Synthesis of Glycolipid Library Reminiscent of Mycobacterial Cell Wall Motif A and its Significance by Microscopy

विद्या वाचस्पति की
उपाधि की अपेक्षाओं की आंशिक पूर्ति में प्रस्तुत शोध प्रबंध

A Thesis submitted in partial fulfilment of the requirements of the degree of Doctor of Philosophy

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Dedicated to…

My Mother

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CERTIFICATE

Certified that the work incorporated in the thesis entitled, "***Synthesis of Glycolipid Library Reminiscent of Mycobacterial Cell Wall Motif A and its Significance by Microscopy"*** submitted by **Pooja Joshi** 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.

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I declare that this written submission represents my idea in my own words and where others' ideas have been included; I have adequately cited and referenced the original sources. I declare that I have acknowledged collaborative work and discussions wherever such work has been included. 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. The work reported in this thesis is the original work done by me under the guidance of Prof. Srinivas Hotha.

Date: 01/04/2025

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Finally, I dedicate this achievement to my family, who have stood by me through every high and low.

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General Remarks

❖ 1H NMR spectra were recorded on Bruker- 400, JEOL 400, or Bruker 600 MHz spectrometer using tetramethylsilane (TMS) as an internal standard. Chemical shifts are expressed in ppm units downfield to TMS.

❖ 13C NMR spectra were recorded on Bruker 100, JEOL 100, or Bruker 150 MHz spectrometer.

❖ High-resolution mass spectroscopy (HRMS) was performed on Waters Synapt G2 or Applied Biosystems MALDI-ToF-ToF spectrometer.

❖ IR spectra were recorded on Perkin-Elmer 1310 or 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 measured in degrees.

❖ All reactions were monitored by Thin-Layer Chromatography carried out on pre-coated 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 freshly prepared anhydrous solvents under anhydrous conditions, and yields refer to chromatographically homogenous materials unless otherwise stated.

❖ All evaporations were carried out under reduced pressure on Büchi and Heidolph rotary evaporators below 45 °C unless otherwise specified.

❖ Silica gel (100-200) and (230-400) mesh was 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.

Abbreviation

Å – Angstrom
Ac – Acetate
AcBr – Acetyl bromide
AcCl – Acetyl chloride
AcOH – Acetic acid
Ac_2O – Acetic anhydride
AG – Arabinogalactan
Ara*f* – arabinofuranosyl / arabinofuranoside
Bn – Benzyl
BnBr – Benzyl bromide
Boc – t-butylcarbonyl
Bz – Benzoyl
BzCl – Benzoyl chloride
Calcd – Calculated
Cbz – Carbobenzoloxy
CAN – Cerric ammonium nitrate
cat. – catalytic
$CDCl_3$ – Chloroform-D
$CHCl_3$ – Chloroform
COSY– Homonuclear Correlation Spectroscopy
DDQ – 2,3-Dichloro-5,6-dicyano-1,4-benzoquinone
DEPT – Distortionless Enhancement by Polarization Transfer
DMAP – N,N-Dimethylaminopyridine
DMF – N,N‟-Dimethyl formamide
D_2O – Deuterium oxide
δ – delta (in PPM)
EDC – 1-Ethyl-3-(3-dimethylaminopropyl)carbodiimide
eq. – equivalents
Et_3N – Triethyl amine
EtOH – Ethanol
EtOAc – Ethyl acetate
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
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
PMB – p-Methoxy benzyl
Py – Pyridine
PTSA – *p*-Toluene sulfonic acid
ppm – parts per million
Rib*f* – ribofuranoside / ribofuranosyl
rt – room temperature
sat – saturated
TBAF – tetra-n-Butyl ammonium fluoride
TBAI – tetra-n-Butyl ammonium iodide
TBDMS – t-Butyldimethylsilyl
TBDMSCl – t-Butyldimethylchloride
TBDPS – t-Butyldiphenylsilyl
TBDPSCl – t-Butyldiphenylsilylchloride
TfOH – Triflouromethanesulfonic acid
THF – Tetrahydrofuran
TLC – Thin Layer Chromatography
TMSOTf – Trimethylsilyltrifluoromethanesulfonate
μmol – micromolar
μL – microliter

Synopsis

The thesis titled "**Synthesis of Glycolipid Library Reminiscent of Mycobacterial Cell Wall Motif A and Its Significance by Microscopy**" is organized into three chapters. Chapter 1 provides an overview of the importance of carbohydrates, glycosylation, glycosidic linkages, stereoselectivity in chemical glycosylation, gold catalysis in glycosylation, and conformational analysis of carbohydrates. It also covers the characteristics of glycans that make them ideal candidates for glycomaterials. Chapter 2 details the synthesis of a mycobacterial glycolipid library consisting of 31 analogs using [Au]/[Ag]-catalyzed glycosylation. Chapter 3 investigates the impact of glycosidic linkage, saturation, unsaturation, and cyclopropanation in the fatty acid component on the self-assembly of glycolipids.

Chapter 1: Introduction of Glycosylation, glycomaterials, and their Importance. Glycoconjugates, including polysaccharides, glycoproteins, glycolipids, and proteoglycans, are found extensively on cell surfaces and in secreted fluids. They play a crucial role in various biological processes, such as cell-cell recognition, infections caused by viruses and bacteria, inflammation, tumor metastasis, and metabolism. However, obtaining naturally occurring glycoconjugates in their pure form is extremely challenging because of the micro-heterogeneous nature of these biomacromolecules. In this regard, chemical and chemo-enzymatic synthesis of glycans is highly significant, as these methods allow the production of pure glycoconjugates with precisely defined structures. Over the past few decades, the literature has reported the development of various glycosyl donors, mild catalytic activation methods, and biomimetic chemo-enzymatic processes. The recently developed gold-catalysed glycosylation reaction has created new opportunities for synthesizing difficult glycosides, owing to its milder activation conditions and remarkable compatibility with diverse substrates. Glycans are particularly challenging due to their stereoselectivity, lower yield in conjugates, and conformational variability. Due to the complexity and inherent flexibility of glycans, their conformational analysis has been hindered for years, resulting in a significantly less developed understanding of carbohydrate structures compared to those of peptides and proteins. Recent advancements have reinvigorated the structural analysis of glycans, demonstrating that they can form defined secondary structures. The fine-tuning of these glycomaterial analogs resulted in the creation of novel, chiral self-assembled materials with controllable shapes and properties. Considering all these factors, the Hotha lab sought to explore the synthesis of glycolipids containing arabinose, a five-membered sugar primarily found in mycobacterial cell walls and associated with mycolic

acid mimics. These glycolipids exhibit a tendency to form diverse self-assembled structures, influenced by variations in the hydrophobic component.

Chapter 2: Synthesis of glycolipid library by using [Au]/[Ag] Catalyzed glycosylation and regioselective esterification.

The cell wall of *Mycobacterium tuberculosis* (MTb) is uniquely characterized by its glycolipid composition, particularly mycolyl arabinogalactan, which contains Araf, Galf, and mycolic acid. The terminal region of arabinogalactan (AG) consists of motif A, a pentaarabinofuranoside featuring two β-1,2 linkages and one each of α-1,5 and α-1,3 linkages. The C5 positions of motif A are esterified with mycolic acids, further modified by distinctive cyclopropane groups. Herein, we synthesized a variety of MTb cell wall glycolipids based on motif A by using an [Au]-[Ag] catalyzed glycosylation strategy.

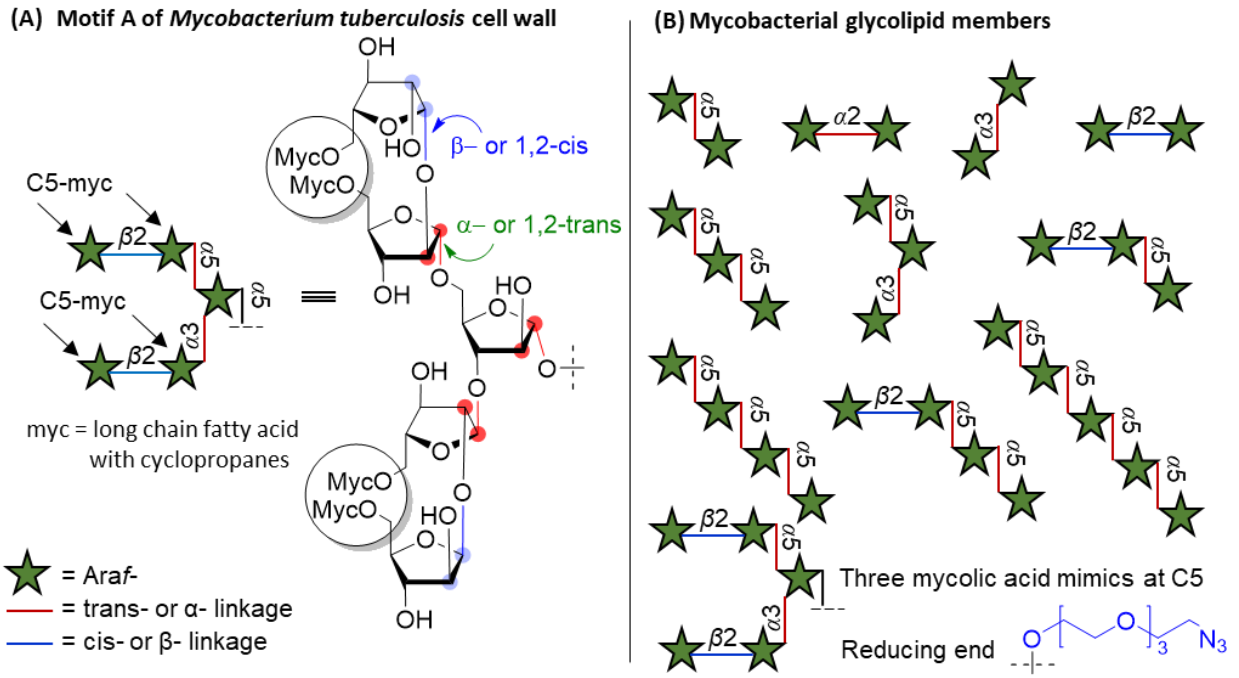


Figure 1. Structure of the terminal pentasaccharide motif A of *Mycobacterium tuberculosis* cell wall (1A) and the targeted glycolipid members (1B).

This collection of glycolipids includes variations with α or β-(1→2, 3, or 5) Ara*f* linkages in di-, tri-, tetra-, and penta-arabinofuranosides, esterified with saturated, doubly unsaturated, or cyclopropanated long-chain fatty acids. In this study, we have used naturally occurring linoleic acid as the lipid component as it contains a couple of *cis* olefins. Also, this chapter focuses on

the regioselective esterification of glycolipids with *trans* glycosidic linkages and showcases the synthesis of *cis* and *trans* cyclopropanation in the hydrophobic component using a modified Simmons-Smith reaction. We conducted an extensive literature review to establish the chirality of these cyclopropanated linoleic acids and discovered that Tomoyuki Nishizaki studied this topic in 2011 (*Cell Physiol. Biochem*. **2011**, *27*, 149-158). In his work, he chemoenzymatically synthesized all four possible cyclopropanated linoleic acid derivatives. Nishizaki noted that determining the stereochemistry of these cyclopropanated esters is a complex task and further demonstrated that the stereochemistry could be confirmed by measuring the specific optical rotation of the cyclopropane derivatives. Based on the literature, we determined the absolute stereochemistry of the cyclopropane rings we synthesized.

Chapter 3: Self-assembly analysis of glycolipid library by using Transmission Electron Microscopy (TEM)

The successful synthesis of our 31 target glycolipids which replicate the terminal pentasaccharide Motif A of *Mycobacterium tuberculosis* has paved the way to explore their biophysical significance. Recent studies have emphasized how short biomolecular sequences can organize into distinct supramolecular structures with significant potential in medicine and pathogenesis. The glycolipids we synthesized, featuring long lipid chains, are well-suited for interdigitation, potentially forming complex hierarchical, supramolecular self-assembling structures that can be visualized using transmission electron microscopy (TEM). TEM analysis of the resulting self-assemblies showed that slight changes in the anomeric linkages, glycan length, and the presence or absence of cyclopropanes affected the morphology of the self-assembled structures. Understanding the link between the hierarchical structures of glycolipids in MTb and their material properties is essential, as these self-assemblies can play a key role in influencing pathogenicity. In a control experiment, TEM images of self-assembled glycans A4, B4, C4, and D4, each with different interarabinofuranosidic linkages, were taken under identical conditions and showed no significant changes in morphology. These results indicate that the β1,2-Araf linkage and cyclopropanated lipid play a crucial role in promoting interdigitation, balancing hydrophilicity and hydrophobicity, and facilitating the formation of stable self-assembled structures.

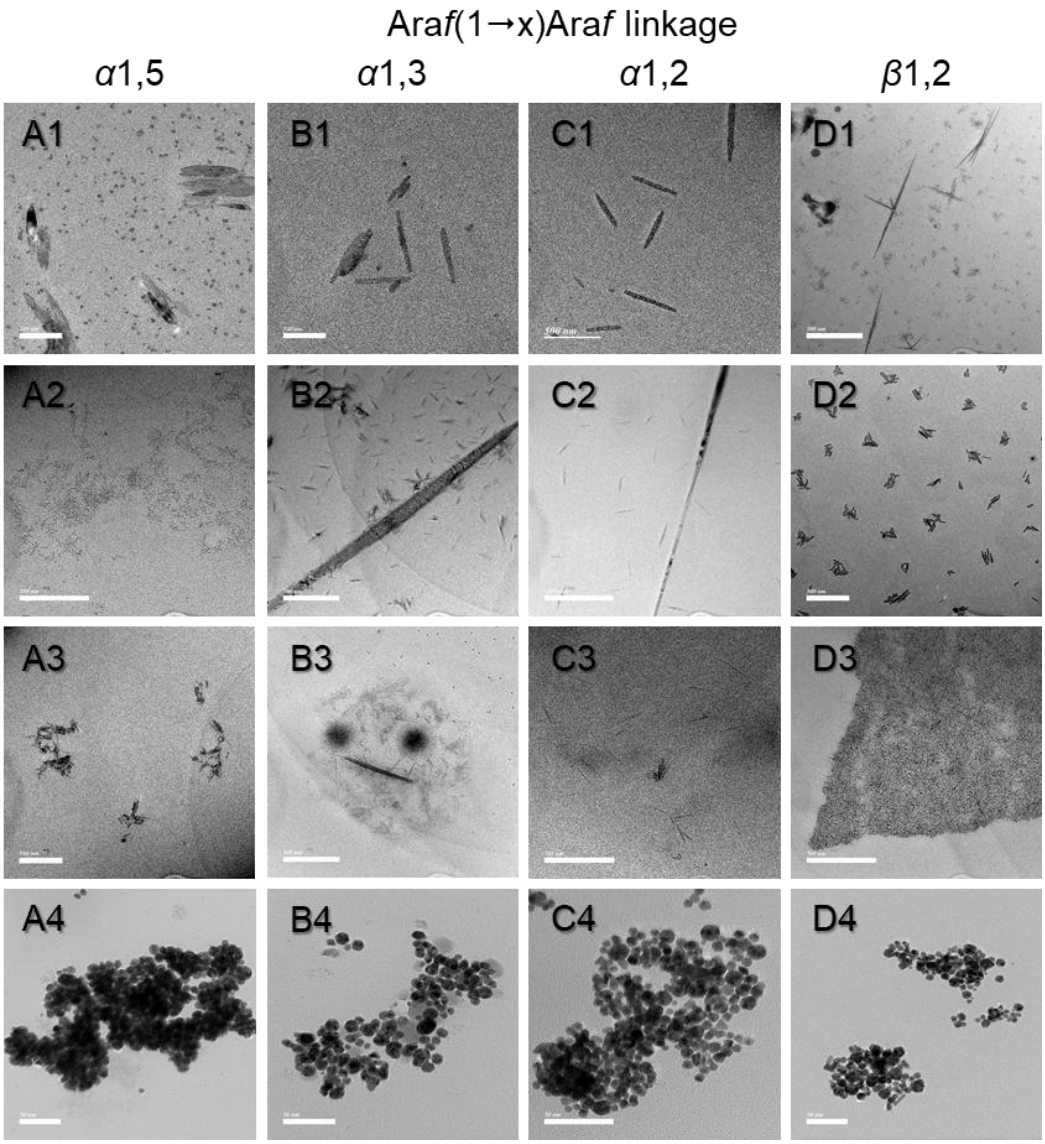


Figure 2. Supramolecular structures with disaccharide glycolipids. TEM images of glycolipids prepared by drop casting (1 mg/mL in 10% acetone-water) for disaccharide glycolipid with 1,5 *trans* glycosidic linkage (A1, A2, A3), disaccharide glycolipid with 1,3 *trans* glycosidic linkage (B1, B2, B3), disaccharide glycolipid with 1,2 *trans* glycosidic linkage (C1, C2, C3), disaccharide glycolipid with 1,2 *cis* glycosidic linkage (D1, D2, D3) [Scale bars: 500 nm for all except D3 (200nm)]. TEM images of glycans prepared by drop casting (1 mg/mL in 10% acetone-water) for 7: A4, 13: B4, 11:C4, 23: D4. Scale bars: 50 nm for all.

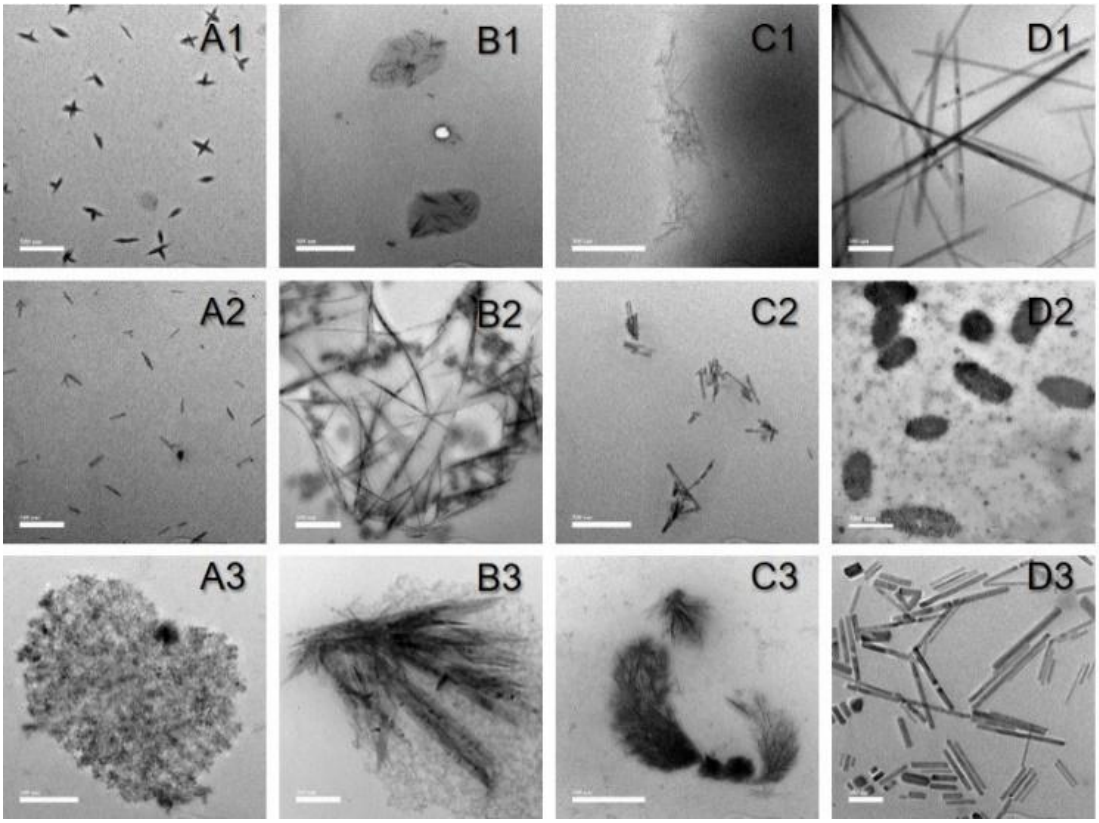


Figure 3. Supramolecular structures with glycolipids. TEM images of prepared by drop casting (1 mg/mL in 10% acetone-water) for trisaccharide glycolipid with 1,5 *trans* glycosidic linkage (A1, A2, A3), trisaccharide glycolipid with 1,5 and 1,3 *trans* glycosidic linkage (B1, B2, B3), trisaccharide glycolipid with 1,5 *trans* and 1,2 *cis* glycosidic linkage (C1, C2, C3), tetrasaccharide glycolipid with 1,5 *trans* and 1,2 *cis* glycosidic linkage (D1), pentasaccharide glycolipid with 1,5 *trans* glycosidic linkage (D2), pentasaccharide glycolipid with 1,5 *trans* and 1,2 *cis* glycosidic linkage (D3), Scale bars: 500 nm for all except D3 (200nm).

In addition to exploring the effects of unsaturation and cis cyclopropanation in the fatty acid portion, we also investigated the impact of *trans* cyclopropanation. We discuss how the presence of both *cis* and *trans* cyclopropanation can significantly influence the self-assembly behavior.

Chapter 1

Introduction of Glycosylation, glycomaterials, and their Importance

Chapter 1

1.1 Introduction of carbohydrates

Carbohydrates, proteins, and fats are fundamental biomolecules and organic compounds made mainly of carbon, hydrogen, oxygen, and occasionally nitrogen. They are crucial for providing energy to the body.[1,2] Carbohydrates widely occur in Nature, including in-plant cellulose, bacterial cell walls, fungal and algal structures, animal exoskeletons (such as chitin), and within the human body (such as glucose). Additionally, carbohydrates can link with other biomolecules like proteins or lipids to form complex structures called glycoconjugates. These glycoconjugates are essential for numerous biological processes and are central to many cellular functions. While carbohydrates have traditionally been recognized primarily as an energy source, recent decades have revealed their crucial roles in various biological processes, including protein folding, signal transduction, fertilization, blood transfusion, hormonal regulation, and cell proliferation. Glycoconjugates exist in micro and heterogeneous forms and are typically found in very low concentrations.[3,4,5] Isolating these molecules from food or natural sources is challenging, making it difficult to study their natural functions in living organisms. Consequently, chemical or enzymatic synthesis is often used to produce sufficient quantities of glycoconjugates for research purposes. In contrast to nucleic acids and protein synthesis, synthesizing oligosaccharides and glycoconjugates faces several major challenges: (i) Complex branching and asymmetric structures, (ii) the need to form either α- or β-glycosidic linkages, (iii) the requirement for multiple protecting group strategies in chemical synthesis, and (iv) the limited availability of diverse glycosyl transferases.[6,7]

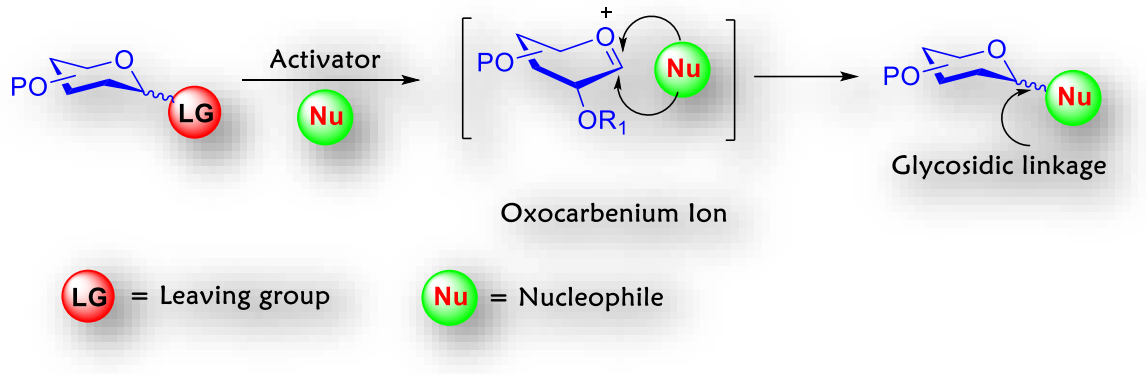
1.2 A brief overview of glycosylation

Glycosylation is commonly defined as the process in which carbohydrate molecules are covalently linked to a target macromolecule, usually proteins or lipids. Adding glycans through glycosylation reactions on various biomacromolecules significantly influences biological processes including fertilization, viral replication, cell growth, cell-cell adhesion, and inflammation.[8,9] In prokaryotic cells, glycosylation reactions occur at the interface of the cytoplasmic membrane or within the periplasm. In eukaryotic cells, the process occurs in the endoplasmic reticulum and Golgi apparatus, and it may also occur in the nucleus and cytosol.[10]

Millions of years of biological evolution have shaped and refined the enzymes responsible for glycosylation in cells, which are classified as glycosyltransferases, glycosidases, and glycosynthases[11]. In this site-specific and stereoselective reaction, a new covalent bond is created between a glycosyl donor and a glycosyl acceptor.

1.3 Chemical Glycosylation

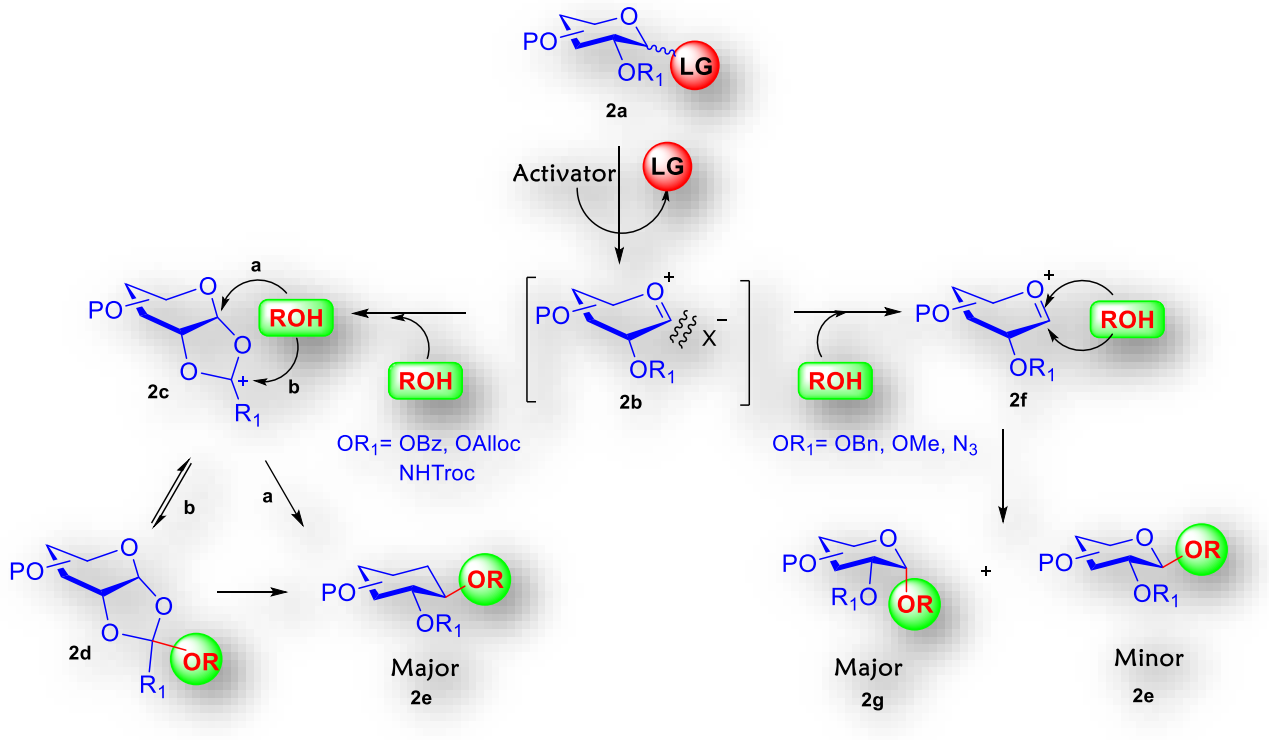
A chemical glycosylation reaction can be explained as a nucleophilic displacement of a leaving group attached to the anomeric carbon of a glycosyl donor, facilitated by various promoters such as (Lewis acids, Brønsted acids, neutral reagents, inorganic salts, etc). Once the leaving group is displaced, an oxocarbenium ion intermediate is generated, which is then attacked by a glycosyl acceptor (nucleophile) to create a new glycosidic bond[12].



Scheme 1.1: **General glycosylation reaction**

Two significant challenges are linked to the chemical synthesis to achieve complete regio- and stereoselectivity of the newly formed glycosidic bond. Regioselectivity issues can be managed by leaving one hydroxyl group free for the reaction, employing a protecting group strategy on the glycosyl acceptor. However, stereospecificity is considerably more complex, as it is influenced by various stereoelectronic factors. In general, the nature of the functional group at the C-2 position of the glycosyl donor dictates the stereochemical outcome, resulting in either 1,2-*cis* or 1,2-*trans* glycoside formation. A carbonyl group at the C-2 position, present as an ester, carbonate, or carbamate, leads to the formation of 1,2-*trans* glycosides due to anchimeric assistance, also referred to as neighbouring group participation, which results in the creation of a more stable acycloxonium ion.[13] The formation of the acycloxonium intermediate limits the approach of the incoming nucleophile to one side, predominantly leading to the formation of 1,2-

trans glycosides. In contrast, ethers at the C-2 position, including benzyl, methyl, and azide, yield a mixture of 1,2-*trans* and 1,2-*cis* glycosides. This is due to the acceptor having an equal chance to attack the oxocarbenium ion (**2b**) from either the axial or equatorial direction. The precise ratio of 1,2-*trans* and 1,2-*cis* glycosides depends on stereoelectronic effects.



Scheme 1.2: General mechanism for glycosidic bond formation

In most cases, axial glycosides are favored as the major products despite steric hindrance, largely due to the well-known anomeric effect. Several factors, such as the structure of the glycosyl donor and acceptor, solvent, temperature, conformation, protecting groups, promoters, and leaving groups, control chemical glycosylation reactions.[13]

1.4 Types of glycosidic linkages[14]

Two types of glycosidic linkages can occur depending on the relative orientation of the functional groups at the C-1 and C-2 positions. If the groups at these positions are co-planar, it is classified as a 1,2-*cis* linkage. On the other hand, if the groups are non-coplanar, it is referred to as a 1,2-*trans* linkage. In the absence of any functional group at the C-2 position (as seen in 2-

deoxy sugars), the assignment of 1,2-*cis* and 1,2-*trans* linkages relies solely on the orientation of the functional groups at the C-1 position.

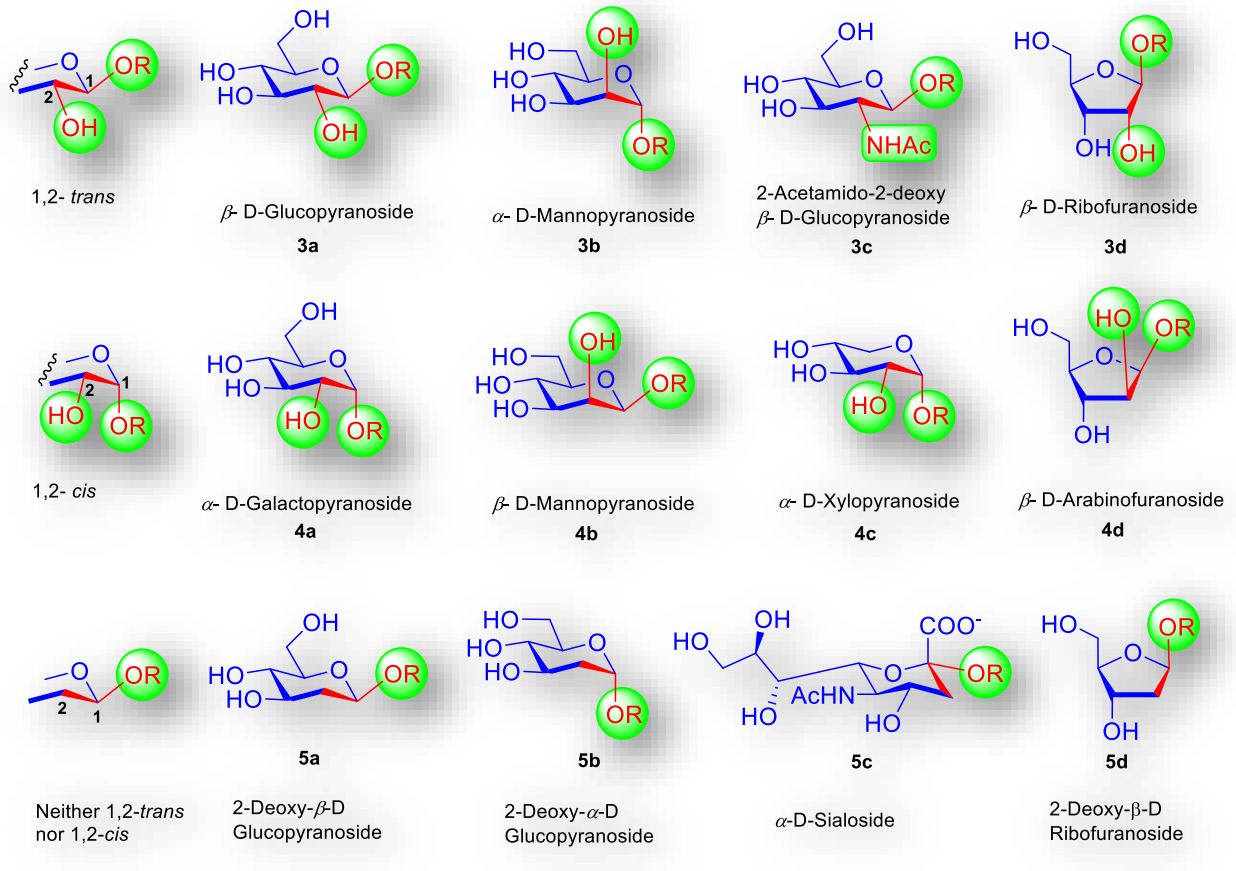


Figure 1.3: Types of Glycosidic-linkages

1.5 Stereoselectivity in chemical glycosylation

1.5.1- 1,2- *trans* selective approaches: 1,2-*trans* Glycosidic linkages can be readily formed with neighboring group participation from C-2 esters on the donor unit. When the glycosyl donor is activated and the leaving group departs, it generates an oxocarbenium ion, which is then trapped by a five-membered dioxolenium ion intermediate through the anchimeric effect of the C-2 ester groups. Nucleophiles (reactive acceptors) facilitate the trans-cleavage at C-1 of the dioxolenium ion, leading to the desired formation of 1,2-*trans* glycosides. Less reactive acceptors often attack the dioxolenium ion intermediate instead of the C-1 carbon, leading to the formation of orthoesters. These orthoesters can then isomerize in the presence of a suitable acid to produce 1,2-*trans* glycosides, as previously mentioned.

1.5.2- 1,2- *Cis* selective approaches in pyranose: The synthesis of 1,2-*cis* glycosidic linkages is more challenging than that of 1,2-*trans* linkages. One key criterion for forming 1,2-*cis* linkages is the presence of a non-participating group at the C-2 position of the glycosyl donor. With a non-participating group present, the anomeric effect promotes the formation of 1,2-*cis* glycosides, and the degree of 1,2-*cis* selectivity depends on the reaction conditions as well as the reactivity of both the glycosyl donor and acceptor. Achieving 1,2-*cis* stereoselectivity is one of the major challenges in glycoside synthesis. There is no universal method for exclusively producing 1,2-*cis* stereoisomers; instead, various groups around the world have devised different strategies to address this issue.

In 1997, the Crich group introduced the concept of pre-activating sulfoxide donors with a Tf_2O activator at low temperatures, generating a triflate intermediate. In this process, the axial triflate ion is attacked by the acceptor from the equatorial position in an S_N2 manner, promoting the formation of 1,2-*cis* stereoisomers. However, this method was restricted to benzylidene-protected mannose glycosyl donors for producing 1,2-*cis* mannosides.[15] In addition to the cyclic 4,6-benzylidene protecting group, a variety of cyclic protecting groups have been developed for 1,2-*cis* glycosylation over the past few decades. Examples include 2,3- or 3,4-acetals, 3,5- or 4,6-di-^{tert}-butyldimethylsilylene, and 3,5- or 4,6-O-(1,1,3,3-tetra-isopropyl-1,3-disiloxanylidene).

In this context, a significant report by Boons *et al*. involved the introduction of a chiral auxiliary as a protecting group within the donor motif itself. When the chiral auxiliary is in the S-configuration, a *trans*-decalin intermediate is proposed. The formation of this *trans*-decalin is believed to occur to minimize steric repulsion associated with the *cis*-decalin intermediate. At the *trans*-decalin intermediate, the acceptor molecule can only access the axial or α-face, leading to the formation of 1,2-*cis* glycosides. In contrast, when the chiral auxiliary is in the R-configuration, the *cis*-decalin intermediate is favored, leading to the formation of 1,2-*trans* glycosides.[16]

Recently, Demchenko *et al*. uncovered the H-bond mediated aglycon delivery (HAD) technique by utilizing remote picolinyl (Pic) or picoloyl (Pico) protecting groups. In this approach, the nitrogen atom forms hydrogen bonds with the incoming acceptor molecule, facilitating access to the *cis*-face of the donor for 1,2-*cis* glycosylation.[17]

1.5.3- 1,2- *Cis* selective approaches in furanose: Five-membered furanosides are conformationally more flexible than pyranoside sugars due to their intrinsic flexibility, allowing the furanoside oxocarbenium ion to adopt twenty different conformations in solution. As a result, controlling 1,2-*cis* stereoselectivity in furanosylations is challenging. Additionally, the absence of the anomeric effect in furanosides further complicates the tuning of stereoselectivity.

One strategy for achieving stereoselectivity is to inhibit the flexibility of furanose rings by locking or freezing the intermediate formed during the glycosylation reaction into a rigid conformation. Several groups have developed various methods using this approach. In this context, Boon's group proposed a method for stereoselective glycosylation of furanosides in 2006. They achieved this by locking the C-3 and C-5 hydroxyl groups with a di-^{t}-butyl silane protecting group, which was believed to impart rigidity to the furanoside oxocarbenium ion intermediate formed during the glycosylation process. The oxocarbenium ion exhibits a double bond character between the ring oxygen and the C-1 carbon atom, causing the C-4, ring oxygen, C-1, and C-2 to become co-planar. The C-3 carbon can either position itself below the plane (E^3-conformer) or above the plane (^{3}E-conformer) to minimize the potential energy and ring strain of the oxocarbenium ion. The Newman projection of the E^3 and $_3$E conformer suggests that the staggered attack favors the eclipsed attack because interactions in the eclipsed conformer disfavor the nucleophilic attack. However, it was suggested by DFT and other theoretical calculations that ^{3}E conformation is distorted and internal ring strain is responsible for less probability of product formation *via* this conformation. Hence, 1,2-*cis* stereoselective product formation occurs *via* syn attack of the nucleophile on the E_3 conformation.[18]

Stereoselective glycosylation was achieved by utilizing the rigidity provided by the di-tert-butyl silane moiety in furanosides. However, complete selectivity cannot be attained for all furanosides using this method. Consequently, *cis*-stereoselective glycosylation continues to be a promising area for researchers to explore.

Lowary's group introduced a comparable approach to attain 1,2-*cis* selectivity by employing a 2,3-*O*-xylylene-protected glycosyl donor. The selectivity was achieved by locking the oxocarbenium ion intermediate into the most stable and conformationally rigid E_3 conformation, where C-3 remains positioned below the plane while all other ring atoms are aligned in the same plane due to the partial double bond character between the ring oxygen and C-1 carbon atoms.

The unfavorable eclipse effect at the top of the plane compels nucleophiles to attack from below the plane.[19]

1.6 -Gold catalysis in glycosylation: Most gold-catalyzed reactions involve gold in the +1 and +3 oxidation states, as Au(0) is generally inert. The use of gold catalysis in glycoside synthesis was entirely unexplored until 2006. Inspired by the Au(III)-catalyzed Ferrier-type reaction involving a 3-*O*-propargyl derivative, Hotha and Kashyap reported the activation of an anomeric propargyl glycosyl donor using catalytic $AuCl_3$ for the first time in 2006.[20] Reports from the Zhu group[21] detailed the $AuCl_3$-mediated activation of alkyne-functionalized 2,2-dimethylbut-3-ynyl thioglycosides, while the Hotha group[22,23] focused on glycosyl propargyl 1,2-orthoester donors for 1,2-*trans* glycosylation are considered as important advancements in the field. Later, Hotha and Kayastha discovered that 1-ethynylcyclohexanyl glycoside donors can be activated at room temperature using $AuCl_3$ with AgOTf as a co-catalyst, are significantly more reactive than propargyl glycosides.[24] Vankar et al. successfully activated the well-known trichloroacetimidate donor using Au(III) salts.[25] The Yu group discovered *o*-hexynylbenzoate glycosyl donors that can be activated in the presence of $Ph_3PAuOTf$ or $Ph_3PAuNTf_2$ forming various glycosides and saccharide-containing natural products.[26,27] Mishra, Neralkar and Hotha successfully developed a mild Au(I)/Ag(I) co-catalyzed glycosylation method using a 1-ethynylcyclohexyl glycosyl carbonate donors.[28] Au(I)-catalyzed glycosylation methods are milder than traditional glycosylation approaches, which often rely on strong Lewis acids or Brønsted acid activators. Therefore, these relatively new methods are attracting more attention for their ability to synthesize many glycosides that are otherwise challenging to produce.

1.7- 1-ethynyl cyclohexyl glycosyl carbonate donor: After nearly a decade of refining reaction conditions since the initial report of gold-catalyzed glycosylation by the Hotha group, Mishra et al. developed a mild, easily scalable, and rapid glycosylation method using shelf-stable glycosyl 1-ethynylcyclohexyl carbonate donors along with Au(I) phosphite and AgOTf as co-catalysts.[28] This new donor has demonstrated potential for synthesizing a variety of glycoconjugates and oligosaccharides. The *O*-glycosylation reaction is completed within 15 minutes at room temperature. The first oligosaccharide synthesized using this method was a heneicosasaccharyl mannose-capped arabinomannan[29] followed by the synthesis of arabinogalactan[30] fragments, found in the cell wall of M. tuberculosis. Recently, the Hotha

group successfully synthesized a more complex branched glycan fragment found in chlorovirus ATCV-1.[31] The application of this donor has been instrumental in creating a successful and efficient synthetic route for the core pentasaccharide of the life-saving drug Fondaparinux.[32] This donor has also been utilized to develop a novel solid-phase synthesis method that significantly reduces the time required to produce oligosaccharides.[33] The significance of the glycosyl alkynyl carbonate donor in synthesizing various glycosides, as well as the properties of the 1-ethynyl cyclohexyl carbonate moiety as a leaving group, will be discussed in detail in the next chapters of the thesis.

1.8- Conformational analysis of carbohydrate: The nomenclature for the pyranose and furanose ring conformations is based on the rules governing six- and five-membered rings, respectively. For cyclohexane, a standard six-membered ring composed of six equivalent carbon atoms, five distinct conformers are recognized: chair (C), boat (B), twist/skew-boat (S), half-chair (H), and envelope (E) conformations. In pyranoses, the presence of the ring oxygen and the C6 carbon allows all ring carbons to be distinguishable. Due to this asymmetry, a total of 38 distinct conformers are identified for the pyranose ring: 2 chairs (C), 6 boat (B), 6 twist/skew-boat (S), 12 half-chair (H), and 12 envelopes (E) conformations. The nomenclature for five-membered rings, using cyclopentane as the typical example, is similarly applied to the furanose ring. Cyclopentane has two distinct conformers: the envelope (E) and twist (T) conformations. In contrast, the furanose ring is defined by 20 distinct conformers, with 10 each of the E and T conformations.[34] These conformers are characterized numerically using Cremer–Pople puckering coordinates.[35]

1.9- Site of Conformational variation in oligosaccharides

1.9.1- Glycosidic bond: The structure of oligosaccharides comprises two or more monosaccharide units linked together in either a linear or branched arrangement via acetal linkages (i.e., glycosidic linkages). The most prevalent glycosidic linkage in glycoconjugates features an O1−C1−O_{ring} However, S-, N-, and C-glycosides, in which O1 is substituted with sulfur, nitrogen, or carbon, do exist. This linkage comprises two rotatable bonds characterized by the torsion angles ψ and ϕ along the fragment. In (1→5)-linked furanosides, the ψ angle denotes the orientation of the C4−C5−O1′−C1′ atoms, while the torsion of the C5−O1′−C1′−O4′ atoms

define the ϕ angle. Steric interactions and stereo-electronic effects, including the endo-anomeric[36a-36c] and exo-anomeric effects[37] influence the conformational preferences in this glycosidic fragment.

1.9.2- Exocyclic hydroxymethyl group: Another site of conformational significance is found in both pyranose and furanose forms, involving the exocyclic hydroxymethyl group (i.e., C5−C6 in hexopyranoses and C4−C5 in pentofuranoses). The conformational preferences of this group are characterized by the torsion angle ω, which denotes the dihedral angle formed by the atoms O5, C5, C4, and O4 in furanoses. In this fragment, the two hydrogen atoms of the CH_2 group are prochiral and referred to as pro-*R* and pro-*S*. Free rotation around this exocyclic bond can produce an infinite variety of staggered, eclipsed, and partially eclipsed conformations, also known as rotamers.[38a,38b]

1.9.3- Rotamers about C-OH bonds: Additional conformational diversity comes from the rotamers around C−OH bonds found either on the carbohydrate ring or in exocyclic fragments. Determining the preferred orientations of these bonds experimentally has been challenging due to the presence of exchangeable hydroxyl protons. The combination of computational methods and NMR spectroscopy has successfully identified specific conditions influencing C−OH orientation, including the presence of inter-residue hydrogen bonds[39] in disaccharides, the absence of such bonds,[40] and the replacement of intra-residue hydrogen bonds with water bridges.[41]

1.9.4- Ring conformation: The pyranose monosaccharide units in oligosaccharides typically exist in single, well-defined, energetically favorable chair conformations, with minimal ring strain and significant energy barriers separating them, except for a few exceptions like iduronic acid.[42] In contrast, furanosides exhibit greater ring strain, allowing them to adopt multiple conformational states that are separated by relatively low energy barriers. Early studies on the conformation of furanosides by Angyal[43] suggested that the preferred conformational positions are those that place the anomeric substituent and the hydroxymethyl group in pseudoaxial and pseudoequatorial orientations, respectively, while placing the other ring substituents in a staggered arrangement. This conformational preference arises from several steric and stereoelectronic effects, including both endo- and exo-anomeric effects. The

preference for staggered orientations of the remaining substituents is due to the gauche effect.[44] This stereoelectronic effect is equally significant as the anomeric effects refers to the tendency of two adjacent electronegative substituents to adopt a gauche orientation. It plays a vital role in influencing the rotamer populations of the hydroxymethyl group and the ring conformation of furanosides.

1.9.5- Pseudorotation: To describe the conformational behavior of furanose-containing molecules, the concept of pseudorotation is utilized, which was first introduced in 1947 by Pitzer and his colleagues in their research on cyclopentane conformation.[45] Pseudorotation occurs due to the tendency of an n-membered ring (where n > 3) to adopt a puckered shape, which helps to minimize torsional strain. Since its conception, pseudorotation theory has been widely employed as a tool for studying the conformations of various ring systems, particularly in the case of five-membered rings.[46a-d] A five-membered ring can pucker in one of two ways: One atom can move out of the plane of the other four, giving rise to an envelope (E) conformation or alternatively two atoms can pucker above and below the plane of the other three, giving a twist (T) conformer.

1.10 Appealing features of glycans to build programmable architectures[46d]

Carbohydrates, also known as glycans or polysaccharides, hold significant potential for developing programmable architecture. With more than 100 naturally occurring monosaccharides, they are capable of forming a broad range of diverse glycan structures. The monosaccharides are connected through glycosidic bonds with different stereochemical and regiochemical configurations, creating either linear or branched structures, in contrast to peptides, which are exclusively linear. The abundant hydroxyl groups and chiral centers in glycans present multiple opportunities for directional, site-specific functionalization, enabling fine-tuned control over their structure and function.[46d] These characteristics make glycans attractive for creating foldamers that can adopt a significantly broader range of conformations compared to peptide-based foldamers.[46f] Moreover, carbohydrates can engage in a range of intermolecular and intramolecular interactions, enabling the formation of hierarchical materials that are advantageous for developing programmable supramolecular assemblies.[46g, 46h] Yet, well-defined glycans have attracted minimal attention in materials science and supramolecular chemistry to date.

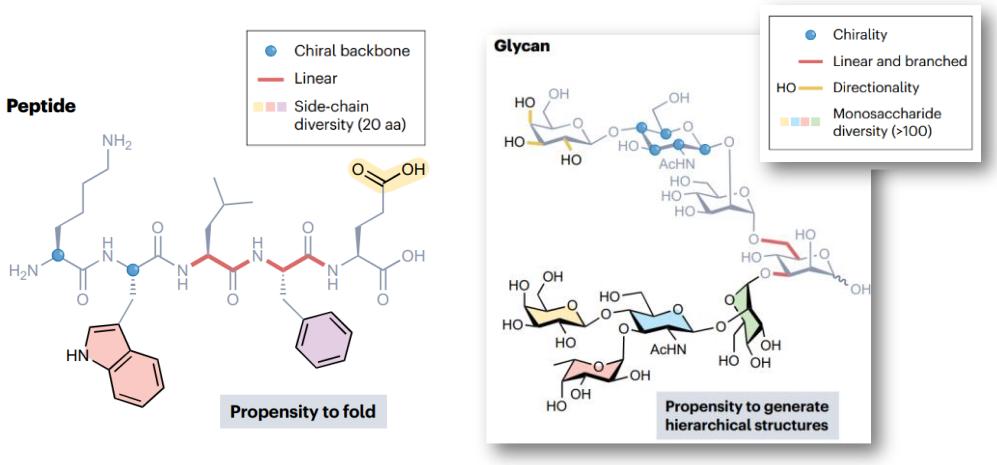


Figure 1.4. Appealing features of glycans to build programmable architectures[46d]

1.11- Intermolecular and intramolecular interaction in carbohydrates: Stereo electronic effects play a significant role in stabilizing glycan conformations. The glycosidic dihedral angles Φ and Ψ are primarily influenced by the exo-anomeric effect, which involves hyperconjugation between the lone pair of electrons on the exocyclic oxygen and the antibonding orbital (σ*) of the endocyclic C–O bond and by steric effects. Likewise, the dihedral angle ω prefers to adopt the gauche–gauche (gg) or gauche–trans (gt) conformations rather than the antiperiplanar conformation (tg), (that is gauche effect). The multiple hydroxyl groups enable the formation of various directional intermolecular and intramolecular hydrogen bonds which are in constant competition with surrounding water molecules. When interacting with proteins, coordination with metal ions and carbohydrate–aromatic interactions contribute to stabilizing specific conformations and enhancing binding affinity. These intermolecular and intramolecular interactions help stabilize the secondary structures of glycans found in nature and a wide range of higher-order assemblies, including crystalline materials, helical superstructures, and inclusion complexes.

1.12-The different labels of glycan structure:

The sequence of monosaccharides in a glycan, along with the regiochemistry and stereochemistry of the glycosidic bonds, determines its primary structure. The conformational

space that a glycan can occupy is influenced by stereoelectronic factors. Rotamer stabilization is due to hyperconjugation, including effects such as exo-anomeric and gauche effects.[47] Intramolecular hydrogen bonds and steric factors influence the conformation of glycosidic bonds and, consequently, give the secondary structure of glycans.[48a,48b] Water plays a crucial role in the folding process by competing with intramolecular hydrogen bonds and influencing the relative populations of rotamers, which contributes to the flexibility of glycans.[49a,49b] Their flexibility has led to the common misconception that these biomolecules lack a distinct shape and that they only adopt helical or ribbon-like conformations at high degrees of polymerization. Glycans can participate in various intermolecular interactions—including hydrogen bonds, carbohydrate–aromatic interactions, hydrophobic interactions, van der Waals forces, and coordination with metal ions, resulting in the formation of assemblies and hierarchical structures. These interactions guide the formation of crystalline materials like cellulose and chitin,[50] helical superstructures (like carrageenans[51] and β-glucans[52]) and inclusion complexes (such as the amylose–iodine complex).[53]

1.12.1 Glycan Foldamers: Drawing inspiration from the extensive literature on peptide foldamers, a glycan was engineered to spontaneously adopt a stable secondary structure.[54] Linking two naturally occurring glycan structural motifs, a rigid turn, and two stacking strands, resulted in a glycan hairpin, a structure not found in nature. The turning unit, inspired by the trisaccharide LeX, was similarly stabilized by an unconventional C−H···O hydrogen bond[55] and was modified to enable conjugation with the two strands in a parallel orientation. The two stacking strands were inspired by cellulose chains and adopted a rigid rod conformation, which is stabilized by intramolecular hydrogen bonds and hydrophobic interactions.[56] In the future, a wider variety of conformations may be achievable through different combinations of monosaccharides, glycan motifs, and non-canonical residues. The ability to manipulate the conformation of glycans could, in turn, result in predictable functions and properties, with potential applications in catalysis[57] and nanotechnology.[58]

1.12.2 Glycan Assemblies: Self-assembly is a crucial process in living organisms where polymeric structures are constructed from repetitive "building blocks" typically through noncovalent interactions, leading to greater diversity and complexity.[59a] Synthetic carbohydrate assemblies are not frequently discussed in the literature. In these instances, specific

characteristics of carbohydrates, such as amphiphilicity, chirality, and the capacity to form multiple directional hydrogen bonds—have been utilized to direct the aggregation process. The amphiphilic properties of certain glycans, sometimes enhanced by adding non-natural aromatic substituents, promoted the formation of supramolecular structures, varying from fibers to particles.[59b] Electron microscopy investigations of a disaccharide model identified the crucial intermolecular interactions that drive its assembly into crystalline, twisted fibers.[60] Strategic placement of aromatic substituents facilitated C−H···π edge-to-face interactions between the aromatic rings, while certain hydroxyl groups on the glycan backbone engaged in hydrogen bonding, forming highly ordered assemblies.[61] In most instances, the self-assembling motifs (such as peptides[62] or aromatic platforms[63]) directed the assembly process. These systems demonstrated that factors like stereochemistry, the type of glycosidic bond, and the balance between hydrophilic and hydrophobic regions of the covalently linked carbohydrate component are critical in determining the final morphology.[64]

1.13 Glycopeptide Assemblies: Glycopeptides (GPps) are peptides in which carbohydrate groups are covalently bonded to the side chains of amino acid residues (oligopeptides) via a glycosyl linkage such as O-, N-, or S-linked. Evidence has shown that the size and structure[65a,65b] of glycans can affect the self-assembly properties of peptides, as well as the chirality and micromorphology of the resulting supramolecular structures.[66a,66b] The carbohydrate components in these systems also contribute O-H-based hydrogen bonding and steric effects, which can interfere with other hydrophobic interactions, such as π−π stacking.[67a, 67b] Although developing glycopeptide-based supramolecular assemblies presents challenges, recent studies have highlighted the successful use of these biomimetic scaffolds to enhance cell adhesion and proliferation,[68] Human mesenchymal cell therapy,[69] immunosuppression,[70] and DNA delivery[71] highlight the potential of glycans and underscore the importance of further research to understand their irreplaceable roles.

1.14 Glycolipid Assemblies: These amphiphilic molecules consist of a sugar moiety and one or more alkyl chains. Their amphiphilic nature (with both hydrophilic and hydrophobic properties) enables the formation of self-aggregating structures at the nanoscale. Synthetic branched-chain glycolipids have gained significant attention in biomimetic research as they offer a viable alternative to natural glycolipids, which are challenging to extract from natural

sources.[72] In recent decades, glycolipids having six-membered sugar as a polar head group have garnered significant attention for their self-assembly capabilities and potential as biosurfactants. Various types of synthetic branched-chain glycolipids have already been synthesized, including 1,2-dialkyl/diacylglycerol-based glycolipids[73-74] which have been studied by Mannock *et al.*, and 1,3-glycosylglycerol-based glycolipids, which were studied by Minamikawa *et al.*[75]

Diacetylene-containing glycolipids are a distinct class of compounds capable of self-assembly, forming ordered supramolecular structures. Polymerizable diacetylene glycolipids, which serve as low molecular weight gelators, are particularly fascinating molecules with the potential to develop stimuli-responsive smart materials.[76] The self-assembly of glycolipids is primarily governed by factors such as molecular architecture, concentration, and solvent environment, and is driven by non-covalent interactions, including hydrogen bonding, pi–pi stacking, and electrostatic forces.[77] Spherical micelles have gained considerable attention as drug carriers,[78] particularly due to their ability to encapsulate hydrophobic drugs. This encapsulation enhances the drugs' water solubility, reduces toxicity, and contributes to more sustained release profiles.[79a-79c] Recent developments in this field emphasize the addition of functional groups such as peptides,[80a] antibodies,[80b] or carbohydrates,[80c] to the surface of drug carriers, facilitating interaction with specific cell receptors for targeted drug delivery. Glycolipids also are used as low molecular weight gelators (LMWGs), are intriguing small molecules that can form reversible supramolecular gels in organic solvents or aqueous solutions.[81a] The resulting gels are used as soft materials in applications such as drug delivery, enzyme immobilization, tissue engineering scaffolds, and beyond.[81b] The gelation efficiency of glycolipid derivatives is influenced by the structure of their acyl chains and the anomeric position of the sugar head group, both of which are critical to the self-assembly process.[82]

Furanoses (five-membered sugar) play a crucial role in the backbone of nucleic acids (RNA and DNA) and are also prevalent in the complex polysaccharides found in organisms such as bacteria, protozoa, fungi, and plants. The conformational characteristics of furanoses impact the structure and recognition of the polymers they constitute. Unlike six-membered sugar rings (pyranoses), five-membered forms (furanoses) show considerable internal ring flexibility.[83] For saturated five-membered rings, the issue is even more complex due to their intrinsic conformational flexibility. These rings are known to exist as a mixture of various puckered

conformations, where each atom can adopt multiple relative positions.[84a, 84b] Conformer exchange mechanisms include inversion, where envelope (E) and twist (T) nonplanar forms interconvert through the planar (P) form, and pseudorotation, where these conformers rapidly exchange without involving the P form.[85a, 85b] The addition of substituents that disturb this balance, leading to the exclusion of certain conformers and favoring others, further complicates the analysis.

This thesis focuses on the conformational change of arabinose, a mycobacterial sugar attached to the fatty acid at the non-reducing end. The conformational changes of the glycolipid can be observed through various self-assembly or morphological alterations which are visualized using Transmission Electron Microscopy (TEM). The study of these glycolipids is crucial due to the lack of sufficient information available in the existing literature about their biophysical significance. One section of this thesis also examines the impact of saturation, unsaturation, and cyclopropanation in the fatty acid portion of glycolipids.

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Chapter 2

Synthesis of glycolipid library by using [Au]/[Ag] Catalyzed glycosylation and regioselective esterification

Chapter 2

2.1 Introduction

Tuberculosis (TB) remains one of the leading causes of death worldwide and continues to be one of the deadliest communicable diseases in human history.[1] The cause of tuberculosis remained unknown until Dr. Robert Koch identified it in 1882 and named the bacillus *Mycobacterium* tuberculosis (Mtb).[2] It is estimated that approximately 2 billion people worldwide have been infected with *M. tuberculosis*. According to a 2019 report by the WHO, tuberculosis ranked the 13th among the leading causes of death globally and was the most common infectious agent, surpassing HIV/AIDS.[3-4]

Tuberculosis is caused by *Mycobacterium tuberculosis*, which spreads when infected individuals release bacteria into the air, such as through coughing. Tuberculosis primarily affects the lungs (pulmonary TB), but it can also impact other organs. People who are HIV-positive, diabetic, smokers, or heavy alcohol consumers are at a higher risk of developing TB. The most recommended frontline drugs are isoniazid and rifampicin. The Bacille Calmette-Guérin (BCG) vaccine, developed nearly 100 years ago, is licensed to prevent TB, and has been widely used to protect children from severe forms of the disease. However, no vaccine currently exists that effectively prevents TB in adults, either before or after infection.[5]

2.2 Structure of MTb cell wall

The bacterial cell wall is often referred to as the mycolyl-arabinogalactan-peptidoglycan (mAGP) complex. It consists of three main components: i) peptidoglycan, ii) lipopolysaccharides (including arabinogalactan, lipoarabinomannan, and lipomannan), and iii) the outer membrane (which contains mycolic acid, various glycolipids, and phthiocerol dimycocerosates)

Peptidoglycan: The peptidoglycan is found outside the mycobacterial inner or plasma membrane. It comprises alternating N-acetylglucosamine and muramic acid (which can be either N-acetylated or N-glycosylated) residues, connected by (1→4) bonds.[6]

LM, LAM, and PIMs: The inner membrane of the mycobacterial cell wall contains a mixture of three lipoglycans: lipomannan (LM), lipoarabinomannan (LAM), and phosphatidyl myo-inositol mannosides (PIMs).[7] PIMs are primarily linked to the two mannose units. LM consists of long chains of mannan or branches featuring the α-D-(1→2) monopyranose unit. LAM, the longest glycopolymer chain, is made up of D-mannan and D-arabinan, which are anchored to a phosphatidyl myo-inositol (PI) group in the mycobacterial cell wall. The highly branched D-

mannan structure features an α-(1→6) linked mannopyranose (Man*p*) backbone, with single Man*p* units substituted at the C2 position.[8]

Arabinogalactan: Arabinogalactan is a heteropolysaccharide covalently linked to the muramic acid residue of peptidoglycan through a phosphodiester bond. It is located between the cytoplasmic membrane and the outer mycolic acid layer of the Mtb cell. It consists of arabinose

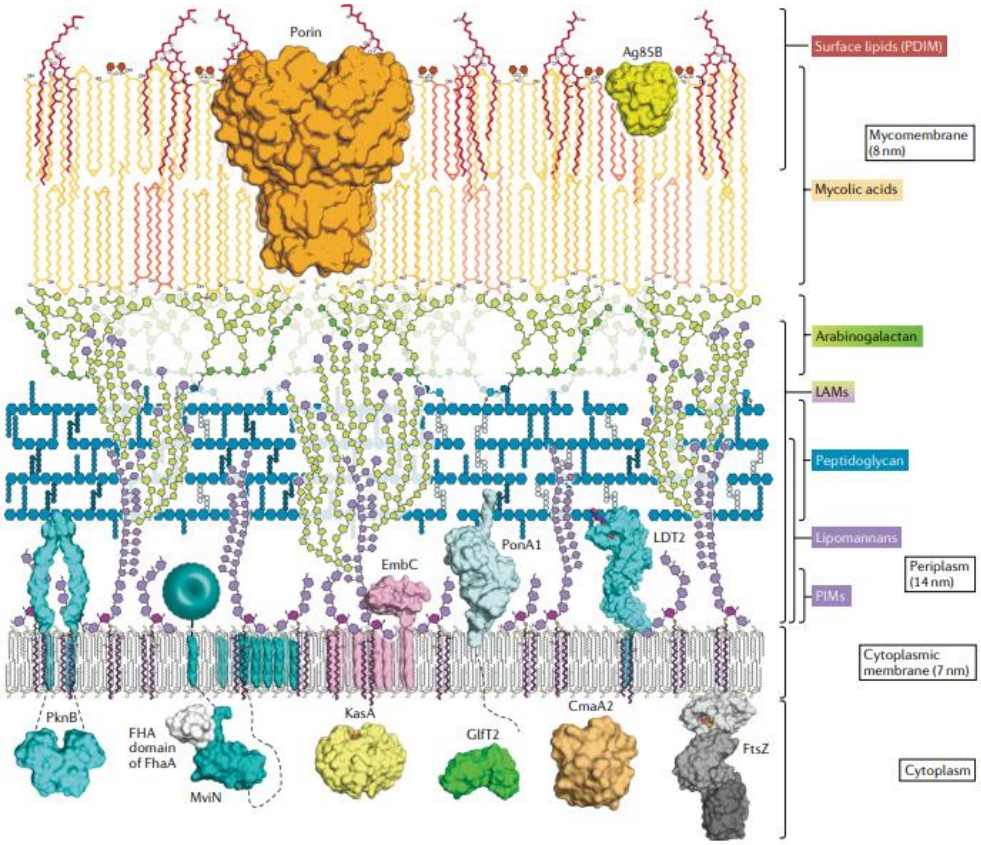


Figure 1: Structure of *Mycobacterium tuberculosis* cell wall[9]

and galactose sugars in their furanoside forms. The AG component is made up of roughly 30 linear alternating β-(1→5) and β-(1→6) Gal*f* residues, forming the D-galactose portion, which is further linked to the rhamnopyrnosyl residue of the linker unit. The galactan region consists of a linear alternation of 5- and 6-linked β-D-Gal*f* residues. Three tricosarabinoside (23mer) moieties are attached to the C5 hydroxyl group of the β(1→6) linked Gal*f* unit. This arabinan portion is highly branched, featuring a linear α(1→5) linked polysaccharide backbone with branching introduced by the 3,5-α-D-Ara*f* residue. Additionally, the non-reducing termini feature a structural motif [β-D-Ara*f*-(1→2)-α-D-Ara*f*]$_2$-3,5-α-D-Ara*f*-(1→5)-α-D-Ara*f* that forms a distinctive hexaarabinose moiety.

Mycolic acid: As part of the outer membrane, trehalose-containing glycolipids and phthiocerol dimycocerosates are interspersed with mycolic acid. These components also play a vital role in the immune response when interacting with the host. Mycolic acids are key and distinctive lipid components of the mycobacterial cell envelope, playing a crucial role in the survival of mycobacterium species, which include the causative agents of tuberculosis and leprosy. Mycolic acid primarily consists of α-alkyl, and β-hydroxy long-chain fatty acids (C_{70}–C_{90}) referred to as mycolic acids. These highly lipophilic fatty acids are classified based on the presence of unsaturation or cyclopropyl groups ("α-mycolic acid"), as well as modifications such as methoxy or keto functions in the main chain.[10-11] Mycolic acids are found either as free acids or esterified to the arabinogalactan layer, trehalose, glucose (glucose mono mycolate, GMM) or glycerol.[12-14] Moody and co-workers showed that the *R,R* stereochemistry of the α-alkyl, β-hydroxy carboxylic acid is essential for T cell recognition of glucose monomycolate[15].

Cyclopropane fatty acids are common in mycobacteria, and their concentration increases when exposed to harsh environments, suggesting they play a role in protecting membranes.[16-17] The impact of cyclopropane and unsaturated fatty acids, in both *cis* and *trans* configurations, on the packing, order, and fluidity of lipid bilayers is examined through molecular dynamics simulations. It has been demonstrated that cyclopropane fatty acids disrupt lipid packing, promote the formation of gauche defects in the chains, and increase lipid lateral diffusion, indicating they enhance fluidity.[18-19] Specifically, an increase in the concentration of cyclopropane fatty acids in the membranes of various bacteria has been linked to tolerance against high osmotic pressure,[20-23] elevated temperature,[20,24] low pH,[25-29] nutrient deprivation,[30,31] and high alcohol concentrations.[27,29] Cyclopropane mycolic acids also influence the host's innate immune response.[32,33] The stereochemistry of the cyclopropane ring is crucial. *Trans*-cyclopropanated mycolic acids play a key role in regulating and limiting the virulence of M. tuberculosis.[34] About 70% of the mycolic acid in *Mycobacterium* is α-mycolic acid, as the double bonds are especially prone to oxidation. It has been hypothesized that their methylenation enhances resistance to superoxide, singlet oxygen, ozonolysis, and oxidative stress overall.[35]

2.3 Importance and biological function of AG-Mycolic acid

The diversity, unique structures, and crucial roles of cell envelope lipids in the physiology and pathogenicity of Mtb are essential factors in its behavior and infection mechanisms. These

characteristics contribute to the specificity and therapeutic effectiveness of first- and second-line TB drugs like isoniazid (INH) and ethionamide (ETH) which work by inhibiting mycolic acid biosynthesis.[36] Additionally, ethambutol (EMB) inhibits the formation of the arabinan domains of ManLAM and AG. Ethambutol (EMB) primarily affects the polymerization steps involved in the biosynthesis of the arabinan component of the cell wall arabinogalactan (AG) in *Mycobacterium smegmatis*. Any disruption in the biosynthesis of these components, especially mycolic acids, AG, or peptidoglycan, would undermine the integrity of the macromolecular structure[37]. The effects of EMB are highly pleiotropic, with proposed primary sites of action including trehalose dimycolate (TDM)[38] and mycolate metabolism,[39] AG synthesis,[40] glucose metabolism,[41] and spermidine biosynthesis.[42] Mycolic acid methyltransferases, which are crucial for the viability of *M. tuberculosis*, cell wall integrity, and intrinsic antibiotic resistance are key drug targets.[43]

2.4 Present work

The cell wall of *Mycobacterium tuberculosis* (Mtb) is defined by its distinctive glycolipid composition particularly mycolyl arabinogalactan, which contains Ara*f*, Gal*f* and mycolic acid. My thesis focuses on the terminal portion of arabinogalactan (AG), motif A, a pentaarabinofuranoside characterized by two β-1,2 linkages and one each of α-1,5 and α-1,3 linkages. The C5 positions of motif A are esterified with mycolic acids, which are further modified by unusual cyclopropanes. In this study, we synthesized a variety of Mtb cell wall glycolipids inspired by motif A and examined their self-assembly behavior through microscopy. This glycolipid collection includes variations with α or β-(1→2, 3, or 5) Ara*f* linkages in di-, tri-, tetra-, and penta- arabinofuranosides esterified with saturated, doubly unsaturated, or cyclopropanated long-chain fatty acids.

Synthetic analysis of a glycolipid library designed to mimic terminal pentasaccharide of Mtb cell wall.

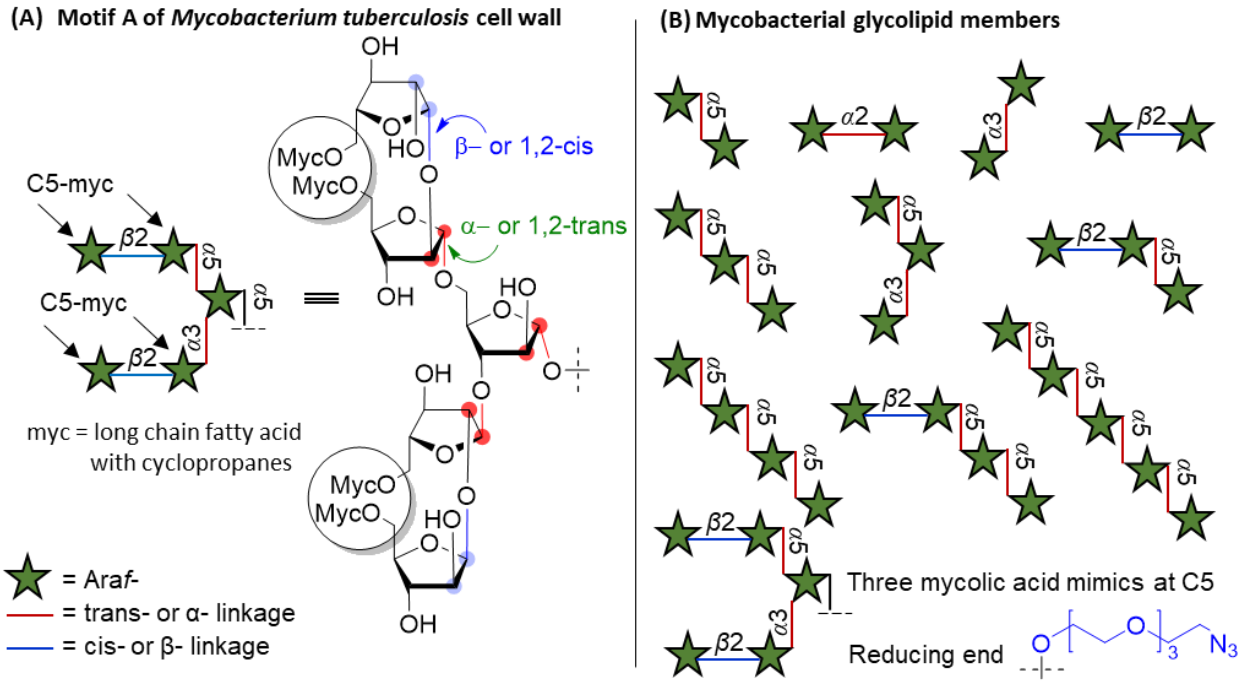
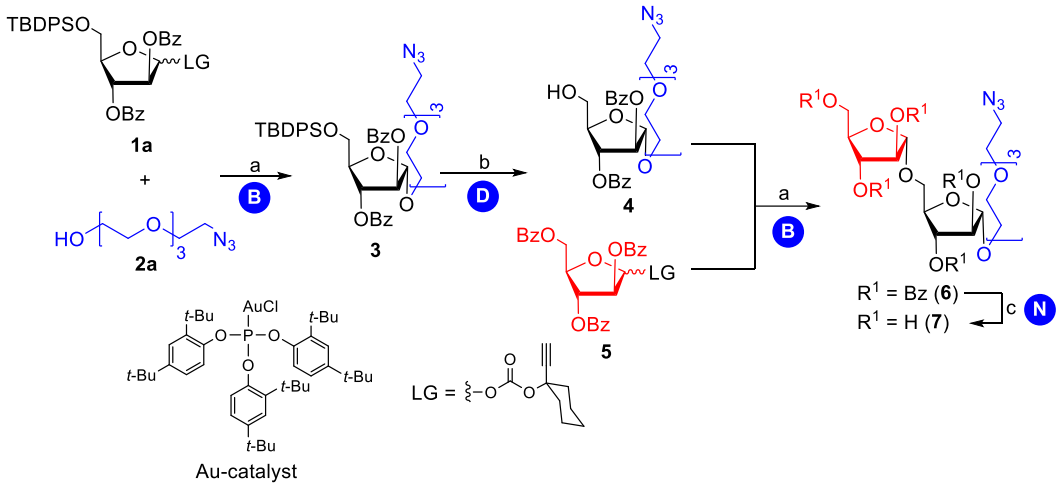


Figure 2: (a) Structure of the terminal pentasaccharide Motif A of *Mycobacterium tuberculosis* cell wall (b) Mycobacterial glycolipids library.

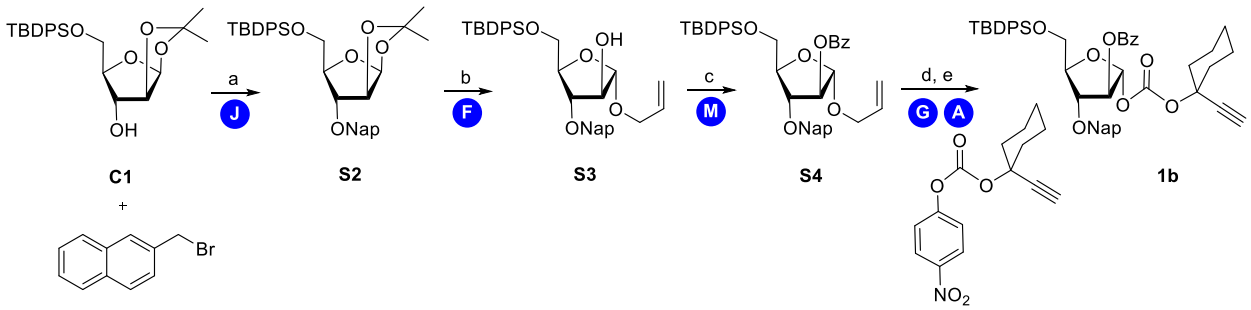
2.5 Synthesis of Disaccharide Glycolipids

2.5.1 Synthesis of disaccharide building block • Disaccharide building block **7** was prepared from compounds **1a** and **2a**. The first Glycosylation between acceptor **2a** and donor **1a** employing [Au]/[Ag]-catalysis in CH_2Cl_2 afforded glycoside **3** in good yield. Consecutively, C5-*O*-TBDPS deprotection of compound **3** using HF•py, followed by glycosylation with donor **5** in the presence of Au-Ag catalysts produced compound **6**. The global deprotection of benzoates has resulted in the formation of compound **7**. In the ^{1}H NMR spectrum of compound **7**, two 1,2-*trans* Ara*f* anomeric protons appeared as doublets at δ 4.95 and 4.91 ppm with coupling constant of 1.3 Hz and 1.4 Hz respectively. In the ^{13}C NMR spectrum, characteristic C1 and C2 carbons were found at δ 109.7 and 109.6 ppm and methylene carbon adjacent to the azide group appeared at 51.7 ppm. (Scheme 1)



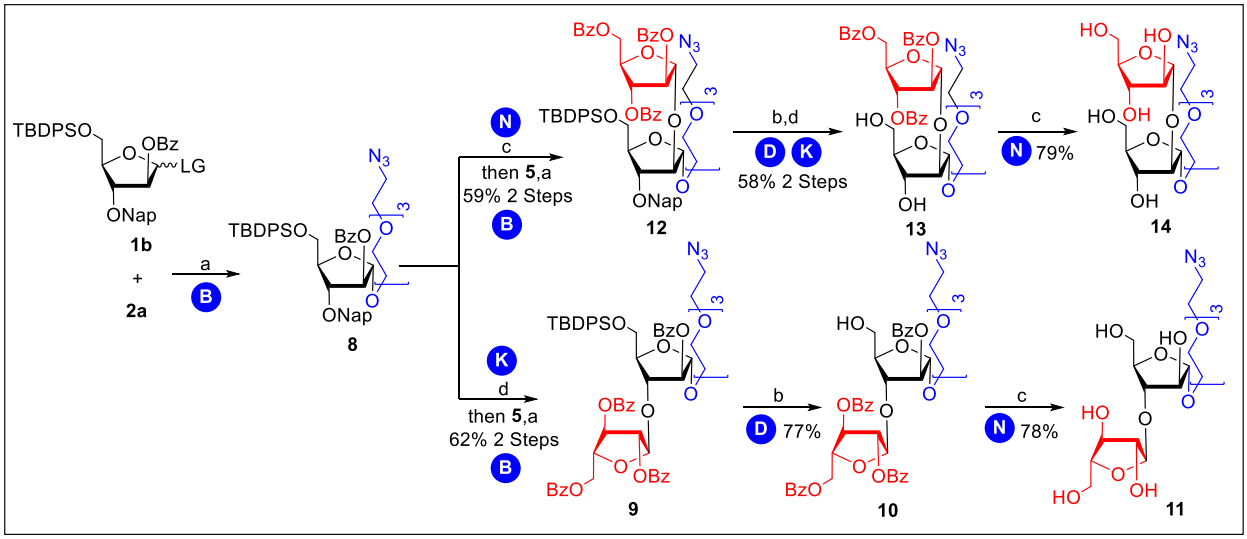
Scheme 1. a) 8mol% each of Au-catalyst and AgOTf, CH_2Cl_2, 4Å MS powder, 25 °C, 1 h, 78% for **3**, 76% for **6** b) HF·py, py., 0-25 °C, 3 h, 78% for **4**; c) NaOMe, MeOH-CH_2Cl_2 (3:1), 25 °C, 1 h, 82% for **7**.

Next, synthesis of disaccharides **11** and **14** was initiated with the synthesis of compound **1b** that was achieved in five steps by doing Nap protection of the C-3 OH of **C1** to afford **S2**, followed by PTSA mediated ring opening of 1,2-acetonide in the presence of allyl alcohol to result in compund **S3**; benzoyl protection at C-2 OH to get S4 which upon hydrolysis of the allyl group using $PdCl_2$ resulted in a hemiacetals which were treated with ethynyl cyclohexyl (4-nitro phenyl) carbonate afforded the desired donor **1b** (Scheme 2).



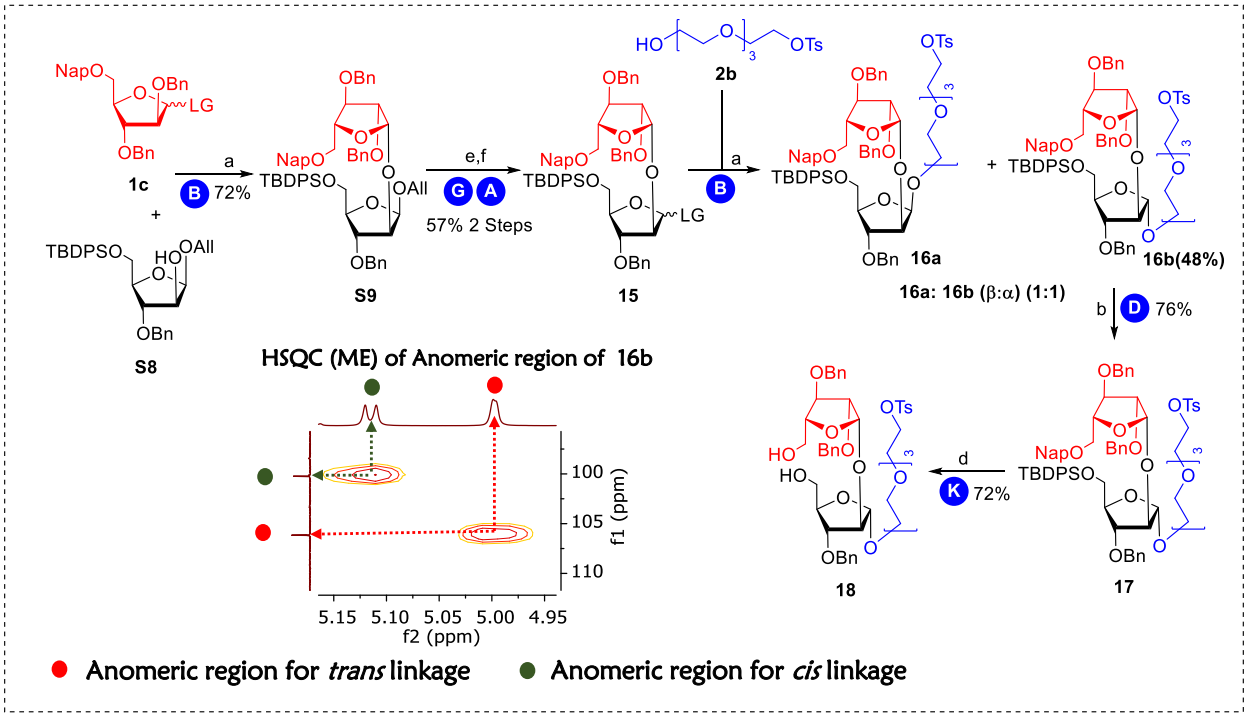
Scheme 2. a) NapBr, NaH, DMF, 0 °C-RT, 3h, 72% b) Allyl alcohol, P-TSA, CH_2Cl_2, RT-60 °C, 2h, (α:β = 1:1) (separated α- isomer, 48%) (c) BzCl, DMAP, Py, 0 °C-RT, 3h, 79% d) $PdCl_2$, MeOH-CH_2Cl_2 (4:1), 25 °C, 4 h, e) 1-ethynylcyclohexyl (4-nitrophenyl) carbonate, CH_2Cl_2, DMAP, 25°C, 3 h, 56% after 2 steps.

After successfully synthesizing donor **1b**, Ag-assisted Au-catalyzed glycosylation was performed between donor **1b** and acceptor **2a** to obtain a good yield of arabinoside **8**. At this stage, compound **8** was split into two portions; one portion was converted into corresponding disaccharide **11** having 1,2 *trans* glycosidic linkage by deprotecting the Nap group and subsequent glycosylation with **5** to produce disaccharide **9** followed by the deprotection of silyl ether using HF•py and global deprotection of benzoates using NaOMe. In the ^{1}H NMR spectrum of compound **11**, two 1,3-*trans* Araf anomeric protons appeared as a doublet at δ 5.07 and 4.94 ppm with coupling constant (J = 1.6 Hz) and (J = 1.2Hz) respectively. In the ^{13}C NMR spectrum, characteristic C1 and C2 carbons were found at δ 109.7 and 109 ppm and methylene carbon adjacent to the azide group appears at 51.7 ppm. On the other hand, disaccharide **14** having 1,3 *trans* glycosidic linkages, was obtained from the second portion of compound **8** through a five-step sequence starting with benzoyl deprotection and subsequent glycosylation with donor **5** to produce disaccharide **12** whose silyl ether was deprotected in the presence of HF•py. The resulting compound was subjected DDQ mediated Nap-ether deprotection and global deprotection of benzoates by using NaOMe in methanol afforded the desired disaccharide **14** (Scheme 3). In the ^{1}H NMR spectrum of compound **14**, two 1,2-*trans* Araf anomeric protons appeared as a doublet at δ 5.48 and 5.22 ppm with coupling constant (J = 1.6 Hz) and (J = 1.2Hz) respectively. In the ^{13}CNMR spectrum, characteristic C1 and C2 carbons were found at δ 106.7 and 105.4 ppm.



Scheme 3. a) 8mol% each of Au-catalyst and AgOTf, CH_2Cl_2, 4Å MS powder, 25°C, 1 h, 73% for **8** b) HF·py, py, 0-25°C, 3 h; c) NaOMe, MeOH-CH_2Cl_2 (3:1), 25°C, 1 h; d) DDQ, MeOH-CH_2Cl_2 (4:1), 25 °C, 4 h.

2.5.2 Synthesis of *cis*-disaccharide carbonate • The synthesis of 1,2-*cis* arabinofuranosyl disaccharide started from glycosyl donor **1c** and glycosyl acceptor **S8** by the literature procedures.[44a] Glycosyl acceptor **S8** is a sterically hindered and less reactive acceptor. Earlier studies from our lab showed less reactive and more sterically crowded Ara*f* acceptors afforded 1,2-*cis* (*β*) Ara*f* disaccharide.[44b] Having synthesized glycosyl donor **1c** and glycosyl acceptor **S8**, the furanosylation was carried out between them under [Au]/[Ag]-catalytic conditions at -78°C to furnish 1,2-*cis* or *β*-disaccharide **S9** (Scheme 4).



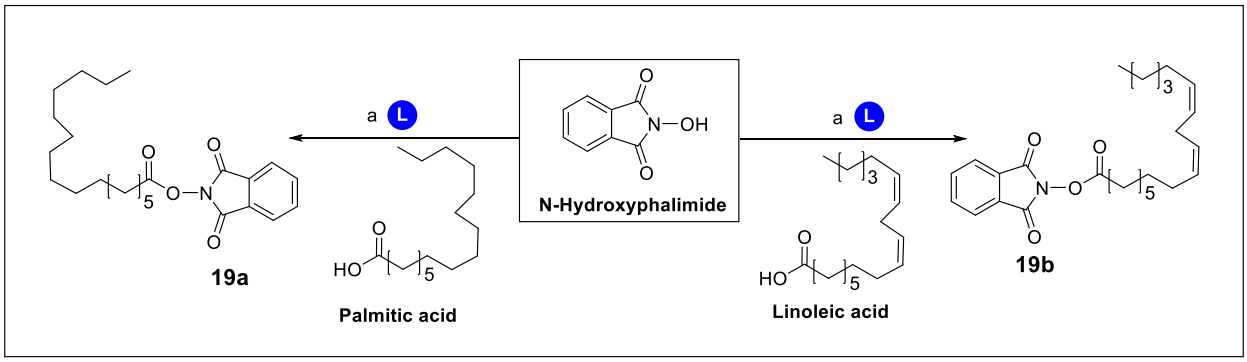
Scheme 4. a) 8mol% each of Au-catalyst and AgOTf, CH_2Cl_2, 4Å MS powder, -78°C - RT, 5h; b) HF·py, py., 0-25 °C, 3 h; d) DDQ, MeOH-CH_2Cl_2 (4:1), 25 °C, 4h; e) $PdCl_2$, MeOH-CH_2Cl_2 (4:1), 25 °C, 4h; f) 1-ethynylcyclohexyl (4-nitrophenyl) carbonate, CH_2Cl_2, DMAP, 25 °C, 3h.

The 1,2-*cis* configuration of disaccharide **S9** was verified by the ^{1}H and ^{13}C NMR spectroscopy. In the ^{1}HNMR spectrum of compound **S9**, 1,2-*cis* anomeric protons were noticed at δ 5.2 (d, J = 3.9 Hz, 2x1H) ppm while in the ^{13}C NMR spectra, diagnostic 1,2-*cis* anomeric carbons were recognized at δ 98.7 and 99.0 ppm. In continuation, glycosyl carbonate donor **15** was obtained

from disaccharide **S9** by the $PdCl_2$ mediated hydrolysis of the allyl group followed by the treatment with 1-ethynyl cyclohexyl (4-nitrophenyl) carbonate and a catalytic amount of DMAP.

No major stereoselectivity was noticed when the glycosylation between donor **15** and acceptor **2b** was performed at -78 or 25 °C. At 25°C, glycosylation between donor **15** and acceptor **2b** showed ββ:αβ = 1:1 mixture of disaccharides. In the ^{1}H NMR spectrum of compound **16b**, 1,2-*cis* anomeric protons were noticed at δ 5.12 (d, 1H) ppm, and 1,2 *trans* proton was noticed at δ 4.99 (S, 1H) ppm. In the ^{13}C NMR spectrum, diagnostic 1,2-*cis* anomeric carbon was recognized at δ 100.6 and 106.3 ppm for 1,2 *trans* anomeric carbon. In continuation, TBDPS deprotection of compound **16** was carried out using HF•py to obtain compound **17** that was subjected to the Nap deprotection to successfully prepare compound **18**. (Scheme-4)

2.5.3 Synthesis of active ester 19a, 19b, 19c



Scheme 5. a) DIC, DMAP, CH_2Cl_2, RT, 3h. 70% for 19a and 68% for 19b.

Having synthesized all the four disaccharides, the synthesis of lipid counterparts was taken up. Accordingly, commercially available *N*-Hydroxypthalimide was treated with DIC/DMAP and palmitic acid or Linoleic acid to obtain N-hydroxypthalimidyl esters **19a** and **19b**. The synthesis of cyclopropanated lipid **19c** was commenced from commercially available linoleic acid. At first, the linoleic acid methyl ester **C2** was cyclopropanated under modified Simmons-Smith conditions (Et_2Zn, CH_2I_2, $ClCH_2CH_2Cl$) to obtain lipid **C3** that was saponified under alkaline conditions to obtain the corresponding carboxylic acid **C4** that was smoothly converted to the desired lipid **19c** under aforementioned conditions. All the three lipids were characterised thoroughly by NMR spectroscopy.

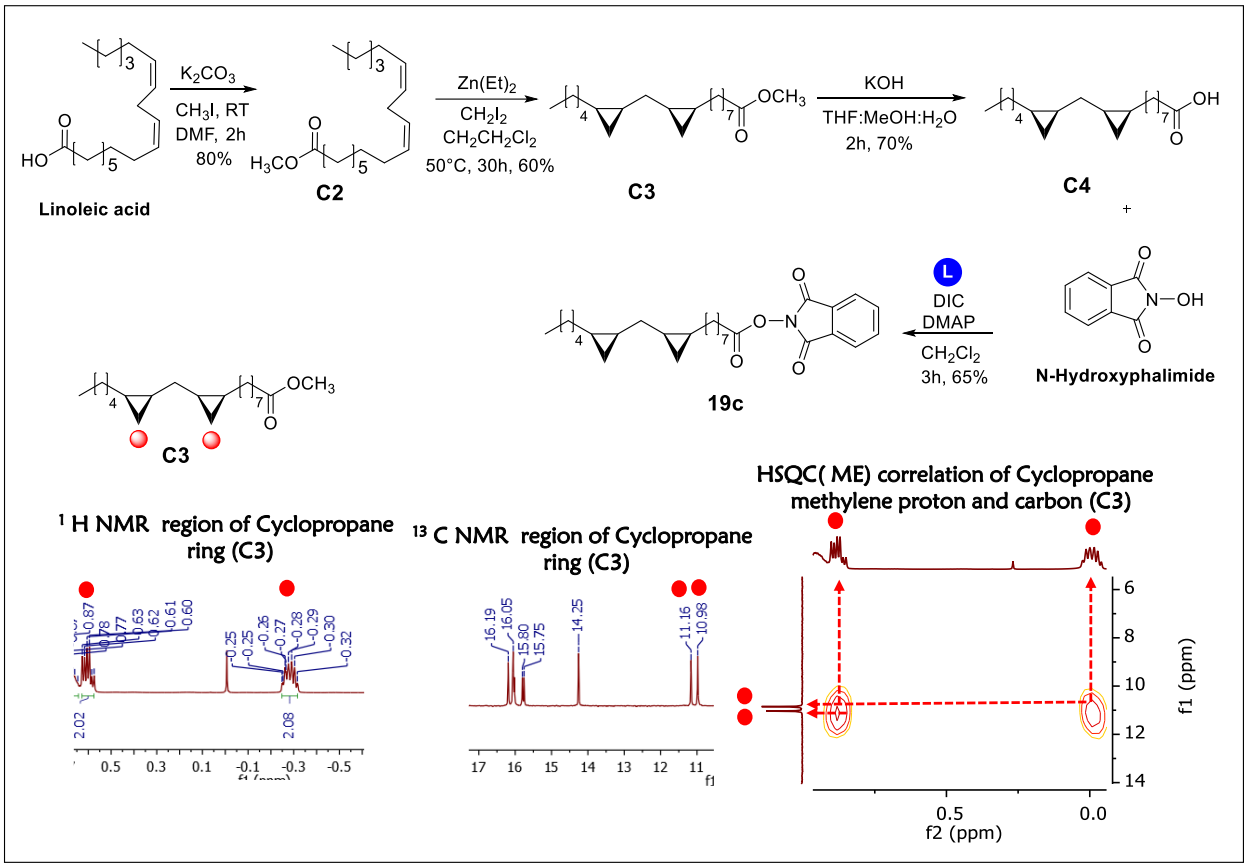
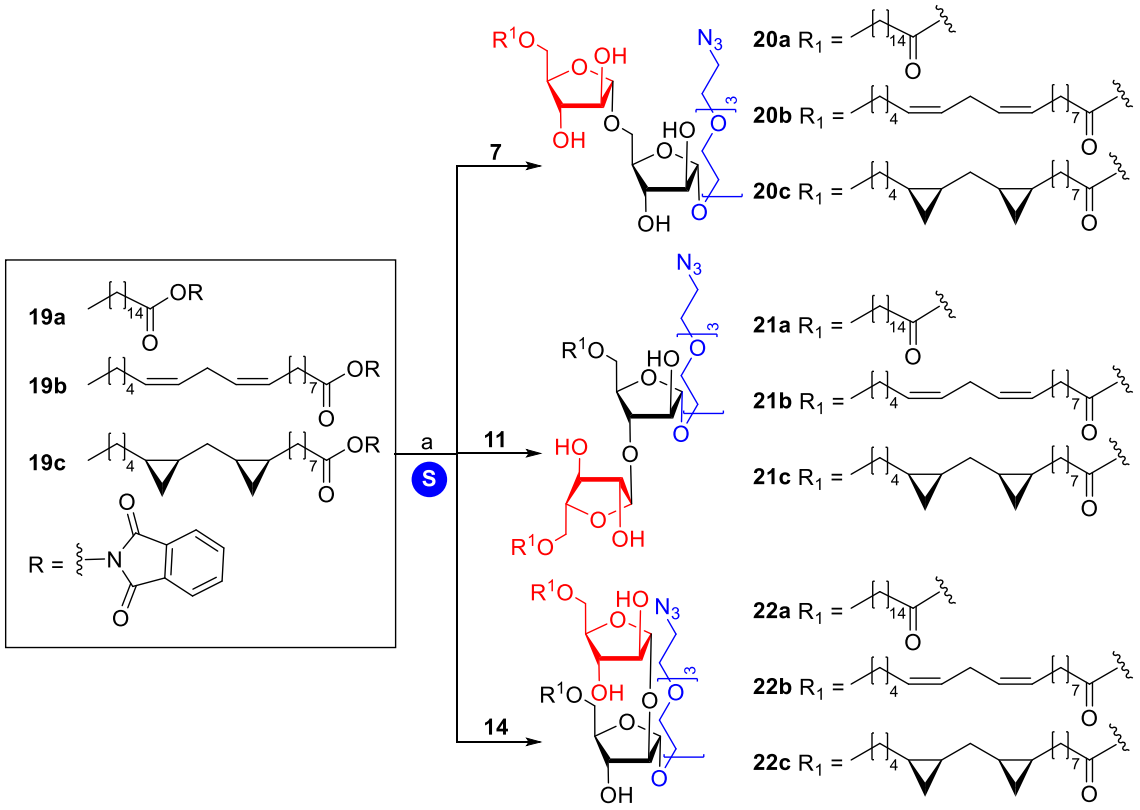


Figure-3 Synthetic scheme of cyclopropanation reaction (**C3**) characterized by ^{1}H, ^{13}C, and HSQC (Multiplicity edited) spectra.

2.5.4 Regioselective Esterification of Disaccharides having 1,5 *trans* glycosidic linkages

• The regioselective esterification at primary OH of compound **7** in the presence of secondary was performed by using an active ester of palmitic acid (**19a**), linoleic acid (**19b**), and cyclopropane derivative of Linoleic acid (**19c**) in DIPEA and DMAP in pyridine. After 35-40h we isolated glycolipids **20a, 20b,** and **20c** (Scheme-6). The rate of reaction was very slow because of the high dilution conditions; low dilutions led to the mixture of esters coming from primary and secondary hydroxyl groups. The regioselectivity of the esterification was confirmed from their HMBC (Hetero Multi Bond Correlation) spectra where the C5-CH_2 of sugar showed a cross peak with carbonyl carbon of the ester group. In the ^{1}H NMR spectrum of compound **20a**, two 1,2-*trans* Ara*f* anomeric protons appeared at δ 5.05 (d, 1H) and 5.02 (s, 1H) ppm. In the ^{13}C NMR spectrum, characteristic two anomeric carbons were found at δ 108 and 107.8 ppm. Further, the appearance of carbonyl resonances at δ 173.9 ppm disclosed the presence of the ester group of palmitic acid. The terminal CH_3 group of fatty acid was noticed at δ 14.3. Similarly, In

the ^{1}HNMR spectrum of compound **20b** two anomeric protons appeared at δ 5.03 (d, 2H) ppm, and olefin protons were noticed at δ 5.41-5.26 (m, 4H) ppm. In the ^{13}C NMR spectrum, four olefin carbons appeared at 130.34, 130.16, 128.17, and 128.03. Characteristic two anomeric carbons were found at δ 108 and 107.8 ppm. Further, the appearance of carbonyl resonances at δ 173.8 ppm disclosed the presence of the ester group of Linoleic acid. The terminal CH_3 group of fatty acid was noticed at δ14.24 and the methylene group adjacent to azide appeared at 50.74. Similarly, In the ^{1}HNMR spectrum of compound **20c**, two anomeric protons appeared at δ 4.93 and 4.97 ppm, and methylene protons of cyclopropane rings were noticed at δ -0.21 to -0.28 (m, 2H) ppm and 0.65 (td, 2H) ppm. In the ^{13}C NMR spectrum, methylene carbons of the cyclopropane ring appeared at δ 11.74 and 11.60 ppm. Characteristic two anomeric carbons were found at δ 109.7 and 109.6 ppm. Further, the appearance of carbonyl peaks at δ 175.2 ppm disclosed the attachment of the ester group of cyclopropane derivative of linoleic acid. The terminal CH_3 group of cyclopropane fatty acid appeared at δ14.48 and the methylene group adjacent to azide was noticed at δ 51.8 ppm. (Table-1)



Scheme 6. a) DIPEA, DMAP, py., 25 °C, 48 h, 20-25%

Entry	Starting Sugar	Active Ester (eq)	DIPEA (eq)	DMAP (eq)	Time (h)	Solvent (mL/0.1g)	Tem.(°C)	Yield	
								Di(%)	Mono(%)
(1)	7	1.1	1	0.1	24	DMF(3)	25	-	10
(2)	7	1.1	1	0.1	24	Pyridine(3)	25	-	30
(3)	7	1.1	1	0.1	24	Pyridine(2)	50	-	5
(4)	7	2	2	0.2	50	Pyridine(2)	25	-	46
(5)	14	2.2	2	0.2	24	Pyridine(2)	25	10	40
(6)	14	3	3	0.3	55	Pyridine(2)	25	25	30
(7)	11	2.2	2	0.2	55	Pyridine(2)	25	28	32
(8)	11	3	3	0.3	96	Pyridine(2)	25	30	25

Table 1- Reaction optimization table for regioselective esterification

2.5.5 Regioselective esterification of disaccharides having (1,3) *trans* glycosidic linkages

Next, we performed regioselective esterification in **11** having 1,3 *trans* glycosidic linkage by using active ester **19a**, **19b**, **19c.** While having all the active ester in hand we started regioselective esterification of **11** in the presence of active ester, DIEA, and DMAP in pyridine as a solvent at RT. After 30-35h we achieved **21a, 21b**, **21c.** In compound **11** due to the presence of two primary OH, the di-substituted as well as mono-substituted products were observed. From HMBC (Hetero Multi Bond correlation spectroscopy) we confirmed the regioselectivity of compounds **21a**, **21b**, and **21c.** Where the two CH_2 at the C-5 position of sugar showed a cross peak with two carbonyl carbons of the ester group. In the ^{1}HNMR spectrum of compound **21a**, two 1,2-*trans* Araf anomeric protons appeared at δ 5.14 (s, 1H) and 5.00 (s, 1H) ppm. The 6H of terminal CH_3 resonates at 0.87 (t, 6H). In the ^{13}C NMR spectrum, characteristic two anomeric carbons were found at δ 108.6 and 107.9 ppm. Further, the appearance of carbonyl peaks at δ 173.79 and 173.67 ppm disclosed the attachment of the ester group of palmitic acid at sugar moiety and their correlation with methylene proton at the C-5 position of sugar confirmed their regioselectivity.

In the ^{1}H NMR spectrum of compound **21b**, two 1,2-*trans* Araf anomeric protons appeared at δ 5.14 (s, 1H) and 4.98 (d, 1H) ppm. The 6H of terminal CH_3 resonates at 0.88 (m, 6H), and eight olefin protons were noticed at δ 5.43-5.27 (m, 8H) ppm. In the ^{13}C NMR spectrum, characteristic two anomeric carbons were found at δ 108.6 and 107.9 ppm and eight olefin carbons appeared at 130.36(2C), 130.17(2C), 128.18(2C), and 128.04(2C). Further, the appearance of carbonyl peaks at δ 173.72 and 173.62 ppm disclosed the attachment of the Ester group of Linoleic acid at sugar moiety and their correlation with methylene proton at the C-5 position of sugar confirmed their regioselectivity.

In the ^{1}HNMR spectrum of compound **21c**, two 1,2-*trans* Araf anomeric protons appeared at δ 5.15 (s, 1H) and 5.00 (s, 1H) ppm and eight methylene protons of cyclopropane rings were noticed at -0.24 – -0.33 (m, 4H) ppm and 0.60 (td, 4H). In the ^{13}C NMR spectrum, two characteristic anomeric carbons were found at δ 108.7 and 107.9 ppm and four methylene carbons of the cyclopropane ring appeared at 11.17(2C) and 10.97(2C). Further, the appearance of carbonyl peaks at δ 173.72 and 173.95 ppm disclosed the attachment of the ester group of cyclopropane derivative of linoleic acid at sugar moiety and their correlation with methylene proton at the C-5 position of sugar with the help of HMBC confirmed their regioselectivity. (Scheme 6) (Table 1)

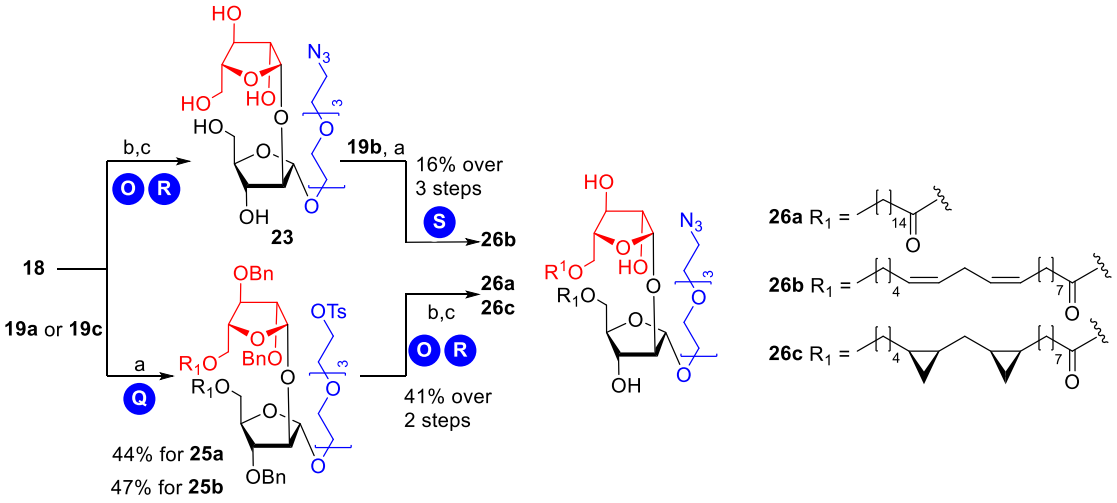
2.5.6 Regioselective esterification of disaccharides having (1,2) *trans* glycosidic linkages

• After successfully confirming the regioselectivity of 1,3 *trans* disaccharide, we applied the similar reaction conditions of regioselective esterification for 1,2 *trans* disaccharide **14** because apart from the sugar linkage everything was the same in both the disaccharides. by using active ester **19a**, **19b**, and **19c** to obtain glycolipids **22a**, **22b**, and **22c**. Regioselectivity of all the 3-glycolipids was confirmed by HMBC spectroscopy. In the ^{1}HNMR spectrum of compound **22a**, two 1,2-*trans* Ara*f* anomeric protons appeared at δ 5.15 (s, 1H) and 5.14(s, 1H) ppm whereas the six protons of terminal CH_3 resonated at δ 0.87 (t, 2x3H) ppm. In the ^{13}C NMR spectrum, resonances due to the characteristic anomeric carbons were found at δ 107.6 and 106.1 ppm. Further, the appearance of carbonyl peaks at δ 174.24 and 173.77 ppm disclosed the attachment of the ester group of palmitic acid at sugar moiety and their correlation with methylene proton at the C-5 position of sugar confirmed their regioselectivity. In the ^{1}H NMR spectrum of compound **22b**, two 1,2-*trans* Ara*f* anomeric protons appeared at δ 5.16 (s, 1H) and

5.13 (d, 1H) ppm whereas the six protons of terminal CH_3s resonated at δ 0.88 (t, 6H), and eight olefin protons were noticed at δ 5.42-5.28 (m, 8H) ppm. In the ^{13}C NMR spectrum, two anomeric carbons were found at δ 107.63 and 107.69 ppm and eight olefin carbons appeared at 130.36(2C), 130.17(2C), 128.19(2C), 128.03(2C). Further, the appearance of carbonyl peaks at δ 174.18 and 173.69 ppm disclosed the attachment of the ester group of linoleic acid at sugar moiety and their correlation with methylene proton at the C-5 position of sugar confirmed their regioselectivity by using HMBC spectroscopy.

In the ^1H NMR spectrum of compound **22c**, two 1,2-*trans* Ara*f* anomeric protons appeared at δ 5.16 (s, 1H) and 5.14 (s, 1H) ppm and eight methylene protons of cyclopropane rings were noticed between δ -0.25 and -0.32 (m, 4H) and 0.61 (td, 4H) ppm. In the ^{13}C NMR spectrum, two anomeric carbons were identified at δ 107.6 and 106.1 ppm and four methylene carbons of the cyclopropane ring appeared at δ 11.17(2C) and 10.97(2C) ppm (Scheme 6) (Table 1)

2.5.7 Esterification of disaccharides having (1,2) *cis* glycosidic linkages • In the case of 1,2 *cis* disaccharide, disaccharide **18** was split into two portions and the first portion was converted into compound **23** via hydrogenolysis and subsequent S_N2 substitution of tosyl group with an azide.



Scheme 7. a) DIPEA, DMAP, py., 25 °C, 48 h; b) Pd $(OH)_2$, EtOAc, H_2, 25 °C, 6 h; c) NaN_3, DMF, 25 °C, 5 h.

The regioselective esterification was performed on compound **23** using active ester **19b**, DIPEA, and DMAP in pyridine at 25 °C. After 36 h, compound **26b** was isolated. In the ^{1}HNMR

spectrum of compound **26b**, two Ara*f* anomeric protons appeared at δ 5.06 (dd, 2H) ppm whereas two characteristic anomeric carbons were found at δ 109.2 ppm for 1,2 *trans* linkage and 102 ppm for 1,2 *cis* linkage in the ^{13}C NMR spectrum. In parallel, the second portion of compound **18** was esterified with **19a** and **19c** under DIPEA/DMAP conditions. In the ^{1}H NMR spectrum of compound **25a**, two Ara*f* anomeric protons appeared at δ 5.10 (s, 1H) and 5.00 (d, 1H) ppm. In the ^{13}C NMR spectrum, two characteristic anomeric carbons were found at δ 106.4 ppm for 1,2 *trans* linkage and 100.8 ppm for 1,2 *cis* linkage. The tolyl methyl resonated at δ 2.43 (s, 3H) as evident in the ^{1}H NMR spectrum and δ 21.73 in the ^{13}C NMR spectroscopy. Further, the appearance of carbonyl peaks at δ 173.68 and 173.52 ppm confirmed the attachment of the ester group of palmitic acid at sugar moiety. and their correlation with methylene proton at the C-5 position of sugar was also confirmed by HMBC. Next, compound **25a** was converted into **26a** by using $Pd(OH)_2$/ethyl acetate, followed by azidation of the tosyl group in the presence of NaN_3/DMF condition. Compound **26a** was confirmed by NMR and HRMS. In the ^{1}H NMR spectrum of compound **26a**, two Araf anomeric protons appeared at δ 5.06 (m, 2H) ppm. In the ^{13}C NMR spectrum, characteristic two anomeric carbons were found at δ 105.5 and 102.1. The methylene CH_2 adjacent to the terminal azide group resonates at 3.39 (t, J = 5.1 Hz, 2H), in ^{1}H NMR and δ 50.74 in ^{13}CNMR. Further, the appearance of carbonyl peaks at δ 174.13 and 173.93 ppm disclosed the attachment of the Ester group of palmitic acid at sugar moiety and their correlation with methylene proton at the C-5 position of sugar with the help of HMBC spectroscopy.

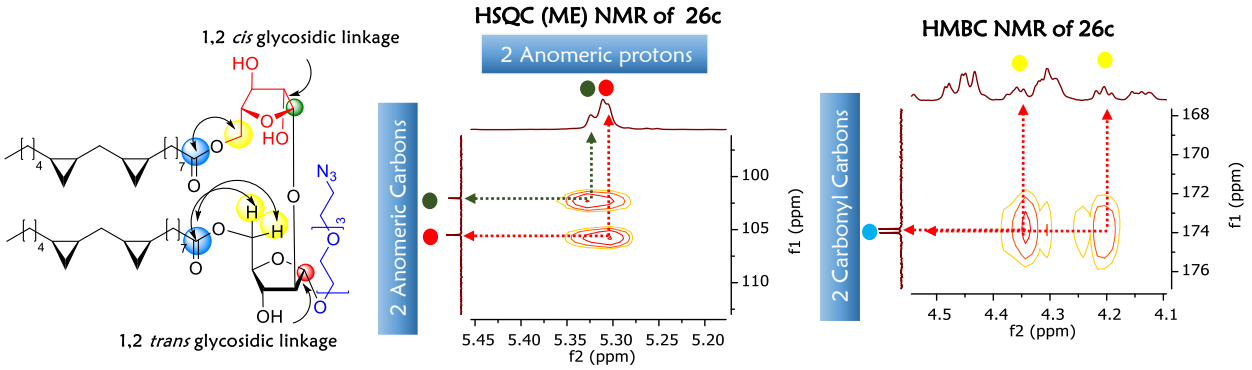


Figure 4: Heteronuclear Single Quantum Coherence (Multiplicity Edited) Spectroscopy and Heteronuclear Multiple bond Correlation Spectroscopy of compound 26c.

The synthesis of **25b** was performed as per the aforementioned procedure for **25a** except for the fatty acid part. Compound **25b** was converted into glycan **26c** using $Pd(OH)_2$/ethyl acetate, followed by azidation of the tosyl group in the presence of NaN_3/DMF conditions. In the ^1H NMR spectrum of compound **26c**, two Ara*f* anomeric protons appeared at δ 5.06 (m, 2H) ppm, and eight methylene protons of cyclopropane rings were noticed at δ -0.25 – -0.32 (m, 4H) ppm and δ 0.61 (td, 4H) ppm. In the ^{13}C NMR spectrum, characteristic anomeric carbons were established at δ 105.6 and 102.1 ppm and four methylene carbons of the cyclopropane ring appeared at 11.15(2C) and 10.96(2C). Further, the appearance of carbonyl peaks at δ 174.10 and 173.90 ppm disclosed the attachment of the ester group of cyclopropane derivative of linoleic acid at sugar moiety and their correlation with methylene proton at the C-5 position of sugar (Scheme 7) (Figure 4). The absolute stereochemistry of the cis cyclopropane ring was established based on existing literature. (Table-2)

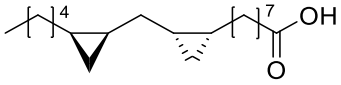
Structure	*Cell Physiol. Biochem.* **2011**, *27*, 149-158	Our value
	$[\alpha]_D^{23}$ [*c*10] = -0.45°	
	$[\alpha]_D^{23}$ [*c*1.0] = -9.9°	
	$[\alpha]_D^{23}$ [*c*0.9] =+9.9°	
	$[\alpha]_D^{23}$ [*c*10] = +0.47°	$[\alpha]_D^{19}$ [*c*10] = +0.58°

Table-2 As per the above table, it is evident that our cyclopropanation resulted in the formation of the (*R*,*R*),(*S*,*R*)-derivative. *Cell Physiol. Biochem.* **2011**, *27*, 149-158

To investigate the impact of a *cis* or *trans* cyclopropane ring on the self-assembly of the molecule, the synthesis of a 1,2-*cis* disaccharide with a *trans* cyclopropane is needed. This necessitated the preparation of an active ester containing trans cyclopropane as outlined

explained below (Figure-5). For the trans derivatives, we have used the linolelaidic acid instead of linoleic acid.

2.5.8 Synthesis of active ester having *trans* cyclopropane in fatty acid.

Synthesis of Compound **C8** started from commercially available linolelaidic acid.

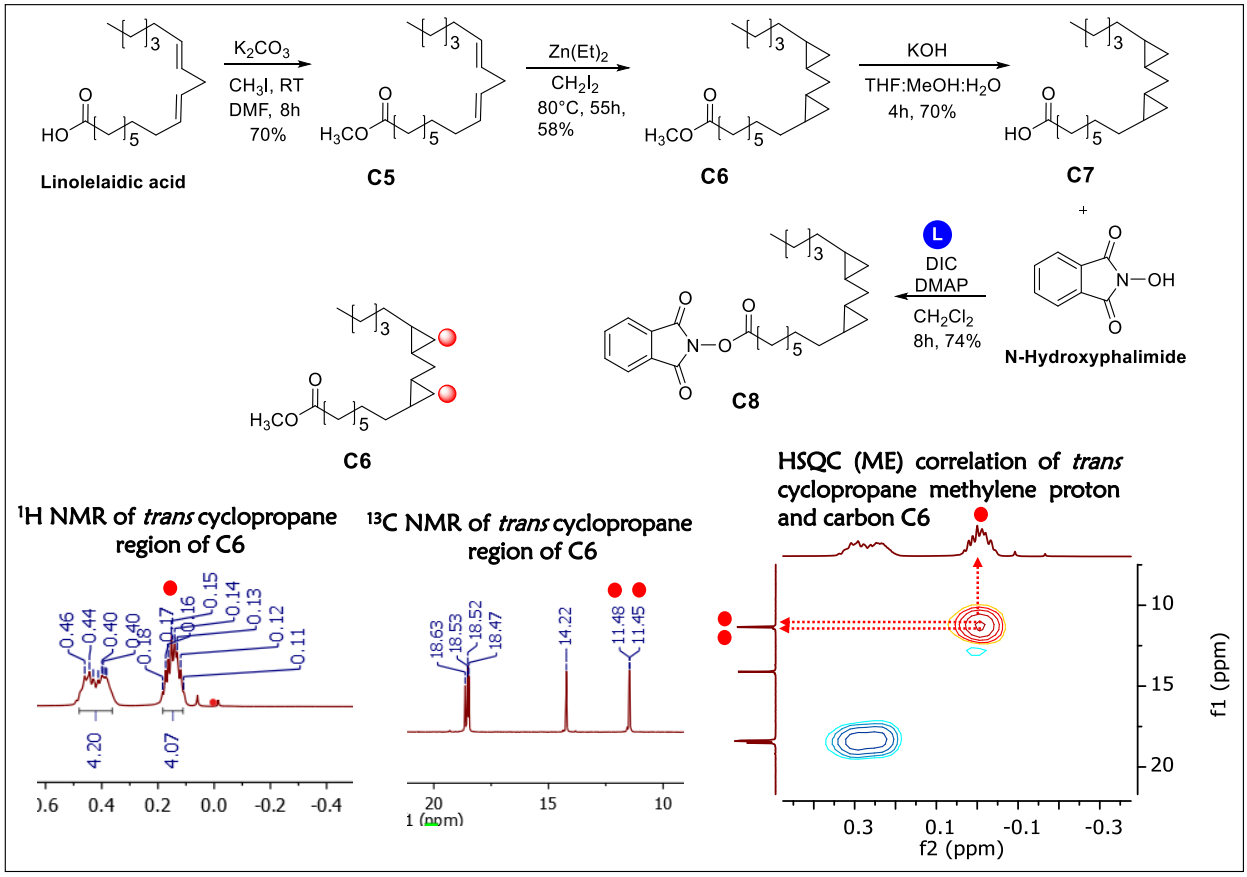
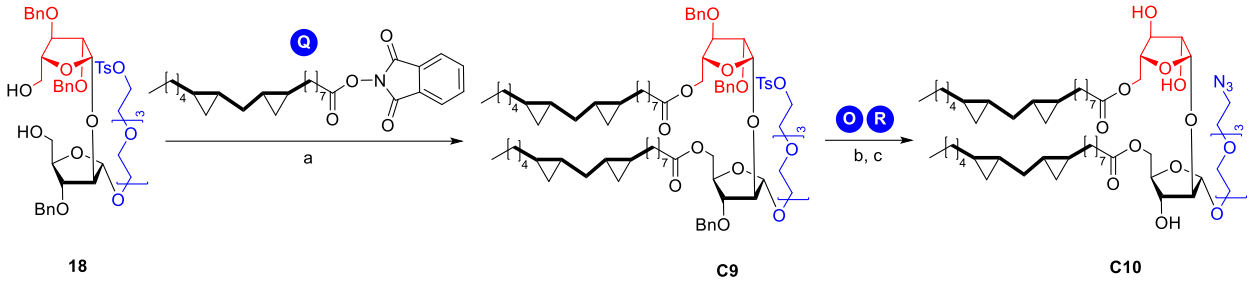


Figure-5 Synthetic scheme of trans cyclopropanation reaction (**C6**) characterized by ^{1}H, ^{13}C, and HSQC (Multiplicity edited) spectra.

1H and 13C NMR values of methylene proton and carbon of *cis* cyclopropane ring	1H and 13C NMR values of methylene proton and carbon of *trans* cyclopropane ring
-0.25- -0.32ppm (2H) and 0.50-0.60 ppm (2H)	0.11-0.88 ppm (4H)
10.98ppm (1C) and 11.16ppm (1C)	11.45ppm (2H) 11.48ppm(2H)

Table 3- Characteristic proton and carbon value of cis or trans cyclopropane ring

2.6.6 Regioselective Esterification of Disaccharides having (1,2) *cis* glycosidic linkages with active ester having trans cyclopropane ring.



Scheme 8. a) DIPEA, DMAP, py., 25 °C, 8 h; b) Pd $(OH)_2$, EtOAc, H_2, 25 °C, 6 h; c) NaN_3, DMF, 25 °C, 5 h.

The disaccharide **18** synthesized vide supra was esterified with the activated ester **C8** to obtain the compound **C9** which upon hydrogenolysis using $Pd(OH)_2$/ethyl acetate followed by azidation of the tosyl group in the presence of NaN_3/DMF conditions afforded the compound **C10**. The successful synthesis of the compound **C10** was confirmed by the NMR spectroscopic studies. In the ^1H NMR spectrum of compound **C10**, two Ara*f* anomeric protons appeared at δ 5.05 (dd, 2H) ppm, and eight methylene protons of cyclopropane rings were noticed at 0.19- 0.12 (m, 8H) ppm. (Scheme 8) (Figure 6).

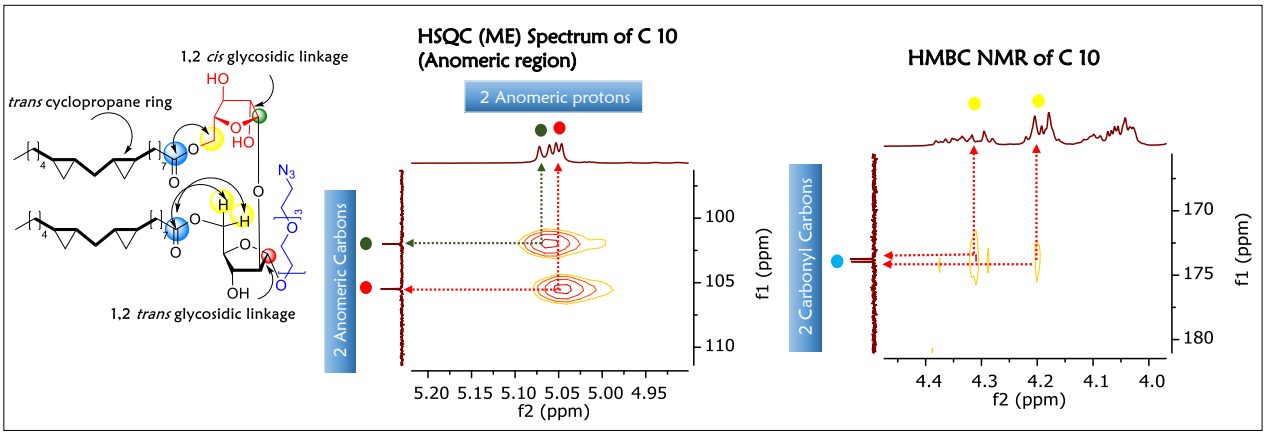


Figure 6: Heteronuclear Single Quantum Coherence (Multiplicity Edited) Spectroscopy and Heteronuclear Multiple bond Correlation Spectroscopy of compound C10.

In the ^{13}C NMR spectrum of compound **C10**, two anomeric carbons were found at δ 105.6 and 102.1 ppm and four methylene carbons of the cyclopropane ring appeared at 11.5(4C). Further, the appearance of carbonyl peaks at δ 174.1 and 173.9 ppm disclosed the attachment of the ester group of cyclopropane derivative of linoleic acid having trans cyclopropane ring at sugar moiety and their correlation with methylene proton at the C-5 position of sugar with the help of HMBC.

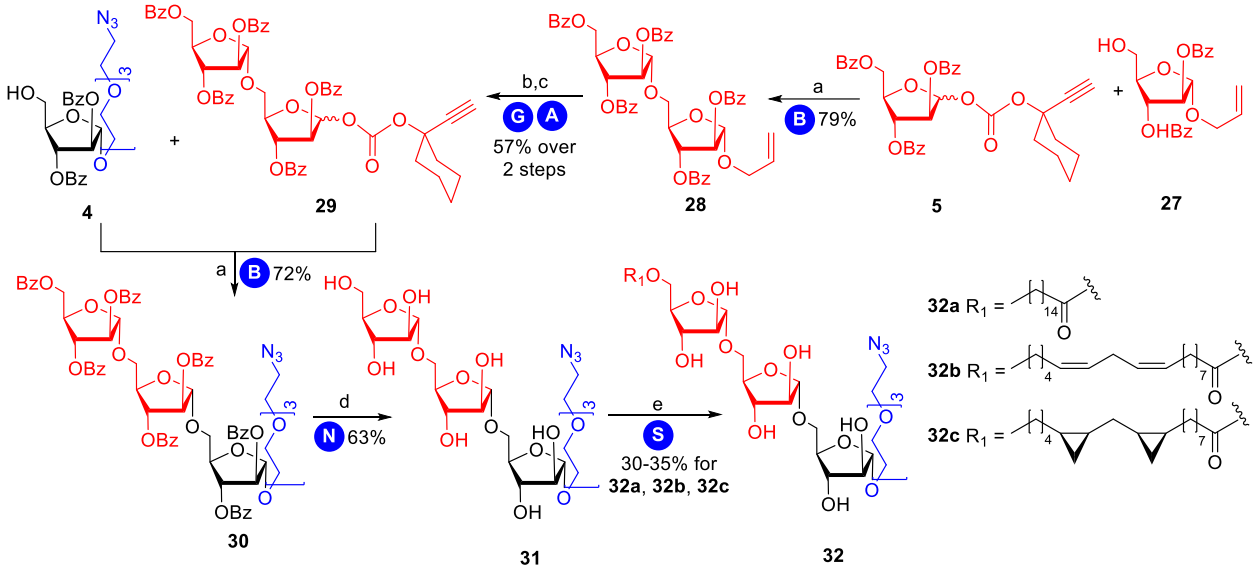
The successful synthesis of twelve glycolipids encouraged us to move to the preparation of the trisaccharide glycolipids. The linear trisaccharide synthesis with 1,5-glycosidic linkages started from the glycosylation of glycosyl donor **29** and glycosyl acceptor **4**. Glycosyl donor **29** was synthesized from compounds **5** and **27** by following literature procedures and glycosylations under Au-Ag conditions to afford compound **28**.[45] Glycosyl carbonate donor **29** was obtained from disaccharide **28** by the $PdCl_2$ mediated hydrolysis of the allyl group and protection of resulting hemiacetal with reagent 1-ethynyl cyclohexyl (4-nitrophenyl) carbonate and a catalytic amount of DMAP.

2.6 Synthesis of linear trisaccharide glycolipids:

2.6.1 Synthesis of linear trisaccharide glycolipids having (1,5 *trans* glycosidic linkages) •

The gold/silver mediated glycosylation between donor **29** and acceptor **4** afforded 76% of the linear trisaccharide **30**. In the ^{1}H NMR spectrum of trisaccharide **30**, three anomeric protons were noticed as three singlets δ 5.46, 5.40, and 5.27 ppm that was identified with the help of HSQC (Hetero Single Bond Correlation) (multiplicity edited) spectroscopy. In the ^{13}C NMR spectrum, characteristic three anomeric carbons were found at δ 106.1, 105.9, 105.8 ppm, and seven carbonyl peaks of the benzoyl moiety appeared at δ 166.4, 165.9, 165.8, 165.8, 165.5, 165.4 and 165.3 ppm. Further, the methylene protons adjacent to the azide were found at δ 50.8 ppm. Furthermore, trisaccharide **30** was debenzoylated using NaOMe/MeOH to obtain trisaccharide **31** whose ^{1}H NMR spectrum showed three Ara*f* anomeric protons at δ 4.98 – 4.95 (m, 2H), 4.93 (d, J = 1.3 Hz, 1H) ppm. In the ^{13}C NMR spectrum of trisaccharide **31**, the three anomeric carbons were found at δ 109.7, 109.7, and 109.6 ppm. The next step of regioselective esterification of primary OH in the presence of secondary hydroxyl underwent smoothly with active esters **19a, 19b**, and **19c** in the presence of DIPEA and DMAP in pyridine to afford

glycolipids **32a**, **32b** and **32c** respectively. The formation of **32a**, **32b,** and **32c** was confirmed by NMR and MALDI.

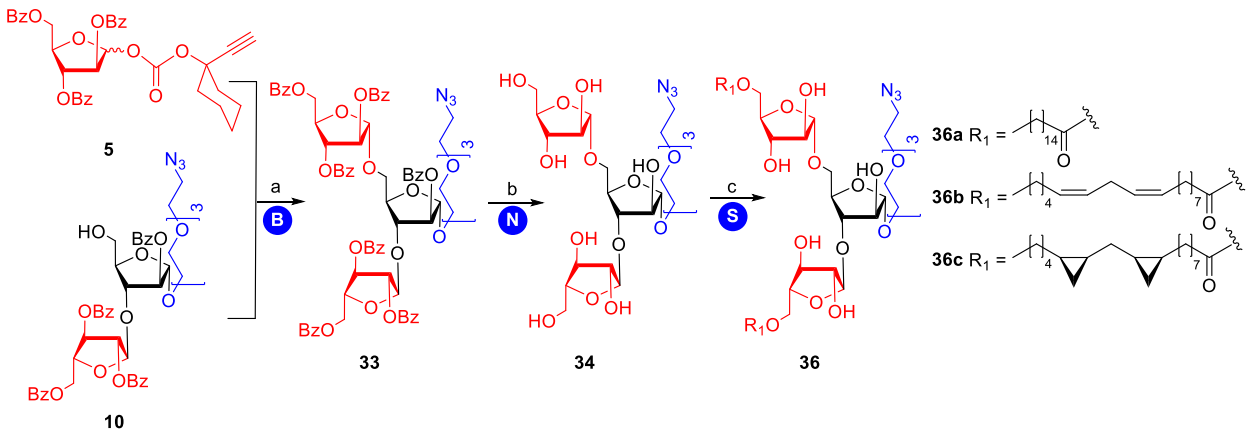


Scheme 8. a) 8mol% each of Au-catalyst and AgOTf, CH_2Cl_2, 4Å MS powder, RT, 30min; b)$PdCl_2$, MeOH-CH_2Cl_2 (4:1), 25 °C, 4 h; c) 1-ethynyl cyclohexyl (4-nitrophenyl) carbonate, CH_2Cl_2, DMAP, 25 °C, 3 h: d) NaOMe, MeOH-CH_2Cl_2 (3:1), 25 °C, 1 h; e) DIPEA, DMAP, py., 25 °C, 48 h.

In the ^{1}HNMR spectrum of compound **32a**, three 1,2-*trans* Ara*f* anomeric protons appeared at δ 5.00- δ 4.95 (s, 2H), 4.92 (s, 1H) ppm. The terminal CH_3 group showed resonances at 0.91 ppm (t, J = 6.8 Hz, 3H) and those of CH_2-N_3 were observed at δ 3.37 (m, 2H) ppm. In the ^{13}C NMR spectrum, characteristic three anomeric carbons were found at 109.7 (2C) and 109.6 ppm. Further, the appearance of carbonyl peaks at δ 175.3 ppm disclosed the presence of the ester group of the palmitic acid. HMBC spectra confirmed the regioselectivity by showing a cross peak between the methylene group of sugar at the C-5 position and the carbonyl group of ester. Similarly, in the ^{1}H NMR spectrum of compound **32b**, three anomeric protons appeared at δ 4.96 – 4.88 (m, 3H) ppm, and olefin protons were noticed at δ 5.40-5.29 (m, 4H) ppm. In the ^{13}C NMR spectrum of glycolipid **32b**, four olefinic carbons appeared at δ 131.0, 130.9, 129.1, and 129.1 ppm. Characteristic three anomeric carbons were found at δ 109.7(2C) and 109.6 ppm. Further, the appearance of carbonyl peaks at δ 175.2 ppm disclosed the presence of the ester group of linoleic acid and regioselectivity explained by the help of the HMBC spectrum. The

terminal CH_3 group of fatty acid was noticed at δ 14.5 ppm and the methylene group adjacent to azide appeared at δ 51.8. Similarly, in the ^{1}HNMR spectrum of compound **32c**, three anomeric protons appeared at δ 4.97 (s, 2H), 4.94 (d, J = 1.4 Hz, 1H) ppm, and methylene protons of cyclopropane rings were noticed at δ - 0.24 (dd, 2H) ppm and 0.66 (q, 2H) ppm. In the ^{13}C NMR spectrum of glycolipid **32c**, methylene carbons of the cyclopropane ring appeared at δ 11.7 and 11.6 ppm. Characteristic three anomeric carbons were found at δ 109.7, 109.7, and 109.6 ppm (Scheme 8).

2.6.2 Synthesis of branch trisaccharide glycolipids having (1,5 and 1,3 *trans* glycosidic linkages) • Trisaccharide **33** having 1,5 and 1,3 *trans* glycosidic linkages, was assembled by the glycosylation of donor **5** and acceptor **10** under the promotion of gold(I) and AgOTf catalysis. In this direction, monosaccharide glycosyl donor **5** and disaccharide acceptor **10** were glycosylated under gold-silver catalytic conditions. The *trans* configuration of trisaccharide **33** was verified by the ^{1}H and ^{13}CNMR spectroscopy. In the ^{1}H NMR spectrum of compound **33**, three anomeric protons were noticed in three singlets at δ 5.61, 5.37, and 5.27 ppm.



Scheme 9. a) 8mol% each of Au-catalyst and AgOTf, CH_2Cl_2, 4Å MS powder, RT, 30min,73% b) NaOMe, MeOH-CH_2Cl_2 (3:1), 25 °C, 1 h, 82%; c) DIPEA, DMAP, py., 25 °C, 48 h, 30-35%.

In the ^{13}C NMR spectrum, three diagnostic *trans* anomeric carbons were recognized at δ 106.2, 106.1, and 105.5 ppm whilst the presence of resonances δ 166.3(2C), 166.1, 165.8, 165.7, 165.7, 165.3 ppm for seven carbonyls confirmed the presence of seven benzoates. In continuation, compound **33** was subjected to global deprotection under the NaOMe/MeOH conditions and

esterified regioselectively at C5-OH using active esters **19a, 19b,** and **19c**/DIPEA/DMAP to obtain desired glycolipids **36a**, **36b** and **36c** respectively.

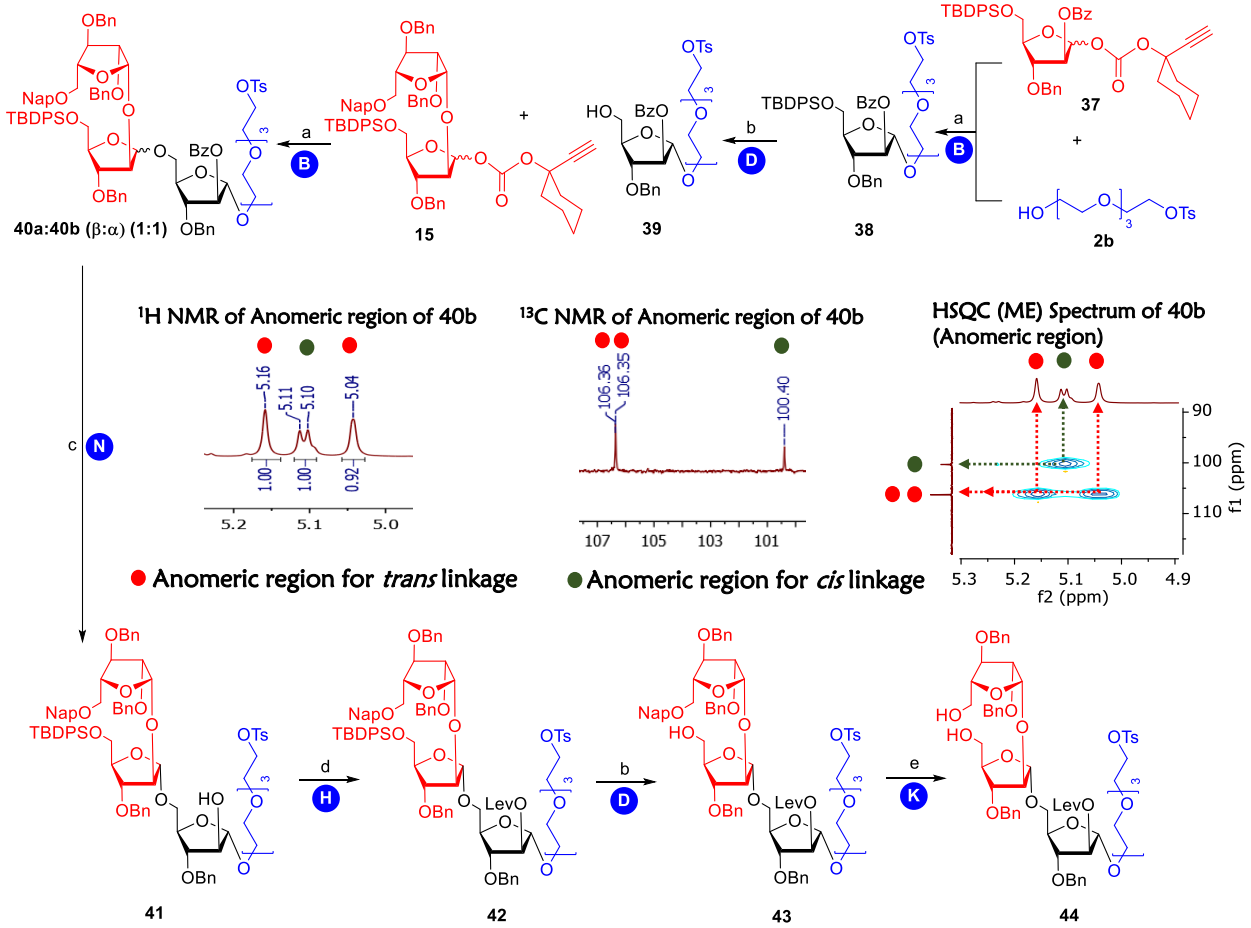
In the ^{1}HNMR spectrum of compound **36a**, three *trans*-Ara*f* anomeric protons were noticed as three singlets at δ 5.13, 5.05, 5.00 ppm whilst the terminal CH_3 group resonated at δ 0.87 (t, J = 6.8 Hz, 6H) and the adjacent methylene group of azide was noticed at δ 3.42 – 3.38 (m, 2H) ppm. In the ^{13}C NMR spectrum, characteristic three anomeric carbons were found at δ 108.4, 108.3 and 108.2 ppm. Further, the appearance of carbonyl peaks at δ 173.8 and 173.6 ppm disclosed the presence of the two palmitates, and the regioselectivity was confirmed by HMBC spectra which showed a cross peak between the two-methylene group of sugar at the C-5 position and the carbonyl group of esters.

Similarly, in the ^{1}H NMR spectrum of compound **36b**, three anomeric protons appeared at δ 5.13 (s, 1H), 5.05 (s, 1H), 4.99 (s, 1H) ppm and eight olefinic protons were noticed at δ 5.35 (m, 8H) ppm. In the ^{13}C NMR spectrum of glycolipid **36b**, eight olefinic carbons appeared at 130.2(2C), 130.0(2C), 128.1(2C), and 127.9(2C). Characteristic three anomeric carbons were found at δ 108.2, 108.2, 108.1 ppm. Further, the appearance of carbonyl peaks at δ δ 173.79, and 173.7 ppm disclosed the presence of the two-esters, and regioselectivity was confirmed by the help of HMBC spectra. The terminal CH_3 group of fatty acid was noticed at δ_C 14.3 ppm and the methylene group adjacent to azide appeared at δ_C 51.6. Similarly, the structural homogeneity of the compound **36c** was established by exhaustive NMR and Mass spectral analysis (Scheme 9).

2.6.3 Synthesis of branch trisaccharide glycolipids having (1,5 *trans* and 1,2 *cis* glycosidic linkages)

• Absence of the neighboring group at the C2 position makes the stereoselective synthesis of trisaccharide **40** as a difficult task. The glycosylations at both 25 and -78 °C did not result in any stereoselectivity. Nevertheless, glycosyl donor **15** was subjected to the glycosylation with glycosyl acceptor **39** under [Au]/[Ag]-catalyzed conditions at 25°C to afford an equal ratio of both isomers from which desired isomer **40b** was separated by 200-400 mesh silica gel column chromatography. The glycosyl acceptor **39** was prepared from precursor **38** followed by [Au]/[Ag]-catalyzed glycosylation between **37** and **2b**.[46] The two isomers were separated and characterized thoroughly by NMR and MS spectroscopic studies. In the ^{1}H NMR spectrum of compound **40b**, three Ara*f* anomeric protons were identified at δ 5.16 (s, 1H), 5.04

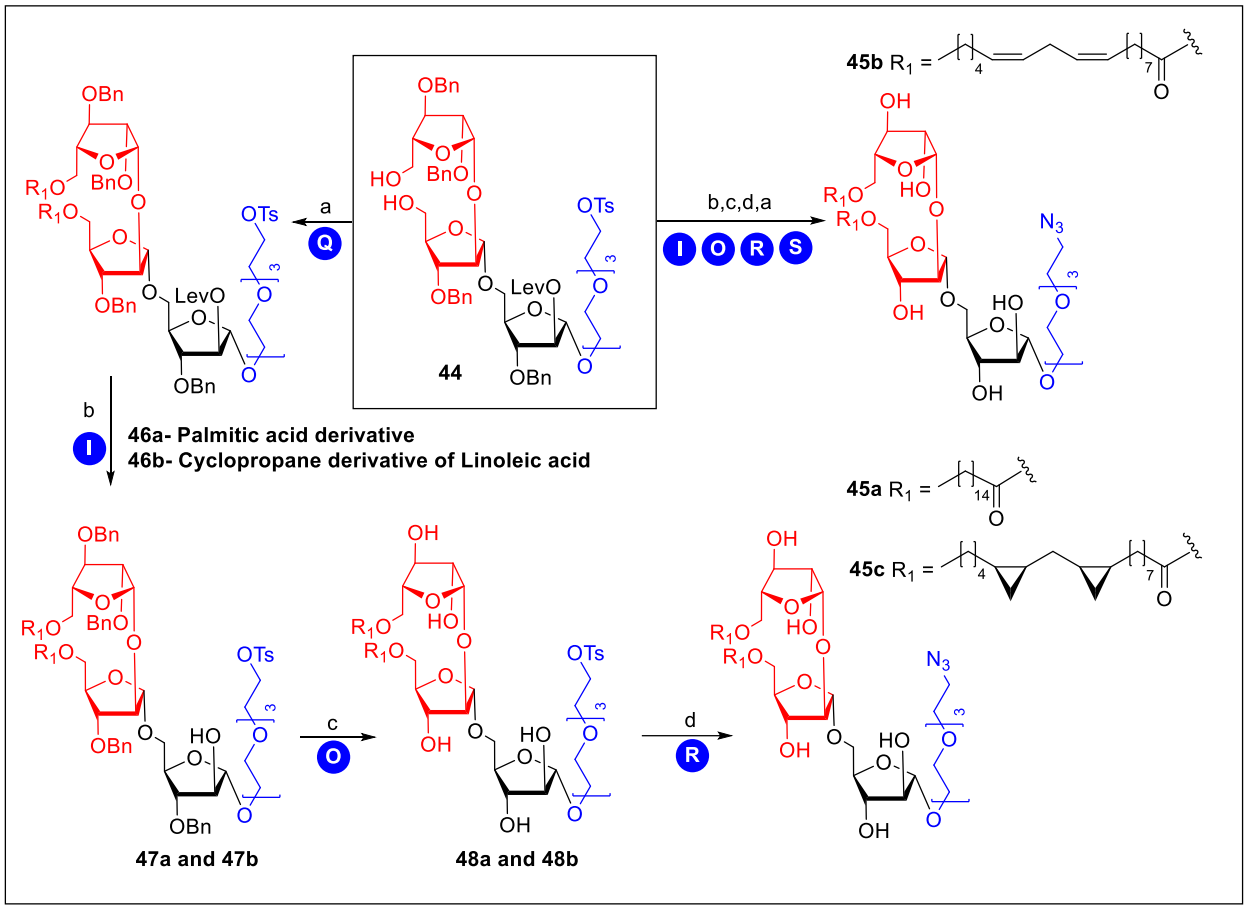
(s, 1H) ppm for two 1,2-*trans* and lone *cis* anomeric proton resonated at δ 5.11 as doublet (*J* = 4.3 Hz) ppm which was confirmed by HSQC (Hetero Single Bond Correlation) (Multiplicity edited) spectroscopy. In the ^{13}C NMR spectrum of compound **40b**, characteristic 1,2-*trans* Ara*f* linkages appeared at δ 106.4(2C) ppm whereas anomeric carbons corresponding to 1,2 *cis* were identified at δ 100.4 ppm. Further, HRMS analysis disclosed m/z for $C_{92}H_{102}O_{20}SSi$ $[M+Na]^+$: 1609.6352, which was in good agreement with the calculated m/z value of 1609.6360.



Scheme 10. a) 8mol% each of Au-catalyst and AgOTf, CH_2Cl_2, 4Å MS powder, RT, 30min,76% for 38 and -78°C for 48% for 40b; b) HF·py, py., 0-25 °C, 3 h, 76% for 39 and 72% for 43 ; c) NaOMe, MeOH-CH_2Cl_2 (3:1), 25 °C, 1 h, 70% for 41; d) Levulinic acid, DIC, DMAP, CH_2Cl_2, RT, 1h,71% e) DDQ, MeO10-CH_2Cl_2 (4:1), 25 °C, 4 h, 66%.

Later, the benzoyl group of trisaccharide **40b** was deprotected by NaOMe/MeOH conditions and protected as levulinate by using levulinic acid/DIC/DMAP in CH_2Cl_2 to afford compound **42** which upon deprotection of the TBDPS group by successive use of HF•py/THF followed by Nap deprotection gave compound **44** which was thoroughly characterized by NMR and MS

spectroscopy. In the ^{13}C NMR spectrum of compound **44**, characteristic two 1,2-*trans* Araf anomeric carbons resonate at δ 106.44, 106.14 ppm whereas anomeric carbons corresponding to 1,2-*cis* linkage showed resonances at δ 100.4 ppm. Further, HRMS analysis disclosed m/z for $C_{63}H_{78}O_{21}S$ $[M+Na]^+$: 1225.4654, which was almost matching with the calculated m/z value of 1225.4670.



Scheme 11. a) DIPEA, DMAP, py., 25 °C, 48 h, 20-25% (over 4 steps) for **45a**, **45b**, **45c**; b) $NH_2NH_2.H_2O$, $Py.CH_3COOH$, CH_2Cl_2, RT, 1h, 70% c) $Pd(OH)_2$, EtOAc, H_2, 25°C, 6 h, 69%; d) NaN_3, DMF, 25 °C, 5 h.

For regioselective esterification, compound **44** was split into two portions, and one portion was converted into compound **45** by deprotection of Lev group followed by hydrogenolysis and subsequent transformation of tosyl group into azide. The regioselective esterification was affected on compound **45** using active ester **19b**, DIPEA/DMAP in pyridine for 2.5 days to afford compound **45b**. In the ^1H NMR spectrum of compound **45b**, three anomeric protons

appeared at δ 5.12 (dd, 1H), 5.06 (d, 1H), 5.04 – 4.99 (m, 1H) ppm, and eight olefin protons were noticed at δ 5.41 – 5.29 (m, 8H) ppm. In the ^{13}C NMR spectrum, eight olefinic carbons appeared at δ 130.39(2C), 130.20(2C), 128.20(2C), and 128.05(2C). Characteristic three anomeric carbons were found at δ 107.84, 105.77, 102.14 ppm.

On the other hand, compound **44** was esterified with **19a** and **19c** under DIPEA/DMAP conditions to obtain compounds **46a** and **46b** respectively. In the ^{13}C NMR spectrum of compound **46a**, characteristic two 1,2-*trans* Ara*f* anomeric carbons resonated at δ 106.54 and 106.20 ppm whereas anomeric carbons corresponding to 1,2-*cis* showed resonances at δ 100.8 ppm. Further, HRMS analysis disclosed m/z for $C_{95}H_{138}O_{23}S$ $[M+Na]^+$: 1701.9247, almost matching the calculated m/z value of 1701.9255. In continuation, compound **46a** was successfully converted into **45a** by hydrogenolysis using $Pd(OH)_2$/ethyl acetate followed by azidation of the tosyl group in the presence of NaN_3/DMF.

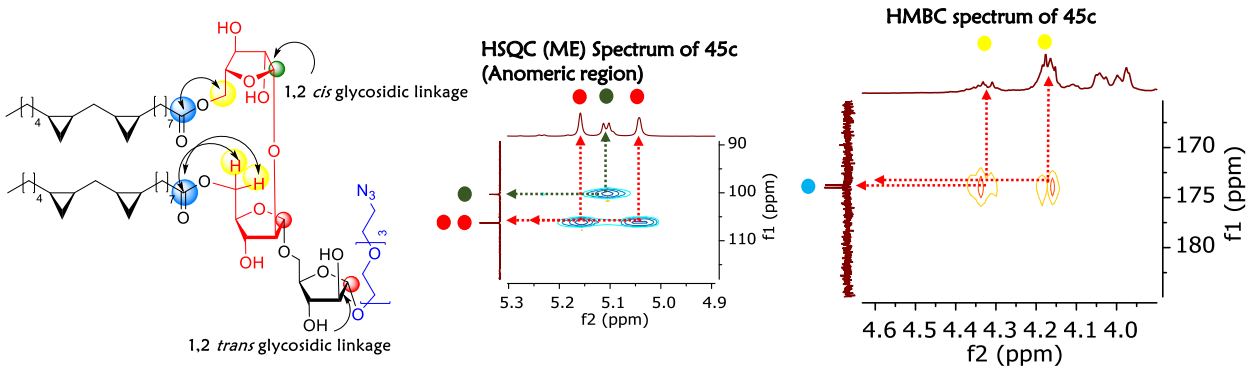
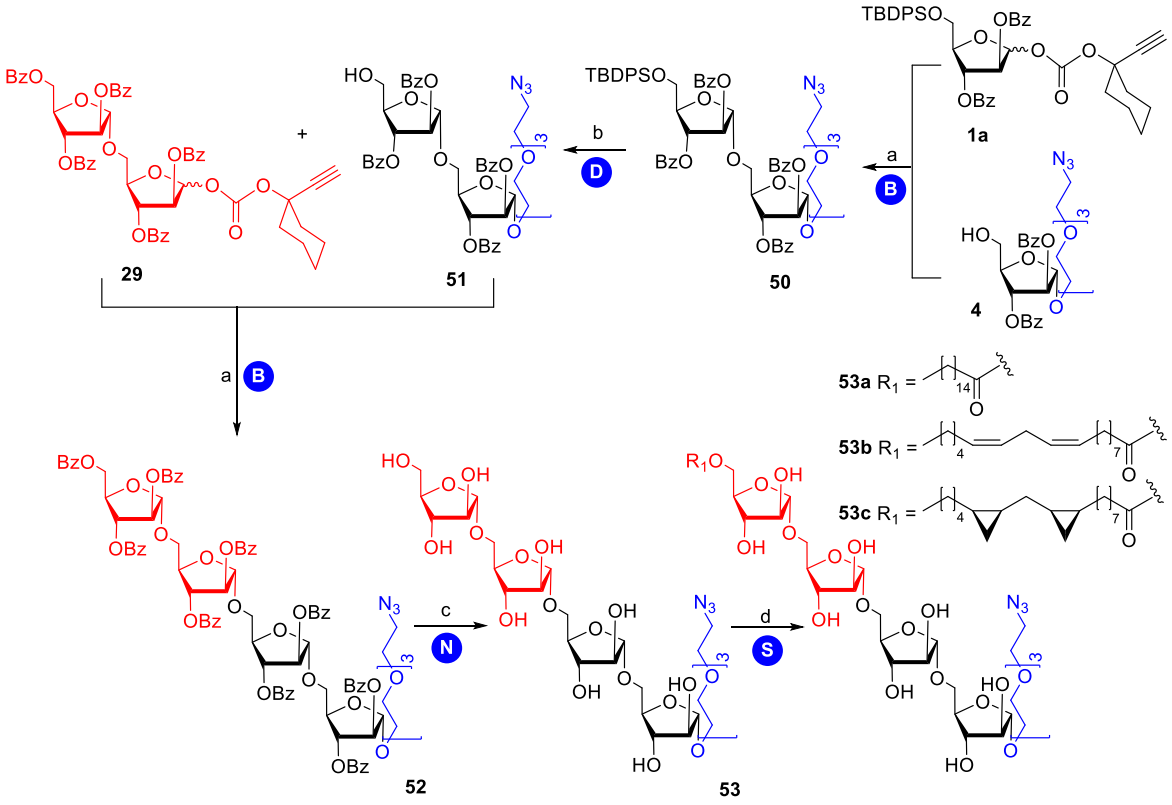


Figure 5: Heteronuclear Single Quantum Coherence (Multiplicity Edited) Spectroscopy and Heteronuclear Multiple bond Correlation Spectroscopy of compound 45c.

The synthesis of **46b** was carried out similarly to that of compound **46a** except for the fatty acid part. Compound **46b** was converted into compound **45c** by using NH_2NH_2/py: CH_3COOH/CH_2Cl_2 reaction conditions for lev-deprotection followed by hydrogenolysis using Pd $(OH)_2$/ethyl acetate, conversion of tosylate to azide in the presence of NaN_3/DMF condition. Structural homogeneity of the compound **45c** was established through analysis of NMR and MS spectroscopy. The characteristic anomeric were identified at δ 107.9, 105.8 and 102.1 ppm while the HRMS analysis confirmed *m/z* for $C_{63}H_{109}N_3O_{18}$ $[M+Na]^+$: 1218.7604 which almost matched with that of the calculated *m/z* value of 1218.7690 for compound **45c** (Figure 5).

2.7 Synthesis of tetrasaccharide glycolipids:

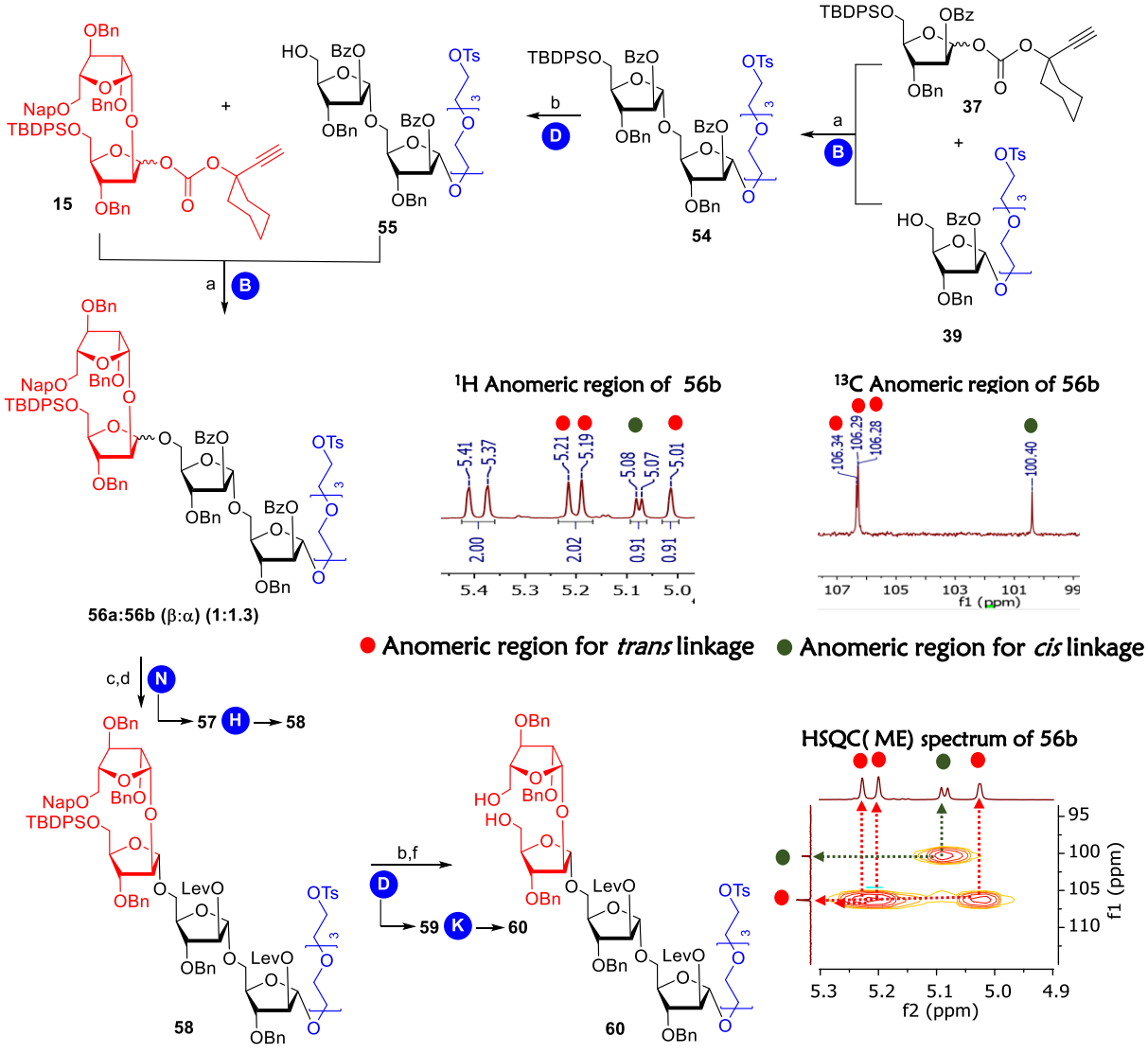
2.7.1 Synthesis of tetrasaccharide glycolipids having (1,5-*trans* glycosidic linkage) • After successfully synthesizing nine glycolipids of trisaccharide, we moved to the preparation of tetrasaccharide glycolipids. We commenced the synthesis of linear tetrasaccharide having 1,5 *trans* glycosidic linkages starting from glycosyl donor **29** and glycosyl acceptor **51**. Accordingly, disaccharide donor **29** and acceptor **51** were subjected to the [Au]/[Ag]-catalysed glycosidation to afford linear tetrasaccharide **52** in very good yield. In the ^{1}H NMR spectrum of compound **52**, all four Ara*f* anomeric protons appeared as singlets at δ 5.46, 5.42, 5.40, and 5.28 ppm whilst four corresponding carbons were found at δ 106.0, 106.0, 105.9, 105.8 ppm in the ^{13}C NMR spectrum. Furthermore, global deprotection of all benzoates of tetrasaccharide **52** was carried out using NaOMe/MeOH to obtain compound **53**. The fully deprotected tetrasaccharide **53** was regioselectively esterified with active esters **19a**, **19b,** and **19c** to obtain glycolipids **53a**, **53b,** and **53c** respectively under the aforementioned conditions (Scheme 12).



Scheme 12. a) 8mol% each of Au-catalyst and AgOTf, CH_2Cl_2, 4Å MS powder, RT, 30min,76% for 50 and 72% for 52; b) HF·py, py., 0-25 °C, 3 h, 76%; c) NaOMe, MeOH-CH_2Cl_2 (3:1), 25 °C, 1 h, 70% d) DIPEA, DMAP, py., 25 °C, 48 h, 20-25% for **53a**, **53b**, **53c**.

2.7.2 Synthesis of branch tetrasaccharide glycolipids having (1,5 *trans* and 1,2 *cis* glycosidic linkages

• The synthesis of tetrasaccharide **56** is challenging due to the lack of any neighboring group at the C-2 position. The glycosylation at 25°C produced 1:1 stereoselectivity whereas at -78 °C, the stereoselectivity slightly improved to 1.3:1 (α: β) which could be separated by 230-400 mesh silica gel to obtain the desired isomer **56b** in sufficient quantities. Synthesis of glycosyl acceptor **55** confirmed by NMR and Mass spectral analysis.



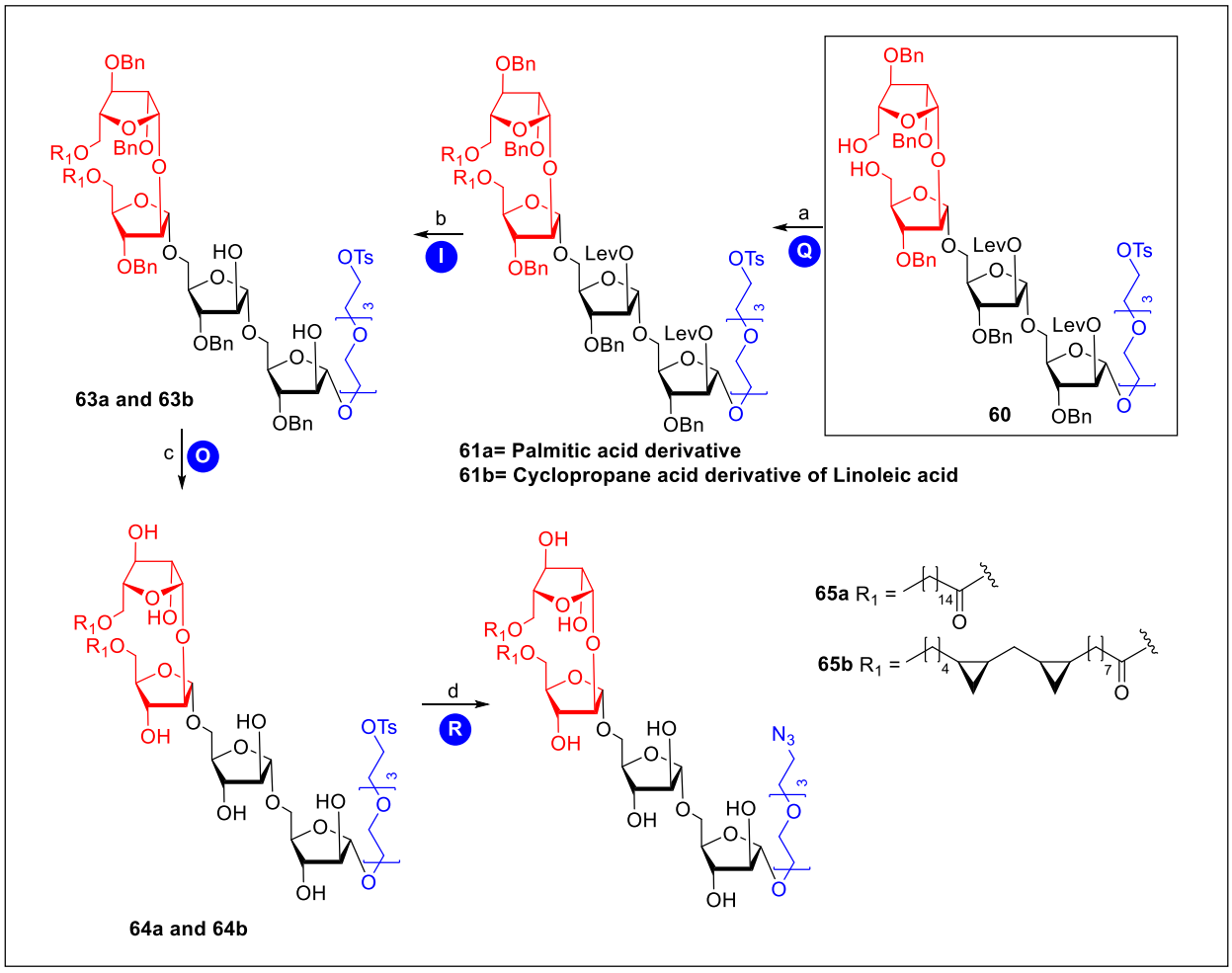
Scheme 13. a) 8mol% each of Au-catalyst and AgOTf, CH_2Cl_2, 4Å MS powder, RT, 30min,76% for 54 and -78°C for (56a:56b) 57% for 56b; b) HF·py, py., 0-25 °C, 3 h, 74% for 55 and 79% for 59; c) NaOMe, MeOH-CH_2Cl_2 (3:1), 25 °C, 1 h, 92% for 57%: d) Levulinic acid, DIC, DMAP, CH_2Cl_2, RT, 1h, 80% for 58: e) DDQ, MeOH-CH_2Cl_2 (4:1), 25 °C, 4 h 67%.

In the ^{1}H NMR spectrum of **55**, two *trans*-linked anomeric protons showed resonances as two singlets at δ 5.27 and 5.22 ppm; the two anomeric carbons appeared at δ_C 106.7 and 106.6 ppm. Further, HRMS analysis gave satisfactory matching of m/z values for $C_{53}H_{60}O_{17}S[M+Na]^+$: 1023.3440.

In the ^{1}H NMR spectrum of compound **56b**, among four Ara*f* anomeric protons, three *trans* anomeric protons resonated as singlets at δ 5.20, 5.01, 4.76 ppm whereas the lone *cis*-anomeric proton resonated at δ 5.08 (d, J = 4.3 Hz, 1H) ppm. In the ^{13}C NMR spectrum of compound **56b**, characteristic *trans*-linked Ara*f* anomeric carbons appeared at δ 106.3, 106.3, and 106.3 ppm whereas the anomeric carbon corresponding to the 1,2-*cis* linkage was identified at δ 100.4 ppm. Further, HRMS analysis disclosed m/z for $C_{111}H_{120}O_{25}SSi$ $[M+Na]^+$: 1935.7506, which was in good agreement with the calculated m/z value of 1935.7517.

Later, the benzoate ester of compound **56b** was cleaved off by NaOMe/MeOH and reprotected as levulinate to afford compound **58** which upon deprotection of TBDPS and Nap moieties resulted in the successful synthesis of compound **60**. In the ^{1}H NMR spectrum of compound **60**, among the four Ara*f* anomeric protons, three *trans*-disposed anomeric protons were noticed as three singlets at δ 5.10, 5.03, and 5.02 ppm, and the remaining *cis*-linked anomeric proton was noticed at 5.07 as doublet (J = 4.6 Hz) ppm. In the ^{13}C NMR spectrum of compound **60**, characteristic three *trans*-Ara*f* anomeric carbons resonated at δ 106.5, 106.1, and 106.0 ppm whereas anomeric carbons corresponding to 1,2 *cis* linkage showed resonances at δ 100.4 ppm. In the case of tetrasaccharide having one *cis* and three conditions. Thus, successfully synthesized tetrasaccharide **60** was esterified with active esters **19a** and **19b** under the aforementioned conditions and characterized. For example, in the ^{1}H NMR spectrum of compound **61a**, among four Araf anomeric protons, three *trans* anomeric protons were noticed at δ 5.08 (s, 1H), 5.03 (s, 1H), 5.03 (s, 1H) ppm and one *cis* anomeric proton noticed at δ 5.14 – 5.11 (m, 1H) ppm. In the ^{13}C NMR spectrum of compound **61a**, characteristic three *trans*-Araf anomeric carbons resonate at δ 106.6, 106.2, and 106.1 ppm whereas anomeric carbons corresponding to 1,2 *cis* appended

residue showed resonances at δ 100.8 ppm. Further, HRMS analysis disclosed m/z for $C_{112}H_{158}O_{29}S$ $[M+Na]^+$: 2023.0507, almost matching the calculated m/z value of 2023.0570.



Scheme14. a) DIPEA, DMAP, py., 25 °C, 55h-60h, 20-25% for **65a**, **65b** over 4 steps; b) $NH_2NH_2.H_2O$, $Py.CH_3COOH$, CH_2Cl_2, RT, 1h: c) $Pd(OH)_2$, EtOAc, H_2, 25°C, 6h; d) NaN_3, DMF, 25°C, 5h.

Further, the appearance of carbonyl peaks at δ 173.61, and 173.41 ppm disclosed the attachment of the ester group of palmitic acid, and their correlation with methylene proton at the C-5 position of sugar was also confirmed by HMBC. The two carbonyl groups of ketones of the Lev group resonated at δ 171.86 and 171.80 ppm and the carbonyl group of esters resonated at δ 206.34 and 206.17 ppm. Next, compound **61a** was converted into **65a** by doing Lev deprotection, hydrogenation using $Pd(OH)_2$/ethyl acetate, followed by azidation of the tosyl group in the presence of NaN_3/DMF condition. Compound **65a** was confirmed by NMR. In the

^{1}H NMR spectrum of compound **65a**, four anomeric protons resonate at δ 5.14 – 5.11 (m, 1H), 5.05 (d, *J* = 4.1 Hz, 1H), 5.01 (s, 2H) ppm. The terminal CH_3 group resonates at 0.87 (t, 6H) and the adjacent methylene group of azide was noticed at 3.42 – 3.35 (m, 2H) ppm. In the ^{13}C NMR spectrum of compound **65a**, characteristic three *trans*-Araf anomeric carbons resonate at 108.0, 107.8, and 105.8 ppm whereas anomeric carbons corresponding to 1,2 *cis* showed resonances at δ 102.5 ppm. The esterification was confirmed by HMBC spectra which showed a cross peak between the two-methylene group of sugar at the C-5 position and the carbonyl group of esters. The two terminal CH_3 groups of fatty acid were noticed at 14.3(2C). Further, HRMS analysis disclosed m/z for $C_{60}H_{109}N_3O_{22}$ $[M+Na]^+$: 1246.7400 which exactly matched with the calculated m/z value of 1246.7400.

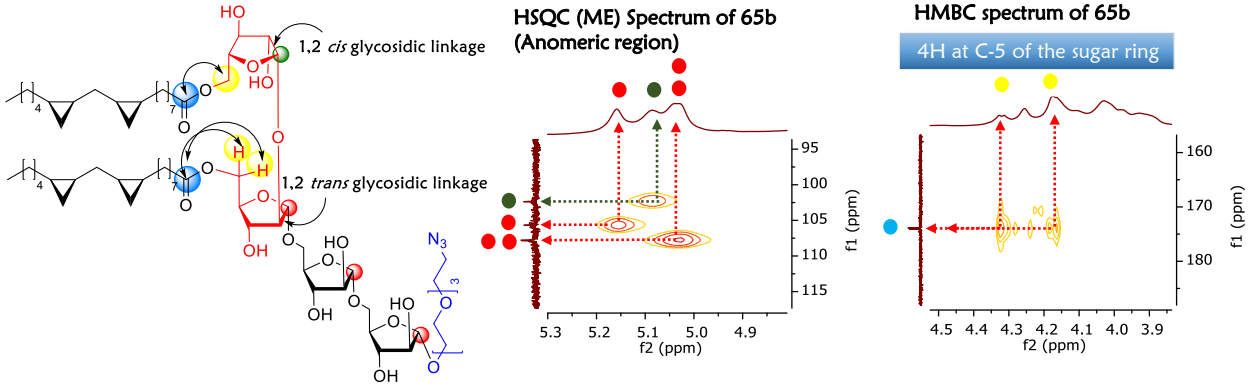


Figure 6: Heteronuclear Single Quantum Coherence (Multiplicity Edited) Spectroscopy and Heteronuclear Multiple bond Correlation Spectroscopy of compound 65b

The synthesis of glycolipid **61b** was similar to that of glycolipid **61a** except for the fatty acid. The ^{1}H NMR spectrum of compound **61b** showed three *trans*-linked anomeric protons at δ 5.08 (s, 1H), 5.03 (s, 1H), 5.03 (s, 1H), and the remaining *cis*-linked anomeric proton merged with other sugar ring protons. In the ^{13}C NMR spectrum, methylene carbons of the cyclopropane ring appeared at 11.1(2C) and 10.9(2C) whereas characteristic three *trans* anomeric carbons were found at δ 106.6, 106.2, 106.1 and the *cis*-oriented anomeric carbon appeared at δ 100.8 ppm thereby confirming the structural homogeneity of the compound **61b**. Further, the appearance of carbonyl peaks at δ 173.60, and 173.40 ppm disclosed the attachment of the ester group of cyclopropane derivative of linoleic acid at sugar moiety. The two carbonyl groups of ketones of the levulinate resonated at δ 171.86 and 171.80 ppm and the carbonyl group of esters resonated

at δ 206.4 and 206.2 ppm. Next, compound **61b** was converted into glycolipid **65b** by Lev deprotection, hydrogenolysis, and azidation of the tosyl group.

The ^{1}H NMR spectrum of compound **65b** methylene protons of cyclopropane rings was noticed at δ 0.62 – 0.57 (m, 4H), -0.29 (dd, *J* = 11.6, 5.2 Hz, 4H) ppm. In the ^{13}C NMR spectrum, methylene carbons of the cyclopropane ring appeared at 11.2(2C) and 11.0(2C). Characteristic three *trans* anomeric carbons were found at δ 108.0, 107.9, 105.8, and lone *cis*-configured anomeric carbon appeared at δ102.4 ppm. Further, the appearance of carbonyl peaks at δ 174.2, and 174.0 ppm proved the attachment of the ester group of cyclopropane derivative of linoleic acid to the sugar moiety. The presence of the azide group confirmed by IR analysis and HRMS disclosed m/z for $C_{68}H_{117}N_3O_{22}$ $[M+Na]^+$:1350.8026, which was almost matching with the calculated m/z value of 1350.8035 (Figure 6).

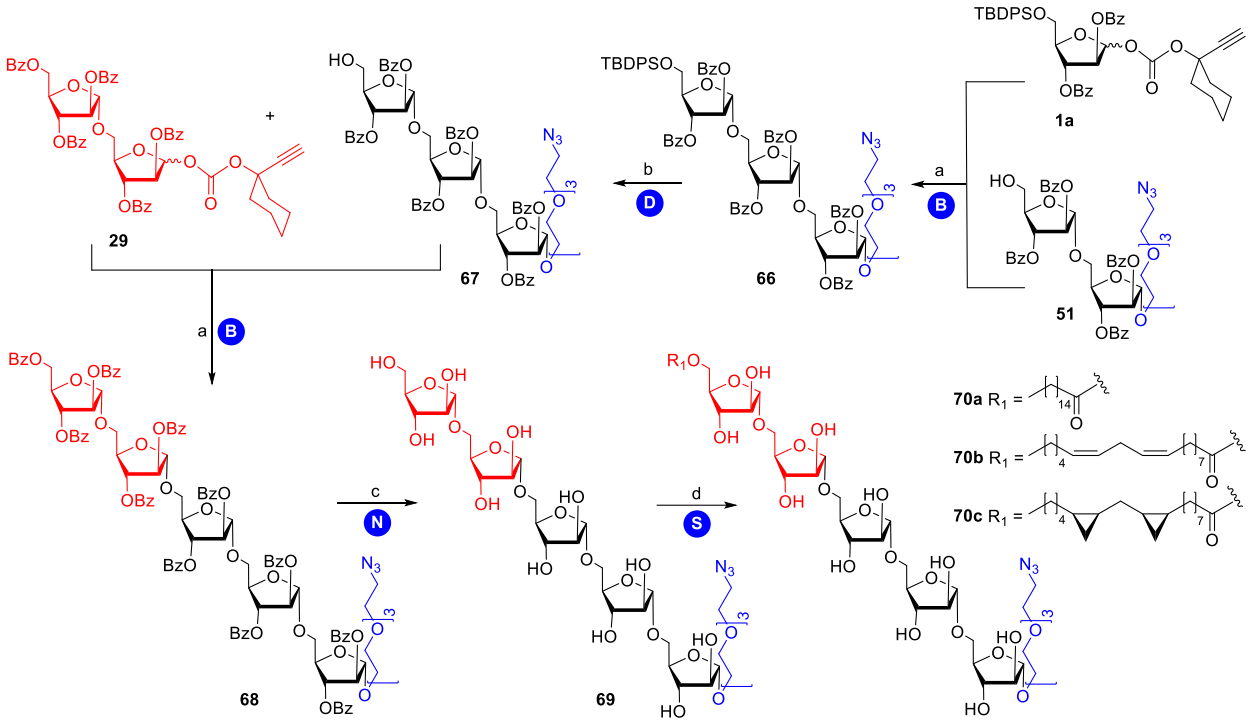
2.8 Synthesis of Pentasaccharide glycolipids:

2.8.1 Synthesis of pentasaccharide glycolipids having (1,5 *trans* glycosidic linkage) •

After successfully synthesizing five glycolipids of tetrasaccharide, we moved to prepare pentasaccharide glycolipids. For that, we started, the synthesis of linear pentasaccharide with glycosyl donor **29** and glycosyl acceptor **67** by silver-assisted gold-catalyzed glycosidation conditions. In the ^{1}H NMR spectrum of compound **68,** all the five anomeric protons of arabinan were noticed at δ 5.45-5.28 ppm as singlets whereas anomeric carbons resonated between δ 106.0 - 105. 8 ppm along with eleven carbonyl peaks of the benzoyl groups at δ 166.29, 165.79, 165.76, 165.70(2C), 165.67, 165.42, 165.28, 165.22, 165.20(2C) ppm established the assigned structure for compound **68**. Further, the appearance of methylene proton adjacent to azide was found at δ 50.7 ppm. The presence of the azide group was confirmed by IR analysis and HRMS disclosed m/z for $C_{110}H_{103}N_3O_{35}$ $[M+Na]^+$: 2046.6113 that was almost matched with that of the calculated m/z value of 2046.6119.

Furthermore, compound **68** was converted into fully deprotected pentasaccharide **69** by simple debenzoylation in NaOMe/MeOH. In the ^{1}H NMR spectrum of compound **69**, five Ara*f* anomeric protons were noticed between δ 4.98 – 4.94 ppm. In the ^{13}C NMR spectrum, anomeric carbons were found between δ 109.6 and 109.3 ppm. After global deprotection, the regioselective esterification of primary OH in the presence of secondary alcohols was performed

using active esters **19a, 19b,** and **19c** under the aforementioned conditions to afford glycolipids **70a**, **70b,** and **70c** respectively in satisfactory yields. In the ^{1}H NMR spectrum of compound **70a**, five *trans*-linked Ara*f* anomeric protons appeared around δ 4.95 ppm. The terminal CH_3 group showed resonances at δ 0.93 ppm (t, J = 6.6 Hz, 3H) and the adjacent methylene group of azide was noticed at δ 3.42 (m, 2H) ppm. In the ^{13}C NMR spectrum, characteristic five anomeric carbons were found at 109.69(4C) and 109.63 ppm.



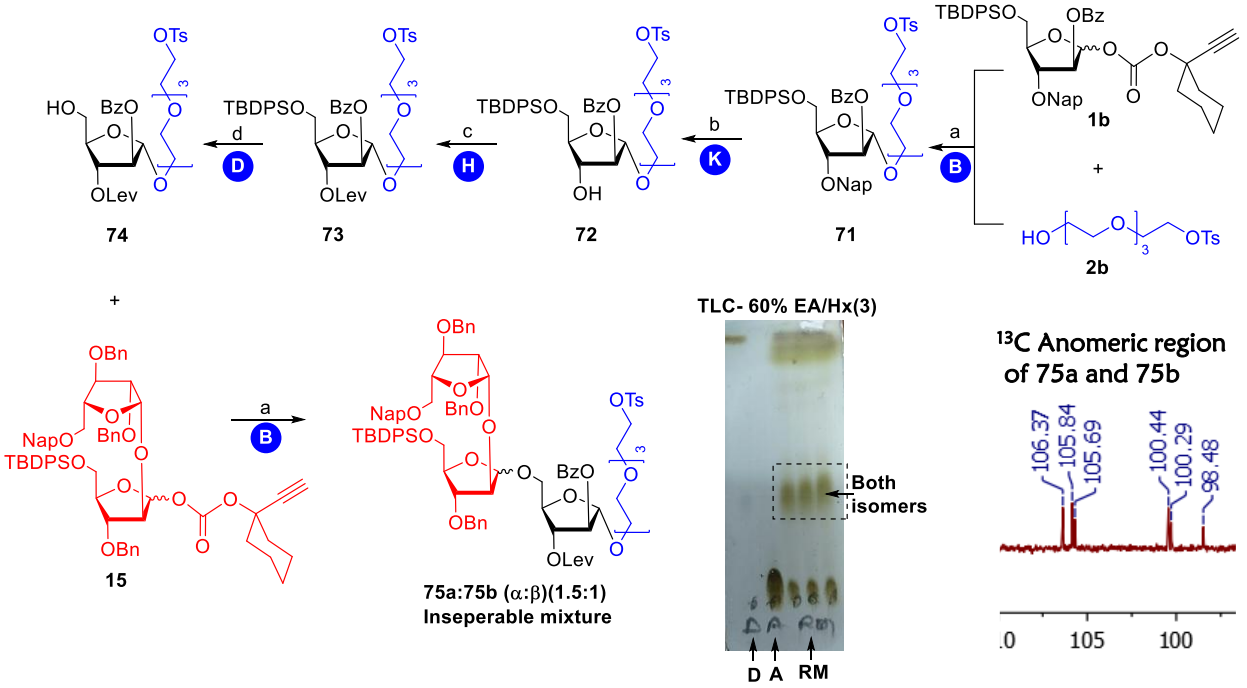
Scheme 15. a) 8mol% each of Au-catalyst and AgOTf, CH_2Cl_2, 4Å MS powder, RT, 30min, 74% for 66 and 70% for 68; b) HF·py, py., 0-25 °C, 3 h, 75%; c) NaOMe, MeOH-CH_2Cl_2 (3:1), 25 °C, 1 h, 70% d) DIPEA, DMAP, py., 25 °C, 48 h, 20-25% for **70a**, **70b**, **70c**.

Further, the appearance of carbonyl peaks at δ 175.52 ppm disclosed the presence of the ester group of palmitic acid. The regioselectivity was confirmed by the HMBC spectrum that showed a cross peak between the methylene group of sugar at the C-5 position and the carbonyl group of esters. The terminal CH_3 group of fatty acid was noticed at δ 14.5 ppm. Similarly, In the ^{1}H NMR spectrum of compound **70b**, five anomeric protons appeared at δ 4.95 (m, 5H) ppm, and olefin protons were noticed at δ 5.40 – 5.33 (m, 4H) ppm. In the ^{13}C NMR spectrum, four olefin carbons appeared at δ 130.94, 130.89, 129.10, and 129.05 ppm. Characteristic five anomeric

carbons were found at δ 109.67(4C), 109.62 ppm. The terminal CH_3 group of fatty acid was noticed at δ14.5 and the methylene group adjacent to azide appeared at δ 51.8 (Scheme 15). Similarly, in the ^{1}H NMR spectrum of compound **70c**, five anomeric protons centered around δ 4.95 ppm and the methylene protons of cyclopropane rings showed resonance at δ 0.65 (dt, J = 8.3, 4.2 Hz, 2H) and -0.21 – -0.28 (m, 2H) ppm. In the ^{13}C NMR spectrum, methylene carbons of the cyclopropane ring appeared at δ 11.7 and 11.6; five anomeric carbons were found at δ 109.7(4C) and 109.6 ppm. Further, the appearance of carbonyl peaks at δ 175.3 ppm disclosed the attachment of the ester group of cyclopropane derivative of linoleic acid at sugar moiety. The terminal CH_3-group of cyclopropane fatty acid appeared at δ 14.5 ppm and the methylene group adjacent to azide was noticed at δ 51. 8 ppm. The HRMS disclosed m/z for, $C_{53}H_{91}N_3O_{25}$ $[M+Na]^+$: 1192.5839 which almost matched the calculated m/z value of 1192.5840.

2.8.2 Synthesis of pentasaccharide buiding block having 1,2 *cis* and 1,5 *trans* glycosidic linkages •

Pentasaccharide **77** was envisaged through the glycosylation of donor **15** and acceptor **76a** under the promotion of gold(I) and AgOTf catalysis. In this direction,



Scheme 16. a) 8mol% each of Au-catalyst and AgOTf, CH_2Cl_2, 4Å MS powder, RT, 30min,78% for 71 and -78°C, 6h for (75a:75b), 72%; b) DDQ, MeOH-CH_2Cl_2 (4:1), 25 °C, 4 h, 70%; c)Levulinic acid, DIC, DMAP, CH_2Cl_2, RT, 1h, 71%; d) HF·py, py., 0-25°C, 3 h, 76%.

monosaccharide **74** was prepared by Nap deprotection of compound **71** using DDQ/CH_2Cl_2: MeOH followed by its Lev protection utilizing Levulinic acid/ DIC/DMAP conditions and at the end the TBDPS deprotection using HF•pyridine. Compound **74** was verified by the ^{1}H and ^{13}C NMR spectroscopy. In the ^{1}HNMR spectrum of compound **74**, 1,2-*trans* anomeric protons were noticed at δ 5.23 (s, 1H) ppm while in the ^{13}C NMR spectrum, 1,2-*trans* anomeric carbons were recognized at δ 105.7 ppm. Apart from that, the carbonyl groups of ketone of the Lev group showed resonances at δ 172.5 ppm, those of the carbonyl group of ester at δ 206.5 ppm, and the carbonyl carbon at δ 165.4 ppm confirmed the presence of the benzoyl group (Scheme 16).

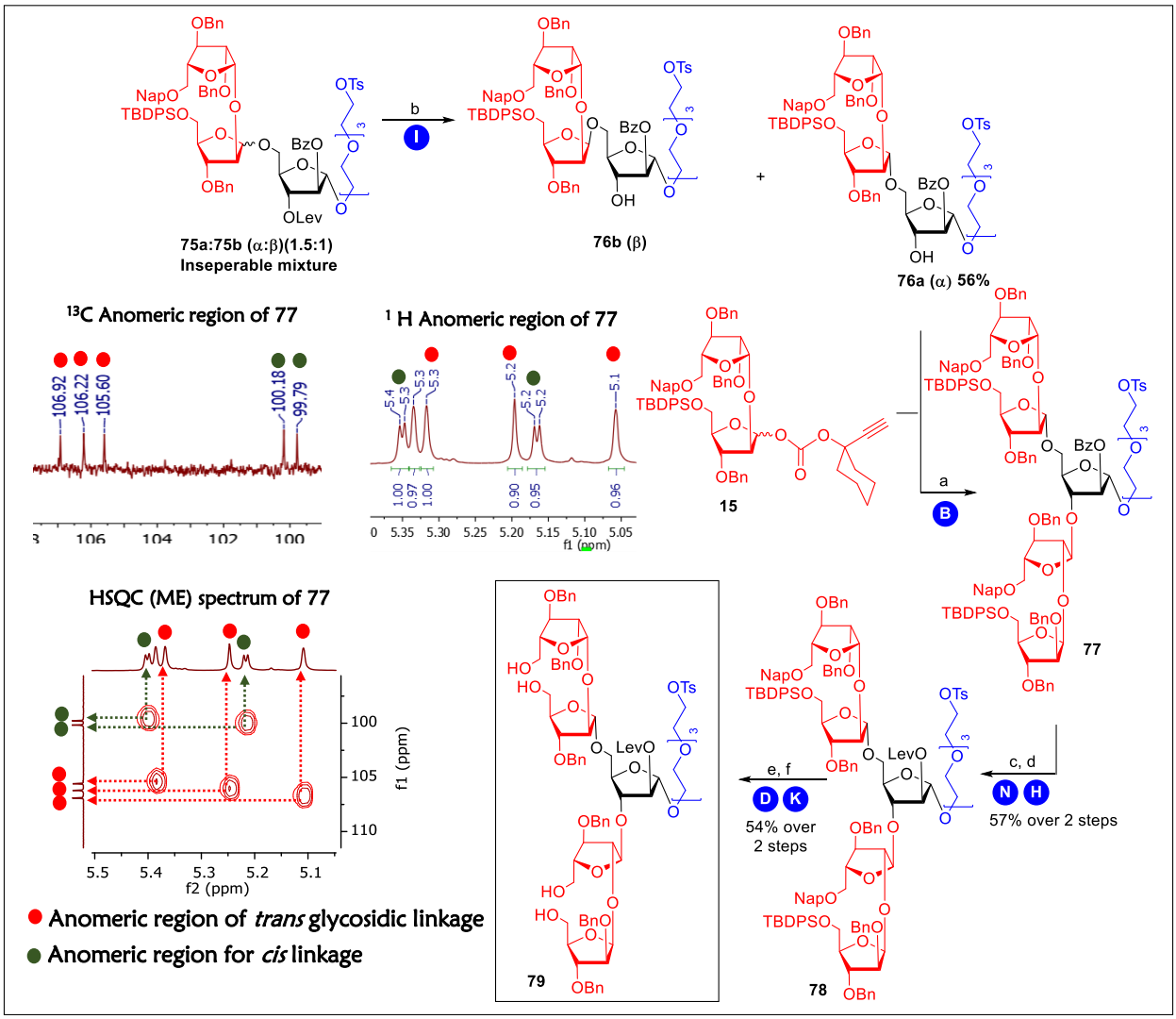
At 25 °C, glycosylation between donor **15** and acceptor **74** showed a 1:1 (α:β) mixture of trisaccharides, however, lowering the temperature of the glycosylation to -78 °C surprisingly afforded α:β = 1.5:1 mixture in favor of the required trisaccharide **75a**. The enhanced α-diastereoselectivity can be rationalized by previously reported $^{3}E_{gg}$ conformation of the oxocarbenium ion intermediate wherein sterically crowded TBDPS unit shielded the β face; therefore, the incoming acceptor can predominantly access the α-face. The diastereoselective mixture of **75a** and **75b** was subjected to the Lev deprotection that enabled us to separate the two diastereomers to get the glycosyl acceptor **76a** (Scheme 17).

The [Ag]/[Au]-catalyzed glycosidation between the trisaccharide acceptor **76a** and glycosyl donor **15** smoothly afforded the desired pentasaccharide **77** that was confirmed by NMR and Mass spectral analysis. In the ^{1}H NMR spectrum, the two 1,2 *cis* anomeric protons displayed resonances around δ 5.37 – 5.34 (m, 1H) ppm and δ 5.37 – 5.34 (m, 1H) ppm, and three *trans* anomeric protons noticed at δ 5.06, 5.20, and 5.33 ppm. In the ^{13}C NMR spectrum of compound **77**, distinctive 1,2-*trans* anomeric carbons were noticed at δ 106.9, 106.2, and 105.6 ppm while the appearance of two resonances at δ 100.2, and 99.8 ppm confirmed the presence of two 1,2-*cis* linkages.

Later, the benzoyl group of pentasaccharide **77** was cleaved off by the above-mentioned NaOMe/MeOH method and protected as Levulinate to afford compound **78** which is converted to pentasaccharide **79** by the deprotection of TBDPS and Nap moieties. The structural integrity of compound **79** was confirmed by the NMR and Mass spectroscopy. In the ^{13}C NMR spectrum of compound **79**, three distinctive 1,2-*trans* anomeric carbons were noticed at δ106.0, 105.8, and 105.4 ppm whilst two resonances at δ 100.4, and 99.6 ppm confirmed the presence of two 1,2-*cis*

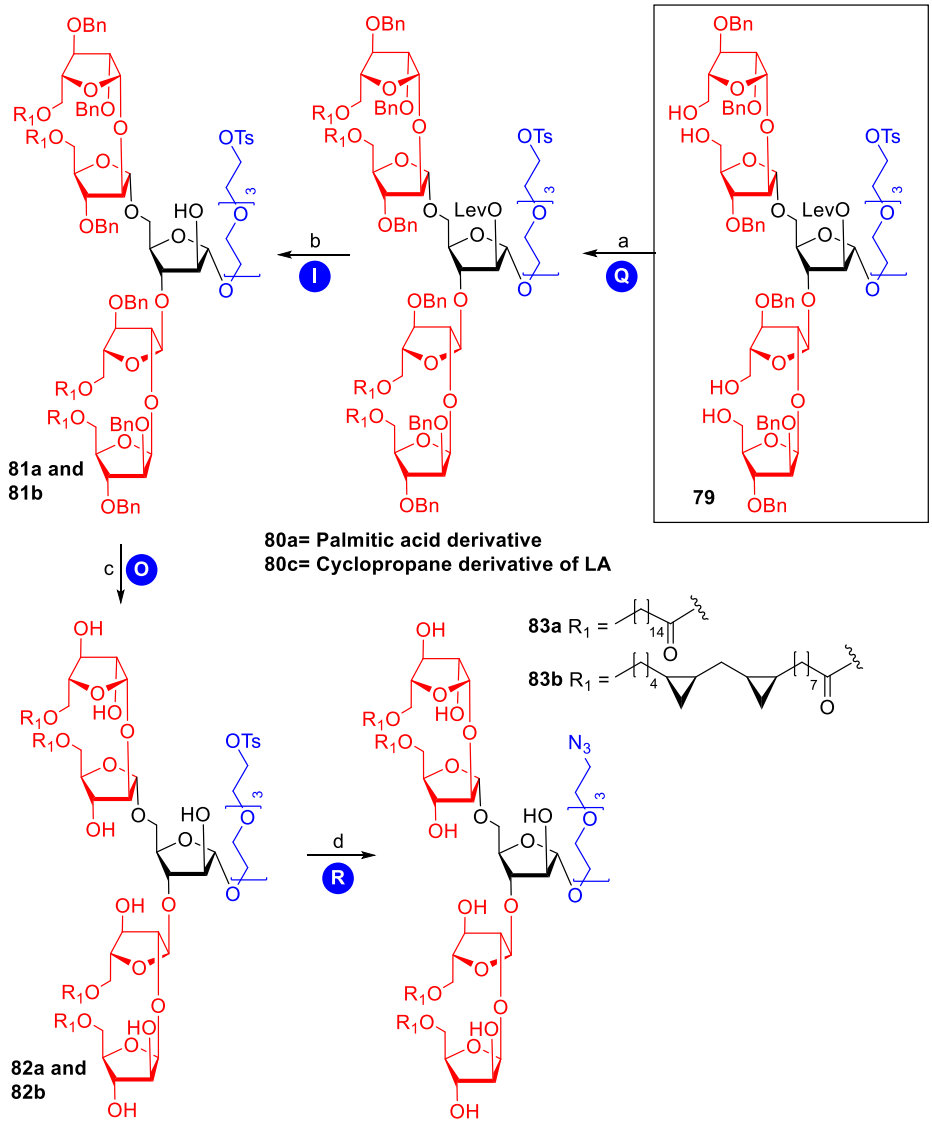
linkages. Further, HRMS disclosed m/z for, $C_{87}H_{106}O_{28}S[M+Na]^+$:1653.6489 which almost matched the calculated m/z value of 1653.6490 (Scheme 17).

In continuation, the pentasaccharide **79** was transesterified with activated N-phthalamidyl esters **19a** and **19c** under DIEA/DMAP conditions. In the ^{1}HNMR spectrum of compound **80a** among five anomeric protons of Ara*f*, three *trans*-disposed anomeric protons were noticed at δ 5.08,



Scheme 17. a) 8mol% each of Au-catalyst and AgOTf, CH_2Cl_2, 4Å MS powder, RT, 30min, 60% for 77; b) $NH_2NH_2.H_2O$, $Py.CH_3COOH$, CH_2Cl_2, RT, 1h; c) NaOMe, MeOH-CH_2Cl_2 (3:1), 25 °C, 1 h, 70%; d) Levulinic acid, DIC, DMAP, CH_2Cl_2, RT, 1h,71%; e) HF·py, py., 0-25°C, 3 h; f) DDQ, MeOH-CH_2Cl_2 (4:1), 25 °C, 4 h; c)

5.05, and 5.29 ppm as three singlets and two *cis*-oriented anomeric protons were identified at 5.26 (d, J = 4.1 Hz, 1H), 5.17 – 5.13 (m, 1H) ppm. In the ^{13}C NMR spectrum of compound **80a**,



Scheme18. a) DIPEA, DMAP, py., 25 °C, 55-60h, 20-25% for **83a**, **83b** (over 4 steps); b) $NH_2NH_2.H_2O$, $Py.CH_3COOH$, CH_2Cl_2, RT, 1h, 70% c) $Pd(OH)_2$, EtOAc, H_2, 25°C, 6 h; d) NaN_3, DMF, 25 °C, 5 h.

characteristic three *trans*-Ara*f* anomeric carbons resonate at δ 106.8, 106.0, and 105.6 ppm whereas two anomeric carbons corresponding to 1,2 *cis* linkages showed resonances at δ 100.7, 100.3 ppm. Further, the appearance of four carbonyl peaks at δ 173.6, 173.6, 173.5, and 173.4 ppm disclosed the attachment of the four-ester group of palmitic acids and their correlation with methylene proton at the C-5 position of sugar was also confirmed by HMBC. The carbonyl

groups of ketone of Lev group showed resonances at δ 172.1 ppm and the carbonyl group of ester resonances were identified at δ 206.1 ppm and 206.2. Next, the Lev-ester of compound **80a** was deprotected under standard conditions to obtain compound **83a** upon hydrogenolysis

in the presence of Pearlman's catalyst and hydrogen followed by azidation of the tosyl group in the presence of NaN_3/DMF condition afforded the desired compound **83a**. In the ^{1}HNMR spectrum of compound **83a**, five anomeric protons resonated from δ 5.17 to 5.05 ppm. The terminal 4xCH_3 groups resonated at δ 0.88 (m, 12H). Three anomeric carbons resonated at δ 108.2, 105.6, and 105.5 ppm whereas two anomeric carbons corresponding to 1,2-*cis* linkages showed resonances at δ 102.7, 102.4 ppm confirming the structural homogeneity of the compound **83a**. The occurrence of four esters was confirmed in the HMBC spectra wherein a cross peak was noticed between the four-methylene groups of sugar at the C-5 position and the carbonyl group of esters. The four terminal CH_3 groups of fatty acid were noticed at 14.3(4C). Further, HRMS analysis disclosed m/z for $C_{60}H_{109}N_3O_{22}$ $[M+Na]^+$: 1246.7400 which exactly matched with the calculated m/z value of 1246.7400.

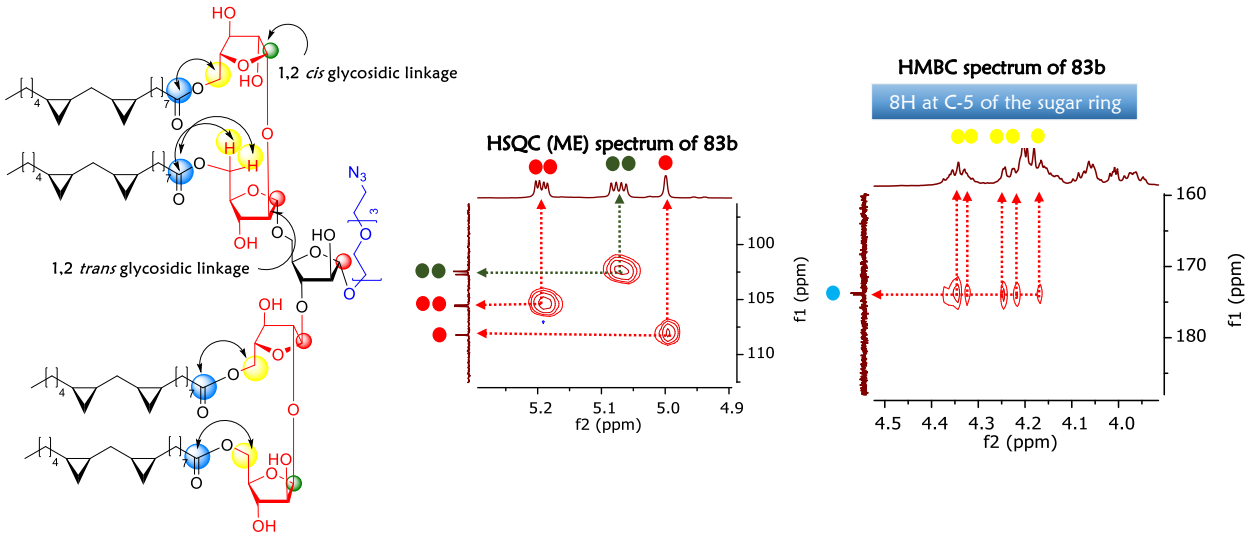


Figure 7: Heteronuclear Single Quantum Coherence (Multiplicity Edited) Spectroscopy and Heteronuclear Multiple bond Correlation Spectroscopy of compound 83b.

The compound **80b** was synthesized exactly following the procedure for compound **80a**. The ^{1}H NMR spectrum of compound **80b** showed three *trans*-linked anomeric protons as three singlets at δ 5.30, 5.08, and 5.06 ppm and two *cis*-oriented anomeric protons appeared as doublets at δ 5.26 (J = 4.1 Hz), 5.15 (J = 3.8 Hz) ppm. The CH_2-protons of cyclopropanes were noticed from

δ 0.63 – to -0.28 as multiplets. In the ^{13}CNMR spectrum, methylene carbons of the cyclopropane ring appeared at 11.1(4C) and 11.0(4C) where five anomeric carbons were found at δ 106.8, 106.0, and 105.6 ppm (for 3x*trans*), 100.7, 100.2 (for 2x*cis*) ppm thereby establishing the structure.

Further, the appearance of four carbonyl peaks at δ 173.61, 173.55, 173.40, and 172.42 ppm disclosed the attachment of the four ester groups of cyclopropane derivative of LA at sugar moiety. and their correlation with methylene proton at the C-5 position of sugar was also confirmed by HMBC. The carbonyl groups of ketones of the Lev group resonated at δ 172.1 ppm and the carbonyl group of esters resonated at δ 206.1 ppm. Next, compound **80b** was converted into **83b** by doing Lev deprotection, and hydrogenation by using $Pd(OH)_2$/ethyl acetate, followed by azidation of the tosyl group in the presence of NaN_3/DMF condition. Compound **83b** was confirmed by NMR.

The ^{1}H NMR spectrum of compound **83b** explained, describes three *trans* anomeric protons appearing at δ 5.16 (dd, J = 9.1, 3.4 Hz, 2H), and 5.00 (s, 1H) ppm. and two *cis* anomeric protons appeared at δ 5.05 (d, J = 4.5 Hz, 2H) ppm which was confirmed by HSQC (Hetero Single Bond Correlation) (Multiplicity edited) spectroscopy. methylene protons of cyclopropane rings were noticed at δ 0.61 to -0.28 ppm as multiplets. In the ^{13}C NMR spectrum, methylene carbons of the cyclopropane ring appeared at 11.1(4C) and 11.0(4C). Characteristic three *trans* anomeric carbons were found at δ 107.4, 105.5, and 105.5 ppm, and two *cis* anomeric carbons appeared at δ102.8, and 102.3 ppm. Further, the appearance of four carbonyl peaks at δ 174.16, 174.12, 173.96, and 173.90 ppm disclosed the attachment of the four-ester groups of cyclopropane derivative of LA at sugar moiety and their correlation with methylene proton at the C-5 position of sugar was also confirmed by HMBC spectroscopy. Furthermore, the HRMS spectrum disclosed m/z for $C_{68}H_{117}N_3O_{22}$ $[M+Na]^+$:1350.8026 which almost matched with the calculated m/z value of 1350.8035(Scheme 18) (Figure 7).

Conclusions

In conclusion, we have developed a comprehensive route for the synthesis of a library of glycolipids reminiscent of *Mycobacterium tuberculosis* cell wall. All the furanosylations were carried out by the activation of arabinofuranosyl ethynylcyclohexyl carbonates using [Au]/[Ag]-

catalysts. The 1,2-*trans* selectivity was obtained through the neighboring group participation. The 1,2-*cis* selectivity was obtained by steric buttressing and conducting the reactions at low temperatures or separation of diastereomeric mixtures. All the synthesized glycans were lapidated with palmitic acid, linoleic acid, and cyclopropanated-LA. Overall, we have synthesized a library of 31 glycolipids in this endeavor. The library members have an azide at the reducing end so that it can used as a handle for attaching biomolecules or surfaces for further biological evaluation.

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2.9 General Experimental Procedures

Procedure A Synthesis of ethynyl cyclohexyl glycosyl carbonate donors: To a rapidly stirring CH_2Cl_2 solution of arabinofuranosyl hemiacetal (1.0 mmol) and DMAP (1.2 mmol) at 25 ºC, ethynyl cyclohexyl (4-nitrophenyl) carbonate (1.2 mmol) **15** was added and continued stirring at 25 ºC for 2 h. After complete consumption of the hemiacetals, the reaction mixture was concentrated *in vacuo* and purified by silica gel column chromatography (*n*-hexane/EtOAc) to afford ethynylcyclohexyl glycosyl carbonate donors containing a trace quantity of the 4-nitrophenol. Eluents containing the compound were concentrated, redissolved in CH_2Cl_2, and washed with sat. aq. $NaHCO_3$ solution to get compound in 75-80% yield.

Procedure B Glycosylation using ethynylcyclohexyl glycosyl carbonate donors: To a solution of acceptor (1.0 mmol) and donor (1.0 mmol) in anhydrous CH_2Cl_2, was added freshly activated 4Å MS powder at 25 ºC. After 10 minutes, 8 mol% each of chloro[tris(2,4-di-tert-butylphenyl)phosphite]gold(I) (**3**) and AgOTf were added to the reaction mixture and 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 arrested by adding excess Et_3N and filtered through a bed of Celite®. The filtrate was concentrated *in vacuo* and the residue was purified by silica gel column chromatography using *n*-hexane/EtOAc as mobile phase to afford glycosides in 72-80% yield.

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

Procedure D Deprotection of the TBDPS-ethers: HF•py (3 mmol) was added dropwise under an inert atmosphere to a solution of silyl ether (1 mmol) in pyridine (3 times to the volume of HF•py) at 0 °C. The reaction mixture was stirred for 5 h at 25 °C, 2*N* HCl was added to quench the reaction at 0 °C, diluted with EtOAc, and washed successively with ice-cold water, saturated solution of $NaHCO_3$ (aq), and brine solution. The 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.

Procedure E Protection of alcohols as benzyl ethers: A solution of the alcohol (1 mmol) in anhydrous DMF, was cooled to 0 °C under a nitrogen atmosphere and NaH (60% oil dispersion, 1.3 mmol per alcohol) was added, and stirred for 10 minutes at 0 °C, benzyl bromide (1.2 mmol per alcohol) was added dropwise and stirred for 2 h at 25 °C. The reaction mixture was poured into cold water with vigorous shaking and extracted with ethyl acetate, and combined EtOAc layers were washed with cold water, and 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 syrups.

Procedure F Synthesis of Allyl glycoside from 1,2-acetonide: Allyl alcohol (4 mmol) followed by PTSA (0.2 mmol) were added to a vigorously stirred solution of acetonide (1 mmol) in freshly prepared anhydrous CH_2Cl_2 at 25 °C. After completion of the reaction, Et_3N was added, the solvent was evaporated *in vacuo* and the crude residue was purified by conventional silica gel column chromatography (ethyl acetate/hexanes) to obtain the desired allyl glycoside.

procedure G Deprotection of allyl glycosides: To a solution of the allyl glycoside (1 mmol) in CH_2Cl_2 (10 mL), $PdCl_2$ (0.2 mmol) in MeOH (40 mL) were added in five portions at 25 °C and stirred for 4-5 h. After completion of the reaction, an excess amount of Et_3N was added and the solid residue was filtered off through a pad of Celite®. The volatile 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.

Procedure H Protection of levulinoate: A solution of the alcohol (1 mmol), DMAP (0.5 mmol) and levulinic acid (1.3 mmol) in dry CH_2Cl_2 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.

Procedure I Deprotection of levulinoate: Hydrazine hydrate (4 mmol), Py-CH_3COOH were added to a solution of levulinoate (1 mmol) in CH_2Cl_2 at 25 °C and stirred for 45 minutes. The

reaction was quenched by adding acetone and washed successively with ethyl acetate, 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.

Procedure J Protection of alcohols as NAP ethers:[48] A solution of the alcohol (1 mmol) in anhydrous DMF was cooled to 0°C under a nitrogen atmosphere and NaH (60% oil dispersion, 1.3mmol per alcohol) was added and stirred for 10 minutes at 0°C, 2-bromomethyl naphthalene (1.2 mmol per alcohol) was added dropwise and stirred for 2 h at 25°C. The reaction mixture was poured into cold water with vigorous shaking, extraction with ethyl acetate, and combined EtOAc layers were washed with cold water, and 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.

Procedure K Deprotection of NAP ethers:[48] 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°C. After 4h, the reaction mixture was quenched by the addition of Et_3N (the reaction mixture turns black from brown) the 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.

Procedure L Synthesis of Active ester (19a, 19b): Carboxylic acid (1.0eq), N-Hydroxyphthalimide (1.0 eq), DMAP (0.1eq) in anhydrous CH_2Cl_2 was stirred vigorously at 25 °C. DIC (1.1 eq) was added dropwise and the mixture was stirred until the carboxylic acid was completely consumed (determined by TLC). The reaction mixture was filtered (over Celite®, SiO2, or through a fritted funnel) and rinsed with additional CH_2Cl_2. The solvent was evaporated under reduced pressure and purification by column chromatography afforded corresponding activated esters.

Procedure M Synthesis of benzoates: 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 °C. The reaction mixture was poured into cold water with vigorous shaking, neutralized by adding 2*N* HCl solution, extracted with ethyl acetate, and combined EtOAc layers were 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.

Procedure N Saponification of benzoates: NaOMe (0.1 mmol per benzoate) was added to a solution of the benzoate (1 mmol) in MeOH and stirred for 8 h at 25 °C. The reaction mixture was concentrated *in vacuo* to obtain a residue that was purified by silica gel column chromatography (ethyl acetate/hexanes) to obtain alcohol.

Procedure O Hydrogenolysis of compound: A solution of the compound in EtOAc under hydrogen atmosphere (balloon pressure) was added 10% $Pd(OH)_2$ and stirred for 36 h at 25 °C. The reaction mixture was filtered through a pad of Celite® and the filtrate was evaporated *in vacuo* first and subsequently lyophilized to afford the target compound as white solids.

Procedure P Synthesis of allyl arabinofuranoside from 1,2-acetonide: Allyl alcohol (30.8 mmol) was added to a solution of acetonide (15.4 mmol) in CH_2Cl_2, stirred at 60 °C. After 5 min, PTSA (3.1 mmol) was added and continued stirring for an additional 1 h; the reaction mixture was neutralized by the addition of Et_3N (excess), diluted with water, and extracted with CH_2Cl_2. Combined CH_2Cl_2 layers were washed with a brine solution, dried over anhydrous sodium sulfate, 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 allyl arabinofuranoside as a pale-yellow syrup.

Procedure Q Esterification: A solution of the alcohol (1 mmol) in anhydrous pyridine (2 mL), activated ester (1.1 mmol), DIPEA (0.2 mmol), and DMAP (0.2 mmol) was stirred under nitrogen atmosphere at 25 °C for 5 h. The reaction mixture was neutralized by adding 1*N* HCl solution, extracted with ethyl acetate, and combined EtOAc layers were washed with cold water, and 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 silica gel column chromatography (ethyl acetate/hexanes) to obtain the required product.

Procedure R Azidation: A solution of the tosyl compound (1 mmol) in anhydrous DMF and sodium azide (5 mmol) was stirred under nitrogen atmosphere at 25 °C for 8 h. After completion, the reaction mixture was diluted and extracted with ethyl acetate, and combined EtOAc layers were washed with brine solution, and dried over Na_2SO_4. The EtOAc solution was

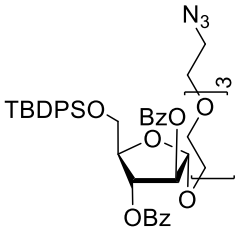
decanted and evaporated *in vacuo* to obtain a residue that was purified by column chromatography (ethyl acetate/hexanes) to obtain the required product.

Procedure S Regioselective Esterification: A solution of the alcohol (1 mmol) in anhydrous pyridine (2 mL), activated ester (1.1mmol), DIPEA (0.2 mmol), and DMAP (0.2 mmol) was stirred under a nitrogen atmosphere at 25°C for 48-60h. The reaction mixture was neutralized by adding 1*N* HCl solution, extracted with ethyl acetate, and combined EtOAc layers were washed with cold water, and 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 product.

2.10 Compound Characterization Data

(2-(2-(2-(2-azidoethoxy)ethoxy)ethoxy)ethyl)-2,3 di-*O*-benzoyl-5-*tert*butyldiphenylsilyl-α-D-arabinofuranoside (**3**):

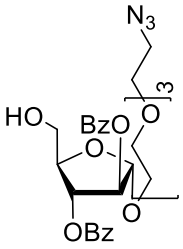
The glycosyl donor **1a**[45] and the glycosyl acceptor **2a**[47] were glycosylated according to the general reaction **Procedure B** as detailed above to give the compound **3**. (Yield 78%, pale yellow syrup). **$[\alpha]_D^{25}$** = +9.8 (*c* = 0.06, $CHCl_3$); **IR** (cm^{-1}, $CHCl_3$): 2930, 2300, 2110, 1720, 1354, 1260, 1109, 988, 870; **^{1}H NMR** (400 MHz, $CDCl_3$): δ 8.07 (d, *J* = 7.5 Hz, 2H), 7.99 (d, *J* = 7.4 Hz, 2H), 7.72 (dd, *J* = 5.8, 2.0 Hz, 4H), 7.61 – 7.54 (m, 2H), 7.46 (t, *J* = 7.7 Hz, 2H), 7.41 – 7.32 (m, 8H), 5.62 (d, *J* = 5.1 Hz, 1H), 5.50 (s, 1H), 5.28 (s, 1H), 4.41 (q, *J* = 4.6 Hz, 1H), 4.02 (d, *J* = 4.5 Hz, 2H), 3.96 – 3.88 (m, 1H), 3.77 – 3.72 (m, 3H), 3.70 (dd, *J* = 6.0, 3.5 Hz, 2H), 3.65 – 3.62 (m, 8H), 3.37 – 3.33 (m, 2H), 1.06 (s, 9H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 165.7, 165.5, 135.8, 135.8, 135.8, 135.8, 133.4, 133.4, 133.4, 133.3, 130.0, 130.0, 130.0, 130.0, 129.8, 129.8, 129.6, 129.4, 128.5, 128.5, 128.5, 128.5, 127.8, 127.8, 127.8, 127.8, 106.0, 83.1, 82.5, 77.6, 70.8, 70.8, 70.8, 70.7, 70.4, 70.1, 66.8, 63.6, 50.8, 26.9, 26.9, 26.9, 19.4; **HRMS** (ESI-MS): m/z calcd. For $C_{43}H_{51}N_3O_{10}Si$ $[M+Na]^+$: 820.3241; Found: 820.3244.



3

(2-(2-(2-(2-azidoethoxy)ethoxy)ethoxy)ethyl)-2,3-di-*O*-benzoyl-α-D-arabinofuranoside (4)

Compound **3** was converted to compound **4** according to the general experimental **Procedure D** (Yield 78%, pale yellow syrup): **$[\alpha]_D^{25}$** = + 12.8 (*c* = 0.06, $CHCl_3$); **IR** (cm^{-1}, $CHCl_3$): 3540, 2830, 2350, 2180, 1740, 1344, 1250, 1108, 990, 870; **^{1}H NMR** (400 MHz, $CDCl_3$): δ 8.08 – 8.02 (m, 4H), 7.60 – 7.55 (m, 2H), 7.47 – 7.42 (m, 4H), 5.55 (s, 1H), 5.42 – 5.40 (m, 1H), 5.29 (s, 1H), 4.35 (q, *J* = 4.2 Hz, 1H), 3.99 (td, *J* = 11.3, 10.7, 3.7 Hz, 2H), 3.95 – 3.86 (m, 1H), 3.76 – 3.70 (m, 3H), 3.67 – 3.57 (m, 10H), 3.34 (t, *J* = 5.0 Hz, 2H); **^{13}C NMR** (101 MHz, $CDCl_3$): δ 166.2, 165.4, 133.6, 133.6, 130.0, 130.0, 129.9, 129.9, 129.3, 129.2, 128.6, 128.6, 128.6, 128.6, 105.7, 83.7, 81.9, 78.0, 70.8, 70.8, 70.7, 70. 7, 70.4, 70.1, 66.8, 62.5, 50.7; **HRMS** (ESI-MS): m/z calcd. For $C_{27}H_{33}N_3O_{10}$ $[M+Na]^+$: 582.2064; Found: 582.2066.

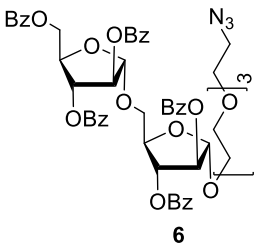


4

(2-(2-(2-(2-azidoethoxy)ethoxy)ethoxy)ethyl)-2,3-di-*O*-benzoyl-5-*O*-(2,3-di-*O*-benzoyl-5-*O*-benzoyl-α-D-arabinofuranosyl)-α-D-arabinofuranoside (6):

The glycosyl donor **5**[49]and the glycosyl acceptor **4** were glycosylated according to the general reaction **Procedure B** as detailed above to give the **7**. (Yield 76%, pale yellow syrup): **$[\alpha]_D^{25}$** = +24.8 (*c* = 0.06, $CHCl_3$); **IR** (cm^{-1}, $CHCl_3$): 2830, 2380, 2155, 1720, 1577, 1450, 1244, 1106,

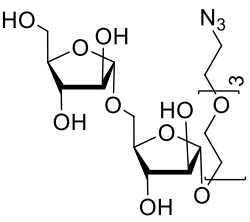
970, 860; **^{1}H NMR** (400 MHz, $CDCl_3$): δ 8.08 – 7.91 (m, 10H), 7.62 – 7.35 (m, 12H), 7.34 – 7.21 (m, 5H), 5.63 (d, *J* = 6.0 Hz, 2H), 5.58 (d, *J* = 6.1 Hz, 2H), 5.46 (s, 1H), 5.29 (s, 1H), 4.84 (dd, *J* = 11.8, 3.2 Hz, 1H), 4.78 – 4.73 (m, 1H), 4.67 (dd, *J* = 11.9, 4.6 Hz, 1H), 4.52 – 4.46 (m, 1H), 4.24 (dd, *J* = 11.3, 4.5 Hz, 1H), 4.01 – 3.87 (m, 2H), 3.74 – 3.58 (m, 13H), 3.35 (t, *J* = 5.0 Hz, 2H); **^{13}C NMR** (101 MHz, $CDCl_3$): δ 166.3, 165.9, 165.8, 165.5, 165.3, 133.6, 133.6, 133.5, 133.4, 133.1, 130.0, 130.0, 130.0, 130.0, 129.9, 129.9, 129.9, 129.9, 129.9, 129.9, 129.8, 129.4, 129.2, 129.1, 129.0, 128.6, 128.6, 128.6, 128.6, 128.6, 128.6, 128.4, 128.4, 128.4, 128.4, 106.0, 105.8, 82.0, 82.0, 81.9, 81.3, 77.9, 77.4, 70.8, 70.8, 70.7, 70.7, 70.3, 70.1, 66.8, 66.2, 63.8, 50.7; **HRMS** (ESI-MS): m/z calcd. For $C_{53}H_{53}N_3O_{17}$ $[M+Na]^+$: 1026.3273; Found: 1026.3253.



6

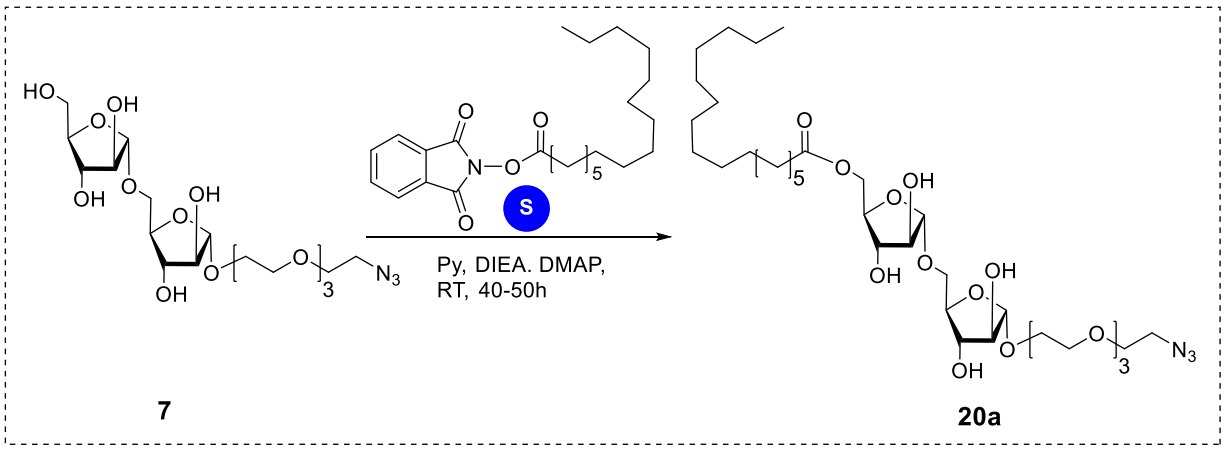
(2-(2-(2-(2-azidoethoxy)ethoxy)ethoxy)ethyl)-5-*O*-(-α-D-arabinofuranosyl)-α-D-arabino furanoside (7):

Compound **6** was converted to compound **7** according to the general experimental **procedure N** (Yield 82%, pale yellow syrup) **$[\alpha]_D^{25}$** = +40.8 (*c* =1.0, $CHCl_3$); **IR** (cm^{-1}, $CHCl_3$): 3560, 2954, 2330, 2160, 1740, 1360, 1094, 990, 870; **^{1}H NMR** (400 MHz, CD_3OD): δ 4.95 (d, *J* = 1.3 Hz, 1H), 4.91 (d, *J* = 1.4 Hz, 1H), 4.07 – 4.03 (m, 1H), 3.99 (ddd, *J* = 6.2, 3.0, 1.3 Hz, 3H), 3.90 – 3.87 (m, 1H), 3.86 – 3.79 (m, 3H), 3.75 (dd, *J* = 11.8, 3.4 Hz, 1H), 3.69 – 3.62 (m, 15H), 3.40 – 3.36 (m, 2H); **^{13}C NMR** (101 MHz, CD_3OD): δ 109.7, 109.6, 85.9, 83.8, 83.4, 83.1, 79.2, 78.7, 71.5, 71.5, 71.5, 71.5, 71.4, 71.1, 68.1, 67.9, 63.1, 51.7; **HRMS** (ESI-MS): m/z calcd. For $C_{18}H_{33}N_3O_{12}$ $[M+Na]^+$: 506.962; Found: 506.965.



7

(2-(2-(2-(2-azidoethoxy)ethoxy)ethoxy)ethyl)-5-*O*-(5-*O*-(hexadecanoyl)-α-D-arabinofuranosyl)-α-D-arabinofuranoside (20a):

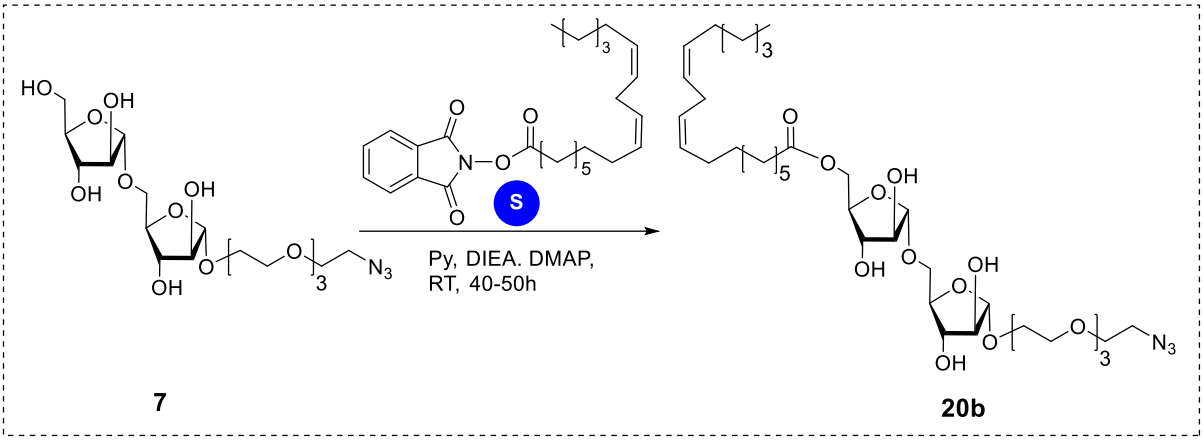


7 **20a**

Compound **7** was converted to compound **20a** according to the general experimental **Procedure S.** (Yield 21%, pale yellow syrup): **$[\alpha]_D^{25}$** = +59.9 (*c* = 1.0, $CHCl_3$); **IR** (cm^{-1}, $CHCl_3$): 3738, 3414, 2924, 2858, 2308, 2107, 1735, 1457, 1358, 1298, 1098, 1013; **^{1}H NMR** (400 MHz, $CDCl_3$): δ 5.05 (d, *J* = 3.4 Hz, 1H), 5.02 (s, 1H), 4.30 (dd, *J* = 11.6, 3.1 Hz, 1H), 4.24 – 4.16 (m, 3H), 4.08 (d, *J* = 5.2 Hz, 2H), 3.97 (d, *J* = 11.6 Hz, 2H), 3.90 – 3.85 (m, 2H), 3.70 – 3.60 (m, 14H), 3.39 (t, *J* = 5.0 Hz, 2H), 2.34 (t, *J* = 7.6 Hz, 2H), 1.60 (q, *J* = 6.9 Hz, 2H), 1.26 (d, *J* = 10.7 Hz, 24H), 0.87 (t, *J* = 6.8 Hz, 3H); **^{13}C NMR** (101 MHz, $CDCl_3$): δ 173.9, 108.1, 108.0, 83.1, 81.0, 80.7, 78.1, 78.0, 77.4, 70.7, 70.6, 70.6, 70.4, 70.3, 70.1, 66. 7, 66.1, 64.2, 50.7, 34.2, 32.1, 29.8, 29.8, 29.8, 29.8, 29.6, 29.6, 29.5, 29.4, 29.4, 29.3, 25.0, 22.8, 14.3. **HRMS** (ESI-MS): m/z calcd. For $C_{34}H_{63}N_3O_{13}$ $[M+Na]^+$: 744.4259; Found: 744.4245.

(2-(2-(2-(2-azidoethoxy)ethoxy)ethoxy)ethyl)-5-*O*-(5-*O*-(9*Z*,12*Z*-octadecadienoyl)-α-D-arabinofuranosyl)-α-D-arabinofuranoside (20b):

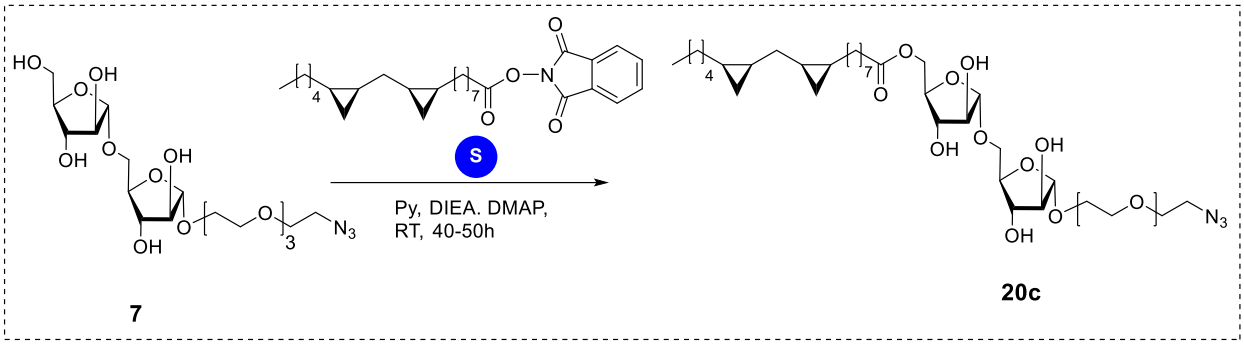
Compound **7** was converted to compound **20b** according to the general experimental



7 **20b**

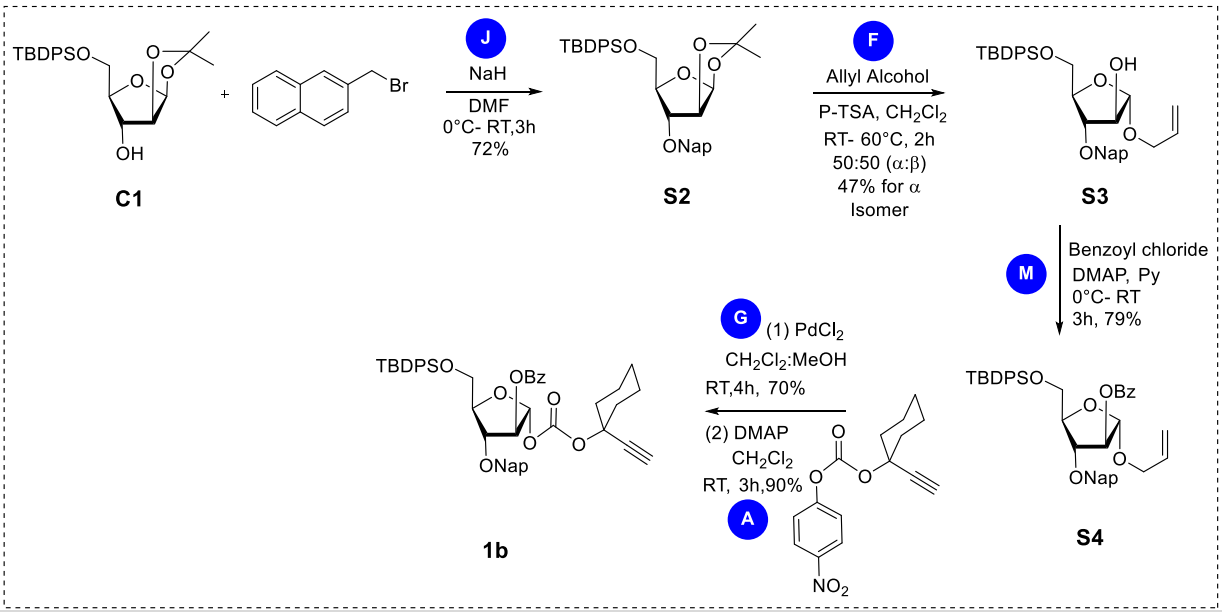
Procedure S. (Yield 23%, pale yellow syrup): **$[\alpha]_D^{25}$** = +28.8 (*c* = 0.06, $CHCl_3$); **IR** (cm^{-1}, $CHCl_3$): 3480, 2925, 2858, 2170, 1730, 1450, 1367, 1300, 1160, 980; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 5.41 – 5.26 (m, 4H), 5.03 (d, *J* = 3.2 Hz, 2H), 4.29 (dd, *J* = 11.5, 3.2 Hz, 1H), 4.23 – 4.17 (m, 3H), 4.08 (d, *J* = 5.7 Hz, 2H), 4.02 – 3.94 (m, 3H), 3.90 – 3.86 (m, 2H), 3.67 – 3.63 (m, 13H), 3.40 – 3.38 (m, 2H), 2.76 (t, *J* = 6.5 Hz, 2H), 2.34 (s, 2H), 2.06 – 2.01 (m, 4H), 1.63 – 1.59 (m, 2H), 1.31 – 1.27 (m, 14H), 0.87 (s, 3H); **^{13}C NMR** (101 MHz, $CDCl_3$): δ 173.9, 130.3, 130.2, 128.2, 128.0, 108.1, 107.9, 84.9, 83.1, 81.0, 80.5, 78.2, 77.9, 70.7, 70.6, 70.6, 70.4, 70.3, 70.1, 66.7, 66.0, 64.2, 50.7, 34.2, 32.1, 31.6, 29.8, 29.8, 29.5, 29.3, 29.3, 27.3, 25.8, 22.8, 22.7, 14.2; **HRMS** (ESI-MS): m/z calcd. For $C_{36}H_{63}N_3O_{13}$ $[M+Na]^+$: 768.4259; Found: 768.4243.

(2-(2-(2-(2-azidoethoxy)ethoxy)ethoxy)ethyl)-5-*O*-(5-*O*-(8-(2-((2-pentylcyclopropyl) methyl)cyclopropyl)octanoyl)-α-D-arabinofuranosyl)-α-D-arabinofuranoside (20c):

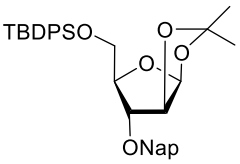


Compound **7** was converted to compound **20c** according to the general experimental **Procedure S.** (Yield 23%, pale yellow syrup): **$[\alpha]_D^{25}$** = +34.8 (*c* = 1.0, $CHCl_3$); **IR** (cm^{-1}, $CHCl_3$): 3735, 3406, 2923, 2859, 2310, 2105, 1734, 1455, 1357, 1293, 1095, 1024; **^{1}H NMR** (400 MHz, $MeOD_4$): δ 4.98 – 4.95 (m, 1H), 4.94 – 4.92 (m, 1H), 4.32 (dd, *J* = 11.7, 3.6 Hz, 1H), 4.19 (dd, *J* = 11.7, 6.1 Hz, 1H), 4.11 (td, *J* = 6.0, 3.4 Hz, 1H), 4.08 – 4.03 (m, 2H), 4.02 – 3.99 (m, 1H), 3.93 – 3.82 (m, 4H), 3.71 – 3.66 (m, 14H), 3.42 – 3.38 (m, 2H), 2.38 (t, *J* = 7.4 Hz, 2H), 1.67 – 1.62 (m, 2H), 1.37 – 1.31 (m, 20H), 0.93 (d, *J* = 4.2 Hz, 3H), 0.83 (td, *J* = 7.7, 7.2, 5.2 Hz, 2H), 0.77 – 0.70 (m, 2H), 0.65 (td, *J* = 8.3, 4.1 Hz, 2H), -0.21 – -0.28 (m, 2H); **^{13}C NMR** (101 MHz, $MeOD_4$): δ 175.3, 109.7, 109.7, 83.8, 83.5, 83.2, 82.8, 79.2, 79.2, 71.6, 71.6, 71.5, 71.5, 71.5, 71.1, 68.3, 67.9, 65.0, 51.8, 34.9, 33.1, 31.3, 31.0, 30.8, 30.6, 30.5, 30.1, 29.2, 29.1, 26.0, 23.8, 17.1, 17.0, 16.7, 16. 7, 14.5, 11.7, 11.6; **HRMS** (ESI-MS): m/z calcd. For $C_{38}H_{67}N_3O_{13}$ $[M+Na]^+$: 796.4572; Found: 796.4561.

Synthesis of **1b**:



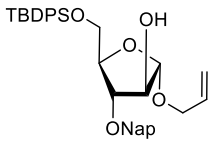
1,2-*O*-isopropylidine-3-*O*-napthylmethyl-5-*O*-^{tert}butyldiphenylsilyl-D-arabinofuranoside (S2): Compound **C1**[44a] was converted to compound **S2** according to the general experimental **Procedure J** (Yield 72%, pale yellow syrup) **$[\alpha]_D^{25}$** = -12.0 (*c* = 0.06, $CHCl_3$); **IR** (cm^{-1}, $CHCl_3$): 3059, 2938, 2862, 1465, 1376, 1099, 1017, 858; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.85 – 7.78 (m, 4H), 7.67 – 7.64 (m, 4H), 7.50 – 7.39 (m, 5H), 7.35 (t, *J* = 7.1 Hz, 4H), 5.92 (d, *J* = 4.1 Hz, 1H), 4.78 (d, *J* = 2.3 Hz, 2H), 4.72 (d, *J* = 4.1 Hz, 1H), 4.28 (s, 2H), 3.83 (d, *J* = 7.0 Hz, 2H), 1.35 (s, 3H), 1.31 (s, 3H), 1.02 (s, 9H); **^{13}C NMR** (101 MHz, $CDCl_3$): δ 135.7, 135.7, 135.1, 134.9, 133.4, 133.4, 133.2, 133.2, 129.9, 129.8, 128.5, 128.1, 127.9, 127.9, 127.9, 127.9, 127.8, 127.8, 126.7, 126.3, 126.1, 125.8, 112.6, 105.9, 85.4, 85.3, 83.0, 71.9, 63.6, 27.1, 26.9, 26.9, 26.9, 26.3, 19.3; **HRMS** (ESI-MS): m/z calcd. For $C_{35}H_{40}O_5Si$ $[M+Na]^+$: 591.2543; Found: 591.2542.



S2

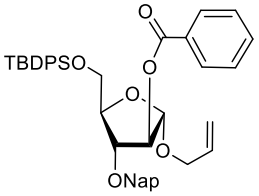
Allyl 3-*O*-naphthylmethyl-5-*O*-^{tert}butyldiphenylsilyl-α-D-arabinofuranoside (S3):

Compound **S2** was converted to compound **S3** according to the general experimental **Procedure F** (Yield 47%, 50:50 (α:β), pale yellow syrup, used only α isomer): **$[\alpha]_D^{25}$** = +18.8 (*c* = 0.06, $CHCl_3$); **IR** (cm^{-1}, $CHCl_3$): 3550, 3360, 3050, 2988, 1376, 1099, 1017, 880; **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.74 – 7.66 (m, 4H), 7.57 – 7.53 (m, 2H), 7.44 – 7.40 (m, 2H), 7.39 – 7.23 (m, 7H), 7.17 – 7.12 (m, 2H), 5.92 – 5.81 (m, 1H), 5.25 (dt, *J* = 17.2, 1.4 Hz, 1H), 5.13 – 5.08 (m, 1H), 5.03 (s, 1H), 4.77 (d, *J* = 12.4 Hz, 1H), 4.60 (d, *J* = 12.4 Hz, 1H), 4.22 – 4.13 (m, 3H), 3.98 (ddd, *J* = 14.7, 7.0, 1.8 Hz, 2H), 3.71 (dd, *J* = 11.2, 2.3 Hz, 1H), 3.47 (dd, *J* = 11.2, 2.0 Hz, 1H), 3.20 (dd, *J* = 10.2, 3.8 Hz, 1H), 0.89 (s, 9H); **^{13}C NMR** (101 MHz, $CDCl_3$): δ135.7, 135.6, 135.4, 134.48, 134.5, 133.3, 133.1, 132.4, 130.0, 130.0, 130.0, 128.4, 128.0, 128.0, 127.9, 127.9, 127.9, 127.8, 127.8, 126.8, 126.2, 126.0, 125.9, 117.3, 108.0, 84.6, 84.4, 78.1, 72.2, 68.2, 64.2, 26.8, 26.8, 26.8, 19.2; **HRMS** (ESI-MS): m/z calcd. For $C_{35}H_{40}O_5Si$ $[M+Na]^+$: 591.2543; Found: 591.2562.



S3

Allyl 2-*O*-benzoyl-3-*O*-naphthylmethyl-5-*O*-^{tert}butyldiphenylsilyl-α-D-arabinofuranoside (S4): Compound **S3** was converted to compound **S4** according to the general experimental **Procedure M** (Yield 79%, pale yellow syrup): **$[\alpha]_D^{25}$** = +15.5 (*c* = 0.06, $CHCl_3$); **IR** (cm^{-1}, $CHCl_3$): 2990, 2910, 2862, 1455, 1366, 1090, 1010, 980; **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.95 (dd, *J* = 8.3, 1.2 Hz, 2H), 7.79 – 7.72 (m, 3H), 7.69 – 7.63 (m, 3H), 7.61 – 7.54 (m,

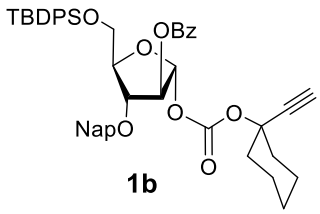


S4

3H), 7.44 – 7.36 (m, 7H), 7.32 – 7.28 (m, 4H), 5.96 (m, 1H), 5.48 (d, *J* = 1.3 Hz, 1H), 5.36 (dq, *J* = 17.2, 1.5 Hz, 1H), 5.23 – 5.20 (m, 2H), 4.94 (d, *J* = 12.3 Hz, 1H), 4.76 (d, *J* = 12.3 Hz, 1H), 4.33 – 4.25 (m, 2H), 4.19 (d, *J* = 5.5 Hz, 1H), 4.10 (ddt, *J* = 13.1, 6.2, 1.2 Hz, 1H), 3.84 (dd, *J* = 4.1, 2.7 Hz, 2H), 0.95 (s, 9H); **^{13}C NMR** (101 MHz, $CDCl_3$): δ 165.6, 135.8, 135.7, 135.2, 134.2, 134.2, 133.5, 133.4, 133.4, 133.3, 133.2, 129.9, 129.9, 129.9, 129.8, 130.0, 129.6, 128.5, 128.5, 128.5, 128.4, 128.0, 127.8, 127.8, 127.8, 127.8, 127.1, 126.1, 126.0, 126.0, 117.7, 105.3, 83.6, 83.0, 82.5, 72.5, 68.0, 63.4, 26.8, 26.8, 26.8, 19.4; **HRMS** (ESI-MS): m/z calcd. For $C_{42}H_{44}O_6Si$ $[M+Na]^+$: 695.2805; Found: 695.2880.

1-*O*-(((1-ethylnylcyclohexyl)oxy)carbonyl)-2-*O*-dibenzyl-3-*O*-naphthylmethyl-5-*O*-*^{tert}*butyldi phenylsilyl-α-D-arabinofuranoside (1b):

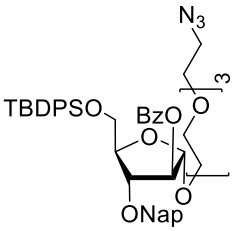
Compound **S4** was converted to compound **1b** according to the general experimental **procedure G** (Yield 63% over 2 steps, pale yellow syrup) and then the general experimental **Procedure A** (Yield 72%, pale yellow syrup): **$[\alpha]_D^{25}$** = +22.8 (*c* = 0.06, $CHCl_3$); **IR** (cm^{-1}, $CHCl_3$): 2980, 2822, 2310, 2250, 1450, 1365, 1060, 1010, 960, 850; **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.95 – 7.91 (m, 2H), 7.80 – 7.70 (m, 4H), 7.60 – 7.54 (m, 5H), 7.47 – 7.34 (m, 7H), 7.28 (d, *J* = 7.4 Hz, 4H), 6.27 (s, 1H), 5.63 (s, 1H), 4.99 (d, *J* = 12.2 Hz, 1H), 4.81 (d, *J* = 12.2 Hz, 1H), 4.48 (q, *J* = 4.4 Hz, 1H), 4.31 (d, *J* = 4.8 Hz, 1H), 3.82 (d, *J* = 4.4 Hz, 2H), 2.64 (s, 1H), 2.21 (td, *J* = 14.4, 14.0, 6.9 Hz, 2H), 1.95 – 1.85 (m, 2H), 1.69 – 1.57 (m, 4H), 1.37 – 1.25 (m, 2H), 0.91 (s, 9H); **^{13}C NMR** (101 MHz, $CDCl_3$): δ 165.4, 151.5, 135.7, 135. 7, 135.0, 133.6, 133.6, 133.4, 133.2, 133.2, 133.2, 130.0, 130.0, 130.0, 130.0, 129.8, 129.2, 128.6, 128.6, 128.4, 128.1, 127.8, 127.8, 127.8, 127.8, 127.8, 127.1, 126.2, 126.0, 125.9, 103.2, 85.9, 82.8, 82.5, 81.6, 78.4, 75.3, 72.6, 62.9, 37.0, 36.8, 26.8, 26.8, 26.8, 25.1, 22.7, 22.7, 19.3; **HRMS** (ESI-MS): m/z calcd. For $C_{48}H_{50}O_8Si$ $[M+Na]^+$: 805.3173; Found: 805.3180.



1b

(2-(2-(2-(2-azidoethoxy)ethoxy)ethoxy)ethyl)-2-*O*-benzoyl-3-*O*-naphthylmethyl-5-*O* *^{tert}*butyldi phenylsilyl-α-D-arabinofuranoside (9):

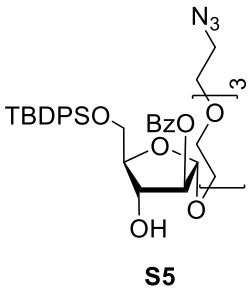
The glycosyl donor **1b** and the glycosyl acceptor **2a**[47] were glycosylated according to the general reaction **Procedure B** as detailed above to give the **8**. (Yield 73%, pale yellow syrup): **$[\alpha]_D^{25}$** = + 36.6 (*c* = 1.0, $CHCl_3$); **IR** (cm^{-1}, $CHCl_3$): 3090, 2890, 2262, 2160,1450, 1365, 1050, 1010, 980; **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.96 (dd, *J* = 8.3, 1.1 Hz, 2H), 7.79 – 7.68 (m, 4H), 7.65 – 7.55 (m, 5H), 7.44 – 7.36 (m,



8

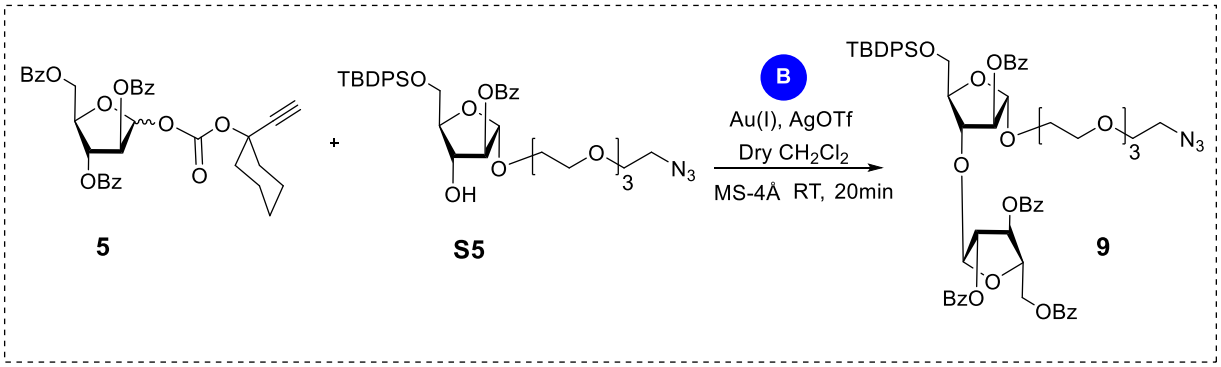
7H), 7.32 – 7.28 (m, 4H), 5.49 (d, *J* = 1.2 Hz, 1H), 5.23 (s, 1H), 4.95 (d, *J* = 12.1 Hz, 1H), 4.75 (d, *J* = 12.2 Hz, 1H), 4.30 (q, *J* = 4.2 Hz, 1H), 4.20 (d, *J* = 5.5 Hz, 1H), 3.90 (dd, *J* = 9.7, 5.3 Hz, 1H), 3.84 (q, *J* = 4.3 Hz, 2H), 3.74 – 3.67 (m, 5H), 3.64 – 3.60 (m, 8H), 3.34 (t, *J* = 5.1 Hz, 2H), 0.95 (s, 9H); **^{13}C NMR** (101 MHz, $CDCl_3$): δ 165.6, 135.8, 135.7, 135.2, 133.4, 133.4, 133.4, 133.3, 133.2, 129.9, 129.9, 129.9, 130.0, 130.0, 129.6, 128.5, 128.5, 128.3, 128.0, 127.8, 127.8, 127.8, 127.8, 127.8, 127.8, 127.1, 126.1, 126.0, 126.0, 106.5, 83.6, 83.1, 82.4, 72.5, 70.8, 70.8, 70.8, 70.7, 70.4, 70.1, 66.8, 63.3, 50.8, 26.8, 26.8, 26.8, 19.4; **HRMS** (ESI-MS): m/z calcd. For $C_{47}H_{55}N_3O_9Si$ $[M+Na]^+$: 856.3605; Found: 856.3605.

(2-(2-(2-(2-azidoethoxy)ethoxy)ethoxy)ethyl)-2-*O*-benzoyl-5-*O*-*tert*butyldiphenylsilyl-α-D-arabinofuranoside (S5): Compound **8** was converted to Glycosyl acceptor **S5** according to the general experimental **Procedure K**. (Yield 79%, pale yellow syrup): **$[\alpha]_D^{25}$** = + 42.4(*c* = 0.06, $CHCl_3$); **IR** (cm^{-1}, $CHCl_3$): 3550, 3420, 3050, 2840, 2270, 2170,1400, 1335, 1030, 1010, 980; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.93 (dd, *J* = 8.3, 1.2 Hz, 2H), 7.68 (dt, *J* = 7.9, 1.3 Hz, 4H), 7.59 – 7.54 (m, 1H), 7.42 – 7.30 (m, 9H), 5.26 (s, 1H), 5.19 – 5.17 (m, 1H), 4.25 (q, *J* = 4.6 Hz, 2H), 3.97 – 3.90 (m, 1H), 3.88 (dd, *J* = 4.5, 2.3 Hz, 2H), 3.73 – 3.63 (m, 14H), 3.37 (t, *J* = 5.1 Hz, 2H), 1.04 (s, 9H); **^{13}C NMR** (101 MHz, $CDCl_3$): δ 166.4, 135.7, 135.7, 135.7, 133.5, 133.4, 129.9, 129.9, 129.9, 129.8, 129.8, 129.8, 128.5, 128.5, 128.5, 127.8, 127.8, 127.8, 127.8, 105.3, 85.4, 85.0, 76.8, 70.8, 70.7, 70.7, 70.7, 70.2, 70.1, 66.1, 63.7, 50.7, 26.9, 26.9, 26.9, 19.4; **HRMS** (ESI-MS): m/z calcd. For $C_{36}H_{47}N_3O_9Si$ $[M+Na]^+$: 716.2979; Found: 716.2980.



S5

(2-(2-(2-(2-azidoethoxy)ethoxy)ethoxy)ethyl)-2-*O*-benzoyl-5-*O*-*tert*butyldiphenylsilyl-3-*O*-(2,3-di-*O*-benzoyl-5-*O*-benzoyl-α-D-arabinofuranosyl)-α-D-arabinofuranoside (9):

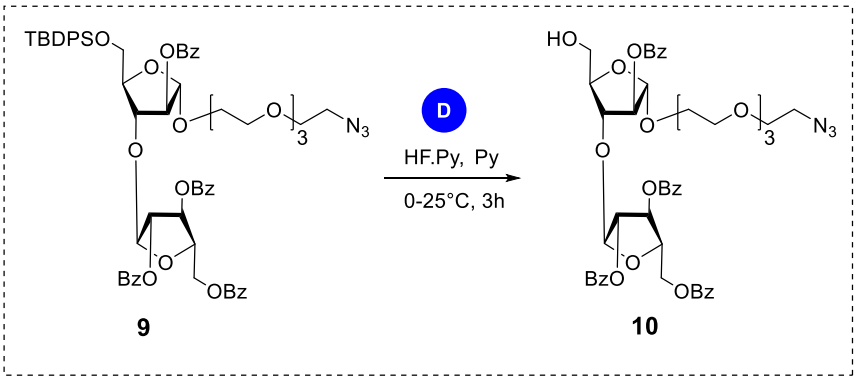


Compound **8** was converted to Glycosyl acceptor **S5** according to the general experimental **Procedure K**. Then Glycosyl accepter **S5** glycosylated with glycosyl donor **5**[49]according to the

general **Procedure B** gave compound **9** (Yield 76 %, pale yellow syrup). **$[\alpha]_D^{25}$** = +34.4 (*c* = 1.0, $CHCl_3$); **IR** (cm^{-1}, $CHCl_3$): 3010, 2870, 2242, 2170,1440, 1360, 1010, 980, 900; **^{1}H NMR** (400 MHz, $CDCl_3$): δ 8.08 (d, *J* = 7.2 Hz, 2H), 8.03 – 8.00 (m, 2H), 7.98 (s, 1H), 7.97 – 7.95 (m, 2H), 7.94 (s, 1H), 7.65 – 7.61 (m, 4H), 7.56 (dt, *J* = 11.2, 7.4 Hz, 3H), 7.43 (dt, *J* = 23.6, 7.5 Hz, 7H), 7.36 – 7.27 (m, 6H), 7.17 (t, *J* = 7.9 Hz, 2H), 5.67 (s, 1H), 5.60 (s, 1H), 5.56 (d, *J* = 4.5 Hz, 1H), 5.42 (s, 1H), 5.29 (s, 1H), 4.60 (dd, *J* = 12.2, 3.8 Hz, 2H), 4.53 (dd, *J* = 12.0, 4.5 Hz, 1H), 4.33 (dt, *J* = 13.0, 4.8 Hz, 2H), 3.90 (d, *J* = 4.4 Hz, 3H), 3.77 – 3.71 (m, 3H), 3.71 – 3.66 (m, 3H), 3.64 – 3.61 (m, 8H), 3.36 – 3.32 (m, 2H), 0.99 (s, 9H); **^{13}C NMR** (101 MHz, $CDCl_3$): δ166.3, 165.8, 165.7, 165.4, 135.7, 135.6, 133.7, 133.6, 133.5, 133.3, 133.2, 133.1, 130.1, 130.1, 130.1, 130.0, 130.0, 130.0, 129.9, 129.8, 129.8, 129.8, 129.8, 129.5, 129.3, 129.2, 128.7, 128.7, 128.6, 128.6, 128.5, 128.5, 128.4, 128.4, 127.9, 127.8, 127.8, 127.8, 127.8, 127.8, 106.4, 104.9, 83.6, 82.6, 82.0, 81.8, 80.0, 77.9, 70.9, 70.8, 70.8, 70.7, 70.4, 70.1, 66.8, 63.7, 63.1, 50.8, 26.9, 26.9, 26.9, 19.4; **HRMS** (ESI-MS): m/z calcd. For $C_{62}H_{67}N_3O_{16}Si$ $[M+Na]^+$: 1160.4188; Found: 1160.4198.

(2-(2-(2-(2-azidoethoxy)ethoxy)ethoxy)ethyl-2-*O*-benzoyl-3-*O*-(2,3-di-*O*-benzoyl-5-*O*-benzoyl-α-D-arabinofuranosyl)-α-D-arabinofuranoside (10):

Compound **9** was converted to compound **10** according to the general experimental **Procedure D.** (Yield 77%, pale yellow syrup): **$[\alpha]_D^{25}$** = +30.8 (*c* = 0.06, $CHCl_3$); **IR** (cm^{-1}, $CHCl_3$): 3530, 3410, 2820, 2260, 2170,1400, 1335, 1030, 1010, 970; **^{1}H NMR** (400 MHz, $CDCl_3$): δ 8.09 (d, *J* = 7.8 Hz, 2H), 8.01 (d, *J* = 7.6 Hz, 5H), 7.59 (dd, *J* = 11.5, 7.2 Hz, 3H), 7.44 (dq, *J* = 21.9, 7.5 Hz, 8H), 7.27 (d, *J* = 2.0 Hz, 2H), 5.65 (s, 1H), 5.63 (s, 1H), 5.56 (d, *J* = 4.6 Hz, 1H), 5.41 (s, 1H), 5.27 (s, 1H), 4.77 (dd, *J* = 11.9, 3.5 Hz, 1H), 4.66 (dd, *J* = 11.9, 5.2 Hz, 1H), 4.56 (q, *J* = 4.5 Hz, 1H), 4.43 (d, *J* = 5.5 Hz, 1H), 4.30 (q, *J* = 3.7 Hz, 1H), 3.91 (ddd, *J* = 21.7, 10.8, 3.2 Hz, 2H), 3.84 – 3.79 (m, 1H), 3.77 – 3.62 (m, 13H), 3.35 (t, *J* = 5.0 Hz, 2H); **^{13}C NMR** (101 MHz, $CDCl_3$): δ 166.3, 165.8, 165.6, 165.4, 133.7, 133.6, 133.5, 133.2, 130.0, 130.0, 130.0, 130.0, 129.9, 129.9, 129.8, 129.8, 129.7, 129.4, 129.2, 129.1, 128.7, 128.6, 128.6, 128.6, 128.6, 128.6, 128.4, 128.4, 106.2, 105.4, 83.0, 82.9, 81.9, 81.6, 80.6, 77.9,

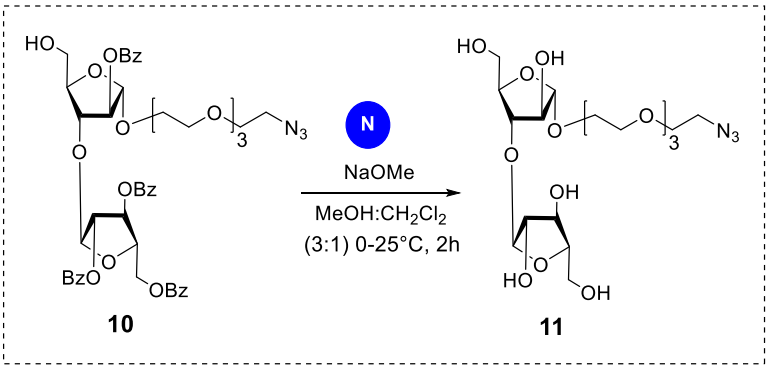


9 **10**

70.8, 70.8, 70.7, 70.6, 70.4, 70.0, 66.8, 63.9, 62.0, 50.7; **HRMS** (ESI-MS): m/z calcd. For $C_{46}H_{49}N_3O_{16}$ $[M+Na]^+$: 922.3011; Found: 922.3091.

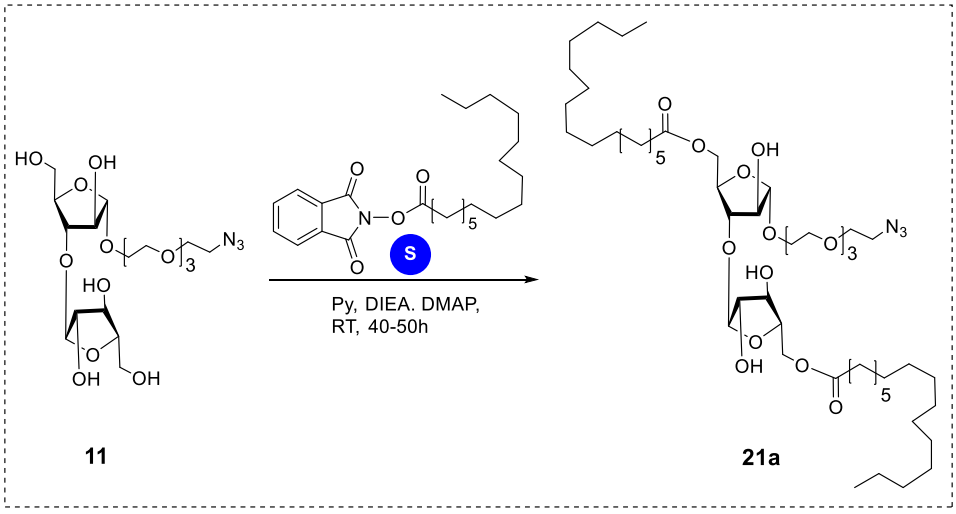
(2-(2-(2-(2-azidoethoxy)ethoxy)ethoxy)ethyl)-3-*O*-(-α-D-arabinofuranosyl)-α-D-arabinofurano side (11):

Compound **10** was converted to compound **11** according to the general experimental **Procedure N.** (Yield 78%, pale yellow syrup): $[\alpha]_D^{25}$ = +28.8 (*c* = 1.0, $CHCl_3$); **IR** (cm^{-1}, $CHCl_3$): 3570, 2950, 2320, 2150, 1710, 1380, 1064, 980, 870; **^{1}H NMR** (400 MHz, CD_3OD): δ 5.07 (d, *J* = 1.6 Hz, 1H), 4.94 (d, *J* = 1.2 Hz, 1H), 4.59 (s, 1H), 4.14 (dd, *J* = 3.1, 1.4 Hz, 1H), 4.06 (ddd, *J* = 6.4, 5.1, 3.0 Hz, 1H), 4.01 – 3.98 (m, 2H), 3.93 (ddd, *J* = 6.4, 5.5, 3.1 Hz, 1H), 3.83 (dq, *J* = 8.4, 3.0 Hz, 3H), 3.79 (dd, *J* = 5.1, 3.1 Hz, 1H), 3.75 – 3.73 (m, 1H), 3.71 – 3.65 (m, 14H), 3.41 – 3.38 (m, 2H); **^{13}C NMR** (101 MHz, CD_3OD): δ 109.7, 109.0, 85.5, 84.1, 83.9, 83.6, 82.1, 78.7, 71.6, 71.6, 71.6, 71.5, 71.4, 71.1, 67.9, 63.0, 62.8, 51.8; **HRMS** (ESI-MS): m/z calcd. For $C_{18}H_{33}N_3O_{12}$ $[M+Na]^+$: 506.1962; Found: 506.1952.



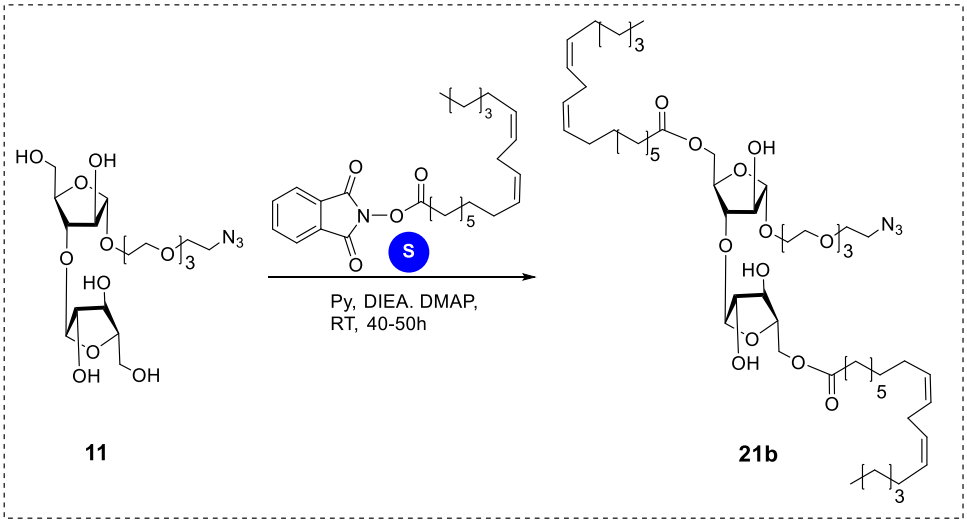
(2-(2-(2-(2-azidoethoxy)ethoxy)ethoxy)ethyl)-5-*O*-(hexadecanoyl)-3-*O*(5-*O*-hexadecanoyl-α-D-arabinofuranosyl)-α-D-arabinofuranoside (21a):

Compound **11** was converted to compound **21a** according to the general experimental **Procedure S**: (Yield 18%, pale yellow syrup): $[\alpha]_D^{25}$ = +42.8 (*c* = 0.06, $CHCl_3$); **IR** (cm^{-1}, $CHCl_3$): 3560, 3350, 2850, 2250, 2140, 1710, 1425,1310, 1080, 1020; **^{1}H NMR** (400 MHz, $CDCl_3$): δ 5.14 (s, 1H), 5.00 (s, 1H), 4.36 – 4.30 (m, 1H), 4.26 (d, *J* = 3.9 Hz, 2H), 4.23 (dd, *J* = 3.1, 1.7 Hz, 2H), 4.18 –



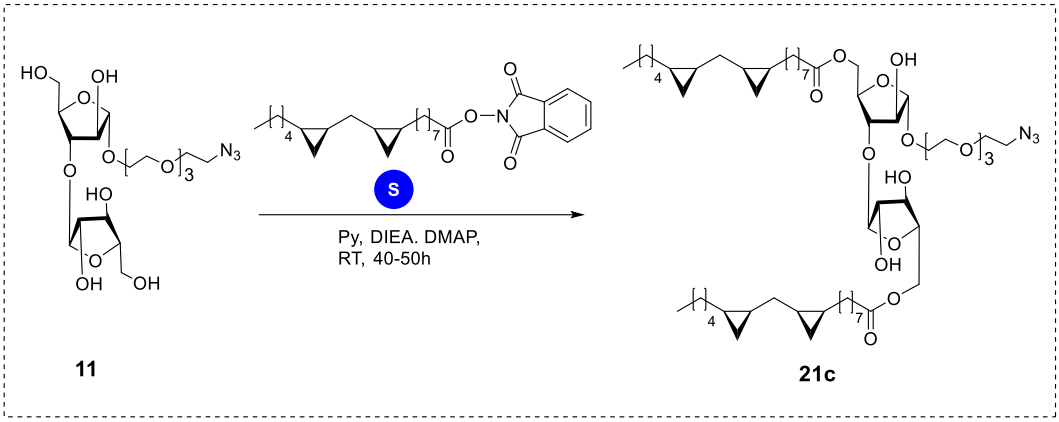
4.13 (m, 2H), 3.98 (dd, *J* = 5.2, 3.2 Hz, 1H), 3.90 – 3.85 (m, 2H), 3.66 (q, *J* = 5.3, 4.5 Hz, 14H), 3.42 – 3.39 (m, 2H), 2.33 (t, *J* = 7.6 Hz, 4H), 1.63 – 1.58 (m, 4H), 1.25 (s, 48H), 0.87 (t, 6H); **^{13}C NMR** (101 MHz, $CDCl_3$): δ 173.8, 173.7, 108.7, 107.9, 83.0, 83.0, 80.9, 80.4, 80.0, 77.6, 70.7, 70.7, 70.6, 70.5, 70.5, 70.1, 67.5, 63.8, 63.6, 50.8, 34.3, 34.2, 32.1, 32.1, 32.1, 29.9, 29.9, 29.8, 29.8, 29.8, 29.8, 29.8, 29.8, 29.8, 29.6, 29.6, 29.5, 29.5, 29.5, 29.4, 29.4, 29.3, 29.3, 25.0, 25.0, 22.8, 22.8, 22.8, 14.3, 14.3; **HRMS** (ESI-MS): m/z calcd. For $C_{50}H_{93}N_3O_{14}$ $[M+Na]^+$: 982.6555; Found: 982.6560.

(2-(2-(2-(2-azidoethoxy)ethoxy)ethoxy)ethyl)-5-*O*-(9*Z*,12*Z*-octadecadienoyl)-3-*O*(5-*O*-9*Z*,12*Z*-octadecadienoyl-α-D-arabinofuranosyl)-α-D-arabinofuranoside (21b): Compound **11** was converted to compound **21b** according to the general experimental **Procedure S.** (Yield 21%, pale ellow syrup): **$[\alpha]_D^{25}$** = +16.6 (*c* = 0.06, $CHCl_3$); **IR** (cm^{-1}, $CHCl_3$): 3560, 3005, 2310, 2160, 1775, 1420, 1340, 1300, 1090, 1010; **^{1}H NMR** (400 MHz, $CDCl_3$): δ 5.43 – 5.27 (m, 8H), 5.14 (s, 1H), 5.01 – 4.98 (d, 1H), 4.36 – 4.31 (m, 1H), 4.25 (dt, *J* = 8.2, 3.7 Hz, 5H), 4.18 – 4.12 (m, 2H), 3.97 (dd, *J* = 5.2, 3.2 Hz, 1H), 3.89 – 3.83 (m, 2H), 3.68 – 3.61 (m, 14H), 3.41 – 3.38 (m, 2H), 2.76 (t, *J* = 6.6 Hz, 4H), 2.33 (t, *J* = 7.6 Hz, 4H), 2.04 (q, *J* = 6.9 Hz, 8H), 1.64 – 1.58 (m, 4H), 1.28 (dd, *J* = 9.4, 2.9 Hz, 28H), 0.88 (m, 6H); **^{13}C NMR** (101 MHz, $CDCl_3$): δ 173.7, 173.6, 130.4, 130.4, 130.2, 130.2, 128.2, 128.2, 128.1, 128.0, 108.6, 108.0, 83.0, 82.8, 80.9, 80.4, 80.1, 77.6, 70.7, 70.7, 70.6, 70.6, 70.5, 70.1, 67.4, 63.9, 63.7, 50.8, 34.2, 34.2, 32.1, 31.7, 29.8, 29.8, 29.8, 29.8, 29.8, 29.5, 29.5, 29.3, 29.3, 29.3, 29.3, 29.3, 29.2, 27.3, 27.3, 25.8, 25.0, 24.9, 22.8, 22.7, 14.3, 14.2; **HRMS** (ESI-MS): m/z calcd. For $C_{54}H_{93}N_3O_{14}$ $[M+Na]^+$: 1030.6555; Found: 1030.6568.



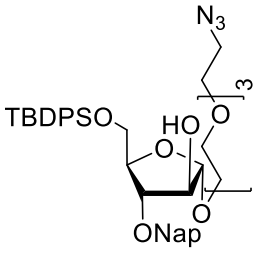
(2-(2-(2-(2-azidoethoxy)ethoxy)ethoxy)ethyl)-5-*O*-(8-(2-((2-pentylcyclopropyl) methyl)cyclopropyl)octanoyl)-3-*O*-(5-*O*-(8-(2-((2-pentylcyclopropyl) methyl)cyclopropyl)octanoyl)-α-D-arabinofuranosyl)-α-D-arabinofuranoside (21c):

Compound **11** was converted to compound **21c** according to the general experimental **Procedure S**. (Yield 22%, pale yellow syrup): **$[\alpha]_D^{25}$** = +28.8 (*c* = 0.06, $CHCl_3$); **IR** (cm^{-1}, $CHCl_3$): 3590, 3310, 2735, 2270, 2180, 1710, 1455, 1370, 1210, 1080, 1010; **^{1}H NMR** (400 MHz, $CDCl_3$): δ 5.15 (s, 1H), 5.00 (s, 1H), 4.37 – 4.30 (m, 1H), 4.29 – 4.21 (m, 5H), 4.20 – 4.12 (m, 2H), 3.97 (dd, *J* = 5.3, 3.0 Hz, 1H), 3.91 – 3.83 (m, 2H), 3.66 (q, *J* = 5.3, 4.5 Hz, 13H), 3.43 – 3.38 (m, 2H), 2.34 (t, *J* = 7.5 Hz, 4H), 1.64 – 1.59 (m, 4H), 1.32 – 1.25 (m, 40H), 0.89 – 0.87 (m, 6H), 0.81 – 0.74 (m, 4H), 0.72 – 0.64 (m, 4H), 0.60 (td, *J* = 8.3, 4.0 Hz, 4H), -0.24 – -0.33 (m, 4H); **^{13}C NMR** (101 MHz, $CDCl_3$): δ 173.7, 173.6, 108.7, 108.0, 83.1, 82.7, 80.8, 80.4, 80.0, 77.6, 70.7, 70.7, 70.6, 70.6, 70.5, 70.1, 67.5, 63.8, 63.7, 50.8, 34.2, 34.2, 32.1, 32.0, 31.1, 30.3, 30.0, 29.8, 29.8, 29.8, 29.8, 29.7, 29.6, 29.5, 29.3, 29.3, 29.0, 29.0, 28.9, 28.9, 28.2, 28.0, 25.0, 25.0, 23.0, 22.8, 16.2, 16.1, 16.1, 16.1, 16.0, 15.8, 15.8, 14.3, 11.2, 11.2, 11.0, 11.0; **HRMS** (ESI-MS): m/z calcd. For $C_{58}H_{101}N_3O_{14}$ $[M+Na]^+$: 1086.7181; Found: 1086.7166.



(2-(2-(2-(2-azidoethoxy)ethoxy)ethoxy)ethyl)-3-*O*-naphthylmethyl-5-*O*-*tert*butyldiphenylsilyl-α-D-arabinofuranoside (S6):

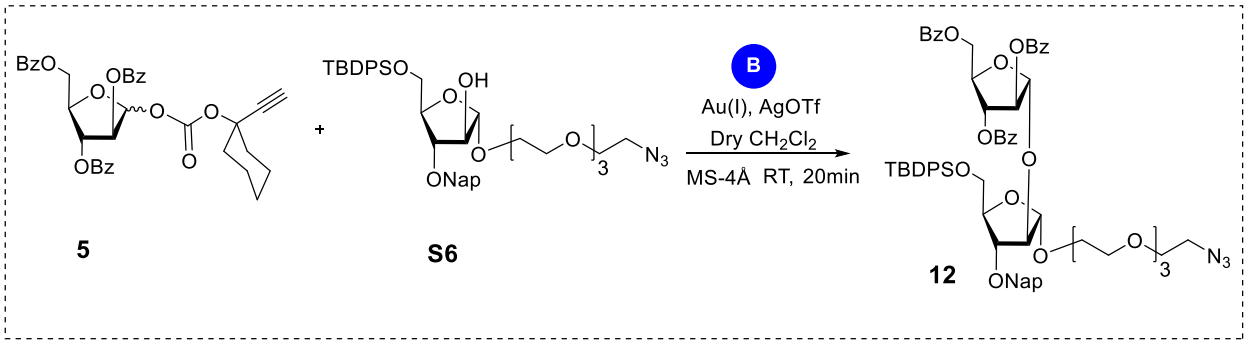
Compound **8** was converted to Glycosyl acceptor **S6** according to the general experimental **Procedure N**. (Yield 67%, pale yellow syrup): **$[\alpha]_D^{25}$** = +24.4 (*c* = 0.06, $CHCl_3$); **IR** (cm^{-1}, $CHCl_3$): 3550, 3400, 3010, 2860, 2270, 2110, 1440, 1355, 1050, 1010, 980; **^{1}H NMR** (400 MHz, $CDCl_3$):δ 7.84 – 7.76 (m, 4H), 7.65 (dd, *J* = 7.8, 1.3 Hz, 2H), 7.55 (d, *J* = 6.9 Hz, 2H), 7.48 – 7.33 (m, 7H), 7.28 – 7.24 (m, 2H), 5.12 (s, 1H), 4.86 (d, *J* = 12.2 Hz, 1H), 4.70 (d, *J* = 12.3 Hz, 1H), 4.30 (s, 1H), 4.22



(q, *J* = 2.7 Hz, 1H), 4.06 (dd, *J* = 3.8, 1.6 Hz, 1H), 3.89 (dt, *J* = 8.4, 4.4 Hz, 1H), 3.81 (dd, *J* = 11.2, 2.6 Hz, 1H), 3.74 – 3.65 (m, 5H), 3.61 (q, *J* = 3.4 Hz, 9H), 3.35 – 3.31 (m, 2H), 0.99 (s, 9H); **^{13}C NMR** (101 MHz, $CDCl_3$): δ 135.7, 135.6, 135.5, 133.3, 133.1, 132.7, 132.6, 130.0, 129.9, 128.3, 128.3, 128.0, 128.0, 127.9, 127.9, 127.9, 127.8, 127.8, 126.7, 126.2, 126.0, 125.9, 109.3, 84.5, 83.9, 78.6, 72.2, 70.7, 70.7, 70.7, 70.6, 70.6, 70.0, 67.2, 64.1, 50.7, 26.8, 26.8, 26.8, 19.2; **HRMS** (ESI-MS): m/z calcd. For $C_{40}H_{51}N_3O_8Si[M+Na]^+$: 752.3343; Found: 752.3360.

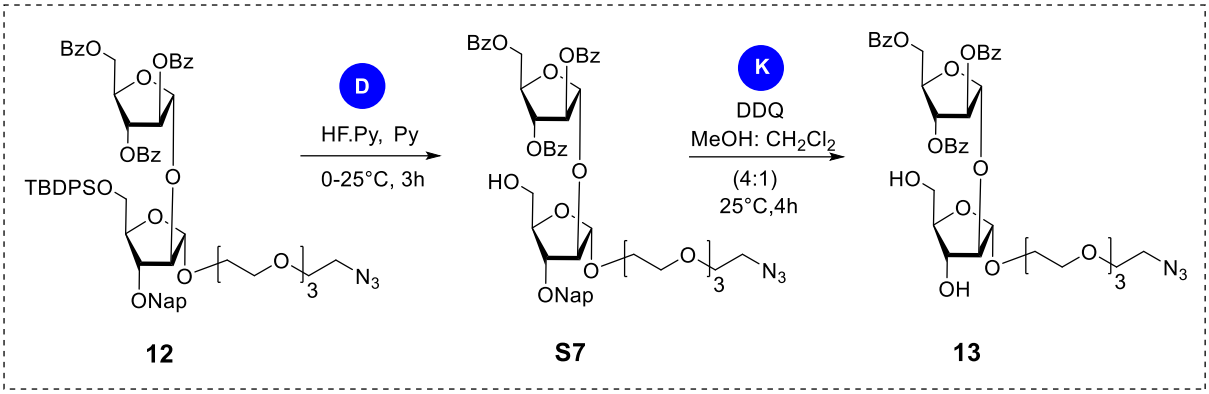
(2-(2-(2-(2-azidoethoxy)ethoxy)ethoxy)ethyl)-3-*O*-napthylmethyl-5-*O*-^{tert}butyldiphenylsilyl-2-*O*-(2,3-di-*O*-benzoyl-5-*O*-benzoyl-α-D-arabinofuranosyl)-α-D-arabinofuranoside (12):

Compound **8** was converted to glycosyl acceptor **S6** according to the general experimental **Procedure N** and then glycosyl accepter **S6** glycosylated with glycosyl donor **5**[49] according to the general **Procedure B** gave compound **12**. (88%, pale yellow syrup):



[α]$_D^{25}$ = +28.8 (*c* = 0.06, $CHCl_3$); **IR** (cm^{-1}, $CHCl_3$): 3030, 2830, 2210, 2150,1400, 1320, 1010, 980, 900; **^{1}H NMR** (400 MHz, $CDCl_3$): δ 8.04 (dd, *J* = 8.3, 1.2 Hz, 2H), 7.99 (ddd, *J* = 8.3, 4.7, 1.2 Hz, 4H), 7.77 – 7.58 (m, 9H), 7.52 (dtd, *J* = 10.2, 7.5, 1.3 Hz, 2H), 7.44 – 7.34 (m, 9H), 7.34 – 7.26 (m, 6H), 5.58 – 5.55 (m, 1H), 5.45 (d, *J* = 1.3 Hz, 1H), 5.34 (s, 1H), 5.16 (s, 1H), 4.84 – 4.66 (m, 4H), 4.60 (q, *J* = 4.9 Hz, 1H), 4.40 – 4.37 (m, 1H), 4.21 (q, *J* = 4.4 Hz, 1H), 4.13 (dd, *J* = 6.0, 2.4 Hz, 1H), 3.86 – 3.81 (m, 3H), 3.67 – 3.56 (m, 14H), 3.34 – 3.30 (m, 2H), 0.99 (s, 9H); **^{13}C NMR** (101 MHz, $CDCl_3$): δ 166.3, 165.8, 165.4, 135.8, 135.7, 135.4, 133.7, 133.6, 133.5, 133.5, 133.3, 133.2, 133.1, 130.0, 130.0, 130.0, 130.0, 129.9, 129.9, 129.8, 129.8, 129.8, 129.1, 128.7, 128.7, 128.7, 128.6, 128.6, 128.6, 128.5, 128.5, 128.5, 128.3, 128.0, 127.8, 127.8, 127.8, 127.8, 127.7, 126.8, 126.1, 125.9, 125.8, 107.0, 105.5, 86.6, 83.0, 82.6, 82.6, 81.5, 77.8, 72.3, 70.7, 70.7, 70.7, 70.7, 70.4, 70.1, 66.9, 63.9, 63.8, 50.7, 26.9, 26.9, 26.9, 19.4; **HRMS** (ESI-MS): m/z calcd. For $C_{66}H_{71}N_3O_{15}Si[M+Na]^+$: 1196.4552; Found: 1196.4560.

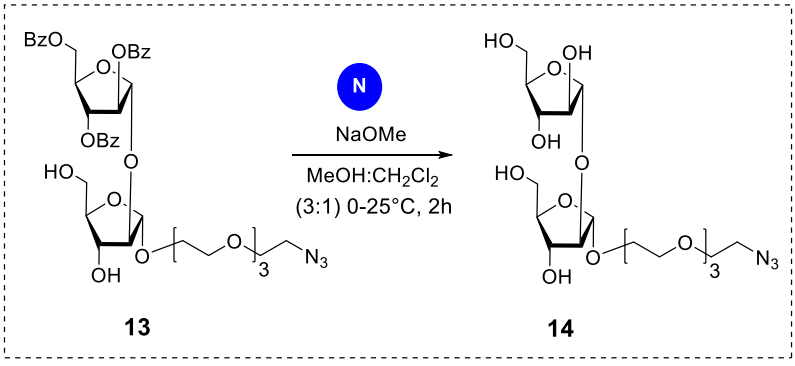
(2-(2-(2-(2-azidoethoxy)ethoxy)ethoxy)ethyl)-2-*O*-(2,3-di-*O*-benzoyl-5-*O*-benzoyl-α-D-arabinofuranosyl)-α-D-arabinofuranoside (13):



Compound **12** was converted to **S7** according to the general experimental **Procedure D** and without purification, directly **S7** converted to **13** according to the general **Procedure K**. (Yield 58% over two steps, pale yellow syrup): **$[\alpha]_D^{25}$** = +11.8 (*c* = 0.06, $CHCl_3$); **IR** (cm^{-1}, $CHCl_3$): 3530, 3410, 2820, 2260, 2170,1400, 1335, 1030, 1010, 970; **^{1}H NMR** (400 MHz, $CDCl_3$): δ 8.07 – 8.03 (m, 4H), 7.99 (d, *J* = 8.3 Hz, 2H), 7.61 – 7.56 (m, 2H), 7.54 – 7.44 (m, 4H), 7.42 – 7.37 (m, 2H), 7.31 (s, 1H), 5.60 (d, *J* = 4.9 Hz, 1H), 5.48 (d, *J* = 2.7 Hz, 2H), 5.22 (s, 1H), 4.82 (dd, *J* = 11.9, 3.5 Hz, 1H), 4.69 (dd, *J* = 11.9, 4.9 Hz, 1H), 4.61 (q, *J* = 4.7 Hz, 1H), 4.27 – 4.25 (m, 1H), 4.18 (q, *J* = 3.7 Hz, 1H), 4.12 (d, *J* = 2.7 Hz, 1H), 3.93 – 3.80 (m, 4H), 3.64 (t, *J* = 3.7 Hz, 12H), 3.37 (t, *J* = 5.0 Hz, 2H); **^{13}C NMR** (101 MHz, $CDCl_3$): δ 166.3, 165.8, 165.7, 133.8, 133.7, 133.2, 130.0, 130.0, 130.0, 130.0, 129.8, 129.8, 129.7, 129.0, 128.8, 128.6, 128.6, 128.6, 128.6, 128.4, 128.4, 106.0, 105.4, 86.3, 86.1, 82.5, 81.5, 77.6, 76.0, 70.7, 70.6, 70.6, 70.5, 70.1, 70.0, 65.7, 63.7, 62.8, 50.7; **HRMS** (ESI-MS): m/z calcd. For $C_{39}H_{45}N_3O_{15}$ $[M+Na]^+$: 818.2748; Found: 818.2750

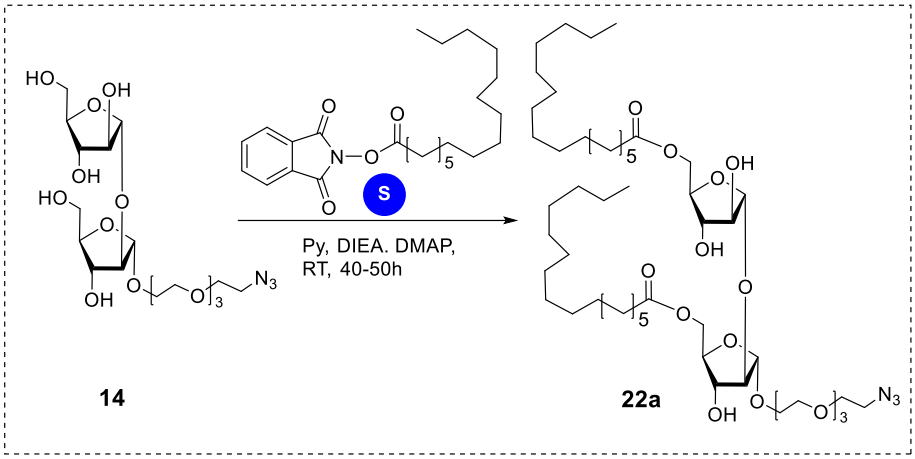
(2-(2-(2-(2-azidoethoxy)ethoxy)ethoxy)ethyl)-2-*O*-(-α-D-arabinofuranosyl)-α-D-arabinofuranoside

(14):Compound **13** was converted to compound **14** according to the general experimental **Procedure N**. (Yield 79%, pale yellow syrup): **$[\alpha]_D^{25}$** = +12.8 (*c* = 0.06, $CHCl_3$); **IR** (cm^{-1}, $CHCl_3$): 3540, 2940, 2310, 2140, 1710, 1370, 1044, 970, 870; **^{1}H NMR** (400 MHz, CD_3OD): δ 5.09 (d, *J* = 1.1 Hz,



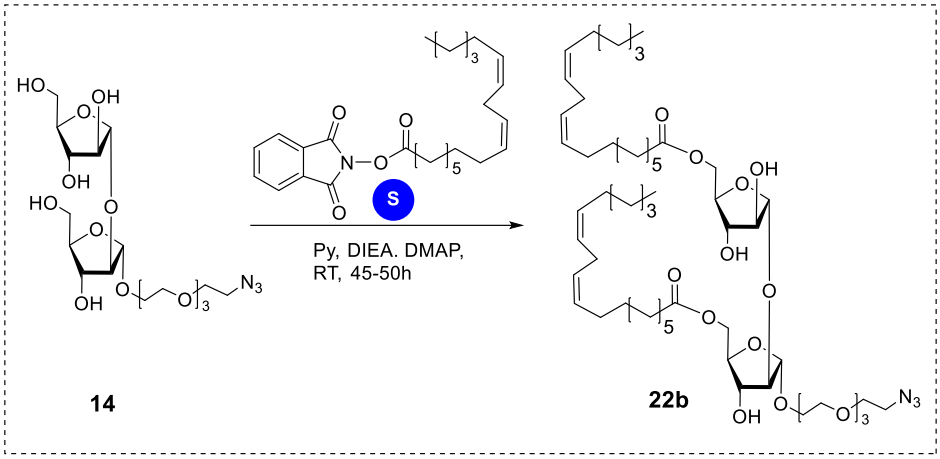
1H), 5.08 (d, *J* = 1.6 Hz, 1H), 4.06 (dd, *J* = 3.5, 1.4 Hz, 1H), 4.01 (dd, *J* = 3.8, 1.7 Hz, 1H), 3.96 (qd, *J* = 7.5, 3.0 Hz, 3H), 3.88 – 3.83 (m, 2H), 3.81 – 3.78 (m, 1H), 3.76 (t, *J* = 2.6 Hz, 1H), 3.71 – 3.62 (m, 16H), 3.42 – 3.39 (m, 2H); **^{13}C NMR** (101 MHz, CD_3OD): δ 109.4, 108.1, 89.8, 85.6, 84.5, 83.8, 78.7, 77.4, 71.6, 71.6, 71.5, 71.5, 71.4, 71.1, 67.8, 63.0, 62.7, 51.8; **HRMS** (ESI-MS): m/z calcd. For $C_{18}H_{33}N_3O_{12}$ [M+Na]$^+$: 506.1962; Found: 506.1962.

(2-(2-(2-(2-azidoethoxy)ethoxy)ethoxy)ethyl)-5-*O*-(hexadecanoyl)-2-*O*-(5-*O* hexadecanoyl-α-D-arabinofuranosyl)-α-D-arabinofuranoside (22a): Compound **14** was converted to **22a** according to the general experimental **Procedure S**. (Yield 19%, pale yellow syrup) **$[\alpha]_D^{25}$** = +16.6 (*c* = 0.06, $CHCl_3$); **IR** (cm^{-1}, $CHCl_3$): 3520, 3340, 2840, 2220, 2180, 1700, 1455,1310, 1060, 1010; **^{1}H NMR** (400 MHz, $CDCl_3$): δ 5.15 (s, 1H), 5.14 (s, 1H), 4.29 – 4.23 (m, 3H), 4.22 – 4.16 (m, 3H), 4.15 – 4.11 (m, 2H), 3.94 – 3.88 (m, 3H), 3.68 – 3.59 (m, 13H), 3.41 – 3.37 (m, 2H), 2.34 (td, *J* = 7.6, 2.4 Hz, 4H), 1.64 – 1.58 (m, 4H), 1.25 (s, 48H), 0.87 (t, *J* = 6.8 Hz, 6H); **^{13}C NMR** (101 MHz, $CDCl_3$): δ 174.2, 173.8, 107.7, 106.2, 85.8, 83.1, 83.0, 81.0, 77.8, 76.4, 70.8, 70.7, 70.6, 70.5, 70.2, 70.1, 66.0, 63.9, 63.8, 50.8, 34.3, 34.2, 32.1, 32.1, 29.8, 29.8, 29.8, 29.8, 29.8, 29.8, 29.8, 29.8, 29.8, 29.8, 29.8, 29.8, 29.6, 29.6, 29.5, 29.5, 29.4, 29.4, 29.3, 29.3, 25.0, 25.0, 22.8, 22.8, 14.3, 14.3; **HRMS** (ESI-MS): m/z calcd. For $C_{50}H_{93}N_3O_{14}$ [M+Na]$^+$: 982.6555; Found: 982.6581.



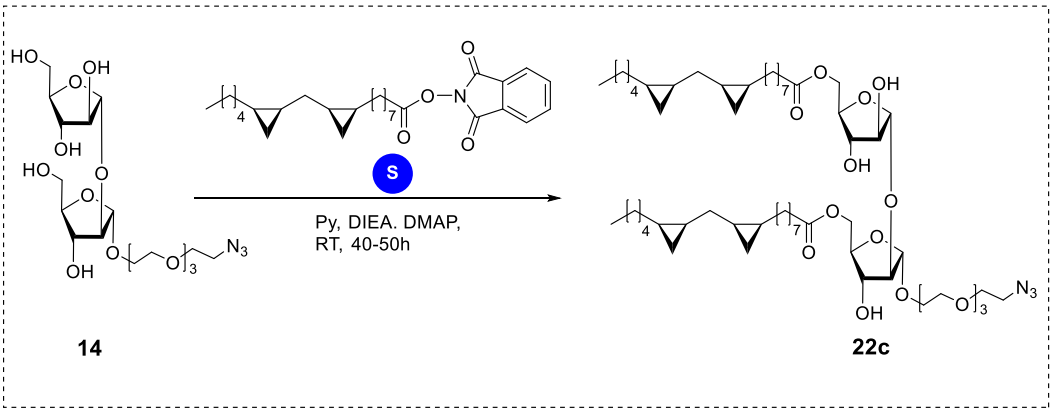
(2-(2-(2-(2-azidoethoxy)ethoxy)ethoxy)ethyl)-5-*O*-(9*Z*,12*Z*-octadecadienoyl)-2-*O*-(5-*O*-9*Z*,12*Z*-octadecadienoyl-α-D-arabinofuranosyl)-α-D-arabinofuranoside (22b): Compound **14** was converted to **22b** according to the general experimental **Procedure S**. (Yield 18%, pale yellow syrup): **$[\alpha]_D^{25}$** = +28.8 (*c* = 0.06, $CHCl_3$); **IR** (cm^{-1}, $CHCl_3$): 3580, 3050, 2310, 2150, 1755, 1400, 1330, 1250, 1080, 1010; **^{1}H NMR** (400 MHz, $CDCl_3$): δ 5.42 – 5.28 (m, 8H), 5.16 (s, 1H), 5.15 – 5.13 (d, 1H), 4.28 – 4.11 (m, 8H), 3.91 (ddd, *J* = 9.8, 6.1, 3.3 Hz, 3H), 3.68 – 3.59 (m, 13H), 3.41 – 3.37 (m, 2H), 2.76 (t, *J* = 6.6 Hz, 4H), 2.34 (td, *J* = 7.6, 2.3 Hz, 4H), 2.04 (q, *J* = 6.8 Hz, 8H), 1.65 – 1.58 (m, 4H), 1.37 – 1.27 (m, 28H), 0.88 (t, *J* = 6.9 Hz, 6H); **^{13}C NMR** (101 MHz,

$CDCl_3$): δ 174.2, 173.7, 130.4, 130.4, 130.2, 130.2, 128.2, 128.2, 128.0, 128.0, 107.6, 106.1, 85.6, 83.3, 83.1, 80.9, 77.8, 76.3, 70.8, 70.7, 70.7, 70.5, 70.2, 70.1, 65.9, 63.8, 63.7, 50.8, 34.3, 34.2, 31.7, 29.8, 29.7, 29.5, 29.5, 29.3, 29.3, 29.3, 29.3, 29.2, 29.2, 29.2, 29.2, 27.3, 27.3, 27.3, 27.3, 25.8, 25.0, 24.9, 22.7, 22.7, 14.2, 14.2; **HRMS** (ESI-MS): m/z calcd. For $C_{54}H_{93}N_3O_{14}$ $[M+Na]^+$: 1030.6555; Found: 1030.6578



(2-(2-(2-(2-azidoethoxy)ethoxy)ethoxy)ethyl)-5-*O*-(8-(2-((2-pentylcyclopropyl) methyl)cyclopropyl)octanoyl)-2-*O*-(5-*O*-(8-(2-((2-pentylcyclopropyl) methyl)cyclopropyl)octanoyl)-α-D-arabinofuranosyl)-α-D-arabinofuranoside (22c):

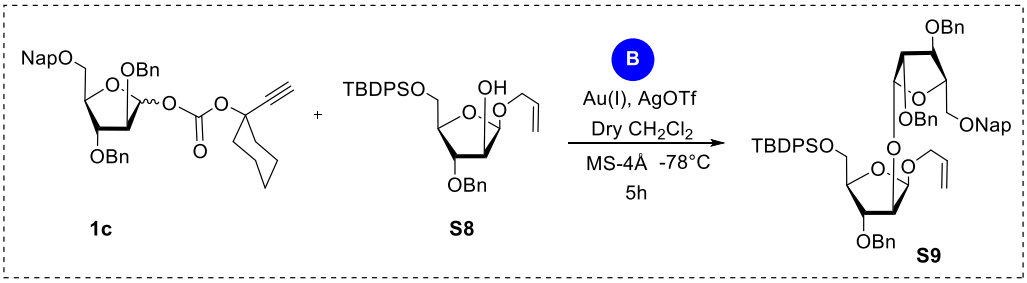
Compound **14** was converted to **22c** according to the general experimental **Procedure S**. (Yield 18%, pale yellow syrup): **$[\alpha]_D^{25}$** = +37.2 (*c* = 0.06, $CHCl_3$); **IR** (cm^{-1}, $CHCl_3$): 3540, 3210, 2730, 2260, 2160, 1710, 1425, 1360, 1210, 1070, 980; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 5.16 (s, 1H), 5.14 (s, 1H), 4.28 – 4.11 (m, 7H), 3.95 – 3.86 (m, 3H), 3.71 – 3.54 (m, 14H), 3.42 – 3.37 (m, 2H), 2.34 (td, *J* = 7.6, 2.3 Hz, 4H), 1.64 – 1.59 (m, 4H), 1.34 – 1.24 (m, 40H), 0.89 – 0.86 (m, 6H), 0.81 – 0.75 (m, 4H), 0.71 – 0.65 (m, 4H), 0.61 (dt, *J* = 8.3, 4.1 Hz, 4H), -0.25 – -0.32 (m, 4H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 174.2, 173.7, 107.7, 106.1, 85.7, 83.2, 83.1, 80.9, 77.8, 76.3, 70.8, 70.7, 70.6, 70.5, 70.2, 70.1, 66.0, 63.8, 63.7, 50.8, 34.3, 34.2, 32.1, 32.0, 30.3,



30.0, 29.8, 29.6, 29.6, 29.5, 29.5, 29.3, 29.3, 29.0, 29.0, 28.8, 28.8, 28.2, 28.0, 25.0, 25.0, 22.9, 22.9, 16.2, 16.2, 16.1, 16.1, 16.0, 16.0, 16.0, 15.8, 15.7, 14.3, 14.3, 11.2, 11.2, 11.0, 11.0; **HRMS** (ESI-MS): m/z calcd. For $C_{58}H_{101}N_3O_{14}$ $[M+Na]^+$: 1086.7181; Found: 1086.7170.

Allyl 2-*O*-(2,3-*O*-dibenzyl-5-*O*-naphthylmethyl-β-D-arabinofuranosyl)-3-*O*-benzyl-5-*O*-*tert*butyldiphenylsilyl-β-D-arabinofuranoside (S9):

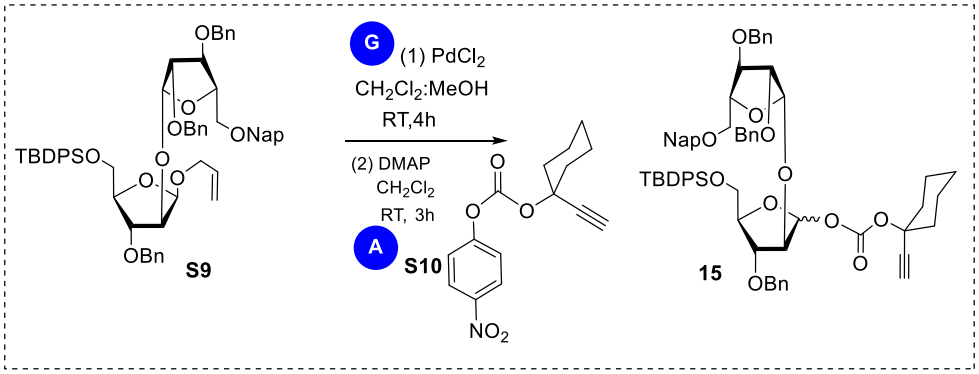
The glycosyl donor **1c**[44a] and the glycosyl acceptor **S8**[44a] were glycosylated according to the general reaction **Procedure B** as detailed above to give the **S9**. (Yield 72%, pale yellow syrup): **$[\alpha]_D^{25}$** = -50.0 (*c* = 1.0, $CHCl_3$); **IR** (cm^{-1}, $CHCl_3$): 3032, 2931, 1458, 1360, 1230, 1103, 1030, 698; **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.80 – 7.71 (m, 3H), 7.68 – 7.59 (m, 5H), 7.46 – 7.27 (m, 15H), 7.23 (s, 10H), 5.75 (ddt, *J* = 16.8, 11.6, 5.9 Hz, 1H), 5.16 (d, *J* = 17.0 Hz, 3H), 5.05 (d, *J* = 10.3 Hz, 1H), 4.80 (d, *J* = 11.4 Hz, 1H), 4.72 – 4.67 (m, 1H), 4.62 – 4.53 (m, 4H), 4.50 – 4.39 (m, 3H), 4.26 (t, *J* = 6.0 Hz, 1H), 4.12 (ddd, *J* = 20.6, 11.2, 4.9 Hz, 5H), 3.90 (dd, *J* = 12.8, 6.8 Hz, 1H), 3.77 – 3.70 (m, 2H), 3.60 (dd, *J* = 22.8, 8.6 Hz, 2H), 1.05 (s, 9H); **^{13}C NMR** (101 MHz, $CDCl_3$): δ 138.4, 138.3, 138.1, 135.8, 135.7, 135.7, 135.7, 135.7, 134.0, 133.5, 133.4, 133.1, 129.8, 129.8, 128.5, 128.5, 128.4, 128.4, 128.4, 128.4, 128.2, 128.2, 128.2, 128.0, 127.9, 127.9, 127.9, 127.8, 127.8, 127.8, 127.8, 127.8, 127.8, 127.8, 127.8, 127.7, 127.6, 126.4, 126.1, 125.9, 125.8, 117.8, 99.0, 98.7, 84.0, 83.2, 82.9, 82.3, 81.0, 79.5, 73.3, 72.8, 72.4, 72.4, 71.8, 68.2, 66.0, 27.0, 27.0, 27.0, 19.4. **HRMS** (ESI-MS): m/z calcd. For $C_{61}H_{66}O_9Si$ $[M+Na]^+$: 993.4374; Found: 993.4379.



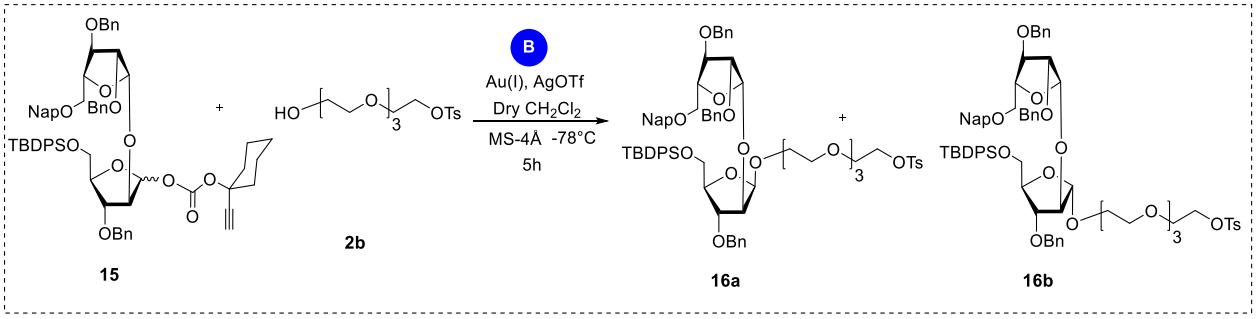
1-*O*-(((1-ethylnylcyclohexyl)oxy)carbonyl)-2-*O*-(2,3-*O*-dibenzyl-5-*O*-naphthylmethyl-β-D-arabinofuranosyl)-3-*O*-benzyl-5-*O*-*tert*butyldiphenylsilyl-α-D-arabinofuranoside (15):

Compound **S9** was converted to **15** according to the general experimental **Procedure G and** general experimental **Procedure A** (57% over 2 steps, pale yellow syrup): **$[\alpha]_D^{25}$** = +12.2 (*c* = 1.0, $CHCl_3$); **IR** (cm^{-1}, $CHCl_3$): 3010, 2911, 2180, 2100, 1498, 1340, 1260, 1102, 1050, 890; **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.79 – 7.68 (m, 3H), 7.66 – 7.61 (m, 5H), 7.46 – 7.25 (m, 15H), 7.23 (dd, *J* = 4.5, 2.5 Hz, 10H), 6.05 (s, 1H), 5.19 (d, *J* = 3.6 Hz, 1H), 4.67 (d, *J* = 11.8 Hz, 1H), 4.63 – 4.58 (m, 2H), 4.58 – 4.54 (m, 2H), 4.51 (d, *J* = 11.2 Hz, 3H), 4.47 (d, *J* = 11.8 Hz, 1H), 4.36 (q,

J = 5.3 Hz, 1H), 4.17 – 4.12 (m, 2H), 4.11 – 4.07 (m, 2H), 3.83 – 3.77 (m, 2H), 3.61 – 3.53 (m, 2H), 2.62 (s, 1H), 2.19 (t, *J* = 14.0 Hz, 2H), 1.87 (dq, *J* = 12.1, 6.1, 3.7 Hz, 2H), 1.62 (ddd, *J* = 18.0, 9.8, 4.5 Hz, 4H), 1.36 – 1.25 (m, 2H), 1.02 (s, 9H); **^{13}C NMR** (101 MHz, $CDCl_3$): δ 151.6, 138.2, 138.0, 137.7, 135.8, 135.7, 135.5, 133.5, 133.4, 133.3, 133.1, 129.8, 129.8, 128.6, 128.6, 128.5, 128.5, 128.4, 128.4, 128.3, 128.3, 128.1, 128.1, 128.0, 128.0, 127.9, 127.9, 127.9, 127.9, 127.9, 127.8, 127.8, 127.8, 127.8, 127.7, 127.6, 127.6, 126.4, 126.2, 126.0, 125.7, 103.3, 100.3, 85.6, 84.7, 83.9, 83.9, 82.9, 82.9, 80.2, 78.1, 75.3, 73.3, 72.6, 72.5, 72.3, 72.2, 63.7, 37.0, 36.8, 27.0, 27.0, 27.0, 25.1, 22.7, 22.7, 19.4; **HRMS** (ESI-MS): m/z calcd. For $C_{67}H_{72}O_{11}Si$ $[M+Na]^+$: 1103.4742; Found: 1103.4741.



(2-(2-(2-(2-tosylethoxy)ethoxy)ethoxy)ethyl)-2-*O*-(2,3-*O*-dibenzyl-5-*O*-naphthylmethyl-β-D-arabinofuranosyl)-3-*O*-benzyl-5-*O*-*tert*butyldiphenylsilyl-α-D-arabinofuranoside(16b): The

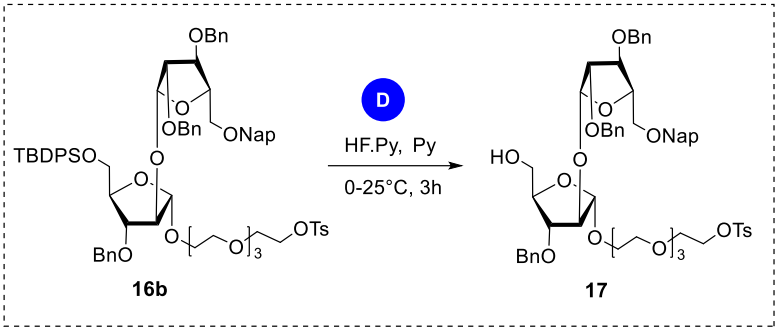


glycosyl donor **15** and the glycosyl acceptor **2b**[47] were glycosylated according to the general reaction **Procedure B** as detailed above to give both isomers (1:1). Separated compound **16b** from other isomers (Yield 48%, pale yellow syrup): **$[\alpha]_D^{25}$** = +33.3 (*c* = 0.06, $CHCl_3$); **IR** (cm^{-1}, $CHCl_3$): 3080, 3015, 2920, 2768, 2308, 1750, 1578, 1428, 1270, 1107, 1000; **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.78 (d, *J* = 8.2 Hz, 3H), 7.72 (d, *J* = 8.7 Hz, 1H), 7.69 – 7.64 (m, 5H), 7.61 (s, 1H), 7.45 – 7.41 (m, 2H), 7.40 – 7.36 (m, 2H), 7.35 – 7.28 (m, 12H), 7.24 (d, *J* = 2.3 Hz, 6H), 7.20 (s, 4H), 5.11 (d, *J* = 4.0 Hz, 1H), 5.00 (s, 1H), 4.64 (dd, *J* = 19.1, 10.4 Hz, 3H), 4.58 – 4.52 (m, 3H), 4.49 – 4.42 (m, 2H), 4.37 – 4.33 (m, 1H), 4.15 – 4.10 (m, 5H), 4.09 – 4.05 (m, 2H), 3.80 (dt, *J* = 7.7, 4.8 Hz, 3H), 3.65 – 3.52 (m, 15H), 2.41 (s, 3H), 1.03 (s, 9H); **^{13}C NMR** (101 MHz,

$CDCl_3$): δ 144.9, 138.2, 138.2, 137.9, 135.8, 135.8, 135.6, 133.6, 133.6, 133.3, 133.1, 133.0, 129.9, 129.9, 129.8, 128.6, 128.6, 128.4, 128.4, 128.4, 128.4, 128.2, 128.1, 128.1, 128.1, 128.1, 128.1, 128.1, 128.0, 128.0, 127.8, 127.8, 127.8, 127.8, 127.8, 127.8, 127.8, 127.7, 127.7, 127.7, 127.7, 127.6, 126.4, 126.1, 125.9, 125.7, 106.2, 100.3, 85.9, 84.1, 83.9, 83.2, 82.7 80.2, 73.3, 72.5, 72.5, 72.4, 72.3, 70.8, 70.7, 70.7, 70.6, 70.5, 69.3, 68.7, 66.9, 64.2, 27.0, 27.0, 27.0, 21.7, 19.4; **HRMS** (ESI-MS): m/z calcd. For $C_{73}H_{84}O_{15}SSi[M+Na]^+$: 1283.5198; Found: 1283.5180.

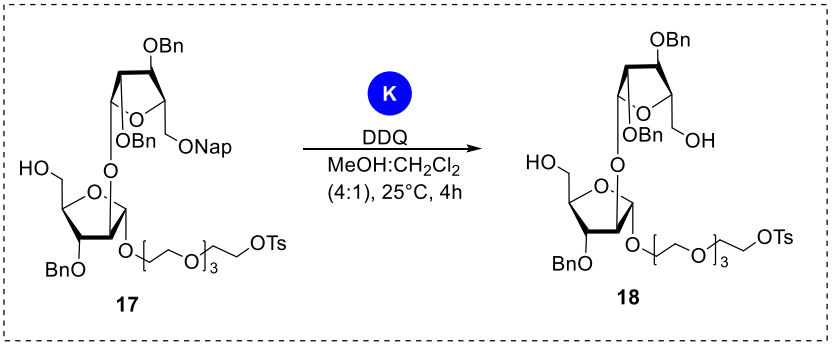
(2-(2-(2-(2-tosylethoxy)ethoxy)ethoxy)ethyl)-2-*O*-(2,3-*O*-dibenzyl-5-*O*-naphthylmethyl-β-D-arabinofuranosyl)-3-*O*-benzyl-α-D-arabinofuranoside (17):

Compound **16b** was converted to **17** according to the general experimental **Procedure D**. (Yield 76%, pale yellow syrup): **$[\alpha]_D^{25}$** = +16.6 (*c* = 1.0, $CHCl_3$); **IR** (cm^{-1}, $CHCl_3$): 3580, 3350, 3080, 2890, 2718, 2318, 1720, 1538, 1408, 1260, 1107, 1000; **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.83 – 7.67 (m, 7H), 7.47 – 7.24 (m, 19H), 5.10 – 5.04 (m, 1H), 4.99 (s, 1H), 4.68 – 4.55 (m, 8H), 4.43 (d, *J* = 11.7 Hz, 1H), 4.30 (s, 1H), 4.10 (d, *J* = 23.3 Hz, 8H), 3.69 – 3.54 (m, 16H), 2.41 (s, 3H); **^{13}C NMR** (101 MHz, $CDCl_3$): δ 144.9, 138.1, 138.1, 137.7, 135.5, 133.3, 133.1, 133.1, 129.9, 129.9, 128.6, 128.4, 128.4, 128.4, 128.4, 128.3, 128.2, 128.2, 128.1, 128.1, 128.1, 128.0, 127.8, 127.8, 127.8, 127.8, 127.8, 127.7, 127.7, 127.7, 126.5, 126.2, 126.0, 125.8, 106.4, 100.5, 85.6, 84.1, 83.5, 83.2, 82.8, 80.2, 73.3, 72.7, 72.6, 72.3, 72.1, 70.8, 70.7, 70.7, 70.5, 70.5, 69.3, 68.7, 66.8, 62.6, 21.7; **HRMS** (ESI-MS): m/z calcd. For $C_{57}H_{66}O_{15}S$ $[M+Na]^+$: 1045.4020; Found: 1045.4038.



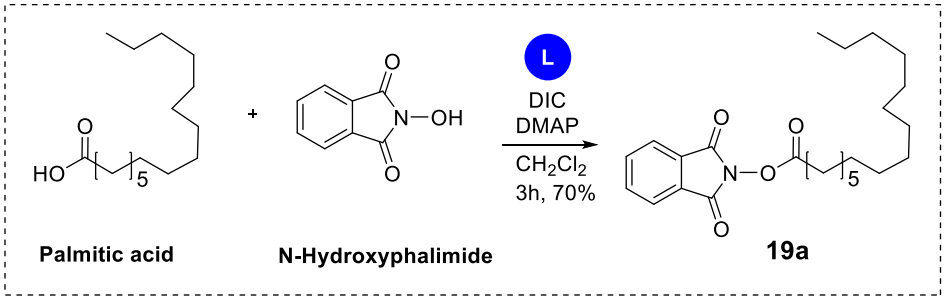
(2-(2-(2-(2-tosylethoxy)ethoxy)ethoxy)ethyl)-2-*O*-(2,3-*O*-dibenzyl-β-D-arabinofuranosyl)-3-*O*-benzyl-α-D-arabinofuranoside (18):

Compound **17** was converted to **18** according to the general experimental **Procedure K.** (yield 72%, pale yellow syrup): **$[\alpha]_D^{25}$** = +20.4 (*c* = 0.06, $CHCl_3$); **IR** (cm^{-1}, $CHCl_3$): 3560, 3480, 3140, 2880, 2628, 2180,

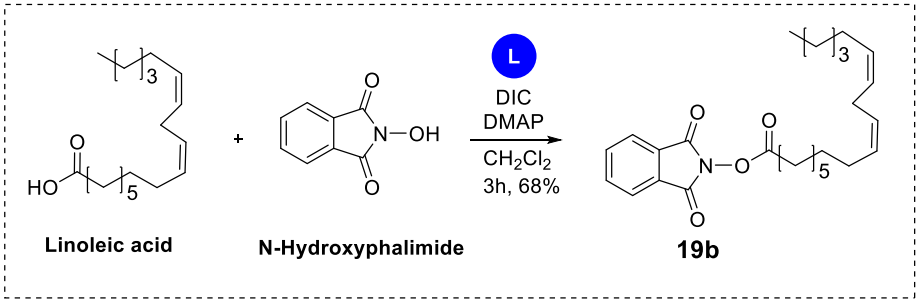


1720, 1530, 1408, 1240, 1120, 990; **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.80 – 7.77 (m, 2H), 7.35 (d, *J* = 4.0 Hz, 4H), 7.34 – 7.27 (m, 14H), 5.05 (d, *J* = 4.6 Hz, 1H), 5.03 (s, 1H), 4.69 (dd, *J* = 14.7, 11.8 Hz, 2H), 4.61 – 4.57 (m, 3H), 4.52 (d, *J* = 11.9 Hz, 1H), 4.25 – 4.22 (m, 2H), 4.18 (dd, *J* = 5.8, 2.5 Hz, 1H), 4.14 – 4.11 (m, 3H), 4.08 (dd, *J* = 7.3, 4.6 Hz, 1H), 3.98 (ddd, *J* = 6.4, 5.1, 3.0 Hz, 1H), 3.84 – 3.77 (m, 2H), 3.66 – 3.60 (m, 8H), 3.59 – 3.54 (m, 8H), 2.43 (s, 3H); **^{13}C NMR** (101 MHz, $CDCl_3$): δ 144.9, 138.1, 137.9, 137.6, 133.1, 129.9, 129.9, 128.7, 128.7, 128.5, 128.5, 128.5, 128.5, 128.2, 128.2, 128.2, 128.1, 128.1, 127.9, 127.9, 127.9, 127.9, 127.8, 127.8, 106.5, 100.7, 86.7, 84.2, 83.0, 82.8, 82.0, 80.6, 72.8, 72.8, 72.4, 70.8, 70.7, 70.6, 70.6, 70.4, 69.4, 68.8, 66.8, 63.4, 62.3, 21.7; **HRMS** (ESI-MS): m/z calcd. For $C_{46}H_{58}O_{15}S$ $[M+Na]^+$: 905.3394; Found: 905.3390.

1,3-dioxoisoindolin-2-yl palmitate (19a): Compound **19a** synthesized from commercially available N-Hydroxyphalimide and palmitic acid according to the general experimental **Procedure L**. (Yield-70%); **IR** (cm^{-1}, $CHCl_3$): 2200, 1790, 1730, 1488, 1322, 1260, 1003, 970, 900, 870; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.88 (tt, *J* = 4.8, 2.2 Hz, 2H), 7.79 (td, *J* = 5.2, 1.9 Hz, 2H), 2.66 (t, *J* = 7.5 Hz, 2H), 1.78 (t, *J* = 7.5 Hz, 2H), 1.47 – 1.40 (m, 2H), 1.25 (s, 22H), 0.89 – 0.85 (m, 3H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 169.7, 162.1, 162.1, 134.7, 134.7, 128.9, 128.9, 123.9, 123.9, 31.9, 31.1, 29.7, 29.7, 29.6, 29.6, 29.6, 29.5, 29.3, 29.7, 29.3, 28.8, 24.9, 22.7, 14.3; **HRMS** (ESI-MS): m/z calcd. For $C_{24}H_{35}NO_4[M+Na]^+$: 401.2566; Found: 401.2570.

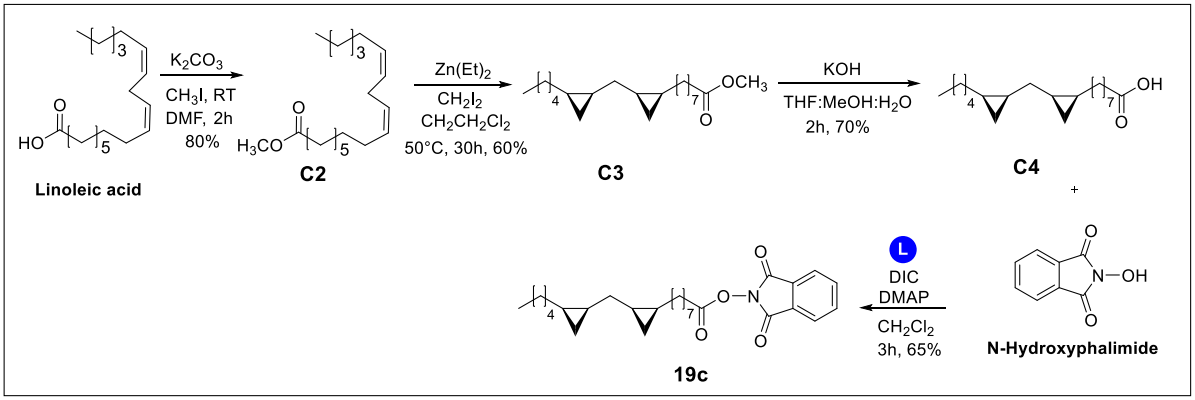


1,3-dioxoisoindolin-2-yl (9Z,12Z)-octadeca-9,12-dienoate(19b): Compound **19b** synthesized from commercially available N-hydroxyphalimide and Linoleic acid according to the general experimental **Procedure L**. (Yield-68%); **IR** (cm^{-1}, $CHCl_3$): 2210, 1730, 1680, 1640, 1488, 1322, 1260, 1003, 970, 900, 840; **^{1}H**



NMR (400 MHz, $CDCl_3$) δ 7.88 (dd, *J* = 5.5, 3.1 Hz, 2H), 7.78 (dd, *J* = 5.5, 3.1 Hz, 2H), 5.36 (tdd, *J* = 10.9, 6.9, 3.9 Hz, 4H), 2.77 (t, *J* = 6.4 Hz, 2H), 2.66 (t, *J* = 7.5 Hz, 2H), 2.04 (q, *J* = 6.7, 5.6 Hz, 4H), 1.78 (p, *J* = 7.5 Hz, 2H), 1.37 – 1.28 (m, 14H), 0.88 (t, *J* = 6.9 Hz, 3H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 169.7, 162.2, 162.2, 134.8, 134.8, 130.4, 130.4, 129.8, 129.7, 128.2, 128.0, 124.0, 124.0, 31.6, 31.1, 29.6, 29.4, 29.4, 29.4, 28.9, 27.3, 27.3, 25.7, 24.7, 22.7, 14.9; **HRMS** (ESI-MS): m/z calcd. For $C_{26}H_{35}NO_4[M+Na]^+$: 425.2566; Found: 401.2588.

Synthesis of 19c:



Methyl 8-(2-((2-pentylcyclopropyl)methyl)cyclopropyl)octanoate(C3):

Compound **19c** synthesized from commercially available linoleic acid converted into **C3** over two steps. To a solution of linoleic acid methyl ester **C2** (1eq, 340µmol) in $CH_2CH_2Cl_2$, a 1.1 M n-hexane solution of diethyl zinc (25eq, 8.49mmol) was added under a nitrogen atmosphere with cooling with ice bath and stirred for 1h. Diiodomethane (50eq, 16.98mmol) was then added and the mixture was stirred at 60°C for 40h. After completing the reaction, the diethyl zinc was diluted by adding hexane, and then the reaction mixture was filtered through a pad of Celite®, and the filtrate was evaporated *in vacuo*. After that, the reaction mixture was transferred to a separating funnel and extracted with ethyl acetate. The combined organic layers were washed with cold water and brine solution, the organic layer was dried over anhydrous Na_2SO_4, concentrated *in vacuo* and the residue was purified by silica gel column chromatography (ethyl acetate/hexanes) to obtain the desired product. (Yield 48% over 2 steps, pink syrup): **IR** (cm^{-1}, $CHCl_3$): 2280, 1830, 1680, 1640, 1420, 1320, 1210, 1000, 950, 900, 810; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 3.66 (s, 3H), 2.30 (t, *J* = 7.6 Hz, 2H), 1.66 – 1.57 (m, 3H), 1.52 – 1.37 (m, 6H), 1.31 – 1.25 (m, 10H), 1.19 – 0.98 (m, 3H), 0.90 – 0.86 (m, 3H), 0.83 – 0.73 (m, 2H), 0.72 – 0.64 (m, 2H), 0.61 (dt, *J* = 8.3, 4.1 Hz, 2H), -0.25 – -0.32 (m, 2H); **^{13}C NMR**



C3

(101 MHz, $CDCl_3$ δ 174.5, 51.6, 34.3, 32.0, 30.3, 30.0, 29.6, 29.4, 29.3, 29.0, 28.8, 28.0, 25.1, 22.9,16.2, 16.1, 15.8, 15.8, 14.3, 11.2, 11.0; **HRMS** (ESI-MS): m/z calcd. For $C_{21}H_{38}O_2$ $[M+Na]^+$: 322.2872; Found:322.2800.

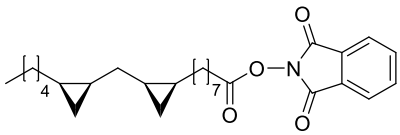
8-(2-((2-pentylcyclopropyl)methyl)cyclopropyl)octanoic acid (C4): Aqueous solution of KOH (3.5 eq, 705.36 µmol in 800µL Milli-Q water) was added dropwise to a solution of compound **C3**(1eq, 201.53 µmol) in THF: MeOH at 0°C. The reaction mixture was stirred for 5 h at 25°C. After completing the reaction 2*N* HCl was added to quench the reaction at 0°C, diluted with EtOAc, and washed successively with ice-cold water, saturated solution of $NaHCO_3$ (aq), and brine solution. The 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. (Yield 70%, light pink syrup): **IR** (cm^{-1}, $CHCl_3$): 2810, 2730, 2280, 1840, 1488, 1320, 1220, 1010, 960, 900, 830; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 2.35 (t, *J* = 7.5 Hz, 2H), 1.66 – 1.60 (m, 2H), 1.39 – 1.27 (m, 17H), 1.13 (dd, *J* = 12.5, 4.4 Hz, 2H), 1.03 (dt, *J* = 14.2, 7.9 Hz, 1H), 0.88 (d, *J* = 4.3 Hz, 3H), 0.82 – 0.74 (m, 2H), 0.73 – 0.65 (m, 2H), 0.61 (td, *J* = 8.3, 4.0 Hz, 2H), -0.28 (dq, *J* = 10.0, 5.1, 4.7 Hz, 2H); **^{13}C NMR** (101 MHz, $CDCl_3$ δ 180.3, 34.2, 32.0, 30.3, 30.0, 29.8, 29.6, 29.4, 29.2, 28.9, 28.0, 24.8, 22.9, 16.2, 16.1, 15.8, 15.8, 14.3, 11.2, 11.0;**HRMS** (ESI-MS): m/z calcd. For $C_{20}H_{36}O_2$ $[M+Na]^+$: 308.2715; Found:308.2760.



C4

1,3-dioxoisoindolin-2-yl 8-(2-((2-pentylcyclopropyl)methyl)cyclopropyl)octanoate(19c):

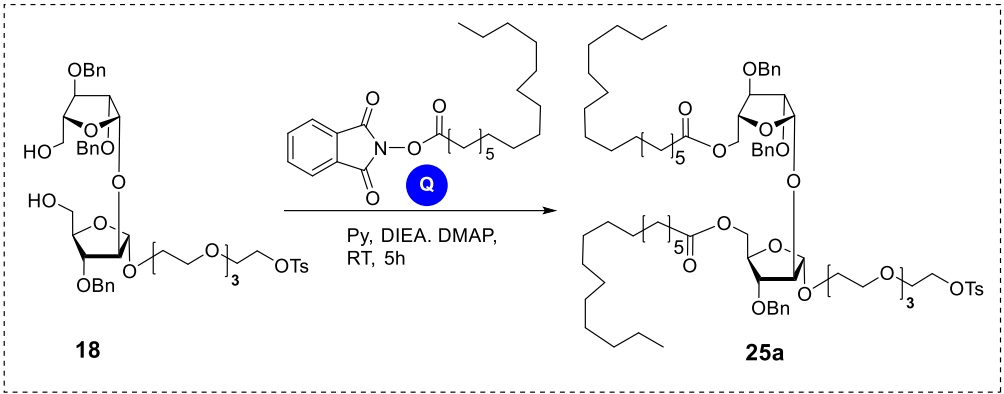
The cyclopropane derivative carboxylic acid **C4** (1.0eq, 162.07µmol), N-Hydroxyphalimide (1.0 eq, 178.28µmol), and DMAP (0.1eq, 16.21µmol) in anhydrous CH_2Cl_2 were stirred at 25°C. DIC (1.1 eq, 162.07µmol) was then added dropwise, and the mixture was allowed to stir until the acid was consumed (determined by TLC). The mixture was filtered (over Celite, SiO2, or through a fritted funnel) and rinsed with additional CH_2Cl_2. The solvent was removed under reduced pressure and purification by column chromatography afforded corresponding activated esters. (Yield- 65%); **IR** (cm^{-1}, $CHCl_3$): 2280, 2230, 1770, 1640, 1480, 1320, 1230, 1020, 960, 900; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.87 (td, *J* = 5.1, 1.9 Hz, 2H), 7.78 (dd, *J* = 5.5, 3.1 Hz, 2H), 2.66 (t, *J* = 7.5 Hz, 2H), 1.78 (p, *J* = 7.5 Hz, 2H), 1.53 – 1.35 (m, 12H), 1.29 (dd, *J* = 8.7, 5.7 Hz, 4H), 1.25 (d, *J* = 2.7 Hz, 1H), 1.22 – 0.98 (m, 3H), 0.91 – 0.86 (m, 3H), 0.83 – 0.74 (m, 2H), 0.74 – 0.65 (m, 2H), 0.60 (dtt, *J* = 8.3, 4.0, 2.0 Hz, 2H), -0.24 – -0.31 (m, 2H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 169.7,



19c

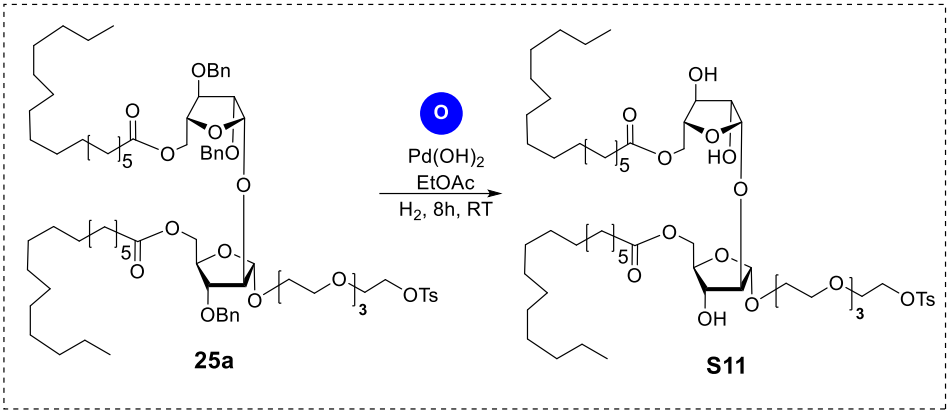
162.1, 162.1, 134.8, 134.8, 129.8, 129.8, 124.5, 124.5, 32.2, 31.2, 30.4, 30.2, 29.9, 29.9, 28.8, 28.8, 28.5, 28.0, 24.8, 22.8, 16.8, 16.4, 15.9, 15.7, 14.4, 11.6, 10.9; **HRMS** (ESI-MS): m/z calcd. For $C_{28}H_{39}NO_4[M+Na]^+$: 453.2879; Found: 453.2890.

(2-(2-(2-(2-tosylethoxy)ethoxy)ethoxy)ethyl)-3-*O*- benzyl-5-*O*-(hexadecanoyl)-2-*O*-(2,3di-*O*-benzyl-5-*O*-hexadecanoyl-β-D-arabinofuranosyl)-α-D-arabinofuranoside (25a) : Compound **18** was converted to **25a** according to the general experimental **Procedure Q.** (yield- 44%, pale yellow syrup): **$[\alpha]_D^{25}$** = +44.4(*c* = 1.0, $CHCl_3$); **IR** (cm^{-1}, $CHCl_3$): 3058, 2890, 2810, 2310, 1740, 1658, 1328, 1250, 1055, 960, 910; **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.79 (d, *J* = 7.7 Hz, 2H), 7.33 (d, *J* = 9.7 Hz, 17H), 5.10 (s, 1H), 5.00 (s, 1H), 4.70 (d, *J* = 11.5 Hz, 2H), 4.55 (dt, *J* = 33.8, 12.0 Hz, 5H), 4.33 – 4.20 (m, 5H), 4.14 – 4.09 (m, 5H), 3.97 – 3.93 (m, 1H), 3.84 – 3.80 (m, 1H), 3.66 – 3.54 (m, 13H), 2.43 (s, 3H), 2.30 (dt, *J* = 14.5, 7.6 Hz, 4H), 2.23 – 2.18 (m, 2H), 1.59 – 1.53 (m, 4H), 1.25 (s, 47H), 0.90 – 0.86 (m, 6H); **^{13}C NMR** (101 MHz, $CDCl_3$): δ 173.7, 173.5, 144.9, 137.9, 137.9, 137.6, 129.9, 129.9, 128.7, 128.7, 128.6, 128.6, 128.5, 128.5, 128.2, 128.2, 128.2, 128.1, 128.0, 127.9, 127.9, 127.9, 127.8, 127.8, 127.8, 127.8, 106.4, 100.8, 86.1, 84.4, 83.9, 82.7, 80.0, 79.0, 72.7, 72.7, 72.5, 70.8, 70.7, 70.7, 70.6, 70.5, 69.3, 68.8, 66.9, 66.1, 63.8, 34.2, 32.1, 32.1, 29.9, 29.8, 29.8, 29.8, 29.8, 29.8, 29.8, 29.8, 29.8, 29.8, 29.8, 29.7, 29.6, 29.5, 29.5, 29.5, 29.4, 29.3, 29.3, 29.2, 25.0, 24.9, 24.9, 22.8, 22.8, 21.8, 14.3, 14.3; **HRMS** (ESI-MS): m/z calcd. For $C_{78}H_{118}O_{17}S$ $[M+Na]^+$:1381.7987; Found: 1381.7990.



(2-(2-(2-(2-tosylethoxy)ethoxy)ethoxy)ethyl)-5-*O*-(hexadecanoyl)-2-*O*(5-*O* hexadecanoyl-β-D-arabinofuranosyl)-α-D-arabinofuranoside (S11) :

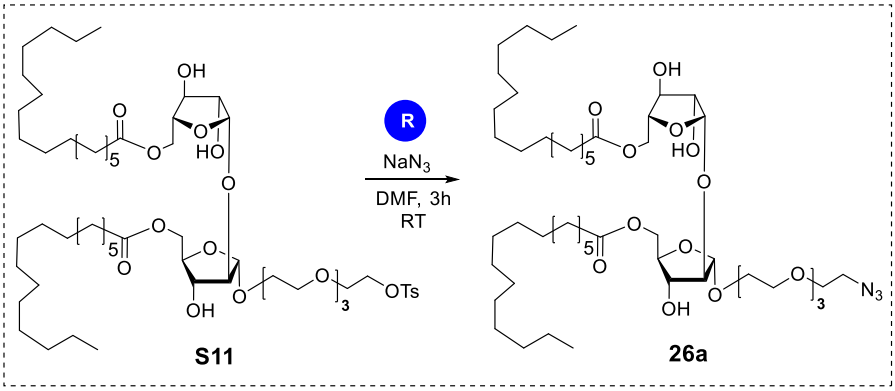
Compound **25a** was converted to **S11** according to the general experimental **Procedure O**. (yield- 55%, pale yellow syrup): **$[\alpha]_D^{25}$** = +40.8 (*c* = 1.0, $CHCl_3$); **IR** (cm^{-1}, $CHCl_3$): 3520, 3240, 3010, 2855, 2320, 1720, 1608, 1340, 1230, 1050, 960, 910; **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.79 (d, *J* = 8.1 Hz, 2H), 7.33 (d, *J* = 8.1 Hz, 2H), 5.04 (d, *J* = 2.7 Hz, 2H), 4.29 (dt, *J* = 9.9, 5.9 Hz, 2H), 4.21 – 4.14 (m, 5H), 4.08 (d, *J* = 4.7 Hz, 1H), 4.03 (d, *J* = 5.6 Hz, 3H), 3.95 – 3.92 (m, 1H),



3.86 (dd, *J* = 7.1, 4.3 Hz, 1H), 3.69 – 3.66 (m, 2H), 3.63 – 3.57 (m, 11H), 2.43 (s, 3H), 2.32 (t, *J* = 7.5 Hz, 4H), 1.62 – 1.57 (m, 4H), 1.24 (s, 48H), 0.86 (s, 6H); **^{13}C NMR** (101 MHz, $CDCl_3$): δ 174.1, 173.9, 145.0, 133.0, 130.0, 130.0, 128.1, 128.1, 105.6, 102.2, 89.3, 80.1, 80.0, 77.6, 76.2, 75.9, 70.8, 70.6, 70.5, 70.5, 70.4, 69.4, 68.8, 67.2, 65.4, 63.7, 34.2, 34.2, 34.0, 32.0, 32.0, 29.8, 29.8, 29.8, 29.8, 29.8, 29.8, 29.8, 29.7, 29.6, 29.6, 29.6, 29.5, 29.5, 29.4, 29.4, 29.4, 29.3, 29.2, 25.0, 25.0, 25.0, 22.8, 22.8, 21.7, 14.2, 14.2; **HRMS** (ESI-MS): m/z calcd. For $C_{57}H_{100}O_{17}S$ $[M+Na]^+$: 1111.6579; Found: 1111.6580.

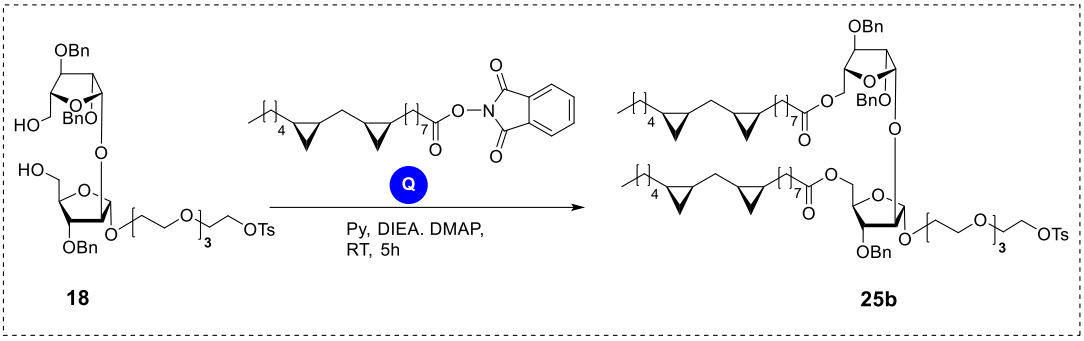
(2-(2-(2-(2-azidoethoxy)ethoxy)ethoxy)ethyl-5-*O*-(hexadecanoyl)-2-*O*-(5-*O* hexadecanoyl-β-D-arabinofuranosyl)-α-D-arabinofuranoside (26a):

Compound **S11** was converted to **26a** according to the general experimental **Procedure R**. (yield- 73%, pale yellow syrup): **$[\alpha]_D^{25}$** = +24.8 (*c* = 1.0, $CHCl_3$); **IR** (cm^{-1}, $CHCl_3$): 3510, 3210, 3000, 2850, 2160, 1710, 1640, 1310, 1230, 1020, 970, 900; **^{1}H NMR** (400 MHz, $CDCl_3$): δ 5.06 – 5.02 (m, 2H), 4.30 (dd, *J* = 9.5, 5.1 Hz, 2H), 4.22 – 4.16 (m, 3H), 4.11 – 4.02 (m, 4H), 3.95 – 3.92 (m, 1H), 3.87 (dd, *J* = 7.4, 4.1 Hz, 1H), 3.65 (m, 13H), 3.39 (t, *J* = 5.1 Hz, 2H), 2.33 (t, *J* = 7.6 Hz, 4H), 1.62 – 1.58 (m, 4H), 1.24 (s, 51H), 0.87 (s, 6H); **^{13}C NMR** (101 MHz, $CDCl_3$): δ 174.1, 173.9, 105.6, 102.2, 89.1, 80.2, 80.1, 77.7, 76.3, 76.0, 70.7, 70.7, 70.6, 70.5, 70.4, 70.1, 67.2, 65.4, 63.7, 50.7, 34.2, 34.2, 32.0, 32.0, 29.8, 29.8, 29.8, 29.8, 29.8, 29.8, 29.8, 29.8, 29.7, 29.6, 29.6, 29.6, 29.5, 29.5, 29.5, 29.4, 29.4, 29.3, 29.2, 25.0, 25.0, 24.9, 22.8, 22.8, 14.2, 14.2; **HRMS** (ESI-MS): m/z calcd. For $C_{50}H_{93}N_3O_{14}$ $[M+Na]^+$: 982.6555; Found: 982.6553.



(2-(2-(2-(2-tosylethoxy)ethoxy)ethoxy)ethyl)-3-*O*-benzyl-5-*O*-(8-(2-((2-pentylcyclopropyl) methyl)cyclopropyl)octanoyl)-2-*O*-(2,3-di-*O*-benzyl-5-*O*-(8-(2-((2-pentylcyclopropyl) methyl)cyclopropyl)octanoyl)-β-D-arabinofuranosyl)-α-D-arabinofuranoside (25b) :

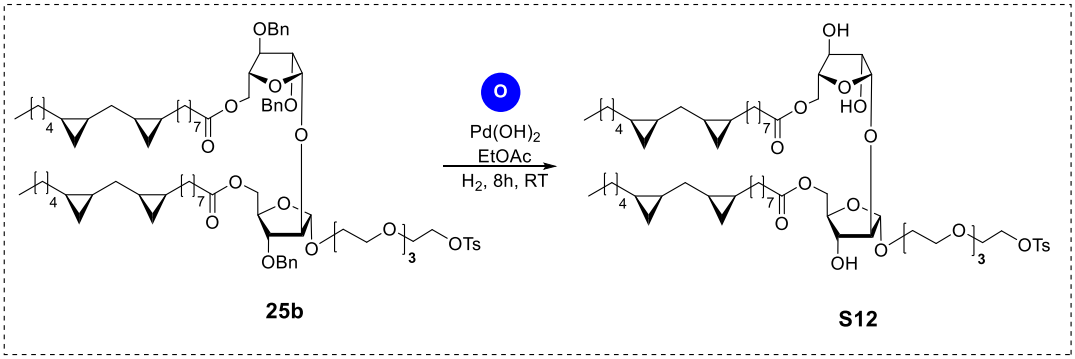
Compound **18** was converted to **25b** according to the general experimental **Procedure Q**. (Yield 47%, pale yellow syrup): **$[\alpha]_D^{25}$** = +28.4 (*c* = 0.06, $CHCl_3$); **IR** (cm^{-1}, $CHCl_3$): 3018, 2910, 2835,



2310, 1742, 1608, 1318, 1260, 1050, 980, 900; **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.79 (d, *J* = 8.3 Hz, 2H), 7.35 – 7.28 (m, 17H), 5.10 (d, *J* = 3.1 Hz, 1H), 5.00 (s, 1H), 4.70 (d, *J* = 11.6 Hz, 2H), 4.63 – 4.55 (m, 3H), 4.53 – 4.47 (m, 1H), 4.33 (d, *J* = 3.6 Hz, 1H), 4.28 – 4.20 (m, 3H), 4.16 – 4.11 (m, 5H), 4.10 – 4.07 (m, 2H), 3.94 (dd, *J* = 6.1, 2.7 Hz, 1H), 3.85 – 3.80 (m, 1H), 3.66 – 3.55 (m, 13H), 2.43 (s, 3H), 2.28 (t, *J* = 7.6 Hz, 2H), 2.21 (td, *J* = 7.5, 2.1 Hz, 2H), 1.39 (dt, *J* = 11.7, 5.7 Hz, 12H), 1.32 – 1.25 (m, 26H), 1.16 – 1.09 (m, 4H), 1.02 (dt, *J* = 14.2, 7.9 Hz, 2H), 0.91 – 0.87 (m, 7H), 0.78 (td, *J* = 8.1, 3.8 Hz, 4H), 0.70 – 0.66 (m, 3H), 0.63 – 0.58 (m, 4H), -0.24 – -0.31 (m, 4H); **^{13}C NMR** (101 MHz, $CDCl_3$): δ 173.7, 173.5, 144.9, 137.9, 137.9, 137.6, 133.2, 130.0, 130.0, 128.7, 128.7, 128.6, 128.6, 128.5, 128.5, 128.2, 128.2, 128.2, 128.2, 128.1, 128.0, 127.9, 127.9, 127.9, 127.9, 127.8, 106.4, 100.8, 86.1, 84.4, 83.9, 82.7, 80.0, 79.0, 72.8, 72.7, 72.5, 70.9, 70.7, 70.7, 70.6, 70.5, 69.4, 68.8, 66.9, 66.1, 63.9, 34.2, 32.0, 30.3, 30.3, 30.0, 30.0, 30.0, 29.8, 29.6, 29.6, 29.5, 29.5, 29.3, 29.3, 29.0, 29.0, 28.9, 28.9, 28.2, 28.0, 25.0, 25.0, 22.9, 22.9, 21.8, 16.2, 16.2, 16.1, 16.1, 16.1, 16.0, 15.8, 15.8, 14.3, 14.3, 11.2, 11.2, 11.0, 11.0; **HRMS** (ESI-MS): m/z calcd. For $C_{86}H_{126}O_{17}S$ $[M+Na]^+$: 1485.8613; Found: 1485.8650.

(2-(2-(2-(2-tosylethoxy)ethoxy)ethoxy)ethyl)-5-*O*-(8-(2-((2-pentylcyclopropyl) methyl)cyclopropyl)octanoyl)-2-*O*-(5-*O*-(8-(2-((2-pentylcyclopropyl)methyl)cyclopropyl)octanoyl)-β-D-arabinofuranosyl)-α-D-arabin ofuranoside (S12) :

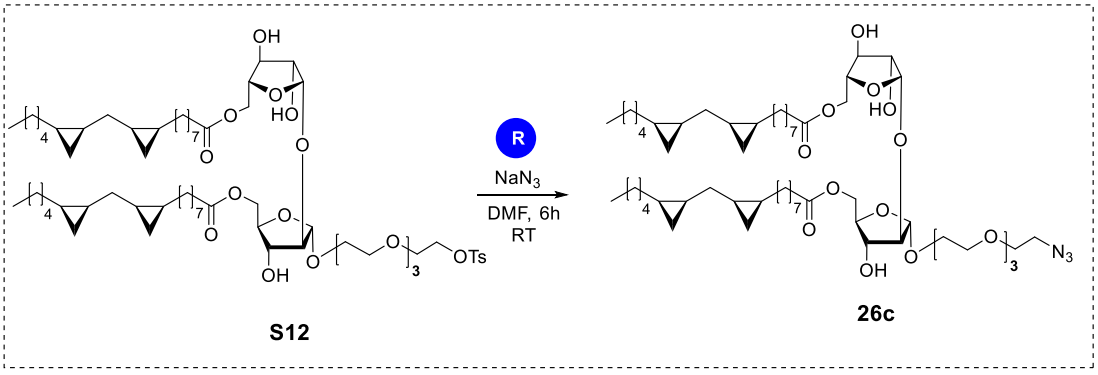
Compound **25b** was converted to **S12** according to the general experimental **procedure O.** (Yield 53%, pale yellow syrup): **$[\alpha]_D^{25}$** = +22.8 (*c* = 0.06, $CHCl_3$); **IR** (cm^{-1}, $CHCl_3$): 3560, 3340, 3010, 2835, 2310, 1722, 1608, 1348, 1250, 1040, 970, 920; **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.80



(d, *J* = 8.3 Hz, 2H), 7.35 (d, *J* = 8.1 Hz, 2H), 5.08 – 5.03 (m, 2H), 4.37 – 4.28 (m, 2H), 4.22 – 4.16 (m, 5H), 4.13 – 4.09 (m, 1H), 4.05 (dq, *J* = 6.0, 3.3 Hz, 3H), 3.97 – 3.93 (m, 1H), 3.87 (dd, *J* = 6.9, 4.1 Hz, 1H), 3.71 – 3.68 (m, 2H), 3.65 – 3.59 (m, 11H), 2.45 (s, 3H), 2.37 – 2.32 (m, 4H), 1.65 – 1.59 (m, 4H), 1.39 – 1.26 (m, 37H), 1.18 – 1.11 (m, 4H), 1.05 – 1.01 (m, 1H), 0.88 (d, *J* = 4.0 Hz, 6H), 0.78 (d, *J* = 6.6 Hz, 3H), 0.71 – 0.66 (m, 3H), 0.61 (q, *J* = 4.2 Hz, 4H), -0.24 – -0.30 (m, 4H); **^{13}C NMR** (101 MHz, $CDCl_3$): δ 174.1,173.9, 145.0, 133.0, 130.0, 130.0, 128.1, 128.1, 105.6, 102.2, 89.3, 80.2, 80.1, 77.7, 76.4, 76.0, 70.8, 70.7, 70.6, 70.5, 70.4, 69.4, 68.8, 67.3, 65.4, 63.7, 34.2, 34.2, 32.0, 32.0, 30.3, 30.0, 30.0, 29.8, 29.8, 29.6, 29.6, 29.5, 29.5, 29.3, 29.0, 29.0, 28.8, 28.8, 28.2, 28.0, 25.0, 25.0, 22.8, 22.8, 21.8, 16.2, 16.2, 16.0, 16.0, 16.0, 16.0, 16.0, 15.7, 14.2, 14.2, 11.2, 11.1, 11.0, 11.0; **HRMS** (ESI-MS): m/z calcd. For $C_{65}H_{108}O_{17}S$ $[M+Na]^+$: 1215.7205; Found: 1215.7235.

(2-(2-(2-(2-azidoethoxy)ethoxy)ethoxy)ethyl)-5-*O*-(8-(2-((2-pentylcyclopropyl) methyl)cyclopropyl)octanoyl)-2-*O*-(5-*O*-(8-(2-((2-pentylcyclopropyl) methyl)cyclopropyl)octanoyl)-β-D-arabinofuranosyl)-α-D-arabinofuranoside (26c) :

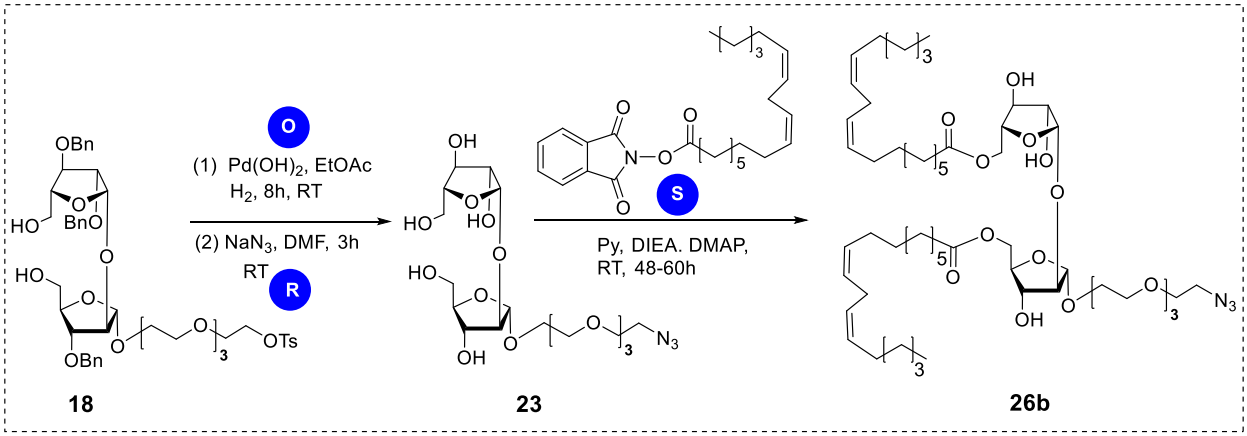
Compound **S12** was converted to **26c** according to the general experimental **Procedure R.** (Yield 67%, pale yellow syrup): **$[\alpha]_D^{25}$** = +16.8 (*c* = 0.06, $CHCl_3$); **IR** (cm^{-1}, $CHCl_3$): 3540, 3310, 3010, 2855, 2180, 1710, 1608, 1340, 1230, 1030, 950, 900; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 5.07 –



5.02 (m, 2H), 4.38 – 4.24 (m, 2H), 4.21 – 4.15 (m, 3H), 4.12 – 4.07 (m, 1H), 4.07 – 4.00 (m, 3H), 3.96 – 3.91 (m, 1H), 3.89 – 3.84 (m, 1H), 3.68 – 3.60 (m, 13H), 3.41 – 3.37 (m, 2H), 2.34 (t, *J* = 7.6 Hz, 4H), 1.64 – 1.59 (m, 4H), 1.38 (s, 9H), 1.31 – 1.24 (m, 25H), 1.16 – 1.09 (m, 4H), 1.05 – 1.00 (m, 1H), 0.90 – 0.86 (m, 7H), 0.80 – 0.74 (m, 4H), 0.67 (dd, *J* = 10.8, 5.5 Hz, 4H), 0.60 (dt, *J* = 8.3, 4.1 Hz, 4H), -0.25 – -0.32 (m, 4H); **^{13}C NMR** (101 MHz, $CDCl_3$): δ 174.1, 173.9, 105.6, 102.1, 89.1, 80.3, 80.1, 77.7, 76.4, 76.0, 70.7, 70.7, 70.6, 70.6, 70.4, 70.1, 67.2, 65.4, 63.7, 50.8, 34.2, 32.0, 32.0, 30.3, 30.0, 30.0, 29.8, 29.8, 29.6, 29.6, 29.5, 29.5, 29.3, 29.0, 29.0, 28.8, 28.8, 28.2, 28.0, 25.0, 25.0, 22.8, 22.8, 16.2, 16.2, 16.0, 16.0, 16.0, 16.0, 16.0, 15.8, 15.7, 14.2, 14.2, 11.2, 11.2, 11.0, 11.0; **HRMS** (ESI-MS): m/z calcd. For $C_{58}H_{101}N_3O_{14}$ $[M+Na]^+$: 1086.7181; Found: 1086.7180.

(2-(2-(2-(2-azidoethoxy)ethoxy)ethoxy)ethyl)-2-*O*-(-β-D-arabinofuranosyl)-α-D-arabinofuranoside (23):

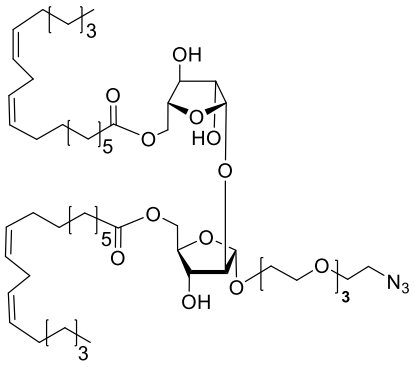
Compound **18** was converted to compound **23** according to the general experimental **Procedure O** and **R**: **$[\alpha]_D^{25}$** = +16.8 (*c* = 0.06, $CHCl_3$); **IR** (cm^{-1}, $CHCl_3$): 3540, 2940, 2310, 2140, 1710, 1370, 1044, 970, 870; **^{1}H NMR** (400 MHz, CD_3OD): δ 5.04 (d, *J* = 2.1 Hz, 1H), 5.01



(d, *J* = 3.9 Hz, 1H), 4.12 (dd, *J* = 4.8, 2.2 Hz, 1H), 4.05 (dd, *J* = 7.7, 4.9 Hz, 1H), 4.00 (t, *J* = 4.9 Hz, 2H), 3.93 (dt, *J* = 4.9, 2.2 Hz, 1H), 3.86 (dq, *J* = 7.2, 2.9, 1.8 Hz, 1H), 3.78 (ddd, *J* = 12.8, 5.8, 3.0 Hz, 3H), 3.72 (d, *J* = 3.1 Hz, 1H), 3.69 – 3.65 (m, 14H), 3.41 – 3.37 (m, 2H). **^{13}C NMR** (101 MHz, CD_3OD) δ 107.5, 102.4, 89.3, 84.4, 84.0, 78.8, 76.4, 75.8, 71.6, 71.5, 71.5, 71.5, 71.4, 71.1, 68.1, 64.4, 62.4, 51.8.; **HRMS** (ESI-MS): m/z calcd. For $C_{18}H_{33}N_3O_{12}$ $[M+Na]^+$: 506.1962; Found: 506.1962.

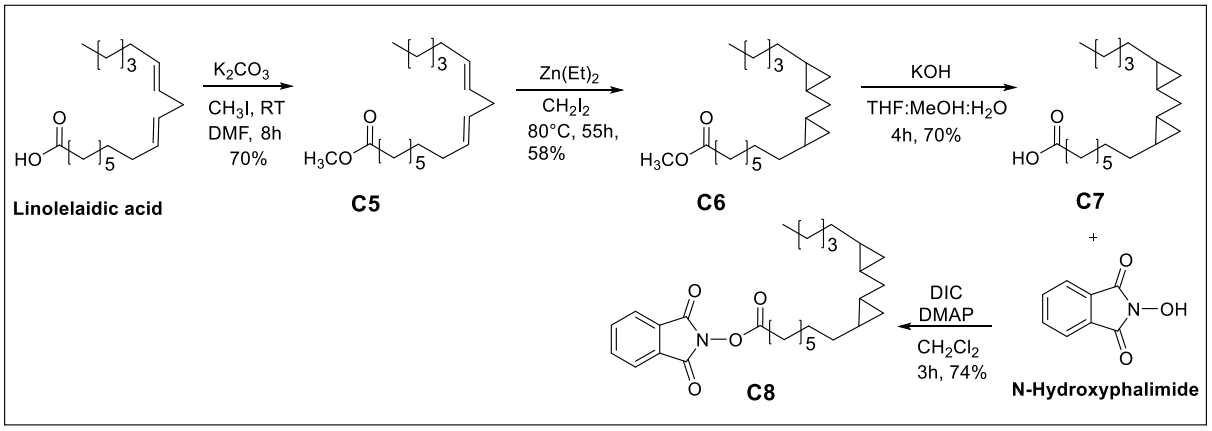
(2-(2-(2-(2-azidoethoxy)ethoxy)ethoxy)ethyl)-5-*O*-(9*Z*,12*Z*-octadecadienoyl)-2-*O*-(5-*O*-9*Z*,12*Z*-octadecadienoyl-β-D-arabinofuranosyl)-α-D-arabinofuranoside (26b) : Compound **23** was converted to **26b** according to the general experimental procedure **S**. (Yield 16% over 3

steps, pale yellow syrup): **$[\alpha]_D^{25}$** = +20.8(*c* = 0.06, $CHCl_3$); **IR** (cm^{-1}, $CHCl_3$): 3480, 3150, 2210, 2050, 1750, 1400, 1330, 1250, 1080, 1010; **^{1}H NMR** (400 MHz, $CDCl_3$): δ 5.38 – 5.32 (m, 8H), 5.06 (dd, *J* = 7.5, 3.4 Hz, 2H), 4.29 – 4.25 (m, 2H), 4.18 (ddd, *J* = 16.9, 5.6, 4.0 Hz, 3H), 4.07 – 4.03 (m, 2H), 3.98 – 3.83 (m, 5H), 3.66 (d, *J* = 6.1 Hz, 12H), 3.42 – 3.38 (m, 2H), 2.77 (t, *J* = 6.2 Hz, 4H), 2.35 (s, 4H), 2.05 (d, *J* = 6.6 Hz, 8H), 1.62 – 1.61 (m, 4H), 1.25 (s, 28H), 0.88 (s, 6H); **^{13}C NMR** (101 MHz, $CDCl_3$): δ 130.4, 130.4, 130.2, 130.2, 128.2, 128.2, 128.1, 128.1, 109.2, 102.0, 97.4, 93.1, 89.5, 87.0, 82.5, 77.7, 70.8, 70.7, 70.6, 70.4, 70.1, 70.1, 64.1, 63.6, 62.3, 50.8, 34.2, 32.1, 32.1, 31.7, 31.7, 29.9, 29.9, 29.9, 29.9, 29.9, 29.9, 29.9, 29.9, 29.8, 29.8, 29.8, 29.5, 29.5, 27.4, 27.4, 25.8, 25.8, 22.8, 22.7, 14.3, 14.2; **HRMS** (ESI-MS): m/z calcd. For $C_{54}H_{93}N_3O_{14}$ $[M+Na]^+$: 1030.6555; Found: 1030.6570.

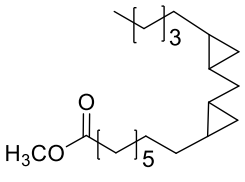


26b

Synthesis of C8:



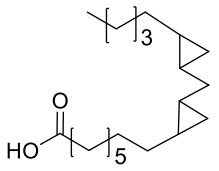
Methyl 8-(2-((2-pentylcyclopropyl)methyl)cyclopropyl)octanoate(C6): Compound **C8** synthesized from commercially available linolelaidic acid converted into **C6** over two steps. To a solution of linolelaidic acid methyl ester **C6**(1eq, 289.83µmol) in a liquid form, a 1.1 M n-hexane solution of diethyl zinc (50eq, 14.94mmol) was added under a nitrogen atmosphere with cooling with ice bath and stirred for 1h. Diiodomethane (100eq, 29.88mmol) was then added and the mixture was stirred at 80°C for 55h without a solvent. After completing the reaction, the diethyl zinc was diluted by adding hexane and then the reaction mixture was



C6

filtered through a pad of Celite® and the filtrate was evaporated *in vacuo*. After that, the reaction mixture was transferred to a separating funnel and extracted with ethyl acetate. The combined organic layers were washed with cold water and brine solution, the organic layer was dried over anhydrous Na_2SO_4, concentrated *in vacuo* and the residue was purified by silica gel column chromatography (ethyl acetate/hexanes) to obtain the desired product. (Yield 40% over 2 steps, pink syrup): **IR** (cm^{-1}, $CHCl_3$): 2210, 1800, 1780, 1620, 1440, 1311, 1240, 1010, 970, 900, 840; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 3.65 (s, 3H), 2.29 (t, *J* = 7.5 Hz, 2H), 1.62 – 1.58 (m, 2H), 1.33 – 1.23 (m, 20H), 0.87 (s, 3H), 0.48 – 0.36 (m, 4H), 0.15 (dq, *J* = 8.5, 5.2, 4.5 Hz, 4H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 174.4, 51.5, 39.0, 38.9, 34.4, 34.4, 34.2, 31.9, 31.9, 29.7, 29.4, 29.3, 25.1, 22.8, 18.6, 18.5, 18.5, 18.5, 14.2, 11.5, 11.5; **HRMS** (ESI-MS): m/z calcd. For $C_{21}H_{38}O_2$ $[M+Na]^+$: 322.2872; Found:322.2800

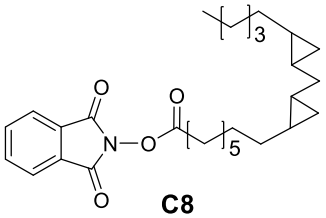
8-(2-((2-pentylcyclopropyl)methyl)cyclopropyl)octanoic acid (C7): Aqueous solution of KOH(7eq, 2.17mmol in 1 mL of MilliQ water) was added dropwise to a solution of compound **C6**(1eq, 310.05µmol) in THF: MeOH (3:1) at 0°C. The reaction mixture was stirred for 7 h at 25°C. After completing the reaction 2*N* HCl was added to quench the reaction at 0°C, diluted with EtOAc, and washed successively with ice-cold water, saturated solution of $NaHCO_3$ (aq), and brine solution. The 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. (Yield 70%, pale yellow syrup): **IR** (cm^{-1}, $CHCl_3$): 2910, 2730, 1880, 1620, 1410, 1322, 1230, 1000, 950, 900, 840; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 2.34 (t, *J* = 7.5 Hz, 2H), 1.66 – 1.60 (m, 2H), 1.38 – 1.25 (m, 20H), 0.89 (s, 3H), 0.44 (dt, *J* = 18.8, 6.5 Hz, 4H), 0.16 (tq, *J* = 9.4, 4.0 Hz, 4H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 180.3, 39.0, 39.0, 34.5, 34.4, 34.2, 31.9, 29.9, 29.8, 29.5, 29.4, 24.8, 22.9, 18.7, 18.6, 18.6, 18.5, 14.3, 11.5, 11.5; **HRMS** (ESI-MS): m/z calcd. For $C_{20}H_{36}O_2$ $[M+Na]^+$:308.2715; Found:308.2760.



C7

1,3-dioxoisoindolin-2-yl 8-(2-((2-pentylcyclopropyl)methyl)cyclopropyl)octanoate(C8):

The cyclopropane derivative carboxylic acid **C7** (1.0eq, 113.15µmol), N-Hydroxyphalimide (1.0eq, 124.80µmol), and DMAP (0.1eq, 11.35µmol) in anhydrous CH_2Cl_2 were stirred at 25°C. DIC (1.1 eq, 113.45µmol) was then added dropwise, and the mixture was allowed to stir until the acid was consumed (determined by TLC). The mixture was filtered (over Celite, SiO2, or

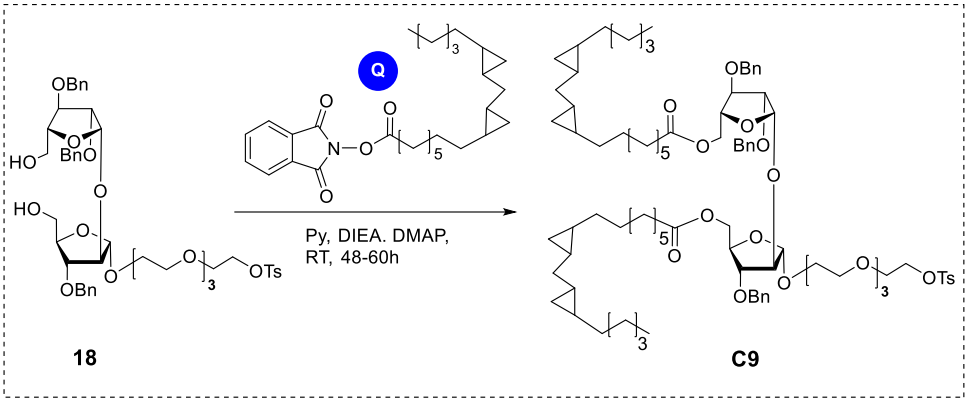


C8

through a fritted funnel) and rinsed with additional CH_2Cl_2. The solvent was removed under reduced pressure and purification by column chromatography afforded corresponding activated esters. (Yield- 65%); **IR** (cm^{-1}, $CHCl_3$): 2280, 2230, 1770, 1640, 1480, 1320, 1230, 1020, 960, 900; **^{1}H NMR** (400 MHz, $CDCl_3$)δ 7.88 (dd, *J* = 5.5, 3.1 Hz, 2H), 7.78 (dd, *J* = 5.5, 3.1 Hz, 2H), 2.66 (t, *J* = 7.5 Hz, 2H), 1.82 – 1.74 (m, 2H), 1.45 – 1.20 (m, 20H), 0.88 (t, *J* = 6.9 Hz, 3H), 0.50 – 0.38 (m, 4H), 0.16 (dtd, *J* = 9.2, 4.7, 4.0, 2.1 Hz, 4H); **^{13}C NMR** (101 MHz, $CDCl_3$)δ 169.8, 162.1, 162.1, 134.8, 134.8, 129.1, 129.1, 124.1, 124.1, 39.0, 34.4, 31.9, 31.1, 29.7, 29.5, 29.4, 29.3, 29.0, 24.8,24.4, 22.9, 18.7, 18.6, 18.5, 18.5, 14.3, 11.5, 11.5; **HRMS** (ESI-MS): m/z calcd. For $C_{28}H_{39}NO_4[M+Na]^+$: 453.2879; Found: 453.2890

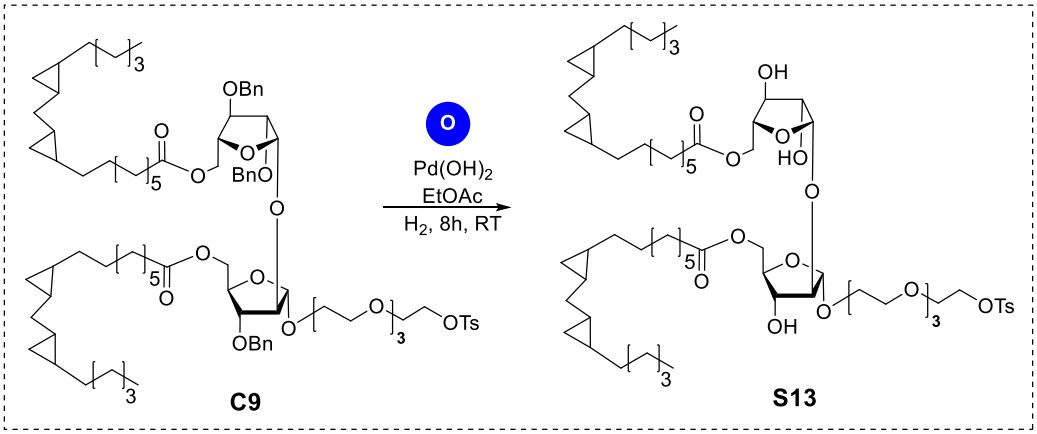
(2-(2-(2-(2-tosylethoxy)ethoxy)ethoxy)ethyl)-3-*O*-benzyl-5-*O*-(8-(2-((2-pentylcyclopropyl) methyl)cyclopropyl)octanoyl)-2-*O*-(2,3-di-*O*-benzyl-5-*O*-(8-(2-((2-pentylcyclopropyl) methyl)cyclopropyl)octanoyl)-β-D-arabinofuranosyl)-α-D-arabinofuranoside (C9):

Compound **18** was converted to **C9** according to the general experimental **Procedure Q**. (Yield 47%, pale yellow syrup): **$[\alpha]_D^{25}$** = +40.0 (*c* = 0.06, $CHCl_3$); **IR** (cm^{-1}, $CHCl_3$): 3018, 2910, 2835, 2310, 1742, 1608, 1318, 1260, 1050, 980, 900; **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.78 (d, *J* = 8.3 Hz, 2H), 7.34 – 7.26 (m, 17H), 5.10 (s, 1H), 5.00 (s, 1H), 4.70 (d, *J* = 11.6 Hz, 2H), 4.62 – 4.55 (m, 3H), 4.50 (s, 1H), 4.34 – 4.32 (m, 1H), 4.27 – 4.20 (m, 3H), 4.15 – 4.11 (m, 5H), 4.08 (s, 1H), 3.94 (dd, *J* = 5.7, 2.1 Hz, 1H), 3.86 – 3.80 (m, 3H), 3.66 – 3.60 (m, 7H), 3.56 (d, *J* = 12.9 Hz, 5H), 2.43 (s, 3H), 2.28 (t, *J* = 7.6 Hz, 2H), 2.21 (dt, *J* = 7.8, 3.9 Hz, 2H), 1.59 – 1.51 (m, 4H), 1.36 – 1.25 (m, 40H), 0.88 (s, 6H), 0.48 – 0.38 (m, 8H), 0.18 – 0.12 (m, 8H); **^{13}C NMR** (101 MHz, $CDCl_3$):δ 173.7, 173.5, 144.9, 137.9, 137.9, 137.6, 133.2, 129.9, 129.9, 128.7, 128.7, 128.6, 128.6, 128.5, 128.5, 128.5, 128.2, 128.2, 128.2, 128.1, 128.1, 128.0, 127.9, 127.8, 127.8, 127.8, 106.4, 100.8, 86.1, 84.4, 83.9, 82.7, 80.0, 79.0, 72.7, 72.6, 72.5,



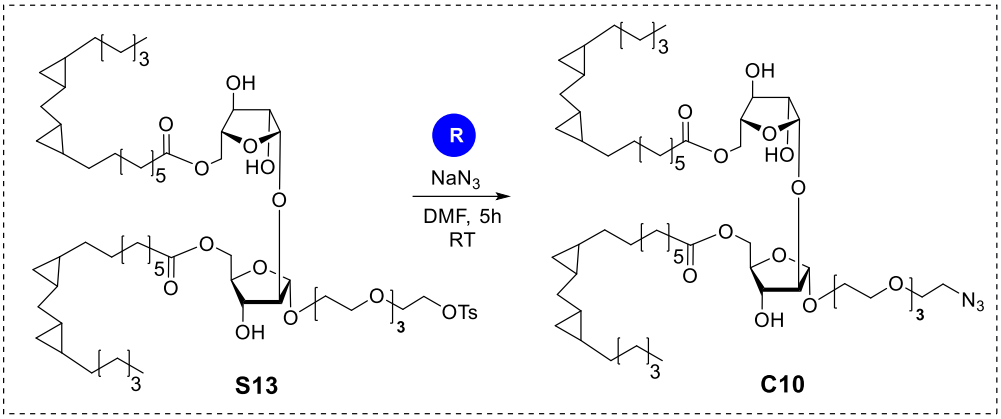
70.8, 70.7, 70.7, 70.6, 70.5, 69.3, 68.8, 66.9, 66.1, 63.9, 39.0, 38.9, 34.4, 34.4, 34.4, 34.4, 34.2, 32.1, 31.9, 31.9, 29.8, 29.8, 29.8, 29.8, 29.5, 29.5, 29.5, 29.5, 29.3, 29.3, 25.0, 25.0, 22.9, 21.8, 18.7, 18.6, 18.5, 18.5, 18.5, 18.5, 18.5, 18.5, 14.3, 14.3, 11.5, 11.5, 11.5, 11.5; **HRMS** (ESI-MS): m/z calcd. For $C_{86}H_{126}O_{17}S$ $[M+Na]^+$: 1485.8613; Found: 1485.8650.

(2-(2-(2-(2-tosylethoxy)ethoxy)ethoxy)ethyl)-5-*O*-(8-(2-((2-pentylcyclopropyl) methyl)cyclopropyl)octanoyl)-2-*O*-(5-*O*-(8-(2-((2-pentylcyclopropyl)methyl)cyclopropyl)octanoyl)-β-D-arabinofuranosyl)-α-D-arabinofuranoside (S13): Compound **C9** was converted to **S13** according to the general experimental **procedure O.** (Yield 53%, pale yellow syrup): **$[\alpha]_D^{25}$** = +18.8 (*c* = 0.06, $CHCl_3$); **IR** (cm^{-1}, $CHCl_3$): 3560, 3340, 3010, 2835, 2310, 1722, 1608, 1348, 1250, 1040, 970, 920; **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.80 (d, *J* = 8.3 Hz, 2H), 7.34 (d, *J* = 8.1 Hz, 2H), 5.05 (d, *J* = 3.4 Hz, 2H), 4.32 (td, *J* = 9.2, 8.5, 4.6 Hz, 2H), 4.21 – 4.16 (m, 5H), 4.11 – 4.03 (m, 4H), 3.96 – 3.92 (m, 1H), 3.87 (dd, *J* = 7.0, 3.8 Hz, 1H), 3.70 (d, *J* = 4.9 Hz, 2H), 3.65 – 3.59 (m, 11H), 2.45 (s, 3H), 2.35 (d, *J* = 8.2 Hz, 4H), 1.64 – 1.59 (m, 4H), 1.38 – 1.26 (m, 40H), 0.88 (s, 6H), 0.43 (dt, *J* = 16.5, 5.7 Hz, 8H), 0.16 (tt, *J* = 8.3, 4.9 Hz, 8H); **^{13}C NMR** (101 MHz, $CDCl_3$): δ 174.1, 173.8, 145.0, 133.1, 130.0, 130.0, 128.1, 128.1, 105.6, 102.3, 89.4, 80.2, 80.1, 77.7, 76.6, 75.9, 70.8, 70.7, 70.6, 70.5, 70.5, 69.4, 68.8, 67.3, 65.3, 63.7, 39.0, 38.9, 34.5, 34.5, 34.5, 34.5, 34.3, 34.2, 31.9, 29.8, 29.8, 29.8, 29.8, 29.5, 29.5, 29.5, 29.5, 29.3, 29.3, 25.0, 25.0, 22.9, 22.8, 21.8, 18.7, 18.7, 18.6, 18.6, 18.5, 18.5, 18.5, 18.5, 14.3, 14.3, 11.5, 11.5, 11.5, 11.5; **HRMS** (ESI-MS): m/z calcd. For $C_{65}H_{108}O_{17}S$ $[M+Na]^+$: 1215.7205; Found: 1215.7235.



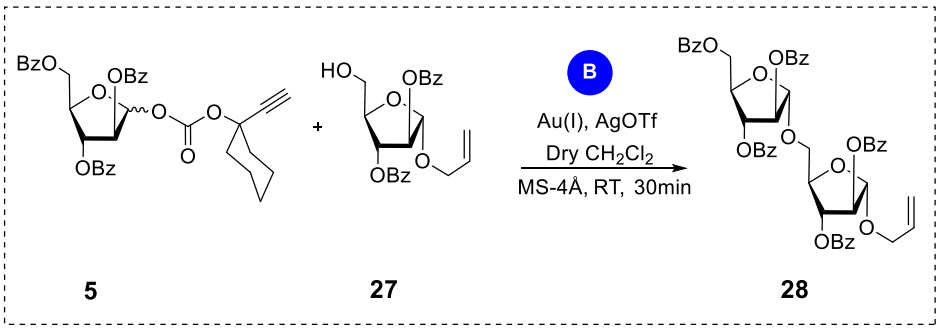
(2-(2-(2-(2-azidoethoxy)ethoxy)ethoxy)ethyl)-5-*O*-(8-(2-((2-pentylcyclopropyl) methyl)cyclopropyl)octanoyl)-2-*O*-(5-*O*-(8-(2-((2-pentylcyclopropyl) methyl)cyclopropyl)octanoyl)-β-D-arabinofuranosyl)-α-D-arabinofuranoside (C10):

Compound **S13** was converted to **C10** according to the general experimental **Procedure R.** (Yield 67%, pale yellow syrup): **$[\alpha]_D^{25}$** = +22.2 (*c* = 0.06, $CHCl_3$); **IR** (cm^{-1}, $CHCl_3$): 3540, 3310, 3010, 2855, 2180, 1710, 1608, 1340, 1230, 1030, 950, 900; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 5.05 (dd, *J* = 6.6, 3.6 Hz, 2H), 4.36 – 4.29 (m, 2H), 4.20 – 4.17 (m, 2H), 4.09 (d, *J* = 4.6 Hz, 1H), 4.07 – 4.02 (m, 3H), 3.96 – 3.93 (m, 1H), 3.88 (dd, *J* = 7.1, 4.3 Hz, 1H), 3.66 (td, *J* = 7.7, 6.7, 4.1 Hz, 14H), 3.42 – 3.39 (m, 2H), 2.34 (t, *J* = 7.2 Hz, 4H), 1.64 – 1.60 (m, 4H), 1.37 – 1.26 (m, 40H), 0.88 (d, *J* = 2.3 Hz, 6H), 0.50 – 0.38 (m, 8H), 0.19 – 0.12 (m, 8H); **^{13}C NMR** (101 MHz, $CDCl_3$): δ 174.1, 173.9, 105.6, 102.1, 89.2, 80.3, 80.2, 77.8, 76.7, 76.0, 70.8, 70.8, 70.7, 70.6, 70.4, 70.1, 67.2, 65.3, 63.6, 50.8, 39.0, 39.0, 38.9, 38.9, 34.5, 34.5, 34.3, 32.1, 31.9, 31.9, 29.8, 29.8, 29.8, 29.8, 29.5, 29.5, 29.5, 29.3, 29.3, 25.0, 25.0, 22.9, 22.9, 22.8, 18.7, 18.7, 18.6, 18.6, 18.5, 18.5, 18.5, 18.5, 14.3, 14.3, 11.5, 11.5, 11.5, 11.5; **HRMS** (ESI-MS): m/z calcd. For $C_{58}H_{101}N_3O_{14}$ $[M+Na]^+$: 1086.7181; Found: 1086.7180.



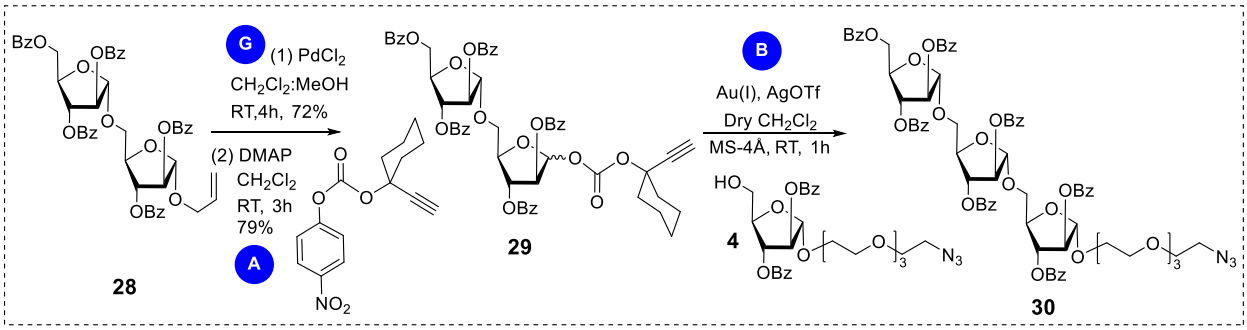
Allyl 2,3-di-*O*-benzoyl-5-*O*-(2,3-di-*O*-benzoyl-5-*O*-(2,3-di-*O*-benzoyl-5-*O*-benzoyl-α-D-arabinofuranosyl)-α-D-arabinofuranosyl)-α-D-arabinofuranoside (28):

The glycosyl donor **5**[49] and the glycosyl acceptor **27**[45] were glycosylated according to the general reaction **Procedure B** as detailed above to give the **28**. (Yield-77%, pale yellow syrup): **$[\alpha]_D^{25}$** = +22.6 (*c* = 0.06, $CHCl_3$); **IR** (cm^{-1}, $CHCl_3$): 2630, 2280, 2125, 1710, 1527, 1440, 1244, 1006, 980, 850; **^{1}H NMR** (400 MHz, $CDCl_3$): δ 8.07 – 7.94 (m, 10H), 7.59 – 7.54 (m, 2H), 7.52 – 7.36 (m, 9H), 7.27 (dt, *J* = 15.4, 8.1 Hz, 4H), 5.94 (ddt, *J* = 16.3, 10.6, 5.3 Hz, 1H), 5.65 (d, *J* = 4.8 Hz, 2H), 5.61 – 5.55 (m, 2H), 5.47 (s, 1H),



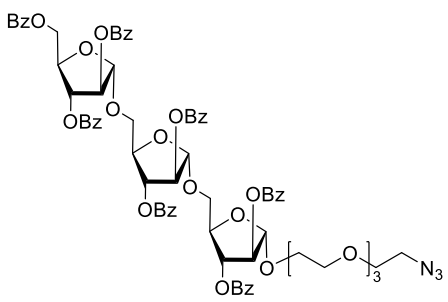
5.39 – 5.32 (m, 1H), 5.28 (s, 1H), 5.23 – 5.17 (m, 1H), 4.85 (dd, *J* = 11.8, 3.1 Hz, 1H), 4.76 (q, *J* = 4.5 Hz, 1H), 4.67 (dd, *J* = 11.8, 4.7 Hz, 1H), 4.50 (q, *J* = 4.5 Hz, 1H), 4.31 – 4.22 (m, 2H), 4.09 (dd, *J* = 13.1, 6.0 Hz, 1H), 3.98 (dd, *J* = 11.2, 2.7 Hz, 1H); **^{13}C NMR** (101 MHz, $CDCl_3$): δ 166.3, 165.9, 165.8, 165.5, 165.4, 133.8, 133.6, 133.6, 133.5, 133.4, 133.1, 130.0, 130.0, 130.0, 130.0, 129.9, 129.9, 129.9, 129.9, 129.9, 129.9, 129.9, 129.3, 129.2, 129.1, 129.0, 128.6, 128.6, 128.6, 128.6, 128.6, 128.6, 128.4, 128.4, 128.4, 128.4, 117.5, 106.0, 104.9, 82.0, 82.0, 82.0, 81.4, 77.9, 77.4, 67.9, 66.2, 63.8; **HRMS** (ESI-MS): m/z calcd. For $C_{48}H_{42}O_{14}$ $[M+Na]^+$: 865.2472; Found: 865.2480.

1-*O*-(((1-ethylnylcyclohexyl)oxy)carbonyl)-2,3-di-*O*-benzoyl-5-*O*-(2,3-di-*O*-benzoyl-5-*O*-benzoyl -α-D-arabinofuranosyl)-α-D-arabinofuranoside (29):



Compound **28** was converted into compound **29** according to the general experimental **Procedures G** and **A.** (Yield 79%, pale yellow syrup): **$[\alpha]_D^{25}$** = + 24.8 (*c* = 0.06, $CHCl_3$); **IR** (cm^{-1}, $CHCl_3$): 2960, 2410, 2185, 1720, 1577, 1435, 1284, 1102, 960, 880**; ^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.07 (d, *J* = 7.4 Hz, 2H), 8.05 – 7.98 (m, 6H), 7.95 (d, *J* = 7.7 Hz, 2H), 7.61 – 7.55 (m, 2H), 7.53 – 7.36 (m, 9H), 7.34 – 7.25 (m, 4H), 6.35 (s, 1H), 5.73 (d, *J* = 5.4 Hz, 2H), 5.61 – 5.56 (m, 2H), 5.44 (s, 1H), 4.81 (dd, *J* = 11.7, 2.9 Hz, 1H), 4.74 – 4.62 (m, 3H), 4.24 (dd, *J* = 11.3, 4.1 Hz, 1H), 3.99 (dd, *J* = 11.3, 2.9 Hz, 1H), 2.65 (s, 1H), 2.21 (t, *J* = 13.8 Hz, 2H), 1.92 (dd, *J* = 15.5, 6.2 Hz, 2H), 1.72 – 1.59 (m, 4H), 1.43 – 1.11 (m, 2H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 166.3, 165.8, 165.6, 165.3, 165.1, 151.3, 133.8, 133.7, 133.5, 133.4, 133.2, 130.1, 130.1, 130.00, 130.00, 129.9, 129.9, 129.9, 129.9, 129.8, 129.8, 129.8, 129.7, 129.5, 129.3, 128.7, 128.6, 128.6, 128.6, 128.6, 128.5, 128.5, 128.4, 128.4, 128.4, 128.4, 106.2, 102.3, 84.3, 82.6, 81.9, 81.4, 81.0, 78.5, 77.8, 76.8, 75.9, 66.2, 63.7, 36.9, 36.8, 25.0, 22.5, 22.5; **HRMS** (ESI-MS): m/z calcd. For $C_{54}H_{48}O_{16}$ $[M+Na]^+$: 952.2942; Found: 952.2972

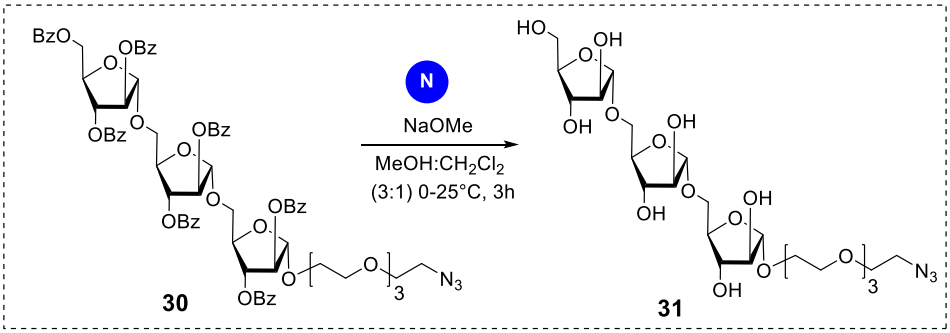
(2-(2-(2-azidoethoxy)ethoxy)ethyl)-2,3-di-*O*-benzoyl-5-*O*-(2,3-di-*O*-benzoyl-5-*O*-(2,3-di-*O*-benzoyl-5-*O*-benzoyl-α-D-arabinofuranosyl)-α-D-arabinofuranosyl)-α-D-arabinofuranoside (30) : Compound **28** was converted into compound **29** according to the general experimental **Procedures G** and **A**, then compound **29** was glycosylated with glycosyl acceptor **4** and converted into compound **30** according to general **Procedure B** (Yield 72%, pale yellow syrup): **$[\alpha]_D^{25}$** = -1.4 (*c* = 0.06, $CHCl_3$); **IR** (cm^{-1}, $CHCl_3$): 2780, 2160, 1600, 1440, 1250, 1100, 690; **^{1}H NMR** (400 MHz, $CDCl_3$): δ 8.01 (q, *J* = 9.0, 8.1 Hz, 10H), 7.93 – 7.88 (m, 4H), 7.59 – 7.54 (m, 2H), 7.53 – 7.46 (m, 3H), 7.46 – 7.35 (m, 11H), 7.28 (d, *J* = 2.9 Hz, 3H), 7.23 (d, *J* = 8.0 Hz, 2H), 5.65 (d, *J* = 3.6 Hz, 2H), 5.61 (d, *J* = 5.8 Hz, 2H), 5.58 – 5.54 (m, 2H), 5.46 (s, 1H), 5.40 (s, 1H), 5.27 (s, 1H), 4.82 (dd, *J* = 11.8, 3.2 Hz, 1H), 4.72 (q, *J* = 4.6 Hz, 1H), 4.64 (dd, *J* = 11.8, 4.6 Hz, 2H), 4.45 (q, *J* = 4.5 Hz, 1H), 4.21 (td, *J* = 12.7, 4.3 Hz, 2H), 3.99 – 3.86 (m, 3H), 3.70 – 3.59 (m, 13H), 3.35 (t, *J* = 5.1 Hz, 2H); **^{13}C NMR** (101 MHz, $CDCl_3$): δ 166.4, 165.9, 165.8, 165.8, 165.5, 165.4, 165.3, 133.6, 133.6, 133.6, 133.5, 133.4, 133.3, 133.1, 130.0, 130.0, 130.0, 130.0, 130.0, 130.0, 130.0, 129.9, 129.9, 129.9, 129.9, 129.9, 129.9, 129.9, 129.5, 129.3, 129.2, 129.2, 129.1, 128.7, 128.6, 128.6, 128.6, 128.6, 128.6, 128.6, 128.6, 128.5, 128.4, 128.4, 128.4, 128.4, 128.4, 128.4, 128.4, 106.1, 105.9, 105.8, 82.2, 82.1, 82.0, 81.9, 81.7, 81.4, 77.9, 77.5, 77.4, 70.9, 70.9, 70.8, 70.8, 70.4, 70.1, 66.8, 66.1, 66.0, 63.8, 50.8; **HRMS** (ESI-MS): m/z calcd. For $C_{72}H_{69}N_3O_{23}$ $[M+Na]^+$: 1366.4220; Found: 1366.4204.



30

(2-(2-(2-azidoethoxy)ethoxy)ethyl)5-*O*-(5-*O*-(α-D-arabinofuranosyl)-α-D-arabinofura nosyl)-α-D-arabinofuranoside (31) :

Compound **30** was converted to compound **31** according to the general experimental **Procedure N**. (Yield 63%, pale yellow syrup): **$[\alpha]_D^{25}$** = -10.4 (*c* = 0.06, $CHCl_3$); **IR** (cm^{-1}, $CHCl_3$): 3570, 3390, 2700, 2160, 1650, 1420, 1240, 1150, 700; **^{1}H NMR** (400 MHz, CD_3OD): δ 4.98 – 4.95 (m, 2H), 4.93 (d, *J* = 1.3 Hz, 1H), 4.08 (dtd, *J* = 13.1, 5.3, 3.9 Hz, 2H), 4.01 (ddt, *J* = 5.9, 3.5, 1.5 Hz, 4H), 3.92 (dt, *J* = 5.7, 2.9

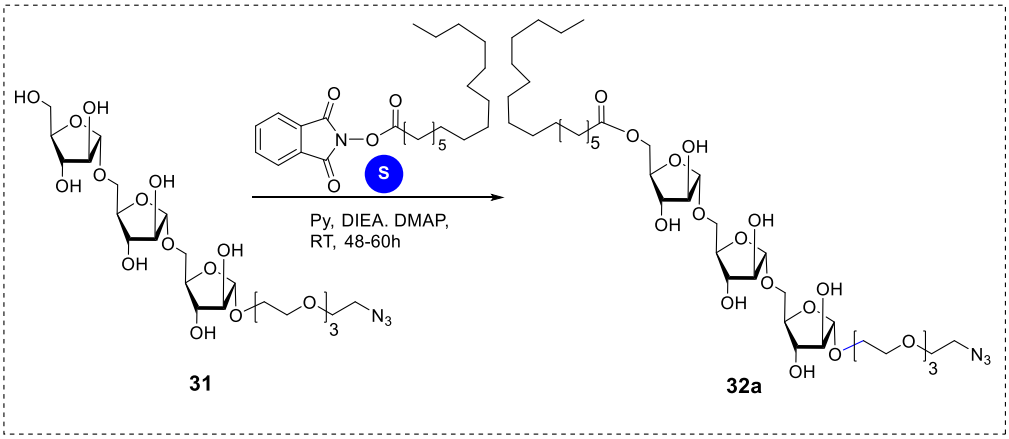


30 **31**

Hz, 2H), 3.89 – 3.82 (m, 4H), 3.76 (dd, *J* = 11.8, 3.3 Hz, 1H), 3.71 – 3.62 (m, 16H), 3.43 – 3.38 (m, 2H); **^{13}C NMR** (101 MHz, CD_3OD): δ 109.7, 109.7, 109.6, 85.9, 84.1, 84.0, 83.4, 83.2, 83.1, 79.2, 79.1, 78.8, 71.6, 71.5, 71.5, 71.5, 71.4, 71.1, 68.2, 68.2, 67.9, 63.1, 51.8; **HRMS** (ESI-MS): m/z calcd. For $C_{23}H_{41}N_3O_{16}$[M+Na]$^+$: 638.2385; Found: 638.2390.

(2-(2-(2-azidoethoxy)ethoxy)ethoxy)ethyl)-5-*O*-(5-*O*-(5-O-(hexadecanoyl)-α-D-arabinofura nosyl)-α-D-arabinofuranosyl)-α-D-arabinofuranoside (32a) :

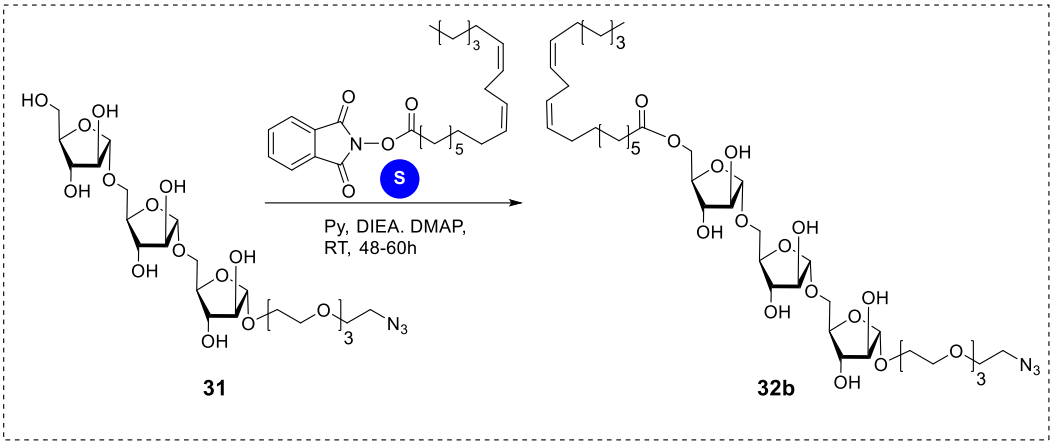
Compound **31** was converted to compound **32a** according to the general experimental **Procedure S.** (Yield 39%, pale yellow syrup): **[α]$_D^{25}$** = +30.5 (*c* = 1.0, $CHCl_3$); **IR** (cm^{-1}, $CHCl_3$): 3300, 2825, 2350, 2150, 1730, 1454, 1353, 1320, 1070, 1020; **^{1}H NMR** (600 MHz, CD_3OD): δ 4.95 (s, 2H), 4.92 (s, 1H), 4.31 (dd, *J* = 11.7, 3.2 Hz, 1H), 4.18 (dd, *J* = 11.7, 6.0 Hz, 1H), 4.11 – 4.04 (m, 3H), 4.03 – 3.98 (m, 3H), 3.92 – 3.88 (m, 2H), 3.87 – 3.83 (m, 4H), 3.67 (s, 15H), 3.40 – 3.37 (m, 2H), 2.37 (t, *J* = 7.5 Hz, 2H), 1.65 – 1.62 (m, 2H), 1.32 (m, 24H), 0.91 (t, *J* = 6.8 Hz, 3H); **^{13}C NMR** (151 MHz, CD_3OD): δ 175.3, 109.7, 109.7, 109.6, 84.1, 83.9, 83.5, 83.3, 83.2, 82.8, 79.2, 79.2, 79.1, 71.7, 71.6, 71.6, 71.6, 71.5, 71.2, 68.3, 68.2, 67.9, 65.0, 51.8, 34.9, 33.1, 30.8, 30.8, 30.8, 30.7, 30.6, 30.5, 30.4, 30.2, 30.2, 26.0, 26.0, 23.7, 14.5; **HRMS** (ESI-MS): m/z calcd. For $C_{39}H_{71}N_3O_{17}$ [M+Na]$^+$: 876.4681; Found: 876.4690.



(2-(2-(2-azidoethoxy)ethoxy)ethoxy)ethyl)5-*O*-(5-*O*-(5-*O*-(9*Z*,12*Z*-octadecadienoyl)-α-D-arabinofuranosyl)-α-D-arabinofuranosyl)-α-D-arabinofuranoside (32b) :

Compound **31** was converted to compound **32b** according to the general experimental **Procedure S**. (Yield 42%, pale yellow syrup): **[α]$_D^{25}$** = +36.6 (*c* = 0,06, $CHCl_3$); **IR** (cm^{-1}, $CHCl_3$): 3389, 2925, 2310, 2106, 1734, 1454, 1357, 1300, 1090, 1018; **^{1}H NMR** (400 MHz, CD_3OD): δ 5.40 – 5.29 (m, 4H), 4.96 – 4.88 (m, 3H), 4.30 (dd, *J* = 11.7, 3.6 Hz, 1H), 4.17 (dd, *J* = 11.7, 6.1 Hz, 1H), 4.12 – 3.95 (m, 6H), 3.88 (dt, *J* = 6.2, 3.1 Hz, 2H), 3.86 – 3.77 (m, 4H), 3.70 – 3.54 (m, 15H), 3.41 – 3.34 (m, 2H), 2.78 (t, *J* = 6.3 Hz, 2H), 2.37 (q, *J* = 7.4, 6.9 Hz, 2H), 2.06 (q, *J* = 6.5

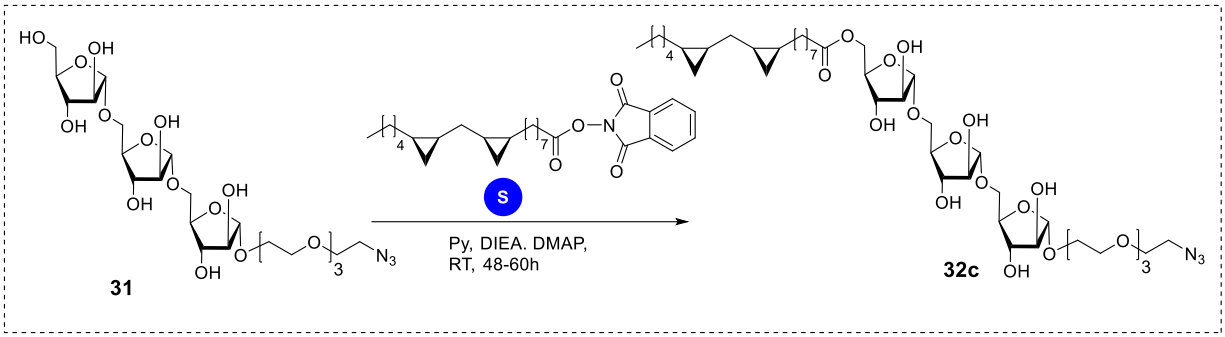
Hz, 4H), 1.65 – 1.60 (m, 2H), 1.38 – 1.29 (m, 14H), 0.91 (t, *J* = 6.8 Hz, 3H); **^{13}C NMR** (101 MHz, CD_3OD): δ 175.3, 131.0, 130.9, 129.1, 129.1, 109.7, 109.7, 109.7, 84.1, 83.9, 83.5, 83.3, 83.2, 82.8, 79.2, 79.2, 79.2, 79.2, 71.7, 71.6, 71.6, 71.6, 71.5, 71.2, 68.3, 68.2, 67.9, 65.0, 51.8, 34.9, 32.7, 30.7,



30.5, 30.3, 30.2, 30.2, 28.2, 26.6, 26.0, 25.9, 23.6, 14.5; **HRMS** (ESI-MS): m/z calcd. For $C_{41}H_{71}N_3O_{17}$ $[M+Na]^+$: 900.4681; Found: 900.4688.

(2-(2-(2-(2-azidoethoxy)ethoxy)ethoxy)ethyl-5-*O*-(5-*O*-(5-*O*-(8-(2-((2-pentylcyclopropyl) methyl)cyclopropyl)octanoyl)-α-D-arabinofuranosyl) -α-D-arabinofuranosyl)-α-D-arabinofuranoside (32c) :

Compound **31** was converted to compound **32c** according to the general experimental **Procedure S**. (Yield 45%, pale yellow syrup): **$[\alpha]_D^{25}$** = +54.5 (*c* = 0.06, $CHCl_3$); **IR** (cm^{-1}, $CHCl_3$):

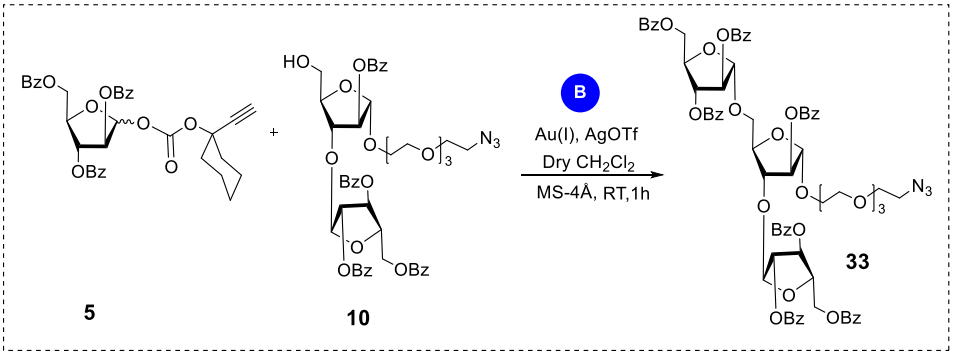


3300, 2775, 2250, 2130, 1750, 1434, 1380, 1220, 1090, 1010; **^{1}H NMR** (400 MHz, CD_3OD): δ 4.97 (s, 2H), 4.94 (d, *J* = 1.4 Hz, 1H), 4.33 (dd, *J* = 11.7, 3.6 Hz, 1H), 4.20 (dd, *J* = 11.7, 6.1 Hz, 1H), 4.12 (ddd, *J* = 10.1, 5.7, 2.7 Hz, 2H), 4.09 – 4.00 (m, 4H), 3.92 (dt, *J* = 6.1, 3.0 Hz, 2H), 3.86 (ddt, *J* = 9.8, 6.8, 3.8 Hz, 4H), 3.72 – 3.66 (m, 15H), 3.42 – 3.39 (m, 2H), 2.39 (t, *J* = 7.3 Hz, 2H), 1.68 – 1.64 (m, 2H), 1.44 – 1.36 (m, 17H), 1.22 (dd, *J* = 11.6, 4.3 Hz, 2H), 1.13 – 1.04 (m, 1H), 0.93 (d, *J* = 4.4 Hz, 3H), 0.87 – 0.81 (m, 2H), 0.77 – 0.72 (m, 2H), 0.66 (q, *J* = 4.2 Hz, 2H), -0.24 (dd, *J* = 12.6, 4.7 Hz, 2H); **^{13}C NMR** (101 MHz, CD_3OD): δ 175.3, 109.7, 109.7, 109.6, 84.1, 83.8, 83.5, 83.2, 83.1, 82.8, 79.2, 79.2, 79.1, 71.6, 71.6, 71.5, 71.5, 71.5, 71.1,

68.3, 68.2, 67.9, 65.0, 51.8, 34.9, 33.1, 31.3, 31.0, 30.8, 30.6, 30.5, 30.2, 30.1, 29.9, 29.2, 29.1, 26.0, 23.8, 17.1, 17.0, 16.7, 14.5, 11.6; **HRMS** (ESI-MS): m/z calcd. For $C_{43}H_{75}N_3O1_7$ $[M+Na]^+$: 928.4994; Found: 928.4991.

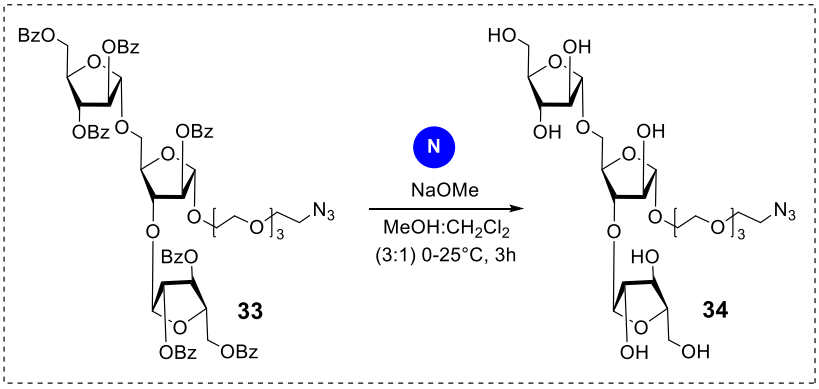
(2-(2-(2-(2-azidoethoxy)ethoxy)ethoxy)ethyl)-2-*O*-benzoyl-3-*O*-(2,3-di-*O*-benzoyl-5-*O*-benzoyl-α-D-arabinofuranosyl)-5-*O*-(2,3-di-*O*-benzoyl-5-*O*-benzoyl -α-D-arabinofuranosyl)-α-D-arabino furanoside (33) :

The glycosyl donor **5**[S4] and the glycosyl acceptor **10** were glycosylated according to the general reaction **Procedure B** as detailed above to give the **33.** (Yield 73%, pale yellow syrup): $[\alpha]_D^{25}$ = +14.4 (*c* = 0.06, $CHCl_3$); **IR** (cm^{-1}, $CHCl_3$): 2788, 2160, 1600, 1440, 1250, 1100, 690; **^{1}H NMR** (400 MHz, $CDCl_3$): δ 8.08 – 8.05 (m, 2H), 8.01 – 7.98 (m, 5H), 7.97 – 7.93 (m, 6H), 7.60 – 7.52 (m, 3H), 7.51 – 7.38 (m, 11H), 7.31 (dt, *J* = 18.6, 7.9 Hz, 5H), 7.23 (d, *J* = 6.3 Hz, 4H), 5.61 (s, 1H), 5.58 (s, 1H), 5.56 (s, 2H), 5.52 (d, *J* = 4.2 Hz, 1H), 5.46 – 5.44 (m, 1H), 5.37 (s, 1H), 5.27 (s, 1H), 4.78 (dd, *J* = 11.3, 2.8 Hz, 1H), 4.70 (dd, *J* = 11.5, 3.6 Hz, 1H), 4.60 (td, *J* = 10.2, 9.1, 4.9 Hz, 4H), 4.52 (d, *J* = 6.0 Hz, 1H), 4.40 (dt, *J* = 6.2, 2.3 Hz, 1H), 4.09 (dd, *J* = 11.4, 4.6 Hz, 1H), 3.92 – 3.85 (m, 2H), 3.71 – 3.61 (m, 13H), 3.36 – 3.32 (m, 2H); **^{13}C NMR** (101 MHz, $CDCl_3$): δ 166.3, 166.1, 165.8, 165.7, 165.7, 165.3, 165.3, 133.7, 133.6, 133.6, 133.5, 133.5, 133.1, 133.1, 130.1, 130.1, 130.0, 130.0, 130.0, 130.0, 129.9, 129.9, 129.9, 129.9, 129.8, 129.8, 129.8, 129.8, 129.7, 129.3, 129.2, 129.1, 129.1, 129.0, 128.7, 128.7, 128.6, 128.6, 128.6, 128.6, 128.6, 128.6, 128.6, 128.5, 128.5, 128.4, 128.4, 128.4, 128.4, 106.2, 106.1, 105.5, 82.8, 81.9, 81.8, 81.7, 81.7, 81.5, 80.9, 78.0, 77.8, 70.8, 70.8, 70.7, 70.7, 70.3, 70.1, 66.8, 65.9, 63.8, 63.8, 50.8; **HRMS** (ESI-MS): m/z calcd. For $C_{72}H_{69}N_3O_{23}$ $[M+Na]^+$: 1366.4220; Found: 1366.4204.



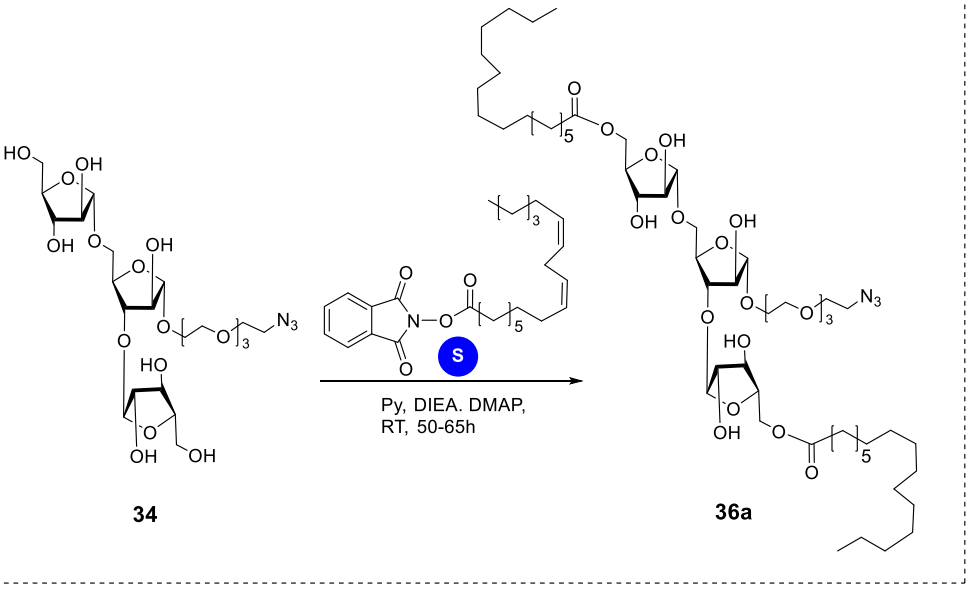
(2-(2-(2-(2-azidoethoxy)ethoxy)ethoxy)ethyl)-3-*O*-(α-D-arabinofuranosyl)-5-*O*-(α-D-arabinofura nosyl)-α-D-arabinofuranoside (34)

Compound **33** was converted to compound **34** according to the general experimental **Procedure N.** (Yield 82%, pale yellow syrup): **$[\alpha]_D^{25}$** = -10.4 (*c* = 0.06, $CHCl_3$); **IR** (cm^{-1}, $CHCl_3$): 3570, 3390, 2700, 2160, 1650, 1420, 1240, 1150, 700; **^{1}H NMR** (400 MHz, CD_3OD): δ 5.06 (d, *J* = 1.4 Hz, 1H), 4.96 (d, *J* = 1.1 Hz, 1H), 4.94 – 4.92 (m, 1H), 4.18 – 4.12 (m, 2H), 4.06 – 3.99 (m, 4H), 3.95 – 3.91 (m, 2H), 3.85 – 3.76 (m, 4H), 3.74 (t, *J* = 2.7 Hz, 2H), 3.72 – 3.67 (m, 3H), 3.66 (d, *J* = 1.1 Hz, 12H), 3.40 – 3.37 (m, 2H); **^{13}C NMR** (101 MHz, CD_3OD): δ 109.7, 109.5, 109.1, 85.9, 85.6, 84.3, 83.5, 83.0, 82.7, 82.0, 78.8, 78.7, 71.6, 71.6, 71.5, 71.5, 71.4, 71.1, 67.9, 67.7, 63.1, 63.0, 51.7; **HRMS** (ESI-MS): m/z calcd. For $C_{23}H_{41}N_3O_{16}[M+Na]^+$: 638.2385; Found: 638.2390.



(2-(2-(2-(2-azidoethoxy)ethoxy)ethoxy)ethyl-5-*O*-(5-*O*-(hexadecanoyl)-α-D-arabinofuranosyl)-3-*O*-(5-*O*-(hexadecanoyl)-α-D-arabinofuranosyl)-α-D-arabinofuranoside (36a) :

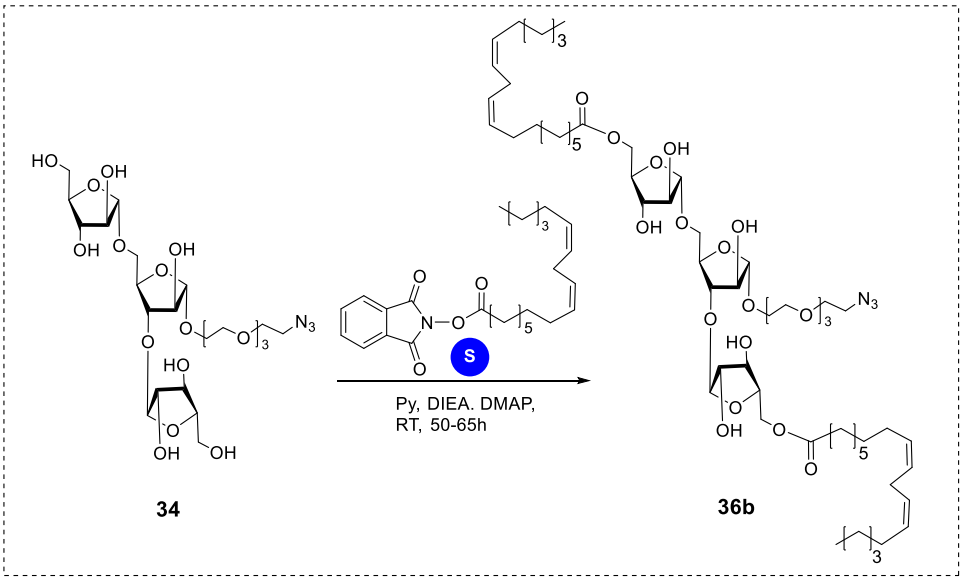
Compound **34** was converted to compound **36a** according to the general experimental **Procedure S.** (Yield 37%, pale yellow syrup): **$[\alpha]_D^{25}$** = +54.5 (*c* = 1.0, $CHCl_3$); **IR** (cm^{-1}, $CHCl_3$): 3570, 3300, 2855, 2300, 2150, 1730, 1455, 1333, 1310, 1090, 1020; **^{1}H NMR** (400 MHz, $CDCl_3$): δ 5.13 (s, 1H), 5.05 (s, 1H), 5.00 (s, 1H), 4.27 (ddd, *J* = 28.7, 14.2, 7.6 Hz, 6H), 4.12



(dd, *J* = 17.3, 7.7 Hz, 4H), 4.03 – 3.98 (m, 1H), 3.93 – 3.79 (m, 4H), 3.65 (d, *J* = 10.5 Hz, 14H), 3.42 – 3.38 (m, 2H), 2.34 (t, *J* = 7.5 Hz, 4H), 1.65 – 1.56 (m, 4H), 1.26 (d, *J* = 11.5 Hz, 48H), 0.87 (t, *J* = 6.8 Hz, 6H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ: 173.9, 173.9, 108.4, 108.3, 108.2, 83.6, 83.2, 82.4, 80.8, 80.0, 77.9, 77.7, 75.9, 73.3, 70.7, 70.6, 70.6, 70.5, 70.4, 70.4, 70.1, 64.1, 64.0, 64.0, 50.8, 34.2, 32.1, 32.1, 29.9, 29.9, 29.9, 29.9, 29.9, 29.9, 29.8, 29.8, 29.8, 29.8, 29.8, 29.8, 29.8, 29.8, 29.8, 29.7, 29.5, 29.5, 29.5, 29.5, 29.3, 29.3, 25.0, 22.8, 22.8, 14.3, 14.3; **HRMS** (ESI-MS): m/z calcd. For $C_{55}H_{101}N_3O_{18}$ $[M+Na]^+$: 1114.6978; Found: 1114.6980.

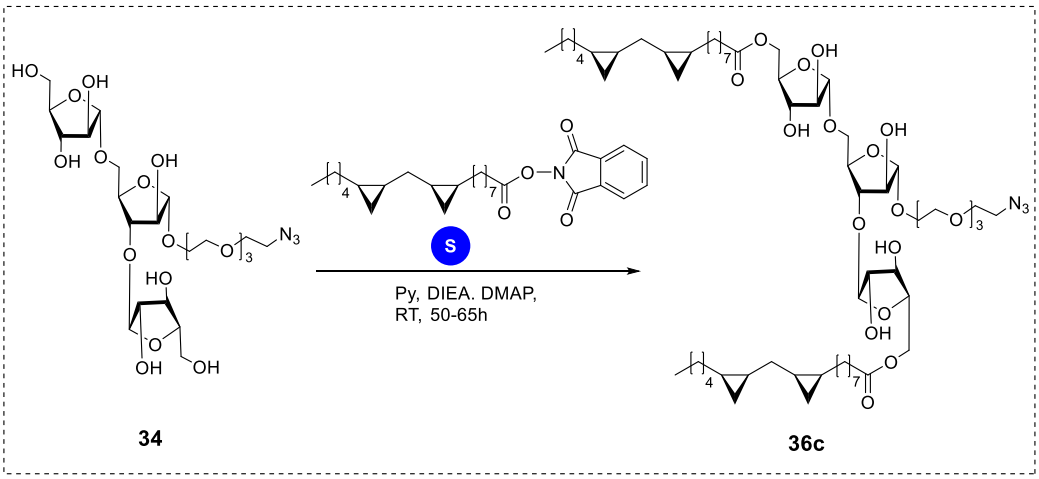
(2-(2-(2-(2-azidoethoxy)ethoxy)ethoxy)ethyl-5-*O*-(5-*O*-(9*Z*,12*Z*-octadecadienoyl)-α-D-arabinofuranosyl)-3-*O*-(5-*O*-(9*Z*,12*Z*-octadecadienoyl)-α-D-arabinofuranosyl)-α-D-arabinofuranoside (36b) :

Compound **34** was converted to compound **36b** according to the general experimental **Procedure S.** (Yield 38%, pale yellow syrup): **$[\alpha]_D^{25}$** = +30.5 (*c* = 0,06, $CHCl_3$); **IR** (cm^{-1}, $CHCl_3$): 3580, 3025, 2410, 2160, 1774, 1424, 1350, 1300, 1090, 1010; **^{1}H NMR** (400 MHz, $CDCl_3$): δ 5.35 (m, 8H), 5.13 (s, 1H), 5.05 (s, 1H), 4.99 (s, 1H), 4.32 – 4.16 (m, 7H), 4.10 (dd, *J* = 17.1, 7.2 Hz, 4H), 4.02 – 3.98 (m, 1H), 3.88 (s, 2H), 3.85 – 3.82 (m, 1H), 3.66 (q, *J* = 9.9, 9.5 Hz, 14H), 3.40 (t, *J* = 4.8 Hz, 2H), 2.76 (t, *J* = 6.4 Hz, 4H) , 2.34 (t, *J* = 7.6 Hz, 4H), 2.04 (q, *J* = 6.7 Hz, 8H), 1.64 – 1.57 (m, 4H), 1.32 (m, 28H), 0.88 (t, *J* = 6.8 Hz, 6H); **^{13}C NMR** (101 MHz, $CDCl_3$): δ 173.8, 173.7, 130.2, 130.2, 130.0, 130.0, 128.1, 128.1, 127.9, 127.9, 108.2, 108.2, 108.1, 83.5, 82.3, 80.7, 80.7, 80.0, 79.9, 77.7, 77.6, 77.2, 70.5, 70.5, 70.5, 70.4, 70.3, 70.0, 69.9, 66.8, 66.2, 64.0, 50.6, 34.1, 31.5, 31.5, 29.7, 29.6, 29.6, 29.4, 29.4, 29.4, 29.4, 29.3, 29.2, 29.2, 29.2, 29.1, 27.2, 27.2, 27.2, 27.2, 27.2, 27.2, 25.6, 25.6, 24.8, 22.6, 22.6, 14.1, 14.1; **HRMS** (ESI-MS): m/z calcd. For $C_{59}H_{101}N_3O_{16}$ $[M+Na]^+$: 1162.6978; Found: 1162.6980.

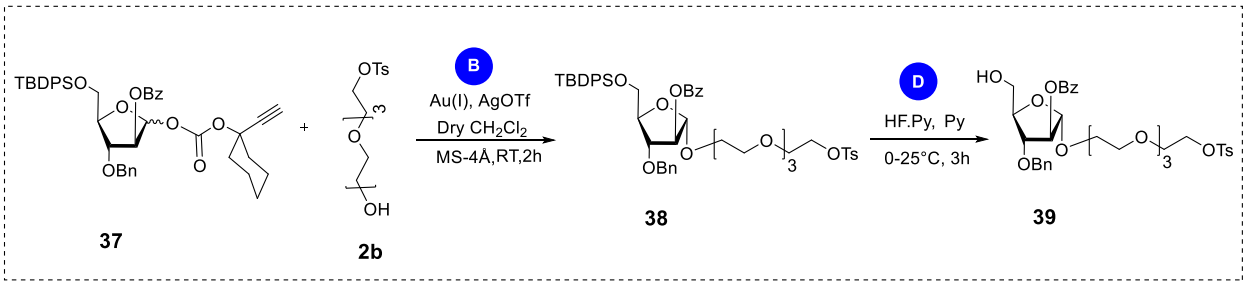


(2-(2-(2-(2-azidoethoxy)ethoxy)ethoxy)ethyl)-5-*O*-(5-*O*-(8-(2-((2-pentylcyclopropyl) methyl) cyclopropyl)octanoyl)-α-D-arabinofuranosyl)-3-*O*-(5-*O*-(8-(2-((2-pentylcyclopropyl)methyl)cy clopropyl)octanoyl)-α-D-arabinofuranosyl)-α-D-arabinofuranoside (36c):

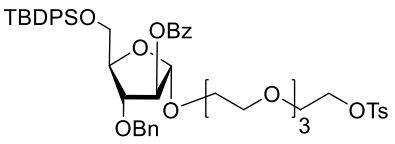
Compound **34** was converted to compound **36c** according to the general experimental **Procedure S.** (Yield 35%, pale yellow syrup): **$[\alpha]_D^{25}$** = +44.5 (*c* = 0.06, $CHCl_3$); **IR** (cm^{-1}, $CHCl_3$): 3570, 3350, 2755, 2250, 2180, 1710, 1435, 1340, 1210, 1070, 1010; **^{1}H NMR** (400 MHz, $CDCl_3$): δ 5.15 (s, 1H), 5.06 (s, 1H), 5.02 (s, 1H), 4.29 – 4.26 (m, 2H), 4.22 (dd, *J* = 6.8, 3.0 Hz, 3H), 4.19 – 4.11 (m, 3H), 4.07 (dd, *J* = 6.4, 2.4 Hz, 1H), 4.01 (dd, *J* = 11.0, 3.3 Hz, 1H), 3.95 – 3.88 (m, 2H), 3.84 (dd, *J* = 9.2, 5.9 Hz, 2H), 3.71 (d, *J* = 3.4 Hz, 1H), 3.70 – 3.62 (m, 14H), 3.41 (t, *J* = 5.0 Hz, 2H), 2.35 (t, *J* = 7.5 Hz, 4H), 1.65 – 1.59 (m, 5H), 1.39 (s, 8H), 1.31 – 1.25 (m, 26H), 1.17 – 1.10 (m, 4H), 1.03 (dt, *J* = 14.3, 7.9 Hz, 2H), 0.89 (m, 6H), 0.82 – 0.75 (m, 4H), 0.69 (dd, *J* = 10.8, 5.3 Hz, 3H), 0.61 (td, *J* = 8.3, 4.1 Hz, 4H), -0.28 (dq, *J* = 9.8, 5.1 Hz, 4H); **^{13}C NMR** (151 MHz, $CDCl_3$): δ 173.8, 173.7, 108.7, 108.1, 108.1, 83.7, 83.6, 83.6, 82.3, 80.6, 80.5, 79.8, 77.9, 77.7, 77.4, 70.7, 70.7, 70.6, 70.5, 70.1, 70.1, 67.1, 66.6, 64.0, 63.9, 50.8, 34.2, 32.0, 32.0, 30.3, 30.0, 30.0, 29.9, 29.9, 29.6, 29.5, 29.3, 29.0, 29.0, 28.9, 28.9, 28.2, 28.0, 25.0, 22.9, 22.9, 22.9, 16.2, 16.2, 16.1, 16.1, 16.1, 16.1, 16.1, 16.0, 16.0, 15.8, 15.8, 14.3, 14.3, 11.2, 11.2, 11.0, 11.0; **HRMS** (ESI-MS): m/z calcd. For $C_{63}H_{109}N_3O_{18}$ $[M+Na]^+$: 1218.7604; Found: 1218.7604.



Synthesis of Compound 39:

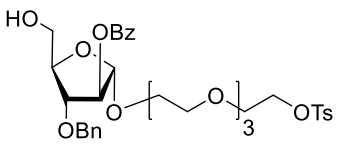


(2-(2-(2-(2-tosylethoxy)ethoxy)ethoxy)ethyl)-2-*O*-benzoyl-3-*O*-benzyl-5-*O*-*tert*butyldiphenylsilyl-α-D-arabinofuranoside (38) : The glycosyl donor **37**[49]and the glycosyl acceptor **2b**[47] were glycosylated according to the general reaction **Procedure B** as detailed above to give the **38**. (Yield 78%, pale yellow syrup). **$[\alpha]_D^{25}$** = +13.4 (*c* = 0.06, $CHCl_3$); **IR** (cm^{-1}, $CHCl_3$): 2910, 2860, 2270, 2100, 1440, 1315, 1020, 1000, 950, 900; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.98 – 7.95 (m, 2H), 7.79 (d, *J* = 8.3 Hz, 2H), 7.66 – 7.61 (m, 4H), 7.59 – 7.55 (m, 1H), 7.42 – 7.37 (m, 4H), 7.35 – 7.29 (m, 7H), 7.28 – 7.22 (m, 4H), 5.42 (s, 1H), 5.21 (s, 1H), 4.78 (d, *J* = 12.0 Hz, 1H), 4.57 (d, *J* = 12.0 Hz, 1H), 4.25 (q, *J* = 4.3 Hz, 1H), 4.15 – 4.12 (m, 3H), 3.84 (dd, *J* = 11.2, 4.7 Hz, 3H), 3.69 (s, 3H), 3.66 – 3.63 (m, 4H), 3.59 – 3.53 (m, 6H), 2.42 (s, 3H), 1.00 (s, 9H); **^{13}C NMR** (101 MHz, $CDCl_3$): δ 165.6, 144.9, 137.8, 135.8, 135.7, 133.4, 133.4, 133.4, 133.1, 129.9, 129.9, 129.8, 129.8, 129.6, 128.5, 128.5, 128.5, 128.5, 128.5, 128.5, 128.1, 128.1, 128.1, 128.0, 128.0, 127.8, 127.8, 127.8, 127.8, 127.8, 127.8, 106.4, 83.6, 83.3, 82.3, 72.4, 70.8, 70.8, 70.7, 70.6, 70.4, 69.4, 68.7, 66.7, 63.3, 26.9, 26.9, 26.9, 21.8, 19.4; **HRMS** (ESI-MS): m/z calcd. For $C_{50}H_{60}O_{12}SSi[M+Na]^+$: 953.3472; Found: 953.3482.



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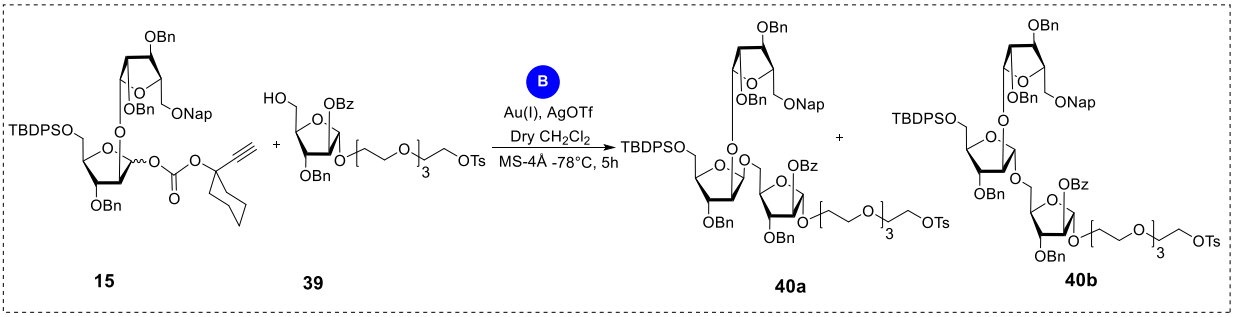
(2-(2-(2-(2-tosylethoxy)ethoxy)ethoxy)ethyl)-2-*O*-benzoyl-3-*O*-benzyl-α-D-arabinofuranoside (39) :Compound **38** was converted to compound **39** according to the general experimental **Procedure D** (Yield 72%, pale yellow syrup): **$[\alpha]_D^{25}$** = +16.4 (*c* = 0.06, $CHCl_3$); **IR** (cm^{-1}, $CHCl_3$): 3560, 3370, 2900, 2810, 2230, 2140, 1410, 1305, 1020, 940, 900; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.01 (dd, *J* = 8.3, 1.2 Hz, 2H), 7.79 (d, *J* = 8.3 Hz, 2H), 7.61 – 7.56 (m, 1H), 7.45 (t, *J* = 7.7 Hz, 2H), 7.34 – 7.27 (m, 7H), 5.40 (d, *J* = 1.5 Hz, 1H), 5.21 (s, 1H), 4.81 (d, *J* = 12.0 Hz, 1H), 4.60 (d, *J* = 12.0 Hz,



39

1H), 4.26 (ddd, *J* = 5.8, 4.3, 3.1 Hz, 1H), 4.15 – 4.13 (m, 2H), 4.05 – 4.03 (m, 1H), 3.91 – 3.84 (m, 2H), 3.73 – 3.63 (m, 9H), 3.60 – 3.55 (m, 5H), 2.43 (s, 3H); **^{13}C NMR** (101 MHz, $CDCl_3$): δ 165.5, 144.9, 137.7, 133.6, 133.1, 129.9, 129.9, 129.9, 129.8, 129.5, 128.6, 128.6, 128.5, 128.5, 128.1, 128.1, 128.0, 128.0, 128.0, 106.4, 83.2, 83.2, 82.2, 72.6, 70.8, 70.8, 70.6, 70.4, 69.4, 68.7, 66.9, 62.2, 21.7; **HRMS** (ESI-MS): m/z calcd. For $C_{34}H_{42}O_{12}S[M+Na]^+$: 697.2295; Found: 697.2281

(2-(2-(2-(2-tosylethoxy)ethoxy)ethoxy)ethyl)-2-*O*-benzoyl-3-*O*-benzyl-5-*O*-(2-*O*-(2,3-di-*O*-benzyl-5-*O*-(naphthylmethyl)-β-D-arabinofuranosyl)-3-*O*-benzyl-5-*O*-*tert*butyldiphenylsilyl-α-D-arabinofuranosyl)-α-D-arabinofuranoside (40b) :

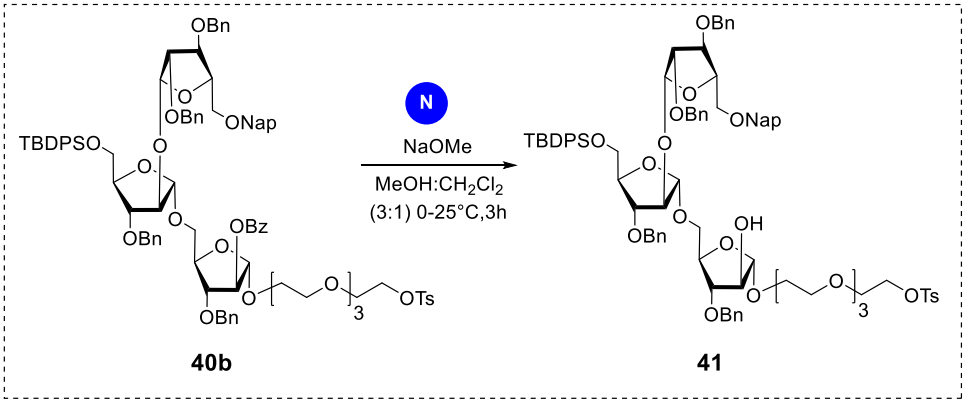


The glycosyl donor **15** and the glycosyl acceptor **39** were glycosylated according to the general reaction **Procedure B** as detailed above to give the **40a and 40b** (Both isomers 1:1). separated desired isomer **40b.** (Yield 42% of **40b**, pale yellow syrup) : **$[\alpha]_D^{25}$** = + 3.35 (*c* = 0.06, $CHCl_3$); **IR** (cm^{-1}, $CHCl_3$): 3840, 3512, 3018, 2928, 2768, 2308, 1710, 1578, 1418, 1272, 1107; **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.99 (d, *J* = 7.2 Hz, 2H), 7.78 (d, *J* = 8.2 Hz, 2H), 7.73 – 7.59 (m, 8H), 7.44 – 7.42 (m, 2H), 7.37 – 7.28 (m, 15H), 7.23 (dt, *J* = 6.4, 3.9 Hz, 10H), 7.19 – 7.13 (m, 7H), 5.40 – 5.38 (m, 1H), 5.16 (s, 1H), 5.11 (d, *J* = 4.3 Hz, 1H), 5.04 (s, 1H), 4.71 (d, *J* = 11.9 Hz, 1H), 4.64 (d, *J* = 12.0 Hz, 1H), 4.59 – 4.52 (m, 4H), 4.46 (dd, *J* = 12.0, 8.7 Hz, 3H), 4.41 – 4.35 (m, 2H), 4.30 (dt, *J* = 6.2, 3.5 Hz, 1H), 4.11 (dt, *J* = 9.9, 5.2 Hz, 7H), 4.04 – 4.00 (m, 1H), 3.93 – 3.83 (m, 2H), 3.77 (t, *J* = 4.0 Hz, 2H), 3.69 – 3.61 (m, 8H), 3.57 – 3.51 (m, 8H), 2.41 (s, 3H), 1.02 (s, 9H); **^{13}C NMR** (101 MHz, $CDCl_3$): δ 165.6, 144.8, 138.2, 138.2, 137.9, 137.8, 135.8, 135.7, 133.6, 133.5, 133.4, 133.3, 133.1, 133.0, 129.9, 129.9, 129.9, 129.9, 129.9, 129.9, 129.8, 129.8, 129.6, 128.6, 128.6, 128.6, 128.6, 128.4, 128.4, 128.4, 128.4, 128.4, 128.4, 128.3, 128.3, 128.2, 128.1, 128.1, 128.1, 128.1, 128.0, 128.0, 128.0, 128.0, 128.0, 127.9, 127.8, 127.8, 127.8, 127.8, 127.8, 127.8, 127.8, 127.7, 127.6, 127.5, 127.5, 126.4, 126.2, 125.9, 125.7, 106.4, 106.4, 100.4, 85.8, 84.0, 83.8, 83.6, 83.3, 83.0, 82.4, 81.6, 80.2, 73.3, 72.7, 72.5, 72.5, 72.4, 72.2,

70.8, 70.8, 70.7, 70.6, 70.3, 69.3, 68.7, 66.8, 65.9, 64.1, 27.0, 27.0, 27.0, 21.7, 19.4; **HRMS** (ESI-MS): m/z calcd. For $C_{92}H_{102}O_{20}SSi$ $[M+Na]^+$: 1609.6352; Found: 1609.6360.

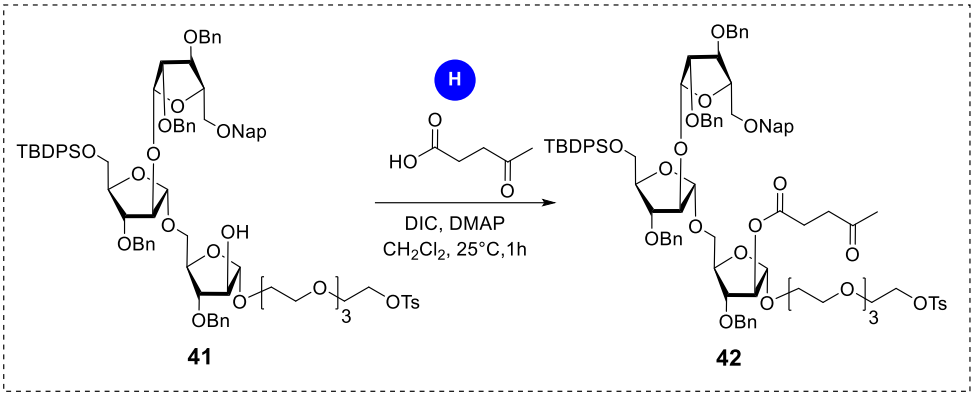
(2-(2-(2-(2-tosylethoxy)ethoxy)ethoxy)ethyl)-3-*O*-benzyl-5-*O*-(2-*O*-(2,3-*O*-dibenzyl-5-*O*-(naphthylmethyl)-β-D-arabinofuranosyl)-3-*O*-benzyl-5-*O*-*tert*butyldiphenylsilyl-α-D-arabinofuranosyl)-α-D-arabinofuranoside (41):

Compound **40b** was converted to compound **41** according to the general experimental **Procedure N.** (Yield 73%, pale yellow syrup) **$[\alpha]_D^{25}$** = +15.5 (*c* = 0.06, $CHCl_3$); **IR** (cm^{-1}, $CHCl_3$): 3751, 3526, 3040, 2300, 1716, 1437,1519, 1102, 1010**; ^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.78 (dd, *J* = 8.7, 4.7 Hz, 3H), 7.71 (t, *J* = 8.9 Hz, 2H), 7.67 – 7.60 (m, 6H), 7.44 – 7.41 (m, 2H), 7.38 – 7.30 (m, 10H), 7.27 (d, *J* = 5.1 Hz, 7H), 7.24 – 7.21 (m, 11H), 5.05 (d, *J* = 3.9 Hz, 1H), 4.98 (d, *J* = 2.6 Hz, 2H), 4.63 (dd, *J* = 11.9, 4.7 Hz, 2H), 4.58 – 4.52 (m, 3H), 4.47 (td, *J* = 12.1, 11.4, 4.7 Hz, 5H), 4.31 (s, 1H), 4.24 – 4.21 (m, 1H), 4.15 – 4.04 (m, 8H), 3.89 (d, *J* = 3.9 Hz, 1H), 3.81 (dd, *J* = 10.8, 7.2 Hz, 2H), 3.74 (d, *J* = 3.4 Hz, 2H), 3.66 – 3.60 (m, 9H), 3.55 (m, 5H), 3.52 – 3.48 (m, 2H), 2.41 (s, 3H), 1.03 (s, 9H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 144.9, 138.2, 138.1, 137.9, 137.8, 135.7, 135.7, 135.7, 135.7, 135.6, 133.5, 133.3, 133.1, 133.0, 129.9, 129.9, 129.8, 129.8, 128.6, 128.6, 128.5, 128.5, 128.4, 128.4, 128.4, 128.4, 128.2, 128.1, 128.1, 128.1, 128.1, 128.0, 128.0, 127.9, 127.9, 127.8, 127.8, 127.8, 127.8, 127.8, 127.8, 127.8, 127.8, 127.7, 127.7, 127.7, 127.7, 126.4, 126.2, 125.9, 125.7, 109.4, 105.7, 99.9, 85.3, 84.5, 84.1, 83.9, 83.3, 83.1, 82.8, 80.2, 79.3, 73.3, 72.5, 72.4, 72.2, 72.1, 72.1, 70.8, 70.7, 70.7, 70.6, 70.5, 69.4, 68.8, 67.0, 66.4, 64.1, 27.0, 27.0, 27.0, 21.7, 19.4; **HRMS** (ESI-MS): m/z calcd. For $C_{85}H_{98}O_{19}SSi$ $[M+Na]^+$: 1505.6090; Found: 1505.6091



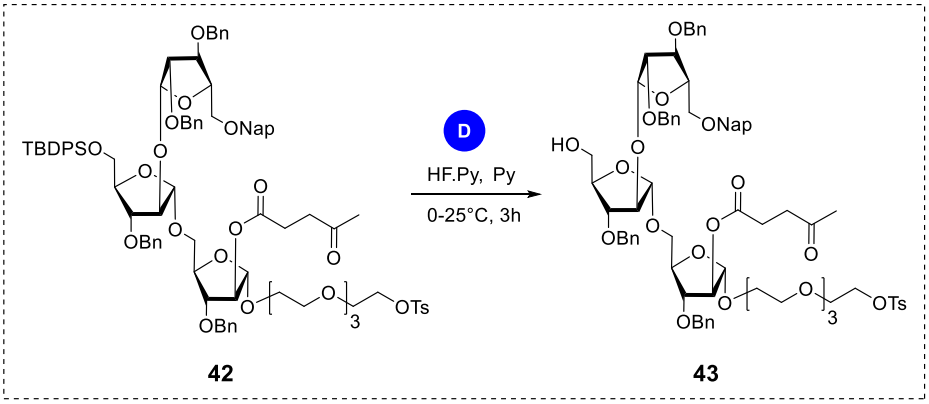
(2-(2-(2-(2-tosylethoxy)ethoxy)ethoxy)ethyl)-2-*O*-(4-oxopentanoyl)-3-*O*-benzyl-5-*O*-(2-*O*-(2,3-*O*-dibenzyl-5-*O*-(naphthylmethyl)-β-D-arabinofuranosyl)-3-*O*-benzyl-5-*O*-*tert*butyldiphenylsilyl-α-D-arabinofuranosyl)-α-D-arabinofuranoside (42):

Compound **41** was converted to compound **42** according to the general experimental **Procedure H.** (Yield 84%, pale yellow syrup) **$[\alpha]_D^{25}$** = +20.0 (*c* = 0.06, $CHCl_3$); **IR** (cm^{-1}, $CHCl_3$): 3220, 3140, 2300, 1736, 1430,1599, 1102, 1010, 950; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.78 (dd, *J* = 8.8, 4.5 Hz, 3H), 7.71 (d, *J* = 8.5 Hz, 1H), 7.69 – 7.64 (m, 5H), 7.59 (s, 1H), 7.46 – 7.42 (m, 2H), 7.37 (td, *J* = 6.9, 2.7 Hz, 2H), 7.34 – 7.29 (m, 11H), 7.28 – 7.26 (m, 4H), 7.22 (m, 12H), 5.15 – 5.12 (m, 2H), 5.03 (d, *J* = 7.8 Hz, 2H), 4.66 (d, *J* = 11.7 Hz, 2H), 4.63 – 4.57 (m, 3H), 4.55 – 4.49 (m, 3H), 4.48 – 4.45 (m, 2H), 4.40 (d, *J* = 20.0 Hz, 2H), 4.21 (dt, *J* = 6.4, 3.5 Hz, 1H), 4.15 – 4.08 (m, 7H), 3.96 (d, *J* = 5.8 Hz, 1H), 3.83 (ddd, *J* = 23.5, 12.7, 3.5 Hz, 4H), 3.67 – 3.58 (m, 10H), 3.55 (d, *J* = 9.7 Hz, 5H), 2.60 – 2.54 (m, 2H), 2.50 – 2.44 (m, 2H), 2.41 (s, 3H), 2.06 (s, 3H), 1.03 (s, 9H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 206.3, 172.0, 144.9, 138.2, 138.2, 137.9, 137.8, 135.8, 135.7, 135.6, 133.6, 133.5, 133.3, 133.1, 133.0, 129.9, 129.9, 129.9, 129.9, 129.8, 128.6, 128.6, 128.4, 128.4, 128.4, 128.4, 128.4, 128.4, 128.2, 128.1, 128.1, 128.1, 128.1, 128.1, 128.0, 127.9, 127.9, 127.9, 127.9, 127.8, 127.8, 127.8, 127.8, 127.8, 127.8, 127.7, 127.7, 127.6, 127.6, 127.5, 126.4, 126.2, 125.9, 125.7, 106.4, 106.2, 100.3, 85.7, 84.0, 84.0, 83.5, 83.2, 82.8, 82.0, 81.8, 80.1, 73.3, 72.6, 72.5, 72.5, 72.4, 72.3, 70.8, 70.7, 70.7, 70.6, 70.2, 69.4, 68.7, 66.7, 65.9, 64.1, 37.8, 29.8, 27.9, 27.0, 27.0, 27.0, 21.7, 19.4; **HRMS** (ESI-MS): m/z calcd. For $C_{90}H_{104}O_{21}SSi$ $[M+Na]^+$: 1603.6458; Found: 1603.6469.



(2-(2-(2-(2-tosylethoxy)ethoxy)ethoxy)ethyl)-2-*O*-(4-oxopentanoyl)-3-*O*-benzyl-5-*O*-(2-*O*-(2,3-*O*-dibenzyl-5-*O*-(naphthylmethyl)-β-D-arabinofuranosyl)-3-*O*-benzyl-α-D-arabinofuranosyl)-α-D-arabinofuranoside (43):

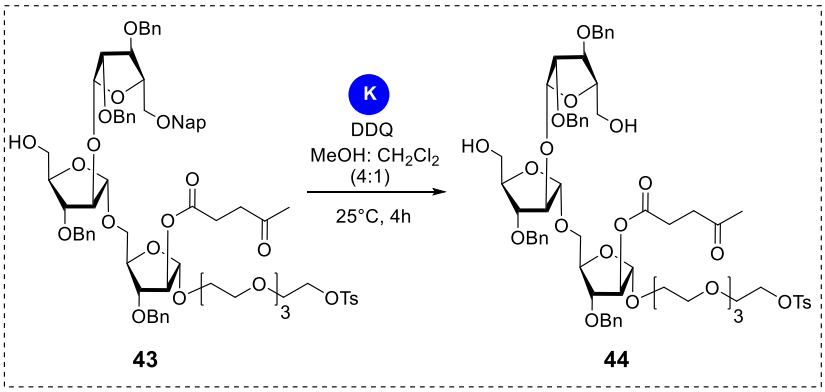
Compound **42** was converted to compound **43** according to the general experimental **Procedure D.** (Yield 79%, pale yellow syrup) **$[\alpha]_D^{25}$** = +68.8 (*c* = 0.06, $CHCl_3$); **IR** (cm^{-1}, $CHCl_3$): 3566, 3015, 2909, 1720, 1405, 1320, 1100**; ^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.80 – 7.71 (m, 6H), 7.66 (s, 1H), 7.46 – 7.43 (m, 2H), 7.38 – 7.34 (m, 5H), 7.30 (m, 9H), 7.25 – 7.23 (m, 8H), 5.14 – 5.13 (m, 1H), 5.09 (d, *J* = 4.3 Hz, 1H), 5.03 (s, 2H), 4.66 (dt, *J* = 12.6, 6.4 Hz, 3H), 4.58 (s, 3H), 4.47 (dt, *J* = 29.7, 11.9 Hz, 4H), 4.33 – 4.31 (m, 1H), 4.22 (dd, *J* = 5.8, 3.2 Hz, 1H), 4.13 (s, 3H),



4.10 – 4.05 (m, 2H), 4.03 – 3.94 (m, 2H), 3.85 – 3.79 (m, 2H), 3.74 – 3.60 (m, 12H), 3.57 – 3.54 (m, 7H), 2.56 (t, *J* = 6.2 Hz, 2H), 2.49 – 2.44 (m, 2H), 2.42 (s, 3H), 2.07 (s, 3H);**^{13}C NMR** (101 MHz, $CDCl_3$) δ 206.4, 171.9, 144.9, 138.1, 138.1, 137.9, 137.6, 135.5, 133.3, 133.1, 133.0, 129.9, 129.9, 128.6, 128.6, 128.4, 128.4, 128.4, 128.4, 128.4, 128.4, 128.4, 128.3, 128.1, 128.1, 128.1, 128.1, 128.1, 127.9, 127.9, 127.9, 127.8, 127.8, 127.8, 127.8, 127.7, 127.6, 127.6, 126.5, 126.2, 126.0, 125.8, 106.5, 106.1, 100.5, 85.4, 84.0, 83.6, 83.4, 83.3, 82.8, 81.9, 81.7, 80.1, 73.3, 72.6, 72.5, 72.4, 72.3, 72.1, 70.8, 70.7, 70.7, 70.5, 70.2, 69.3, 68.7, 66.7, 65.8, 62.5, 37.8, 29.8, 27.8, 21.7; **HRMS** (ESI-MS): m/z calcd. For $C_{74}H_{86}O_{21S}[M+Na]^+$: 1365.5280; Found: 1365.5299.

(2-(2-(2-(2-tosylethoxy)ethoxy)ethoxy)ethyl-2-*O*-(4-oxopentanoyl)-3-*O*-benzyl-5-*O*-(2-*O*-(2,3-*O*-dibenzyl-β-D-arabinofuranosyl)-3-*O*-benzyl-α-D-arabinofuranosyl)-α-D-arabinofuranoside (44):

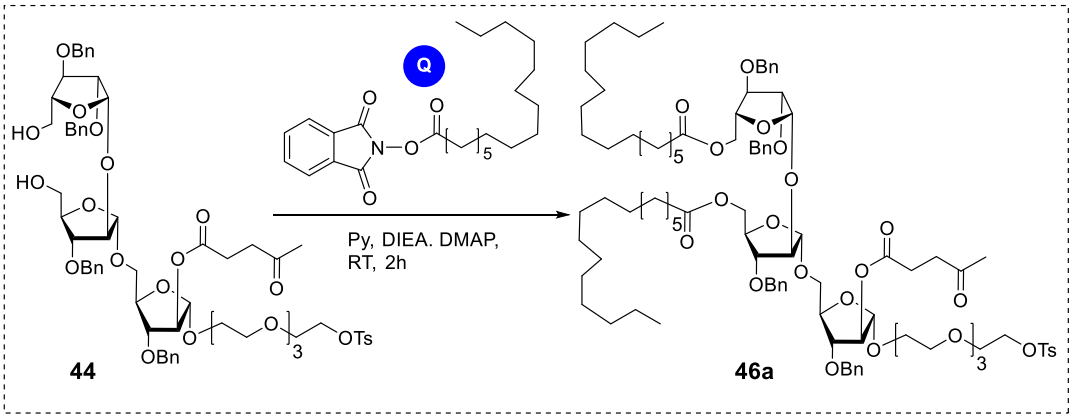
Compound **43** was converted to compound **44** according to the general experimental **Procedure K.** (Yield 72%, pale yellow syrup): **$[\alpha]_D^{25}$** = +9.09 (*c* = 0.06, $CHCl_3$); **IR** (cm^{-1}, $CHCl_3$): 3566, 3015, 2803, 1690, 1505, 1320, 1100, 1008**; ^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.79 (d, *J* = 8.3 Hz, 2H), 7.35 – 7.28 (m, 22H), 5.14 (d, *J* = 1.3 Hz, 1H), 5.07 (d, *J* = 4.6 Hz, 1H), 5.04 (d, *J* = 6.5 Hz, 2H), 4.71 (d, *J* = 12.1 Hz, 2H), 4.64 (d, *J* = 12.0 Hz, 1H), 4.61 – 4.56 (m, 3H), 4.52 (d, *J* = 12.0 Hz, 2H), 4.28 (d, *J* = 1.7 Hz, 1H), 4.22 (dd, *J* = 6.2, 3.1 Hz, 2H), 4.16 – 4.13 (m, 3H), 4.08 (dd, *J* = 7.2, 4.5 Hz, 1H), 4.02 – 3.94 (m, 3H), 3.86 – 3.73 (m, 4H), 3.67 – 3.60 (m, 10H), 3.56 (m, 6H), 2.66 – 2.62 (m, 2H), 2.50 (td, *J* = 6.5, 2.2 Hz, 2H), 2.43 (s, 3H), 2.12 (s, 3H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 206.6,



171.9, 144.9, 138.1, 137.9, 137.9, 137.6, 133.1, 129.9, 129.9, 128.6, 128.6, 128.5, 128.5, 128.5, 128.5, 128.4, 128.4, 128.1, 128.1, 128.1, 128.0, 128.0, 127.9, 127.9, 127.9, 127.9, 127.8, 127.8, 127.8, 127.7, 127.7, 106.4, 106.1, 100.5, 86.2, 84.1, 83.3, 83.1, 82.9, 82.1, 81.8, 81.7, 80.7, 72.7, 72.6, 72.3, 72.3, 70.8, 70.7, 70.7, 70.5, 70.2, 69.3, 68.7, 66.7, 65.9, 63.5, 62.2, 37.8, 29.8, 27.8, 21.7; **HRMS** (ESI-MS): m/z calcd. For $C_{63}H_{78}O_{21}S$ $[M+Na]^+$: 1225.4654; Found: 1225.4670.

(2-(2-(2-(2-tosylethoxy)ethoxy)ethoxy)ethyl)-2-*O*-(4-oxopentanoyl)-3-*O*-benzyl-5-*O*-(2-*O*-(2,3-*O*-dibenzyl-5-*O*-(hexadecanoyl)-β-D-arabinofuranosyl)-3-*O*-benzyl-5-*O*-(hexadecanoyl)-α-D-arabinofuranosyl)-α-D-arabinofuranoside(46a):

Compound **44** was converted to compound **46a** according to the general experimental **Procedure Q.** (Yield 47%, pale yellow syrup) $[\alpha]_D^{25}$ = + 17.7(*c* = 1.0, $CHCl_3$); **IR** (cm^{-1}, $CHCl_3$):

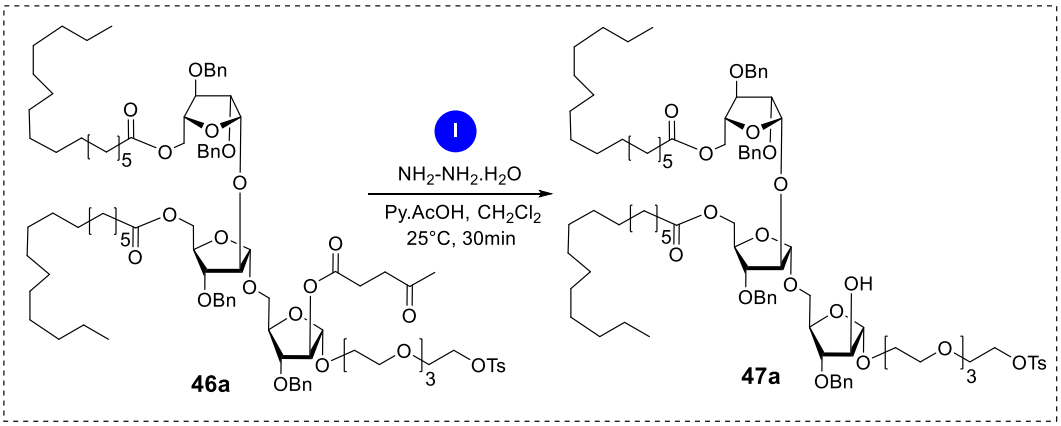


3630, 3060, 2911, 2815, 1704, 1428, 1360, 1213, 1022, 960, 905; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.79 (d, *J* = 8.3 Hz, 2H), 7.35 – 7.27 (m, 22H), 5.14 (d, *J* = 1.4 Hz, 1H), 5.12 (d, *J* = 2.0 Hz, 1H), 5.03 (d, *J* = 4.2 Hz, 2H), 4.70 (d, *J* = 3.2 Hz, 1H), 4.67 (d, *J* = 3.3 Hz, 2H), 4.62 – 4.58 (m, 2H), 4.54 – 4.47 (m, 3H), 4.35 – 4.34 (m, 1H), 4.24 (dd, *J* = 9.2, 6.5 Hz, 2H), 4.22 – 4.18 (m, 2H), 4.15 – 4.13 (m, 4H), 4.09 (d, *J* = 4.5 Hz, 2H), 3.97 – 3.93(m, 2H), 3.88 – 3.77 (m, 5H), 3.67 – 3.64 (m, 3H), 3.63 – 3.60 (m, 4H), 3.56 (m, 5H), 2.63 (td, *J* = 6.4, 3.1 Hz, 2H), 2.49 (q, *J* = 6.4, 5.9 Hz, 2H), 2.43 (s, 3H), 2.31 (s, 1H), 2.26 (t, *J* = 7.6 Hz, 2H), 2.19 (td, *J* = 7.5, 2.1 Hz, 2H), 2.12 (s, 3H), 1.26 (s, 51H), 0.88 (s, 6H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 206.3, 173.7, 173.5, 171.9, 144.9, 137.9, 137.9, 137.9, 137.5, 133.1, 129.9, 129.9, 128.7, 128.7, 128.6, 128.6, 128.5, 128.5, 128.5, 128.5, 128.2, 128.2, 128.2, 128.1, 128.1, 128.0, 128.0, 128.0, 127.9, 127.8, 127.8, 127.8, 127.7, 127.7, 106.5, 106.2, 100.8, 86.1, 84.4, 83.8, 83.4, 82.8, 82.0, 81.7, 80.2, 79.0, 72.7, 72.6, 72.5, 72.5, 70.8, 70.8, 70.7, 70.6, 70.2, 69.4, 68.8, 66.8, 66.0, 66.0, 63.7, 37.9, 34.1, 32.0, 29.8, 29.8, 29.8, 29.8, 29.8, 29.8, 29.8, 29.8, 29.8, 29.7, 29.7, 29.6, 29.6, 29.5, 29.5, 29.4,

29.4, 29.3, 29.3, 27.9, 25.0, 24.9, 23.6, 23.6, 22.8, 21.8, 14.2, 14.2; **HRMS** (ESI-MS): m/z calcd. For $C_{95}H_{138}O_{23}S$ $[M+Na]^+$: 1701.9247; Found: 1701.9255.

(2-(2-(2-(2-tosylethoxy)ethoxy)ethoxy)ethyl)-3-*O*-benzyl-5-*O*-(2-O-(2,3-*O*-dibenzyl-5-*O*-(hexadecanoyl)-β-D-arabinofuranosyl)-3-*O*-benzyl-5-*O*-(hexadecanoyl)-α-D-arabinofuranosyl)-α-D-arabinofuranoside (47a):

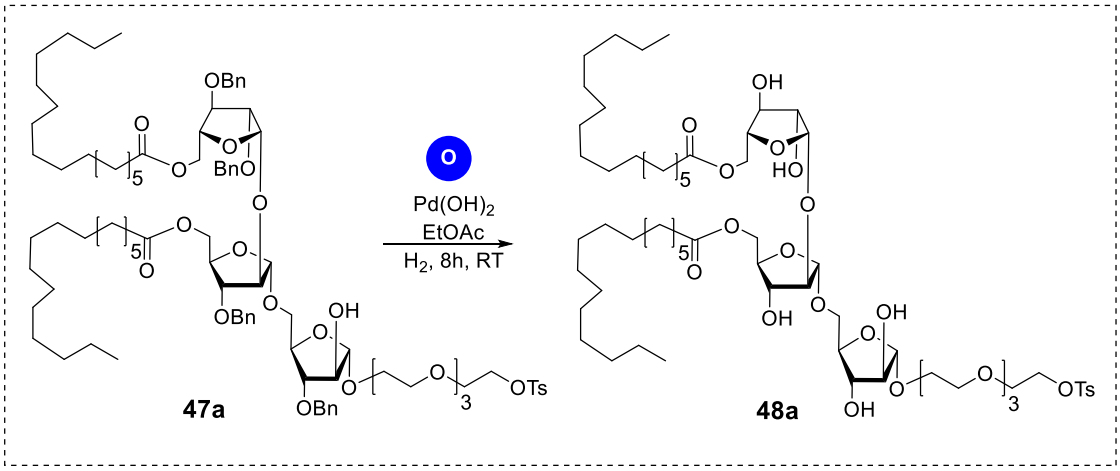
Compound **46a** was converted to compound **47a** according to the general experimental **Procedure I.** (Yield 67%, pale yellow syrup): **$[\alpha]_D^{25}$** = +44.8 (*c* = 0.06, $CHCl_3$); **IR** (cm^{-1}, $CHCl_3$)



3630, 3207, 2804, 2105, 1702, 1410, 1326, 1050, 1022, 870**; ^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.79 (d, *J* = 8.3 Hz, 2H), 7.31 (m, 22H), 5.03 (d, *J* = 3.6 Hz, 1H), 4.99 (s, 2H), 4.70 – 4.65 (m, 2H), 4.61 (d, *J* = 10.2 Hz, 1H), 4.57 – 4.54 (m, 1H), 4.52 (d, *J* = 7.1 Hz, 1H), 4.49 (d, *J* = 7.6 Hz, 1H), 4.27 (d, *J* = 1.5 Hz, 1H), 4.22 (dd, *J* = 4.4, 2.2 Hz, 1H), 4.17 – 4.13 (m, 5H), 4.12 – 4.07 (m, 3H), 4.05 (q, *J* = 4.6, 3.7 Hz, 3H), 3.90 – 3.78 (m, 7H), 3.67 – 3.61 (m, 8H), 3.57 (d, *J* = 3.8 Hz, 5H), 2.43 (s, 3H), 2.29 – 2.20 (m, 4H), 1.57 (dd, *J* = 15.2, 7.6 Hz, 4H), 1.26 (s, 48H), 0.88 (s, 6H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 173.5, 173.4, 144.9, 138.0, 137.8, 137.5, 137.5, 133.1, 129.9, 129.9, 128.6, 128.6, 128.5, 128.5, 128.5, 128.5, 128.5, 128.5, 128.5, 128.2, 128.1, 128.1, 128.1, 128.0, 128.0, 128.0, 127.9, 127.9, 127.9, 127.8, 127.8, 127.8, 109.4, 105.8, 100.4, 85.0, 84.6, 83.8, 83.8, 82.6, 82.5, 81.2, 79.3, 78.9, 72.7, 72.6, 72.3, 72.1, 70.8, 70.7, 70.7, 70.5, 70.5, 69.3, 68.7, 67.0, 66.3, 65.8, 63.7, 34.1, 32.0, 29.8, 29.8, 29.8, 29.8, 29.8, 29.8, 29.8, 29.8, 29.7, 29.7, 29.7, 29.6, 29.6, 29.5, 29.4, 29.4, 29.4, 29.4, 29.3, 29.2, 24.9, 24.9, 23.6, 23.6, 23.6, 23.6, 22.8, 22.8, 21.7, 14.2, 14.2; **HRMS** (ESI-MS): m/z calcd. For $C_{90}H_{132}O_{21}S$ $[M+Na]^+$: 1603.8880; Found: 1603.8891.

(2-(2-(2-(2-tosylethoxy)ethoxy)ethoxy)ethyl)-5-*O*-(2-*O*-(-5-*O*-(hexadecanoyl)-β-D-arabinofuranosyl)-5-*O*-(hexadecanoyl)-α-D-arabinofuranosyl)-α-D-arabinofuranoside (48a):

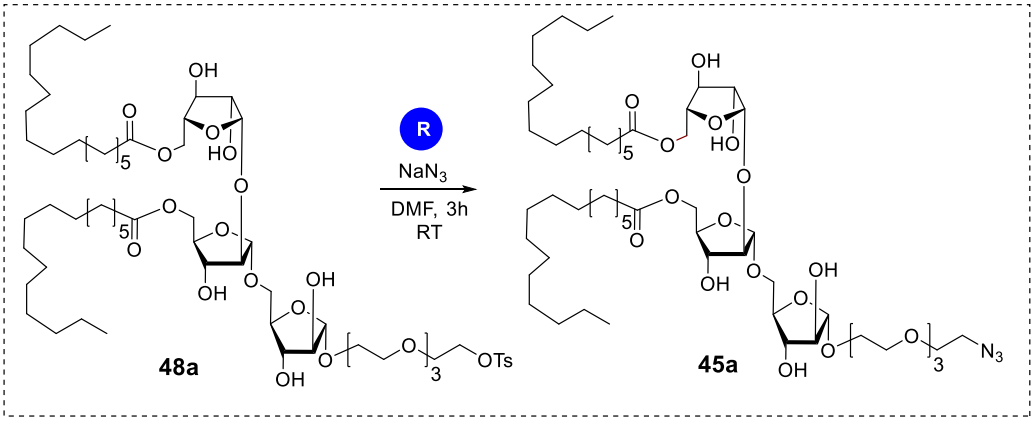
Compound **47** was converted to compound **48** according to the general experimental **Procedure O.** (Yield 52%, pale yellow syrup**): $[\alpha]_D^{25}$** = +27.2 (*c* = 0.06, $CHCl_3$); **IR** (cm^{-1}, $CHCl_3$)



3610, 3535, 2720, 2700, 2009, 1612, 1205, 1310, 1110, 1013; 900; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.78 (d, *J* = 8.0 Hz, 2H), 7.33 (d, *J* = 8.0 Hz, 2H), 5.08 (d, *J* = 2.1 Hz, 1H), 5.01 (d, *J* = 4.2 Hz, 2H), 4.29 (d, *J* = 8.5 Hz, 2H), 4.20 – 4.08 (m, 8H), 4.04 – 3.93 (m, 7H), 3.89 – 3.82 (m, 2H), 3.81 – 3.75 (m, 2H), 3.68 – 3.65 (m, 2H), 3.58 (m, 8H), 2.43 (s, 3H), 2.32 (q, *J* = 7.3 Hz, 4H), 1.61 – 1.56 (m, 4H), 1.25 (m, 48H), 0.86 (s, 6H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 174.1, 173.9, 145.0, 133.0, 130.0, 130.0, 128.1, 128.1, 107.8, 105.8, 102.2, 89.2, 80.2, 80.1, 78.0, 77.4, 76.0, 76.0, 76.0, 75.6, 70.7, 70.5, 70.5, 70.4, 70.2, 69.4, 68.8, 67.4, 65.9, 65.5, 63.6, 34.2, 34.1, 32.0, 32.0, 29.8, 29.8, 29.8, 29.8, 29.8, 29.8, 29.8, 29.8, 29.8, 29.8, 29.7, 29.7, 29.6, 29.5, 29.4, 29.4, 29.4, 29.3, 25.0, 24.9, 23.5, 23.5, 22.8, 22.8, 21.7, 14.2, 14.2; **HRMS** (ESI-MS): m/z calcd. For $C_{62}H_{108}O_{21}S$ $[M+Na]^+$: 1243.7002; Found: 1243.7009.

(2-(2-(2-(2-Azidoethoxy)ethoxy)ethoxy)ethyl-5-*O*-(2-*O*-(-5-*O*-(hexadecanoyl)-β-D-arabinofuranosyl)-5-*O*-(hexadecanoyl)-α-D-arabinofuranosyl)-α-D-arabinofuranoside (45a):

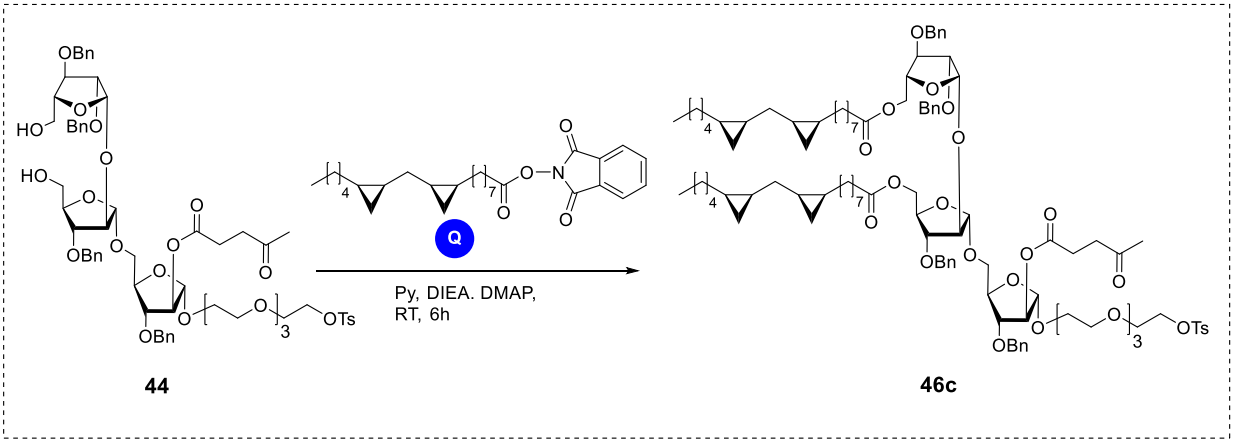
Compound **48a** was converted to compound **45a** according to the general experimental **Procedure R.** (Yield 60%, pale yellow syrup): **$[\alpha]_D^{25}$** = +43.4 (*c* = 0.06, $CHCl_3$); **IR** (cm^{-1},



$CHCl_3$): 3787, 3400, 2900, 2815, 2160, 1727,1499, 1338, 1300, 1105, 890; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 5.08 (d, *J* = 2.4 Hz, 1H), 5.03 (s, 1H), 5.02 (s, 1H), 4.31 (dt, *J* = 9.8, 5.8 Hz, 2H), 4.17 (q, *J* = 6.2, 4.9 Hz, 4H), 4.12 – 4.08 (m, 1H), 4.05 – 4.00 (m, 3H), 3.99 – 3.96 (m, 3H), 3.88 (dd, *J* = 8.6, 4.6 Hz, 1H), 3.72 (dd, *J* = 11.4, 2.9 Hz, 1H), 3.68 – 3.59 (m, 14H), 3.41 – 3.37 (m, 2H), 2.34 (d, *J* = 7.7 Hz, 4H), 1.60 (q, *J* = 6.7 Hz, 4H), 1.24 (s, 48H), 0.87 (t, *J* = 6.8 Hz, 6H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 174.2, 173.9, 107.9, 105.8, 102.2, 89.2, 85.2, 85.1, 80.2, 78.1, 77.5, 77.4, 76.1, 75.6, 70.7, 70.6, 70.6, 70.4, 70.3, 70.1, 67.4, 66.0, 65.4, 63.7, 50.8, 34.2, 34.2, 32.0, 32.0, 29.8, 29.8, 29.8, 29.8, 29.8, 29.8, 29.8, 29.8, 29.8, 29.8, 29.8, 29.8, 29.8, 29.6, 29.6, 29.5, 29.5, 29.5, 29.4, 29.3, 25.0, 25.0, 22.8, 22.8, 14.2, 14.2; **HRMS** (ESI-MS): m/z calcd. For $C_{55}H_{101}N_3O_{18}$ $[M+Na]^+$: 1114.6978; Found: 1114.6980.

(2-(2-(2-(2-tosylethoxy)ethoxy)ethoxy)ethyl)-2-*O*-(4-oxopentanoyl)-3-*O*-benzyl-5-*O*-(2-*O*-(2,3-*O*-dibenzyl-5-*O*-(8-(2-((2-pentylcyclopropyl)methyl)cyclopropyl)octanoyl)-β-D-arabinofuranosyl)-3-*O*-benzyl-5-*O*-(8-(2-((2-pentylcyclopropyl) methyl)cyclopropyl)octanoyl)-α-D-arabinofuranosyl)-α-D-arabinofuranoside (46c):

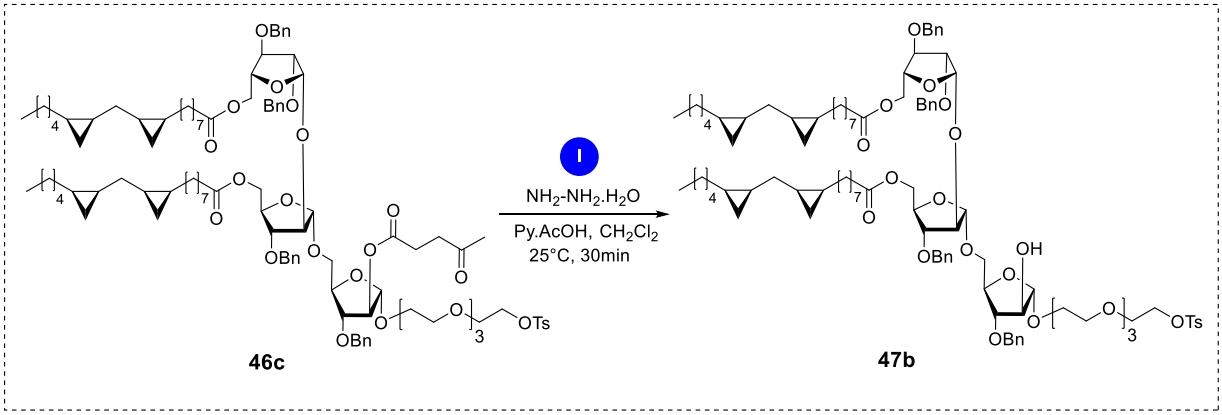
Compound **44** was converted to compound **46c** according to the general experimental **Procedure Q.** (Yield 45%, pale yellow syrup)**: [α]$_D^{25}$** = +21.2 (*c* = 0.06, $CHCl_3$); **IR** (cm^{-1}, $CHCl_3$):



3155, 3008, 2911, 2815, 2300, 1712, 1604, 1408, 1338, 1280, 1053, 980, 902; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.79 (d, *J* = 8.3 Hz, 2H), 7.36 – 7.27 (m, 22H), 5.14 (d, *J* = 1.5 Hz, 1H), 5.12 (d, *J* = 2.2 Hz, 1H), 5.03 (d, *J* = 4.4 Hz, 2H), 4.70 (d, *J* = 2.9 Hz, 1H), 4.68 (d, *J* = 3.1 Hz, 1H), 4.61 (d, *J* = 1.7 Hz, 1H), 4.59 (d, *J* = 1.8 Hz, 1H), 4.54 – 4.47 (m, 3H), 4.34 (d, *J* = 2.0 Hz, 1H), 4.27 – 4.19 (m, 3H), 4.17 – 4.07 (m, 9H), 3.96 – 3.93 (m, 2H), 3.87 – 3.78 (m, 2H), 3.67 – 3.64 (m, 3H), 3.63 – 3.60 (m, 4H), 3.56 (d, *J* = 9.3 Hz, 7H), 2.63 (td, *J* = 6.3, 3.0 Hz, 2H), 2.49 (q, *J* = 6.3, 5.8 Hz, 2H), 2.43 (s, 3H), 2.27 (t, *J* = 7.6 Hz, 2H), 2.20 (td, *J* = 7.5, 2.2 Hz, 2H), 2.12 (s, 3H), 1.42 – 1.36 (m, 10H), 1.33 – 1.26 (m, 32H), 0.88 (m, 9H), 0.80 – 0.74 (m, 4H), 0.71 – 0.65 (m, 3H),

0.63 – 0.58 (m, 4H), -0.28 (dq, *J* = 9.5, 3.3, 2.5 Hz, 4H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 206.3, 173.7, 173.5, 172.0, 144.9, 137.9, 137.9, 137.9, 137.5, 133.2, 129.9, 129.9, 128.7, 128.7, 128.6, 128.6, 128.5, 128.5, 128.5, 128.5, 128.2, 128.2, 128.2, 128.1, 128.1, 128.0, 128.0, 128.0, 127.9, 127.8, 127.8, 127.8, 127.7, 127.7, 106.5, 106.2, 100.8, 86.1, 84.4, 83.9, 83.4, 82.8, 82.0, 81.7, 80.2, 79.0, 72.7, 72.6, 72.5, 72.5, 70.8, 70.8, 70.7, 70.6, 70.3, 69.4, 68.8, 66.8, 66.1, 66.0, 63.8, 37.9, 34.1, 34.1, 32.1, 32.0, 30.3, 30.3, 30.0, 29.8, 29.8, 29.8, 29.6, 29.6, 29.5, 29.5, 29.5, 29.3, 29.3, 29.0, 28.8, 28.2, 28.0, 27.9, 24.9, 22.9, 22.9, 22.8, 21.8, 16.2, 16.1, 16.0, 16.0, 16.0, 15.8, 15.7, 14.3, 14.3, 11.2, 11.2, 11.0, 11.0; **HRMS** (ESI-MS): m/z calcd. For $C_{103}H_{146}O_{23}S[M+Na]^+$:1805.9873; Found: 1805.9880.

(2-(2-(2-(2-tosylethoxy)ethoxy)ethoxy)ethyl)-3-*O*-benzyl-5-*O*-(2-*O*-(2,3-*O*-dibenzyl-5-*O*-(8-(2-((2-pentylcyclopropyl)methyl)cyclopropyl)octanoyl)-β-D-arabinofuranosyl)-3-*O*-benzyl-5-*O*-(8-(2-((2-pentylcyclopropyl)methyl)cyclopropyl)octanoyl)-α-D-arabinofuranosyl)-α-D-arabinofuranoside (47b):



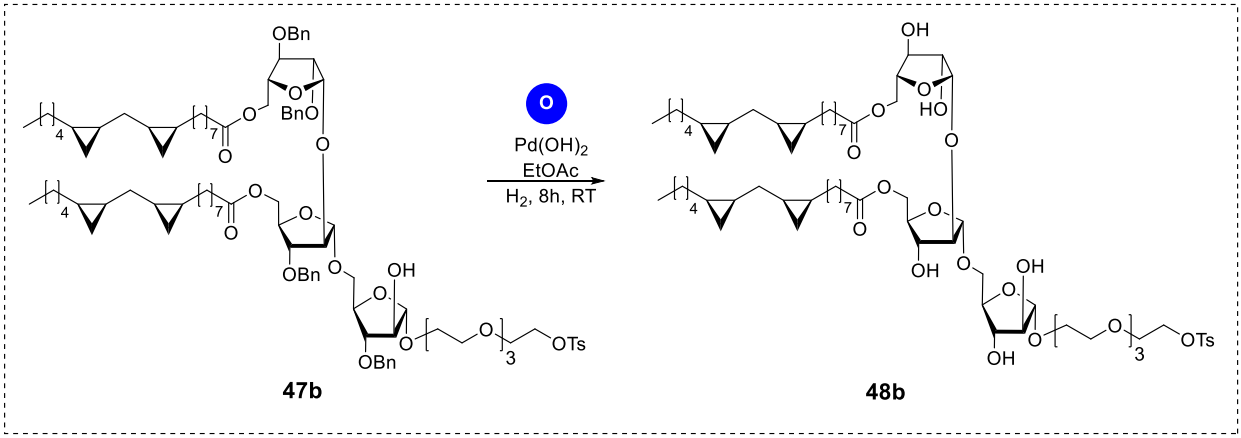
46c 47b

Compound **46c** was converted to compound **47b** according to the general experimental **Procedure I.** (Yield 71%, pale yellow syrup): **$[\alpha]_D^{25}$** = +58.8 (*c* = 0.06, $CHCl_3$); **IR** (cm^{-1}, $CHCl_3$) 3638, 3307, 2909, 2101, 1730, 1450, 1396, 1098, 1000, 870; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.80 – 7.77 (m, 2H), 7.30 (m, 22H), 5.03 (d, *J* = 3.7 Hz, 1H), 4.99 (s, 2H), 4.69 – 4.64 (m, 2H), 4.62 – 4.56 (m, 2H), 4.54 – 4.49 (m, 2H), 4.46 (d, *J* = 11.7 Hz, 1H), 4.27 (d, *J* = 1.4 Hz, 1H), 4.24 – 4.21 (m, 1H), 4.17 – 4.13 (m, 5H), 4.06 (ddd, *J* = 14.7, 11.3, 6.1 Hz, 6H), 3.89 – 3.78 (m, 4H), 3.68 – 3.61 (m, 9H), 3.59 – 3.56 (m, 6H), 2.43 (s, 3H), 2.25 (dd, *J* = 11.3, 7.5 Hz, 4H), 1.59 – 1.45 (m, 6H), 1.41 – 1.37 (m, 8H), 1.31 – 1.25 (m, 25H), 1.16 – 1.10 (m, 4H), 1.03 (dt, *J* = 14.3, 7.9 Hz, 2H), 0.89 (s, 6H), 0.81 – 0.75 (m, 4H), 0.71 – 0.66 (m, 3H), 0.62 (dd, *J* = 8.3, 4.0 Hz, 4H), -0.24 – -0.31 (m, 4H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 173.5, 173.5, 144.9, 138.1, 137.9, 137.5, 137.5, 133.1, 129.9, 129.9, 128.7, 128.7, 128.6, 128.6, 128.5, 128.5, 128.5, 128.5, 128.5,

128.2, 128.2, 128.1, 128.1, 128.0, 128.0, 128.0, 128.0, 127.9, 127.9, 127.9, 127.8, 127.8, 109.4, 105.8, 100.4, 85.1, 84.6, 83.9, 83.8, 82.6, 82.6, 81.3, 79.3, 79.0, 72.7, 72.6, 72.4, 72.1, 70.8, 70.8, 70.7, 70.6, 70.5, 69.4, 68.8, 67.0, 66.3, 65.9, 63.8, 34.1, 32.0, 32.0, 30.3, 30.3, 30.0, 30.0, 29.8, 29.6, 29.6, 29.5, 29.5, 29.3, 29.3, 29.0, 29.0, 28.8, 28.8, 28.2, 28.0, 25.0, 22.9, 22.9, 22.8, 21.8, 16.2, 16.2, 16.1, 16.0, 16.0, 16.0, 15.8, 15.7, 14.3, 14.3, 11.2, 11.2, 11.0, 11.0; **HRMS** (ESI-MS): m/z calcd. For $C_{98}H_{140}O_{21}S$ $[M+Na]^+$: 1707.9506; Found: 1707.9511.

(2-(2-(2-(2-tosylethoxy)ethoxy)ethoxy)ethyl)-5-*O*-(2-*O*-(-5-*O*-(8-(2-((2-pentylcyclopropyl)methyl)cyclopropyl)octanoyl)-β-D-arabinofuranosyl)-5-*O*-(8-(2-((2-pentylcyclopropyl) methyl)cyclopropyl)octanoyl)-α-D-arabinofuranosyl)-α-D-arabinofuranoside (48b):

Compound **47b** was converted to compound **48b** according to the general experimental **Procedure O.** (Yield 52%, pale yellow syrup): **$[\alpha]_D^{25}$** = +50.5 (*c* = 0.06, $CHCl_3$); **IR** (cm^{-1}, $CHCl_3$):

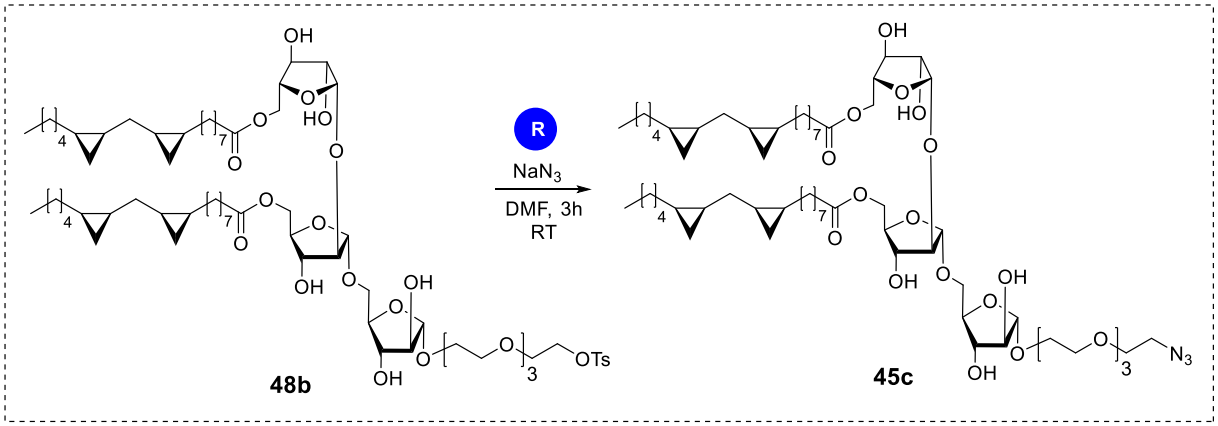


3666, 3595, 2830, 2750, 2200, 1610, 1205, 1322, 1100, 1001, 900; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.80 (d, *J* = 8.3 Hz, 2H), 7.35 (d, *J* = 8.0 Hz, 2H), 5.10 – 5.01 (m, 3H), 4.33 (ddt, *J* = 14.1, 7.4, 4.7 Hz, 3H), 4.20 – 4.15 (m, 6H), 4.13 – 4.10 (m, 1H), 4.07 – 4.02 (m, 3H), 4.00 – 3.97 (m, 3H), 3.88 (dd, *J* = 7.4, 4.9 Hz, 1H), 3.75 – 3.67 (m, 5H), 3.61 (m, 9H), 2.45 (s, 3H), 2.35 (d, *J* = 7.6 Hz, 4H), 1.64 – 1.59 (m, 4H), 1.39 (s, 8H), 1.32 – 1.26 (m, 28H), 1.16 – 1.12 (m, 3H), 1.03 (dt, *J* = 14.2, 7.9 Hz, 2H), 0.89 (d, *J* = 4.0 Hz, 6H), 0.81 – 0.76 (m, 4H), 0.71 – 0.66 (m, 3H), 0.63 – 0.59 (m, 4H), -0.28 (dd, *J* = 11.5, 5.4 Hz, 4H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 174.1, 173.9, 145.0, 133.0, 130.0, 130.0, 128.1, 128.1, 107.8, 105.8, 102.2, 89.2, 85.6, 80.2, 80.1, 79.8, 78.1, 77.6, 76.3, 75.5, 70.8, 70.6, 70.5, 70.5, 70.3, 69.4, 68.8, 67.5, 65.8, 65.3, 63.6, 34.3, 34.2, 32.0, 32.0, 30.3, 30.0, 30.0, 29.8, 29.6, 29.6, 29.5, 29.5, 29.3, 29.3, 29.0, 29.0, 28.8, 28.8, 28.2, 28.0, 25.0, 25.0, 22.9, 22.9, 21.8, 16.2, 16.2, 16.1, 16.0, 16.0, 16.0, 15.8, 15.7, 14.3, 14.3, 11.2, 11.2,

11.0, 11.0; **HRMS** (ESI-MS): m/z calcd. For $C_{70}H_{116}O_{21}S$ $[M+Na]^+$: 1347.7628; Found: 1347.7644.

(2-(2-(2-(2-azidoethoxy)ethoxy)ethoxy)ethyl)-5-*O*-(2-*O*-(-5-*O*-(8-(2-((2-pentylcyclopropyl)methyl)cyclopropyl)octanoyl)-β-D-arabinofuranosyl)-5-*O*-(8-(2-((2-pentylcyclopropyl)methyl)cyclopropyl)octanoyl)-α-D-arabinofuranosyl)-α-D-arabinofuranoside (45c):

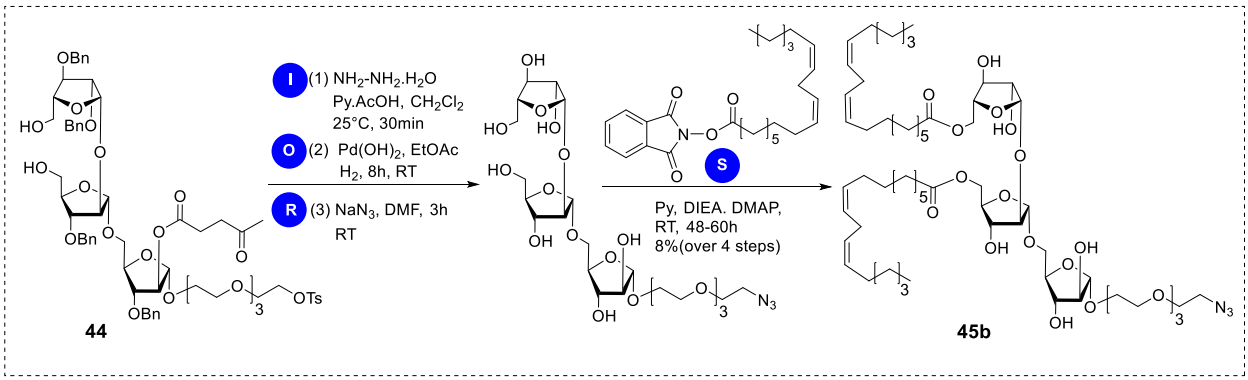
Compound **48b** was converted to compound **45c** according to the general experimental **Procedure R.** (Yield 60%, pale yellow syrup): **$[\alpha]_D^{25}$** = + 15.1 (*c* = 0.06, $CHCl_3$); **IR** (cm^{-1},



$CHCl_3$): 3705, 3366, 2904, 2898, 2300, 2160, 1722, 1412, 1360, 1000, 900; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 5.06 (d, *J* = 17.8 Hz;3H), 4.39 – 4.25 (m, 3H), 4.17 (d, *J* = 10.0 Hz, 4H), 4.03 (dd, *J* = 21.9, 16.8 Hz, 6H), 3.94 – 3.84 (m, 2H), 3.76 – 3.58 (m, 14H), 3.44 – 3.38 (m, 2H), 2.34 (q, *J* = 7.3 Hz, 4H), 1.65 – 1.59 (m, 4H), 1.40 (d, *J* = 8.1 Hz, 8H), 1.33 – 1.26 (m, 26H), 1.16 – 1.10 (m, 4H), 1.02 (dt, *J* = 14.3, 7.9 Hz, 2H), 0.90 – 0.86 (m, 7H), 0.81 – 0.75 (m, 4H), 0.68 (dd, *J* = 10.6, 5.4 Hz, 3H), 0.61 (dt, *J* = 8.2, 4.1 Hz, 4H), -0.28 (dq, *J* = 9.8, 4.9, 4.4 Hz, 4H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 174.2, 173.9, 107.9, 105.8, 102.2, 89.2, 85.7, 80.2, 80.1, 79.8, 78.0, 77.6, 76.3, 75.5, 70.7, 70.6, 70.6, 70.4, 70.2, 70.1, 67.6, 65.8, 65.3, 63.6, 50.8, 34.3, 34.2, 32.1, 32.0, 32.0, 30.3, 30.0, 30.0, 29.8, 29.8, 29.8, 29.6, 29.6, 29.5, 29.5, 29.3, 29.3, 29.0, 28.8, 28.2, 28.0, 25.0, 25.0, 22.9, 22.9, 22.8, 16.2, 16.1, 16.1, 16.0, 15.8, 15.8, 14.3, 14.3, 11.2, 11.2, 11.0, 11.0; **HRMS** (ESI-MS): m/z calcd. For $C_{63}H_{109}N_3O_{18}$ $[M+Na]^+$: 1218.7604; Found: 1218.7604.

(2-(2-(2-(2-Azidoethoxy)ethoxy)ethoxy)ethyl)-5-*O*-(2-*O*-(-5-*O*-(hexadecanoyl)-β-D-arabinofuranosyl)-5-*O*-(hexadecanoyl)-α-D-arabinofuranosyl)-α-D-arabinofuranoside (45b):

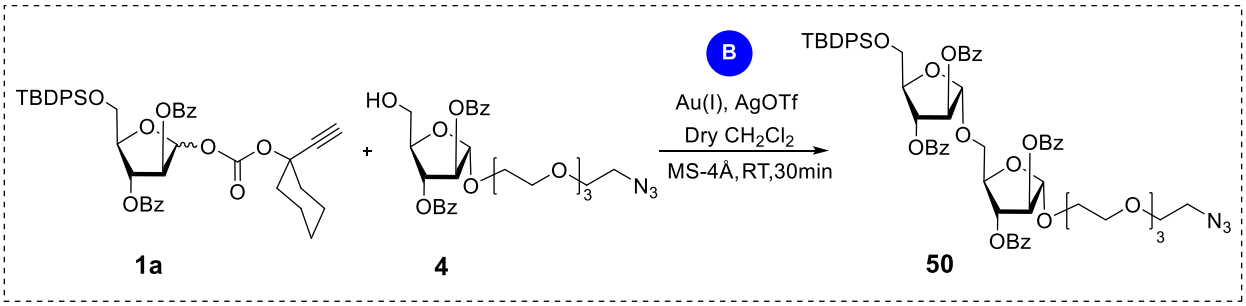
Compound **44** was converted to compound **45b** according to the general experimental **Procedure I, O, R, and S.** (Yield 8% over 4 steps), pale yellow syrup: **$[\alpha]_D^{25}$** = +39.8 (*c* = 0.06,



$CHCl_3$); **IR** (cm^{-1}, $CHCl_3$): 3680, 3540, 2980, 2815, 2160, 1780,1680, 1630, 1340, 1300, 1100, 920; **^{1}H NMR** (600 MHz, $CDCl_3$) δ 5.41 – 5.29 (m, 8H), 5.12 (dd, *J* = 19.4, 7.2 Hz, 1H), 5.06 (d, *J* = 10.1 Hz, 1H), 5.04 – 4.99 (m, 1H), 4.39 – 4.31 (m, 1H), 4.26 (ddd, *J* = 17.8, 7.0, 4.4 Hz, 2H), 4.22 – 4.20 (m, 1H), 4.18 – 4.15 (m, 2H), 4.13 – 4.09 (m, 2H), 4.03 (dd, *J* = 12.7, 5.5 Hz, 2H), 4.00 – 3.96 (m, 2H), 3.93 – 3.87 (m, 2H), 3.86 – 3.82 (m, 1H), 3.66 (m, 14H), 3.41 – 3.38 (m, 2H), 2.77 (t, *J* = 6.8 Hz, 4H), 2.35 (dd, *J* = 12.9, 5.5 Hz, 4H), 2.05 (q, *J* = 6.9 Hz, 8H), 1.62 (s, 4H), 1.32 (m, 28H), 0.89 (s, 6H); **^{13}C NMR** (151 MHz, $CDCl_3$) δ 174.1, 173.8, 130.4, 130.4, 130.2, 130.1, 128.2, 128.2, 128.1, 128.1, 107.8, 105.8, 102.1, 89.2, 86.0, 86.0, 80.3, 80.1, 79.5, 78.1, 77.7, 75.5, 70.8, 70.7, 70.7, 70.6, 70.5, 70.1, 67.6, 65.7, 65.2, 63.5, 50.8, 34.2, 34.0, 32.1, 31.7, 29.9, 29.8, 29.8, 29.8, 29.8, 29.5, 29.5, 29.3, 29.3, 29.2, 27.4, 27.4, 27.3, 25.8, 25.0, 25.0, 24.9, 24.9, 22.8, 22.7, 14.3, 14.2; **HRMS** (ESI-MS): m/z calcd. For $C_{59}H_{101}N_3O_{18}$ $[M+Na]^+$: 1139.7080; Found: 1139.7009

(2-(2-(2-azidoethoxy)ethoxy)ethyl)-2,3-di-*O*-benzoyl-5-*O*-(2,3-di-*O*-benzoyl-5-*O*-*tert*butyldiphenylsilyl-α-D-arabinofuranosyl)-α-D-arabinofuranoside (50):

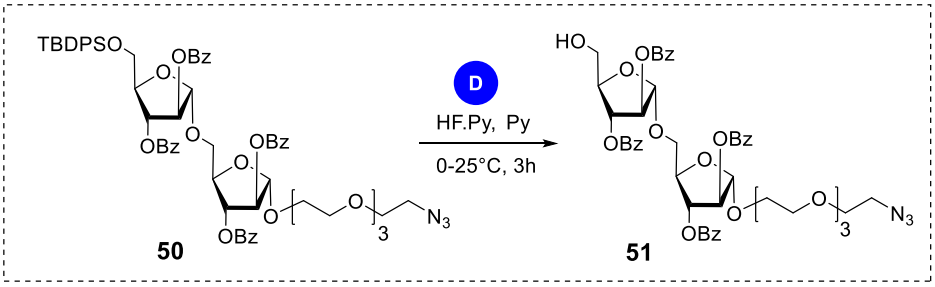
The glycosyl donor **1a**[45] and the glycosyl acceptor **4** were glycosylated according to the general reaction **Procedure B** as detailed above to give the **50**. (Yield 76%, pale yellow syrup):



[α]$_D^{25}$ = +7.57 (*c* = 0.06, $CHCl_3$); **IR** (cm^{-1}, $CHCl_3$): 3066, 2930, 2310, 2180, 2104,1723, 1602, 1453, 1356, 1266, 1176, 1108, 900; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.09 – 8.05 (m, 2H), 7.99 (d, *J* = 7.4 Hz, 4H), 7.95 – 7.92 (m, 2H), 7.71 (ddd, *J* = 7.7, 3.7, 1.5 Hz, 4H), 7.60 – 7.54 (m, 2H), 7.50 – 7.44 (m, 3H), 7.42 – 7.29 (m, 13H), 5.63 (t, *J* = 4.7 Hz, 2H), 5.58 – 5.55 (m, 2H), 5.38 (s, 1H), 5.29 (s, 1H), 4.52 (dq, *J* = 7.9, 4.5 Hz, 2H), 4.21 (dd, *J* = 11.2, 4.5 Hz, 1H), 4.00 (d, *J* = 4.3 Hz, 2H), 3.97 – 3.90 (m, 2H), 3.72 (s, 3H), 3.70 – 3.66 (m, 2H), 3.62 (q, *J* = 4.9 Hz, 9H), 3.37 – 3.33 (m, 2H), 1.03 (s, 9H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 165.8, 165.6, 165.4, 165.3, 135.8, 135.8, 133.5, 133.5, 133.4, 133.3, 133.2, 133.2, 130.1, 130.1, 130.0, 130.0, 129.9, 129.9, 129.9, 129.9, 129.8, 129.8, 129.5, 129.4, 129.4, 129.1, 128.6, 128.6, 128.5, 128.5, 128.5, 128.5, 128.3, 128.3, 127.8, 127.8, 127.8, 127.8, 127.8, 127.8, 106.1, 105.9, 83.3, 82.3, 82.0, 81.8, 77.6, 77.4, 70.9, 70.8, 70.8, 70.7, 70.4, 70.1, 66.8, 66.1, 63.5, 50.8, 26.9, 26.9, 26.9, 19.4; **HRMS** (ESI-MS): m/z calcd. For $C_{62}H_{67}N_3O_{16}Si$ $[M+Na]^+$: 1160.4188; Found: 1160.4156.

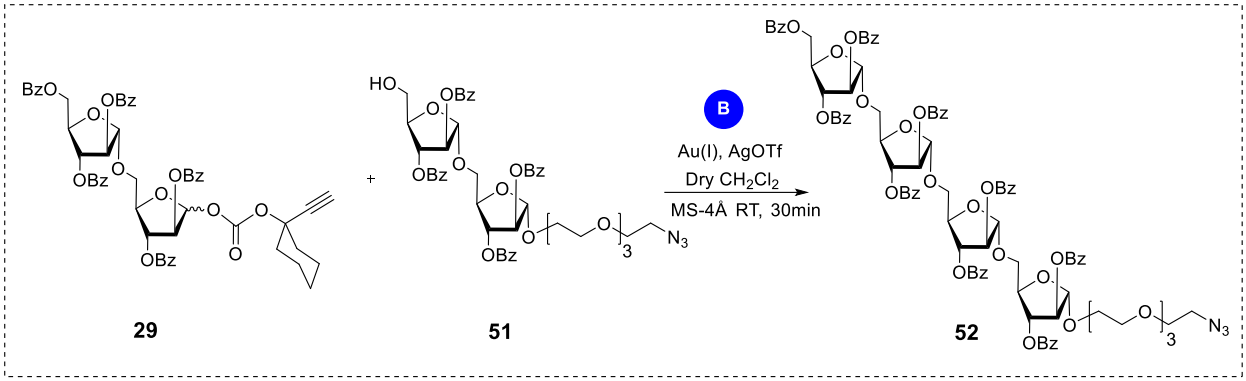
(2-(2-(2-(2-azidoethoxy)ethoxy)ethoxy)ethyl)-2,3-di-*O*-benzoyl-5-*O*-(2,3-di-*O*-benzoyl-α-D-arabinofuranosyl)-α-D-arabinofuranoside (51):

Compound **50** was converted to compound **51** according to the general experimental **Procedure D** (Yield 78%, pale yellow syrup): **[α]$_D^{25}$** = -1.51 (*c* = 0.06, $CHCl_3$); **IR** (cm^{-1}, $CHCl_3$): 3068, 2926, 2310, 2155, 1722, 1597, 1453, 1264, 1108, 969, 866; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.06 – 8.01 (m, 6H), 7.96 – 7.91 (m, 2H), 7.61 – 7.56 (m, 2H), 7.53 – 7.38 (m, 8H), 7.29 (t, *J* = 7.8 Hz, 2H), 5.64 (d, *J* = 1.3 Hz, 1H), 5.60 (d, *J* = 5.1 Hz, 1H), 5.56 (d, *J* = 1.3 Hz, 1H), 5.44 – 5.42 (m, 1H), 5.41 (s, 1H), 5.29 (s, 1H), 4.49 (dq, *J* = 7.8, 4.4 Hz, 2H), 4.20 (dd, *J* = 11.2, 4.6 Hz, 1H), 4.04 – 3.87 (m, 4H), 3.73 – 3.65 (m, 5H), 3.64 – 3.59 (m, 8H), 3.35 (t, *J* = 5.0 Hz, 2H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ^{13}C NMR (101 MHz, $CDCl_3$) δ 166.2, 165.8, 165.5, 165.2, 133.6, 133.6, 133.5, 133.4, 130.0, 130.0, 130.0, 130.0, 129.9, 129.9, 129.9, 129.9, 129.4, 129.3, 129.2, 129.1, 128.6, 128.6, 128.6, 128.6, 128.6, 128.6, 128.4, 128.4, 105.9, 105.8, 83.8, 81.9, 81.9, 81.8, 77.9, 77.4, 70.8, 70.8, 70.7, 70.7, 70.4, 70.1, 66.8, 66.2, 62.4, 50.7; **HRMS** (ESI-MS): m/z calcd. For $C_{46}H_{49}N_3O_{16}$ $[M+Na]^+$: 922.3011; Found: 922.3005.



(2-(2-(2-(2-azidoethoxy)ethoxy)ethoxy)ethyl)-2,3-di-*O*-benzoyl-5-*O*-(2,3-di-*O*-benzoyl-5-*O*-(2,3-di-*O*-benzoyl-5-*O*-(2,3-di-*O*-benzoyl-5-*O*-benzoyl-α-D-arabinofuranosyl)-α-D-arabinofuranosyl)-α-D-arabinofuranosyl)-α-D-arabinofuranoside (52):

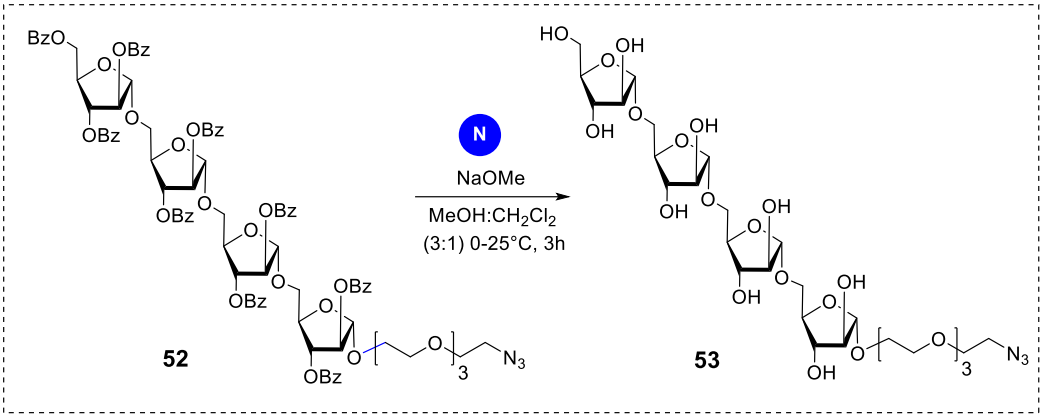
The glycosyl donor **29** and the glycosyl acceptor **51** were glycosylated according to the general reaction **Procedure B** as detailed above to give the **52**. (Yield 71%, pale yellow syrup):



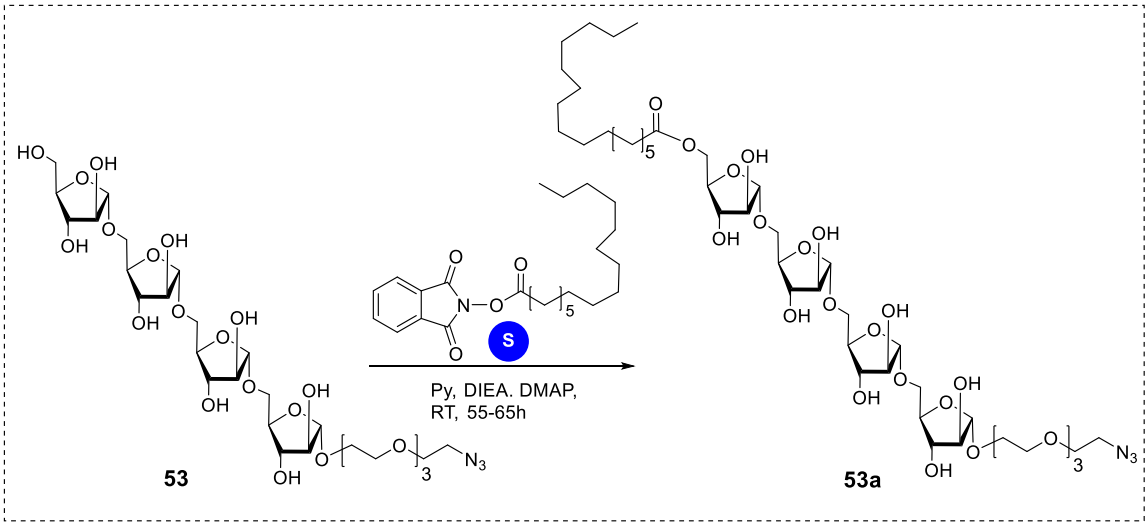
[α]$_D^{25}$ = + 15.5 (*c* = 0.06, $CHCl_3$); **IR** (cm^{-1}, $CHCl_3$): 3090, 2930, 2877, 2170, 1725, 1600, 1490, 1453, 1259, 1176, 1106, 1069, 1026, 965; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.01 (m, 12H), 7.93 – 7.86 (m, 6H), 7.59 – 7.53 (m, 2H), 7.50 (q, *J* = 6.9, 6.4 Hz, 4H), 7.45 – 7.35 (m, 14H), 7.27 (d, *J* = 3.8 Hz, 2H), 7.23 (d, *J* = 7.9 Hz, 5H), 5.65 (s, 4H), 5.62 (s, 2H), 5.58 – 5.55 (m, 2H), 5.46 (s, 1H), 5.42 (s, 1H), 5.40 (s, 1H), 5.28 (s, 1H), 4.82 (dd, *J* = 11.9, 2.2 Hz, 1H), 4.72 (q, *J* = 3.5 Hz, 1H), 4.68 – 4.59 (m, 3H), 4.49 – 4.44 (m, 1H), 4.21 (dt, *J* = 9.3, 4.4 Hz, 3H), 3.99 – 3.87 (m, 4H), 3.71 (d, *J* = 6.8 Hz, 3H), 3.68 – 3.65 (m, 2H), 3.61 (m, 8H), 3.34 (t, *J* = 5.1 Hz, 2H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 166.3, 165.8, 165.8, 165.7, 165.7, 165.4, 165.3, 165.2, 165.2, 133.5, 133.5, 133.5, 133.5, 133.5, 133.4, 133.3, 133.2, 133.1, 130.0, 130.0, 130.0, 130.0, 129.9, 129.9, 129.9, 129.9, 129.9, 129.9, 129.9, 129.9, 129.9, 129.8, 129.8, 129.8, 129.4, 129.2, 129.2, 129.2, 129.2, 129.2, 129.2, 129.1, 129.0, 128.6, 128.6, 128.6, 128.6, 128.6, 128.6, 128.5, 128.5, 128.5, 128.5, 128.4, 128.4, 128.4, 128.4, 128.4, 128.4, 128.4, 128.4, 128.4, 106.0, 106.0, 105.9, 105.8, 82.2, 82.1, 82.0, 82.0, 81.9, 81.7, 81.7, 81.3, 77.9, 77.4, 77.3, 77.3, 70.8, 70.8, 70.7, 70.7, 70.3, 70.1, 66.7, 66.1, 66.0, 65.9, 63.7, 50.7; **HRMS** (ESI-MS): m/z calcd. For $C_{91}H_{85}N_3O_{29}$ $[M+Na]^+$:1706.5166 ; Found: 1706.5150.

(2-(2-(2-(2-azidoethoxy)ethoxy)ethoxy)ethyl)5-*O*-(5-*O*-(5-*O*-(-α-D-arabinofuranosyl)-α-D-arabinofuranosyl)-α-D-arabinofuranosyl)-α-D-arabinofuranoside (53):

Compound **52** was converted to compound **53** according to the general experimental **Procedure N.** (Yield 70%, pale yellow syrup): **$[\alpha]_D^{25}$** = +34.4 (*c* = 0.06, $CHCl_3$); **IR** (cm^{-1}, $CHCl_3$): 3482, 2925, 2109, 1737, 1645, 1455, 1356, 1304, 1089, 1018, 868; **^{1}H NMR** (400 MHz, CD_3OD) δ 4.95 (s, 3H), 4.93 (d, *J* = 1.2 Hz, 1H), 4.08 (ddd, *J* = 10.9, 4.7, 1.5 Hz, 3H), 4.00 (ddd, *J* = 7.0, 3.3, 1.8 Hz, 5H), 3.92 – 3.88 (m, 3H), 3.87 – 3.82 (m, 5H), 3.75 (dd, *J* = 11.8, 3.3 Hz, 1H), 3.67 (m, 17H), 3.41 – 3.38 (m, 2H); **^{13}C NMR** (101 MHz, CD_3OD) δ 109.7, 109.6, 109.6, 109.6, 85.9, 84.1, 84.1, 84.0, 83.3, 83.1, 83.1, 83.0, 79.1, 79.1, 79.1, 78.7, 71.5, 71.5, 71.4, 71.4, 71.4, 71.4, 71.0, 68.2, 68.1, 67.9, 63.0, 51.7; **HRMS** (ESI-MS): m/z calcd. For $C_{28}H_{49}N_3O_{20}$ $[M+Na]^+$: 770.2807; Found: 770.2803.



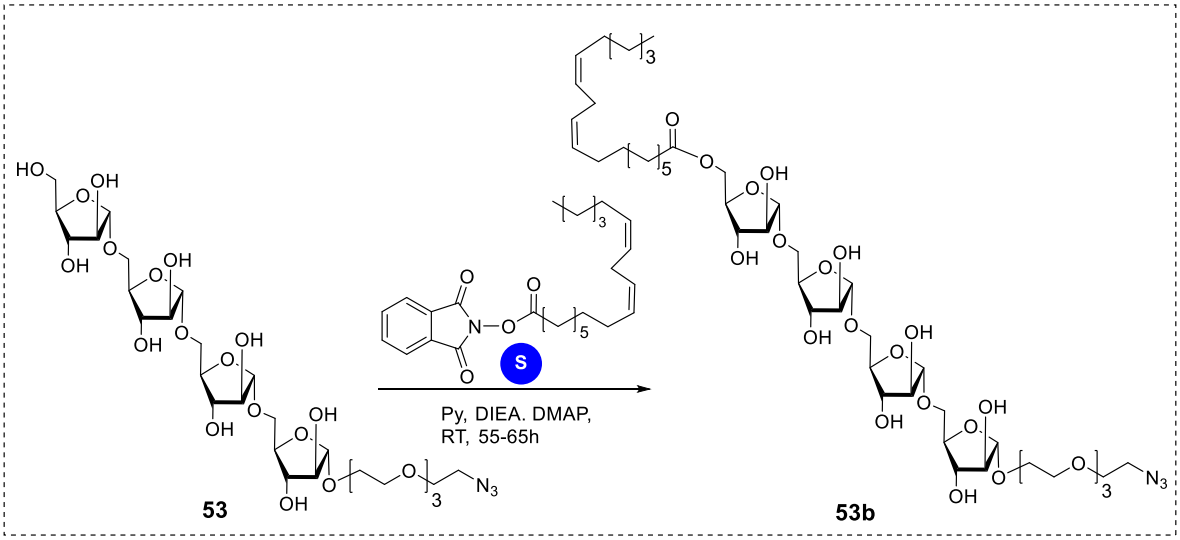
(2-(2-(2-(2-azidoethoxy)ethoxy)ethoxy)ethyl-5-*O*-(-5-*O*-(-5-*O*-(-5-*O*-(hexadecanoyl)-α-D-arabinofuranosyl)-α-D-arabinofuranosyl)-α-D-arabinofuranosyl)-α-D-abinofuranoside (53a):



Compound **53** was converted to compound **53a** according to the general experimental **Procedure S.** (Yield 35%, pale yellow syrup). **$[\alpha]_D^{25}$** = +45.5 (*c* = 1.0, $CHCl_3$); **IR** (cm^{-1}, $CHCl_3$): 3400, 2855, 2330, 2180, 1720, 1434, 1350, 1310, 1090, 1020; **^{1}H NMR** (400 MHz, CD_3OD) δ 4.96 (s, 3H), 4.93 (d, *J* = 1.3 Hz, 1H), 4.19 (dd, *J* = 11.7, 6.1 Hz, 1H), 4.13 – 3.98 (m, 8H), 3.91 (dt, *J* = 6.2, 3.2 Hz, 3H), 3.88 – 3.82 (m, 5H), 3.76 (dd, *J* = 11.8, 3.3 Hz, 1H), 3.71 – 3.67 (m, 15H), 3.41 – 3.38 (m, 2H), 2.39 (q, *J* = 7.1 Hz, 2H), 1.67 – 1.61 (m, 2H), 1.35 – 1.31 (m, 24H), 0.94 – 0.90 (m, 3H); **^{13}C NMR** (101 MHz, CD_3OD) δ 175.3, 109.7, 109.7, 109.7, 109.6, 84.1, 84.1, 83.8, 83.5, 83.2, 83.2, 82.8, 79.2, 79.2, 79.1, 79.1, 79.0, 71.6, 71.6, 71.5, 71.5, 71.5, 71.1, 68.3, 68.2, 68.2, 67.9, 65.0, 63.1, 51.8, 34.9, 33.1, 30.8, 30.8, 30.8, 30.8, 30.7, 30.6, 30.5, 30.4, 30.2, 26.0, 25.9, 23.7, 14.5; **HRMS** (ESI-MS): m/z calcd. For $C_{44}H_{79}N_3O_{21}$ $[M+Na]^+$: 1008.5104; Found: 1008.5106

(2-(2-(2-(2-azidoethoxy)ethoxy)ethoxy)ethyl)5-*O*-(5-*O*-(5-*O*-(5-*O*-(*9Z*,*12Z*-octadecadienoyl)-α-D-arabinofuranosyl)-α-D-arabinofuranosyl)-α-D-arabinofuranosyl) -α-D-arabinofuranoside (53b):

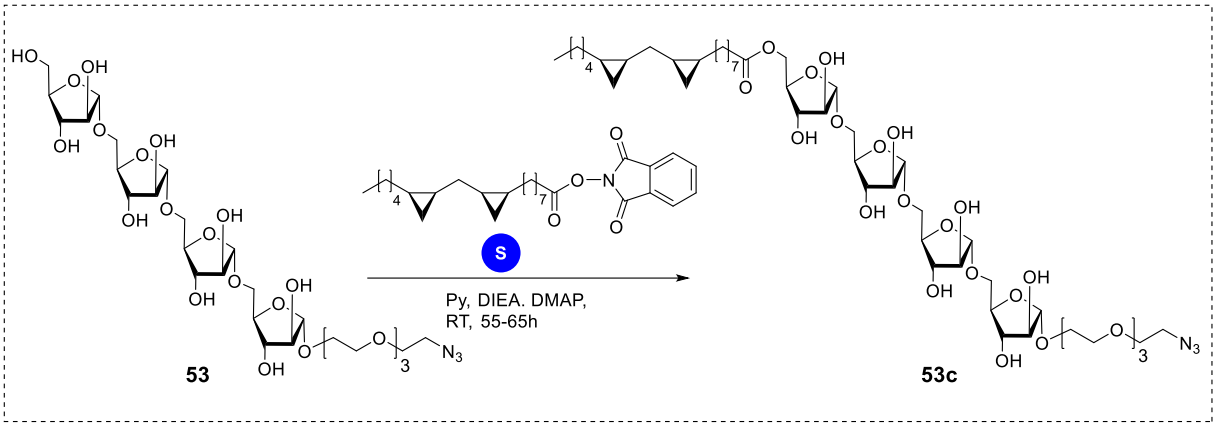
Compound **53** was converted to compound **53b** according to the general experimental **Procedure S.** (Yield 38%, pale yellow syrup).



$[\alpha]_D^{25}$ = +50.0(*c* = 0.06, $CHCl_3$); **IR** (cm^{-1}, $CHCl_3$): 3390, 2900, 2350, 2180, 1734, 1444, 1350, 1350, 1080, 1018, 950**; ^{1}H NMR** (400 MHz, CD_3OD) δ 5.42 – 5.31 (m, 4H), 4.98 – 4.92 (m, 4H), 4.19 (dd, *J* = 11.7, 6.1 Hz, 1H), 4.14 – 4.07 (m, 3H), 4.03 (m, 5H), 3.91 (dd, *J* = 6.3, 3.2 Hz, 3H), 3.85 (ddd, *J* = 10.0, 6.9, 4.8 Hz, 5H), 3.81 – 3.72 (m, 1H), 3.71 – 3.65 (m, 16H), 3.42 – 3.38 (m, 2H), 2.80 (t, *J* = 6.3 Hz, 2H), 2.39 (q, *J* = 7.1 Hz, 2H), 2.09 (q, *J* = 6.6 Hz, 4H), 1.68 – 1.62 (m, 2H), 1.34 (m,14H), 0.93 (t, *J* = 6.8 Hz, 3H); **^{13}C NMR** (101 MHz, CD_3OD) δ 175.3, 130.9, 130.9,

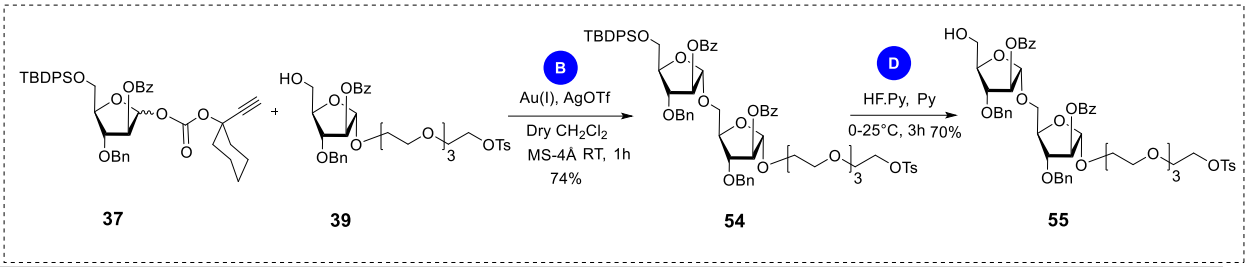
129.1, 129.1, 109.7, 109.7, 109.7, 109.6, 84.1, 84.1, 83.8, 83.5, 83.2, 83.2, 83.1, 82.8, 79.2, 79.2, 79.1, 79.1, 71.6, 71.6, 71.5, 71.4, 71.1, 68.2, 68.2, 67.9, 65.0, 63.1, 59.9, 51.8, 34.9, 32.7, 30.7, 30.5, 30.3, 30.2, 30.2, 28.2, 26.5, 26.0, 25.9, 23.6, 14.5; **HRMS** (ESI-MS): m/z calcd. For $C_{46}H_{79}N_3O_{21}$ $[M+Na]^+$; Found 1032.5104: 1032.5100

(2-(2-(2-(2-azidoethoxy)ethoxy)ethoxy)ethyl)-5-*O*-(5-*O*-(5-*O*-(5-*O*-(8-(2-((2-pentylcyclopropyl)methyl)cyclopropyl)octanoyl)-α-D-arabinofuranosyl)-α-D-arabinofuranosyl)-α-D-arabinofuranosyl)-α-D-arabinofuranoside (53c):



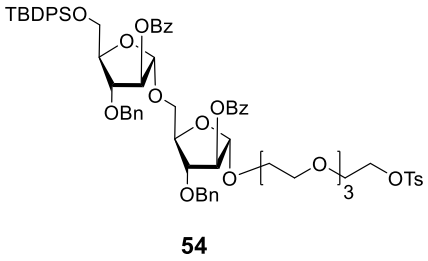
Compound **53** was converted to compound **53c** according to the general experimental **Procedure S.** (Yield 41%, pale yellow syrup): **$[\alpha]_D^{25}$** = +51.5(*c* = 0.06, $CHCl_3$); **IR** (cm^{-1}, $CHCl_3$): 3350, 2770, 2280, 2150, 1780, 1424, 1390, 1210, 1070, 1010; **^{1}H NMR** (400 MHz, CD_3OD) δ 4.98 – 4.92 (m, 4H), 4.19 (dd, *J* = 11.7, 6.1 Hz, 1H), 4.15 – 3.99 (m, 8H), 3.91 (dt, *J* = 6.2, 3.3 Hz, 3H), 3.85 (ddt, *J* = 11.6, 6.4, 3.1 Hz, 5H), 3.76 (dd, *J* = 11.8, 3.3 Hz, 1H), 3.71 – 3.64 (m, 16H), 3.42 – 3.38 (m, 2H), 2.39 (q, *J* = 7.1 Hz, 2H), 1.68 – 1.61 (m, 2H), 1.43 (s, 5H), 1.36 – 1.31 (m, 12H), 1.24 – 1.18 (m, 2H), 1.14 – 1.03 (m, 1H), 0.95 – 0.91 (m, 3H), 0.82 (ddd, *J* = 14.3, 8.2, 6.0 Hz, 2H), 0.77 – 0.69 (m, 2H), 0.65 (td, *J* = 8.3, 4.1 Hz, 2H), -0.21 – -0.28 (m, 2H); **^{13}C NMR** (101 MHz, CD_3OD) δ 175.3, 109.7, 109.7, 109.7, 109.6, 84.1, 84.1, 83.8, 83.5, 83.2, 83.2, 83.1, 82.8, 79.2, 79.2, 79.1, 79.1, 71.6, 71.6, 71.5, 71.5, 71.1, 68.2, 68.2, 67.9, 65.0, 63.1, 59.9, 51.8, 34.9, 33.0, 31.2, 31.0, 30.5, 30.2, 30.1, 29.9, 29.2, 29.1, 26.0, 25.9, 23.8, 17.1, 17.0, 16.7, 14.5, 11.7, 11.6; **HRMS** (ESI-MS): m/z calcd. For $C_{48}H_{83}N_3O_{21}$ $[M+Na]^+$: 1060.5417; Found: 1060.5416

Synthesis of 55:



(2-(2-(2-(2-tosylethoxy)ethoxy)ethoxy)ethyl)-2-*O*-benzoyl-3-*O*-benzyl-5-*O*-(2-*O*-benzoyl-3-*O*-benzyl-5-*O* *tert*butyldiphenylsilyl-α-D-arabinofuranosyl)-α-D-arabinofuranoside (54):

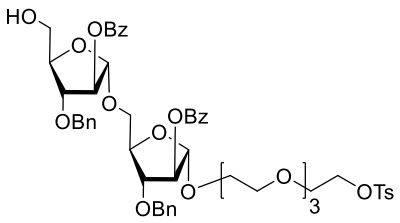
The glycosyl donor **37**[49] and the glycosyl acceptor **39** were glycosylated according to the general reaction **Procedure B** as detailed above to give the **54**. (Yield 74%, pale yellow syrup). **$[\alpha]_D^{25}$** = +22.4 (*c* = 0.06, $CHCl_3$); **IR** (cm^{-1}, $CHCl_3$): 3020, 2970, 2810, 2230, 2100, 1430, 1344, 1080, 1000, 950, 900; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.04 (d, *J* = 8.0 Hz, 2H), 7.96 (d, *J* = 8.0 Hz, 2H), 7.78 (d, *J* = 8.2 Hz, 2H), 7.65 – 7.59 (m, 4H), 7.55 (d, *J* = 7.6 Hz, 2H), 7.43 – 7.37 (m, 6H), 7.31 (m, 9H), 7.24 – 7.18 (m, 7H), 5.43 (s, 2H), 5.28 (s, 1H), 5.22 (s, 1H), 4.77 (d, *J* = 12.0 Hz, 1H), 4.61 (t, *J* = 12.1 Hz, 2H), 4.46 (d, *J* = 12.1 Hz, 1H), 4.38 – 4.34 (m, 1H), 4.14 (dd, *J* = 11.7, 6.9 Hz, 5H), 3.95 – 3.86 (m, 2H), 3.75 (d, *J* = 11.1 Hz, 3H), 3.69 (d, *J* = 5.5 Hz, 3H), 3.65 – 3.62 (m, 4H), 3.58 – 3.53 (m, 6H), 2.41 (s, 3H), 0.98 (s, 9H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 165.5, 165.3, 144.8, 137.8, 137.7, 135.6, 135.6, 133.4, 133.3, 133.1, 129.9, 129.8, 129.8, 129.8, 129.8, 129.8, 129.8, 129.8, 129.8, 129.7, 129.7, 129.5, 129.5, 128.6, 128.5, 128.5, 128.5, 128.4, 128.4, 128.3, 128.3, 128.0, 128.0, 127.9, 127.9, 127.7, 127.7, 127.7, 127.7, 127.7, 127.7, 127.7, 127.7, 127.6, 106.3, 106.2, 83.8, 83.5, 83.0, 82.1, 82.0, 81.7, 72.5, 72.1, 70.7, 70.7, 70.6, 70.5, 70.3, 69.3, 68.6, 66.7, 65.5, 63.1, 26.8, 26.8, 26.8, 21.7, 19.3; **HRMS** (ESI-MS): m/z calcd. For $C_{69}H_{78}O_{17}SSi[M+Na]^+$: 1261.4627; Found: 1261.4665



54

(2-(2-(2-(2-tosylethoxy)ethoxy)ethoxy)ethyl)-2-*O*-benzoyl-3-*O*-benzyl-5-*O*-(2-*O*-benzoyl-3-*O*-benzyl-α-D-arabinofuranosyl)-α-D-arabinofuranoside(55):

Compound **54** was converted to compound **55** according to the general experimental **Procedure D** (Yield 70%, pale yellow syrup): **$[\alpha]_D^{25}$** = +26.4 (*c* = 0.06, $CHCl_3$); **IR** (cm^{-1}, $CHCl_3$): 3580, 3470, 3000, 2990, 2860, 2210, 2140, 1410, 1324, 1040, 1020, 940, 900; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.05 – 7.98 (m, 4H), 7.78 (d, *J* = 8.3 Hz, 2H), 7.59 – 7.52 (m, 2H), 7.42 (q, *J* =

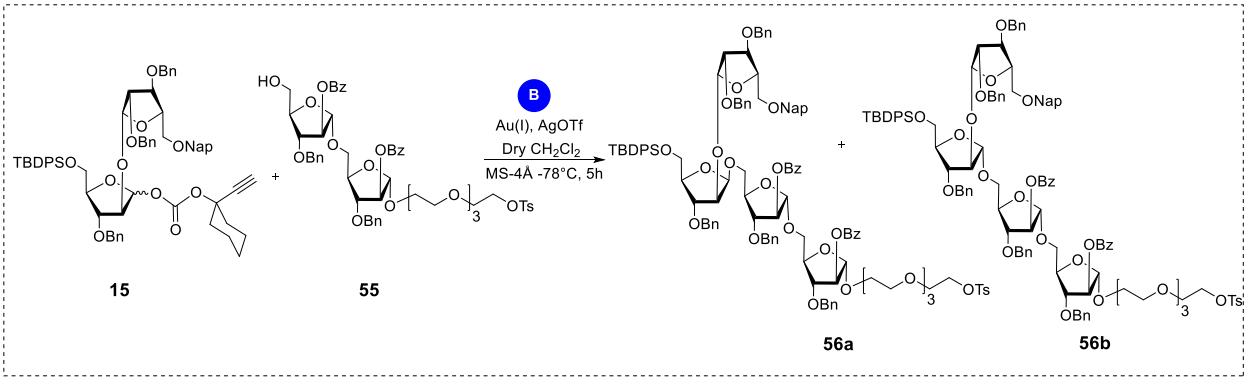


55

7.5 Hz, 4H), 7.35 – 7.26 (m, 6H), 7.23 (q, *J* = 3.8 Hz, 6H), 5.43 (d, *J* = 1.2 Hz, 1H), 5.40 – 5.38 (m, 1H), 5.27 (s, 1H), 5.22 (s, 1H), 4.80 (d, *J* = 12.0 Hz, 1H), 4.65 – 4.60 (m, 2H), 4.47 (d, *J* = 12.1 Hz, 1H), 4.36 (q, *J* = 4.0 Hz, 1H), 4.16 – 4.12 (m, 3H), 4.11 – 4.07 (m, 1H), 3.98 (d, *J* = 5.5 Hz, 1H), 3.90 (td, *J* = 11.1, 5.5 Hz, 2H), 3.77 (ddd, *J* = 12.2, 9.7, 3.3 Hz, 2H), 3.68 (q, *J* = 3.9 Hz, 3H), 3.65 – 3.62 (m, 4H), 3.60 – 3.53 (m, 7H), 2.42 (s, 3H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 165.5, 165.3, 144.8, 137.8, 137.6, 133.5, 133.4, 133.0, 129.9, 129.8, 129.8, 129.8, 129.8, 129.7, 129.5, 129.4, 128.6, 128.6, 128.6, 128.6, 128.4, 128.4, 128.4, 128.4, 128.0, 128.0, 128.0, 128.0, 127.8, 127.8, 127.8, 127.7, 106.3, 106.2, 83.5, 83.4, 82.9, 82.0, 81.9, 81.7, 72.4, 72.2, 70.7, 70.7, 70.6, 70.5, 70.3, 69.3, 68.6, 66.8, 65.8, 62.0, 21.7; **HRMS** (ESI-MS): m/z calcd. For $C_{53}H_{60}O_{17}S[M+Na]^+$: 1023.3449; Found: 1023.3460.

(2-(2-(2-(2-tosylethoxy)ethoxy)ethoxy)ethyl-2-*O*-benzoyl-3-*O*-benzyl-5-*O*-(2-*O*-benzoyl-3-*O*-benzyl-5-*O*-(2-*O*-(2,3-*O*-dibenzyl-5-*O*-(naphthylmethyl)-β-D-arabinofuranosyl)-3-*O*-benzyl-5-*O* *tert*butyldiphenylsilyl-α-D-arabinofuranosyl)-α-D-arabinofuranosyl)-α-D-arabinofuranoside (56b):

The glycosyl donor **15** and the glycosyl acceptor **55** were glycosylated according to the general reaction **Procedure B** as detailed above to give the **S36a: S36b (1.3:1**). Then separate the desired isomer **56b.** (Yield 45%, pale yellow syrup): **$[\alpha]_D^{25}$** = -1.51 (*c* = 0.06, $CHCl_3$); **IR** (cm^{-1},

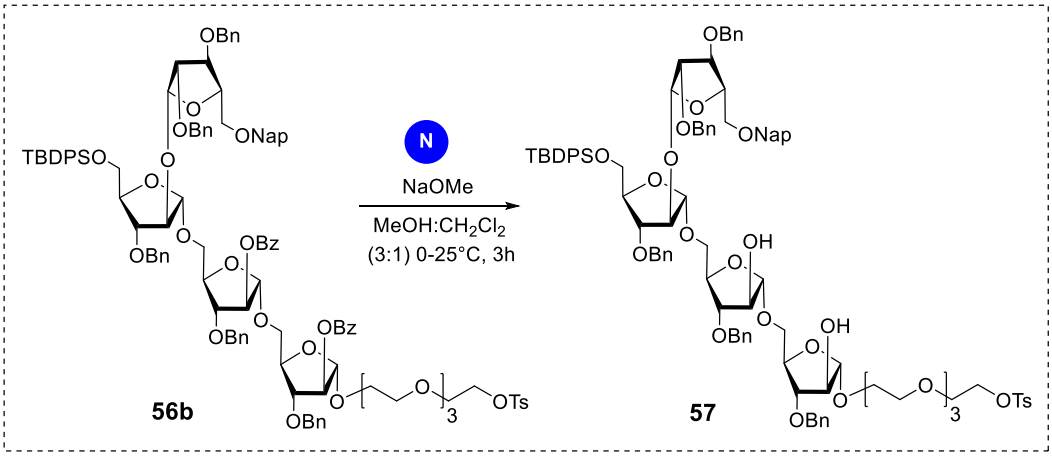


$CHCl_3$): 3160, 3320, 3058, 2928, 2868, 2310, 1721, 1598, 1458, 1359, 1272, 1107; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.04 – 7.95 (m, 4H), 7.78 (d, *J* = 8.2 Hz, 3H), 7.72 – 7.50 (m, 8H), 7.44 – 7.39 (m, 4H), 7.38 – 7.26 (m, 17H), 7.24 – 7.18 (m, 10H), 7.17 – 7.08 (m, 10H), 5.39 (d, *J* = 14.8 Hz, 2H), 5.20 (d, *J* = 10.4 Hz, 2H), 5.08 (d, *J* = 4.3 Hz, 1H), 5.01 (s, 1H), 4.76 (d, *J* = 12.0 Hz, 1H), 4.65 – 4.57 (m, 3H), 4.56 – 4.50 (m, 3H), 4.49 – 4.42 (m, 4H), 4.39 (d, *J* = 16.7 Hz, 1H), 4.33 (d, *J* = 6.8 Hz, 2H), 4.15 – 4.11 (m, 4H), 4.10 – 4.03 (m, 5H), 4.02 – 3.99 (m, 1H),

3.87 (ddd, *J* = 19.9, 11.4, 4.1 Hz, 3H), 3.73 (dd, *J* = 17.8, 3.9 Hz, 2H), 3.68 – 3.59 (m, 9H), 3.55 (m, 8H), 2.41 (s, 3H), 1.02 (s, 9H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 165.5, 165.4, 144.8, 138.2, 138.1, 137.9, 137.8, 137.7, 135.7, 135.7, 135.5, 133.5, 133.5, 133.4, 133.4, 133.3, 133.1, 133.0, 129.9, 129.9, 129.9, 129.9, 129.9, 129.9, 129.8, 129.8, 129.7, 129.7, 129.6, 129.5, 128.6, 128.6, 128.6, 128.5, 128.5, 128.4, 128.4, 128.4, 128.4, 128.3, 128.3, 128.3, 128.3, 128.2, 128.0, 128.0, 128.0, 128.0, 128.0, 127.9, 127.8, 127.8, 127.8, 127.8, 127.8, 127.8, 127.7, 127.7, 127.7, 127.7, 127.7, 127.7, 127.7, 127.7, 127.6, 127.5, 127.4, 127.4, 126.3, 126.1, 125.9, 125.6, 106.3, 106.3, 106.3, 100.4, 85.7, 84.0, 83.7, 83.5, 83.4, 83.2, 83.0, 82.1, 82.1, 81.9, 81.8, 80.1, 73.2, 72.5, 72.4, 72.4, 72.4, 72.3, 72.1, 70.8, 70.7, 70.7, 70.5, 70.3, 69.3, 68.7, 66.8, 65.8, 65.7, 64.0, 27.0, 26.9, 26.9, 21.7, 19.4; **HRMS** (ESI-MS): m/z calcd. For $C_{111}H_{120}O_{25}SSi$ $[M+Na]^+$: 1935.7506; Found: 1935.7517.

(2-(2-(2-(2-tosylethoxy)ethoxy)ethoxy)ethyl)-3-*O*-benzyl-5-*O*-(3-O-benzyl-5-*O*-(2-*O*-(2,3-*O*-dibenzyl-5-*O*-(naphthylmethyl)-β-D-arabinofuranosyl)-3-*O*-benzyl-5-*O* *tert*butyldiphenylsilyl-α-D-arabinofuranosyl)-α-D-arabinofuranosyl)-α-D-arabinofuranoside (57):

Compound **56b** was converted to compound **57** according to the general experimental **Procedure N**. (Yield 92%, pale yellow syrup): **$[\alpha]_D^{25}$** = -19.6 (*c* = 0.06, $CHCl_3$); **IR** (cm^{-1}, $CHCl_3$): 3851, 3736, 3467, 3063, 2310, 1726, 1457,1559, 1108, 1023; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.80 – 7.60 (m, 10H),

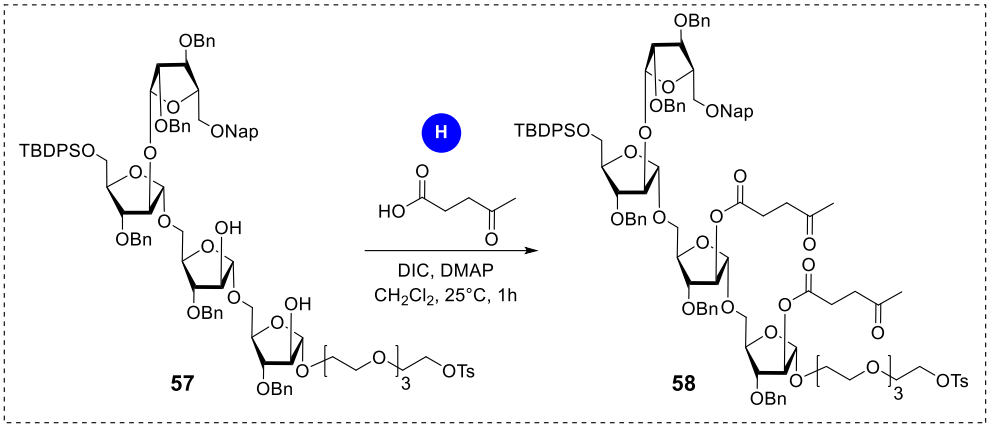


7.44 – 7.30 (m, 15H), 7.28 – 7.19 (m, 21H), 5.04 (s, 1H), 4.98 (d, *J* = 3.4 Hz, 1H), 4.93 (s, 2H), 4.69 – 4.45 (m, 10H), 4.42 – 4.32 (m, 2H), 4.24 (d, *J* = 17.4 Hz, 2H), 4.16 – 4.01 (m, 8H), 3.96 – 3.90 (m, 1H), 3.82 (d, *J* = 9.5 Hz, 2H), 3.78 – 3.69 (m, 5H), 3.67 – 3.60 (m, 9H), 3.56 (d, *J* = 4.7 Hz, 7H), 3.45 (d, *J* = 11.0 Hz, 2H), 2.41 (s, 3H), 1.04 (s, 9H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 144.8, 138.2, 138.1, 137.8, 137.7, 137.4, 135.7, 135.7, 135.5, 133.4, 133.4, 133.3, 133.1, 133.0, 129.9, 129.9, 129.9, 129.8, 129.8, 128.5, 128.5, 128.5, 128.5, 128.5, 128.5, 128.5, 128.4, 128.4,

128.4, 128.4, 128.2, 128.2, 128.2, 128.1, 128.1, 128.0, 128.0, 127.9, 127.9, 127.9, 127.9, 127.8, 127.8, 127.8, 127.8, 127.8, 127.8, 127.8, 127.8, 127.7, 127.7, 127.7, 127.7, 127.7, 126.3, 126.1, 125.9, 125.7, 109.6, 108.5, 105.4, 99.9, 85.0, 84.3, 84.2, 84.2, 84.0, 83.7, 83.2, 83.1, 83.1, 80.1, 78.7, 77.8, 73.2, 72.4, 72.3, 72.1, 72.0, 72.0, 71.6, 70.8, 70.7, 70.7, 70.6, 70.4, 69.3, 68.7, 66.9, 66.1, 66.0, 64.0, 27.0, 27.0, 27.0, 21.7, 19.4; **HRMS** (ESI-MS): m/z calcd. For $C_{97}H_{112}O_{23}SSi$ $[M+Na]^+$: 1727.6982; Found: 1727. 6957.

(2-(2-(2-(2-tosylethoxy)ethoxy)ethoxy)ethyl)-2-*O*-(4-oxopentanoyl)-3-*O*-benzyl-5-*O*-(2-*O*-(4-oxopentanoyl)-3-*O*-benzyl-5-*O*-(2-*O*-(2,3-*O*-dibenzyl-5-*O*-(naphthylmethyl)-β-D-arabinofuranosyl)-3-*O*-benzyl-5-*O* *tert*butyldiphenylsilyl-α-D-arabinofuranosyl)-α-D-arabinofuranosyl)-α-D-arabinofuranoside (58):

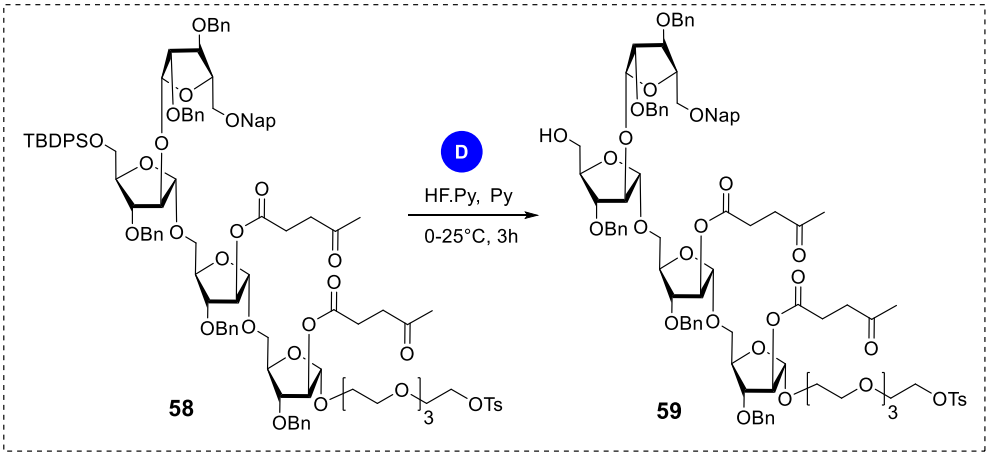
Compound **57** was converted to compound **58** according to the general experimental **Procedure H**. (Yield 80%, pale yellow syrup) **$[\alpha]_D^{25}$** = -57.5 (*c* = 1.0, $CHCl_3$); **IR** (cm^{-1}, $CHCl_3$): 3864, 3735, 3596, 3056, 2925, 2310, 1732,1457, 1360,1108; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.78 (d, *J* = 8.3 Hz, 3H), 7.72 – 7.59 (m, 7H), 7.45 – 7.41 (m, 2H), 7.38 – 7.31 (m, 8H), 7.30 – 7.25 (m, 11H), 7.22 (m, 15H), 5.14 (d, *J* = 4.7 Hz, 3H), 5.08 (s, 1H), 5.04 (d, *J* = 5.9 Hz, 2H), 4.70 – 4.64 (m, 3H), 4.63 – 4.60 (m, 2H), 4.59 – 4.52 (m, 3H), 4.50 (s, 2H), 4.48 – 4.42 (m, 3H), 4.37 (s, 1H), 4.21 (q, *J* = 4.2 Hz, 1H), 4.15 – 4.07 (m, 8H), 3.94 (dd, *J* = 19.8, 5.3 Hz, 2H), 3.85 – 3.78 (m, 4H), 3.66 – 3.59 (m, 10H), 3.57 – 3.53 (m, 7H), 2.63 – 2.42 (m, 8H), 2.41 (s, 3H), 2.11 (s, 3H), 2.04 (s, 3H), 1.04 (s, 9H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 206.3, 206.2, 171.8, 171.8, 144.8, 138.2, 138.2, 138.0, 137.9, 137.8, 135.7, 135.7, 135.5, 133.5, 133.5, 133.2, 133.1, 133.0, 129.9, 129.9, 129.9, 129.9, 129.7, 128.5, 128.5, 128.4, 128.4, 128.4, 128.4, 128.4, 128.4, 128.4, 128.3, 128.3, 128.3, 128.3, 128.1, 128.0, 128.0, 128.0, 128.0, 128.0, 127.9, 127.9, 127.9, 127.9, 127.9, 127.8, 127.8, 127.7, 127.7, 127.7, 127.7, 127.7, 127.7, 127.6, 127.6, 127.5, 126.3, 126.1, 125.9, 125.6, 106.5, 106.1, 106.1, 100.2, 85.7, 84.0, 83.9, 83.6, 83.4, 83.1, 82.8, 82.1, 81.8, 81.8, 81.8, 80.1, 73.2, 72.5, 72.4, 72.4, 72.3, 72.3, 72.2, 70.8, 70.8, 70.7, 70.7, 70.5, 70.2, 69.3, 68.7, 66.7, 65.7, 64.1, 37.8, 37.7,



29.8, 29.7, 27.9, 27.8, 27.0, 26.9, 26.9, 21.7, 19.4; **HRMS** (ESI-MS): m/z calcd. For $C_{107}H_{124}O_{27}SSi$ $[M+Na]^+$: 1923.7718; Found: 1923.7770.

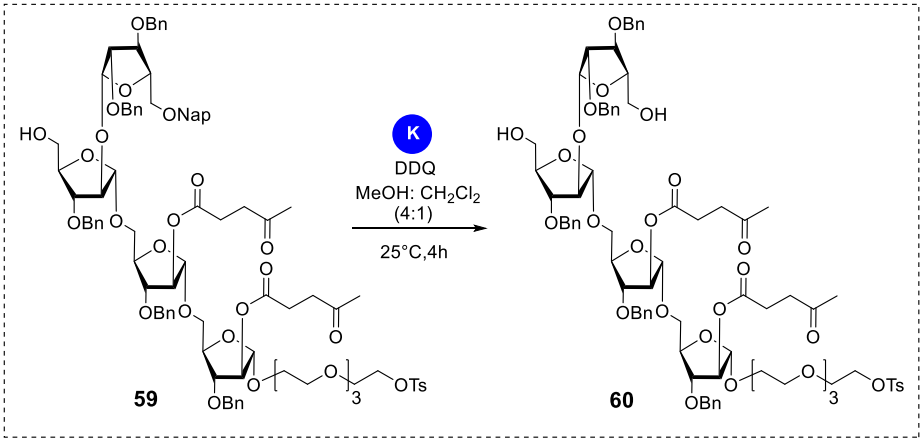
(2-(2-(2-(2-tosylethoxy)ethoxy)ethoxy)ethyl-2-*O*-(4-oxopentanoyl)-3-*O*-benzyl-5-*O*-(2-*O*-(4-oxopentanoyl)-3-*O*-benzyl-5-*O*-(2-*O*-(2,3-*O*-dibenzyl-5-*O*-(naphthylmethyl)-β-D-arabinofuranosyl)-3-*O*-benzyl-α-D-arabinofuranosyl)-α-D-arabinofuranosyl)-α-D-arabinofuranoside (59):

Compound **58** was converted to compound **59** according to the general experimental **Procedure D**. (Yield 79%, pale yellow syrup): **$[\alpha]_D^{25}$** = -78.7 (c = 1.0, $CHCl_3$); **IR** (cm^{-1}, $CHCl_3$): 3737, 3516, 3045, 2923, 1730, 1455, 1360, 1108; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.82 – 7.65 (m, 6H), 7.47 – 7.42 (m, 2H), 7.38 – 7.31 (m, 6H),7.30 – 7.26 (m, 10H), 7.25 – 7.20 (m, 12H), 5.14 (d, *J* = 7.2 Hz, 2H), 5.08 (s, 2H), 5.02 (s, 2H), 4.67 (dd, *J* = 11.9, 4.1 Hz, 3H), 4.59 (dt, *J* = 10.4, 4.2 Hz, 5H), 4.55 – 4.45 (m, 3H), 4.42 (d, *J* = 11.8 Hz, 1H), 4.31 (s, 1H), 4.22 (d, *J* = 4.1 Hz, 1H), 4.15 – 4.05 (m, 7H), 4.01 (d, *J* = 2.9 Hz, 1H), 3.95 (d, *J* = 4.7 Hz, 1H), 3.91 (d, *J* = 4.8 Hz, 1H), 3.80 (dt, *J* = 6.9, 2.9 Hz, 3H), 3.73 – 3.69 (m, 1H), 3.62 (m, 10H), 3.54 (m, 8H), 2.66 – 2.42 (m, 8H), 2.41 (s, 3H), 2.12 (s, 3H), 2.05 (s, 3H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 206.3, 206.3, 171.8, 171.8, 144.8, 138.1, 138.1, 138.0, 137.9, 137.6, 135.4, 133.2, 133.0, 133.0, 129.8, 129.8, 129.8, 128.6, 128.6, 128.4, 128.4, 128.4, 128.4, 128.3, 128.3, 128.3, 128.2, 128.1, 128.0, 128.0, 128.0, 128.0, 128.0, 127.9, 127.9, 127.9, 127.7, 127.7, 127.7, 127.7, 127.7, 127.7, 127.7, 127.6, 127.5, 127.5, 126.4, 126.2, 125.9, 125.7, 106.5, 106.1, 106.0, 100.4, 85.4, 83.9, 83.5, 83.4, 83.4, 83.3, 82.8, 81.9, 81.8, 81.7, 81.7, 80.1, 73.2, 72.5, 72.5, 72.3, 72.3, 72.0, 70.7, 70.7, 70.6, 70.5, 70.2, 69.3, 68.6, 66.7, 65.8, 65.6, 62.4, 60.4, 37.8, 37.7, 29.8, 29.7, 27.9, 27.8, 21.7; **HRMS** (ESI-MS): m/z calcd. For $C_{91}H_{106}O_{27}S[M+Na]^+$: 1685.6540; Found: 1685.6565



(2-(2-(2-(2-tosylethoxy)ethoxy)ethoxy)ethyl)-2-*O*-(4-oxopentanoyl)-3-*O*-benzyl-5-*O*-(2-*O*-(4-oxopentanoyl)-3-*O*-benzyl-5-*O*-(2-*O*-(2,3-*O*-dibenzyl)-β-D-arabinofuranosyl)-3-*O*-benzyl-α-D-arabinofuranosyl)-α-D-arabinofuranosyl)-α-D-arabinofuranoside (60):

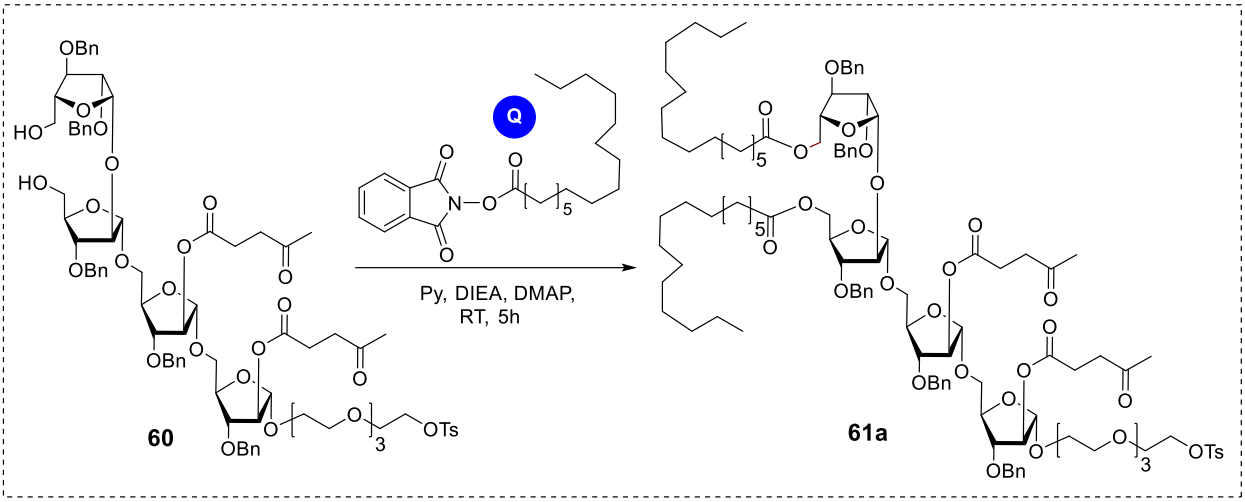
Compound **59** was converted to compound **60** according to the general experimental **Procedure K**. (Yield 67%, pale yellow syrup): **$[\alpha]_D^{25}$** = +12.2 (*c* = 1.0, $CHCl_3$); **IR** (cm^{-1}, $CHCl_3$): 3536, 3075, 2823, 1710, 1555, 1360, 1108, 1008; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.78 (d, *J* = 8.3 Hz, 2H), 7.35 – 7.28 (m, 27H), 5.14 (dd, *J* = 9.8, 1.2 Hz, 2H), 5.10 (s, 1H), 5.07 (d, *J* = 4.6 Hz, 1H), 5.03 (s, 2H), 4.72 – 4.65 (m, 4H), 4.62 – 4.56 (m, 3H), 4.54 (d, *J* = 5.8 Hz, 2H), 4.50 (s, 1H), 4.27 – 4.19 (m, 3H), 4.16 – 4.07 (m, 6H), 4.00 – 3.91 (m, 4H), 3.84 – 3.74 (m, 5H), 3.62 (m, 10H), 3.55 (d, *J* = 2.8 Hz, 6H), 2.63 (q, *J* = 6.7 Hz, 4H), 2.51 – 2.46 (m, 4H), 2.42 (s, 3H), 2.13 (s, 3H), 2.10 (s, 3H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 206.5, 206.4, 171.8, 171.8, 144.8, 138.0, 138.0, 137.9, 137.9, 137.5, 133.0, 129.9, 129.9, 128.6, 128.6, 128.5, 128.5, 128.5, 128.4, 128.4, 128.4, 128.4, 128.3, 128.3, 128.1, 128.1, 128.0, 128.0, 128.0, 128.0, 127.9, 127.9, 127.8, 127.8, 127.7, 127.7, 127.7, 127.7, 127.7, 127.6, 106.5, 106.1, 106.0, 100.4, 86.2, 84.0, 83.4, 83.4, 83.1, 82.8, 82.0, 82.0, 81.8, 81.7, 81.6, 80.7, 72.7, 72.6, 72.3, 72.3, 72.3, 70.7, 70.6, 70.6, 70.5, 70.1, 69.3, 68.6, 66.6, 65.8, 65.7, 63.5, 62.2, 37.8, 37.8, 29.8, 29.8, 27.9, 27.8, 21.7; **HRMS** (ESI-MS): m/z calcd. For $C_{80}H_{98}O_{27}S$ $[M+Na]^+$: 1545.5914; Found: 1545.5900



(2-(2-(2-(2-tosylethoxy)ethoxy)ethoxy)ethyl)-2-*O*-(4-oxopentanoyl)-3-*O*-benzyl-5-*O*-(2-*O*-(4-oxopentanoyl)-3-*O*-benzyl-5-*O*-(2-*O*-(2,3-*O*-dibenzyl-5-*O*-(hexadecanoyl)-β-D-arabinofuranosyl)-3-*O*-benzyl-5-*O*-(hexadecanoyl)-α-D-arabinofuranosyl)-α-D-arabinofuranosyl)-α-D-arabinofuranoside (61a):

Compound **60** was converted to compound **61a** according to the general experimental **Procedure Q.** (Yield 52%, pale yellow syrup): **$[\alpha]_D^{25}$** = +18.1 (*c* = 0.06, $CHCl_3$); **IR** (cm^{-1}, $CHCl_3$): 3736, 3069, 2921, 2855, 1714, 1458, 1367, 1283, 1082, 969, 903; **^{1}H NMR** (400 MHz,

$CDCl_3$) δ 7.79 (d, *J* = 8.3 Hz, 2H), 7.31 (m, *J* = 14.9, 3.8 Hz, 27H), 5.15 (d, *J* = 1.3 Hz, 1H), 5.14 – 5.11 (m, 2H), 5.08 (s, 1H), 5.03 (d, *J* = 5.1 Hz, 2H), 4.68 (dt, *J* = 12.0, 3.9 Hz, 4H), 4.60 (d, *J* =

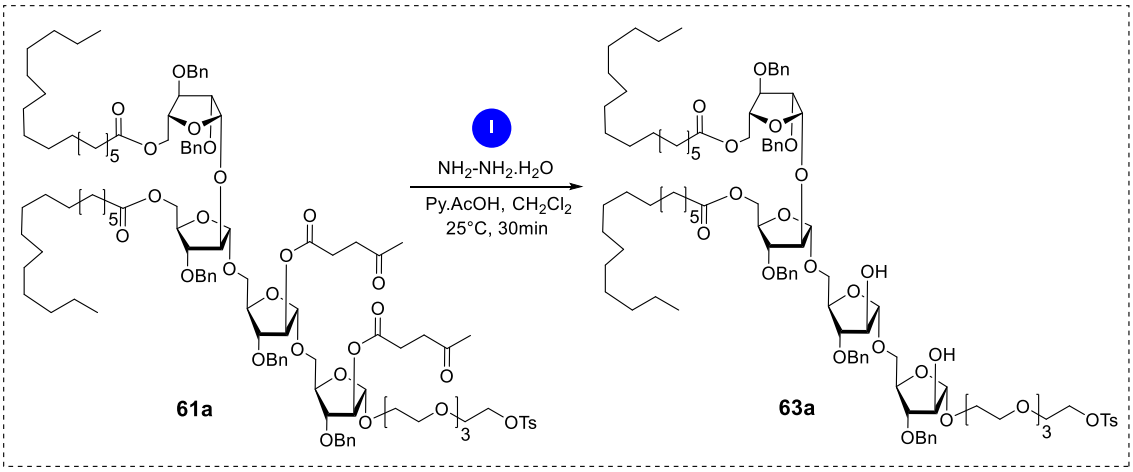


10.8 Hz, 2H), 4.51 (ddd, *J* = 11.6, 9.2, 5.3 Hz, 4H), 4.33 (d, *J* = 2.0 Hz, 1H), 4.27 – 4.19 (m, 3H), 4.16 – 4.07 (m, 9H), 3.97 – 3.90 (m, 3H), 3.81 (ddd, *J* = 10.7, 6.0, 3.9 Hz, 3H), 3.67 – 3.60 (m, 9H), 3.57 – 3.54 (m, 6H), 2.66 – 2.59 (m, 4H), 2.48 (qd, *J* = 6.4, 5.2, 1.9 Hz, 4H), 2.43 (s, 3H), 2.26 (t, *J* = 7.6 Hz, 2H), 2.19 (td, *J* = 7.4, 2.1 Hz, 2H), 2.13 (s, 3H), 2.11 (s, 3H), 1.54 (dt, *J* = 19.5, 6.9 Hz, 4H), 1.28 – 1.22 (m, 48H), 0.88 (t, *J* = 6.8 Hz, 6H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 206.3, 206.2, 173.6, 173.4, 171.9, 171.8, 144.8, 138.0, 138.0, 137.9, 137.9, 137.5, 133.1, 129.9, 129.9, 128.6, 128.6, 128.5, 128.5, 128.5, 128.5, 128.4, 128.4, 128.4, 128.4, 128.1, 128.1, 128.1, 128.1, 128.1, 128.0, 127.9, 127.8, 127.8, 127.8, 127.8, 127.8, 127.8, 127.7, 127.7, 127.7, 127.7, 106.6, 106.2, 106.1, 100.8, 86.1, 84.4, 83.8, 83.5, 83.4, 82.8, 82.0, 81.9, 81.8, 81.7, 80.2, 78.9, 72.6, 72.6, 72.5, 72.4, 72.3, 70.8, 70.7, 70.7, 70.6, 70.2, 69.4, 68.7, 68.7, 66.7, 66.0, 65.8, 63.7, 37.8, 37.8, 34.1, 34.1, 32.0, 32.0, 29.8, 29.8, 29.8, 29.8, 29.8, 29.8, 29.8, 29.8, 29.7, 29.6, 29.6, 29.5, 29.5, 29.4, 29.4, 29.3, 29.2, 27.9, 27.9, 24.9, 22.8, 22.8, 21.7, 14.2, 14.2; **HRMS** (ESI-MS): m/z calcd. For $C_{112}H_{158}O_{29}S$ $[M+Na]^+$: 2023.0507; Found: 2023.0570.

(2-(2-(2-(2-tosylethoxy)ethoxy)ethoxy)ethyl)-3-*O*-benzyl-5-*O*-(-3-*O*-benzyl-5-*O*-(2-*O*-(2,3-*O*-dibenzyl-5-*O*-(hexadecanoyl)-β-D-arabinofuranosyl)-3-*O*-benzyl-5-*O*-(hexadecanoyl)-α-D-arabinofuranosyl)-α-D-arabinofuranosyl)-α-D-arabinofuranoside (63a):

Compound **61a** was converted to compound **63a** according to the general experimental **Procedure I.** (Yield 72%, pale yellow syrup):

[α]$_D^{25}$ = +50.5 (*c* = 0.06, $CHCl_3$); **IR** (cm^{-1}, $CHCl_3$): 3638, 3307, 2824, 2100, 1708, 1450, 1346, 1070, 1023, 870; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.79 (d, *J* = 8.3 Hz, 2H), 7.35 – 7.28 (m, 27H),

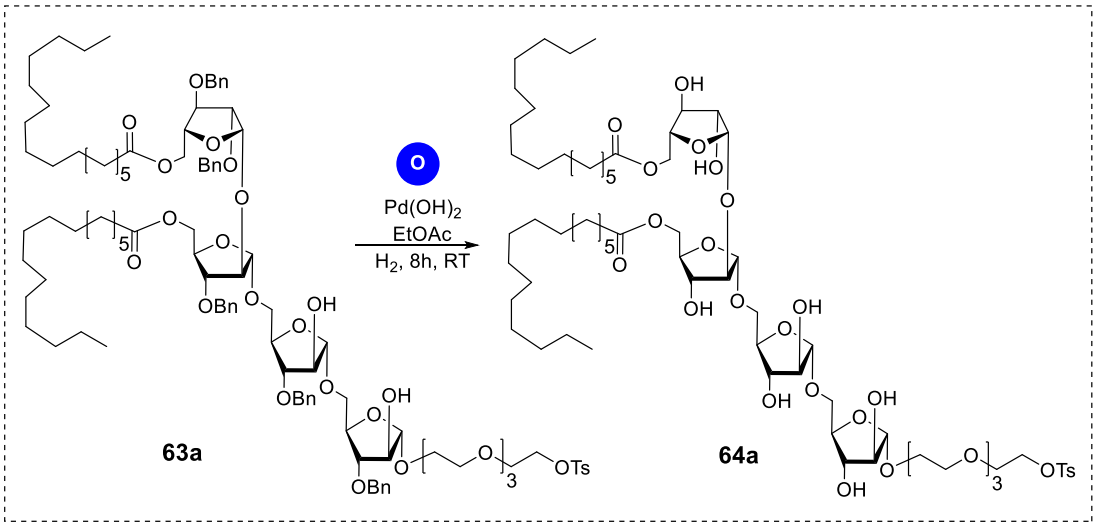


5.04 (s, 1H), 4.97 (d, *J* = 4.0 Hz, 1H), 4.94 (s, 2H), 4.72 – 4.66 (m, 2H), 4.57 (d, *J* = 11.9 Hz, 3H), 4.53 – 4.48 (m, 3H), 4.39 (dd, *J* = 14.4, 12.3 Hz, 2H), 4.29 – 4.26 (m, 1H), 4.16 (dd, *J* = 9.1, 4.4 Hz, 4H), 4.13 – 3.99 (m, 9H), 3.88 – 3.82 (m, 4H), 3.75 (ddd, *J* = 16.3, 5.1, 2.6 Hz, 3H), 3.68 – 3.62 (m, 9H), 3.60 – 3.57 (m, 6H), 2.43 (s, 3H), 2.30 – 2.26 (m, 2H), 2.22 (t, *J* = 7.6 Hz, 2H), 1.58 (dt, *J* = 15.3, 7.2 Hz, 4H), 1.26 (s, 48H), 0.88 (s, 6H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 173.5, 173.4, 144.9, 138.1, 137.8, 137.5, 137.4, 137.3, 133.1, 129.9, 129.9, 128.6, 128.6, 128.6, 128.5, 128.5, 128.5, 128.5, 128.5, 128.3, 128.3, 128.2, 128.1, 128.1, 128.1, 128.1, 128.1, 128.1, 128.0, 128.0, 128.0, 128.0, 127.9, 127.9, 127.8, 127.8, 127.8, 109.6, 108.5, 105.4, 100.4, 84.9, 84.3, 83.9, 83.8, 83.6, 83.5, 83.0, 82.5, 81.8, 79.0, 78.8, 77.8, 72.7, 72.6, 72.3, 72.0, 71.7, 70.8, 70.7, 70.7, 70.6, 70.4, 69.3, 68.8, 66.9, 66.1, 65.9, 65.8, 63.6, 34.1, 32.0, 32.0, 29.8, 29.8, 29.8, 29.8, 29.8, 29.8, 29.8, 29.8, 29.8, 29.7, 29.7, 29.7, 29.6, 29.6, 29.5, 29.5, 29.5, 29.4, 29.3, 29.2, 24.9, 24.9, 22.8, 22.8, 21.7, 14.2, 14.2; **HRMS** (ESI-MS): m/z calcd. For $C_{102}H_{146}O_{25}S$ $[M+Na]^+$: 1825.9772; Found: 1825.9980.

(2-(2-(2-(2-tosylethoxy)ethoxy)ethoxy)ethyl)5-*O*-(-5-*O*-(2-*O*-(-5-*O*-(hexadecanoyl)-β-D-arabinofuranosyl)-5-*O*-(hexadecanoyl)-α-D-arabinofuranosyl)-α-D-arabinofuranosyl)-α-D-arabinofuranoside (64a):

Compound **63a** was converted to compound **64a** according to the general experimental **Procedure O.** (Yield 60%, pale yellow syrup): **[α]$_D^{25}$** = +30.3 (*c* = 1.0, $CHCl_3$); **IR** (cm^{-1}, $CHCl_3$): 3660, 3635, 2734, 2750, 2009, 1610, 1225, 1340, 1109, 1003, 900; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.78 (d, *J* = 8.2 Hz, 2H), 7.34 (d, *J* = 8.1 Hz, 2H), 5.15 – 4.98 (m, 4H), 4.31 – 4.21 (m, 4H), 4.16 – 4.12 (m, 5H), 4.07 (s, 2H), 3.92 (m, 10H), 3.71 – 3.56 (m, 15H), 2.43 (s, 3H), 2.32 (q, *J* = 7.4 Hz, 4H), 1.62 – 1.55 (m, 4H), 1.25 (m, 48H), 0.86 (t, *J* = 6.8 Hz, 6H); **^{13}C NMR** (101 MHz,

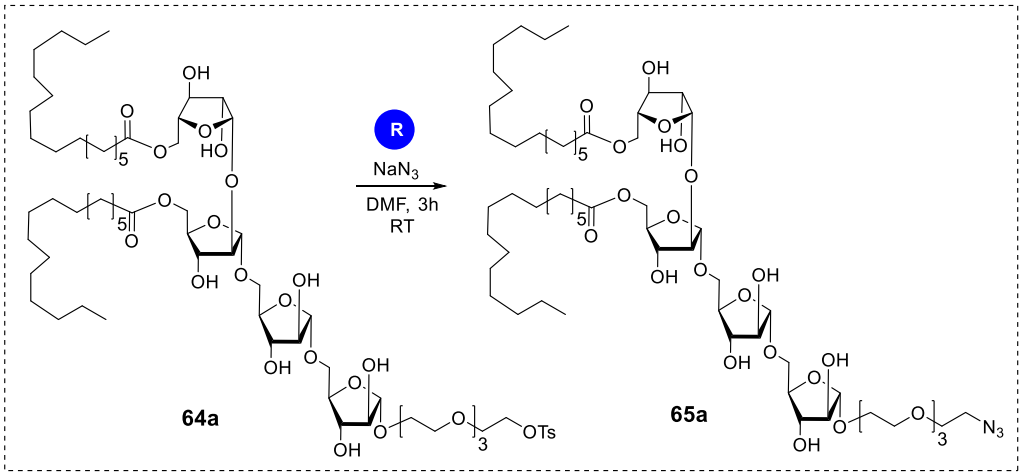
$CDCl_3$) δ 174.1, 174.0, 145.0, 133.0, 130.0, 130.0, 128.1, 128.1, 108.0, 107.9, 105.8, 102.5, 89.7, 84.2, 84.2, 81.1, 80.9, 80.0, 79.8, 78.1, 78.0, 77.9, 75.7, 75.4, 70.7, 70.5, 70.4, 70.4, 70.3,



69.4, 68.7, 67.7, 66.5, 66.1, 65.6, 63.8, 34.2, 34.1, 32.0, 32.0, 32.0, 29.8, 29.8, 29.8, 29.8, 29.8, 29.8, 29.8, 29.8, 29.8, 29.8, 29.8, 29.7, 29.5, 29.5, 29.5, 29.5, 29.3, 29.3, 24.9, 22.8, 22.8, 22.8, 21.8, 14.2, 14.2; **HRMS** (ESI-MS): m/z calcd. For $C_{67}H_{116}O_{25}S$ $[M+Na]^+$: 1375.7424; Found: 1375.7430

(2-(2-(2-(2-Azidoethoxy)ethoxy)ethoxy)ethyl)5-*O*-(-5-*O*-(2-*O*-(-5-*O*-(hexadecanoyl)-β-D-arabinofuranosyl)-5-*O*-(hexadecanoyl)-α-D-arabinofuranosyl)-α-D-arabinofuranosyl)-α-D-arabinofuranoside (65a) :

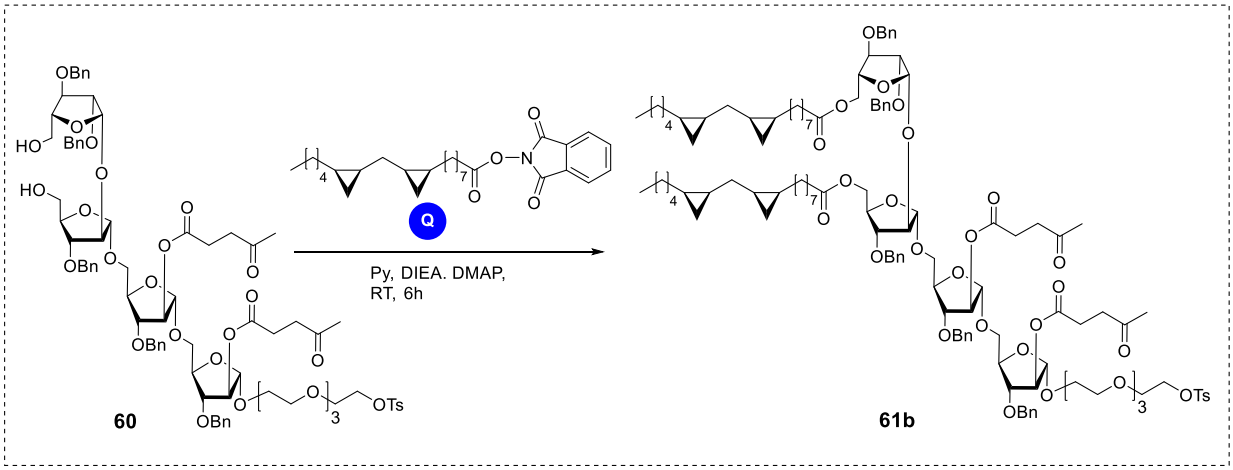
Compound **64a** was converted to compound **65a** according to the general experimental **Procedure R.** (Yield 72%, pale yellow syrup): **$[\alpha]_D^{25}$** = +51.5 (*c* = 1.0, $CHCl_3$); **IR** (cm^{-1}, $CHCl_3$): 3737, 3409, 2920, 2855, 2107, 1737,1459, 1358, 1301, 1100, 897; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 5.14 – 5.11 (m, 1H), 5.05 (d, *J* = 4.1 Hz, 1H), 5.01 (s, 2H), 4.33 – 4.28 (m, 2H), 4.26 – 4.22 (m, 2H), 4.18 – 4.12 (m, 5H),



4.07 (s, 2H), 4.02 – 3.89 (m, 9H), 3.70 – 3.59 (m, 14H), 3.42 – 3.35 (m, 2H), 2.34 (q, *J* = 7.5 Hz, 4H), 1.63 – 1.56 (m, 4H), 1.25 (s, 48H), 0.87 (t, *J* = 6.8 Hz, 6H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 174.2, 174.0, 108.0, 107.8, 105.8, 102.5, 89.7, 84.4, 84.3, 81.1, 80.7, 80.1, 79.9, 78.1, 77.9, 77.3, 75.8, 75.4, 70.7, 70.6, 70.6, 70.4, 70.3, 70.1, 67.7, 66.5, 66.0, 65.6, 63.7, 50.7, 34.2, 34.2, 32.1, 32.1, 32.1, 29.9, 29.9, 29.9, 29.9, 29.9, 29.9, 29.8, 29.8, 29.8, 29.8, 29.8, 29.8, 29.8, 29.7, 29.5, 29.5, 29.5, 29.5, 29.3, 25.0, 25.0, 22.8, 22.8, 14.3, 14.2; **HRMS** (ESI-MS): m/z calcd. For $C_{60}H_{109}N_3O_{22}$ $[M+Na]^+$: 1246.7400; Found: 1246.7400

(2-(2-(2-(2-tosylethoxy)ethoxy)ethoxy)ethyl)-2-*O*-(4-oxopentanoyl)-3-*O*-benzyl-5-*O*-(2-*O*-(4-oxopentanoyl)-3-*O*-benzyl-5-*O*-(2-*O*-(2,3-*O*-dibenzyl-5-*O*-(8-(2-((2-pentylcyclopropyl)methyl)cyclopropyl)octanoyl)-β-D-arabinofuranosyl)-3-*O*-benzyl-5-*O*-(8-(2-((2-pentylcyclopropyl)methyl)cyclopropyl)octanoyl)-α-D-arabinofuranosyl)-α-D-arabinofuranosyl)-α-D-arabinofuranoside (61b):

Compound **60** was converted to compound **61b** according to the general experimental **Procedure Q**. (Yield 54%, pale yellow syrup) **$[\alpha]_D^{25}$** = +19.6 (*c* = 0.06, $CHCl_3$); **IR** (cm^{-1}, $CHCl_3$):

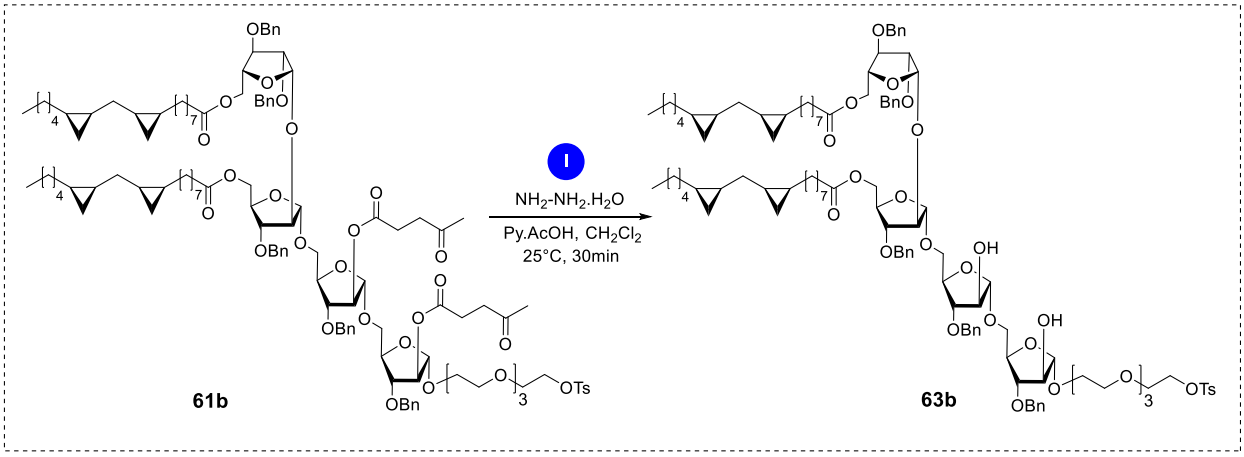


3735, 3068, 2921, 2855, 2309, 1732, 1644, 1458, 1368, 1281, 1083, 970, 903; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.79 (d, *J* = 8.3 Hz, 2H), 7.31 (dt, *J* = 14.6, 3.9 Hz, 27H), 5.16 – 5.11 (m, 3H), 5.08 (s, 1H), 5.03 (d, *J* = 5.3 Hz, 2H), 4.68 (dt, *J* = 12.0, 4.0 Hz, 4H), 4.60 (d, *J* = 11.1 Hz, 2H), 4.51 (ddd, *J* = 11.7, 8.9, 5.2 Hz, 4H), 4.34 (d, *J* = 2.0 Hz, 1H), 4.26 – 4.19 (m, 3H), 4.16 – 4.07 (m, 9H), 3.97 – 3.90 (m, 3H), 3.81 (ddd, *J* = 10.7, 6.7, 3.8 Hz, 3H), 3.67 – 3.60 (m, 9H), 3.58 – 3.54 (m, 6H), 2.66 – 2.59 (m, 4H), 2.53 – 2.45 (m, 4H), 2.43 (s, 3H), 2.27 (t, *J* = 7.6 Hz, 2H), 2.19 (td, *J* = 7.5, 2.2 Hz, 2H), 2.13 (s, 3H), 2.11 (s, 3H), 1.53 (ddd, *J* = 28.6, 13.7, 6.9 Hz, 6H), 1.41 – 1.36 (m, 9H), 1.29 (m, 23H), 1.08 (ddt, *J* = 44.0, 14.3, 7.1 Hz, 6H), 0.89 (t, *J* = 6.8 Hz, 6H), 0.81 – 0.75 (m, 4H), 0.72 – 0.64 (m, 4H), 0.62 (dd, *J* = 8.9, 3.4 Hz, 4H), -0.24 – -0.32 (m, 4H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 206.3, 206.2, 173.6, 173.4, 171.9, 171.8, 144.8, 138.0,

137.9, 137.8, 137.8, 137.5, 133.1, 129.9, 129.9, 128.6, 128.6, 128.6, 128.5, 128.5, 128.5, 128.5, 128.5, 128.4, 128.4, 128.4, 128.4, 128.4, 128.1, 128.1, 128.1, 128.0, 128.0, 127.9, 127.9, 127.8, 127.8, 127.8, 127.8, 127.8, 127.7, 127.7, 106.6, 106.1, 106.1, 100.8, 86.1, 84.4, 83.8, 83.5, 83.4, 82.8, 81.9, 81.9, 81.8, 81.7, 80.1, 78.9, 72.6, 72.6, 72.6, 72.5, 72.4, 72.3, 70.8, 70.7, 70.7, 70.6, 70.2, 69.4, 68.7, 66.7, 66.0, 65.8, 63.7, 37.8, 37.8, 34.1, 34.1, 32.0, 30.3, 30.2, 30.0, 29.8, 29.8, 29.6, 29.5, 29.5, 29.4, 29.3, 29.2, 29.0, 28.8, 28.8, 28.1, 28.0, 27.9, 27.9, 24.9, 22.8, 21.7, 16.1, 16.0, 16.0, 16.0, 16.0, 15.8, 15.7, 14.2, 14.2, 11.1, 11.1, 10.9, 10.9; **HRMS** (ESI-MS): m/z calcd. For $C_{120}H_{166}O_{29}S$ $[M+Na]^+$: 2126.1133; Found: 2126.1169

(2-(2-(2-(2-tosylethoxy)ethoxy)ethoxy)ethyl)-3-*O*-benzyl-5-*O*-(-3-*O*-benzyl-5-*O*-(2-*O*-(2,3-*O*-dibenzyl-5-*O*-(8-(2-((2-pentylcyclopropyl)methyl)cyclopropyl)octanoyl)-β-D-arabinofuranosyl)-3-O-benzyl-5-O-(8-(2((2-pentylcyclopropyl)methyl)cyclopropyl)octanoyl)-α-D-arabinofuranosyl)-α-D-arabinofuranosyl)-α-D-arabinofuranoside (63b):

Compound **61b** was converted to compound **63b** according to the general experimental **Procedure I**. (Yield 73%, pale yellow syrup): **$[\alpha]_D^{25}$** = +57.5 (*c* = 0.06, $CHCl_3$); **IR** (cm^{-1}, $CHCl_3$):

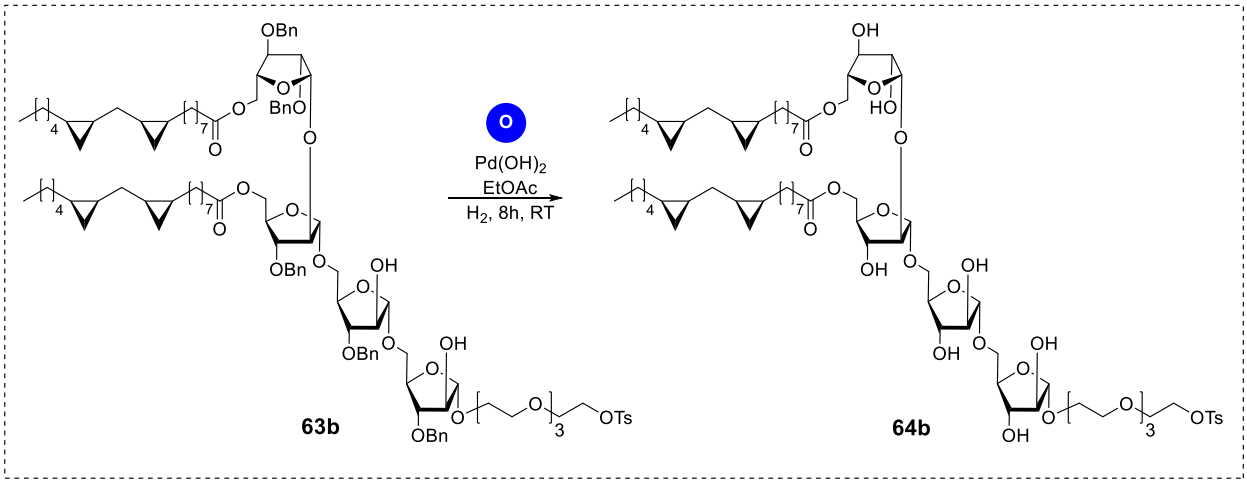


3738, 3387, 2924, 2107, 1738, 1454, 1356, 1090, 1003, 876; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.79 (d, *J* = 8.3 Hz, 2H), 7.35 – 7.27 (m, 27H), 5.04 (s, 1H), 4.97 (d, *J* = 4.0 Hz, 1H), 4.93 (s, 2H), 4.71 – 4.65 (m, 2H), 4.59 – 4.55 (m, 3H), 4.53 – 4.48 (m, 3H), 4.39 (dd, *J* = 14.5, 12.3 Hz, 2H), 4.28 – 4.26 (m, 1H), 4.15 (dt, *J* = 9.3, 4.5 Hz, 5H), 4.11 – 4.05 (m,4H), 4.03 (dt, *J* = 8.0, 4.0 Hz, 3H), 3.84 (dd, *J* = 9.2, 5.3 Hz, 4H), 3.75 (ddd, *J* = 16.2, 5.1, 2.6 Hz, 3H), 3.66 (q, *J* = 4.4, 3.8 Hz, 6H), 3.63 (dd, *J* = 3.6, 2.1 Hz, 2H), 3.61 – 3.56 (m, 8H), 2.43 (s, 3H), 2.30 – 2.20 (m, 4H), 1.54 (ddt, *J* = 28.3, 14.1, 6.7 Hz, 6H), 1.41 – 1.36 (m, 10H), 1.28 (m, 23H), 1.14 (td, *J* = 8.0, 2.6 Hz, 4H), 1.06 – 0.99 (m, 1H), 0.91 – 0.87 (m, 6H), 0.78 (td, *J* = 8.0, 4.1 Hz, 4H), 0.73 – 0.65 (m, 4H), 0.63 – 0.58 (m, 4H), -0.24 – -0.31 (m, 4H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 173.5, 173.4,

144.9, 138.1, 137.8, 137.5, 137.4, 137.3, 133.1, 129.9, 129.9, 129.9, 128.6, 128.6, 128.6, 128.6, 128.5, 128.5, 128.5, 128.5, 128.5, 128.5, 128.3, 128.3, 128.2, 128.1, 128.1, 128.1, 128.1, 128.0, 128.0, 128.0, 128.0, 127.9, 127.9, 127.8, 127.8, 127.8, 109.6, 108.5, 105.4, 100.4, 84.9, 84.2, 83.9, 83.8, 83.6, 83.5, 83.0, 82.5, 81.8, 79.0, 78.8, 77.8, 72.7, 72.6, 72.3, 72.0, 71.7, 70.8, 70.7, 70.7, 70.6, 70.4, 69.3, 68.8, 66.9, 66.1, 65.9, 65.8, 63.6, 34.1, 34.1, 32.0, 32.0, 30.3, 30.3, 30.0, 30.0, 29.8, 29.6, 29.6, 29.5, 29.4, 29.3, 29.3, 29.0, 29.0, 28.8, 28.8, 28.1, 28.0, 24.9, 24.9, 22.8, 21.7, 16.1, 16.1, 16.0, 16.0, 16.0, 16.0, 15.8, 15.7, 14.2, 14.2, 11.1, 11.1, 11.0, 10.9; **HRMS** (ESI-MS): m/z calcd. $C_{110}H_{154}O_{25}S$ $[M+Na]^+$: 1930.0398; Found: 1930.0370

(2-(2-(2-(2-tosylethoxy)ethoxy)ethoxy)ethyl)5-*O*-(-5-*O*-(2-*O*-(-5-*O*-(8-(2-((2-pentylcyclopropyl)methyl)cyclopropyl)octanoyl)-β-D-arabinofuranosyl)-5-*O*-(8-(2((2-pentylcyclopropyl)methyl)cyclopropyl)octanoyl)-α-D-arabinofuranosyl)-α-D-arabinofuranosyl)-α-D-arabinofuranoside (64b):

Compound **63b** was converted to compound **64b** according to the general experimental **Procedure O.** (Yield 58%, pale yellow syrup):

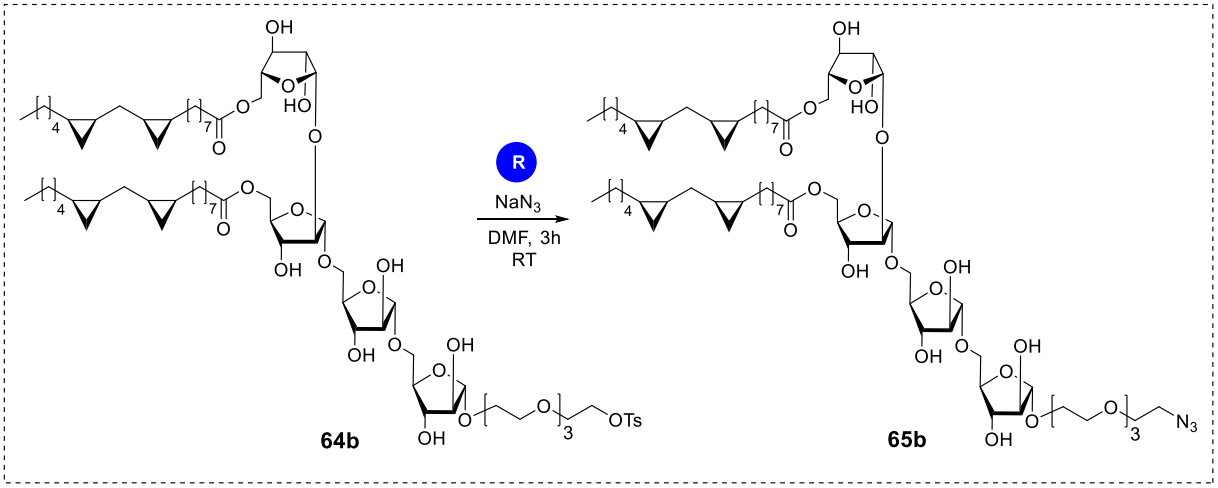


$[\alpha]_D^{25}$ = +48.4 (*c* = 0.06, $CHCl_3$); **IR** (cm^{-1}, $CHCl_3$): 3766, 3735, 2834, 2850, 2209, 1630, 1255, 1342, 1101, 1002, 900; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.78 (d, *J* = 8.1 Hz, 2H), 7.33 (d, *J* = 8.0 Hz, 2H), 5.16 – 4.98 (m, 4H), 4.33 – 4.21 (m, 5H), 4.15 – 4.07 (m, 9H), 4.01 – 3.87 (m, 9H), 3.70 – 3.65 (m, 4H), 3.61 (t, *J* = 7.9 Hz, 6H), 3.57 (s, 3H), 2.43 (s, 3H), 2.33 (q, *J* = 7.3 Hz, 4H), 1.62 – 1.56 (m, 4H), 1.50 – 1.37 (m, 10H), 1.30 – 1.22 (m, 25H), 1.07 (ddd, *J* = 34.7, 14.2, 6.7 Hz, 6H), 0.87 (t, *J* = 6.7 Hz, 6H), 0.80 – 0.73 (m, 4H), 0.69 – 0.4 (m, 3H), 0.59 (dt, *J* = 8.2, 4.1 Hz, 4H), -0.30 (dd, *J* = 11.5, 5.4 Hz, 4H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ174.0, 173.9, 144.9, 132.9, 129.9, 129.9, 128.0, 128.0, 107.9, 107.8, 105.7, 102.4, 89.7, 84.1, 81.0, 80.8, 79.9, 79.9, 79.7, 77.9, 77.8, 77.1, 75.6, 75.3, 72.5, 70.6, 70.4, 70.3, 70.3, 70.1, 69.3, 68.6, 66.4, 66.0, 65.6,

63.7, 60.4, 34.1, 34.0, 31.9, 31.9, 30.2, 29.9, 29.9, 29.9, 29.7, 29.5, 29.4, 29.4, 29.2, 28.9, 28.9, 28.7, 28.7, 28.1, 27.9, 24.8, 22.7, 22.7, 21.7, 21.0, 16.1, 16.1, 15.9, 15.9, 15.9, 15.9, 15.9, 15.7, 15.6, 14.2, 14.1, 11.1, 11.0, 10.9, 10.8; **HRMS** (ESI-MS): m/z calcd. For $C_{75}H_{124}O_{25}S$ $[M+Na]^+$: 1479.8050; Found: 1479.8060

(2-(2-(2-(2-Azidoethoxy)ethoxy)ethoxy)ethyl)5-*O*-(-5-*O*-(2-*O*-(-5-*O*-(8-(2-((2-pentylcyclopropyl)methyl)cyclopropyl)octanoyl)-β-D-arabinofuranosyl)-5-*O*-(8-(2((2-pentylcyclopropyl)methyl)cyclopropyl)octanoyl)-α-D-arabinofuranosyl)-α-D-arabinofuranosyl)-α-D-arabinofuranoside (65b):

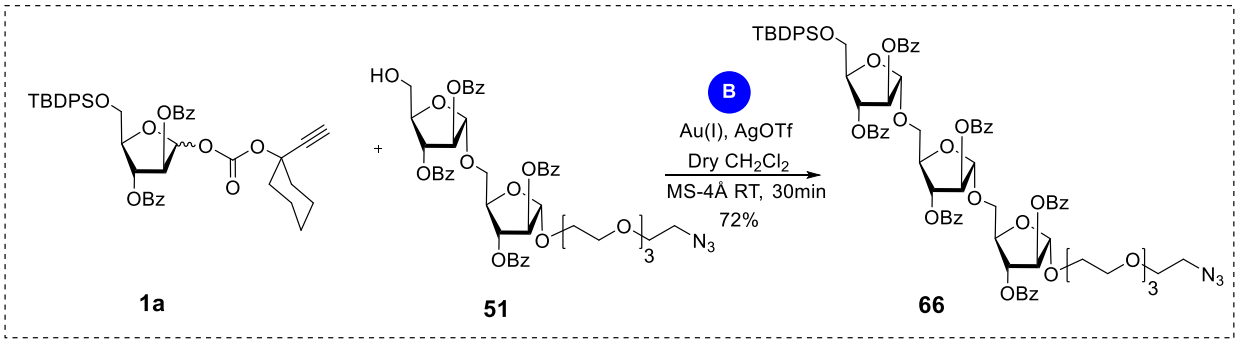
Compound **64b** was converted to compound **65b** according to the general experimental **Procedure R.** (Yield 72%, pale yellow syrup): **$[\alpha]_D^{25}$** = +22.7 (*c* = 0.06, $CHCl_3$); **IR** (cm^{-1}, $CHCl_3$):



3863, 3735, 3396, 2924, 2858, 2309, 2108, 1736, 1455, 1362, 1106, 1002, 900; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 5.15 – 5.00 (m, 4H), 4.34 – 4.23 (m, 5H), 4.17 – 4.07 (m, 7H), 4.02 – 3.89 (m, 8H), 3.65 (s, 14H), 3.39 (t, *J* = 4.7 Hz, 2H), 2.37 – 2.31 (m, 4H), 1.63 – 1.57 (m, 4H), 1.38 (s, 11H), 1.27 (m, 24H), 1.16 – 1.09 (m, 4H), 1.06 – 0.99 (m, 1H), 0.88 (t, *J* = 6.9 Hz, 6H), 0.80 – 0.74 (m, 4H), 0.70 – 0.64 (m, 4H), 0.62 – 0.57 (m, 4H), -0.29 (dd, *J* = 11.6, 5.2 Hz, 4H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 174.2, 174.0, 108.0, 107.9, 105.8, 102.5, 89.8, 84.4, 84.3, 81.1, 80.8, 80.0, 79.8, 78.0, 77.9, 77.4, 75.8, 75.4, 70.6, 70.5, 70.5, 70.4, 70.2, 70.1, 70.1, 67.7, 66.1, 65.6, 63.8, 50.7, 34.2, 34.2, 32.0, 32.0, 32.0, 32.0, 30.3, 30.0, 30.0, 30.0, 30.0, 29.6, 29.6, 29.5, 29.4, 29.0, 29.0, 28.8, 28.8, 28.2, 28.0, 25.0, 22.9, 22.8, 16.2, 16.2, 16.1, 16.0, 16.0, 16.0, 15.8, 15.7, 14.3, 14.3, 11.2, 11.2, 11.0, 11.0; **HRMS** (ESI-MS): m/z calcd. For $C_{68}H_{117}N_3O_{22}$ $[M+Na]^+$:1350.8026; Found: 1350.8035

(2-(2-(2-azidoethoxy)ethoxy)ethyl)2,3-di-*O*-benzoyl-5-*O*-(2,3-di-*O*-benzoyl-5-*O*-(2,3-di-*O*-benzoyl-5-*O*-*tert*butyldiphenylsilyl-α-D-arabinofuranosyl)-α-D-arabinofuranosyl)-α-D-arabinofuranoside (66):

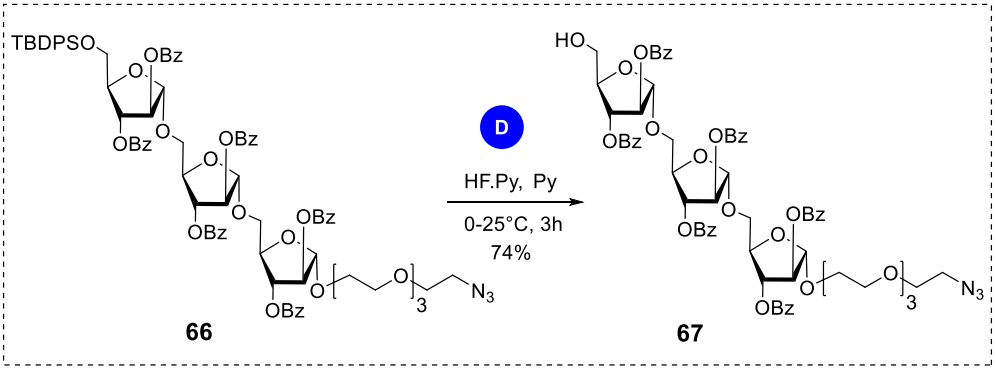
The glycosyl donor **1a**[45] and the glycosyl acceptor **51** were glycosylated according to the general reaction **Procedure B** as detailed above to give the **66**. (Yield 72%, pale yellow syrup):



[α]$_D^{25}$ = +15.5 (*c* = 1.0, $CHCl_3$); **IR** (cm^{-1}, $CHCl_3$): 3067, 2931, 2309, 2105, 1724, 1598, 1455, 1354, 1265, 1108, 968, 870; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.05 – 8.01 (m, 3H), 8.00 – 7.95 (m, 5H), 7.91 (t, *J* = 6.9 Hz, 4H), 7.72 – 7.66 (m, 4H), 7.54 (dt, *J* = 17.5, 8.8 Hz, 3H), 7.46 – 7.34 (m, 11H), 7.32 – 7.24 (m, 10H), 5.63 (q, *J* = 4.9, 4.3 Hz, 4H), 5.56 (d, *J* = 4.3 Hz, 2H), 5.39 (s, 1H), 5.38 (s, 1H), 5.28 (s, 1H), 4.63 (d, *J* = 3.5 Hz, 1H), 4.52 – 4.44 (m, 2H), 4.20 (ddd, *J* = 11.1, 6.7, 4.5 Hz, 2H), 3.98 – 3.87 (m, 5H), 3.69 (dt, *J* = 9.3, 6.0 Hz, 5H), 3.62 (m, 8H), 3.35 (t, *J* = 5.0 Hz, 2H), 1.01 (s, 9H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 165.8, 165.7, 165.6, 165.5, 165.3, 165.3, 135.8, 135.8, 133.5, 133.5, 133.5, 133.4, 133.4, 133.3, 133.3, 133.2, 130.1, 130.1, 130.0, 130.0, 129.9, 129.9, 129.9, 129.9, 129.9, 129.9, 129.9, 129.8, 129.7, 129.4, 129.4, 129.4, 129.3, 129.2, 129.2, 128.6, 128.6, 128.6, 128.6, 128.6, 128.5, 128.5, 128.5, 128.5, 128.4, 128.4, 128.3, 128.3, 127.8, 127.8, 127.8, 127.8, 127.8, 106.1, 106.0, 105.8, 83.3, 82.2, 82.2, 82.0, 81.9, 81.6, 77.5, 77.4, 77.4, 70.9, 70.8, 70.8, 70.7, 70.4, 70.1, 66.8, 66.0, 65.9, 63.5, 50.8, 26.9, 26.9, 26.9, 19.4; **HRMS** (ESI-MS): m/z calcd. For $C_{81}H_{83}N_3O_{22}Si[M+Na]^+$: 1500.5133; Found: 1500.5137

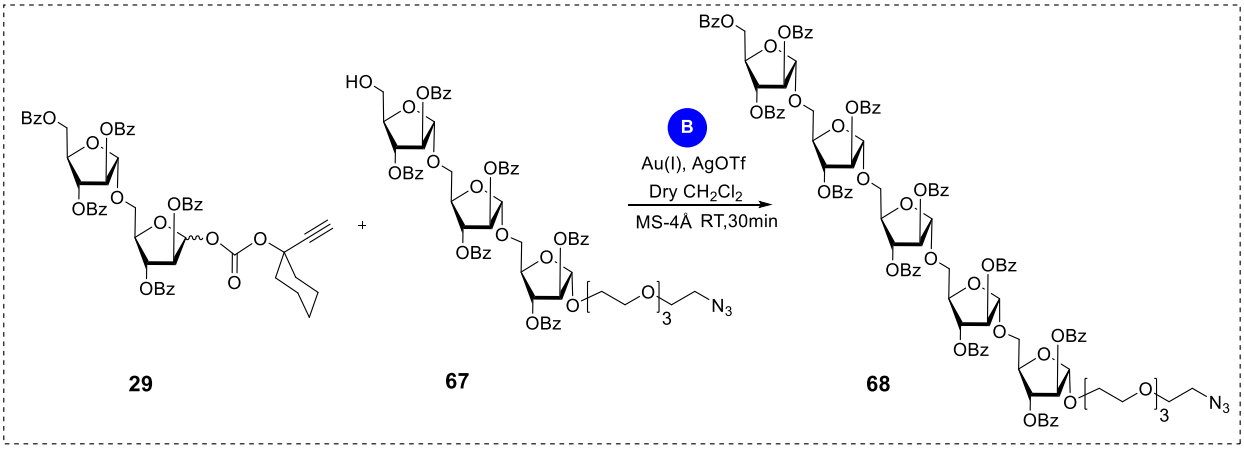
(2-(2-(2-azidoethoxy)ethoxy)ethyl)2,3-di-*O*-benzoyl-5-*O*-(2,3-di-*O*-benzoyl-5-*O*-(2,3-di-*O*-benzoyl-α-D-arabinofuranosyl)-α-D-arabinofuranosyl)-α-D-arabinofuranoside (67): Compound **66** was converted to compound **67** according to the general experimental **Procedure D** (Yield 74%, pale yellow syrup): **[α]$_D^{25}$** = + 31.3 (*c* = 0.06, $CHCl_3$); **IR** (cm^{-1}, $CHCl_3$): 3450, 3060, 2910, 2310, 2160, 1720, 1588, 1445, 1304, 1215, 1101, 960; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.07 – 8.00 (m, 8H), 7.90 (dd, *J* = 7.6, 1.7 Hz, 3H), 7.58 (td, *J* = 7.4, 3.2 Hz, 2H),

7.53 – 7.48 (m, 2H), 7.42 (m,11H), 7.29 – 7.26 (m, 3H), 7.25 (d, *J* = 3.7 Hz, 1H), 5.68 – 5.59 (m, 4H), 5.57 – 5.54 (m, 1H), 5.42 (s, 1H), 5.42 (s, 1H), 5.40 (s, 1H), 5.28 (s, 1H), 4.62 (q, *J* = 4.2 Hz, 1H), 4.46 (p, *J* = 4.4 Hz, 2H), 4.19 (dt, *J* = 11.0, 4.5 Hz, 2H), 4.02 – 3.87 (m, 5H), 3.73 – 3.65 (m, 5H), 3.64 – 3.58 (m, 8H), 3.35 (t, *J* = 5.1 Hz, 2H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 166.2, 165.8, 165.8, 165.4, 165.3, 165.2, 133.6, 133.6, 133.5, 133.5, 133.4, 133.3, 130.0, 130.0, 130.0, 130.0, 129.9, 129.9, 129.9, 129.9, 129.9, 129.9, 129.9, 129.9, 129.4, 129.3, 129.2, 129.2, 129.2, 129.1, 128.6, 128.6, 128.6, 128.6, 128.6, 128.6, 128.6, 128.6, 128.4, 128.4, 128.4, 128.4, 105.9, 105.9, 105.8, 83.8, 82.1, 82.0, 81.9, 81.8, 81.7, 77.8, 77.4, 77.4, 70.8, 70.8, 70.7, 70.7, 70.4, 70.1, 66.8, 66.2, 66.0, 62.4, 50.8; **HRMS** (ESI-MS): m/z calcd. For $C_{65}H_{65}N_3O_{22}$ [M+Na]$^+$: 1262.3957; Found: 1262.3925.



(2-(2-(2-(2-azidoethoxy)ethoxy)ethoxy)ethyl)2,3-di-*O*-benzoyl-5-*O*-(2,3-di-*O*-benzoyl-5-*O*-(2,3-di-*O*-benzoyl-5-*O*-(2,3-di-*O*-benzoyl-5-*O*-(2,3-di-*O*-benzoyl-5-*O*-benzoyl-α-D-arabinofuranosyl)-α-D-arabinofuranosyl)-α-D-arabinofuranosyl)-α-D-arabinofuranosyl)-α-D-arabinofuranoside (68):

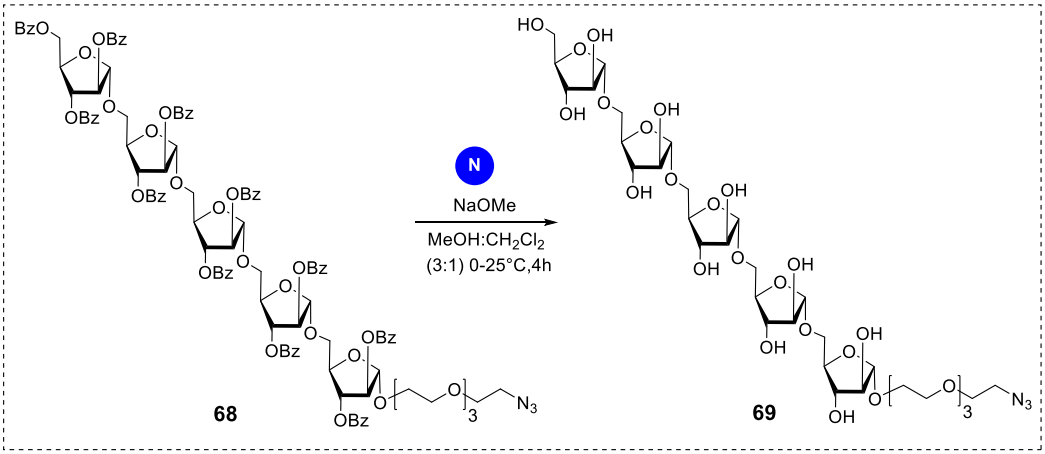
The glycosyl donor **29** and the glycosyl acceptor **67** were glycosylated according to the general reaction **Procedure B** as detailed above to give the **S47**. (Yield 64%, pale yellow syrup): **$[\alpha]_D^{25}$**



= +40.8 (*c* = 0.06, $CHCl_3$); **IR** (cm^{-1}, $CHCl_3$): 3090, 2900, 2870, 2150, 1725, 1600, 1480, 1433, 1239, 1166, 1105, 1068, 1025, 965; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.05 – 7.97 (m, 15H), 7.89 (m,, 8H), 7.58 – 7.54 (m, 2H), 7.49 (q, *J* = 6.5, 5.6 Hz, 5H), 7.45 – 7.34 (m, 18H), 7.27 – 7.26 (m, 1H), 7.25 – 7.21 (m, 6H), 5.63 (d, *J* = 10.5 Hz, 8H), 5.57 (d, *J* = 5.9 Hz, 2H), 5.45 (s, 1H), 5.40 (s, 3H), 5.28 (s, 1H), 4.81 (d, *J* = 11.6 Hz, 1H), 4.71 (d, *J* = 4.2 Hz, 1H), 4.67 – 4.57 (m, 4H), 4.48 – 4.44 (m, 1H), 4.19 (t, *J* = 9.2 Hz, 4H), 3.98 – 3.87 (m, 5H), 3.72 – 3.65 (m, 5H), 3.61 (d, *J* = 5.7 Hz, 8H), 3.36 – 3.33 (m, 2H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ166.3, 165.8, 165.8, 165.7, 165.7, 165.7, 165.4, 165.3, 165.2, 165.2, 165.2, 133.5, 133.5, 133.5, 133.5, 133.5, 133.5, 133.4, 133.3, 133.2, 133.2, 133.1, 130.0, 130.0, 130.0, 130.0, 130.0, 130.0, 129.9, 129.9, 129.9, 129.9, 129.9, 129.9, 129.9, 129.9, 129.9, 129.9, 129.9, 129.9, 129.8, 129.8, 129.8, 129.8, 129.8, 129.4, 129.2, 129.2, 129.2, 129.2, 129.2, 129.2, 129.2, 129.1, 129.1, 129.0, 128.6, 128.6, 128.6, 128.6, 128.6, 128.6, 128.6, 128.5, 128.5, 128.5, 128.4, 128.4, 128.4, 128.4, 128.4, 128.4, 128.4, 128.3, 128.3, 128.3, 106.0, 106.0, 106.0, 105.9, 105.8, 82.2, 82.2, 82.1, 82.0, 82.0, 81.9, 81.7, 81.6, 81.6, 81.3, 77.9, 77.4, 77.4, 77.3, 77.3, 70.8, 70.8, 70.7, 70.7, 70.3, 70.1, 66.7, 66.1, 66.0, 65.9, 65.9, 63.7, 50.7; **HRMS** (ESI-MS): m/z calcd. For $C_{110}H_{103}N_3O_{35}$ $[M+Na]^+$: 2046.6113; Found: 2046.6139.

(2-(2-(2-(2-azidoethoxy)ethoxy)ethoxy)ethyl)5-*O*-(5-*O*-(5-*O*-(5-*O*-(-α-D-arabinofuranosyl)-α-D-arabinofuranosyl)-α-D-arabinofuranosyl)-α-D-arabinofuranosyl)-α-D-arabinofuranoside (69):

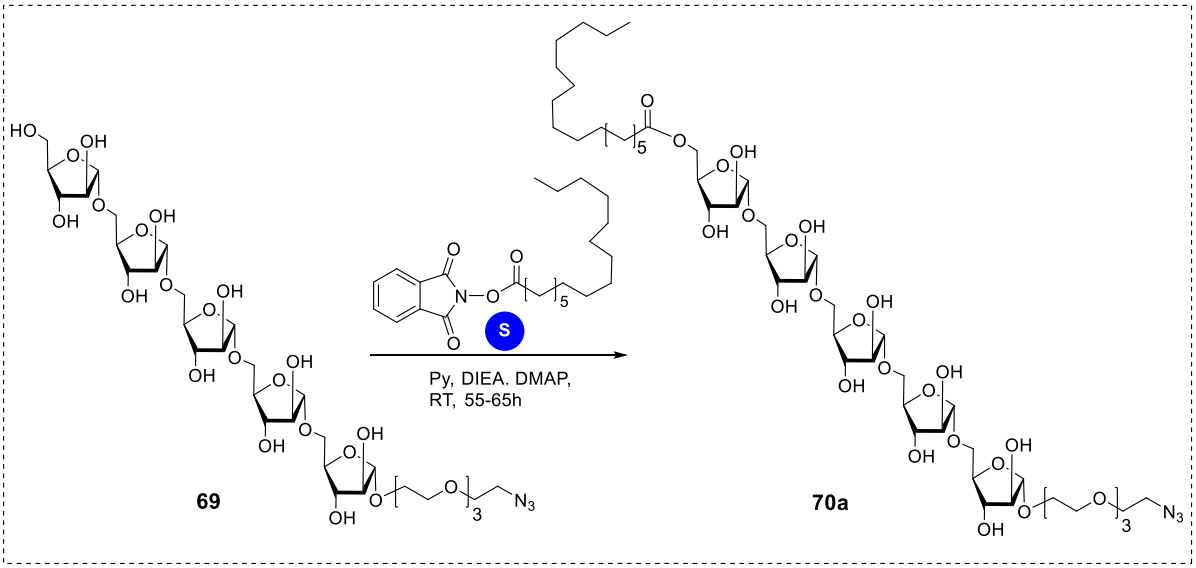
Compound **68** was converted to compound **69** according to the general experimental **Procedure N.** (Yield 75%, pale yellow syrup) **$[\alpha]_D^{25}$** = +81.8 (*c* = 0.06, $CHCl_3$); **IR** (cm^{-1}, $CHCl_3$): 3596, 2924, 2310, 2106, 1740, 1367, 1094, 990, 880; **^{1}H NMR** (400 MHz, CD_3OD) δ 4.98 (s, 4H), 4.95 – 4.94 (m, 1H), 4.13 – 4.00 (m, 10H), 3.95 – 3.84 (m, 10H), 3.78 (d, *J* = 8.6 Hz, 1H), 3.72 – 3.62 (m, 18H), 3.44 – 3.39 (m, 2H); **^{13}C NMR** (101 MHz, CD_3OD) δ 109.6, 109.6, 109.6, 109.6, 109.6,



85.9, 84.1, 84.1, 84.1, 83.8, 83.4, 83.2, 83.2, 83.2, 83.1, 79.2, 79.1, 79.1, 79.1, 78.7, 71.6, 71.6, 71.5, 71.5, 71.5, 71.4, 71.1, 68.2, 68.2, 68.1, 67.9, 63.1, 51.7; **HRMS** (ESI-MS): m/z calcd. For $C_{33}H_{57}N_3O_{24}[M+Na]^+$: 902.3230; Found: 902.3280

(2-(2-(2-(2-azidoethoxy)ethoxy)ethoxy)ethyl-5-*O*-(-5-*O*-(-5-*O*-(-5-*O*-(-5-*O*-(hexadecanoyl)-α-D-arabinofuranosyl)-α-D-arabinofuranosyl)-α-D-arabinofuranosyl)- α-D-arabinofuranosyl)-α-D-arabinofuranoside (70a):

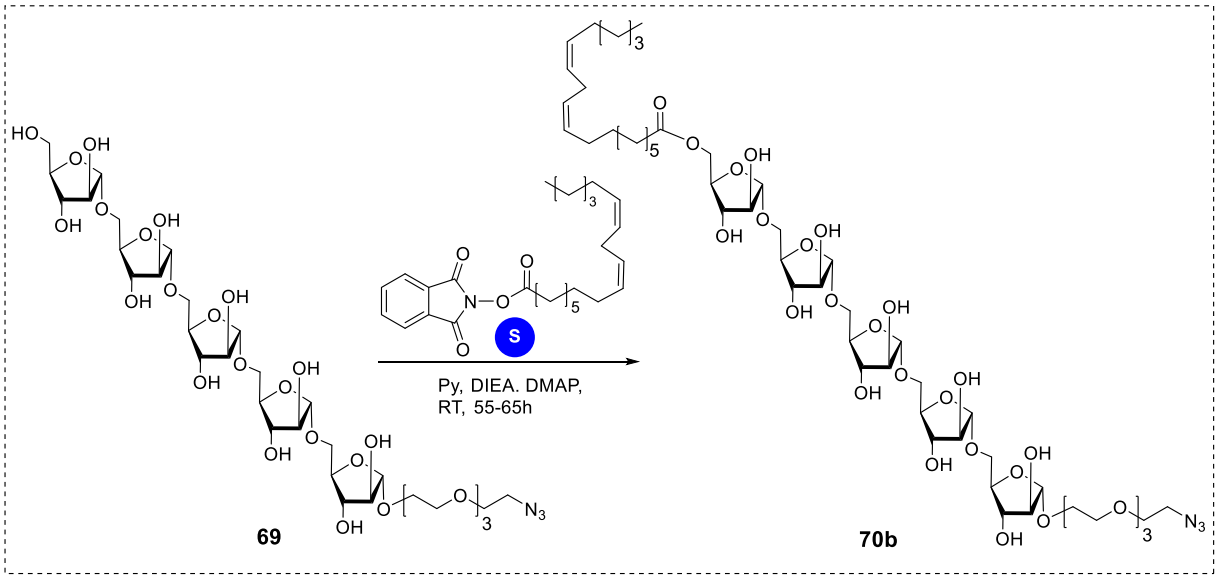
Compound **69** was converted to compound **70a** according to the general experimental **Procedure S.** (Yield 31%, pale yellow syrup):



$[\alpha]_D^{25}$ = +48.8 (*c* = 0.06, $CHCl_3$); **IR** (cm^{-1}, $CHCl_3$): 3540, 2815, 2230, 2170, 1710, 1430, 1330, 1300, 1050, 1020; **^{1}H NMR** (400 MHz, CD_3OD) δ 4.95 (d, *J* = 12.5 Hz, 5H), 4.19 (dd, *J* = 11.7, 6.1 Hz, 1H), 4.14 – 4.07 (m, 4H), 4.05 – 4.00 (m, 5H), 3.91 (dt, *J* = 7.9, 4.8 Hz, 4H), 3.88 – 3.81 (m, 6H), 3.79 – 3.73 (m, 1H), 3.69 (m, 18H), 3.42 – 3.38 (m, 2H), 2.39 (d, *J* = 7.2 Hz, 2H), 1.67 – 1.61 (m, 2H), 1.32 (m, 24H), 0.93 (d, *J* = 6.6 Hz, 3H); **^{13}C NMR** (101 MHz, CD_3OD) δ 177.8, 109.7, 109.7, 109.7, 109.7, 109.6, 84.1, 84.1, 83.8, 83.5, 83.2, 83.2, 83.2, 83.2, 83.1, 82.8, 79.2, 79.2, 79.1, 79.0, 78.8, 71.6, 71.6, 71.5, 71.5, 71.5, 71.4, 71.1, 68.2, 68.2, 67.9, 65.0, 63.1, 51.8, 49.6, 35.1, 33.1, 30.8, 30.8, 30.8, 30.7, 30.7, 30.6, 30.5, 30.4, 30.3, 30.2, 26.1, 23.7, 14.5; **HRMS** (ESI-MS): m/z calcd. For $C_{49}H_{87}N_3O_{25}$ $[M+Na]^+$: 1140.5526; Found: 1140.5570

(2-(2-(2-(2-azidoethoxy)ethoxy)ethoxy)ethyl)5-*O*-(5-*O*-(5-*O*-(5-*O*-(5-*O*-(*9Z,12Z*-octadecadienoyl)-α-D-arabinofuranosyl)-α-D-arabinofuranosyl)-α-D-arabinofuranosyl) -α-D-arabinofuranosyl)-α-D-arabinofuranoside (70b):

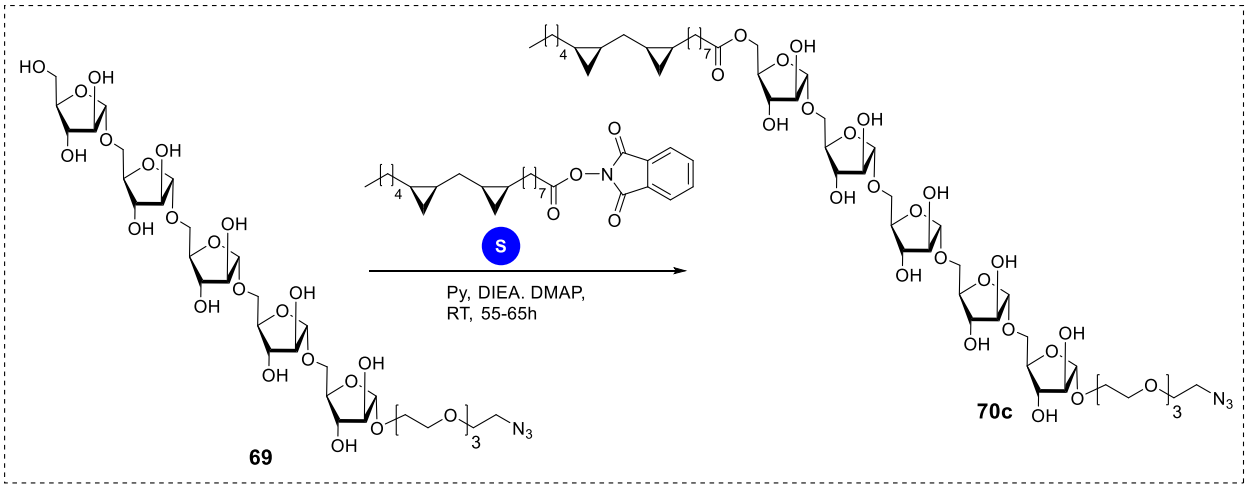
Compound **69** was converted to compound **70b** according to the general experimental **Procedure S.** (Yield 36%, pale yellow syrup)



$[\alpha]_D^{25}$ = +52.2 (*c* = 0.06, $CHCl_3$); **IR** (cm^{-1}, $CHCl_3$): 3480, 2900, 2330, 2170, 1730, 1440, 1330, 1310, 1070, 1010, 950; **^{1}H NMR** (400 MHz, CD_3OD) δ 5.40 – 5.33 (m, 4H), 4.95 (d, *J* = 13.7 Hz, 5H), 4.19 (dd, *J* = 11.7, 6.1 Hz, 1H), 4.10 (dq, *J* = 8.9, 4.8, 3.7 Hz, 4H), 4.05 – 4.00 (m, 5H), 3.91 (dd, *J* = 6.0, 3.0 Hz, 4H), 3.89 – 3.81 (m, 6H), 3.80 – 3.73 (m, 1H), 3.71 – 3.60 (m, 18H), 3.42 – 3.38 (m, 2H), 2.80 (t, *J* = 6.2 Hz, 2H), 2.39 (q, *J* = 7.1 Hz, 2H), 2.11 – 2.06 (m, 4H), 1.67 – 1.62 (m, 2H), 1.36 – 1.31 (m, 14H), 0.93 (t, *J* = 6.8 Hz, 3H); **^{13}C NMR** (101 MHz, CD_3OD) δ 130.9, 130.9, 129.1, 129.1, 109.7, 109.7, 109.7, 109.7, 109.6, 85.9, 84.1, 84.1, 83.8, 83.5, 83.2, 83.2, 83.2, 83.1, 82.8, 79.2, 79.2, 79.1, 79.1, 78.8, 71.6, 71.6, 71.5, 71.5, 71.5, 71.5, 71.4, 71.1, 68.2, 68.2, 67.9, 65.0, 51.8, 34.9, 32.7, 30.7, 30.5, 30.3, 30.2, 30.2, 28.2, 26.5, 26.0, 25.9, 23.6, 14.5; **HRMS** (ESI-MS): m/z calcd. For $C_{51}H_{87}N_3O_{25}$ $[M+Na]^+$: 1164.5526 Found: 1164.5513

(2-(2-(2-(2-azidoethoxy)ethoxy)ethoxy)ethyl)-5-*O*-(5-*O*-(5-*O*-(5-*O*-(5-*O*-(8-(2-((2-pentylcyclopropyl)methyl)cyclopropyl)octanoyl)-α-D-arabinofuranosyl)-α-D-arabinofuranosyl)-α-D-arabinofuranosyl)-α-D-arabinofuranosyl)-α-D-arabinofuranoside (70c):

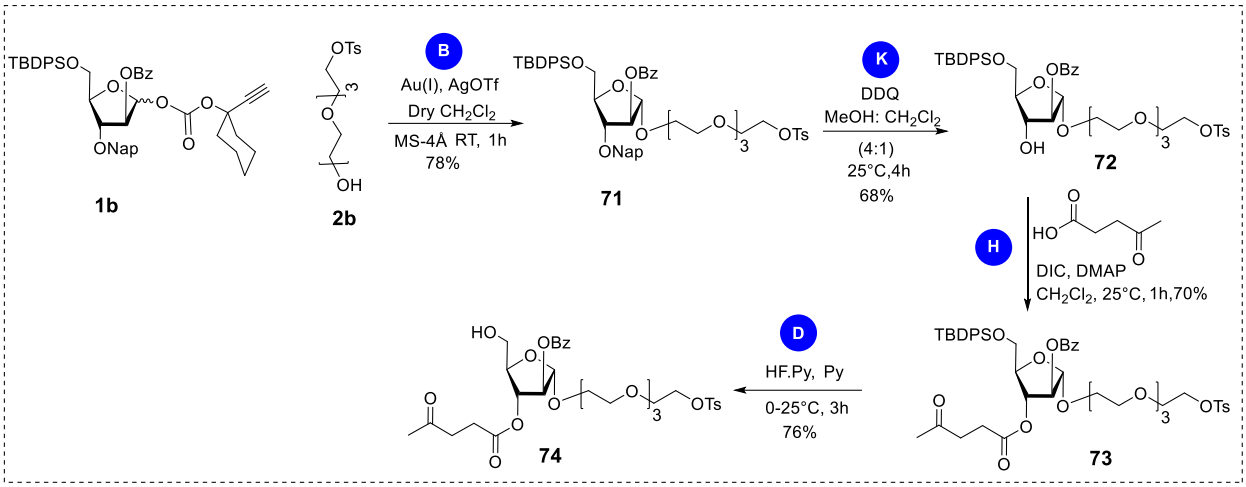
Compound **69** was converted to compound **70c** according to the general experimental **Procedure S.** (Yield 40%, pale yellow syrup: $[\alpha]_D^{25}$ = +52.5 (*c* = 1.0, $CHCl_3$); **IR** (cm^{-1}, $CHCl_3$):



3450, 2670, 2280, 2140, 1770, 1420, 1380, 1200, 1020, 1000; **^{1}H NMR** (400 MHz, CD_3OD) δ 4.95 (d, *J* = 12.8 Hz, 5H), 4.19 (dd, *J* = 11.7, 6.1 Hz, 1H), 4.12 – 4.06 (m, 4H), 4.04 – 3.99 (m, 5H), 3.94 – 3.89 (m, 4H), 3.88 – 3.81 (m, 6H), 3.79 – 3.72 (m, 1H), 3.68 (m, 18H), 3.42 – 3.38 (m, 2H), 2.39 (q, *J* = 7.2 Hz, 2H), 1.67 – 1.61(m, 2H), 1.52 (t, *J* = 6.8 Hz, 1H), 1.44 – 1.42 (m, 3H), 1.38 – 1.30 (m, 13H), 1.22 (dd, *J* = 15.0, 6.4 Hz, 2H), 1.07 (dt, *J* = 14.3, 7.9 Hz, 1H), 0.95 – 0.91 (m, 3H), 0.82 (ddd, *J* = 14.1, 8.2, 6.0 Hz, 2H), 0.77 – 0.69 (m, 2H), 0.65 (dt, *J* = 8.3, 4.2 Hz, 2H), -0.21 – -0.28 (m, 2H);

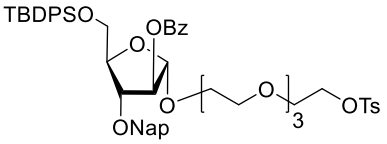
^{13}C NMR (101 MHz, CD_3OD) δ 175.3, 109.7, 109.7, 109.7, 109.7, 109.6, 85.9, 84.1, 84.1, 84.1, 83.9, 83.4, 83.2, 83.2, 83.2, 82.8, 79.2, 79.2, 79.1, 79.1, 78.8, 71.6, 71.6, 71.5, 71.5, 71.4, 71.1, 68.3, 68.3, 68.3, 67.9, 65.0, 63.1, 51.8, 34.9, 33.0, 31.3, 31.0, 30.2, 30.1, 29.9, 29.2, 29.1, 26.0, 26.0, 23.8, 17.1, 17.0, 16.7, 16.7, 14.5, 11.7, 11.6; **HRMS** (ESI-MS): m/z calcd. For $C_{53}H_{91}N_3O_{25}$ $[M+Na]^+$: 1192.5839; Found: 1192.5844.

Synthesis of compound 74:



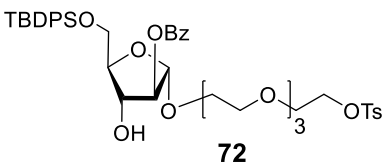
(2-(2-(2-(2-tosylethoxy)ethoxy)ethoxy)ethyl)-2-*O*-benzoyl-3-*O*-naphthylmethyl-5-*O*-*tert*butyldiphenylsilyl-α-D-arabinofuranoside(71):

The glycosyl donor **1b** and the glycosyl acceptor **2b**[47] were glycosylated according to the general reaction **Procedure B** as detailed above to give the **71**. (Yield 78%, pale yellow syrup): **[α]$_D^{25}$** = +19.8 (*c* = 0.06, $CHCl_3$); **IR** (cm^{-1}, $CHCl_3$): 2980, 2340, 2130, 1750, 1394, 1240, 1180, 980, 879; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.98 (d, *J* = 8.2 Hz, 2H), 7.78 (dd, *J* = 17.1, 8.5 Hz, 5H), 7.71 – 7.56 (m, 6H), 7.46 – 7.38 (m, 7H), 7.32 (dt, *J* = 7.1, 3.1 Hz, 6H), 5.51 (s, 1H), 5.26 (s, 1H), 4.97 (d, *J* = 12.1 Hz, 1H), 4.77 (d, *J* = 12.1 Hz, 1H), 4.33 (d, *J* = 3.9 Hz, 1H), 4.23 (d, *J* = 5.4 Hz, 1H), 4.17 – 4.13 (m, 2H), 3.89 (dt, *J* = 13.8, 4.3 Hz, 3H), 3.74 (d, *J* = 6.2 Hz, 3H), 3.66 (dt, *J* = 13.4, 4.5 Hz, 4H), 3.60 – 3.57 (m, 2H), 3.54 (s, 4H), 2.42 (s, 3H), 0.97 (s, 9H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 165.5, 144.8, 135.7, 135.6, 135.1, 133.4, 133.3, 133.3, 133.2, 133.1, 129.8, 129.8, 129.8, 129.8, 129.8, 129.7, 129.7, 129.5, 128.5, 128.5, 128.3, 128.0, 128.0, 128.0, 127.9, 127.7, 127.7, 127.7, 127.7, 127.7, 127.7, 127.0, 126.1, 125.9, 125.9, 106.4, 83.5, 83.0, 82.3, 72.4, 70.7, 70.7, 70.7, 70.5, 70.3, 69.3, 68.6, 66.7, 63.2, 26.7, 26.7, 26.7, 21.7, 19.3; **HRMS** (ESI-MS): m/z calcd. For $C_{54}H_{62}O_{11}SSi$ $[M+Na]^+$: 969.3680; Found: 969.3622.



(2-(2-(2-(2-tosylethoxy)ethoxy)ethoxy)ethyl)-2-*O*-benzoyl-3-*O*-naphthylmethyl-α-D-arabinofuranoside(72):

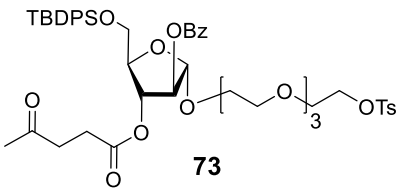
Compound **71** was converted to compound **72** according to the general experimental **Procedure K** (Yield 68%, pale yellow syrup): **$[\alpha]_D^{25}$** = +22.8 (*c* = 0.06, $CHCl_3$); **IR** (cm^{-1}, $CHCl_3$): 3450, 3200, 2990, 2300, 2230, 1710, 1290, 1240, 1120, 980, 870; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.92 (dd, *J* = 8.3, 1.2 Hz, 2H), 7.79 (d, *J* = 8.3 Hz, 2H), 7.69 – 7.66 (m, 4H), 7.57 (dt, *J* = 14.9, 1.2 Hz, 1H), 7.41 – 7.35 (m, 5H), 7.34 – 7.30 (m, 5H), 5.25 (s, 1H), 5.17 – 5.15 (m, 1H), 4.25 (dd, *J* = 9.3, 4.4 Hz, 2H), 4.16 – 4.13 (m, 2H), 3.95 – 3.86 (m, 3H), 3.70 – 3.62 (m, 9H), 3.58 (s, 4H), 2.43 (s, 3H), 1.03 (s, 9H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 166.4, 144.9, 135.7, 135.7, 133.5, 133.4, 133.1, 129.9, 129.9, 129.9, 129.9, 129.8, 129.8, 129.3, 128.6, 128.6, 128.1, 128.1, 127.8, 127.8, 127.8, 127.8, 127.8, 127.8, 127.8, 105.3, 85.4, 85.0, 76.8, 70.8, 70.7, 70.6, 70.6, 70.3, 69.4, 68.8, 66.1, 63.7, 26.9, 26.9, 26.9, 21.7, 19.4; **HRMS** (ESI-MS): m/z calcd. For $C_{43}H_{54}O_{11}SSi$ $[M+Na]^+$: 829.3054; Found: 829.3010.



72

(2-(2-(2-(2-tosylethoxy)ethoxy)ethoxy)ethyl)-2-*O*-benzoyl-3-*O*-(4-oxopentanoyl)-5-*O*-*tert*butyldiphenylsilyl-α-D-arabinofuranoside(73):

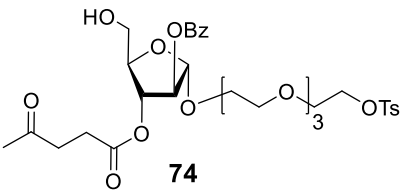
Compound **72** was converted to compound **73** according to the general experimental **Procedure H** (Yield 70%, pale yellow syrup): **$[\alpha]_D^{25}$** = +24.8 (*c* = 0.06, $CHCl_3$); **IR** (cm^{-1}, $CHCl_3$): 3005, 2990, 2350, 2230, 1870, 1770, 1280, 1270, 1130, 980, 870; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.95 (dd, *J* = 8.3, 1.2 Hz, 2H), 7.79 (d, *J* = 8.3 Hz, 2H), 7.70 (ddd, *J* = 7.9, 3.0, 1.5 Hz, 4H), 7.56 – 7.52 (m, 1H), 7.40 – 7.32 (m, 10H), 5.39 (dd, *J* = 5.4, 1.3 Hz, 1H), 5.32 (d, *J* = 1.5 Hz, 1H), 5.20 (s, 1H), 4.22 (q, *J* = 4.3 Hz, 1H), 4.15 – 4.13 (m, 2H), 3.91 (d, *J* = 4.2 Hz, 2H), 3.87 – 3.82 (m, 1H), 3.71 – 3.65 (m, 7H), 3.61 (dd, *J* = 5.8, 3.1 Hz, 2H), 3.56 (s, 4H), 2.81 – 2.69 (m, 2H), 2.63 – 2.59 (m, 2H), 2.43 (s, 3H), 2.18 (s, 3H), 1.04 (s, 9H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 206.4, 172.0, 165.5, 144.9, 135.8, 135.8, 133.4, 133.4, 133.4, 133.1, 130.0, 130.0, 129.9, 129.9, 129.8, 129.8, 129.3, 128.5, 128.5, 128.1, 128.1, 127.8, 127.8, 127.8, 127.8, 127.8, 127.8, 106.0, 82.8, 82.6, 77.2, 70.9, 70.8, 70.8, 70.6, 70.4, 69.4, 68.8, 66.8, 63.3, 38.0, 30.0, 28.0, 26.9, 26.9, 26.9, 21.8, 19.4; **HRMS** (ESI-MS): m/z calcd. For $C_{48}H_{60}O_{13}SSi$ $[M+Na]^+$: 927.3422; Found: 927.3460



73

(2-(2-(2-(2-tosylethoxy)ethoxy)ethoxy)ethyl)-2-*O*-benzoyl-3-*O*-(4-oxopentanoyl)-α-D-arabinofuranoside(74):

Compound **73** was converted to compound **74** according to the general experimental **Procedure D.** (Yield 76%, pale yellow syrup): **$[\alpha]_D^{25}$** = +22.8 (*c* = 0.06, $CHCl_3$); **IR** (cm^{-1}, $CHCl_3$):

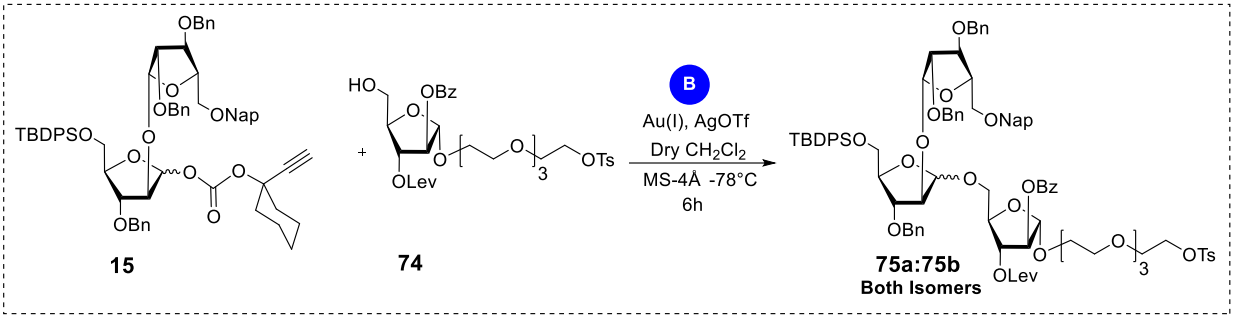


74

3520, 3300, 2970, 2320, 2230, 1870, 1780, 1250, 1210, 1160, 990, 870; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.01 (d, *J* = 8.3 Hz, 2H), 7.79 (d, *J* = 7.8 Hz, 2H), 7.61 – 7.55 (m, 1H), 7.44 (t, *J* = 7.6 Hz, 2H), 7.34 (d, *J* = 8.0 Hz, 2H), 5.37 (s, 1H), 5.23 (s, 1H), 5.19 (d, *J* = 5.2 Hz, 1H), 4.22 (q, *J* = 4.1 Hz, 1H), 4.17 – 4.13 (m, 2H), 3.95 – 3.80 (m, 3H), 3.75 – 3.65 (m, 7H), 3.64 – 3.60 (m, 2H), 3.58 (s, 4H), 2.78 (tt, *J* = 12.6, 6.6 Hz, 2H), 2.70 – 2.55 (m, 2H), 2.44 (s, 3H), 2.18 (s, 3H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 206.5, 172.5, 165.4, 144.9, 133.6, 133.0, 129.9, 129.9, 129.9, 129.9, 129.2, 128.6, 128.6, 128.0, 128.0, 105.7, 83.1, 82.0, 77.5, 70.8, 70.7, 70.7, 70.6, 70.3, 69.3, 68.7, 66.8, 62.2, 37.9, 29.9, 27.9, 21.7; **HRMS** (ESI-MS): m/z calcd. For $C_{32}H_{42}O_{13}Si$ $[M+Na]^+$: 689.2244; Found: 689.2260

(2-(2-(2-(2-tosylethoxy)ethoxy)ethoxy)ethyl)-2-*O*-benzoyl-3-*O*-(4-oxopentanoyl)-5-*O*-(2-*O*-(2,3-*O*-dibenzyl-5-*O*-(naphthylmethyl)-β-D-arabinofuranosyl)-3-*O*-benzyl-5-*O* *tert*butyldiphenylsilyl-α-D-arabinofuranosyl)-α-D-arabinofuranoside(75a:75b) Both Isomers:

The glycosyl donor **15** and the glycosyl acceptor 7**4** were glycosylated according to the general reaction **Procedure B** as detailed above to give the **75a:75b (both isomers, 1.5:1)**. (Yield 61% for both isomers, pale yellow syrup):

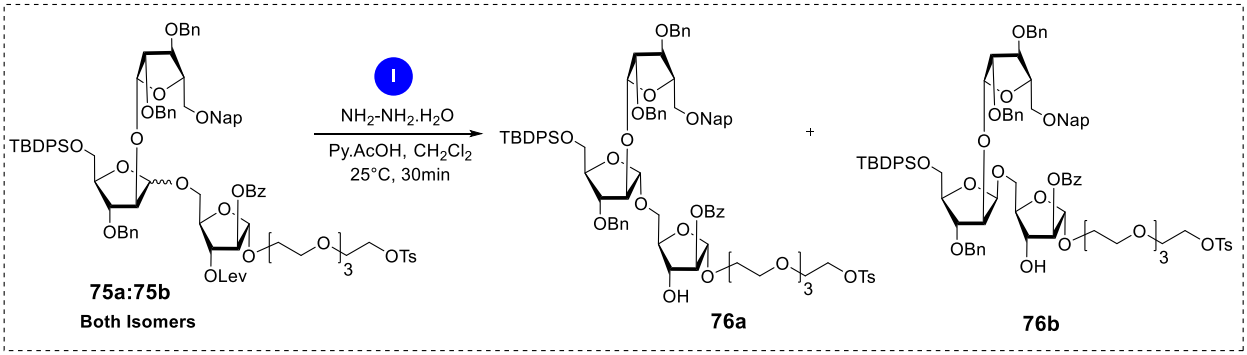


$[\alpha]_D^{25}$ = +14.5 (*c* = 0.06, $CHCl_3$); **IR** (cm^{-1}, $CHCl_3$): 3030, 2300, 2240, 1880, 1760, 1710, 1630, 1515, 1430, 1200, 1010**; ^{1}H NMR** (400 MHz, CDCl3) δ 8.01 – 7.98 (m, 3H), 7.80 – 7.76 (m, 5H), 7.72 (dd, *J* = 8.6, 4.3 Hz, 2H), 7.70 – 7.64 (m, 5H), 7.64 – 7.59 (m, 4H), 7.45 – 7.42 (m, 4H), 7.41 – 7.37 (m, 3H), 7.37 – 7.29 (m, 21H), 7.29 – 7.25 (m, 4H), 7.25 – 7.21 (m, 12H), 7.19 – 7.14 (m, 5H), 5.34 – 5.32 (m, 1H), 5.29 (s, 1H), 5.24 (d, *J* = 4.2 Hz, 1H), 5.21 (d, *J* = 1.5 Hz, 1H), 5.16 (s, 1H), 5.12 (d, *J* = 4.4 Hz, 1H), 5.05 – 5.01 (m, 2H), 4.83 (d, *J* = 11.4 Hz, 1H), 4.65 (dd, *J* = 11.8, 8.2 Hz, 1H), 4.58 (d, *J* = 5.4 Hz, 2H), 4.57 – 4.55 (m, 2H), 4.53 (s, 1H), 4.51 (d, *J* = 3.8 Hz, 1H), 4.49 (d, *J* = 5.4 Hz, 2H), 4.47 (s, 1H), 4.43 (d, *J* = 3.1 Hz, 1H), 4.40 (d, *J* = 3.6

Hz, 1H), 4.38 (dd, *J* = 3.1, 1.3 Hz, 1H), 4.25 (ddd, *J* = 16.5, 8.9, 5.3 Hz, 3H), 4.16 – 4.12 (m, 5H), 4.09 (dd, *J* = 5.2, 3.5 Hz, 3H), 4.02 (ddd, *J* = 11.4, 7.9, 5.4 Hz, 3H), 3.96 (dd, *J* = 11.4, 2.3 Hz, 1H), 3.85 – 3.70 (m, 6H), 3.68 – 3.62 (m, 10H), 3.62 – 3.58 (m, 4H), 3.58 – 3.50 (m, 14H), 2.71 – 2.66 (m, 2H), 2.60 (dt, *J* = 17.2, 6.6 Hz, 4H), 2.51 – 2.46 (m, 1H), 2.41 (s, 5H), 2.10 (s, 2H), 2.09 (s, 2H), 1.03 (s, 9H), 1.00 (s, 6H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 206.4, 206.1, 172.0, 171.9, 165.5, 165.4, 144.9, 144.9, 138.4, 138.2, 138.2, 138.2, 138.2, 137.8, 135.8, 135.7, 135.6, 135.6, 133.6, 133.5, 133.5, 133.4, 133.3, 133.3, 133.1, 133.0, 130.1, 129.9, 129.9, 129.9, 129.9, 129.9, 129.8, 129.7, 129.7, 129.3, 129.1, 128.6, 128.5, 128.5, 128.5, 128.5, 128.5, 128.5, 128.4, 128.4, 128.4, 128.4, 128.4, 128.4, 128.4, 128.4, 128.4, 128.3, 128.3, 128.3, 128.3, 128.3, 128.3, 128.3, 128.2, 128.2, 128.1, 128.1, 128.1, 128.1, 128.1, 128.1, 128.1, 128.0, 128.0, 128.0, 127.9, 127.9, 127.8, 127.8, 127.8, 127.8, 127.8, 127.8, 127.8, 127.8, 127.8, 127.8, 127.8, 127.8, 127.7, 127.7, 127.7, 127.7, 127.7, 127.7, 127.6, 127.6, 127.6, 127.5, 127.5, 126.4, 126.3, 126.3, 126.1, 126.1, 126.1, 125.9, 125.9, 125.8, 125.8, 125.7, 125.7, 106.4, 105.8, 105.7, 100.4, 100.3, 98.5, 86.0, 84.4, 84.0, 83.7, 83.3, 83.2, 83.0, 82.7, 82.4, 82.3, 81.9, 81.7, 81.4, 81.0, 80.1, 79.0, 77.6, 77.3, 73.2, 73.2, 72.7, 72.5, 72.5, 72.4, 72.4, 72.2, 72.2, 71.8, 70.8, 70.8, 70.7, 70.7, 70.7, 70.7, 70.6, 70.6, 70.3, 70.2, 69.4, 69.3, 68.7, 68.7, 67.3, 66.8, 66.8, 66.3, 65.8, 64.0, 37.9, 37.8, 29.8, 29.8, 27.9, 27.8, 27.0, 27.0, 27.0, 27.0, 26.9, 26.9, 21.7, 21.7, 19.4, 19.3; **HRMS** (ESI-MS): m/z calcd. For $C_{90}H_{89}O_{21}SSi$ $[M+Na]^+$: 1565.5386; Found: 1565.5370

(2-(2-(2-(2-tosylethoxy)ethoxy)ethoxy)ethyl)-2-*O*-benzoyl-5-*O*-(2-*O*-(2,3-*O*-dibenzyl-5-*O*(naphthylmethyl)-β-D-arabinofuranosyl)-3-*O*-benzyl-5-*O* ^{tert}butyldiphenylsilyl-α-D-arabinofuranosyl)-α-D-arabinofuranoside (76a):

Compound (**75a:75b)** was converted to compounds **76a** and **76b (76a:76b, 1.5:1)** according to the general experimental **Procedure I,** and at this step both the isomers separated. (Yield 56%

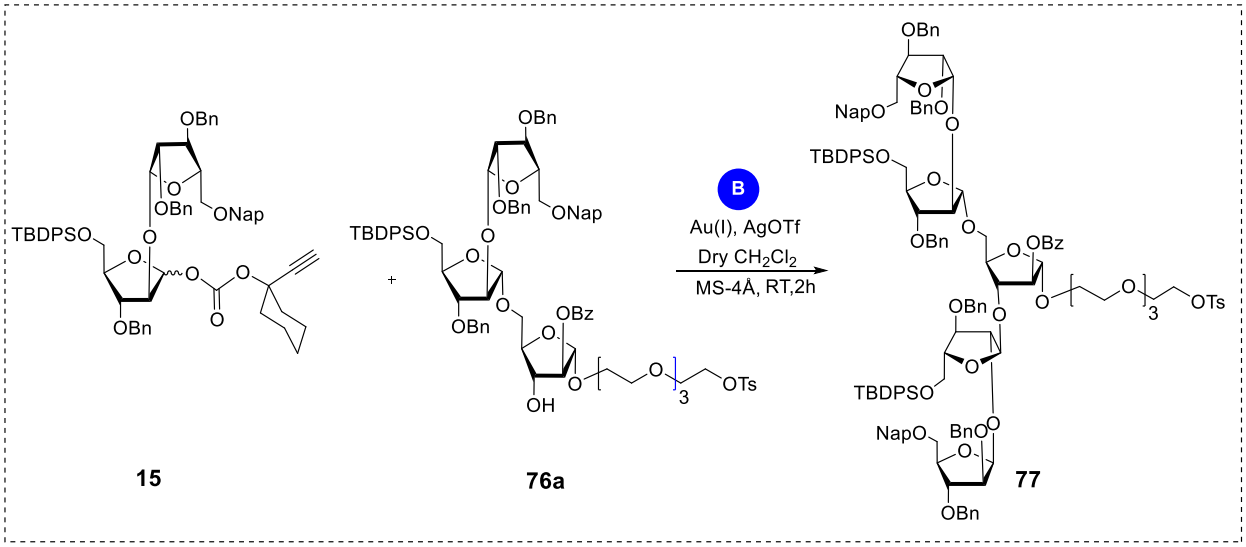


for **41a**, pale yellow syrup: **$[\alpha]_D^{25}$** = +4.54 (*c* = 0.06, $CHCl_3$); **IR** (cm^{-1}, $CHCl_3$): 3750, 3522, 3030,

2300, 1710, 1433, 1515, 1100, 1010**; ^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.02 – 7.97 (m, 2H), 7.77 (dd, *J* = 8.9, 4.2 Hz, 3H), 7.73 – 7.59 (m, 7H), 7.51 – 7.46 (m, 1H), 7.45 – 7.41 (m, 2H), 7.40 – 7.33 (m, 6H), 7.32 – 7.26 (m, 10H), 7.23 – 7.21 (m, 5H), 7.16 (qd, *J* = 5.3, 4.6, 2.0 Hz, 5H), 5.23 (s, 1H), 5.15 (d, *J* = 2.5 Hz, 1H), 5.09 (d, *J* = 4.3 Hz, 1H), 5.06 – 5.03 (m, 1H), 4.65 (d, *J* = 11.9 Hz, 1H), 4.59 (d, *J* = 5.0 Hz, 1H), 4.57 – 4.51 (m, 3H), 4.51 – 4.46 (m, 2H), 4.44 – 4.39 (m, 1H), 4.36 (dd, *J* = 3.0, 1.4 Hz, 1H), 4.26 (q, *J* = 4.6 Hz, 1H), 4.21– 4.16 (m, 2H), 4.15 – 4.12 (m, 2H), 4.11 – 4.03 (m, 4H), 3.96 – 3.87 (m, 2H), 3.82 – 3.74 (m, 2H), 3.70 (dd, *J* = 11.3, 4.5 Hz, 1H), 3.62 (m, 9H), 3.54 (d, *J* = 4.4 Hz, 6H), 2.40 (s, 3H), 1.02 (s, 9H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 166.6, 144.8, 138.2, 138.0, 137.8, 135.7, 135.7, 135.6, 133.5, 133.5, 133.5, 133.3, 133.1, 133.0, 129.9, 129.9, 129.9, 129.9, 129.8, 129.3, 128.6, 128.6, 128.5, 128.5, 128.4, 128.4, 128.3, 128.3, 128.2, 128.1, 128.1, 128.0, 128.0, 128.0, 127.9, 127.8, 127.8, 127.8, 127.8, 127.8, 127.8, 127.7, 127.7, 127.7, 127.7, 127.6, 127.6, 127.6, 127.6, 126.3, 126.1, 125.9, 125.7, 106.2, 105.4, 100.2, 85.6, 85.4, 84.0, 83.6, 83.2, 83.0, 82.8, 80.1, 77.4, 73.2, 72.5, 72.4, 72.4, 72.2, 70.8, 70.7, 70.7, 70.5, 70.2, 69.3, 68.7, 66.5, 66.5, 64.1, 27.0, 27.0, 27.0, 21.7, 19.4; **HRMS** (ESI-MS): m/z calcd. For $C_{85}H_{96}O_{19}SSi$ $[M+Na]^+$: 1503.5933; Found: 1503.5950.

(2-(2-(2-(2-tosylethoxy)ethoxy)ethoxy)ethyl)2-*O*-benzoyl-3,5-di-*O*-(2-*O*-(2,3-di-*O*-benzyl-5-*O*-(naphthalen-1-ylmethyl)-β-D-arabinofuranosyl)-3-*O*-benzyl-5-*O*-^{tert}butyldiphenylsilyl-α-D-arabinofuranosyl)-α-D-arabinofuranoside (77):

The glycosyl donor **15** and the glycosyl acceptor **76a** were glycosylated according to the general reaction **Procedure B** as detailed above to give the **77.** (Yield 60%, pale yellow syrup): **$[\alpha]_D^{25}$** =

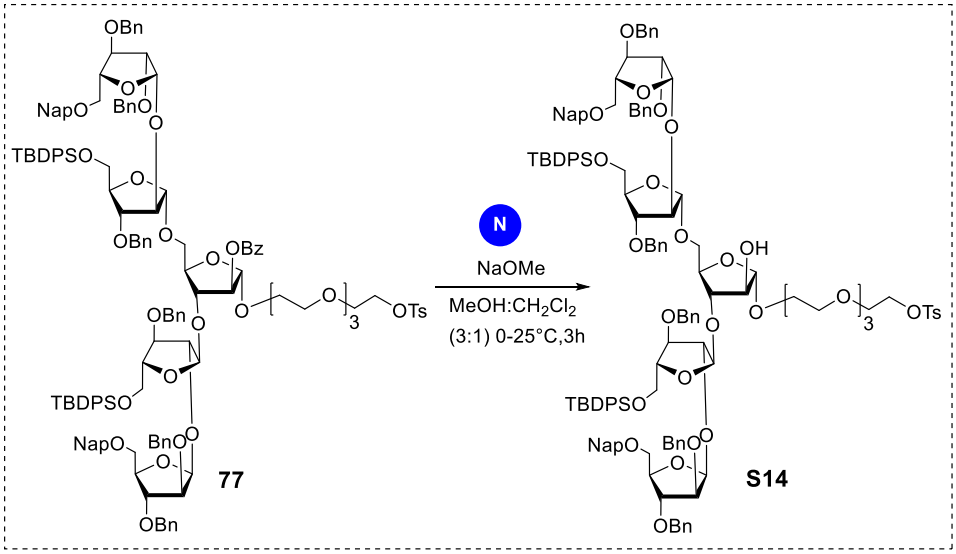


-22.8 (*c* = 0.06, $CHCl_3$); **IR** (cm^{-1}, $CHCl_3$): 3032, 2929, 1601, 1452**,** 1433, 1515, 1228, 1100,1010**,** 695**; ^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.95 – 7.94 (m, 1H), 7.78 – 7.75 (m, 3H), 7.73 –

7.66 (m, 3H), 7.63 (dd, *J* = 11.2, 7.0 Hz, 4H), 7.59 (d, *J* = 7.6 Hz, 6H), 7.43 – 7.37 (m, 4H), 7.36 – 7.25 (m, 18H), 7.25 – 7.09 (m, 34H), 5.37 – 5.34 (m, 1H), 5.33 (d, *J* = 10.7 Hz, 2H), 5.20 (s, 1H), 5.17 (d, *J* = 4.3 Hz, 1H), 5.06 (s, 1H), 4.69 (d, *J* = 11.8 Hz, 2H), 4.64 (d, *J* = 11.9 Hz, 1H), 4.61 – 4.57 (m, 3H), 4.55 – 4.52 (m, 3H), 4.48 (dd, *J* = 12.5, 7.8 Hz, 3H), 4.45 – 4.42 (m, 3H), 4.41 – 4.38 (m, 3H), 4.24 (s, 1H), 4.16 – 4.13 (m, 3H), 4.09 (dt, *J* = 9.0, 4.2 Hz, 7H), 4.01 – 3.95 (m, 2H), 3.75 (tdt, *J* = 22.8, 11.2, 5.7 Hz, 7H), 3.60 – 3.53 (m, 14H), 3.48 (s, 4H), 2.39 (s, 3H), 1.00 (s, 9H), 0.94 (s, 9H); **^{13}C NMR** (151 MHz, $CDCl_3$) δ^{13}C NMR (151 MHz, $CDCl_3$) δ 165.7, 144.8, 138.3, 138.3, 138.3, 138.2, 138.0, 137.8, 135.8, 135.7, 135.7, 135.7, 133.6, 133.5, 133.5, 133.4, 133.4, 133.3, 133.3, 133.1, 133.0, 133.0, 129.9, 129.9, 129.9, 129.9, 129.9, 129.9, 129.9, 129.7, 129.7, 129.7, 129.7, 129.7, 129.7, 129.5, 128.6, 128.5, 128.5, 128.5, 128.5, 128.5, 128.4, 128.4, 128.4, 128.4, 128.4, 128.4, 128.4, 128.4, 128.4, 128.3, 128.2, 128.2, 128.2, 128.2, 128.2, 128.2, 128.1, 128.1, 128.0, 128.0, 128.0, 128.0, 127.9, 127.8, 127.8, 127.8, 127.8, 127.8, 127.8, 127.8, 127.8, 127.8, 127.8, 127.8, 127.8, 127.8, 127.8, 127.7, 127.7, 127.6, 127.6, 127.5, 127.5, 127.5, 126.3, 126.3, 126.1, 126.1, 125.9, 125.9, 125.7, 125.7, 106.9, 106.2, 105.6, 100.2, 99.8, 85.7, 85.0, 84.1, 84.0, 83.7, 83.7, 83.6, 83.5, 83.1, 82.7, 82.3, 82.1, 81.6, 80.2, 80.1, 73.3, 73.2, 72.6, 72.6, 72.4, 72.4, 72.4, 72.3, 72.3, 72.1, 70.8, 70.7, 70.7, 70.5, 70.3, 69.3, 68.7, 66.6, 66.3, 63.9, 63.8, 27.0, 27.0, 27.0, 26.9, 26.9, 26.9, 21.7, 19.4, 19.3.

(2-(2-(2-(2-tosylethoxy)ethoxy)ethyl)-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*-^{tert}butyldiphenylsilyl-α-D-arabinofuranosyl)-α-D-arabinofuranoside (S14):

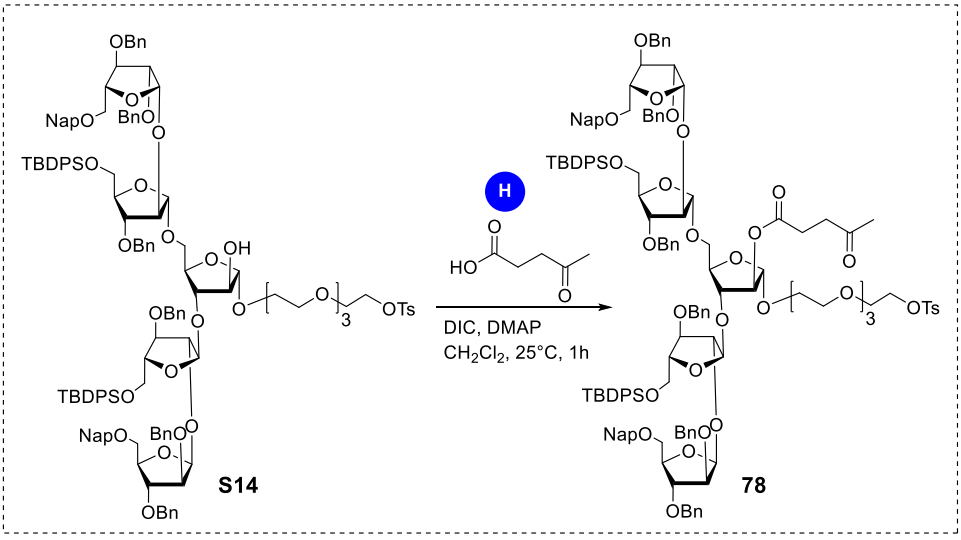
Compound **77** was converted to compound **S14** according to the general experimental **Procedure N.** (Yield 80 %, pale yellow syrup): **$[\alpha]_D^{25}$** = - 14.4 (*c* = 0.06, $CHCl_3$); **IR** (cm^{-1}, $CHCl_3$): 3580, 3060, 2969, 1500, 1462**,** 1403, 1330, 1208, 1100,1010**,** 680; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.77 (d, *J* = 7.9 Hz, 4H), 7.70 (ddd, *J* = 9.5, 7.5, 2.9 Hz, 4H), 7.65 – 7.59 (m, 10H), 7.41 (dd, *J* = 6.2, 3.2 Hz,



4H), 7.33 – 7.25 (m, 26H), 7.23 – 7.19 (m, 20H), 5.09 (dd, *J* = 7.5, 3.7 Hz, 3H), 5.00 (s, 1H), 4.95 (s, 1H), 4.69 – 4.62 (m, 3H), 4.60 (d, *J* = 5.4 Hz, 3H), 4.56 (dd, *J* = 10.4, 5.4 Hz, 4H), 4.49 (dt, *J* = 13.0, 6.7 Hz, 6H), 4.42 (d, *J* = 11.3 Hz, 2H), 4.37 (d, *J* = 8.2 Hz, 2H), 4.21 (dd, *J* = 10.0, 4.5 Hz, 2H), 4.09 (m, *J* = 12.0, 6.8, 6.1 Hz, 15H), 3.76 (s, 4H), 3.56 (m, *J* = 18.3, 10.0, 6.1 Hz, 13H), 3.48 (s, 3H), 2.37 (s, 3H), 1.01 (s, 9H), 1.00 (s, 9H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 144.8, 138.2, 138.2, 138.2, 138.0, 137.8, 137.7, 135.7, 135.7, 135.6, 135.6, 133.5, 133.4, 133.4, 133.3, 133.3, 133.3, 133.3, 133.1, 133.0, 133.0, 129.9, 129.9, 129.9, 129.9, 129.9, 129.9, 129.8, 129.8, 129.7, 129.7, 129.7, 129.7, 128.6, 128.6, 128.6, 128.5, 128.5, 128.5, 128.4, 128.4, 128.4, 128.4, 128.3, 128.3, 128.3, 128.3, 128.3, 128.3, 128.2, 128.2, 128.1, 128.1, 128.0, 128.0, 128.0, 128.0, 128.0, 128.0, 128.0, 127.9, 127.9, 127.9, 127.8, 127.8, 127.8, 127.8, 127.8, 127.8, 127.7, 127.7, 127.7, 127.7, 127.7, 127.7, 127.6, 127.6, 127.6, 127.6, 127.6, 126.3, 126.3, 126.1, 125.9, 125.7, 125.7, 108.9, 106.4, 106.1, 100.2, 99.6, 85.8, 84.6, 84.1, 84.0, 83.9, 83.6, 83.5, 83.4, 83.2, 83.1, 82.9, 82.5, 80.2, 80.0, 79.8, 73.2, 73.2, 72.7, 72.5, 72.4, 72.4, 72.3, 72.3, 72.1, 72.1, 70.7, 70.6, 70.6, 70.5, 70.3, 69.3, 68.7, 67.0, 66.6, 64.0, 63.7, 27.0, 27.0, 27.0, 26.9, 26.9, 26.9, 21.7, 19.4, 19.3.

(2-(2-(2-(2-tosylethoxy)ethoxy)ethoxy)ethyl)2-*O*-(4-oxopentanoyl)-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*-*tert*butyldiphenylsilyl-α-D-arabinofuranosyl)-α-D-arabinofuranoside (78):

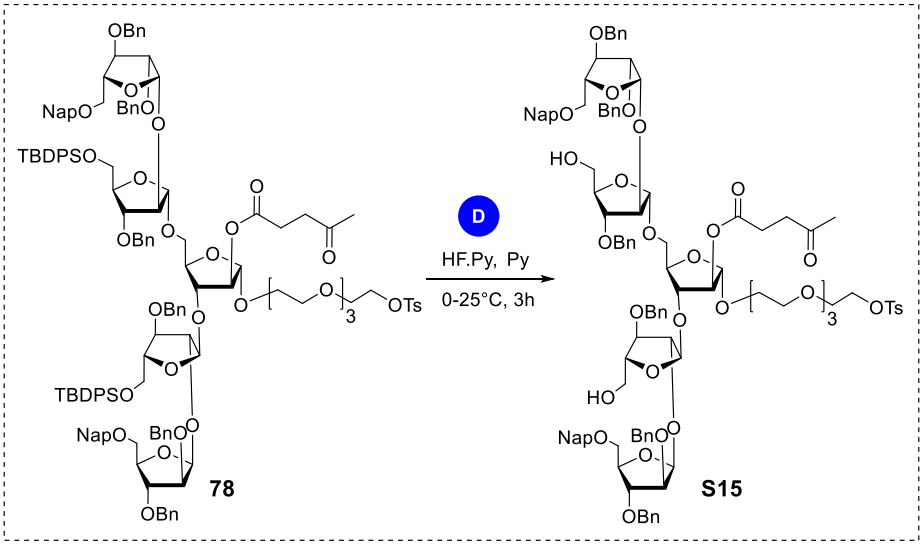
Compound **S14** was converted to compound **78** according to the general experimental **Procedure H**. (Yield 70%, pale yellow syrup)**: [α]$_D^{25}$** = - 24.8 (*c* = 0.06, $CHCl_3$); **IR** (cm^{-1}, $CHCl_3$): 3030, 2920, 1880, 1740, 1600, 1442**,** 1430, 1220, 1100,1010**,** 690; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.78 – 7.75 (m, 4H), 7.72 – 7.66 (m, 5H), 7.65 – 7.59 (m, 9H), 7.43 – 7.40 (m, 3H), 7.36 – 7.33 (m, 3H), 7.32 – 7.25 (m, 24H), 7.24 – 7.21 (m, 11H), 7.20 – 7.17 (m, 9H), 5.28 (s, 2H), 5.21 (d, *J* =



4.2 Hz, 1H), 5.09 (s, 1H), 5.05 (d, *J* = 4.3 Hz, 2H), 4.67 (dd, *J* = 11.9, 5.3 Hz, 3H), 4.63 – 4.55 (m, 6H), 4.51 (s, 1H), 4.50 – 4.46 (m, 3H), 4.45 – 4.38 (m, 5H), 4.10 (m, 13H), 3.95 (dd, *J* = 12.1, 2.8 Hz, 1H), 3.80 – 3.74 (m, 5H), 3.62 – 3.48 (m, 19H), 2.59 – 2.40 (m, 3H), 2.39 (s, 3H), 2.37 – 2.29 (m, 1H), 1.86 (s, 3H), 1.00 (d, *J* = 10.3 Hz, 18H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 206.1, 172.1, 144.8, 138.3, 138.3, 138.3, 138.2, 138.0, 137.8, 135.8, 135.7, 135.7, 135.7, 135.7, 135.6, 133.6, 133.5, 133.5, 133.4, 133.3, 133.3, 133.3, 133.1, 133.0, 133.0, 129.9, 129.9, 129.9, 129.8, 129.7, 129.7, 129.7, 128.5, 128.5, 128.5, 128.5, 128.5, 128.5, 128.4, 128.4, 128.4, 128.4, 128.3, 128.3, 128.3, 128.3, 128.3, 128.3, 128.3, 128.3, 128.2, 128.1, 128.1, 128.1, 128.1, 128.1, 128.0, 128.0, 128.0, 128.0, 128.0, 127.9, 127.9, 127.9, 127.8, 127.8, 127.8, 127.8, 127.8, 127.7, 127.7, 127.7, 127.7, 127.6, 127.6, 127.6, 127.5, 127.5, 127.5, 127.5, 126.3, 126.3, 126.1, 126.1, 125.9, 125.9, 125.7, 125.7, 107.1, 106.0, 105.6, 99.9, 99.7, 85.6, 84.9, 84.1, 83.9, 83.8, 83.7, 83.3, 83.2, 83.0, 82.7, 82.6, 82.2, 81.4, 80.1, 80.1, 73.2, 73.2, 72.7, 72.6, 72.3, 72.3, 72.3, 72.2, 72.2, 70.7, 70.7, 70.7, 70.5, 70.2, 69.3, 69.3, 68.7, 68.7, 66.5, 65.7, 63.9, 37.7, 29.5, 27.7, 27.0, 27.0, 27.0, 26.9, 26.9, 26.9, 21.7, 19.4, 19.3.

(2-(2-(2-(2-tosylethoxy)ethoxy)ethoxy)ethyl)2-*O*-(4-oxopentanoyl)-3,5-di-O-(2-*O*-(2,3-di-*O*-benzyl-5-*O*-(naphthalen-1-ylmethyl)-β-D-arabinofuranosyl)-3-*O*-benzyl-α-D-arabinofuranosyl)-α-D-arabinofuranoside (S15):

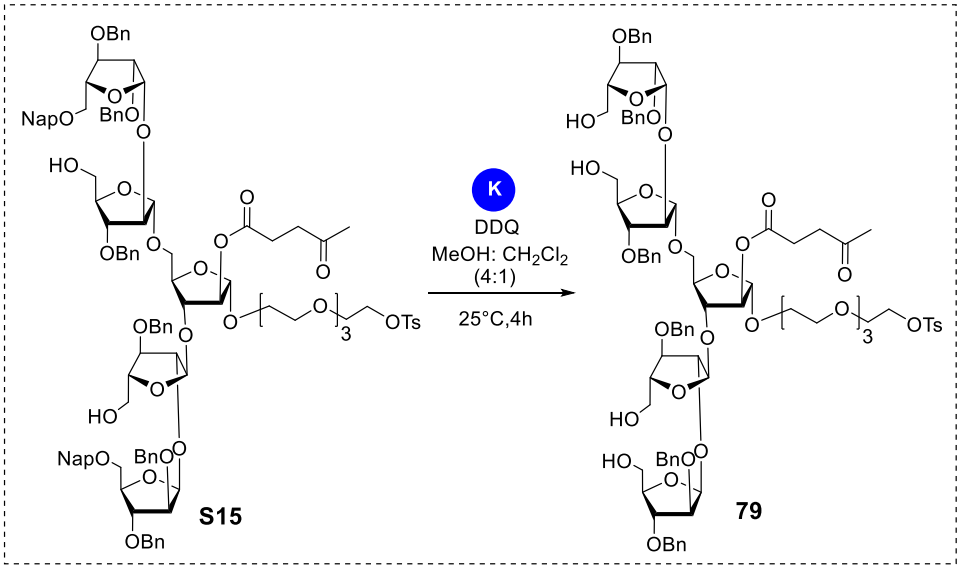
Compound **78** was converted to compound **S15** according to the general experimental **Procedure D.** (Yield 74%, pale yellow syrup): **$[\alpha]_D^{25}$** = +22.8 (*c* = 0.06, $CHCl_3$); **IR** (cm^{-1}, $CHCl_3$): 3516, 3045, 2923, 1730, 1455, 1360, 1108, 1010, 710; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.80 – 7.75 (m, 5H), 7.74 – 7.70 (m, 3H), 7.64 (d, *J* = 7.1 Hz, 2H), 7.44 (dt, *J* = 5.9, 2.3 Hz, 4H), 7.38 (d, *J* = 8.0 Hz, 3H), 7.33 (d, *J* = 4.4 Hz, 7H), 7.31 – 7.27 (m, 6H), 7.24 – 7.19 (m, 18H), 5.27 (s, 1H), 5.26 – 5.22 (m, 1H), 5.10 (s, 1H), 5.08 – 5.05 (m, 2H), 5.00 (s, 1H), 4.68 (d, *J* = 5.0 Hz, 1H), 4.65 (d, *J* = 5.1 Hz, 2H), 4.63 (d, *J* = 6.8 Hz, 1H),



4.60 (d, *J* = 5.5 Hz, 3H), 4.56 (d, *J* = 4.5 Hz, 5H), 4.52 (s, 1H), 4.49 (d, *J* = 4.6 Hz, 1H), 4.42 – 4.37 (m, 3H), 4.35 (s, 1H), 4.19 – 4.11 (m, 10H), 4.09 – 4.05 (m, 2H), 3.96 (d, *J* = 5.5 Hz, 1H), 3.90 (d, *J* = 9.4 Hz, 2H), 3.83 – 3.75 (m, 2H), 3.67 – 3.55 (m, 18H), 3.53 (s, 3H), 2.40 (s, 3H), 2.35 (s, 4H), 1.85 (s, 3H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 206.5, 172.1, 144.8, 138.2, 138.1, 138.1, 138.0, 137.8, 137.6, 135.5, 135.5, 133.3, 133.3, 133.1, 133.0, 133.0, 129.9, 129.9, 129.9, 129.9, 128.6, 128.6, 128.6, 128.6, 128.6, 128.6, 128.4, 128.4, 128.4, 128.4, 128.4, 128.4, 128.4, 128.4, 128.4, 128.4, 128.4, 128.4, 128.3, 128.2, 128.2, 128.2, 128.1, 128.1, 128.1, 128.0, 128.0, 128.0, 127.8, 127.8, 127.8, 127.8, 127.8, 127.7, 127.7, 127.6, 126.5, 126.4, 126.2, 126.2, 126.0, 125.9, 125.8, 125.7, 106.2, 105.9, 105.5, 100.7, 99.8, 86.0, 85.0, 84.2, 84.0, 83.8, 83.7, 83.4, 83.3, 83.0, 82.8, 82.7, 81.4, 80.8, 80.1, 80.1, 73.3, 72.7, 72.5, 72.5, 72.4, 72.3, 72.3, 72.2, 72.1, 70.8, 70.7, 70.7, 70.5, 70.2, 69.3, 69.3, 68.7, 68.7, 66.5, 64.6, 63.1, 37.6, 29.5, 27.7, 21.7, 21.5; **HRMS** (ESI-MS): m/z calcd. For $C_{109}H_{122}O_{28}S[M+Na]^+$: 1933.7741; Found: 1933.7750.

(2-(2-(2-(2-tosylethoxy)ethoxy)ethoxy)ethyl)2-*O*-(4-oxopentanoyl)-3,5-di-*O*-(2-O-(2,3-di-*O*-benzyl-β-D-arabinofuranosyl)-3-*O*-benzyl-α-D-arabinofuranosyl)-α-D-arabinofuranoside (79):

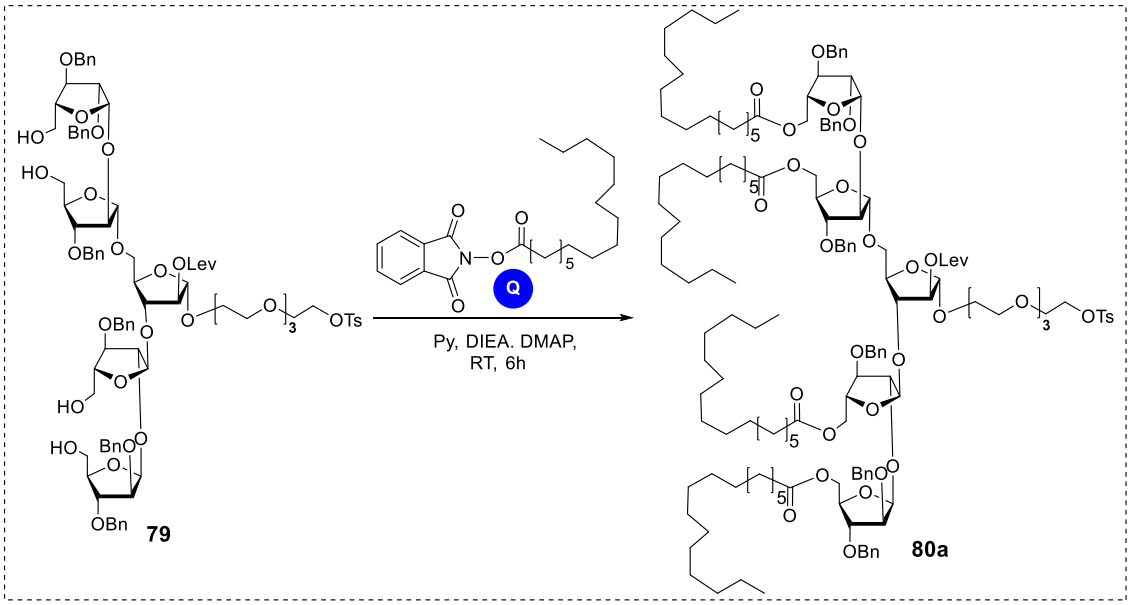
Compound **S15** was converted to compound **79** according to the general experimental **Procedure K.** (Yield 74%, pale yellow syrup)**: [α]$_D^{25}$** = +18.8 (*c* = 1.0, $CHCl_3$); **IR** (cm^{-1}, $CHCl_3$): 3550, 3280, 3040, 2903, 1730, 1433, 1330, 1102, 1010, 700; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.78 (d, *J* = 8.3 Hz, 2H), 7.40 – 7.37 (m, 2H), 7.35 (d, *J* = 4.3 Hz, 7H), 7.30 (m, 23H), 5.28 (s, 1H), 5.22 (d, *J* = 4.4 Hz, 1H), 5.11 (s, 1H), 5.09 – 5.06 (m, 2H), 5.03 (s, 1H), 4.72 (d, *J* = 5.2 Hz, 1H), 4.70 – 4.65 (m, 3H), 4.63 (d, *J* = 1.8 Hz, 1H), 4.59 – 4.57 (m, 2H), 4.57 – 4.55 (m, 2H), 4.54 (d, *J* = 3.4 Hz, 1H), 4.52 (d, *J* = 3.6 Hz, 1H), 4.48 (d, *J* = 12.0 Hz, 1H), 4.35 (dt, *J* = 4.9, 2.1 Hz, 2H), 4.25 – 4.16 (m, 6H), 4.12 (q, *J* = 4.5 Hz, 4H), 4.09 – 4.03 (m, 4H), 3.98 (dt, *J* = 6.1, 3.2 Hz, 3H), 3.92 (dd, *J* = 11.3, 2.7



Hz, 1H), 3.83 – 3.79 (m, 1H), 3.76 (s, 1H), 3.74 – 3.72 (m, 1H), 3.70 – 3.67 (m, 1H), 3.64 (dd, *J* = 7.9, 3.1 Hz, 6H), 3.60 (d, *J* = 4.4 Hz, 3H), 3.57 (d, *J* = 6.1 Hz, 3H), 3.54 (s, 4H), 2.51 – 2.42 (m, 4H), 2.42 (s, 3H), 1.94 (s, 3H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 206.7, 172.1, 144.8, 138.1, 138.0, 137.9, 137.7, 137.7, 137.6, 133.1, 129.9, 129.9, 129.9, 129.9, 128.6, 128.6, 128.6, 128.6, 128.6, 128.5, 128.5, 128.5, 128.5, 128.5, 128.5, 128.5, 128.4, 128.4, 128.4, 128.2, 128.2, 128.1, 128.0, 128.0, 127.9, 127.9, 127.9, 127.8, 127.8, 127.8, 127.8, 127.8, 127.8, 127.7, 106.0, 105.8, 105.4, 100.4, 99.6, 86.0, 85.4, 84.0, 83.9, 83.4, 83.3, 83.1, 83.1, 82.6, 82.1, 82.0, 81.5, 81.0, 80.8, 80.7, 72.7, 72.6, 72.6, 72.5, 72.4, 72.3, 70.8, 70.7, 70.7, 70.5, 70.2, 69.3, 68.7, 66.5, 64.8, 63.7, 63.6, 62.9, 62.8, 37.7, 29.6, 27.8, 21.7; **HRMS** (ESI-MS): m/z calcd. For $C_{87}H_{106}O_{28}S[M+Na]^+$: 1653.6489; Found: 1653.6490.

(2-(2-(2-(2-tosylethoxy)ethoxy)ethoxy)ethyl)2-*O*-(4-oxopentanoyl)-3,5-di-*O*-(2-*O*-(2,3-di-*O*-benzyl-5-*O*-(hexadecanoyl)-β-D-arabinofuranosyl)-3-*O*-benzyl-5-O-(hexadecanoyl)-α-D-arabinofuranosyl)-α-D-arabinofuranoside (80a) :

Compound **79** was converted to compound **80a** according to the general experimental **Procedure Q.** (Yield 41%, pale yellow syrup): **$[\alpha]_D^{25}$** = + 20.5(*c* = 0.06, $CHCl_3$); **IR** (cm^{-1}, $CHCl_3$):

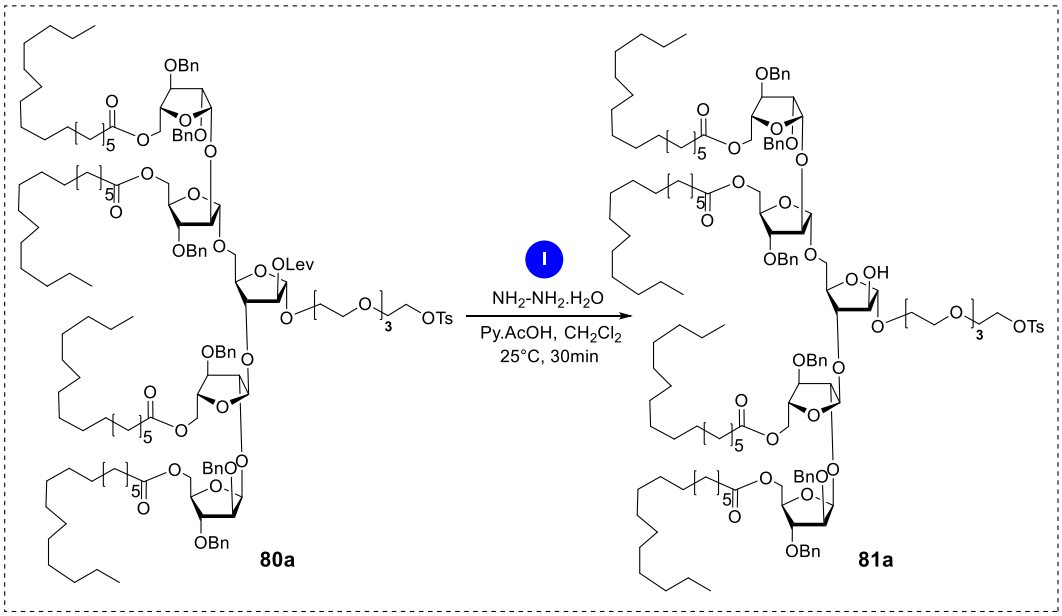


3080, 2910, 2705, 2230, 1750, 1624, 1478, 1320, 1250, 1002, 970, 900; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.78 (d, *J* = 8.3 Hz, 2H), 7.39 – 7.27 (m, 32H), 5.29 (s, 1H), 5.26 (d, *J* = 4.1 Hz, 1H), 5.17 – 5.13 (m, 1H), 5.08 (s, 1H), 5.05 (s, 1H), 5.04 (s, 1H), 4.72 – 4.66 (m, 5H), 4.62 – 4.59 (m, 2H), 4.57 (d, *J* = 4.5 Hz, 1H), 4.51 (d, *J* = 4.5 Hz, 1H), 4.49 – 4.46 (m, 2H), 4.42 (d, *J* = 2.4 Hz, 1H), 4.37 (d, *J* = 2.1 Hz, 1H), 4.26 (m, 11H), 4.17 – 4.12 (m, 8H), 4.09 (d, *J* = 6.2 Hz, 2H), 3.96 (dd, *J* = 5.7, 2.7 Hz, 2H), 3.88 – 3.82 (m, 7H), 3.66 – 3.63 (m, 2H), 3.60 – 3.57 (m, 5H), 3.54 (s,

2H), 2.58 – 2.45 (m, 2H), 2.43 (s, 3H), 2.40 (d, *J* = 7.8 Hz, 2H), 2.28 – 2.17 (m, 8H), 1.94 (s, 3H), 1.57 – 1.48 (m, 8H), 1.24 (m, 96H), 0.88 (t, *J* = 6.8 Hz, 12H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 206.1, 173.6, 173.6, 173.5, 173.4, 172.1, 144.9, 137.9, 137.9, 137.9, 137.8, 137.7, 137.5, 133.1, 129.9, 129.9, 128.6, 128.6, 128.6, 128.6, 128.5, 128.5, 128.5, 128.5, 128.5, 128.5, 128.5, 128.5, 128.1, 128.1, 128.1, 128.1, 128.1, 128.1, 127.9, 127.9, 127.9, 127.8, 127.8, 127.8, 127.8, 127.8, 127.8, 127.8, 127.8, 127.6, 127.6, 106.8, 106.0, 105.6, 100.7, 100.3, 86.0, 85.1, 84.4, 84.2, 83.9, 83.7, 83.3, 82.9, 82.7, 82.0, 81.0, 80.1, 80.0, 78.9, 78.9, 72.6, 72.6, 72.6, 72.5, 72.5, 72.4, 70.8, 70.7, 70.7, 70.6, 70.2, 69.4, 69.4, 68.8, 66.5, 66.2, 66.0, 63.6, 63.4, 37.7, 34.1, 34.1, 34.1, 34.1, 34.0, 32.1, 32.0, 32.0, 32.0, 32.0, 32.0, 29.9, 29.9, 29.8, 29.8, 29.8, 29.8, 29.8, 29.8, 29.8, 29.8, 29.8, 29.8, 29.8, 29.8, 29.8, 29.7, 29.7, 29.7, 29.7, 29.6, 29.6, 29.5, 29.5, 29.5, 29.5, 29.5, 29.5, 29.4, 29.4, 29.3, 29.3, 29.3, 29.3, 24.9, 24.9, 23.6, 23.6, 23.6, 23.6, 23.6, 23.6, 23.6, 23.6, 23.6, 22.8, 22.8, 22.8, 22.8, 21.7, 14.2, 14.2, 14.2, 14.2.

(2-(2-(2-(2-tosylethoxy)ethoxy)ethoxy)ethyl)-3,5-di-*O*-(2-*O*-(2,3-di-*O*-benzyl-5-*O*-(hexadecanoyl)-β-D-arabinofuranosyl)-3-*O*-benzyl-5-*O*-(hexadecanoyl)-α-D-arabinofuranosyl)-α-D-arabinofuranoside (81a):

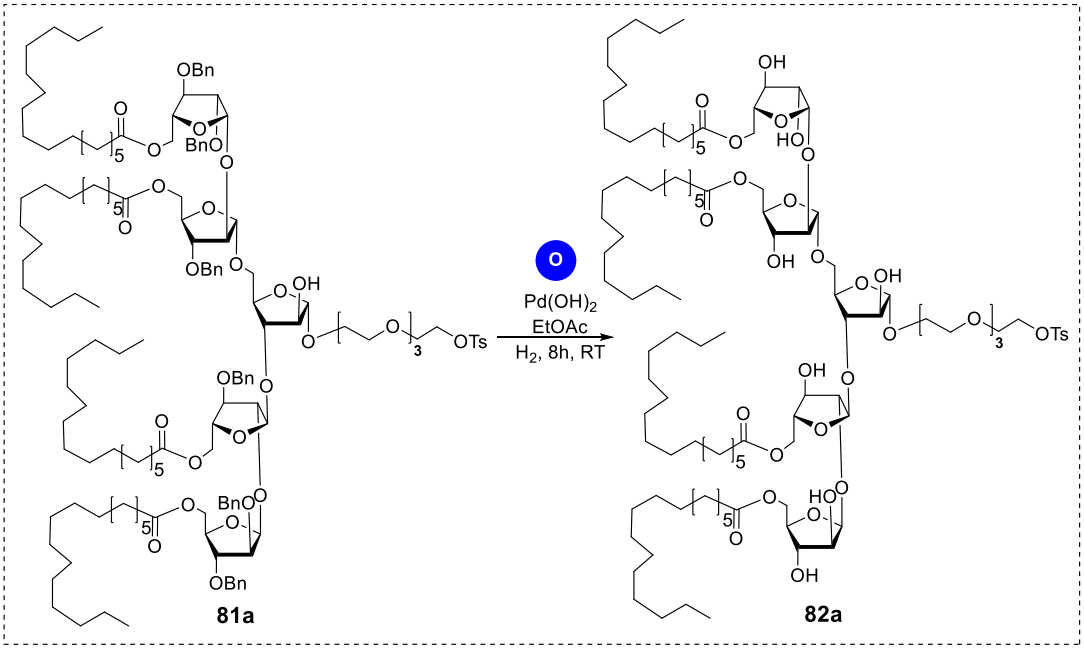
Compound **80a** was converted to compound **81a** according to the general experimental **Procedure I.** (Yield 84%, pale yellow syrup): **$[\alpha]_D^{25}$** = +22.8 (*c* = 0.60, $CHCl_3$); **IR** (cm^{-1}, $CHCl_3$): 3500, 3470, 3160, 2950, 2705, 2300, 1890,1620, 1418, 1308, 1290, 1000, 980, 900; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.78 (d, *J* = 8.3 Hz, 2H), 7.35 – 7.27 (m, 31H), 7.25 – 7.23 (m, 1H), 5.09 (s, 1H), 5.07 (d, *J* = 2.4 Hz, 2H), 5.02 (s, 1H), 4.95 (s, 1H), 4.68 (dt, *J* = 11.4, 5.6 Hz, 4H), 4.62 – 4.58 (m, 2H), 4.56 (d, *J* = 6.9 Hz, 2H), 4.52 (s, 1H), 4.50 (d, *J* = 4.0 Hz, 1H), 4.47 (d, *J* = 3.7 Hz, 1H), 4.29 (dd, *J* = 13.0, 3.2 Hz, 3H), 4.23 – 4.16 (m, 8H),



4.14 – 4.12 (m, 3H), 4.11 – 4.07 (m, 8H), 4.06 – 4.04 (m, 2H), 3.96 (dt, *J* = 10.2, 2.5 Hz, 2H), 3.92 (dd, *J* = 4.9, 2.0 Hz, 1H), 3.86 – 3.77 (m, 4H), 3.64 (q, *J* = 5.9, 4.8 Hz, 3H), 3.58 – 3.52 (m, 8H), 2.42 (s, 3H), 2.28 – 2.18 (m, 8H), 1.58 – 1.49 (m, 8H), 1.27 – 1.22 (m, 96H), 0.88 (t, *J* = 6.8 Hz, 12H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 173.5, 173.5, 173.5, 173.5, 144.9, 137.9, 137.9, 137.8, 137.6, 137.5, 137.5, 133.1, 129.9, 129.9, 128.7, 128.7, 128.6, 128.6, 128.6, 128.6, 128.6, 128.5, 128.5, 128.5, 128.3, 128.2, 128.2, 128.2, 128.2, 128.2, 128.2, 128.1, 128.1, 128.0, 128.0, 128.0, 128.0, 128.0, 127.9, 127.9, 127.9, 127.8, 127.8, 127.8, 127.8, 127.8, 108.9, 106.2, 105.9, 100.7, 100.4, 86.0, 84.8, 84.1, 83.9, 83.8, 83.7, 82.9, 82.8, 82.7, 82.7, 81.1, 80.0, 79.7, 79.0, 78.9, 72.8, 72.7, 72.6, 72.6, 72.5, 72.4, 70.8, 70.7, 70.6, 70.5, 70.4, 69.3, 68.8, 66.8, 66.2, 66.1, 65.9, 63.7, 63.5, 34.1, 34.1, 34.1, 34.1, 32.1, 32.1, 32.1, 32.0, 32.0, 32.0, 29.9, 29.9, 29.8, 29.8, 29.8, 29.8, 29.8, 29.8, 29.8, 29.8, 29.8, 29.8, 29.8, 29.8, 29.8, 29.8, 29.8, 29.8, 29.7, 29.7, 29.7, 29.7, 29.6, 29.6, 29.6, 29.5, 29.5, 29.5, 29.5, 29.4, 29.4, 29.3, 29.3, 29.3, 29.3, 24.9, 24.9, 24.9, 24.9, 23.6, 23.6, 23.6, 23.6, 23.6, 23.6, 22.8, 22.8, 22.8, 22.8, 21.7, 14.2, 14.2, 14.2, 14.2.

(2-(2-(2-(2-tosylethoxy)ethoxy)ethoxy)ethyl)-3,5-di-O-(2-O-(5-O-(hexadecanoyl)-β-D-arabinofuranosyl)-5-O-(hexadecanoyl)-α-D-arabinofuranosyl)-α-D-arabinofuranoside(82a):

Compound **81a** was converted to compound **82a** according to the general experimental **Procedure O.** (Yield 72%, pale yellow syrup): **$[\alpha]_D^{25}$** = +24.8 (*c* = 0.06, $CHCl_3$); **IR** (cm^{-1}, $CHCl_3$):

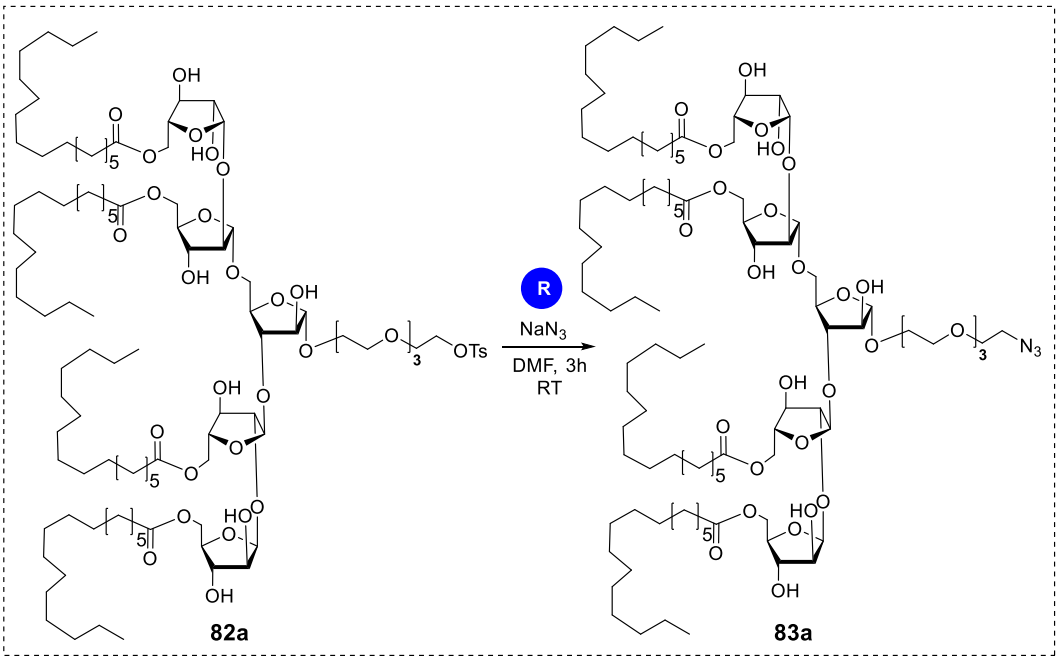


650, 3460, 3250, 2744, 2810, 2202, 1620, 1250, 1322, 1109, 1000, 900; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.80 (d, *J* = 8.3 Hz, 2H), 7.35 (d, *J* = 8.1 Hz, 2H), 5.18 (dd, *J* = 5.6, 3.5 Hz, 2H), 5.05 (dd, *J* = 8.9, 4.5 Hz, 2H), 4.97 (s, 1H), 4.33 – 4.26 (m, 5H), 4.24 – 4.20 (m, 2H), 4.18 – 4.15 (m,

5H), 4.14 – 4.07 (m, 5H), 4.03 (t, *J* = 6.7 Hz, 4H), 3.99 (dd, *J* = 6.0, 3.1 Hz, 2H), 3.93 (dd, *J* = 10.0, 3.5 Hz, 3H), 3.82 – 3.77 (m, 3H), 3.71 – 3.68 (m, 2H), 3.62 (m, 10H), 2.45 (s, 3H), 2.36 – 2.31 (m, 8H), 1.63 – 1.57 (m, 8H), 1.25 (s, 96H), 0.87 (t, *J* = 6.8 Hz, 12H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 174.2, 174.1, 174.0, 173.9, 145.2, 132.9, 130.1, 130.1, 128.1, 128.1, 108.2, 105.7, 105.6, 102.7, 102.5, 90.1, 89.8, 89.8, 83.6, 82.2, 80.5, 80.1, 80.0, 79.7, 79.6, 77.3, 76.0, 75.7, 75.2, 75.1, 70.7, 70.5, 70.4, 70.4, 70.4, 70.4, 69.4, 68.8, 66.8, 66.1, 65.8, 65.5, 63.7, 34.2, 34.2, 34.2, 34.2, 32.1, 32.1, 32.1, 32.1, 32.1, 29.9, 29.9, 29.9, 29.9, 29.9, 29.9, 29.9, 29.9, 29.9, 29.9, 29.8, 29.8, 29.8, 29.8, 29.8, 29.8, 29.8, 29.8, 29.8, 29.8, 29.7, 29.7, 29.7, 29.7, 29.5, 29.5, 29.5, 29.5, 29.5, 29.5, 29.4, 29.3, 29.3, 29.3, 29.3, 25.0, 25.0, 25.0, 25.0, 22.8, 22.8, 22.8, 22.8, 22.8, 22.8, 21.8, 14.3, 14.3, 14.3, 14.3.

(2-(2-(2-(2-azidoethoxy)ethoxy)ethoxy)ethyl)-3,5-di-*O*-(2-*O*-(5-*O*-(hexadecanoyl)-β-D-arabinofuranosyl)-5-*O*-(hexadecanoyl)-α-D-arabinofuranosyl)-α-D-arabinofuranoside(83a):

Compound **82a** was converted to compound **83a** according to the general experimental **Procedure R.** (Yield 43%, pale yellow syrup: **$[\alpha]_D^{25}$** = +29.8 (*c* = 0.06, $CHCl_3$); **IR** (cm^{-1}, $CHCl_3$):

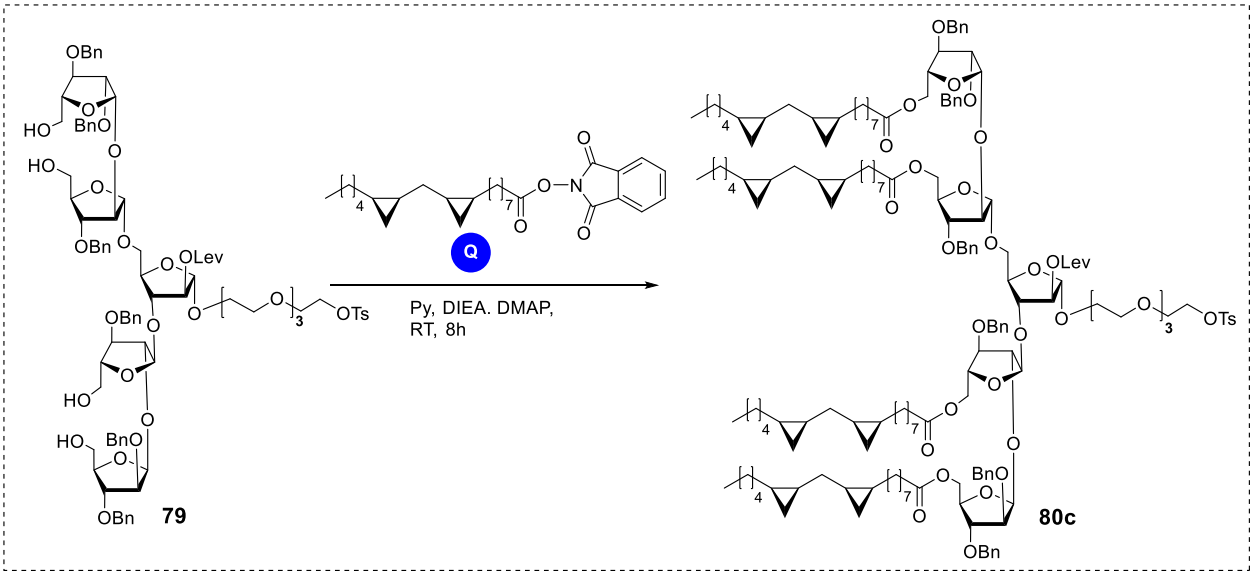


3630, 3440, 3150, 2844, 2810, 2202, 2180, 1640, 1280, 1320, 1109, 1000, 900; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 5.17 (dd, *J* = 6.3, 3.4 Hz, 2H), 5.05 (dd, *J* = 6.9, 4.7 Hz, 2H), 4.97 (s, 1H), 4.31 (dd, *J* = 12.6, 4.1 Hz, 4H), 4.22 (d, *J* = 11.0 Hz, 2H), 4.19 – 4.17 (m, 2H), 4.14 (t, *J* = 5.1 Hz, 5H), 4.07 – 4.02 (m, 4H), 3.99 (dd, *J* = 5.6, 3.6 Hz, 2H), 3.96 – 3.91 (m, 3H), 3.83 – 3.77 (m,

3H), 3.66 (m, 14H), 3.43 – 3.39 (m, 2H), 2.34 (q, *J* = 7.2 Hz, 8H), 1.64 – 1.58 (m, 8H), 1.27 (m, 96H), 0.88 (t, *J* = 6.6 Hz, 12H); **^{13}C NMR** (151 MHz, $CDCl_3$) δ 174.2, 174.1, 174.0, 173.9, 108.2, 105.6, 105.5, 102.7, 102.4, 90.0, 89.7, 83.5, 82.3, 80.4, 80.1, 80.1, 79.7, 79.6, 77.5, 77.4, 76.0, 75.8, 75.1, 75.1, 70.6, 70.6, 70.5, 70.4, 70.4, 70.0, 66.9, 66.2, 65.7, 65.4, 63.6, 63.6, 50.7, 34.3, 34.2, 34.2, 34.2, 32.1, 32.1, 32.1, 32.1, 32.1, 32.1, 29.9, 29.9, 29.9, 29.9, 29.9, 29.9, 29.9, 29.9, 29.9, 29.9, 29.9, 29.9, 29.8, 29.8, 29.8, 29.8, 29.8, 29.8, 29.8, 29.8, 29.8, 29.8, 29.7, 29.7, 29.7, 29.7, 29.5, 29.5, 29.5, 29.5, 29.5, 29.5, 29.5, 29.4, 29.3, 29.3, 29.3, 25.0, 25.0, 25.0, 25.0, 22.8, 22.8, 22.8, 22.8, 14.3, 14.3, 14.3, 14.3.

(2-(2-(2-(2-tosylethoxy)ethoxy)ethoxy)ethyl)2-*O*-(4-oxopentanoyl)-3,5-di-*O*-(2-*O*-(2,3-di-*O*-benzyl-5-*O*-(8-(2-((2-pentylcyclopropyl)methyl)cyclopropyl)octanoyl)-β-D-arabinofuranosyl)-3-*O*-benzyl-5-*O*-(8-(2-(2-pentylcyclopropyl)methyl)cyclopropyl)octanoyl)-α-D-arabinofuranosyl)-α-D-arabinofuranoside (80c):

Compound **79** was converted to compound **80c** according to the general experimental **Procedure Q.** (Yield 39%, pale yellow syrup): **[α]$_D^{25}$** = + 15.5(*c* = 0.06, $CHCl_3$); **IR** (cm^{-1}, $CHCl_3$):



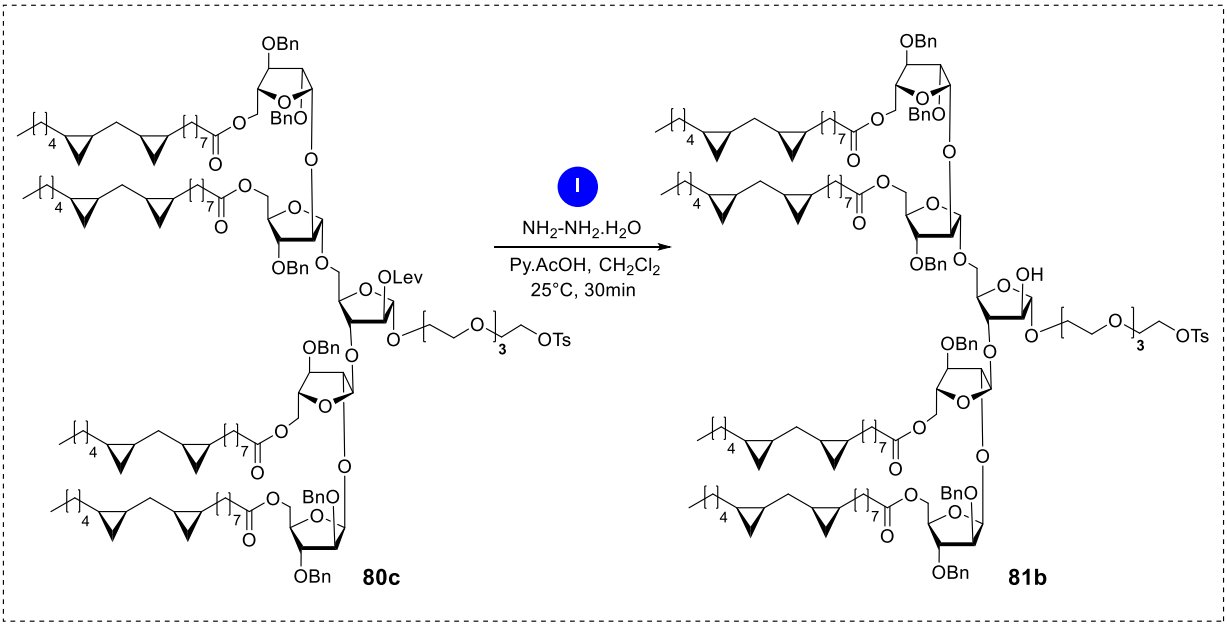
3060, 2911, 2805, 2300, 1730, 1604, 1488, 1322, 1260, 1003, 970, 900; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.78 (d, *J* = 8.3 Hz, 2H), 7.39 – 7.26 (m, 32H), 5.30 (s, 1H), 5.26 (d, *J* = 4.1 Hz, 1H), 5.15 (d, *J* = 2.8 Hz, 1H), 5.08 (s, 1H), 5.05 (d, *J* = 7.0 Hz, 2H), 4.72 – 4.69 (m, 2H), 4.67 (d, *J* = 1.9 Hz, 2H), 4.63 – 4.56 (m, 3H), 4.52 (d, *J* = 4.2 Hz, 1H), 4.50 – 4.46 (m, 2H), 4.42 (d, *J* = 2.5 Hz, 1H), 4.37 (d, *J* = 2.2 Hz, 1H), 4.23 (td, *J* = 9.7, 4.7 Hz, 9H), 4.17 – 4.08 (m, 13H), 3.96 (dd, *J*

= 5.6, 2.6 Hz, 2H), 3.91 – 3.76 (m, 7H), 3.66 – 3.63 (m, 2H), 3.61 – 3.57 (m, 5H), 3.54 (s, 2H), 2.59 – 2.44 (m, 3H), 2.43 (s, 3H), 2.41 – 2.36 (m, 1H), 2.28 – 2.17 (m, 8H), 1.94 (s, 3H), 1.51 (m, 12H), 1.42 – 1.35 (m, 22H), 1.31 – 1.21 (m, 51H), 1.07 – 0.96 (m, 4H), 0.91 – 0.87 (m, 12H), 0.82 – 0.74 (m, 8H), 0.69 (dq, *J* = 13.1, 6.9, 6.5 Hz, 7H), 0.63 – 0.58 (m, 8H), -0.28 (ddt, *J* = 9.8, 6.7, 3.9 Hz, 8H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 206.1, 173.6, 173.5, 173.5, 173.4, 172.1, 144.9, 137.9, 137.9, 137.9, 137.8, 137.7, 137.5, 133.1, 129.9, 129.9, 129.9, 128.6, 128.6, 128.6, 128.6, 128.6, 128.6, 128.5, 128.5, 128.5, 128.5, 128.5, 128.5, 128.5, 128.5, 128.5, 128.1, 128.1, 128.1, 128.1, 127.9, 127.9, 127.9, 127.8, 127.8, 127.8, 127.8, 127.8, 127.7, 127.7, 127.6, 127.6, 106.8, 105.9, 105.6, 100.7, 100.2, 86.0, 85.0, 84.4, 84.2, 83.9, 83.7, 83.3, 82.9, 82.7, 82.0, 81.0, 80.1, 79.9, 78.9, 78.9, 72.6, 72.5, 72.5, 72.5, 72.5, 72.4, 72.4, 70.8, 70.7, 70.7, 70.6, 70.2, 69.3, 68.7, 66.5, 66.3, 66.0, 63.6, 63.4, 37.7, 37.7, 36.8, 36.8, 34.1, 34.1, 34.1, 34.0, 32.0, 32.0, 32.0, 32.0, 30.3, 30.3, 30.3, 30.3, 30.0, 30.0, 30.0, 30.0, 29.8, 29.6, 29.6, 29.6, 29.5, 29.5, 29.4, 29.3, 29.3, 29.3, 29.0, 29.0, 29.0, 29.0, 29.0, 29.0, 28.8, 28.8, 28.8, 28.8, 28.8, 28.8, 28.1, 28.0, 24.9, 24.9, 24.8, 23.6, 23.6, 23.6, 23.6, 23.6, 23.6, 23.6, 23.6, 22.8, 21.7, 16.2, 16.2, 16.2, 16.2, 16.0, 16.0, 16.0, 16.0, 16.0, 16.0, 15.8, 15.8, 15.7, 15.7, 14.2, 14.2, 14.2, 14.2, 11.1, 11.1, 11.1, 11.1, 11.0, 11.0, 10.9, 10.9.

(2-(2-(2-(2-tosylethoxy)ethoxy)ethoxy)ethyl)-3,5-di-*O*-(2-*O*-(2,3-di-*O*-benzyl-5-*O*-(8-(2-((2-pentylcyclopropyl)methyl)cyclopropyl)octanoyl)-β-D-arabinofuranosyl)-3-*O*-benzyl-5-*O*-(8-(2-(2-pentylcyclopropyl)methyl)cyclopropyl)octanoyl)-α-D-arabinofuranosyl)-α-D-arabinofuranoside (81b):

Compound **80c** was converted to compound **81b** according to the general experimental **Procedure I.** (Yield 76%, pale yellow syrup)**: $[\alpha]_D^{25}$** = +22.8 (*c* = 0.60, $CHCl_3$); **IR** (cm^{-1}, $CHCl_3$): 3480, 3060, 2900, 2805, 2300, 1870,1602, 1448, 1302, 1200, 1000, 970, 900; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.78 (d, *J* = 8.3 Hz, 2H), 7.32 (m, 30H), 7.24 (d, *J* = 6.9 Hz, 2H), 5.10 (s, 1H), 5.08 – 5.05 (m, 2H), 5.02 (s, 1H), 4.95 (s, 1H), 4.68 (dt, *J* = 10.6, 5.2 Hz, 4H), 4.62 – 4.58 (m, 2H), 4.57 – 4.55 (m, 2H), 4.52 (s, 1H), 4.50 (d, *J* = 3.9 Hz, 1H), 4.47 (d, *J* = 3.6 Hz, 1H), 4.33 – 4.27 (m, 3H), 4.24 – 4.19 (m, 2H), 4.18 – 4.14 (m, 5H), 4.13 (d, *J* = 4.8 Hz, 3H), 4.11 – 4.06 (m, 8H), 4.05 (d, *J* = 3.8 Hz, 2H), 3.98 – 3.91 (m, 3H), 3.85 – 3.74 (m, 2H), 3.64 (q, *J* = 6.4, 4.8 Hz, 3H), 3.59 – 3.51 (m, 11H), 2.42 (s, 3H), 2.29 – 2.19 (m, 8H), 1.56 – 1.45 (m, 10H), 1.42 – 1.35 (m, 22H), 1.31 – 1.25 (m, 48H), 1.13 – 0.99 (m, 9H), 0.90 – 0.87 (m, 12H), 0.81 – 0.74 (m, 8H), 0.71 – 0.65 (m, 7H), 0.61 (dd, *J* = 8.2, 3.9 Hz, 8H), -0.28 (dq, *J* = 9.8, 3.6, 3.0 Hz, 8H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 173.5, 173.5, 173.5, 173.5, 144.9, 137.9, 137.9, 137.8, 137.6, 137.5, 137.5, 133.1, 129.9, 129.9, 128.7, 128.7, 128.7, 128.7, 128.6, 128.6, 128.6, 128.6, 128.5, 128.5, 128.5,

128.5, 128.5, 128.5, 128.3, 128.3, 128.2, 128.2, 128.2, 128.1, 128.1, 128.1, 128.0, 128.0, 128.0, 128.0, 127.9, 127.8, 127.8, 127.8, 127.8, 127.8, 108.9, 106.2, 105.8, 100.7, 100.4, 85.9, 84.8, 84.1, 83.9, 83.8, 83.7, 82.9, 82.8, 82.8, 82.7, 81.1, 80.0, 79.7, 79.0, 78.9, 72.8, 72.7, 72.6, 72.6, 72.5, 72.4, 70.8, 70.7, 70.6, 70.5, 70.4, 69.3, 68.8, 66.8, 66.3, 66.1, 65.9, 63.7, 63.5, 34.1, 34.1,

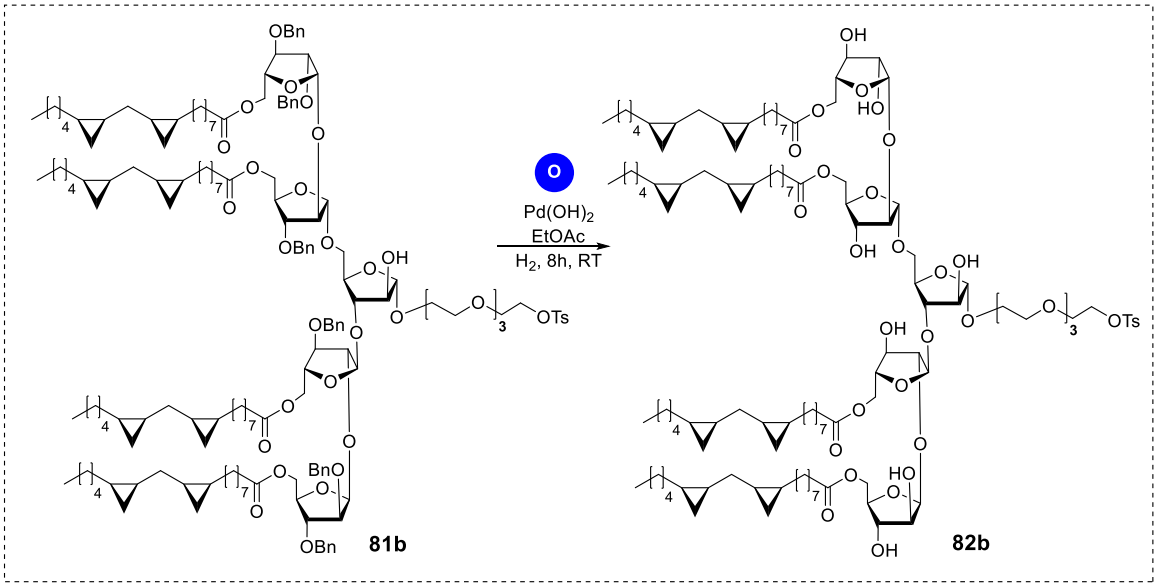


34.1, 34.1, 32.0, 32.0, 32.0, 32.0, 30.3, 30.3, 30.3, 30.3, 30.0, 30.0, 30.0, 30.0, 30.0, 30.0, 29.8, 29.8, 29.7, 29.7, 29.6, 29.6, 29.6, 29.6, 29.5, 29.5, 29.3, 29.3, 29.3, 29.3, 29.0, 29.0, 29.0, 29.0, 28.8, 28.8, 28.8, 28.8, 28.2, 28.2, 28.0, 28.0, 24.9, 24.9, 24.9, 23.6, 23.6, 22.8, 22.8, 22.8, 21.8, 16.2, 16.2, 16.2, 16.2, 16.1, 16.0, 16.0, 16.0, 16.0, 16.0, 15.8, 15.8, 15.7, 15.7, 14.3, 14.3, 14.3, 14.2, 11.2, 11.2, 11.2, 11.2, 11.0, 11.0, 11.0, 11.0.

(2-(2-(2-(2-tosylethoxy)ethoxy)ethoxy)ethyl)3,5-di-*O*-(2-*O*-(5-*O*-(8-(2-((2-pentylcyclopropyl)methyl)cyclopropyl)octanoyl)-β-D-arabinofuranosyl)-5-*O*-(8-(2-(2-pentylcyclopropyl)methyl)cyclopropyl)octanoyl)-α-D-arabinofuranosyl)-α-D-arabinofuranoside (82b):

Compound **81b** was converted to compound **82b** according to the general experimental **Procedure O.** (Yield 60%, pale yellow syrup): **$[\alpha]_D^{25}$** = +27.7 (*c* = 0.06, $CHCl_3$); **IR** (cm^{-1}, $CHCl_3$): 3660, 3440, 3200, 2834, 2850, 2209, 1630, 1255, 1342, 1101, 1002, 900; **^{1}H NMR** (400 MHz, CDCl3) δ 7.80 (d, *J* = 8.3 Hz, 2H), 7.36 (d, *J* = 8.0 Hz, 2H), 5.17 (d, *J* = 3.0 Hz, 2H), 5.05 (t, *J* = 4.1 Hz, 2H), 5.00 (s, 1H), 4.32 (ddt, *J* = 14.5, 9.5, 4.4 Hz, 5H), 4.22 (s, 1H), 4.18 (dd, *J* = 9.2, 3.9 Hz, 6H), 4.15 – 4.08 (m, 5H), 4.06 – 4.01 (m, 4H), 4.00 – 3.97 (m, 2H), 3.95 – 3.92 (m, 2H), 3.80 (ddd, *J* = 10.3, 8.4, 3.9 Hz, 2H), 3.72 – 3.69 (m, 2H), 3.63 (m, 12H), 2.45 (s, 3H), 2.34 (m, 8H), 1.64 – 1.60 (m, 9H), 1.53 – 1.46 (m, 4H), 1.41 – 1.37 (m, 16H), 1.32 – 1.29 (m, 27H), 1.26

(m, 23H), 1.16 – 1.11 (m, 8H), 1.05 – 0.99 (m, 4H), 0.88 (d, *J* = 3.8 Hz, 11H), 0.81 – 0.75 (m, 8H), 0.71 – 0.66 (m, 6H), 0.60 (td, *J* = 8.3, 4.1 Hz, 8H), -0.28 (dq, *J* = 9.8, 5.0 Hz, 8H); **^{13}C NMR**

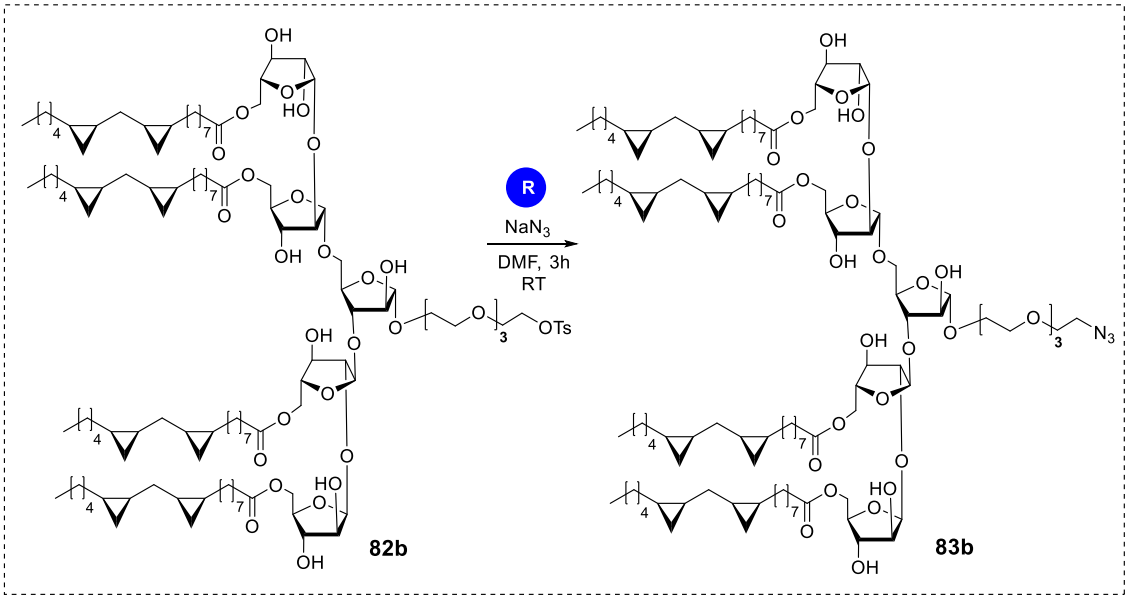


(151 MHz, $CDCl_3$) δ 174.1, 174.1, 173.9, 173.9, 145.2, 132.8, 130.1, 130.1, 128.1, 128.1, 108.3, 105.6, 105.5, 102.8, 102.5, 90.0, 89.7, 83.6, 82.3, 80.3, 80.1, 80.1, 80.1, 79.7, 79.7, 79.7, 76.2, 75.9, 75.1, 74.9, 70.7, 70.6, 70.4, 70.4, 70.3, 69.4, 68.8, 66.9, 66.5, 65.7, 65.4, 63.6, 63.5, 34.3, 34.2, 34.2, 34.2, 32.1, 32.0, 32.0, 32.0, 32.0, 30.3, 30.3, 30.1, 30.0, 30.0, 30.0, 30.0, 29.9, 29.9, 29.8, 29.8, 29.8, 29.7, 29.6, 29.6, 29.6, 29.5, 29.5, 29.5, 29.4, 29.4, 29.3, 29.3, 29.0, 29.0, 29.0, 29.0, 28.9, 28.9, 28.9, 28.9, 28.2, 28.2, 28.0, 28.0, 25.0, 25.0, 22.9, 22.9, 22.9, 22.9, 22.8, 21.8, 16.2, 16.2, 16.2, 16.2, 16.1, 16.1, 16.1, 16.1, 16.1, 16.0, 16.0, 16.0, 15.8, 15.8, 15.8, 15.8, 14.3, 14.3, 14.3, 14.3, 11.2, 11.2, 11.2, 11.2, 11.0, 11.0, 11.0, 11.0.

(2-(2-(2-(2-azidoethoxy)ethoxy)ethoxy)ethyl)3,5-di-*O*-(2-*O*-(5-*O*-(8-(2-((2-pentylcyclopropyl)methyl)cyclopropyl)octanoyl)-β-D-arabinofuranosyl)-5-*O*-(8-(2-(2-pentylcyclopropyl)methyl)cyclopropyl)octanoyl)-α-D-arabinofuranosyl)-α-D-arabinofuranoside (83b):

Compound **82b** was converted to compound **83b** according to the general experimental **Procedure R.** (Yield 61%, pale yellow syrup)**: [α]D^{25}** = +32.8 (*c* = 1.0, $CHCl_3$); **IR** (cm^{-1}, $CHCl_3$): 3440, 3200, 2834, 2850, 2209, 2160 1600, 1235, 1302, 1118, 1000, 900; **^{1}H NMR** (600 MHz, $CDCl_3$) δ 5.16 (dd, *J* = 9.1, 3.4 Hz, 2H), 5.05 (d, *J* = 4.5 Hz, 2H), 5.00 (s, 1H), 4.36 – 4.29 (m, 5H), 4.22 – 4.16 (m, 7H), 4.13 (dd, *J* = 11.0, 5.8 Hz, 3H), 4.05 (dd, *J* = 12.7, 5.1 Hz, 4H), 4.01 – 3.99 (m, 2H), 3.97 – 3.93 (m, 3H), 3.84 – 3.76 (m, 3H), 3.68 – 3.63 (m, 12H), 3.44 – 3.41 (m, 2H), 2.35 (d, *J* = 7.3 Hz, 8H), 1.41 – 1.37 (m, 22H), 1.31 (s, 27H), 1.25 (m, 31H), 1.14 (m,

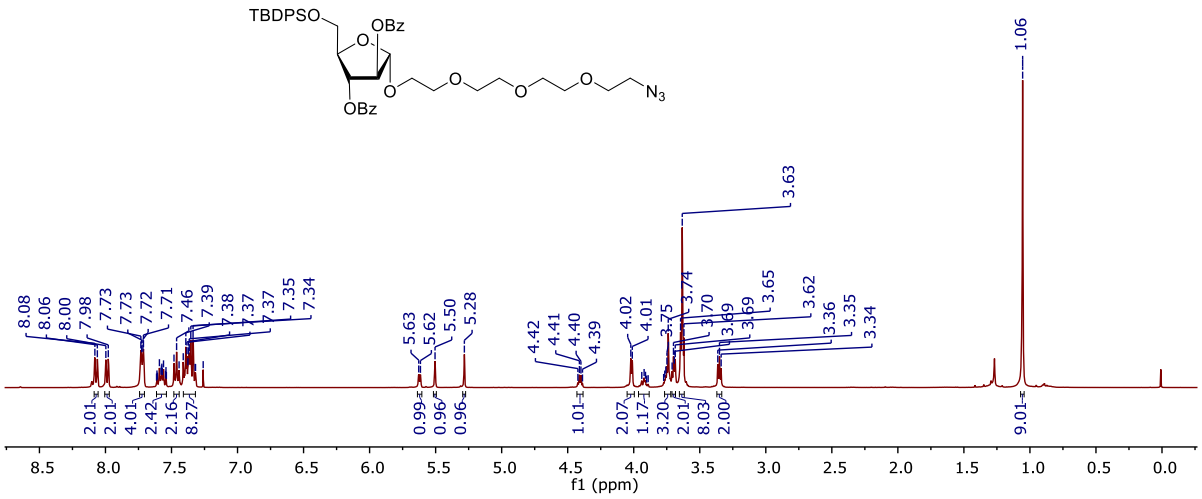
8H), 1.05 – 1.00 (m, 4H), 0.88 (d, *J* = 6.4 Hz, 11H), 0.80 – 0.76 (m, 8H), 0.68 (dd, *J* = 8.4, 3.1 Hz, 5H), 0.61 (td, *J* = 8.3, 4.2 Hz, 8H), -0.28 (dq, *J* = 15.2, 4.9 Hz, 8H); **^{13}C NMR** (151 MHz,



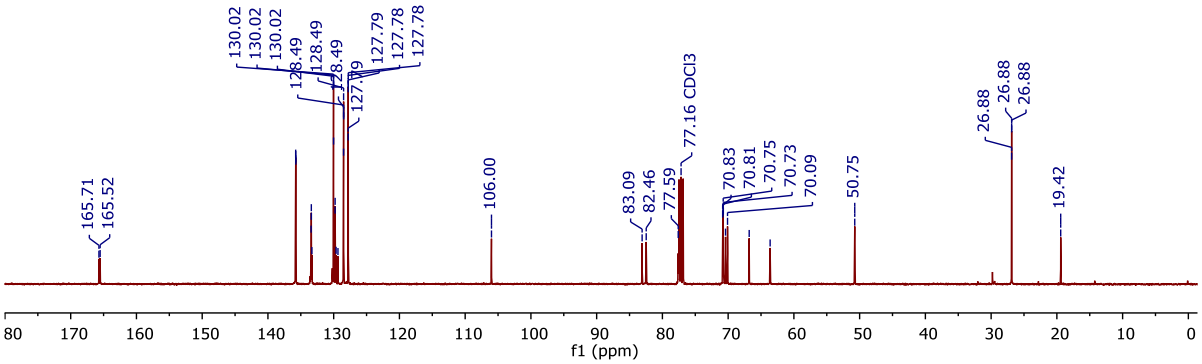
$CDCl_3$) δ 174.2, 174.1, 174.0, 173.9, 107.4, 105.5, 105.5, 102.7, 102.4, 90.0, 90.0, 89.6, 89.5, 83.5, 83.5, 82.3, 82.2, 80.1, 80.1, 80.1, 79.7, 79.7, 77.5, 77.5, 70.6, 70.6, 70.4, 70.4, 70.4, 70.4, 70.0, 70.0, 67.0, 65.6, 65.6, 65.4, 50.7, 34.3, 34.2, 34.2, 34.2, 34.0, 32.1, 32.1, 32.0, 32.0, 32.0, 31.6, 30.3, 30.3, 30.0, 30.0, 29.8, 29.8, 29.8, 29.8, 29.8, 29.8, 29.8, 29.8, 29.7, 29.6, 29.6, 29.6, 29.6, 29.5, 29.5, 29.4, 29.4, 29.4, 29.3, 29.3, 29.2, 29.1, 29.0, 29.0, 28.9, 28.9, 28.2, 28.2, 28.0, 28.0, 25.0, 25.0, 25.0, 25.0, 22.9, 22.9, 22.8, 22.8, 16.2, 16.2, 16.1, 16.1, 16.1, 16.1, 16.0, 15.8, 15.8, 15.8, 15.8, 14.3, 14.3, 14.3, 14.3, 11.2, 11.2, 11.2, 11.2, 11.0, 11.0, 11.0, 11.0.

2.11 NMR Spectral charts

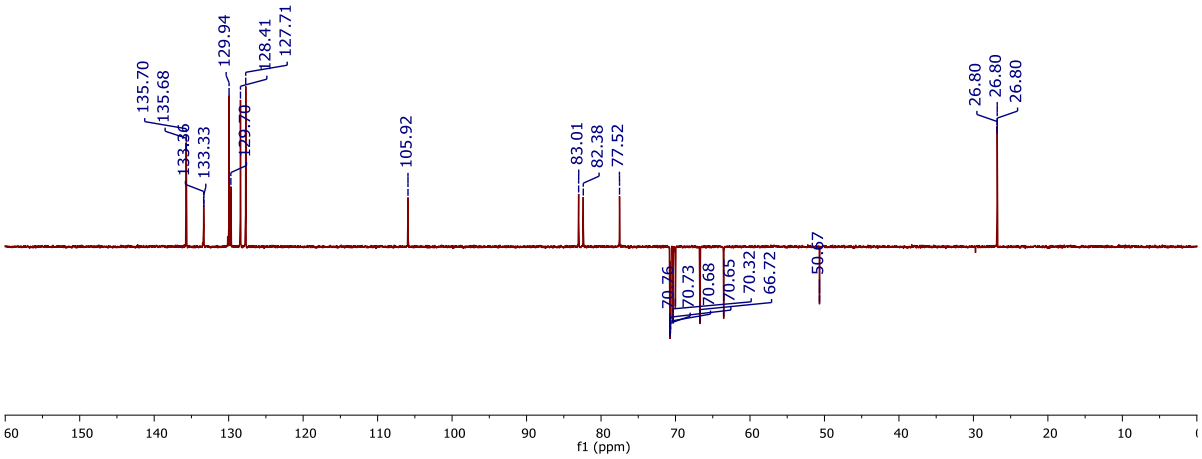
^{1}H NMR Spectrum (400.31 MHz, $CDCl_3$) of Compound **3**



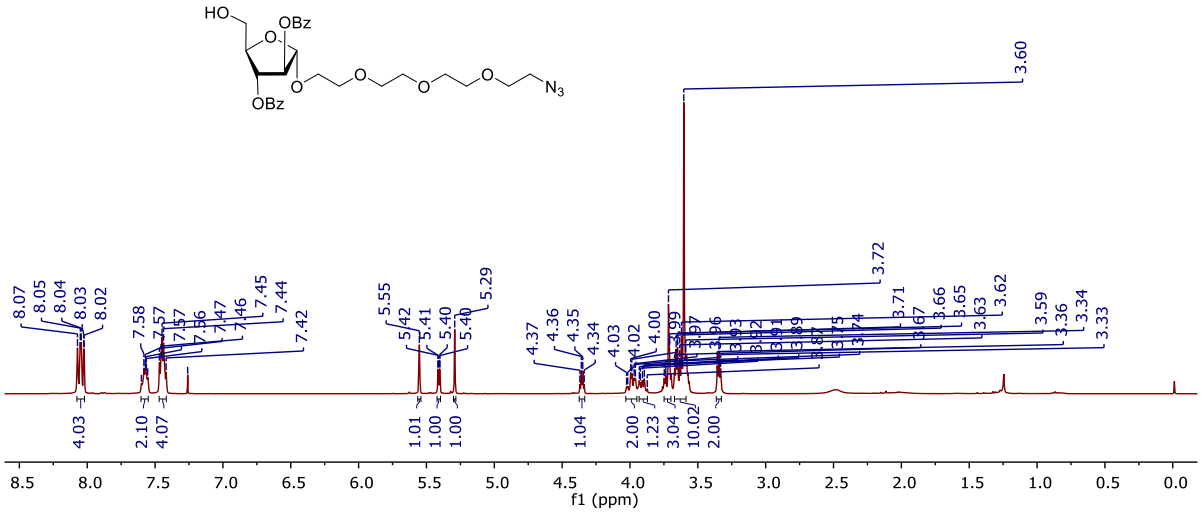
^{13}C NMR Spectrum (100.53 MHz, $CDCl_3$) of Compound **3**



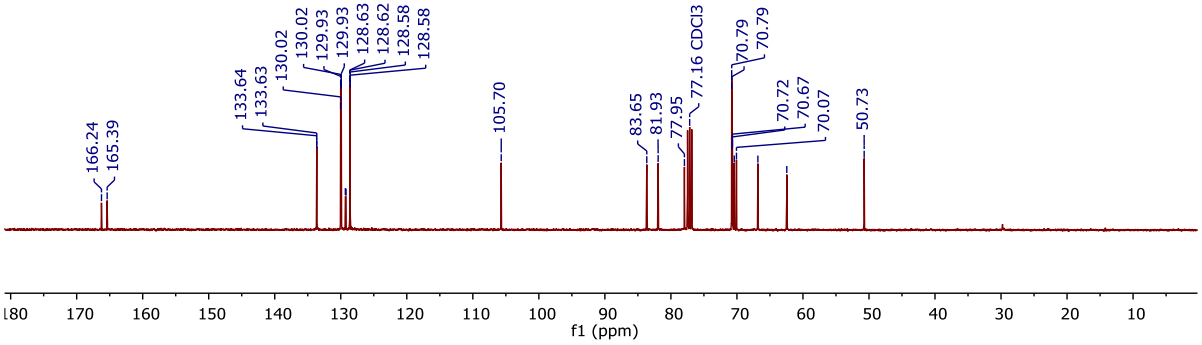
DEPT NMR Spectrum (100.53 MHz, $CDCl_3$) of Compound **3**



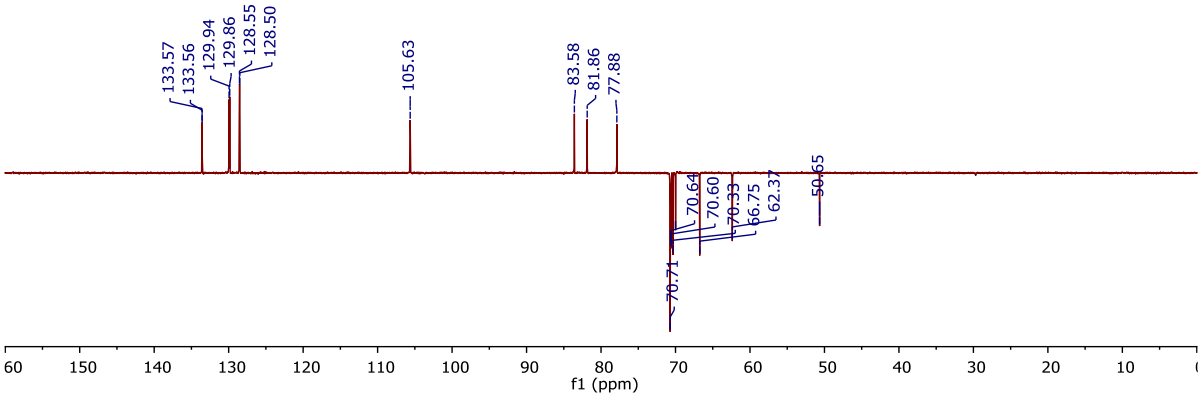
^{1}H NMR Spectrum (400.31 MHz, $CDCl_3$) of Compound **4**



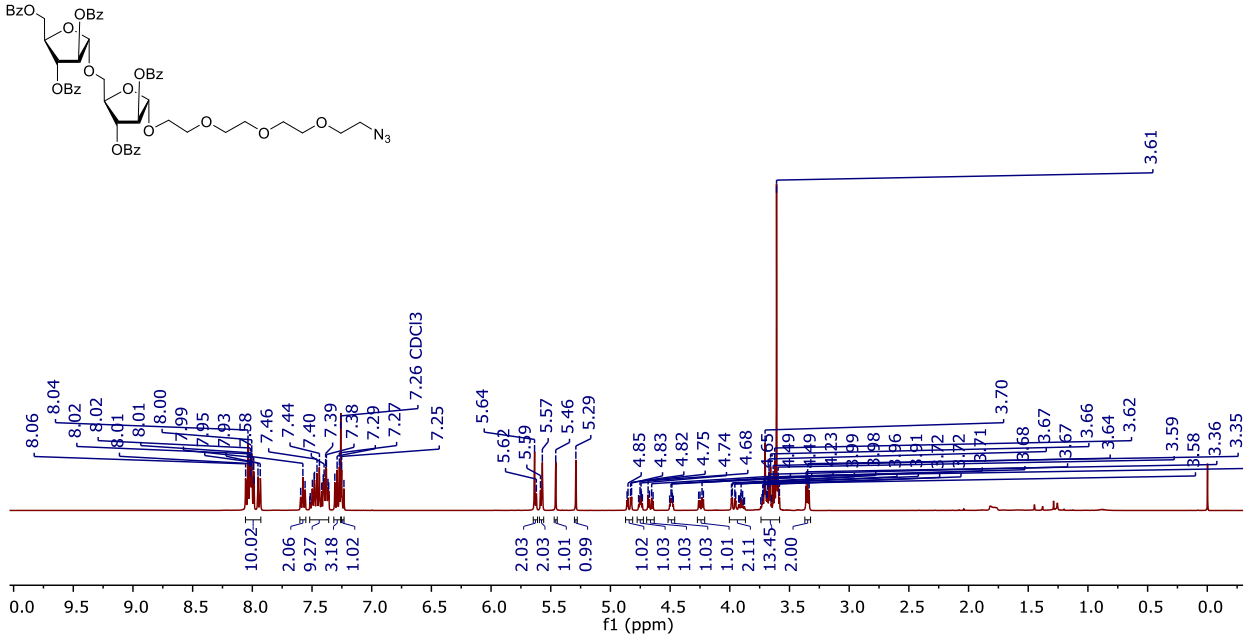
^{13}C NMR Spectrum (100.53 MHz, $CDCl_3$) of Compound **4**



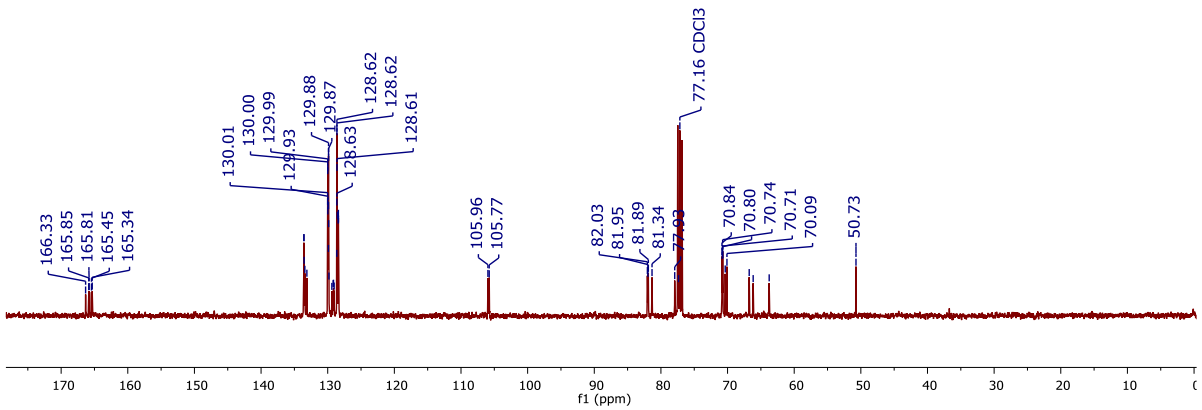
DEPT NMR Spectrum (100.53 MHz, $CDCl_3$) of Compound **4**



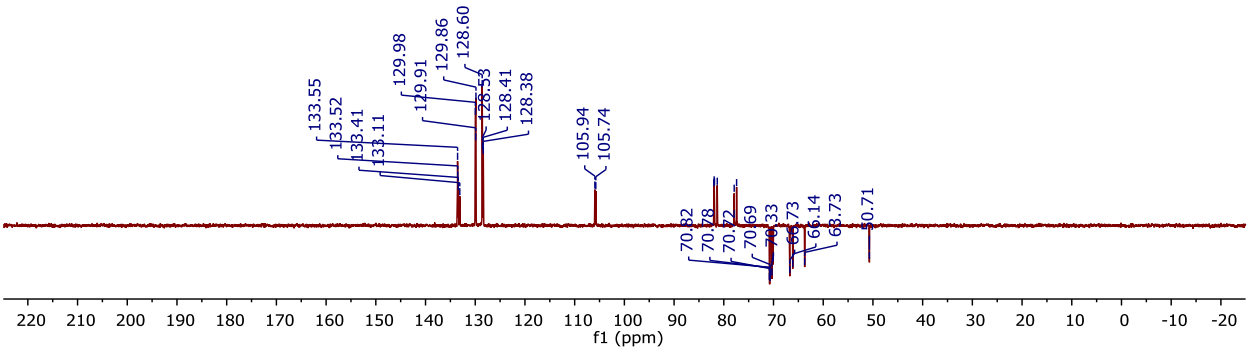
^{1}H NMR Spectrum (400.31 MHz, $CDCl_3$) of Compound **6**



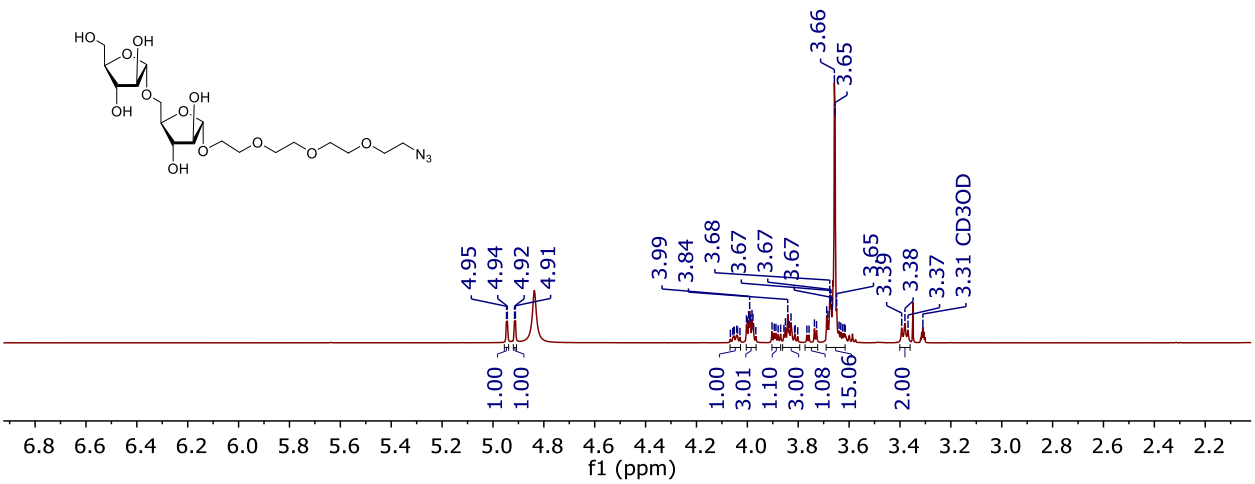
^{13}C NMR Spectrum (100.53 MHz, $CDCl_3$) of Compound **6**



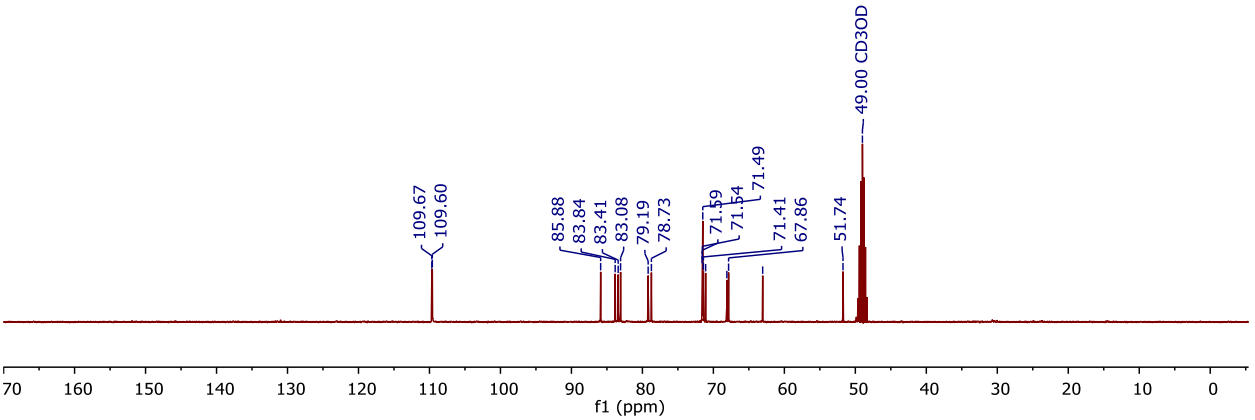
DEPT-NMR Spectrum (100.53 MHz, $CDCl_3$) of Compound **6**



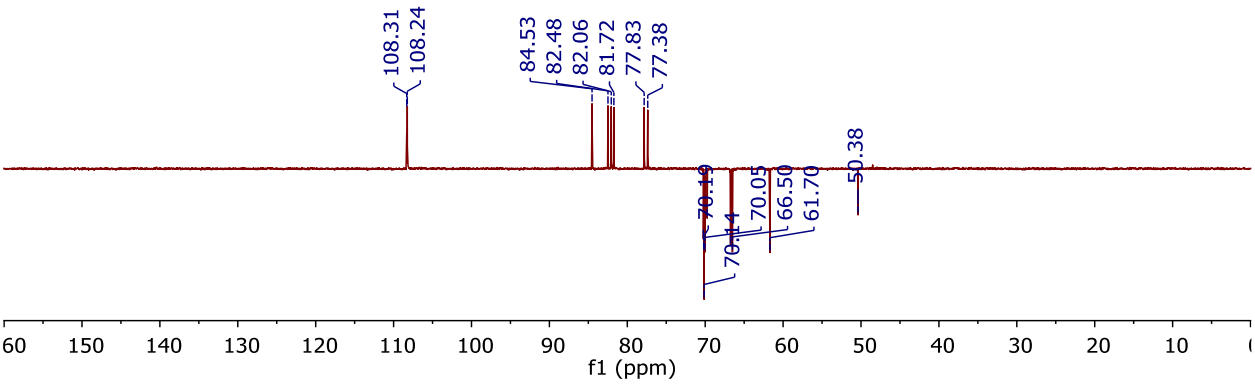
^{1}H NMR Spectrum (400.31 MHz, CD_3OD) of Compound **7**



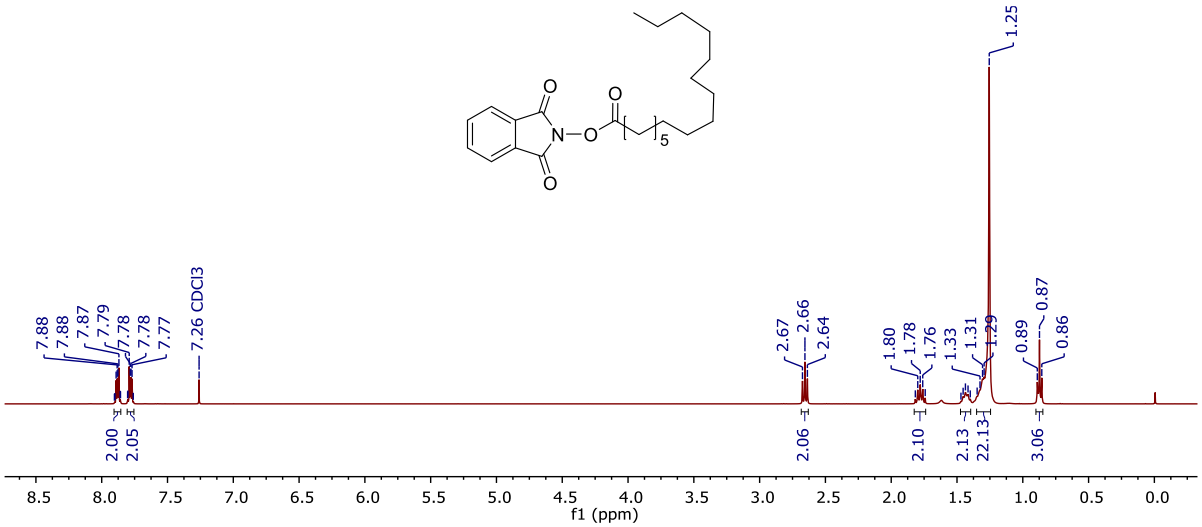
^{13}C NMR Spectrum (100.53 MHz, $CDCl_3$) of Compound **7**



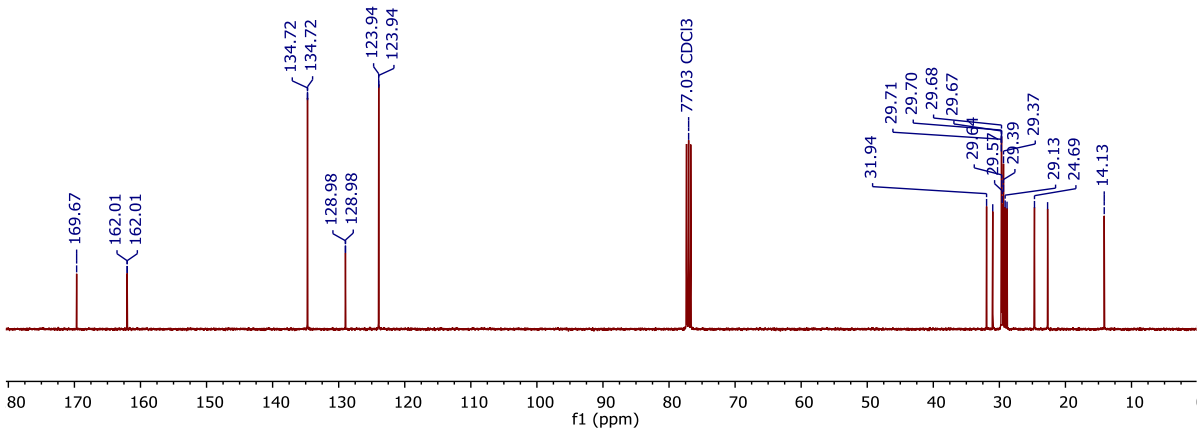
DEPT-NMR Spectrum (100.53 MHz, $CDCl_3$) of Compound **7**



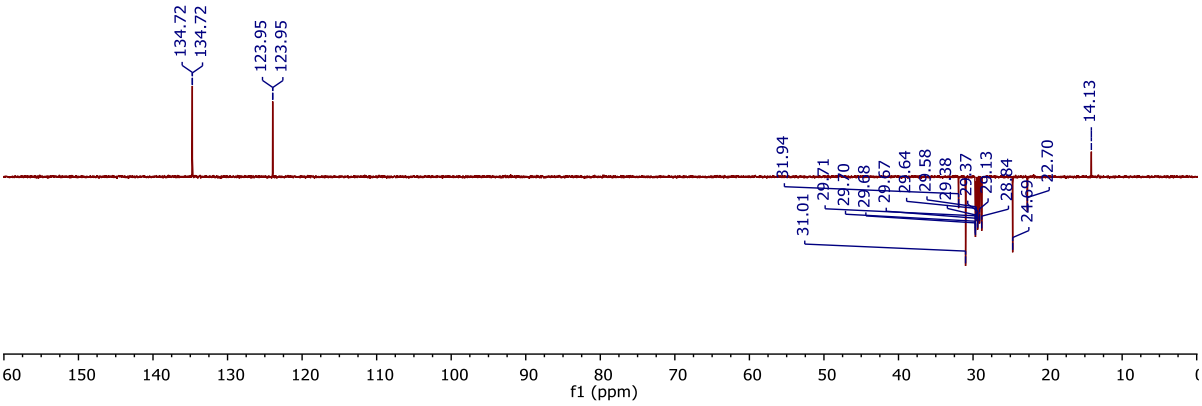
^{1}H NMR Spectrum (400.31 MHz, $CDCl_3$) of Compound **19a**



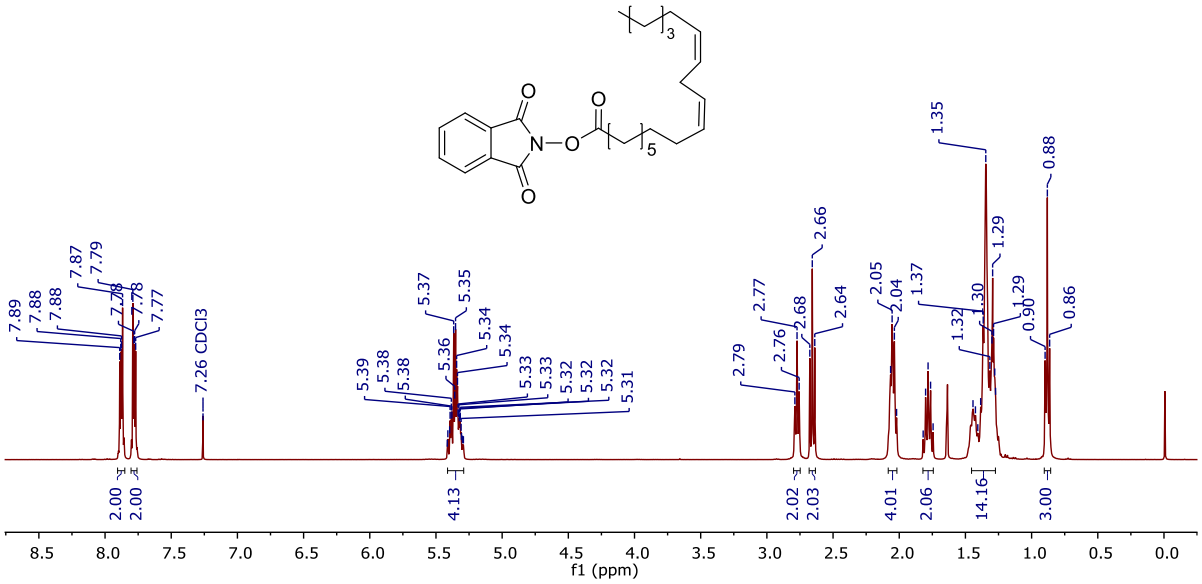
^{13}C NMR Spectrum (100.53 MHz, $CDCl_3$) of Compound **19a**



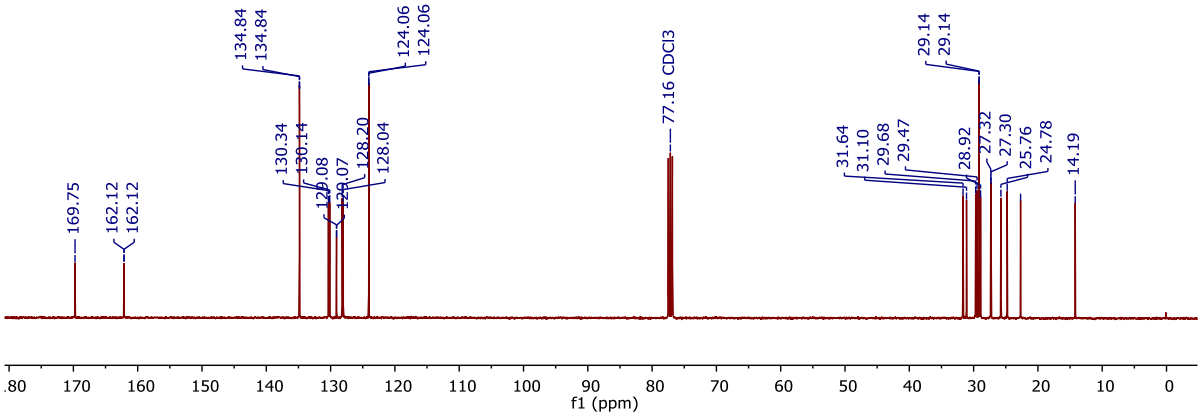
DEPT NMR Spectrum (100.53 MHz, $CDCl_3$) of Compound **19a**



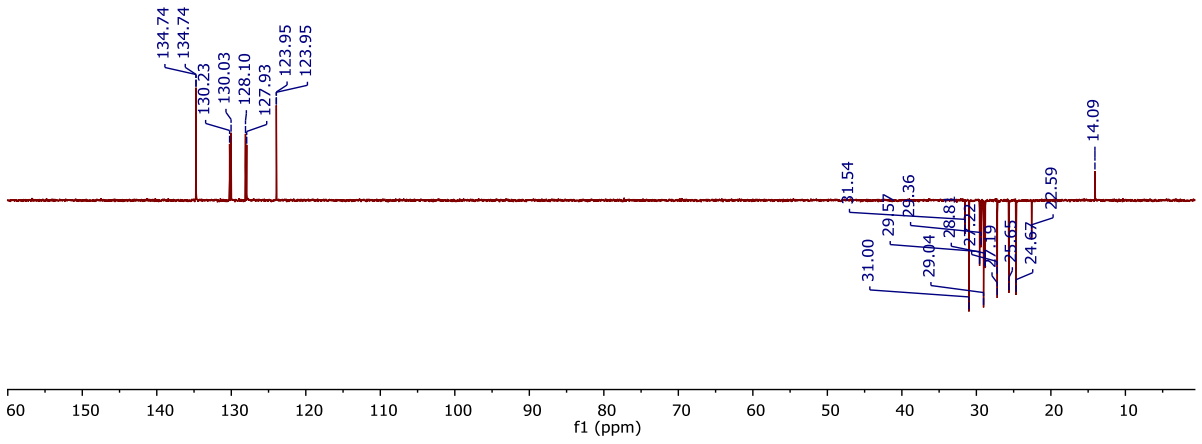
^{1}H NMR Spectrum (400.31 MHz, $CDCl_3$) of Compound **19b**



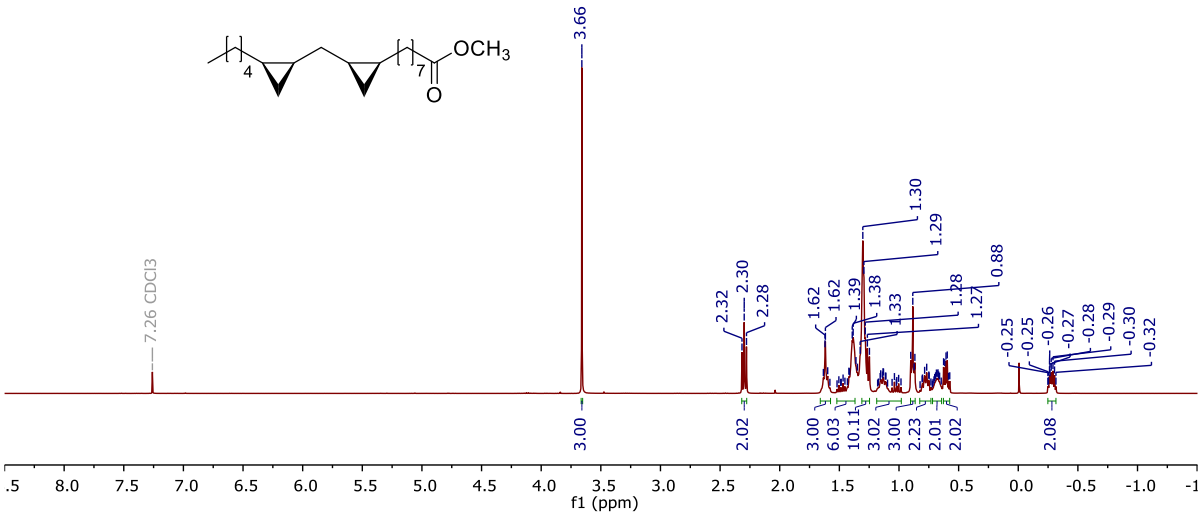
^{13}C NMR Spectrum (100.53 MHz, $CDCl_3$) of Compound **19b**



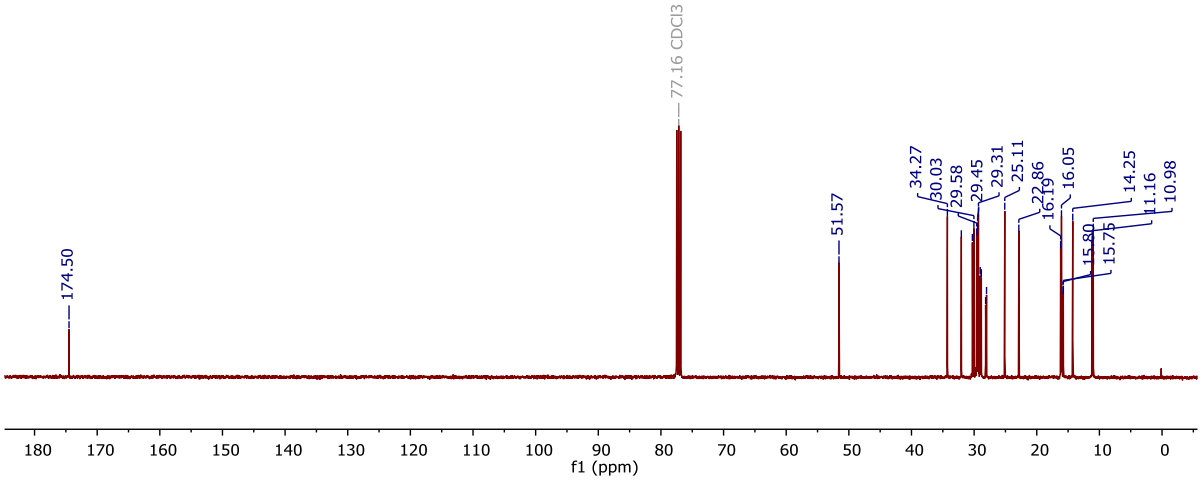
DEPT NMR Spectrum (100.53 MHz, $CDCl_3$) of Compound **19b**



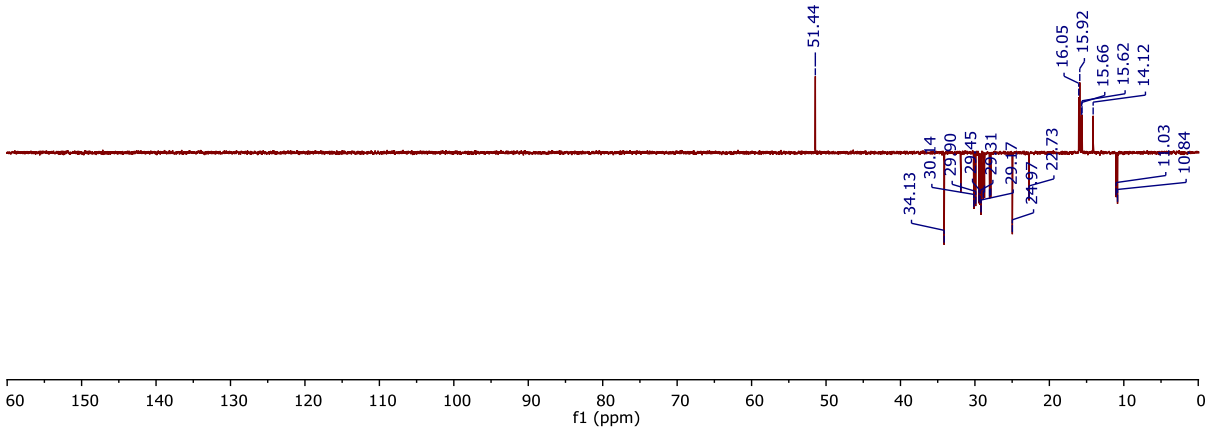
^{1}H NMR Spectrum (400.31 MHz, $CDCl_3$) of Compound **C3**



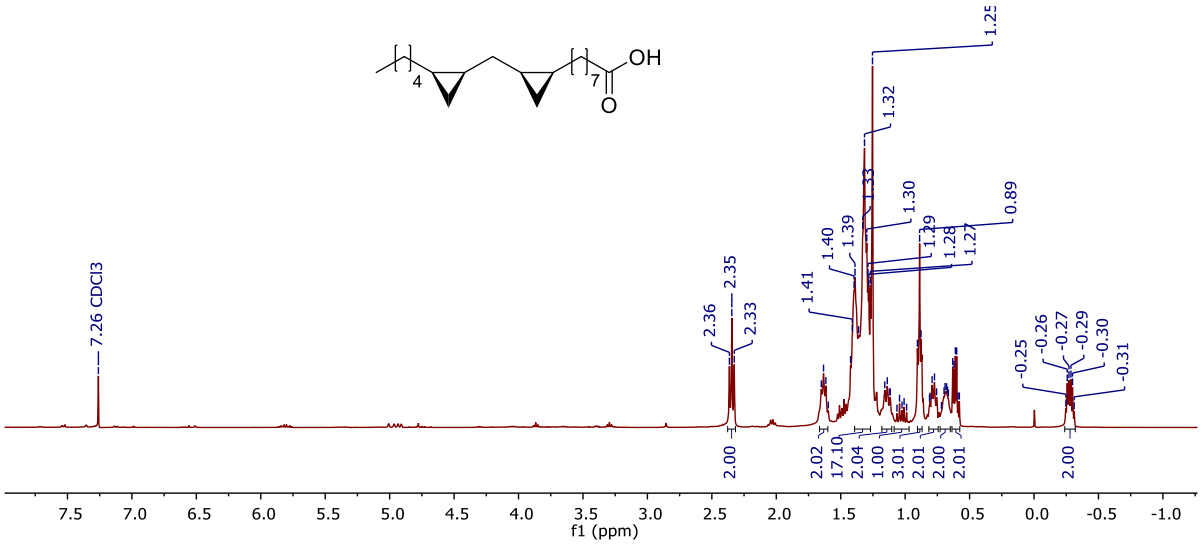
^{13}C NMR Spectrum (100.53 MHz, $CDCl_3$) of Compound **C3**



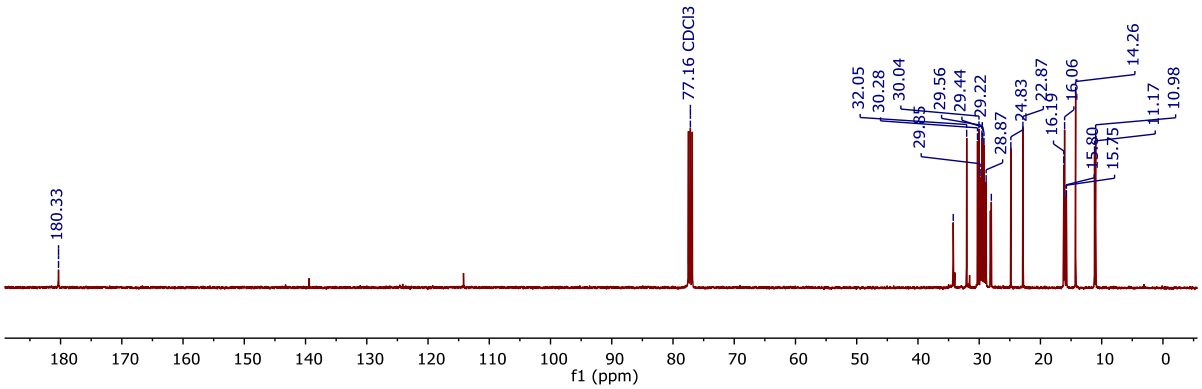
DEPT NMR Spectrum (100.53 MHz, $CDCl_3$) of Compound **C3**



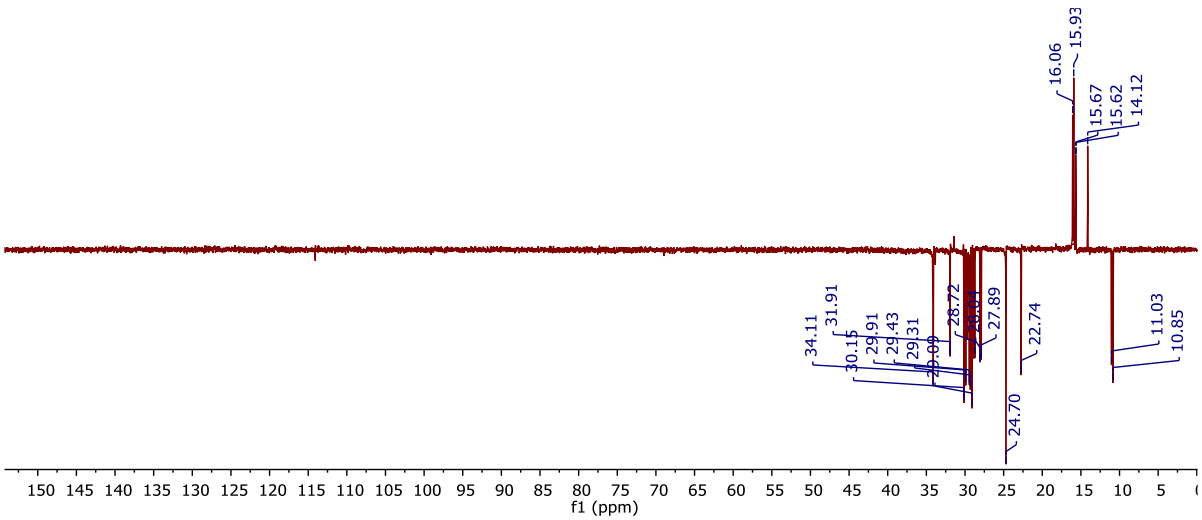
^{1}H NMR Spectrum (400.31 MHz, $CDCl_3$) of Compound **C4**



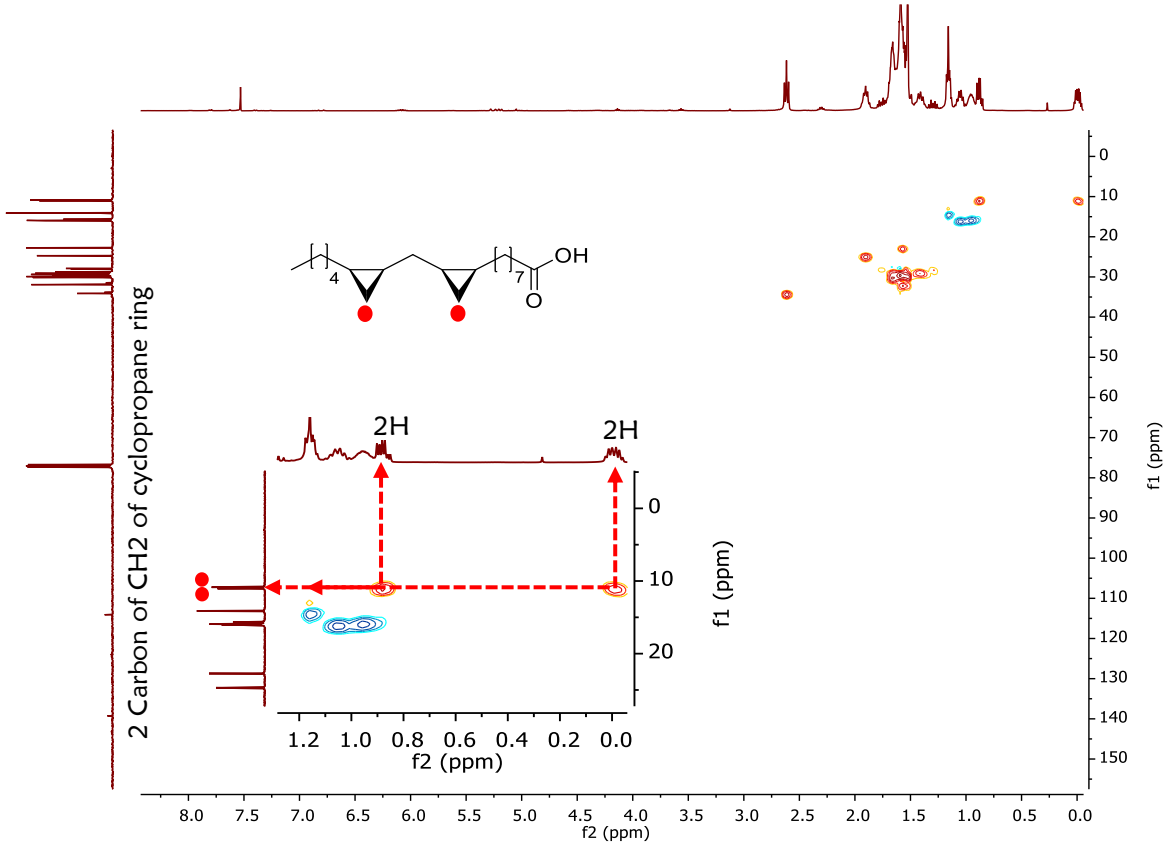
^{13}C NMR Spectrum (100.53 MHz, $CDCl_3$) of Compound **C4**



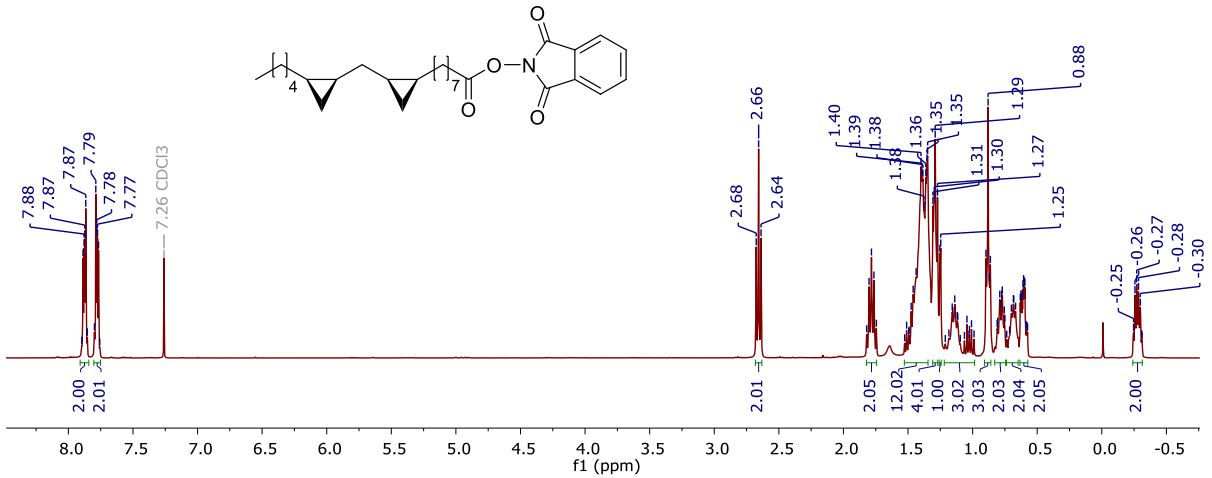
DEPT NMR Spectrum (100.53 MHz, $CDCl_3$) of Compound **C4**



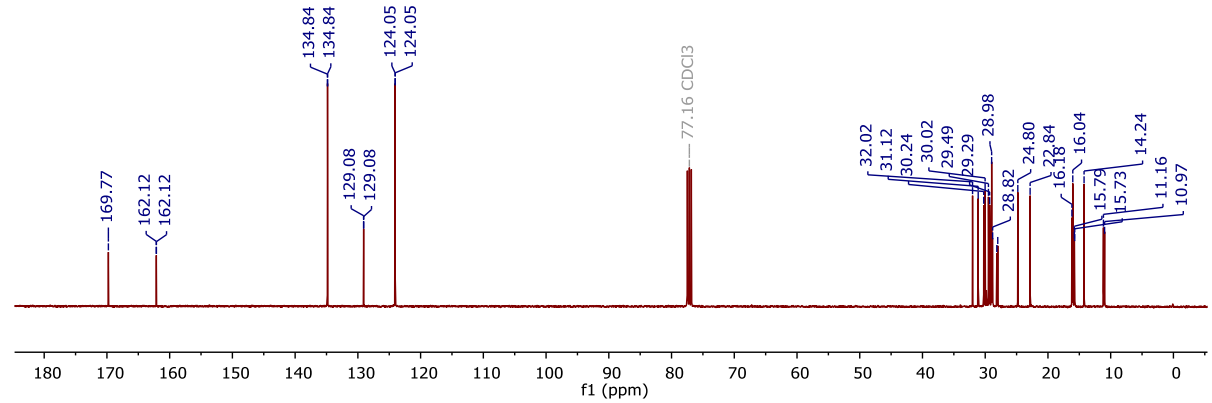
HMBC NMR Spectrum of Compound **C4**



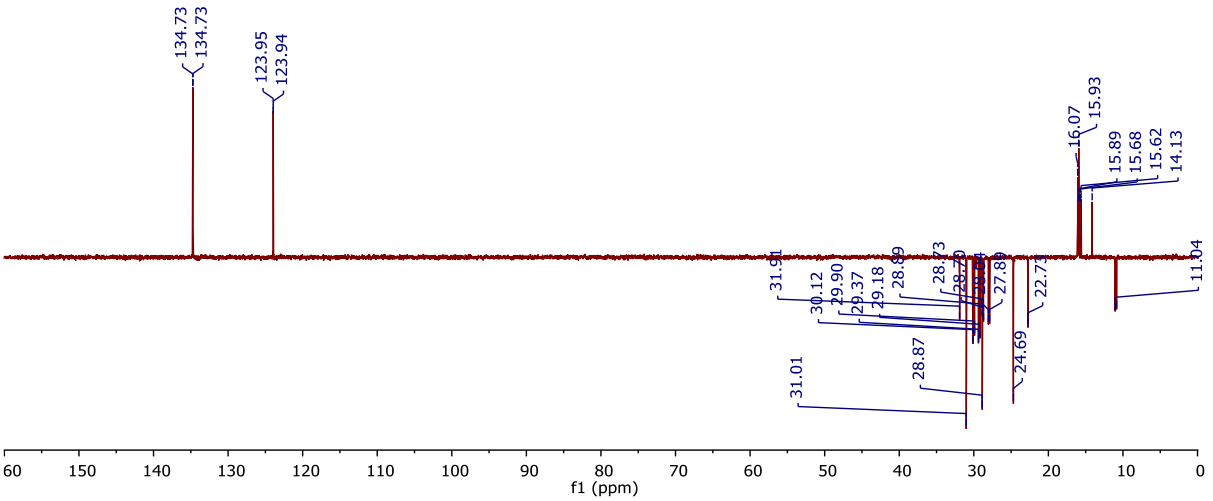
^{1}H NMR Spectrum (400.31 MHz, $CDCl_3$) of Compound **19c**



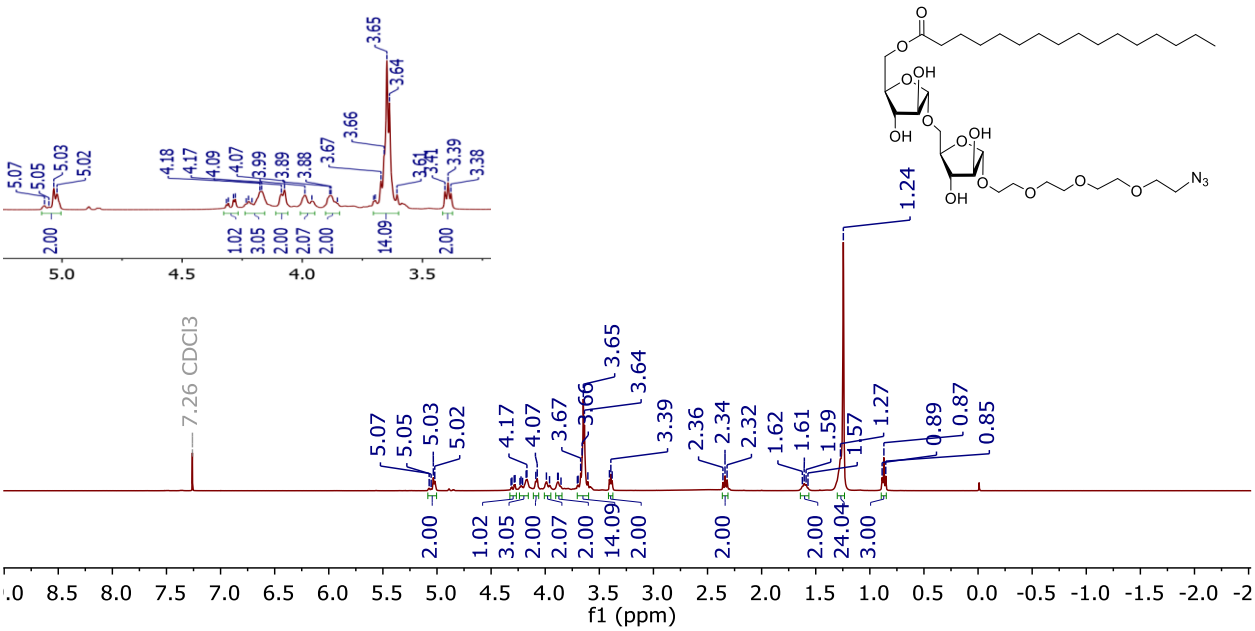
^{13}C NMR Spectrum (100.53 MHz, $CDCl_3$) of Compound **19c**



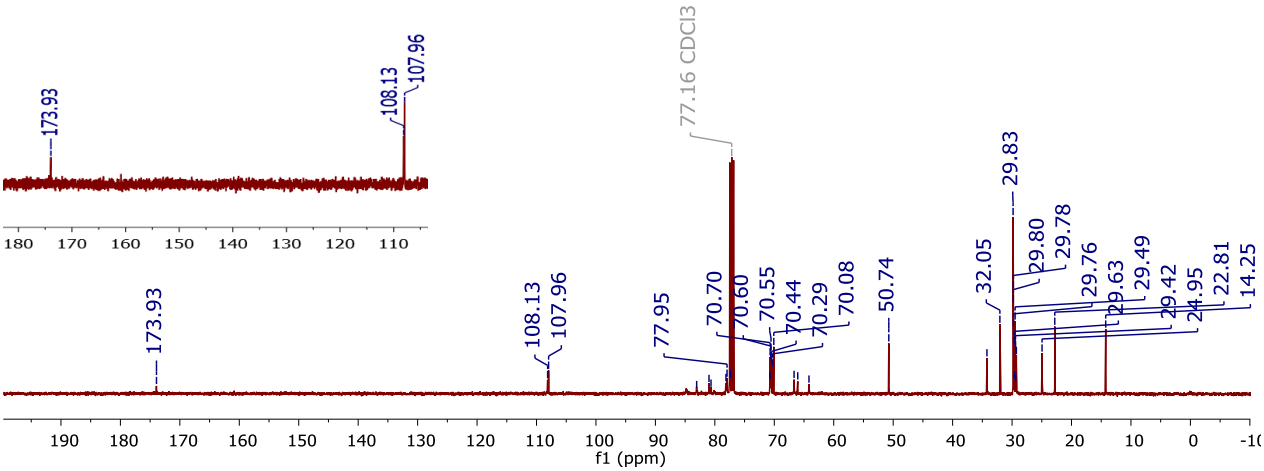
DEPT NMR Spectrum (100.53 MHz, $CDCl_3$) of Compound **19c**



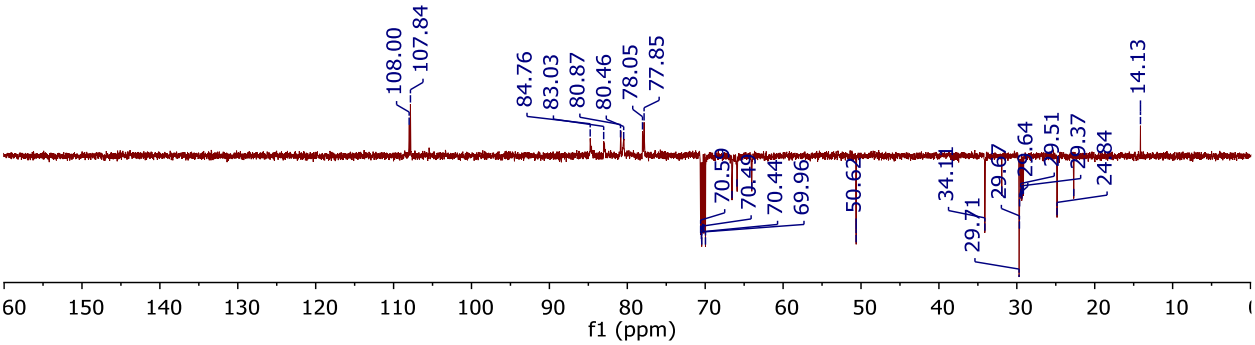
^{1}H NMR Spectrum (400.31 MHz, $CDCl_3$) of Compound **20a**



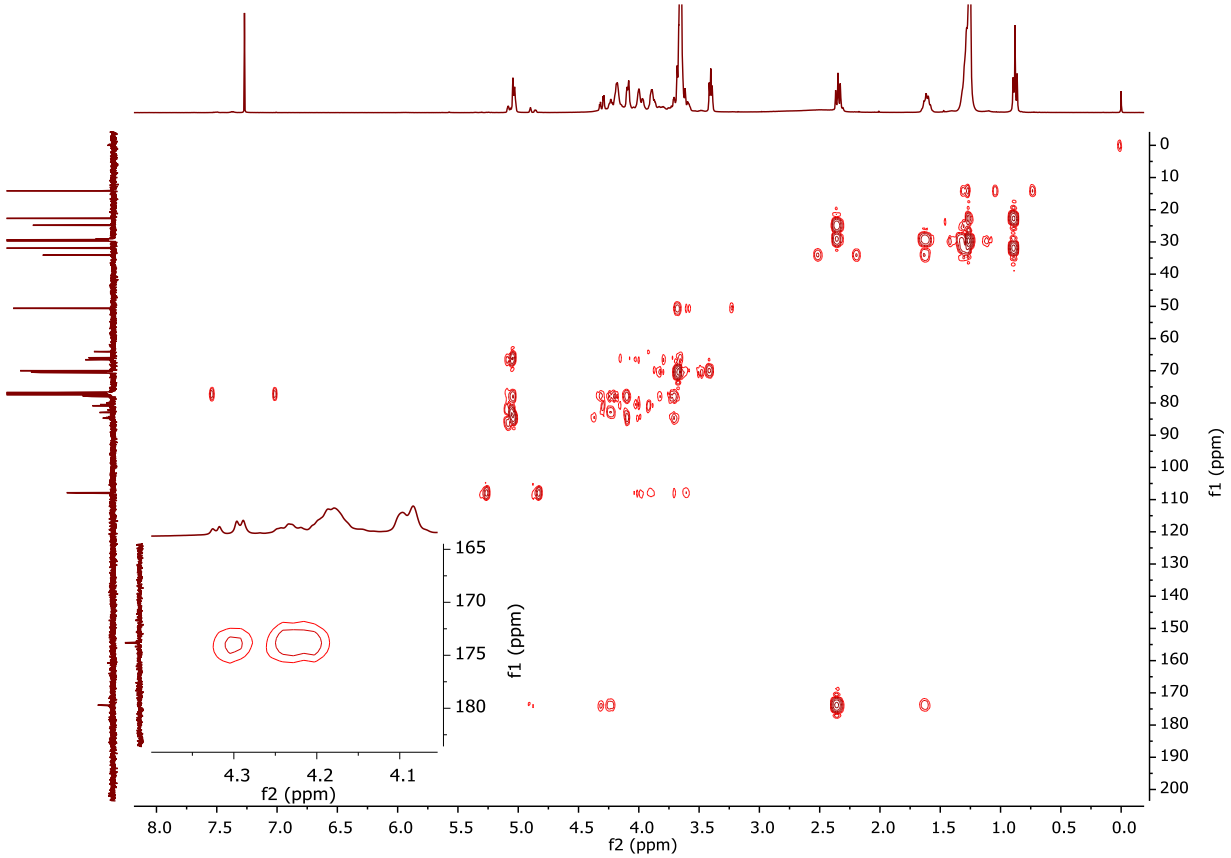
^{13}C NMR Spectrum (100.53 MHz, $CDCl_3$) of Compound **20a**



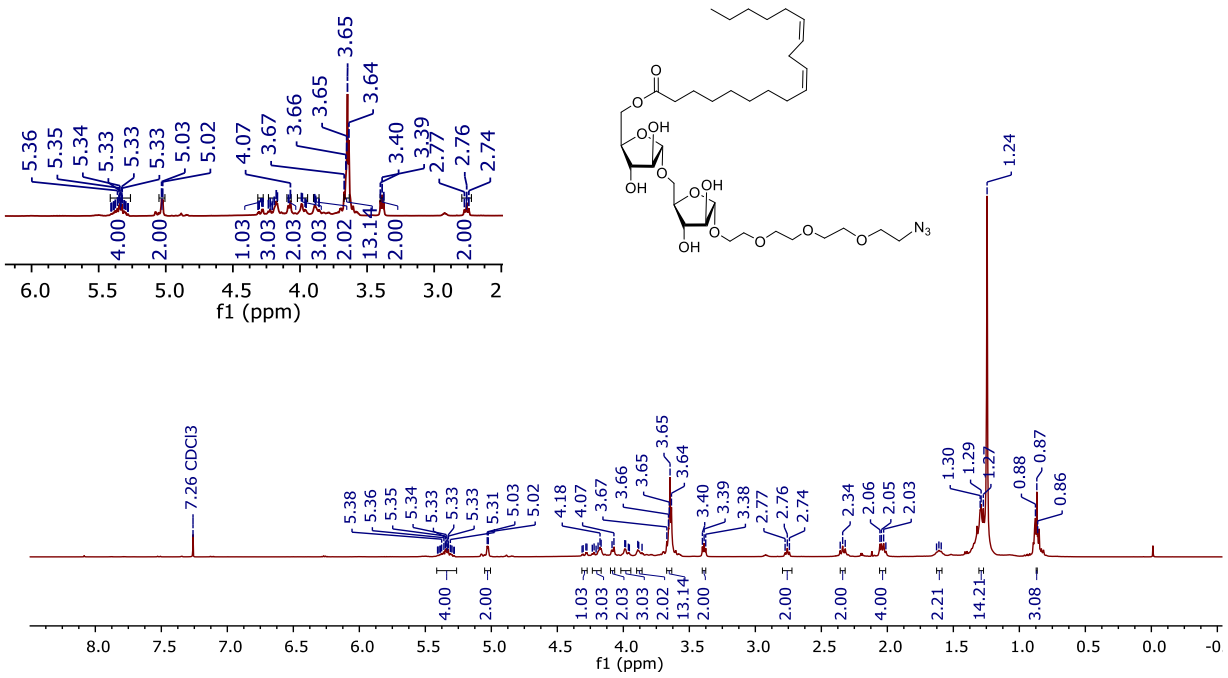
DEPT-NMR Spectrum (100.53 MHz, $CDCl_3$) of Compound **20a**



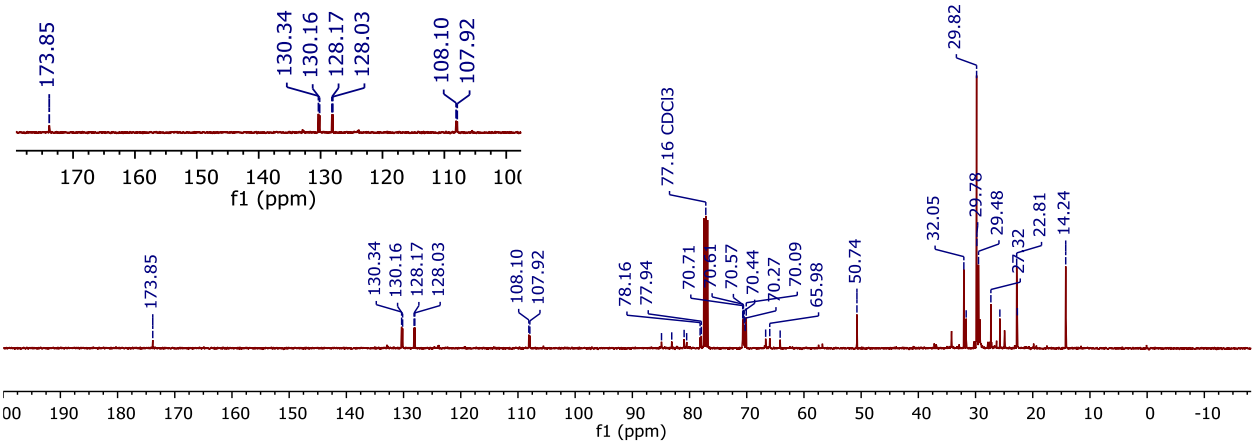
HMBC NMR Spectrum of Compound **20a**



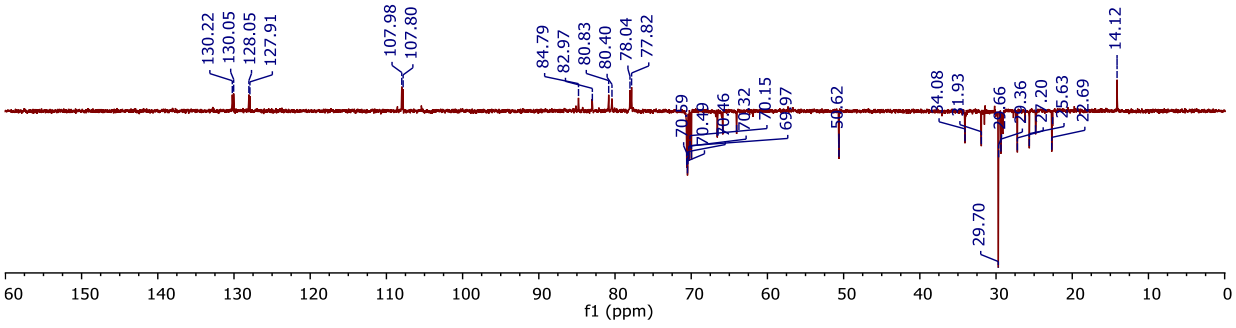
^{1}H NMR Spectrum (400.31 MHz, $CDCl_3$) of Compound **20b**



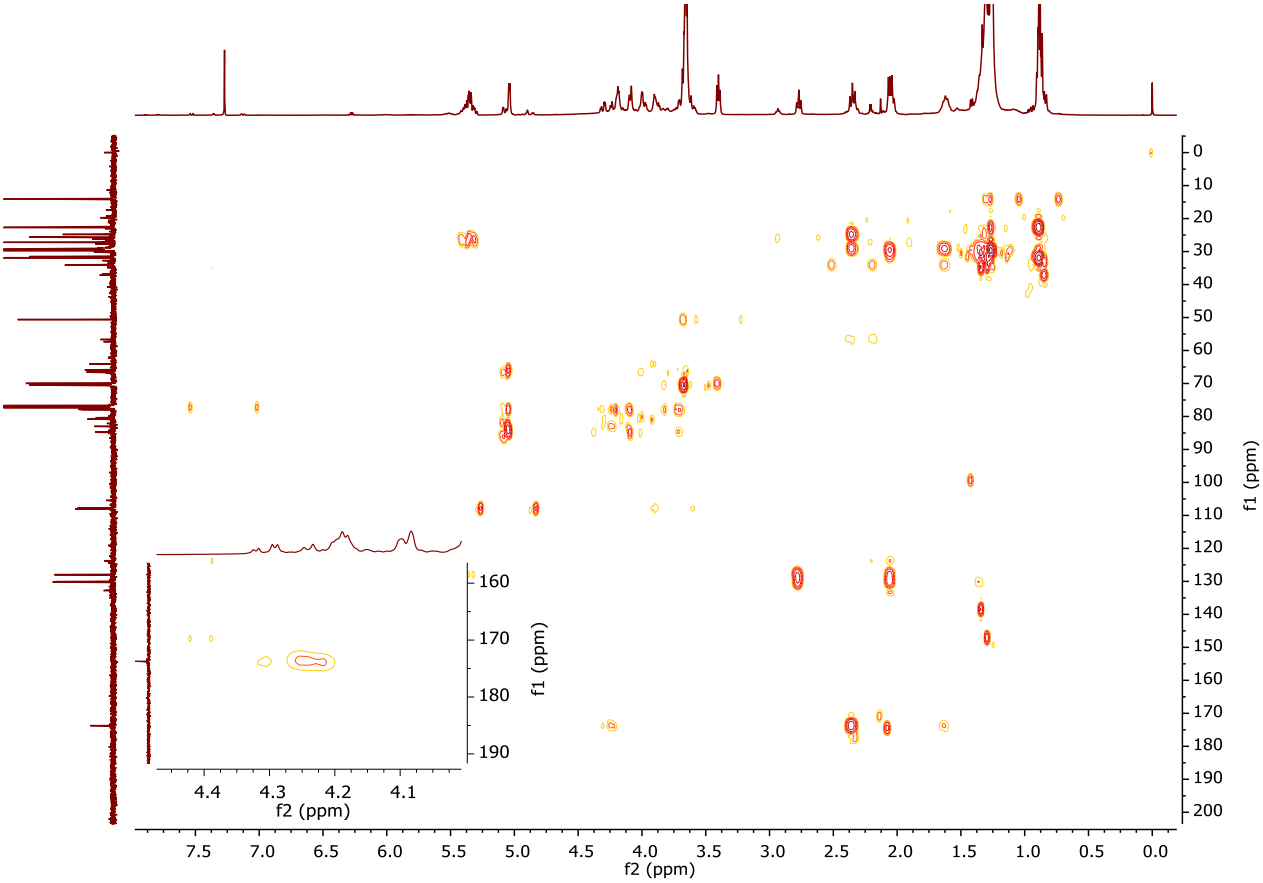
^{13}C NMR Spectrum (100.53 MHz, $CDCl_3$) of Compound **20b**



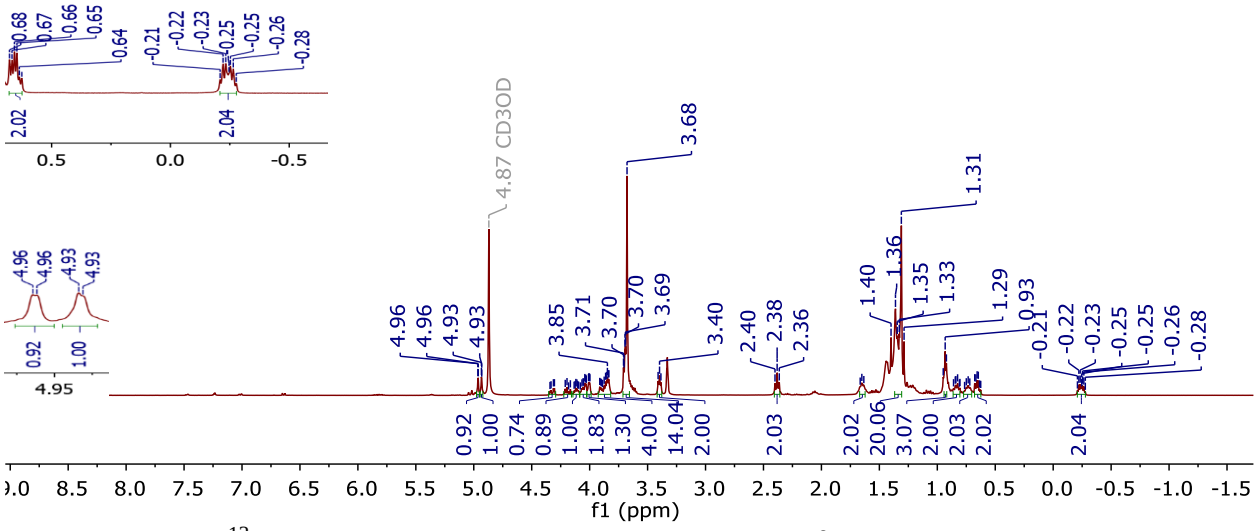
DEPT-NMR Spectrum (100.53 MHz, $CDCl_3$) of Compound **20b**



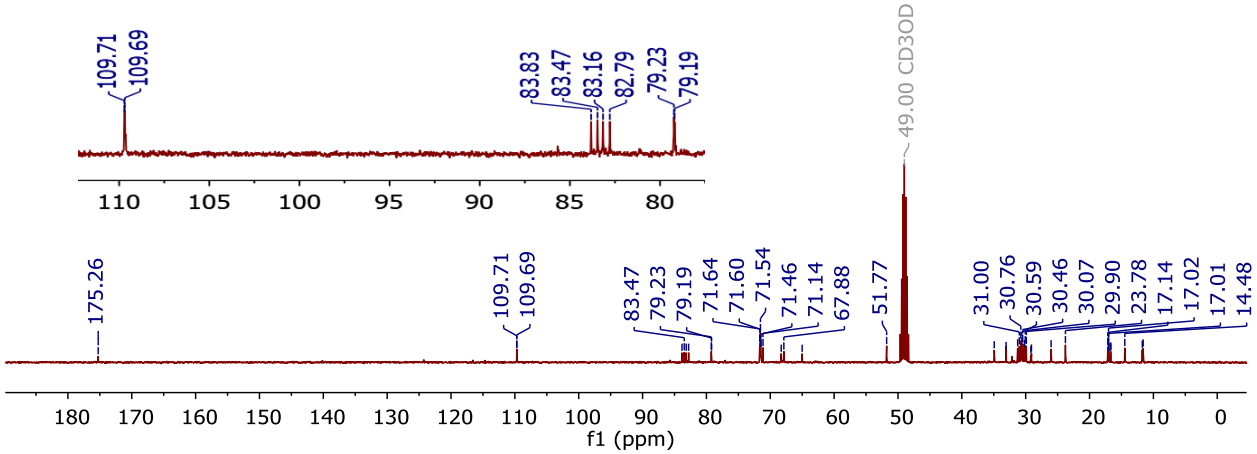
HMBC NMR Spectrum of Compound **20b**



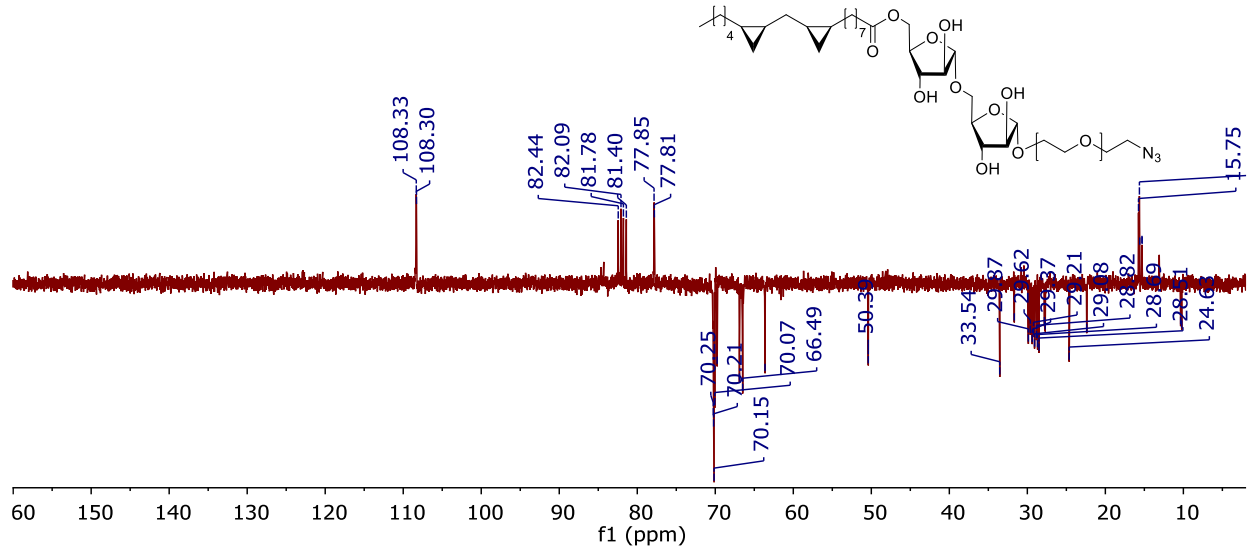
^{1}H NMR Spectrum (400.31 MHz, CD_3OD) of Compound **20c**



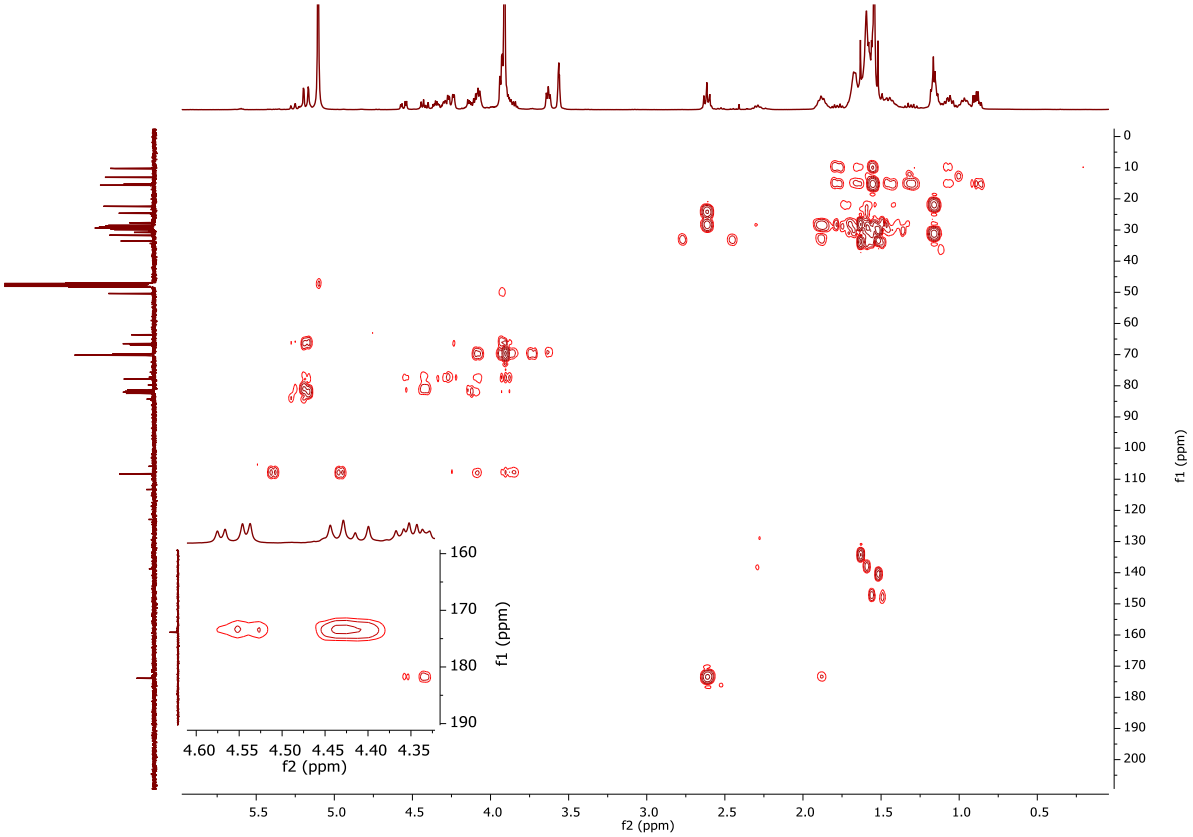
^{13}C NMR Spectrum (100.53 MHz, CD_3OD) of Compound **20c**



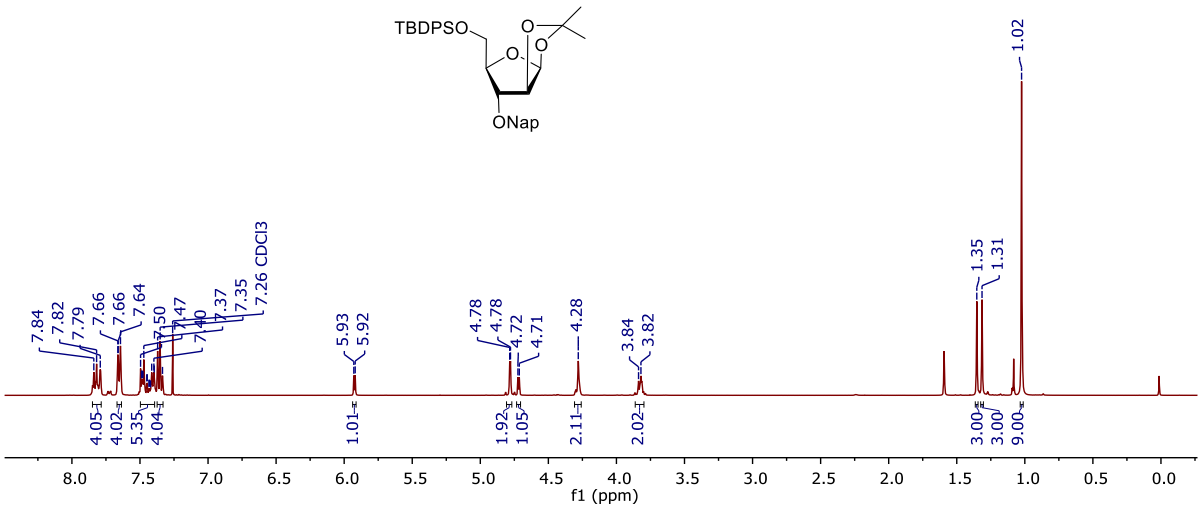
DEPT-NMR Spectrum (100.53 MHz, CD_3OD) of Compound **20c**



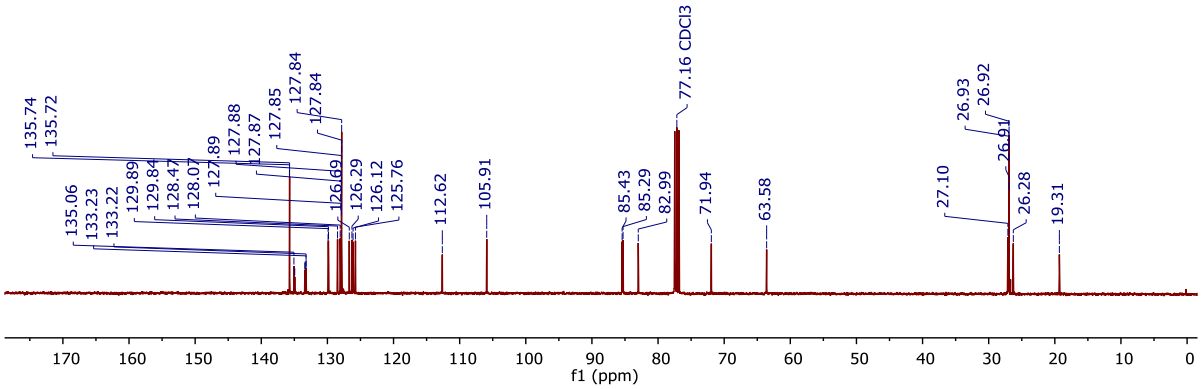
HMBC NMR Spectrum of Compound **20c**



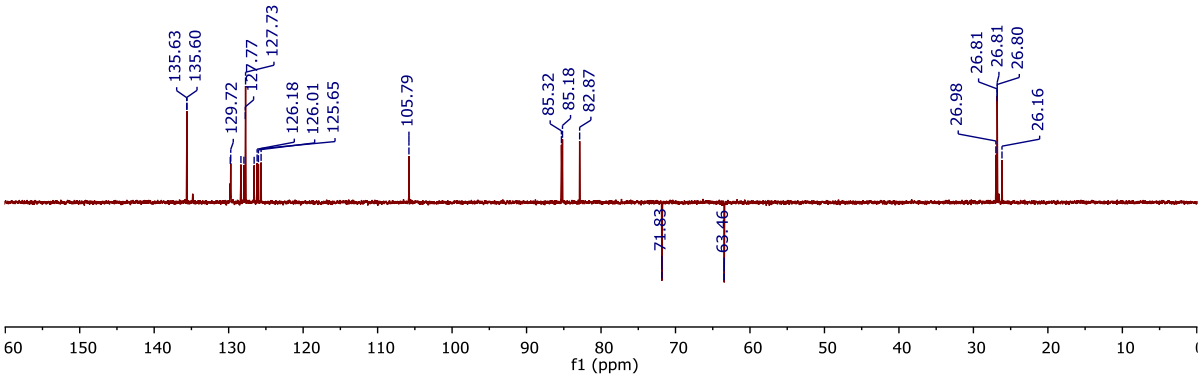
^{1}H NMR Spectrum (400.31 MHz, $CDCl_3$) of Compound **S2**



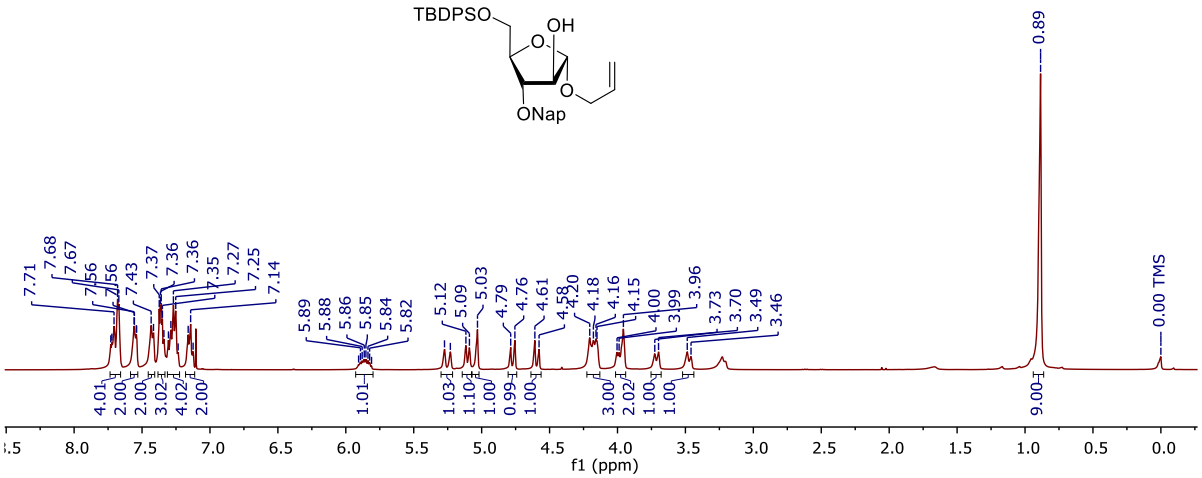
^{13}C NMR Spectrum (100.53 MHz, $CDCl_3$) of Compound **S2**



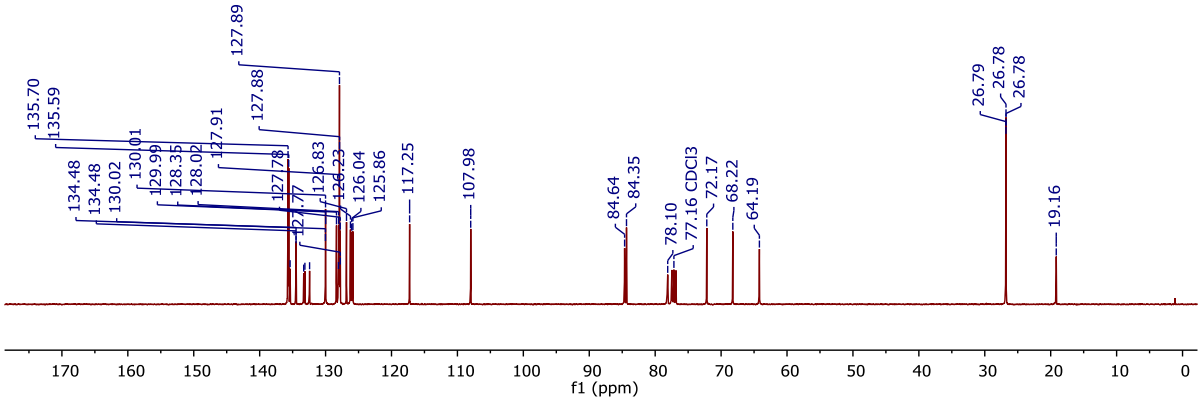
DEPT NMR Spectrum (100.53 MHz, $CDCl_3$) of Compound **S2**



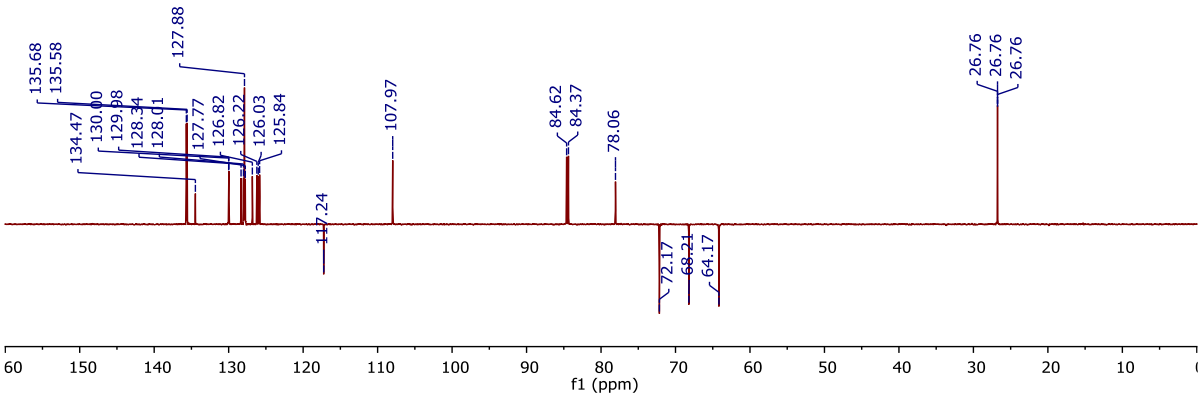
^{1}H NMR Spectrum (400.31 MHz, $CDCl_3$) of Compound **S3**



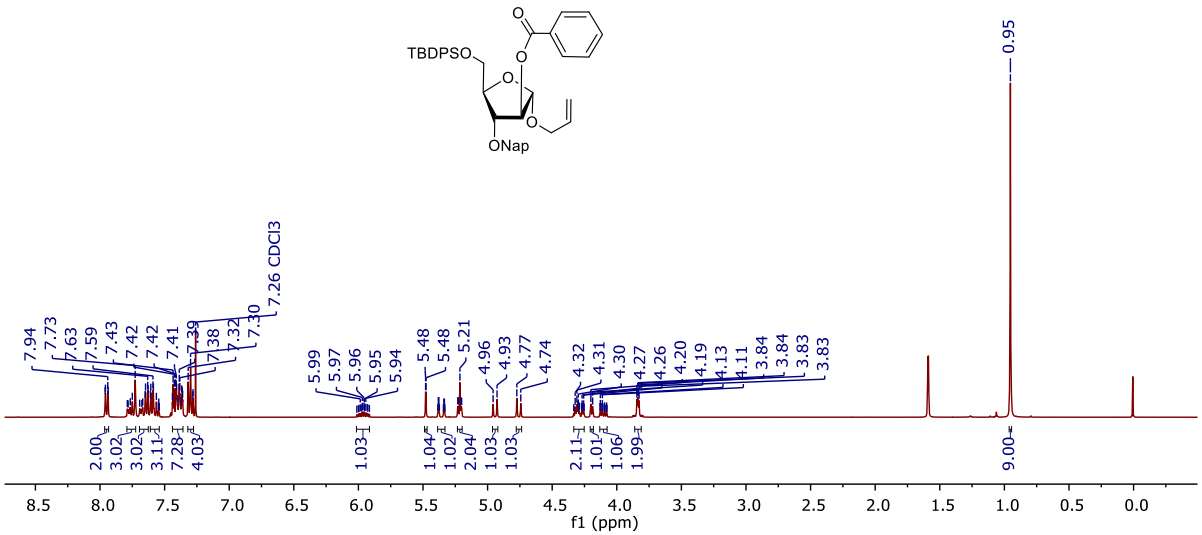
^{13}C NMR Spectrum (100.53 MHz, $CDCl_3$) of Compound **S3**



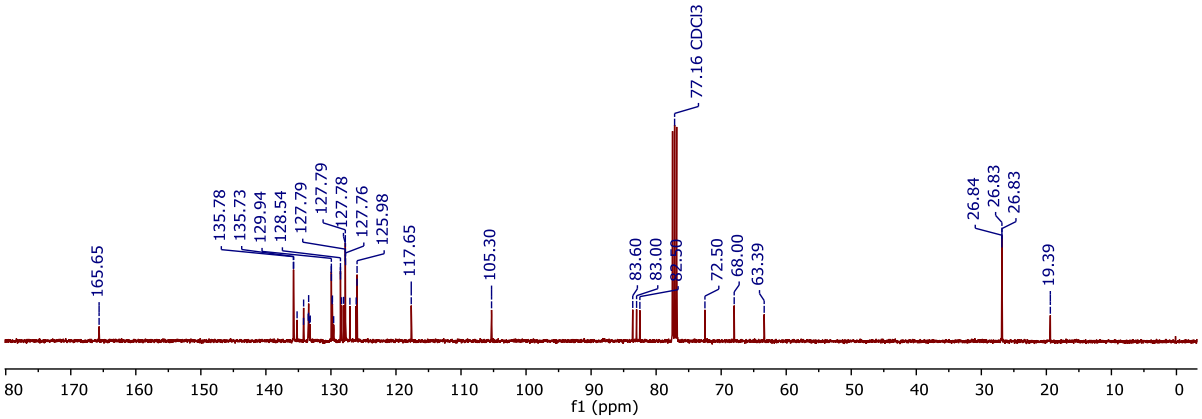
DEPT NMR Spectrum (100.53 MHz, $CDCl_3$) of Compound **S3**



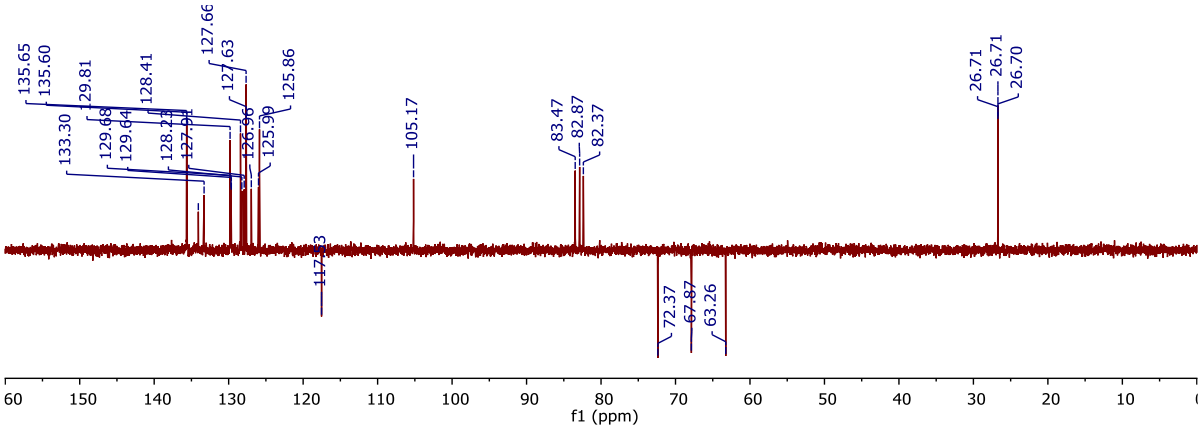
^{1}H NMR Spectrum (400.31 MHz, $CDCl_3$) of Compound **S4**



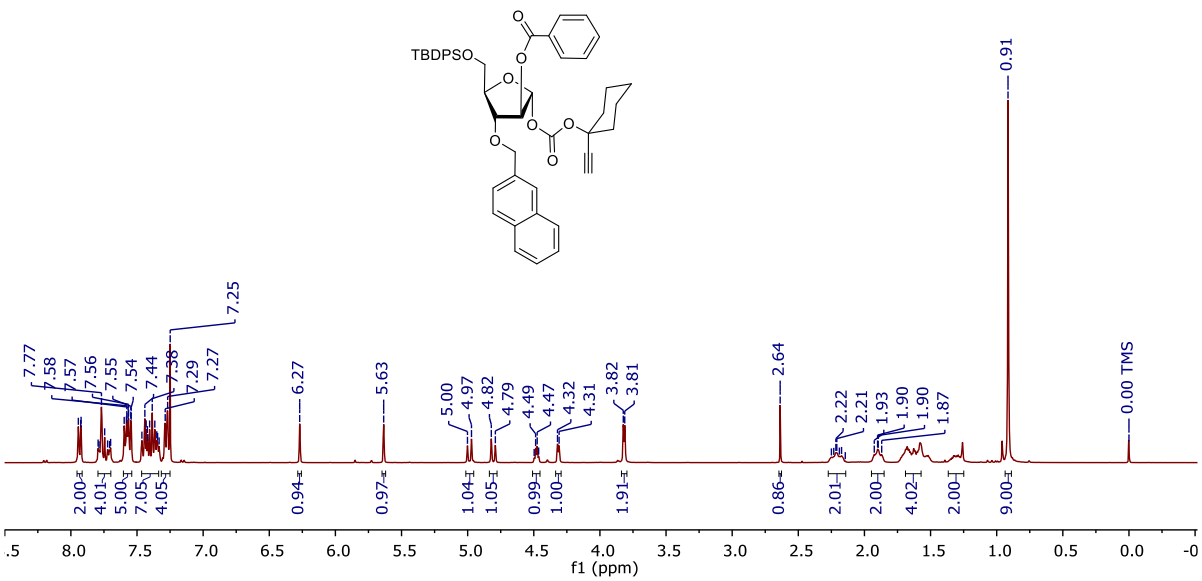
^{13}C NMR Spectrum (100.53 MHz, $CDCl_3$) of Compound **S4**



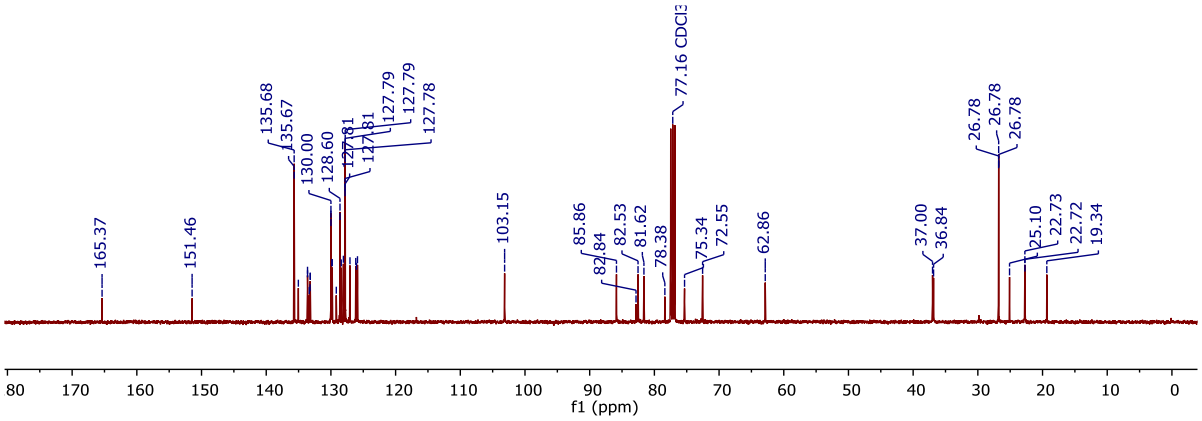
DEPT NMR Spectrum (100.53 MHz, $CDCl_3$) of Compound **S4**



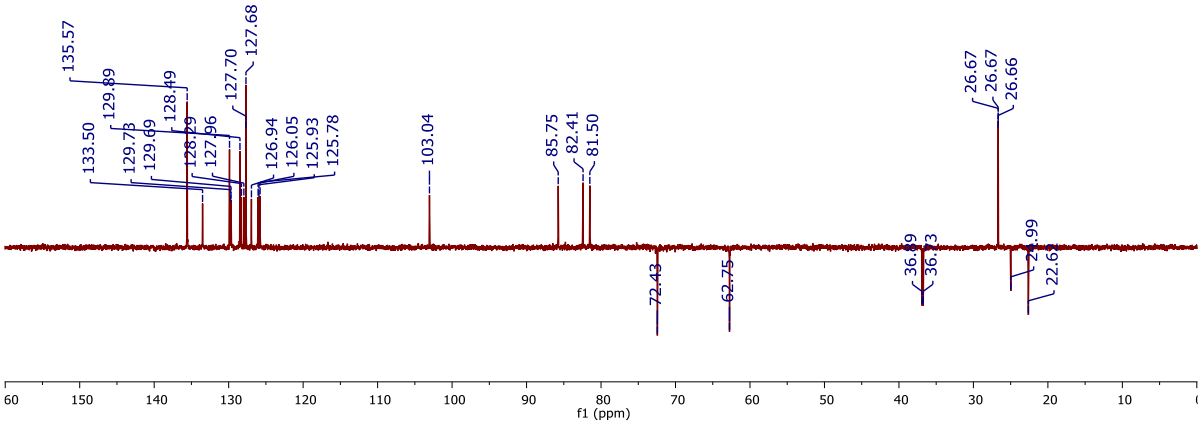
^{1}H NMR Spectrum (400.31 MHz, $CDCl_3$) of Compound **1b**



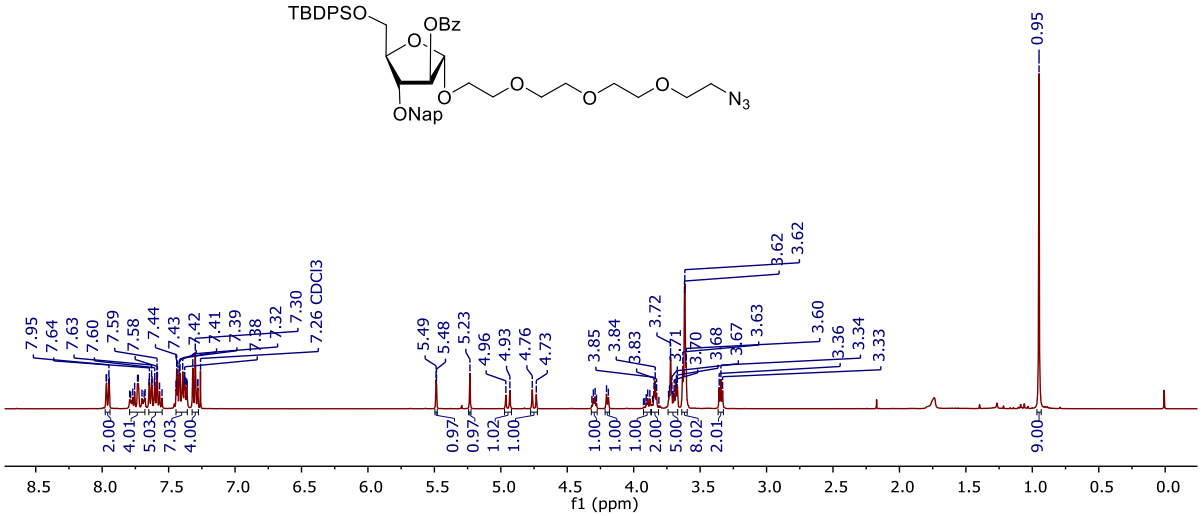
^{13}C NMR Spectrum (100.53 MHz, $CDCl_3$) of Compound **1b**



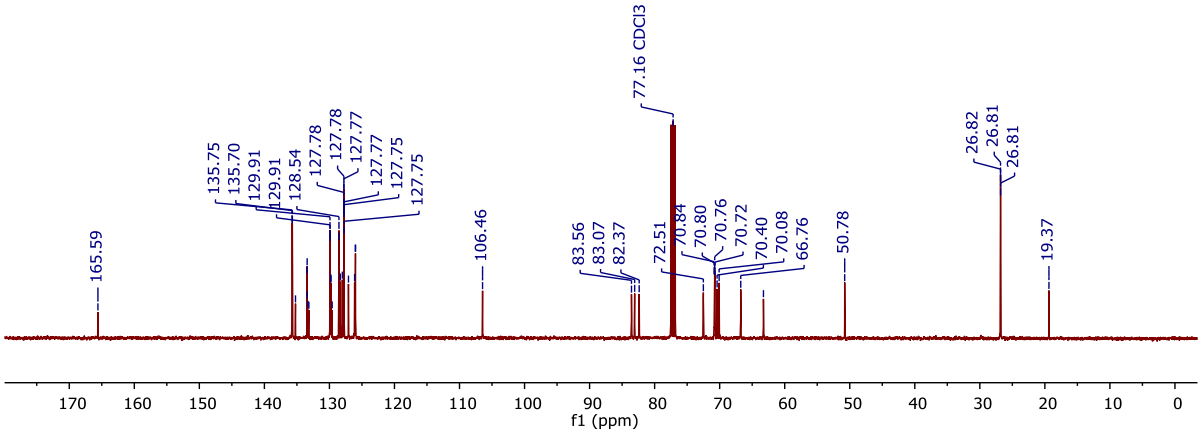
DEPT NMR Spectrum (100.53 MHz, $CDCl_3$) of Compound **1b**



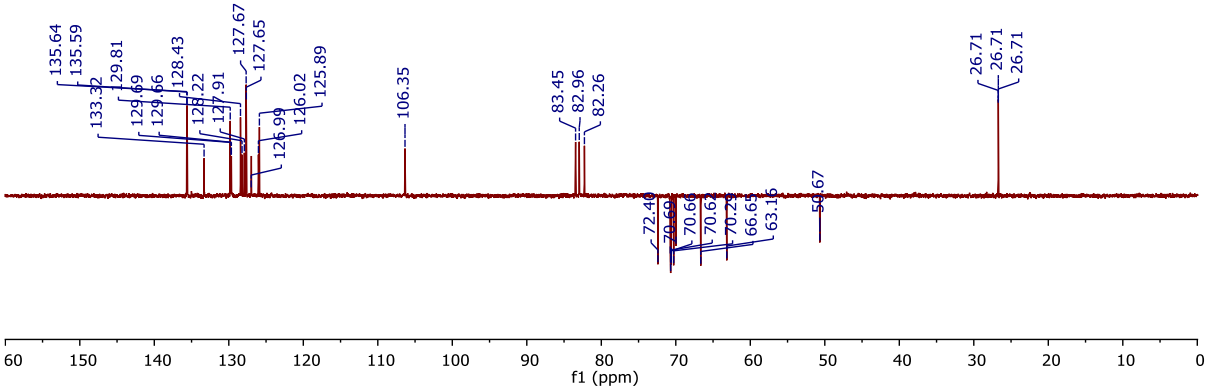
^{1}H NMR Spectrum (400.31 MHz, $CDCl_3$) of Compound **8**



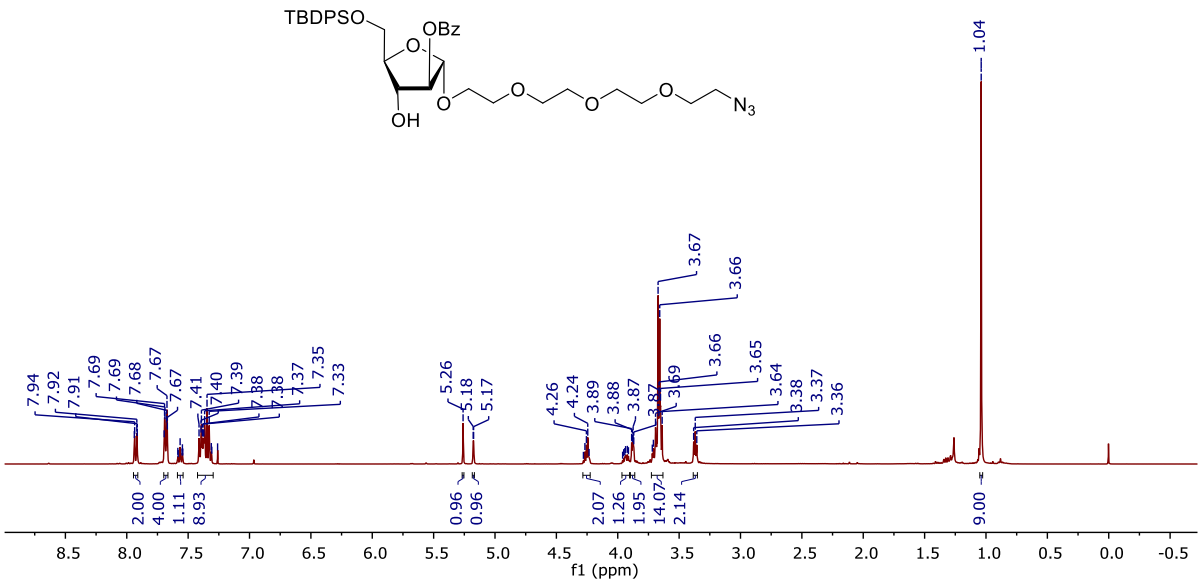
^{13}C NMR Spectrum (100.53 MHz, $CDCl_3$) of Compound **8**



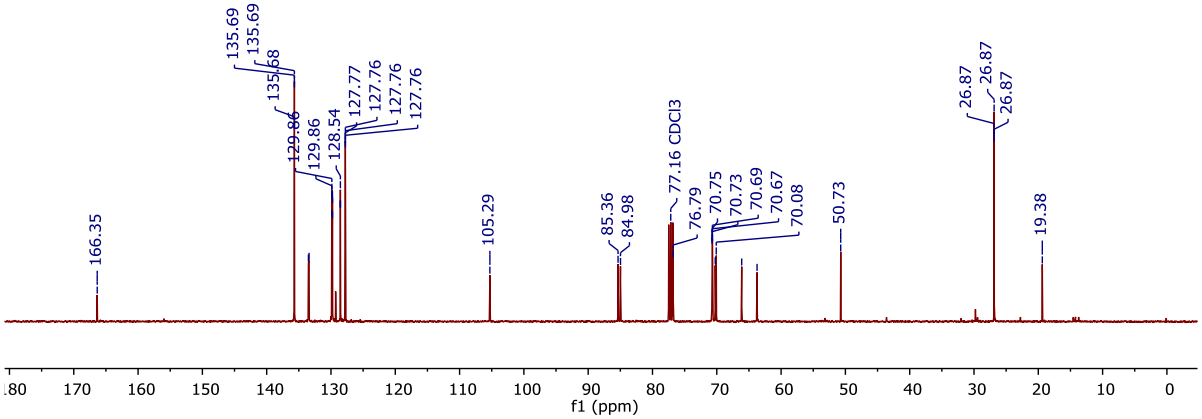
DEPT NMR Spectrum (100.53 MHz, $CDCl_3$) of Compound **8**



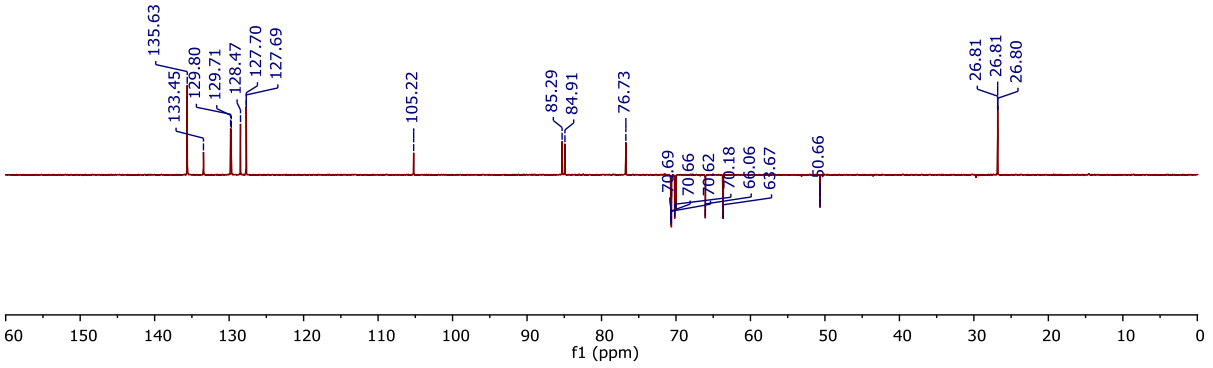
^{1}H NMR Spectrum (400.31 MHz, $CDCl_3$) of Compound **S5**



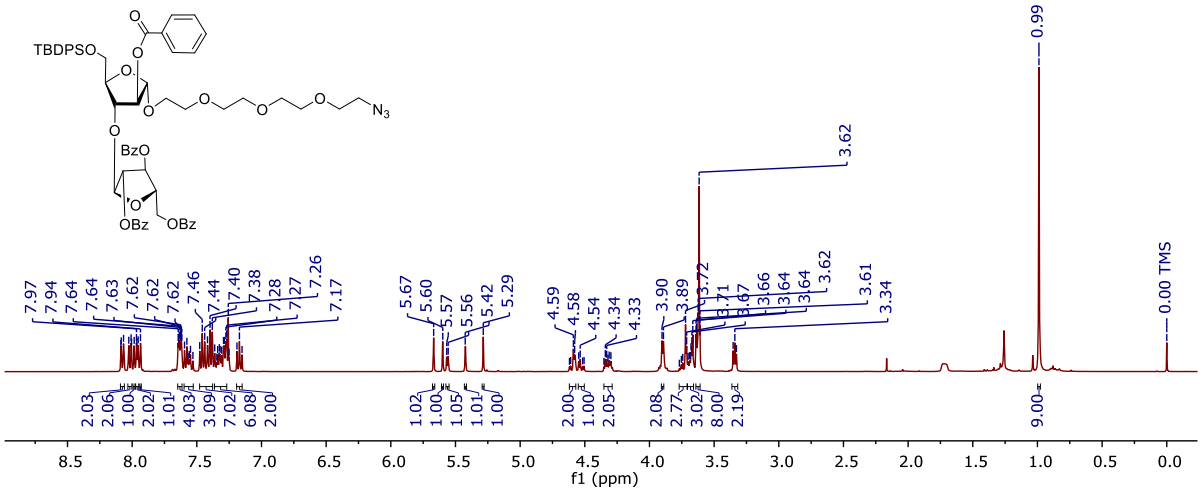
^{13}C NMR Spectrum (100.53 MHz, $CDCl_3$) of Compound **S5**



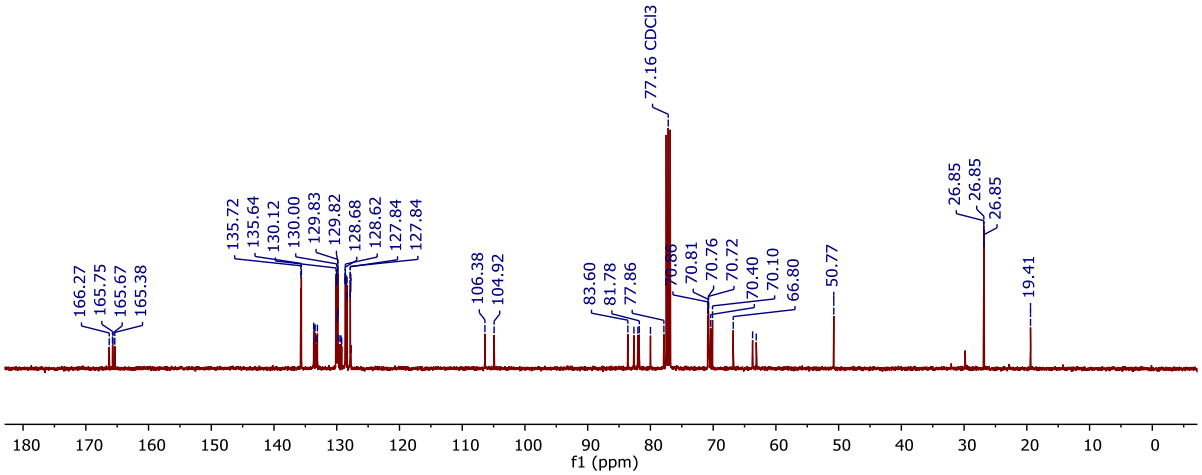
DEPT NMR Spectrum (100.53 MHz, $CDCl_3$) of Compound **S5**



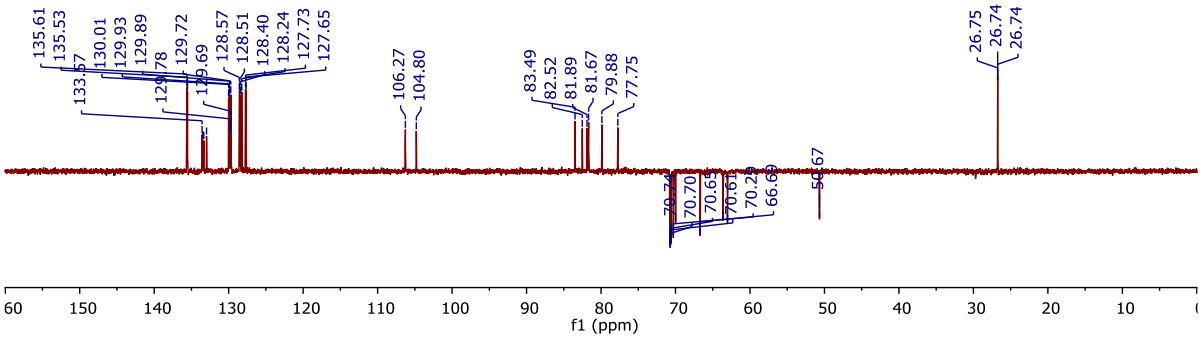
^{1}H NMR Spectrum (400.31 MHz, $CDCl_3$) of Compound **9**



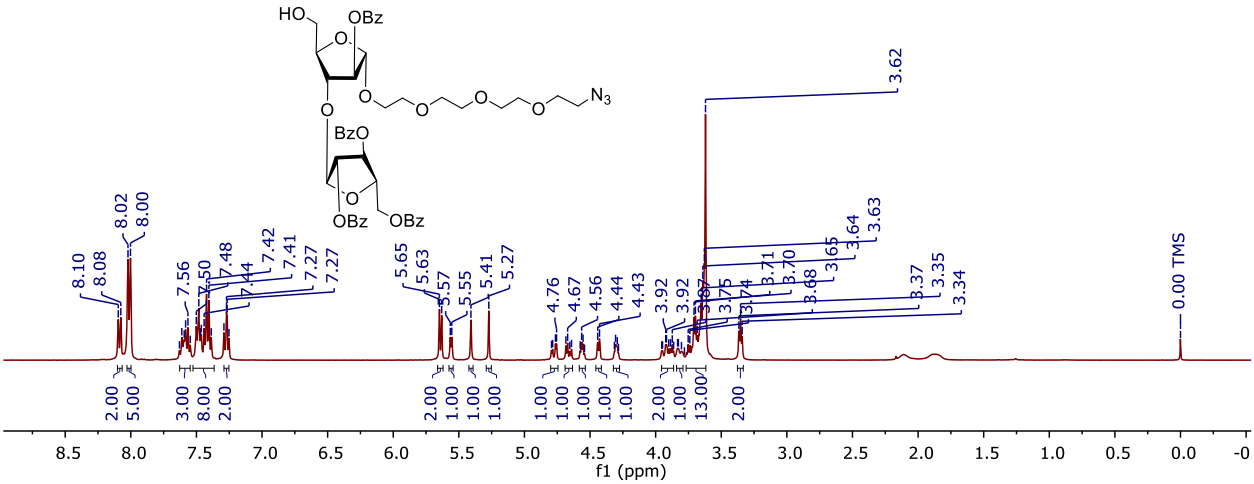
^{13}C NMR Spectrum (100.53 MHz, $CDCl_3$) of Compound **9**



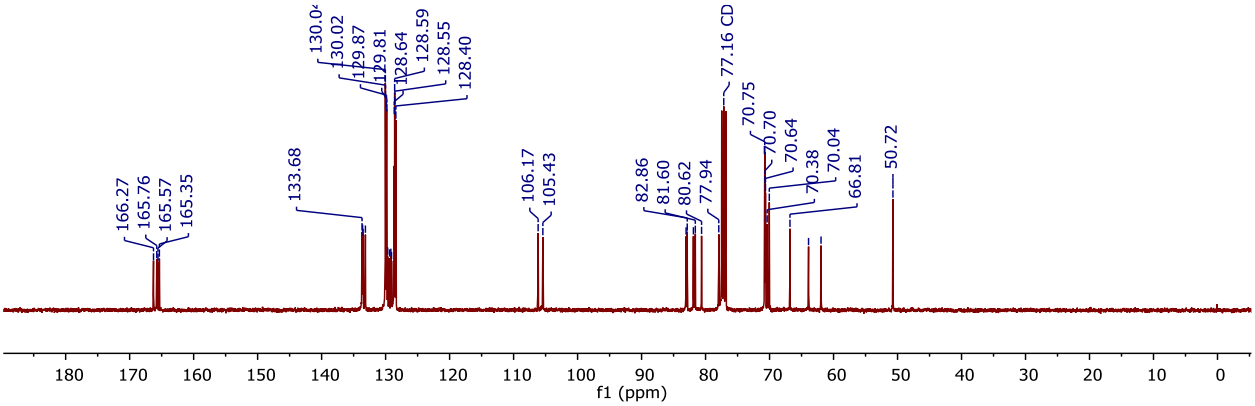
DEPT-NMR Spectrum (100.53 MHz, $CDCl_3$) of Compound **9**



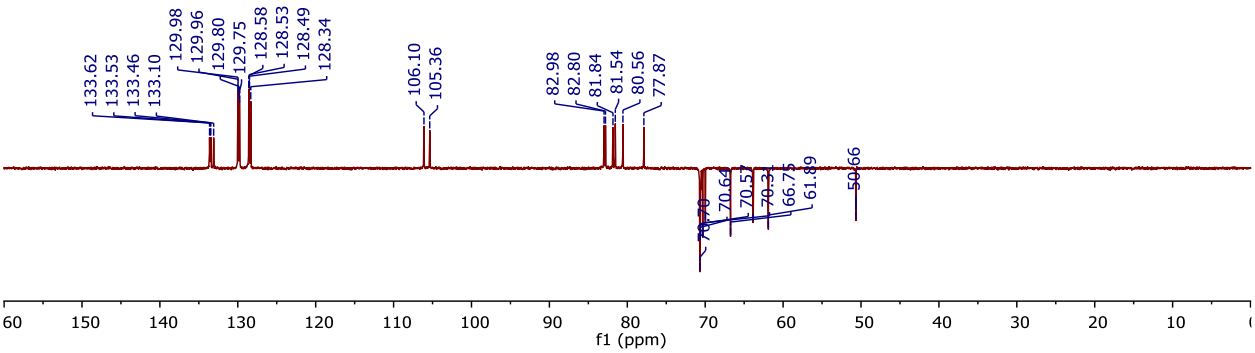
^{1}H NMR Spectrum (400.31 MHz, $CDCl_3$) of Compound **10**



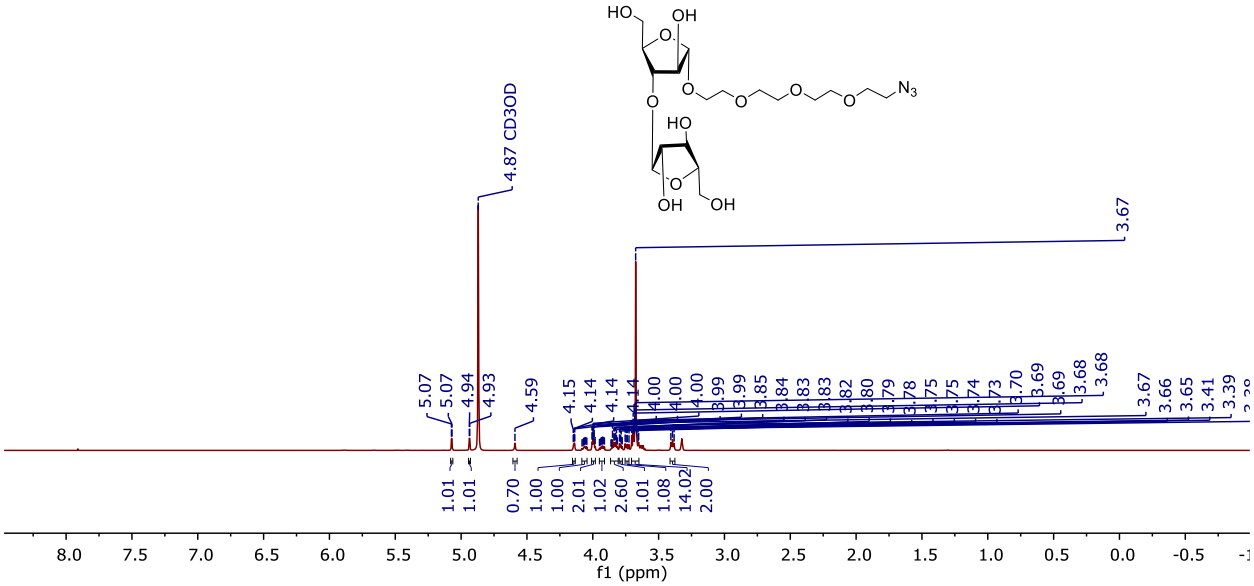
^{13}C NMR Spectrum (100.53 MHz, $CDCl_3$) of Compound **10**



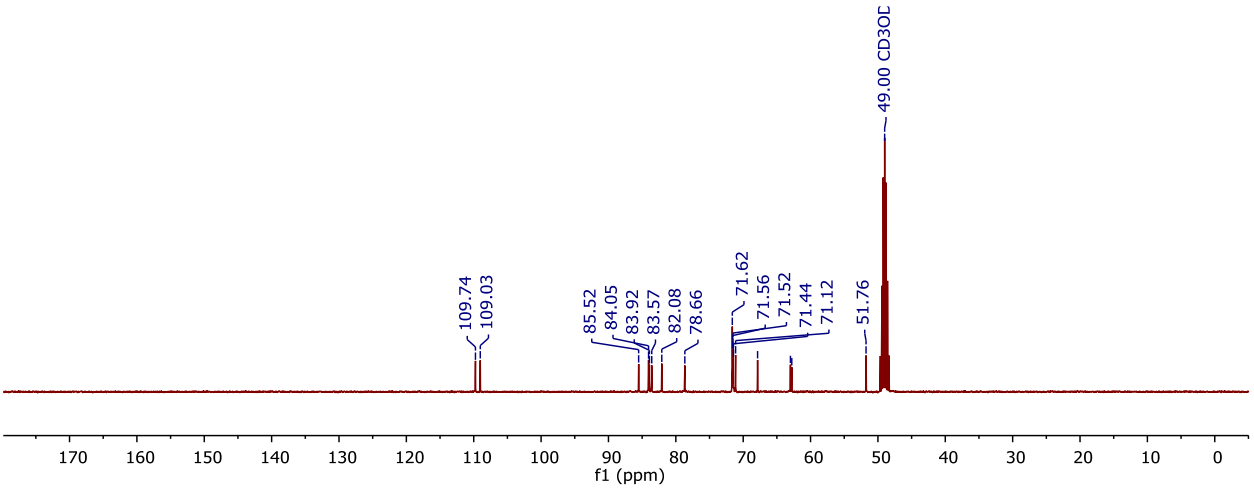
DEPT-NMR Spectrum (100.53 MHz, $CDCl_3$) of Compound **10**



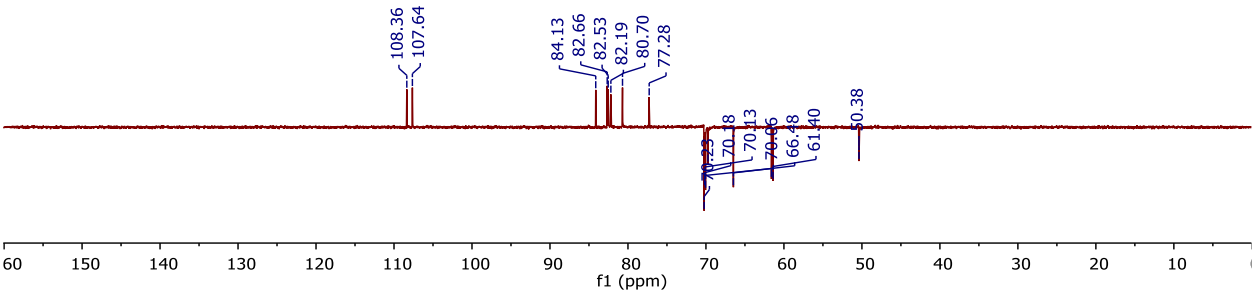
^{1}H NMR Spectrum (400.31 MHz, CD_3OD) of Compound **11**



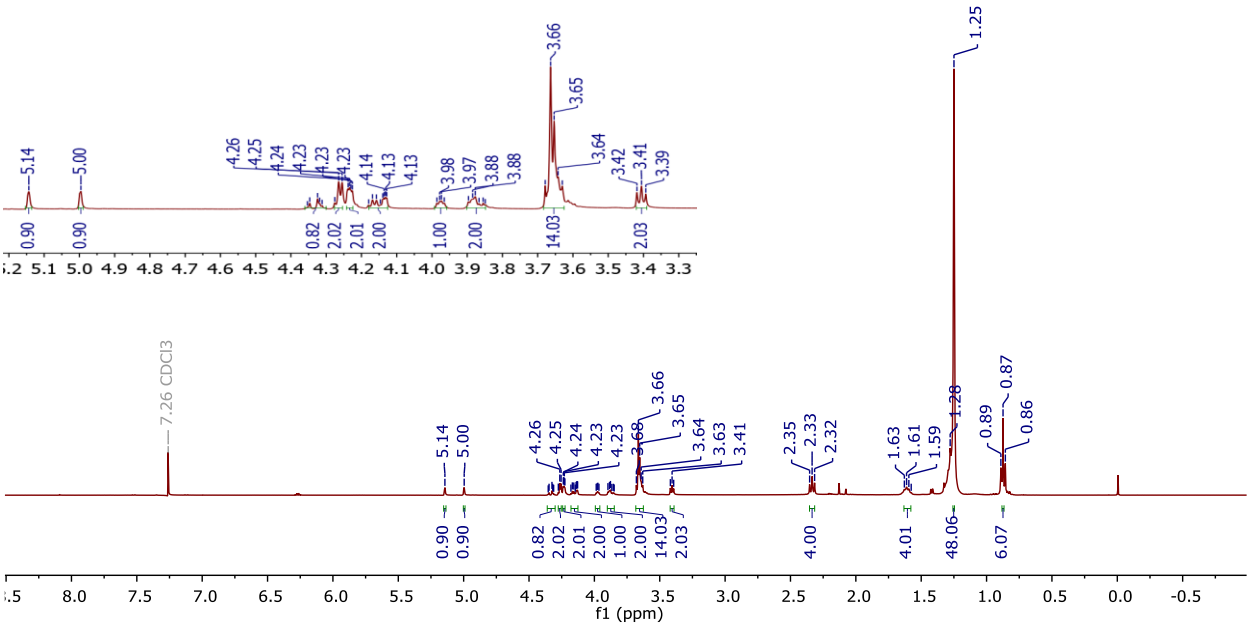
^{13}C NMR Spectrum (100.53 MHz, CD_3OD) of Compound **11**



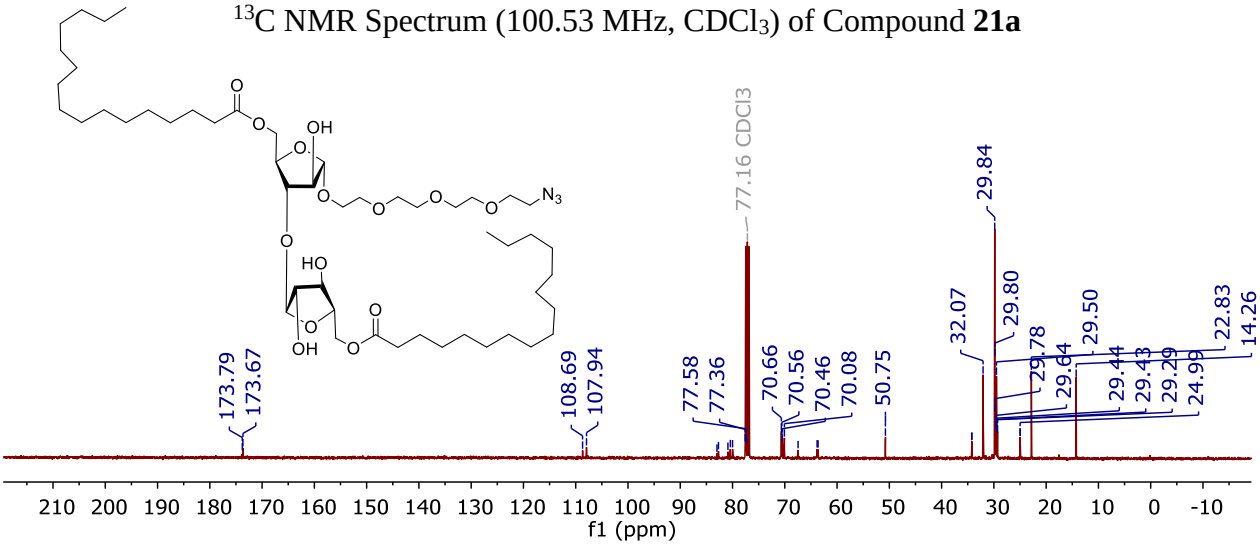
DEPT-NMR Spectrum (100.53 MHz, CD_3OD) of Compound **11**



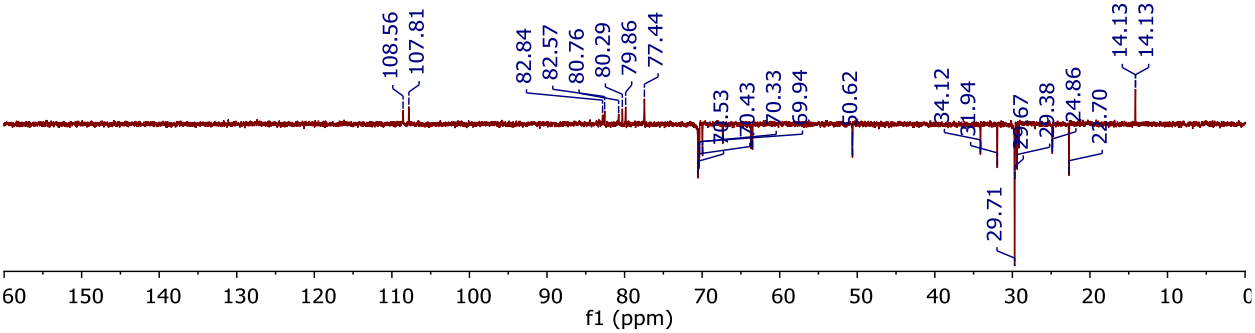
^{1}H NMR Spectrum (400.31 MHz, $CDCl_3$) of Compound **21a**



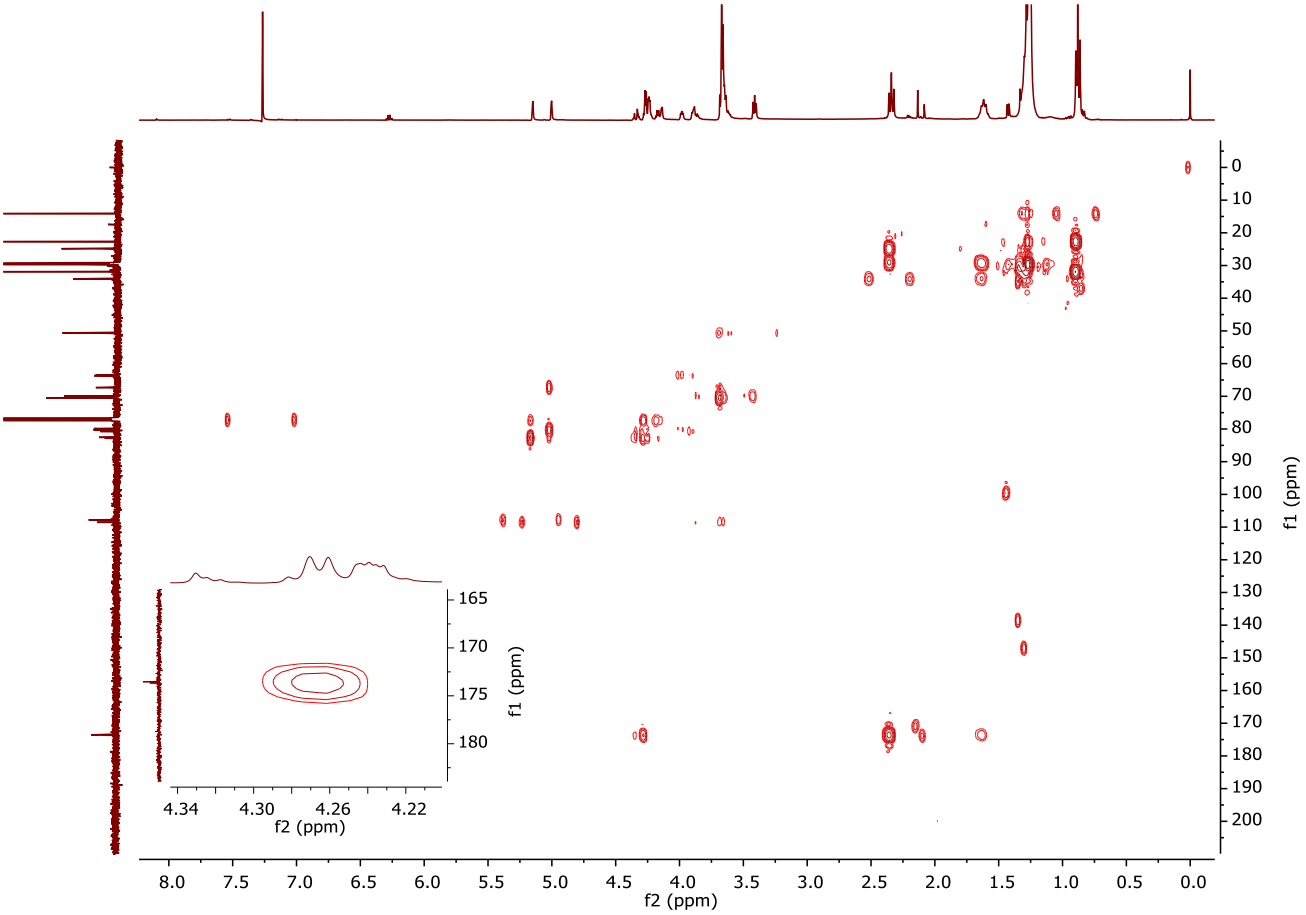
^{13}C NMR Spectrum (100.53 MHz, $CDCl_3$) of Compound **21a**



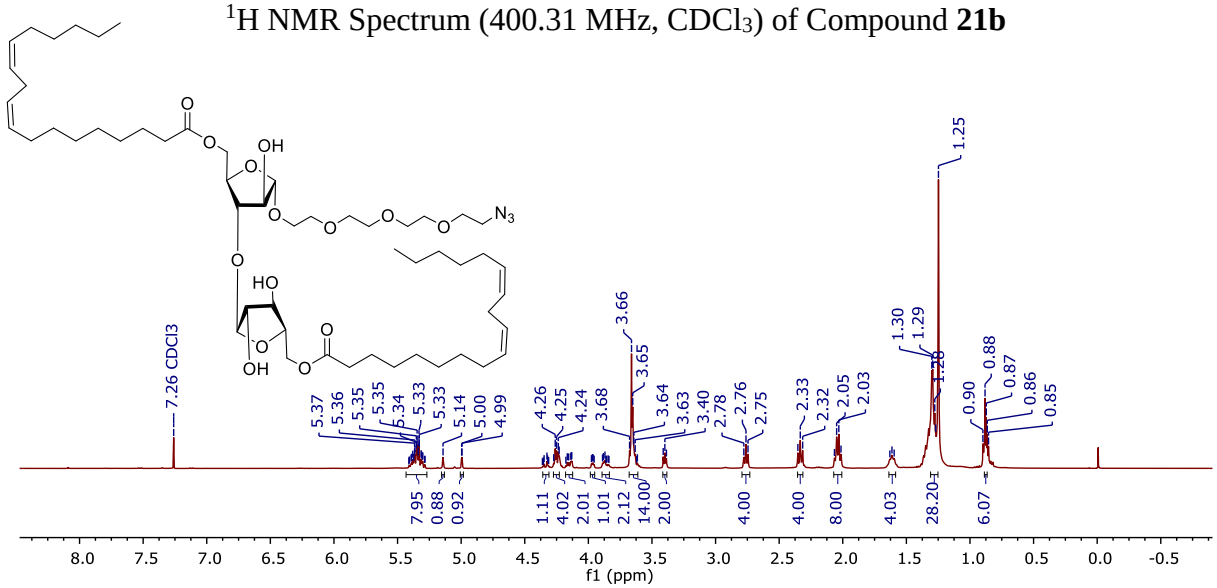
DEPT-NMR Spectrum (100.53 MHz, $CDCl_3$) of Compound **21a**



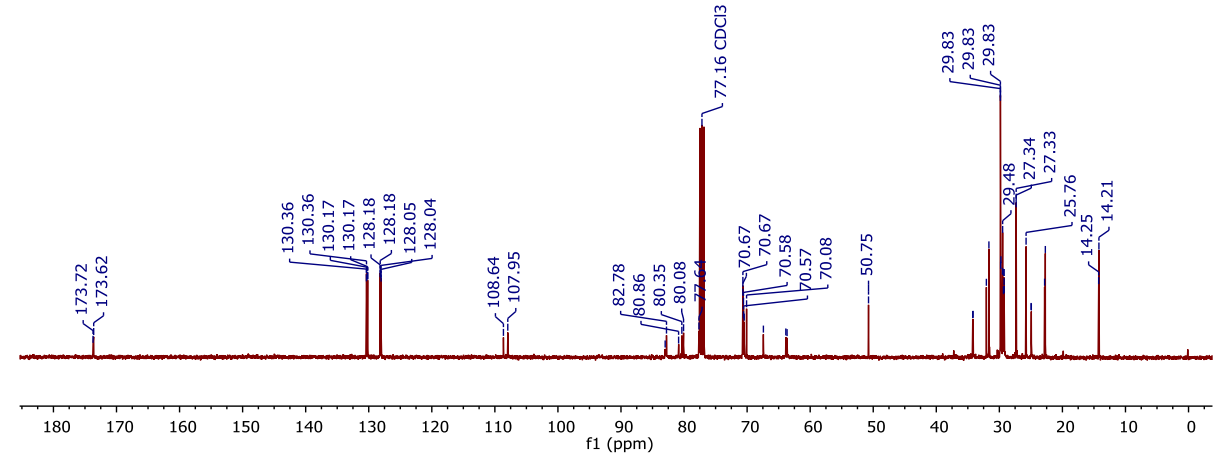
HMBC NMR Spectrum of Compound **21a**



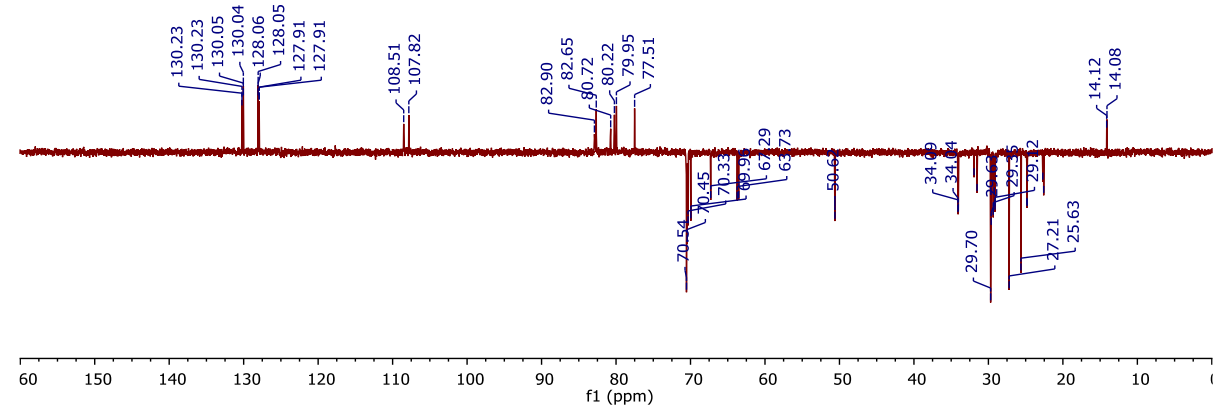
^{1}H NMR Spectrum (400.31 MHz, $CDCl_3$) of Compound **21b**



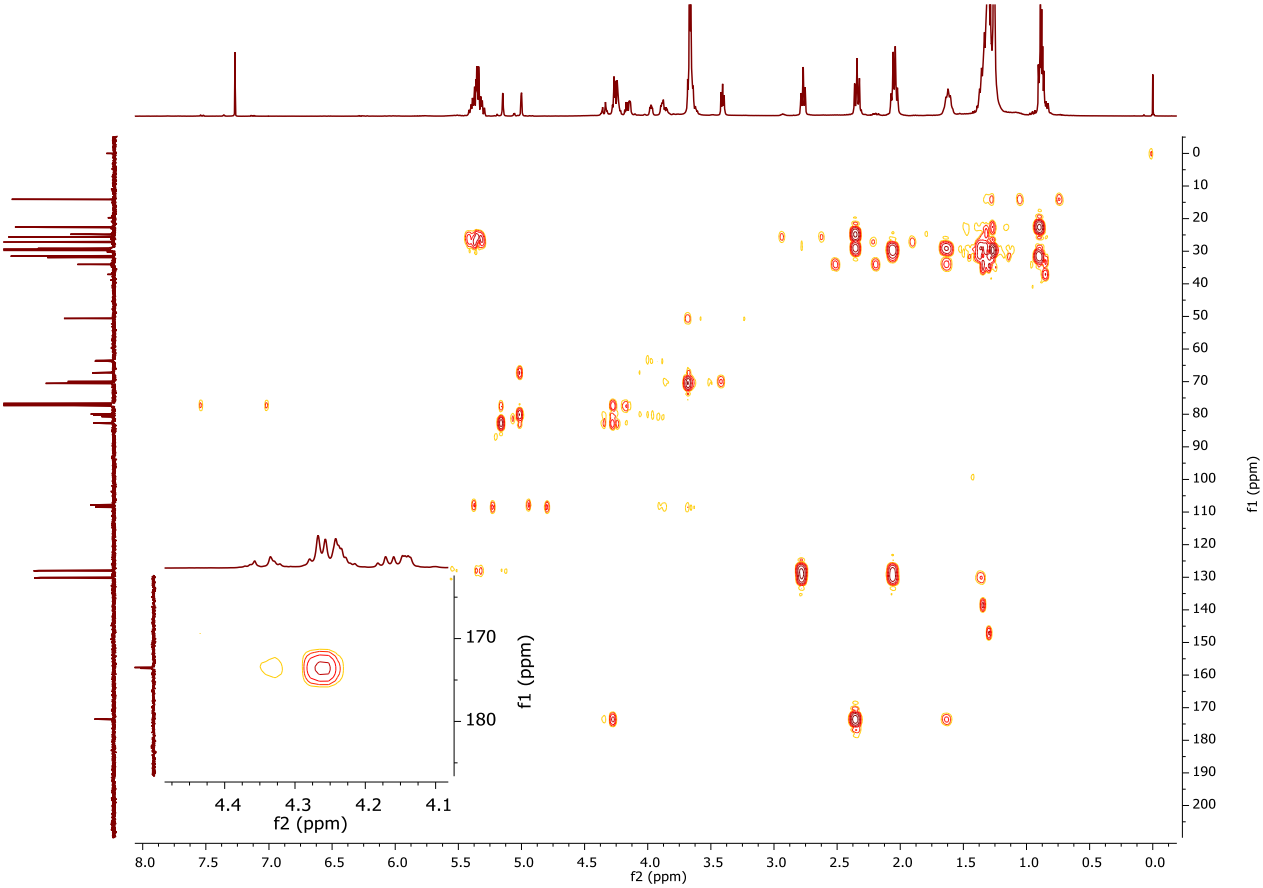
^{13}C NMR Spectrum (100.53 MHz, $CDCl_3$) of Compound **21b**



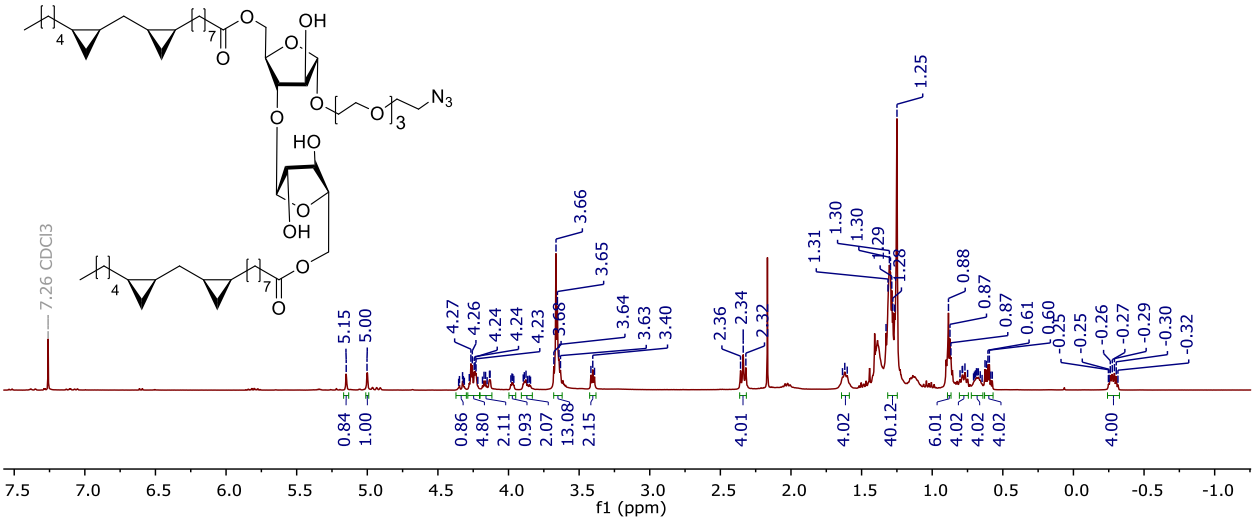
DEPT-NMR Spectrum (100.53 MHz, $CDCl_3$) of Compound **21b**



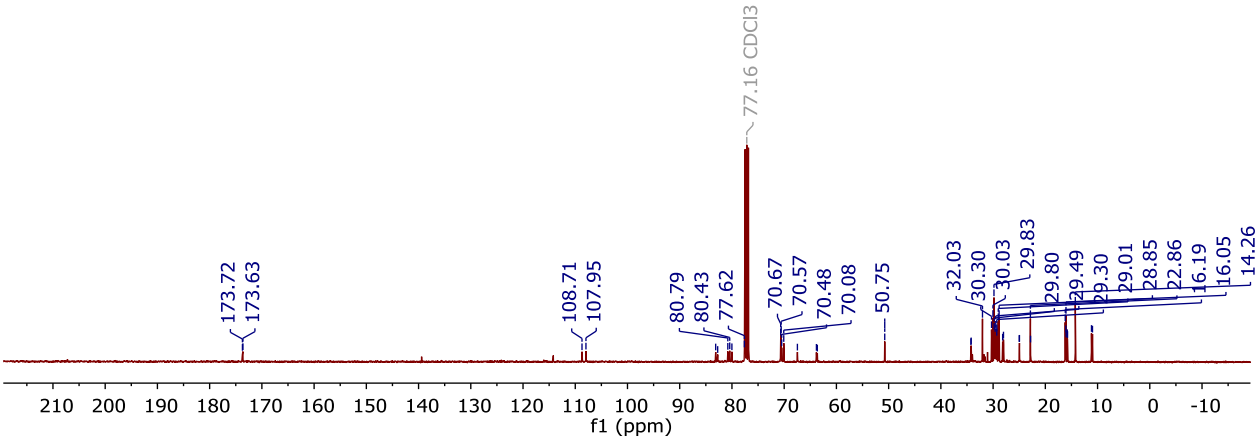
HMBC NMR Spectrum of Compound **21b**



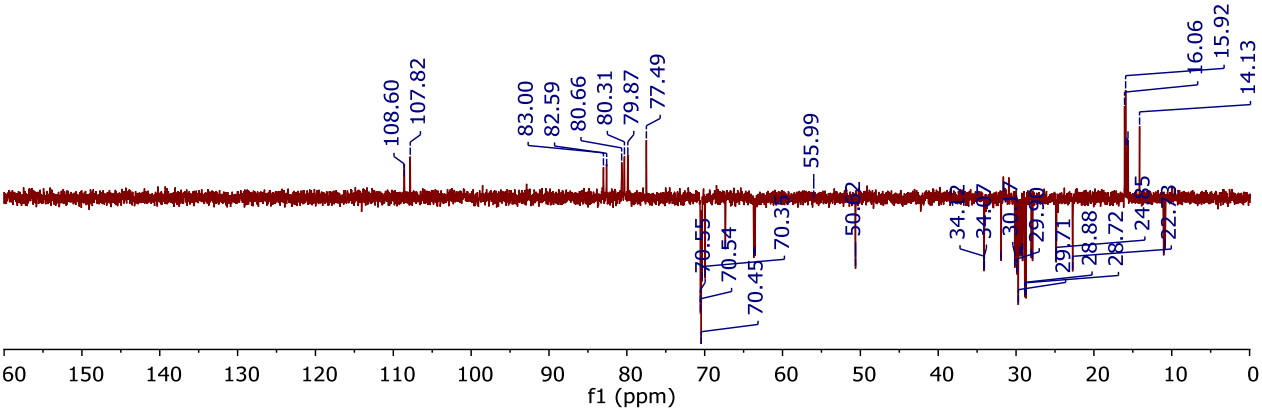
^{1}H NMR Spectrum (400.31 MHz, $CDCl_3$) of Compound **21c**



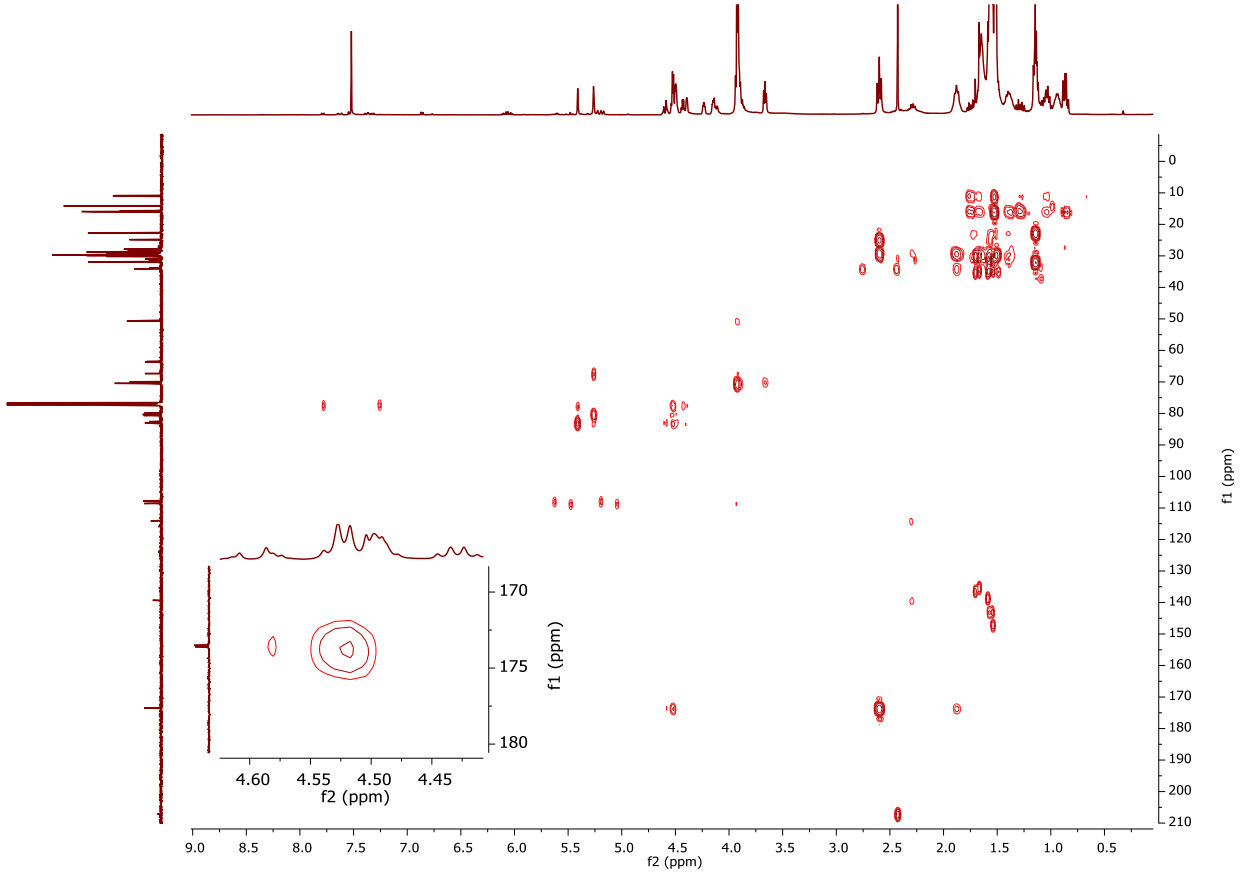
^{13}C NMR Spectrum (100.53 MHz, $CDCl_3$) of Compound **21c**



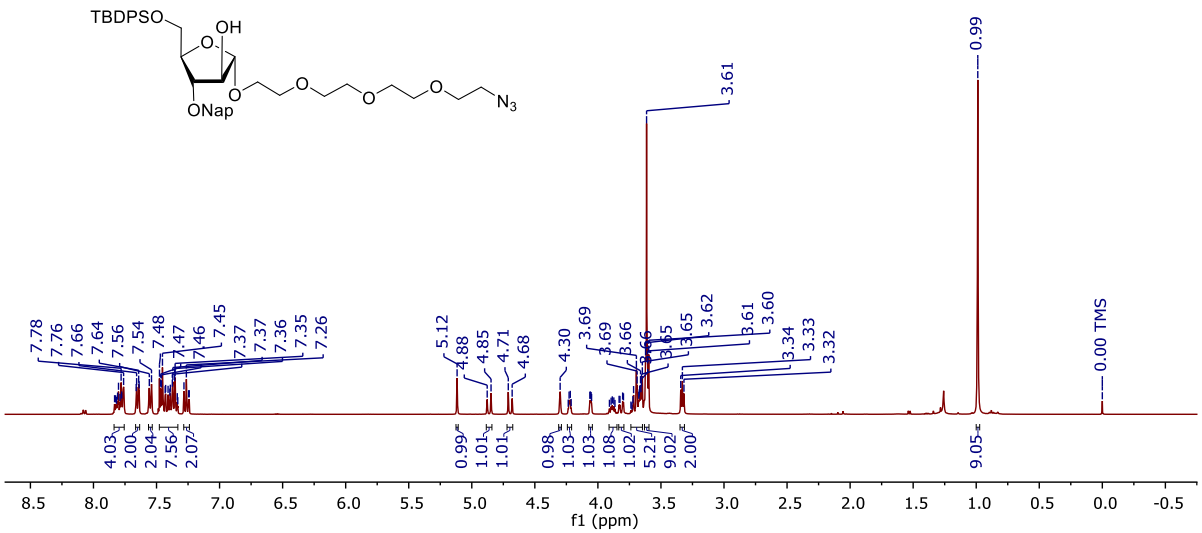
DEPT-NMR Spectrum (100.53 MHz, $CDCl_3$) of Compound **21c**



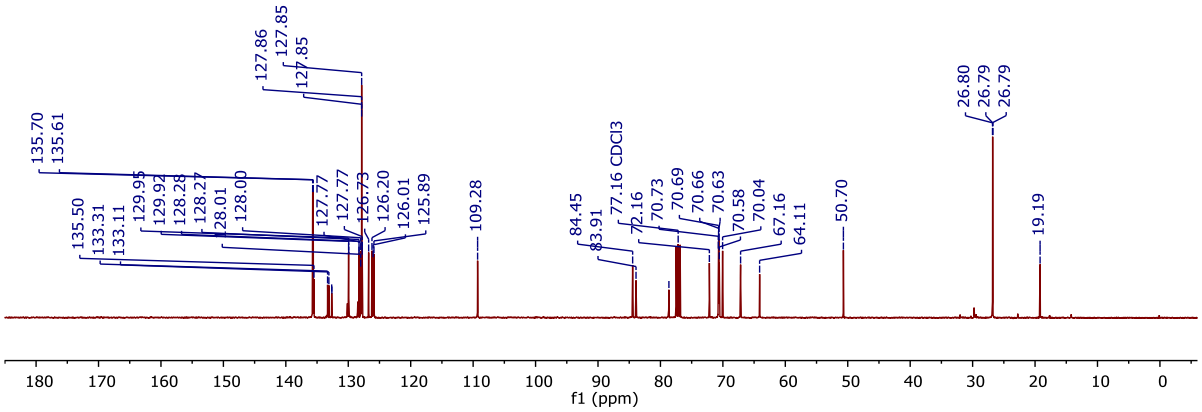
HMBC NMR Spectrum of Compound **21c**



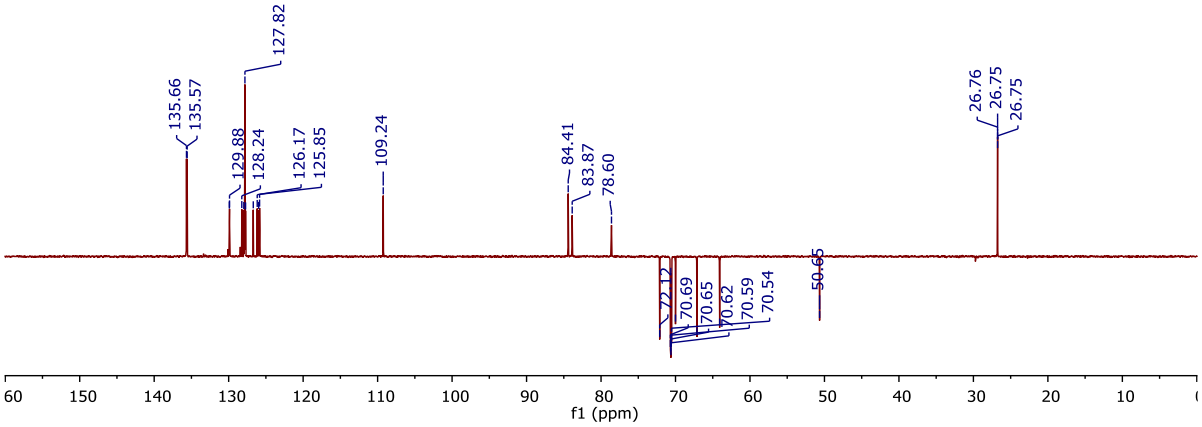
^{1}H NMR Spectrum (400.31 MHz, $CDCl_3$) of Compound **S6**



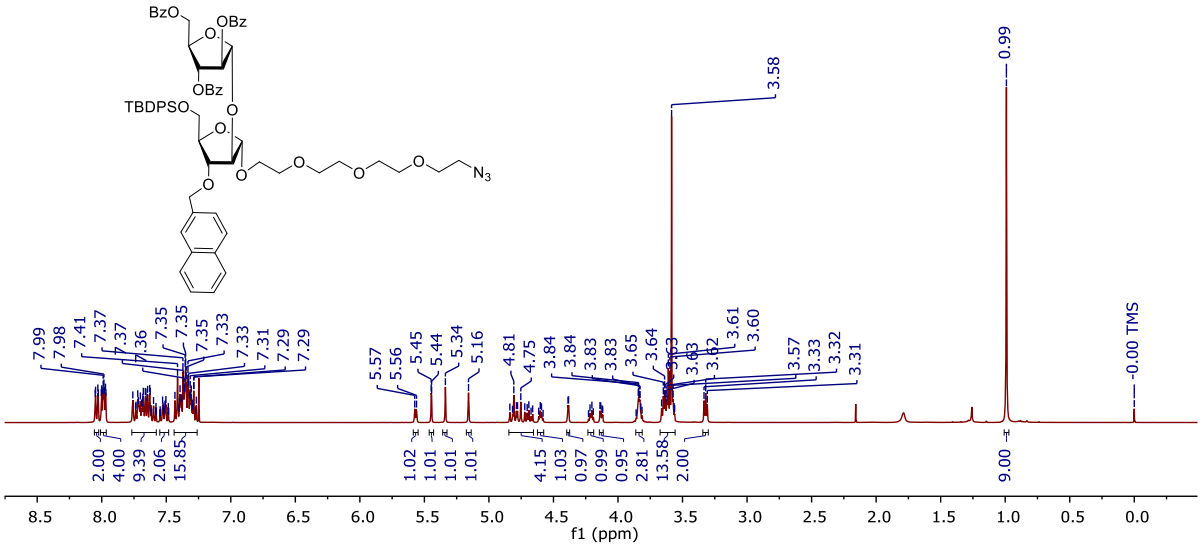
^{13}C NMR Spectrum (100.53 MHz, $CDCl_3$) of Compound **S6**



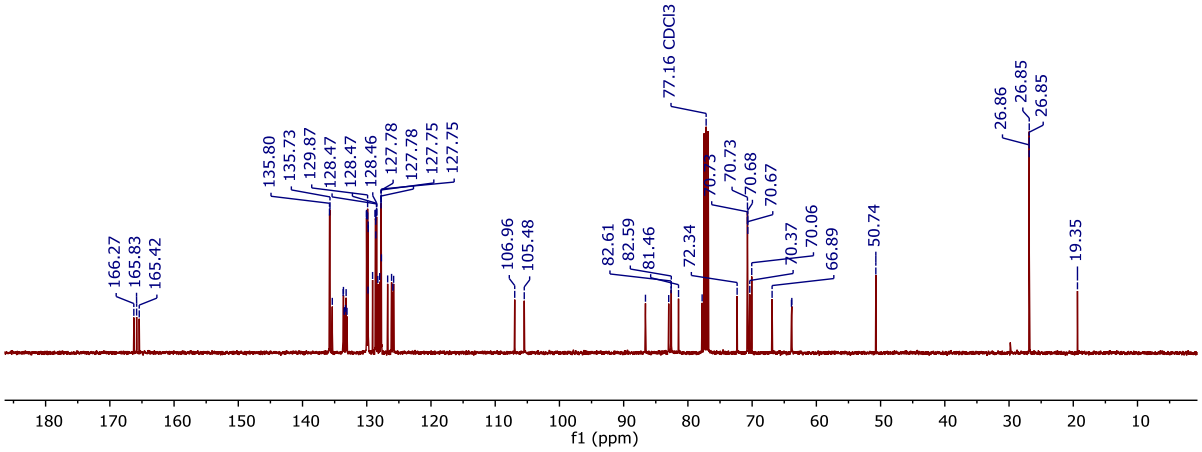
DEPT NMR Spectrum (100.53 MHz, $CDCl_3$) of Compound **S6**



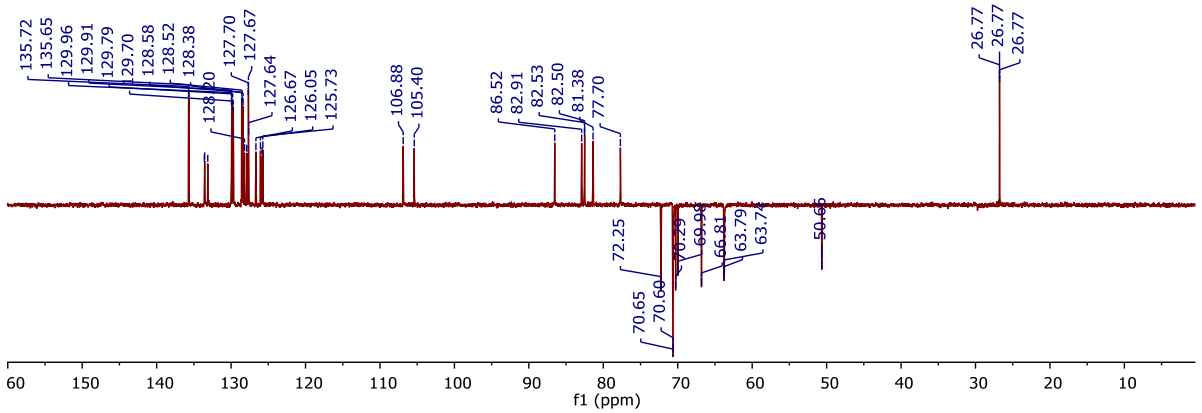
^{1}H NMR Spectrum (400.31 MHz, $CDCl_3$) of Compound **12**



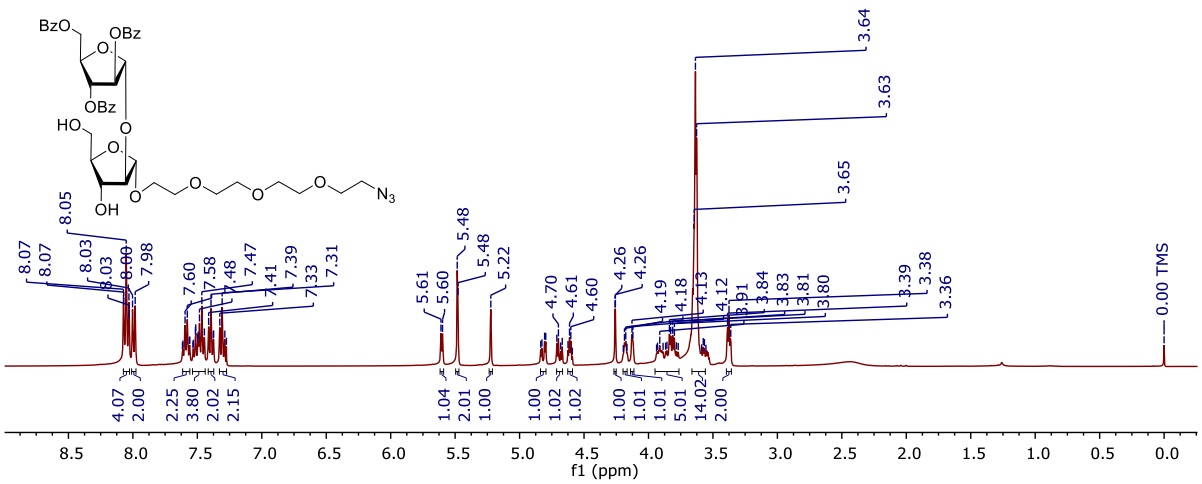
^{13}C NMR Spectrum (100.53 MHz, $CDCl_3$) of Compound **12**



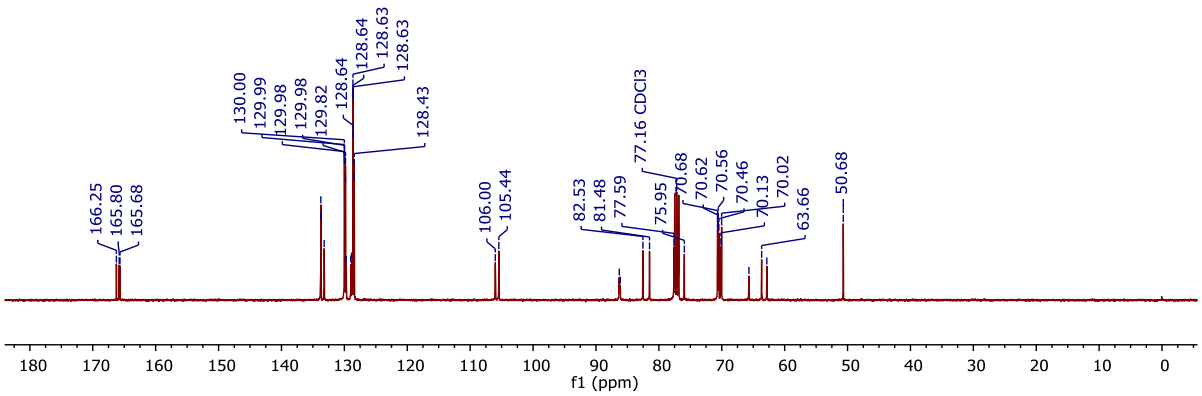
DEPT-NMR Spectrum (100.53 MHz, $CDCl_3$) of Compound **12**



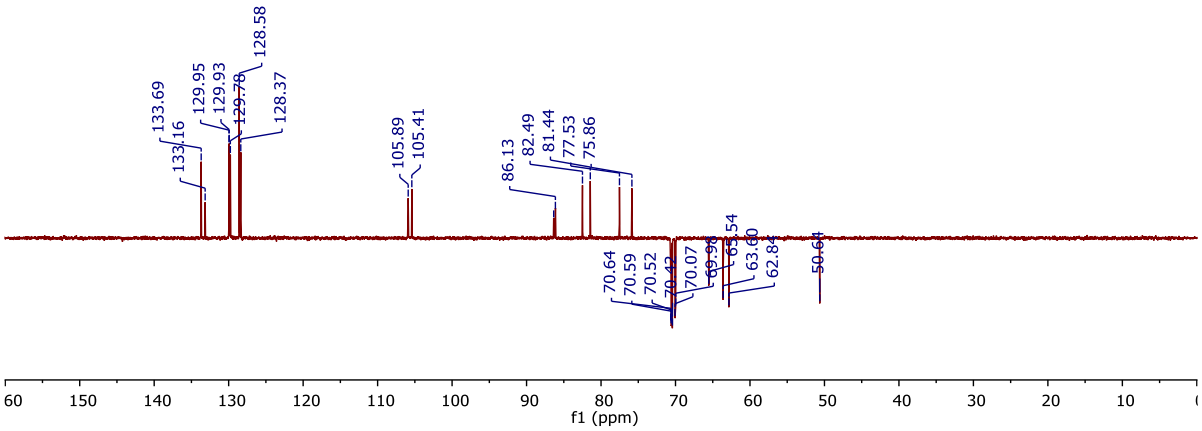
^{1}H NMR Spectrum (400.31 MHz, $CDCl_3$) of Compound **13**



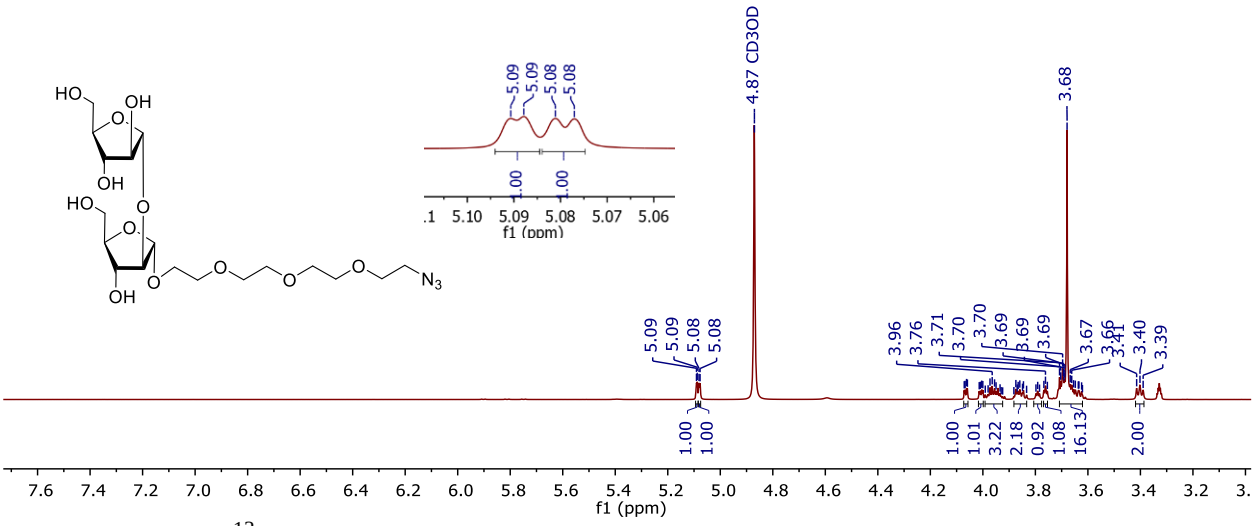
^{13}C NMR Spectrum (100.53 MHz, $CDCl_3$) of Compound **13**



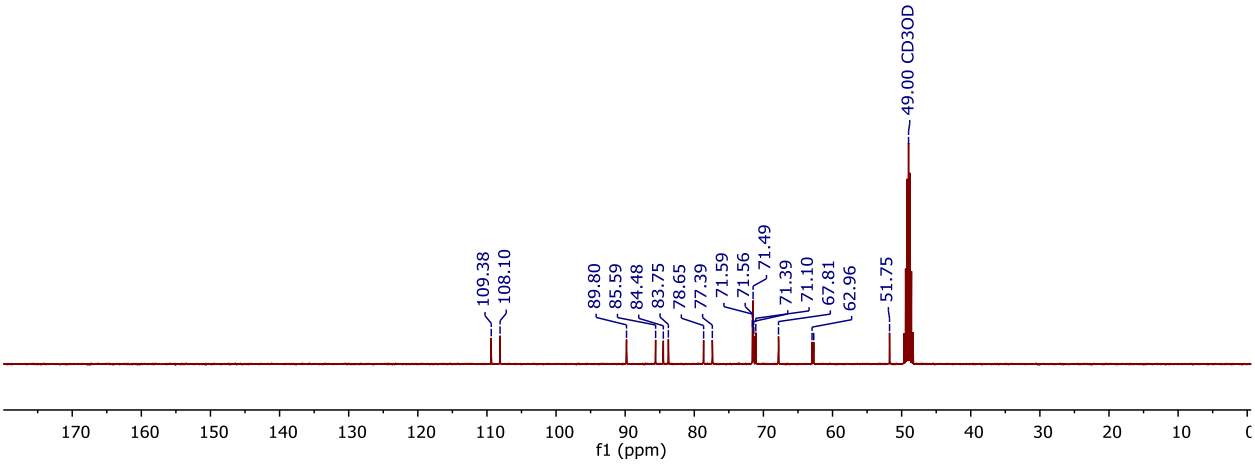
DEPT-NMR Spectrum (100.53 MHz, $CDCl_3$) of Compound **13**



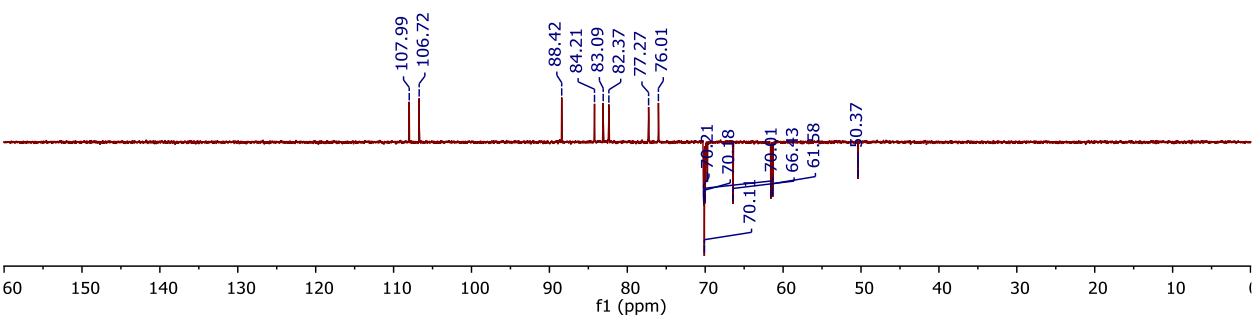
^{1}H NMR Spectrum (400.31 MHz, CD_3OD) of Compound **14**



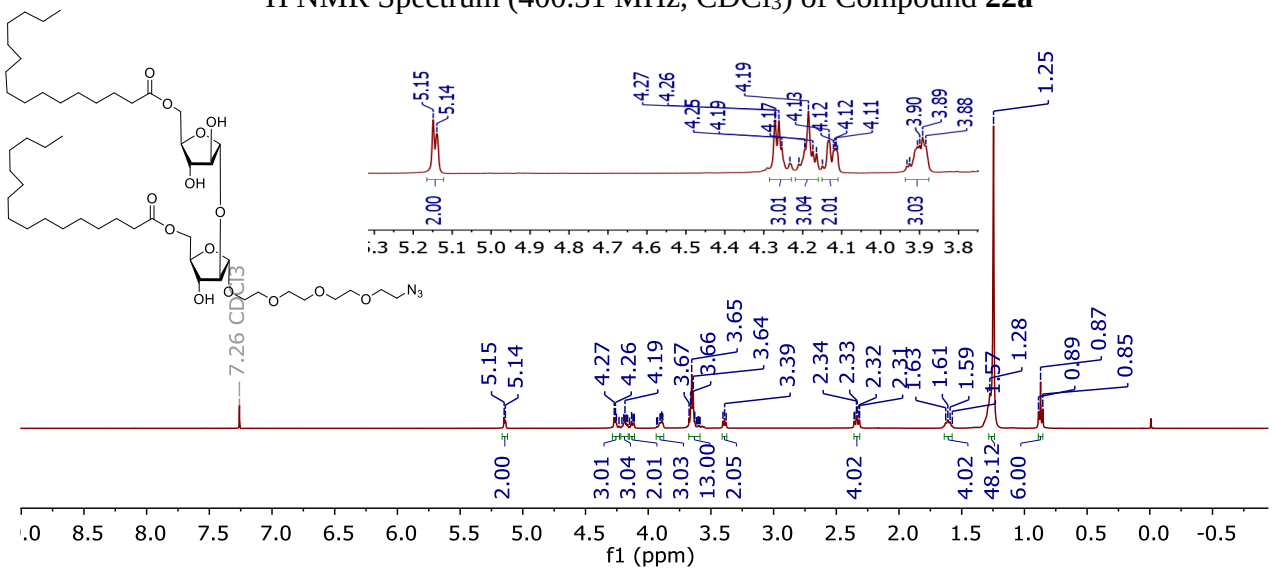
^{13}C NMR Spectrum (100.53 MHz, CD_3OD) of Compound **14**



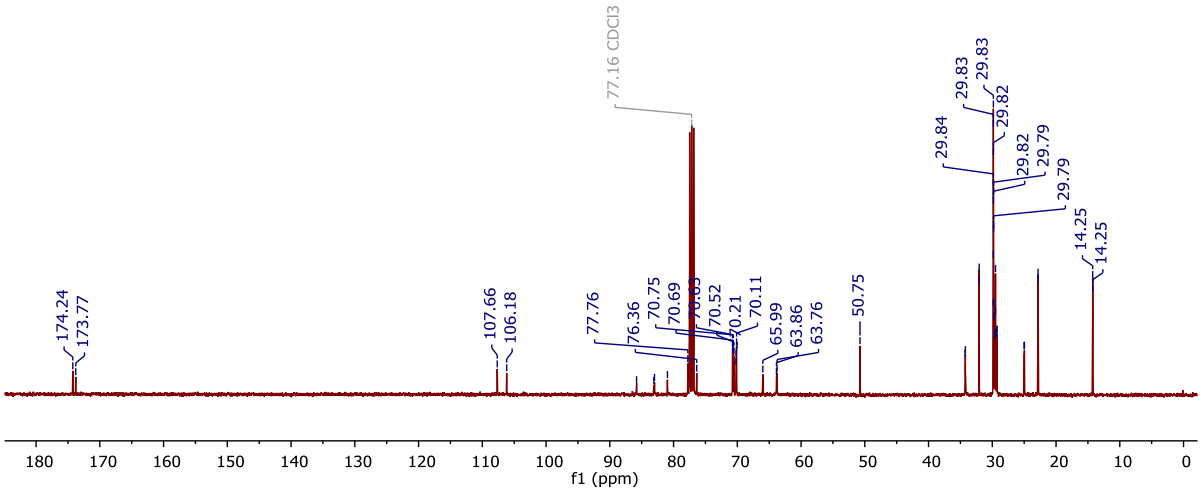
DEPT-NMR Spectrum (100.53 MHz, CD_3OD) of Compound **14**



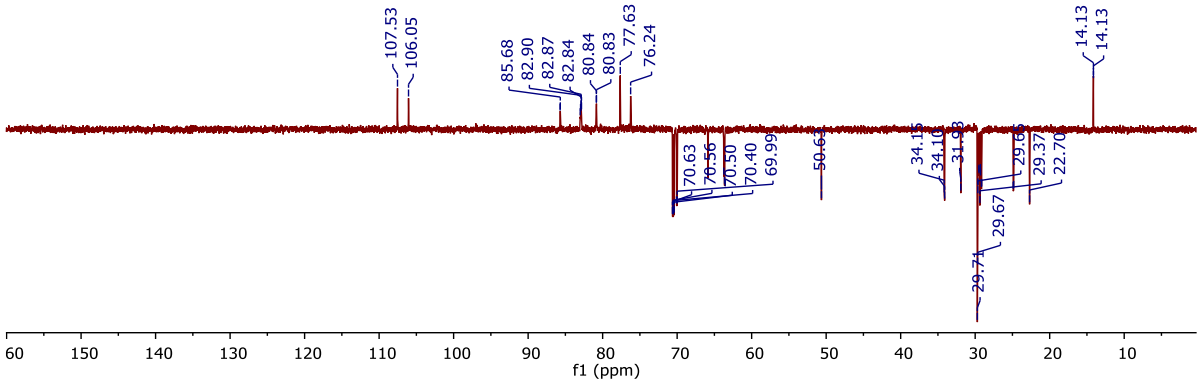
^{1}H NMR Spectrum (400.31 MHz, $CDCl_3$) of Compound **22a**



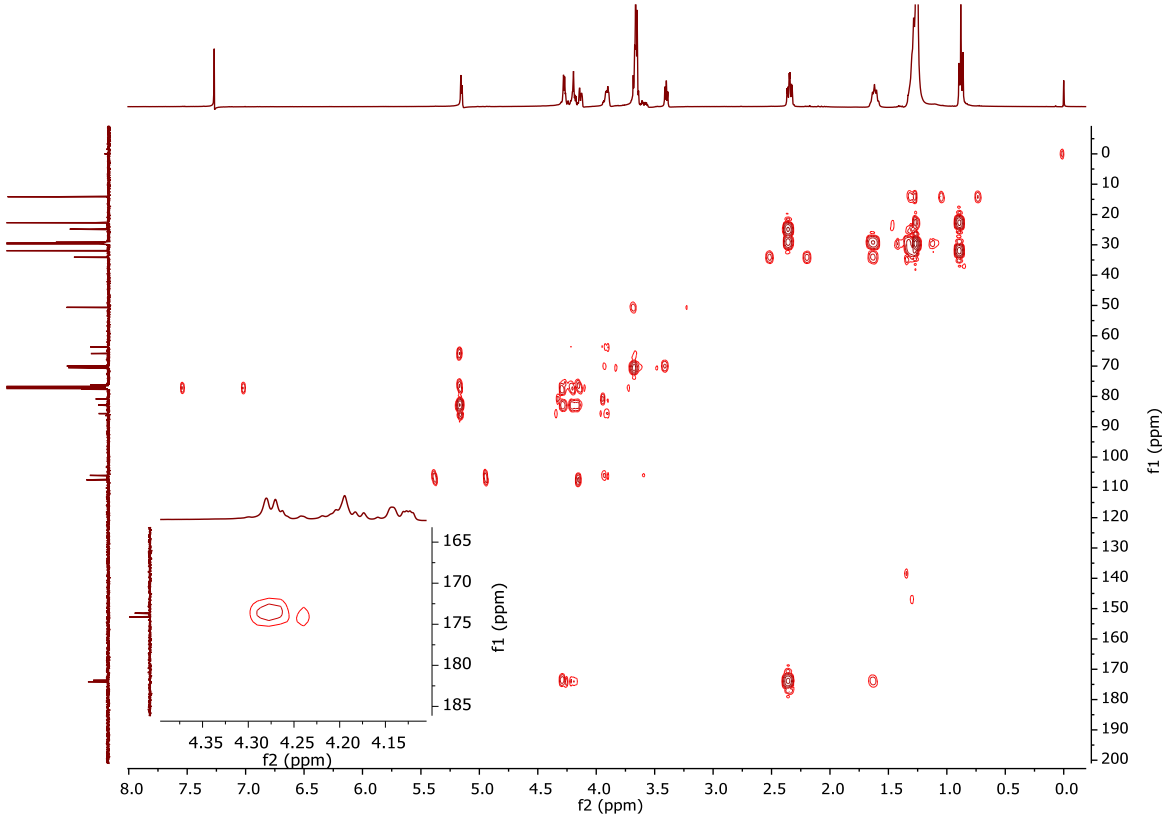
^{13}C NMR Spectrum (100.53 MHz, $CDCl_3$) of Compound **22a**



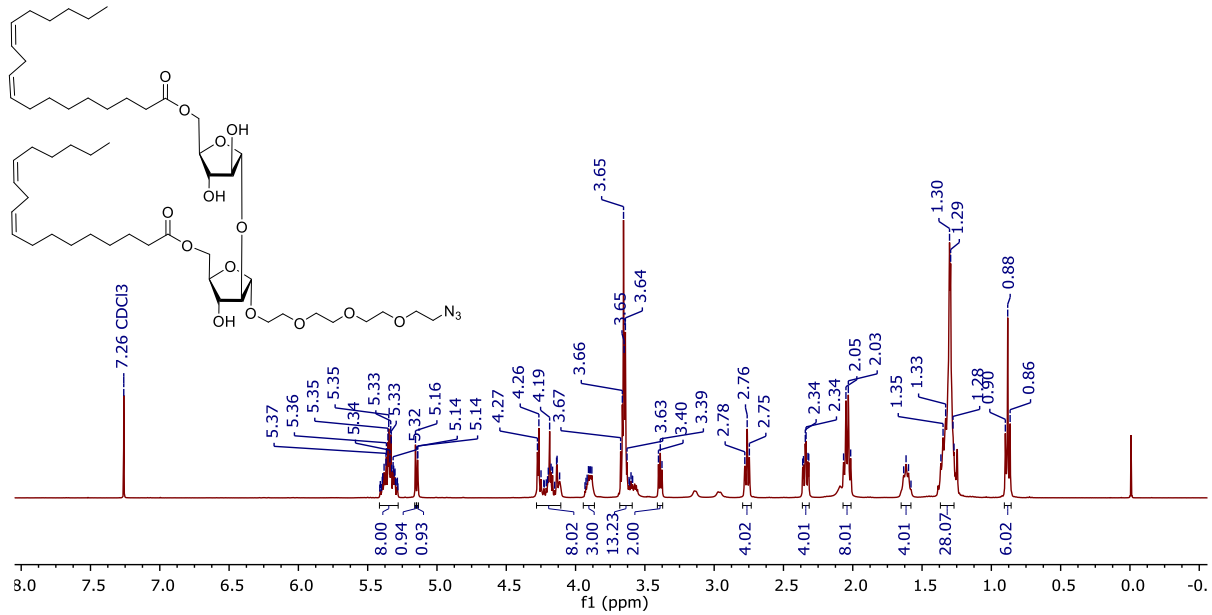
DEPT-NMR Spectrum (100.53 MHz, $CDCl_3$) of Compound **22a**



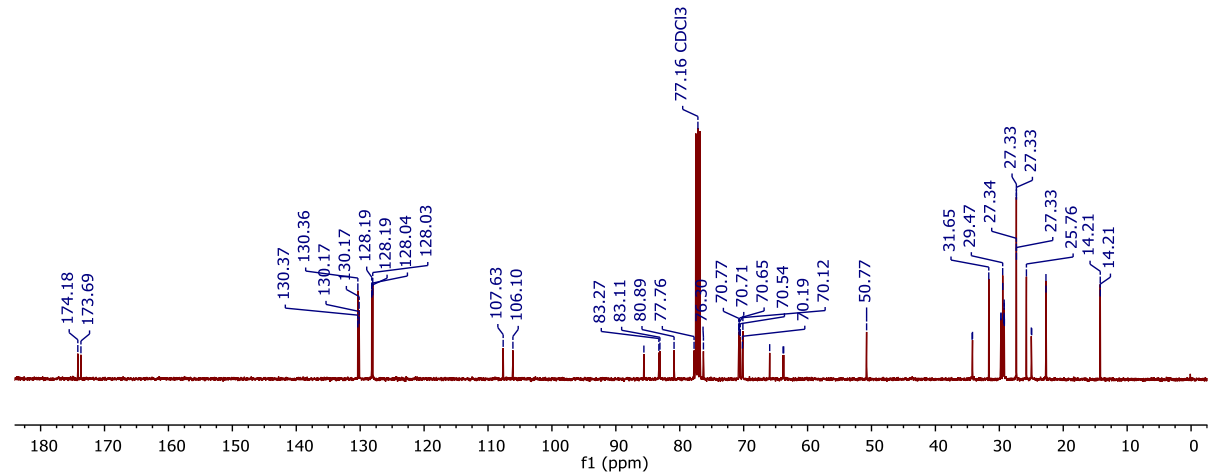
HMBC NMR Spectrum of Compound **22a**



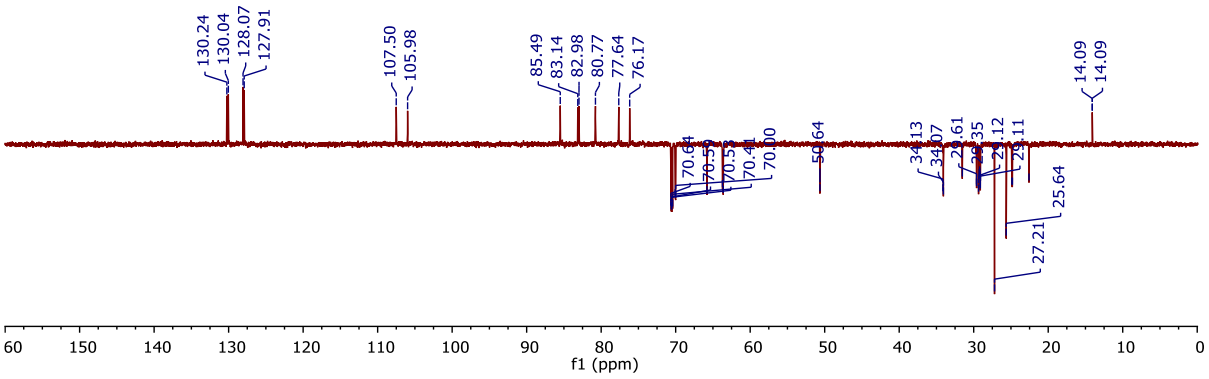
^{1}H NMR Spectrum (400.31 MHz, $CDCl_3$) of Compound **22b**



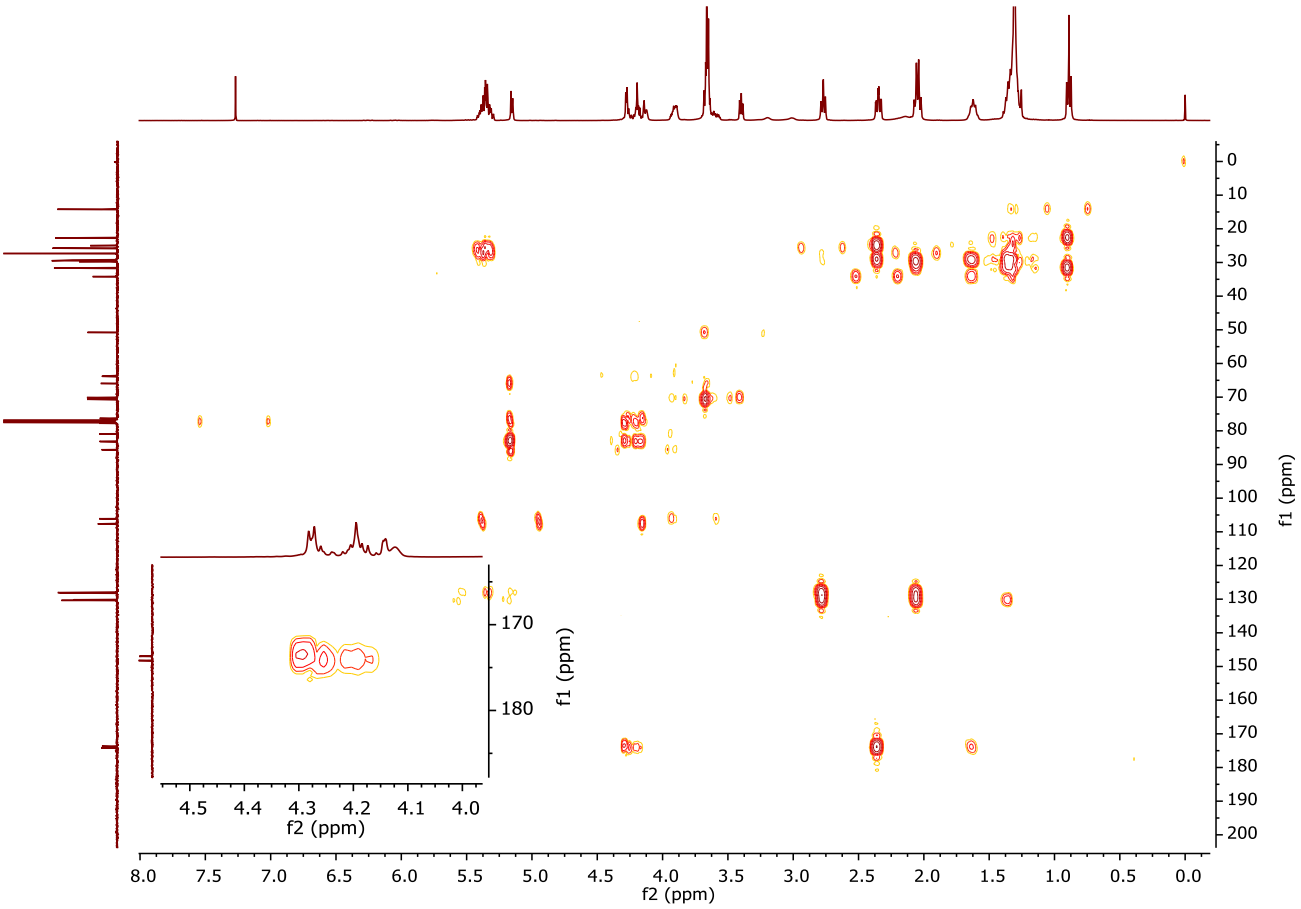
^{13}C NMR Spectrum (100.53 MHz, $CDCl_3$) of Compound **22b**



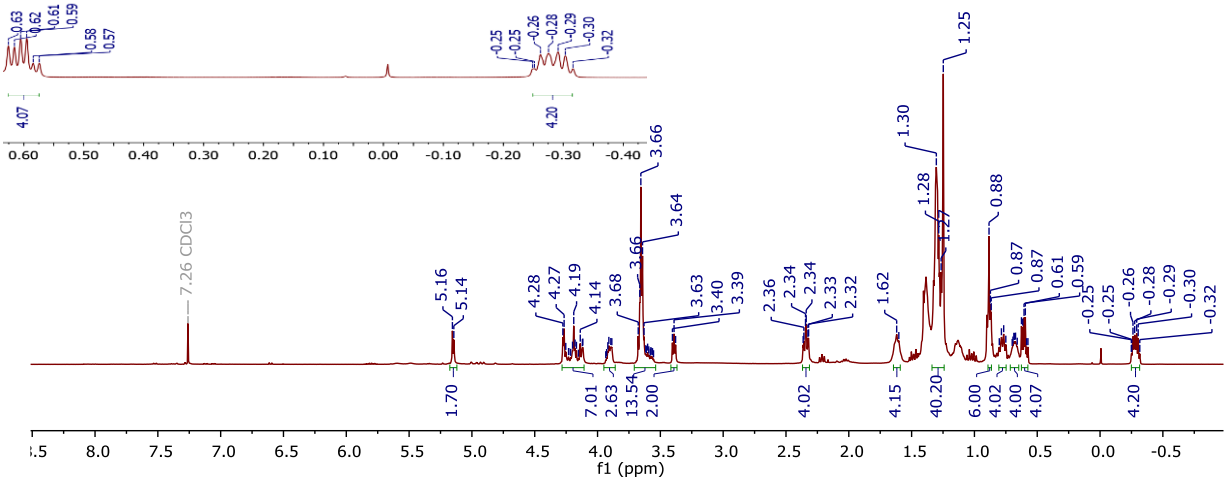
DEPT-NMR Spectrum (100.53 MHz, $CDCl_3$) of Compound **22b**



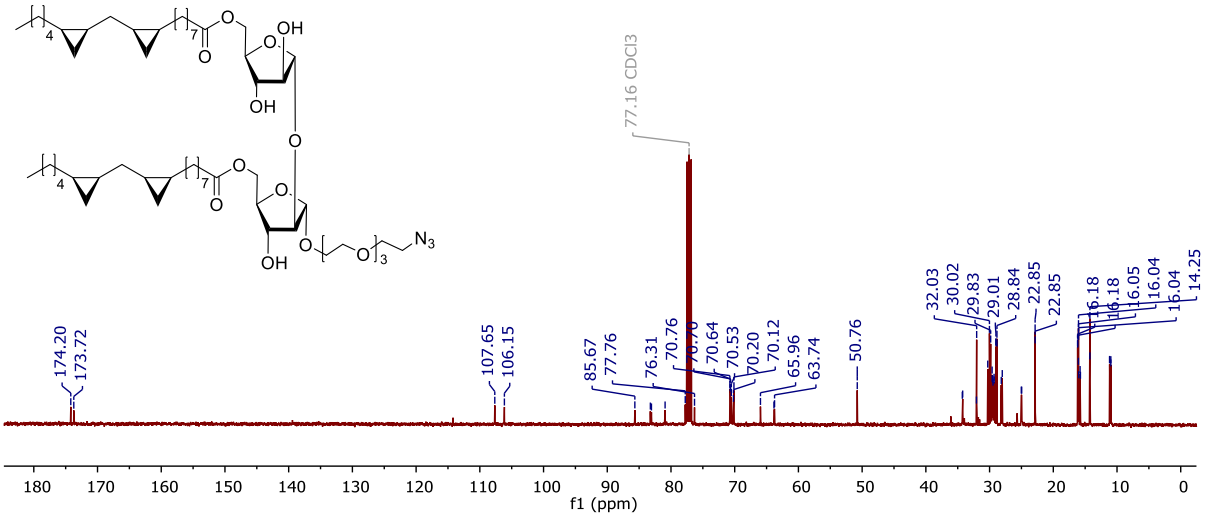
HMBC NMR Spectrum of Compound **22b**



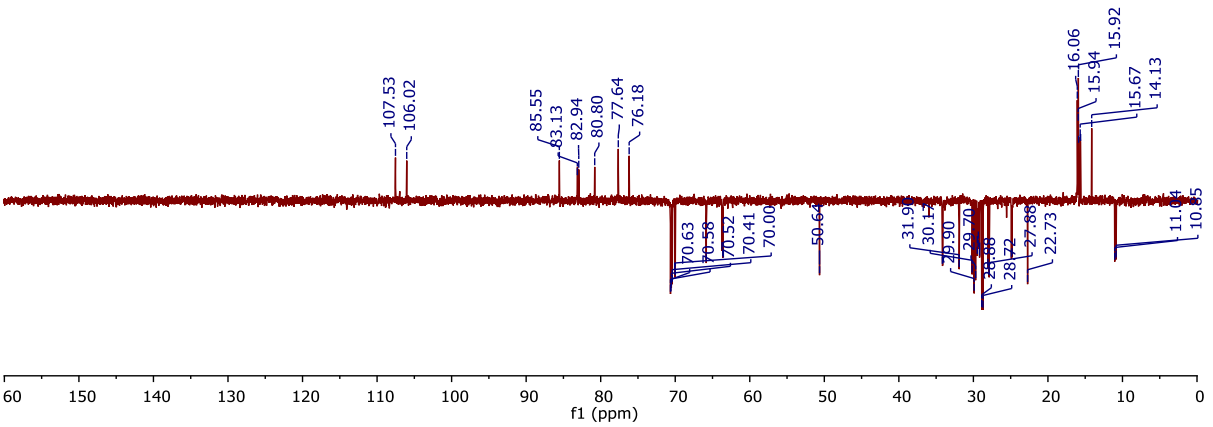
^{1}H NMR Spectrum (400.31 MHz, $CDCl_3$) of Compound **22c**



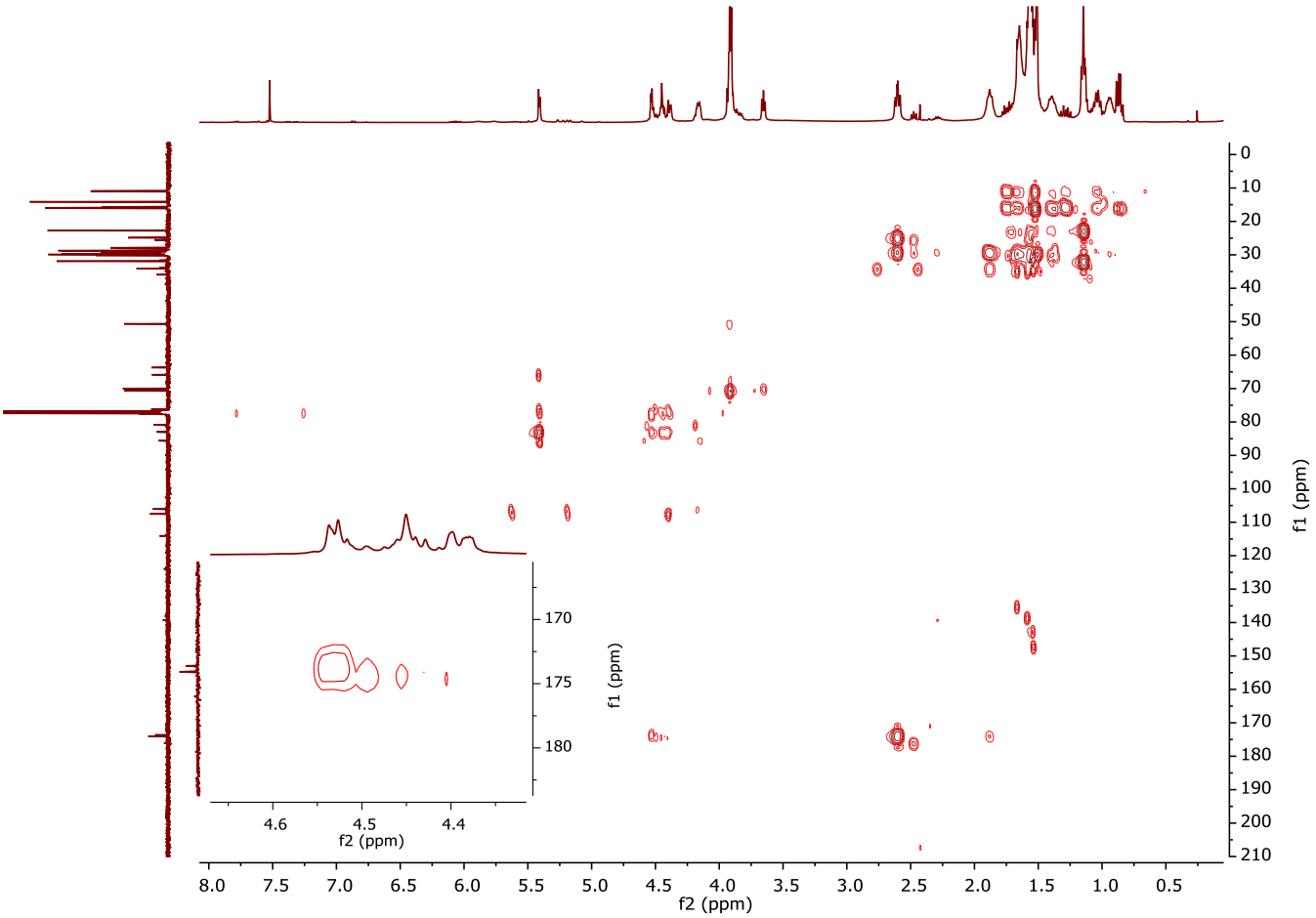
^{13}C NMR Spectrum (100.53 MHz, $CDCl_3$) of Compound **22c**



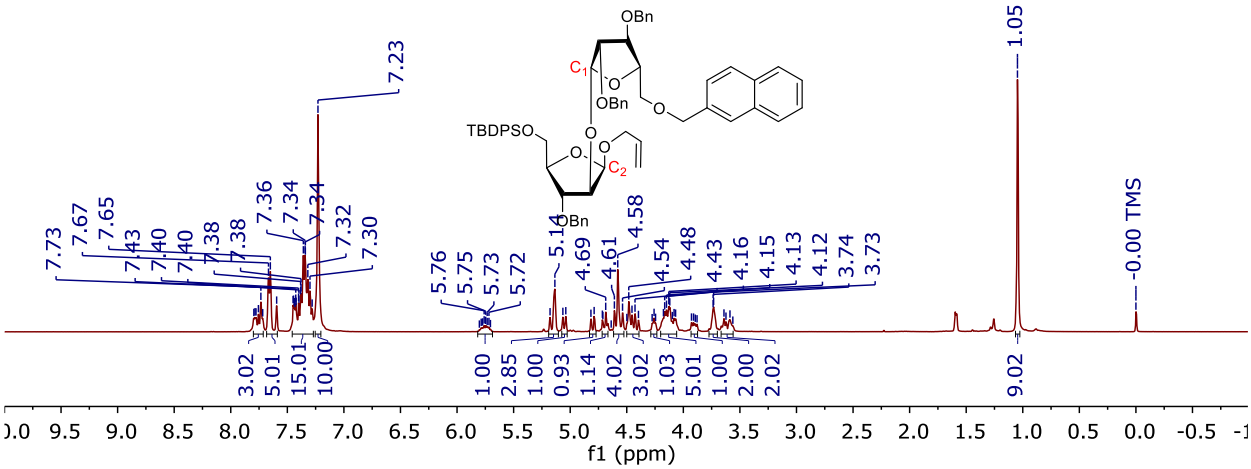
DEPT-NMR Spectrum (100.53 MHz, $CDCl_3$) of Compound **22c**



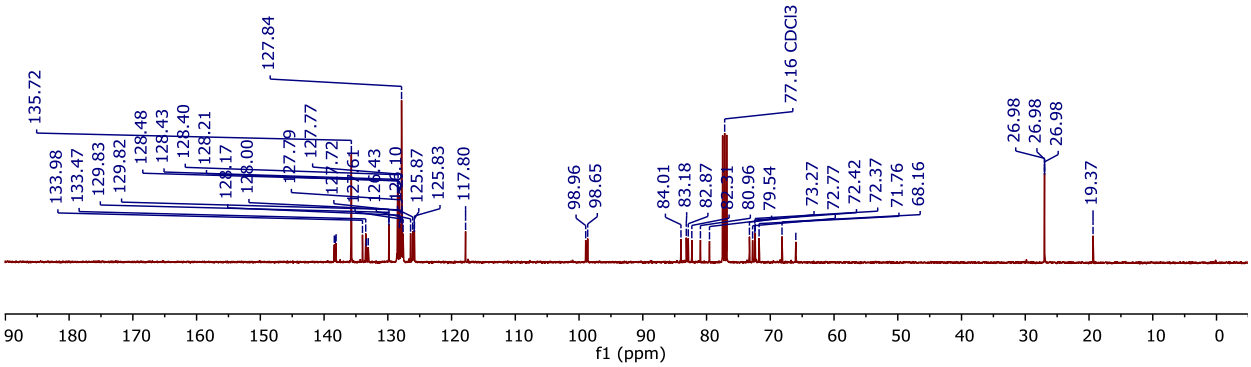
HMBC NMR Spectrum of Compound **22c**



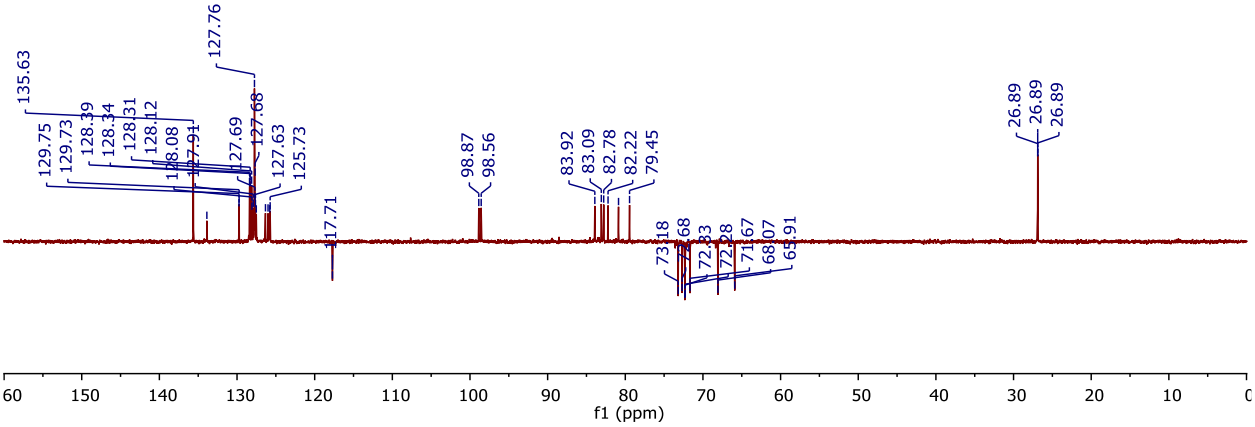
^{1}H NMR Spectrum (400.31 MHz, $CDCl_3$) of Compound **S9**



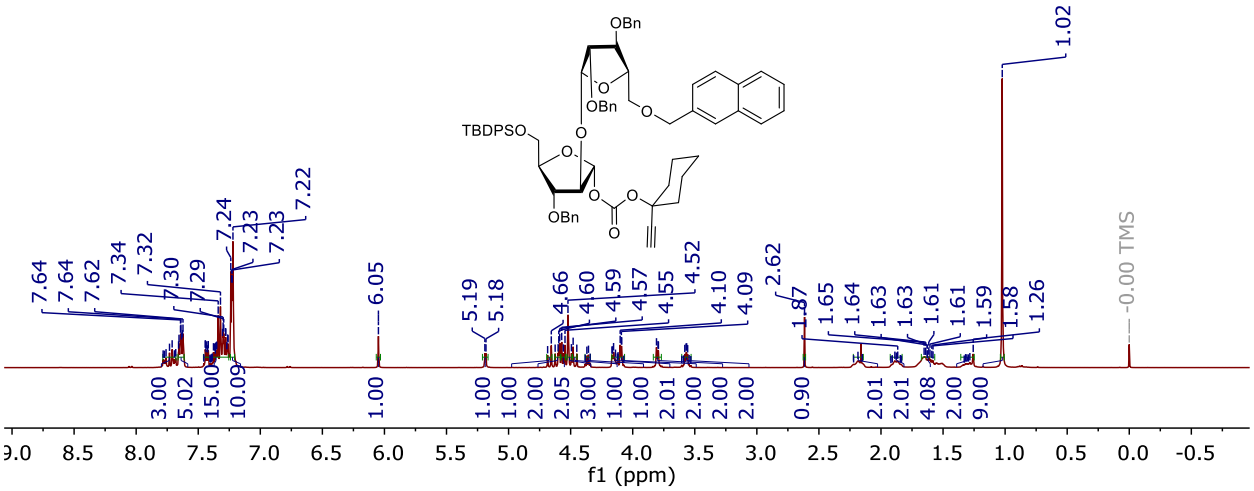
^{13}C NMR Spectrum (100.53 MHz, $CDCl_3$) of Compound **S9**



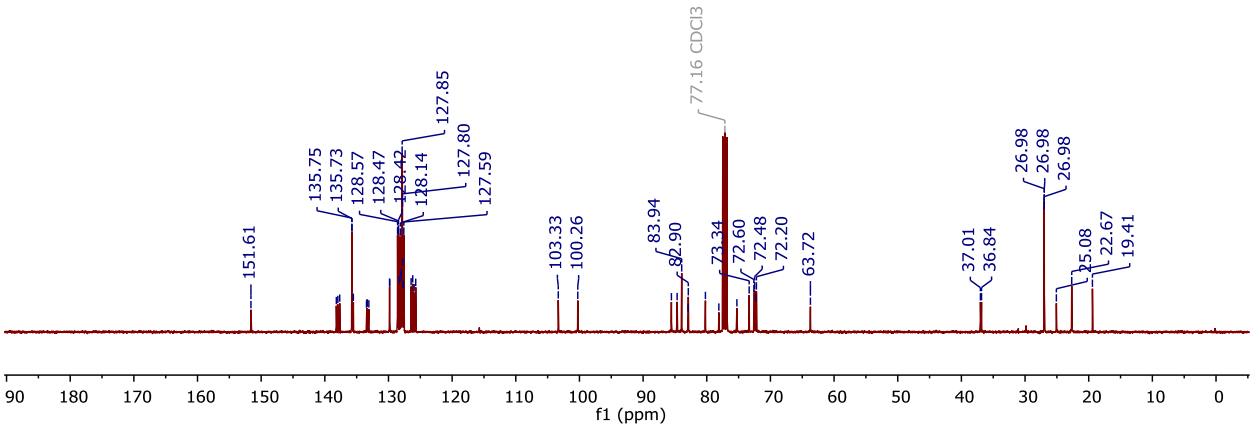
DEPT-NMR Spectrum (100.53 MHz, $CDCl_3$) of Compound **S9**



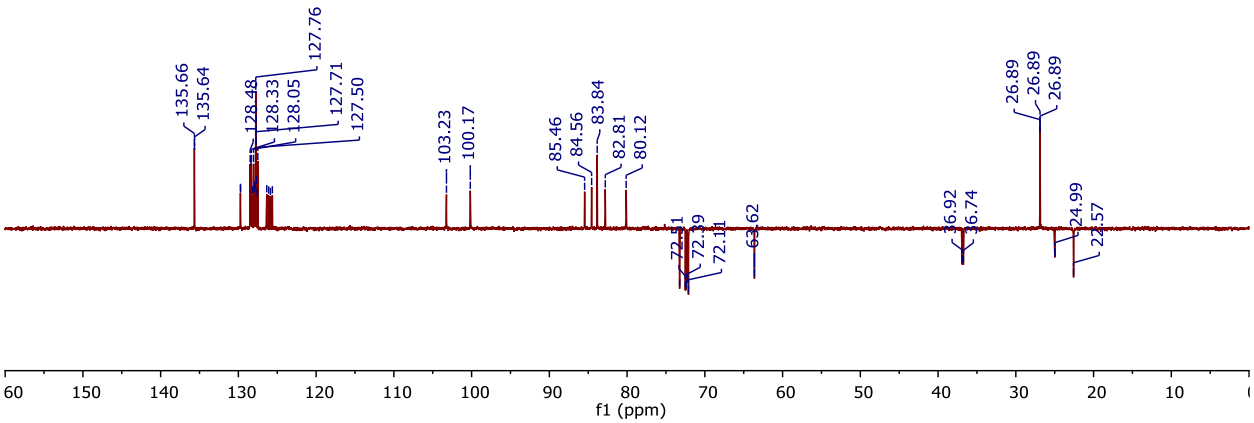
^{1}H NMR Spectrum (400.31 MHz, $CDCl_3$) of Compound **15**



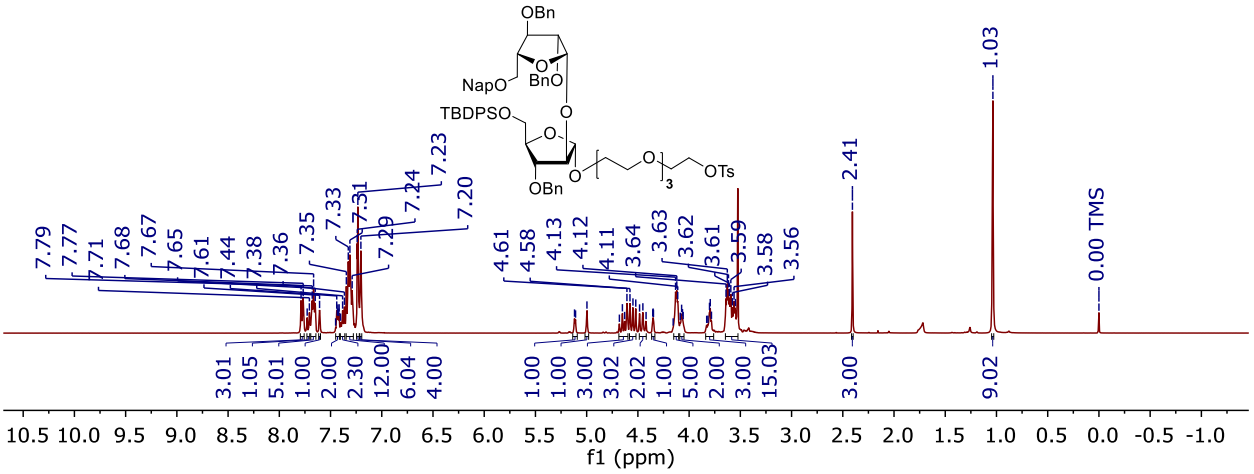
^{13}C NMR Spectrum (100.53 MHz, $CDCl_3$) of Compound **15**



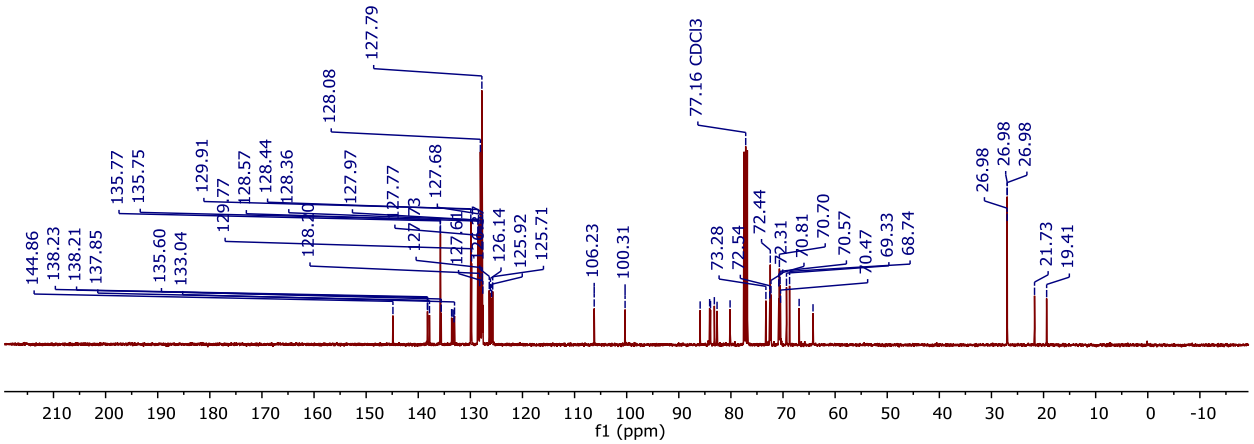
DEPT-NMR Spectrum (100.53 MHz, $CDCl_3$) of Compound **15**



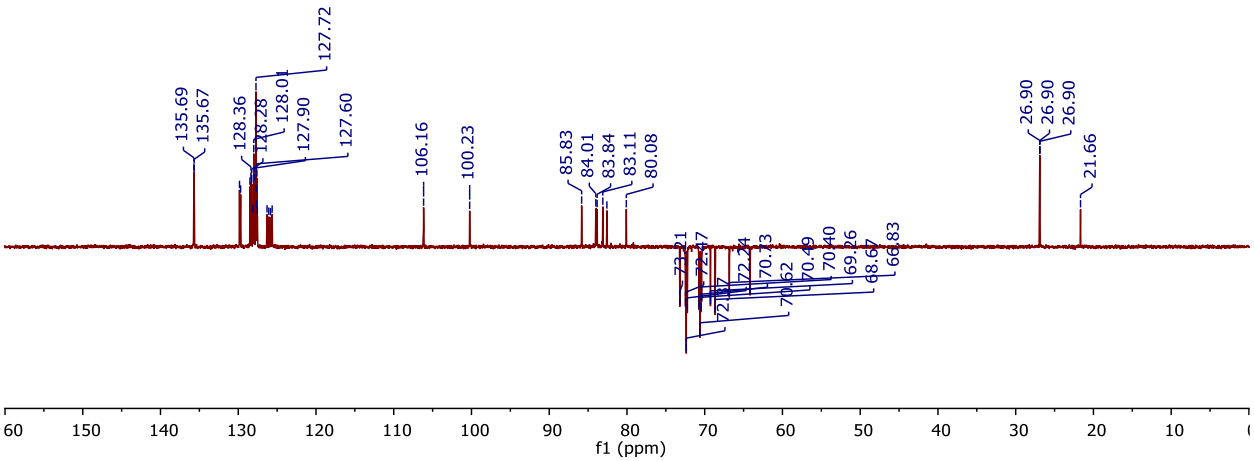
^{1}H NMR Spectrum (400.31 MHz, $CDCl_3$) of Compound **16b**



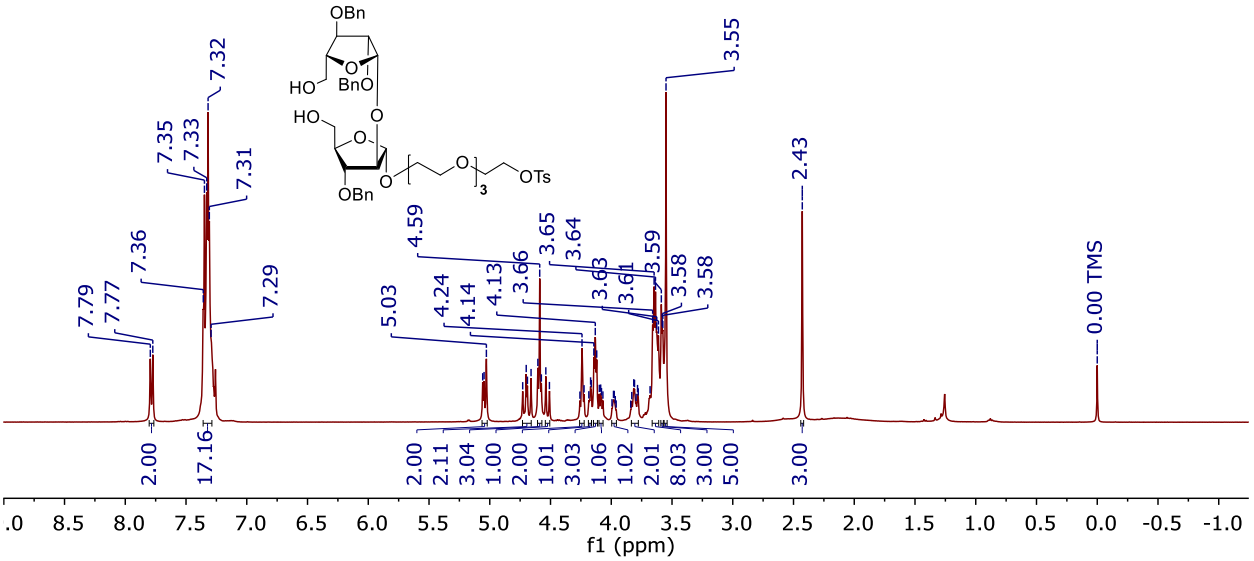
^{13}C NMR Spectrum (100.53 MHz, $CDCl_3$) of Compound **16b**



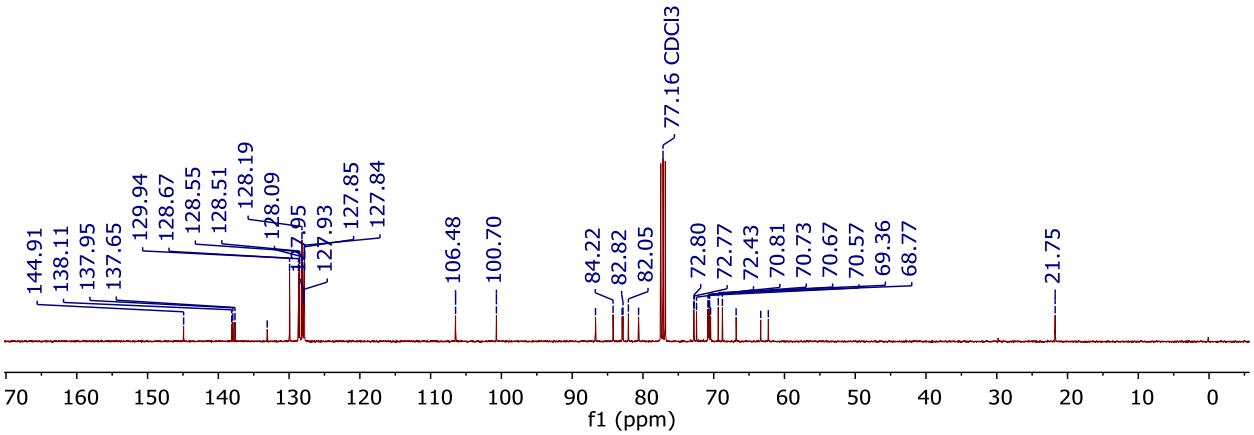
DEPT-NMR Spectrum (100.53 MHz, $CDCl_3$) of Compound **16b**



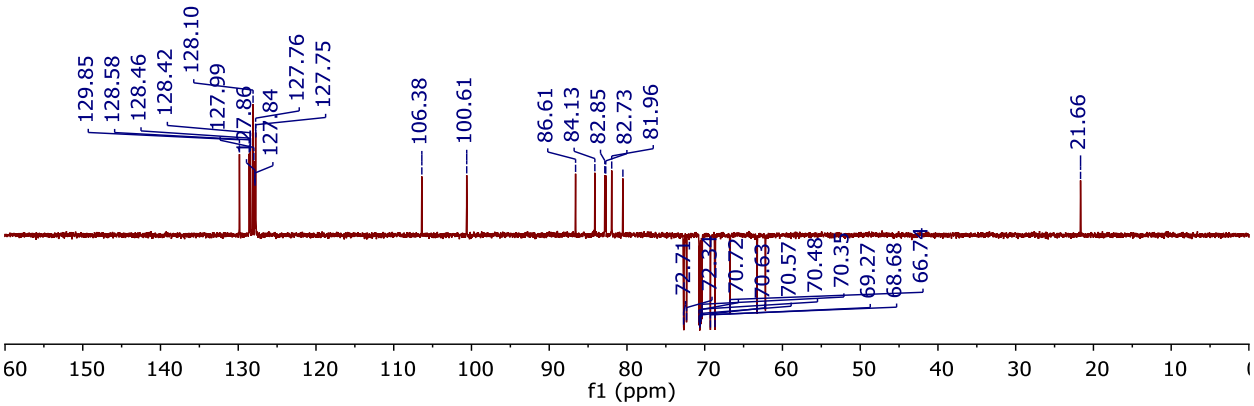
^{1}H NMR Spectrum (400.31 MHz, $CDCl_3$) of Compound **18**



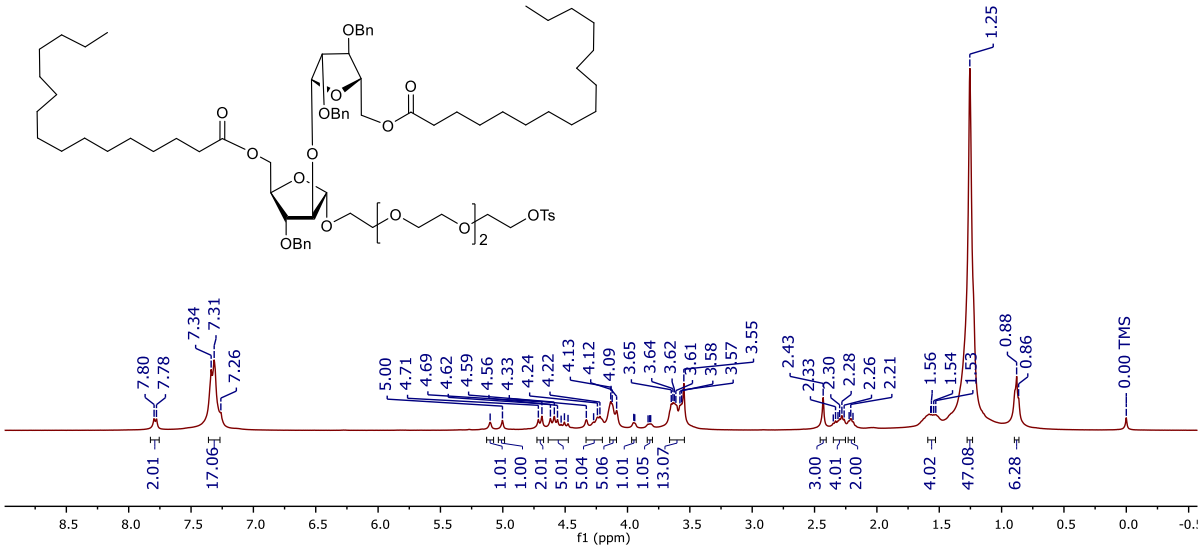
^{13}C NMR Spectrum (100.53 MHz, $CDCl_3$) of Compound **18**



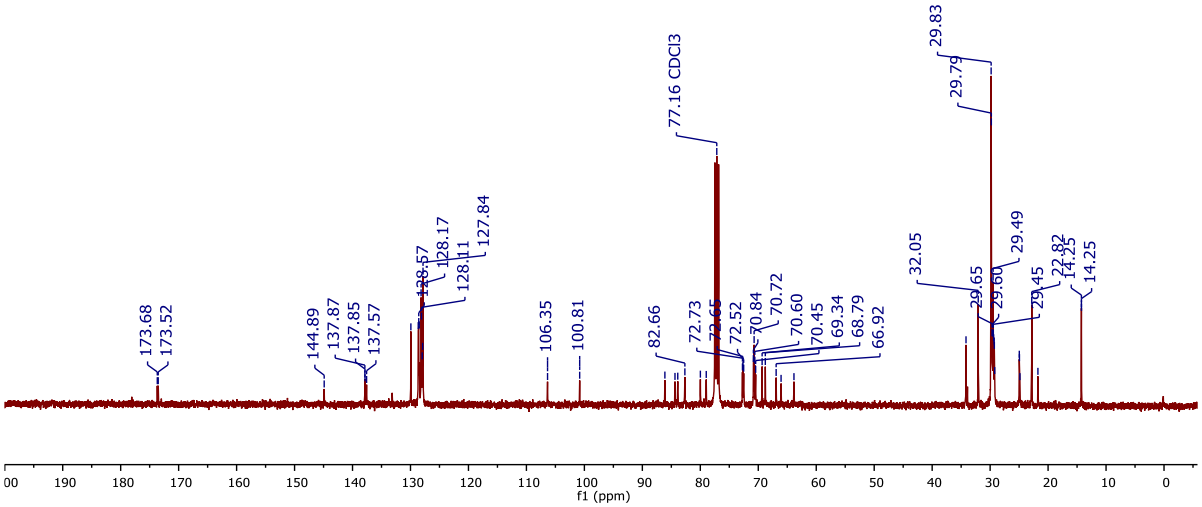
DEPT-NMR Spectrum (100.53 MHz, $CDCl_3$) of Compound **18**



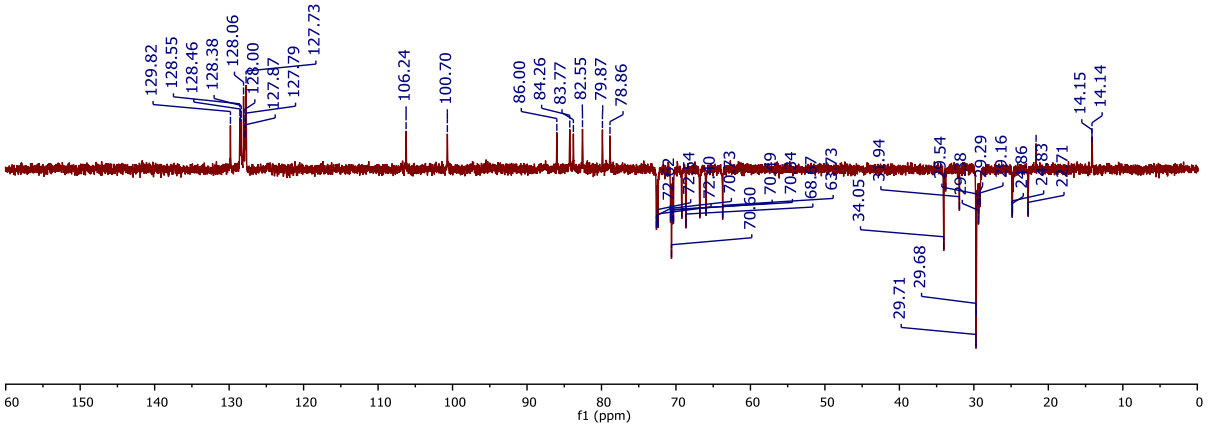
^{1}H NMR Spectrum (400.31 MHz, $CDCl_3$) of Compound **25a**



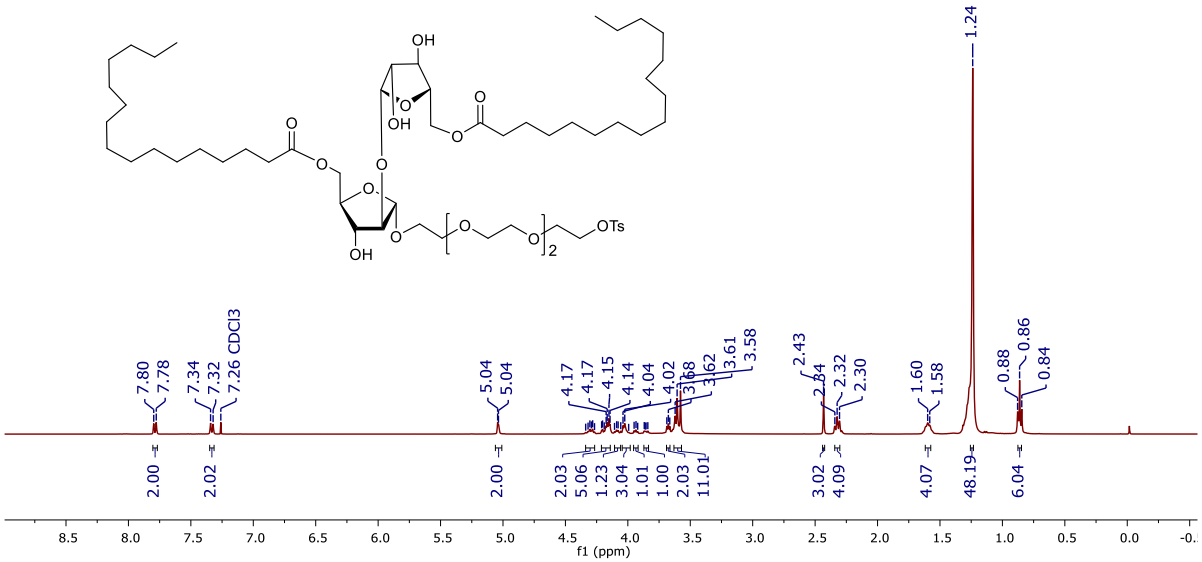
^{13}C NMR Spectrum (100.31 MHz, $CDCl_3$) of Compound **25a**



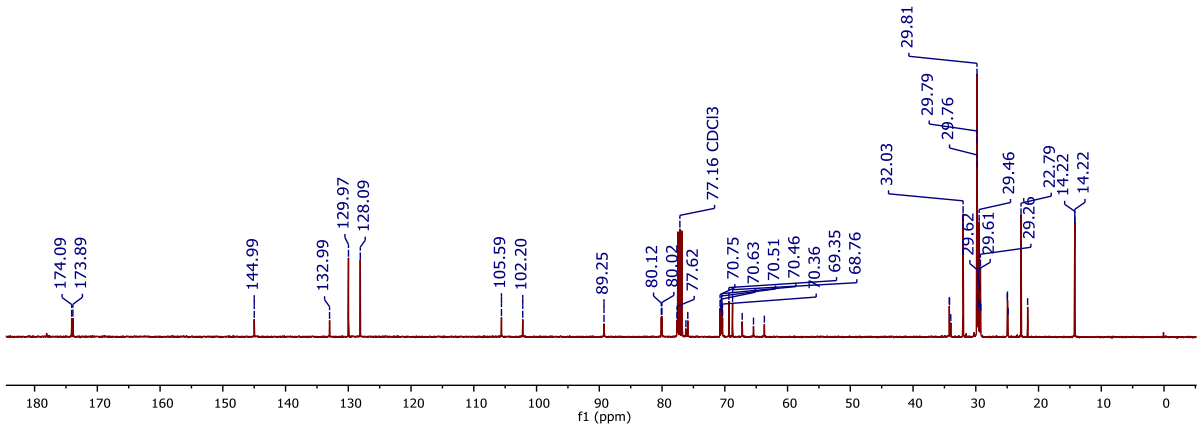
DEPT NMR Spectrum (100.31 MHz, $CDCl_3$) of Compound **25a**



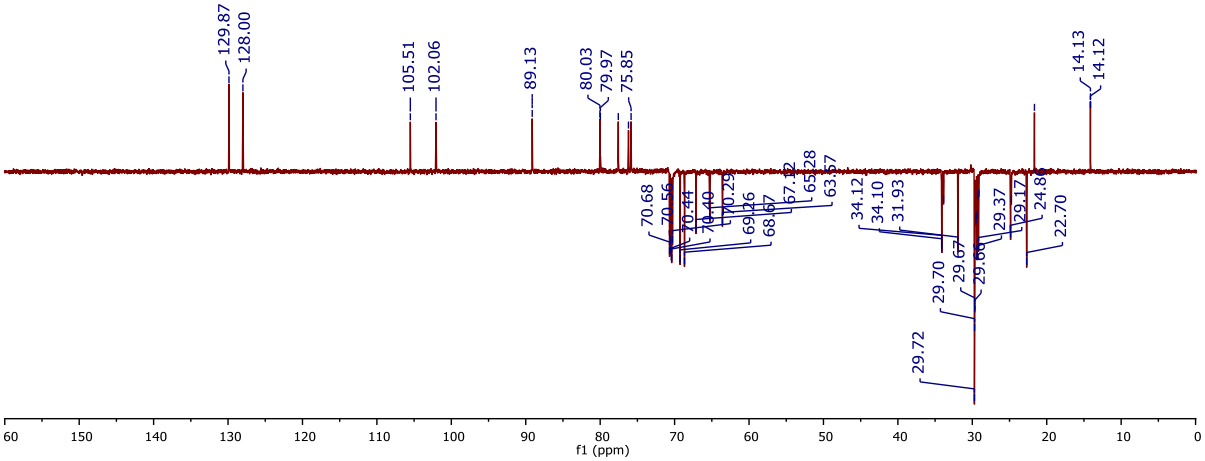
^{1}H NMR Spectrum (400.31 MHz, $CDCl_3$) of Compound **S11**



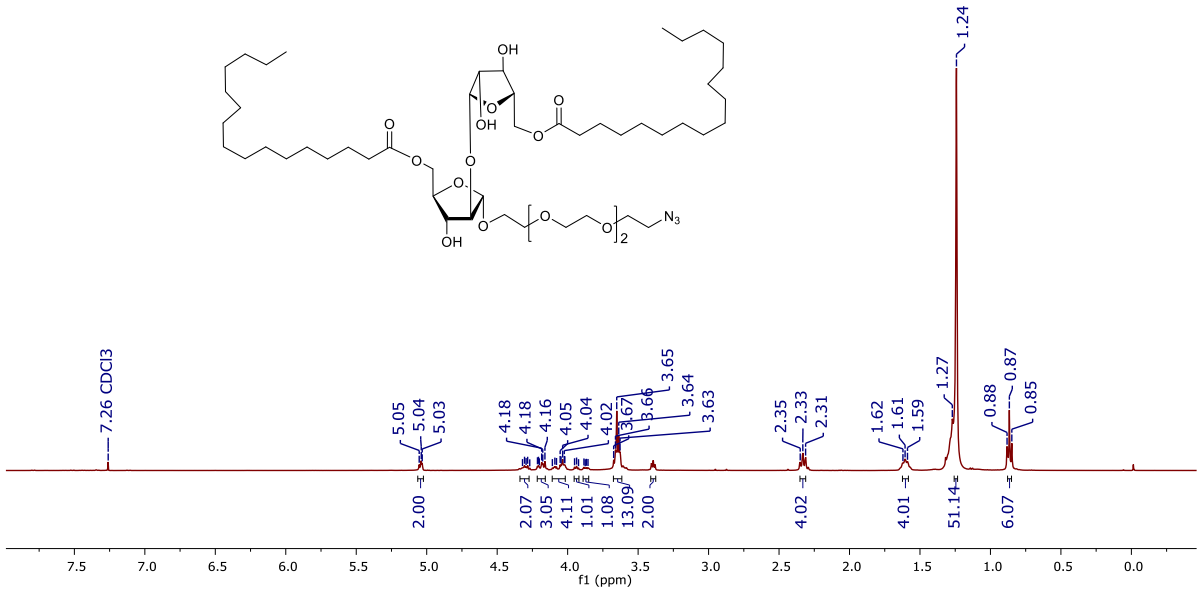
^{13}C NMR Spectrum (100.53 MHz, $CDCl_3$) of Compound **S11**



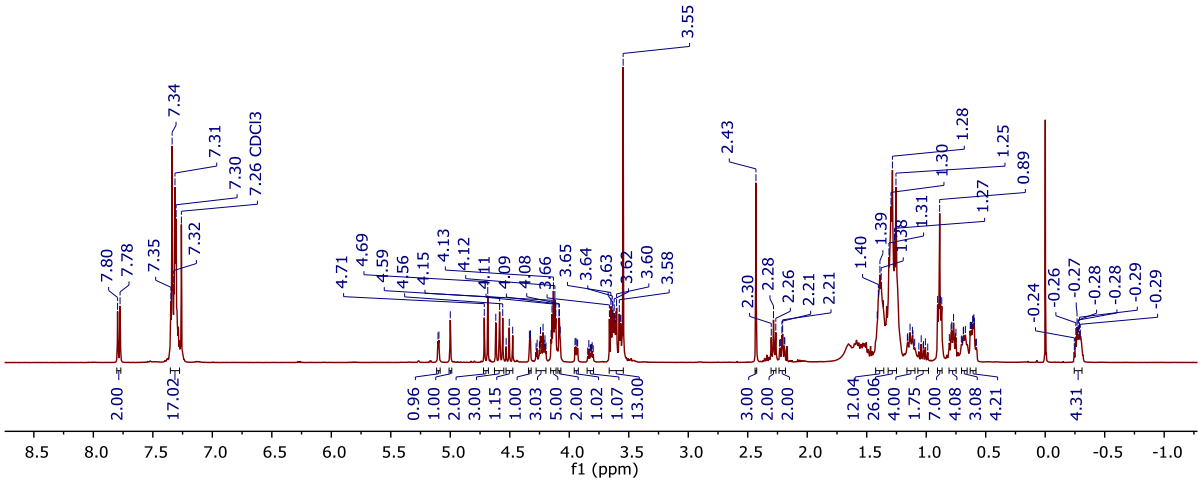
DEPT NMR Spectrum (100.53 MHz, $CDCl_3$) of Compound **S11**



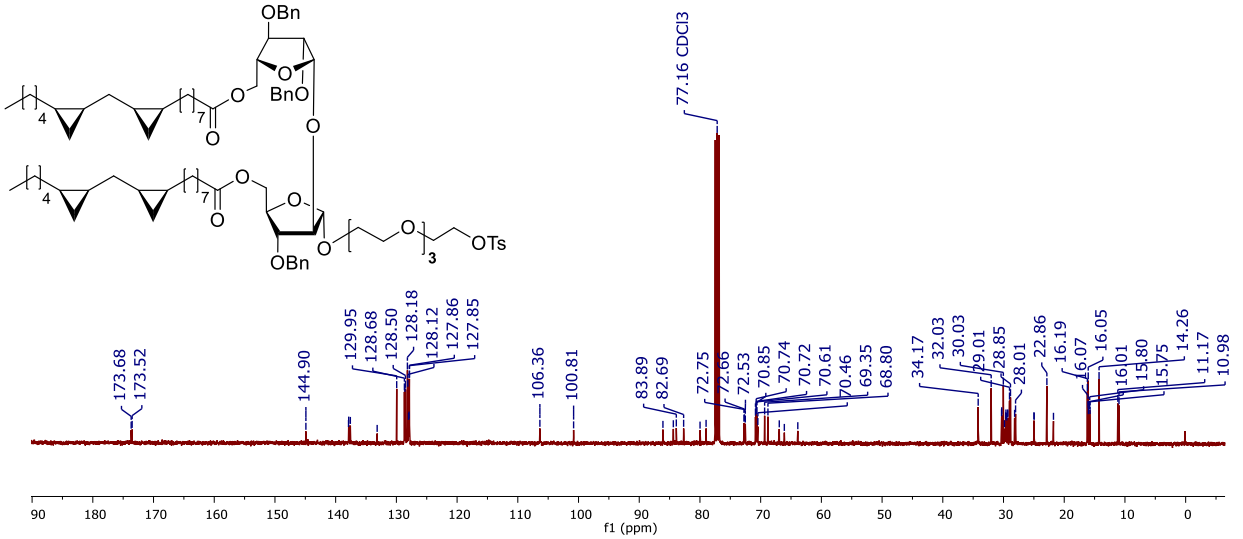
^{1}H NMR Spectrum (400.31 MHz, $CDCl_3$) of Compound **26a**


OH
O
OH
O
O
O

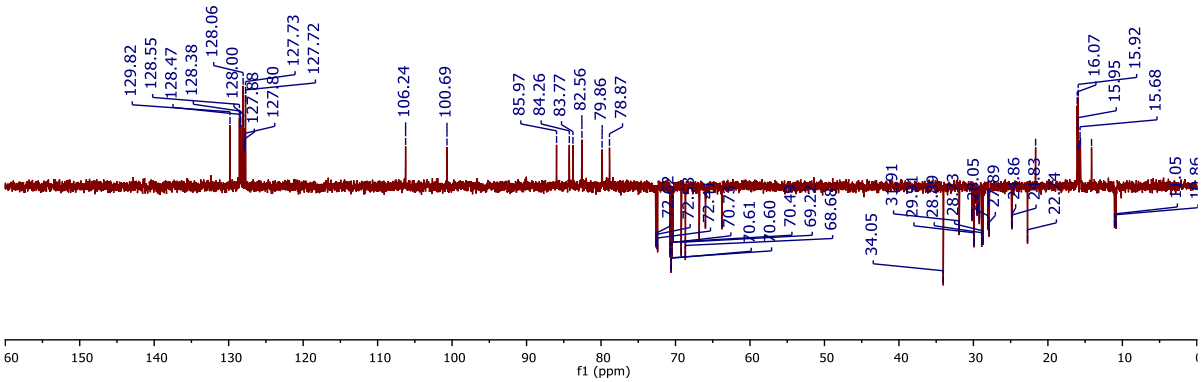
^{1}H NMR Spectrum (400.31 MHz, $CDCl_3$) of Compound **25b**



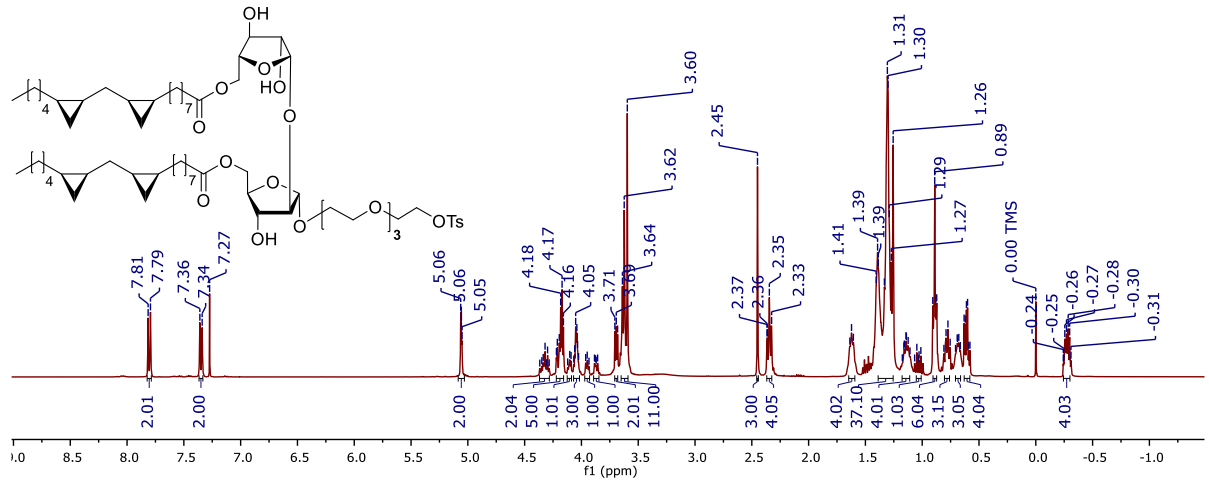
^{13}C NMR Spectrum (100.53 MHz, $CDCl_3$) of Compound **25b**



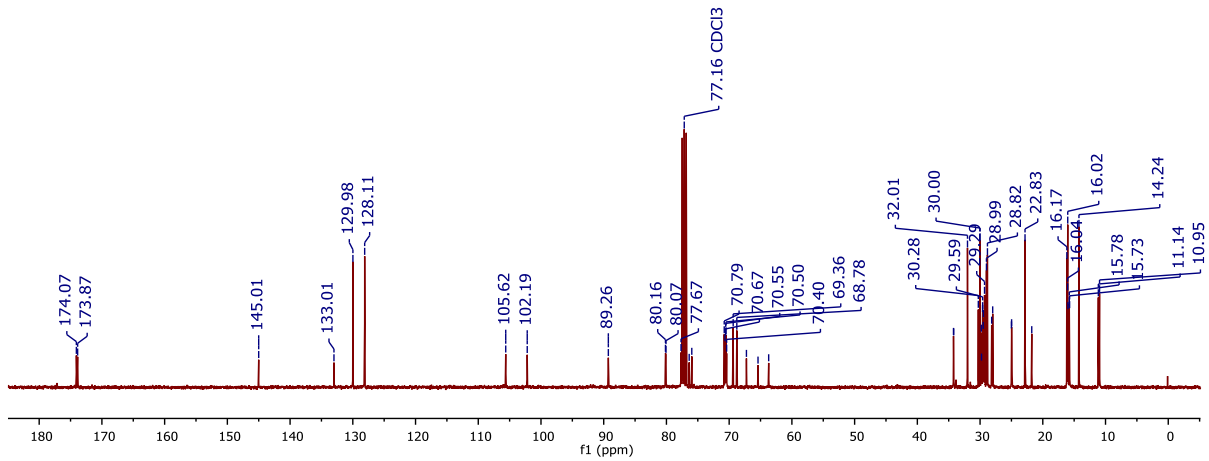
DEPT NMR Spectrum (100.31 MHz, $CDCl_3$) of Compound **25b**



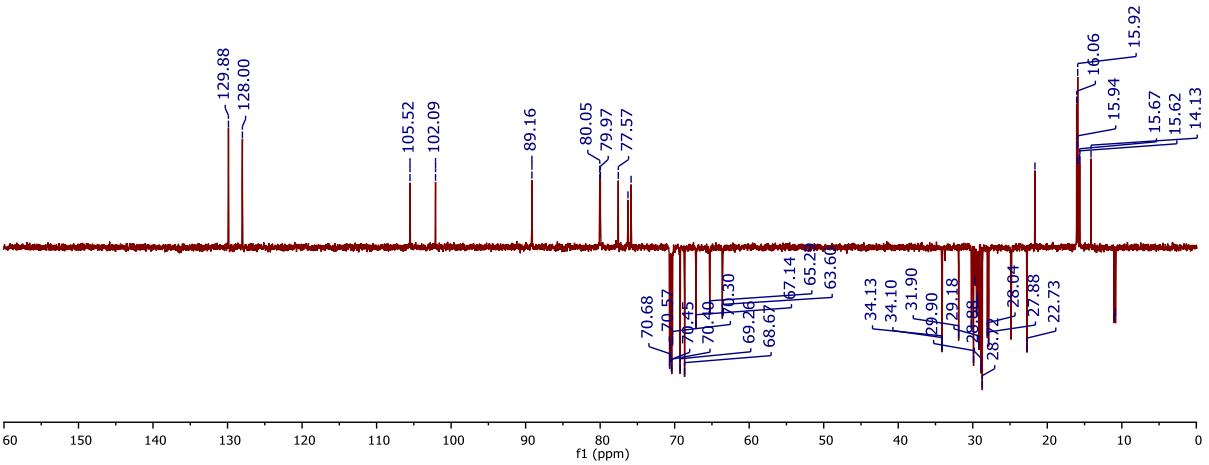
^{1}H NMR Spectrum (400.31 MHz, $CDCl_3$) of Compound **S12**



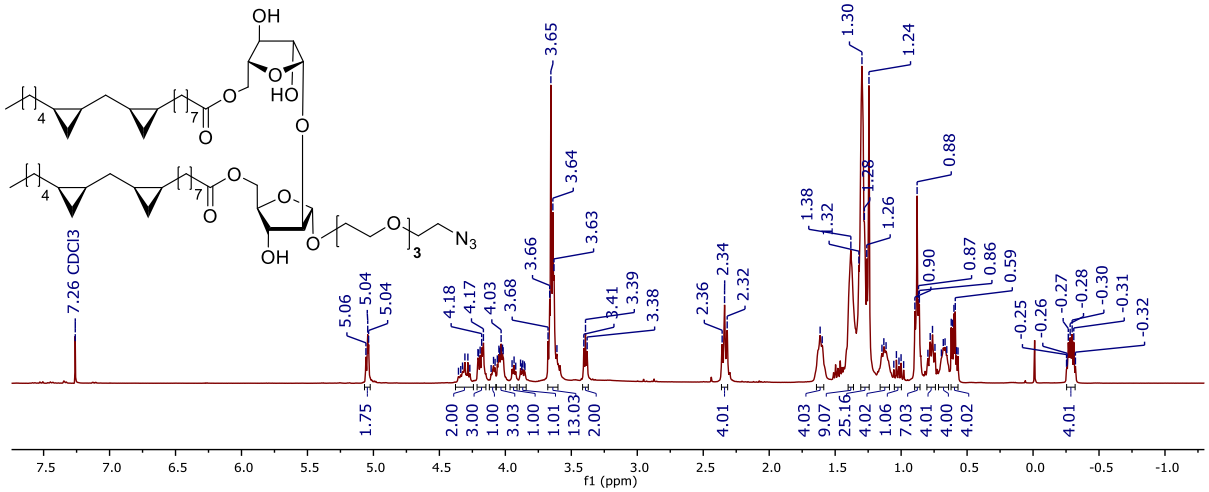
^{13}C NMR Spectrum (100.53 MHz, $CDCl_3$) of Compound **S12**



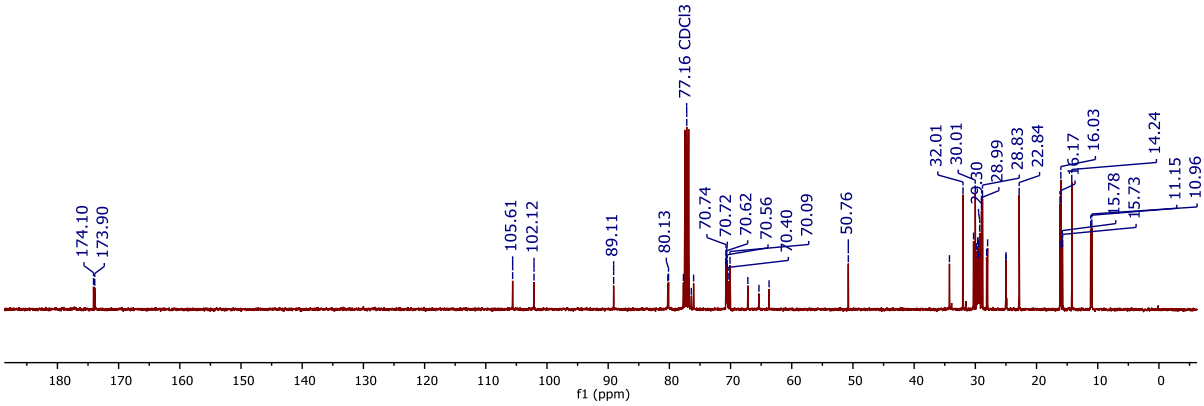
DEPT NMR Spectrum (100.53 MHz, $CDCl_3$) of Compound **S12**



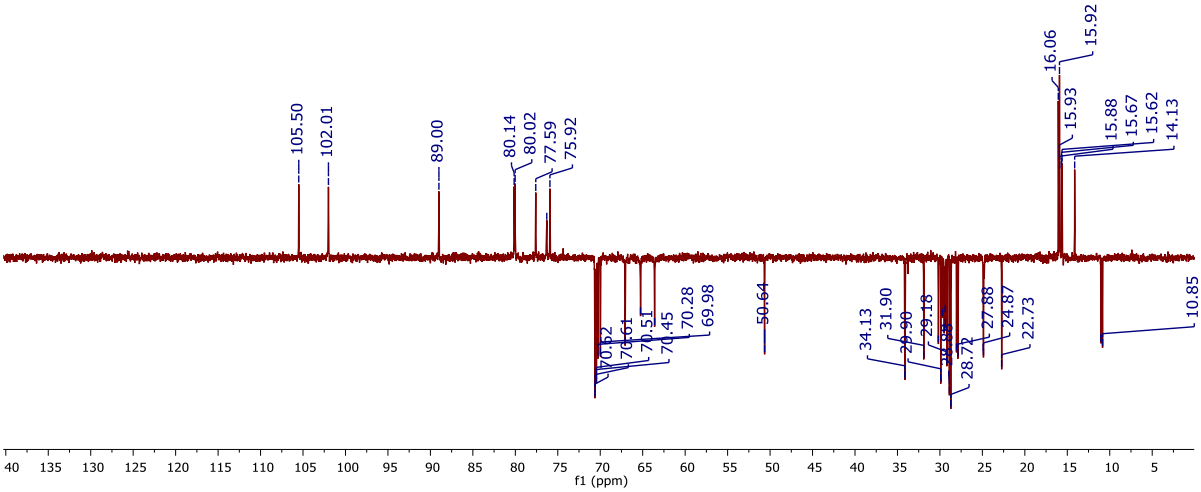
^{1}H NMR Spectrum (400.31 MHz, $CDCl_3$) of Compound **25c**



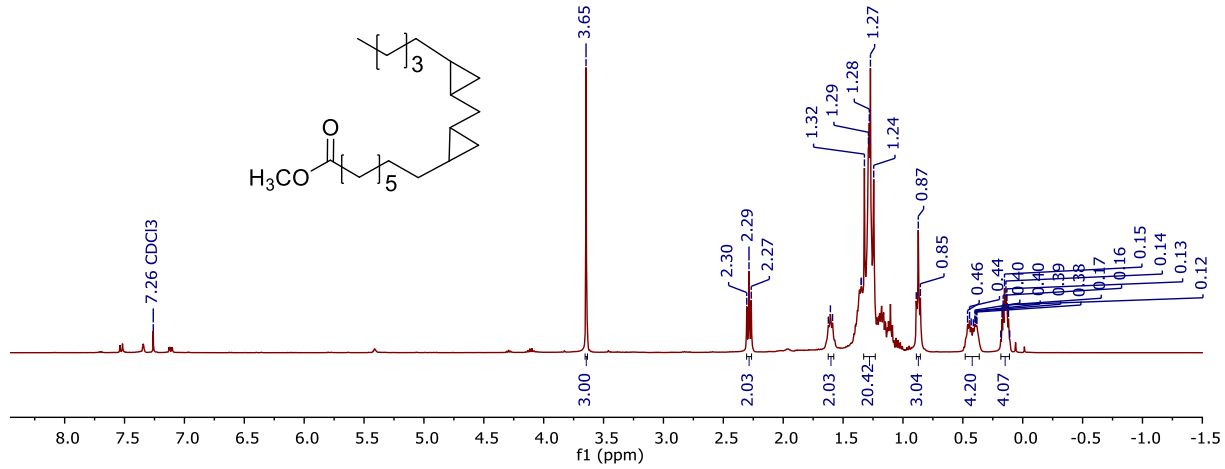
^{13}C NMR Spectrum (100.53 MHz, $CDCl_3$) of Compound **25c**



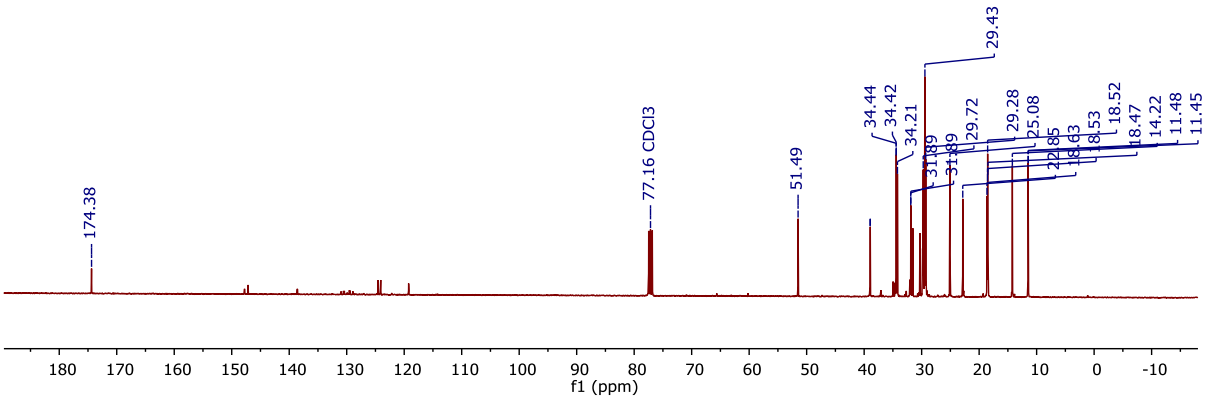
DEPT NMR Spectrum (100.53 MHz, $CDCl_3$) of Compound **25c**



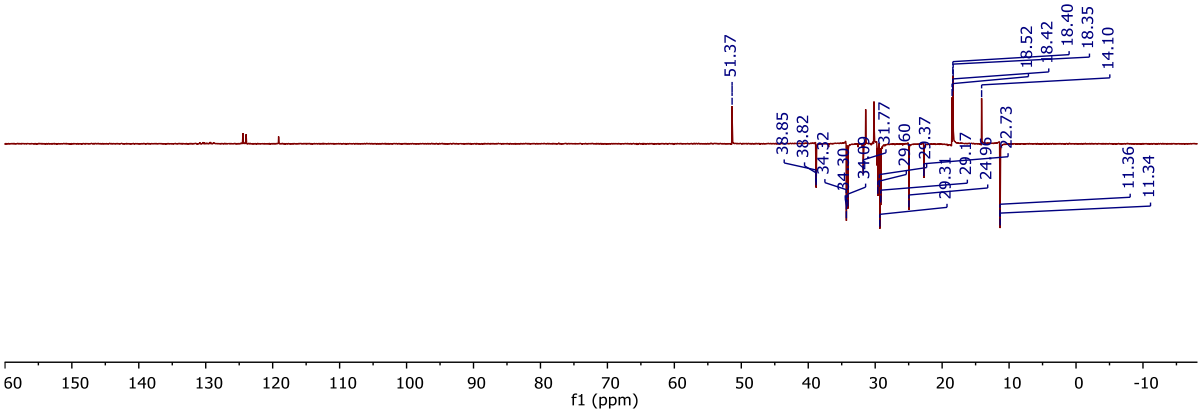
^{1}H NMR Spectrum (400.31 MHz, $CDCl_3$) of Compound **C6**



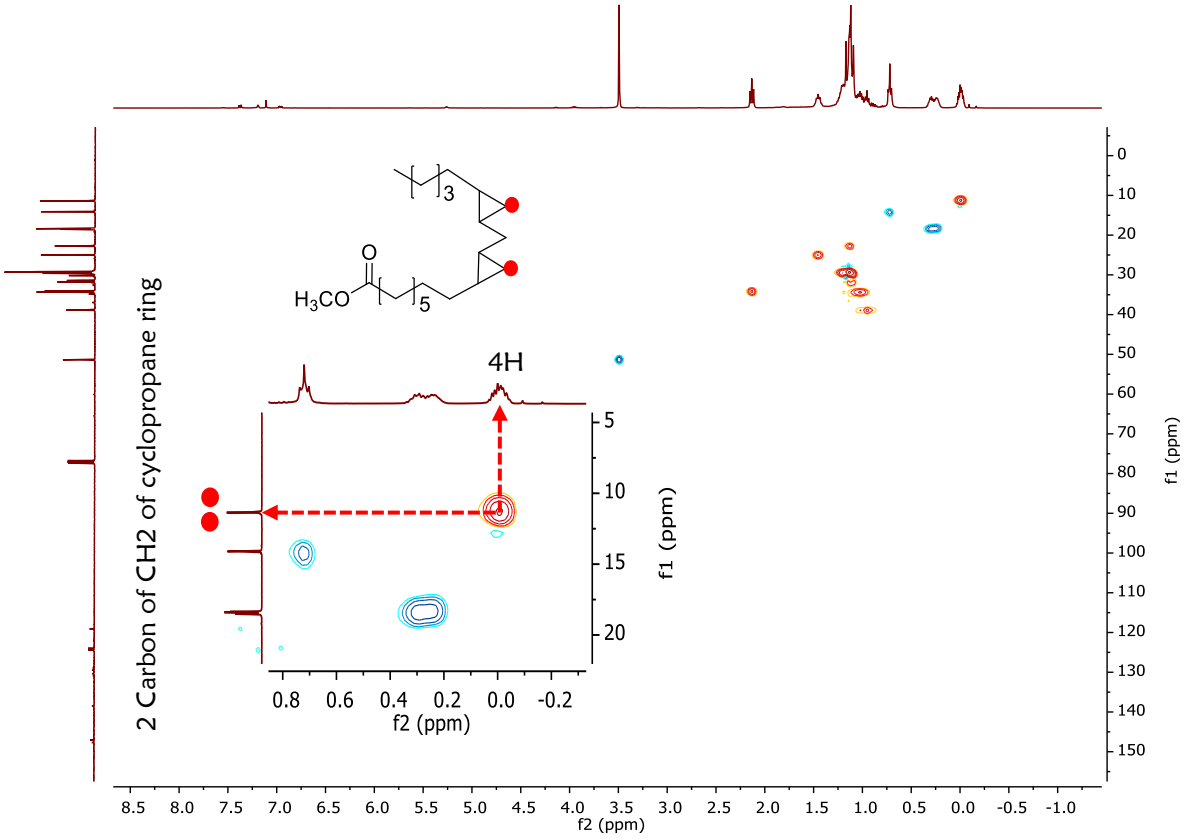
^{13}C NMR Spectrum (100.53 MHz, $CDCl_3$) of Compound **C6**



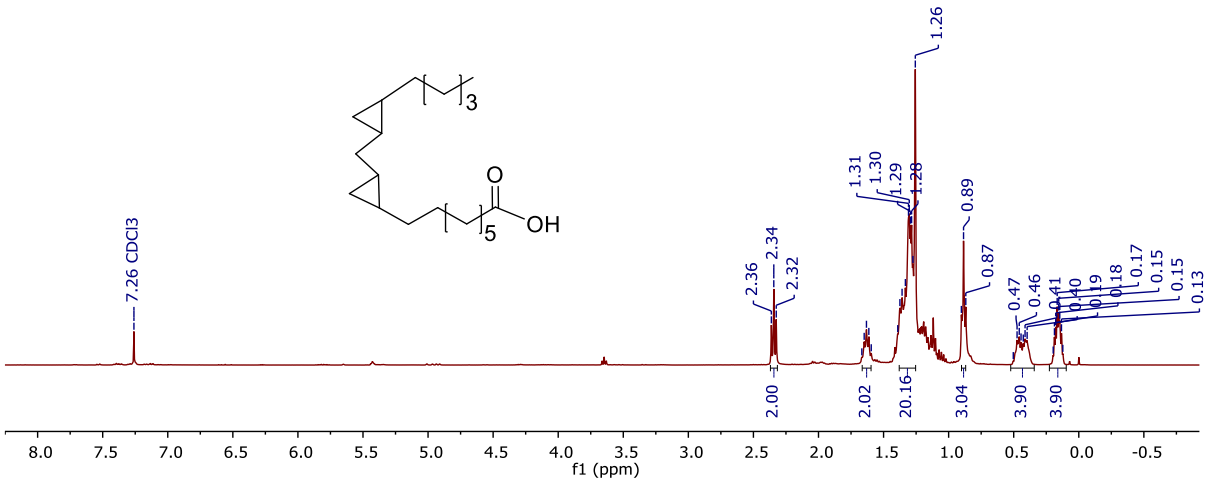
DEPT NMR Spectrum (100.53 MHz, $CDCl_3$) of Compound **C6**



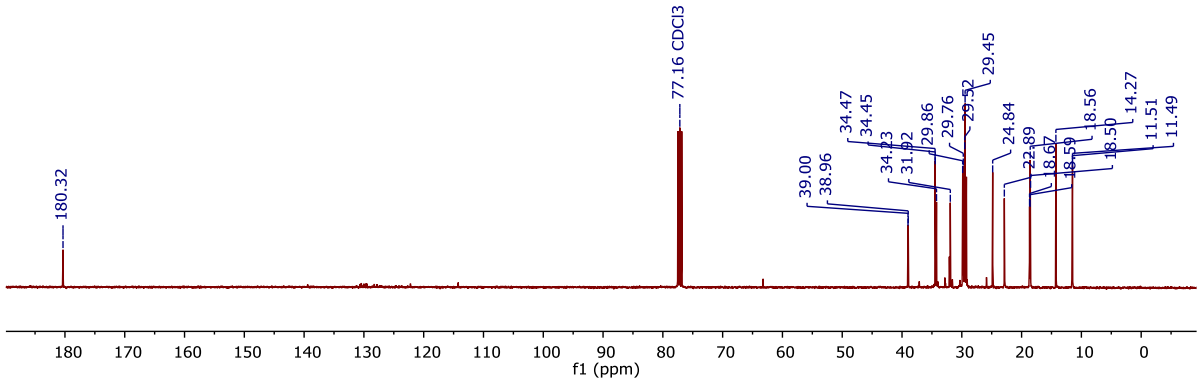
HMBC NMR Spectrum of Compound **C6**



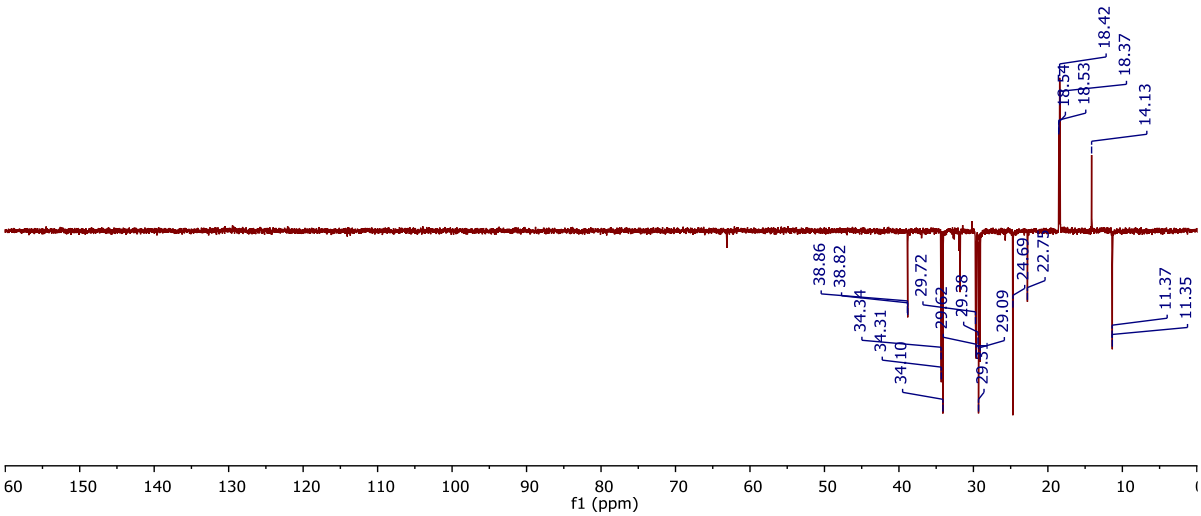
^{1}H NMR Spectrum (400.31 MHz, $CDCl_3$) of Compound **C7**



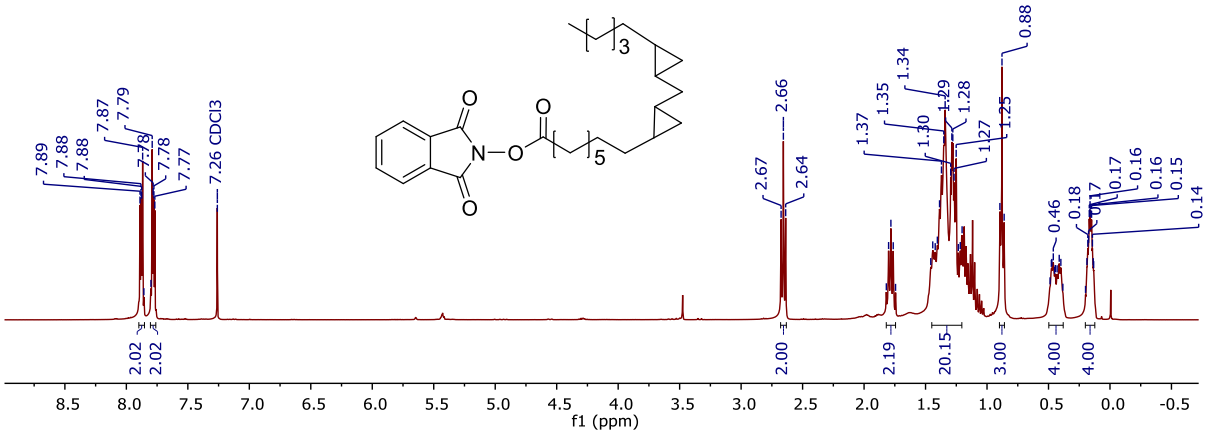
^{13}C NMR Spectrum (100.53 MHz, $CDCl_3$) of Compound **C7**



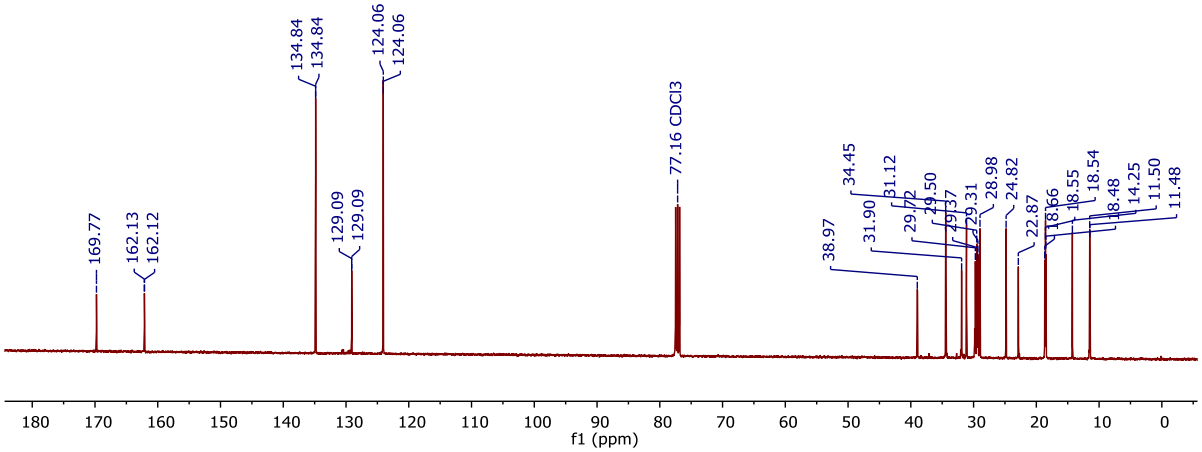
DEPT NMR Spectrum (100.53 MHz, $CDCl_3$) of Compound **C7**



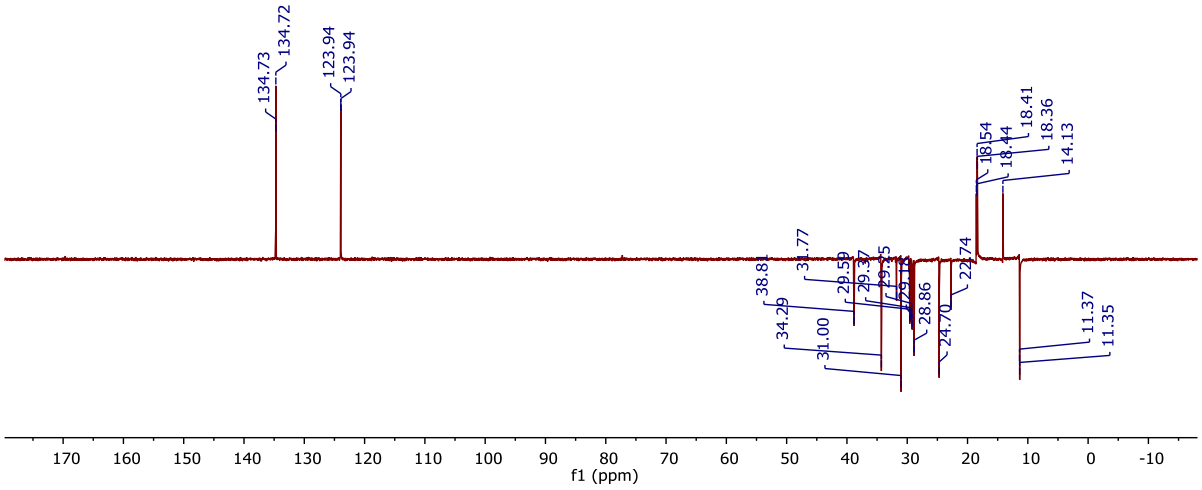
^{1}H NMR Spectrum (400.31 MHz, $CDCl_3$) of Compound **C8**



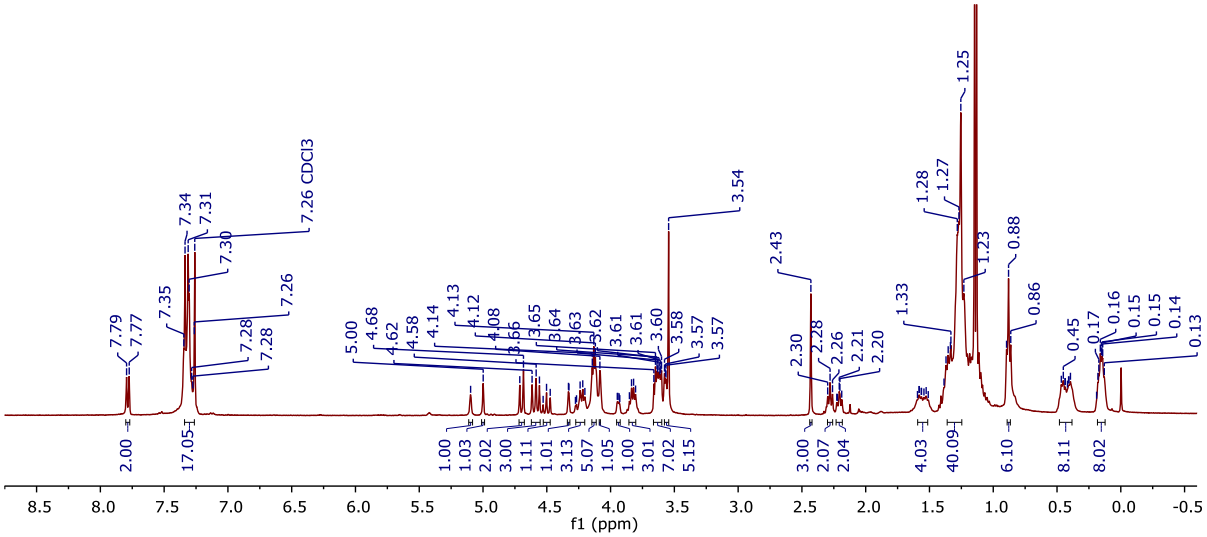
^{13}C NMR Spectrum (100.53 MHz, $CDCl_3$) of Compound **C8**



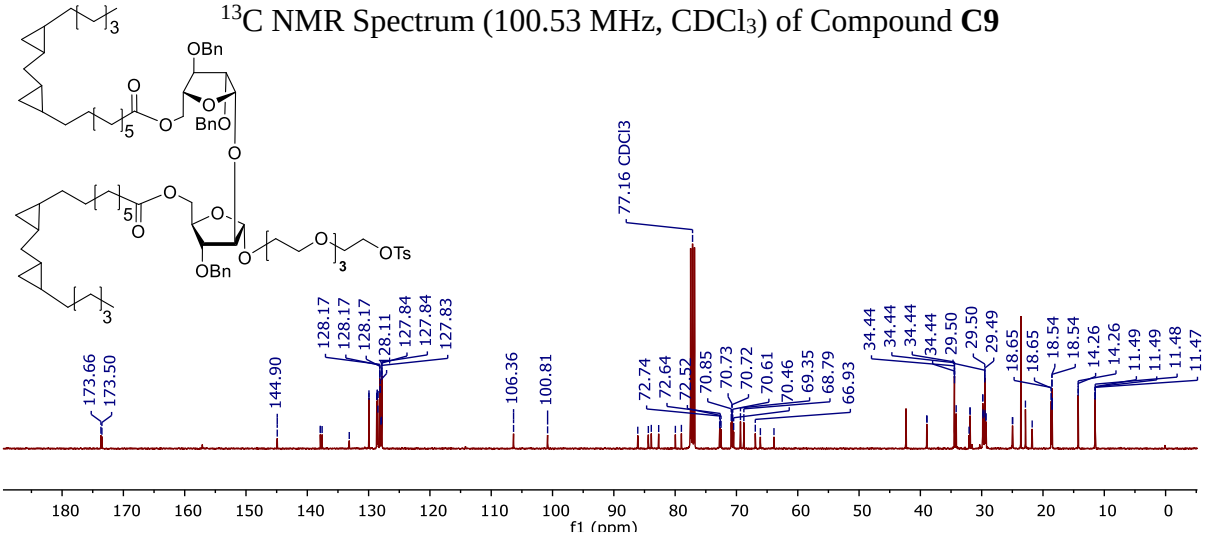
DEPT NMR Spectrum (100.53 MHz, $CDCl_3$) of Compound **C8**



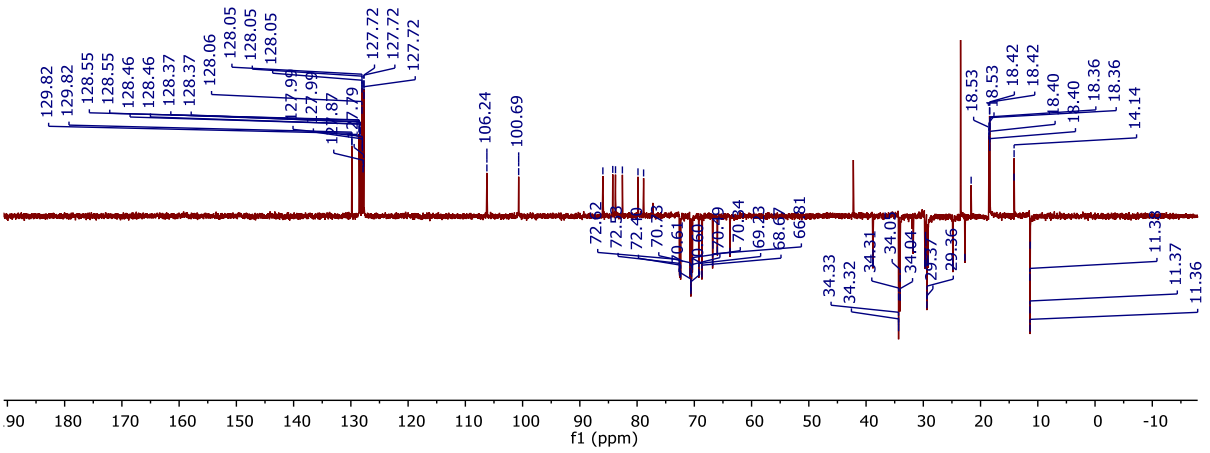
^{1}H NMR Spectrum (400.31 MHz, $CDCl_3$) of Compound **C9**



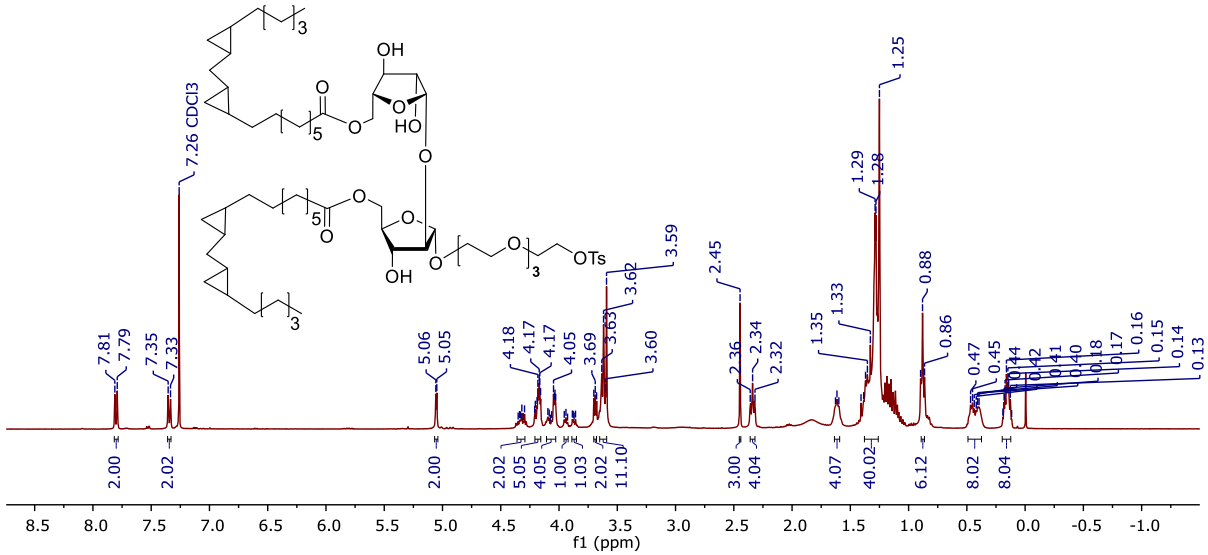
^{13}C NMR Spectrum (100.53 MHz, $CDCl_3$) of Compound **C9**



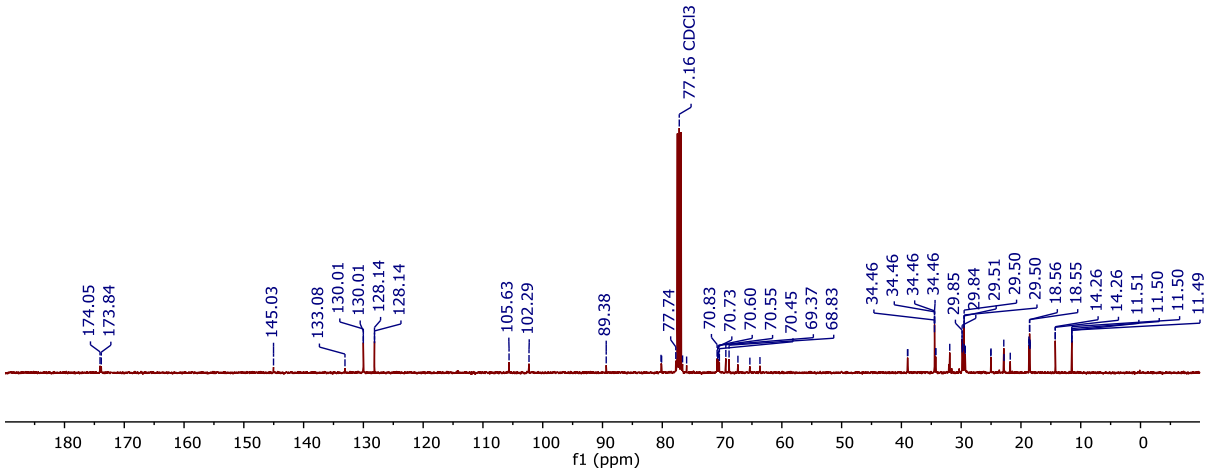
DEPT NMR Spectrum (100.53 MHz, $CDCl_3$) of Compound **C9**



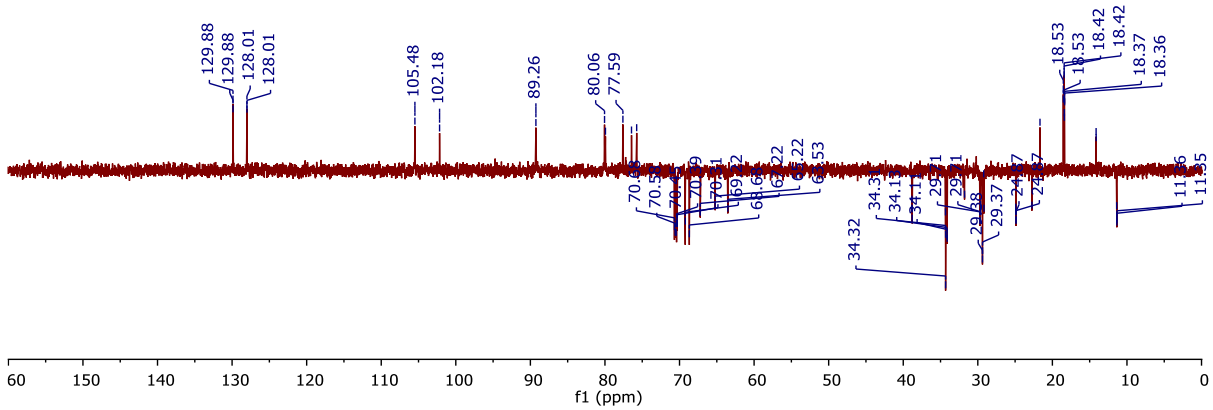
^{1}H NMR Spectrum (400.31 MHz, $CDCl_3$) of Compound **S13**



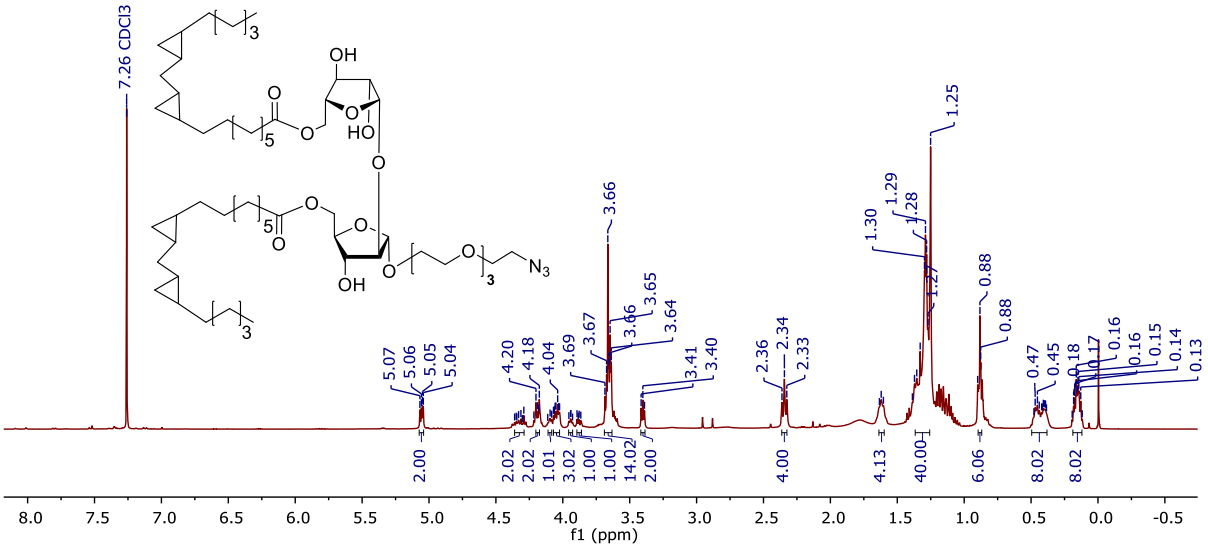
^{13}C NMR Spectrum (100.53 MHz, $CDCl_3$) of Compound **S13**



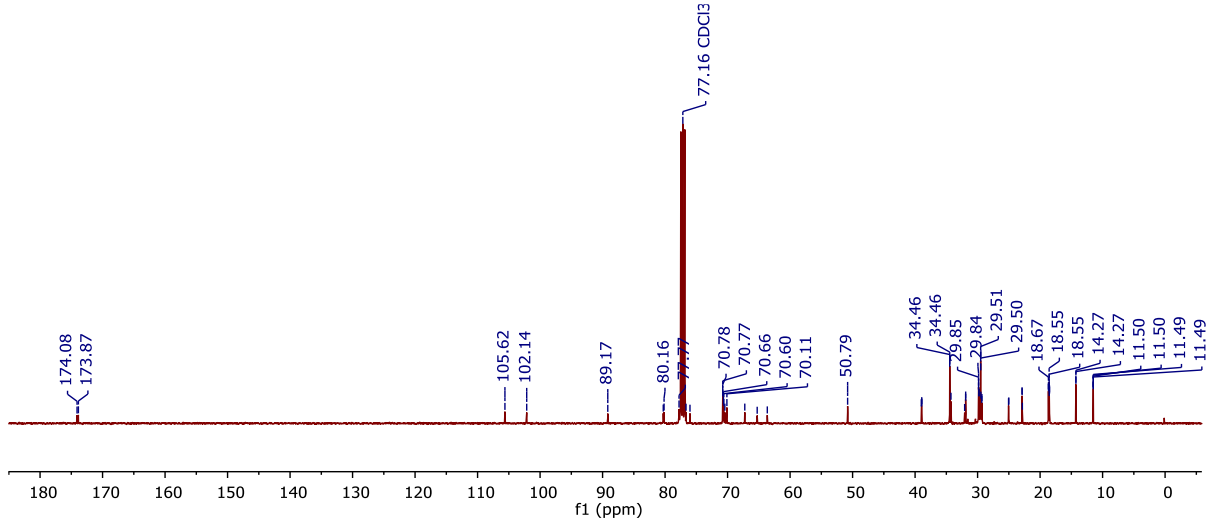
^{13}C NMR Spectrum (100.53 MHz, $CDCl_3$) of Compound **S13**



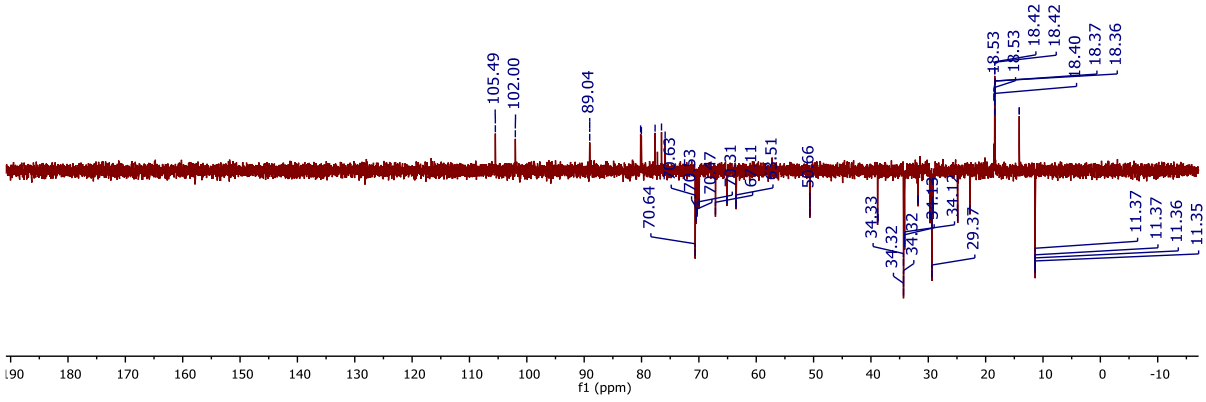
^{1}H NMR Spectrum (400.31 MHz, $CDCl_3$) of Compound **C10**



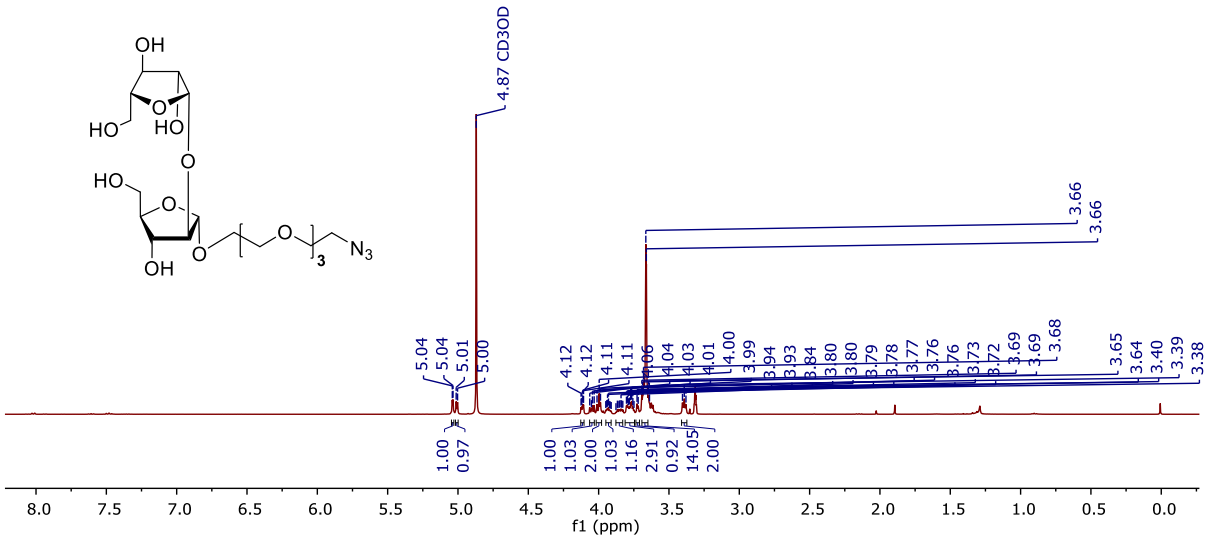
^{13}C NMR Spectrum (100.53 MHz, $CDCl_3$) of Compound **C10**



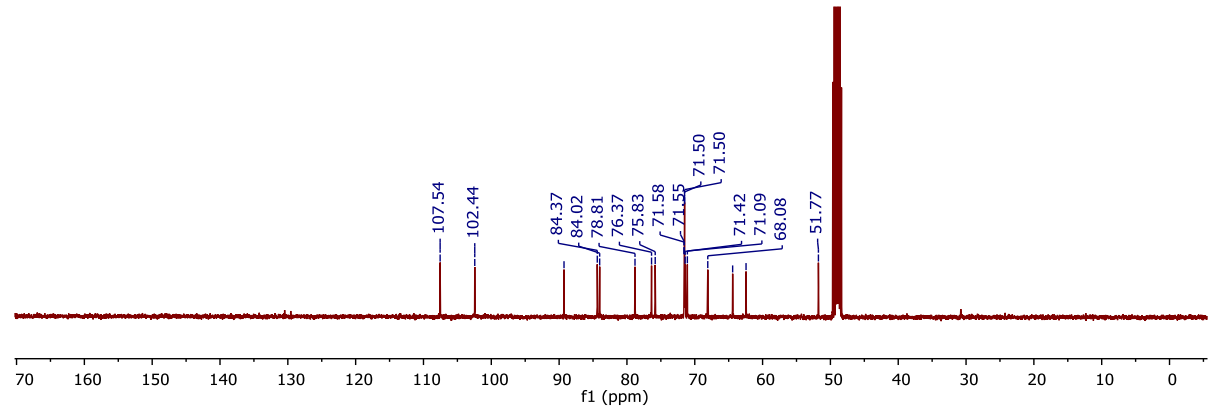
DEPT NMR Spectrum (100.53 MHz, $CDCl_3$) of Compound **C10**



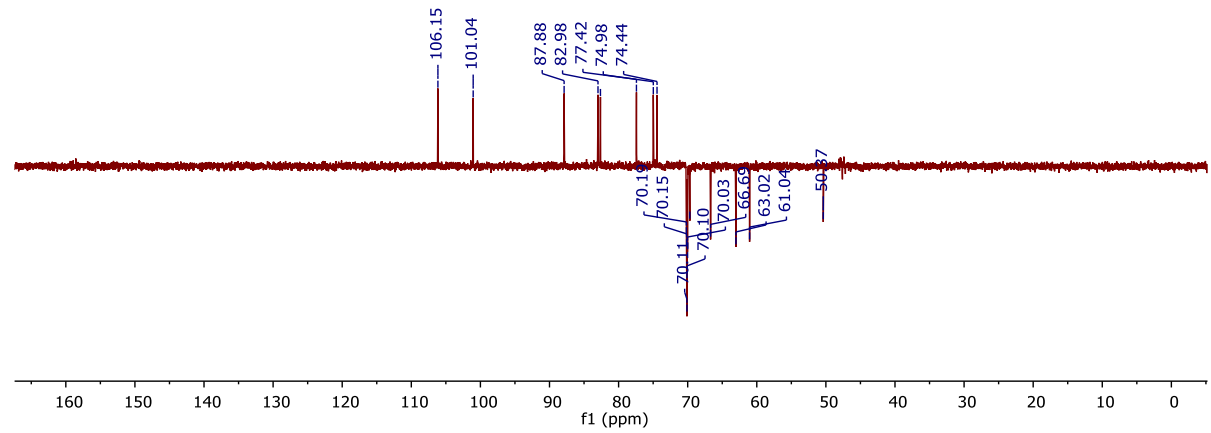
^{1}H NMR Spectrum (400.31 MHz, $CDCl_3$) of Compound **23**



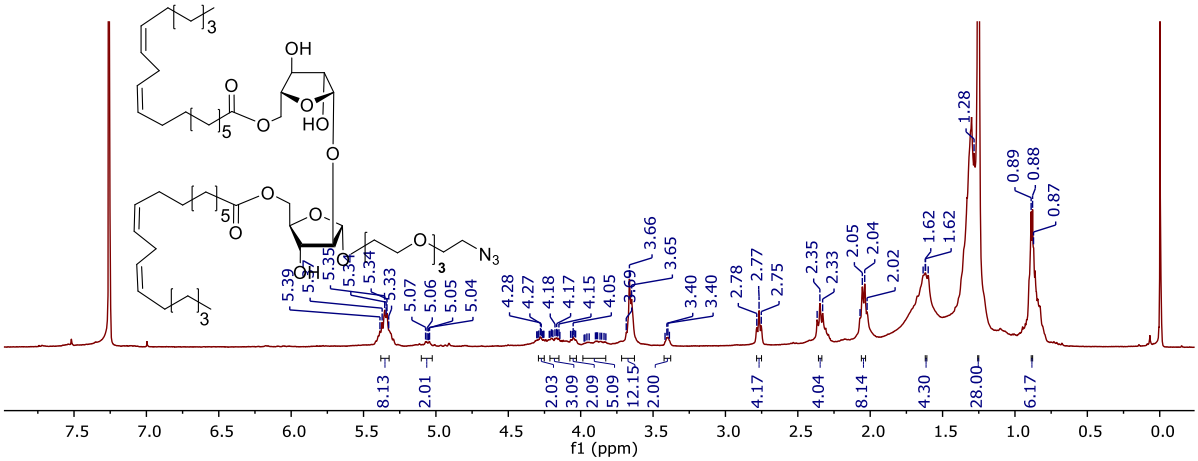
^{13}C NMR Spectrum (100.53 MHz, $CDCl_3$) of Compound **23**



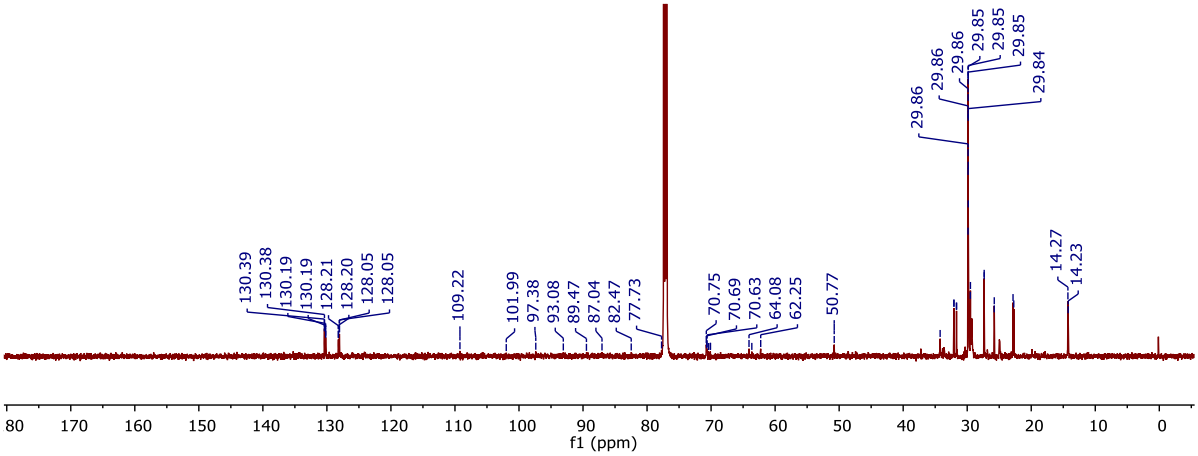
DEPT NMR Spectrum (100.53 MHz, $CDCl_3$) of Compound **23**



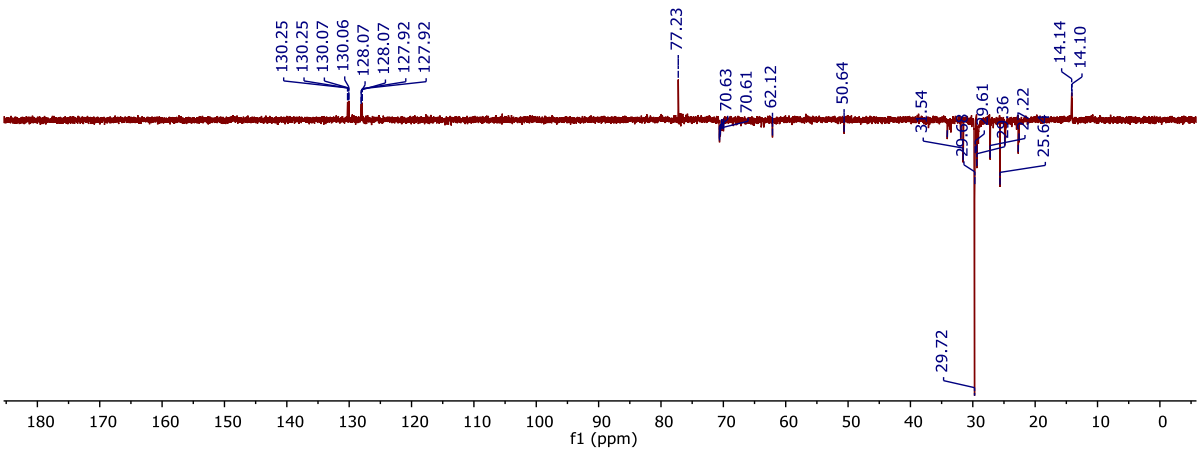
^{1}H NMR Spectrum (400.31 MHz, $CDCl_3$) of Compound **26b**



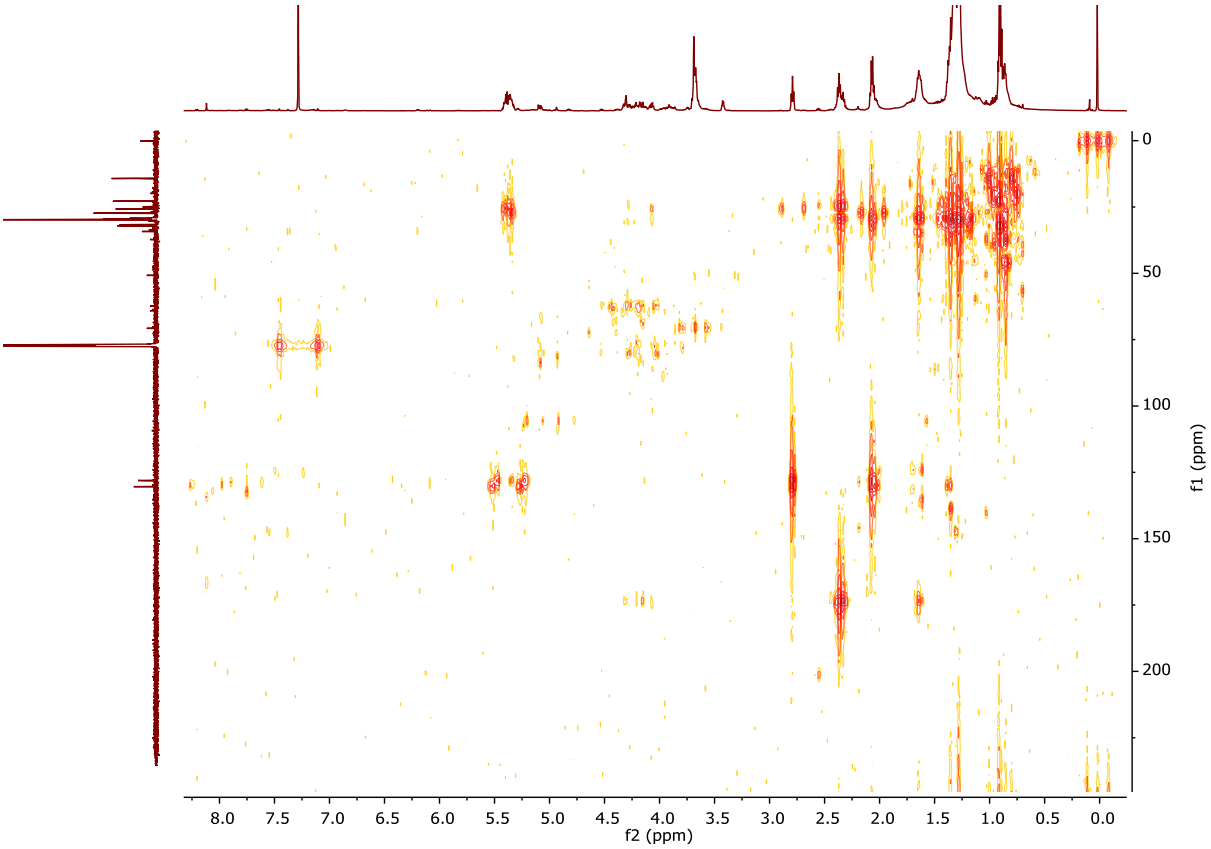
^{13}C NMR Spectrum (100.53 MHz, $CDCl_3$) of Compound **26b**



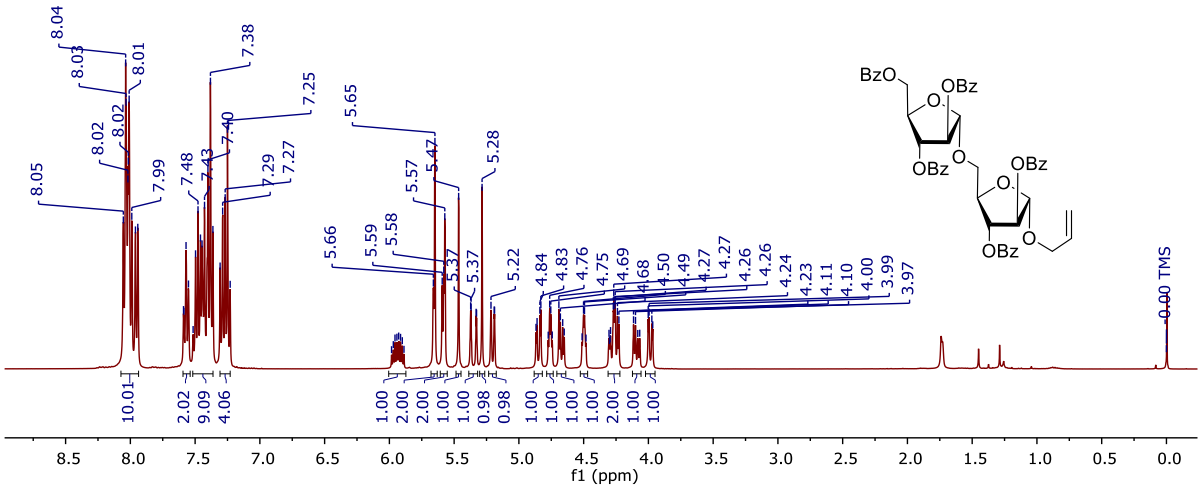
DEPT NMR Spectrum (100.53 MHz, $CDCl_3$) of Compound **26b**



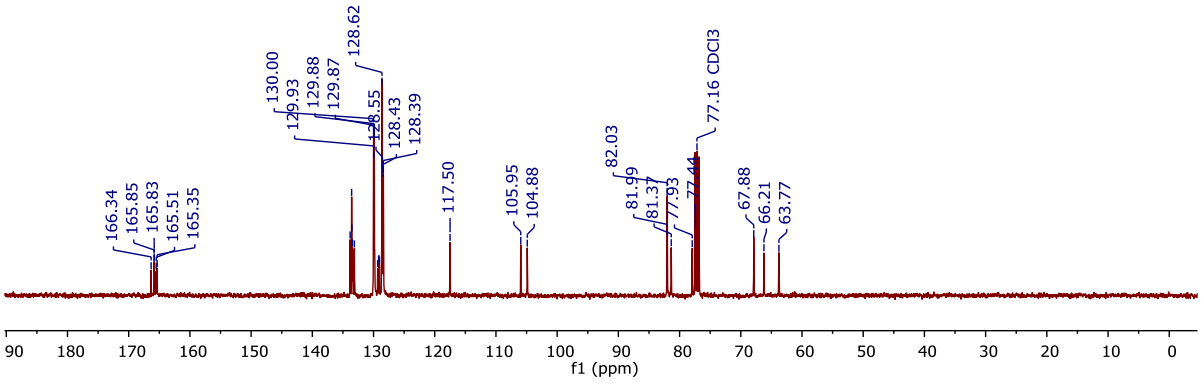
HMBC NMR Spectrum of Compound **26b**



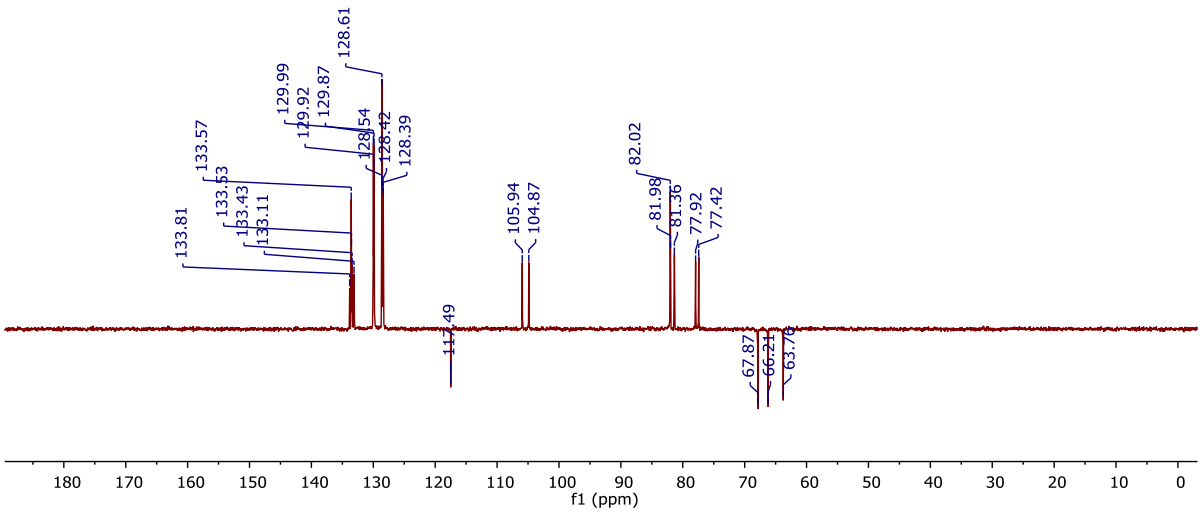
^{1}H NMR Spectrum (400.31 MHz, $CDCl_3$) of Compound **28**



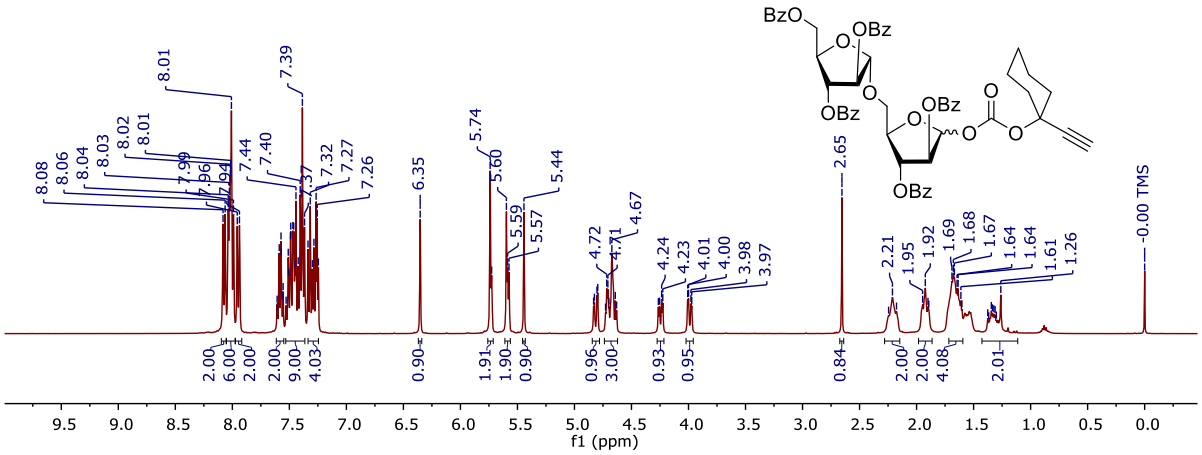
^{13}C NMR Spectrum (100.53 MHz, $CDCl_3$) of Compound **28**



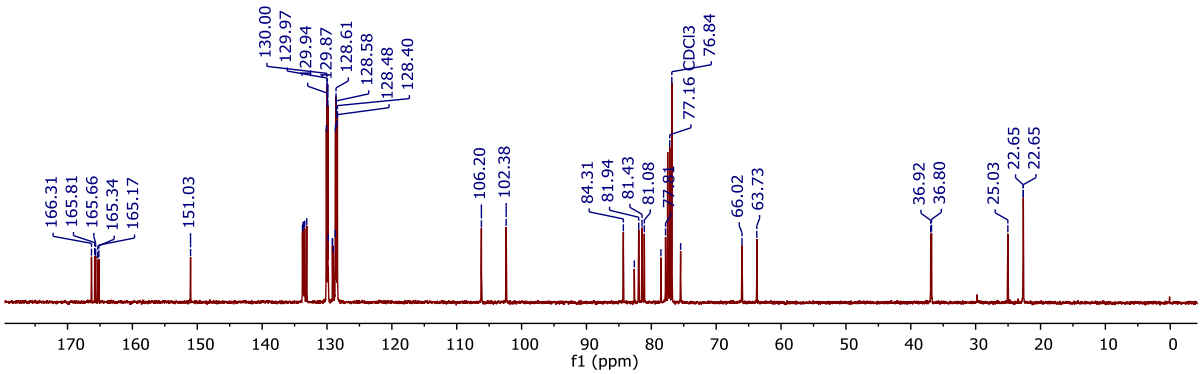
DEPT NMR Spectrum (100.53 MHz, $CDCl_3$) of Compound **28**



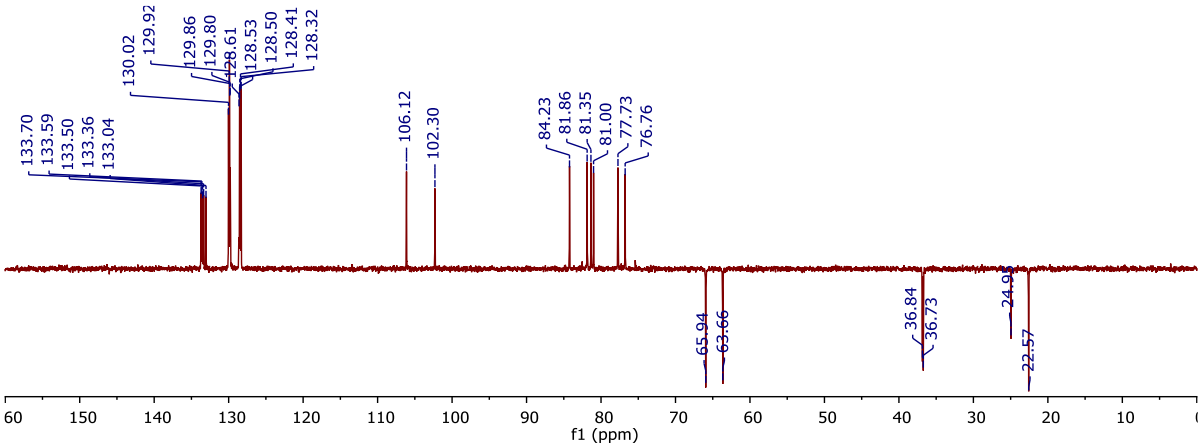
^{1}H NMR Spectrum (400.31 MHz, $CDCl_3$) of Compound **29**



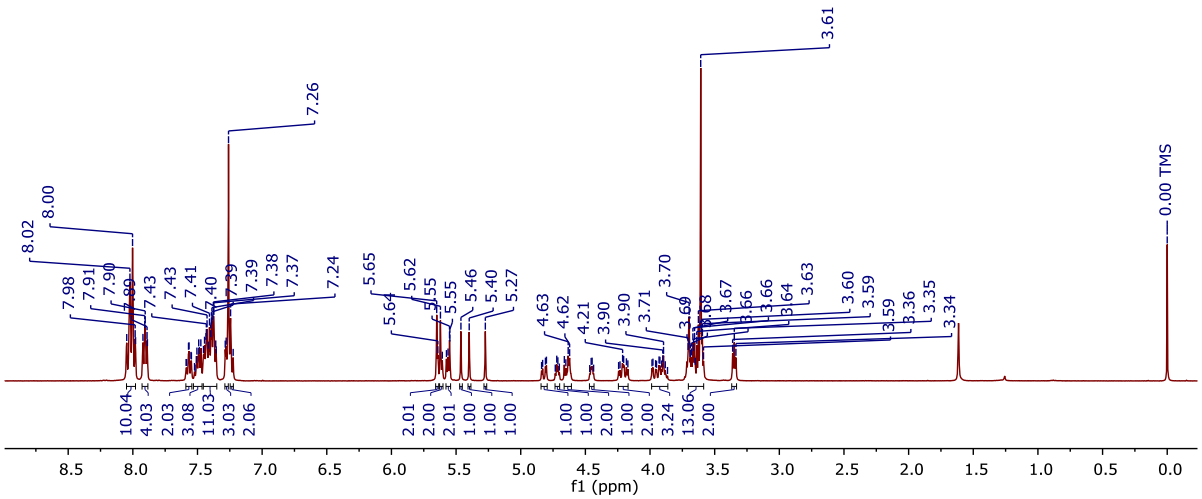
^{13}C NMR Spectrum (100.53 MHz, $CDCl_3$) of Compound **29**



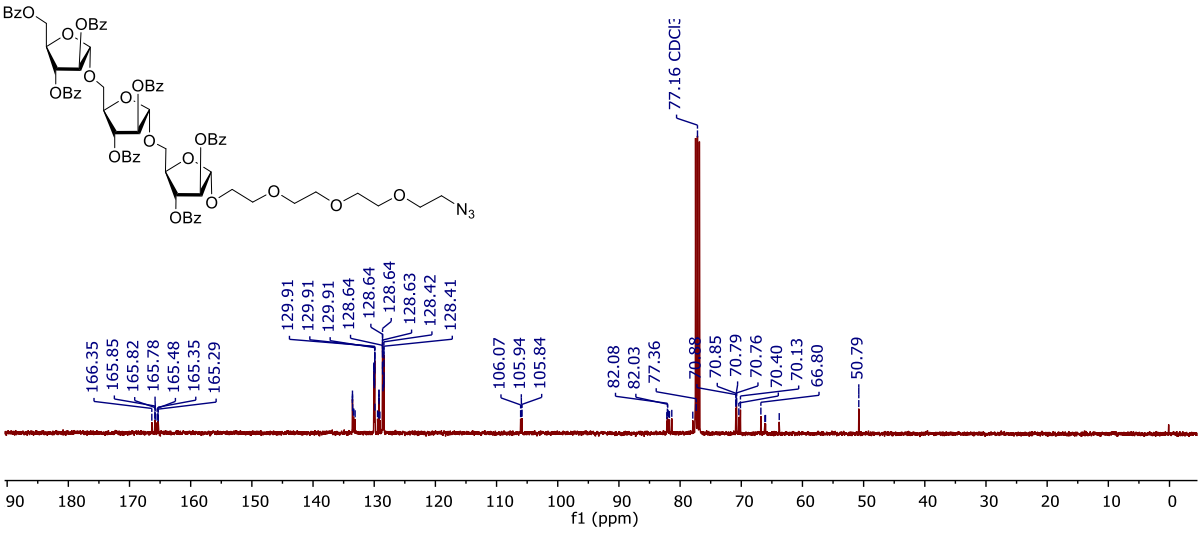
DEPT NMR Spectrum (100.53 MHz, $CDCl_3$) of Compound **29**



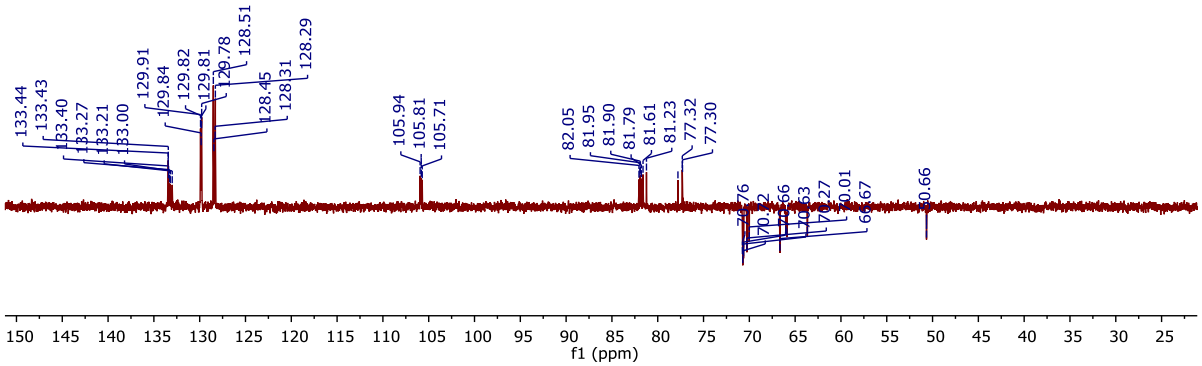
^{1}H NMR Spectrum (400.31 MHz, $CDCl_3$) of Compound **30**



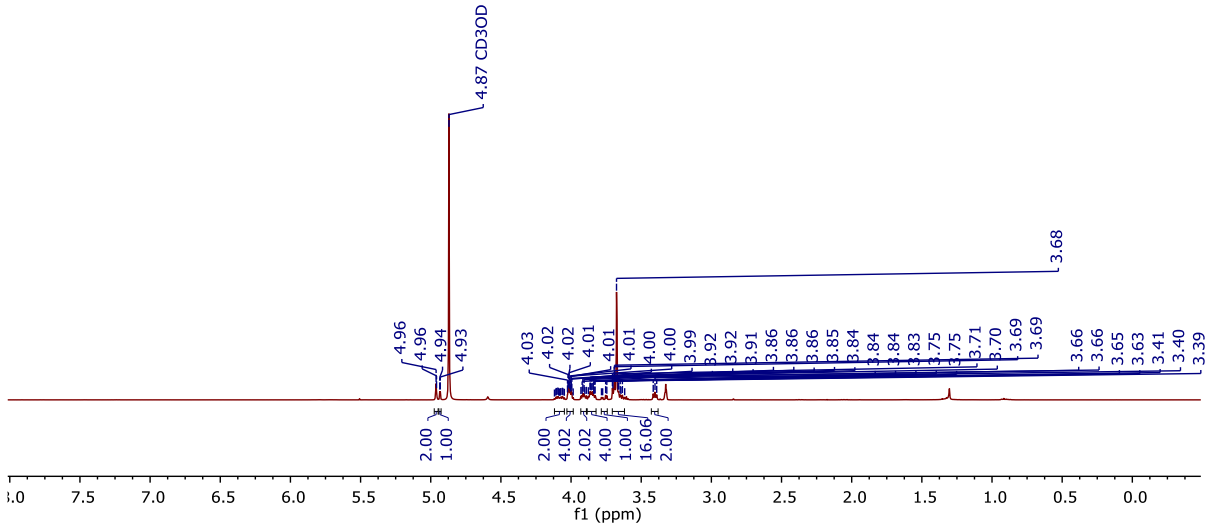
^{13}C NMR spectrum (100.53 MHz) of compound **30**



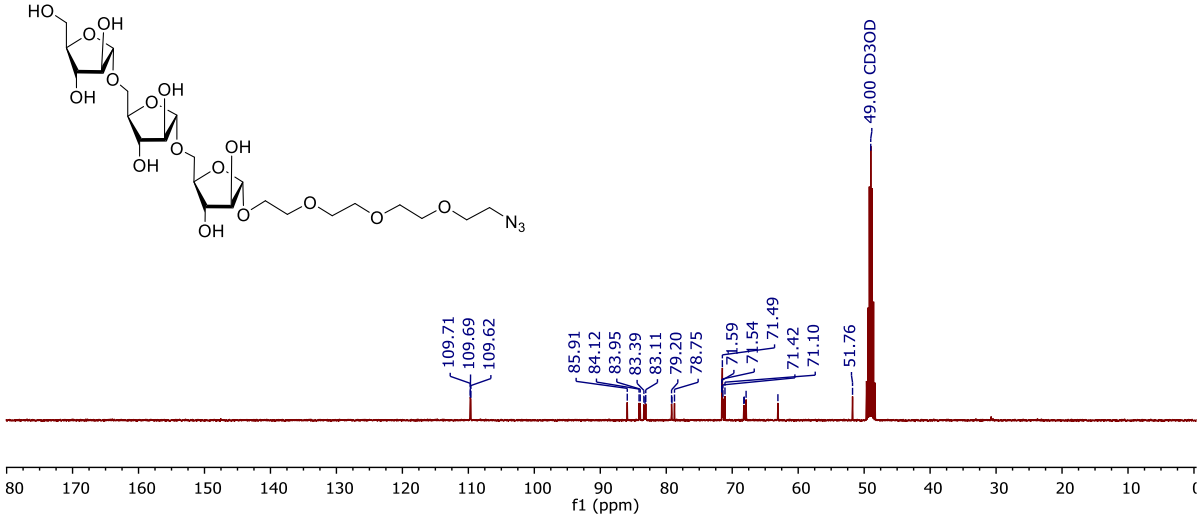
DEPT NMR spectrum (100.53 MHz) of compound **30**



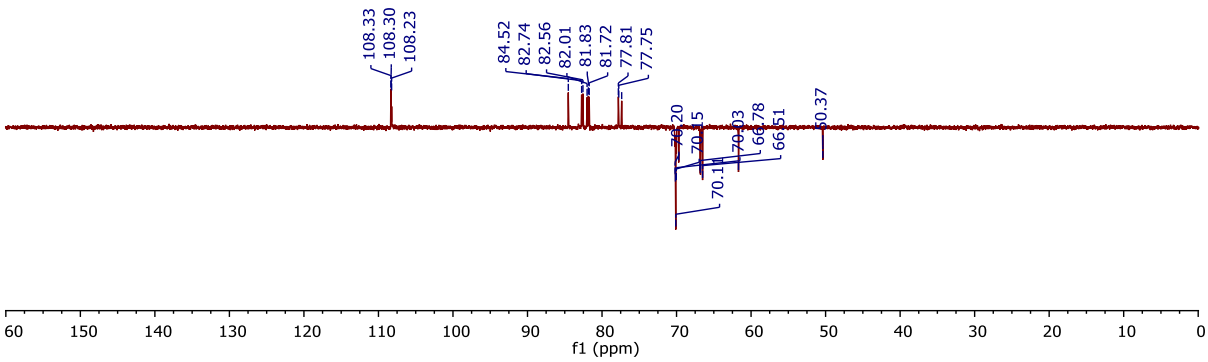
^{1}H NMR spectrum (400.31 MHz, CD_3OD) of compound **31**



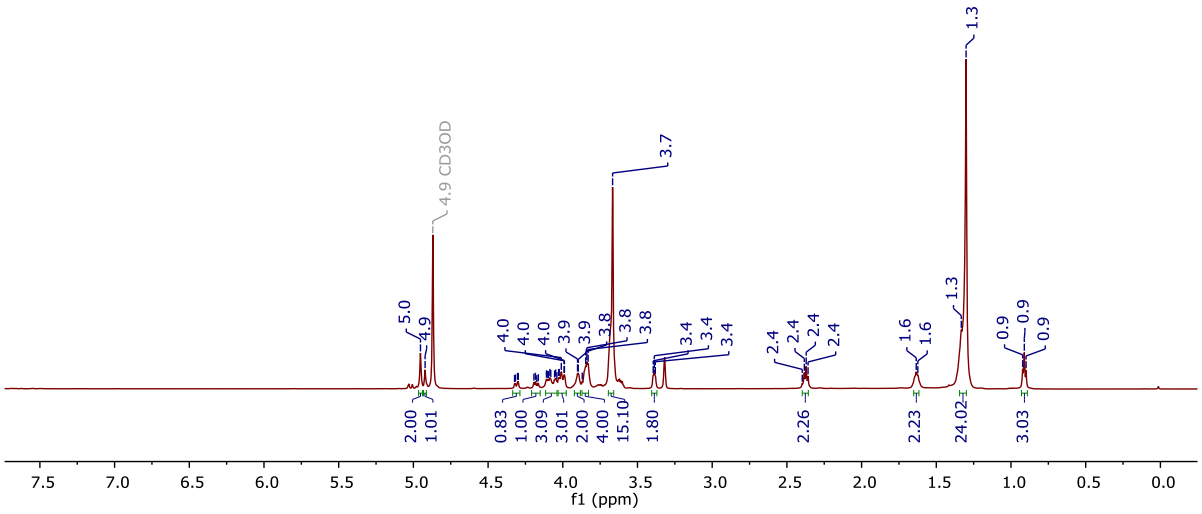
^{13}C NMR spectrum (100.53 MHz, CD_3OD) of compound **31**



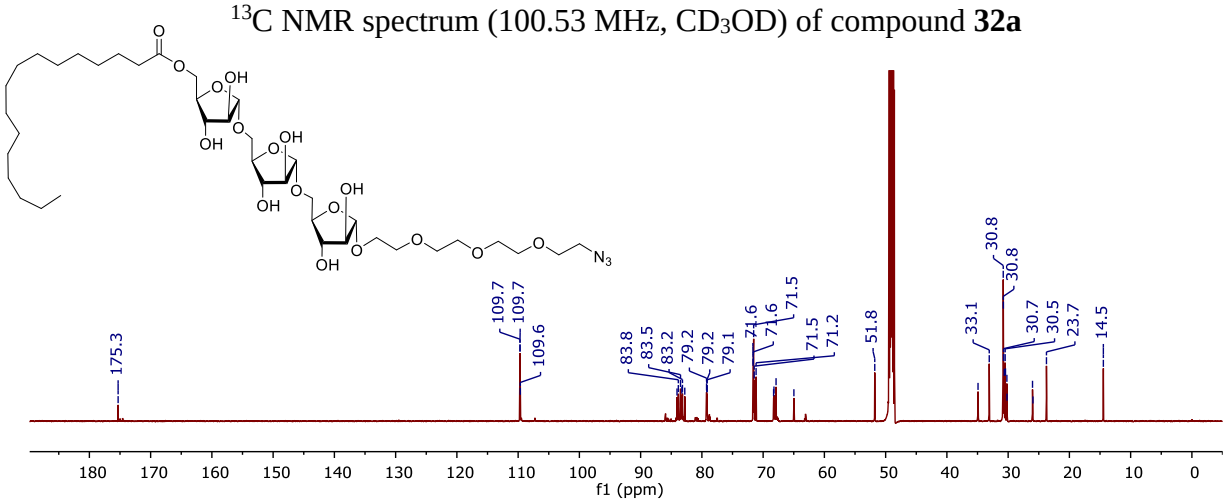
DEPT NMR spectrum (100.53 MHz, CD_3OD) of compound **31**



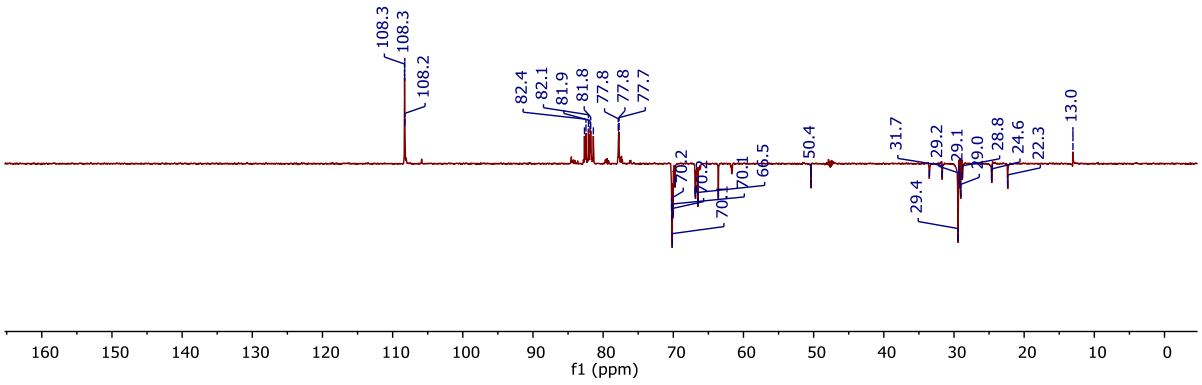
^{1}H NMR spectrum (400.31 MHz, CD_3OD) of compound **32a**



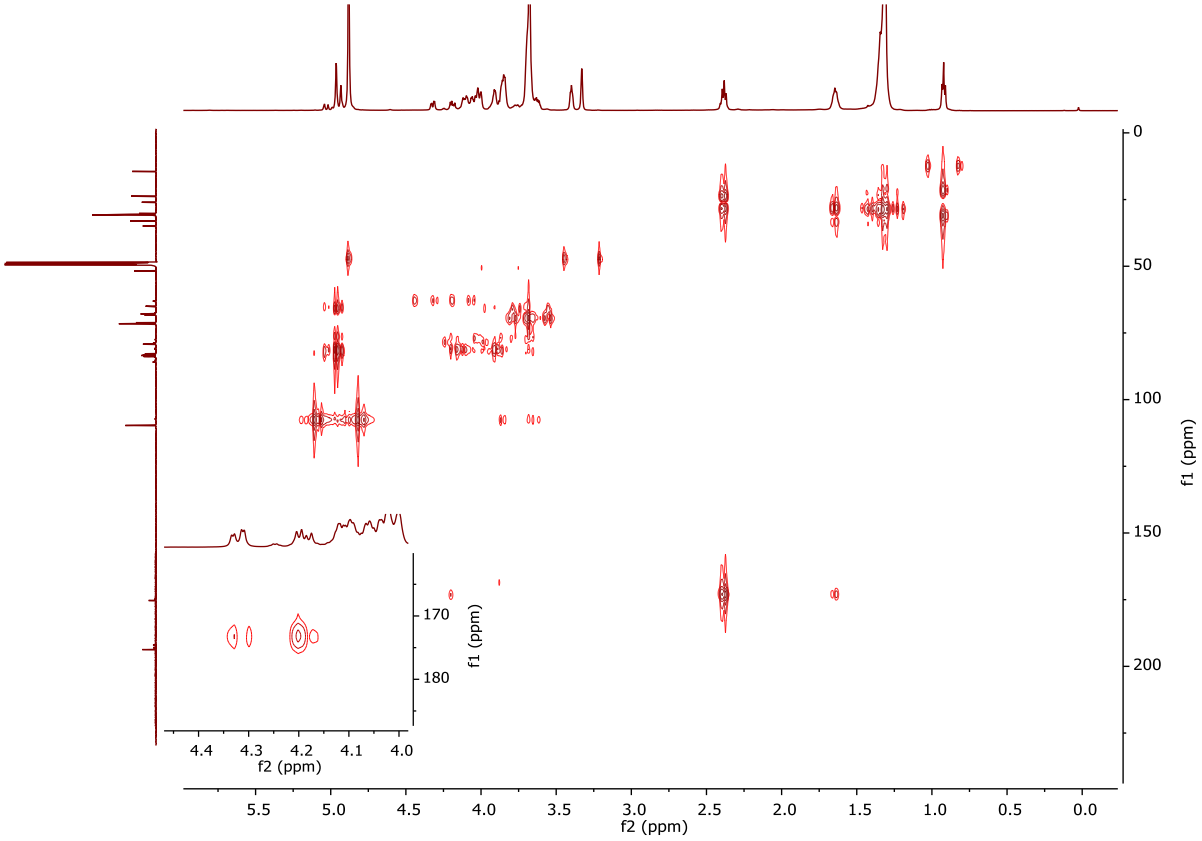
^{13}C NMR spectrum (100.53 MHz, CD_3OD) of compound **32a**



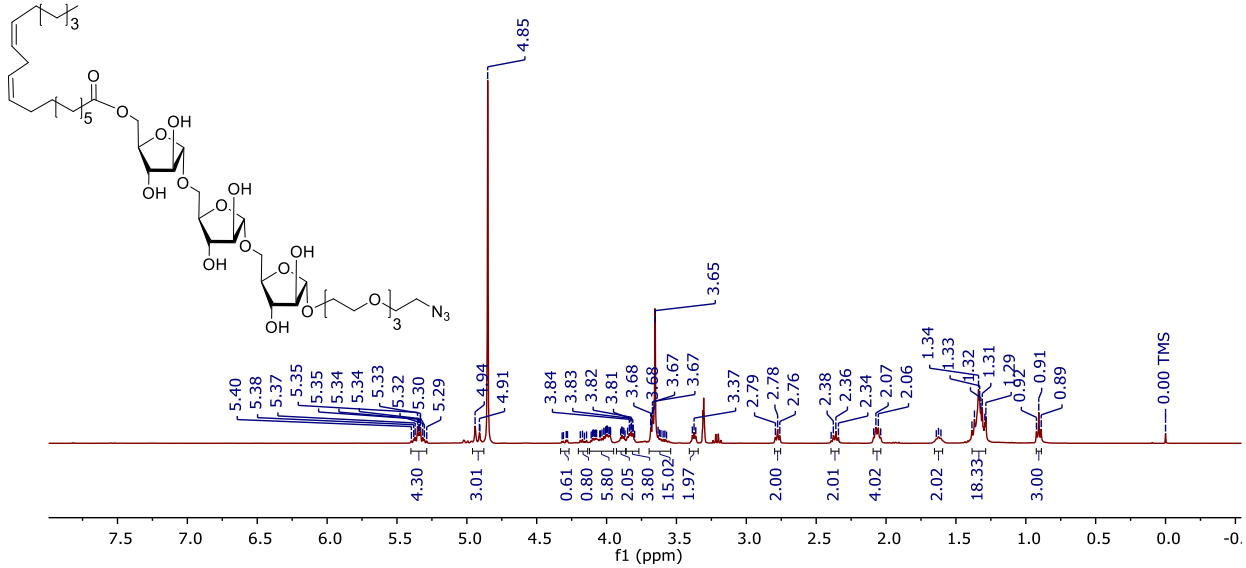
DEPT NMR spectrum (100.53 MHz, CD_3OD) of compound **32a**



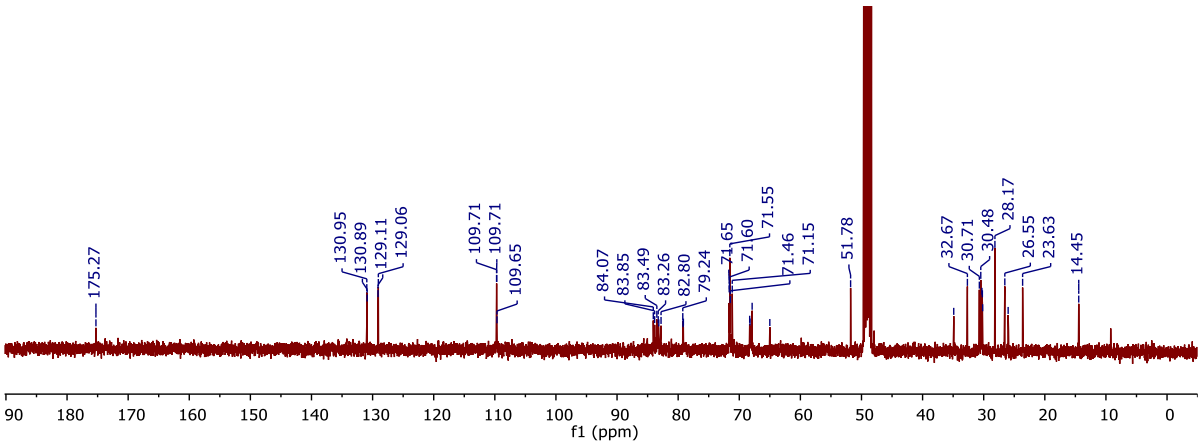
HMBC NMR of compound **32a**



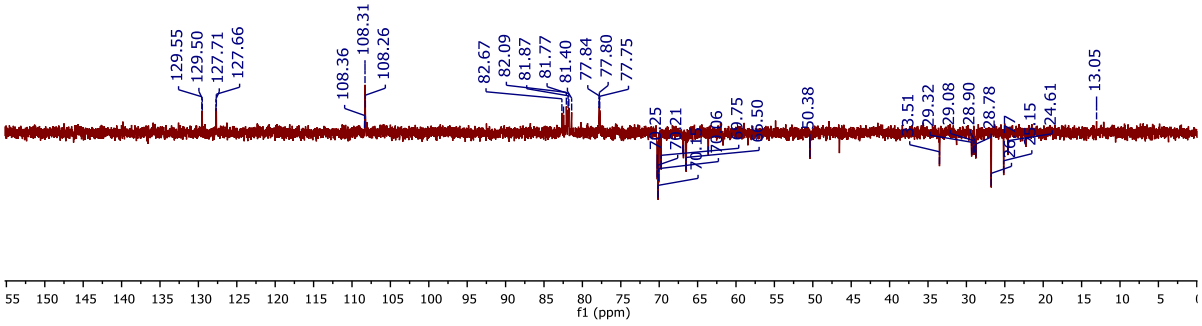
^{1}H NMR spectrum (400.31 MHz, CD_3OD) of compound **32a**



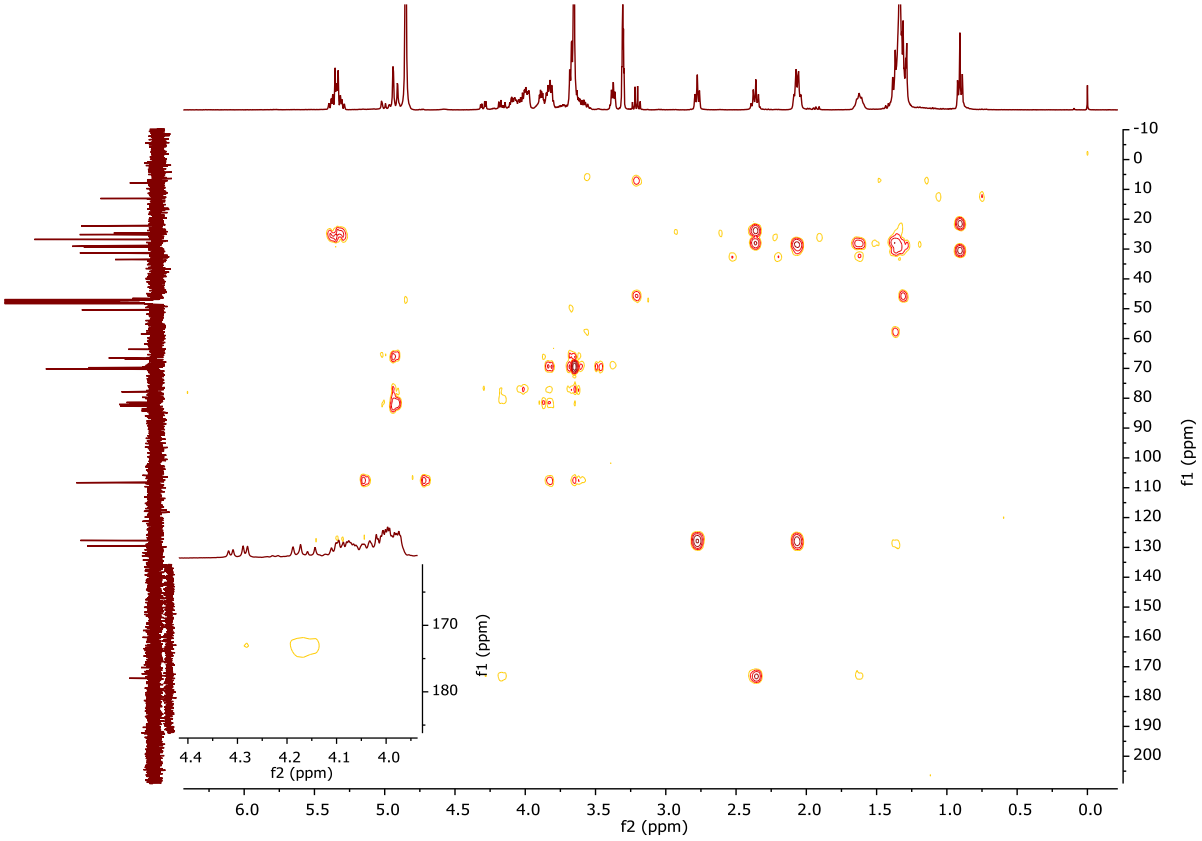
^{13}C NMR spectrum (100.53 MHz, CD_3OD) of compound **32b**



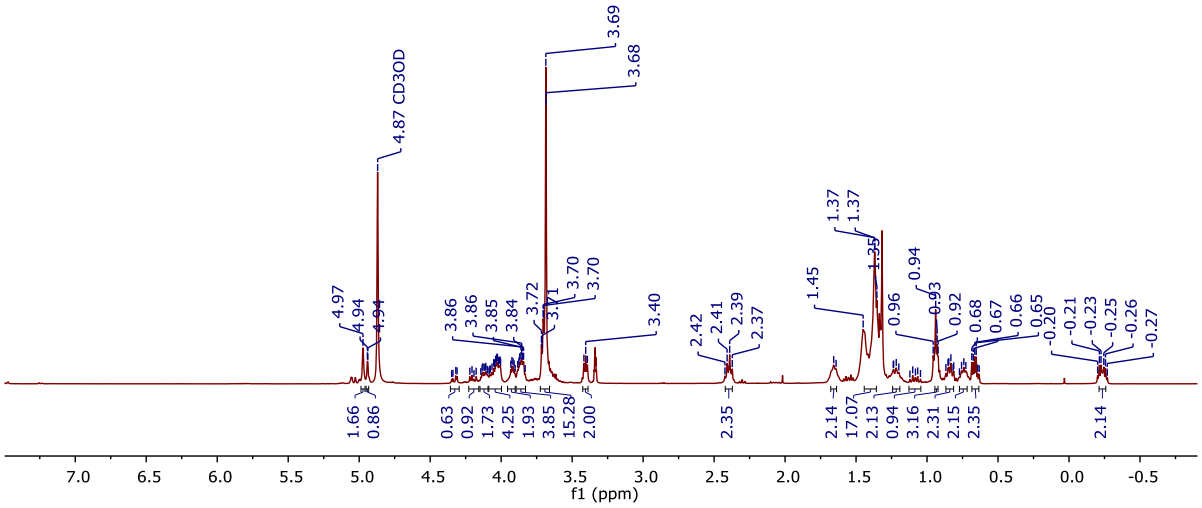
DEPT NMR spectrum (100.53 MHz, CD_3OD) of compound **32b**



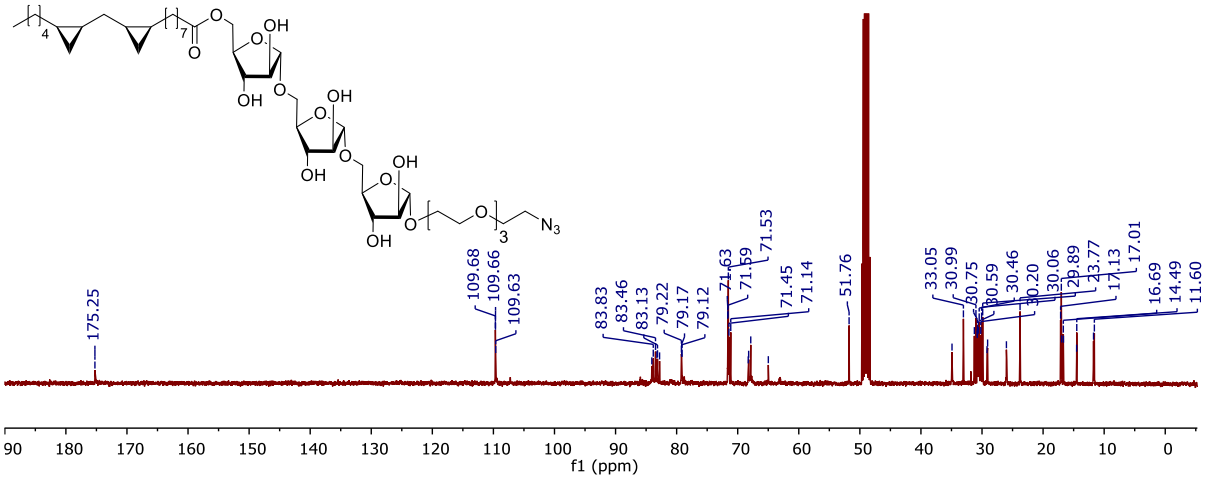
HMBC NMR of compound **32b**



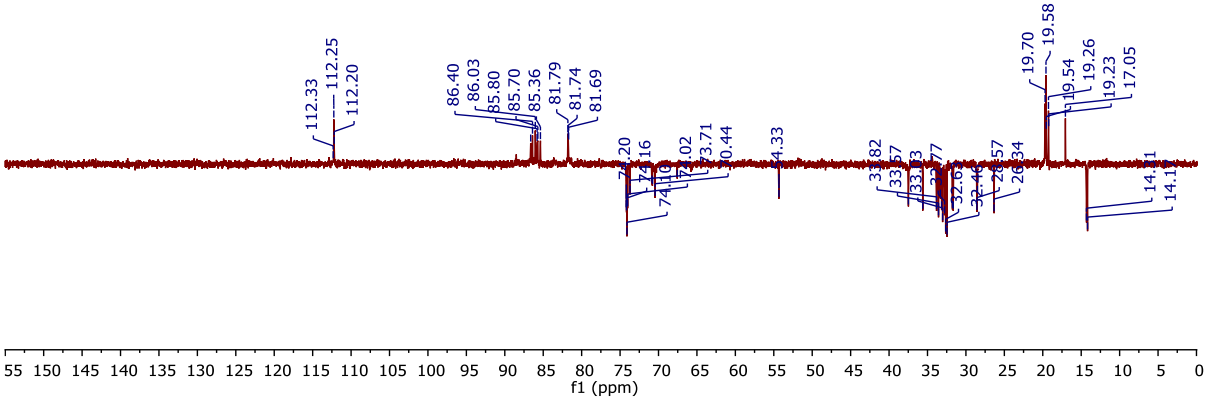
^{1}H NMR spectrum (400.31 MHz, CD_3OD) of compound **32c**



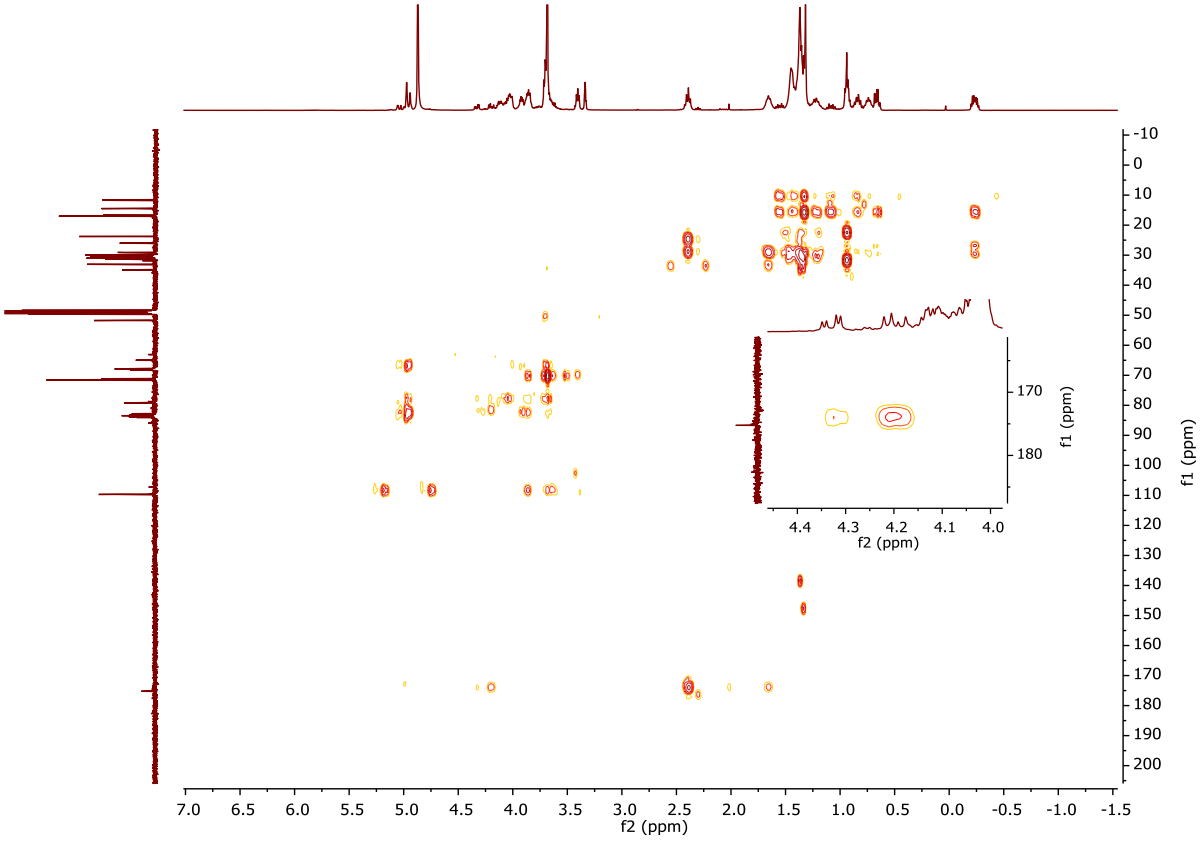
^{13}C NMR spectrum (100.53 MHz, CD_3OD) of compound **32c**



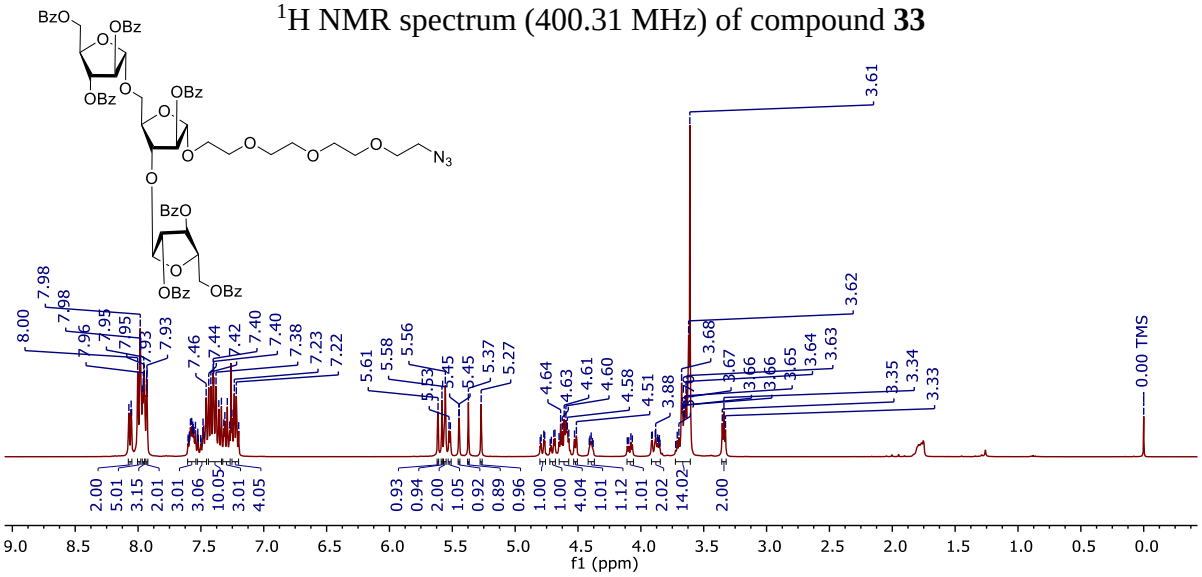
DEPT NMR spectrum (100.53 MHz, CD_3OD) of compound **32c**



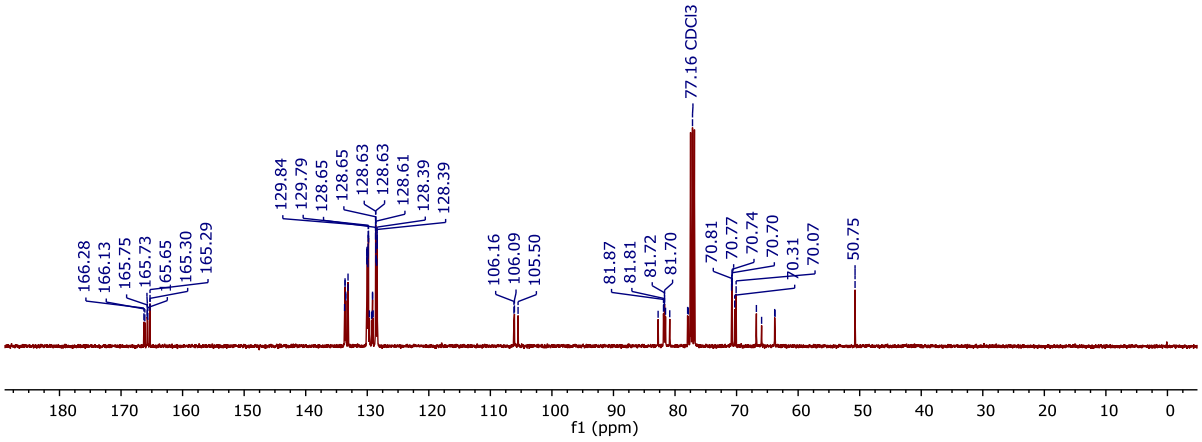
HMBC NMR of compound **32c**



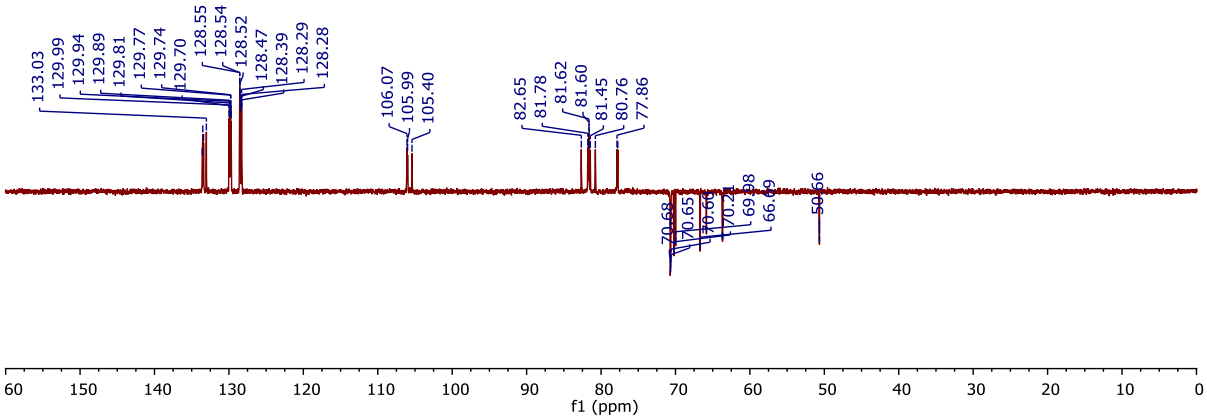
^{1}H NMR spectrum (400.31 MHz) of compound **33**



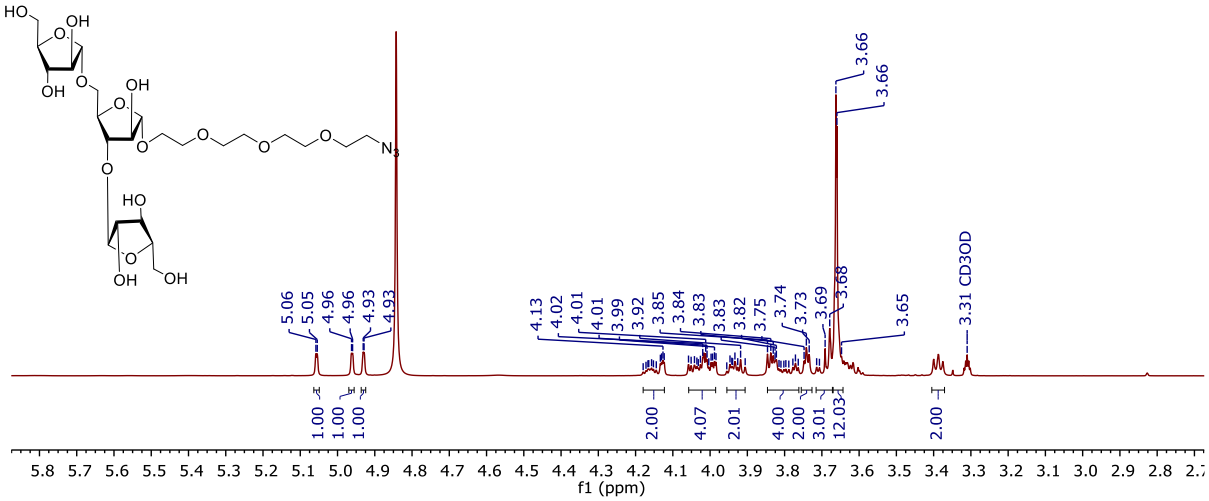
^{13}C NMR spectrum (100.53 MHz) of compound **33**



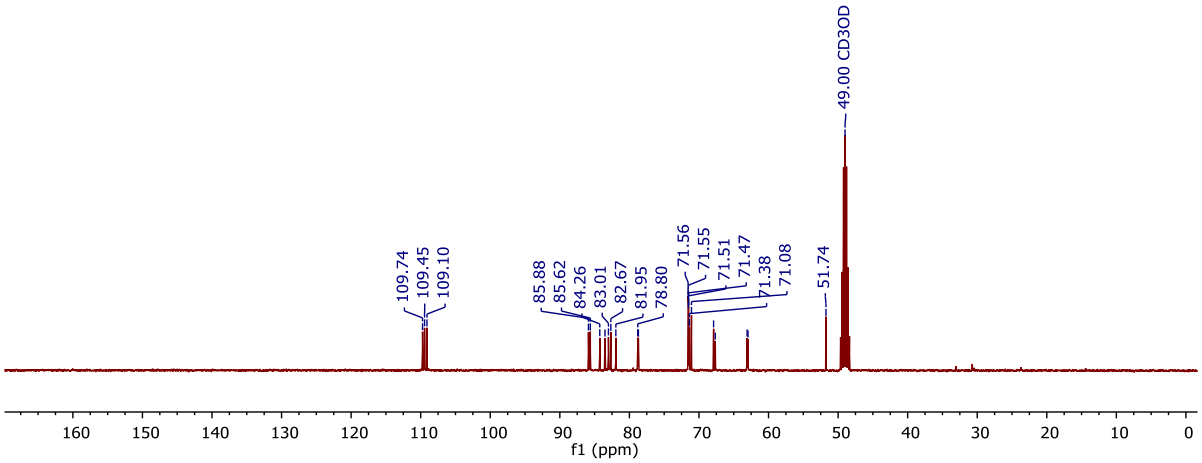
DEPT NMR spectrum (100.53 MHz) of compound **33**



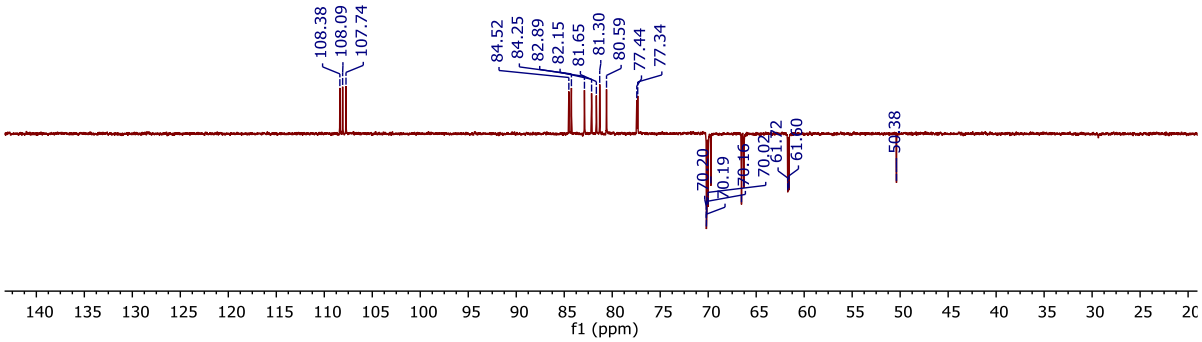
^{1}H NMR spectrum (400.31 MHz, CD_3OD) of compound **34**



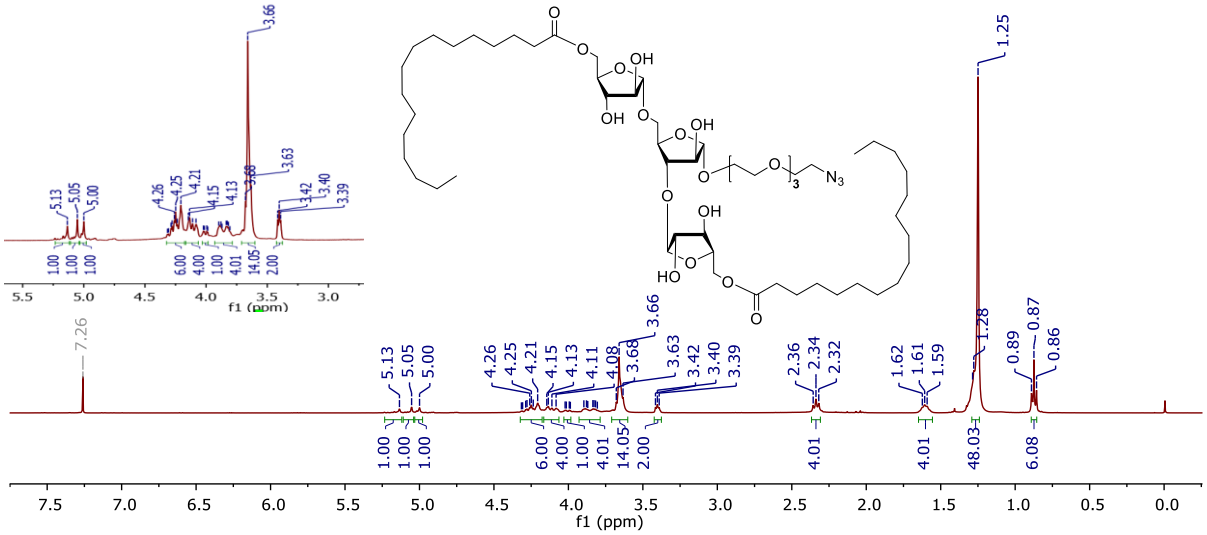
^{13}C NMR spectrum (100.53 MHz, CD_3OD) of compound **34**



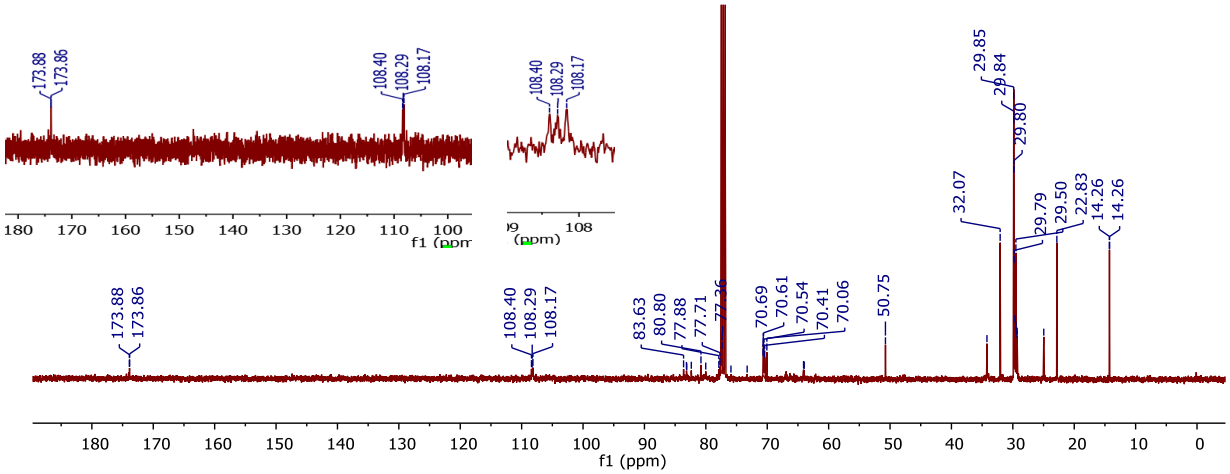
DEPT NMR spectrum (100.53 MHz, CD_3OD) of compound **34**



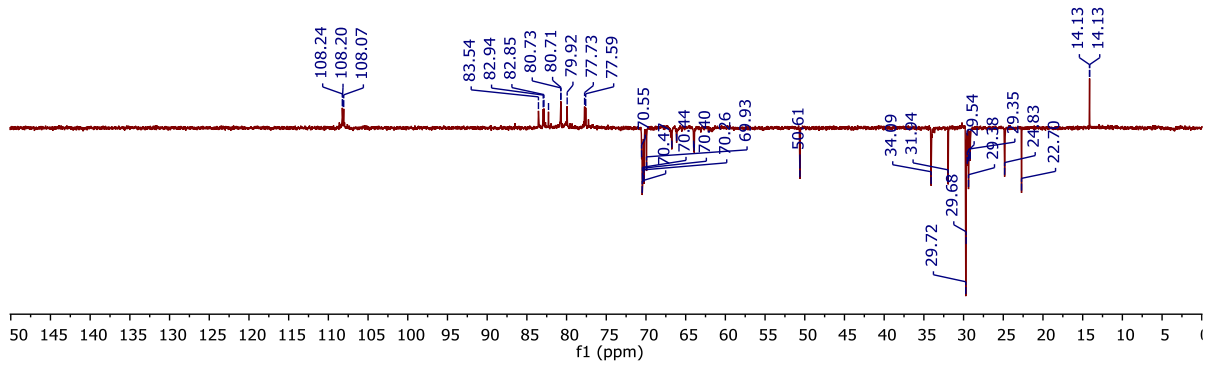
^{1}H NMR spectrum (400.31 MHz) of compound **36a**



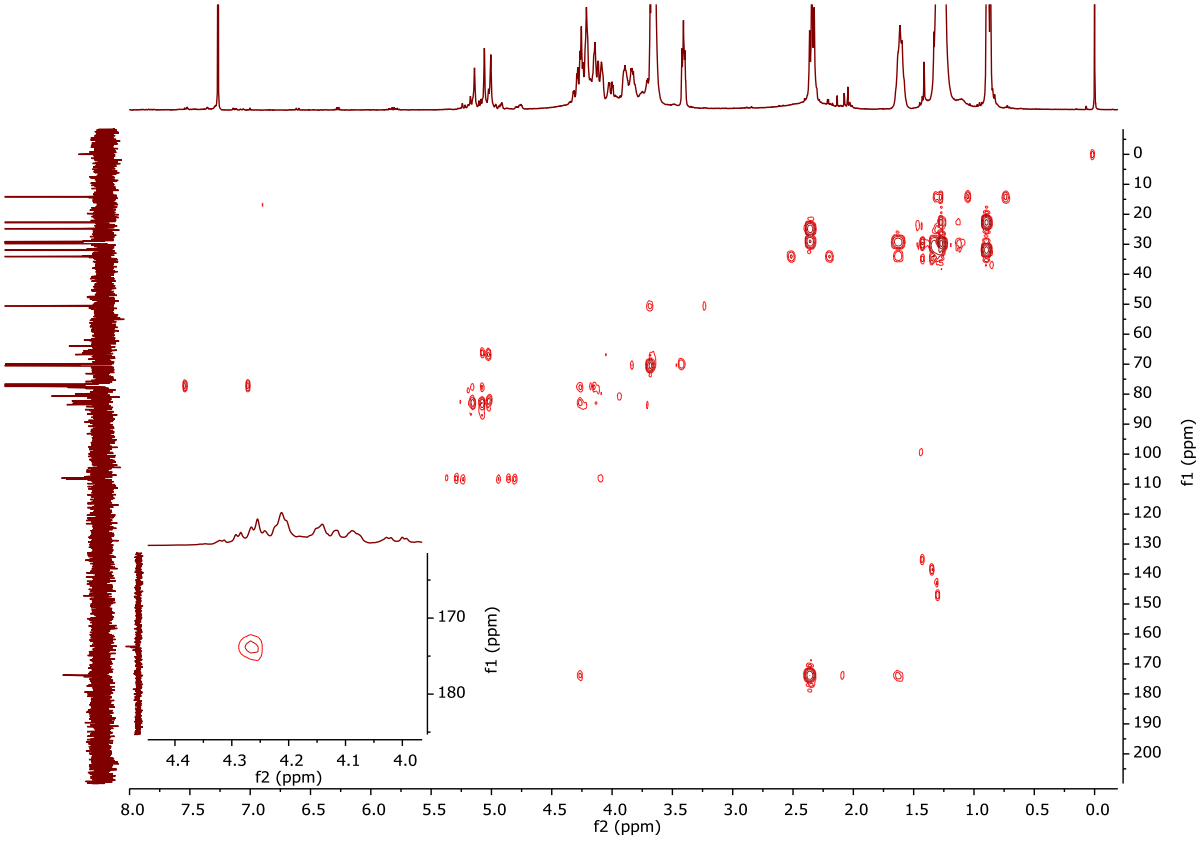
^{13}C NMR spectrum (100.53 MHz) of compound **36a**



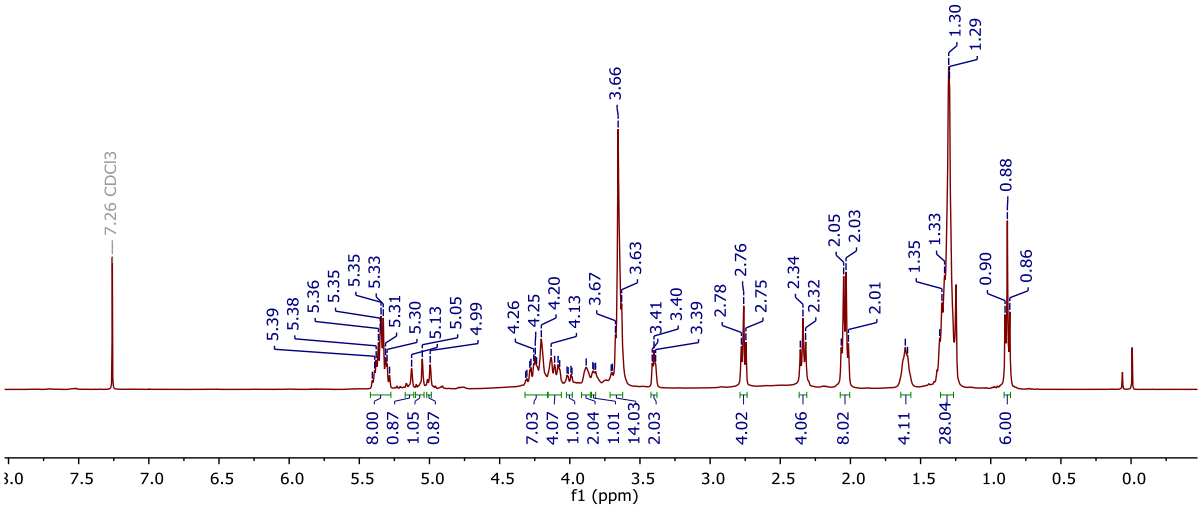
DEPT NMR spectrum (100.53 MHz) of compound **36a**



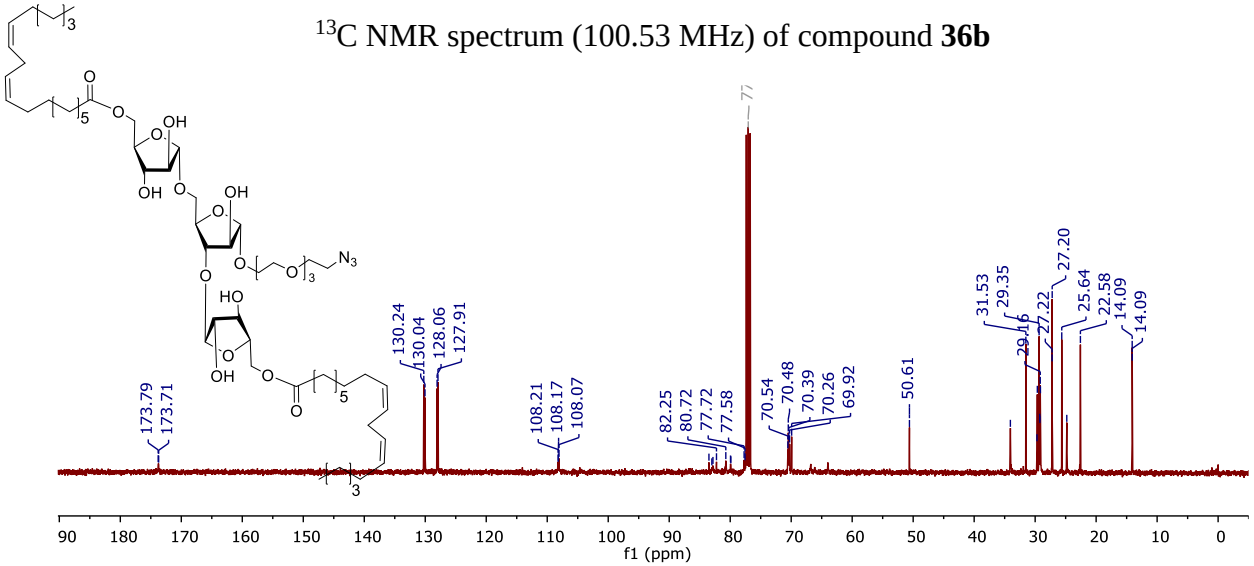
HMBC NMR of compound **36a**



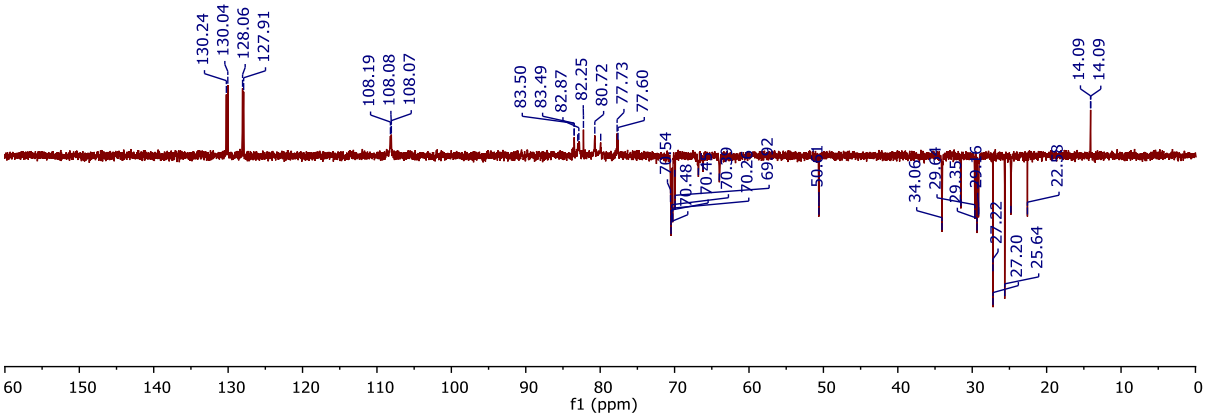
^{1}H NMR spectrum (400.31 MHz) of compound **36b**



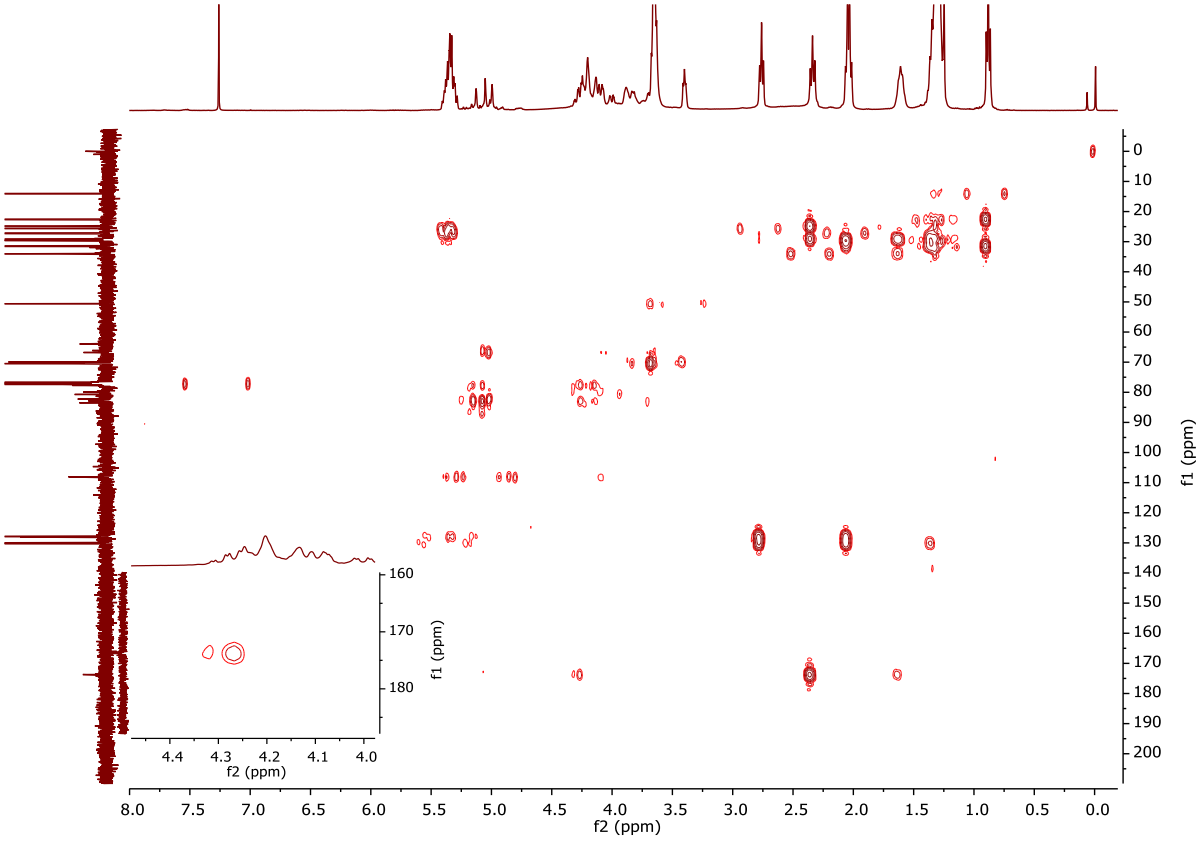
^{13}C NMR spectrum (100.53 MHz) of compound **36b**



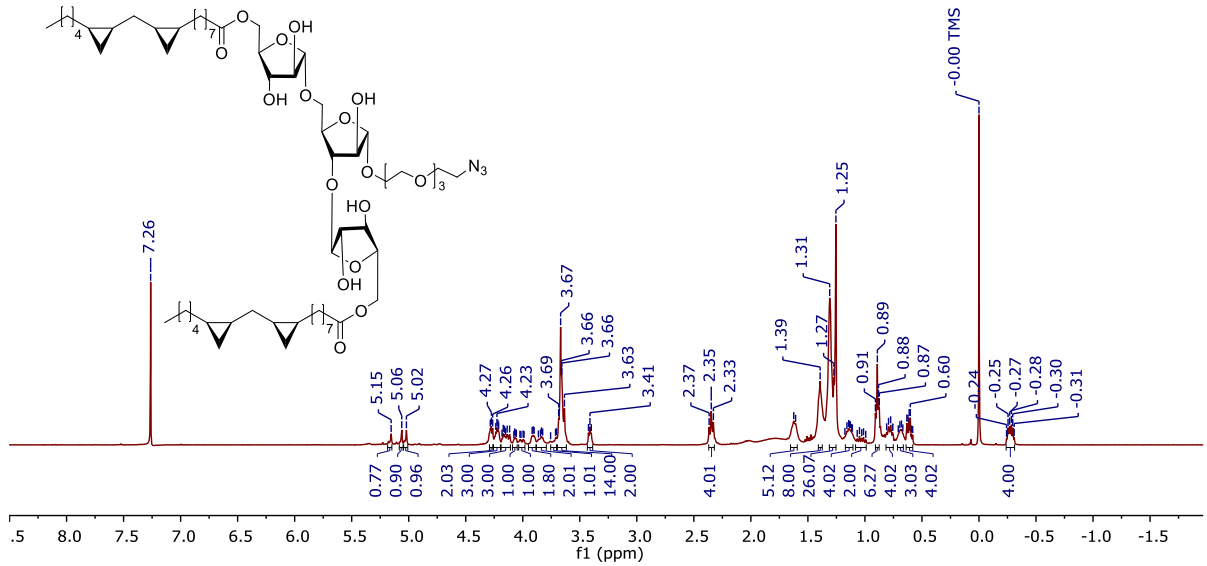
DEPT NMR spectrum (100.53 MHz) of compound **36b**



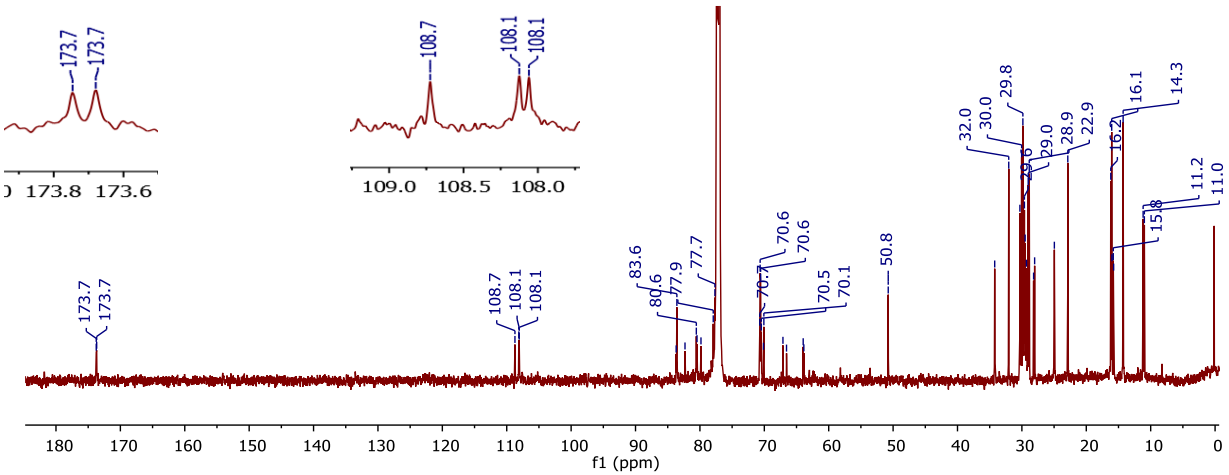
HMBC NMR of compound **36b**



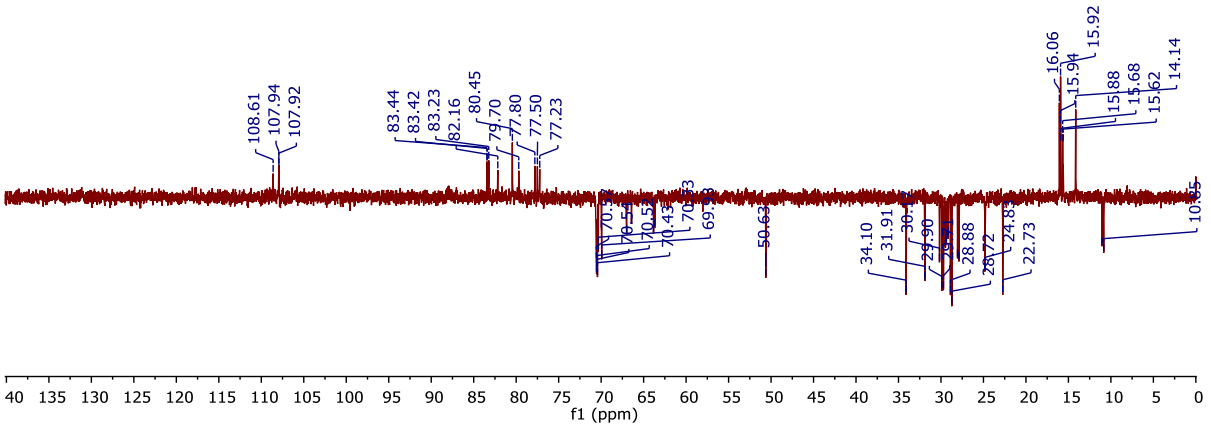
^{1}H NMR spectrum (400.31 MHz) of compound **36c**



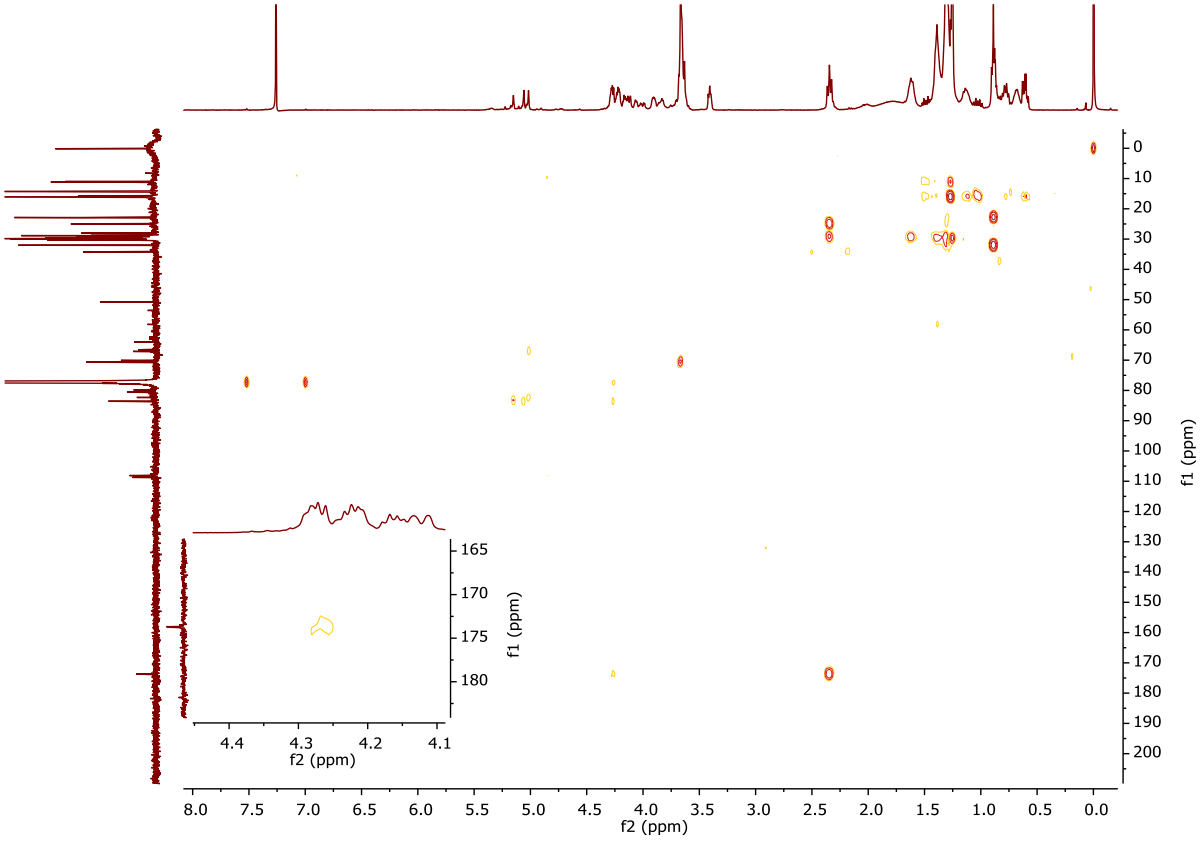
^{13}C NMR spectrum (100.53 MHz) of compound **36c**



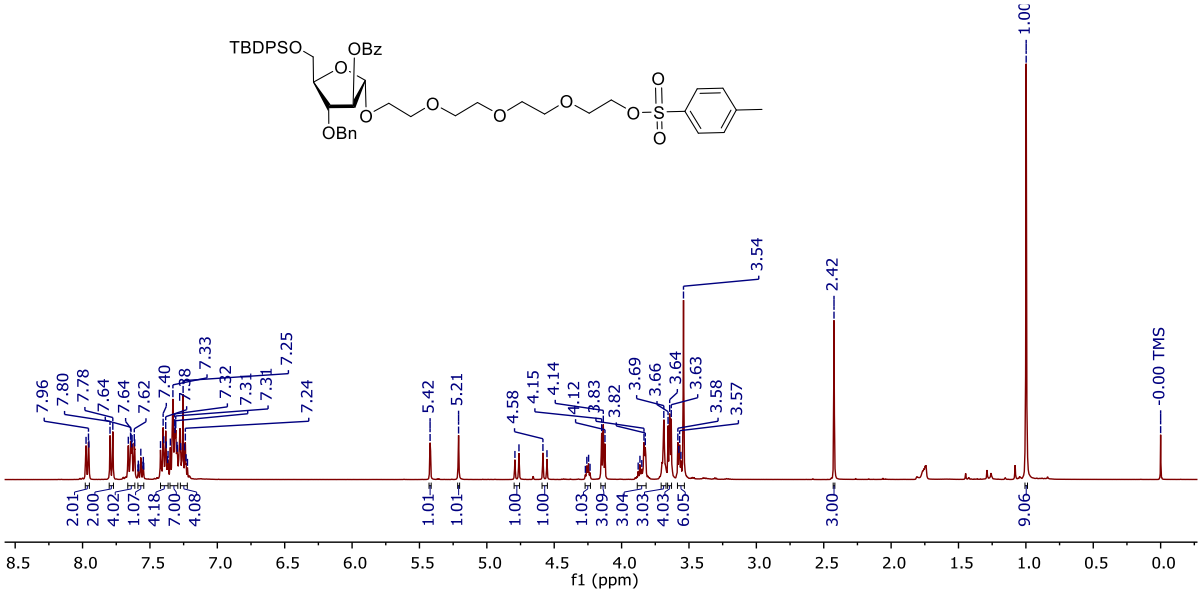
DEPT NMR spectrum (100.53 MHz) of compound **36c**



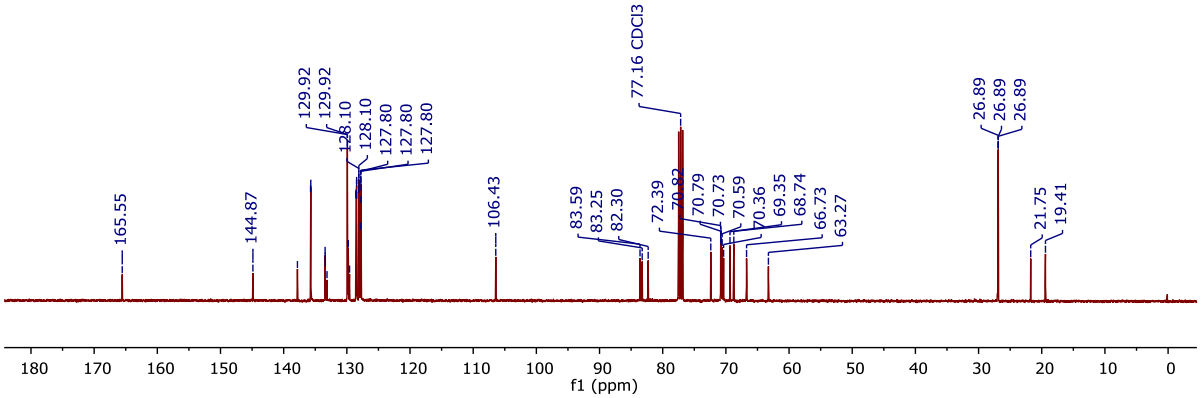
HMBC NMR of compound **36c**



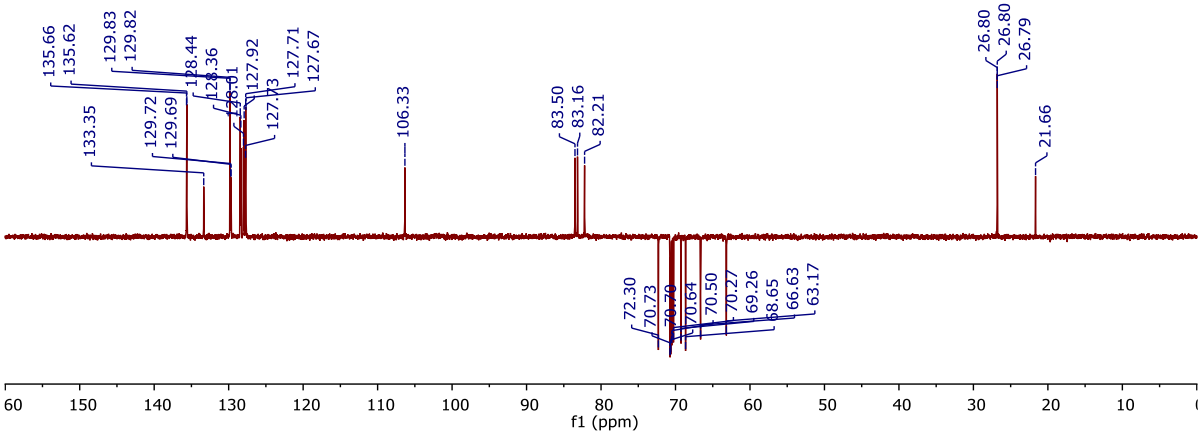
^{1}H NMR Spectrum (400.31 MHz, $CDCl_3$) of compound **38**



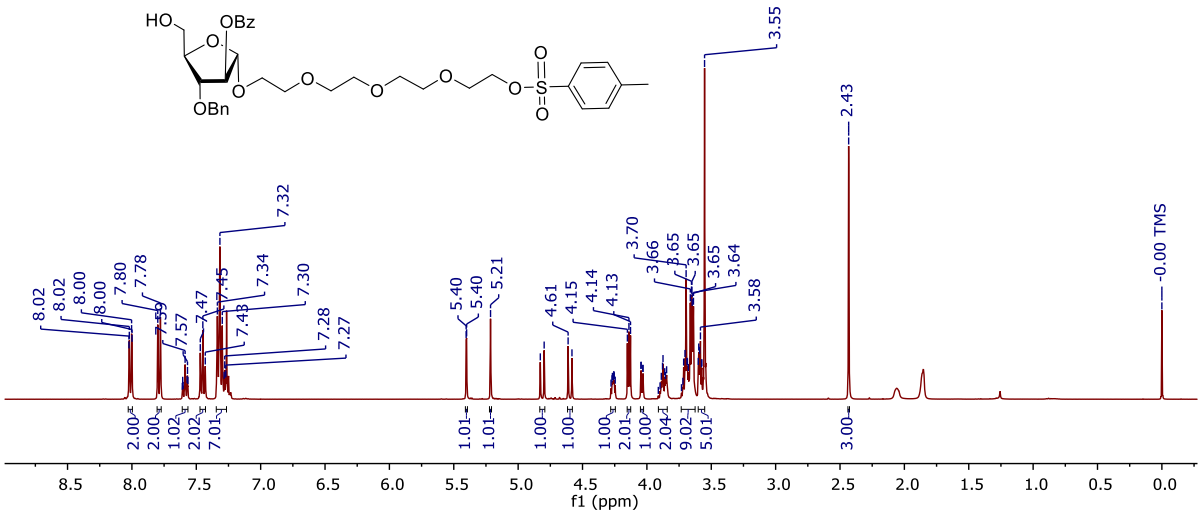
^{13}C NMR Spectrum (100.53 MHz, $CDCl_3$) of compound **38**



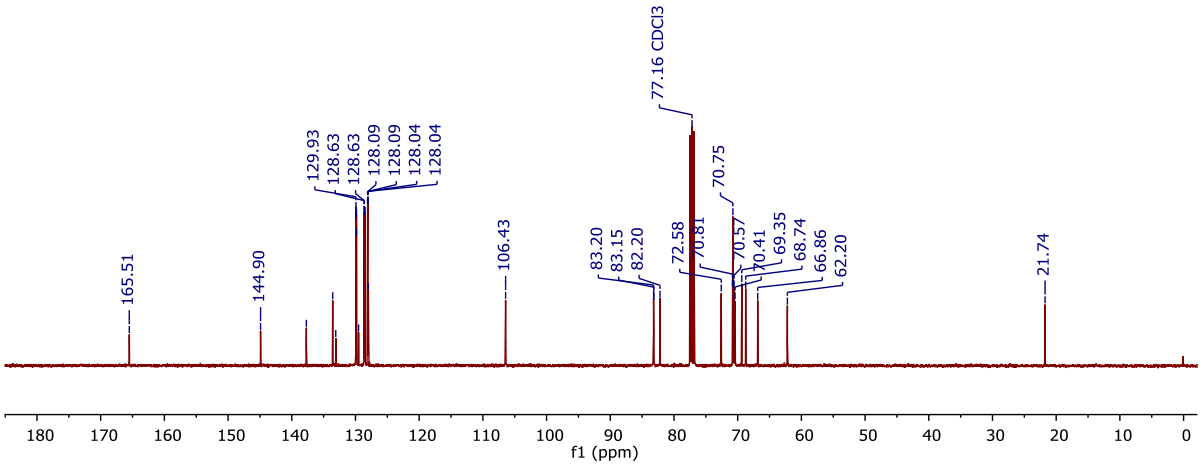
^{13}C NMR Spectrum (100.53 MHz, $CDCl_3$) of compound **38**



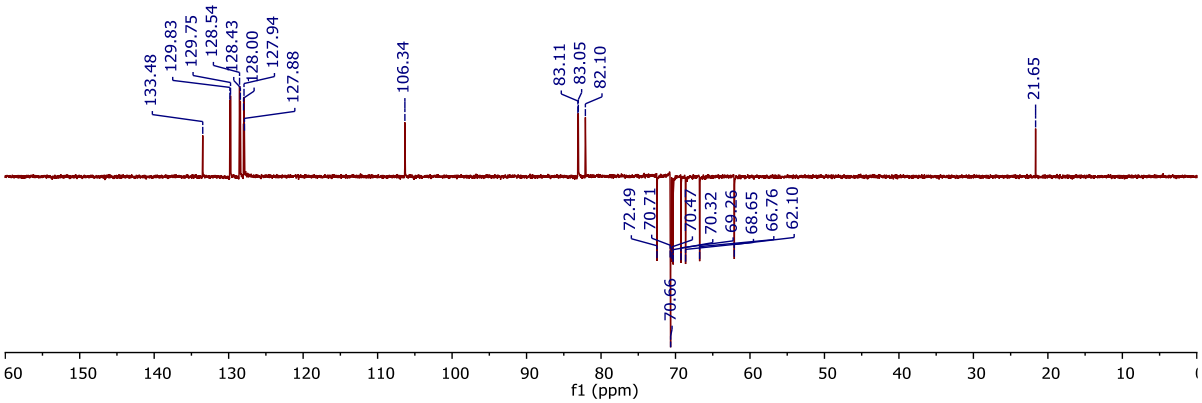
^{1}H NMR Spectrum (400.31 MHz, $CDCl_3$) of compound **39**



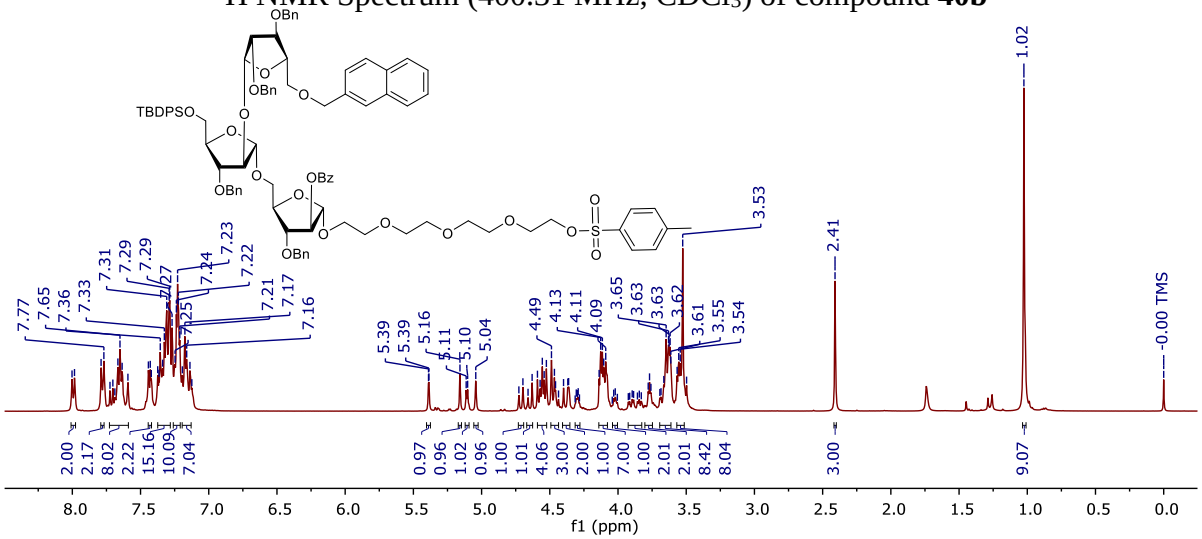
^{13}C NMR Spectrum (100.53MHz, $CDCl_3$) of compound **39**



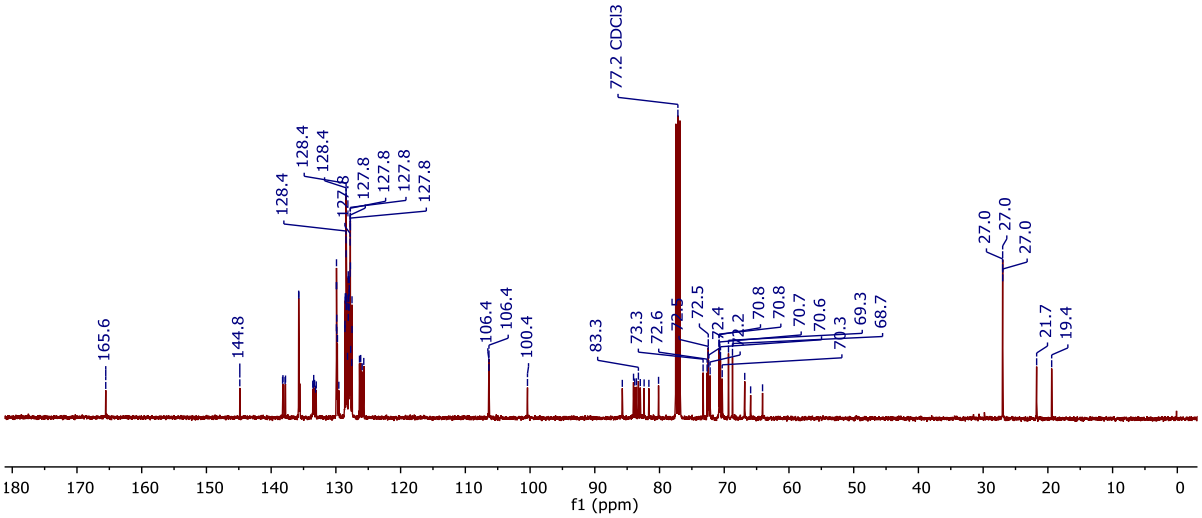
DEPT NMR Spectrum (100.53 MHz, $CDCl_3$) of compound **39**



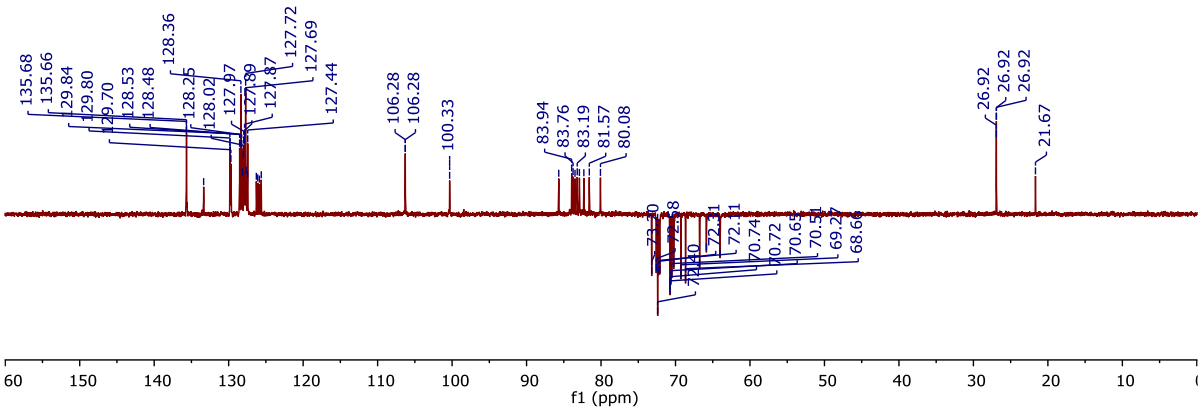
^{1}H NMR Spectrum (400.31 MHz, $CDCl_3$) of compound **40b**



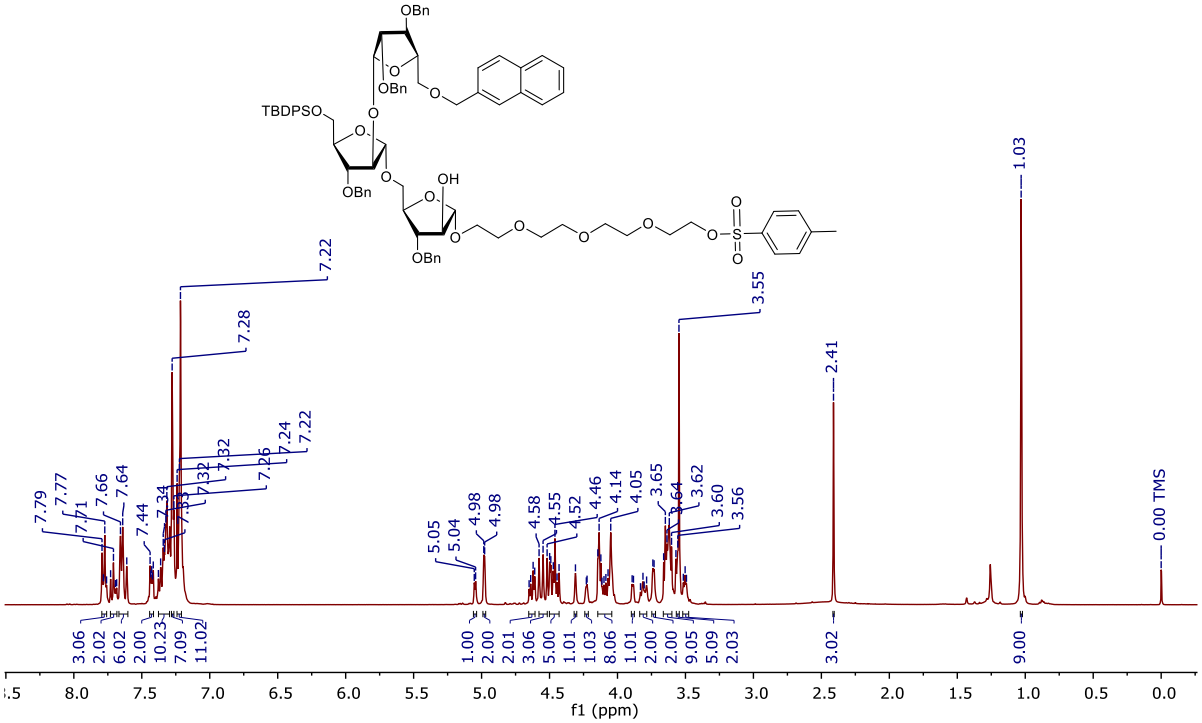
^{13}C NMR Spectrum (100.53 MHz, $CDCl_3$) of compound **40b**



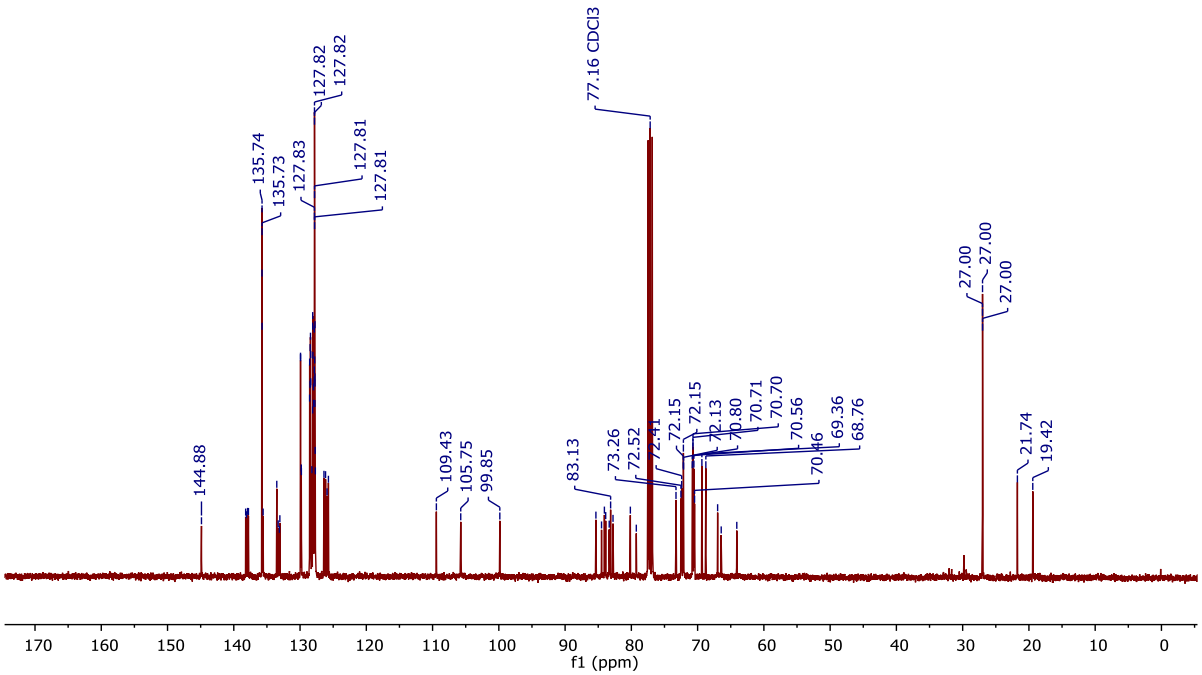
DEPT NMR Spectrum (100.53 MHz, $CDCl_3$) of compound **40b**



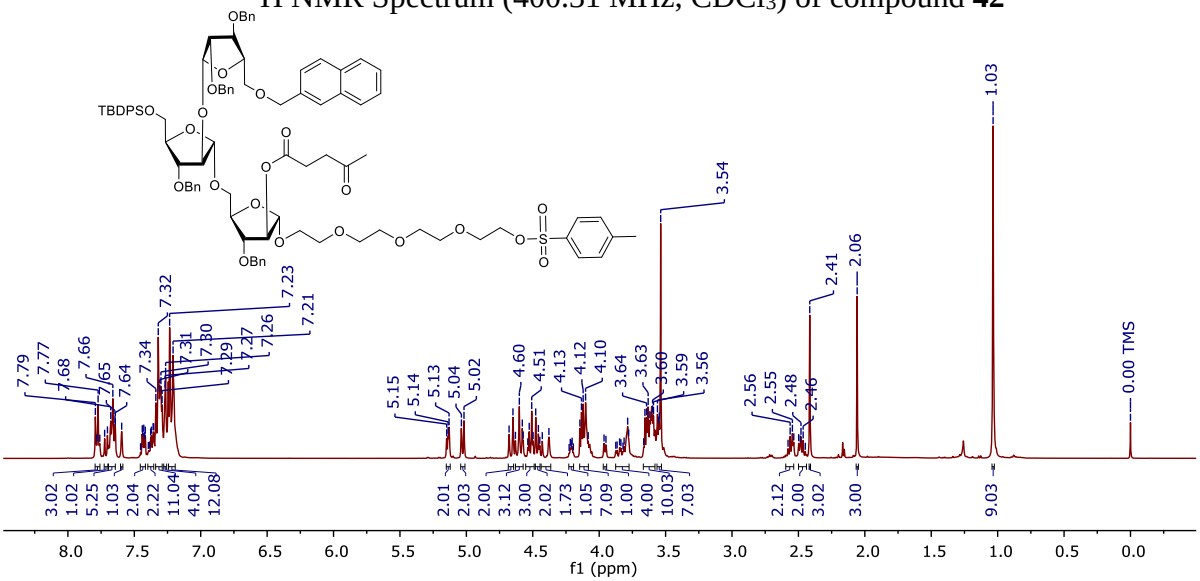
^{1}H NMR Spectrum (400.31 MHz, $CDCl_3$) of compound **41**



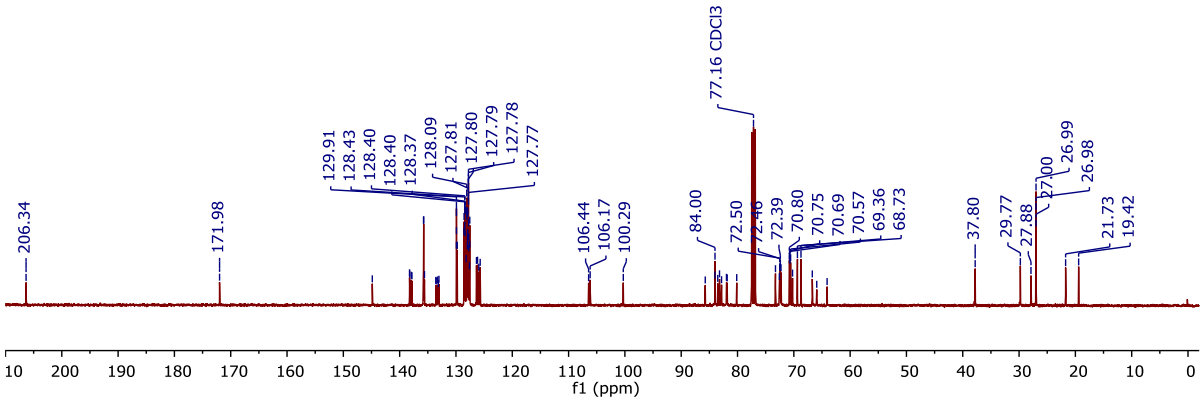
^{13}C NMR Spectrum (100.53 MHz, $CDCl_3$) of compound **41**



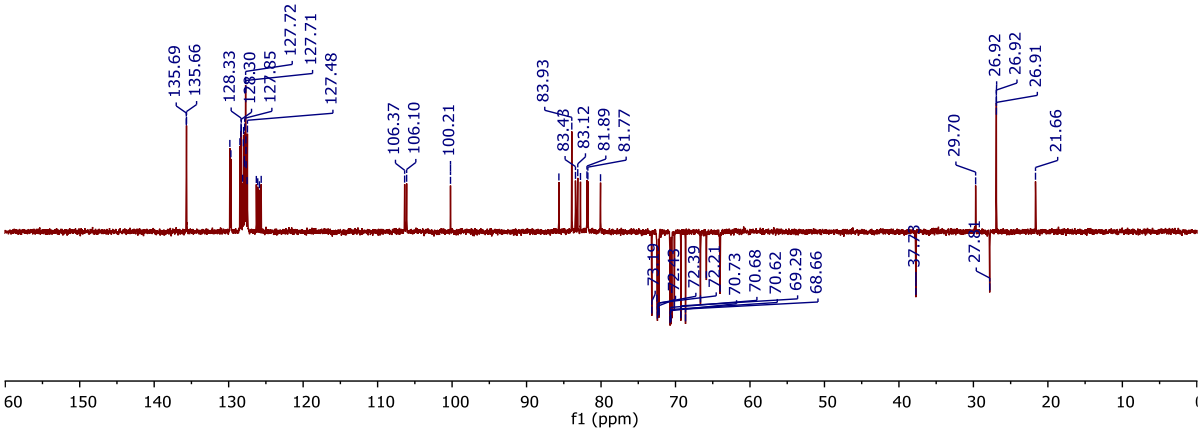
^{1}H NMR Spectrum (400.31 MHz, $CDCl_3$) of compound **42**



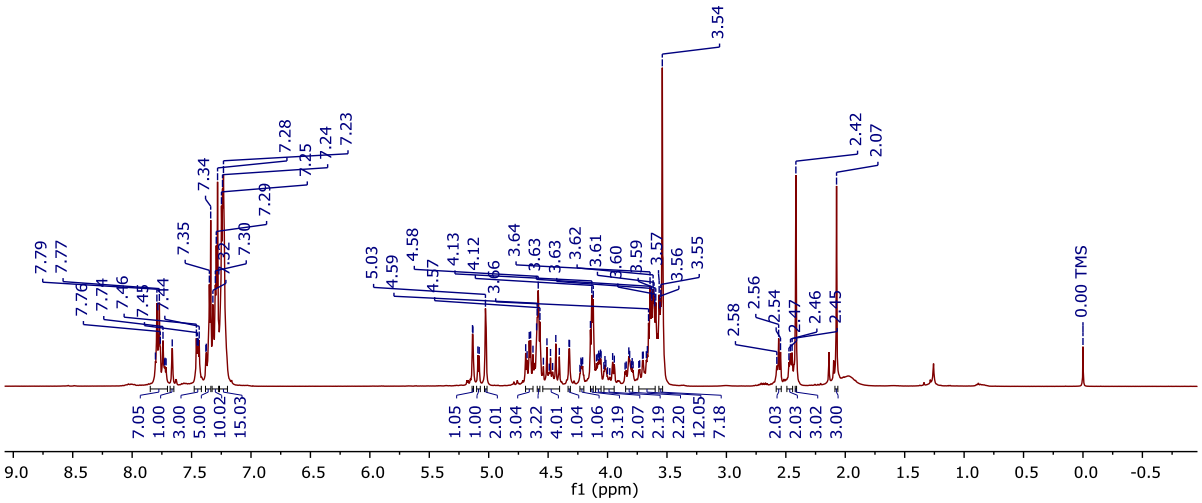
^{13}C NMR Spectrum (100.53 MHz, $CDCl_3$) of compound **42**



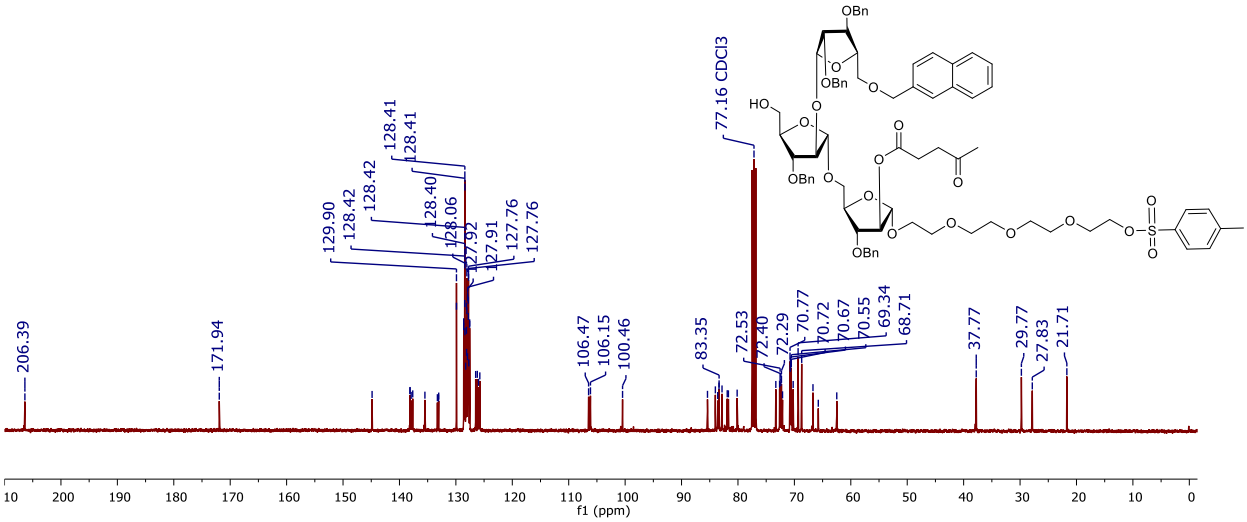
DEPT NMR Spectrum (100.53 MHz, $CDCl_3$) of compound **42**



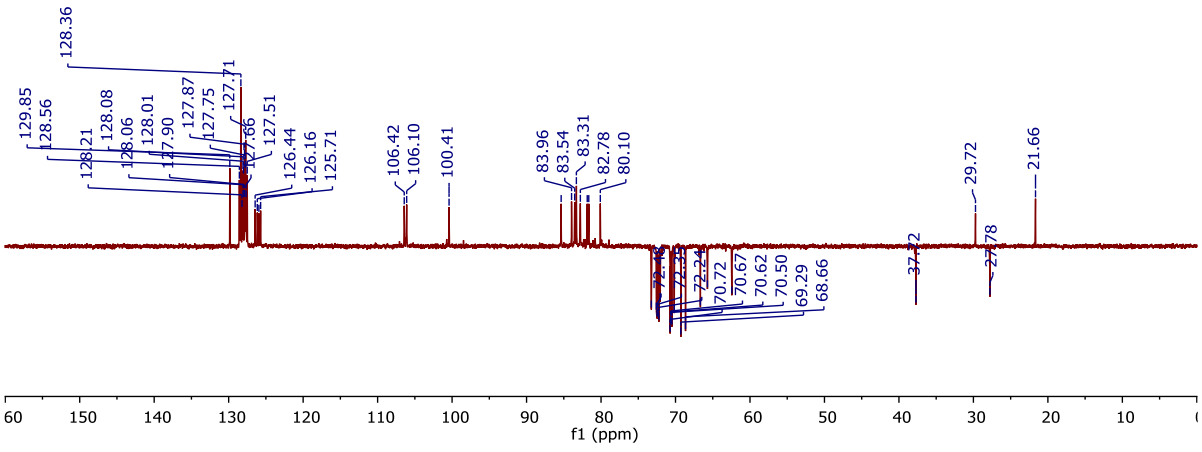
^{1}H NMR Spectrum (400.31 MHz, $CDCl_3$) of compound **43**



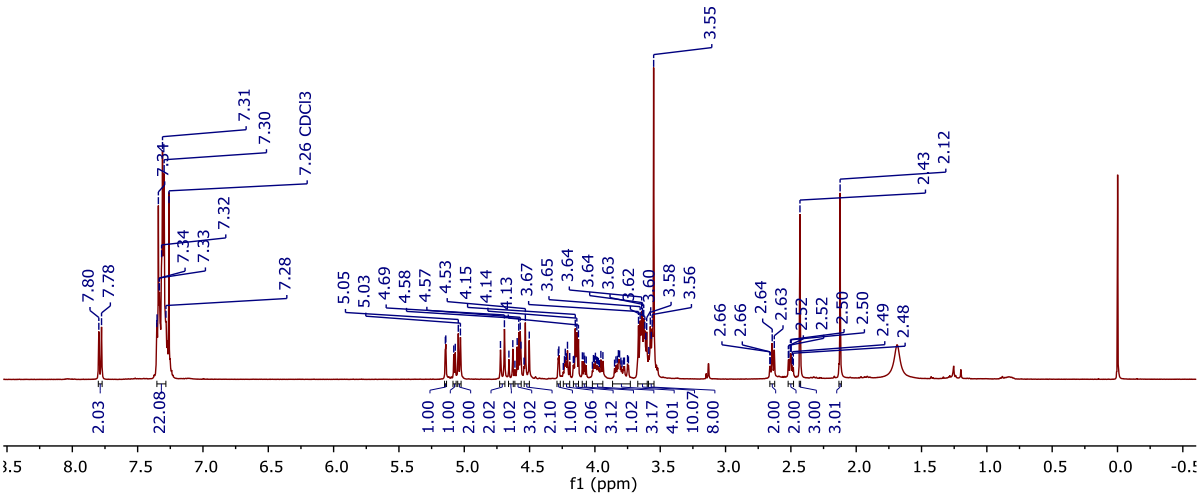
^{13}C NMR Spectrum (100.53 MHz, $CDCl_3$) of compound **43**



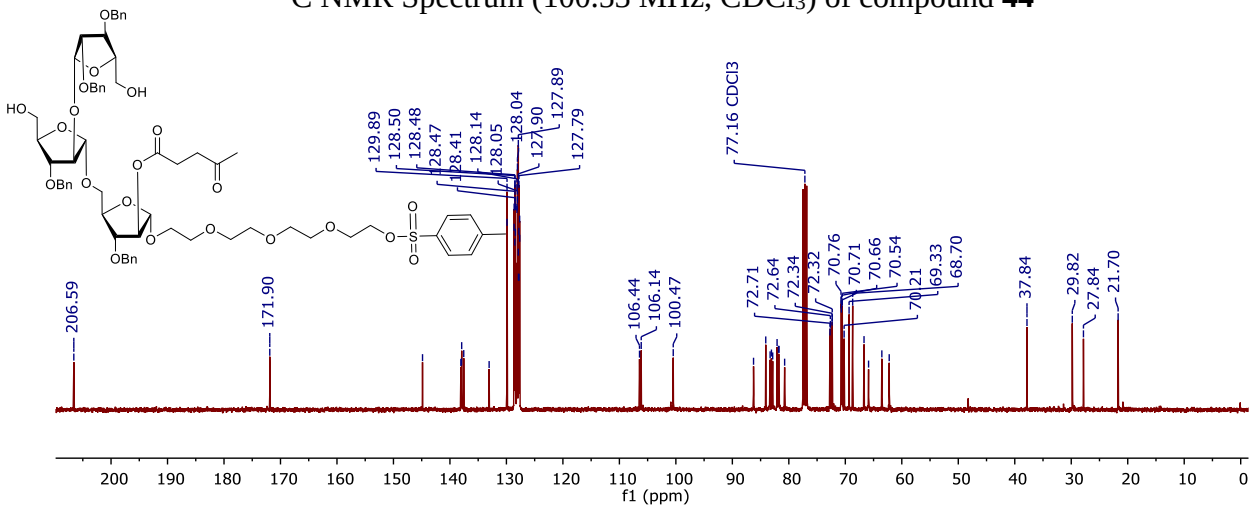
DEPT NMR Spectrum (100.53 MHz, $CDCl_3$) of compound **43**



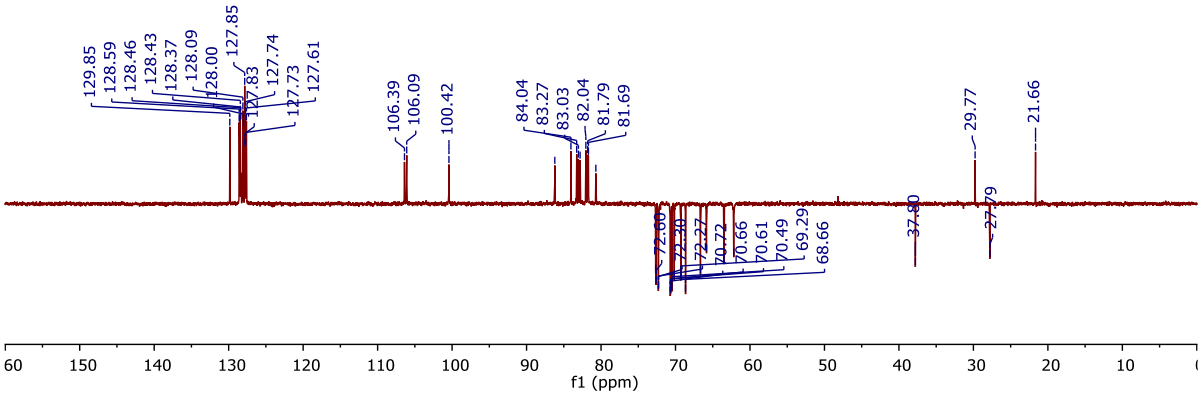
^{1}H NMR Spectrum (400.31 MHz, $CDCl_3$) of compound **44**



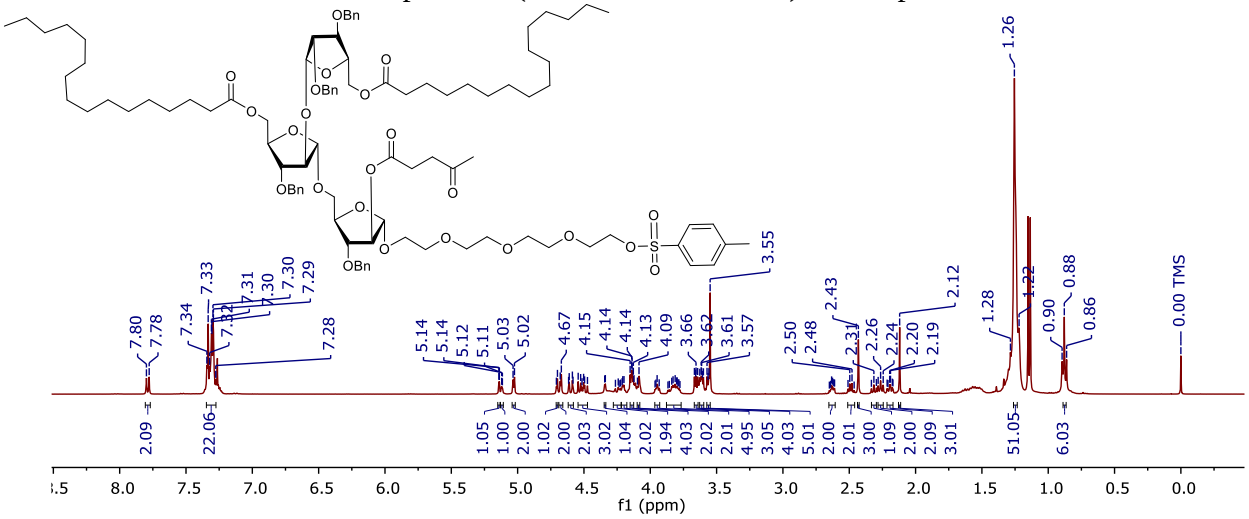
^{13}C NMR Spectrum (100.53 MHz, $CDCl_3$) of compound **44**



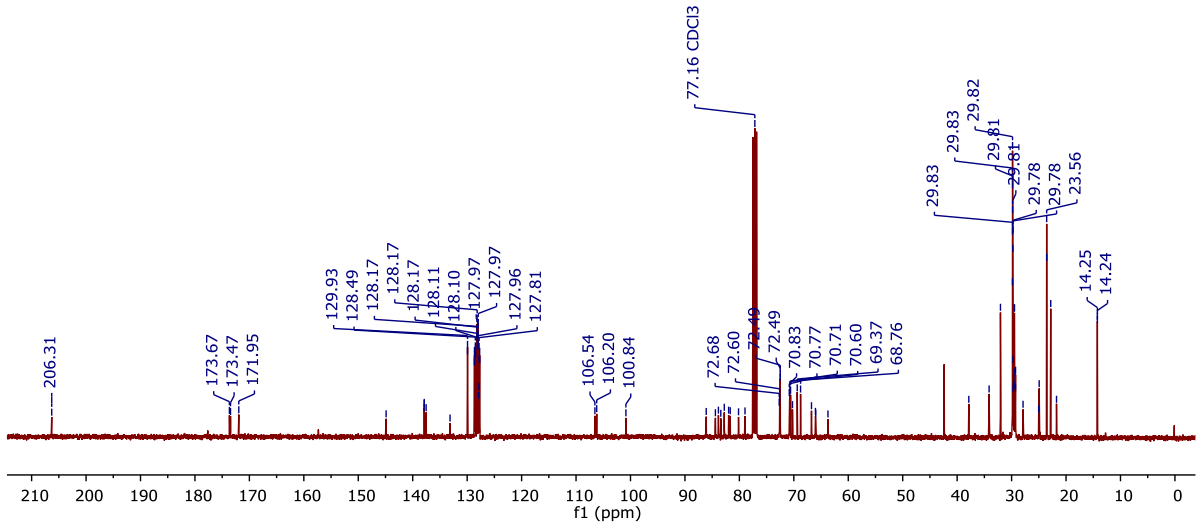
DEPT NMR Spectrum (100.53 MHz, $CDCl_3$) of compound **44**



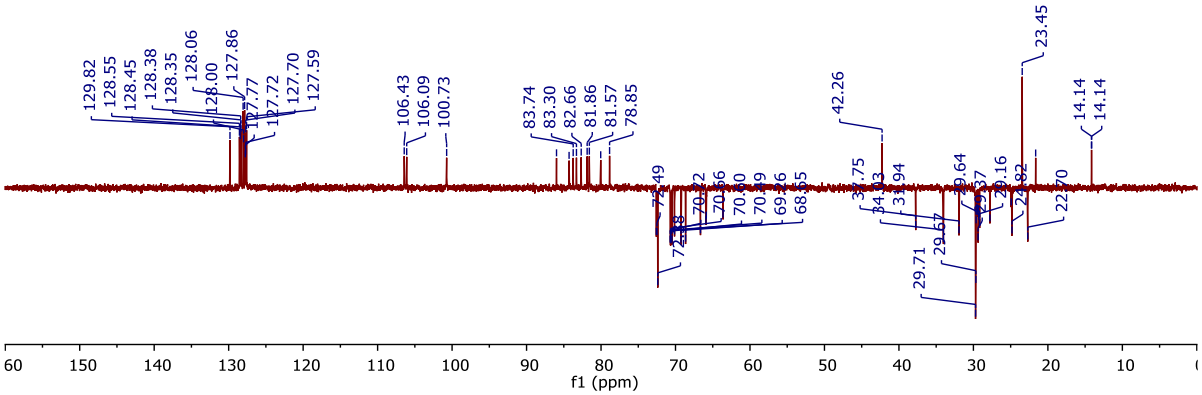
^{1}H NMR Spectrum (400.31 MHz, $CDCl_3$) of compound **46a**



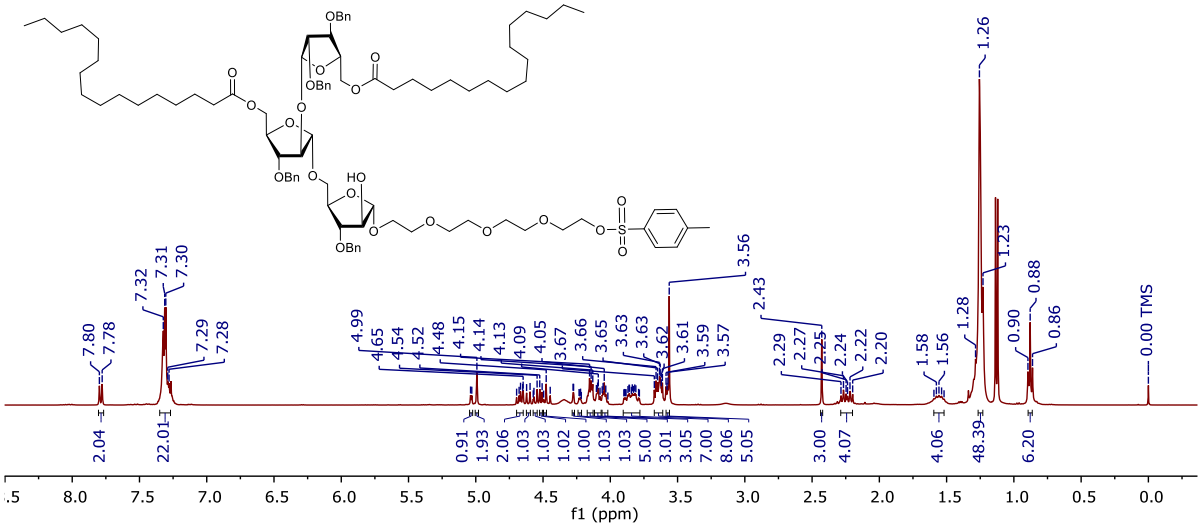
^{13}C NMR Spectrum (100.53 MHz, $CDCl_3$) of compound **46a**



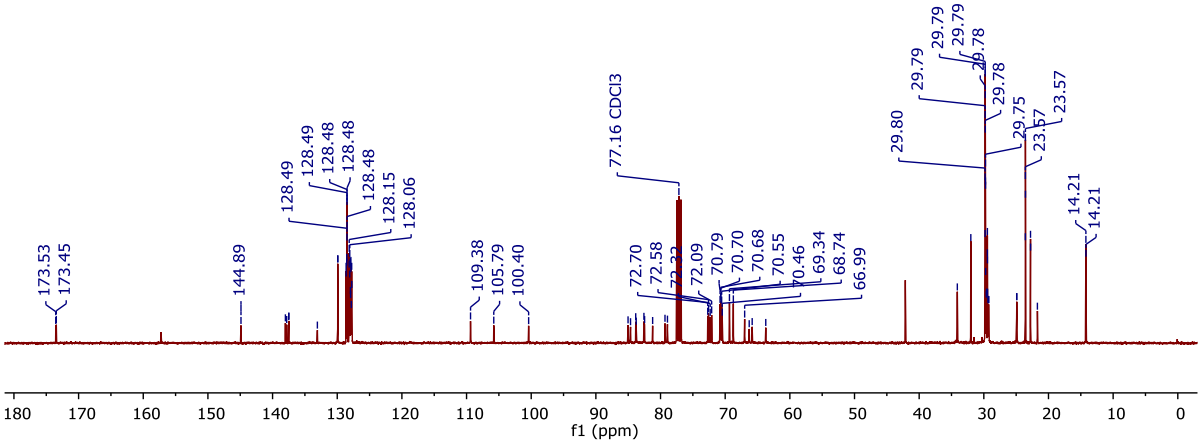
DEPT NMR Spectrum (100.53 MHz, $CDCl_3$) of compound **46a**



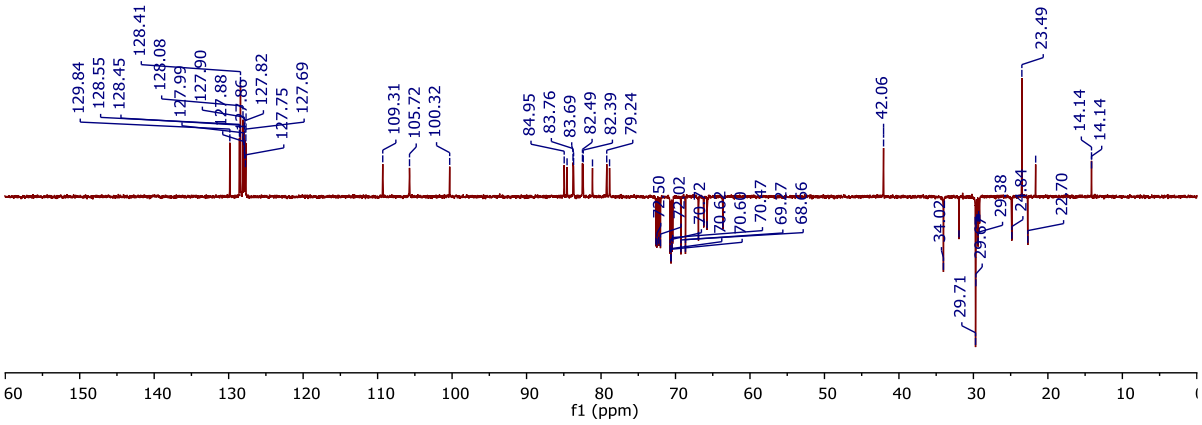
^{1}H NMR Spectrum (400.31 MHz, $CDCl_3$) of compound **47a**



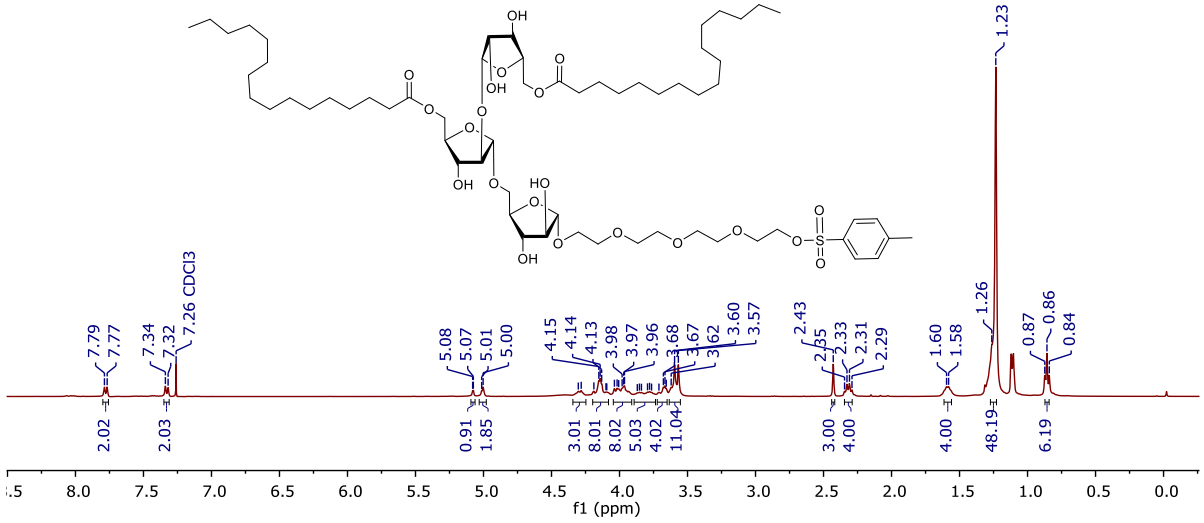
^{13}C NMR Spectrum (100.53 MHz, $CDCl_3$) of compound **47a**



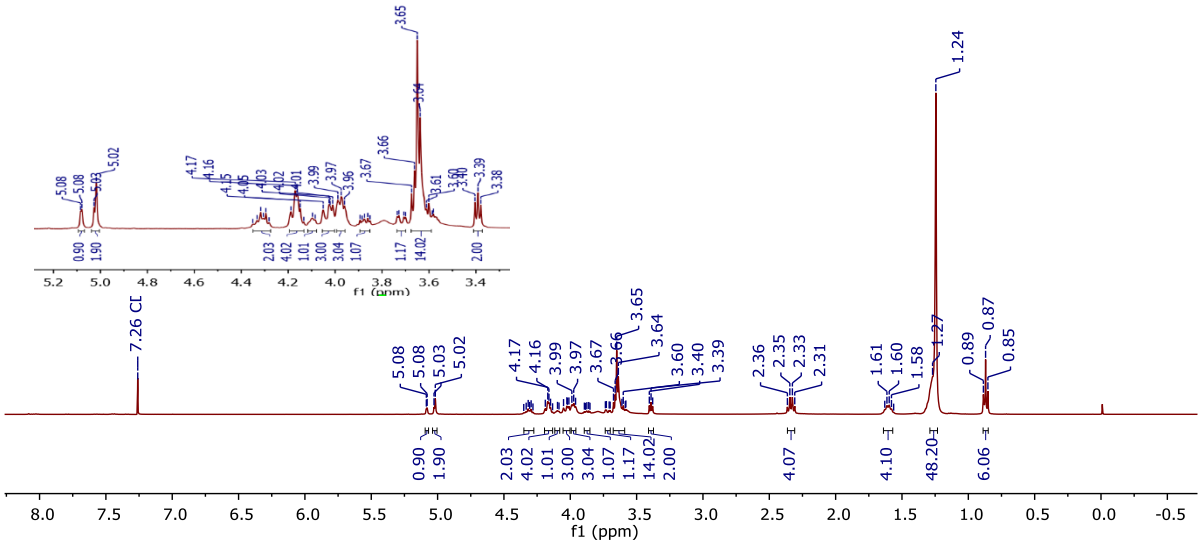
DEPT NMR Spectrum (100.53 MHz, $CDCl_3$) of compound **47a**



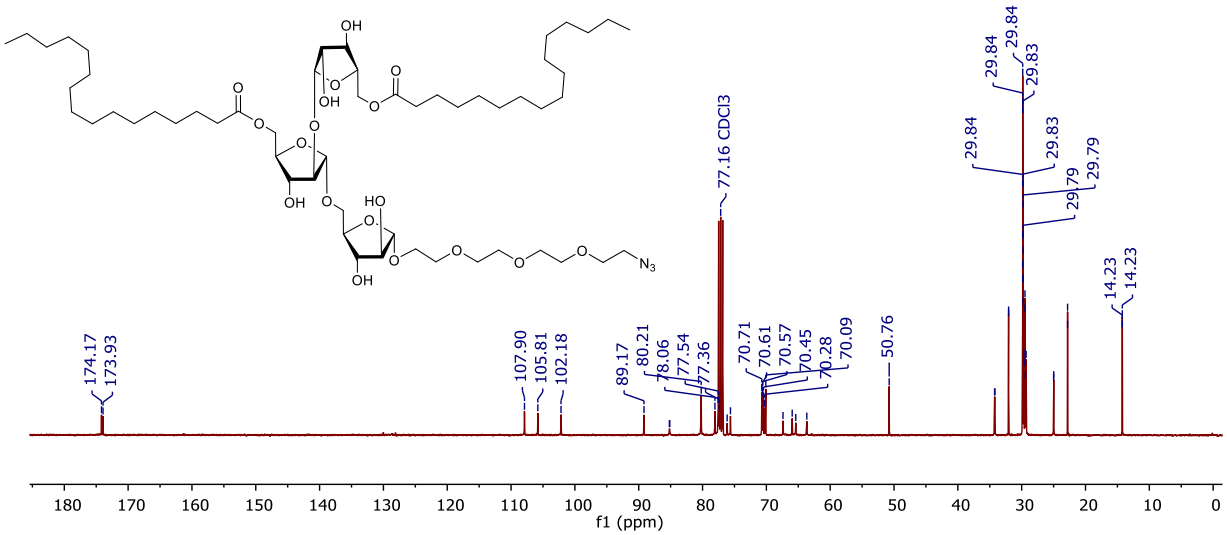
^{1}H NMR Spectrum (400.31 MHz, $CDCl_3$) of compound **48a**


OH
OH
OH
HO
OH
O
O
O

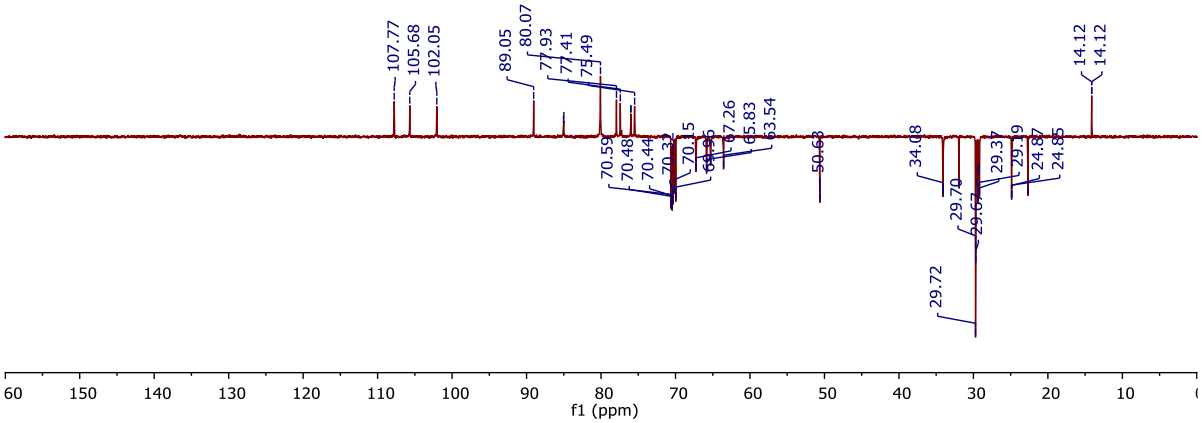
^{1}H NMR Spectrum (400.31 MHz, $CDCl_3$) of compound **45a**



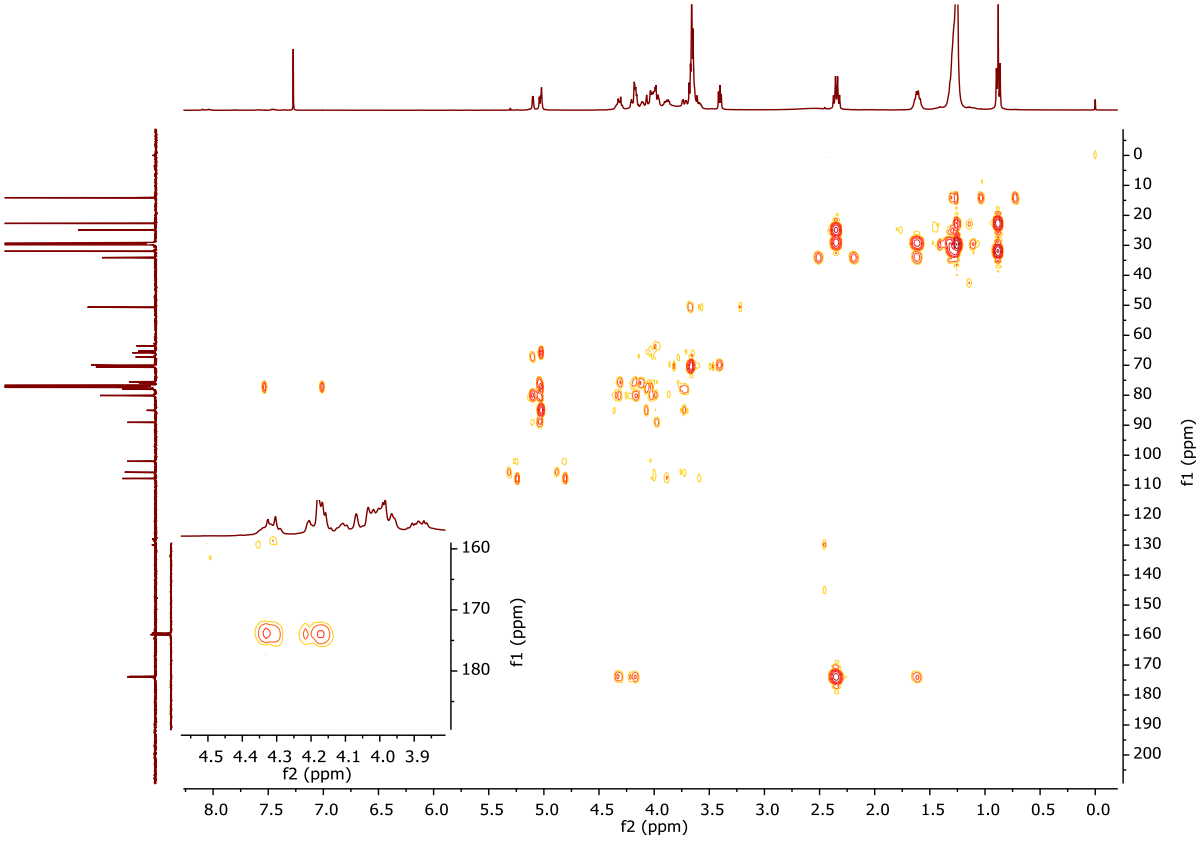
^{13}C NMR Spectrum (100.53 MHz, $CDCl_3$) of compound **45a**



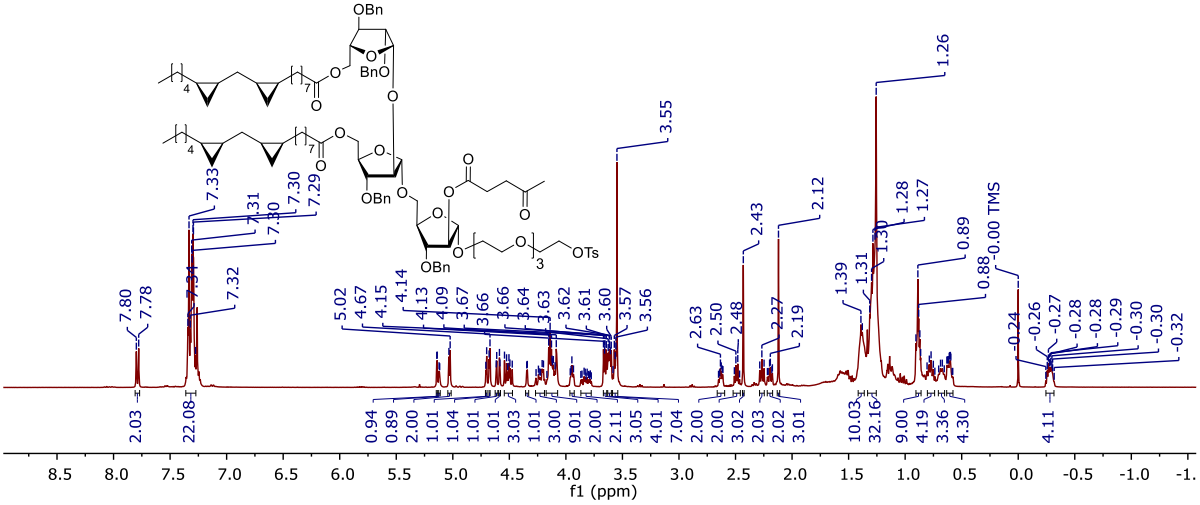
DEPT NMR Spectrum (100.53 MHz, $CDCl_3$) of compound **45a**



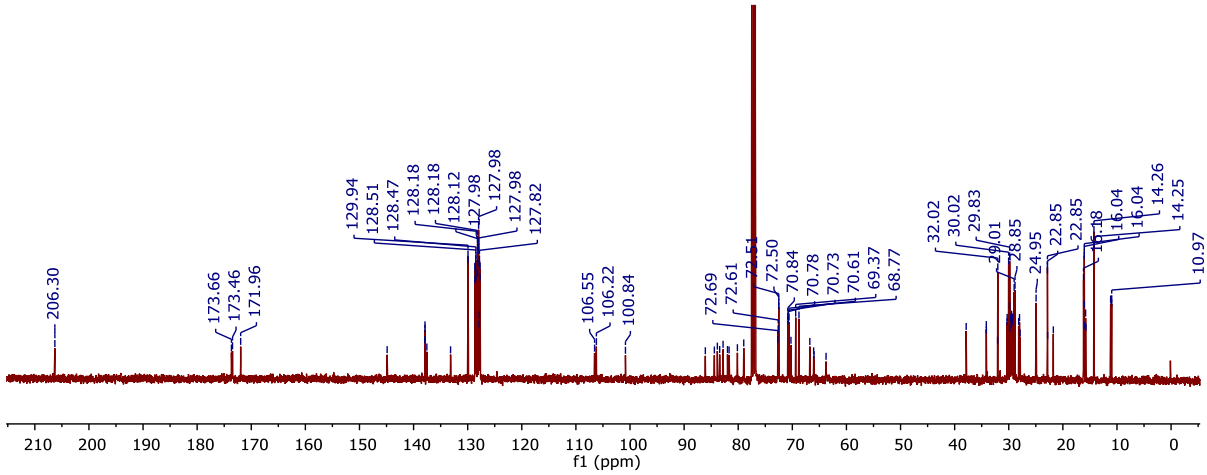
HMBC NMR Spectrum of compound **45a**



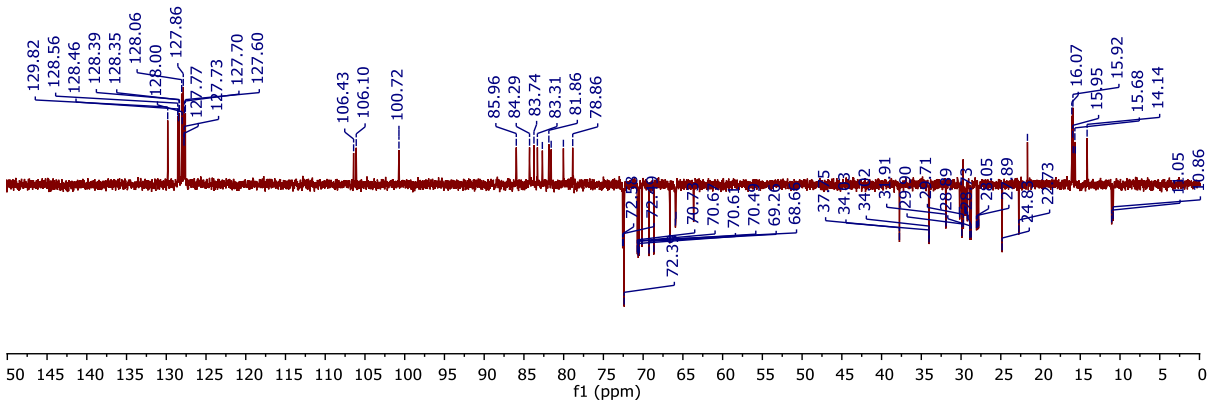
^{1}H NMR Spectrum (400.31 MHz, $CDCl_3$) of compound **46b**



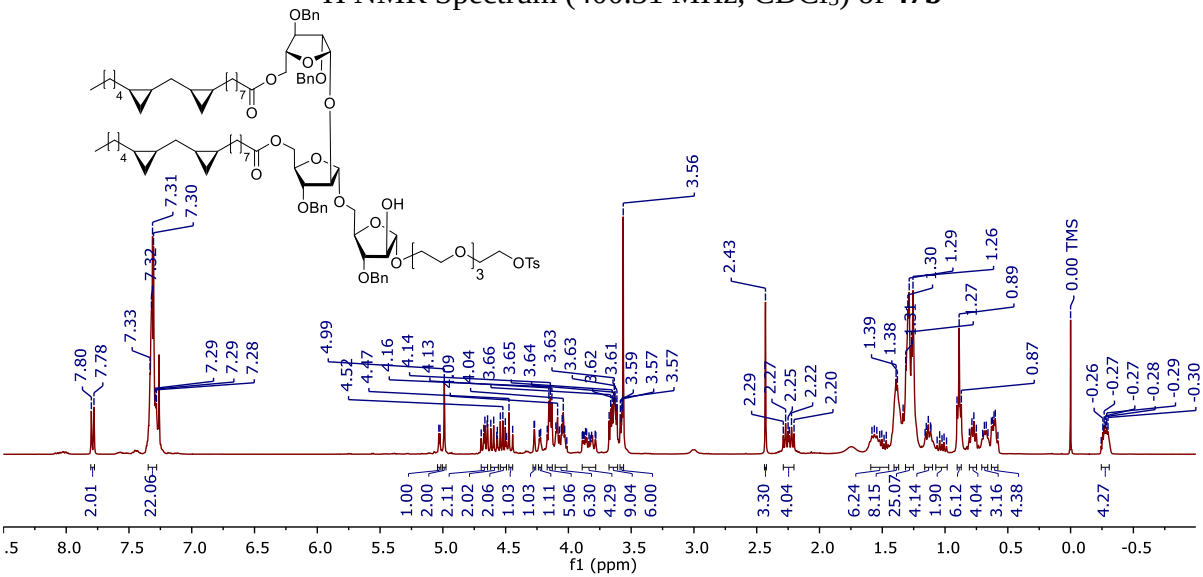
^{13}C NMR Spectrum (100.53 MHz, $CDCl_3$) of compound **46b**



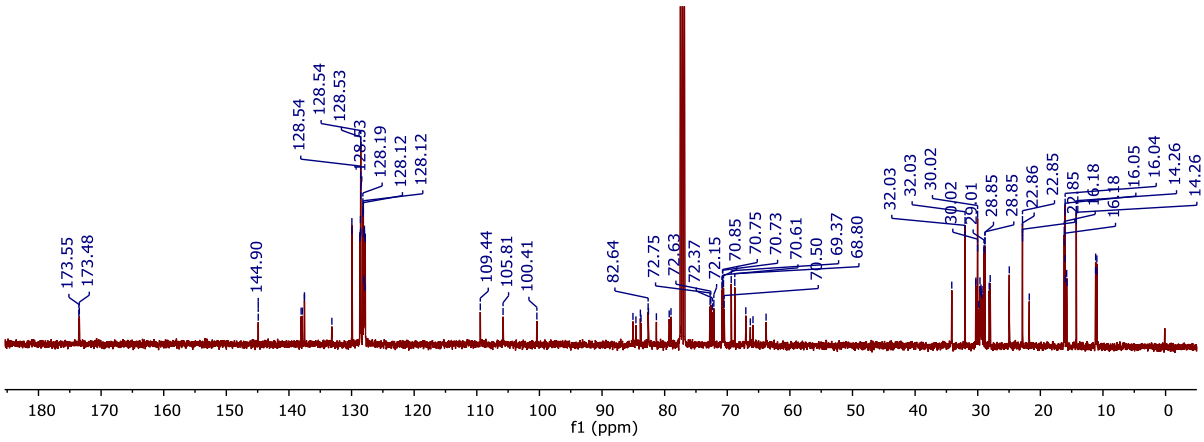
DEPT NMR Spectrum (100.53 MHz, $CDCl_3$) of compound **46b**



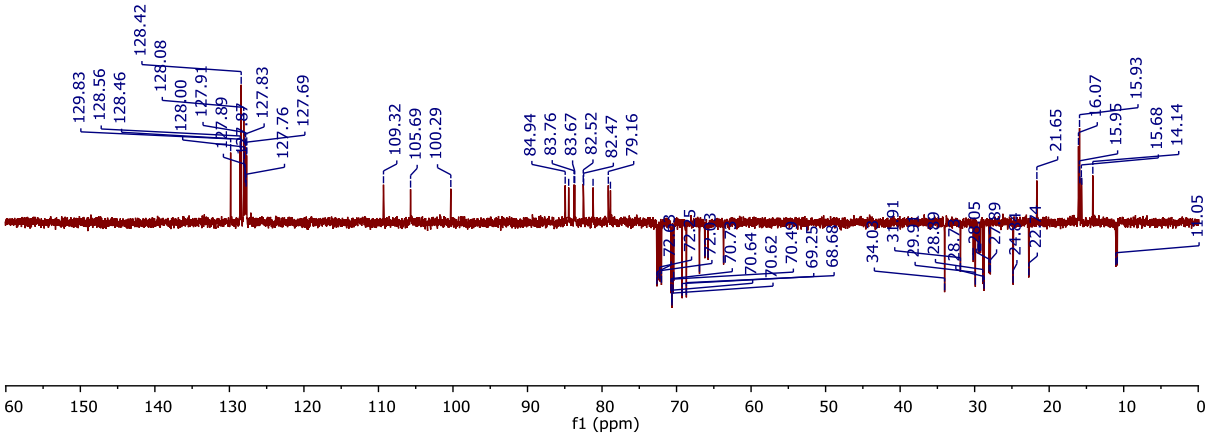
^{1}H NMR Spectrum (400.31 MHz, $CDCl_3$) of **47b**



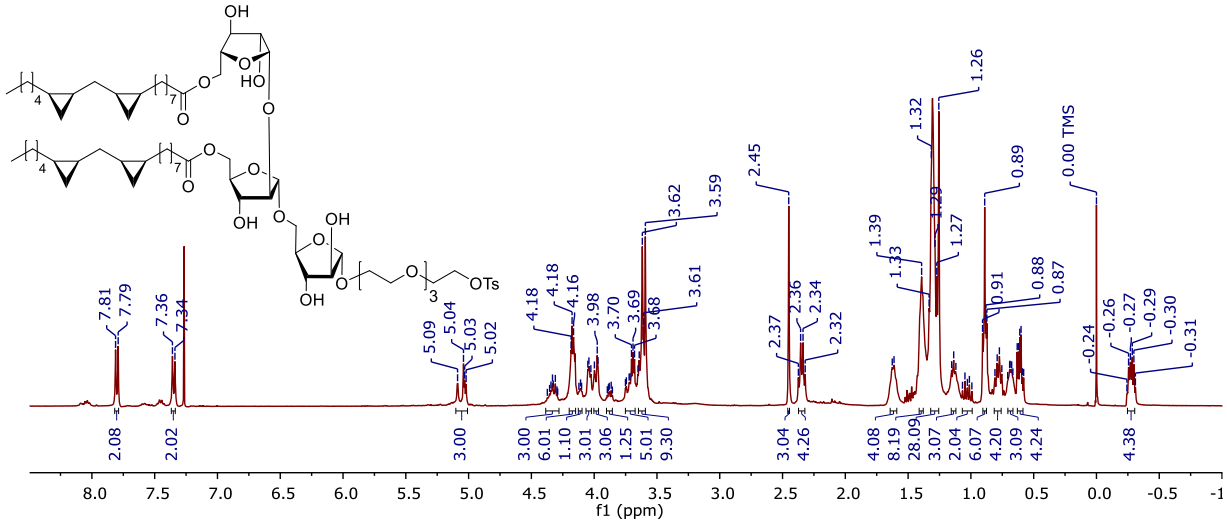
^{13}C NMR Spectrum (100.53 MHz, $CDCl_3$) of compound **47b**



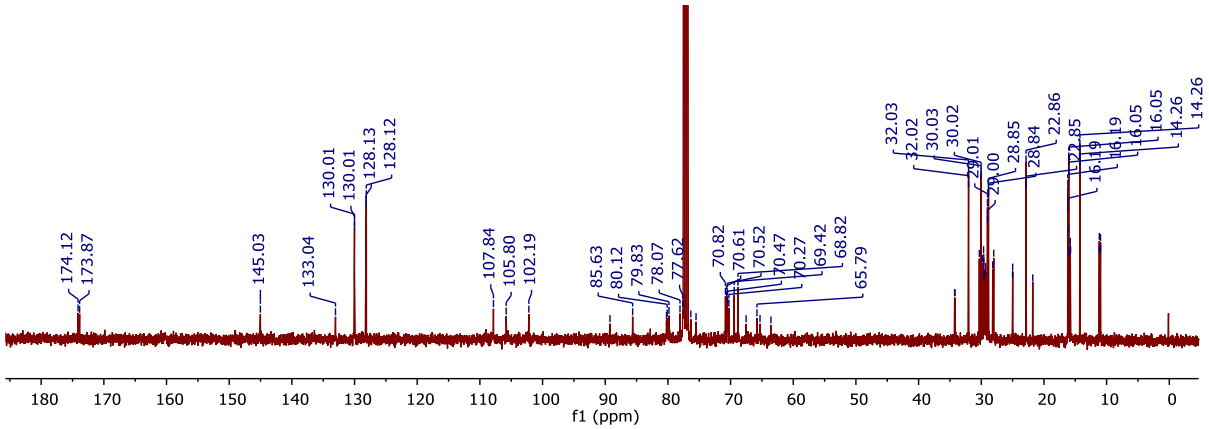
DEPT NMR Spectrum (100.53 MHz, $CDCl_3$) of compound **47b**



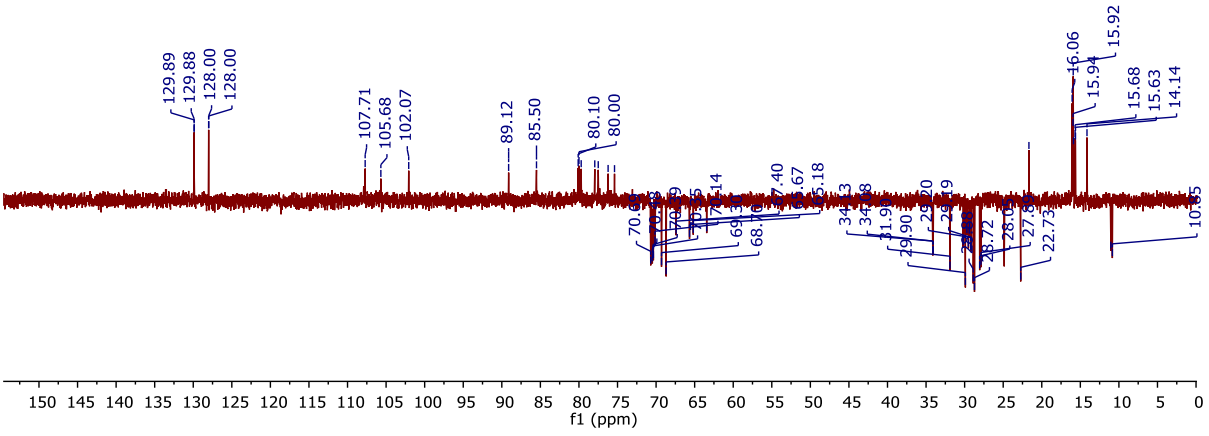
^{1}H NMR Spectrum (400.31 MHz, $CDCl_3$) of compound **48b**



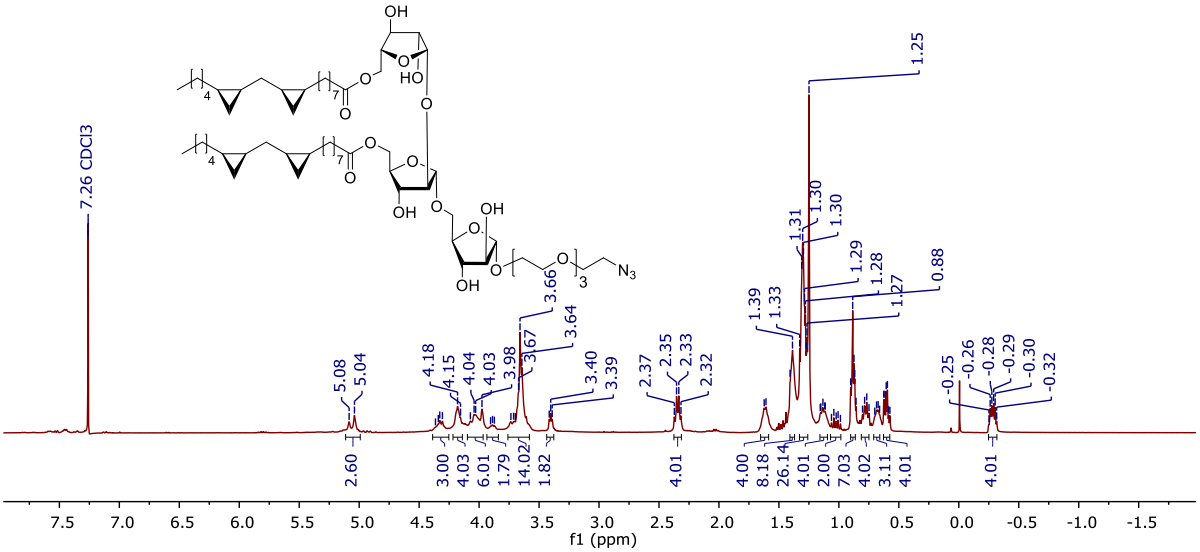
^{13}C NMR Spectrum (100.53 MHz, $CDCl_3$) of compound **48b**



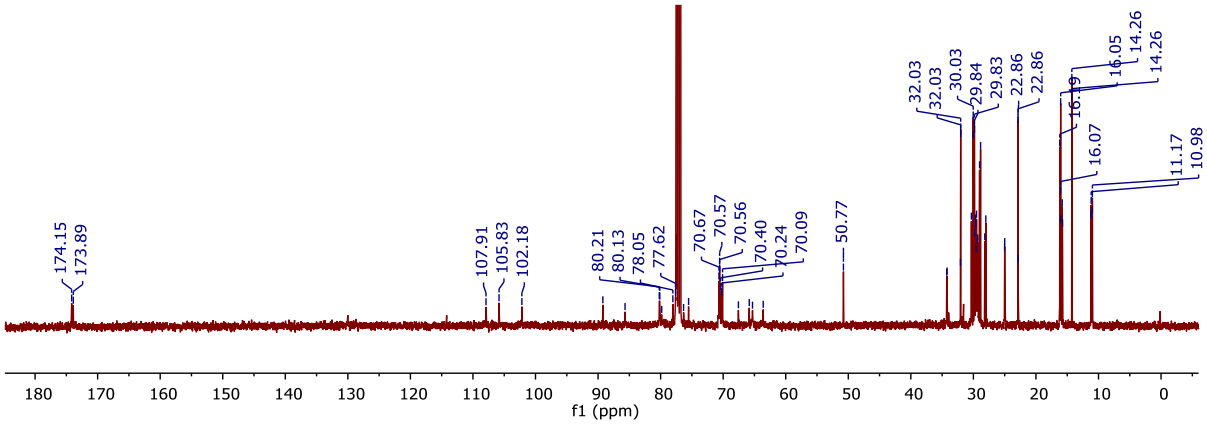
DEPT NMR Spectrum (100.53 MHz, $CDCl_3$) of compound **48b**



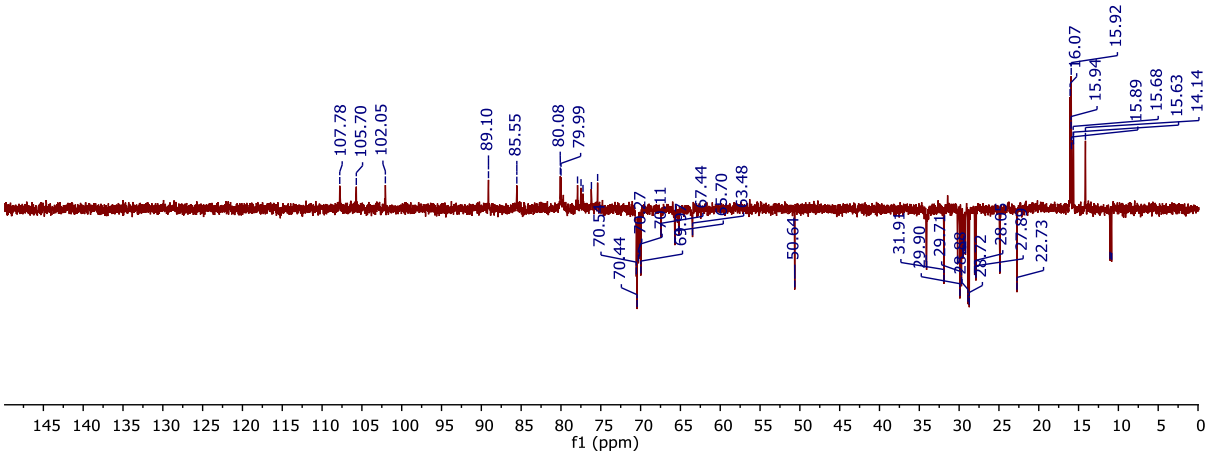
^{1}H NMR Spectrum (400.31 MHz, $CDCl_3$) of compound **45b**



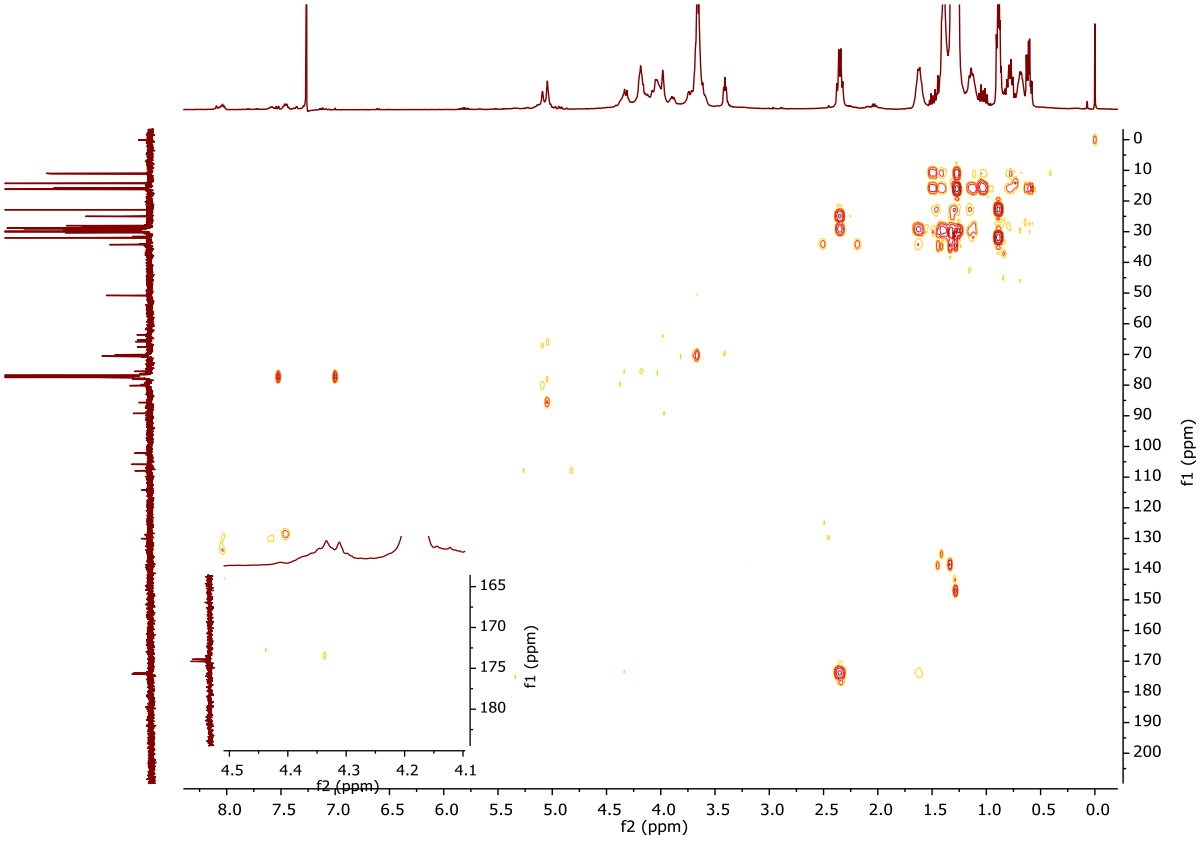
^{13}C NMR Spectrum (100.53 MHz, $CDCl_3$) of compound **45b**



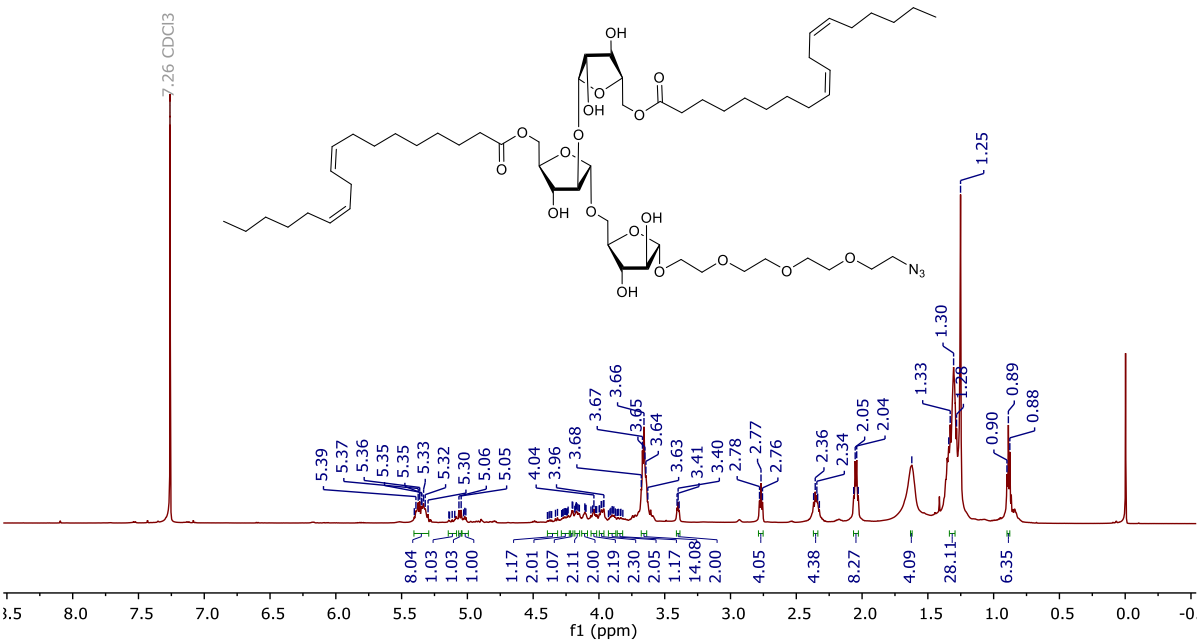
DEPT NMR Spectrum (100.53 MHz, $CDCl_3$) of compound **45b**



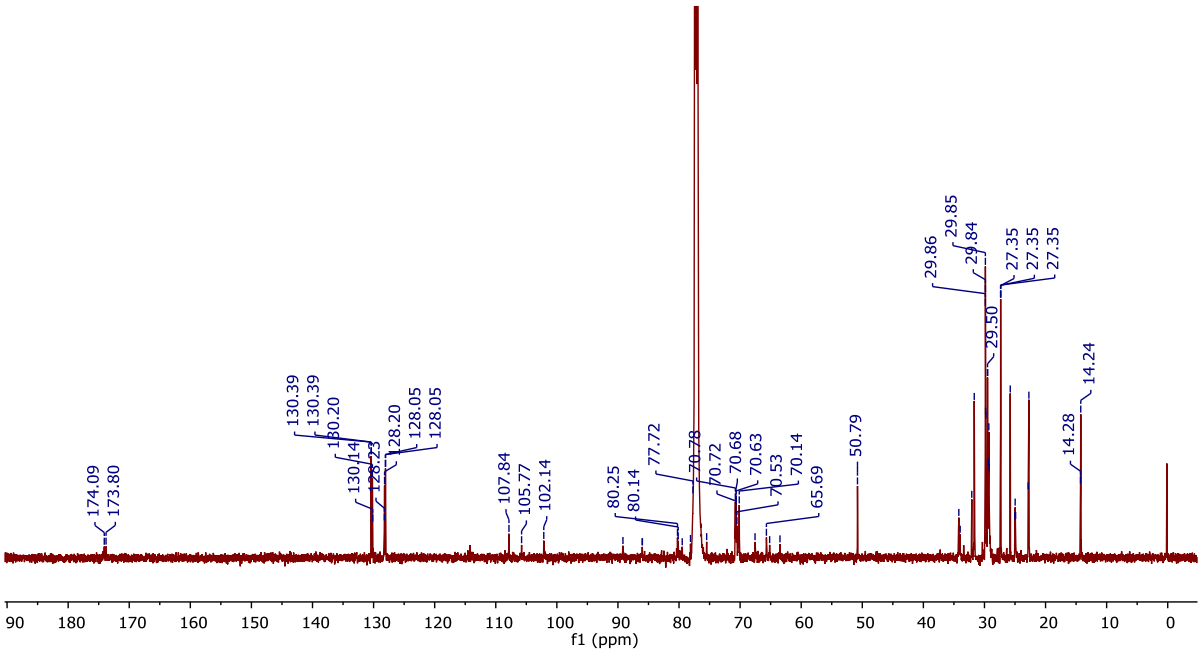
HMBC NMR Spectrum of compound **45b**



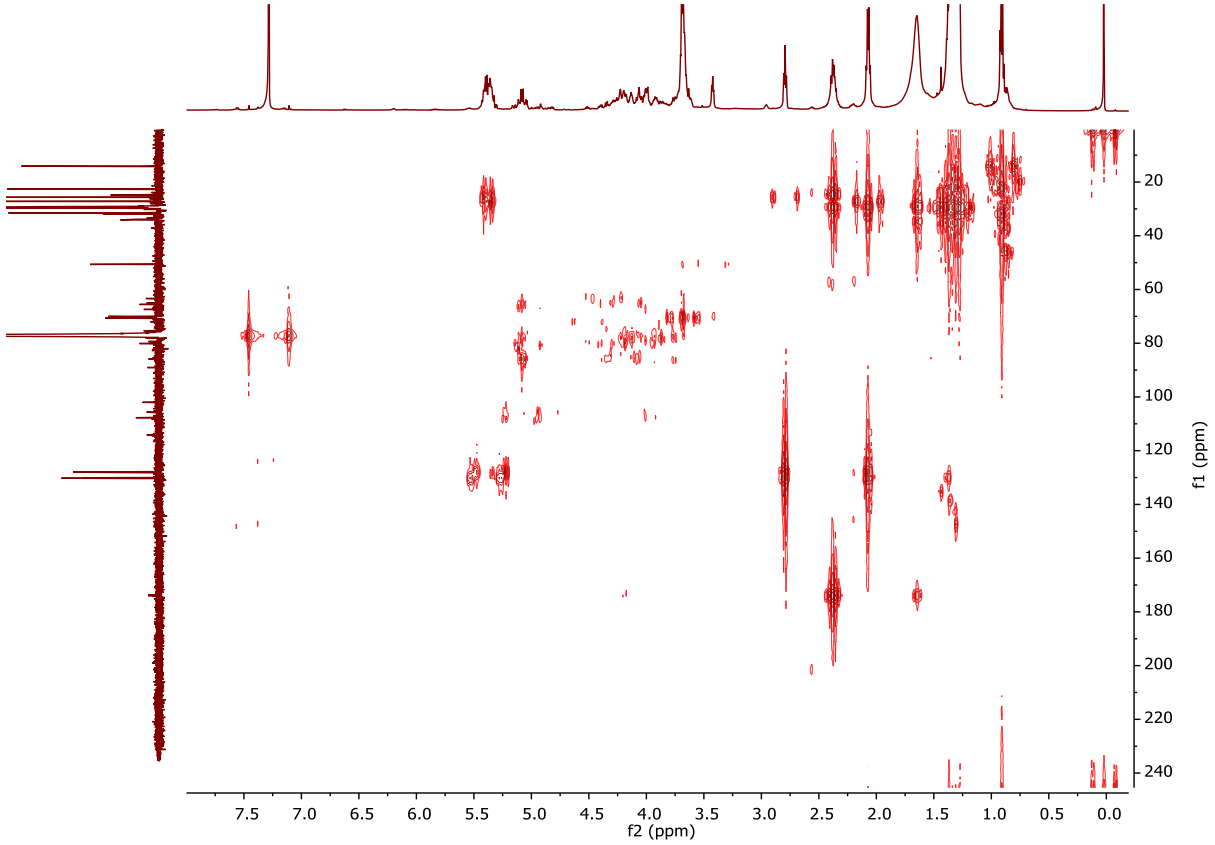
^{1}H NMR Spectrum (400.31 MHz, $CDCl_3$) of compound **45b**



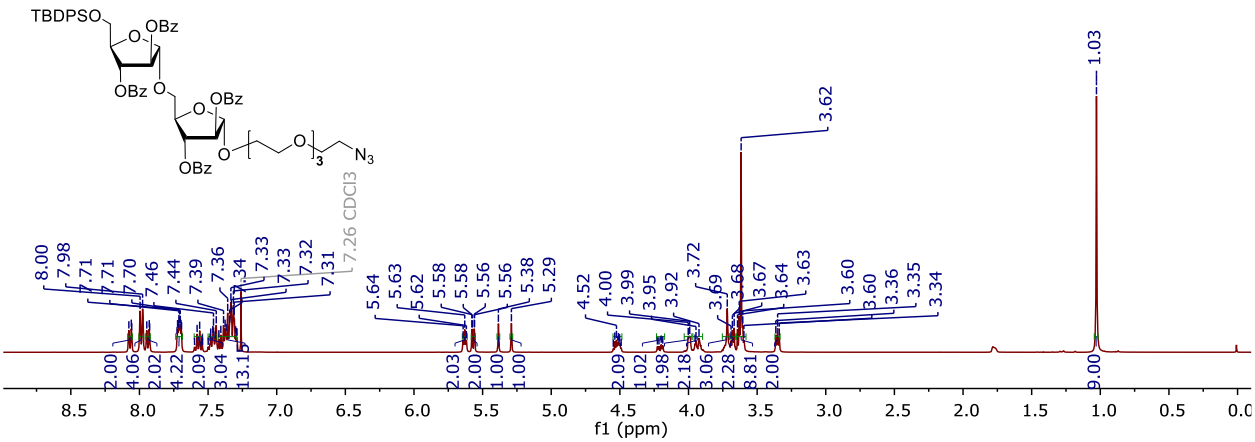
^{13}C NMR Spectrum (100.53 MHz, $CDCl_3$) of compound **45b**



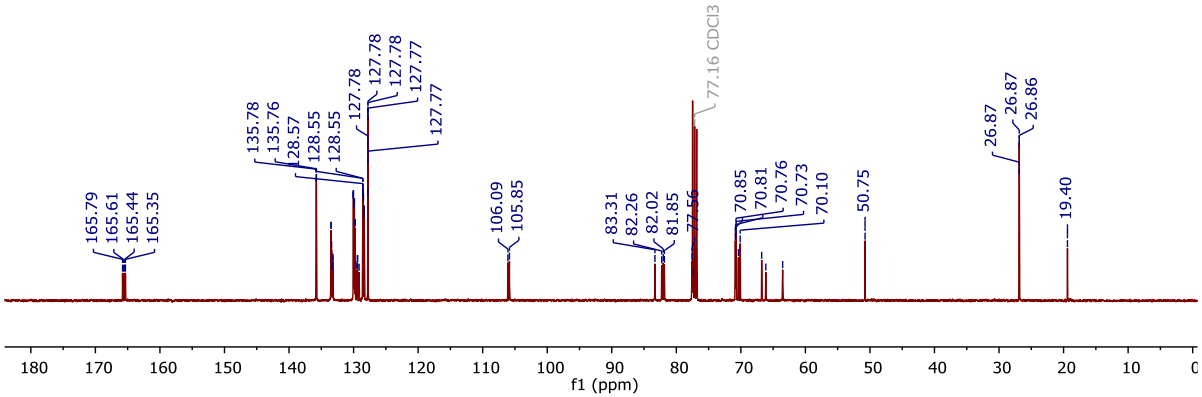
HSQC NMR Spectrum of compound **45b**



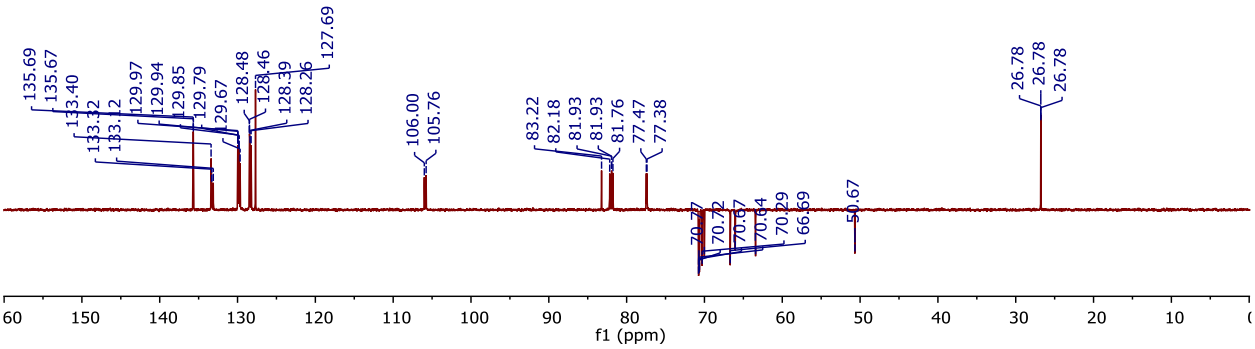
^{1}H NMR Spectrum (400.31 MHz, $CDCl_3$) of Compound **50**



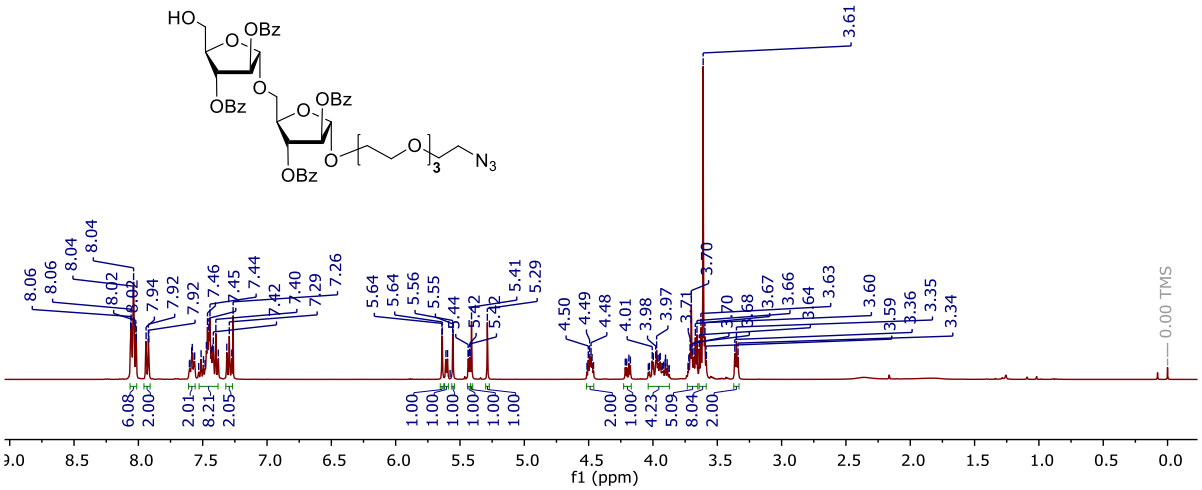
^{13}C NMR Spectrum (100.53 MHz, $CDCl_3$) of Compound **50**



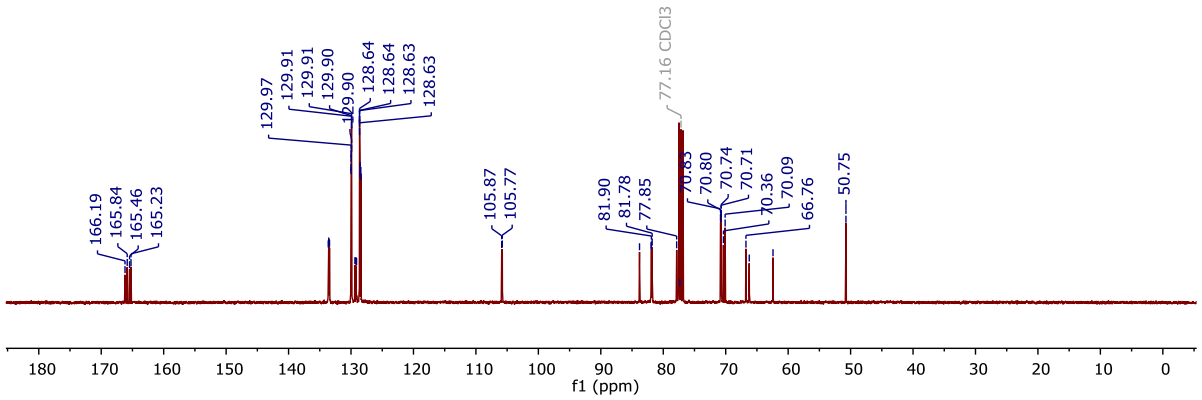
DEPT-NMR Spectrum (100.53 MHz, $CDCl_3$) of Compound **50**



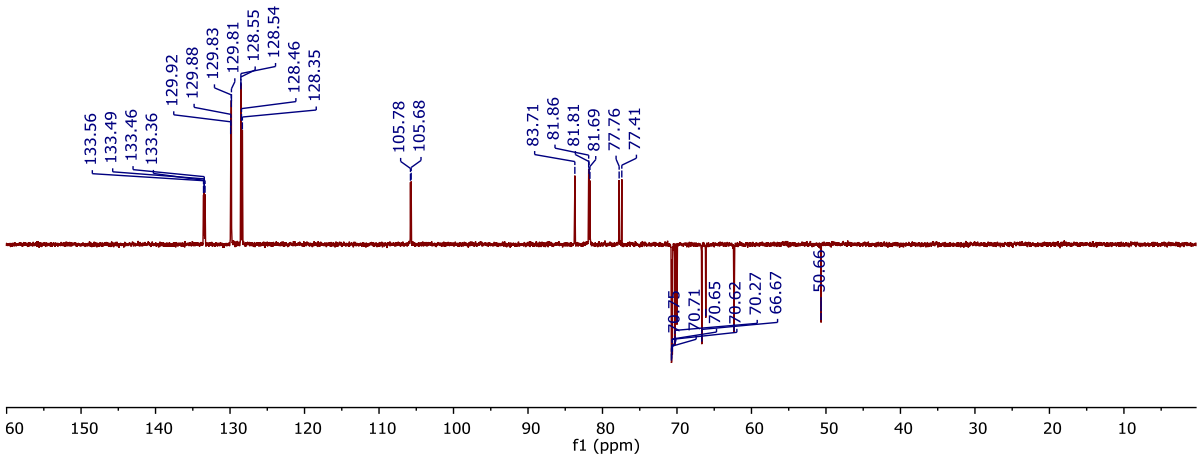
^{1}H NMR Spectrum (400.31 MHz, $CDCl_3$) of Compound **51**



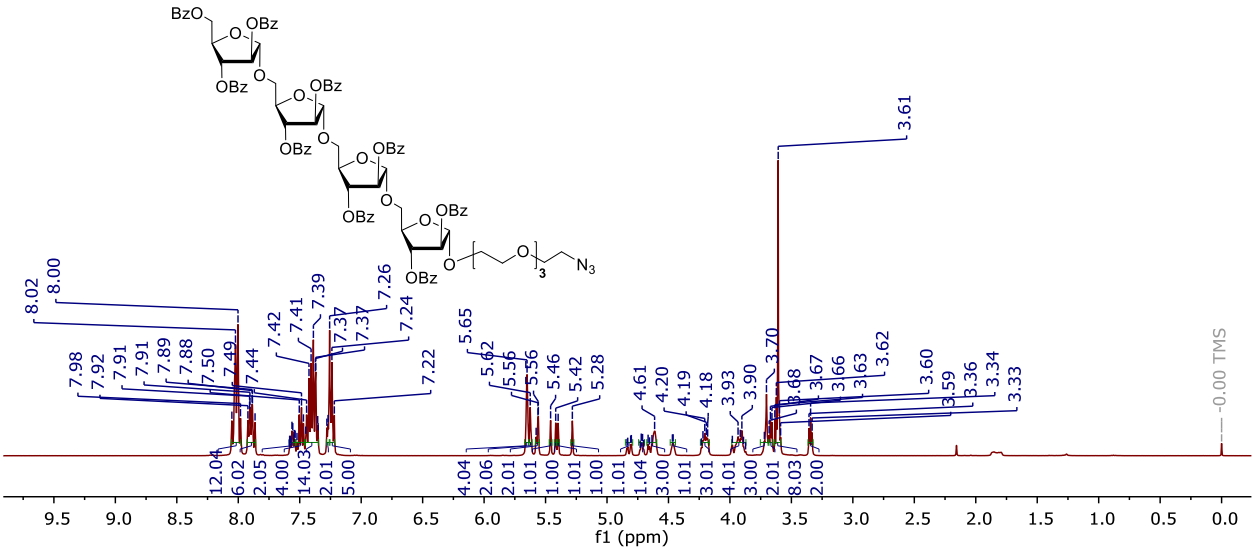
^{13}C NMR Spectrum (100.53 MHz, $CDCl_3$) of Compound **51**



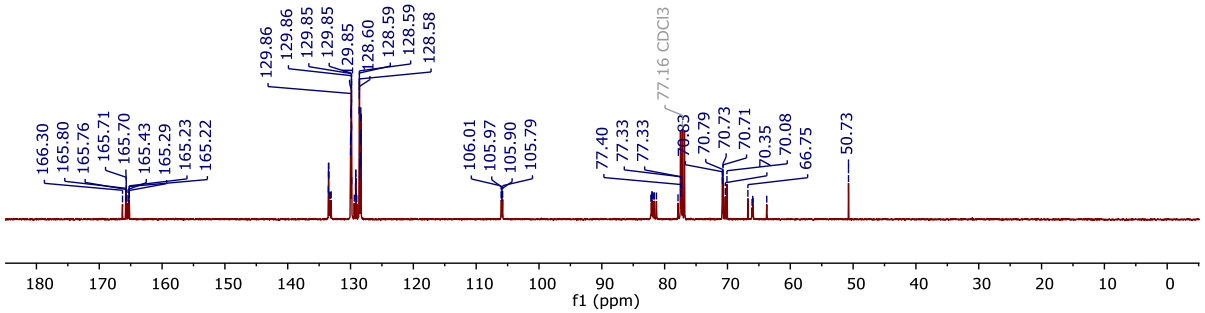
DEPT NMR Spectrum (100.53 MHz, $CDCl_3$) of Compound **51**



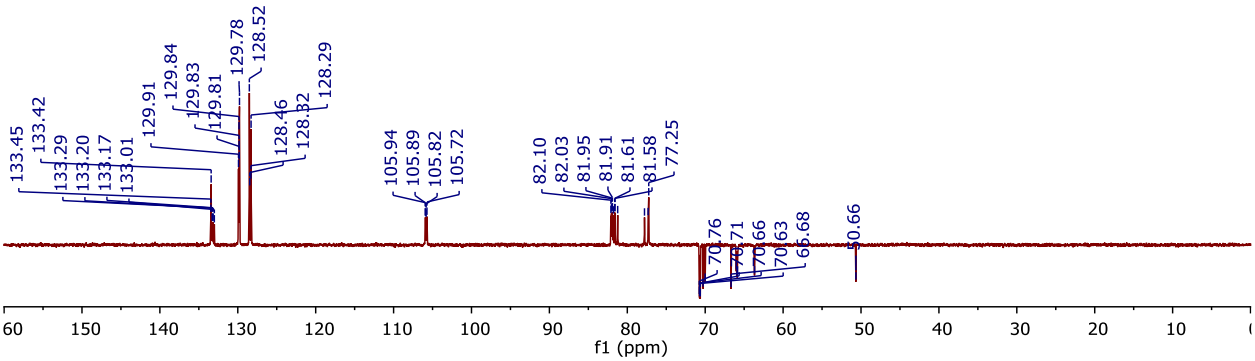
^{1}H NMR Spectrum (400.31 MHz, $CDCl_3$) of Compound **52**



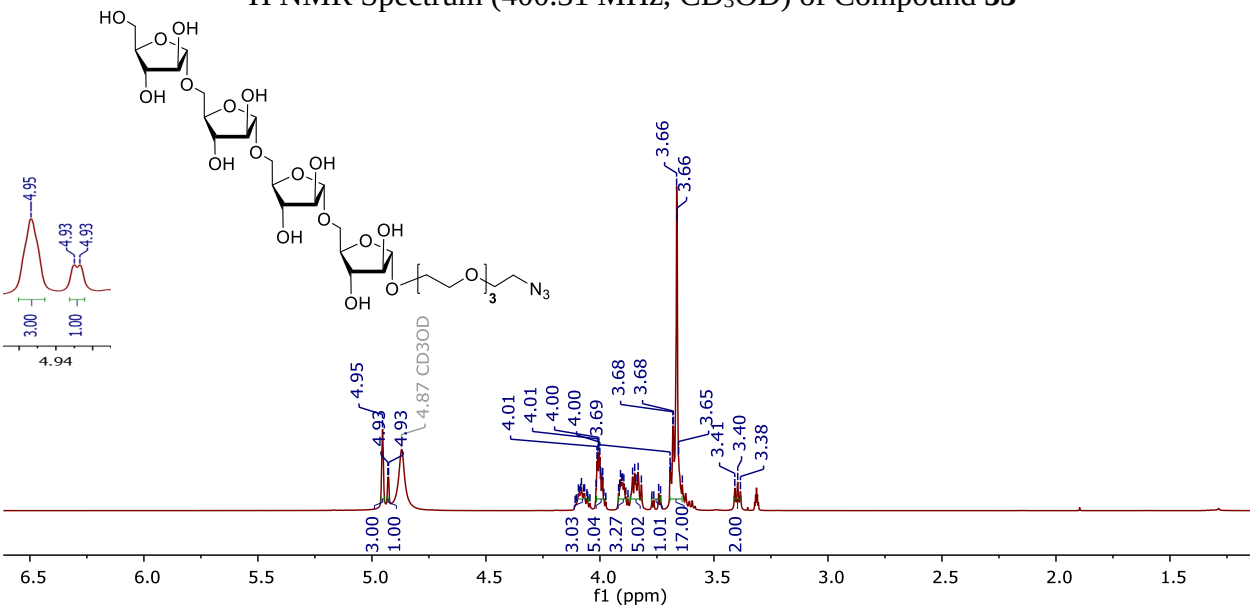
^{13}C NMR Spectrum (100.53 MHz, $CDCl_3$) of Compound **52**



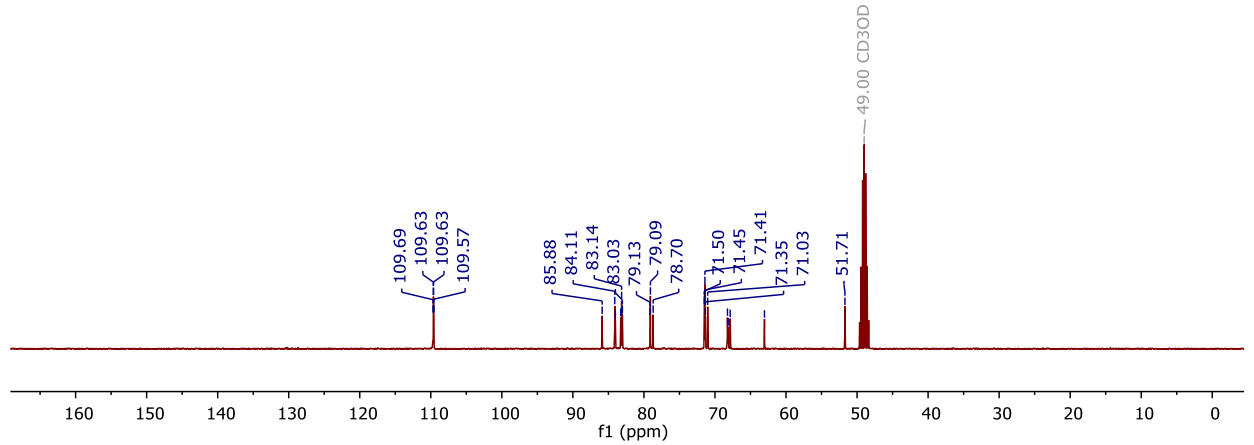
DEPT-NMR Spectrum (100.53 MHz, $CDCl_3$) of Compound **52**



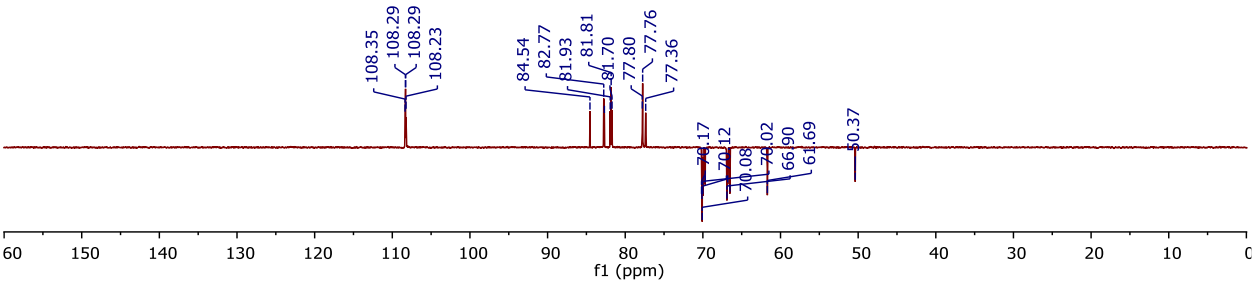
^{1}H NMR Spectrum (400.31 MHz, CD_3OD) of Compound **53**



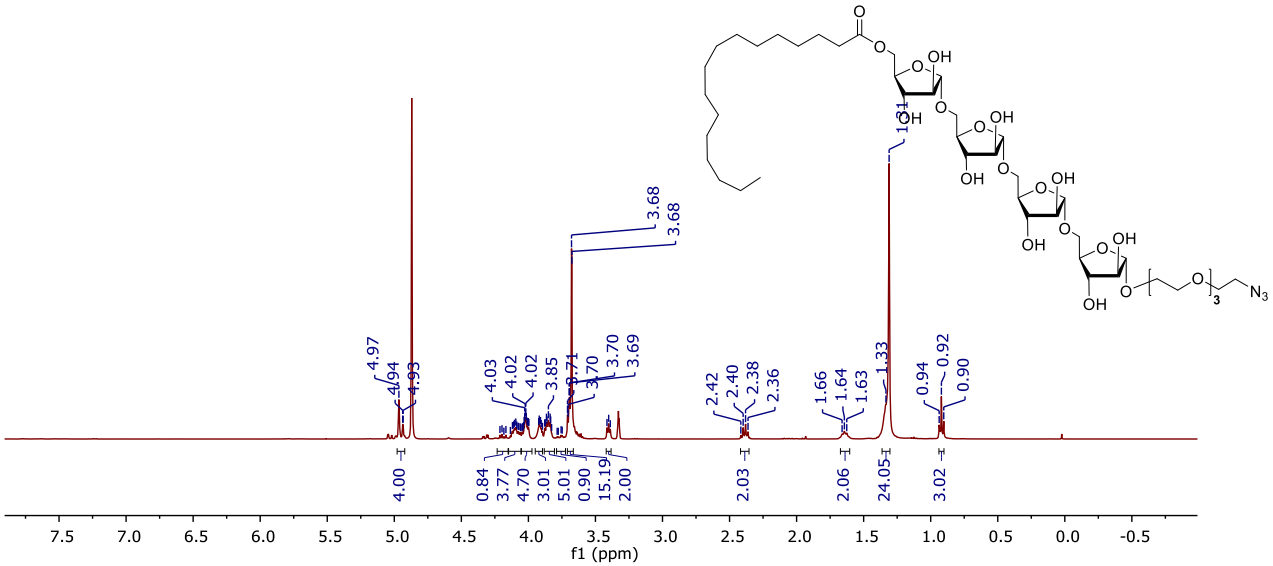
^{13}C NMR Spectrum (100.53 MHz, CD_3OD) of Compound **53**



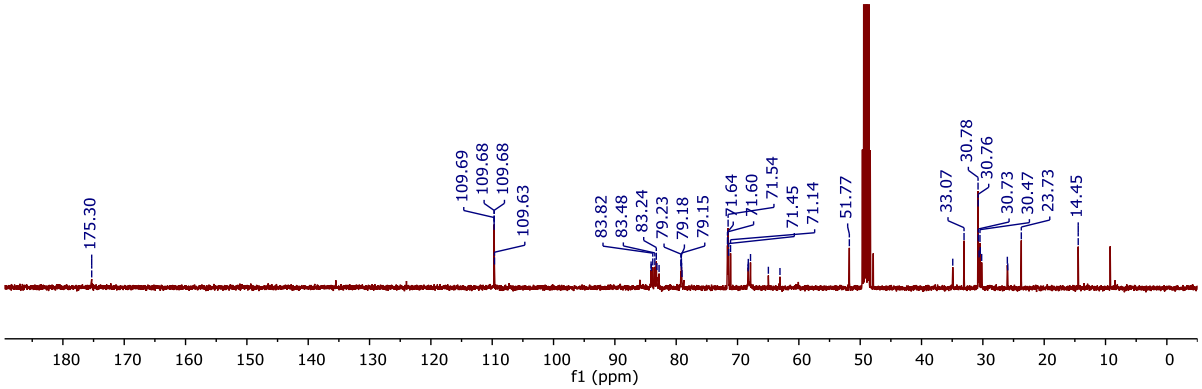
DEPT-NMR Spectrum (100.53 MHz, CD_3OD) of Compound **53**



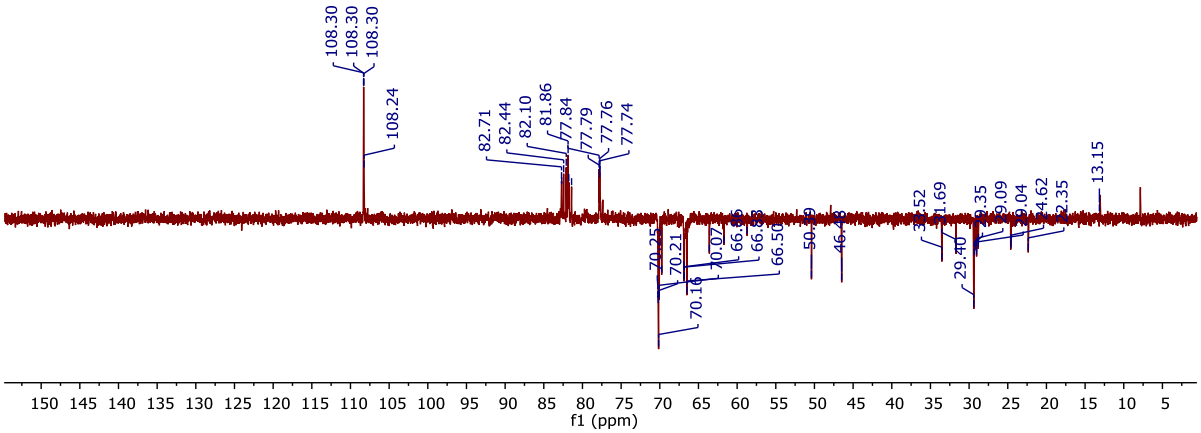
^{1}H NMR Spectrum (400.31 MHz, CD_3OD) of Compound **53a**



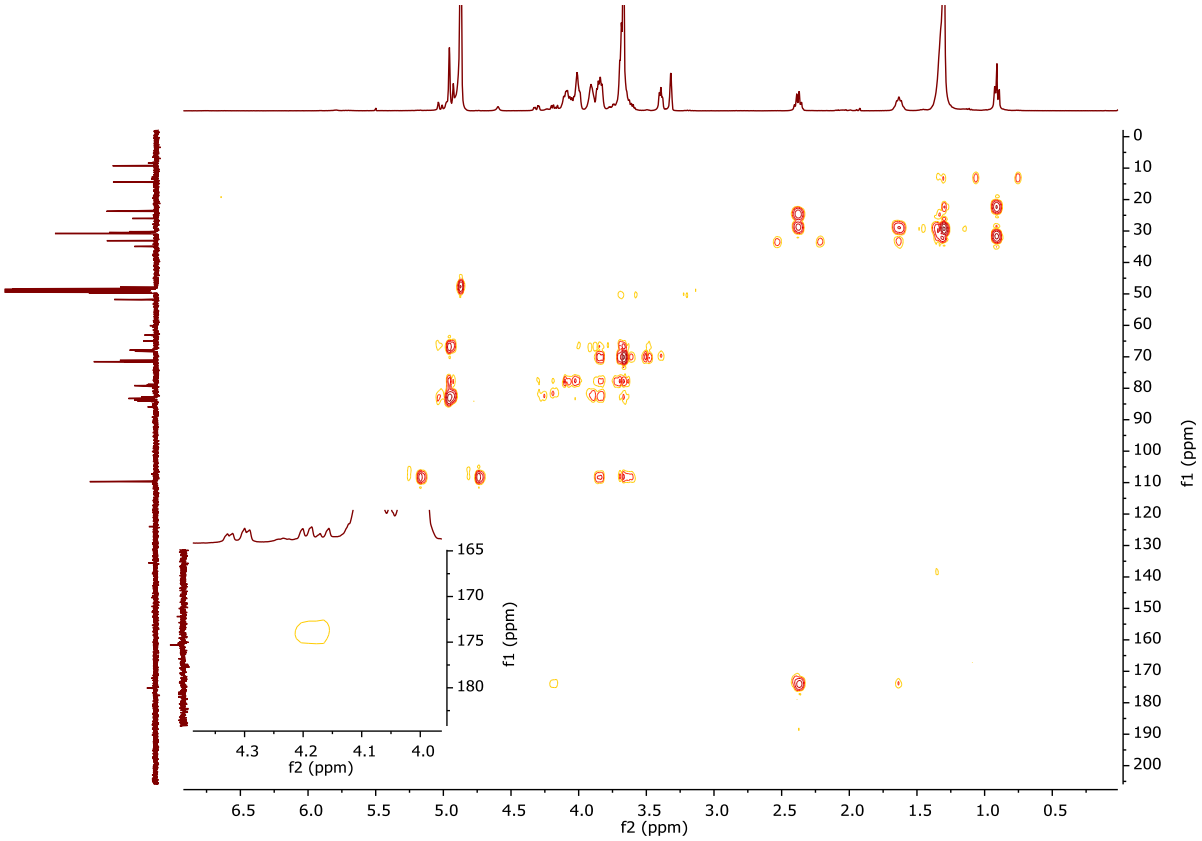
^{13}C NMR Spectrum (100.53 MHz, CD_3OD) of Compound **53a**



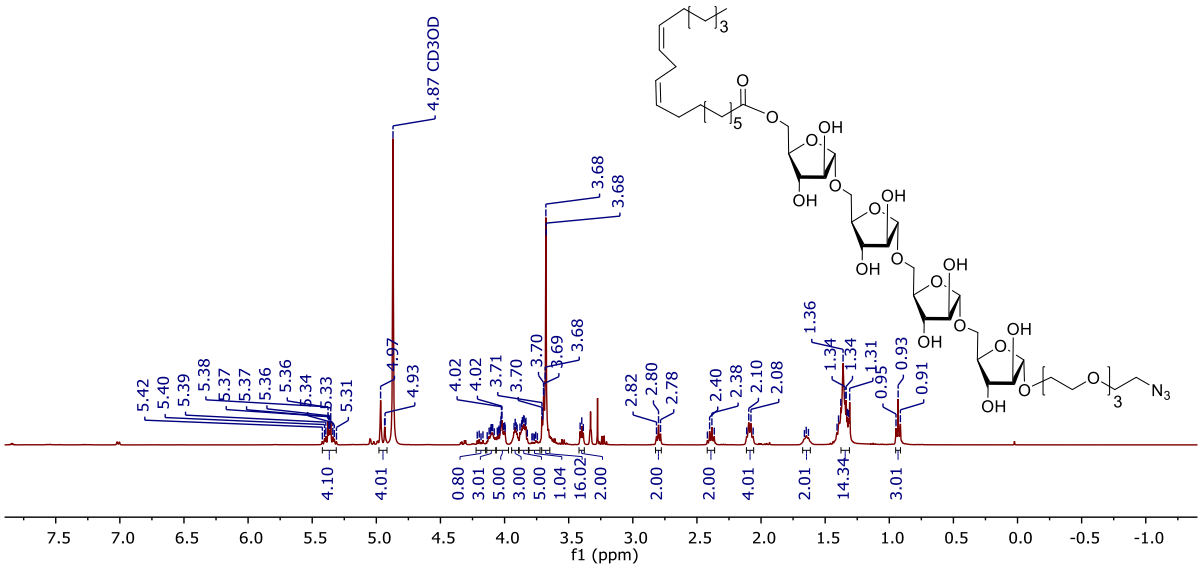
DEPT NMR Spectrum (100.53 MHz, CD_3OD) of Compound **53a**



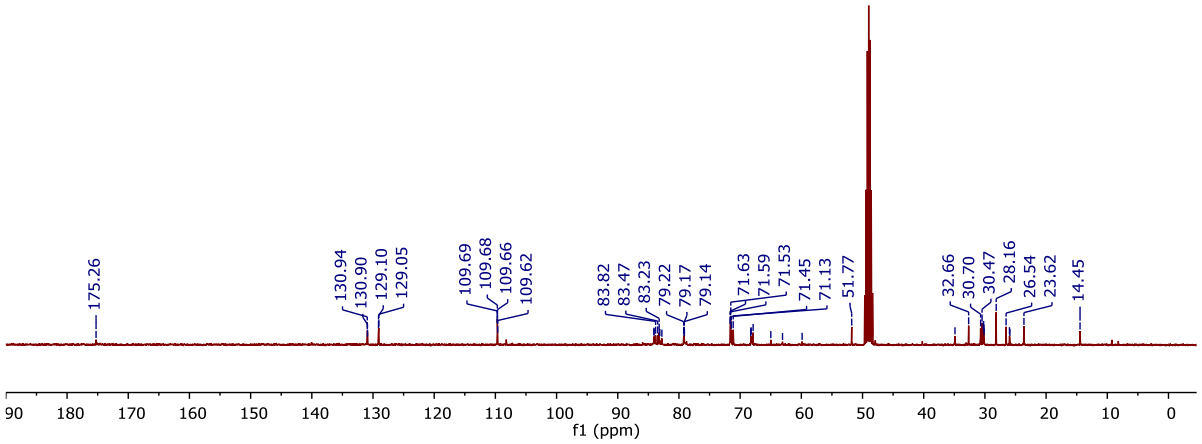
HMBC NMR Spectrum of Compound **53a**



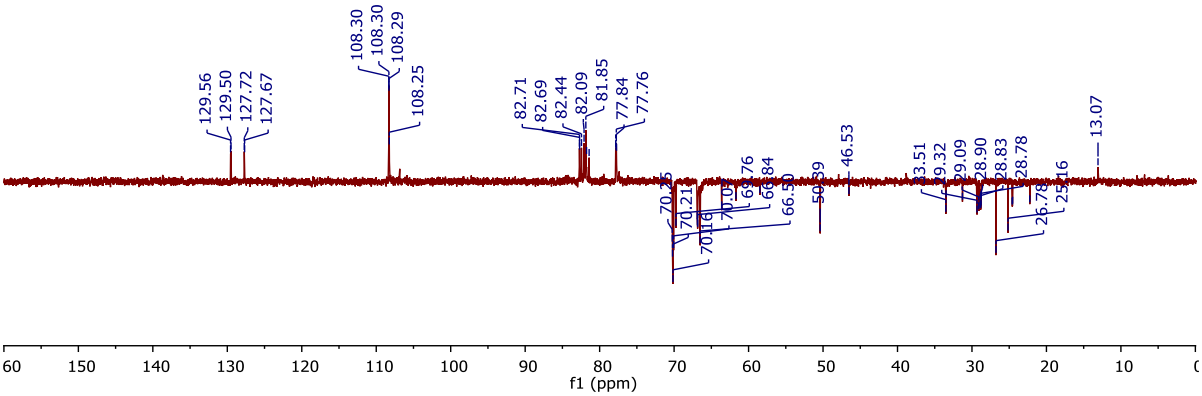
^{1}H NMR Spectrum (400.31 MHz, CD_3OD) of Compound **53b**



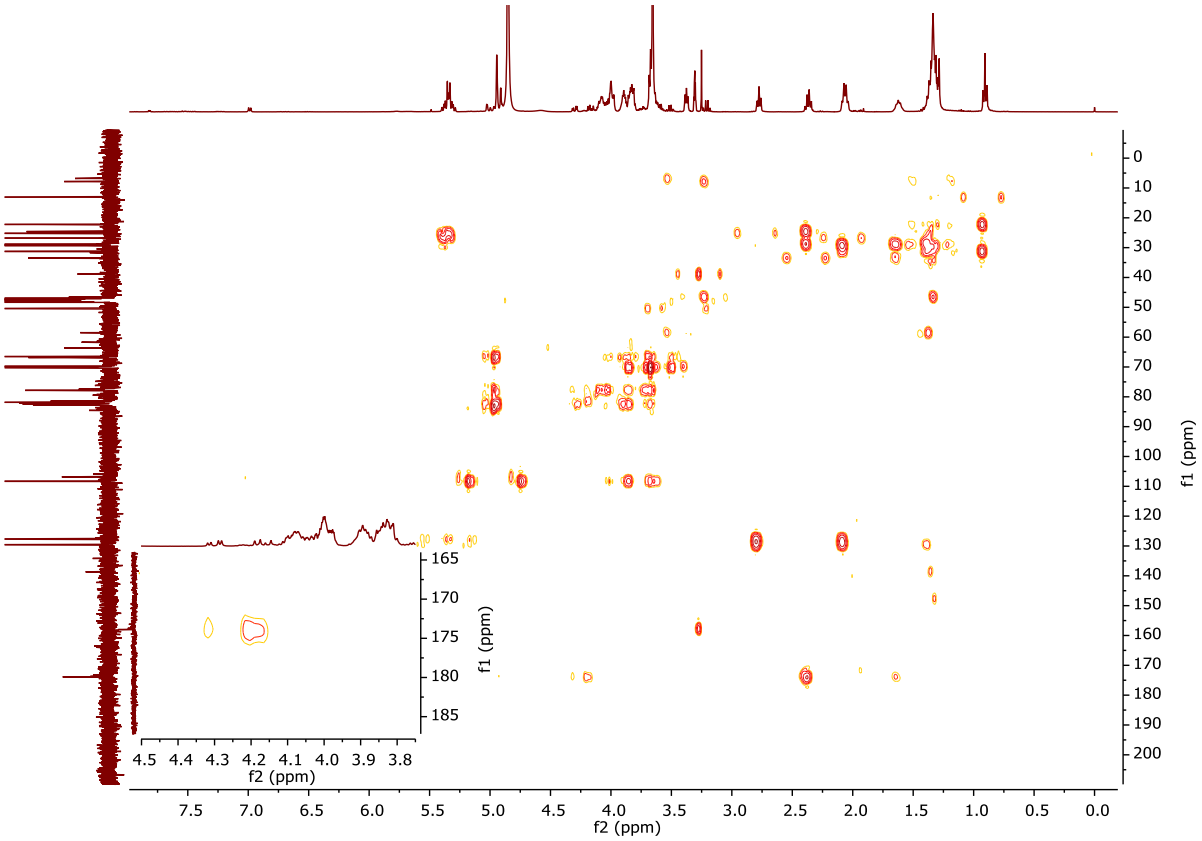
^{13}C NMR Spectrum (100.53 MHz, CD_3OD) of Compound **53b**



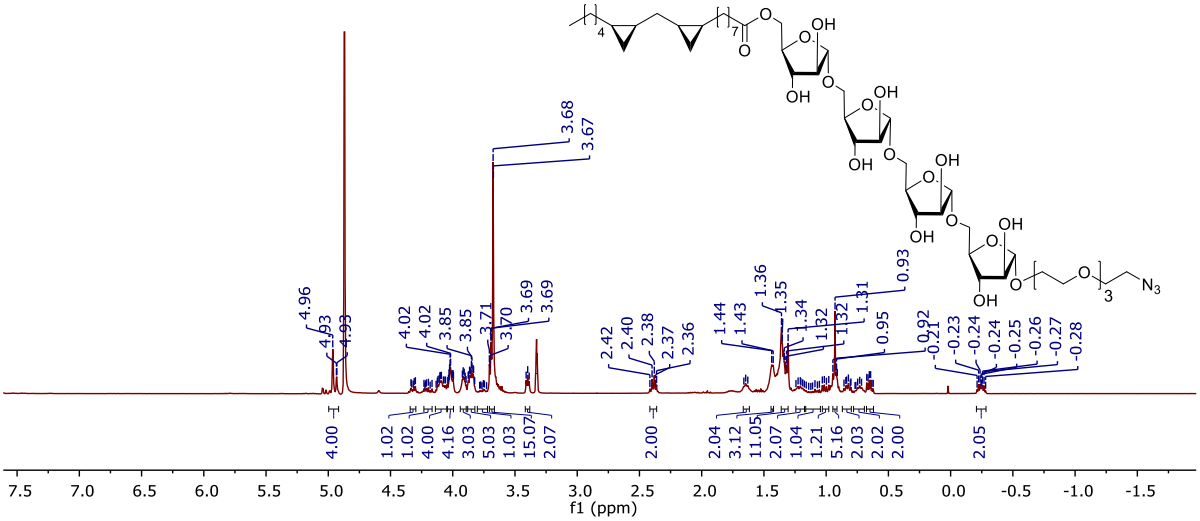
DEPT NMR Spectrum (100.53 MHz, CD_3OD) of Compound **53b**



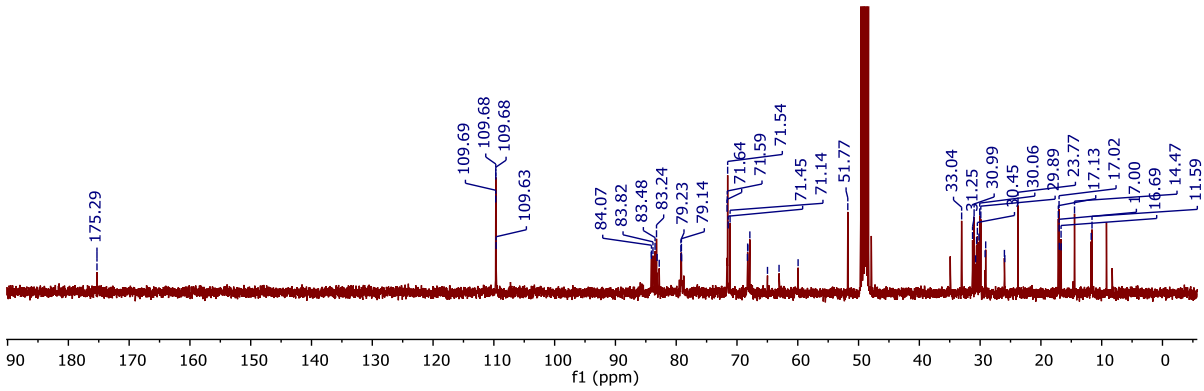
HMBC NMR Spectrum of Compound **53b**



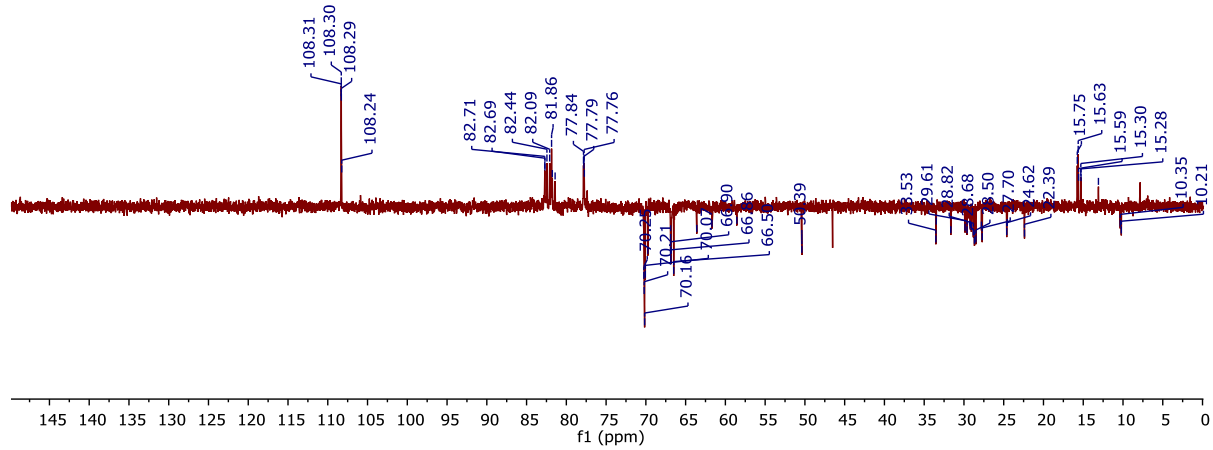
^{1}H NMR Spectrum (400.31 MHz, CD_3OD) of Compound **53c**



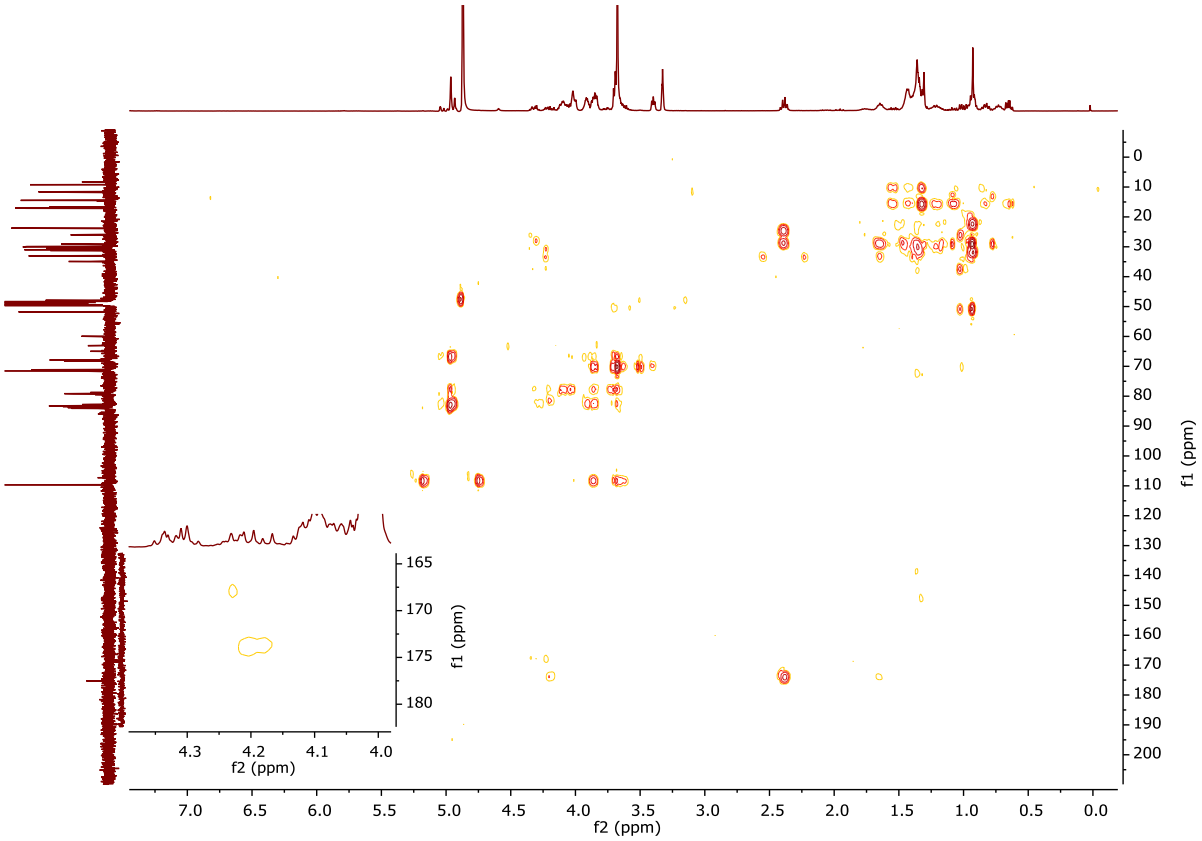
^{13}C NMR Spectrum (100.53 MHz, CD_3OD) of Compound **53c**



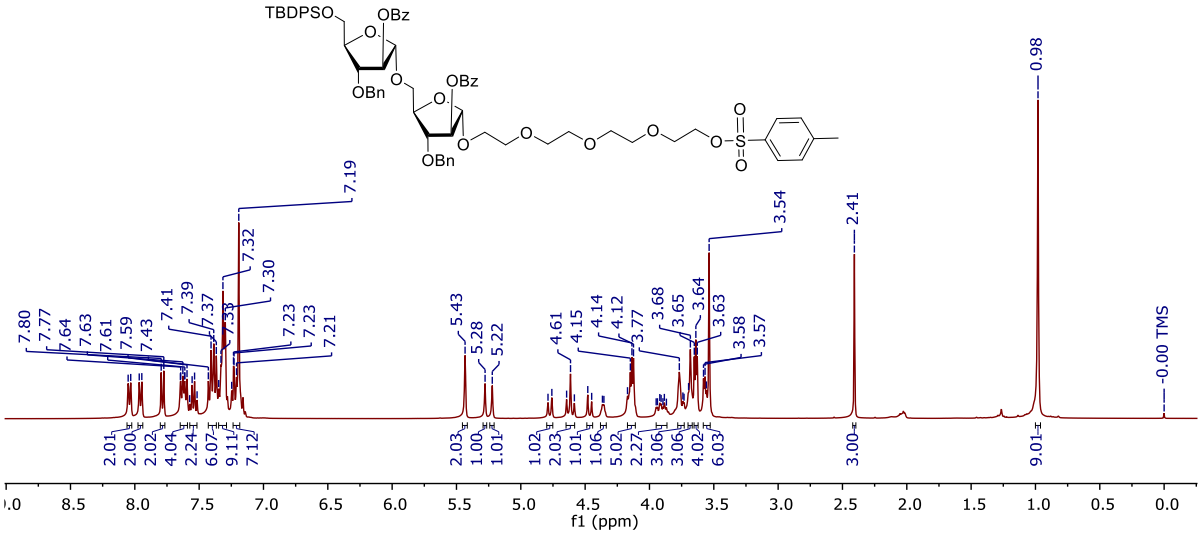
DEPT NMR Spectrum (100.53 MHz, CD_3OD) of Compound **53c**



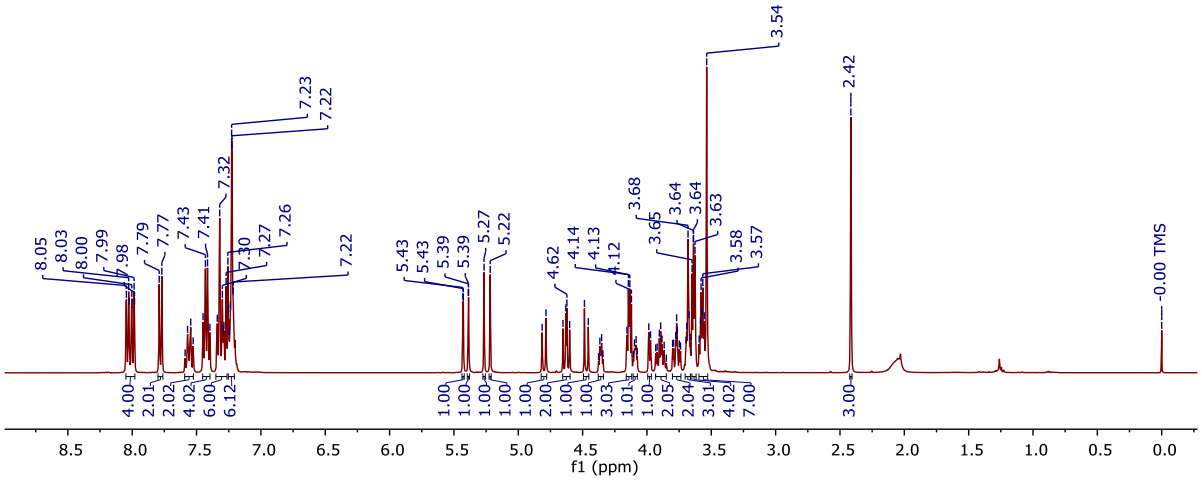
HMBC NMR Spectrum of Compound **53c**



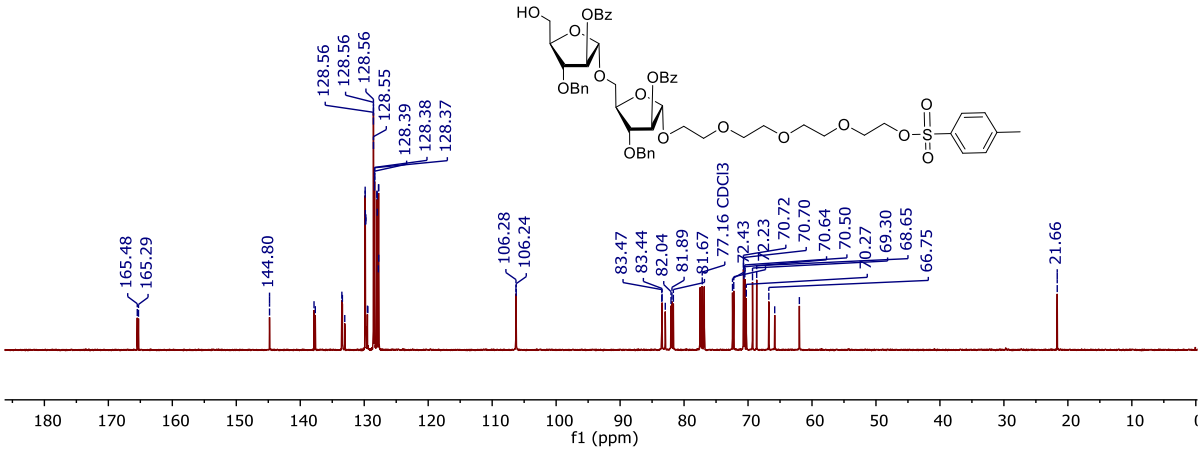
^{1}H NMR Spectrum (400.31 MHz, $CDCl_3$) of Compound **54**


TBDPSO
OBz
OBn
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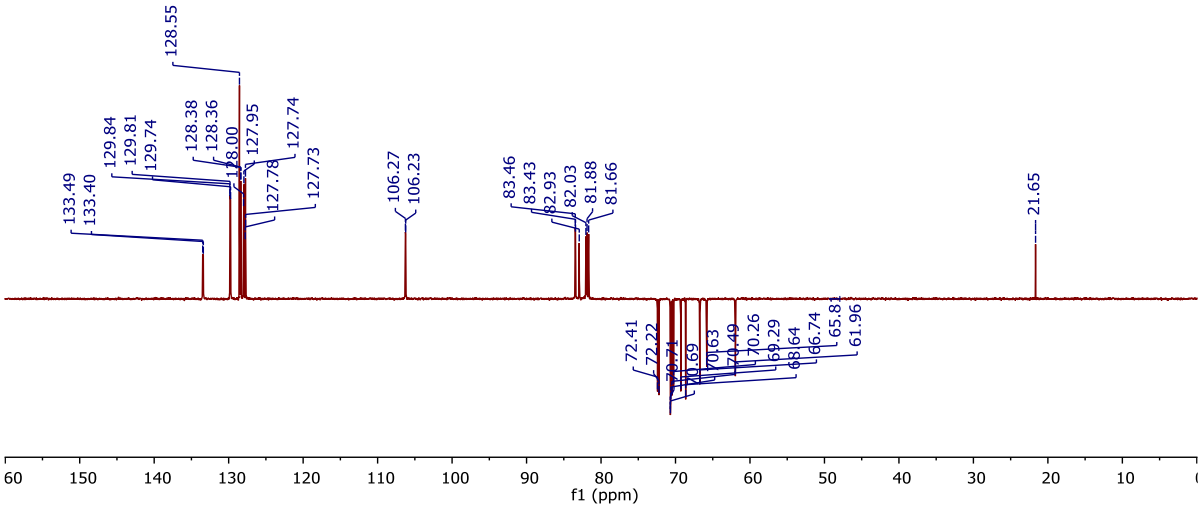
^{1}H NMR Spectrum (400.31 MHz, $CDCl_3$) of Compound **55**



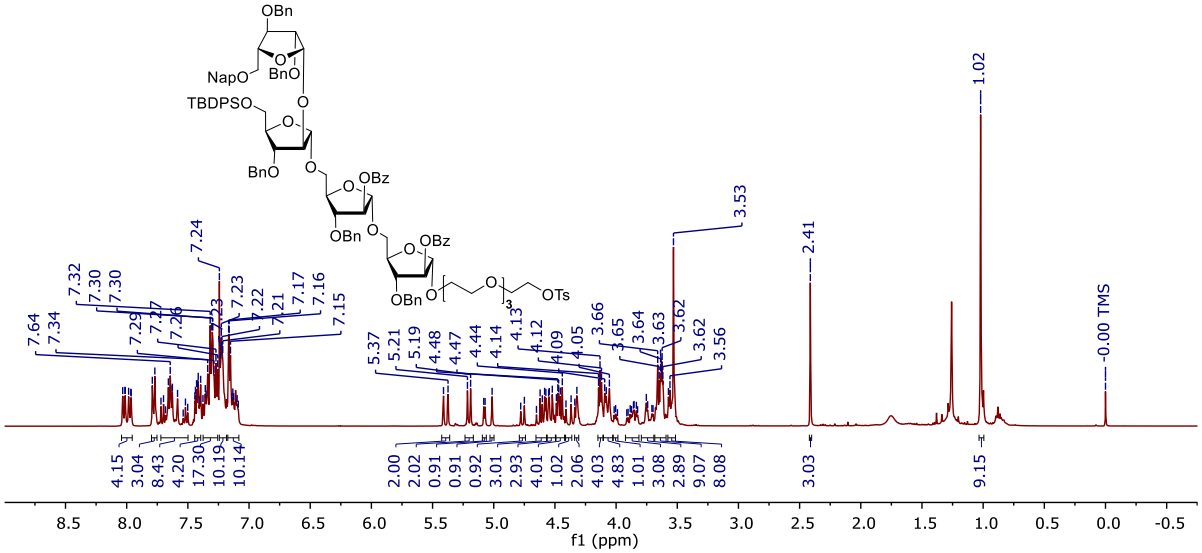
^{13}C NMR Spectrum (100.53 MHz, $CDCl_3$) of Compound **55**



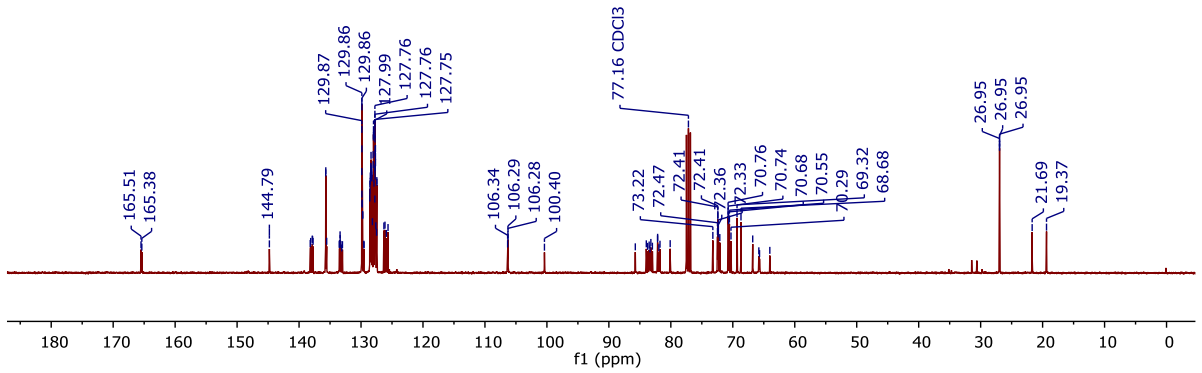
DEPT NMR Spectrum (100.53 MHz, $CDCl_3$) of Compound **55**



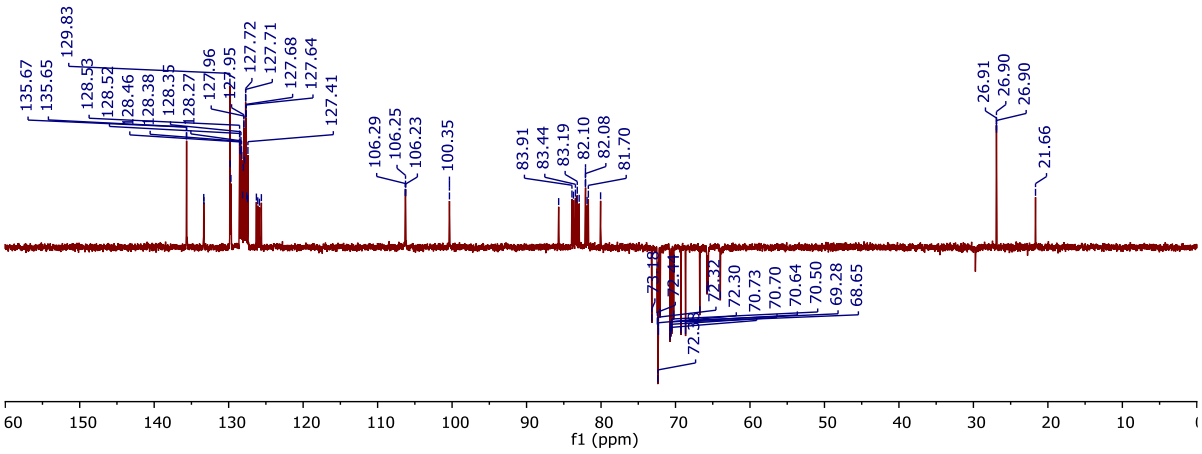
^{1}H NMR Spectrum (400.31 MHz, $CDCl_3$) of Compound **56b**



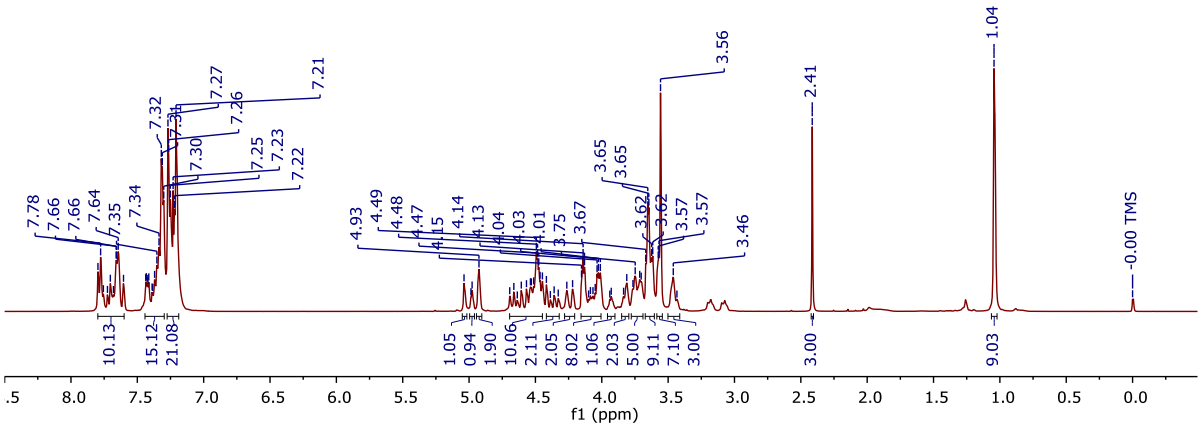
^{13}C NMR Spectrum (100.53 MHz, $CDCl_3$) of Compound **56b**



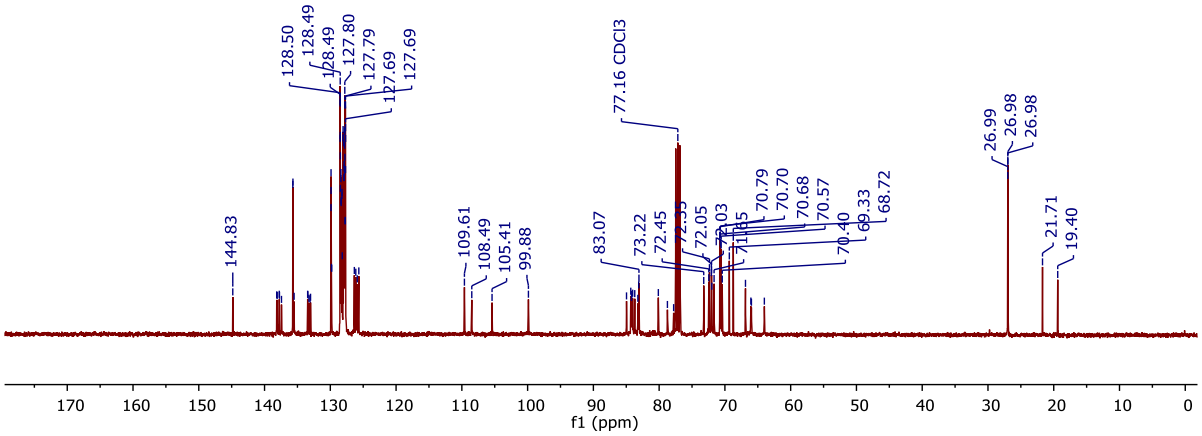
DEPT NMR Spectrum (100.53 MHz, $CDCl_3$) of Compound **56b**



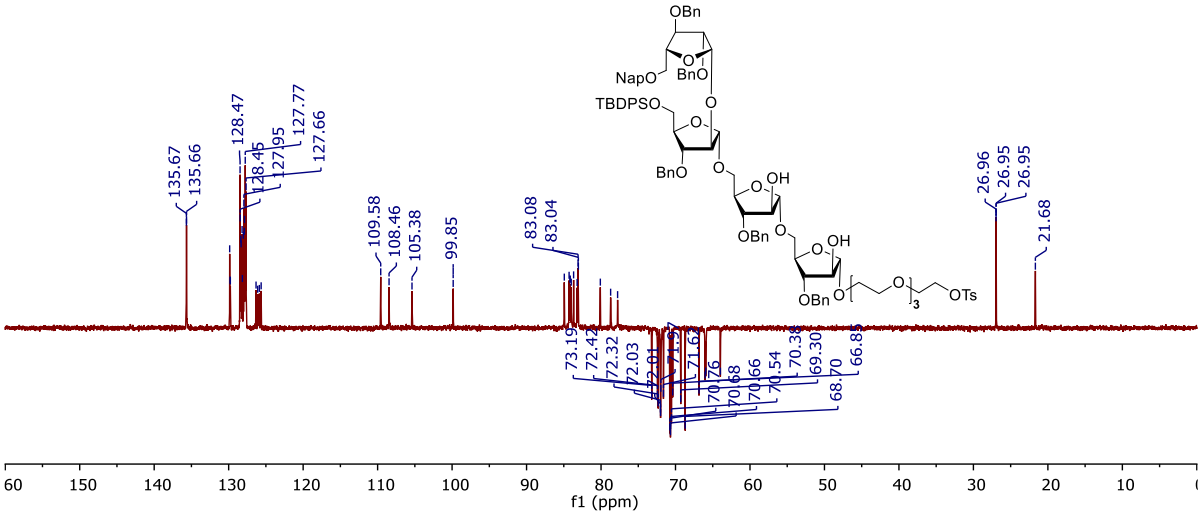
^{1}H NMR Spectrum (400.31 MHz, $CDCl_3$) of Compound **57**



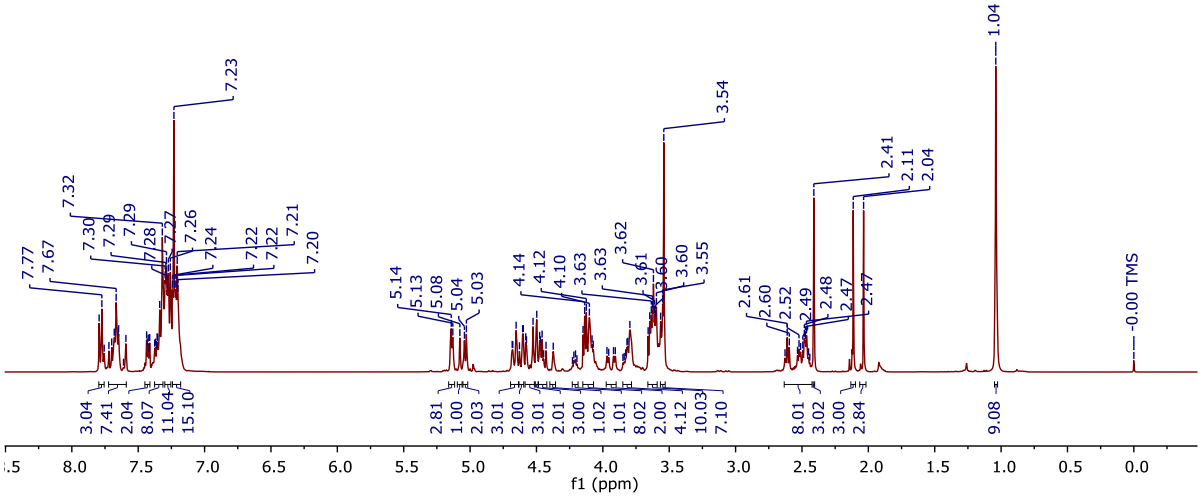
^{13}C NMR Spectrum (100.53 MHz, $CDCl_3$) of Compound **57**



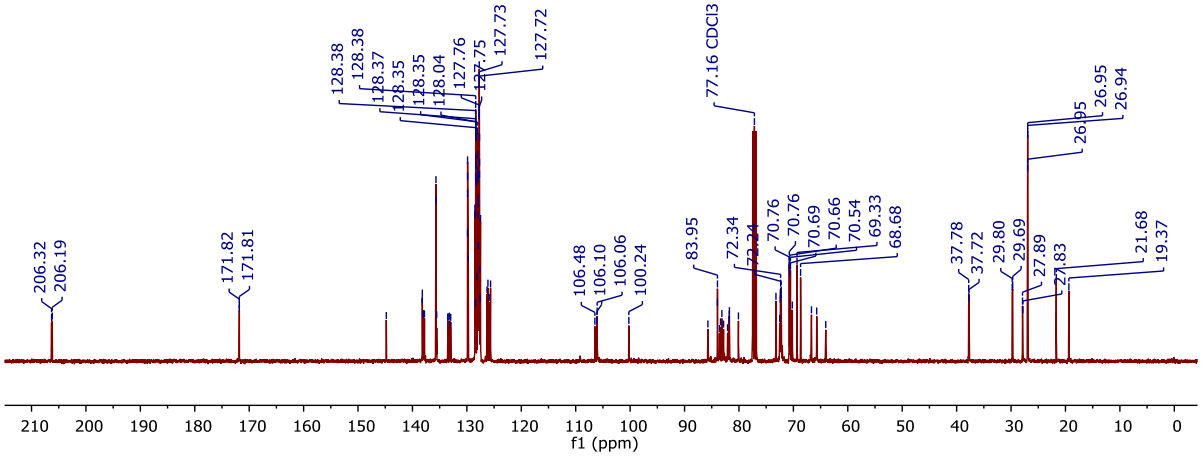
DEPT NMR Spectrum (100.53 MHz, $CDCl_3$) of Compound **57**



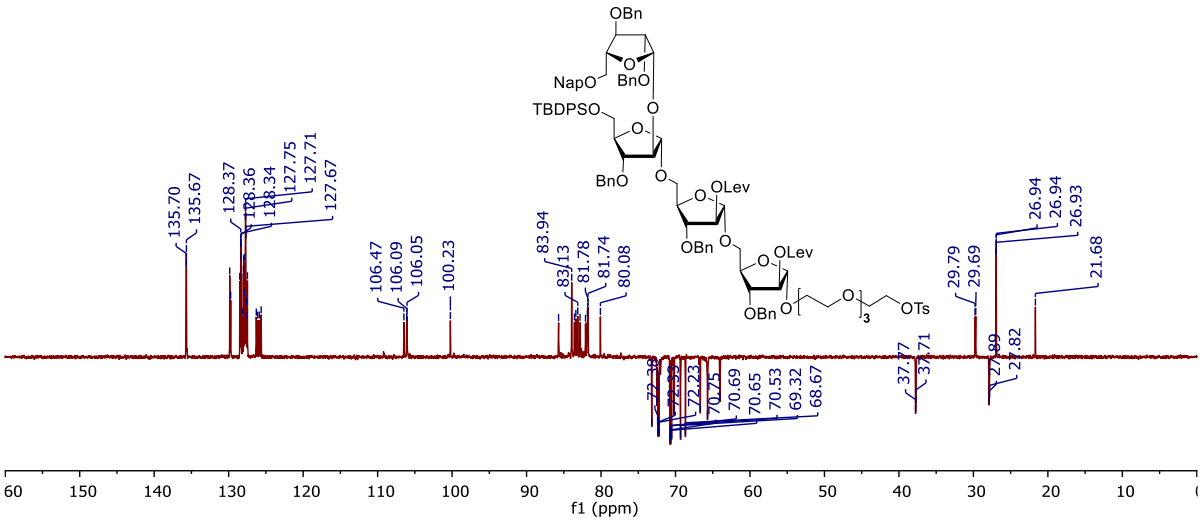
^{1}H NMR Spectrum (400.31 MHz, $CDCl_3$) of Compound **58**



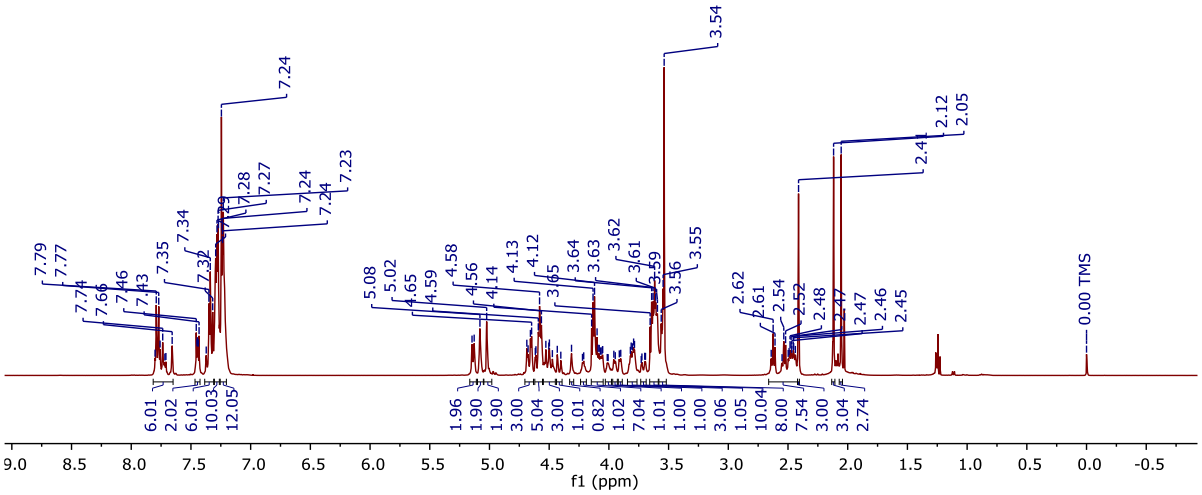
^{13}C NMR Spectrum (100.53 MHz, $CDCl_3$) of Compound **58**



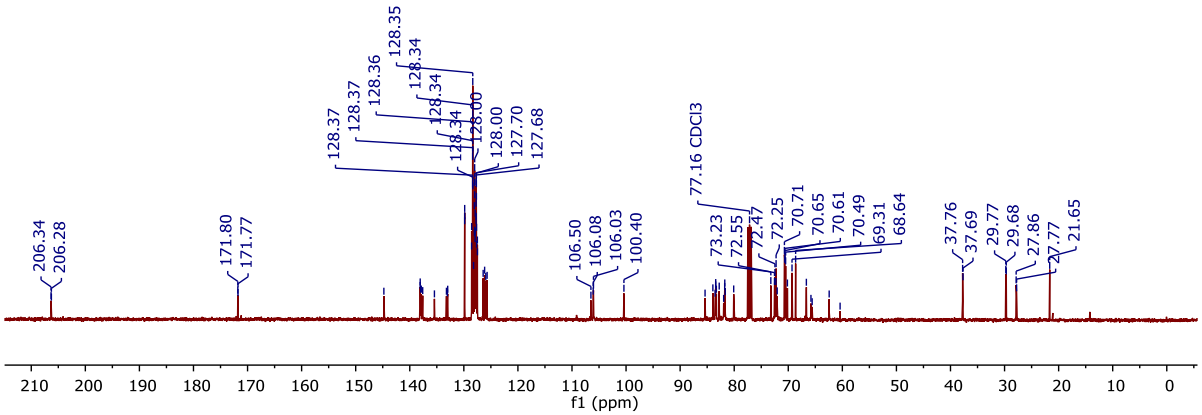
DEPT NMR Spectrum (100.53 MHz, $CDCl_3$) of Compound **58**



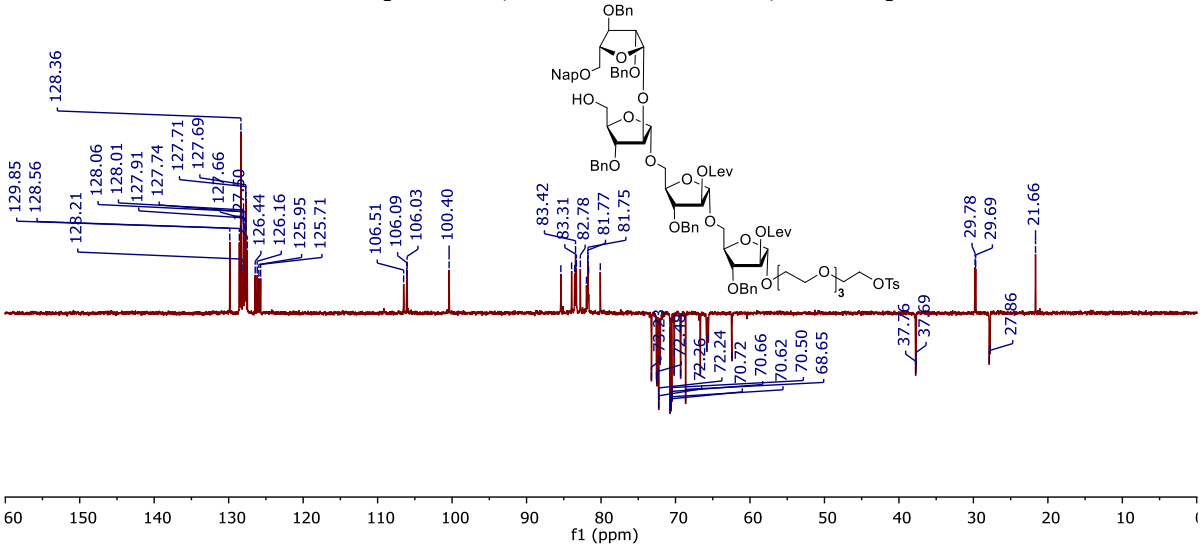
^{1}H NMR Spectrum (400.31 MHz, $CDCl_3$) of Compound **59**



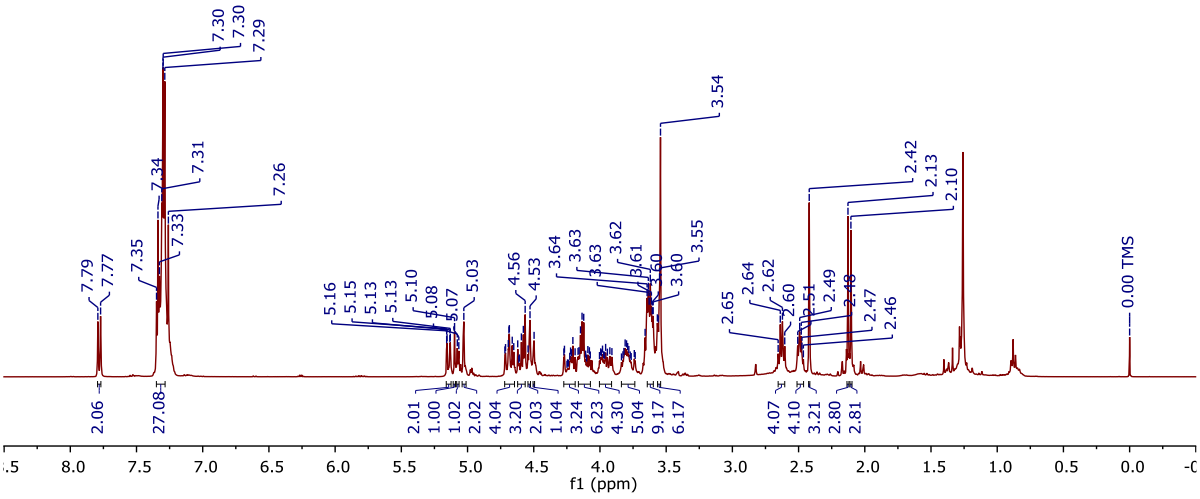
^{13}C NMR Spectrum (100.53 MHz, $CDCl_3$) of Compound **59**



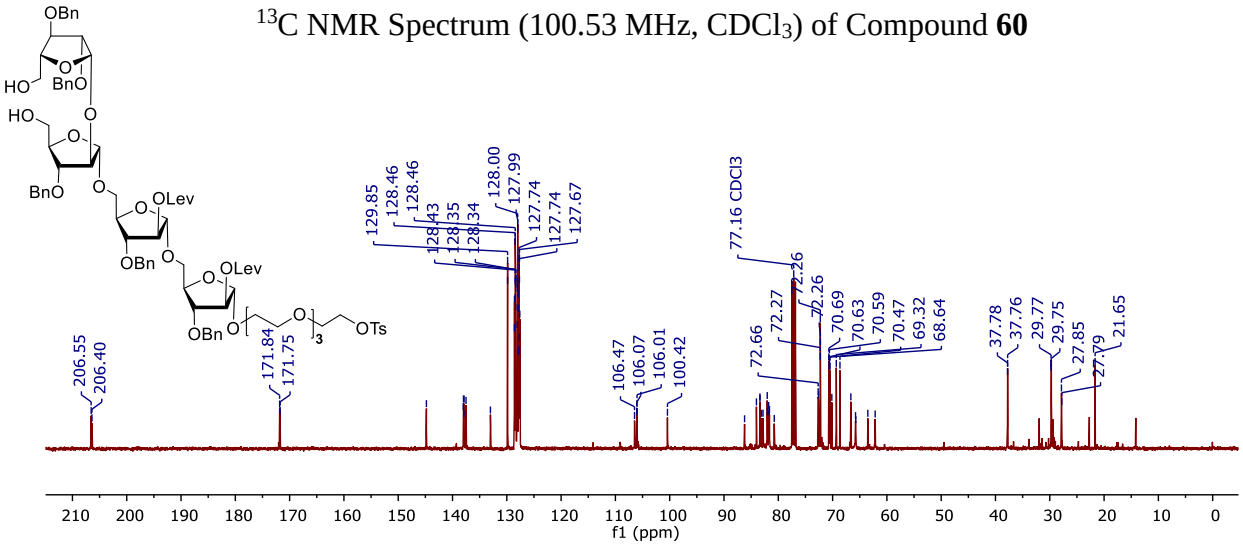
DEPT NMR Spectrum (100.53 MHz, $CDCl_3$) of Compound **59**



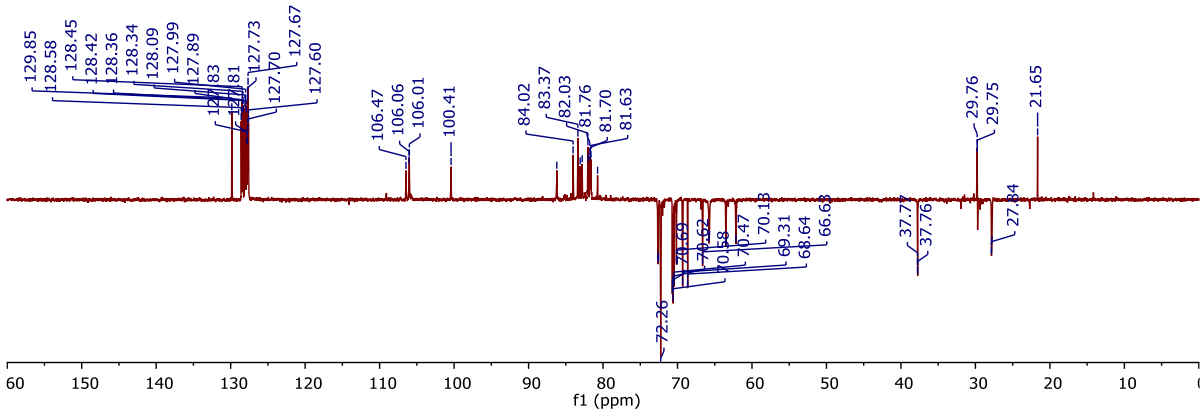
^{1}H NMR Spectrum (400.31 MHz, $CDCl_3$) of Compound **60**



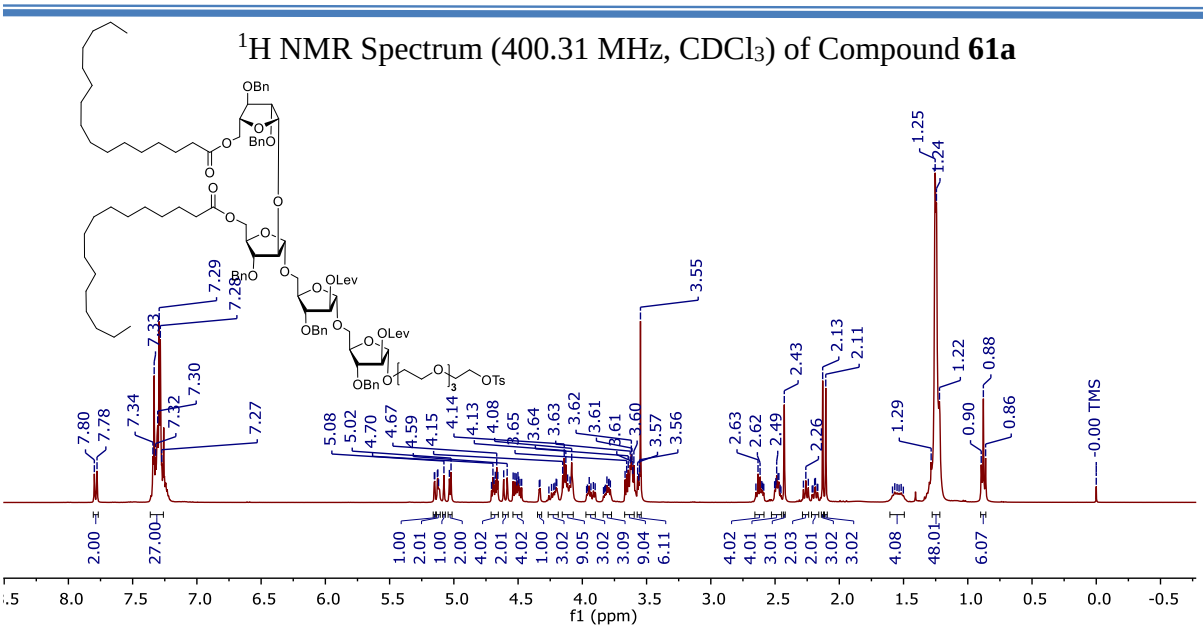
^{13}C NMR Spectrum (100.53 MHz, $CDCl_3$) of Compound **60**



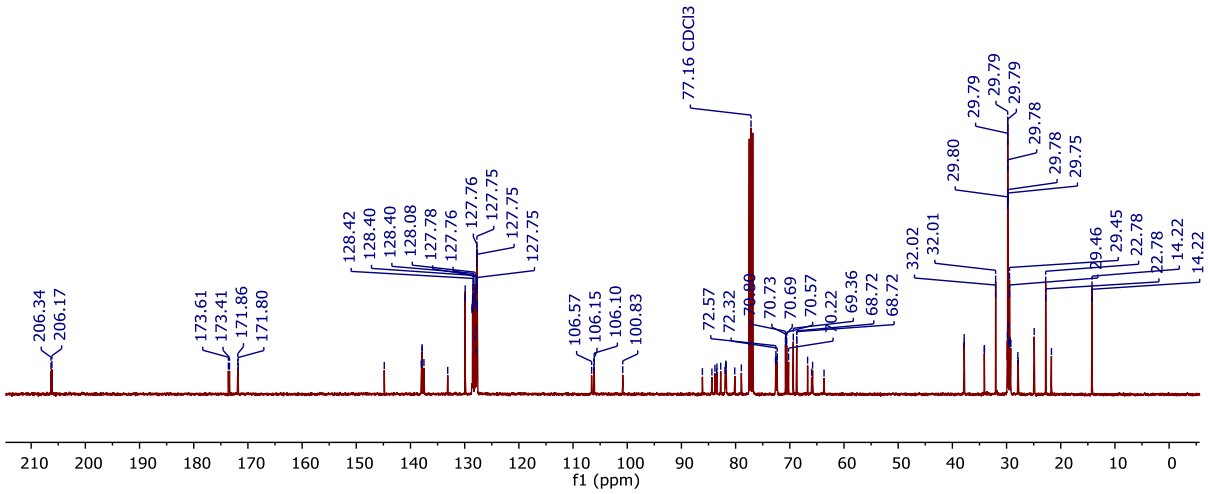
DEPT NMR Spectrum (100.53 MHz, $CDCl_3$) of Compound **60**



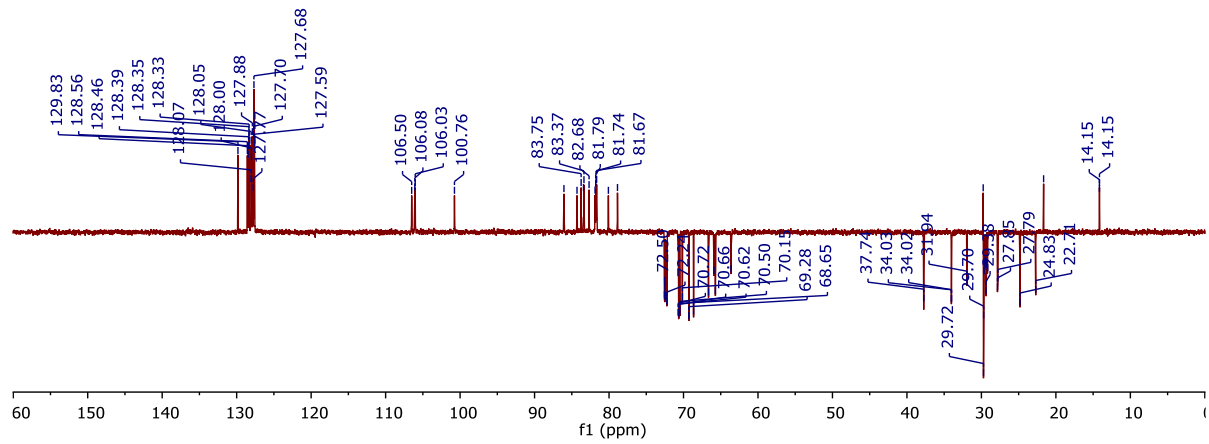
^{1}H NMR Spectrum (400.31 MHz, $CDCl_3$) of Compound **61a**



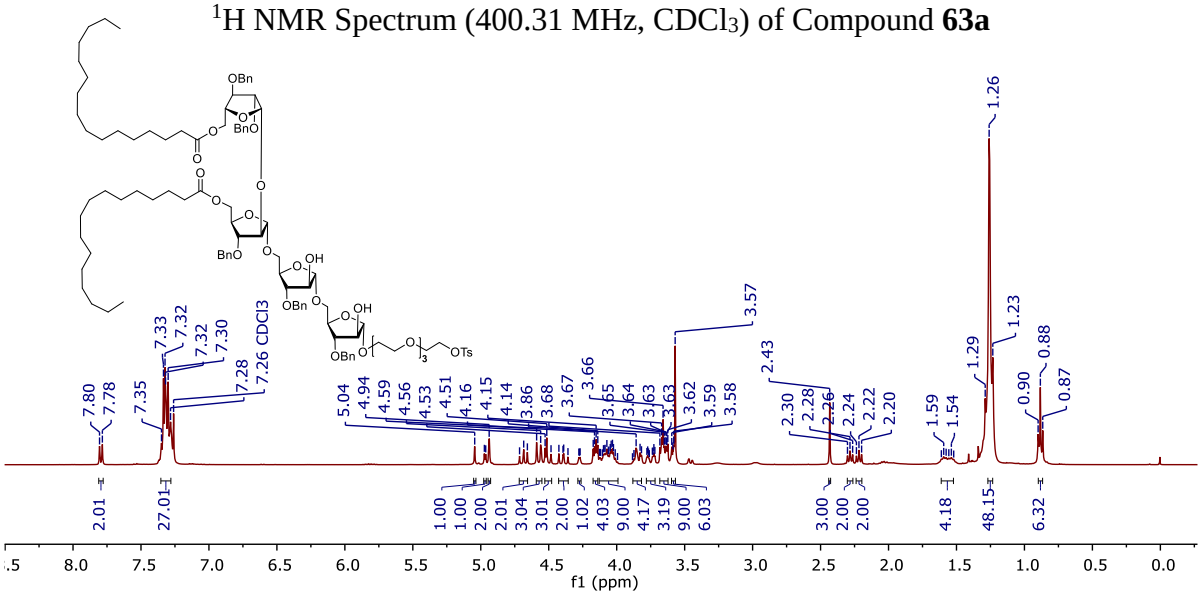
^{13}C NMR Spectrum (100.53 MHz, $CDCl_3$) of Compound **61a**



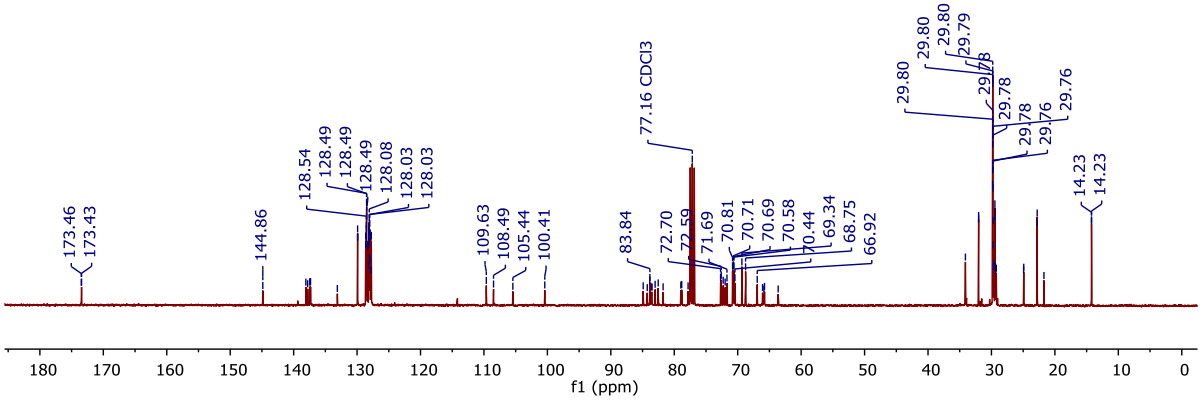
DEPT NMR Spectrum (100.53 MHz, $CDCl_3$) of Compound **61a**



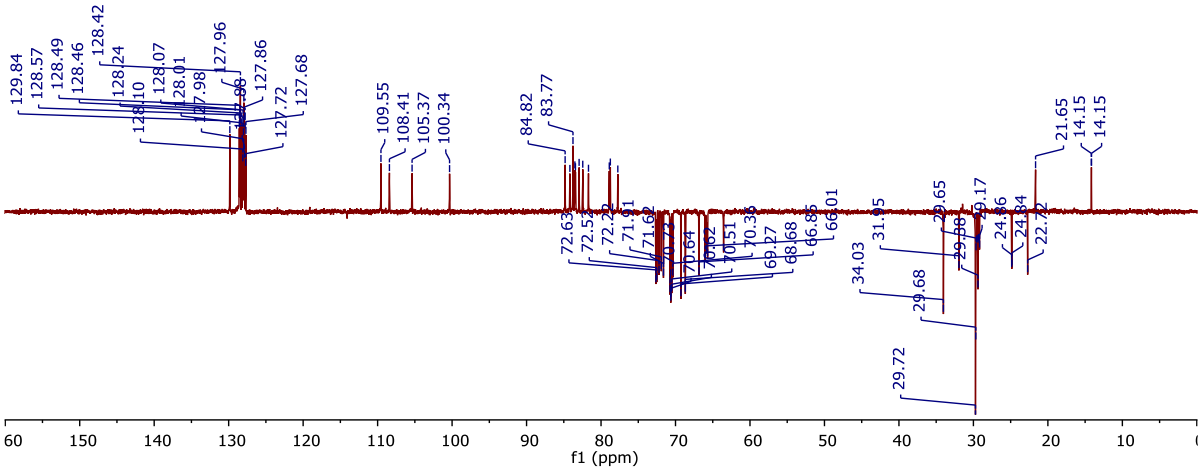
^{1}H NMR Spectrum (400.31 MHz, $CDCl_3$) of Compound **63a**



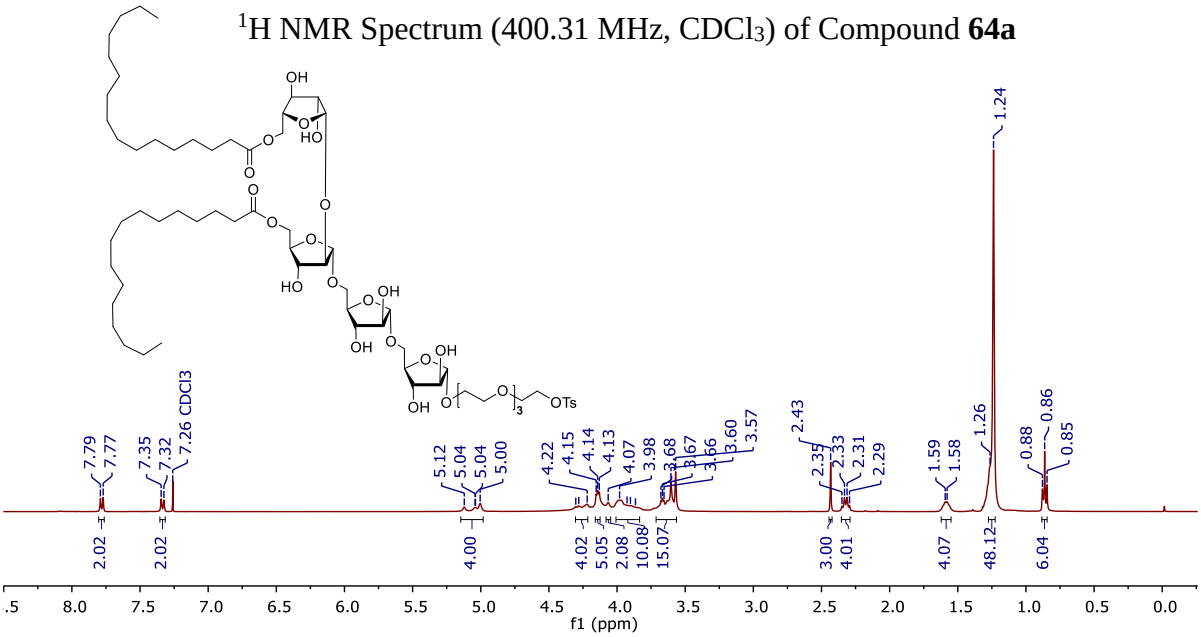
^{13}C NMR Spectrum (100.53 MHz, $CDCl_3$) of Compound **63a**



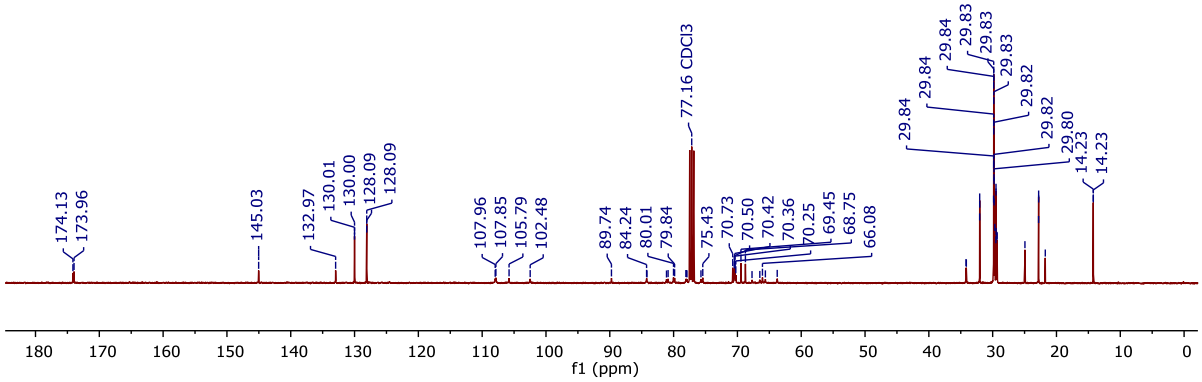
DEPT NMR Spectrum (100.53 MHz, $CDCl_3$) of Compound **63a**



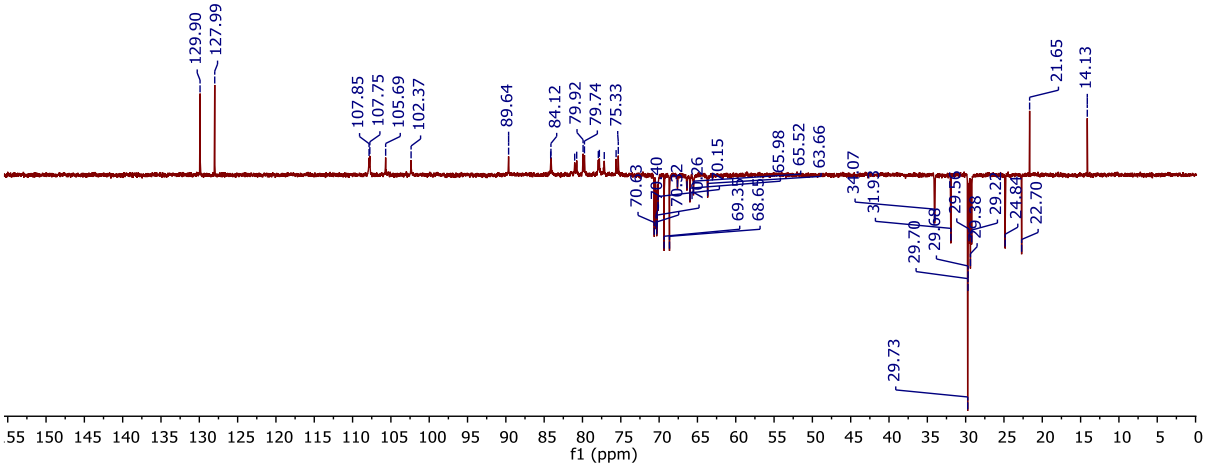
^{1}H NMR Spectrum (400.31 MHz, $CDCl_3$) of Compound **64a**



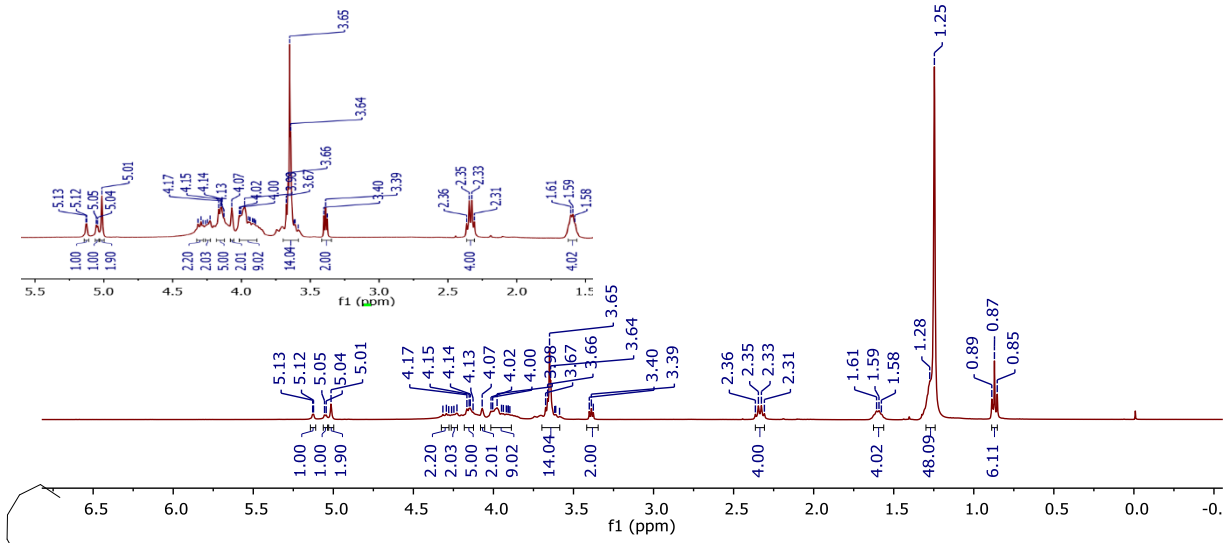
^{13}C NMR Spectrum (100.53 MHz, $CDCl_3$) of Compound **64a**



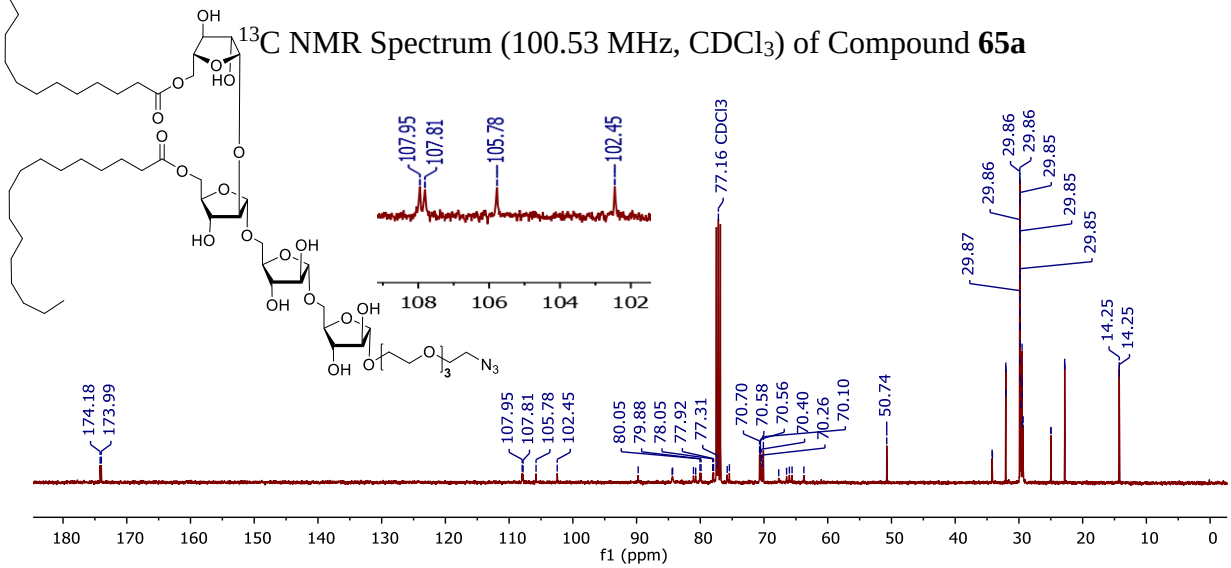
DEPT NMR Spectrum (100.53 MHz, $CDCl_3$) of Compound **64a**



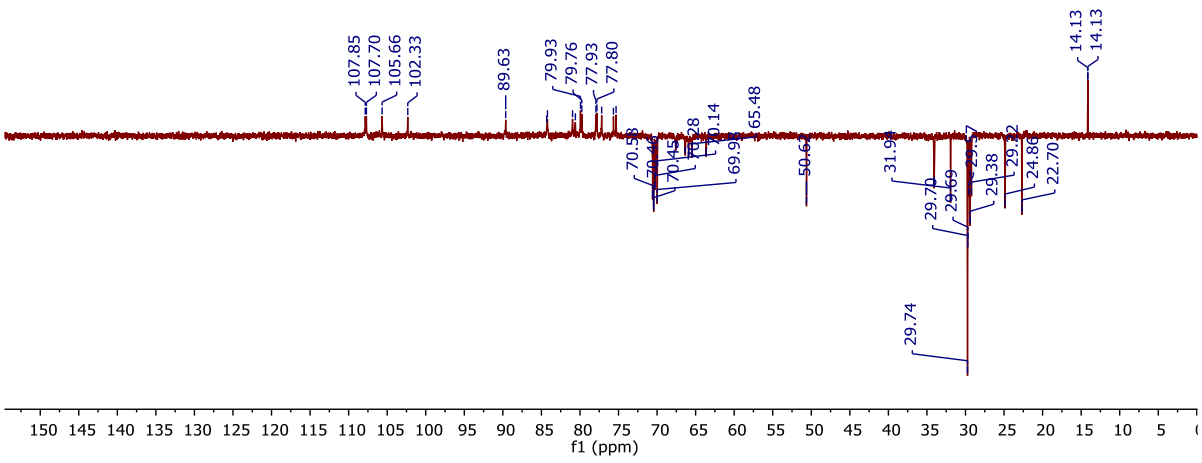
^{1}H NMR Spectrum (400.31 MHz, $CDCl_3$) of Compound **65a**



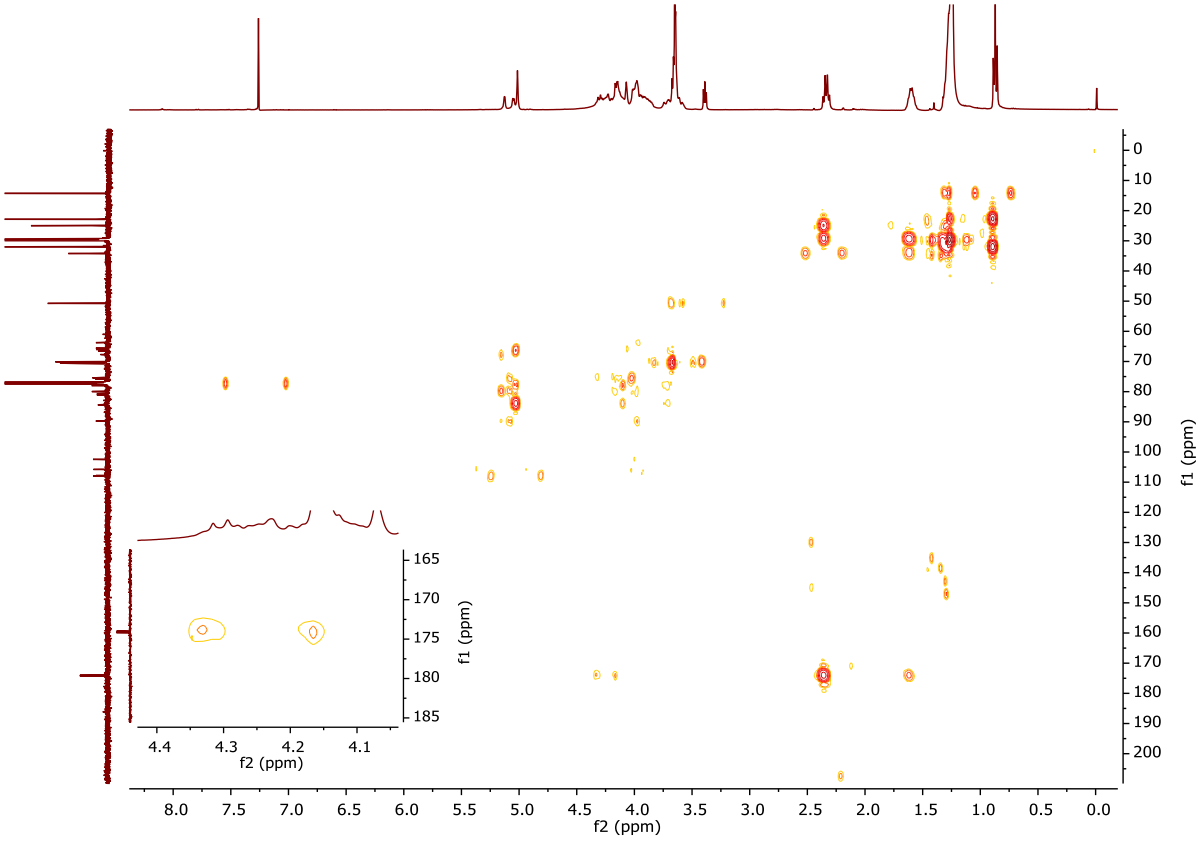
^{13}C NMR Spectrum (100.53 MHz, $CDCl_3$) of Compound **65a**



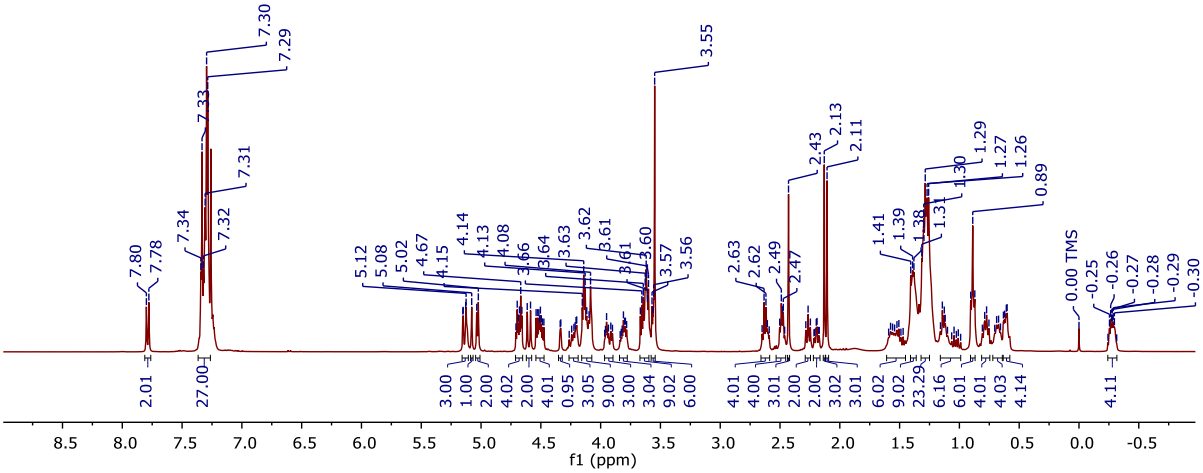
DEPT NMR Spectrum (100.53 MHz, $CDCl_3$) of Compound **65a**



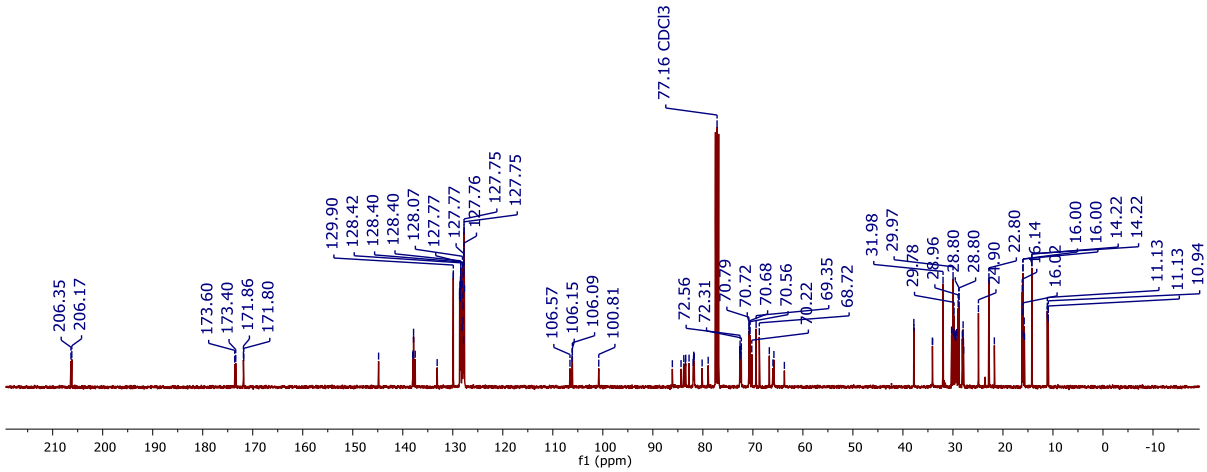
HMBC NMR Spectrum of Compound **65a**



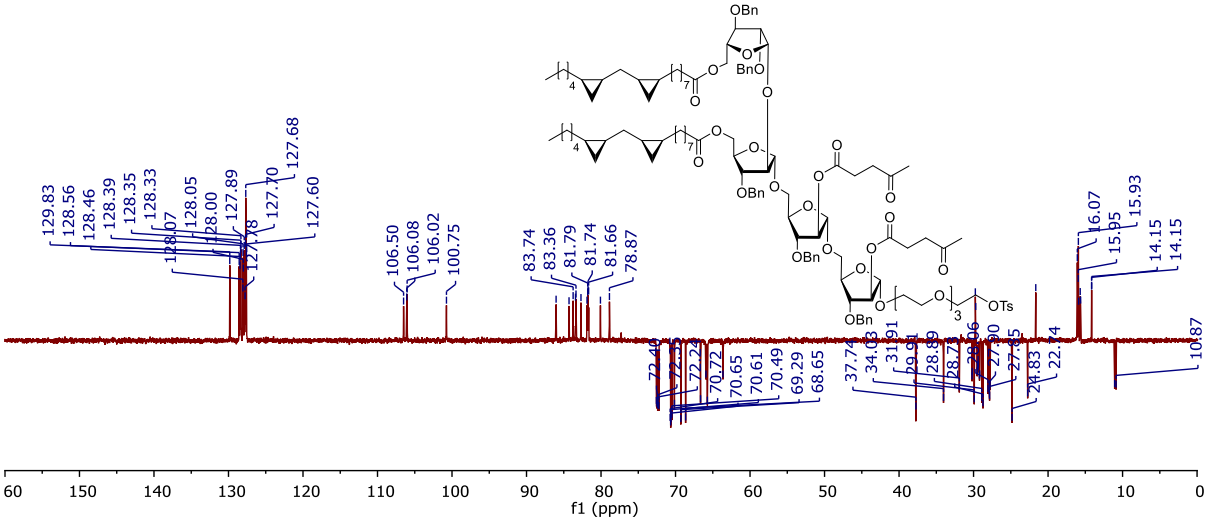
^{1}H NMR Spectrum (400.31 MHz, $CDCl_3$) of Compound **61b**



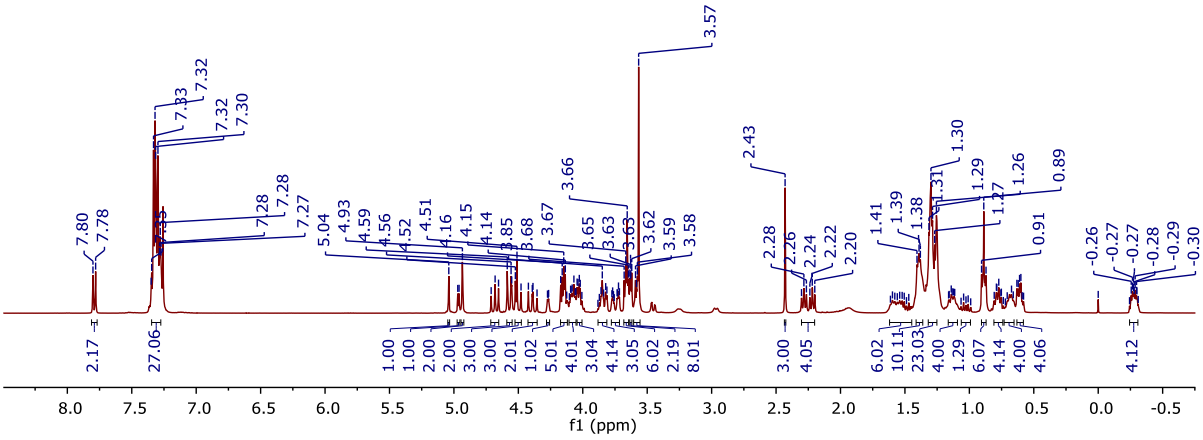
^{13}C NMR Spectrum (100.53 MHz, $CDCl_3$) of Compound **61b**



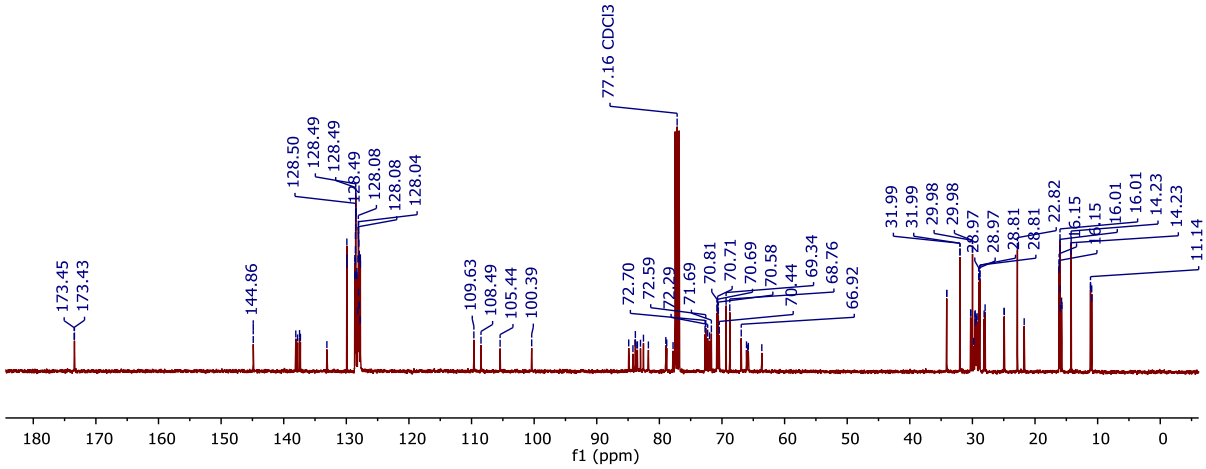
DEPT NMR Spectrum (100.53 MHz, $CDCl_3$) of Compound **61b**



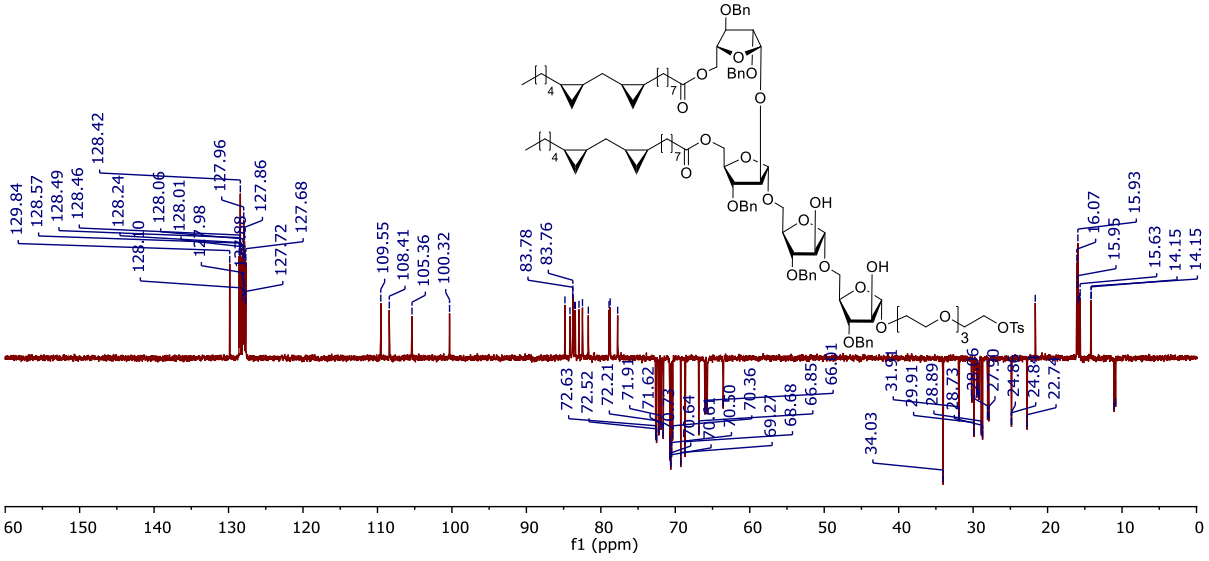
^{1}H NMR Spectrum (400.31 MHz, $CDCl_3$) of Compound **63b**



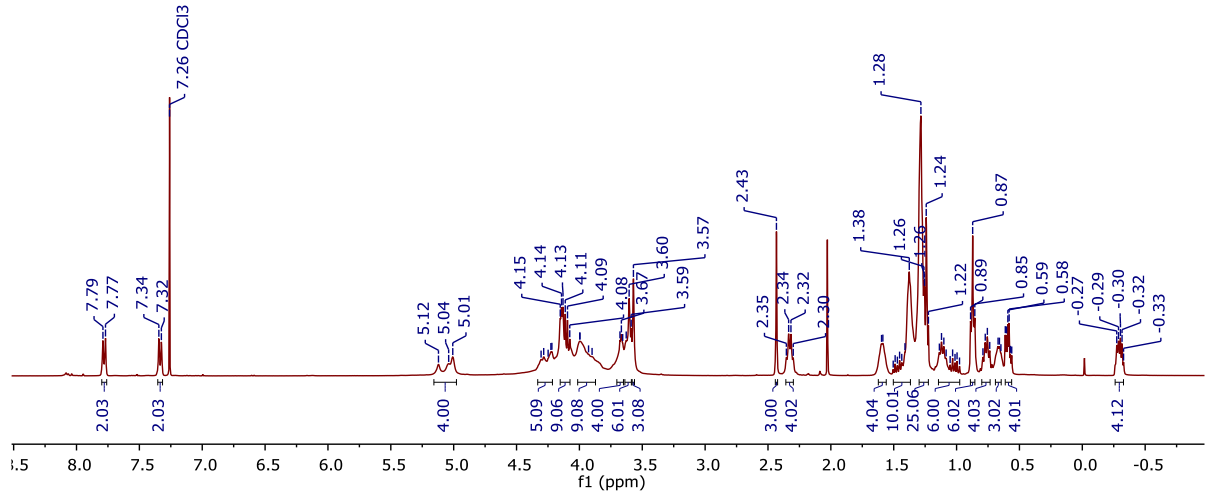
^{13}C NMR Spectrum (100.53 MHz, $CDCl_3$) of Compound **63b**



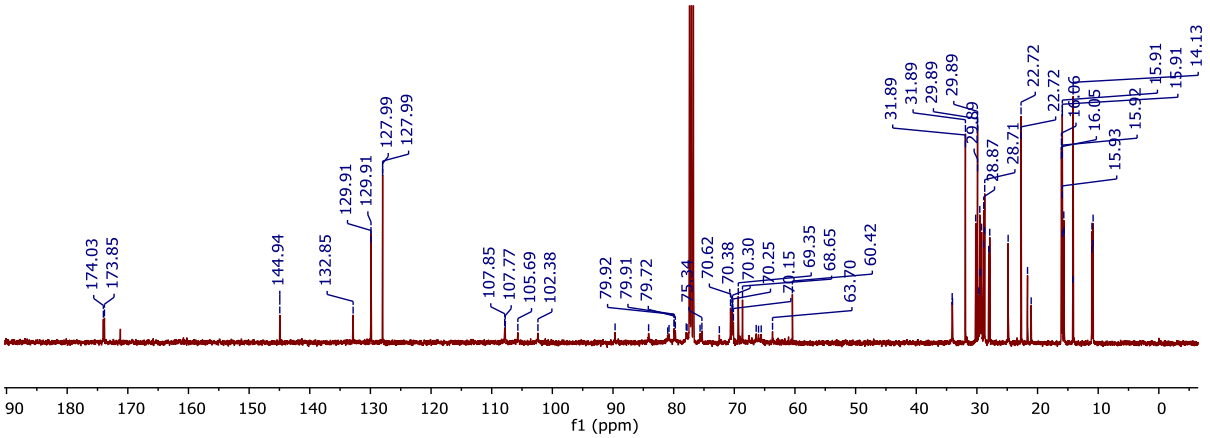
DEPT NMR Spectrum (100.53 MHz, $CDCl_3$) of Compound **63b**



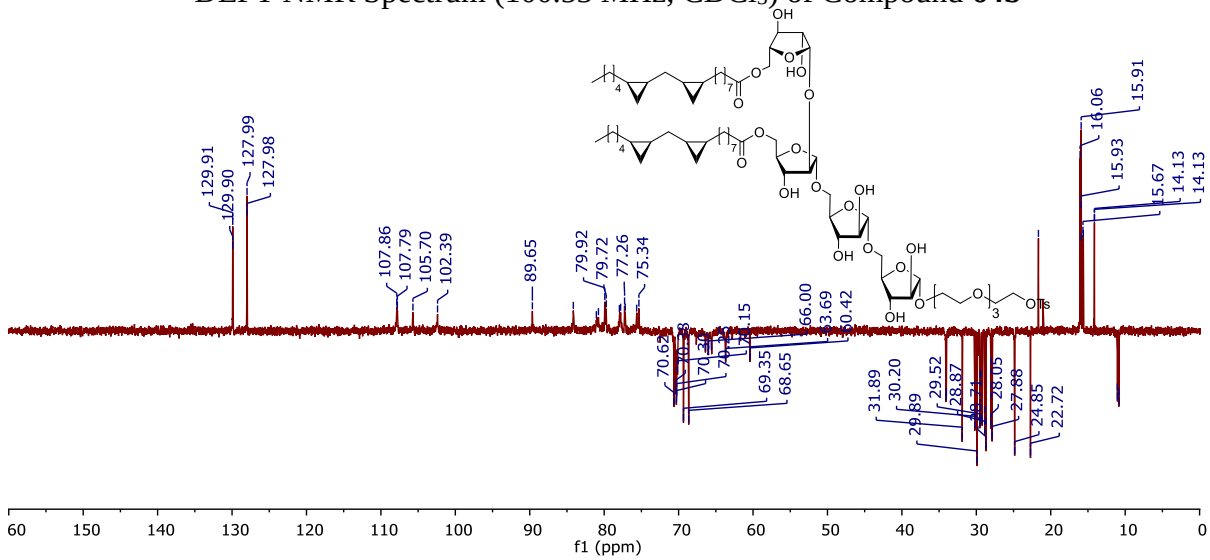
^{1}H NMR Spectrum (400.31 MHz, $CDCl_3$) of Compound **64b**



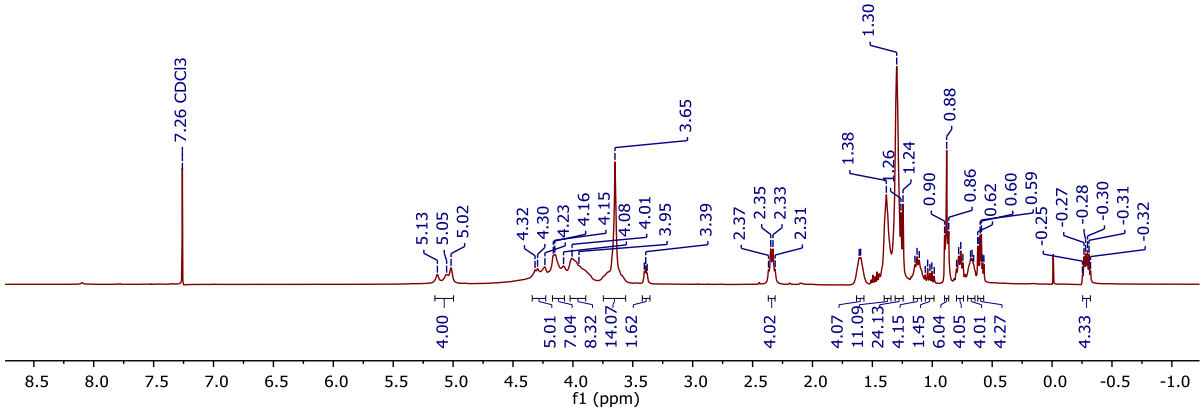
^{13}C NMR Spectrum (100.53 MHz, $CDCl_3$) of Compound **64b**



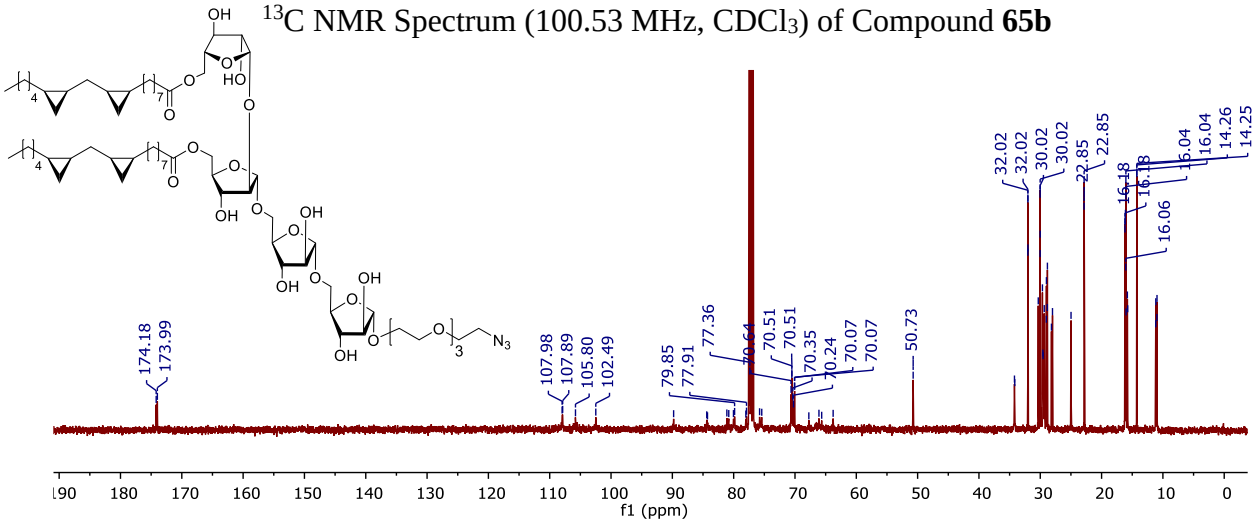
DEPT NMR Spectrum (100.53 MHz, $CDCl_3$) of Compound **64b**



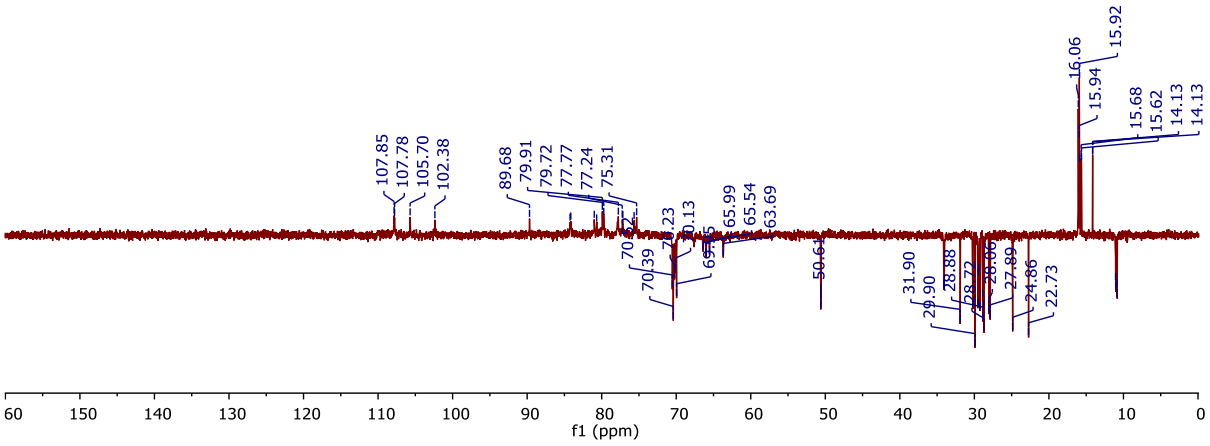
^{1}H NMR Spectrum (400.31 MHz, $CDCl_3$) of Compound **65b**



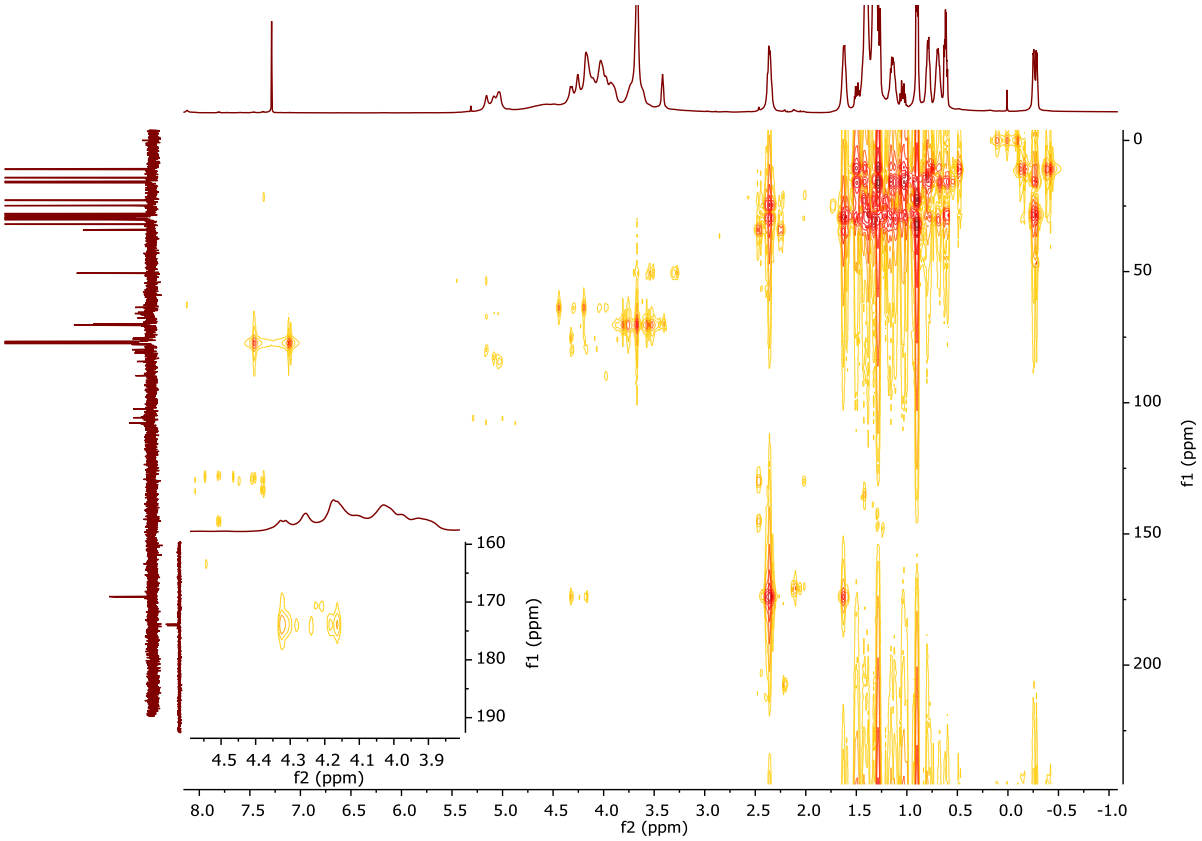
^{13}C NMR Spectrum (100.53 MHz, $CDCl_3$) of Compound **65b**



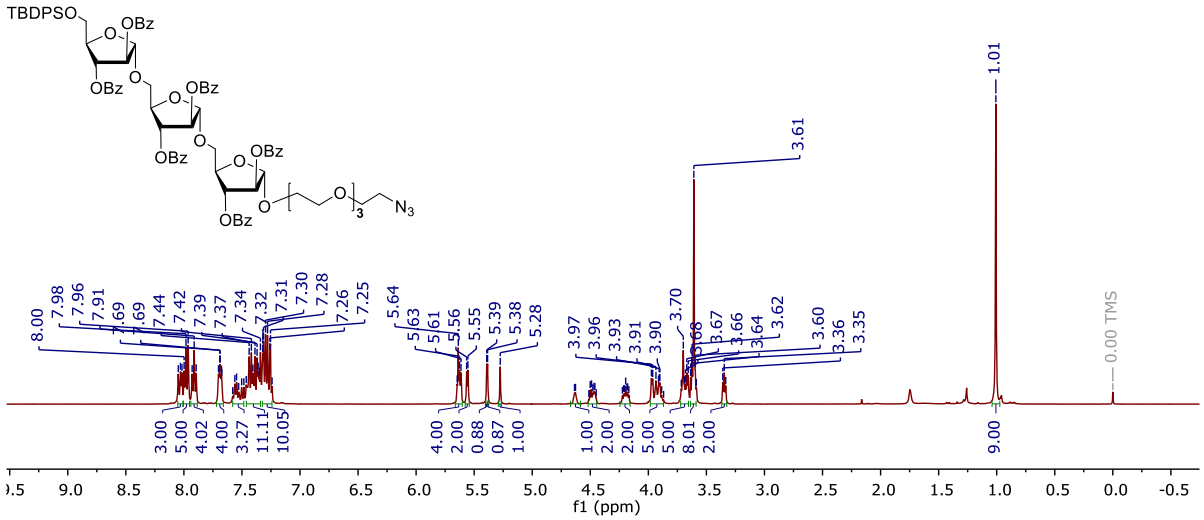
DEPT NMR Spectrum (100.53 MHz, $CDCl_3$) of Compound **65b**



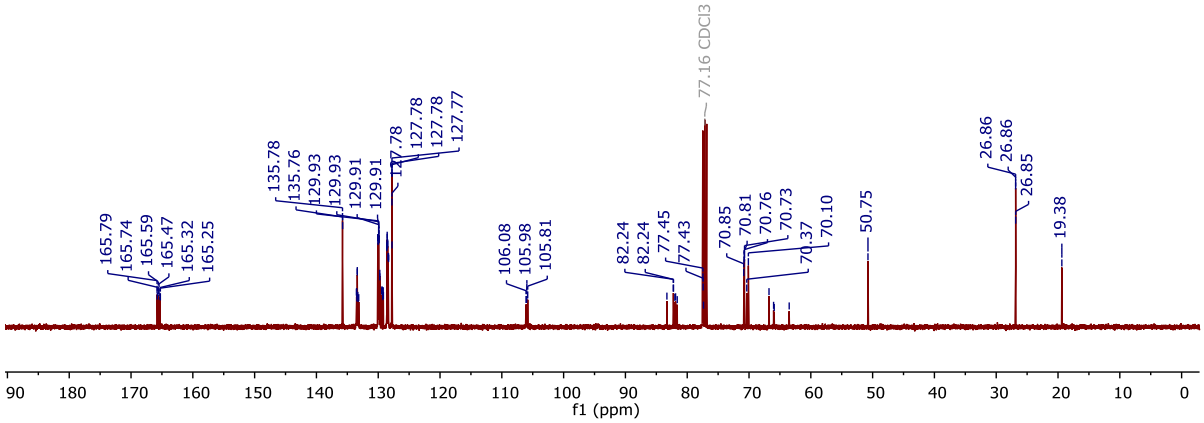
HMBC NMR Spectrum of Compound **65b**



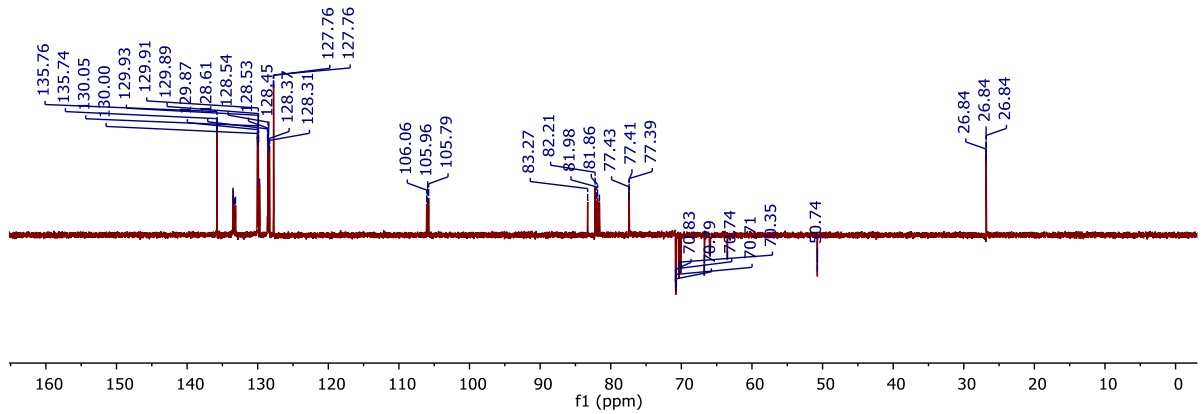
^{1}H NMR Spectrum (400.31 MHz, $CDCl_3$) of Compound **66**



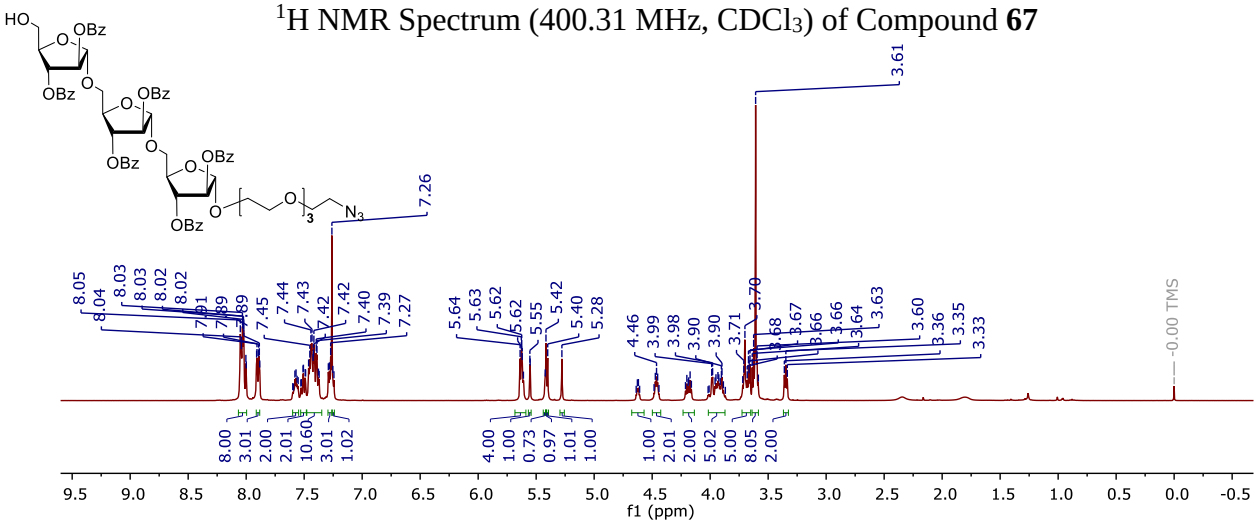
^{13}C NMR Spectrum (100.53 MHz, $CDCl_3$) of Compound **66**



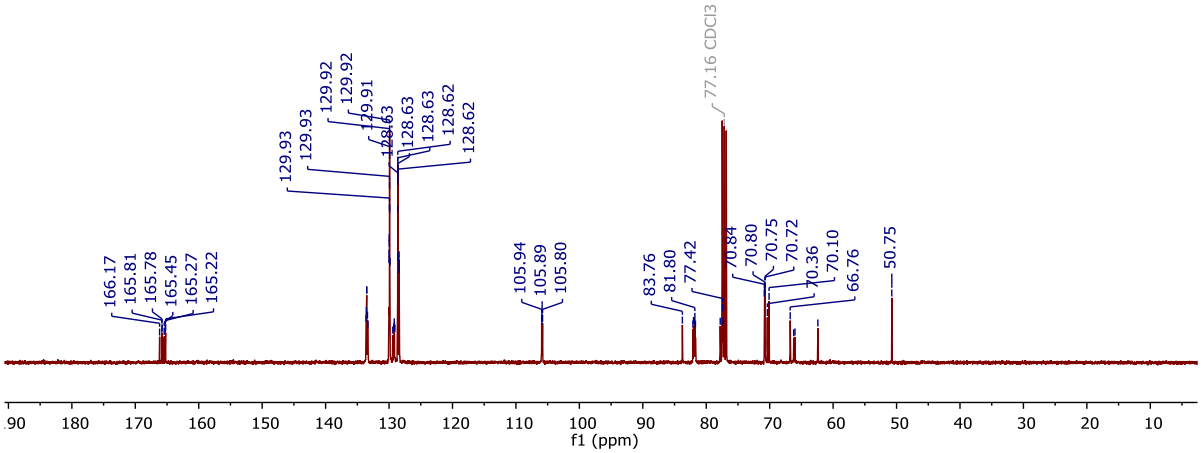
DEPT NMR Spectrum (100.53 MHz, $CDCl_3$) of Compound **66**



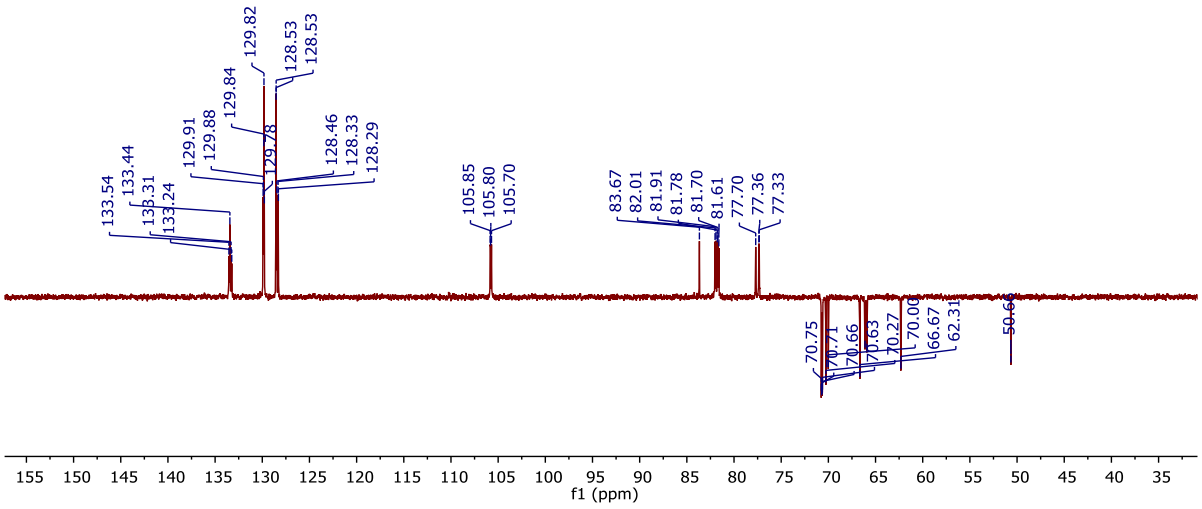
^{1}H NMR Spectrum (400.31 MHz, $CDCl_3$) of Compound **67**



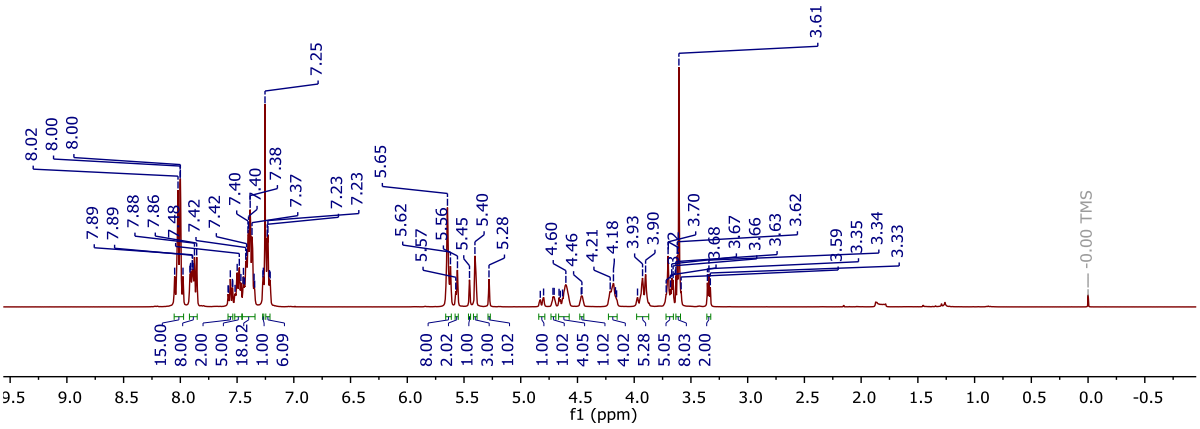
^{13}C NMR Spectrum (100.53 MHz, $CDCl_3$) of Compound **67**



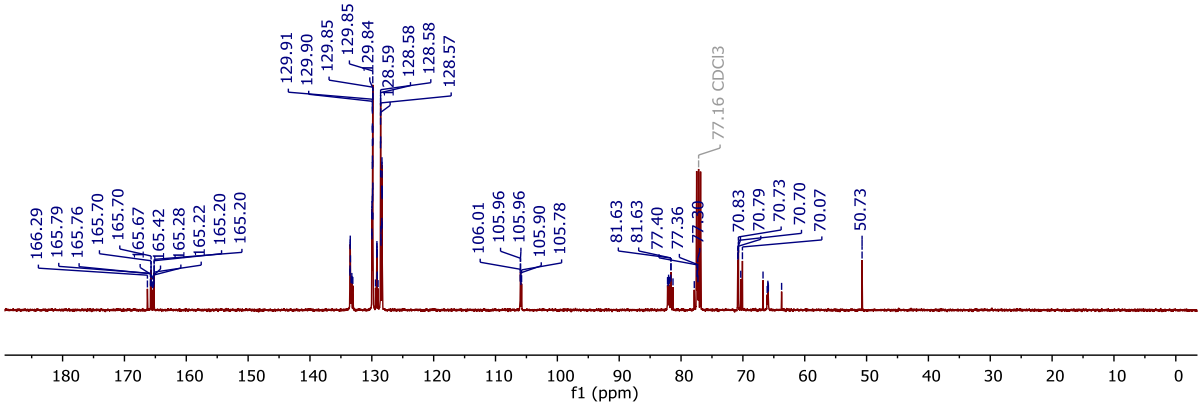
DEPT NMR Spectrum (100.53 MHz, $CDCl_3$) of Compound **67**



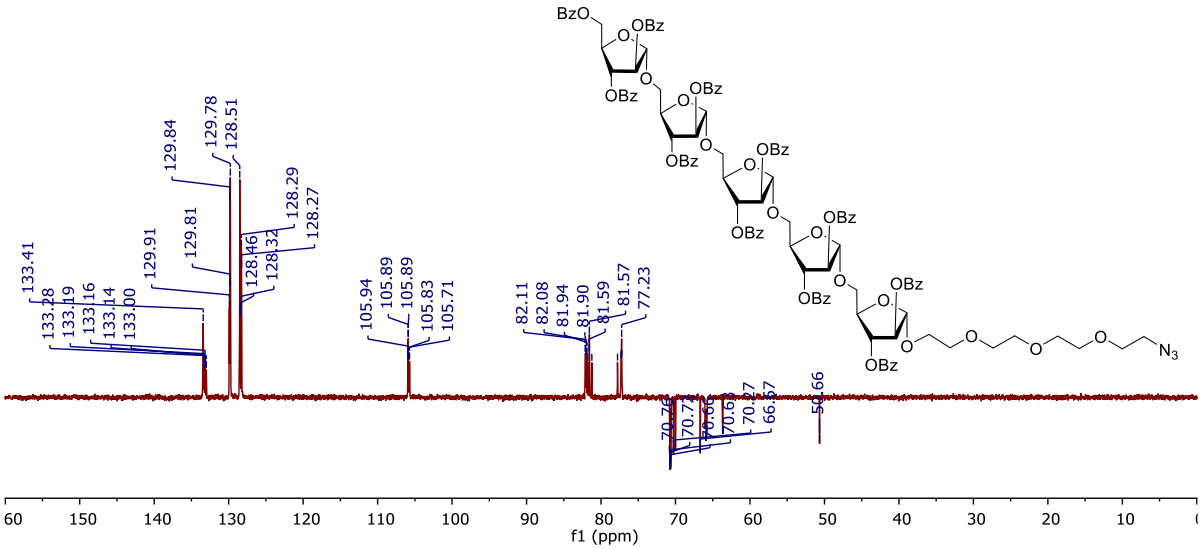
^{1}H NMR Spectrum (400.31 MHz, $CDCl_3$) of Compound **68**



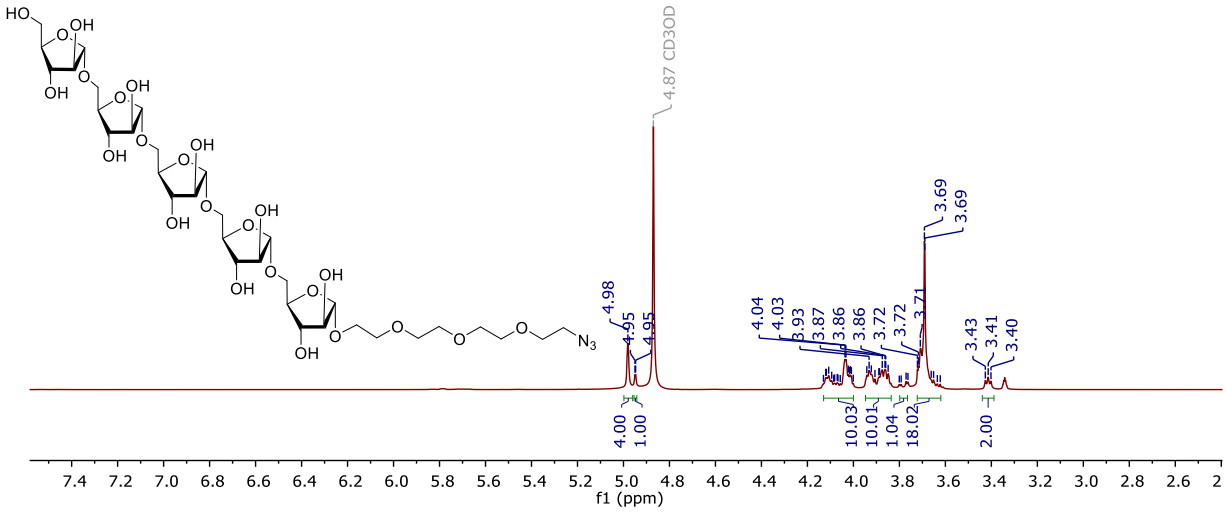
^{13}C NMR Spectrum (100.53 MHz, $CDCl_3$) of Compound **68**



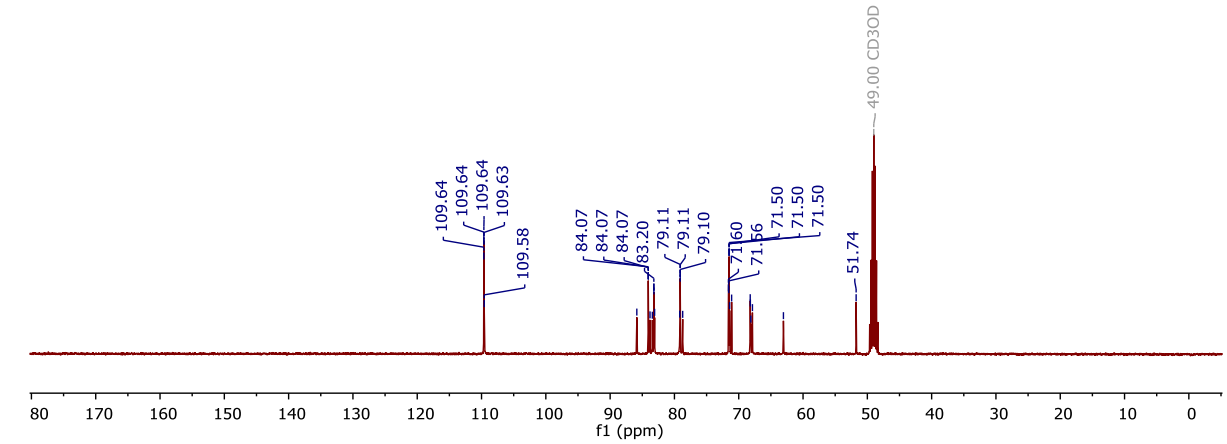
DEPT NMR Spectrum (100.53 MHz, $CDCl_3$) of Compound **68**



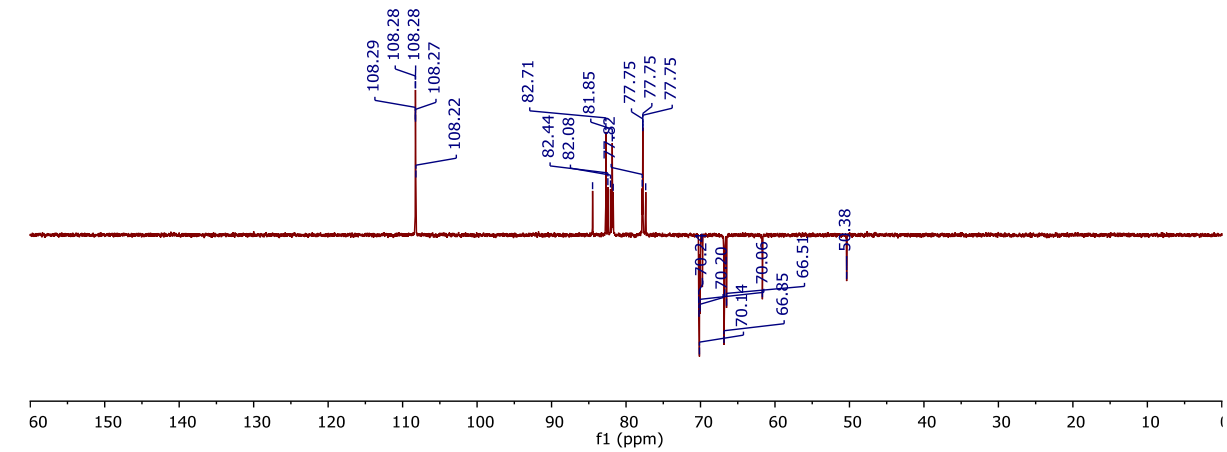
^{1}H NMR Spectrum (400.31 MHz, CD_3OD) of Compound **69**



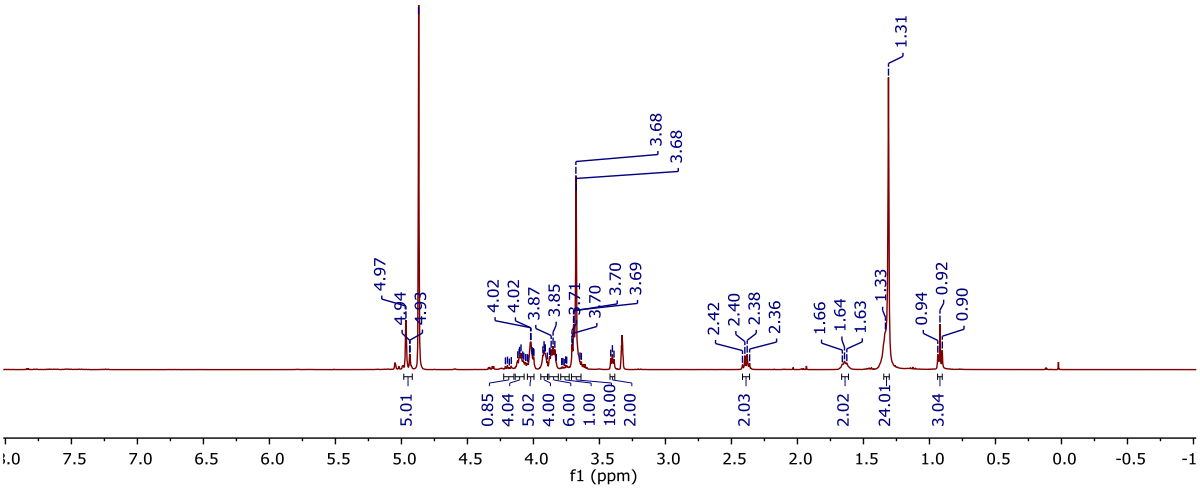
^{13}C NMR Spectrum (100.53 MHz, CD_3OD) of Compound **69**



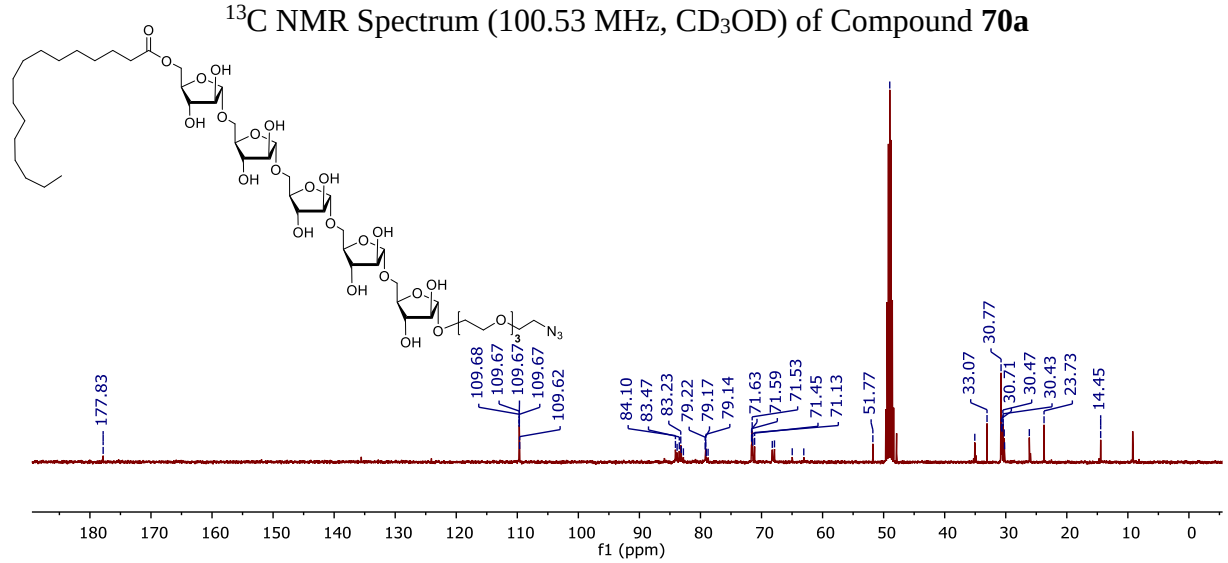
DEPT NMR Spectrum (100.53 MHz, CD_3OD) of Compound **69**



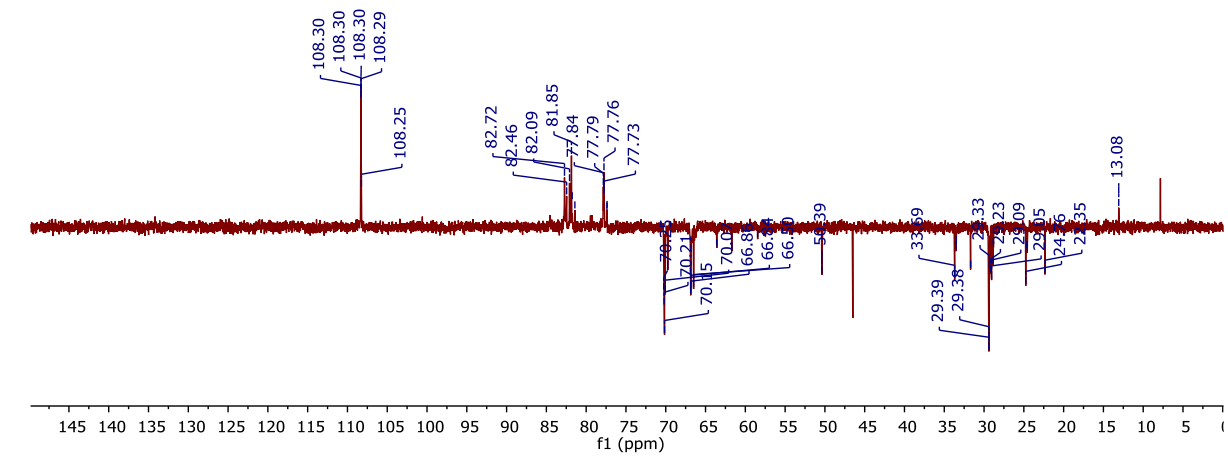
^{1}H NMR Spectrum (400.31 MHz, CD_3OD) of Compound **70a**



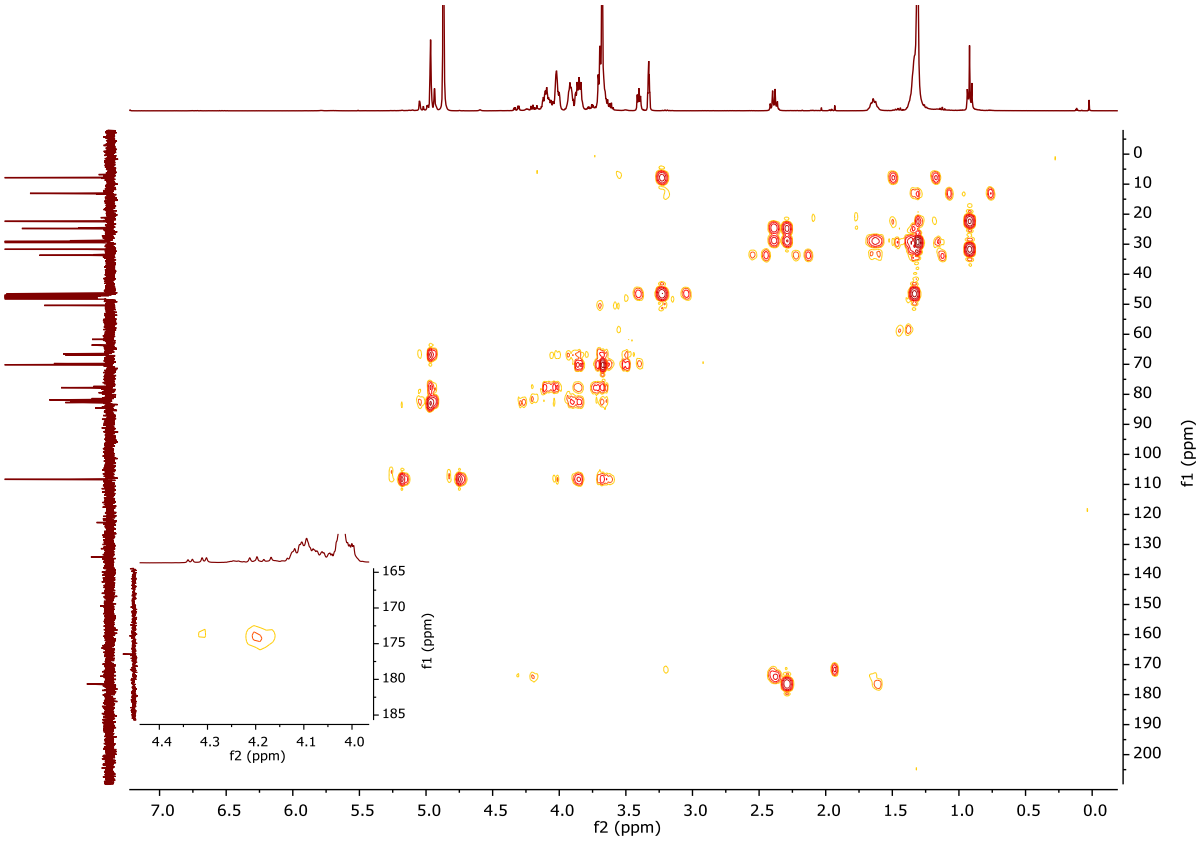
^{13}C NMR Spectrum (100.53 MHz, CD_3OD) of Compound **70a**



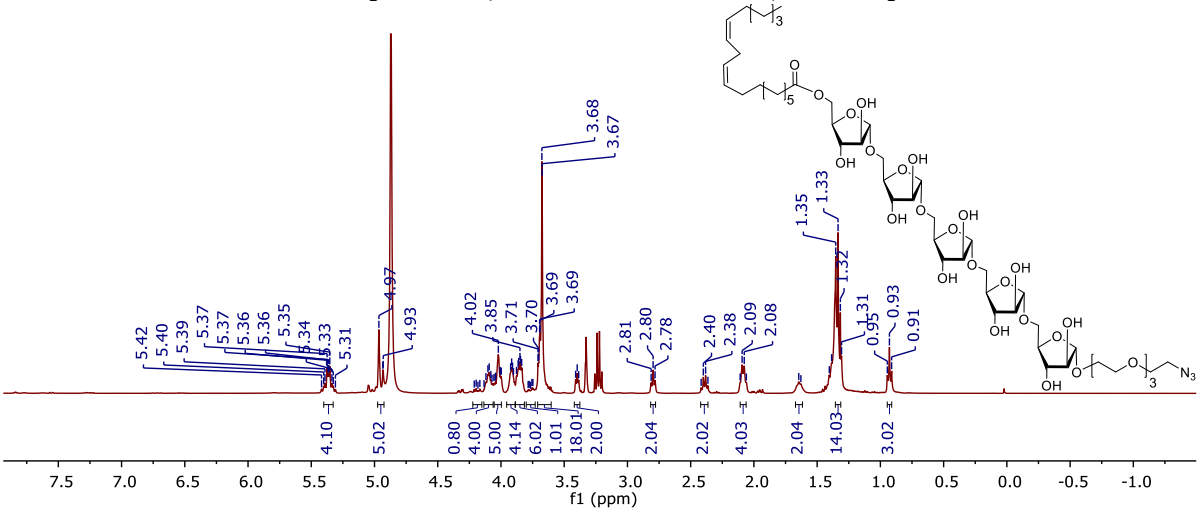
DEPT NMR Spectrum (100.53 MHz, CD_3OD) of Compound **70a**



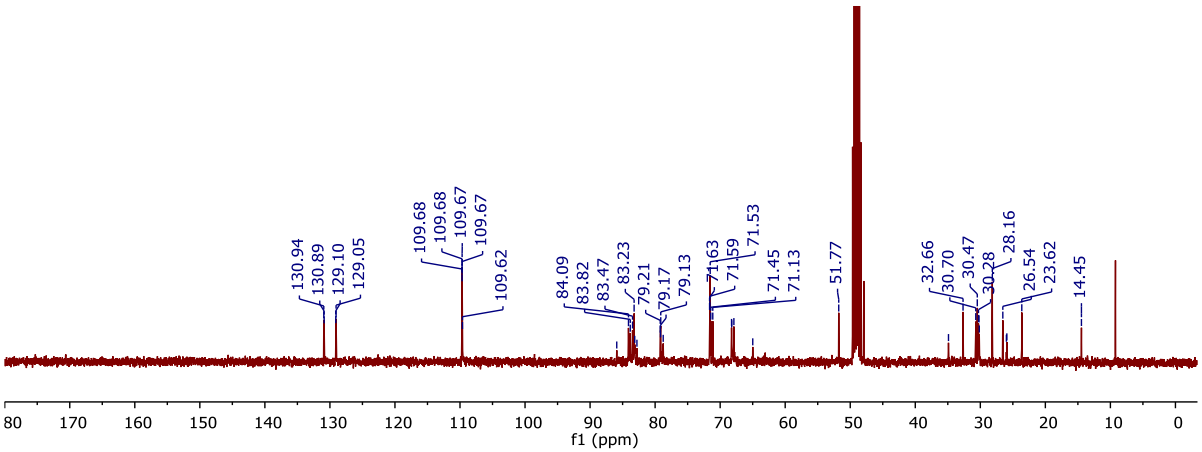
HMBC NMR Spectrum of Compound **70a**



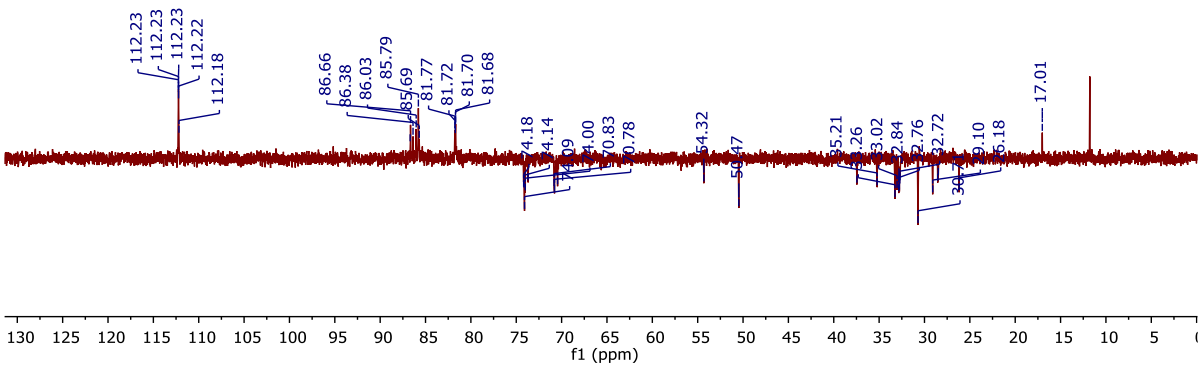
^{1}H NMR Spectrum (400.31 MHz, CD_3OD) of Compound **70b**



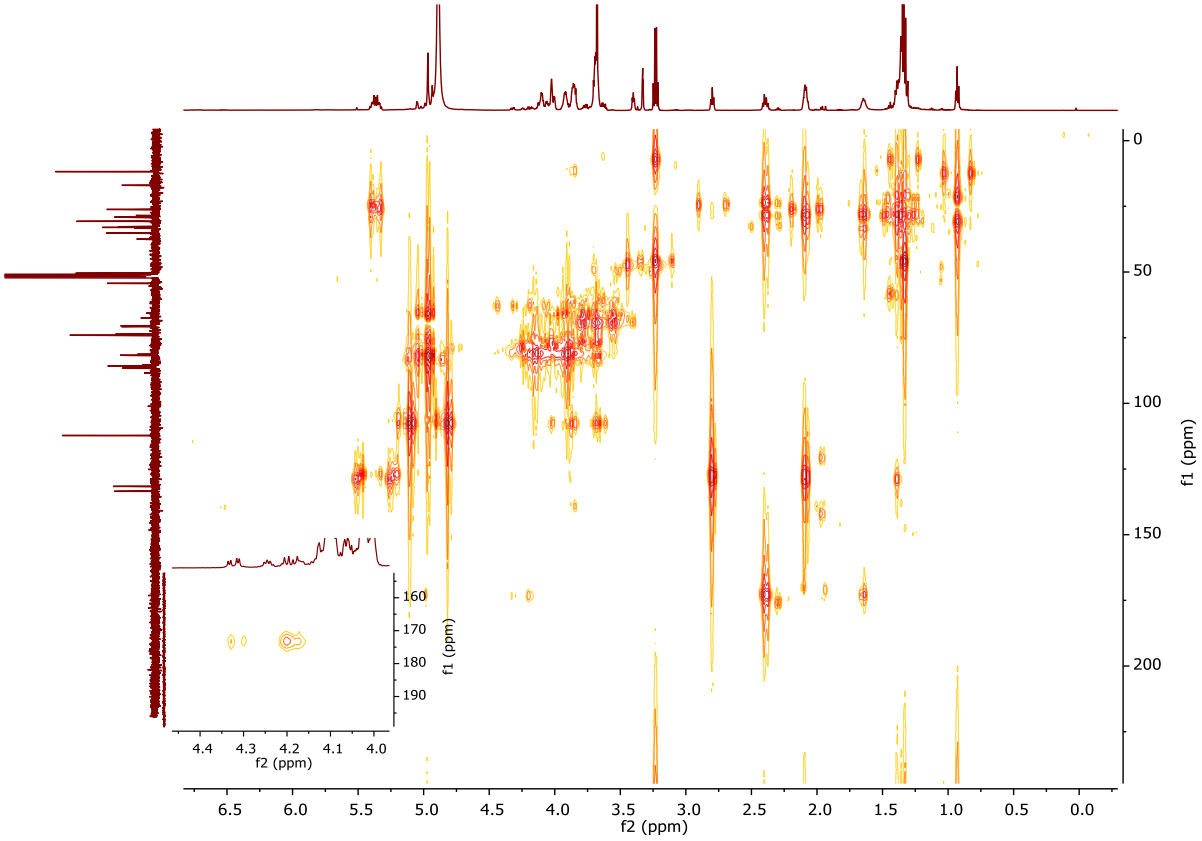
^{13}C NMR Spectrum (100.53 MHz, CD_3OD) of Compound **70b**



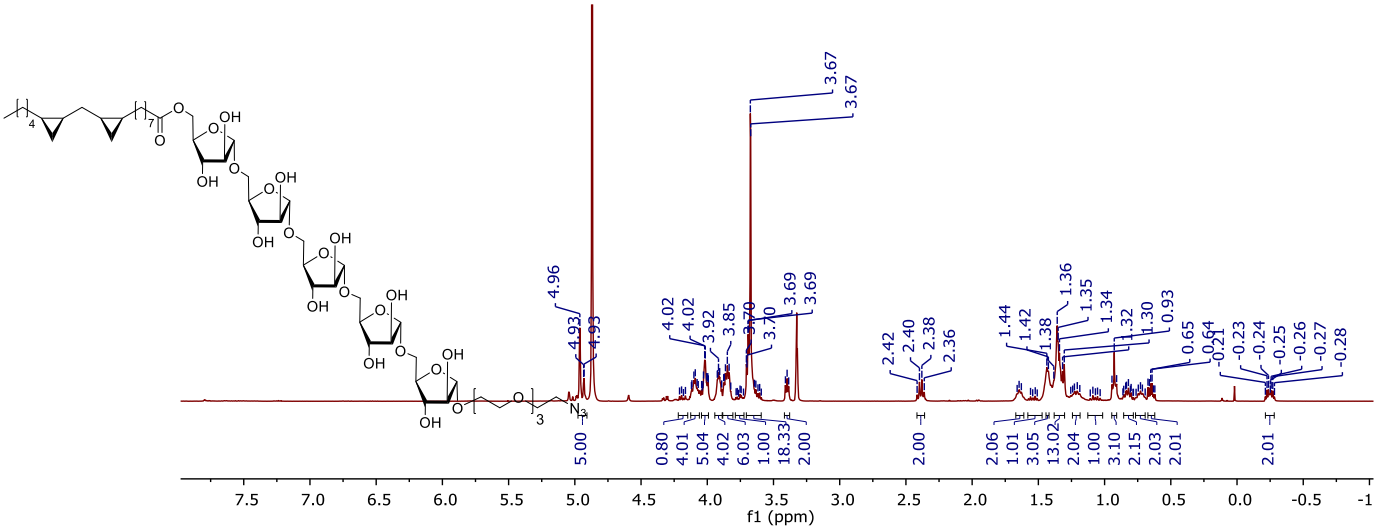
DEPT NMR Spectrum (100.53 MHz, CD_3OD) of Compound **70b**



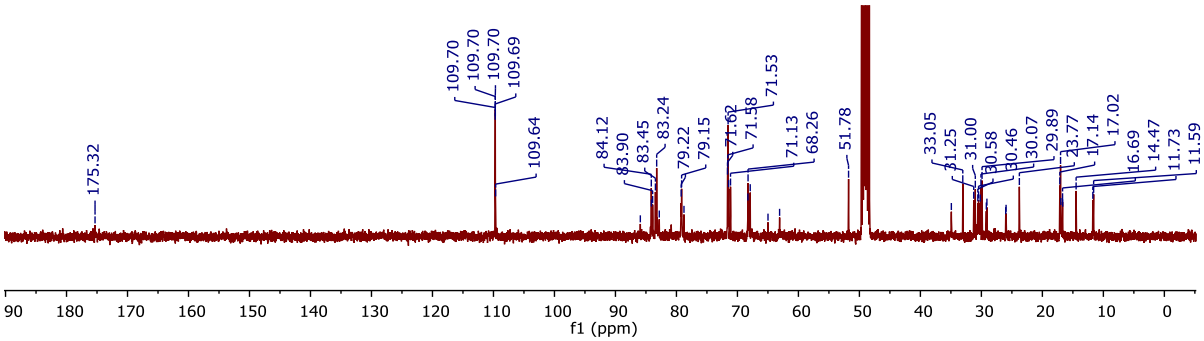
HMBC NMR Spectrum of Compound **70b**



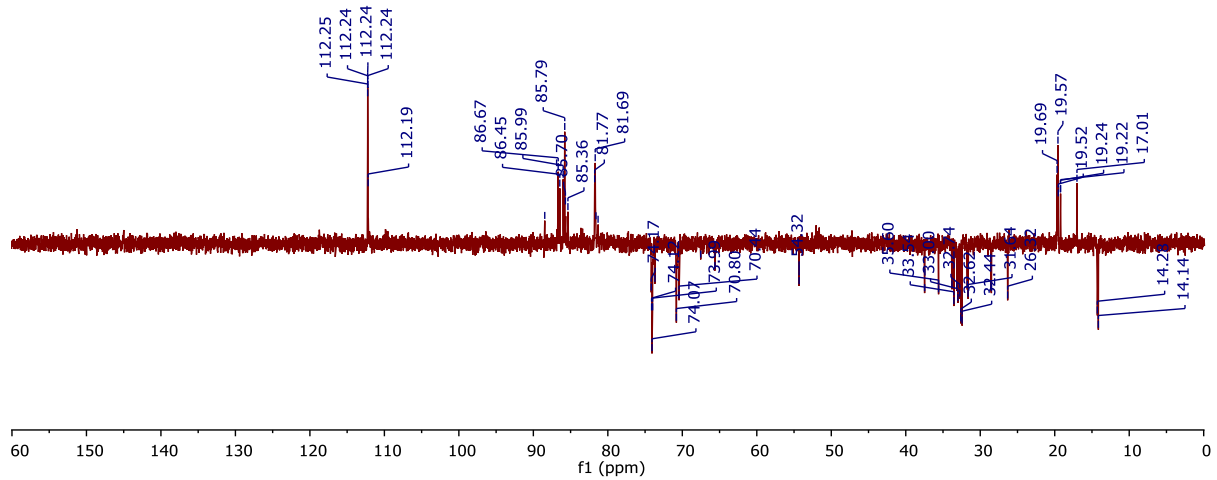
^{1}H NMR Spectrum (400.31 MHz, CD_3OD) of Compound **70c**



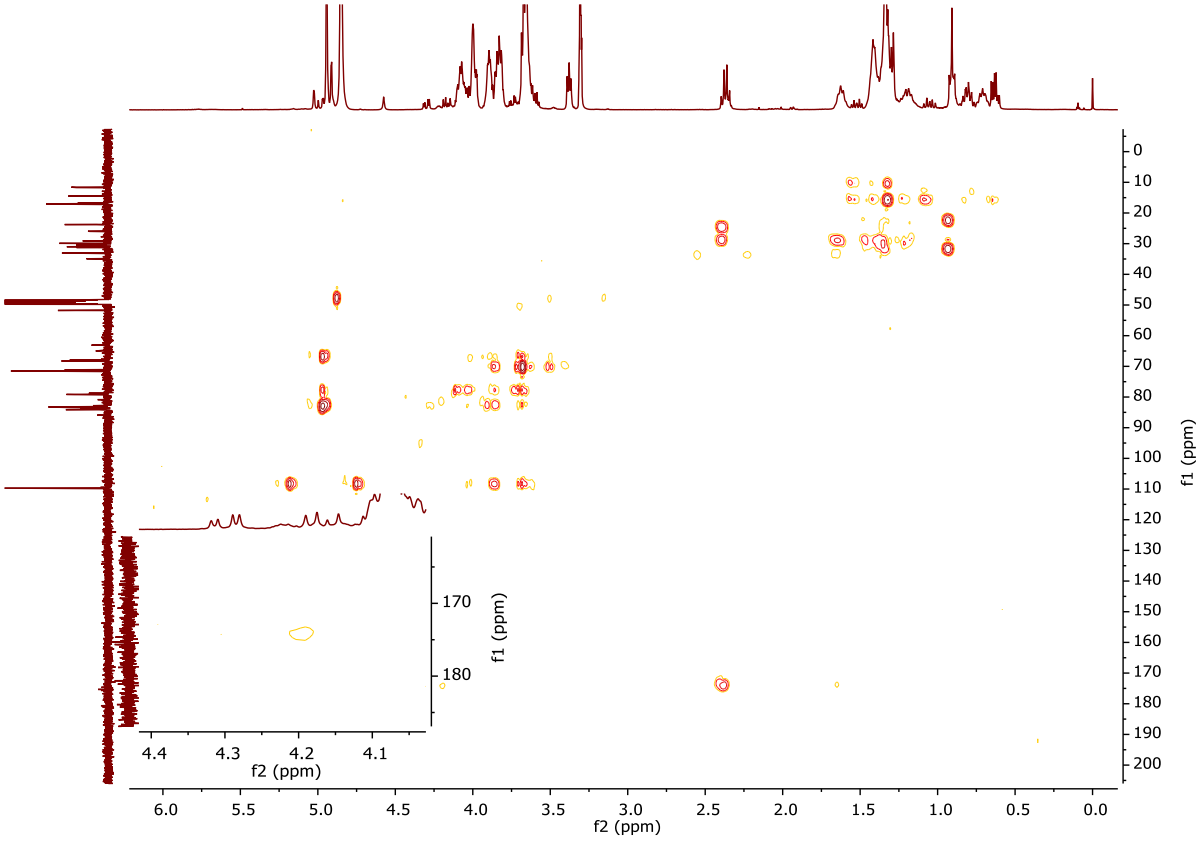
^{13}C NMR Spectrum (100.53 MHz, CD_3OD) of Compound **70c**



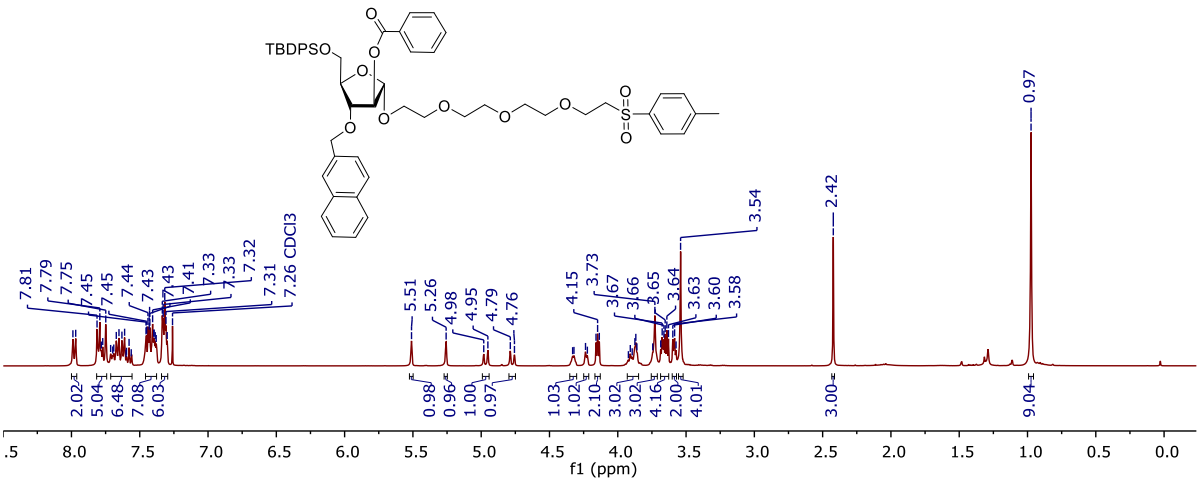
DEPT NMR Spectrum (100.53 MHz, CD_3OD) of Compound **70c**



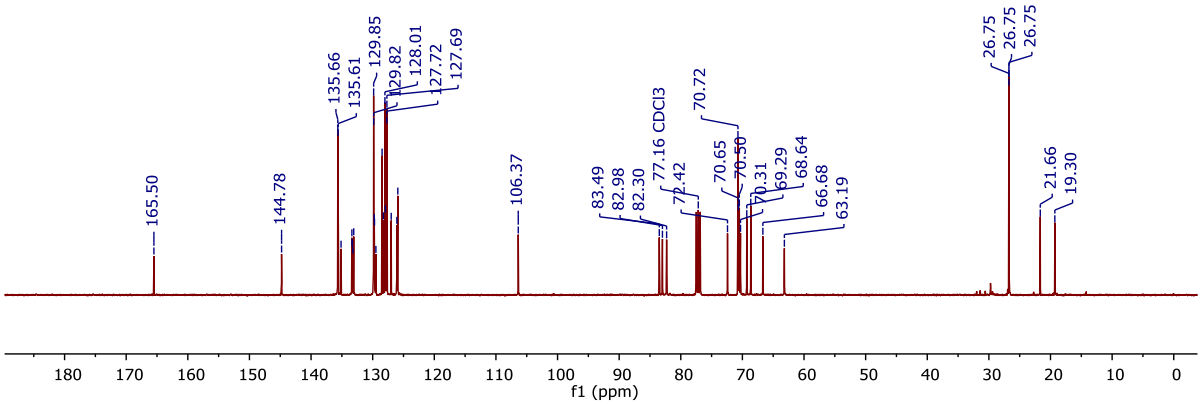
HMBC NMR Spectrum of Compound **70c**



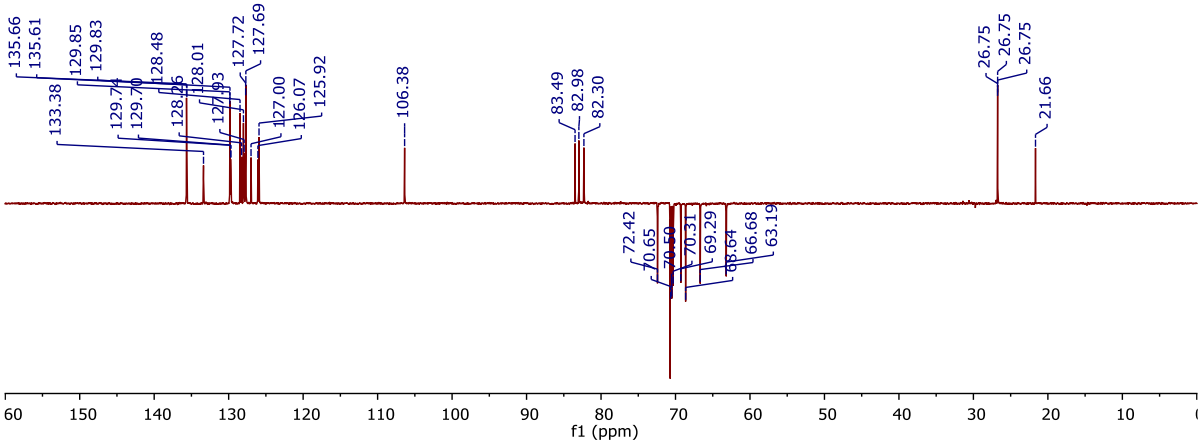
^{1}H NMR Spectrum (400.31 MHz, $CDCl_3$) of compound **71**



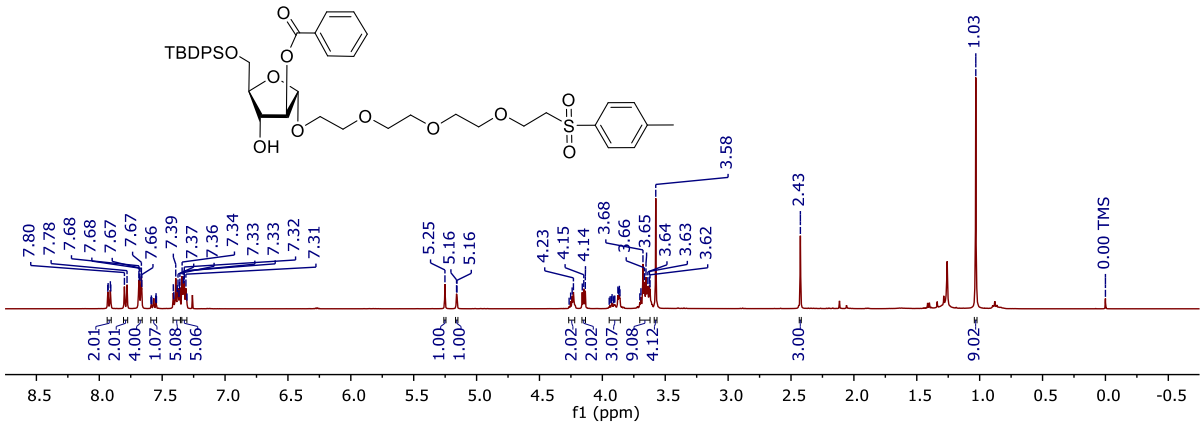
^{13}C NMR Spectrum (100.53 MHz, $CDCl_3$) of compound **71**



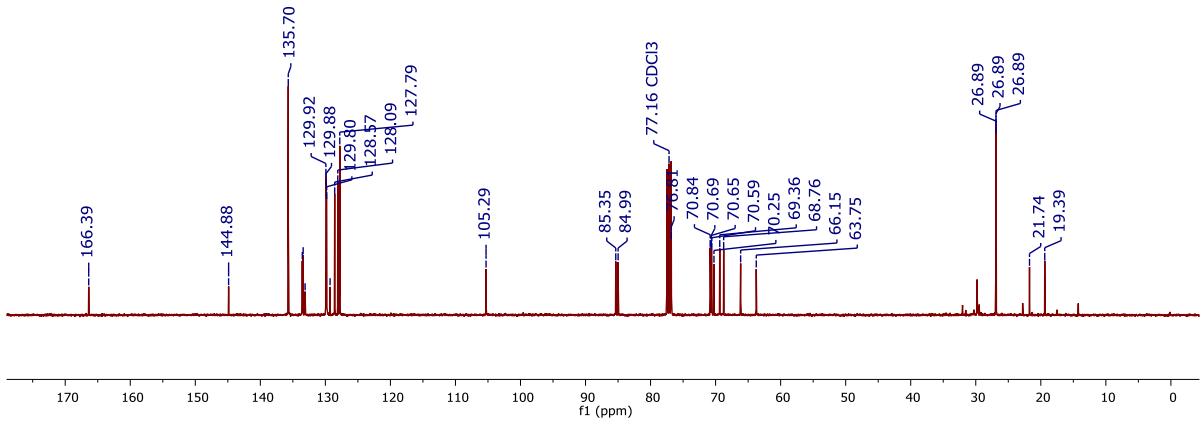
DEPT NMR Spectrum (100.53 MHz, $CDCl_3$) of compound **71**



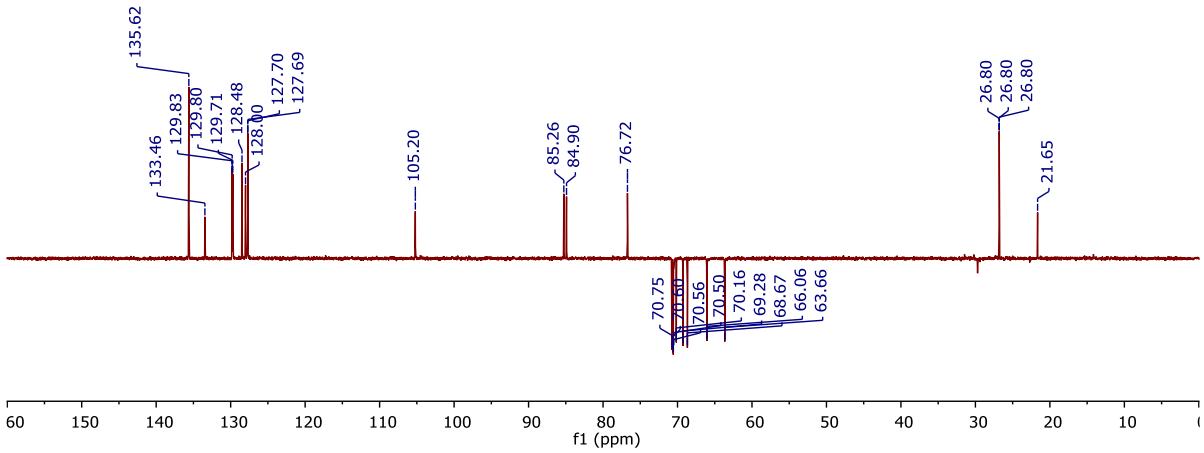
^{1}H NMR Spectrum (400.31 MHz, $CDCl_3$) of compound **72**



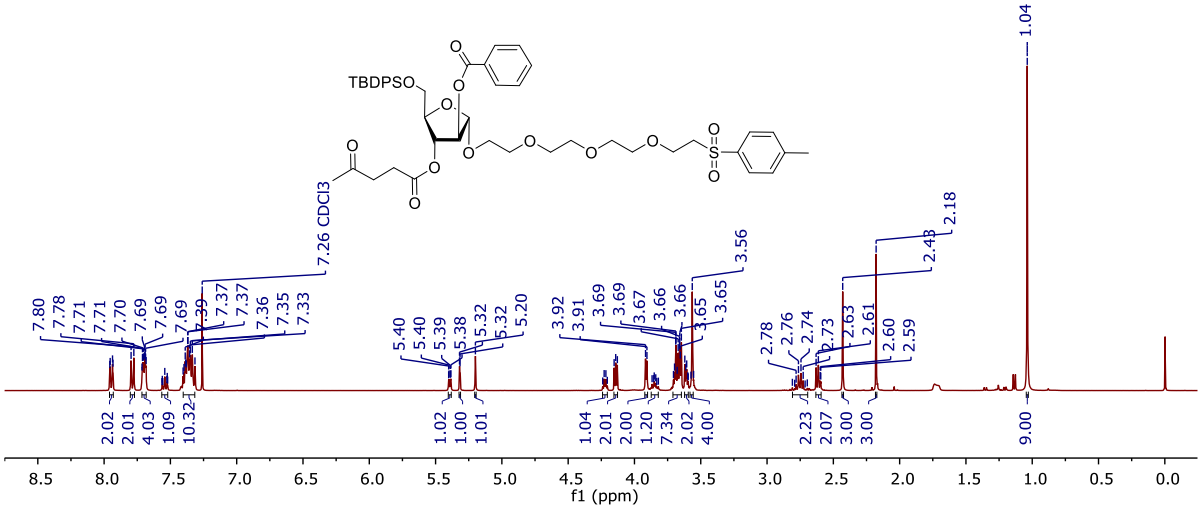
^{13}C NMR Spectrum (100.53 MHz, $CDCl_3$) of compound **72**



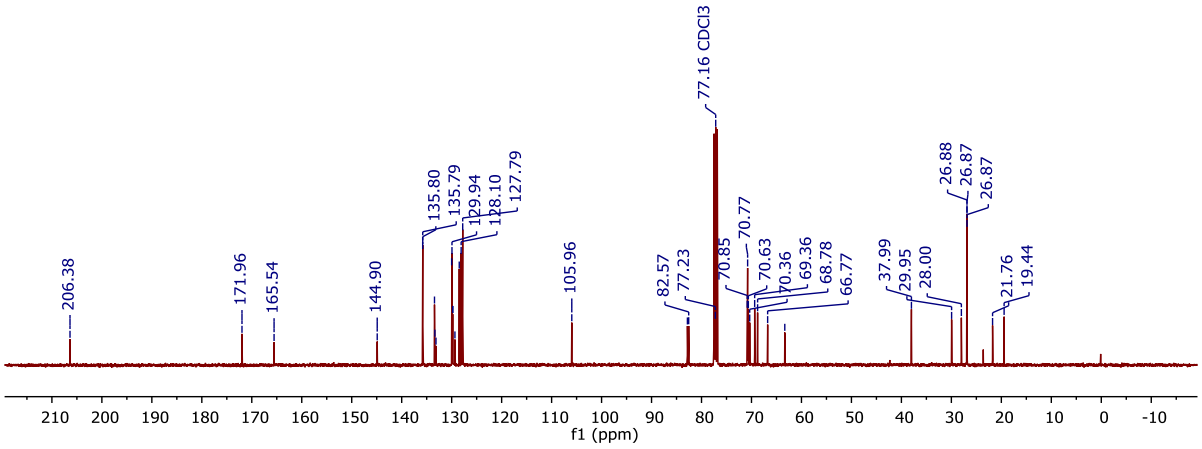
DEPT NMR Spectrum (100.53 MHz, $CDCl_3$) of compound **72**



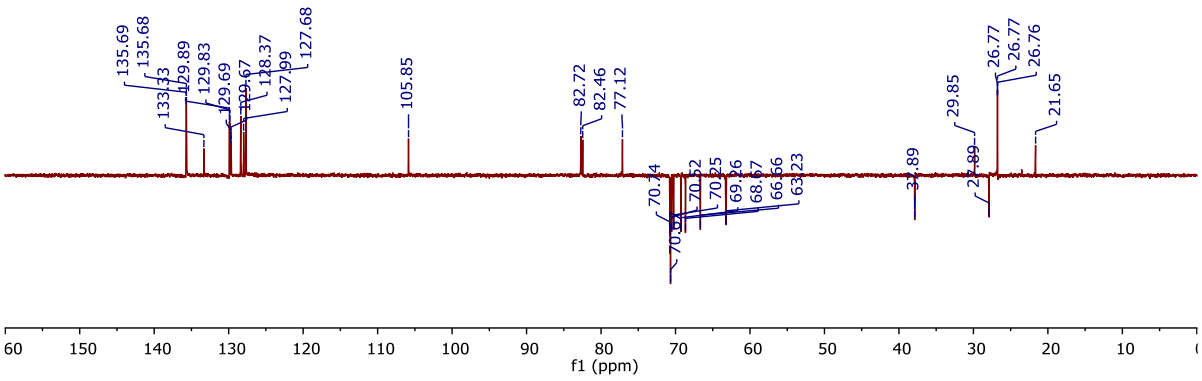
^{1}H NMR Spectrum (400.53 MHz, $CDCl_3$) of compound **73**



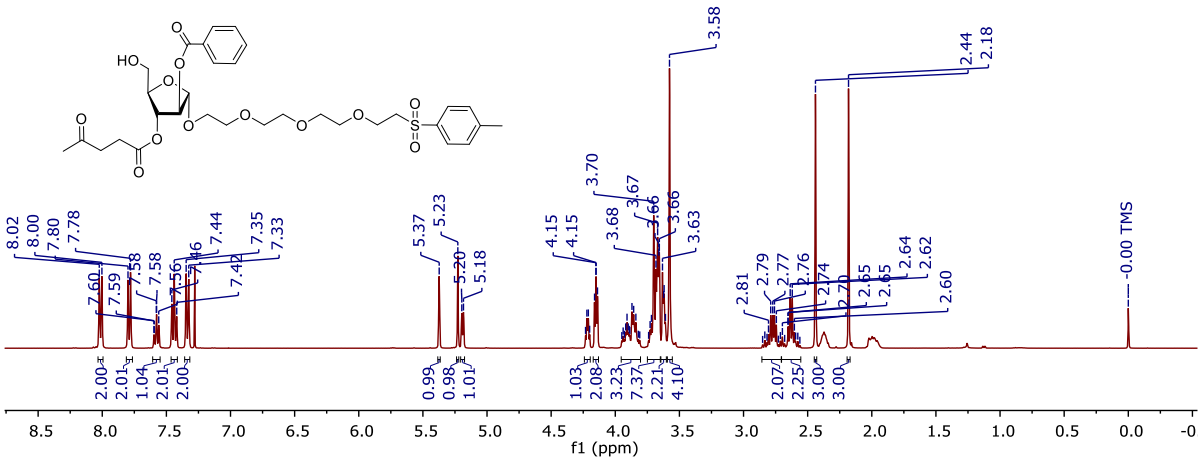
^{13}C NMR Spectrum (100.53 MHz, $CDCl_3$) of compound **73**



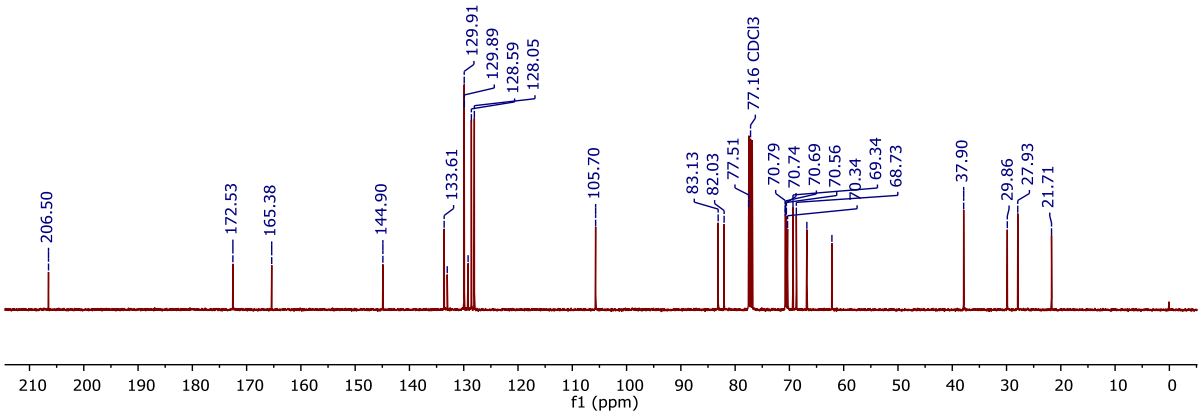
DEPT NMR Spectrum (100.53 MHz, $CDCl_3$) of compound **73**



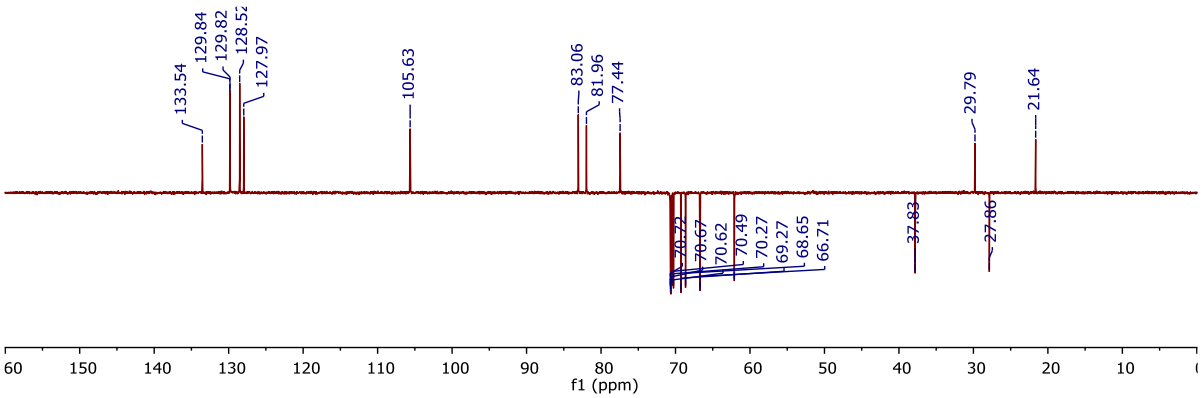
^{1}H NMR Spectrum (400.31 MHz, $CDCl_3$) of compound **74**



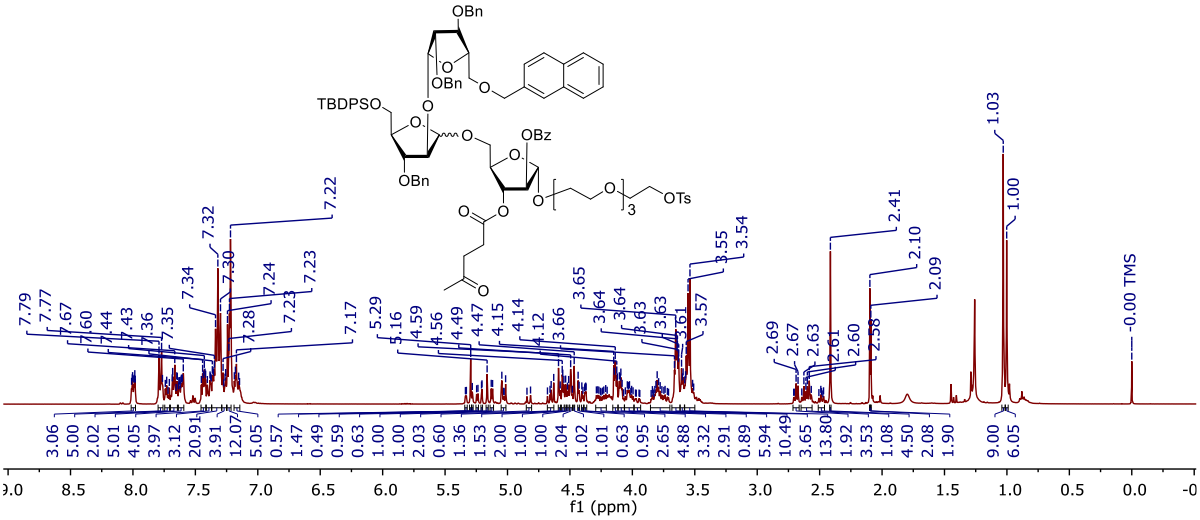
^{13}C NMR Spectrum (100.53 MHz, $CDCl_3$) of compound **74**



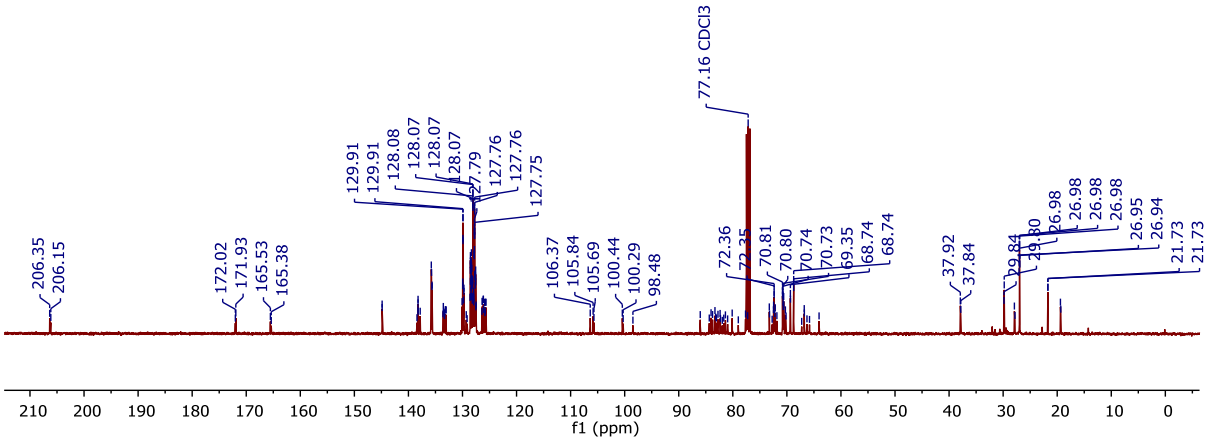
DEPT NMR Spectrum (100.31 MHz, $CDCl_3$) of compound **74**



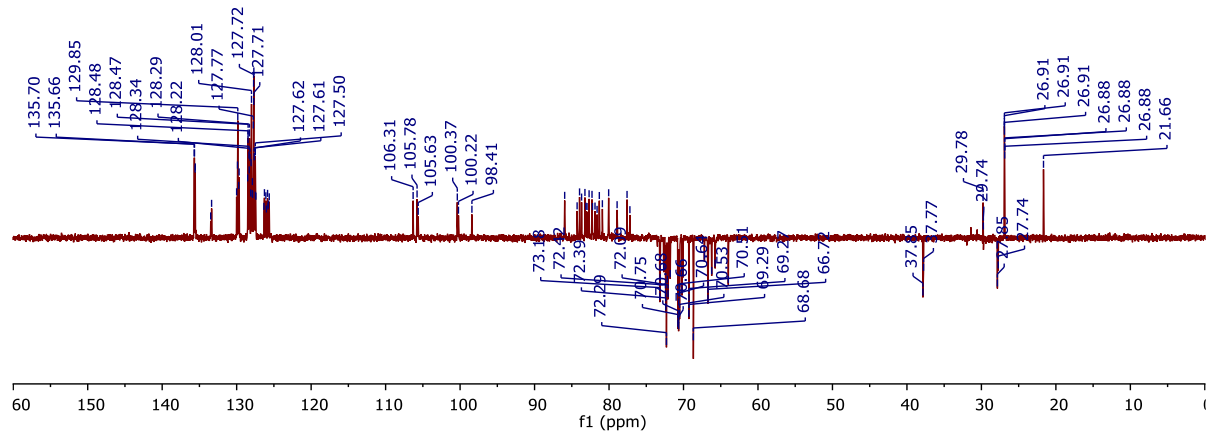
^{1}H NMR spectrum (400.31 MHz, $CDCl_3$) of compound **75a:75b** (Both isomers)



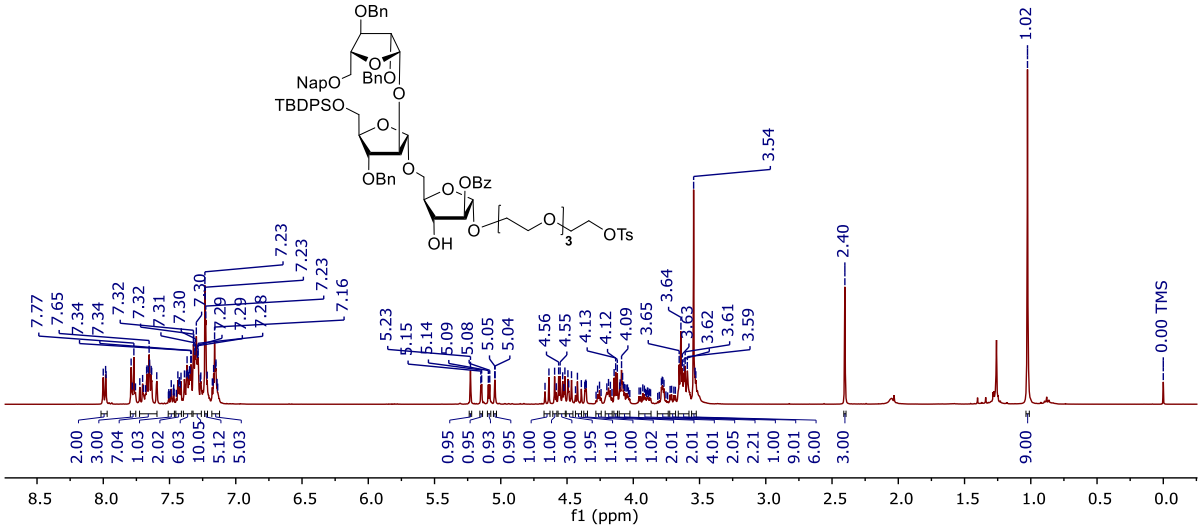
^{13}C NMR Spectrum (100.53 MHz, $CDCl_3$) of compound **75a:75b** (Both isomers)



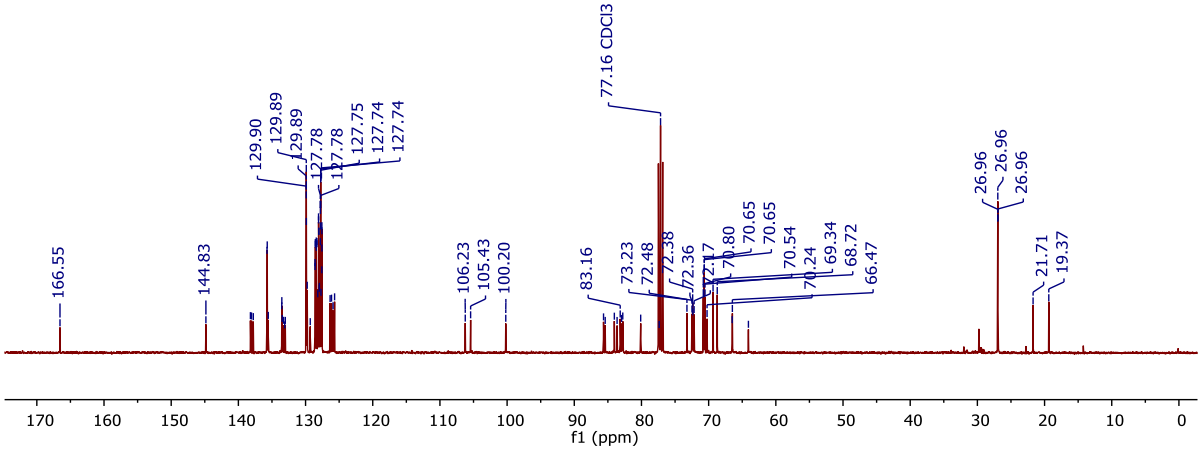
DEPT NMR Spectrum (100.53 MHz, $CDCl_3$) of compound **75a:75b** (Both isomers)



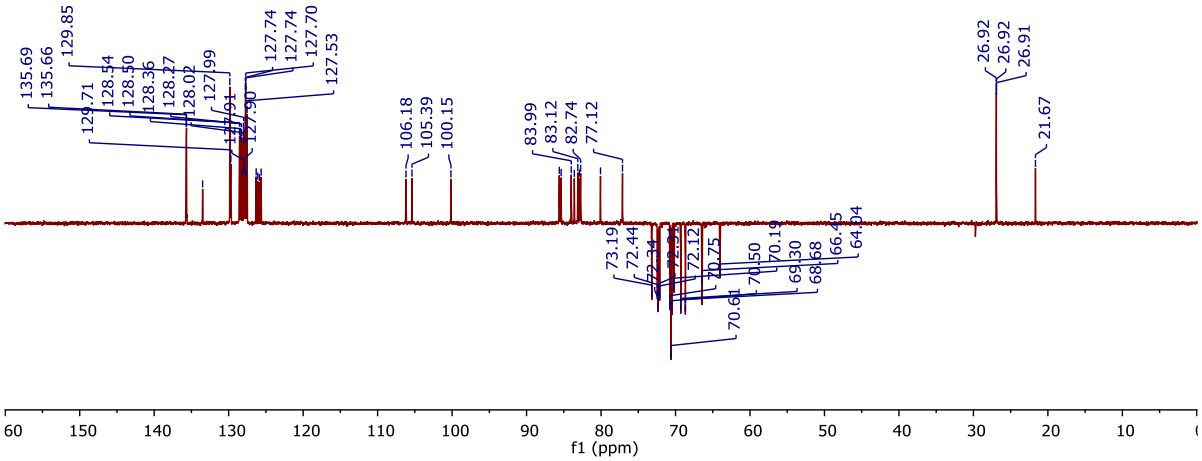
^{1}H NMR Spectrum (400.31 MHz, $CDCl_3$) of compound **76a**



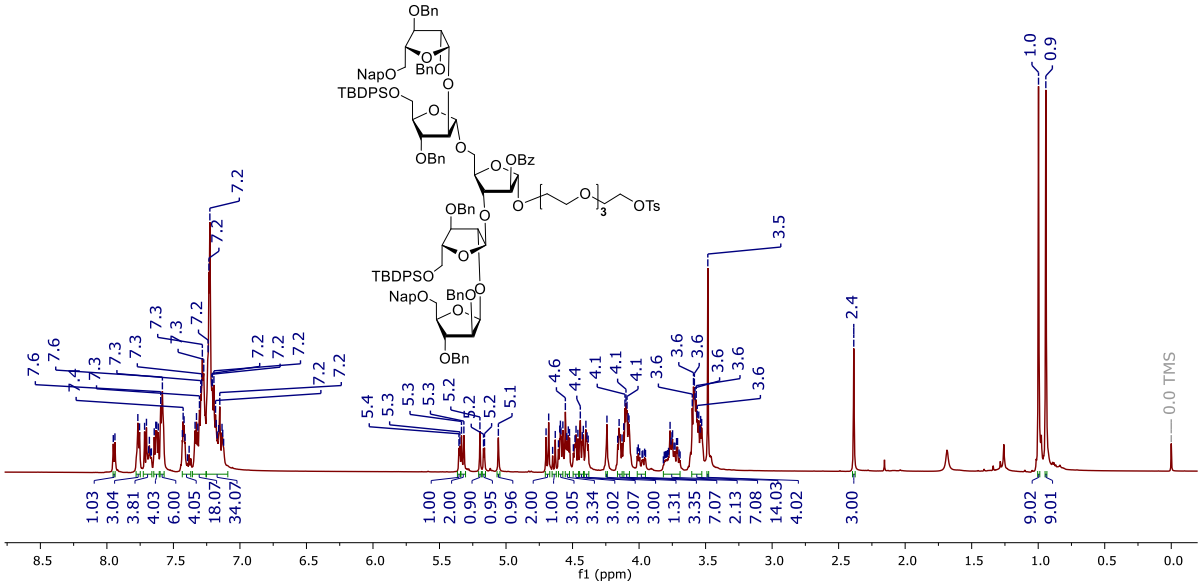
^{13}C NMR Spectrum (100.53 MHz, $CDCl_3$) of compound **76a**



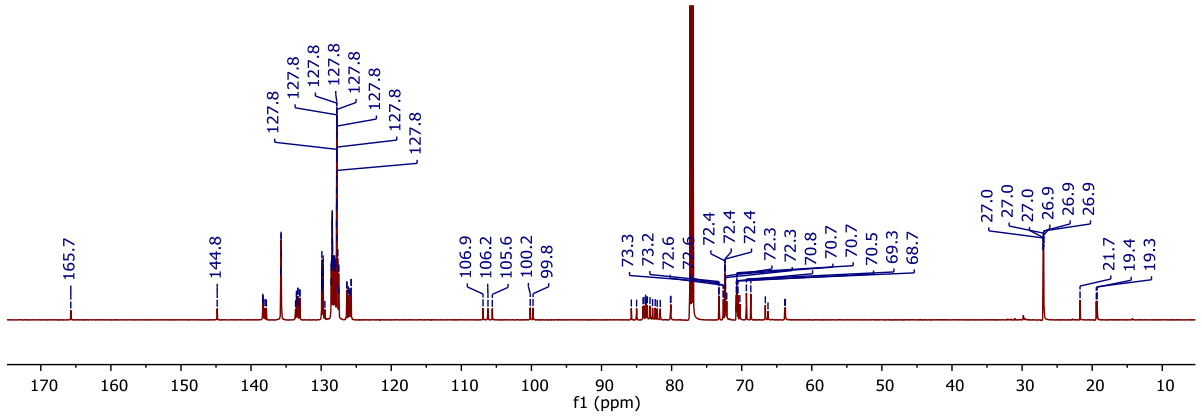
DEPT NMR Spectrum (100.53 MHz, $CDCl_3$) of compound **76a**



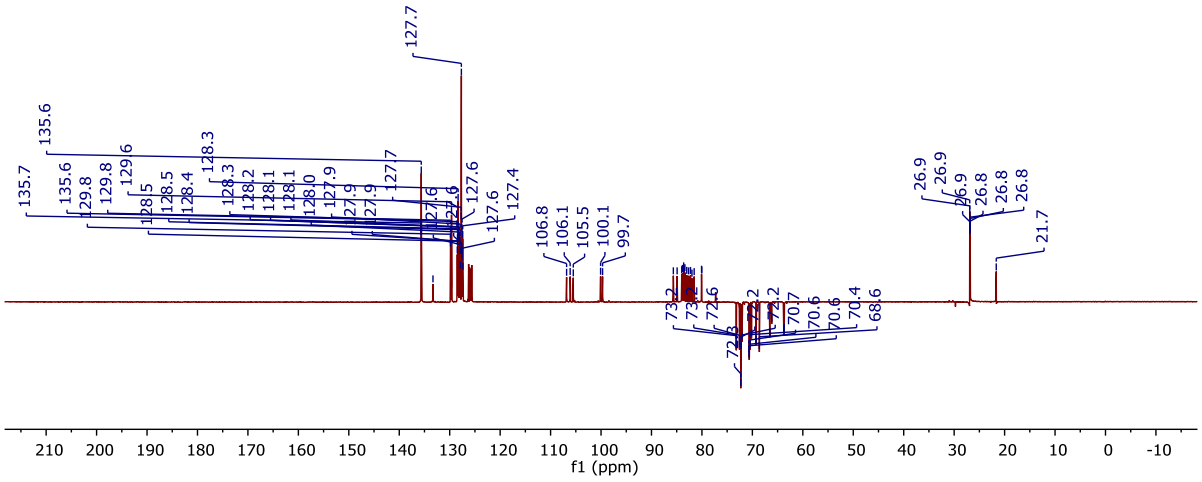
^{1}H NMR Spectrum (400.31 MHz, $CDCl_3$) of compound **77**



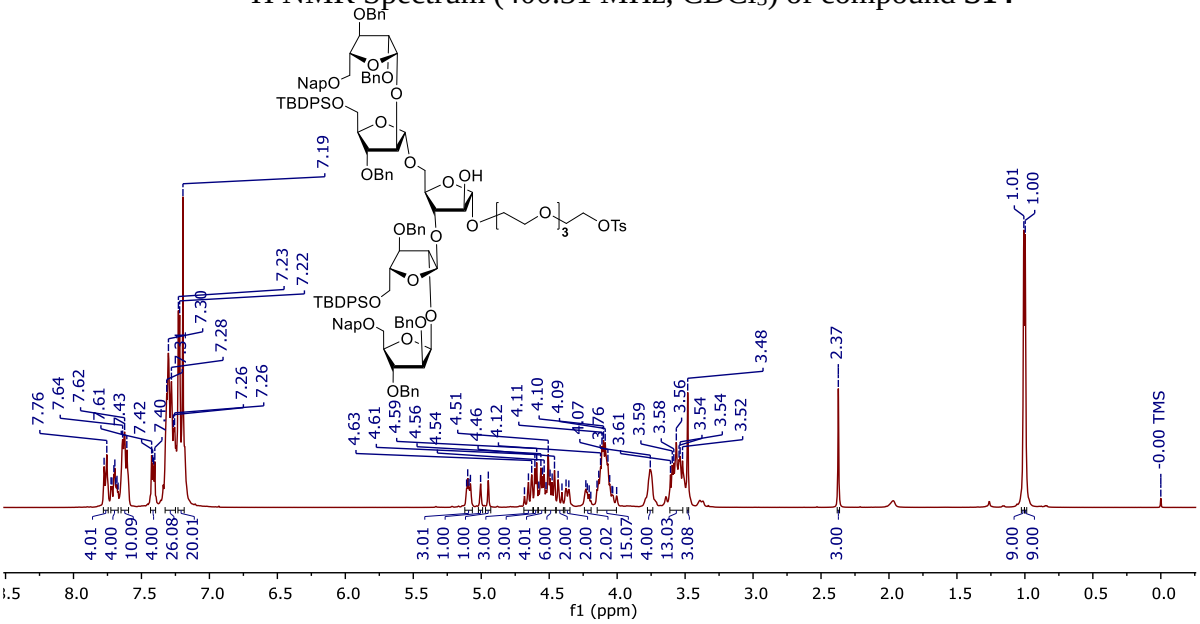
^{13}C NMR Spectrum (100.53 MHz, $CDCl_3$) of compound **77**



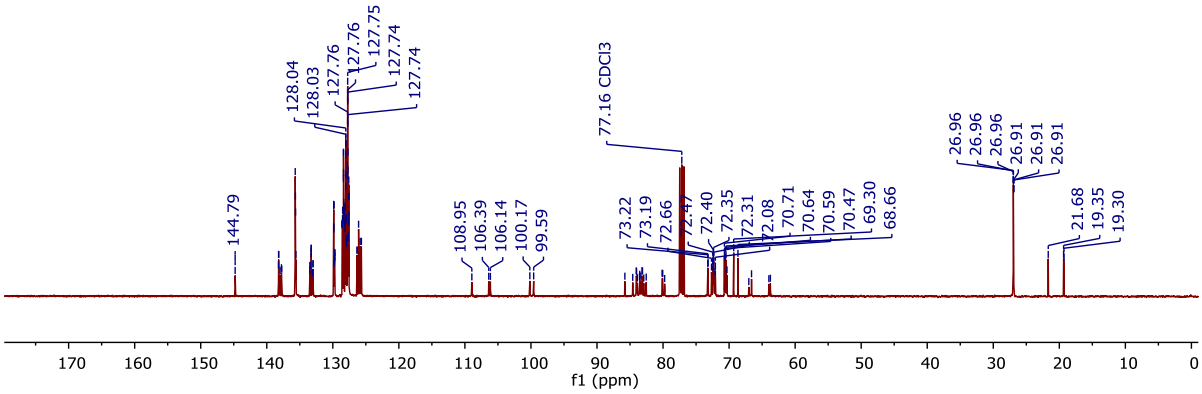
DEPT NMR Spectrum (100.53 MHz, $CDCl_3$) of compound **77**



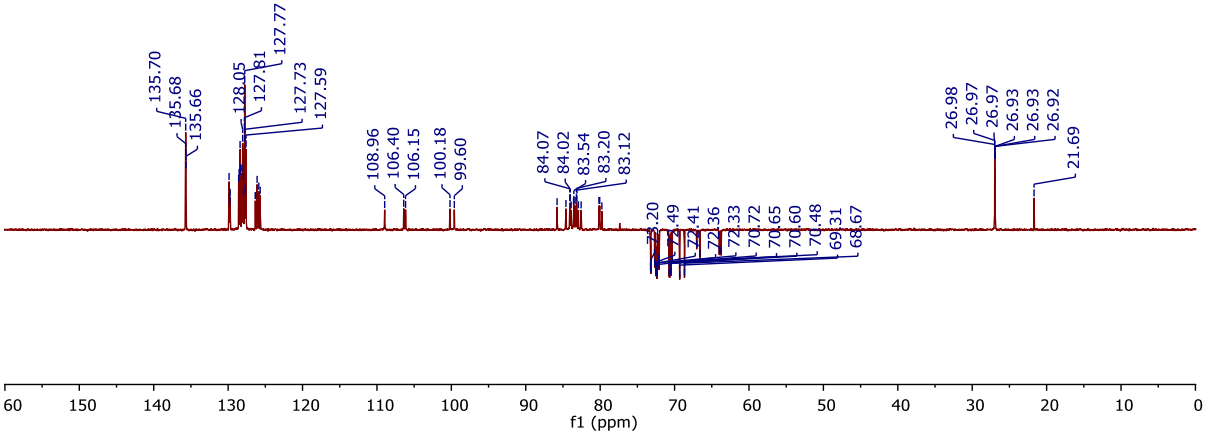
^{1}H NMR Spectrum (400.31 MHz, $CDCl_3$) of compound **S14**



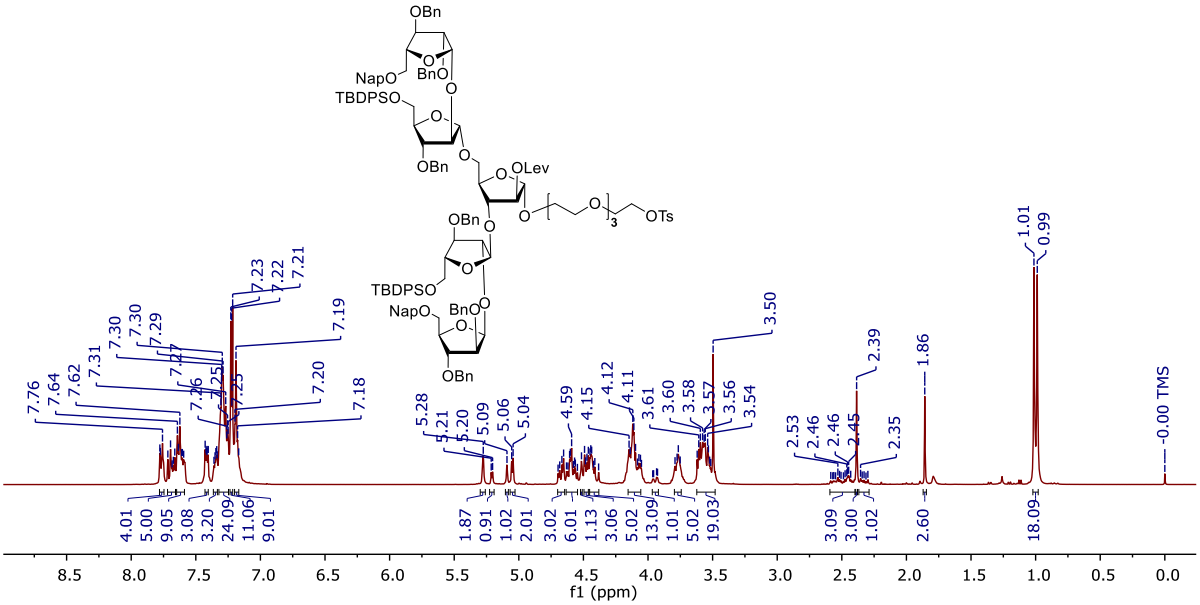
^{13}C NMR Spectrum (100.53 MHz, $CDCl_3$) of compound **S14**



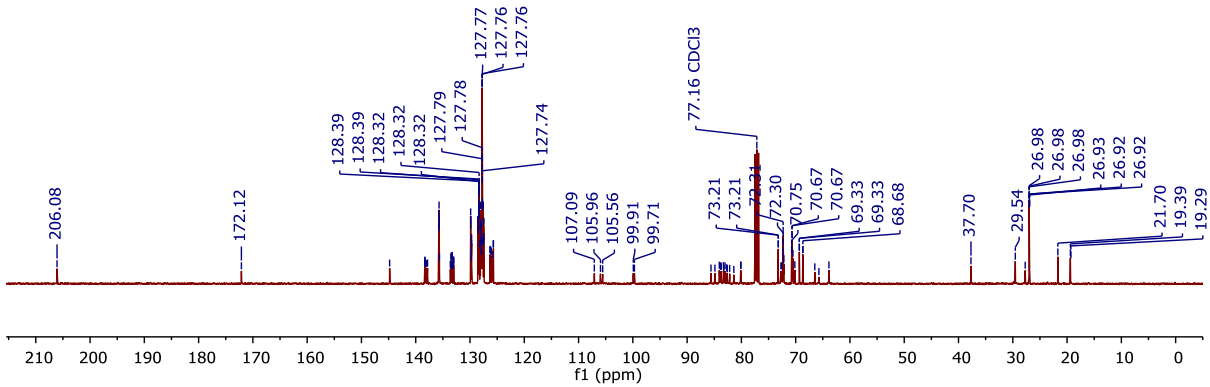
DEPT NMR Spectrum (100.53 MHz, $CDCl_3$) of compound **S14**



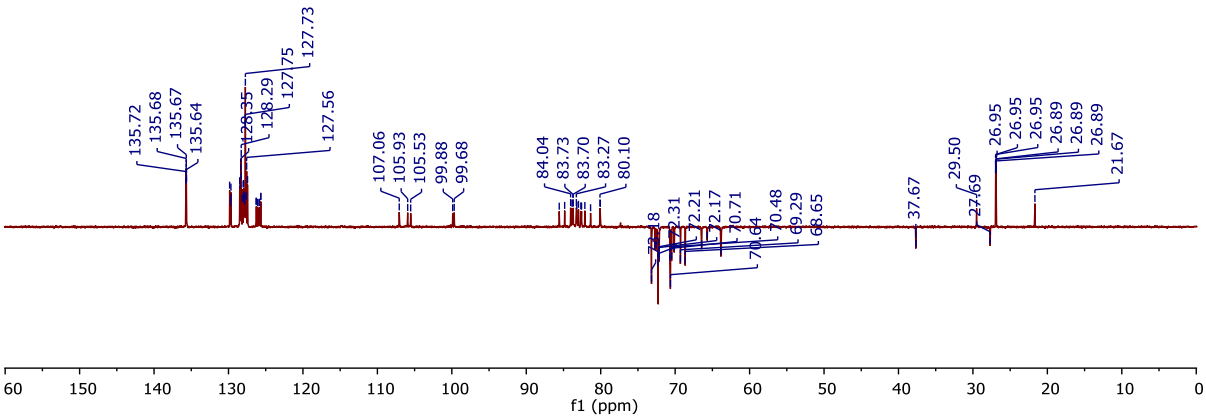
^{1}H NMR Spectrum (400.31 MHz, $CDCl_3$) of compound **78**



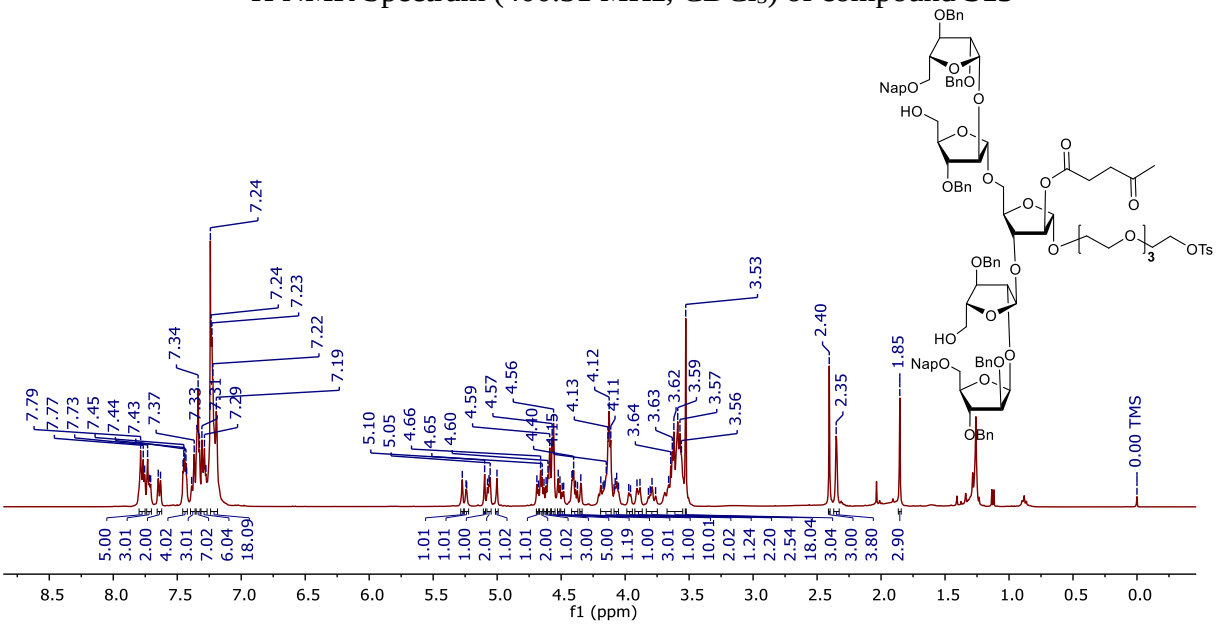
^{13}C NMR Spectrum (100.53 MHz, $CDCl_3$) of compound **78**



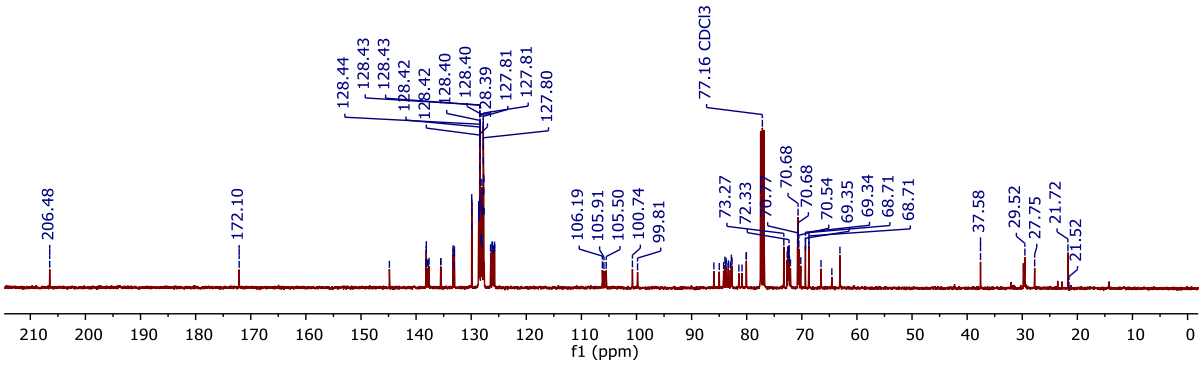
DEPT NMR Spectrum (100.53 MHz, $CDCl_3$) of compound **78**



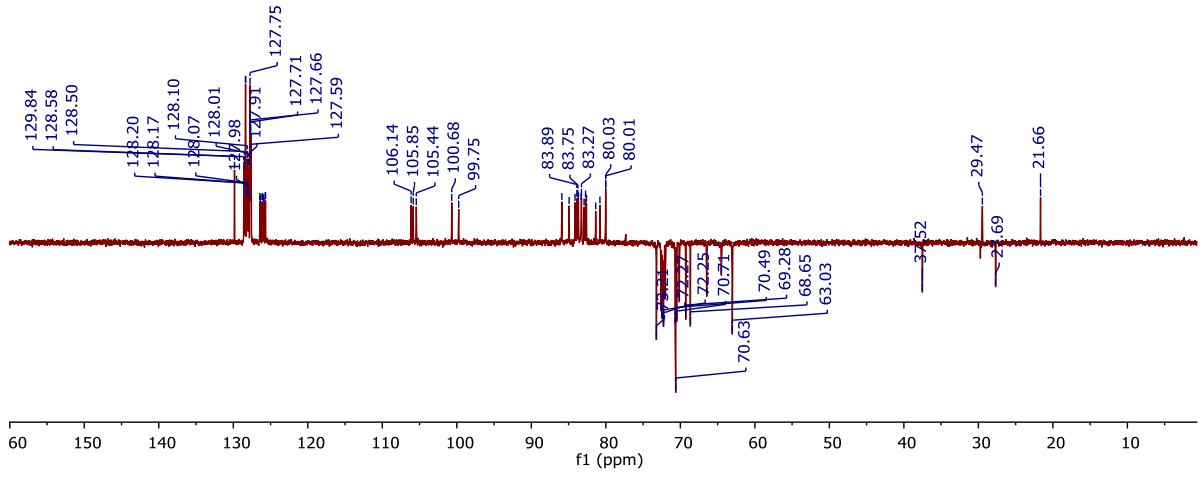
^{1}H NMR Spectrum (400.31 MHz, $CDCl_3$) of compound **S15**



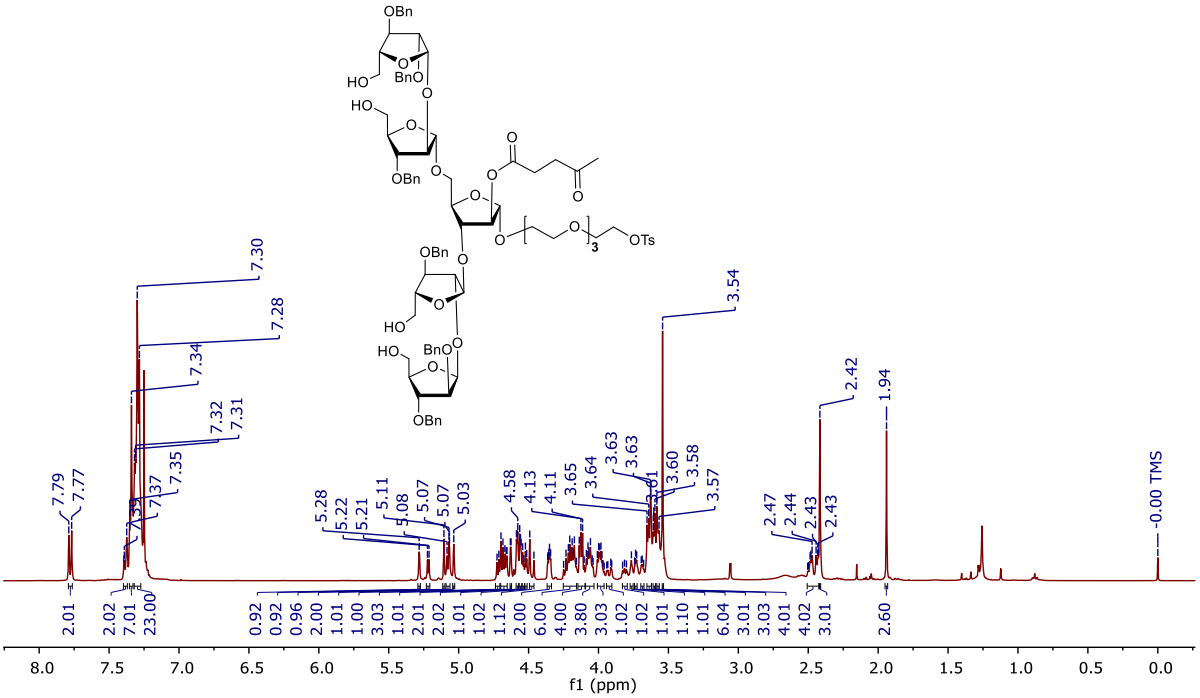
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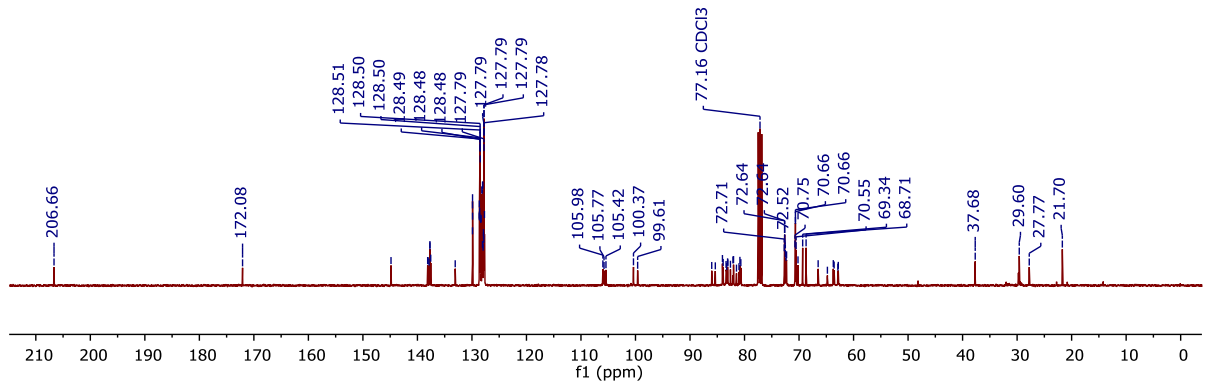
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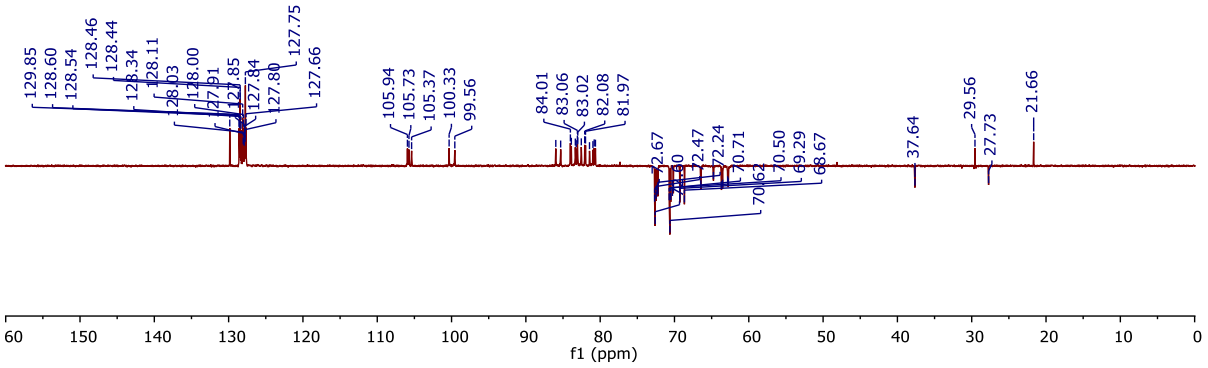
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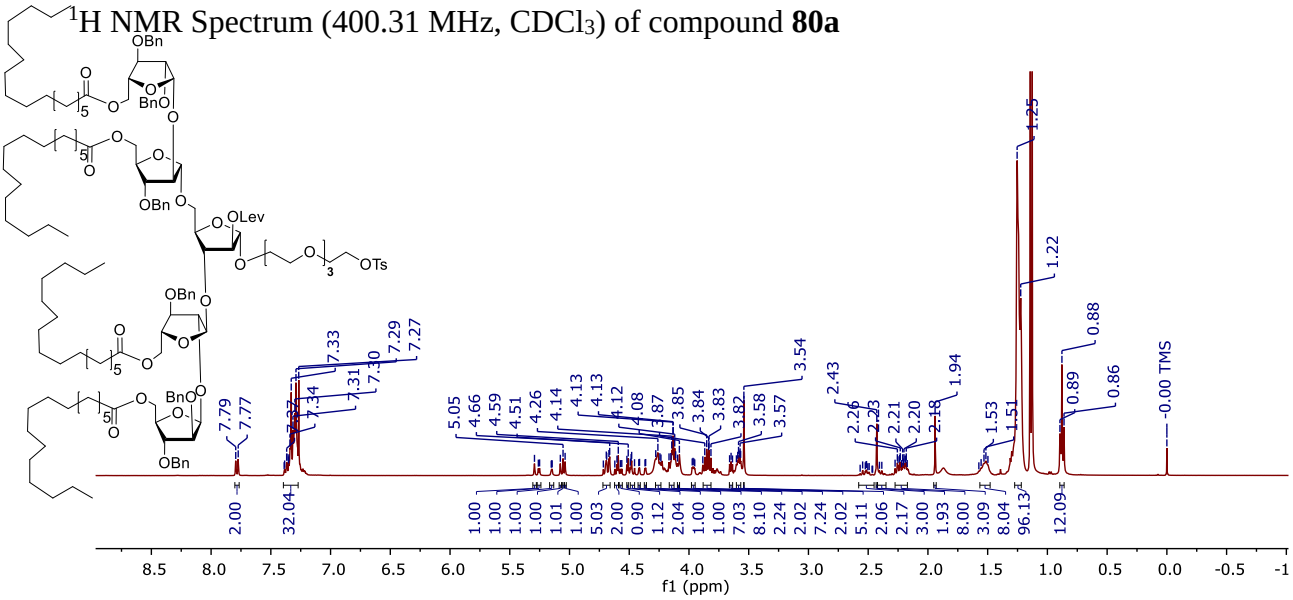
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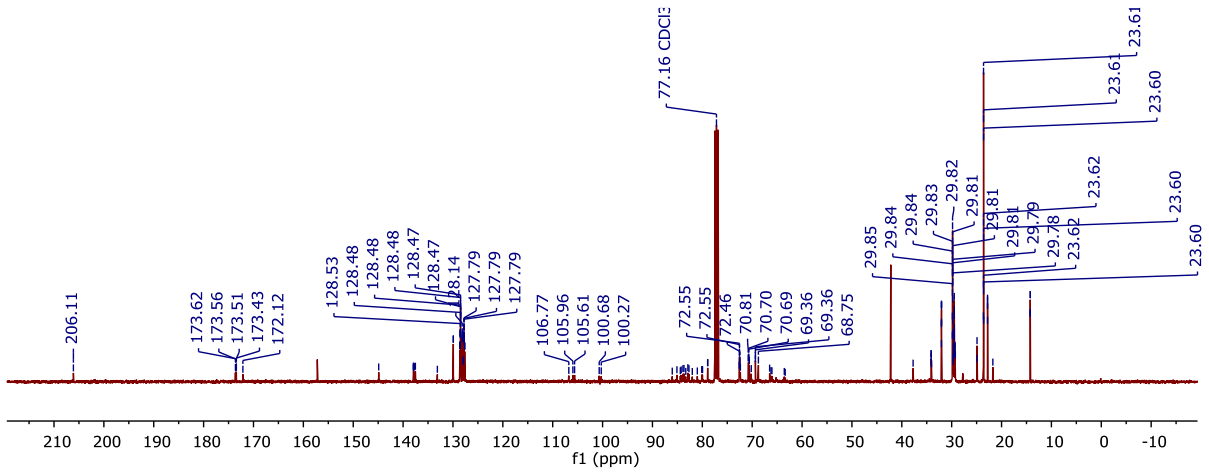
DEPT NMR Spectrum (100.53 MHz, $CDCl_3$) of compound **79**



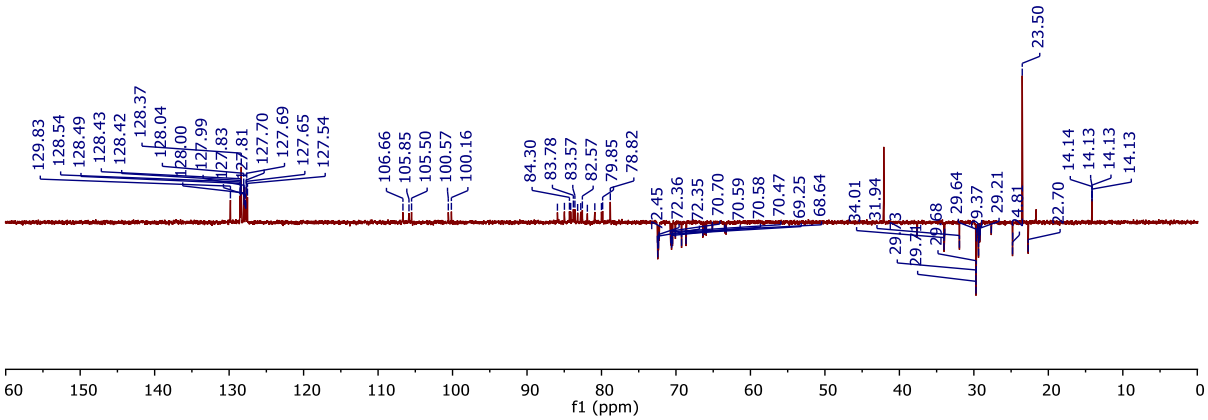
^{1}H NMR Spectrum (400.31 MHz, $CDCl_3$) of compound **80a**



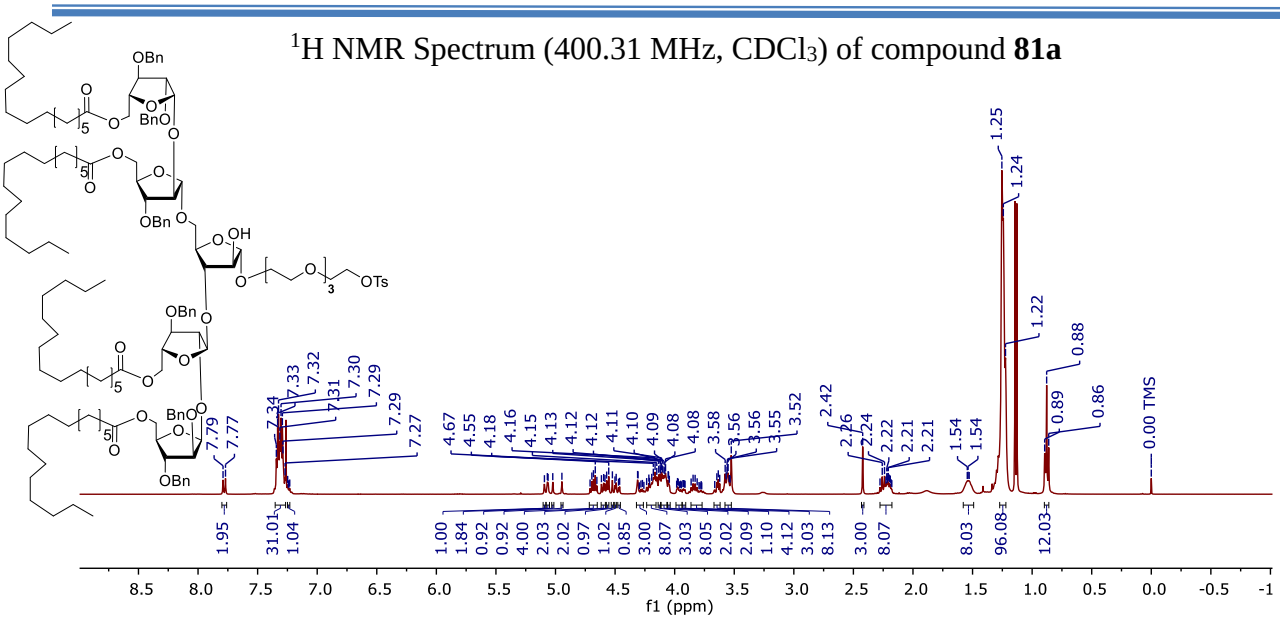
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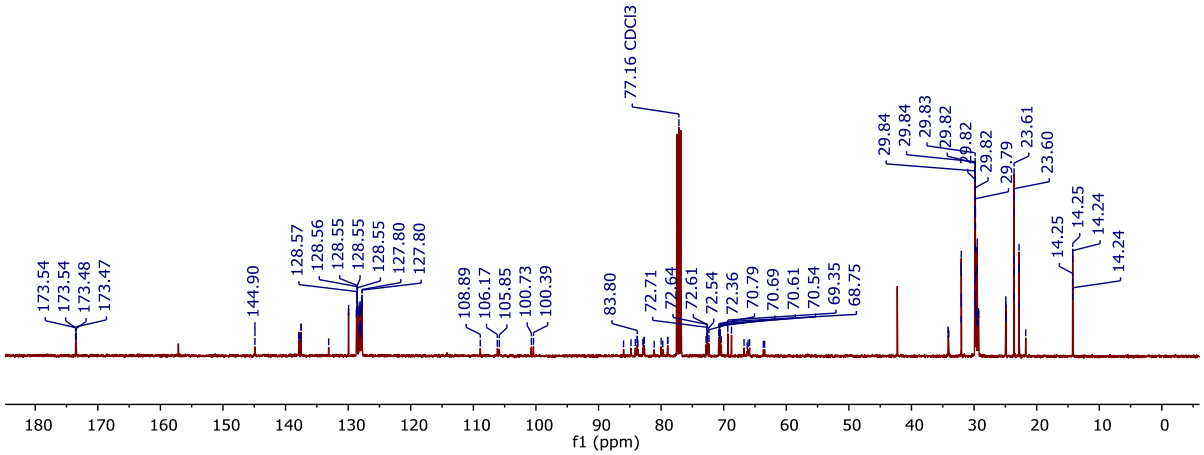
DEPT NMR Spectrum (100.53 MHz, $CDCl_3$) of compound **80a**



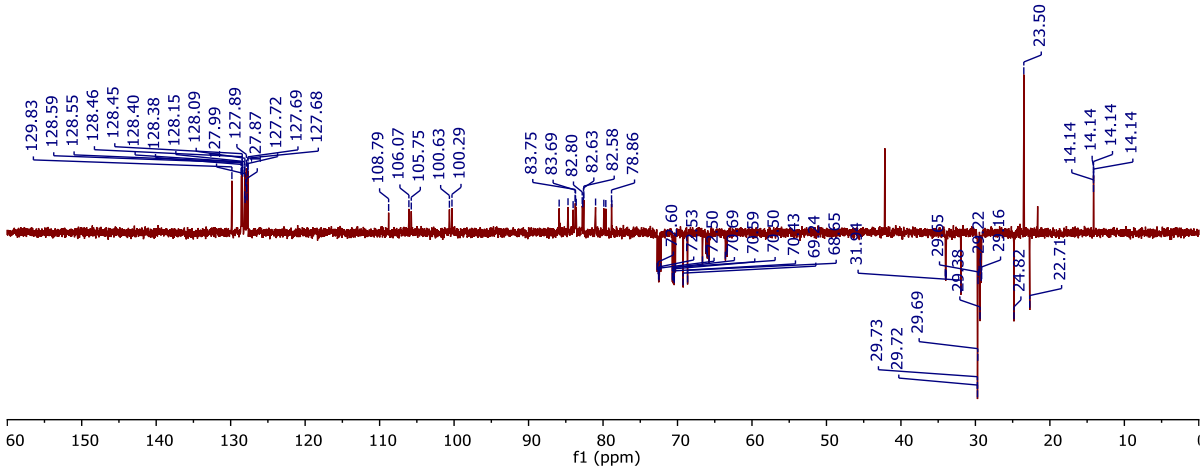
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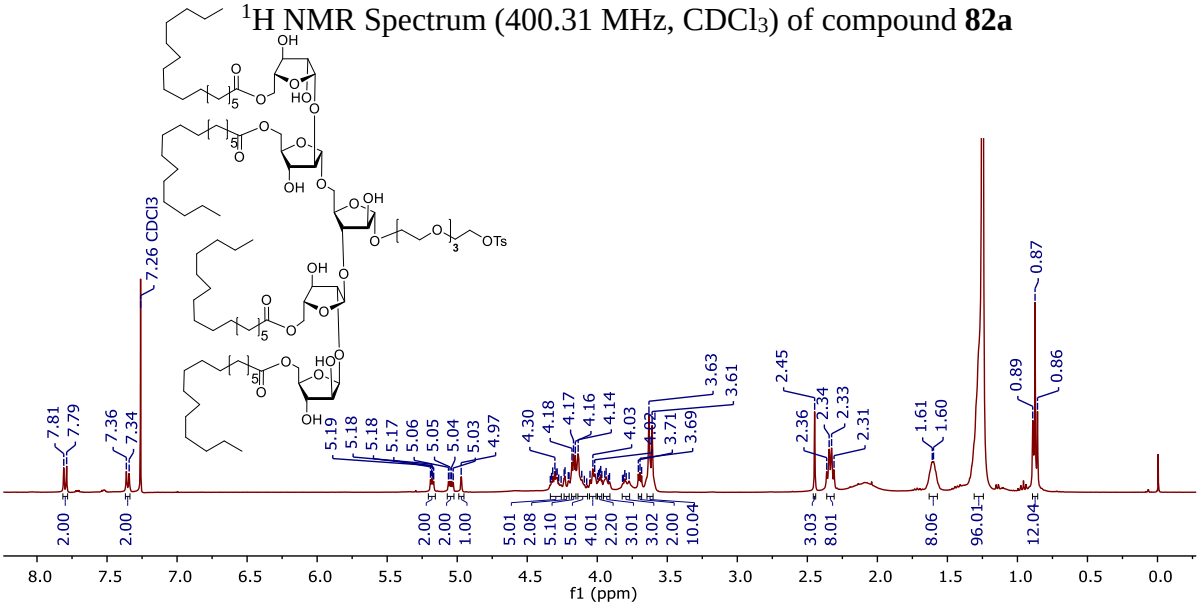
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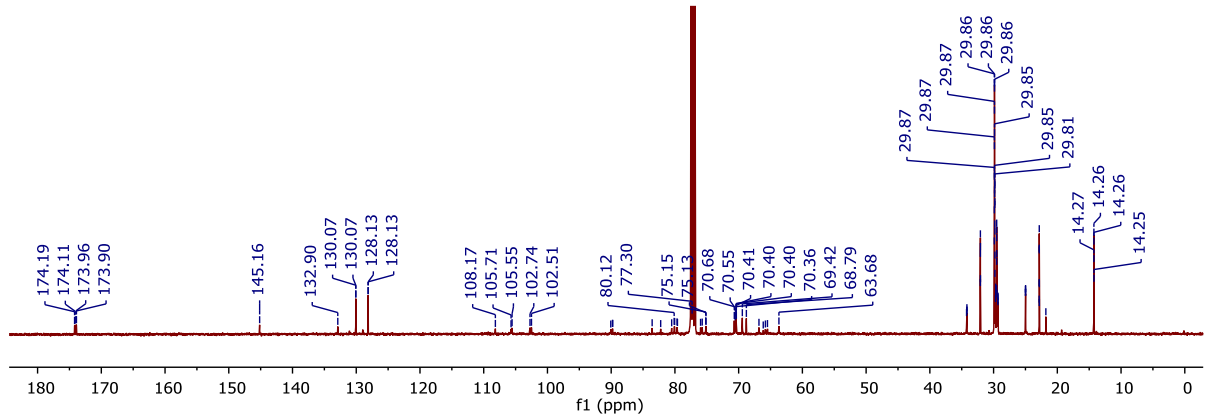
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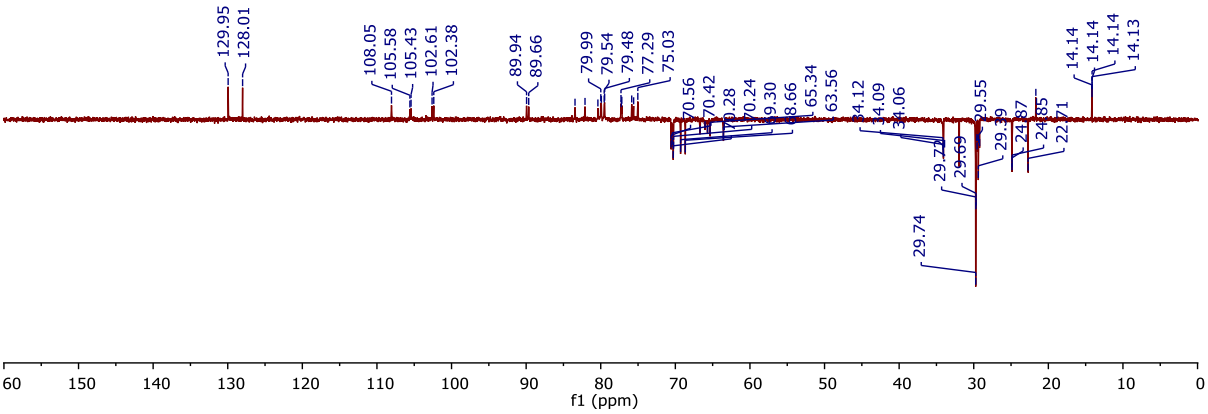
^{1}H NMR Spectrum (400.31 MHz, $CDCl_3$) of compound **82a**



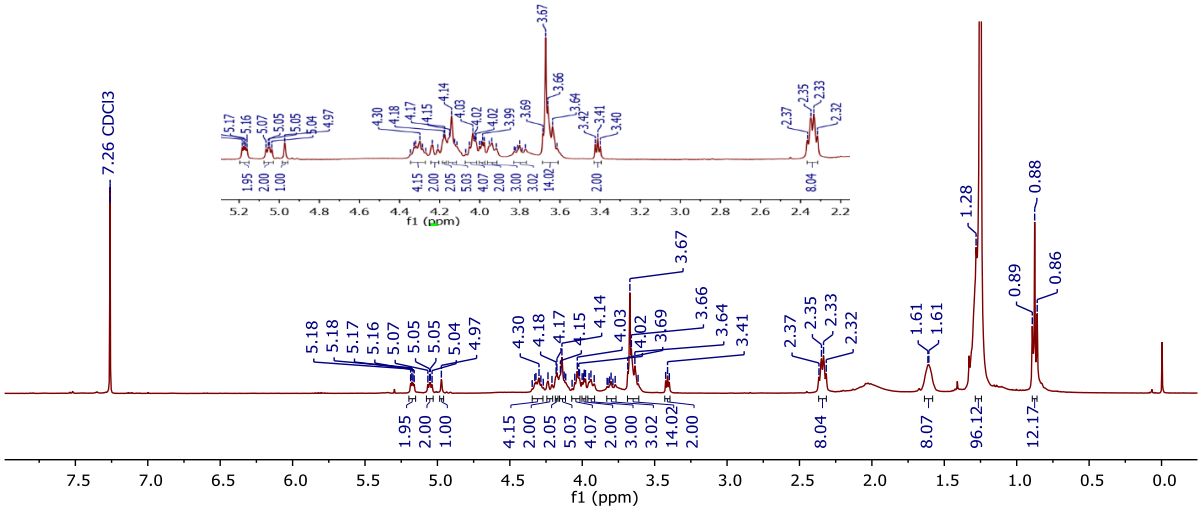
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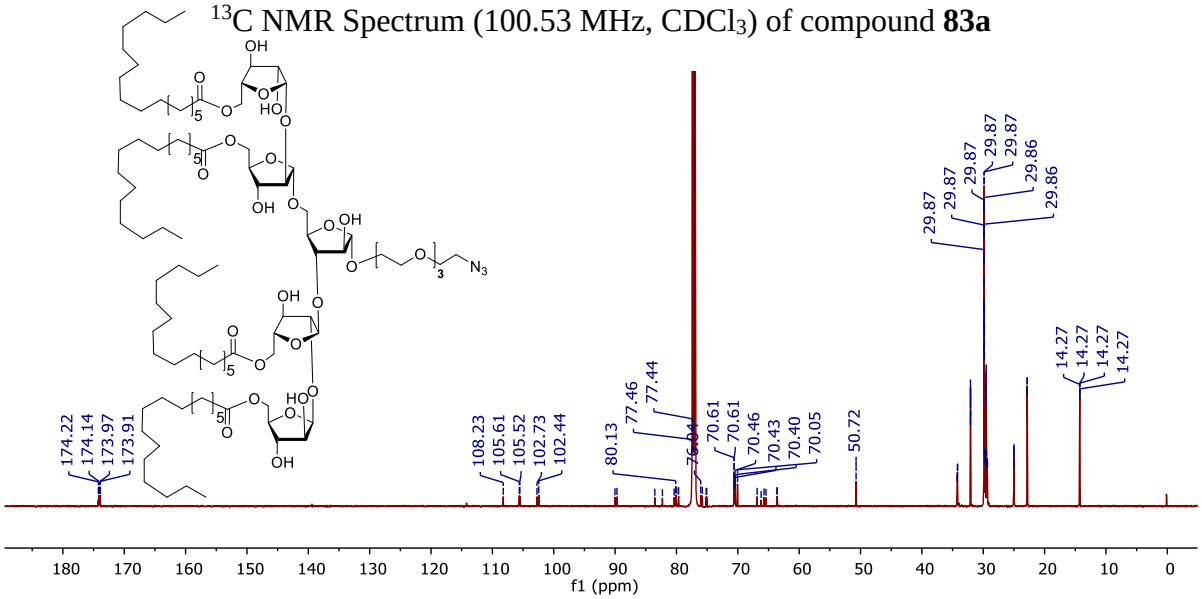
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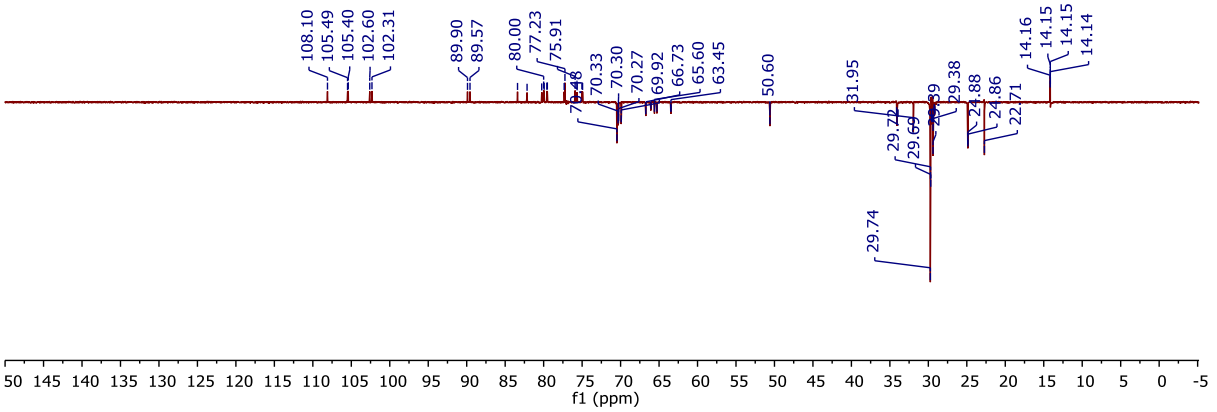
^{1}H NMR Spectrum (400.31 MHz, $CDCl_3$) of compound **83a**



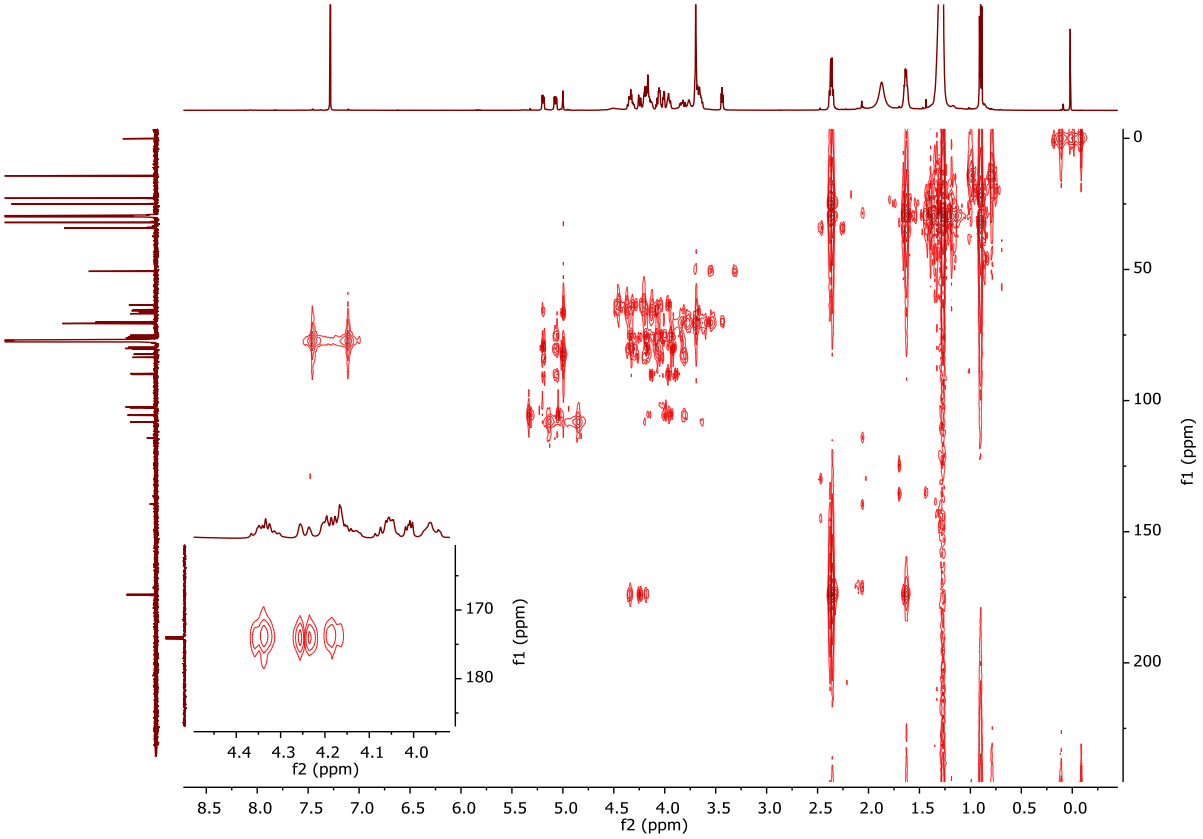
^{13}C NMR Spectrum (100.53 MHz, $CDCl_3$) of compound **83a**



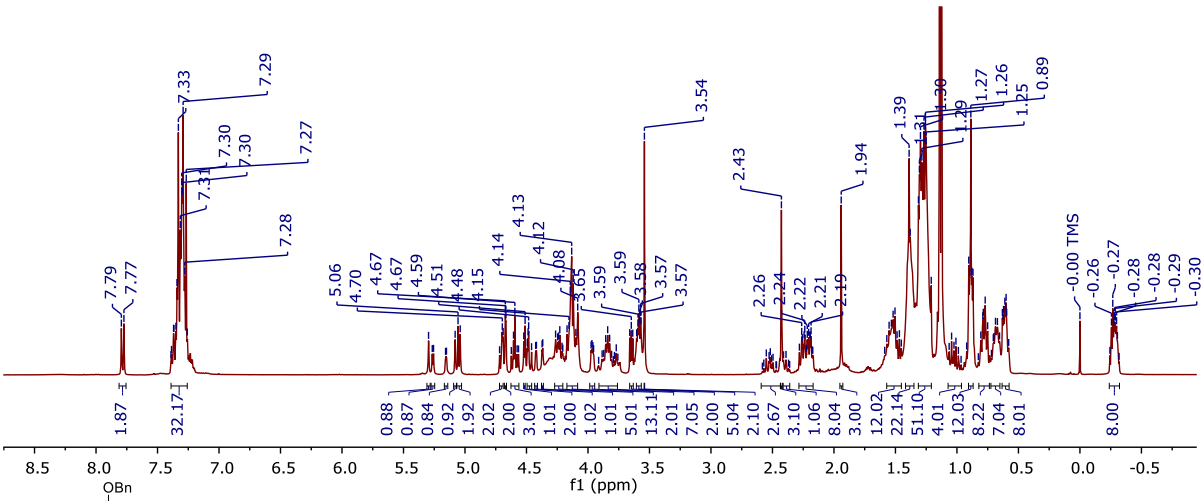
DEPT NMR Spectrum (100.53 MHz, $CDCl_3$) of compound **83a**

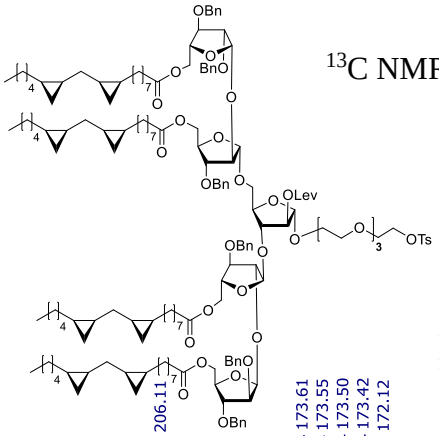


HMBC NMR of compound 83a

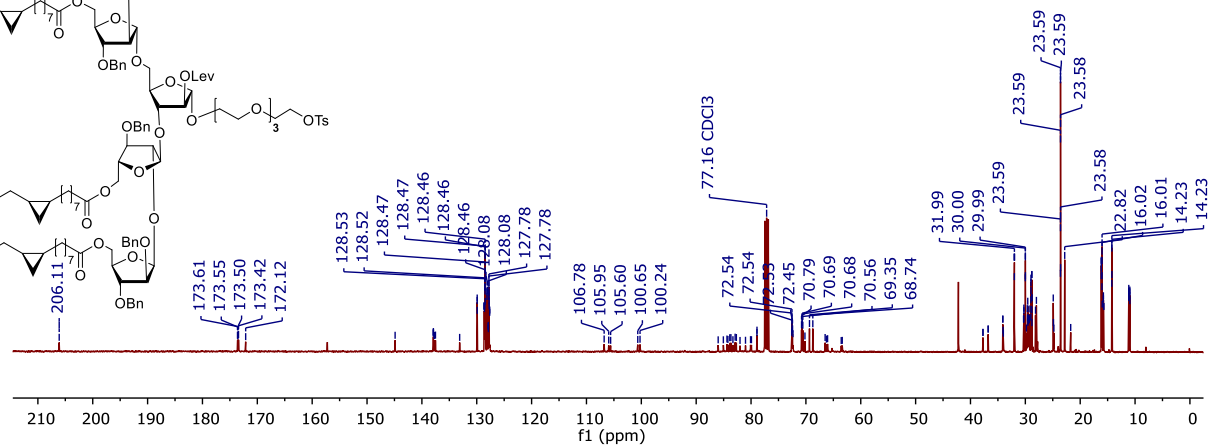


^{1}H NMR Spectrum (400.31 MHz, $CDCl_3$) of compound **80b**

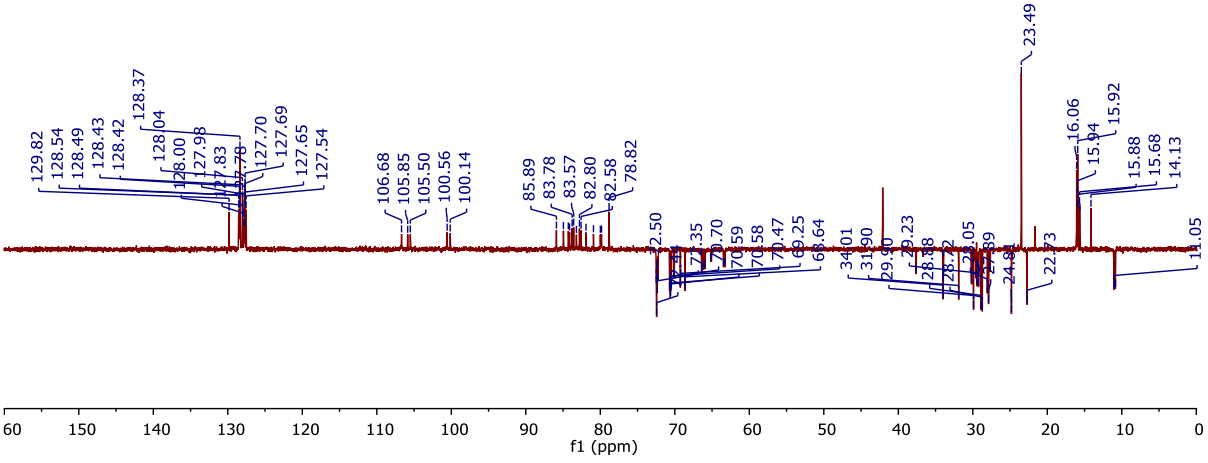




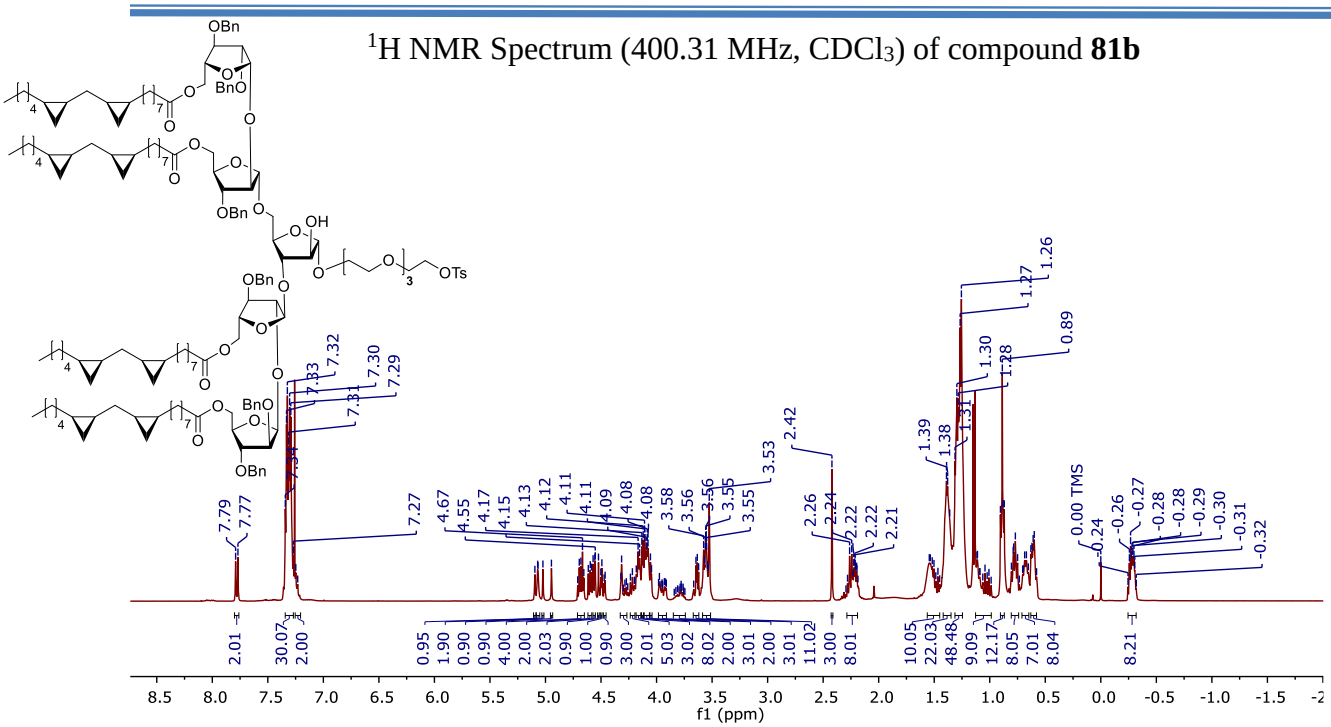
^{13}C NMR Spectrum (100.53 MHz, $CDCl_3$) of compound **80b**



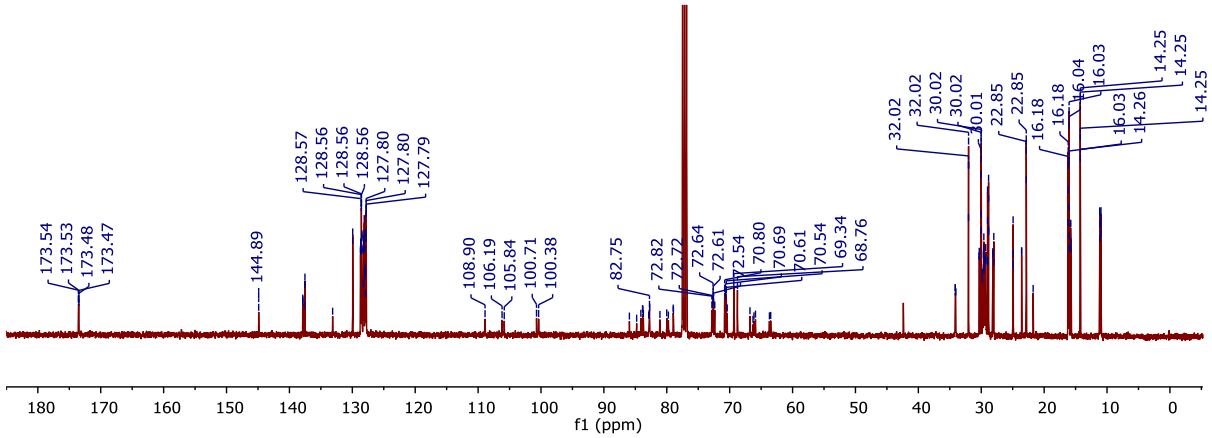
DEPT NMR Spectrum (100.53 MHz, $CDCl_3$) of compound **80b**



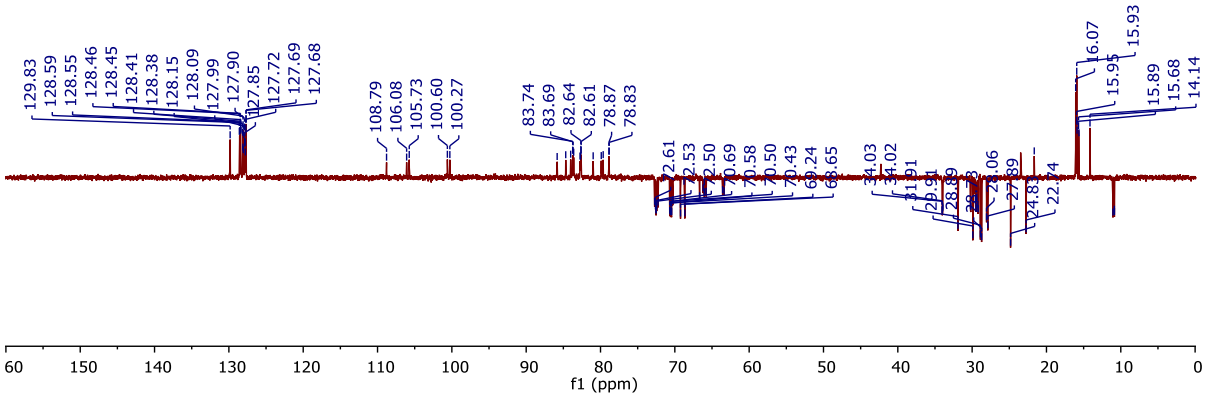
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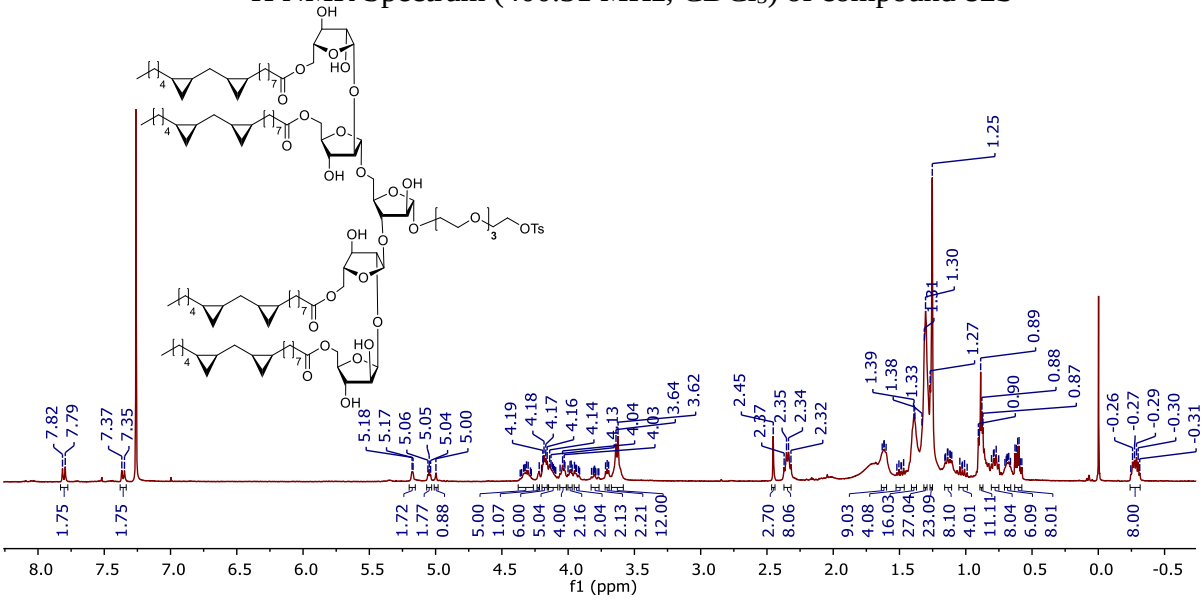
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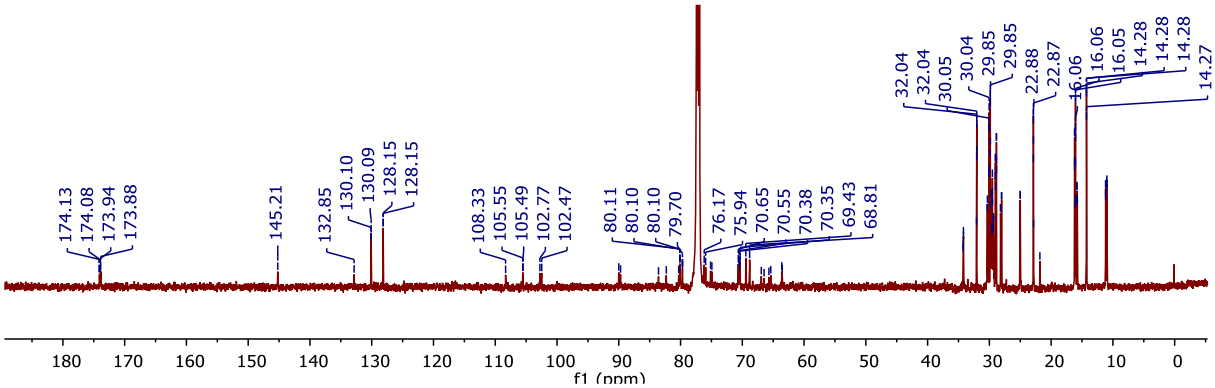
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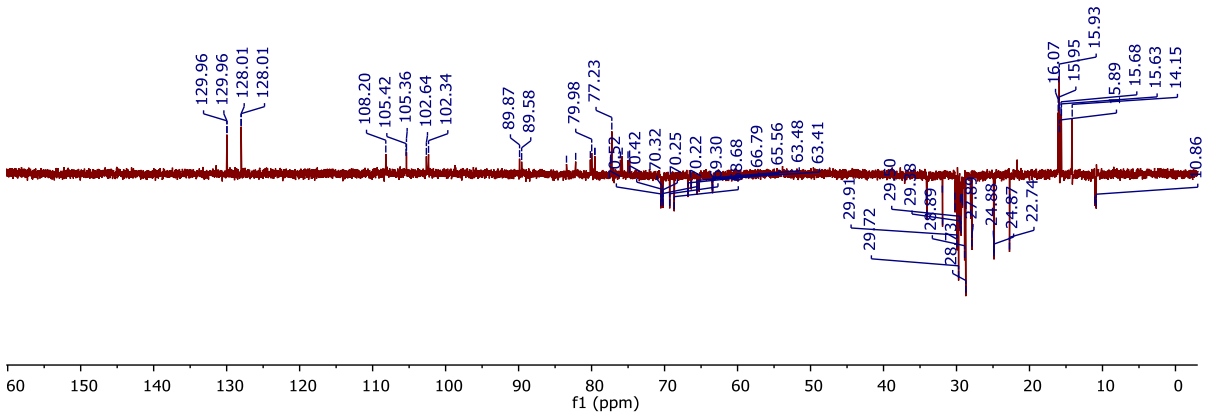
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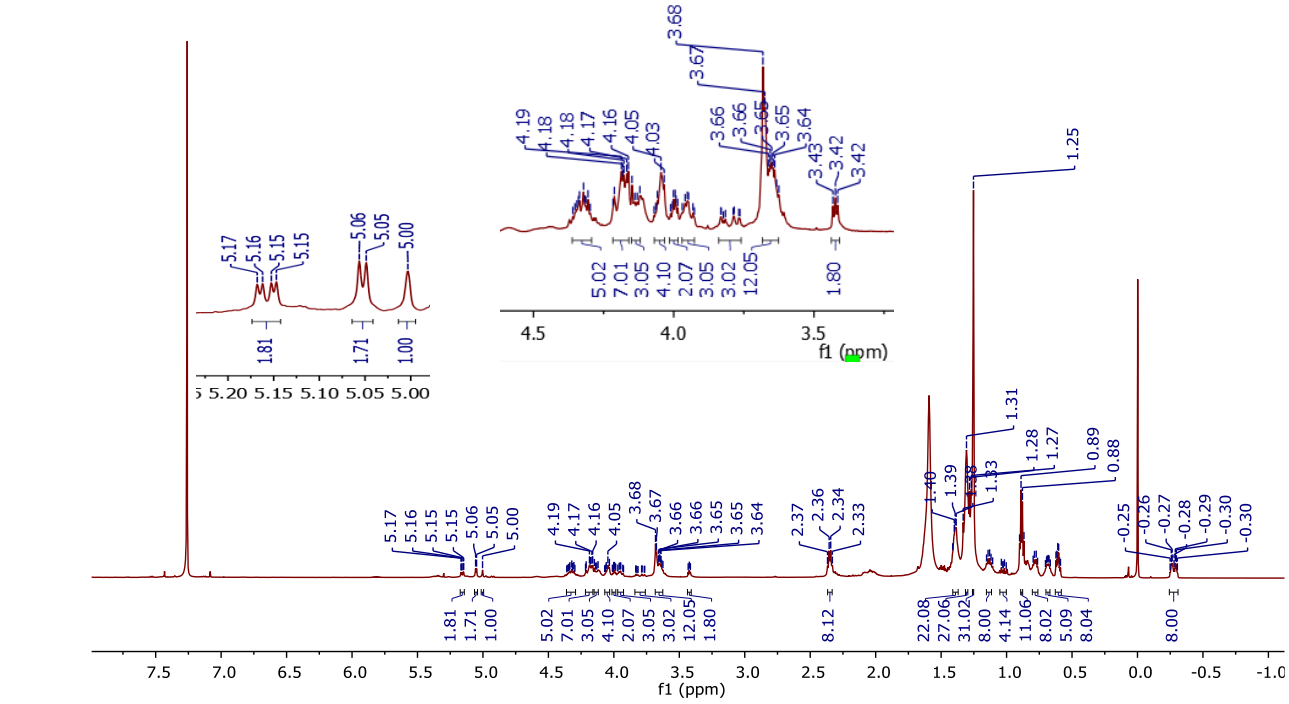
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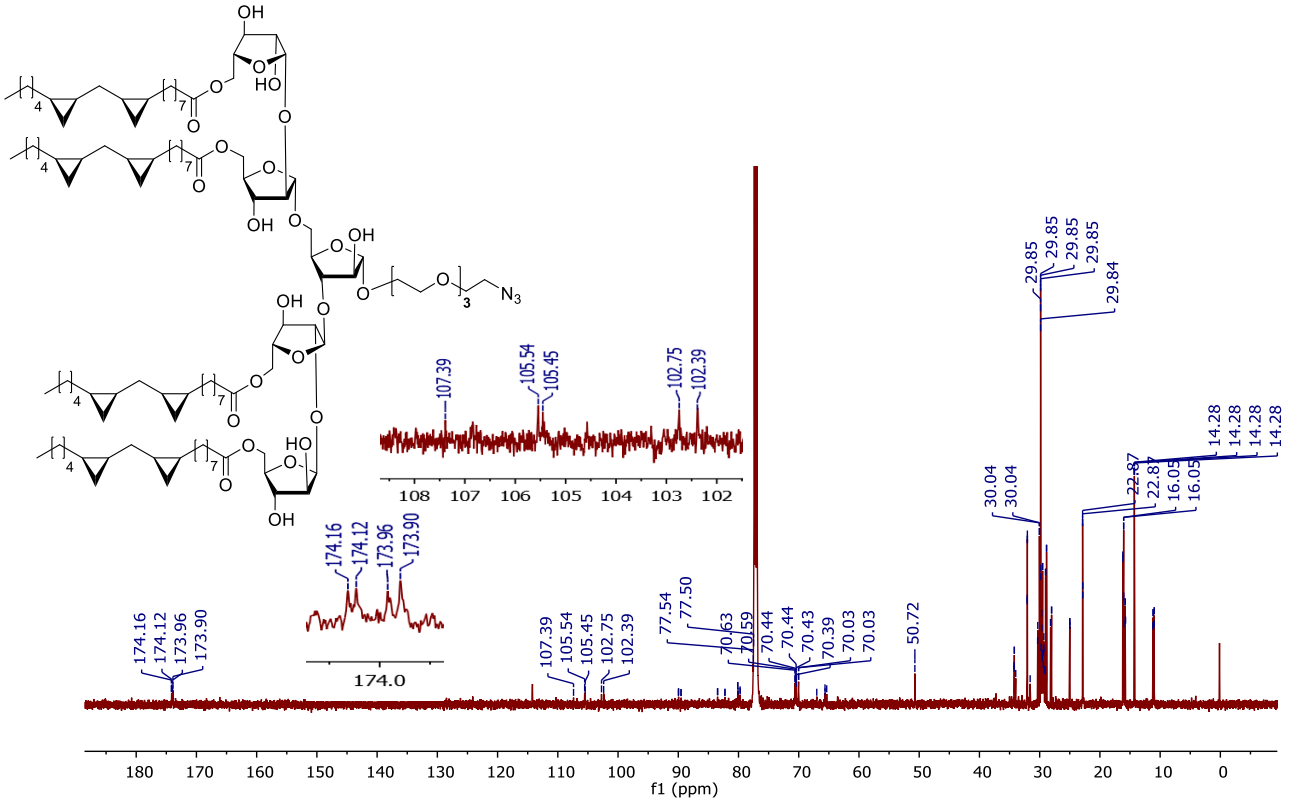
DEPT NMR Spectrum (100.53 MHz, $CDCl_3$) of compound **82b**



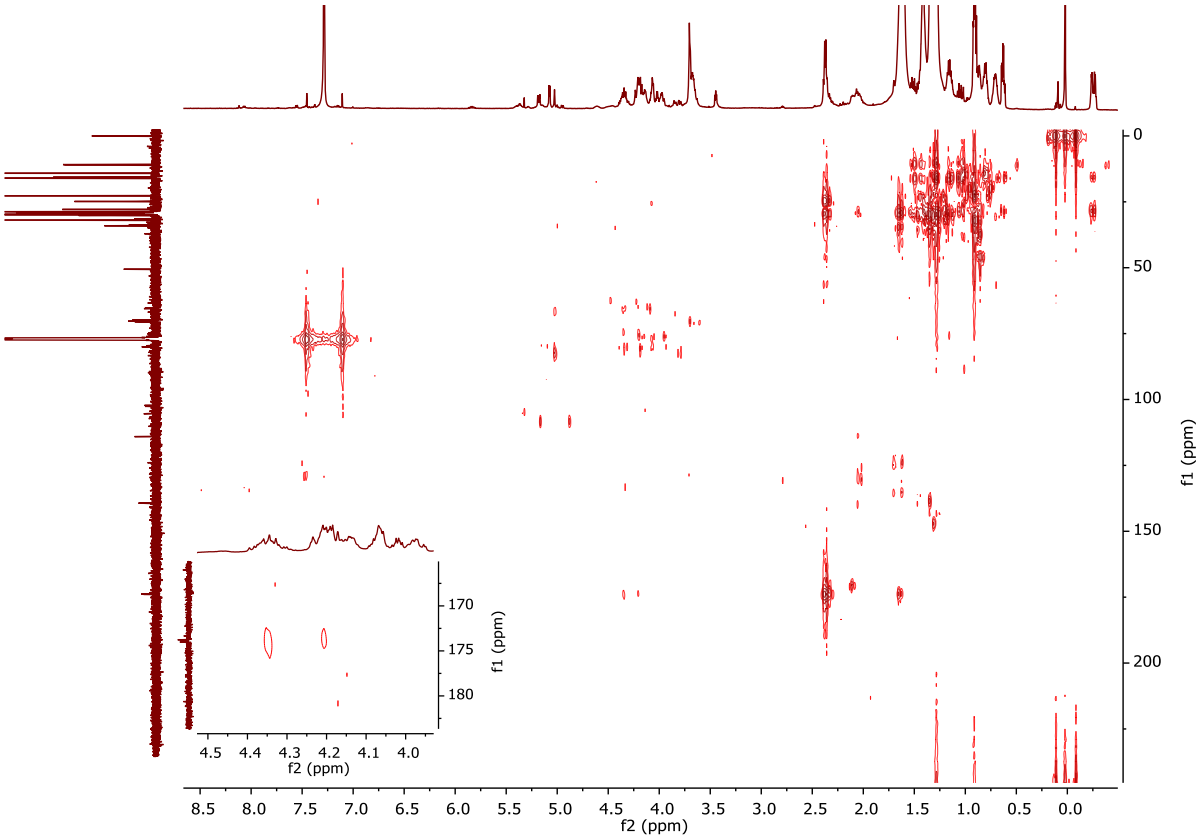
^{1}H NMR Spectrum (400.31 MHz, $CDCl_3$) of compound **83b**



^{13}C NMR Spectrum (100.53 MHz, $CDCl_3$) of compound **83b**



HMBC NMR of compound **83b**



Chapter 3

Self-assembly analysis of glycolipid library by using Transmission Electron Microscopy (TEM)

Chapter 3

3.1 Introduction

Mycobacterium tuberculosis (Mtb) has been recognized as the causative agent of tuberculosis since the time of Robert Koch.[1] Koch also noted that the thick, waxy cell wall of Mtb could contribute to its prolonged dormancy.[1] For decades, tuberculosis was considered a disease of the past. However, the HIV epidemic led to a significant rise in TB cases. Additionally, the emergence of antibiotic-resistant Mtb strains and the limited effectiveness of the BCG vaccine have brought TB back into focus. With nearly two million deaths annually, the World Health Organization has declared tuberculosis a global emergency.[1] In the 1980s, Brennan proposed a tentative structure of the Mtb cell wall based on mass spectrometric studies identifying two major oligosaccharides: Arabinogalactan (AG) and Lipoarabinomannan (LAM). Interestingly, arabinose in LAM/AG and galactose in AG was found to exist in the furanosyl form. Additionally, the non-reducing end of AG is capped by mycolic acids.[2]

3.2 Fine structure of arabinogalactan (AG)

Using GC-MS, NMR, and FAB MS spectroscopic techniques, a detailed analysis of the partially depolymerized polysaccharides revealed that AG primarily consists of arabinan and galactan motifs. The galactan core is made up of approximately 30 linear alternating β(1→5) and β(1→6) galactofuranoside (Gal*f*) residues[3]. Furthermore, the galactan core is extended by an arabinan chain consisting of approximately 31 arabinofuranoside (Ara*f*) units, attached to the C5 position of the β(1→6) Gal*f* unit. MS spectrometric analysis has revealed that the arabinan motifs are attached at the 8th, 10th, and 12th positions of the β(1→6) galactan core.[4] In arabinan, α(1→5) linked Ara*f* residues are arranged in a linear fashion with branching at the C3 position. It contains four 1,2-*cis* and twenty-six 1,2-*trans* interglycosidic linkages. The non-reducing end of arabinan is terminated by a unique hexa-arabinofuranosyl motif: [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 the terminal 1,2-*cis* Ara*f* and the penultimate 1,2-*trans* Ara*f* at C5-O are capped by mycolic acids.[5] In addition to the well-defined structure mentioned above, AG exhibits slight modifications that vary between species.

3.3 Structure of Mycolic acid (MA)

Stodola et al. were the first to isolate long-chain mycolic acids from Mtb extracts which are attached to the non-reducing end of branched hexa-arabinofuranosides.[3a] Later, Asselineau and

colleagues proposed that mycolic acid is composed of a β-hydroxycarboxylic acid with a long α-alkyl side chain.[3b] Additionally, mycobacterial mycolic acids can be distinguished from those of other genera by the following characteristics: (i) they contain approximately 70-90 carbon atoms with 24 carbons typically saturated at the α-branch and 40-60 carbons in the meromycolate chains and (ii) within the meromycolate chain, there are two distinctive positions occupied by double bonds, a cyclopropane ring, or oxygen-containing functional groups. Based on the presence of oxygen-containing functional groups, mycolic acids can be further classified into three subgroups. i.e. a) Mycolic acids without any oxygen-containing functional groups are referred to as α-mycolic acids. b) Mycolic acids that contain methoxy- and keto-functional groups are called methoxy- and keto-mycolic acids, respectively. α-Mycolic acid is the most abundant form, constituting over 70%, while methoxy- and keto-mycolic acids are minor components, making up 20 to 30%[6].

With a focus on fine structural details, numerous research groups have targeted the inhibition of galactofuranosyl transferases or arabinofuranosyl transferases in the biosynthesis of AG to develop novel therapeutic agents. For example, ethambutol and benzothiazinones, two drugs currently used in TB treatment, are known to block arabinan biosynthesis. Additionally, glycolipids from Mtb are currently being explored as potential targets for drug discovery. The xenobiotic nature of furanosyl forms of arabinose, galactose, and cyclopropanes in lipids raises several questions: (i) Why did Mtb choose furanoses over pyranoses? (ii) Why did Mtb select Ara*f* over other pentoses? (iii) What is the reason for the presence of rare cyclopropanes in the Mtb cell wall? (iv) Why does Mtb require two additional steps to synthesize the 1,2-*cis* Ara*f* at the non-reducing end? (v) Why didn't Mtb use 1,2-*trans* Ara*f* or 1,2-*trans* Rib*f* at the non-reducing end? (vi) Is there a connection between the arabino lipids 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 previously synthesized all possible analogs of the terminal position of *Mycobacterium tuberculosis* glycolipid mimics, followed by their physicochemical studies by exploiting modern spectroscopic and microscopic techniques.

3.4 Present work

The mycobacterial AG complex is crucial for the survival of *Mycobacterium tuberculosis* (Mtb). Although the role of mycolic acids remains underexplored, their presence at the outer cell surface

suggests they play a key role in bacterial growth within macrophages, effectively allowing the bacteria to evade the host immune system.[7] Recently, the 'flexible scaffold hypothesis' suggested that the high ring flexibility of furanose rings, compared to pyranose rings, promotes the tight packing of mycolic acids, resulting in a dense, low-permeability hydrophobic barrier that protects against foreign antibiotics.[8] To test the above hypothesis, the Lowary[9a] and Jayaraman[9b] groups independently synthesized a series of arabinofuranosides with hydrophobic lipids at the non-reducing and reducing ends, respectively. Lowary *et al.* observed in their NMR experiments that lipids have minimal impact on the furanose conformation while Jayaraman *et al.* based on their biophysical studies, claimed that hydrophobic alkyl chains are essential for mycobacterial growth. In the previous studies, the library of glycolipids was limited to exploring the impact of fatty acid chains on the sugar conformation.

In the previous chapter, we synthesized a glycolipid library consisting of 31 analogs of the terminal pentasaccharide. Instead of using the actual mycolic acid, we incorporated three different types of fatty acid components: palmitic acid (C_{16} saturated carbon chain), Linoleic acid (C_{18} with two *cis* double bonds), and a cyclopropane derivative of linoleic acid (containing two *cis* cyclopropane rings). After synthesizing the glycolipids, which are the combination of a hydrophilic sugar component and a hydrophobic fatty acid component, we explored their potential for self-assembled supramolecular structures. This section of my thesis will discuss how the saturation, unsaturation, and cyclopropanation of the fatty acid chain influence the self-assembly and morphology of the glycolipids.

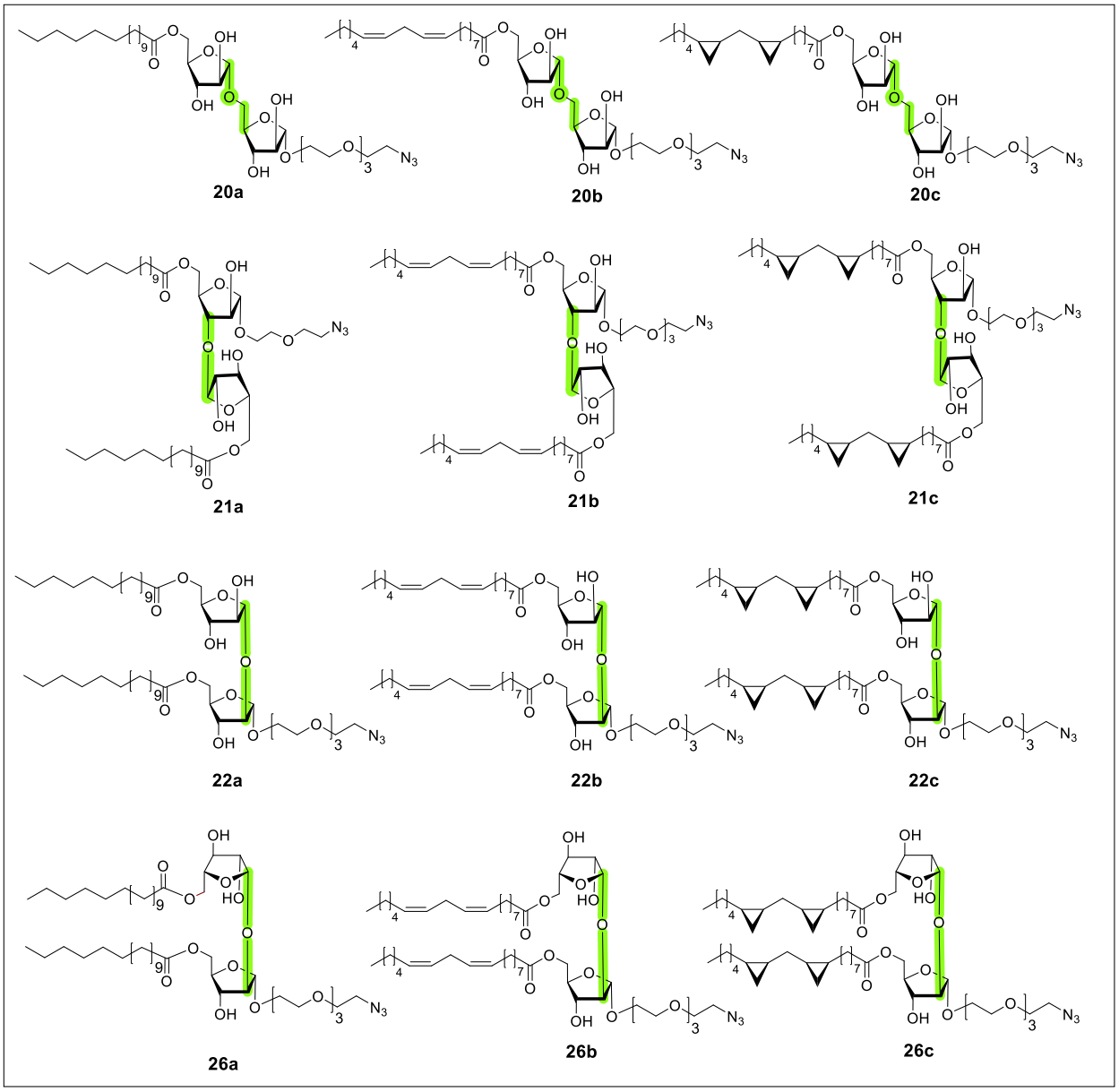
3.5 Sample preparation method

Step-1: 1 mg of the glycolipid was added to a 9:1 sonicated solution (water: acetone) and sonicated again for 5 min.

Step 2: Then drop casted (2-3 μL) aqueous suspensions of glycolipids prepared in Step 1 on glow-discharged carbon-coated copper grids. Allowed to settle for approximately 1 min, then carefully blotted away with filter paper.

Step-3: Samples were kept in a vacuum desiccator for 2 days and then images were obtained using TEM (Transmission Electron Microscopy) without negative staining.

3.6 Library of disaccharide glycolipids



The successful synthesis of our target glycolipids represents a significant step forward, as it allows us to explore their biophysical properties and potential applications in greater depth. Recent studies[9] have emphasized the fascinating ability of short biomolecular sequences to self-organize into distinct and highly ordered supramolecular structures. These structures are not only of great interest in fundamental research but also hold substantial promise in both medical and pathogenic contexts[10]. In our case, the glycolipids we have synthesized are equipped with long

lipid chains, which enhance their ability to interdigitate, meaning the lipid chains can weave into each other in a way that supports the formation of complex, hierarchical assemblies. Such assemblies may exhibit advanced self-organization, which could be highly relevant for a variety of processes, including drug delivery and membrane formation. Moreover, these intricate structures are well-suited to be visualized using transmission electron microscopy (TEM), a powerful imaging technique that can provide detailed insights into their molecular architecture and structural organization.

Our initial focus was on investigating disaccharide glycolipids, as we aimed to understand the role of specific structural components such as the terminal β (1→2)-Ara*f* linkages and the presence of cyclopropane rings in the self-assembly behavior of these molecules. To explore their assembly, we prepared transmission electron microscopy (TEM) grids by drop-casting 1 mg/mL solutions of various glycolipids (compounds **20a-20c**, **21a-21c**, **22a-22c**, and **26a-26c**) dissolved in a 10% acetone-water mixture. The samples were then analyzed using TEM without the application of negative staining[10], which preserves the natural morphology of the structures. TEM image analysis revealed distinct assembly patterns for each glycolipid. For example, glycolipid **20a** formed both particulate structures and broad, needle-like formations, indicating a certain degree of aggregation or structural ordering. In contrast, compound **21b** initially assembled into sharp, well-defined needle-like structures that, over time, transitioned into rod-shaped aggregates as they underwent further self-assembly. Additionally, glycolipid **20c** exhibited a more defined, oval-shaped morphology, suggesting a different mode of organization compared to the other compounds. These observations highlight the diverse ways in which the structural features of these glycolipids influence their self-assembly and provide important insights into their potential use in nanotechnology or biomedical applications.

Compounds **20a-20c** (Figure 1) displayed relatively few supramolecular structures, indicating that their ability to self-assemble into well-defined aggregates was limited or less pronounced compared to other glycolipids in our study. In contrast, glycolipids **21a-21c** (Figure 2) exhibited clearly defined and well-organized self-assembled structures, suggesting that these compounds possess a stronger propensity for ordered molecular assembly. Particularly noteworthy was compound **21b**, which formed exceptionally long needle-like structures. These structures likely originated from smaller needle-like aggregates that gradually extended as the self-assembly

process progressed. This trend of forming long, ordered assemblies was also observed in glycolipids **22a-22c** (Figure 3), which displayed similar self-assembled patterns characterized by elongated, needle-shaped morphologies. Interestingly, the naturally occurring β1,2-linked disaccharide compounds **26a-26c** stood out from the rest by forming particularly impressive and highly organized supramolecular assemblies. These glycolipids exhibited more complex and well-developed structures, which could be attributed to the inherent stability and favorable molecular interactions associated with the β1,2 linkage. Overall, these observations underscore the significant impact of the molecular structure on the self-assembly behavior of glycolipids, with specific linkage types fostering more robust and intricate supramolecular architectures.

Compound **26a**, which incorporates a saturated lipid, primarily formed a few fine, elongated needle-like structures, suggesting that the saturation of the lipid chains may limit the diversity of the resulting supramolecular assemblies. On the other hand, compound **26b**, which contains a linoleic ester, exhibited a distinct self-assembly behavior, forming clusters of smaller, more compact needle structures. This variation may be attributed to the unsaturated nature of the linoleic ester, which could influence the packing and arrangement of the lipid molecules, leading to the formation of smaller, less-ordered aggregates. Even more striking, however, was compound **26c**, designed to mimic the mycolic acid found in *Mycobacterium tuberculosis* (Mtb). This compound displayed an extensively bushy and highly branched architecture in the TEM images (Figure 4), suggesting that the structural features of mycolic acid such as the long, branched lipid chains induce a complex and highly organized self-assembly process. The bushy morphology observed for **26c** could provide important insights into how mycolic acids in bacterial membranes contribute to the formation of unique, dense, and protective structural networks in the context of Mtb.

After observing the bushy, branched architectures formed by compound **26c**, which contains a 1,2-*cis* glycosidic linkage and a cis cyclopropane, we were prompted to investigate how changing the configuration of the cyclopropane would affect the self-assembly behavior. Specifically, we were interested in exploring the morphology that would emerge if the cis cyclopropane were replaced with a trans cyclopropane. To address this, we synthesized compound **C10**, which retains the 1,2-*cis* glycosidic linkage but incorporates a trans cyclopropane. This modification was introduced to probe the impact of the cyclopropane's geometric configuration on the

3.6.1 TEM images of **disaccharides glycolipids** having **1,5** ***trans*** glycosidic linkage with palmitic fatty acid analog (20a), Linoleic fatty acid analog (20b), and Cyclopropane derivative of Linoleic acid analog (20c)

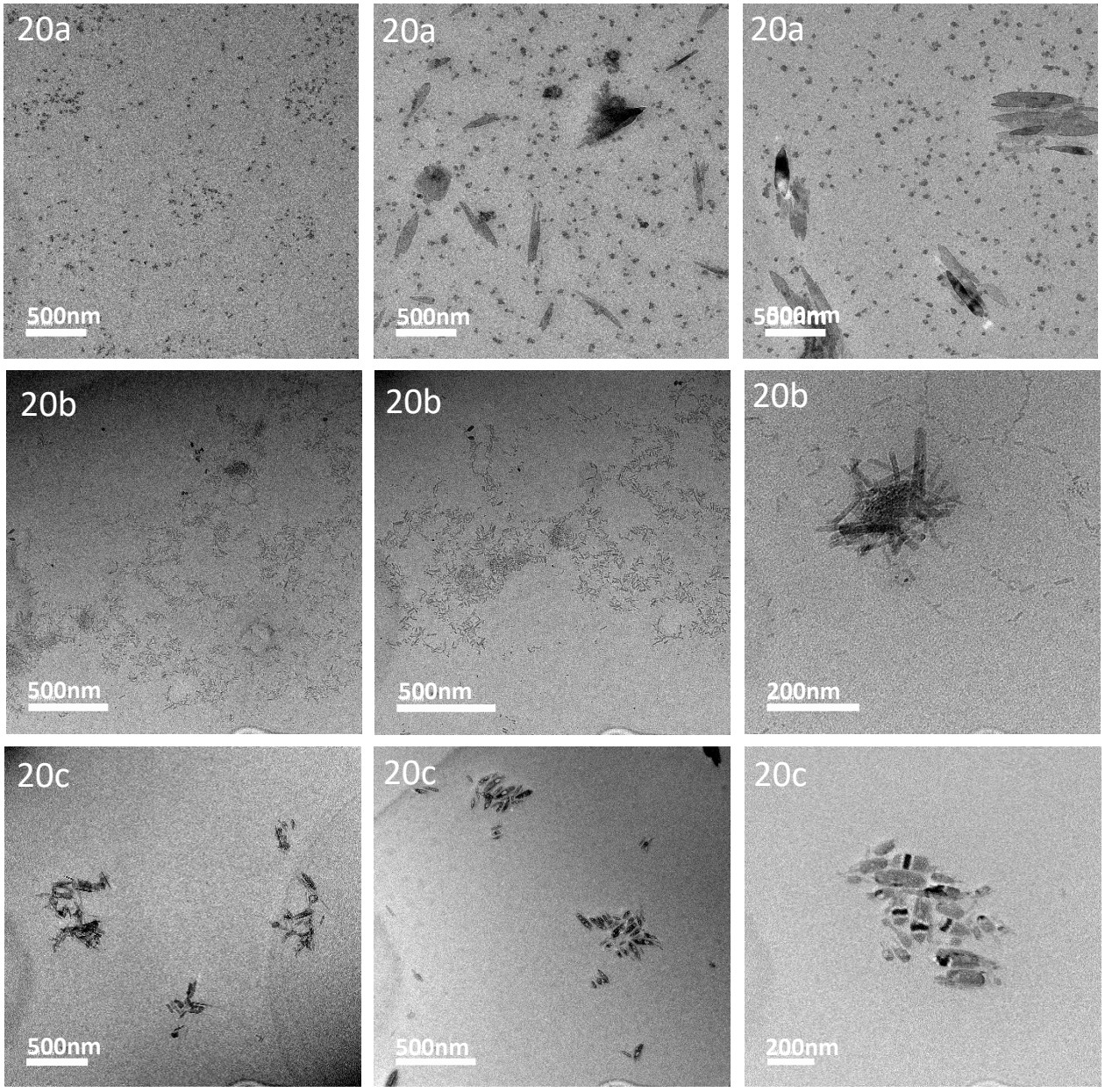


Figure 1- Representative TEM images of 20a, 20b, and 20c from aqueous suspension 1mg/mL in Acetone: Milli-Q water (1:9)

supramolecular organization of the glycolipid. However, when **C10** was subjected to the same solvent conditions used for compound **26c**, no notable self-assembled structures were observed. The lack of distinct assemblies in the TEM images (Figure 5) suggests that the trans cyclopropane configuration may disrupt the molecular interactions necessary for the formation of

organized supramolecular structures, in contrast to the cis cyclopropane found in **26c**, which facilitates the formation of the complex bushy morphology.

3.6.2 TEM images of **disaccharides glycolipids** having **1,3** ***trans*** glycosidic linkage with palmitic fatty acid analog (21a), Linoleic fatty acid analog (21b) and Cyclopropane derivative of Linoleic acid analog(21c)

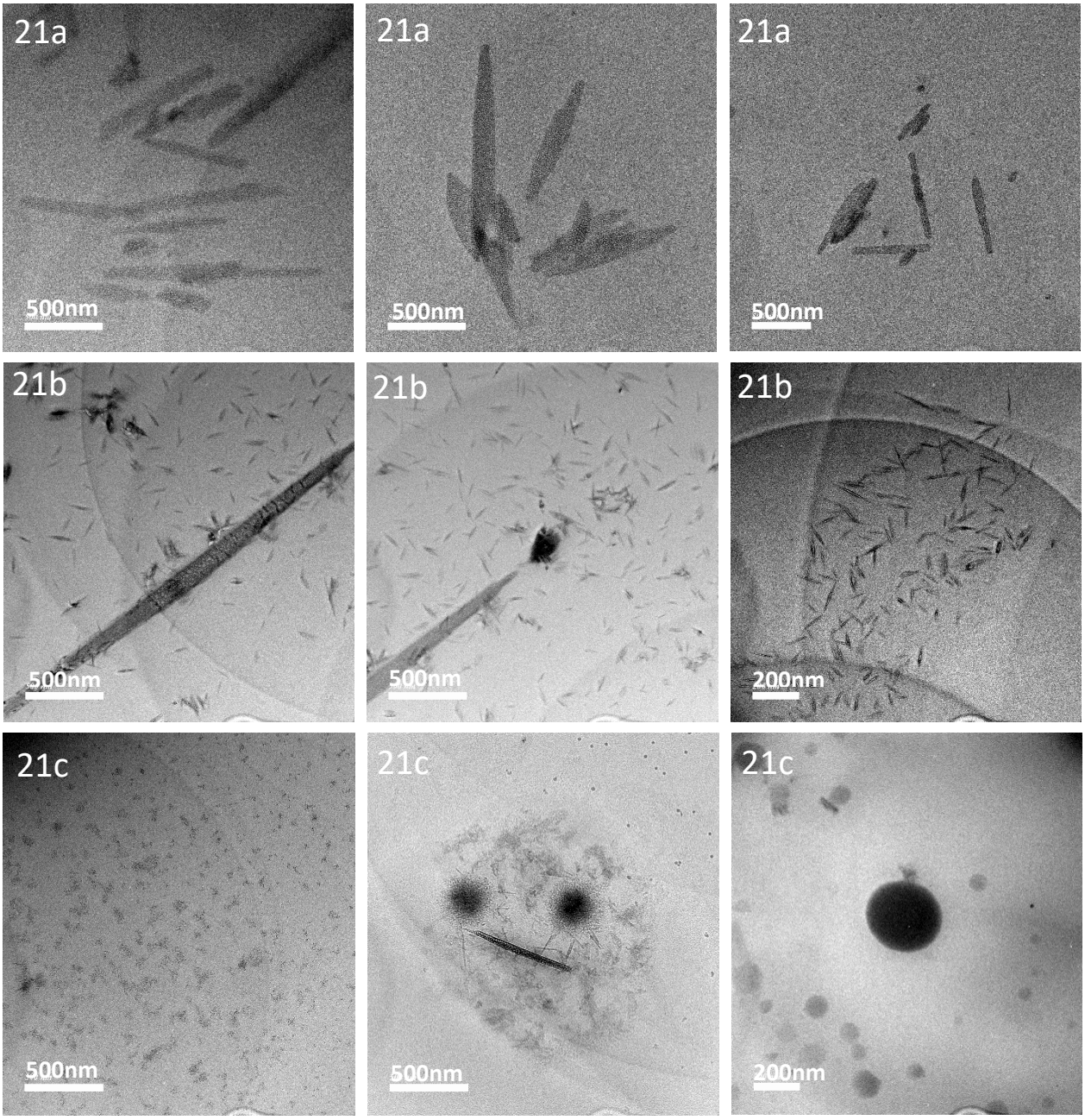


Figure 2- Representative TEM images of 21a, 21b, and 21c from aqueous suspension 1mg/mL in Acetone: Milli-Q water (1:9)

3.6.3 TEM images of **disaccharides glycolipids** having **1,2** ***trans*** glycosidic linkage with palmitic fatty acid analog (22a), Linoleic fatty acid analog (22b), and Cyclopropane derivative of Linoleic acid analog (22c)

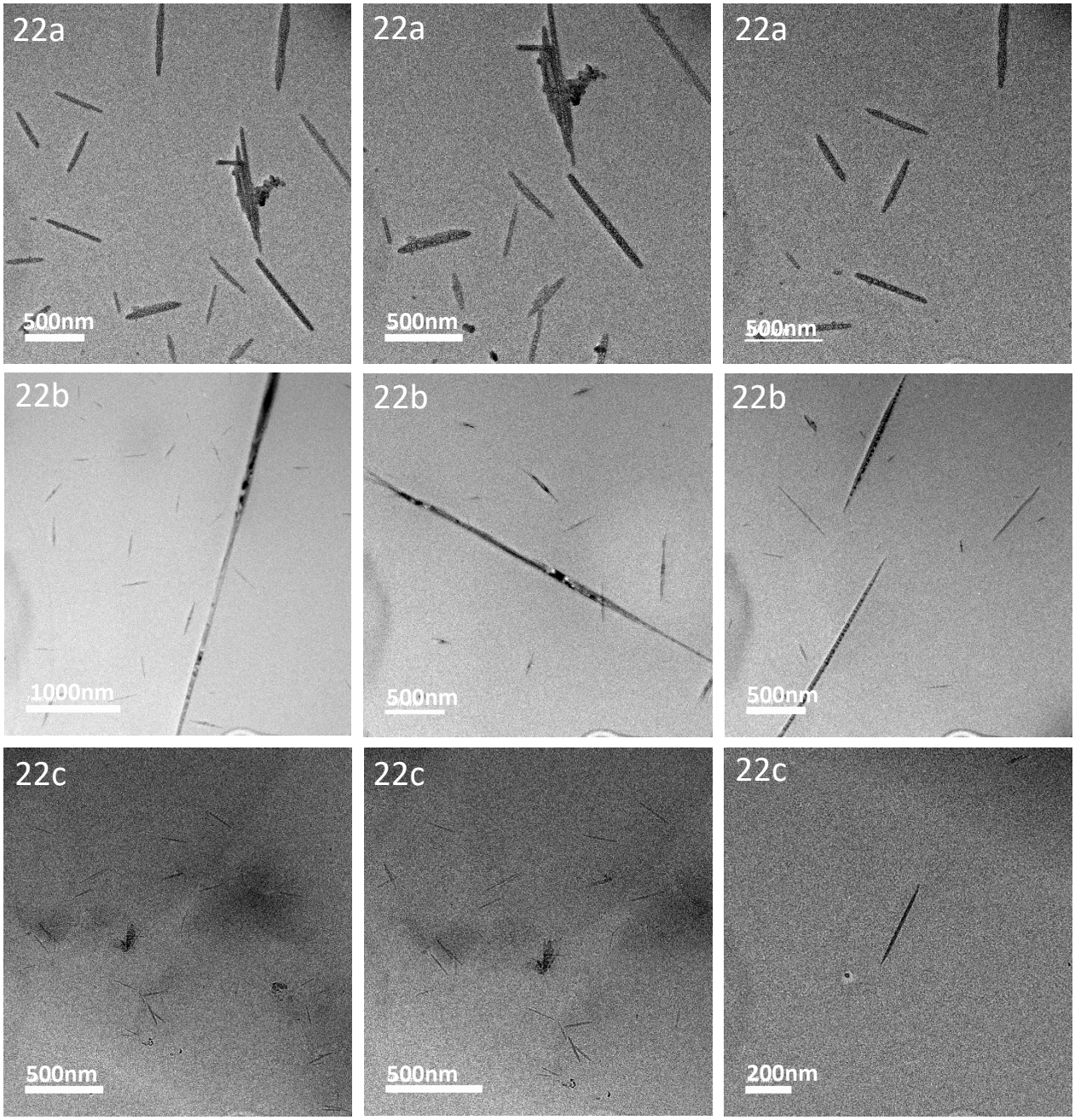


Figure 3- Representative TEM images of 22a, 22b, and 22c from aqueous suspension 1mg/mL in Acetone: Milli-Q water (1:9)

3.6.4 TEM images of **disaccharides glycolipids** having **1,2** ***cis*** glycosidic linkage with palmitic fatty acid analog (26a), Linoleic fatty acid analog (26a), and Cyclopropane derivative of Linoleic acid analog (26a)

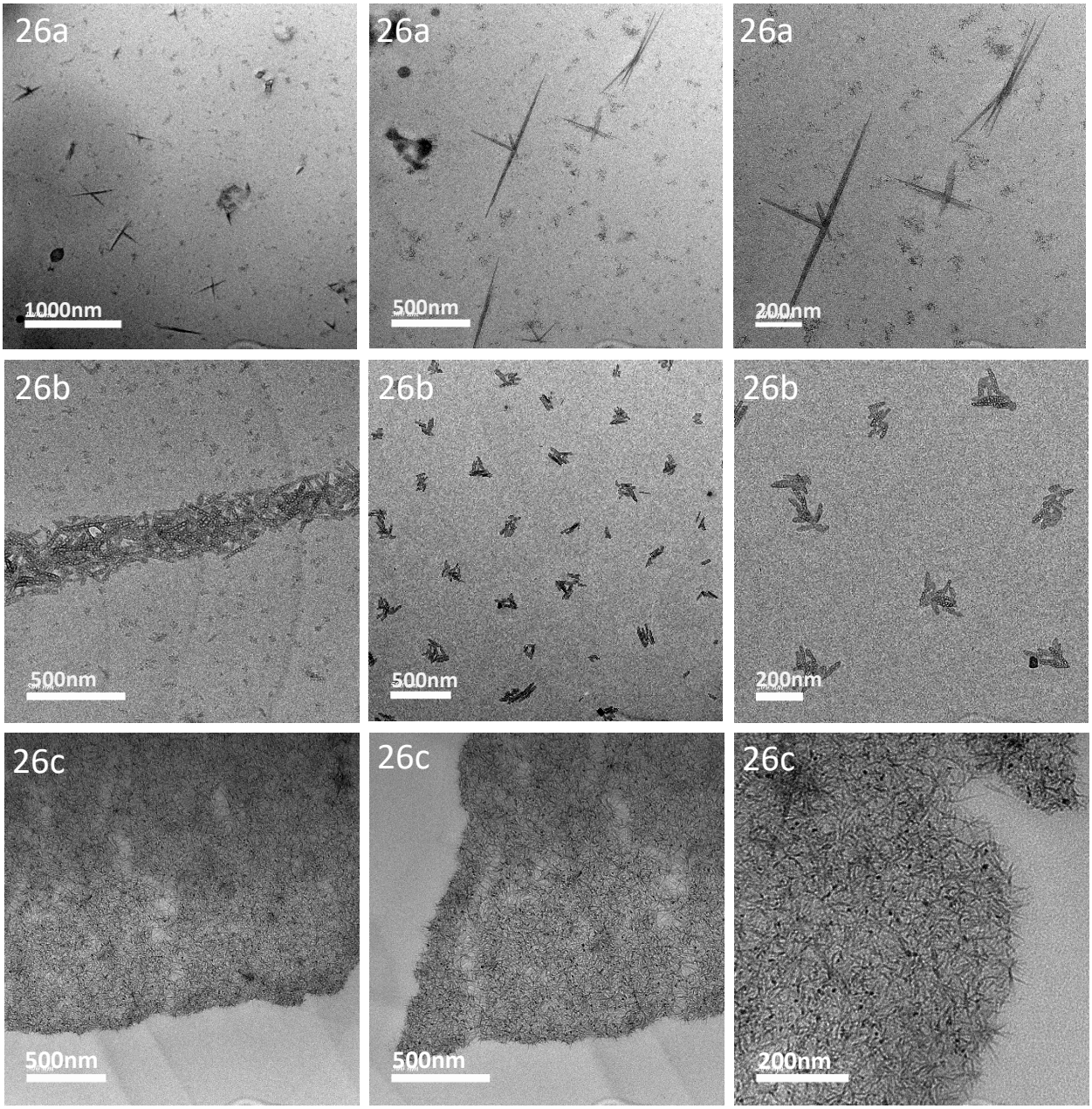


Figure 4- Representative TEM images of 26a, 26b, and 26c from aqueous suspension 1mg/mL in Acetone: Milli-Q water (1:9)

In the case of 1,2 *cis* disaccharide glycolipids, after achieving self-assembly in the Acetone: MilliQ system, it would be intriguing to explore the effect of other solvent conditions on the self-assembly structure. To investigate this, compounds **26a**-**26c** were subjected to THF: MilliQ (1:9)

and Dioxane: MilliQ (1:9) solvent systems. Compound **26a** forms small, thread-like structures in the THF: MilliQ (1:9) system. However, in the Dioxane: MilliQ (1:9) system, **26a** displays poorly defined aggregated structures (Figure-7). Compound **26b** forms small needle-like aggregates in both solvent systems (Figure-8). On the other hand, compound **26c** forms long, intertwined thread-like structures in the THF: MilliQ (1:9) system and exhibits aggregation in the Dioxane: MilliQ solvent system. In all three solvent conditions, Acetone: MilliQ proved to be the most effective (Figure-9). Therefore, for tri-, tetra-, and penta-glycolipids, all self-assembly experiments were conducted using this solvent system.

3.7 Disaccharide glycolipids have a 1,2 *cis* glycosidic linkage and a *trans* cyclopropane ring in the fatty acid part.

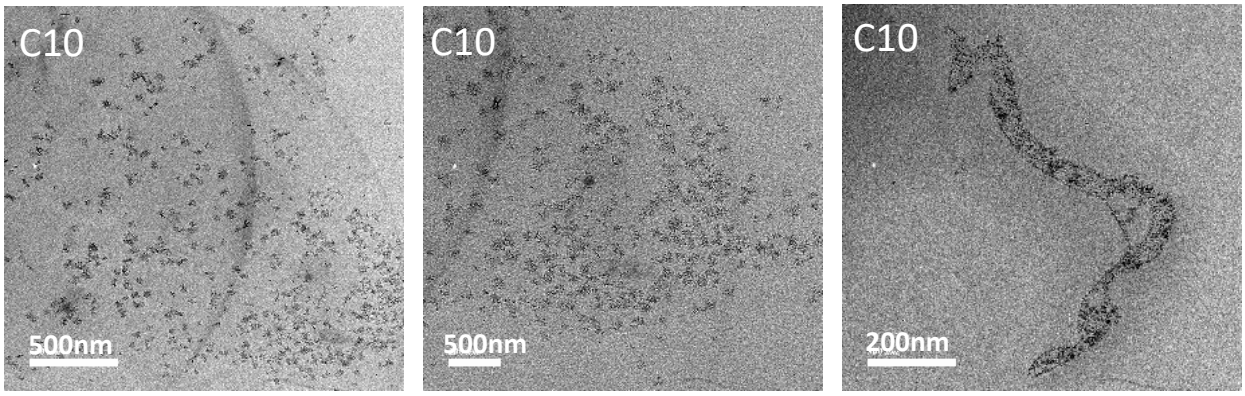


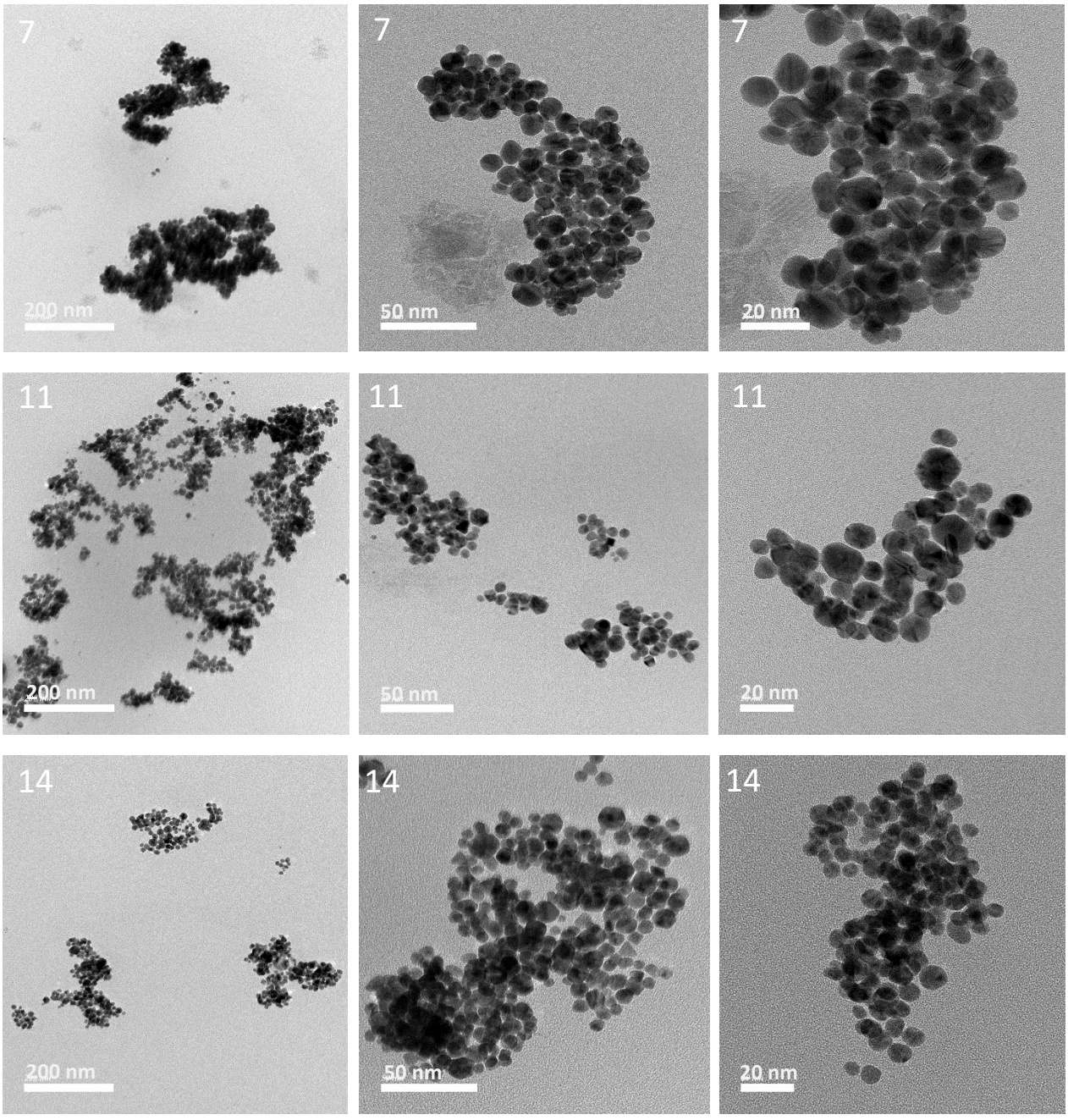
Figure 5- Representative TEM images of **C10** in Acetone: Milli-Q water (1:9), 1mg/mL **(A, B, C** (scalebar 500nm, 500nm, 200nm respectively).

After initially observing the self-assembly structures of various disaccharide glycolipids, we became intrigued by the underlying mechanisms that drive the formation of their unique three-dimensional architectures. To gain a deeper understanding of the factors influencing these structures, we aimed to explore how different glycosidic linkages might affect their self-assembly behavior. As part of this investigation, we focused on compounds **7**, **11**, **14**, and **23** four disaccharides that feature distinct glycosidic linkages but do not contain fatty acid components. By examining these compounds, we sought to isolate the influence of the glycosidic bond structure on the formation of supramolecular assemblies.

In a control experiment, we examined the self-assembly behavior of glycans **7**, **11**, **14**, and **23**, each possessing different intra-abinofuranosidic linkages, under identical experimental conditions. TEM images of these compounds showed no significant changes in their

morphological characteristics, indicating that the variations in glycosidic linkages alone did not have a substantial impact on the self-assembly process.

3.8.1 Disaccharide having 1-5, 1-3, 1-2 *trans* and 1-2 *cis* glycosidic linkage



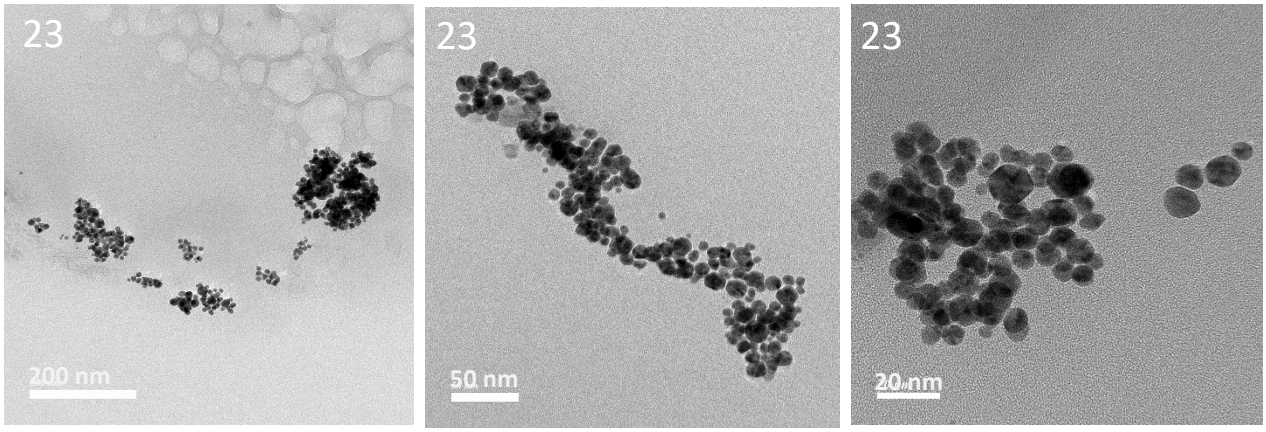


Figure 6-Representative TEM images of **7, 11, 14, 23** in Acetone: Milli-Q water (1:9), 1mg/mL

3.9 Disaccharide glycolipids having 1,2 *cis* glycosidic linkage in a different solvent system

3.9.1 TEM images of **disaccharides glycolipids** having 1,2 *cis* glycosidic linkage with palmitic fatty acid analog (26a).

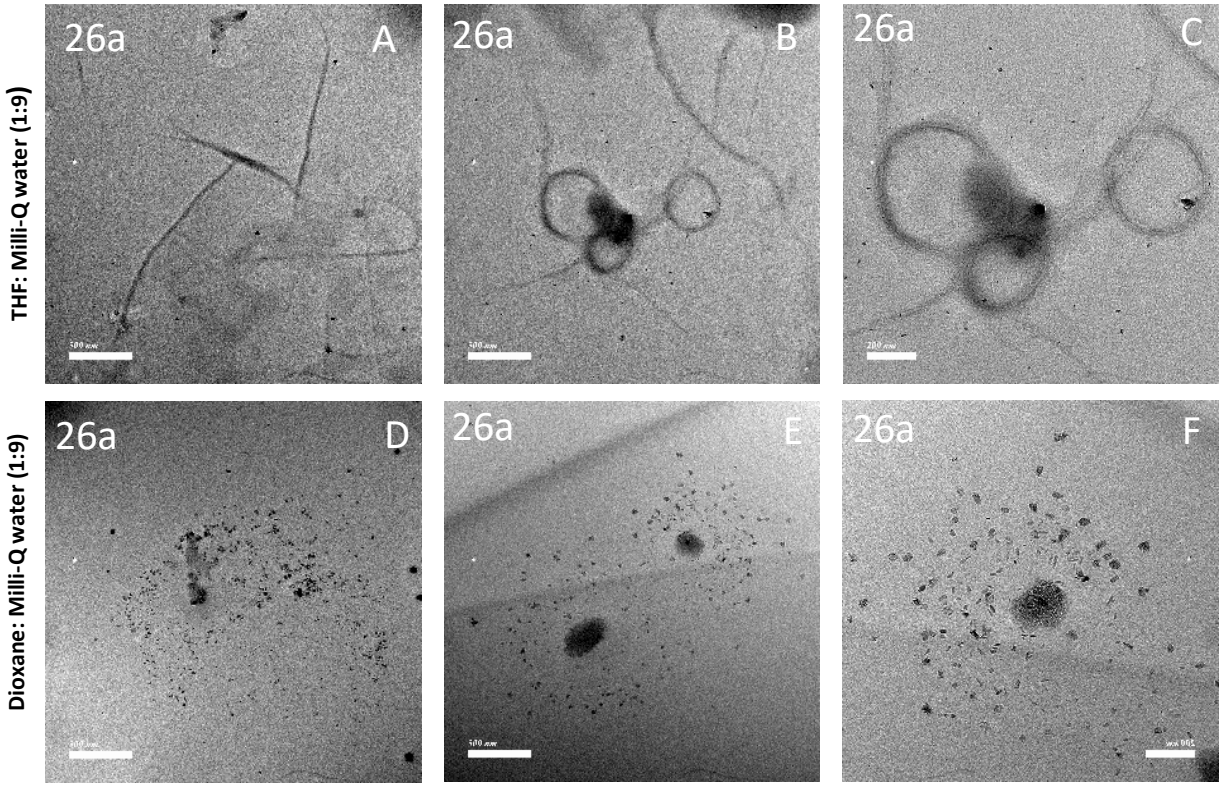


Figure 7- Representative TEM images of **26a** in THF: Milli-Q water (1:9), 1mg/mL **(A, B, C** (scalebar 500nm, 500nm, 200nm respectively) and **26a** in Dioxane: Milli-Q water (1:9), 1mg/mL **(D, E, F** (scalebar 500nm, 500nm, 200nm respectively)

3.9.2 TEM images of **disaccharides glycolipids** having 1,2 *cis* glycosidic linkage with palmitic fatty acid analog (26b).

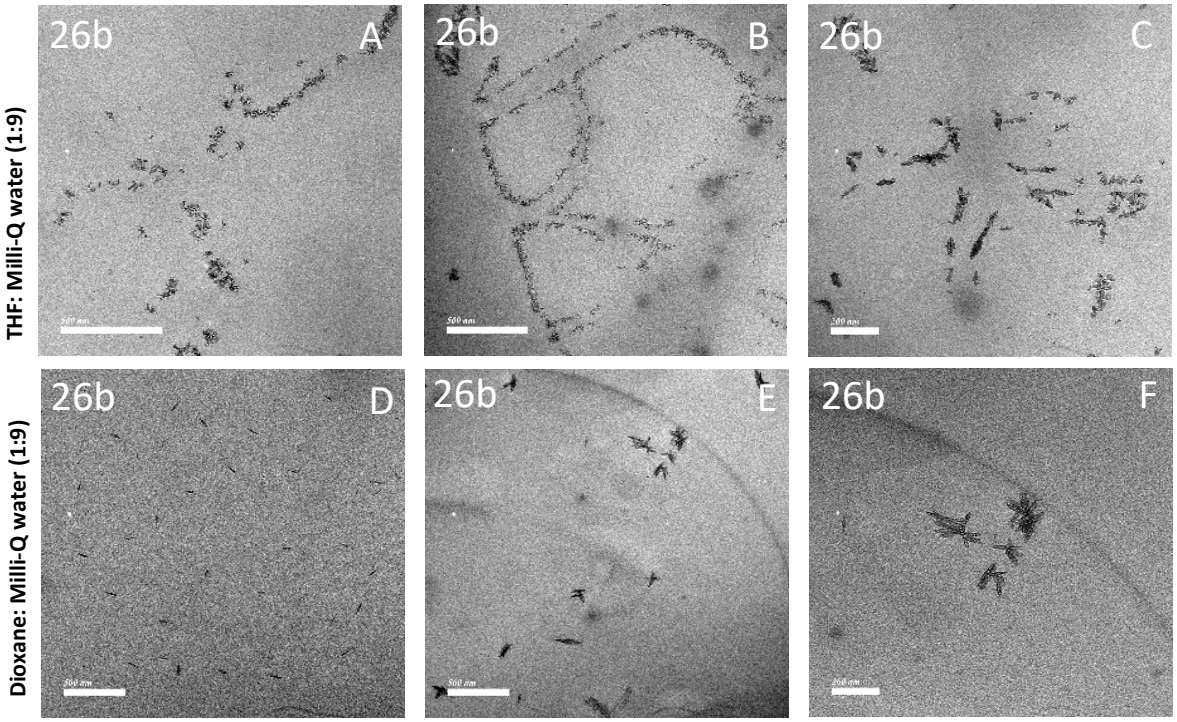


Figure 8- Representative TEM images of **26b** in THF: Milli-Q water (1:9), 1mg/mL **(A, B, C** (scalebar 500nm, 500nm, 200nm respectively) and **26b** in Dioxane: Milli-Q water (1:9), 1mg/mL **(D, E, F** (scalebar 500nm, 500nm, 200nm respectively)

These findings suggest that the specific structural features found in other glycolipids, such as the β1,2-Ara*f* linkage and the presence of a cyclopropanated lipid component, are critical for promoting more effective self-assembly. The β1,2-Araf linkage, in particular, appears to play a key role in facilitating the interdigitation of lipid chains, while the cyclopropane ring contributes to the balance between hydrophilicity and hydrophobicity within the structure. This balance is essential for enabling the formation of stable, robust self-assembled structures that can maintain their integrity and order. The results from this control experiment (Figure 6) underscore the importance of these specific molecular components in driving the formation of complex, well-organized supramolecular assemblies.

3.9.2 TEM images of **disaccharides glycolipids** having 1,2 *cis* glycosidic linkage with palmitic fatty acid analog (26c).

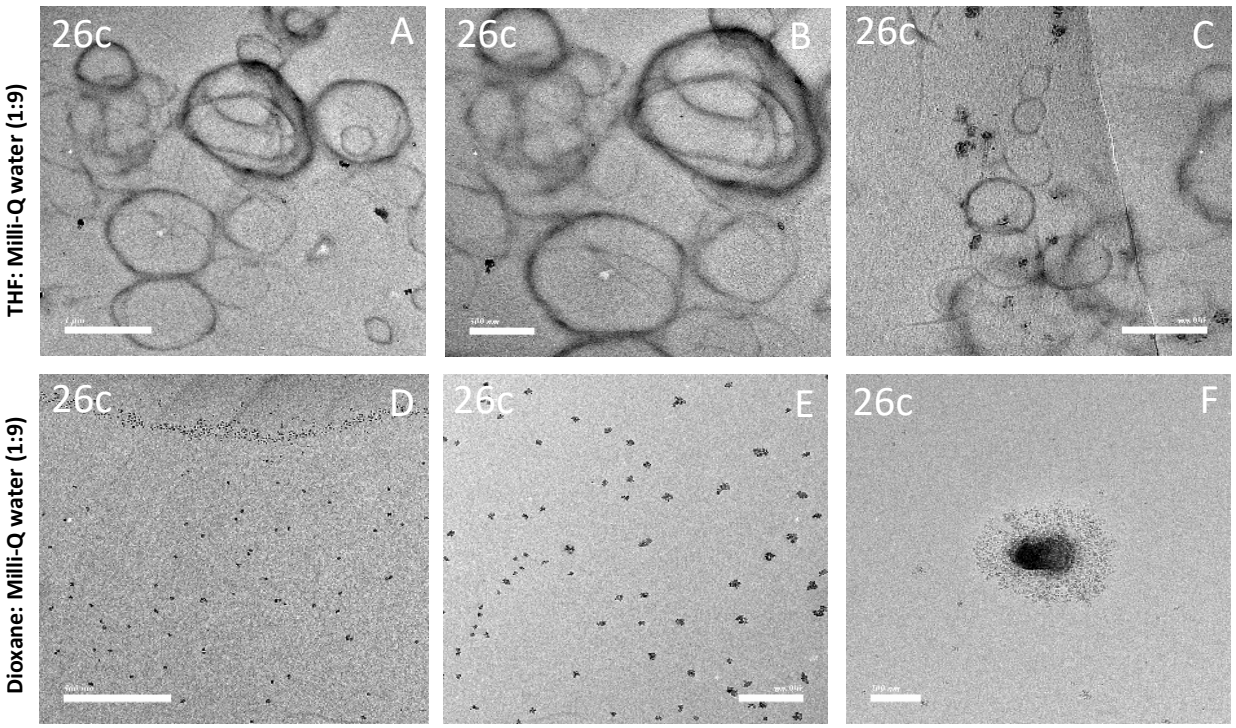
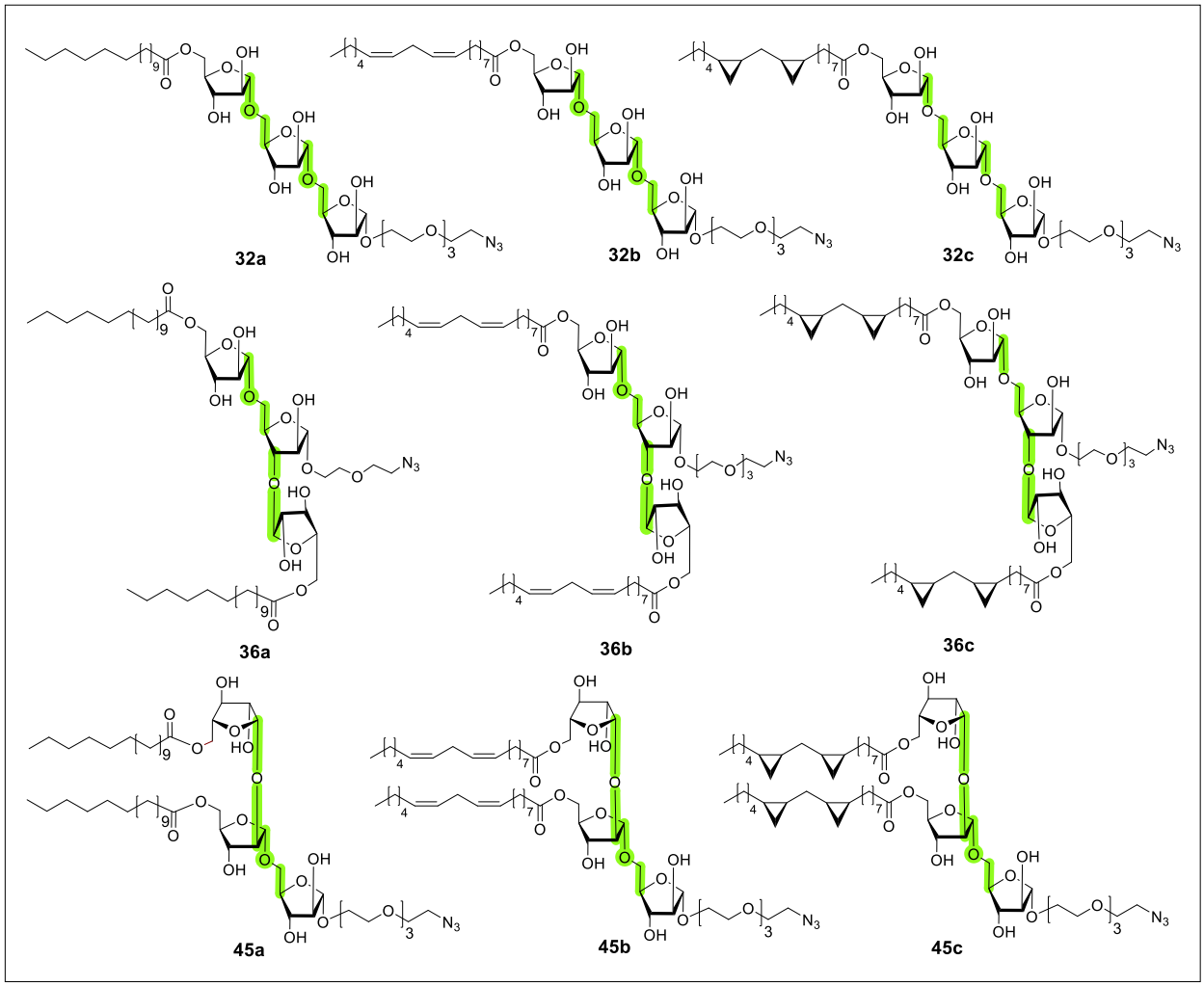


Figure 9- Representative TEM images of **26c** in THF: Milli-Q water (1:9), 1mg/mL **(A, B, C** (scalebar 500nm, 500nm, 200nm respectively) and **26c** in Dioxane: Milli-Q water (1:9), 1mg/mL **(D, E, F** (scalebar 500nm, 500nm, 200nm respectively)

3.10 Library of trisaccharide glycolipids



We further expanded our investigation to include trisaccharide glycolipids (**32a-c**, **36a-c**, **45a-c**) glycolipids. Compound **32a** exhibited a bird-like morphology, formed by the crossing of two broad needles from the center. In contrast, compound 32b displayed a thin, needle-like structure, while compound **32c**, which contains a cyclopropane fatty acid component, resembled numerous self-assembled structures merging to form a cloud-like formation (Figure-10). After examining the self-assembly of linear trisaccharides with 1,5-*trans* glycosidic linkages, we advanced to investigate branched trisaccharides containing both 1,5- and 1,3-*trans* glycosidic linkages. Compound **36a**, with two saturated fatty acid chains, appeared as small needles clustering together in a group. In contrast, compound **36b**, containing two unsaturated fatty acid chains, formed very long needles that intertwined to create a net-like structure.

3.10.1 TEM images of **trisaccharides glycolipids** having **1,5** ***trans*** glycosidic linkage with palmitic fatty acid analog (32a), Linoleic fatty acid analog (32b), and Cyclopropane derivative of Linoleic acid analog(32c)

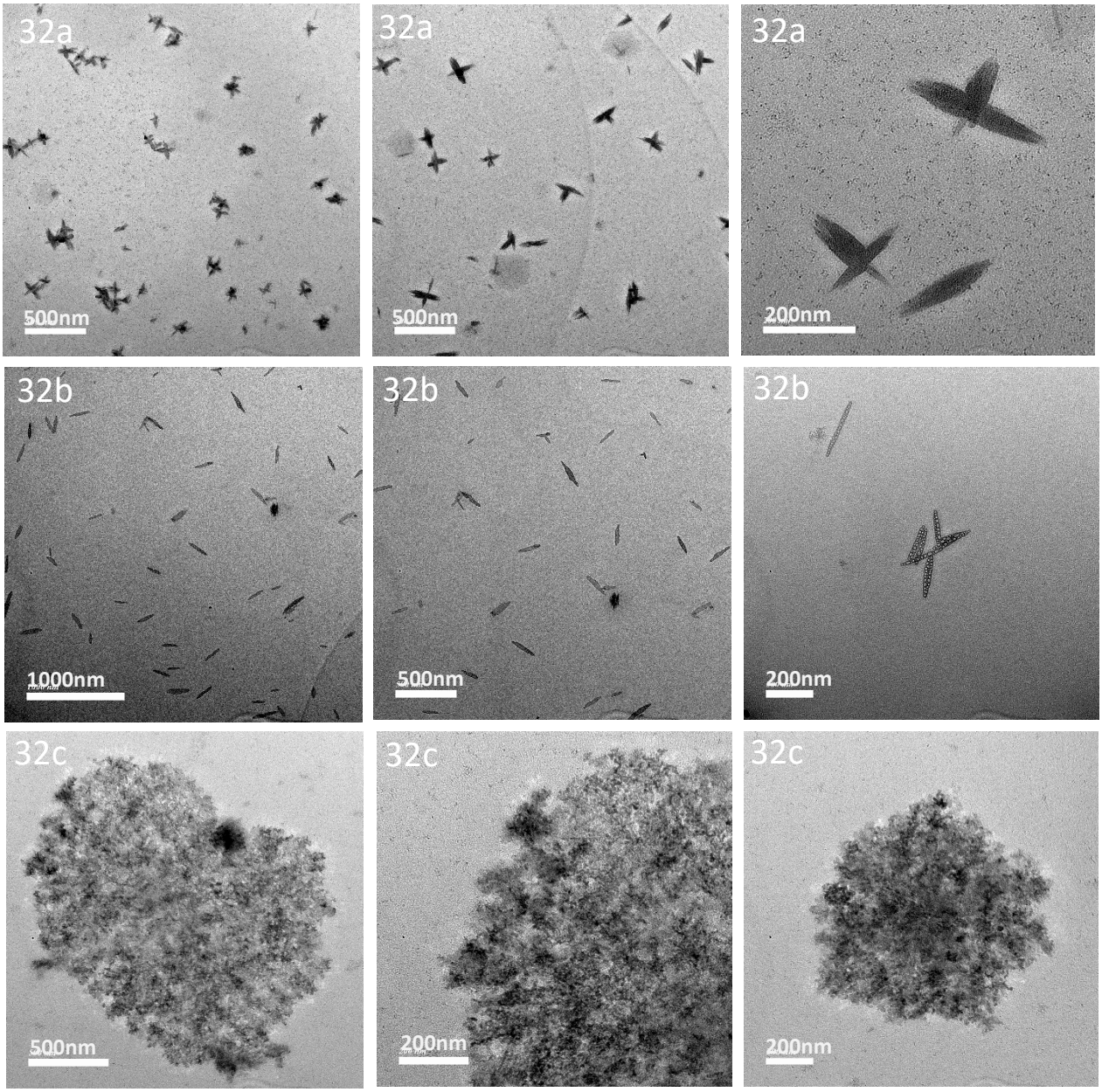


Figure 10- Representative TEM images of 32a, 32b, and 32c from aqueous suspension 1mg/mL in Acetone: Milli-Q water (1:9)

On the other hand, compound **36c**, decorated with two sets of cis cyclopropane fatty acids, exhibited a combination of small and large feather-like self-assemblies (Figure-11). In certain

regions, the structure was small, while in others, it merged to form a larger feather-like architecture.

3.10.2 TEM images of **trisaccharides glycolipids** having **1,5 *trans*** and **1,3 *trans*** glycosidic linkage with palmitic fatty acid analog (36a), Linoleic fatty acid analog (36b), and Cyclopropane derivative of Linoleic acid analog (36c)

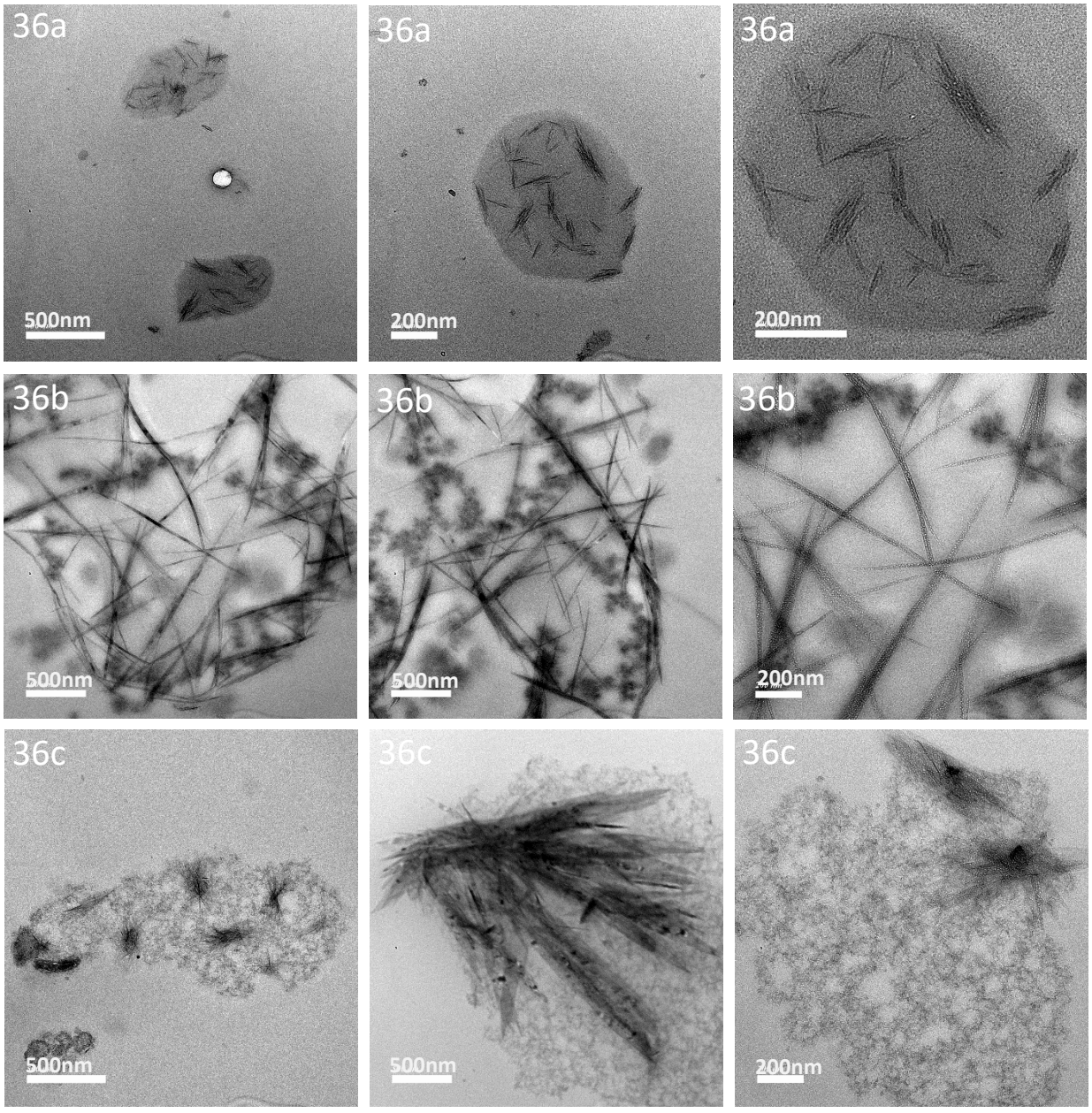


Figure 11- Representative TEM images of 36a, 36b, and 36c from aqueous suspension 1mg/mL in Acetone: Milli-Q water (1:9)

After analyzing the TEM images of branched trisaccharide glycolipids with 1,5- and 1,3-*trans* glycosidic linkages, the study progressed to investigate branched trisaccharides featuring 1,2-*cis* and 1,5-*trans* glycosidic linkages with different fatty acid components.

3.10.3 TEM images of **trisaccharide glycolipids** having **1,2 *cis*** and **1,5 *trans*** glycosidic linkage with palmitic fatty acid analog (45a), Linoleic fatty acid analog (45b), and Cyclopropane derivative of Linoleic acid analog(45c)

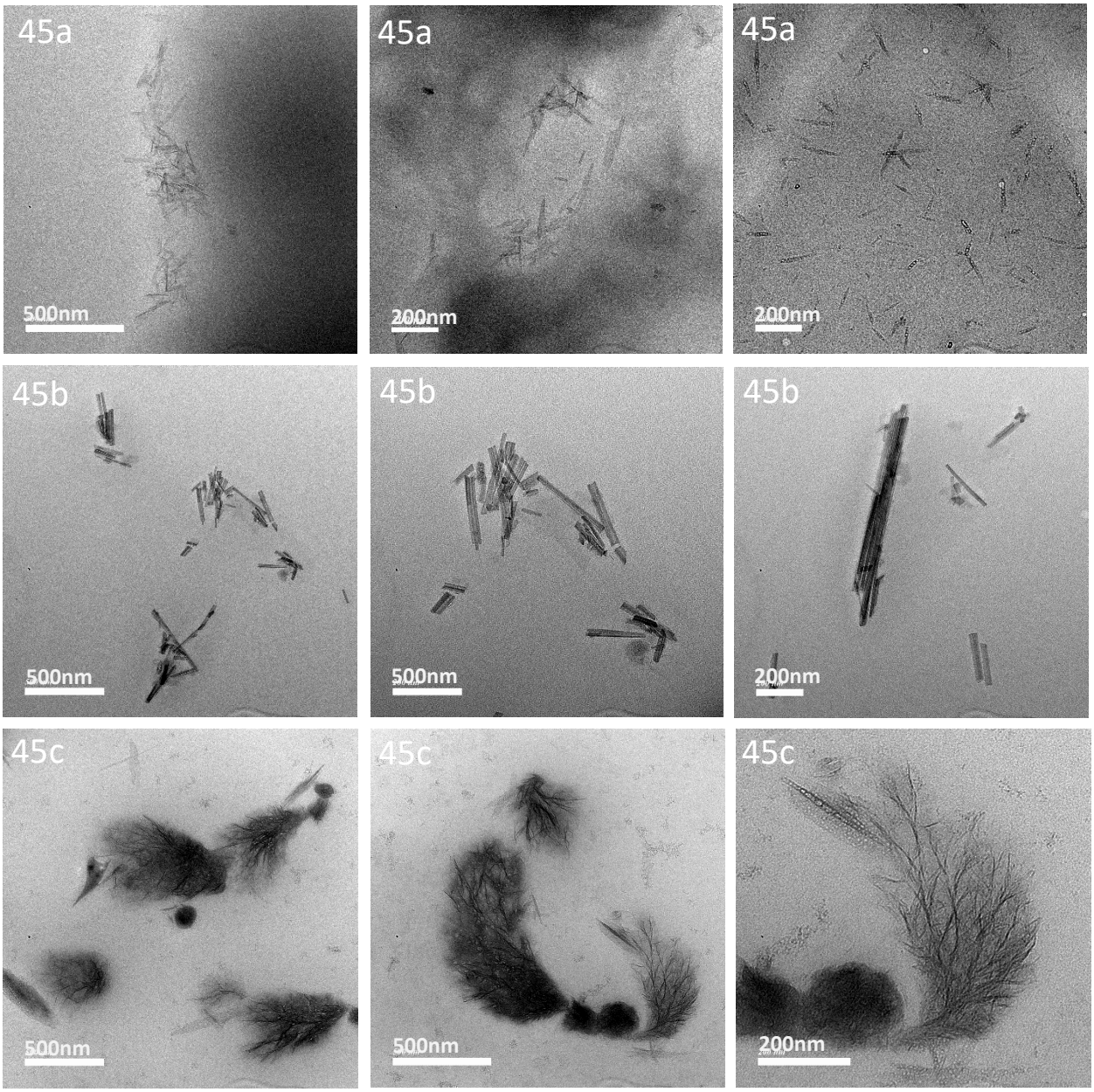
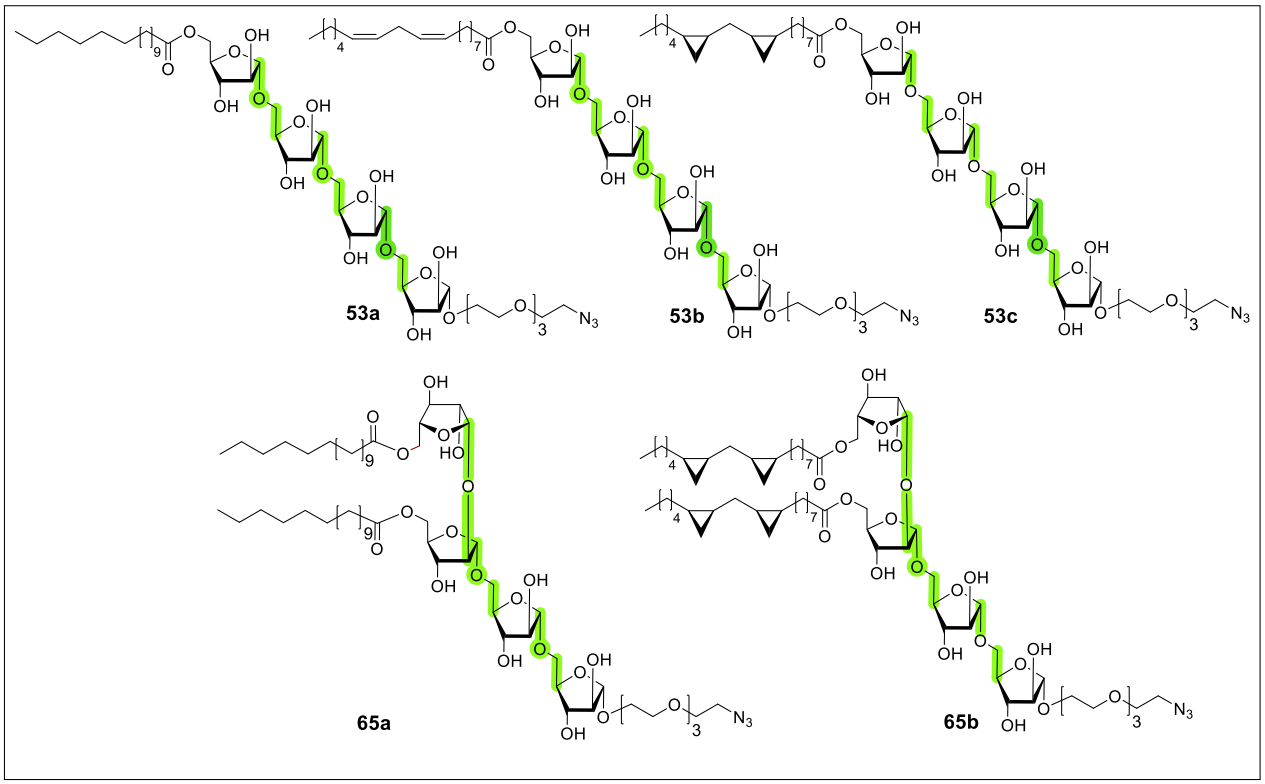


Figure 12- Representative TEM images of 45a, 45b, and 45c from aqueous suspension 1mg/mL in Acetone: Milli-Q water (1:9)

In the case of compound **45a**, which features 1,2-*cis* and 1,5-*trans* glycosidic linkages along with saturated fatty acids, the structure appeared as thin needles, well-dispersed from one another. In contrast, compound **45b**, containing unsaturated fatty acids, resembled a rod-like structure grouped in clusters. The most striking TEM images were observed in the case of **45c**, which contains a 1,2 *cis* and 1,5 *trans* glycosidic linkage along with a cyclopropanated fatty acid component. The TEM images resembled the shape of a bottlebrush flower (Figure-12). It is quite evident from the images that glycans esterified with the cyclopropanated lipid **32c**, **36c**, and **45c** formed strikingly different architectures signifying the presence of cyclopropanes.

3.11 Library of tetrasaccharide glycolipids



After successfully analyzing di- and trisaccharide glycolipids, the focus shifted to linear tetrasaccharides with 1,5-*trans* glycosidic linkages. In the case of compound **53a**, which contains saturated fatty acids, no significant changes in morphology were observed. However, glycolipid **53b** which has unsaturation, exhibited some flower-like structures alongside aggregates. On the

other hand, the linear tetrasaccharide glycolipid **53c**, featuring a cyclopropanated lipid, formed long, flat strips. The self-assembly of linear tetrasaccharide glycolipids was notably low, possibly due to the disruption of the hydrophilic and hydrophobic ratio in the glycolipids. (Figure-13)

3.11.2 TEM images of **tetrasaccharide glycolipids** having **1,5 *trans*** glycosidic linkage with palmitic fatty acid analog (53a), Linoleic fatty acid analog (53b), and Cyclopropane derivative of Linoleic acid analog (53c)

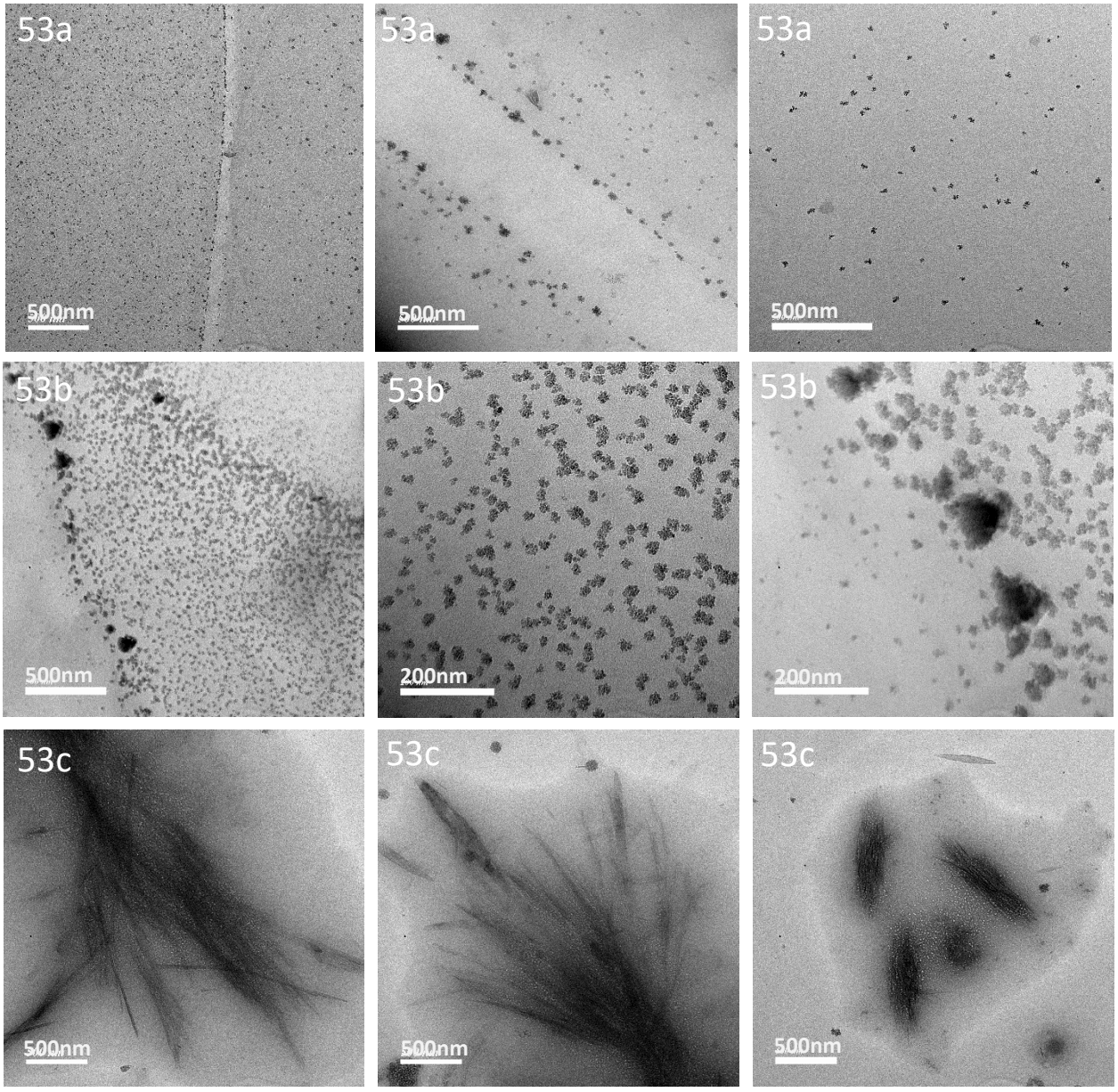


Figure 13- Representative TEM images of 53a, 53b, and 53c from aqueous suspension 1mg/mL in Acetone: Milli-Q water (1:9)

3.11.3 TEM images of **tetrasaccharide glycolipids** having **1,2 *cis*** and **1,5 *trans*** glycosidic linkage with palmitic fatty acid analog (65a) and Cyclopropane derivative of Linoleic acid analog(65b)

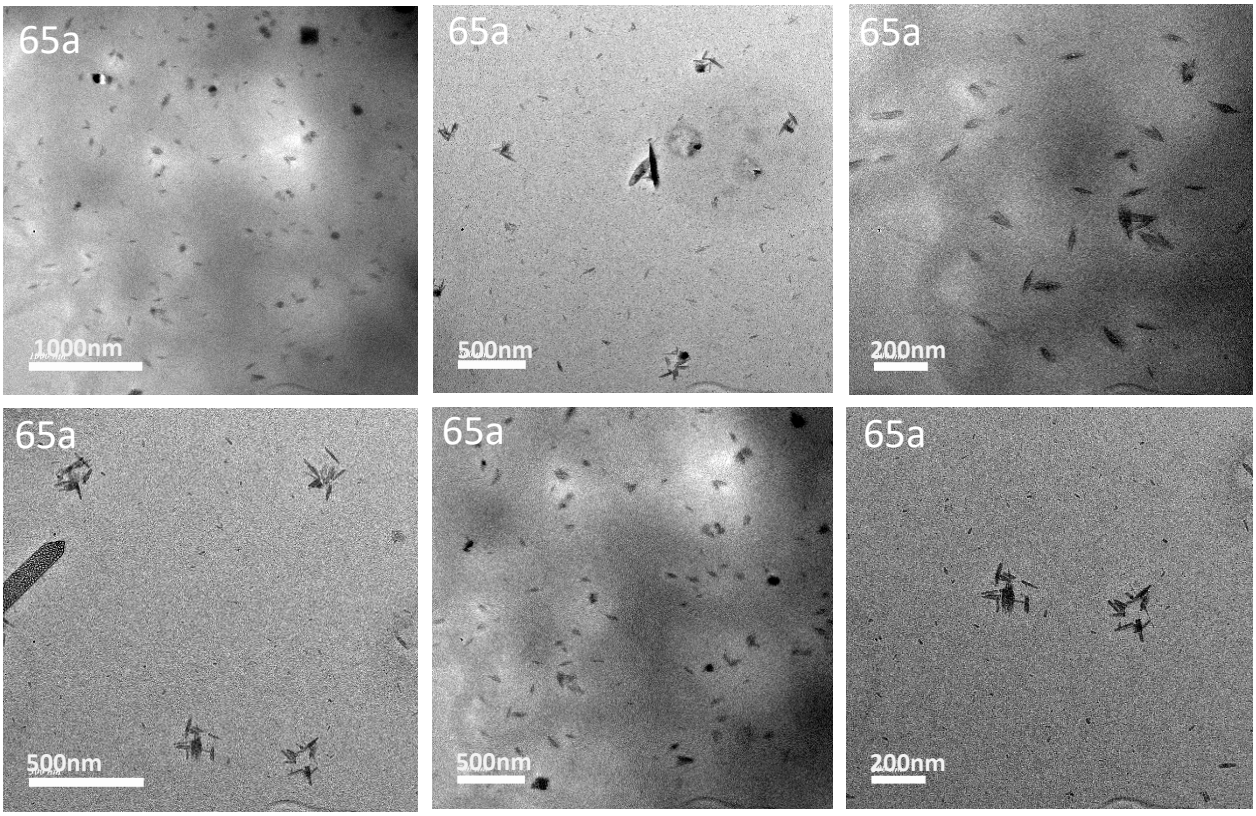


Figure 14- Representative TEM images of 65a from aqueous suspension 1mg/mL in Acetone: Milli-Q water (1:9)

In the case of **65a**, a branched tetrasaccharide featuring one 1,2 *cis* and three 1,5 *trans* glycosidic linkages, along with a saturated fatty acid in its structure, very small needle-like crystals were observed, both dispersed and grouped together. However, the size of the needles remained consistent throughout. (Figure- 14)

In the case of **65b**, a branched tetrasaccharide with one 1,2 *cis* and three 1,3 *trans* glycosidic linkages, along with a cyclopropane fatty acid component, a variety of rod-shaped structures were observed. These structures were well-dispersed and formed cage-like structures when multiple rods combined with one another. The rod self-assembly was highly pronounced, displaying a range of sizes from 200 nm to 1 micron. (Figure- 15)

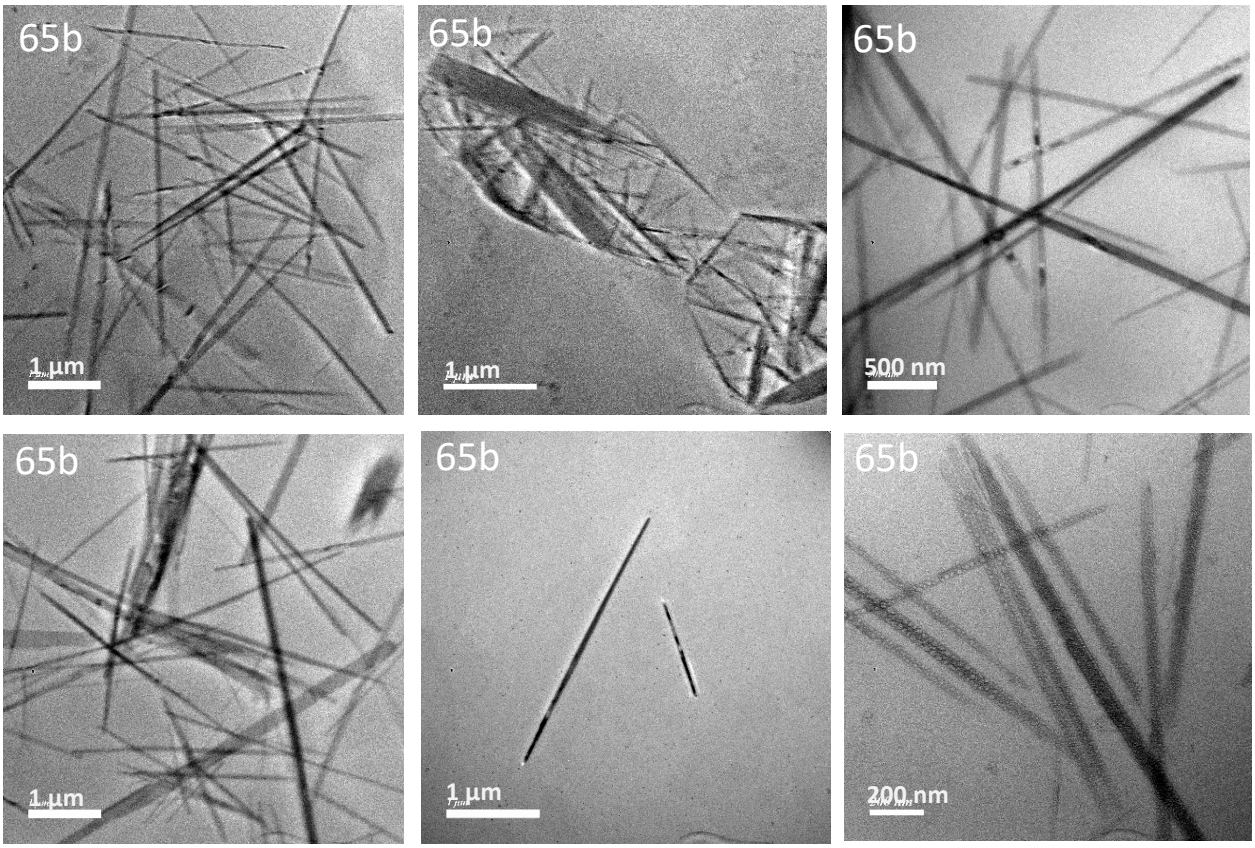
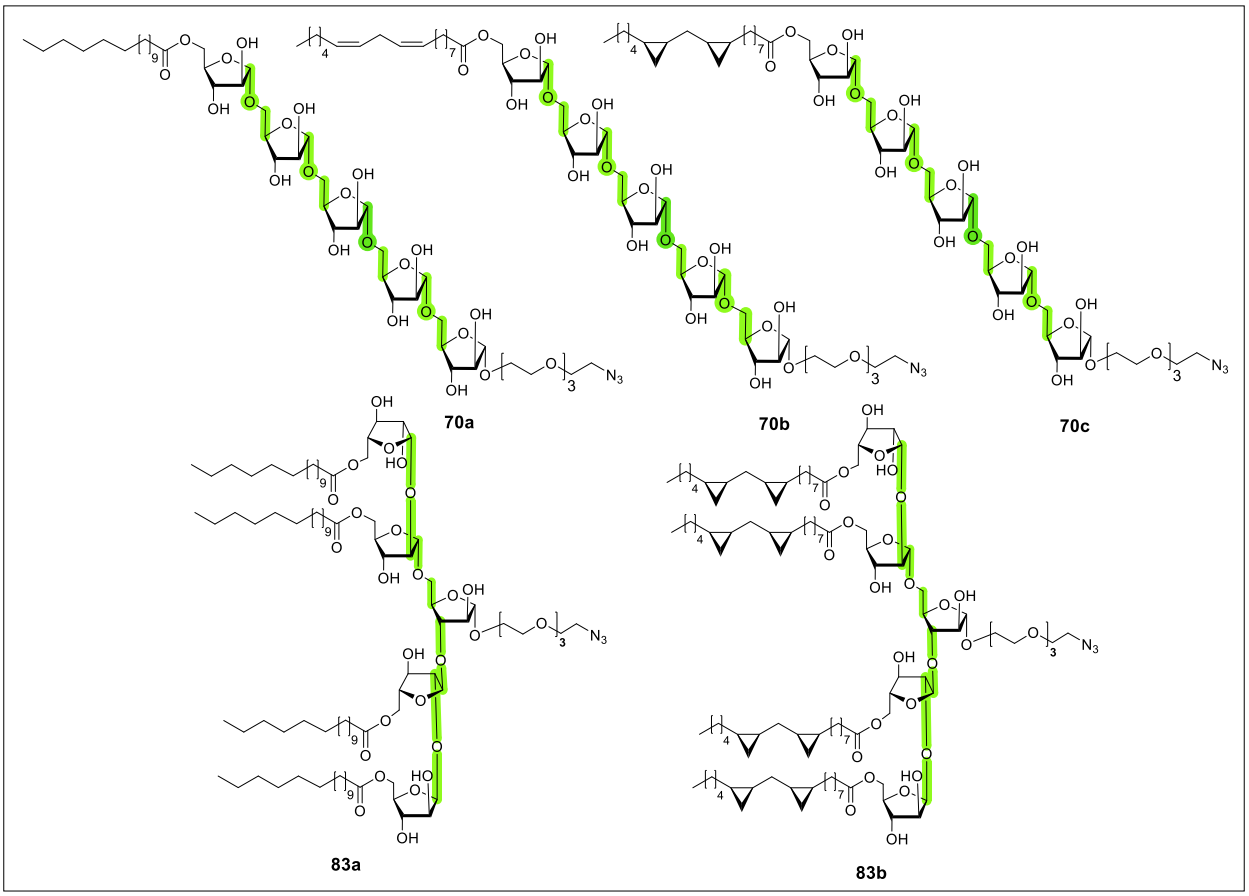


Figure 15- Representative TEM images of 65b from aqueous suspension 1mg/mL in Acetone: Milli-Q water (1:9)

Finally, after successfully analyzing the linear and branched tetrasaccharide glycolipids, the focus shifted to the linear and branched pentasaccharides, which represent the terminal motif A of *Mycobacterium tuberculosis*. In the case of compound **70a**, a linear pentasaccharide with 1,5-*trans* glycosidic linkages and saturated fatty acids, a very thin, needle-like structure was observed, uniformly distributed throughout. Compound **70b**, a linear pentasaccharide with unsaturation in the fatty acid portion, forms spherical, furry ball-like self-assembly structures. In contrast, compound **70c**, which is a linear pentasaccharide with 1,5 *trans* glycosidic linkage with cyclopropane group in the fatty acid portion, exhibited a broad bean-like morphology, appearing as a structure formed by the aggregation of multiple needle-like shapes (Figure-16). Similarly, for di-, tri-, and tetrasaccharide glycolipids, the presence of a cyclopropane group in the fatty acid portion leads to the formation of distinct architectural structures, suggesting that the cyclopropane ring has a unique effect on the self-assembly of the molecules. This effect,

however, was observed only with cis-cyclopropane, while glycolipids containing trans-cyclopropane showed no significant changes in their self-assembly.

3.12 Library of Pentasaccharide glycolipids



Finally, after successfully analyzing the TEM images of linear pentasaccharides, the study progressed to the branched pentasaccharide, which contains the terminal Motif A with two 1,2-*cis*, one 1,3-*trans*, and two 1,5-*trans* glycosidic linkages, along with saturated and cyclopropane fatty acid components in its structure. For compound **83a**, a branched pentasaccharide with four saturated fatty acid components, an asymmetrical rod-like morphology was observed, with the structures tightly packed together (Figure-17). In contrast, compound **83b**, a branched pentasaccharide containing four *cis*-cyclopropane fatty acids, displayed a clean rod-shaped morphology with varying sizes (Figure- 18). Upon analyzing the glycolipid library, ranging from disaccharides to pentasaccharides, it became clear that the effects of unsaturation and cyclopropane in the fatty

3.12.1 TEM images of **Pentasaccharides glycolipids** having **1,5 *trans*** glycosidic linkage with palmitic fatty acid analog (70a), Linoleic fatty acid (70b), and Cyclopropane derivative of Linoleic acid analog(70c)

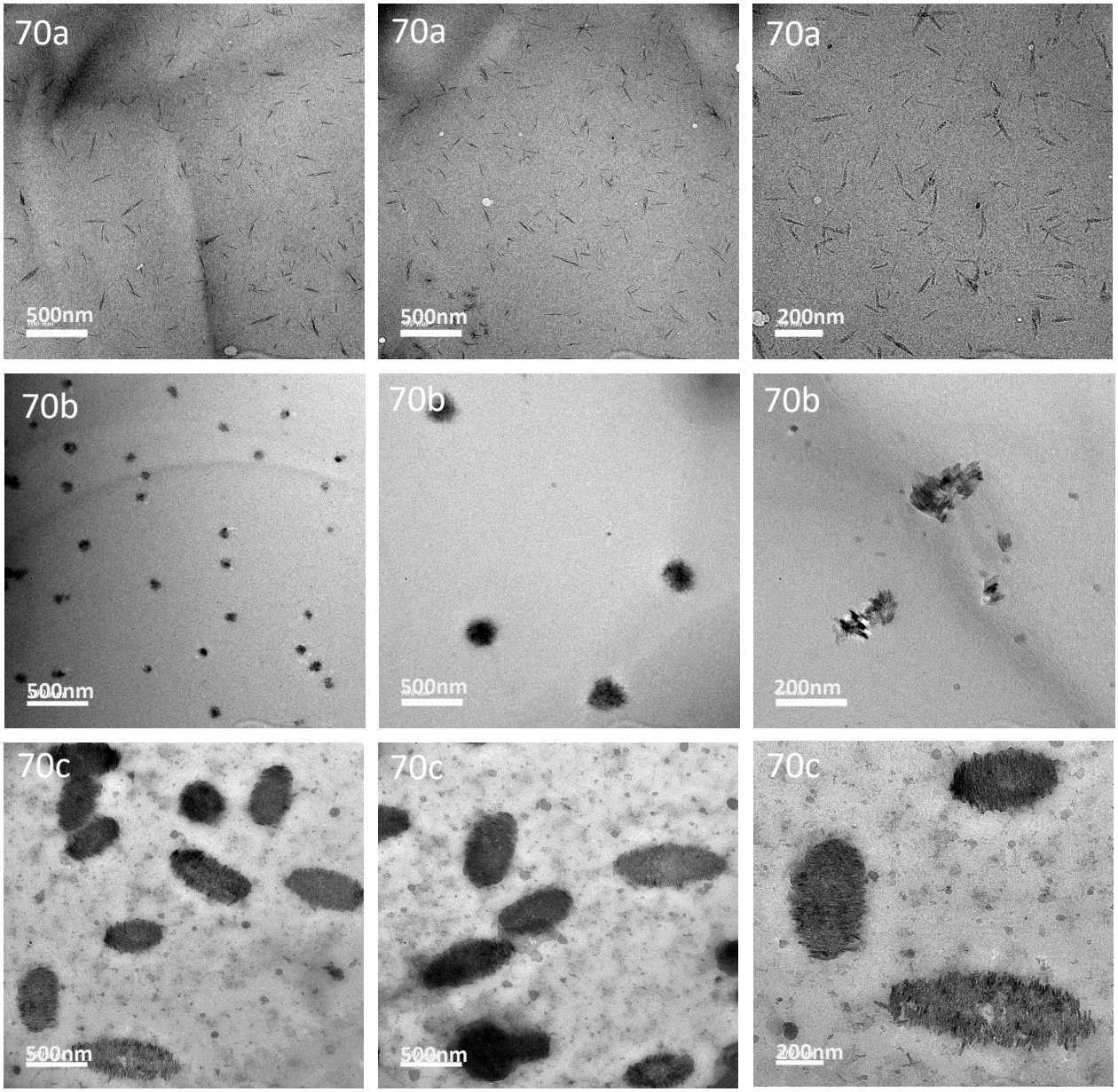


Figure 16- Representative TEM images of 70a, 70b, and 70c from aqueous suspension 1mg/mL in Acetone: Milli-Q water (1:9)

3.12.2 TEM images of **Pentasaccharides glycolipids** having **1,2 *cis*, 1,3 *trans*, 1,5 *trans*** glycosidic linkage with palmitic fatty acid analog (83a) and Cyclopropane derivative of Linoleic acid analog(83b)

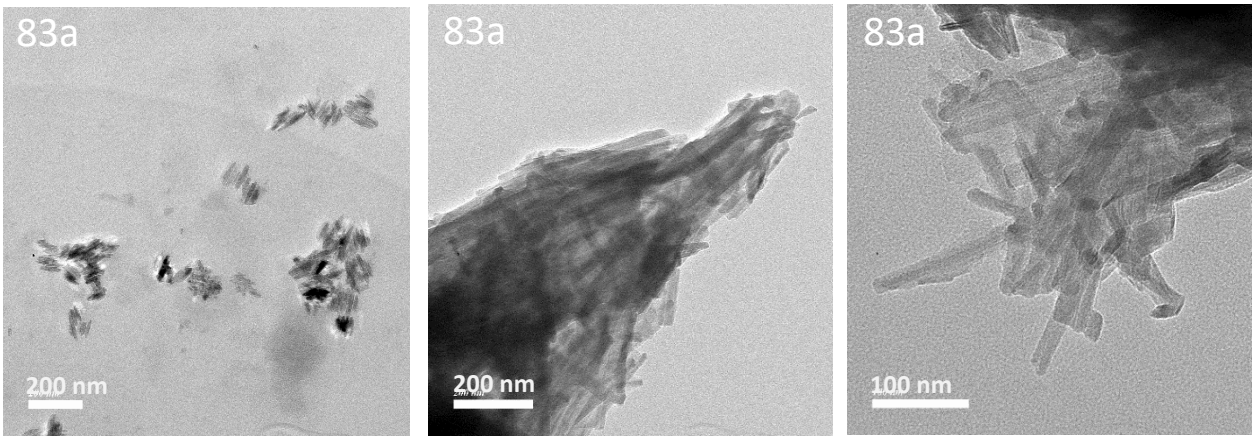


Figure 17- Representative TEM images of 83a from aqueous suspension 1mg/mL in Acetone: Milli-Q water (1:9)

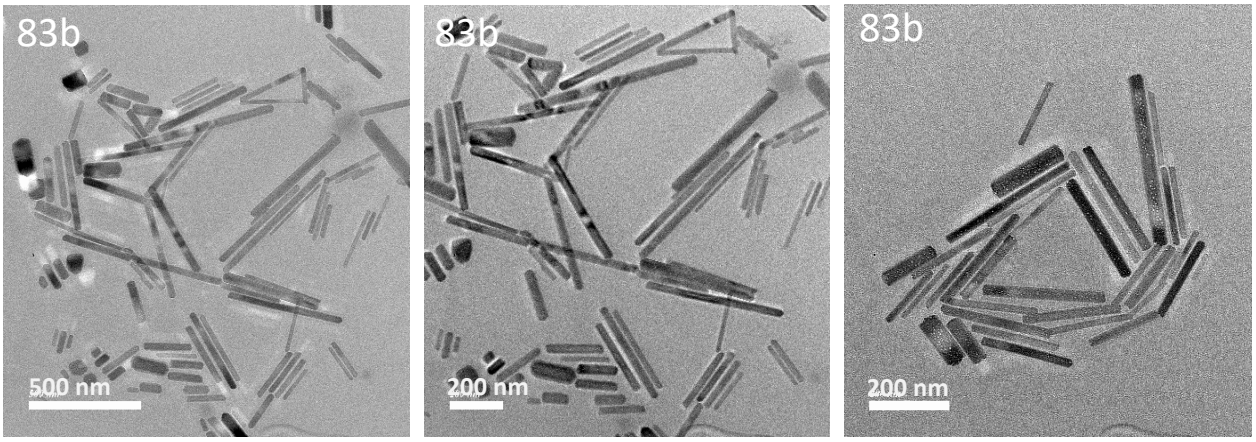


Figure 18- Representative TEM images of 83b from aqueous suspension 1mg/mL in Acetone: Milli-Q water (1:9)

acid portion was prominent. In particular, glycolipids containing cyclopropane displayed a morphology that was both unique and distinct from the saturated and unsaturated forms.

Conclusions

In summary, we have synthesized a series of glycolipids inspired by motif A of the *Mycobacterium tuberculosis* cell wall. All the glycolipids are synthesized by using the [Au]/[Ag]-catalyzed glycosidations; the 1,2-*trans* linkages were formed through neighboring

group participation while the 1,2-*cis* linkages were installed by strategically managing steric effect. Linoleic acid was chosen as a mycolic acid mimic since it has two *cis*-double bonds which can be converted easily to cyclopropanated lipids. The glycolipids encompass a diverse range of α or β-Ara*f* linkages featuring di-, tri-, tetra-, and penta-arabinofuranosides motifs esterified with either saturated, unsaturated, or cyclopropanated fatty acids. All the glycolipids are allowed to self-assemble in aqueous acetone and imaged to notice subtle variations in linkages and stereochemistry that dramatically influence their self-assembled structures. These findings reveal how specific molecular features influence the self-assembly of complex glycolipids, opening exciting avenues for further exploration. Further studies on the structure-self-assemblies-property relationship for tissue engineering are currently underway in our laboratory[10].

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List of Publications

(1) Synthesis of Glycolipid Library Reminiscent of Mycobacterial Cell Wall Motif A and its Significance by Microscopy. **Pooja Joshi**, V Srinidhi and Srinivas Hotha*. (Recently accepted in Angew. chem. (https://doi.org/10.1002/anie.202502837)

(2) Synthesis of an Immunologically Active Heptamannoside of Mycobacterium tuberculosis by the [Au]/[Ag]-Catalyzed Activation of Ethynylcyclohexyl Glycosyl Carbonate Donor. Ganesh P. Shinde, Yogesh Sutar, Niteshlal Kasdekar, **Pooja Joshi**, Omid Rasool, Lech Ignatowicz, Beston Hamasur* and Srinivas Hotha*, *Org. Lett.* **2024**, *26*, 10, 2034-2038.

(3) Selective Binding of C2-linked Arabinose Functionalized Polystyrene Microbeads to Identify Staphylococcus Aureus. Gulab Walke, Cristina Santi, Calum Haydon, **Pooja Joshi**, Yuiko Takebayashi, Sylvain Rama, Josephine Dorh, Srinivas Hotha, * James Spencer, * M. Carmen Galan*, *JACS* Au **2024**, *4*, 4537−4543.

(4) Synthesis of Water-Soluble Thioglycosylated trans-A2B2 Type Porphyrins: Cellular Uptake Studies and Photodynamic Efficiency. Vijayalakshmi Pandey, Md Kausar Raza, **Pooja Joshi**, Iti Gupta*, *J. Org. Chem*. **2020**, *85*, 6309-6322.

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RESEARCH ARTICLE

Synthesis of Glycolipid Library Reminiscent of Mycobacterial Cell Wall Motif A and Its Significance by Microscopy

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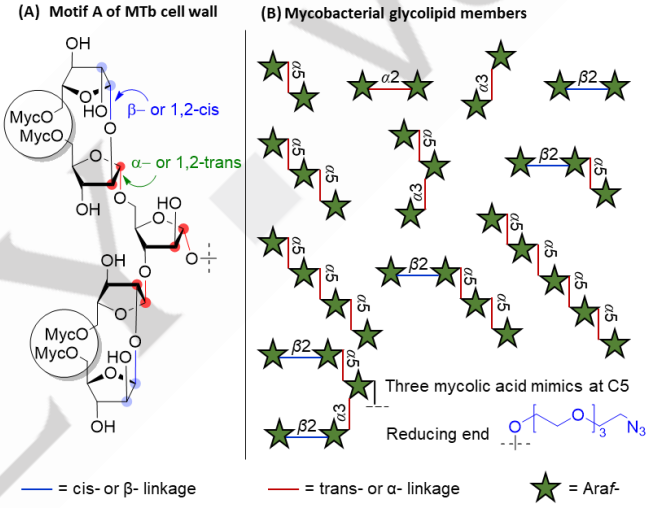
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Abstract: The cell wall of *Mycobacterium tuberculosis* (MTb) is distinguished by its unique glycolipid composition, notably mycolyl arabinogalactan, that features Ara*f*, Gal*f*, and mycolic acid. The terminal portion of arabinogalactan (AG) is motif A, a pentaarabinofuranoside characterized by two *β*-1,2 linkages and one each of *α*-1,5 and *α*-1,3 linkages. The C5 positions of motif A are esterified with mycolic acids, further enriched by unusual cyclopropanes. In this study, we synthesized a diverse array of MTb cell wall glycolipids inspired by motif A and explored their self-assembly behavior using microscopy. This collection of glycolipids includes variations with α or *β*-(1→2, 3, or 5) Ara*f* linkages in di-, tri-, tetra-, and penta-arabinofuranosides, esterified with saturated, doubly unsaturated, or cyclopropanated long-chain fatty acids. The TEM analysis of the resulting self-assemblies revealed that subtle modifications in the anomeric linkages, length of the glycan, and the presence or absence of cyclopropanes impacted the morphology of the self-assembled structures.

Introduction

Every year, tuberculosis (TB) claims over 1.5 million lives, a stark reminder of its relentless threat to global health.[1] Despite advances in medicine, the emergence of multi-drug resistant tuberculosis (MDR-TB) and extensively drug-resistant tuberculosis (XDR-TB) poses a serious challenge.[2] This urgent crisis underscores the need for innovative therapeutic agents, grounded in a deeper biochemical and biophysical understanding of the disease's causative agent, *Mycobacterium tuberculosis* (MTb).[3] Central to this challenge is the complex, greasy cell wall of MTb, which serves as a critical target for novel treatment strategies.[4] While main stream antibiotics such as penicillin and vancomycin effectively target bacterial cell walls, frontline TB drugs isoniazid and ethambutol specifically inhibit MTb's cell wall biosynthesis.[5] The MTb cell wall comprises a thick layer of peptidoglycan, lipoarabinomannan (LAM), mycolyl arabinogalactan (AG), and trehalose-linked lipids.[4] Notably, the chemical architecture of LAM and AG features a distinct pentaarabinofuranosyl motif A (Figure 1A), which plays a pivotal role in the bacterium's virulence.[6] The motif A is attached to a dimannopyranoside in LAM whereas it is esterified with mycolic acids in AG.[4b] Various arabinan motifs of AG are synthesized during the past decades without lipid tether at the terminal C5-position.[7] The presence of the *β*-1,2 linkages at the terminal C5-position of motif A and the cycloprapanes in the mycolic acid

Figure 1. Structure of the terminal pentasaccharide motif A of *Mycobacterium tuberculosis* cell wall (1A) and the targeted glycolipid members (1B).



are intriguing as they are essential for the MTb's long-term persistence and pathogenicity.[8] Consequently, the biosynthetic pathways involved in *β*-1,2 linkages (DprE1, DprE2) and cyclopropane synthetases are investigated for drug development.[9] Understanding the relationship between the hierarchical architectures of glycolipids in MTb and their material properties is crucial, as these self-assemblies can significantly influence pathogenicity.[8b] In this context, we hypothesized that creating a library of glycolipids modeled after motif A will offer insights on the roles of terminal *β*-1,2 Araf linkages and cyclopropanes in this context. Accordingly, we envisioned an azidotriethylene glycol at the reducing end of the collection of molecules so that it could become a powerful handle for further studies and all the glycosidation can be accomplished by our gold-catalyzed glycosidation. The *β*-1,2 Ara*f* linkages were created by exploiting steric buttressing whilst the α-Ara*f* linkages were envisioned through the neighboring group participation of C2-esters. All glycosides were subjected to esterification with linoleic acid to obtain glycolipids with olefins, which were then cyclopropanated to isolate fully saturated or cyclopropanated glycolipids, respectively.

Results and Discussion

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Synthesis of an Immunologically Active Heptamannoside of *Mycobacterium tuberculosis* by the [Au]/[Ag]-Catalyzed Activation of Ethynylcyclohexyl Glycosyl Carbonate Donor

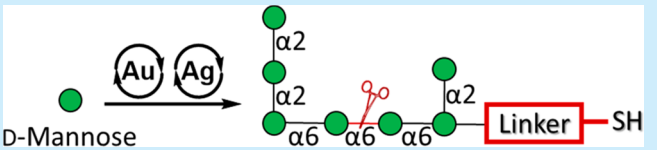
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Ganesh P. Shinde, Yogesh Sutar, Niteshlal Kasdekar, Pooja Joshi, Omid Rasool, Lech Ignatowicz, Beston Hamasur,* and Srinivas Hotha*

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ABSTRACT: Tuberculosis (TB) is one of the most dreadful diseases, killing more than 3 million humans annually. *M. tuberculosis* (MTb) is the causative agent for TB and has a thick and waxy cell wall, making it an attractive target for immunological studies. In this study, a heptamannopyranoside containing 1 → 2 and 1 → 6 α-mannopyranosidic linkages has been explored for the immunological evaluations. The conjugation-ready heptamannopyranoside was synthesized by exploiting the salient features of recently discovered [Au]/[Ag]-glycosidation of ethynylcyclohexyl glycosyl carbonate donors. The glycan was conjugated to the ESAT6, an early secreted protein of MTb for further characterization as a potential subunit vaccine candidate.



Tuberculosis is a disease that has one of the longest histories of burden to mankind with no sigh of relief.[1] *Mycobacterium tuberculosis* (MTb) is the causative agent for tuberculosis (TB) and is known to be dormant in the host until the immunity of the host is compromised, becoming active when the host immunity is compromised (e.g., HIV-AIDS).[1b,c] The current prognosis for TB includes multidrug therapy over a prolonged time. According to the World Health Organization, vaccination is considered to be the most cost-effective strategy for controlling infectious disease.[1d] Unfortunately, today, the only vaccine available against TB is the *Mycobacterium bovis* bacillus Calmette−Guerin (BCG).[1e] Although BCG has been shown to provide good protection against disseminated TB in children, its protective efficacy often fades in adolescence and fails to protect against pulmonary TB. The reported efficacy of BCG[1e] against adult pulmonary TB varies hugely (0−80%). Several mycobacterial protein antigens have been employed alone, together with BCG, or as booster vaccines but without much success.[1e] A better understanding of the immunology of carbohydrates has paved the way for the development of more safe and efficient carbohydrate-based vaccines.[2] Indeed, many vaccines developed against bacterial infections are carbohydrate vaccines. Unfortunately, carbohydrate antigens are T-cell-independent and provide poor immunogenicity unless they are converted to T-cell-dependent through conjugation to a carrier protein.[2] *Mycobacterium tuberculosis* cell-wall-associated glycolipids LAM, LM, and PIM have been shown to modulate host immune responses through interaction with several pivotal immune cells.[3a] While LAM of TB has been suggested in many studies as a vaccine candidate against mycobacterial infection,[3] the protective efficacy of mycobacterium PIM is not yet explored. This is very interesting since, in contrast to LAM, PIM has been shown to exert potent anti-inflammatory activities.[3d]

The chemical structure of the highly conserved LAM revealed that it comprises α-1,6 and α-1,2 mannopyranosyl linkages which are further attached to a phosphatidylinositol moiety.[4] Our long-standing interest in the synthesis of oligosaccharides coupled with their biological evaluation enticed us to hypothesize that a branched heptamannopyranoside (**1**), equipped with α-1,6 and α-1,2 mannopyranosides, could become a potential vaccine candidate against TB after conjugating with ESAT-6,[5] an early secreted protein of MTb.

Heptamannopyranoside (**1**) can be synthesized from the glycosyl donor **2** and the aglycone **3** in [4+3] fashion. The presence of the benzoate at the C2-position ensures the formation of an α-linkage through neighboring group participation. Azide is useful, as it can be reduced to an amine while performing hydrogenolysis at the last stages of the synthesis. Saccharides **2** and **3** can be synthesized from the four monosaccharide building blocks **4**−**7** (Scheme 1). The synthesis of compound **1** has been envisioned by the presence of three

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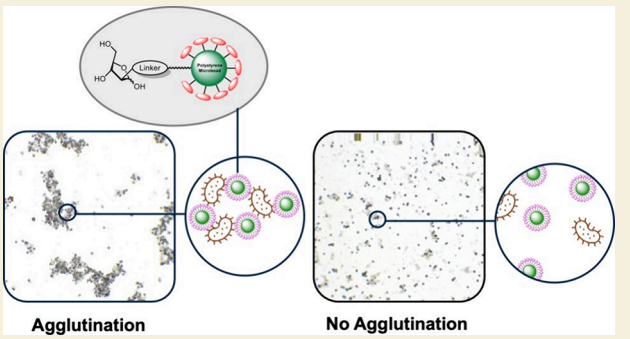
C2-Linked Arabinose-Functionalized Polystyrene Microbeads Selectively Target *Staphylococcus aureus*

Gulab Walke,[⊥] Cristina Santi,[⊥] Calum Haydon, Pooja Joshi, Yuiko Takebayashi, Sylvain Rama, Josephine Dorh, Srinivas Hotha,* James Spencer,* and M. Carmen Galan*

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ABSTRACT: Carbohydrates play pivotal roles in the first stages of microbial infections and can be exploited as decoys to hijack the interactions between bacteria and the host cell. Multivalent glycan probes mimicking the natural presentation of glycans in living cells have been successfully employed to study fundamental carbohydrate/protein interactions in microbial systems; however, most pathogenic glycan receptors exhibit a shared specificity for commonly found sugars present in both healthy and pathogenic cells, posing a challenge for target selectivity. In this study, we report the synthesis of a small library of D-arabinose multivalent probes, a sugar absent in human physiology, and their evaluation in a bacteria agglutination assay using cluster analysis. Our findings reveal preferential binding to *Staphylococcus aureus* of C2-linked arabinose moieties over C1- or C5-linked probes, underscoring the importance of glycan presentation in targeting specificity. Furthermore, we demonstrate the selectivity of the C2-linked probe toward *S. aureus* across a panel of common bacterial pathogens. Additionally, these probes are able to disrupt biofilm formation in *S. aureus* SH1000, thereby further proving the cell surface interactions with *S. aureus*



KEYWORDS: *antimicrobial probes, oligosaccharide synthesis, nonmamalian glycans, bacteria targeting, agglutination*

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Bacterial adhesion to host cells is a crucial step in the infection process. Bacteria exploit interactions with specific carbohydrates via lectins (glycan-binding proteins), which recognize specific cell surface glycans on host cells and tissue surfaces, as part of the processes of colonization and infection.[1−4] In the same manner that bacteria may exploit glycan mimics to hijack host biology to establish infection,[5] it is possible to develop glycan-based tools as antagonists of such interactions for use as antiadhesive agents[6−9] and diagnostic tools.[10,11]

To design probes to exploit bacterial interactions with carbohydrates for detection, structurally defined oligosaccharides as well as probes able to replicate physiological multivalent carbohydrate presentation and so overcome the often low binding affinities of monovalent glycosides are needed. Another important consideration is that glycan receptors are found in both human cells and pathogens and in some instances share similar specificities for the same carbohydrate moieties.[12] For instance, many strains of uropathogenic *Escherichia coli* (UPEC) type 1 encode the virulence factor FimH, which is a mannose-specific lectin,[13] while the DC-SIGN lectin also binds specifically to mannose (and fucose) residues.[14] Therefore, the identification of glycan(s) and scaffold type, size, and degree of multivalency that allow for specific interactions with bacteria but do not interfere with the host or other species is the key to successful downstream applications.

Staphylococcus aureus (*S. aureus*) is a Gram-positive bacterium commonly found in the natural environment and as a human commensal and one of the so-called "ESKAPE" human pathogens,[15,16] which has been linked to life-threatening diseases such as pneumonia, meningitis, septicaemia, and endocarditis.[17,18] Moreover, under favorable conditions, *S. aureus* can produce enterotoxins, one of the most common causes of food-borne diseases.[19] Due to the prevalence of *S. aureus* infections in healthcare settings and the rise of antimicrobial resistance, there is a pressing need to develop fast and accurate point-of-care diagnostic tools.[17,20−25] However, most methods for *S. aureus* detection in clinical settings are time-consuming and costly, being based on bacterial culture, nucleic acid amplification, or antibody-based immune- or immuno-PCR assays.[17]

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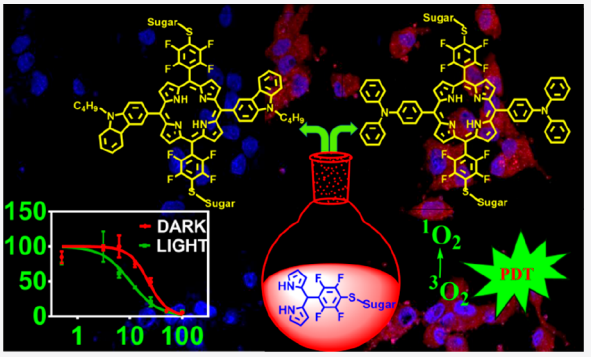
Synthesis of Water-Soluble Thioglycosylated *trans*-A_2B_2 Type Porphyrins: Cellular Uptake Studies and Photodynamic Efficiency

Vijayalakshmi Pandey, Md Kausar Raza, Pooja Joshi, and Iti Gupta*

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ABSTRACT: The synthesis of water-soluble thioglycosylated A_2B_2 type porphyrins and their zinc(II) complexes is reported. The water-soluble *trans*-A_2B_2 porphyrins were synthesized in two steps, via [2+2] condensation between thioglycosylated dipyrromethanes and aromatic aldehydes in 15−21% yields. The thioglycosylated *trans*-A_2B_2 porphyrins showed decent *in vitro* singlet oxygen generation, which was supported by the intracellular DCFDA study. The *in vitro* cellular investigations of thioglycosylated A_2B_2 porphyrins were carried out in lung cancer cells (A549) to test their photodynamic therapeutic (PDT) activity. The PDT study revealed significant cytotoxicities of porphyrins with IC_{50} values between 23.3 and 44.2 μM in the dark, whereas, after visible light exposure, the photosensitizers exhibited IC_{50} values around 11.1−23.8 μM. The water-soluble thioglycosylated zinc(II) porphyrins having two *meso*-*N*-butylcarbazole groups exhibited an excellent degree of photocytotoxicity (IC_{50} = 4.6−8.8 μM). The flow cytometry analysis revealed that cellular uptake and ROS (reactive oxygen species) generation efficiency of water-soluble thioglycosylated zinc(II) porphyrins were considerably higher than nonmetalated porphyrins. Confocal microscopy images displayed substantial distribution in the endoplasmic reticulum with partial colocalization in mitochondria and lysosomes of water-soluble thioglycosylated zinc(II) porphyrins in A549 cells.



INTRODUCTION

Carbohydrates play a vital role in many biological processes like neuronal development, hormone activities, cell communication, and inflammatory responses.[1,2] Manmade glycoconjugates and oligosaccharides have shown possible applications as bioimaging agents and drug delivery systems in medicinal chemistry.[3−5] Photodynamic therapy (PDT) is widely used to treat different types of cancers, e.g., skin cancer, lung cancer, digestive tract, and age-related macular degeneration.[6,7] The PDT combines visible/near-infrared light, a photosensitizer, and cellular oxygen to kill cancer cells.[8−16] Clinically approved porphyrin-based PDT drugs Foscan and Photofrin are nonspecific and have side effects on healthy tissues.[17−24] Most of the currently available porphyrin-based photosensitizers, like palladium bacteriochlorin, texaphyrin, silicon phthalocyanines, and Sn(II)etiopurpurin, are hydrophobic compounds, and some of them have a relatively long retention time in tissues.[25−27] The water solubility of the photosensitizer can be enhanced by attachment of oligonucleotides,[28,29] carrier peptides,[30,31] and oligosaccharides. The uptake of PDT drugs into cancer cells can occur by active or passive transport. Passive transport involves nonspecific interactions and diffusion of molecules through the cell membrane.[32] On the other hand, active transport requires specific cell-molecule recognition and cell receptors, which can shuttle the drugs across the cell membrane.[15] The malignant cells are known to overexpress carbohydrate-binding proteins.[33−36] The porphyrin-based molecules can be targeted toward cell surface receptors particularly known as carbohydrate-binding lectins, by linking hexose sugars/oligosaccharides on the molecules.[37−39] Glycoconjugated porphyrinoids have been nicely summarized in the recent review by Drain and co-workers, such molecules have shown good solubility and higher cellular uptake due to enhanced interactions with tumor cell receptors.[40] Thus, carbohydrate−porphyrin conjugates are promising candidates for PDT; attachment of sugars make them amphiphilic in nature and helps in their cellular uptake in tumor cells.[41−45] However, the ongoing research on novel glycoporphyrin conjugates for PDT is challenging, due to the lack of straightforward synthetic protocols to prepare such molecules in large quantities. The well-established methods of porphyrin syntheses reported by Lindsey and co-workers and Alder and co-workers are not favorable to prepare glycosylated porphyrins in good yields.[46,47] The available glycoconjugates of porphyrins were synthesized either by condensation of pyrrole with carbohydrate-linked

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