Functional and biologically active oligosaccharide mimics of carbohydrate processing enzymes and their application for pathogen detection: An exercise with *Mycobacterium tuberculosis*

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BY

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(Research Guide)

ORGANIC CHEMISTRY DIVISION
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Aai, aba ani gurus

Samarpit

DECLARATION

The research work embodied in this thesis has been carried out at National Chemical Laboratory, Pune under the supervision of **Dr. C. V. Ramana**, Organic Chemistry Division, National Chemical Laboratory, Pune – 411008. This work is original and has not been submitted in part or full, for any degree or diploma of this or any other university.

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CERTIFICATE

The research work presented in thesis entitled **"Functional and biologically active oligosaccharide mimics of carbohydrate processing enzymes and their application for pathogen detection: An exercise with *Mycobacterium tuberculosis*"** has been carried out under my supervision and is a bonafide work of **Mr. Rahul Shivaji Patil**. This work is original and has not been submitted for any other degree or diploma of this or any other University.

Pune – 411008
May–2012

Dr. C. V. Ramana
(Research Guide)

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Rahul Shivaji Patil

DEFINATIONS AND ABBREVIATIONS

Ac	–	Acetyl
Ac_2O	–	Acetic anhydride
AcOH	–	Acetic acid
AIBN	–	Azobisisobutyronitrile
Bu	–	Butyl
Bn	–	Benzyl
Bz	–	Benzoyl
Cat.	–	Catalytic/catalyst
DCM	–	Dichloromethane
Conc.	–	Concentrated
COSY	–	Correlation spectroscopy
DIAD	–	Diisopropyl azodicarboxylate
DMP	–	2,2'-Dimethoxypropane
DMF	–	*N,N*-Dimethylformamide
DMAP	–	*N,N'*-Dimethylaminopyridine
DMSO	–	Dimethyl sulfoxide
Et	–	Ethyl
HRMS	–	High Resolution Mass Spectrometry
LDA	–	Lithium diisopropylamide
Liq.	–	Liquid
m-CPBA	–	3-Chloroperbenzoic acid
Ms/Mesyl	–	Methanesulfonyl
Me	–	Methyl
MIC	–	Minimum Inhibitory Concentration
NIS	–	*N*-iodosuccinamide
NMR	–	Nuclear Magnetic Resonance
NOESY	–	Nuclear overhauser effect spectroscopy
Py	–	Pyridine
p-TSA	–	*para*-Toluenesulfonic acid
Ph	–	Phenyl

i-PrOH	–	*iso*-Propanol
rt	–	Room temperature
Sat.	–	Saturated
TBDMS	–	*tert*-Butyldimethyl chlorosilane
TBDPS	–	*tert*-Butyldiphenyl chlorosilane
TBAB		Tetra-*n*-butylammonium bromide
TBAF	–	Tetra-*n*-butylammonium fluoride
THF	–	Tetrahydrofuran
TMSOI	–	Trimethylsulfoxonium iodide
TMSOTf		Timethylsilyl trifluromethanesulfonate
TPP	–	Triphenylphosphine

Abbreviations used for NMR spectral informations:

br	Broad	q	Quartet
d	Doublet	s	Singlet
m	Multiplet	t	Triplet

GENERAL REMARKS

- ^{1}H NMR spectra were recorded on AV–200 MHz, AV–400 MHz, and DRX–500 MHz spectrometer using tetramethylsilane (TMS) as an internal standard. Chemical shifts have been expressed in ppm units downfield from TMS.
- ^{13}C NMR spectra were recorded on AV–50 MHz, AV–100 MHz, and DRX–125 MHz spectrometer.
- EI Mass spectra were recorded on Finngan MAT–1020 spectrometer at 70 *eV* using a direct inlet system.
- Infrared spectra were scanned on Shimadzu IR 470 and Perkin-Elmer 683 or 1310 spectrometers with sodium chloride optics and are measured in cm^{-1}.
- Optical rotations were measured with a JASCO DIP 370 digital polarimeter.
- All reactions are monitored by Thin Layer Chromatography (TLC) carried out on 0.25 mm E-Merck silica gel plates (60F–254) with UV light, I_2, and anisaldehyde in ethanol as developing agents.
- All reactions were carried out under nitrogen or argon atmosphere with dry, freshly distilled solvents under anhydrous conditions unless otherwise specified. Yields refer to chromatographically and spectroscopically homogeneous materials unless otherwise stated.
- All evaporations were carried out under reduced pressure on Buchi rotary evaporator below 45 °C unless otherwise specified.
- Silica gel (60–120), (100–200), and (230–400) mesh were used for column chromatography.

CONTENTS

ABSTRACT

ABSTRACT

The thesis entitled "**Functional and biologically active oligosaccharide mimics of carbohydrate processing enzymes and their application for pathogen detection: an exercise with *Mycobacterium tuberculosis***" consist of five part namely i. Introduction, ii. Results and Discussion, iii. Experimental, iv. Spectra and v. References. The introduction is an overview of *Mtb* cell wall structure and the literature survery of *C*-glycoside analogues of β-DPA and Motif C disaccharide. The second part results and discussion deals with 1. Strategy and synthesis of 1-α and β-d-arabinofuranosyl-undec-10-ene, 2. Synthesis of Motif C carba-disaccharide analogues, 3. Studies toward the synthesis of Motif C and B *C*-glycoside analogues. Also second part comprises 4. Anti-mycobacterium activity of *C*-arabinofuranosides, SAR and preliminary studies toward the imaging of *M. Bovis* BCG are described.

1. Strategy and synthesis of 1-α and β-D-arabinofuranosyl-undec-10-ene

The arabinofuranosyl transferases (AraTs) are the enzymes involved in the biosynthesis of polysaccharides Arabinogalactan (AG) and Lipoarabinomannan (LAM) which are the basic constituents of the *Mycobacterium tuberculosis* (*Mtb*) cell wall. All the known AraTS utilize a single substrate i.e. β-decaprenyl-D-arabinofuranosyldiphosphate (Figure 1, β-DPA).

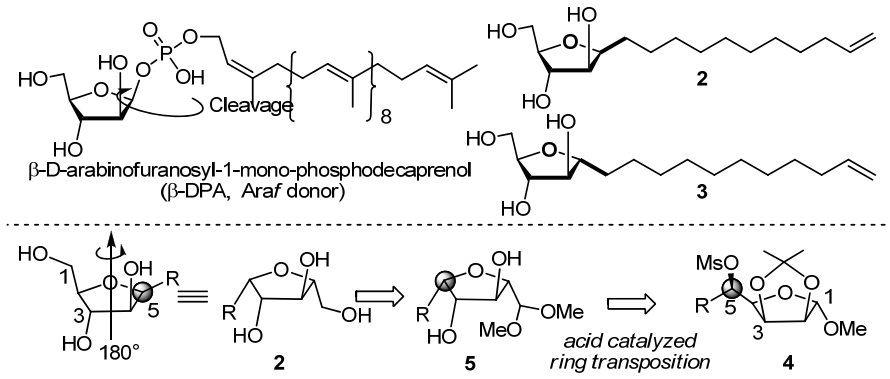
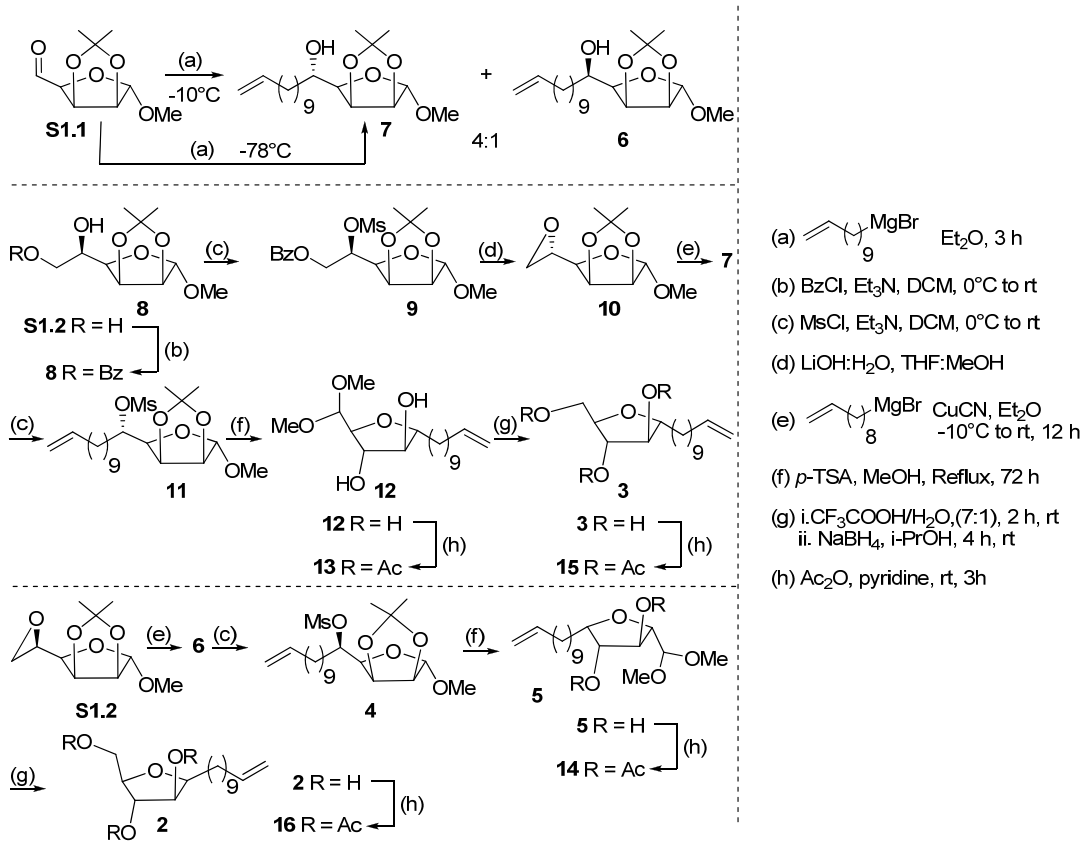


Figure 1: *β-DPA, 1-α and β-D-arabinofuranosyl-undec-10-ene and general strategy for C-D-arabinofuranoside*

We have intended to synthesize the *C*-glycoside analogues of β-DPA as potential anti-mycobacterial agents. Considering the lack of a single method for the stereoselective selective synthesis of either of the anomeric *C*-glycosides in general, and *C*-arabinofuranosides in particular we devised a new strategy featuring furan ring transposition reaction (FRT) as the key step. The 1-α- and β-D-arabinofuranosyl-undec-10-enes **2** (potential β-DPA analogue) and **3** have been selected as the initial targets (Figure 1) and the salient features of our approach are described in Figure 1. The acid mediated ring transposition of a suitable D-mannofuranoside **4** should lead to the acetal **5** which upon hydrolysis and reduction should provide the target compound **2**.



Scheme 1: *Synthesis of 1-α and β-D-arabinofuranosyl-undec-10-ene*

The synthesis started with the Grignard reaction of known aldehyde **S1.1** with 10-undecenylmagnesium bromide (Scheme 1). The Grignard addition was found to give a 4:1 diastereoselectivity at –10 °C, and at –78 °C gave exclusively **7**. The stereochemistry of the newly created centre in alcohol **7** was determined at a later stage as undesired 5*S*.

Also alcohol **7** was prepared from epoxide **10** to confirm the configuration. The mesylation of free –OH in **7** followed by refluxing **7** in MeOH with cat. *p*-TSA gave the dimethyl acetal **12**. The acetal **12** on hydrolysis and reduction gave the α-*C*-D-arabinofuranoside **3**. Similarly, the synthesis of **2** was achieved in 5 steps from methyl-D-lyxofuranoside epoxide **9** in 44% overall yield. The acetates of acetal **13**/**12** were prepared to learn about the validity of nOe correlations in *C*-furanosides - which are conformationally labile. Also triacetates **15/16** were synthesised to compare their data reported for known triacetate of the β-*C*-allyl arabinofuranoside.

2. Synthesis of Motif C carba-disaccharide analogues

Having been established a common approach for the stereospecific synthesis of α-/β-*C*-arabinofuranosides, we next proceeded to extend our strategy for the synthesis of carba-disaccharide analogues of Motif C. The linear chain of arabinan polymer is made up of repeating disaccharide α-D-Ara*f*-(1→5)-α-D-Ara*f* which is trivially called as motif C (Figure 2).

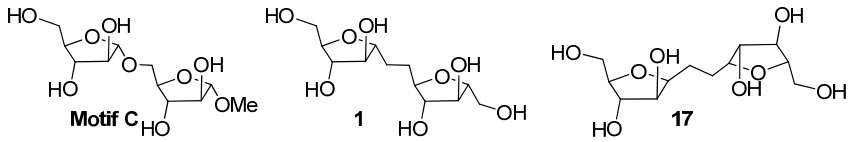
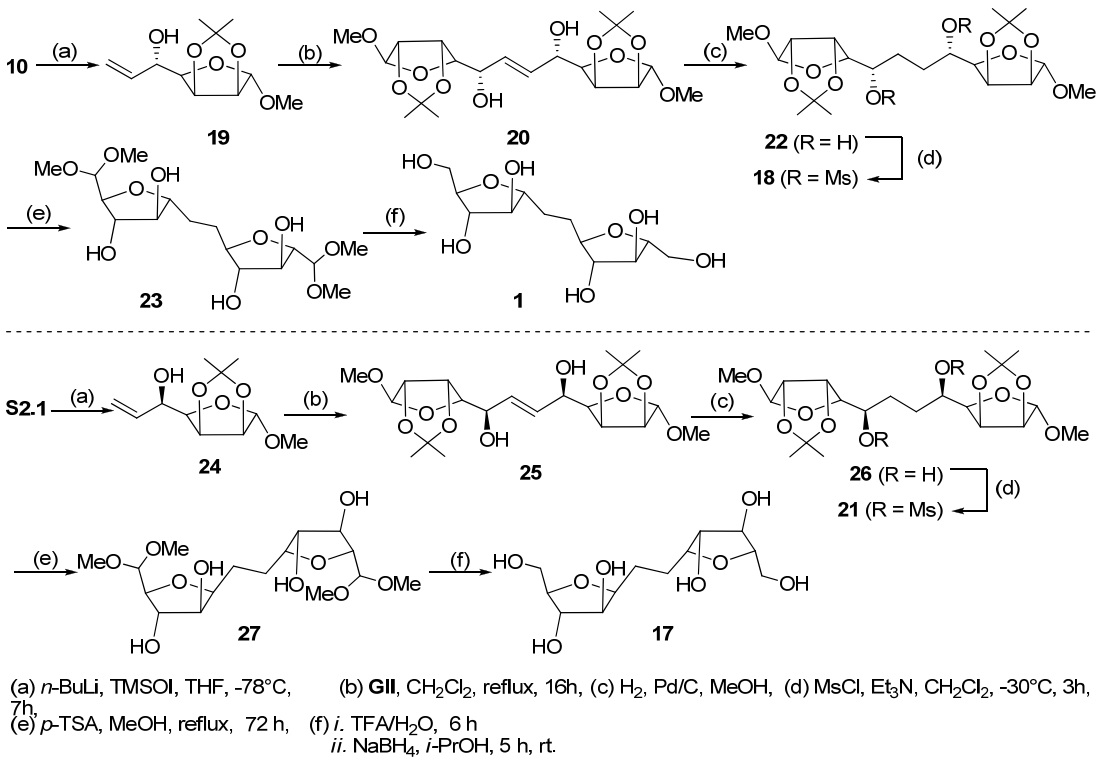


Figure 2*: Structure of motif C and carba-disaccharide analogues **1** and **17***

The synthesis of carba-disaccharide **1** commenced with Mioskowski's one carbon homologation of epoxide **10** (Scheme 2) followed by the homo-dimerization of resulting allyl alcohol **19** with Grubb's 2nd generation catalyst (**GII**). The dimer **20** thus obtained was subjected for the olefin hydrogenolysis followed by dimesylation to obtain the dimesylate **18**. The key double ring transposition of **18** proceeded smoothly under the established conditions (refluxing in methanol in presence of catalytic *p*-TSA for 72 h) to afford the C_2-symmetric diacetal **23**. Following the acetal hydrolysis and the reduction of dialdehyde with sodium borohydride gave the known carba-disaccharide **1** in seven steps with 37% overall yield. Similarly the synthesis of carba-disaccharide **17** was completed in 7 steps with an overall 41% yield.



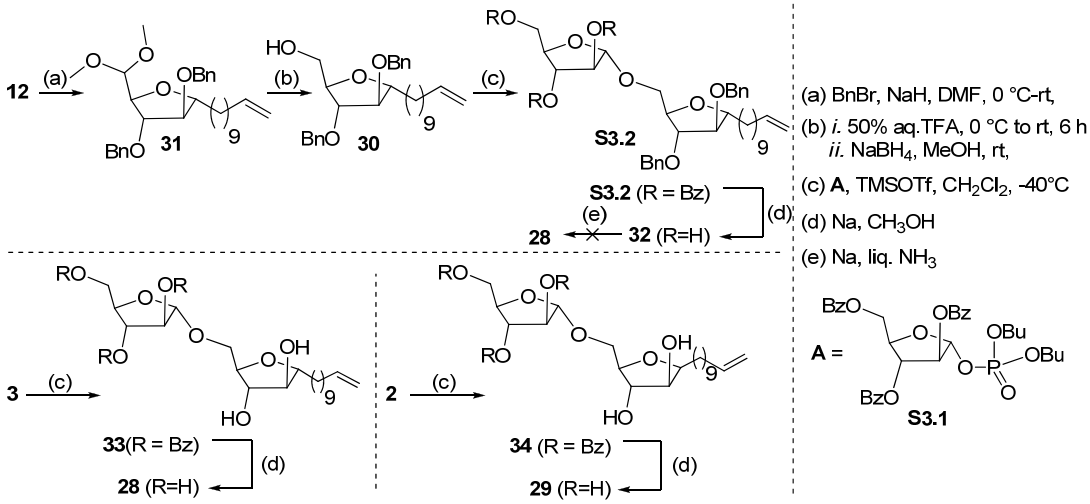
Scheme 2: *A double furan ring transposition and synthesis of Motif C carba-saccharide analogues (**1\17**)*

3. Studies toward the synthesis of Motif C and B *C*-glycoside analogues

Synthesis of *C*-glycoside motif C analogues

Having synthesized the Motif C carba-disaccharide analogues, we next targeted the Motif C *C*-glycoside mimics **28**/**29** (Scheme 3). The key step will be the selective *O*-glycosylation employing a suitable glycosyl acceptor. The di-*n*-butyl D-arabinofuranosyl phosphate **S3.1** was selected as the glycosyl donor. The glycosyl acceptor **30** was synthesized from acetal **12** in 3 steps and the key glycosylation was achieved by treating a mixture of **S3.1** and **30** with TMSOTf at –40^{o}C in DCM to procure the disaccharide **S3.2** in moderate yield. The debenzoylation of **S3.2** gave the di-*O*-benzyl disaccharide **32**. The attempted debenzylation of **32** using Na/Liq.NH_3 (in order to keep the olefin unit intact) ended with unidentified mixture of products. Finally, use of the free α-*C*-glycoside **3** as acceptor and the glycosylation using **S3.1** under the conditions mentioned above gave the disaccharide **33**, which after saponification using Na/MeOH provided the

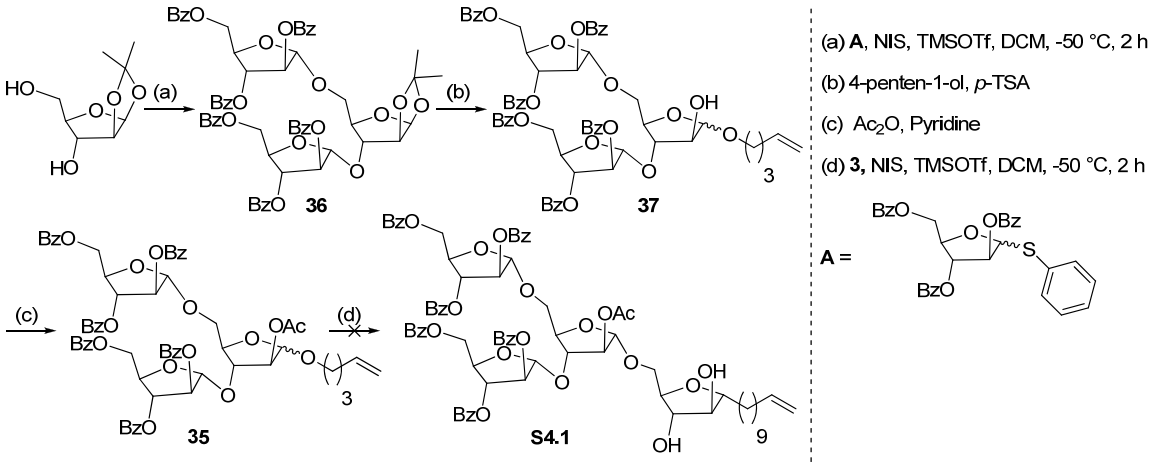
desired Motif C analogue **28**. By employing a similar strategy, the *β-C*-glycoside analogue of Motif C **29** has been synthesized.



Scheme 3: *Synthesis of α-D-arabinofuranosyl-(1→5)-1-α-D-arabinofuranosyl-undec-10-ene and α-D-arabinofuranosyl-(1→5)-1-β-D-arabinofuranosyl-undec-10-ene*

Synthetic studies toward the Motif B analogue

After the synthesis of motif C analogues, we opted for the synthesis of tetrasaccharide analogue (motif B) of cell wall AG and LAM complex, keeping 1-α-D-arabinofuranosyl-undec-10-ene monosaccharide as one of the unit. Synthesis of motif B analogue was started with the preparation of key trisaccharide **36**.



Scheme 4: *Synthetic studies toward Motif B C-glycoside analogue*

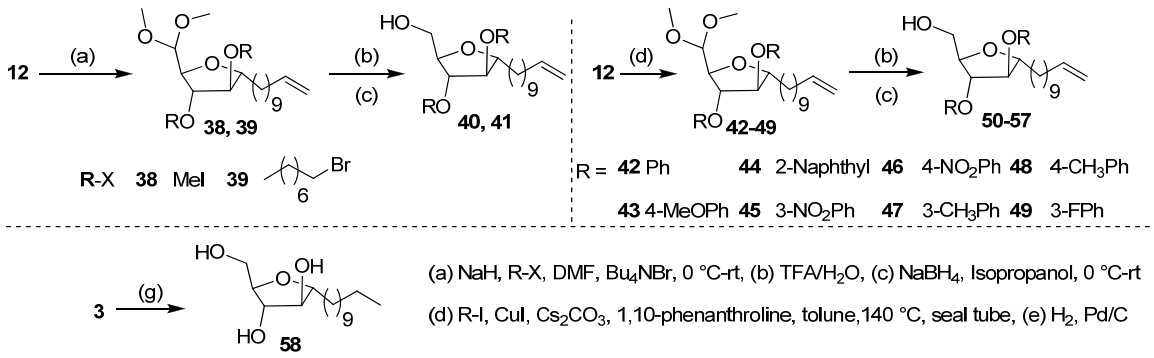
The trisaccharide **36** was prepared by treatment of a mixture of *S*-thiophenyl-2,3,5-tribenzoyl-D-arabinofuranoside and 1,2-*O*-isopropylidene-D-arabinofuranose with TMSOTf at –50 °C. The 1,2-isopropylidene trisaccharide **36** was hydrolyzed in the presence of 4-penten-1-ol with *p*-TSA to get the anomeric mixture of *O*-glycosides **37**. The acetylation of free –OH in **37** gave the desired glycosyl donor **35**. All the attempts for glycosylation of **3** with **35** met with failures.

4. Anti-mycobacterium activity of *C*-arabinofuranosides, SAR and preliminary studies toward the imaging of *M. Bovis* BCG

The mono (**2**, **3** and **30**) and the disaccharides (**28**, **29** and **32**) analogues were subjected for anti-mycobacterial evaluation. All *C*-glycosides (except **29**) displayed significant anti-mycobacterial effect at concentrations of 1 μg/mL. The 2,3-dibenzyl-1-α-D-arabinofuranosyl-undec-10-ene **30** is the best, among all the *C*-glycosides with IC_{50} 12 nm. The α–glycoside **3** displayed significant anti-mycobacterial effect at concentrations of 1 μg/mL. Surprisingly the 1-β-D-arabinofuranosyl-undec-10-ene **2** was found to be less potent than the α-analogue **3**. The disaccharide **28** and **29** are less potent than **2** and **3** which revealed that addition of an extra arabinofuranosyl residue has a negative effect.

Synthesis of 2, 3-di-*O*-alkyl/di-*O*-aryl-1-α-D-arabinofuranosyl-undec-10-ene and their evaluation against *M. Bovis* BCG

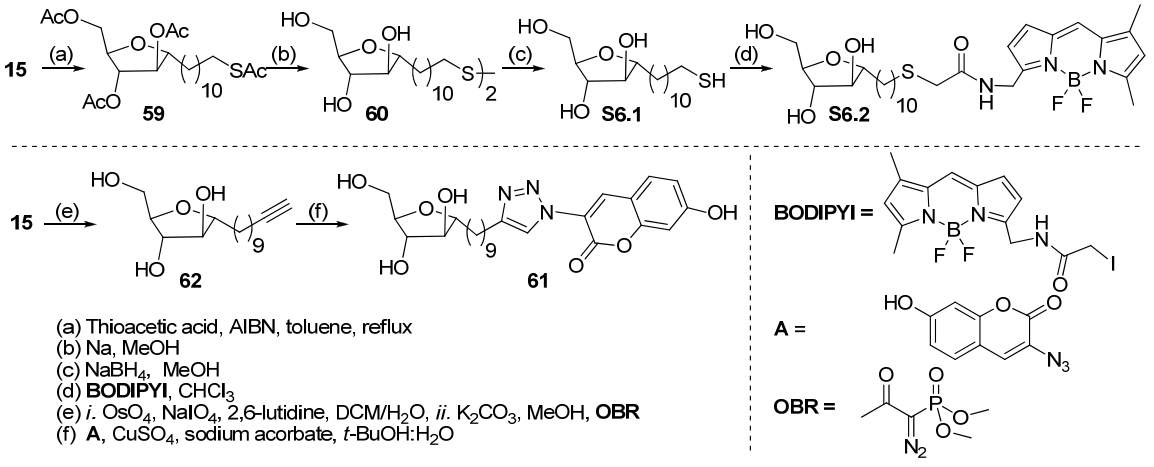
Inspired with the excellent anti-mycobacterial activity of 2,3-dibenzyl-1-α-D-arabinofuranosyl-undec-10-ene **30**, we have synthesized corresponding 2,3-dialkyl ether derivatives **40** and **41**, by diakylation of acetal **12** and subsequent acetal hydrolysis/reduction. The 2,3-diaryl derivatives **50–57** have been also synthesized by using the Buchwald coupling as the key reaction. The biological activity screening of all these compounds against *M. Bovis* BCG revealed that except the dimethyl derivative **40**, the entire collection of compounds synthesized are inactive (less than 19% at 20 μg/mL).



Scheme 5: *Synthesis of 2,3-O-dialkyl/diaryl-1-α-C-undec-10-enyl-D-arabinofuranosides*

Synthesis and preliminary study of imaging of *M. Bovis* BCG by BODIPY and coumarine conjugate 1-α-D-arabinofuranosyl-undec-10-ene

Considering the better inhibitory profile of the α-*C*-arabinofuranoside **3**, we have next deployed it for imaging business in the pursuit of developing new diagnostic tools for *M. Tuberculosis*. In this regard, the BODIPY conjugate **S6.2** has been synthesized from **15**, using known set of reactions - first thioacetylation followed by acetate deprotection to arrive at the disulphide **60**.



Scheme 6: *Synthesis of Bodipy- and coumarine-conjugate fluorescent tag of **3***

The thiol **S6.1** was prepared in situ by reduction of the disulfide **60** with $NaBH_4$ and coupled immediately with the iodoacetamido BODIPY to afford the fluorescent probe **S6.2.** The preliminary imaging (*M* Bovis BCG) experiments using **S6.2** are promising.

Since the BODIPY fluorescent conjugate **S6.2** was unstable, it's difficult to characterize and expensive to scale up, the coumarine conjugate **61** has been synthesized as a viable alternative. The synthesis involves the Cu-catalyzed cycloaddition of the alkyne **62** (prepared from **15** in 2 steps) and the easily accessible coumarinyl azide. Further experiments probing the use of **61** for the imaging of *M. Bovis* BCG are currently in progress.

To summarize, we have developed a strategy for synthesis of 1-α and β-D-arabinofuranosyl-undec-10-ene from D-mannose using furan ring transposition as the key reaction also synthesized their Motif C analogues and attempted for corresponding Motif B analogues. The carba-disaccharide *Motif C* analogues have been synthesized featuring a double furan ring transposition reaction. One of the *C*-arabinofuranosides **30** was found to have the MIC better than frontline anti-tubercular drug Ethambutol. We further explored the possibility imaging *M. Bovis* BCG using *BODIPY* as a fluorescent tag. The coumarine conjugate of **3** has been synthesized as a simple alternative for *Mycobacterium* imaging.

INTRODUCTION

1. Introduction

1.1 Tuberculosis

TB kills 1.4 million people each year or more than one person every 20 seconds.[1] It generally infects the lungs (pulmonary TB) as well as it can also affect other organs (extra pulmonary TB). Robert Koch discovered the cause of contagious bacterial infection tuberculosis that is *Mycobacterium tuberculosis* in 1882. Figure 1 is a schematic representation of different stages of *M. tuberculosis* infection.[1] The cycle starts by transmission of the disease from pulmonary TB infected people to healthy individual as they expel bacteria in air through coughing or sneezing. Interestingly, out of this infected people only small portion (5%) of individual will go on to develop *M. tuberculosis*. However, there is more possibility to develop TB to those with poor immune system such as person infected by Human Immunodeficiency syndrome (50%). Diabetes patients, patients who are taking heavy dose of chemotherapy and the population with deprived nutrition are also vulnerable to develop TB. Another fact about TB is that men are more susceptible to develop TB than woman and the adult mortality rate is more than other age group (2/3 TB cases are between 15 to 59 age group).[2]

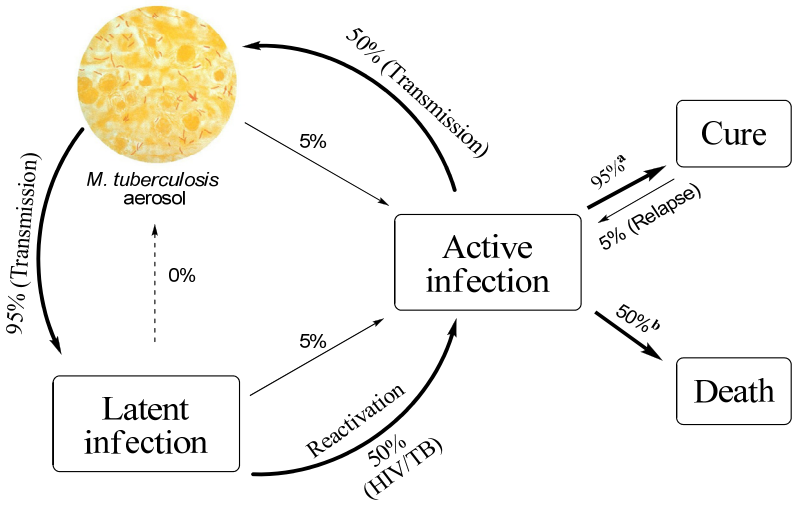


Figure 1: Different stages of *M. tuberculosis* infection *Progress and transmission of infectious (active) or non infectious latent by M. tuberculosis aerosol. Latent infection is not infectious but there is chance of 5% for active infection and 50% in case of HIV patient.* [a] *In cases of drug-susceptible (DS)-TB there 95% cure and 5% relapse and if it is untreated there is 50% chances of death* [b] *TB untreated*

Since the discovery of chemotherapy to treat TB in 1950s, the disease scenario is dramatically changed (in clinical trial 90% patient are cured).[3] However, the TB drug regimen in general takes 6–24 months to cure and is too complicated to administer.[3] In the recent years, TB has resurged as one of the world's deadliest pandemic diseases because of the emergence of drug resistance and propelled by global poverty and the AIDS epidemic.[4] Despite the flaws with and growing resistance to current TB treatments, no new TB drugs have been developed in nearly 50 years. This recent uprising of TB has invoked many of the public funding agencies and non government organizations (NGOs) sponsoring programs across the academic and industrial sectors to develop new anti-mycobacterial drugs.[5] Despite this, during the last decade there were only about 10 compounds progressed into clinical development[6] (Figure 2) out of that 6 were New Chemical Entities (NCE) and four compounds were redeveloped or repurposed the existing drug. Redeveloped drugs Rifapentine, Linezolid are in Phase II clinical trials. The inhibitors (DNA gyrase) Gatifloxacin, Moxifloxacin are in Phase III clinical trials.

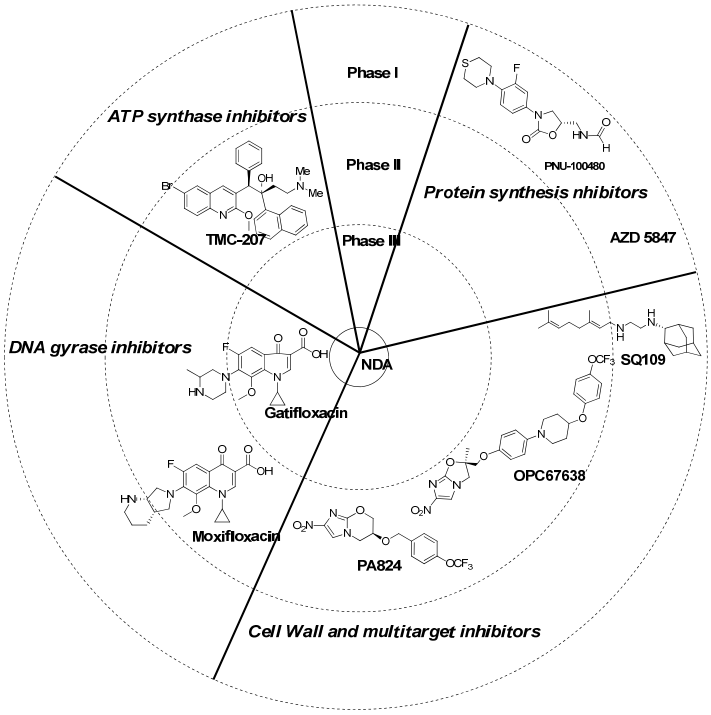


Figure 2: *Compounds in clinical trials for the treatment of tuberculosis with their mode of action*

The new drug SQ-109 (2004) having similar structure to Ethambutol (TB drug) shown good results against MDR and XDR tuberculosis and currently is in phase I trials (Figure 2).[2a, 7] The compounds PNU-100480(2010) and AZD-5847 (2009) discovered respectively by Pfizer and AstraZeneca, belong to oxazolidinone class of drugs and are currently in phase I clinical trials.[8] Both these compounds are shown to target Ribosome. The compounds P-A824 (2000), OPC67683 (2006) are developed by TB Alliance and Otsuka respectively, belong to nitroimidazole class of drugs. These compounds are known to inhibit mycolic acid biosynthesis and are currently in Phase II clinical trials. Quite interestingly, these compounds showed high activity against drug-persistent culture in vitro. The J & J Tibotec and TB Alliance have developed the TMC-207 (2005) which is a Phase II drug and it acts on enzyme ATP Synthase.[8]

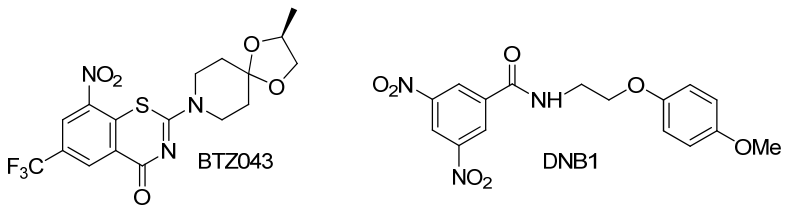


Figure 3: *Structure of Benzothiazinone 043 and Dinitrobenzamide*

Benzothiazinone, BTZ the Dinitrobenzamide (Figure 3) are two classes of compounds in preclinical trials and are showing very good results against *M. tuberculosis* including MDR-TB and XDR-TB strains.[8] Interestingly both compounds are having the same target enzyme that is decaprenylphosphoryl-β-D-ribose 2`-epimerase which is an essential enzyme in *M. tuberculosis* cell wall biosynthesis. Although about 10 compounds are currently in clinical trials raising hopes for future tuberculosis chemotherapy, but high attrition in clinical trials along with ease with which the *M. tuberculosis* acquires resistance towards a new drug is posing attention towards new drug discovery along and novel target search.[9] In search of novel target for tuberculosis drug development, its cell wall biosynthesis is in spotlight since it is known that cell wall makes *Mtb* to survive in adverse physiological as well biological conditions. Also several enzymes involved in its biosynthesis and their substrate were characterized.[10]

The work that has been presented in this thesis focus mainly on the development of new inhibitors cell wall synthesis designed around the substrate of the

arabinofuranosyl transferases. The conjugation of potent inhibitors with a fluorescent tag and use of these fluorescent probes for imaging the *M. tuberculosis* has been attempted. In this regard, a brief description about the recent developments in diagnosis and a comprehensive summary of cell wall structure, details about the arabinofuranosyl transferases (Afts) - important enzymes involved in the cell wall biosynthesis, various substrate mimics of β-DPA (common substrate of all the known arabinofuranosyl transferases) that have developed as potential anti-tubercular compounds has been provided in the proceeding sections.

1.1.1 Tuberculosis diagnosis

The second obstacle in fighting against tuberculosis disease is diagnosis as *M. tuberculosis* active infection does not show any symptoms in initial stage. In advance stage, cough (usually cough up mucus), coughing up blood, excessive sweating (especially at night), fatigue, fever, unintentional weight loss are some of the symptoms and usually patient will be taken for medical assistance at this stage.[11] In advanced stage of tuberculosis, commonly used test is sputum smear microscopy. This test developed more than 100 year ago is unreliable. Advanced TB tests such as culture methods or use of rapid molecular tests are available in developed countries for TB diagnosis. However are not cost effective and unaffordable in undeveloped and developing countries.[11]

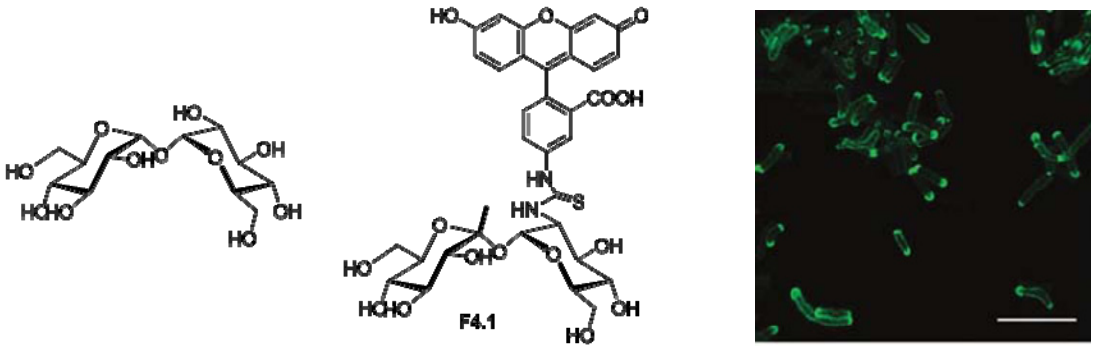


Figure 4: *Trehalose and fluorescein isothiocyanate (FITC) labeled trehalose derivative*

In 2011 Davis *et al* reported[12] a new method for *M. tuberculosis* diagnosis by using fluorescent label trehalose (Figure 4, F4.1). It is the first example of *M. tuberculosis* imaging by small molecular fluorescent probe (Image Figure 4). Davis *et al*

first investigated that enzymes trehalose mycolyltransferases are efficiently processing trehalose more than (MIC/MIC_{50}) 200 µg/ml and trehalose analogue are successfully anchored not only to *M. tuberculosis* in vitro but also to macrophages.

1.1.2. Cell wall structure of *Mycobacterium tuberculosis*

The cell wall of *M. tuberculosis* differentiates it from prokaryotes and is unique in its own.[13] The outer layer of cell wall is made up of densely packed mycolic acid. Intensive efforts from chemical biologists resulted in an almost complete description of cell wall components at the molecular level. The structure of *M. tuberculosis* cell wall (Figure 5) is made up of - plasma membrane, peptidoglycan, arabinogalactan (AG), mycolic acid esters as major components.[13]

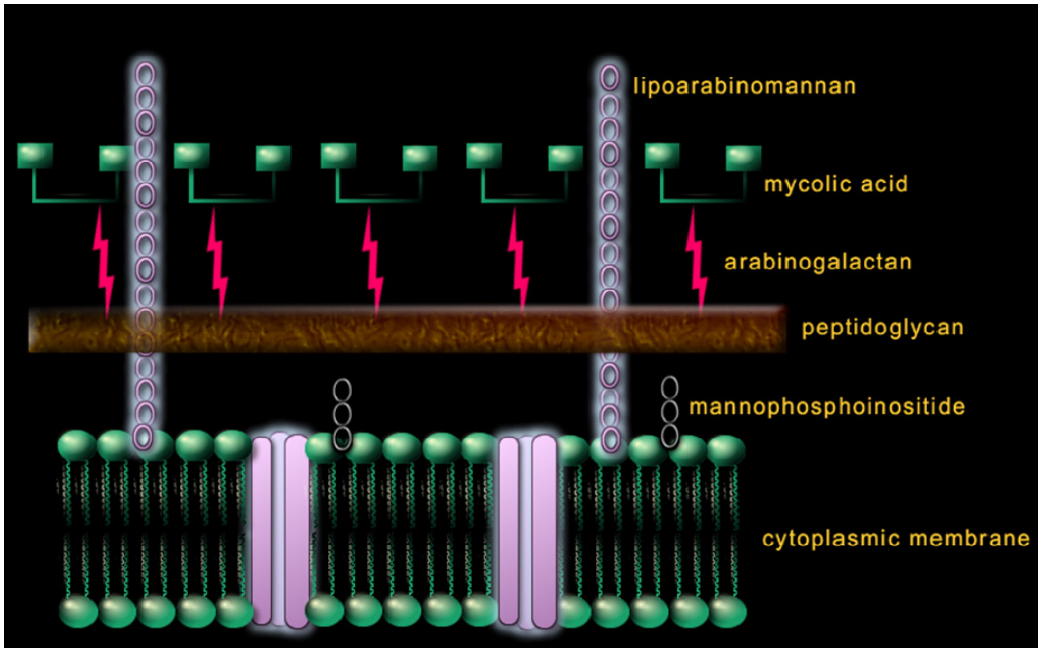


Figure 5: *Cross section of Mycobacterium tuberculosis cell envelope*

The strong portion of cell wall is its outer layer comprising mycolic acid, which is connected covalently with AG complex by an ester bond. AG complex is pendent on peptidoglycan which is further supported by mannophosphoinositide to stay bounded with plasma membrane. The Lipoarabinomannan (LAM) is a polysaccharide containing mannose and arabinose posing outer cell wall is directly connected with plasma membrane. Peptidoglycan is the back bone of cell wall skeleton and covalently linked to

AG chains via phosphoryl-*N*-acetylglucosaminosyl-rhamnosyl linkage units. This peptidoglycan made up of polysaccharide chains constitutes alternating units of N-acetylglucosamine and N-glycolylmuramic acid. The muramic acid is further modified by tetrapeptide (L-alanyl-D-isoglutaminyl-meso-diaminopimelyl-D-alanine).[13]

1.1.3 Arabinogalctan (AG) polysaccharide complex

The AG (Figure 6) complex is a polysaccharide made up of arabinofuranose and galactofuranose is a major portion of *Mycobacterium* cell wall. The galactan is attached to the 6-position of some of the muramic acid residues of the peptidoglycan via an α-L-Rha*p*-(1→3)-α-D-GlcNAc-(1→P).[13] Galactan is a linear portion of AG complex with about 30 alternation of 5 and 6 linked β-D-Gal*f* residues.

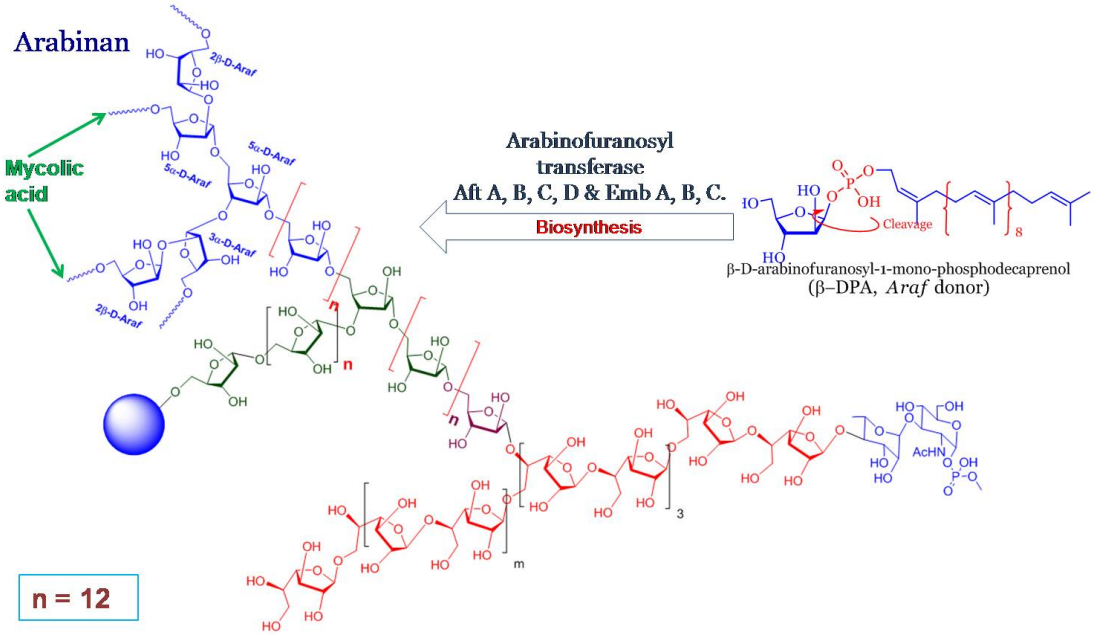


Figure 6: *Mycolyl Arabinogalctan (AG) Complex and structure of β-DPA*

The arabinan polymer is attached to the 5th carbon of some of the 6-linked Gal*f* residues. Most of the arabinofuranose polysaccharide is composed of 5- linked α- D-Ara*f* with branching introduced by 3,5-α-D-Ara*f* residues and comprising about 70 arabinofuranosyl residues. Motif A hexa-saccharide (Figure 6 [β-D-Ara*f*-(1→2)-α-D-Ara*f*]$_2$-3,5-α- D-Ara*f*-(1→5)-α-D-Ara*f*) is present at non-reducing terminal of AG. At the terminal residue of Motif A, that is β-D-Ara*f* `s C(5)–hydroxy group is covalently bonded

to mycolic acid by ester linkage. The linear chain of arabinan polymer is made up of repeating disaccharide α-D-Ara*f*-(1→5)-α-D-Ara*f* which is trivially called as Motif B.

The biosynthesis of AG and LAM portion of cell wall involves several arabinofuranosyl transferases (AraTs) enzymes, out of which AftA is the main AraTs and donate the first Ara*f* on the galactan. AftB is a capping AraTs which terminate the arabinan chain probably after branching has been introduced by EmbA/EmbB. Remaining two enzymes AftC and AftD are shown to exhibit internal branching activity. All AraTs are important in *Mycobacterium* survival and quite interestingly, all the known arabinofuranosyl transferases utilize a single substrate i.e. β-Decaprenyl-D-arabinofuranosyldiphosphate (β-DPA figure 6), which is an attractive target for drug discovery.[13]

1.2 Survey of *C*-glycoside synthesis and biological significance

C-glycosides are carbohydrate mimics where the glycosidic oxygen is replaced by carbon. The *C*-glycosides are metabolically stable compared to *O*-glycosides in various chemical as well as physiological conditions.[14,15] The stability of *C*-glycoside makes them in principle promising inhibitors for enzymes glycosyl transferases, but in practice the difficulties with mimicking *O*-glycosides will be the conformational difference between *O*- and *C*-glycosides due to absence of *endo* and *exo* anomeric effect (resulting from the glycosidic oxygen) in *C*-glycosides.[14] The solution state conformational structure is responsible for biological activity and *C*-glycosides having different conformations from corresponding *O*-glycosides resulted in diminished biological activity. However there are several instances where the *C*-glycosides shown with retained or enhanced biological activity.[16]

The occurrence of *C*-glycosides in natural products (1970s) inspired chemist for their synthesis and afterwards several *C*-glycosylation methods and *C*-glycoside (Mono, di and oligosaccharides) synthesis were reported. However, the current discussion will be limited mainly to the *C*-glycoside syntheses (Figure 7) involving the arabinofuranosyl units. In Figure 7, transformations of common interconnected sugar synthons **F7.A** to **F7.E** is shown. Synthons when treated with acids or base or radical initiator or metal

complex will generate electrophilic, nucleophilic, radical, π-complex intermediates at anomeric center, further treatment of generated intermediates with suitable aglycon partner resulted in to *C*-glycosides.[17]

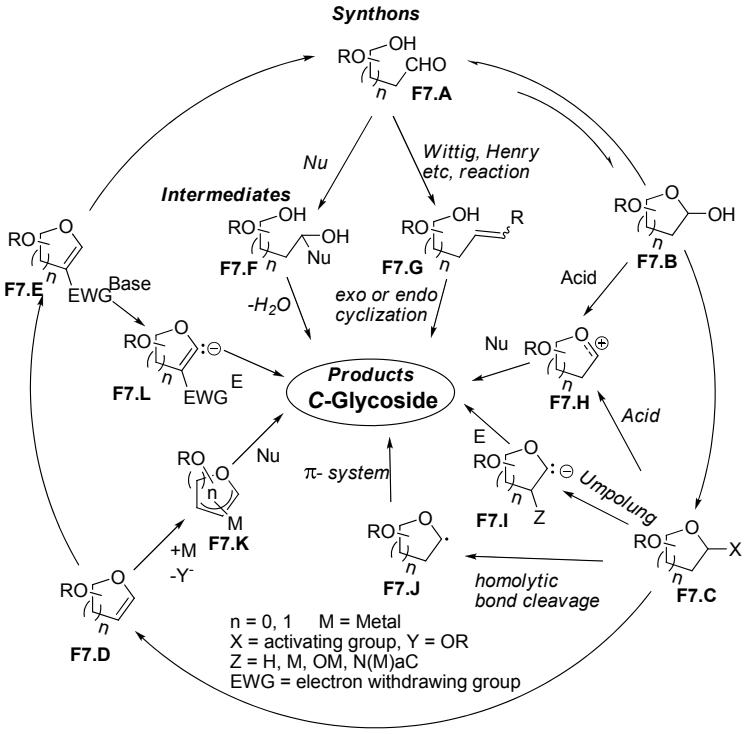


Figure 7: *General strategies employed in C-glycoside synthesis*

The most common *C*-glycoside donors are electrophilic (**F7.F, G, H**) in nature as they are easily accessible along with their stability and reaction simplicity. Commonly employed electrophilic donors (Figure 8) are glycosyl lactone, glycal, 1,2-anhydro sugars and sugars with a good leaving group at anomeric position like hydroxyl, halide, imidate, and acetate.

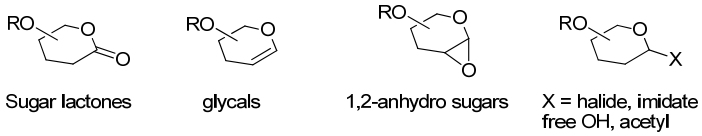


Figure 8: *Common electrophilic donors in C-glycoside synthesis*

C-glycosylation through anomeric anionic intermediate also received attention (**F7.H, L**) as a complementary strategy to electrophilic glycosylations. In most of the

cases the deprotonation at anomeric center was employed to generate anion, generally lithiated glycosyl donor (Figure 9) are used as anionic intermediate in synthesis of *C*-glycoside.

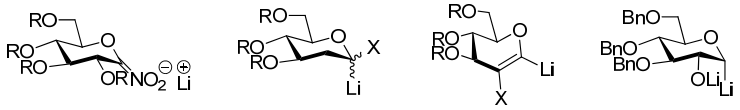


Figure 9: *Commonly employed sugar nucleophiles in C-glycoside synthesis*

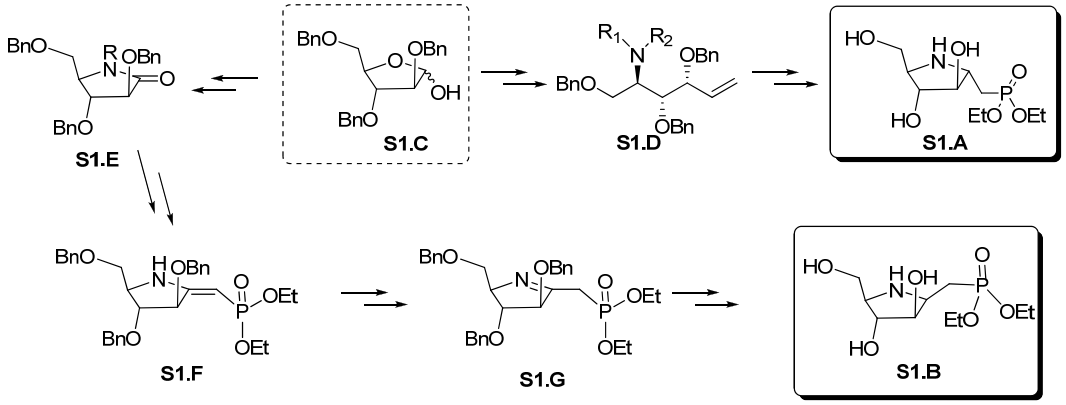
Intermolecular radical (**F7.J**) approach is also a choice of method in some cases for *C*-glycoside synthesis. An anomeric radical is α-alkoxyalkyl radical having the elevated HOMO which can interact with the LUMO of electron poor aglycons like acrylonitrile, acroleine to form a C–C bond. The protecting group tolerance and slow down of elimination and/or epimerization due to absence of anion are merits of radical approach. The leaving groups such as halide, phophate, and sulphonate are generally used to generate an anomeric radical. Along with these classical approaches, these days the *C*-glycosylation has been also performed by using metal π-complex at anomeric center (**F7.K**) as intermediate and employing an appropriate *C*-nucleophilic aglycon. Although several methods are reported for *C*-glycoside synthesis, there is no general protocol available for stereoselective *C*-glycosylation. This poses opportunity and challenges for developing new strategies for the *C*-glycoside synthesis by using methods other than the direct C–C bond formation at anomeric position.

1.3 Literature report about arabinofuranosyl transferases inhibitor development

The following literature survey will deal mainly with the synthesis of *C*-glycoside analogues of β-DPA and their inhibition studies against the Mycobacterium.

1.3.1 Eustache`s synthesis of azasugar-derived phosphonate (1997)

Eustache group[18] first reported the synthesis of azasugar derivative with arabino configuration as AraTs inhibitor. Synthesis of azasugars (**S1.A, S1.B**) started from D-arabinose derived tribenzyl lactol **S1.C** which by one carbon Wittig homologation and two successive Mitsunobu reactions by *p*-nitro benzoic acid and phthalimide amine furnished **S1.D**. The intermediate **S1.D** was further subjected for iodo cyclization to get pyrrolidine, subsequent replacement of iodo with diethyl phosphate and protecting group removal afforded alpha azasugar analogue of β-DPA **S1.A**. Dimethoxy phosphonomethyl lithium is added to lactam **S1.E** and hemiketal intermediate subjected for deoxygation procured **S1.F** conjugate phophonate. **S1.F** was isomerized to get iminium ion **S1.G** and subsequently iminium ion and benzyl group in **S1.G** were reduced to get the aza-sugar analogue **S1.B** with required stereochemistry as of β-DPA.

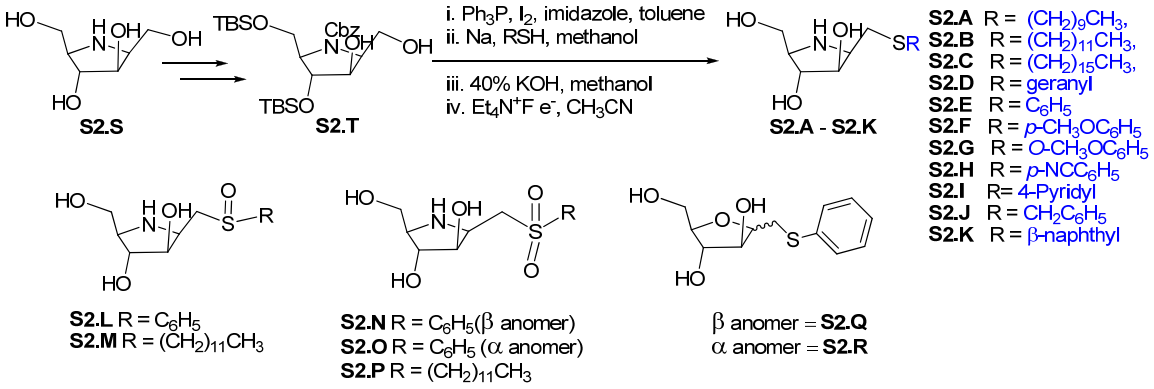


Scheme 1: *Synthesis of azasugar C-phosphonate analogue of DPA*

1.3.2 Maddry`s synthesis and evaluation of DPA azasugar analogue as antimicrobacterial agents (1998)

Maddry *et al*[19] synthesized hydrolytically stable DPA azasugar analogues where the phosphorous atom was replaced by a sulfur atom. The synthesis of the thioether,

sulfoxide and sulfone DPA derivatives (**S2.A–S2.R**) started by protecting group manipulation of (**S2.S**) pyrrolidine to give **S2.T**. Selectively primary hydroxyl in **S2.T** was converted into iodo and displacement of the iodine with the appropriate sodium salt of an alkyl thiol or a thiophenol followed by the deprotection the N-Cbz and TBS groups furnished azasugar thioethers **S2.A–S2.R**. Further, the thioethers **S2.B** and **S2.E** were oxidized to afford sulfoxides **S2.L** and **S2.M** and sulfones **S2.N–S2.P**. For comparison of biological activity, α and β furanose analogues **S2.Q–S2.R** have been also prepared.



Scheme 2: *Synthesis of azasugar thioether, sulfoxide and sulfone derivative of azasugar*

The DPA analogues **S2.A–S2.R** were tested in vitro against *M. tuberculosis* strain H37Ra and also against a panel of 5 clinical MAC isolated. It was found that most of the compounds were not showing good activity against mycobacterium up to noncytotoxic levels, surprisingly **S2.E** was showing consistently and reproducibly active against 3 strains of MAC at 4 μg/ml in infected macrophages. In addition, no Structure-Activity Relations were observed with the prepared set of molecules and in vivo study of **S2.E** in TB infected mouse was not reproducible and the authors concluded that the mechanism of action of **S2.E** is unclear and the inactivity of the compound against mycobacterium in assays may argue against inhibition of cell wall synthesis.

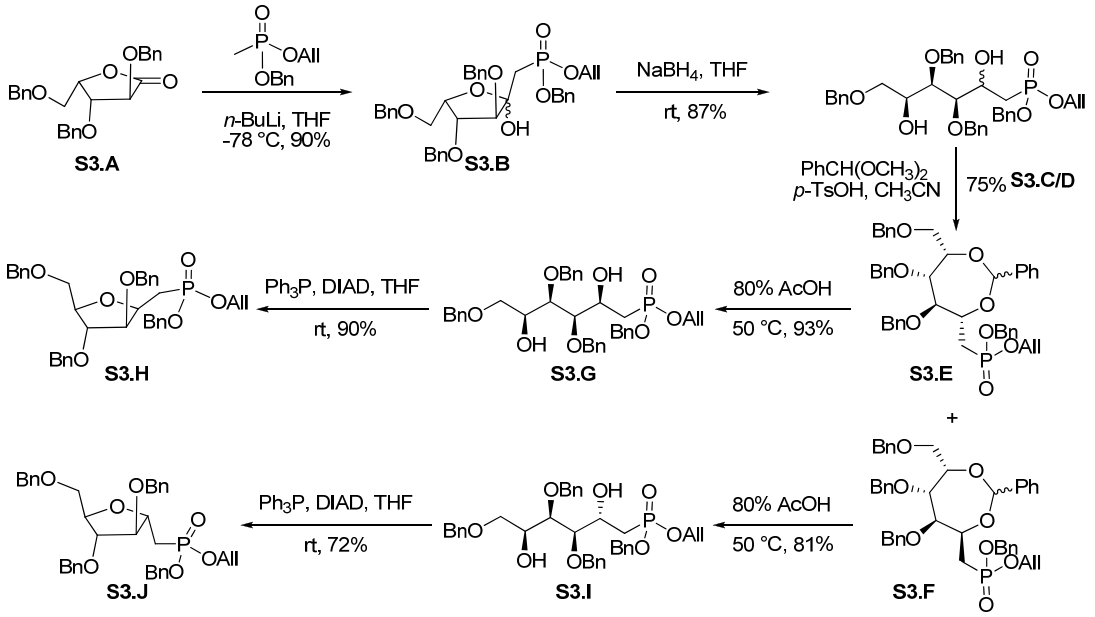
Table 1: *Structures and Biological Activities of arabinose Analogues* [a, b]

Compound	R	MIC[c] (μg/ml)	MBC[c] (μg/ml)	BACTEC % Inhibition at 12.5 μg/ml	Macrophage (*M. avium*)
S2.A	$(CH2)_9CH_3$	32-128	>128	ND	ND
S2.B	$(CH2)_{11}CH_3$	16-32	64 to 128	ND	C
S2.C	$(CH2)_{13}CH_3$	16-64	64 to 128	ND	ND
S2.D	geranyl	64 to 128	ND	ND	C
S2.E	C_6H_5	>128	ND	0	4 μg/ml
S2.F	*p*-$OCH_3C_6H_5$	>128	ND	ND	ND
S2.G	*o*-$OCH_3C_6H_5$	>128	ND	ND	ND
S2.H	*p*-NCC_6H_5	>128	ND	5	ND
S2.I	4-pyridyl	>128	ND	6	ND
S2.J	$CH_2C_6H_5$	>128	ND	ND	ND
S2.K	β-naphthyl	>128[d]	ND	18	ND
S2.L	C_6H_5	>128	ND	18	1
S2.M	$(CH_2)_{11}CH_3$	32-64	≥128	ND	ND
S2.N	C_6H_5	>128	ND	6	1
S2.O	$(CH_2)_{11}CH_3$	32 to 128	≥128	ND	C
S2.P	β-Araf	>128	ND	ND	>64 μg/ml
S2.Q	α-Araf	>128	ND	ND	>64 μg/ml
S2.R		>12.8- ≤ 128	ND	ND	ND

[a]See Scheme (2) and figure **S2.A**–**S2.R** for structures; [b] abbreviations : MIC, minimum inhibitory concentration; MBC, minimum bactericidal concentration; ND, not determined; C, cytotoxic to macrophages; I, inactive in macrophages. [c] Numbers represent the range of values obtained with the various strains (specific strains used are *M tuberculosis* strain H37Ra and on MAC strains NJ 168 (serovar 1), NJ 211 (serovar 4,6), NJ 1854 (serovar 8), NJ 3009 (serovar 4), and NJ 3404 (serovar 4)); the following compounds were used as controls: Ethambutol, 8-32; isoniazid, 0.03 *(M. tuberculosis),* 0.5->2 (MAC). [d]Partial inhibition at 128 ~μg/mL.

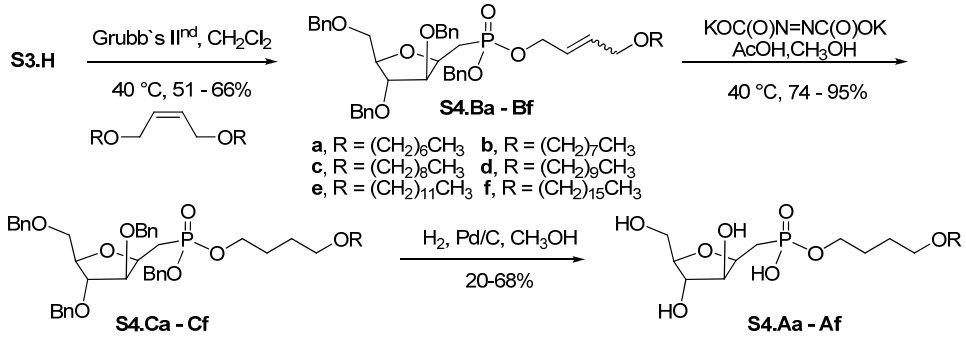
1.3.3 Lowary`s synthesis and evaluation of *C*-phosphonate arabinofuranose analogues as DPA mimics and their evaluation as substrates for the arabinofuranosyltransferase inhibition (2002)

In 2002 Lowary *et al*[20] reported synthesis of *C*-phosphonate analogues (Scheme 3) of β-DPA after encountering with several failures. Synthesis of **S3.Aa–Af** started from nucleophilic addition of lithiated phosphonate to L-xylofurano lactone **S3.A**. The resulting hemiketal **S3.B** was reduced to afford diastereomeric diols **S3.C/D**. These hemi diols were separated as their benzylidene acetals **S3.E**/**S3.F**. The separated acetals were subjected for the acetal deprotection and the resulting pure diols were further cyclized to the corresponding *C*-furanoside **S3.H/ S3.J** using Mitsunobu reaction.



Scheme 3: *Synthesis of C-phosphonate analogues of DPA*

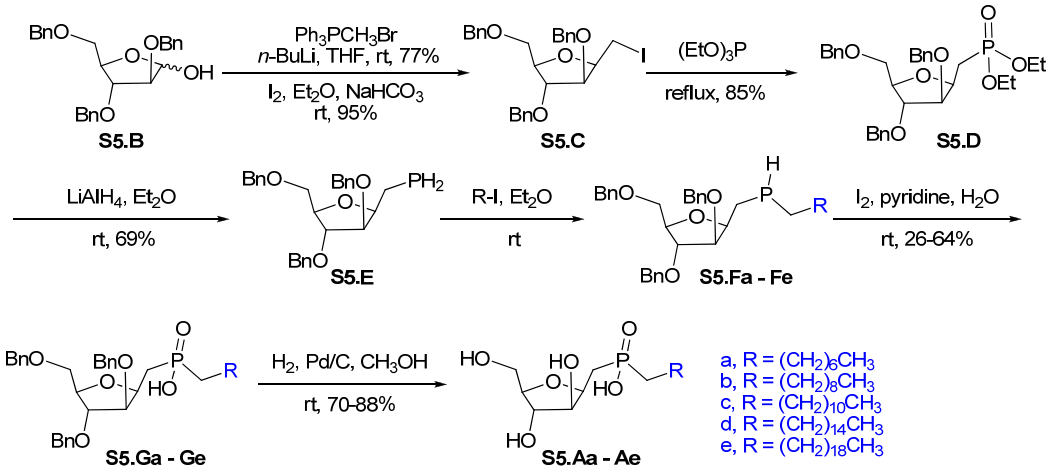
Further, the phosphonate allyl ester **S3.H** coupled with various alkenes by cross metathesis and subsequently the olefin units in phosphonates **S4.Ba–Bf** were reduced by diimide. The final hydrogenolysis of the benzyl groups afforded desired DPA analogues **S4.Aa–S4.Af**. Screening of these phosponate analogues against *M.* tuberculosis in vitro reveled that one of the compound **S4.Af** possessed anti-tubercular activity with an MIC value of 3.13 µg/mL.



Scheme 4: *Synthesis of C-phosphonate analogues of DPA*

1.3.4 Synthesis of glycosyl phosphinic acids (2003)

In 2003, the Lowary group[21] has reported the synthesis of *C*-phosphinic acid analogues of β-DPA and their evaluation as novel anti-tubercular compounds.



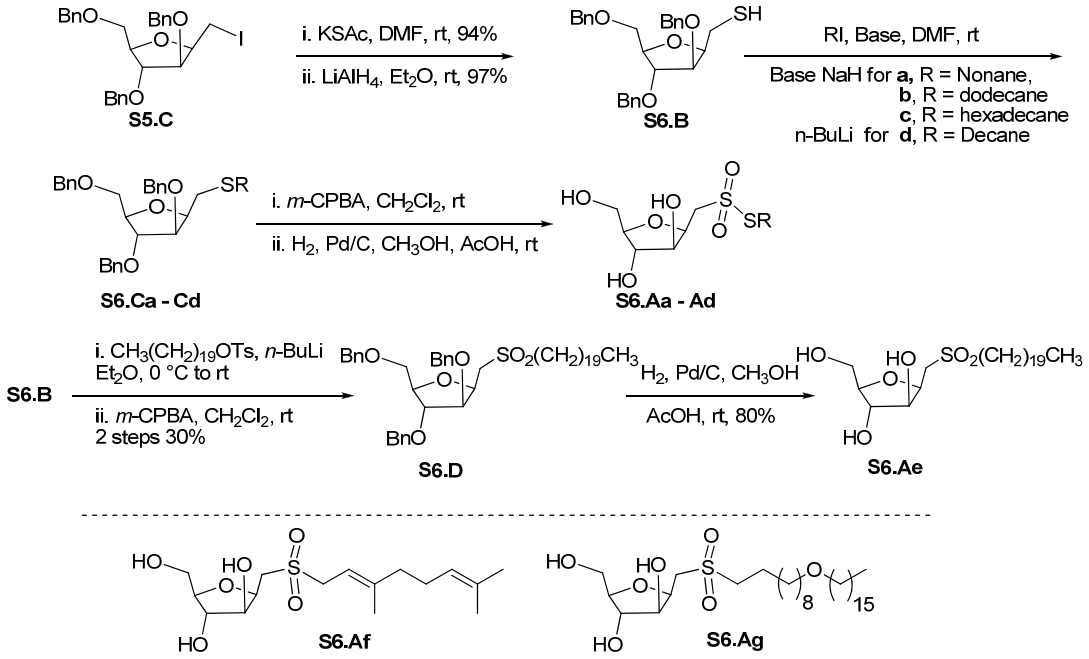
Scheme 5: *Synthesis of glycosyl phosphinic acids*

Synthesis of arabinofuranosyl phosphinic acids **S5.Aa–Ae** was started by one carbon Wittig homologation of tribenzylarabinofuranose and iodo-etherification of the *C*-furanosides **S5.B** to get **S5.C** with exclusive beta configuration. The pendant iodo group in **S5.C** was replaced by trimethyl phosphite and the resulting phosphonate **S5.D** was reduced by lithium aluminum hydride to get corresponding phosphine **S5.E**. The unstable phosphine **S5.E** was immediately subjected for alkylation using various long chain alkyl (hexyl, octyl, decyl, tetradacyl, octadacyl) iodides to get monoalkylated products **S5.Fa–Fe**. Subsequent phosphine oxidation followed by benzyl group deprotection furnished phosphinic acid analogue of β-DPA **S5.Aa–S5.Ae**.

1.3.5 Synthesis of arabinofuranosyl sulfone analogues of β-DPA as anti-tuberculosis agents

After successful synthesis of *C*-glycosyl phosphonate and phosphonic acid, Lowary *et al* designed and synthesized sulfone analogue of β-DPA.[22] For the synthesis of sulfone analogue (Scheme 6) Lowary group employed similar strategy as used in synthesis of phosphonic acid analogue (2002). The synthesis of sulfone analogues **S6.Aa–Ag** started from **S5.C** where the iodo group was replaced by thioacetate and

resultant thioester was reduced with lithium aluminum hydride to get the thiol **S6.B**. This thiol was further alkylated using long chain alkyl iodides. The resulting thioethers **S6.Ca–S6.Cd** were oxidized to corresponding sulfones and then subjected for hydrogenolysis using H_2, Pd/C to afford the sulfone analogue **S6.Aa–Ad**. Similarly, compound **S6.Af** was synthesized using geranyl tosylate and **S6.Ag** was synthesized by using 10-(hexadecyloxy) decyl benzenesulfonate as alkylation agent.



Scheme 6: *Synthesis of arabinofuranosyl sulfone analogue of β-DPA*

1.3.6 Screening of phosphonate, phosphonic acid and sulfone analogues as anti-tuberculosis agents[22]

The *C*-phosphonate analogues **S4.Aa–Af,** phosphonic acids **S5.Aa–Ae** and sulfones **S6.Aa–Ag** have been screened for their ability to prevent the growth of *M. tuberculosis* strain H37Rv using the fluorescence-based almar Blue microplate assay and the results given are summarized in Table 2. The phosphonate DPA analogue **S4.Af** was found to be the best amongst the all the compounds screened. The sulfone and phosphonic acid analogues have not shown any significant inhibition except the sulfone **S6.Ac** with decyl chain showing 45% inhibition. The results clearly demonstrate that no clear correlation exist between structure and antituberculosis activity. However, in

phosphonate **S4.Aa–Af** DPA analogues the activity seem to be depend upon the chain length of the aglycon.

Table 2. *Activity of against M. tuberculosis strain $H_{37}Rv$*[a]

Entry	Compound	% of **Inhibition**
1	**S4.Af**[b] (Phosphonate analogue)	92
2	**S6.Aa** (Sulfone analogue)	0
3	**S6.Ab** (Sulfone analogue)	21
4	**S6.Ac** (Sulfone analogue)	45
5	**S6.Ad** (Sulfone analogue)	0
6	**S6.Ae** (Sulfone analogue)	4
7	**S6.Af** (Sulfone analogue)	0
8	**S6.Ag** (Sulfone analogue)	20
9	**S5.Aa** (Phosphinic acid analogue)	0
10	**S5.Ab** (Phosphinic acid analogue)	0
11	**S5.Ac** (Phosphinic acid analogue)	17
12	**S5.Ad** (Phosphinic acid analogue)	0
13	**S5.Ae** (Phosphinic acid analogue)	0

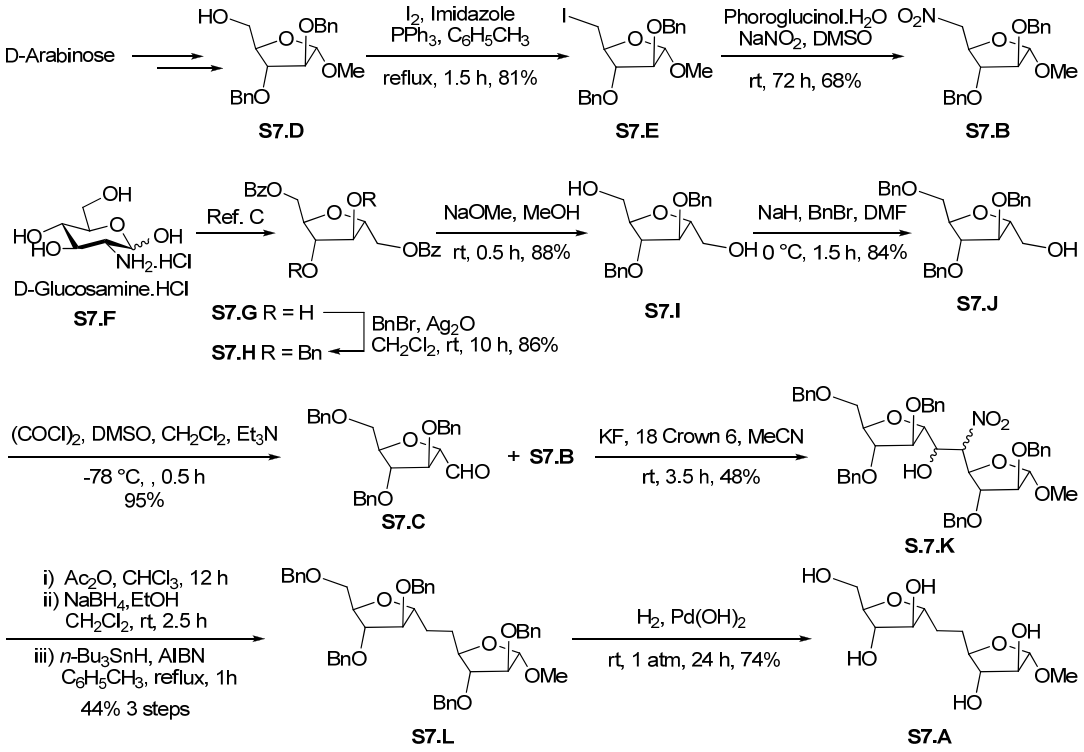
[a] All compounds were screened at a concentration of 6.25l g/mL using the Alamar Blue assay.[b] **S4.Af** has a MIC of 3.13l g/mL.

1.4 Synthesis of *carba*-disaccharide analogues of Motif C

1.4.1 Gurjar`s Synthesis of *C*-disaccharide methyl-α-*C*-D-arabinofuranose-(1–5)-α-D-arabinofuranoside (2002)

In 2002 Gurjar *et al*[23] published first *C*-analogue (**S7.A)** synthesis of Motif C utilizing nitro aldol as a key reaction to join two monosaccharide units. Retro synthesis simplifies that disaccharide could be obtain from two units, one is 5-nitro-D-arabinose monosaccharide **S7.B** which was procured from D-arabinose and second monosaccharide **S7.C** unit was synthesized from D-glucosamine hydrochloride. The synthesis of **S7.A** started with conversion of the C-5 hydroxyl of **S7.D** to iodo derivative **S7.E**. Subsequently iodo was replaced by nitro group using sodium nitrite to get the nitro partner **S7.B**. Synthesis of second monosaccharide unit **S7.C** was started by diazotization-mediated ring contraction reaction of D-glucosamine-hydrochloride **S7.F** and subsequent transformations to get dibenzoyl protected compound **S7.G**. The benzylation of diol in **S7.G** and subsequent saponification provided **S7.I** which was

subjected for selective monobenzylation to get **S7.J**. The free (C)-5hydroxyl in **S7.J** was oxidized to aldehyde **S7.C** under Swern conditions. The coupling between nitro **S7.B** and aldehyde **S7.C** was furnished by using KF in acetonitrile to get **S7.K**. The hydroxyl group of **S7.K** was eliminated and resulting conjugate olefin reduction followed by denitration procured pentabenzyl Motif C analogue **S7.L** where all benzyl groups were deprotected by using Pd $(OH)_2$ to get motif C analogue **S7.A**.

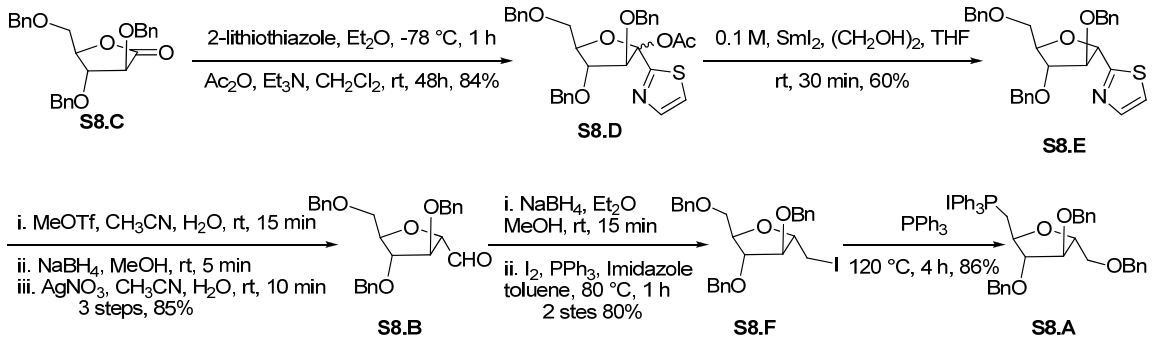


Scheme 7: *First synthesis of methyl-α-C-D-arabinofuranosyl-(1–5)-α-D-arabinofuranoside*

1.4.2 Dondoni`s approach for α-(1–5)-D-arabinofuranose *C*-oligosaccharide by iterative Wittig reaction (2003)

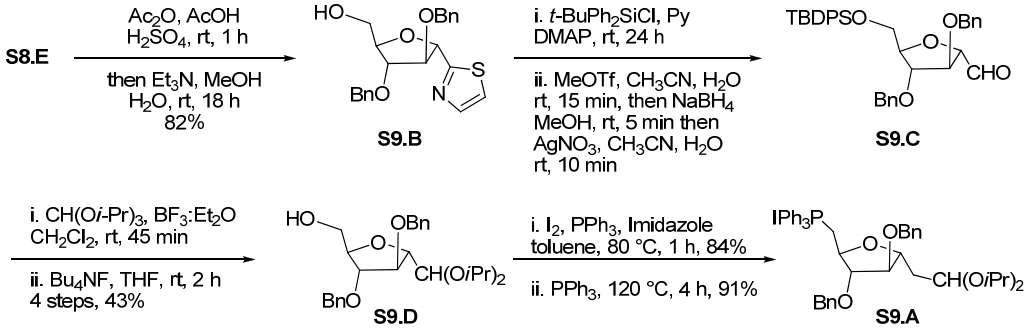
Dondoni *et al*[24] synthesized *C*-disaccharide **1** and trisaccharide **S10.A** of arabinofuranose by iterative Wittig olefination. For synthesis of di- and trisaccharides three arabinofuranose building blocks were designed. Two were triphenyl phoshine salts **S8.A**, **S9.A** and one was the aldehyde **S8.B**. Synthesis of first building block (Scheme 8) started by addition of 2-lithiothiazole to lactone **S8.C**. The resulting hemiketal was acetylated by acetic anhydride to get α/β-1-*O*-acetyl derivative **S8.D**. The *O*-acetyl

thiazolyl derivative was then subjected for deoxygenation with samarium (II) iodide in ethylene glycol to procure the α-deoxy product **S8.E**.



Scheme 8: *Synthesis of aldehyde and monofuctionalized (Wittig salt) building block*

Next, the thiazole group in **S8.E** was unmasked to an aldehyde by a sequence of reactions involving *N*-methylation, borohydride reduction and silver assisted hydrolysis of thiazolidine to get *C*- formyl arabinoside **S8.B** without any epimerization. The second monofuctionalized building block (Scheme 8), i.e. the tribenzylated phosphonium salt **S8.A** was obtained from the aldehyde **S8.B** by reduction and subsequent iodination of primary hydroxyl to get iodo compound **S8.F**. Treatment of the iodo **S8.F** with neat triphenylphosphine at 120 °C (69%, three steps) resulted in to **S8.A.**

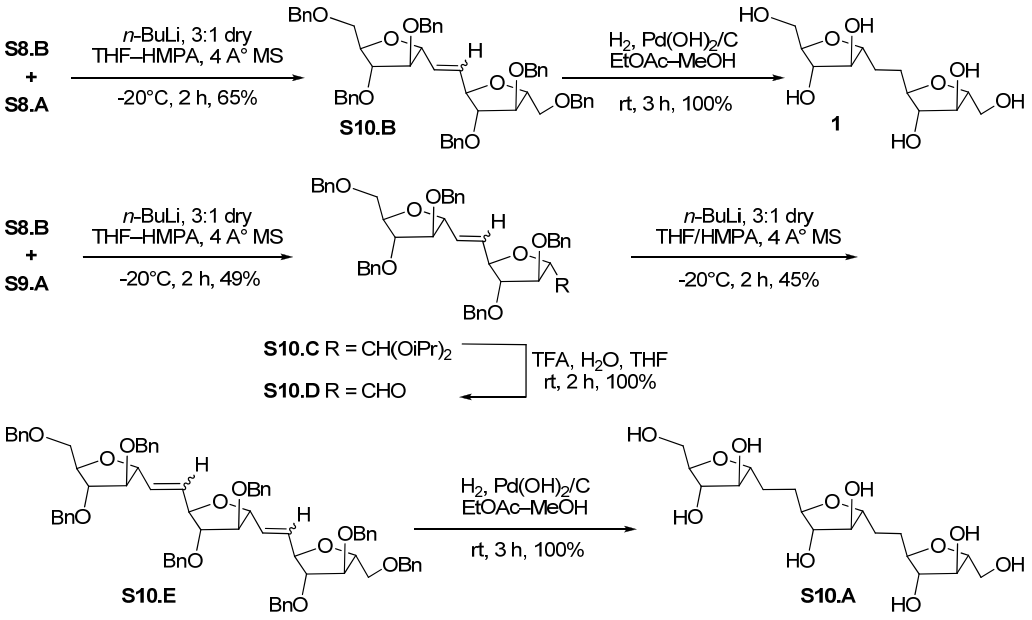


Scheme 9: *Synthesis of second Wittig salt building block*

The third building block **S9.A** was prepared by a long sequence of reactions. The sequence started with the benzyl deprotection in **S8.E** and TBDPS protection of (C)-5 hydroxyl of **S9.B** then unmasking of the thiazolyl unit to aldehyde **S9.C** followed by protection of aldehyde as its acetal by isopropyl orthoester and TBDPS deprotection to

arrive at the acetal **S9.D**. The alcohol **S9.D** was finally transformed into the target phosphonium salt **S9.A** via the corresponding iodide derivative.

The synthesis of disaccharide **1** (Scheme 10) started with treatment of aldehyde building block **S8.B** with in situ generated ylide from **S8.A** to get the disaccharide **S10.B**. The perhydrogenolysis using $Pd(OH)_2/C$ gave the fully the disaccharide **1**. Similarly trisaccharide (Scheme 10) **S10.A** synthesis was completed by first assembling disaccharide building block **S10.C** by Wittig reaction of **S8.B** and **S9.A** and subsequent diisopropyl deprotection by TFA/H_2O to get aldehyde **S10.D** which upon second Wittig reaction with salt **S8.A** and global deprotection resulted in the trisaccharide **S10.A**.

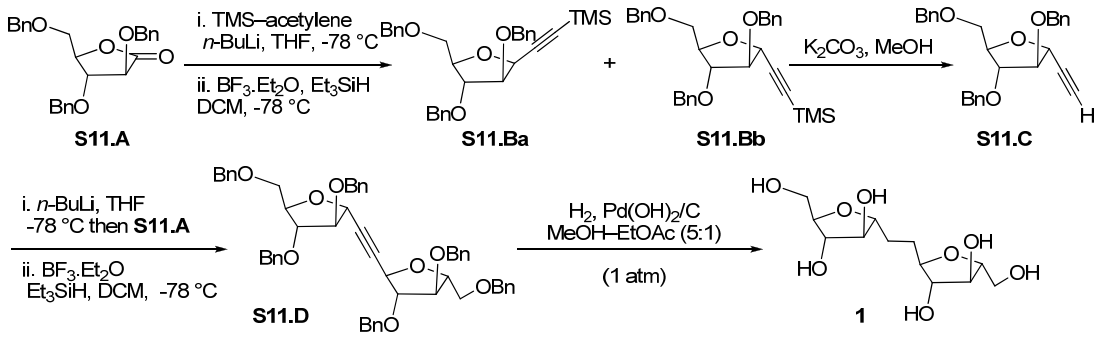


Scheme 10: *Synthesis of C-disaccharide and trisaccharide analogue of cell wall of Mtb*

1.4.3 Wightman`s synthesis of Motif C *C*-disaccharide analogue (2005)

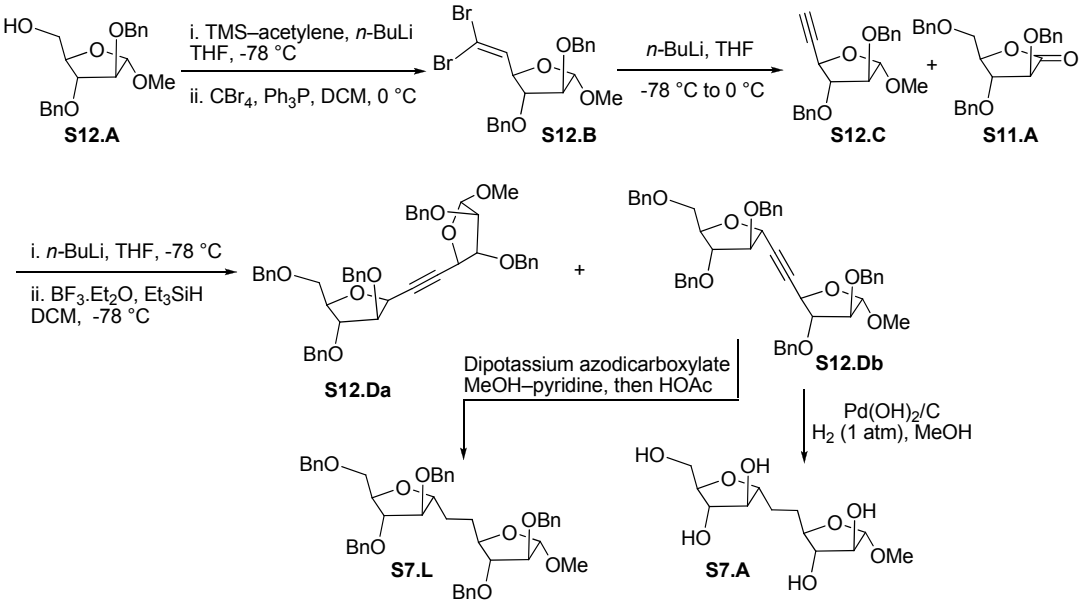
Wightman *et al*[25] reported synthesis of two *C*-disaccharide Motif C analogues (**1/S12.A**) by using nucleophilic alkyne addition at anomeric position as a key reaction to couple two monosaccharide derivative in synthesis of both disaccharides. Synthesis of first *C*-disaccharide analogue **1** commenced with addition of lithium trimethyl silyl acetalide to the tribenzyl lactone **S11.A** and subsequent reduction of the intermediate hemiacetal with $BF_3.Et_2O/Et_3SiH$ to afford a mixture of *C*-alkynes **S11.Ba/b**. The alkyne

alpha anomer **S11.Bb** was separated and trimethyl silyl group was deprotected using K_2CO_3 in MeOH to get **S11.C**. Next the lithiated alkyne **S11.C** was added to the lactone **S11.A** and resulting hemiacetal was reduced with $BF_3.Et_2O/Et_3SiH$ to get disaccharide **S11.D** as major isomer. Finally one pot hydrogenolysis of alkyne and *O*-benzyl groups using $Pd(OH)_2/C$ gave the disaccharide **1** in quantitative yield.



Scheme 11: *Synthesis of Motif C-disaccharide*

Next synthesis of methyl disaccharide **S7.A** started by preparation of first alkyne monosaccharide part **S12.C** in 3 step from arabinose derivative **S12.A**. The free hydroxyl in **S12.A** was oxidized by Swern oxidation and the resulting aldehyde was converted in to dibromoalkene **S12.B** by treating with CBr_4-Ph_3P.

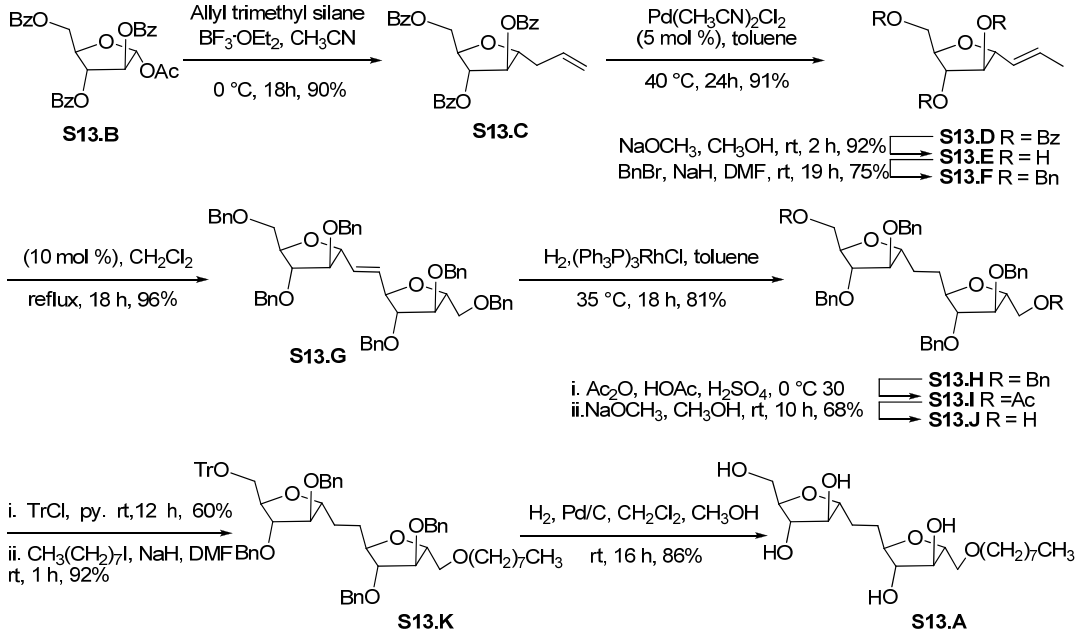


Scheme 12: *Synthesis of Motif C-disaccharide*

Then treatment of **S12.B** with *n*-BuLi gave the alkyne **S12.C**. Further reaction of lithiated alkyne **S12.C** with lactone **S11.A** subsequent reduction of intermediate hemiacetal with Et_3SiH and $BF_3.Et_2O$ gave a mixture of anomers **S12.Da** in 66% and **S12.Db** in 20% yield. The major product **S12.Db** was found to be alpha anomer and was further partially reduced to procured **S7.L** known compound to match the data. Lastly alkyne and benzyls in alpha isomer **S12.Db** were reduced over $Pd(OH)_2/C$ to get **S7.A**.

1.4.4 Lowary`s Synthesis of α-D-arabinofuranose-(1–5)-α-D-arabinofuranose *C*-disaccharide motif (2006)

Lowary *et al*[26] (**2006**) reported synthesis of *C*-disaccharide by using cross metathesis as key reaction. The synthesis started by α-*C*-allylation of arabinose derivative **S13.B** by using allyltrimethylsilane and $BF_3.OEt_2$. The *C*-allyl **S13.B** derivative was then subjected for olefin isomerization using Wilkinson catalyst to get **S13.C**. Cross metathesis of olefin **S13.C** using Grubb`s first generation catalyst met with failure. To overcome this problem, the tribenzyl derivative **S13.F** has been prepared.



Scheme 13*: Synthesis of Motif C-disaccharide*

The initial experiments on the cross metathesis of tribenzyl derivative **S13.F** using Grubb`s 1st generation catalyst resulted in poor yield (10%). Quite surprisingly, the yield

of the cross metathesis was increased dramatically up to 96% when Grubb`s 2nd generation catalyst was deployed for this purpose.

The resulting alkene **S13.G** was reduced using Wilkinson catalyst to get the disaccharide **S13.H**. Selective primary diacetylation of disaccharide dibenzyl **S13.H** followed by acetyl deprotection gave the diol **S13.J**. The selective trityl group protection of **S13.J** gave the monoprotected derivative and the remaining free –OH group in was subsequently alkylated using octyl iodide to obtain the **S13.K**. Then trityl ether was deprotected by acid hydrolysis and then benzyl ethers were deprotected to arrive at the final disaccharide **S13.A**. Preliminary screening results of the disaccharide **S13.A** against the inhibition of the growth not encouraging and no further synthesis of the derivatives related to this compound have been not documented later.

Thus the examination of the available synthesis of *C*-disaccharide Motif C reveals that in majority of the cases lengthy sequence and the options for the synthesis of anomeric analogues are limited. Considering the biological importance of *C*-disaccharide Motif C, we were interested to develop a strategy to provide the *C*-disaccharide Motif C anomeric analogues. The details of our efforts in this direction will be discussed in the Section **2.2**.

RESULTS & DISCUSSION

2. Results and Discussion

2.1.1 Synthesis of 1-α and β-D-arabinofuranosyl-undec-10-ene

Multidrug resistance in tuberculosis posing difficulty to control and eliminate the disease and increased death toll in developing countries.[27] This situation posed challenges for academia as well industry to work for new mechanism based drug discovery.[28] In this regard many biosynthetic pathway and enzymes involved in *M. tuberculosis* cell were discovered. Out of these characterized enzymes, ATP synthase, protein synthase, DNA gyrase, cell wall synthase are some of the current targets for new drug discovery.[2a] The impermeable cell wall of *Mycobacterium tuberculosis* has been identified as one of the reasons for its drug resistance and for the long life in human lungs.[29] The major portion of the cell wall of *Mycobacterium tuberculosis* is made up of the polysaccharides arabinogalactan (AG) and lipoarabinomannan (LAM), in which arabinan chains are linked to C(5)-carbon of galactofuranose by glycoside bond.[10e, 30] Arabinan chains are made up of D-arabinofuranose residues (Araf) and arabinose as such is foreign material to the mammalian cells. These oligosaccharides (AG and LAM) are synthesized inside the infected host cells by complex processes. Therefore the inhibition of the corresponding machinery of the cell-wall biosynthesis of *M. tuberculosis* is a promising approach for the discovery of new anti-tubercular agents.[31]

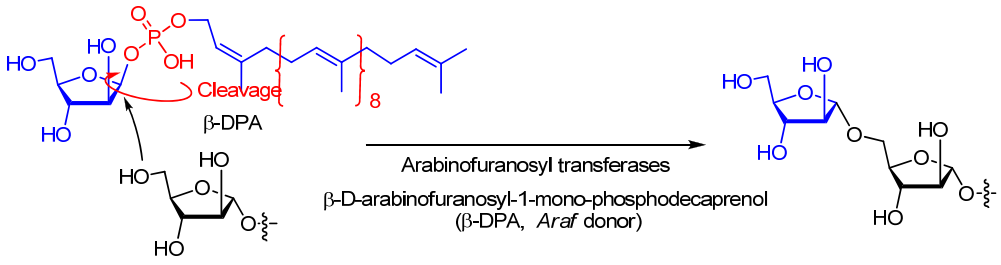


Figure 1: *Putative biosynthesis of arabinan polysaccharide catalyzed by arabinofuranosyl transferases*

Till date, seven arabinofuranosyl transferases (AraTs) involved in biosynthesis of AG and LAM have been discovered. Interestingly, all these AraTs utilize a single substrate i.e. β-decaprenyl-D-arabinofuranosyldiphosphate (Figure 1, β-DPA) for the

biosynthesis of arabinofuranose polysacharide.[32] This has prompted a search for the mimics of the β-DPA as potential inhibitors for AraTs *inter alia* new drug candidates that stop cell wall biosynthesis of *M. Tuberculosis*.[10d, 33] We have been particularly interested in *C*-glycosides in this regard. The *C*-glycosides, which entail methylene substitution for the anomeric oxygen, are non-hydrolysable isosteric mimics of their *O*-glycoside counterparts which offer a great deal of stability without substantial conformational amendment.[34] The 1-β-D-arabinofuranosyl-undec-10-ene **2** (Figure 2) was selected as β-DPA analogue, where the decaprenyl phosphate aglycon partner has been replaced by undec-1-ene. The undec-1-ene unit has been selected for three reasons - i. as a simple hydrophobic side chain to mimic decaprenyl; ii. aglycon easy availability; iii. the provision of a terminal olefin for further functional group modifications and for conjugation to afford a fluroscent probe. Also α-analogue **3** was selected as a substrate for control experiments.

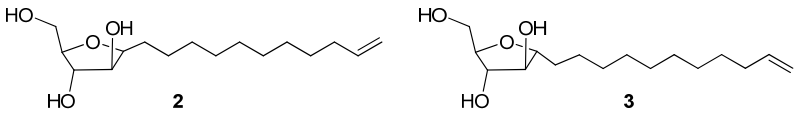


Figure 2: *Structure of 1-β and α-D-arabinofuranosyl-undec-10-ene*

In literature, the lack of suitable protocol for stereoselective synthesis for *C*-arabinofuranosides prompted us to devise a new stratgy for their stereoselective synthesis in general and for synthesis of **2** and **3** in particular.

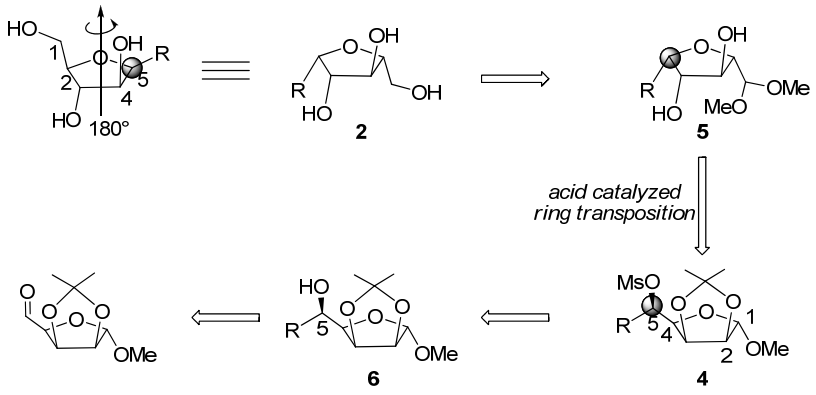
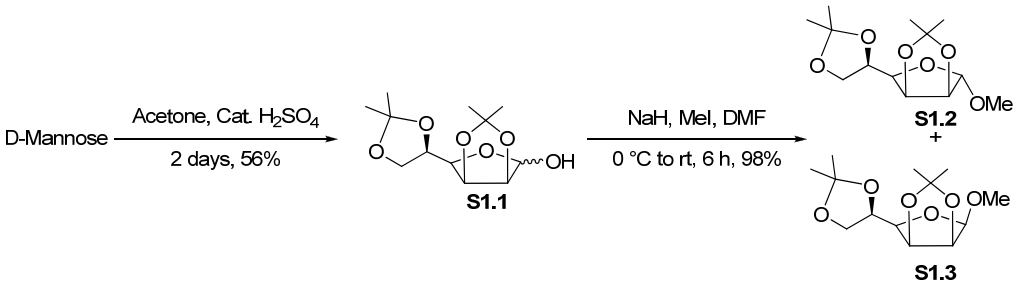


Figure 3: *Strategy for C-alkyl-D-arabinofuranoside*

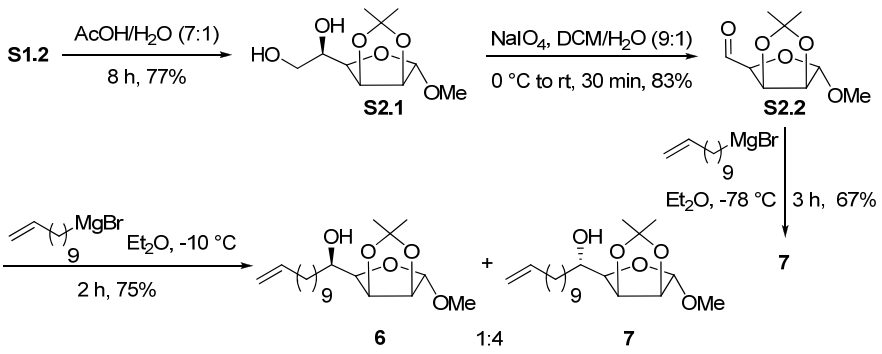
For synthesis of **2**, we relied on acid mediated furan ring transposition (FRT) of a mesylate **4** as the key reaction (Figure 3).[35] The proposed FRT involves multiple C–O bond ruptures and formations happen in one pot to yield acetal **5** having *C*-glycoside core structure. The acetal **5** can be easily transformed into **2** by hydrolysis of acetal group and subsequent reduction of resulting aldehyde. Mesylate **4** can be prepared from alcohol **6** which was planned to synthesize from D-lyxo aldehyde by Grignard addition of undecenyl magnesium bromide. The synthesis of D-lyxo aldehyde has been reported from D-mannose in 4 steps.

Initially, the selected β-DPA analogue 1-β-D-arabinofuranosyl-undec-10-ene (**2**) synthesis began with the usual diacetonide protection of D-mannose in acetone by catalytic sulphuric acid (Scheme 1). The diacetonide **S1.1** was subjected for methylation using sodium hydride and methyl iodide in DMF to get separable anomeric mixture of methyl glycoside **S1.2** and **S1.3**. Anomeric proton in **S1.2** shows singlet at 4.48 ppm which is characteristic of alpha anomer and that of **S1.3** shows doublet at 4.62 ppm corresponds to β-anomer in ^{1}H NMR.



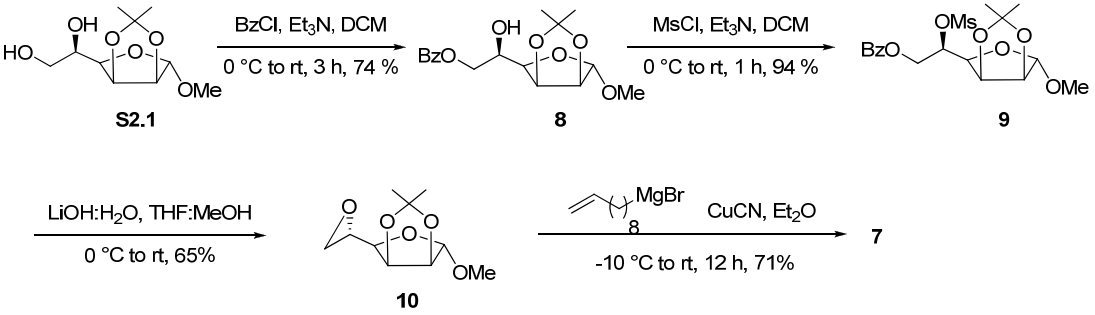
Scheme 1: *Synthesis methyl-2,3,5,6-diisopropylidene-D-mannofuranose*

The aldehyde **S2.2** was prepared from major alpha methyl glycoside **S1.2** by selective deprotection of 5,6-acetonide in aqueous acetic acid followed by cleavage of resulted diol **S2.1** in dichloromethane using sodium periodate. Subsequent addition of 10-undecenylmagnesium bromide on aldehyde at –10 °C found to give a 1:4 epimeric mixture of alcohols **6** and **7** (Ratio of epimers determined from ^{1}H NMR). When the reaction was conducted at –78 °C, the exclusive formation of one diastereomer **7** has been observed.



Scheme 2: *Synthesis methyl-6-deoxy-6-dec-16-ene-2,3-O-isopropylidene-α-L-Gulose and methyl-6-deoxy-6-dec-16-ene-2,3-O-isopropylidene-α-D-Mannose*

Initially, the relative stereochemistry of the major alcohol **7** was determined after the ring transposition and with the help of 2D NMR analysis of the diacetate of the acetal **13** vide-infra found to possess the 5*S*-configuration, which was not the one what we intended. Later, we have also prepared this compound from the L-*gulo* epoxide **10** (Scheme 3).[36] The epoxide **10** was synthesized by selective mono benzoylation of primary hydroxyl of the diol **S2.1** followed by mesylation of secondary hydroxyl group and subsequent saponification and cyclization mediated by LiOH in THF-MeOH.



Scheme 3: *Synthesis methyl-6-deoxy-6-dec-16-ene-2,3-O-isopropylidene-α-L-Gulose*

The epoxide was opened by 9-decenyl magnesium bromide in presence of cuprous cyanide to get alcohol **7** in 71% yield. The spectral and analytical data of product obtained from Grignard addition to aldehyde and epoxide opened were identical.

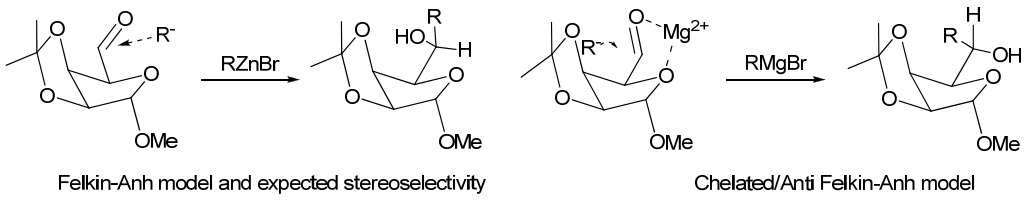
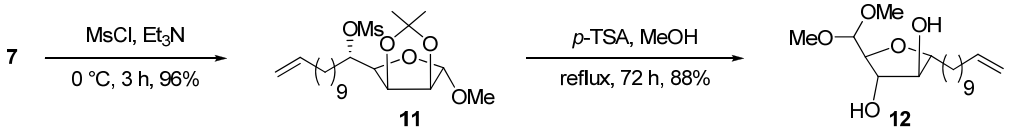


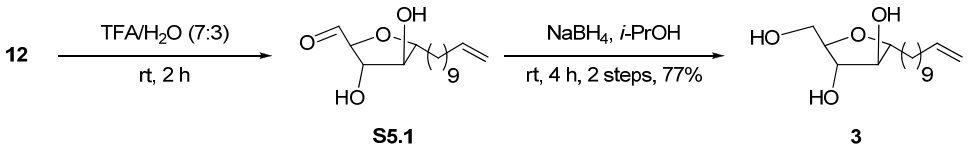
Figure 4: *Hypothetical models for selectivity in Barbier and Grignard reaction*

The results of Grignard reaction were opposite with respect to the diastereomeric outcome in the Zn-mediated allylation/propargylations of D-lyxo aldehyde. In the later case, the 5R-diastereomer was obtained as the main product.[35f] *The stereochemical outcome of Barbier reaction could be explained by considering Felkin Anh model*[37] *(Figure 4), where direct nucleophile attacks on aldehyde from less hindered side. Whereas chelation controlled model explains the outcome of Grignard reaction (Figure 4). The magnesium coordinates with oxygen atom of adjacent chiral carbon and delivers the nucleophile from the pro-S face.*



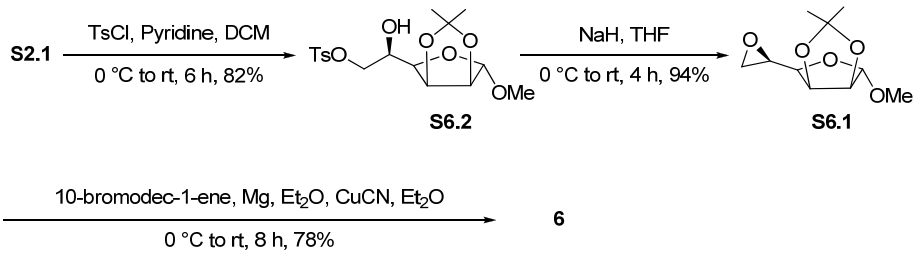
Scheme 4: *Synthesis of methyl-6-deoxy-6-dec-16-ene-2, 3-O-isopropylidene-α-L-Gulose*

After establishing configuration at C(5) center of **7**, we next proceeded for its mesylation and subsequent ring transposition reaction. The mesylation of compound **7** using mesyl chloride and triethyl amine gave the mesylate **11** in 96% yield (Scheme 4). The characteristic peak of mesyl group was resonated at δ 3.10 as a singlet in ^{1}H NMR and at δ 38.5 as a quartet in ^{13}C NMR. The key furan ring transposition reaction of mesylate **11** was carried out in methanol using catalytic *p*-TSA at reflux temperature for 3 days to obtain the dimethyl acetal **12** with α-D-arabino configuration. The structure was fully supported by analytical data. In ^{1}H NMR spectrum acetal –OCH_3 protons were resonated at δ 3.41 (s, 3H), 3.45 (s, 3H) and –CH of acetal at 4.35 (d, J = 4.8 Hz, 1H). A strong peak corresponding to *m/z* HRMS: ([M+Na]$^{+}$, 100%) observed in the mass spectrum of compound **12**.



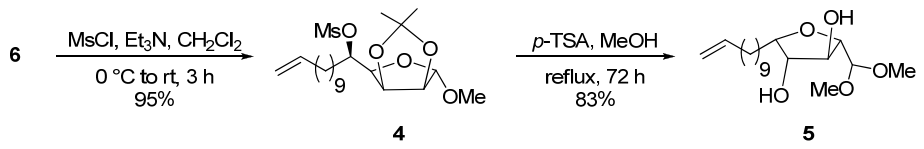
Scheme 5: *Synthesis of 1-α-D-arabinofuranosyl-undec-10-ene*

Next, the synthesis of α-*C*-arabinofuranoside **3** was completed (in 77% yield, 2 steps) by hydrolysis of acetal group in **12** using 70% aq. TFA to get aldehyde **S5.1**, which was subsequently reduced by sodium borohydride in *iso*-propanol to get triol **3**. The structure of **3** was well supported by spectral data. The two C(5) methylene protons resonated at δ 3.61 (dd, J = 5.3, 11.8 Hz, 2H), 3.69 (dd, J = 3.5, 11.8 Hz, 1H) ^{1}H NMR and at δ 63.3 (t) in ^{13}C NMR suggested the structure and it was further confirmed by the presence of strong peak in HRMS: *m/z* 309.2052 ([M+Na]$^{+}$, 100%).



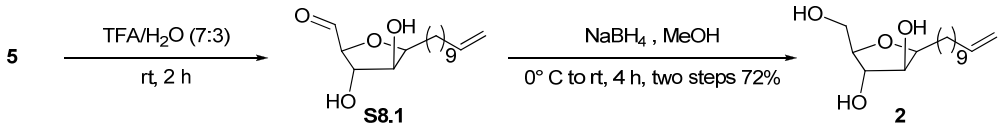
Scheme 6: *Synthesis of methyl 6-deoxy-6-dec-16-ene-2,3-O-isopropylidene-α-D-mannofuranoside*

As the intended synthesis of **2** resulted in the preparation of α-*C*-arabinofuranoside **3**, we opted for the Grignard addition to epoxide **S6.1**[38] with the required and existing *R* configuration at C(5) (Scheme 6) for the synthesis of **2**. This epoxide was prepared according to the reported procedure from diol **S2.1** by selective tosylation of primary hydroxyl followed by treatment of resulting tosylate **S6.2** with sodium hydride. The oxirane opening **S6.1** under previously standardized conditions delivered undecenyl alcohol **6** in 78% yield. In ^{1}H NMR spectrum the signal corresponding to C(5) C-H was observed at δ 3.81–3.93 as a multiplet and the presence of (s, 1C), (d, 6C), (t, 10C), (q, 4C) signals in ^{13}C NMR along with peaks oberved at *m/z* 379.37 ([M+Na]$^{+}$) in mass spectrum (ESI-MS) defend the structure of alcohol **6**.



Scheme 7: *Synthesis of 5-dideoxy-dimethylacetal-1-α-D-arabinofuranosyl-undec-10-ene*

Mesylation of the alcohol **6** under standard conditions gave the mesylate **4** in 95% yield. The acid mediated ring transposition of **4** proceeded smoothly and the acetal **5** was obtained in excellent yields. The structure of acetal **5** was assigned with the help of spectral and analytical data. For example, in the ^{1}H NMR spectrum of compound **5**, the acetal C(5)–H was appeared as doublet at δ 4.36 with J = 3 Hz and two singlets correspond to the methyl groups of acetal resonated at δ 3.48, 3.54. A strong peak observed at *m/z* 353.2330 ([M+Na]$^{+}$ 100%) in mass spectra (HRMS) further supported constitution of acetal **5**.



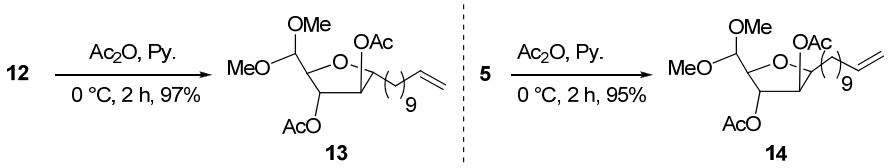
Scheme 8: *Synthesis of 1-β-D-arabinofuranosyl-undec-10-ene*

Finally, the hydrolysis of the dimethyl acetal **5** by using 70% aq. trifluroacetic acid gave aldehyde **S8.1** which was used for the next step without any purification. The reduction of the crude aldehyde **S8.1** using sodium borohydride in *iso*-propanol gave the required α-*C*-arabinofuranoside **2**. The structure of **2** was fully supported by analytical data. In ^{1}H NMR spectra, C(5) methylene appeared as dd at δ 3.63 (J = 4.8, 11.5 Hz, 1H), 3.68 (J = 3.9, 11.5 Hz, 1H) where as in ^{13}C NMR of compound **2**, a signal at δ 63.7 (t) and base peak at *m/z* 309.2011 in HRMS mass spetra corresponds to ([M+Na]$^{+}$, 100%) confirmed the structure of 1-β-D-arabinofuranosyl-undec-10-ene.

2.1.2 Synthesis and Structural Characterization of Diacetates (13/14) and triacetates (15/16) of α-/β-*C*-arabinofuranosides

Initially, to fix the newly generated stereocenter of the compound **7** resulting from the Grignard addition, the diacetate **13** of the acetal **12** has been prepared (Scheme 9).

Later, we have also prepared the diacetate **14** from the acetal **5** to learn about the validity of nOe correlations in establishing the relative stereochemistry *C*-furanosides - which are conformationally more labile.



Scheme 9: *Synthesis of 5-deoxy-5-dimethylacetal-2,3-di-O-acetyl-1-α and β-D-arabinofuranosyl-undec-10-ene and its nOe interactions*

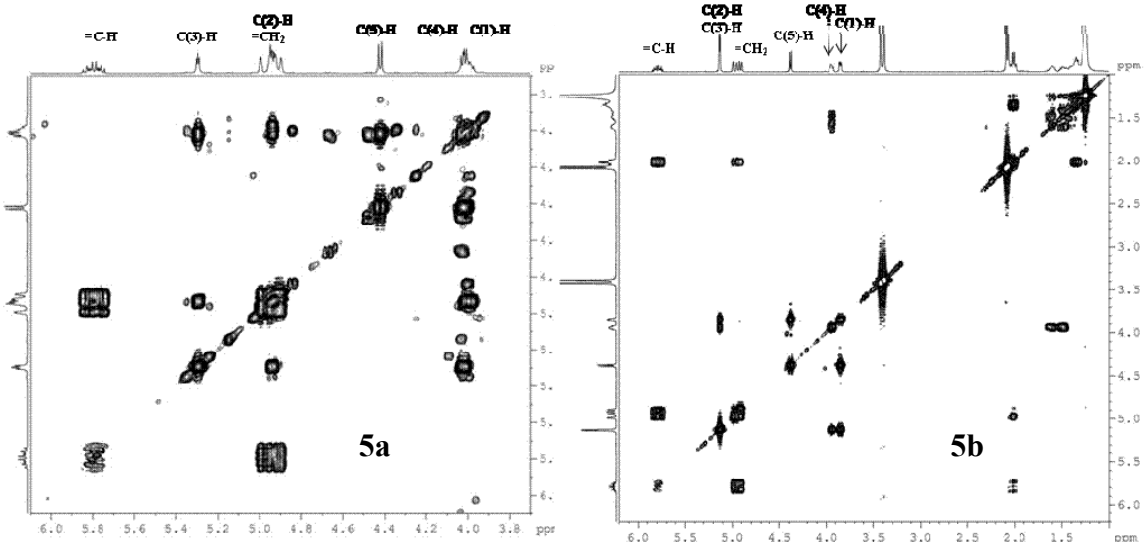
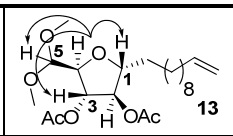
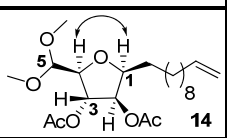


Figure 5: *Expansion of COSY spectrum diacetate **13** and **14***

Table 1: *Ring C–H position of diacetate **13** and **14** using COSY*

Camparison of Chemical Shift (δ ppm) and Coupling constant (Hz) of **13** and **14**		
C-H	 **13**	 **14**
C(1)-H	3.99, dt, *J* = 4.0, 6.0	3.94, dt, *J* = 3.6, 6.0
C(2)-H	4.93, dd, *J* = 3.0, 4.0	5.13, d, *J* = 3.5
C(3)-H	5.29, dd, *J* = 2.8, 3.8	
C (4)-H	4.02, dd, *J* = 4.0, 6.0	3.84, dd, *J* = 3.7, 6.4
C(5)-H	4.42, d, *J* = 6.1	4.38, d, *J* = 6.4

The sequence of the spectral analysis is as follows. First with the help of the *COSY* (Correlation spectroscopy) (Figure 5a/5b), all the inter residual connectivities of diacetates **13** and **14** have been established, the ring C–H peaks were assigned and coupling constants determined (Table 1). The stereochemistry at the C(1) carbon of the diacetate **13** [C(5) in **7**] was confirmed by NOSEY analysis. In the nOe spectrum (Figure 6a) of **13**, anomeric C(1)–H has shown strong through spatial interaction with C(3)–H and C(5)–H (C–H of the acetal) indicating a 1,3-cis and 1,4-trans relations thus establish anomeric configuration as alpha and that the stereochemistry at C(5) in the Grignard product **7** as 5*S*. As expected, in the diacetate **14**, the C(1)–H showed close spatial proximity only with the C(4)–H. In addition there was no cross peak present between C(3)–H and C(1)–H. This indicated 1,4-cis and 2,4-cis configuration in diacetate **14**.

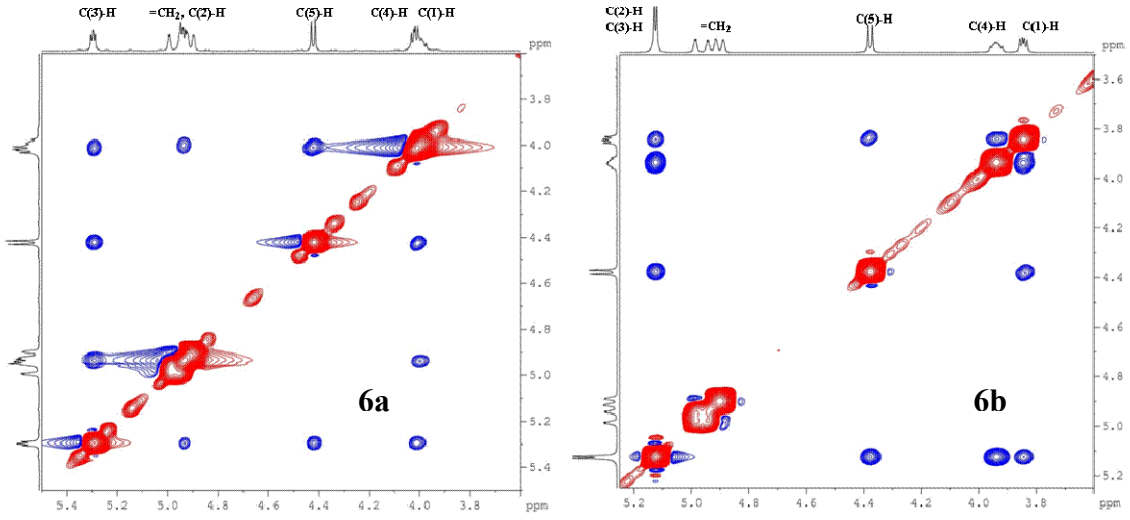
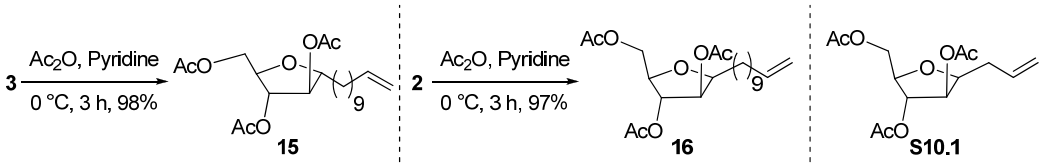


Figure 6: *nOe spectrum of diacetate **13** and **14***

To further support the assigned α-glycosidic configuration in compound **3**, the triacetate **15** has been prepared and its spectral data was compared with the data reported for known triacetate of the β-*C*-allyl arabinoside.[35f] Later, the triacetate **16** of the β-*C*-glycoside **2** was also prepared to understand how the chemical shifts of the ring carbons in *C*-furanosides was influenced by the anomeric configuration. Table 2 provides the comparative chemical shifts and coupling constants of the triacetates **15**, **16** and **S10.1**.



Scheme 10: *Synthesis of 2,3,5-tri-O-acetyl-α and β-D-arabinofuranosyl-undec-10-ene*

Table 2: *Selected ^{1}H and ^{13}C data of peracetates **15**, **16** and **S10.1** C-D-arabinofuranosides*

C-H	β–triacetate 16	β–triacetate S10.1	α–triacetate 15
	^{1}H NMR		
C(1)-H	3.98 (dt, *J* = 3.4, 5.5)	4.03 (dt, *J* = 3.6, 7.0)	4.0 (dt, *J* = 3.7, 6.7)
C(2)-H	5.16 (dd, *J* = 0.8, 3.5)	5.15 (d *J* =3.6)	5.06 (dd, *J* = 2.4, 3.7)
C(3)-H	4.90 (dd, *J* = 0.9, 3.6)	4.88 (d *J* = 3.4)	5.01 (dd, *J* = 2.5, 3.8)
C (4)-H	3.91 (ddd, *J* = 3.3, 4.7, 6.5)	3.92 (ddd, *J* = 3.4, 5.0, 6.5)	4.14 (ddd, *J* = 3.8, 5.0, 6.0)
C(5)-H	4.33 (dd, *J* = 4.7, 11.5)	4.30 (dd *J* = 5.0, 11.5)	4.26 (dd, *J* = 5.0, 11.6)
C(5)`-H	4.12 (dd, *J* = 6.5, 11.5)	4.10 (dd *J* = 6.5, 11.5)	4.22 (dd, *J* = 6.0, 11.6)
^{13}C NMR			
C(1)	77.0 (d)	76.8 (d)	78.9 (d)
C(2)	81.0 (d)	81.2 (d)	81.0 (d)
C(3)	80.9 (d)	80.1 (d)	80.2 (d)
C(4)	79.0 (d)	78.9 (d)	83.2 (d)
C(5)	63.9 (t)	63.8 (t)	63.5 (t)

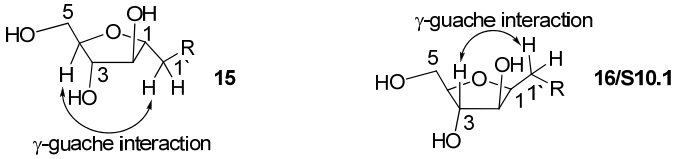


Figure 7: *γ-gauche effect in C-glycoside*

In the ^{13}C NMR (Table 2), the first major difference is that the C(4) carbon of α-*C*-arabinofuranoside **15** is shielded (~3 ppm) than in the β-*C*-arabinofuranosides. This observation can be explained by γ- gauche effect[39] (γ_g) which arises due to internuclear distance between C(4)–H substituent and its gamma gauche carbon C(1)` fall in the

region of the van der Waals potential curve where the interaction changed from attractive to repulsive. As a result, the changes in molecular geometry of **15** caused significant changes in the γ_g effect. Also the C(3) carbon in β-*C*-arabinofuranoside is shielded due to contraction of the C–H bond on the C(3) carbon.

2.2 Synthesis of Motif C carba-disaccharide analogues

Carbohydrates, either in their native form or, more frequently, conjugated (glycol-conjugates) with the proteins (glycoprotein's or proteoglycans) and lipids (glycolipids) play a major role in various biological processes such as inflammation, intra-cellular and host-pathogen recognitions - to name a few.[40] The processing of these complex oligosaccharides and glycoconjugates in biological systems are managed by two classes of enzymes namely glycosidases and glycosyl transferases.[41] The mimicking of the substrates of these enzymes is an important aspect in the development of carbohydrate based drugs.[42] The Arabinofuranosyl transferases are enzymes involved in the cell wall synthesis of *M. tuberculosis* have been recognized as promising targets for the development of new anti-tubercular drugs.[33c] The linear chain of arabinan polymer is made up of repeating disaccharide α-D-Ara*f*-(1→5)-α-D-Ara*f* called as motif C (Figure 8).

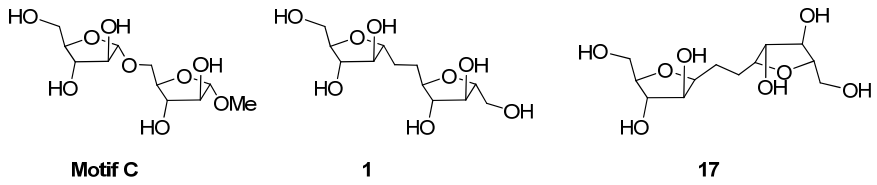


Figure 8*: Structure of motif C and carba-disaccharide analogues **1** and **17***

In this context, the carba-disaccharides where the *O*-glycosidic linkage was replaced by a *C*-glycosidic bond are recognized for their superior physiological stability without substantial conformational change.[14–15] This hypothesis supported by recent progress in *C*-glycoside biological screening which shows the enhanced activity over their *O*-glycoside counterparts.[16] For mimicking motif C, we have designed two carba-disaccharide analogues, where two of the glycoside oxygen were replaced by carbon with (*i*) the same configuration like in **1** which is known and (*ii*) the inverted configuration at both the anomeric centres - **17**.

Dondoni *et al.*[24] had first documented the synthesis of parent **1** and the higher oligomers of motif C by the iterative Wittig reaction. Whiteman *et al.*[25] used alkyne nucleophilic addition on a sugar lactone for the synthesis of **1**. Lowary's group[26] reported the synthesis of the corresponding C(1)-*O*-alkyl derivatives of **1** as potential substrates for the AraTs by self-dimerization of a suitable arabinose derivative via olefin metathesis.

To overcome the known lengthy reaction sequence for synthesis of motif C carba-disaccharide analogues from D-arabinose, we planned a short route from D-mannose by a double furan ring transposition. The proposed key reaction involves a total 12 bonds rearrangement in one pot to get desired motif C analogues.

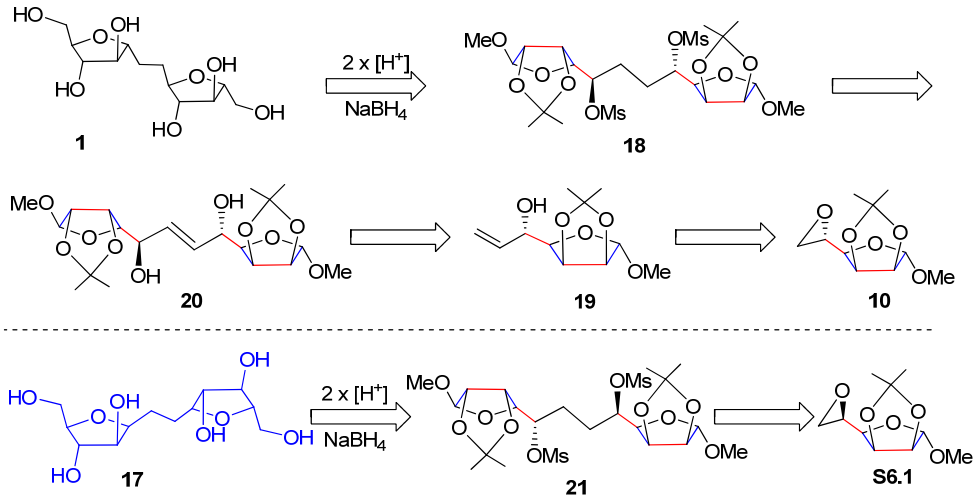
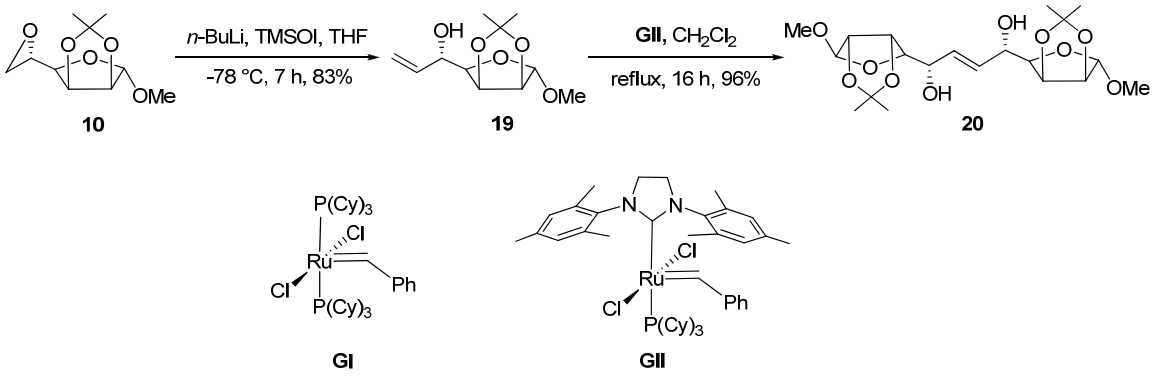


Figure 9: *Synthetic strategy for carba-disaccharide analogues **1** and **17***

Our intended strategy for the synthesis of carba-disaccharide analogues **1** and **17** was illustrated in Figure 9. A double furan ring transposition reaction of C_2-symmetric dimesylate **18** should lead to a diacetal which can be easily converted in to disaccharide **1** following a sequence of hydrolysis and reduction reactions. The dimesylate **18** can be prepared from the allylic alcohol **19** by a simple set of reactions comprising the homo-dimerization, hydrogenation and then mesylation. The allylic alcohol can be made from the known oxirane **10** employing Mioskowski's[43] one carbon homologation. Here, the oxirane functionality serves two purposes - a handle for the introduction of glycon and also prefixes the anomeric configuration. Similarly, the motif *C* carba-disaccharide analogue **17** can be procured by double ring transposition of dimesyl compound **21** which could be easily prepared from epimeric oxirane **S6.1**.

The synthesis of carbadisaccharide **1** commenced with Mioskowski's[43] one carbon homologation of epoxide **10**. Treatment of **10** with in situ generated trimethylsulfoxonium ylide at –78 °C gave the L-gulo configured allyl alcohol **19** in 83% yield. Its structure was well supported by ^{1}H, ^{13}C NMR and mass spectrum. In ^{1}H NMR

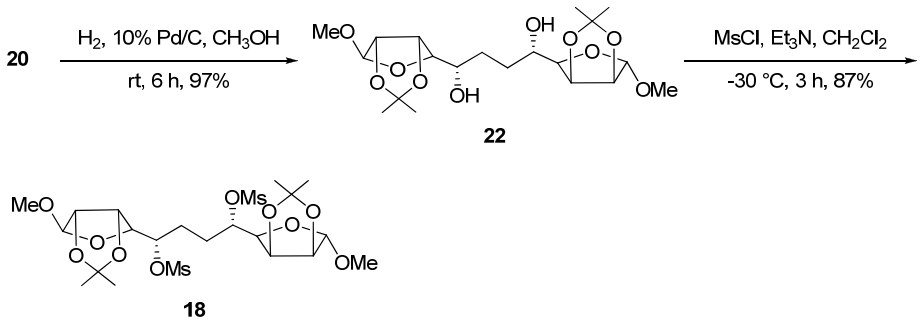
the characteristic epoxide protons at, δ 2.62 (dd, *J* = 2.7, 4.8 Hz, 1H) and 2.89 (t, *J* = 4.5 Hz, 1H) were disappeard. The newly generated C(6), C(7) olefin protons were resonated at δ 5.21 (dt, *J* = 1.5, 10.5 Hz, 1H), 5.39 (dt, *J* = 1.5, 17.3 Hz, 1H), 5.97 (ddd, *J* = 5.4, 10.5, 17.3 Hz, 1H) and at δ 116.5 (t), 135.9 (d) in ^{13}C NMR. Presence of strong peak of highest intensity at (*m/z*) 253.01 ($[M+Na]^+$, 100%) supported the structure **19**.



Scheme 11: *Synthesis of methyl 6,7-dideoxy-2,3:10,11-di-O-isopropylidene -α-D-glycero-D-xylo-L-gulo-dodec-6E-eno-dialdo-(1,4:9,12)-bisfuranoside*

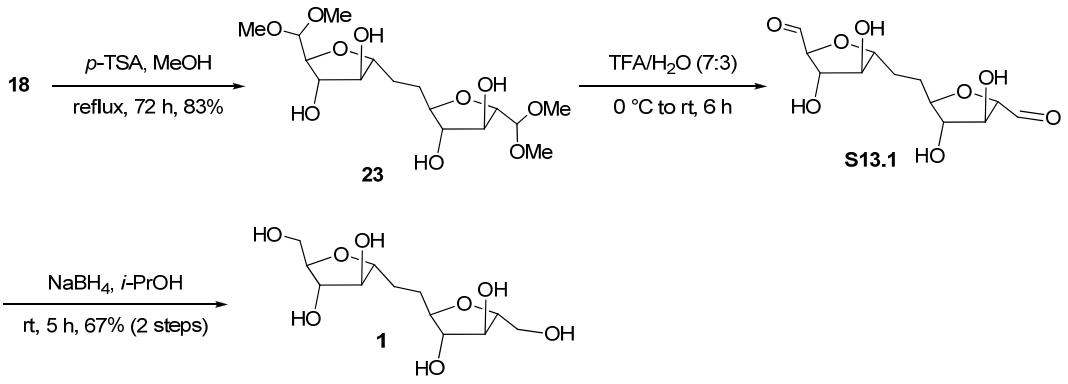
Next, the homodimerization of **19** with Grubbs 1st generation catalyst (**GI**) was not successful, only a little starting material (5%) was consumed even after refluxing for 2 days in dichloromethane. However, by considering the earlier experience of Lowary's[26] group, Grubbs IInd generation catalyst (**GII**) has been opted for this purpose. The homodimerization of **19** with **GII** was facile and the optimized reaction conditions involve the reflux of a solution of allyl alcohol **19** in the presence of 3 mol% of **GII** in dichloromethane for 16 h. The required dimer **20** was obtained in quantitative yields (96%). The structure of the dimer **20** was confirmed by spectral and analytical data. Because of its symmetrical nature (C_2 point group), only nine and ten signals were observed in ^{1}H NMR and ^{13}C NMR spectrums respectively - which are exactly half of the total proton/carbons present. In the ^{1}H NMR spectrum of **20**, the newly generated olefinic protons C(6) and C(7) were resonated at δ 6.01 (dd, *J* = 1.0, 3.0 Hz, 2H) and the anomeric protons C(1)/C(12)–H were appeared as singlet at δ 4.90 (s, 2H). The C(2)/C(11)–H protons were appeared as a doublet at δ 4.52 (*J* = 5.8 Hz, 2H) and that of the C(3)/C(10)–H as double of doublets at δ 4.55 (*J* = 3.0, 6.0 Hz, 2H). The C(4)/C(9)–H were resonated at δ 3.75 (dd, *J* = 3.5, 6.5 Hz, 2H) and the C(5)/C(8)–H at δ 4.55 (ddd, *J* =

1.0, 3.0, 6.0 Hz, 2H). In ^{13}C NMR spectrum, the signal at δ 129.9 (d, 2C) was identified as the olefin signal. Finally a strong peak at *m/z* 455.15 ([M+Na]$^+$, 100%) assured the constitution of the dimer **20**.



Scheme 12: *Synthesis of methyl 5,8-di-O-methanesulfonyl-6,7-dideoxy-2,3:10,11-di-O-isopropylidene-α-D-glycero-D-xylo-L-gulo-dodecadialdo-(1,4:9,12)-bisfuranoside*

The dimer **20** was subjected for the olefin hydrogenation over 10% Pd/C in methanol at 60 psi to secure the 1,4-diol **22** in quantitative yield (97%). The absence of olefinic protons and the appearance of four methylene protons [C(6) and C(7)] as a multiplet between δ 1.72–1.82 indicated the absence of olefine unit in the obtained product. The ^{13}C NMR also exhibited a peak at δ 29.1 (2C) for the two methylene carbons. The base peak in mass spectrum observed at 457.16 ([M+Na]$^+$, 100%) confirmed the structure of diol **22**. After a literature survey we have selected the Corey's[44] procedure for mesylation of 1,4-diol, where competing tetrahydrofuran formation pathway would be avoided. Thus the dimesylation of **22** was carried out at –30 °C using mesyl chloride and triethylamine to get exclusively the dimesylate **18** in 87% yield. The structure of dimesylate was fully supported by the spectral and analytical data. For example, in ^1H and ^{13}C NMR spectra of compound **18**, the characteristic signals respectively at δ 3.10 (6H) and at δ 38.5 (q, 2C) supported the presence of two mesyl groups. Finally the most abundant peak in mass spectrum at (*m/z*) 613.14 ([M+Na]$^+$, 100%) supported the proposed constitution of compound **18**.



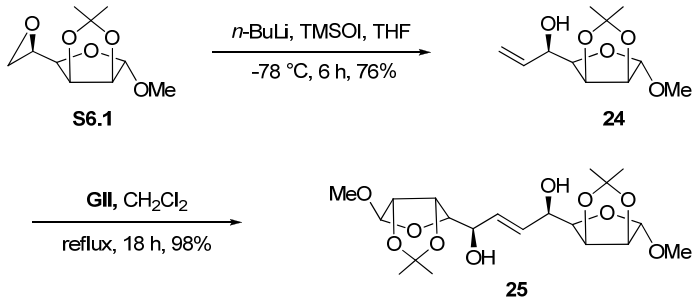
Scheme 13: *Synthesis of 6,7-dideoxy-D-glycero-D-lyxo-D-manno-dodeca-2,5:8,11-dianhydroalditol*

Once the dimesylate **18** was in hand, our next concern was the key double furan ring transposition reaction. The double ring transposition proceeded smoothly under the established conditions (refluxing in methanol in the presence of catalytic *p*-TSA for 72 h) to afford the diacetal **23** in 83% yield. The structure of diacetal was confirmed by ^{1}H, ^{13}C NMR and mass spectrometry. The C_2-symmetry associated with dimesylate was transmitted in to diacetal, which was clear from its ^{1}H and ^{13}C NMR spectrums where only half (8) of the total signals were observed. The ^{1}H NMR provides information to support the presence of two acetal groups, as acetal C–H were resonated at δ 4.40 (d, J = 5.9 Hz, 2H) and methyl protons were observed at δ 3.43 (s, 6H), 3.44 (s, 6H) and also corresponding carbon signals were resonated at δ 105.9 (d, 2C) and at 54.8 (q, 2C), 55.9 (q, 2C) in ^{13}C NMR spectrum. Lastly the strong peak at *m/z* 405.09 ($[M+Na]^+$, 100%) prooved its structure. The key features of acid mediated double ring transposition are, organized multiple bond rearrangement and *in situ* cleavage of two acetonide groups and two furanose rings, followed by two new furan rings formation. This makes it aesthetically pleasing along high yielding practical route for the synthesis of carba-disaccharide.

The two dimethyl acetal groups in **23** were hydrolyzed by using 70% aq. TFA at room temperature for 6 h and resulting dialdehyde **S13.1** was subjected for reduction with sodium borohydride in *iso*-propanol to get the known carba-disaccharide **1.** The carba-disaccaride was prepared in seven steps from oxirane **10** in 37% overall yield. The structure of **1** was fully supported by analytical data. The ^{1}H and ^{13}C NMR data of carba-disaccharide **1** are in well agreement with the data reported by Whiteman's group[25]. For

example in the ^{1}H NMR spectrum of compound **1**, the characteristic peak of diastereotopic methylene [C(1), C(12)] protons were observed at δ 3.67 (dd, *J* = 5.9, 12.2 Hz, 2H), 3.74 (dd, *J* = 3.9, 12.2 Hz, 2H) and in ^{13}C NMR, these carbons were resonated at δ 63.3 (t, 2C). In the mass spectrum of **1** the most abundant peak at (*m/z*) 317.01 ([M+Na]$^{+}$, 100%) confirmed the structure **1**.

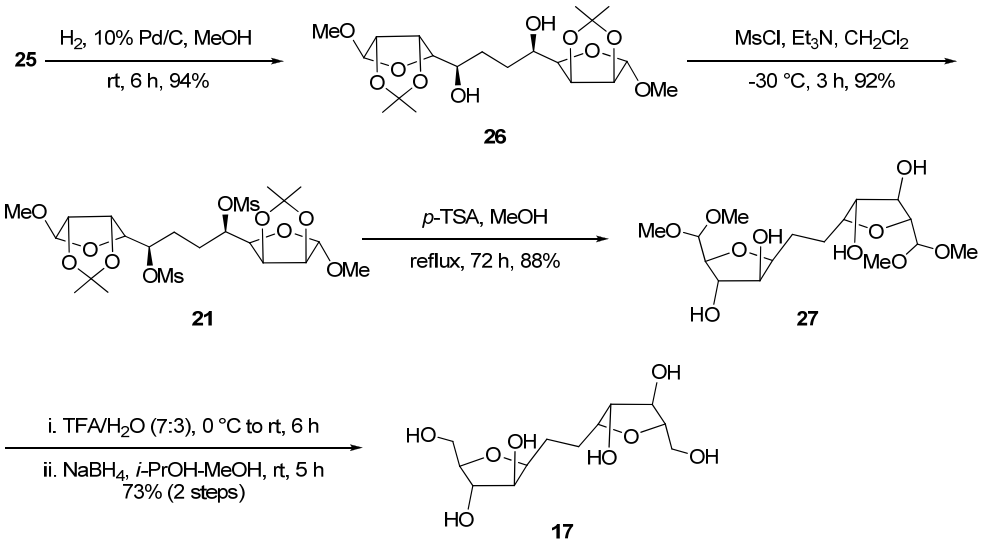
Similarly, the synthesis of carba-disaccharide analogue **17** was started from the known epoxide **S6.1**.[38] The opening of the epoxide with sulphoxonium ylide gave the allyl alcohol **24** in 76% yield. The structure of compound **24** was established with the help of spectral and analytical data. For example, in the ^{1}H NMR spectrum of compound **24**, the olefin protons were resonated at δ 5.97 (ddd, *J* = 5.4, 10.5, 17.3 Hz, 1H), 5.39 (dt, *J* = 1.5, 17.3 Hz, 1H), 5.21 (dt, *J* = 1.5, 10.5 Hz, 1H), whereas carbons at δ 116.0 (t), 137.6 (d) in ^{13}C NMR and strong *m/z* peak at 253.07 ([M+Na]$^{+}$, 100%) in ESI mass proved the structure. The homodimerization of allyl alcohol **24** was executed using Grubbs IInd generation catalyst, to obtain the diol **25** in excellent yield. In ^{1}H and ^{13}C NMR the disappearance of terminal olefin signal and presence of internal olefin peak at δ 6.02 (dd, *J* = 1.0, 2.6 Hz, 2H) and 131.1 (d, 2C) respectively confirmed the proposed structure of dimer **25** and the mass peak at *m/z* 455 further assured its proposed constitution.



Scheme 14: *Synthesis of key mannoconfigured allyl alcohol **24** and its homodimerization*

The double bond in dimer **25** was reduced by H_2 using 10% Pd/C in methanol, the reduced product **26** was well characterized by Mass and NMR techniques. In ^{1}H NMR spectra the olefin protons were absent and 4 protons were appeared at δ 1.63–1.77 (m, 2H), 1.98–2.08 (m, 2H) belongs to methylene signal, similarly at δ 31.5 (t, 2C) were

found in ^{13}C NMR. Finally, the base peak of *m/z* at δ 457.15 ([M+Na]$^+$, 100%) provided the further evidence for proposed structure of compound **26**. The dimesylation of **26** was carried out under the established conditions (mesyl chloride, triethyl amine, dichloromethane, –30 °C)[44] to obtain the dimesylate **21** in 92% yield .The structure of dimesylate was validated from NMR and mass spectral data. The characteristic signal at δ 3.07 (s, 6H) in ^1H NMR spectrum and at δ 38.5 (q, 2C) in ^{13}C NMR spectrum of compound **21** confirmed the presence of two mesyl groups. Further a peak at *m/z* 613.16 ([M+Na]$^+$, 100%) in the mass spectrum of compound **21** gave an additional evidence for its structure.



Scheme 15: *Synthesis of β-configured carba-disaccharide **17***

Subsequently, the dimesylate was subjected for the double ring transposition in refluxing methanol using catalytic *p*-TSA to procure diacetal **27** in 88% yield. The presence of four methyl groups of diacetal was supported by the signals resonated at δ 3.43 (s, 6H), 3.44 (s, 6H) in ^1H NMR and at δ 54.9 (q, 2C), 55.8 (q, 2C) in ^{13}C NMR spectrum. The diacetal was hydrolyzed by 70% aq. TFA and resulting intermediate dialdehyde was immediately subjected for reduction with sodium borohydride in *iso*-propanol to yield the carba-disaccharide **17** (2 steps 73% yield).The ^1H and ^{13}C NMR exhibited the symmetric nature of carba-disaccharide in which the two methylene protons C(1), C(12) appeard at δ 3.64 (dd, *J* = 5.0, 11.5 Hz, 2H), 3.69 (dd, *J* = 3.8, 11.5 Hz, 2H)

and carbons at δ 63.6 (t, 2C) in ^{13}C NMR. Finally strong peak in mass spectra at *m/z* 317.03 ($[M+Na]^+$, 100%) confirmed the structure **17**.

2.3 Studies toward the synthesis of Motif C and B *C*-glycoside analogues

The impermeable cell wall of *Mycobacterium tuberculosis* (*Mtb*) has been identified as one of the reasons for its drug resistance and for the long life in billions of human lungs.[45] The major portion of the cell wall of ***Mtb*** is made up of the polysaccharides arabinogalactan (AG) and lipoarabinomannan (LAM).[10] The AG and LAM polysaccharides are composed of arabinose and are synthesized inside the infected host cells. Since arabinose is foreign to the mammalian cells, the inhibition of the corresponding enzymes responsible for AG and LAM biosynthesis is a promising approach for the discovery of new anti-tubercular agents.[10]

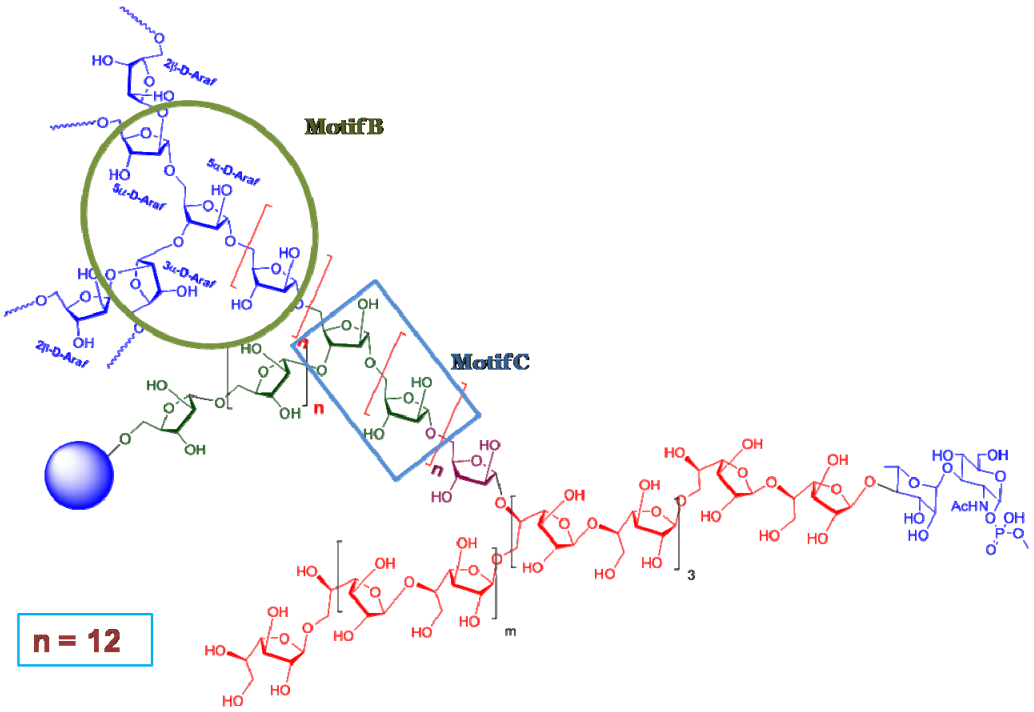


Figure 10: *Structure of AG complex of cell wall of Mtb*

The structure of AG complex (Figure 10) contains approximately 70 arabinose units and major part is repeating disaccharide α-D-Ara*f*-(1→5)-α- D-Ara*f* called as motif C. However to this linear chain there are periodic branched points at which another arabinan linear chain is attached via α-(1→3) linkage. At nonreducing terminal of arabinan hexasaccharide present AG complex is referred as Motif A {[β-D-Ara*f*-(1→2)-α-D-Ara*f*]$_2$-3,5-α-D-Ara*f*-(1→5)-α-D-Ara*f*)} and the tetrasaccharide portion (Highlighted

in figure 10 is called as Motif B). To the hexasaccharide terminal portion of AG complex (motif A) mycolic acids are covalently bound by ester linkage. The mycolic acids are connected in cluster of four at C(5) hydroxy group of last and penultimate Ara*f* unit at the end of arabinan chain. This tetra mycolated hexasaccharide portion determines the physiology of cell including impermeability, strength and long survival in exotic condition.

In the lliterature, it has been shown that the smaller fragments of hexasaccharide such as disaccharide (motif C) or trisaccharide are substrate of AraTs.[46] In this regard we have identified the disaccharide and tetrasaccharide of AG complex as potential drug candidates and we planned to synthesize the *C*-glycoside analogues **28**, **29** and **S23.1** (Figure 11) as potential mimics in this regard.

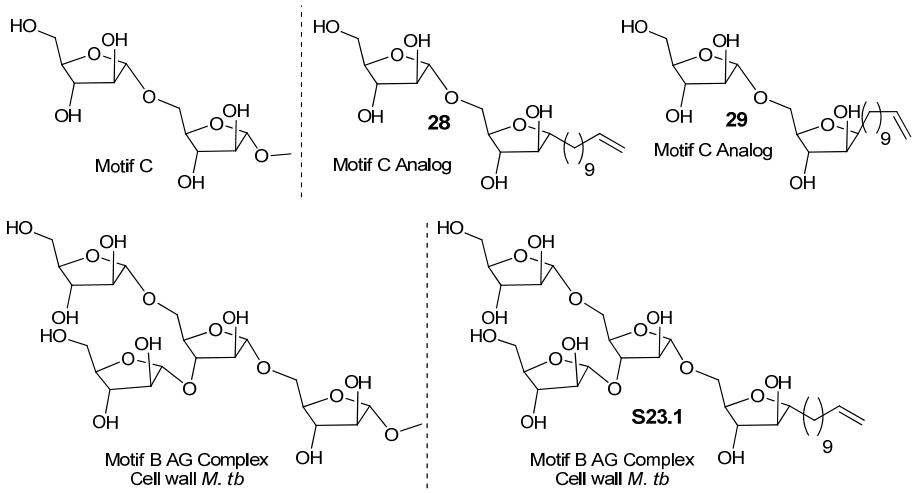


Figure 11*: Structure of motif B, C and their C-glycoside analogues **28, 29** and **S23.1***

2.3.1 Synthesis of *C*-glycoside motif C analogues

A retrosynthetic strategy for motif C **28** disaccharide synthesis is shown in Figure **12**. The key reaction is the glycosylation of the 2,3-di-*O*-benzyl-*C*-arabinofuranoside **30**. The D-arabinofuranosyl phosphate was identified as a glycosyl donor after careful literature search. The synthesis of **30** is a straight forward proposition from acetal **12** in two simple steps. The synthesis of glycosyl donor **S17.5** has been reported by Seeberger's group.[47]

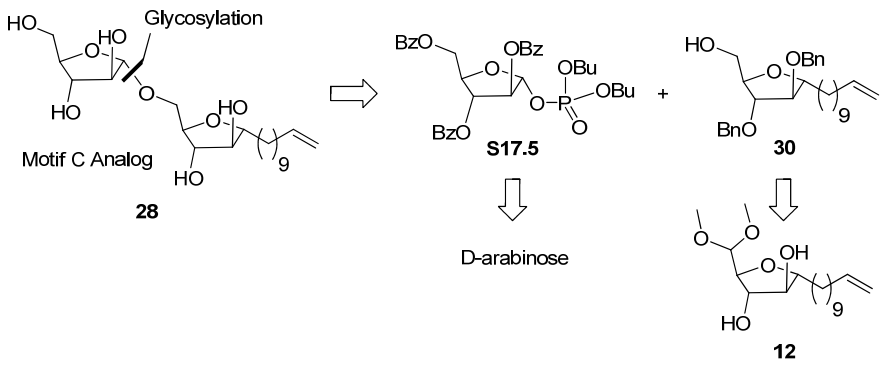
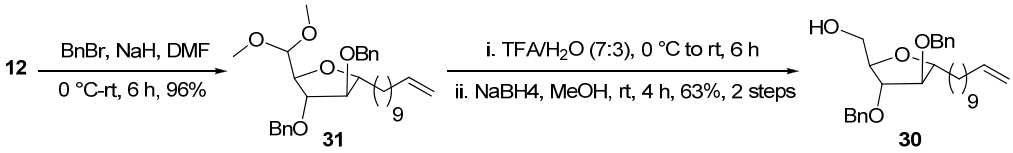


Figure 12: *Key retrosynthetic disconnections for the synthesis of motif C analogue **28***

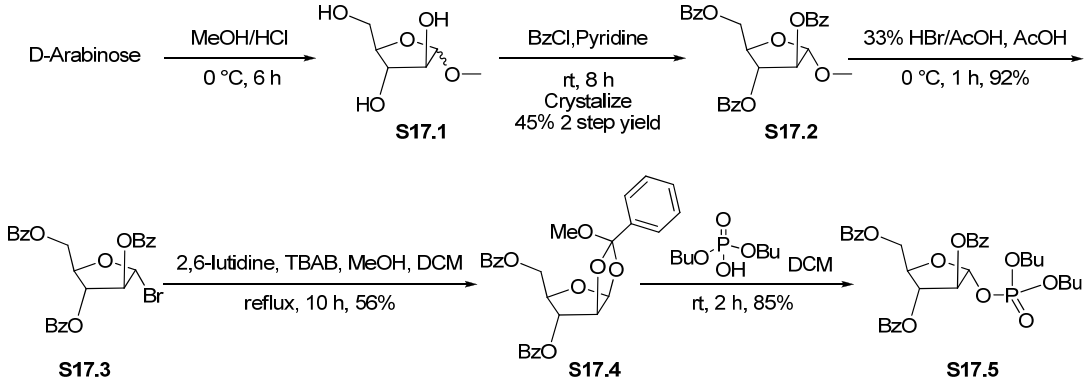
The synthesis of disaccharide **28** commenced with the preparation of glycosyl acceptor **30**. The benzylation of acetal **12** using benzyl bromide and sodium hydride gave **31** in 96% yield. The peaks at δ 4.48 (d, J = 12.0 Hz, 2H), 4.53 (d, J = 12.0 Hz, 1H), 4.62 (d, J = 12.0 Hz, 1H) and at δ 71.6 (t, 2C) respectively in the ^{1}H NMR and ^{13}C NMR spectra of compound **31** were characteristic peaks of benzylic units. The base peak at *m/z* 533.44 ([M+Na]$^{+}$, 100%) in the mass spectrum of **31** confirmed the proposed constitution. Next, the acetal group in compound **31** was hydrolyzed by using 70% aqueous trifluroacetic acid and the resulted aldehyde was reduced immediately by using sodium borohydride in methanol to furnish the key glycosyl acceptor **30** in 63% yield (2 steps). The newly generated methylene group at C(5) was supported from the ^{1}H and ^{13}C NMR signals resonated at δ 3.68–3.70 (m, 2H) and δ 62.6 (t) and structure was ultimately proved by signals present in mass spectrum at *m/z* 489.68 ([M+Na]$^{+}$, 100%), 505.65 ([M+K]$^{+}$, 30%,).



Scheme 16: *Synthesis of 2,3-dibenzyl-1-α-D-arabinofuranosyl-undec-10-ene **30***

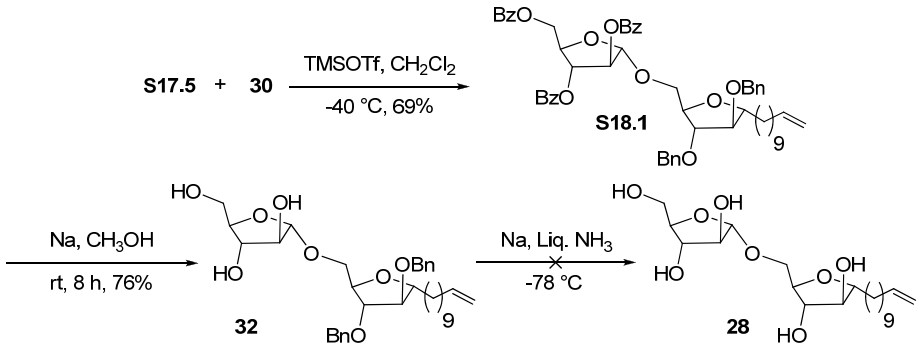
Next, we moved for synthesis of known arabinofuranosyl phosphate **S17.5**. The synthesis was started with kinetic methylation of D-arabinose to get methyl furanoside **S17.1**, which was subsequently subjected for benzoylation with benzoyl chloride and pyridine. The resulting tribenzoate was purified by recrystallisation in ethanol to get

crystalline alpha anomer **S17.2**.[48] This was converted in to the arabinofurnosyl bromide by using HBr/AcOH and subsequently to orthoester by refluxing the bromide **S17.3** in dichloromethane using 2,6-lutidine and methanol. The resulting orthoester **S17.4** was treated with *n*-dibutyl-phosphate in dichloromethane to procure **S17.5** in 85% yield.



Scheme 17: *Synthesis of 2,3,5-tribenzoyl-D-arabinofuranosyl dibutyl phosphate*

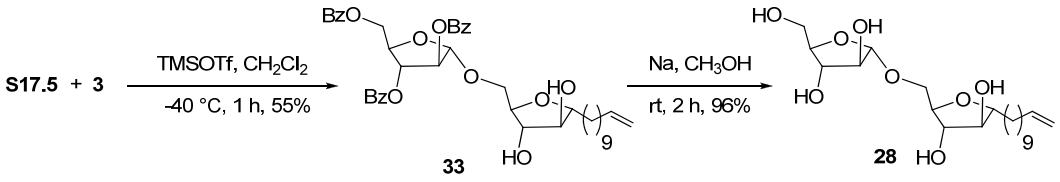
Our next concern was the glycosylation. The employed conditions involve the treatment of a solution of **30** and **S17.5** in dichloromethane with trimethylsilyltriflate at – 40 °C. The protected disaccharide **S18.1** was obtained in moderate yields. The signal resonated at δ 5.57 (s, 1H) indicated an alpha anomeric in **S18.1**.



Scheme 18: *Synthesis attempts of motif C disaccharide **28***

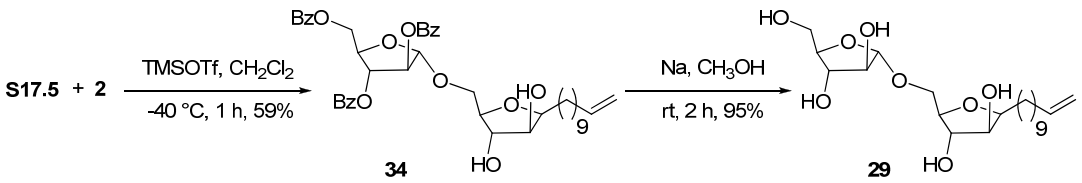
The benzoyl deprotection **S18.1** (Scheme 18) by using Na/MeOH gave the di-O-benzyl disaccharide **32**. The structure of compound **32** was established with the help of spectral and analytical data. The peak at *m/z* 621.78 ($[M+Na]^+$) indicated the constitution the compound **32**. In the ^1H NMR spectrum of **32**, the characteristic anomeric-H peak of

was observed at δ 5.0 (s, 1H) and the corresponding carbon resonated at δ 107.6 (d) in the ^{13}C NMR spectrum. After benzoyl deprotection, we moved to benzyl group removal in Na/NH_3 to keep the olefin intact. However, this reaction ended with unidentified mixture of products. Similarly our efforts for one pot deprotection of benzyl groups and in situ peracetylation using TMSOTf -acetic anhydride was also failed.



Scheme 19: *Synthesis of α-D-arabinofuranosyl-(1→5)-1-α-D-arabinofuranosyl-undec-10-ene*

To attain the synthesis of α-*C*-glycoside motif C **28** analogue keeping terminal olefin intact, we have intended to explore the possibility of using 1-α-D-arabinofuranosyl-undec-10-ene **3** as glycosyl acceptor anticipating selective glycosylation of the C(5)–OH. To this end, using the conditions employed in Scheme 18, the glycosylation of **3** with excess glycosyl donor gave the disaccharide **33** in respectable yields. The structure and the stereochemistry of the newly created glycosidic bond in the resulting disaccharide **33** was established with the help of spectral data. The signal observed at δ 5.38 (s, 1H) in ^{1}H NMR and δ 106.2 (d) in ^{13}C NMR were characteristic C(1) of Ara*f* unit with an α-configuration. The mass peak at *m/z* 753.25 ($[M+Na]^+$, 38%) in ESI mass confirmed the structure **33**. Next the saponification of benzoyl groups in compound **33** proceeded smoothly under Zemplen conditions (cat. Na/MeOH) resulting in the α-*C*-glycoside motif C analogue **28**. The presence of a strong peak of highest *m/z* at 441.21 ($[M+Na]^+$) in the ESI mass spectrum of **28** and the absence of aromatic protons and carbonyl signals in ^{1}H and ^{13}C NMR indicated the successful benzoyl deprotection. Additionally, the presence of anomeric carbon peak at δ 109.6 (d) in ^{13}C NMR suggest the α-Ara*f* unit and all spectral information was in support of the assigned sturcutre of compound **28**.



Scheme 20: *Synthesis of α-D-arabinofuranosyl-(1→5)-1-β-D-arabinofuranosyl-undec-10-ene*

Similarly, the synthesis of β-*C*-glycoside analogue of motif C **29** has been completed by using 1-β-D-arabinofuranosyl-undec-10-ene **2** as glycosyl acceptor. The selective glycosylation of **2** using **S17.5** at –40 °C in DCM provided the disaccharide **34** in 59% yield. The presence of Ara*f* unit was evident from ^{1}H and ^{13}C NMR, showing signals respectively at δ 5.38 (s, 1H) and δ 106.4 (d) corresponding to anomeric proton and corresponding carbon. Similarly, the presence of 3 singlet carbon signals at δ 165.5 (s), 165.9 (s), 166.2 (s) and 15 doublet peaks in aromatic region supported the presence of three benzoyl groups. The benzoyl groups in **34** were hydrolyzed using sodium in methanol to obtain the parent disaccharide **29** in 95% yield. The structure of compound **29** was established with the help of spectral and analytical data. For example, anomeric carbon was resonated at δ 109.6 (d) and there 9 doublets, and 12 triplets altogether in ^{13}C NMR. The observed mass signal at *m/z* 441.10 ([M+Na]$^{+}$) confirmed the proposed constitution of the compound **29**.

2.3.2 Synthetic studies toward the motif B analogue

After the synthesis of motif C analogues, we next proceeded for the synthesis of tetrasaccharide analogue (motif B)[49] of cell wall AG and LAM complex, keeping 1-α-D-arabinofuranosyl-undec-10-ene monosaccharide as the terminal unit. As shown in Figure 13, the synthesis of motif B tetrasaccharide analogue **F.11** was planned from the selective C(5)–O glycosylation of **3** with the trisaccharide **35** as glycosyl donor. The synthesis of donor pentenyl glycoside **35** was planned from the *O*-glycosylation of trisaccharide **36** with 4-penten-1-ol and subsequent C(2)–hydroxyl acetylation. The trisaccharide **36** can be made from the double glycosylation of 1,2-*O*-isopropylidene-D-arabinofuranose[50] and *S*-thiophenyl-2,3,5-tribenzoyl-D-arabinofuranoside as Ara*f* donor.[51]

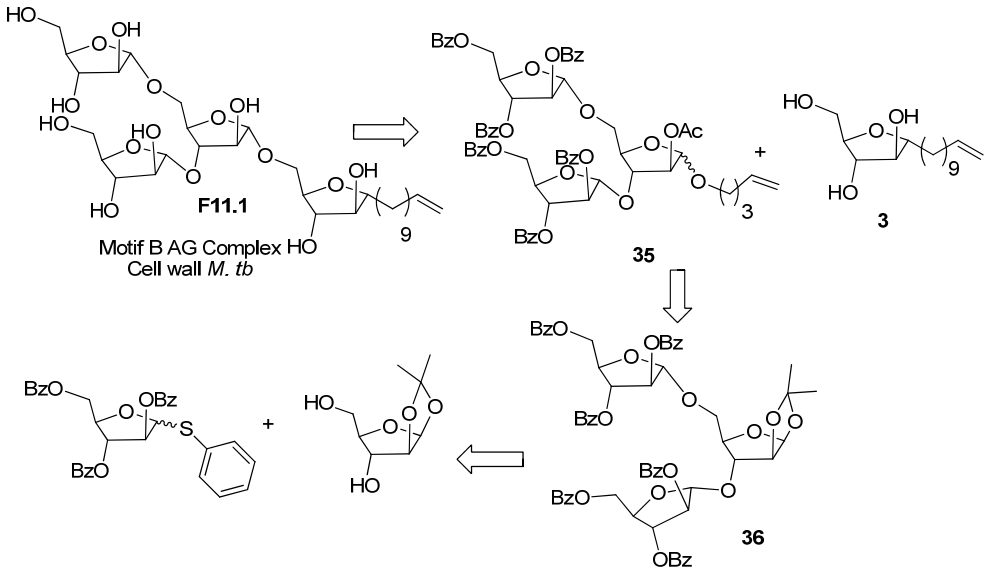
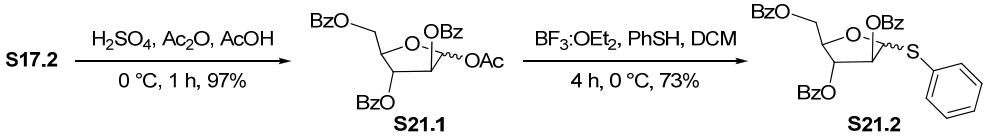


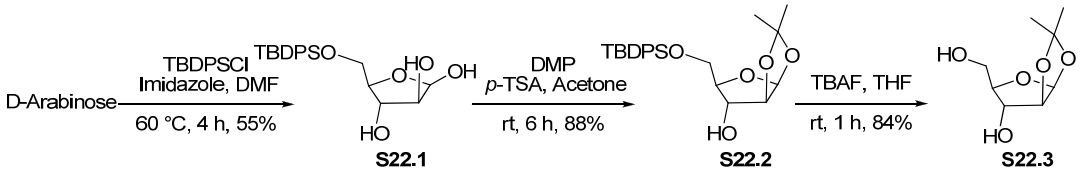
Figure 13: *Retrosynthetic disconnections for the C-glycoside motif B analogue **30***

The synthesis started from preparation of thioglycoside **S21.2**, by acetylation of **S17.2**[52] using acetic anhydride, acetic acid and catalytic amount of H_2SO_4 (97% yield) followed by thioglycosylation using thiophenol and $BF_3{\cdot}Et_2O$ at 0 °C (73% yield).



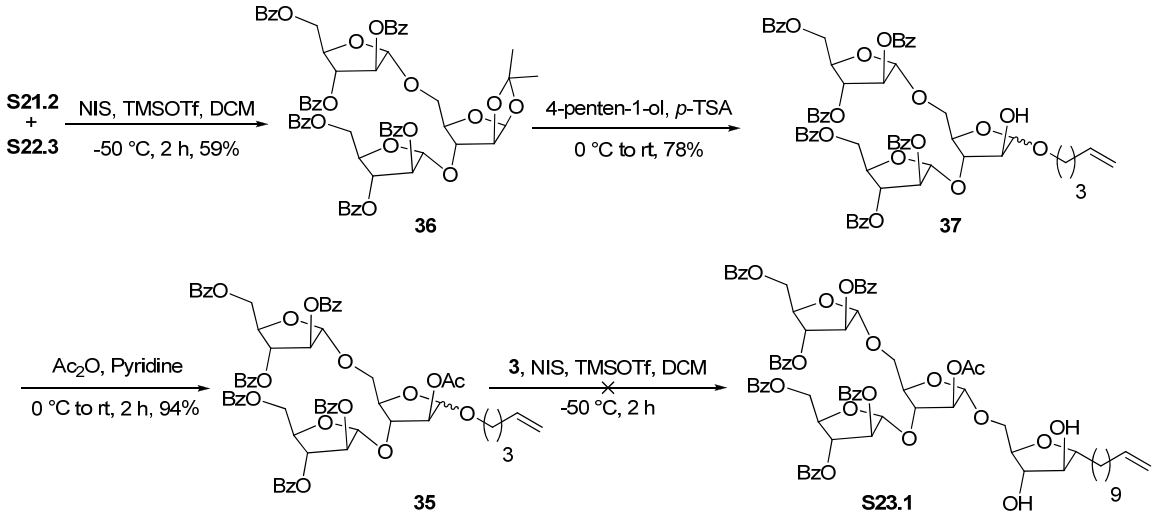
Scheme 21: *Synthesis of 2,3,5-tribenzoyl-S-thiophenyl-D-arabinofuranose*

The glycosyl acceptor **S22.3** was synthesized from D-Arabinose. Selective silylation of C(5) hydroxyl group of D-Arabinose using TBDPSCl and imidazole in DMF gave **S22.1** in 55% yield. Subsequently, the acetonide **S22.3** was procured by acetonide protection of **S22.1** using dimethoxy propane in acetone and *p*-TSA followed by desilylation using TBAF in THF at rt.



Scheme 22: *Synthesis of 1,2-isopropylidene-D-arabinofuranose*

Once both the acceptor and donors are in hand, we next moved for one pot synthesis of key trisaccharide **36**. After exploring several conditions, we concluded that the glycosylation can be successfully carried out by using NIS and TMSOTf at –50 °C in dichloromethane and the trisaccharide **36** was obtained in 59% yield. The structure of the trisaccharide **36** was established with the help of extensive spectral analytical data. In ^{1}H and ^{13}C NMR spectra, the signals corresponding to the anomeric-H two arabinofuranose residues with α-configuration resonated at δ 5.32 (s, 1H), 5.34 (s, 1H) and at δ 105.1 (d), 105.5 (d) respectively. The other anomeric proton and carbon at δ 5.95 (d, J = 4.0 Hz, 1H) indicating the presence of one arabinofuranose unit of the glycosyl acceptor with the β-anomeric configuration. The characteristic signals of isopropylidene were resonated at δ 1.34 (s, 3H), 1.58 (s, 3H) and δ 26.5 (q), 27.2 (q). A strong signal at *m/z* 1101.51 ($[M+Na]^{+}$, 100%) further confirmed the assigned structure and the constitution of the trisaccharide **36**.



Scheme 23: *Synthetic studies toward Motif B C-glycoside analogue*

After having the key trisaccharide in hand we moved for 1,2-isopropylidene opening by 4-penten-1-ol with *p*-TSA to get the anomeric mixture of *O*-glycosides **37**. The structure of compound **37** was well supported by spectral and analytical data. Subsequently, it was acylated by acetic anhydride and pyridine to get the acetate **35** in 94% yield. Having the key glycosyl donor in our hand, we next moved for the final glycosylation. However, the attempted glycosylation of **3** with excess **35** in

dichloromethane using NIS and TMSOTf at –50 °C gave an intractable complex mixture of products. We have explored several other conditions to synthesize **S23.1** (changing stoichiometry of reagents and starting material, temperature etc.) however, without any success.

2.4. Anti-mycobacterium activity of *C*-arabinofuranoside, SAR and preliminary studies toward the imaging of *M. Bovis* BCG

Tuberculosis (TB) caused by *Mycobacterium tuberculosis* (*Mtb*) remains a leading cause of mortality worldwide in 21st century.[53] Tuberculosis is a respiratory transmitted disease affecting nearly 32% of the world's population, more than any other infectious disease. The mortality and spread of this disease has further been aggravated because of synergy of this disease with HIV. Approximately 50% of India's population is reported to be tuberculin test positive and because of TB, every minute one person dies.[54]

Chemotherapy of tuberculosis started in early forties and since then a number of anti-tubercular drugs have been discovered including *p*-aminosalicylic acid (PAS), isoniazid (INH), pyrazinamide (PZA), cycloserine, ethionamide, rifampicin (RMP), and ethambutol.[55] Strategies have been devised to treat TB from time to time and current treatment involves a combination therapy that extends for months at a time, and the pharmacology of these treatment regimens can be complex.[3] Moreover, a number of anti-TB drugs were found to be ineffective against the disease because of development of resistance strains.[4] Initially lack of understanding of drug action and ignorance in the biochemistry of the *Mycobacterium* also the difficulty in manipulating *Mtb* had hindered efforts to define the mode of action of these agents. Based on the recent developments of evaluating the fine structure and biochemistry of *Mycobacterium bacilli*, it is observed that the cell wall of *Mycobacterium* plays a key role in growth and survival of *Mtb*.[13] As the cell wall in *Mtb* being very complex and of very poor permeability, contributes significantly to the resistance against many therapeutic agents and protect it in the human lungs for long time.

The major portion of the cell wall of *Mtb* is made up of the polysaccharides arabinogalactan (AG) and lipoarabinomannan (LAM).[30] The AG and LAM polysaccharides are composed of arabinose and are synthesized inside the infected host cells. Arabinan component present in the polysaccharide contains approx 70 arabinofuranose residues. Since arabinose is foreign to the mammalian cells, the inhibition of the corresponding enzymes arabinofuranosyl transferases (AraTs) play a

critical role in mycobacterial cell wall biosynthesis and its considered as potential drug targets for the treatment of tuberculosis, especially multi-drug resistant forms of *Mtb*.

In this section, the evaluation of anti-tubercular activity of various derivatives of 1-α-D-arabinofuranosyl-undec-10-ene and their disaccharide analogues against *M. Bovis* BCG is presented. Also some 2,3-di-*O*-aryl/di-*O*-alkyl-1-α-D-arabinofuranosyl-undec-10-enes were synthesised for SAR studies. We also describe the synthesis of 1-α-D-arabinofuranosyl-undec-10-ene derived fluorescent conjugate and preliminary studies toward the imaging of *M. Bovis BCG*, using the same.

2.4.1 Anti-mycobacterium activity of *C*-arabinofuranosides

The mono (**2, 3, 30**) and disaccharides (**28, 29, 32**), β-DPA and Motif C analogues (Result and discussion; Section 1 and 3) have been subjected for anti-mycobacterial evaluation. The *M. bovis* BCG strain has been used for this purpose and the inhibition studies have been carried out on the whole cell based HTS assay. Rifampicin and Ethambutol are employed as controls for the inhibition studies. The dose dependent inhibition of *M. bovis* BCG by all the compounds (each at concentrations of 0 (control), 0.05, 0.1, 0.2, 0.3, 0.5 and 1 µg/mL, Table 3) are carried out. The resulting decrease in growth of the organism by compounds was represented as percentage of inhibition of growth in the culture.

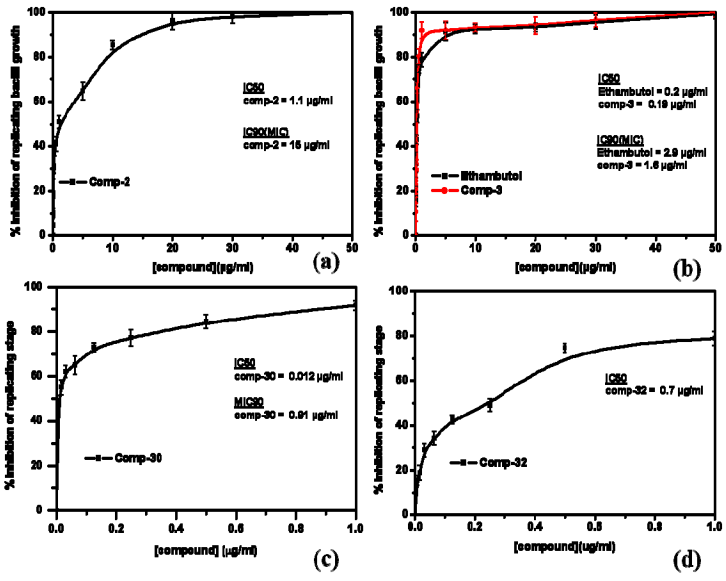
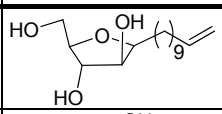
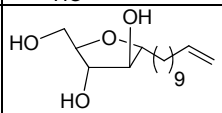
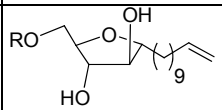
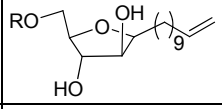
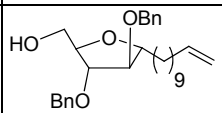
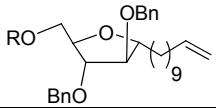
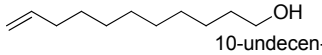
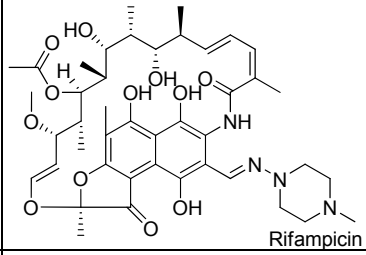
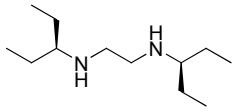
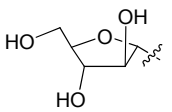


Figure 14: *Dose dependent effect of antimycobacterial inhibitors. (a) Effect of compound **2** (■) (b) compound **3** (●) and Ethambutol (■) (c) compound **30** (■) (d) compound **32** (■), against M. Bovis BCG (Doses of Compound **2**, **3** and Ethambutol dissolved in DMSO ranging from 0.1 to 10 µg/mL and of compound **30** and **32** from 0.1 to 1 µg/mL were added at the time of inoculation and O.D. was measured after 8 days of incubation at 620 nm. Experiments were carried out three times with duplicate cultures and results are mean ± SD)*

Table 3: *% inhibition of Mycobacterium Bovis BCG growth by **2, 3, 28, 29, 30, 32**, 10-undecenol, Rifampicin and Ethambutol at 1 µg/mL concentration, and their IC_{50} & MIC values*

Entry	Compound	% Inhibition	IC50 mg/ml	MIC mg/ml
1	 **2**	48	1.1	15
2	 **3**	85	0.19	1.6
3	 **28**	28	19	-
4	 **29**	<5	>100	-
5	 **30**	>93	12 nm	910 nm
6	 **32**	87	70 nm	-
7	 10-undecen-1-ol	30	-	-
8	 Rifampicin	99 (0.2 mg/ml)	0.02	-
9	 Ethambutol	85	0.2	2.9

R = 

All *C*-glycosides (except **29**) displayed significant anti-mycobacterial effect at concentrations of 1 µg/mL (Table 3). Among all *C*-glycosides, the 2,3-di-*O*-benzyl-1-α-D-arabinofuranosyl-undec-10-ene (**30**) is the best, with IC_{50} 12 nm (Figure 14c). Compound **3** displayed significant anti-mycobacterial effect at concentrations of 1 µg/mL (Figure 14b). Surprisingly the 1-β-D-arabinofuranosyl-undec-10-ene **2** was found to be less potent than α-analogue **3**. Also when extra arabinofuranosyl residue added to **2** and **3,** that is in case of disaccharide **28** and **29** percentage of inhibition of *Mycobacterium* was decreased. It is worth mentioning here that the compound **30** was found to be better than the antitubercular drug ethambutol, and compound **3** have similar inhibition at the same concentrations (Table 3). Control experiments using 10-undecenol revealed it as ineffective against *M. Bovis* BCG.

Next, to evaluate the cytotoxicity of these compounds, we examined the effect of compounds **2, 3, 28** and **29** on the metabolic function of the Thp-1, A431 and HL-60 human monocytic cells using a standard MTT assay. No substantial growth inhibition of these cell lines has been found up to 100 µg/mL concentration of these compounds. Thus, these compounds do not have any significant cytotoxic effect on human cell lines.

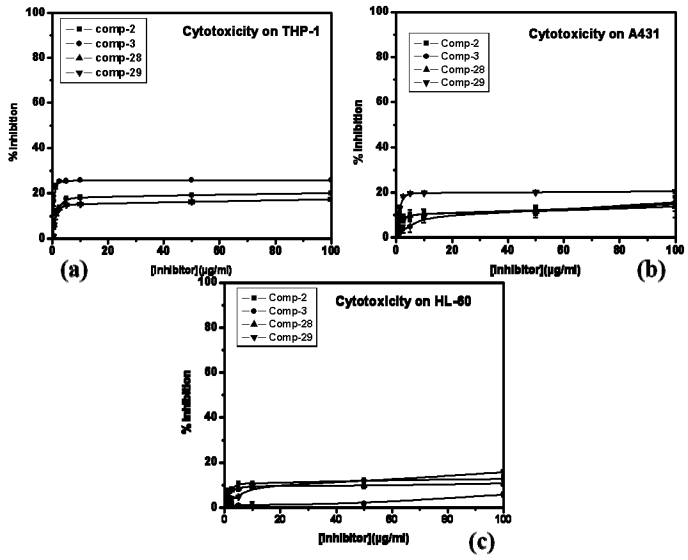
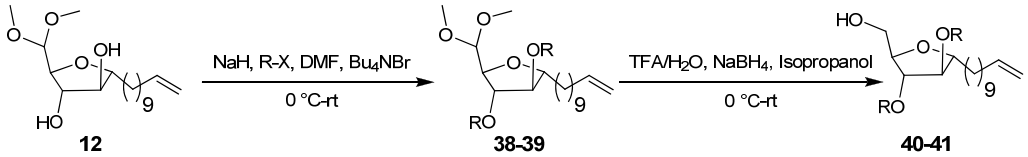


Figure 15: *Dose dependent effect of antimycobacterial inhibitors (**2**, **3**, **28** and **29**) on mammalian cell lines: (a) Thp-1, (b) A431 and (c) HL-60. Doses of compounds dissolved in DMSO ranging from 1 to 10µg/ml were added at the time of inoculation .Reduction of MTT dye indicating the % inhibition. Experiments were carried out three times with duplicate cultures and results are mean ± SD*

2.4.2 Synthesis of 2, 3-di-*O*-alkyl/di-*O*-aryl-1-α-D-arabinofuranosyl-undec-10-enes and their evaluation against *M. Bovis* BCG

Inspired by inhibition of 2,3-di-*O*-benzyl-1-α-D-arabinofuranosyl-undec-10-ene **30** against *Mycobacterium* at nanomolar concentrations, we planned to synthesize various 2,3-di-*O*-alkyl/aryl analogues to get the best lead against Mycobacterium. The synthesis of these 2,3-di-*O*-alkyl/2,3-di-*O*-aryl ether derivatives is a straight forward proposition that involves the dialkylation/diarylation of acetal **12** and subsequent acetal hydrolysis/reduction. The dialkylation was accomplished by using sodium hydride and alkyl halide in DMF. For diaryl ether synthesis, we used Buchwald's protocol[56], Cu(I), Cs_2CO_3 and 1,10-phenanthroline in toluene under heating conditions.

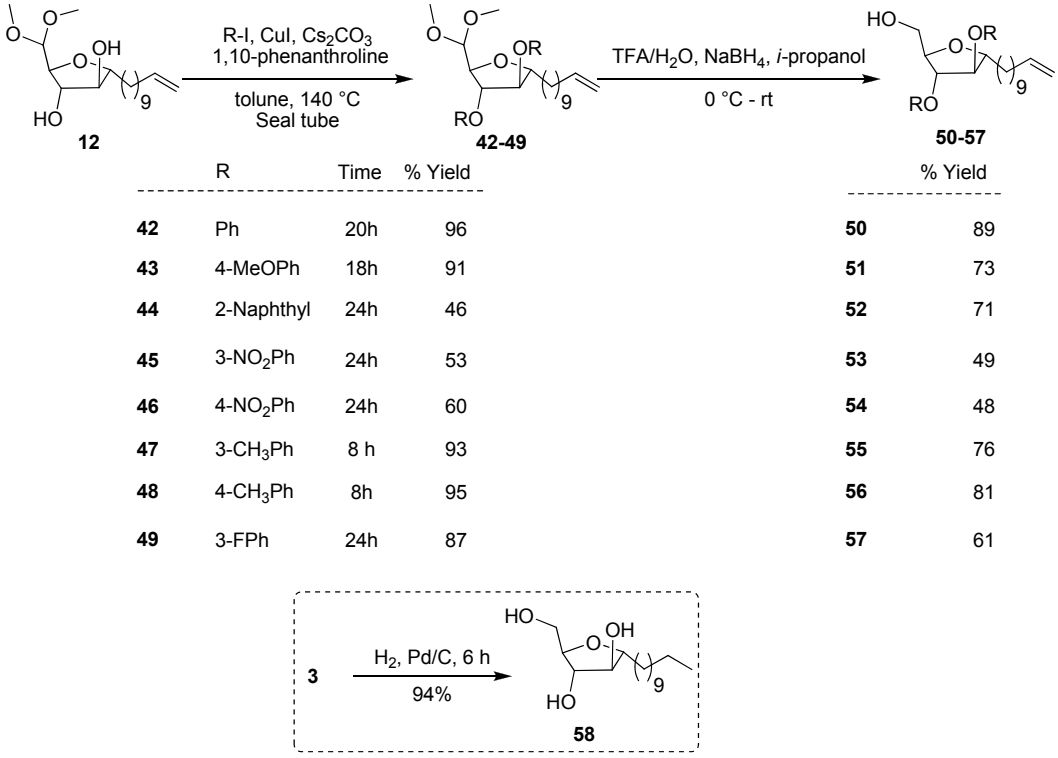
For example the dimethyl derivative **38** was prepared in 92% yield by using methyl iodide and sodium hydride in DMF. Subsequently it was hydrolysed with aqueous TFA and resultant aldehyde was reduced by sodium borohydride in *iso*-propanol. The structure of resulting di-*O*-methyl derivative **40** was established by spectral data. The two singlets at δ 3.37 (s, 3H), 3.38 (s, 3H) in ^{1}H NMR and at 57.3 (q), 57.7 (q) in ^{13}C NMR spectrum corresponds to two methoxy groups. The characteristic signal of C(5) methylene at δ 62.9 (t) and in the mass spectrum, a strong peak at *m/z* 314.46 ($[M+Na]^+$, 100%) confirmed the structure. Employing similar conditions, the di-*O*-octyl derivative was synthesized in 60% overall yield for two steps and it was fully characterized by analytical and spectral data.



	R-X	% Yield		% Yield
38	MeI	92	**40**	88
39		75	**41**	81

Scheme 24: *Synthesis of 2,3-di-O-alkyl-1-α-D-arabinofuranosyl-undec-10-enes*

Next, we proceeded for the di-*O*-aryl derivatives synthesis. The synthesis commenced with the preparation of 2,3-di-*O*-phenyl derivative **50**. The C–O coupling of acetal **12** using iodobenzene, CuI, Cs_2CO_3 and 1,10-phenanthroline in toluene at 140 °C gave **42** in 96% yield. The strong peak at *m/z* 505.29 ($[M+Na]^+$, 100%), and the presence of two phenyl group was supported from signals resonated at δ 6.85–7.02 (m, 6H), 7.21–7.32 (m, 4H) and at δ 115.7 (d, 2C), 115.8 (d, 2C), 121.4 (d), 121.6 (d), 129.6 (d, 2C), 129.7 (d, 2C), 157.0 (s), 157.1 (s) in ^{1}H and ^{13}C NMR respectively. Subsequently, the acetal group in compound **42** was hydrolyzed and the resulting aldehyde was reduced with $NaBH_4$ to obtain the alcohol **50** in 89% yield. The peak present at δ 3.80–3.91 (m, 2H) and 62.3 (t) in ^{1}H NMR and ^{13}C NMR spectra were identity marks of C(5) methylene and peak at *m/z* 461.29 ($[M+Na]^+$, 100%) in ESI mass spectrum confirmed the structure.



	R	Time	% Yield		% Yield
42	Ph	20h	96	**50**	89
43	4-MeOPh	18h	91	**51**	73
44	2-Naphthyl	24h	46	**52**	71
45	3-NO_2Ph	24h	53	**53**	49
46	4-NO_2Ph	24h	60	**54**	48
47	3-CH_3Ph	8 h	93	**55**	76
48	4-CH_3Ph	8h	95	**56**	81
49	3-FPh	24h	87	**57**	61

Scheme 25: *Synthesis of 2,3-O-diaryl-1-α -D-arabinofuranosyl-undec-10-ene*

Scheme 25 presents the generality of this two step strategy. The yields of coupling reactions with nitro, fluro benzene derivatives were less when compared to 4-methoxy, 3-methyl and 4-methyl benzene derivatives (66%, 71% and 76% yield respectively,

Scheme 25). Thus, the outcome of C–O coupling seems to be substrate dependent. In case of electron donating substituent (mesomeric or hyperconjugative) on phenyl group, the reaction was fast and yields are high. A reverse trend has been observed in the case of sterically hindered or with iodobenzenes having the electron withdrawing substituent's. For example, the 3-nitro, 4-nitro and 3-fluro the compounds **53**, **54** and **57** were obtained in an overall yield 26%, 29% and 53% respectively and the di-*O*-naphthyl **52** was obtained in 31% overall yield. All synthesised compounds (**42**–**57**) were well characterised by ^{1}H and ^{13}C NMR and mass spectral data.

As mentioned above, Also, as a part of SAR, we made compound **58** by hydrogenation of **3** to check if olefin has any role in *Mtb* inhibition. The absence of olefin protons and presence of characteristic peak at resonated at δ 0.9 (t, J = 6.6, Hz) corresponds to terminal CH_3 and mass spectral signal at 311.46 ($[M+Na]^+$) confirmed the structure.

Table 4: *% inhibition of Mycobacterium Bovis BCG growth by **38–58** at 20 ug/ml concentration by XTT-Menadion assay*

Entry	Compound	% inhibition	Entry	Compound	% inhibition
dialkyl acetal			dialkyl alcohol		
1	**38**	45	12	**40**	91
2	**39**	23	13	**41**	20
diaryl acetal			diaryl alcohol		
4	**42**	0	15	**50**	0
5	**43**	0	16	**51**	0
6	**44**	0	17	**52**	0
7	**45**	0	18	**53**	0
8	**46**	0	19	**54**	0
9	**47**	0	20	**55**	19
10	**48**	0	21	**56**	0
11	**49**	0	22	**57**	0
12				**58**	94

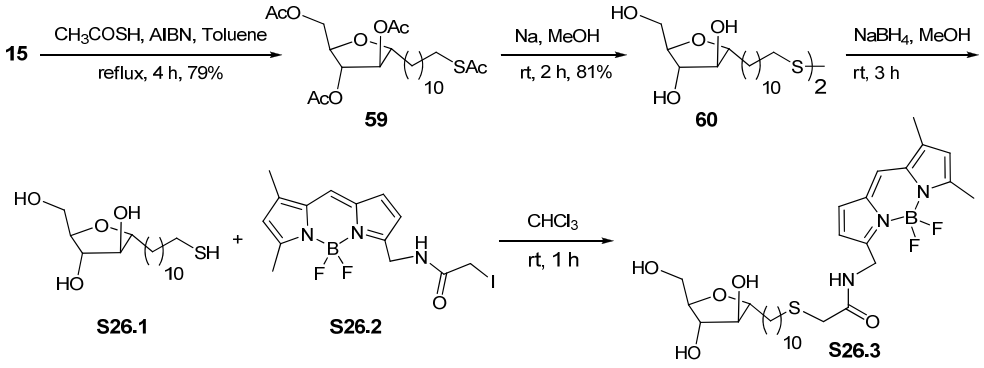
Next the derivatives **38–57** were evaluated against *M. Bovis* BCG and it's found that acetals (**38**–**40** and **42**–**49**) were showing little inhibition compared to compound with -CH_2OH at C(5) group (**40–42**). In case of alkylated derivative, as we increase the length of the chain (hydrophobicity) the activity decreases in proportional like **40** > **41**, the dimethyl derivative **40** was the best among the entire collection made. Surprisingly

the compounds **42**–**57** which were synthesised with inspiration from the inhibitory activity of the dibenzyl derivative **30** are found to be completely inactive even at the concentration of 20 μg/mL. Only, the di-*O*-tolyl derivative **55** showed little inhibition (19%) at the concentration 20 μg/mL. As expected, the reduced compound **58** showed similar inhibition activity as of **3**, at 20 μg/ml it is 94%.

2.4.3 Synthesis and preliminary study of imaging of *M. Bovis* BCG by BODIPY conjugate 1-α-D-arabinofuranosyl-undec-10-ene

As we have already identified a simple lead compound for inhibiting *Mycobacterium***,** next we planned to use this compound for imaging in the pursuit of developing new diagnostic tools for *M. Tuberculosis*.[57]

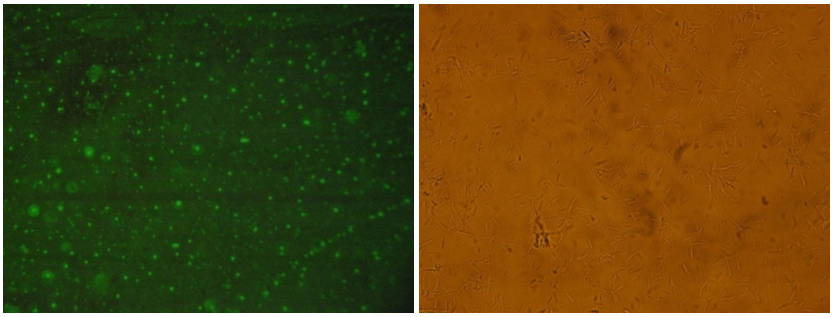
In this regard, first we planned to use BODIPY as a source of fluorescence and to attach this fluorescent tag to **15**, we need a thiol group as an handle. This handle was easily introduced in **15** by thioacetylation of the terminal olefin[58] using thioacetic acid, AIBN in toluene to obtain the thioacetate **59** in 79% yield (Scheme 26). In ^{1}H and ^{13}C NMR spectra, the characteristic signals observed at δ 2.31 (s, 3H), 30.6 (q), 196.0 (s) were due to thioacetyl group and its corresponding signal in the mass spectrum at *m/z* 511.25 ([M+Na]$^{+}$, 100%) proved the structure.



Scheme 26: *Synthesis of fluorescent Bodipy-conjugate of 1-α-D-arabinofuranosyl-undec-10-ene*

Next, the compound **59** was subjected for deacetylation using sodium in methanol to obtain the disulfide **60** in 81% yield. The structure was confirmed from the methylene protons adjacent to sulphur resonated at 2.68 (t, *J* = 7.2 Hz, 4H) in ^{1}H NMR and most

abundant peak at *m/z* 661.19 ($[M+Na]^+$) in ESI mass. The well characterized disulfide **60** has been used as the starting point for the imaging studies which in general were carried out at ≤ 1 mg quantities. The imaging experiment involve the following sequence of reactions. First, the disulfide linkage was broken by using sodium borohydride in methanol and the resulting intermediate thiol **S26.1** was coupled with iodoacetamido BODIPY derivative **S26.2** to afford **S26.3**, which was used for imaging *Mycobacterium* BOVIS BCG and preliminary results are as below (Picture 1).

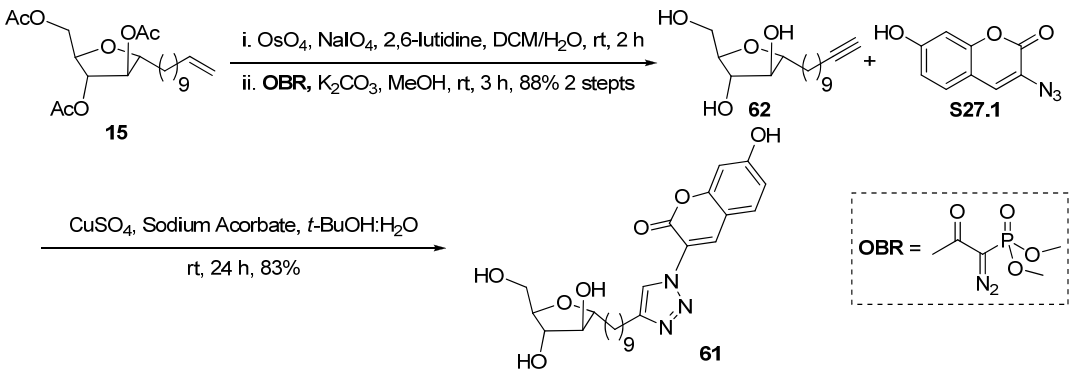


(a) **(b)**

Picture 1: *Fluorescence (a) and UV-Visible image (b) of Bodipy-conjugate of 1-α-D-arabinofuranosyl-undec-10-ene*

2.4.4 Syntheses of fluorescent coumarin conjugate of 1-α-D-arabinofuranosyl-undec-10-ene

Though the imaging results with **S26.3** are promising, however it was unstable and expensive to scale up for the characterization purpose. To overcome these deficiencies, we have synthesised a stable coumarin conjugate **61**, using cheap and easily accessible coumarinyl azide **S27.1**.[59]



Scheme 27: *Synthesis of coumarine -conjugate fluorescent tag of 1-α-D-arabinofuranosyl-undecene*

The synthesis of **61** started with the dihydroxylation of triacetate **15** followed by the oxidative cleavage of resulting diol with osmium tetraoxide in DCM/H_2O[60] and the intermediate crude aldehyde was subjected directly to Ohira-Bestmann alkynylation[61] by using potassium carbonate in methanol to obtain the alkyne **62** in 88%. In ESI-mass spectrum, the peak present at *m/z* 307.05 ($[M+Na]^+$) and the absence of acetyl peaks along with characteristic peak of CH of terminal alkyne resonated at δ 2.13 (t, *J* = 2.3 Hz, 1H) in ^{1}H NMR spectrum established the assigned structure. Next, the alkyne **62** was treated with coumarin azide **S27.1** under Click reaction conditions[62] i.e. $CuSO_4$ *t*-BuOH/H_2O and sodium ascorbate to obtain the conjugate **61** in 83% yield. Its structure was well supported by NMR and mass spectral data. For example, in the ^{1}H NMR spectrum of compound **61**, the characteristic four protons of coumarin moiety were resonated at δ 6.81 (d, *J* = 2.0 Hz, 1H), 6.90 (dd, *J* = 2.0, 8.6 Hz, 1H), 7.64 (d, *J* = 8.6 Hz, 1H), 8.34 (s, 1H) and of the with triazole–H at δ 8.46 (s, 1H). The appearance of the required number of signals in ^{13}C NMR spectrum and a strong peak at *m/z* 510.22 (100%, $[M+Na]^+$) in mass spectrum further supported the assigned structure. The fluorescence maxima (λ_{max}) of coumarin conjugate **61** was at appeared at 426 nm in methanol and water but at 476 nm in DMSO. From the preliminary screenings, this compound was found to inhibit *M. Bovis* BCG in 79% at 20 μg/mL concentration. Further experiments probing the use of this compound for the imaging of *M. Bovis* BCG are currently in progress.

Conclusions:

To summarize**,** a general protocol for the stereoselective synthesis of *α*- and *β*-*C*-arabinofuranosides has been developed. A furan ring transposition reaction has been adopted as key strategy which involves the prior manipulation of stereochemistry at one center in the substrate employed, which ultimately decides the anomeric configuration of the *C*-glycoside synthesized. This is quite important considering the difficulties associated in establishing the stereochemistry at a newly generated anomeric carbon in *C*-glycoside synthesis. Two carba-disaccharide *Motif C* analogues (**1** and **17**) of AG complex of cell wall of *Mtb* have been synthesised in good overall yields (7 steps; **1** with 37% and **17** with 41%). A novel double furan ring transposition reaction has been proposed in this pursuit and executed successfully for the stereospecific synthesis of these two disaccharides. This reaction involves the reorganization of multiple bonds in a synchronised manner with complete regio- and stereoselectivity. The motif C analogues have been synthesized using selective glycosylation at C(5) hydroxyl group of α and β-D-arabinofuranosyl-undec-10-enes **2** and **3**. Attempts were made for the synthesis of corresponding Motif B analogue **4**.

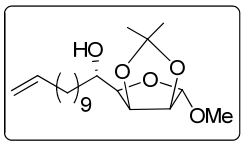
The anti-mycobacterial activity of all the final compounds has been evaluated against the *M. bovis* BCG strain and the inhibition studies have been carried out on the whole cell based HTS assay. One of the *C*-arabinofuranosides **30** was found to have the MIC better than frontline anti-tubercular drug Ethambutol and the other one **3** with similar MIC. Several analogues of **30** were synthesised and found that increasing hydrophobicity and changing electronic and steric environment in **30** decreases the inhibitory activity. Also synthesised the BODIPY, coumarin conjugates of **3** and the preliminary results of *Mycobacterium* imaging using the BODIPY conjugate are encouraging.

EXPERIMENTAL

3. Experimental information

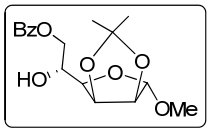
3.1 Synthesis and characterization of compounds 1–62

Methyl 6-deoxy-2,3-*O*-isopropylidene-α-L-*gulo*-hexadec-15-enofuranoside (7):



To a suspension of magnesium turnings (6.2 g, 255 mmol) in anhydrous diethyl ether (100 mL) was added 10-bromo-dec-1-ene (19 mL, 96 mmol) and the contents were heated to reflux for 2 h. The reaction mixture was diluted with diethyl ether (100 mL) and was transferred slowly to an ice-cooled solution of anhydrous cuprous cyanide (14.3 g, 159 mmol) in diethyl ether (100 mL). The contents were stirred for additional 30 min at 0 °C and then treated with a solution of the oxirane **5** (13.8 g, 64 mmol) in diethyl ether (75 mL) and stirred for 1 h at 0 °C and for 6 h at rt. Then the reaction mixture was quenched by adding cold water and extracted with ethyl acetate. The combined organic layer was washed with brine, dried (Na_2SO_4) and concentrated. The crude product was purified by silica gel column chromatography (15:85 EtOAc/Pet ether) and afforded **10** (17.3 g, 71% yield) as colorless oil. R_f = 0.7 (1:3 EtOAc/Pet ether); $[\alpha]_D^{25}$ = +39.9 (*c* 1 $CHCl_3$). **^{1}H NMR (200 MHz, $CDCl_3$):** δ 1.24–1.28 (br m, 17H), 1.45 (s, 3H), 1.51–1.60 (m, 2H), 1.96–2.06 (m, 2H), 2.88 (br s, 1H –OH), 3.31 (s, 3H), 3.75 (dd, *J* = 3.7, 5.2 Hz, 1H), 3.99 (br dt, *J* = 4.0, 6.0 Hz, 1H), 4.54 (d, *J* = 6.0 Hz, 1H), 4.69 (dd, *J* = 3.6, 6.0 Hz, 1H), 4.89 (ddt, *J* = 1.2, 2.3, 10.1 Hz, 1H), 4.97 (ddt, *J* = 1.6, 2.2, 17.0 Hz, 1H), 4.92 (s, 1H), 5.78 (ddt, *J* = 6.7, 10.1, 17.1 Hz, 1H) ppm; **^{13}C NMR (50 MHz, $CDCl_3$):** δ 24.5 (q), 25.3 (t), 25.9 (q), 28.9 (t), 29.1 (t), 29.4 (t), 29.5 (t, 3C), 33.1 (t), 33.8 (t), 54.5 (q), 69.9 (d), 80.5 (d), 81.7 (d), 85.4 (d), 106.7 (d), 112.6 (s), 114.1 (t), 139.2 (d) ppm; **ESI-MS *m/z*:** 379.30 ($[M+Na]^+$,100%), 395.39 ($[M+K]^+$, 3%); **HRMS (MALDI-TOF) *m/z*:** calcd for ($[C_{20}H_{36}O_5Na]^+$) 379.2461, found 379.2495.

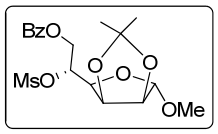
Methyl 6-*O*-benzoyl-2,3-*O*-isopropylidene-α-D-mannofuranoside (8):



At 0 °C, a solution of diol **7** (8.5 g, 36 mmol) in THF (90 mL) and triethylamine (5.8 g, 42 mmol) was treated with benzoyl chloride

(4.2 ml, 36 mmol) dropwise and the contents were stirred at 0 °C for 3 h. The reaction mixture was quenched with water extracted with DCM. The combined organic phase was washed with aq. sodium bicarbonate and water, dried (Na_2SO_4) and evaporated under reduced pressure. The crude product was purified by silica gel column chromatography (1:3 EtOAc/Pet ether) to afford benzoate **8** (9 g, 74% yield) as a yellow oil. R_f = 0.4 (2:3 EtOAc/Pet ether); **[α]** $^{25}_{D}$ = +50.4 (*c* 2.8, $CHCl_3$). **^{1}H NMR (200 MHz, $CDCl_3$):** δ 1.31 (s, 3H), 1.47 (s, 3H), 3.26 (s, 3H), 3.96 (dd, *J* = 3.7, 5.2 Hz, 1H), 4.29 (ddd, *J* = 2.9, 5.7, 8.2 Hz, 1H), 4.46 (dd, *J* = 5.7, 11.7 Hz, 1H), 4.55 (d, *J* = 5.9 Hz, 1H), 4.62 (dd, *J* = 3.0, 11.7 Hz, 1H), 4.85 (d, *J* = 3.7, 5.9 Hz, 1H), 4.90 (s, 1H), 7.35–7.46 (m, 2H), 7.49–7.59 (m, 1H), 8.03–8.10 (m, 2H)) ppm; **^{13}C NMR (50 MHz, $CDCl_3$):** δ 24.6 (q), 25.9 (q), 54.5 (q), 66.9 (t), 68.7 (d), 78.6 (d), 80.0 (d), 84.8 (d), 107.0 (d), 112.7 (s), 128.3 (d, 2C), 129.6 (d, 2C), 129.8 (s), 133.1 (d), 166.7 (s) ppm; **ESI-MS *m/z*:** 361.10 (100%, $[M+Na]^+$); **HRMS (MALDI-TOF) *m/z*:** calcd for ($[C_{17}H_{22}O_7Na]^+$) 361.1264, found 361.1246.

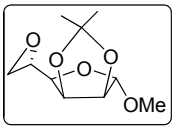
Methyl 6-*O*-benzoyl-5-*O*-mesyl-2,3-*O*-isopropylidene-α-D-mannofuranoside (9):



A solution of alcohol **8** (7 g, 20.7 mmol) in anhydrous DCM (70 mL) and triethyl amine (8.6 mL, 62 mmol) was cooled to 0 °C and treated with mesyl chloride (3.2 mL, 41.3 mmol) stirred at the rt for 1 h. The reaction mixture was diluted with water and extracted with DCM. The combined organic layer was washed with aq. $NaHCO_3$ solution, brine, dried (Na_2SO_4) and concentrated under reduced pressure. The crude product was purified by column chromatography (1:3 EtOAc/Pet ether) to afford **9** (8.1 g, 94% yield) as a yellowish oil. R_f = 0.4 (2:3 EtOAc/Pet ether); **[α]** $^{25}_{D}$ = +40.5 (*c* 1, $CHCl_3$). **^{1}H NMR (200 MHz, $CDCl_3$):** 1.32 (s, 3H), 1.50 (s, 3H), 3.12 (s, 3H), 3.24 (s, 3H), 4.22 (dd, *J* = 3.5, 8.3 Hz, 1H), 4.59 (t, *J* = 6.0 Hz, 1H), 4.62 (t, *J* = 6.0 Hz, 1H), 4.80 (dd, *J* = 3.5, 5.8 Hz, 1H), 4.86 (dd, *J* = 2.0, 12.4 Hz, 1H), 4.92 (s, 1H), 5.21 (ddd, *J* = 2.0, 5.5, 8.0 Hz, 1H), 7.39–7.50 (m, 2H), 7.52–7.61 (m, 1H), 8.05–8.14 (m, 2H) ppm; **^{13}C NMR (50 MHz, $CDCl_3$):** δ 24.6 (q), 25.7 (q), 38.3 (q), 54.4 (q), 64.0 (t), 76.6 (d), 76.8 (d), 78.6 (d), 84.5 (d), 107.9 (d), 112.8 (s), 128.2 (d, 2C), 129.4 (d, 2C), 129.5 (s), 133.0 (d), 165.7 (s) ppm; **ESI-MS *m/z*:**

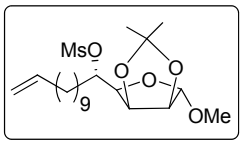
439.03 ([M+Na]$^+$); **HRMS (MALDI-TOF) *m/z*:** calcd for ([$C_{18}H_{24}O_9S$ Na]$^+$) 439.1039, found 439.1027.

Methyl 5,6-anhydro-2, 3-*O*-isopropylidene-β-L-gulofuranoside (10):



A solution of mesylate **9** (7.9 g, 19 mmol) in THF:MeOH (5:3, 80 ml) was cooled to 0 °C and LiOH:H_2O (4.0 g, 94.9 mmol) was added portion wise. The reaction mixture was allowed to stir up to completion of reaction as indicated by TLC. The solvent was evaporated and the crude residue was purified over silica gel column chromatography (1:9 EtOAc/Pet ether) to procure **10** (2.67 g, 65%) as a colorless solid. R_f = 0.6 (3:7 EtOAc/Pet ether); **[α]** $^{25}_{D}$ = +65.0 (*c* 1.2, $CHCl_3$). **^{1}H NMR (200 MHz, $CDCl_3$):** δ 1.30 (s, 3H), 1.48 (s, 3H), 2.62 (dd, *J* = 2.7, 4.8 Hz, 1H), 2.89 (t, *J* = 4.5 Hz, 1H), 3.24 (ddd, *J* = 2.7, 4.3, 7.0 Hz, 1H), 3.32 (s, 3H), 3.45 (dd, *J* = 3.7, 7.0 Hz, 1H), 4.54 (d, *J* = 5.9 Hz, 1H), 4.71 (dd, *J* = 3.7, 5.8 Hz, 1H), 4.95 (s, 1H) ppm; **^{13}C NMR (50 MHz, $CDCl_3$):** δ 24.7 (q), 26.0 (q), 43.6 (t), 49.9 (d), 54.7 (q), 80.5 (d), 82.2 (d), 85.0 (d), 107.4 (d), 112.9 (d) ppm; **ESI-MS *m/z*:** 238.99 (100% [M+Na]$^+$); **HRMS (MALDI-TOF) *m/z*:** calcd for ([$C_{10}H_{16}O_5Na^+$) 239.0896, found 239.0877.

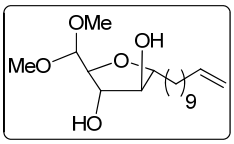
Methyl 6-deoxy-2,3-*O*-isopropylidene-5-*O*-methanesulfonyl-α-L-*gulo*-hexadec-15-enofuranoside (11):



At 0 °C, a solution of alcohol **10** (4.5 g, 12.62 mmol) in anhydrous DCM (60 mL) and triethyl amine (5 mL, 38 mmol) was treated with mesyl chloride (1.2 mL, 15 mmol) and stirred at rt for 2 h. The reaction mixture was quenched with ice water and extracted with DCM. The combined organic layer was washed with aq. $NaHCO_3$ solution, brine, dried (Na_2SO_4) and concentrated. The crude product was purified by column chromatography (15:85 EtOAc/Pet ether) to afford **11** (5.3 g, 96% yield) as light yellow oil. R_f = 0.7 (1:3 EtOAc/Pet ether); **[α]** $^{25}_{D}$ = +36.9 (*c* 1, $CHCl_3$). **^{1}H NMR (200 MHz, $CDCl_3$):** δ 1.20–1.35 (br m, 17H), 1.44 (s, 3H), 1.63–1.81 (m, 2H), 1.96–2.06 (m, 2H), 3.10 (s, 3H), 3.28 (s, 3H), 3.98 (dd, *J* = 3.4, 9.0 Hz, 1H), 4.55 (d, *J* = 5.9 Hz, 1H), 4.64 (dd, *J* = 3.5, 5.9 Hz,

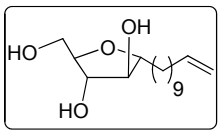
1H), 4.85 (br dt, *J* = 3.3, 9.0 Hz, 1H), 4.86–4.95 (m, 1H), 4.96 (ddt, *J* = 1.6, 2.2, 17.2 Hz, 1H), 4.89 (s, 1H), 5.79 (ddt, *J* = 6.7, 10.1, 17.2 Hz, 1H) ppm; **^{13}C NMR (50 MHz, $CDCl_3$):** 24.4 (t), 24.8 (q), 26.0 (q), 28.8 (t), 29.0 (t), 29.2 (t), 29.2 (t), 29.4 (t), 29.4 (t), 31.0 (t), 33.7 (t), 38.5 (q), 54.5 (q), 79.4 (d), 81.0 (d), 83.3 (d), 85.0 (d), 106.9 (d), 112.8 (s), 114.0 (t), 139.2 (d) ppm; **ESI-MS *m/z*:** 457.41 ($[M+Na]^+$,15%); **HRMS (MALDI-TOF) *m/z*:** calcd for ($[C_{21}H_{38}O_7SNa]^+$) 457.2236, found 457.2234.

5-Deoxy-5-dimethylacetal-1-β-D-arabinofuranosyl-undec-10-ene (12):



To a solution of mesylate **11** (4.3 g, 9.9 mmol) in anhydrous methanol (110 mL) was added *p*-TSA (340 mg, 1.98 mmol) and allowed to reflux at 80 ºC for 48 h. The reaction mixture was cooled and treated with solid $NaHCO_3$ and stirred for 1 h. The contents were filtered through *celite* and concentrated under reduced pressure. The crude product was purified by column chromatography (3:7 EtOAc/Pet ether) to obtain **12** (2.90 gm 88%) as pale yellow oil. R_f = 0.4 (1:1 EtOAc/Pet ether); $[\alpha]_D^{25}$ = +20.0 (*c* 1, $CHCl_3$). **^{1}H NMR (200 MHz, $CDCl_3$):** δ 1.20–1.40 (br m, 14H), 1.50–1.60 (m, 2H), 1.94–2.04 (m, 2H), 3.41 (s, 3H), 3.45 (s, 3H), 3.67 (br s, 1H –OH), 3.61–3.80 (br m, 2H), 3.83 (t, *J* = 5.0 Hz, 1H), 3.97 (br s, 1H –OH), 4.14 (br t, *J* = 4.4 Hz, 1H), 4.35 (d, *J* = 4.8 Hz, 1H), 4.86 (ddt, *J* = 1.2, 2.2, 10.1 Hz, 1H), 4.95 (ddt, *J* = 1.5, 2.2, 17.1 Hz, 1H), 5.76 (ddt, *J* = 6.7, 10.1, 17.1 Hz, 1H) ppm; **^{13}C NMR (50 MHz, $CDCl_3$):** δ 25.6 (t), 28.8 (t), 29.0 (t), 29.4 (t), 29.5 (t, 2C), 29.6 (t), 33.2 (t), 33.7 (t), 55.0 (q), 56.4 (q), 78.4 (d), 81.0 (d), 82.0 (d), 83.6 (d), 105.4 (d), 114.0 (t), 139.1 (d) ppm; **ESI-MS *m/z*:** 353.26 ($[M+Na]^+$,100%); **HRMS (MALDI-TOF) *m/z*:** calcd for ($[C_{18}H_{34}O_5Na^+$) 353.2304, found 353.2292.

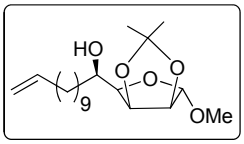
1-α-D-Arabinofuranosyl-undec-10-ene (3):



The dimethyl acetal **12** (350 mg, 1.06 mmol) was dissolved in 7 mL ice cold 70% aq. trifluoroacetic acid (TFA) and stirred at rt for 4 h. After complete consumption of the acetal **12** as indicated by TLC, the reaction mixture was concentrated under reduced pressure and the resulting crude (301 mg) was dissolved in isopropanol and treated with a solution of $NaBH_4$ (120 mg, 3.18 mmol) in water (1.5 mL) and stirred at rt for 2 h. The reaction mixture was brought

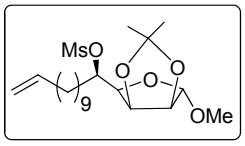
to acidic pH by adding 1N hydrochloric acid and then extracted with diethyl ether (15 x 3 mL). The combined organic layer was washed with brine, dried (Na_2SO_4) and concentrated under reduced pressure. The crude product was purified by column chromatography (1:9 CH_3OH/CH_2Cl_2) to afford compound **3** (233 mg, 77% yield) as a colorless gum. R_f = 0.2 (1:9 CH_3OH/CH_2Cl_2); **[α]** $^{25}_{D}$ = +29.77 (*c* 0.8, $CHCl_3$); **^{1}H NMR (400 MHz, $CDCl_3$):** δ 1.28–1.40 (br m, 14H), 1.56–1.63 (m, 2H), 2.02–2.06 (m, 2H), 3.61 (dd, *J* = 5.3, 11.8 Hz, 2H), 3.69 (dd, *J* = 3.5, 11.8 Hz, 1H), 3.71–3.74 (br m, 2H), 3.76 (dt, *J* = 3.5, 5.3 Hz, 2H), 3.93 (t, *J* = 5.5 Hz, 1H), 4.91 (ddt, *J* = 1.1, 2.2, 10.2 Hz, 1H), 4.98 (br ddt, *J* = 1.6, 2, 17.1 Hz, 1H), 5.80 (ddt, *J* = 6.7, 10.2, 17.1 Hz., 1H) ppm; **^{13}C NMR (100 MHz, $CDCl_3$):** δ 26.7 (t), 31.0 (t), 30.2 (t), 30.6 (t), 30.7 (t, 2C), 30.8 (t), 34.7 (t), 34.9 (t), 63.4 (t), 79.1 (d), 82.7 (d), 84.1 (d), 84.5 (d), 114.7 (t), 140.1 (d) ppm; **ESI-MS *m/z*:** 309.22 ($[M+Na]^+$,100%), 301.28 (22%); **HRMS (MALDI-TOF) *m/z*:** calcd for ($[C_{16}H_{30}O_4Na]^+$) 309.2042, found 309.2052.

Methyl 6-deoxy-2,3-*O*-isopropylidene-α-D-*manno*-hexadec-15-enofuranoside (6):



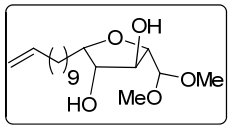
Following the procedure used for preparation of compound **7**, the epoxide **S6.1** (7.56 g, 35 mmol) was converted to the corresponding alcohol **6** (9.7 g, 78% yield) as a low melting solid; R_f = 0.7 (1:3 EtOAc/Pet ether); **[α]** $^{25}_{D}$ = +59.7 (*c* 1.0 $CHCl_3$); **^{1}H NMR (200 MHz, $CDCl_3$):** δ 1.23–1.30 (br m, 17H), 1.46 (s, 3H), 1.50–1.68 (m, 2H), 1.96–2.06 (m, 2H), 2.52 (d, *J* = 5.7 Hz, 1H), 3.29 (s, 3H), 3.74 (dd, *J* = 3.6, 7.3 Hz, 1H), 3.81–3.93 (m, 1H), 4.53 (d, *J* = 6.0 Hz, 1H), 4.79 (dd, *J* = 3.7, 6.0 Hz, 1H), 4.89 (ddt, *J* = 1.2, 2.2, 10.2 Hz, 1H), 4.90 (s, 1H), 4.98 (ddt, *J* = 1.6, 3.6, 16.0 Hz, 1H), 5.78 (ddt, *J* = 6.7, 10.2, 17.2 Hz, 1H) ppm; **^{13}C NMR (50 MHz, $CDCl_3$):** δ 24.6 (q), 25.5 (t), 25.9 (q), 28.9 (t), 29.1 (t), 29.4 (t), 29.5 (t), 29.5 (t), 29.7 (t), 33.7 (t), 34.5 (t), 54.5 (q), 70.3 (d), 80.1 (d), 81.8 (d), 84.8 (d), 106.9 (d), 112.5 (s), 114.0 (t), 139.1 ppm; **ESI-MS *m/z*:** 379.37 ($[M+Na]^+$ 3%),; **HRMS (MALDI-TOF) *m/z*:** calcd for ($[C_{20}H_{36}O_5Na]^+$) 379.2461, found 379.2425.

Methyl 6-deoxy-2,3-*O*-isopropylidene-5-*O*-methanesulfonyl-α-D-*manno*-hexadec-15-enofuranoside (4):



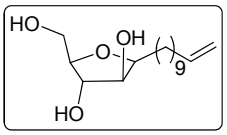
The alcohol **6** (8.8 g, 25 mmol) was mesylated according to the procedure used in the preparation of **11** to obtain mesylate **4** (10.2 g, 95% yield) as light yellow oil. R_f = 0.7 (1:3 EtOAc/Pet ether); $[\alpha]_D^{25}$ = +12.8 (*c* 1, $CHCl_3$). **^{1}H NMR (200 MHz, $CDCl_3$):** δ 1.23–1.28 (br m, 17H), 1.45 (s, 3H), 1.70–1.93 (m, 2H), 1.96–2.00 (m, 2H), 3.06 (s, 3H), 3.30 (s, 3H), 3.98 (dd, *J* = 3.4, 8.4 Hz, 1H), 4.55 (d, *J* = 5.9 Hz, 1H), 4.69 (dd, *J* = 3.5, 5.8 Hz, 1H), 4.86 (s, 1H), 4.87–4.93 (br m, 2H), 4.96 (ddt, *J* = 1.3, 2.0, 17.0 Hz, 1H), 5.78 (ddt, *J* = 6.7, 10.2, 17.2 Hz, 1H) ppm; **^{13}C NMR (50 MHz, $CDCl_3$):** δ 23.6 (t), 24.9 (q), 26.0 (q), 28.9 (t), 29.1 (t), 29.3 (t), 29.4 (t, 2C), 29.6 (t), 32.2 (t), 33.8 (t), 38.3 (q), 54.7 (q), 78.8 (d), 79.0 (d), 80.2 (d), 84.8 (d), 107.0 (d), 112.8 (s), 114.0 (t), 139.2 (d) ppm; **ESI-MS *m/z*:** 457.34 ($[M+Na]^+$, 11%); **HRMS (MALDI-TOF) *m/z*:** calcd for ($[C_{21}H_{38}O_7SNa]^+$) 457.2236, found 457.2235.

5-Deoxy-5-dimethylacetal-1-β-D-arabinofuranosyl-undec-10-ene (5):



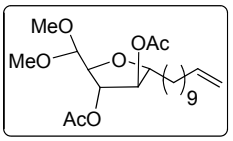
Acetal **5** (2.52 g, 83% yield) was prepared from the mesylate **4** (4.0 g, 9.2 mmol) following the procedure used for preparation of compound **12**. Light yellow oil; R_f = 0.5 (1:1 EtOAc/Pet ether); $[\alpha]_D^{25}$ = +20.8 (*c* 1, $CHCl_3$). **^{1}H NMR (200 MHz, $CDCl_3$):** δ 1.24–1.37 (br m, 14H), 1.59–1.65 (m, 2H), 1.97–2.06 (m, 2H), 3.3 (br d, *J* = 11.1 Hz, 1H), 3.48 (s, 3H), 3.54 (s, 3H), 3.74 (dd, *J* = 2.6, 11.0 Hz, 1H), 3.82 (dd, *J* = 1.7, 2.9 Hz, 1H), 3.92 (dt, *J* = 2.7, 6.8 Hz, 1H) 4.25 (brs, 1H), 4.36 (d, *J* = 3 1H), 4.89 (ddt, *J* = 1.3, 2.3, 10.1 Hz, 1H), 4.96 (ddt, *J* = 1.5, 2.2, 17.1 Hz, 1H), 5.79 (ddt, *J* = 6.7, 10.1, 17.2 Hz, 1H) ppm; **^{13}C NMR (50 MHz, $CDCl_3$):** δ 26.1 (t), 28.2 (t), 28.9 (t), 29.1 (t), 29.5 (t, 3C), 29.7 (t), 33.7 (t), 56.4 (q), 57.8 (q), 77.1 (d), 77.9 (d), 82.1 (d), 85.7 (d), 105.2 (d), 114.1 (t), 139.2 (d) ppm; **ESI-MS *m/z*:** 301.27 ($[M+1]^+$, 100%), 353.35 ($[M+Na]^+$, 100%), 369.35 ($[M+K]^+$, 6%); **HRMS (MALDI-TOF) *m/z*:** calcd for ($[C_{18}H_{34}O_5Na^+$) 353.2304, found 353.2330.

1-β-D-Arabinofuranosyl-undec-10-ene (2):



According to the procedure used in the preparation of **3**, the hydrolysis of dimethyl acetal **5** (500 mg, 1.5 mmol) and subsequent reduction with $NaBH_4$ gave **2** (313 mg, 72% yield) as a colorless gum; R_f = 0.3 (1:9 CH_3OH/CH_2Cl_2); **[α]** $^{25}_{D}$ = +25.9 (*c* 0.6, $CHCl_3$). **^{1}H NMR (400 MHz, $CDCl_3$):** δ 1.31–1.44 (br s, 14H), 1.61–1.66 (m, 2H), 2.01–2.07 (m, 2H), 3.63 (dd, *J* = 4.8, 11.5 Hz, 1H), 3.68 (dd, *J* = 3.9, 11.5 Hz, 1H), 3.73 (ddd, *J* = 2.5, 3.7, 4.6 Hz, 1H), 3.78 (br dd, *J* = 0.9, 3.0 Hz, 1H), 3.91 (dt, *J* = 3.1, 6.9 Hz, 1H), 3.96 (br dd, *J* = 1.0, 2.4 Hz, 1H), 4.91 (ddt, *J* = 1.2, 2.2, 10.1 Hz 1H), 4.98 (ddt, *J* = 1.5, 2.2, 17.1 Hz 1H), 5.81 (ddt, *J* = 6.8, 10.2, 17.1 Hz, 1H) ppm; **^{13}C NMR (100 MHz, $CDCl_3$):** δ 27.4 (t), 29.8 (t), 30.2 (t), 30.3 (t), 30.7 (t), 30.8 (t, 2C), 31.1 (t), 35.0 (t), 63.7 (t), 78.9 (d), 80.7 (d), 81.2 (d), 87.4 (d), 114.8 (t), 140.3 (d) ppm; **ESI-MS *m/z*:** 287.40 ($[M+H]^+$ 2%), 309.29 ($[M+Na]^+$, 100%), 325.37 ($[M+K]^+$, 2%), 301.21 (11%); **HRMS (MALDI-TOF) *m/z*:** calcd for ($[C_{16}H_{30}O_4Na]^+$) 309.2042, found 309.2011.

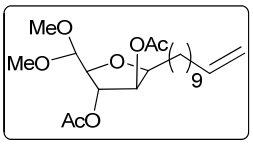
5-Deoxy-5-dimethylacetal-2,3-di-*O*-acetyl-1-α-D-arabinofuranosyl-undec-10-ene (13):



To an ice cooled solution of diol **12** (30 mg, 91 μmol) in pyridine (0.3 mL) acetic anhydride (0.2 mL), was added and the reaction mixture was stirred for 2 h. The contents were poured in water and extracted with ethyl acetate. Combined organic layer was washed with sat. $CuSO_4$ solution, water followed by brine. The organic layer was dried over Na_2SO_4, concentrated under reduced pressure and the crude was purified by column chromatography (30:70 EtOAc/Pet ether) to afford **13** (36 mg, 97%) as a yellowish gum. R_f = 0.3 (30:70 EtOAc/Pet ether). **[α]** $^{25}_{D}$ = +32.1 (*c* 1.3, $CHCl_3$). **IR ($CHCl_3$):** *v* 3019, 2929, 2856, 1743, 1371, 1216**,** 1048, 757**,** 668; **^{1}H NMR (400 MHz, $CDCl_3$):** δ 1.20–1.30 (br m, 12H), 1.34–1.37 (m, 2H), 1.55–1.64 (m, 2H), 1.99–2.05 (m, 2H), 2.06 (s, 6H), 3.42 (s, 6H), 3.99 (dt, *J* = 4.0, 6.0 Hz, 1H), 4.02 (dd, *J* = 4.0, 6.0 Hz, 1H), 4.42 (d, *J* = 6.1 Hz, 1H), 4.99 (dd, *J* = 3.0, 4.0 Hz, 1H), 4.90 (ddt, *J* = 1.2, 2.1, 10.2 Hz, 1H), 4.98

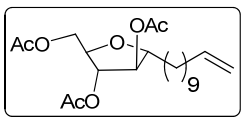
(br ddt, *J* = 1.7, 2.0, 17.2 Hz, 1H), 5.29 (dd, *J* = 2.8, 3.8 Hz, 1H), 5.79 (ddt, *J* = 6.7, 10.2, 17.1 Hz, 1H) ppm; **^{13}C NMR (100 MHz, $CDCl_3$):** δ 20.9 (q, 2C), 25.4 (t), 28.9 (t), 29.1 (t), 29.4 (t, 2C), 29.5 (t), 29.7 (t), 32.4 (t), 33.8 (t), 53.9 (q), 55.3 (q), 78.6 (d), 81.2 (d, 2C), 83.2 (d), 103.4 (d), 114.1 (t), 139.2 (d), 169.8 (s), 170.1 (s) ppm; **ESI-MS *m/z*:** calcd for $[(C_{22}H_{38}O_7K)^+]$ 437.52 found 437.38 ($[M+K]^+$, 100%).

5-Deoxy-5-dimethylacetal-2,3-di-*O*-acetyl-1-β-D-arabinofuranosyl-undec-10-ene (14):



Following the procedure for synthesis of **13**, the diol **4** (25 mg, 76 μmol) was converted to the corresponding diacetate (30 mg, 95%). R_f = 0.4 (30:70 EtOAc/Pet ether). $[\alpha]_D^{25}$ = +13.3 (*c* 2, $CHCl_3$); **IR ($CHCl_3$):** ν 3019, 2928, 2855, 1743, 1372, 1215**,** 1088, 1047, 755**,** 668; **^{1}H NMR (400 MHz, $CDCl_3$):** δ 1.20–1.30 (br m, 14H), 1.32–1.38 (m, 2H), 1.99–2.04 (m, 2H), 2.07 (s, 3H), 2.09 (s, 3H), 3.39 (s, 3H), 3.42 (s, 3H), 3.84 (dd, *J* = 3.7, 6.4 Hz 1H), 3.94 (br dt, *J* = 3.6, 6.0 Hz, 1H), 4.38 (d, *J* = 6.4 Hz 1H), 4.90 (ddt, *J* = 1.1, 2.0, 10.0 Hz, 1H), 4.96 (ddt, *J* = 1.5, 2.6, 17.1 Hz, 1H), 5.13 (br d, *J* = 3.5 Hz, 2H), 5.79 (ddt, *J* = 6.7, 10.2, 17.1 Hz, 1H) ppm; **^{13}C NMR (50 MHz, $CDCl_3$):** δ 20.7 (q), 20.9 (q), 25.9 (t), 28.3 (t), 28.9 (t), 29.1 (t), 29.39 (t), 29.4 (t, 2 C), 29.6 (t), 33.8 (t), 53.8 (d), 55.1 (d), 77.3 (d), 78.9 (d), 81.0 (d), 82.2 (d), 103.6 (d), 114.1 (t), 139.2 (d), 169.4 (s),169.6 (s) ppm; **ESI-MS *m/z*:** calcd for $[(C_{22}H_{38}O_7Na)^+]$ 437.52 found 437.32 ($[M+Na]^+$, 100%), 453.30 ($[M+K]^+$, 27.7%).

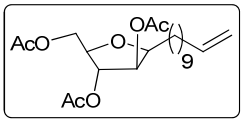
2,3,5-Triacetyl-1-α-D-arabinofuranosyl-undec-10-ene (15):



Following the procedure for synthesis of **13**, the triol **3** (35 mg, 122 μmol) was converted to the corresponding triacetate **15** (48 mg, 98%). R_f = 0.6 (20:80 EtOAc/Pet ether); $[\alpha]_D^{25}$ = +16.50 (*c* 0.761, $CHCl_3$). **^{1}H NMR (400 MHz, $CDCl_3$):** δ 1.26 (bs, 14H), 1.34–1.38 (m, 2H), 1.59–1.63 (m, 2H), 2.08 (s, 6H), 2.09 (s, 3H), 4.0 (ddd, *J* = 3.8, 7.0, 13.7 Hz 1H), 4.14 (ddd, *J* = 3.9, 5.0, 8.7 Hz 1H), 4.22 (dd, *J* = 6.0, 11.6 Hz 1H), 4.26 (dd, *J* = 5, 11.6 Hz 1H), 4.91

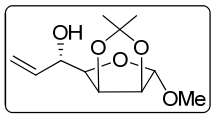
(ddt, *J* = 1.2, 2.4, 10.3 Hz 1H), 4.97 (ddt, *J* = 1.1, 2.1, 17.1 Hz 1H), 5.01 (d, 2.9 Hz, 1H), 5.06 (dd, *J* = 2.4, 3.7 Hz 1H), 5.80 (ddt, *J* = 6.7, 10.2, 17.1 Hz, 1H) ppm; **^{13}C NMR (100 MHz, $CDCl_3$):** δ 20.80 (q), 20.82 (q), 20.90 (q), 25.46 (t), 28.92 (t), 29.10 (t), 29.39 (t), 29.44 (t)**,** 29.46 (t, 2C), 32.43 (t), 33.78 (t), 63.46 (t), 78.92 (d), 80.21 (d), 80.95 (d), 83.15 (d), 114.10 (t), 139.21 (d),170.02 (s), 170.05 (s), 170.72 (s) ppm; **ESI-MS *m/z*:** Calcd for [$(C_{22}H_{36}O_7Na)^+$] 435.51 found 435.31 ([M+Na]$^+$,100%). **HRMS (MALDI-TOF) *m/z*:** Calcd for [$(C_{22}H_{36}O_7H)^+$] 413.2359 found 413.2712.

2,3,5-Tri-*O*-acetyl-1-β-D-arabinofuranosyl-undec-10-ene (16):



Following the procedure for synthesis of **13**, the triol **2** (42 mg, 146 µmol) was converted to the corresponding triacetate (58 mg, 97%). R_f = 0.7 (25:75 EtOAc/Pet ether); $[\alpha]_D^{25}$ = +6.4 (*c* 3.4, $CHCl_3$). **^{1}H NMR (400 MHz, $CDCl_3$):** δ 1.24 (bs, 14H), 1.48–1.63 (m, 2H), 1.95–2.04 (m, 2H), 2.06 (s, 6H), 2.09 (s, 3H), 3.91 (ddd, *J* = 3.5, 5.9, 7.1 Hz, 1H), 3.97 (ddd, *J* = 3.5, 4.7, 6.4 Hz, 1H), 4.12 (dd, *J* = 6.5, 11.5 Hz, 1H), 4.33 (dd, *J* = 4.7, 11.5 Hz, 1H), 4.89 (dd, *J* = 0.7, 3.7 Hz, 1H), 4.91 (dd, *J* = 0.9, 3.5 Hz, 1H), 4.95 (ddt, *J* = 1.7, 2.2, 17.2 Hz, 1H), 5.16 (dd, *J* = 0.9, 3.5 Hz, 1H), 5.77 (ddt, *J* = 6.8, 10.1, 17.2 Hz, 1H) ppm; **^{13}C NMR (100 MHz, $CDCl_3$):** δ 20.68 (q), 20.74 (q), 20.79 (q), 25.92 (t), 28.24 (t), 28.83 (t), 29.03 (t), 29.32 (t), 29.36 (t), 29.38 (t), 29.49 (t), 33.72 (t), 63.90 (t), 76.99 (d), 79.01 (d), 80.92 (d), 80.99 (d), 114.05 (t), 139.13 (d), 169.64 (s), 169.71 (s),170.71 (s) ppm; **ESI-MS *m/z*:** calcd for [$(C_{22}H_{36}O_7Na)^+$] 435.51 found 435.19 ([M+Na]$^+$, 100%), 451.15 ([M+K]$^+$, 3%). **HRMS (MALDI-TOF) *m/z*:** calcd for ([$C_{22}H_{36}O_7Na]^+$) 435.2359 found 435.2328.

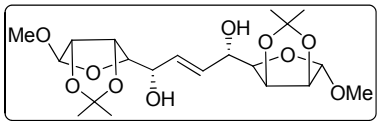
Methyl 6-deoxy-2,3-*O*-isopropylidene-α-L-*gulo*-hept-6-enofuranoside (19):



A solution of trimethyl sulphonium iodide (6.6 g, 32.4 mmol) in THF (35 mL) was cooled to –78 °C and treated with *n*-BuLi (17.3 ml, 27.7 mmol) and stirred for 20 min. To this, a solution of **10** (1 g, 4.6 mmol) in THF (15 mL) was added slowly and stirred at –78 °C for 1 h and at rt for 6 h. The reaction mixture was partitioned between water and EtOAc and the aqueous phase

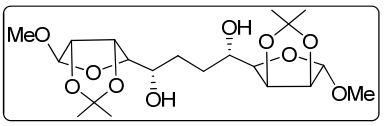
was extracted with EtOAc. The combined organic phase was dried (Na_2SO_4), filtered and concentrated under reduced pressure. The purification of crude product by silica gel column chromatography (1:4 EtOAc/Pet ether) gave **19** (883 mg, 83%) as low melting solid. R_f = 0.4 (3:7 EtOAc/Pet ether); $[\alpha]_D^{25}$ = +64.6 (*c* 1, $CHCl_3$). **^{1}H NMR (200 MHz, $CDCl_3$):** δ 1.28 (s, 3H), 1.46 (s, 3H), 2.80 (br s, 1H), 3.31 (s, 3H), 3.77 (dd, *J* = 3.5, 6.5 Hz, 1H), 4.52 (d, *J* = 5.7 Hz, 1H), 4.54 (d, *J* = 6.0 Hz, 1H), 4.68 (dd, *J* = 3.5, 6.0 Hz, 1H), 4.93 (s, 1H), 5.23 (br dt, *J* = 1.6, 10.6 Hz, 1H), 5.45 (br dt, *J* = 1.6, 17.3 Hz, 1H), 5.97 (ddd, *J* = 5.1, 10.6, 17.3 Hz, 1H) ppm; **^{13}C NMR (100 MHz, $CDCl_3$):** δ 24.5 (q), 25.9 (q), 54.6 (q), 70.9 (d), 80.6 (d), 82.2 (d), 85.3 (d), 106.9 (d), 112.7 (s), 116.5 (t), 135.9 (d) ppm; **ESI-MS *m/z*:** 253.01 (100%, $[M+Na]^+$); **HRMS (MALDI-TOF) *m/z*:** calcd for ($[C_{11}H_{18}O_5Na]^+$) 253.1052, found 253.1041.

Methyl 6,7-diedeoxy-2,3:10,11-di-*O*-isopropylidene-α-D-*glycero*-D-*xylo*-L-*gulo*-dodec-6*E*-eno-dialdo-(1,4:9,12)-bisfuranoside (20):



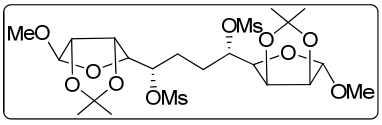
To a degassed solution of alcohol **19** (450 mg, 2 mmol) in anhydrous dichloromethane (8 mL) was added Grubbs` 2nd generation catalyst (49 mg, 30 μmol). The solution was refluxed for 16 h. The reaction mixture was concentrated and the crude mixture was purified by column chromatography (1:1 EtOAc/Pet ether) to afford **20** (405 mg, 96%) as colorless solid. R_f = 0.15 (1:1 EtOAc/Pet ether); mp 122–123 °C; $[\alpha]_D^{25}$ = +51.4 (*c* 0.4, $CHCl_3$). **^{1}H NMR (200 MHz, $CDCl_3$):** δ 1.25 (s, 6H), 1.43 (s, 6H), 2.75 (br s, 2H), 3.29 (s, 6H), 3.75 (dd, *J* = 3.5, 6.5 Hz, 2H), 4.52 (d, *J* = 5.8 Hz, 2H), 4.55 (dd, *J* = 3.0, 6.0 Hz, 2H), 4.65 (dd, *J* = 3.5, 6.0 Hz, 2H), 4.90 (s, 2H), 6.01 (dd, *J* = 1.0, 3.0 Hz, 2H); **^{13}C NMR (50 MHz, $CDCl_3$):** δ 24.6 (2C), 25.9 (2C), 54.6 (2C), 70.3 (2C), 79.8 (2C), 82.5 (2C), 85.2 (2C), 106.9 (2C), 112.5 (2C), 129.9 (2C) ppm; **ESI-MS *m/z*:** 455.15 (100%, $[M+Na]^+$); **HRMS (MALDI-TOF) *m/z*:** calcd for ($[C_{20}H_{32}O_{10}K]^+$) 471.1632, found 471.1602.

Methyl 6,7-diedeoxy-2,3:10,11-di-*O*-isopropylidene-α-D-*glycero*-D-*xylo*-L-*gulo*-dodecadialdo-(1,4:9,12)-bisfuranoside (22):



To a solution of olefin **20** (400 mg, 924 µmol) in methanol (10 ml) was added 10% Pd/C (20 mg) and the reaction mixture was stirred at 60 psi hydrogen pressure for 6 h. The reaction mixture was filtered over *celite* and the filtrate was concentrated under reduced pressure to gave **22** (389 mg, 97% yield) as colorless solid. R_f = 0.15 (1:1 EtOAc/Pet ether); mp 97–102 °C; $[\alpha]_D^{25}$ = +67.3 (*c* 4.8, $CHCl_3$). **^{1}H NMR (200 MHz, $CDCl_3$):** δ 1.24 (s, 6H), 1.41 (s, 6H), 1.72–1.82 (m, 4H), 3.28 (s, 6H), 3.78 (dd, *J* = 3.5, 5.8 Hz, 2H), 3.98–4.08 (m, 2H), 4.51 (d, *J* = 5.9 Hz, 2H), 4.68 (dd, *J* = 3.5, 5.9 Hz, 2H), 4.89 (s, 2H); **^{13}C NMR (50 MHz, $CDCl_3$):** δ 24.4 (2C), 25.8 (2C), 29.1 (2C), 54.5 (2C), 69.7 (2C), 80.2 (2C), 81.7 (2C), 85.2 (2C), 106.6 (2C), 112.5 (2C) ppm; **ESI-MS *m/z*:** 457.16 (100%, $[M+Na]^+$); **HRMS (MALDI-TOF) (*m/z*):** calcd for ($[C_{20}H_{34}O_{10}\ Na]^+$) 457.205, found 457.2033.

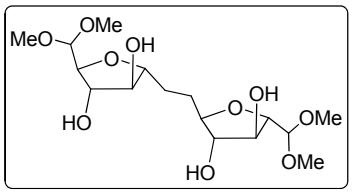
Methyl 5,8-di-*O*-methanesulfonyl-6,7-diedeoxy-2,3:10,11-di-*O*-isopropylidene-α-D-*glycero*-D-*xylo*-L-*gulo*-dodecadialdo-(1,4:9,12)-bisfuranoside (18):



At –30 °C, a solution of diol **22** (260 mg, 600 µmol) and Et_3N (250 µL, 1.8 mmol) in dichloromethane (7 mL) was treated with methanesulfonyl chloride (110 µL, 1.4 mmol). The reaction mixture was allowed to warm to rt during 1 h and then quenced by adding a few drops of water. The reaction mixture was partioned between ethyl aceate/water and the layers separated. The aq. layer was re-extracted with EtOAc and the combined organic layer was washed with brine, dried (Na_2SO_4) and concentrated. The resulting crude products was purified over colum chromatography (3:7 EtOAc/Pet ether) and gave **18** (307 mg, 87% yield) as colorless solid. R_f = 0.5 (1:1 EtOAc/Pet ether); mp 116 –117 °C; $[\alpha]_D^{25}$ = +31.8 (*c* 1.1, $CHCl_3$). **^{1}H NMR (200 MHz, $CDCl_3$):** δ 1.27 (s, 6H), 1.43 (s, 6H), 1.92–2.02 (m, 4H), 3.10 (s, 6H), 3.26 (s, 6H), 4.00 (dd, *J* = 3.4, 9.0 Hz, 2H), 4.54 (d, *J* = 5.8 Hz, 2H), 4.67 (d, *J* = 3.5, 5.8 Hz, 2H), 4.80–4.94 (m, 2H), 4.88 (s, 2H); **^{13}C NMR (50 MHz, $CDCl_3$):** δ 24.6 (2C), 26.0 (2C), 26.7 (2C), 38.5 (2C), 54.5

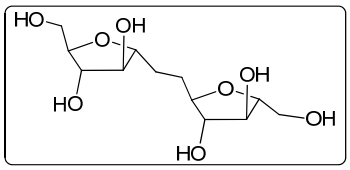
(2C), 79.2 (2C), 80.9 (2C), 82.5 (2C), 84.9 (2C), 107.1 (2C), 112.9 (2C) ppm; **ESI-MS *m/z*:** 613.14 (100%, $[M+Na]^+$); **HRMS (MALDI-TOF) *m/z*:** calcd for ($[C_{22}H_{38}O_{14}S_2Na]^+$) 613.1601, found 613.1597.

6,7-Diedeoxy-D-*glycero*-D-*lyxo*-D-*manno*-bis(1,12-dimethylacetal)-dodeca-2,5:8,11-dianhydroalditol (23):



To a solution of dimesylate **18** (280 mg, 474 µmol) in anhydrous methanol (10 mL) was added *p*-TSA (340 mg, 190 µmol). The solution was allowed to reflux at 80 °C for 72 h. After complete consumption of **18** as indicated by TLC, the reaction mixture was cooled and treated with solid $NaHCO_3$ and stirred for 1 h. The contents were filtered through *celite* and concentrated under reduced pressure. The crude product was purified by column chromatography (7:3 EtOAc/Pet ether) to procure **23** (150 mg 83%) as a colorless syrup. R_f = 0.3 (1:9 MeOH/DCM); $[\alpha]_D^{25}$ = +43.4 (*c* 2.4, MeOH**). ^{1}H NMR (400 MHz, MeOH-d4):** δ 1.65–1.80 (m, 4H), 3.43 (s, 6H), 3.44 (s, 6H), 3.71–3.78 m, 4H), 3.79 (dd, *J* = 4.8, 5.9 Hz, 2H), 4.08 (ddd, *J* = 4.2, 7.3, 9.4 Hz, 2H), 4.40 (d, *J* = 5.9 Hz, 2H); **^{13}C NMR (50 MHz, $CDCl_3$):** δ 30.3 (2C), 54.8 (2C), 55.9 (2C), 79.9 (2C), 82.6 (2C), 84.2 (2C), 84.5 (2C), 105.9 (2C) ppm; **ESI-MS *m/z*:** 405.09 (100%, $[M+Na]^+$); **HRMS (MALDI-TOF) *m/z*:** calcd for ($[C_{16}H_{30}O_{10}Na]^+$) 405.1737, found 405.1749.

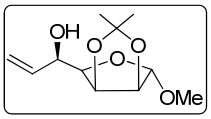
6,7-Diedeoxy-D-*glycero*-D-*lyxo*-D-*manno*-dodeca-2,5:8,11-dianhydroalditol (1):



The diacetal **23** (100 mg, 261 µmol) was dissolved in 4 mL ice cold 70% aq. trifluoroacetic acid (TFA) and stirred at rt until the TLC indicated the complete consumption of the acetal (6h) **23**. The reaction was concentrated under reduced pressure and the resulting crude product (68 mg, 234 µmol) was dissolved (isopropanol) and treated with a solution of $NaBH_4$ (35 mg, 937 µmol) in water (0.5 mL) and stirred at rt for 5 h. The reaction mixture was brought to acidic pH by adding 1N Hydrochloric acid and the solvent was then evaporated at reduced pressure. The crude product was purified by column chromatography (15:85 CH_3OH/CH_2Cl_2) to

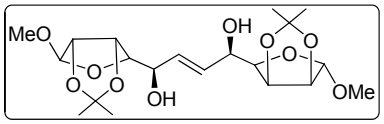
afford compound **1** (46 mg, 67% yield) as a solid (hygroscopic). R_f = 0.3 (2:8 CH_3OH/CH_2Cl_2); $[\alpha]_D^{25}$ = +62.8 (*c* 1.25, MeOH). **^{1}H NMR (400 MHz, MeOH-d4):** δ 1.75 (br m, 4H), 3.61 (ddd, *J* = 2.3, 5.6, 11.8 Hz, 2H), 3.69 (dt, *J* = 3.0, 11.8 Hz, 2H), 3.75–3.82 (m, 6H), 3.93 (ddd, *J* = 2.4, 5.6, 8.0 Hz, 2H); **^{13}C NMR (100 MHz, MeOH-d4):** δ 30.4 (2C), 63.3 (2C), 79.0 (2C), 82.5 (2C), 83.7 (2C), 84.5 (2C) ppm; **^{1}H NMR (400 MHz, D_2O):** δ 1.70–1.80 (m, 4H), 3.67 (dd, *J* = 5.9, 12.2 Hz, 2H), 3.74 (dd, *J* = 3.9, 12.2 Hz, 2H), 3.80–3.88 (m, 4H), 3.91 (t, *J* = 6.0 Hz, 2H), 4.0 (t, *J* = 6.0 Hz, 2H); **^{13}C NMR (100 MHz, D_2O):** δ 28.7 (2C), 61.7 (2C), 77.2 (2C), 80.7 (2C), 82.1 (2C), 82.6 (2C) ppm; **ESI-MS *m/z*:** 317.01 (100%, $[M+Na]^+$); **HRMS (MALDI-TOF) *m/z*:** calcd for ($[C_{12}H_{22}O_8Na]^+$) 317.1213, found 317.1205.

Methyl 6, 7-dideoxy-2, 3-*O*-isopropylidene-α-D-manno-hept-6-enfuranose (24):



Following the procedure used for the synthesis of **19**, the epoxide **S6.1** (4 g, 18.5 mmol) was converted to the corresponding allyl alcohol **24** (3.2 g, 76%). Colorless oil; R_f = 0.4 (3:7 EtOAc/Pet ether); $[\alpha]_D^{25}$ +8.4 (*c* 1, $CHCl_3$). **^{1}H NMR (200 MHz, $CDCl_3$):** δ 1.28 (s, 3H), 1.45 (s, 3H), 2.93 (br d, *J* = 5.94 Hz, 1H), 3.27 (s, 3H), 3.77 (dd, *J* = 3.6, 7.1 Hz, 1H), 4.41 (dd, *J* = 5.6, 10.9 Hz, 1H), 4.52 (d, *J* = 5.9 Hz, 1H), 4.78 (dd, *J* = 3.6, 5.9 Hz, 1H), 4.91 (s, 1H), 5.21 (dt, *J* = 1.5, 10.5 Hz, 1H), 5.39 (dt, *J* = 1.5, 17.3 Hz, 1H), 5.97 (ddd, *J* = 5.4, 10.5, 17.3 Hz, 1H) ppm; **^{13}C NMR (100 MHz, $CDCl_3$):** δ 24.5, 25.8, 54.5, 70.9, 80.0, 81.1, 84.7, 106.9, 112.6, 116.0, 137.6 ppm; **ESI-MS *m/z*:** 253.07 (100%, $[M+Na]^+$); **HRMS (MALDI-TOF) *m/z*:** calcd for ($[C_{11}H_{18}O_5Na]^+$) 253.1052, found 253.1028.

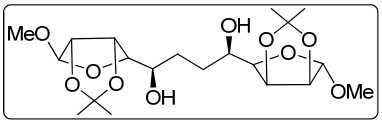
Methyl 6,7-dideoxy-2,3:10,11-di-*O*-isopropylidene-α-D-*glycero*-D-*lyxo*-D-*manno*-dodec-6*E*-eno-dialdo-(1,4:9,12)-bisfuranoside (25):



The diol **25** (276 mg, 98% yield) was prepared from the allyl alcohol **24** (300 mg, 1.3 mmol) following the procedure used for the synthesis of **20**. The diol **25** was found as a colorless solid; R_f = 0.15 (1:1 EtOAc/Pet ether); mp 119–120 °C; $[\alpha]_D^{25}$ = +62.3 (*c* 1.3, $CHCl_3$); **1H NMR (200 MHz, $CDCl_3$):** δ 1.28 (s, 6H), 1.46 (s, 6H), 2.99 (d,

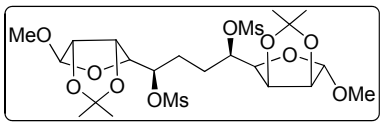
J = 6.7 Hz, 2H), 3.29 (s, 6H), 3.81 (dd, *J* = 3.6, 6.7 Hz, 2H), 4.49 (dd, *J* = 2.4, 6.6 Hz, 2H), 4.52 (d, *J* = 6.0 Hz, 2H), 4.80 (dd, *J* = 3.6, 5.9 Hz, 2H), 4.92 (s, 2H), 6.02 (dd, *J* = 1.0, 2.6 Hz, 2H) ppm; **^{13}C NMR (50 MHz, $CDCl_3$):** δ 24.5 (2C), 25.9 (2C), 54.6 (2C), 70.3 (2C), 80.2 (2C), 81.1 (2C), 84.8 (2C), 107.0 (2C), 112.7 (2C), 131.1 (2C) ppm; **ESI-MS *m/z*:** 455.13 (100% $[M+Na]^+$); **HRMS (MALDI-TOF) *m/z*:** calcd for ($[C_{20}H_{32}O_{10}K]^+$) 471.1632, found 471.1609.

Methyl 6,7-diedeoxy-2,3:10,11-di-*O*-isopropylidene-α-D-*glycero*-D-*lyxo*-D-*manno*-dodecadialdo-(1,4:9,12)-bisfuranoside (26):



The hydrogenation of the olefin **25** (200 mg, 462 μmol) according to the procedure used in the preparation of **22** gave diol **26** (188 mg, 94% yield) as a colorless solid; R_f = 0.15 (1:1 EtOAc/Pet ether); mp 92–96 °C; $[\alpha]_D^{25}$ = +27.9 (*c* 0.1, $CHCl_3$). **^{1}H NMR (200 MHz, $CDCl_3$):** δ 1.31 (s, 6H), 1.47 (s, 6H), 1.63–1.77 (m, 2H), 1.98–2.08 (m, 2H), 3.30 (s, 6H), 3.76 (dd, *J* = 3.6, 7.4 Hz, 2H), 3.93 (br t, *J* = 8.2 Hz, 2H), 4.55 (d, *J* = 5.8 Hz, 2H), 4.83 (dd, *J* = 3.7, 5.8 Hz, 2H), 4.91 (s, 2H); **^{13}C NMR (50 MHz, $CDCl_3$):** δ 24.6 (2C), 26.0 (2C), 31.5 (2C), 54.5 (2C), 70.7 (2C), 80.1 (2C), 81.9 (2C), 84.9 (2C), 107.0 (2C), 112.7 (2C) ppm; **ESI-MS *m/z*:** 457.15 (100%, $[M+Na]^+$); **HRMS (MALDI-TOF) *m/z*:** calcd for ($[C_{20}H_{34}O_{10}K^+$) 473.1789, found 473.176.

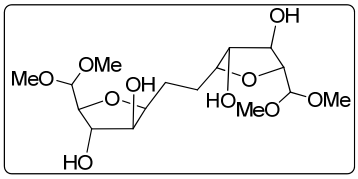
Methyl 5,8-methanesulfonyl-6,7-diedeoxy-2,3:10,11-di-*O*-isopropylidene-α-D-*glycero*-D-*lyxo*-D-*manno*-dodecadialdo-(1,4:9,12)-bisfuranoside (21):



The diol **21** (180 mg, 414 μmol) was mesylated according to the procedure used in the preparation of **18** to obtain dimesylate **21** (225 mg, 92%) as a colorless solid; R_f = 0.5 (1:1 EtOAc/Pet ether); mp 122–126 °C; $[\alpha]_D^{25}$ = +14.1 (*c* 1.0, $CHCl_3$). **^{1}H NMR (200 MHz, $CDCl_3$):** δ 1.28 (s, 6H), 1.45 (s, 6H), 1.98–2.08 (m, 2H), 2.19–2.28 (m, 2H), 3.07 (s, 6H), 3.31 (s, 6H), 4.00 (dd, *J* = 3.5, 8.5 Hz, 2H), 4.55 (d, *J* = 5.8 Hz, 2H), 4.70 (dd, *J* = 3.5, 5.8 Hz, 2H), 4.85 (s, 2H), 4.98 (dt, *J* = 4.0, 8.4 Hz, 2H); **^{13}C NMR (50 MHz, $CDCl_3$):** δ 24.9 (2C), 26.0 (2C), 26.5 (2C), 38.5 (2C), 54.8 (2C), 78.4 (2C), 78.9

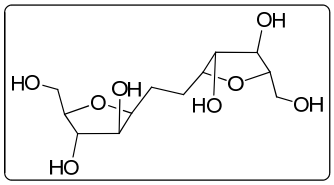
(2C), 79.0 (2C), 84.8 (2C), 107.0 (2C), 112.9 (2C) ppm; **ESI-MS *m/z*:** 613.16 (100%, [M+Na]+); **HRMS (MALDI-TOF) *m/z*:** calcd for ($[C_{22}H_{38}O_{14}S_2Na]^+$) 613.1601, found 613.1559.

6,7-Diedeoxy-D-*glycero*-D-*xylo*-L-*gulo*-bis(1,12-dimethyl acetal)-dodeca-2,5:8,11-dianhydroalditol (**27**)



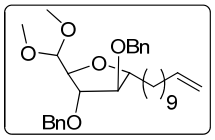
Following the procedure for synthesis of **23**, the dimesylate **21** (200 mg, 338 μmol) was converted to the corresponding tetrol **27** (114 mg 88%) as a colorless oil. R_f = 0.3 (1:9 MeOH/DCM); $[\alpha]_D^{25}$ = +25.5 (*c* 0.6, MeOH). **^{1}H NMR (400 MHz, MeOH-d4):** δ 1.65–1.73 (m, 2H), 1.75–1.83 (m, 2H), 3.43 (s, 6H), 3.44 (s, 6H), 3.72 (dd, *J* = 2.1, 6.6 Hz, 2H), 3.85 (dd, *J* = 0.8, 3.0 Hz, 2H), 3.98 (ddd, *J* = 3.0, 6.7, 9.6 Hz, 2H), 4.06 (d, *J* = 0.9, 2.1 Hz, 2H) 4.39 (d, *J* = 6.7 Hz, 2H); **^{13}C NMR (100 MHz, MeOH-d4):** δ 26.1 (2C), 54.9 (2C), 55.8 (2C), 78.6 (2C), 80.1 (2C), 82.9 (2C), 86.6 (2C), 106.0 (2C) ppm; **ESI-MS *m/z*:** 405.11 (100%, $[M+Na]^+$); **HRMS (MALDI-TOF) *m/z*:** calcd for ($[C_{16}H_{30}O_{10}K]^+$) 421.1476, found 421.1461.

6,7-Diedeoxy-D-*glycero*-D-*xylo*-L-*gulo*-dodec-2,5:8,11- dianhydroalditol (**17**)**:**



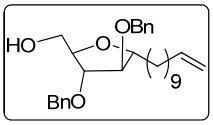
Following the procedure for synthesis of **17**, the diacetal **27** (40 mg, 104 μmol) was converted to the corresponding hexol **1** (22 mg, 73% yield) as a solid (hygroscopic); R_f = 0.2 (1:4 CH_3OH/CH_2Cl_2); $[\alpha]_D^{25}$ = +17.4 (*c* 0.5, MeOH); **^{1}H NMR (400 MHz, MeOH-d4):** δ 1.67–1.73 (m, 2H), 1.77–1.84 (m, 2H), 3.64 (dd, *J* = 5.0, 11.5 Hz, 2H), 3.69 (dd, *J* = 3.8, 11.5 Hz, 2H), 3.75 (ddd, *J* = 3.0, 5.0, 6.7 Hz, 2H), 3.85 (dd, *J* = 1.0, 3.0 Hz, 2H), 3.96 (dd, *J* = 1.0, 3.0 Hz, 2H), 3. 97–4. 00 (m, 2H); **^{13}C NMR (100 MHz, MeOH-d4):** δ 26.2 (2C), 63.6 (2C), 78.9 (2C), 80.5 (2C), 82.9 (2C), 87.3 (2C) ppm; **ESI-MS *m/z*:** 317.03 (100%, $[M+Na]^+$); **HRMS (MALDI-TOF) *m/z*:** calcd for ($[C_{12}H_{22}O_8K]^+$) 333.0952, found 333.0938.

2,3-di-*O*-benzyl-1-α-D-arabinofuranosylundec-ene (31):



To a solution of alcohol **12** (900 mg, 2.7 mmol) in dry DMF (7 mL), NaH (60% disperse 326 mg, 8.7 mmol) was added portion wise at 0 °C and stirred for 20 min, followed by drop wise addition of benzyl bromide (0.7 mL, 6.0 mmol). After stirring for additional 6 h at room temperature the reaction mixture was quenched by adding small pieces of ice and poured into water and extracted with ethyl acetate. The combined organic phases were washed with water, brine, dried (Na_2SO_4) and concentrated. Purification of the crude by column chromatography gave the dibenzyl derivative **31** (1.4 g, 96%) as colorless oil, R_f = 0.4 (Pet ether/EtOAc 7:3). **[α]$_D^{25}$:** +20.0 (*c* 1, $CHCl_3$). **^{1}H NMR (400 MHz, $CDCl_3$):** δ 1.19–1.45 (br m, 14H), 1.50–1.70 (m, 2H), 1.96–2.11 (m, 2H), 3.41 (s, 3H), 3.44 (s, 3H), 3.77 (dd, *J* = 2.3, 4.4 Hz, 1H), 3.99 (ddd, *J* = 4.7, 6.5, 13.0 Hz, 1H), 4.07 (dd, *J* = 3.0, 8.0 Hz, 1H), 4.10 (dd, *J* = 4.0, 7.2 Hz, 1H), 4.38 (d, *J* = 6.0 Hz, 1H), 4.48 (d, *J* = 12.0 Hz, 2H), 4.53 (d, *J* = 12.0 Hz, 1H), 4.62 (d, *J* = 12.0 Hz, 1H), 4.92 (ddt, *J* = 1.5, 2.6, 10.0 Hz, 1H), 4.99 (ddt, *J* = 1.6, 2.1, 17.0 Hz, 1H), 5.81 (ddt, *J* = 6.7, 10.1, 17.0 Hz, 1H), 7.26–7.40 (br m, 10H) ppm; **^{13}C NMR (100 MHz, $CDCl_3$):** δ 25.7 (t), 28.9 (t), 29.1 (t), 29.4 (t), 29.5 (t, 2C), 29.5 (t), 33.0 (t), 33.8 (t), 53.7 (q), 55.5 (q), 71.6 (t, 2C), 82.4 (d), 82.7 (d), 85.0 (d), 87.5 (d), 103.6 (d), 114.1 (t), 127.6 (d), 127.6 (d), 127.7 (d, 2C), 127.7 (d), 127.9 (d), 128.3 (d, 2C), 128.3 (d, 2C), 137.8 (s), 138.0 (s), 139.2 (d) ppm; **ESI-MS *m/z*:** calcd [$(C_{32}H_{46}O_5Na)^+$] 533.69 found 533.44 ([M+Na]$^+$, 100%).

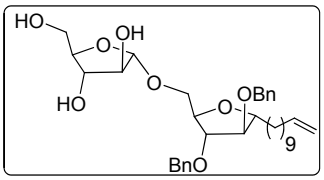
2,3-Di-*O*-benzyl-1-α-D-arabinofuranosylundec-10-ene (30):



Colourless liquid, yield 63%, 2 steps, **[α]$_D^{25}$:** + 24.7 (*c* 3.6, $CHCl_3$). **^{1}H NMR (400 MHz, $CDCl_3$):** δ 1.20–1.40 (m, 14H), 1.56–1.64 (m, 2H), 1.99–2.08 (m, 2H), 2.16 (br s, 1H, -OH), 3.68–3.70 (m, 2H), 3.82 (dd, *J* = 0.7, 2.6 Hz, 1H), 3.96–4.04 (br m, 2H), 4.09 (dd, *J* = 4.3, 9.2 Hz, 1H), 4.53 (s, 2H), 4.55 (s, 2H), 4.88–5.06 (br m, 2H), 5.85 (ddt, *J* = 6.6, 10.3, 17.0 Hz, 1H), 7.26–7.40 (br m, 10H) ppm; **^{13}C NMR (100 MHz, $CDCl_3$):** δ 25.6 (t), 28.8 (t), 29.0 (t), 29.4 (t, 3C), 32.9 (t), 33.7 (t, 2C), 62.6 (t), 71.5 (t), 71.9 (t), 82.6 (d), 82.7 (d), 84.4 (d), 87.2 (d), 114.0 (t), 127.6 (d), 127.6 (d, 2C), 127.7 (d), 128.3 (t, 2C), 128.3 (t, 2C), 137.5

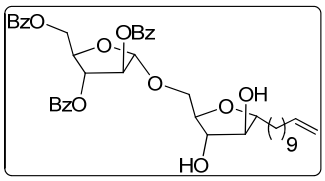
(s), 137.6 (s), 139.0 (s) ppm; **ESI-MS *m/z*:** calcd [$(C_{30}H_{42}O_4Na)^+$] 489.64 found 489.68 ([M+Na]$^+$, 100%), 505.65 ([M+K]$^+$, 30%).

α-D-Arabinofuranosyl-(1→5)-2,3-di-*O*-benzyl-1-α-D-arabinofuranosylundec-ene (32):



To a solution of crude tribenzoate **S18.1** (210 mg, 230 μmol) in methanol (5 mL) catalytic amount of Na was added and stirred for 2 h. The reaction mixture was concentrated and purified by column chromatography (10:90 CH_2Cl_2/CH_3OH) to obtain **32** (98 mg, 76% yield). Colourless gum, 76% yield. **[α]** $^{25}_{D}$ **:** +34.1 (*c* 0.8, $CHCl_3$). **^{1}H NMR (400 MHz, $CDCl_3$):** δ 1.20–1.40 (br m, 14H), 1.55–1.64 (m, 2H), 2.00–2.05 (m, 2H), 2.87 (s, 1H), 2.95 (s, 1H), 3.56 (dd, *J* = 3.8, 10.3 Hz, 1H), 3.70–3.80 (m, 2H), 3.83 (dd, *J* = 6.2, 10 Hz, 1H), 3.86 (dd, *J* = 1.8, 3.6 Hz, 1H), 3.95 (s, 1H), 3.97 (m, 1H), 3.99 (s, 1H), 4.02 (s, 1H), 4.12 (ddd, *J* = 3.8, 5.9, 9.4 Hz, 1H), 4.40–4.57 (m, 4H), 5.0 (s, 1H), 4.89–5.02 (br m, 2H), 5.80 (ddt, *J* = 6.6, 10.3, 16.9 Hz, 1H), 7.26–7.38 (br m, 10H) ppm; **^{13}C NMR (100 MHz, $CDCl_3$):** δ 28.9 (t), 29.1 (t), 29.3 (t), 29.5 (t), 29.7 (t, 3C), 31.9 (t), 33.8 (t), 62.0 (t), 66.6 (t), 71.7 (t), 71.8 (t), 78.0 (d), 78.9 (d), 81.1 (d), 83.0 (d), 85.4 (d), 87.1 (d), 87.3 (d), 107.6 (d), 114.1 (t), 127.7 (d), 128.0 (d, 4C), 128.5 (d, 4C), 129.7 (d), 137.5 (s, 2C), 139.2 (s) ppm; **ESI-MS *m/z* :** calcd [$(C_{35}H_{50}O_8Na)^+$] 621.76 found 621.78 ([M+Na]$^+$, 100%).

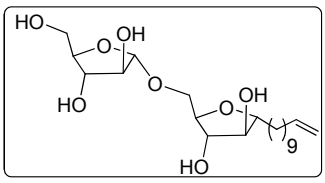
2,3,5-Tri-*O*-benzoyl-α-D-arabinofuranosyl-(1→5)-1-α-D-arabinofuranosyl-undec-10-ene (33):



At 0 °C, to a solution of orthoester (393 mg, 824 μmol) **S17.4** in anhydrous dichloromethane (6 mL) was added dibutyl phosphate (654 μl, 3.3 mmol) and stirred for 2 h at room temperature. The reaction mixture was treated with triethyl amine (3 mL) and concentrated under reduced pressure. The resulting crude product was purified on flash silica gel to get the phosphate **S17.5** (394 mg, 73%yield) which was immediately subjected to next reaction.

At –40 °C, in a solution of triol **3** (115 mg, 401 μmol) and phosphate **S17.5** (394 mg, 602 μmol) in anhydrous dichloromethane was added TMSOTf (0.2 mL, 1.05 mmol) and stirred for 1 h at same temperature, to this triethylamine (3 mL) was added allowed to come at room temperature. The reaction mixture was concentrated under reduced pressure and purified by column chromatography (50:50 EtOAc/Pet ether) to procure the disaccharide **33** (161 mg, 55% yield) as a colourless gum; R_f = 0.2 (50:50 EtOAc/Pet ether); **[α]** $^{25}_{D}$**:** +7.6 (*c* 0.5**,** $CHCl_3$). **^{1}H NMR (400 MHz, $CDCl_3$):** *δ* 1.22–1.38 (br m, 14H), 1.58–1.61 (m, 2H), 2.0–2.04 (m, 2H,), 3.2 (br s, 2H –OH), 3.77 (dd, *J* = 4.0, 10.8 Hz, 1H), 3.84 (dd, *J* = 6.3, 12.5 Hz, 1H), 3.86 (t, *J* = 5.2 Hz, 1H), 3.95 (dd, *J* = 3.8, 10.9 Hz, 1H), 3.98 (dt, *J* = 4.0, 5.7 Hz, 1H), 4.24 (t, *J* = 5.2 Hz, 1H), 4.61 (dt, *J* = 3.5, 4.8 Hz, 1H), 4.65 (dd, *J* = 4.8, 11.8 Hz, 1H), 4.81 (dd, *J* = 3.3, 11.8 Hz, 1H), 4.92 (ddt, *J* = 1.2, 2.0, 10.2 Hz, 1H), 4.98 (ddt, *J* = 1.7, 2.0, 17.1 Hz, 1H), 5.38 (s, 1H), 5.53 (d, *J* = 1.4, 1H), 5.59 (dd, *J* = 1.4, 5.1 Hz, 1H), 5.80 (ddt, *J* = 6.7, 10.2, 17.1 Hz, 1H), 7.28 (t, *J* = 7.8 Hz, 2H), 7.37 (t, *J* = 7.8 Hz, 2H), 7.43 (t, *J* = 7.8 Hz, 2H), 7.49 (t, *J* = 1.2, 7.2 Hz, 1H), 7.54–7.58 (m, 2H), 7.97 (dd, *J* = 1.2, 8.1 Hz, 2H), 8.02 (dd, *J* = 1.2, 8.1 Hz, 2H), 8.13 (dd, *J* = 1.2, 8.2 Hz, 2H) ppm; **^{13}C NMR (100 MHz, $CDCl_3$):** *δ* 25.6 (t), 28.9 (t), 29.1 (t), 29.4 (t), 29.5 (t, 2C), 29.6 (t), 33.3 (t), 33.8 (t), 63.6 (t), 67.6 (t), 77.6 (d), 79.5 (d), 80.9 (d), 81.0 (d), 82.0 (d), 82.3 (d), 83.5 (d), 106.2 (d), 114.1 (t), 128.3 (d, 2C), 128.5 (d, 4C), 128.7 (s), 128.8 (s),129.5 (s), 129.7 (d, 2C), 129.9 (d, 2C), 130.0 (d, 2C), 133.1 (d, 2C), 133.5 (d), 133.6 (d), 139.2 (d), 165.7 (s), 165.8 (s), 166.3 (s) ppm; **MALDI-TOF *m/z*:** calcd [($C_{42}H_{50}O_{11}Na)^+$] 753.83 found 753.11 ([M+Na]$^+$, 47%), 769.03 ([M+K]$^+$, 18%).

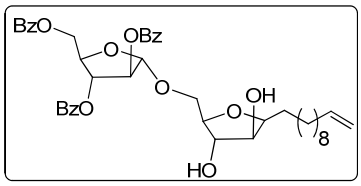
α-D-arabinofuranosyl-(1→5)-1-α-D-arabinofuranosyl-undec-10-ene (28):



To a solution of tribenzoate **33** (40 mg, 54 μmol) in methanol (5 mL) catalytic amount of Na was added and stirred for 2 h. The reaction mixture was concentrated and purified by column chromatography (10:90 CH_2Cl_2/CH_3OH) to obtain **28** (22 mg, 96% yield). R_f = 0.2 (10:90 CH_2Cl_2/CH_3OH); **[α]** $^{25}_{D}$**:** +31.1 (*c* 0.4, CH_3OH). **^{1}H NMR (400 MHz, $CDCl_3$):** *δ* 1.29–137 (br m, 14H), 1.56–1.63 (m, 2H), 2.02–2.07 (m, 2H), 3.59 (dd, *J* = 3.6, 10.7 Hz, 1H), 3.62 (d, *J* = 5.2 Hz, 1H), 3.65 (d, *J* =

5.4 Hz, 1H), 3.71–3.74 (m, 2H), 3.75 (t, *J* = 3.3 Hz 1H), 3.82 (dd, *J* = 5.3, 11 Hz, 1H), 3.83 (dd, *J* = 3.0, 6.0 Hz, 1H), 3.87 (dt, *J* = 3.8, 5.3 Hz, 1H), 3.97 (dd, *J* = 3.3, 5.7 Hz, 1H), 3.98–4.02 (br m, 2H), 4.92 (ddt, *J* = 1.1, 2.0, 10.1 Hz, 1H), 4.93 (d, *J* = 1.3 Hz, 1H), 4.97 (ddt, *J* = 1.6, 2.0, 17.2 Hz, 1H), 5.80 (ddt, *J* = 6.7, 10.2, 17.0 Hz, 1H) ppm; **^{13}C NMR (100 MHz, $CDCl_3$):** δ 26.7 (t), 30.1 (t), 30.2 (t), 30.6 (t), 30.7 (t, 2C), 30.8 (t), 34.6 (t), 34.9 (t), 63.1 (t), 68.7 (t), 78.9 (d), 79.6 (d), 82.8 (d), 82.9 (d), 83.2 (d), 84.3 (d), 85.9 (d), 109.6 (d), 114.7 (t), 140.2 (d) ppm; **MALDI-TOF *m/z*:** calcd $[(C_{21}H_{38}O_8Na)^+]$ 441.51 found 441.10 ($[M+Na]^+$, 100%).

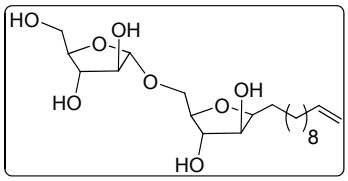
2,3,5-Tri-*O*-benzoyl-α-D-arabinofuranosyl-(1→5)-1-β-D-arabinofuranosyl-undec-10-ene (34):



The glycosylation of the compound **2** (100 mg, 350 μmol) was carried out as outlined in the preparation of **33** employing freshly prepared phosphonate (172mg, 260 μmol), the crude was purified by column chromatography (50:50 EtOAc/Pet ether) to get the tribenzoyl disaccharide **34** (150 mg, 59% yield) as a colourless gum; R_f = 0.3 (50:50 EtOAc/Pet ether). **$[\alpha]_D^{25}$:** +1.7 (*c* 1, $CHCl_3$). **^{1}H NMR (400 MHz, $CDCl_3$):** δ 1.24–1.31 (br s, 14H), 1.65–1.70 (m, 2H), 1.99–2.07 (m, 2H), 3.82 (br t, *J* = 2.5 Hz, 1H), 3.87 (dd, *J* = 2.9, 11.0 Hz, 1H), 3.88–3.89 (br m, 1H), 3.90 (dt, *J* = 2.7, 6.8 Hz, 1H), 3.97 (dd, *J* = 2.1, 11.0 Hz, 1H), 4.26 (d, *J* = 2.2 Hz, 1H), 4.59 (ddd, *J* = 3.3, 4.8, 5.3 Hz, 1H), 4.67 (dd, *J* = 4.8, 11.9 Hz, 1H), 4.84 (dd, *J* = 3.2, 11.9 Hz, 1H), 4.91 (br ddt, *J* = 1.2, 2.0, 10.1 Hz, 1H), 4.98 (br ddt, *J* = 1.7, 2.2, 17.0 Hz, 1H), 5.38 (s, 1H), 5.50 (d, *J* = 1.2 Hz, 1H), 5.60 (dd, *J* = 1.0, 5.2 Hz, 1H), 5.80 (ddt, *J* = 6.7, 10.2, 17.0 Hz, 1H), 7.28 (t, *J* = 7.9 Hz 2H), 7.38 (t, *J* = 7.9 Hz, 2H), 7.44 (t, *J* = 7.9 Hz, 2H), 7.49 (t, *J* = 1.3, 7.5 Hz, 1H), 7.56–7.59 (m, 2H), 7.98 (dd, *J* = 1.3, 7.9 Hz, 2H), 8.02 (dd, *J* = 1.3, 7.9 Hz, 2H), 8.13 (dd, *J* = 1.3, 7.9 Hz, 2H) ppm; **^{13}C NMR (100 MHz, $CDCl_3$):** δ 26.2 (t), 28.1 (t), 28.9 (t), 29.4 (t), 29.5 (t), 29.8 (t), 29.7 (t), 29.8 (t), 33.8 (t), 63.6 (t), 67.4 (t), 77.6 (d), 78.5 (d), 79.7 (d), 81.4 (d), 82.0 (d), 82.2 (d), 84.3 (d), 106.4 (d), 114.1 (t), 128.3 (d, 2C), 128.4 (d, 2C), 128.5 (d, 2C), 128.7 (s), 128.8 (s), 129.6 (s), 129.7 (d, 2C), 129.9 (d,2C), 130.1 (d, 2C), 133.1 (d), 133.6 (d), 133.6 (d), 139.2 (d), 165.5 (s), 165.9 (s),

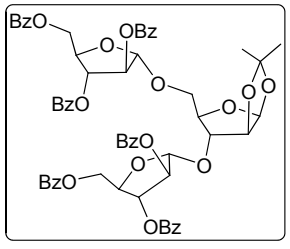
166.2 (s) ppm; **MALDI-TOF *m/z*:** calcd [$(C_{42}H_{50}O_{11}Na)^+$] 753.83 found 753.25 ([M+Na]$^+$, 38%), 769.20 ([M+K]$^+$, 10%).

α-D-Arabinofuranosyl-(1→5)-1-β-D-arabinofuranosyl-undec-10-ene (29):



The tribenzoate **34** (50 mg, 68 μmol) was taken in methanol (5 mL) and a catalytic Na was added. After 2 h stirring at room temperature, the reaction mixture was concentrated and purified by column chromatography (10:90 CH_2Cl_2/CH_3OH) to procure the free disaccharide **29** (27 mg, 95% yield). R_f = 0.2 (10:90 CH_2Cl_2/CH_3OH); **[α]$_D^{25}$:** + 61.7 (*c* 1, CH_3OH). **^{1}H NMR (400 MHz, $CDCl_3$):** δ 1.29–136 (br m, 14H), 1.61–1.66 (m, 2H), 2.02–2.07 (m, 2H), 3.59 (dd, *J* = 4, 9.7 Hz, 1H), 3.63 (dd, *J* = 5.4, 11.9 Hz, 1H), 3.73 (dd, *J* = 3.4, 11.9 Hz, 1H), 3.79–3.85 (m, 5H), 3.89 (dt, *J* = 3.4, 7.0 Hz, 1H), 3.96–3.97 (br m, 2H) 3.98 (d, *J* = 1.1 Hz, 1H), 4.90 (ddt, *J* = 1.2, 2.1, 10.1 Hz, 1H), 4.93 (d, *J* = 1.2 Hz, 1H), 4.97 (ddt, *J* = 1.7, 2.1, 17.0 Hz, 1H) 5.81 (ddt, *J* = 6.7, 10.2, 17.1 Hz, 1H) ppm; **^{13}C NMR (100 MHz, $CDCl_3$):** δ 27.3 (t), 29.7 (t), 30.2 (t), 30.3 (t), 30.7 (t), 30.8 (t), 30.9 (t), 31.0 (t), 35.0 (t), 63.2 (t), 69.1 (t), 78.8 (d), 79.2 (d), 80.9 (d), 83.2 (d), 83.3 (d), 85.6 (d), 86.1 (d), 109.7 (d), 114.8 (t), 140.3 (d) ppm; **MALDI-TOF *m/z*:** calcd [$(C_{21}H_{38}O_8Na)^+$] 441.51 found 441.21 ([M+Na]$^+$, 100%), 457.21 ([M+K]$^+$, 39%).

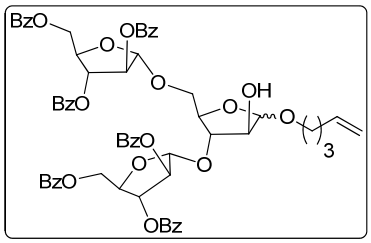
2,3,5-tri-*O*-benzoyl-α-D-arabinofuranosyl-(1→3)-[2,3,5-tri-*O*-benzoyl-α-D-arabinofuranosyl-(1→5)]1,2-isopropylidene-β-D-arabinofuranose (36):



At –40 °C, to a vigorously stirring suspension of diol **S22.3** (250mg, 1.32 mmol), thioglycoside **S21.2** (1.9 g, 3.42 mmol) and powdered molecular sieves (250mg) in dry CH_2Cl_2 (10 mL) were added N-iodosuccinimide (805 mg, 3.6 mmol) and TMSOTf (0.14 mL, 0.8 mmol). After stirring for 30 min at –40 °C, Et_3N (1.0 mL) was introduced and the reaction mixture was diluted with CH_2Cl_2 (15 mL) and filtered through Celite. The combined filtrate was washed successively with a saturated aqueous solution of $Na_2S_2O_3$, water, and brine. After drying (Na_2SO_4), the

organic phase was filtered and concentrated and the residue was purified by chromatography (50:50 EtOAc/Pet ether) to give **36** (155 mg, 59%) as a syrup; R_f = 0.5 (50:50 EtOAc/Pet ether); **[α]$_D^{25}$:** +1.7 (*c* 1, $CHCl_3$). **^{1}H NMR (400 MHz, $CDCl_3$):** δ 1.34 (s, 3H), 1.58 (s, 3H), 3.78 (dd, *J* = 4.7, 10.4 Hz, 1H), 4.09 (ddd, *J* = 6.0, 10.4, 16.6 Hz, 1H), 4.32 (ddd, *J* = 4.2, 5.9, 9.5 Hz, 1H), 4.47 (d, *J* = 3.5 Hz, 1H), 4.56–4.90 (m, 7H), 5.32 (s, 1H), 5.34 (s, 1H), 5.46 (d, *J* = 1.2 Hz, 1H), 5.55 (d, *J* = 1.0 Hz, 1H), 5.60 (dd, *J* = 1.0, 4.7 Hz, 1H), 5.57 (dd, *J* = 1.2, 4.7 Hz, 1H), 5.95 (d, *J* = 4.0 Hz, 1H), 7.20–7.65 (m, 18H), 7.95–8.13 (m, 12H) ppm; **^{13}C NMR (100 MHz, $CDCl_3$):** δ 26.5 (q), 27.2 (q), 63.4 (t), 63.7 (t), 66.4 (t), 77.2 (d), 77.5 (d), 77.7 (d), 80.3 (d), 81.3 (d), 81.5 (d), 81.9 (d), 82.1 (d), 83.3 (d), 105.1 (d), 105.5 (d), 105.6 (d), 113.4 (t), 128.3 (d, 2C), 128.3 (d, 2C), 128.4 (d, 2C), 128.5 (d, 2C), 128.6 (d, 4C), 129.7 (d, 4C), 129.8 (d, 4C), 129.9 (d, 4C), 129.9 (d, 4C), 130.0 (d, 2C), 133.0 (s), 133.1 (s), 133.2 (s), 133.4 (s), 133.5 (s), 133.3 (s), 165.3 (s), 165.5 (s), 165.6 (s), 165.8 (s), 166.0 (s), 166.2 (s) ppm; **ESI-MS *m/z*:** calcd $[(C_{60}H_{54}O_{19}Na)^+]$ 1102.05 found 1101.51 ($[M+Na]^+$, 100%).

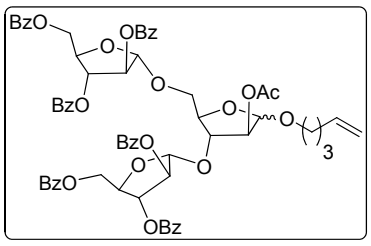
Pent-3-enyl-2,3,5-tri-*O*-benzoyl-α-D-arabinofuranosyl-(1→3)-[2,3,5-tri-*O*-benzoyl-α-D-arabinofuranosyl-(1→5)]-α/β-D-arabinofuranoside (37):



At 0 °C, to a solution of trisaccharide (200 mg, 185 μmol) **36** in anhydrous dichloromethane (6 mL) was added 4-penten-1-ol (1.2 mL, 11 mmol), *p*-TSA (47 mg, 278 μmol) and stirred for 6 h at room temperature. The reaction mixture was treated with triethyl amine (4 mL) and concentrated under reduced pressure. The resulting crude product was purified on flash silica gel (60:40 EtOAc/Pet ether) to get **37** (160 mg, 78% yield) as a syrup; R_f = 0.4 (50:50 EtOAc/Pet ether). **^{1}H NMR (400 MHz, $CDCl_3$):** δ 1.60–1.70 (m, 2H), 2.02–2.14 (m, 2H), 3.37–3.47 (m, 1H), 3.37–3.47 (m, 1H), 3.68 (dt, *J* = 6.7, 9.7 Hz, 0.3H, minor), 3.75 (dd, *J* = 3.3, 10.5 Hz, 0.7H, major), 3.84 (dt, *J* = 6.5, 9.6 Hz, 0.7H, major), 3.90 (dd, *J* = 2.0, 11.8 Hz, 0.3H, minor), 3.95 (dd, *J* = 6.2, 10.5 Hz, 0.7H, major), 4.05 (dd, *J* = 2.7, 11.8 Hz, 0.3H, minor), 4.17–4.23 (m, 0.7H), 4.25–4.29 (m, 0.3H), 4.30–4.42 (m, 2H), 4.57 (dd, *J* = 4.7, 8.9 Hz, 0.3H, minor), 4.61–4.64 (m, 0.7H), 4.65–4.77 (m, 3H), 4.80 (dd, *J* = 8.4, 10.7 Hz, 0.3H, minor), 4.84 (dd, *J* = 3.1, 11.7 Hz, 0.7H, major), 4.90–5.04

(m, 3H), 5.32 (s, 0.7H, major), 5.36 (s, 0.3H, minor), 5.44 (s, 0.3H, minor), 5.52–5.58 (m, 2H), 5.59–5.63 (m, 1.4 H, major), 5.64 (s, 0.7H, major), 5.66–5.18 (m, 1H), 7.10–7.60 (m, 19H), 7.95–8.10 (m, 11H) ppm; **^{13}C NMR (100 MHz, $CDCl_3$):** δ 28.5 (t, 2C, major), 28.6 (t, minor), 30.1 (t, minor), 30.1 (t, 2C), 63.5 (t, major), 63.7 (t, minor), 65.2 (t, minor), 66.8 (t, minor), 67.6 (t, major), 68.1 (t, major), 77.5 (d, major), 77.5 (d, minor), 77.6 (d, minor), 77.7 (d, major), 79.5 (d, 2C, major), 80.6 (d, minor), 81.1 (d, minor), 81.2 (d, minor), 81.3 (d, 2C, major), 81.4 (d, major), 81.6 (d, minor), 81.7 (d, major), 81.9 (d, major), 82.1 (d, minor), 82.4 (d, minor), 83.2 (d, minor), 100.9 (d, 2C,), 105.2 (d, major), 105.4 (d, major), 105.9 (d, minor), 107.9 (d, minor), 114.8 (t, minor), 114.9 (t, major), 125.2 (d, minor), 128.1 (d, 2C, major), 128.2 (d, 2C, major), 128.2 (d, major), 128.2 (d, minor), 128.3 (d, minor), 128.3 (d, minor), 128.4 (d, minor), 128.4 (d, 2C, major), 128.5 (d, minor), 128.7 (s, minor), 128.8 (s, minor), 128.8 (s, minor), 128.8 (s, minor), 128.93 (d, minor), 129.0 (s, minor), 129.0 (s, minor), 129.5 (s, 2C, major), 129.6 (d, major), 129.6 (s, 2C, major), 129.7 (d, major), 129.8 (d, major), 129.9 (d, major), 129.9 (d, minor), 132.9 (d, major), 133.0 (d, major), 133.0 (d, 2C, minor), 133.4 (s, major),133.5 (d, major), 133.5 (d, minor), 133.6 (s, major), 137.7 (d, major), 138.0 (d, minor), 165.2 (s, major), 165.3 (s, major), 165.4 (s, minor), 165.6 (s, major), 165.6 (s, minor), 165.6 (s, minor), 165.7 (s, 2C, minor), 165.7 (s, minor), 166.0 (s, 2C, major), 166.1 (s, major) ppm; **ESI-MS *m/z*:** calcd $[(C_{62}H_{58}O_{19}K)^+]$ 1145.32 found 1145.54 ($[M+K]^+$, 20%).

Pent-3-enyl-2,3,5-tri-*O*-benzoyl-α-D-arabinofuranosyl-(1→3)-[2,3,5-tri-*O*-benzoyl-α-D-arabinofuranosyl-(1→5)]-2-*O*-acetyl-α/β-D-arabinofuranoside (35):



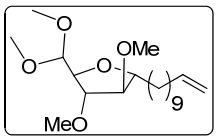
Following the procedure used in synthesis of **13**, the alcohol **37** (110 mg, 99 μmol) was converted to the corresponding acetate **35** (107 mg, 94%); R_f = 0.4 (30:70 EtOAc/Pet ether); R_f = 0.5 (50:50 EtOAc/Pet ether); **^{1}H NMR (400 MHz, $CDCl_3$):** δ 1.55–1.72 (m, 2H), 2.02 (s, 1.5H, major), 2.08 (s, 1.5H, minor), 1.18–2.17 (m, 4H), 3.28 (dt, *J* = 6.9, 9.7 Hz, 0.7H, major), 3.43 (dt, *J* = 6.9, 9.7 Hz, 0.3H, minor), 3.45 (dd, *J* = 2.0, 7.0 Hz, 0.7H, major), 3.71 (dd, *J* = 6.8, 9.7 Hz, 0.3H, minor), 3.17–4.01 (m, 2H), 4.04 (d5, *J* = 4.7, 9.6 Hz,

0.5H, minor), 4.22 (dt, J = 4.1, 6.3 Hz, 0.5H, major), 4.27–4.34 (m, 0.5H), 4.30 (br d, J = 6.0 Hz, 0.5H, minor), 4.55–4.72 (m, 4H), 4.74–4.86 (m, 2H), 4.86–4.94 (m, 1H), 4.86–4.94 (m, 1H), 4.95–5.05 (m, 2H), 5.16 (d, J = 1.2 Hz, 0.5H, minor), 5.23 (d, J = 4.5 Hz, 0.5H, minor), 5.33 (s, 0.5H, major), 5.37 (s, 0.5H, minor), 5.42 (s, 0.5H, major), 5.51–5.62 (m, 2.5H), 5.64–5. 85 (m, 1H), 7.22–7.64 (m, 18H), 7.91–8.11 (m, 12H); ppm; **^{13}C NMR (100 MHz, $CDCl_3$):** δ 28.5 (t, major), 28.6 (t, minor), 30.0 (t, minor), 30.1 (t, major), 63.5 (t, major), 63.6 (t, minor), 63.6 (t, major), 63.7 (t, minor), 65.8 (t, minor), 66.5 (t, major), 67.3 (t, major), 68.3 (t, minor), 77.5 (d, major), 77.6 (d, minor), 77.7 (d, minor), 77.8 (d, major), 78.4 (d, major), 78.5 (d, minor), 79.0 (d, major), 80.8 (d, minor), 81.2 (d, minor), 81.4 (d, major), 81.5 (d, major), 81.6 (d, 2C, major), 81.7 (d, 2C, minor), 81.7 (d, major), 81.8 (d, minor), 82.5 (d, minor), 99.5 (d, minor), 105.4 (d, major), 105.5 (d, minor), 105.6 (d, major), 105.8 (d, minor), 105.9 (d, major), 114.8 (t, 2C), 128.2 (d, 4C, minor), 128.3 (d, major), 128.4 (d, 4C, major), 128.5 (d, 4C, major), 128.8 (s, minor), 128.9 (s, major), 128.9 (s, minor), 129.0 (s, major), 129.0 (s, minor), 129.0 (s, major), 129.5 (s, minor), 129.5 (s, major), 129.6 (s, 4C), 129.63 (d, 4C minor), 129.8 (d, 5C, minor), 129.8 (d, major), 129.9 (d, minor), 132.9 (d, major), 137.7 (d, major), 137.9 (d, minor), 165.1 (s, major), 165.2 (s, major), 165.5 (s, 2C), 165.6 (s, major), 165.7 (s, minor), 165.9 (s, 2C, major), 166.1 (s, 2C, minor), 170.1 (s, minor), 170.3 (s, major) ppm; **ESI-MS *m/z*:** calcd $[(C_{64}H_{60}O_{20}Na)^+]$ 1171.36 found 1171.53 ($[M+Na]^+$, 100%), 1187.53 ($[M+K]^+$, 30%).

General procedure for *O*-alkylation:

To a solution of alcohol (1.0 mmol) in dry DMF (7 mL), NaH (3.2 mmol) was added portion wise at 0 °C and stirred for 20 min, followed by drop wise addition of alkyl halide (2.2 mmol). After stirring for additional 6 h at room temperature the reaction mixture was quenched by adding small pieces of ice and poured into water and extracted with ethyl acetate. The combined organic phases were washed with water, brine, dried (Na_2SO_4) and concentrated. Purification of the crude by column chromatography gave the di-*O*-alkyl derivative

5-Deoxy-5-dimethylacetal-2,3-di-*O*-methyl-1-α-D-arabinofuranosyl-undec-10-ene (38):

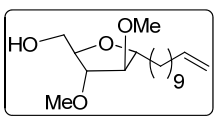


Colourless liquid, 92% yield. **$[\alpha]_D^{25}$:** + 17.1 (*c* 2.4, $CHCl_3$). **^{1}H NMR (200 MHz, $CDCl_3$):** δ 1.21–1.45 (m, 14H), 1.50–1.70 (m, 2H), 1.94–2.11 (m, 2H), 3.32–3.52 (m, 13H), 3.75–3.85 (m, 1H), 3.87 (dd, *J* = 4.3, 7.5 Hz, 1H), 3.95 (dd, *J* = 1.8, 3.0 Hz, 1H), 4.34 (dd, *J* = 1.0, 6.5 Hz, 1H), 4.85–5.10 (m, 2H), 5.80 (ddt, *J* = 6.2, 10.0, 17.0 Hz, 1H); **^{13}C NMR (50 MHz, $CDCl_3$):** 25.8 (t), 28.9 (t), 29.1 (t), 29.5 (t, 4C), 33.1 (t), 33.8 (t), 53.7 (q), 55.4 (q), 57.3 (q), 57.5 (q), 82.0 (d), 82.7 (d), 87.0 (d), 89.6 (d), 103.6 (d), 114.1 (t), 139.2 (d) ppm; **ESI-MS *m/z***: calcd [$(C_{20}H_{38}O_5Na)^+$] 381.26 found 381.24 ([M+Na]$^+$, 100%).

General procedure for acetal hydrolysis and reduction:

The dimethyl acetal (1.0 mmol) was dissolved in 10 mL ice cold 70% aq. trifluoroacetic acid (TFA) and stirred at rt for 8 h. After complete consumption of the acetal as indicated by TLC, the reaction mixture was concentrated under reduced pressure and the resulting crude was dissolved in isopropanol (5 ml) and treated with a solution of $NaBH_4$ (3.0 mmol) in water (0.5 mL) and stirred at rt for 2 h. The reaction mixture was brought to acidic pH by adding 1N hydrochloric acid and then extracted with diethyl ether (20 x 3 mL). The combined organic layer was washed with brine, dried (Na_2SO_4) and concentrated under reduced pressure. The crude product was purified by column chromatography.

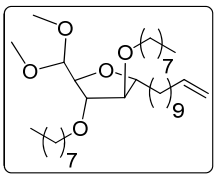
2,3-Di-*O*-methyl-1-α-D-arabinofuranosyl-undec-10-ene (40):



Colourless liquid, 88% yield. **$[\alpha]_D^{25}$:** + 33.6 (*c* 2.6, $CHCl_3$). **^{1}H NMR (200 MHz, $CDCl_3$):** δ 1.20–1.40 (m, 14H), 1.53–1.70 (m, 2H), 1.97–2.07 (m, 2H), 2.16 (s, 1H, -OH), 3.37 (s, 3H), 3.38 (s, 3H), 3.47–3.55 (m, 1H),), 3.66–3.75 (m, 3H), 3.91 (dd, *J* = 3.4, 8.3 Hz, 1H), 3.99 (dd, *J* = 4.0, 8.2 Hz, 1H), 4.85–5.06 (m, 2H), 5.85 (ddt, *J* = 6.7, 10.0, 17.0 Hz, 1H); **^{13}C NMR (50 MHz, $CDCl_3$):** 25.8

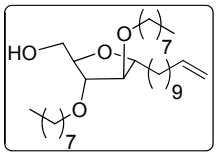
(t), 28.9 (t), 29.1 (t), 29.5 (t, 4C), 33.0 (t), 33.8 (t), 57.3 (q), 57.7 (q), 62.9 (t), 82.4 (d), 82.8 (d), 86.3 (d), 89.3 (d), 114.1 (t), 139.2 (d) ppm; **ESI-MS *m/z***: calcd $[(C_{18}H_{34}O_4)^+]$ 314.25 found 314.46 ($[M]^+$, 100%).

5-Deoxy-5-dimethylacetal-2,3-di-*O*-octyl-1-α-D-arabinofuranosyl-undec-10-ene (39):



Colourless liquid, 75% yield. **$[\alpha]_D^{25}$:** + 7.8 (*c* 0.8, $CHCl_3$). **^{1}H NMR (200 MHz, $CDCl_3$):** δ 0.86 (t, *J* = 6.0 Hz, 6H), 1.21–1.40 (m, 34H), 1.48–1.64 (m, 6H), 1.97–2.06 (m, 2H), 3.40 (s, 6H), 3.42–3.51 (m, 4H), 3.54 (dd, *J* = 2.4, 4.0 Hz, 1H), 3.82 (t, *J* = 2.4 Hz, 1H), 3.87 (dd, *J* = 2.2, 6.5 Hz, 1H), 3.93 (dd, *J* = 2.8, 6.8 Hz, 1H), 4.35 (d, *J* = 6.8 1H), 4.86–5.05 (m, 2H), 4.79 (ddt, *J* = 6.7, 10.1, 16.9 Hz, 1H); **^{13}C NMR (50 MHz, $CDCl_3$):** 14.1 (q, 2C), 22.6 (t, 2C), 25.8 (t), 26.2 (t, 2C), 28.9 (t), 29.1 (t), 29.3 (t, 2C), 29.4 (t, 2C), 29.5 (t), 29.52 (t, 2C), 29.6 (t), 29.7 (t), 29.8 (t), 31.8 (t, 3C), 33.3 (t), 33.8 (t), 53.5 (q), 55.0 (q), 69.9 (t, 2C), 82.2 (d), 82.9 (d), 85.6 (d), 88.1 (d), 114.1 (t), 139.2 (d) ppm; **ESI-MS *m/z***: calcd $[(C_{34}H_{66}O_5Na)^+]$ 577.48 found 577.55 ($[M+Na]^+$, 100%).

2,3-Di-*O*-octyl-1-α-D-arabinofuranosyl-undec-10-ene (41):

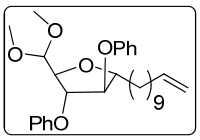


Colourless liquid, 81% yield. **$[\alpha]_D^{25}$:** + 22.2 (*c* 2.1, $CHCl_3$). **^{1}H NMR (200 MHz, $CDCl_3$):** δ 0.9 (t, *J* = 6.6, Hz, 6H), 1.20–1.40 (m, 34H), 1.48–1.65 (m, 6H), 1.97–2.08 (m, 2H), 3.39–3.52 (m, 4H), 3.59 (dd, *J* = 2.6, 3.2 Hz, 1H), 3.65–3.72 (m, 2H), 3.73 (dd, *J* = 2.4, 4.0 Hz, 1H), 3.90 (ddd, *J* = 3.6, 5.6, 8.5 Hz, 1H), 3.99 (ddd, *J* = 4.0, 5.0, 9.0 Hz, 1H), 4.86–5.05 (m, 2H), 5.80 (ddt, *J* = 6.7, 10.0, 16.9 Hz, 1H); **^{13}C NMR (50 MHz, $CDCl_3$):** 14.1 (q, 2C), 22.6 (t, 2C), 25.9 (t), 26.1 (t, 2C), 28.9 (t), 29.1 (t), 29.3 (t, 2C), 29.4 (t, 2C), 29.5 (t, 4C), 29.8 (t), 31.8 (t, 3C), 33.1 (t), 33.8 (t), 63.1 (t), 69.9 (t), 70.2 (t), 82.6 (d), 82.9 (d), 85.0 (d), 87.8 (d), 114.1 (t), 139.2 (d) ppm; **ESI-MS *m/z***: calcd $[(C_{32}H_{62}O_4Na)^+]$ 533.45 found 533.56 ($[M+Na]^+$, 100%), 549.51 ($[M+K]^+$, 5%).

General procedure for Cu(I) catalyzed C–O coupling of aryl halide:

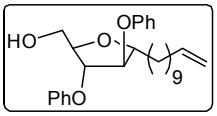
A test tube was charged with CuI (0. 8 μmol), 1,10-phenanthroline (0. 3 μmol), Cs_2CO_3 (8 μmol), iodobenzene (9.6 μmol) and **12** (1.6 mmol). The test tube was sealed and the reaction mixture was stirred at 120 °C (external temp.) for 8 to 24 h. The resulting suspension was cooled to room temperature and filtered through a pad of silica gel eluting with ethyl acetate. The filtrate was concentrated and purified by column chromatography to afford the coupled product**.**

5-Deoxy-5-dimethylacetal-2,3-di-*O*-phenyl-1-α-D-arabinofuranosyl-undec-10-ene (42):



Colourless liquid, 96% yield. **$[\alpha]_D^{25}$:** –4.0 (*c* 1.0, $CHCl_3$). **^{1}H NMR (200 MHz, $CDCl_3$):** δ 1.20–1.40 (m, 14H), 1.60–1.89 (m, 2H), 1.97–2.11 (m, 2H), 3.42 (s, 3H), 3.43 (s, 3H), 4.25 (ddd, *J* = 2.4, 6.3, 8.0 Hz, 1H), 4.30 (dd, *J* = 1.8, 7.3 Hz, 1H), 4.61 (d, *J* = 7.3 Hz, 1H), 4.63 (d, *J* = 2.3 Hz, 1H), 4.87 (d, *J* = 1.8 Hz, 1H), 4.92 (ddt, *J* = 1.3, 2.4, 10.2 Hz, 1H), 5.00 (ddd, *J* = 1.6, 3.8, 10.2 Hz, 1H), 5.81 (ddt, *J* = 6.7, 10.2, 17.1 Hz, 1H), 6.85–7.02 (m, 6H), 7.21–7.32 (m, 4H); **^{13}C NMR (50 MHz, $CDCl_3$):** 25.7 (t), 28.9 (t), 29.1 (t), 29.4 (t, 4C), 32.9 (t), 33.8 (t), 53.0 (q), 55.2 (q), 82.1 (d), 83.0 (d), 83.9 (d), 85.5 (d), 102.8 (t), 114.1 (d), 115.7 (d, 2C), 115.8 (d, 2C), 121.4 (d), 121.6 (d), 129.6 (d, 2C), 129.7 (d, 2C), 139.2 (d), 157.0 (s), 157.1 (s) ppm; **ESI-MS *m/z***: calcd [$(C_{30}H_{42}O_5Na)^+$] 505.29 found 505.29 ([M+Na]$^+$, 100%).

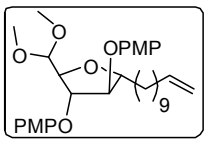
2,3-Di-*O*-phenyl-1-α-D-arabinofuranosyl-undec-10-ene (50):



Colourless liquid, 89% yield. **$[\alpha]_D^{25}$:** + 1.6 (*c* 1.1, $CHCl_3$). **^{1}H NMR (200 MHz, $CDCl_3$):** δ 1.20–1.40 (m, 16H), 1.99–2.10 (m, 2H), 2.17 (s, 1H, -OH), 3.80–3.91 (m, 2H), 4.23 (ddd, *J* = 1.8, 5.4, 11.0 Hz, 1H), 4.30 (ddd, *J* = 4.1, 7.5, 12.1 Hz, 1H), 4.65 (m, 1H), 4.85 (d, *J* = 3.2 Hz, 1H), 4.93 (ddd, *J* = 1.2, 3.5, 10.2 Hz, 1H), 4.93 (ddd, *J* = 1.6, 3.5, 16.5 Hz, 1H), 5.85 (ddt, *J* = 6.6, 10.2, 16.5 Hz, 1H), 6.65–7.05 (m, 6H), 7.22–7.33 (m, 4H); **^{13}C NMR (50 MHz, $CDCl_3$):**

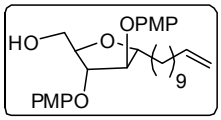
25.7 (t), 28.9 (t), 29.1 (t), 29.4 (t), 29.5 (t, 3C), 32.2 (t), 33.8 (t), 62.3 (t), 82.4 (d), 82.8 (d), 82.3 (d), 85.6 (d), 114.1 (t), 115.7 (d, 2C), 115.8 (d, 2C), 121.7 (d, 2C), 129.7 (d, 4C), 139.2 (d), 157.0 (s), 157.1 (s) ppm; **ESI-MS *m/z*:** calcd [$(C_{28}H_{38}O_4Na)^+$] 461.27 found 461.29 ([M+Na]$^+$, 100%,), 499.14 ([M+K]$^+$, 20%).

2,3-Di-*O*-(4-methyoxy phenyl)-1-α-D-arabinofuranosyl-undec-10-ene (43):



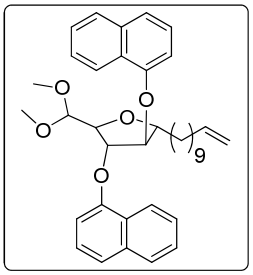
Colourless liquid, 91% yield. **$[\alpha]_D^{25}$:** +11.8 (*c* 2.0, $CHCl_3$). **^{1}H NMR (200 MHz, $CDCl_3$):** δ 1.20–1.39 (m, 14H), 1.60–1.90 (m, 2H), 1.95–2.10 (m, 2H), 3.39 (s, 3H), 3.42 (s, 3H), 3.75 (s, 6H), 4.21 (ddd, *J* = 2.5, 6.5, 9.8 Hz, 1H), 4.25 (dd, *J* = 1.9, 7.4 Hz, 1H), 4.49 (d, *J* = 2.5 Hz, 1H), 4.56 (d, *J* = 7.4 Hz, 1H), 4.75 (d, *J* = 1.9 Hz, 1H), 4.91 (ddt, *J* = 1.2, 2.3, 10.2 Hz, 1H), 4.98 (ddd, *J* = 1.6, 3.8, 17.2 Hz, 1H), 5.81 (ddt, *J* = 6.7, 10.2, 17.1 Hz, 1H), 6.76–6.92 (m, 8H); **^{13}C NMR (50 MHz, $CDCl_3$):** 25.8 (t), 28.9 (t), 29.1 (t), 29.5 (t, 4C), 32.9 (t), 33.8 (t), 53.1 (q), 55.0 (q), 55.6 (q, 2C), 82.0 (d), 83.7 (d), 83.9 (d), 86.2 (d), 102.7 (d), 114.1 (t), 114.6 (d, 2C), 114.7 (d, 2C), 116.9 (d, 2C), 117.0 (d, 2C), 139.2 (d), 151.1 (s), 151.2 (s), 154.3 (s), 154.4 (s) ppm; **ESI-MS *m/z*:** calcd [$(C_{32}H_{46}O_7Na)^+$] 565.31 found 565.28 ([M+Na]$^+$, 100%).

2,3-Di-*O*-(4-methyoxy phenyl)-1-α-D-arabinofuranosyl-undec-10-ene (51):



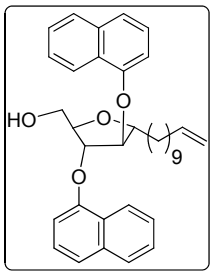
Colourless liquid, 73% yield. **$[\alpha]_D^{25}$:** + 29.7 (*c* 2.3, $CHCl_3$). **^{1}H NMR (200 MHz, $CDCl_3$):** δ 1.20–1.40 (m, 14H), 1.55–1.78 (m, 2H), 1.97–2.07 (m, 2H), 2.16 (s, 1H), 3.75 (S, 6H), 3.76–3.85 (m, 2H), 4.18 (ddd, *J* = 2.2, 5.3, 8.7 Hz, 1H), 4.26 (ddd, *J* = 3.9, 5.3, 8.74 Hz, 1H), 4.52 (dd, *J* = 1.3, 2.2 Hz, 1H), 4.71 (dd, *J* = 1.3, 3.3 Hz, 1H), 4.91 (ddd, *J* = 1.2, 2.6, 10.2 Hz, 1H), 4.98 (ddd, *J* = 1.4, 2.6, 17.0 Hz, 1H), 5.80 (ddt, *J* = 6.7, 10.2, 17.0 Hz, 1H), 6.78–6.83 (m, 8H); **^{13}C NMR (50 MHz, $CDCl_3$):** 25.8 (t), 29.0 (t), 29.2 (t), 29.4 (t), 29.5 (t, 3C), 32.4 (t), 33.8 (t), 55.7 (q, 2C), 62.4 (t), 82.8 (d), 83.2 (d), 83.3 (d), 86.5 (d), 114.1 (t), 114.8 (d, 4C), 117.0 (d, 2C), 117.2 (d, 2C), 139.26 (d), 151.1 (s), 151.2 (s), 154.6 (s), 158.0 (s) ppm; **ESI-MS *m/z*:** cacld [$(C_{30}H_{42}O_6Na)^+$] 521.29 found 521.64 ([M+Na]$^+$, 100%).

2,3-Di-*O*-(1-naphthyl)-1-α-D-arabinofuranosyl-undec-10-ene (44):



Colourless liquid, 46% yield. $[\alpha]_D^{25}$ **:** –102.1 (*c* 2.4, $CHCl_3$). **^{1}H NMR (200 MHz, $CDCl_3$):** δ 1.11–1.43 (m, 14H), 1.59–1.83 (m, 2H), 1.92–2.06 (m, 2H), 3.40 (s, 3H), 3.47 (s, 3H), 4.47 (dd, *J* = 7.0, 12.0 Hz, 1H), 4.51 (d, *J* = 7.0 Hz, 1H), 4.78 (d, *J* = 7.3 Hz, 1H), 4.86–5.05 (m, 3H), 5.24 (s, 1H), 5.80 (ddt, *J* = 6.7, 10.2, 17.0 Hz, 1H), 6.75 (d, *J* = 7.5 Hz, 1H), 6.99 (d, *J* = 7.5 Hz, 1H), 7.23 (d, *J* = 7.5 Hz, 1H), 7.32 (d, *J* = 7.5 Hz, 1H), 7.42 (d, *J* = 2.4 Hz, 1H), 7.47 (d, *J* = 2.4 Hz, 1H), 7.50 (d, *J* = 3.3 Hz, 1H), 7.53 (d, *J* = 3.3 Hz, 1H), 7.76–7.90 (m, 2H), 8.29 (t, *J* = 3.3 Hz, 2H), 8.32 (t, *J* = 3.3 Hz, 2H); **^{13}C NMR (50 MHz, $CDCl_3$):** δ 25.8 (t), 28.9 (t), 29.1 (t), 29.5 (t, 3C), 29.7 (t), 33.2 (t), 33.8 (t), 53.0 (q), 55.4 (q), 82.2 (d), 83.1 (d), 84.1 (d), 85.7 (d), 102.9 (d), 106.1 (d), 106.6 (d), 114.1 (t), 121.0 (d), 121.1 (d), 121.8 (d), 121.9 (d), 125.4 (d), 125.5 (d), 125.7 (d), 125.8 (s), 125.9 (d), 126.5 (d), 126.6 (d), 127.6 (d, 2C), 134.6 (s, 2C), 134.7 (s), 139.2 (d), 152.6 (s), 152.7 (s) ppm; **ESI-MS *m/z*:** cacld $[(C_{38}H_{46}O_5Na)^+]$ 605.32 found 605.38 ($[M+Na]^+$, 100%).

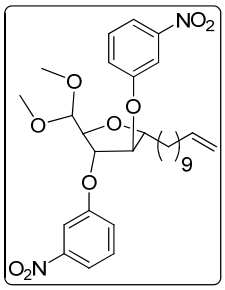
2,3-Di-*O*-(1-naphthyl)-1-α-D-arabinofuranosyl-undec-10-ene (52):



Colourless liquid, 71% yield. $[\alpha]_D^{25}$ **:** –66.5 (*c* 1.2, $CHCl_3$). **^{1}H NMR (200 MHz, $CDCl_3$):** δ 1.20–1.40 (m, 14H), 1.53–1.86 (m, 2H), 1.98–2.07 (m, 2H), 2.15 (s, 1H, -OH), 3.96 (d, *J* = 4.7 Hz, 2H), 4.44 (ddd, *J* = 1.6, 5.3, 7.9 Hz, 1H), 4.52 (ddd, *J* = 2.9, 4.6, 7.9 Hz, 1H), 4.92 (ddd, *J* = 1.2, 3.5, 10.2 Hz, 1H), 4.98 (ddd, *J* = 1.6, 3.6, 17.0 Hz, 1H), 5.00 (s, 1H), 5.23 (d, *J* = 3.0 Hz, 1H), 5.8 (ddt, *J* = 6.6, 10.2, 17.0 Hz, 1H), 6.72 (d, *J* = 7.6 Hz, 1H), 6.86 (d, *J* = 7.6 Hz, 1H), 7.25 (t, *J* = 8.3 Hz, 1H), 7.26 (t, *J* = 7.8 Hz, 1H), 7.42–7.58 (m, 6H), 7.75–7.85 (m, 2H), 8.28 (dd, *J* = 3.0, 5.8 Hz, 1H), 8.32 (dd, *J* = 3.0, 5.8 Hz, 1H); **^{13}C NMR (50 MHz, $CDCl_3$):** δ 25.7 (t), 28.9 (t), 29.1 (t), 29.4 (t), 29.5 (t, 3C), 32.3 (t), 33.8 (t), 62.4 (t), 82.7 (d), 83.1 (d), 83.4 (d), 85.6 (d), 106.1 (d), 106.3 (d), 114.1 (t), 121.2 (d, 2C), 121.7 (d), 121.8 (d), 125.5 (d), 125.6 (d), 125.7 (d), 125.7 (d), 125.8 (d), 125.8 (d), 126.6 (d), 126.7 (d), 127.6 (d, 2C), 134.7 (d, 2C), 139.2 (d),

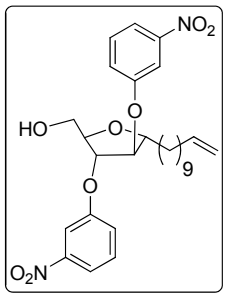
152.6 (s), 152.7 (s) ppm; **ESI-MS *m/z*:** cacld $[(C_{36}H_{42}O_4Na)^+]$ 561.30 found 561.32 ($[M+Na]^+$, 100%).

2,3-Di-*O*-(3-nitro phenyl)-1-α-D-arabinofuranosyl-undec-10-ene (45):



Yellow liquid, 53% yield. $[\alpha]_D^{25}$ **:** –15.2 (*c* 1.9, $CHCl_3$). **^{1}H NMR (200 MHz, $CDCl_3$):** δ 1.22–1.45 (m, 14H), 1.75–1.85 (m, 2H), 1.95–2.10 (m, 2H), 3.45 (s, 3H), 3.53 (s, 3H), 4.24 (dd, *J* = 2.0, 6.0 Hz, 1H), 4.29 (ddd, *J* = 4.5, 5.8, 10.2 Hz, 1H), 4.57 (d, *J* = 6.1 Hz, 1H), 4.72 (dd, *J* = 1.0, 4.2 Hz, 1H), 4.86–4.95 (m, 2H), 4.99 (ddt, *J* = 1.9, 3.5, 17.0 Hz, 1H), 5.79 (ddt, *J* = 6.7, 10.2, 17.0 Hz, 1H), 7.24 (ddd, *J* = 1.0, 2.4, 8.2 Hz, 1H), 7.42 (dt, *J* = 1.6, 8.1 Hz, 3H), 7.77 (t, *J* = 2.2 Hz, 1H), 7.82 (t, *J* = 1.8 Hz, 1H), 7.88 (t, *J* = 1.8 Hz, 1H), 8.06 (t, *J* = 2.2 Hz, 1H); **^{13}C NMR (50 MHz, $CDCl_3$):** 25.7 (t), 28.9 (t), 29.1 (t), 29.4 (t, 4C), 33.0 (t), 33.8 (t), 53.8 (q), 56.3 (q), 82.2 (d), 82.9 (d), 83.8 (d), 87.2 (d), 103.4 (d), 110.0 (d), 110.1 (d), 114.1 (t), 116.8 (d, 2C), 122.3 (d), 123.0 (d), 130.1 (d), 130.4 (d), 139.2 (d), 149.2 (s, 2C), 157.5 (s), 157.7 (s) ppm; **ESI-MS *m/z*:** cacld $[(C_{30}H_{40}N_2O_9Na)^+]$ 595.26 found 595.35 ($[M+Na]^+$, 100%), 611.32 ($[M+K]^+$, 5%).

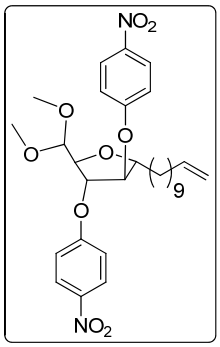
2,3-Di-*O*-(3-nitro phenyl)-1-α-D-arabinofuranosyl-undec-10-ene (53)



Colourless liquid, 49% yield. $[\alpha]_D^{25}$ **:** + 8.5 (*c* 2.3, $CHCl_3$). **^{1}H NMR (200 MHz, $CDCl_3$):** δ 1.20–1.48 (m, 14H), 1.71–1.87 (m, 2H), 1.98–2.10 (m, 2H), 2.14 (br s, 1H, -OH), 3.78–3.90 (m, 2H), 3.96 (dd, *J* = 4.2, 11.7 Hz, 1H), 4.26 (ddd, *J* = 3.1, 5.3, 8.7 Hz, 1H), 4.31 (dd, *J* = 4.4, 8.7 Hz, 1H), 4.75 (dd, *J* = 1.9, 2.8 Hz, 1H), 4.87–5.07 (m, 3H), 5.85 (ddt, *J* = 6.6, 10.2, 17.0 Hz, 1H), 7.23–7.36 (m, 2H), 7.45 (t, *J* = 8.2 Hz, 1H), 7.46 (t, *J* = 8.2 Hz, 1H), 7.75 (t, *J* = 2.2 Hz, 1H), 7.82–7.90 (m, 3H); **^{13}C NMR (50 MHz, $CDCl_3$):** δ 25.6 (t), 28.9 (t), 29.1 (t), 29.3 (t), 29.4 (t, 3C), 32.4 (t), 33.8 (t), 61.7 (t), 81.9 (d), 82.6 (d), 82.8 (d), 86.6 (d), 109.8 (d), 110.1 (d), 114.1 (t), 116.9 (d, 2C), 122.2 (d), 122.6 (d), 130.4 (d, 2C), 139.2 (d), 149.2 (s, 2C), 157.5 (s, 2C) ppm; **ESI-**

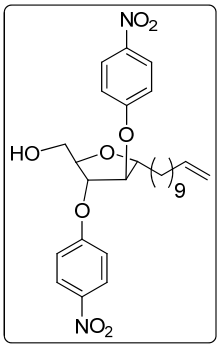
MS *m/z*: cacld [($C_{28}H_{36}N_2O_8Na$)$^+$] 551.24 found 551.32 ([M+Na]$^+$, 100%), 567.28 ([M+K]$^+$, 5%).

2,3-Di-*O*-(4-nitro phenyl)-1-α-D-arabinofuranosyl-undec-10-ene (46):



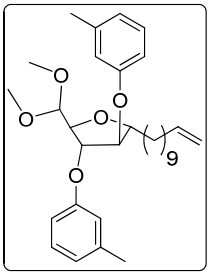
Yellow liquid, 60% yield. **$[\alpha]_D^{25}$:** + 31.8 (*c* 2.8, $CHCl_3$). **^{1}H NMR (200 MHz, $CDCl_3$):** δ 1.21–1.41 (m, 14H), 1.66–1.85 (m, 2H), 1.96–2.07 (m, 2H), 3.42 (s, 3H), 3.48 (s, 3H), 4.22 (dd, *J* = 1.7, 6.0 Hz, 1H), 4.29 (ddd, *J* = 4.0, 5.6, 11.7 Hz, 1H), 4.54 (d, *J* = 6.1 Hz, 1H), 4.73 (d, *J* = 3.4 Hz, 1H), 4.85–5.05 (m, 3H), 5.79 (ddt, *J* = 6.6, 10.2, 17.0 Hz, 1H), 6.96 (d, *J* = 9.3 Hz, 2H), 7.11 (d, *J* = 9.3 Hz, 2H), 8.18 (d, *J* = 9.3 Hz, 2H); **^{13}C NMR (50 MHz, $CDCl_3$):** δ 25.7 (t), 28.9 (t), 29.1 (t), 29.4 (t, 4C), 33.0 (t), 33.8 (t), 53.8 (q), 56.2 (q), 82.1 (d), 83.2 (d), 83.4 (d), 86.7 (d), 103.2 (d), 114.1 (t), 115.4 (d, 2C), 115.6 (d, 2C), 126.0 (d, 2C), 126.1 (d, 2C), 139.2 (d), 142.2 (s, 2C), 161.7 (s), 161.9 (s) ppm; **ESI-MS *m/z*:** cacld [($C_{30}H_{40}N_2O_9Na$)$^+$] 595.26 found 595.35 ([M+Na]$^+$, 100%).

2,3-Di-*O*-(4-nitro phenyl)-1-α-D-arabinofuranosyl-undec-10-ene (54):



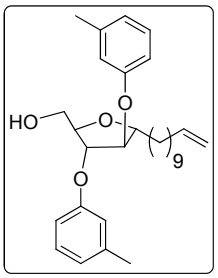
Yellow liquid, 48% yield. **$[\alpha]_D^{25}$:** + 35.8 (*c* 2.6, $CHCl_3$). **^{1}H NMR (200 MHz, $CDCl_3$):** δ 1.20–1.48 (m, 14H), 1.57–1.75 (m, 2H), 1.97–2.07 (m, 2H), 2.16 (s, 1H, -OH), 3.75–3.90 (m, 2H), 3.94 (dd, *J* = 4.4, 11.7 Hz, 1H), 4.21 (dd, *J* = 2.5, 4.9 Hz, 1H), 4.28 (dd, *J* = 4.4, 8.5 Hz, 1H), 4.75 (br s, 1H), 4.85–5.10 (m, 3H), 5.79 (ddt, *J* = 6.7, 10.2, 17.0 Hz, 1H), 6.95 (d, *J* = 9.2 Hz, 2H), 7.05 (d, *J* = 9.2 Hz, 2H), 8.15 (d, *J* = 1.2 Hz, 2H), 8.19 (d, *J* = 1.2 Hz, 2H); **^{13}C NMR (50 MHz, $CDCl_3$):** δ 25.6 (t), 28.9 (t), 29.1 (t), 29.3 (t), 29.4 (t, 3C), 32.3 (t), 33.7 (t), 61.6 (t), 82.0 (d), 82.6 (d), 82.8 (d), 86.5 (d), 114.1 (t), 115.4 (d, 4C), 126.1 (d, 4C), 139.1 (d), 142.3 (s, 2C), 161.7 (s, 2C), 161.8 (s, 2C) ppm; **ESI-MS *m/z*:** cacld [($C_{28}H_{36}N_2O_8Na$)$^+$] 551.24 found 551.33 ([M+Na]$^+$, 100%).

2,3-Di-*O*-(3-methyl phenyl)-1-α-D-arabinofuranosyl-undec-10-ene (47):



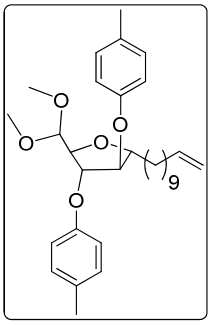
Colourless liquid, 93% yield. **$[\alpha]_D^{25}$:** – 2.1 (*c* 1.8, $CHCl_3$). **^{1}H NMR (200 MHz, $CDCl_3$):** δ 1.21–1.40 (m, 14H), 1.65–1.85 (m, 2H), 1.97–2.09 (m, 2H), 2.28 (s, 3H), 2.29 (s, 3H), 3.42 (s, 3H), 3.44 (s, 3H), 4.23 (ddd, *J* = 2.3, 6.3, 10.2 Hz, 1H), 4.28 (dd, *J* = 1.7, 7.4 Hz, 1H), 4.60 (dd, *J* = 7.3 Hz, 1H), 4.59 (d, *J* = 2.4 Hz, 1H), 4.85 (d, *J* = 1.6 Hz, 1H), 4.91 (ddt, *J* = 1.3, 2.3, 10.2 Hz, 1H), 5.00 (ddt, *J* = 1.8, 2.3, 17.0 Hz, 1H), 5.81 (ddt, *J* = 6.6, 10.2, 17.0 Hz, 1H), 6.64–6.85 (m, 6H), 7.08–7.21 (m, 2H); **^{13}C NMR (50 MHz, $CDCl_3$):** δ 21.5 (q, 2C), 25.8 (t), 28.9 (t), 29.1 (t), 29.4 (t, 4C), 32.9 (t), 33.8 (t), 53.0 (q), 55.0 (q), 82.2 (d), 83.0 (d), 84.0 (d), 85.4 (d), 102.8 (d), 112.7 (d, 2C), 114.1 (t), 116.7 (d, 2C), 122.2 (d), 122.4 (d), 129.3 (d), 129.4 (d), 139.2 (d), 139.6 (s), 139.7 (s), 157.0 (s), 157.2 (s) ppm; **ESI-MS *m/z*:** cacld $[(C_{32}H_{46}O_5Na)^+]$ 533.32 found 533.41 ($[M+Na]^+$, 100%), 549.36 ($[M+K]^+$, 5%).

2,3-Di-*O*-(3-methyl phenyl)-1-α-D-arabinofuranosyl-undec-10-ene (55):



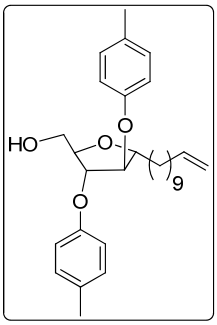
Colourless liquid, 76% yield. **$[\alpha]_D^{25}$:** + 11.6 (*c* 1.2, $CHCl_3$). **^{1}H NMR (200 MHz, $CDCl_3$):** δ 1.20–1.48 (m, 14H), 1.59–1.79 (m, 2H), 1.99–2.16 (m, 2H), 2.28 (s, 6H), 3.78–3.88 (m, 2H), 4.16–4.25 (m, 2H), 4.29 (dd, *J* = 4.4, 8.5 Hz, 1H), 4.62 (br s, 1H), 4.80 (d, *J* = 2.9 Hz, 1H), 4.87–5.07 (m, 2H), 5.81 (ddt, *J* = 6.7, 10.1, 17.0 Hz, 1H), 6.68 (d, *J* = 2.2 Hz, 2H), 6.72 (d, *J* = 7.0 Hz, 2H), 7.70 (d, *J* = 6.8 Hz, 2H), 7.14 (t, *J* = 7.6 Hz, 2H); **^{13}C NMR (50 MHz, $CDCl_3$):** δ 21.4 (q, 2C), 25.8 (t), 28.9 (t), 29.1 (t), 29.4 (t), 29.5 (t, 3C), 32.2 (t), 33.8 (t), 61.3 (t), 82.4 (d), 83.0 (d), 83.4 (d), 85.5 (d), 112.5 (d), 112.6 (d), 114.1 (t), 116.6 (d), 116.8 (d), 122.5 (d, 2C), 129.4 (d, 2C), 139.2 (d), 139.8 (s, 2C), 157.0 (s), 157.2 (s) ppm; **ESI-MS *m/z*:** cacld $[(C_{30}H_{42}O_4Na)^+]$ 489.30 found 489.35 ($[M+Na]^+$, 100%).

2,3-Di-*O*-(4-methyl phenyl)-1-α-D-arabinofuranosyl-undec-10-ene (48):



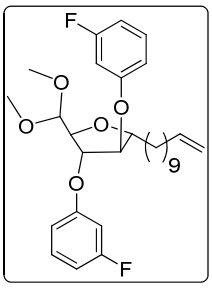
Colourless liquid, 95% yield. **$[\alpha]_D^{25}$:** + 4.5 (*c* 1.6, $CHCl_3$). **^{1}H NMR (200 MHz, $CDCl_3$):** δ 1.21–1.42 (m, 14H), 1.66–1.86 (m, 2H), 1.97–2.10 (m, 2H), 2.27 (s, 6H), 3.40 (s, 3H), 3.42 (s, 3H), 4.21 (dd, *J* = 2.0, 6.5 Hz, 1H), 4.28 (dd, *J* = 1.6, 7.4 Hz, 1H), 4.56–4.63 (m, 2H), 4.82 (d, *J* = 1.4 Hz, 1H), 4.86–5.07 (m, 2H), 5.81 (ddt, *J* = 6.7, 10.2, 17.0 Hz, 1H), 6.77 (d, *J* = 8.5 Hz, 2H), 6.87 (d, *J* = 8.5 Hz, 2H), 7.05 (d, *J* = 8.5 Hz, 4H); **^{13}C NMR (50 MHz, $CDCl_3$):** δ 20.4 (q, 2C), 25.8 (t), 28.9 (t), 29.1 (t), 29.4 (t, 4C), 32.9 (t), 33.8 (t), 52.9 (q), 55.9 (q), 82.1 (d), 83.1 (d), 83.9 (d), 85.5 (d), 102.7 (d), 114.1 (t), 115.6 (d, 4C), 129.9 (d, 2C), 130.1 (d, 2C), 130.6 (s), 130.8 (s), 139.2 (d), 154.9 (s), 155.0 (s) ppm; **ESI-MS *m/z*:** cacld $[(C_{32}H_{46}O_5Na)^+]$ 533.32 found 533.41 ($[M+Na]^+$, 100%), 549.36 ($[M+K]^+$, 5%).

2,3-Di-*O*-(4-methyl phenyl)-1-α-D-arabinofuranosyl-undec-10-ene (56):



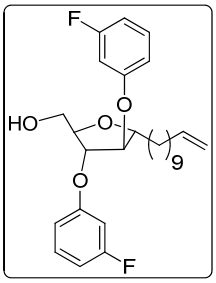
Colourless liquid, 81% yield. **$[\alpha]_D^{25}$:** + 22.44 (*c* 3.8, $CHCl_3$). **^{1}H NMR (200 MHz, $CDCl_3$):** δ 1.20–1.48 (m, 14H), 1.59–1.84 (m, 2H), 1.98–2.10 (m, 2H), 2.27 (s, 6H), 3.78–3.88 (m, 2H), 4.16–4.24 (m, 2H), 4.27 (dd, *J* = 4.0, 8.6 Hz, 1H), 4.59 (br s, 1H), 4.77 (d, *J* = 3 Hz, 1H), 4.86–5.06 (m, 2H), 5.81 (ddt, *J* = 6.7, 10.1, 17.0 Hz, 1H), 6.77 (d, *J* = 6.7 Hz, 2H), 6.81 (d, *J* = 6.7 Hz, 2H), 7.05 (d, *J* = 8.4 Hz, 4H); **^{13}C NMR (50 MHz, $CDCl_3$):** δ 20.4 (q, 2C), 25.8 (t), 28.9 (t), 29.1 (t), 29.4 (t), 29.5 (t, 3C), 32.2 (t), 33.8 (t), 62.3 (t), 82.5 (d), 82.9 (d), 83.2 (d), 85.6 (d), 114.1 (t), 115.5 (d, 2C), 115.7 (d, 2C), 130.1 (d, 4C), 130.9 (s, 2C), 139.2 (d), 154.8 (s), 155.0 (s) ppm; **ESI-MS *m/z*:** cacld $[(C_{30}H_{42}O_4Na)^+]$ 489.30 found 489.29 ($[M+Na]^+$, 100%).

2,3-Di-*O*-(3-fluro phenyl)-1-α-D-arabinofuranosyl-undec-10-ene (49):



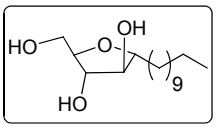
Colourless liquid, 87% yield. **$[\alpha]_D^{25}$:** –9.8 (*c* 2.2, $CHCl_3$). **^{1}H NMR (200 MHz, $CDCl_3$):** δ 1.21–1.40 (m, 14H), 1.66–1.84 (m, 2H), 1.96–2.11 (m, 2H), 3.44 (s, 3H), 3.45 (s, 3H), 4.22 (dd, *J* = 2.8, 6.8 Hz, 1H), 4.26 (dd, *J* = 1.7, 6.8 Hz, 1H), 4.56 (dd, *J* = 6.9 Hz, 1H), 4.57–4.62 (m, 1H), 4.83 (br s, 1H), 4.87–5.08 (m, 2H), 5.82 (ddt, *J* = 6.7, 10.1, 17.1 Hz, 1H), 6.56–6.85 (m, 6H), 7.14–7.28 (m, 2H); **^{13}C NMR (50 MHz, $CDCl_3$):** δ 25.7 (t), 28.9 (t), 29.1 (t), 29.4 (t, 4C), 32.9 (t), 33.8 (t), 53.2 (d), 55.5 (d), 82.0 (d), 83.3 (d), 83.6 (d), 86.1 (d), 102.9 (d), 103.4 (d, *J* = 2.5 Hz), 103.9 (d, *J* = 2.5 Hz), 103.6 (d, *J* = 25 Hz), 103.7 (d, *J* = 25 Hz), 108.4 (d, *J* = 21.4 Hz), 108.6 (d, *J* = 21.4 Hz), 111.1 (d, *J* = 2.8 Hz), 111.4 (d, *J* = 2.8 Hz), 114.1 (d), 130.5 (t, *J* = 9.6 Hz), 139.2 (d), 158.2 (d, *J* = 10.7 Hz), 158.3 (d, *J* = 10.7 Hz), 161.1 (s), 163.0 (d, *J* = 246.6 Hz) ppm; **ESI-MS *m/z*:** cacld $[(C_{30}H_{40}F_2O_5Na)^+]$ 541.27 found 541.35 ($[M+Na]^+$, 100%).

2,3-Di-*O*-(3-fluro phenyl)-1-α-D-arabinofuranosyl-undec-10-ene (57):



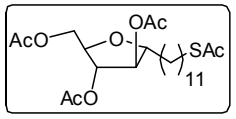
Colourless liquid, 61% yield. **$[\alpha]_D^{25}$:** + 8.4 (*c* 2.4, $CHCl_3$). **^{1}H NMR (200 MHz, $CDCl_3$):** δ 1.20–1.45 (m, 14H), 1.59–1.82 (m, 2H), 1.97–2.11 (m, 2H), 2.24 (s, 1H), 3.77 (dd, *J* = 5.5, 11.7 Hz, 1H), 3.89 (dd, *J* = 4.6, 11.9 Hz, 1H), 4.19 (dd, *J* = 2.3, 5.3 Hz, 1H), 4.27 (dd, *J* = 4.4, 8.7 Hz, 1H), 4.62 (dd, *J* = 1.3, 2.2 Hz, 1H), 4.83 (d, *J* = 3.0 Hz, 1H), 4.88–5.06 (m, 2H), 5.81 (ddt, *J* = 6.7, 10.1, 17.0 Hz, 1H), 6.60–6.75 (m, 6H), 7.17 (d, *J* = 7.9 Hz, 2H), 7.24 (t, *J* = 7.6 Hz, 2H); **^{13}C NMR (50 MHz, $CDCl_3$):** δ 25.8 (t), 28.9 (t), 29.1 (t), 29.3 (t), 29.4 (t, 3C), 32.2 (t), 33.8 (t), 61.9 (t), 82.4 (d), 82.5 (d), 83.0 (d), 86.0 (d), 103.4 (d, *J* = 2.5 Hz), 103.9 (d, *J* = 2.5 Hz), 103.6 (d, *J* = 25 Hz), 103.7 (d, *J* = 25 Hz), 108.7 (d, *J* = 21.2 Hz, 2C), 111.0 (d, *J* = 2.8 Hz), 111.2 (d, *J* = 2.8 Hz), 114.0 (d), 130.5 (d, *J* = 9.9 Hz), 139.2 (s), 158.2 (d, *J* = 10.7 Hz), 158.3 (d, *J* = 10.7 Hz), 163.0 (d, *J* = 246.6 Hz) ppm; **ESI-MS *m/z*:** cacld $[(C_{28}H_{36}F_2O_4Na)^+]$ 497.25 found 497.26 ($[M+Na]^+$, 100%), 511.26 ($[M+K]^+$, 20%).

1-α-D-Arabinofuranosylundecane (58):



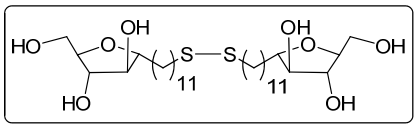
To a solution of olefin **3** (100 mg, 349 μmol) in methanol (12 ml), 20 mg of 10% Pd/C was added and the reaction mixture was stirred at 60 psi for 6 h. The contents were filtered over celite and the filtrate was concentrated under reduced pressure to obtain pure **58** (94 mg, 94% yield). R_f = 0.15 (50:50 EtOAc/Pet ether); $[\alpha]_D^{25}$: + 39.9 (*c* 0.6, $CHCl_3$). **^{1}H NMR (200 MHz, $CDCl_3$):** δ 0.9 (t, *J* = 6.6, Hz, 3H), 1.20–1.40 (m, 18H), 1.56–1.64 (m, 2H), 1.99–2.08 (m, 2H), 2.16 (br s, 1H, -OH), 3.68–3.70 (m, 2H), 3.82 (dd, *J* = 0.7, 2.6 Hz, 1H), 3.96–4.04 (m, 2H), 4.09 (dd, *J* = 4.3, 9.2 Hz, 1H), 4.53 (s, 2H), 4.55 (s, 2H); **^{13}C NMR (50 MHz, $CDCl_3$):** δ 14.3 (q), 25.6 (t), 28.8 (t), 29.0 (t), 29.4 (t, 3C), 32.9 (t), 33.7 (t, 2C), 62.6 (t), 71.5 (t), 71.9 (t), 82.6 (d), 82.7 (d), 84.4 (d), 87.2 (d) ppm; **ESI-MS *m/z*:** cacld $[(C_{16}H_{32}O_4Na)^+]$ 311.22 found 311.46 ($[M+Na]^+$, 100%).

2,3,5-tri-*O*-acetyl-11-*S*-acetyl-1-α-D-arabinofuranosylundene (59):



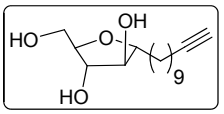
To a degassed solution of compound **15** (200 mg, 486 μmol) in toluene was added thioacetic acid (0.5 mL, 7.3 mmol), AIBN (16mg, 97 μmol) and reaction mixture was refluxed until disappearance of the olefin (4 h) as monitored by TLC. After the reaction was complete toluene was evaporated under vacuum and the crude was subjected for column purification to afford tetra acetate **59** in 79% yield as yellow liquid. $[\alpha]_D^{25}$ **:** + 19.6 (*c* 1.0, $CHCl_3$). **^{1}H NMR (200 MHz, $CDCl_3$):** δ 1.20–1.38 (m, 16H), 1.48–1.68 (m, 4H), 2.08 (s, 6H), 2.09 (s, 3H), 2.31 (s, 3H), 2.85 (t, *J* = 7.0 Hz, 2H), 4.00 (dt, *J* = 3.6, 6.6 Hz, 1H), 4.10–4.20 (m, 1H), 4.15 (dd, *J* = 3.6, 5.3 Hz, 1H), 4.24 (dd, *J* = 2.4, 5.1 Hz, 1H), 5.0 (dd, *J* = 2.5, 3.6 Hz, 1H), 5.65 (dd, *J* = 2.4, 3.6 Hz, 1H); **^{13}C NMR (50 MHz, $CDCl_3$):** δ 20.8 (q), 20.8 (q), 20.9 (q), 25.4 (t), 28.8 (t), 29.5 (t, 4C), 29.1 (t), 29.4 (t), 29.4 (t), 29.5 (t), 30.6 (q), 32.4 (t), 63.4 (t), 78.9 (d), 80.2 (d), 80.9 (d), 83.1 (d), 170.0 (s), 170.0 (s), 170.7 (s), 196.0 (s) ppm; **ESI-MS *m/z*:** cacld $[(C_{24}H_{40}O_8SNa)^+]$ 511.23 found 511.25 ($[M+Na]^+$, 100%).

Bis(1-α-D-arabinofuranosylundec-disulfide) (60):



To a, ice-cooled solution of compound **59** (110 mg, 225 µmol) in methanol was added a small piece of sodium methoxide and reaction mixture was stirred for 2 h and concentrated under vacuum. The resulting solid was purified over column chromatography to get disulfide **60** (116 mg, 81% yield) as a colorless solid. **$[\alpha]_D^{25}$:** + 42.57 (*c* 1.0, MeOH); **^{1}H NMR (500 MHz, MeOH-d4):** δ 1.26–1.74 (br m, 4H, -0H), 2.68 (t, J = 7.2 Hz, 4H), 3.61 (dd, J = 5.3, 11.7 Hz, 2H), 3.68 (dd, J = 3.3, 11.7 Hz, 2H), 3.70–3.74 (m, 4H), 3.76 (ddd, J = 3.6, 5.7, 11.4 Hz, 1H), 3.92 (t, J = 5.7 Hz, 2H); **^{13}C NMR (125 MHz, MeOH-d4):** δ 26.8 (t, 2C), 29.5 (t, 2C), 30.2 (t, 2C), 30.3 (t, 2C), 30.6 (t, 2C), 30.7 (t, 6C), 30.8 (t, 2C), 34.7 (t, 2C), 39.9 (t, 2C), 63.4 (t, 2C), 79.2 (d, 2C), 82.8 (d, 2C), 84.1 (d, 2C), 84.5 (d, 2C) ppm; **ESI-MS *m/z*:** cacld $[(C_{32}H_{62}O_8S_2Na)^+]$ 661.38 found 661.19 ($[M+Na]^+$, 100%).

1-α-D-arabinofuranosylundec-10-yne (62):

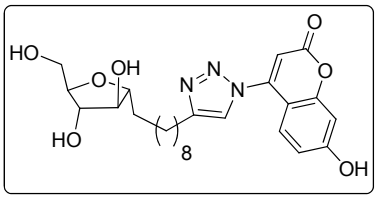


To a solution of compound **15** (160 mg, 387 µmol) in dioxane-water (3:1, 2 mL), were added 2,6-lutidine (0.8 mL, 775 µmol), OsO_4 (20 mg, 0.7 mL, 0.1 molar in toluene, 77 µmol), and $NaIO_4$ (331 mg, 1.55 mmol). Stirring was continued until (2 h), the TLC showed the complete disappearance of **15**. After completion, water (1 mL) and CH_2Cl_2 (7 mL) were added. The organic layer was separated, and aqueous was layer extracted with CH_2Cl_2 3 X 3 mL. The combined organic layer was washed with brine, dried over Na_2SO_4 and procured aldehyde **S27.1** (158 mg) as colorless oil.

In crude solution of aldehyde **S27.1** (158 mg, 370 µmol) and K_2CO_3 (110 mg, 814 µmol) in methanol was added dimethyl-1-diazo-2-oxopropylphosphonate (147 mg, 814 µmol) and stir at same condition for 3 h and reaction mixture was concentrated and crude product was purified over silica gel column chromatography to afford **62** (80 mg 88% yield, 2 steps) as colorless solide.

$[\alpha]_D^{25}$: + 38.1 (*c* 1.0, $CHCl_3$). **^{1}H NMR (200 MHz, MeOH-d4):** δ 1.20–1.70 (m, 16H), 2.13 (t, *J* = 2.3 Hz, 1H), 2.15–2.22 (m, 2H), 3.59 (dd, *J* = 5.4, 11.7 Hz, 1H), 3.66 (d, *J* = 3.4 Hz, 1H), 3.67–3.86 (m, 3H), 3.92 (t, *J* = 5.8 Hz 1H); **^{13}C NMR (50 MHz, $CDCl_3$):** δ 19.0 (t), 26.7 (t), 29.7 (t), 29.8 (t), 30.2 (t), 30.6 (t), 30.6 (t), 30.7 (t), 34.7 (t), 63.4 (t), 69.4 (s), 79.1 (d), 82.7 (d), 84.1 (d), 84.5 (d), 85.1 (d) ppm; **ESI-MS *m/z*:** cacld $[(C_{16}H_{28}O_4Na)^+]$ 307.19 found 307.05 ($[M+Na]^+$, 100%).

Compound (61):



The heterogeneous mixture of alkyne **62** (17 mg, 60 µmol) and 7-hydroxy-3-azidocoumarin (25 mg, 119 µmol), sodium ascorbate (11 mg, 60 µmol), copper (II) sulphate pentahydrate (8 mg, 47 µmol) in *t*-butanol and water (3:2, 5 mL) was vigorously stirred for one day in the dark at room temperature. The *t*-butanol was removed and the residue was diluted with water/ethyl acetate and layers are separated water layer was washed with ethyl acetate twice and combined organic layers are washed with saturated sodium chloride, dried over sodium sulphate and concentrated in vacuum, resulted crude was purified over column chromatography (90:10 EtOAc/Pet ether) and afforded **61** (45 mg, 83% yield) as yellow solid. **$[\alpha]_D^{25}$:** + 30.1 (*c* 0.3, $CHCl_3$). **^{1}H NMR (200 MHz, MeOH-d4):** δ 1.25–1.50 (m, 12H), 1.55–1.89 (m, 4H), 2.79 (t, *J* = 7.2 Hz, 2H), 3.63 (dd, *J* = 5.4, 11.7 Hz, 1H), 3.70 (d, *J* = 3.4 Hz, 1H), 3.77 (dd, *J* = 5.4, 8.0 Hz, 1H), 3.78–3.84 (m, 2H), 3.97 (d, *J* = 5.6 Hz, 1H), 6.81 (d, *J* = 2.0 Hz, 1H), 6.90 (dd, *J* = 2.0, 8.6 Hz, 1H), 7.64 (d, *J* = 8.6 Hz, 1H), 8.34 (s, 1H), 8.46 (s, 1H); **^{13}C NMR (50 MHz, MeOH-d4):** δ 26.2 (t), 26.7 (t), 29.7 (t), 30.2 (t), 30.4 (t, 2C), 30.6 (t), 30.6 (t), 30.7 (t), 34.7 (t), 63.4 (t), 79.1 (d), 82.7 (d), 84.1 (d), 84.5 (d), 103.1 (d), 103.4 (d), 112.0 (s), 115.5 (d), 120.9 (s), 131.8 (d), 136.9 (d), 156.4 (s), 158.1 (s), 164.2 (s) ppm; **ESI-MS *m/z*:** cacld $[(C_{25}H_{33}N_3O_7Na)^+]$ 510.22 found 510.22 ($[M+Na]^+$, 100%).

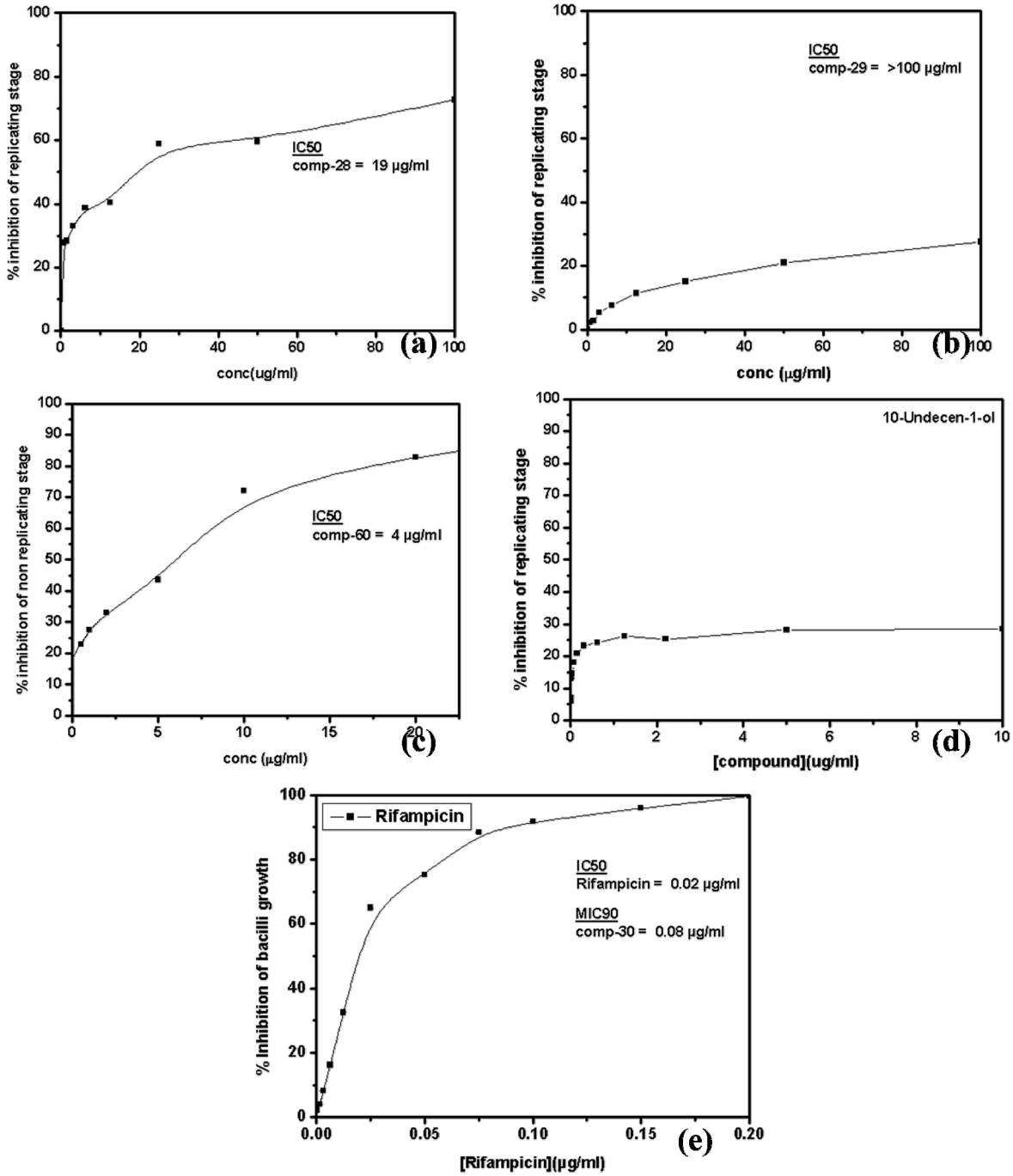
3.2 Protocols for Evaluation of compounds against *M. Bovis* BCG and Cytotoxicity assesment

Growth conditions for Bacterial strains and cell lines: *M. Bovis* BCG Culture:

Sub-culturing of the Strain was routinely done in Dubos albumin agar slants or plates. Liquid inoculum of the organism was added in Dubos tween albumin broth medium and incubated at 37 °C and 150 rpm shaking conditions. One percent of 1.0 O.D at 620 nm of the culture was used as standard inoculum size for all the experiments, yielding a final inoculum of approximately 105 CFU/ml. viable cell counts were measured by following an earlier described method.[63] **Thp-1, MCF-7 and HL-60 cell line:** Cells obtained were at passage numbers 90-93. Cells were cultured at 37 °C with 5% CO_2 and 90% humidity in T-75 tissue culture flasks (Corning 430641). Cells were maintained in the culture medium used Minimum essential medium (MEM) without phenol red with 2.5 mM L-glutamine (Sigma, US) and supplemented with 10% fetal bovine serum.

Effect of inhibitors on growth of the bacilli:

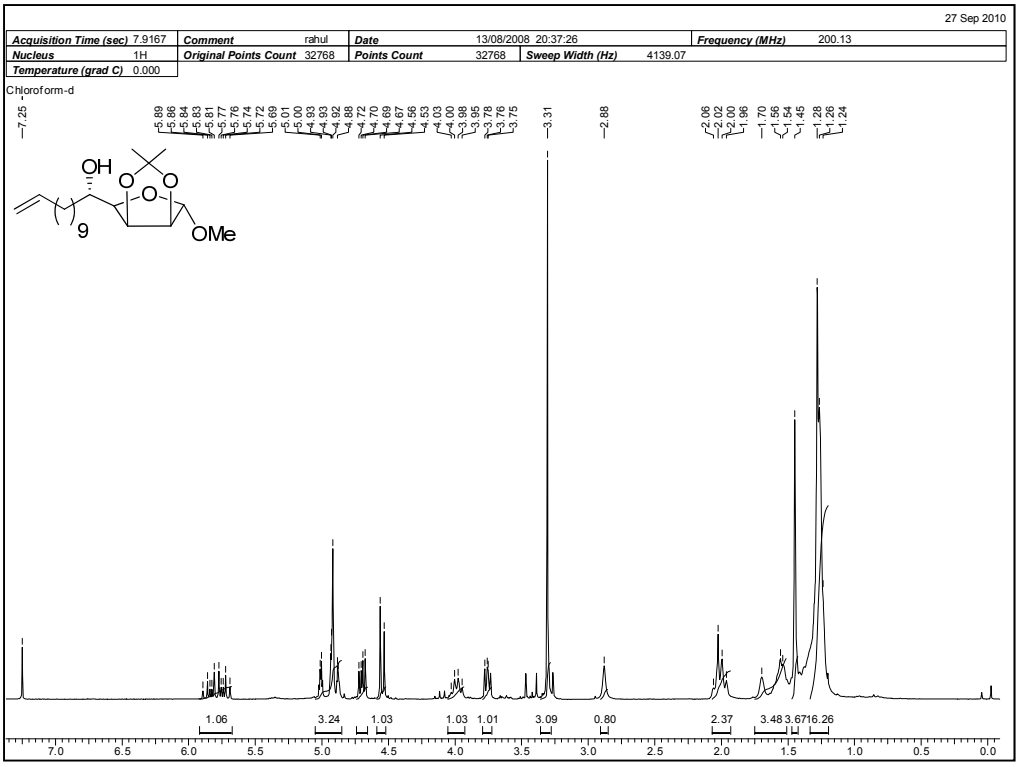
The inhibitory effect of the compounds was monitored by following an earlier described method.[64] Briefly, 247.5 µl of 1% of 1 O.D at 620 nm *M. bovis* BCG culture was taken in Dubos medium without ADS enrichment in microplate wells. Already having 2.5 µl of inhibitor in DMSO. The plate was then covered with a sterile sealer and incubated at 37 °C for 8 days. Then the growth of the bacilli was measured by reading the absorbance at 620 nm as well as by determining CFU/ml of the culture at different time intervals. The lowest concentration of drugs yielding a differential absorbance (620 nm) of approximately zero was defined as MIC. The well representing positive controls have only DMSO (vehicle) and the negative controls were having rifampicin and Ethambutol at their respective IC_{50} values.



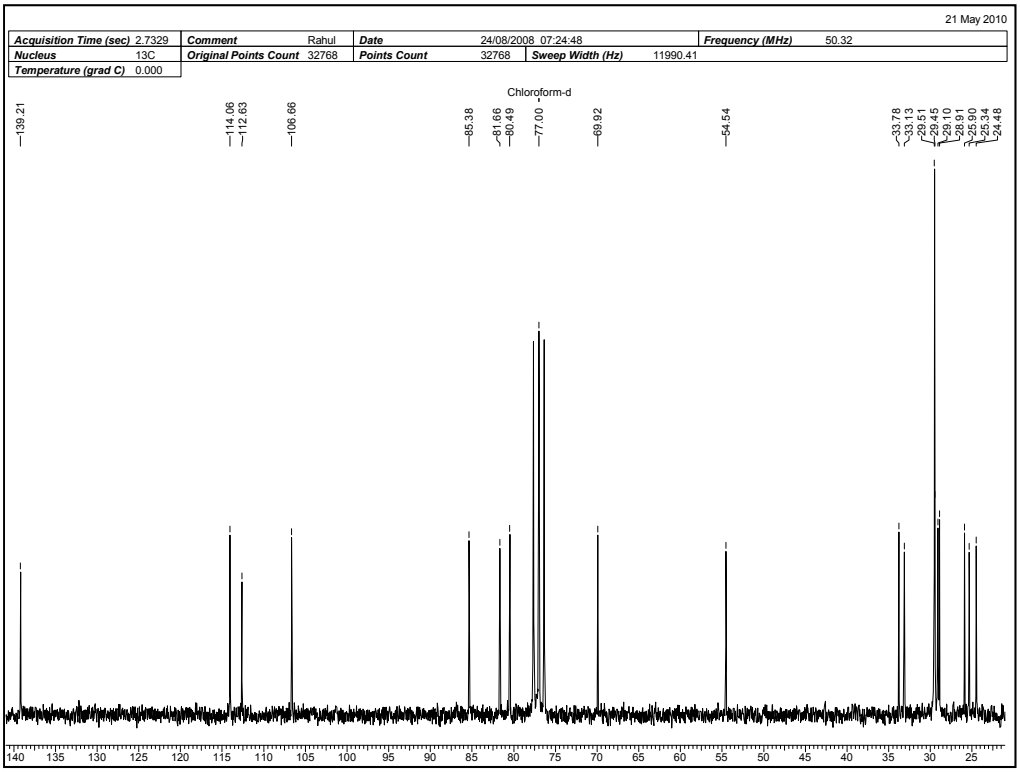
Experimetnal figure 1: Dose dependent effect of antimycobacterial inhibitors: **a)** compound **28** (■), **b)** compound **29** (■), **c)** Compound **60** (■), **d)** 10-uncen-1-ol (■), **e)** rifampicin (■) against *M. bovis* BCG . Doses of all Compounds dissolved in DMSO ranging from 0.1 to 100 µg/ml were added at the time of inoculation and O.D was measured after 8 days of incubation at 620nm. Experiments were carried out three times with duplicate cultures and results are mean ± SD.

Cytotoxicity assessment of the inhibitors: To test the in vitro viability/cytotoxicity of the compounds, we selected THP-1, A431 and HL-60 human cell lines. The effect of the compounds were examined on metabolic function of the cells using a standard MTT assay.[65] a widely adopted method of measuring cellular proliferation. The MTT assay consists of a yellow tetrazolium 3-(4,5-dimethylthiazolyl)-2,5-diphenyltetrazolium bromide) dye that is reduced by mitochondrial dehydrogenase enzymes to form purple formazan which gets precipitated within viable cells. The concentration of formazan formed is proportional to the number of viable cells. These crystals of reduced MTT dye i.e. formazan, absorbs light at 490 nm. The absorbance of light at 490 nm should be proportional to the viable cell count. For this, 100µl of the culture containing 10,000 cells/ml was added to each of the 96 wells of the tissue culture plate containing 2.5µl of inhibitors. Then, the cells were incubated in a CO_2 incubator supplied with 5% CO_2, 95% humidity at 37 ºC. At the end of the incubation period, 10µl MTT (5mg/ml) was added and incubated at 37 ºC for 1 h. Then, add 200µl of 100% isopropyl alcohol in all the wells and keep it at rt for 4 h. The reading was taking at 490nm by using a plate reader (Model SPECTRA max PLUS^{384} from Molecular Devices, USA). In positive control there was no inhibitor added in the wells and in negative controls only medium was used instead of culture. Here, the values obtained from positive and negative controls are considered to have 100% and 0% equivalent growth of the cells respectively.

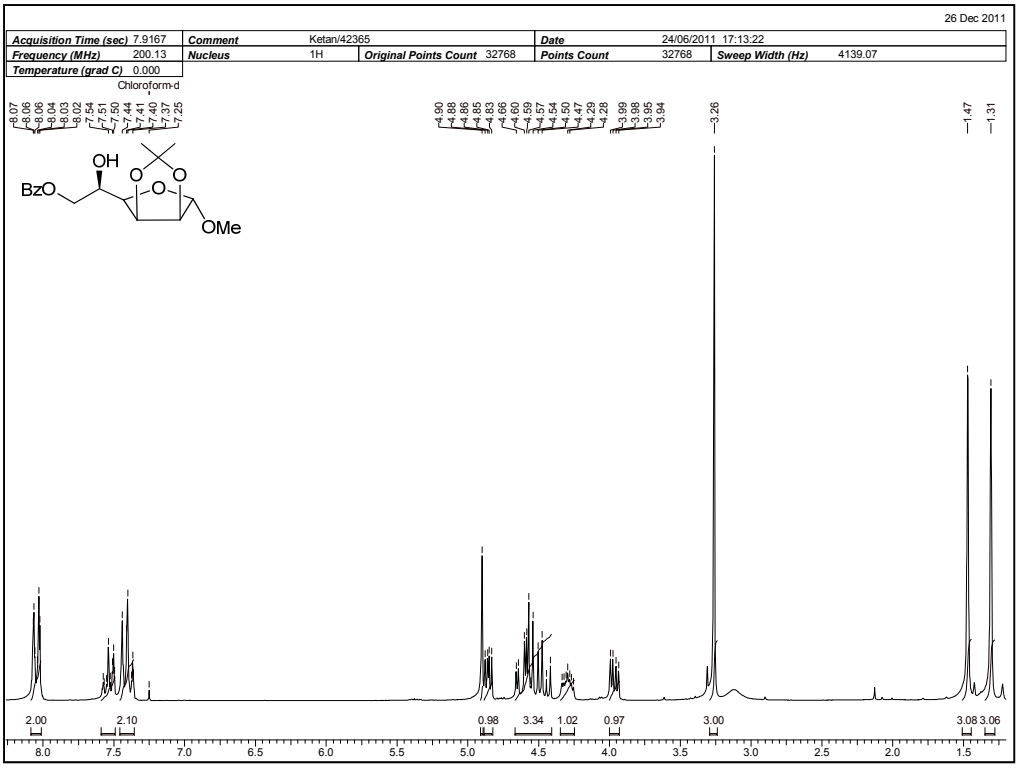
SPECTRA



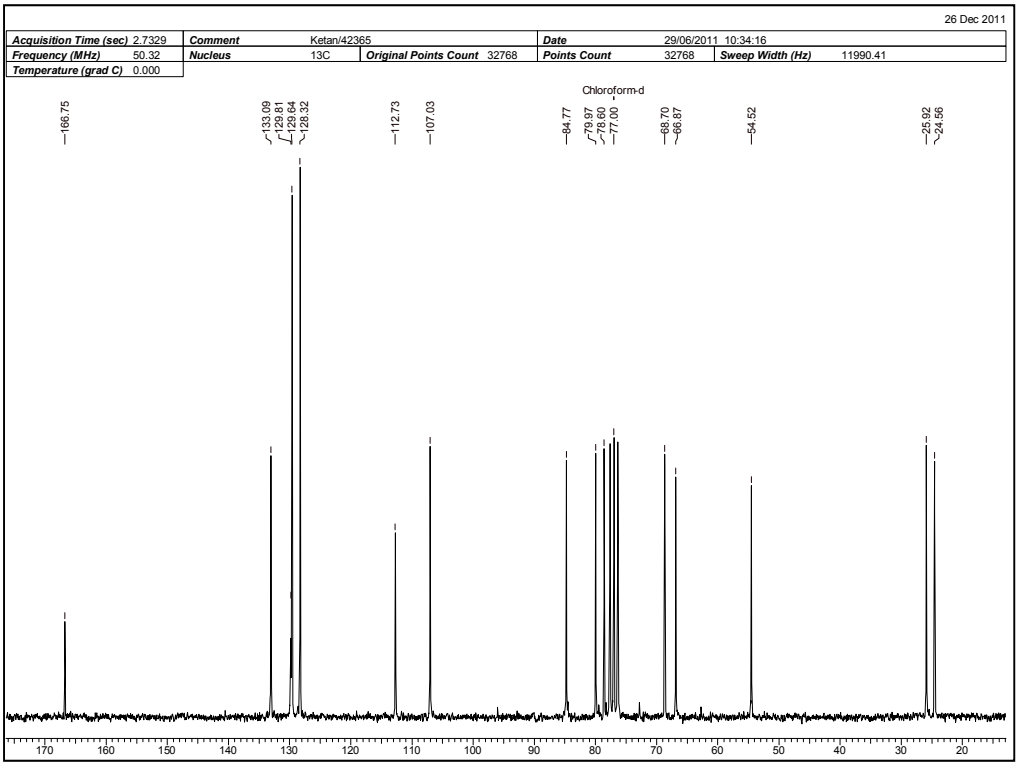
^{1}H NMR Spectrum of 7 in $CDCl_3$



^{13}C NMR Spectrum of 7 in $CDCl_3$



^{1}H NMR Spectrum of 8 in $CDCl_3$



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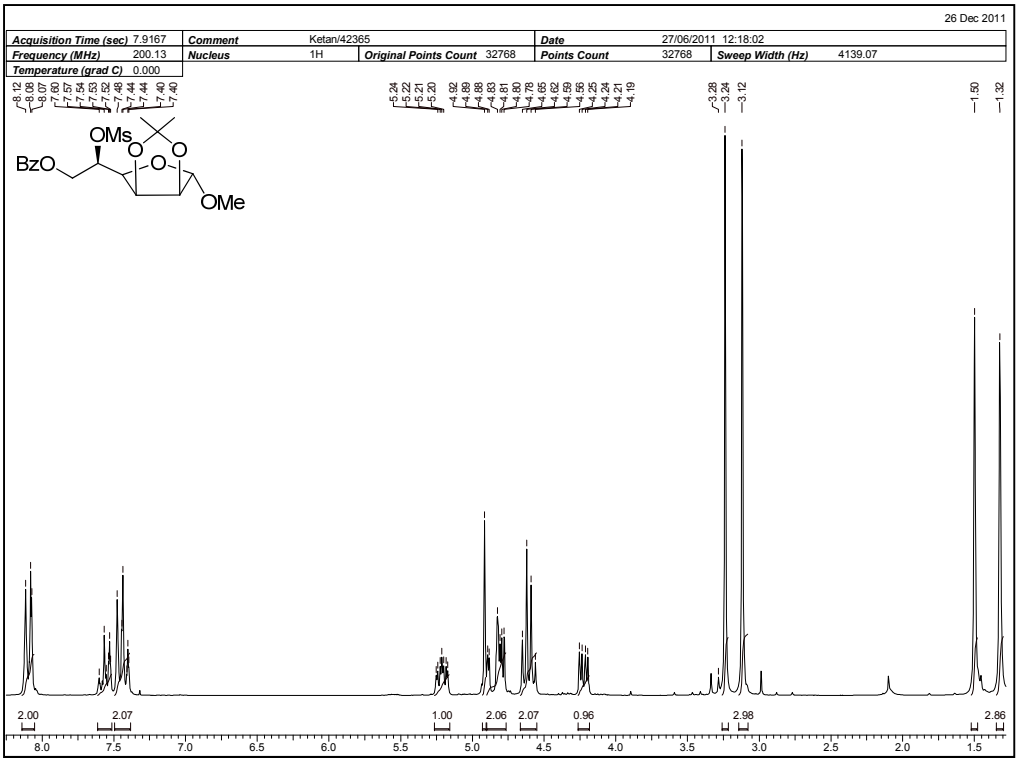
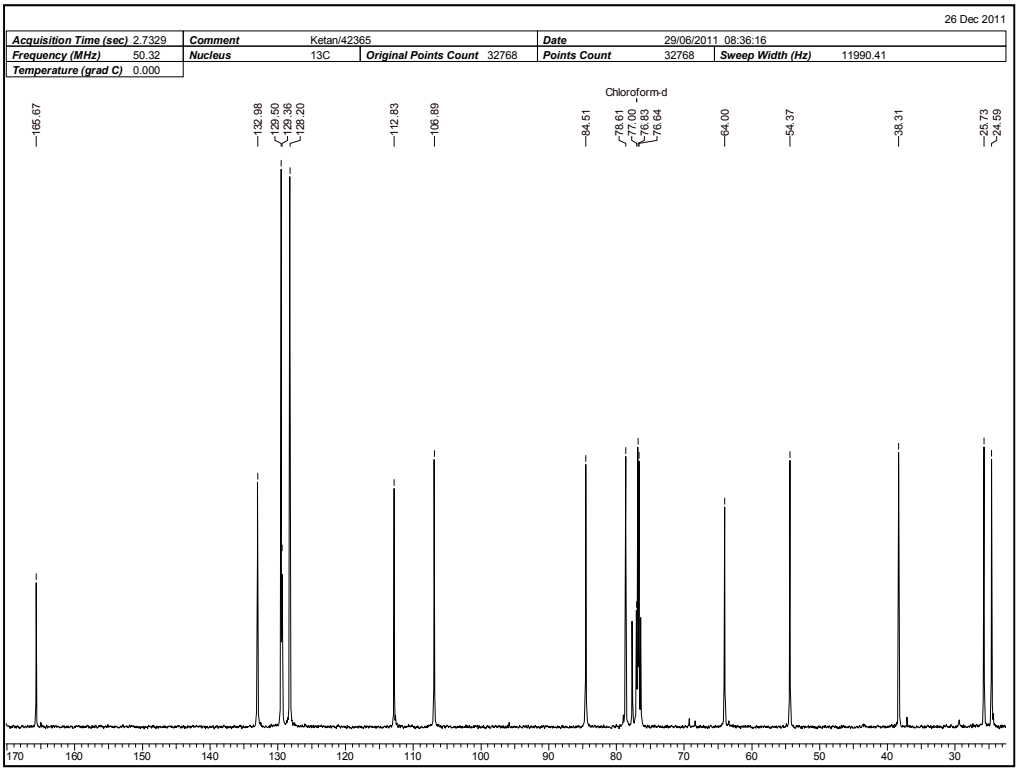


^{1}H NMR Spectrum of 9 in $CDCl_3$



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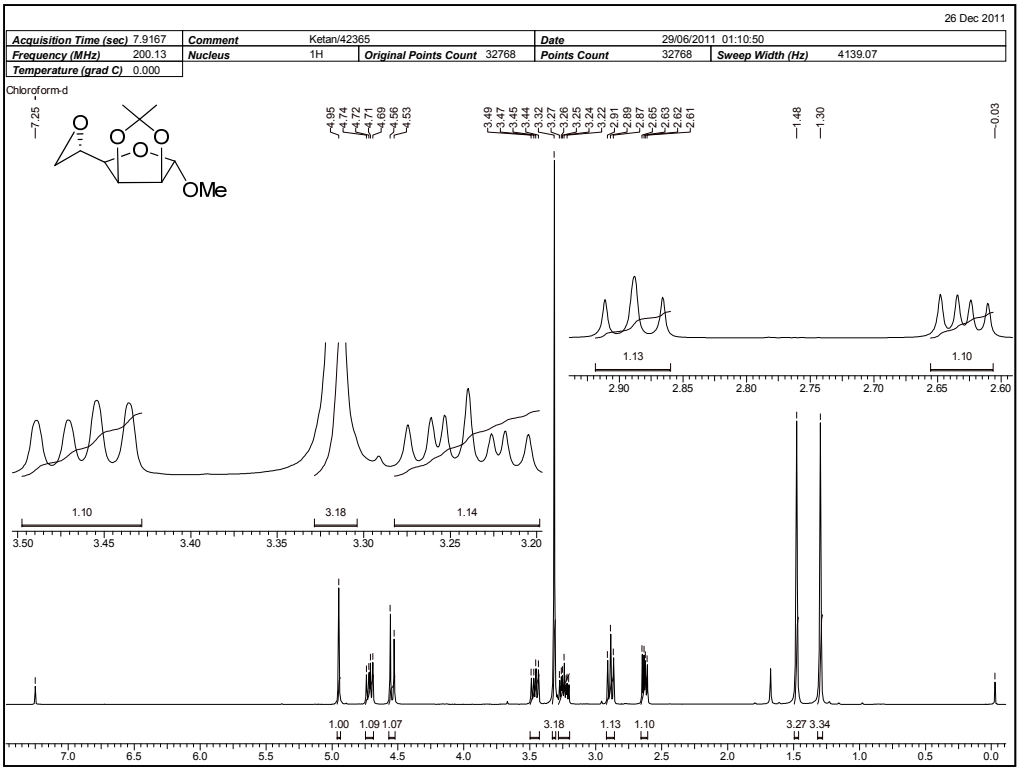
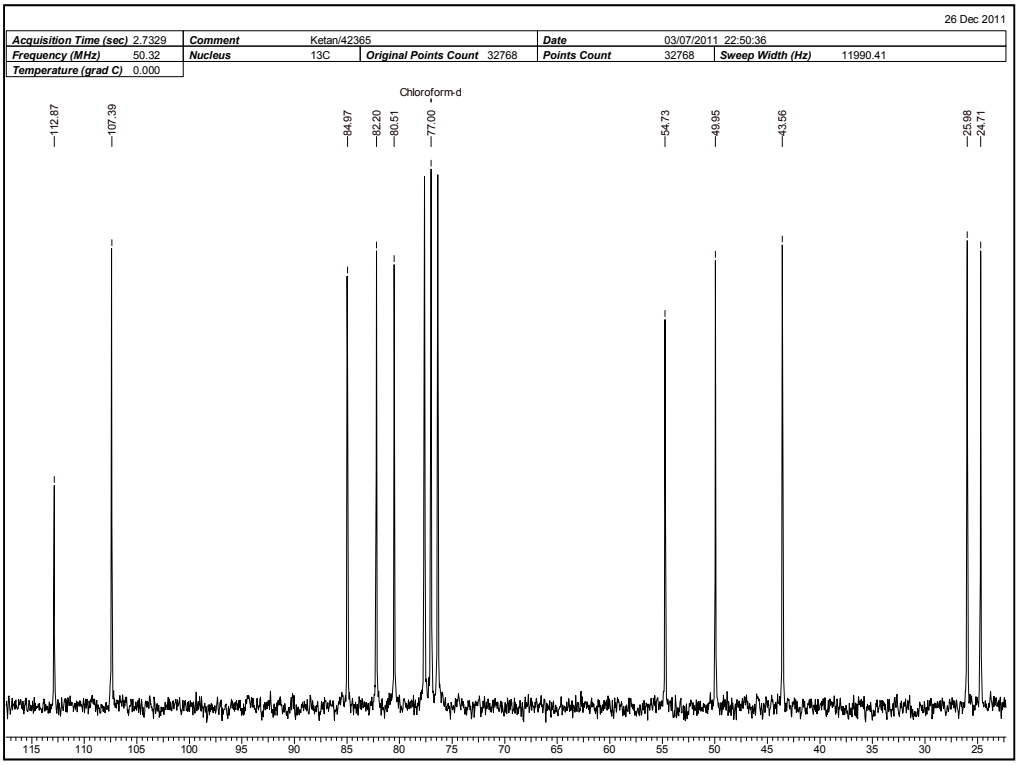


^{1}H NMR Spectrum of 10 in $CDCl_3$



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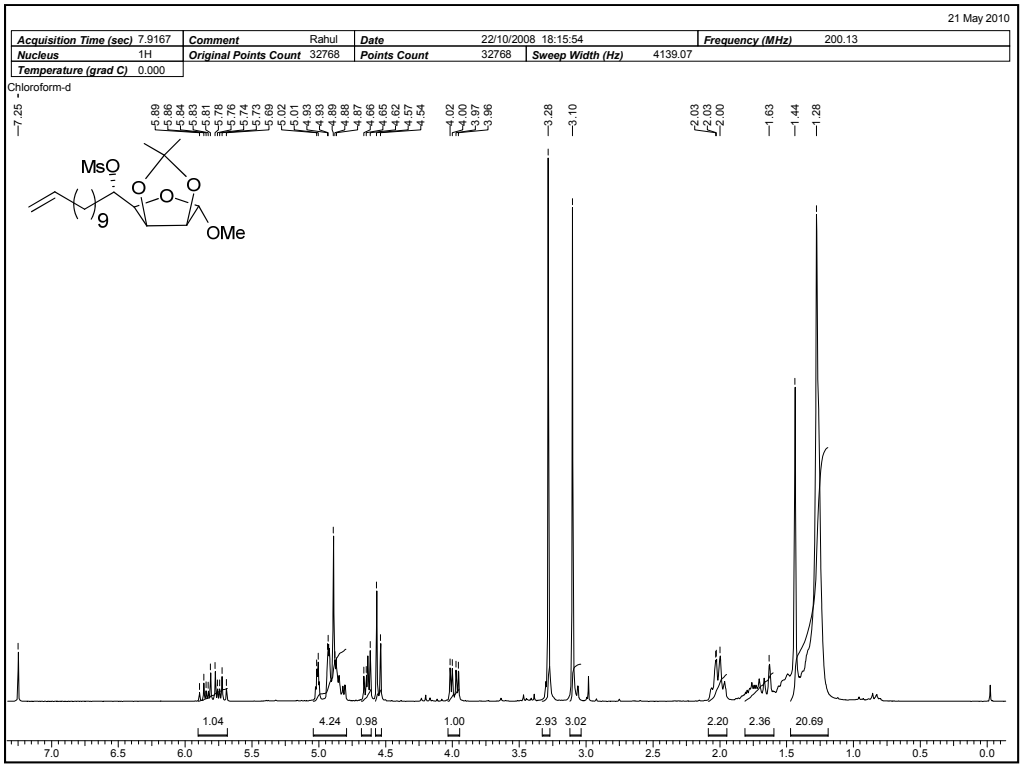

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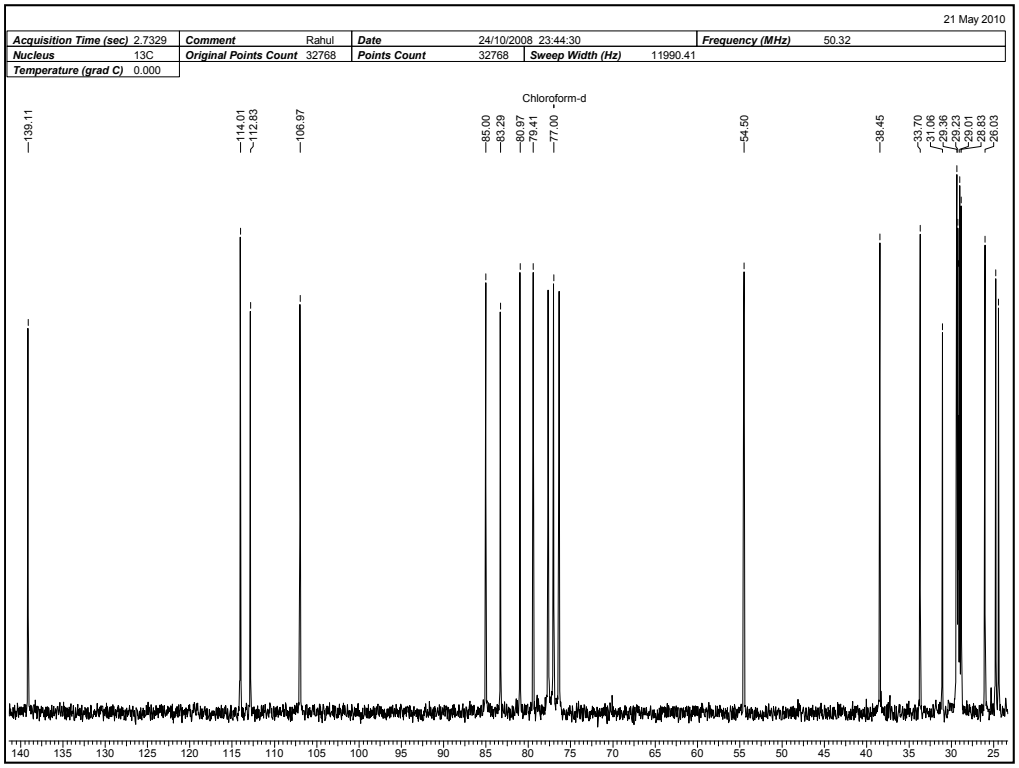

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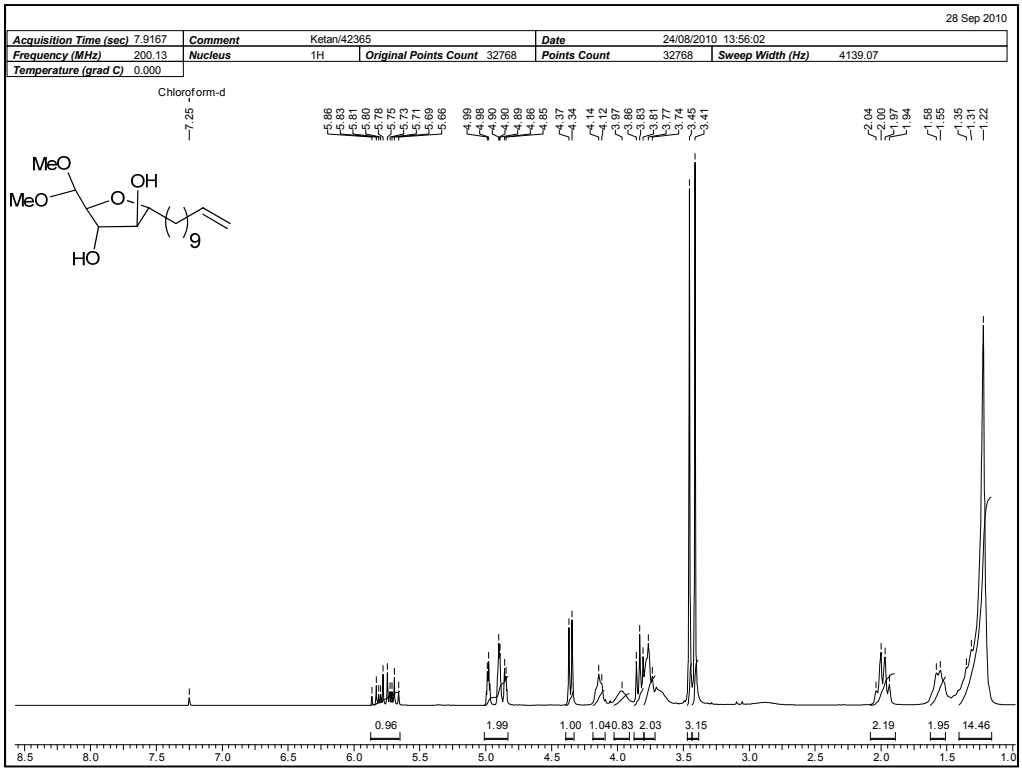

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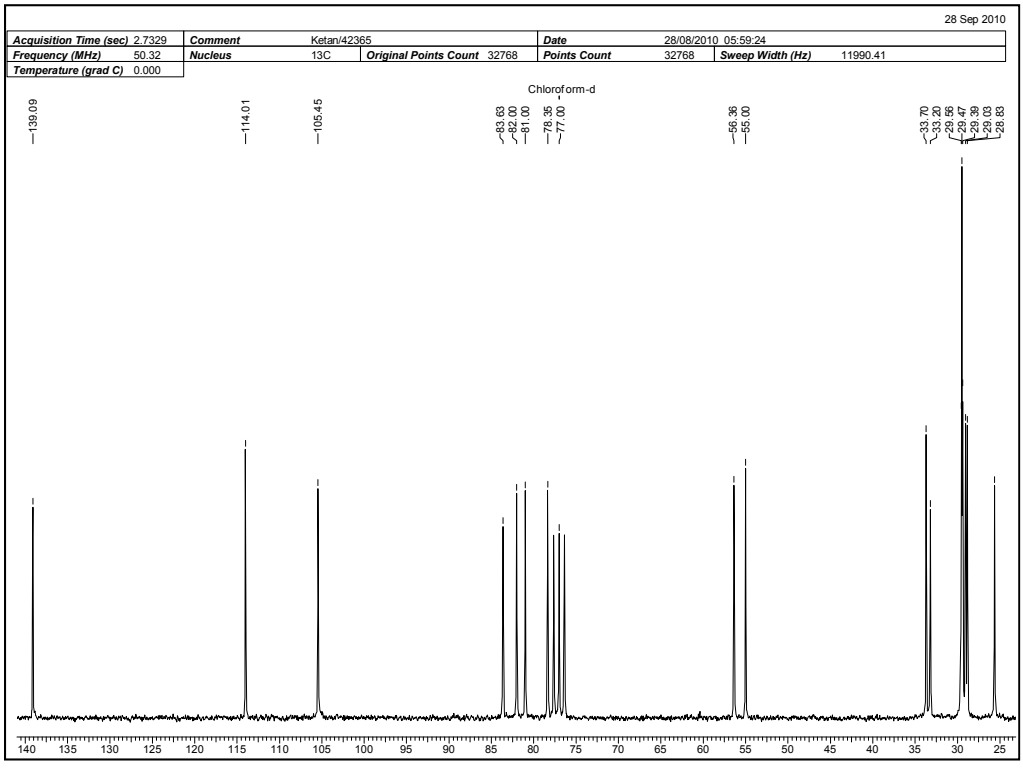
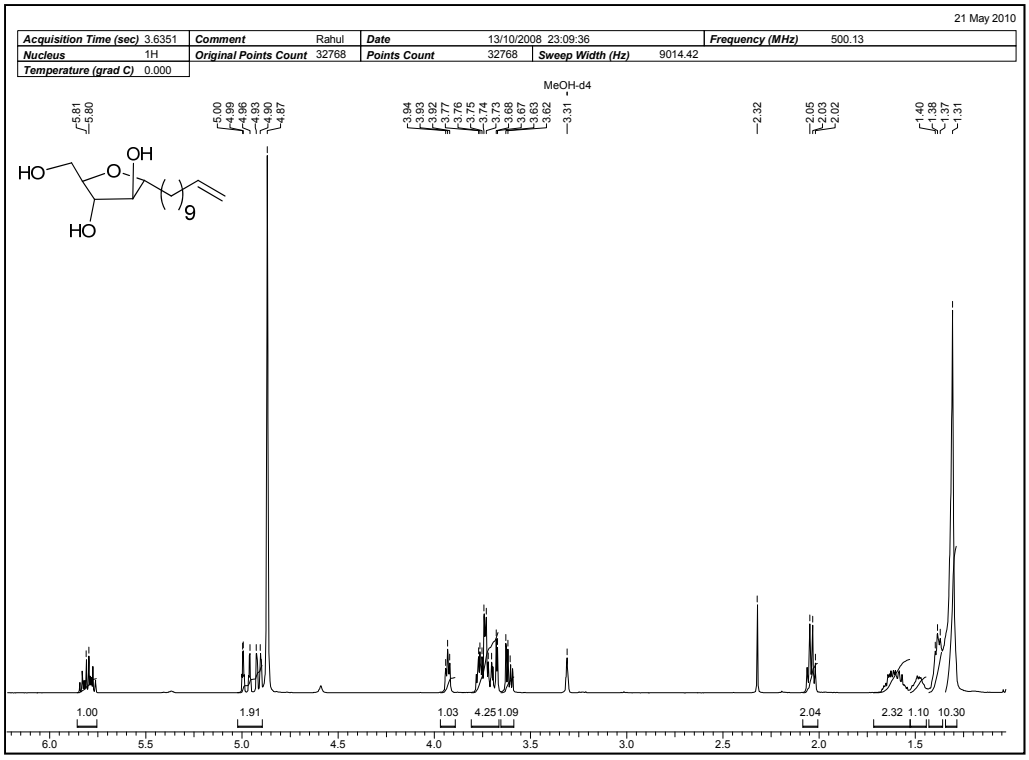
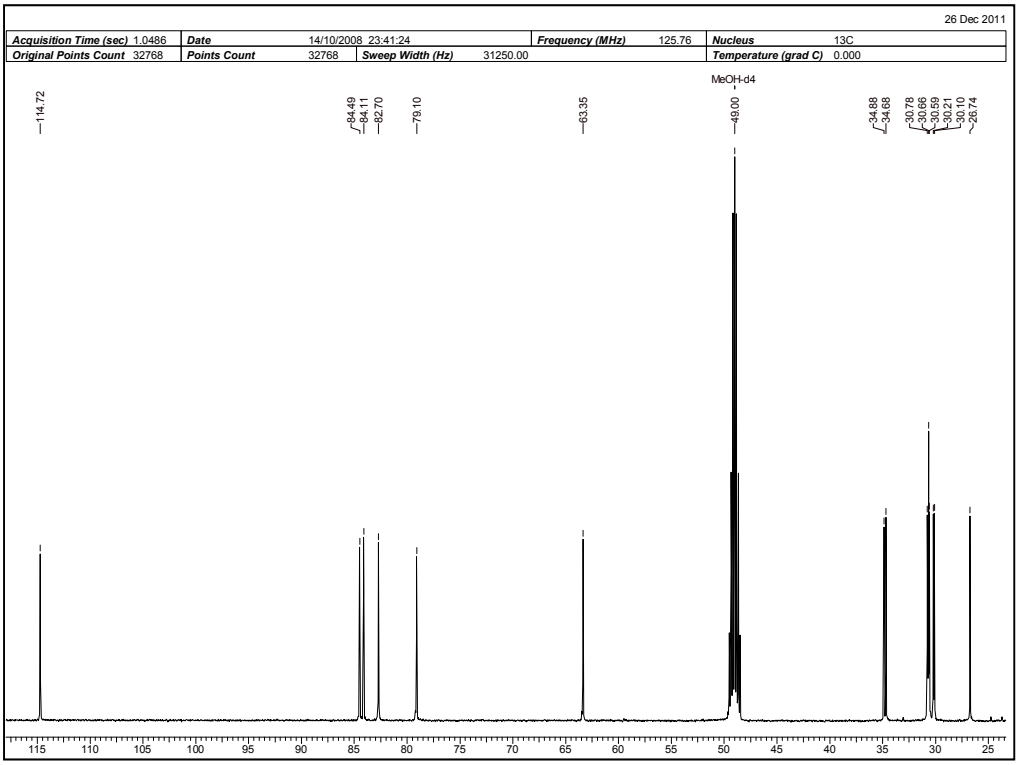


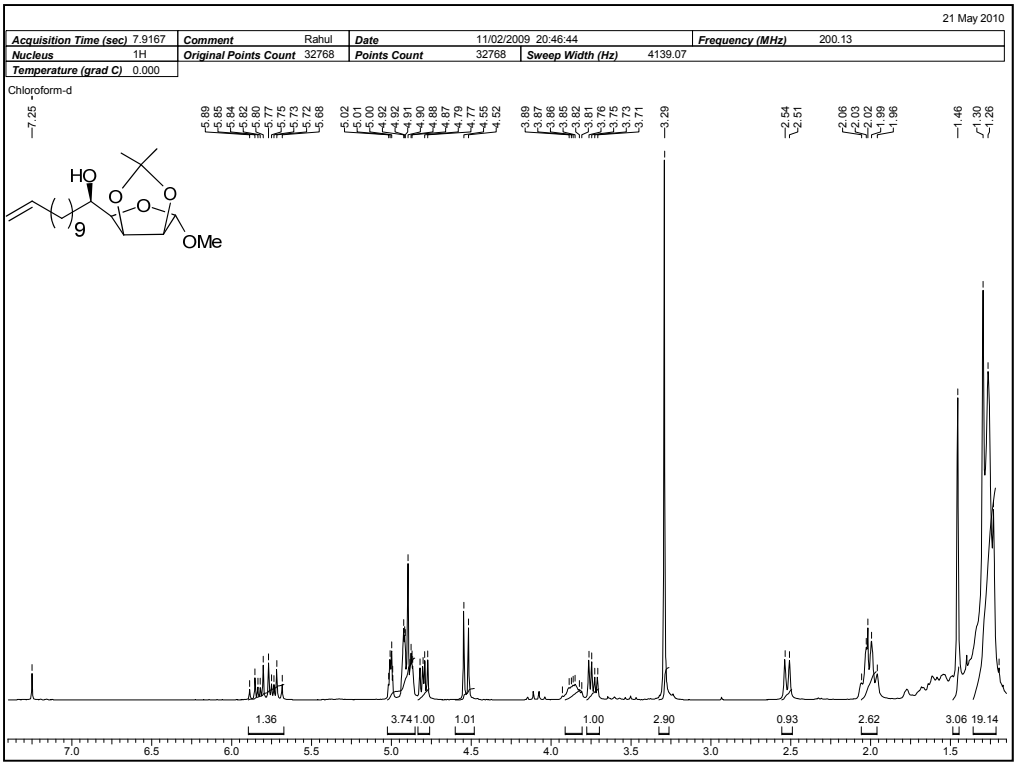
^{13}C NMR Spectrum of 12 in $CDCl_3$



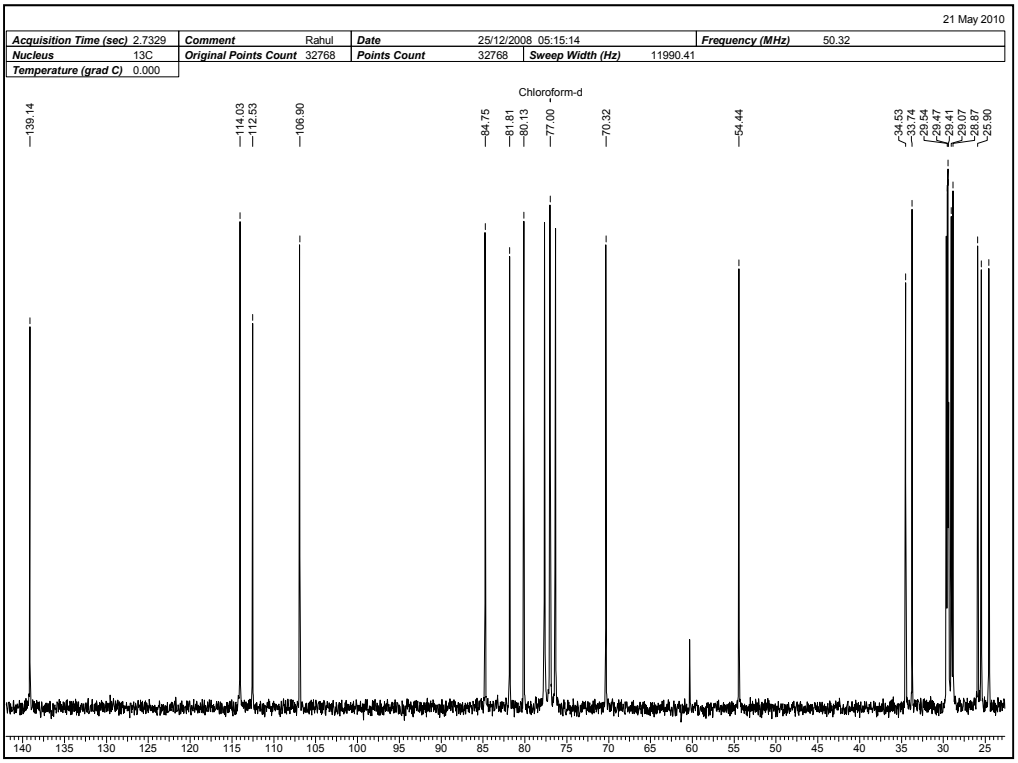
^{1}H NMR Spectrum of 3 in MeOH-D4



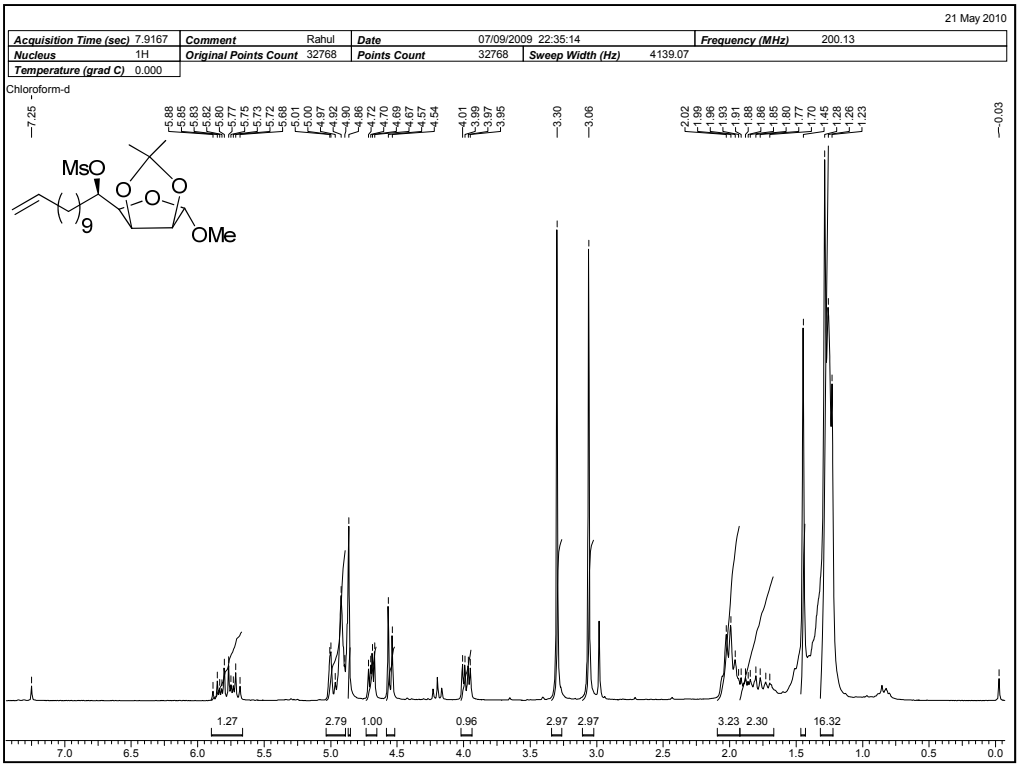
^{13}C NMR Spectrum of 3 in MeOH-D4



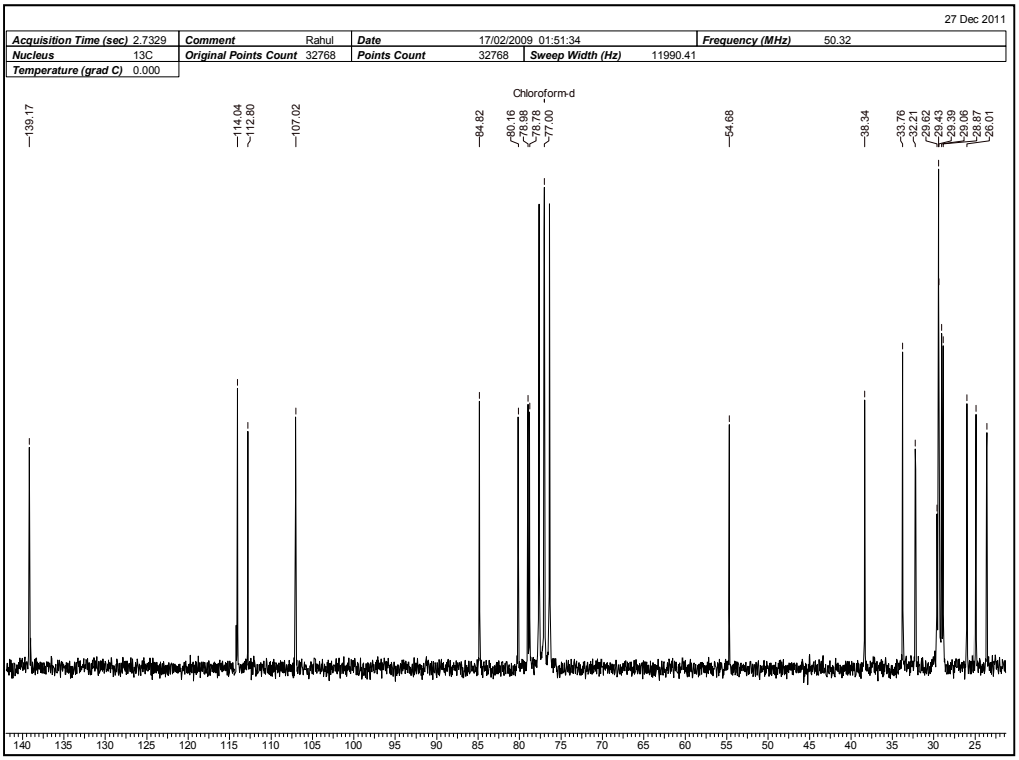
^{1}H NMR Spectrum of 6 in $CDCl_3$



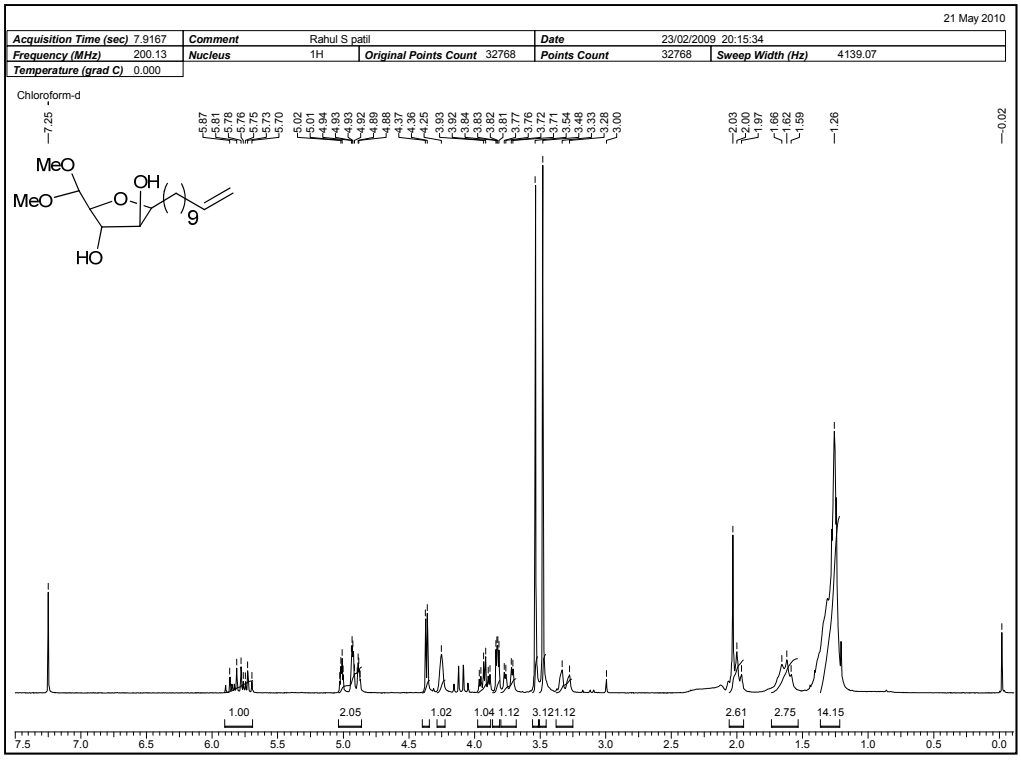
^{13}C NMR Spectrum of 6 in $CDCl_3$



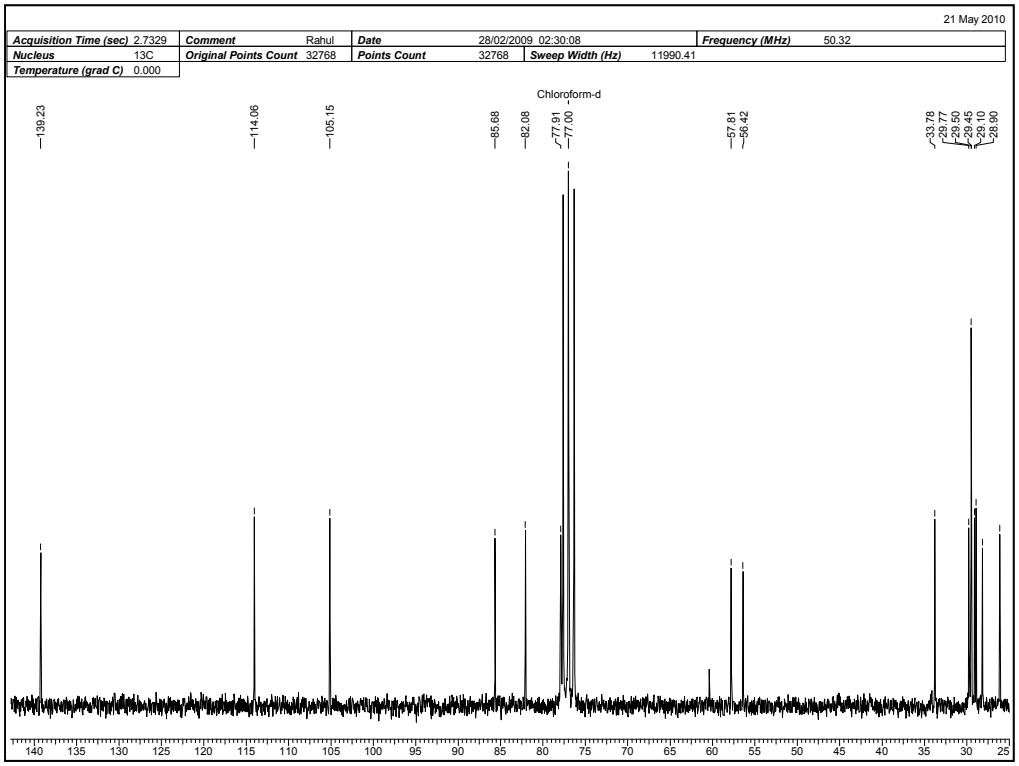
^{1}H NMR Spectrum of 4 in $CDCl_3$



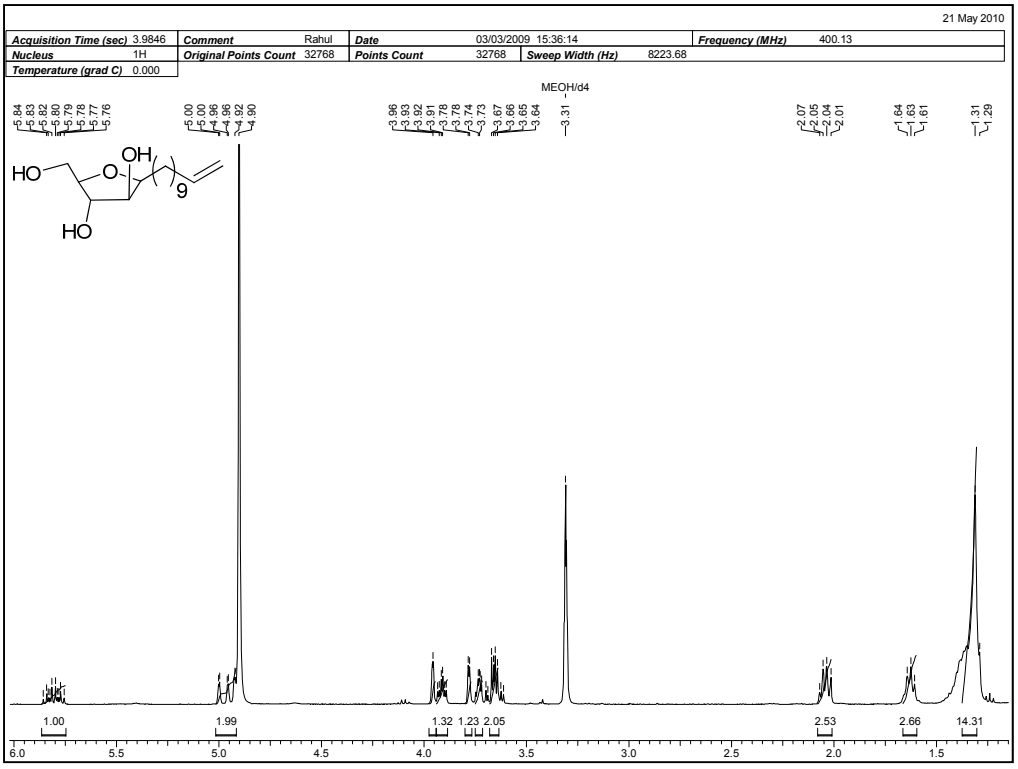
^{13}C NMR Spectrum of 4 in $CDCl_3$



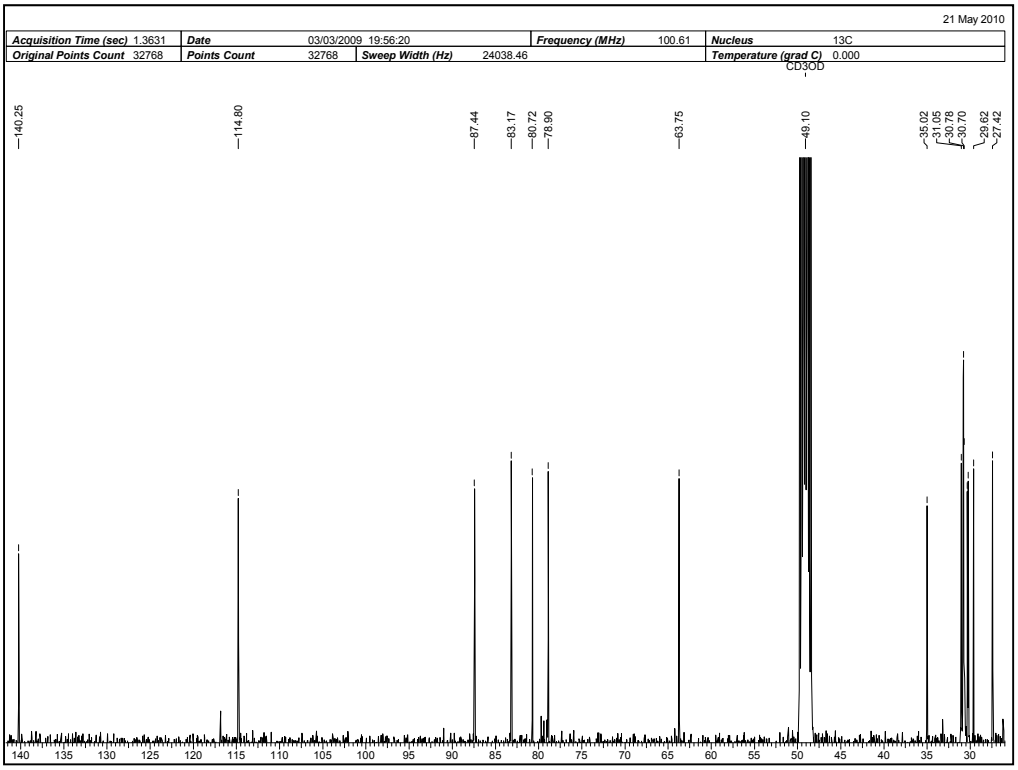
^{1}H NMR Spectrum of 5 in $CDCl_3$



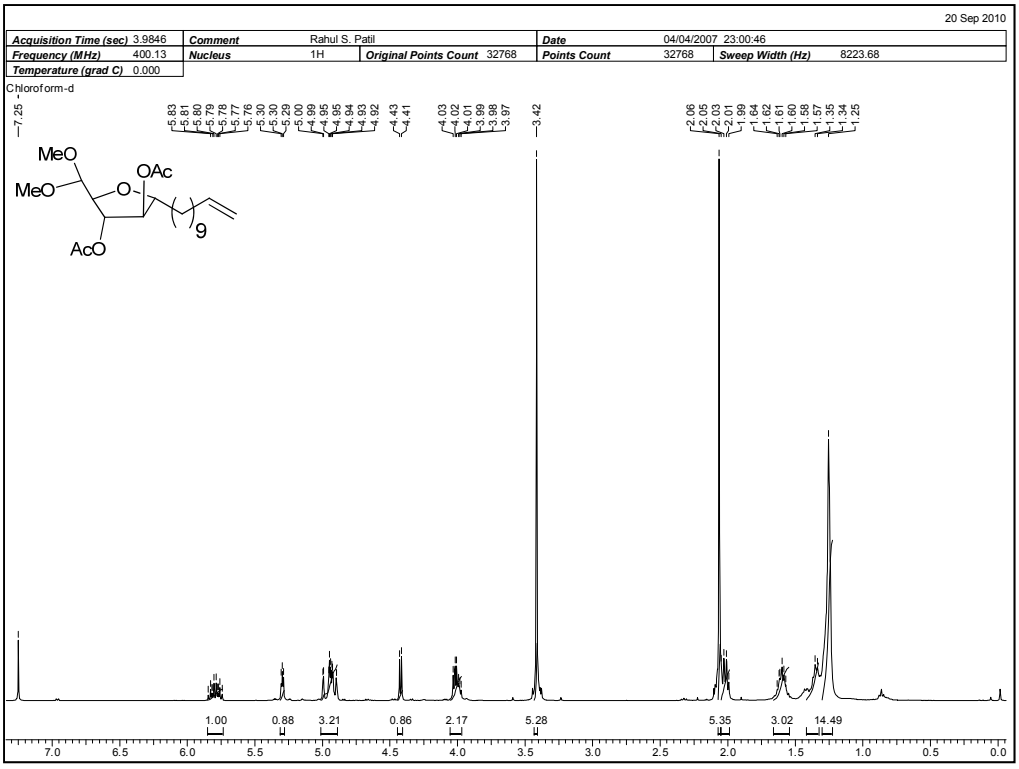
^{13}C NMR Spectrum of 5 in $CDCl_3$



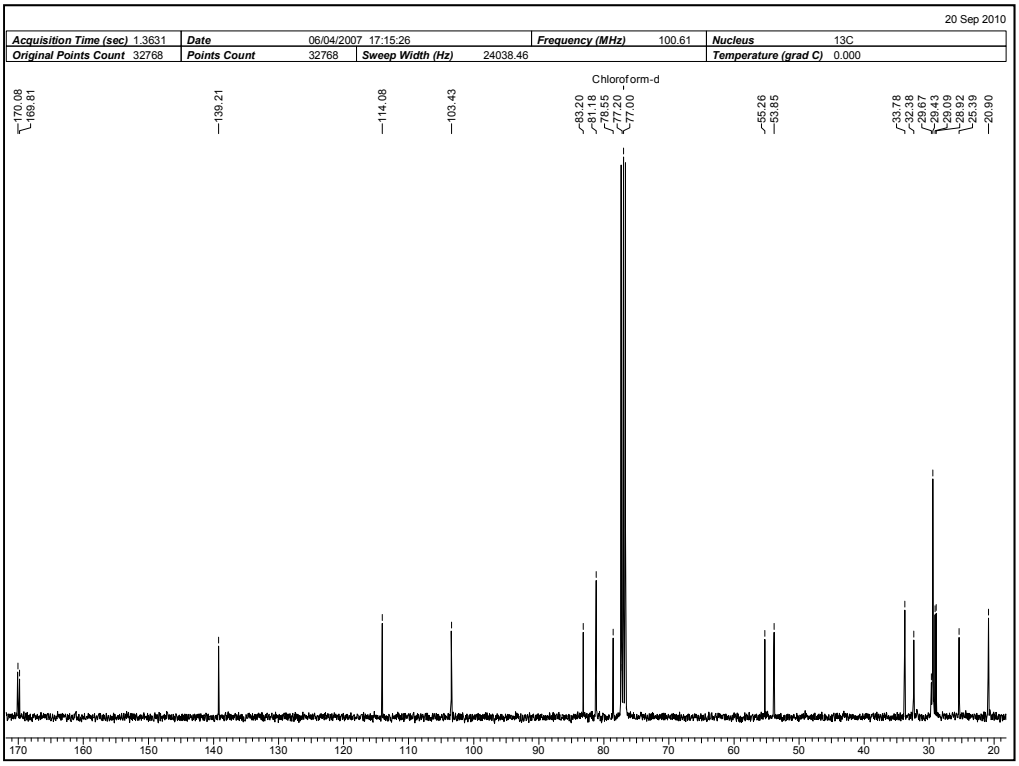
^{1}H NMR Spectrum of 2 in MeOH-D4



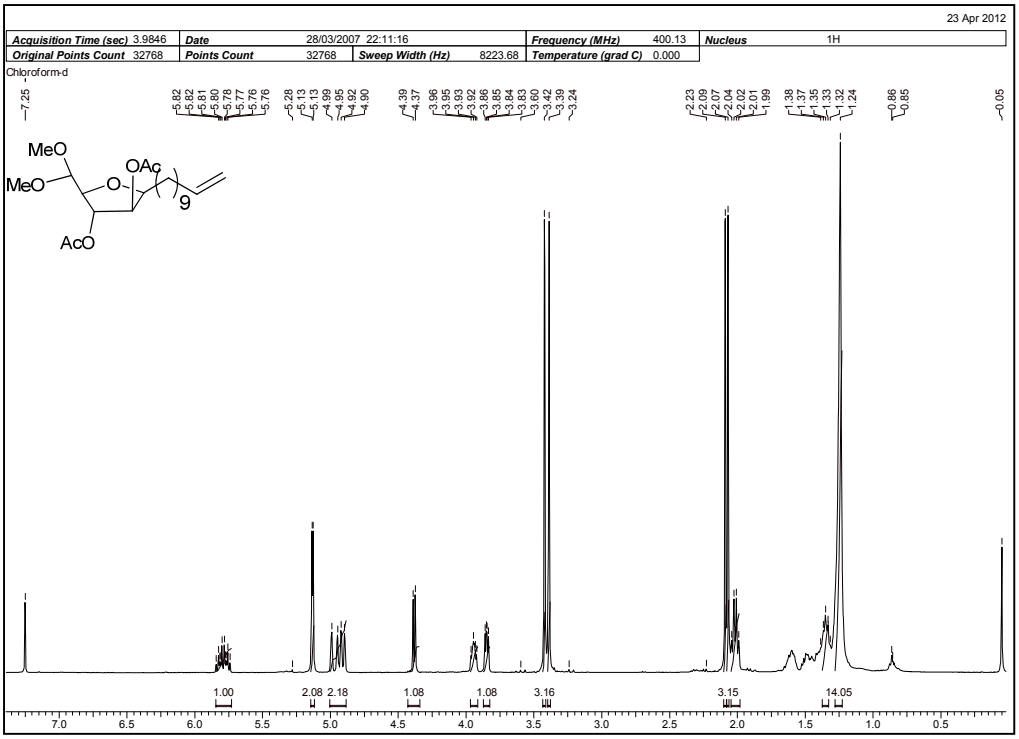
^{13}C NMR Spectrum of 2 in MeOH-D4



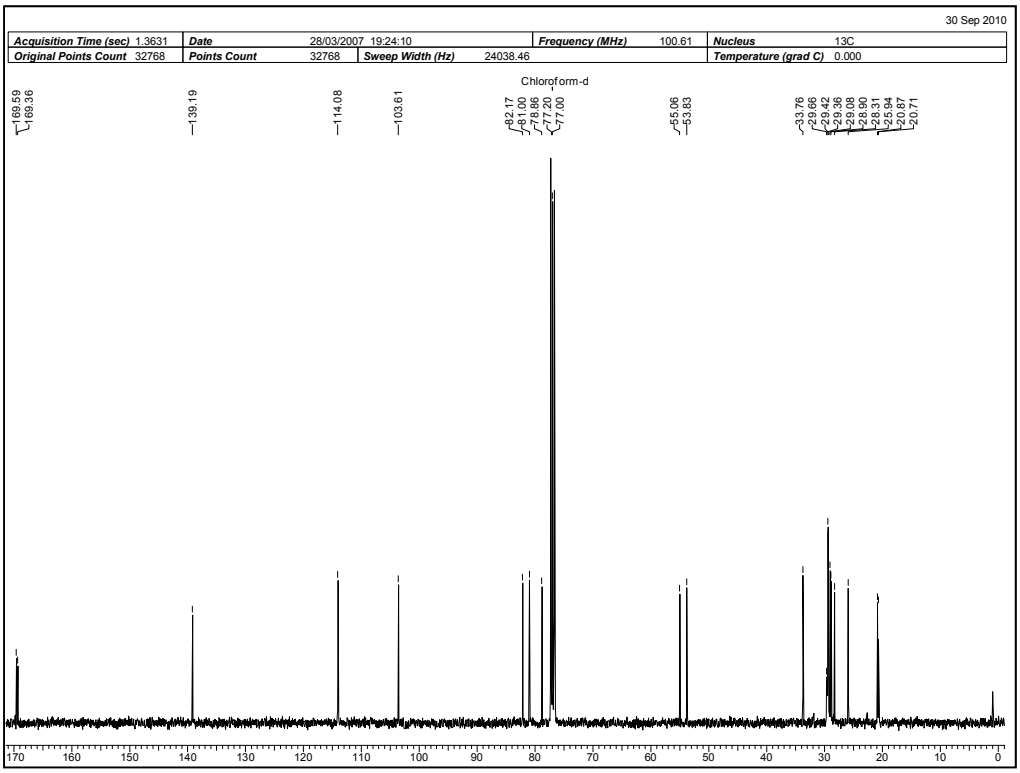
^{1}H NMR Spectrum of 13 in $CDCl_3$



^{13}C NMR Spectrum of 13 in $CDCl_3$



^{1}H NMR Spectrum of 14 in $CDCl_3$



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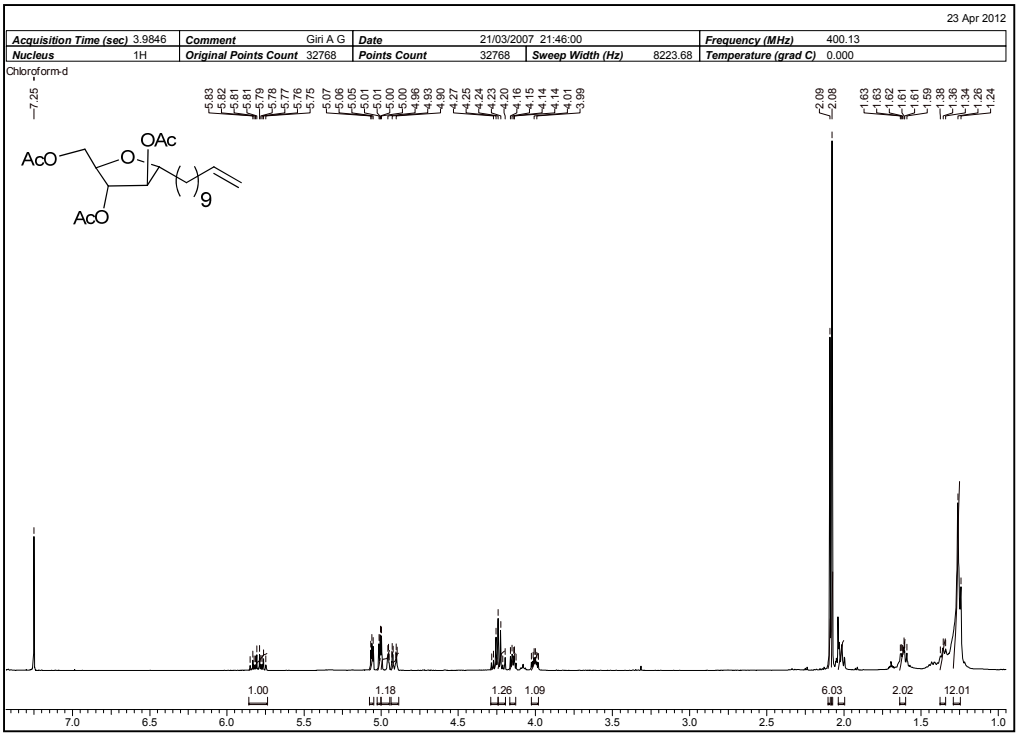

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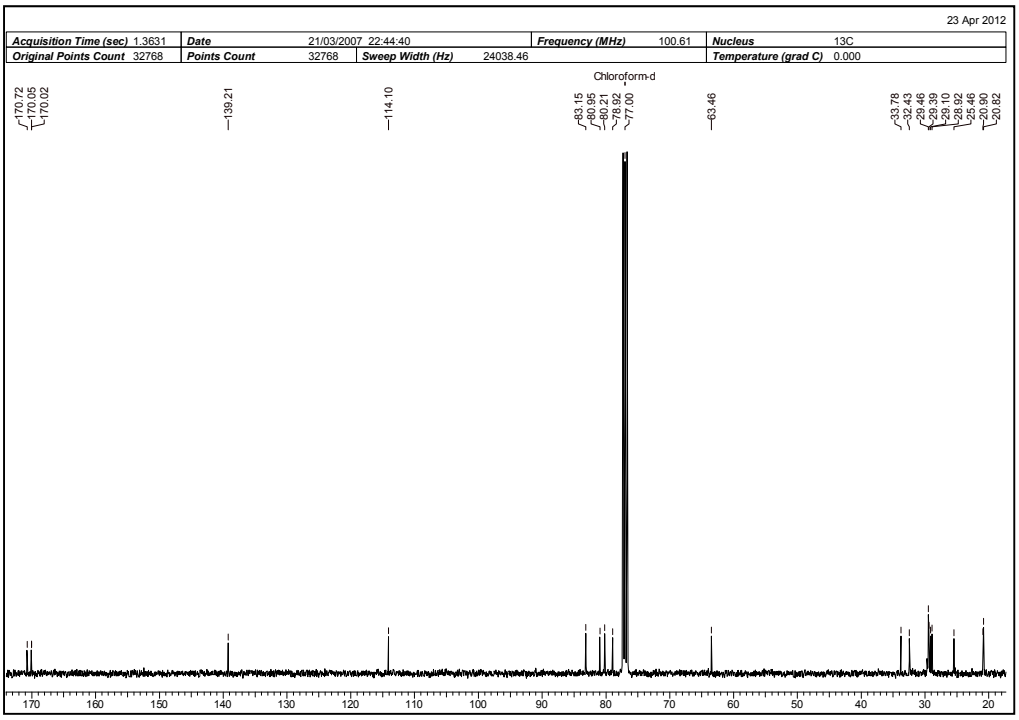
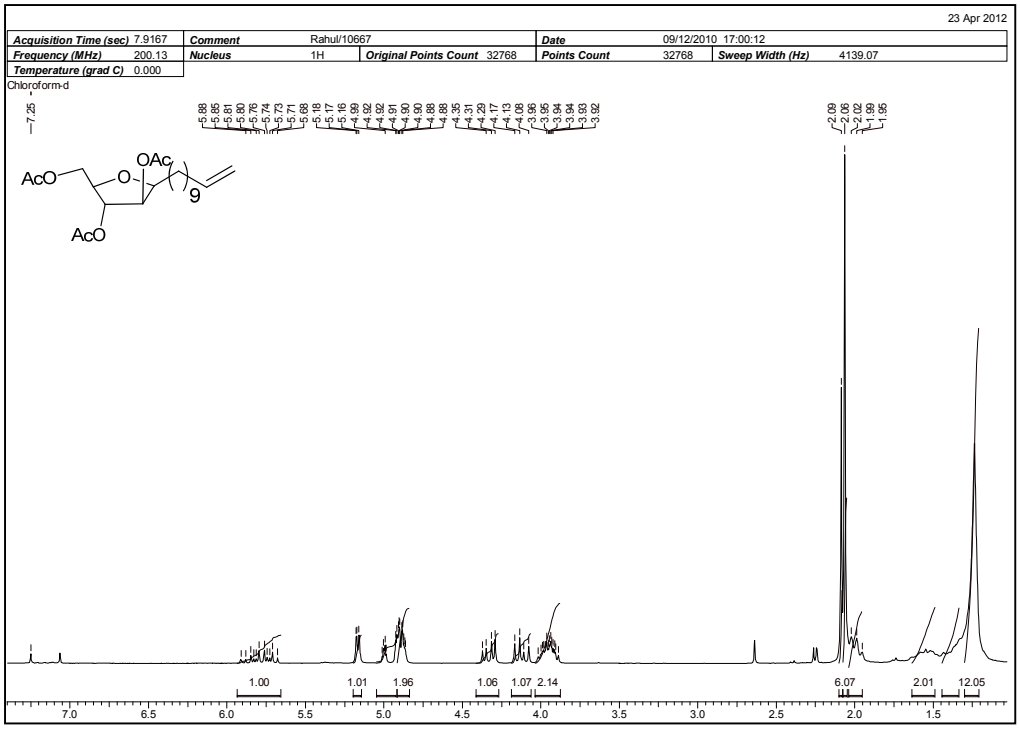


^{13}C NMR Spectrum of 15 in $CDCl_3$



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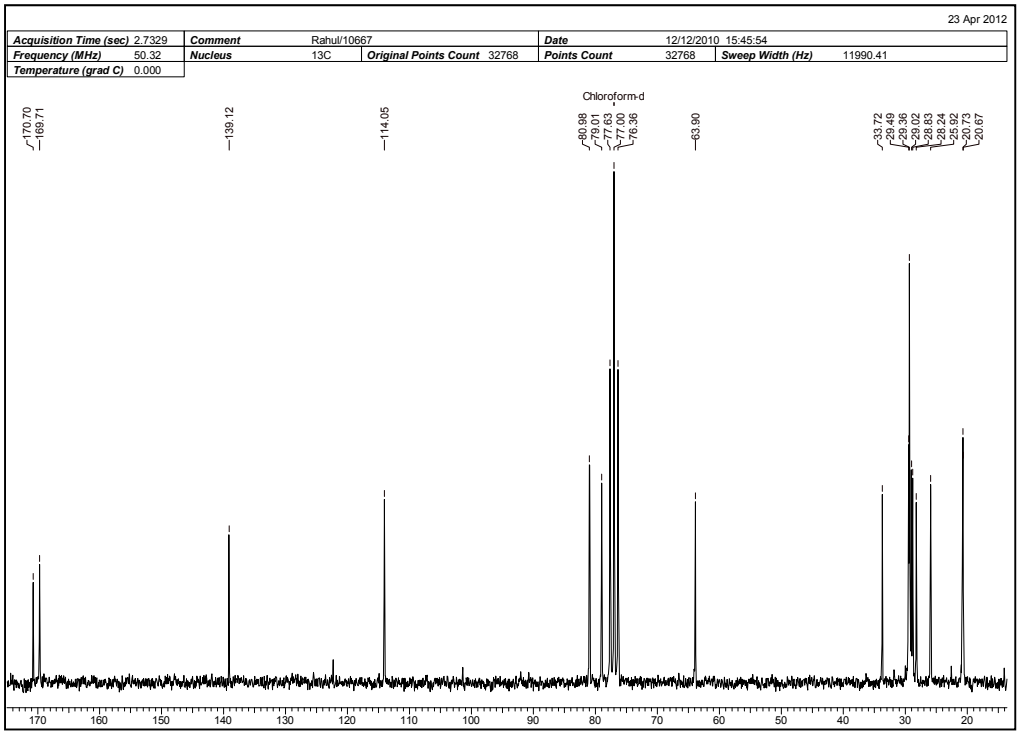
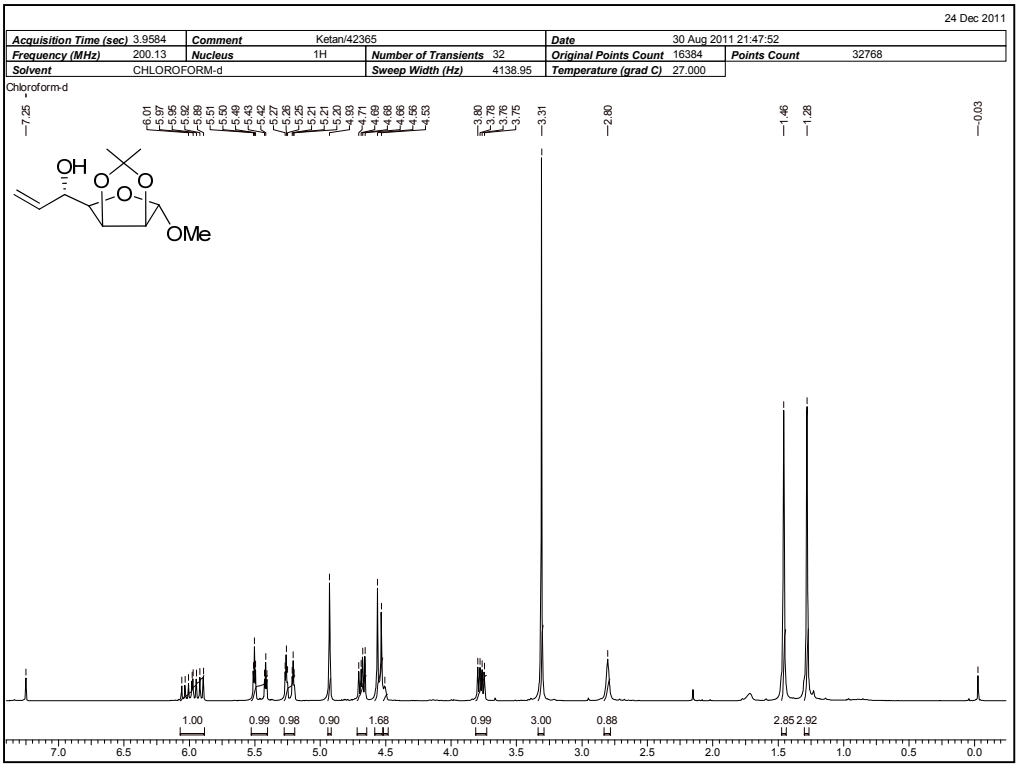


^{13}C NMR Spectrum of 16 in $CDCl_3$



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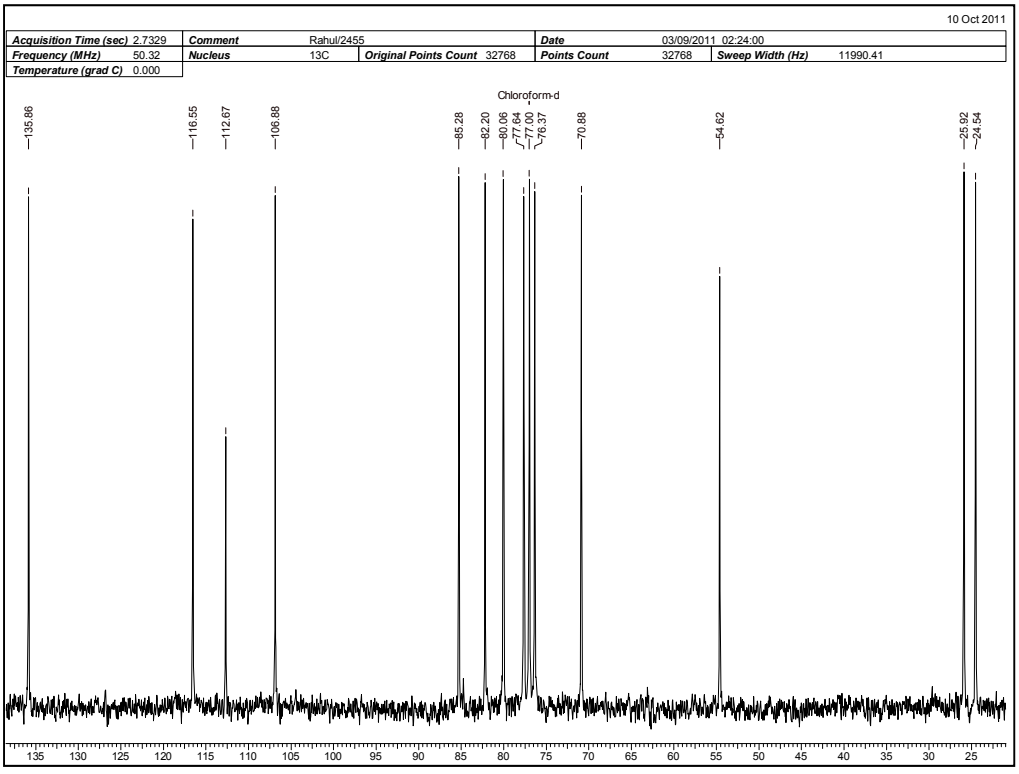
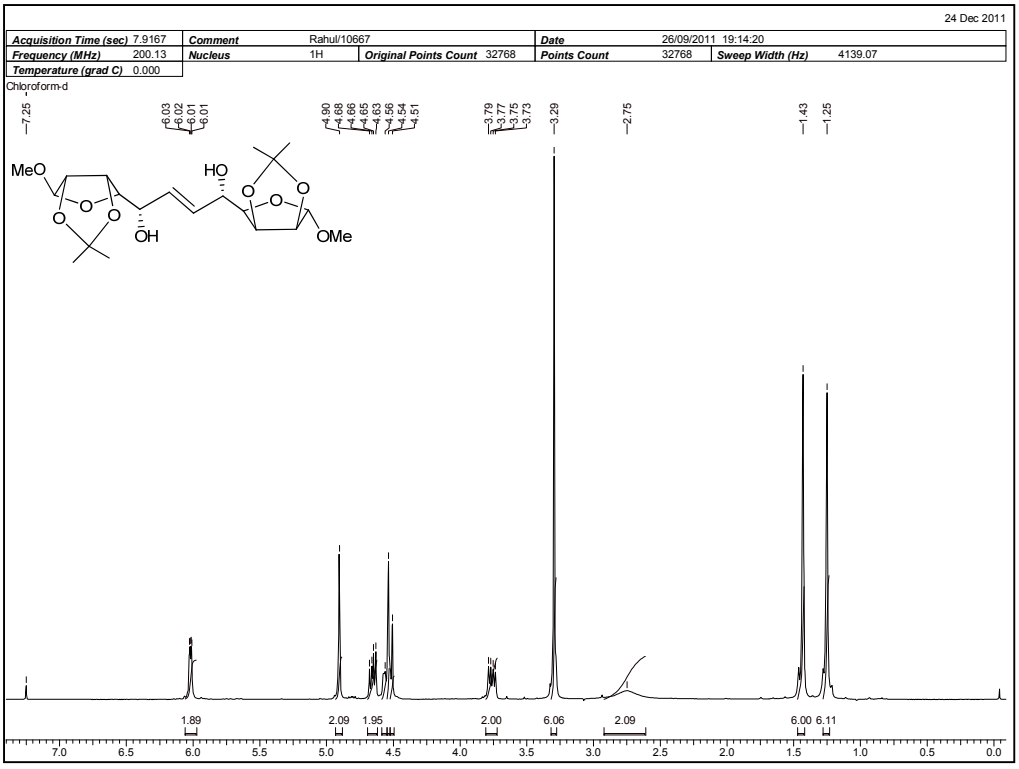


^{13}C NMR Spectrum of 19 in $CDCl_3$



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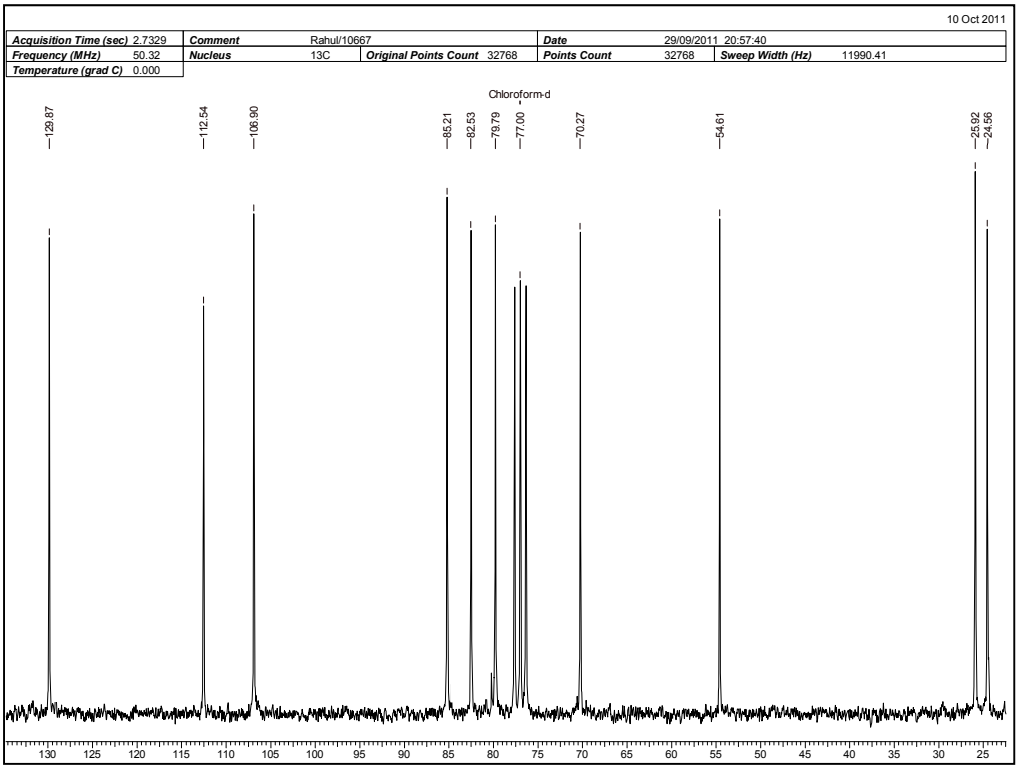

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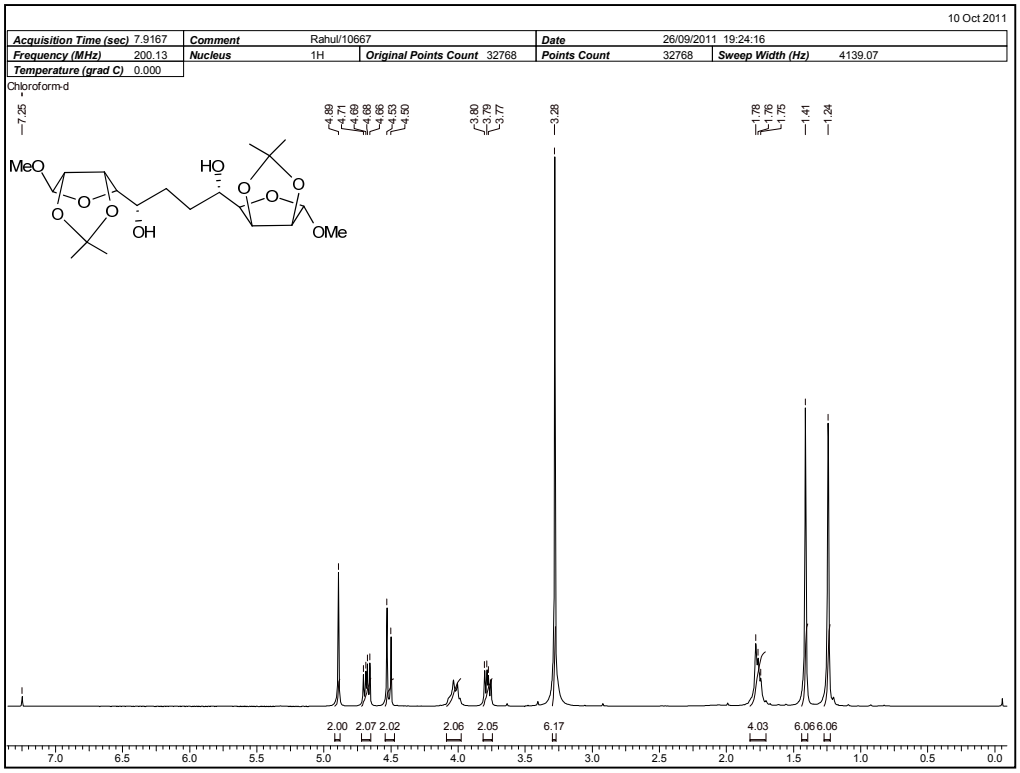

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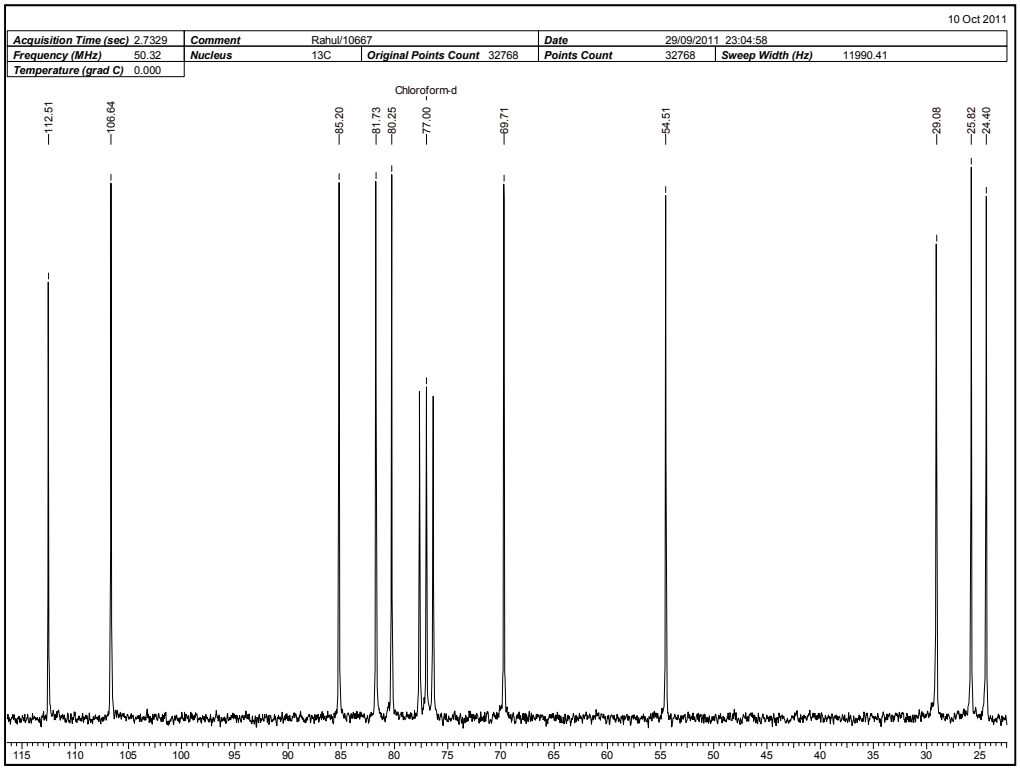
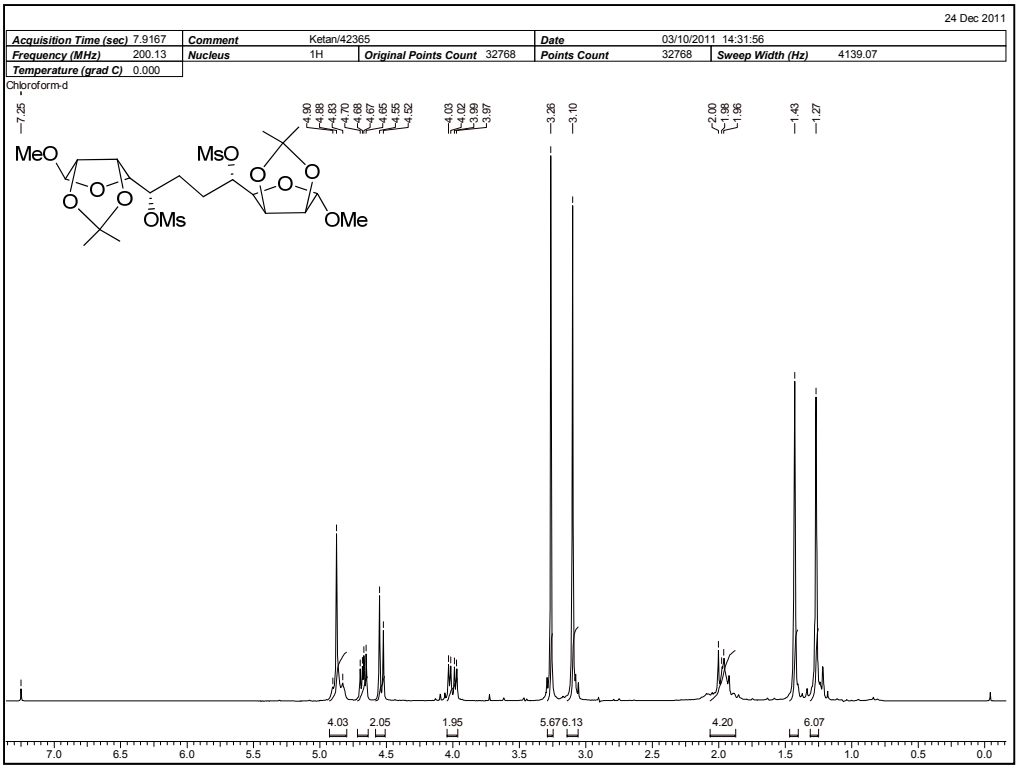


^{13}C NMR Spectrum of 22in $CDCl_3$



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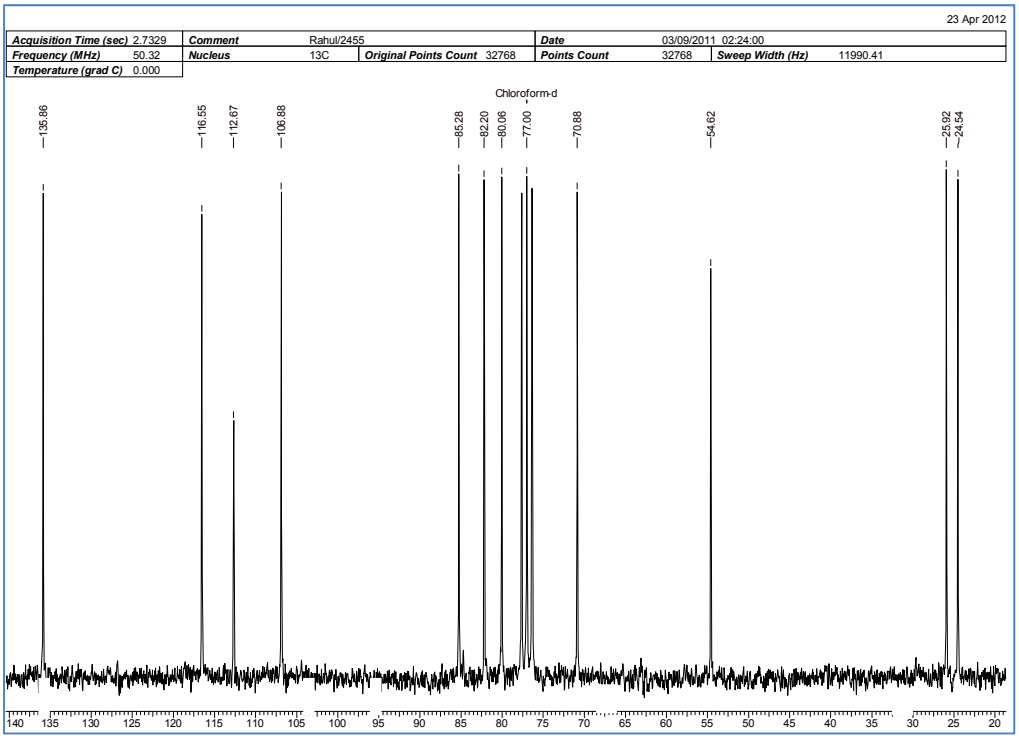
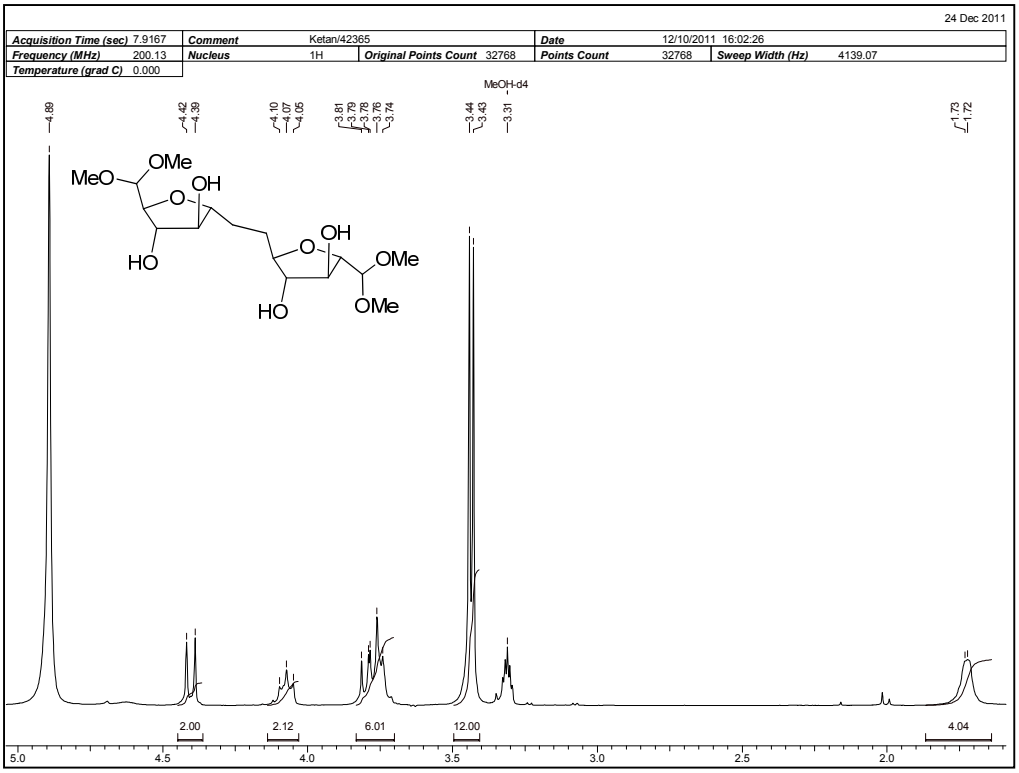
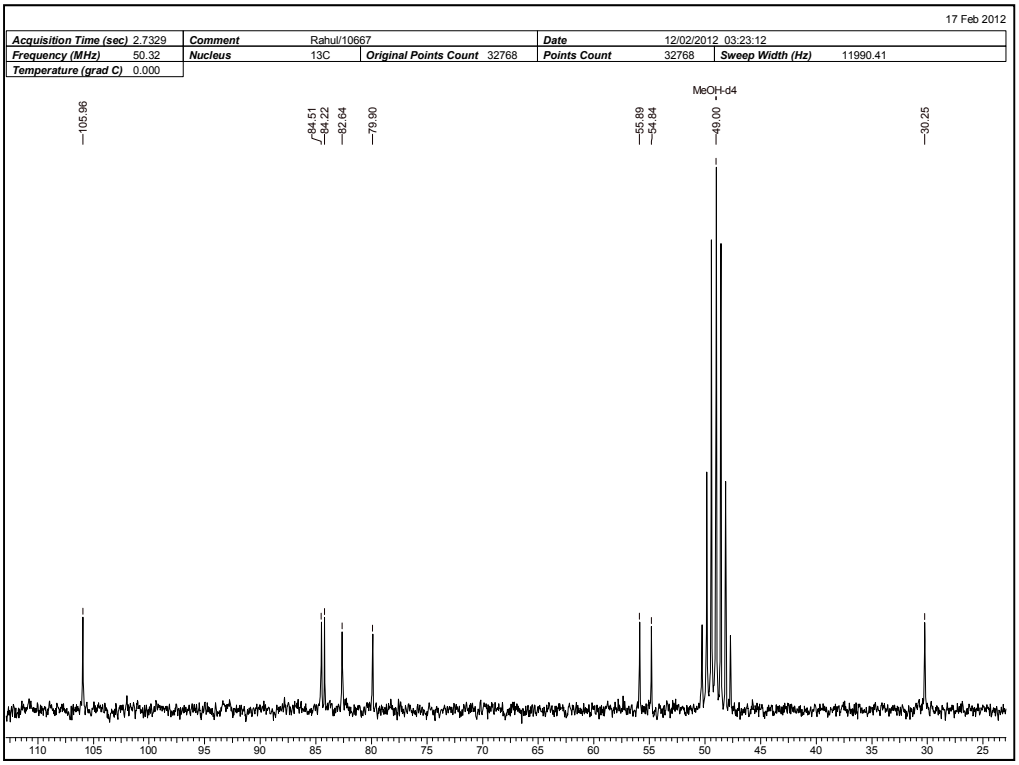


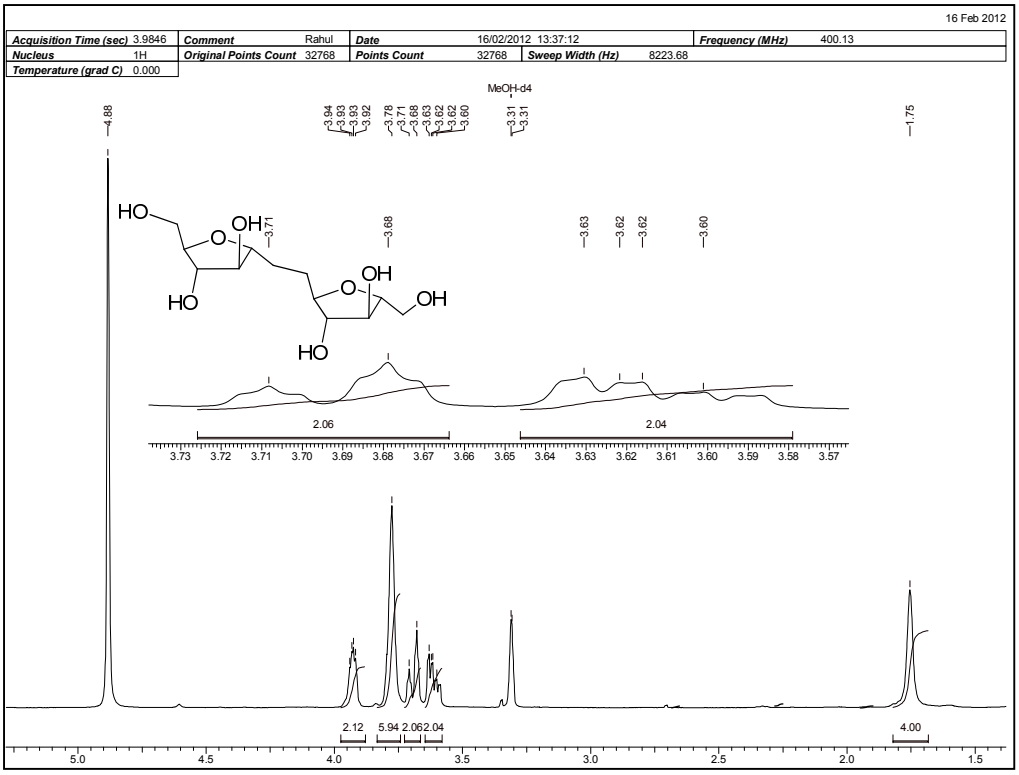
^{13}C NMR Spectrum of 18 in $CDCl_3$



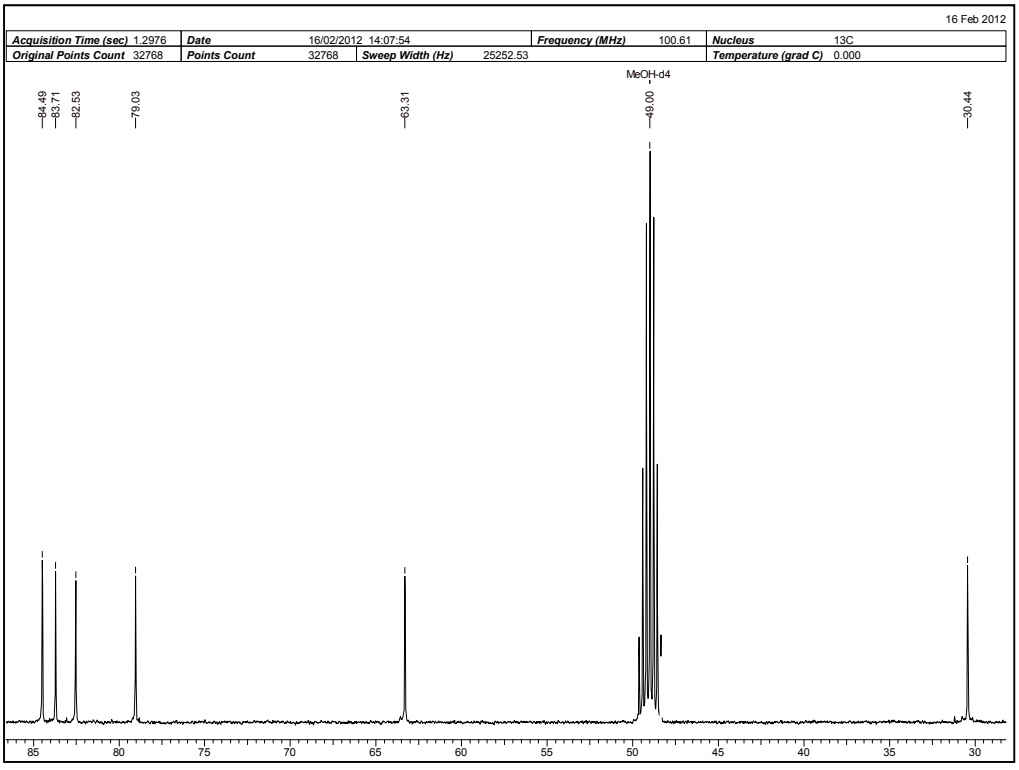
^{1}H NMR Spectrum of 23 in MeOH-D4



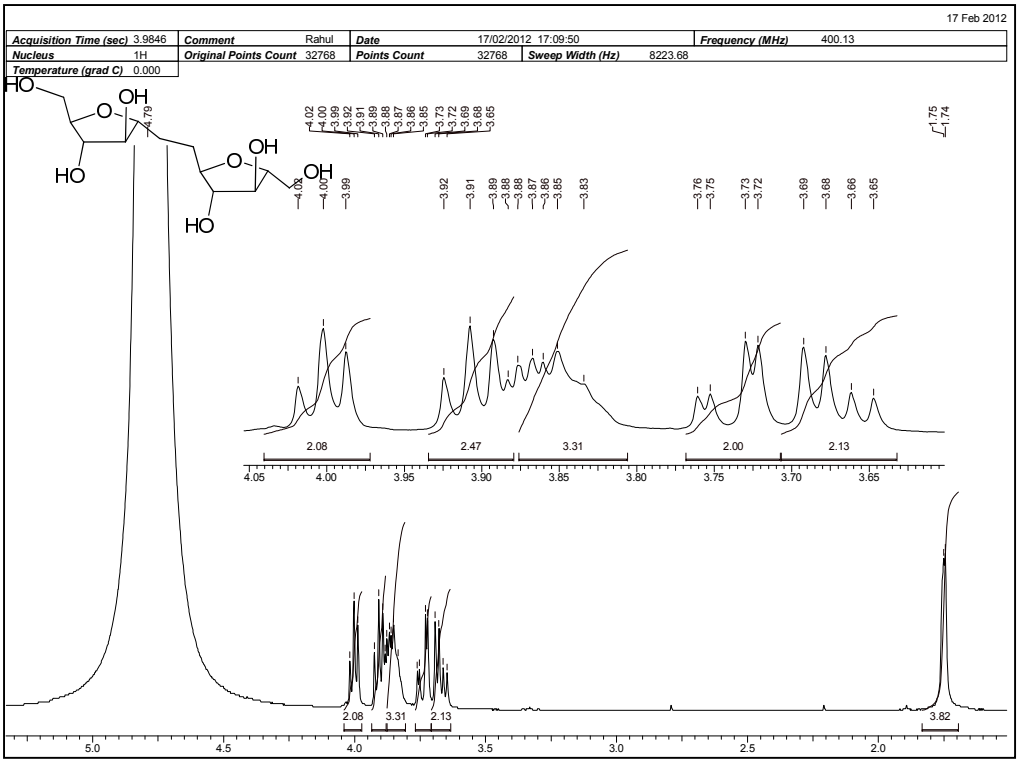
^{13}C NMR Spectrum of 23 in MeOH-D4



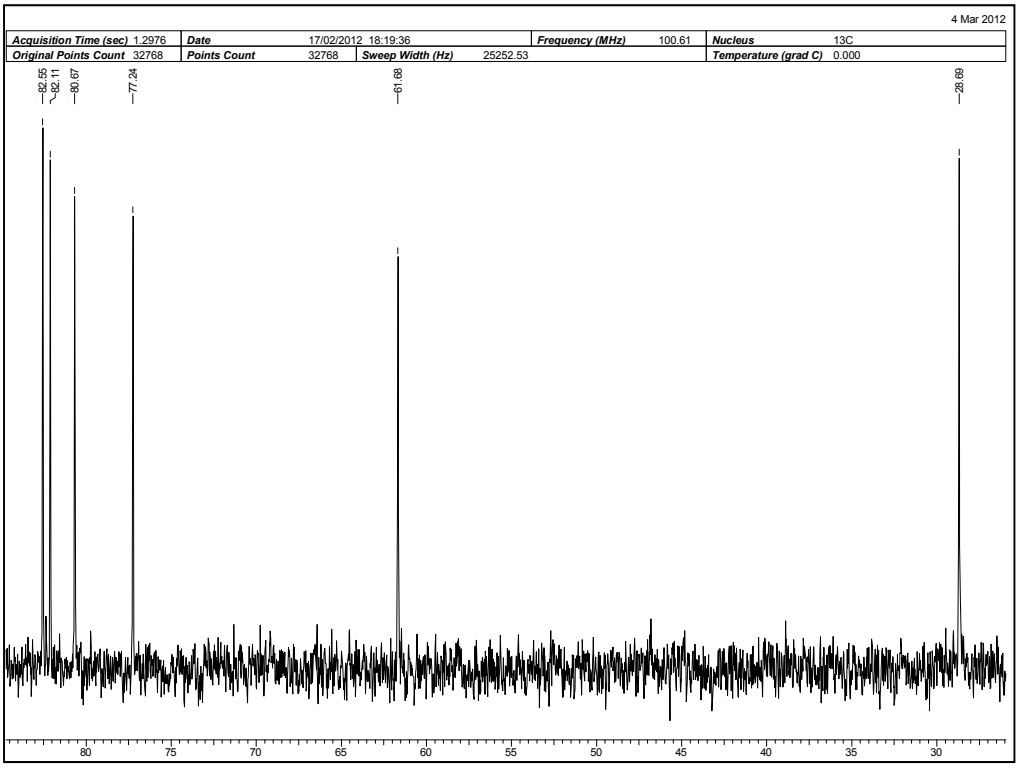
^{1}H NMR Spectrum of 1 in MeOH-D4



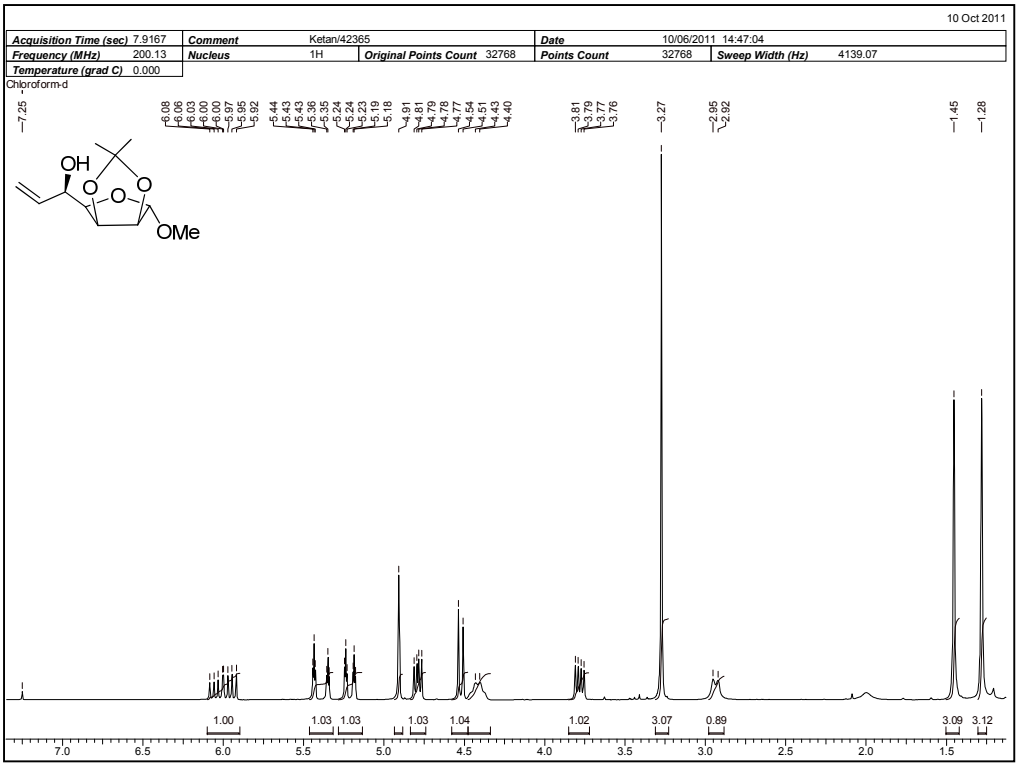
^{13}C NMR Spectrum of 1 in MeOH-4



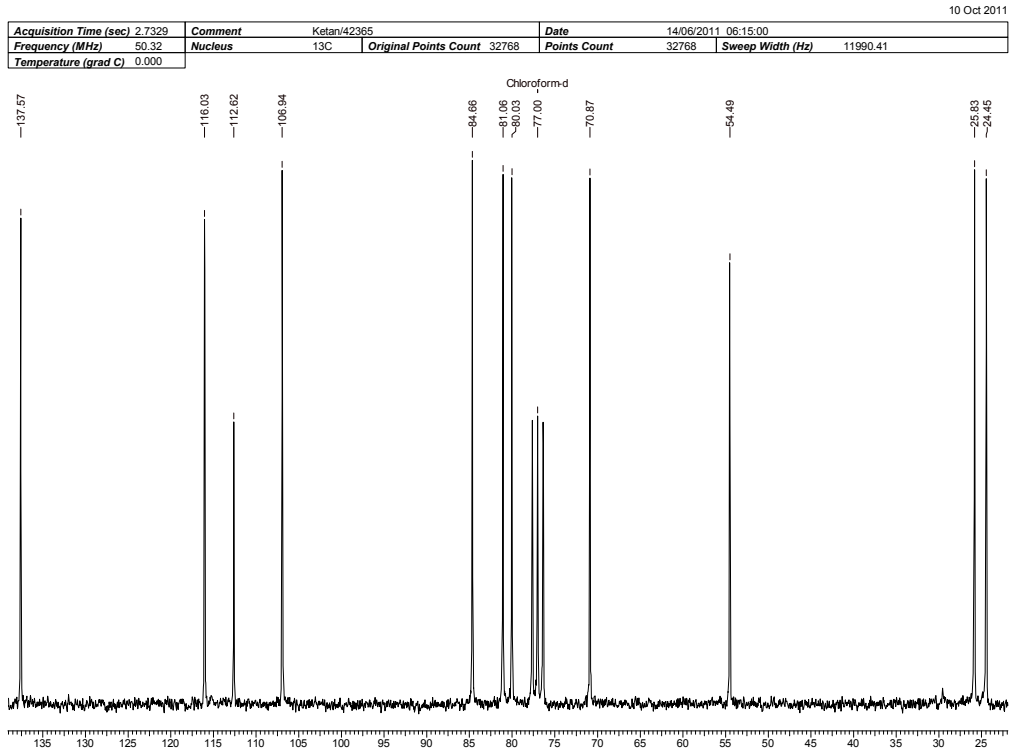
^{1}H NMR Spectrum of 1 in D_2O



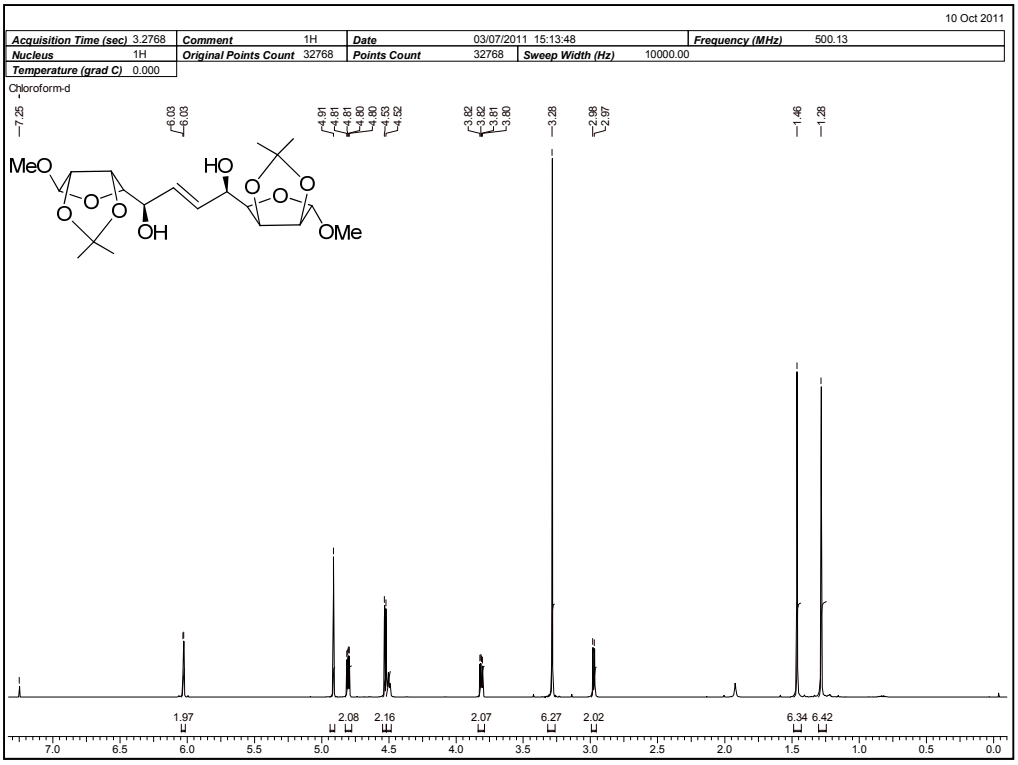
^{13}C NMR Spectrum of 1 in D_2O



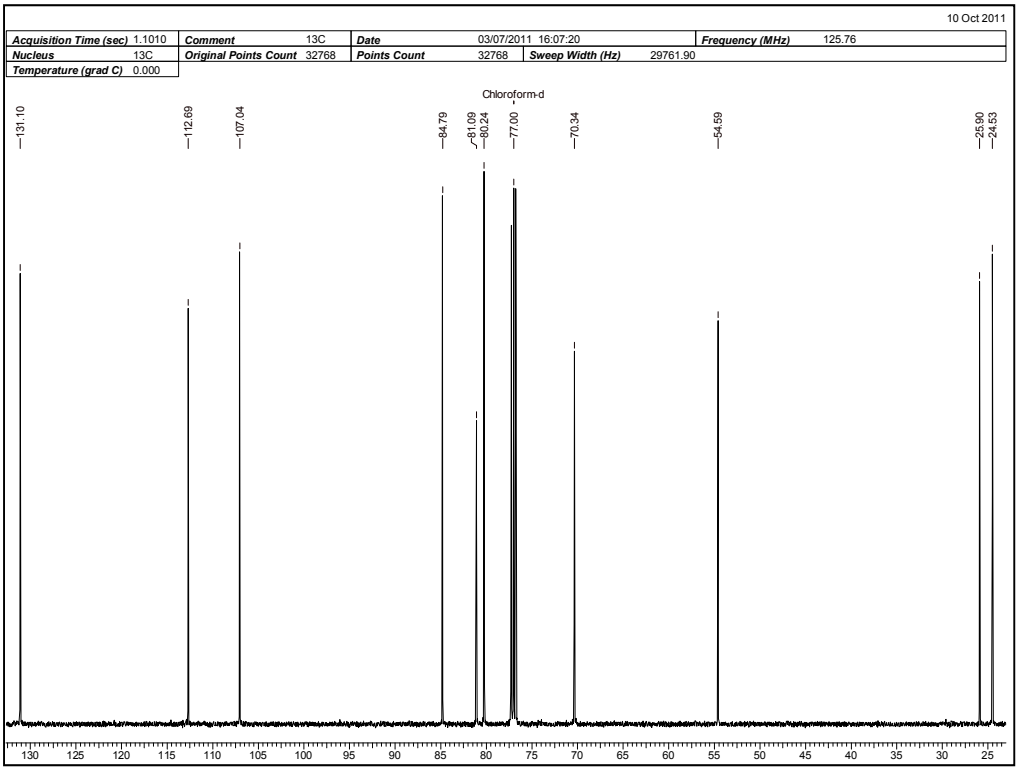
^{1}H NMR Spectrum of 24 in $CDCl_3$



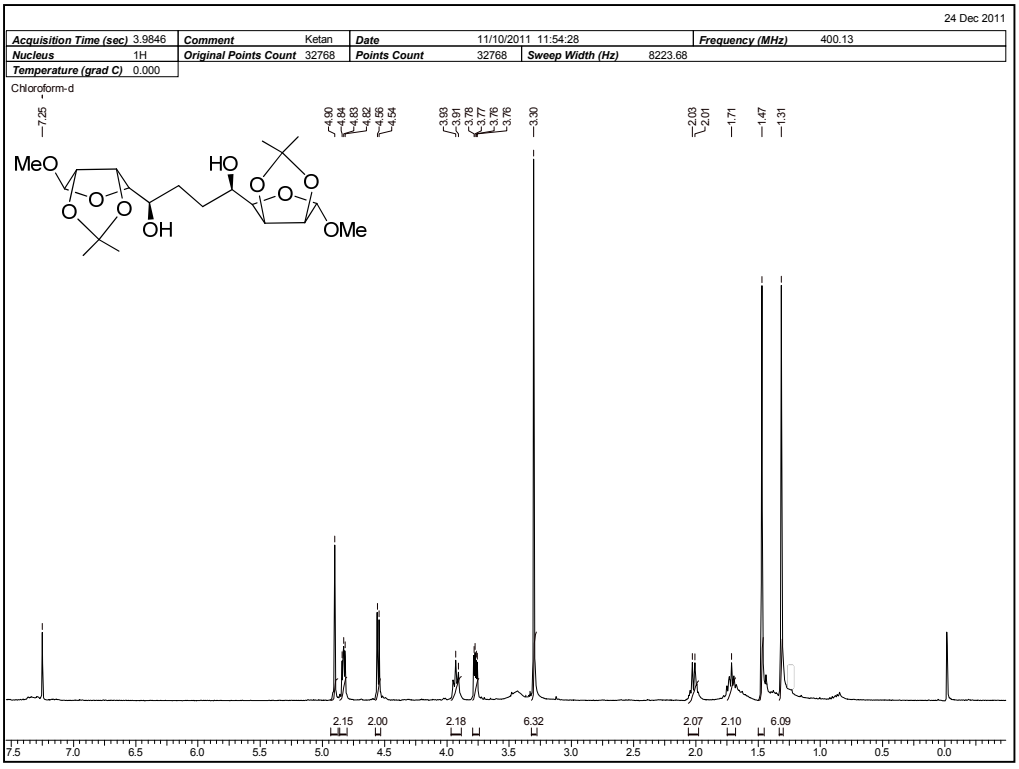
^{13}C NMR Spectrum of 24 in $CDCl_3$



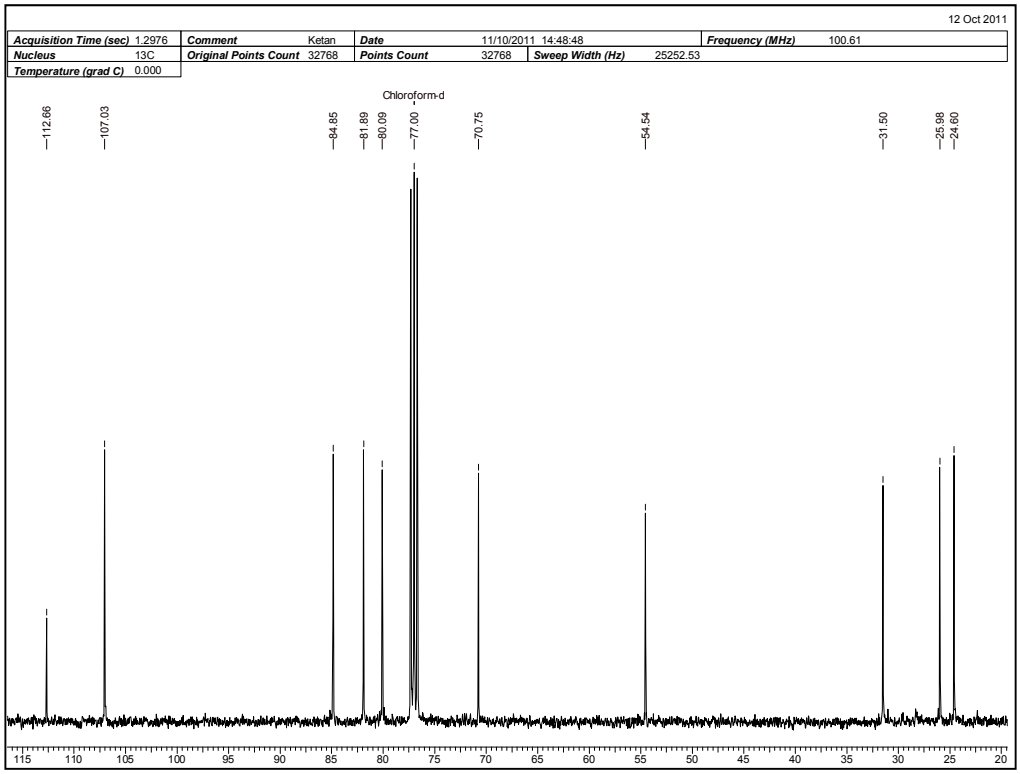
^{1}H NMR Spectrum of 25 in $CDCl_3$



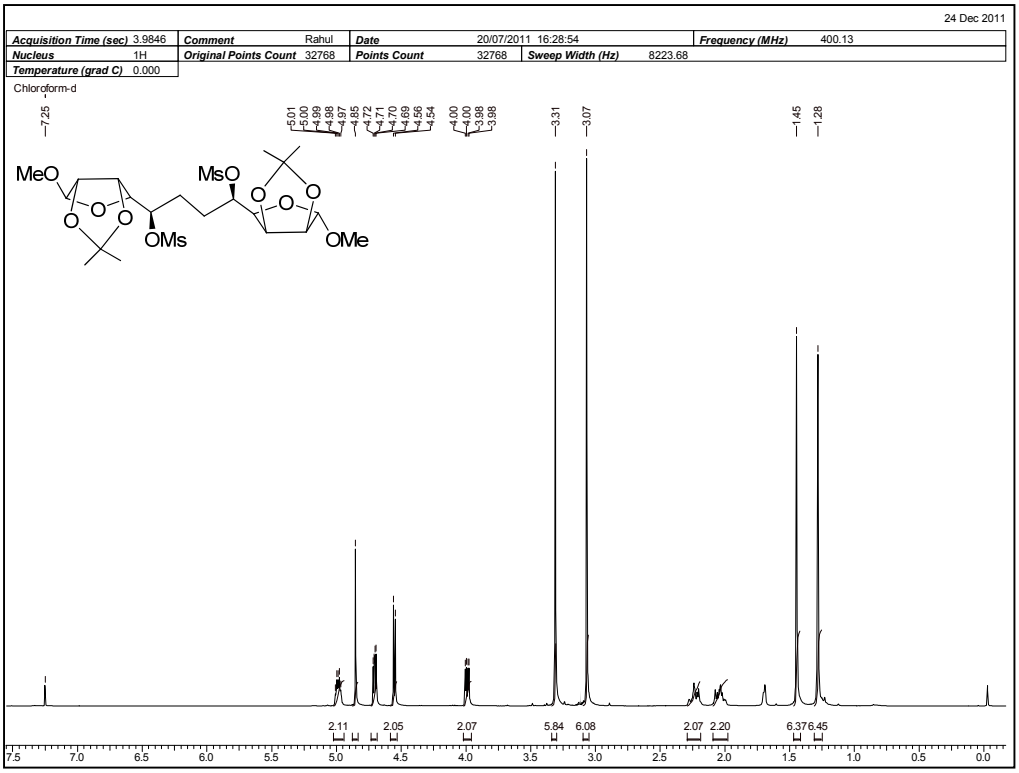
^{13}C NMR Spectrum of 25 in $CDCl_3$



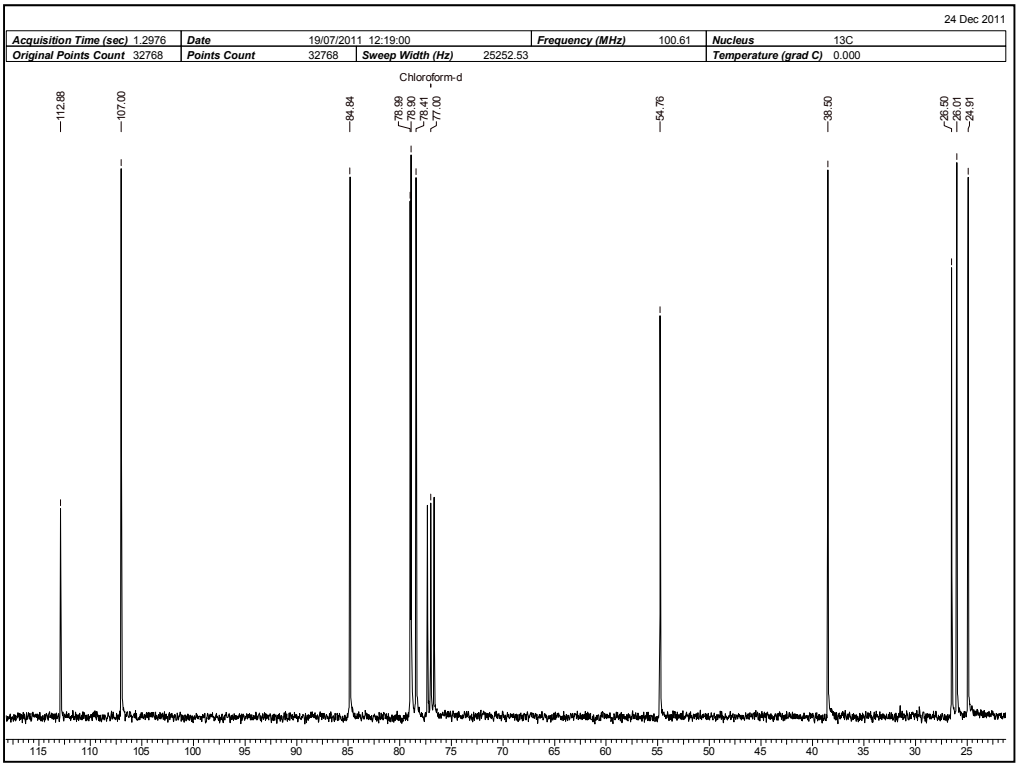
^{1}H NMR Spectrum of 26 in $CDCl_3$



^{13}C NMR Spectrum of 26 in $CDCl_3$

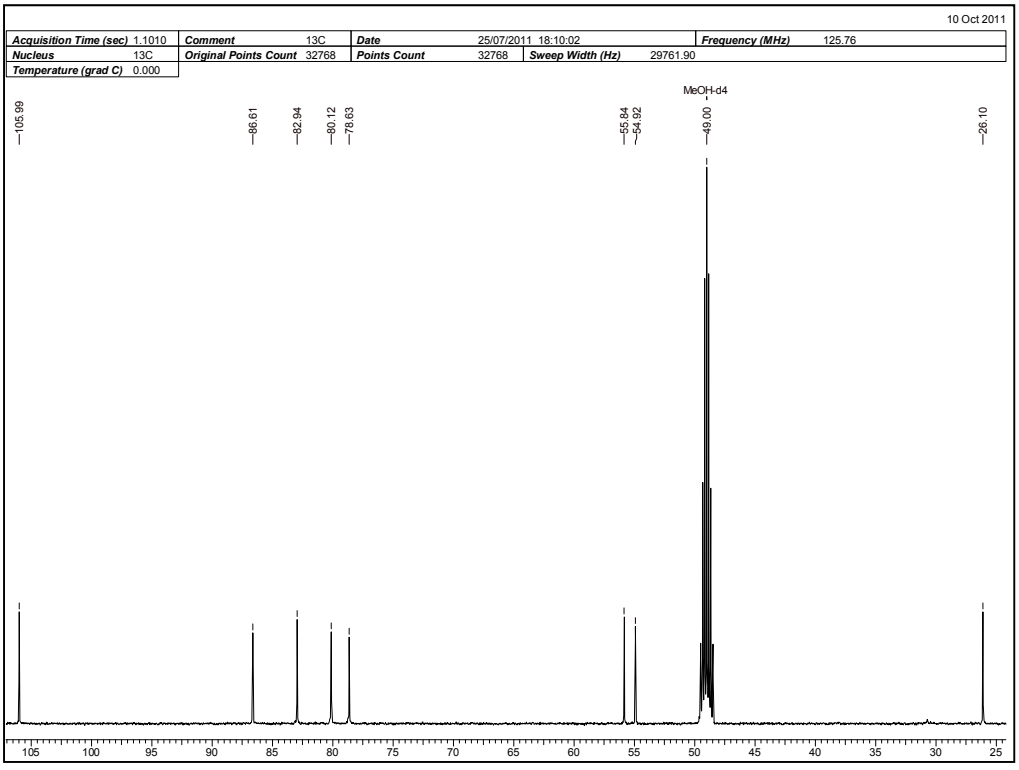


^{1}H NMR Spectrum of 21 in $CDCl_3$

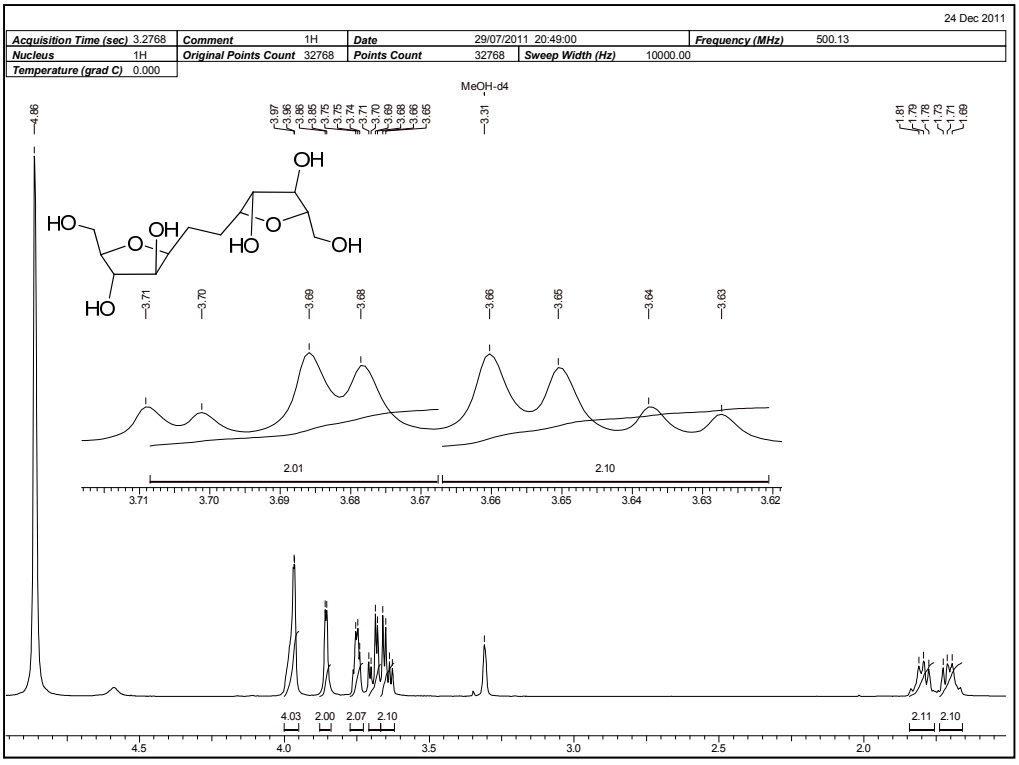


^{13}C NMR Spectrum of 21 in $CDCl_3$

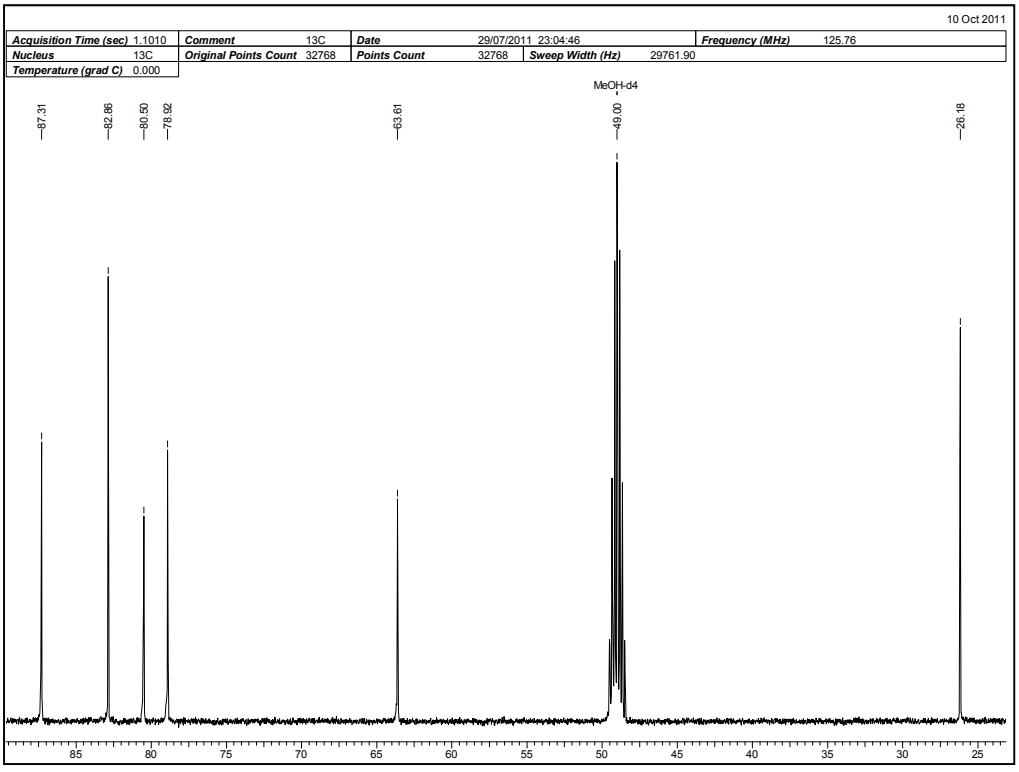
^{1}H NMR Spectrum of 27 in MeOH-D4



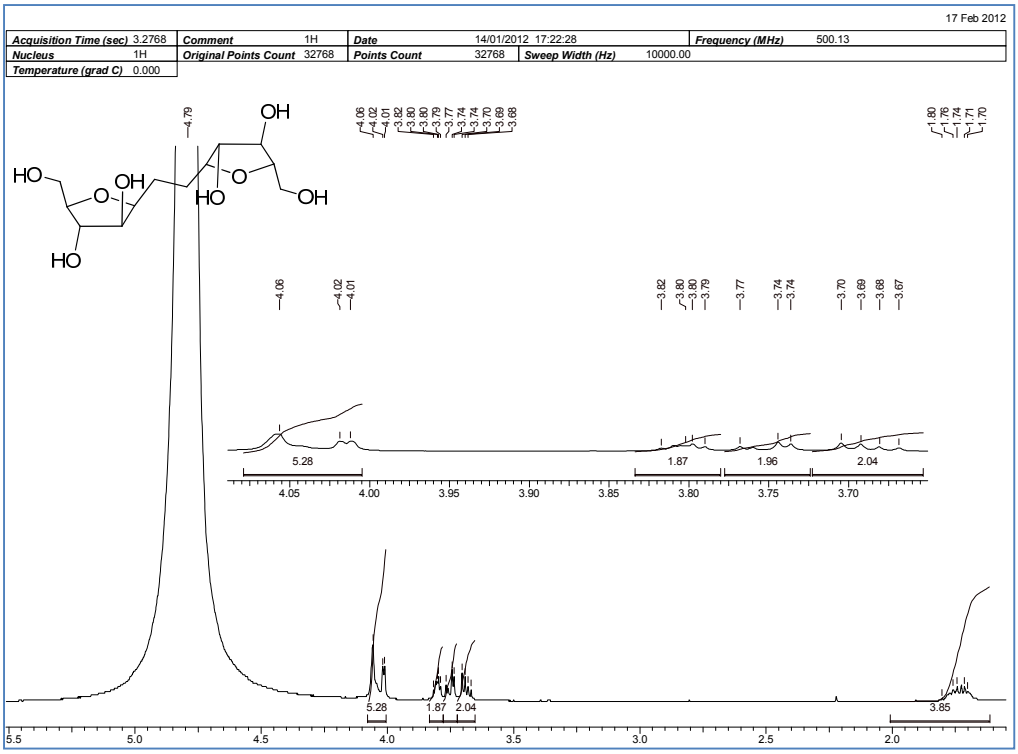
^{13}C NMR Spectrum of 27 in MeOH-D4



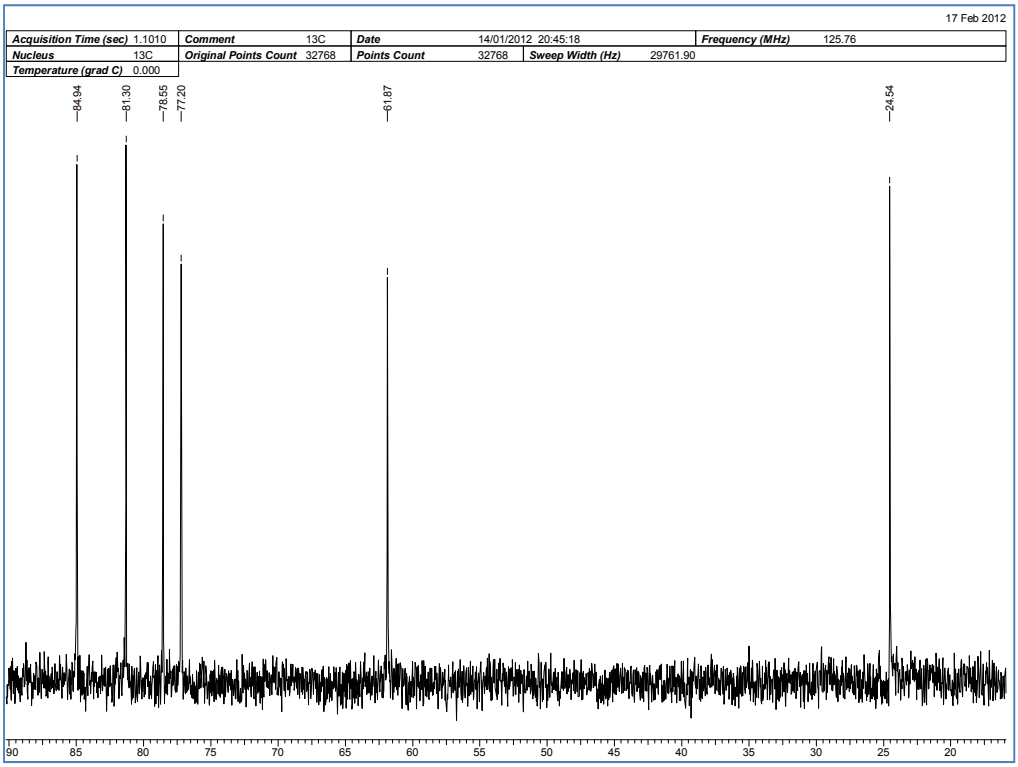
^{1}H NMR Spectrum of 17 in MeOH-D4



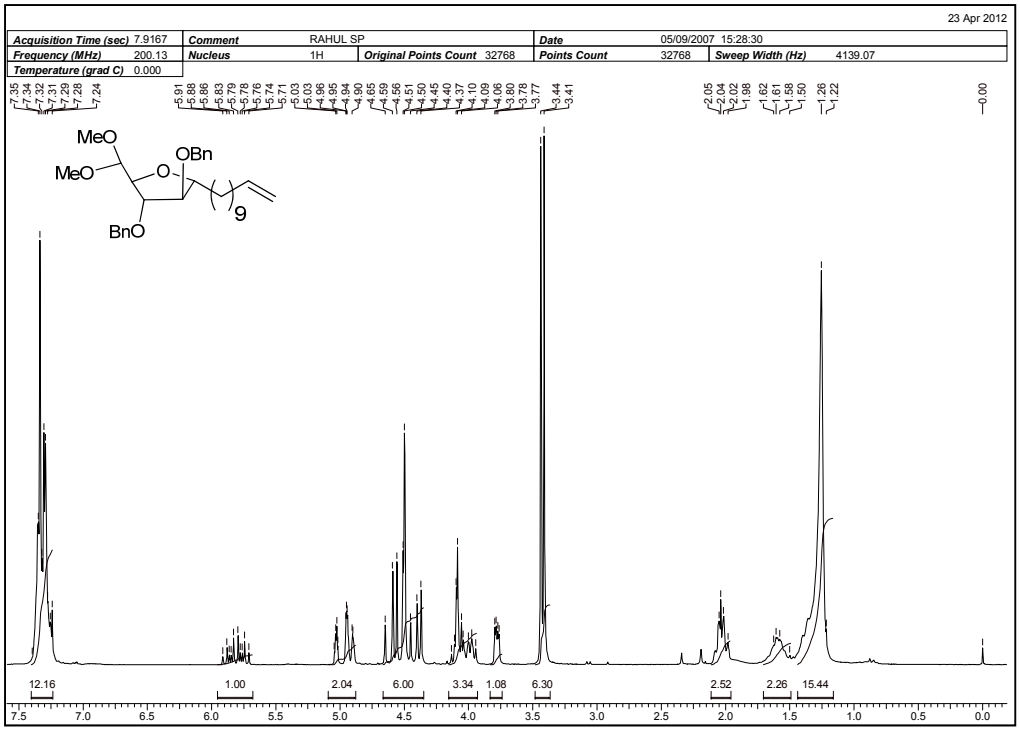
^{13}C NMR Spectrum of 17 in MeOH-D4



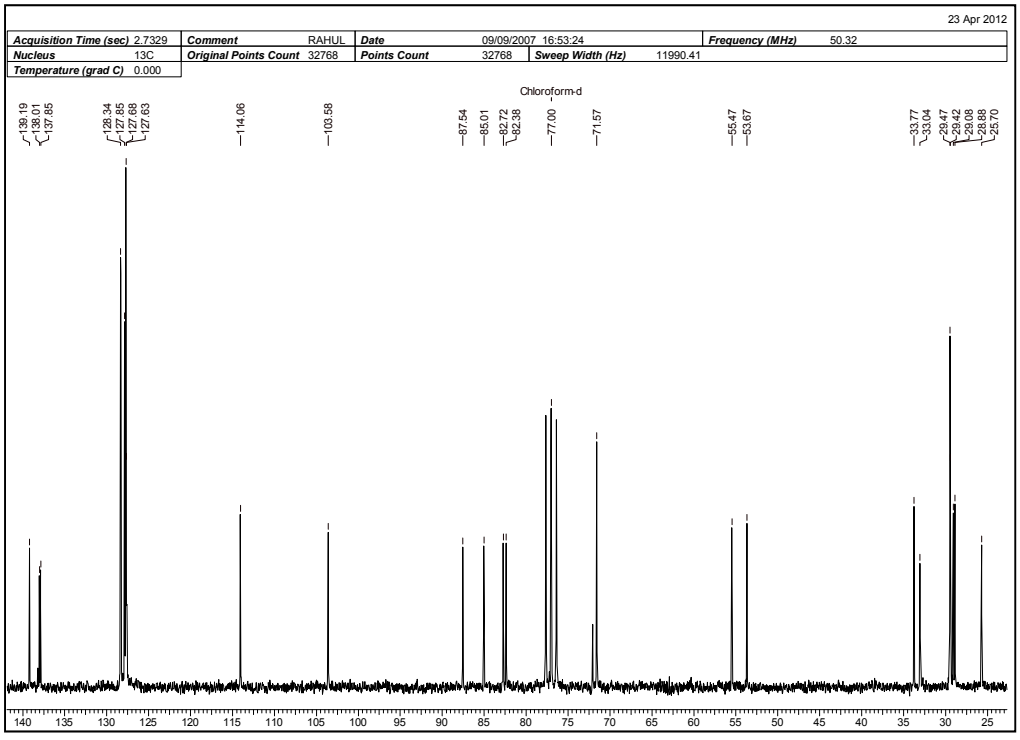
^{1}H NMR Spectrum of 17 in D_2O



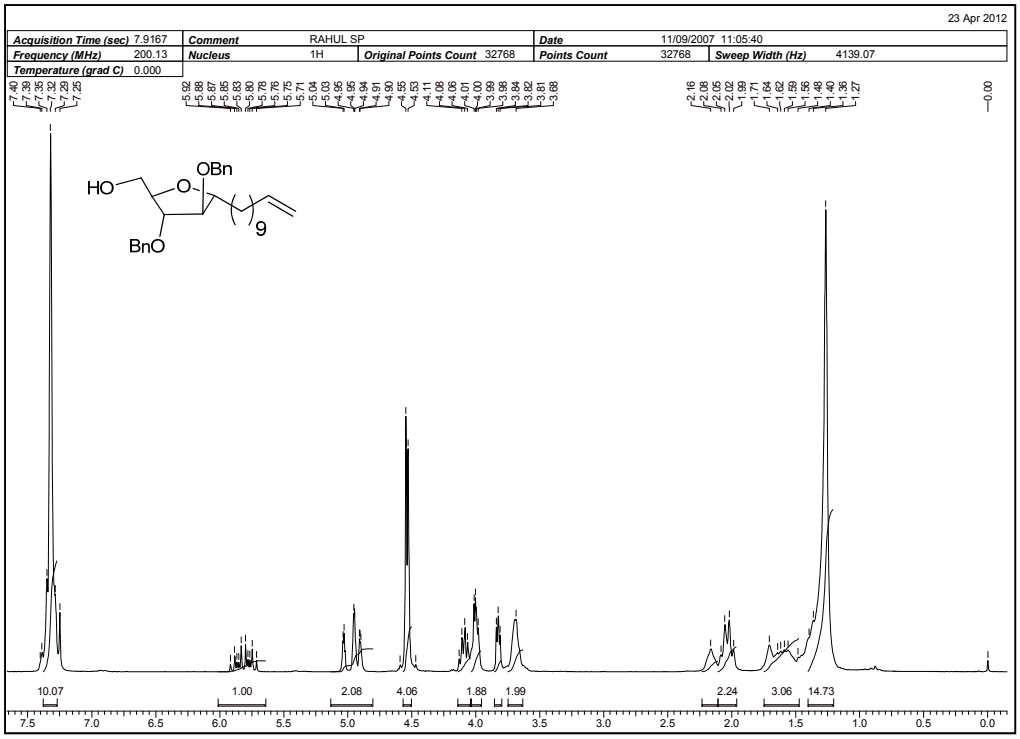
^{13}C NMR Spectrum of 17 in D_2O



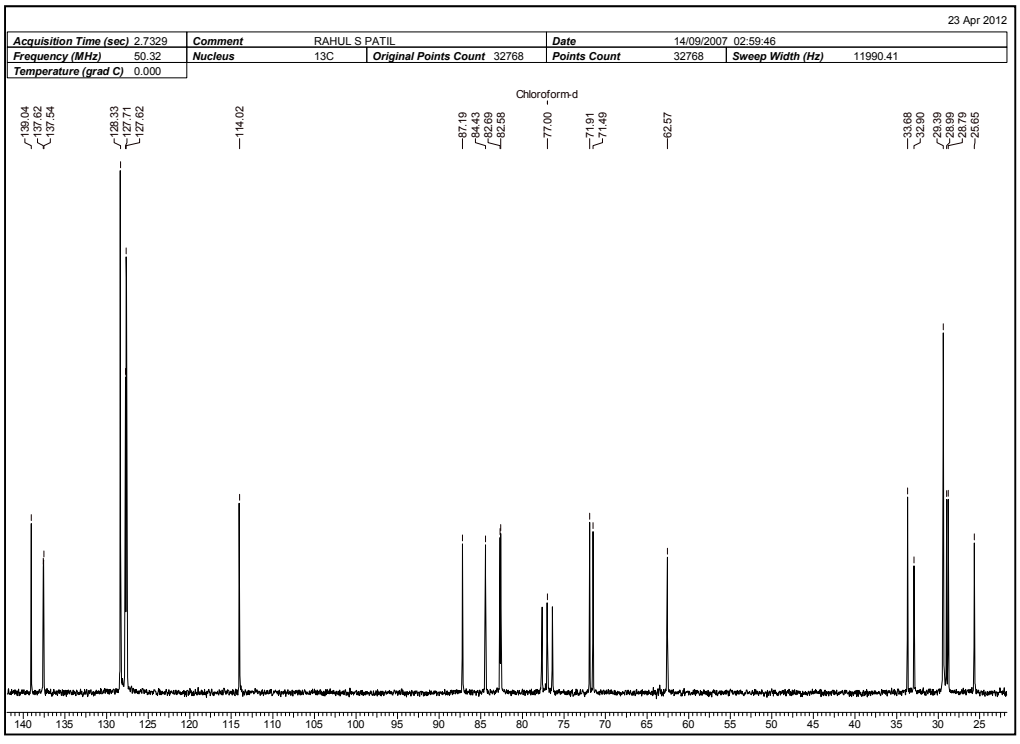
^{1}H NMR Spectrum of 31 in $CDCl_3$



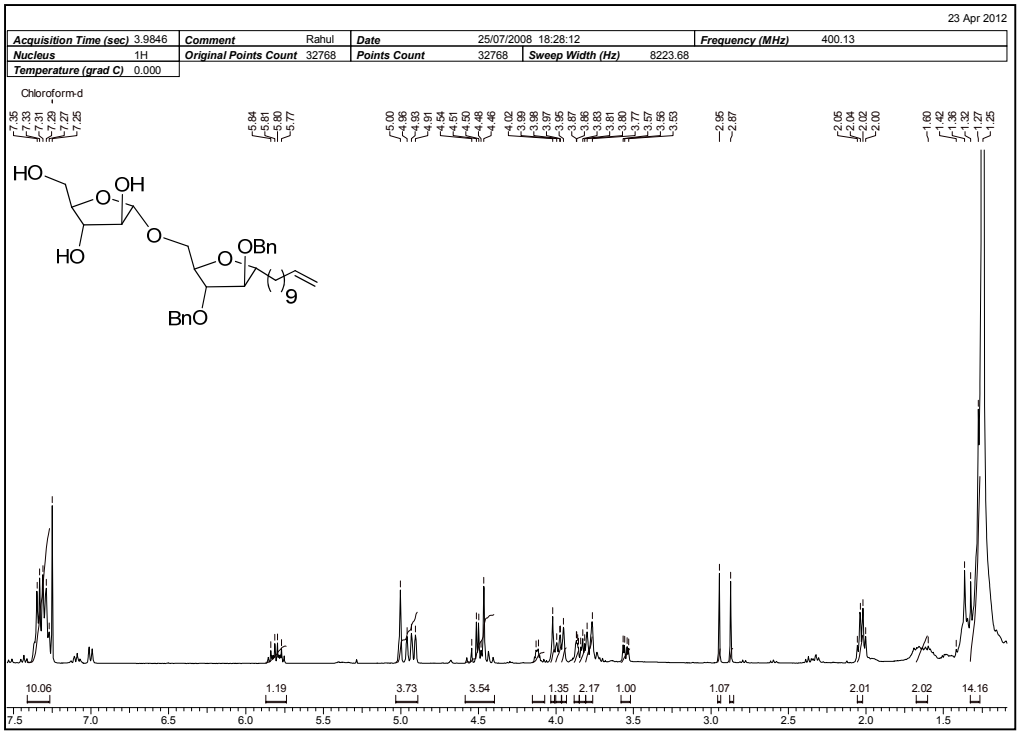
^{13}C NMR Spectrum of 31 in $CDCl_3$



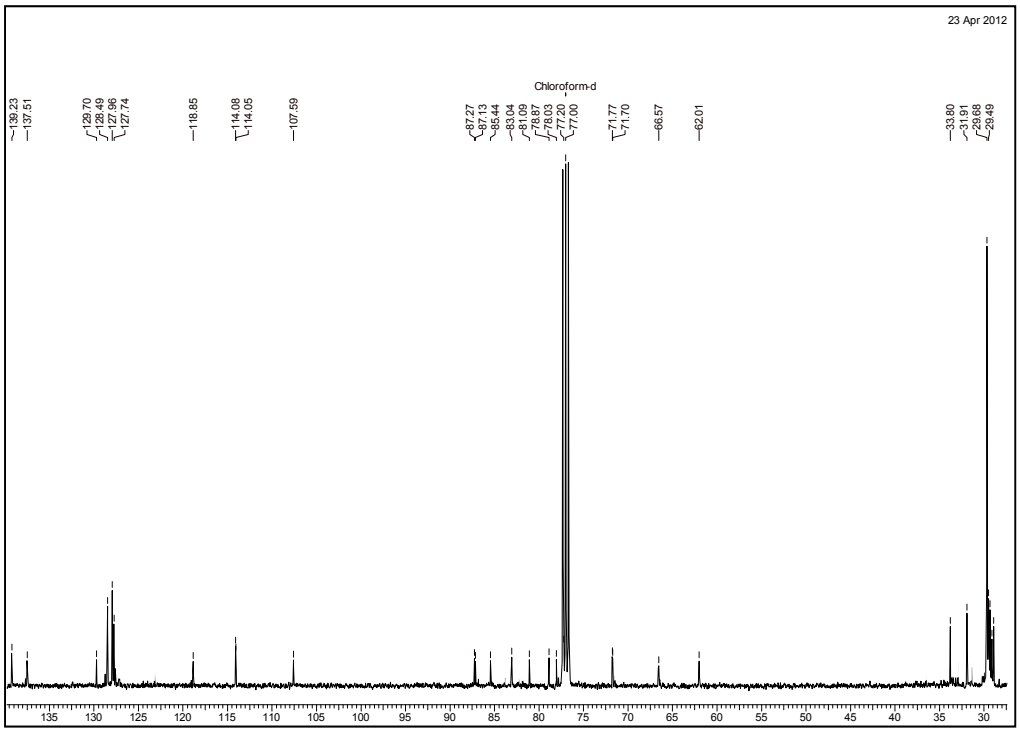
^{1}H NMR Spectrum of 30 in $CDCl_3$



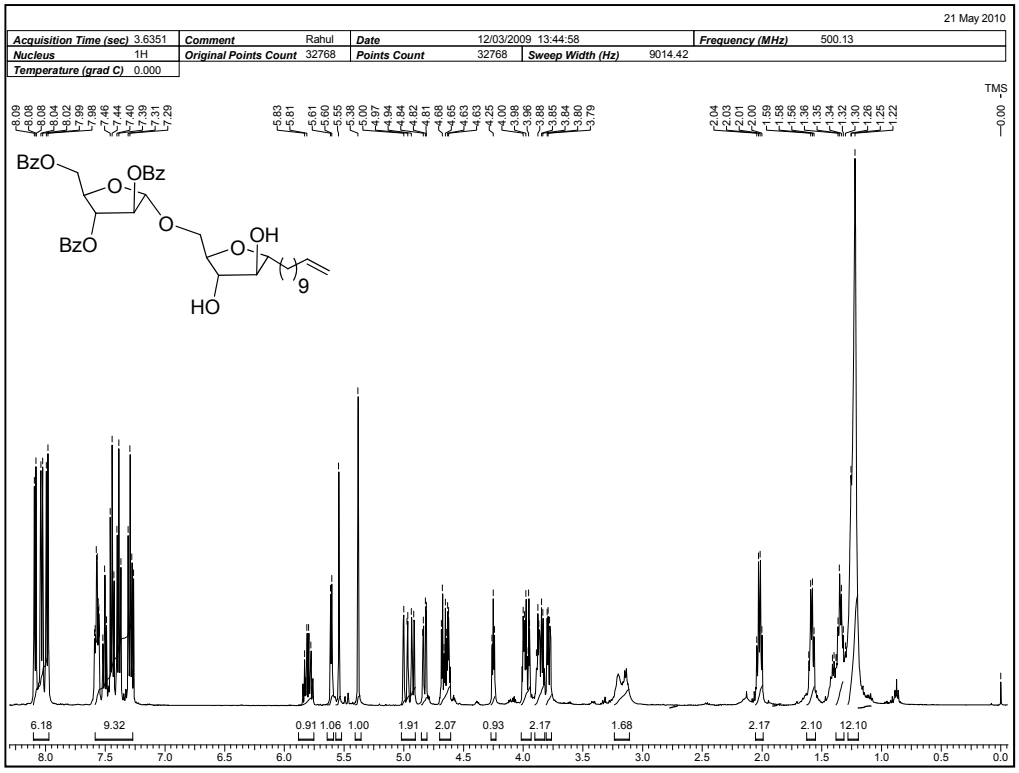
^{13}C NMR Spectrum of 30 in $CDCl_3$



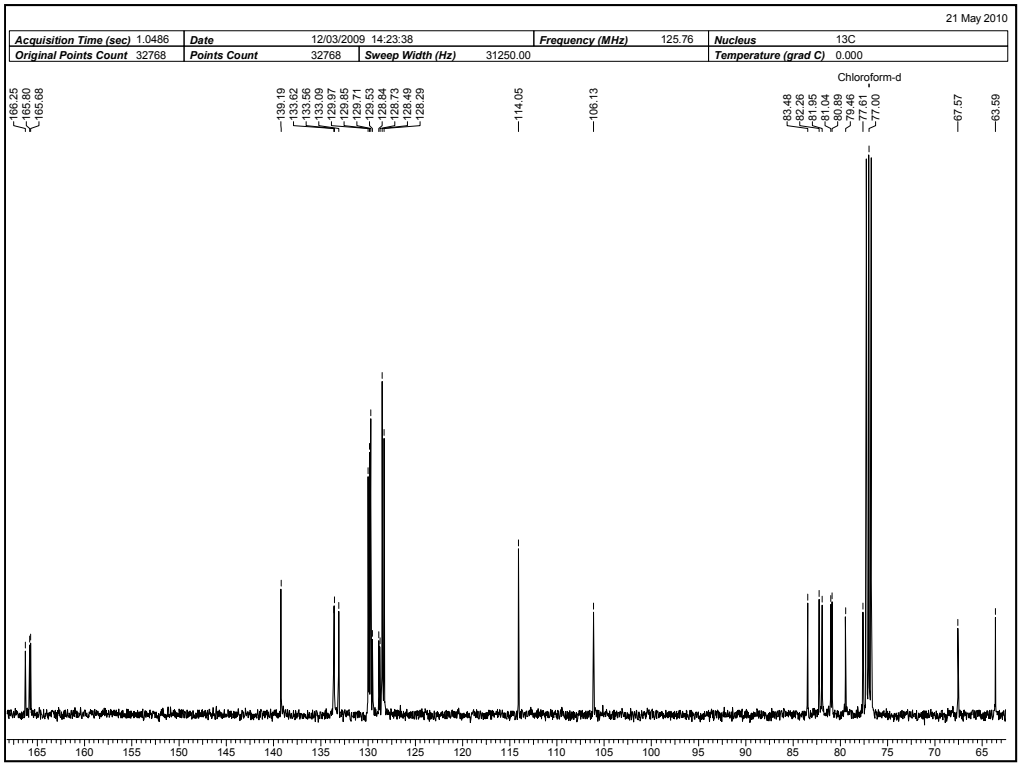
^{1}H NMR Spectrum of 32 in $CDCl_3$



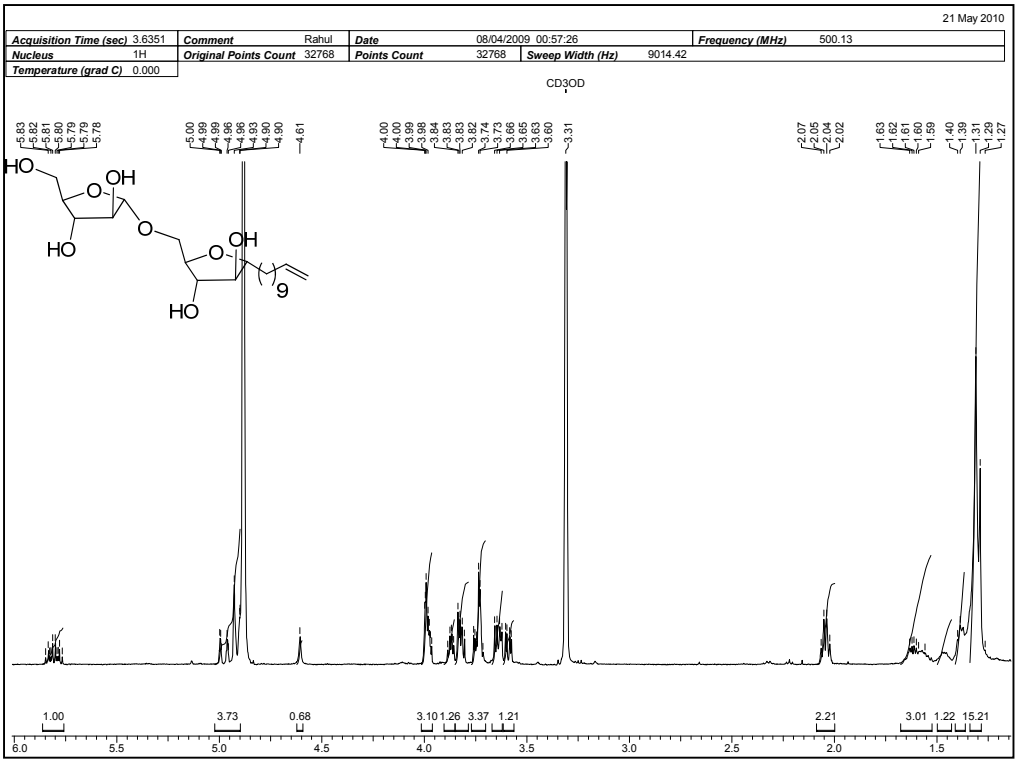
^{13}C NMR Spectrum of 32 in $CDCl_3$



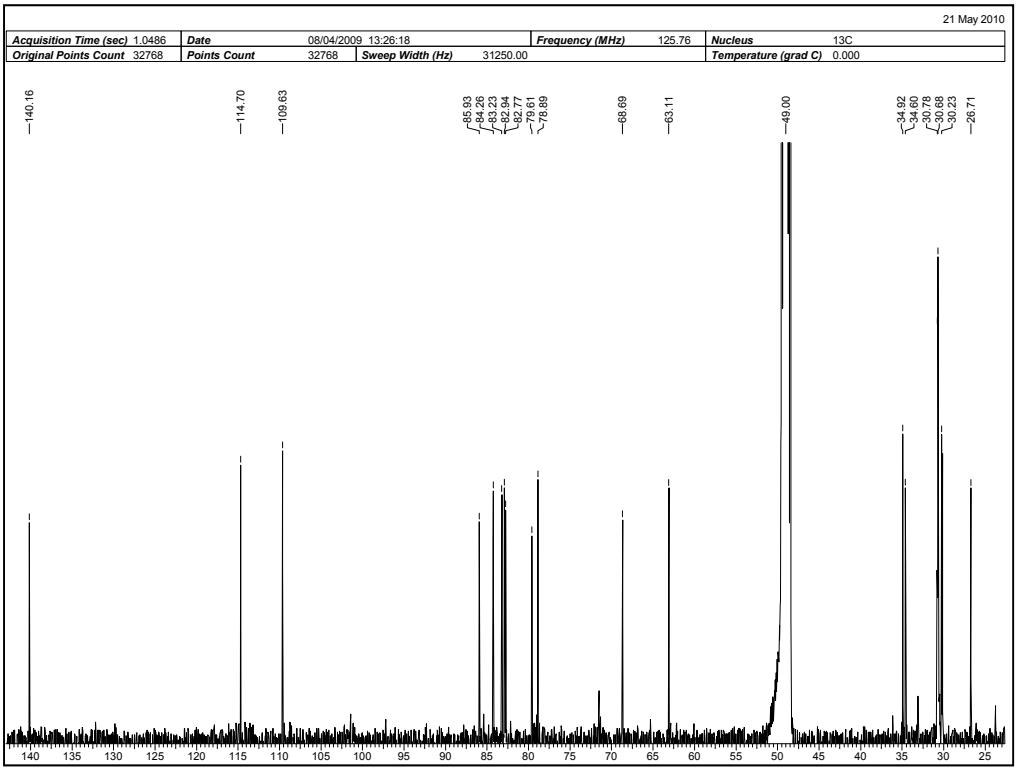
^{1}H NMR Spectrum of 33 in $CDCl_3$



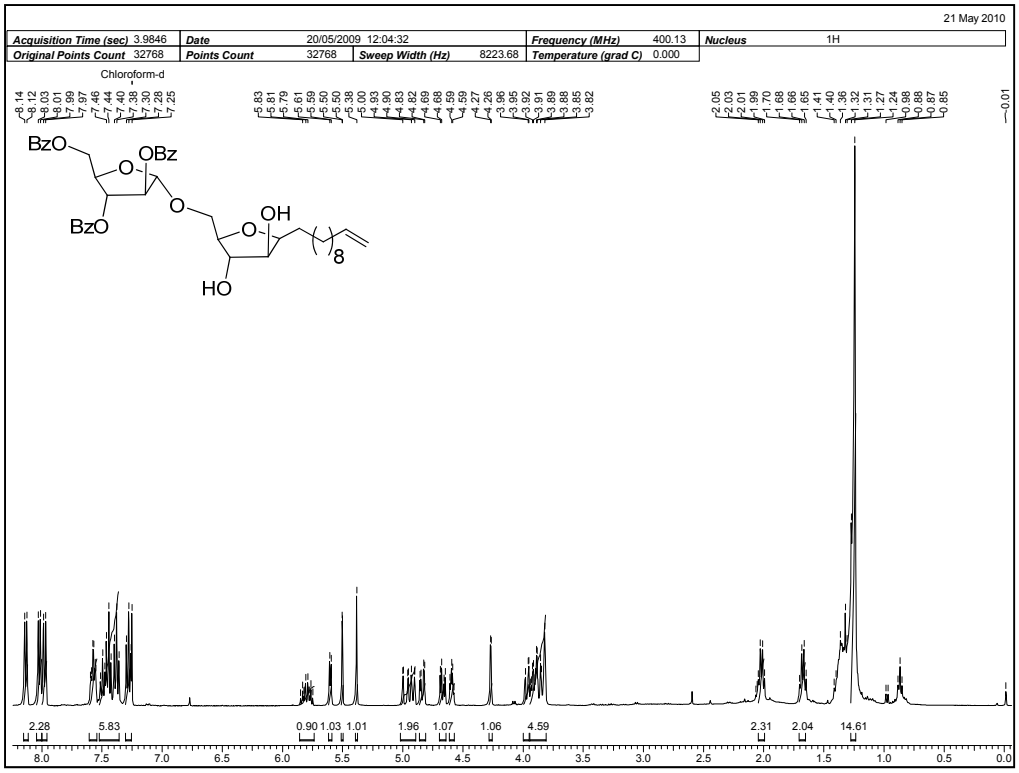
^{13}C NMR Spectrum of 33 in $CDCl_3$



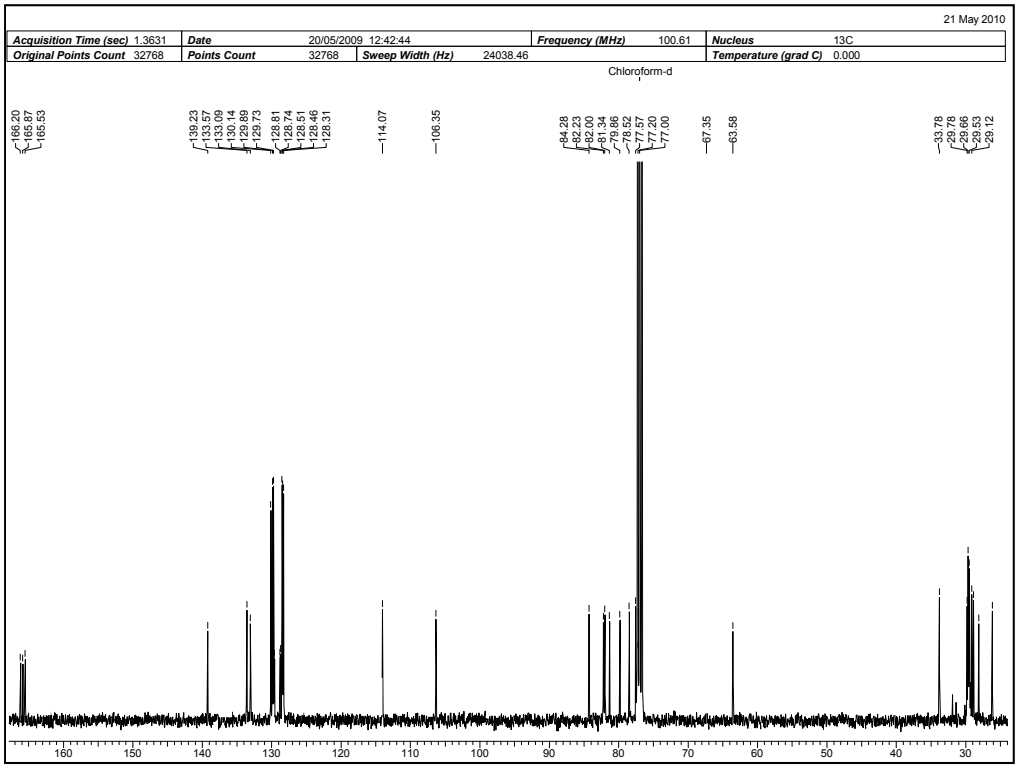
^{1}H NMR Spectrum of 28 in MeOH-D4



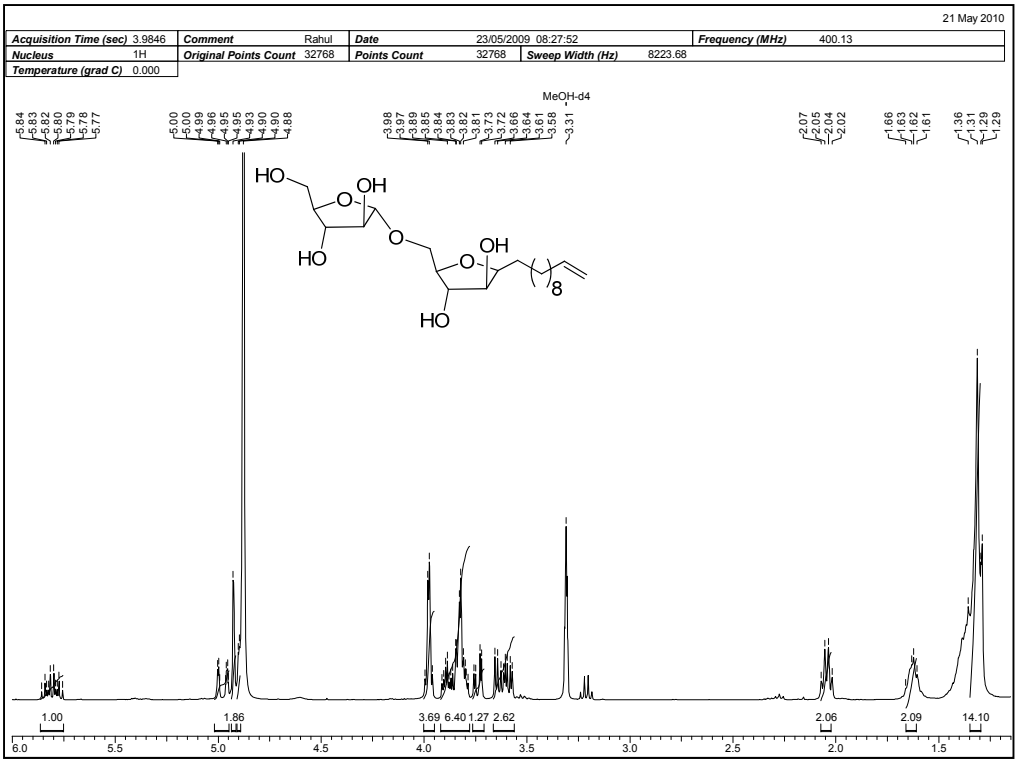
^{13}C NMR Spectrum of 28 in MeOH-D4



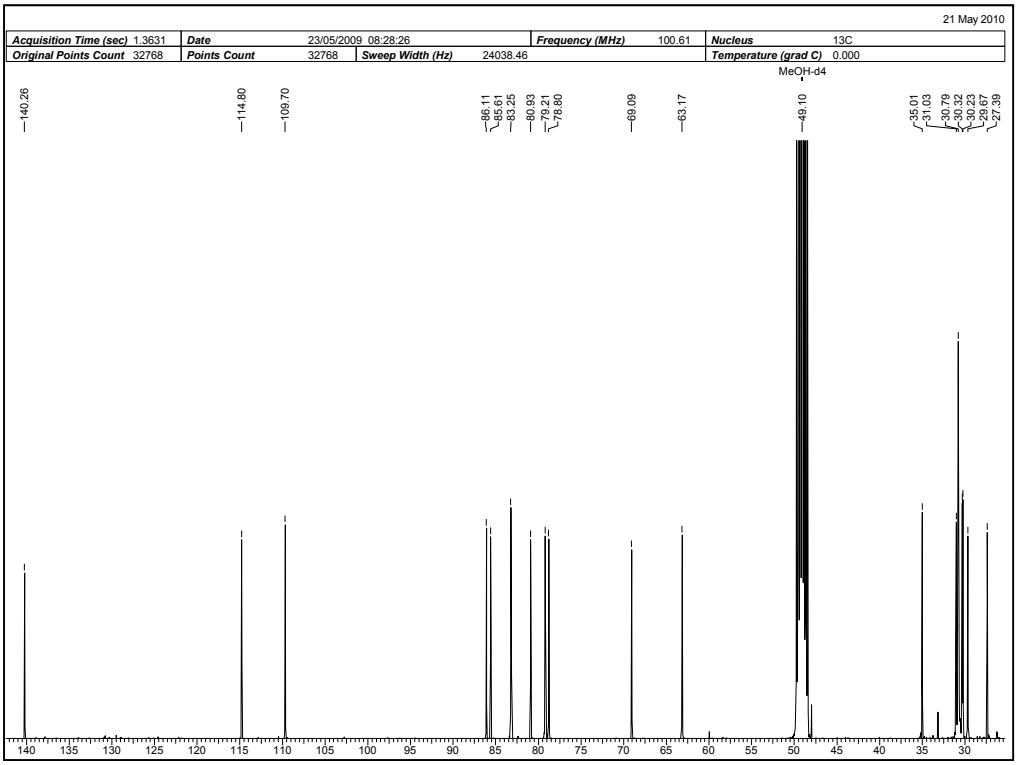
^{1}H NMR Spectrum of 34 in $CDCl_3$



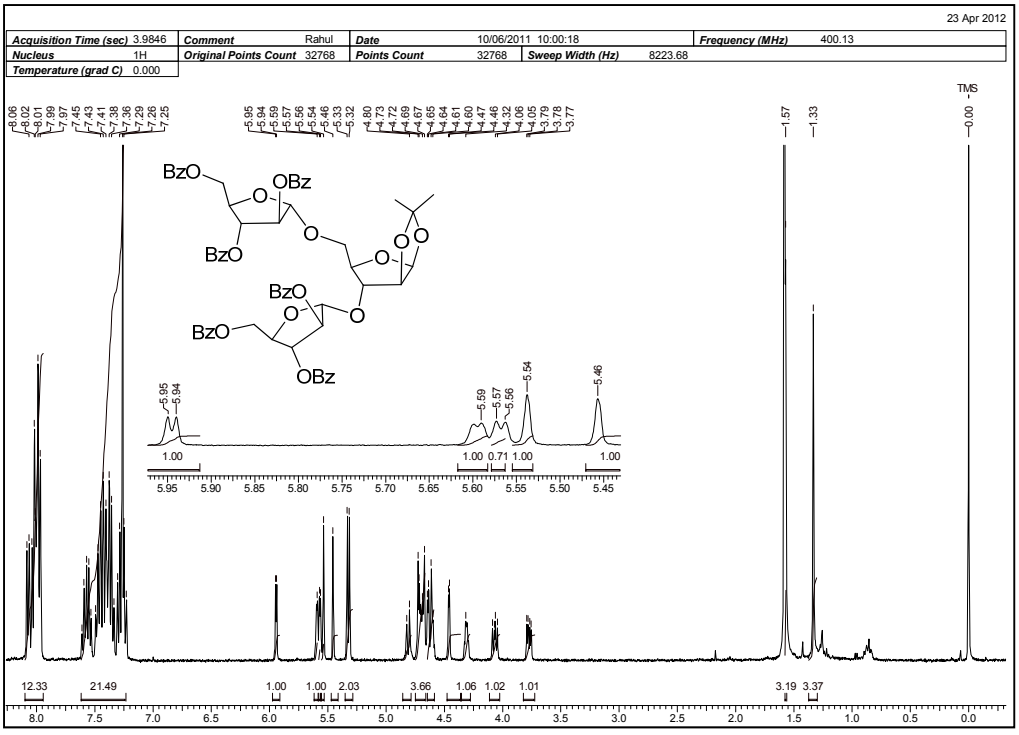
^{13}C NMR Spectrum of 34 in $CDCl_3$



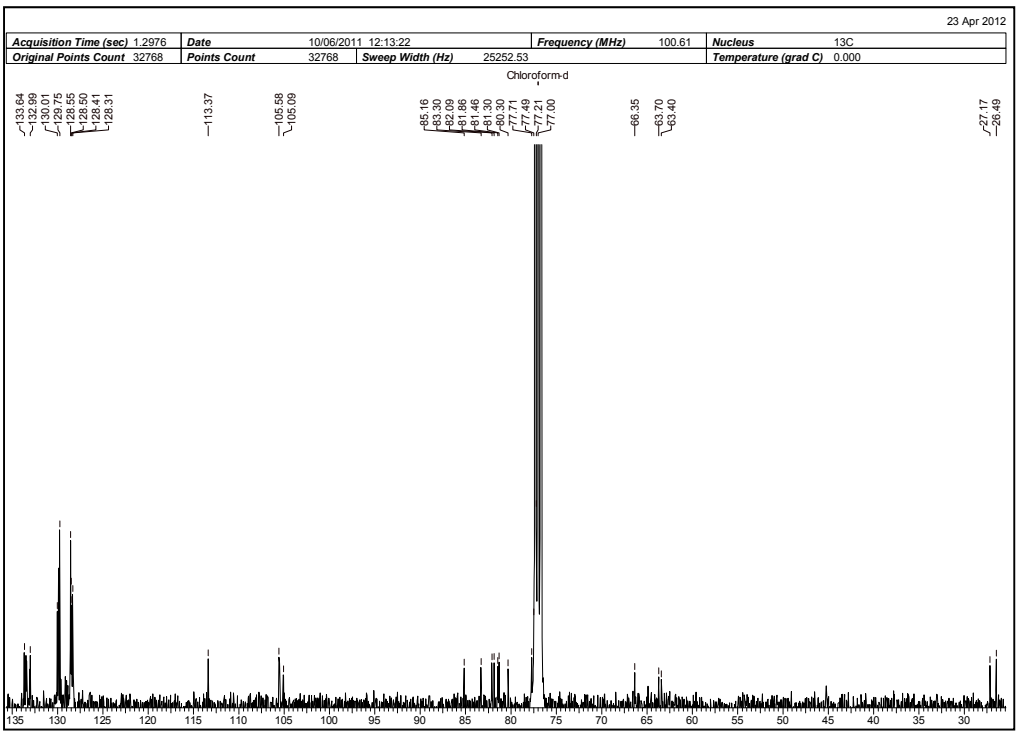
^{1}H NMR Spectrum of 29 in MeOH-D4



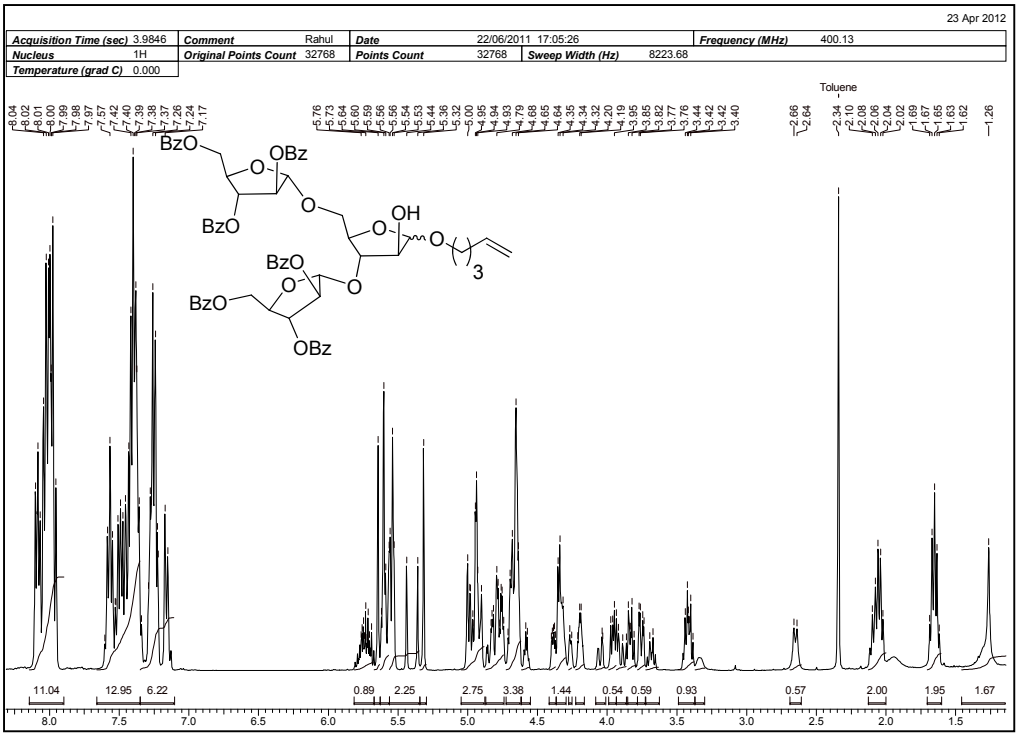
^{13}C NMR Spectrum of 29 in MeOH-D4



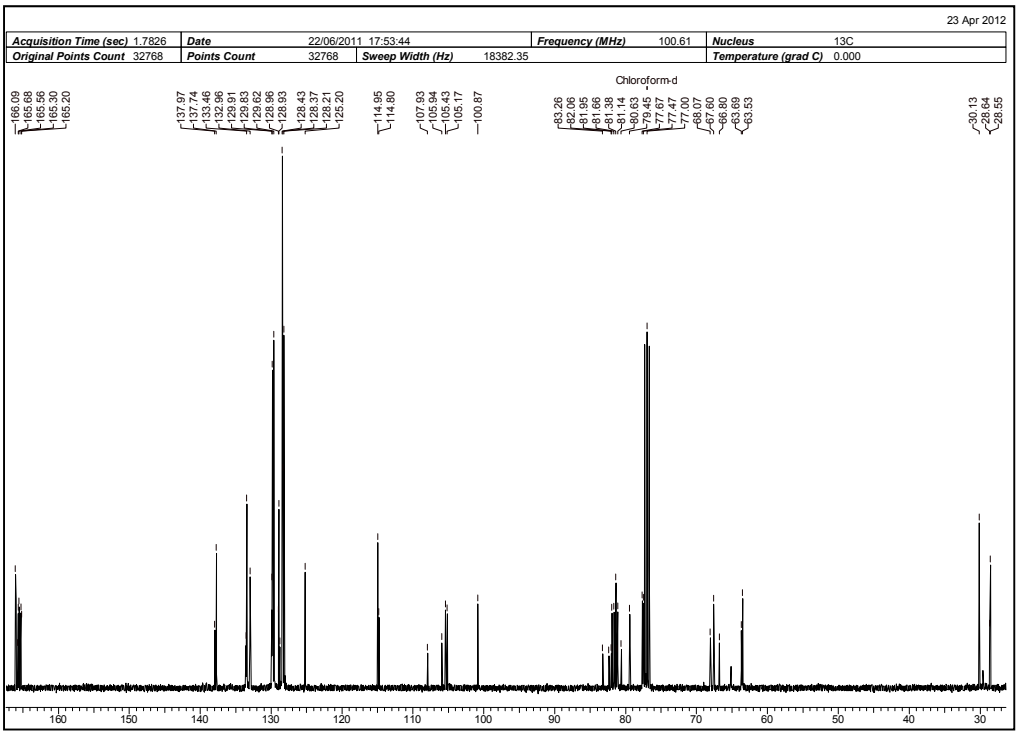
^{1}H NMR Spectrum of 36 in $CDCl_3$



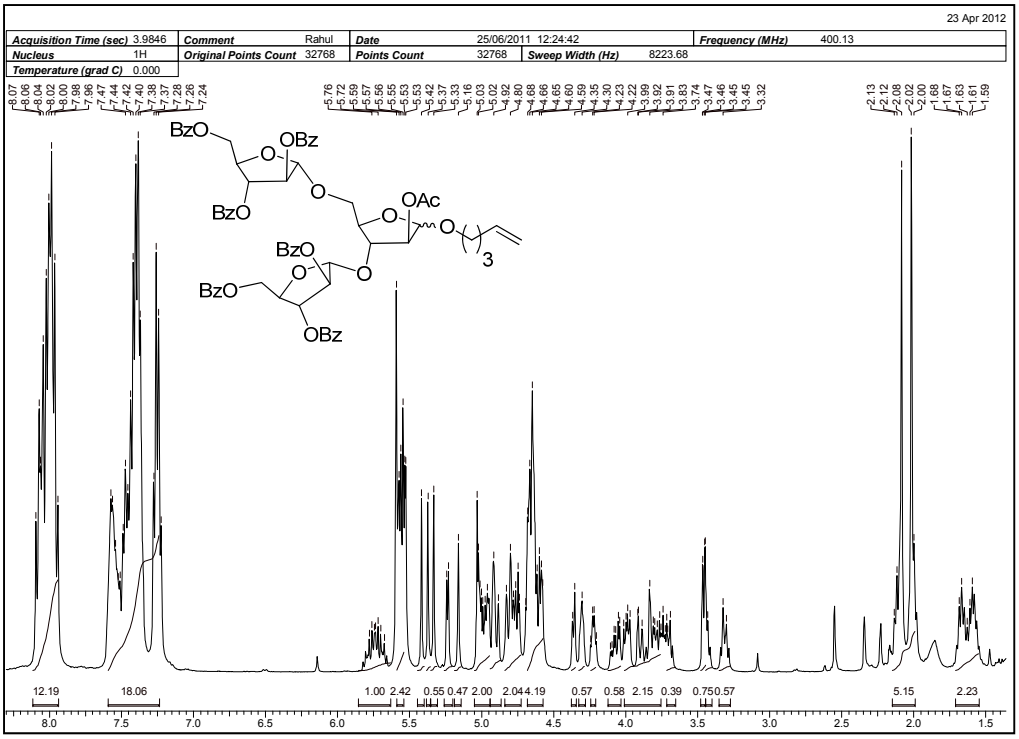
^{13}C NMR Spectrum of 36 in $CDCl_3$



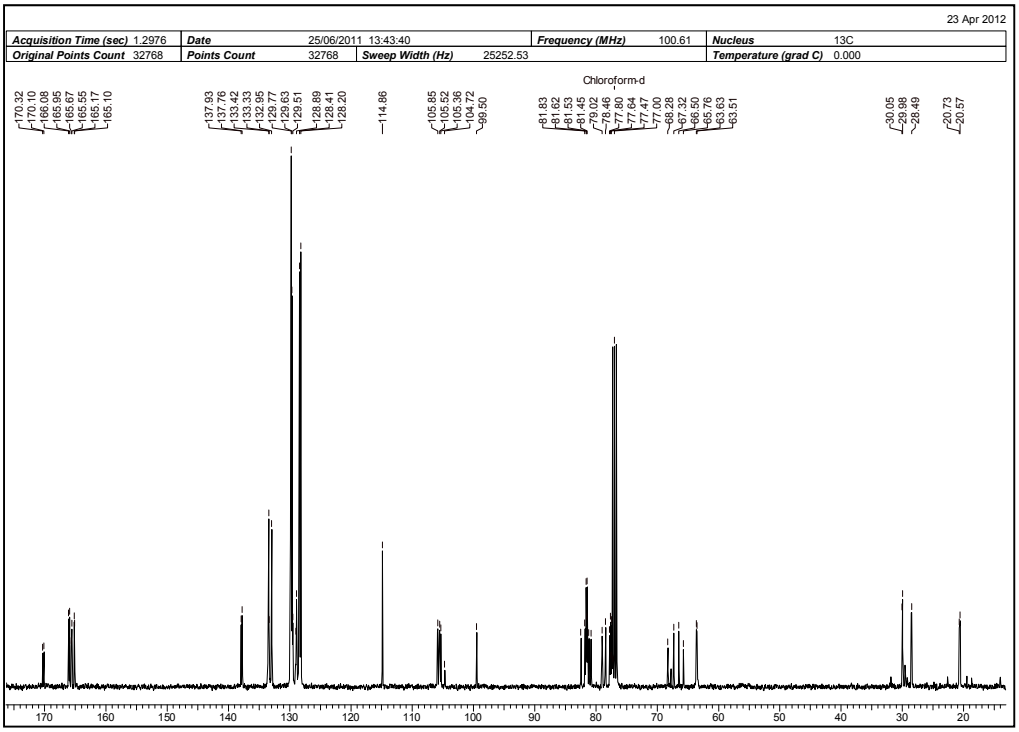
^{1}H NMR Spectrum of 37 in $CDCl_3$



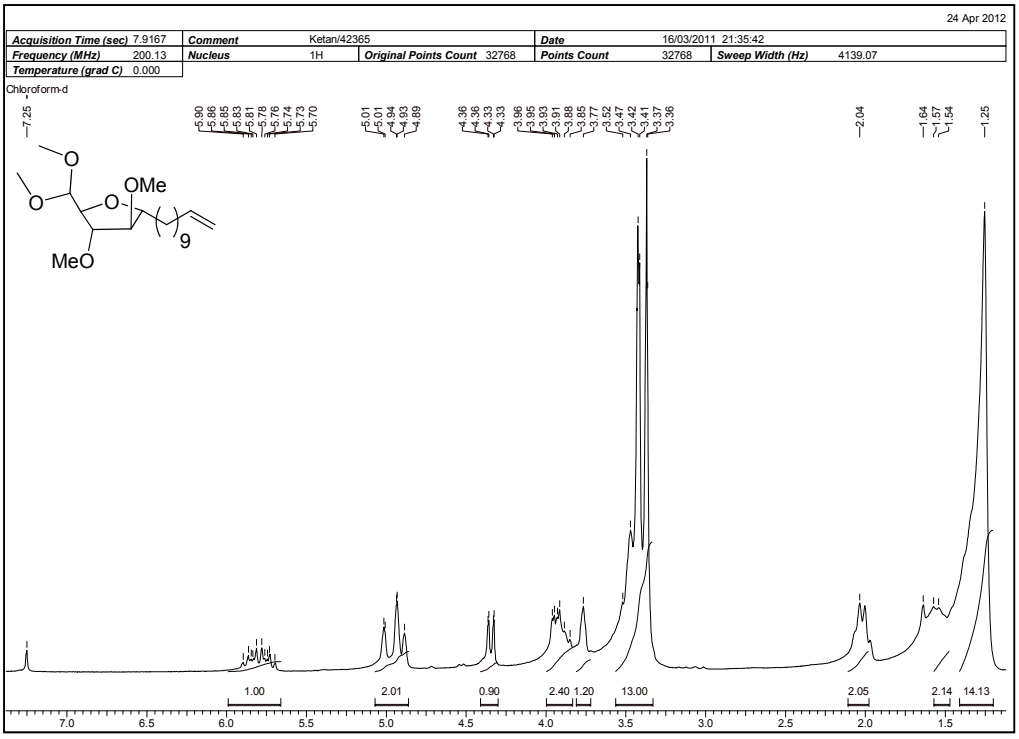
^{13}C NMR Spectrum of 37 in $CDCl_3$



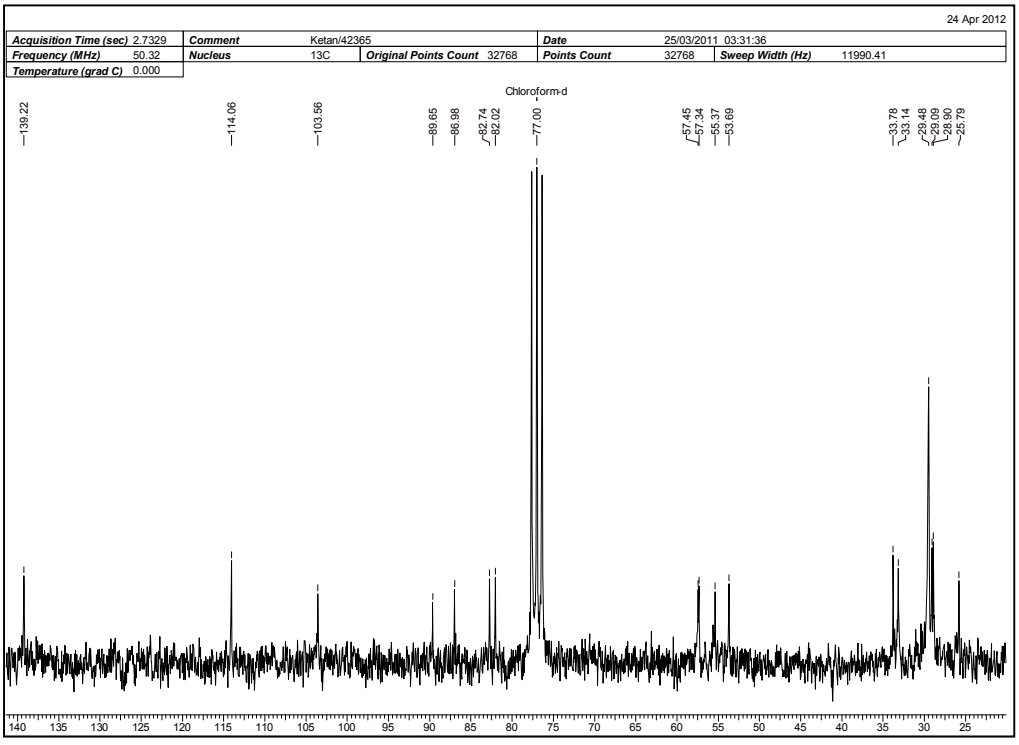
^{1}H NMR Spectrum of 35 in $CDCl_3$



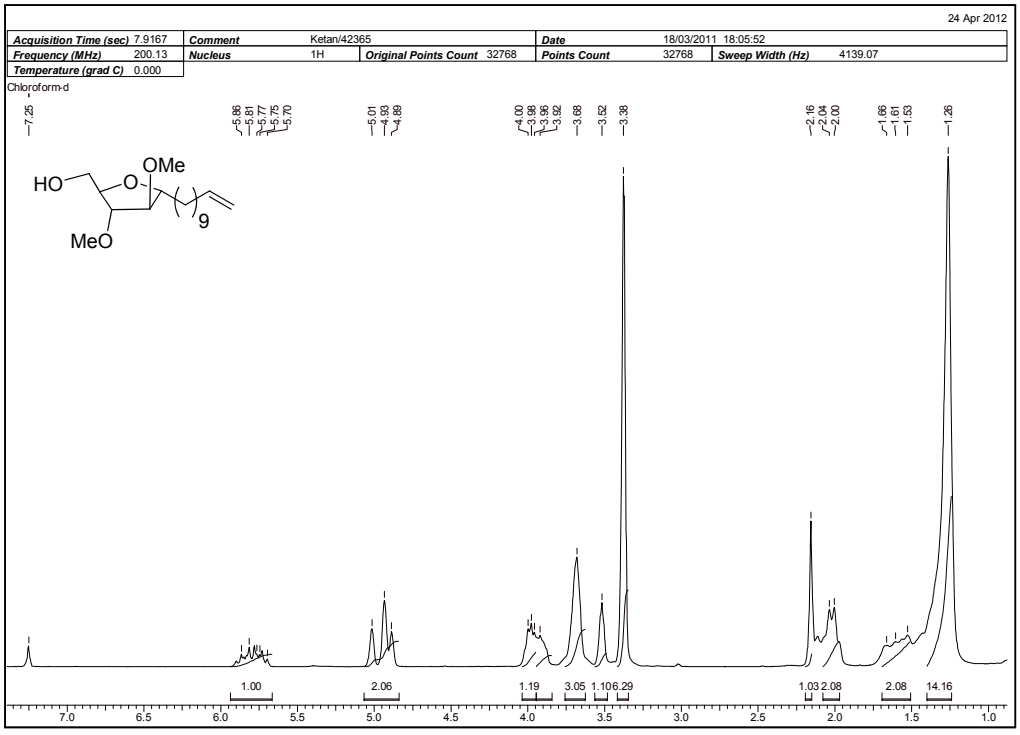
^{13}C NMR Spectrum of 35 in $CDCl_3$



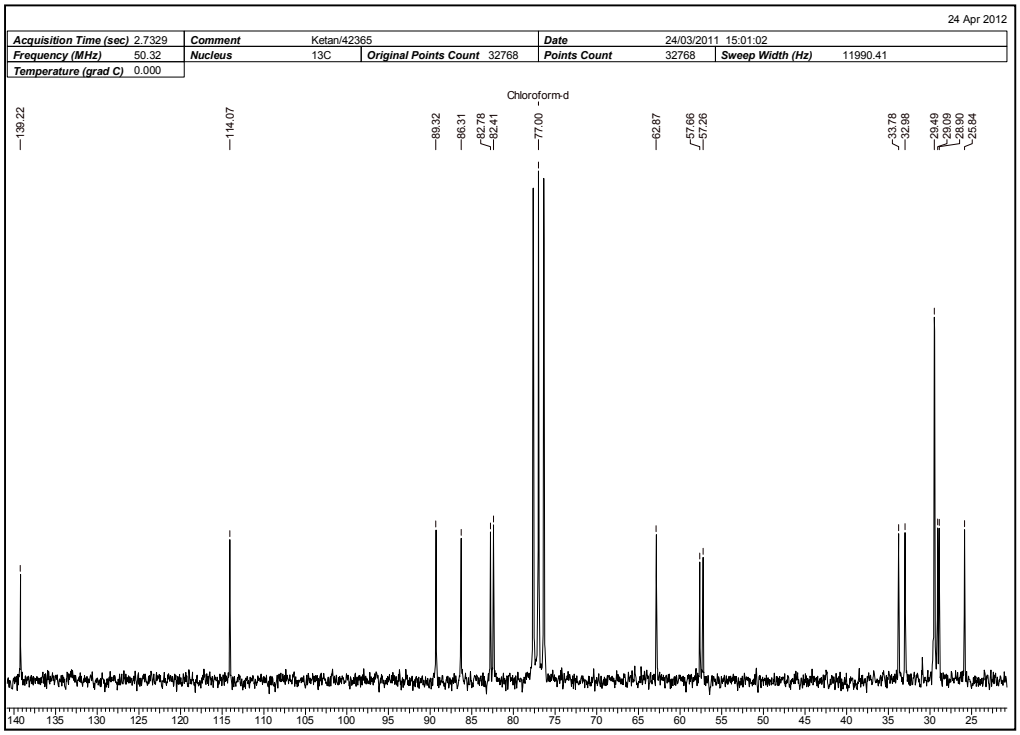
^{1}H NMR Spectrum of 38 in $CDCl_3$



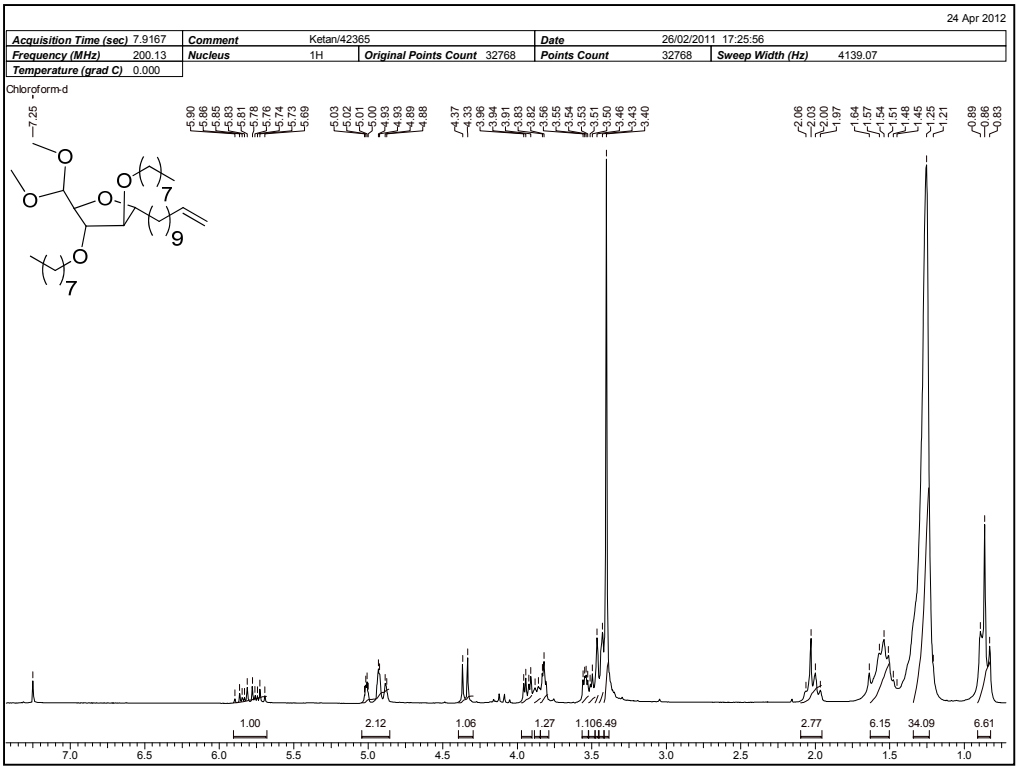
^{13}C NMR Spectrum of 38 in $CDCl_3$



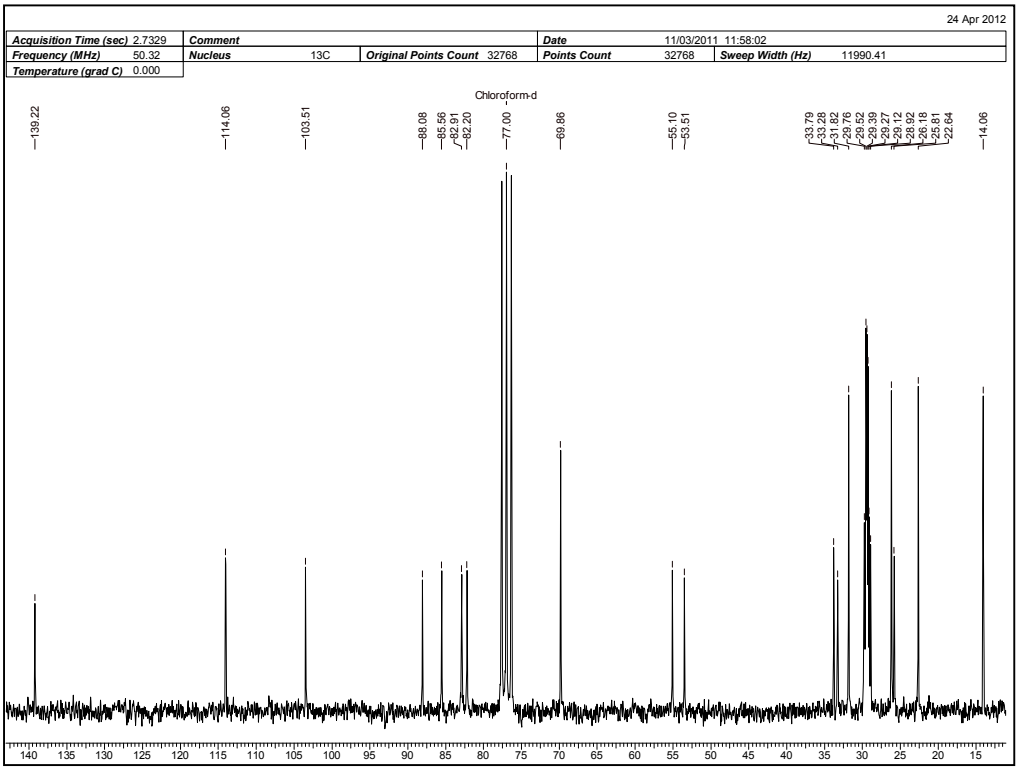
^{1}H NMR Spectrum of 40 in $CDCl_3$



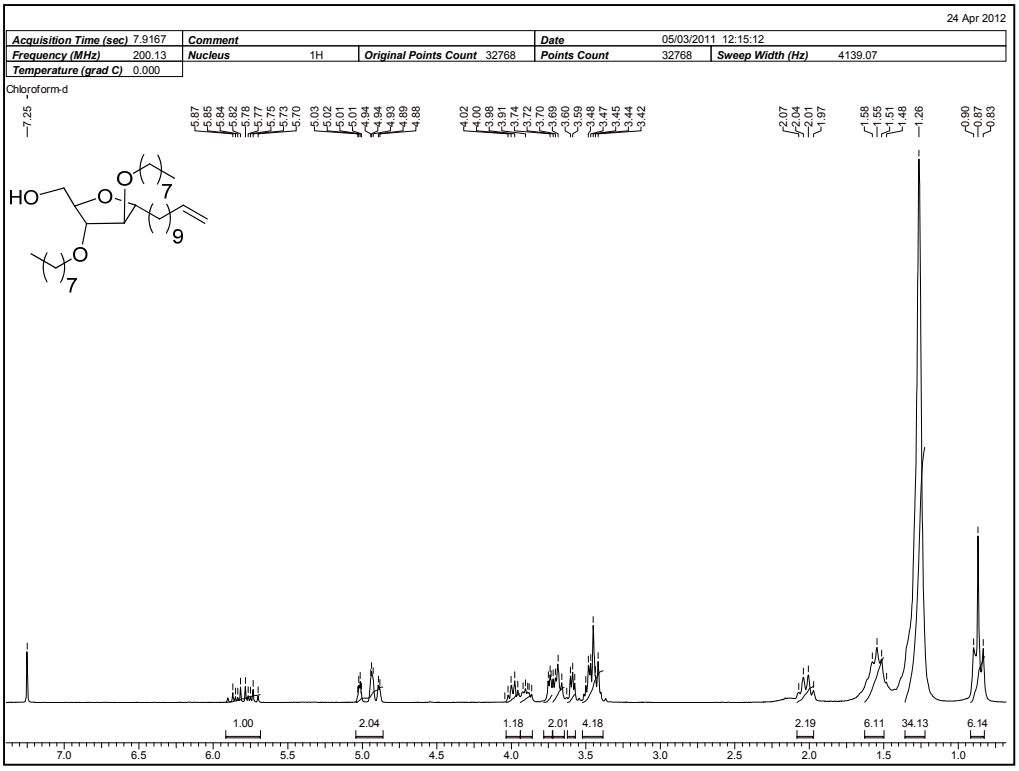
^{13}C NMR Spectrum of 40 in $CDCl_3$



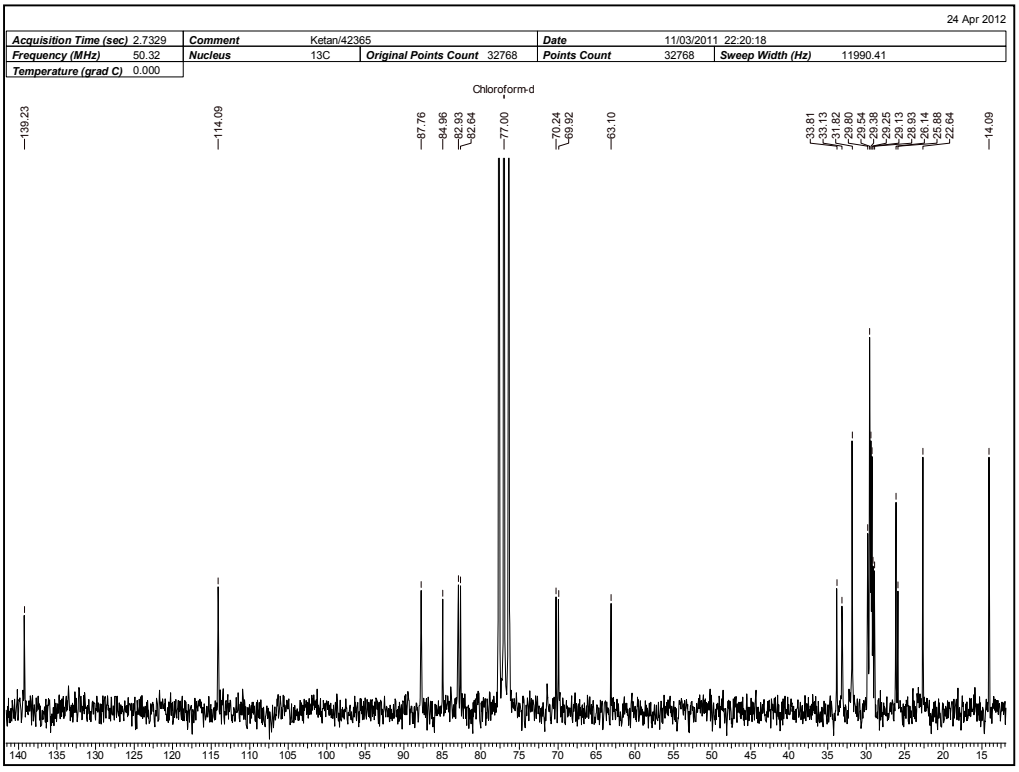
^{1}H NMR Spectrum of 39 in $CDCl_3$



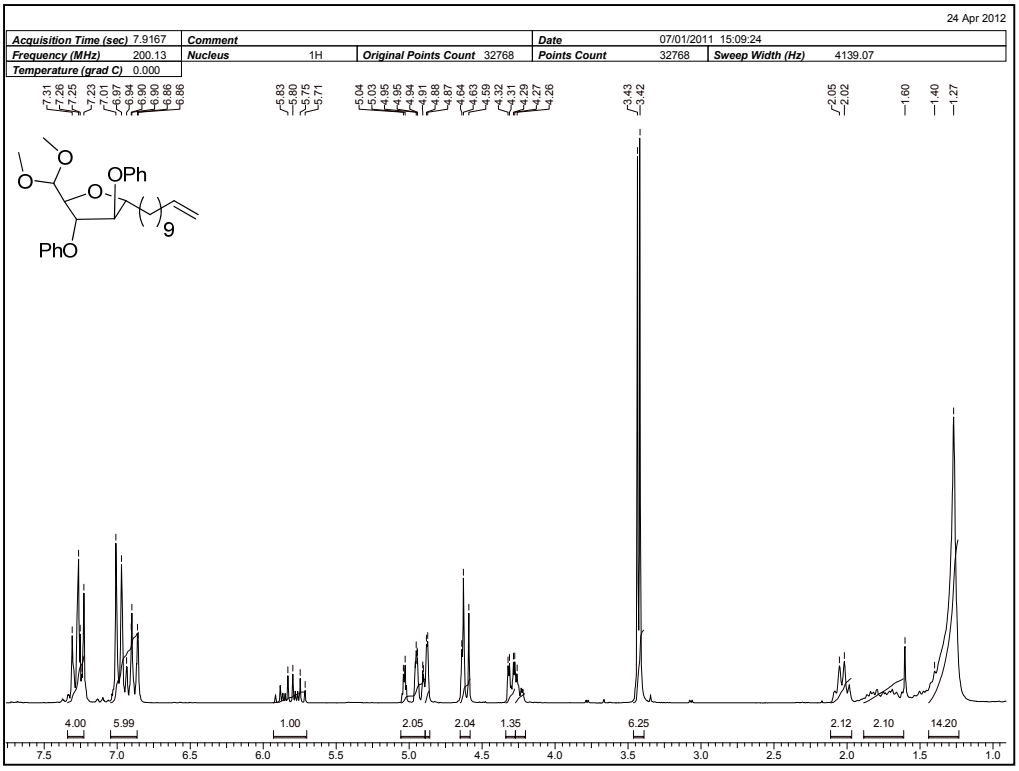
^{13}C NMR Spectrum of 39 in $CDCl_3$



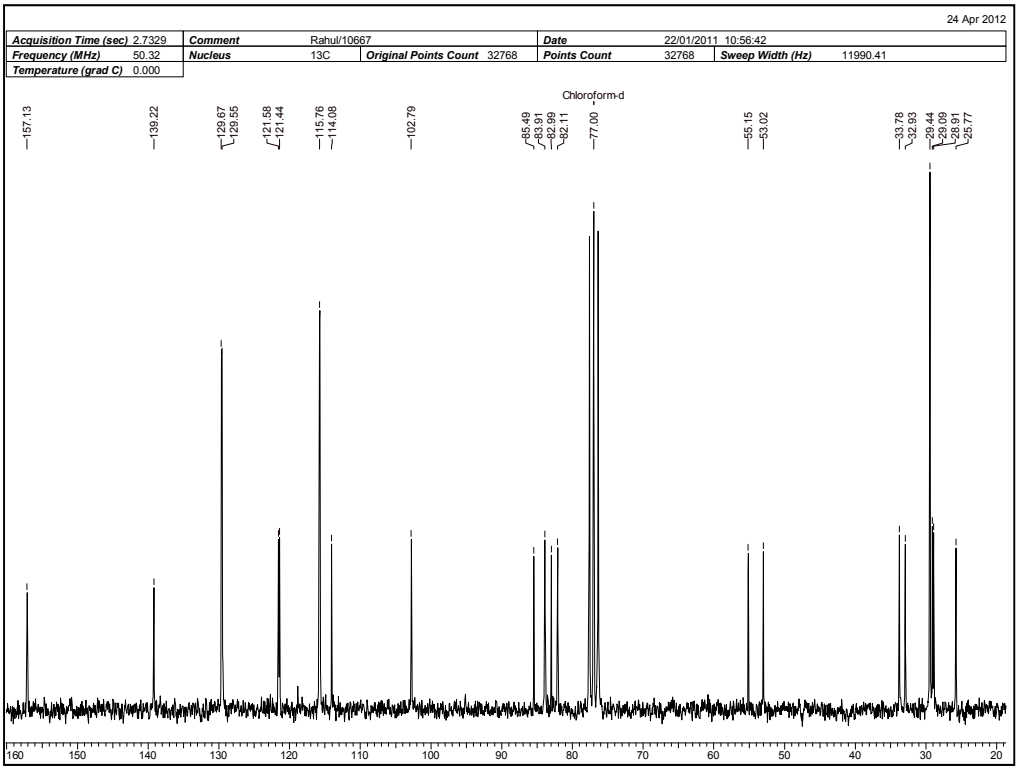
^{1}H NMR Spectrum of 41 in $CDCl_3$



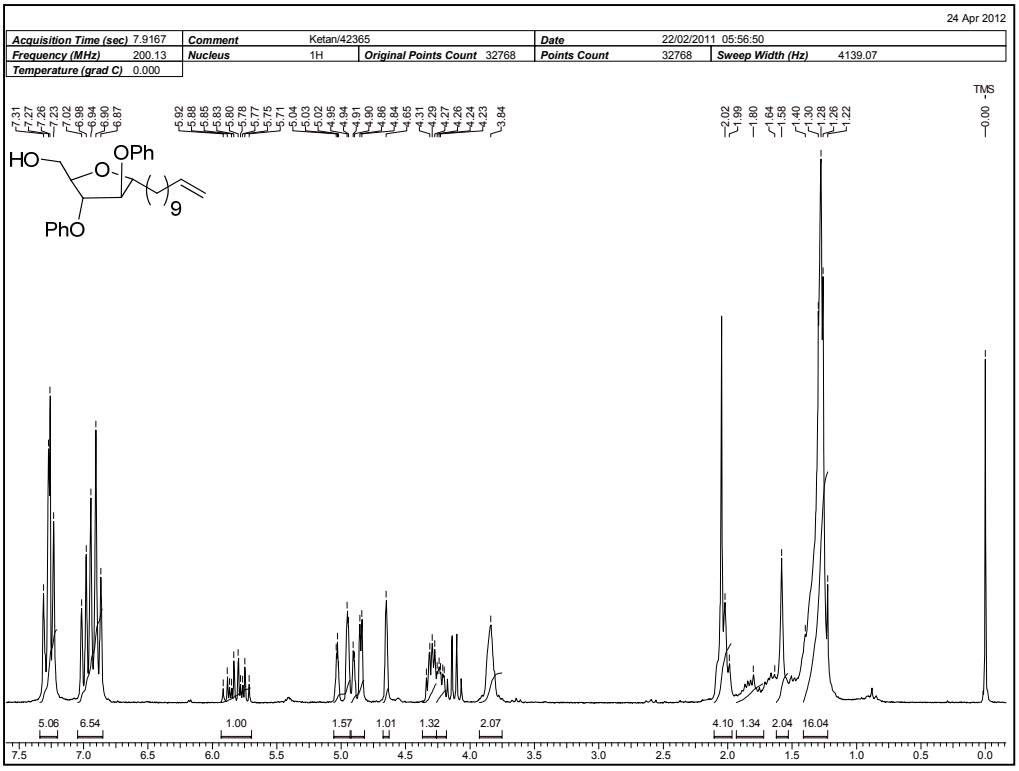
^{13}C NMR Spectrum of 41 in $CDCl_3$



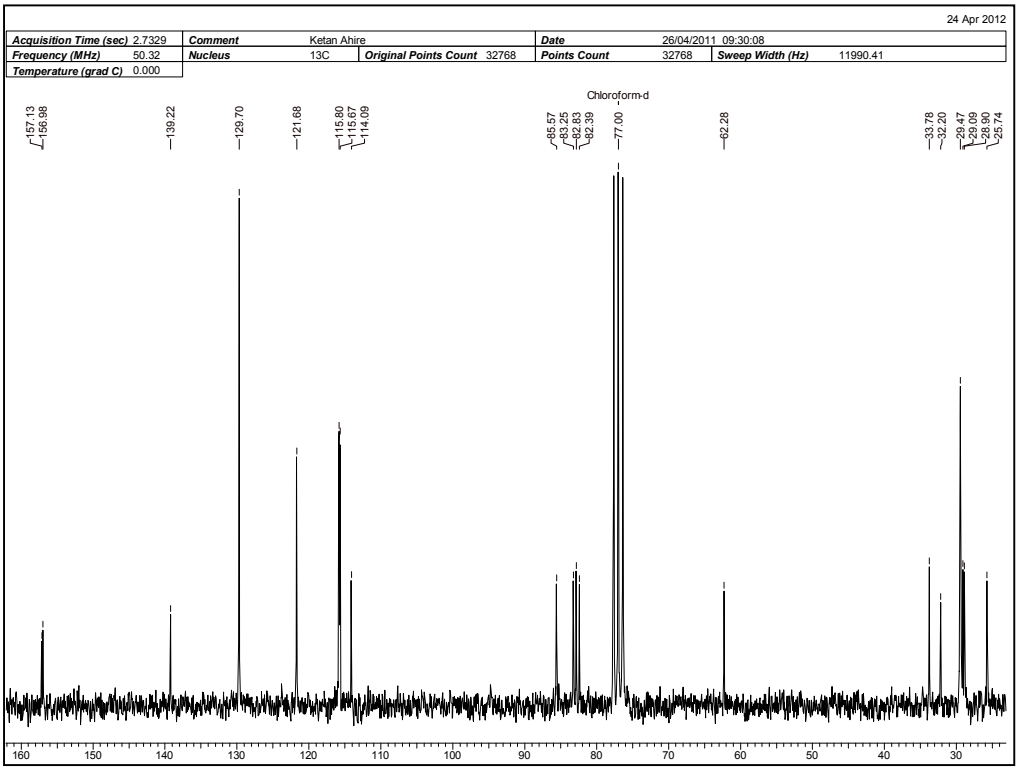
^{1}H NMR Spectrum of 42 in $CDCl_3$



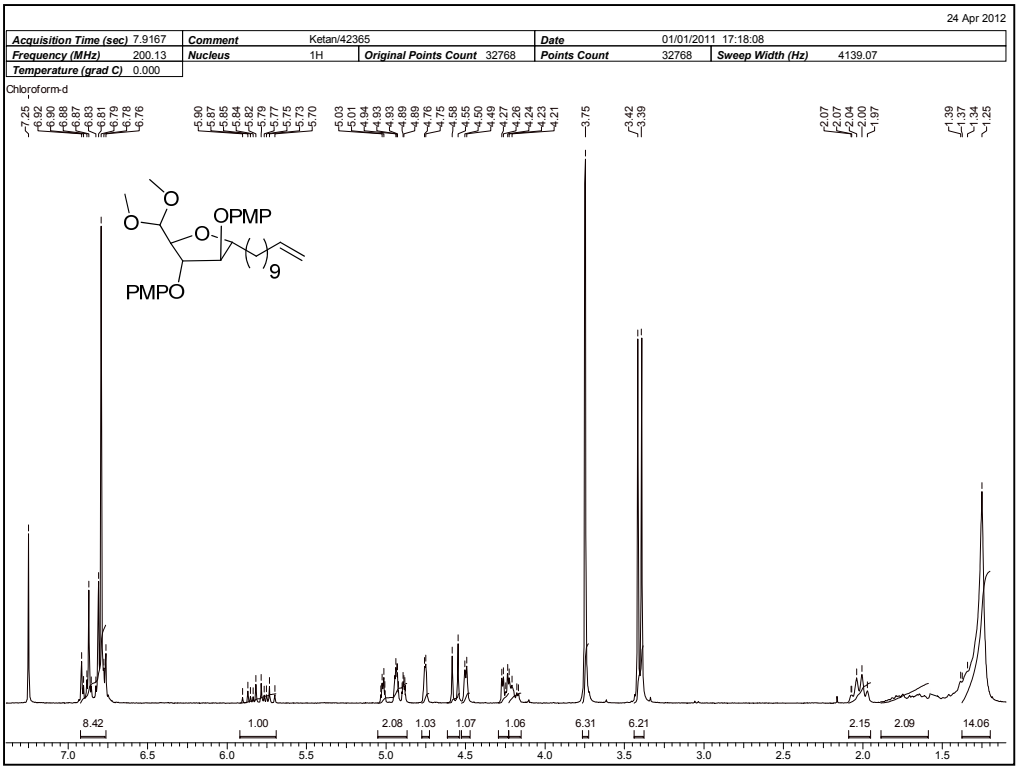
^{13}C NMR Spectrum of 42 in $CDCl_3$



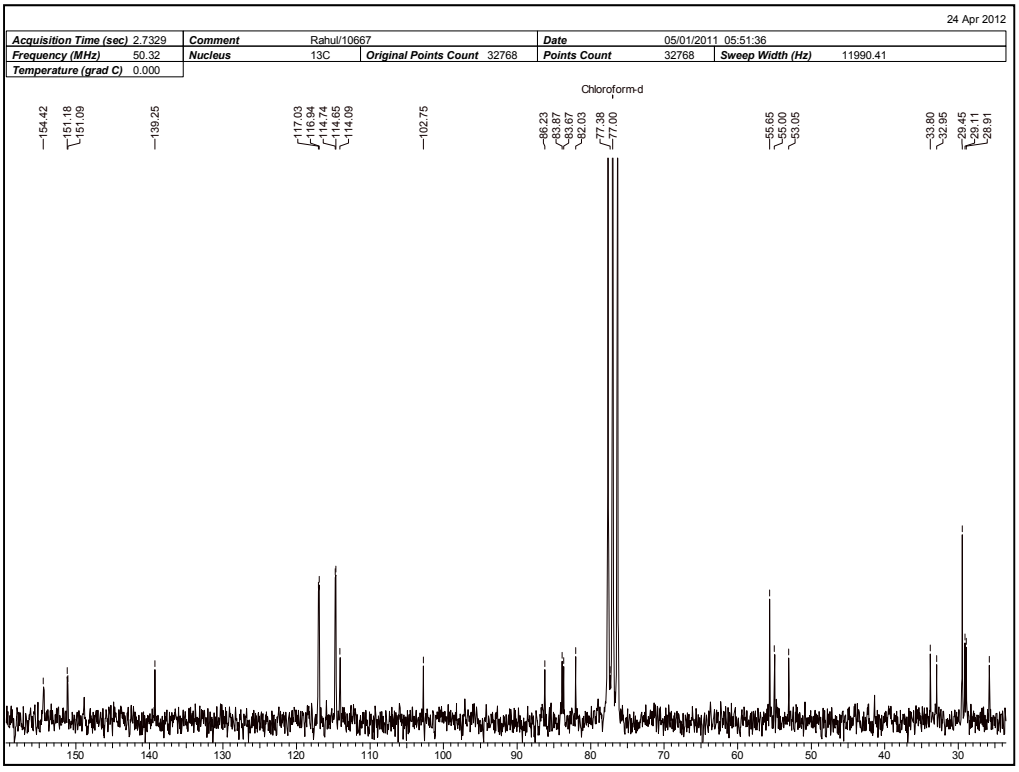
^{1}H NMR Spectrum of 50 in $CDCl_3$



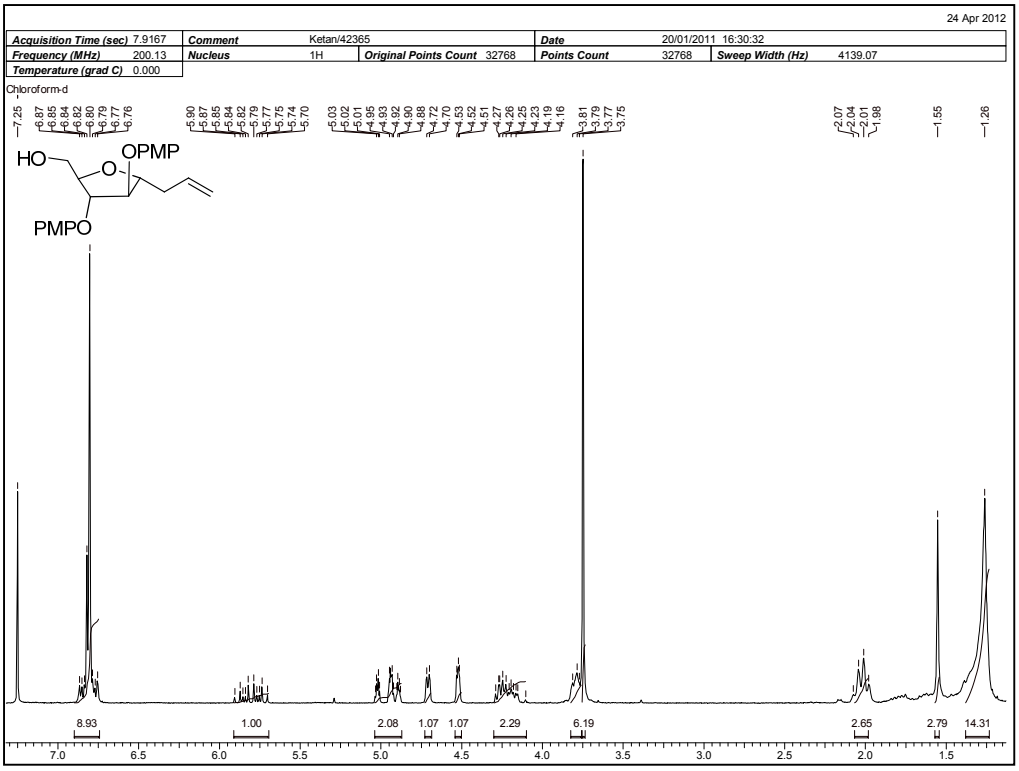
^{13}C NMR Spectrum of 50 in $CDCl_3$



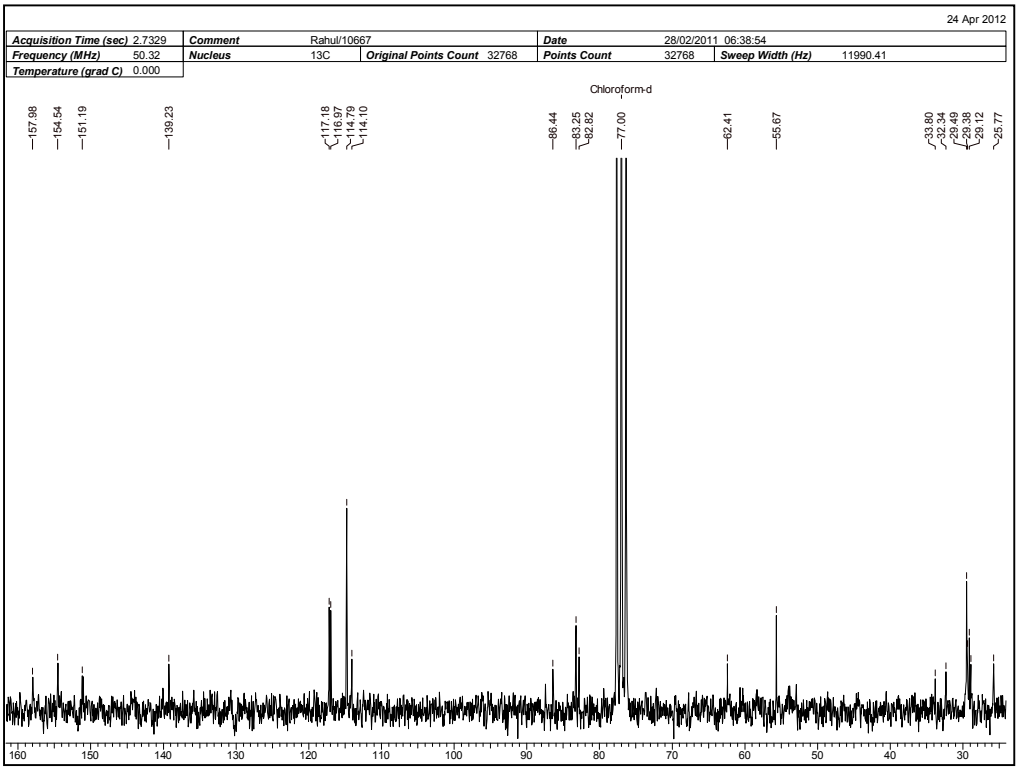
^{1}H NMR Spectrum of 43 in $CDCl_3$



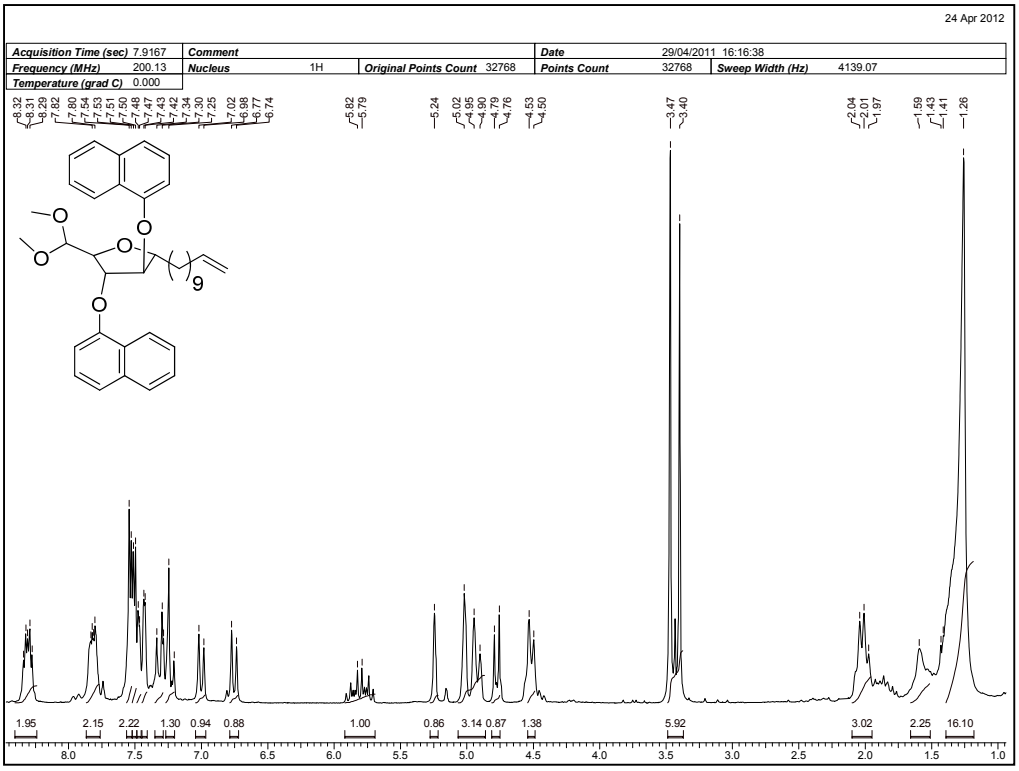
^{13}C NMR Spectrum of 43 in $CDCl_3$



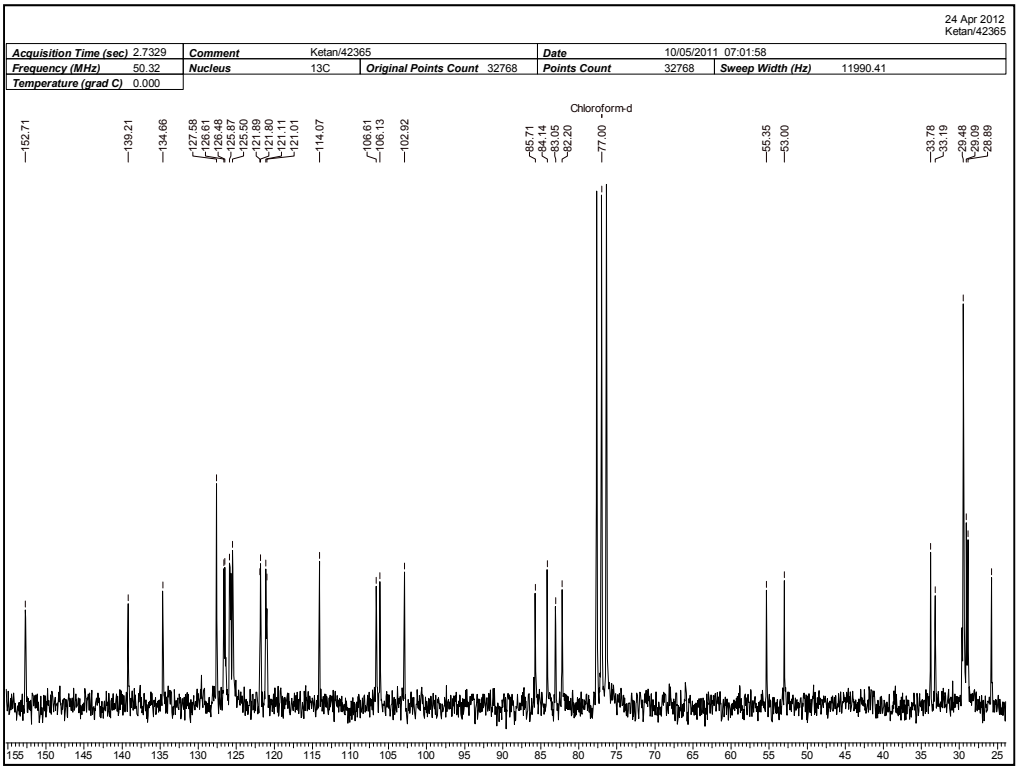
^{1}H NMR Spectrum of 51 in $CDCl_3$



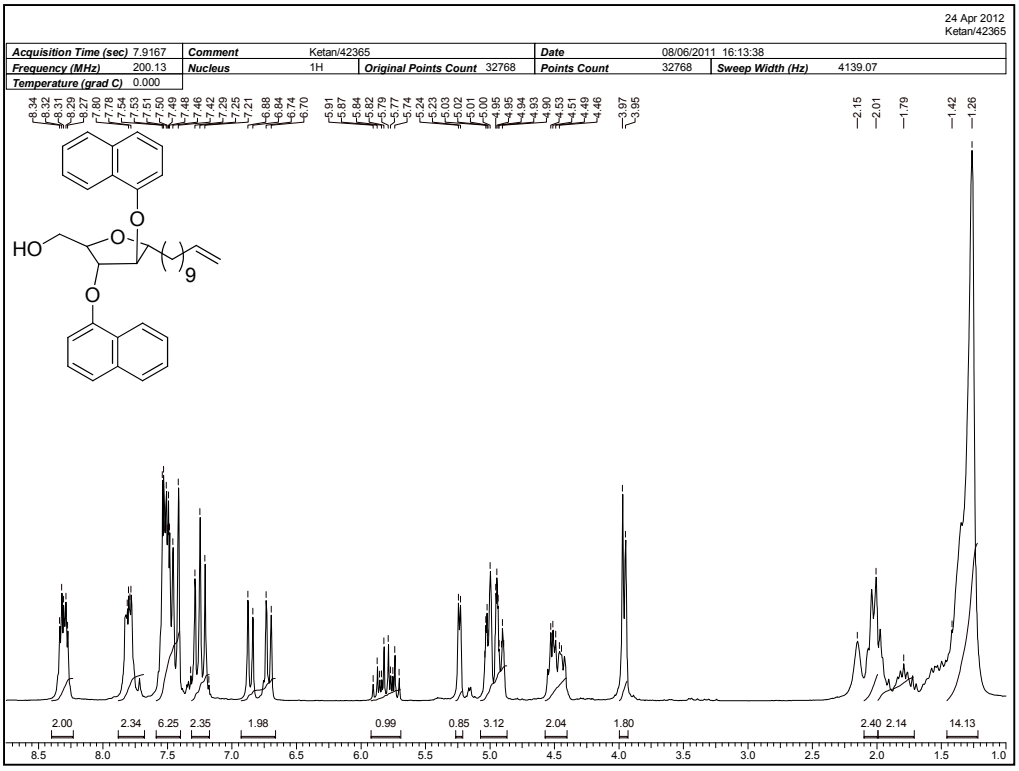
^{13}C NMR Spectrum of 51 in $CDCl_3$



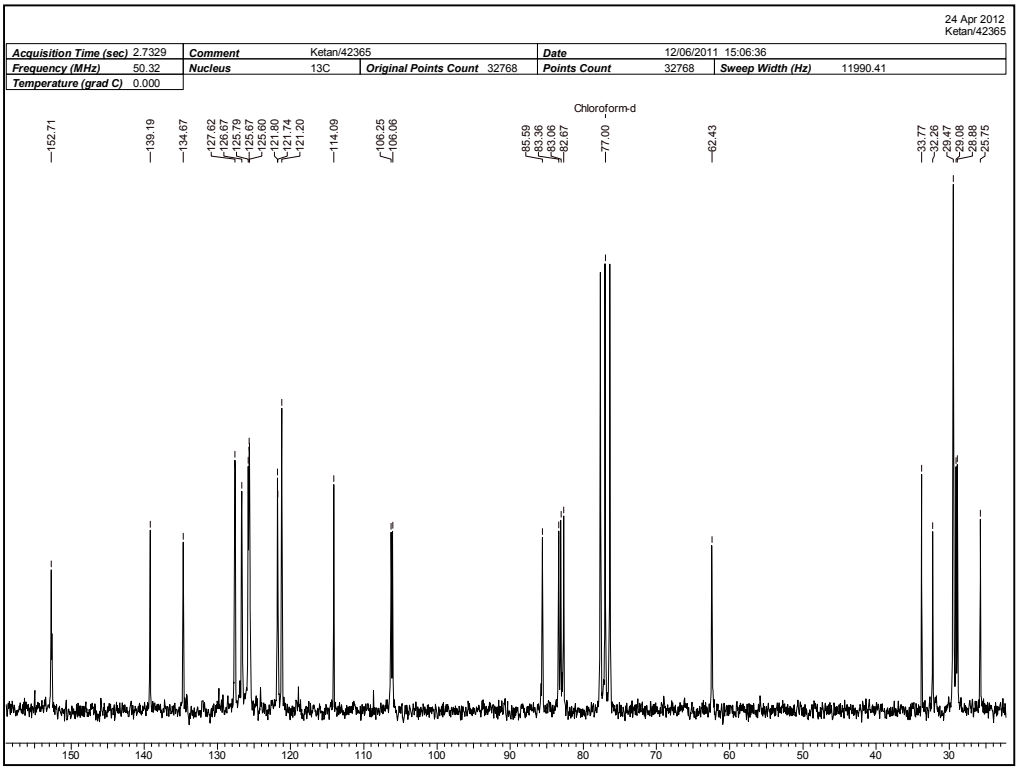
^{1}H NMR Spectrum of 44 in $CDCl_3$



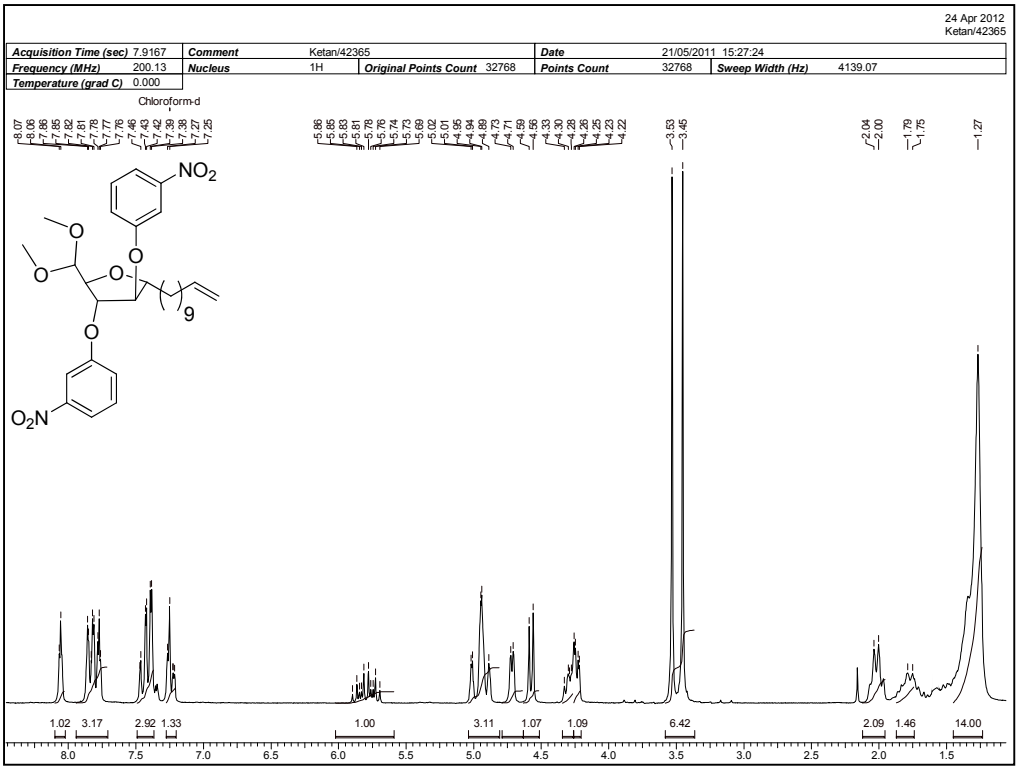
^{13}C NMR Spectrum of 44 in $CDCl_3$



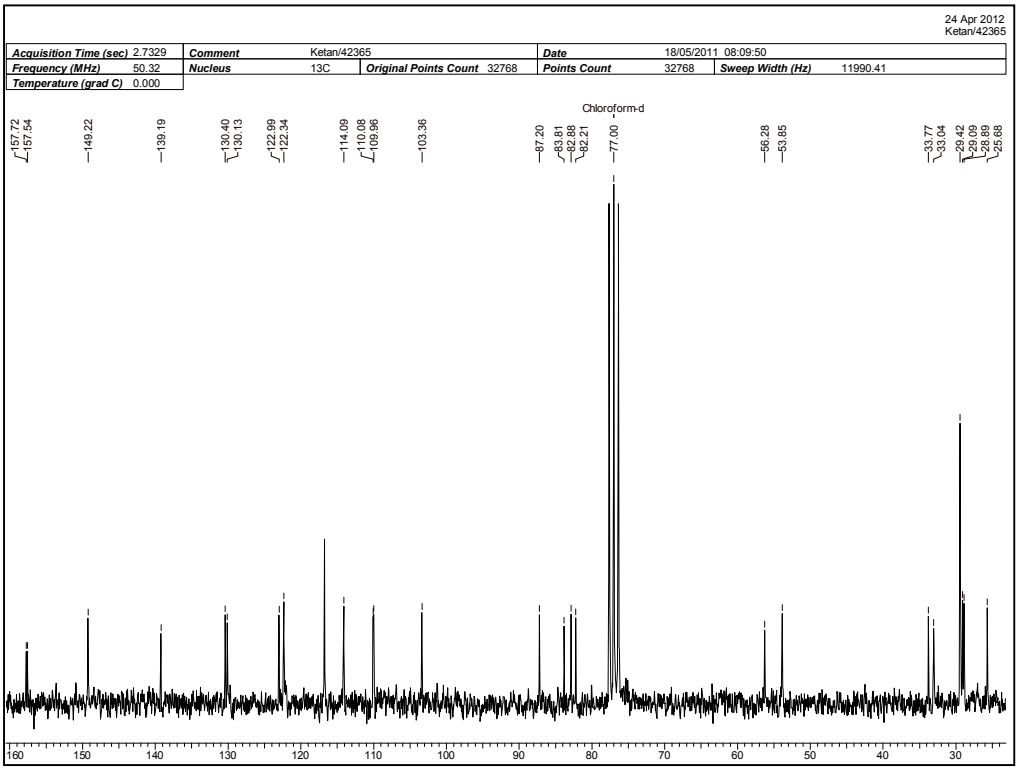
^{1}H NMR Spectrum of 52 in $CDCl_3$



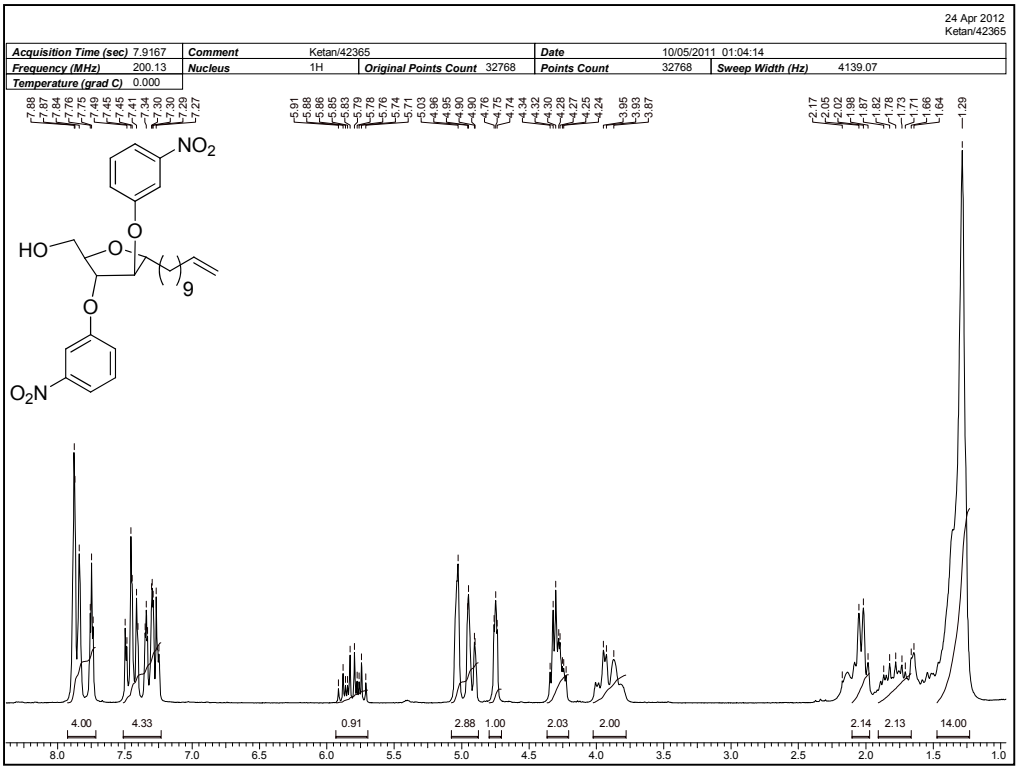
^{13}C NMR Spectrum of 52 in $CDCl_3$



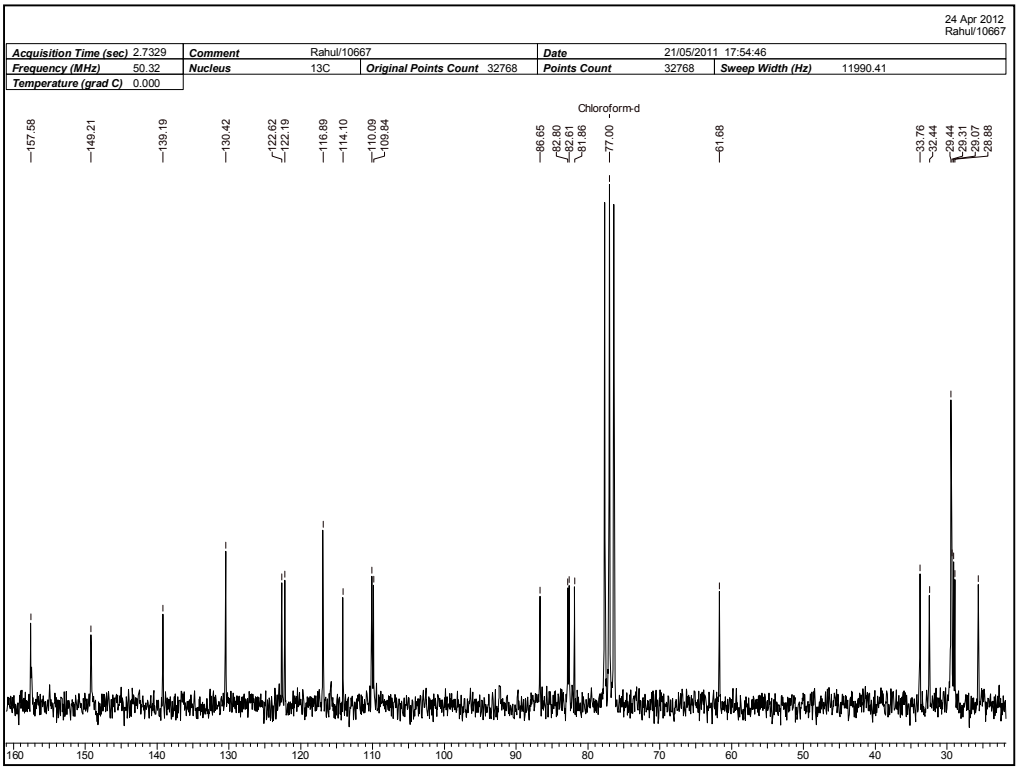
^{1}H NMR Spectrum of 45 in $CDCl_3$



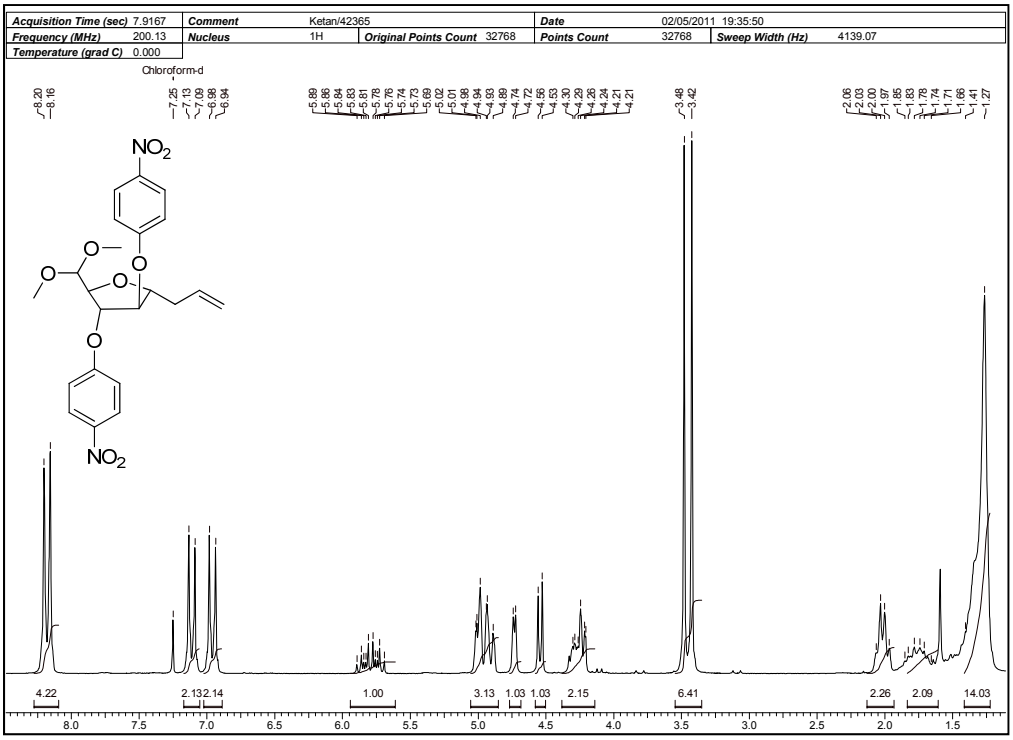
^{13}C NMR Spectrum of 45 in $CDCl_3$



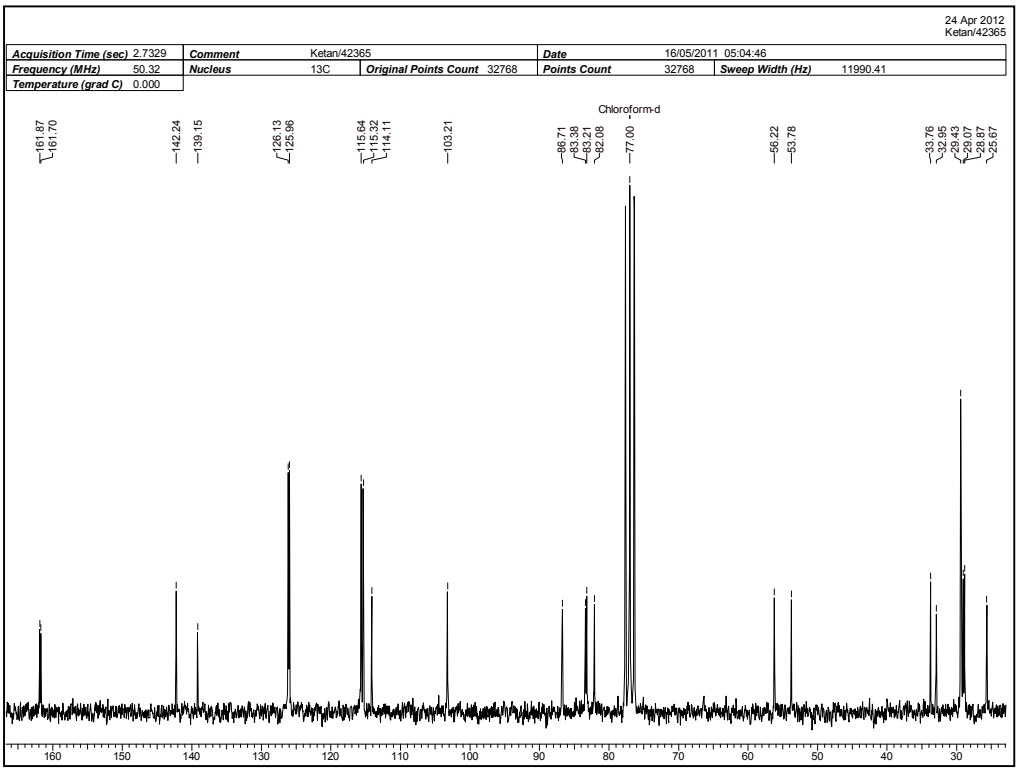
^{1}H NMR Spectrum of 53 in $CDCl_3$



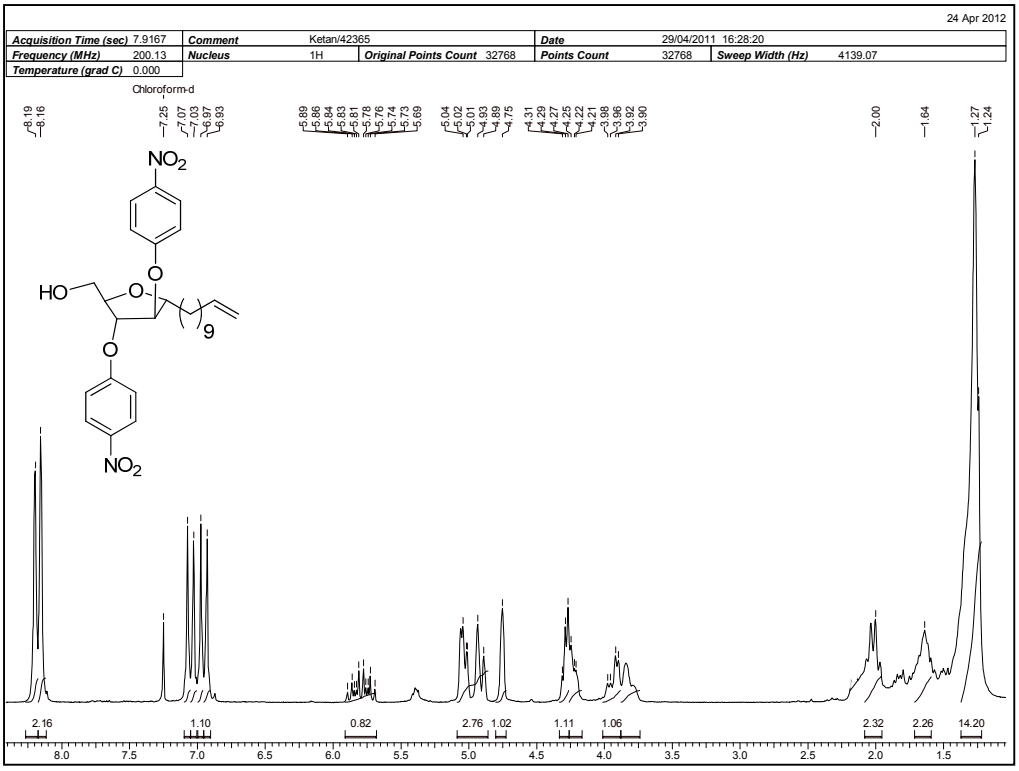
^{13}C NMR Spectrum of 53 in $CDCl_3$



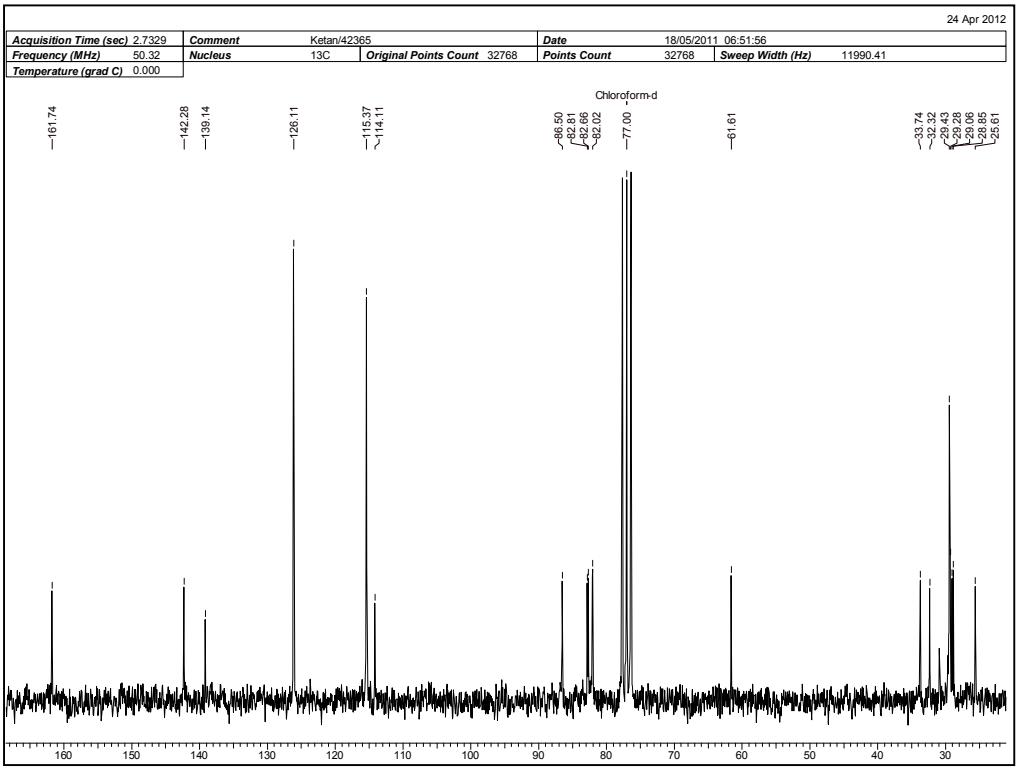
^{1}H NMR Spectrum of 46 in $CDCl_3$



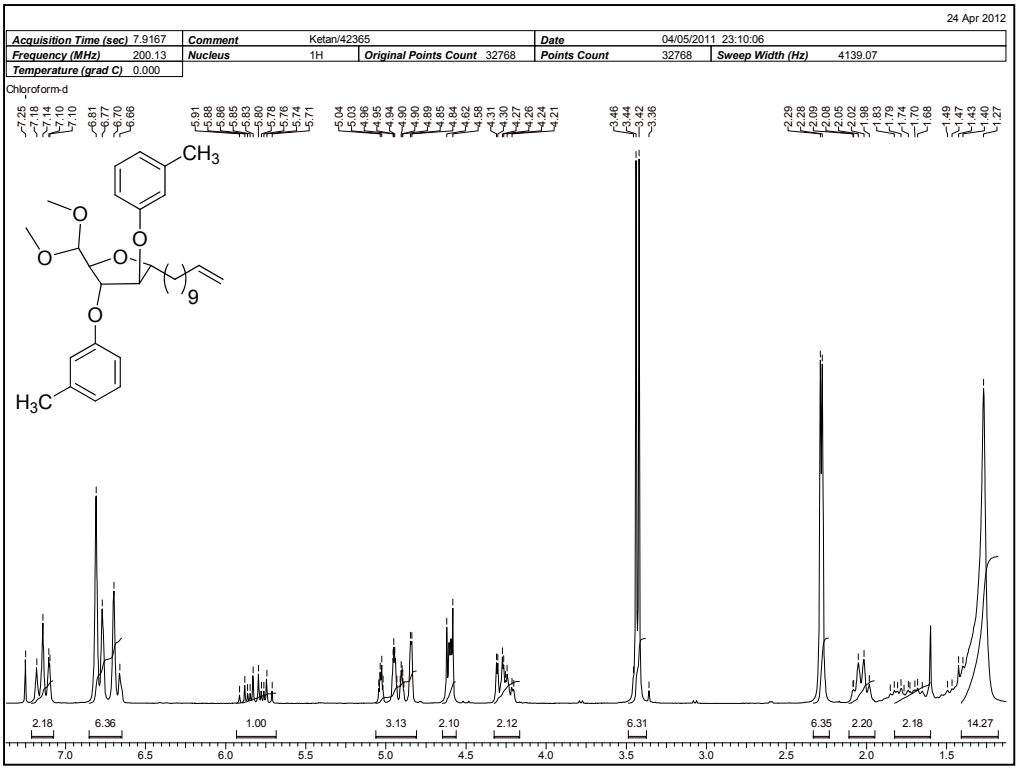
^{13}C NMR Spectrum of 46 in $CDCl_3$



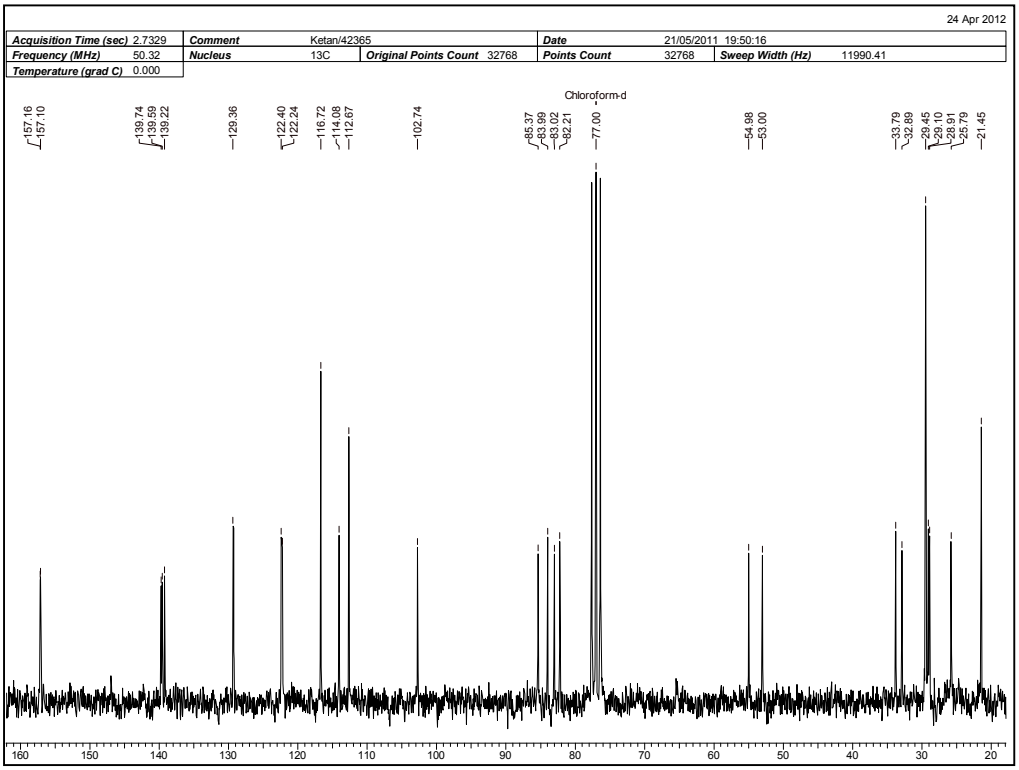
^{1}H NMR Spectrum of 54 in $CDCl_3$



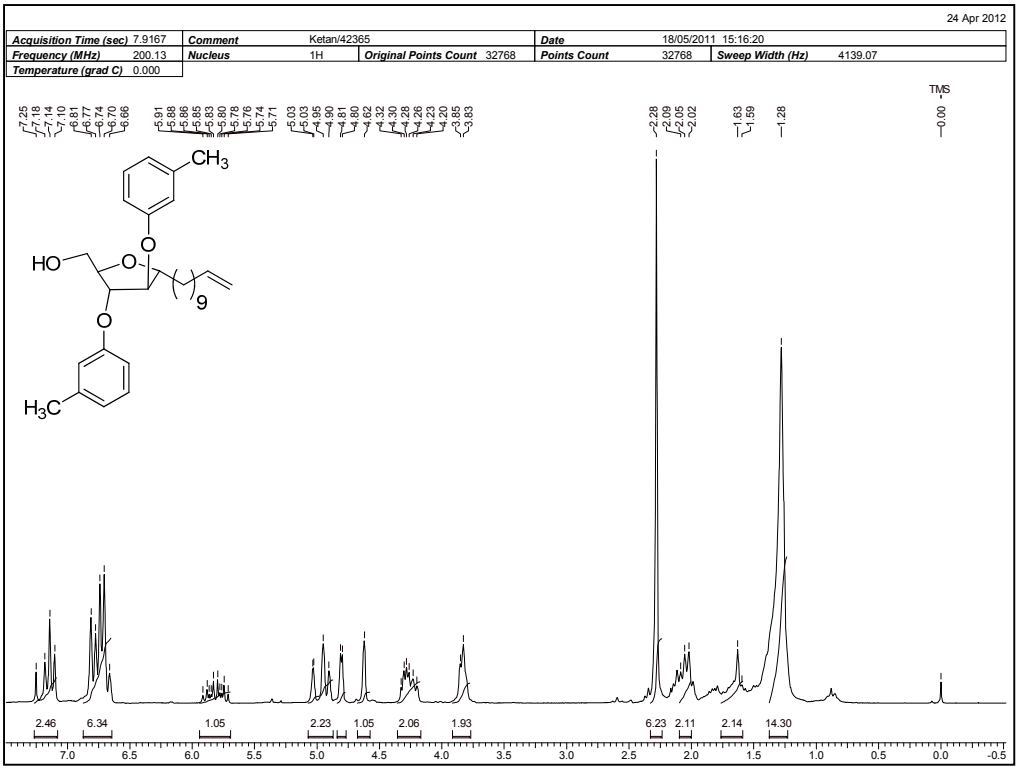
^{13}C NMR Spectrum of 54 in $CDCl_3$



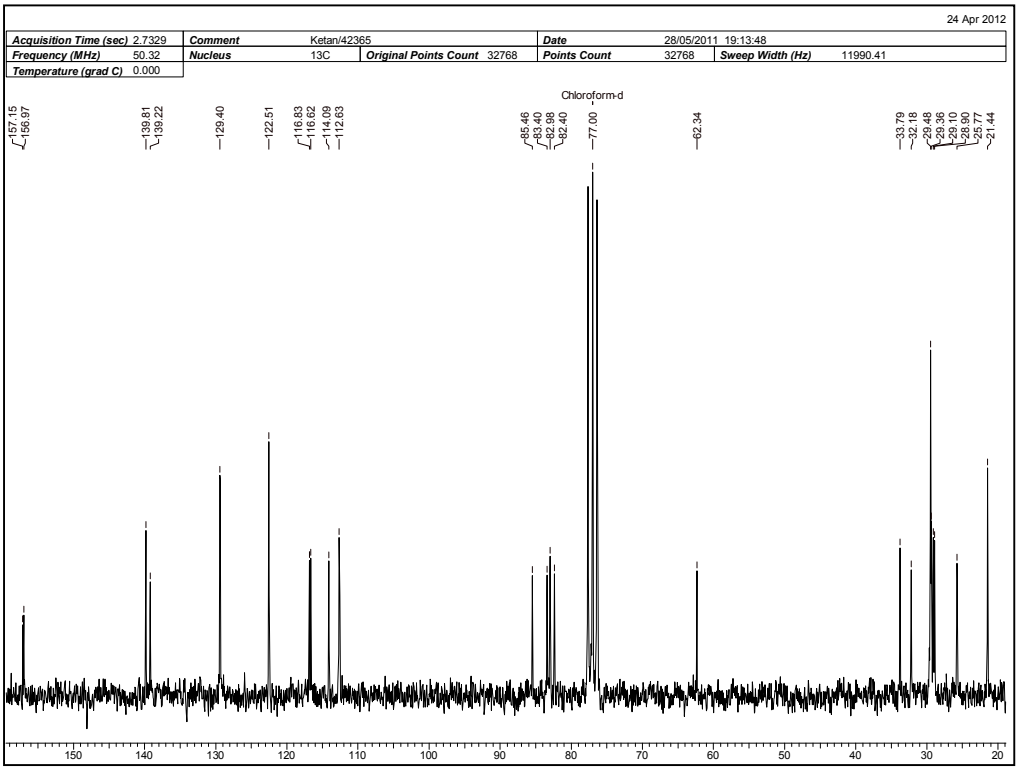
^{1}H NMR Spectrum of 47 in $CDCl_3$



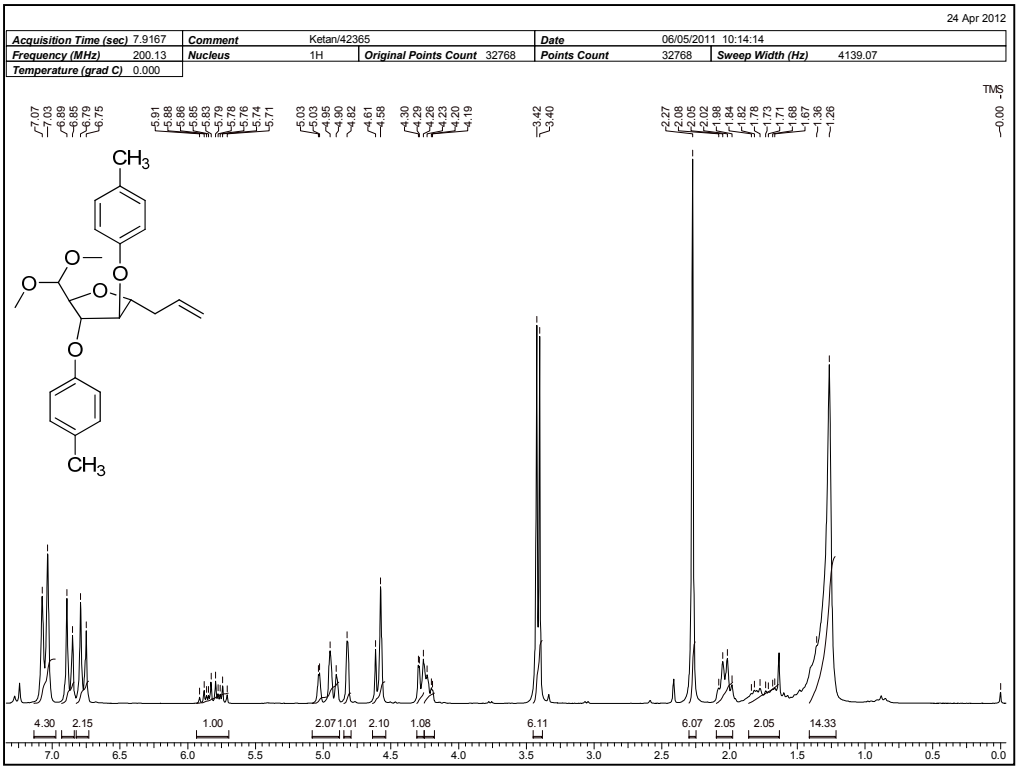
^{13}C NMR Spectrum of 47 in $CDCl_3$



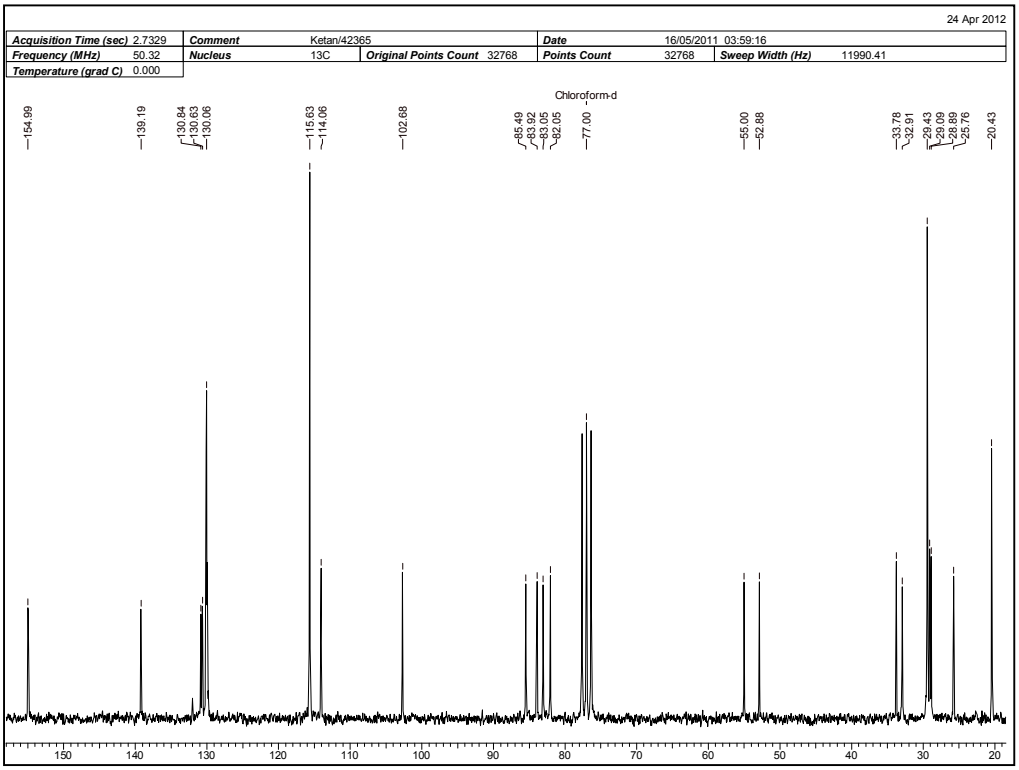
^{1}H NMR Spectrum of 55 in $CDCl_3$



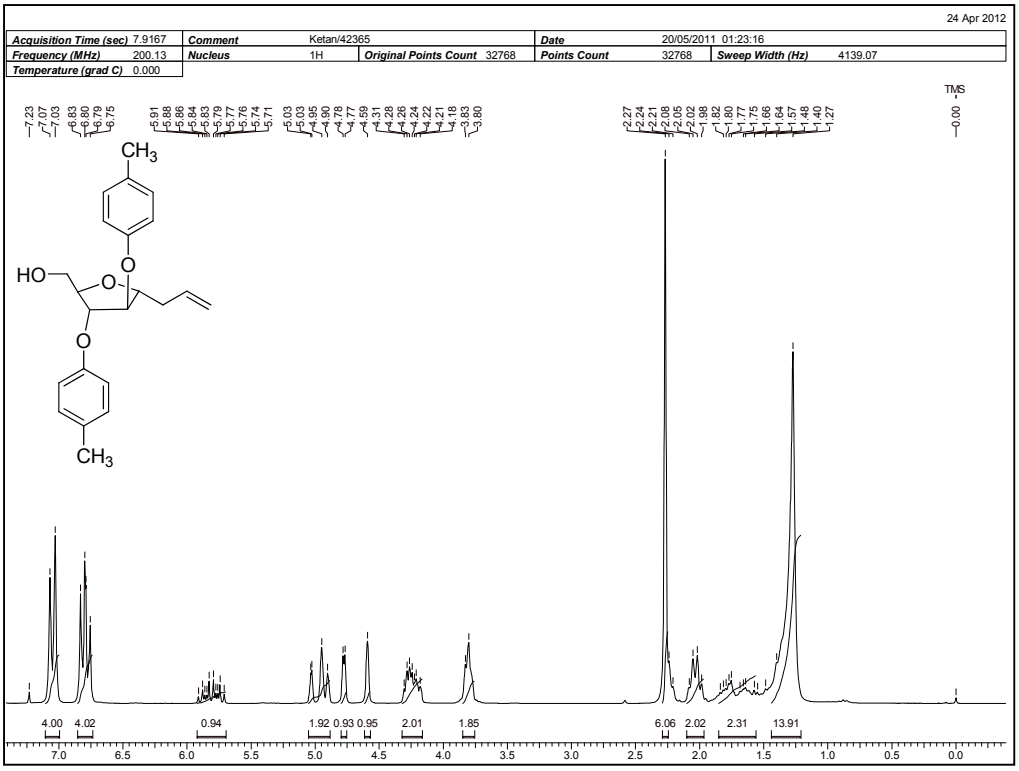
^{13}C NMR Spectrum of 55 in $CDCl_3$



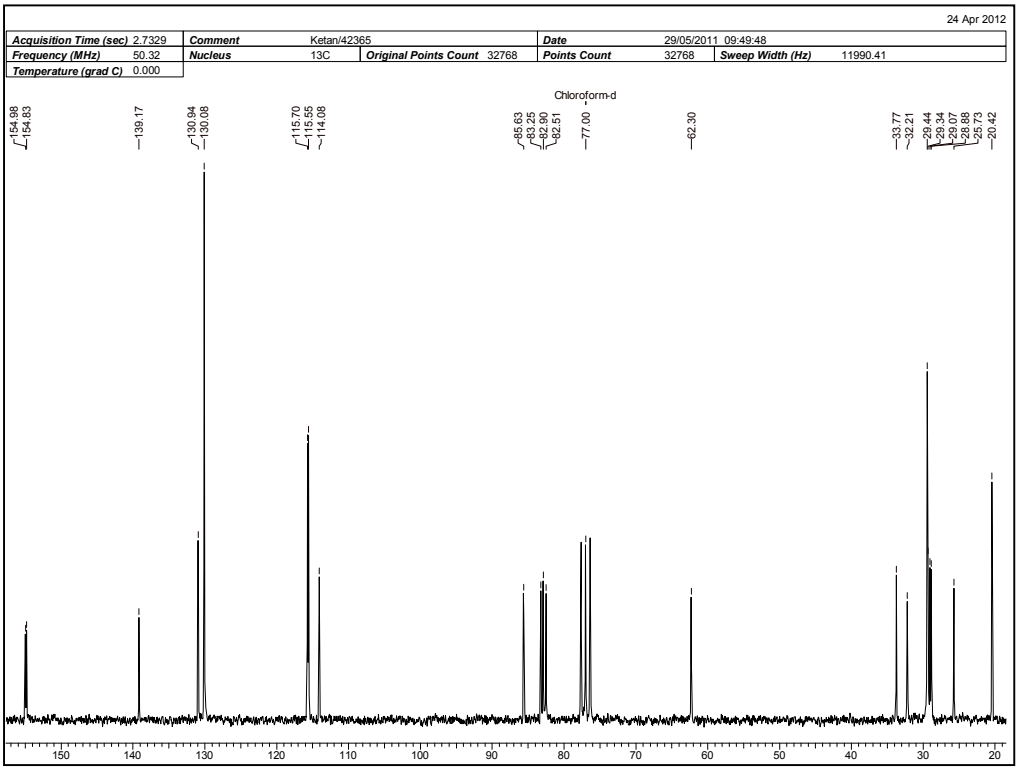
^{1}H NMR Spectrum of 48 in $CDCl_3$



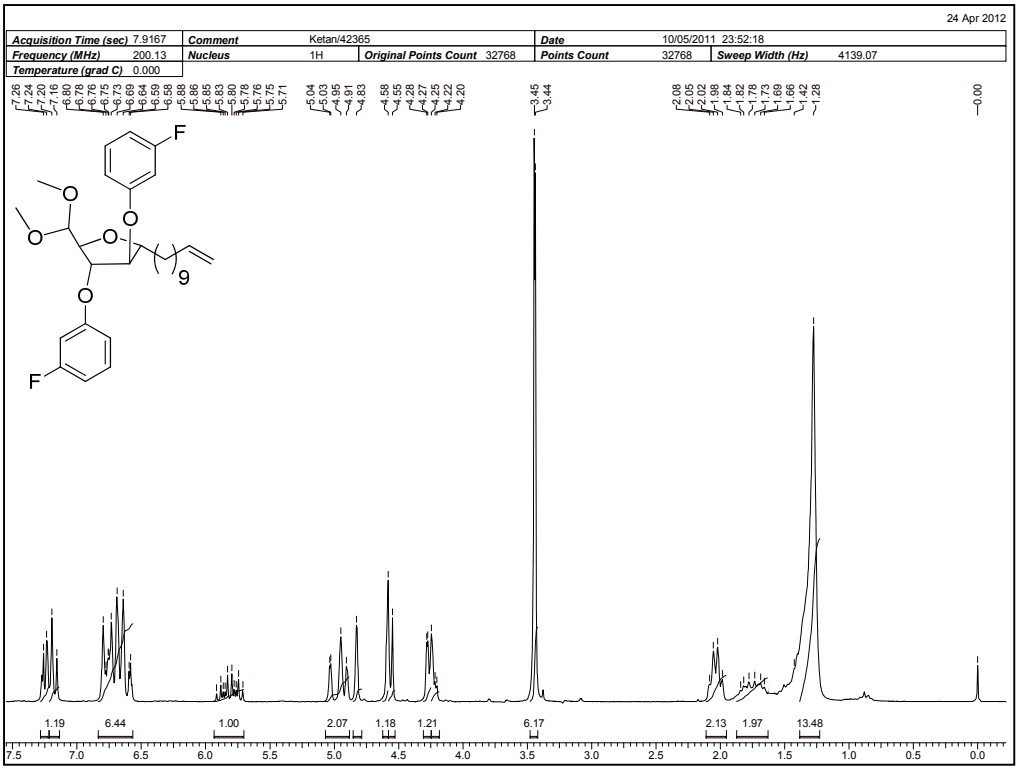
^{13}C NMR Spectrum of 48 in $CDCl_3$



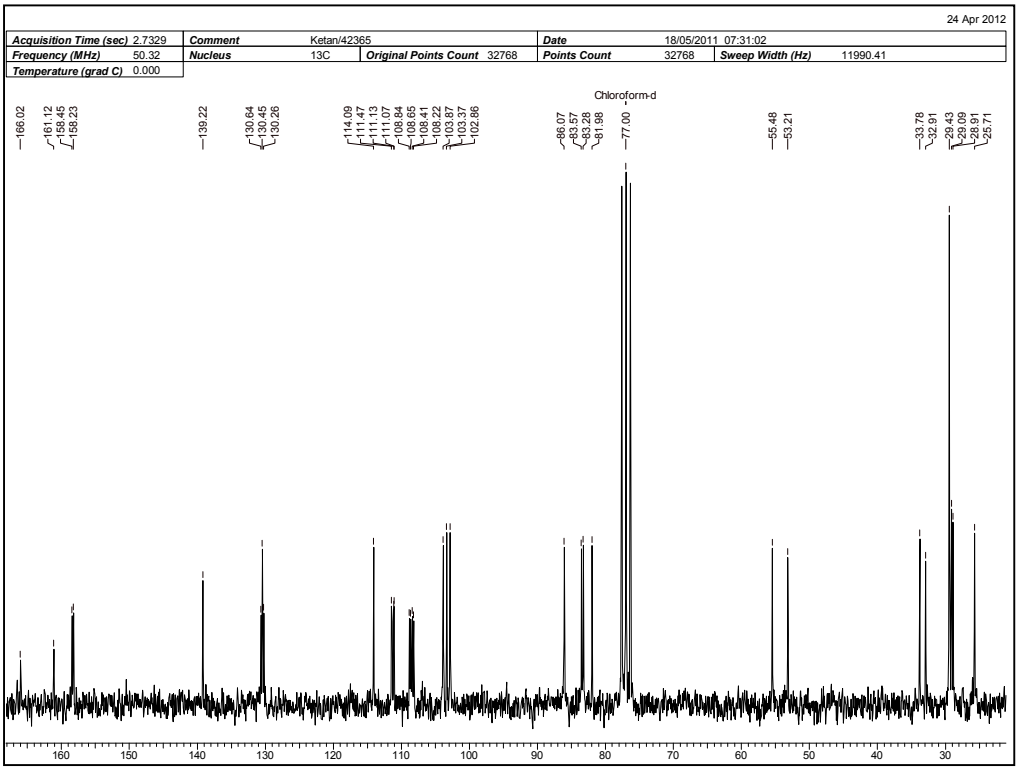
^{1}H NMR Spectrum of 56 in $CDCl_3$



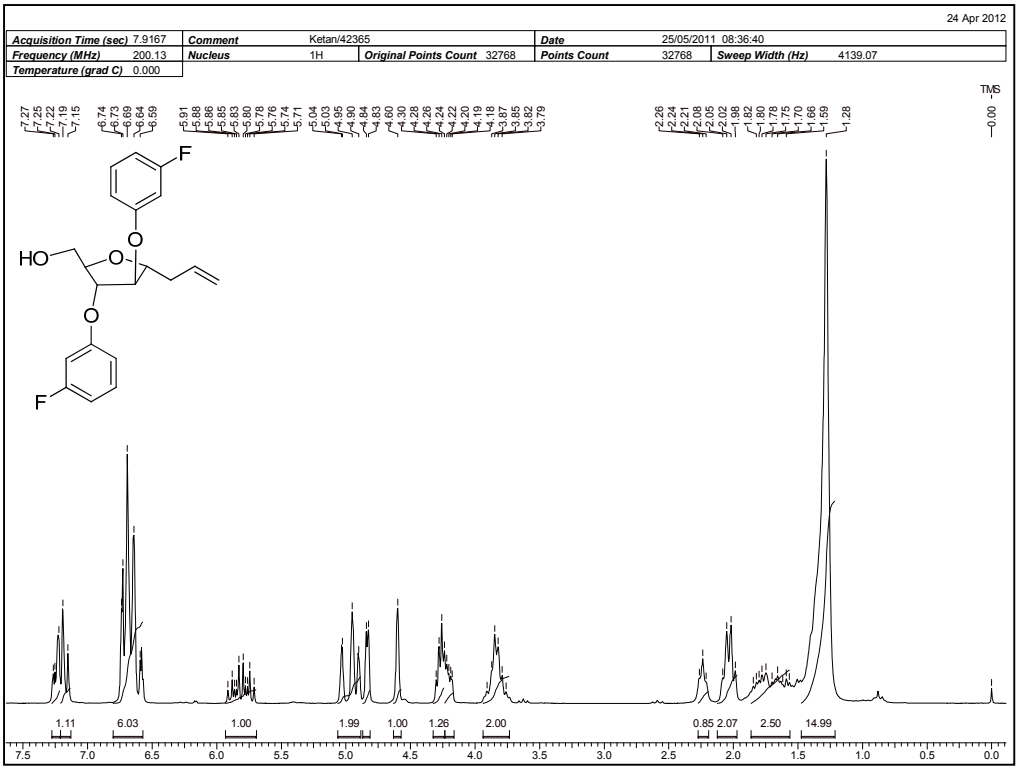
^{13}C NMR Spectrum of 56 in $CDCl_3$



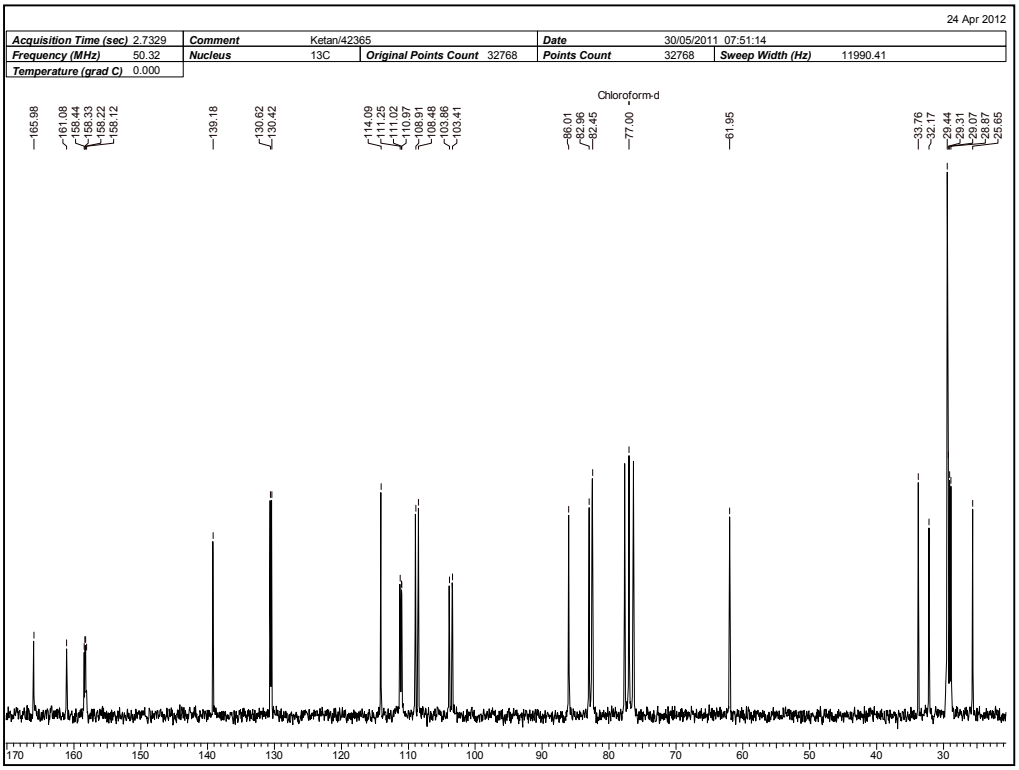
^{1}H NMR Spectrum of 49 in $CDCl_3$



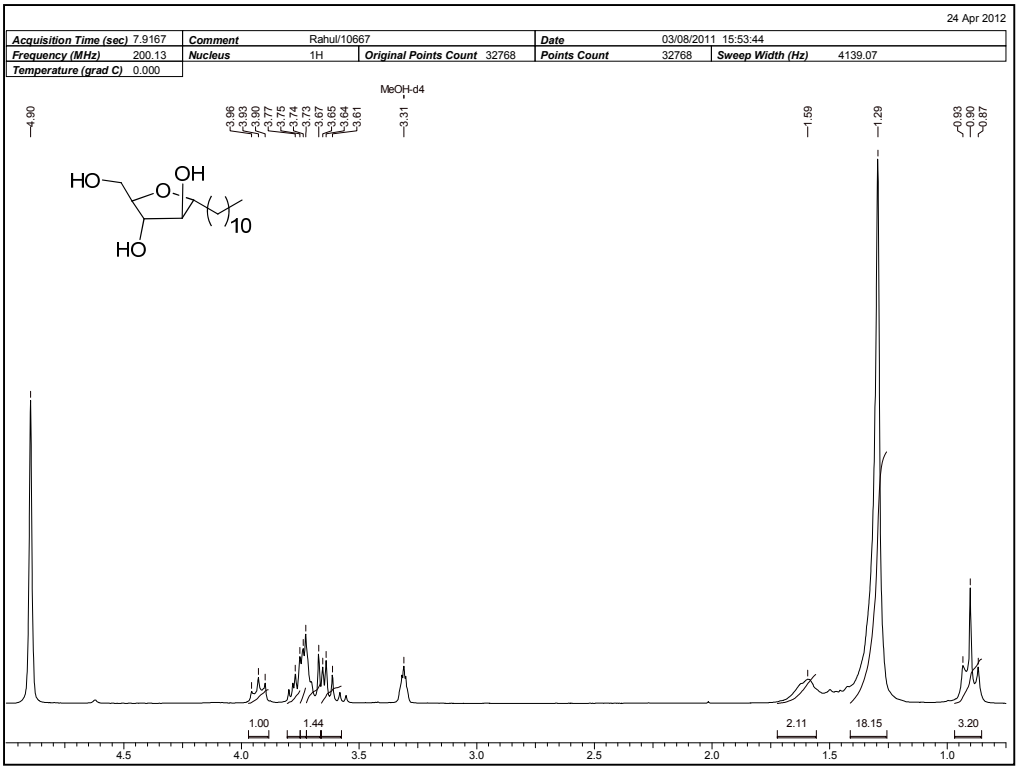
^{13}C NMR Spectrum of 49 in $CDCl_3$



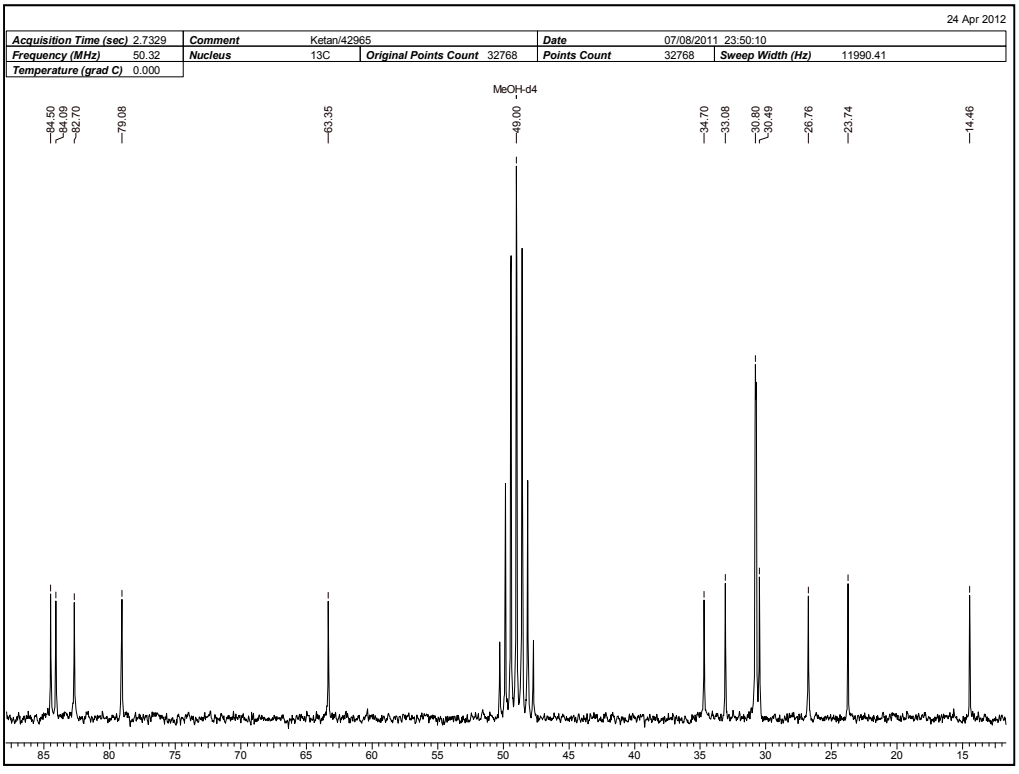
^{1}H NMR Spectrum of 57 in $CDCl_3$



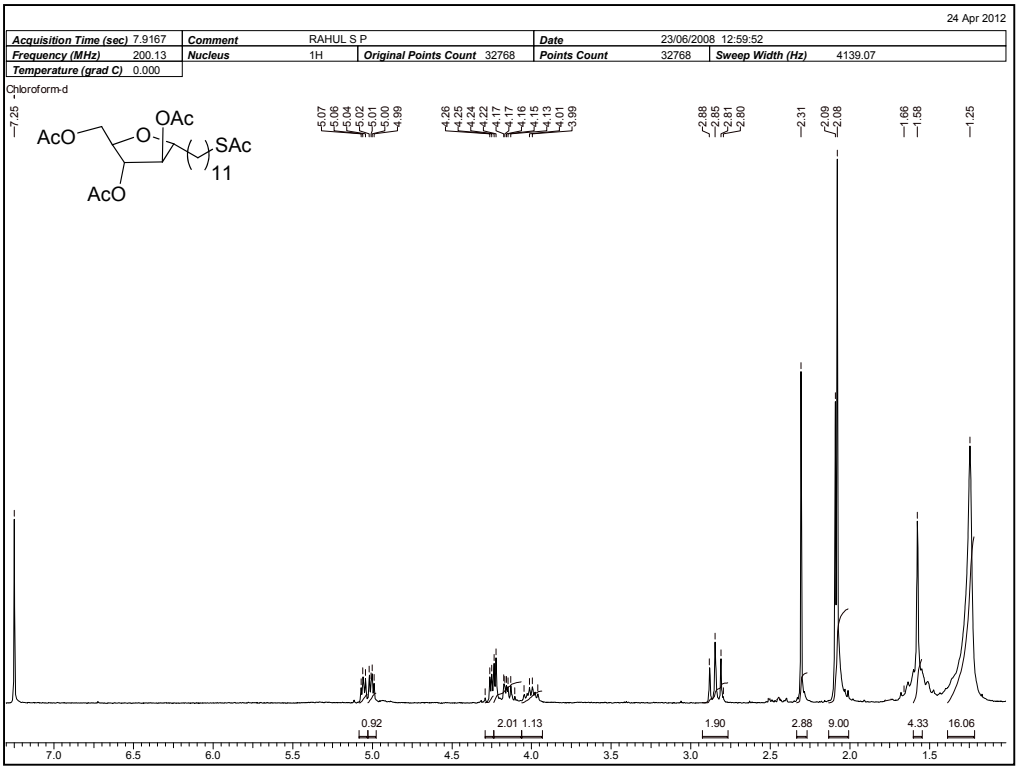
^{13}C NMR Spectrum of 57 in $CDCl_3$



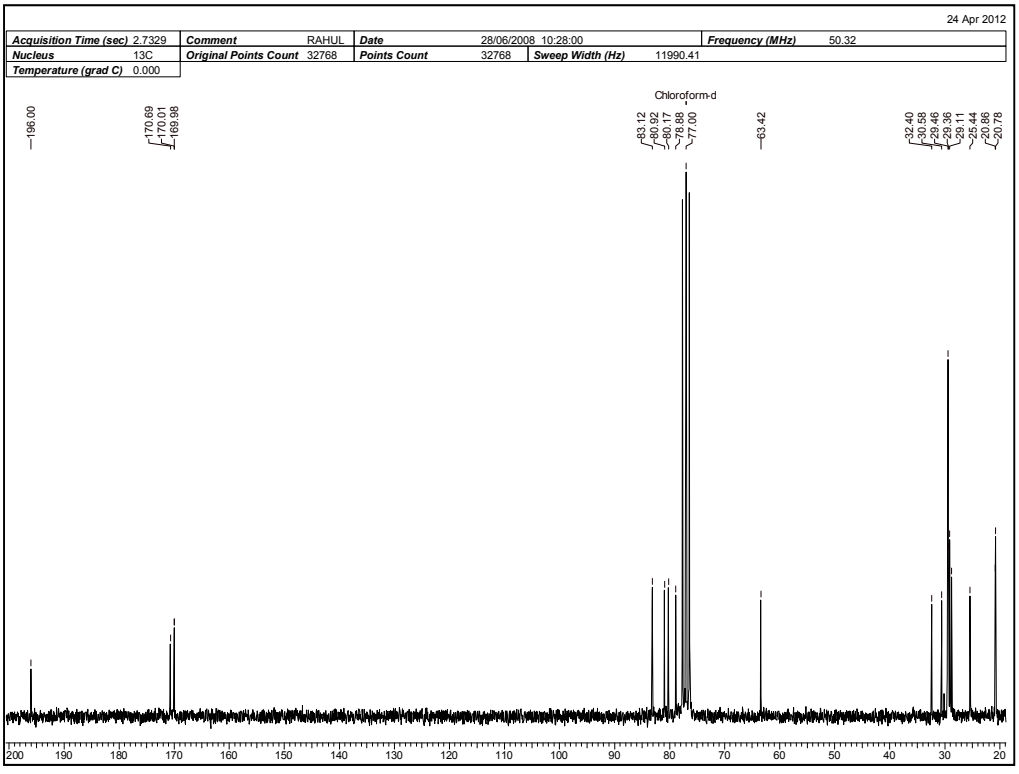
^{1}H NMR Spectrum of 58 in MeOH-D4



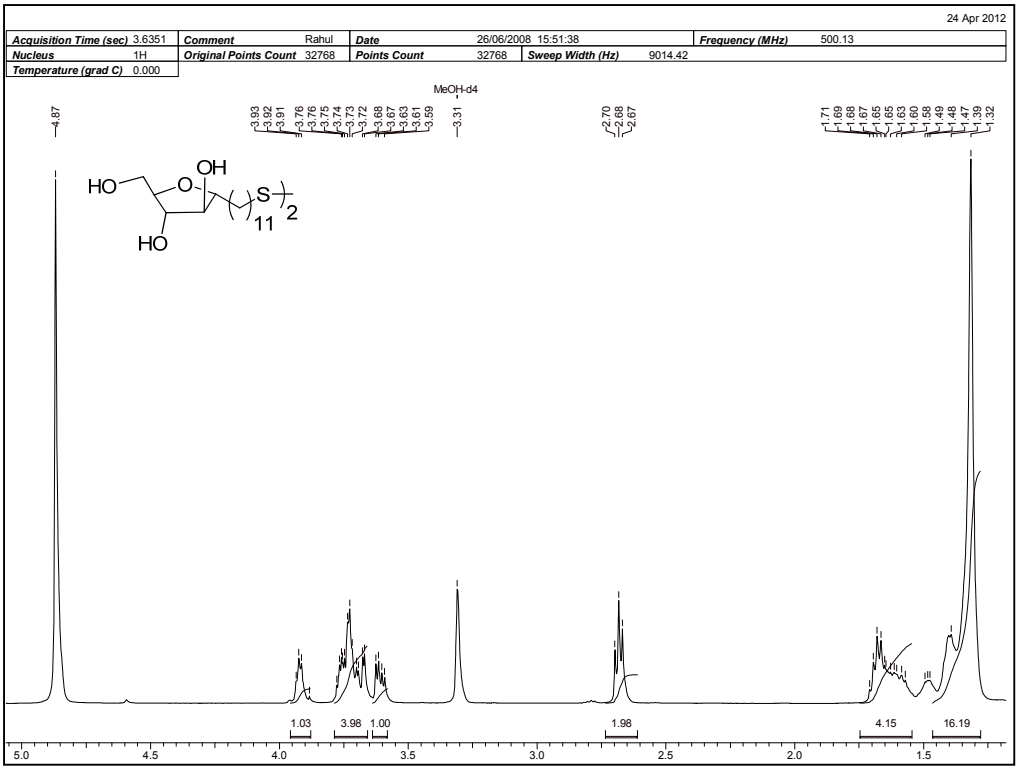
^{13}C NMR Spectrum of 58 in MeOH-D4



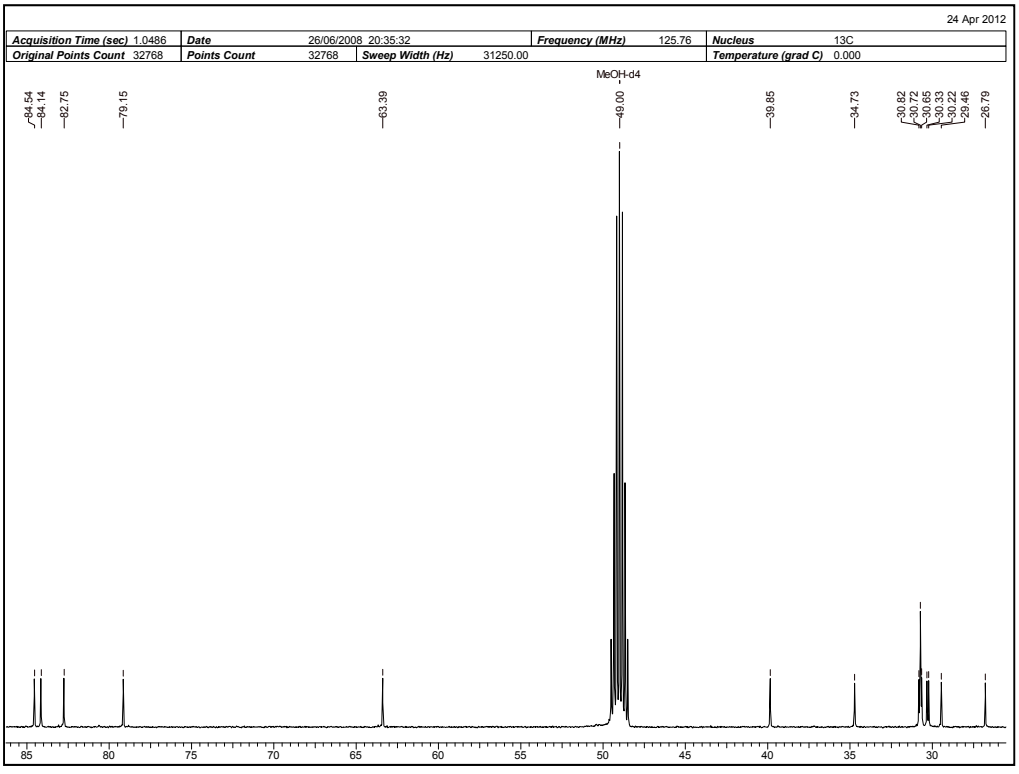
^{1}H NMR Spectrum of 59 in $CDCl_3$



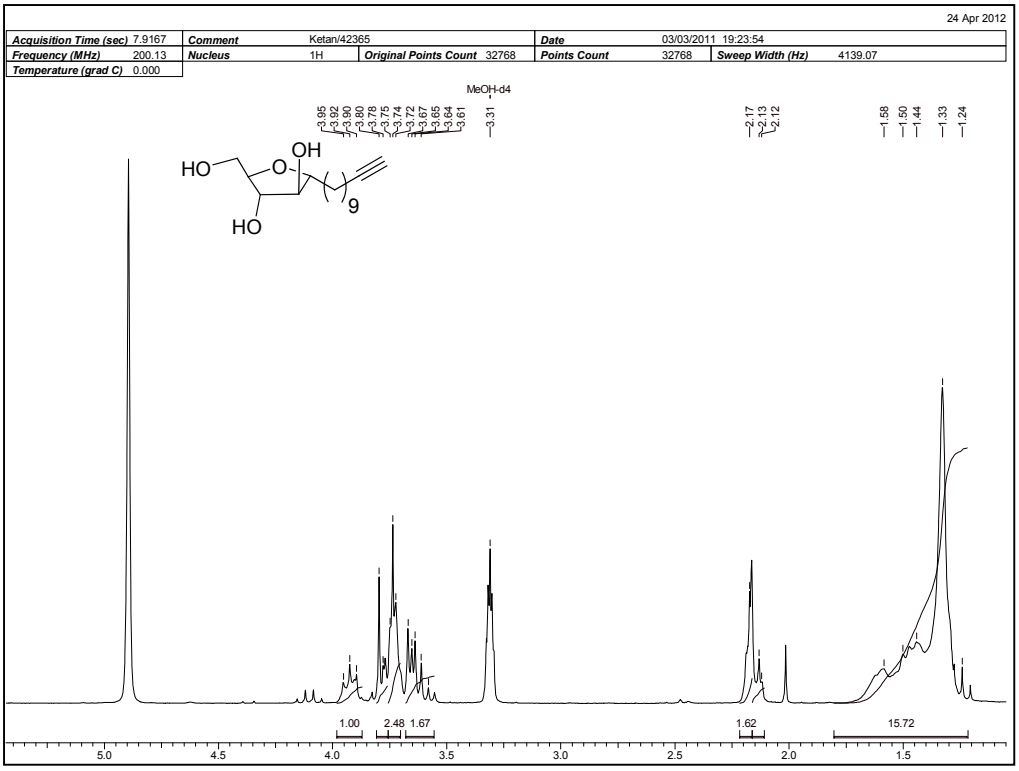
^{13}C NMR Spectrum of 59 in $CDCl_3$



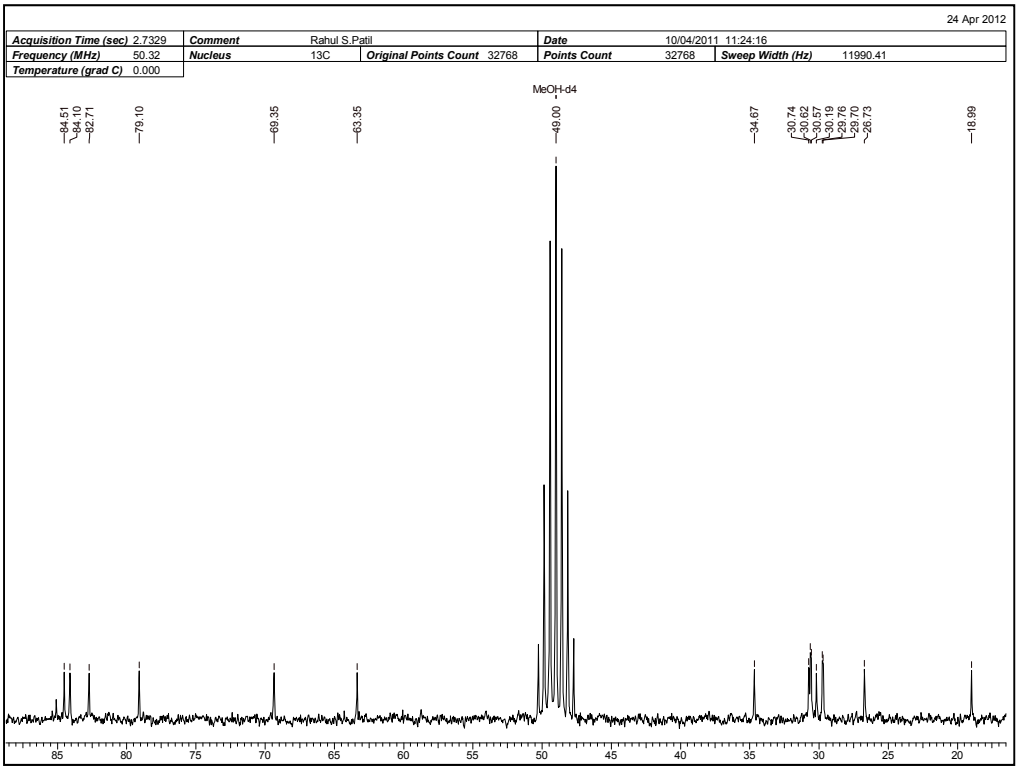
^{1}H NMR Spectrum of 60 in MeOH-D4



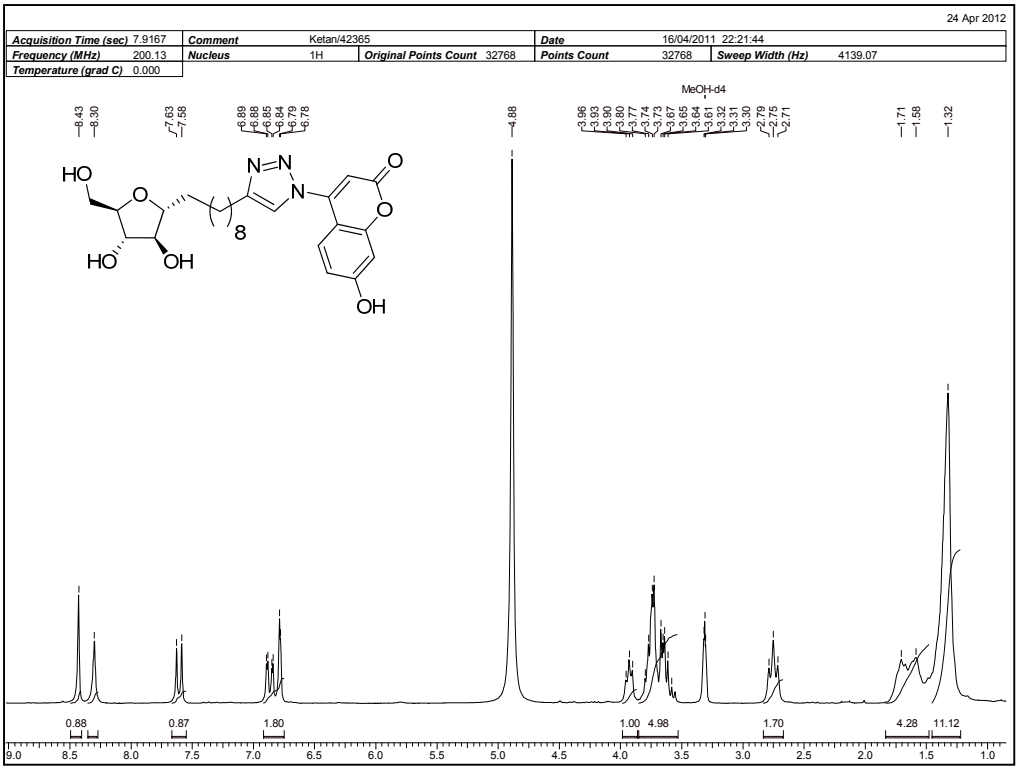
^{13}C NMR Spectrum of 60 in MeOH-D4



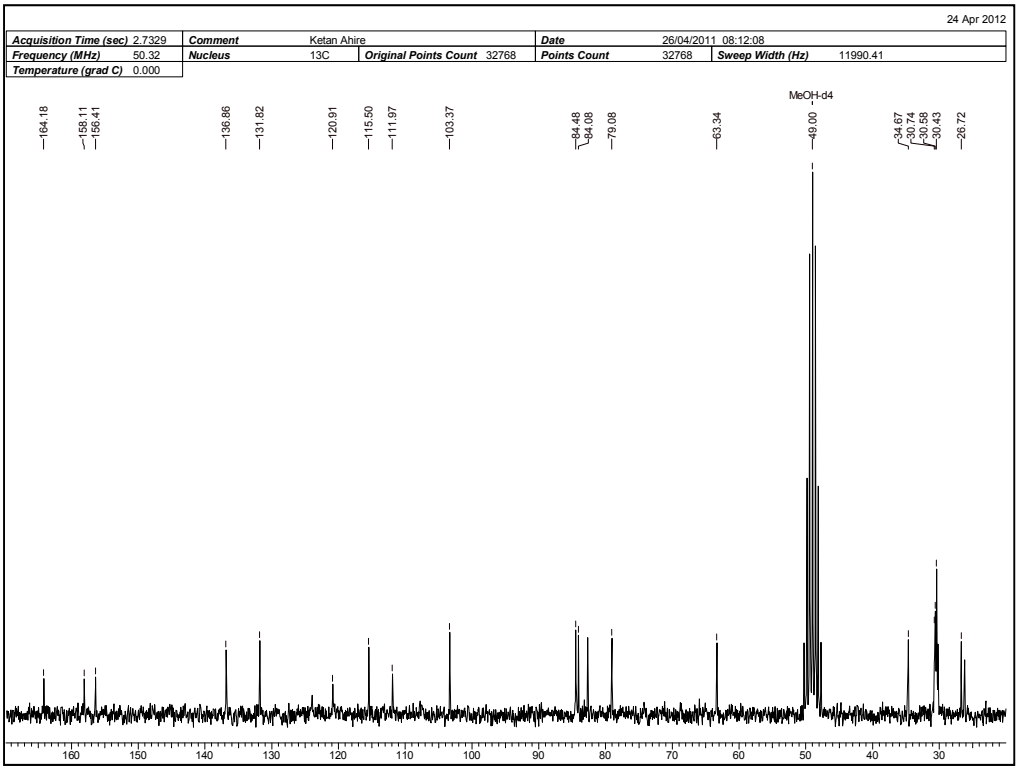
^{1}H NMR Spectrum of 62 in MeOH-D4



^{13}C NMR Spectrum of 62 in MeOH-D4



^{1}H NMR Spectrum of 61 in MeOH-D4



^{13}C NMR Spectrum of 61 in MeOH-D4

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List of Publication

1. "Synthesis of 10-undecenyl *C*-arabinosides as potential anti-mycobacterial agents" C. V. Ramana, D. Sarkar, R. S Patil and S. Sarkar, Provisional Patent, Filing No. 2655DEF2011 Filing Date: 14 Sept **2011.**

2. "A Furan Ring Transposition Reaction for the Stereospecific Synthesis of *C*-Arabinofuranosides" R. S. Patil, C. V. Ramana Communicated.

3. Antimicrobial activity of *C*-Arabinofuranoside and Synthesis of 2,3-*O*-diaryl/dialkyl-10-undecenyl *C*-Arabinofuranosides and their evaluation as potential anti-mycobacterial agents" R. S Patil, S. Sarkar, D. Sarkar and C. V. Ramana, To be communicated.

Erratum