Novel Transformations of 2,3-Unsaturated Sugars

A thesis submitted for the degree of

DOCTOR OF PHILOSOPHY

by

Intzar Ali

School of Chemistry
University of Hyderabad
Hyderabad-500 046

INDIA

June, 2023

To

All My teachers,

My family,

My friends, and Indian soldiers

Contents

Statement

I here declare that, the overall material contained in this thesis is the outcome of research accomplished by me in the school of chemistry, University of Hyderabad, Hyderabad, India, under the supervision of ***Prof. Perali Ramu Sridhar.***

In keeping with the general trend of reporting scientific observations, due acknowledgements have been made wherever the work described is based on the findings of other investigations. Any omission, which might have occurred by oversight or error, is regretted.

Intzar Ali

Hyderabad
June, 2023

Dr. P. Ramu Sridhar
Professor
Work: 91-40-66794823
Fax: +91-40-23012460
Email: p_ramu_sridhar@uohyd.ac.in

School of Chemistry
University of Hyderabad
Prof. C. R. Rao Road
Gachibowli, Hyderabad
Telangana - 500046

Certificate

Certified that the work pertaining to the thesis entitled "**Novel Transformations of 2,3-Unsaturated Sugars**" has been carried out by **Mr. Intzar Ali** under my supervision and that the aforementioned work has not been submitted elsewhere for obtaining degree.

Further the student has passed the following courses towards fulfilment of course work requirement for Ph.D.

S.No.	Course. No	Title	Credits	Pass/Fail
1.	CY-801	Research Proposal	4	Pass
2.	CY-805	Instrumental Methods A	4	Pass
3.	CY-806	Instrumental Methods B	4	Pass

P. Ramu Sridhar
Prof. Perali Ramu Sridhar
(Supervisor)

Dr. P. Ramu Sridhar
Professor
School of Chemistry
University of Hyderabad
Hyderabad-500 046, India.

21/06/2023

Dean
School of Chemistry
University of Hyderabad

Dean
SCHOOL OF CHEMISTRY
University of Hyderabad
Hyderabad-500 046

Acknowledgements

All thanks to Almighty Allah who is Omniscient, Omnipresent, and Omnipotent for the blessings that has been extended to me and helping me to reach at this stage of my life.

I express my sincere gratitude and profound regard to my supervisor ***Prof. Perali Ramu Sridhar,*** *for his able guidance, encouragement, valuable suggestions, and constructive discussions at every stage of my research work. Not only chemistry, he also helped me in understanding the philosophy of life, taught how to handle a tuff situation, and overcome it. Such an approach has been instrumental in nurturing positive growth in me, both personally and professionally. Thus, his supervision is incomparable and it has been a great privilege and honour to be associated with him.*

I am also thankful to my doctoral committee members, ***Prof. R. Balamurugan*** *and* ***Prof. Tushar Jana,*** *for their support and help during my entire course.*

I would like to thank Prof. ***Ashwini Nangia****, Dean, School of Chemistry for providing the research facilities and the former Dean Prof.* ***K. C. Kumara Swamy,*** *for their kind help on various instances. I would also like to thank all the faculty members of School of Chemistry for their kind help on many occasions.*

I am thankful to all my lab mates and fellow researchers specially Dr. Uma Maheshwara Rao (post Doctorate, USA), Dr. Akanksha Gupta (Women scientist), Dr. Mahesh (post Doctorate USA), Dr. Venkatesh, Dr. Anjaneyulu Bandi (post Doctorate USA). My PhD journey would have been a nightmare without my very special friend, mentor, colleague and labmate M. V. Kamalalakshmi, who stood by me through all ups and downs. My hard-core vegetarian friend has even turned me partially into one, which I do not like sometimes. But friendship goals are much higher than just food. And finally thanks my others juniors who gave me cool Environment inside the lab Mr. A. Praveen, Mrs. Drisya C.S , Ms. Shree Vidya, Mr. Kemong Sapong, Ms.Gundumalla Sravani.

I would like to thank few M. Sc project students namely, Ms. Priyadarshini, Ms laxmi, Mr. Zoyab, Ms. Grace, Ms. Joyti, Ms. Ganga Bhawani, Mr.Vamsi, Mr. Bhanu parsad, Mr. Vinay, Mr. Suman, Ms. Ashlesha, Ms.Amrita,

I further thanks my friends, batchmate and juniors, Mr. Ishfaq , Mr. Asif Ali, Mr. Nurul Huda, Mr. Mujahid Husain, Ms Isha Mishra, Ms. Navaneetha, Mrs. Hema Kumari, Mr. Dinesh, Ms. Bhuwana, Mr. Irfan, Ms. Anju Josaf, Mr. Arun, Mr, Shabbir Ahamad, Ms. Reena, Mrs. Drodi, Mr. sachin, Mr. Satyam, Mr. Ajay Rawat, Mr. Hafijur, Mr. Ravi Ahlawat, Mr. Rajesh Gotam, Dr. Gola Ramesh, Dr. Akram Hussain, Dr. Pritam Roy, Mrs, Mansha, Mr. Ashok, Mr. Vamshi, Ms. Ramiya, Ms. Sravanthi,

I take this occasion to express my love to the people who are with me under any conditions like Mrs. Tabassum khan, Mrs. Sneha Banerjee, Dr. Jahangeer Alam, Dr. Mohd. Shiraz, Mr. Mohd. Danish

I would like to express my special thanks to Dr. Rajesh, Ms. Sneha Dandugula for their support and encouragement in Research.

I am very grateful to all my friends and colleagues in the School of Chemistry Dr. Kalyani, Dr. Ravindra, Dr. Suman, Narshima, Jhansi, Rani, Jishu, Vinay, Vinod, Smruthi, Upasna, Moon, Liyaqat Ali, Jeevani kodru, Shyam, Shibani, Rajkiran, Chandrika, Sarvan Kumar, Kondal Rao, Anjali, Argdeep, Avinash,

I am deeply thankful to technicians, without them, this thesis would have not been possible, Mr. Durgesh kumar Singh, and G. Mahender for all their help in the NMR facility. Mrs. Asia Pervez and Dr. Manasi Dalai for helping in mass determination analysis and Mr. Mahesh for crystal structure determination.

I express my heartfelt thanks to all my childhood friends Akash (Pipe), Ankur, Suraj bhan singh, Gulpham, Mohd.Adnan, Mohd farman, Dr. Kulsum who helped me to deal with my stressful days. I would like to specially thank all my M.Sc friends, Dr. Saquibh Tanveer , Dr Owais Zaleel, Dr Sameer Ahamad, Dr. Abudarda Jilli, Dr faisal Umar, Dr. Aktar Alam, Mohd Danih , Aqaha Iqbal, Dr megha, Nikhat Jabeen, Priyanka, who guided to overcome several experimental problems.

Finally, I find no way to express my deep gratitude and profound reverence to my most precious and loving parents ***Mr. Akhatar Ali*** *and* ***Mrs. Jaitun Begum,*** *my brother* ***Guljar Ali,*** *my sisters* ***(Gulshana Parveen, Saiba Parveen, Aisha Parveen, Sultana Parveen)*** *and finally, I am thankful to my wife* ***Mrs. Sarika Ali*** *for providing me support, motivation, and encouragement to make this*

venture a success. I hope I can fulfil their wishes someday and bring as much joy to them as they do to me by being my family.

Intzar Ali

List of Abbreviations

α	alpha
Å	angstrom
Ac	acetyl AcOH acetic acid
β	beta
Bn	benzyl
NIS	N-Iodosuccinimide
BnOH	benzyl Alcohol
DBU	1,8-Diazabicyclo[5.4.0]undec-7-ene
br.	Broad
calcd.	calculated
COSY	correlation spectroscopy
δ	delta
d	doublet
dd	doublet of doublet
DIPA	diisopropylamine
DMF	dimethylformamide
Dt	doublet of triplet
DMSO	dimethyl sulfoxide
EtOAc	ethyl acetate
ESI	electrospray ionization
equiv.	equivalent
g	gram(s)

h/hr	hour(s)
HRMS	High resolution mass spectrometry
Hz	hertz
IR	infrared
J	coupling constant in Hz (NMR) xiv
m	multiplet
MHz	megahertz
mL	milliliter
mmol	millimolar
MeOH	methanol
ms	molecular sieves
NOESY	nuclear Overhauser effect spectroscopy
NMR	nuclear magnetic resonance
PNB	p-nitrobenzoate
Ppm	parts per million
Rf	retardation factor
Ref	reference
s	singlet
p-TsOH	p-toluenesulfonic acid
t	triplet
TBAF	tetra-n-butylammonium fluoride
TBSCl	tert-butyldimethylsilyl chloride
THF	tetrahydrofuran TLC thin-layer chromatography
TMSOT	trimethylsilyl trifluromethanesulfonate
UV	ultraviolet

List of publications

1. Synthesis of Hexenuloses and a Library of Disaccharides Possessing 3-oxo-glycal Unit

   Perali Ramu Sridhar**, Intzar Ali** and M V Kamala Lakshmi *J. Org. Chem.* **2022**, *87*, 14, 8939–8955; https://doi.org/10.1021/acs.joc.2c00663

2. A Ring Expansion─Stereoselective Cycloaddition of Carbohydrate-Derived Donor–Acceptor Cyclopropanes: Synthesis of Bridged Oxepanone–Indole Hybrids

   M V Kamala Lakshmi, **Intzar Ali** and Perali Ramu Sridhar *J. Org. Chem.* **2022**, *87*, 18, 12370–12385; https://doi.org/10.1021/acs.joc.2c01652

3. An Iterative Protocol for the Synthesis of Digitoxose Donor glycoside: Synthesis of Digoxin and Gitoxin derivatives (*Manuscript submitted*)

   Intzar Ali, M V Kamala Lakshmi and Ramu Sridhar Perali

4. Synthesis of 2*C*-branched *C*-glycosides via Claisen rearrangement (*Manuscript submitted*)

   Intzar Ali, Ramu Sridhar Perali

Posters and flash presentations

1. Talk in **CHEMFEST 2021** "Synthesis of Hexenuloses and a Library of Disaccharides Possessing 3-oxo-glycal Unit" organized by the **University of Hyderabad.**
2. Oral presentation at International Conference on Chemistry And Allied Sciences **(ICCAS-2022**) on "Synthesis of Hexenuloses and a Library of Disaccharides Possessing 3-oxo-glycal Unit" held in **NIT Warangal**.
3. Attended International Carbohydrate Conference **(CARBO-XXXIV)-2019**, organized by University of Lucknow in association with **NIPER-R and ACCTI**
4. Poster presentation at International Carbohydrate Conference **CARBO XXXVI 2022** on "Synthesis of Hexenuloses and a Library of Disaccharides Possessing 3-oxo-glycal Unit" held in **IIT Bombay**.

Synopsis

Name of the Candidate	Mr. Intzar Ali
Degree Registered	Ph. D. in Chemistry (17CHPH37)
Title of the Thesis	**Novel Transformations of 2,3-Unsaturated Sugars**
Research Supervisor	Prof. Perali Ramu Sridhar, School of Chemistry, University of Hyderabad

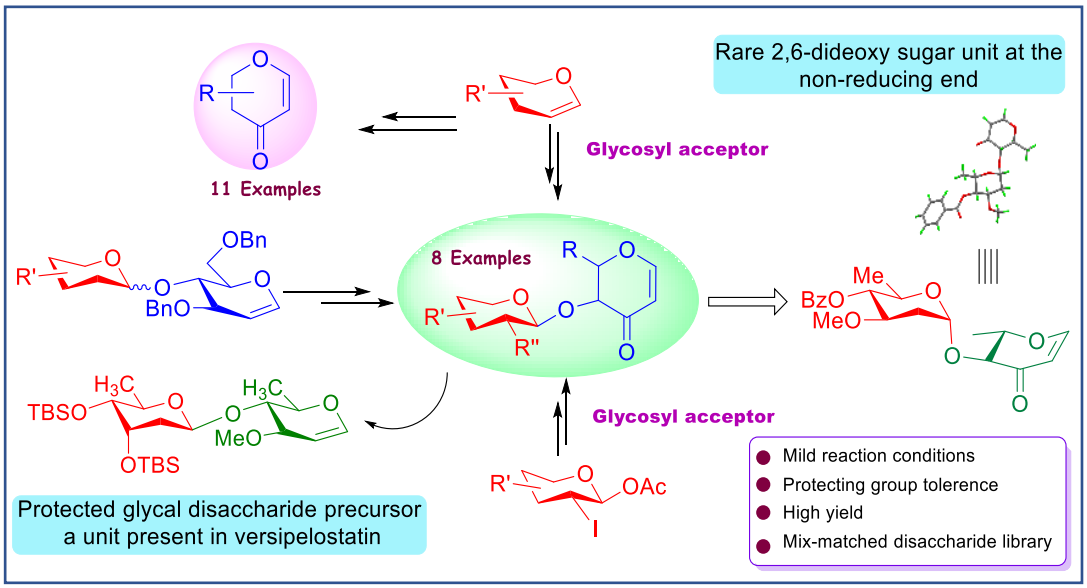
The thesis entitled **"Novel Transformations of 2,3-Unsaturated Sugars"** consists four chapters:

Chapters 1: Introduction of Glycals and 2,3 Unsaturated sugars

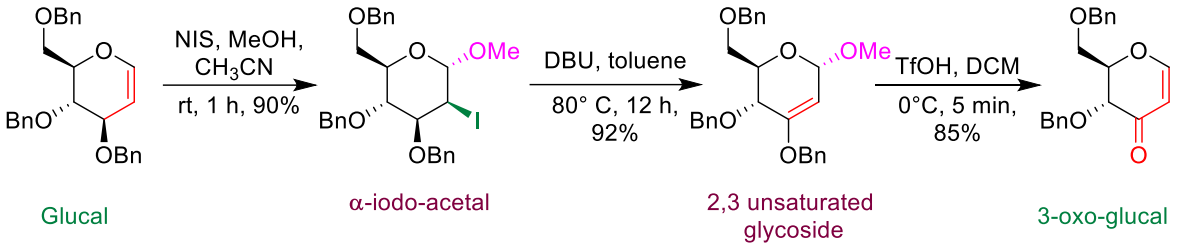
Initial part of this chapter mainly describes the reactivity and applications of simple endocyclic glycals. Glycals also called as the cyclic enol ethers, are well known scaffolds in the synthetic carbohydrate chemistry. Due to the presence of electron rich double bond in glycals, various chemical transformations were introduced in mono- and disaccharide derived glycals with good regio- and stereo selectivity. Few straightforward synthetic applications like cyclopropanation, glycosylation, halo-acetalization, synthesis of deoxy sugars, carbon branched sugar and imino sugar are highlighted. Inspired by this chemistry, this chapter deals with yet another powerful synthon, the 2,3-unsaturated systems. In this context, this chapter further describes the synthetic route, reactivity, and applications of these "hex-2-enopyranoses".

Although an enormous research work has been carried out in the past 50 years on the 1,2-unsaturated sugar derivatives, 2,3-unsaturated systems has also contributed immensely in the advancement of carbohydrate chemistry. The basic idea and motivation of the thesis work is specified over the advancement of the chemistry and the application of 2,3-unsaturated sugar derivatives.

Chapters 2: Synthesis of Hexenuloses and a Library of Disaccharides Possessing 3-oxo-glycal unit



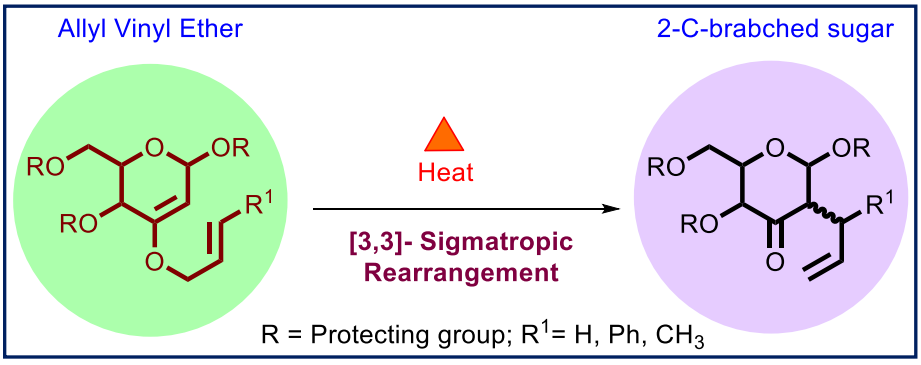
The chapter mainly describes an expeditious method for the synthesis of monosaccharides and disaccharides possessing 3-oxo-glycal unit. The methodology has been designed with glycals as the starting material. Incorporating the three key steps of this methodology: halo-alkoxylation, dehydrohalogenation, and ketalyzation reactions, several monosaccharide glycals are converted to the corresponding hexenuloses. A model substrate, tribenzyl glucal, when subjected to the regio- and stereoselective iodo-methoxylation using NIS/MeOH, provided methyl 2-iodo glycosides α and β in 4:1 ratio, respectively. Among the anomers, α-glycoside is treated with DBU, which effected the dehydrohalogenation reaction forming the 2,3-unsaturated vinyl ether in excellent yield. Further, the trifluoromethanesulfonic acid (TfOH) catalyzed ketalyzation, gives the glucal derived hexenuloses in good yield (Scheme 1). The methodology highlights the efficient conversion of the 1,2-unsaturated sugars (glycals) to 2,3-unsaturated glycosides by base mediated dehydrohalogenation of iodo-acetals. Further, this highly reactive vinyl ether is transformed into the corresponding 3-oxo-glycal derivative using catalytic amount of TfOH.



Scheme 1: Synthesis of 3-oxo-glucal from glucal.

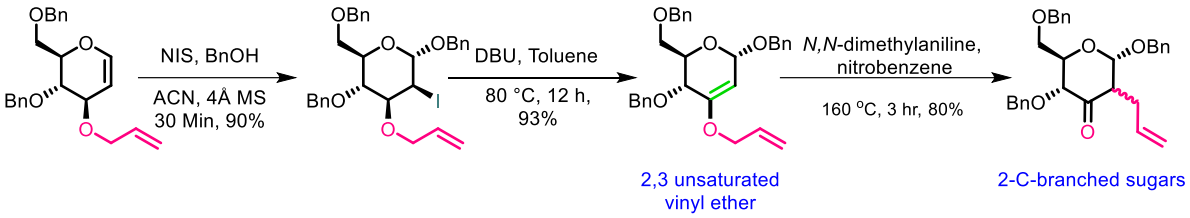
Several 3-oxo-glycals are synthesized to show the importance of methodology and generality of the reaction. Further, the protocol is successfully applied to synthesize disaccharides possessing 3-oxo-glycals. A library of disaccharides with mix and match monosaccharides was constructed. Finally, the effective application of the methodology is demonstrated *via* synthesizing the disaccharide unit, comprised of rare-monosaccharide, present in natural product, versipelostatin.

Chapter 3: Synthesis of 2*C*-branched sugars via Claisen rearrangement



This chapter encompasses the Claisen rearrangement of carbohydrate-derived allyl-vinyl ethers for effective construction of 2-C-branched sugar derivatives. A suitable 3-O-alkenylated glycal is synthesized as the key precursor. The methodology is designed with 3 key steps: 1) iodo-benzoxylation 2) dehydrohalogenation and 3) Claisen rearrangement. 2-C-branched sugar derivates were obtained as mixtures in excellent yield. The model substrate, glucose-derived 3-*O*-allylated glucal was subjected to iodo-benzoxylation using NIS-BnOH to give the

corresponding 2-iodo glycoside with high α-anomeric stereoselectivity. DBU mediated dehydrohalogenation of this glycoside provided the 2,3-unsaturated vinyl ether derivative. Finally, subjecting this vinyl ether substrate to Claisen rearrangement in the presence of *N*,*N*-dimethyl aniline as catalyst, nitrobenzene as solvent, provided the glucal-derived 2-C-branched sugar derivative as inseparable mixtures in good yield (Scheme 2).

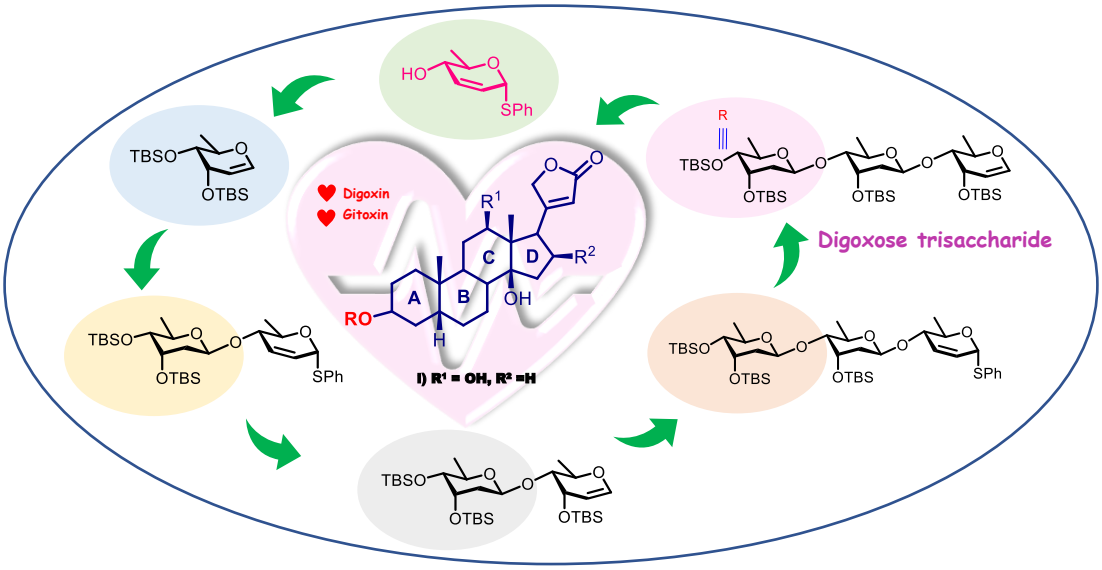


Scheme 2: Synthesis of 2-C- branched sugar via Claisen rearrangement of 2,3 unsaturated glycosides.

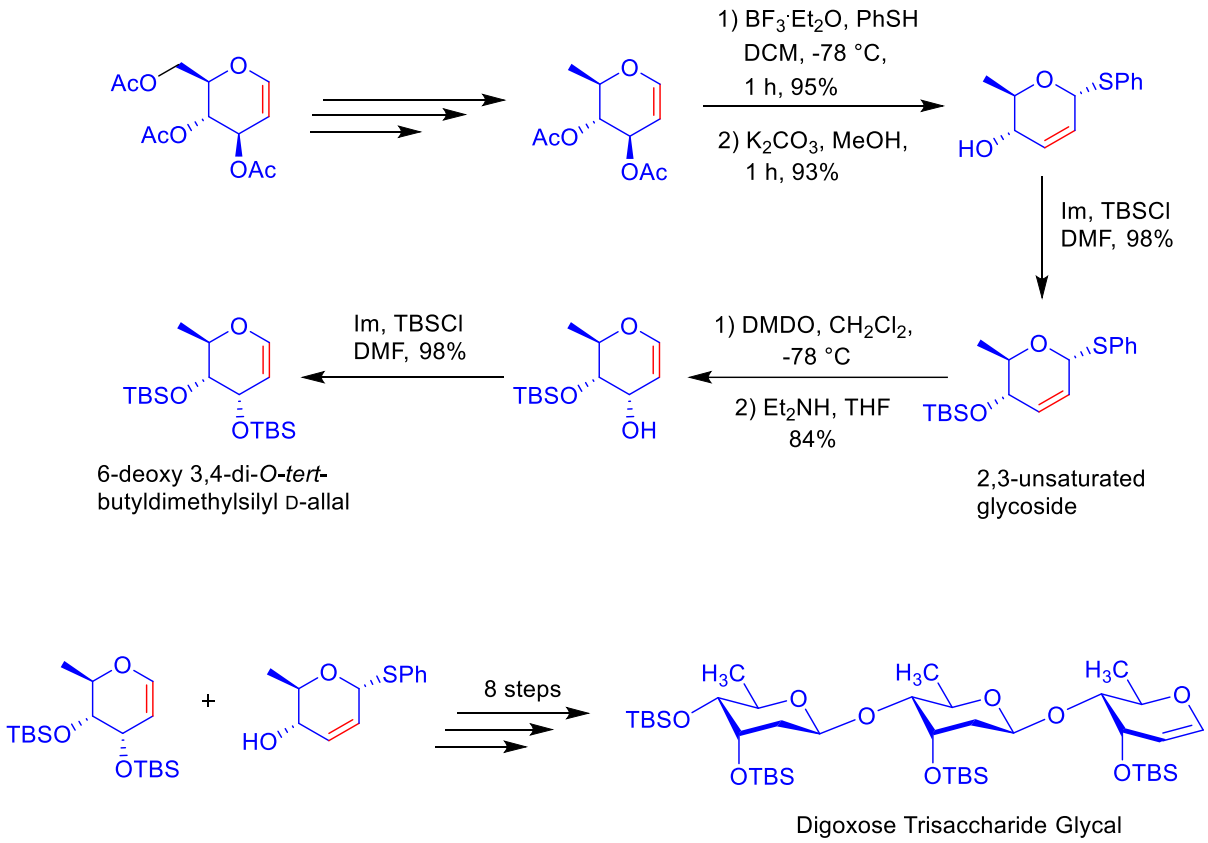
The effective use of 2,3-unsaturated system as one of the significant synthons in carbohydrate chemistry is emphasized in the current chapter. The generalization of developed methodology is projected by synthesizing a few 2-C-branched sugars from an array of alkenylated monosaccharide glycal-derivatives. Major contribution and applicability of this methodology is highlighted by constructing the 2-C-branched disaccharide derivatives via the Claisen rearrangement for the first time.

Chapter 4: An Efficient Method for the Synthesis of Digoxose Trisaccharide Glycal Donor *via* Mislow-Evans Rearrangement

Milsow-Evans rearrangement, a class of [2,3]-sigmatropic rearrangement, has evolved as a valuable chemical reaction in organic chemistry. Danishefsky's application of the Mislow−Evans rearrangement to prepare 6-deoxy D-allal derivative has paved the way in the field of carbohydrate chemistry. However, this has not been explored further in view of its applicability on sugar molecules. This chapter has efficiently adopted the Mislow-Evans rearrangement for the synthesis of 6-deoxy 3,4-di-*O*-*tert*-butyldimethylsilyl D-allal (Scheme 3). Two synthetic routes have been developed for its preparation involving this [2,3]-sigmatropic rearrangement which startes from triacetyl-D-glucal. The accessibility of this [2,3]-sigmatropic rearrangement reaction



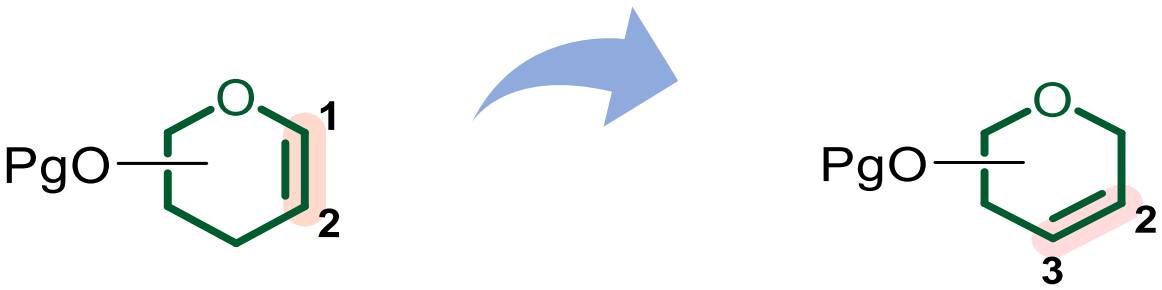
on disaccharide and trisaccharide precursors is the key contribution highlighted in this work. The strategy allows the construction of both donor and acceptor from single starting material, stereoselective glycosylation and further application of Mislow-Evans rearrangement on the di- and trisaccharide. The developed protocol has proved itself to be a realiable and perfectly compatible on the higher order oligosaccharides. Alongside, this strategy establishes an imperative pathway for the gram scale synthesis of digoxose trisaccharide glycal moiety. Furthermore, the post synthetic application is also showcased by performing the stereoselective synthesis of two main CG derivatives, digoxin and gitoxin. This unique strategy utilizes the very stable and commercially available triacetyl-D-glucal as the starting material. This approach is mild, efficient and equally amenable to the preparation of various analogues of CGs.



Scheme 3: Synthesis of Digoxose trisaccharide by using Mislow- Evan rearrangement.

Chapter 1

Glycals: A powerful transformation tool in glyco-chemistry



Abstract

Glycals also called as the cyclic enol ethers, are well known scaffolds in the synthetic carbohydrate chemistry. Due to the presence of electron rich double bond in glycals, various chemical transformations are introduced in mono- and disaccharide derived glycals with good regio- and stereo selectivity. Few straightforward synthetic applications like cyclopropanation, glycosylation, halo-acetalization, synthesis of deoxy sugars, carbon branched sugar and imino sugar are highlighted. Although an enormous research work has been carried out in the past 50 years on the 1,2-unsaturated sugar derivatives, 2,3-unsaturated systems has also contributed immensely in the advancement of carbohydrate chemistry. The basic idea and motivation of the thesis work is specified over the advancement of the chemistry and the application of 2,3-unsaturated sugar derivatives.

1.1 Introduction

Carbohydrates frequently act as structural building blocks and biosynthetic precursors needed to support all living things. They have been proven to be the most prevalent, omnipresent organic compounds in nature, and some of them are serving as vital sources of energy and energy storage. They can be found in less complicated glycosides like mono- and disaccharides or more complex glycosides like glycolipids, glycoproteins, peptido- and proteoglycans, nucleic acids, poly- and lipopolysaccharides.[1] Given the abundance of chiral centres and hydrophilic functionalities in natural carbohydrates, many organic chemists believed that among the biomolecules (nucleic acids, carbohydrates, lipids, and proteins), the study of natural carbohydrates was particularly difficult to handle. However, this belief has recently changed. With growing admiration for the role of carbohydrate molecules in disease, biological processes, human health, and their applications in the advancement of pharmaceutical goals, this deficiency had recently been dramatically corrected by grasping their hidden benefits in chemical synthesis.

Emil Fisher[2] (Figure 1.1) (1852-1919), the father of carbohydrate chemistry, was one of the pioneering scientists from the area of organic chemistry in his time. This distinguished scientist established the first major milestone in the study of carbohydrates in the 1880s. With the limited analytical capability of his study era, Emil Fisher had explained the stereochemistry of all simple carbohydrates, providing the Le Bel-Van't Hoff hypothesis of stereoisomerism with the indisputable evidence it required,[3] of which he was the chemist who received the 1902 Nobel Prize as the first in organic chemistry and second ever awarded. The effects of this work on the advancement of both organic chemistry and carbohydrate chemistry have been thoroughly discussed.

Figure 1.1
Emil Fischer

Due to the vast structural diversity of carbohydrates and their numerous uses in glycobiology, microbiology, medicinal chemistry, and biochemistry, synthetic carbohydrate chemistry is one of the most important and rapidly growing subfields in organic chemistry.[1] Due to the sugars' low cost, large natural abundance, and accessibility in enantiomeric pure forms with

direct stereocenters, this topic has drawn the attention of many scientists.[4] With the intention of using them in the investigation of potential biological processes occurring in living organisms, sugars have also been used as the precursors for the constructing biologically active synthetic molecules as well as naturally occurring important molecules.

1.2 Glycals

Glycals are the 1,2-unsaturated cyclic enol ethers, which possess a double bond between C1 and C2 positions of the furan or pyran moieties of the carbohydrate compound (Figure 1.2).[5] While "glycal" is a generic term, particular derivatives formed from glucose are referred to as "glucals," whereas those derived from galactose are frequently referred to as "galactals".[5] Apart from these, there are modified glycals such as deoxy glycals. Due to the substantial growth in the various synthesis and applications such as epoxidation, halogenation, as well as cyclopropanation reactions etc. in organic synthesis, many benefits of the unsaturated sugars like glycals have been investigated. Glycals are also converted into stereo- and regioselective molecular scaffolds, which is induced by the oxygen present in the ring as well as the size and electronic make-up of the substituents in glycals. Glycals are a crucial component in the synthesis of numerous sugar derivatives, including *O*-glycosides, *C*-glycosides, *N*-glycosides, and *S*-glycosides, as well as medically relevant natural products.

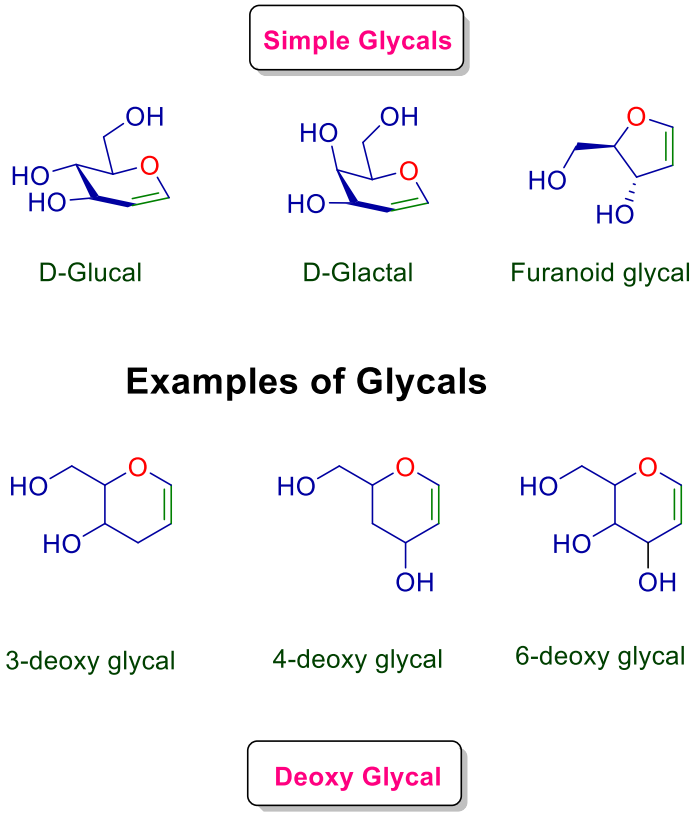


Figure 1.2: Examples of glycals.

1.3 Synthetic applications of glycals

Glycals are well acknowledged to be one of the excellent precursors in synthetic sugar chemistry due to their many synthetic applications, (Figure1.3). Glycals have a double bond, which has allowed for the introduction of diverse functional groups into mono- and disaccharides with strong stereo- and regioselectivity. Due to the involvement of endo-cyclic oxygen, the enol-ether exhibits nucleophilic substitution and electrophilic addition reactions, leading to the production of products, such as the synthesis of polysaccharides from the modified monosaccharide derivatives.

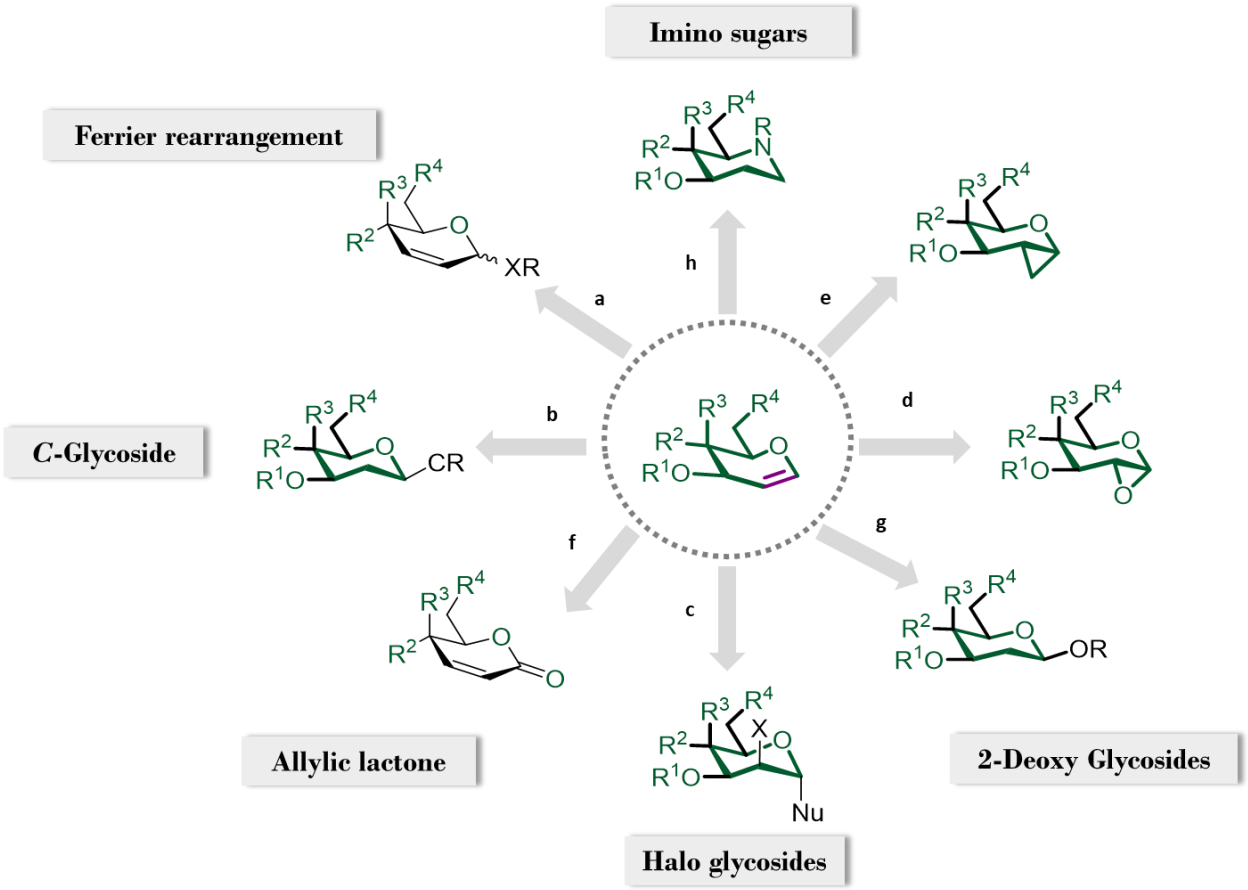


Figure 1.3: Few synthetic applications of simple glycals in sugar chemistry.

Through an allylic rearrangement in nucleophilic substitution reaction to make 2,3-unsaturated glycosides, Ferrier rearrangement[7] is one of the highly exerted reactions of glycals which Ferrier initially reported. Prior to Ferrier's publication, Emil Fischer had studied a similar type of reaction using water as the nucleophile.[8] Ferrier has researched the stereoselective synthesis of the related 2,3-unsaturated glycosides using a variety of nucleophiles, including *O*-, *C*-, *N*-, and *S*-nucleophiles.[9] (Figure1.3a). Researchers had focused on creating novel methods for *C*-Glycoside[10] synthesis due to their stability in metabolic processing. Such *C*-glycosides could be made using glycals as well (Figure1.3b). One of the early glycosylation techniques described by Lemieux is haloglycosylation[11], which uses glycals as glycosyl donors to produce halo-glycosides (Figure1.3c). These halo-glycosides have been used to synthesise a few biologically active oligosaccharides and natural products like ciclamycin[12], ivermectin, etc. Danishefsky[13] has created

a systematic procedure for creating 1,2-Anhydro sugars (also known as 1,2-epoxy sugars) by oxidising glycals with DMDO. Following that, these glycosides were utilised as exceptional glycosyl donors to create various higher order glycosides of glucose, mannose, and galactose (Figure1.3d).[12] In addition, glycals are also used to produce modified carbohydrate residues such as 1,2-cyclopropanated sugars[14] (Figure1.3e), allylic lactones[15] (Figure1.3f), 2-deoxy glycosides[16] (Figure1.3g) and imino sugars[17] (Figure1.3h), which are then synthesised into new sugar molecules, natural products, their advanced intermediates, and secondary metabolites produced by living organisms.

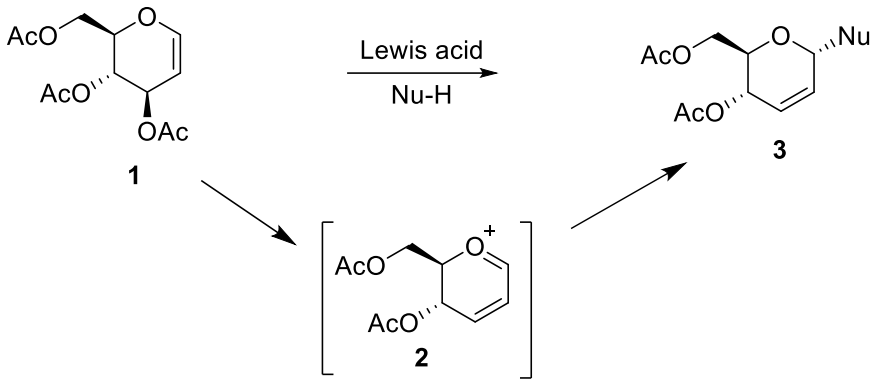
1.4 The journey towards 2,3-unsaturated sugars from 1,2-unsaturation

Glycals have emerged as a powerful transformation tool in the synthetic carbohydrate chemistry. The versatile reactivity of the endocyclic oxygen and the 1,2-unsaturation has obtained significant importance. However, the double bond shift from 1,2 to 2,3 position of the sugar, has uplifted the interests of several research groups. In a similar way, we were attracted to know more about the 2,3-unsaturated sugar derivatives because they are very much undermined and less explored till date. Further part of this section, emphasizes the value of $\Delta^{2,3}$ unsaturated carbohydrate derivatives, it's reactivity and synthetic routes reported till date. The rich chemistry of 2,3-unsaturated pyranoses is shown further in this context by the array of transformations carried out.

1.5 2,3-unsaturated Sugar derivatives

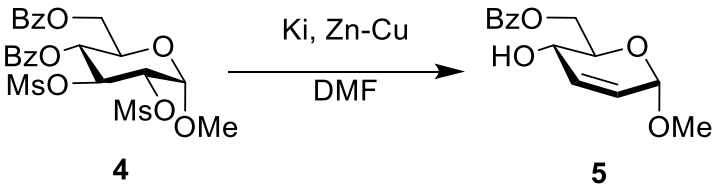
Although there are enormous reports of literature accessible over simple-glycals and its application, over the past 50 years, mechanistic and synthetic advances in carbohydrate chemistry have been made possible by 2,3-unsaturated pyranose derivative or hex-2-enopyranoses, **3**. They are also called pseudoglycals.[18] Fischer[19] was the first one to declare the existence of a molecule in this category, but it took Bergmann[20] ten years to determine the precise structure of that molecule.

1.6 Synthetic Path to Hex-2-enopyranosides using Glycal precursors



Scheme 1. Formation of hex-2-enopyranoses **3** *via* Ferrier rearrangement of glucal **1**

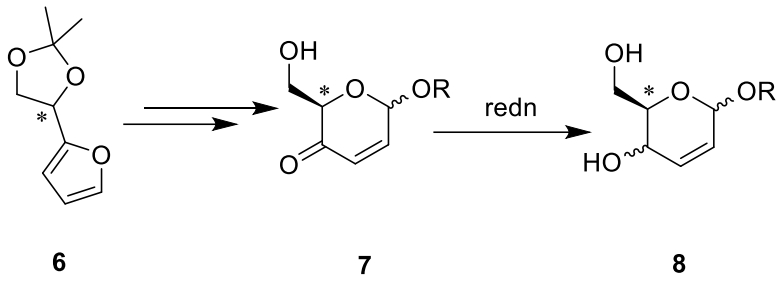
Ferrier and Prasad became the first to render the route **1→3** (Scheme 1), which produced the widely used synthetic intermediates hex-2-enopyranosides, available on a preparative scale in 1969.[21] The cationic intermediate **2**, which was produced in this reaction, has been important since then in numerous carbohydrate transformations, and is now referred as the Ferrier-I rearrangement.[22,23] This widely used method incorporated Lewis acid, like $BF_3{\cdot}OEt_2$, as promoters. In addition to the Ferrier rearrangement, which is depicted in Scheme 1, other methods of obtaining hex-2-enopyranoses from carbohydrate derived precursors have been discovered. In order to access **5** (Scheme 2), Boctor and Fraser-Reid used the reductive removal of adjacent/vicinal disulfonates from compound **4**.[24]



Scheme 2. Boctor and Fraser-Reid's method to the synthesis of hex-2-eno-pyranosides.

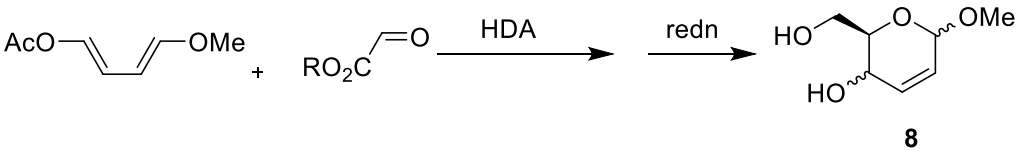
In another report, Zamojski and Achmatowicz developed a route to allylic pyranosides which used non-carbohydrate sources (Scheme 3).[25] According to their report, hex-2-eno-pyranosides **8** was obtained from 2-furanylcarbinols via oxidative rearrangement and forming highly functionalized

pyranones, e.g., **6→7.** As a result, additional ready pathways from non-carbohydrate precursors become available from that point forward. This technique has the benefit of preserving the inherent or original conformation of the alcohol functionality present in the furylcarbinol, making the procedure applicable to the synthesis of both D- and L-series compounds.



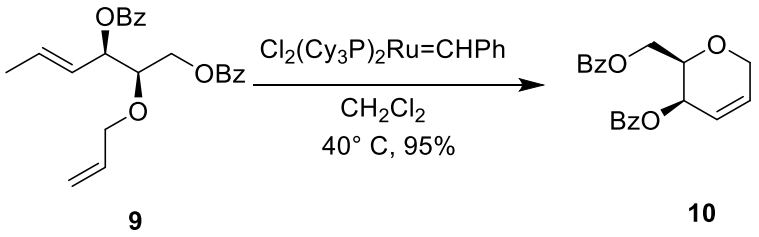
Scheme 3: Synthesis of hex-2-enopyranosides from furylcarbinols**.**

Further account for synthesis of 2,3-unsaturated hexoses system is the contribution of hetero Diels-Alder reaction (HDA) which was first developed by Danishefsky's group for synthesis of hexenuloses. This has been widely employed in the synthesis of hexoses, with 2,3-unsaturated sugar derivatives serving as crucial intermediates in several methods. The Lewis acid catalysed HDA reaction of activated carbonyl compounds like glyoxylates and substituted 1,4-dialkoxy-1,3-dienes provided the hex-2-enopyranosides, e.g., **8**, from non-carbohydrate sources (Scheme 4) [26].



Scheme 4. Route to the synthesis of hex-2-eno-pyranosides *via* Hetero Diels-Alder (HDA)

Carbohydrate derivatives with a terminal double bond are suitable precursors for the synthesis of cyclic frameworks *via* olefin self-metathesis (SM) and olefin cross-metathesis (CM) processes. This has involved the preparation of several hex-2,3-enopyranose molecules and its derivatives. One such reaction being the ring-closing metathesis of dibenzoate **9** to yield 1-deoxy-hex-2,3-enopyranose **10** (Scheme 5).[27]



Scheme 5. Synthesis of hex-2-eno-pyranose derivatives via ring-closing metathesis

1.7 Reactions of Hex-2-enopyranoside

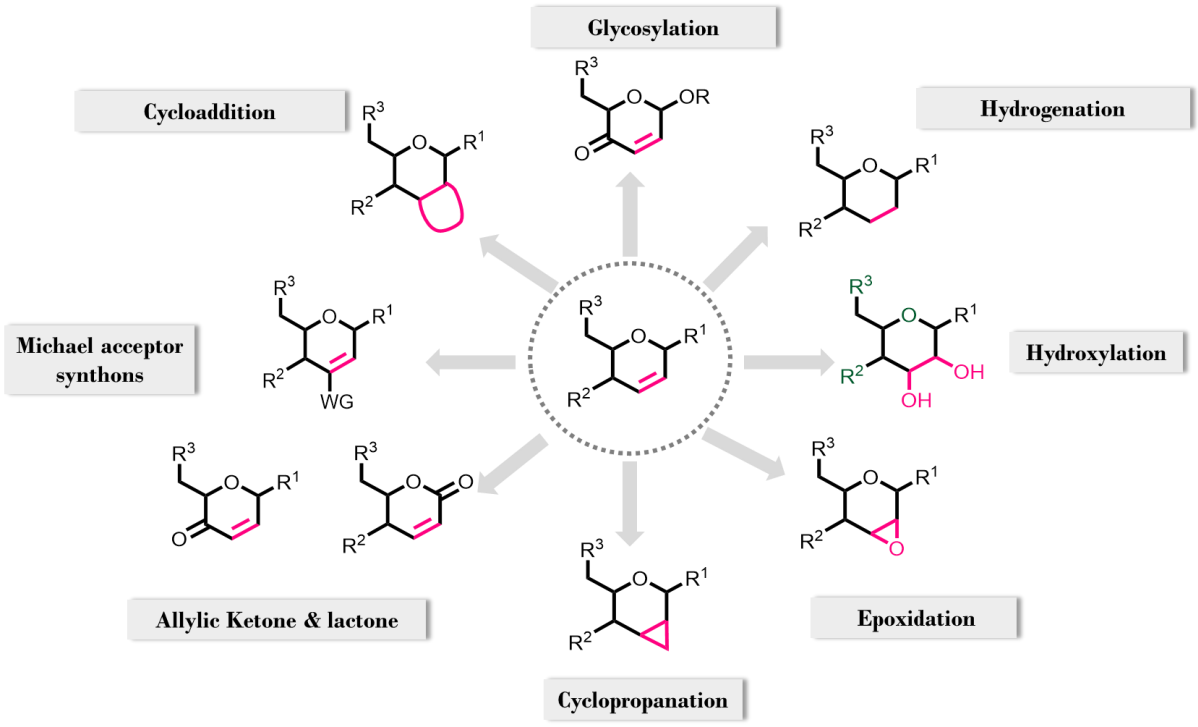
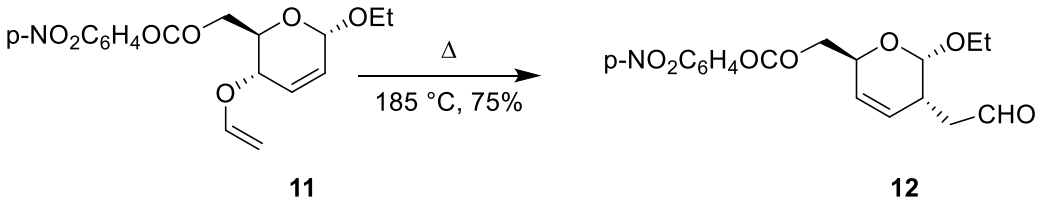


Figure 1.7: A few reactions of 2,3-unsaturated sugar system

One of the motivations for the broad application of hex-2-enopyranosides in carbohydrate chemistry could be its high synthetic application (Figure 1.7).[28] They are prone to undergo standard alkene-addition reactions which includes hydroxylation, hydrogenation, epoxidation, or oxyamination and more frequently with high stereoselectivity, if not complete. Integration of extra functionality that polarises the alkene group, like sulphonyl or nitro substituents, allows for

Michael-like additions, with regiospecific nucleophile incorporation. Apart from these, a few research groups have explored the incorporation of 2,3-unsaturated hexenopyaranoses as unique substrate for glycosylation reactions.[29]

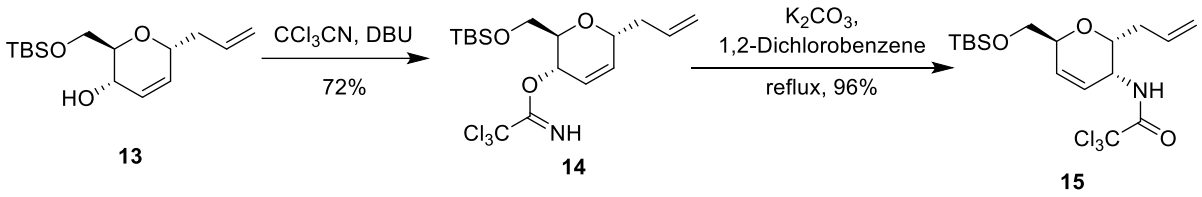
1.7.1. [3,3]-sigmatropic rearrangement:



11 **12**

Scheme 6. Representative example of Claisen rearrangement

These unsaturated sugar derivatives have also proven to undergo [3,3]-sigmatropic rearrangement to form the *C*-*C* bonds or the C-heteroatom bonds. The Claisen rearrangement[30] and Overman rearrangement[31] has contributed immensely in this regard (Scheme 6). For example, Ferrierr et al. reported the Claisen rearrangement of 4-vinyl 2,3-enopyranoside **11** under heating condition at 185° C and got the branched-chain aldehyde **12**. Further this methodology was improvised by several groups for the construction of several types of glycosides.[32]



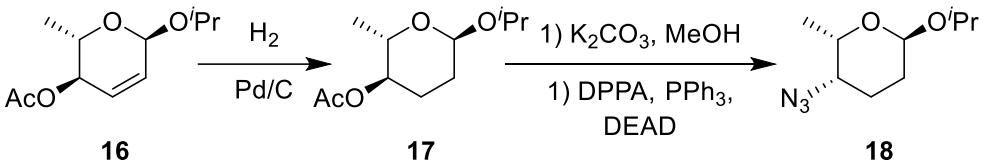
13 **14** **15**

Scheme 7. Representative example of Overman rearrangement

In a similar way, Overman [3,3]-sigmatropic rearrangements has been utilised to introduce amine functionalities at the *C*-2 position of hex-2,3-enopyaranosides.[33] The C-allyl glycoside **13** allowed the formation of allylic trichloroacetimidate **14** and subsequently caused the effective and efficient linking of a secondary amine over the *C*-2 on compound **15** upon boiling in 1,2-dichlorobenzene solvent in presence of base K_2CO_3 (Scheme 7).

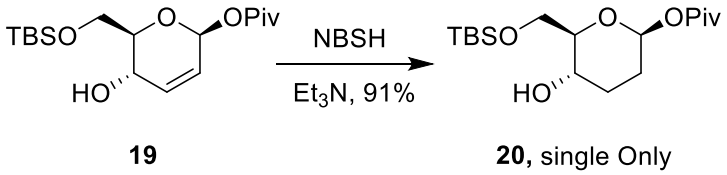
1.7.2 Addition Reactions:

Addition reactions over the 2,3-unsaturated sugar derivative have generated extreme interest by providing opportunity to perform numerous reactions. Firstly, the hydrogenation reaction over the 2,3-enopyranosides has allowed the construction of uncommon deoxy sugars which are further incorporated for post-synthetic transformation. In this context, Zhang *et al.* has employed 2,3-eno-pyranosides **16** for a typical palladium on carbon hydrogenation for the reduction of double bond to give compound **17** which was further transformed into azido deoxy sugar substrate **18** involving the Mitsunobu reaction conditions (Scheme 8).[34]



Scheme 8: Zhang's synthesis of 4-substituted uncommon sugar.

In a similar way, *O'Doherty* group reported the direct hydrogenation of 2,3-unsaturated sugars with allylic alcohol **19** using *o*-nitrobenzenesulfonyl hydrazide (NBSH) and triethyl amine to afford the 2,3-deoxy sugar glycoside **20** (Scheme 9).[35]

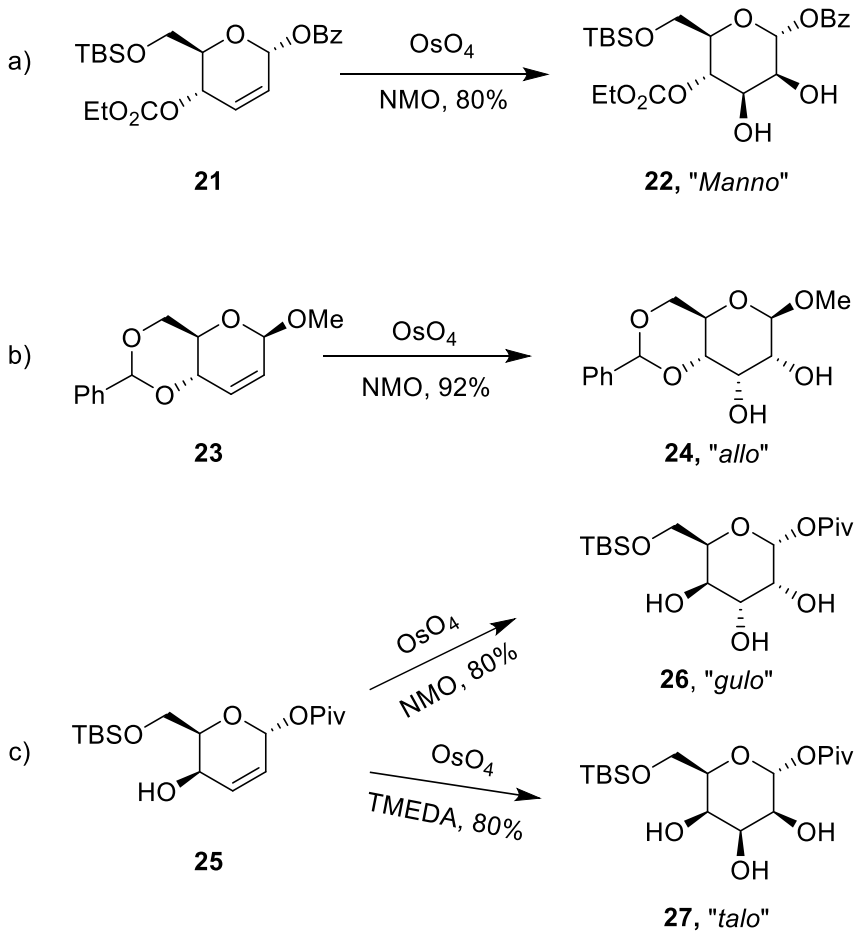


NBSH= o-nitrobenzenesulfonylhydrazide

Scheme 9: Diimide reduction of 2,3-enopyranosides.

Cis-hydroxylation of alkene double bond has evolved as another powerful addition reaction. Under common conditions, stereospecific addition of dihydroxyls is a great challenge and is exclusively used in natural product synthesis. A simple report involving sugar substrates normally

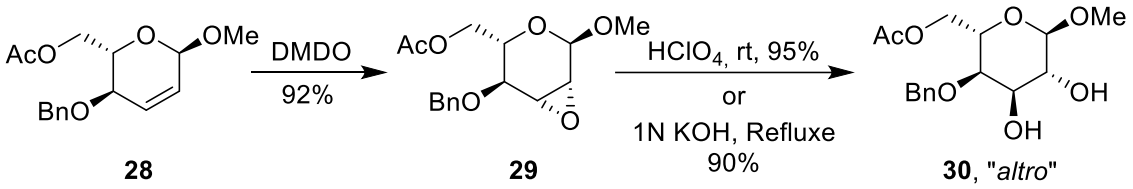
occurs from the sterically more accessible face. For example, the dihydroxylation reaction of 2,3-dideoxy-α-D-erythro hex-2-enopyranoside **21**, where both the 4-substituent and the anomeric substituent are placed below the ring, occurs exclusively from the upper face of the molecule, resulting in the formation of α-D-mannopyranoside **22** (Scheme 10a).[36] However, osmylation of β-D-erythro-2-enopyranoside **23**, where the *C*-1 and *C*-4 substituents are projected in opposite faces of the pyranose, provided exclusively to β-D-allopyranoside **24**, (Scheme 10b).[37] In contrast, when allylic alcohol **25** was exposed to OsO_4/NMO in H_2O/*t*-BuOH, it yielded gulose isomer **26** in good yield (80%), but the protected isomer of talose **27** was preferrebly formed when **25** was treated with TMEDA adduct of OsO_4. (Scheme 10c).[36]



Scheme 10: OsO_4 mediated *Cis*-dihydroxylation of 2,3-unsaturation in hex-2,3-enopyranosides

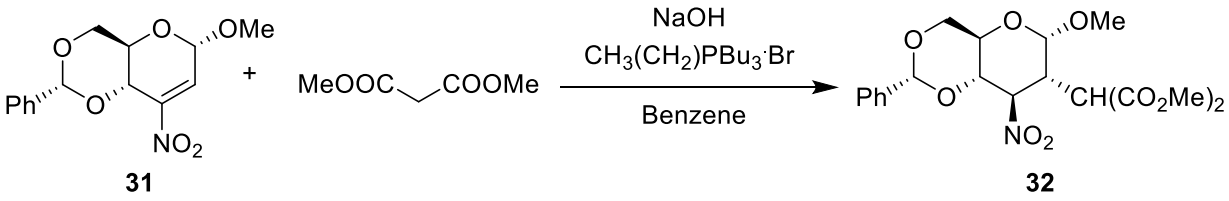
Another interesting utilization of the 2,3-unnsated of sugars lies in the epoxidation reaction, which is highly stereoselective and the formed epoxides act as valuable tool for further ring opening dihydroxylation reactions. This is a complementary approach to the above mentioned *cis*-

hydroxylation and provides the trans-diaxial products based on Furst-Platnner rule. For example, when the 2,3-unsaturated substrate **28** was treated with DMDO, gave a highly stereoselective epoxide **29** and subsequent ring opening by acid or base gave exclusively L-altropyranoside **30** (Scheme 11).[38]



Scheme 11: *Trans*-dihydroxylation of hex-2,3-enopyranosides *via* epoxide ring opening.

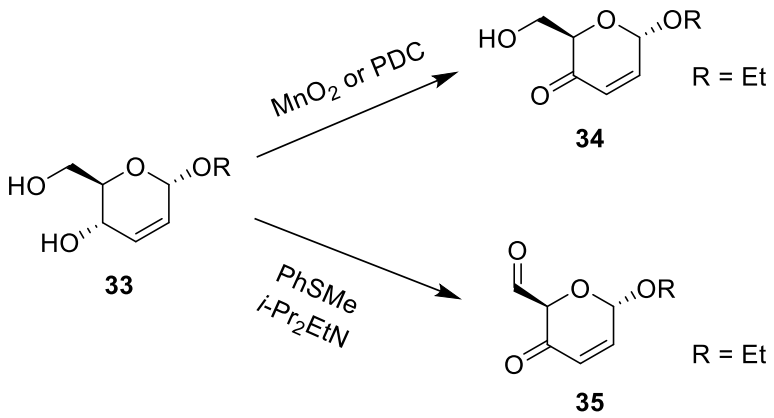
Michael addition reaction adds on as a valuable tool for addition reactions. In the 2,3-unsaturated sugar derivative, incorporation of the chemical functionality such as nitro or sulfone helps in alkene bond polarization and favours the Michael-type additions leading to regioselective introduction of nucleophiles. For example, Sakakibara reported the reaction of active methylene group with Michael synthon **31** in a stereo- and regioselective manner at the *C*-2 position to obtain Michael adduct **32** (Scheme 12).[39]



Scheme 12: Michael addition reaction over 3-nitro-hex-2-enopyranosides **31**

1.7.3 Oxidative transformations:

Allylic lactone, *α,β*-unsaturated ketone and 6-formyl derivatives can be synthesised by oxidative transformation of hex-2,3-enopyranosides and develop a synthetic value of both the compounds. For example, regioselective oxidation of diol[40] **33,** by MnO_2 or PDC provided the allylic ketone **34** whereas selective oxidation of the *O*-6 hydroxyl group gave the corresponding aldehyde **35** (Scheme 13).[41]



Scheme 13: Chemo- and regio-selective oxidation of 2,3-unsaturated diol 33

1.7.4 Cycloaddition Reactions:

Chmielewski's group has contributed immensely in the study of cycloaddition of nitrones to *δ*-lactones derived from carbohydrate to construct several biologically relevant iminosugars.

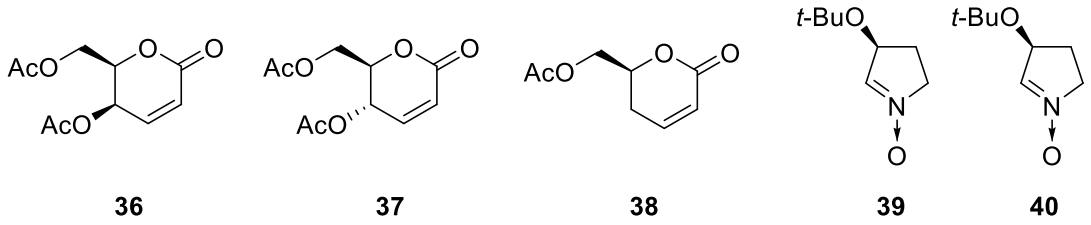
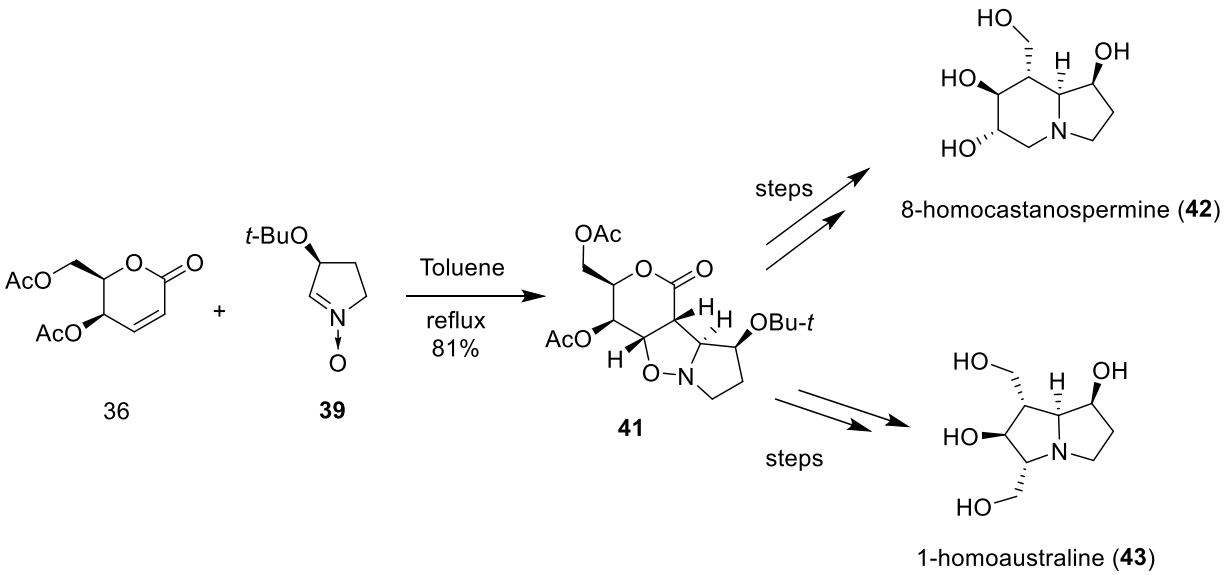


Table 1: 2,3-unsaturated anomeric lactones and chiral nitrones.

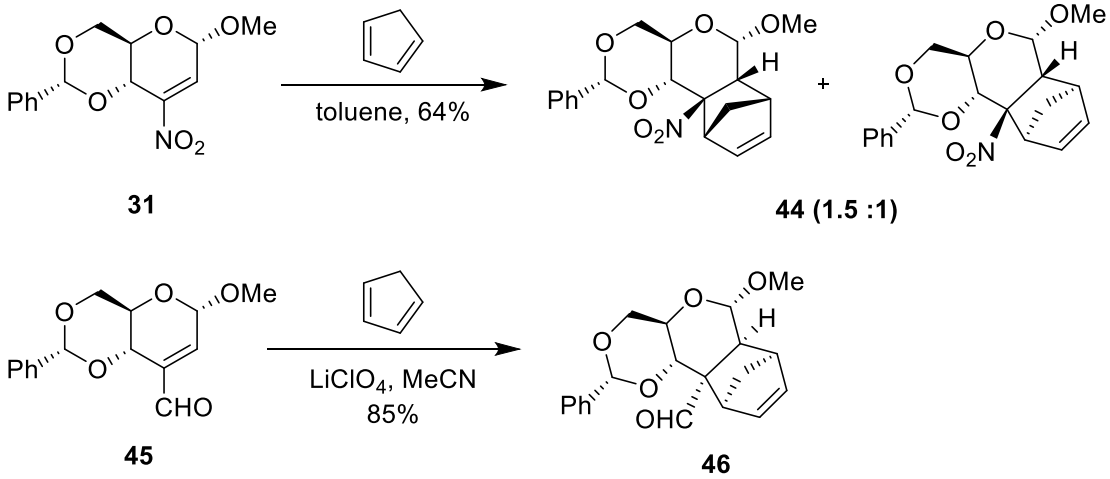
The anomeric lactones **36-38** were reacted in 1,3-dipolar addition fashion with cyclic nitrones **39-40** (Table 1). For example, lactone **36** and nitrone **39** reacted to give a stereoselective tricyclic derivative **41** with *exo*-orientation which was further employed for the synthesis of cyclic

iminosugar such as 8-homocastanospermine **42** (Scheme 14).[42] In a similar way, the tricyclic adduct was also employed for the synthesis of 1-homoaustraline **43** (Scheme 14).[43]



Scheme 14: Chmielewski's approach of cycloaddition on 2,3-unsaturated lactone

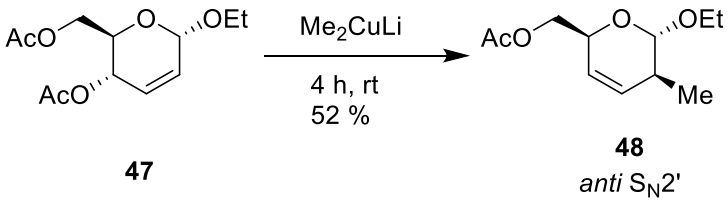
Diels-Alder reaction is another efficient tool of cycloaddition reaction for successful synthesis of polycyclic systems. In this context, cyclopentadiene is employed for Diels-Alder reaction with different 2,3-unsaturated sugar derivative such as **31** and **45** (Scheme 15). The reaction gave the corresponding cycloadducts **44** and **46**.[44]



Scheme 15: Diels-Alder reaction of cyclopentadiene and 2,3-unsaturated sugar derivative

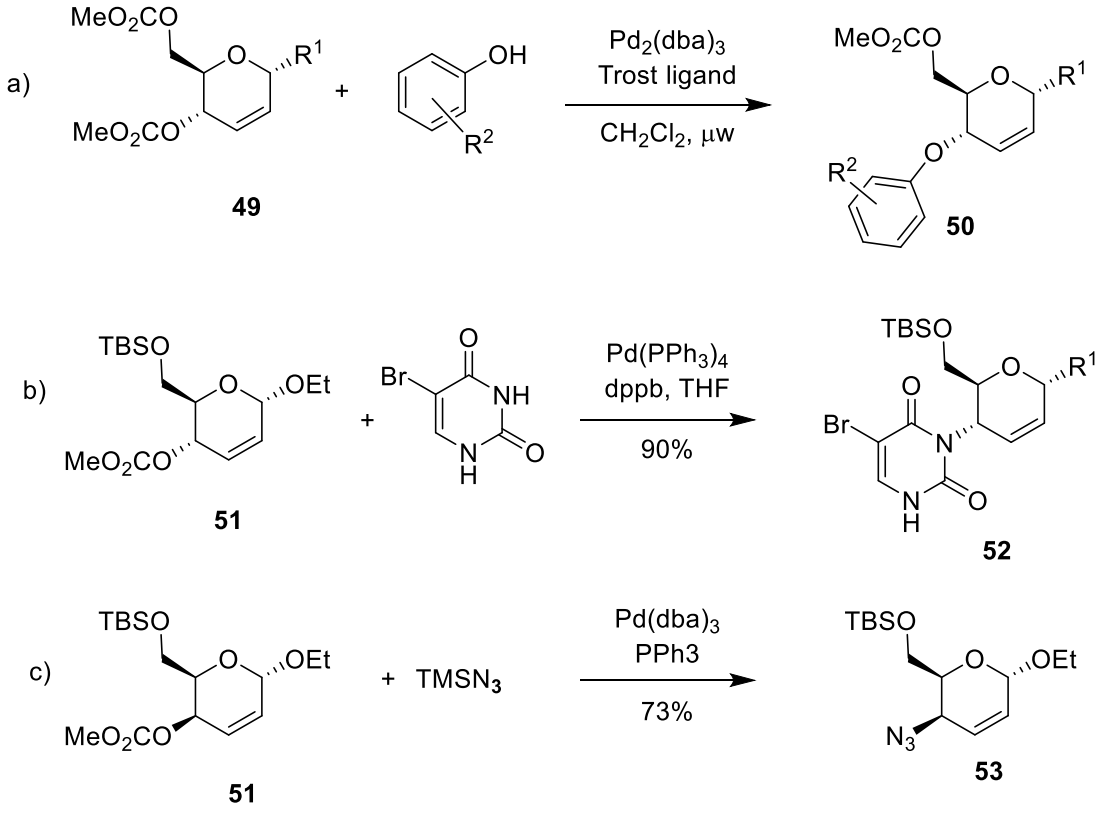
1.7.5 Nucleophilic substitutions:

The shift of the *C*-4 allylic group present on 2,3-enopyranosides opens possibilities for various functionalization. Several reports for nucleophilic allylic substitution relies majorly on copper and palladium reagent.



Scheme 16: Allylic substitution reaction on 2,3-enopyranoneside **47**

A particular report by Yves Chapleur et al. allowed the stereospecific *C*-*C* bond formation when allylic acetate **47** is reacted with lithium dimethyl cuprate in ether at 0°C afforded the alkene **48** in 52% yield (Scheme 16).[45]

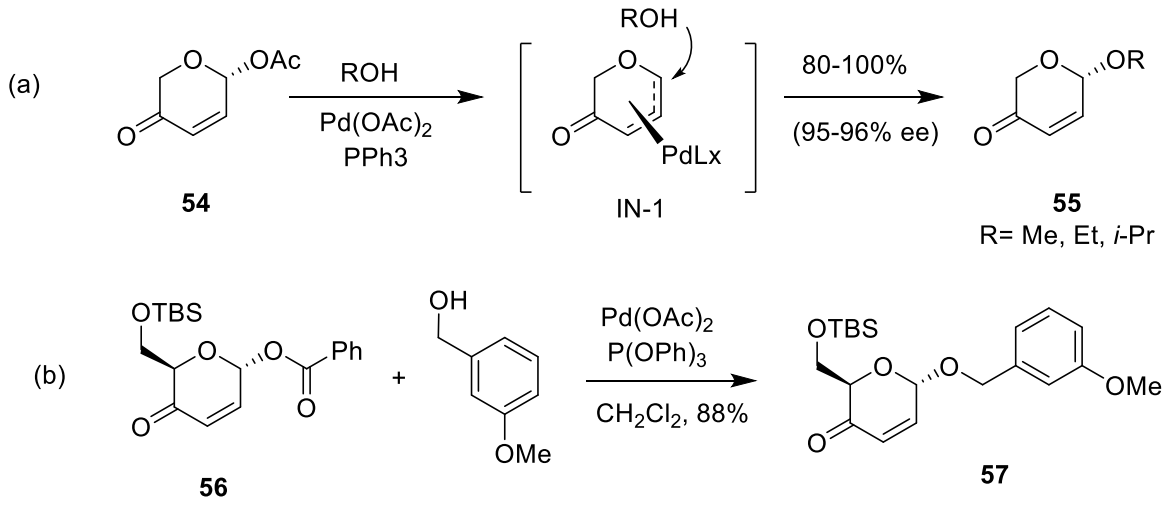


Scheme 17: Palladium facilitated allylic substitution reaction

Similar way palladium-catalysed substitution of carbonates or allylic esters by nitrogen and carbon nucleophiles have been of great relevance. The methodology also accounts for the formation of highly regio- and stereoselective products. For example, when nucleophilic substitution was carried out on alkenes **49** and **51**, a very high stereo- and regioselective *C*-4 substituted derivatives **50** and **52**, respectively were obtained (Scheme 17a,b). Similarly, the azido derivative **53** is obtained when **51** is subjected to palladium-catalysed allylic substitution reaction with $TMSN_3$ (Scheme 17c).[46]

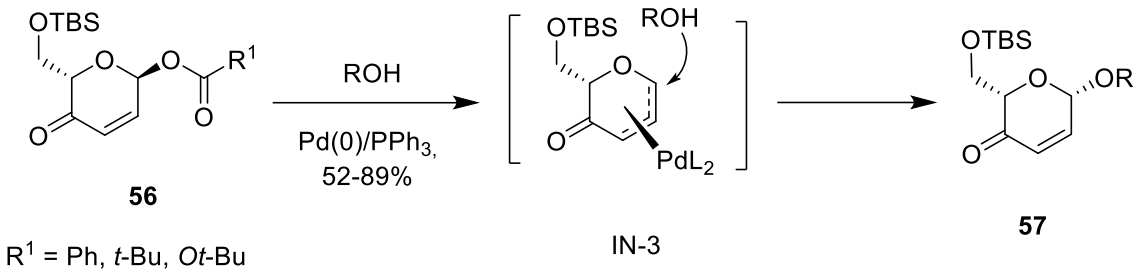
1.7.6 Glycosylation:

Palladium catalysts have also played exclusive role in the glycosylation reaction. Feringa and O'Doherty's group have extensively worked on glycosylation reaction with 2,3-unsaturated hexoses by incorporating it as glycosyl donor.



Scheme 18: Feringa and co-workers' allylic substitution using palladium catalysis.

Feringa and co-workers demonstrated stereoselective palladium acetate catalysed glycosylation of pyranones donors like **54** and **56** to afford stereoselective glycosylated products **55** and **57** respectively (Scheme 18). The approach was particularly useful in synthesis of *O*-glycosides, since the newly created glycosidic link retains stereochemistry at allylic acetal moiety.[47]



Scheme 19: Pd-catalyzed glycosylation with pyranone donors by O'Doherty and co-workers

Similarly, O'Doherty's group reported a highly stereoselective and stereospecific palladium-catalysed glycosylation reaction that selectively converts the pyranone donors **56** into *O*-glycosides **57**.[48] The same group further explored the palladium catalysed glycosylation of 2,3-unsaturated sugar derivative with various glycosyl donors, their reactivity and selectivity. Also, they employed this methodology for synthesis of oligosaccharides (Scheme 19).[49]

1.8 Motivation for the work presented in this thesis

Although several reports are available on the hex-2,3-enopyranosides, we strongly believed that these 2,3-unsaturated sugar skeletons could be used in such a way to attain the important skeletons having biological, medicinal applications or could be used in the syntheses of natural products. In the latter chapters of the thesis, we have presented a reasonable work carried out to explore the direct synthetic applications of 2,3-unsaturated sugar substrates.

1.9 References

1. (a) Levy, D. E.; Fugedi, P. The Organic Chemistry of Sugars. Taylor & Francis: *CRC press*, **2006**. (b) Ernst, B.; Hart, G. W.; Sinay, P. Carbohydrates in Chemistry and Biology. *Molecules* **2000**, *5*, 1520-1521.
2. (a) Lichtenthaler, F. W. Emil Fischer, His Personality, His Achievements, and His Scientific Progeny. *Eur. J. Org. Chem.* **2002**, (24), 4095-4122. (b) Kunz, H. Emil Fischer–Unequalled Classicist, Master of Organic Chemistry Research,and Inspired Trailblazer of Biological Chemistry. *Angew. Chem. Int. Ed.* **2002**, *41* (23), 4439-4451. (c) Goodman, M.; Cai, W. B.; Smith, N. D. The Bold Legacy of Emil Fischer. *J. Pept. Sci.* **2003**, *9* (9), 594-603.

3. Lichtenthaler, F. W. Emil Fischer's Proof of the Configuration of Sugars: A Centennial Tribute. *Angew. Chem. Int. Ed.* **1992**, *31* (12), 1541-1556.
4. Hollingsworth, R. I.; Wang, G. J. Toward a Carbohydrate-Based Chemistry: Progress in the Development of General-Purpose Chiral Synthons from Carbohydrates. *Chem. Rev.* **2000**, *100*, 4267-4282.
5. McNaught, A. D. Nomenclature of carbohydrates. Carbohydrate Research, **1997**, *297*, 1-92.
6. Zhao, J. Z.; Wei, S. Q.; Ma, X. F.; Shao, H. W. A simple and convenient method for the synthesis of pyranoid glycals *Carbohydrate Research*. **2010,** 345, 168–171.
7. (a) Ferrier, R.J. Unsaturated carbohydrates. Part II. Three reactions leading to unsaturated glycopyranosides. *J. Chem. Soc.* **1964**, 5443-5449. (b) Somsak, L. Carbanionic Reactivity of the Anomeric Center in Carbohydrates. *Chem. Rev.* **2001**, *101* (1), 81-135. (c) Fraser-Reid. Some Progeny of 2,3-Unsaturated Sugars They Little Resemble Grandfather Glucose. *Acc. Chem. Res*, **1996**, *29*, No. 2, 59. (d) Ferrier, R. J.; Prasad, N. Unsaturated carbohydrates. Part IX. Synthesis of 2, 3-dideoxy-α-D-erythro-hex-2-enopyranosides from tri-O-acetyl-D-glucal. *J. Chem. Soc. C* **1969**, 570-575. **(e)** De Raadt, A.; Ferrier, R. J. Syntheses and reactions of saturated and 2,3-unsaturated vinyl and 1'-substituted-vinyl glycosides. *Carholydrare Research*, **1991**, *2 16* ,93 – 107. (f) Ferrier, R. J.; Zubkov, O. A. Transformation of Glycals into 2,3-Unsaturated Glycosyl Derivatives. *Org. React. (N. Y.)* **2003**, *62*, 569- 736.
8. Fischer, E. Über neue Reduktionsprodukte des Traubenzuckers: Glucal und Hydro-glucal *Ber. Dtsch. Chem. Ges.* **1922**, 393-407.
9. (a) Gomez, A. M.; Lobo, F.; Uriel, C.; Lopez, J. C. Recent Developments in the Ferrier Rearrangement. *Eur. J. Org. Chem.***2013**, 7221–7262. (b) Ansari, A. A.; Lahiri, R.; Vankar, Y. D. The Carbon—Ferrier Rearrangement: An Approach Towards the Synthesis of C-Glycosides. *ARKIVOC* **2013**, 316-362.
10. Du, Y.; Linhardt, R. J.; Vlahov, I. R. Recent Advances in Stereoselective C-Glycoside Synthesis. *Tetrahedron* **1998**, *54* (34), 9913-9959.
11. (a) Lemieux, R. U.; Levine, S. Synthesis of alkyl 2-Deoxy-α-D glucopyranoside and their 2-Deuterio derivatives *Can. J. Chem*. 1964, *42*, 1473-80. (b) Lemieux, R. U.; Fraser-Reid, B. The mechanisms of the halogenations and halogenomethoxylations of D-glucal triacetate, D-galactal triacetate, and 3, 4-dihydropyran. *Can. J. Chem*. **1965**, *43*, 1460-1475.
12. Danishefsky, S. J.; Bilodeau, M. T. Glycals in Organic Synthesis: The Evolution of Comprehensive Strategies for the Assembly of Oligosaccharides and Glycoconjugates of Biological Consequence. *Angew. Chem. Int. Ed. Engl*. **1996**, *35*, 1380-1419
13. Halcomb, R. L.; Danishefsky, S. J. On the direct epoxidation of glycals: application of a reiterative strategy for the synthesis of. beta-linked oligosaccharides. *J. Am. Chem. Soc.* **1989**, *111*, 6661-6666.
14. (a) Harvey, J. E.; Hewitt, R. J.; Moore, P. W.; Somarathne, K. K. Reactions of 1,2-cyclopropyl carbohydrates. *Pure Appl. Chem*. **2014**, *86* (9): 1377–1399 (b) Sridhar, P. R.;

Kumar, P. V.; Seshadri, K.; Satyavathi, R. Synthesis of 2-C-Branched Oligo(glyco–amino acid)s (OGAAs) by RingOpening of 1,2-Cyclopropanecarboxylated Sugar Donors *Chem-Eur. J.* **2009**, *15* (31), 7526-7529. (c) Sridhar, P. R.; Seshadri, K.; Reddy, G. M. Stereoselective synthesis of sugar fused b-disubstituted c-butyro-lactones: C-spiro-glycosides from 1,2-cyclopropanecarboxylated sugars. *Chem. Commun*. **2012**, *48* (5), 756-758. (d) Sridhar, P. R.; Venukumar, P. A Ring ExpansionGlycosylation Strategy toward the Synthesis of Septano-oligosaccharidesOrg. Lett. **2012, 14** (21), 5558- 5561.

15. (a) Momose, T.; Setoguchi, M.; Fujita, T.; Tamura, H.; Chida, N. Chiral synthesis of the CD ring unit of paclitaxel from d-glucal. *Chem. Comm*. **2000**, 2237-2238. (b) Tanimoto, H.; Saito, R.; Chida, N. Formal synthesis of (-)-morphine from D-glucal based on the cascade Claisen rearrangement. *Tetrahedron Lett*. **2008**, *49* (2), 358-362.
16. (a) Lemieux, R. U.; Levine, S. Synthesis of alkyl 2-Deoxy-α-D glucopyranoside and their 2-Deuterio derivatives *Can. J. Chem*. 1964, *42* (6), 1473-80. (b) Bowles, W. A.; Robins, R. K. The Direct Utilization of Glycals for the Preparation of Purine Deoxynucleosides. *J. Am. Chem. Soc*. **1964**, *86*, 1252-1253 (c) Bolitt, V.; Mioskowski, C.; Lee, S. G.; Falck, J. R. Direct Preparation of 2-Deoxy-D-gIucopyranosides from Glucals without Ferrier Rearrangemen. *J. Org. Chem*. **1990**, *55* (23), 5812-5813.
17. (a) Dransfield, P. J.; Gore, P. M.; Shipman, M.; Slawin, A. M. Z. Divergent approach to imino sugar C-glycosides using imino glycals: application to the stereocontrolled synthesis of (+)-deoxoprosophylline. *Chem. Comm.* **2002**, 150-151; (b) Squarcia, A.; Vivolo, F.; Weinig, H.-G.; Passacantilli, P.; Piancatelli, G. Glycal-mediated syntheses of enantiomerically pure polyhydroxylated γ- and δ-lactams. Tetrahedron Lett. **2002**, 43, 4653-4655.
18. (a) Ferrier, R. J.; Zubkov, O. A. Transformation of Glycals into 2,3-Unsaturated Glycosyl Derivatives. *Org. React. (N. Y.)* **2003**, *62*, 569- 736. (b) Ferrier, R. J.; Hoberg, J. O. Synthesis and reaction of unsaturated sugar. *Adv. Carbohydr. Chem. Biochem*. **2003**, *58*, 55.
19. Fischer, E. Concerning new reduction products of dextrose, glucal and hydro-glucal. *Chem. Ber*. **1914**, *47*, 196–210.
20. Bergmann, M. The pseudo-glucal and dihydro-pseudoglucal. Liebigs *Ann. Chem*. **1925**, *443*, 223–242.
21. Ferrier, R.J.; Prasad, N. Unsaturated carbohydrates. IX. Synthesis of 2,3-dideoxy-α-D-erythrohex-2-enopyranosides from tri-O-acetyl-D-glucal. *J. Chem. Soc. (C)*, **1969**, 570–575.
22. Ferrier, R.J. Unsaturated sugars. *Adv. Carbohydr. Chem. Biochem*. **1969**, *24*, 199–266.
23. Ferrier, R.J. Unsaturated sugars. In The Carbohydrates; Pigman, W., Horton, D., Eds.; Academic Press: New York, NY, USA, 1980; Volume 1B, 843.
24. (a) Tipson, R.S.; Cohen, A. Action of zinc dust and sodium iodide in N,N-dimethylformamide on contiguous, secondary sulfonyloxy groups: A simple method for introducing nonterminal unsaturation. *Carbohydr. Res*. **1965**, *1*, 338–340. (b) Fraser-Reid,

B.; Boctor, B. Some aspects of the formation of hex-2-enopyranosides from methyl 2,3-di-O-methanesu1fonyl-α-D-glucopysanosides. *Can. J. Chem.* **1969**, *47*, 393–401.

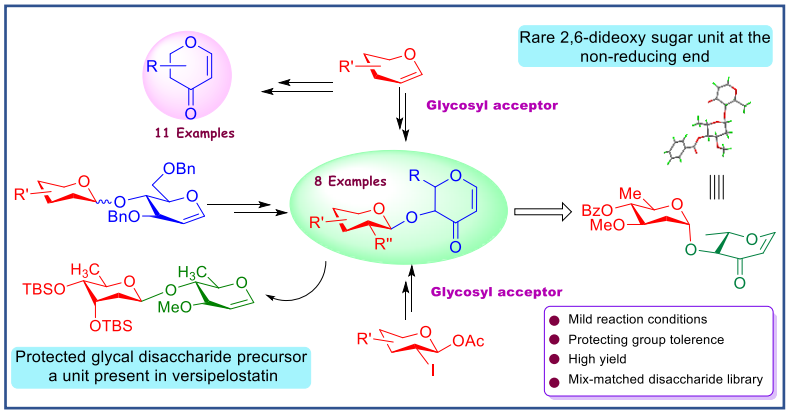
25. (A) Achmatowicz, O.; Bielski, R. Stereoselective total synthesis of methyl α-D and α-L-glucopyranosides. *Carbohydr. Res*. **1977**, *55*, 165–176. 17. (B) Achmatowicz, O.; Bukowski, B.; Szechner, B.; Zwierzchowska, Z.; Zamojski, A. Synthesis of methyl 2,3-dideoxy-DL-alk-2-enopyranosides from furan compounds. A general approach to the total synthesis of monosaccharides. *Tetrahedron* **1971**, *27*, 1973–1996.
26. (A) Angerbauer, R.; Schmidt, R.R. Short synthesis of racemic uronic acids and 2,3-anhydrouronic acids. *Carbohydr. Res*. **1981**, *89*, 159–162. (B) Bataille, C.; Begin, G.; Guillam, A.; Lemiegre, L.; Lys, C.; Maddaluno, J.; Toupet, L. Thermal/hyperbaric heterocycloaddition of 1,4-dialkoxy-1,3-dienes: The de novo (E,Z) way to sugars. *J. Org. Chem*. **2002**, *67*, 8054–8062.
27. Crimmins, M.T.; King, B.W.; Zuercher, W.J.; Choy, A.L. An efficient, general asymmetric synthesis of carbocyclic nucleosides: Application of an asymmetric aldol/ring-closing metathesis strategy. *J. Org. Chem.* **2000**, *65*, 8499–8509.
28. Gomez, A. M.; Lobo, F.; Miranda, S.; Lopez, J. C. A Survey of Recent Synthetic Applications of 2,3-Dideoxy-Hex-2-enopyranosides. *Molecules.* **2015**, *20*, 8357-8394.
29. (a) Comely, A.C.; Eelkema, R.; Minnaard, A.J.; Feringa, B.L. De novo asymmetric bio- and chemocatalytic synthesis of saccharides—Stereoselective formal *O*-glycoside bond formation using palladium catalysis. *J. Am. Chem. Soc***. 2003**, *125*, 8714–8715. (b) Babu, R.S.; O'Doherty, G.A. A palladium-catalyzed glycosylation reaction: The de novo synthesis of natural and unnatural glycosides. *J. Am. Chem. Soc*. **2003**, *125*, 12406–12407.
30. Ferrier, R.J.; Vethaviyasar, N. Unsaturated carbohydrates. XVII. Synthesis of branched-chain sugar derivatives by the Claisen rearrangement. *J. Chem. Soc*. Perkin 1 **1973**, 1791–1793.
31. Montero, A.; Mann, E.; Herradon, B. The Overman rearrangement in carbohydrate chemistry: Stereoselective synthesis of functionalized 3-amino-3,6-dihydro-2H-pyrans and incorporation in peptide derivatives. *Tetrahedron Lett*. **2005**, *46*, 401–405.
32. (a) Krohn, K.; Flörke, U.; Gehle, D. Highly deoxygenated sugars. I. C2-Branched glucose derivatives and carbon linked deoxygenated disaccharides. *J. Carbohydr. Chem*. **2002**, *21*, 431–443. (b) Montero, A.; Mann, E.; Herradon, B. Preparation of sugar amino acids by Claisen-Johnson rearrangement: Synthesis and incorporation into enkephalin analogues. *Eur. J. Org. Chem*. **2004**, 3063–3073.
33. Kriek, N.M.A.J.; van der Hout, E.; Kelly, P.; van Meijgaarden, K.E.; Geluk, A.; Ottenhoff, T.H.M.; van der Marel, G.A.; Overhand, M.; van Boom, J.H.; Valentijn, A.R.P.M.; et al. Synthesis of novel tetrahydropyran-based dipeptide isosters by Overman rearrangement of 2,3-didehydroglycosides. *Eur. J. Org. Chem*. **2003**, 2418–2427.
34. Zhang, G.; Shi, L.; Liu, Q.; Wang, J.; Li, L.; Liu, X. A divergent strategy for constructing a sugar library containing 2,6-dideoxy sugars and uncommon sugars with 4-substitution. *Tetrahedron* **2007**, *63*, 9705–9711.

35. Haukaas, M.H.; O'Doherty, G.A. Enantioselective synthesis of 2-deoxy- and 2,3-dideoxyhexoses. *Org. Lett*. **2002**, *4*, 1771–1774.
36. Harris, J.M.; Keranen, M.D.; O'Doherty, G.A. Syntheses of D- and L-mannose, gulose, and talose via diastereoselective and enantioselective dihydroxylation reactions. *J. Org. Chem*. **1999**, *64*, 2982–2983
37. Murphy, P.V.; O'Brien, J.L.; Smith, A.B., III. Stereospecific synthesis of β-D-allopyranosides by dihydroxylation of β-D-erythro-2,3-dideoxyhex-2-enopyranosides. *Carbohydr. Res*. **2001**, *334*, 327–335.
38. Guaragna, A.; Napolitano, C.; D'Alonzo, D.; Pedatella, S.; Palumbo, G. A versatile route to L-hexoses: Synthesis of L-mannose and -altrose. *Org. Lett*. **2006**, *8*, 4863–4866.
39. Sakakibara, T.; Yamada, M.; Sudoh, R. Phase transfer catalyzed reactions. II. Reactions of methyl 3-deoxy-3-nitro-β-D-hexopyranosides with active methylene compounds. *J. Org. Chem*. **1976**, *41*, 736–737.
40. Fraser–Reid, B.; McLean, A.; Usherwood, E.W.; Yunker, M., Pyranosiduloses. II. The synthesis and properties of some alkyl 2, 3-dideoxy-2-enopyranosid-4-uloses. *Canadian J. Chem.***1970**, *48*, 2877-2884
41. Gomez, A.M.; Lopez, J.C.; Fraser-Reid, B. Stereoselective synthesis of ethyl (Z)- and (E)-octa2,6-dienopyranosideuronates from ethyl 2,3-dideoxy-α-D-erythro-hex-2-eno-pyranoside. *Singlet*. **1993**, 557–560.
42. Pasniczek, K.; Socha, D.; Jurczak, M.; Solecka, J.; Chmielewski, M. Synthesis of 8-homocastanospermine. *Can. J. Chem.* **2006**, *84*, 534–539.
43. Socha, D.; Pasniczek, K.; Jurczak, M.; Solecka, J.; Chmielewski, M. Synthesis of 1-homoaustraline. *Carbohydr. Res*. **2006**, *341*, 2005–2011.
44. (A) Lopez, J.C.; Lameignere, E.; Burnouf, C.; Laborde, M.A.; Ghini, A.; Olesker, A.; Lukacs, G. Efficient routes to pyranosidic homologated conjugated enals and dienes from monosaccharides. *Tetrahedron* **1993**, *49*, 7701–7722. (B) Mangione, M.I.; Sarotti, A.M.; Suarez, A.G.; Spanevello, R.A. Experimental and theoretical study of a Diels-Alder reaction between a sugar-derived nitroalkene and cyclopentadiene. *Carbohydr. Res*. **2011**, *346*, 460–464.
45. Chapleur, Y.; Grapsas. Stereospecific formation of carbon-carbon bonds in ethyl 4,6-di-O-acetyl-2,3-dideoxy-α-D-ribo-hex-3-enopyranoside. *Carbohydrate Research*, **1985** *141*, 153-158
46. Yeager, A.R.; Min, G.K.; Porco, J.A.; Schaus, S.E. Exploring skeletal diversity via ring contraction of glycal-derived scaffolds. *Org. Lett*. **2006**, *8*, 5065–5068.
47. Comely, A.C.; Eelkema, R.; Minnaard, A.J.; Feringa, B.L. De novo asymmetric bio- and chemocatalytic synthesis of saccharides—Stereoselective formal O-glycoside bond formation using palladium catalysis. *J. Am. Chem. Soc*. **2003**, *125*, 8714–8715.
48. Babu, R.S.; O'Doherty, G.A. A palladium-catalyzed glycosylation reaction: The de novo synthesis of natural and unnatural glycosides. *J. Am. Chem. Soc*. **2003**, *125*, 12406–12407.

49. Babu, R.S.; Zhou, M.; O'Doherty, G.O. De novo synthesis of oligosaccharides using a palladium-catalyzed glycosylation reaction. *J. Am. Chem. Soc*. **2004**, *126*, 3428–3429.

Chapter 2

Synthesis of Hexenuloses and a Library of Disaccharides Possessing 3-oxo-glycal Unit



Abstract

An efficient method for the synthesis of monosaccharides and disaccharides possessing 3-oxo-glycal unit is discussed. An array of monosaccharides and disaccharide-derived glycals are converted to the corresponding hexenuloses *via* three key steps involving halo-alkoxylation, dehydrohalogenation, and ketalyzation reactions. Several 3-oxo-glycals are synthesized to show the generality and importance of the methodology. Further, the post-synthetic transformations are carried out to synthesize a rare-sugar disaccharide donor unit present as part of trisaccharide moiety in the reported natural product, versipelostatin.

2.1 Introduction

Hexenuloses are the enones commonly known as 3-oxo-glycals or sugar derived 2,3-dihydro-4*H*-pyran-4-ones. They are the *α,β*-unsaturated-ketone moiety occupying *C*1, *C*2, and *C*3 positions of a sugar molecule (Figure 1). 3-oxo-glycals also possess an electron-donating endocyclic oxygen atom on the *β*-carbon which makes it more reactive substrate in the synthetic carbohydrate chemistry. Its importance, utility and reactivity is discussed further in this chapter.

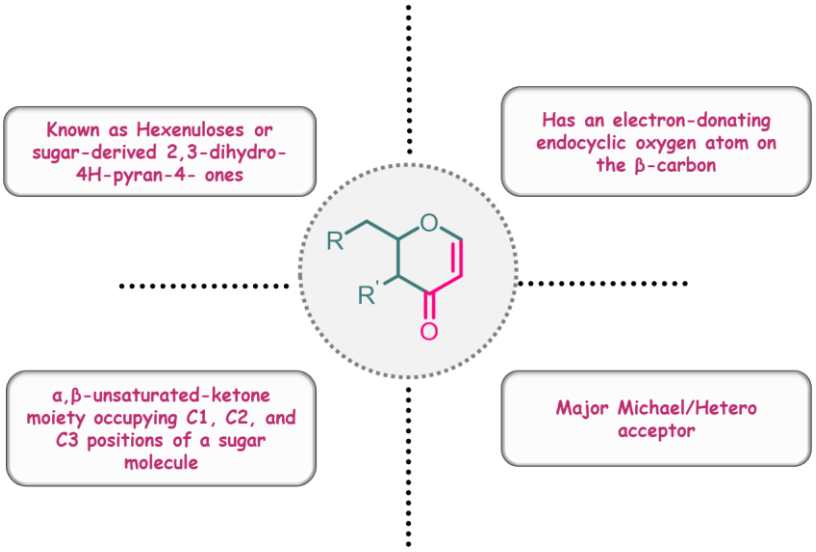


Figure 1: Representative structure of Hexenuloses

Hexenuloses are chiral synthons derived from glycals that are used for synthesis of therapeutically relevant compounds and complicated natural products. Total synthesis of natural compounds such as mycalamides, (+)-decarestrictine L, and thailastatin A-C has recently been accomplished employing 3-oxo-glycals as crucial intermediates.[1] In addition, hexenulose has been the crucial precursor in the total synthesis of several natural products, such as diospongin A, *ent*-diospongin A,[2] 6-*epi*-phomonol,[3] (+)-decarstrictine L[4] are to say a few examples. Protected 3-oxo-glycals have been used as substrates for the preparation of 2-alkynyl 3-oxo-glycals *via* the 2-iodo derivative involving the Sonogashira coupling[5] as well as to synthesize 1-aryl hexenuloses through the Heck coupling with aryl boronic acids.[6] Moreover, due to the presence of a reactive α,β-unsaturated ketone system possessing an electron-donating endocyclic oxygen atom on the β-carbon, these glycals are prone to undergo stereoselective Michael/Hetero Michael addition

reactions. Hence, hexenuloses are excellent precursors for constructing *O*-[7] *S*- and *C*-alkyl[8]/aryl[9] glycosides. Additionally, 3-oxo-glycals have been used as substrates to synthesize septatanoses and septano-oligosaccharides,[10] and rare sugar derivatives[11] such as D-allal *via* stereoselective reduction of the 3-oxo group[12] (Figure 2).

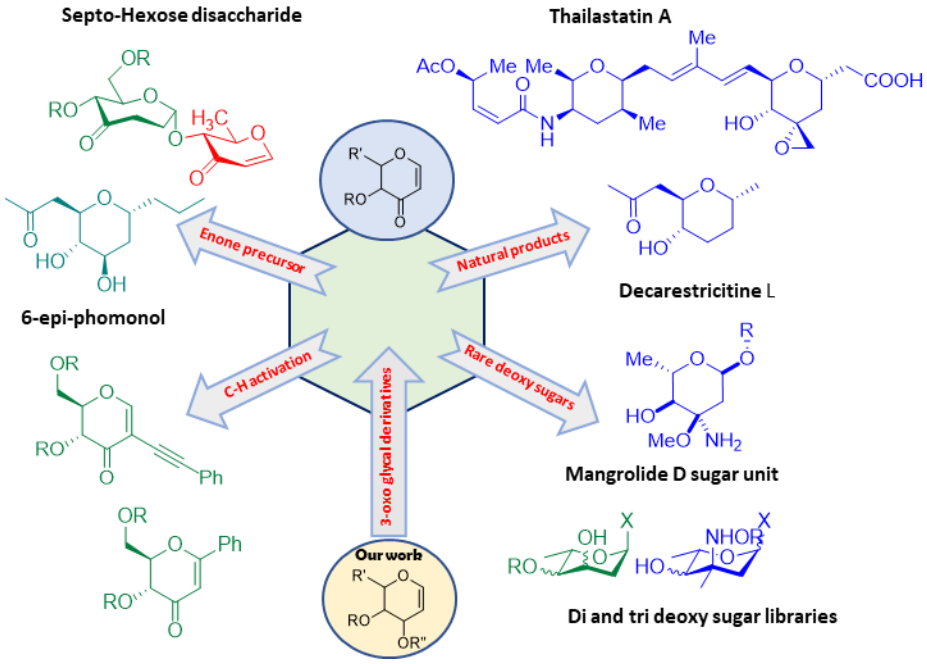


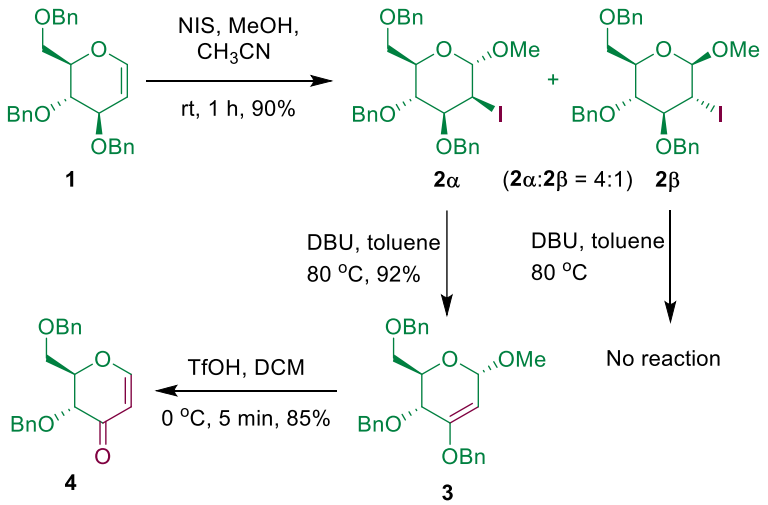
Figure 2. Synthetic application of 3-oxo-glycals in natural products and carbohydrate derivatives.

The discovery of synthetic methods for the manufacture of 3-oxo-glycals is in great demand due to its relevance and application. There are a few reports to synthesize hexenuloses.[13] The reported methods to synthesize hexenuloses primarily includes the allylic oxidation of the corresponding 3-hydroxy glycals by utilizing a variety of oxidizing agents such as PDC,[13a] MnO_2,[13b] NIS and $(Bu_3Sn)_2O$[13c] etc.,[13d] Alongside the allylic oxidation strategy, utilization of hypervalent iodine reagents like PhI(OH)(OTs) (Koser's reagent),[13e] $PhI(OAc)_2$ with Me_3SiN_3[13f] also utilized for the conversion of 3-*O*-protected glycals to 3-oxo-glycal derivatives. Recently, Vankar *et al.* reported the TEMPO catalyzed oxidation of 3-*O*-benzylated/silylated glycals to the corresponding 3-oxo glycals by using $PhI(OCOCF_3)_2$-water system.[13g] However, most of the reported procedures have poor yield, require anhydrous conditions, and are not reproducible. These disadvantages compelled us to seek a possible solution to the aforementioned problems. Proceeding our ongoing

research on glycals to discover their potential applications in the synthesis of novel carbohydrate architectures,[16] we chose to investigate a more acurate, accessible and reliable protocol for synthesising a variety of hexenuloses from easily available starting materials and cost-effective reagents. Herein, we report an expeditious and novel approach to synthesize 3-oxo-glycals from glycals by utilizing halo-alkoxylation, dehydrohalogenation, and ketalyzation as the key reactive steps.

2.2 Results and Discussion

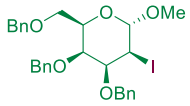
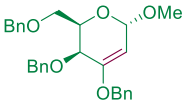
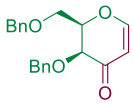
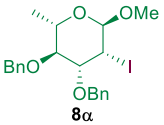
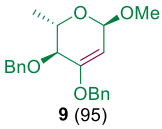
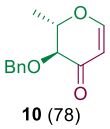
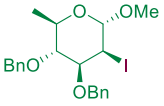
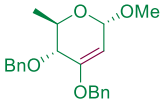
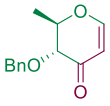
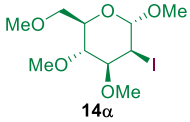
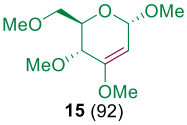
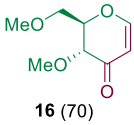
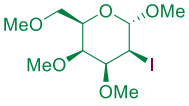
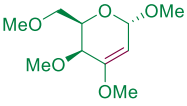
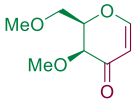
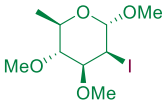
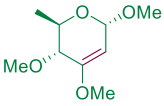
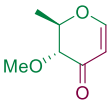
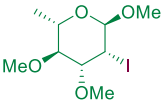
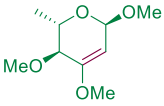
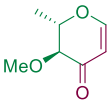
At the onset of our investigation, we explored the regio- and stereoselective iodo-methoxylation of tribenzyl glucal **1**[17] using NIS/MeOH. This reaction led to the isolation of the corresponding methyl 2-iodo glycosides (**2*α*** and **2*β***)[18] in 4:1 ratio, respectively. In the next step, we subjected **2*α*** and **2*β*** separately to the DBU mediated dehydrohalogenation reaction. As expected, the anti-periplanar alignment between the 2*C*-I and 3*C*-H in **2*α*** favoured the formation of the corresponding vinyl ether **3,** whereas **2*β*** remained unreacted. In the last step, vinyl ether **3** was exposed to a catalytic amount of trifluoromethanesulfonic acid (TfOH) in dichloromethane, resulting in the desired 3-oxo-glucal **4**[14] in excellent yield (Scheme 1).



Scheme 1. Synthesis of 4,6-di-*O*-benzyL-3-oxo-glucal from tribenzyl glucal.

Having synthesized the 3-oxo-glucal **4** from tribenzyl glucal **1,** we focused on the generality and efficacy of this methodology on a variety of perbenzylated glycal derivatives. Thus, perbenzyl D-

galactal, L-rhamnal, and 6-deoxy-D-glucal upon iodo-methoxylation in the presence of NIS/MeOH provided the corresponding methyl 2-deoxy-2-iodo glycosides **5*α***, **8*α***, and **11*α*** in good yield. Subsequent DBU mediated dehydrohalogenation resulted in vinyl ethers **6**, **9**, and **12,** which upon reaction with a catalytic amount of triflic acid led to the formation of the 3-oxo glycal derivatives **7**,[15] **10**[15] and **13**,[11a] respectively in good yields (Table 1, entry 1-3).

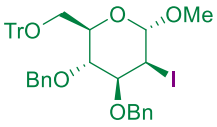
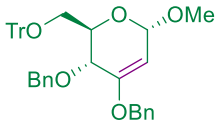
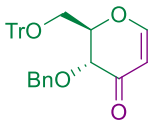
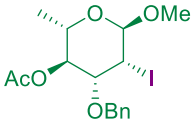
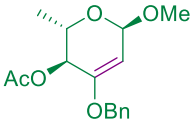
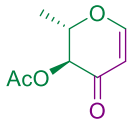
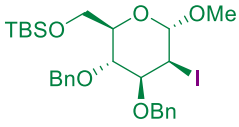
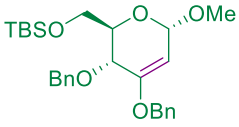
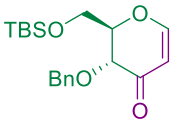
S.No	Iodoacetal	Vinyl ether (%)[a]	3-Oxo-glycal (%)[a]
1	 **5α**	 **6** (90)	 **7** (68)
2	 **8α**	 **9** (95)	 **10** (78)
3	 **11α**	 **12** (95)	 **13** (80)
4	 **14α**	 **15** (92)	 **16** (70)
5	 **17α**	 **18** (97)	 **19** (68)
6	 **20α**	 **21** (84)	 **22** (81)
7	 **23α**	 **24** (78)	 **25** (67)

[a] Yield refers to pure and isolated products.

Table 1. Conversion of perbenzyl and permethylated glycals to the corresponding 3-oxo-glycals.

Further extension of the methodology to the permethylated D-glucal, D-galactal, D-rhamnal, and L-rhamnal, which provided the methyl 2-deoxy- 2-iodo-glycosides **14*α***, **17*α***, **20*α***, and **23*α***, respectively as major products when subjected to iodo- methoxylation reaction conditions. DBU mediated dehydrohalogenation of these iodo-derivatives provided the vinyl ethers **15**, **18**, **21**, and **24**, respectively. Ultimately, the triflic acid-mediated ketalyzation of the obtained vinyl ethers led to the formation of permethyl 3-oxo-glycal derivatives **16**, **19**, **22,** and **25** (table 1, entry 4-7), respectively. To the best of our knowledge, this is one of the very useful methods for the conversion of 3-*O*-methyl glycals to the corresponding 3-oxo-glycals.[19]

We further investigated the protecting group tolerance under the developed reaction conditions. Towards this, 6-*O*-trityl, 4-*O*-acetyl, and 6-*O*-*tert*-butyldimethylsilyl protected 2-deoxy-2-iodo glycosides **26*α***, **29*α***, and **32*α*** were synthesized from the corresponding glycals and subjected to the dehydrohalogenation reaction to give vinyl ethers **27**, **30,** and **33**, respectively. Finally, the triflic acid-catalyzed ketalyzation of respective vinyl ethers provided the orthogonally protected 3-oxo-glycal derivatives **28**, **31**[15], and **34**,[15,] respectively (Table 2, entry 1-3).

S.No	Iodoacetal	Vinyl ether (%)[a]	3-Oxo-glycal (%)[a]
1	 **26**α	 **27** (98)	 **28** (89)
2	 **29**α	 **30** (92)	 **31** (73)
3	 **32**α	 **33** (87)	 **34** (68)

[a] Yield refers to pure and isolated products.

Table 2. Substrate scope for the protecting group tolerance in the preparation of 3-oxo-glycals.

However, the methodology was not successful in the case of methyl 2-deoxy-2-iodo-glycosides **35**-**39**. The probable reason is that, the iodo-methoxylation of 3,4,6-tri-*O*-*tert*-butyldimethylsilyl glucal and 4,6-di-*O*-benzyl-3-*O*-*tert*-butyldimethylsilyl glucal provided the methyl *β*-D-2-deoxy-2-iodo glycoside derivatives **35** and **36**, respectively, as the only diastereomers. One can envisage that compounds **35**[20] and **36** prefer the *tert*-butyldimethylsilyl protecting group at the C-3 position in an axial trajectory and adopt a $^{1}C_{4}$ conformation instead of the $^{4}C_{1}$. Due to the lack of trans-periplanar arrangement of the leaving groups in this conformation, these compounds did not undergo dehydrohalogenation reaction. The 1,2-diaxial conformation of these sugars was confirmed based on NMR coupling constant of the anomeric proton ($J_{1,2}$ = 2.8 Hz). On the other hand, halo-alkoxylation of 3,4-di-*O*-benzyl D- and L-arabinal provided exclusively 2-deoxy-2-iodo derivatives **37** and **38**, respectively. Again, these compounds did not possess the leaving groups in trans-periplanar arrangement, hence no dehydrohalogenation occurred.In the case of 3,4,6-tri-*O*-acetyl-D-glucal derived methyl 2-deoxy-2-iodo glycoside derivative **39,**[21] the relatively larger size of the C=O in the methyl ester, compared to the CH_2 of the 3-*O*-benzyl, prohibits the approach of the DBU for the deprotonation reaction which may hinder the formation of the corresponding vinyl acetate derivative (Figure 2).

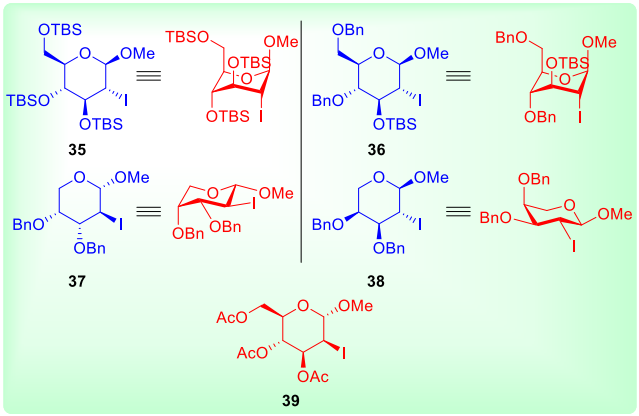
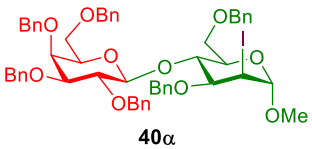
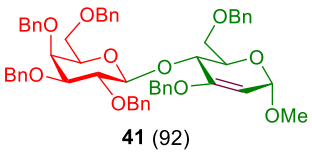
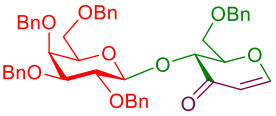
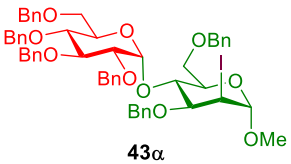
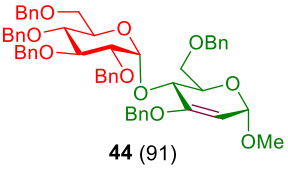
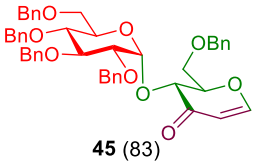
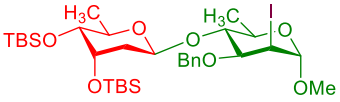
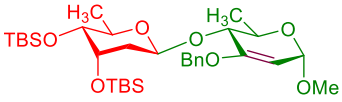
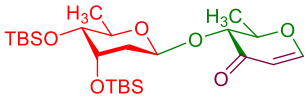
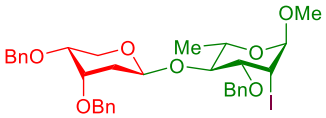
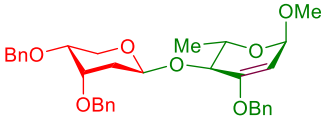
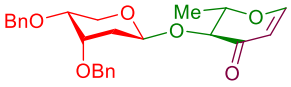
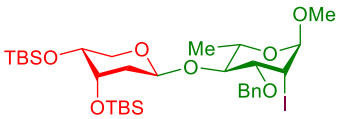
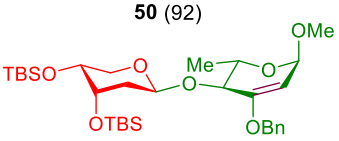
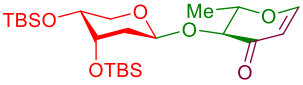
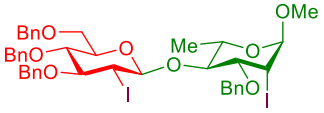
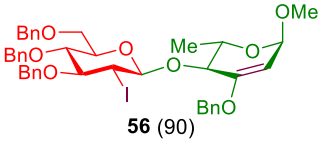
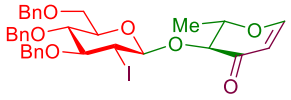
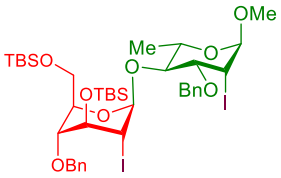
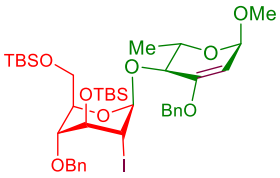
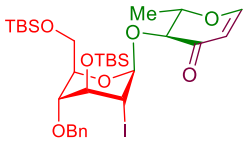


Figure 2. Importance of the conformation concerning the dehydrohalogenation reaction.

Although a few methods are known to synthesize 3-oxo-glycals from the corresponding 3-*O*-protected/non-protected monosaccharide units, extending the same to disaccharide glycals is very rare.[15] Hence, having success in the case of monosaccharides, our vision focused on evaluating the protocol for the synthesis of 3-oxo-glycals in disaccharide derivatives. To initiate this,

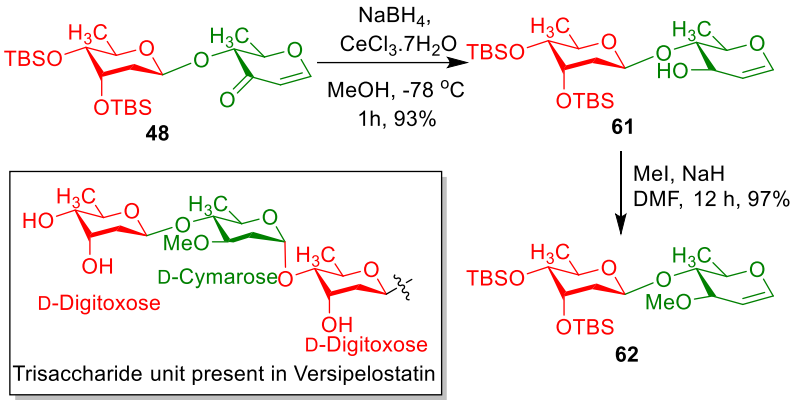
perbenzylated D-lactal was subjected to iodo-methoxylation to obtain the methyl 2-deoxy-2-iodo-lactose derivative **40*α***. DBU mediated dehydrohalogenation of **40*α*,** to give vinyl ether **41,** which upon reacting with catalytic triflic acid provided the 3-oxo-glycal derived disaccharide **42** in good yield. This transformation clearly indicates the stability of the glycosidic linkage under the prescribed reaction conditions. Further, we successfully showcased the application of the methodology by choosing structurally diverse disaccharides. In this regard, dehydrohalogenation of maltose derived 2-deoxy-2-iodo glycoside **43*α*** (where there is an α-glycosidic linkage), 2,6-dideoxy 3,4-di-*O*-*tert*-butyldimethylsilyl allose containing disaccharide **46**, 3,4-di-*O*-benzyl and 3,4-di-*O*-*tert*-butyldimethylsilyl D-arabinose derived iodo glycoside **49** and **52,** respectively, gave vinyl ether derivatives **44**, **47**, **50** and **53**. Further reaction with catalytic triflic acid gave the enone-disaccharides **45**, **48**, **51**, and **54**, respectively (Table 3, entry 2-5) in good to excellent yield.
We further assessed the use of unreactive 2-deoxy-2-iodo glycoside as one of the sugar units in the disaccharide. Hence, disaccharides **55** and **58** were synthesized and subjected to the dehydrohalogenation reaction. As expected, the carbohydrate unit possessing the anti-periplanar leaving groups underwent the reaction providing the vinyl ethers **56** and **59**, which further provided the 3-oxo-glycal containing disaccharides **57** and **60**, respectively (Table 3, entry 6 and 7).

Having established a novel strategy for synthesizing 3-oxo-glycals, we anticipated that our methodology would serve as a valuable toolkit in synthesizing complex natural products possessing rare sugar units. Accordingly, we attempted the synthesis of the disaccharide unit present at the non-reducing end of versipelostatin.[22] Towards this, disaccharide **48** was subjected to Luche reduction, and the corresponding allylic alcohol **61** was obtained as a single diastereomer. Subsequent methylation provided the expected disaccharide glycal precursor **62**, consisting of D-digitoxose and D-cymarose units present in the natural product versipelostatin (Scheme 2).

S.No	Iodoacetal	Vinyl ether (%)[a]	3-Oxo-glycal (%)[a]
1	 **40α**	 **41** (92)	 **42** (87)
2	 **43α**	 **44** (91)	 **45** (83)
3	 **46**	 **47** (92)	 **48** (88)
4	 **49**	 **50** (92)	 **51** (78)
5	 **52**	 **53** (82)	 **54** (72)
6	 **55**	 **56** (90)	 **57** (80)
7	 **58**	 **59** (90)	 **60** (68)

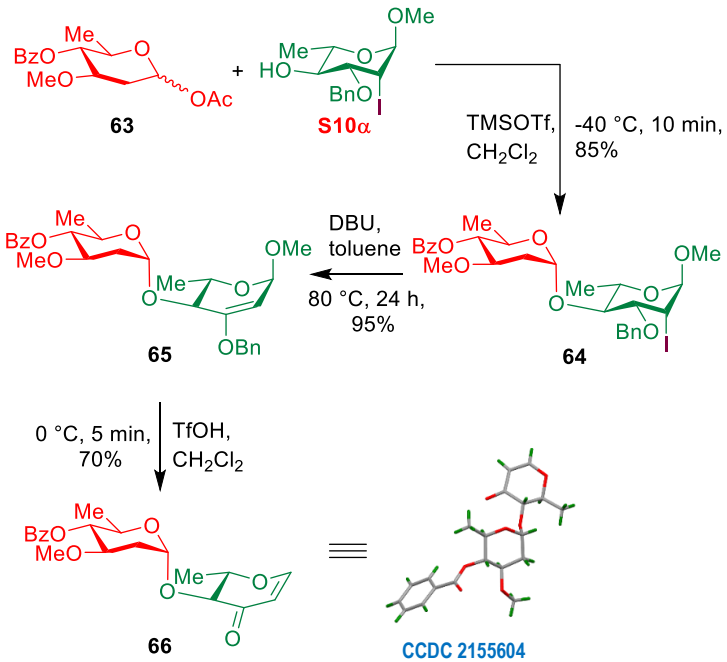
[a]Yield refers to pure and isolated products.

Table 3. Synthesis of disaccharides possessing 3-oxo-glycal unit.



Scheme 2. Synthesis of the disaccharide unit precursor present in the proposed structure of Versipelostatin.

To explore the importance of the methodology, a disaccharide unit with various protecting groups on a non-reducing end was planned to synthesize. Thus, TMSOTf catalyzed glycosylation of donor **63** with acceptor **S10*α*** provided the disaccharide **64** in excellent yield. Dehydrohalogenation of **64** gave vinyl ether **65,** followed by treatment with catalytic triflic acid provided the enone-disaccharide **66** (Scheme 3).



Scheme 3. Synthesis of the disaccharide unit possessing a rare 2,6-dideoxysugar framework at the non-reducing end.

The structure of 66 was also confirmed by single-crystal X-ray diffraction studies (CCDC 2155604). It is important to mention that several natural products possess a similar kind of rare-deoxy sugar units in their molecular framework, for example, apoptolidine,[23] ivermectin[24].

2.3 Conclusion

In conclusion, we reported a general, efficient, and convenient methodology for synthesizing 3-oxo-glycals. The substrate scope and accessibility of the current protocol were successfully shown by synthesizing variably protected hexenuloses of mono- and disaccharides. Finally, the effective application of the methodology was demonstrated via synthesizing the disaccharide unit, comprised of rare-monosaccharide, present in natural product, versipelostatin. Further application of the current protocol in the total synthesis of deoxy-sugar-containing natural products and their analogs is in progress.

2.4 Experimental Section

2.4.1 General Information:

All the reactions were carried out under nitrogen or argon atmosphere and monitored by thin layer chromatography (TLC) using silica gel GF_{254} plates with detection by charring with 5% (v/v) H_2SO_4 in methanol or by phosphomolybdic acid (PMA) stain or by ultra violet (UV) detection. All the chemicals were purchased from local suppliers and Sigma-Aldrich Chemicals Company. Solvents used in the reactions were distilled over dehydrated agents. Silica-gel (100-200 mesh) was used for column chromatography. All NMR spectra were recorded on Bruker 400 MHz and 500 MHz spectrometer in $CDCl_3$. ^1H NMR chemical shifts were reported in ppm (δ) with TMS as internal standard (δ 0.00) and ^{13}C NMR were reported in chemical shifts with solvent reference ($CDCl_3$, δ 77.00). Structural assignments were made with additional information from gCOSY, gNOESY experiments. High resolution mass spectra were obtained in the ESI mode recorded on ESI-TOF spectrometer.

2.4.2 General Experimental Procedures:

General Procedure A: Iodo-acetalyzation of glycals

To a stirred solution of protected glycal (1.0 mmol) in anhydrous ACN (10 mL/mmol) under inert atmosphere was added MeOH (1.8 mmol) followed by NIS (1.5 mmol) at 0°C. The reaction was allowed to raise to room temperature and further stirred until starting material is disappeared. The reaction was quenched with saturated solution of sodium thiosulphate and extracted with EtOAc, dried over anhydrous Na_2SO_4 and concentrated under reduced pressure to obtain crude product. Purification of the crude product by column chromatography over silica gel using hexane and ethyl acetate provided iodo compounds as anomeric mixtures (α:β).

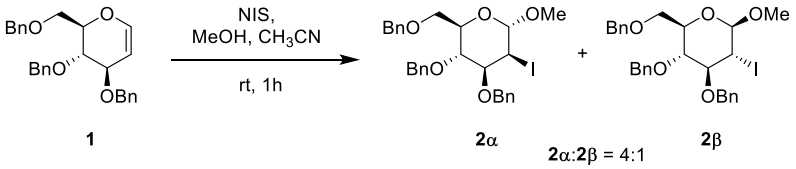
General procedure B: Dehydrohalogenation- Synthesis of vinyl ether

To a stirred solution of iodo derivative (1.0 mmol) in anhydrous Toluene (10 mL/mmol) under inert atmosphere was added DBU (1.1 mmol) at room temperature. The reaction mass was further heated at 80°C using oil bath for 24 hours. After complete conversion of starting material, solvent was concentrated under reduced pressure to obtain crude product which was purified over basic alumina using hexane and ethyl acetate to obtain vinyl ether.

General procedure C: Synthesis of 3-oxoglycals

To a stirred solution of vinyl ether (1.0 mmol) in anhydrous DCM (10 mL/mmol) under inert atmosphere was added TfOH (0.05 mmol) at 0°C for 10 minutes. After complete conversion of starting material, the reaction was quenched with saturated solution of $NaHCO_3$, extracted with DCM, dried over anhydrous Na_2SO_4 and concentrated under reduced pressure to obtain crude product. Purification of the crude product by column chromatography over silica gel using hexane and ethyl acetate provided pure *α,β*-unsaturated ketone.

2.4.3 Experimental procedures and spectral data:



1 **2α** **2α:2β = 4:1** **2β**

Compound **2α** and **2β** were synthesizesynthesized from Tribenzylglucal **1** (300 mg, 0.72 mmol) by following general **procedure A**. Overall yield: 90%, 372.44 mg.

(2*R*,3*R*,4*S*,5*S*,6*S*)-3,4-bis(benzyloxy)-2-((benzyloxy)methyl)-5-iodo-6-methoxytetrahydro-2*H*-pyran (2*α*):

Yield: 72%, 297.95 mg colorless oil. R_f: 0.5 (5% EtOAc/toluene). $[\alpha]_D^{25}$= +4.1 (c 0.9, $CHCl_3$).

^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.17-7.42 (m, 15H), 5.14 (s, 1H), 4.87 (d, 1H, *J* = 10.5 Hz), 4.73 (d, 1H, *J* = 12.5 Hz), 4.70 (d, 1H, *J* = 11.5 Hz), 4.55 (d, 1H, *J* = 12.5 Hz), 4.49-4.53 (m, 3H), 3.91 (t, 1H, *J* = 9.5 Hz), 3.83-3.86 (m, 1H), 3.80 (dd, 1H, *J* = 4.5 Hz, 11.0 Hz), 3.73 (d, 1H, *J* = 10.5 Hz), 3.36 (s, 3H), 3.32 (dd, 1H, *J* = 4.5 Hz, 8.5 Hz).

^{13}C{1H}NMR (125 MHz, $CDCl_3$): δ 138.3, 138.2, 137.7, 128.4, 128.4, 128.3, 128.0, 127.9, 127.8, 127.7, 127.6, 127.4, 102.4, 77.0, 75.8, 75.1, 73.4, 72.0, 70.9, 68.9, 55.0, 33.2.

HRMS (ESI-TOF) *m/z*: $[M+NH_4]^+$ calcd for $C_{28}H_{31}IO_5NH_4$ 592.1554, found 592.1557.

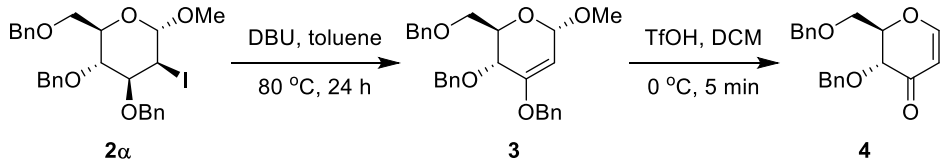
(2*R*,3*R*,4*S*,5*R*,6*R*)-3,4-bis(benzyloxy)-2-((benzyloxy)methyl)-5-iodo-6-methoxytetrahydro-2*H*-pyran (2β):

Yield: 18%, 74.48 mg white solid. R_f: 0.4 (5% EtOAc/toluene), m.p. 90-91 ˚C.

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.17-7.43 (m, 15H), 4.98 (d, 1H, *J* = 10.5 Hz), 4.86 (d, 1H, *J* = 10.0 Hz), 4.80 (d, 1H, *J* = 10.5 Hz), 4.62 (d, 1H, *J* = 12.0 Hz), 4.57 (d, 1H, *J* = 9.0 Hz), 4.54 (d, 1H, *J* = 12.0 Hz), 4.47 (d, 1H, *J* = 9.0 Hz), 3.91 (dd, 1H, *J* = 9.0 Hz, 10.5 Hz), 3.71-3.77 (m, 3H), 6.38 (dd, 1H, *J* = 8.5 Hz, 9.5 Hz), 3.56 (s, 3H), 3.50-3.53 (m, 1H).

^{13}C{1H} NMR (125 MHz, $CDCl_3$): δ 138.0, 137.7, 137.7, 128.5, 128.4, 128.4, 128.1, 127.9, 127.9, 127.8, 127.8, 127.7, 104.1, 85.8, 79.6, 75.5, 75.2, 74.9, 73.5, 68.5, 57.3, 32.6.

HRMS (ESI-TOF) *m/z*: $[M+NH_4]^+$ calcd for $C_{28}H_{31}IO_5NH_4$ 592.1554, found 592.1561.



2α **3** **4**

(2*R*,3*R*,6*S*)-3,4-bis(benzyloxy)-2-((benzyloxy)methyl)-6-methoxy-3,6-dihydro-2*H*-pyran (3):

Compound **3** was synthesized from **2*α*** (300 mg, 0.52 mmol) by following **general procedure B.**

Yield: 214.50 mg, 92%, colorless oil. R_f: 0.5 (10% EtOAc/hexane).

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.17-7.38 (m, 15H), 5.12 (d, 1H, *J* = 3.0 Hz), 4.91 (d, 1H, *J* = 3.5 Hz), 4.88 (d, 1H, *J* = 11.5 Hz), 4.87 (d, 1H, *J* = 11.0 Hz), 4.78 (d, 1H, *J* = 11.5 Hz), 4.65 (d,

1H, *J* = 12.5 Hz), 4.51 (d, 1H, *J* = 12.0 Hz), 4.46 (d, 1H, *J* = 11.0 Hz), 4.29 (d, 1H, *J* = 9.0 Hz), 4.14-4.16 (m, 1H), 3.72-3.73 (m, 2H), 3.44 (s, 3H).

^{13}C{1H} NMR (125 MHz, $CDCl_3$): δ 157.9, 138.2, 138.1, 136.4, 128.4, 128.3, 128.1, 128.1, 127.9, 127.8, 127.6, 127.5, 127.5, 96.9, 95.8, 74.0, 73.3, 71.0, 69.5, 69.4, 68.8, 55.4.

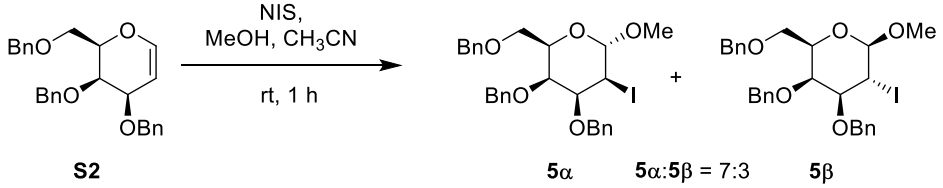
HRMS (ESI-TOF) *m/z*: $[M+Na]^+$ calcd for $C_{28}H_{30}O_5Na$ 469.1997, found 469.1985.

(2*R*,3*R*)-3-(benzyloxy)-2-((benzyloxy)methyl)-2,3-dihydro-4*H*-pyran-4-one (4): Compound **4** was synthesized from **3** (100 mg, 0.22 mmol) by following **general procedure C.** Yield: 61.2 mg, 85%, colorless oil. R_f: 0.5 (20% EtOAc/hexane).

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.28-7.35 (m, 11H), 5.38 (d, 1H, *J* = 6.0 Hz), 5.07 (d, 1H, *J* = 11.0 Hz), 4.57-4.61 (m, 2H), 4.52 (d, 1H, *J* = 12.0 Hz), 4.43 (dt, 1H, *J* =3.0 Hz, 11.5 Hz), 4.24 (d, 1H, *J* = 12.0 Hz), 3.80 (m, 2H).

^{13}C{1H} NMR (125 MHz, $CDCl_3$): δ 193.5, 162.2, 137.5, 137.4, 128.5, 128.4, 128.3, 128.0, 127.9, 127.8, 105.2, 81.0, 74.6, 74.1, 73.6, 67.9.

HRMS (ESI-TOF) *m/z*: $[M+H]^+$ calcd for $C_{20}H_{20}O_4H$ 325.1431, found 325.1431.



S2 **5α** **5α:5β = 7:3** **5β**

Compound **5α and 5β** were synthesized from **S2**[17] (3 g, 7.20 mmol) by following **general procedure A.** Overall yield: 97%, 4.01 g.

(2*R*,3*S*,4*S*,5*S*,6*S*)-3,4-bis(benzyloxy)-2-((benzyloxy)methyl)-5-iodo-6-methoxytetrahydro-2*H*-pyran (5α):

Yield: 67.9%, 2.80 g, colorless oil, R_f: 0.7 (10% EtOAc/hexane). $[\alpha]_D^{25}$= -5.7 (c 0.6, $CHCl_3$).

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.33-7.51 (m, 15H), 5.33 (d, 1H, *J* = 1.2 Hz), 5.14 (d, 1H, *J* = 11.6 Hz), 4.80 (d, 1H, *J* = 11.6 Hz). 4.66 (d, 1H, *J* = 11.6 Hz), 4.59 (d, 1H, *J* = 11.6 Hz), 4.54 (d,

1H, *J* = 11.6 Hz), 4.51 (d, 1H, *J* = 12.0 Hz), 4.43 (d, 1H, *J* = 4.4 Hz), 4.13 (td, 1H, *J* = 2.0 Hz, 6.0 Hz), 4.02 (bs, 1H), 3.75-3.83 (m, 2H), 3.58 (dd, 1H, *J* = 3.2 Hz, 4.4 Hz), 3.42 (s, 3H).

^{13}C{1H} NMR (100 MHz, $CDCl_3$): δ 138.5, 137.9, 137.6, 128.2, 128.2, 128.0, 127.6, 127.5 (2), 127.4, 127.4, 127.2, 103.1, 73.6, 73.3 (2), 73.0, 70.4, 70.3, 69.1, 55.1, 24.2.

HRMS (ESI-TOF) *m/z*: $[M+NH_4]^+$ calcd for $C_{28}H_{31}IO_5NH_4$ 592.1554, found 592.1557.

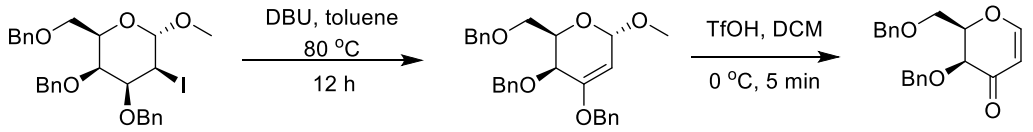
(2*R*,3*S*,4*S*,5*R*,6*R*)-3,4-bis(benzyloxy)-2-((benzyloxy)methyl)-5-iodo-6-methoxytetrahydro-2*H*-pyran (5β):

Yield: 29.1%, 1.20 g, white powder, R_f: 0.6 (10% EtOAc/hexane), $[\alpha]_D^{25}$= +23.3 (c 0.5, $CHCl_3$), m.p. 95-96 ˚C.

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.28-7.50 (m, 15H), 4.88 (d, 1H, *J* = 11.6 Hz), 4.74 (d, 1H, *J* = 10.8 Hz), 4.67 (d, 1H, *J* = 11.2 Hz), 4.57 (d, 1H, *J* = 11.6 Hz), 4.51 (d, 1H, *J* = 8.8 Hz), 4.49 (d, 1H, *J* = 12.0 Hz), 4.45 (d, 1H, *J* = 11.6 Hz), 4.33 (dd, 1H, *J* = 8.8 Hz, *J* = 11.2 Hz), 3.85 (d, 1H, *J* = 2.8 Hz), 3.64 (s, 3H), 3.57 (dd, 1H, *J* = 2.8 Hz, 7.2 Hz), 3.55 (m, 3H).

^{13}C{1H} NMR (100 MHz, $CDCl_3$): δ 138.1, 137.6, 137.1, 128.4, 128.2 (2), 128.1 (2), 128.0, 127.8, 127.8, 127.6, 104.6, 83.6, 74.4, 73.9, 73.5, 72.8, 72.7, 68.4, 57.1, 33.0.

HRMS (ESI-TOF) *m/z*: [M+Na] calcd for $C_{28}H_{31}IO_5Na$ 597.1114, found 597.1111.



5α **6** **7**

(2*R*,3*S*,6*S*)-3,4-bis(benzyloxy)-2-((benzyloxy)methyl)-6-methoxy-3,6-dihydro-2*H*-pyran (6):

Compound **6** was synthesized from **5α** (500 mg, 0.87 mmol) by following **general procedure B.**

Yield: 349.74 mg, 90%, colorless gum, R_f: 0.5 (10% EtOAc/hexane), $[\alpha]_D^{25}$= -5.2 (c 0.9, $CHCl_3$).

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.26-7.37 (m, 15H), 5.16 (d, 1H, *J* = 3.5 Hz), 4.95 (d, 1H, *J* = 3.5 Hz), 4.08-4.82 (m, 3H), 4.58-4.62 (m, 2H), 4.53 (d, 1H, *J* = 12.0 Hz), 4.32 (dt, 1H, *J* = 2.5 Hz, 6.5 Hz), 3.81 (d, 1H, *J* = 2.0 Hz), 3.75-3.78 (m, 2H), 3.44 (m, 3H)

^{13}C{1H} NMR (100 MHz, $CDCl_3$): δ 156.3, 138.2, 138.1, 136.2, 128.5, 128.5, 128.3, 128.2, 128.1, 128.0, 127.6, 127.6, 127.5, 97.0, 96.5, 73.3, 73.0, 71.0, 69.9, 69.3, 69.2, 55.3.

HRMS (ESI-TOF) *m/z*: $[M+Na]^+$ calcd for $C_{28}H_{30}O_5Na$ 469.1985, found 469.1997.

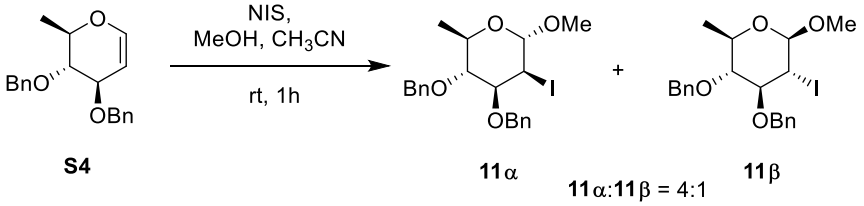
(2*R*,3*S*)-3-(benzyloxy)-2-((benzyloxy)methyl)-2,3-dihydro-4*H*-pyran-4-one (7): Compound **7** was synthesized from **6** (180 mg, 0.43 mmol) by following **general procedure C.** Yield: 88.0 mg, 68%, colorless oil, R_f: 0.4 (10% EtOAc/hexane), $[\alpha]_D^{25}$= -38.8 (c 0.4, $CHCl_3$).

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.28-7.38 (m, 11H), 5.44 (dd, 1H, *J* = 1.6 Hz, 6.0 Hz), 4.70 (d, 1H, *J* = 12.0 Hz), 4.56 (d, 1H, *J* = 12.0 Hz), 4.46-4.2 (m, 3H), 3.91 (dd, 1H, *J* = 7.2 Hz, 10.4 Hz), 3.75 (dd, 1H, *J* = 4.8 Hz, 10.0 Hz), 3.69 (dd, 1H, *J* = 1.6 Hz, 2.4 Hz).

^{13}C{1H} NMR (100 MHz, $CDCl_3$): δ 189.4, 162.7, 137.4, 137.0, 128.5, 128.4, 128.2, 128.0, 128.0, 127.8, 105.1, 80.6, 74.2, 73.6, 72.0, 67.6.

HRMS (ESI-TOF) *m/z*: $[M+H]^+$ calcd for $C_{20}H_{20}O_4H$ 325.1431, found 325.1431.

(2*S*,3*S*,6*R*)-3,4-bis(benzyloxy)-6-methoxy-2-methyl-3,6-dihydro-2*H*-pyran (9) and (2*S*,3*S*)-3-(benzyloxy)-2-methyl-2,3-dihydro-4*H*-pyran-4-one (10): Compounds **9** and **10** are the enantiomers of compounds **12** and **13**, respectively. Hence the spectroscopic data of **9** and **10** is same as reported for **12** and **13**. The NMR spectra of compounds **9** and **10** are provided in the supporting information.



Compound **11α and 11β** were synthesized from **S4**[25] (1.3 g, 4.19 mmol) by following **general procedure A.** Overall yield: 93%, 1.82 g.

(2*R*,3*R*,4*S*,5*S*,6*S*)-3,4-bis(benzyloxy)-5-iodo-6-methoxy-2-methyltetrahydro-2*H*-pyran (11*α*):

Yield: 74%, 1.45 g, colorless oil, R_f: 0.5 (5% EtOAc/hexane), $[\alpha]_D^{25}$= -6.87 (c 0.8, $CHCl_3$).

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.30-7.45 (m,10H), 5.06 (s, 1H), 4.96 (d, 1H, *J* = 11.0 Hz), 4.72 (d, 1H, *J* = 11.5 Hz), 4.65 (d, 1H, *J* = 11.0 Hz), 4.52-4.54 (m, 2H), 3.80-3.85 (m, 1H), 3.52 (t, 1H, *J* = 9.0 Hz), 3.35 (s, 3H), 3.27 (dd, 1H, *J* = 40 Hz, 8.5 Hz), 1.37 (d, 3H, *J* = 6.5 Hz).

^{13}C{1H} NMR (125 MHz, $CDCl_3$): δ 138.3, 137.7, 128.3, 128.2, 127.9, 127.8, 127.7, 127.6, 102.3, 81.4, 76.7, 75.3, 70.7, 68.0, 54.8, 33.9, 17.9.

HRMS (ESI-TOF) *m/z*: $[M+Na]^+$ calcd for $C_{21}H_{25}IO_4Na$ 491.0690, found 491.0692.

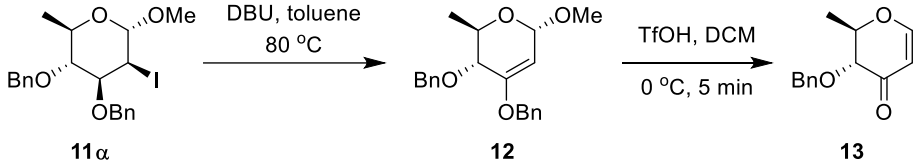
(2*R*,3*R*,4*S*,5*R*,6*R*)-3,4-bis(benzyloxy)-5-iodo-6-methoxy-2-methyltetrahydro-2*H*-pyran (11β):

Yield: 18.6%, 0.36 g, white solid, R_f: 0.4 (5% EtOAc/hexane).

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.29-7.43 (m, 10H), 4.97 (d, 1H, *J* = 10.0 Hz), 4.87 (s, 1H), 4.85 (s, 1H), 4.66 (d, 1H, *J* = 10.5 Hz), 4.45 (d, 1H, *J* = 9.0 Hz), 3.88 (dd, 1H, *J* = 9.0 Hz, 11.0 Hz), 3.69 (dd, 1H, *J* = 9.0 Hz, 11.0 Hz), 3.54 (s, 3H), 3.43-3.48 (m, 1H), 3.0 (t, 1H, *J* = 9.0 Hz), 1.33 (d, 3H, *J* = 6.0 Hz).

^{13}C{1H} NMR (100 MHz, $CDCl_3$): δ 137.7 (2), 128.5, 128.4, 128.2, 128.0, 127.9, 128.7, 103.9, 85.6, 85.1, 75.6, 75.3, 71.5, 57.3, 33.1, 17.6.

HRMS (ESI-TOF) *m/z*: $[M+Na]^+$ calcd for $C_{21}H_{25}IO_4Na$ 491.0690, found 491.0692.



(2*R*,3*R*,6*S*)-3,4-bis(benzyloxy)-6-methoxy-2-methyl-3,6-dihydro-2*H*-pyran (12): Compound **12** was synthesized from **11α** (500 mg, 1.06 mmol) by following **general procedure B.** Yield: 345 mg, 95%, colorless oil, R_f: 0.4 (5% EtOAc/hexane), $[\alpha]_D^{25}$= +74.5 (c 0.9, $CHCl_3$).

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.26-7.39 (m, 10H), 5.02 (d, 1H, *J* = 3.5 Hz), 4.90 (d, 1H, *J* = 5.5 Hz), 4.89 (t, 1H, *J* = 2.0 Hz), 4.86 (s, 1H), 4.78 (d, 1H, *J* = 11.0 Hz), 4.60 (d, 1H, *J* = 11.5 Hz), 4.10-4.15 (m, 1H), 3.83 (d, 1H, *J* = 8.0 Hz), 3.42 (s, 3H), 1.32 (d, 3 H, *J* = 6.0 Hz).

^{13}C{1H} NMR (125 MHz, $CDCl_3$): δ 157.8, 138.3, 136.4, 128.4, 128.2, 128.1, 127.9, 127.5 (2), 96.8, 95.9, 76.9, 73.7, 69.4, 66.0, 55.2, 18.3.

HRMS (ESI-TOF) *m/z*: $[M+Na]^+$ calcd for $C_{21}H_{24}O_4Na$ 363.1567, found 363.1566.

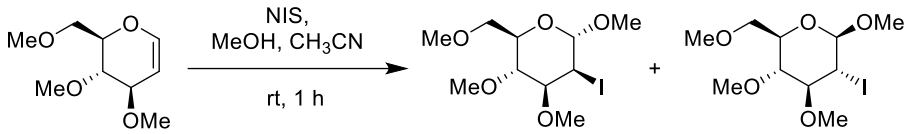
(2*R*,3*R*)-3-(benzyloxy)-2-methyl-2,3-dihydro-4*H*-pyran-4-one (13):

Compound **13** was synthesized from **12** (230 mg, 0.67 mmol) by following **general procedure C.** Yield: 117.92 mg, 80%, colorless oil, R_f: 0.5 (10% EtOAc/hexane), $[\alpha]_D^{25}$= -97.1 (c 0.4, $CHCl_3$).

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.30-7.39 (m, 5H), 7.25 (d, 1H, *J* = 6.0 Hz), 5.36 (d, 1H, *J* = 6.0 Hz), 5.02 (d, 1H, *J* = 11.5 Hz, 4.65 (d, 1H, *J* = 11.5 Hz), 4.44 – 4.50 (m, 1H), 3.71 (d, 1H, *J* = 9.5 Hz), 1.41 (d, 3H, *J* = 6.5 Hz).

^{13}C{1H} NMR (125 MHz, $CDCl_3$): δ 193.1, 162.2, 137.3, 128.4 (2), 128.0, 105.0, 78.6, 78.6, 73.9, 17.1.

HRMS (ESI-TOF) *m/z*: $[M+Na]^+$ calcd for $C_{13}H_{14}O_3Na$ 241.0835, found 241.0837



S5 **14α** **14α:14β= 7:3** **14β**

Compound **14*α* and14β** were synthesized from **S5**[26] (300 mg, 0.72 mmol) by following **general procedure A.** Overall yield: 90%, 372.44 mg.

(2*S*,3*S*,4*S*,5*R*,6*R*)-3-iodo-2,4,5-trimethoxy-6-(methoxymethyl)tetrahydro-2*H*-pyran (14*α*):

Yield: 63%, 260.70 mg, colorless oil. R_f: 0.5 (20% EtOAc/hexane), $[\alpha]_D^{25}$= +11.7 (c 0.9, $CHCl_3$).

^{1}H NMR (500 MHz, $CDCl_3$): δ 5.01 (s, 1H), 4.39 (dd, 1H, *J* = 1.5 Hz, 4.5 Hz), 3.60 (ddd, 1H, *J* = 2.0 Hz, 5.0 Hz, *J* = 9.5 Hz), 3.56 (dd, 1H, *J* = 5.0 Hz, 10.5 Hz), 3.52 (dd, 1H, *J* = 2.0 Hz, *J* = 10.0 Hz), 3.45 (s, 3H), 3.37 (s, 3H), 3.35 (d, 1H, *J* = 9.0 Hz), 3.33 (s, 3H), 3.29 (s, 3H), 2.81 (dd, 1H, *J* = 4.5 Hz, 9.0 Hz).

^{13}C{1H} NMR (125 MHz, $CDCl_3$): δ 102.3, 78.4, 77.5, 71.5, 71.3, 60.6, 59.2, 56.3, 54.9, 32.3.

HRMS (ESI-TOF) *m/z*: $[M+H]^+$ calcd for $C_{10}H_{19}IO_5H$ 347.0351, found 347.0350.

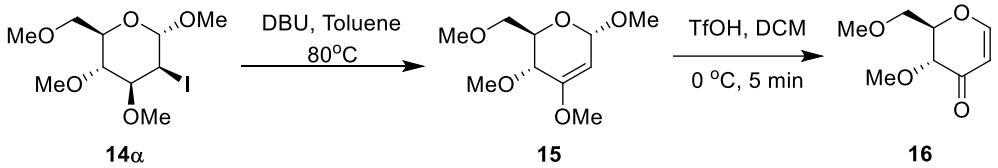
(2*R*,3*R*,4*S*,5*R*,6*R*)-3-iodo-2,4,5-trimethoxy-6-(methoxymethyl)tetrahydro-2*H*-pyran (14β):

Yield: 27 %, 111.73 mg, white solid, R_f: 0.5 (20% EtOAc/hexane), $[\alpha]_D^{25}$= +57.3 (c 0.9, $CHCl_3$), m.p. 108-109 ˚C

^{1}H NMR (500 MHz, $CDCl_3$): δ 4.34 (d, 1H, *J* = 9.5 Hz), 3.67 (dd, 1H, *J* = 9.0 Hz, *J* = 10.5 Hz), 3.62 (s, 3H), 3.59 (d, 1H, *J* = 2.0 Hz), 3.54 (dd, 1H, *J* = 4.5 Hz, 11.0 Hz), 3.49 (s, 3H), 3.47 (s, 3H), 3.36 (s, 3H), 3.26-3.30 (m, 2H), 3.16 (dd, 1H, *J* = 9.0 Hz, 10.0 Hz).

^{13}C{1H} NMR (100 MHz, $CDCl_3$): δ 103.9, 87.4, 81.0, 74.8, 70.7, 60.6, 60.2, 59.2, 57.1, 32.4.

HRMS (ESI-TOF) *m/z*: $[M+NH_4]^+$ calcd for $C_{10}H_{19}IO_5NH_4$ 364.0615, found 347.0641.



14α **15** **16**

(2*R*,3*R*,6*S*)-3,4,6-trimethoxy-2-(methoxymethyl)-3,6-dihydro-2*H*-pyran (15):

Compound **15** was synthesized from **14α** (700 mg, 2.02 mmol) by following **general procedure B.** Yield: 406 mg, 92%, R_f: 0.4 (20% EtOAc/hexane), $[\alpha]_D^{25}$= +148.4 (c 0.8, $CHCl_3$).

^{1}H NMR (500 MHz, $CDCl_3$): δ 5.01 (d, 1H, *J* = 3.5 Hz), 4.71 (d, 1H, *J* = 3.0 Hz), 3.95 (dt, 1H, *J* = 3.5 Hz, 9.5 Hz), 3.88 (d, 1H, *J* = 9.5 Hz), 3.59 (d, 2H, *J* = 3.0 Hz), 3.55 (s, 3H), 3.45 (s, 3H), 3.40 (s, 3H), 3.37 (s, 3H).

^{13}C{1H} NMR (125 MHz, $CDCl_3$): δ 158.4, 96.9, 94.8, 72.5, 71.6, 68.9, 59.2, 59.0, 55.3, 54.6.

HRMS (ESI-TOF) *m/z*: $[M+Na]^+$ calcd for $C_{10}H_{18}O_5Na$ 241.1044, found 241.1046.

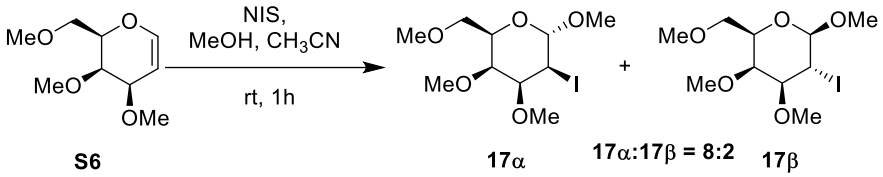
(2*R*,3*R*)-3-methoxy-2-(methoxymethyl)-2,3-dihydro-4*H*-pyran-4-one (16):

Compound **16** was synthesized from **15** (240 mg, 1.10 mmol) by following **general procedure C.** Yield: 120.44 mg, 70%, colorless oil. R_f: 0.4 (20% EtOAc/hexane).

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.29 (, d, 1H, *J* = 5.5 Hz), 5.35 (d, 1H, *J* = 6.0 Hz), 4.34 (dt, 1H, *J* = 3.0 Hz, 11.5 Hz), 3.94 (d, 1H, *J* = 11.5 Hz), 3.74 (d, 2H, *J* = 3.5 Hz), 3.63 (s, 3H), 3.45 (s, 3H).

^{13}C{1H} NMR (125 MHz, $CDCl_3$): δ 193.3, 162.1, 105.1, 81.0, 76.4, 70.4, 60.6, 59.5.

HRMS (ESI-TOF) *m/z*: $[M+H]^+$ calcd for $C_8H_{12}O_4H$ 173.0809, found 173.0808.



S6 **17α** **17α:17β = 8:2** **17β**

Compound **17*α* and 17β** were synthesized from **S6**[26] (300 mg, 1.59 mmol) by following **general procedure A.** Overall yield: 98%, 540.80 mg.

(2*S*,3*S*,4*S*,5*S*,6*R*)-3-iodo-2,4,5-trimethoxy-6-(methoxymethyl)tetrahydro-2*H*-pyran (17*α*):

Yield: 78.4%, 432.64 mg, colorless oil, R_f: 0.5 (20% EtOAc/hexane).

^{1}H NMR (500 MHz, $CDCl_3$): δ 5.15 (s, 1H), 4.20 (d, 1H, *J* = 4.0 Hz), 3.92 (t, 1H, *J* = 6.0 Hz), 3.63 (s, 1H), 3.55-3.61 (m, 2H), 3.48 (s, 3H), 3.37 (s, 3H), 3.35 (s, 3H), 3.32 (s, 3H), 3.16-3.17 (t, 1H, *J* = 3.5 Hz).

^{13}C{1H} NMR (125 MHz, $CDCl_3$): δ. 103.3, 75.4, 75.2, 71.4, 69.9, 60.0, 59.1, 56.4, 55.1, 23.6.

HRMS (ESI-TOF) *m/z*: $[M+Na]^+$ calcd for $C_{10}H_{19}IO_5Na$ 369.0169, found 369.0166.

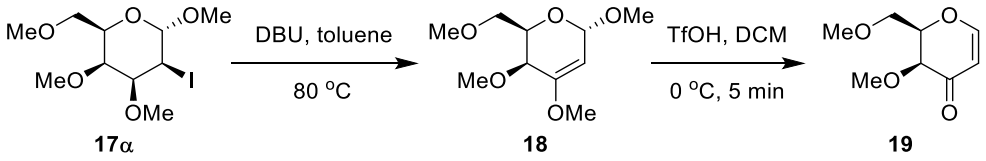
(2*R*,3*R*,4*S*,5*S*,6*R*)-3-iodo-2,4,5-trimethoxy-6-(methoxymethyl)tetrahydro-2*H*-pyran (17β):

Yield: 19.6%, 108.60 mg, white solid, R_f: 0.4 (20% EtOAc/hexane).

^{1}H NMR (500 MHz, $CDCl_3$): δ 4.43 (d, 1H, *J* = 9.0 Hz), 4.07 (dd, 1H, *J* = 9.0 Hz, 11.0 Hz), 3.62 (dd, 1H, *J* = 9.0 Hz, 10.5 Hz), 3.58 (d, 1H, *J* = 2.5 Hz), 3.55-3.56 (m, 4H), 3.53 (d, 1H, J 5.5 Hz), 3.51 (s, 3H), 3.49 (s, 3H), 3.39 (s, 3H), 3.23 (dd, 1H, *J* = 2.5 Hz, 11.0 Hz).

^{13}C{1H} NMR (100 MHz, $CDCl_3$): δ. 104.4, 85.4, 74.3, 73.6, 70.5, 61.2, 59.2, 57.9, 56.9, 32.4.

HRMS (ESI-TOF) *m/z*: $[M+NH_4]$ calcd for $C_{10}H_{19}IO_5NH_4$ 364.0621, found 364.0627.



17α **18** **19**

(2*R*,3*S*,6*S*)-3,4,6-trimethoxy-2-(methoxymethyl)-3,6-dihydro-2*H*-pyran (18):

Compound **18** was synthesized from **17*α*** (350 mg, 1.01 mmol) by following **general procedure B.** Yield: 214.0 mg, 97%, colorless oil, R_f: 0.4 (20% EtOAc/hexane).

^{1}H NMR (500 MHz, $CDCl_3$): δ 5.09 (d, 1H, *J* = 2.5 Hz), 4.81 (d, 1H, *J* = 2.5 Hz), 4.17-4.10 (m, 1H), 3.64 (dd, 1H, *J* = 6.0 Hz, 10.0 Hz), 3.60 (dd, 1H, *J* = 6.5 Hz, 10.0 Hz), 3.58 (s, 3H), 3.46 (d, 1H, *J* = 2.5 Hz), 3.45 (s, 3H), 3.40 (s, 3H), 3.40 (s, 3H).

^{13}C{1H} NMR (125 MHz, $CDCl_3$): δ. 156.6, 96.5, 96.0, 72.7, 71.4, 69.7, 59.2, 58.8, 55.2, 54.4.

HRMS (ESI-TOF) *m/z*: $[M+Na]^+$ calcd for $C_{10}H_{18}O_5Na$ 241.1046, found 241.1047

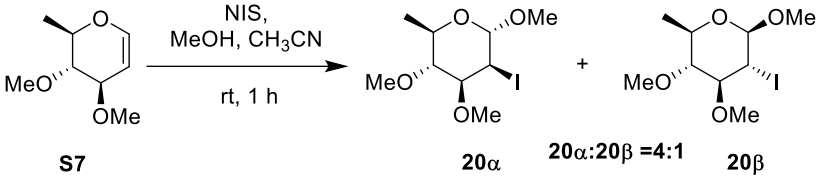
(2*R*,3S)-3-methoxy-2-(methoxymethyl)-2,3-dihydro-4*H*-pyran-4-one (19):

Compound **19** was synthesized from **18** (200 mg, 0.91 mmol) by following **general procedure C.** Yield: 107.29 mg, 68.0%, colorless oil, R_f: 0.3 (20% EtOAc/hexane), $[\alpha]_D^{25}$= +74.6 (c 0.5, $CHCl_3$).

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.34 (d, 1H, *J* = 6.0 Hz), 5.38 (dd, 1H, *J* = 1.5 Hz, 6.0 Hz), 4.43-4.46 (m, 1H), 3.81 (dd, 1H, *J* = 7.5 Hz, 10.5 Hz), 3.70 (dd, 1H, *J* = 5.0 Hz, 10.5 Hz), 3.44 (dd, 1H, *J* = 1.5 Hz, 2.5 Hz), 3.41 (s, 3H), 3.39 (s, 3H).

^{13}C{1H} NMR (125 MHz, $CDCl_3$): δ. 189.1, 162.5, 104.9, 80.3, 77.1, 70.0, 59.3, 58.4.

HRMS (ESI-TOF) *m/z*: $[M+Na]^+$ calcd for $C_8H_{12}O_4Na$ 195.0628, found 195.0629.



S7 **20α** **20β**

Compound **20*α*** and **20β** were synthesized from **S7**[26] (130 mg, 0.82 mmol) by following **general procedure A.** Overall yield: 89%, 231mg.

(2*S*,3*S*,4*S*,5*R*,6*R*)-3-iodo-2,4,5-trimethoxy-6-methyltetrahydro-2*H*-pyran (20*α*):

Yield: 71.2%, 184.80 mg, colorless oil, R_f: 0.5 (5% EtOAc/hexane).

^{1}H NMR (500 MHz, $CDCl_3$): δ 4.99 (s, 1H), 4.45 (dd, 1H, *J* = 1.0 Hz, 4.0 Hz), 3.62-3.67 (m, 1H), 3.53 (s, 3H), 3.37 (s, 3H), 3.32 (s, 3H), 3.07 (t, 1H, *J* = 9.0 Hz), 2.81 (dd, 1H, *J* = 4.0 Hz, 8.5 Hz), 1.30 (d, 3H, *J* = 6.0 Hz).

^{13}C{1H} NMR (125 MHz, $CDCl_3$): δ. 102.3, 83.5, 78.4, 68.1, 61.0, 56.4, 54.9, 33.3, 17.8.

HRMS (ESI-TOF) *m/z*: $[M+H]^+$ calcd for $C_9H_{17}IO_4H$ 317.0244, found 317.0241.

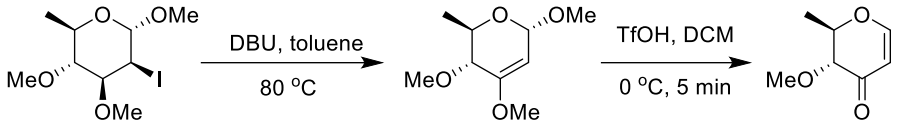
(2*R*,3*R*,4*S*,5*R*,6*R*)-3-iodo-2,4,5-trimethoxy-6-methyltetrahydro-2*H*-pyran (20β):

Yield: 17.8%, 46.20 mg, white solid, R_f: 0.4 (5% EtOAc/hexane),), $[\alpha]_D^{25}$= +33.9 (c 0.5, $CHCl_3$), m.p. 109-110 ˚C.

^{1}H NMR (500 MHz, $CDCl_3$): δ 4.37 (d, 1H, *J* = 9.0 Hz), 3.71 (dd, 1H, *J* = 9.0 Hz, 11.) Hz), 3.66 (s, 3H), 3.56 (s, 3H), 3.51 (s, 3H), 3.30-3.33 (m, 1H), 3.28 (dd, 1H, *J* = 8.5 Hz, 11.0 Hz), 2.80 (dd, 1H, *J* = 8.5 Hz, 9.5 Hz), 1.32 (d, 1H, *J* = 6.5 Hz).

^{13}C{1H} NMR (125 MHz, $CDCl_3$): δ. 103.8, 87.4, 87.1, 71.4, 60.8, 60.8, 57.3, 32.9, 17.4.

HRMS (ESI-TOF) *m/z*: [M+Na] calcd for $C_9H_{17}IO_4Na$ 339.0069, found 339.0065.



20α **21** **22**

(2*R*,3*R*,6*S*)-3,4,6-trimethoxy-2-methyl-3,6-dihydro-2*H*-pyran (21):

Compound **21** was synthesized from **20*α*** (70 mg, 0.22 mmol) by following **general procedure B.** Yield: 34.90 mg, 84%, colorless oil, R_f: 0.4 (5% EtOAc/hexane).

^{1}H NMR (500 MHz, $CDCl_3$): δ 4.94 (d, 1H, 3.5 Hz), 4.70 (d, 1H, *J* = 3.0 Hz), 3.93-3.98 (m, 1H), 3.55 (s, 3H), 3.47 (d, 1H, *J* = 9.0 Hz), 3.44 (s, 3H), 3.36 (s, 3H), 1.27 (d, 3H, *J* = 6.5 Hz).

^{13}C{1H} NMR (125 MHz, $CDCl_3$): δ.158.3, 96.7 , 94.9, 78.5, 65.5, 58.8, 55.1, 54.5, 18.1.

HRMS (ESI-TOF) *m/z*: $[M+Na]^+$ calcd for $C_9H_{16}O_4Na$ 211.0941, found 211.0940.

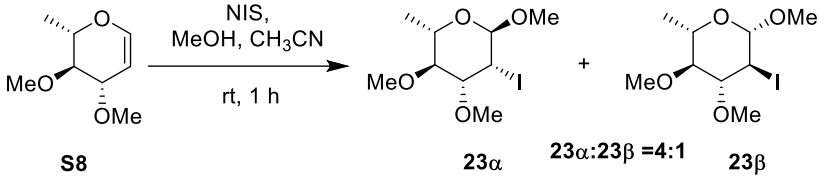
(2*R*,3*R*)-3-methoxy-2-methyl-2,3-dihydro-4*H*-pyran-4-one (22):

Compound **22** was synthesized from **21** (30 mg, 0.15 mmol) by following **general procedure C.** Yield: 18.30 mg, 81%, colorless oil, R_f: 0.5 (10% EtOAc/hexane).

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.26 (d, 1H, *J* = 6.0 Hz), 5.35 (d, 1H, *J* = 6.0 Hz), 4.43-4.49 (m, 1H), 3.60 (s, 3H), 3.50 (d, 1H, *J* = 9.5 Hz), 1.46 (d, 3H, *J* = 6.5 Hz).

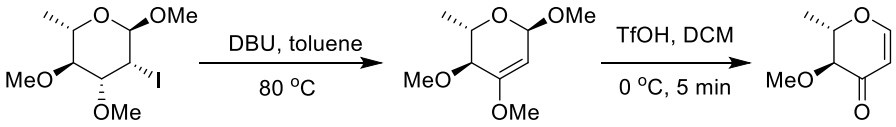
^{13}C{1H} NMR (125 MHz, $CDCl_3$): δ:192.6, 162.1, 104.8, 81.5, 78.6, 60.1, 17.0.

HRMS (ESI-TOF) *m/z*: $[M+Na]^+$ calcd for $C_7H_{10}O_3Na$ 165.0522, found. 165.0519.



S8 23α 23β

(2*R*,3*R*,4*R*,5*S*,6*S*)-3-iodo-2,4,5-trimethoxy-6-methyltetrahydro-2*H*-pyran (23α) and (2*S*,3*S*,4*R*,5*S*,6*S*)-3-iodo-2,4,5-trimethoxy-6-methyltetrahydro-2*H*-pyran (23β): Compounds **23α** and **23β** were synthesized from compound **S8**[26] and are the enantiomers of compounds **20α** and **20β**, respectively. Hence the spectroscopic data of **23α** and **23β** is same as reported for **20α** and **20β**. The NMR spectra of compounds **23α** and **23β** are provided in the supporting information.



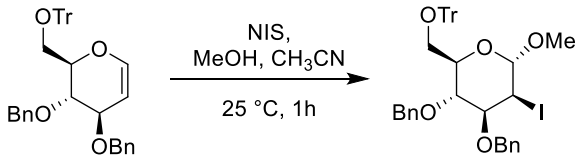
23α 24 25

(2*S*,3*S*,6*R*)-3,4,6-trimethoxy-2-methyl-3,6-dihydro-2*H*-pyran (24):

Compound **24** was synthesized from **23α** (80 mg, 0.25 mmol) by following **general procedure B.** Yield: 37 mg, 78%, colorless oil, R_f: 0.4 (5% EtOAc/hexane). Compound **24** is an enantiomer of compound **21**, hence all the spectral data are same as reported for **21** (The NMR spectra of **24** is provided in the supporting information).

(2*S*,3*S*)-3-methoxy-2-methyl-2,3-dihydro-4*H*-pyran-4-one (25):

Compound **25** was synthesized from **24** (35 mg, 0.17 mmol) by following **general procedure C.** Yield: 17.6 mg, 67%, colorless oil, R_f: 0.5 (10% EtOAc/hexane). Compound **25** is an enantiomer of compound **22**, hence all the spectral data are same as reported for **22** (The NMR spectra of **25** is provided in the supporting information).



S9 26α

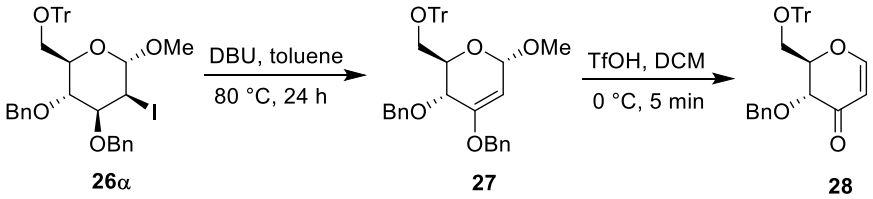
Compound **26α** was synthesized from **S9**[27] (1 g, 1.75 mmol) by following **general procedure A.** Yield 99 % 1.26 gm, white solid, R_f: 0.5 (10% EtOAc/hexane), $[\alpha]_D^{25}$= -3.6 (c 0.5, $CHCl_3$).

(2*R*,3*R*,4*S*,5*S*,6*S*)-3,4-bis(benzyloxy)-5-iodo-6-methoxy-2-((trityloxy)methyl)tetrahydro-2*H*-pyran (26α):

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.20-7.58 (m, 23H), 6.89-6.90 (m, 2H), 5.21 (s, 1H), 4.73 (d, 1H, *J* = 10.0 Hz), 4.71 (d, 1H, *J* = 11.0 Hz), 4.55 (dd, 1H, *J* = 1.0 Hz, 4.0 Hz), 4.54 (d, 1H, *J* = 11.5 Hz), 4.26 (d, 1H, *J* = 10.5 Hz), 4.06 (t, 1H, *J* = 9.5 Hz), 3.82-3.85 (m, 1H), 3.54 (dd, 1H, *J* = 2.0 Hz, 10.0 Hz), 3.39 (s, 3H), 3.30 (dd, 1H, *J* = 4.0 Hz, 8.5 Hz), 3.27 (dd, 1H, *J* = 4.0 Hz, 10.0 Hz).

^{13}C{1H} NMR (100 MHz, $CDCl_3$): δ.144.1, 138.0, 137.8, 128.8, 128.4 , 128.1, 128.0, 127.8, 127.5, 126.8, 102.3, 86.3, 77.0, 76.0, 75.1, 71.9, 71.0, 62.4, 54.9, 33.6.

HRMS (ESI-TOF) *m/z*: [M+K] calcd for $C_{40}H_{39}IO_5K$ 765.1479, found 765.1464.



(2*R*,3*R*,6*S*)-3,4-bis(benzyloxy)-6-methoxy-2-((trityloxy)methyl)-3,6-dihydro-2*H*-pyran (27): Compound **27** was synthesized from **26α** (600 mg, 0.82 mmol) by following **general procedure B.** Yield: 484.4 mg, 98%, white solid, R_f: 0.3 (10% EtOAc/hexane), $[\alpha]_D^{25}$= +55.4 (c 0.5, $CHCl_3$).

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.48-7.50 (m, 6H), 7.12-7.35 (m, 17H), 6.94-6.95 (m, 2H), 5.13 (d, 1H, *J* = 3.5 Hz), 4.90 (d, 1H, *J* = 3.5 Hz), 4.85 (d, 1H, *J* = 11.0 Hz), 4.76 (1H, *J* = 11.5 Hz), 4.1 (d, 1H, *J* = 10.5 Hz), 4.31 (d, 1H, *J* = 10.5 Hz), 4.15-4.21 (m, 2H), 3.49 (s, 3H), 3.45 (dd, 1H, *J* = 2.0 Hz, 10.0 Hz), 319 (dd, 1H, *J* = 5.0 Hz, 10.0 Hz).

^{13}C{1H} NMR (100 MHz, $CDCl_3$): δ.158.0, 144.1, 138.0, 136.4, 128.8, 128.5, 128.2, 128.1, 128.0, 127.7, 127.6, 127.4, 126.9, 96.7, 96.0, 86.4, 74.0, 71.5, 70.0, 69.4, 63.3, 55.2.

HRMS (ESI-TOF) *m/z*: [M+Na] calcd for $C_{40}H_{38}O_5Na$ 621.2617, found 621.2611

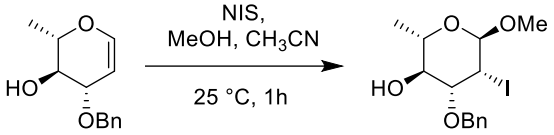
(2*R*,3*R*)-3-(benzyloxy)-2-((trityloxy)methyl)-2,3-dihydro-4*H*-pyran-4-one (28):

Compound **28** was synthesized from **27** (300 mg, 0.50 mmol) by following **general procedure C.** Yield: 212 mg, 89%, colorless oil, R_f: 0.6 (20% EtOAc/hexane), $[\alpha]_D^{25}$ = +105.7 (c 0.4, $CHCl_3$).

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.43-7.45 (m, 5H), 7.38 (d, 1H, *J* = 6.0 Hz), 7.24-730 (m, 13H), 7.12-7.14 (m, 2H), 5.41 (d, 1H, *J* = 6.0 Hz), 4.97 (d, 1H, *J* = 11.0 Hz), 4.49 (d, 1H, *J* = 11.0 Hz), 4.41-4.45 (m, 1H), 4.32 (d, 1H, *J* = 11.5 Hz), 3.62 (dd, 1H, *J* = 2.5 Hz, 10.5 Hz), 3.36 (dd, 1H, *J* = 4.0 Hz, 11.0 Hz).

^{13}C{1H} NMR (100 MHz, $CDCl_3$): δ.193.2, 162.4, 143.5, 137.3 , 128.7, 128.2, 128.2, 127.9, 127.8, 127.7, 127.2, 105.1, 86.9, 81.3, 74.5, 74.4, 61.9.

HRMS (ESI-TOF) *m/z*: [M+NH_4] calcd for $C_{32}H_{28}O_4$ NH_4 494.2331, found 494.2326.



S10α

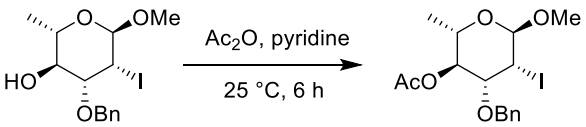
(2*S*,3*S*,4*R*,5*R*,6*R*)-4-(benzyloxy)-5-iodo-6-methoxy-2-methyltetrahydro-2*H*-pyran-3-ol (S10*α*):

Compound **S10*α*** was synthesised from 3-*O*-benzyl *L*-rhamnal[28] (500 mg, 2.26 mmol) by following **general procedure A.** Yield: 85%, 725 mg, colorless oil, R_f: 0.5 (20% EtOAc/hexane). $[\alpha]_D^{25}$ = 31.0 (c 0.8, $CHCl_3$).

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.31-7.41 (m, 5H), 5.05 (s, 1H), 4.66 (d, 1H, *J* = 11.0 Hz), 4.49 (dd, 1H, *J* = 1.0 Hz, 4.0 Hz), 3.73-3.79 (m, 1H), 3.60 (t, 1H, *J* = 9.0 Hz), 3.09 (s, 3H), 3.00-3.02 (m, 1H), 2.36 (bs, 1H), 1.33 (d, 3H, *J* = 6.0 Hz).

^{13}C**{1H} NMR (125 MHz, $CDCl_3$):** δ 137.2, 128.5, 128.2, 128.1, 102.6, 76.2, 73.4, 70.4, 68.4, 54.9, 32.1, 17.7.

HRMS (ESI-TOF) *m/z*: $[M+Na]^+$ calcd for $C_{14}H_{19}IO_4Na$ 401.0226, found 401.0226.



S10α **29α**

To a stirred solution of **S10*α*** (500 mg, 1.32 mmol) in pyridine (10 mL) was added Ac_2O (3 Equiv) at room temperature and stirred for 6 hr. After completion of the reaction, reaction mixture was

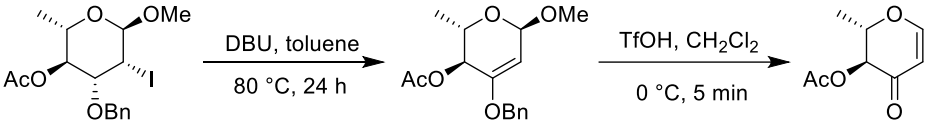
concentrated under reduced pressure. The crude product was purified by column chromatography to obtain the product **29** as colorless oil, R_f: 0.5 (20% EtOAc/hexane), yield: 90%, 500 mg.

(2*S*,3*S*,4*R*,5*R*,6*R*)-4-(benzyloxy)-5-iodo-6-methoxy-2-methyltetrahydro-2*H*-pyran-3-yl acetate (29α):

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.27-7.35 (m, 5H), 5.06 (t, 1H, *J* = 9.0 Hz), 5.03 (s, 1H), 4.64 (d, 1H, *J* = 12.5 Hz), 4.44 (dd, 1H, *J* = 1.5 Hz, 4.0 Hz), 4.39 (d, 1H, *J* = 12.0 Hz), 3.77-3.83 (m, 1H), 3.33 (s, 3H), 3.16 (dd, 1H, *J* = 4.5 Hz, 9.0 Hz), 2.02 (s, 3H), 1.21 (d, 3H, *J* = 6.5 Hz).

^{13}C{1H} NMR (100 MHz, $CDCl_3$): δ 169.7, 137.5, 128.3, 127.6, 127.5, 102.3, 74.0, 73.8, 70.6, 66.9, 55.1, 32.4, 20.8, 17.5.

HRMS (ESI-TOF) *m/z*: [M+Na] calcd for $C_{16}H_{21}IO_5$ Na 443.0331, found 443.0320.



29α **30** **31**

(2*S*,3*S*,6*R*)-4-(benzyloxy)-6-methoxy-2-methyl-3,6-dihydro-2*H*-pyran-3-yl acetate (30): Compound **30** was synthesized from **29*α*** (200 mg, 0.47 mmol) by following **general procedure B.** Yield: 127 mg, 92%, colorless oil, R_f: 0.5(20% EtOAc/hexane).

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.26-7.34 (m, 5H), 5.34 (d, 1H, *J* = 9.0 Hz), 5.03 (d, 1H, *J* = 3.5 Hz), 4.87 (dd, 1H, *J* = 1.0 Hz, 3.0 Hz), 4.77 (d, 1H, *J* = 12.0 Hz), 4.73 (d, 1H, *J* = 12.0 Hz), 4.10-4.16 (m, 1H), 3.41 (s, 3H), 2.05 (s, 3H), 1.25 (d, 3H, *J* = 6.5 Hz).

^{13}C{1H} NMR (100 MHz, $CDCl_3$): δ 170.4, 154.2, 136.1, 128.3, 127.6, 126.7, 96.5(2), 69.4, 69.0, 65.2, 55.2, 20.7, 17.7.

HRMS (ESI-TOF) *m/z*: [M+Na] calcd for $C_{16}H_{20}O_5$ Na 315.1208, found 315.1201.

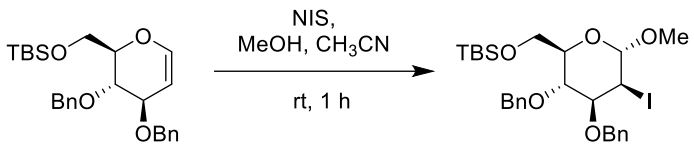
(2*S*,3*S*)-2-methyl-4-oxo-3,4-dihydro-2*H*-pyran-3-yl acetate (31):

Compound **31** was synthesized from **30** (100 mg, 0.34 mmol) by following **general procedure C.** Yield: 42.48 mg, 73%, colorless oil, R_f: 0.4 (20% EtOAc/hexane), $[\alpha]_D^{25}$= +256.2 (c 0.4, $CHCl_3$), m.p. 64-65 ˚C.

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.30 (d, 1H, *J* = 6.0 Hz), 5.40 (d, 1H, *J* = 6.0 Hz), 5.21 (d, 1H, *J* = 12.5 Hz), 4.44-4.50 (m, 1H), 2.16 (s, 3H), 1.42 (d, 3H, *J* = 6.0 Hz).

^{13}C{1H} NMR (125 MHz, $CDCl_3$): δ. 188.3, 169.4, 162.9, 105.1, 77.2, 73.1, 20.4, 17.4.

HRMS (ESI-TOF) *m/z*: [M+Na] calcd for $C_8H_{10}O_4$ Na 193.0477, found 193.0475.



S11 **32α**

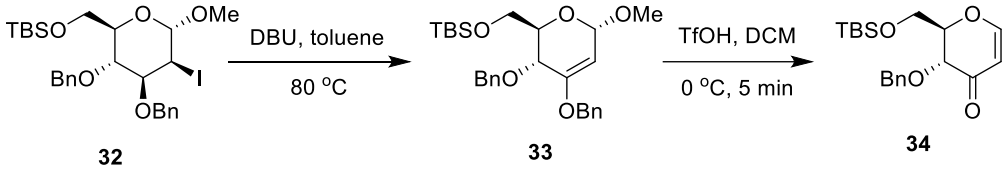
Compound ***32α*** was synthesized from **S11**[29] (500 mg, 1.13 mmol) by following **general procedure A.** Overall yield: 96%, 671.0 mg. colorless oil, R_f: 0.5 (5% EtOAc/hexane).

(((2*R*,3*R*,4*S*,5*S*,6*S*)-3,4-bis(benzyloxy)-5-iodo-6-methoxytetrahydro-2*H*-pyran-2-yl)methoxy)(*tert*-butyl)dimethylsilane (32*α*):

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.30-7.42 (m, 10H), 5.08 (s, 1H), 4.91 (d, 1H, *J* = 10.8 Hz), 4.69 (d, 1H, *J* = 11.6 Hz), 4.62 (d, 1H, *J* = 10.8 Hz), 4.51 (d, 1H, *J* = 11.6 Hz), 4.48 (dd, 1H, *J* = 1.2 Hz, 4.0 Hz), 3.86-3.90 (m, 2H), 3.82 (dd, 1H, *J* = 2.0 Hz, 11.2 Hz), 3.66 (ddd, 1H, *J* = 2.0 Hz, 4.4 Hz, 10.0 Hz), 3.32 (s, 3H), 3.30 (dd, 1H, *J* = 4.4 Hz, 8.8 Hz), 0.93 (s, 9H), 0.12 (s, 3H), 0.08 (s, 3H).

^{13}C{1H} NMR (100 MHz, $CDCl_3$): δ. 138.5, 137.8, 128.4, 128.3, 127.9 (2), 127.7, 127.6, 102.3, 77.0, 75.7, 75.2, 73.1, 71.0, 62.2, 54.7, 33.3, 25.9, 18.3, -5.1, -5.4.

HRMS (ESI-TOF) *m/z*: $[M+Na]^+$ calcd for $C_{27}H_{39}IO_5SiNa$ 621.1502, found 621.1502.



32 **33** **34**

(((2*R*,3*R*,6*S*)-3,4-bis(benzyloxy)-6-methoxy-3,6-dihydro-2*H*-pyran-2-yl)methoxy)(*tert*-butyl)dimethylsilane (33):

Compound **33** was synthesized from **32** (250 mg, 0.41 mmol) by following **general procedure B.** Yield: 171.0 mg, 87% colorless gum, R_f: 0.5 (10% EtOAc/hexane), $[\alpha]_D^{25}$= +49.2 (c 0.4, $CHCl_3$).

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.26-7.37 (m, 10H), 5.06 (d, 1H, *J* = 3.6 Hz), 4.85-4.91 (m, 3H), 4.76 (d, 1H, *J* = 11.6 Hz), 4.57 (d, 1H, *J* = 10.8 Hz), 4.13 (d, 1H, *J* = 9.6 Hz), 4.03 (ddd, 1H, *J* =

2.0 Hz, 5.2 Hz, 9.2 Hz), 3.85 (dd, 1H, *J* = 2.0 Hz, 11.2 Hz), 3.79 (dd, 1H, *J* = 5.2 Hz, 11.6 Hz), 3.42 (s, 3H), 0.91 (s, 9H), 0.08 (s, 6H).

^{13}C{1H} NMR (100 MHz, $CDCl_3$): δ.157.9, 138.3, 136.4, 128.4, 128.2, 128.0, 127.9, 127.6, 127.5, 96.6, 96.0, 73.6, 71.1, 71.0, 69.4, 62.9, 55.2, 25.9, 18.4, -5.2, -5.3.

HRMS (ESI-TOF) *m/z*: $[M+Na]^+$ calcd for $C_{27}H_{38}O_5SiNa$ 493.2386, found 493.2385.

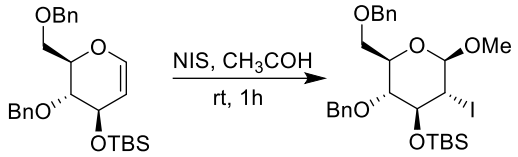
(2*R*,3*R*)-3-(benzyloxy)-2-(((*tert*-butyldimethylsilyl)oxy)methyl)-2,3-dihydro-4*H*-pyran-4-one (34):

Compound **34** was synthesized from **33** (100 mg, 0.21 mmol) by following **general procedure C.** Yield: 50.3 mg, 68%, colorless oil, R_f: 0.4 (10% EtOAc/hexane), $[\alpha]_D^{25}$= +187.3 (c 0.7, $CHCl_3$).

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.29-7.41 (m, 6H), 5.35 (d, 1H, *J* = 5.5 Hz), 5.07 (d, 1H, *J* = 11.0 Hz), 4.63 (d, 1H, *J* = 11.0 Hz), 4.32 (dt, 1H, *J* = 3.0 Hz, 11.0 Hz), 4.23 (d, 1H, *J* = 11.0 Hz), 3.95 (m, 2H), 0.90 (s, 9H), 0.08 (s, 3H), 0.07 (s, 3H).

^{13}C{1H} NMR (125 MHz, $CDCl_3$): δ. 193.6, 162.2, 137.6, 128.4, 128.2, 127.9, 104.9, 82.4, 74.6, 74.2, 61.4, 25.8, 18.3, -5.3, -5.4.

HRMS (ESI-TOF) *m/z*: $[M+Na]^+$ calcd for $C_{19}H_{28}O_4SiNa$ 371.1649, found 371.1640.



36

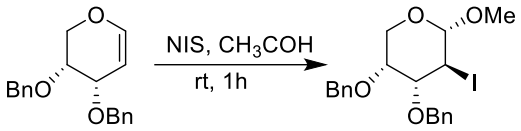
(((2*R*,3*R*,4*S*,5*R*,6*R*)-3-(benzyloxy)-2-((benzyloxy)methyl)-5-iodo-6-methoxytetrahydro-2*H*-pyran-4-yl)oxy)(*tert*-butyl)dimethylsilane (36):

Compound **36** was synthesized from (((2*R*,3*R*,4*R*)-3-(benzyloxy)-2-((benzyloxy)methyl)-3,4-dihydro-2*H*-pyran-4-yl)oxy)(*tert*-butyl)dimethylsilane[13] (300 mg, 0.68 mmol) by following **general procedure A.** Overall yield: 84 %, 342.0 mg. R_f: 0.5 (5% EtOAc/hexane).

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.24-7.37 (m, 10H), 5.08 (s, 1H), 4.82 (d, 1H, *J* = 11.0 Hz), 4.68 (d, 1H, *J* = 12.0 Hz), 4.86-4.54 (m, 2H), 4.27 (dd, 1H, *J* = 1.5 Hz, J= 4.5 Hz), 3.77-3.83 (m, 2H), 3.71-3.75 (m, 2H), 3.67 (dd, 1H, *J* = 1.5 Hz, 10.5 Hz), 3.35 (s, 3H), 0.96 (s, 9H), 0.12 (s, 3H), 0.09 (s, 3H).

^{13}C{1H} NMR (125 MHz, $CDCl_3$): δ138.5, 138.3, 128.3(2), 127.7, 127.6, 127.5, 127.41, 102.5, 77.6, 75.0, 73.4, 72.3, 70.2, 69.1, 55.0, 38.3, 26.0, 18.0, -4.4, -4.5.

HRMS (ESI-TOF) *m/z*: $[M+Na]^+$ calcd for $C_{27}H_{39}IO_5SiNa$ 621.1502, found 621.1505.



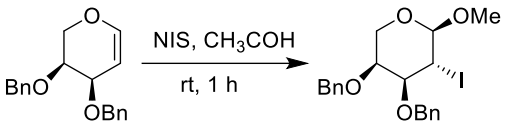
37

(2*S*,3*S*,4*R*,5*R*)-4,5-bis(benzyloxy)-3-iodo-2-methoxytetrahydro-2*H*-pyran (37): Compound **37** was synthesized from (3*R*,4*S*)-3,4-bis(benzyloxy)-3,4-dihydro-2*H*-pyran[26] (500 mg, 1.68 mmol) by following **general procedure A.** Overall yield: 90%, 689.9 mg. R_f: 0.2 (10% EtOAc/hexane), m.p. 77-78 ˚C.

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.26-7.42 (m, 10H), 4.73 (d, 1H, *J* = 12.5 Hz), 4.55-4.64 (m, 3H), 4.44 (d, 1H, *J* = 8.5), 4.32 (dd, 1H, *J* = 8.5 Hz, *J* = 10.5 Hz), 4.12 (dd, 1H, *J* = 2.5 Hz, *J* = 12.5 Hz), 3.62-3.63 (m, 1H), 3.52-3.55 (m, 4H), 3.36 (dd, 1H, *J* = 12.5 Hz).

^{13}C{1H} NMR (125 MHz, $CDCl_3$): δ 137.8, 137.2, 128.3, 128.3 , 128.1, 127.9, 127.9, 127.7, 104.8, 81.5, 71.9, 71.7, 71.1, 63.6, 56.9, 32.4.

HRMS (ESI-TOF) *m/z*: [M+Na] calcd for $C_{20}H_{23}I\,O_4Na$ 477.0539, found 477.0530



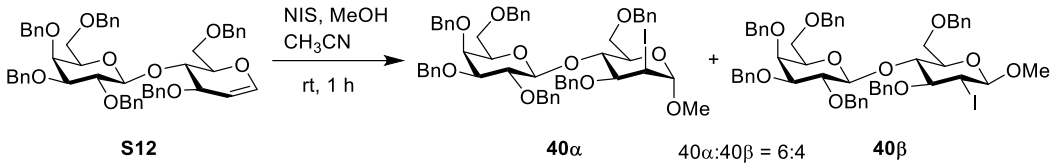
38

(2*R*,3*R*,4*S*,5*S*)-4,5-bis(benzyloxy)-3-iodo-2-methoxytetrahydro-2*H*-pyran (38): Compound **38** was synthesized from **(3*S*,4*R*)-3,4-bis(benzyloxy)-3,4-dihydro-2*H*-pyran[26]** (300 mg, 1.05 mmol) by following **general procedure A.** Overall yield: 95%, 456.81 mg. R_f: 0.3 (10% EtOAc/hexane), m.p. 84-85 ˚C.

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.26-7.41(m, 10H), 4.72 (d, 1H, *J* = 12.5 Hz), 4.54-4.63 (m, 3H), 4.43(d, 1H, *J* = 8.5), 4.31 (dd, 1H, *J* = 8.5 Hz, *J* = 10.5 Hz), 4.14 (dd, 1H, *J* = 2.5 Hz, *J* = 12.5 Hz), 3.61-3.62 (m, 1H), 3.52-3.55 (m, 4H), 3.35 (dd, 1H, *J* = 12.5 Hz).

^{13}C{1H} NMR (125 MHz, $CDCl_3$): δ 137.8, 137.3, 128.4, 128.4, 128.1, 127.9, 127.9, 127.7, 104.8, 81.6, 72.0, 71.7, 71.2, 63.6, 56.9, 32.4.

HRMS (ESI-TOF) *m/z*: [M+K] calcd for $C_{20}H_{23}IO_4K$ 493.0273, found 493.0273.



Compound **40α and 40β** were synthesized from **S12**[30] (400 mg, 0.471 mmol) by following **general procedure A.** Overall yield: 95%, 451.1 mg.

(2*S*,3*R*,4*S*,5*S*,6*R*)-3,4,5-tris(benzyloxy)-2-(((2*R*,3*R*,5*S*,6*S*)-4-(benzyloxy)-2-((benzyloxy)methyl)-5-iodo-6-methoxytetrahydro-2*H*-pyran-3-yl)oxy)-6-((benzyloxy)methyl)tetrahydro-2*H*-pyran (40*α*):

Yield 57 %, 270.60 mg, colorless oil, R_f: 0.5 (5% EtOAc/toluene).

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.22-7.39 (m, 30H), 5.09 (d, 1H, *J* = 2.5 Hz), 4.93 (d, 1H, 4.79 (d, 1H, *J* = 11.0 Hz), 4.71-4.73 (m, 2H), 4.64-4.68 (m, 3H), 4.58 (d, 1H, *J* = 12.0 Hz), 4.56 (d, 1H, *J* = 11.5 Hz), 4.42-4.45 (m, 3H), 4.39 (d, 1H, *J* = 2.5 Hz), 4.28 (d, 1H, *J* = 12.0 Hz), 4.11 (dd, 1H, *J* = 7.0 Hz, 9.0 Hz), 3.82-3.85 (m, 2H), 3.78 (dd, 1H, *J* = 5.0 Hz, 10.5 Hz), 3.73 (dd, 1H, *J* = 7.5 Hz, 10.0 Hz), 3.69 (dd, 1H, *J* = 2.0 Hz, 11.0 Hz), 3.52 (dd, 1H, *J* = 6.5 Hz, 8.5 Hz), 3.44 (dd, 1H, *J* = 5.5 Hz, 9.5 Hz), 3.40 (dd, 2H, *J* = 3.0 Hz, 10.0 Hz), 3.38 (s, 3H), 3.35 (d, 1H, *J* = 6.5 Hz).

^{13}C{1H} NMR (100 MHz, $CDCl_3$): δ.138.8, 138.7, 138.6, 138.5, 138.3, 138.1, 128.3(3), 128.2, 128.1(3), 128.1, 128.0, 127.9, 127.8, 127.6, 127.5(2), 127.4(2), 127.3, 127.2, 103.4, 102.3, 82.5, 79.8, 76.2(2), 75.1, 74.5, 73.5(2), 73.4, 73.1, 72.7, 71.9, 71.7, 68.8, 68.7, 55.2, 32.3.

HRMS (ESI-TOF) *m/z*: $[M+NH_4]^+$ calcd for $C_{55}H_{59}IO_{10}NH_4$ 1024.3497, found 1024.3492.

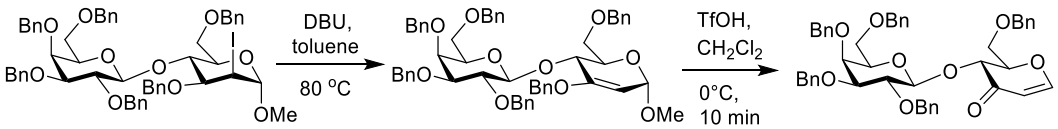
(2*S*,3*R*,4*S*,5*S*,6*R*)-3,4,5-tris(benzyloxy)-2-(((2*R*,3*R*,5*R*,6*R*)-4-(benzyloxy)-2-((benzyloxy)methyl)-5-iodo-6-methoxytetrahydro-2*H*-pyran-3-yl)oxy)-6-((benzyloxy)methyl)tetrahydro-2*H*-pyran (40β):

Yield 38 %, 180.44 mg, colorless oil, R_f: 0.4 (5% EtOAc/toluene), $[\alpha]_D^{25}$= +22.5 (c 0.9, $CHCl_3$).

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.13-7.47 (m, 30H), 5.14 (d, 1H, *J* = 9.5 Hz), 5.01 (d, 1H, *J* = 11.0 Hz), 4.85 (d, 1H, *J* = 11.0 Hz), 4.81 (d, 1H, *J* = 11.5 Hz), 4.74 (s, 1H), 4.73 (s, 1H), 4.66 (d, 1H, *J* = 9.5 Hz), 4.57 (d, 2H, *J* = 11.5 Hz), 4.49 (d, 1H, *J* = 9.5 Hz), 4.42 (d, 1H, *J* = 8.0 Hz), 4.40 (d, 1H, *J* = 12.0 Hz), 4.32 (d, 1H, *J* = 11.5 Hz), 4.20 (d, 1H, *J* = 11.5 Hz), 3.97 (dd, 1H, *J* = 9.0 Hz, 10.0 Hz), 3.94 (d, 1H, *J* = 2.5 Hz), 3.84-3.90 (m, 2H), 3.80 (dd, 1H, *J* = 8.0 Hz, 10.0 Hz), 3.74 (dd, 1H, *J* = 2.0 Hz, 10.5 Hz), 3.63 (dd, 1H, *J* = 9.0 Hz, 11.0 Hz), 3.5 (s, 3H), 3.52 (d, 1H, *J* = 8.5 Hz), 3.39-3.45 (m, 2H), 3.33-3.36 (m, 1H), 3.29 (dd, 1H, *J* = 5.0 Hz, 8.5 Hz).

^{13}C{1H} NMR (125 MHz, $CDCl_3$): δ.139.0, 138.8, 138.5, 138.3, 138.2, 138.0, 128.6, 128.3(3), 128.2(2), 128.2(2), 127.9, 127.8(2), 127.8(3), 127.6, 127.5, 127.4(2), 104.3, 102.8, 83.8, 82.4, 81.0, 77.3, 75.5, 75.4, 75.3, 74.8, 73.7, 73.4, 73.1(2), 72.6, 68.0, 67.8, 57.2, 33.0.

HRMS (ESI-TOF) *m/z*: $[M+Na]^+$ calcd for $C_{55}H_{59}IO_{10}Na$ 1029.3051, found 1029.3052



(2*R*,3*S*,6*S*)-4-(benzyloxy)-2-((benzyloxy)methyl)-6-methoxy-3-(((2*S*,3*R*,4*S*,5*S*,6*R*)-3,4,5-tris(benzyloxy)-6-((benzyloxy)methyl)tetrahydro-2*H*-pyran-2-yl)oxy)-3,6-dihydro-2*H*-pyran (41):

Compound **41** was synthesized from **40α** (150 mg, 0.14 mmol) by following **general procedure B.** Yield: 119.5 mg, 92%, colorless oil, R_f: 0.4 (20% EtOAc/hexane).

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.10-7.38 (m, 30H), 5.05 (d, 1H, *J* = 3.5 Hz), 4.95 (d, 1H, *J* = 11.5 Hz), 4.83 (d, 1H, *J* = 3.0 Hz), 4.81 (d, 1H, *J* = 12.5 Hz), 4.77 (d, 1H, *J* = 11.0 Hz), 4.73 (d, 1H, *J* = 11.5 Hz), 4.68-4.71 (m, 3H), 4.57 (d, 1H, *J* = 12.0 Hz), 4.54 (d, 1H, *J* = 10.5 Hz), 4.47 (d, 1H, *J* = 9.5 Hz), 4.36 (d, 1H, *J* = 9.0 Hz), 4.34 (d, 1H, *J* = 9.5 Hz), 4.26 (d, 1H, *J* = 12.0 Hz), 4.20 (d, 1H, *J* = 8.0 Hz), 4.09-4.12 (m, 1H), 3.87 (d, 1H, *J* = 3.0 Hz), 3.81 (dd, 1H, *J* = 3.5 Hz, 10.5 Hz), 3.77 (dd, 1H, *J* = 7.5 Hz, 9.5 Hz), 3.60 (dd, 1H, *J* = 7.5 Hz, 8.5 Hz), 3.54 (dd, 1H, *J* = 2.0 Hz, 10.5 Hz), 3.35-3.41 (m, 5H), 3.33 (dd, 1H, *J* = 3.0 Hz, 9.5 Hz).

^{13}C{1H} NMR (125 MHz, $CDCl_3$): δ 155.7, 139.1, 138.6, 138.3 , 138.1, 136., 129.0, 128.4, 128.3, 128.3, 128.2, 128.1(2), 128.1(2), 128.1, 128.0, 127.8, 127.8, 127.7, 127.4(2), 127.2, 126.7,

125.3, 103.9, 97.0, 96.8, 82.5, 79.7, 75.0, 74.6, 73.9, 73.5, 73.2(2), 72.7, 71.6, 70.4, 68.9, 68.6, 68.4, 55.3.

HRMS (ESI-TOF) *m/z*: $[M+Na]^+$ calcd for $C_{55}H_{58}O_{10}Na$ 901.3928, found 901.3925.

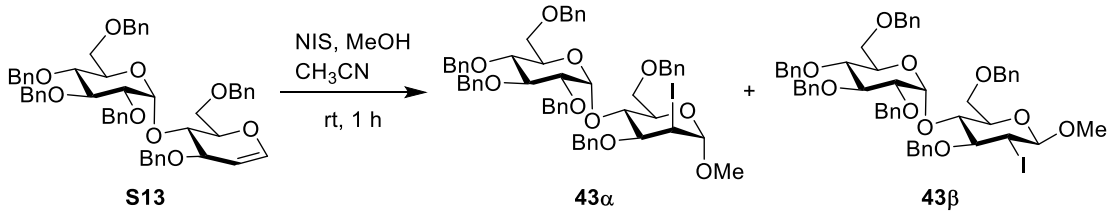
(2*R*,3*R*)-2-((benzyloxy)methyl)-3-(((2*S*,3*R*,4*S*,5*S*,6*R*)-3,4,5-tris(benzyloxy)-6-((benzyloxy)methyl)tetrahydro-2*H*-pyran-2-yl)oxy)-2,3-dihydro-4*H*-pyran-4-one (42): Compound **42** was synthesized from **41** (100 mg, 0.34 mmol) by following **general procedure C.** Yield: 67.4 mg, 87%, colorless oil, R_f: 0.6 (40% EtOAc/hexane).

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.25-7.34 (m, 26H), 5.37 (d, 1H, *J* = 6.0 Hz), 4.92 (d, 1H, *J* = 11.5 Hz), 4.83 (s, 2H), 4.71 (s, 2H), 4.59 (d, 1H, *J* = 11.5 Hz), 4.43-4.50 (m, 5H), 4.39-4.42 (m, 2H), 3.88-3.92 (m, 2H), 3.82 (dd, 1H, *J* = 4.0 Hz, 11.0 Hz), 3.69 (dd, 1H, *J* = 2.5 Hz, 11.0 Hz), 3.61 (dd, 1H, *J* = 7.5 Hz, 9.5 Hz), 3.54 (dd, 1H, *J* = 6.0 Hz, 9.5 Hz), 3.42-3.46 (m, 2H).

^{13}C{1H} NMR (125 MHz, $CDCl_3$): δ. 190.0, 161.6, 138.8, 138.7, 138.4, 138.0, 137.5, 128.4(2), 128.3(2), 128.2, 128.1, 128.1, 127.9, 127.8(2), 127.7, 127.7, 127.5, 127.5, 127.4, 105.5, 103.2, 82.5, 81.2, 79.3, 75.2, 75.0, 74.5, 73.6, 73.4(2), 73.3, 73.0, 68.5, 67.5.

HRMS (ESI-TOF) *m/z*: [M+Na] calcd for $C_{47}H_{48}O_9Na$ 779.3196, found 779.3194

.



Compound **43α and 43β** were synthesized from **S13**[31] (800 mg, 0.94 mmol) by following **general procedure A.** Overall yield: 89%, 844.40 mg.

(2*S*,3*R*,4*S*,5*R*,6*R*)-3,4,5-tris(benzyloxy)-2-(((2*R*,3*R*,5*S*,6*S*)-4-(benzyloxy)-2-((benzyloxy)methyl)-5-iodo-6-methoxytetrahydro-2*H*-pyran-3-yl)oxy)-6-((benzyloxy)methyl)tetrahydro-2*H*-pyran (43α):

Yield 53.4 %, 506.64 mg, colorless oil, R_f: 0.5 (30% EtOAc/hexane).

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.30-7.47 (m, 26H), 7.15-7.21 (m, 4H), 5.80 (d, 1H, *J* = 3.5 Hz), 5.23 (d, 1H, *J* = 1.5 Hz), 5.00 (d, 1H, *J* = 11.0 Hz), 4.85 (d, 1H, *J* = 11.0 Hz), 4.84 (d, 1H, *J* =

10.5 Hz), 4.82 (d, 1H, *J* = 11.5 Hz), 474 (d, 1H, *J* = 11.0 Hz), 4.61-4.63 (m, 3H), 4.59 (d, 1H, J= 4.5 Hz), 4.46-4.49 (m, 3H), 4.37 (d, 1H, *J* = 11.5 Hz), 4.28 (d, 1H, *J* = 12.0 Hz), 4.05-4.08 (m, 1H), 4.00 (dd, 1H, *J* = 4.5 Hz, 11.5 Hz), 3.93 (t, 1H, *J* = 9.5 Hz), 3.81 (dd, 1H, *J* = 1.5 Hz, 11.5 Hz), 3.76-3.78 (m, 1H), 3.71 (dd, 1H, *J* = 8.5 Hz, 10.0 Hz), 3.58-3.63 (m, 2H), 3.54 (dd, 1H, *J* = 4.0 Hz, 10.0 Hz), 3.45 (s, 3H), 3.40 (dd, 1H, *J* = 1.5 Hz, 10.5 Hz).

^{13}C{1H} NMR (125 MHz, $CDCl_3$): δ 138.8, 138.5, 138.3, 137.9, 137.8, 137.3, 128.2, 128.1(3), 128.1(2), 128.1(2), 128.1(2), 127.9, 127.8, 127.6(2), 127.6(2), 127.4, 127.2, 102.0, 96.6, 81.6, 79.2, 77.6, 77.3, 75.4, 74.8, 73.4, 73.2, 72.2, 71.5, 71.2, 70.8, 69.7, 69.1, 67.8, 54.9, 31.9.

HRMS (ESI-TOF) *m/z*: $[M+Na]^+$ calcd for $C_{55}H_{59}IO_{10}Na$ 1024.3497, found 1024.3492.

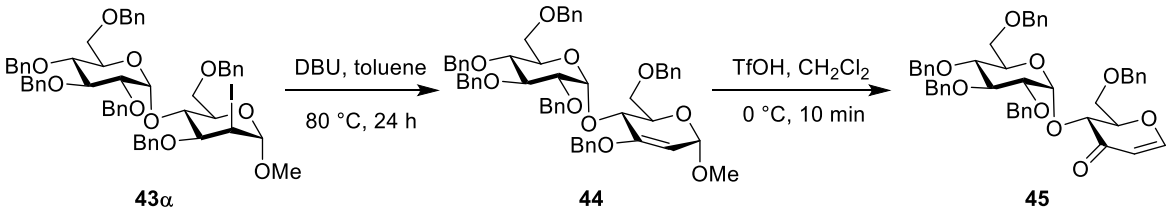
(2*S*,3*R*,4*S*,5*R*,6*R*)-3,4,5-tris(benzyloxy)-2-(((2*R*,3*S*,4*S*,5*S*,6*S*)-4-(benzyloxy)-2-((benzyloxy)methyl)-5-iodo-6-methoxytetrahydro-2*H*-pyran-3-yl)oxy)-6-((benzyloxy)methyl)tetrahydro-2*H*-pyran (43β):

Yield 35.6 %, 337.76 mg, colorless oil, R_f: 0.4 (30% EtOAc/hexane).

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.20-7.47 (m, 30H), 5.50 (d, 1H, *J* = 3.5 Hz), 5.03 (d, 1H, *J* = 10.0 Hz), 4.97 (d, 1H, *J* = 11.0 Hz), 4.84-4.89 (m, 3H), 4.60-4.63 (m, 4H), 4.53-4.57 (m, 3H), 4.23 (d, 1H, *J* = 11.5 Hz), 4.18 (t, 1H, *J* = 9.0 Hz), 4.08 (dd, 1H, *J* = 9.0 Hz, 11.0 Hz), 3.96-4.00 (m, 3H), 3.88-3.90 (m, 1H), 3.84 (dd, 1H, *J* = 2.0 Hz, 11.5 Hz), 3.68 (dd, 1H, *J* = 9.0 Hz, 10.0 Hz), 3.64 (dd, 1H, *J* = 3.5 Hz, 10.5 Hz), 3.61 (s, 3H), 3.57-3.62 (m, 1H), 3.53-3.58 (m, 2H).

^{13}C{1H} NMR (125 MHz, $CDCl_3$): δ 138.8, 138.5, 138.3, 137.9, 137.8, 137.3, 128.2, 128.1(3), 128.1(2), 128.1(2), 128.1(2), 127.9, 127.8, 127.6(2), 127.6(2), 127.4, 127.2, 102.0, 96.6, 81.6, 79.2, 77.6, 77.3, 75.4, 74.8, 73.4, 73.2, 72.2, 71.5, 71.2, 70.8, 69.7, 69.1, 67.8, 54.9, 31.9.

HRMS (ESI-TOF) *m/z*: $[M+Na]^+$ calcd for $C_{55}H_{59}IO_{10}Na$ 1024.3497, found 1024.3492.



(2*R*,3*S*,6*S*)-4-(benzyloxy)-2-((benzyloxy)methyl)-6-methoxy-3-(((2*S*,3*R*,4*S*,5*R*,6*R*)-3,4,5-tris(benzyloxy)-6-((benzyloxy)methyl)tetrahydro-2*H*-pyran-2-yl)oxy)-3,6-dihydro-2*H*-pyran (44):

Compound **44** was synthesized from **43α** (300mg, 0.29 mmol) by following **general procedure B.** Yield: 238.4 mg, 91%, colorless gum, R_f: 0.4 (30% EtOAc/hexane).

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.06-7.30 (m, 30H), 5.74 (d, 1H, *J* = 3.5 Hz), 5.09-5.11 (m, 1H), 4.88-4.91 (m, 2H), 4.66-4.77 (m, 5H), 4.48-4.56 (m, 3H), 4.43 (d, 1H, *J* = 11.0 Hz), 4.36 (d, 1H, *J* = 10.5 Hz), 4.16-4.26 (m, 3H), 3.81-3.88 (m, 2H), 3.68-3.72 (m, 2H), 3.61 (dd, 1H, *J* = 8.5 Hz, 9.5 Hz), 3.35-3.51 (m, 6H).

^{13}C{1H} NMR (125 MHz, $CDCl_3$): δ. 157.9, 138.9, 138.5, 138.2, 138.2, 137.8, 135.9, 128.5, 128.2, 128.2(2), 128.2(3), 128.0, 128.0, 127.8, 127.7(2), 127.6, 127.4, 127.3, 127.3, 127.3(2), 96.7, 96.6, 96.5, 81.3, 79.4, 77.25, 75.4, 74.9, 73.4, 73.2, 71.6, 70.9, 69.9, 69.8, 69.4, 68.1, 66.7, 55.2.

HRMS (ESI-TOF) *m/z*: $[M+Na]^+$ calcd for $C_{55}H_{58}O_{10}Na$ 901.3928, found 901.3917.

(2*R*,3*S*)-2-((benzyloxy)methyl)-3-(((2*S*,3*R*,4*S*,5*R*,6*R*)-3,4,5-*tris*(benzyloxy)-6-((benzyloxy)methyl)tetrahydro-2*H*-pyran-2-yl)oxy)-2,3-dihydro-4*H*-pyran-4-one (45):

Compound **45** was synthesized from **44** (100 mg, 0.11 mmol) by following **general procedure C.** Yield: 73.1 mg, 83%, colorless oil, R_f: 0.5 (30% EtOAc/hexane).

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.22-7.48 (m, 24H), 7.11-7.14 (m, 2H), 5.90 (d, 1H, *J* = 3.6 Hz), 5.40 (d, 1H, *J* = 6.0 Hz), 5.05 (d, 1H, *J* = 11.6 Hz), 5.00 (d, 1H, *J* = 10.8 Hz), 4.82 (d, 1H, *J* = 10.8 Hz), 4.77 (d, 1H, *J* = 2.8 Hz), 4.74 (d, 1H, *J* = 3.6 Hz), 4.71 (d, 1H, *J* = 12.0 Hz), 4.55-4.60 (m, 3H), 4.49 (d, 1H, *J* = 12.4 Hz), 4.43 (d, 1H, *J* = 10.8 Hz), 4.26 (d, 1H, *J* = 12.4 Hz), 3.87-3.93 (m, 2H), 3.82 (dd, 1H, *J* = 2.0 Hz, 7.2 Hz), 3.64-3.69 (m, 3H), 3.49 (dd, 1H, *J* = 2.4 Hz, 10.8 Hz), 3.31-3.34 (m, 1H).

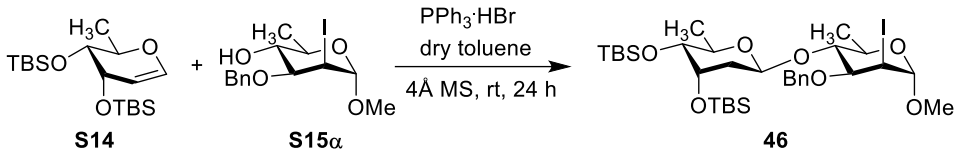
^{13}C{1H} NMR (125 MHz, $CDCl_3$): δ. 193.3, 162.2, 138.9, 138.5, 137.9, 137.9, 137.5, 128.6, 128.4, 128.3, 128.3, 128.3, 128.2, 127.9(4), 127.7, 127.7, 127.6, 127.6, 127.5, 105.2, 96.3, 81.5, 80.6, 79.2, 77.2, 75.6, 75.1, 73.6, 73.4, 72.3, 71.2, 68.8, 68.0, 67.8.

HRMS (ESI-TOF) *m/z*: $[M+Na]^+$ calcd for $C_{47}H_{48}O_9Na$ 779.3196, found 779.3194.

General procedure for $HBr{\cdot}PPh_3$ mediated Glycosylation (general procedure D):

To a stirred solution of donor sugar (1 mmol) and acceptor sugar (2 mmol) in anhydrous Toluene (10 mL/mmol) under inert atmosphere was added 4Å moleculae sieves and stirred for 1 hour. $HBr{\cdot}PPh_3$ (0.2 mmol) was added to the above stirred solution and continued stirring for 24 hours.

After complete conversion of starting material, solvent was concentrated under reduced pressure to obtain crude product which was purified by column chromatography using hexane and ethyl acetate to obtain the glycosylated product.



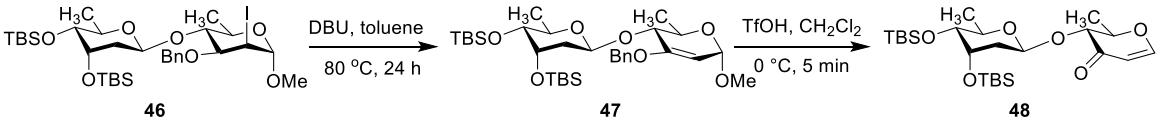
(((2*R*,3*R*,4*S*,6*S*)-6-(((2*R*,3*S*,4*S*,5*S*,6*S*)-4-(benzyloxy)-5-iodo-6-methoxy-2-methyltetrahydro-2*H*-pyran-3-yl)oxy)-2-methyltetrahydro-2*H*-pyran-3,4-diyl)bis(oxy))bis(*tert*-butyldimethylsilane) (46):

Compound **46** was synthesized from compound **S14**[32] (500 mg, 1.39 mmol) and **S15*α***[33] (580 mg, 1.53 mmol) following the **general procedure D.** Yield: 816 mg, 80 %, colorless oil, R_f: 0.5 (10% EtOAc/hexane). $[\alpha]_D^{25}$= +29.4 (c 0.8, $CHCl_3$).

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.42 (d, 2H, *J* = 7.5 Hz), 7.31 (t, 2H, *J* = 7.5 Hz), 7.24-7.27 (m, 1H), 5.09 (dd, 1H, *J* = 2.0 Hz, 9.5 Hz), 4.99 (d, 1H, *J* = 2.0 Hz), 4.66 (d, 1H, *J* = 12.0 Hz), 4.64 (d, 1H, *J* = 12.0 Hz), 4.40 (dd, 1H, *J* = 2.0 Hz, 4.0 Hz), 3.96-3.97 (m, 1H), 3.82 (dd, 1H, *J* = 6.5 Hz, *J* = 9.0 Hz), 3.75 (dd, 1H, *J* = 6.0 Hz, 9.0 Hz), 3.56 (dd, 1H, *J* = 8.0 Hz, 9.0 Hz), 3.32 (s, 3H), 3.28 (dd, 1H, *J* = 4.0 Hz, 7.0 Hz), 3.22 (dd, 1H, *J* = 2.0 Hz, 9.0 Hz), 1.94-1.98 (m, 1H), 1.59-1.62 (m, 1H), 1.29 (d, 3H, *J* = 6.5 Hz), 1.10 (d, 3H, *J* = 6.5 Hz), 0.88 (s, 9H), 0.87 (s, 9H), 0.06 (s, 3H), 0.05 (s, 3H), 0.04 (s, 3H), 0.03 (s, 3H).

^{13}C{1H} NMR (125 MHz, $CDCl_3$): δ.138.5, 128.1, 127.4, 127.3, 102.3, 99.1, 80.5, 76.6, 75.2, 71.5, 70.0, 69.8, 67.9, 55.0, 39.9, 33.3, 26.0, 25.8, 18.4, 18.2, 18.1, 18.1, -3.5, -4.2, -4.6, -4.7.

HRMS (ESI-TOF) *m/z*: $[M+Na]^+$ calcd for $C_{32}H_{57}IO_7Si_2Na$ 759.2585, found 759.2582.



(((2*R*,3*R*,4*S*,6*S*)-6-(((2*R*,3*S*,6*S*)-4-(benzyloxy)-6-methoxy-2-methyl-3,6-dihydro-2*H*-pyran-3-yl)oxy)-2-methyltetrahydro-2*H*-pyran-3,4-diyl)bis(oxy))bis(*tert*-butyldimethylsilane) (47):

Compound **47** was synthesized from **46** (230mg, 0.31 mmol) by following **general procedure B.** Yield: 174.1 mg, 92%, colorless oil, R_f: 0.4(10% EtOAc/hexane). $[\alpha]_D^{25}$= +70.0 (c 0.8, $CHCl_3$).

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.27-7.34 (m, 5H), 5.09 (d, 1H, *J* = 4.5 Hz), 4.98 (d, 1H, *J* = 3.5 Hz), 4.76 (d, 1H, *J* = 3.0 Hz), 4.74 (d, 1H, *J* = 11.5 Hz), 4.69 (d, 1H, *J* = 11.0 Hz), 4.23 (dd, 1H, *J* = 6.5 Hz, 8.5 Hz), 3.96-4.02 (m, 1H), 3.93 (d, 1H, *J* = 9.0 Hz), 3.86 (q, 1H, *J* = 3.0 Hz), 3.40 (s, 3H), 3.22 (dd, 1H, *J* = 2.5 Hz, *J* = 9.0 Hz), 1.95 (ddd, 1H, *J* = 1.5 Hz, 4.0 Hz, 14.5 Hz), 1.65 (ddd, 1H, *J* = 3.0 H, 5.5 Hz, 14.5 Hz), 1.35 (d, 3H, *J* = 6.0 Hz), 1.13 (d, 3H, *J* = 6.5 Hz), 0.89 (s, 18H), 0.05 (s, 3H), 0.02 (s, 6H), 0.00 (s, 3H).

^{13}C{1H} NMR (125 MHz, $CDCl_3$): δ.158.6, 136.6, 128.4, 127.8, 127.4, 98.1, 96.8, 95.0, 75.2, 74.6, 69.2, 68.4, 66.1, 64.5, 55.1, 36.8, 26.0, 25.9, 18.2, 18.1, 18.1, 17.9, -3.6, -3.9, -4.7, -4.8.

HRMS (ESI-TOF) *m/z*: $[M+Na]^+$ calcd for $C_{32}H_{56}O_6Si_2Na$ 631.3457, found 631.3455.

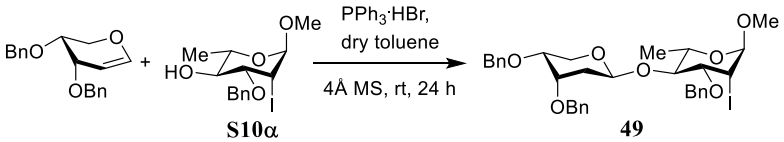
(2*R*)-3-(((2*S*,4*S*,5*R*,6*R*)-4,5-bis((*tert*-butyldimethylsilyl)oxy)-6-methyltetrahydro-2*H*-pyran-2-yl)oxy)-2-methyl-2,3-dihydro-4*H*-pyran-4-one (48):

Compound **48** was synthesized from **47** (90 mg, 0.14 mmol) by following **general procedure C.** Yield: 63.36 mg, 88%, colorless oil, R_f: 0.5 (20% EtOAc/hexane).

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.23 (d, 1H, *J* = 5.5 Hz), 5.38 (d, 1H, *J* = 6.0 Hz), 4.99 (dd, 1H, *J* = 2.0 Hz, 9.5 Hz), 4.46-4.52 (m, 1H), 4.07 (d, 1H, *J* = 10.5 Hz), 3.99-4.00 (m, 1H), 3.83-3.88 (m, 1H), 3.31 (dd, 1H, *J* = 2.5 Hz, 9.0 Hz), 2.01 (ddd, 1H, *J* = 2.0 Hz, 4.0 Hz, 13.5 Hz), 1.75 (ddd, 1H, *J* = 2.0 Hz, 9.5 Hz, 13.0 Hz), 1.47 (d, 3H, *J* = 6.5 Hz), 1.16 (d, 3H, *J* = 6.0 Hz), 0.88 (s, 18H), 0.08 (s 3H), 0.06 (s, 3H), 0.05 (s, 3H), 0.03 (s, 3H).

^{13}C{1H} NMR (125 MHz, $CDCl_3$): δ.191.1, 161.8, 105.5, 98.0, 78.8, 78.4, 74.8, 69.9, 69. 9, 39.4, 26.0, 25.8, 18.2, 18.1, 18.0, 17.1, -3.5, -4.3, -4.6, -4.7.

HRMS (ESI-TOF) *m/z*: $[M+Na]^+$ calcd for $C_{24}H_{46}O_6Si_2Na$ 509.2725, found 509.2724.



S10α **49**

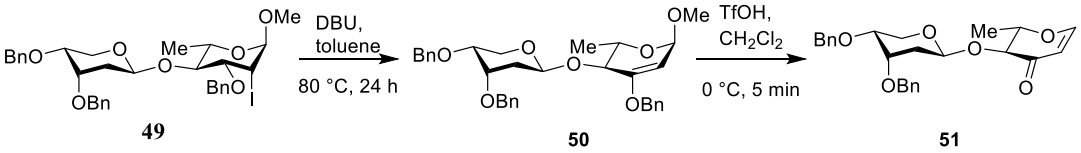
(2*S*,3*S*,4*R*,5*R*,6*R*)-4-(benzyloxy)-3-(((2*S*,4*S*,5*R*)-4,5-bis(benzyloxy)tetrahydro-2*H*-pyran-2-yl)oxy)-5-iodo-6-methoxy-2-methyltetrahydro-2*H*-pyran (49):

Compound **59** was synthesized from compound (3*R*,4*S*)-3,4-bis(benzyloxy)-3,4-dihydro-2*H*-pyran[26] (500 mg, 1.68 mmol) and **S10α** (702 mg, 1.85 mmol) following the **general procedure D.** Yield:1.02 g, 90 %, colorless gum, R_f: 0.3(10% EtOAc/hexane). $[\alpha]_D^{25}$= -10.8 (c 0.5, $CHCl_3$).

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.29-7.39 (m, 15H), 5.37 (t, 1H, *J* = 3.5 Hz), 5.04 (s, 1H), 4.62-4.71 (m, 3H), 4.48-4.50 (m, 3H), 4.38 (d, 1H, *J* = 11.0 Hz), 3.83-3.87 (m, 2H), 3.73-3.76 (m, 2H), 3.66-3.70 (m, 2H), 3.35 (s, 3H), 3.17 (dd, 1H, *J* = 4.5 Hz, 8.5 Hz), 2.19 (dtd, 1H, *J* = 3.5 Hz, 10.0 Hz, 13.0 Hz), 1.76 (dt, 1H, *J* = 3.5 Hz, 13.0 Hz), 1.34 (d, 3H, *J* = 6.5 Hz).

^{13}C{1H} NMR (125 MHz, $CDCl_3$): δ. 138.5, 138.4, 137.3, 128.4, 128.2(2), 127.9, 127.8, 127.6, 127.5, 127.4(2), 102.2, 99.4, 78.9, 76.8, 72.7, 72.2, 71.0, 70.4, 70.2, 67.6, 61.5, 54.9, 33.0, 32.5, 18.2.

HRMS (ESI-TOF) *m/z*: $[M+Na]^+$ calcd for $C_{33}H_{39}IO_7Na$ 697.1638, found 697.1636.



(2*R*,3*R*,6*S*)-4-(benzyloxy)-3-(((2*S*,4*S*,5*R*)-4,5-bis(benzyloxy)tetrahydro-2*H*-pyran-2-yl)oxy)-6-methoxy-2-methyl-3,6-dihydro-2*H*-pyran (50):

Compound **50** was synthesized from **49** (200 mg, 0.29 mmol) by following **general procedure B.** Yield: 149.19 mg, 92%, colorless oil, R_f: 0.5 (20% EtOAc/hexane). $[\alpha]_D^{25}$= -126.3 (c 0.7, $CHCl_3$).

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.27-7.38 (m, 15H), 5.36 (t, 1H, *J* = 3.5 Hz), 5.01 (d, 1H, *J* = 3.5 Hz), 4.85 (d, 1H, *J* = 3.5 Hz), 4.80 (d, 1H, *J* = 11.5 Hz), 4.68-4.73 (m, 3H), 4.47 (d, 1H, *J* = 12.0 Hz), 4.43 (d, 1H, *J* = 12.0 Hz), 3.97-4.01 (m, 2H), 3.80-3.85 (m, 2H), 3.75-3.77 (m, 1H), 3.67 (s, 1H), 3.42 (s, 3H), 2.12-2.18 (dtd, 1H, *J* = 3.5 Hz, 10.5 Hz, 13.0 Hz), 1.86 (dt, 1H, *J* = 3.5 Hz, 13.0 Hz), 1.33 (d, 3H, *J* = 5.5 Hz).

^{13}C{1H} NMR (125 MHz, $CDCl_3$): δ. 157.8, 138.5(2), 136.1, 128.5, 128.3(3), 128.0, 127.7, 127.5, 127.4(2), 99.7, 96.6, 95.4, 74.7, 72.6, 72.2, 71.3, 70.0, 69.4, 66.1, 61.7, 55.2, 31.7, 18.6.

HRMS (ESI-TOF) *m/z*: $[M+K]^+$ calcd for $C_{33}H_{38}O_7K$ 585.2255, found 585.2248.

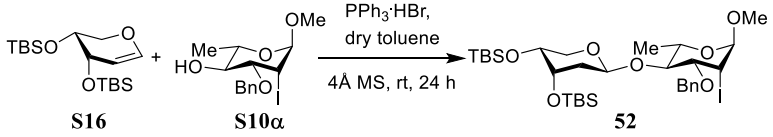
(2*R*,3*R*)-3-(((2*S*,4*S*,5*R*)-4,5-bis(benzyloxy)tetrahydro-2*H*-pyran-2-yl)oxy)-2-methyl-2,3-dihydro-4*H*-pyran-4-one (51):

Compound **51** was synthesized from **50** (50 mg, 0.09 mmol) by following **general procedure C.** Yield: 30.25 mg, 78%, colorless oil, R_f: 0.4 (20% EtOAc/hexane).

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.26-7.39 (m, 11H), 5.43 (t, 1H, *J* = 3.0 Hz), 5.35 (d, 1H, *J* = 6.0 Hz), 4.72 (s, 2H), 4.69 (d, 1H, *J* = 5.0 Hz), 4.60 (d, 1H, *J* = 12.0 Hz), 4.54 (d, 1H, *J* = 12.0 Hz), 4.35-4.41 (m, 1H), 4.08 (d, 1H, *J* = 11.5 Hz), 3.81-3.89 (m, 2H), 3.66-3.70 (m, 1H), 2.33 (ddd, 1H, *J* = 3.5 Hz, 11.0 Hz, 14.5 Hz), 2.06-2.10 (m, 1H), 1.45 (d, 3H, J 6.5 Hz).

^{13}C{1H} NMR (125 MHz, $CDCl_3$): δ. 193.1, 162.3, 138.5, 138.5, 128.6, 128.3(2), 127.8, 127.5, 127.0, 105.1, 98.9, 78.4, 75.6, 72.6, 72.2, 71.5, 70.3, 62.1, 31.4, 17.8.

HRMS (ESI-TOF) *m/z*: $[M+NH_4]^+$ calcd for $C_{25}H_{28}O_6NH_4$ 442.2230, found 442.2228



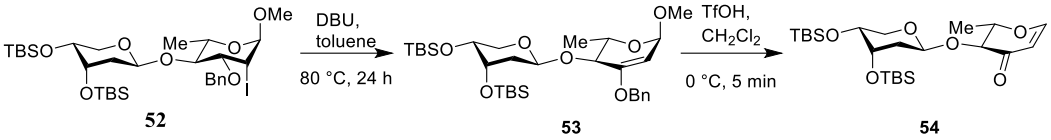
(((3*R*,4*S*,6*S*)-6-(((2*S*,3*S*,4*R*,5*R*,6*R*)-4-(benzyloxy)-5-iodo-6-methoxy-2-methyltetrahydro-2*H*-pyran-3-yl)oxy)tetrahydro-2*H*-pyran-3,4-diyl)bis(oxy))bis(*tert*-butyldimethylsilane) (52):

Compound **52** was synthesized from compound **S16**[34] (200 mg, 0.58 mmol) and **S10α** (241.60 mg, 0.63 mmol) following the **general procedure D.** Yield: 377.67 mg, 90 %, colorless gum, R_f: 0.6 (10% EtOAc/hexane).

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.21-7.31 (m, 5H), 5.14 (t, 1H, *J* = 4.0 Hz), 4.93 (s, 1H), 4.54 (d, 1H, *J* = 12.0 Hz), 4.38 (d, 1H, *J* = 11.5 Hz), 4.32 (d, 1H, *J* = 3.5 Hz), 3.89-3.92 (m, 1H), 3.62-3.67 (m, 3H), 3.54-3.59 (m, 2H), 3.25 (s, 3H), 3.02 (dd, 1H, *J* = 4.0 Hz, 8.5 Hz), 1.97 (dtd, 1H, *J* = 3.0 Hz, 8.5 Hz, 12.0 Hz), 1.50 (dt, 1H, *J* = 4.5 Hz, 8.5 Hz), 1.27 (d, 3H, *J* = 6.0 Hz), 0.82 (s, 9H), 0.79 (s, 9H), 0.00 (s, 6H), -0.02 (s, 3H), -0.04 (s, 3H).

^{13}C{1H} NMR (125 MHz, $CDCl_3$): δ. 137.6, 128.4, 127.9, 127.7, 102.4, 99.5, 79.1, 76.4, 70.5, 70.0, 67.9, 67.7, 64.9, 55.0, 36.3, 33.4, 25.9(2), 18.2(2), 18.2, -4.4(2), -4.7, -4.8.

HRMS (ESI-TOF) *m/z*: $[M+NH_4]^+$ calcd for $C_{31}H_{55}IO_7Si_2NH_4^+$ 740.2869, found 740.2873.



52 53 54

(((3*R*,4*S*,6*S*)-6-(((2*R*,3*R*,6*S*)-4-(benzyloxy)-6-methoxy-2-methyl-3,6-dihydro-2*H*-pyran-3-yl)oxy)tetrahydro-2*H*-pyran-3,4-diyl)bis(oxy))bis(*tert*-butyldimethylsilane) (53):

Compound **53** was synthesized from **52** (200 mg, 0.27 mmol) by following **general procedure B.** Yield: 134.9 mg, 82%, colorless oil, R_f: 0.5 (10% EtOAc/hexane). $[\alpha]_D^{25}$ = -50.7 (c 0.5, $CHCl_3$).

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.28-7.35 (m, 5H), 5.18 (t, 1H, *J* = 3.5 Hz), 4.96 (d, 1H, *J* = 3.0 Hz), 4.81 (d, 1H, *J* = 11.5 Hz), 4.76 (d, 1H, *J* = 3.5 Hz), 4.73 (d, 1H, *J* = 12.0 Hz), 3.93-4.01 (m, 3H), 3.69-3.75 (m, 2H), 3.59 (dd, 1H, *J* = 5.0 Hz, 11.0 Hz), 3.39 (s, 3H), 1.98 (dtd, 1H, *J* = 3.0 Hz, 9.0 Hz, 12.5 Hz), 1.60 (dt, 1H, *J* = 4.0 Hz, 13.0 Hz), 1.34 (d, 3H, *J* = 6.0 Hz), 0.88 (s, 9H), 0.83 (s, 9H), 0.05 (s, 6H), 0.02 (s, 3H), -0.02 (s, 3H).

^{13}C{1H} NMR (125 MHz, $CDCl_3$): δ. 157.8, 136.4, 128.5, 127.9, 127.3, 100.0, 96.7, 95.4, 75.2, 70.0, 69.3, 67.4, 66.3, 65.0, 55.1, 35.5, 25.9(2), 18.5, 18.2, 18.1, -4.5(2), -4.7, -4.8.

HRMS (ESI-TOF) *m/z*: $[M+Na]^+$ calcd for $C_{31}H_{54}O_7Si_2Na$ 617.3300, found 617.3306.

(2*R*,3*R*)-3-(((2*S*,4*S*,5*R*)-4,5-bis((*tert*-butyldimethylsilyl)oxy)tetrahydro-2*H*-pyran-2-yl)oxy)-2-methyl-2,3-dihydro-4*H*-pyran-4-one (54):

Compound **54** was synthesized from **53** (80 mg, 0.13 mmol) by following **general procedure C.** Yield: 45.81 mg, 72%, colorless oil, R_f: 0.6 (20% EtOAc/hexane).

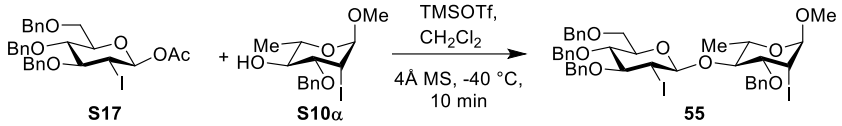
^{1}H NMR (500 MHz, $CDCl_3$): δ 7.25 (d, 1H, *J* = 5.5 Hz), 5.33 (d, 1H, *J* = 5.5 Hz), 5.31 (dd, 1H, *J* = 3.0 Hz, 4.5 Hz), 4.37-4.43 (m, 1H), 4.07 (d, 1H, *J* = 11.0 Hz), 4.00 (dt, 1H, *J* = 3.0 Hz, 8.0 Hz), 3.71-3.73 (m, 1H), 3.63-3.64 (m, 2H), 2.12-2.17 (m, 1H), 1.72 (dt, 1H, *J* = 4.0 Hz, 13.0 Hz), 1.48 (d, 3H, *J* = 6.5 Hz), 0.90 (s, 9H), 0.89 (s, 9H), 0.08 (s, 3H), 0.07 (s, 3H), 0.06 (s, 6H).

^{13}C{1H} NMR (125 MHz, $CDCl_3$): δ. 193.0, 162.2, 105.1, 98.8, 78.5, 75.7, 69.9, 67.6, 65.1, 35.6, 25.9, 25.9, 18.2(2), 17.6, -4.4, -4.5, -4.7, -4.8. .

HRMS (ESI-TOF) *m/z*: $[M+H]^+$ calcd for $C_{23}H_{44}O_6Si_2H$ 473.2749, found 473.2746.

General procedure for TMSOTf mediated Glycosylation (general procedure E):

To a stirred solution of donor sugar (1 mmol) and acceptor sugar (1.2 mmol) in anhydrous CH_2Cl_2 (10 mL/mmol) under inert atmosphere was added 4Å molecular sieves and stirred for 1 hour at room temperature. The reaction mixture was further cooled to -40 ˚C. TMSOTf (0.5 mmol) was added dropwise to the above reaction mixture and continued stirring at -40 ˚C. The reaction was monitored by TLC and quenched by triethylamine (0.6 mmol) at same temperature and allowed to room temperature. Solvent was concentrated under reduced pressure to obtain crude product which was purified by column chromatography using hexane and ethyl acetate to obtain the glycosylated product.



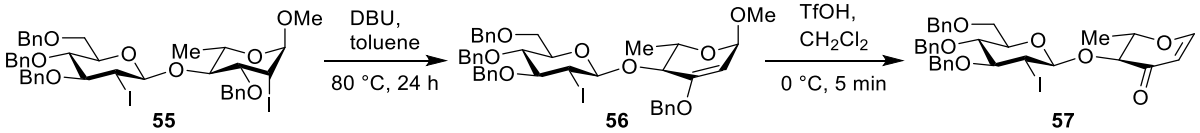
(2*S*,3*S*,4*R*,5*R*,6*R*)-4-(benzyloxy)-3-(((2*S*,4*S*,5*R*)-4,5-bis(benzyloxy)tetrahydro-2*H*-pyran-2-yl)oxy)-5-iodo-6-methoxy-2-methyltetrahydro-2*H*-pyran (55):

Compound **55** was synthesized from compound **S17**[35] (250 mg, 0.41 mmol) and **S10*α*** (188.3 mg, 0.49 mmol) following the **general procedure E.** Yield: 359.1 mg, 94 %, colorless oil, R_f: 0.8 (20% EtOAc/hexane).

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.22-7.53 (m, 20H), 5.07 (s, 1H), 4.99 (d, 1H, *J* = 8.5 Hz), 4.94 (d, 1H, *J* = 10.0 Hz), 4.84 (d, 1H, *J* = 10.0 Hz), 4.78 (d, 1H, *J* = 11.0 Hz), 4.67 (d, 1H, *J* = 10.5 Hz), 4.64 (d, 1H, *J* = 11.0 Hz), 4.56-4.62 (m, 3H), 4.52 (dd, 1H, *J* = 1.0 Hz, 4.5 Hz), 3.71-3.82 (m, 5H), 3.67 (t, 1H, *J* = 9.0 Hz), 3.61 (dd, 1H, *J* = 8.5 Hz, 10.5 Hz), 3.42-3.45 (m, 1H), 3.36-3.38 (m, 4H), 1.36 (d, 3H, *J* = 6.0 Hz).

^{13}C{1H} NMR (125 MHz, $CDCl_3$): δ 138.2, 137.9, 137.9, 137.5, 128.7, 128.4, 128.3(2), 128.3(2), 128.3, 128.0, 127.8(3), 127.5, 102.3, 102.0, 85.6, 79.7, 77.7, 76.7, 75.3, 74.9(2), 73.6, 70.7, 68.6, 67.4, 55.1, 33.3, 32.9, 18.0.

HRMS (ESI-TOF) *m/z*: $[M+NH_4]^+$ calcd for $C_{41}H_{46}I_2O_8NH_4$ 938.1626, found 938.1620.



(2*R*,3*R*,6*S*)-4-(benzyloxy)-3-(((2*S*,3*R*,4*S*,5*R*,6*R*)-4,5-bis(benzyloxy)-6-((benzyloxy)methyl)-3-iodotetrahydro-2*H*-pyran-2-yl)oxy)-6-methoxy-2-methyl-3,6-dihydro-2*H*-pyran (56):

Compound **56** was synthesized from **55** (150 mg, 0.16 mmol) by following **general procedure B.** Yield: 116.2 mg, 90%, colorless oil, R_f: 0.4 (10% EtOAc/hexane).

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.21-7.46 (m, 20H), 5.01 (d, 1H, *J* = 3.5 Hz), 4.97 (d, 1H, *J* = 9.0 Hz), 4.95 (d, 1H, *J* = 10.5 Hz), 4.92 (d, 1H, *J* = 12.0 Hz), 4.87 (d, 1H, *J* = 3.5 Hz), 4.83 (d, 1H, *J* = 10.0 Hz), 4.79 (d, 1H, *J* = 11.0 Hz), 4.77 (d, 1H, *J* = 11.5 Hz), 4.55-4.62 (m, 3H), 4.15 (d, 1H, *J* = 9.0 Hz), 4.05-4.11 (m, 1H), 3.78-3.82 (m, 1H), 3.71 (d, 2H, *J* = 3.0 Hz), 3.60-3.65 (m, 2H), 3.42-3.44 (m, 4H), 1.37 (d, 3H, *J* = 6.0 Hz).

^{13}C{1H} NMR (125 MHz, $CDCl_3$): δ. 157.3, 138.1, 137.8, 137.8, 136.3, 128.4, 128.4, 128.3(2), 128.3, 128.0, 127.9, 127.9, 127.9, 127.8, 127.6, 127.5, 102.0, 96.7, 96.1, 85.8, 79.6, 75.3, 75.0, 74.9, 73.6, 73.3, 69.5, 68.7, 66.3, 55.1, 31.5, 18.1.

HRMS (ESI-TOF) *m/z*: $[M+NH_4]^+$ calcd for $C_{41}H_{45}IO_8NH_4$ 810.2503, found 810.2505.

(2*R*,3*R*)-3-(((2*S*,3*R*,4*S*,5*R*,6*R*)-4,5-bis(benzyloxy)-6-((benzyloxy)methyl)-3-iodotetrahydro-2*H*-pyran-2-yl)oxy)-2-methyl-2,3-dihydro-4*H*-pyran-4-one (57): Compound **57** was synthesized from **56** (80 mg, 0.10 mmol) by following **general procedure C.** Yield: 54.1 mg, 80%, colorless oil, R_f: 0.4 (10% EtOAc/hexane).

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.19-7.43 (m, 16H), 5.39 (d, 1H, *J* = 5.5 Hz), 5.02 (d, 1H, *J* = 9.0 Hz), 4.99 (d, 1H, *J* = 10.5 Hz), 485 (d, 1H, *J* = 10.5 Hz), 4.80 (d, 1H, *J* = 11.0 Hz), 4.56-4.61 (m, 3H), 4.52 (d, 1H, *J* = 12.0 Hz), 4.13 (d, 1H, *J* = 9.0 Hz), 3.82 (dd, 1H, *J* = 9.0 Hz, 10.5 Hz), 3.73 (dd, 1H, *J* = 9.0 Hz, 11.0 Hz), 3.71 (d, 2H, *J* = 3.0 Hz), 3.64 (t, 1H, J – 9.5 Hz), 3.49 (dt, 1H, *J* = 3.0 Hz, 9.5 Hz), 1.45 (d, 3H, *J* = 6.5 Hz).

^{13}C NMR (125 MHz, $CDCl_3$): δ. 190.8, 162.2, 138.0, 137.8(2), 128.5, 128.4, 128.4(2), 128.1, 127.9, 127.8, 127.7, 127.6, 105.1, 101.2, 85.6, 79.5, 78.3, 75.7, 75.6, 75.1, 74.9, 73.4, 68.4, 30.9, 16.6. .

HRMS (ESI-TOF) *m/z*: $[M+Na]^+$ calcd for $C_{33}H_{35}IO_7Na$ 693.1325, found 693.1320.

S18

(2*S*,3*R*,4*S*,5*R*,6*R*)-5-(benzyloxy)-4-((*tert*-butyldimethylsilyl)oxy)-6-(((*tert*-butyldimethylsilyl)oxy)methyl)-3-iodotetrahydro-2*H*-pyran-2-yl acetate (S18):

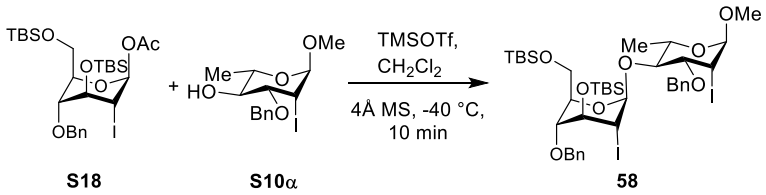
2,4-di-*O*-*tert*-butyldimethylsilyl-3-*O*-benzyl D-glucal[36] (1 g, 3.23 mmol) was dissolved in dry CH_2Cl_2 (15 mL) under nitrogen in a foil-covered round-bottom flask and 4Å MS was added and stirred for 30 mins. To the resulting solution, at room temperature, was added AcOH (1.8 mL, 32.30 mmol) followed by *N*-iodosuccinimide (1.09 g, 4.84 mmol). After 1 h, the starting compound was consumed and the reaction was quenched by the addition of saturated aqueous $Na_2S_2O_3$ (20 mL) and the resulting mixture was stirred vigorously for 5 min. The mixture was diluted with CH_2Cl_2 (30 mL). The organic phase was separated and, dried over Na_2SO_4, filtered, and concentrated. The residue was purified by silica gel column chromatography using hexane and ethyl acetate to obtain the product.

Yield: 1.4 g, 80%, colorless gum, R_f: 0.5 (10% EtOAc/hexane).

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.27-7.36 (m, 5H), 6.36 (d, 1H, *J* = 2.0 Hz), 4.86 (d, 1H, *J* = 11.0 Hz), 4.26 (dd, 1H, *J* = 1.5 Hz, 4.0 Hz), 3.93 (t, 1H, *J* = 9.5 Hz), 3.89 (dd, 1H, *J* = 3.5 Hz, 11.5 Hz), 3.74-3.79 (m, 1H), 3.30 (dd, 1H, *J* = 4.0 Hz, 8.5 Hz), 2.07 (s, 3H), 0.97 (s, 9H), 0.93 (s, 9H), 0.10-0.11 (m, 9H), 0.06 (s, 3H).

^{13}C{1H} NMR (100 MHz, $CDCl_3$): δ. 168.6, 138.4, 128.4, 128.5, 128.2, 127.8, 127.8, 95.7, , 76.8, 75.8, 75.2 , 77.0, 61.7, 36.0, 26.0, 25.9, 20.9, 18.3, 18.0, -4.4, -4.6, -5.0, -5.4.

HRMS (ESI-TOF) *m/z*: $[M+NH_4]^+$ calcd for $C_{27}H_{47}IO_6Si_2NH_4$ 668.2300, found 668.2301.



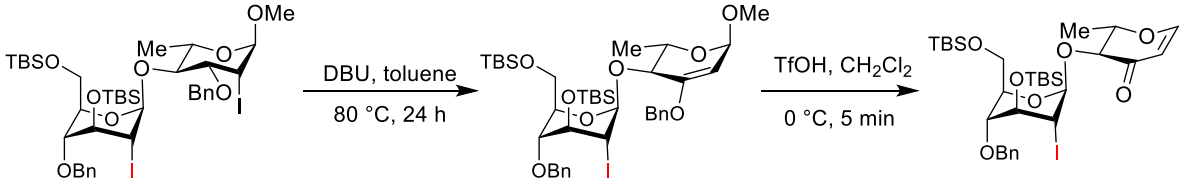
Compound **58** were synthesized from compound **S18** (300 mg, 0.46 mmol) and **S10α** (209 mg, 0.55 mmol) following the **general procedure D.** Yield 45%, colorless gum, R_f: 0.9 (10% EtOAc/hexane). $[\alpha]_D^{25}$ = +17.5 (c 1.1, $CHCl_3$).

(((2*R*,3*R*,4*S*,5*R*,6*S*)-3-(benzyloxy)-6-(((2*S*,3*S*,4*R*,5*R*,6*R*)-4-(benzyloxy)-5-iodo-6-methoxy-2-methyltetrahydro-2*H*-pyran-3-yl)oxy)-2-(((*tert*-butyldimethylsilyl)oxy)methyl)-5-iodotetrahydro-2*H*-pyran-4-yl)oxy)(*tert*-butyl)dimethylsilane (58):

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.25-7.42 (m, 10H), 5.37 (s, 1H), 5.03 (d, 1H, *J* = 1.5 Hz), 480 (d, 1H, *J* = 11.0 Hz), 4.57 (d, 1H, *J* = 11.0 Hz), 4.53 (d, 1H, *J* = 10.5 Hz), 4.51 (dd, 1H, *J* = 1.5 Hz, 4.5 Hz), 4.35 (d, 1H, *J* = 10.5 Hz), 4.23 (dd, 1H, *J* = 1.5 Hz, 4.5 Hz), 3.79-3.85 (m, 2H), 3.75 (dd, 1H, *J* = 6.5 Hz, 9.0 Hz), 3.63 (t, 1H, *J* = 9.0 Hz), 3.41 (dd, 1H, *J* = 2.5 Hz, 11.5 Hz), 3.34-3.35 (m, 4H), 3.26 (dd, 1H, *J* = 4.0 Hz, 8.0 Hz), 3.11 (dd, 1H, *J* = 4.5 Hz, 8.5 Hz), 1.31 (d, 3H, *J* = 6.5 Hz), 0/96 (s, 9H), 0.89 (s, 9H), 0.10 (s, 3H), 0.08 (s, 3H), 0.02 (s, 3H), -0.04 (s, 3H).

^{13}C{1H} NMR (100 MHz, $CDCl_3$): δ. 138.9, 137.2, 128.8, 128.3, 128.2, 127.9, 127.5, 127.3, 102.3, 102.0, 79.5, 77.0, 74.9, 74.7, 73.5, 70.6, 70.0, 68.0, 61.3, 55.1, 38.5, 33.2, 26.0, 25.9, 18.2(2), 18.0, -4.3, -4.5, -5.0, -5.5. .

HRMS (ESI-TOF) *m/z*: $[M+Na]^+$ calcd for $C_{39}H_{62}I_2O_8Si_2Na$ 991.1970, found 991.1966.



(((2*R*,3*R*,4*S*,5*R*,6*S*)-3-(benzyloxy)-6-(((2*R*,3*R*,6*S*)-4-(benzyloxy)-6-methoxy-2-methyl-3,6-dihydro-2*H*-pyran-3-yl)oxy)-2-(((*tert*-butyldimethylsilyl)oxy)methyl)-5-iodotetrahydro-2*H*-pyran-4-yl)oxy)(*tert*-butyl)dimethylsilane (59):

Compound **59** was synthesized from **58** (130 mg, 0.13 mmol) by following **general procedure B.** Yield: 101.5 mg, 90%, colorless oil, R_f: 0.5 (10% EtOAc/hexane).

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.26-7.35 (m, 10H), 5.21 (s, 1H), 5.00 (d, 1H, *J* = 3.0 Hz), 4.95 (d, 1H, *J* = 3.5 Hz), 4.78 (d, 1H, *J* = 11.0 Hz), 4.71 (d, 1H, *J* = 10.5 Hz), 4.64 (d, 1H, *J* = 10.5 Hz), 4.53 (d, 1H, J – 11.5 Hz), 4.13-4.18 (m, 2H), 3.98 (d, 1H, *J* = 9.0 Hz), 3.79-3.81 (m, 1H), 3.70 (t, 1H, *J* = 9.0 Hz), 3.37-3.41 (m, 4H), 3.31 (dd, 1H, *J* = 1.5 Hz, 11.5 Hz), 3.20 (dd, 1H, *J* = 4.0 Hz, 8.5 Hz), 1.28 (d, 3H, *J* = 6.0 Hz), 0.90 (s, 9H), 0.88 (s, 9H), 0.03 (s, 3H), 0.01 (s, 3H), -0.02 (s, 3H), -0.07 (s, 3H).

^{13}C{1H} NMR (125 MHz, $CDCl_3$): δ. 155.5, 138.9, 135.6, 128.8, 128.7, 128.4, 128.1, 127.6, 127.3, 100.9, 97.5, 96.5, 77.2, 76.6, 74.8, 73.8, 70.0, 69.8, 66.0, 61.5, 55.2, 39.4, 26.0, 25.9, 18.4, 18.3, 17.9, -4.5, -4.8, -5.0, -5.5.

HRMS (ESI-TOF) *m/z*: $[M+Na]^+$ calcd for $C_{39}H_{61}IO_8Si_2Na$ 863.2847, found 863.2841.

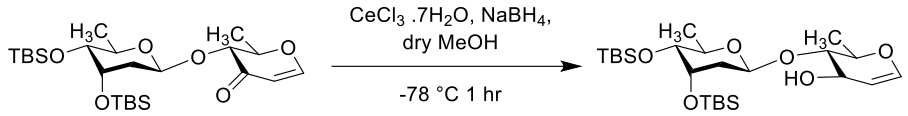
(2*R*,3*R*)-3-(((2*S*,3*R*,4*S*,5*R*,6*R*)-5-(benzyloxy)-4-((*tert*-butyldimethylsilyl)oxy)-6-(((*tert*-butyldimethylsilyl)oxy)methyl)-3-iodotetrahydro-2*H*-pyran-2-yl)oxy)-2-methyl-2,3-dihydro-4*H*-pyran-4-one (60):

Compound **60** was synthesized from **59** (50 mg, 0.05 mmol) by following **general procedure C.** Yield: 29.03 mg, 68%, colorless oil, R_f: 0.4 (10% EtOAc/hexane).

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.31-7.32 (m, 5H), 7.24 (d, 1H, *J* = 6.0 Hz), 5.35 (d, 1H, *J* = 6.0 Hz), 5.25 (s, 1H), 4.83 (d, 1H, *J* = 11.5 Hz), 4.63 (d, 1H, *J* = 11.5 Hz), 4.47-4.52 (m, 1H), 4.36 (dd, 1H, *J* = 1.5 Hz, 4.0 Hz), 4.15-4.17 (m, 1H), 3.98 (d, 1H, *J* = 10.0 Hz), 3.84 (dd, 1H, *J* = 4.0 Hz, 11.5 Hz), 3.80 (dd, 1H, *J* = 8.5 Hz, 9.5 Hz), 3.71 (dd, 1H, *J* = 1.5 Hz, 11.5 Hz), 3.36 (dd, 1H, *J* = 4.0 Hz, 8.5 Hz), 1.45 (d, 3H, *J* = 6.5 Hz), 0.95 (s, 9H), 0.90 (s, 9H), 0.10 (s, 3H), 0.08 (s, 3H), 0.07 (s, 3H), 0.00 (s, 3H).

^{13}C{1H} NMR (125 MHz, $CDCl_3$): δ.190.3, 161.8, 138.7, 128.2, 127.5, 127.4, 105.4, 102.3, 78.2, 78.1, 77.1, 74.7, 74.2, 69.9, 61.9, 38.1, 26.0, 25.9, 18.3, 18.0, 17.0, -4.4, -4.6, -5.0, -5.5.

HRMS (ESI-TOF) *m/z*: $[M+Na]^+$ calcd for $C_{31}H_{51}IO_7Si_2Na$ 741.2116, found 741.2113.



48 61

(2*R*,3*S*,4*S*)-3-(((2*S*,4*S*,5*R*,6*R*)-4,5-bis((*tert*-butyldimethylsilyl)oxy)-6-methyltetrahydro-2*H*-pyran-2-yl)oxy)-2-methyl-3,4-dihydro-2*H*-pyran-4-ol (61):

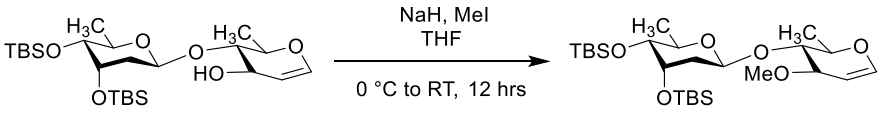
To a stirred solution of *α,β*-unsaturated ketone **48** (30 mg, 0.06 mmol) in anhydrous MeOH (5 mL) under inert atmosphere was added $CeCl_3{\cdot}7H_2O$ (20 mg, 0.061 mmol) and stirred for 15 minutes at room temperature. The reaction mixture was then cooled to -78 ˚C and $NaBH_4$ (2.38 mg, 0.06 mmol) was added to the above reaction mixture and continued stirring for 1 h at same temperature. The reaction was monitored by TLC and quenched by saturated NH_4Cl solution at same temperature and allowed to room temperature. Solvent was concentrated under reduced pressure and extracted with EtOAc and washed with brine. Organic layer was dried over anhydrous $NaSO_4$, concentrated under reduced pressure and purified by column chromatography using hexane and ethyl acetate to obtain the alcohol **61.**

Yield: 28.0 mg, 93%, white solid, R_f: 0.5 (10% EtOAc/hexane).

^{1}H NMR (500 MHz, $CDCl_3$): δ 6.30 (dd, 1H, *J* = 2.0 Hz, 6.0 Hz), 4.92 (dd, 1H, *J* = 2.0 Hz, 10.5 Hz), 4.78 (dd, 1H, *J* = 2.0 Hz, 6.0 Hz), 4.72 (s, 1H), 4.23 (dt, 1H, *J* = 2.0 Hz, 7.0 Hz), 3.99-4.04 (m, 2H), 3.82-3.87 (m, 1H), 3.31 (dd, 1H, *J* = 2.0 Hz, 7.0 Hz), 3.27 (dd, 1H, *J* = 7.5 Hz, 10.0 Hz), 2.03 (ddd, 1H, *J* = 2.0 Hz, 4.0 Hz, 13.5 Hz), 1.73 (ddd, 1H, *J* = 2.0 Hz, 9.5 Hz, 13.0 Hz), 1.32 (d, 3H, *J* = 6.0 Hz), 1.24 (d, 3H, *J* = 6.5 Hz), 0.91 (s, 18H), 0.09 (s, 6H), 0.08 (s, 6H).

^{13}C{1H} NMR (125 MHz, $CDCl_3$): δ. 143.6, 102.5, 99.7, 85.9, 74.8, 72.7, 70.1, 69.7, 68.1, 39.5, 26.0, 25.7, 18.1, 18.1, 18.0, 17.1, -3.5, -4.4, -4.6, -4.8.

HRMS (ESI-TOF) *m/z*: $[M+Na]^+$ calcd for $C_{24}H_{48}O_6Si_2Na^+$ 511.2882, found 511.2884.



61 **62**

(((2*R*,3*R*,4*S*,6*S*)-6-(((2*R*,3*R*,4*S*)-4-methoxy-2-methyl-3,4-dihydro-2*H*-pyran-3-yl)oxy)-2-methyltetrahydro-2*H*-pyran-3,4-diyl)bis(oxy))bis(*tert*-butyldimethylsilane) (62):

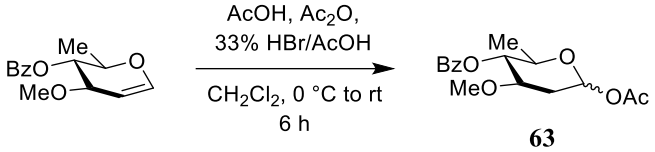
To a stirred solution of alcohol **61** (20 mg, 0.04 mmol) in anhydrous THF (5 mL) under inert atmosphere was added NaH (60%) (2 mg, 0.04 mmol) at 0 ˚C and stirred for 15 minutes at same temperature. To reaction mixture was methyl iodide (33 µL, 0.05 mmol) dropwise at 0 ˚C and continued stirring for 10 hours at room temperature. The reaction was quenched by ice cold water, extracted with EtOAc and washed with brine. Organic layer was dried over anhydrous $NaSO_4$, concentrated under reduced pressure and purified by column chromatography using hexane and ethyl acetate to obtain the product **62.**

Yield: 19.93 mg, 97%, colorless oil, R_f: 0.5 (10% Acetone/hexane).

^{1}H NMR (500 MHz, $CDCl_3$): δ 6.35 (dd, 1H, *J* = 1.0 Hz, 6.0 Hz), 5.05 (dd, 1H, *J* = 2.0 Hz, 9.5 Hz), 4.80 (dd, 1H, *J* = 3.0 Hz, 6.0 Hz), 3.99-4.01 (m, 2H), 3.96 (t, 1H, *J* = 7.0 Hz), 3.88-3.93 (m, 1H), 3.66 (dd, 1H, *J* = 6.0 Hz, 8.0 Hz), 3.38 (s, 3H), 3.31 (dd, 1H, *J* = 2.5 Hz, 9.0 Hz), 1.95 (ddd, 1H, *J* = 2.0 Hz, 4.0 Hz, 13.5 Hz), 1.69 (ddd, 1H, *J* = 2.0 Hz, 9.5 Hz, 13.5 Hz), 1.33 (d, 3H, *J* = 6.5 Hz), 1.20 (d, 3H, *J* = 6.5 Hz), 0.90 (s, 9H), 0.89 (s, 9H), 0.07 (s, 6H), 0.06 (s, 6H).

^{13}C{1H} NMR (125 MHz, $CDCl_3$): δ.144.8, 100.2, 98.3, 77.4, 75.3, 75.0, 73.6, 70.0, 69.5, 54.7, 39.9, 26.0, 25.8, 18.4, 18.1, 18.0, 17.0, -3.5, -4.3, -4.6, -4.7.

HRMS (ESI-TOF) *m/z*: $[M+Na]^+$ calcd for $C_{25}H_{59}O_6Si_2Na$ 525.3044 found 525.3044.



63

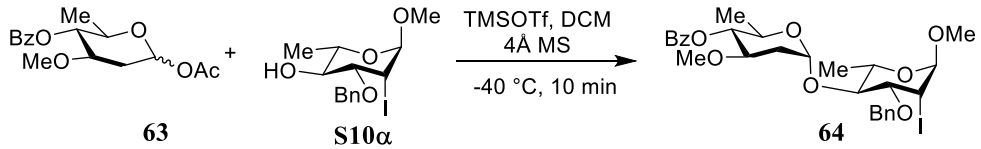
(2*R*,3*R*,4*S*)-6-acetoxy-4-methoxy-2-methyltetrahydro-2*H*-pyran-3-yl benzoate (63):
4-*O*-Benzoyl 3-*O*-methyl-D-rhamnal (500 mg, 2.01 mmol) was dissolved in dry CH_2Cl_2 (2 mL) and purged with argon for 10 min, and cooled to 0 ˚C. Acetic acid (1.09 mL, 19.09 mmol) and acetic anhydride (1.63 mL, 17.28 mmol) were added, and the solution was stirred for 15 min. 33% HBr in acetic acid solution (109 µL, 0.3 Eq of HBr) was added, the solution was allowed to warm to room temperature, and stirred for 6 h. The reaction was quenched by the addition of ice-cold H_2O (20 mL), diluted with CH_2Cl_2 (20 mL) and the organic layer was separated, and washed with ice-cold H_2O (3 × 20 mL), ice-cold sat. aq. $NaHCO_3$ (2 x 20 mL), and ice-cold brine (20 mL). The organic layer was dried over anhydrous $NaSO_4$, the solvent was removed in vacuo, and the resulting residue was purified by silica gel column chromatography using hexane and ethyl acetate to obtain product as an anomeric mixture.

Yield: 524 mg, 85%, colorless oil. R_f: 0.5 (15% EtOAc/hexane).

Selected data for the major anomer. **^{1}H NMR (500 MHz, $CDCl_3$):** δ 8.05-8.08 (m, 2H), 78.56-7.59 (m, 1H), 7.45 (t, 2H, *J* = 7.5 Hz), 6.24 (m, 1H), 4.99 (t, 1H, *J* = 9.5 Hz), 3.97-4.02 (m, 1H), 3.75-3.80 (m, 1H), 3.33 (s, 3H), 2.32 (ddd, 1H, *J* = 1.5 Hz, 5.0 Hz, 13.5 Hz), 2.14 (s, 3H), 1.84 (dd, 1H, *J* = 3.5 Hz, 11.5 Hz, 15.0 Hz), 1.20 (d, 3H, *J* = 6.0 Hz).

^{13}C{1H} NMR (125 MHz, $CDCl_3$): 169.2, 165.6, 133.1, 129.8, 128.3, 91.6, 76.1, 75.4, 71.2, 68.5, 57.3, 33.8, 21.1, 17.6.

HRMS (ESI-TOF) *m/z*: $[M+NH_4]^+$ calcd for $C_{16}H_{20}O_6NH_4$ 326.1604, found 326.1605.



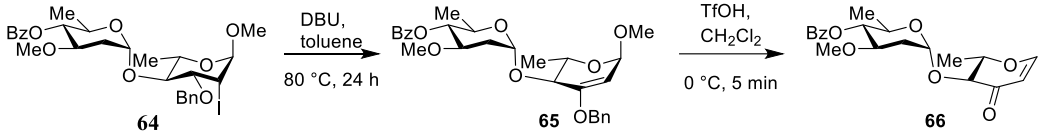
(2*R*,3*R*,4*R*,6*R*)-6-(((2*S*,3*S*,4*R*,5*R*,6*R*)-4-(benzyloxy)-5-iodo-6-methoxy-2-methyltetrahydro-2*H*-pyran-3-yl)oxy)-4-methoxy-2-methyltetrahydro-2*H*-pyran-3-yl benzoate (64):

Compound **64** was synthesized from compound **63** (350 mg, 1.13 mmol) and **S10α** (515 mg, 1.36 mmol) following the **general procedure D.** Yield: 604.53 mg, 85 %, colorless gum, R_f: 0.5 (20% EtOAc/hexane). $[\alpha]_D^{25}$= 40.0 (c 0.7, $CHCl_3$).

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.90 (d, 2H, *J* = 7.0 Hz), 7.51 (t, 1H, *J* = 7.0 Hz), 7.36-7.40 (m, 4H), 7.11-7.18 (m, 3H), 4.99 (s, 2H), 4.76 (t, 1H, *J* = 9.5 Hz), 4.57 (d, 1H, *J* = 10.5 Hz), 4.50 (dd, 1H, *J* = 1.0 Hz, 4.0 Hz), 4.30 (d, 1H, *J* = 11.0 Hz), 4.07-4.12 (m, 1H), 372-3.78 (m, 1H), 3.61-3.67 (m, 2H), 3.29 (s, 3H), 3.23 (s, 3H), 3.08 (dd, 1H, *J* = 4.0 Hz, 8.5 Hz), 2.19 (dd, 1H, *J* = 5..0 Hz, 13.0 Hz), 1.61 (td, 1H, *J* = 3.5 Hz, 12.5 Hz), 1.27 (d, 3H, *J* = 6.5 Hz), 0.71 (d, 3H, *J* = 6.5 Hz).

^{13}C{1H} NMR (125 MHz, $CDCl_3$): δ. 165.7, 137.2, 132.9, 130.2, 129.7, 128.6, 128.3, 128.3, 127.8, 102.3, 97.5, 78.4, 76.8 , 75.8, 74.9, 70.5, 68.6, 66.5 , 57.2, 55.0, 35.0, 33.3, 18.4, 16.9.

HRMS (ESI-TOF) *m/z*: [M+Na] calcd for $C_{28}H_{35}IO_8Na$ 649.1274, found 649.1275.



(2*R*,3*R*,4*R*,6*R*)-6-(((2*S*,3*S*,6*R*)-4-(benzyloxy)-6-methoxy-2-methyl-3,6-dihydro-2*H*-pyran-3-yl)oxy)-4-methoxy-2-methyltetrahydro-2*H*-pyran-3-yl benzoate (65):

Compound **65** was synthesized from **64** (170 mg, 0.27 mmol) by following **general procedure B.** Yield: 128.41 mg, 95%, white solid. R_f: 0.4 (20% EtOAc/hexane). $[\alpha]_D^{25}$= +28.1 (c 0.5, $CHCl_3$).

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.99 (dd, 1H, *J* = 1.5 Hz, 8.5 Hz), 7.58-7.61 (m, 1H), 7.46-7.49 (m, 2H), 7.36-7.38 (m, 2H), 7.21-7.24 (m, 2H), 7.14-7.17 (m, 1H), 5.03 (d, 1H, *J* = 3.5 Hz), 5.00 (d, 1H, *J* = 3.0 Hz), 4.94 (dd, 1H, *J* = 1.0 Hz, 3.5 Hz), 4.77-4.81 (m, 2H), 4.69 (d, 1H, *J* = 10.5 Hz), 4.07-4.15 (m, 2H), 3.99 (d, 1H, *J* = 9.5 Hz), 3.68-3.72 (m, 1H), 3.43 (s, 3H), 3.27 (s, 3H), 2.28 (dd, 1H, *J* = 5.0 Hz, 12.5 Hz), 1.63-1.69 (m, 1H), 1.32 (d, 3H, *J* = 6.5 Hz), 0.68 (d, 3H, *J* = 6.0 Hz).

^{13}C{1H} NMR (125 MHz, $CDCl_3$): 165.7, 155.9, 135.8, 132.9, 130.2, 129.7, 128.7, 128.5, 128.3(2), 97.8, 97.0, 96.7, 76.7, 76.0, 75.7, 70.0, 67.0, 66.6, 57.2, 55.2, 35.3, 18.4, 16.9.

HRMS (ESI-TOF) *m/z*: [M+Na] calcd for $C_{28}H_{34}O_8Na$ 521.2151, found 521.2152.

(2*R*,3*R*,4*R*,6*R*)-4-methoxy-2-methyl-6-(((2*S*,3*S*)-2-methyl-4-oxo-3,4-dihydro-2*H*-pyran-3-yl)oxy)tetrahydro-2*H*-pyran-3-yl benzoate (66):

Compound **66** was synthesized from 65 (100 mg, 0.20 mmol) by following **general procedure C.** Yield: 52.8 mg, 70%, white solid, R_f: 0.5 (30% EtOAc/hexane). $[\alpha]_D^{25}$= -13.5 (c 0.3, $CHCl_3$).

^{1}H NMR (500 MHz, $CDCl_3$): δ 8.08 (dd, 2H, *J* = 1.0 Hz, 8.5 Hz), 754-7.58 (m, 1H), 7.43-7.46 (m, 2H), 7.28 (d, 1H, *J* = 6.0 Hz), 5.39 (d, 1H, *J* = 6.0 Hz), 5.02 (d, 1H, *J* = 3.0 Hz), 4.95 (t, 1H, *J* = 9.5 Hz), 4.54-4.59 (m, 1H), 4.47-4.53 (m, 1H), 4.03 (d, 1H, *J* = 10.0 Hz), 3.83 (ddd, 1H, *J* = 5.0 Hz, 9.0 Hz, 14.0 Hz), 3.32 (s, 3H), 2.36 (dd, 1H, *J* = 1.0 Hz, 5.0 Hz, 13.0 Hz), 1.77 (ddd, 1H, *J* = 4.0 Hz, 11.5 Hz, *J* = 15.5 Hz), 1.48 (d, 3H, *J* = 6.5 Hz), 1.16 (d, 3H, *J* = 6.5 Hz).

^{13}C{1H} NMR (125 MHz, $CDCl_3$): δ 191.2, 165.9, 162.1, 133.0 , 130.1, 129.8, 128.3, 105.5, 98.3, 78.5, 78.0, 76.7, 75.7, 67.0, 57.5, 35.1, 17.3, 17.1

HRMS (ESI-TOF) *m/z*: [M+Na] calcd for $C_{20}H_{24}O_7Na$ 399.1420, found 399.1419.

X-ray Crystal Structure and Details of Compound 66

The absolute configuration of compound **66** was determined by X-ray crystallography analysis. Single crystal of **66** was recrystallized from mixed solvents of Ethyl acetate and Hexane. The data can be obtained free of charge *via* www.ccdc.cam.ac.uk/data_request/cif_or by emailing data_request@ccdc.cam.ac.uk. X-ray reflections were collected on Rigaku Oxford diffraction XtaLAB Synergy and reduction was performed using Olex2 Software. The structure was solved and refined using Olex2.

Table S1: Crystal data and structure refinement for **66**: CCDC: **2155604**

Identification code	PRS26
Empirical formula	$C_{20}H_{24}O_7$
Formula weight	376.39
Temperature/K	297(1)
Crystal system	Orthorhombic
Space group	$P2_12_12_1$
a/Å	8.3836(5)
b/Å	9.3434(6)
c/Å	24.9167(16)
α/°	90
β/°	90
γ/°	90
Volume/Å^3	1951.8(2)
Z	4
ρ_{calc}g/cm^3	1.281
μ/mm^{-1}	0.097
F(000)	800.0
Crystal size/mm^3	0.19 × 0.18 × 0.16
Radiation	Mo Kα (λ = 0.71073)
2Θ range for data collection/°	4.656 to 50.044
Index ranges	$-9 \leq h \leq 8$, $-11 \leq k \leq 11$, $-29 \leq l \leq 29$
Reflections collected	8951
Independent reflections	3352 [R_{int} = 0.0443, R_{sigma} = 0.0617]
Data/restraints/parameters	3352/0/247
Goodness-of-fit on F^2	0.954
Final R indexes [I>=2σ (I)]	R_1 = 0.0497, wR_2 = 0.1083
Final R indexes [all data]	R_1 = 0.0834, wR_2 = 0.1271
Largest diff. peak/hole / e Å^{-3}	0.12/-0.16
Flack parameter	-0.3(10)

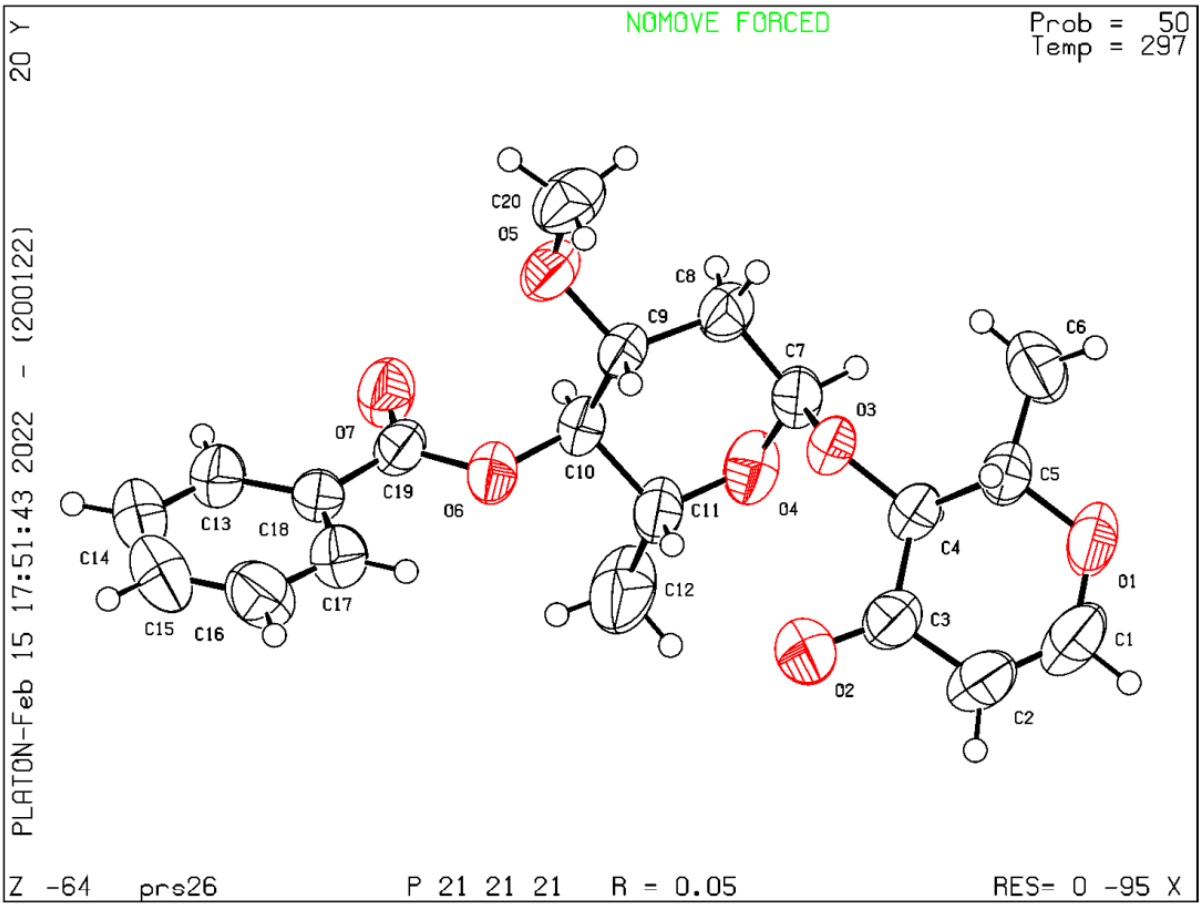
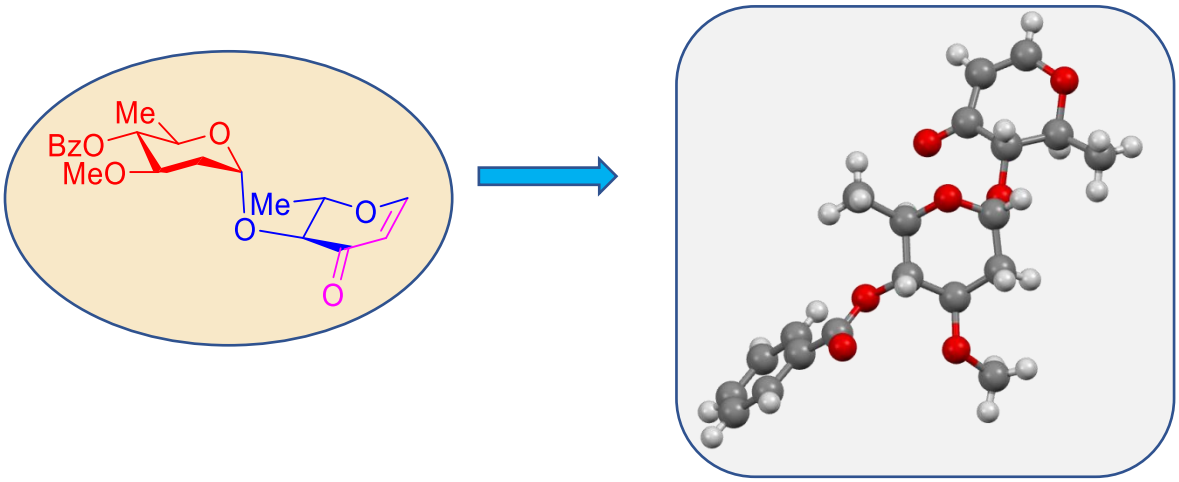


Figure S1: ORTEP diagram of compound **66**



2.5 REFERENCES

1 (a) Nicolaou, K. C.; Rhoades, D.; Mothish Kumar, S. Total Syntheses of Thailanstatins A−C, Spliceostatin D, and Analogues Thereof. Stereodivergent Synthesis of Tetrasubstituted Dihydro- and Tetrahydropyrans and Design, Synthesis, Biological Evaluation, and Discovery of Potent Antitumor Agents. *J. Am. Chem. Soc.*, **2018**, *140*, 8303–8320. (b) Nicolaou, K. C.; Rhoades, D.; Lamani, M.; M. R. Pattanayak S. Mothish Kumar. Total Synthesis of Thailanstatin A. *J. Am. Chem. Soc.* **2016**, 138, 7532–7535.

2 Zúñiga, A.; Pérez, M.; Gándara, Z.; Fall, A.; Gómez, G.; Fall, Y. Synthesis of diospongin A, ent-diospongin A and C-5 epimer of diospongin B from tri-*O*-acetyL-D-glucal. *Arkivoc* **2015**, *7*, 195−215.

3 Garrido, F.; Santalla, H.; Gómez, G.; Fall, Y. First total synthesis of 6-epi-phomonol. *Tetrahedron Lett.* **2016**, *57*, 2631−2632.

4 Zuniga.; Perez, M.; Pazos, G.; Gomez, G.; Fall, Y. A Concise, Enantioselective Synthesis of (+)-Decarestrictine L from Tri-O-acetyL-D-glucal. Synthesis. 2010, 2446−2450.

5 Mal, K.; Sharma, A.; Das, I. Gold(III) Chloride Catalyzed Synthesis of Chiral Substituted 3-Formyl Furans from Carbohydrates: Application in the Synthesis of 1,5-Dicarbonyl Derivatives and Furo[3,2-c]pyridine. *Chem. Eur. J.* **2014**, *20*, 11932 – 11945.

6 Singh, A. K.; Kanaujiya, V. K.; Tiwari, V.; Sabiah, S.; Kandasamy. J. Development of Routes for the Stereoselective Preparation of β-AryL-C-glycosides via C-1 Aryl Enones. *Org. Lett.* **2020**, *22*, 7650–7655.

7 (a) Lin, H. C.; Wu, H. H.; Lin, Z. P.; Lin, C. Y.; Lin, C. H.; Chen, K. L.; Wong, F. F. Microwave-assisted stereoselective a-2-deoxyglycosylation of hex-1-en-3-uloses. *Tetrahedron Lett.*, **2009**, *50*, 7327–7329. (b) Michael, K.; Kessler, H. MICHAEL-Type Additions in the Synthesis of *α*-*O*- and -*S*-2-Deoxyglycosides. Tetrahedron *Lett.* **1996**, *37*, 3453–3456.

8 Goodwin, T. E.; Rothman, N. M.; Salazar, K. L.; Sorrels, S. L.; Evans, F. E. Stereoselectivity reversals in conjugate additions to a 2,3-dihydro-4*H*-pyran-4-one. *J. Org. Chem.* **1992**, *57*, 2469-2471.

9 Ramnauth, J.; Poulin, O.; Bratovanov, S. S.; Rakhit, S.; Maddaford, S. P. Stereoselective C-Glycoside Formation by a Rhodium(I)-Catalyzed 1,4-Addition of Arylboronic Acids to Acetylated Enones Derived from Glycals. *Org. Lett.* **2001**, *3*, 2571-2573.

10 (a) Venukumar, P.; Sudharani, C.; Sridhar, P. R. A one-pot septanoside formation and glycosylation of acyclic dithioacetals derived from 1,2-cyclopropanated sugars. *Chem. Commun.* **2014**, *50*, 2218–2221. (b) Sridhar, P. R.; Venukumar, P. A ring expansion-glycosylation strategy toward the synthesis of septano-oligosaccharides. *Org. Lett.* **2012**, *14*, 5558–5561.

11 (a) Yalamanchili, S.; Miller, W.; Chen, X.; Bennett, C. S. Rapid de Novo Preparation of 2,6-Dideoxy Sugar Libraries through GolD-Catalyzed Homopropargyl Orthoester Cyclization. *Org. Lett.* **2019**, *21*, 9646–9651. (b) Zeng, J.; Sun, G.; Yao, Y. Zhu, W.; Wang, R.; Cai, L.; Liu, K.; Zhang, Q.; Liu, X.-W.; Wan, Q. 3-Aminodeoxypyranoses in Glycosylation: Diversity-Oriented Synthesis and Assembly in Oligosaccharides. *Angew Chem. Int. Ed.* **2017**, *56*, 5227–5231.

12 Fujiwara, T.; Hayashi, M. Efficient Synthesis of Rare Sugar D-Allal via Reversal of Diastereoselection in the Reduction of Protected 1,5-Anhydrohex-1-en-3-uloses: Protecting Group Dependence of the Stereoselection. *J. Org. Chem.* **2008**, *73*, 9161–9163.

13 a) S. Czernecki, K. Vijayakumaran and G. Ville, *J. Org. Chem.*, 1986, **51**, 5472-5475.; b) B. Fraser-reid, D. L. Walker, S. Y-k Tam and N. L. Holder, *Can. J. Chem.* 1973, **51**, 3950-3954. c) S. Czemecki, C. Leteux and A. Veyrières, *Tetrahedron. Lett.*, 1992, **33**, 221-224. d) A. Bouillot, D. do Khac, M. Fétizon, F. Guir and Y. Memoria, *Syn. Commun*, 1993, **23**, 2071–2081.; e) A. Kirschning, *J. Org. Chem.*, 1995, **60**, 1228-1232.; f) A. Kirschning, U. Hary, C. Plumeier, M. Ries and L. Rose, *J. Chem. Soc. Perkin Trans.*, 1999, **1**, 519-528. g) A. Chennaiah, A. K. Verma and Y. D. Vankar, *J. Org. Chem.*, 2018, **83**, 10535–10540.

14 Kirschning, A. Oxidation of Fully Protected Glycals by Hypervalent Iodine Reagents. *J. Org. Chem.* **1995**, *60*, 1228-1232.

15 Kirschning, A.; Hary, U.; Plumeier, C.; Ries, M.; Rose, L. Simple oxidation of 3-*O*-silylated glycals: application in deblocking 3-*O*-protected glycals. *J. Chem. Soc. Perkin Trans.* **1999**, *1*, 519-528.

16 (a) Reddy, G. M.; Sridhar, P. R. The first stereoselective total synthesis of neosemburin and isoneosemburin. *Org. Bio. Chem.* **2014**, *12*, 8408-8414. (b) Sridhar, P. R.; Sudharani, C. Stereoselective synthesis of C-2-methylene and C-2-methyL-C-glycosides by Claisen rearrangement of 2-vinyloxymethyl glycals. RSC *adv.* **2012**, *2*, 8596-8598. (c) Sridhar, P. R.; Rao, B. U.; Drisya, C. S. [1,2]- vs [2,3]-Wittig Rearrangement in Carbohydrate Derived Alkenyl Systems. *Org. Lett.* **2021**, *23*, 3850-3853.

17 Gammon, D. W.; Kinfe, H. H.; De Vos, D. E.; Jacobs, P. A.; Sels, B. F. A New Procedure for Highly Regio- and Stereoselective Iodoacetoxylation of Protected Glycals and α-1,2-Cyclopropanated Sugars. *J. Carbohydr. Chem.*, **2007**, *26*, 141-157.

18 Horton, D.; Priebe, W.; Sznaidman, M. Iodoalkoxylation of 1,5-anhydro-2-deoxy-hex-1-enitols (glycals). *Carbohydr. Res.* **1990**, *205*, 71-86.

19 Boyd, E. C.; Jones, R. V. H.; Quayle, P.; Waring, A. J. "Green" oxidation reactions - Application to carbohydrate chemistry. *Green Chem.* **2003**, *5*, 679–681.

20 Kozlowski, J. S.; Marzabadi, C. H.; Rath, N. P.; Spilling, C. D. Chemistry of glucal halohydrins (II): An unusual protecting group effect in the competitive formation of formyl furanosides and methyl glycosides. *Carbohydr. Res.* **1997**, *300*, 301-313.

21 Liu, L.; Postema, M. H. D. A Unified Approach to Differentially Linked β-C-Disaccharides by Ring-Closing Metathesis. *J. Am. Chem. Soc.* **2001**, *123*, 8602-8603.

22 Park, H.-R.; Furihata, K.; Hayakawa, Y.; Shin-Ya,V. Versipelostatin, a novel GRP78/Bip molecular chaperone down-regulator of microbial origin. *Tetrahedron Lett.* **2002**, *43*, *6941-6945*.

23 Srinivasarao, M.; Park, T.; Chen, Y.; Fuchs, P. L. Noteworthy observations accompanying synthesis of the apoptolidin Disaccharide. *Chem. Commun.* **2011**, *47*, 5858–5860.

24. Mrozik, H.; Eskola, P.; Fisher, M. H. Partial syntheses of avermectin b,a and ivermectin from avermectin B_{2a}. *Tetrahedron Lett.* **1982**, *23*, 2377-2378.

25 Beau, J. M.; Jaurand, G.; Esnault, J.; Sinay, P. Synthesis of the disaccharide C-D fragment found in everninomicin-C and -D, avilamycin-A and -C, and curamycin-A: stereochemistry at the spiro-ortholactone center. *Tethedron Lett.*, **1987**, *28*, 1105-1108.

26 Wang, B.; Xiong, D. C.; Ye, X. S. Direct C–H Trifluoromethylation of Glycals by Photoredox Catalysis. *Org. Lett.* **2015**, *17*, 5698–5701.

27 Ansari, A. A.; Vankar, Y. D. Synthesis of pyrrolidine iminosugars, (−)-lentiginosine, (−)-swainsonine and their 8a-epimers from d-glycals. *RSC Adv.* **2014**, 4, 12555-12567.

28 Yalamanchili, S.; Lloyd, D., Bennett, C. S. Synthesis of the Hexasaccharide Fragment of Landomycin A Using a Mild, Reagent-Controlled Approach. *Org. Lett.* **2019**, *21*, 3674–3677.

29 Lellouche, J-P.; Koeller, S. The Particular Sensitivity of Silyl Ethers of D-Glucal toward Two Vilsmeier-Haack Reagents $POCl_3$·DMF and $(CF_3SO_2)_2O$·DMF. Their Unique and Selective Conversion to the Corresponding C(6)-*O*-Formates. *J. Org. Chem.* 2001, *66*, 693-696.

30 Upreti, M.; Ruhela, D.; Vishwakarma, R. A. Synthesis of the tetrasaccharide cap domain of the antigenic lipophosphoglycan of Leishmania donovani parasite. *Tetrahedron*, 2000, *56*, 6577-6584.

31 Xiao, R; Zeng, J; Grinstaff, M. W. Biologically Active Branched Polysaccharide Mimetics: Synthesis via Ring-Opening Polymerization of a Maltose-Based β-Lactam. *ACS Macro Lett*, 2018, *7*, 772-777.

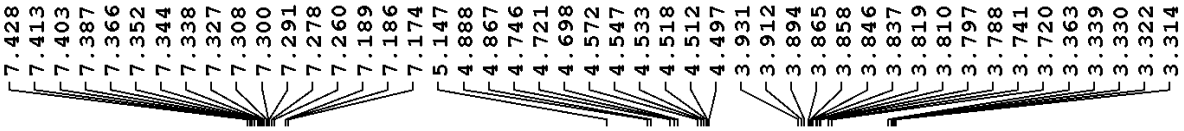
32 Hofferberth, Max. L.; Brueckner, Reinhard. α- and β-Lipomycin: Total Syntheses by Sequential Stille Couplings and Assignment of the Absolute Configuration of All Stereogenic Centers. *Angew. Chem, Int. Ed. Eng.* 2014, *53*, 7328-7334.

33 S15α was synthesized similar to the synthesis of S10α.

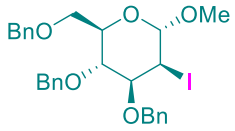
34 Lia, H. H.; Ye, X. S. Regio- and stereo-selective synthesis of aryl 2-deoxy-C-glycopyranosides by palladium-catalyzed Heck coupling reactions of glycals and aryl iodides. *Org. Biomol. Chem.*, 2009, *7*, 3855-3861.

35 Wang, R.; Wu, W-Q.; Li, N.; Shen, J.; Liu, K.; Yu, J. Bronsted Acids of Anionic Chiral Cobalt(III) Complexes as Catalysts for the Iodoglycosylation or Iodocarboxylation of Glycals. *Synlett*, 2019, *30*, 1077-1084.

36 Yamada, H.; Adachi, M.; Isobe, M.; Nishikawa, T. Stereocontrolled Total Synthesis of Polygalolide A. *Chem. Asian J.*, 2013, *8*, 1428-1435.

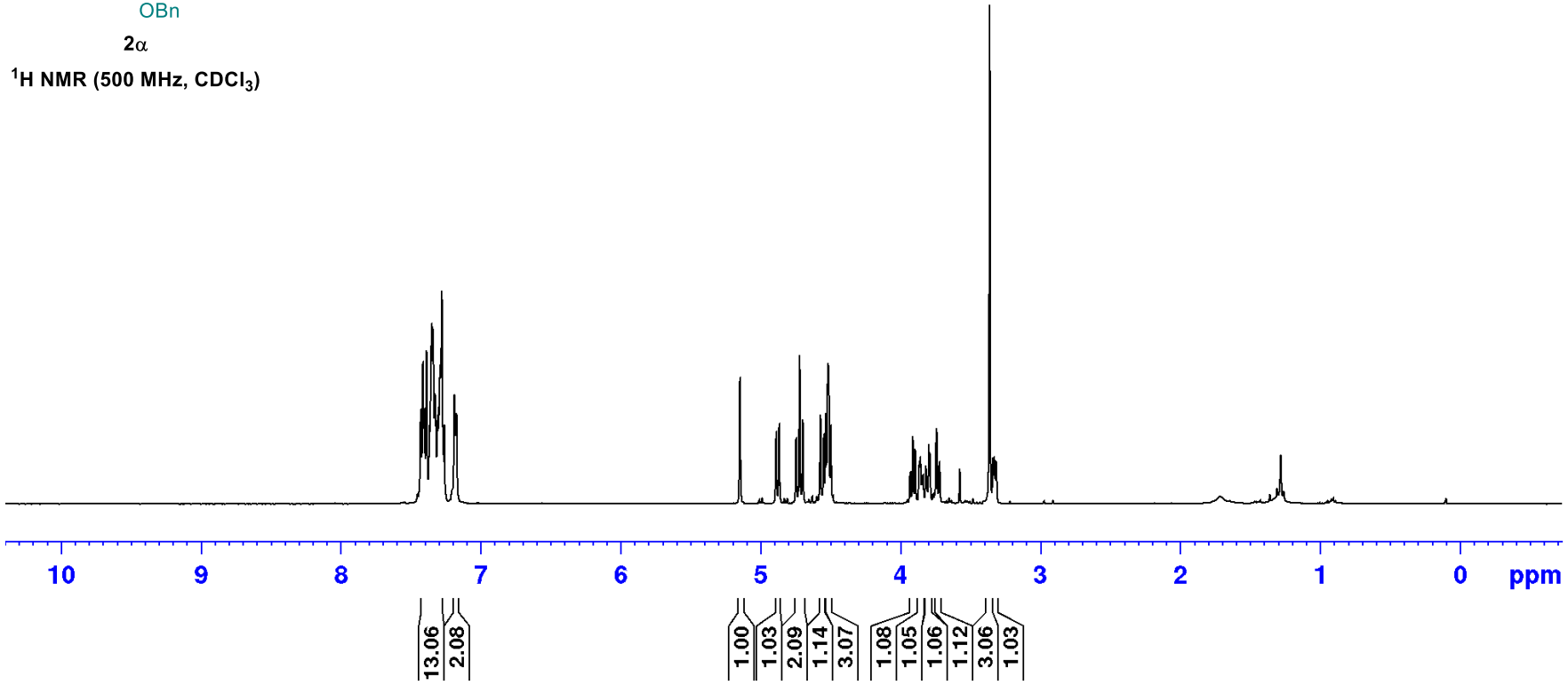


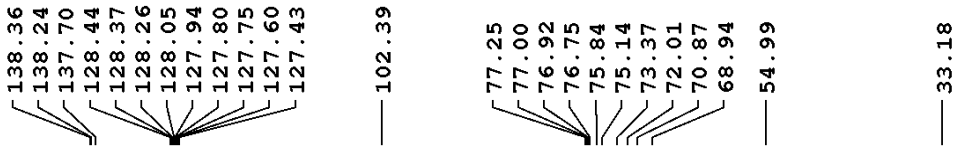
2.6 NMR Spectra

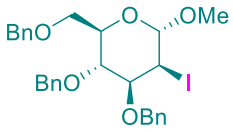


2α

^{1}H NMR (500 MHz, $CDCl_3$)

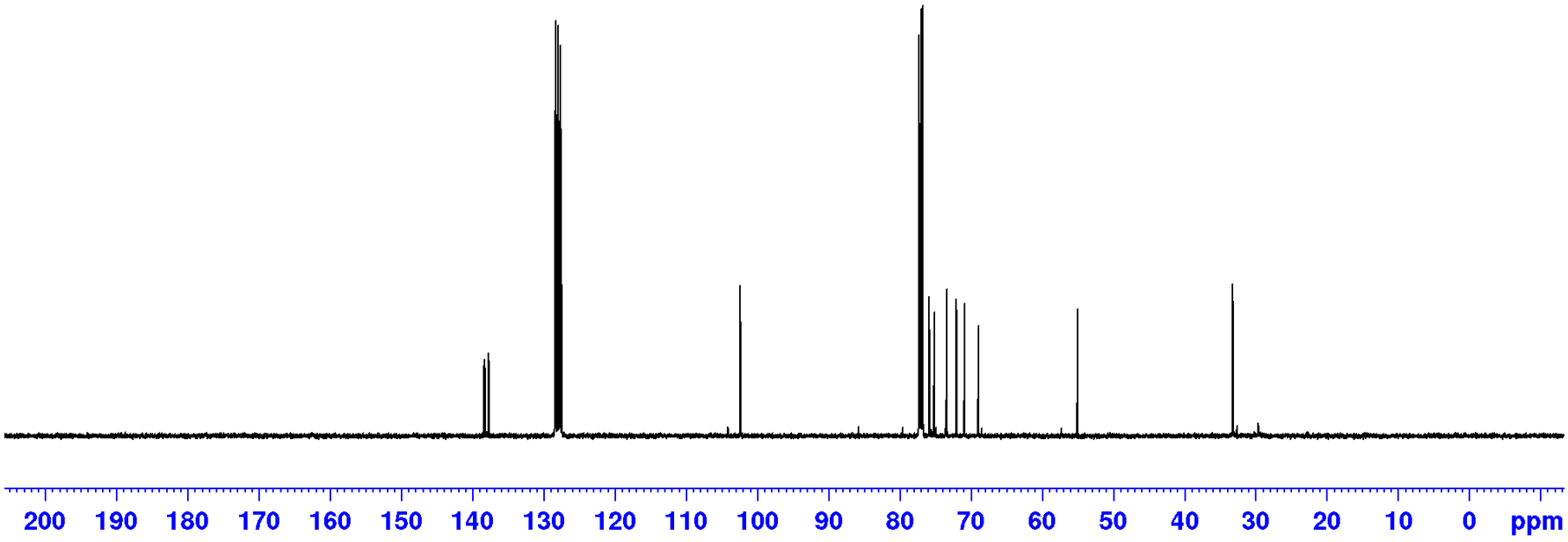


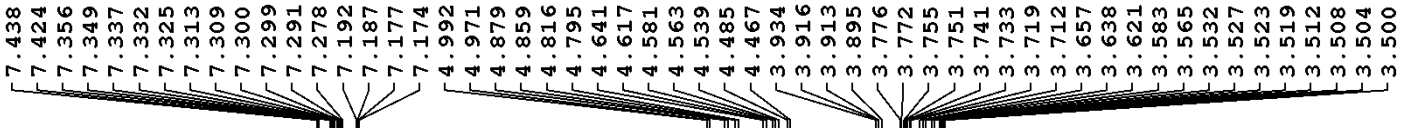


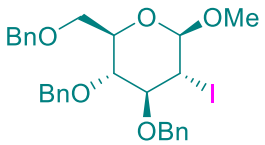


2α

$^{13}C\{^{1}H\}$ NMR (125 MHz, $CDCl_3$)

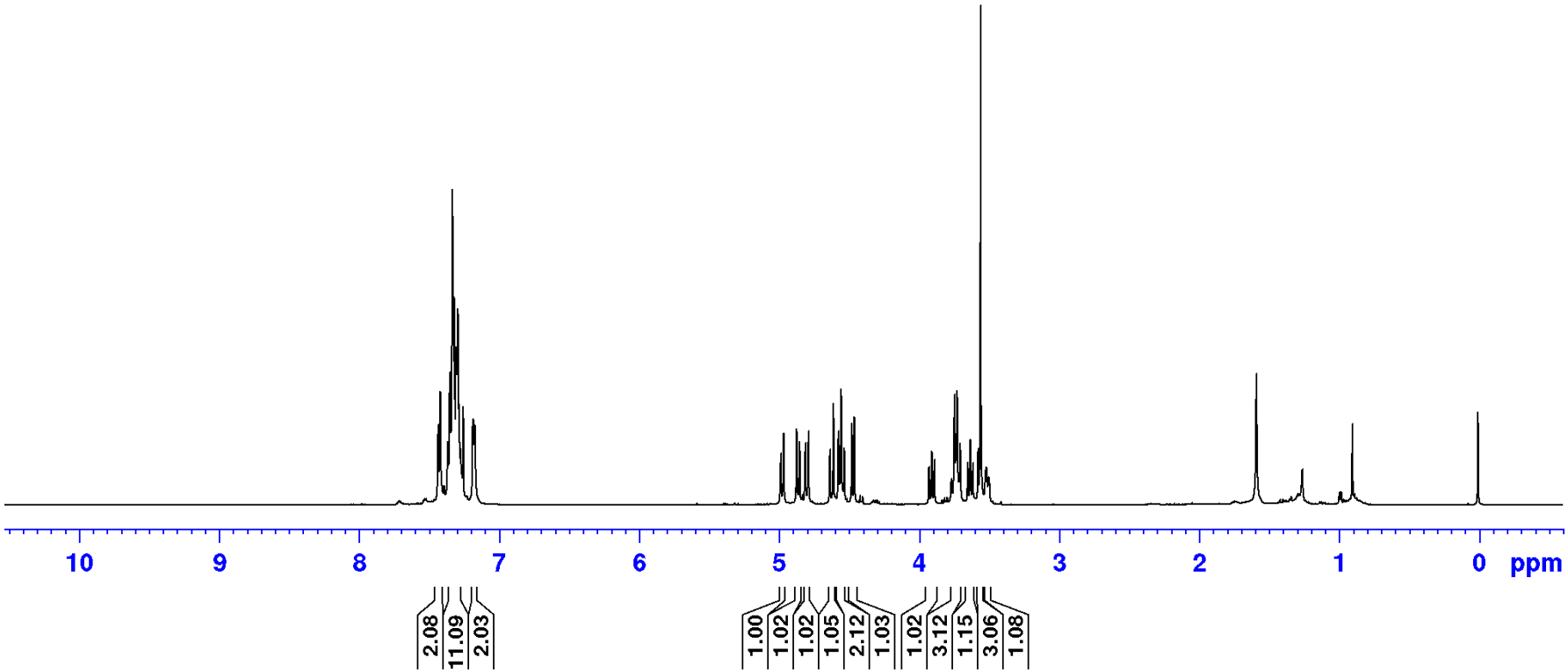


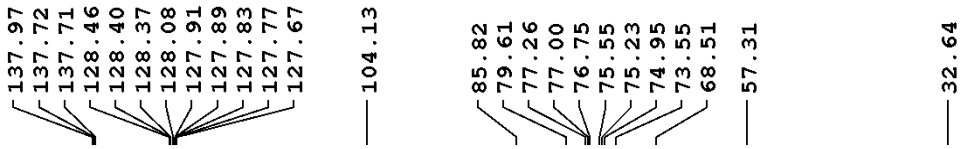


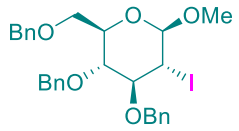


2β

^{1}H NMR (500 MHz, $CDCl_3$)

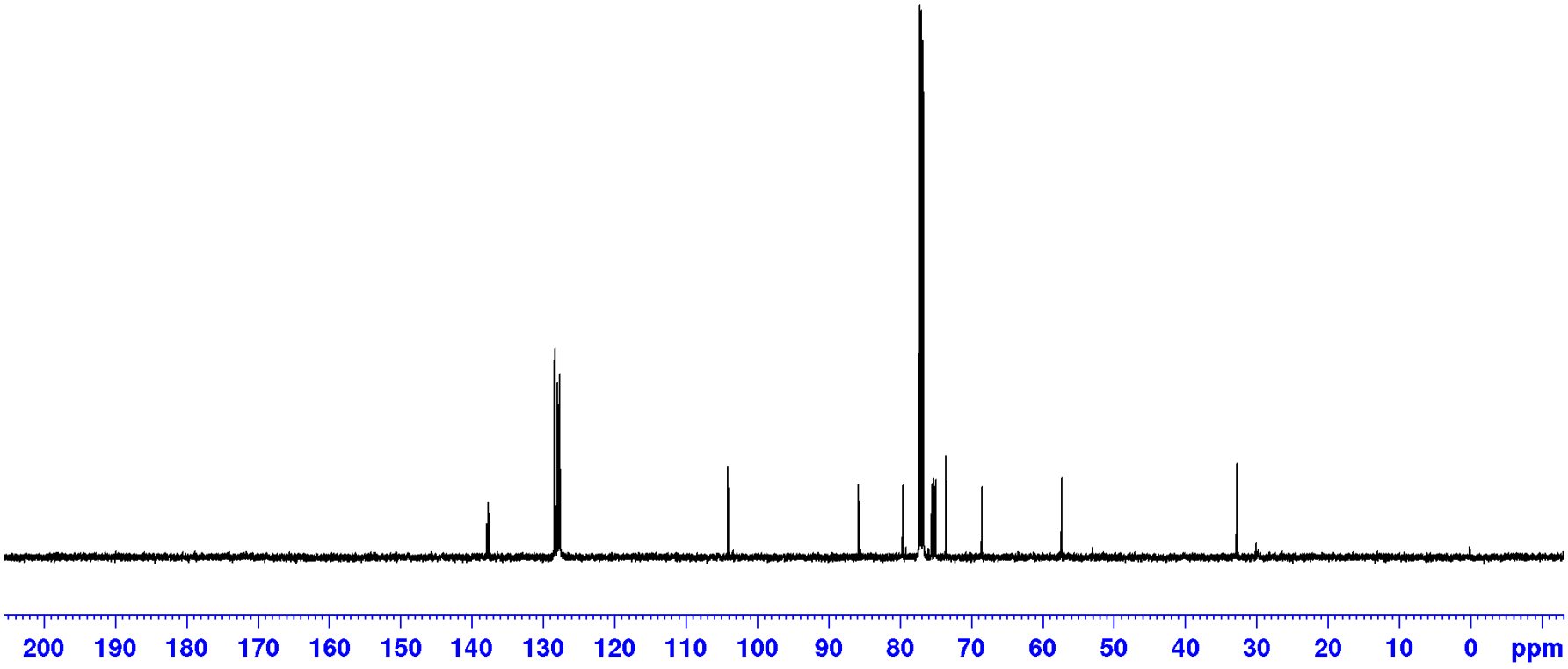


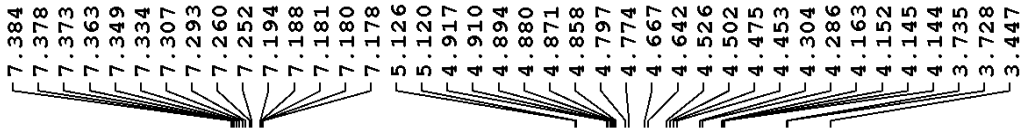


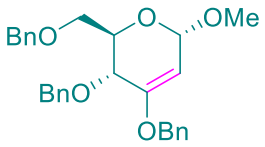


2β

$^{13}C\{^{1}H\}$ NMR (125MHz, $CDCl_3$)

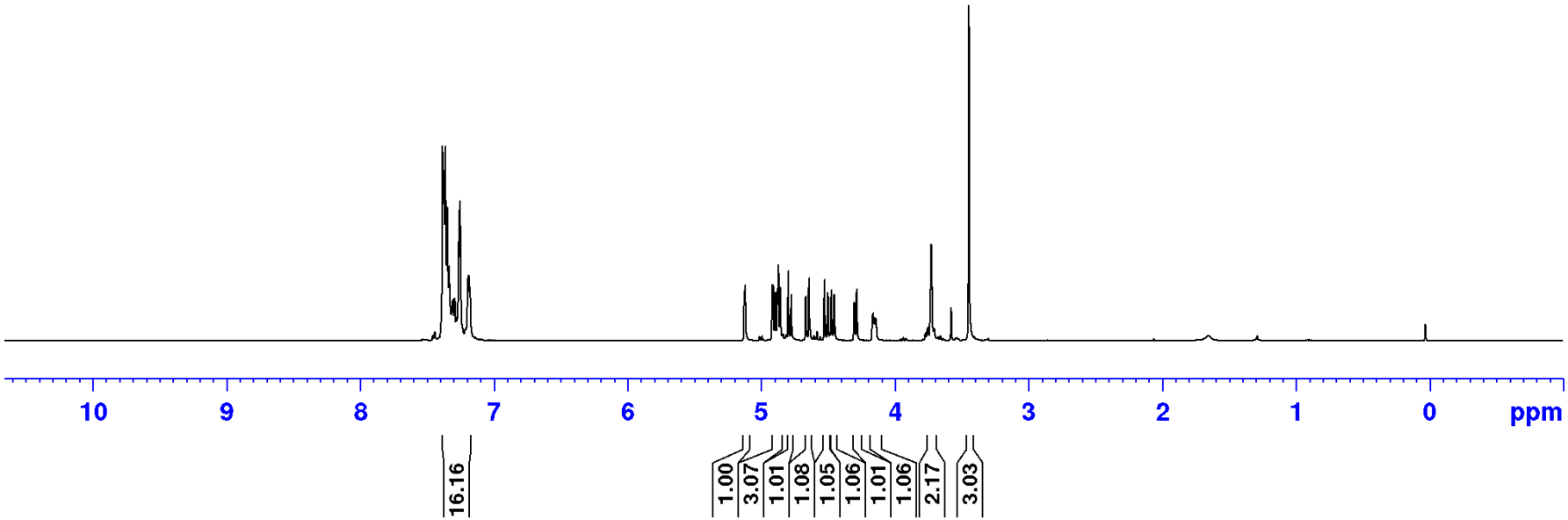


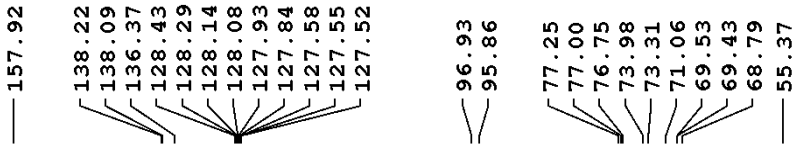


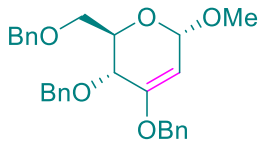


3

^{1}H NMR (500 MHz, $CDCl_3$)

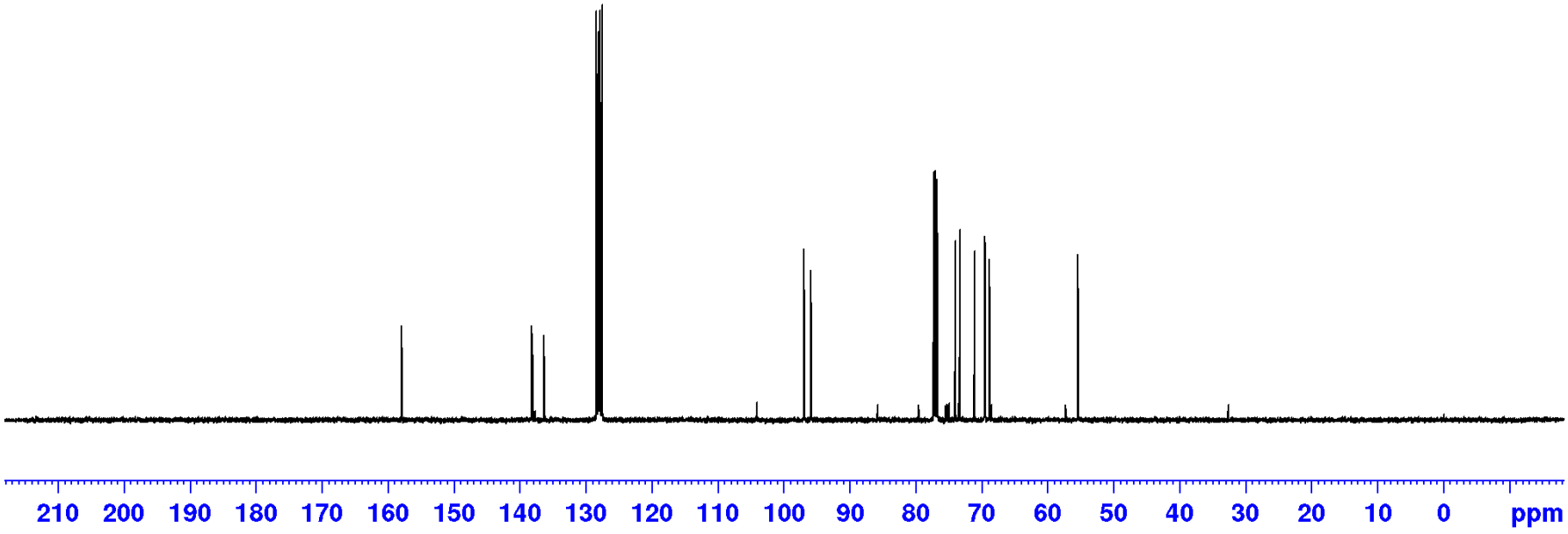


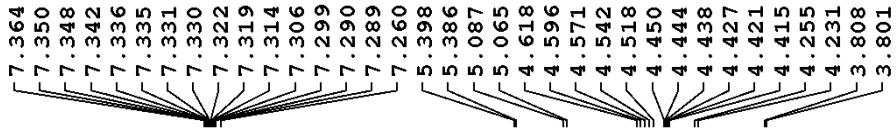


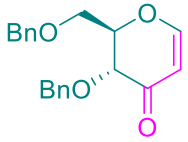


3

$^{13}C\{^{1}H\}$ NMR (125 MHz, $CDCl_3$)

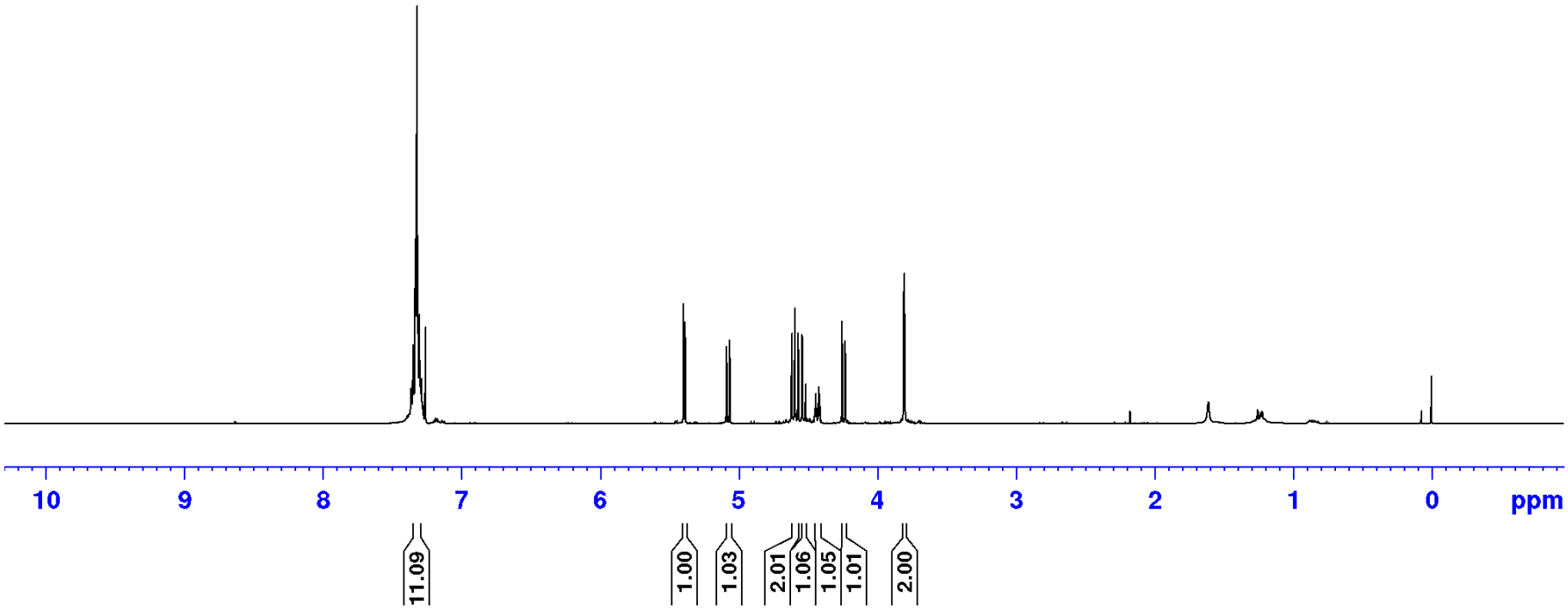


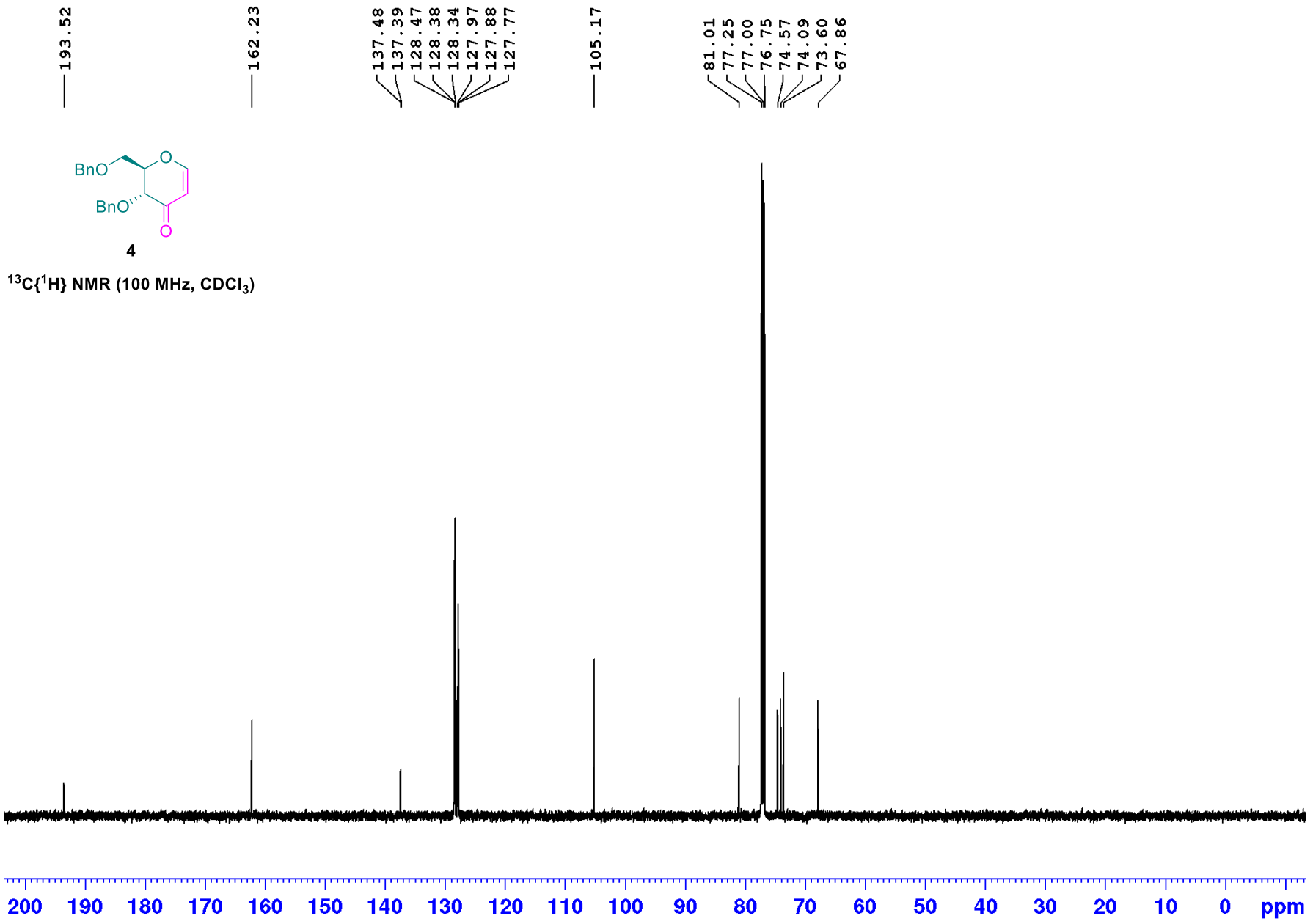


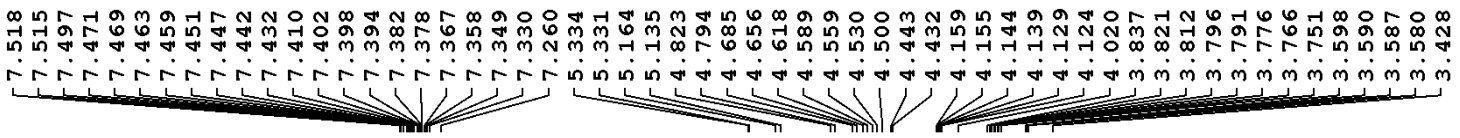


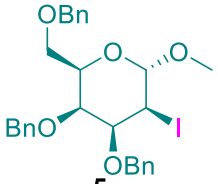
4

^{1}H NMR (400 MHz, $CDCl_3$)



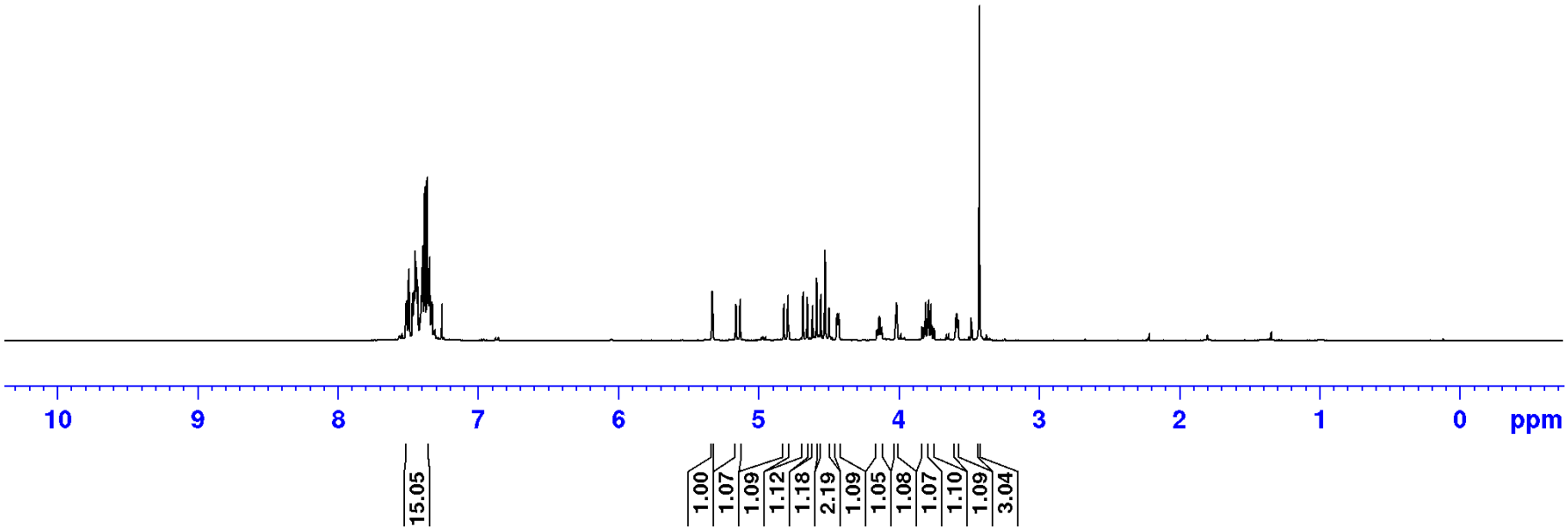

193.52
162.23
137.48
137.39
128.47
128.38
128.34
127.97
127.88
127.77
105.17
81.01
77.25
77.00
76.75
74.57
74.09
73.60
67.86
BnO
BnO
O
O
4
13C{1H} NMR (100 MHz, CDCl3)
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
ppm

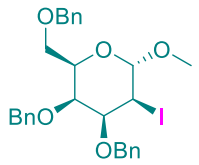




5α

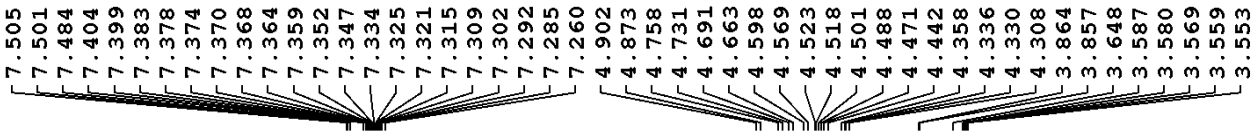
^{1}H NMR (400 MHz, $CDCl_3$)

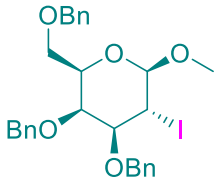




5α

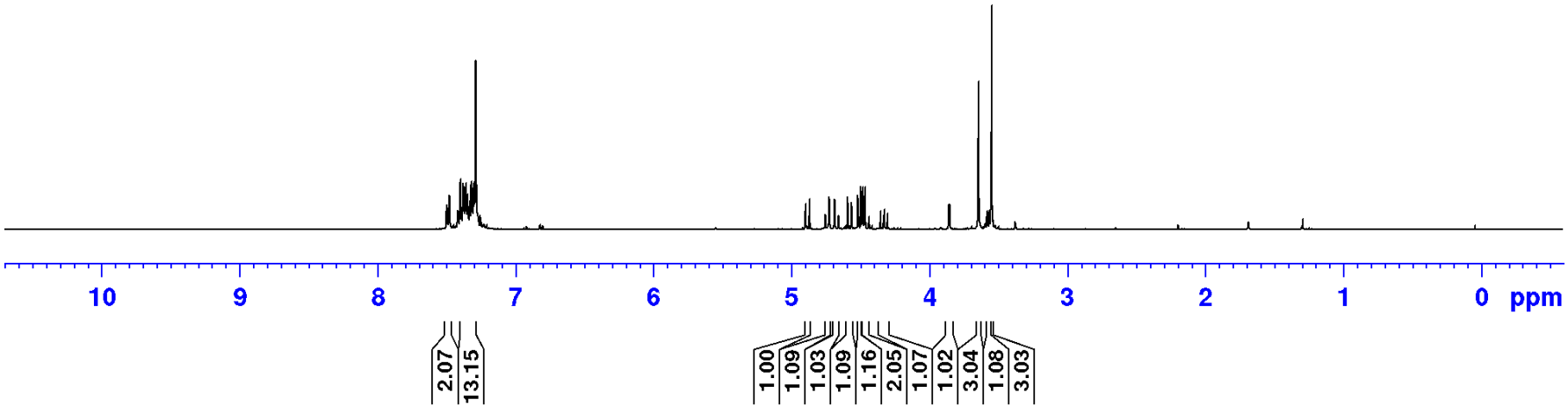
$^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$)

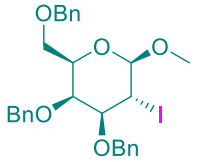




5β

^{1}H NMR (400 MHz, $CDCl_3$)

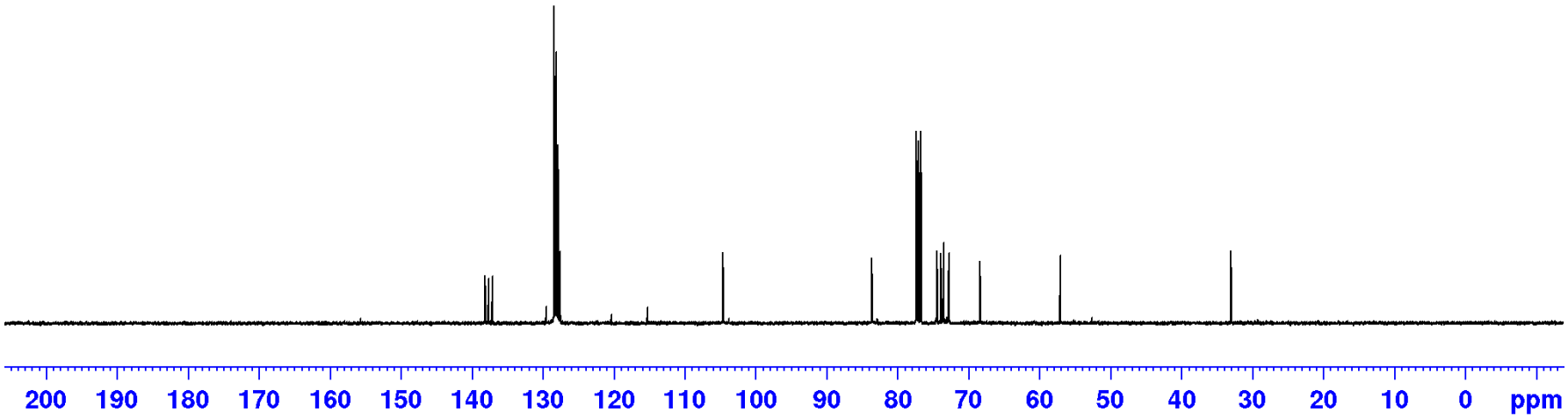


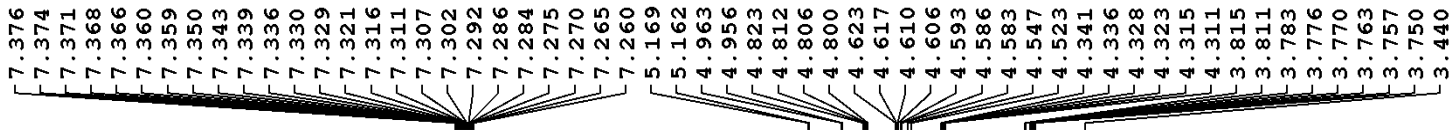


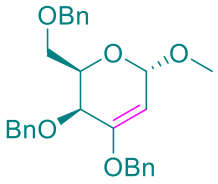
5β

$^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$)

138.12
137.66
137.12
128.38
128.17
128.15
127.96
127.83
127.80
127.59
104.59
83.63
77.32
77.00
76.68
74.44
73.86
73.50
72.80
72.71
68.38
57.07
32.98

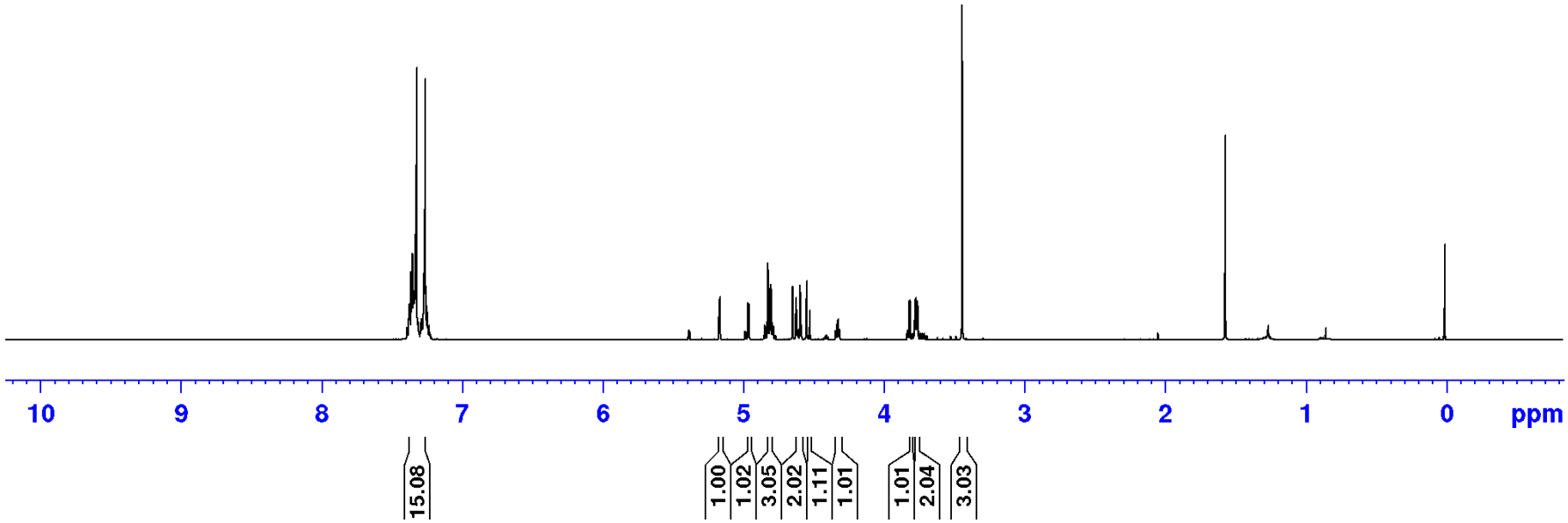


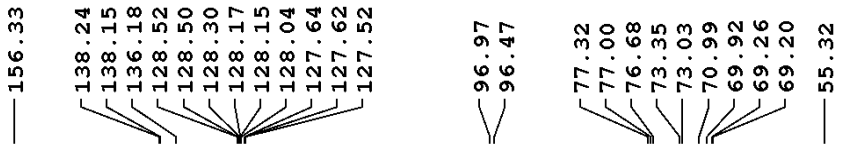


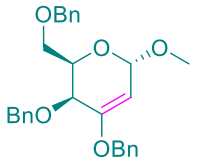


6

^{1}H NMR (500 MHz, $CDCl_3$)

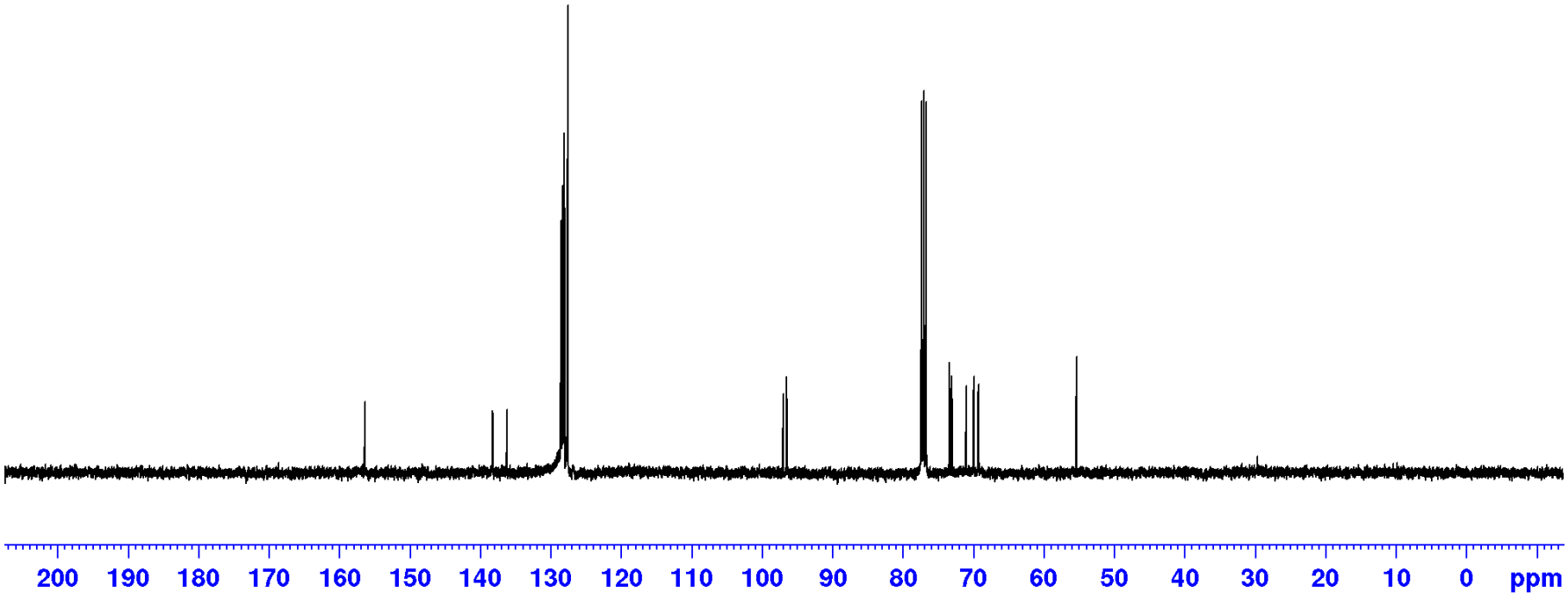


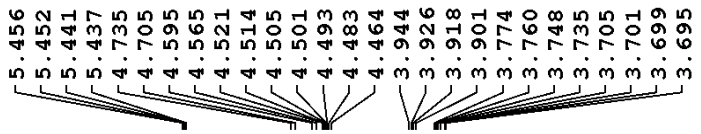


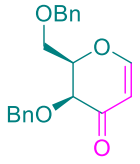


6

$^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$)

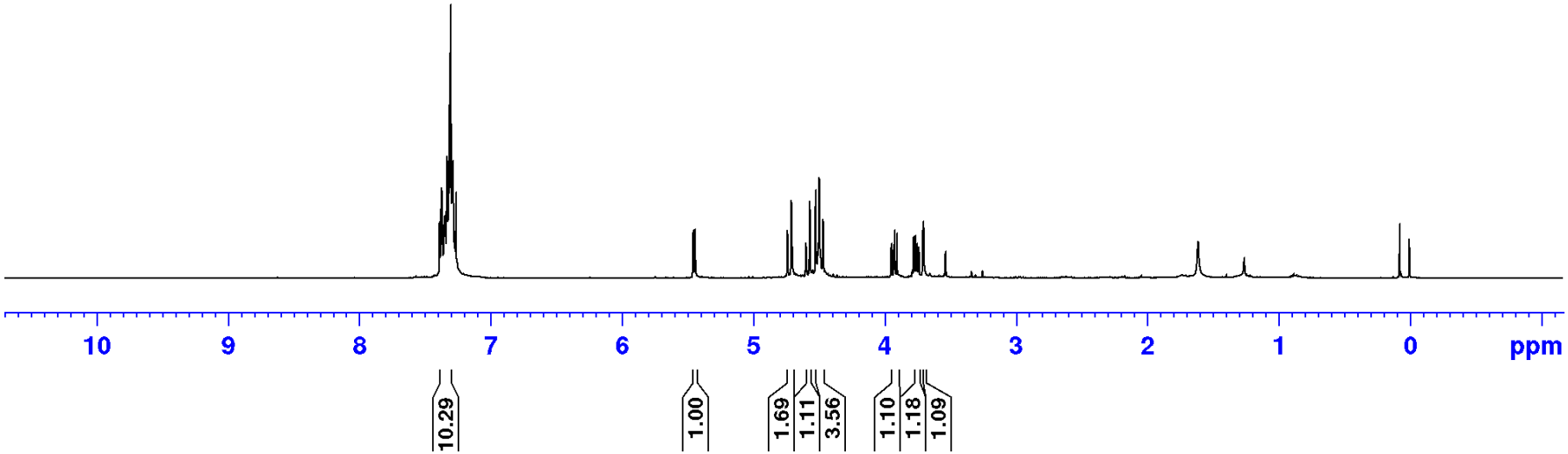


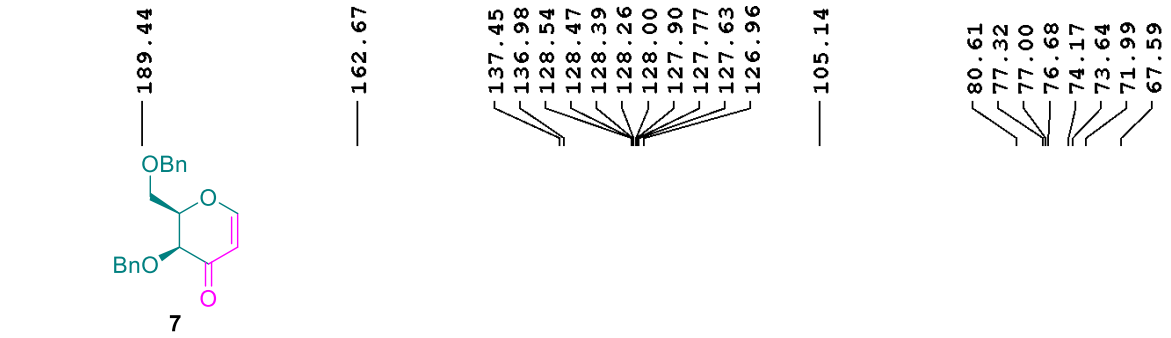




7

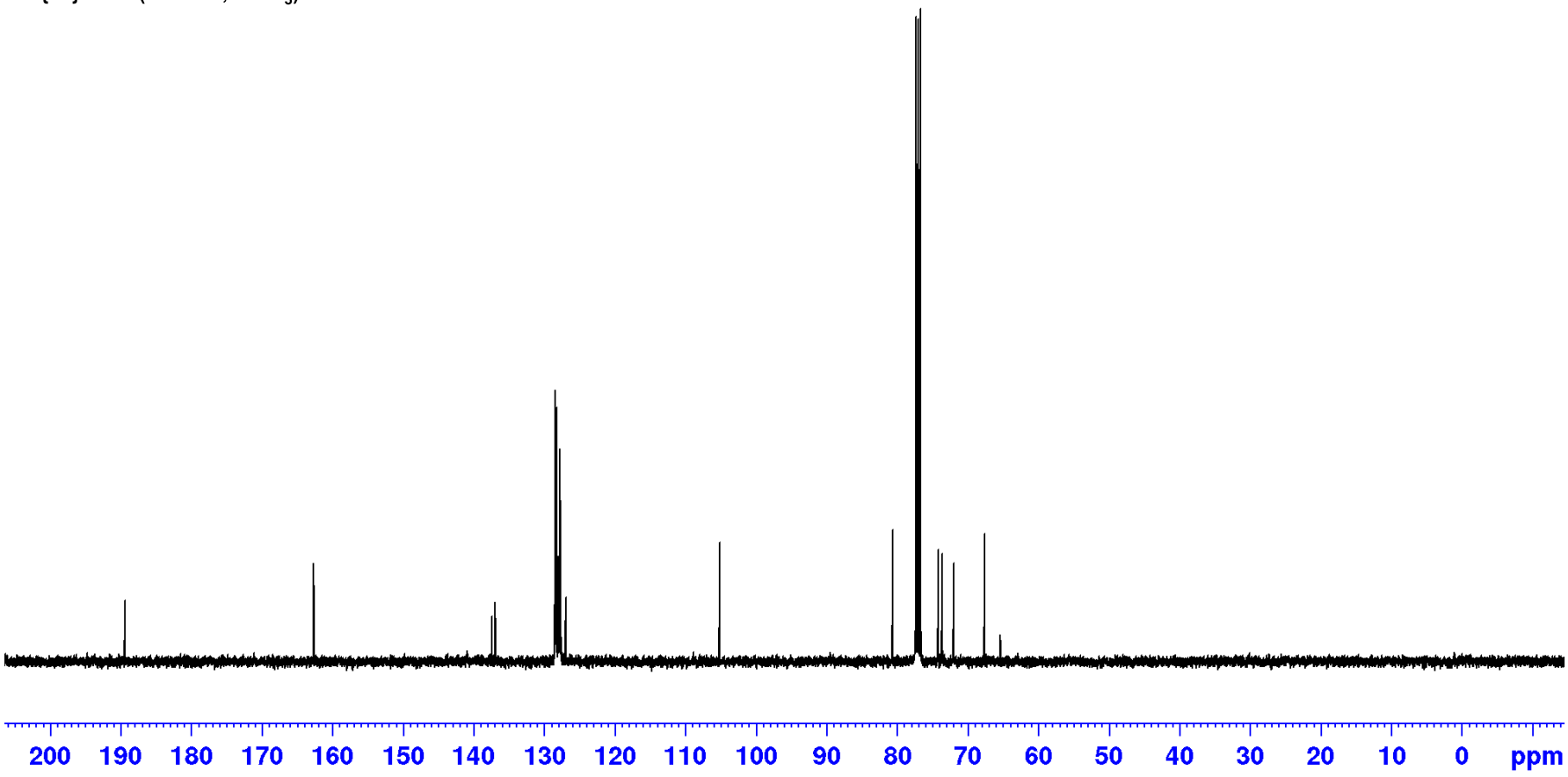
^{1}H NMR (400MHz, $CDCl_3$)

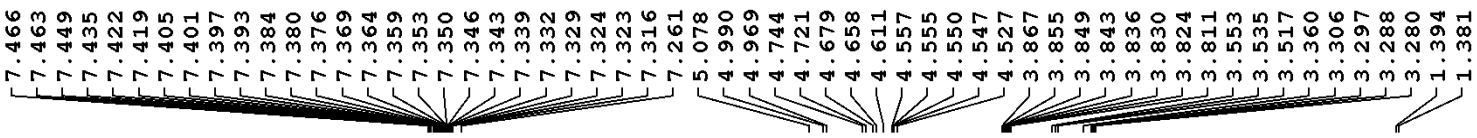


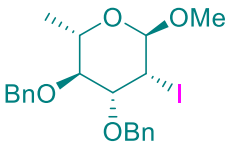


7

$^{13}C\{^{1}H\}$ NMR (100MHz, $CDCl_3$)

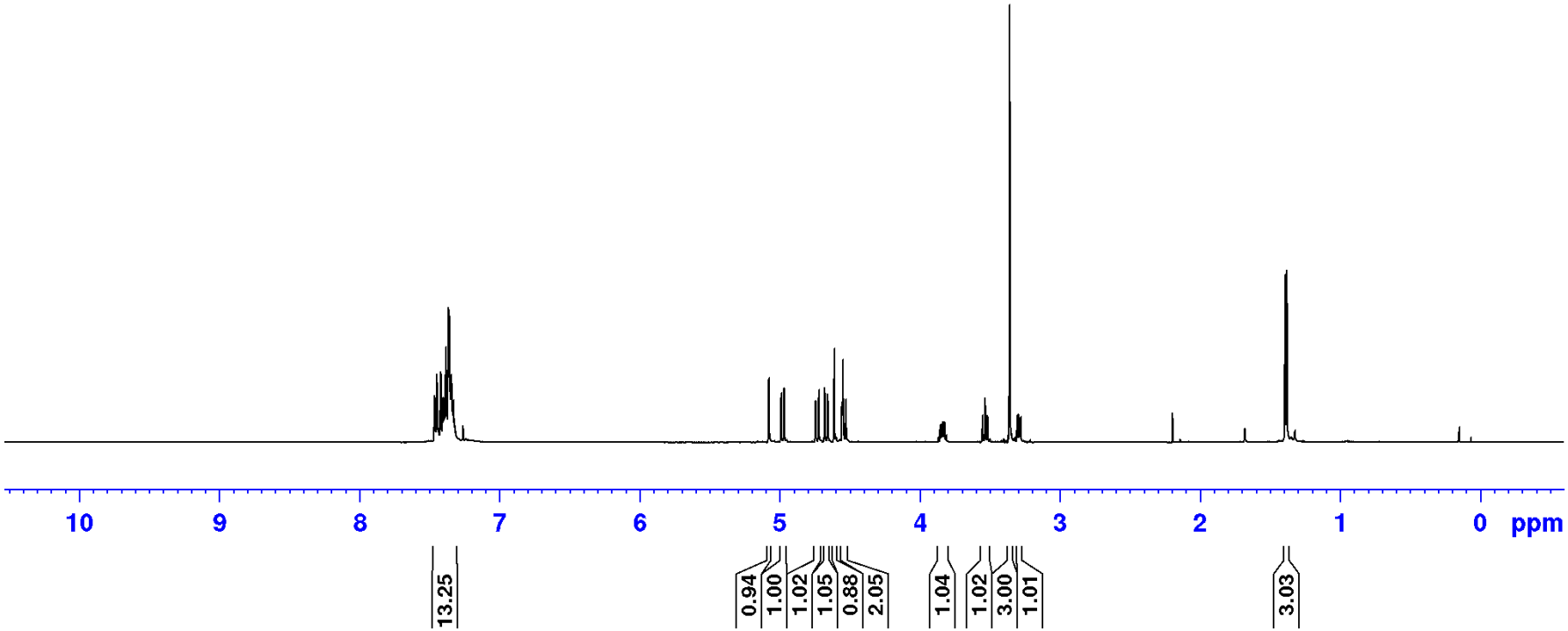


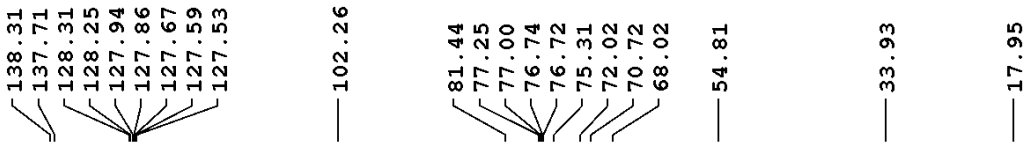


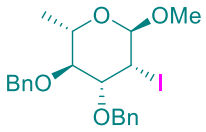


8α

^{1}H NMR (500 MHz, $CDCl_3$)

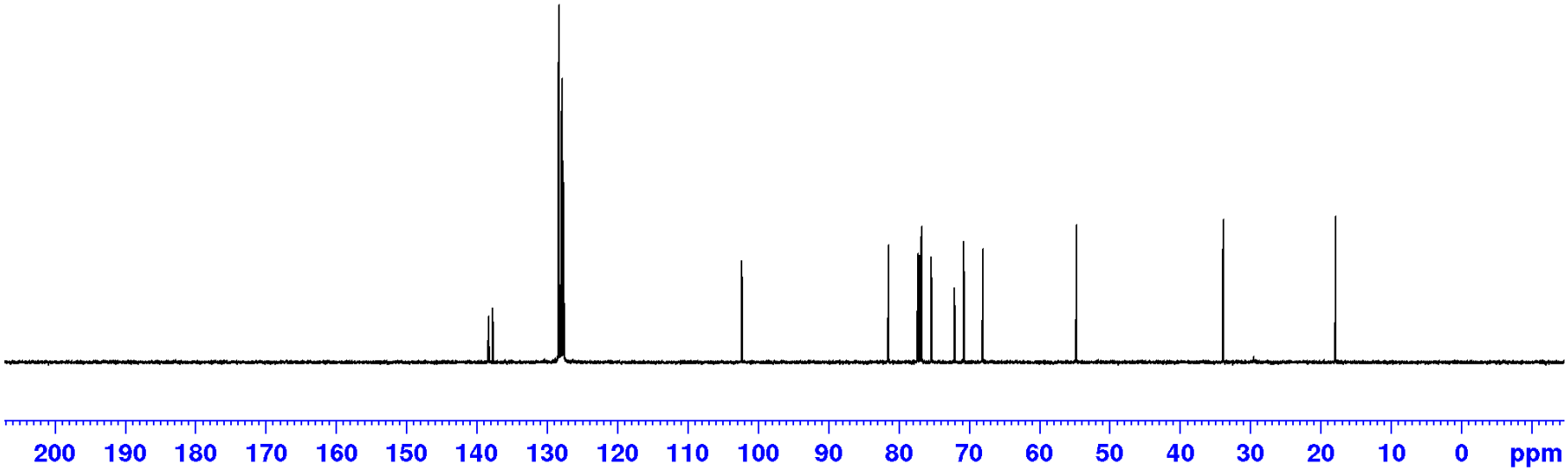


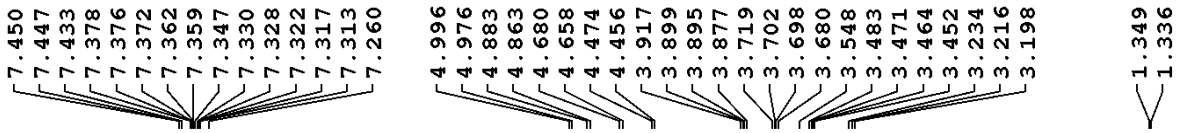


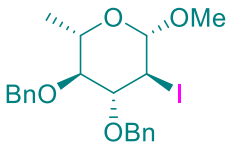


8α

$^{13}C\{^{1}H\}$ NMR (125 MHz, $CDCl_3$)

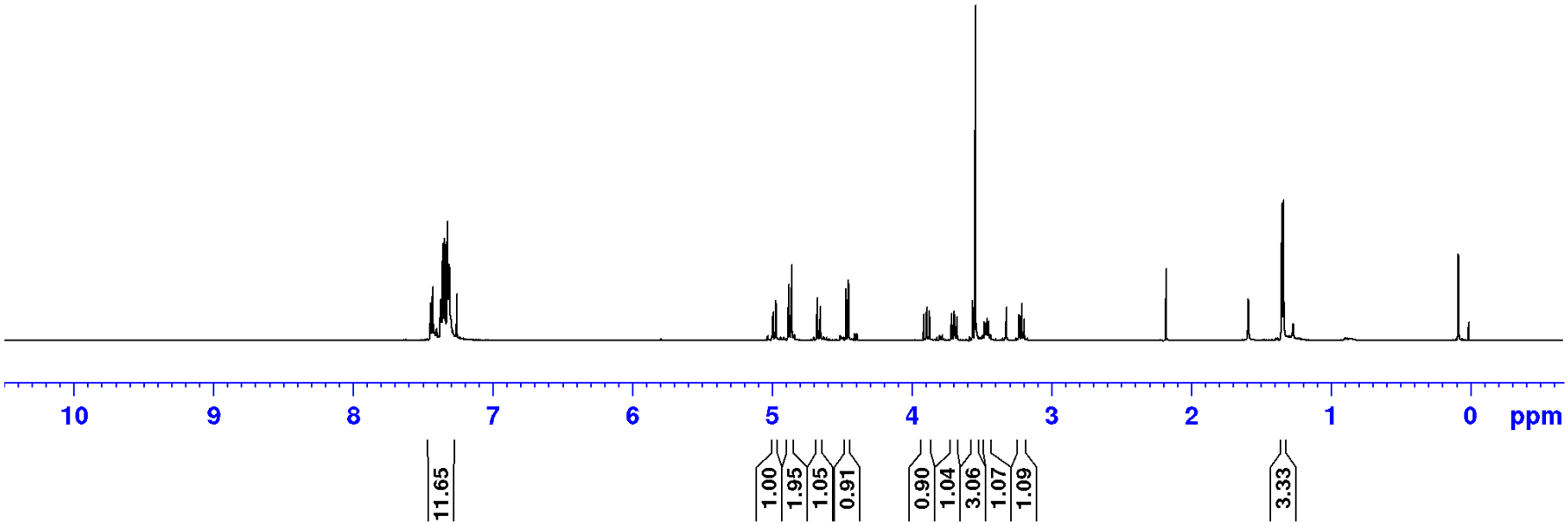


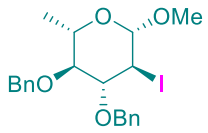




8β

^{1}H NMR (500 MHz, $CDCl_3$)

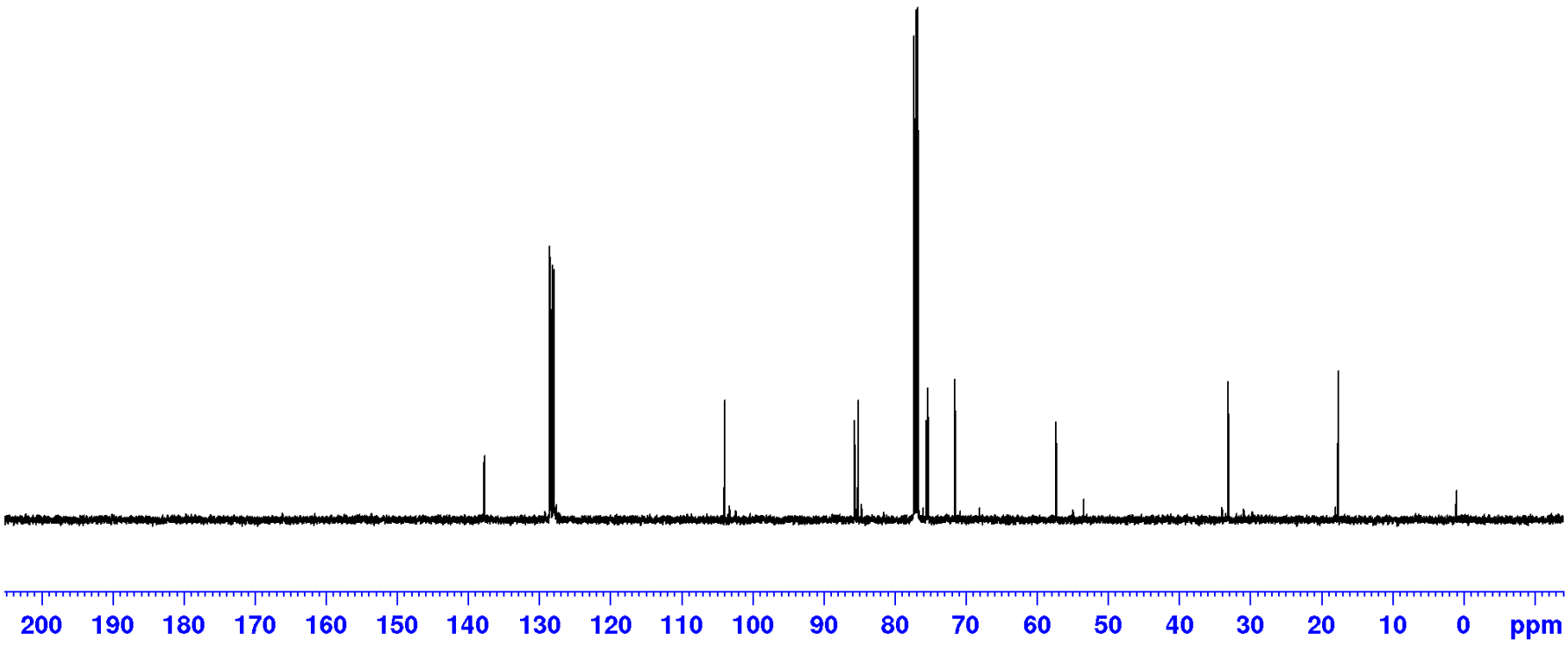


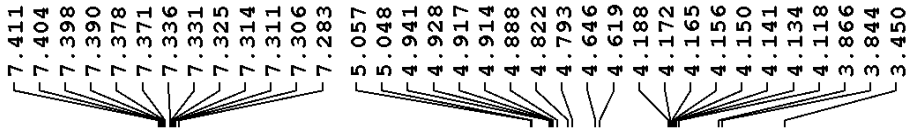


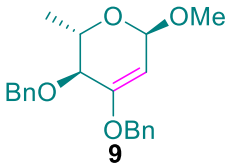
8β

$^{13}C\{^{1}H\}$ NMR (125 MHz, $CDCl_3$)

137.72
128.50
128.40
128.12
127.96
127.92
127.90
103.91
85.66
85.14
77.25
77.00
76.75
75.55
75.30
71.54
57.28
33.07
17.61

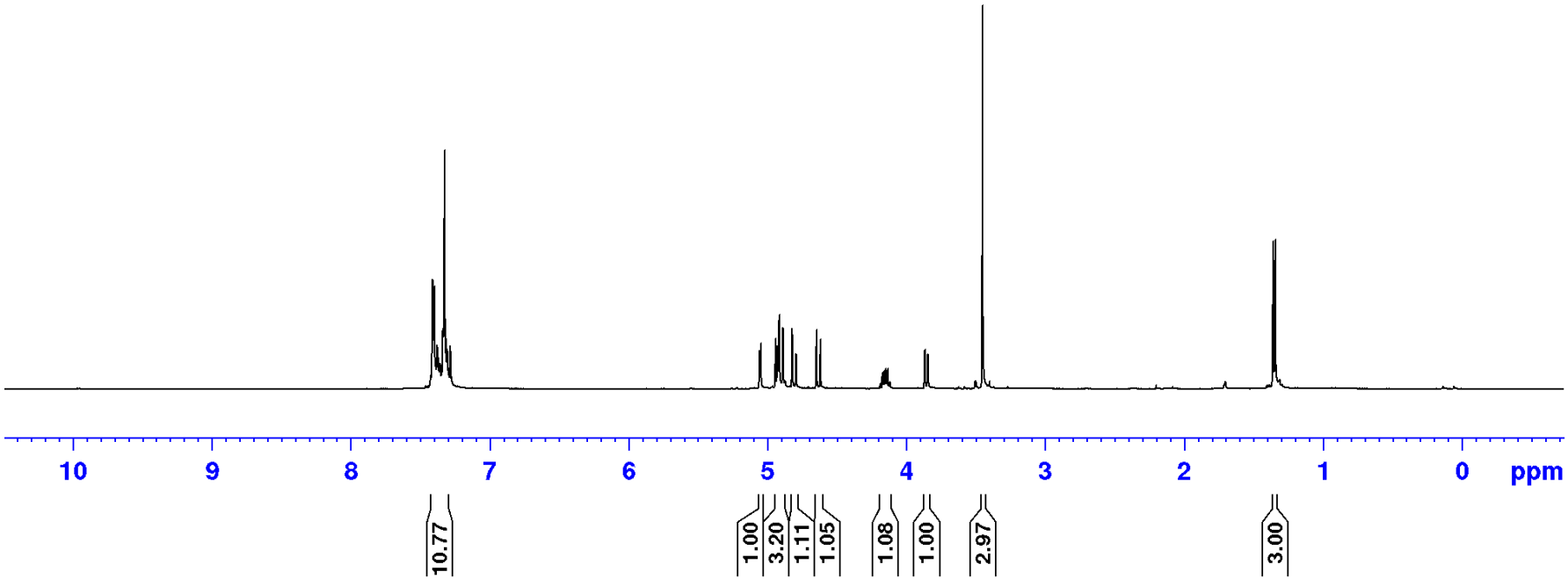


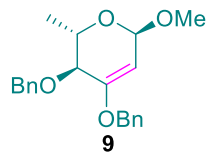




9

^{1}H NMR (400 MHz, $CDCl_3$)

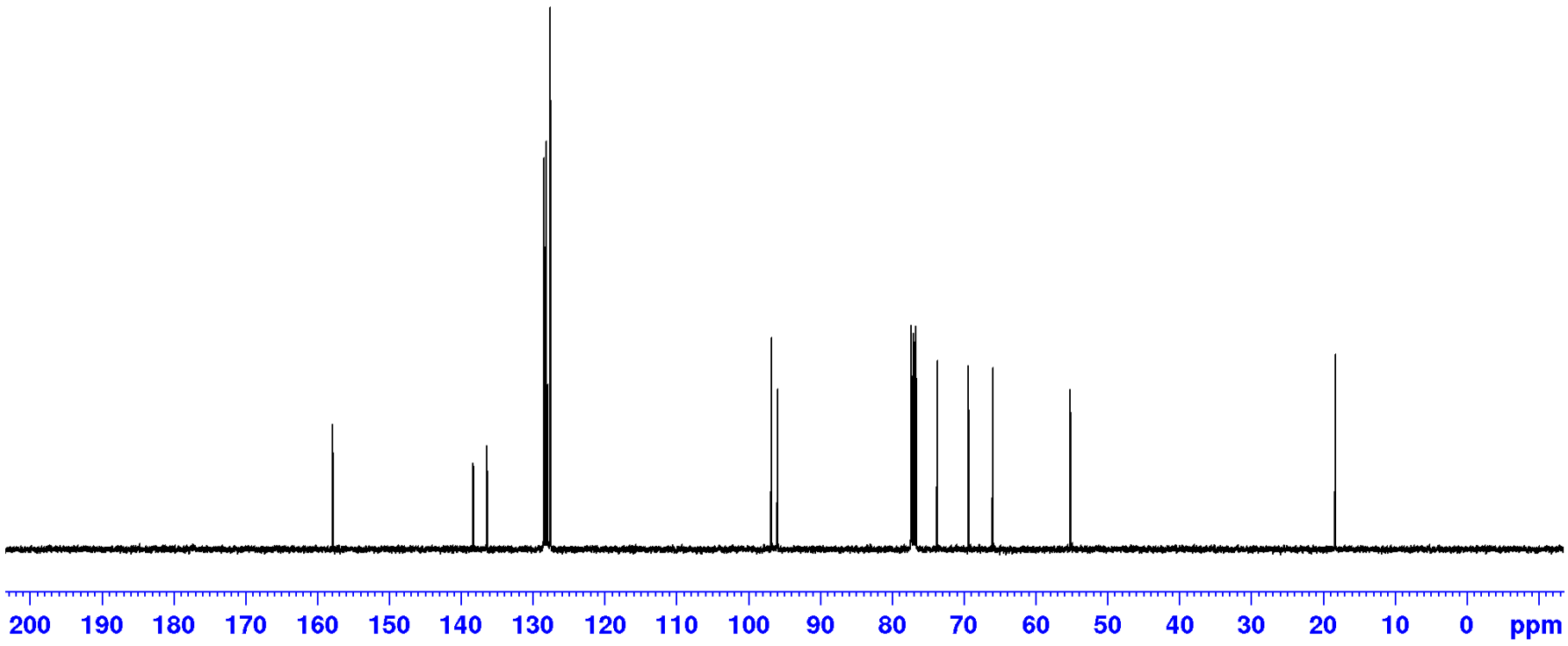


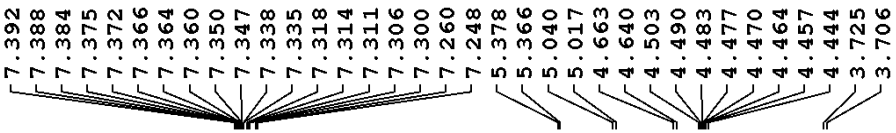


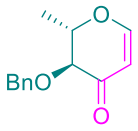
9

$^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$)

157.85
138.28
136.40
128.43
128.16
128.10
127.92
127.55
96.77
95.93
77.32
77.00
76.91
76.68
73.70
69.36
65.95
55.14
18.27

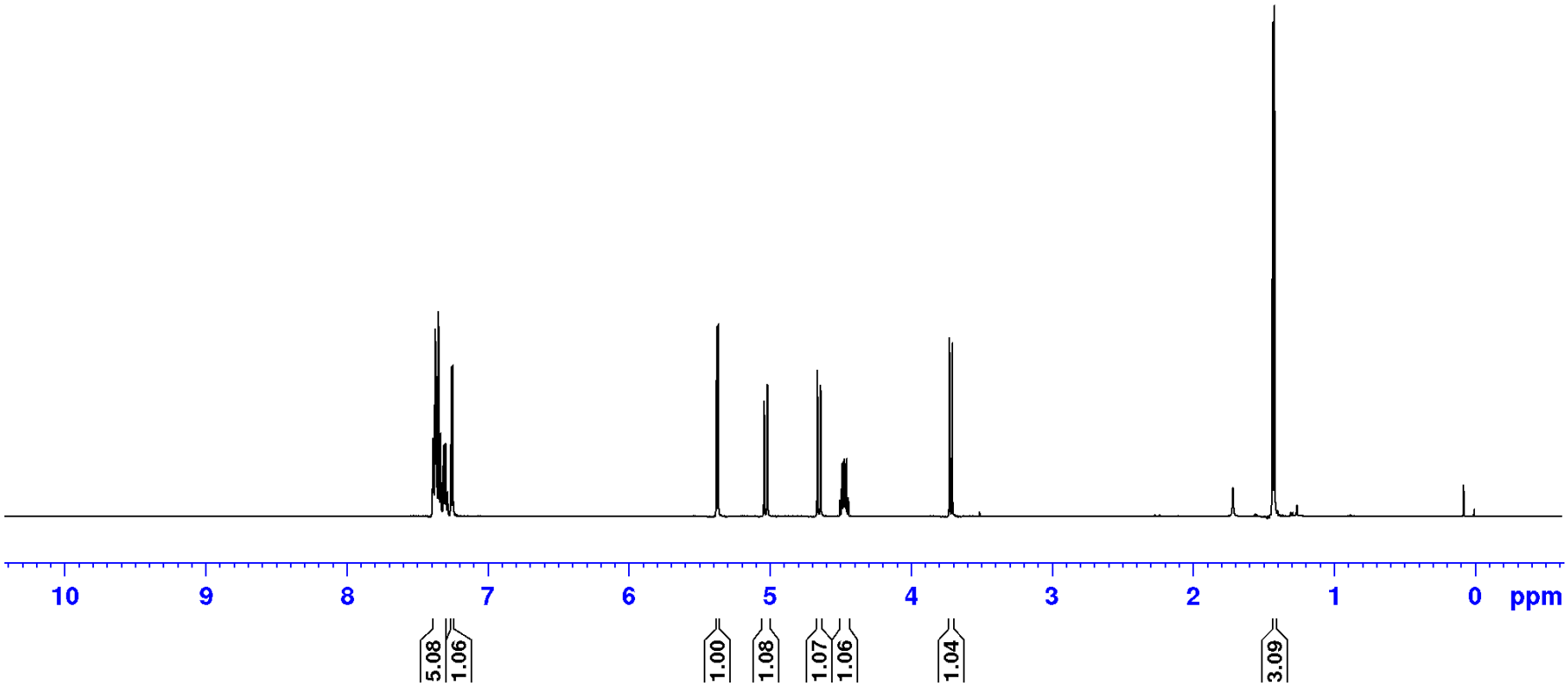


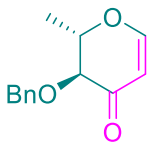




10

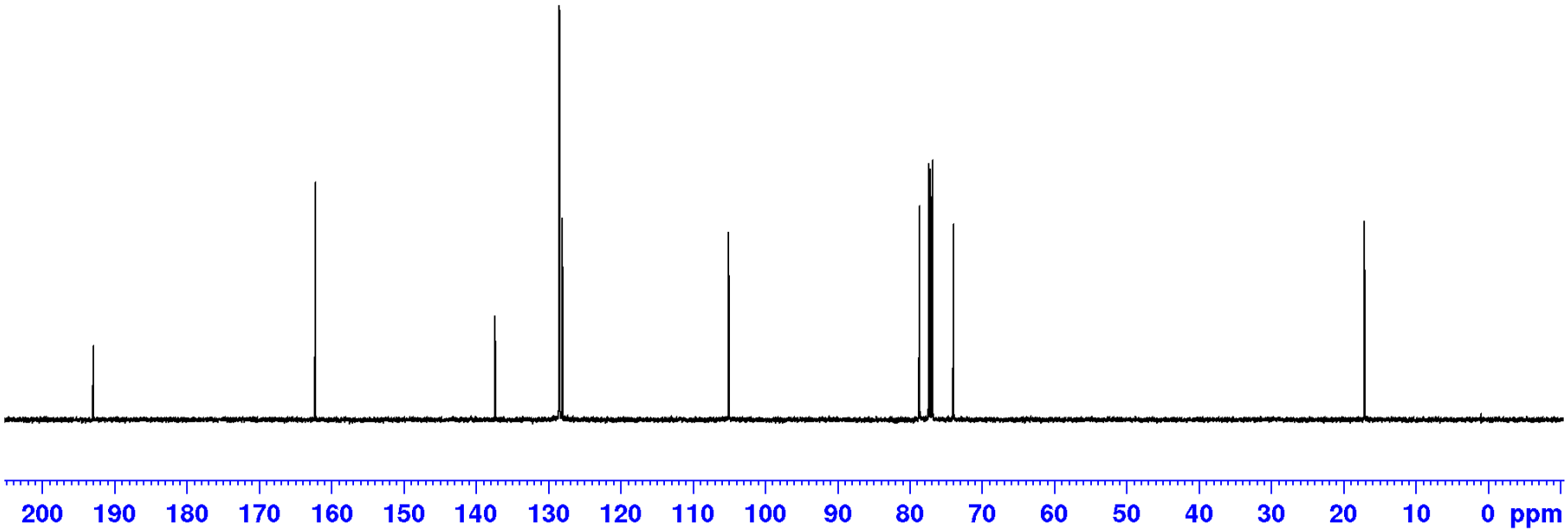
^{1}H NMR (500 MHz, $CDCl_3$)

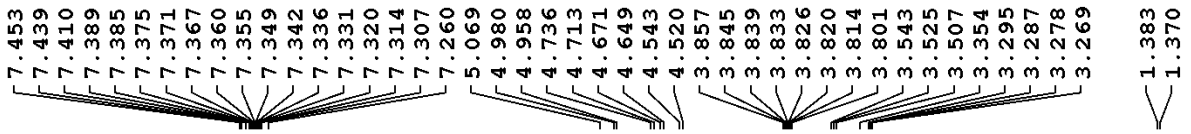


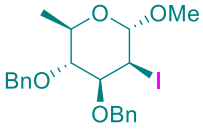


10

$^{13}C\{^{1}H\}$ NMR (125 MHz, $CDCl_3$)

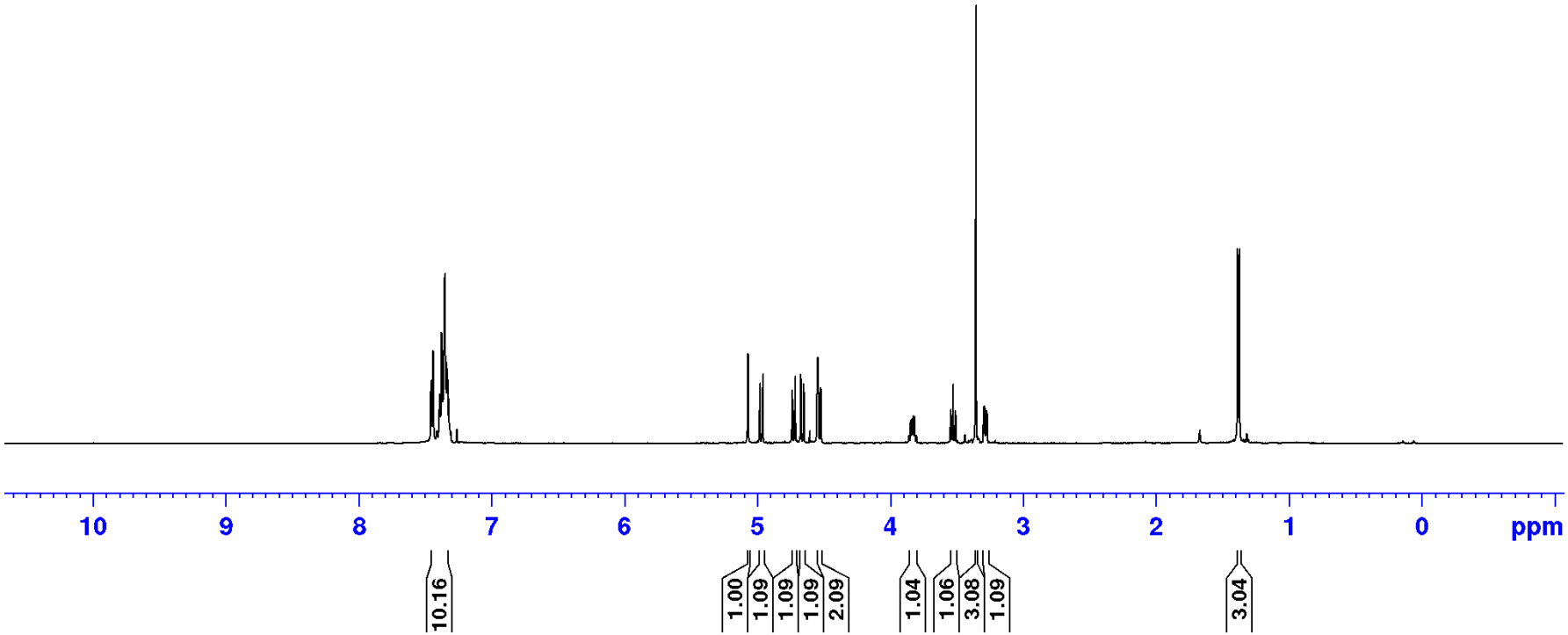


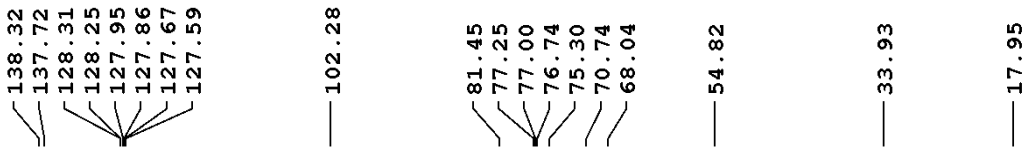


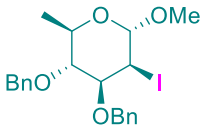


11α

^{1}H NMR (500 MHz, $CDCl_3$)

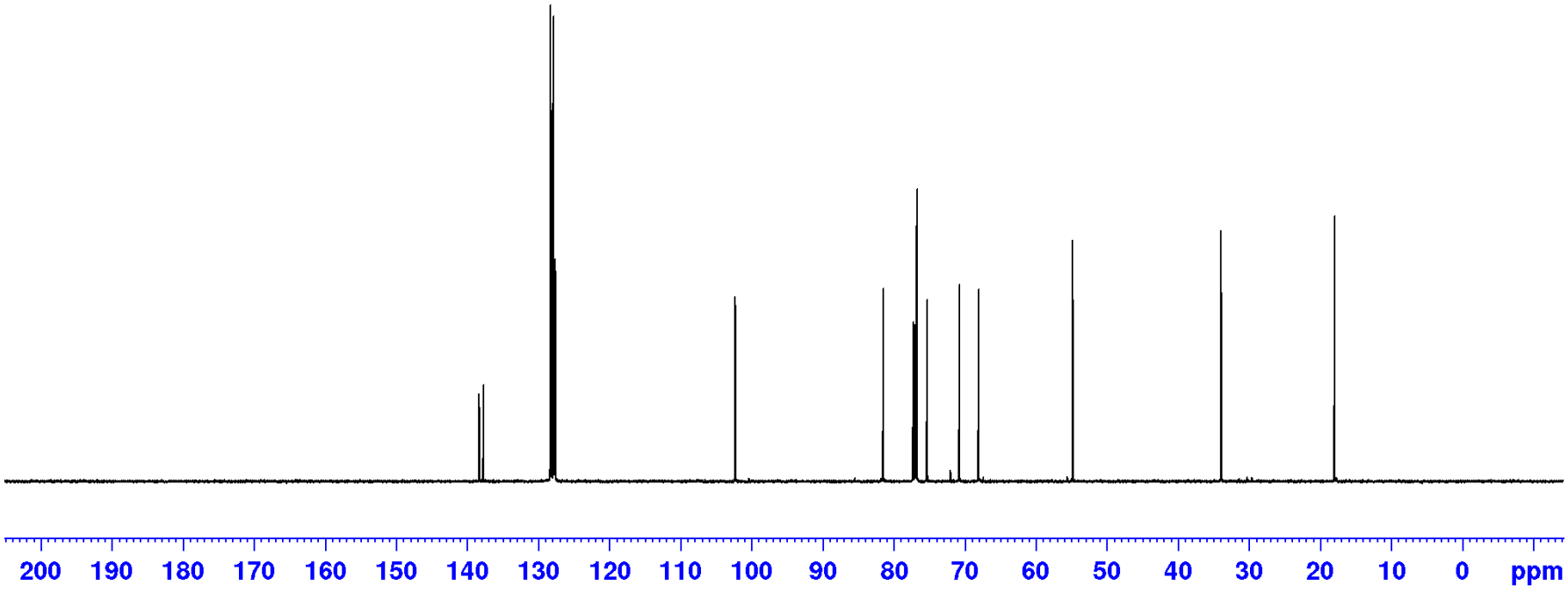


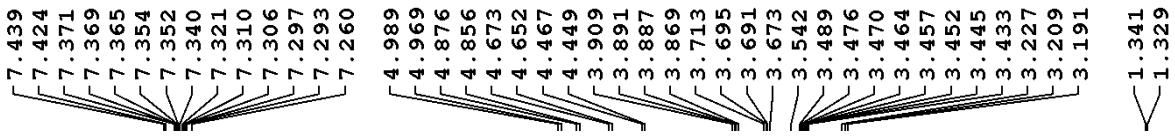


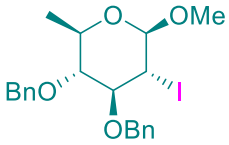


11α

$^{13}C\{^{1}H\}$ NMR (125 MHz, $CDCl_3$)

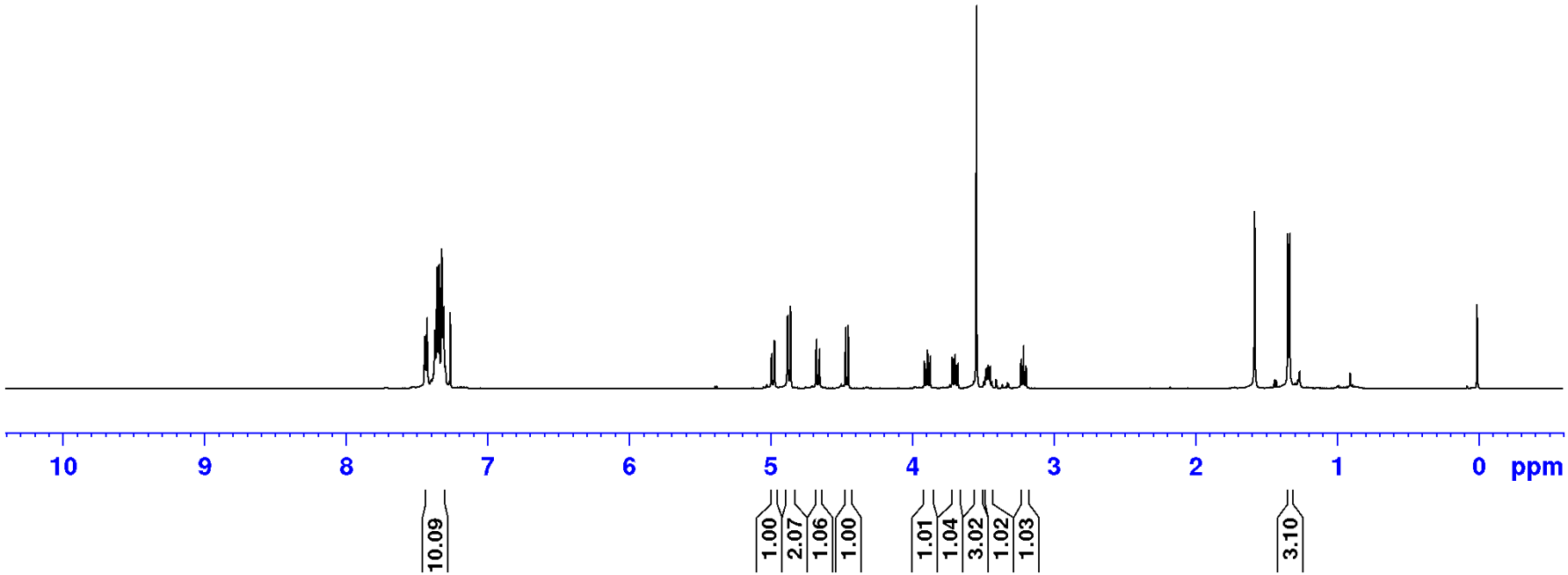


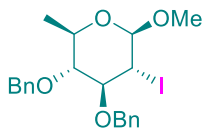




11β

^{1}H NMR (500 MHz, $CDCl_3$)



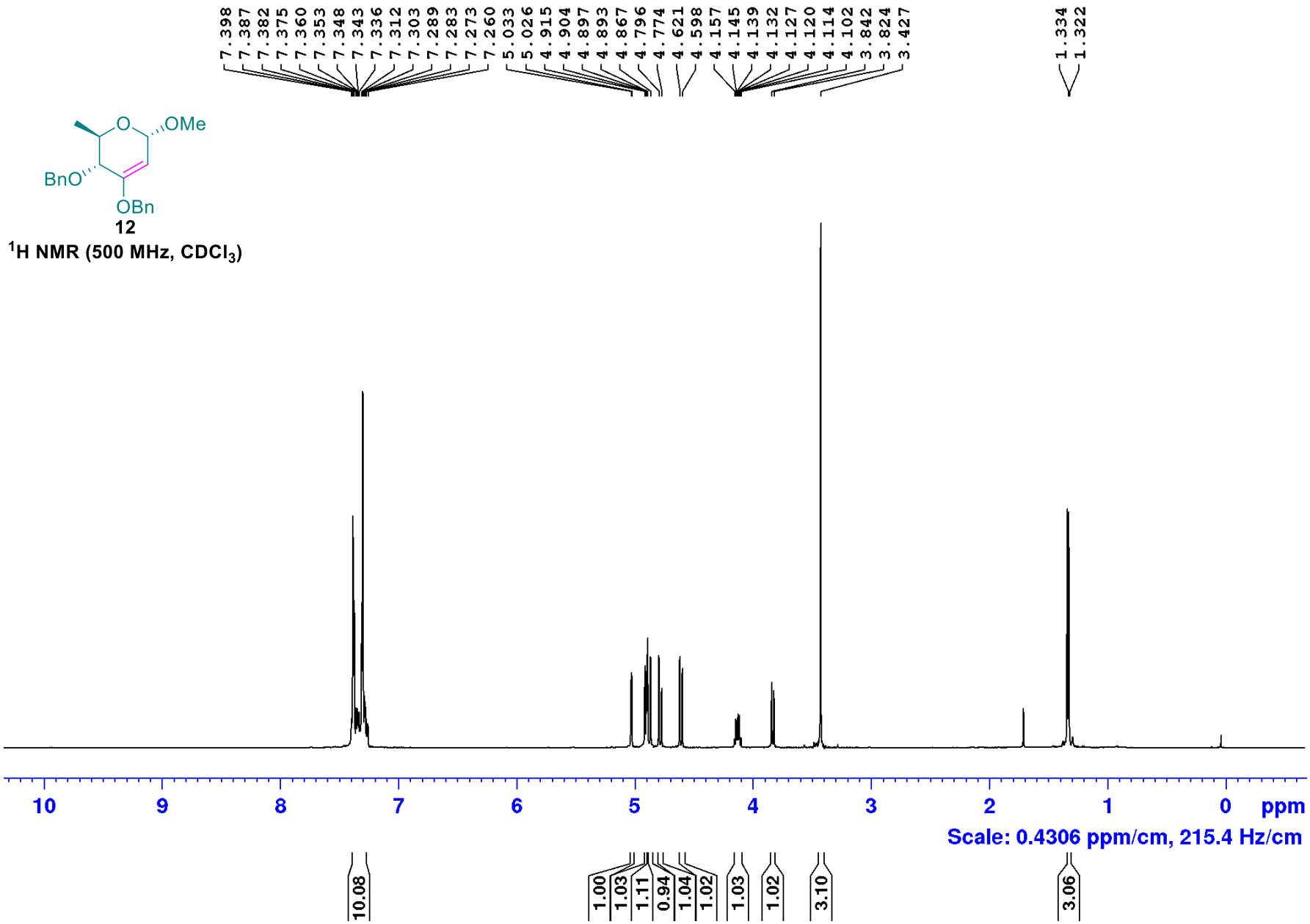


11β

$^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$)

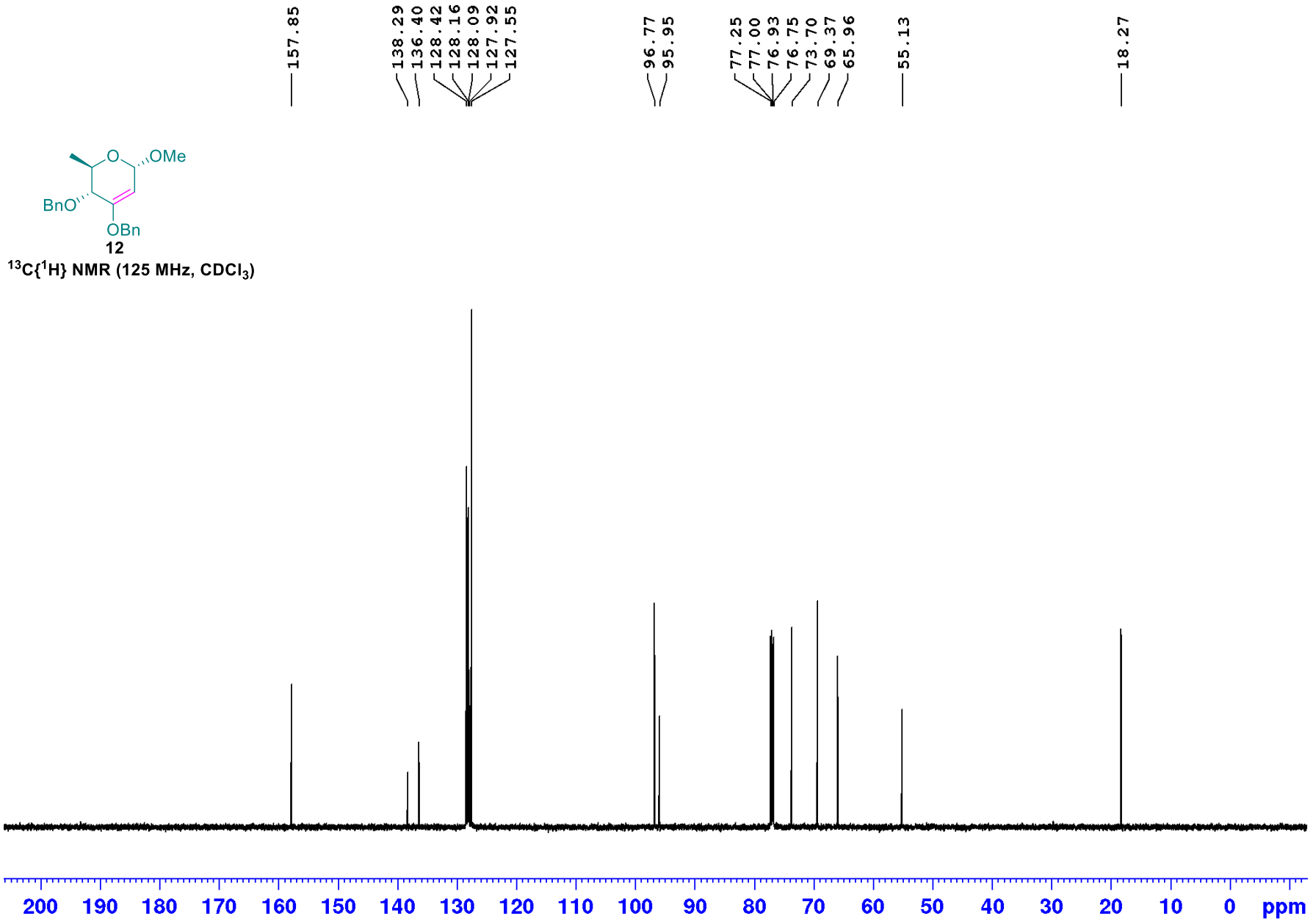
137.69
128.52
128.42
128.14
127.91
103.89
85.63
85.12
77.32
77.00
76.68
75.58
75.32
71.53
57.32
33.06
17.61

200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm



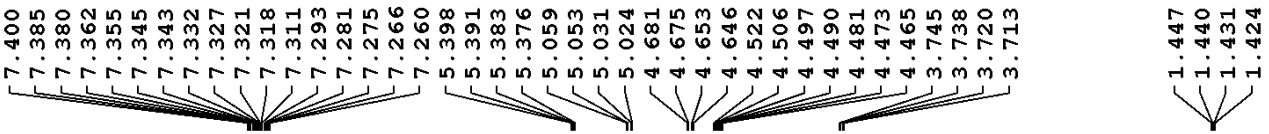
12

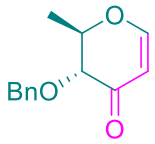
^{1}H NMR (500 MHz, $CDCl_3$)



12

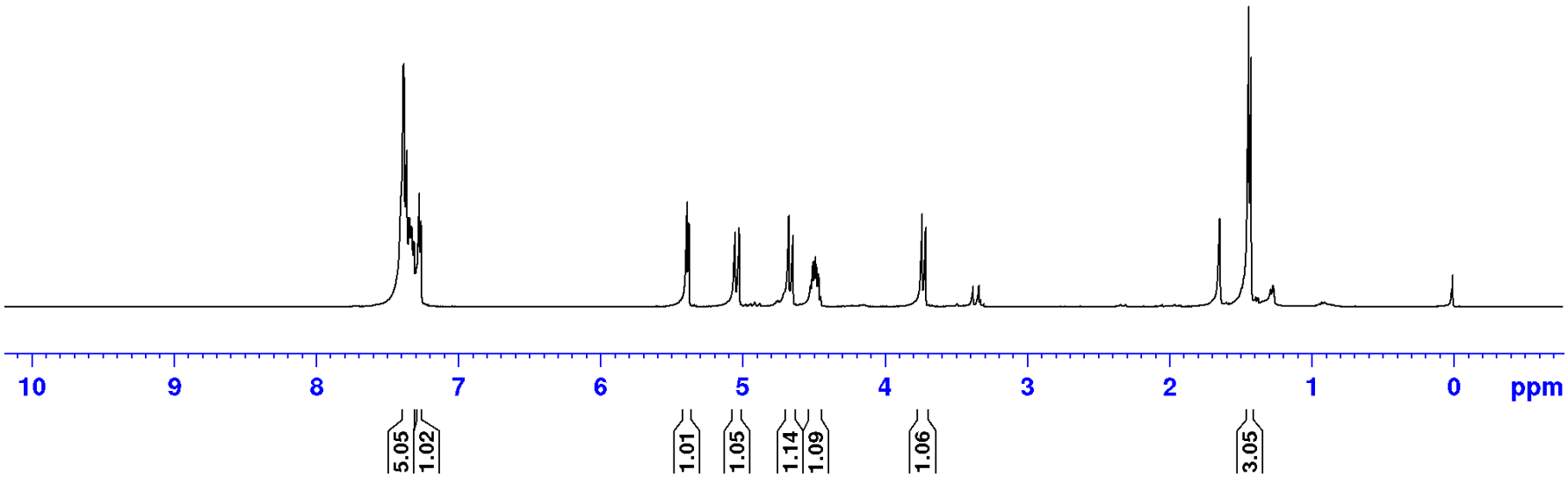
$^{13}C\{^{1}H\}$ NMR (125 MHz, $CDCl_3$)

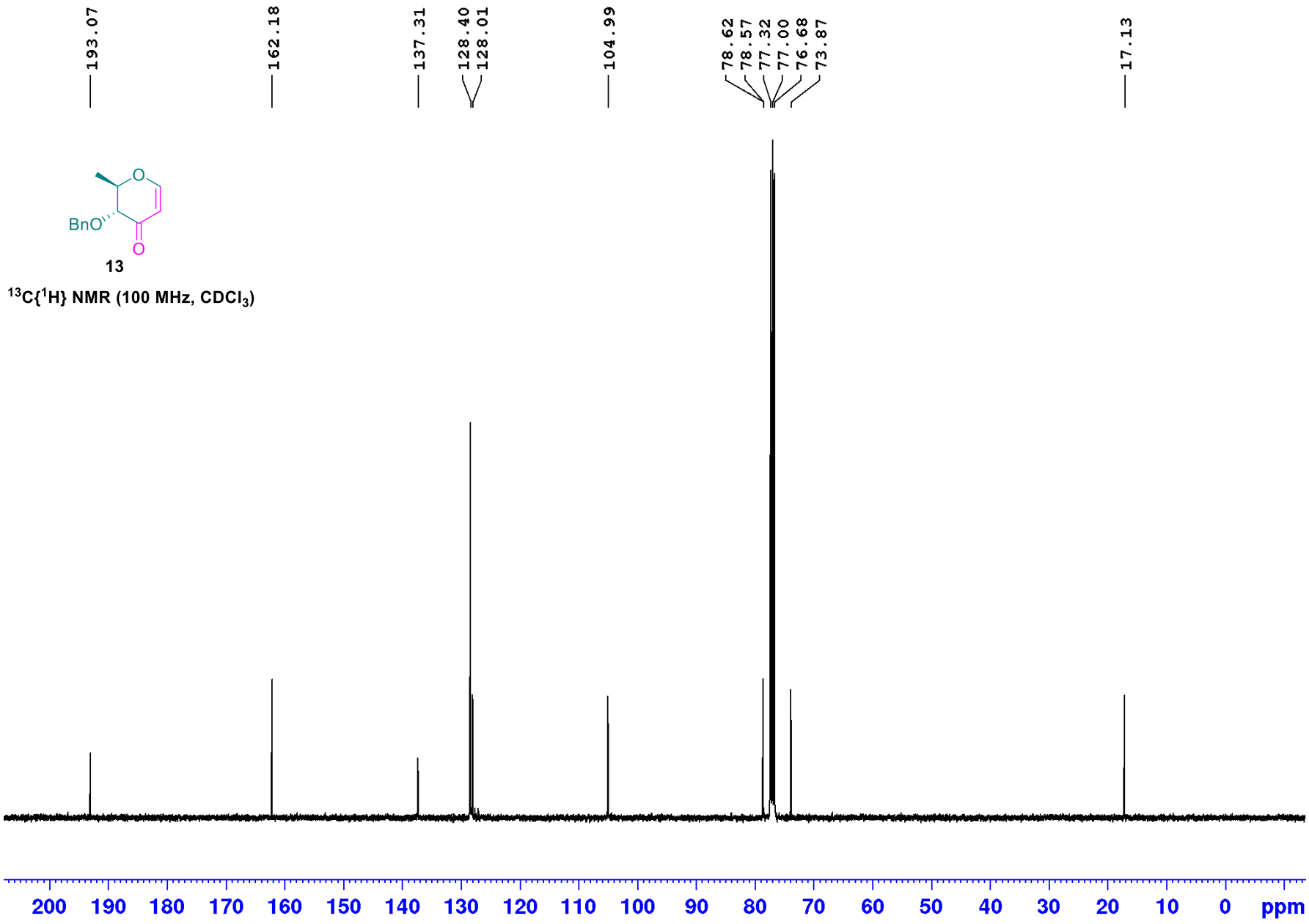




13

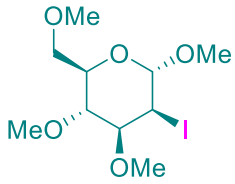
^{1}H NMR (400 MHz, $CDCl_3$)





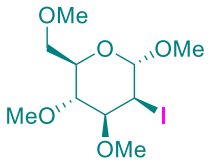
13

$^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$)



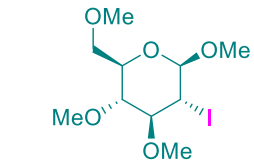
14α

^{1}H NMR (500 MHz, $CDCl_3$)



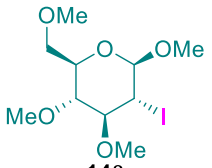
14α

$^{13}C\{^{1}H\}$ NMR (125 MHz, $CDCl_3$)



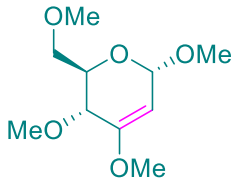
14β

^{1}H NMR (500 MHz, $CDCl_3$)



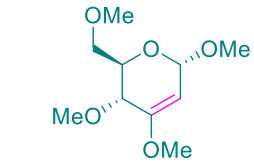
14β

$^{13}C\{^{1}H\}$ NMR (125 MHz, $CDCl_3$)



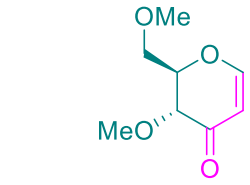
15

^{1}H NMR (500 MHz, $CDCl_3$)



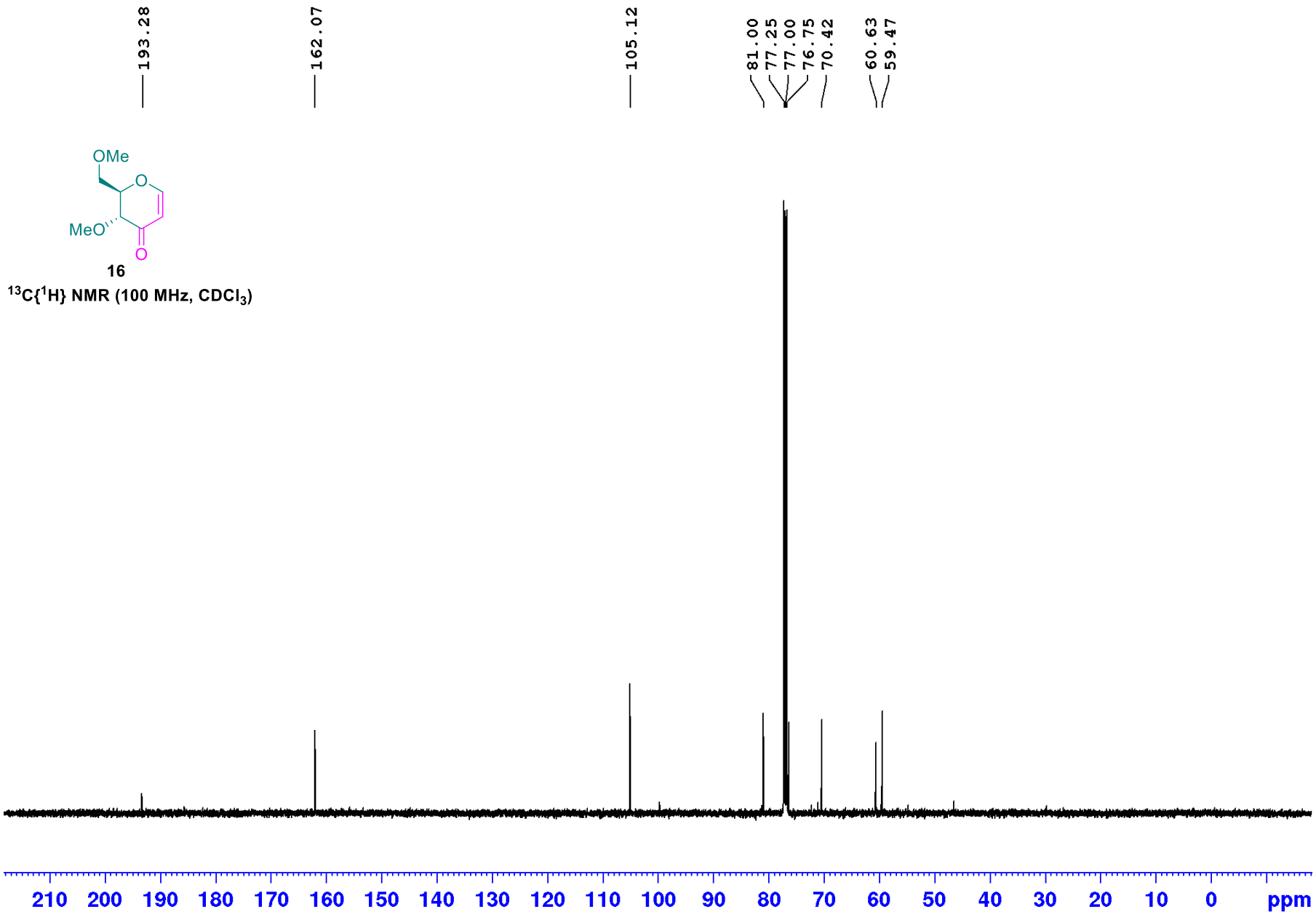
15

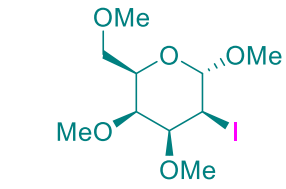
$^{13}C\{^{1}H\}$ NMR (125 MHz, $CDCl_3$)



16

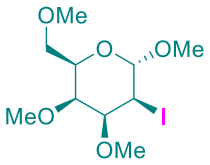
^{1}H NMR (400 MHz, $CDCl_3$)


193.28
162.07
105.12
81.00
77.25
77.00
76.75
70.42
60.63
59.47
OMe
O
MeO
O
16
13C{1H} NMR (100 MHz, CDCl3)
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm



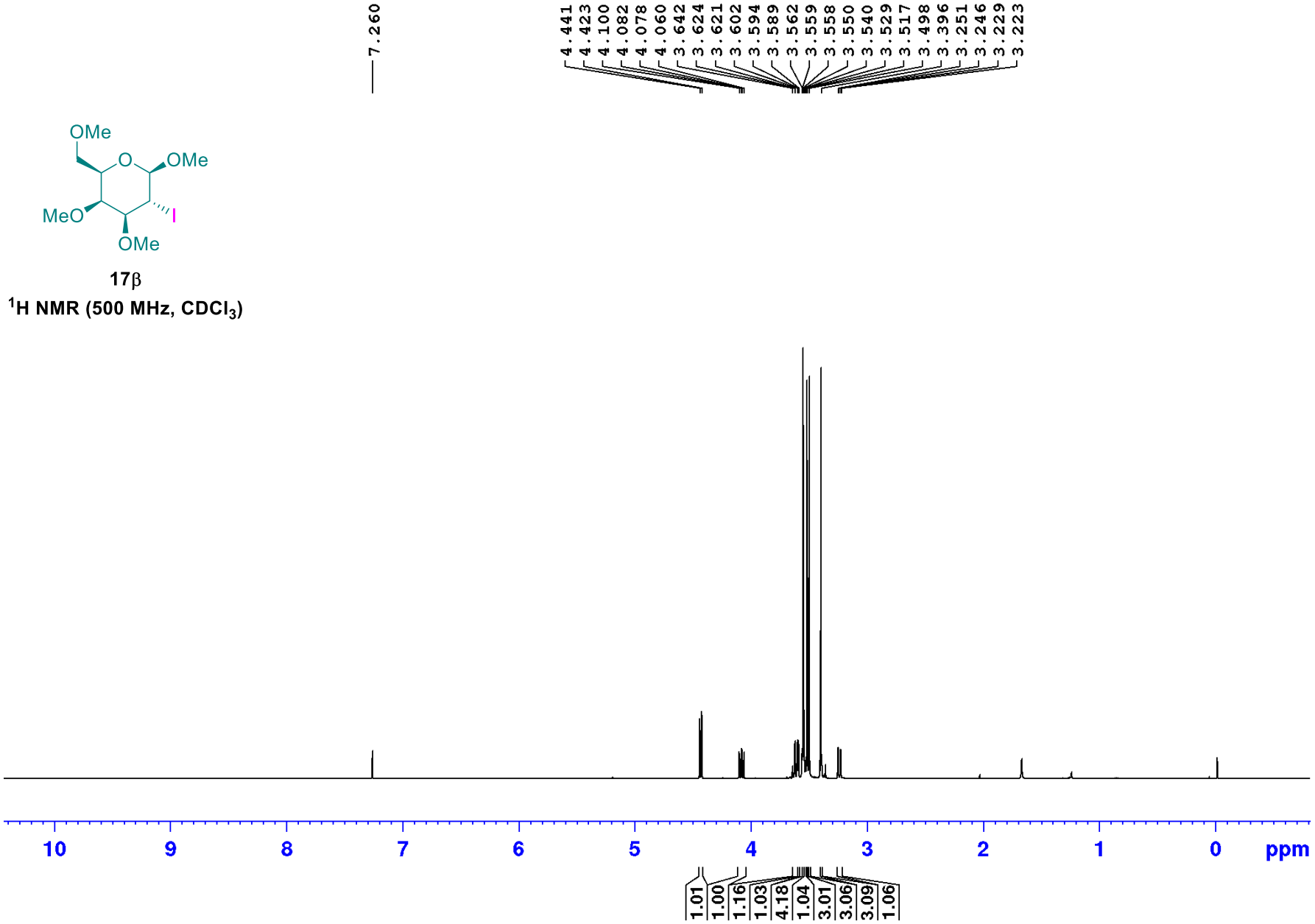
17α

1H NMR(500 MHz, $CDCl_3$)



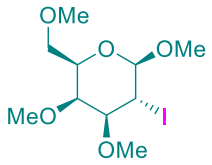
17α

$^{13}C\{^{1}H\}$ NMR(100 MHz, $CDCl_3$)



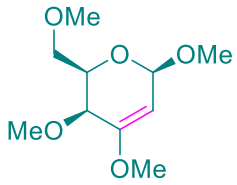
17β

^{1}H NMR (500 MHz, $CDCl_3$)



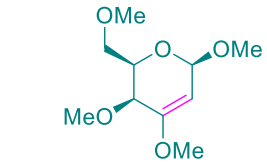
17β

$^{13}C\{^{1}H\}$ NMR (125 MHz, $CDCl_3$)



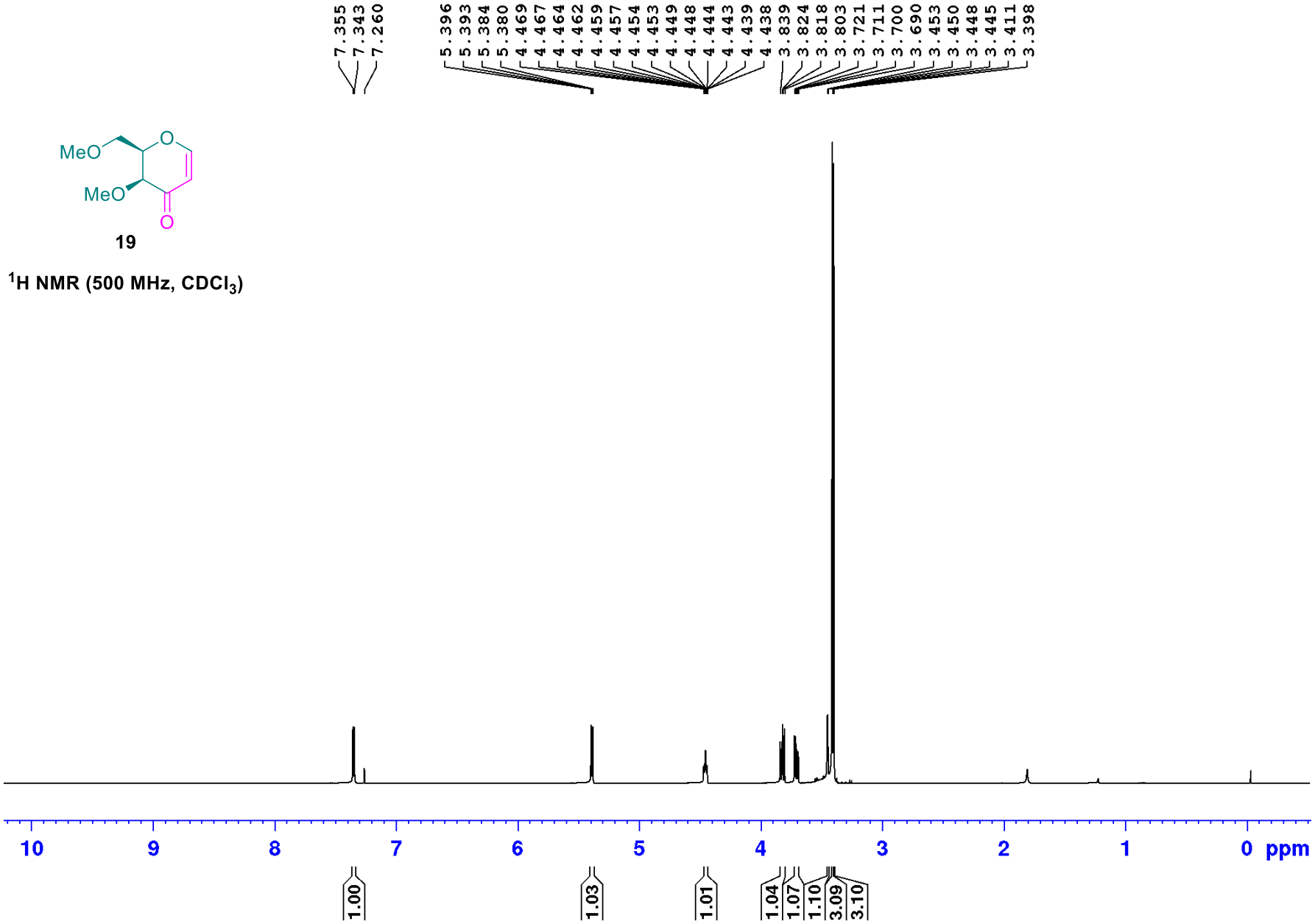
18

^{1}H NMR (500 MHz, $CDCl_3$)



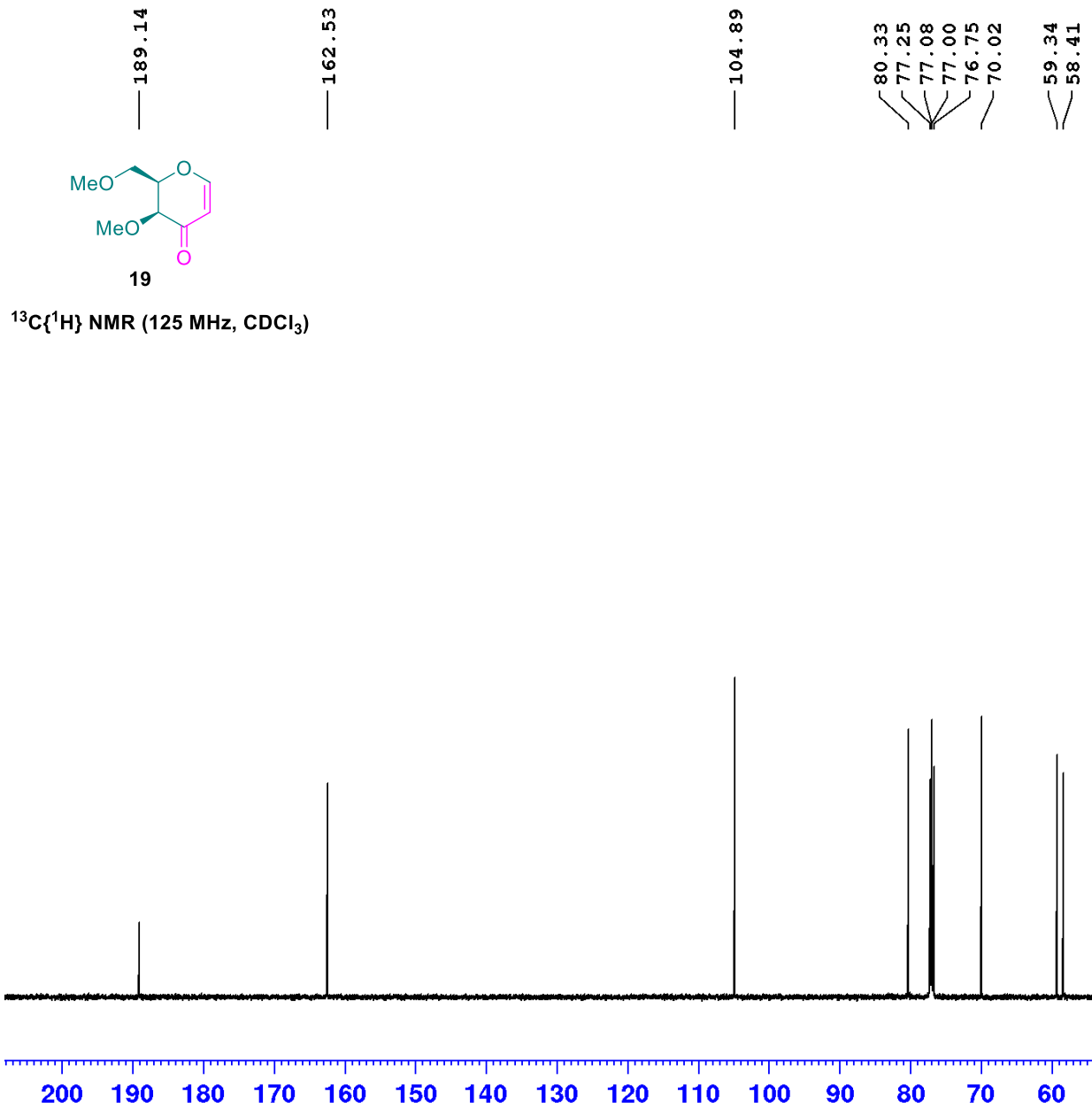
18

$^{13}C\{^{1}H\}$ NMR (125 MHz, $CDCl_3$)



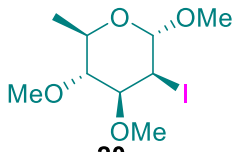
19

^{1}H NMR (500 MHz, $CDCl_3$)



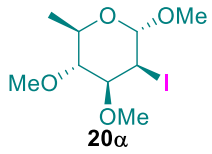
19

$^{13}C\{^{1}H\}$ NMR (125 MHz, $CDCl_3$)



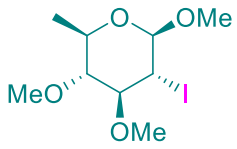
20α

^{1}H NMR (500 MHz, $CDCl_3$)



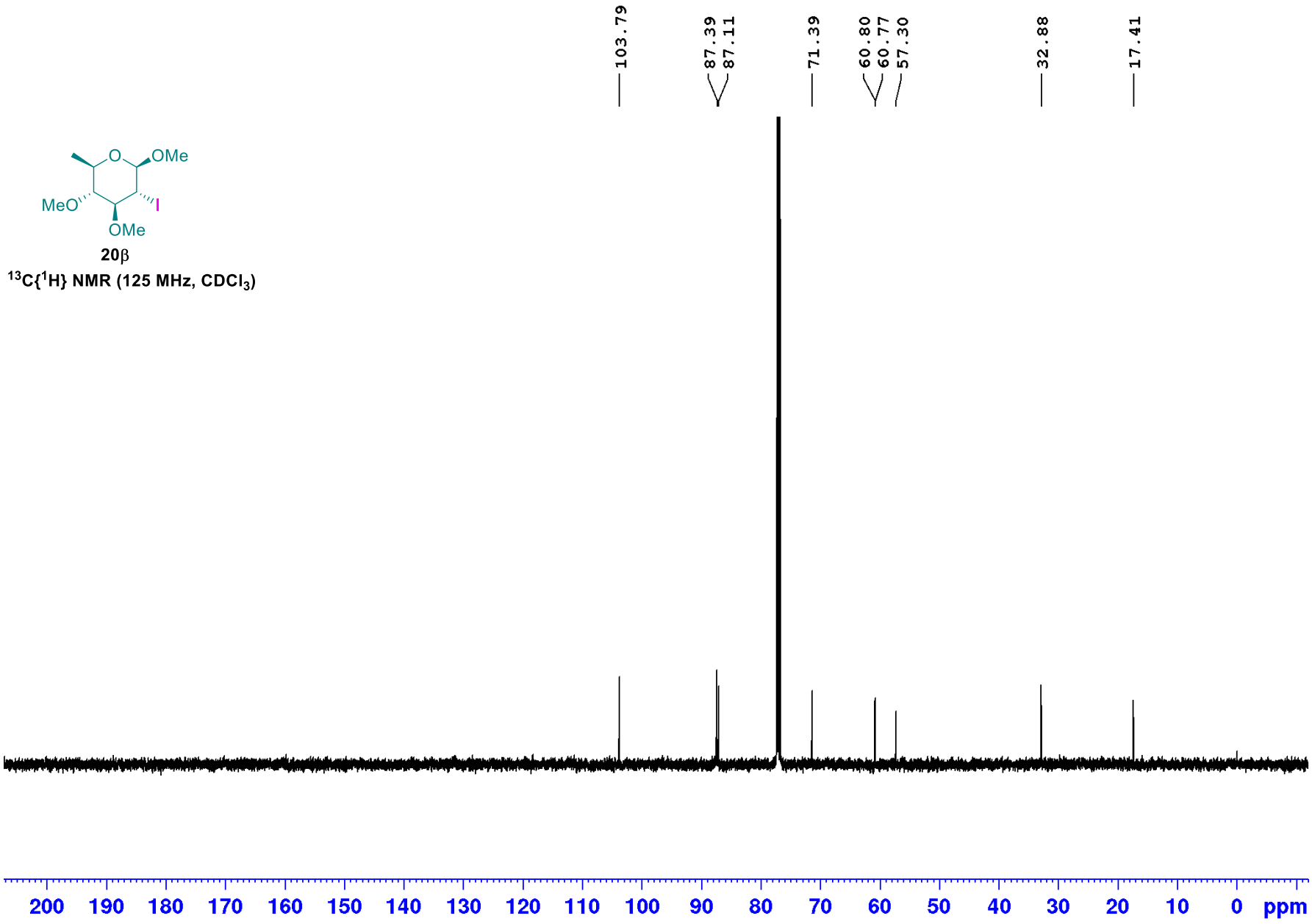
20α

$^{13}C\{^{1}H\}$ NMR (125 MHz, $CDCl_3$)



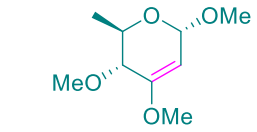
20β

^{1}H NMR (500 MHz, $CDCl_3$)



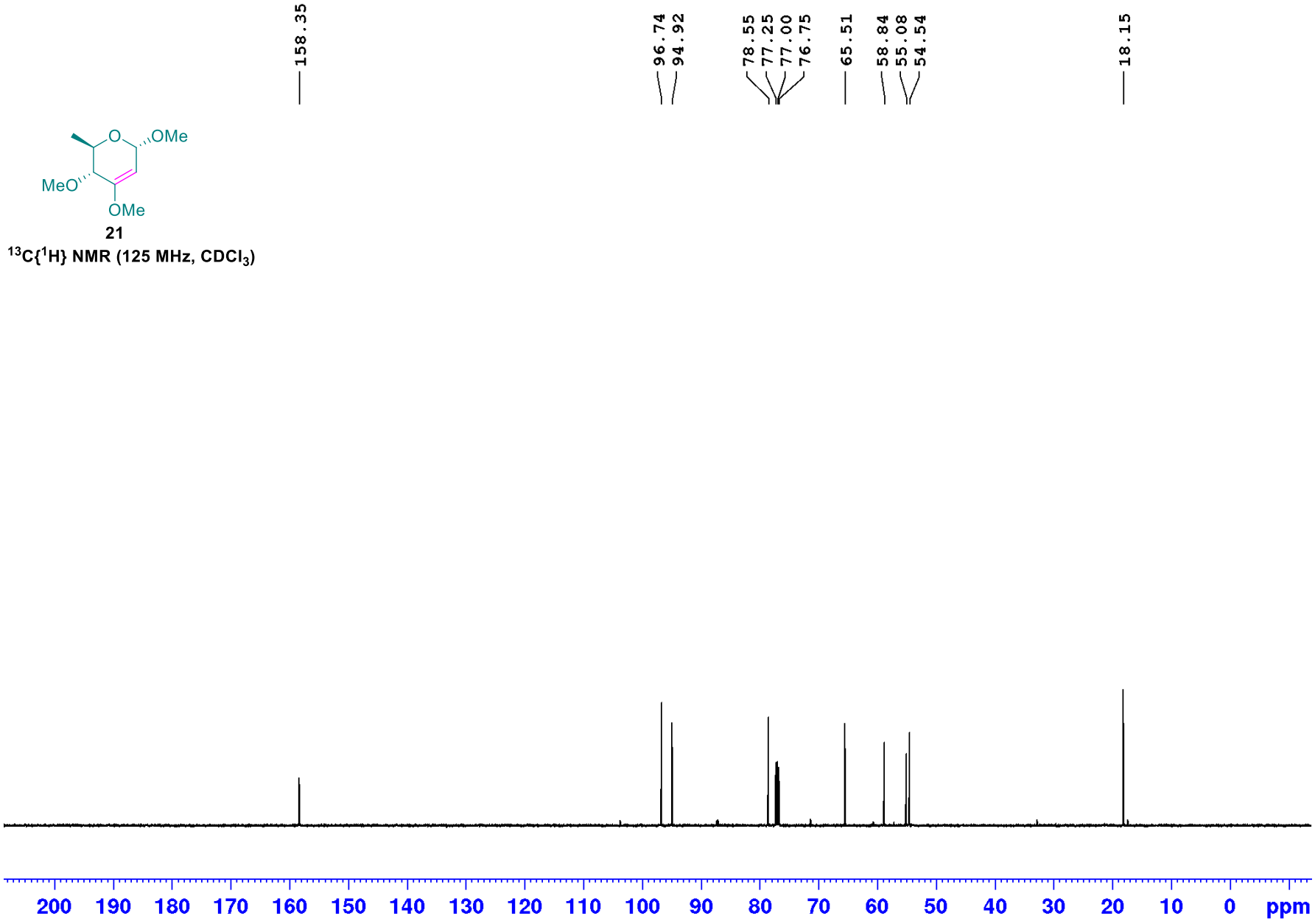
20β

$^{13}C\{^{1}H\}$ NMR (125 MHz, $CDCl_3$)



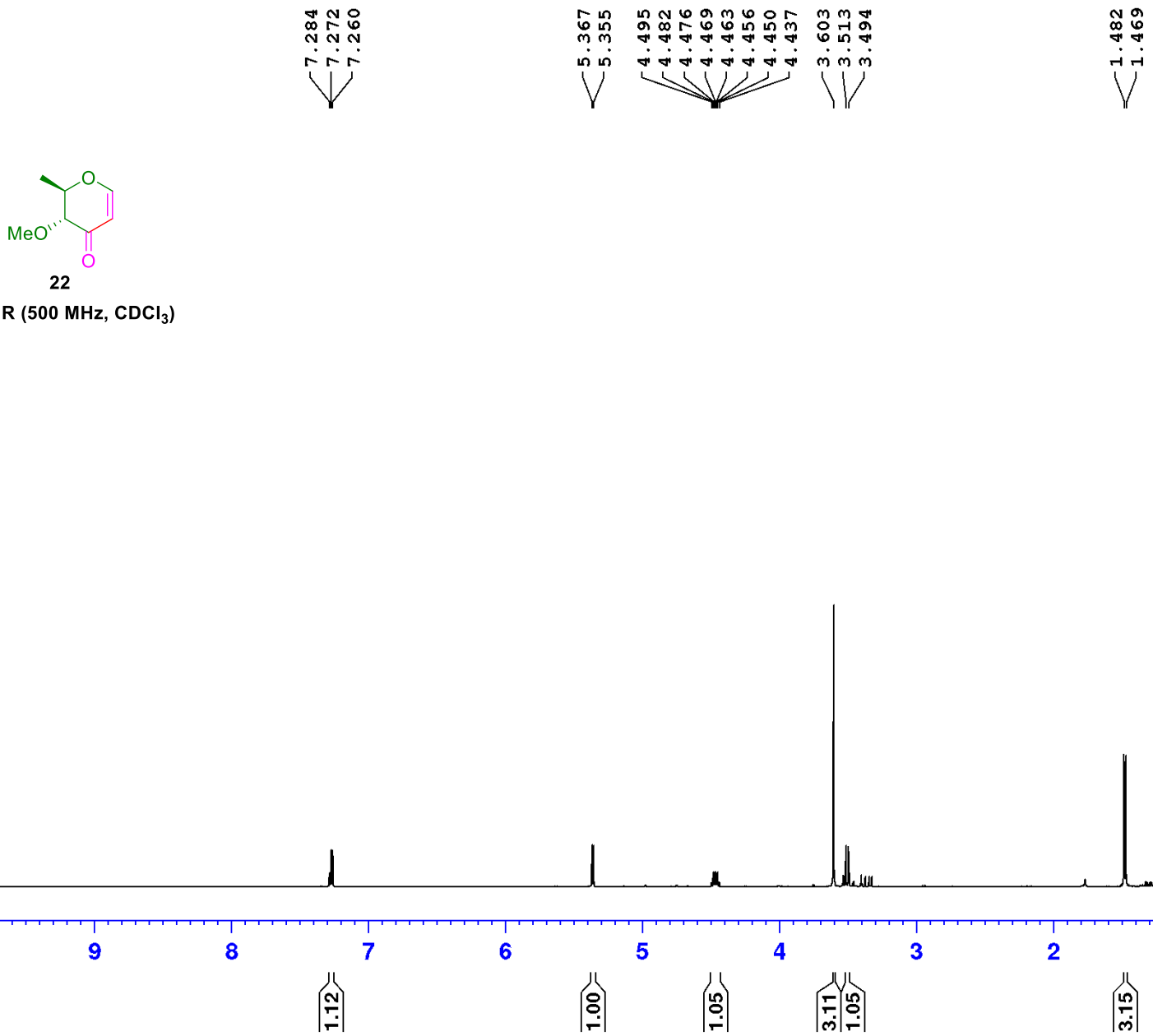
21

^{1}H NMR (500 MHz, $CDCl_3$)



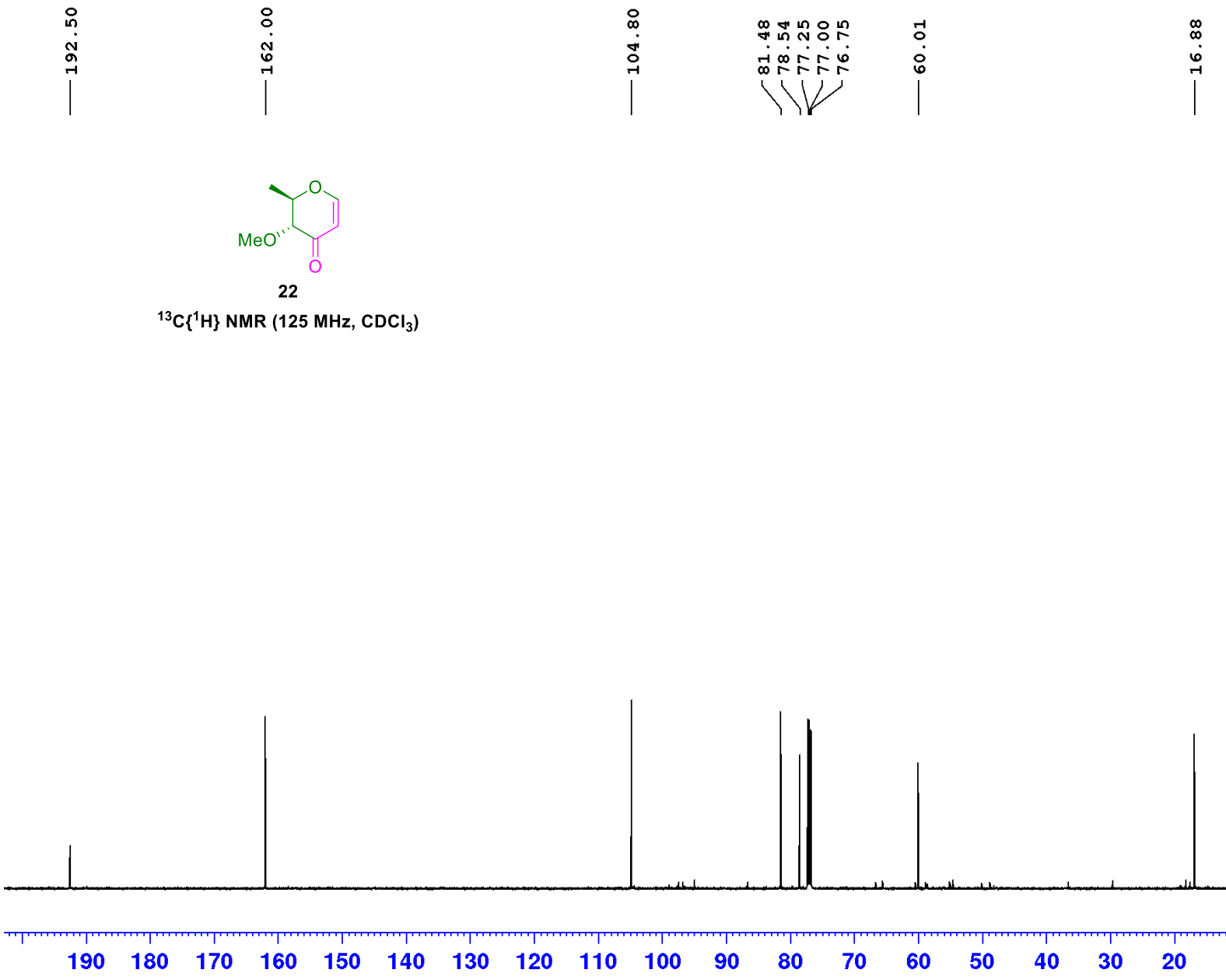
21

$^{13}C\{^{1}H\}$ NMR (125 MHz, $CDCl_3$)



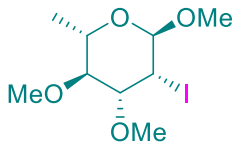
22

^{1}H NMR (500 MHz, $CDCl_3$)



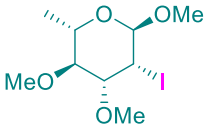
22

$^{13}C\{^{1}H\}$ NMR (125 MHz, $CDCl_3$)



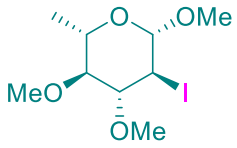
23α

^{1}H NMR (500 MHz,$CDCl_3$)



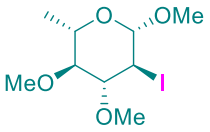
23α

$^{13}C\{^{1}H\}$ NMR (125 MHz,$CDCl_3$)



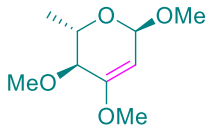
23β

^{1}H NMR (500 MHz,$CDCl_3$)



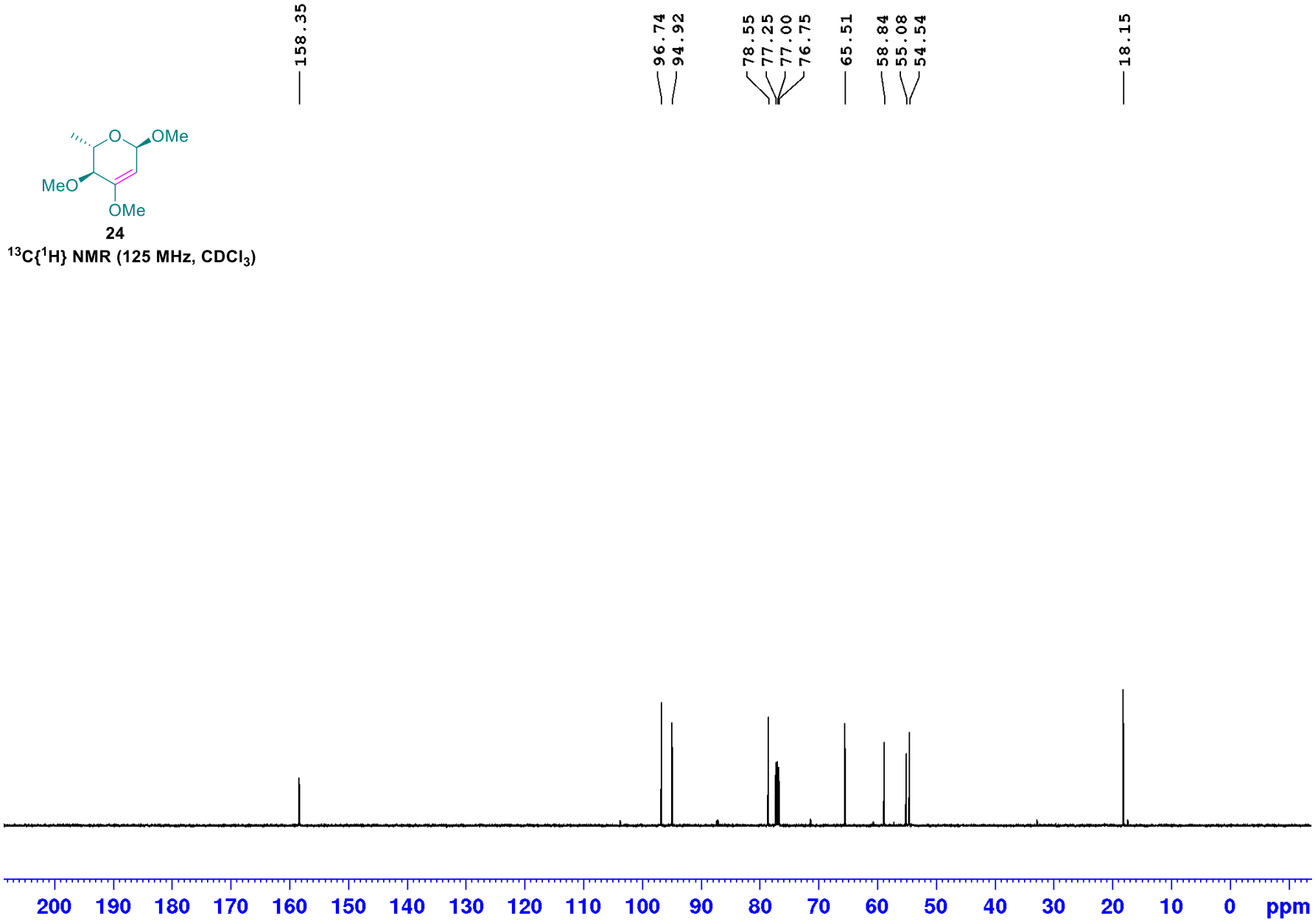
23β

$^{13}C\{^{1}H\}$ NMR (125 MHz,$CDCl_3$)



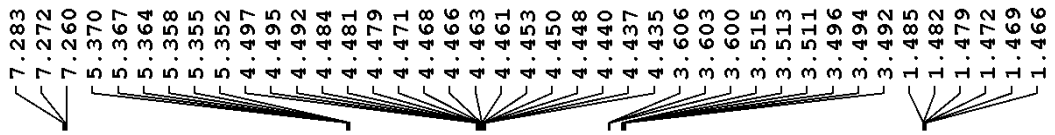
24

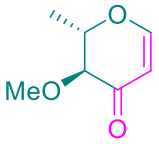
^{1}H NMR (500 MHz, $CDCl_3$)



24

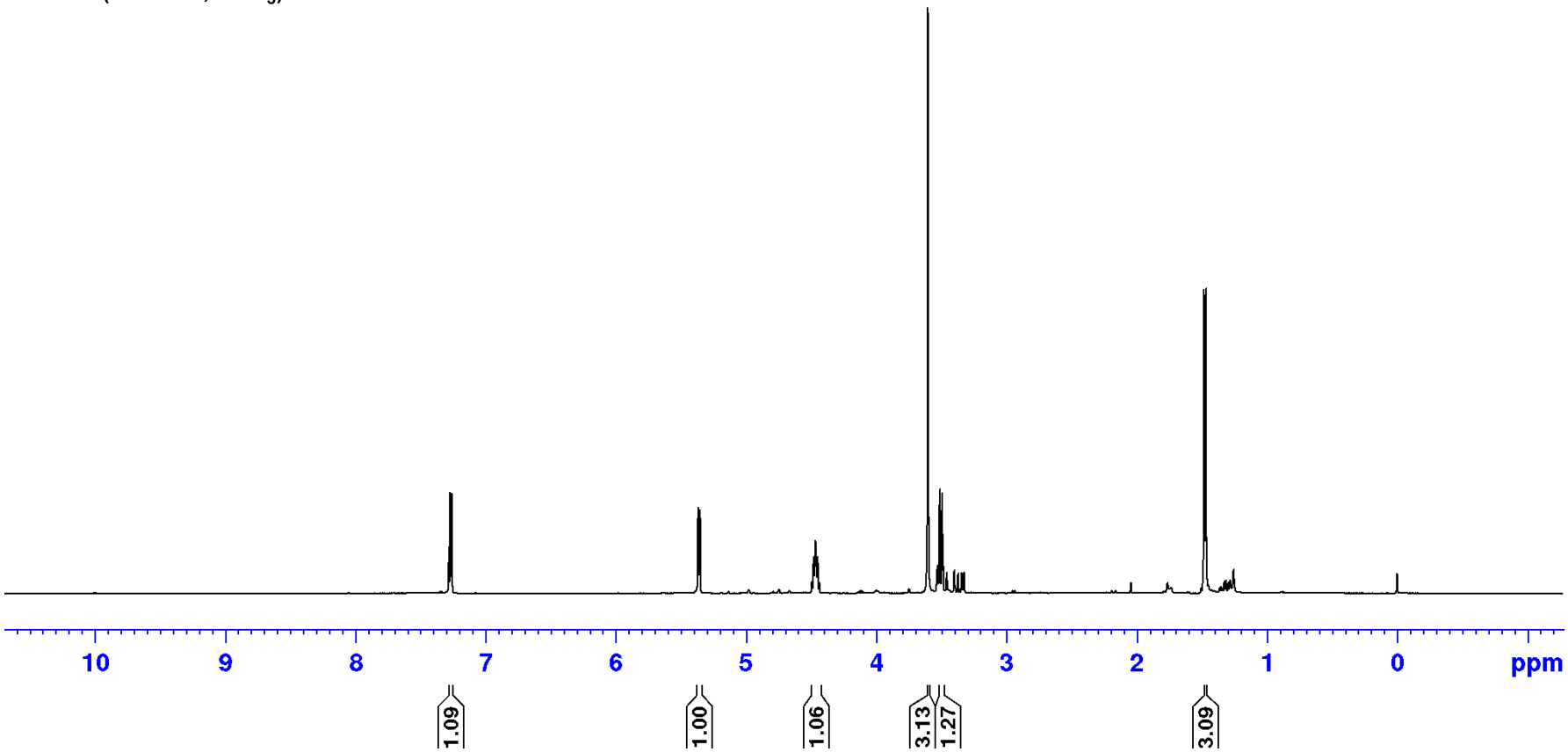
$^{13}C\{^{1}H\}$ NMR (125 MHz, $CDCl_3$)

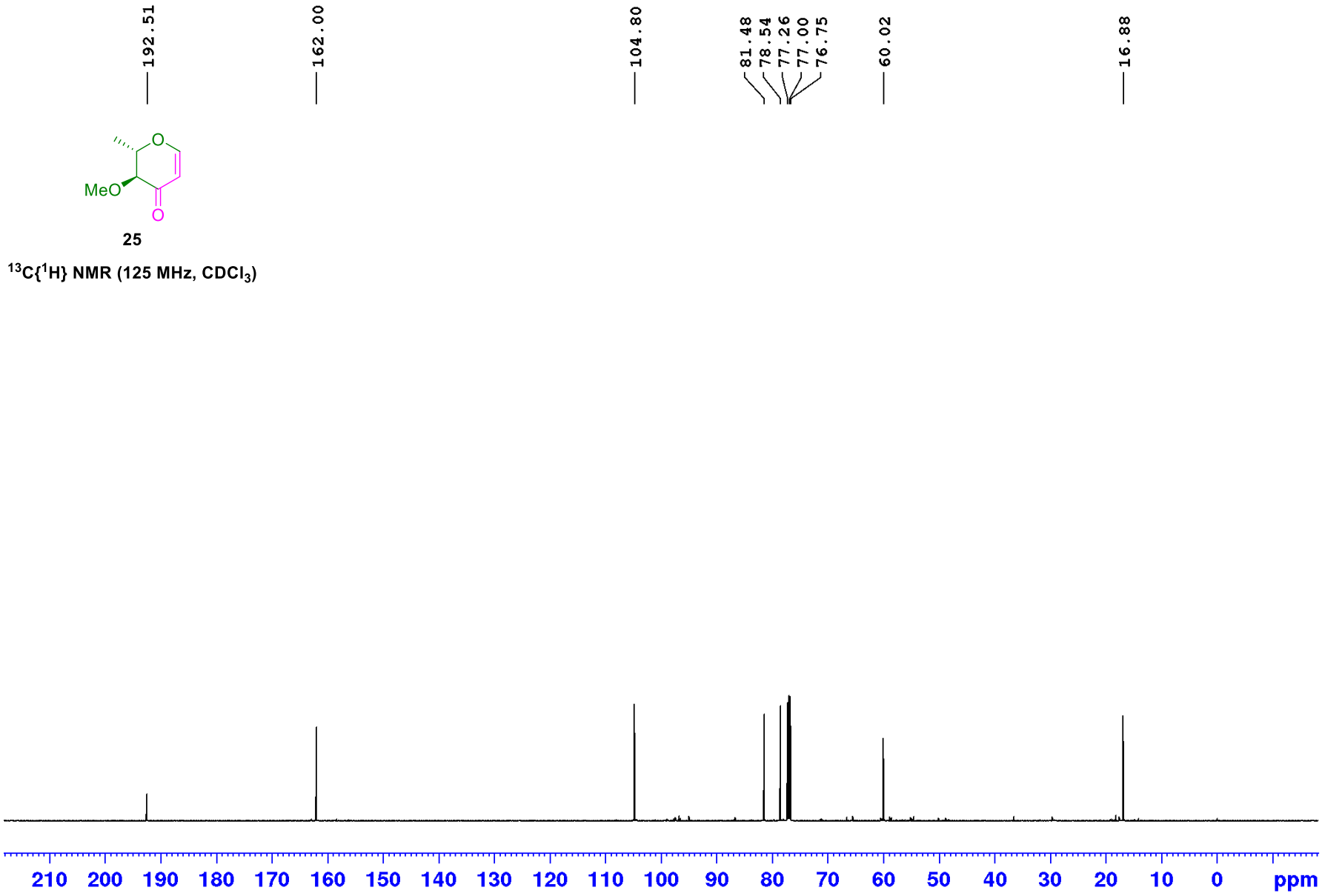




25

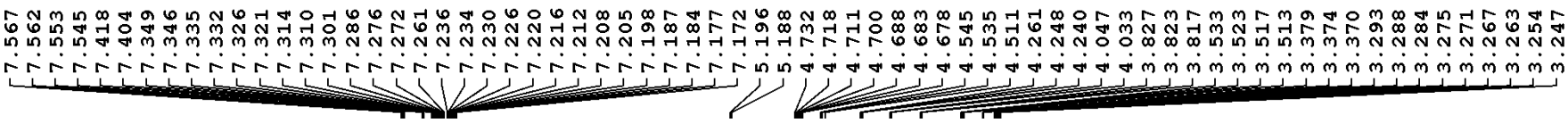
^{1}H NMR (500 MHz,$CDCl_3$)

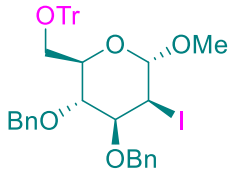




25

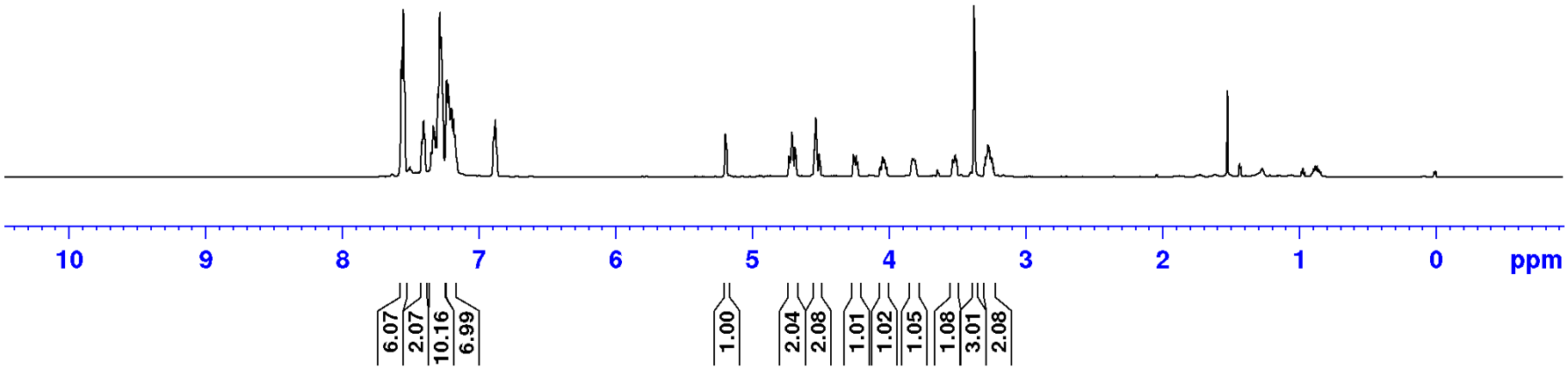
$^{13}C\{^{1}H\}$ NMR (125 MHz, $CDCl_3$)

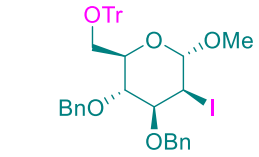




26α

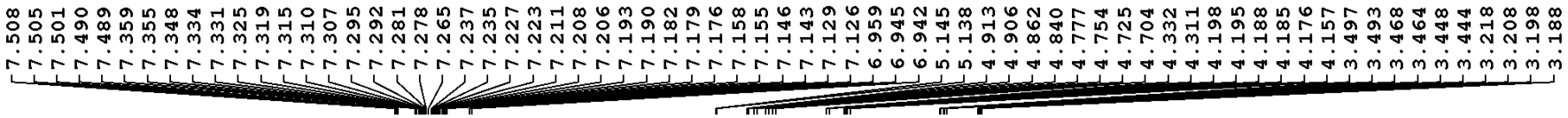
^{1}H NMR (500 MHz, $CDCl_3$)

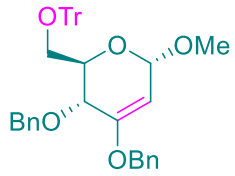




26α

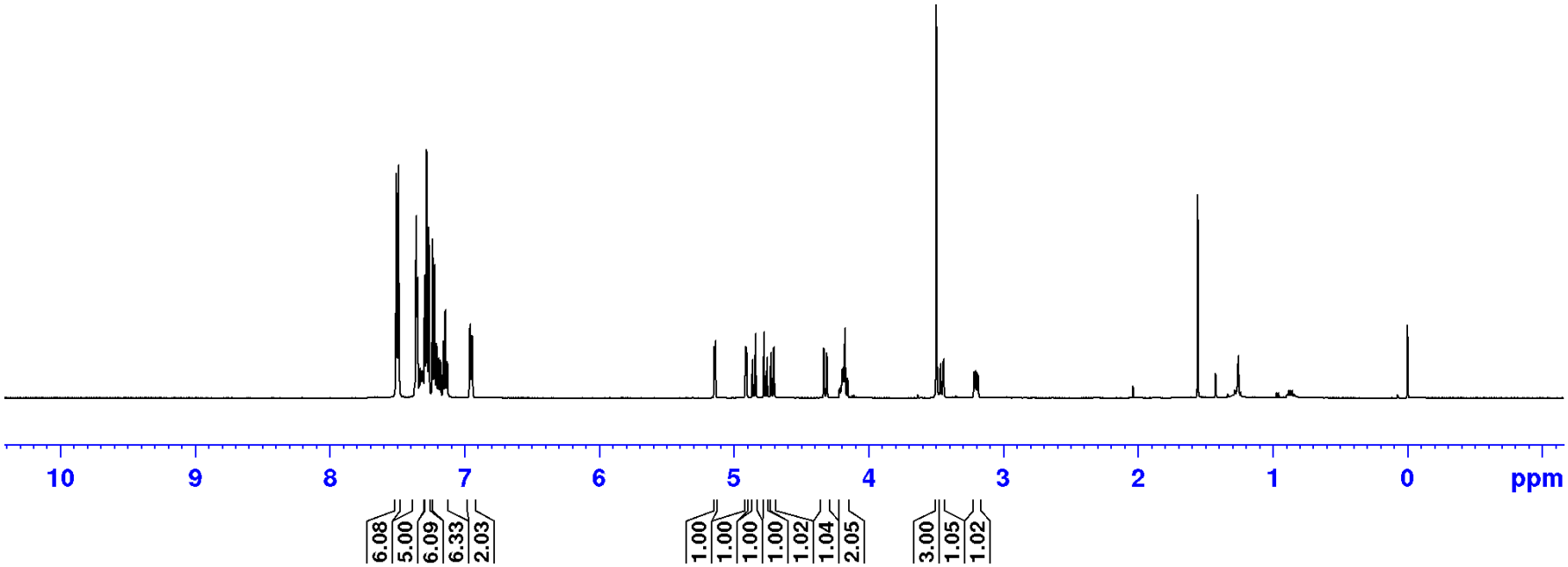
$^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$)

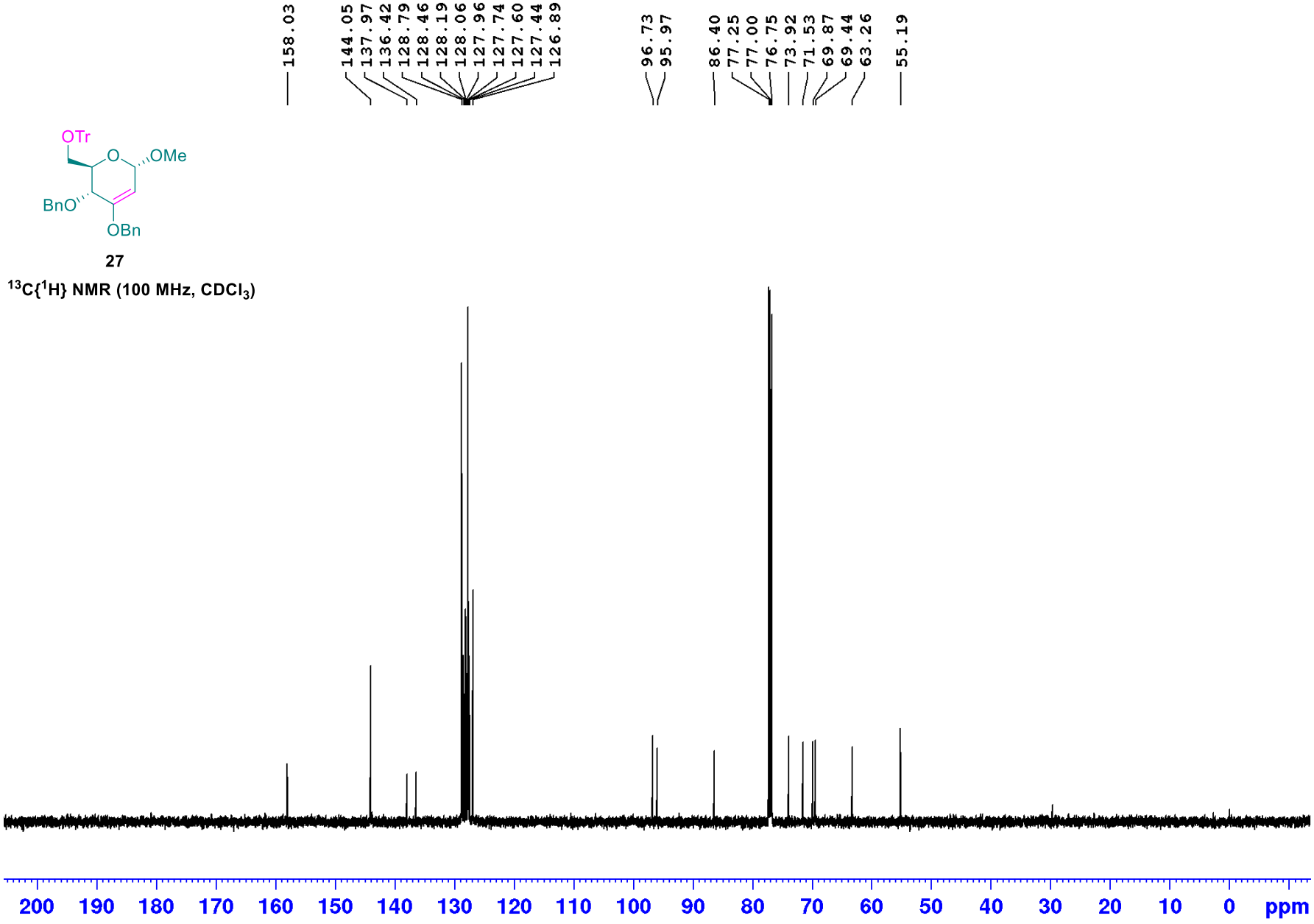




27

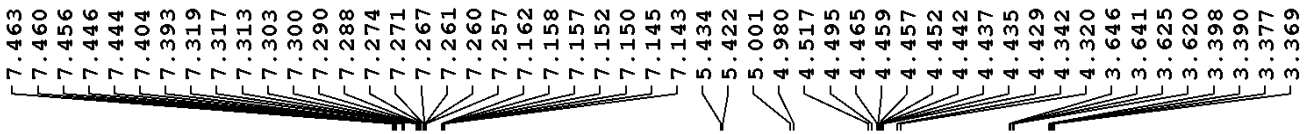
^{1}H NMR (500 MHz, $CDCl_3$)

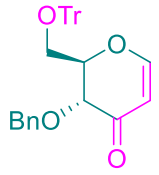




27

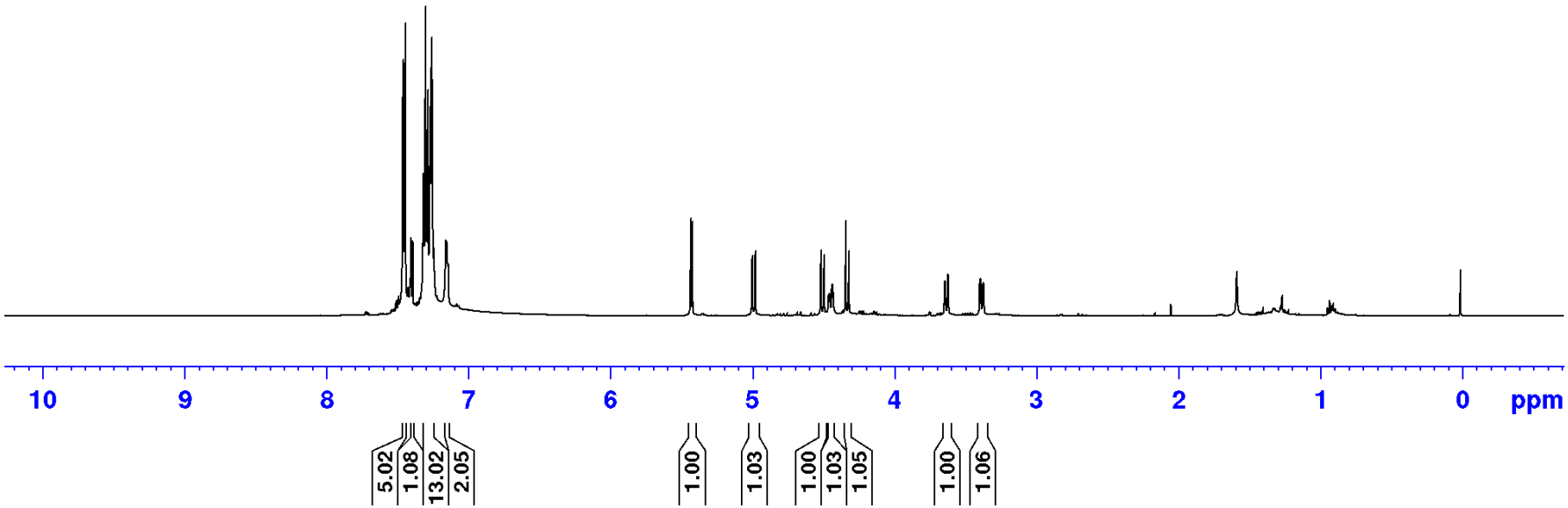
$^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$)



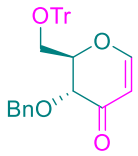


28

^{1}H NMR (500 MHz, $CDCl_3$)

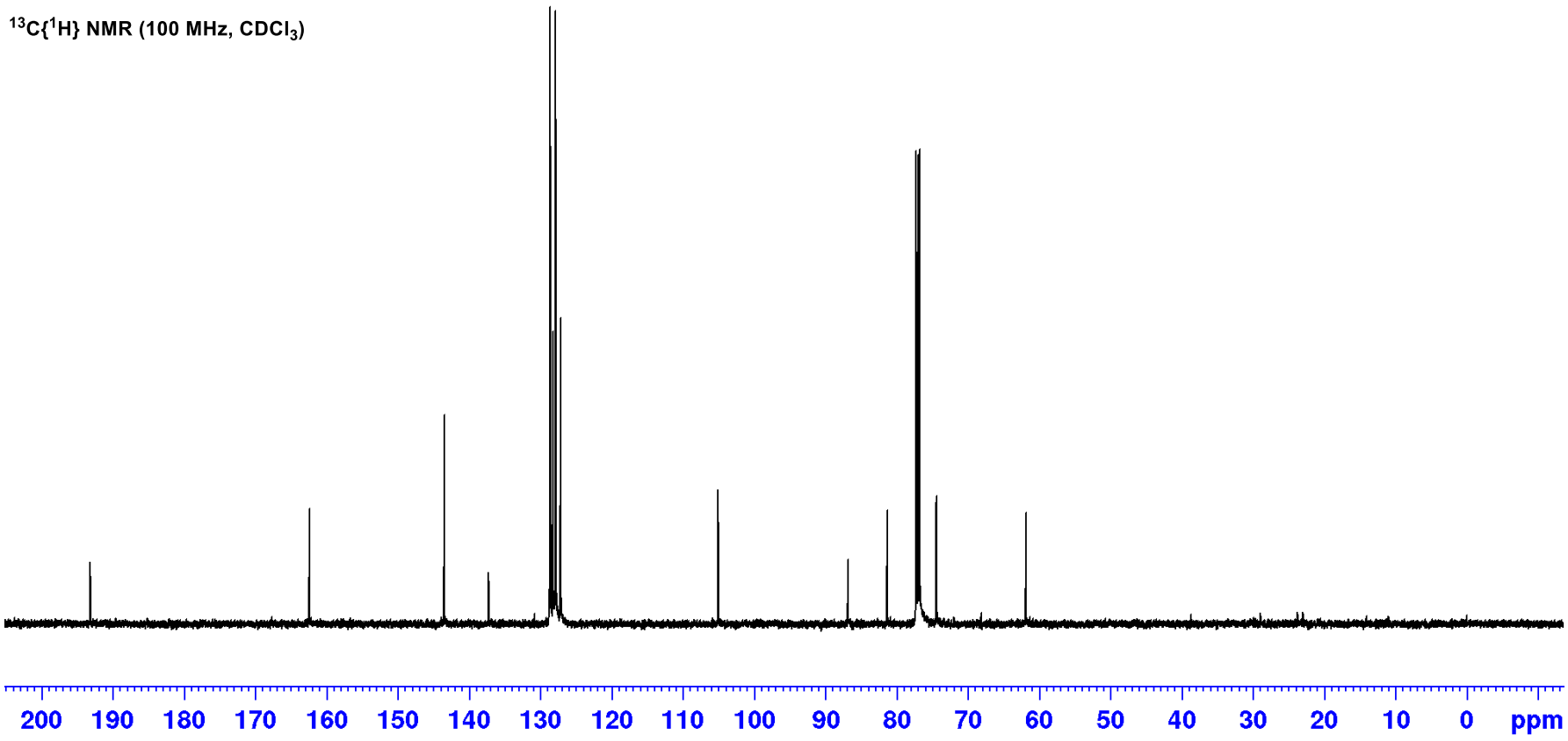


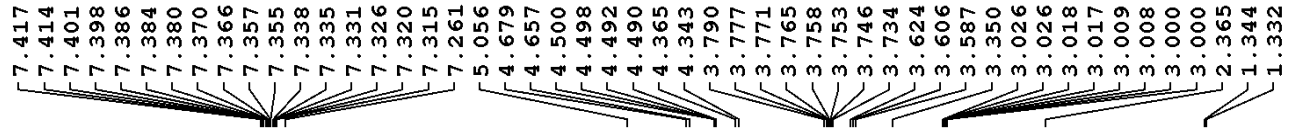
193.20
162.43
143.48
137.25
128.66
128.24
128.21
127.89
127.80
127.17
105.08
86.83
81.33
77.25
77.00
76.75
74.46
74.40
61.84

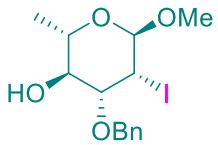


28

$^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$)

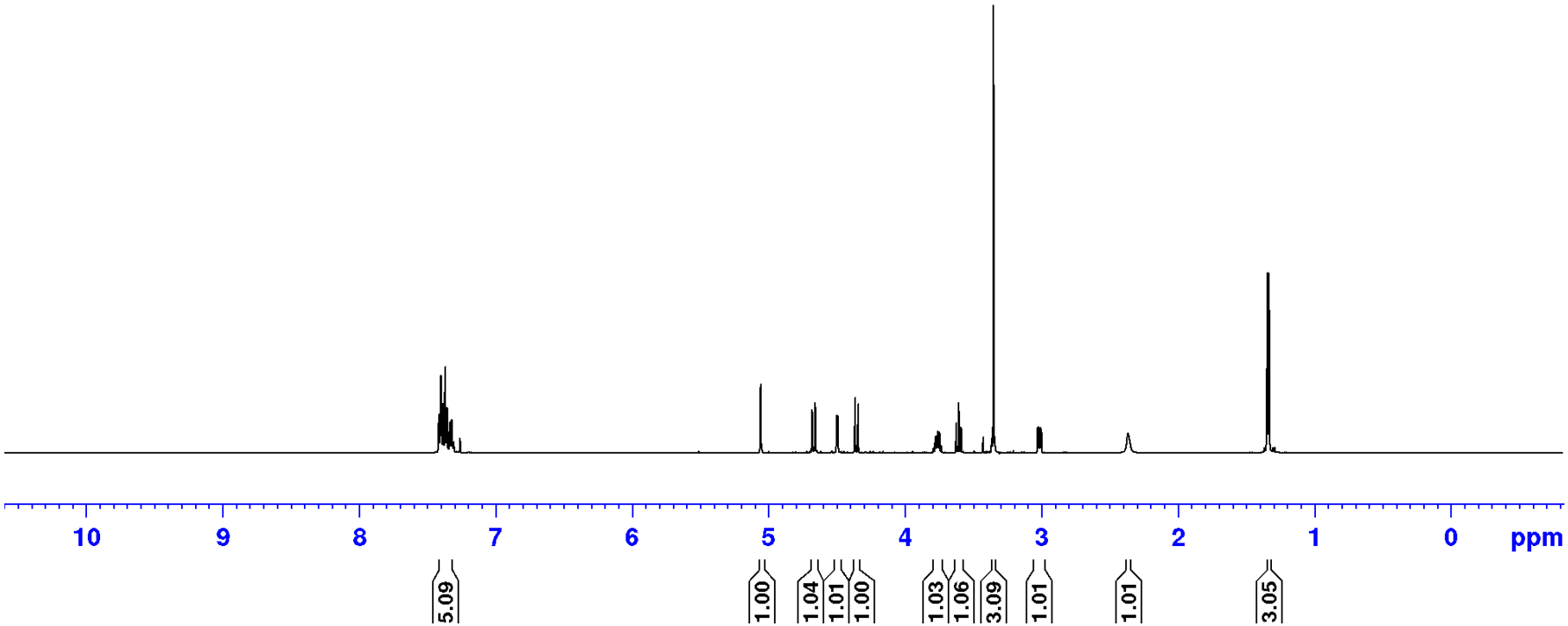


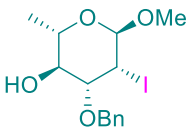




S10α

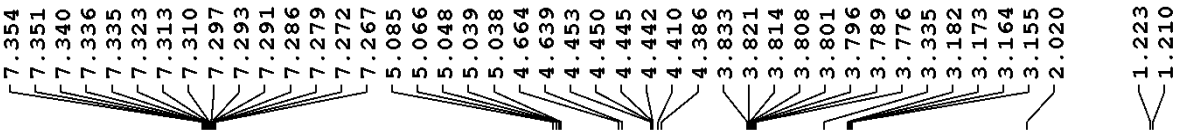
^{1}H NMR (500 MHz, $CDCl_3$)

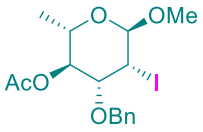




S10α

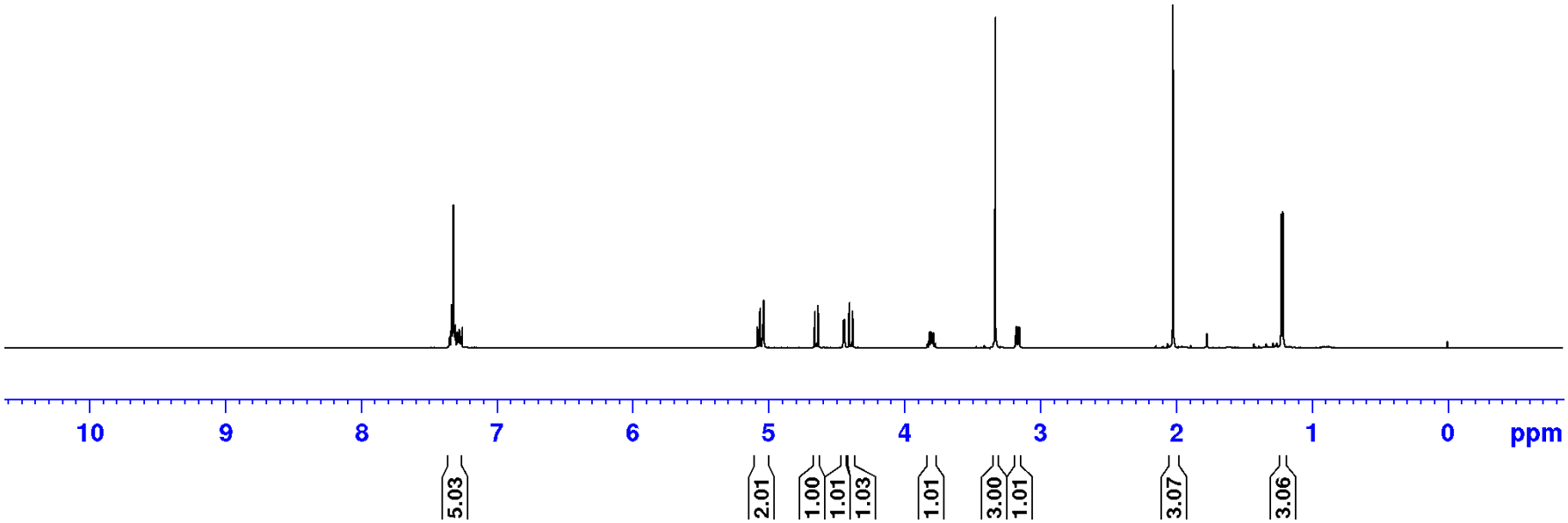
$^{13}C\{^{1}H\}$ NMR (125 MHz, $CDCl_3$)

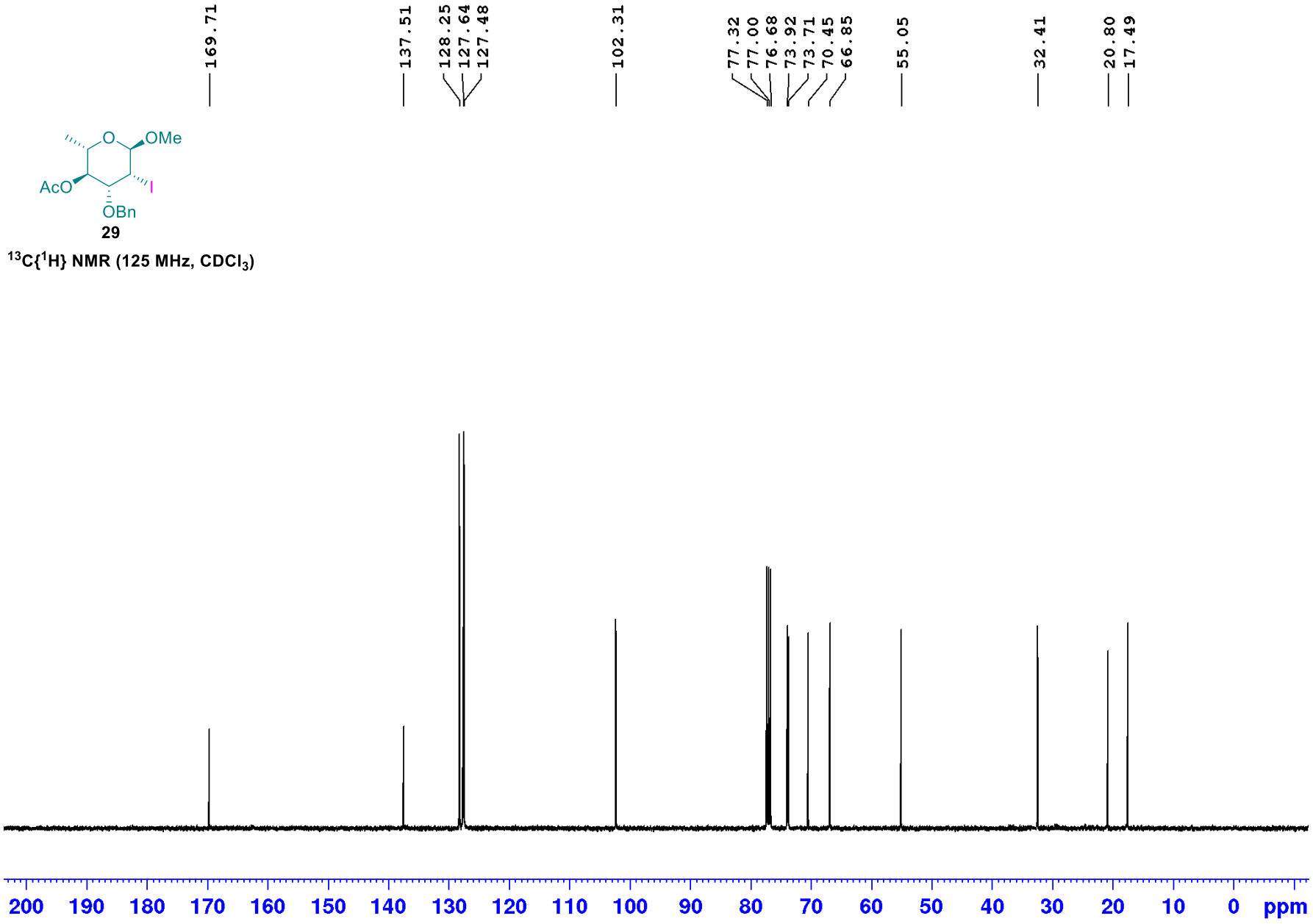




29α

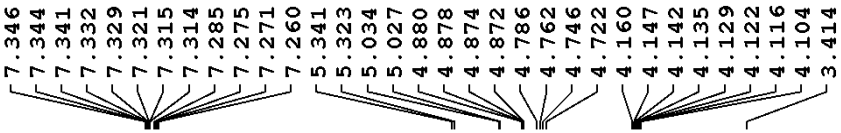
^{1}H NMR (500 MHz, $CDCl_3$)

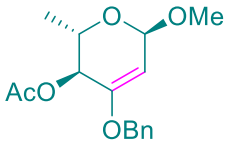




29

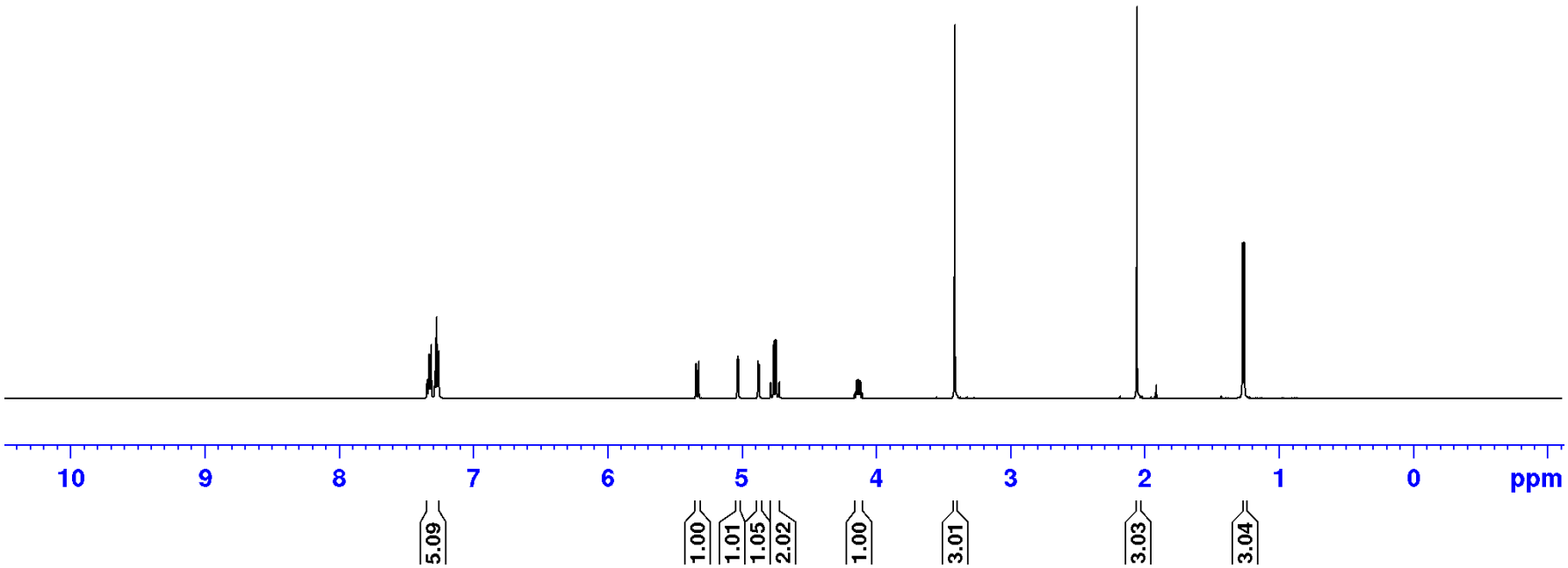
$^{13}C\{^{1}H\}$ NMR (125 MHz, $CDCl_3$)

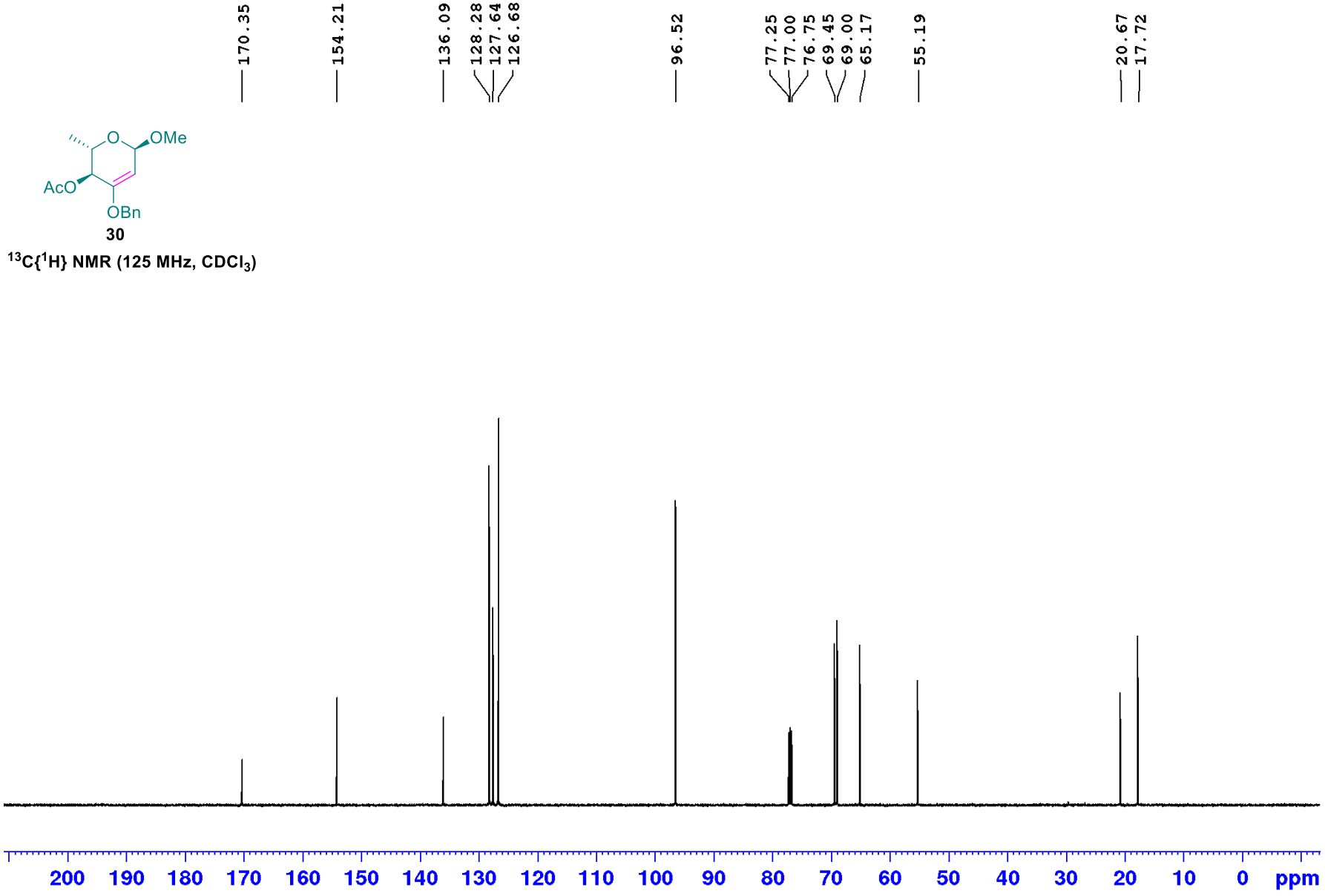




30

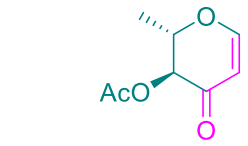
^{1}H NMR (500 MHz, $CDCl_3$)





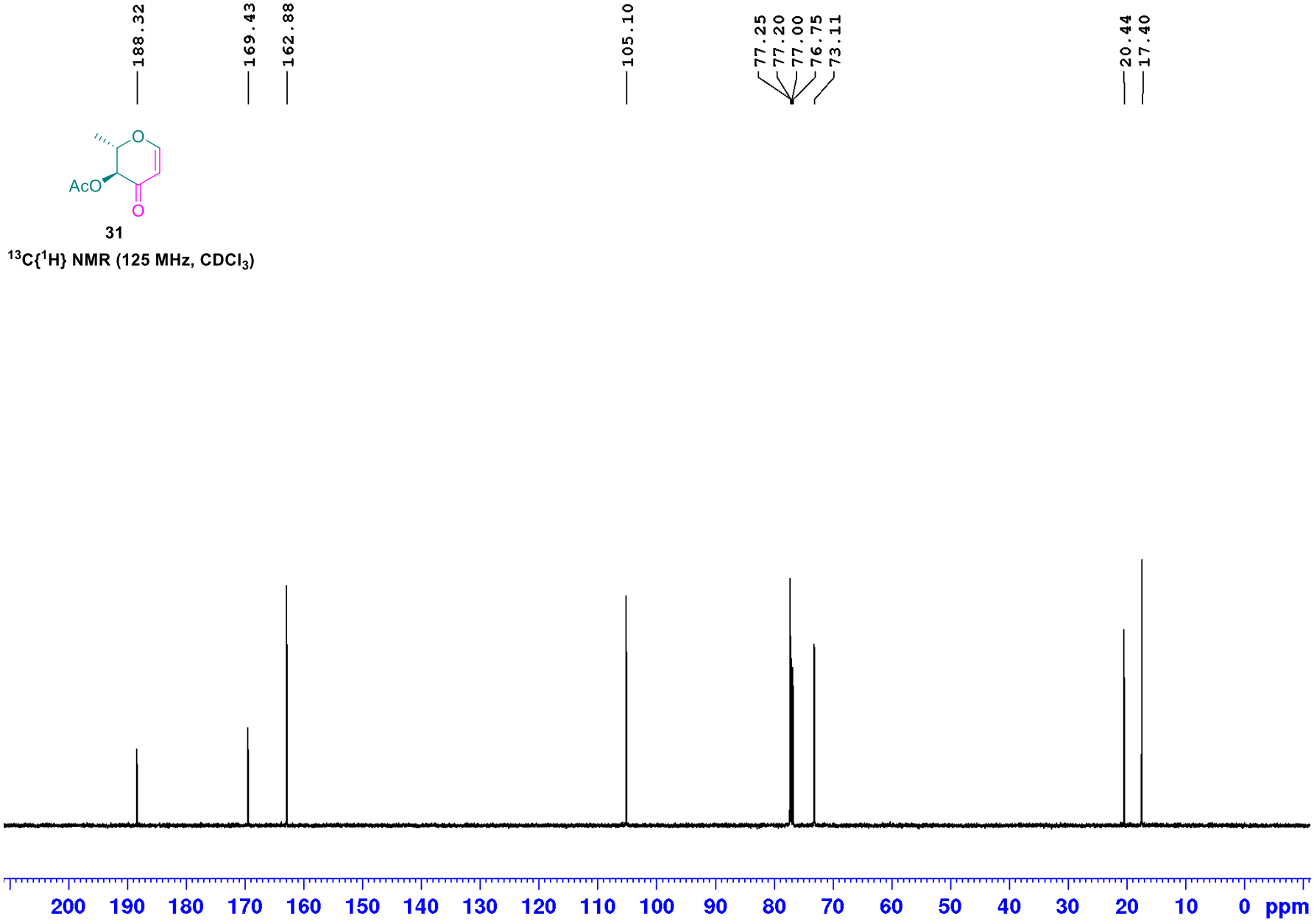
30

$^{13}C\{^{1}H\}$ NMR (125 MHz, $CDCl_3$)



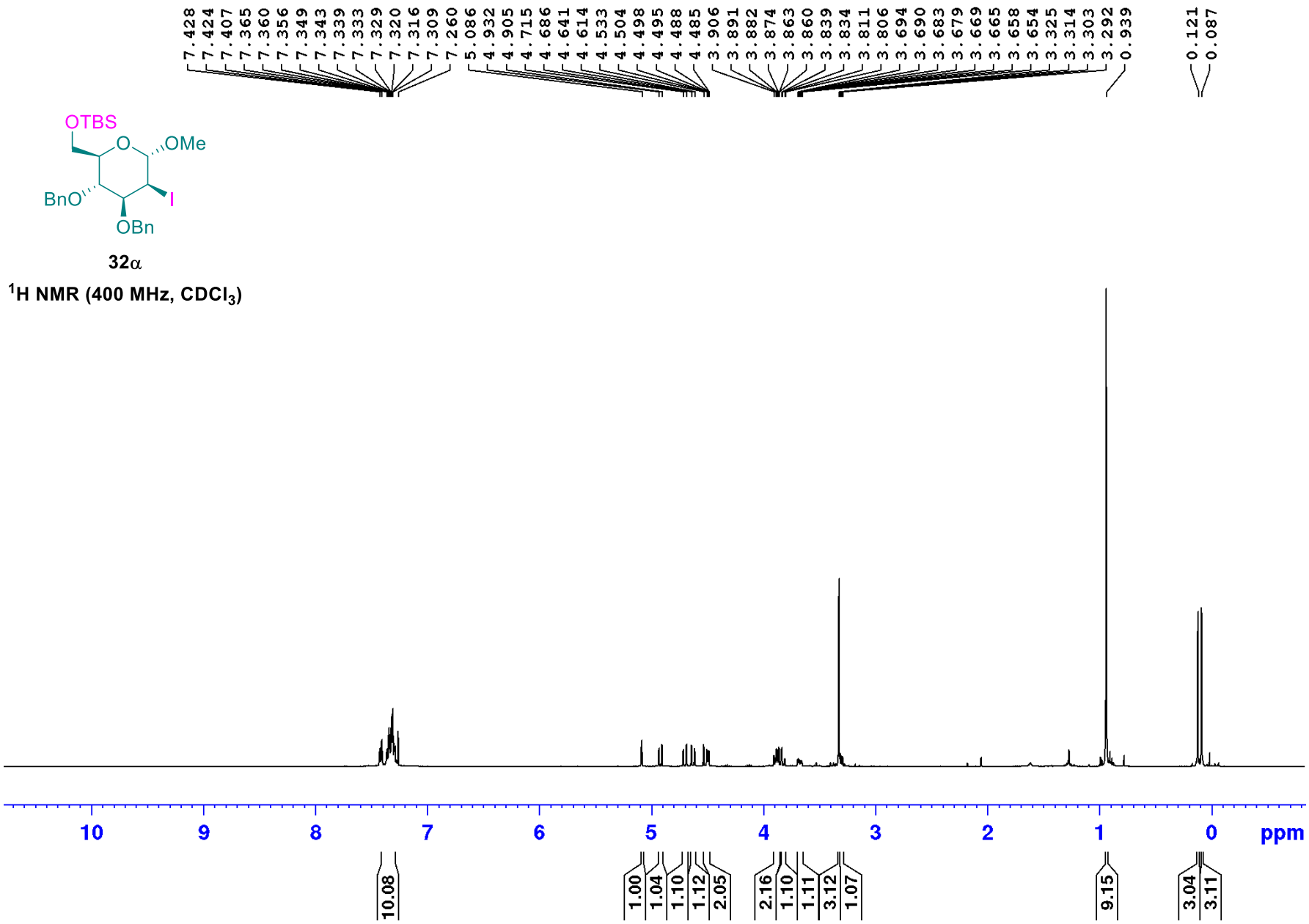
31

^{1}H NMR (500 MHz, $CDCl_3$)



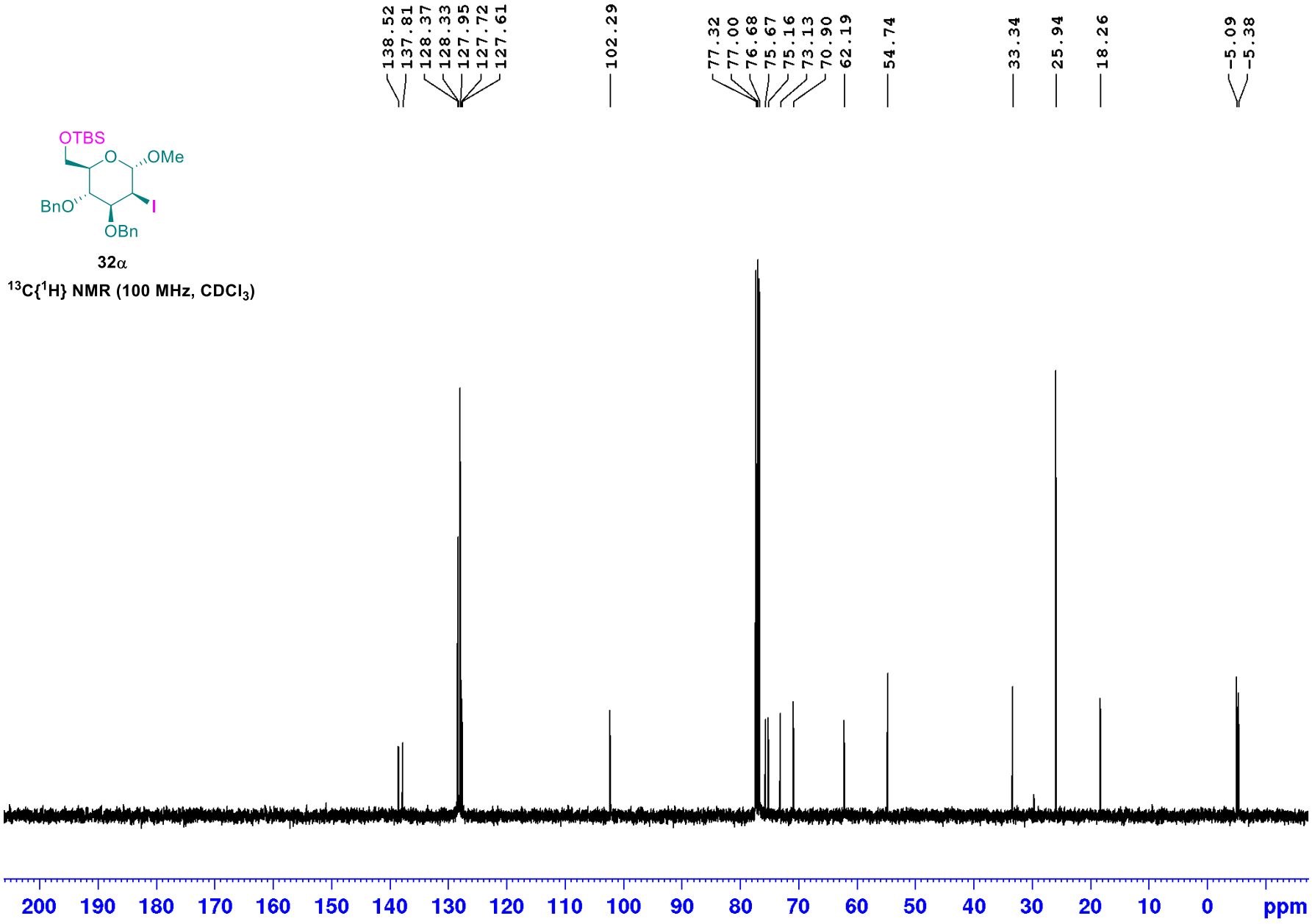
31

$^{13}C\{^{1}H\}$ NMR (125 MHz, $CDCl_3$)



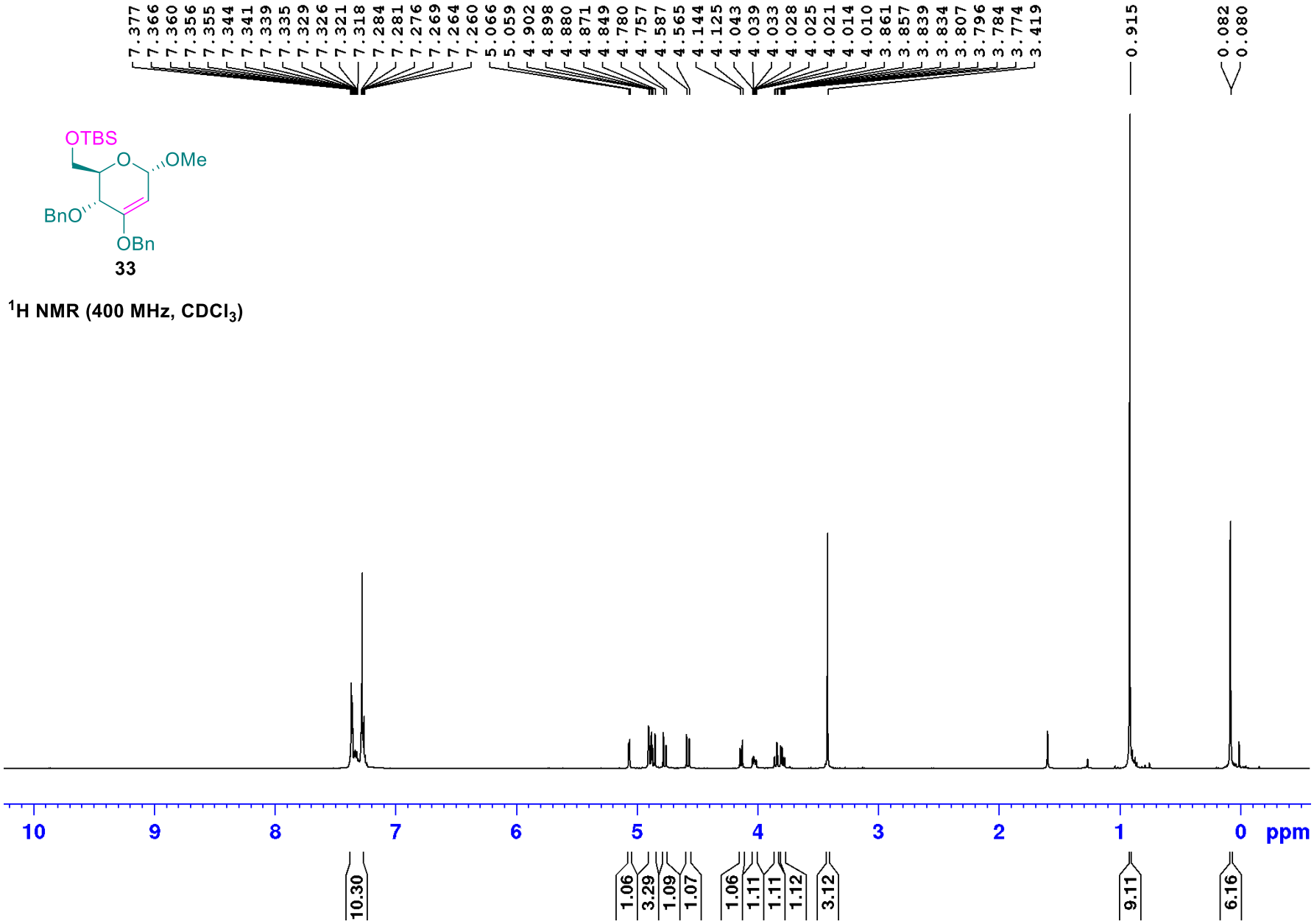
32α

^{1}H NMR (400 MHz, $CDCl_3$)



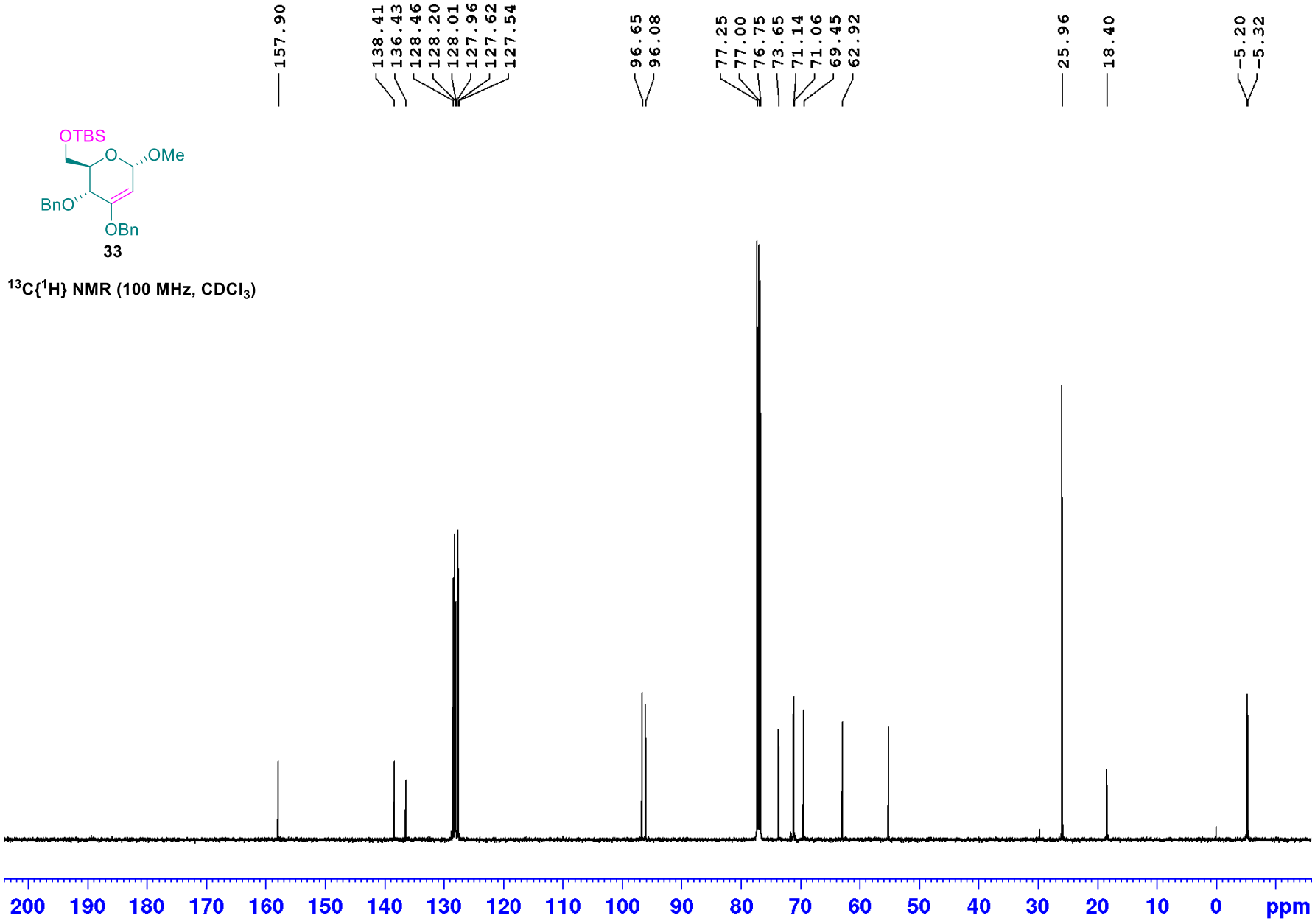
32α

$^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$)



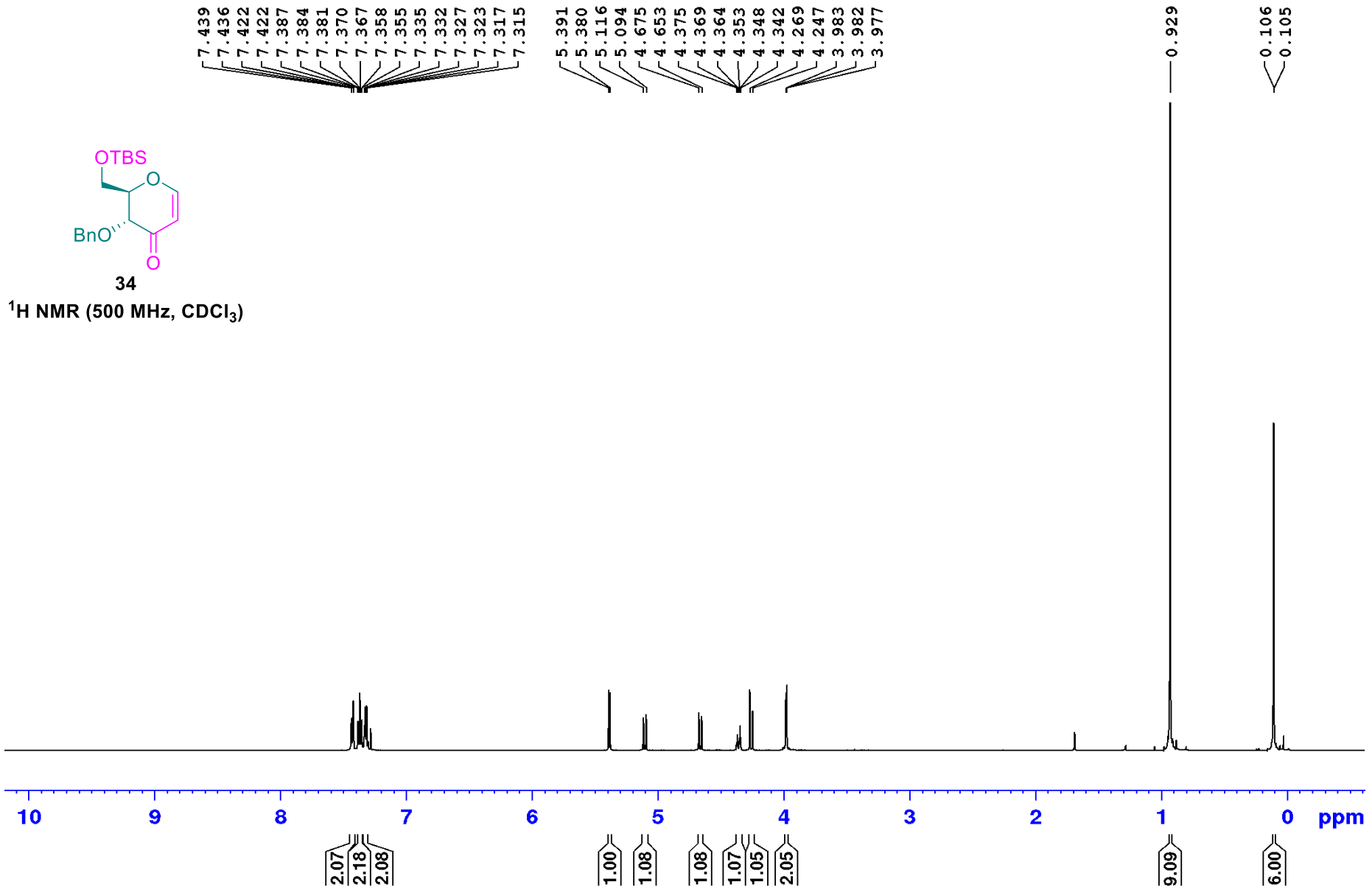
33

^{1}H NMR (400 MHz, $CDCl_3$)



33

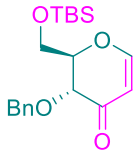
$^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$)



34

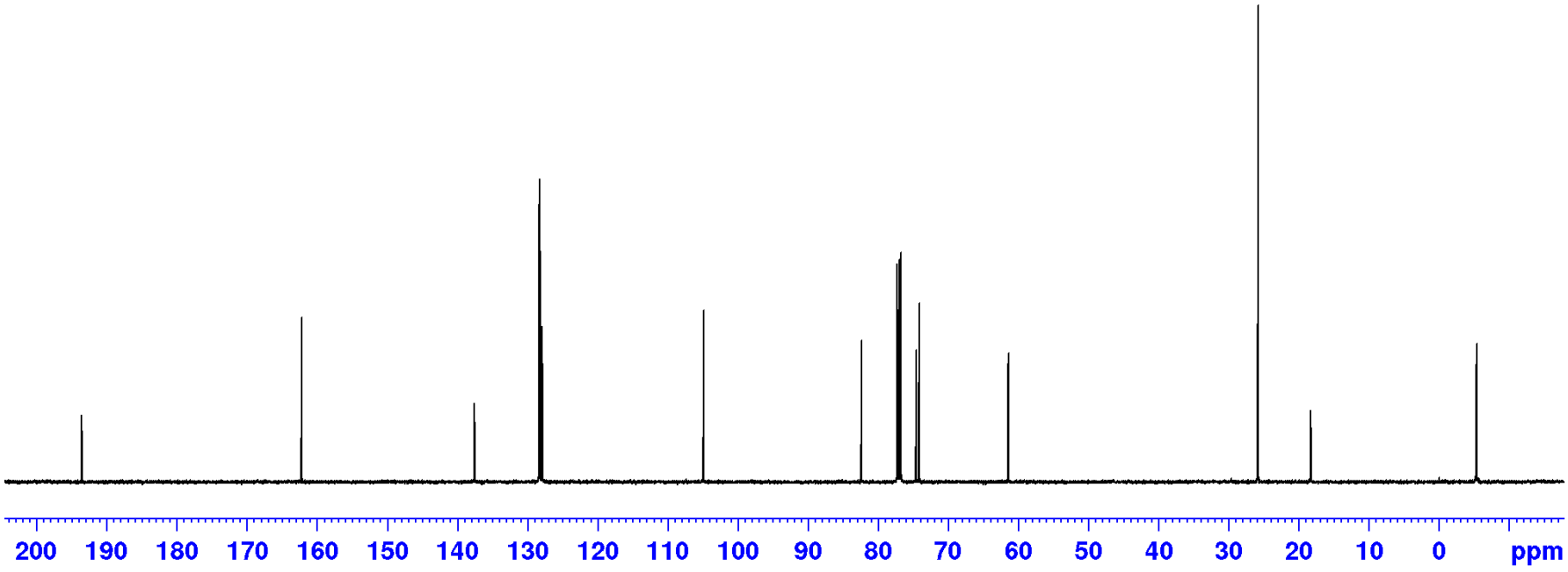
^{1}H NMR (500 MHz, $CDCl_3$)

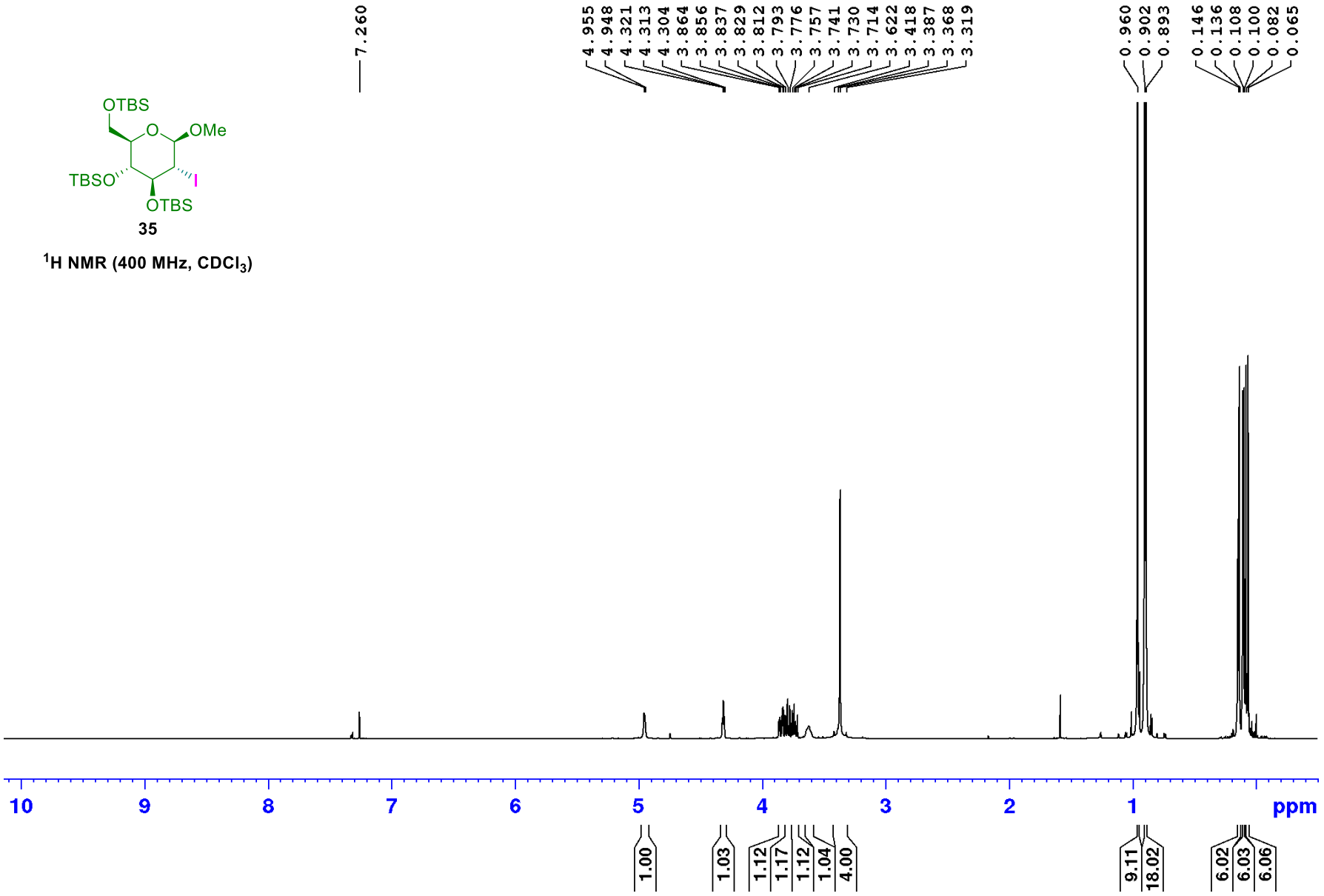
193.57
162.21
137.58
128.35
128.22
127.90
104.87
82.36
77.25
77.00
76.75
74.55
74.15
61.41
25.81
18.30
-5.35
-5.42

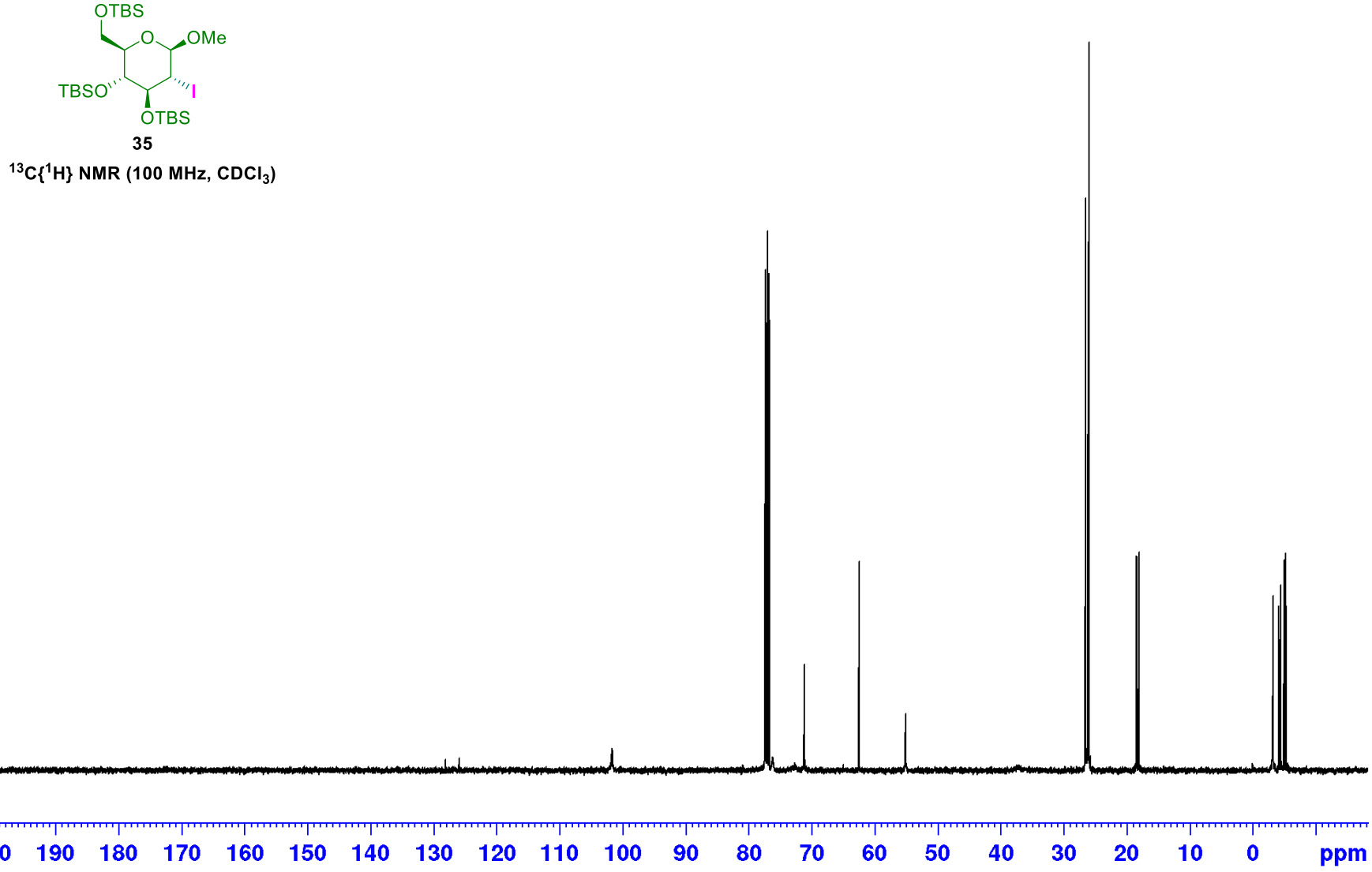


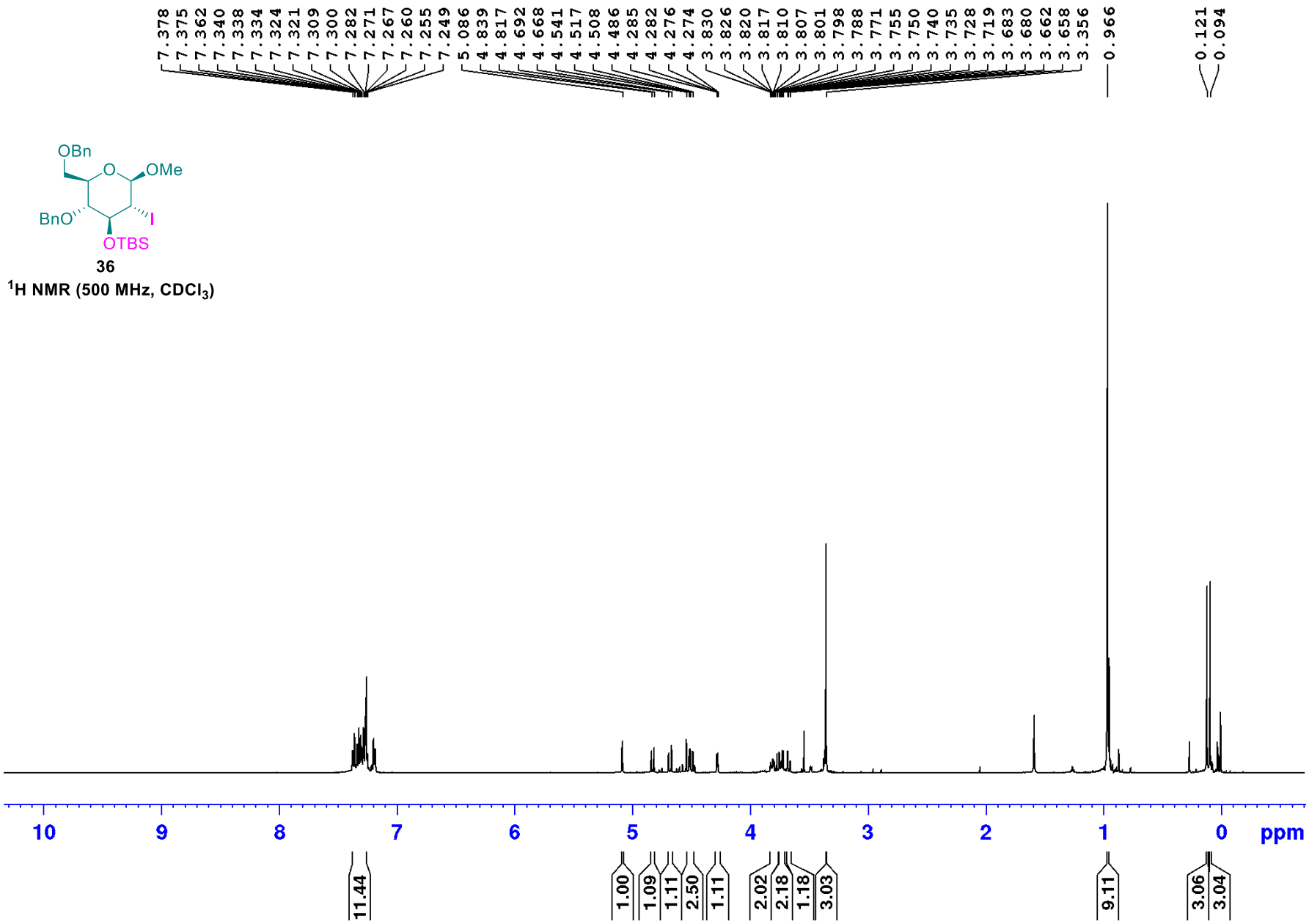
34

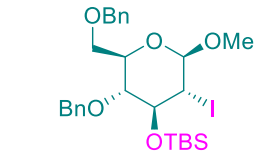
$^{13}C\{^{1}H\}$ NMR (125 MHz, $CDCl_3$)




OTBS
O
OMe
TBSO
I
OTBS
35
1H NMR (400 MHz, CDCl3)
7.260
4.955
4.948
4.321
4.313
4.304
3.864
3.856
3.837
3.829
3.812
3.793
3.776
3.757
3.741
3.730
3.714
3.622
3.418
3.387
3.368
3.319
0.960
0.902
0.893
0.146
0.136
0.108
0.100
0.082
0.065
10
9
8
7
6
5
4
3
2
1
ppm
1.00
1.03
1.12
1.17
1.12
1.04
4.00
9.11
18.02
6.02
6.03
6.06

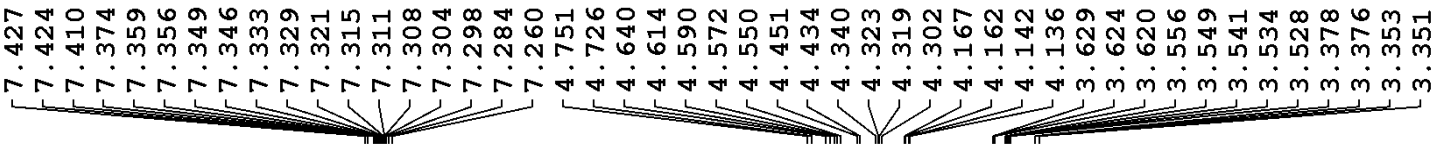

OTBS
O
OMe
TBSO
I
OTBS
35
$^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$)
101.65
77.32
77.00
76.69
71.11
62.45
55.05
26.49
26.08
25.97
18.38
18.36
18.03
-3.26
-4.20
-4.50
-5.00
-5.27
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm

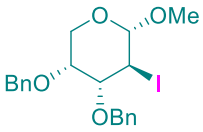

7.378
7.375
7.362
7.340
7.338
7.334
7.324
7.321
7.309
7.300
7.282
7.271
7.267
7.260
7.255
7.249
5.086
4.839
4.817
4.692
4.668
4.541
4.517
4.508
4.486
4.285
4.282
4.276
4.274
3.830
3.826
3.820
3.817
3.810
3.807
3.801
3.798
3.788
3.771
3.755
3.750
3.740
3.735
3.728
3.719
3.683
3.680
3.662
3.658
3.356
0.966
0.121
0.094
OBn
O
OMe
BnO
I
OTBS
36
1H NMR (500 MHz, CDCl3)
10
9
8
7
6
5
4
3
2
1
0
ppm
11.44
1.00
1.09
1.11
2.50
1.11
2.02
2.18
1.18
3.03
9.11
3.06
3.04



36

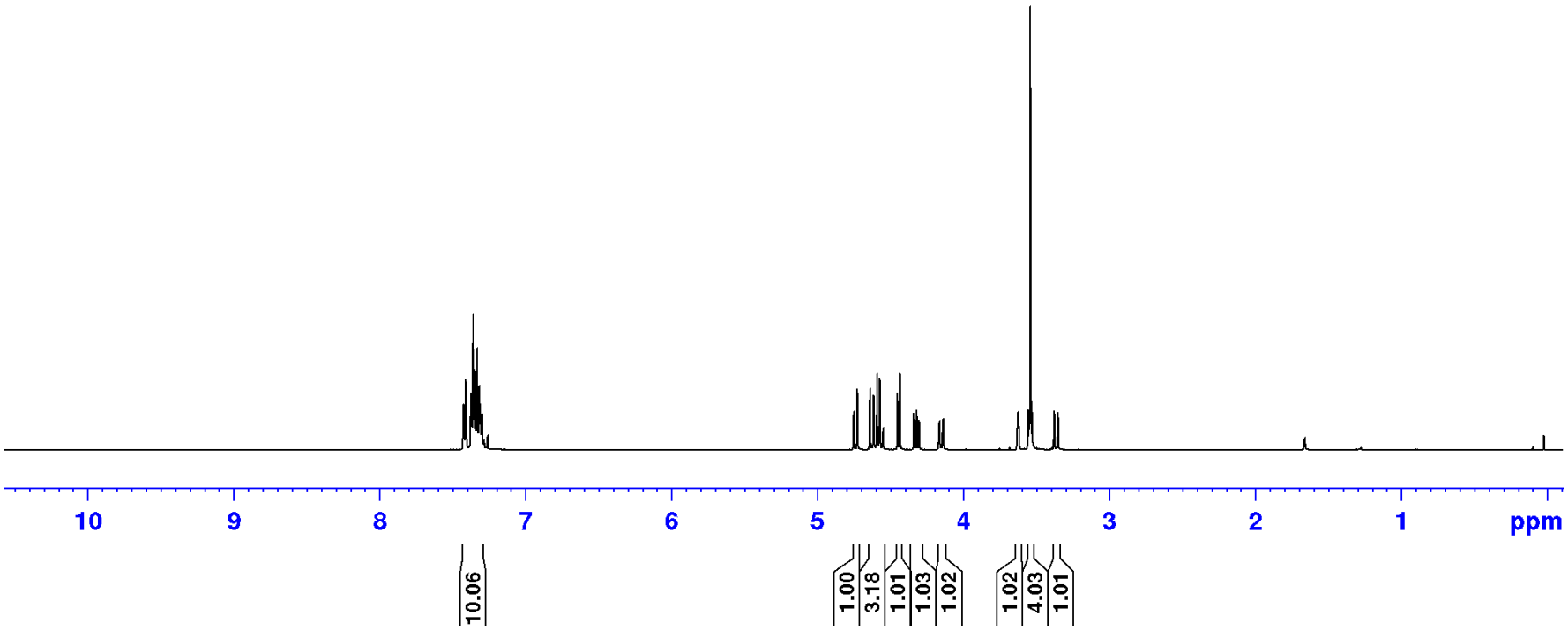
$^{13}C\{^{1}H\}$ NMR (125 MHz, $CDCl_3$)

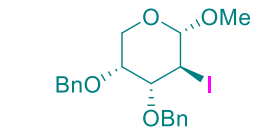




37

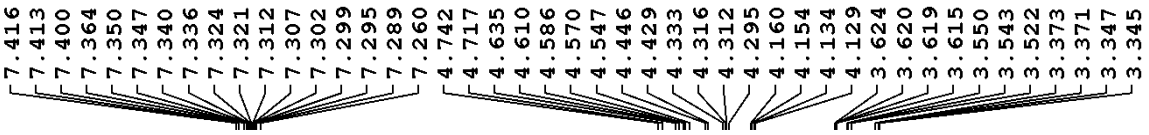
^{1}H NMR (500 MHz, $CDCl_3$)

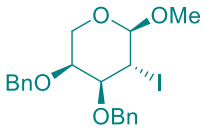




37

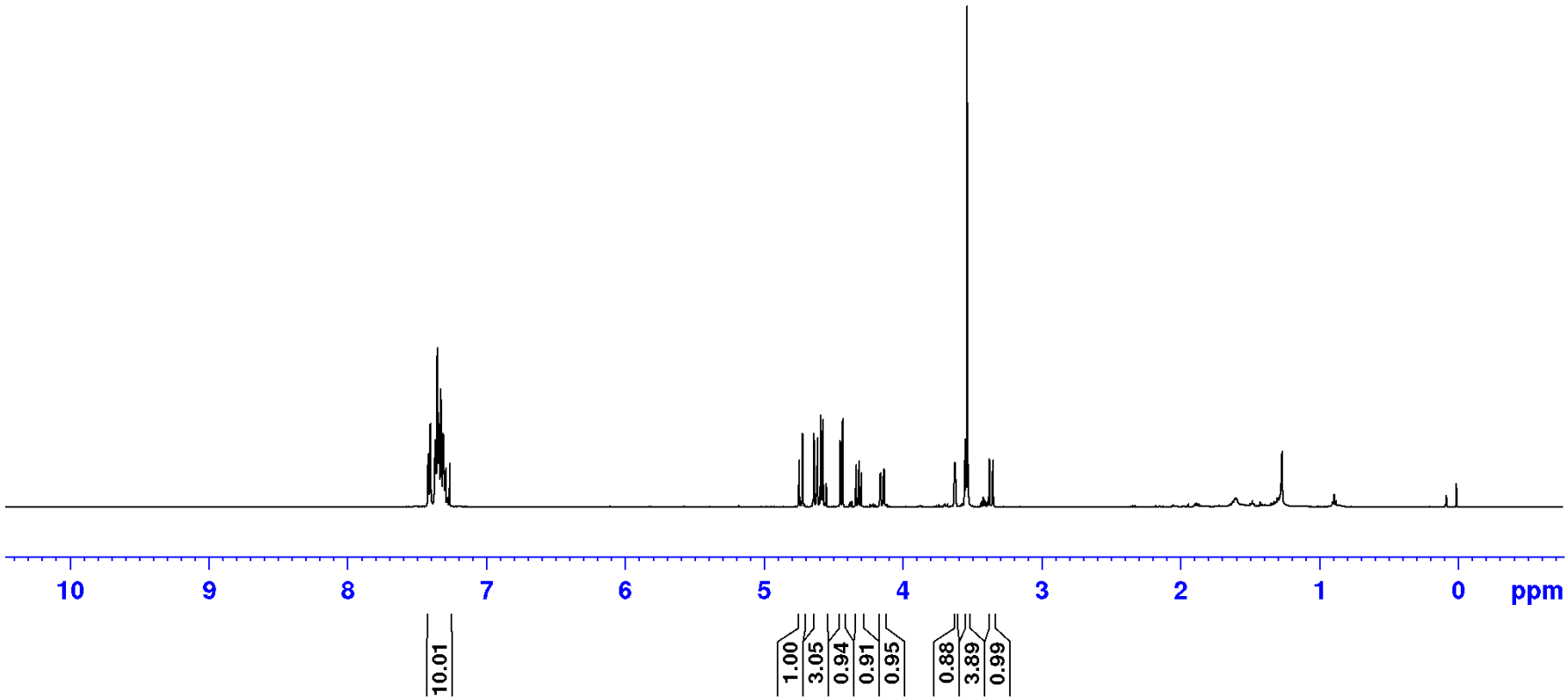
$^{13}C\{^{1}H\}$ NMR (125 MHz, $CDCl_3$)

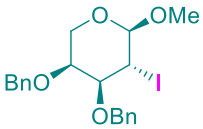




38

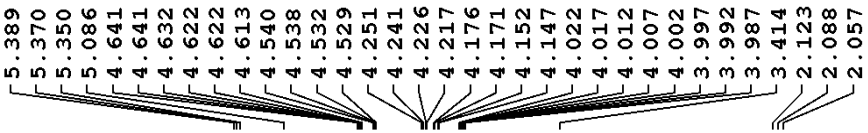
^{1}HNMR (500 MHz, $CDCl_3$)

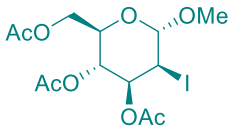




38

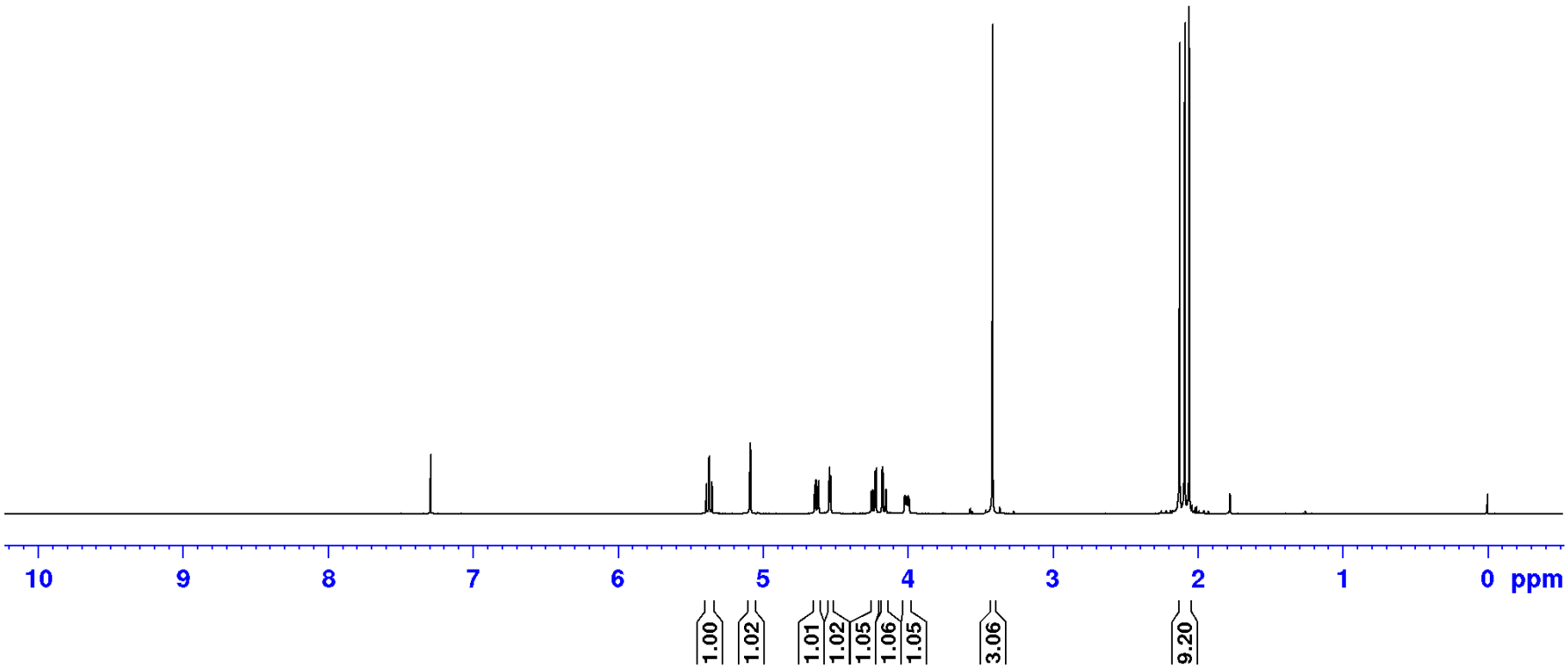
$^{13}C\{^{1}H\}$ NMR (125 MHz, $CDCl_3$)

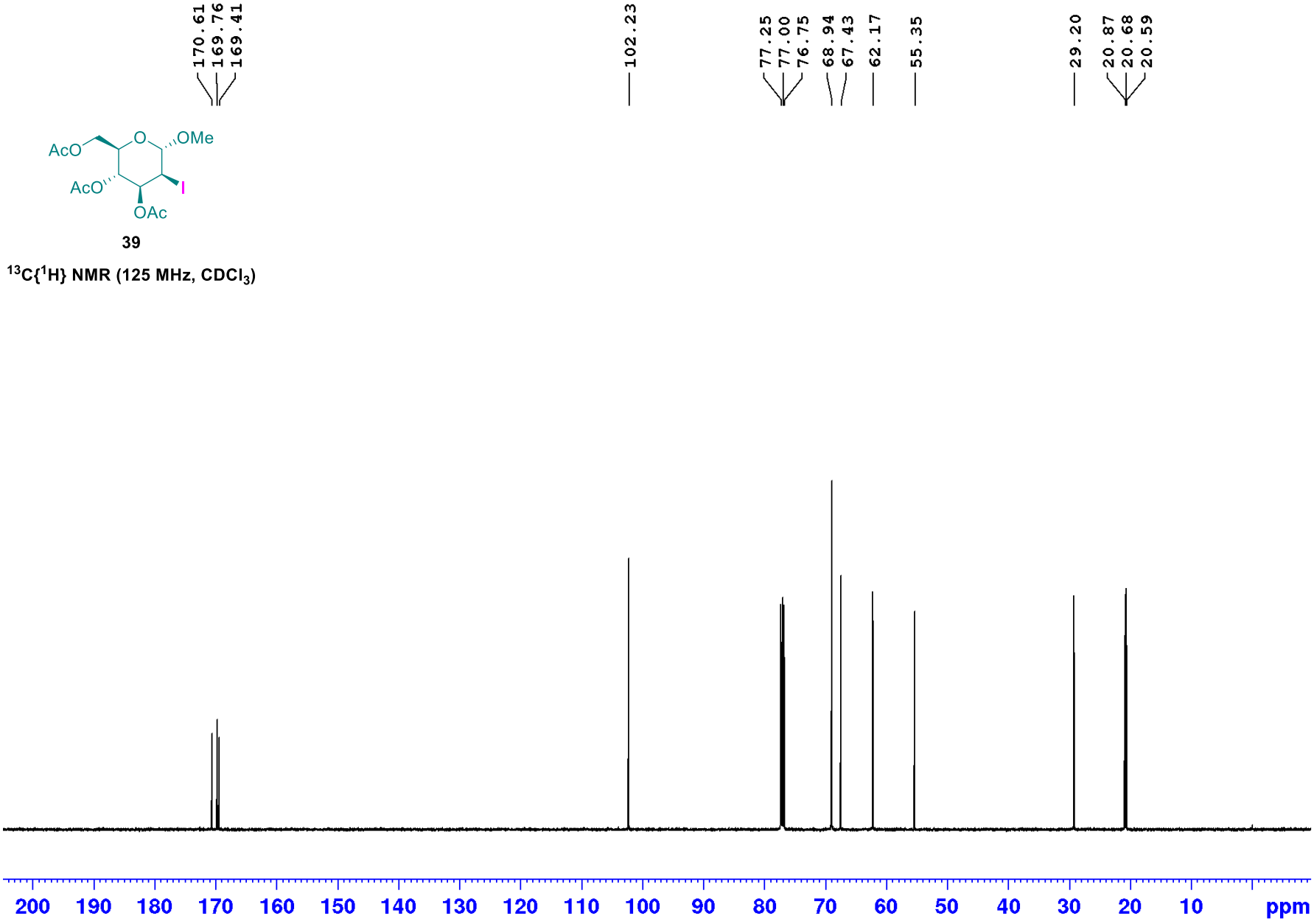




39

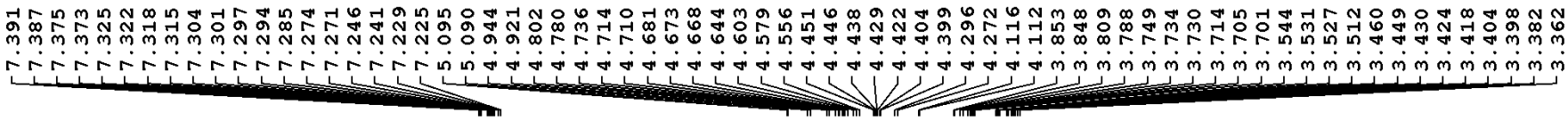
^{1}H NMR (500 MHz, $CDCl_3$)

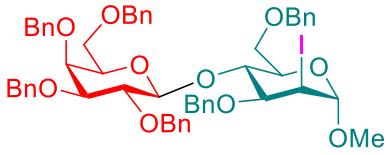




39

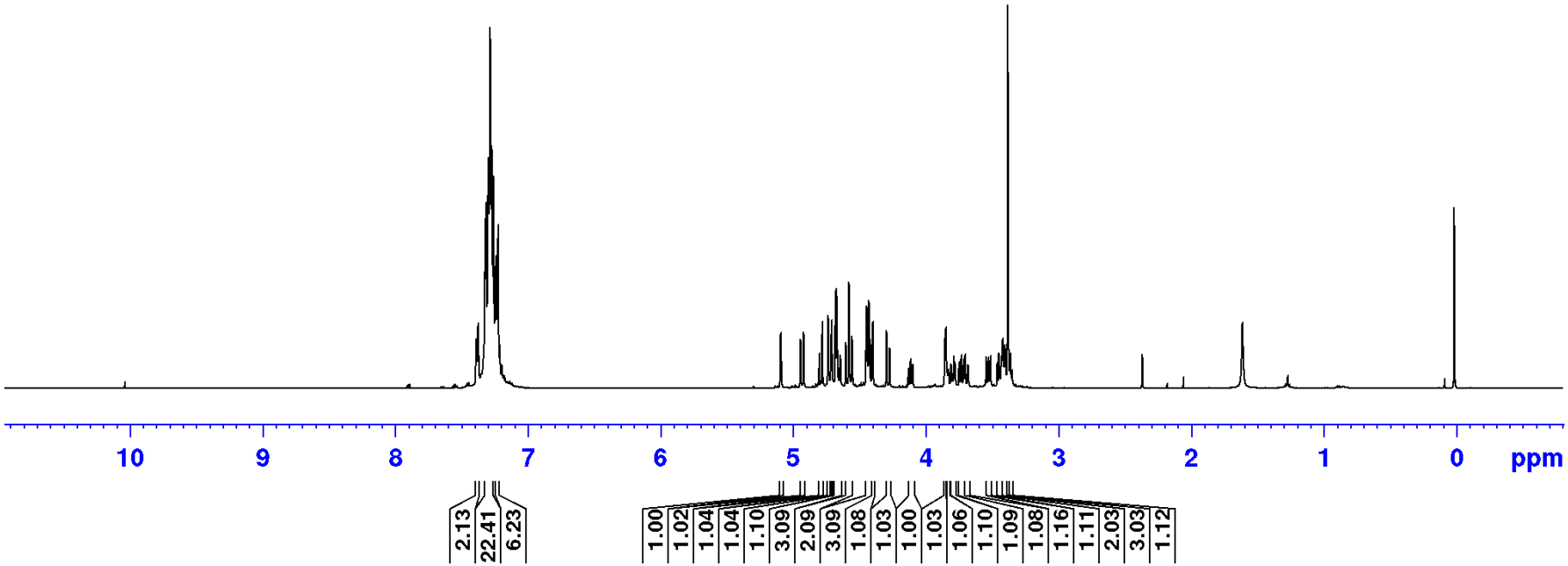
$^{13}C\{^{1}H\}$ NMR (125 MHz, $CDCl_3$)

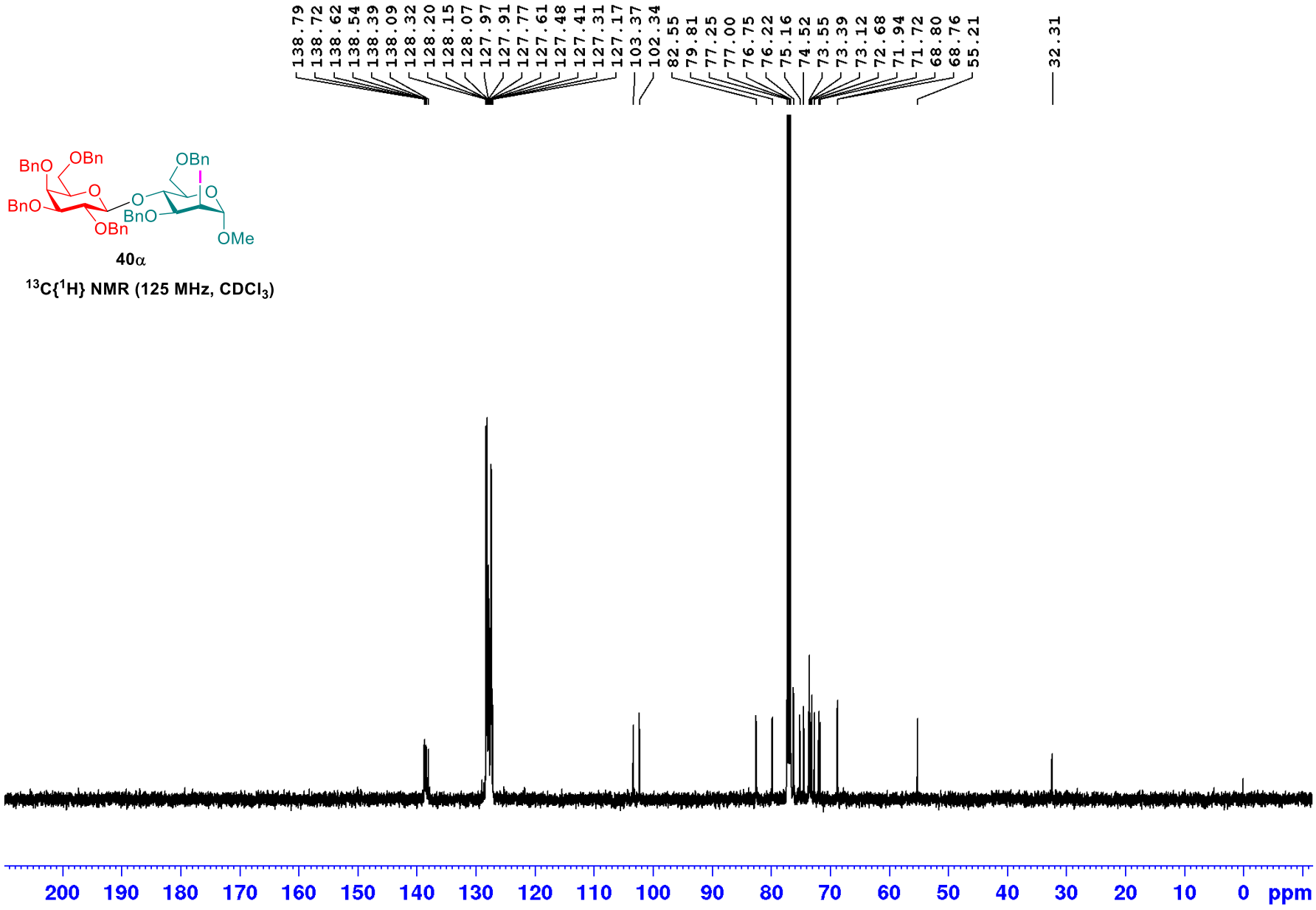




40α

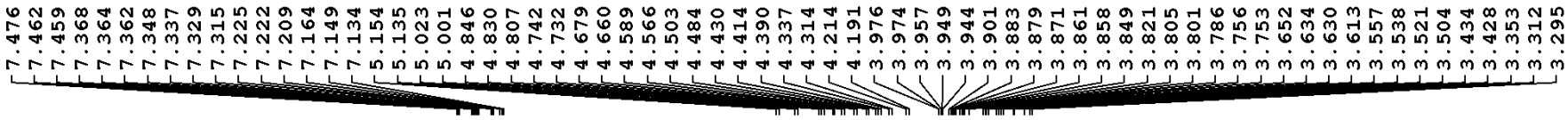
^{1}H NMR (500 MHz, $CDCl_3$)

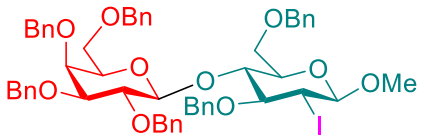




40α

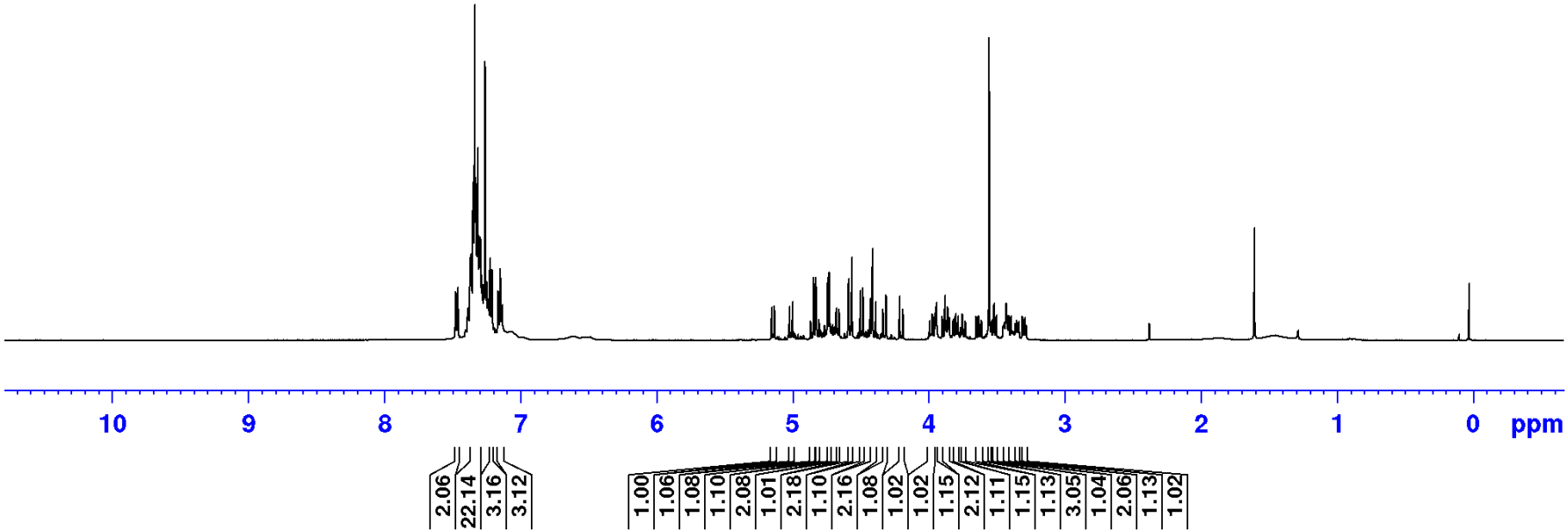
$^{13}C\{^{1}H\}$ NMR (125 MHz, $CDCl_3$)

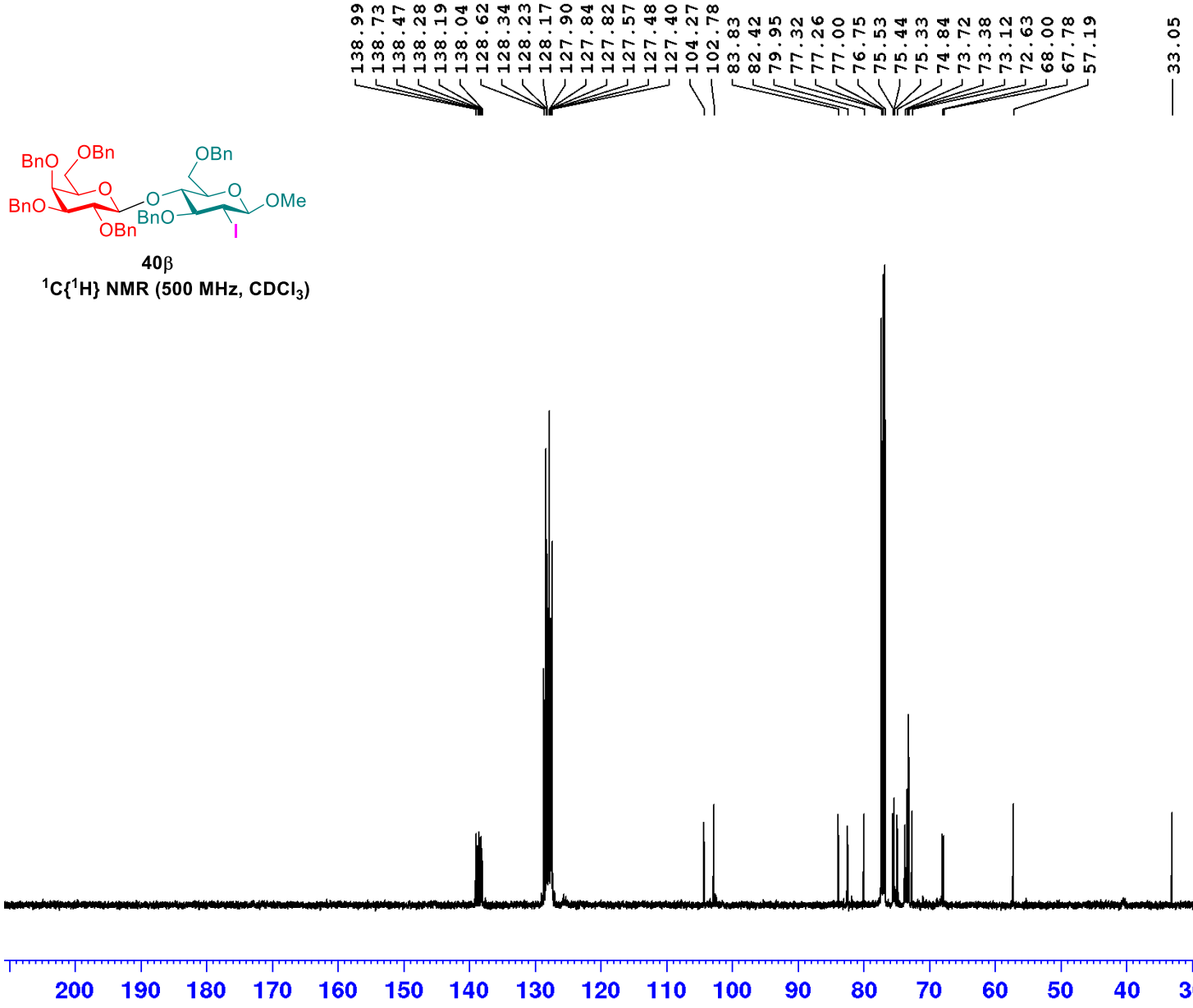




40β

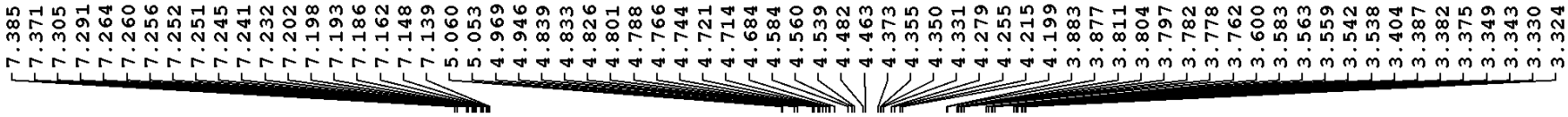
^{1}H NMR (500 MHz, $CDCl_3$)

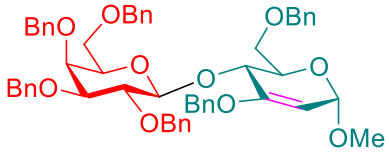




40β

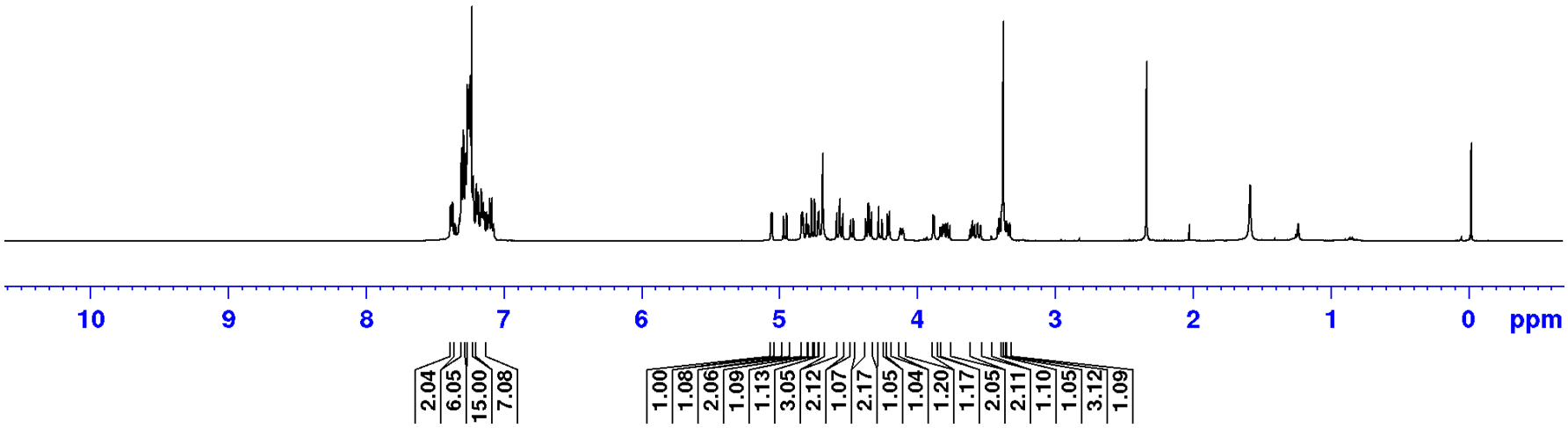
$^{1}C\{^{1}H\}$ NMR (500 MHz, $CDCl_3$)

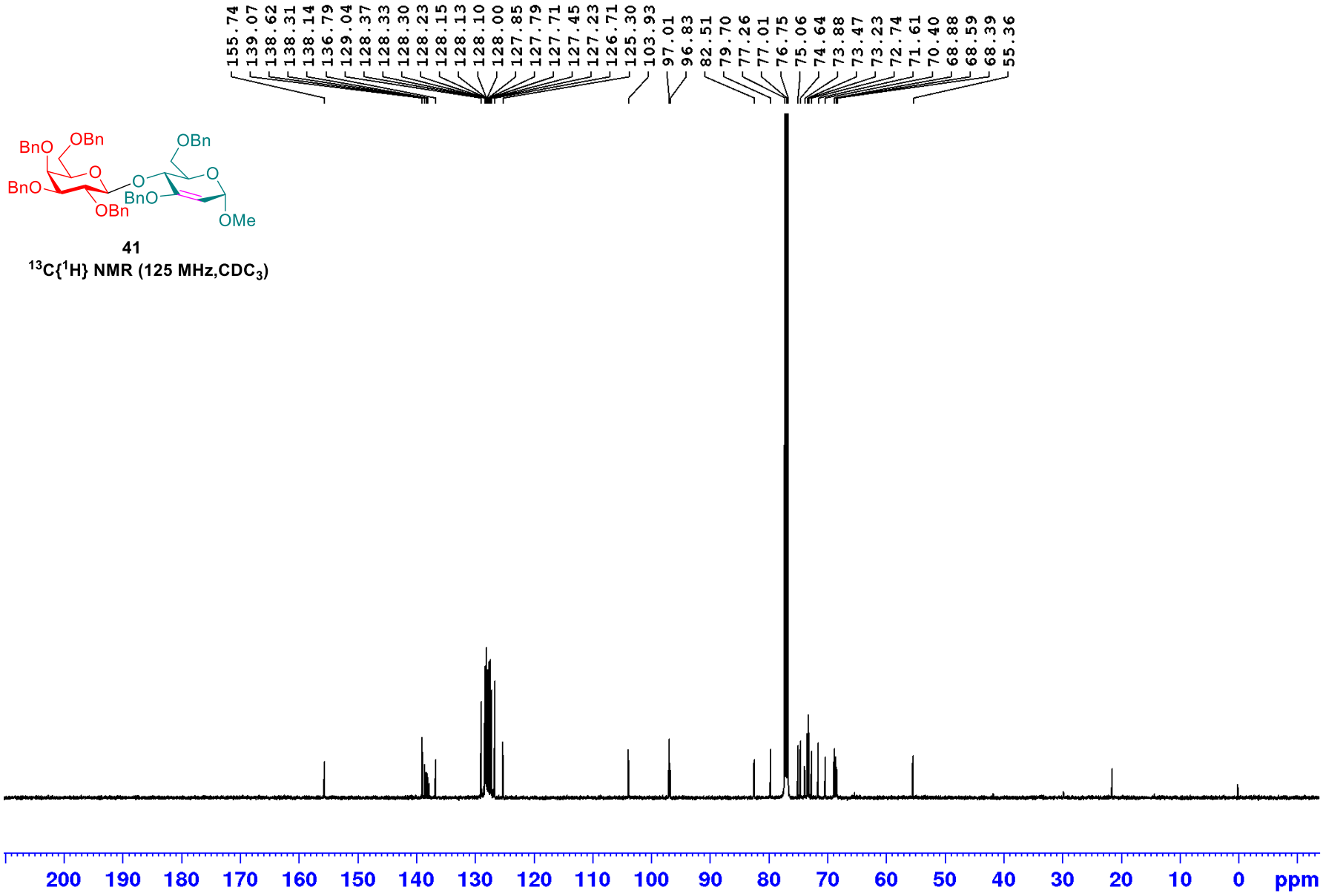




41

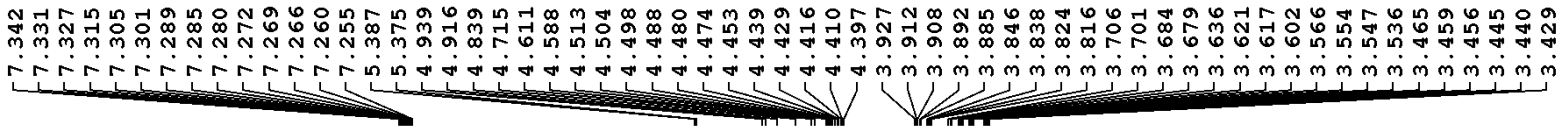
^{1}H NMR (500 MHz,CDC$_3$)

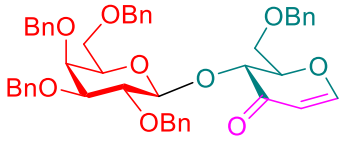




41

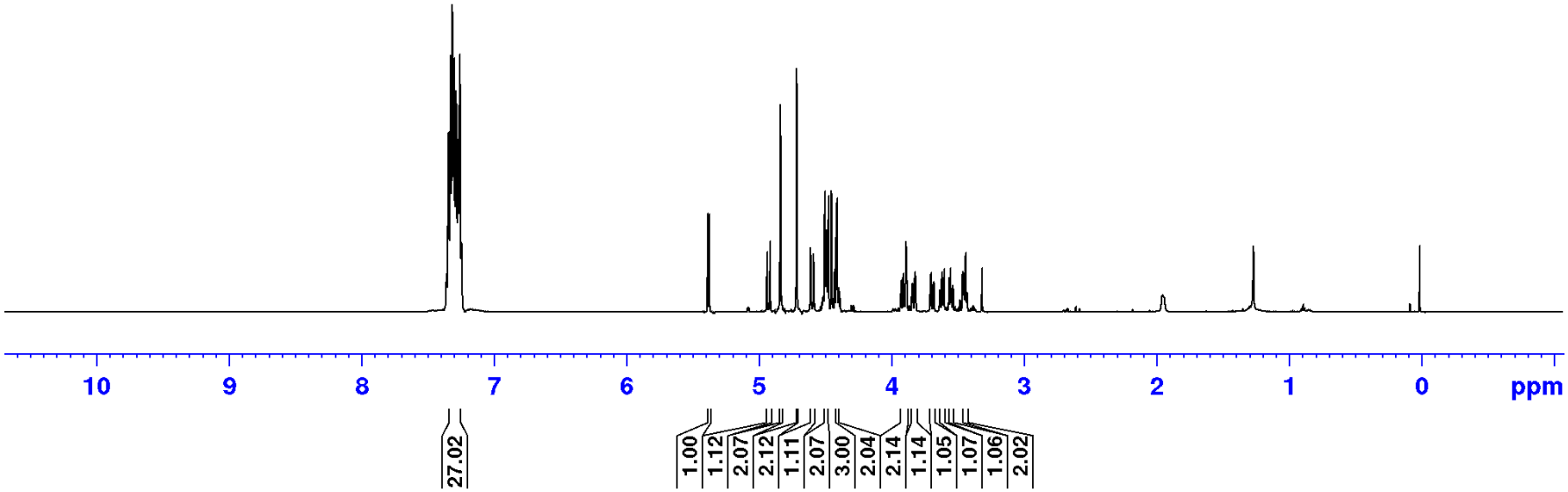
$^{13}C\{^{1}H\}$ NMR (125 MHz,CDC_3)

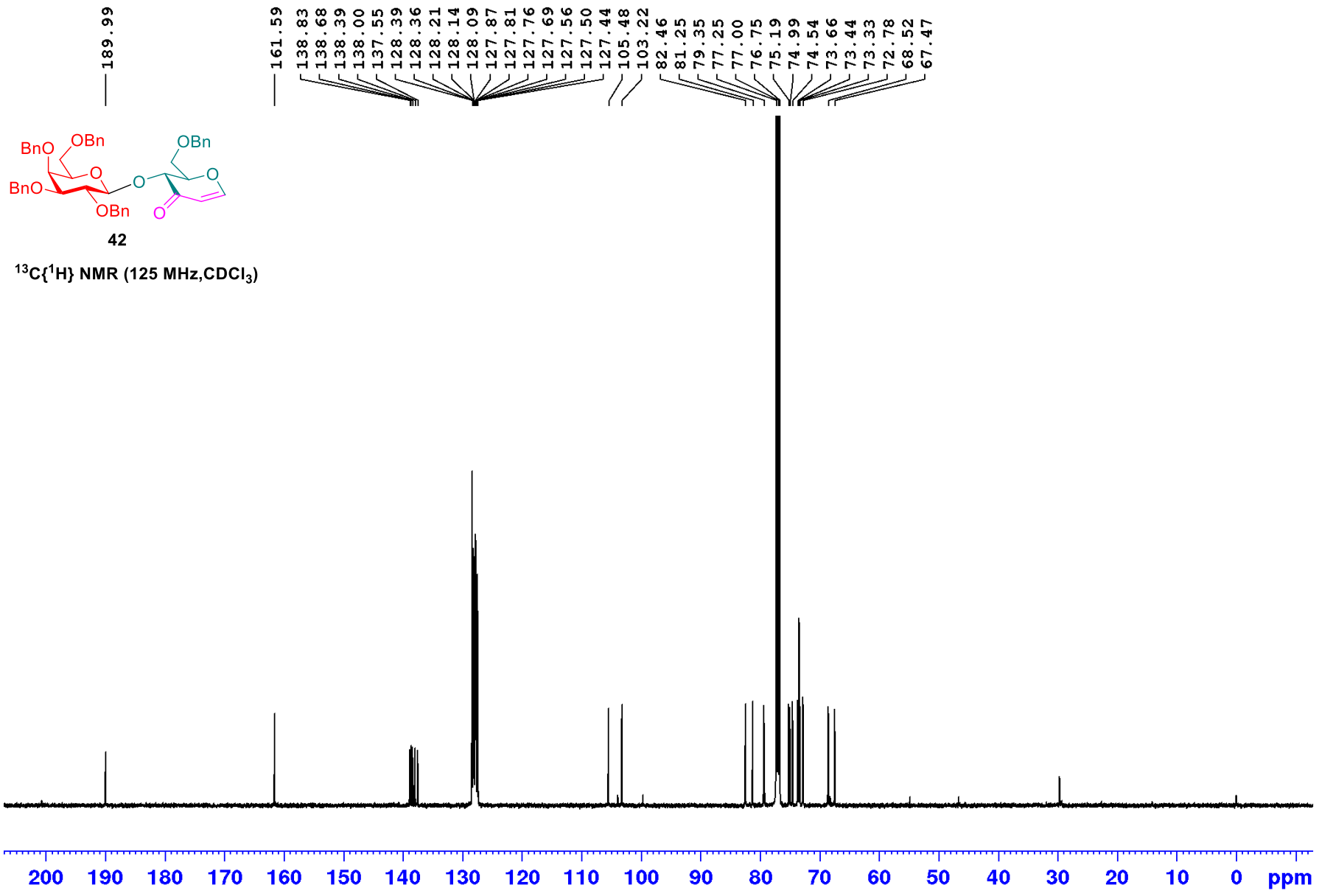




42

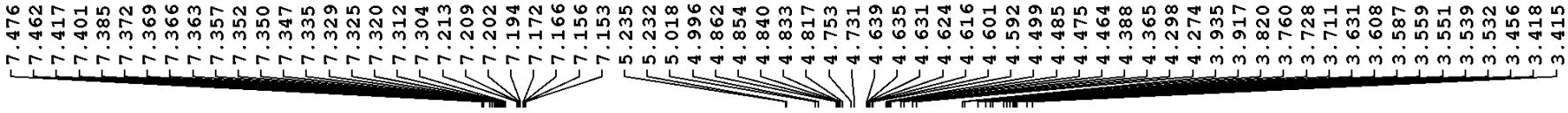
^{1}H NMR (500 MHz,$CDCl_3$)

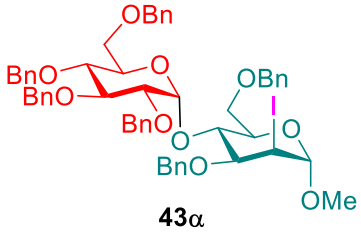




42

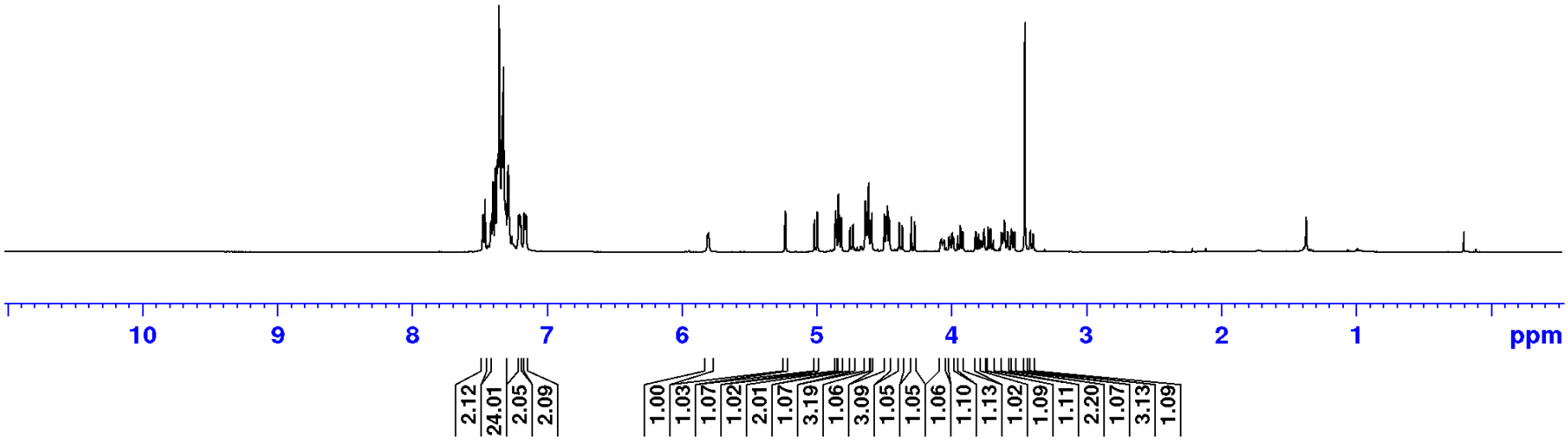
$^{13}C\{^{1}H\}$ NMR (125 MHz,$CDCl_3$)

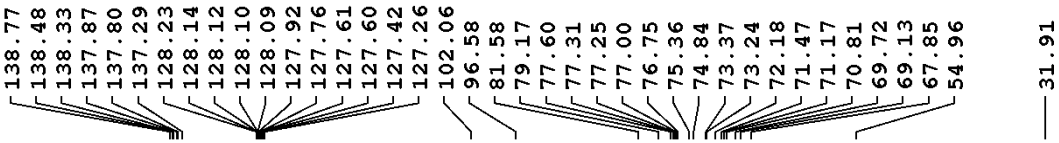


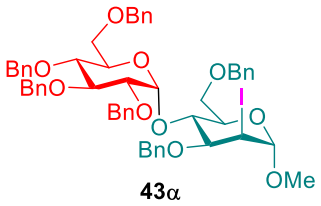


43α

^{1}H NMR (500 MHz,$CDCl_3$)

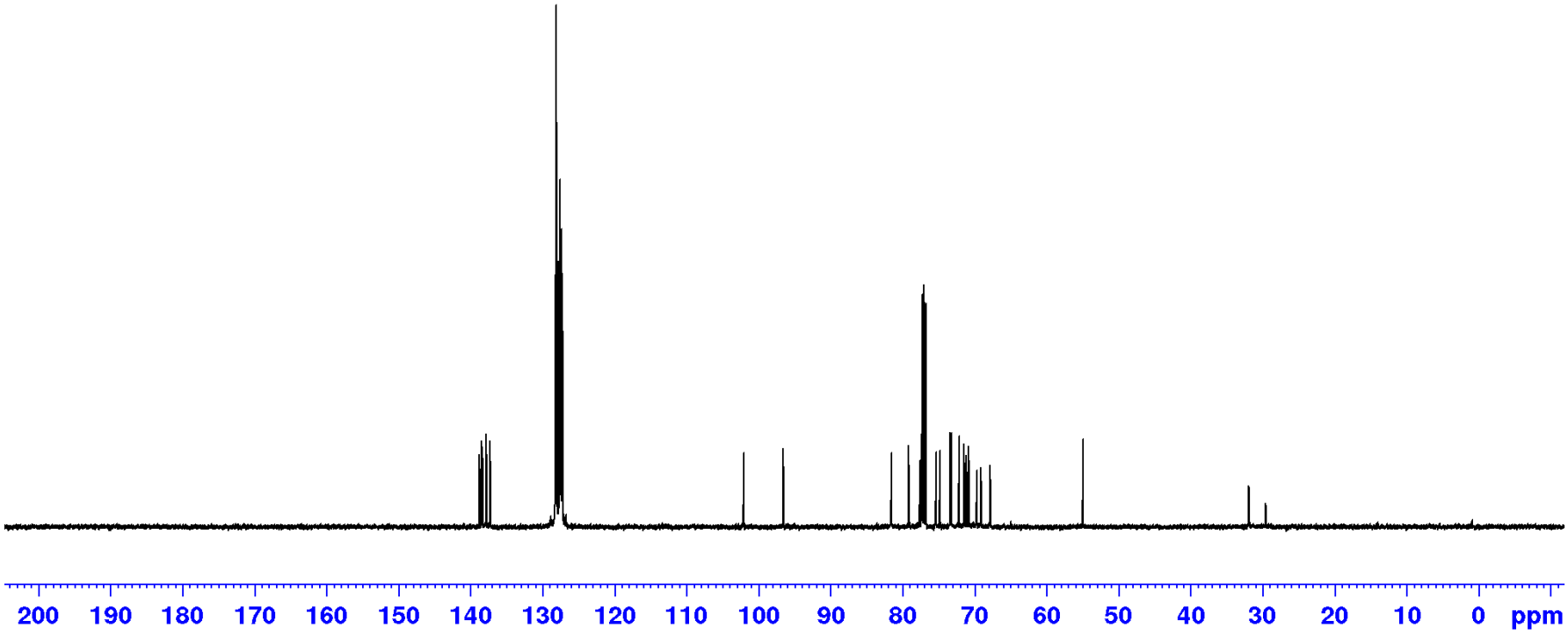


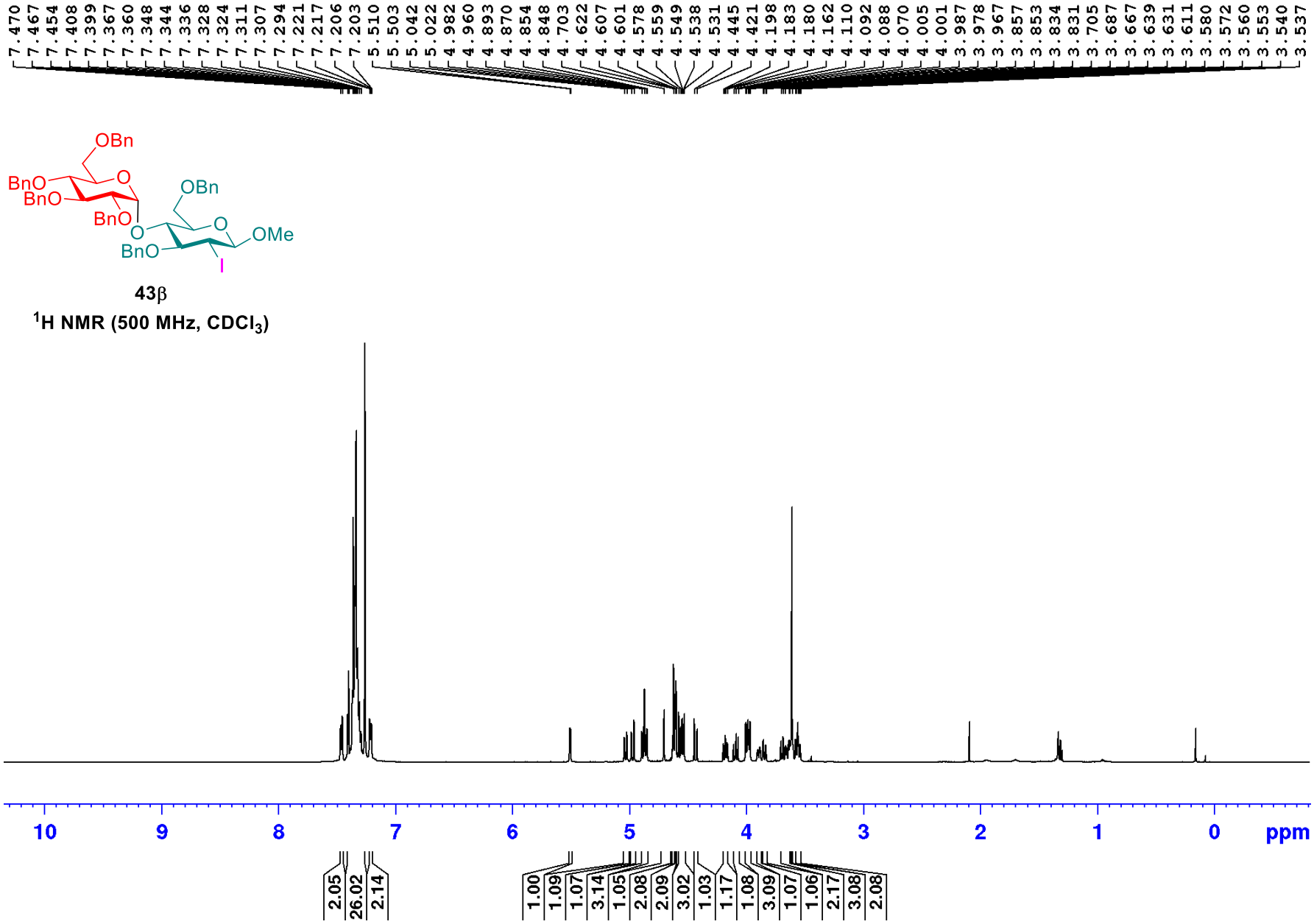




43α

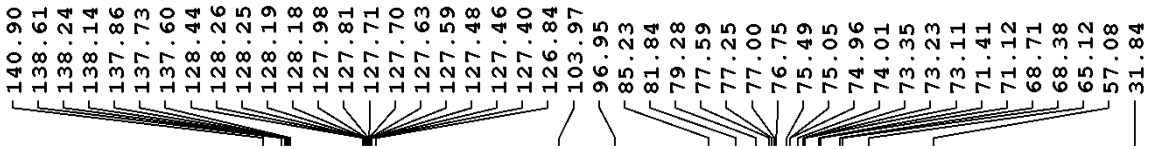
$^{13}C\{^{1}H\}$ NMR (125 MHz,$CDCl_3$)

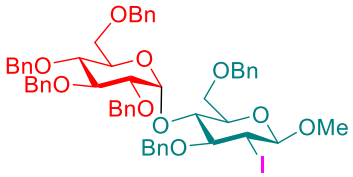




43β

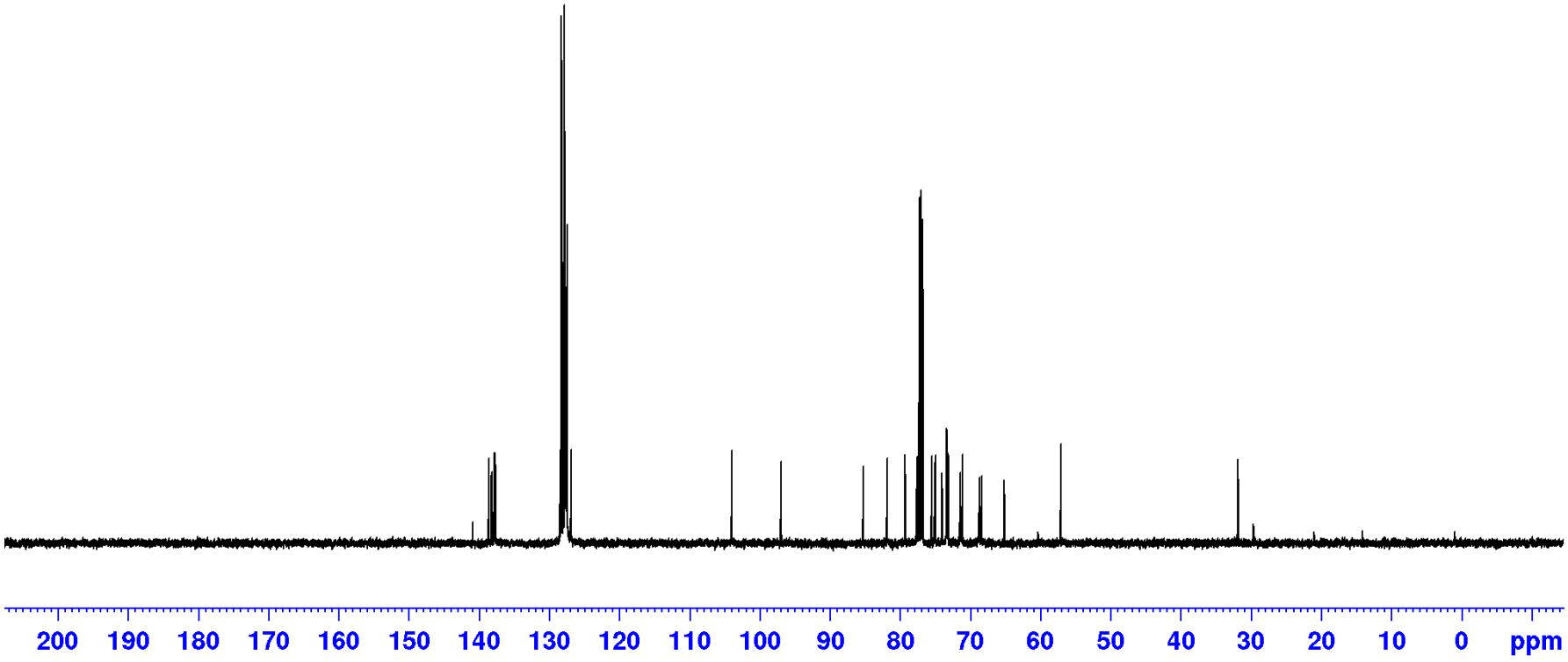
^{1}H NMR (500 MHz, $CDCl_3$)

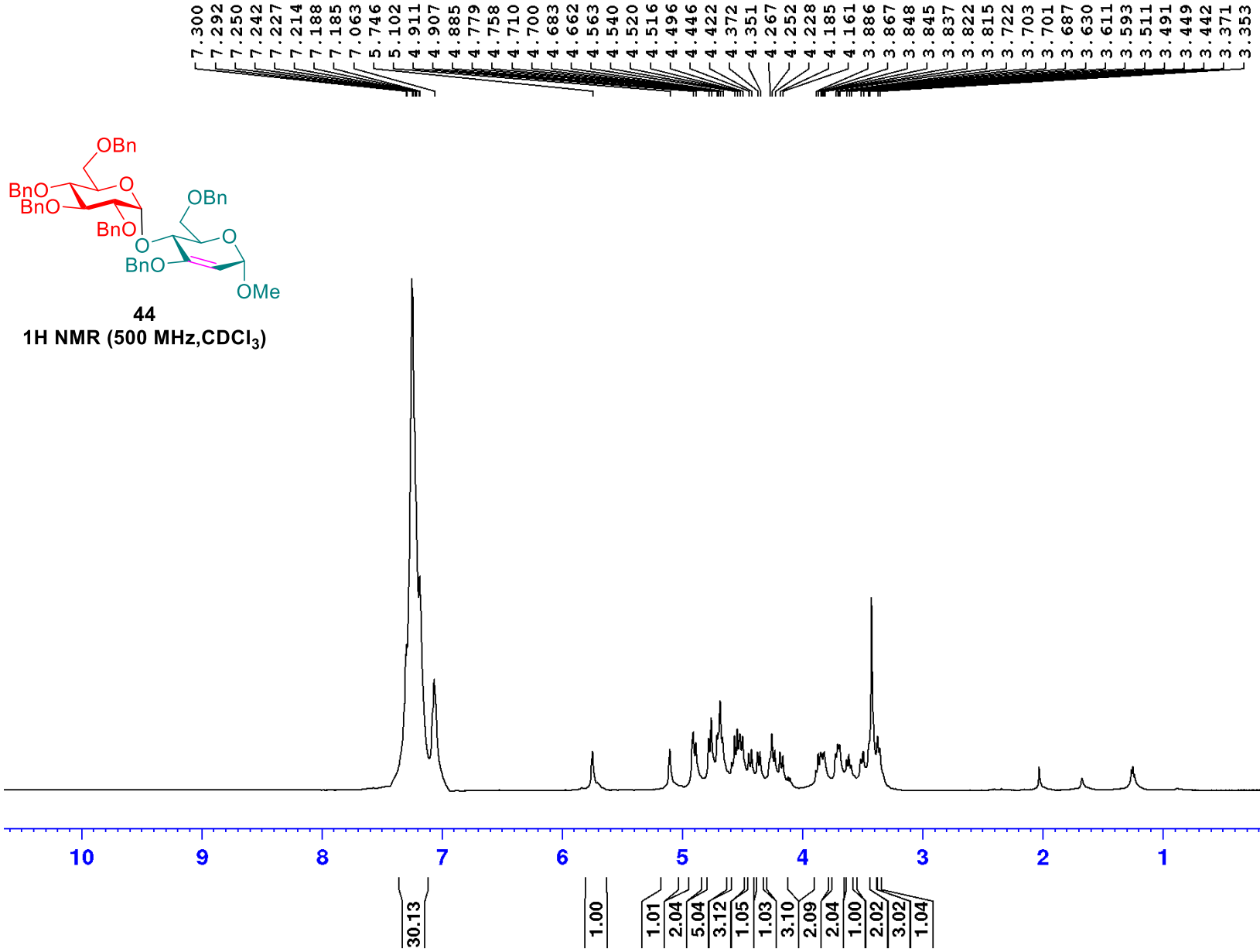


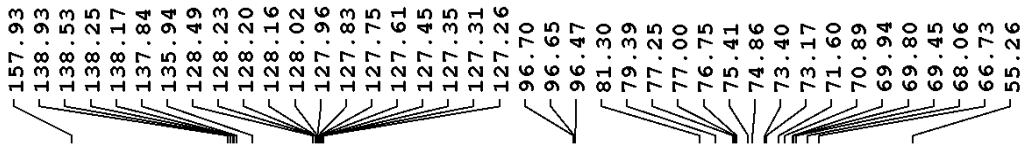


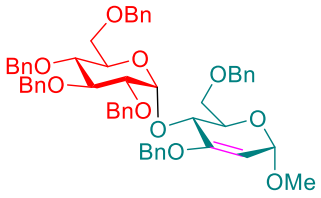
43β

$^{13}C\{^{1}H\}$ NMR (125 MHz, $CDCl_3$)



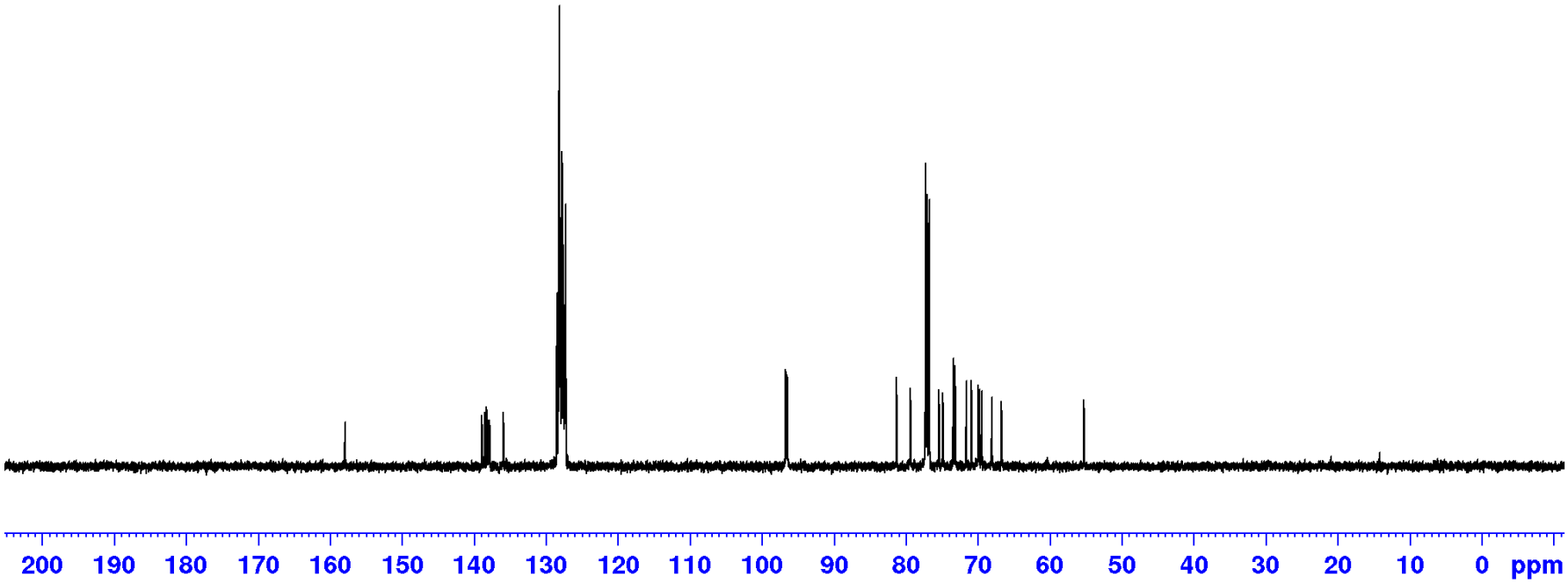

7.300
7.292
7.250
7.242
7.227
7.214
7.188
7.185
7.063
5.746
5.102
4.911
4.907
4.885
4.779
4.758
4.710
4.700
4.683
4.662
4.563
4.540
4.520
4.516
4.496
4.446
4.422
4.372
4.351
4.267
4.252
4.228
4.185
4.161
3.886
3.867
3.848
3.845
3.837
3.822
3.815
3.722
3.703
3.701
3.687
3.630
3.611
3.593
3.511
3.491
3.449
3.442
3.371
3.353
OBn
BnO
BnO
O
BnO
OBn
O
O
BnO
OMe
44
1H NMR (500 MHz,CDCl3)
10
9
8
7
6
5
4
3
2
1
0
ppm
30.13
1.00
1.01
2.04
5.04
3.12
1.05
1.03
3.10
2.09
2.04
1.00
2.02
3.02
1.04

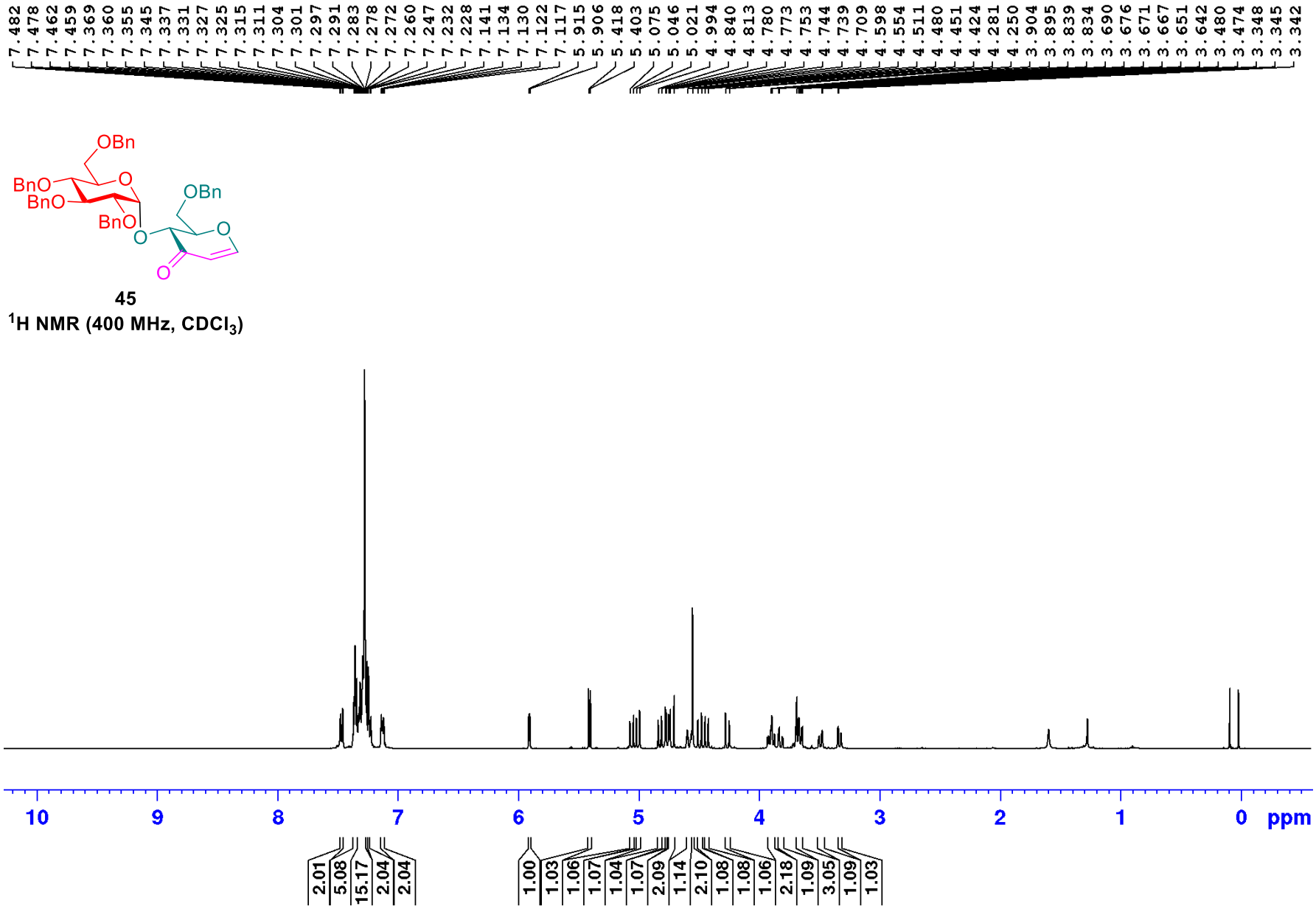




44

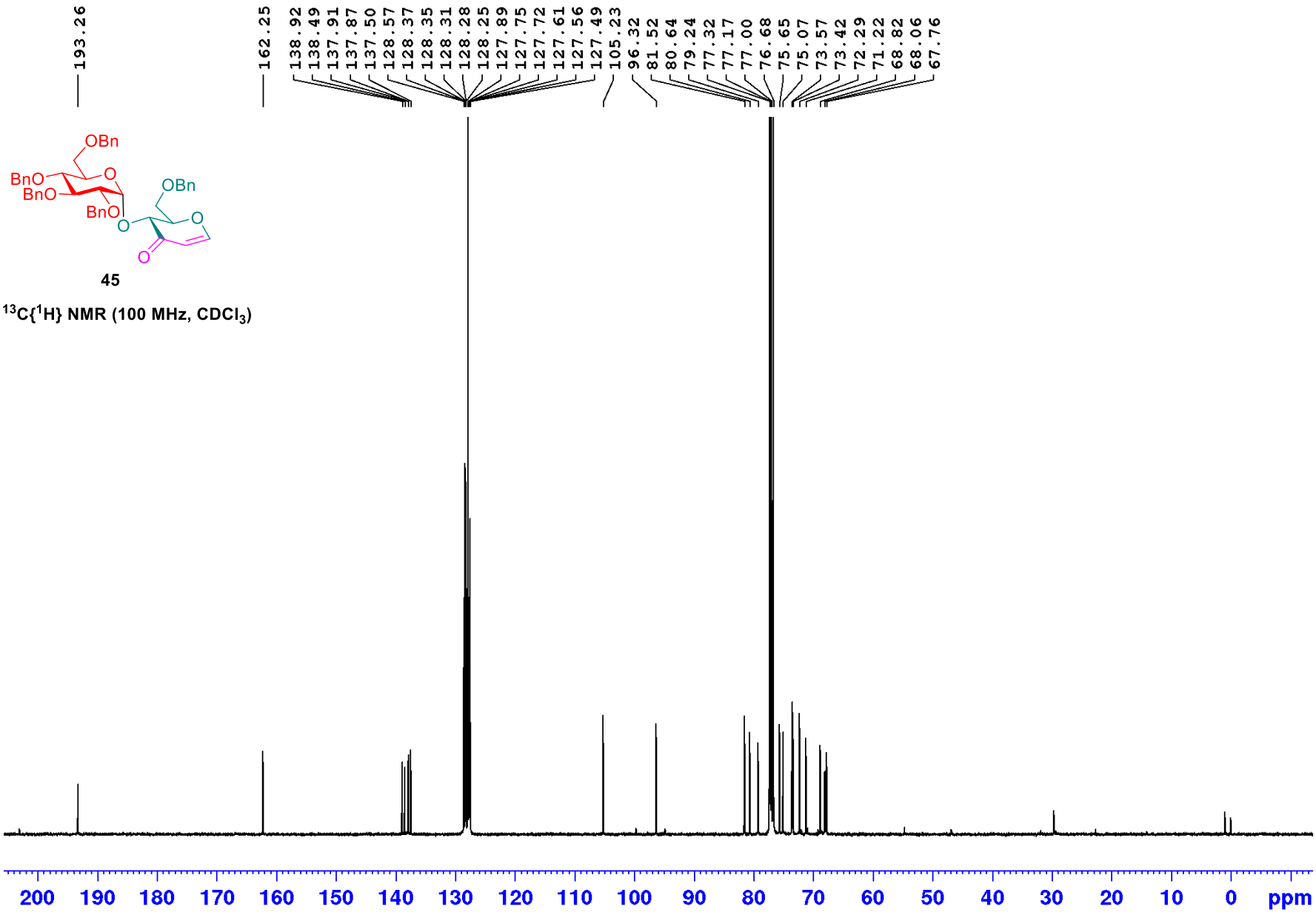
$^{13}C\{^{1}H\}$ NMR (125MHz,$CDCl_3$)





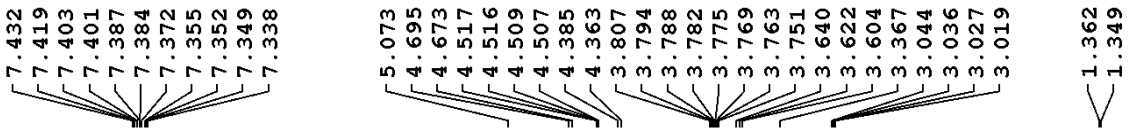
45

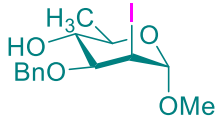
^{1}H NMR (400 MHz, $CDCl_3$)



45

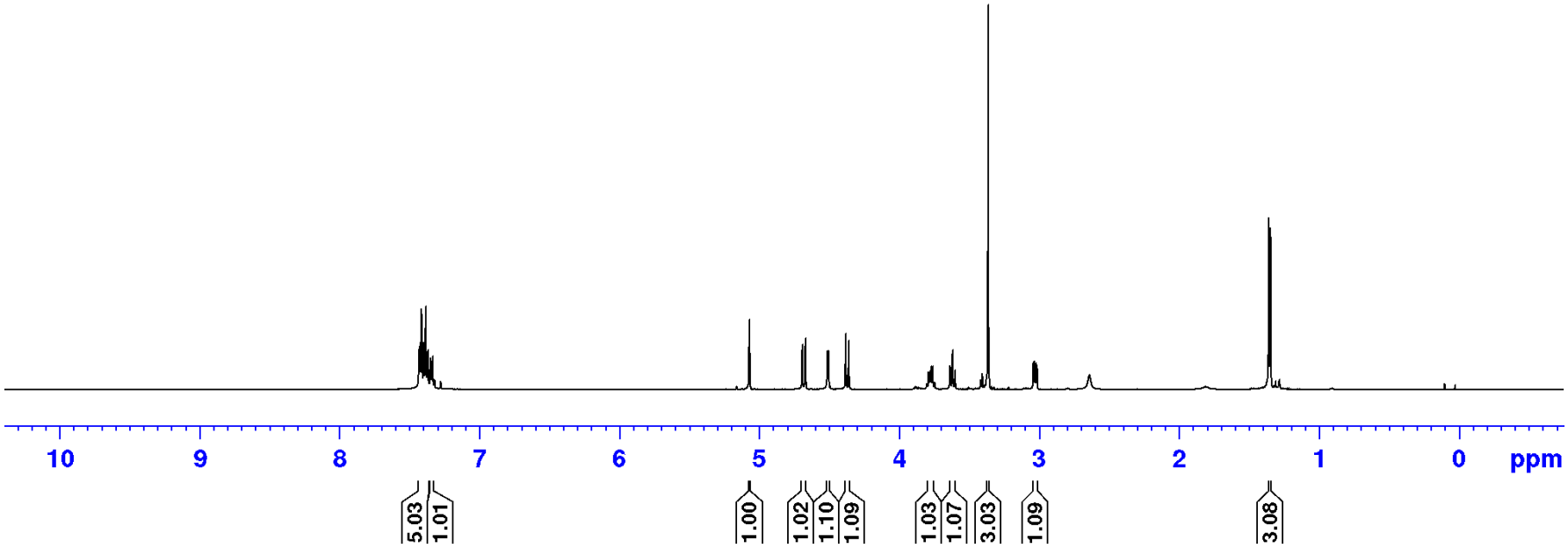
$^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$)

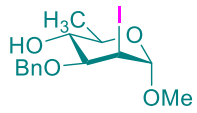




S15α

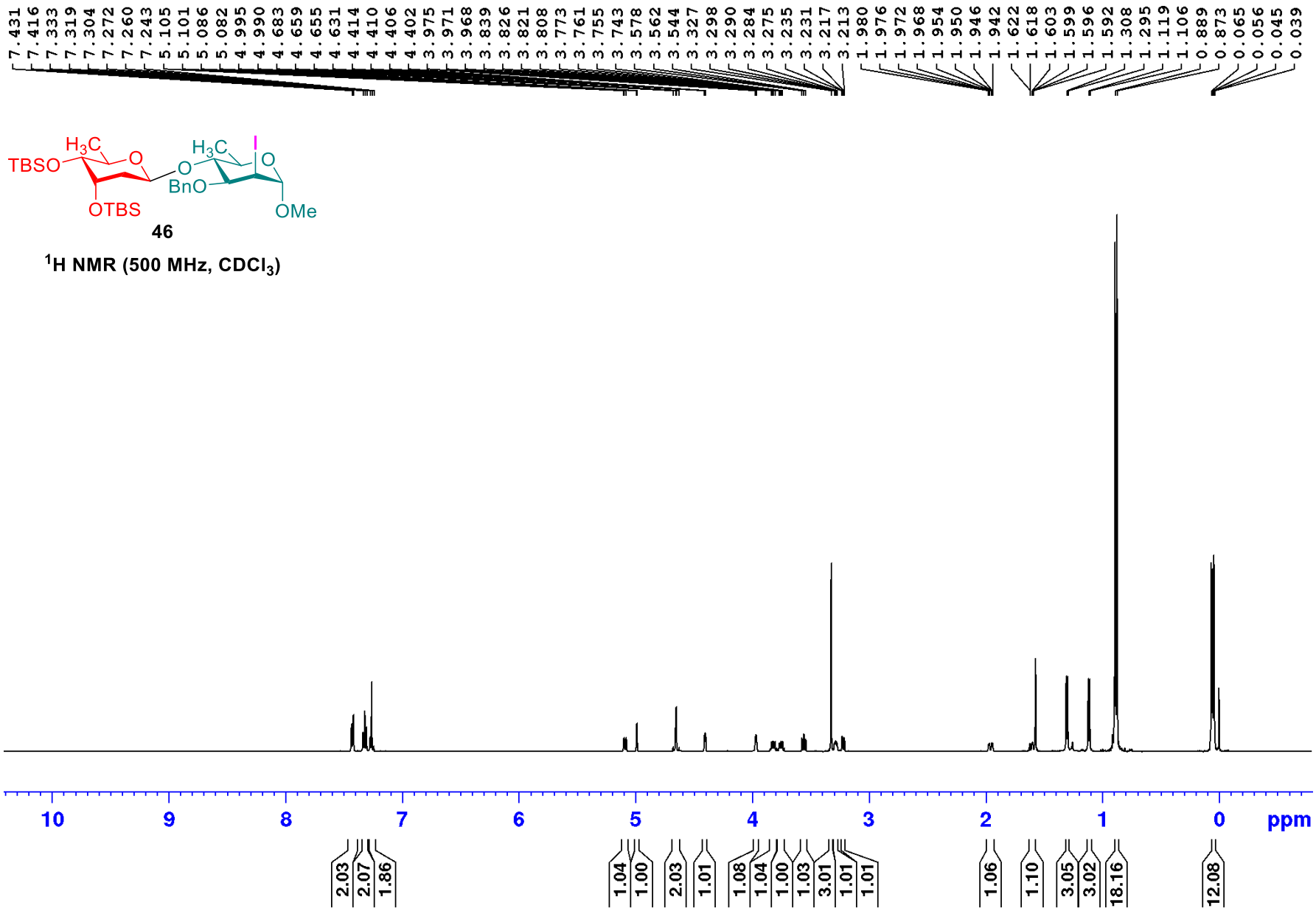
^{1}H NMR (500 MHz, $CDCl_3$)





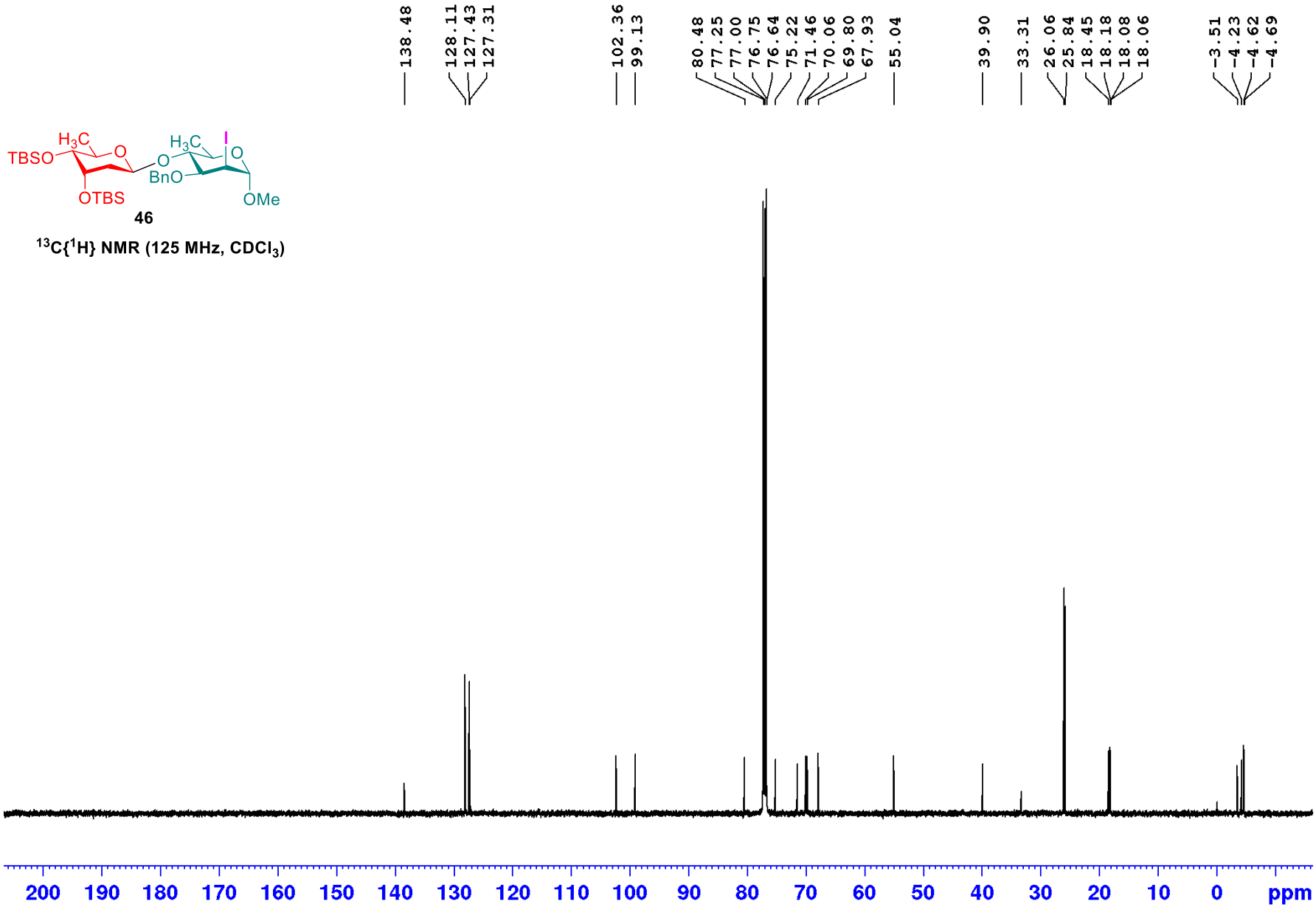
S15α

$^{13}C\{^{1}H\}$ NMR (500 MHz, $CDCl_3$)



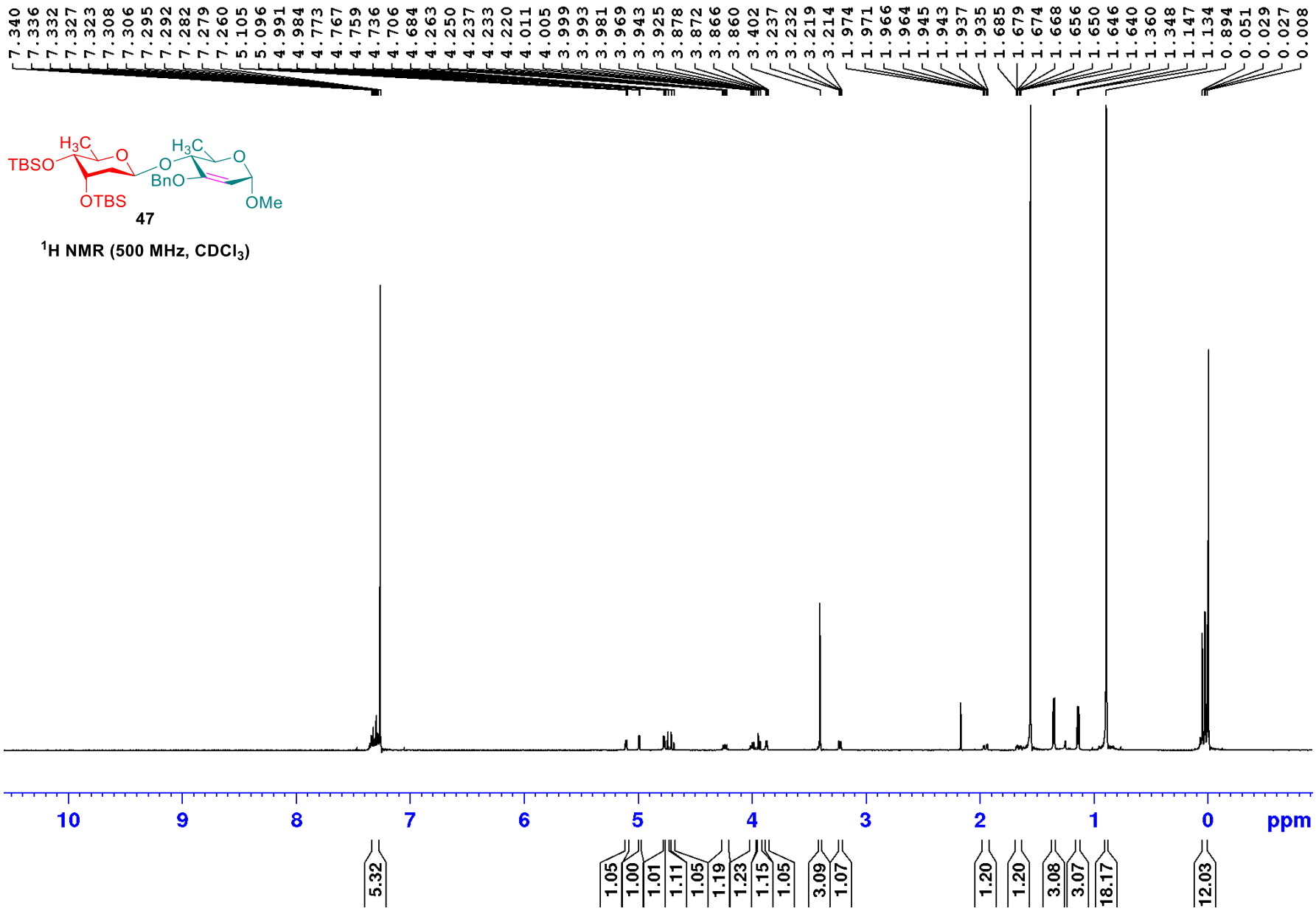
46

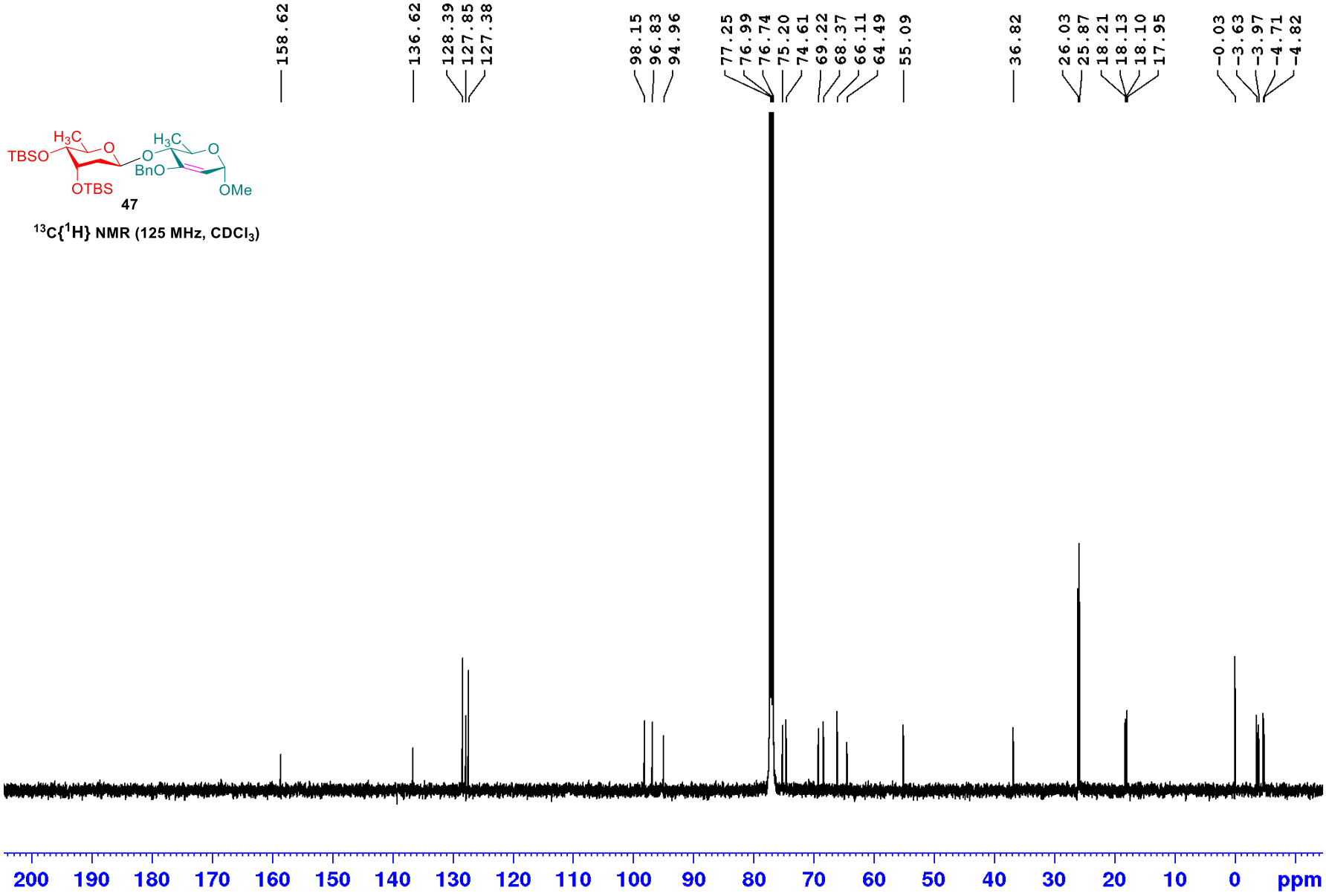
^{1}H NMR (500 MHz, $CDCl_3$)

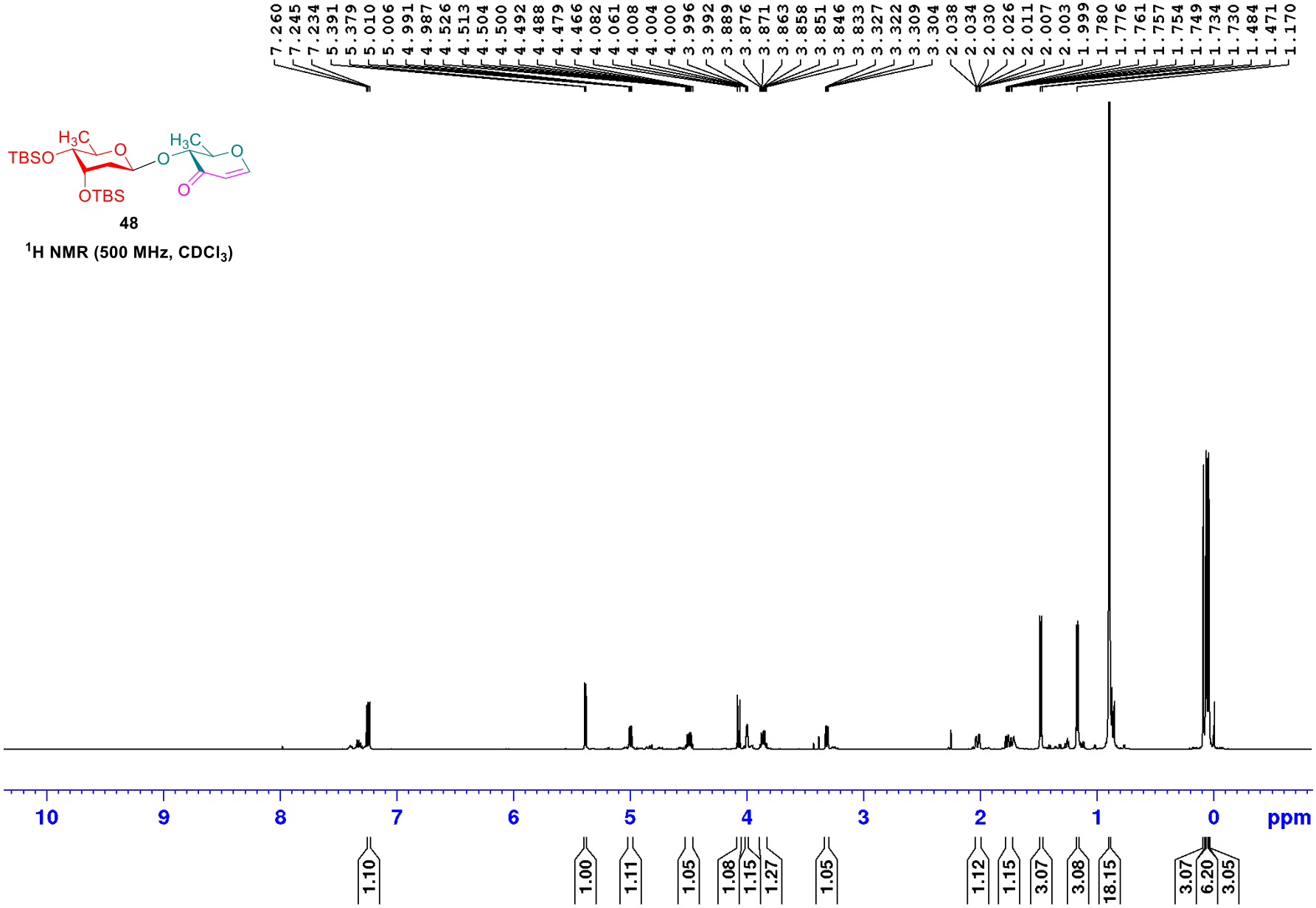


46

$^{13}C\{^{1}H\}$ NMR (125 MHz, $CDCl_3$)

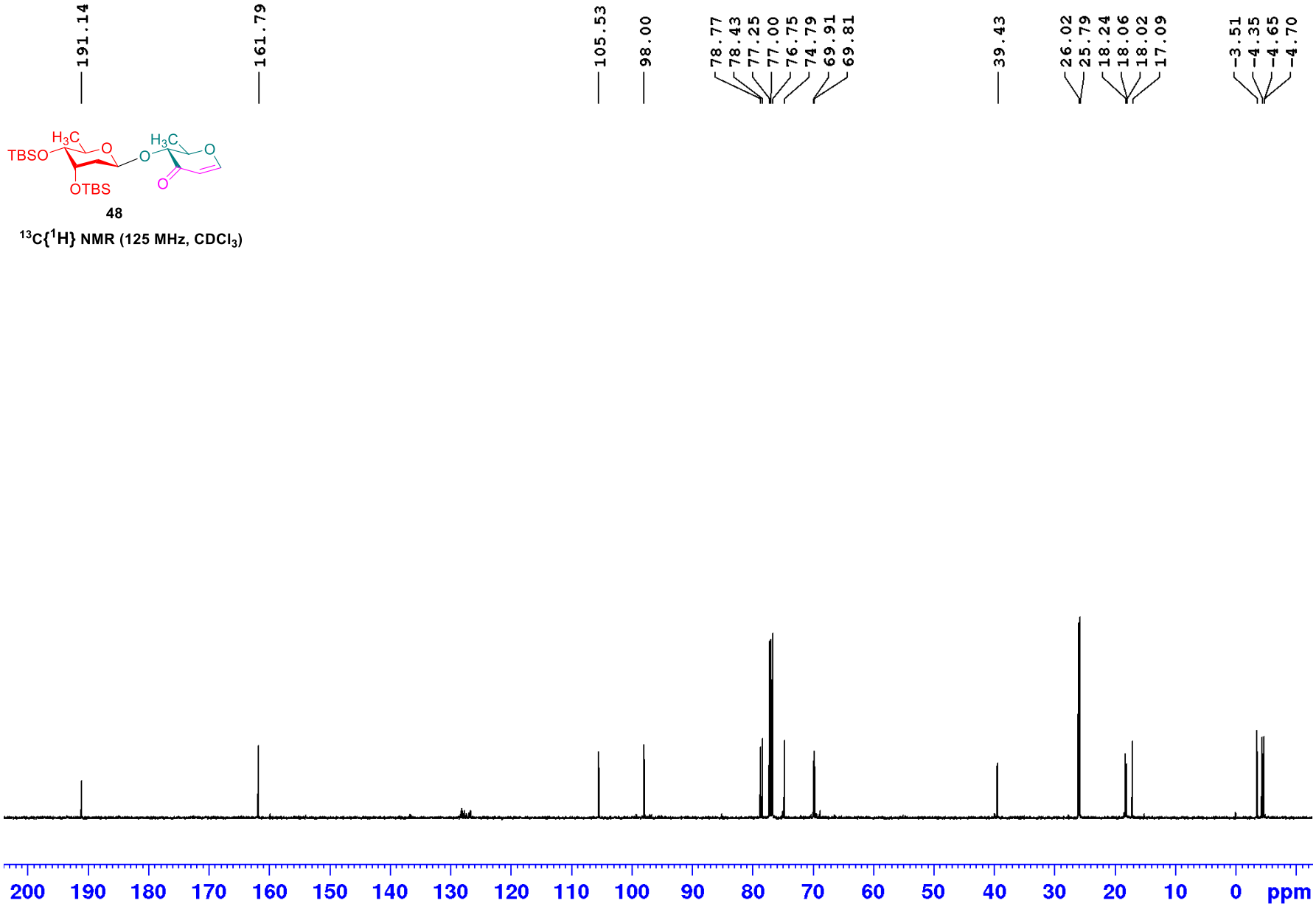

7.340
7.336
7.332
7.327
7.323
7.308
7.306
7.295
7.292
7.282
7.279
7.260
5.105
5.096
4.991
4.984
4.773
4.767
4.759
4.736
4.706
4.684
4.263
4.250
4.237
4.233
4.220
4.011
4.005
3.999
3.993
3.981
3.969
3.943
3.925
3.878
3.872
3.866
3.860
3.402
3.237
3.232
3.219
3.214
1.974
1.971
1.966
1.964
1.945
1.943
1.937
1.935
1.685
1.679
1.674
1.668
1.656
1.650
1.646
1.640
1.360
1.348
1.147
1.134
0.894
0.051
0.029
0.027
0.008
TBSO
H3C
O
OTBS
O
BnO
H3C
O
OMe
47
1H NMR (500 MHz, CDCl3)
10
9
8
7
6
5
4
3
2
1
0
ppm
5.32
1.05
1.00
1.01
1.11
1.05
1.19
1.23
1.15
1.05
3.09
1.07
1.20
1.20
3.08
3.07
18.17
12.03


158.62
136.62
128.39
127.85
127.38
98.15
96.83
94.96
77.25
76.99
76.74
75.20
74.61
69.22
68.37
66.11
64.49
55.09
36.82
26.03
25.87
18.21
18.13
18.10
17.95
-0.03
-3.63
-3.97
-4.71
-4.82
TBSO
OTBS
BnO
OMe
47
$^{13}C\{^{1}H\}$ NMR (125 MHz, $CDCl_3$)
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
ppm



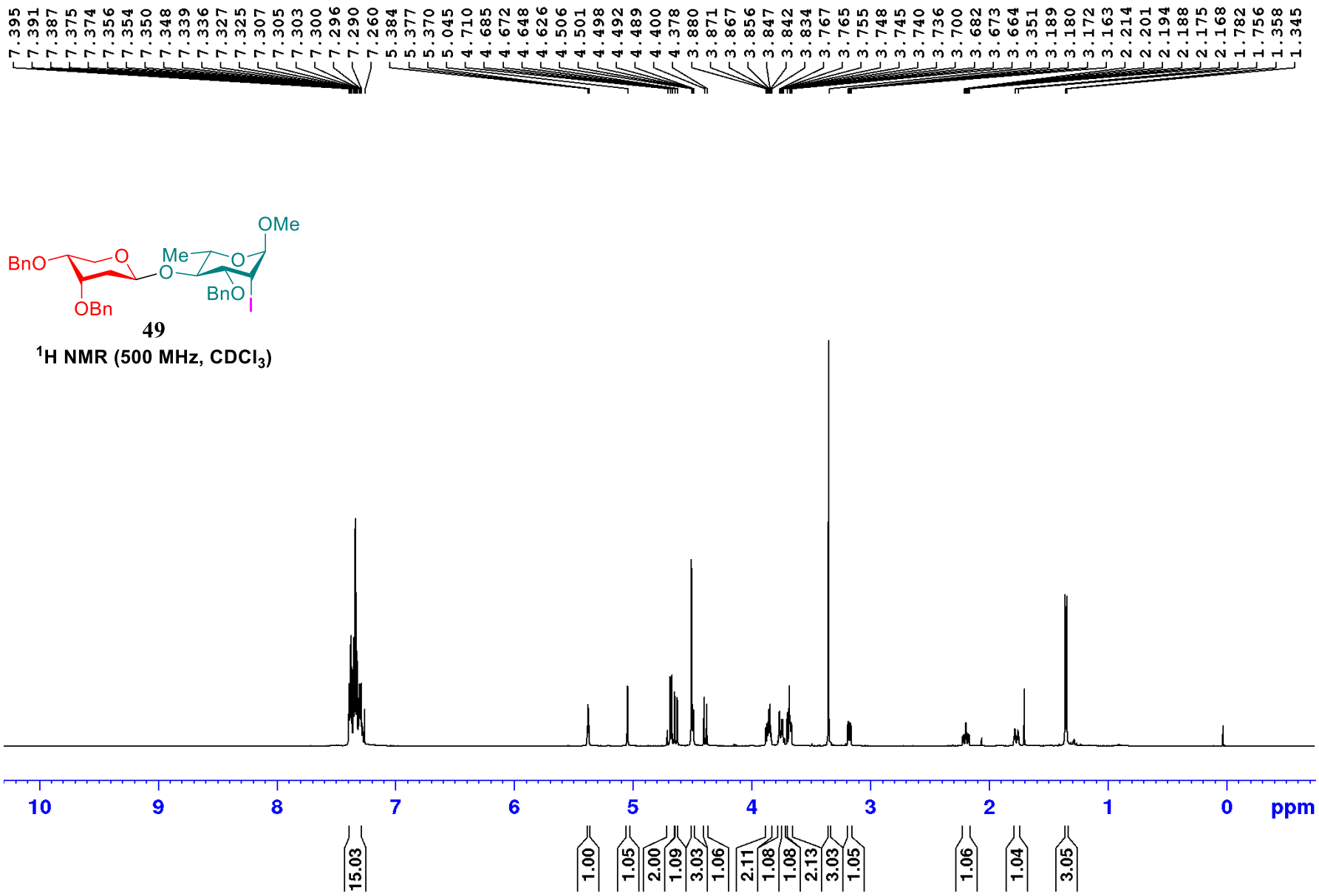
48

^{1}H NMR (500 MHz, $CDCl_3$)



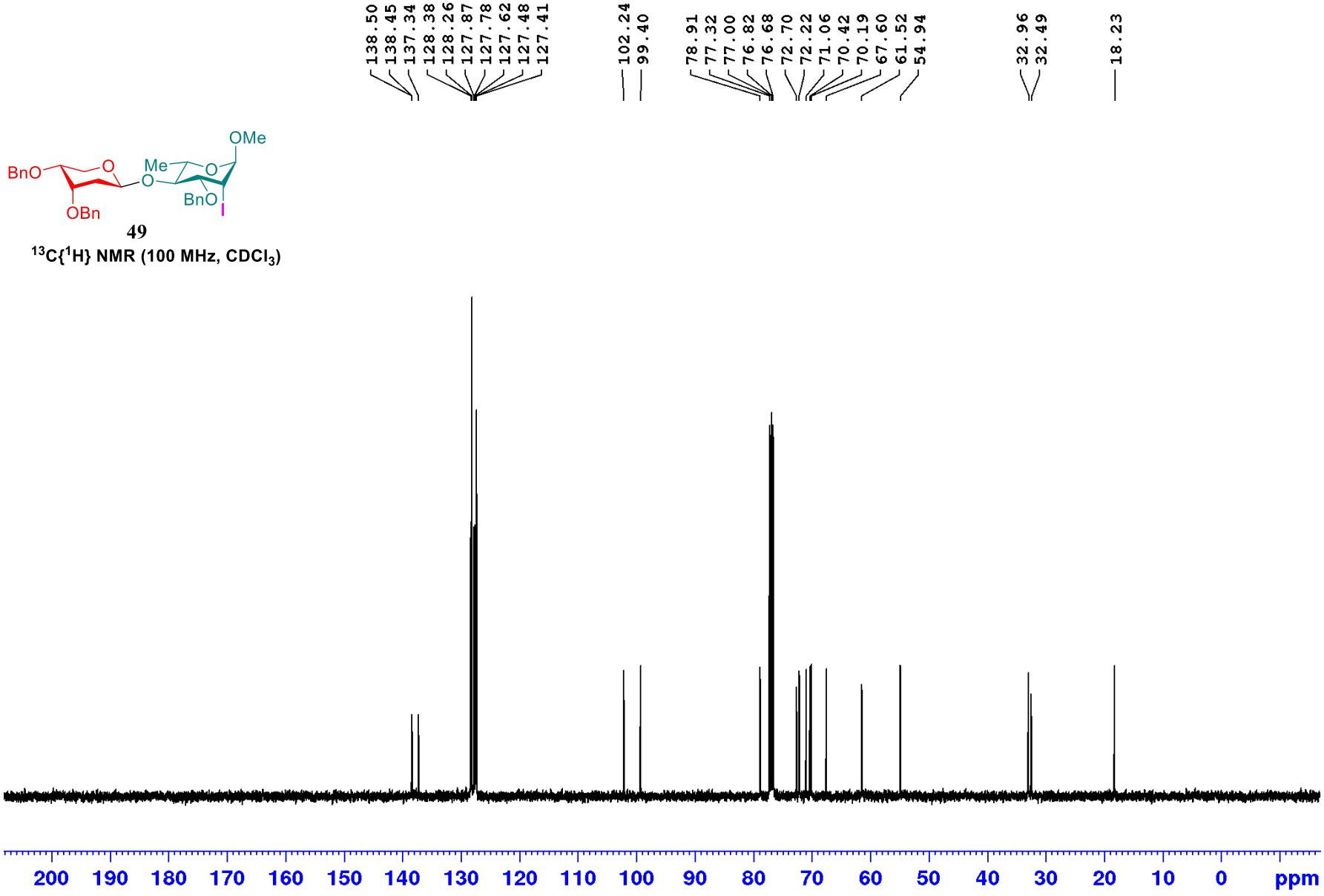
48

$^{13}C\{^{1}H\}$ NMR (125 MHz, $CDCl_3$)



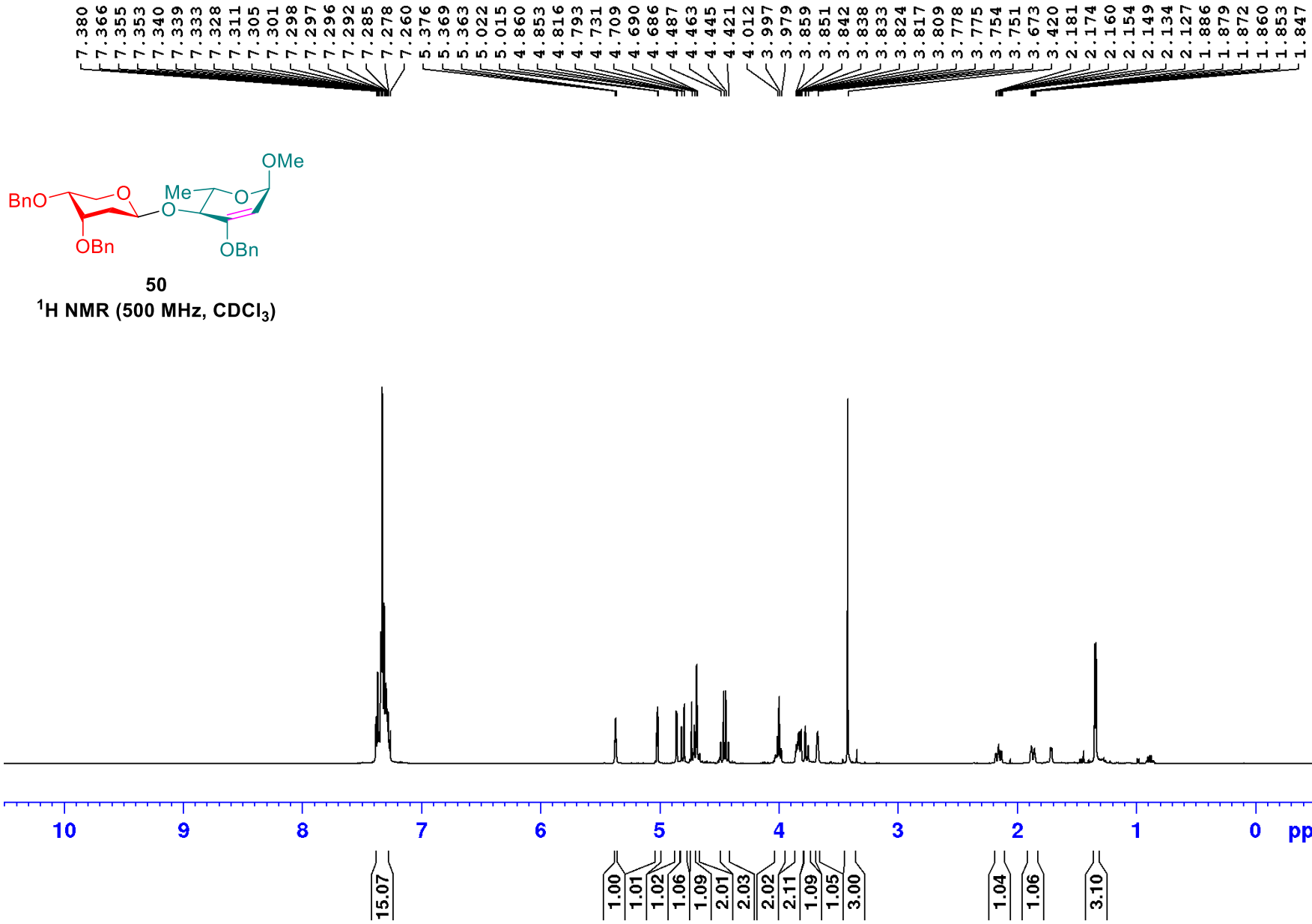
49

^{1}H NMR (500 MHz, $CDCl_3$)



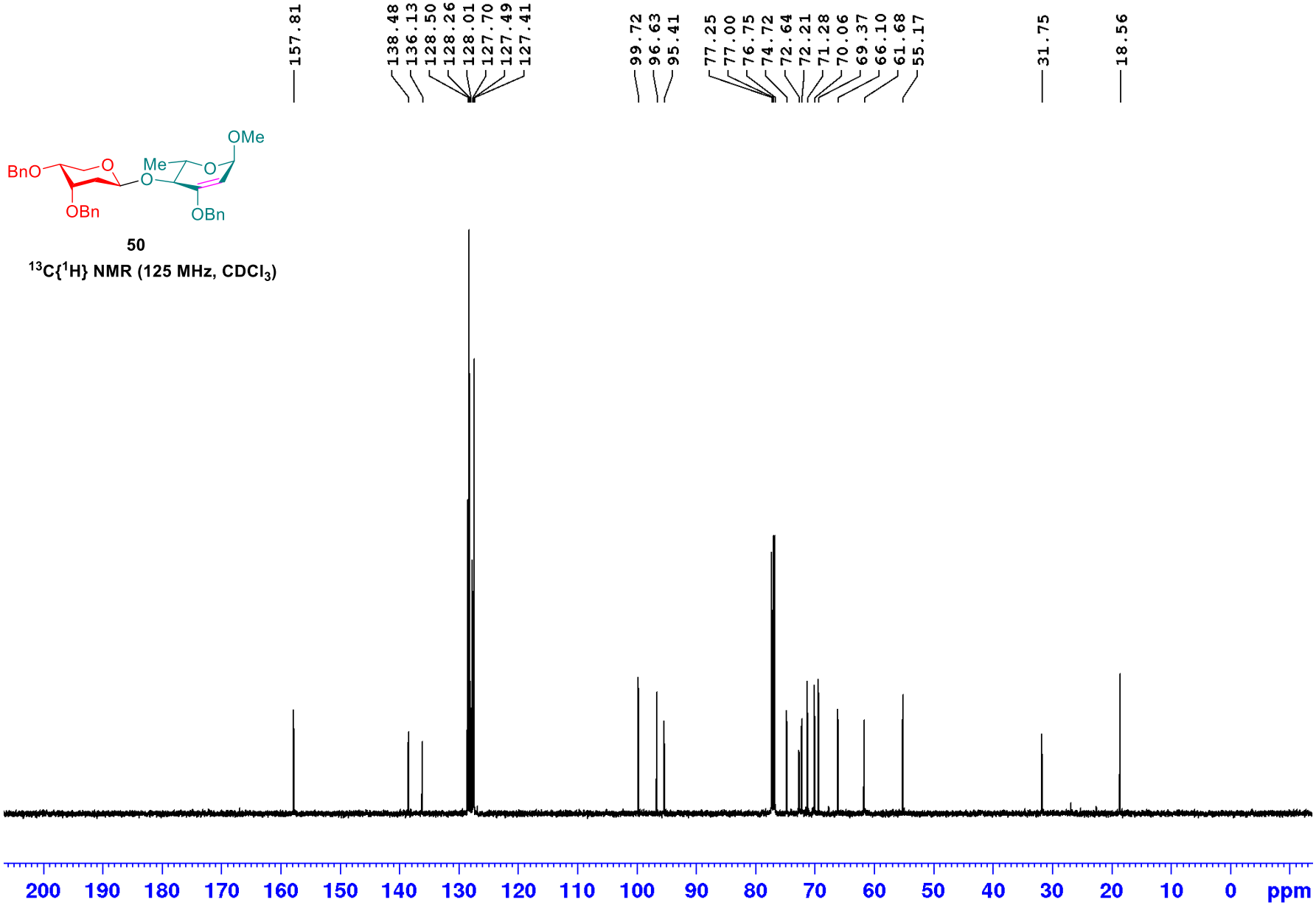
49

$^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$)



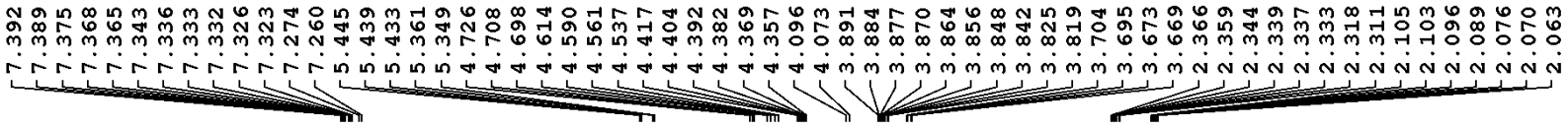
50

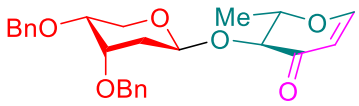
^{1}H NMR (500 MHz, $CDCl_3$)



50

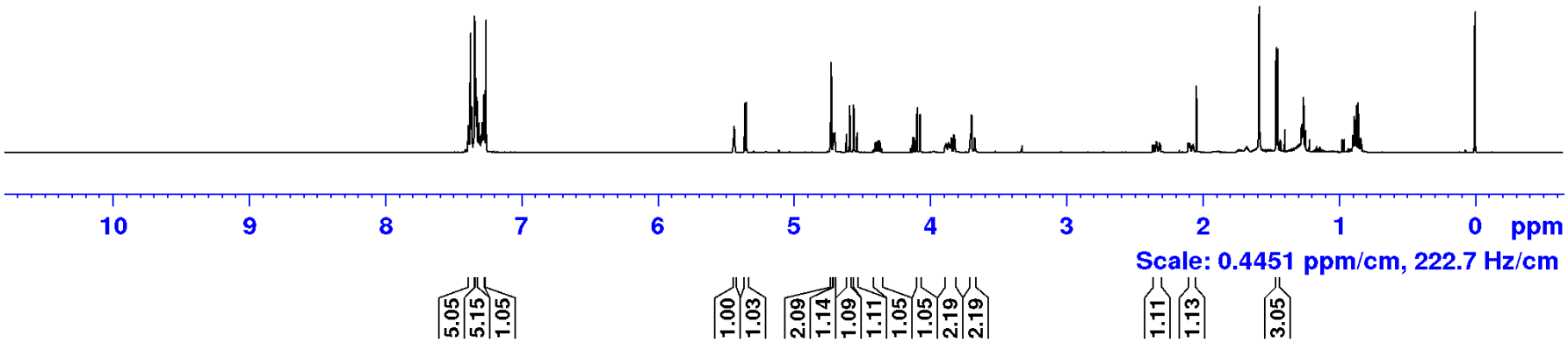
$^{13}C\{^{1}H\}$ NMR (125 MHz, $CDCl_3$)

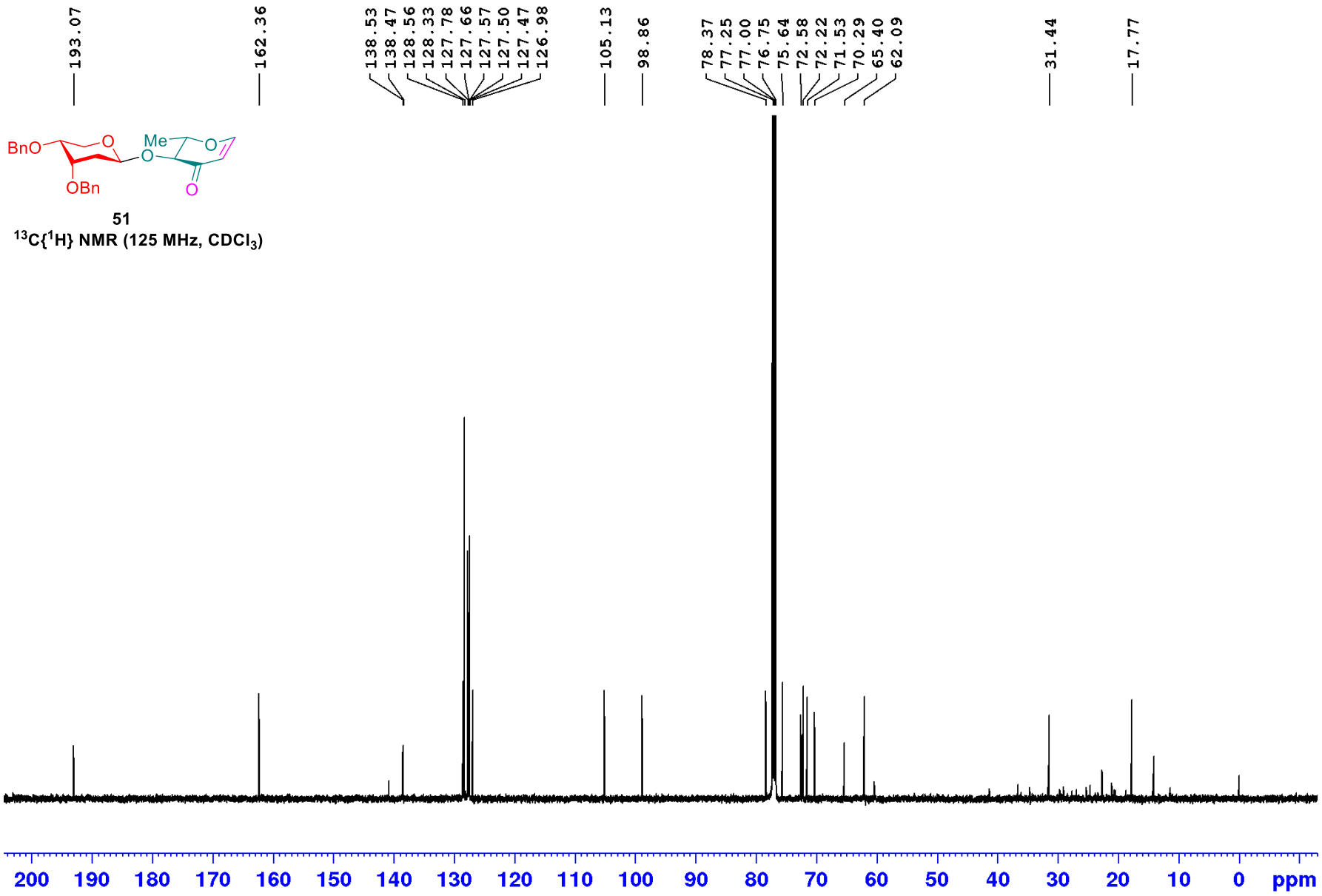




51

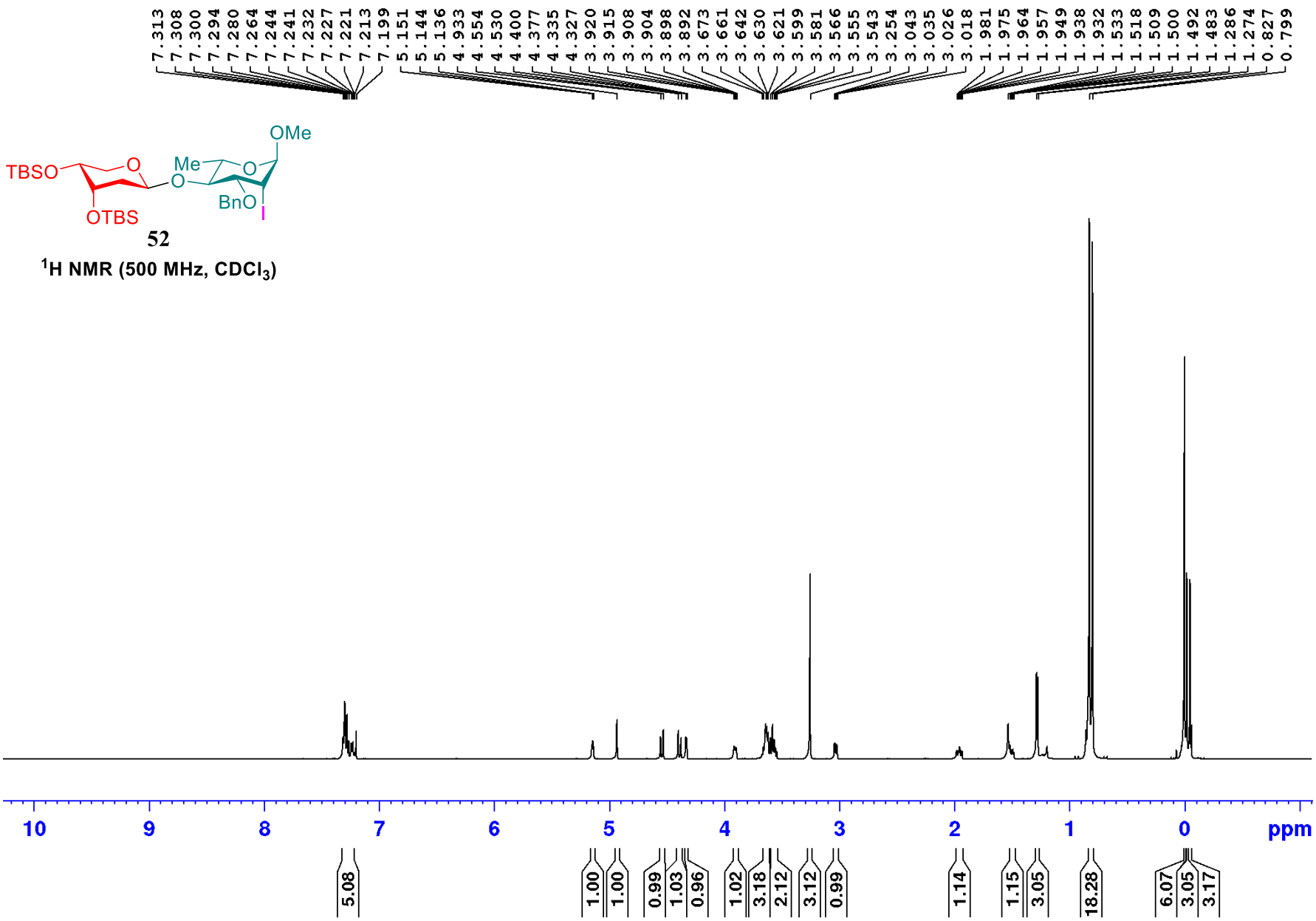
^{1}H NMR (500 MHz, $CDCl_3$)

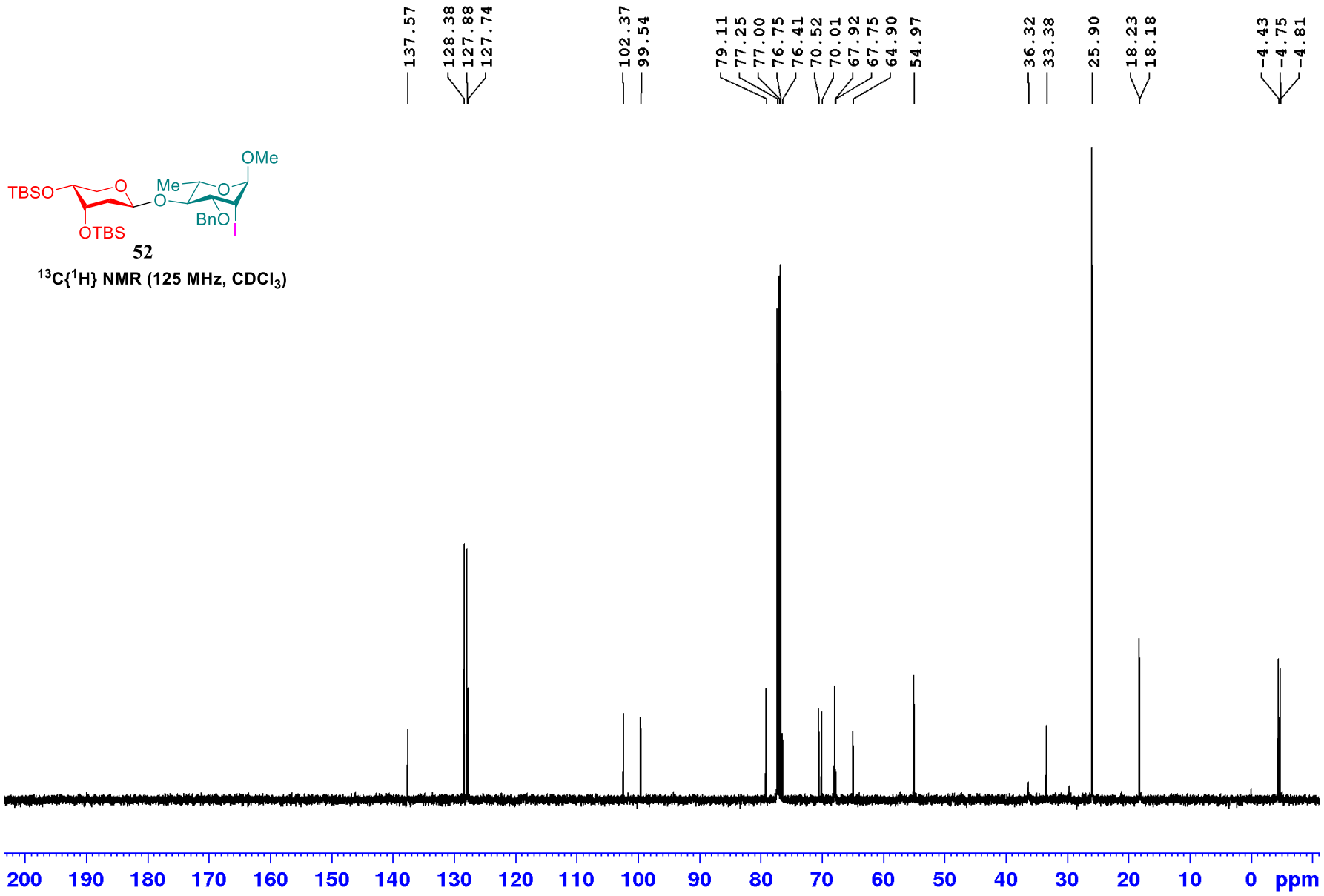


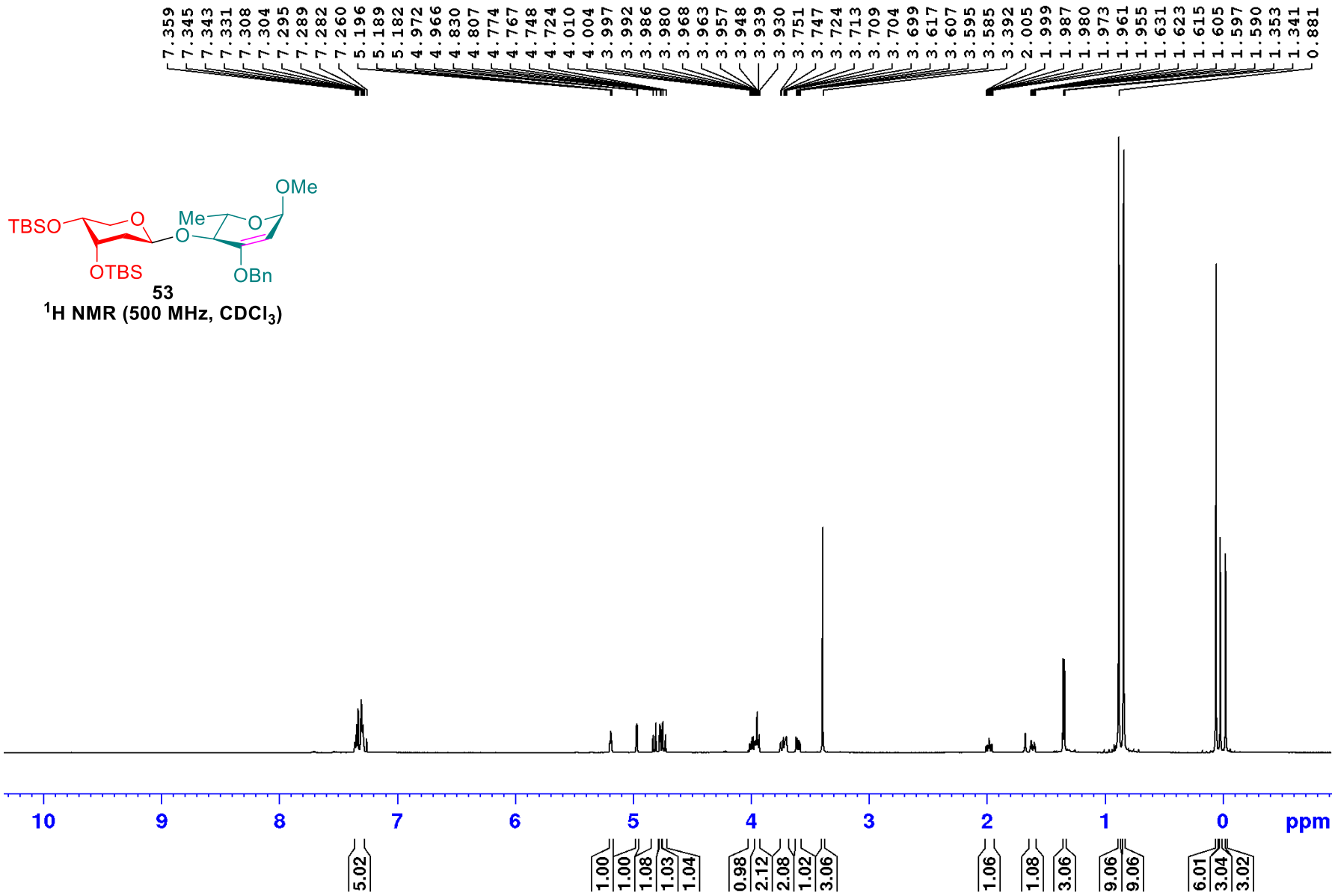


51

$^{13}C\{^{1}H\}$ NMR (125 MHz, $CDCl_3$)

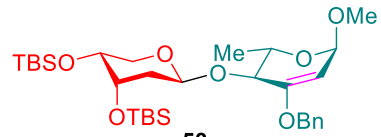

7.313
7.308
7.300
7.294
7.280
7.264
7.244
7.241
7.232
7.227
7.221
7.213
7.199
5.151
5.144
5.136
4.933
4.554
4.530
4.400
4.377
4.335
4.327
3.920
3.915
3.908
3.904
3.898
3.892
3.673
3.661
3.642
3.630
3.621
3.599
3.581
3.566
3.555
3.543
3.254
3.043
3.035
3.026
3.018
1.981
1.975
1.964
1.957
1.949
1.938
1.932
1.533
1.518
1.509
1.500
1.492
1.483
1.286
1.274
0.827
0.799
TBSO
OTBS
O
Me
OMe
BnO
I
52
1H NMR (500 MHz, CDCl3)
10
9
8
7
6
5
4
3
2
1
0
ppm
5.08
1.00
1.00
0.99
1.03
0.96
1.02
3.18
2.12
3.12
0.99
1.14
1.15
3.05
18.28
6.07
3.05
3.17


137.57
128.38
127.88
127.74
102.37
99.54
79.11
77.25
77.00
76.75
76.41
70.52
70.01
67.92
67.75
64.90
54.97
36.32
33.38
25.90
18.23
18.18
-4.43
-4.75
-4.81
TBSO
OTBS
O
Me
O
O
OMe
BnO
I
52
$^{13}C\{^{1}H\}$ NMR (125 MHz, $CDCl_3$)
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
ppm



53

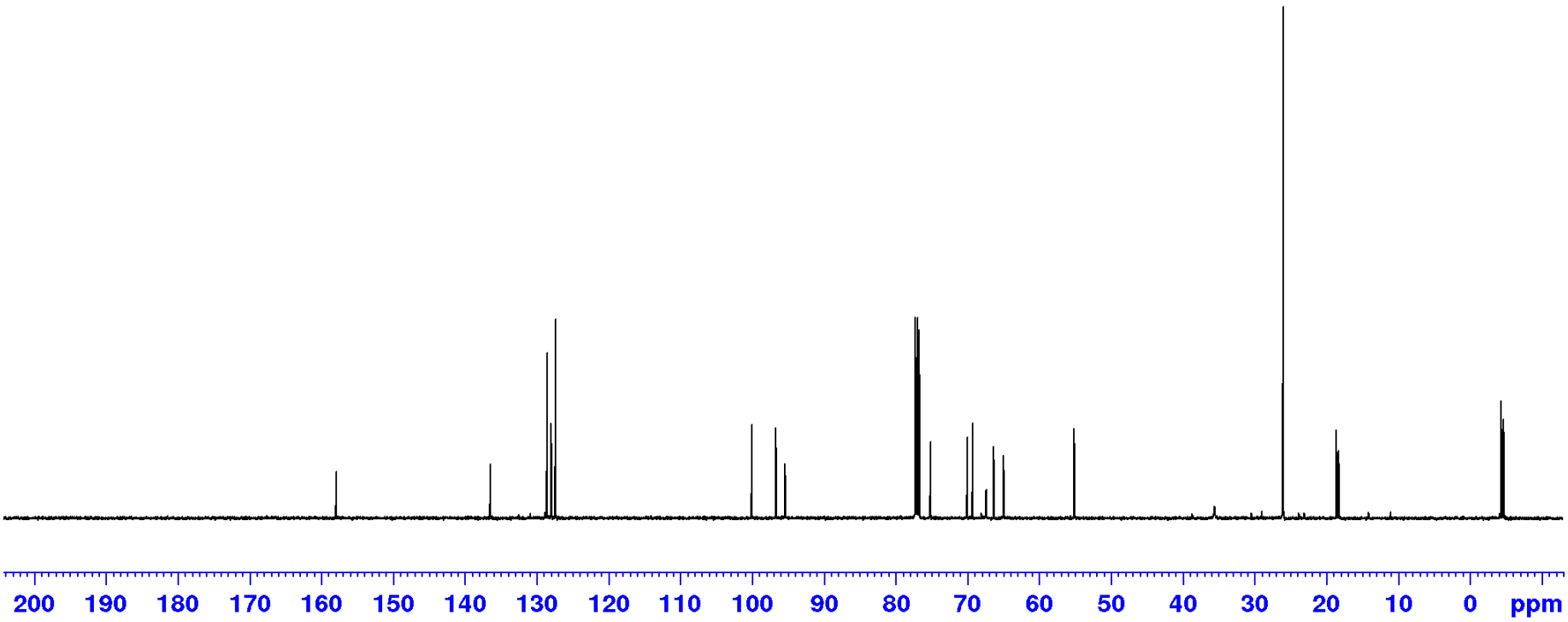
^{1}H NMR (500 MHz, $CDCl_3$)

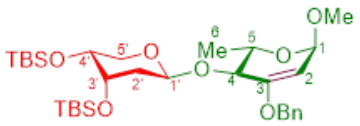


53

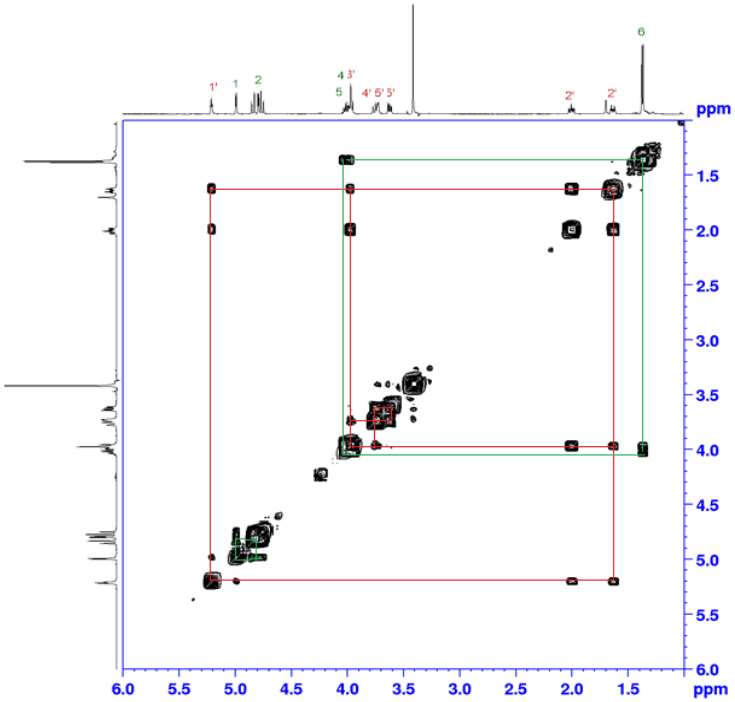
$^{13}C\{^{1}H\}$ NMR (125 MHz, $CDCl_3$)

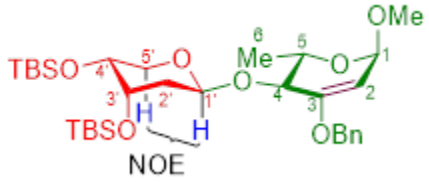
157.85
136.41
128.50
127.89
127.29
100.05
96.70
95.44
77.25
77.00
76.75
75.17
70.04
69.29
67.40
66.35
65.00
55.12
35.49
25.88
18.50
18.22
18.13
-4.47
-4.73
-4.85



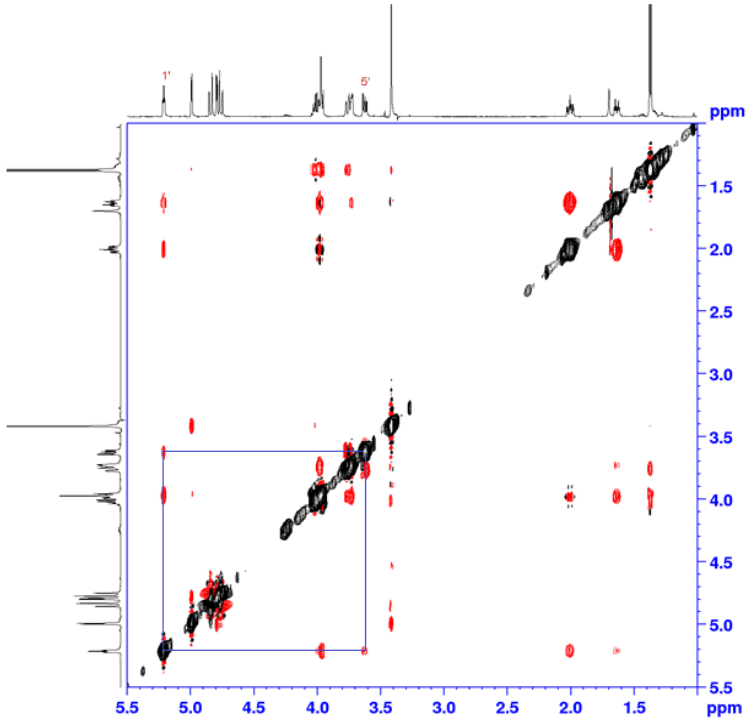


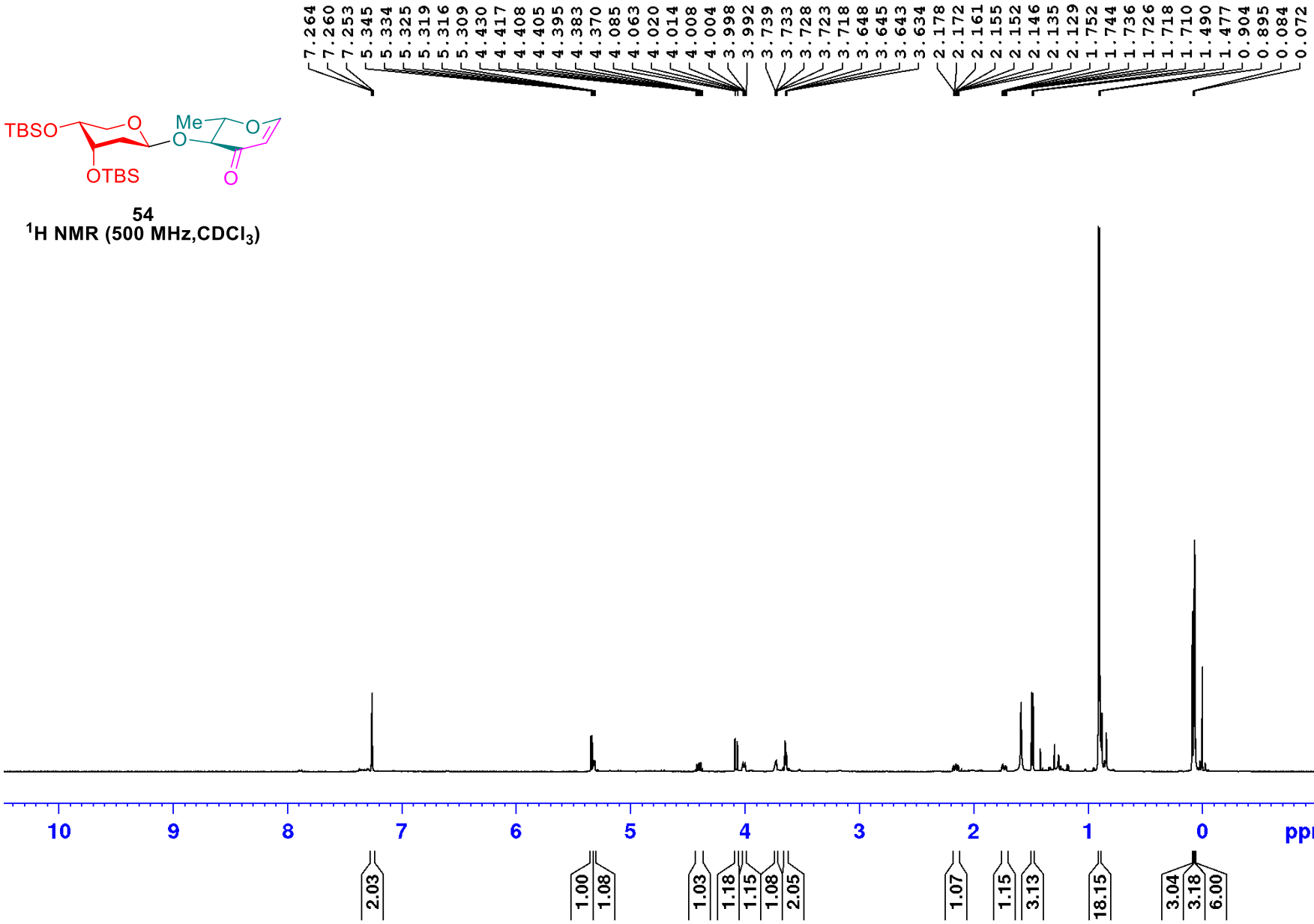
53
(COSY, 500 MHz)

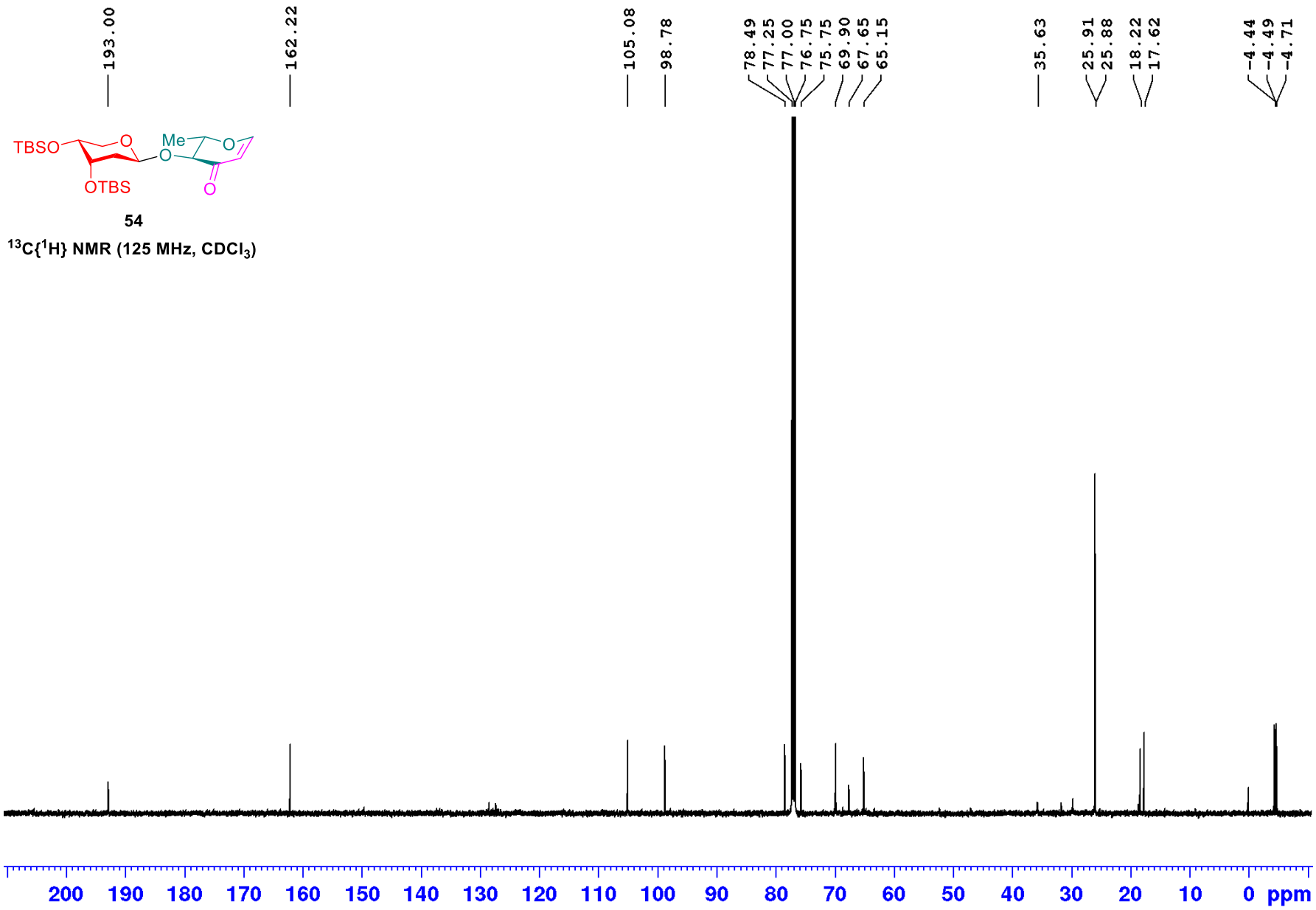




53
(NOESY, 500 MHz)

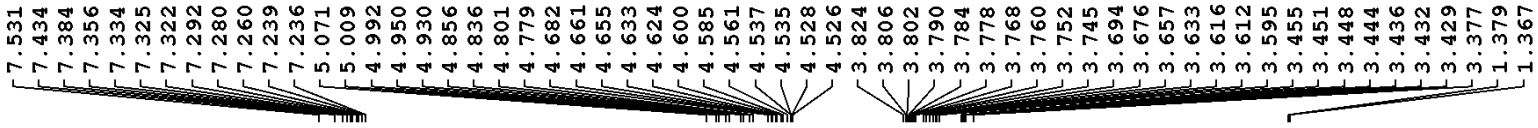


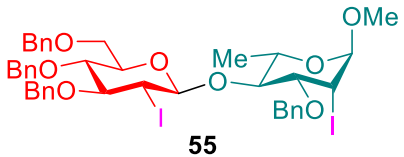

7.264
7.260
7.253
5.345
5.334
5.325
5.319
5.316
5.309
4.430
4.417
4.408
4.405
4.395
4.383
4.370
4.085
4.063
4.020
4.014
4.008
4.004
3.998
3.992
3.739
3.733
3.728
3.723
3.718
3.648
3.645
3.643
3.634
2.178
2.172
2.161
2.155
2.152
2.146
2.135
2.129
1.752
1.744
1.736
1.726
1.718
1.710
1.490
1.477
0.904
0.895
0.084
0.072
TBSO
O
Me
O
O
OTBS
O
54
1H NMR (500 MHz,CDCl3)
10
9
8
7
6
5
4
3
2
1
0
ppm
2.03
1.00
1.08
1.03
1.18
1.15
1.08
2.05
1.07
1.15
3.13
18.15
3.04
3.18
6.00



54

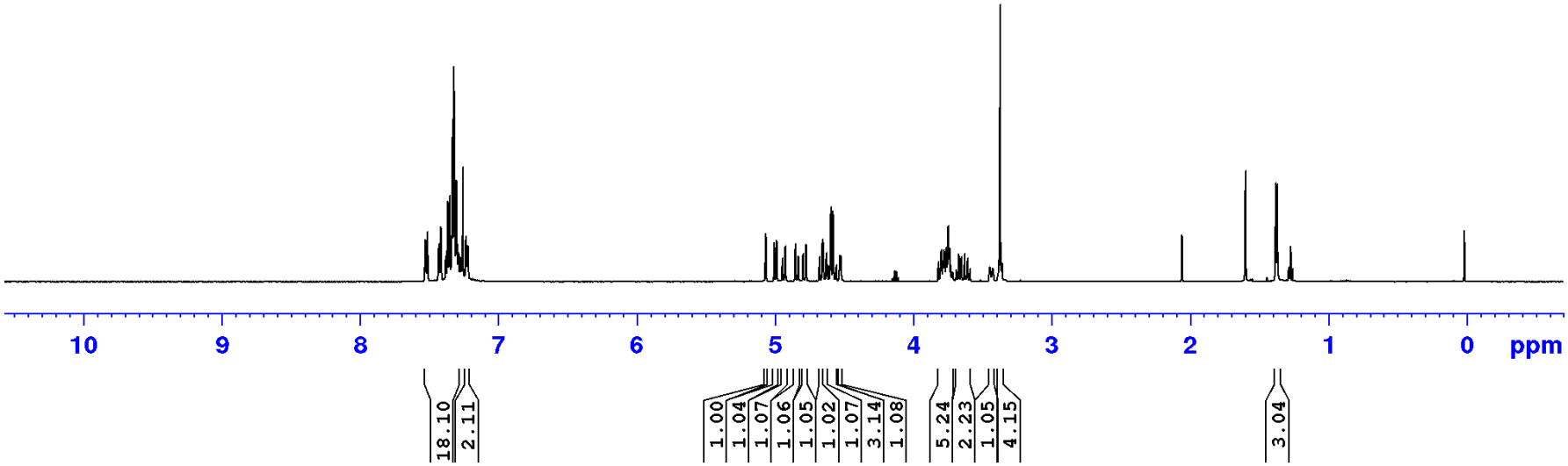
$^{13}C\{^{1}H\}$ NMR (125 MHz, $CDCl_3$)

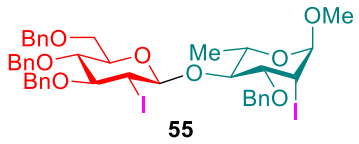




55

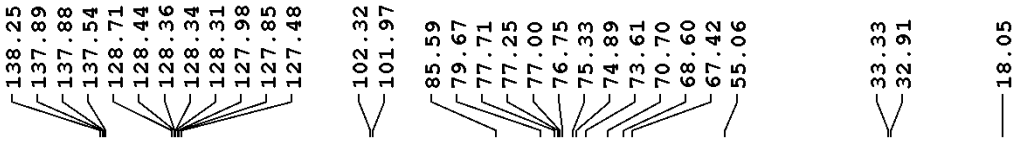
^{1}H NMR (500 MHz, $CDCl_3$)

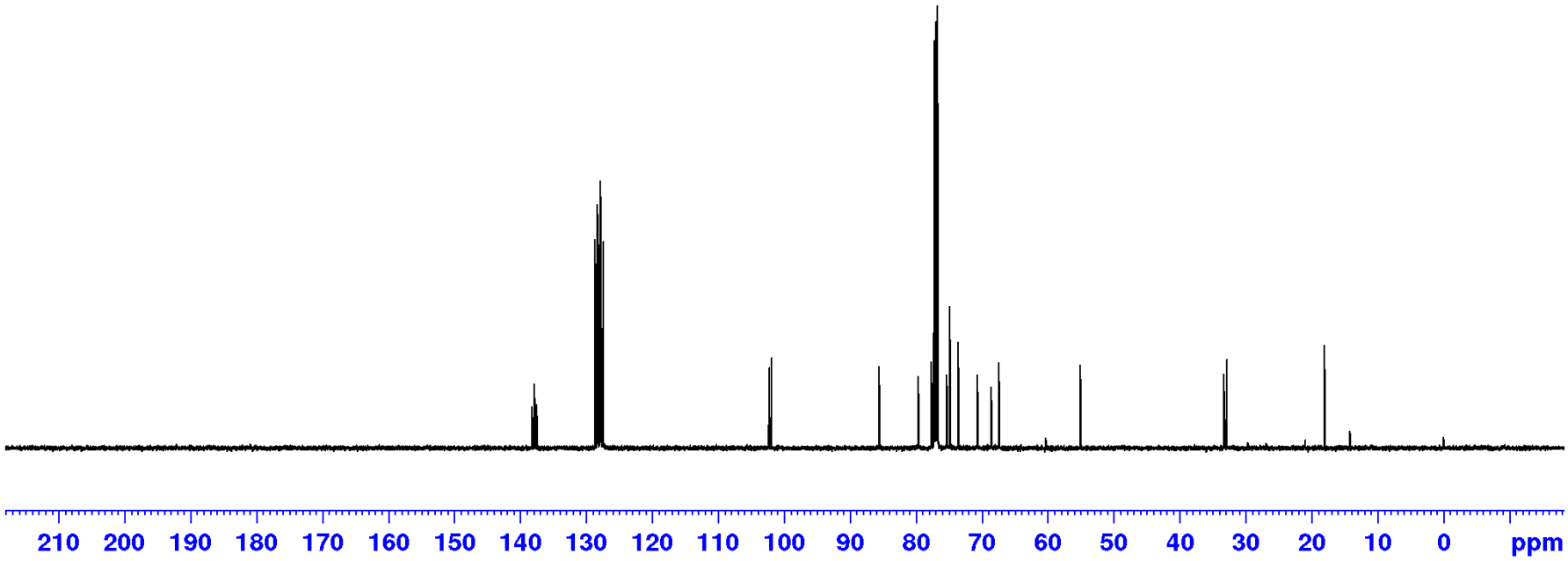


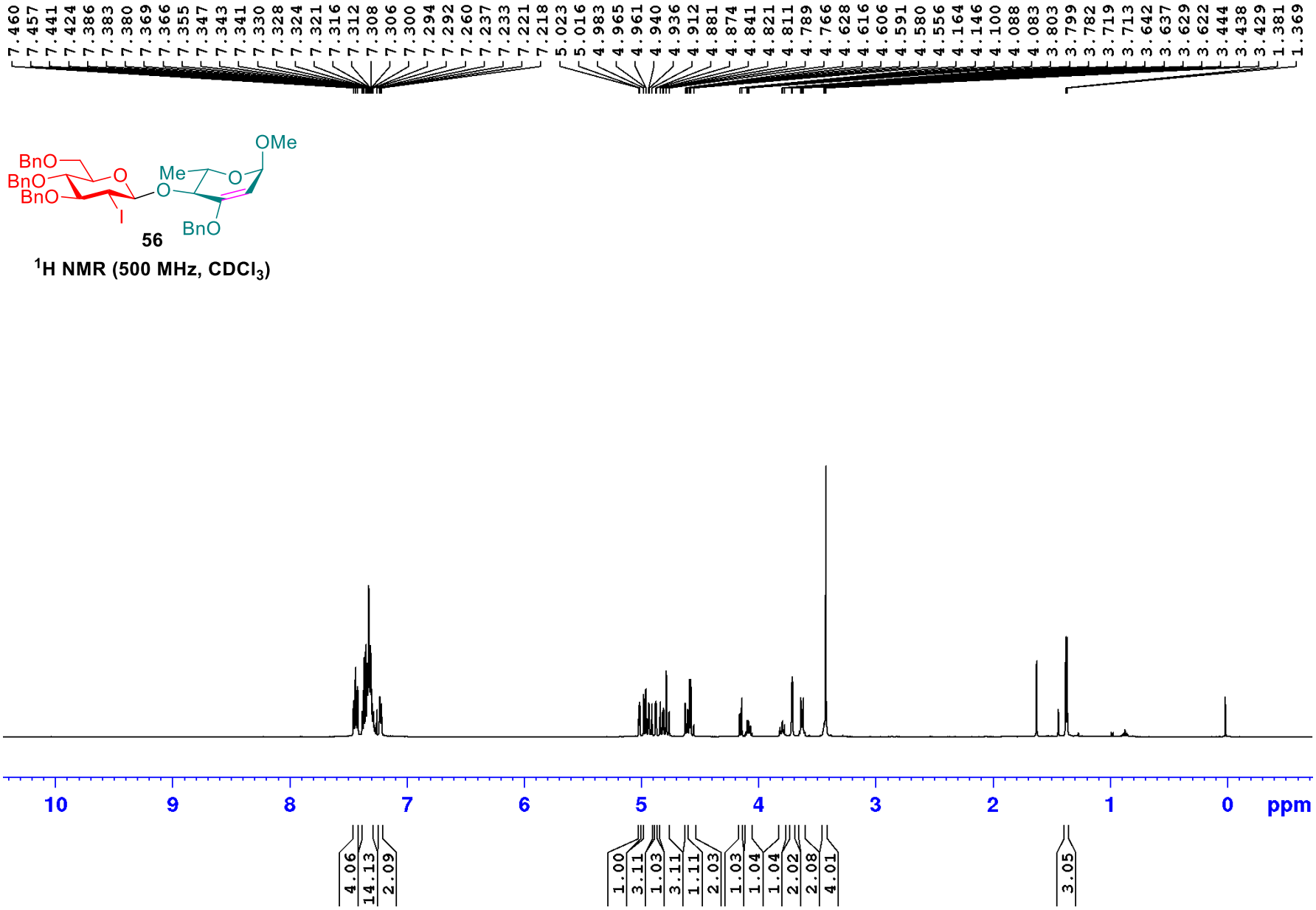


55

$^{13}C\{^{1}H\}$ NMR (125 MHz, $CDCl_3$)

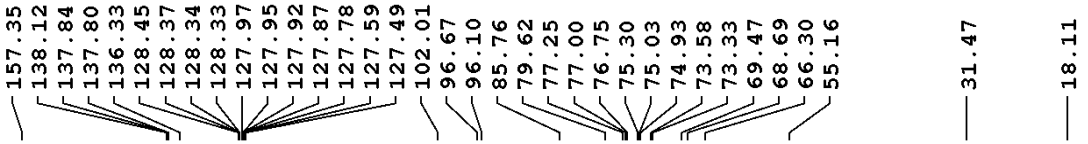


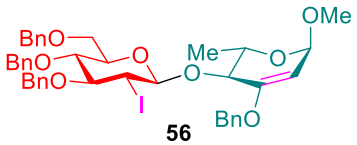




56

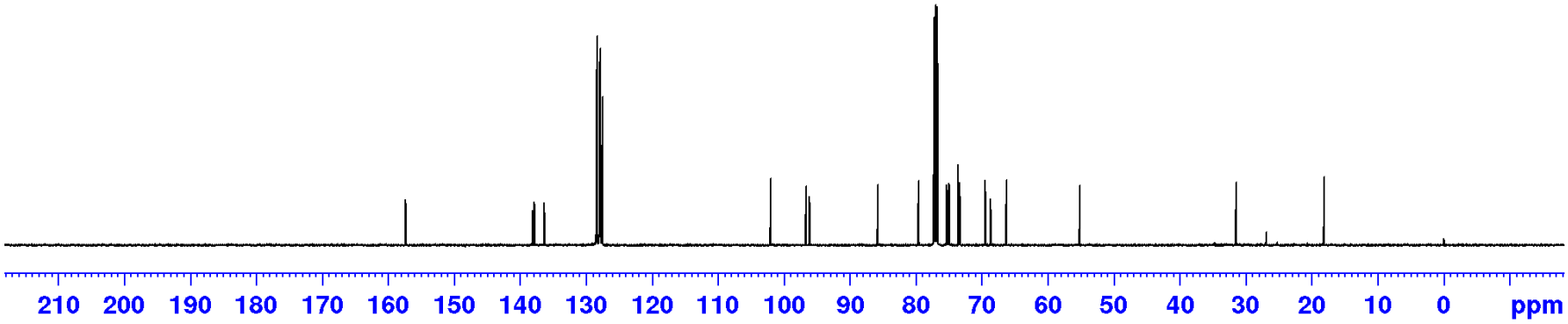
^{1}H NMR (500 MHz, $CDCl_3$)

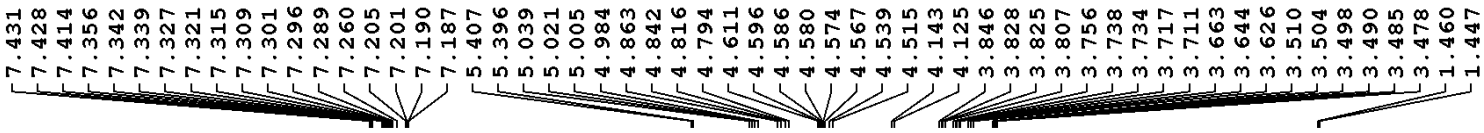


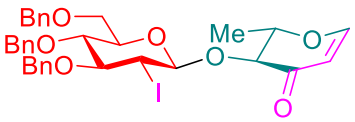


56

$^{13}C\{^{1}H\}$ NMR (125 MHz, $CDCl_3$)

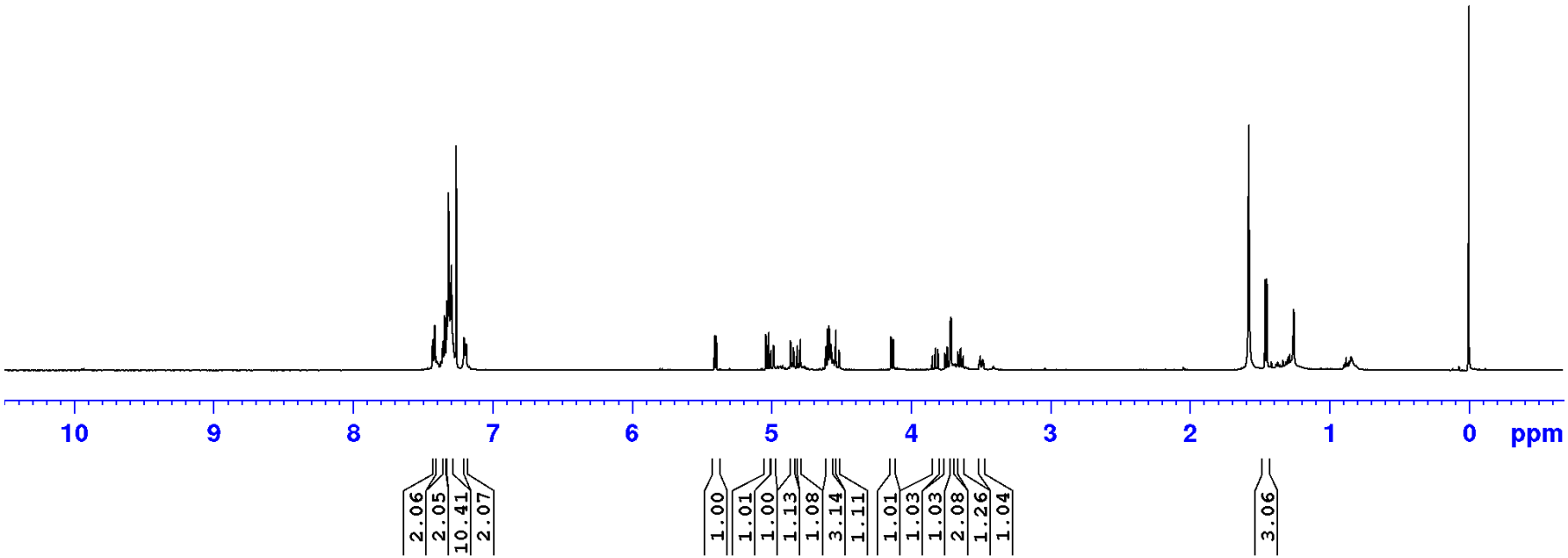


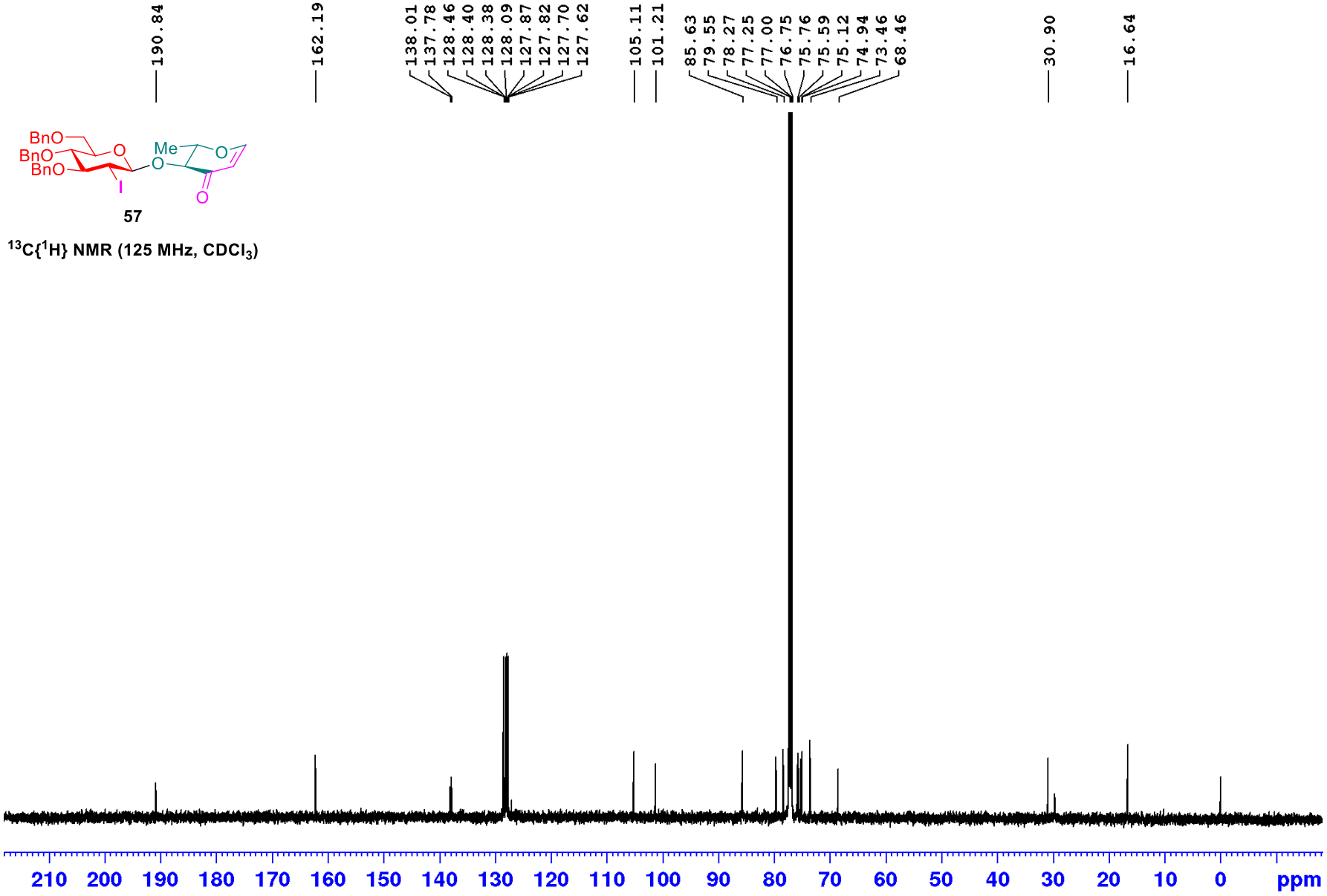




57

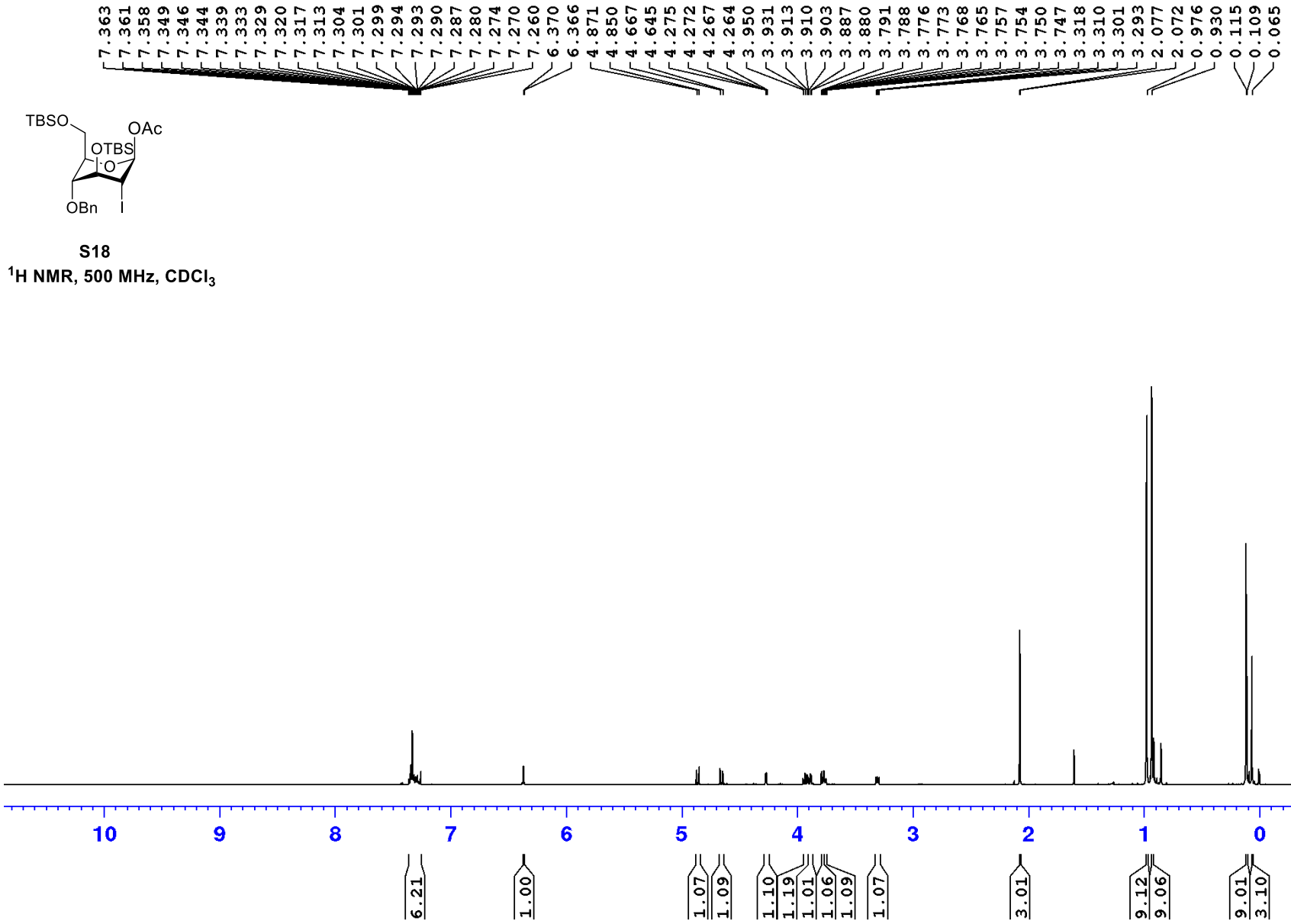
^{1}H NMR (500 MHz, $CDCl_3$)





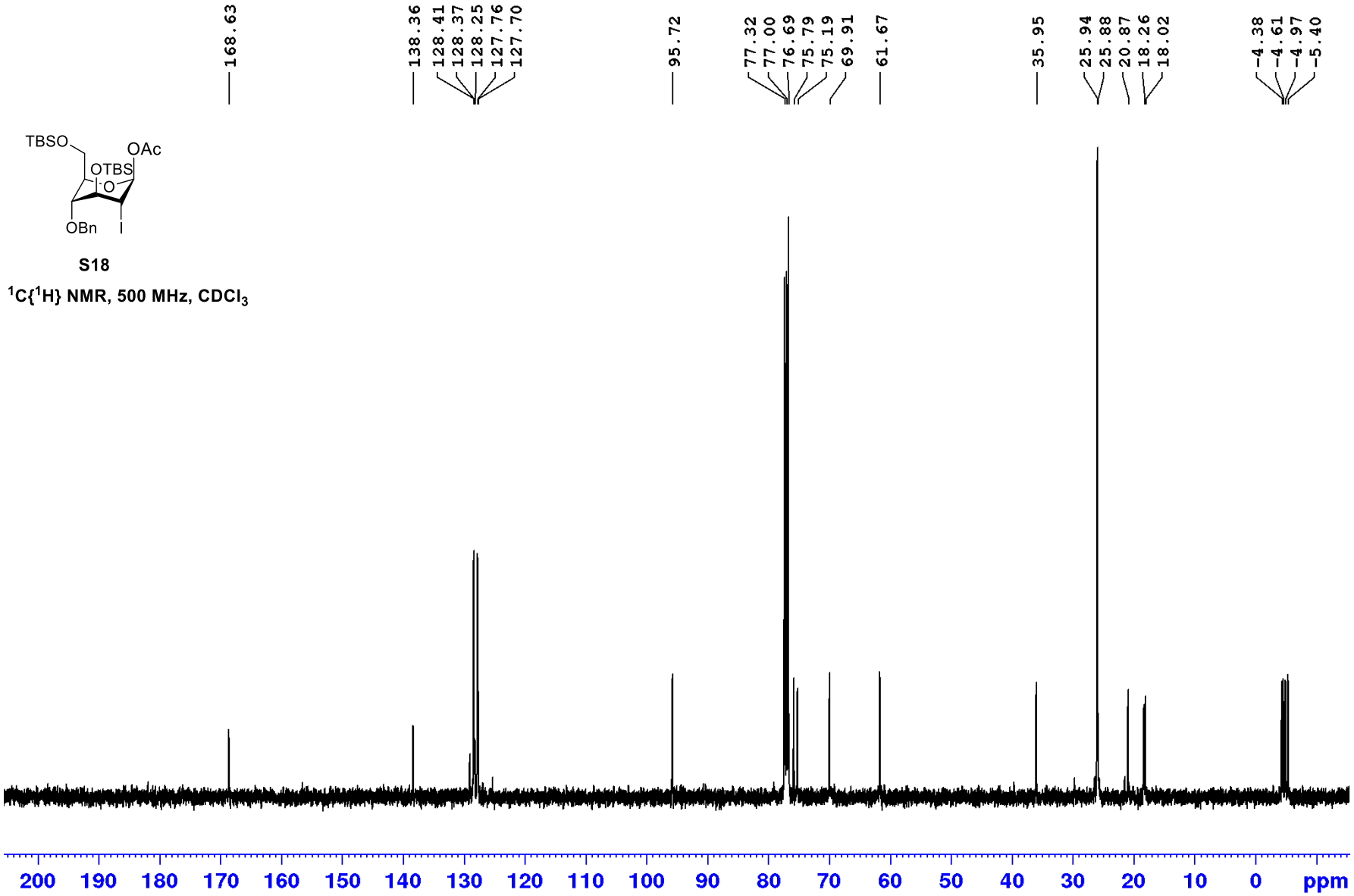
57

$^{13}C\{^{1}H\}$ NMR (125 MHz, $CDCl_3$)



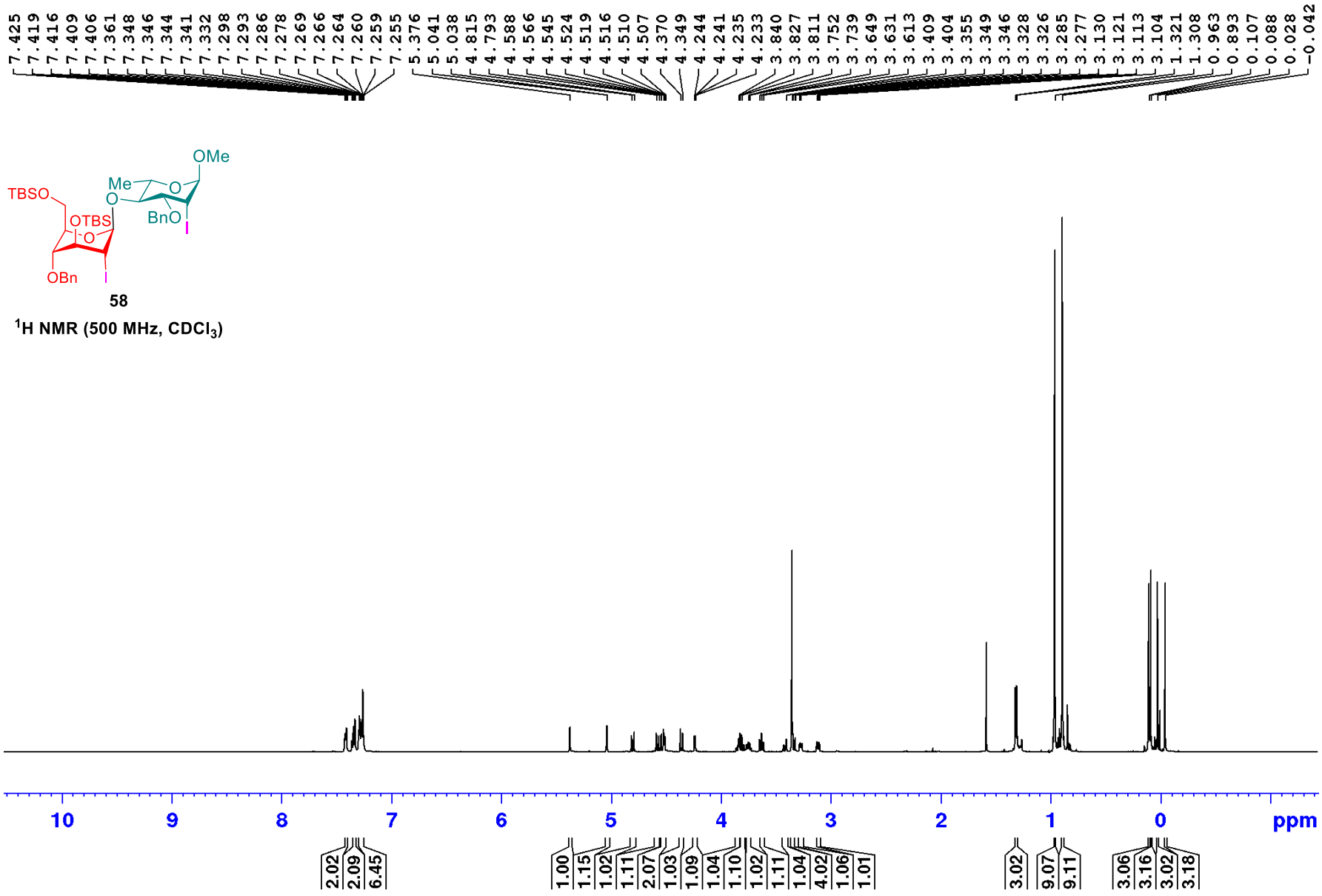
S18

^{1}H NMR, 500 MHz, $CDCl_3$



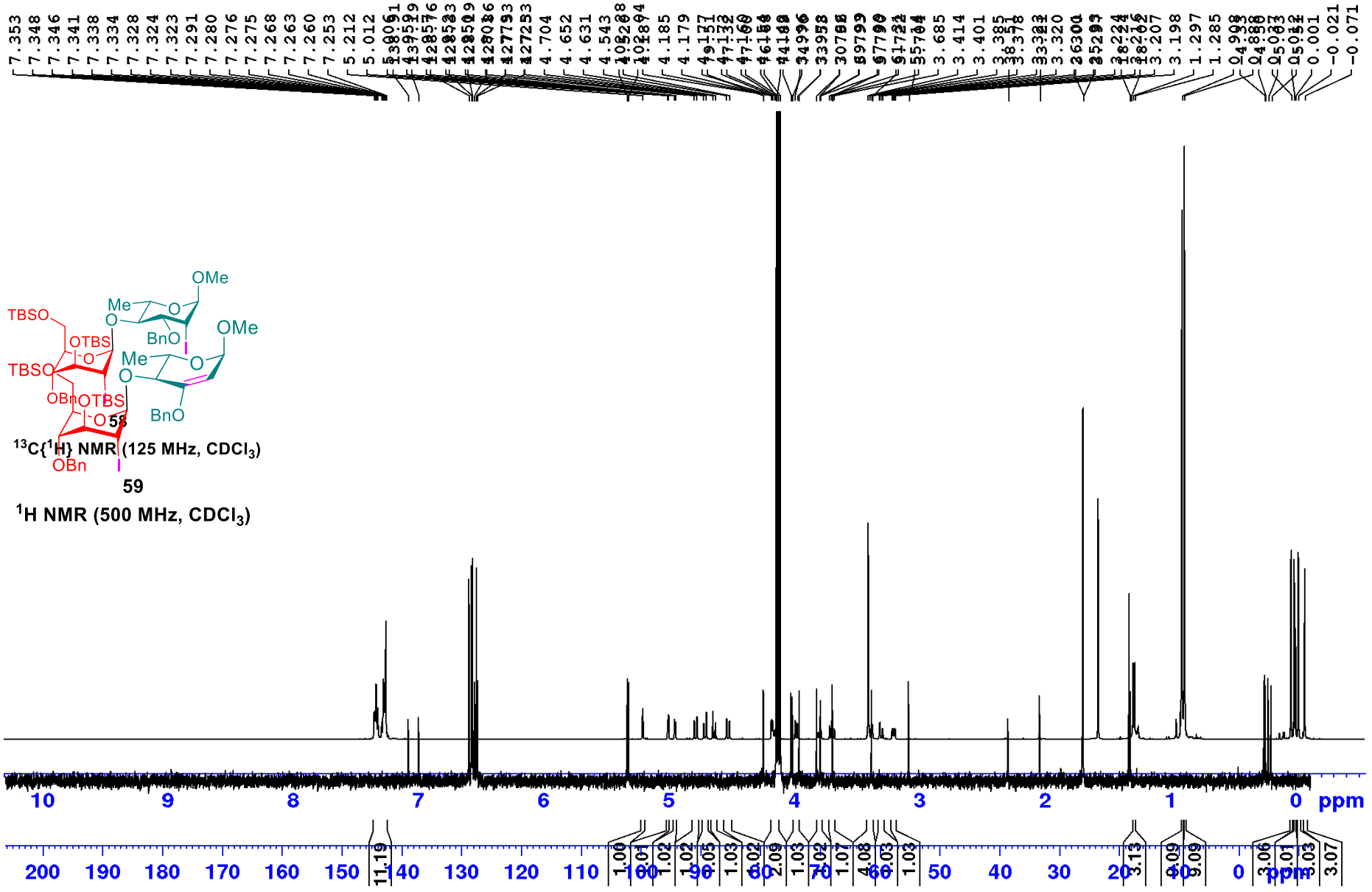
S18

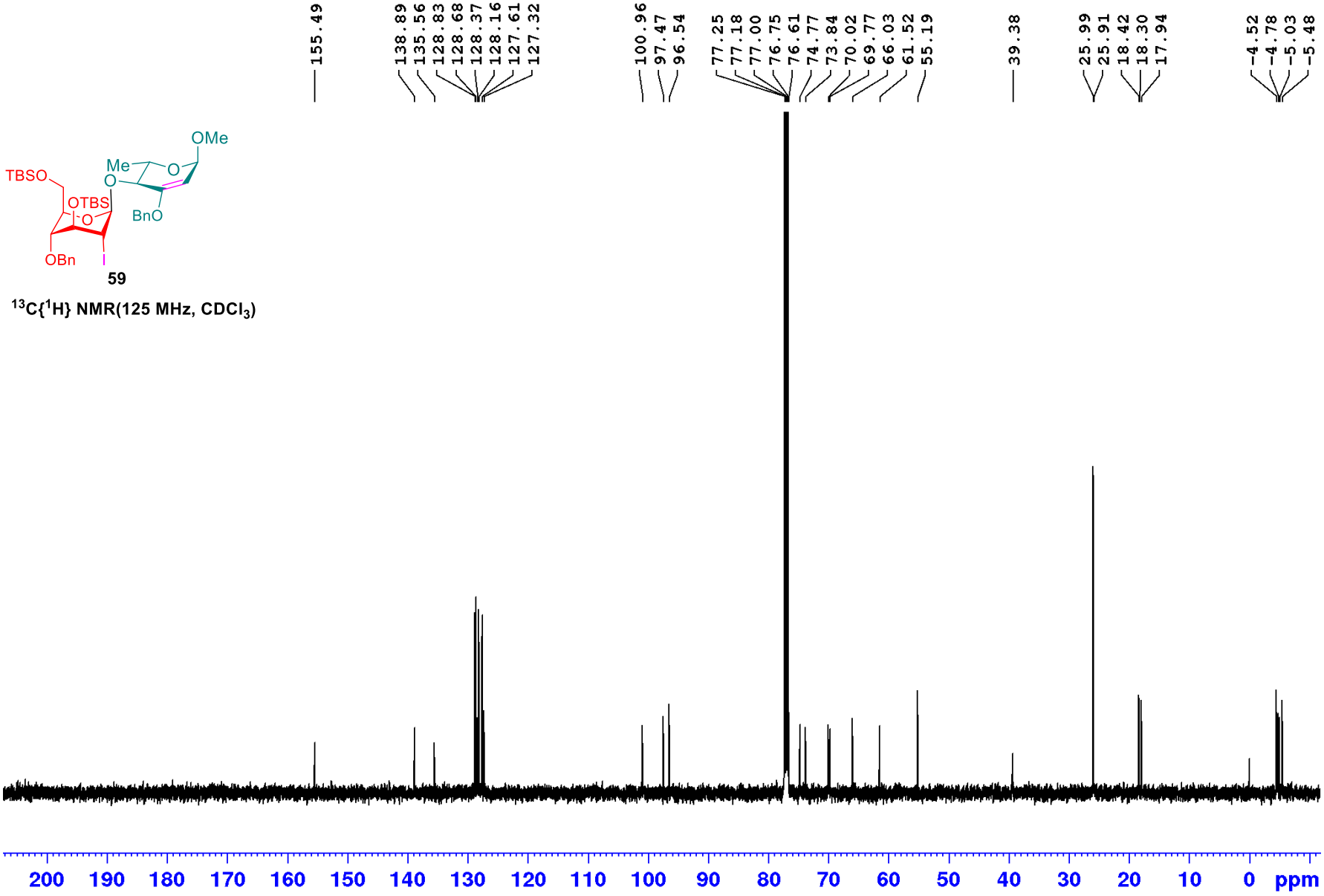
$^{1}C\{^{1}H\}$ NMR, 500 MHz, $CDCl_3$



58

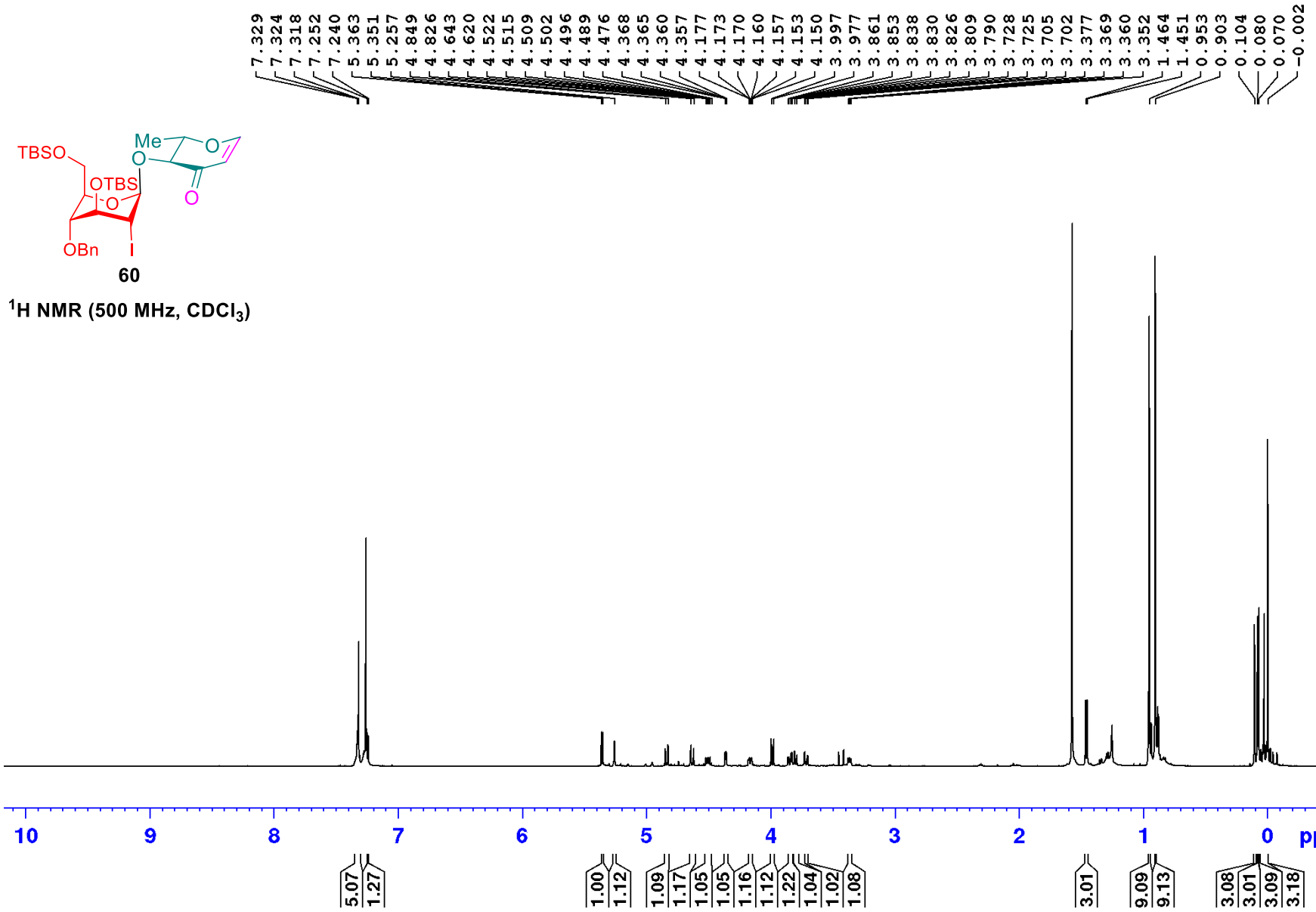
^{1}H NMR (500 MHz, $CDCl_3$)


OMe
Me
O
TBSO
OTBS
BnO
OMe
Me
O
TBSO
OBn
OTBS
BnO
OBn
59
13C{1H} NMR (125 MHz, CDCl3)
59
1H NMR (500 MHz, CDCl3)
ppm



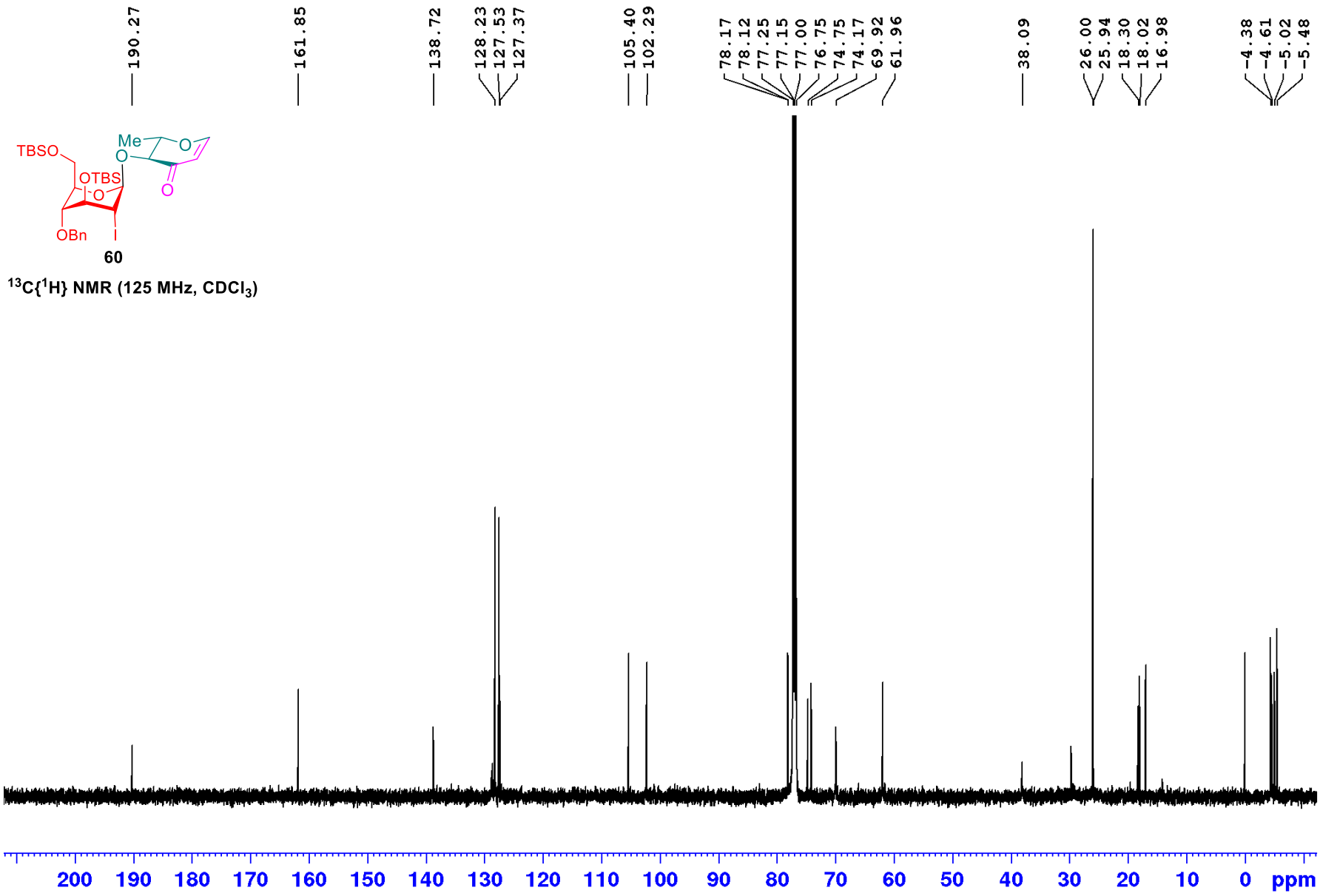
59

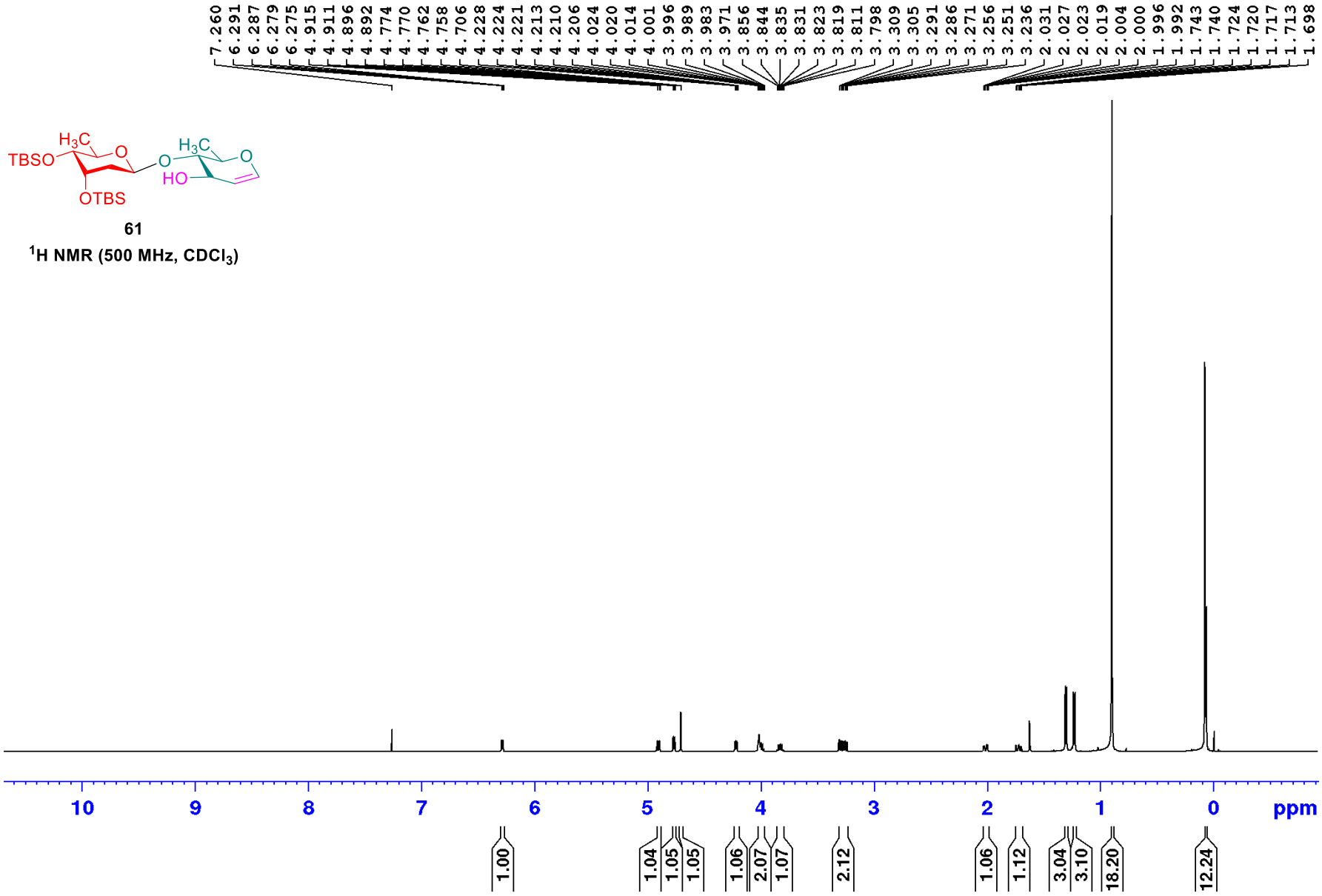
$^{13}C\{^{1}H\}$ NMR(125 MHz, $CDCl_3$)



60

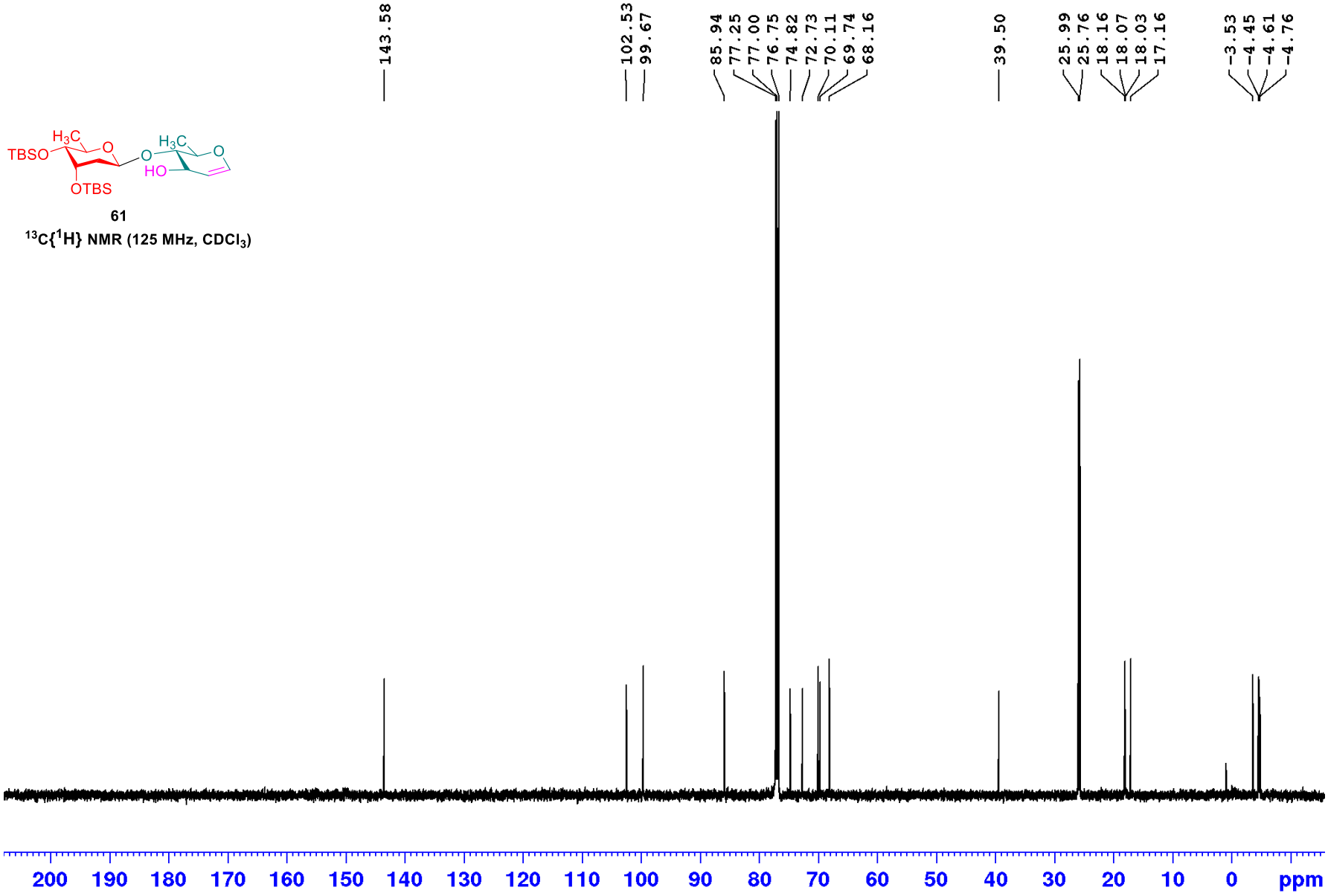
^{1}H NMR (500 MHz, $CDCl_3$)


190.27
161.85
138.72
128.23
127.53
127.37
105.40
102.29
78.17
78.12
77.25
77.15
77.00
76.75
74.75
74.17
69.92
61.96
38.09
26.00
25.94
18.30
18.02
16.98
-4.38
-4.61
-5.02
-5.48
TBSO
OTBS
OBn
Me
O
O
O
O
I
60
13C{1H} NMR (125 MHz, CDCl3)
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
ppm



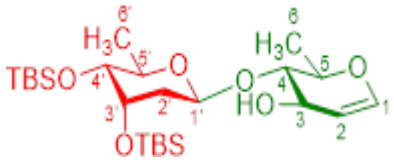
61

^{1}H NMR (500 MHz, $CDCl_3$)

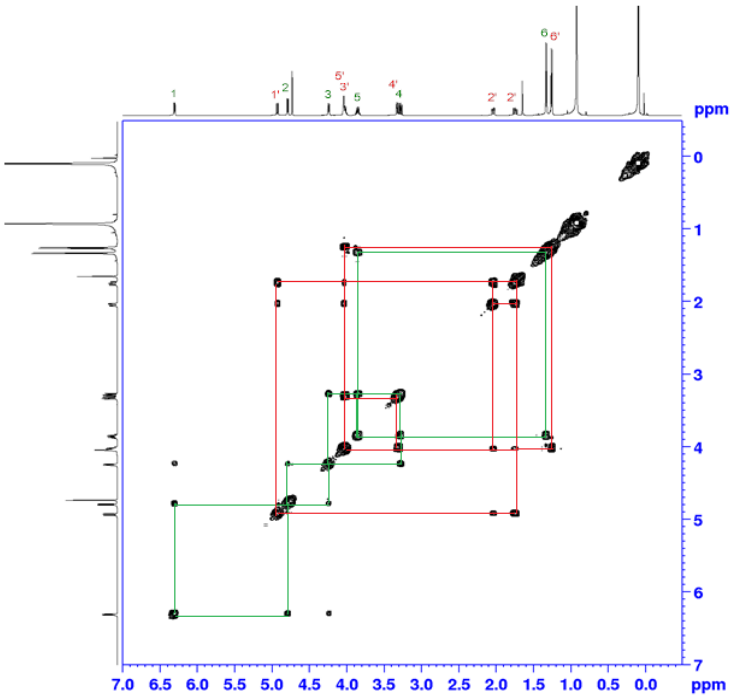


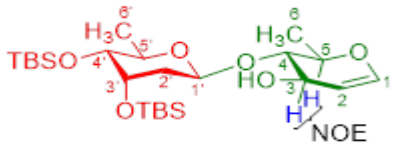
61

$^{13}C\{^{1}H\}$ NMR (125 MHz, $CDCl_3$)

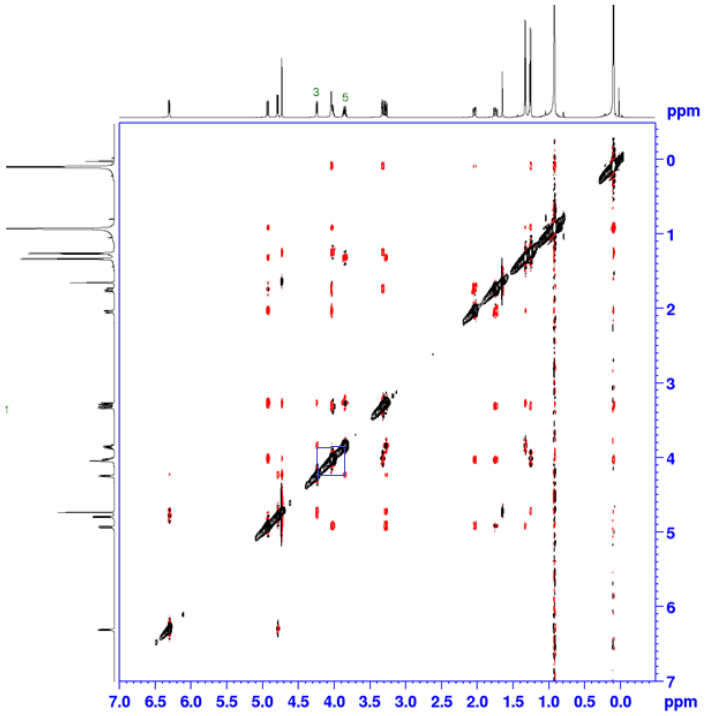


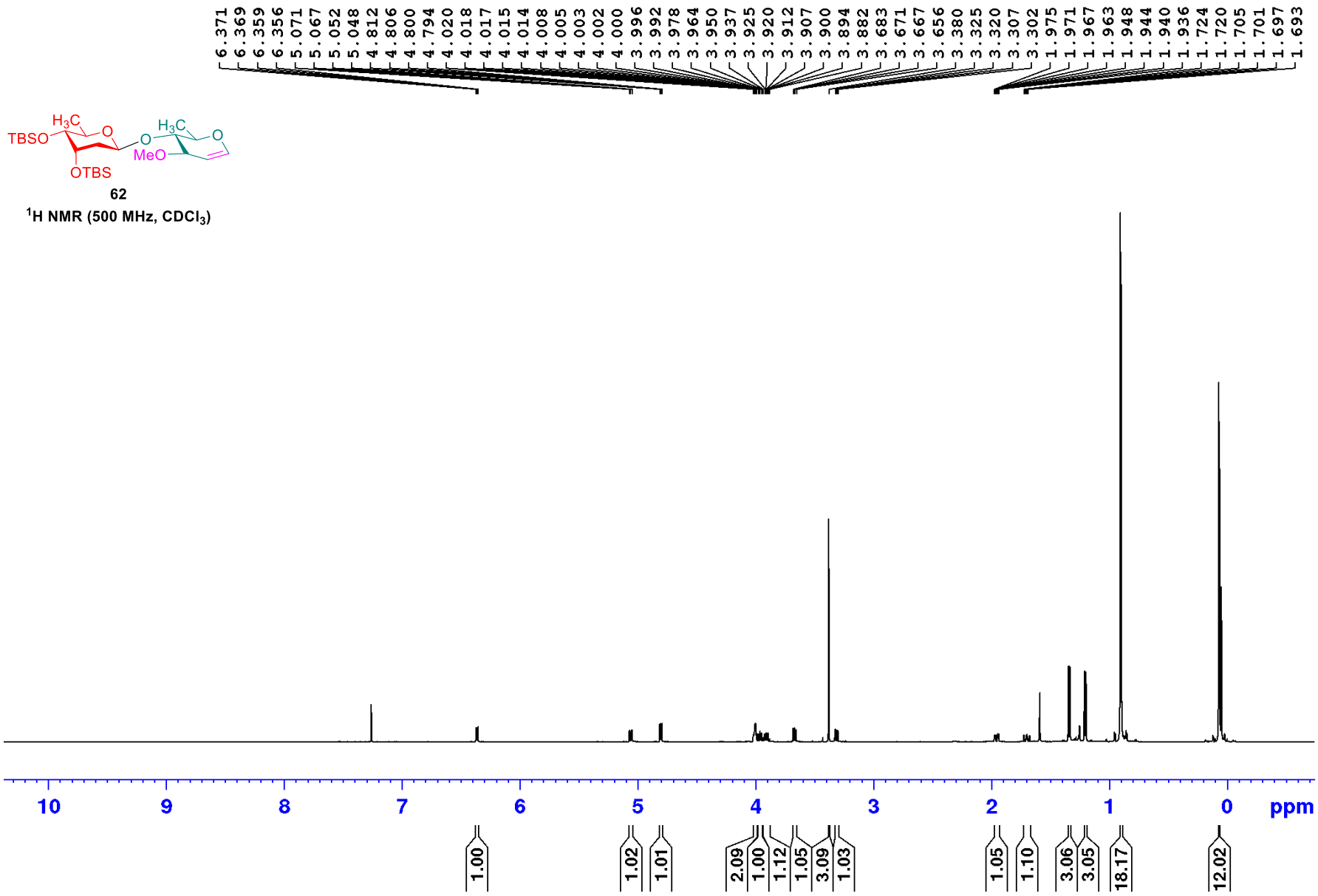
61
(COSY, 500 MHz)





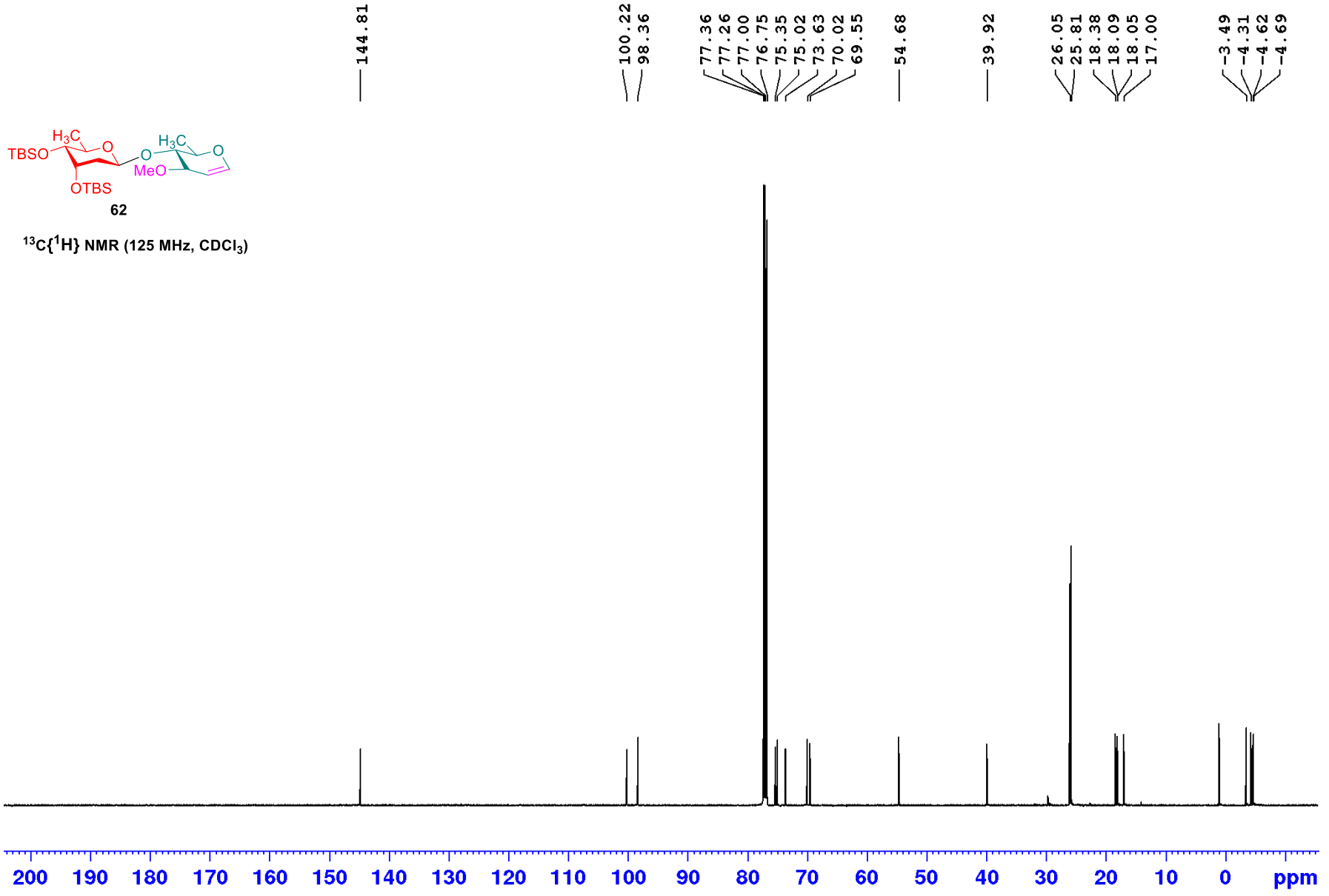
61
(NOESY, 500 MHz)





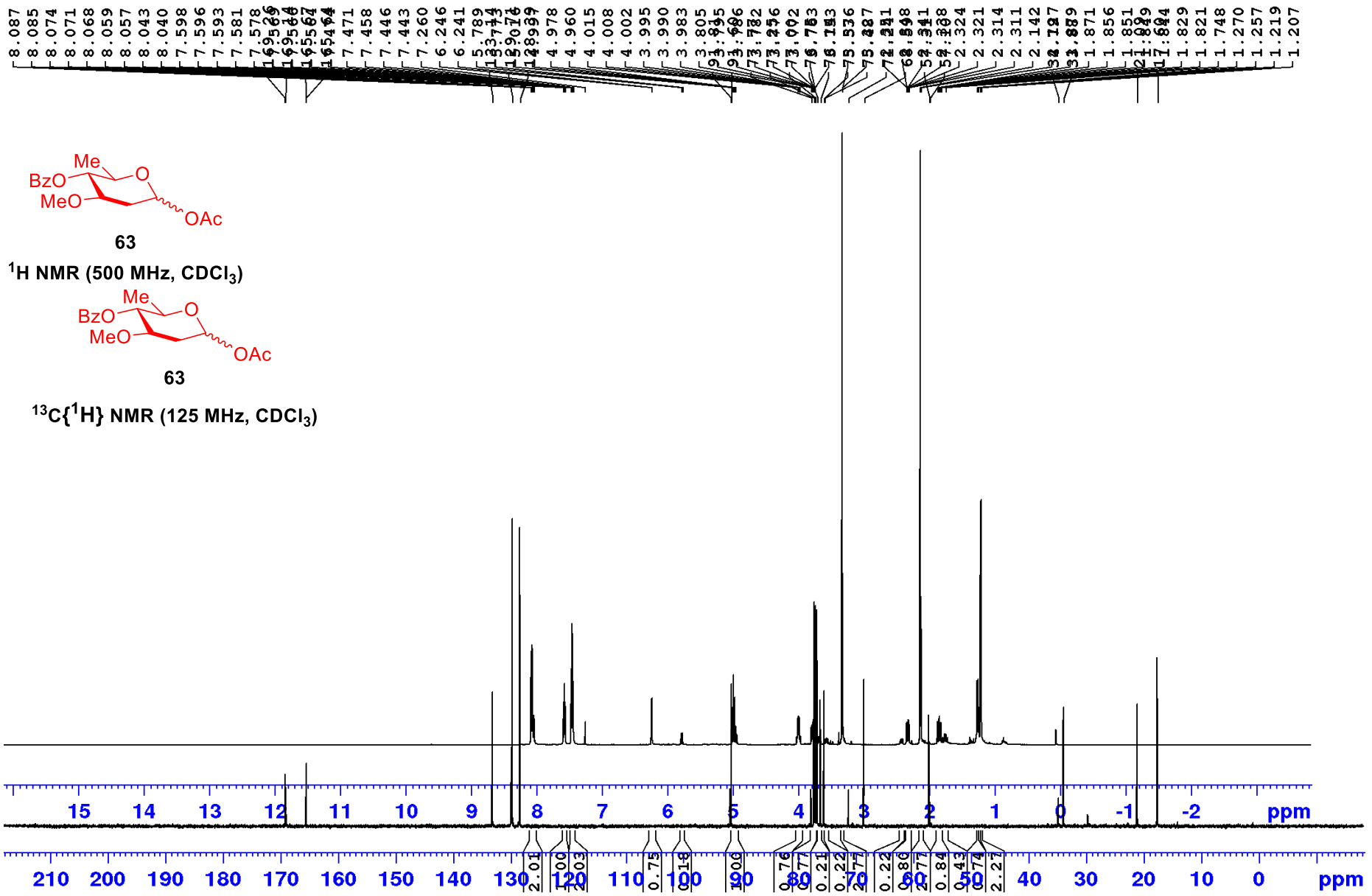
62

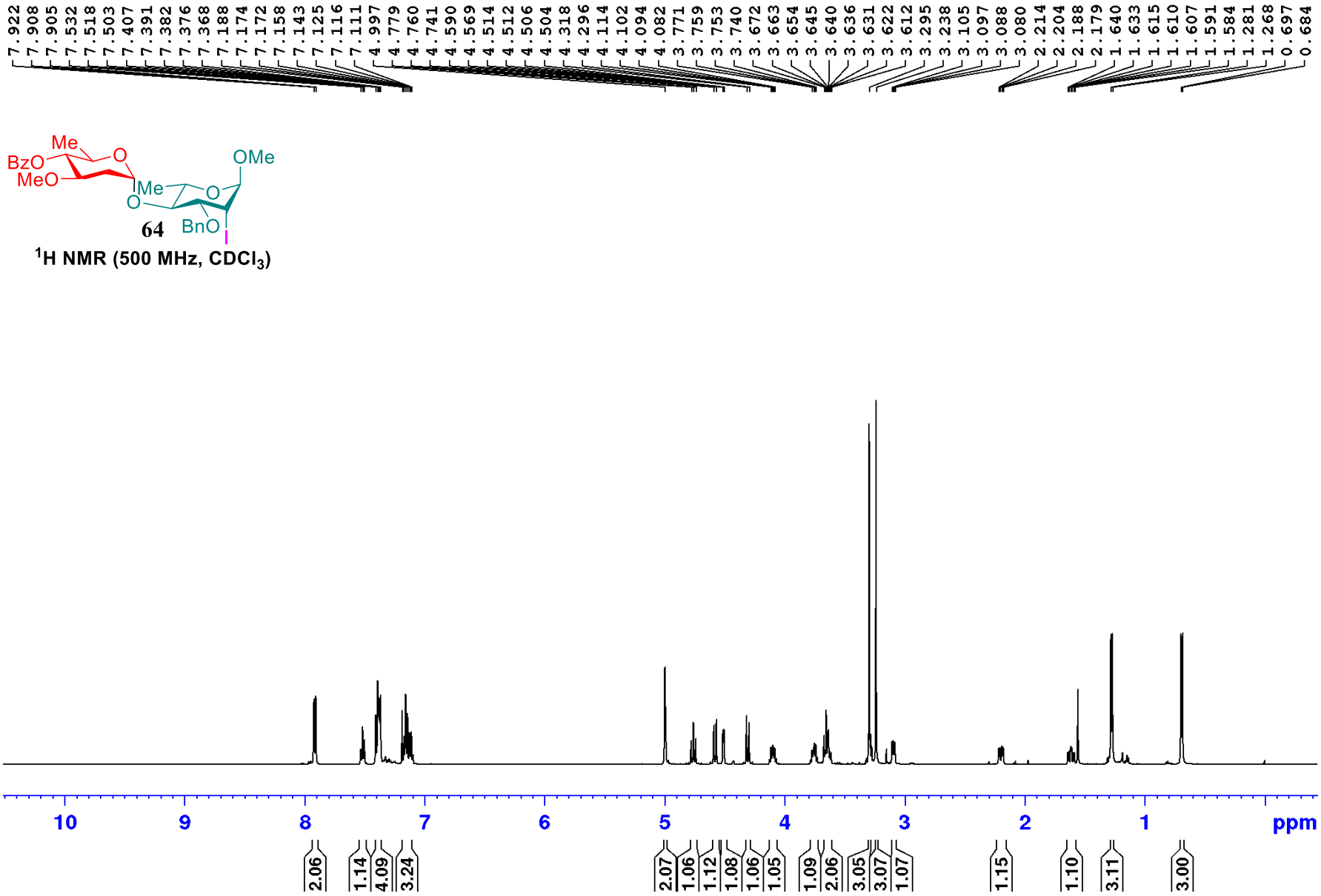
^{1}H NMR (500 MHz, $CDCl_3$)



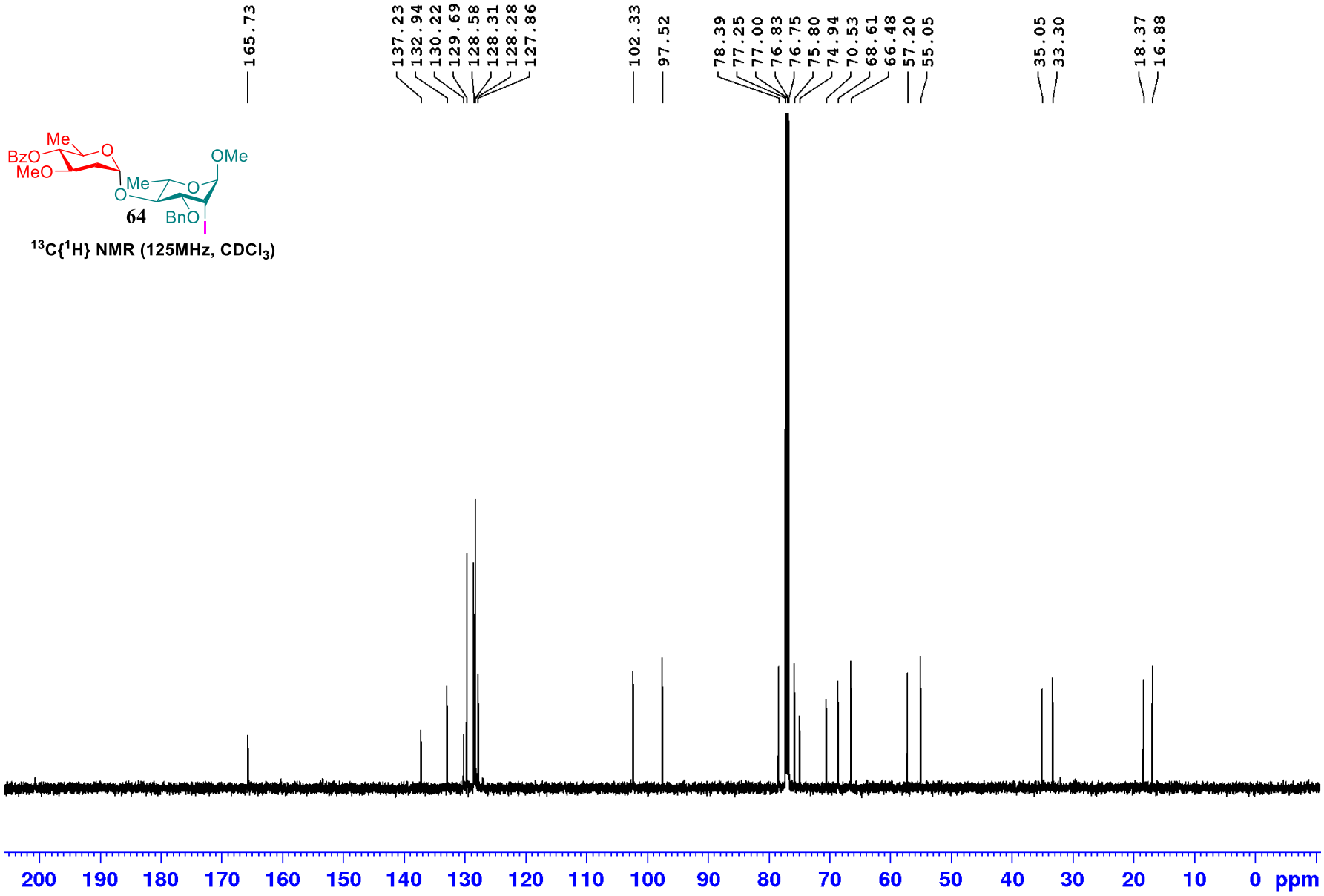
62

$^{13}C\{^{1}H\}$ NMR (125 MHz, $CDCl_3$)

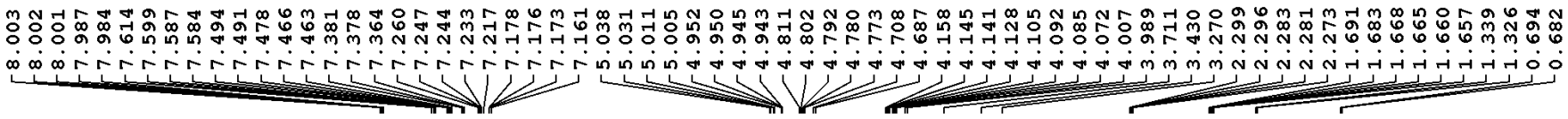

Me
BzO
O
MeO
OAc
63
1H NMR (500 MHz, CDCl3)
Me
BzO
O
MeO
OAc
63
13C{1H} NMR (125 MHz, CDCl3)
ppm
ppm

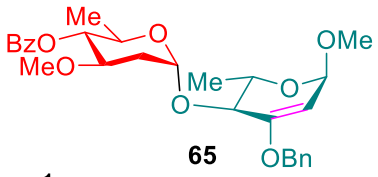


^{1}H NMR (500 MHz, $CDCl_3$)



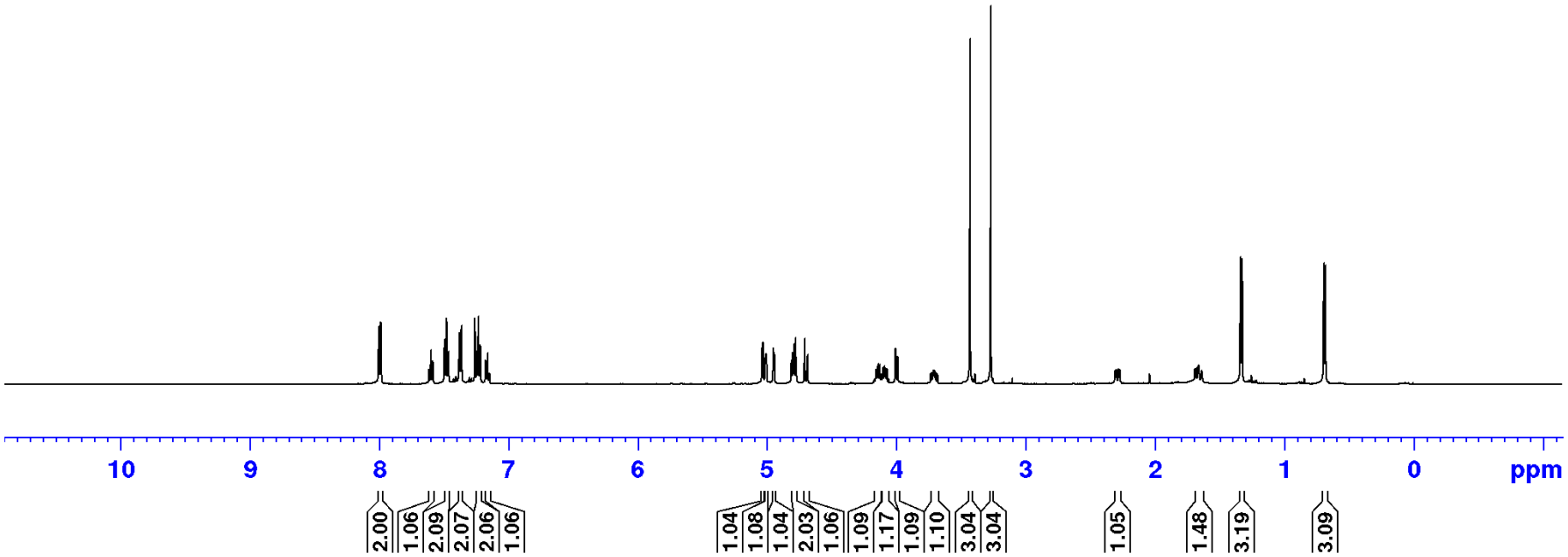
$^{13}C\{^{1}H\}$ NMR (125MHz, $CDCl_3$)

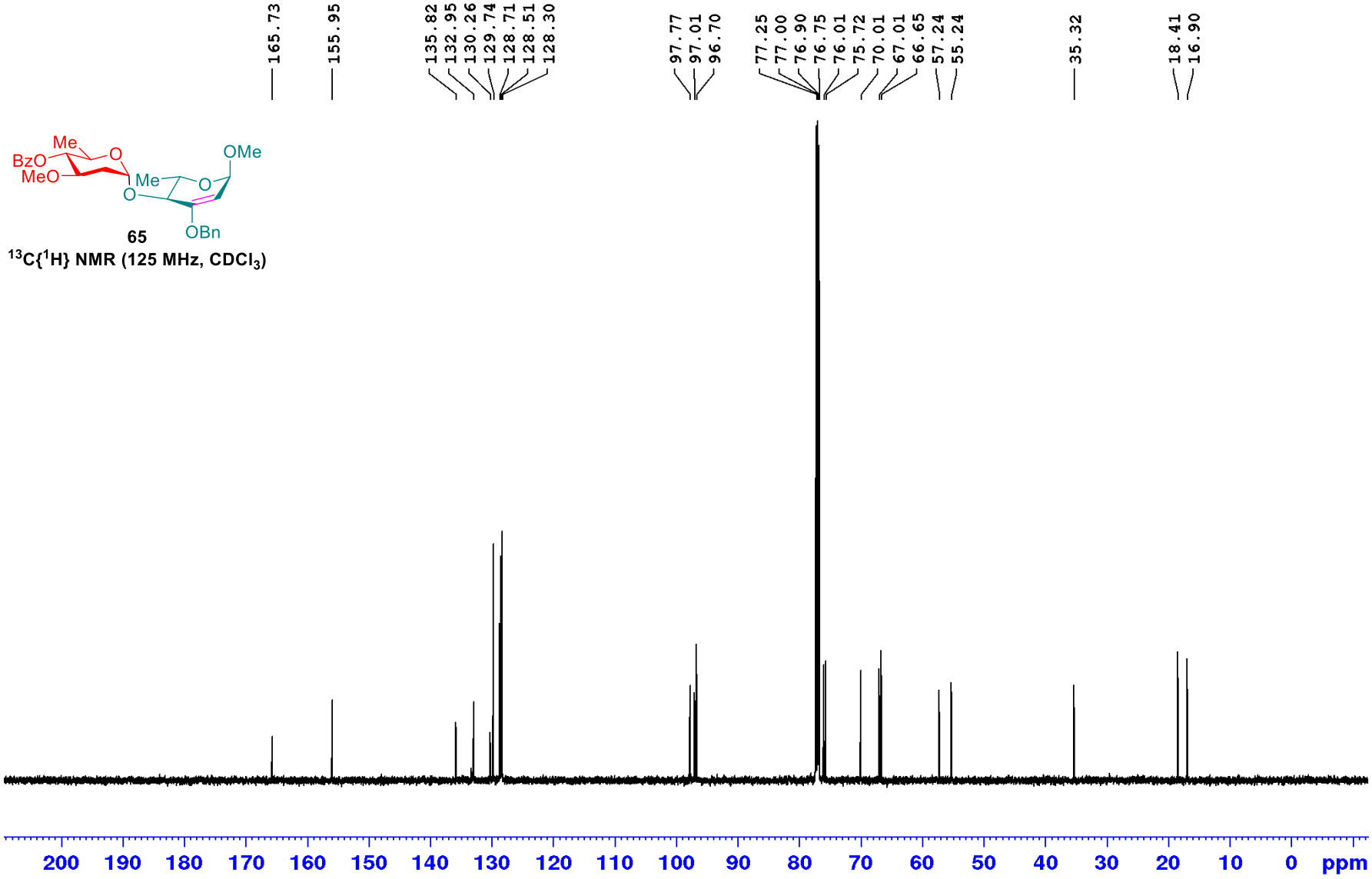




65

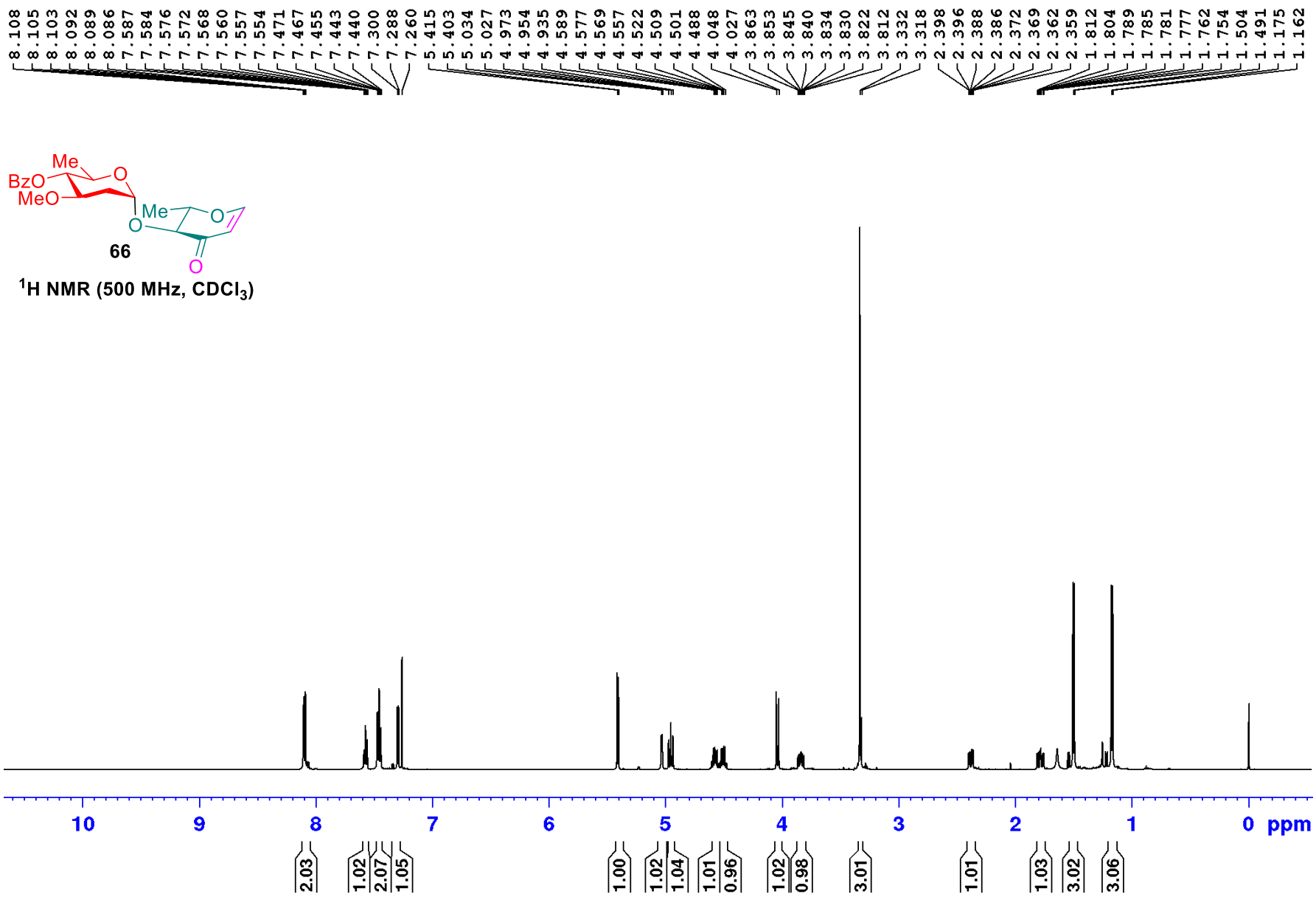
^{1}H NMR (500 MHz, $CDCl_3$)





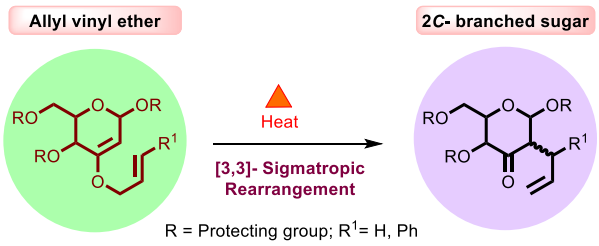
65

$^{13}C\{^{1}H\}$ NMR (125 MHz, $CDCl_3$)


8.108
8.105
8.103
8.092
8.089
8.086
7.587
7.584
7.576
7.572
7.568
7.560
7.557
7.554
7.471
7.467
7.455
7.443
7.440
7.300
7.288
7.260
5.415
5.403
5.034
5.027
4.973
4.954
4.935
4.589
4.577
4.569
4.557
4.522
4.509
4.501
4.488
4.048
4.027
3.863
3.853
3.845
3.840
3.834
3.830
3.822
3.812
3.332
3.318
2.398
2.396
2.388
2.386
2.372
2.369
2.362
2.359
1.812
1.804
1.789
1.785
1.781
1.777
1.762
1.754
1.504
1.491
1.175
1.162
Me
BzO
MeO
O
Me
O
O
66
1H NMR (500 MHz, CDCl3)
10
9
8
7
6
5
4
3
2
1
0 ppm
2.03
1.02
2.07
1.05
1.00
1.02
1.04
1.01
0.96
1.02
0.98
3.01
1.01
1.03
3.02
3.06

Chapter 3

Synthesis of 2C-branched sugars via Claisen rearrangement



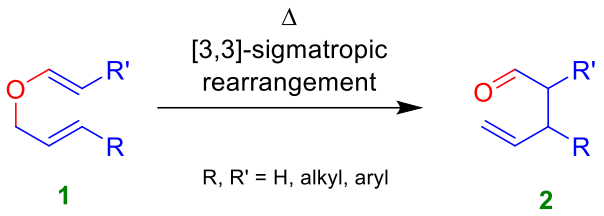
Abstract:

This chapter encompasses the Claisen rearrangement of carbohydrate-derived allyl-vinyl ethers for effective construction of 2-*C*-branched sugar derivatives. A suitable 3-*O*-alkenylated glycal is synthesized as the key precursor. The methodology is designed with 3 key steps: 1) iodo-benzoxylation 2) dehydrohalogenation and 3) Claisen rearrangement. 2-*C*-branched sugar derivates were obtained as mixtures in excellent yield. The substrates were subjected to iodo-benzoxylation using NIS-BnOH to give the corresponding 2-iodo glycoside with high α-anomeric stereoselectivity. DBU mediated dehydrohalogenation of this glycoside provided the 2,3-unsaturated vinyl ether derivative. Finally, subjecting this vinyl ether substrate to Claisen rearrangement in the presence of *N*,*N*-dimethyl aniline as catalyst, nitrobenzene as solvent, provided the glycal-derived 2-*C*-branched sugar derivative as inseparable mixtures in good yield. The applicability of the reaction was showcased by performing Claisen rearrangement over the disaccharide substrates.

3.1 Introduction

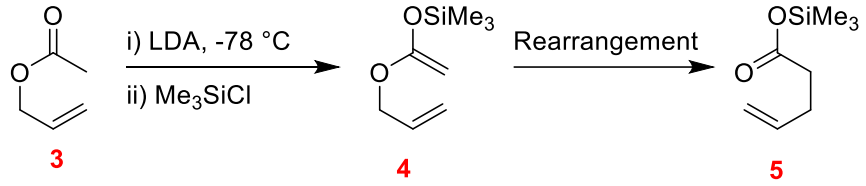
Carbohydrates, like proteins and nucleic acids, play critical roles in biological processes. This includes cell-cell and cell-viral recognition, cell adhesion, cell development, inflammation, and other features that have been well studied in the fields of glycochemistry and glycobiology.[1] These carbohydrates exist in oligomeric forms as glycolipids and glycoproteins, which are referred to collectively as glycoconjugates. Another major endeavour is the design and synthesis of carbohydrate mimics with the goal of discovering superior or alternate biological features.[2] Carbon branched sugars are one among the mimicking compound which are present in a variety of natural compounds, in which the hydroxyl groups on the pyranose/furanose ring are substituted with carbon. *C*-branched carbohydrates, which are abundant in nature and serve as major subunits in numerous antibiotics, bacterial polysaccharides, and macrolides, are of current interest in glycochemistry. One of the most important and demanding aims in organic synthesis is the development of stereocontrolled carbon-carbon bonds. Large efforts have been directed in this arena for the synthesis of carbon branched sugars employing the main class of carbohydrates as synthons. Carbohydrate-derived synthons, in turn, enabled the effective formation of structurally complex, wide-ranging, highly oxygenated natural compounds,[3, 4, 5] as well as significant carbohydrate mimetics [6, 7, 8.]

There are numerous ways for constructing C-glycosides in the literature, but forming a C-C bond at places other than the anomeric centre (at C-1) is quite challenging. Amid them, syntheses of 2-*C*-branched sugars have proven particularly appealing because they allow for manipulation of the anomeric core. Furthermore, in many circumstances, 2-*C*-branched sugars can serve as valuable precursors to produce some biologically important compounds.[9] The synthetic protocols involve pool of reactions for the construction of 2-*C*-branched sugars. Among the different techniques available, heteroatom addition,[10] epoxidation,[11] acid-mediated rearrangements[12] and cycloaddition reactions,[13] are the most significant procedures to produce 2-C-branched sugars. Similarly, The classic Claisen rearrangement, discovered by Claisen in 1912 [14], which represents a broad class of the [3, 3]-sigmatropic reaction, is recognised as one of the most efficient stereoselective carbon-carbon bond-forming synthetic techniques. The thermal Claisen rearrangement of allyl vinyl ether **1** is considered to occur in a stereocontrolled manner through a chair-like transition state, yielding γ,δ-unsaturated carbonyl system **2** (Scheme 1).



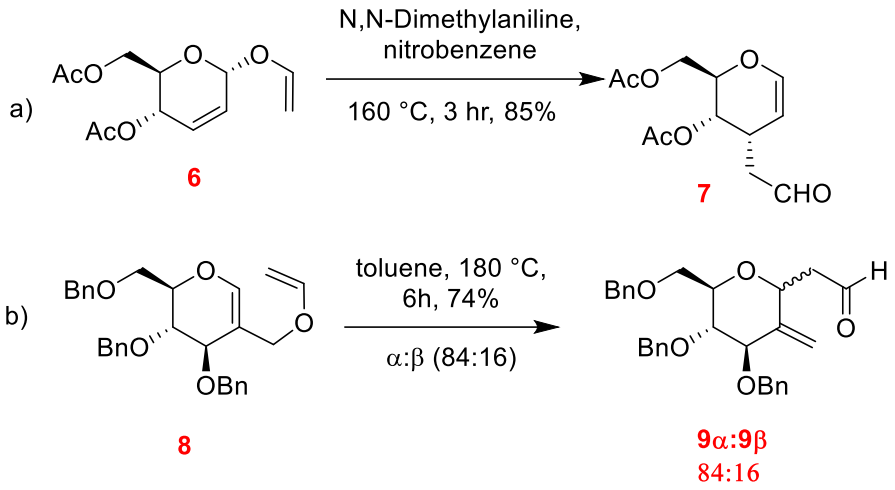
Scheme 1: Claisen rearrangement

To broaden the scope of the previous rearrangement process, a number of modifications were incorporated, including the approach established by Ireland and colleagues in 1972.[15] It involved the base-promoted *O*-sialylation of allyl ester **3** to obtain silyl ketene acetal **4**, followed by its rearrangement to afford γ,δ-unsaturated silyl ester **5** (Scheme 2).



Scheme 2: The Ireland-Claisen rearrangement of silyl ketene acetal

Claisen rearrangement has proven to be a valuable method for the construction of complex sugar framework.[16] Our group has done enormous work and built several *C*-branched sugars, *C*-glycosides and fused molecular frameworks by implementing Claisen rearrangement on the perfectly designed glycal derivative (Scheme 3).[17] For example, allyl vinyl ether derivative **6** under heating condition in nitrobenzene/N,N-dimethylaniline underwent Claisen [3,3]-sigmatropic rearrangement provided the expected 3-C-branched glucal derivative **7** (Scheme 3a). Similarly in another work, when 2-vinyloxymethyl glucal derivative **8** was heated to 180 °C in toluene for 6 h, the reaction provided the expected C-2-methylene-C-glycosides **9α** and **9β** in 84:16 ratio, respectively (Scheme 3b)

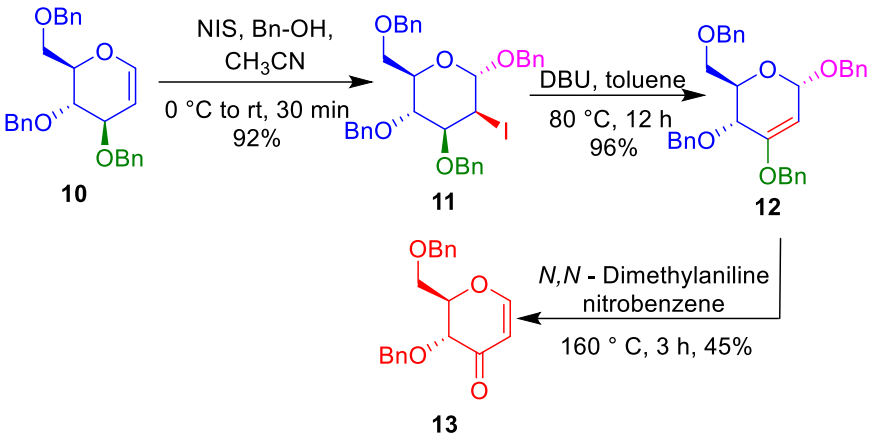


Scheme 3: Claisen rearrangement on the perfectly designed glycal derivative.

In this view, we further concentrate on the synthesis of pyranoid sugars with *C*-2 branching using the Claisen rearrangement involving a 2,3-unsaturated sugar derivative as the synthons.

3.2 Results and Discussions

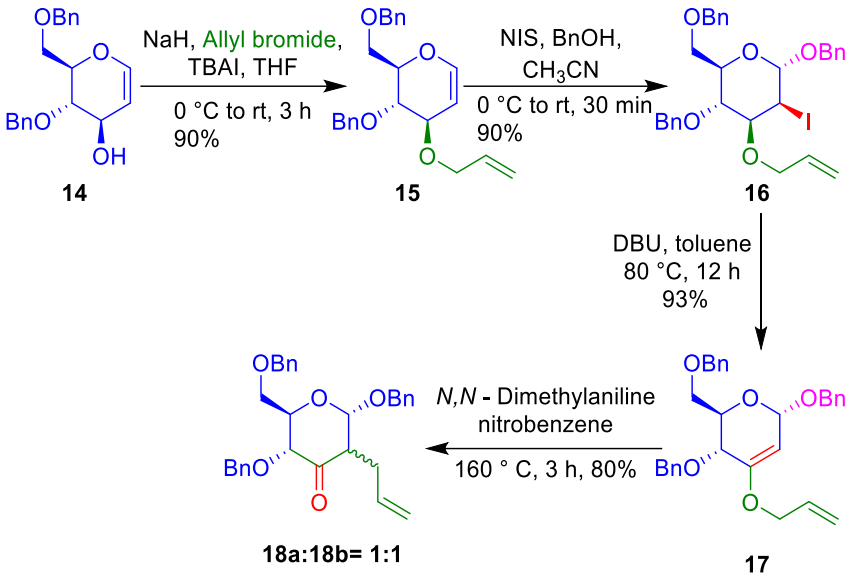
Towards this, we started our investigation by employing tribenzyl-D-glucal **10** as the initial substrate. Compound **10** was haloalkoxylation using NIS and BnOH in acetonitrile, provided the α-anomer **11** in 92% yield as the only product. Further, this iodo-acetal was subjected to dehydrohalogenation using DBU to obtain vinyl ether compound **12** in 96% yield. Finally, compound **12** was subjected to Claisen rearrangement reaction under heating conditions in nitrobenzene/*N*,*N*-dimethylaniline provided the unexpected 3-oxo-glucal **14** as the only product (Scheme 4).



Scheme 4. Unexpected product 3-oxo-glucal 13 from tribenzyl glucal by Claisen rearrangement

It was noticed that the olefin of the benzene ring did not participate in the rearrangement and instead underwent ketalyzation to give the corresponding 3-oxo-glucal **13**. As the phenylic double bond was not suitable for Claisen rearrangement, reactivity of allylic double bond was investigated for the rearrangement reaction.

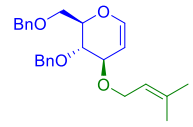
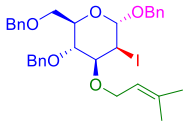
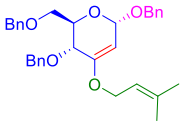
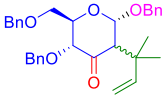
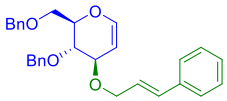
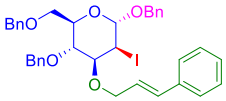
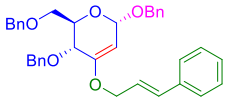
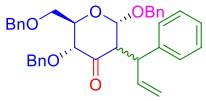
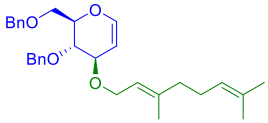
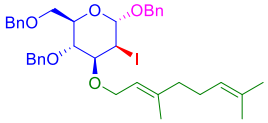
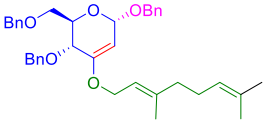
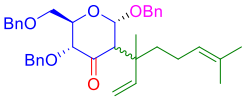
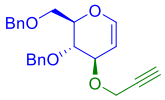
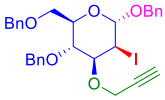
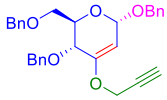
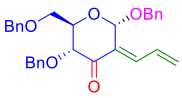
At the onset of our investigation, 3-OH-4,6-dibenzyl glucal **14** was subjected to allylation using NaH and allyl bromide in the presence of dry THF. The 3-*O*-allylated product **15** was obtained in 90% yield. Subsequently, compound **6** was subjected to iodoacetalization using NIS/BnOH in acetonitrile which gave compound **16** in 90% yield as a single anomeric isomer. In the next step, 2-iodo-glycoside **16** was subjected to DBU mediated dehydrohalogenation which gave the corresponding vinyl ether **17** in excellent yield of 93%. Ultimately, the Claisen [3,3]-sigmatropic rearrangement of compound **17** effected by heating in nitrobenzene/*N*,*N*-dimethylaniline provided the expected product **18**, the 2*C*-branched sugar, as the isomeric mixture (**18a:18b=1:1**) in 80% overall yield (Scheme 5).



Scheme 5. Expected Claisen product **18** from **17** by Claisen rearrangement.

It is worth noting that the methodology effectively uses the 2,3-unsaturated vinyl ether type of molecule for the construction of 2*C*-branched sugars. After the successful formation of Claisen adduct, the methodology was explored for the substrate scope. In this regard, several 3-*O*-alkenylated glucal (**19**, **23** and **27**) was synthesized from **14**. Firstly, 3-*O*-prenylated glucal **19** was synthesised from **14** in 92% yield. Further, **19** was subjected to iodoacetalyzation using NIS/BnOH to get the 2-iodo-glycoside **20** in 95% yield. Then DBU mediated dehydrohalogenation was performed over **20** to obtain the vinyl ether **21** in excellent yield. Further, the thermal, [3,3]-sigmatropic Claisen rearrangement of **21** gave the corresponding 2C-branched sugar **22** as (**22α:22β = 1:1**) mixture in 88% yield. Similarly, the alkenylated glucal substrates **23** and **27** underwent iodoacetalyzation in the presence of NIS/BnOH and provided the corresponding benzyl 2-deoxy-2-iodo glycosides **24** and **28** in good yield. Subsequent DBU mediated dehydrohalogenation resulted in vinyl ethers **25** and **29** respectively, which upon reaction with a catalytic amount of *N*,*N*-dimethyl aniline in nitrobenzene solvent under heating condition led to the formation of the 2C-branched sugar derivatives **26a:26b** and **30a:30b** respectively in good yields (Table 1, entry 2-3). Next, the 3-*O*-akynylated substrate **31** was specially synthesised from **14** to see the substrate effect. When the substrate **31** was subjected to iodoacetalyzation using NIS/BnOH in acetonitrile provided compound **32** in 80% yield. The obtained halo-glycoside **32** was subjected to DBU mediated dehydrohalogenation to get the corresponding vinyl ether **33** in

90% yield. Finally, this Claisen precursor **33** was subjected to Claisen rearrangement under optimised condition. However, in this case the Claisen adduct was not observed instead a diene compound **34** was formed in 67% yield (Table 1, entry 4) and the reason behind its formation is unknown.

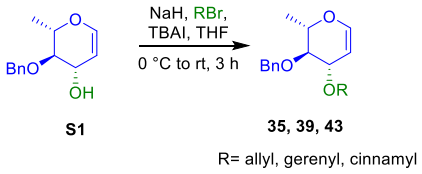
S.No	3-*O*-alkyl product (%)[a]	Iodoacetal (%)[a]	Vinyl ether (%)[a]	Claisen product as a Mixture (%)[b]
1	 **19**, 92%	 **20**, 95%	 **21**, 97%	 **22a : 22b = 1:1**, 88%
2	 **23**,90%	 **24**, 96%	 **25**, 95%	 **26a :26b = 1:1** 82%
3	 **27**, 95%	 **28**, 90%	 **29**, 98%	 **30a :30b = 1:1** 87%
4	 **31**, 92%	 **32**, 80%	 **33**, 90%	 **34**, 67%[a]

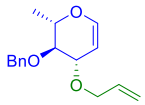
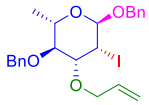
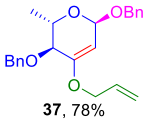
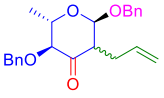
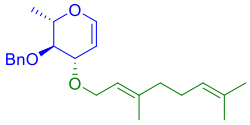
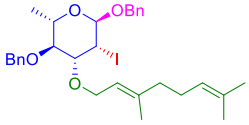
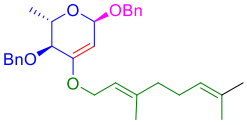
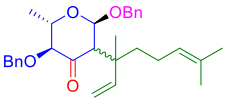
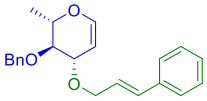
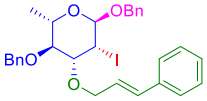
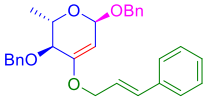
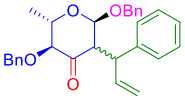
[a] Yield refers to pure and isolated products; [b]Isolated as mixtures.

Table 1: Synthesis of 2*C*-Branched sugars via Claisen rearrangements of 3-*O*-alkenylated 2,3-unsaturated Glucal derivative.

Having synthesized the library of 2*C*-branched sugar derivatives from 3-*O*-alkenylated 2,3-unsaturated glucal derivatives, we focused on the generality and efficacy of this methodology on a variety of 3-*O*-alkenylated L-rhamnal derivatives (Table 2, entry 1-3). The substrates **35**, **39** and **43** were synthesised from L-rhamnal derived glycal **S1.** The allylated, gernylated and cinnamylated L-rhamnal substrates **35**, **39** and **43** respectively, underwent iodo-benzoxylation in the presence of NIS/BnOH and provided the corresponding 2-iodo glycosides **36**, **40**, and **44** in good yield. Subsequent DBU mediated dehydrohalogenation of these, resulted in vinyl ethers **37**,

41, and **45** respectively which upon reaction under Claisen rearrangement conditions, product **38a:38b**, **42a:42b** and **46a:46b**, respectively in good yields (Table 2, entry 1-3).



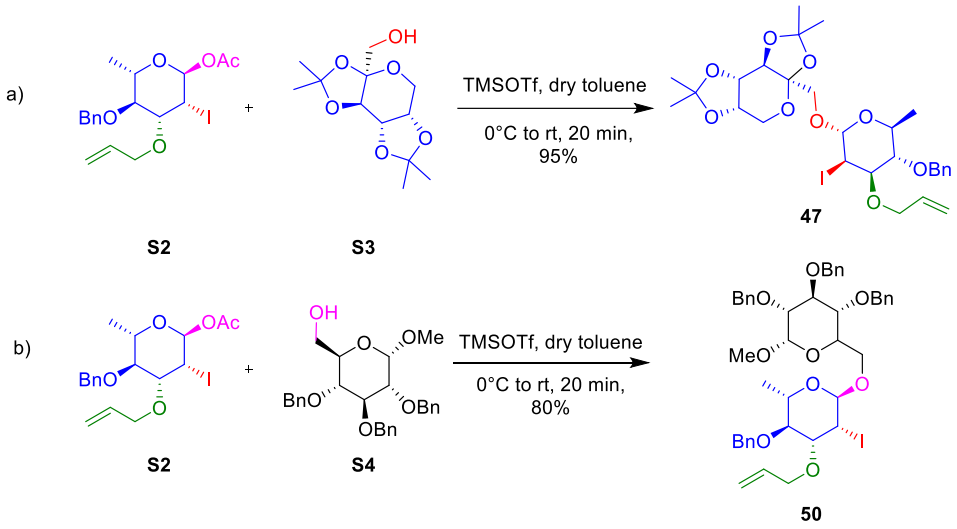
S.No	3-*O*-alkyl product (%)[a]	Iodoacetal (%)[a]	Vinyl ether (%)[a]	Claisen product as a Mixture(%)[b]
1	 **35**, 78%	 **36**, 80%	 **37**, 78%	 **38a:38b = 1:1**, 58%
2	 **39**, 90%	 **40**, 95%	 **41**, 96%	 **42a :42b = 7:3** 90%
3	 **43** 92%	 **44**, 95%	 **45**, 93%	 **46a :46b = 1:1**,88%

[a] Yield refers to pure and isolated products; [b]Isolated as mixtures.

Table 2: Synthesis of 2*C*-Branched sugars via Claisen rearrangements of 3-*O*-alkenylated 2,3-unsaturated Rhamnal derivative.

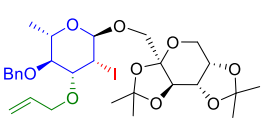
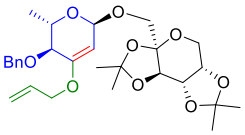
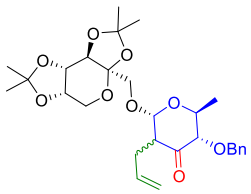
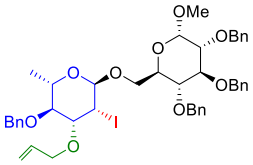
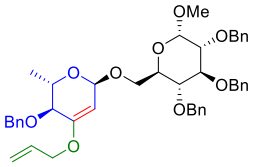
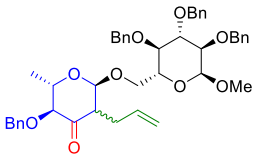
Having success in the case of monosaccharides, our vision focused on evaluating the protocol for the synthesis of carbon branched sugars in disaccharide derivatives. To initiate this, structurally diverse disaccharides **47**, **50, 53 and 56** having non-reducing and reducing end, were synthesized (Scheme 6 and Scheme 7).

The donor **S2** and acceptor **S3** was subjected to TMSOTf mediated glycosylation at 0 °C in toluene to obtain the disaccharide **47,** with non-reducing end, in 95% yield (Scheme 6a). Under the similar glycosylation conditions, another disaccharide **50**, with a non-reducing end, was synthesised in 80% yield using **S4** alcohol acceptor (Scheme 6b).



Scheme 6: Synthesis of disaccharide precursors with non-reducing end for Claisen rearrangement

Having obtained the disaccharides **47** and **50**, these substrates were subjected to DBU mediated dehydrohalogenation which provided the vinyl ethers **48** and **51** respectively in excellent yield. Finally, these 2,3-unsaturated vinyl ethers were subjected to the key step, the [3,3]-sigmatropic Claisen rearrangement reaction, using catalytic amount of *N*,*N*-dimethyl aniline in nitrobenzene solvent under heating condition. As a result, the Claisen adducts **49a:49b** and **52a:52b** were obtained as a mixture at the newly formed *C*-*C* bond which were separable by column chromatography (Table 3, entry 1-2).

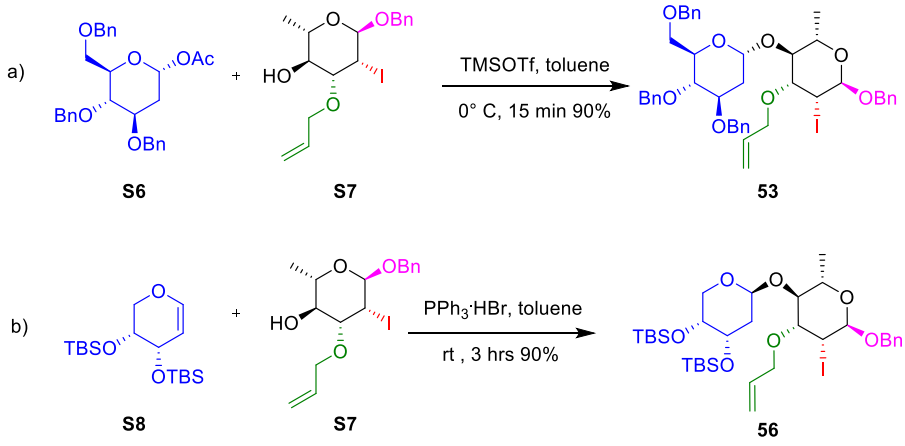
S.No	Iodoacetal	Vinyl ether (%)[a]	Claisen product as a mixture (%)[b]
1			
	47	48, 97%	49a:49b = 1.1 95%
2			
	50	51, 95%	52a:52b = 1:1 87%

[a] Yield refers to pure and isolated products; [b]Isolated as mixtures.

Table 3: Application of Claisen rearrangement on the disaccharides with non-reducing ends.

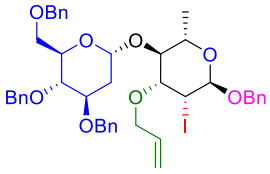
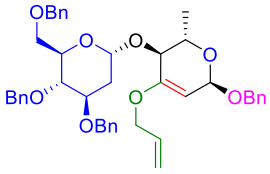
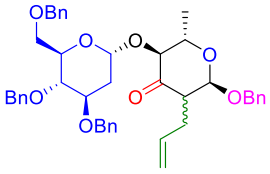
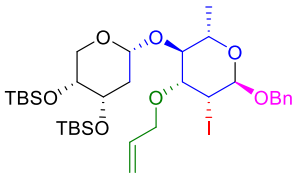
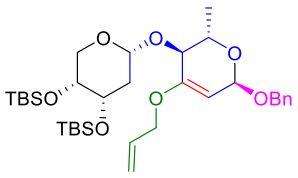
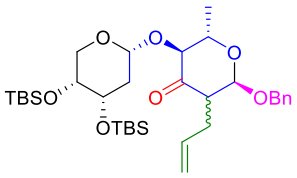
Hence, for the first time, we successfully applied the Claisen rearrangement over the disaccharide substrate to obtain the C-branched sugar derivatives.

In a similar way, we successfully showcased the applicability of the methodology over the disaccharides with the reducing end. In this view, the disaccharides **53 and 56** were synthesised (Scheme 7).



Scheme 7: Synthesis of disaccharide precursors with reducing end for Claisen rearrangement

The donor **S6** and alcohol acceptor **S7** were subjected to TMSOTf mediated glycosylation at 0 °C in toluene to obtain the disaccharide **53,** with reducing end, in 90% yield (Scheme 7a). Disaccharide **56** was synthesised via PPh_3·HBr mediated glycosylation reaction using **S8** as the glycosyl donor (Scheme 7b). The synthesized disaccharides **53** and **56** were treated with DBU to give the corresponding vinyl ether **54** and **57** in excellent yield. Ultimately, under thermal conditions in the presence of catalytic amount of *N*,*N*-dimethyl aniline in nitrobenzene solvent, the 2,3-unsaturated disaccharide systems were efficiently transformed to the corresponding carbon branched sugars **55a:55b** and **58a:58b** as mixtures. These transformations over the disaccharides clearly indicates the potential applicability of the Claisen rearrangement (Table 4, entry 1-2).

S.No	Iodoacetal	Vinyl ether (%)[a]	Claisen product as a mixture (%)[a]
1			
	53	**54**, 93%	**55a: 55b = 9: 1** 87%
2			
	56	**57**, 90%	**58a: 58b = 9:1** 90%

[a] Yield refers to pure and isolated products; [b]Isolated as mixtures.

Table 4: Application of Claisen rearrangement on the disaccharides with reducing ends.

3.3 Conclusion

In conclusion, we reported a general, efficient, and convenient methodology for synthesizing 2*C*-branched sugar derivatives via Claisen rearrangement. The methodology adopts one of the most powerful tools, that is the [3,3]-sigmatropic rearrangement. The substrate opportunity and approachability of the current protocol were successfully shown by synthesizing 2*C*-branced sugar derivatives of mono- and disaccharides.

3.4 Experimental Section

3.4.1 General Information:

All the reactions were carried out under nitrogen or argon atmosphere and monitored by thin layer chromatography (TLC) using silica gel GF_{254} plates with detection by charring with 5% (v/v) H_2SO_4 in methanol or by phosphomolybdic acid (PMA) stain or by ultra violet (UV) detection. All the chemicals were purchased from local suppliers and Sigma-Aldrich Chemicals Company. Solvents used in the reactions were distilled over dehydrated agents. Silica-gel (100-200 mesh) was used for column chromatography. ^{1}H, ^{13}C, DEPT, COSY, NOESY spectra were recorded on Bruker 400 MHz and 500 MHz spectrometer in $CDCl_3$. ^{1}H NMR chemical shifts were reported in ppm (δ) with TMS as internal standard (δ 0.00) and ^{13}C NMR were reported in chemical shifts with solvent reference ($CDCl_3$, δ 77.00). High resolution mass spectra (HRMS) were obtained in the ESI mode.

Iodo-acetalyzation of glycals (General Procedure A):

To a stirred solution of protected glycal in anhydrous ACN (10 mL/mmol) under inert atmosphere was added Bn-OH (5 eq) followed by NIS (1.5 eq) at 0°C. The reaction was allowed to raise to room temperature and further stirred until starting material is disappeared. The reaction was quenched with saturated solution of sodium thiosulphate and extracted with EtOAc. dried over anhydrous Na_2SO_4 and concentrated under reduced pressure to obtain crude product. Purification of the crude product by column chromatography over silica gel using hexanes and ethyl acetate provided Iodo compounds.

Dehydrohalogenation-synthesis of vinyl ether (General procedure B):

To a stirred solution of compound in anhydrous Toluene (10 mL/mmol) under inert atmosphere was added DBU (1.1 eq) at room temperature. The reaction mass was further heated at 80°C for 24 hours. After complete conversion of starting material, solvent was concentrated under reduced pressure to obtain crude product which was purified over basic alumina to obtain vinyl ether.

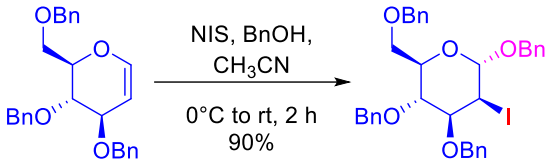
Claisen rearrangement of vinyl ether (General procedure C):

Vinyl glycoside 4 (2.4 mmol, 1 equiv.) was mixed with N,N-dimethylaniline (0.2 mL) in nitrobenzene (10 mL), and the mixture was heated at 150–170 °C until the starting material was

completely consumed (5–6 h). The resulting mixture was instantly loaded onto a silica gel column, and the product was purified by eluting with hexanes and ethyl acetate to obtain the 2-C-branched 3-oxo-glycal derivative in a respectable yield.

General procedure for alkylation of benzyl protected glycal derivatives (D): The benzyl protected *C*-3-OH glycal was dissolved in anhydrous THF (3 mL/mmol) under an inert atmosphere and the mixture was cooled to 0 ^{o}C. NaH (1.5 eq, 60%) was added portion wise with stirring over a period of 20 minutes. After continues stirring for a further 1 hour at 0 ^{o}C, alkyl halide (1.25 eq) and TBAI (0.1 eq) were added at 0 ^{o}C and the mixture was stirred overnight at 25 ^{o}C. After completion of the reaction (monitored by TLC cold water was added dropwise and the obtained solution was extracted with ethyl acetate. The combined organic layer were dried over anhydrous Na_2SO_4 and concentrated under reduced pressure to obtain the crude alkyl protected glycal derivatives.

3.4.2 Experimental procedures and spectral data



10 **11**

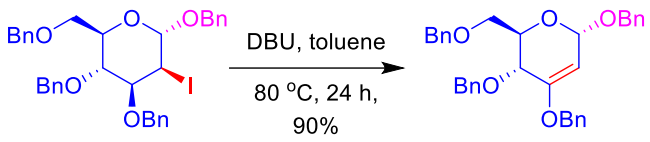
(2*S*,3*S*,4S,5R,6R)-2,4,5-tris(benzyloxy)-6-((benzyloxy)methyl)-3-iodotetrahydro-2*H*-pyran (11): Compound **11** was synthesised from Tribenzylglucal **10** (1g, 2.402 mmol) by following general **procedure A.**

Yield: 1.43g, 92 % colourless gel. R_f: 0.5 (10% EtOAc/Hx).

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.30-7.44 (m, 20H), 5.14 (s, 1H), 4.88-4.92 (m, 1H), 4.78 (d, 1H, *J* = 15.0 Hz), 4.75 (s, 1H), 4.72 (s, 1H), 4.58-4.61 (m, 2H), 4.53-4.56 (m, 2H), 4.51 (d, 1H, *J*= 15.0 HZ), 3.97-3.99 (m, 2H), 3.83-3.86 (m, 1H), 3.75 (8, 1H, *J*= 13.5 Hz), 3.40-3.43 (m, 1H).

^{13}C NMR (125 MHz, $CDCl_3$): δ 138.3, 138.1, 137.6, 136.8 , 128.4, 128.3, 128.3, 128.2, 128.0, 128.0, 127.9, 127.9, 127.7, 127.6, 127.6, 127.4, 100.6, 76.7, 75.8, 75.2, 73.3, 72.3, 70.9, 69.4, 68.7, 33.4

HRMS (ESI-TOF) *m/z*: [M+NH_4] calcd for $C_{34}H_{35}IO_5NH_4$ 668.1873, found 668.1871.



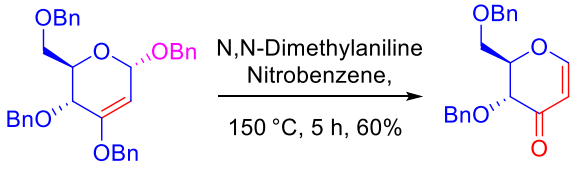
11 **12**

(2*R*,3*R*,6*S*)-3,4,6-tris(benzyloxy)-2-((benzyloxy)methyl)-3,6-dihydro-2*H*-pyran (12): Compound **12** was synthesised from **11** (1 g, 1.53 mmol) by following **general procedure B.** Yield: 771.1 mg, 96%, colureless gel . R_f: 0.4 (10% EtOAc/hexane).

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.27-7.41 (m, 20H), 5.36 (d, 1H, *J* = 4.5 Hz), 4.88-4.96 (m, 3H), 4.81 (t, 2H, *J* = 16.0 Hz), 4.67 (d, 1H, *J* = 15.5 Hz), 4.63 (d, 1H, *J* = 14.5 Hz), 4.52 (d, 1H, *J* = 15.0 Hz), 4.47 (d, 1H, *J* = 14.0 Hz), 4.34 (d, 1H, *J* = 12.0 Hz), 4.21- 4.25 (m, 1H), 3.72-3.76 (m, 1H), 3.64 (dd , 1H, J_1 = 2.5, J_2 = 27 Hz).

^{13}C NMR (125 MHz, $CDCl_3$): δ 158.0, 138.2, 138.2, 138.1 , 136.4 , 128.4 , 128.3(2), 128.2, 128.1, 128.0, 127.9, 127.9, 127.6, 127.6, 127.6, 127.5, 95.8, 95.4, 74.1, 73.3, 71.1, 69.8, 69.7, 69.4, 68.6

HRMS (ESI-TOF) *m/z*: [M+NH_4] calcd for $C_{34}H_{34}O_5NH_4$ 540.2750, found 540.2755



12 **13**

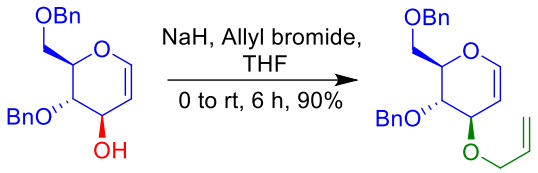
(2*R*,3*R*)-3-(benzyloxy)-2-((benzyloxy)methyl)-2,3-dihydro-4*H*-pyran-4-one (13): Compound **13** was synthesised from **12** (500 mg, 0.95 mmol) by following general **procedure C.** Yield: 139.6 mg, 45%, colureless gel . R_f: 0.6 (15% EtOAc/hexane).

IR (neat): 2968, 1738, 1366, 1215 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.28-7.35 (m, 11H), 5.38 (d, 1H, *J* = 6.0 Hz), 5.07 (d, 1H, *J* = 11.0 Hz), 4.57-4.61 (m, 2H), 4.52 (d, 1H, *J* = 12.0 Hz), 4.43 (dt, 1H, *J* =3.0 Hz, 11.5 Hz), 4.24 (d, 1H, *J* = 12.0 Hz), 3.80 (m, 2H).

^{13}C NMR (125 MHz, $CDCl_3$): δ 193.5, 162.2, 137.5, 137.4, 128.5, 128.4, 128.3, 128.0, 127.9, 127.8, 105.2, 81.0, , 74.6, 74.1, 73.6, 67.9.

HRMS (ESI-TOF) *m/z*: $[M+H]^+$ calcd for $C_{20}H_{20}O_4H$ 325.1431, found 325.1431.



14 15

(2*R*,3*S*,4*R*)-4-(allyloxy)-3-(benzyloxy)-2-((benzyloxy)methyl)-3,4-dihydro -2*H*-pyran (15):

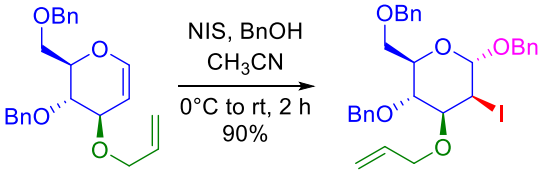
Compound **15** was synthesised from **14** (500 mg, 1.53 mmol) by following general **procedure D.** Yield: 505.2 mg, 90%, colureless gel. R_f: 0.8 (10% EtOAc/hexane).

IR (neat): 3028, 2920, 2860, 1737, 1646 cm^{-1}

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.28-7.36 (m, 10H), 6.43 (dd, 1H, J_1 = 0.5 Hz, J_2 = 6.0 Hz), 5.90-5.98 (m, 1H), 5.24 (dd, 1H, J_1 = 1.5 Hz, J_2 = 17.0 Hz), 5.20 (dd, 1H, J_1 = 3.0 Hz, J_2 = 10.5 Hz), 4.85-4.87 (m, 2H), 4.67 (d, 1H, J = 11.5 Hz), 4.57-4.64 (m, 2H), 4.12-4.16 (m, 2H), 4.03-4.09 (m, 2H), 3.83- 3.84 (m 1H), 3.80 (d, 1H, J = 4.5 Hz), 3.77-3.80 (m, 1H).

^{13}C NMR (125 MHz, $CDCl_3$): δ 144.6, 138.2, 138.0, 134.8, 128.4, 128.3 , 127.9, 127.8, 127.7, 127.6, 116.8, 100.1, 76.7, 75.7, 74.3, 73.7, 73.5, 69.4, 68.5.

HRMS (ESI-TOF) *m/z*: [M+Na] calcd for $C_{23}H_{26}O_4Na$ 389.1729, found 389.1724.



15 16

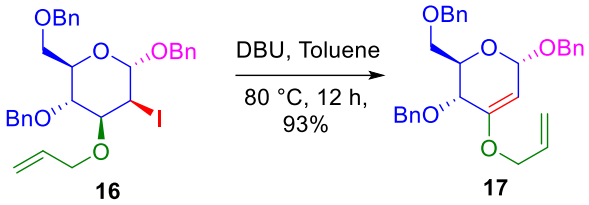
(2*S*,3*S*,4*S*,5*R*,6*R*)-4-(allyloxy)-2,5-bis(benzyloxy)-6-((benzyloxy)methyl)-3-iodotetrahydro-2*H*-pyran (16): Compound **16** was synthesised from **15** (300 mg, 0.81 mmol) by following general **procedure A.** Yield: 442.5 mg, 90%, colureless gel. R_f: 0.8 (10% EtOAc/hexane).

IR (neat): 3027, 2920, 1738, 1452 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.24-7.7.40 (m, 15H), 5.94-6.0 (m, 1H), 5.37 (d, 1H, J = 17.5 Hz), 5.33 (s, 1H), 5.22 (d, 1H, J = 10.0 Hz), 4.89 (d, 1H, J = 11.0 Hz), 4.70 (d, 1H, J = 12.5 Hz), 4.70 (d, 1H, J = 11.5), 4.49-4.58 (m, 4H), 4.182 (dd, 1H, J_1 = 5.5 Hz, J_2 = 12.5 Hz), 4.04 (dd, 1H, J_1 = 5.5 Hz, J_2 = 13.0 Hz), 3.89-3.95 (m 2H), 3.80 (dd, 1H, J_1 = 7.0 Hz, J_2 = 10.5 Hz), 3.71 (d, 1H, J = 10.5 Hz), 3.26-3.29 (m, 1H).

^{13}C NMR (125 MHz, $CDCl_3$): δ, 138.4, 138.2, 136.9, 134.3, 128.4, 128.3, 128.3, 128.1, 128.0, 128.0, 127.7, 127.6, 127.4, 117.3, 100.7, 76.7, 76.0, 75.2, 73.4, 72.4, 70.0, 69.5, 68.9, 33.7.

HRMS (ESI-TOF) *m/z*: $[M+Na]^+$ calcd for $C_{30}H_{33}IO_5Na$ 623.1265, found 623.1266.



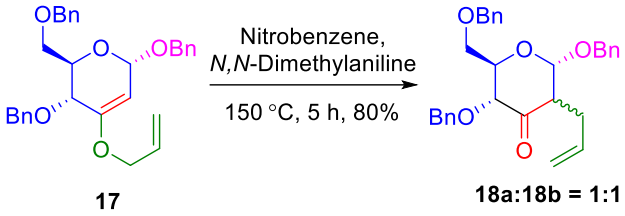
(2*R*,3*R*,6*S*)-4-(allyloxy)-3,6-bis(benzyloxy)-2-((benzyloxy)methyl)-3,6-dihydro-2*H*-pyran(8): Compound **17** was synthesised from **16** (300 mg, 0.49 mmol) by following general **procedure B.** Yield: 219.5 mg, 93%, colureless gel . R_f: 0.7 (10% EtOAc/hexane.

IR (neat): 3027, 2918, 1738, 1665 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.27-7.7.38 (m, 15H), 5.98-6.0 (m, 1H), 5.37-5.41 (m, 1H), 5.32 (d, 1H, *J* = 3.5 Hz), 5.26-5.29 (m, 1H), 4.92 (d, 1H, *J* = ^{11}.0 Hz), 4.82 (d, 1H, *J* = 3.5 Hz), 4.79-4.81 (m, 1H), 4.65 (d, 1H, *J* = 12.5), 4.60 (d, 1H, *J* = 12.0 Hz), 4.49 (s, 2H, *J* = 12.5 Hz), 4.5-4.38 (m 1H), 4.29-4.38 (m, 1H), 4.27 (s, 1H), 4.1-4.20 (m, 1H). 3.71 (dd, 1H, J_1 = 4.0 Hz, J_2 = 10.5 Hz), 3.61 (dd, 1H, J_1 = 2.5 Hz, J_2 = 11.0 Hz),

^{13}C NMR (125 MHz, $CDCl_3$): δ 157.7, 138.4, 138.2, 138.1, 132.7, 128.3(3), 128.2, 128.1, 128.0, 127.9, 127.6, 127.5, 117.5, 95.7, 95.3, 74.0, 73.3, 71.1, 69.7, 69.7, 68.7, 68.1 .

HRMS (ESI-TOF) *m/z*: $[M+NH_4]^+$ calcd for $C_{30}H_{32}O_5NH_4$ 490.2588, found 495.2589



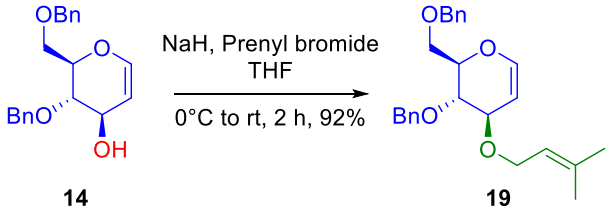
(2*S*,5*R*,6*R*)-3-allyl-2,5-bis(benzyloxy)-6-((benzyloxy)methyl)tetrahydro-4*H*-pyran-4-one (18a:18b): Compound (**18a:18b)** was synthesised from **17** (200mg, 0.42 mmol) by following general **procedure C.** Yield: 159.9 mg, 80%, colureless gel . R_f: 0.7. (10% EtOAc/hexane).

IR (neat): 3027, 2968, 2922, 1734 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.30-7.7.36 (m, 15H), 5.68-5.75 (m, 1H), 5.20 (d, 1H, *J* = 3.5 Hz), 4.99-5.04 (m, 2H), 4.91(d, 1H, *J* = 11.0 Hz), 4.67 (t, 2H, *J* = 12.0 Hz), 4,53-4.55 (m, 1H), 4.47 (d, 1H, *J* = 12.0 Hz), 4.41 (d, 1H, *J* = 11.0 Hz), 4.25 (d, 1H, *J* = 10.0 Hz), 4.07 (d, 1H, *J* = 9.5 Hz), 3.79-3.82 (m 1H), 3.72 (d, 1H, *J* = 10.5 Hz), 2.80-2.84 (m, 1H), 2.57-2.62 (m, 1H), 2.18-2,24(m, 1H).

^{13}C NMR (125 MHz, $CDCl_3$): δ 204.5, 137.9, 137.5, 136.8, 135.0, 128.4, 128.3(2), 128.2, 128.0, 127.9, 127.8, 127.8, 127.7, 116.9, 100.0, 79.0, 73.6, 73.3, 73.3, 69.3, 68.5, 53.3, 28.1

HRMS (ESI-TOF) *m/z*: $[M+Na]^+$ calcd for $C_{30}H_{32}O_5Na$ 495.2147, found 495.2145



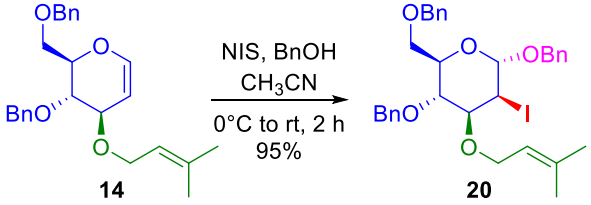
14 **19**

(2*R*,3*S*,4*R*)-3-(benzyloxy)-2-((benzyloxy)methyl)-4-((3-methylbut-2-en-1-yl)oxy)-3,4-dihydro-2*H*-pyran (19): Compound **19** was synthesised from **14** (400 mg, 1.22 mmol) by following general **procedure D.** Yield: 444.7 mg, 92%, colureless gel . R_f: 0.5 (10% EtOAc/hexane).

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.30-7.37 (m, 10H), 6.44 (d, 1H, *J* = 6.0 Hz), 5.38 (t, 1H, *J* = 5.5 Hz), 4.88-4.90 (m, 2H), 4.58-4.69 (m, 3H), 4.11-4.15 (m, 2H), 4.02-4.11 (m, 2H), 3.78-3.84 (m, 3H), 1.77 (s, 3H), 1.69 (s, 3H).

^{13}C NMR (125 MHz, $CDCl_3$): δ 144.4, 138.3, 138.0, 136.8, 128.3, 128.3 , 127.8, 127.7, 127.6, 127.6, 121.1, 100.3, 76.7, 75.4, 74.3, 73.6, 73.4, 68.6, 64.9, 25.7, 18.0

HRMS (ESI-TOF) *m/z*: $[M+H]^+$ calcd for $C_{25}H_{30}O_4H$ 395.2222, found 395.2217



14 **20**

(2*S*,3*S*,4*S*,5*R*,6*R*)-2,5-bis(benzyloxy)-6-((benzyloxy)methyl)-3-iodo-4-((3-methylbut-2-en-1-yl)oxy)tetrahydro-2*H*-pyran(11): Compound **20** was synthesised from **14** (300 mg, 0.76 mmol)

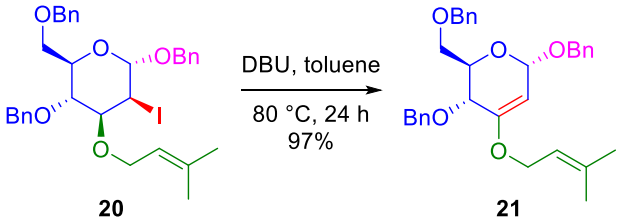
by following general **procedure A.** Yield: 454.1 mg, 95%, colureless gel . R_f: 0.6 (10% EtOAc/hexane).

IR (neat): 2922, 2016, 1738 cm−1

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.25-7.41 (m, 15H), 5.43-5.47 (m, 1H), 5.35 (s, 1H), 4.93 (d, 1H, *J* = 10.5 Hz), 4.72-4.77 (m, 2H), 4.56-4.60 (m, 2H), 4.51-4.53 (m, 2H) 4.17-4.21 (m, 1H), 3.93-4.00 (m, 2H), 3.89 (s, 1H, *J* = 8.5 Hz), 3.82 (dd, 1H, J_1 = 4.5 Hz, *J* = 11.0Hz), 3.74 (dd, 1H, J_1 = 2 Hz, *J* = 11.0Hz), 3.26-3.28 (m, 1H), 1.74 (s, 3H), 1.71 (s, 3H).

^{13}C NMR (125 MHz, $CDCl_3$): δ 138.4(2), 137.5, 136.9, 128.4, 128.3, 128.3(2), 128.0, 128.0, 127.9, 127.6, 127.4, 120.6, 100.7, 76.5, 75.8, 75.2, 73.3, 72.4, 69.4, 68.9, 65.3, 34.0, 25.8, 18.1.

HRMS (ESI-TOF) *m/z*: $[M+Na]^+$ calcd for $C_{32}H_{37}IO_5Na$ 651.1583, found 651.1578.



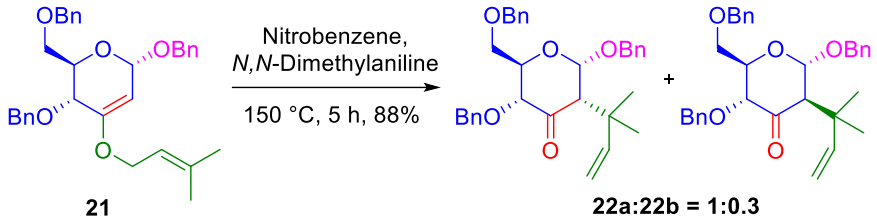
20 **21**

(2*R*,3*R*,6*S*)-3,6-bis(benzyloxy)-2-((benzyloxy)methyl)-4-((3-methylbut-2-en-1-yl)oxy)-3,6-dihydro-2*H*-pyran (21): Compound **21** was synthesised from **20** (350 mg, 0.55 mmol) by following general **procedure B.** Yield: 270.3 mg, 97%, colureless gel . R_f: 0.5 (10% EtOAc/hexane).

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.23-7.34 (m, 15H), 5.39-5.42 (m, 1H), 5.29 (d, 1H, *J* = 3.5 Hz), 4.85 (d, 1H, *J* = 11.0), 4.75-4.79 (m, 2H), 4.61 (d, 1H, *J* = 12.0 Hz), 4.57 (d, 1H, *J* = 11.5 Hz), 4.44 (d, 1H, *J* = 12.0 Hz), 4.44 (d, 1H, *J* = 11.0 Hz), 4.27-4.31 (m, 1H), 4.21-4.24 (m, 2H), 4.14-4.17 (m, 1H), 3.67 (dd, 1H, J_1 = 4.0 Hz, *J* = 10.5 Hz), 3.58 (dd, 1H, J_1 = 2 Hz, *J* = 10.5 Hz), 1.76 (s, 3H), 1.67 (s, 3H).

^{13}C NMR (125 MHz, $CDCl_3$): δ 158.0, 138.5, 138.3, 138.2, 137.7, 128.3 (2), 128.2, 128.1, 128.1, 127.9, 127.6, 127.5, 127.5, 119.3, 95.5, 95.2, 73.7, 73.3, 71.1, 69.7, 69.6, 68.7, 64.3, 25.7, 18.2.

HRMS (ESI-TOF) *m/z*: $[M+NH_4]^+$ calcd for $C_{32}H_{36}O_5NH_4$ 518.2906, found 518.2901.

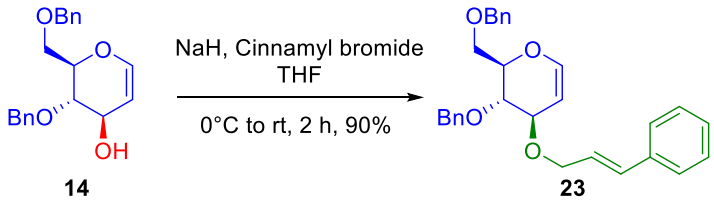


(2*S*,3*S*,5*R*,6*R*)-2,5-bis(benzyloxy)-6-((benzyloxy)methyl)-3-(2-methylbut-3-en-2-yl)tetrahydro-4*H*-pyran-4-one (22a:22b): Compound (**22a:22b)** was synthesised from **21** (200 mg, 0.399 mmol) by following general **procedure C.** Yield: 175.9 mg, 88%, colureless gel . R_f: 0.5. (10% EtOAc/hexane).

^{1}H NMR (500 MHz, $CDCl_3$): mixture δ 7.30-7.35 (m, 15H), 5.90-5.97 (m, 1H) 4.89-4.94 (m, 2H), 4.84 (d, 1H, *J* = 11.0 Hz), 4.69 (d, 1H, *J* = 12.5 Hz), 4.63-4.66 (m, 2H), 4.51 (d, 1H, *J* = 2.5 Hz), 4.24 (d, 1H, *J* = 10.0 Hz), 4.09-4.14 (m, 1H), 3.73-3.78 (m, 2H), 3.67-3.71 (m, 1H), 1.20 (d, 2H, *J* = 17.0 Hz), 1.70 (s, 3H), 1.09 (s, 3H).

^{13}C NMR (125 MHz, $CDCl_3$) Mixture: δ 206.3, 203.9, 146.7, 145.3, 138.2, 137.9, 137.5, 137.3, 137.1, 136.4, 128.5, 128.4, 128.3, 128.3, 128.3, 128.0, 127.9, 127.9, 127.8, 127.8, 127.7, 127.6, 127.5, 127.4, 112.5, 111.1, 100.1, 99.0, 79.5, 78.5, 73.6, 73.5, 73.4, 73.3, 73.2, 72.2, 69.2, 69.0, 68.8, 68.5, 65.9, 61.3, 37.8, 37.0, 27.7, 26.4, 24.6, 23.7

HRMS (ESI-TOF) *m/z*: $[M+NH_4]^+$ calcd for $C_{32}H_{36}O_5NH_4$ 518.2906, found 518.2950.



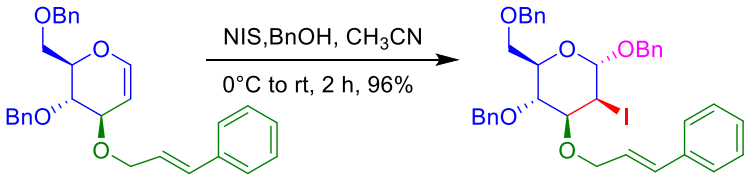
(2*R*,3*S*,4*R*)-3-(benzyloxy)-2-((benzyloxy)methyl)-4-(cinnamyloxy)-3,4-dihydro-2*H*-pyran (23): Compound **14** was synthesised from **23** (400 mg, 1.22 mmol) by following general **procedure D.** Yield: 488.1 mg, 90%, colureless gel. R_f: 0.6 (10% EtOAc/hexane).

IR (neat): 3025, 2968, 2924,1738 cm^{-1}

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.27-7.39 (m, 15H), 6.63 (d, 1H, *J* = 15.5 Hz), 6.46 (d, 1H, *J* = 6.0 Hz), 6.27-6.33 (m, 1H), 4.88-4.91 (m, 2H), 4.67-4.76 (m, 1H), 4.62 (q, 2H, *J* = 12.0 Hz), 4.28-4.32 (m, 1H), 4.20-4.24 (m, 2H), 4.08-4.12 (m, 1H), 3.86-3.89 (m, 1H), 3.83-3.85 (m, 1H), 3.80-3.83 (m, 1H).

^{13}C NMR (125 MHz, $CDCl_3$): δ 144.7, 138.2, 137.9, 136.6, 132.2, 128.5, 128.4, 128.3, 127.9, 127.7, 127.7, 127.6, 127.6, 126.4, 126.1,100.1, 76.7, 75.7, 74.4, 73.8,73.5, 69.1 ,68.5

HRMS (ESI-TOF) *m/z*: $[M+Na]^+$ calcd for $C_{29}H_{30}O_4Na$ 465.2036, found 465.2035.



23 **24**

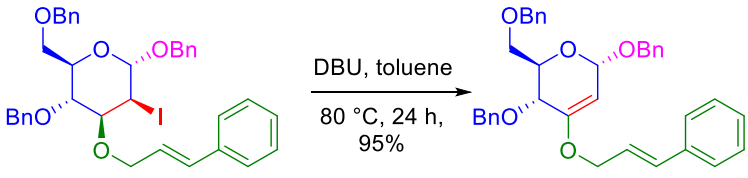
(2*S*,3*S*,4*S*,5*R*,6*R*)-2,5-bis(benzyloxy)-6-((benzyloxy)methyl)-4-(cinnamyloxy)-3-iodotetrahydro-2*H*-pyran (24): Compound **24** was synthesised from **23** (400 mg, 0.90 mmol) by following general **procedure A.** Yield: 587.1 mg, 96%, colureless gel . R_f: 0.7 (10% EtOAc/hexane).

IR (neat): 3026, 2922, 1738 ,1449 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.27-744 (m, 20H), 6.69 (d, 1H, *J* = 16.0 Hz), 6.33-6.38 (m, 1H), 5.36 (s, 1H), 4.95 (d, 1H, *J* = 11.0 Hz), 4.70 (d, 1H, *J* = 12.5 Hz), 4.73 (d, 1H, *J* = 11.5 Hz), 5.46-4.61 (m, 3H), 4.52 (d, 1H, *J* = 12.0 Hz), 4.35-4.38 (m, 1H), 4.21-4.25 (m, 1H), 3.97 (d, 2H, *J* = 5.0 Hz), 3.83-3.86 (m, 1H), 3.75 (d, 1H, *J* = 10.5 Hz), 1.64 (s, 1H).

^{13}C NMR (125 MHz, $CDCl_3$): δ 138.3, 138.2, 136.8, 136.5, 132.8, 128.5 , 128.4(2), 128.3, 128.3, 128.0, 128.0, 127.9, 127.7, 127.6, 127.5, 126.5, 125.5, 100.7, 76.7, 75.2, 73.4, 72.4, 69.8, 69.4(2), 68.8, 33.9.

HRMS (ESI-TOF) *m/z*: $[M+Na]^+$ calcd for $C_{36}H_{37}IO_5Na$ 699.1578, found 699.1578



24 **25**

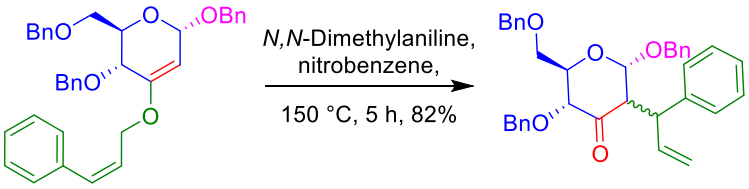
(2*R*,3*R*,6*S*)-3,6-bis(benzyloxy)-2-((benzyloxy)methyl)-4-(cinnamyloxy)-3,6-dihydro-2*H*-pyran (25): Compound **25** was synthesised from **24** (400 mg, 0.59 mmol) by following general procedure B. Yield: 308.1 mg, 95%, colureless gel . R_f: 0.6 (10% EtOAc/hexane).

IR (neat): 3025, 2968, 2925, 1737 ,1599 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.27-7.38 (m, 20H), 6.69 (d, 1H, *J* = 16.0 Hz), 6.32-6.38 (m, 1H), 5.33 (d, 1H, *J* = 3.5 Hz), 4.92 (d, 1H, *J* = 11.5 Hz), 4.88 (d, 1H, *J* = 3.5 Hz), 4.80 (d, 1H, *J* = 11.5 Hz), 4.65 (d, 1H, *J* = 12.5 Hz), 4.61 (d, 1H, *J* = 11.5 Hz), 4.49-4.54 (m, 3H), 4.20-4.45 (m, 1H), 4.30 (d, 1H, *J* = 9.5 Hz), 4.19-4.22 (m, 1H), 3.72 (dd, 1H, J_1 = 4.0 Hz, J_2 = 10.5 Hz), 3.62 (dd, 1H, J_1 = 2.0 Hz, J_2 = 10.5 Hz),

^{13}C NMR (125 MHz, $CDCl_3$): δ 157.8, 138.4, 138.3, 138.2, 136.4, 133.0, 128.6, 128.3, 128.2, 128.1, 128.0, 127.9, 127.9, 127.6, 127.6, 127.5, 126.5, 123.9, 95.9, 95.4, 74.0, 73.4, 71.3, 69.8, 68.8, 68.0

HRMS (ESI-TOF) *m/z*: $[M+Na]^+$ calcd for $C_{36}H_{36}O_5Na$ 571.2455, found 571.2454



25 **26a:26b = 1:1**

(2*S*,5*R*,6*R*)-2,5-bis(benzyloxy)-6-((benzyloxy)methyl)-3-(1-phenylallyl)tetrahydro-4*H*-pyran-4-one (26a:26b): Compound (**26a:26b**) was synthesised from **25** (245.9 mg, 0.54 mmol) by following general **procedure C.** Yield: 245.9 mg, 82%, colureless gel . R_f: 0.6. (10% EtOAc/hexane).

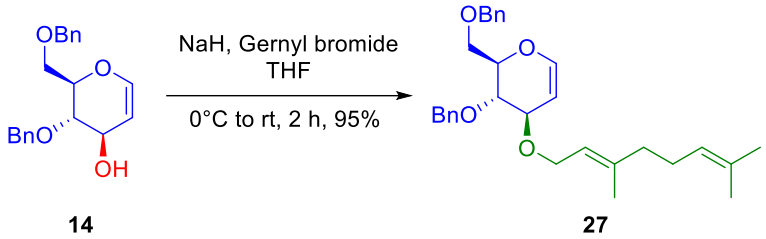
IR (neat): 3026, 2968, 2922, 1736 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.19-7.37 (m, 20H), 5.88-5.97 (m, 2H), 5.03-5.50 (m, 1H), 4.88 (d, 1H, *J* = 14.0 Hz), 4.76 (s, 1H), 4.70 (d, 1H, *J* = 15.0 Hz), 4.60 (d, 1H, *J* = 15.0 Hz), 4.55 (d, 1H, *J* = 15.0 Hz), 4.43 (d, 1H, *J* = 14.0 Hz), 4.33-4.38 (m, 2H), 4.08-4.11 (m, 1H), 3.83 (dd, 1H, J_1 = 4.5 Hz, J_2 = 13.5 Hz), 3.72-3.77 (m, 2H), 3.11 (d, 1H, *J* = 14.5 Hz).

^{13}C NMR (125 MHz, $CDCl_3$): δ 205.6, 140.6, 138.3, 138.1, 137.4, 136.9, 129.0, 128.4, 128.4, 128.4, 128.3, 128.0, 127.6(2), 127.5(3), 127.2, 116.2, 99.9, 77.4, 73.6, 73.4, 73.1, 69.3, 68.8, 61.9, 50.6 .

HRMS (ESI-TOF) *m/z*: $[M+Na]^+$ calcd for $C_{36}H_{36}O_5Na$ 571.2455, found 571.2454

.



14 27

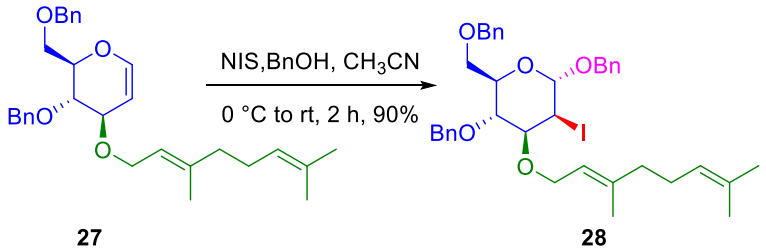
(2*R*,3*S*,4*R*)-3-(benzyloxy)-2-((benzyloxy)methyl)-4-(((E)-3,7-dimethylocta-2,6-dien-1-yl)oxy)-3,4-dihydro-2*H*-pyran (27): Compound **27** was synthesised from **14** (500 mg, 1.53 mmol) by following general **procedure D.** Yield: 673.24 mg, 95%, colorless gel. R_f: 0.6 (10% EtOAc/hexane).

IR (neat): 2968,2932, 1738 ,1647 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.32-7.39 (m, 10H), 6.46 (dd, 1H, J_1 = 1.0 Hz, J_2 = 6.0 Hz), 5.39-5.42 (m, 1H), 5.13-5.16 (m, 1H), 4.91-4.92 (m, 1H), 4.90 (d, 1H, J = 2.5 Hz), 4.70 (d, 1H, J = 11.5 Hz), 4.65 (d, 1H, J = 12.5 Hz), 4.16-4.20 (m, 2H), 4.07-4.12 (m, 2H), 3.82-3.87 (m, 3H), 2.12-2.18 (m, 2H), 2.07-2.10 (m, 2H), 1.73 (d, 3H, J = 1.0 Hz), 1.70 (s, 3H), 1.65 (s, 3H).

^{13}C NMR (125 MHz, $CDCl_3$): δ 144.5, 140.1, 138.4, 138.1, 131.7, 128.4, 128.4, 127.9, 127.8, 127.7, 127.7, 124.0, 121.0, 100.5, 76.8, 75.6 , 74.4, 73.7, 73.5, 68.7, 65.1, 39.6, 26.4, 25.8, 17.8, 16.6.

HRMS (ESI-TOF) *m/z*: $[M+H]^+$ calcd for $C_{28}H_{30}O_5H$ 463.2843, found 463.2844.



27 28

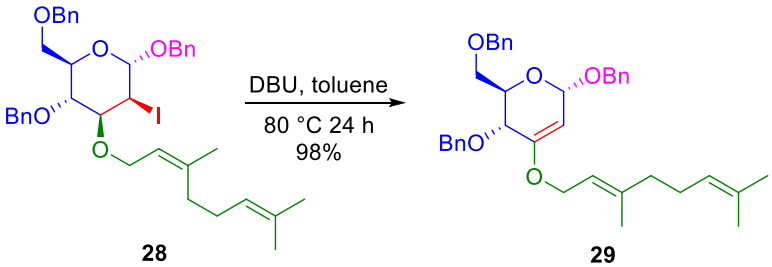
(2*S*,3*S*,4*S*,5*R*,6*R*)-2,5-bis(benzyloxy)-6-((benzyloxy)methyl)-4-(((E)-3,7-dimethylocta-2,6-dien-1-yl)oxy)-3-iodotetrahydro-2*H*-pyran(28): Compound **28** was synthesised from **27** (500 mg, 1.08 mmol) by following general **procedure A.** Yield: 677.7 mg, 90%, colureless gel . R_f: 0.6 (10% EtOAc/hexane).

IR (neat): 3025, 2968, 1738 ,1451 cm−1.

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.21-7.7.41 (m, 15H), 5.44 (t, 1H, *J* = 6.5 Hz), 5.34 (s, 1H), 5.11 (t, 1H, *J* = 6.5 Hz), 4.92 (d, 1H, *J* = 10.5 Hz), 4.70-4.76 (m, 1H), 4.56 (d, 2H, *J* = 12.0 Hz), 4.49-4.52 (m, 2H), 4.19-4.23 (m, 1H), 3.99-4.03 (m, 1H), 3.92-3.95 (m, 1H), 3.86-3.90 (m, 1H), 3.81 (dd, 1H, J_1 = 4.5 Hz, J_2 = 10.5 Hz) 3.71-3.73 (m, 1H), 3.25-3.27 (m, 1H), 2.09-2.12 (m, 2H), 2.04-2.07 (m, 2H), 1.69 (s, 6H), 1.61 (s, 2H), 1.59 (s, 1H)

^{13}C NMR (125 MHz, $CDCl_3$): δ 140.8, 138.5, 137.0, 131.7, 128.5, 128.3, 128.3(2), 128.1, 128.0, 128.0, 127.6(2), 127.5, 123.9, 120.4, 100.8, 76.6, 75.9, 75.2, 73.4, 72.5, 69.5, 69.0, 65.5, 39.6, 34.2, 26.4,25.7, 17.7, 16.6

HRMS (ESI-TOF) *m/z*: $[M+NH_4]^+$ calcd for $C_{37}H_{45}IO_5H$ 714.2655, found 714.2650.



28 **29**

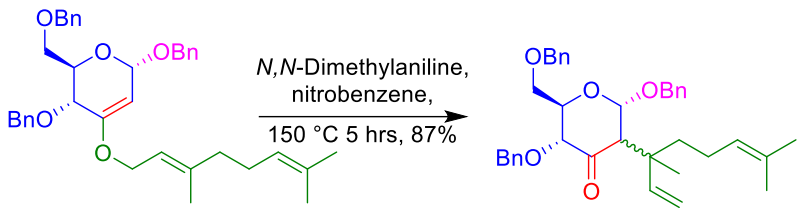
(2*R*,3*R*,6*S*)-3,6-bis(benzyloxy)-2-((benzyloxy)methyl)-4-(((E)-3,7-dimethylocta-2,6-dien-1-yl)oxy)-3,6-dihydro-2*H*-pyran(29): Compound **29**was synthesised from **28** (500 mg, 0.71 mmol) by following general procedure B. Yield: 399.9 mg, 98%, colureless gel . R_f: 0.6 (10% EtOAc/hexane).

IR (neat): 3026, 2968, 1738, 1661 cm−1.

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.23-7.35 (m, 15H), 5.40-5.43 (m, 1H), 5.29 (d, 1H, *J* = 4.0 Hz), 5.07-5.10 (m, 1H), 4.86 (d, 1H, *J* = 10.5 Hz), 4.78-4.79 (m, 1H), 4.75 (s, 1H), 4.61 (d, 1H, *J* = 12.5 Hz), 4.57 (d, 1H, *J* = 12.0 Hz), 4.43 (d, 1H, *J* = 11.0 Hz), 4.30-4.33 (m, 1H), 4.24-4.26 (m, 1H), 4.22 (d, 1H, *J* = 9.5 Hz), 4.14-4.17 (m, 1H), 3.67 (dd, 1H, J_1 = 4.0 Hz, *J* = 10.5 Hz), 2.08-2.11 (m, 2H), 2.03-2.06 (m, 2H), 1.03 (s, 6H), 1.59 (s, 3H),

^{13}C NMR (125 MHz, $CDCl_3$): δ 158.0, 141.0, 138.5, 138.3, 138.2, 131.8 , 128.4, 128.2 128.2, 128.1, 127.9, 127.6, 127.6, 127.6, 123.8, 119.1, 95.5, 95.3, 77.3, 73.8, 73.4, 71.1, 69.8, 69.7, 68.8, 64.3, 39.5, 26.4, 25.7, 17.7, 16.6

HRMS (ESI-TOF) *m/z*: $[M+NH_4]$ calcd for $C_{37}H_{44}O_5NH_4$ 586.3532, found 586.3509.



29 **30a : 30b 1 : 1**

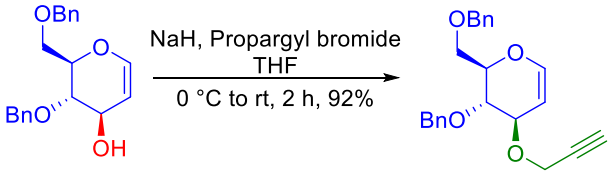
(2*S*,5*R*,6*R*)-2,5-bis(benzyloxy)-6-((benzyloxy)methyl)-3-(3,7-dimethylocta-1,6-dien-3-yl)tetrahydro-4*H*-pyran-4-one(30a:30b,1:1): Compound (30a,30b,1:1) was synthesised from **29** (250 mg, 0.43 mmol) by following general **procedure C.** Yield: 217.4 mg, 87%, colureless gel . *R*$_f$: 0.5. (10% EtOAc/hexane).

IR (neat): 2923 ,1955, 1736 cm−1.

^{1}H NMR (500 MHz, CDCl$_3$): Mixture: δ 7.29-7.36 (m, 15H), 5.85-5.92 (m, 1H), 5.22 (d, 1H, *J* = 13.0 Hz), 5.04-5.07 (m, 2H), 4.88-4.93 (m, 1H), 4.83-4.87 (m, 1H), 4.83-493 (m, 2H), 4.64-4.71 (m, 2H), 4.53 (d, 1H, *J* = 3.5 Hz), 4.50 (d, 1H, *J* = 4.0 Hz), 4.42 (d, 1H, *J* = 14.0 Hz), 4.18 (d, 1H, *J* = 12.5 Hz), 4.07-4.12 (m, 1H), 3.75-3.79 (m, 1H), 3.70-3.73 (m, 1H), 2.75 (s, 1H), 1.93-12.03 (m, 1H), 1.82-1.93 (m, 1H), 1.63-1.70 (m, 4H), 1.59 (d, 3H, *J* = 11.5 Hz), 1,14 (s, 2H).

^{13}C NMR (125 MHz, CDCl$_3$): δ 158.0, 141.0, 138.5, 138.3, 138.2, 131.8 , 128.4, 128.2 128.2, 128.1, 127.9, 127.6, 127.6, 127.6, 123.8, 119.1, 95.5, 95.3, 77.3, 73.8, 73.4, 71.1, 69.8, 69.7, 68.8, 64.3, 39.5, 26.4, 25.7, 17.7, 16.6

HRMS (ESI-TOF) *m/z*: [M+H] calcd for $C_{37}H_{44}O_5H$ 569.3262, found 569.3267.



14 **31**

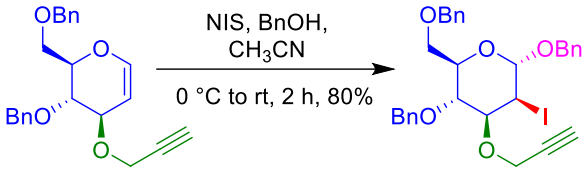
(2*R*,3*S*,4*R*)-3-(benzyloxy)-2-((benzyloxy)methyl)-4-(prop-2-yn-1-yloxy)-3,4-dihydro-2*H*-pyran(31): Compound **31** was synthesised from **14** (400 mg, 1.22 mmol) by following general **procedure D.** Yield: 410.8 mg, 92%, colureless gel . R$_f$: 0.5 (10% EtOAc/hexane).

IR (neat): 3288, 2863, 1647,1495 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.31-7.38 (m, 10H), 6.46 (dd, 1H, *J* = 1.5 Hz, *J* = 7.5 Hz), 4.90-4.91 (m, 1H), 4.88 (d, 1H, *J* = 5.0 Hz), 4.67-4.70 (m, 1H), 4.62 (s, 1H), 4.61 (s, 1H), 4.33-4.36 (m, 1H), 4.25-4.26 (m, 2H), 4.08-4.13 (m, 1H), 3.85-3.87 (m, 1H), 3.83 (d, 1H, *J* = 7.0 Hz), 3.81 (d, 1H, *J* = 4.0), 2.46 (t, 1H, *J* = 5.0).

^{13}C NMR (125 MHz, $CDCl_3$): δ 145.1, 138.2, 138.0, 128.4(2), 128.0, 127.8, 127.8, 127.7, 99.4, 80.0, 76.8, 75.4, 74.5, 74.2, 73.7, 73.5, 68.5, 55.9

HRMS (ESI-TOF) *m/z*: $[M+NH_4]^+$ calcd for $C_{23}H_{24}O_4NH_4$ 382.2013, found 382.2013



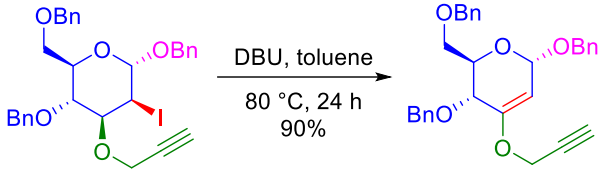
31 **32**

(2*S*,3*S*,4*S*,5*R*,6*R*)-2,5-bis(benzyloxy)-6-((benzyloxy)methyl)-3-iodo-4-(prop-2-yn-1-yloxy)tetrahydro-2*H*-pyran(32): Compound **32** was synthesised from **31** (300 mg, 0.82 mmol) by following general **procedure A.** Yield: 394.19 mg, 80%, colureless gel . R_f: 0.6 (10% EtOAc/hexane).

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.27-7.41 (m, 15H), 5.32-5.33 (m, 1H), 5.39 (d, 1H, *J* = 11.0 Hz), 7.14 (d, 1H, *J* = 12.0 Hz), 4.72 (d, 1H, *J* = 12.0 Hz), 4.56-4.60 (m, 2H), 4.50-4.54 (m, 2H), 4.36 (dd, 1H, J_1 = 2.0 Hz, *J* = 15.5), 4.27 (dd, 1H, *J* = 2.5, *J* = 16.0 Hz), 3.91-3.94 (m, 2H), 3.80-3.83 (m, 1H), 3.70- 3.73 (m, 1H), 3.48-3.51 (m, 1H), 2.48 (t, 1H, *J* = 2.5 Hz).

^{13}C NMR (125 MHz, $CDCl_3$): δ 138.4, 138.2, 136.9, 128.5, 128.4, 128.3, 128.2, 128.1, 128.0, 127.8, 127.7, 127.5, 100.7, 79.3, 76.7, 76.0, 75.3, 75.1, 73.4, 72.4, 69.5, 68.8, 56.8, 33.1

HRMS (ESI-TOF) *m/z*: $[M+Na]^+$ calcd for $C_{30}H_{31}IO_5Na$ 621.1108, found 621.1107.



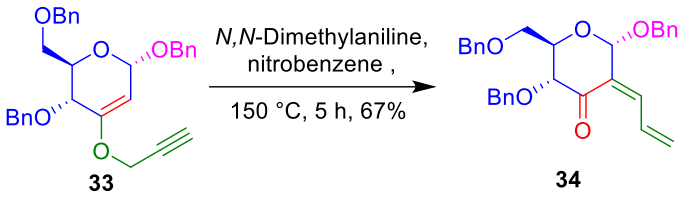
32 **33**

(2*R*,3*R*,6*S*)-3,6-bis(benzyloxy)-2-((benzyloxy)methyl)-4-(prop-2-yn-1-yloxy)-3,6-dihydro-2H-pyran (33): Compound **33** was synthesised from **32** (300 mg, 0.50 mmol) by following general procedure **B**. Yield: 212.2 mg, 90%, colureless gel . R_f: 0.5 (10% EtOAc/hexane).

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.28-7.37 (m, 15H), 5.32-5.34 (m, 1H,), 4.88-4.93 (m, 2H,), 4.79 (d, 1H, *J* = 12.0 Hz), 4.59-4.65 (m, 2H), 4.54 (dd, 1H, *J* = 24 Hz, *J* = 50.5), 4.45-4.51 (m, 3H), 4,28 (d, 1H, *J* = 9.0 Hz), 4.16-4.21 (m, 1H), 3.70 (dd, 1H, J_1 = 4.0 Hz, J_2 = 10.5 hz), 3.61 (dd, 1H, J_1 = 2.0 Hz, J_2 = 10.5 Hz), 2.54 (s, 1H, 2.5).

^{13}C NMR (125 MHz, $CDCl_3$): δ 156.9, 138.3, 138.1(2), 128.4(3), 128.3, 128.2, 128.1, 127.9, 127.7, 127.6, 96.7, 95.1, 77.9, 75.7, 74.1, 73.4, 71.0, 69.9, 69.7, 68.6, 55.2

HRMS (ESI-TOF) *m/z*: $[M+Na]^+$ calcd for $C_{30}H_{30}O_5Na$ 493.1985, found 493.1986.



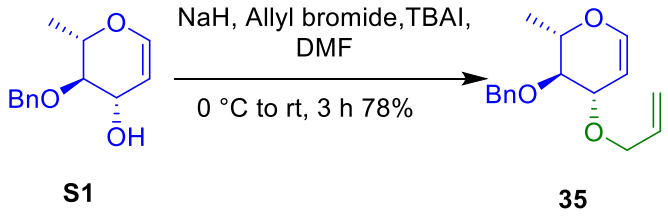
(2*S*,5*R*,6*R*,*Z*)-3-allylidene-2,5-bis(benzyloxy)-6-((benzyloxy)methyl)tetrahydro-4*H*-pyran-4-one (34): Compound **34** was synthesised from **33** (200 mg, 0.42 mmol) by following general **procedure C.** Yield: 133.9 mg, 67%, colureless gel . R_f: 0.5. (10% EtOAc/hexane).

IR (neat): 2921, 2853 ,2230, 1729 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.31-7.36 (m, 15H), 7.17 (d, 1H, *J* = 15.0 Hz), 6.30-6.39 (m, 1H), 5.77 (t, 2H, *J* = 11.5 Hz), 5.65 (d, 1H, *J* = 12.5 Hz), 5.10 (d, 1H, *J* = 13.5 Hz), 4.81 (d, 1H, *J* = 15.0 Hz), 4.63-4.69 (m, 2H), 4.53-4.4.62 (m, 2H), 4.35-4.39 (m, 1H), 4.12 (d, 1H, *J* = 13.0 Hz), 3.76 (dd, 1H, J_1 = 5.0 Hz, J_2 = 13.0), 3.68 (dd, 1H, J_1 = 2.5 Hz, J_2 = 13.5),

^{13}C NMR (100 MHz, $CDCl_3$): δ 197.1, 139.4(2), 137.9, 137.7, 137.0, 132.1, 130.6, 129.7, 128.4, 128.4, 128.4, 128.3, 128.3, 128.0, 127.8, 127.7, 95.2, 77.2, 74.7, 73.5, 69.3, 69.1, 68.7

HRMS (ESI-TOF) *m/z*: $[M+Na]^+$ calcd for $C_{30}H_{30}O_5Na$ 493.1985, found 493.1985.

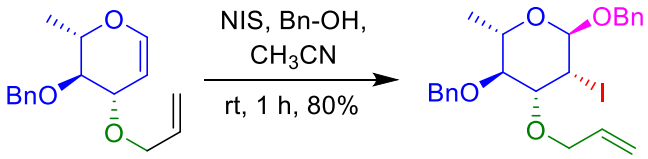


(2*S*,3*S*,4*S*)-4-(allyloxy)-3-(benzyloxy)-2-methyl-3,4-dihydro-2*H*-pyran(35): Compound **35** was synthesised from **S1** (500 mg, 2.27 mmol) by following general **procedure D.** Yield: 460.9 mg, 78%, colureless gel . R_f: 0.7 (10% EtOAc/hexane).

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.29-7.37 (m, 5H), 6.34 (dd, 1H, J_1 = 1.0 Hz, J_2 = 6.0 Hz), 5.90-5.98 (m, 1H), 5.28-5.33 (m, 1H), 5.17-5.19 (m, 1H), 4.88 (d, 1H, J = 11.5 Hz), 4.82 (dd, 1H, J_1 = 2.5 Hz, J_2 = 6.0 Hz), 4.70 (d, 1H, J = 11.5 Hz), 4.12-4.15 (m, 2H), 4.02-4.06 (m, 1H), 3.91-3.96 (m, 1H), 3.41-3.44 (m, 1H), 1.37 (d, 3H, J = 6.0 Hz).

^{13}C NMR (125 MHz, $CDCl_3$): δ 144.7, 138.3 , 135.0, 128.4, 128.0, 127.8, 116.8, 100.3, 79.5, 76.5, 74.1, 74.0, 69.5, 17.5

HRMS (ESI-TOF) *m/z*: [M+H] calcd for $C_{16}H_{20}O_3H$ 261.1491, found 261.1493.



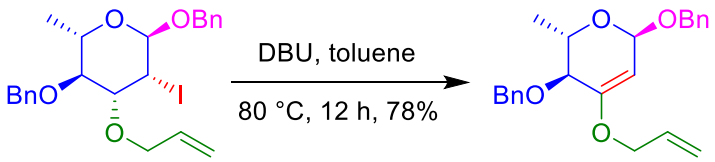
35 **36**

(2*R*,3*R*,4*R*,5*S*,6*S*)-4-(allyloxy)-2,5-bis(benzyloxy)-3-iodo-6-methyltetrahydro-2*H*-pyran(36): Compound **36** was synthesised from **35** (400 mg, 1.15 mmol) by following general **procedure A.** Yield: 607.7 mg, 80%, colureless gel . R_f: 0.5 (10% EtOAc/hexane).

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.33-7.39 (m, 10H), 5.93-6.00 (m, 1H), 5.33-5.38 (m, 1H), 5.21 (s, 2H), 4.94 (d, 1H, J = 11.0 Hz), 4.66 (d, 1H, J = 12.0 Hz), 4.63 (d, 1H, J = 10.5 Hz), 4.52 (dd, 1H, J = 1.0 Hz, J = 4.0 Hz), 4.46 (d, 1H, J = 11.5 Hz), 4.13-4.17 (m, 1H), 4.00-4.03 (m, 1H), 3.83-3.89 (m, 1H), 3.47 (t, 1H, J = 9.0 Hz), 3.18-3.20 (m, 1H), 1.32 (d, 3H, J = 6.0 Hz).

^{13}C NMR (125 MHz, $CDCl_3$): δ 138.3, 137.0 , 134.3, 128.6, 128.5, 128.4(2), 128.3, 128.1(2), 128.0, 128.0, 127.8, 117.3, 100.7, 81.7, 76.6, 75.5, 70.0, 69.4, 68.5, 34.5, 18.0

HRMS (ESI-TOF) *m/z*: [M+Na] calcd for $C_{23}H_{27}IO_4Na$ 5170852, found 5170856.



36 **37**

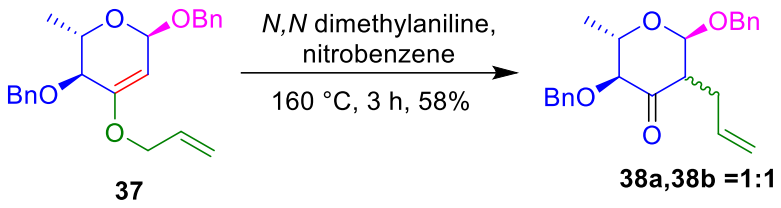
(2*S*,3*S*,6*R*)-4-(allyloxy)-3,6-bis(benzyloxy)-2-methyl-3,6-dihydro-2*H*-pyran(37): Compound **37** was synthesised from **36** (300 mg, 0.60 mmol) by following general **procedure B.** Yield: 173.4 mg, 78%, colureless gel . R_f: 0.4 (10% EtOAc/hexane).

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.32-7.36 (m, 10H), 5.96-6.03 (m, 1H), 5.36 (dd, 1H, J_1 = 1.5 Hz, J_2 = 17.5), 5.25 (dd, 1H, J_1 = 1.0 Hz, J_2 = 10.5 Hz), 5.20 (d, 1H, J = 3.5 Hz), 4.93 (d, 1H, J =

11.0 Hz), 4.78 (d, 1H, *J* = 3.0 Hz), 4.74 (d, 1H, *J* = 12.0 Hz), 4.56-4.61 (m, 2H), 4.32-4.35 (m, 1H), 4.24-4.28 (m, 1H), 4.12-4.16 (m, 1H), 3.77 (d, 1H, *J* = 9.0 Hz), 1.24 (d, 3H, *J* = 6.5 Hz),

^{13}C NMR (125 MHz, $CDCl_3$): δ 157.7, 138.4, 138.3, 132.7, 128.5, 128.3, 128.2, 128.1, 127.9, 127.6, 127.5, 117.5, 95.8, 95.2, 73.8, 69.6, 68.1, 66.1, 18.2

HRMS (ESI-TOF) *m/z*: [M+NH_4] calcd for $C_{23}H_{26}O_4NH_4$ 384.2174, found 384.2175.

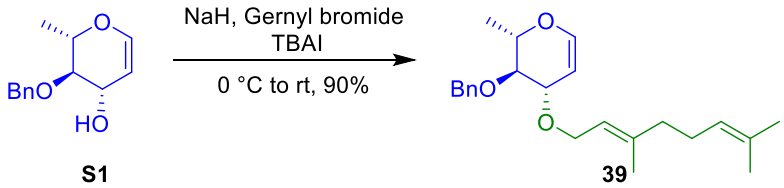


(2*R*,5*S*,6*S*)-3-allyl-2,5-bis(benzyloxy)-6-methyltetrahydro-4*H*-pyran-4-one(29a,29b): Compound (**38a,38b)** was synthesised from **37** (100 mg, 0.27 mmol) by following general **procedure C.** Yield: 57.9 mg, 58%, colureless gel . R_f: 0.4 (10% EtOAc/hexane).

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.29-7.40 (m, 10H), 5.66-5.77 (m, 1H), 5.06-5.09 (m, 1H), 5.036 (d, 1H, *J* = 6.5 Hz), 4.94-5.00 (m, 2H), 4.874.90-4.92 (m, 1H, *J* = 11.0), .65-4.69 (m, 1H, *J* = 11.5), 4.6.43-4.505 (m, 2H), 3.66-3.67 (m, 1H), 2.72-2.76 (m, 1H), 2.55-2.61 (m, 1H), 2.17-2.23 (m, 1H), 1.24 (d, 3H, *J* = 6.5 Hz).

^{13}C NMR (125 MHz, $CDCl_3$): δ 206.3, 204.0, 137.6, 137.0, 135.2, 128.4(2), 128.4, 128.3, 128.0, 116.9, 99.8, 84.6, 73.1, 70.2, 69.2, 53.7, 28.2, 19.0

HRMS (ESI-TOF) *m/z*: [M+NH_4] calcd for $C_{23}H_{26}O_4NH_4$ 384.2174, found 384.2172

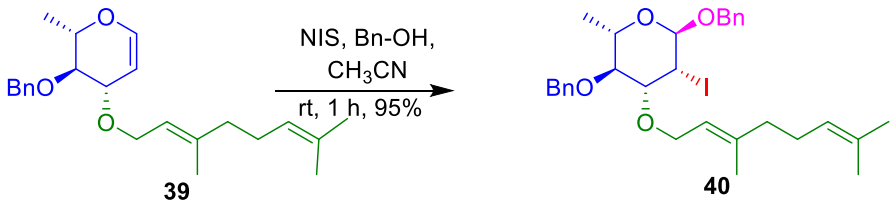


(2*S*,3*S*,4*S*)-3-(benzyloxy)-4-(((E)-3,7-dimethylocta-2,6-dien-1-yl)oxy)-2-methyl-3,4-dihydro-2*H*-pyran(39): Compound **39** was synthesised from **S1** 500 mg, 2.27 mmol) by following general **procedure D.** Yield: 728.32 mg, 90%, colureless gel . R_f: 0.6 (10% EtOAc/hexane).

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.31-7.40 (m, 5H), 4.87 (d, 1H, *J* = 5.5 Hz), 5.39-5.42 (m, 1H), 5.11-5.12 (m, 1H), 4.91-4.94 (m, 1H), 4.85-4.88 (m, 1H), 4.72-4.75 (m, 1H), 4.13-4.20 (m, 2H), 4.0-4.10 (m, 1H), 3.93-3.98 (m, 1H), 3.42-3.46 (m, 1H), 2.11-2.16 (m, 2H), 2.07-2.08 (m, 2H), 1.70 (s, 6H), 1.63 (s, 3H), 1.38-1.40 (m, 3H).

^{13}C NMR (125 MHz, $CDCl_3$): δ 144.5, 140.0, 138.4, 131.6, 128.3, 127.9, 127.6, 123.9, 121.0, 100.6, 79.5, 76.2, 73.9(2), 65.0, 39.6, 26.3, 25.6, 17.7, 17.5, 16.5

HRMS (ESI-TOF) *m/z*: [M+Na] calcd for $C_{23}H_{32}O_3Na$ 379.2249, found 379.2252



39 40

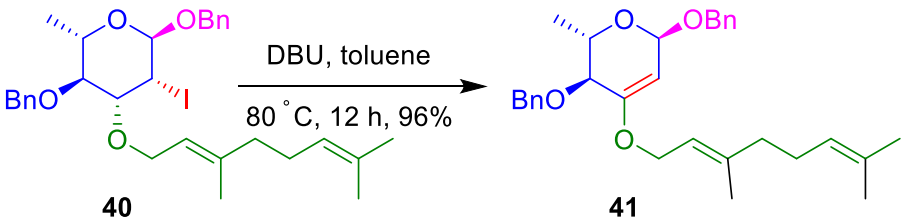
(2*R*,3*R*,4*R*,5*S*,6*S*)-2,5-bis(benzyloxy)-4-(((E)-3,7-dimethylocta-2,6-dien-1-yl)oxy)-3-iodo-6-methyltetrahydro-2*H*-pyran(40): Compound **40** was synthesised from39 (400 mg, 1.12 mmol) by following general **procedure A.** Yield: 627.7 mg, 95%, colureless gel . R_f: 0.7 (10% EtOAc/hexane).

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.30-7.36 (m, 10H), 5.42-5.45 (m, 1H), 5.22 (s, 1H), 5.09-5.11 (m, 1H), 4.97 (d, 1H, *J* = 11.0 Hz), 4.66-4.69 (m, 1H), 4.63 (d, 1H, *J* = 11.0 Hz), 4.56 (dd, 1H, J_1 = 1.5 Hz, J_2 = 4.0 Hz), 4.47 (d, 1H, *J* = 12.0 Hz), 4.19 (dd, 1H, J_1 = 7.0 Hz, J_2 = 11.5 Hz), 3.97-4.01 (m, 1H), 3.84-3.88 (m, 1H), 3.45 (t, 1H, *J* = 9.0 Hz), 3.17-3.19 (m, 1H), 2.08-2.13 (m, 2H), 2.03-2.06 (m, 2H), 1.68 (s, 6H), 1.60 (s, 3H), 1.33 (d, 3H, *J* = 6.5 Hz),

^{13}C NMR (125 MHz, $CDCl_3$): δ 140.6, 138.5, 137.0, 131.6 , 128.4, 128.3, 128.0, 127.9, 127.9, 127.6, 123.9, 120.4, 100.7, 81.6, 76.4, 75.4, 69.4, 68.5, 65.4, 39.6, 35.0, 26.3, 25.6, 18.0, 17.7, 16.6

HRMS (ESI-TOF) *m/z*: [M+Na] calcd for $C_{30}H_{39}IO_4Na$ 613.1791, found 613.1790

.



40 41

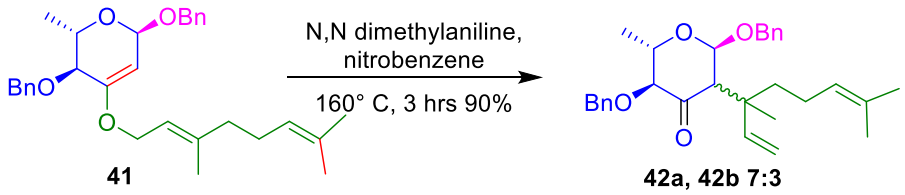
(2*S*,3*S*,6*R*)-3,6-bis(benzyloxy)-4-(((E)-3,7-dimethylocta-2,6-dien-1-yl)oxy)-2-methyl-3,6-dihydro-2*H*-pyran(41): Compound 41 was synthesised from 31 450 mg, 0.76 mmol) by

following general procedure B. Yield: 328.1 mg, 96%, colureless gel . R_f: 0.6 (10%EtOAc/hexane).

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.28-7.36 (m, 10H), 5.41-5.44 (m, 1H), 5.20 (d, 1H, *J* = 3.5 Hz), 5.08-5.11 (m, 1H), 4.88 (d, 1H, *J* = 11.0 Hz), 4.78 (d, 1H, *J* = 3.0 Hz), 4.74 (d, 1H, *J* = 12.0 Hz), 4.58 (d, 1H, *J* = 3.5 Hz), 4.56 (d, 1H, *J* = 4.5 Hz), 4.30-4.34 (m, 1H), 4.25 (dd, 1H, J_1 = 6.5, J_2 = 11.5 Hz), 4.10-4.16 (m, 1H), 3.75 (d, 1H, *J* = 9.0 Hz), 2.09-2.12 (m, 2H), 2.04-2.07 (m, 2H), 1.67 (s, 6H), 1.60 (s, 3H), 1.24 (d, 3H, *J* = 6.0 Hz),

^{13}C NMR (125 MHz, $CDCl_3$): δ 157.9, 140.9, 138.5, 138.4, 131.8, 128.3(2), 128.2(3), 128.0, 127.6, 127.5, 123.8, 119.1, 95.3, 73.5, 69.6, 66.1, 64.3, 39.5, 26.3, 25.7, 18.2, 17.7, 16.6

HRMS (ESI-TOF) *m/z*: [M+Na] calcd for $C_{30}H_{38}O_4Na$ 485.2668, found 485.2666

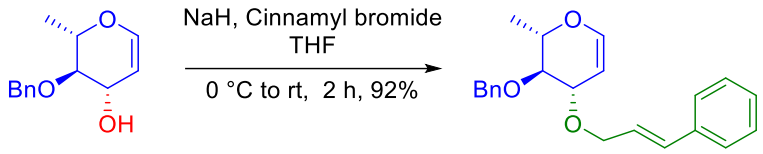


(2*R*,5*S*,6*S*)-2,5-bis(benzyloxy)-3-(3,7-dimethylocta-1,6-dien-3-yl)-6-methyltetrahydro-4*H*-pyran-4-one(42a,42b 7:3) Compound (42a,42b,7:3) was synthesised from 41 (300 mg, 0.64 mmol) by following general **procedure C.** Yield: 269.9 mg, 90%, colureless gel . R_f: 0.6 (10% EtOAc/hexane).

^{1}H NMR (500 MHz, $CDCl_3$): Mixture δ 7.29-7.34 (m, 15H), 5.79-5.85 (m, 1H), 5.40-5.43 (m, 1H), 5.19 (d, 1H, *J* = 3.5 Hz), 5.07-5.10 (m, 1H), 5.05 (s, 1H), 5.01-5.04 (m, 1H), 4.86-4.89 (m, 2H), 4.71-4.77 (m, 2H), 4.30-4.33 (m, 1H), 4.23-4.26 (m, 1H), 4.23-4.26 (m, 1H), 4.63 (d, 1H, *J* = 12.5 Hz), 4.57 (dd, 1H, J_1 = 4.5 Hz, J_2 = 11.0 Hz), 4.44-4.48 (m, 2H), 4.30-4.33 (m, 1H), 4.23-4.26 (m, 1H), 4.11-4.15 (m, 1H), 3.99-4.05 (m, 1H), 3.71-3.76 (m, 1H), 3.62 (d, 1H, *J* = 9.5), 1.66-1.67 (m, 9H), 1.58 (d, 6H, *J* = 11.5 Hz), 1.28 (d, 3H, *J* = 6.5 Hz), 1.23 (d, 3H, *J* = 6.5 Hz).

^{13}C NMR (125 MHz, $CDCl_3$):Inseparable Mixture δ 205.7, 158.0, 144.1, 143.7, 141.0, 138.6, 138.4 , 137.4, 137.2, 134.6, 131.8, 131.7, 129.3, 129.2, 128.6, 128.6, 128.5, 128.4, 128.4, 128.2, 128.0, 127.7, 127.7, 127.6, 127.5, 127.0, 124.1, 123.8, 123.5, 119.1, 113.3, 112.5, 112.4, 98.6, 95.4, 84.0, 73.5, 73.0, 69.6, 68.9, 68.8, 66.1, 65.3, 64.3, 40.5, 39.5, 39.4, 29.7, 26.4, 25.7, 22.5, 21.8, 18.9, 18.2, 17.7, 17.6, 16.6

HRMS (ESI-TOF) *m/z*: [M+NH_4] calcd for $C_{30}H_{38}O_4NH_4$ 480.3114, found 480.3120



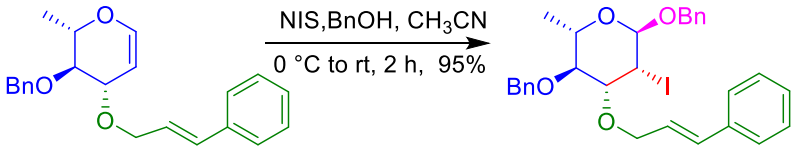
S1 **43**

(2*S*,3*S*,4*S*)-3-(benzyloxy)-4-(cinnamyloxy)-2-methyl-3,4-dihydro-2*H*-pyran(43): Compound **43** was synthesised from **S1** (500 mg, 2.27 mmol) by following general **procedure D.** Yield: 702.5 mg, 92%, colureless gel . R_f: 0.7 (10% EtOAc/hexane).

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.30-7.39 (m, 10H), 6.55 (d, 1H, *J* = 1.0 Hz), 6.37 (dd, 1H, J_1 = 1.0 Hz, J_2 = 6.0 Hz), 6.28-6.33 (m, 1H), 4.92 (d, 1H, *J* = 11.0 Hz), 4.87 (dd, 1H, J_1 = 2.5 Hz, J_2 = 6.0 Hz), 4.75 (d, 1H, *J* = 11.0 Hz), 4.29-4.33 (m, 1H), 4.19-4.29 (m, 2H), 3.93-3.99 (m, 1H), 3.47 (dd, 1H, J_1 = 6.5 Hz, J_2 = 9.0 Hz), 1.40 (d, 3H, *J* = 6.5 Hz).

^{13}C NMR (125 MHz, $CDCl_3$): δ 144.8, 138.3, 136.7, 132.2, 128.5(2), 128.4(2), 127.9, 127.7, 127.6, 126.5(2), 126.2, 100.3, 79.6, 76.4, 74.1, 74.0, 69.2, 17.5

HRMS (ESI-TOF) *m/z*: [M+Na] calcd for $C_{22}H_{24}O_3Na$ 359.1623, found 359.1622



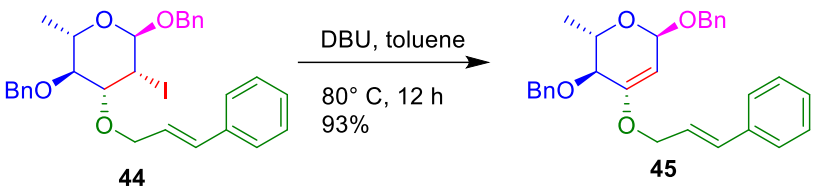
43 **44**

(2*R*,3*R*,4*R*,5*S*,6*S*)-2,5-bis(benzyloxy)-4-(cinnamyloxy)-3-iodo-6-methyltetrahydro-2*H*-pyran(44): Compound **44** was synthesised from **43** (400 mg, 1.18 mmol) by following general **procedure A.** Yield: 644.4 mg, 95%, colureless gel . *R_f:* 0.7 (10% EtOAc/hexane).

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.27-7.38 (m, 15H), 6.67 (d, 1H, *J* = 16.0 Hz), 6.30-6.35 (m, 1H), 5.23 (s, 1H), 5.49 (d, 1H, *J* = 0.01 Hz), 4.68 (d, 1H, *J* = 1.0 Hz), 4.66 (d, 1H, *J* = 2.5 Hz), 4.57-4.58 (m, 1H), 4,47 (d, 1H, *J* = 11.5 Hz), 4.31-4.35 (m, 1H), 4.18-4.22 (m, 1H), 3.86-3.92 (m, 1H), 3.51 (t, 1H, *J*= 9.0 Hz), 3.26-3.29 (m, 1H), 1.35 (d, 3H, *J* = 6.5 Hz).

^{13}C NMR (125 MHz, $CDCl_3$): δ 138.4, 137.0, 136.6, 132.7, 128.5(2), 128.4(2), 128.4, 128.0(2), 127.9(2), 127.9, 127.7, 127.7, 126.5(2), 125.6, 100.7, 81.7, 77.2, 76.6, 75.5, 69.7, 69.4, 68.6, 34.7, 18.0

HRMS (ESI-TOF) *m/z*: [M+Na] calcd for $C_{29}H_{31}IO_4Na$ 593.1165, found 593.1161



44 45

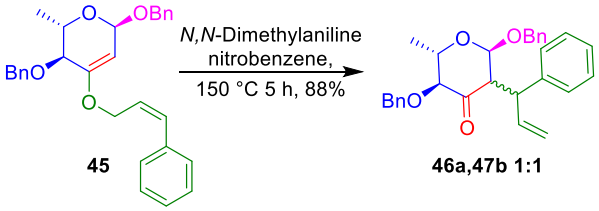
(2*S*,3*S*,6*R*)-3,6-bis(benzyloxy)-4-(cinnamyloxy)-2-methyl-3,6-dihydro-2*H*-pyran(45):

Compound **44** was synthesised from **44** (400 mg, 0.70 mmol) by following general procedure **B**. Yield: 288.5 mg, 93%, colureless gel . R_f: 0.6 (10% EtOAc/hexane).

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.26-7.38 (m, 15H), 6.68 (d, 1H, *J* = 16.0 Hz), 6.31-6.37 (m, 1H), 5.22 (d, 1H, *J* = 3.5 Hz), 4.94 (d, 1H, *J* = 11.5 Hz), 4.85 (d, 1H, *J* = 3.5 Hz), 4.76 (d, 1H, *J* = 12.0 Hz), 4.63 (d, 1H, *J* = 11.0 Hz), 4.58 (d, 1H, *J* = 12.0 Hz), 4.48-4.52 (m, 1H), 4.39-4.43 (m, 1H), 4.14-4.19 (m, 1H), 3.80 (d, 1H, *J* = 9.0 Hz), 1.26 (d, 3H, *J* = 6.5 Hz).

^{13}C NMR (125 MHz, $CDCl_3$): δ 157.7, 138.4, 138.3, 136.4, 133.0, 128.6(3), 128.3(3), 128.3, 128.1, 128.0(2), 127.9, 127.6, 127.5, 126.5(2), 123.9, 95.9, 95.2, 77.1, 73.7, 69.6, 67.9, 66.1, 18.2

HRMS (ESI-TOF) *m/z*: $[M+Na]^+$ calcd for $C_{29}H_{30}O_5Na$ 469.1997, found 469.1985.



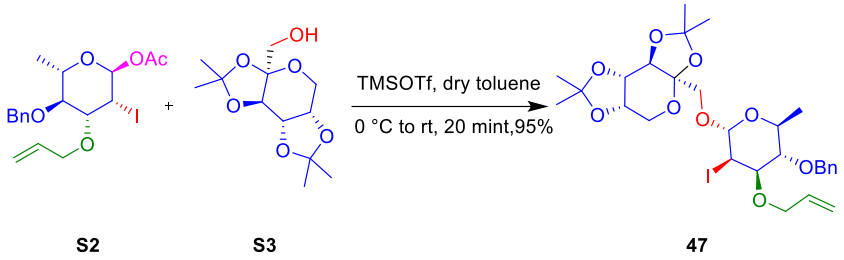
45 46a,47b 1:1

(2*R*,5*S*,6*S*)-2,5-bis(benzyloxy)-6-methyl-3-(1-phenylallyl)tetrahydro-4*H*-pyran-4-one(46a, 46b): Compound (46a,46b 1:1) was synthesised from 45 (200 mg, 0.45 mmol) by following general **procedure C.** Yield: 175.9 mg, 88%, colureless gel . R_f: 0.6 (10% EtOAc/hexane).

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.18-7.39 (m, 15H), 5.90-5.97 (m, 1H), 5.07 (s, 1H), 5.05 (d, 1H, *J* = 4.0 Hz), 4.94 (d, 1H, *J* = 12.0 Hz), 4.66 (s, 1H), 4.57 (d, 1H, *J* = 12.0 Hz), 4.47 (d, 1H, *J* = 12.0Hz), 4.31 (d, 1H, *J* = 12.0 Hz), 4.06-4.12 (m, 1H), 3.88 (d, 1H, *J* = 9.5 Hz), 3.62-3.66 (m, 1H), 3.10 (d, 1H, *J* = 12.0 Hz), 1.41 (d, 3H, *J* = 6.0 Hz).

^{13}C NMR (125 MHz, $CDCl_3$): Inseparable Mixture δ 205.2, 140.6, 138.1, 137.4, 136.9, 129.0(3), 128.4(2), 128.3, 128.3, 128.2(2), 128.0, 127.6, 127.5, 127.3(2), 127.2, 116.1, 99.6, 83.0, 72.8, 69.8, 69.2, 62.0, 50.9, 18.9

HRMS (ESI-TOF) *m/z*: [M+Na] calcd for $C_{29}H_{30}O_4Na$ 465.2042, found 465.2045

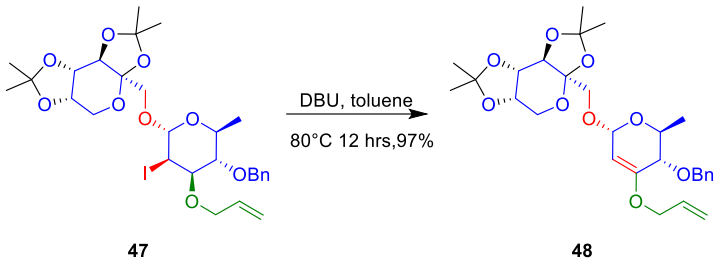


(3a*R*,5a*S*,8a*S*,8b*R*)-3a-((((2*S*,3*R*,4*R*,5*S*,6*S*)-4-(allyloxy)-5-(benzyloxy)-3-iodo-6-methyltetrahydro-2*H*-pyran-2-yl)oxy)methyl)-2,2,7,7-tetramethyltetrahydro-5*H*-bis([1,3]dioxolo)[4,5-b:4',5'-d]pyran(47):

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.29-7.36 (m, 5H), 5.91-5.99 (m, 1H), 5.32 (dd, 1H, J_1 = 1.5Hz, J_2 = 17.0 Hz), 5.22 (s, 1H), 5.15 (dd, 1H, J_1 = 1.5 Hz, J = 10.5 Hz), 4.93 (d, 1H, J = 11.0 Hz), 4.63 (d, 1H, J = 10.5 Hz), 4.56-4.58 (m, 1H), 4.52 (d, 1H, J = 4.0 Hz), 4.31 (d, 1H, J = 2.5 Hz), 4.20-4.22 (m, 1H), 4.13-4.17 (m, 1H), 4.00-4.03 (m, 1H), 3.88-3.91 (m, 1H), 3.68-3.79 (m, 3H), 3.56 (d, 1H, J = 11 Hz), 3.463 (t, 1H), 3.07-3.10 (m, 1H), 1.53 (s, 3H), 1.43 (s, 3H), 1.37 (s, 3H), 1.31 (s, 3H), 1.29 (d, 3H, J = 6.5 Hz),

^{13}C NMR (125 MHz, $CDCl_3$): δ 138.3, 134.4, 128.5, 128.3, 127.9, 117.6, 108.9, 108.5, 102.1, 101.6, 81.5, 76.5, 75.7, 70.9, 70.1, 69.9, 69.8, 68.7, 67.7, 61.1, 33.7, 26.6, 25.8, 25.4, 23.9, 17.8

HRMS (ESI-TOF) *m/z*: [M+Na] calcd for $C_{28}H_{39}IO_9Na$ 669.1536, found 669.1537.

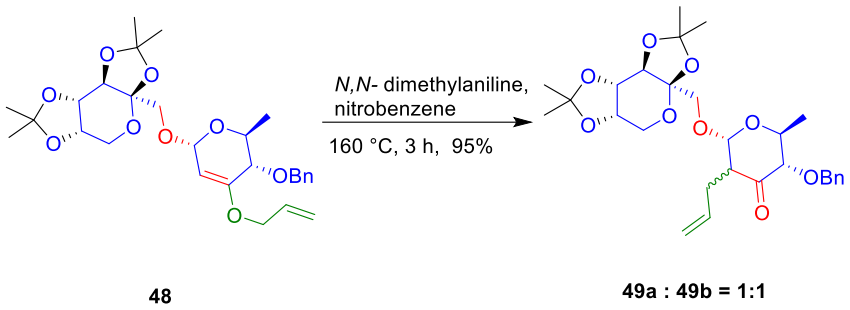


(3a*R*,5a*S*,8a*S*,8b*R*)-3a-((((2*R*,5*S*,6*S*)-4-(allyloxy)-5-(benzyloxy)-6-methyl-5,6-dihydro-2*H*-pyran-2-yl)oxy)methyl)-2,2,7,7-tetramethyltetrahydro-5*H*-bis([1,3]dioxolo)[4,5-b:4',5'-d]pyran(48): Compound **48** was synthesised from **47** (150 mg, 0.232 mmol) by following general procedure **B**. Yield: 116.6 mg, 97%, colureless gel . R_f: 0.5 (20% EtOAc/hexane).

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.28-7.38 (m, 5H), 5.95-6.02 (m, 1H), 5.36 (dd, 1H, J_1 = 1.5Hz, J_2 = 17.5 Hz), 5.29 (dd, 1H, J_1 = 1.5 Hz, J_2 = 10.5 Hz), 5.14 (d, 1H, J = 3.5 Hz), 4.94 (d, 1H, J = 11.0 Hz), 4.76 (d, 1H, J = 3.0 Hz), 4.59 (d, 1H, J = 11.0 Hz), 4.56 (dd, 1H, J_1 = 2.5 Hz, J = 8.0 Hz), 4.38 (d, 1H, J = 2.5 Hz), 4.20-4.32 (m, 3H), 4.00-4.06 (m, 1H), 3.90 (dd, 1H, J_1 = 2.0 Hz, J_2 = 13.0 Hz), 3.71-3.79 (m, 3H), 3.62 (d, 1H, J = 10.5 Hz), 1.53 (s, 3H), 1.46 (s, 3H), 1.40 (s, 3H), 1.32 (s, 3H), 1,26 (d, 3H, J = 6.5 Hz),

^{13}C NMR (125 MHz, $CDCl_3$): δ 157.6, 138.3, 132.7, 128.3(3), 127.7, 117.5, 108.8, 108.4, 102.6, 95.7, 95.6, 76.7, 74.4, 71.0, 70.1, 70.0, 68.1, 66.2, 61.0, 26.6, 25.9, 25.5, 24.0, 18.0

HRMS (ESI-TOF) *m/z*: [M+Na] calcd for $C_{28}H_{38}O_9Na$ 541.2414, found 541.2419.



48 **49a : 49b = 1:1**

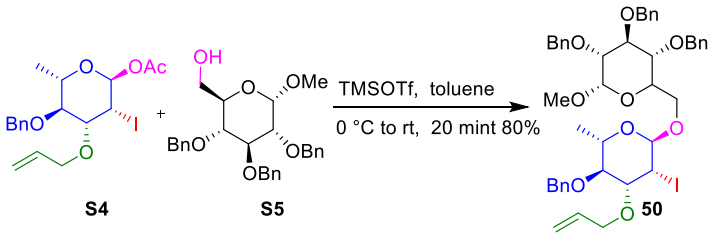
(2*R*,5*S*,6*S*)-3-allyl-5-(benzyloxy)-6-methyl-2-(((3a*R*,5a*S*,8aS,8b*R*)-2,2,7,7-tetramethyltetrahydro-3a*H*-bis([1,3]dioxolo)[4,5-b:4',5'-d]pyran-3a-yl)methoxy)tetrahydro-4*H*-pyran-4-one(49a:49b= 1:1): Compound **(49a,49b 1:1)** was synthesised from **48** (100 mg, 0.19 mmol) by following general **procedure C.** Yield: 94.9 mg, 95%, colureless gel . R_f: 0.5. (20% EtOAc/hexane).

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.33-7.41 (m, 5H), 5.74-5.79 (m, 1H), 5.11-5.16 (m, 1H), 5.07 (d, 1H, *J* = 10.5 Hz), 5.03 (d, 1H, *J* = 4.0 Hz), 4.95 (d, 1H, *J* = 11.5 Hz), 4.56 (dd, 1H, J_1 = 2.5 Hz, *J* = 8.0 Hz), 4.50 (d, 1H, *J* = 11.5 Hz), 4.30 (d, 1H, *J* = 2.5 Hz), 4.22 (dd, 1H, J_1 = 1.0 Hz, *J* = 8.0 Hz), 3.98-4.02 (m, 1H), 3.94 (dd, 1H, J_1 = 1.5 Hz, *J* = 13.0 Hz), 3.77 (d, 1H, *J* = 10.0 Hz), 3.96-3.374 (m, 2H), 3.43 (d, 1H, *J* = 10.0 Hz), 2.75-2.79 (m, 1H), 2.49-2.55 (m, 1H), 2.25-2.32 (m, 1H), 1.54 (s, 3H), 1.45 (s, 3H), 1.40 (s, 3H), 1.36 (d, 3H, *J* = 6.5 Hz), 1.32 (s, 3H).

^{13}C NMR (125 MHz, $CDCl_3$): Spot 1 δ 204.0, 137.4, 134.9, 128.5, 128.4, 128.1, 117.4, 108.8, 108.8, 101.7, 100.7, 84.6, 73.1, 71.0, 70.4, 69.8, 69.5, 67.9, 61.0, 53.5, 27.9, 26.6, 25.9, 25.7, 23.8, 18.8

^{13}C NMR (125 MHz, $CDCl_3$): Spot 2 δ 206.2, 137.2, 133.6, 128.5, 128.4, 128.1, 118.0, 108.8, 108.7, 102.0, 101.5, 82.0, 73.2, 70.9, 69.8, 69.7, 69.6, 67.2, 61.0, 56.2, 34.4, 26.6, 25.8, 25.3, 23.9, 18.7

HRMS (ESI-TOF) *m/z*: [M+Na] calcd for $C_{28}H_{38}O_9Na$ 541.2414, found 541.2419



S4 **S5** **50**

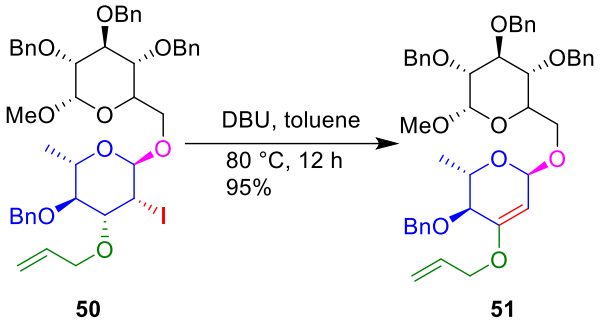
(2*S*,3*S*,4*R*,5*R*,6*R*)-4-(allyloxy)-3-(benzyloxy)-5-iodo-2-methyl-6-(((3R,4S,5R,6S)-3,4,5-tris(benzyloxy)-6-methoxytetrahydro-2H-pyran-2-yl)methoxy)tetrahydro-2*H*-pyran(50):

IR (neat): 2928, 2246, 1730 ,195 cm−1.

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.32-7.36 (m, 20H), 5.92-6.00 (m, 1H), 5.34 (dd, 1H, J_1 = 1.5 Hz, J_2 = 17.5 Hz), 5.19 (dd, 1H, J_1 = 1.0 Hz, J_2 = 10.0 Hz), 5.50 (d, 2H, J = 0.01 Hz), 4.93 (d, 1H, J = 11.0 Hz), 4.89 (d, 1H, J = 11.0 Hz), 4.78-4.83 (m, 2H), 2.37 (d, 1H, J = 12.0 Hz), 4.61 (d, 1H, J = 11.0 Hz), 4.54-4.57 (m, 2H), 4.34-4.35 (m, 1H), 4.11-4.15 (m, 1H), 3.97-4.01 (m, 2H), 3.77-3.80 (m, 2H), 3.69-3.72 (m, 1H), 3.50 (dd, 1H, J_1 = 3.5 Hz, J_2 = 13.5 Hz), 3.40-3.46 (m, 3H), 3.35 (t, 3H, J = 14.0 Hz), 3.09 (dd, 1H, J_1 = 4.0 Hz, J_2 = 8.5 Hz), 1.27 (d, 3H, J = 6.5 Hz).

^{13}C NMR (125 MHz, $CDCl_3$): δ 138.6, 138.3, 138.0, 134.4, 128.4, 128.4(2), 128.4, 128.4, 128.1, 128.1, 128.0, 127.9, 127.9, 127.7, 127.7, 117.3, 101.3, 97.8, 82.1, 81.6, 80.0, 77.4
76.3, 75.8, 75.4, 74.8, 73.3(2), 69.9, 69.8, 68.2, 66.4, 55.0, 34.3, 17.9

HRMS (ESI-TOF) *m/z*: [M+NH_4] calcd for $C_{44}H_{51}IO_9NH_4$ 868.2932, found 868.2932.



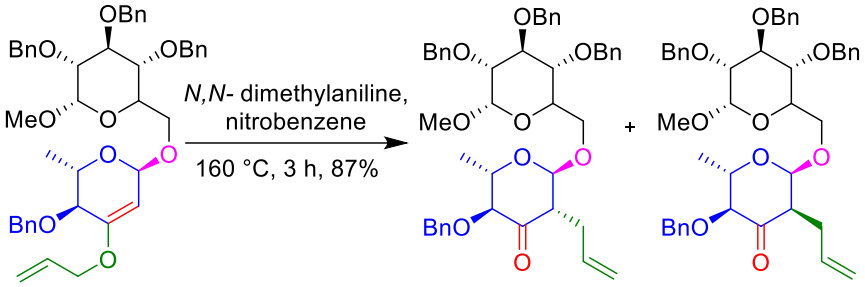
50 51

(2*S*,3*S*,6*R*)-4-(allyloxy)-3-(benzyloxy)-2-methyl-6-(((3*R*,4*S*,5*R*,6*S*)-3,4,5-tris(benzyloxy)-6-methoxytetrahydro-2*H*-pyran-2-yl)methoxy)-3,6-dihydro-2*H*-pyran(51): Compound **51** was synthesised from **50** (100 mg, 0.11 mmol) by following general procedure B. Yield: 80.7 mg, 95%, colureless gel . R_f: 0.5 (20% EtOAc/hexane).

IR (neat): 3028, 2927, 2254, 1738 ,1647 cm−1.

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.30-7.38 (m, 20H), 5.98-6.05 (m, 1H), 5.40 (dd, 1H, J_1 = 1.5 Hz, J_2 = 17.5 Hz), 5.27 (dd, 1H, J_1 = 1.5 Hz, J_2 = 12.0 Hz), 5.01-5.04 (m, 2H), 4.90-4.95 (m, 2H), 4.80-4.85 (m, 2H), 4.67-4.70 (m, 2H), 4.59-4.61 (m, 2H), 4.30-4.34 (m, 1H), 4.23-4.27 (m, 1H), 4.08-4.13 (m, 1H), 4.03 (t, 1H, J = 9.0 Hz), 3.93 (dd, 1H, J_1 = 2.0 Hz, J_2 = 11.0 Hz), 3.73-3.79 (m, 2H), 3.62 (dd, 1H, J_1 = 5.0 Hz, J_2 = 11.0 Hz), 3.51-3.57 (m, 2H), 3.39 (s, 3H), 1.29 (s, 1H), 1.26 (d, 3H, J = 6.5 Hz).

^{13}C NMR (125 MHz, $CDCl_3$): δ 157.5, 138.8, 138.5, 138.3, 138.2, 132.8, 128.4, 128.4, 128.4(3), 128.2(3), 128.1(3), 128.1(3), 127.9, 127.9, 127.8, 127.7, 127.6, 127.5, 117.5, 98.0, 96.2, 95.6, 82.1, 80.0, 77.9, 77.0, 75.7, 74.9, 74.0, 73.3, 70.1, 68.0, 66.5, 66.1, 55.1, 18.2
HRMS (ESI-TOF) *m/z*: [M+NH_4] calcd for $C_{44}H_{50}O_9NH_4$ 740.3799, found 740.3799.



51 **52a, 52b 1:1**

(2*R*,3*S*,5*S*,6*S*)-3-allyl-5-(benzyloxy)-6-methyl-2-(((3R,4S,5R,6S)-3,4,5-tris(benzyloxy)-6-methoxytetrahydro-2H-pyran-2-yl)methoxy)tetrahydro-4*H*-pyran-4-one(52a,52b,1:1):
Compound **(52a,52b 1:1)** was synthesised from **51** (70 mg, 0.09 mmol) by following general **procedure C.** Yield: 60.8 mg, 87%, colureless gel . R_f: 0.5 (20% EtOAc/hexane).
IR (neat): 2929, 2247, 1729, 1495 cm−1
^{1}H NMR (500 MHz, $CDCl_3$): δ 7.30-7.36 (m, 20H), 5.61-5.68 (m, 1H), 5.04-5.08 (m, 2H), 4.98 (d, 1H, *J* = 11.0 Hz), 4.88 (dd, 2H, J_1 = 3.0 Hz, J_2 = 11.5 Hz), 4.76-4.80 (m, 2H), 4.73 (s, 1H), 4.64 (d, 1H, *J* = 12.0 Hz), 4.50-4.52 (m, 2H), 4.44-4.47 (m, 1H), 4.03-4.07 (m, 1H), 3.94-3.99 (m, 1H), 3.77-3.80 (m, 1H), 3.69-3.72 (m, 1H), 3.65 (d, 1H, *J* = 10.0 Hz), 3.45-3.50 (m, 3H), 3.33 (s, 3H), 2.63 (t, 1H, *J* = 8.0 Hz), 2.31-2.39 (m, 2H), 1.30 (d, 3H, *J* = 6.5 Hz).

^{13}C NMR (125 MHz, $CDCl_3$): Spot 1 206.1, 138.7, 138.3, 138.1, 137.3, 133.8, 128.4, 128.4, 128.1, 128.0, 127.9, 127.9, 127.7, 127.7, 127.5, 117.8, 101.4, 97.8, 82.0, 82.0, 80.0, 77.7
77.2, 75.7, 74.9, 73.4, 73.1, 69.7, 69.0, 66.2, 56.0, 55.1, 34.4, 18.7

^{13}C NMR (125 MHz, $CDCl_3$): Spot 2 206.8, 138.7, 138.3, 138.1, 137.2, 134.6, 128.5, 128.5, 128.4(2), 128.4, 128.1, 128.1(2), 127.9, 127.8, 127.7, 117.2, 101.1, 98.2, 82.5, 82.0, 80.0, 77.6, 75.9, 75.2, 73.5, 73.2, 71.9, 69.9, 67.1, 56.1, 55.2, 29.7, 29.6, 19.0

HRMS (ESI-TOF) *m/z*: [M+NH_4] calcd for $C_{44}H_{50}O_9NH_4$ 740.3799, found 740.3794.

S6 S7 53

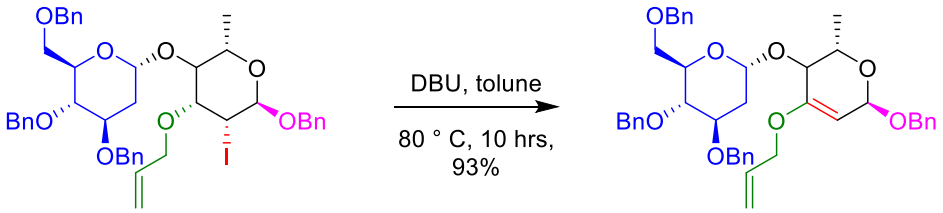
(2*R*,3*R*,4*R*,6*S*)-4-(allyloxy)-2-(benzyloxy)-5-(((2*R*,4*R*,5*S*,6*R*)-4,5-bis(benzyloxy)-6-((benzyloxy)methyl)tetrahydro-2*H*-pyran-2-yl)oxy)-3-iodo-6-methyltetrahydro-2*H*-pyran(53):

IR (neat): 3028, 2915, 1738 ,1495 cm−1.

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.23-7.38 (m, 20H), 5.90-5.98 (m, 1H), 5.28-5.32 (m, 1H), 5.23 (d, 1H, *J* = 1.5 Hz), 5.18 (d, 1H, *J* = 3.0 Hz), 5.15 (dd, 1H, J_1 = 5.5 Hz, J_2 = 10.0 Hz), 4.91 (d, 1H, *J* = 11.0 Hz), 4.68-4.72 (m, 4H), 4.55 (d, 1H, *J* = 11.0 Hz), 4.48-4.54 (m, 3H), 4.14-4.17 (m, 1H), 4.01-4.06 (m, 1H), 3.91-3.986 (m, 2H), 3.84-3.88(m, 1H), 3.81 (dd, 1H, J_1 = 3.0 Hz, J_2 = 10.5 Hz), 3.67-3.74 (m, 3H), 3.08 (dd, 1H, J_1 = 4.0 Hz, J_2 = 8.5 Hz), 2.27-2.31(m, 1H), 1.73-1.79 (m, 1H), 1.31 (d, 3H, *J* = 6.5 Hz).

^{13}C NMR (125 MHz, $CDCl_3$): δ 138.9, 138.7, 138.3, 137.0 , 134.2, 128.5, 128.3, 128.2, 128.2(2), 127.9, 127.9, 127.6, 127.5, 127.5, 127.3, 117.8, 100.5, 97.9, 78.4, 78.2, 77.3, 75.2, 74.7, 73.4, 71.8, 71.0, 69.9, 69.5, 68.9, 68.9, 35.5, 33.9, 18.3

HRMS (ESI-TOF) *m/z*: [M+NH_4] calcd for $C_{43}H_{49}IO_8NH_4$ 838.2816, found 838.2816.



53 54

(2*S*,6*R*)-4-(allyloxy)-6-(benzyloxy)-3-(((2*R*,4*R*,5*S*,6*R*)-4,5-bis(benzyloxy)-6-((benzyloxy)methyl)tetrahydro-2*H*-pyran-2-yl)oxy)-2-methyl-3,6-dihydro-2*H*-pyran(54):

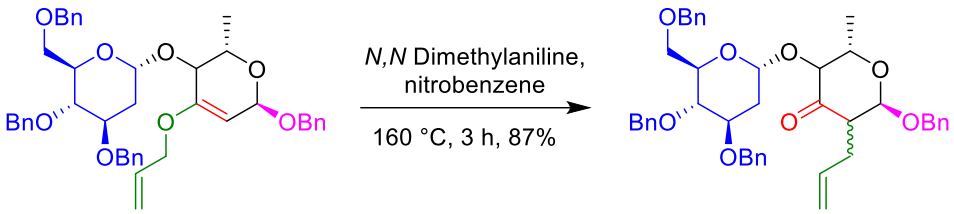
Compound 54 was synthesised from 53 (170 mg, 0.20 mmol) by following general procedure B. Yield: 133.4 mg, 93%, colureless gel . R_f: 0.5 (20% EtOAc/hexane).

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.27-7.37 (m, 20H), 5.89-5.94 (m, 1H), 5.30 (dd, 1H, J_1 = 1.0 Hz, J_2 = 17.0 Hz), 5.17-5.20 (m, 2H), 5.09 (d, 1H, *J* = 3.0 Hz), 4.90 (d, 1H, *J* = 11.0 Hz), 4.84 (d, 1H, *J* = 2.5 Hz), 4.75 (d, 1H, *J* = 12.0 Hz), 4.65 (t, 3H, *J* = 12.0 Hz), 4.57 (t, 2H, *J* = 12.5 Hz), 4.48 (d, 1H, *J* = 12.5 Hz), 4.19-4.26 (m, 4H), 3.96-4.00 (m, 2H), 3.79 (dd, 1H, J_1 = 3.0 Hz, J_2 =

10.5 Hz), 3.69 (t, 1H, *J* = 9.5 Hz), 3.60-3.61 (m, 1H), 2.29-2.32 (m, 1H), 1.74 (td, 1H, J_1 = 3.5 Hz, J_2 = 12.5 Hz), 1.25 (d, 3H, *J* = 6.5 Hz).

^{13}C NMR (125 MHz, $CDCl_3$): δ 155.7, 139.0, 138.8, 138.4, 138.3, 132.6, 128.4, 128.4, 128.3, 128.2, 128.0, 127.9, 127.6, 127.6(2), 127.5, 127.5, 127.4, 118.5, 97.9, 96.9, 95.1, 78.3, 77.5, 75.9, 74.6, 73.5, 72.0, 71.3, 69.6, 69.0, 68.5, 67.0, 35.9, 18.4

HRMS (ESI-TOF) *m/z*: [M+NH_4] calcd for $C_{43}H_{48}O_8NH_4$ 710.3693, found 710.3693.



54 **55a,55b = 9:1**

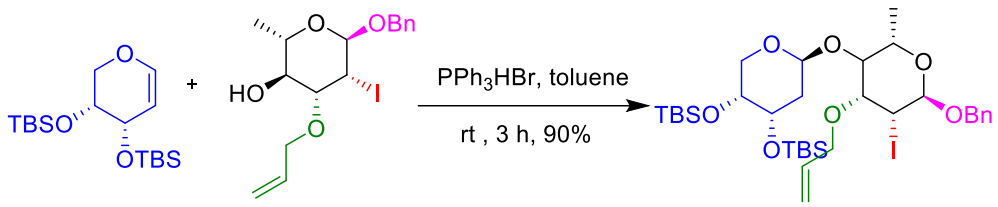
(2*R*,6*S*)-3-allyl-2-(benzyloxy)-5-(((2*R*,4*R*,5*S*,6*R*)-4,5-bis(benzyloxy)-6-((benzyloxy)methyl)tetrahydro-2*H*-pyran-2-yl)oxy)-6-methyltetrahydro-4*H*-pyran-4-one(46a,46b 9:1): Compound **(55a,55b 9:1)** was synthesised from **54** (100 mg, 0.14 mmol) by following general **procedure C.** Yield: 86.65 mg, 87%, colureless gel . R_f: 0.5 (20% EtOAc/hexane).

IR (neat): 3028, 2914, 1732 ,1495 cm−1.

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.27-7.37 (m, 20H), 5.59-5.67 (m, 1H), 5.06 (dd, 1H, J_1 = 1.5 Hz, J_2 = 17.0 Hz), 4.97-4.99 (m, 2H), 4.89 (d, 2H, *J* = 11.0 Hz), 4.65-4.67 (m, 3H), 4.59 (d, 1H, *J* = 12.0 Hz), 4.54 (d, 1H, *J* = 11.0 Hz), 4.48 (d, 1H, *J* = 12.5 Hz), 4.44 (d, 1H, *J* = 12.0 Hz), 4.33-4.36 (m, 1H), 4.03-4.10 (m, 2H), 3.96 (d, 1H, *J* = 9.5 Hz), 3.78 (dd, 1H, J_1 = 3.0 Hz, J_2 = 13.5 Hz), 3.66 (t, 1H, *J* = 9.5 Hz), 3.49 (dd, 1H, J_1 = 2.0 Hz, J_2 = 10.5 Hz), 2.71 (t, 1H, *J* = 8.0 Hz), 2.33-2.44 (m, 3H), 1.74-1.80 (m, 1H), 1.33 (d, 3H, *J* = 6.0 Hz).

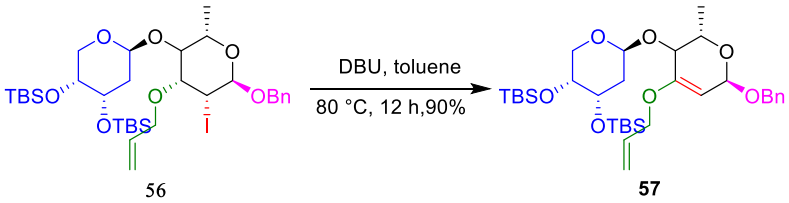
^{13}C NMR (125 MHz, $CDCl_3$): δ 204.1, 138.8, 138.8, 138.1, 137.0, 133.8, 128.4(2), 128.3, 128.3(2), 128.2, 127.9(2), 127.8, 127.7, 127.6, 127.6, 127.5(2), 127.5, 127.3, 117.8, 100.5, 99.4, 82.0, 78.2, 77.4, 74.5, 73.4, 72.1, 71.3, 69.8, 69.1, 68.6

HRMS (ESI-TOF) *m/z*: [M+NH_4] calcd for $C_{43}H_{48}O_8NH_4$ 710.3693, found 710.3695.



S8 S9 56

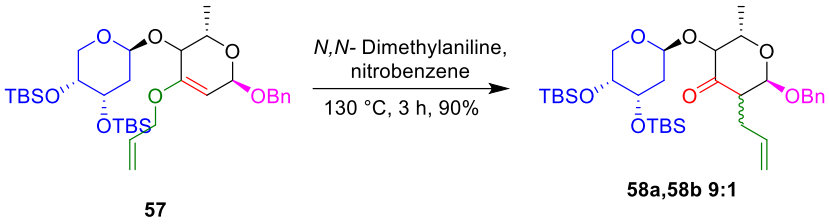
(((3*R*,4*S*,6*S*)-6-(((2*S*,4*R*,5*R*,6*R*)-4-(allyloxy)-6-(benzyloxy)-5-iodo-2-methyltetrahydro-2*H*-pyran-3-yl)oxy)tetrahydro-2*H*-pyran-3,4-diyl)bis(oxy))bis(tert-butyldimethylsilane)(56):
IR (neat): 2952, 2927, 2884, 2855, 1461 cm−1
^{1}H NMR (500 MHz, $CDCl_3$): δ 7.29-7.37 (m, 5H), 5.89-5.93 (m, 1H), 5.28-5.31 (m, 1H), 5.16-5.19 (m, 3H), 4.67 (d, 1H, *J* = 11.5 Hz), 4.45-4.48 (m, 2H), 4.05-4.09 (m, 1H), 3.97-4.00 (m, 1H), 3.89-3.93 (m, 1H), 3.76-3.81 (m, 1H), 3.69-3.71 (m, 1H), 3.60-3.66 (m, 4H), 3.00 (dd, 1H, J_1 = 4.0 Hz, J_2 = 8.5 Hz), 2.01-2.06 (m, 1H), 1.34 (d, 3H, *J* = 6.5 Hz), 0.90 (s, 9H), 0.89 (s, 9H), 0.06-0.07 (m, 12H),
^{13}C NMR (125 MHz, $CDCl_3$): δ 137.1, 134.4, 128.5, 128.0, 117.4, 100.7, 99.6, 79.3, 76.3, 70.0, 69.6, 69.4, 68.3, 68.1, 64.8, 33.8, 26.0, 26.0, 18.3, 18.3, 18.2, -4.4, -4.7, -4.8
HRMS (ESI-TOF) *m/z*: [M+NH_4] calcd for $C_{33}H_{57}IO_7Si_2NH_4$ 766.3031, found 766.3029.



56 57

(((3*R*,4*S*,6*S*)-6-(((2*S*,6*R*)-4-(allyloxy)-6-(benzyloxy)-2-methyl-3,6-dihydro-2*H*-pyran-3-yl)oxy)tetrahydro-2*H*-pyran-3,4-diyl)bis(oxy))bis(tert-butyldimethylsilane)(57): Compound **57** was synthesised from **56** (200 mg, 0.285 mmol) by following general procedure B. Yield: 147.11 mg, 90%, colureless gel . R_f: 0.6 (10% EtOAc/hexane).

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.29-739 (m, 5H), 5.90-5.98 (m, 1H), 5.30 (dd, 1H, J_1 = 1.5 Hz, J_2 = 17.5 Hz), 5.20-5.24 (m, 3H), 4.76 (d, 1H, *J* = 11.5 Hz), 4.72 (d, 1H, *J* = 3.5 Hz), 4.58 (d, 1H, *J* = 12.0 Hz), 4.21-4.30 (m, 2H), 4.03-4.07 (m, 1H), 3.99-4.02 (m, 1H), 3.93 (d, 1H, *J* = 9.0 Hz), 3.69-3.74 (m, 2H), 3.65 (dd, 1H, J_1 = 6.0 Hz, J_2 = 11.0 Hz), 2.04-2.09 (m, 1H), 1.64-1.69 (m, 1H), 1.32 (d, 3H, *J* = 6.5 Hz), 0.92 (s, 9H), 0.91 (s, 9H), 0.07-0.09 (m, 12H).
^{13}C NMR (125 MHz, $CDCl_3$): δ157.6, 138.4, 132.8, 128.4(2), 128.0(2), 127.5, 117.6, 99.9, 95.2, 95.2, 75.2, 70.1, 69.6, 68.1, 68.0, 66.5, 64.8, 26.0, 26.0, 18.4, 18.3, 18.2, -4.4, -4.7, -4.8
HRMS (ESI-TOF) *m/z*: [M+NH_4] calcd for $C_{33}H_{56}O_7Si_2NH_4$ 638.3908, found 638.3908.



57 58a,58b 9:1

(2*R*,6*S*)-3-allyl-2-(benzyloxy)-5-(((2*S*,4*S*,5*R*)-4,5-bis((tertbutyldimethylsilyl)oxy)tetrahydro-2*H*-pyran-2-yl)oxy)-6-methyltetrahydro-4*H*-pyran-4-one (58): Compound **(58a, 58b 9:1)** was synthesised from **57** (100 mg, 0.61 mmol) by following general **procedure C.** Yield: 89.9 mg, 90%, colureless gel . R_f: 0.5 (10% EtOAc/hexane).

IR (neat): 2952, 2928, 2886, 2856, 11731 cm−1

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.27-7.34 (m, 5H), 5.60-5.68 (m, 1H), 5.08 (dd, 1H, J_1 = 1.5 Hz, J_2 = 17.0 Hz), 5.03-5.05 (m, 1H), 4.95-4.98 (m, 1H), 4.90 (s, 1H), 4.66 (d, 1H, J = 12.0 Hz), 4.48 (d, 1H, J = 12.0 Hz), 3.99-4.08 (m, 3H), 3.71-3.73 (m, 1H), 3.64 (dd, 1H, J_1 = 2.5 Hz, J_2 = 11.5 Hz), 3.57-3.61 (m, 1H), 2.94-2.95 (m, 1H), 2.71 (t, 1H, J = 8.0 Hz), 2.38-2.43 (m, 1H), 2.12-2.17 (m, 1H), 1.71-1.75 (m, 1H), 1.39 (d, 3H, J = 6.0 Hz), 0.89 (s, 9H), 0.89 (s, 9H), 0.06-0.08 (m, 12H).

^{13}C NMR (125 MHz, $CDCl_3$): δ 205.8, 137.1, 133.7, 128.4(2), 127.8, 127.7(2), 117.8, 100.6, 97.9, 69.9, 69.2, 69.0, 65.2, 56.1, 34.3, 25.9, 25.9, 19.0, 18.2, 18.2, -4.4, -4.5, -4.7, -4.8

HRMS (ESI-TOF) *m/z*: [M+NH_4] calcd for $C_{33}H_{56}O_7Si_2NH_4$ 638.3908, found 638.3906.

3.5 References

1) a) Varki, A. Biological roles of oligosaccharides: all of the theories are correct. *Glycobiology*, **1993**, *3*, 97–130. b) Werz, D. B.; Seeberger, P. H. Carbohydrates as the Next Frontier in Pharmaceutical Research. *Chem. Eur. J*, **2005**, 11, 3194–3206. c) Seeberger, P. H.; Werz, D. B. Synthesis and medical applications of oligosaccharides. *Nature*, 2007, *446*, 1046–1051. d) Galonic, D. P.; Gin, D. Y. Chemical glycosylation in the synthesis of glycoconjugate antitumour vaccines. *Nature*, **2007**, *446*, 1000–1007. e) Golster, T. M.; Vocadlo, D. J. Developing inhibitors of glycan processing enzymes as tools for enabling glycobiology. *Nature Chem. Biol*, **2012**, *8*, 683–694. f) Dam, T. K.; Brewer, C. F. Thermodynamic studies of lectin-carbohydrate interactions by isothermal titration calorimetry. *Adv. Carbohydr. Chem. Biochem*, **2010**, *63*, 139–164. g) B. Ernst, G. W. Hart, P. Sinaÿ, *Carbohydrates in Chemistry and Biology*, vol. **3 and 4**, Wiley-VCH,

Weinheim, Germany, **2000**. h) Varki A. *Essentials of Glycobiology*., Cold Spring Harbor Laboratory Press, New York, 2008. i) Mariño, K.; Bones, J.; Kattla, J. J.; Rudd, P. M. A systematic approach to protein glycosylation analysis: a path through the maze *Nature Chem. Biol*, 2010, *6*, 713–723.

2) a) Li, X.; Uchiyama, T.; Raetz, C. R.; Hindsgaul, O. Synthesis of a carbohydrate-derived hydroxamic acid inhibitor of the bacterial enzyme (LpxC) involved in lipid A biosynthesis. *Org. Lett*, 2003, *5*, 539–541. b) Koester, D. C.; Holkenbrink, A.; Werz, D. B. Recent Advances in the Synthesis of Carbohydrate Mimetics. *Synthesis*, 2010, 3217–3242. c) Bernardi, A.; Cheshev, P. Interfering with the Sugar Code:Design and Synthesis of Oligosaccharide Mimics. *Chem. Eur. J*, 2008, *14*, 7434–7441. d) Jackman, J. E.; Fierke, C. A.; Tumey, L. N.; Pirrung, M.; Uchiyama, T.; Tahir S. H.; Hindsgaul, O.; Raetz, C. R. Antibacterial agents that target lipid A biosynthesis in gram-negative bacteria. Inhibition of diverse UDP-3-O-(r-3-hydroxymyristoyl)-n-acetylglucosamine deacetylases by substrate analogs containing zinc binding motifs. *J. Biol. Chem*, 2000, *275*, 11002–11009. e) Hang, H. C.; Bertozzi, C. R. Ketone isosteres of 2-N-acetamidosugars as substrates for metabolic cell surface engineering. *J. Am. Chem. Soc*, 2001, *123*, 1242–1243. f) Liu, X.; Guo, Y.; Li, Y.; Jiang, Y.; Chubb, S.; Azuma, A.; Huang, P.; Matsuda, A.; Hittelman, W.; Plunkett, W. Molecular Basis for G_2 Arrest Induced by 2′-*C*-Cyano-2′-Deoxy-1-β-d *Arabino*-Pentofuranosylcytosine and Consequences of Checkpoint Abrogation. *Cancer Res*, 2005, *65*, 6874–6881. g) P. G. Reddy, D. Bao, W. Chang, B.-K. Chun, J. Du, D. Nagarathnam, S. Rachakonda, B. S. Ross, H.-R. Zhang, S. Bansal, C. L. Espiritu, M. Keilman, A. M. Lam, C. Niu, H. M. Steuer, P. A. Furman, M. J. Otto, M. J. Sofia, Bioorg. *Med. Chem. Lett*, 2010, *20*, 7376–7380. h) Lepenies, B.; Yin, J.; Seeberger, P. H. Applications of synthetic carbohydrates to chemical biology. *Curr. Opin. Chem. Biol*, 2010, *14*, 404–411. i) Bouché, L.; Reissig, H.-U. Synthesis of novel carbohydrate mimetics via 1,2-oxazines. *Pure Appl. Chem*, 2012, *84*, 23–36.

3) a) Paterson, L.; Keown, L. E. Studies in marine macrolide synthesis: stereocontrolled synthesis of the F-ring subunit of Spongistatin 1 (Altohyrtin A). *Tetrahedron Lett*, **1997**, *38*, 5727–5730. b) Smith, AB III.; Zhuang, L.; Brook, C.S.; Boldi, A.M.; McBriar, M.D. Spongistatin synthetic studies. 1. Construction of A C (29-48) subtarget. *Tetrahedron Lett*, **1997**, *38*, 8667–8670.

4) a) Hanessian, S. Reflection on the total synthesis of natural products: art, craft, logic, and the chiron approach. *Pure & Appl Chem*, **1993**, *65*, 1189–1204. b) Hanessian, S. Total synthesis of natural products: The "Chiron" approach. Pergamon Press, Oxford, **1983** pp 40–183.

5) Lundt, L.; madsen, R. Synthetically Useful Base-Induced Rearrangements of Aldonolactones. topic. *Curr. Chem*, 1997, *187*, 117–153.

6) Du, Y.; Linhardt, R.J.; Vlahov, I.R. Recent advances in stereoselective C-glycoside synthesis. *Tetrahedron* 1998, 54, 9913–9959.

7) a) Levy D, Tang EC (1995) The chemistry of C-glycosides tetrahedron organic chemistry series, vol 13. Pergamon Press, Oxford. b) Nicotra, F. Synthesis of C-glycosides of biological interest. *Topics Curr Chem*, 1997, 187, 55–83.

8) Postema, M.H.D. Recent developments in the synthesis of C-glycosidase. *Tetrahedron*, 1992, 48, 8545–8599.

9) Vankar, Y. D.; Linker, T.; Recent Developments in the Synthesis of 2-C-Branched and1,2-Annulated Carbohydrates. *Eur. J. Org. Chem*., **2015**, 7633–7642.

10) Lgarashi. K.; Honma, T. *J. Org. Chem.* **1970**, *35*, 617-620.

11) Halcomb, R. L.; Danishefsky, S. J. *J. Am. Chem. Soc.* **1989**, *111*, 6661-6666.

12) Ferrier, R. J.; Prasad, N. Unsaturated Carbohydrates. Part 1X.l Synthesis of 2,3-Dideoxy-a-~-eryfhro-hex-2-enopyranosides from Tri-0-acetyl-D-glucal. *J. Chem. Soc. C.* **1969**, 581-586.

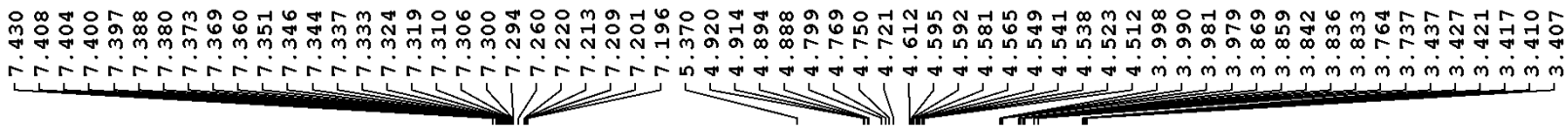
13) Henry, K. J.; Fraser-Reid. B. Cyclopropanation of Glycals: Application to the Synthesis of 2-Deoxy-ZVinyl Glycosidesl. *Tetrahedron Lett*. **1995**, *36*, 8901-8904.

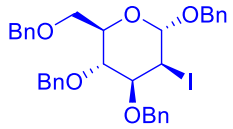
14) Claisen, L. Über Umlagerung von Phenol-allyläthern in *C*-Allyl-phenole. *Ber Dtsch Chem Ges*, *1912*, *45*, 3157–3166.

15) a) Ireland, R.E.; Mueller, R.H. The Claisen rearrangement of allyl esters. *J. Am.Chem. Soc*, **1972**, *94*, 5897–5898. b) Ireland, R.E.; Mueller, R.H.; Willard, A.K. The ester enolate Claisen rearrangement. stereochemical control through Stereoselective enolate formation. *J. Am. Chem Soc***, 1976**, 98, 2868–2877. c) Thiem, J. Alternative approaches towards glycosylated eight-membered ring compounds employing Claisen rearrangement of mono and disaccharide allyl vinyl ether precursors. *Tetrahedron Asymmetry*, **2005,** *16*, 569–576.

16) S. Dubbu, J. Santhi, R. Hevey, *Helv. Chim. Acta* 2022, **105**, e202200135.

17) a) Sridhar, P. R. Reddy, G. M.; Seshadri, K. Stereoselective synthesis of cis-fused perhydrofuro[2,3-b] furan derivatives from sugar-derived allyl vinyl ethers. *Eur. J. Org. Chem.* **2012,** 6228-6235. b) Reddy, G. M.; Sridhar, P. R. Stereoselective Construction of 2,8-Dioxabicyclo[3.3.1]nonane/nonene Systems from 3-C-Branched Glycals *European Journal of Organic Chemistry*. *Eur. J. Org. Chem*., **2014, *7***, 1496- 1504. c) Reddy, G. M.; Sridhar, P. R.The first stereoselective total synthesis of neosemburin and isoneosemburin. *Org. Biomol. Chem.*, **2014**, *12*, 8408–8414.

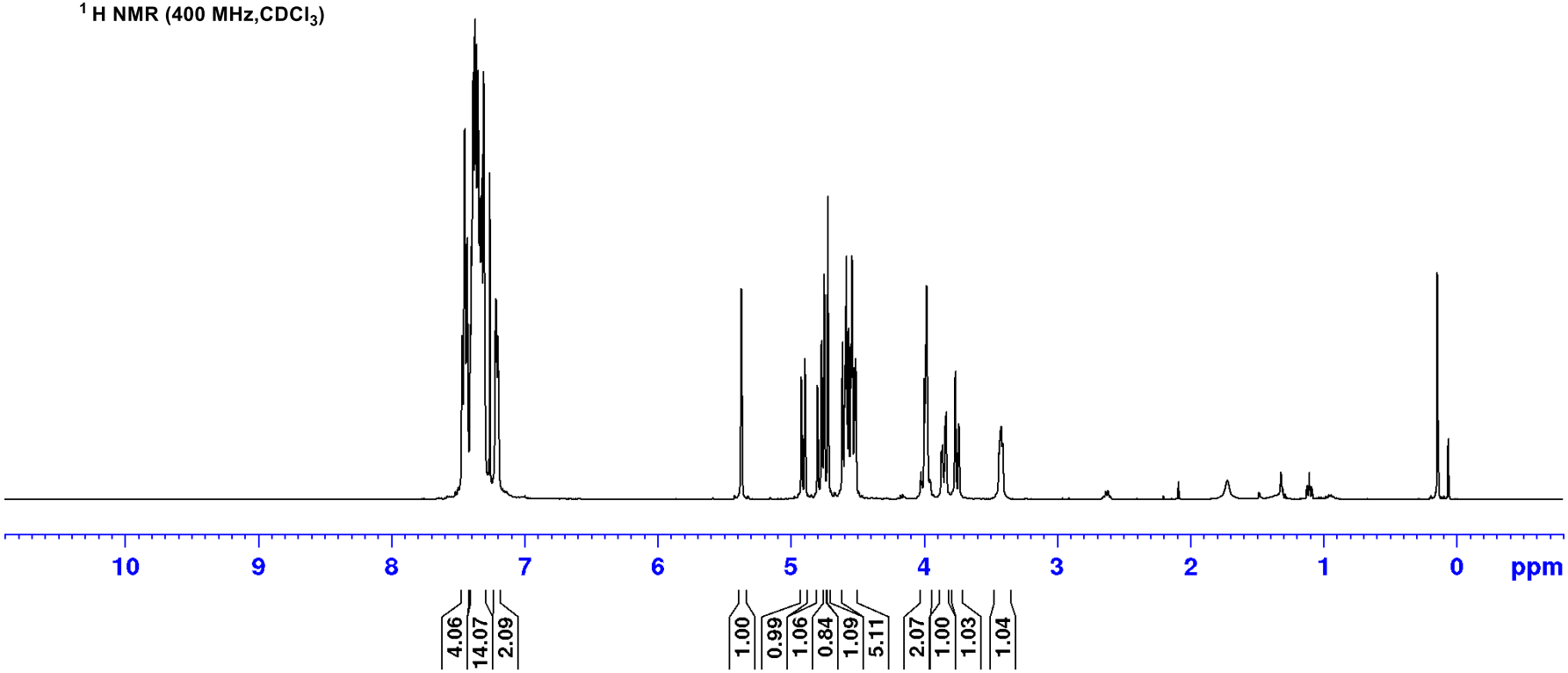


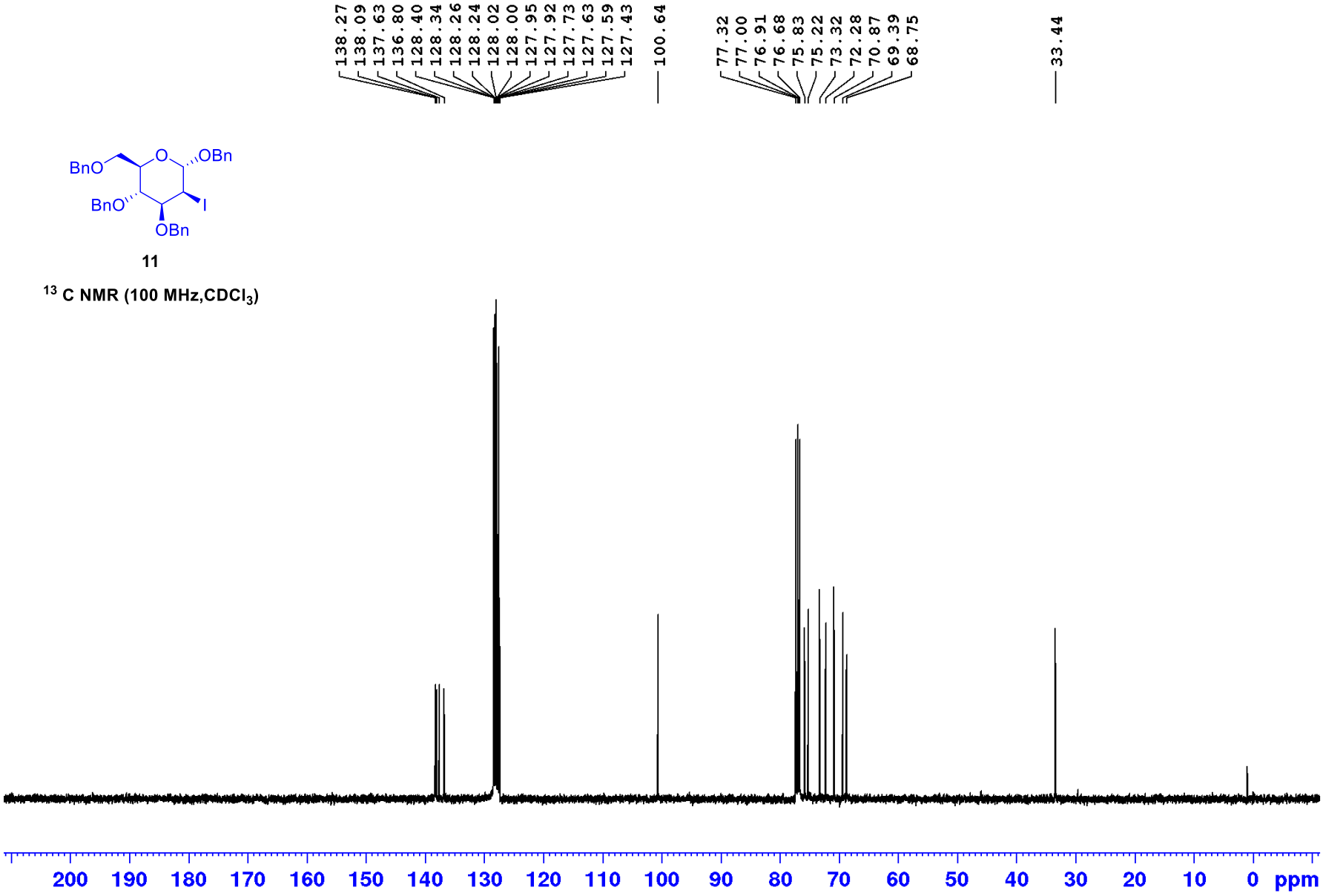


11

^{1}H NMR (400 MHz,$CDCl_3$)

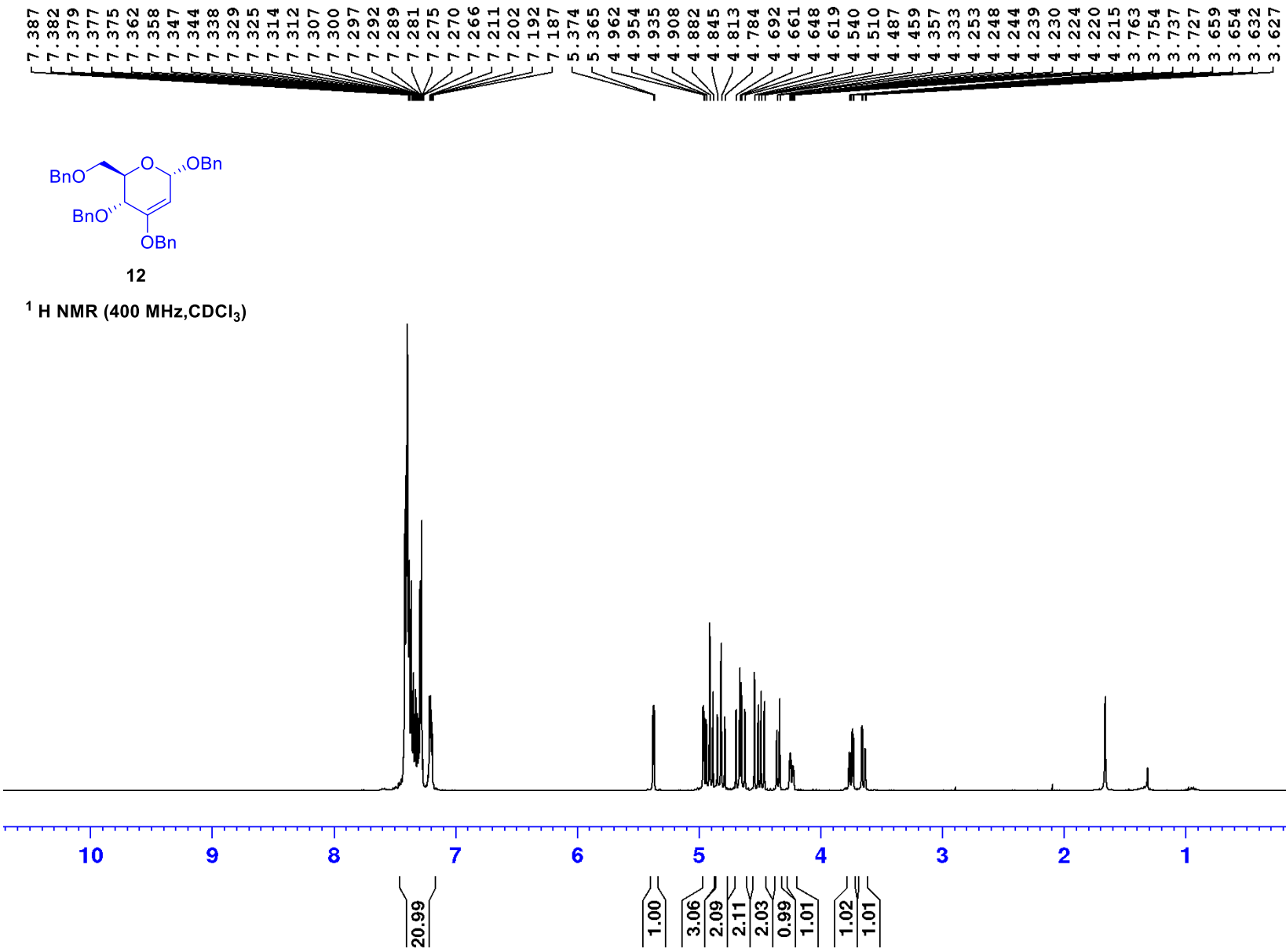
3.6 NMR Spectra

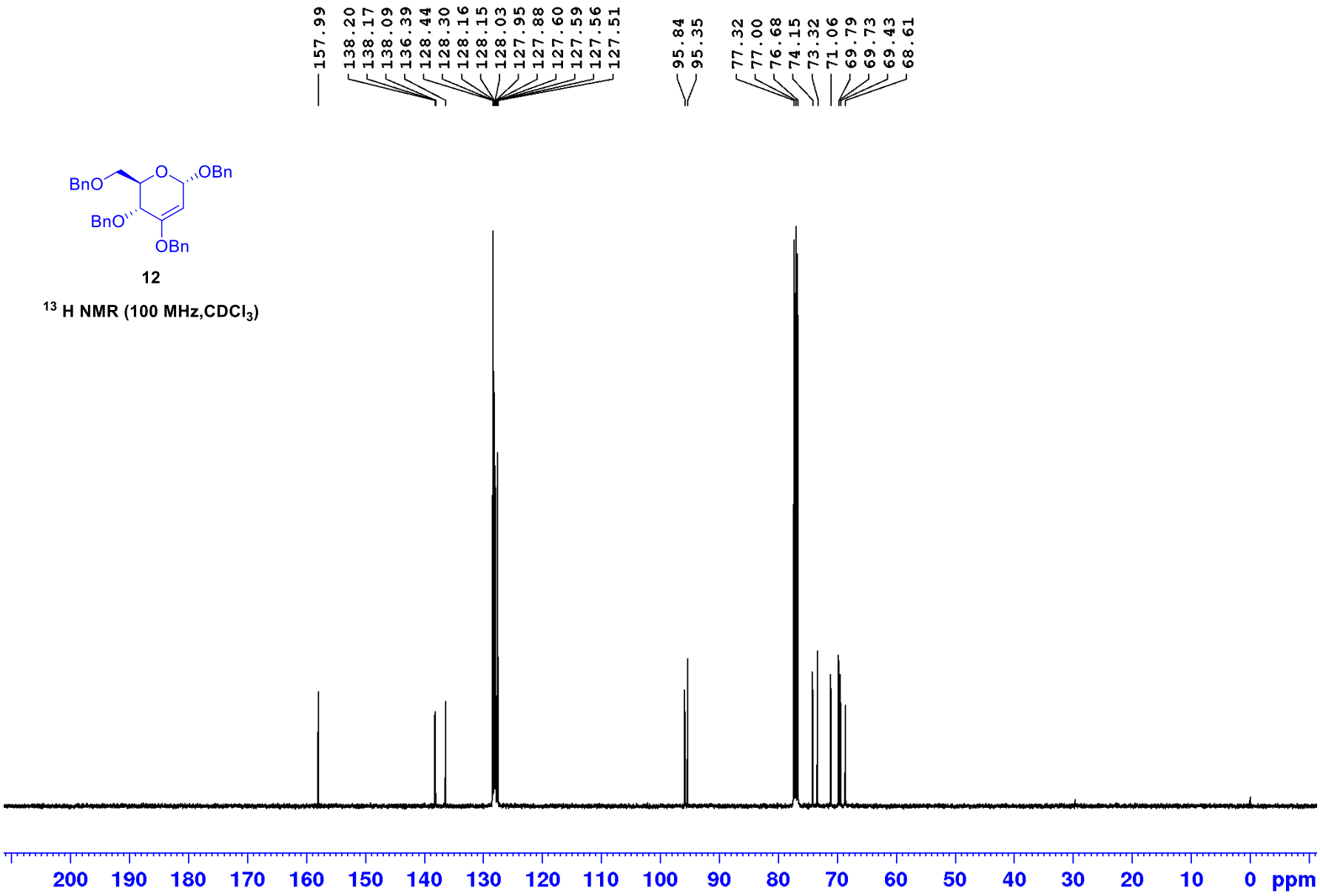




11

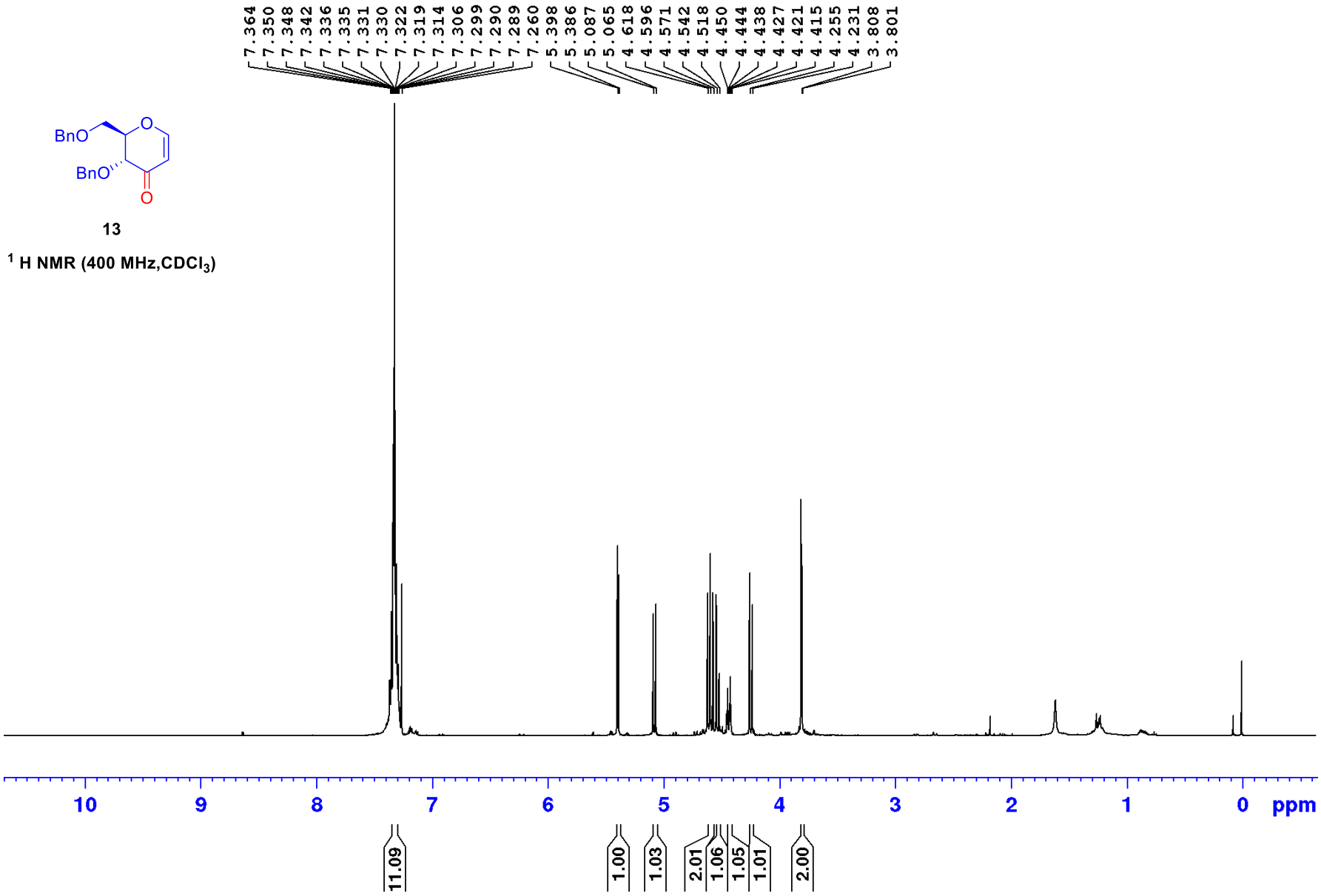
^{13}C NMR (100 MHz,$CDCl_3$)


7.387
7.382
7.379
7.377
7.375
7.362
7.358
7.347
7.344
7.338
7.329
7.325
7.314
7.312
7.307
7.300
7.297
7.292
7.289
7.281
7.275
7.270
7.266
7.211
7.202
7.192
7.187
5.374
5.365
4.962
4.954
4.935
4.908
4.882
4.845
4.813
4.784
4.692
4.661
4.648
4.619
4.540
4.510
4.487
4.459
4.357
4.333
4.253
4.248
4.244
4.239
4.230
4.224
4.220
4.215
3.763
3.754
3.737
3.727
3.659
3.654
3.632
3.627
BnO
O
OBn
BnO
OBn
12
1 H NMR (400 MHz,CDCl3)
10
9
8
7
6
5
4
3
2
1
0
ppm
20.99
1.00
3.06
2.09
2.11
2.03
0.99
1.01
1.02
1.01



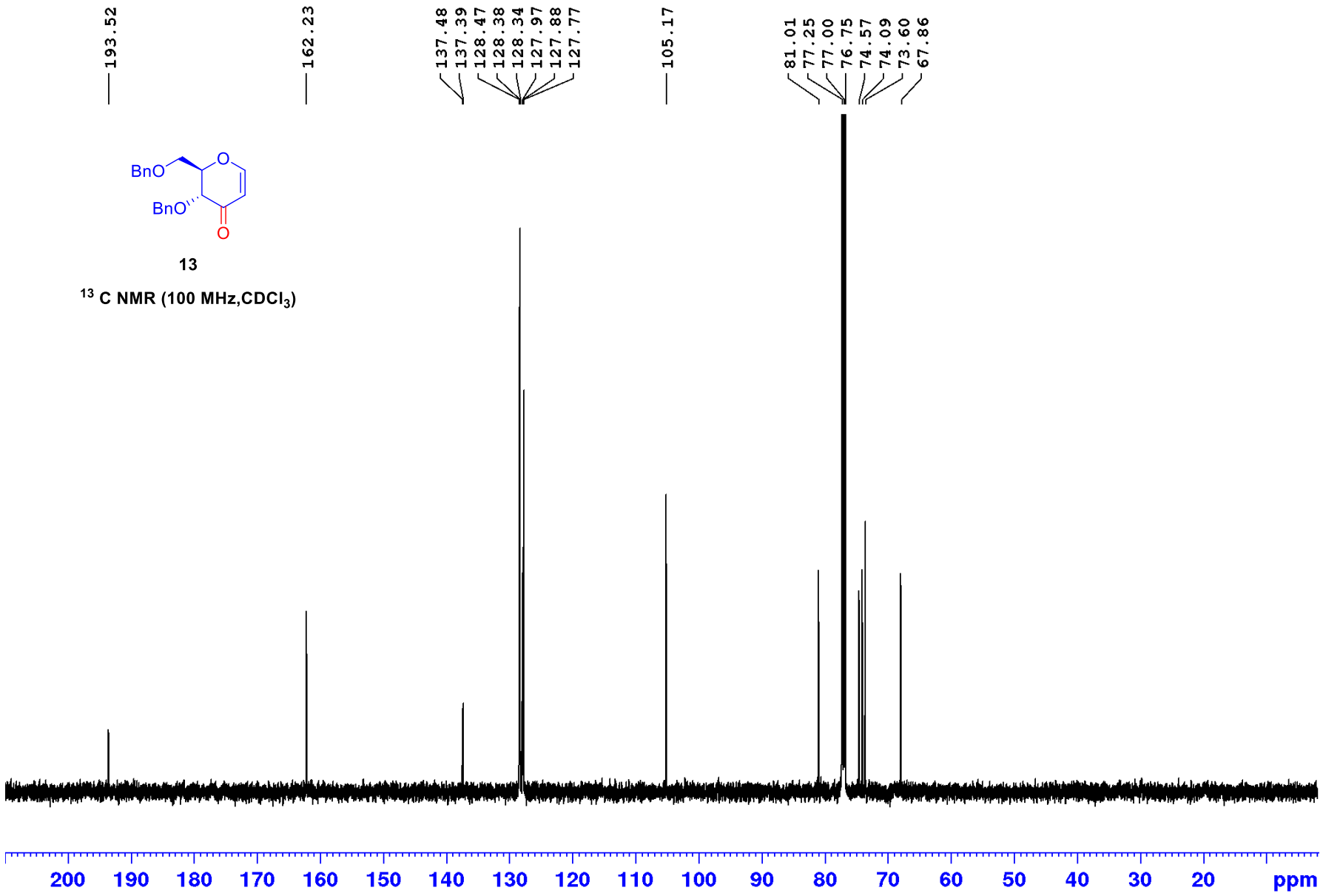
12

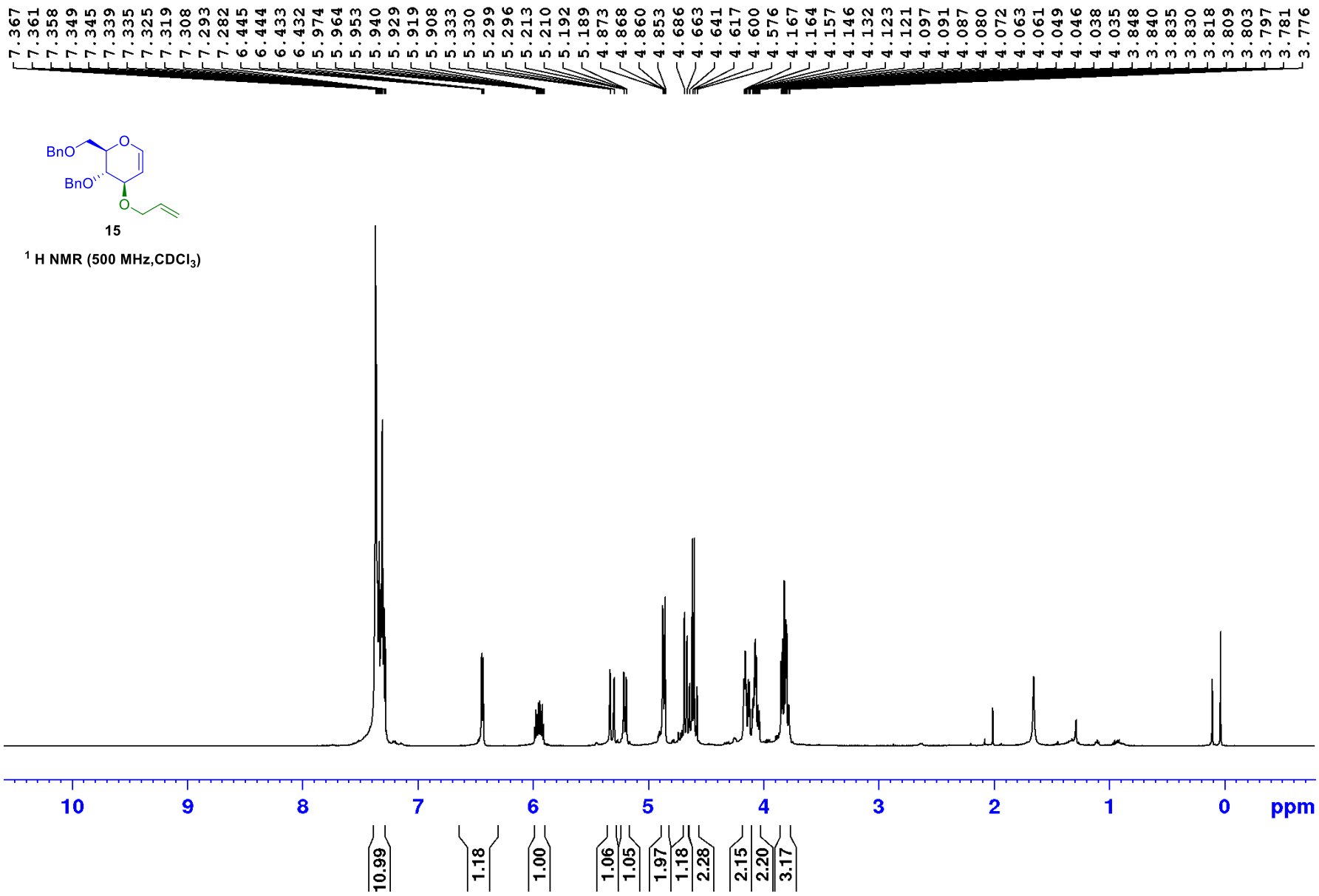
^{13} H NMR (100 MHz,$CDCl_3$)

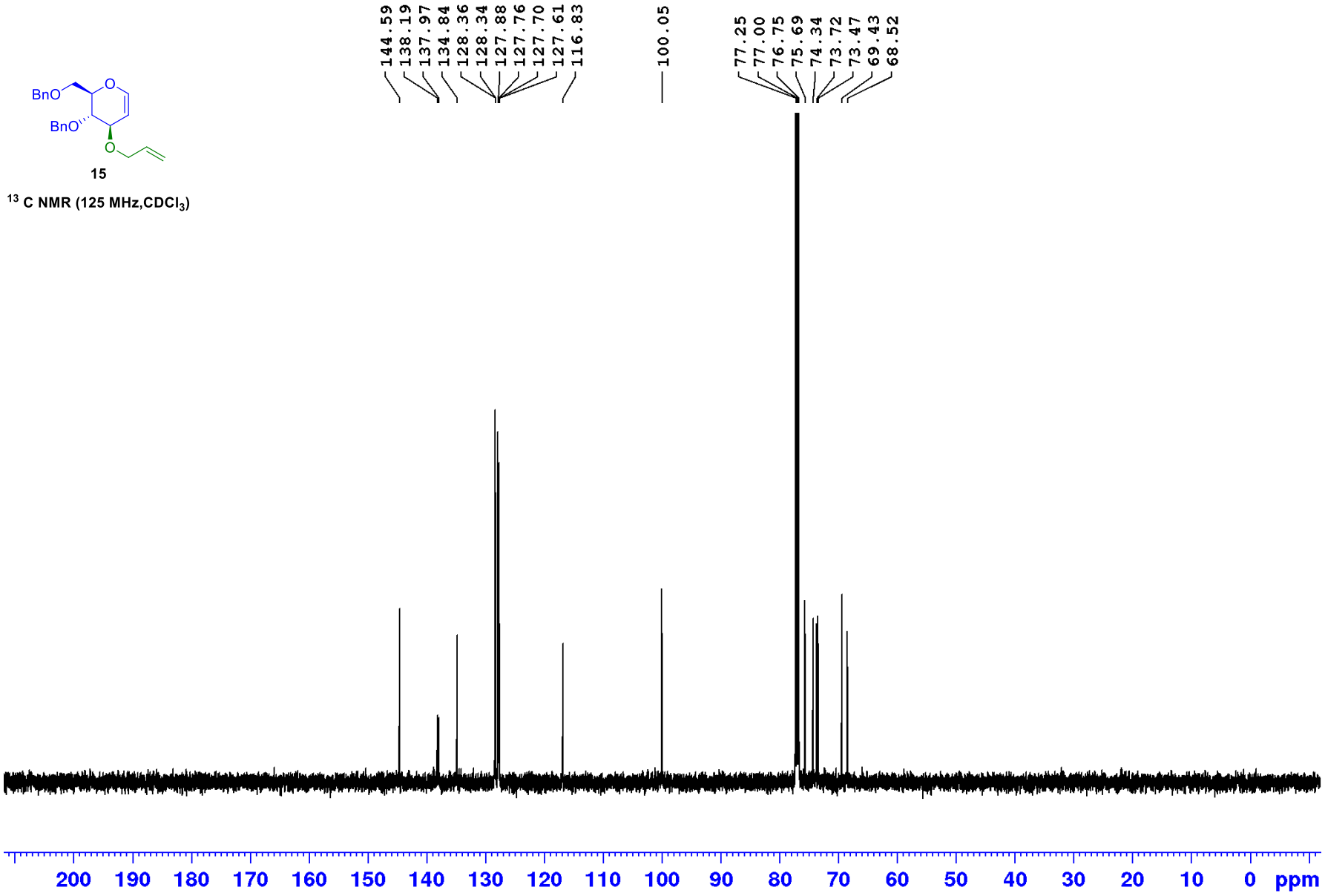


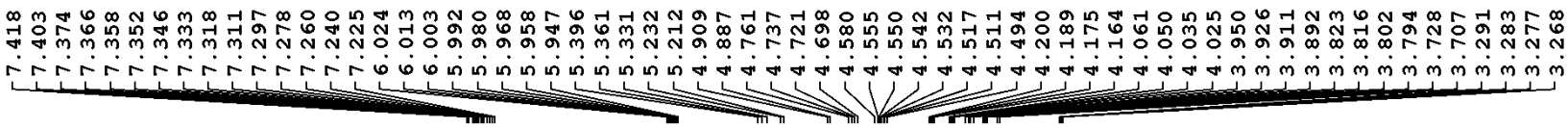
13

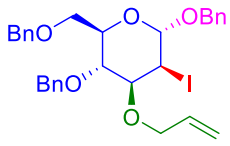
^{1}H NMR (400 MHz,$CDCl_3$)


193.52
162.23
137.48
137.39
128.47
128.38
128.34
127.97
127.88
127.77
105.17
81.01
77.25
77.00
76.75
74.57
74.09
73.60
67.86
BnO
BnO
O
O
13
13 C NMR (100 MHz,CDCl3)
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
ppm


7.367
7.361
7.358
7.349
7.345
7.339
7.335
7.325
7.319
7.308
7.293
7.282
6.445
6.444
6.433
6.432
5.974
5.964
5.953
5.940
5.929
5.919
5.908
5.333
5.330
5.299
5.296
5.213
5.210
5.192
5.189
4.873
4.868
4.860
4.853
4.686
4.663
4.641
4.617
4.600
4.576
4.167
4.164
4.157
4.146
4.132
4.123
4.121
4.097
4.091
4.087
4.080
4.072
4.063
4.061
4.049
4.046
4.038
4.035
3.848
3.840
3.835
3.830
3.818
3.809
3.803
3.797
3.781
3.776
BnO
BnO
O
O
15
1 H NMR (500 MHz,CDCl3)
10
9
8
7
6
5
4
3
2
1
0
ppm
10.99
1.18
1.00
1.06
1.05
1.97
1.18
2.28
2.15
2.20
3.17

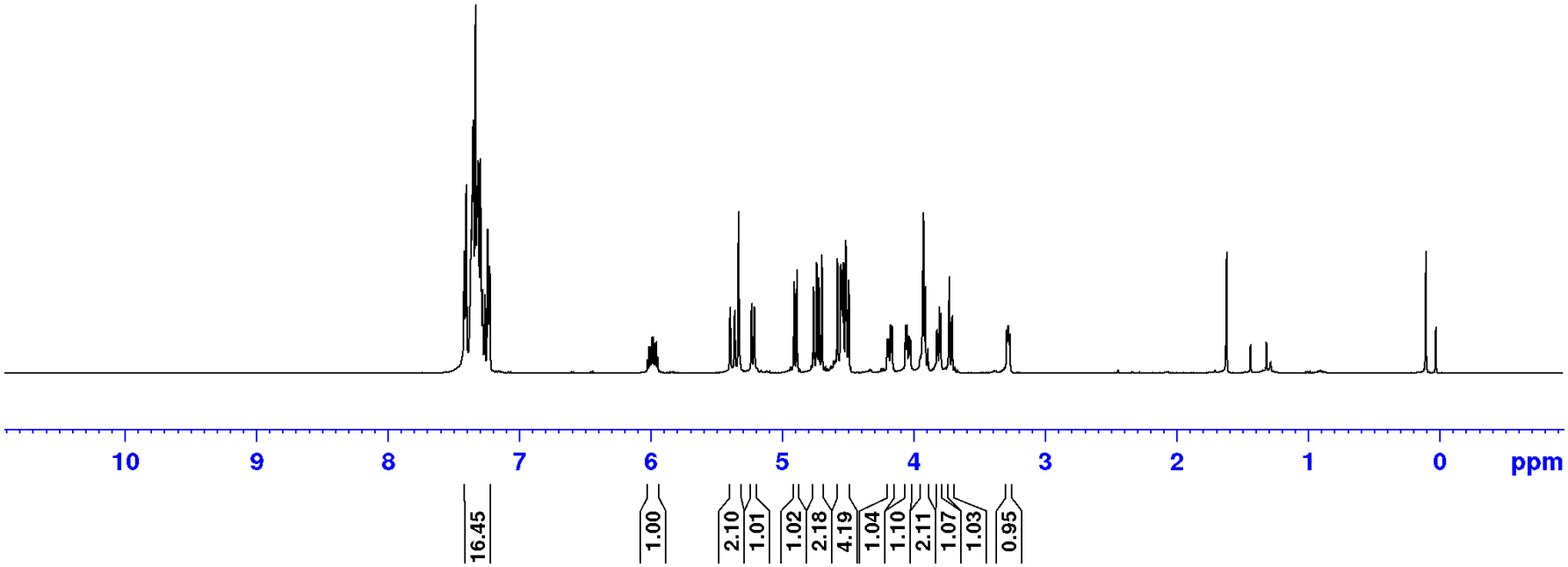

BnO
BnO
O
O
15
13 C NMR (125 MHz,CDCl3)
144.59
138.19
137.97
134.84
128.36
128.34
127.88
127.76
127.70
127.61
116.83
100.05
77.25
77.00
76.75
75.69
74.34
73.72
73.47
69.43
68.52
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm

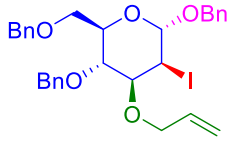




16

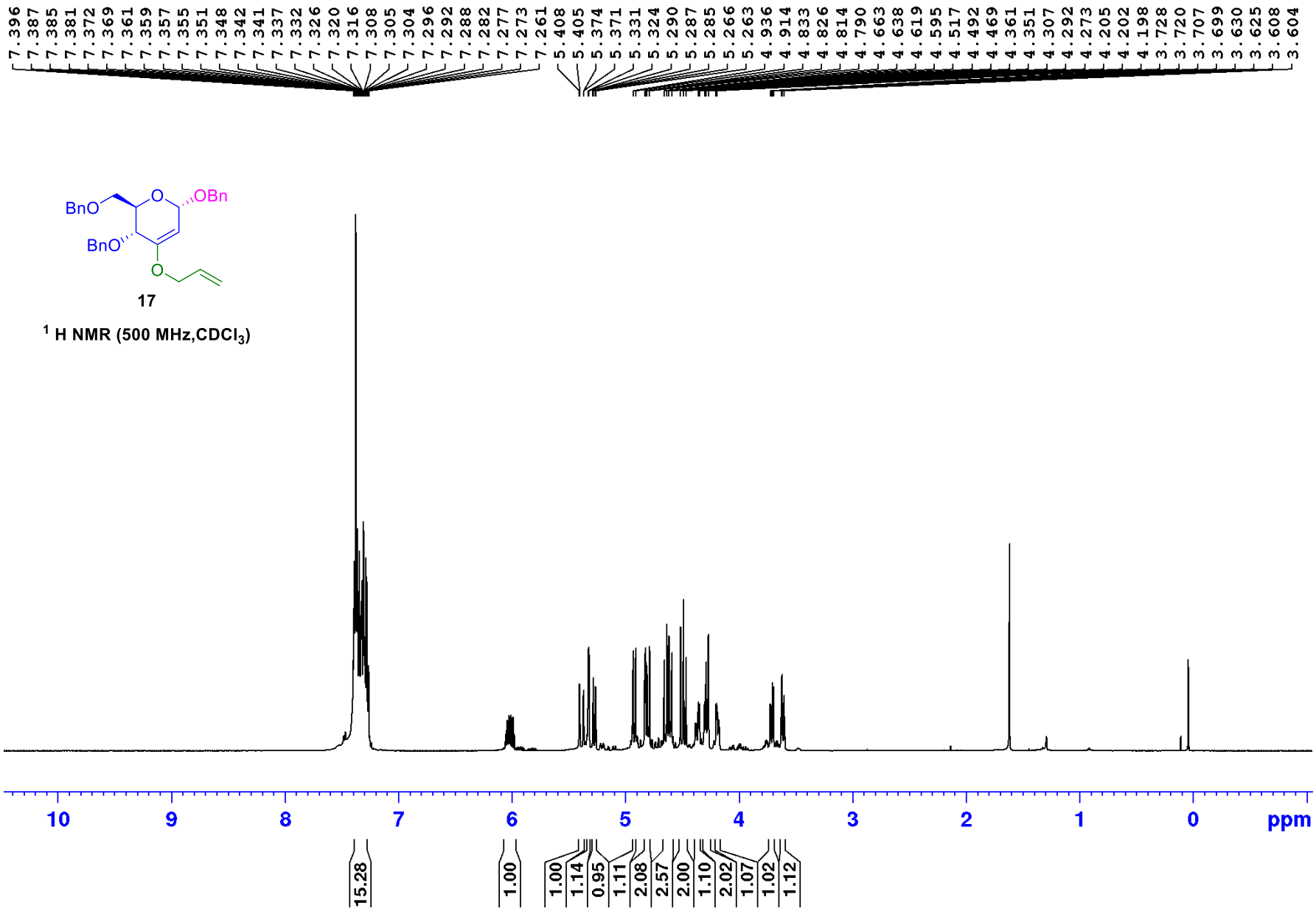
^{1}H NMR (500 MHz,$CDCl_3$)

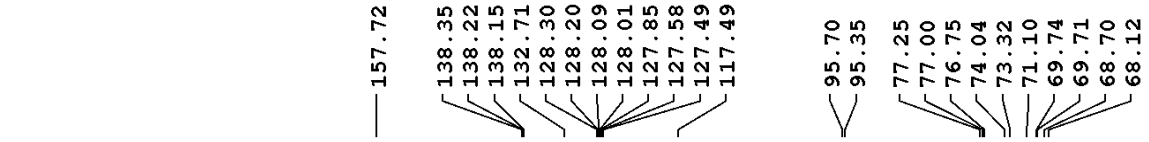


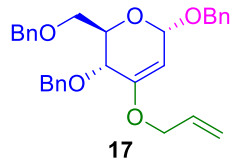


16

^{13} C NMR (125 MHz,$CDCl_3$)

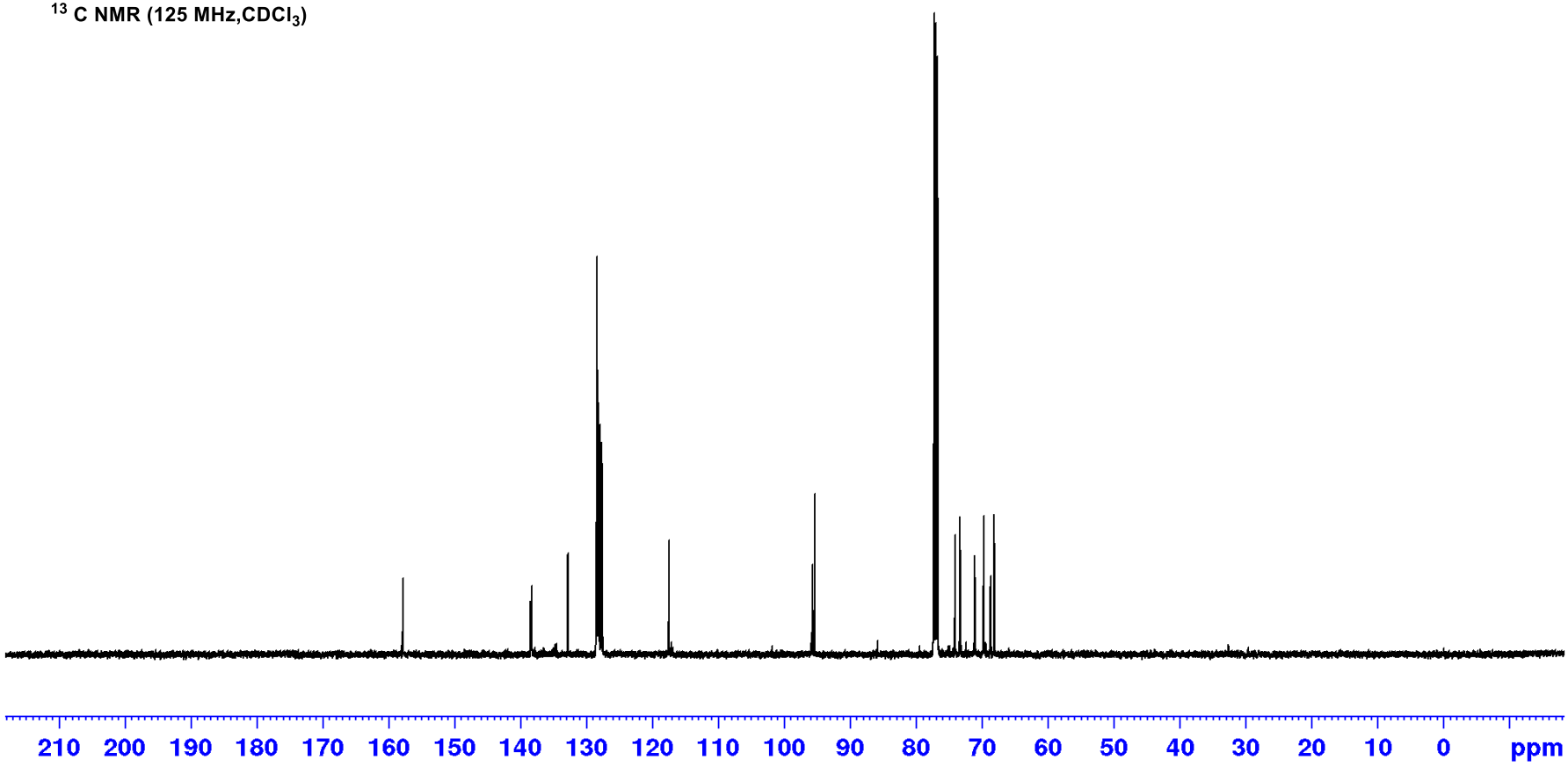

7.396
7.387
7.385
7.381
7.372
7.369
7.361
7.359
7.357
7.355
7.351
7.348
7.342
7.341
7.337
7.332
7.326
7.320
7.316
7.308
7.305
7.304
7.296
7.292
7.288
7.282
7.277
7.273
7.261
5.408
5.405
5.374
5.371
5.331
5.324
5.290
5.287
5.285
5.266
5.263
4.936
4.914
4.833
4.826
4.814
4.790
4.663
4.638
4.619
4.595
4.517
4.492
4.469
4.361
4.351
4.307
4.292
4.273
4.205
4.202
4.198
3.728
3.720
3.707
3.699
3.630
3.625
3.608
3.604
BnO
OBn
BnO
O
O
17
1 H NMR (500 MHz,CDCl3)
10
9
8
7
6
5
4
3
2
1
0
ppm
15.28
1.00
1.00
1.14
0.95
1.11
2.08
2.57
2.00
1.10
2.02
1.07
1.02
1.12

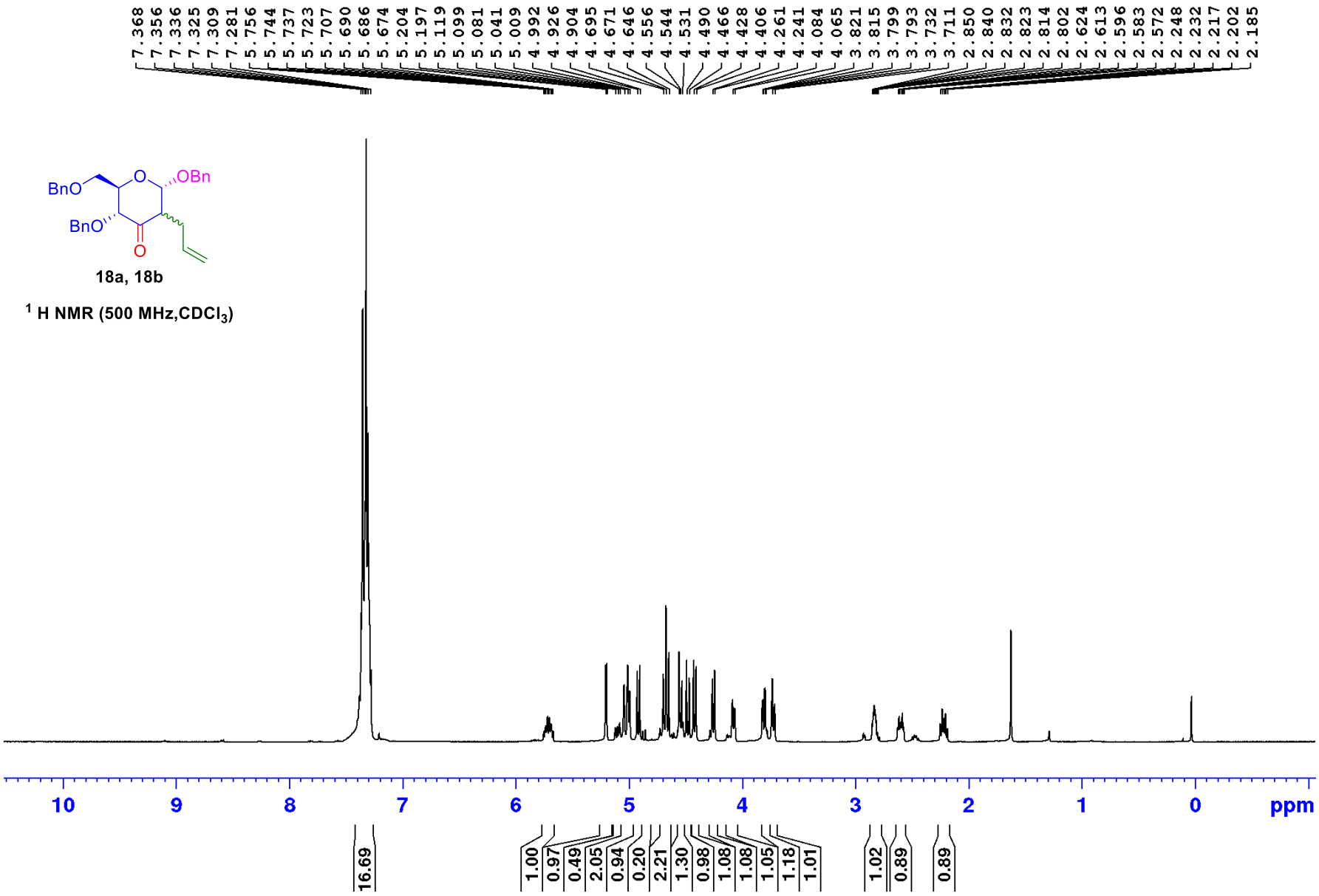


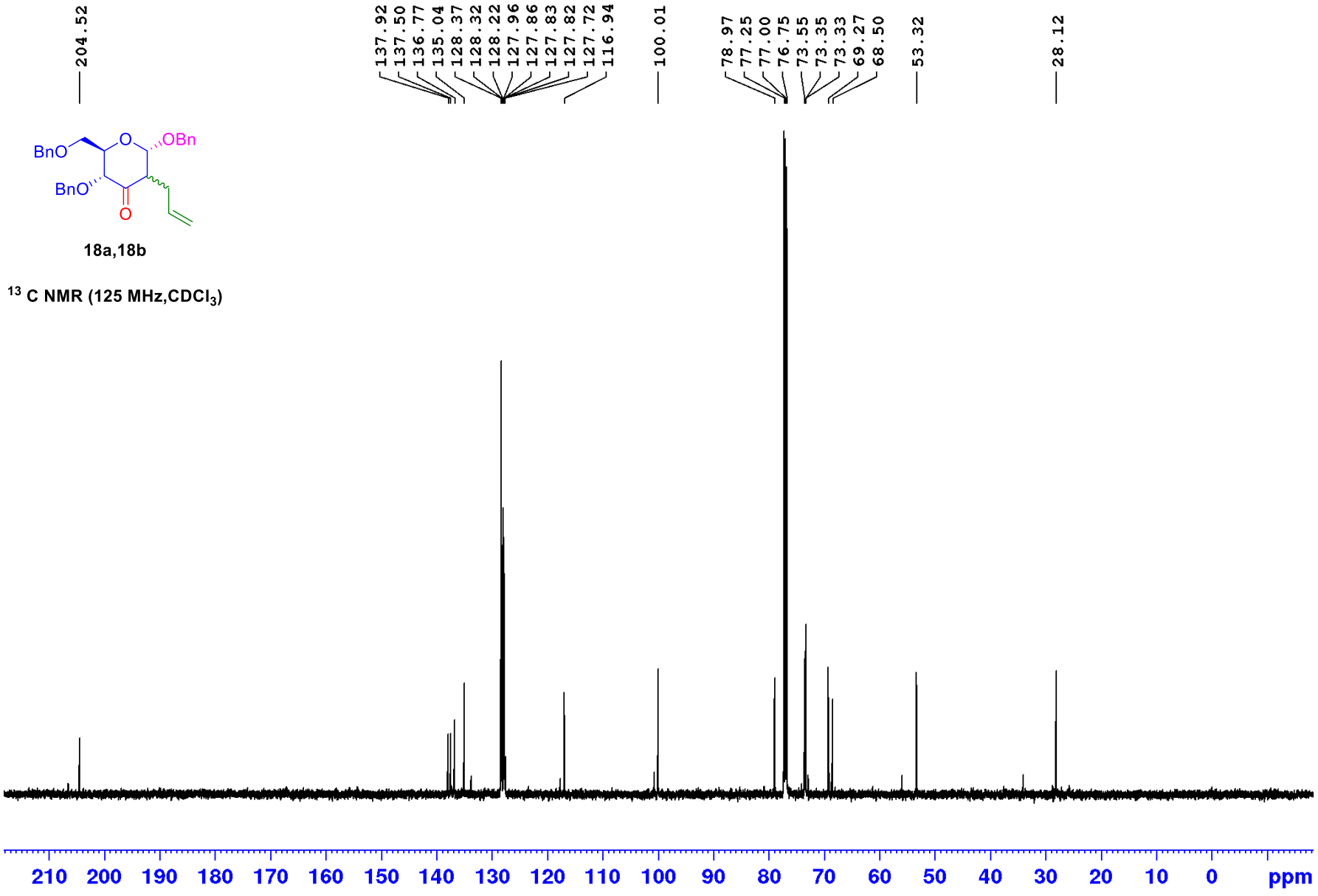


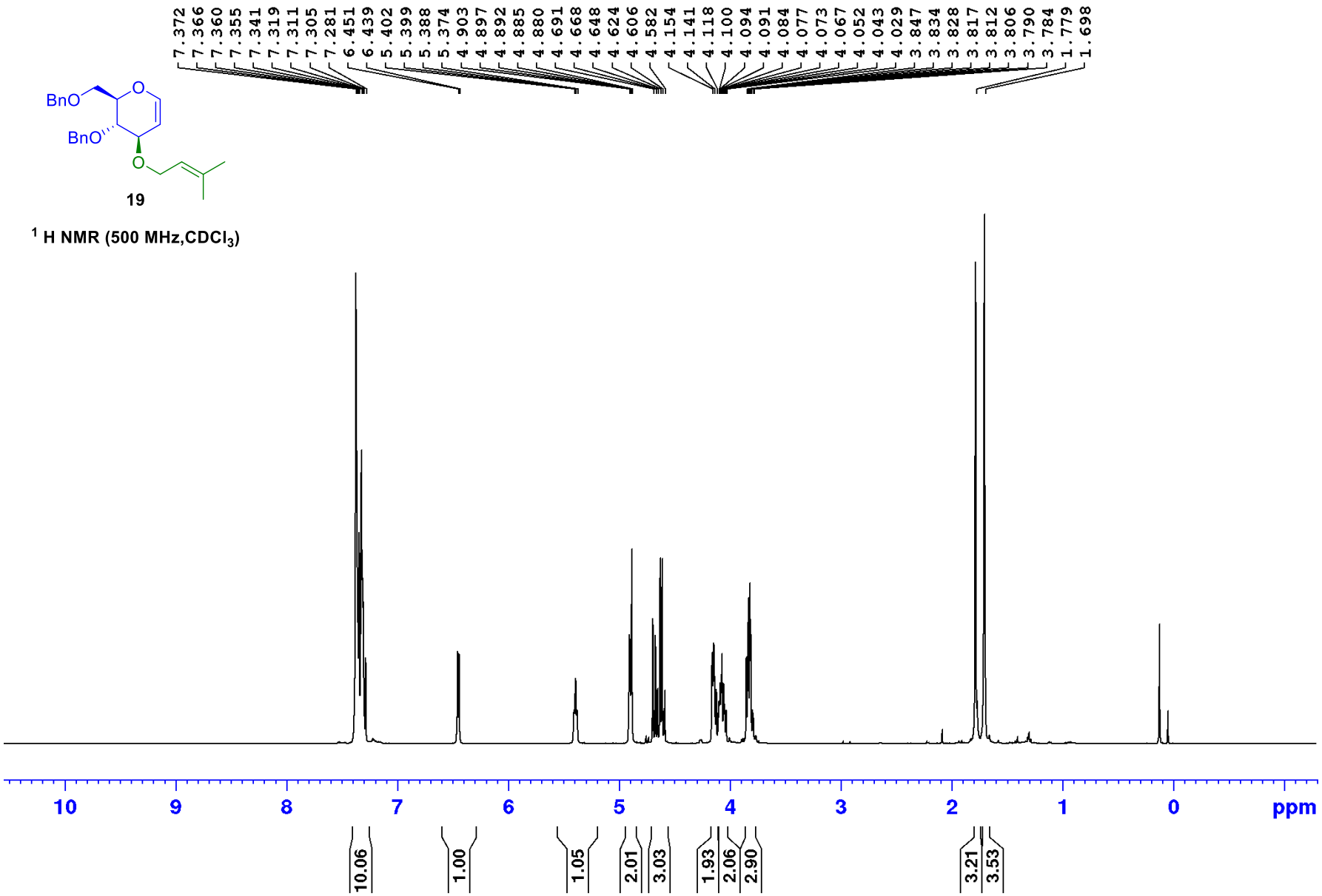
17

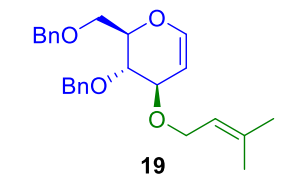
^{13} C NMR (125 MHz,$CDCl_3$)




7.368
7.356
7.336
7.325
7.309
7.281
5.756
5.744
5.737
5.723
5.707
5.690
5.686
5.674
5.204
5.197
5.119
5.099
5.081
5.041
5.009
4.992
4.926
4.904
4.695
4.671
4.646
4.556
4.544
4.531
4.490
4.466
4.428
4.406
4.261
4.241
4.084
4.065
3.821
3.815
3.799
3.793
3.732
3.711
2.850
2.840
2.832
2.823
2.814
2.802
2.624
2.613
2.596
2.583
2.572
2.248
2.232
2.217
2.202
2.185
BnO
OBn
BnO
O
O
18a, 18b
1 H NMR (500 MHz,CDCl3)
10
9
8
7
6
5
4
3
2
1
0
ppm
16.69
1.00
0.97
0.49
2.05
0.94
0.20
2.21
1.30
0.98
1.08
1.08
1.05
1.18
1.01
1.02
0.89
0.89

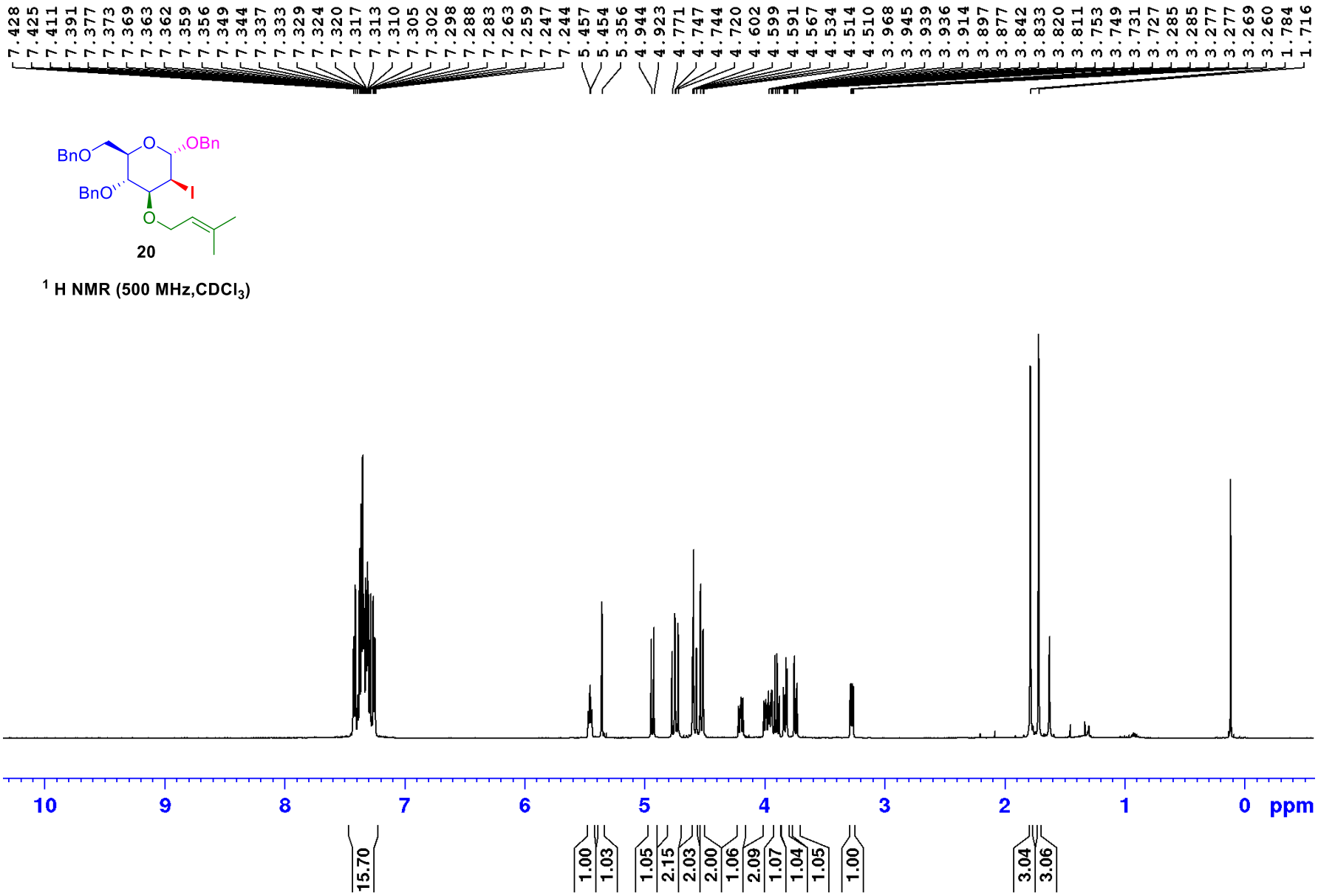

204.52
137.92
137.50
136.77
135.04
128.37
128.32
128.22
127.96
127.86
127.83
127.82
127.72
116.94
100.01
78.97
77.25
77.00
76.75
73.55
73.35
73.33
69.27
68.50
53.32
28.12
BnO
OBn
BnO
O
O
18a,18b
13 C NMR (125 MHz,CDCl3)
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm

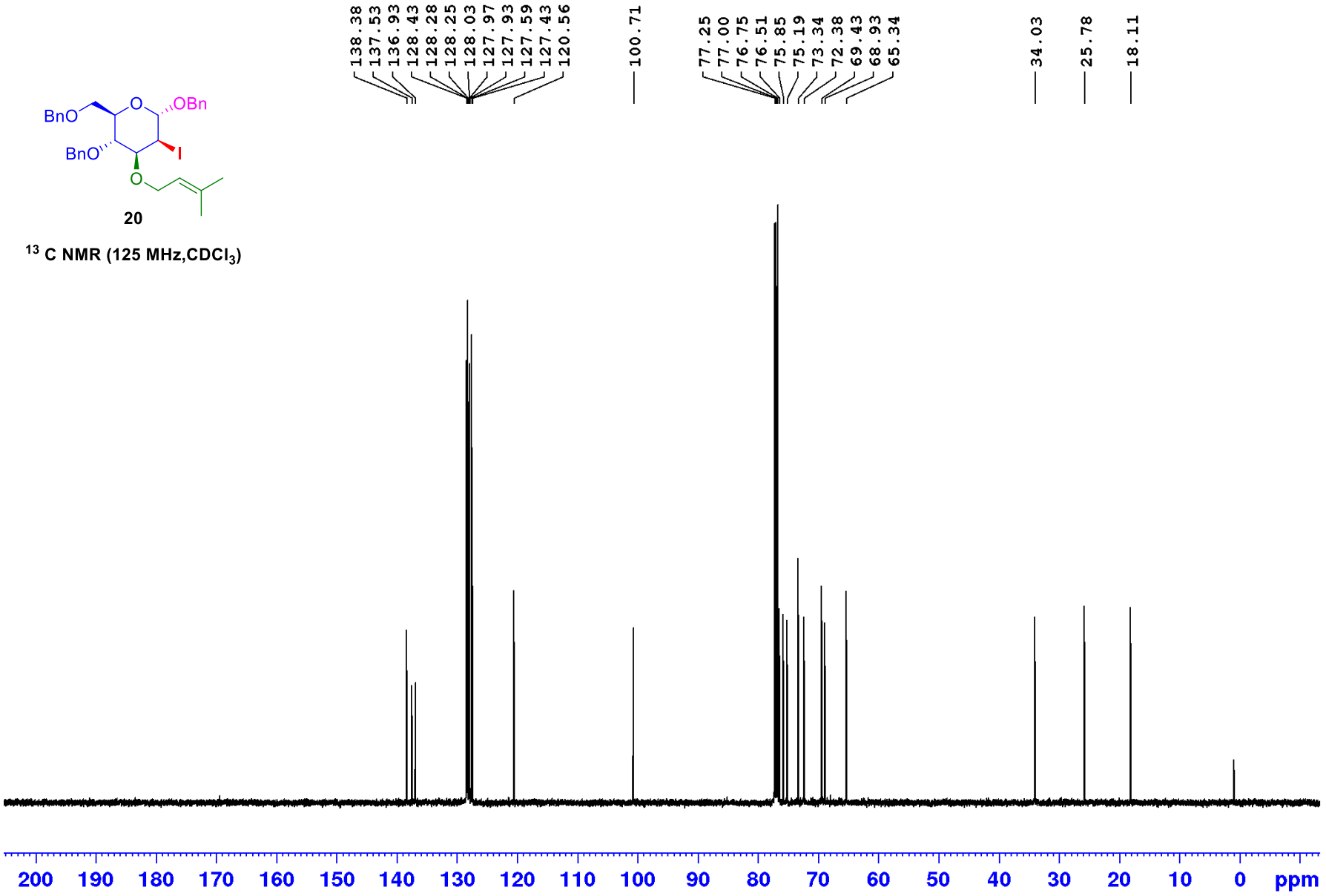

7.372
7.366
7.360
7.355
7.341
7.319
7.311
7.305
7.281
6.451
6.439
5.402
5.399
5.388
5.374
4.903
4.897
4.892
4.885
4.880
4.691
4.668
4.648
4.624
4.606
4.582
4.154
4.141
4.118
4.100
4.094
4.091
4.084
4.077
4.073
4.067
4.052
4.043
4.029
3.847
3.834
3.828
3.817
3.812
3.806
3.790
3.784
1.779
1.698
BnO
BnO
O
O
19
1 H NMR (500 MHz,CDCl3)
10
9
8
7
6
5
4
3
2
1
0
ppm
10.06
1.00
1.05
2.01
3.03
1.93
2.06
2.90
3.21
3.53



19

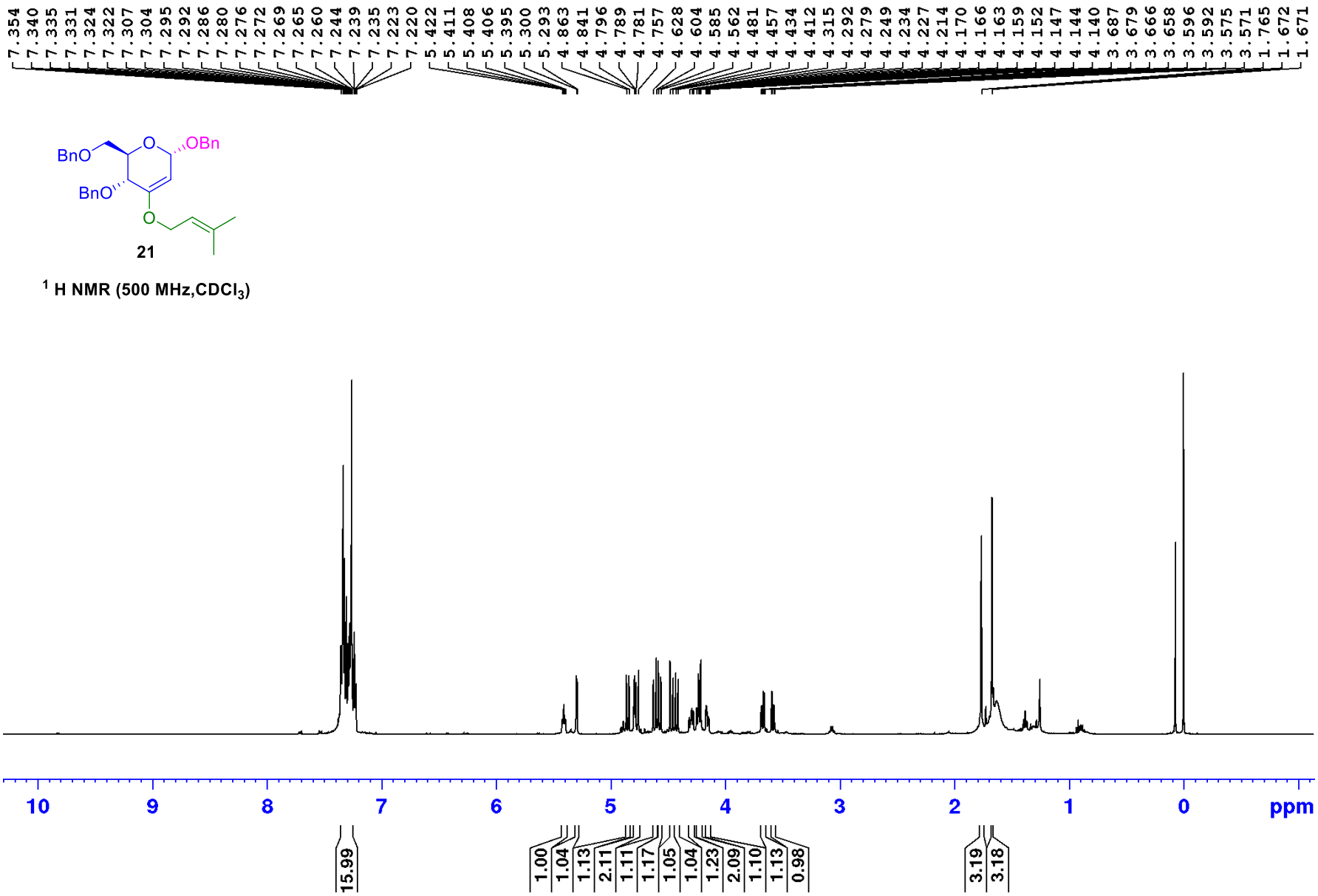
^{13} C NMR (125 MHz,$CDCl_3$)


7.428
7.425
7.411
7.391
7.377
7.373
7.369
7.363
7.362
7.359
7.356
7.349
7.344
7.337
7.333
7.329
7.324
7.320
7.317
7.313
7.310
7.305
7.302
7.298
7.288
7.283
7.263
7.259
7.247
7.244
5.457
5.454
5.356
4.944
4.923
4.771
4.747
4.744
4.720
4.602
4.599
4.591
4.567
4.534
4.514
4.510
3.968
3.945
3.939
3.936
3.914
3.897
3.877
3.842
3.833
3.820
3.811
3.753
3.749
3.731
3.727
3.285
3.285
3.277
3.277
3.269
3.260
1.784
1.716
BnO
O
OBn
BnO
I
O
20
1 H NMR (500 MHz,CDCl3)
10
9
8
7
6
5
4
3
2
1
0
ppm
15.70
1.00
1.03
1.05
2.15
2.03
2.00
1.06
2.09
1.07
1.04
1.05
1.00
3.04
3.06



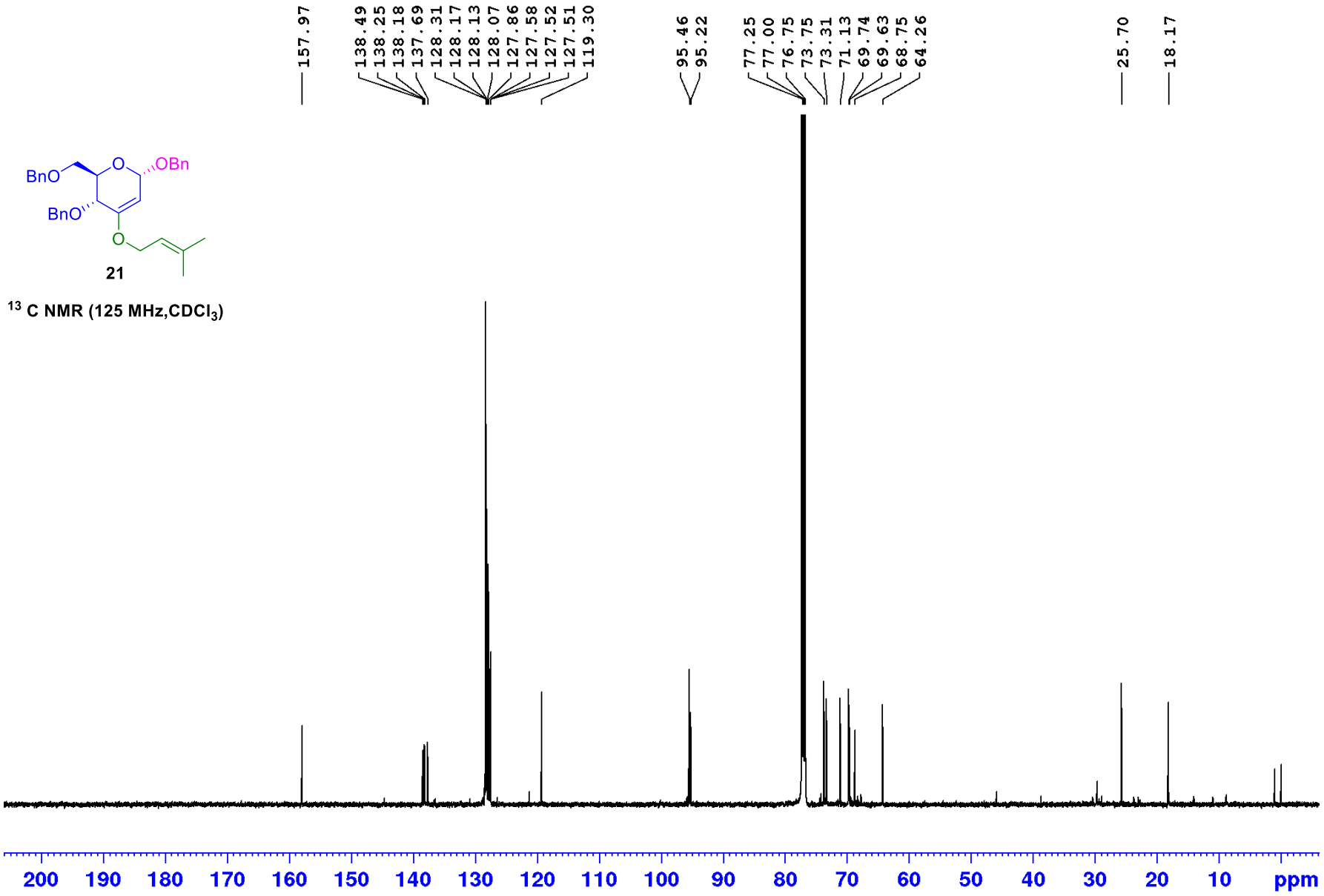
20

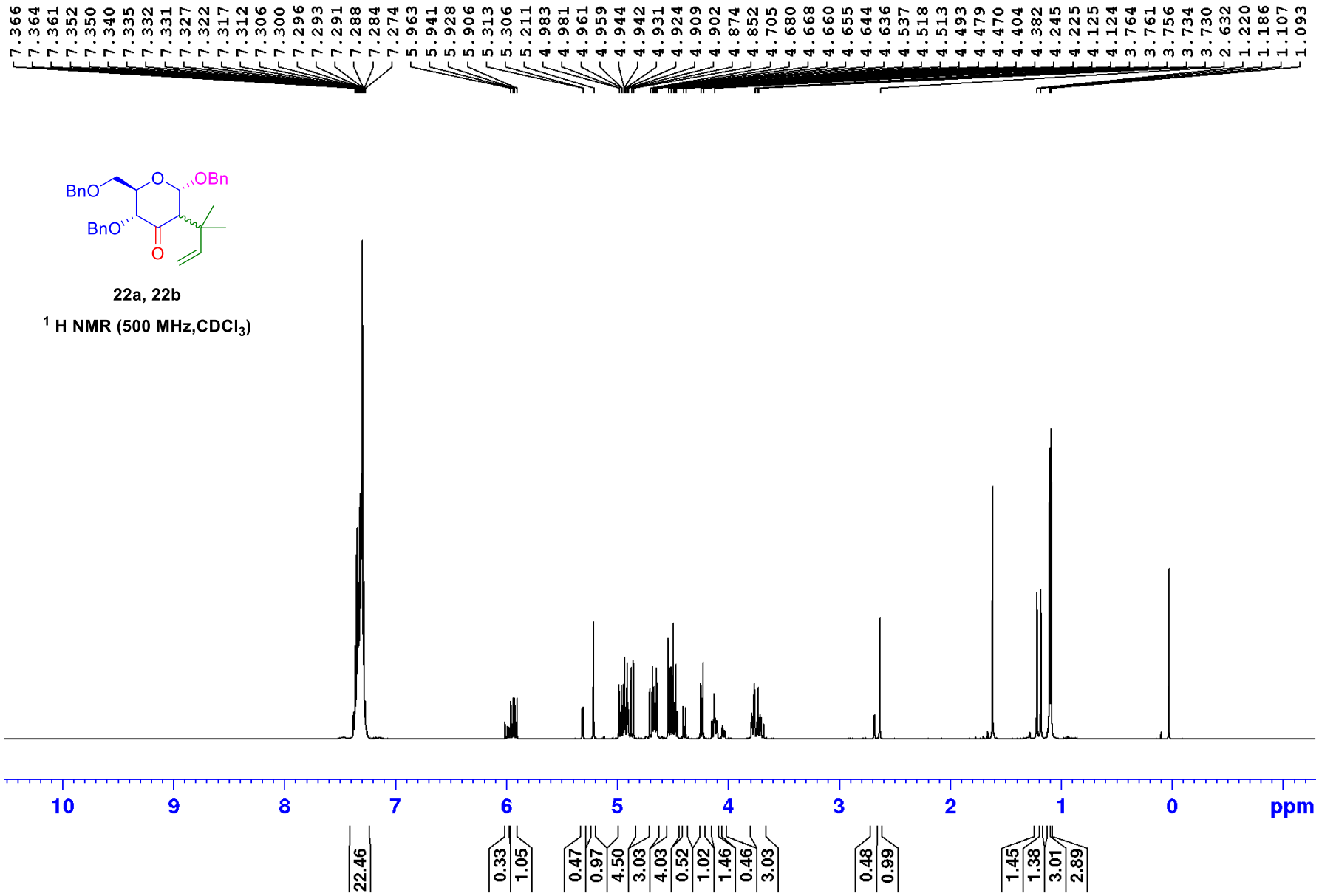
^{13}C NMR (125 MHz,$CDCl_3$)

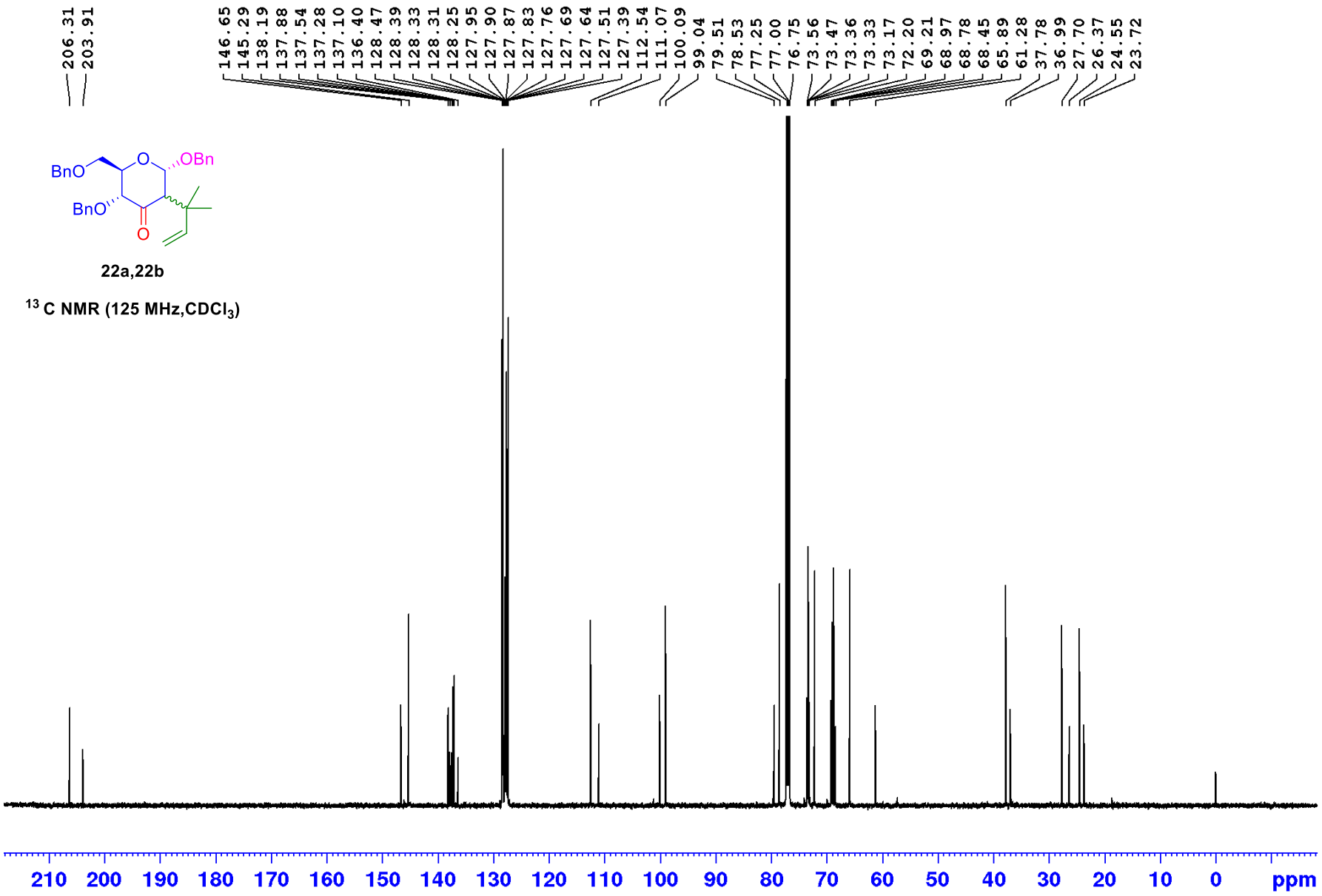


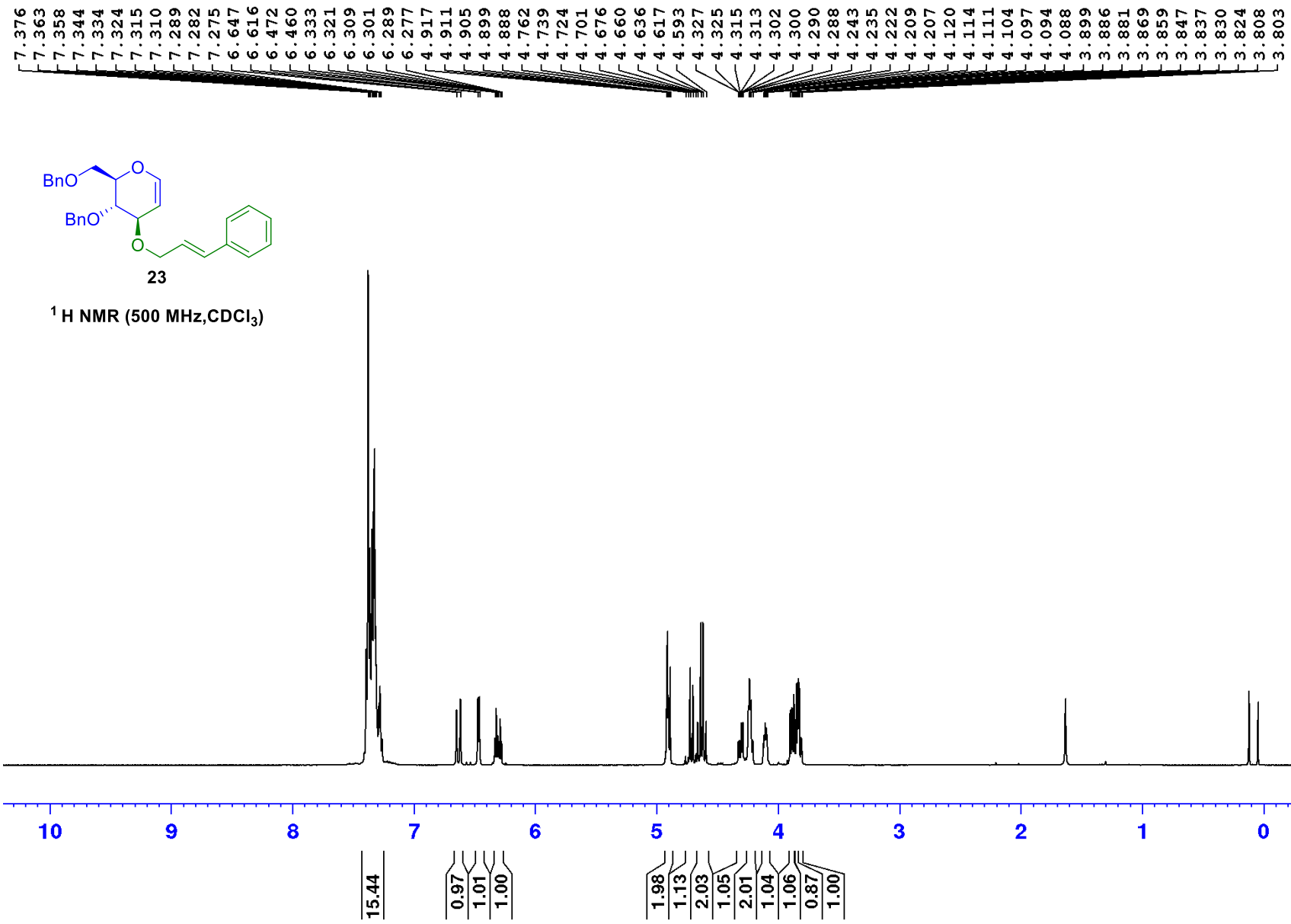
21

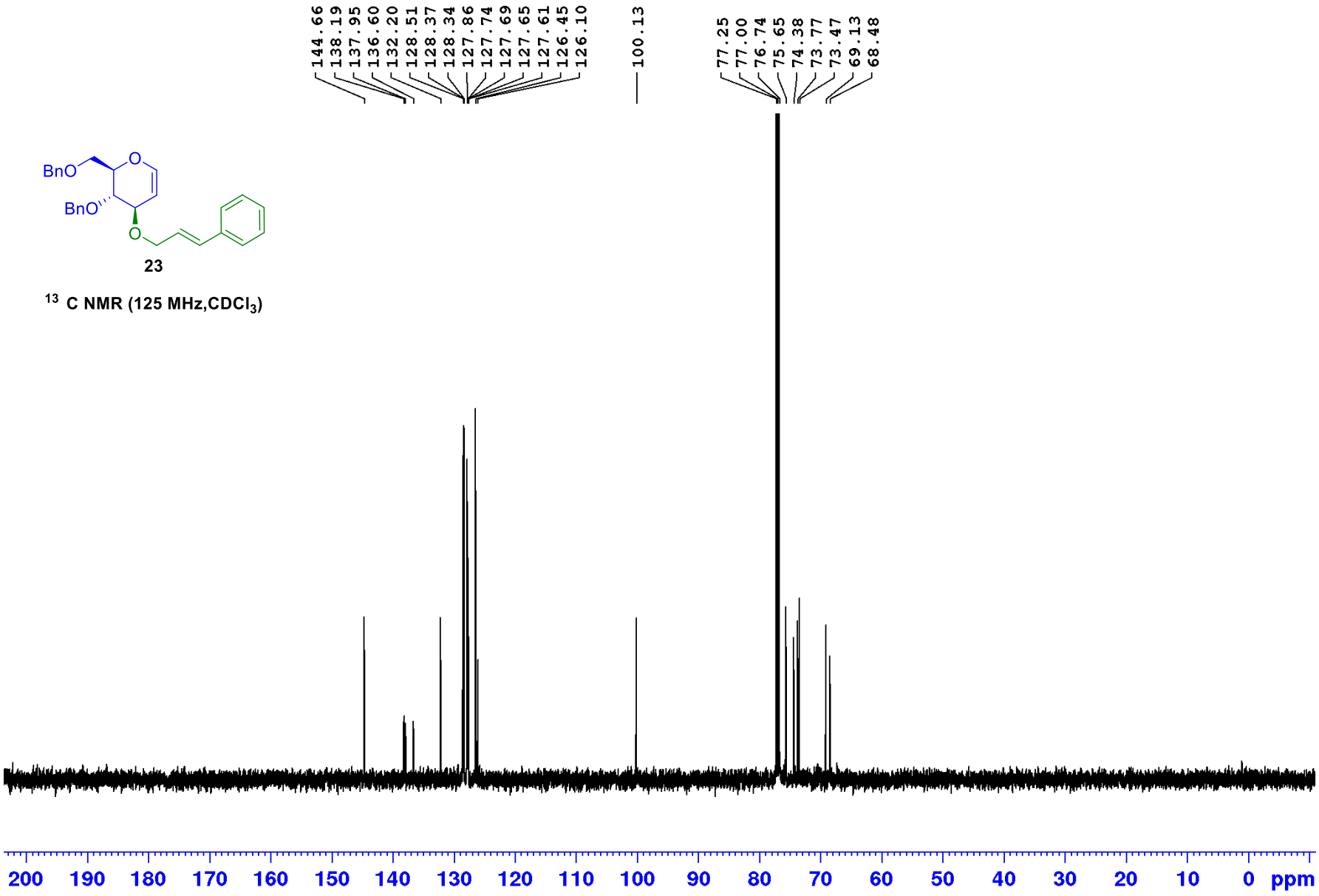
^{1} H NMR (500 MHz,$CDCl_3$)


157.97
138.49
138.25
138.18
137.69
128.31
128.17
128.13
128.07
127.86
127.58
127.52
127.51
119.30
95.46
95.22
77.25
77.00
76.75
73.75
73.31
71.13
69.74
69.63
68.75
64.26
25.70
18.17
BnO
OBn
BnO
O
O
21
13 C NMR (125 MHz,CDCl3)
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm


7.366
7.364
7.361
7.352
7.350
7.340
7.335
7.332
7.331
7.327
7.322
7.317
7.312
7.306
7.300
7.296
7.293
7.291
7.288
7.284
7.274
5.963
5.941
5.928
5.906
5.313
5.306
5.211
4.983
4.981
4.961
4.959
4.944
4.942
4.931
4.924
4.909
4.902
4.874
4.852
4.705
4.680
4.668
4.660
4.655
4.644
4.636
4.537
4.518
4.513
4.493
4.479
4.470
4.404
4.382
4.245
4.225
4.125
4.124
3.764
3.761
3.756
3.734
3.730
2.632
1.220
1.186
1.107
1.093
BnO
BnO
O
OBn
O
22a, 22b
1 H NMR (500 MHz,CDCl3)
10
9
8
7
6
5
4
3
2
1
0
ppm
22.46
0.33
1.05
0.47
0.97
4.50
3.03
4.03
0.52
1.02
1.46
0.46
3.03
0.48
0.99
1.45
1.38
3.01
2.89

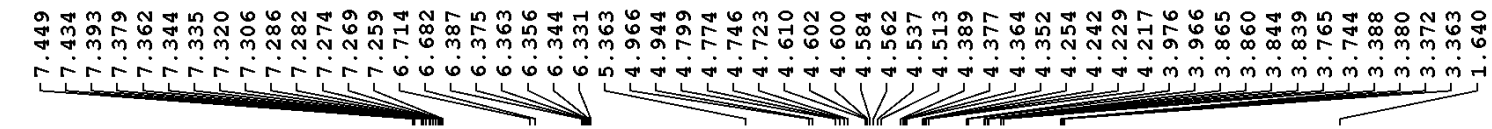

206.31
203.91
146.65
145.29
138.19
137.88
137.54
137.28
137.10
136.40
128.47
128.39
128.33
128.31
128.25
127.95
127.90
127.87
127.83
127.76
127.69
127.64
127.51
127.39
112.54
111.07
100.09
99.04
79.51
78.53
77.25
77.00
76.75
73.56
73.47
73.36
73.33
73.17
72.20
69.21
68.97
68.78
68.45
65.89
61.28
37.78
36.99
27.70
26.37
24.55
23.72
BnO
OBn
BnO
O
O
22a,22b
13 C NMR (125 MHz,CDCl3)
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
ppm

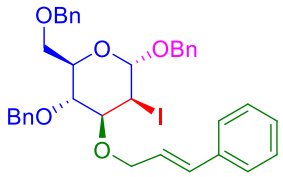

7.376
7.363
7.358
7.344
7.334
7.324
7.315
7.310
7.289
7.282
7.275
6.647
6.616
6.472
6.460
6.333
6.321
6.309
6.301
6.289
6.277
4.917
4.911
4.905
4.899
4.888
4.762
4.739
4.724
4.701
4.676
4.660
4.636
4.617
4.593
4.327
4.325
4.315
4.313
4.302
4.300
4.290
4.288
4.243
4.235
4.222
4.209
4.207
4.120
4.114
4.111
4.104
4.097
4.094
4.088
3.899
3.886
3.881
3.869
3.859
3.847
3.837
3.830
3.824
3.808
3.803
BnO
BnO
O
O
23
1 H NMR (500 MHz,CDCl3)
10
9
8
7
6
5
4
3
2
1
0
ppm
15.44
0.97
1.01
1.00
1.98
1.13
2.03
1.05
2.01
1.04
1.06
0.87
1.00



23

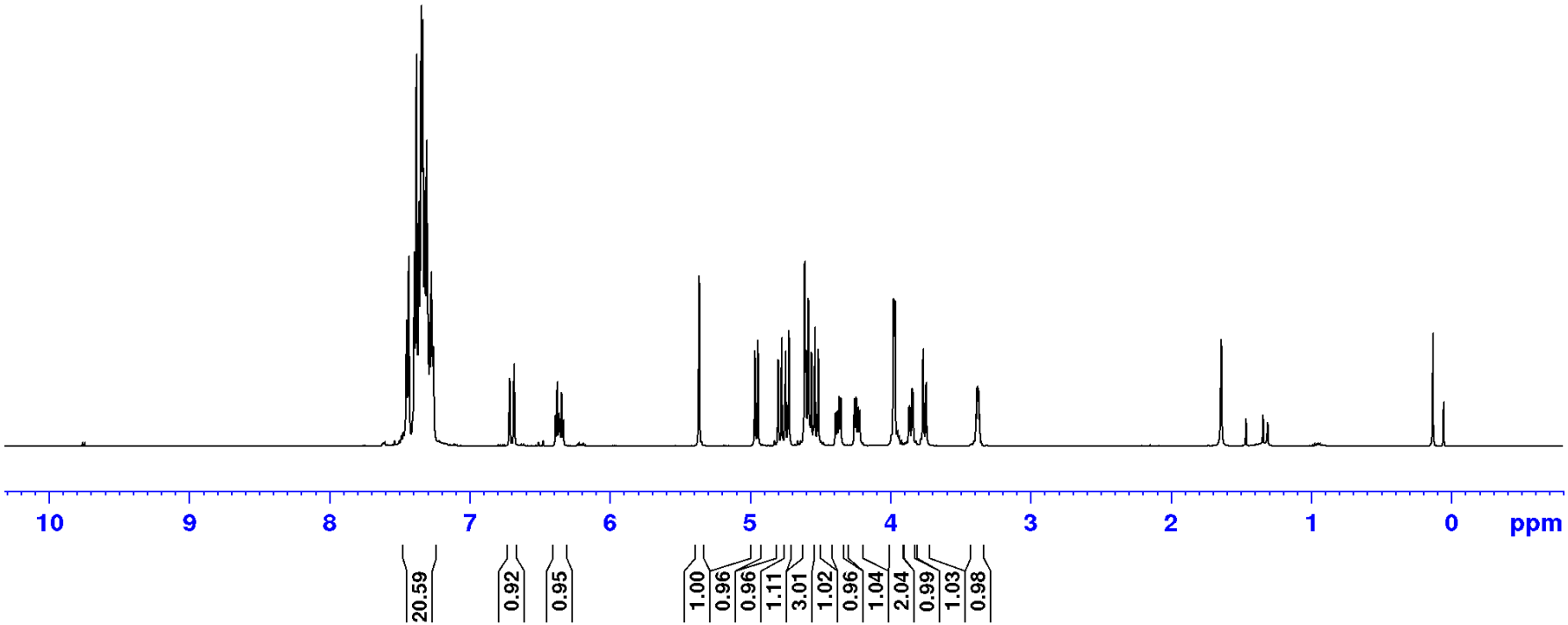
^{13} C NMR (125 MHz,$CDCl_3$)

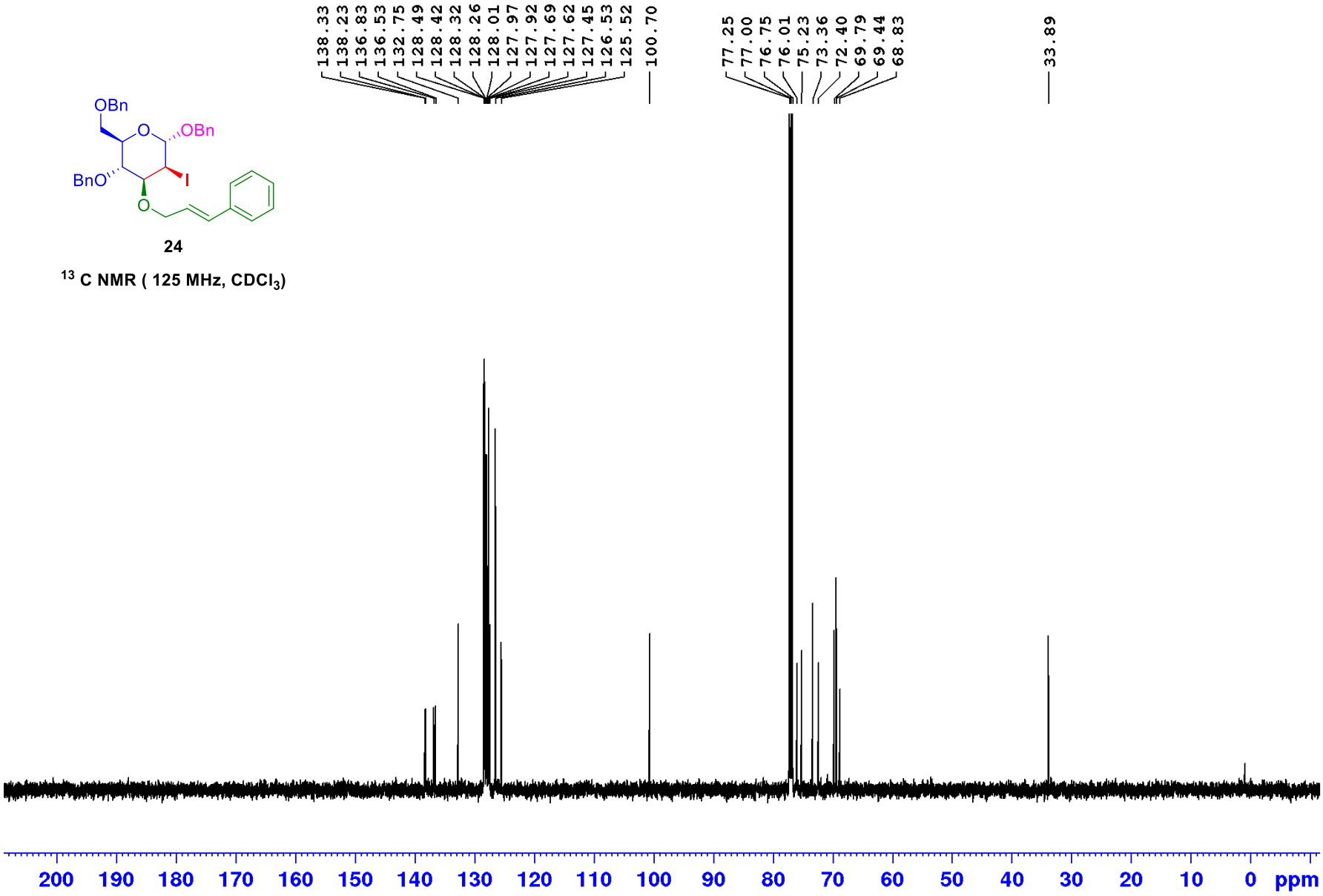




24

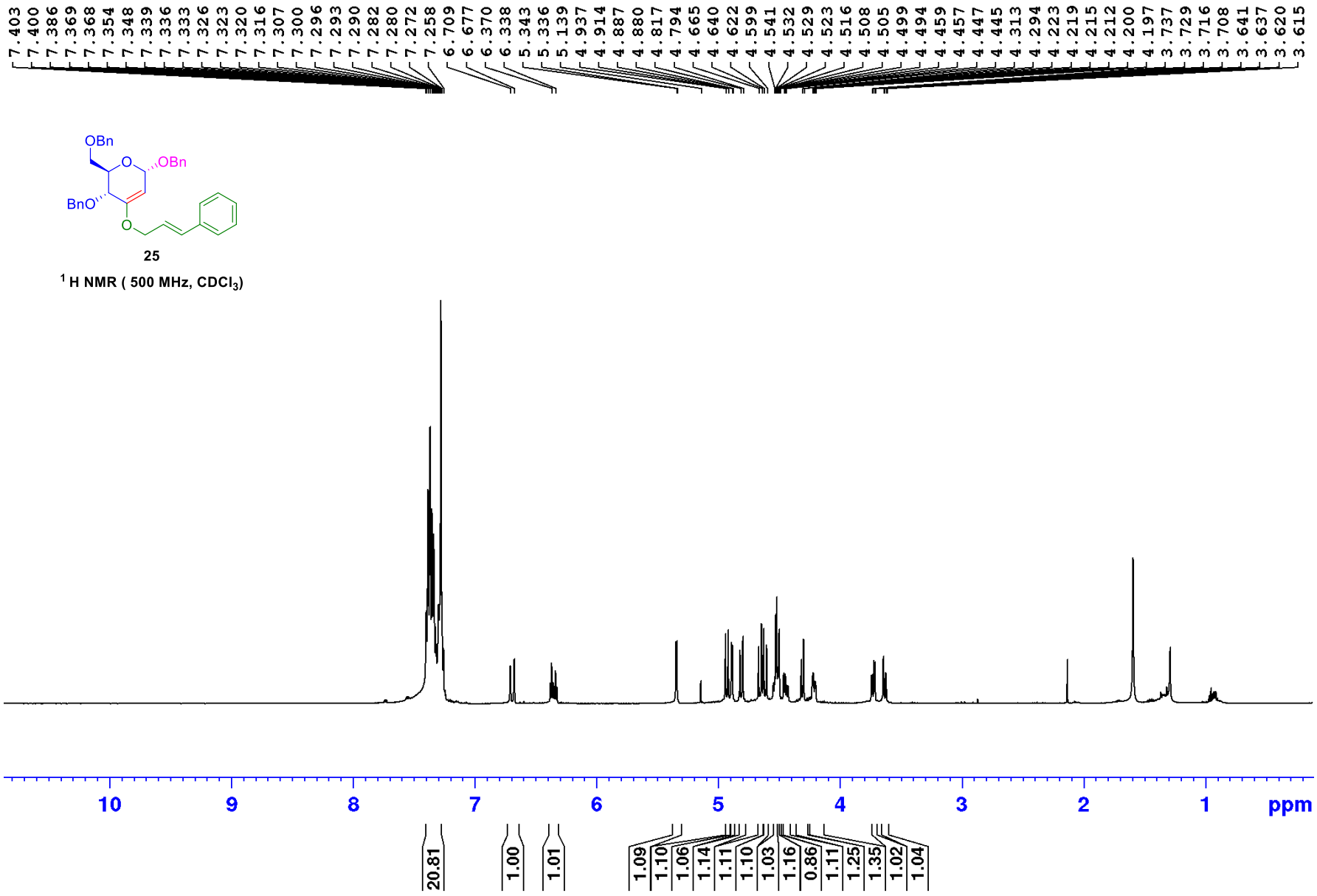
^{1}H NMR (500 MHz,$CDCl_3$)

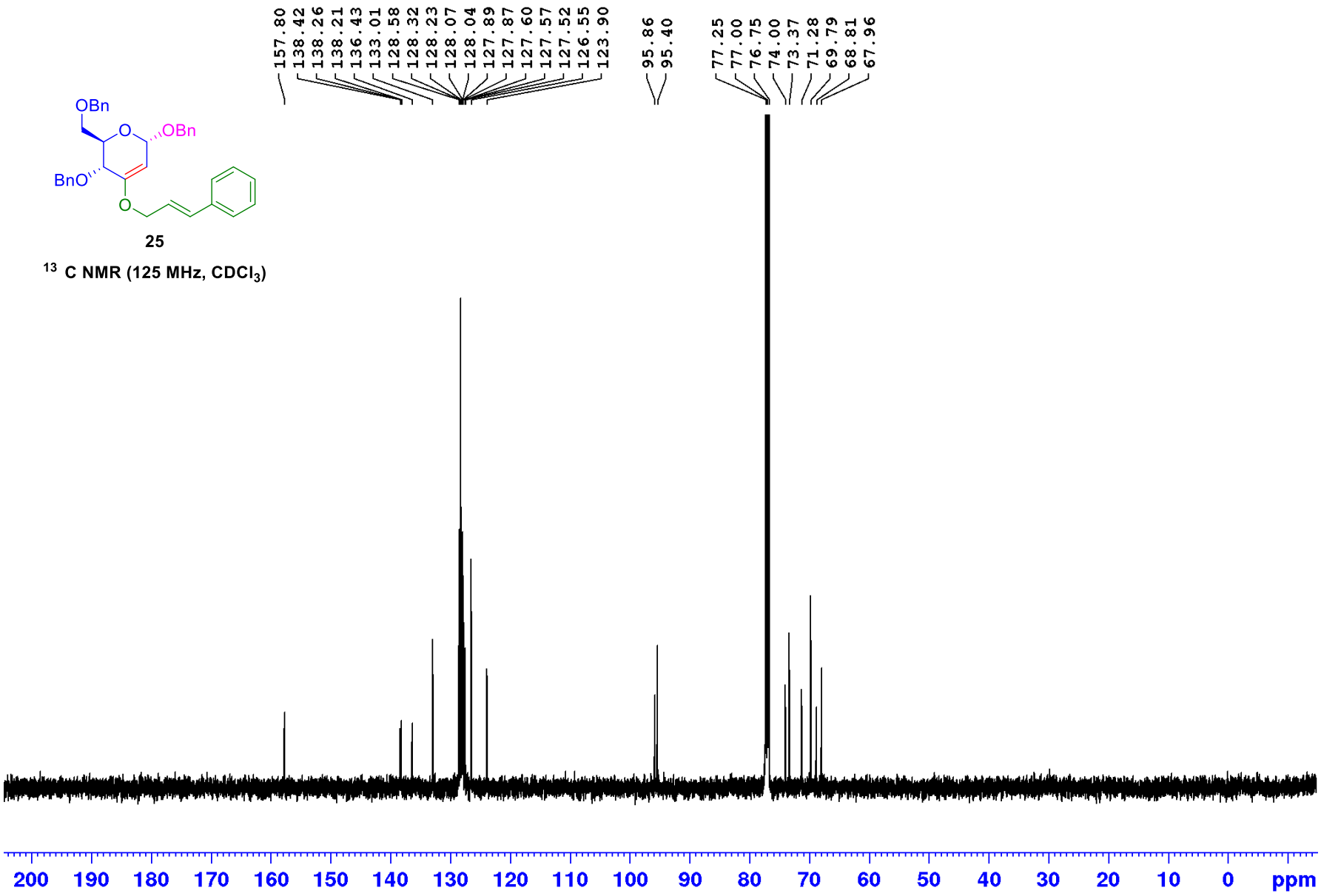




24

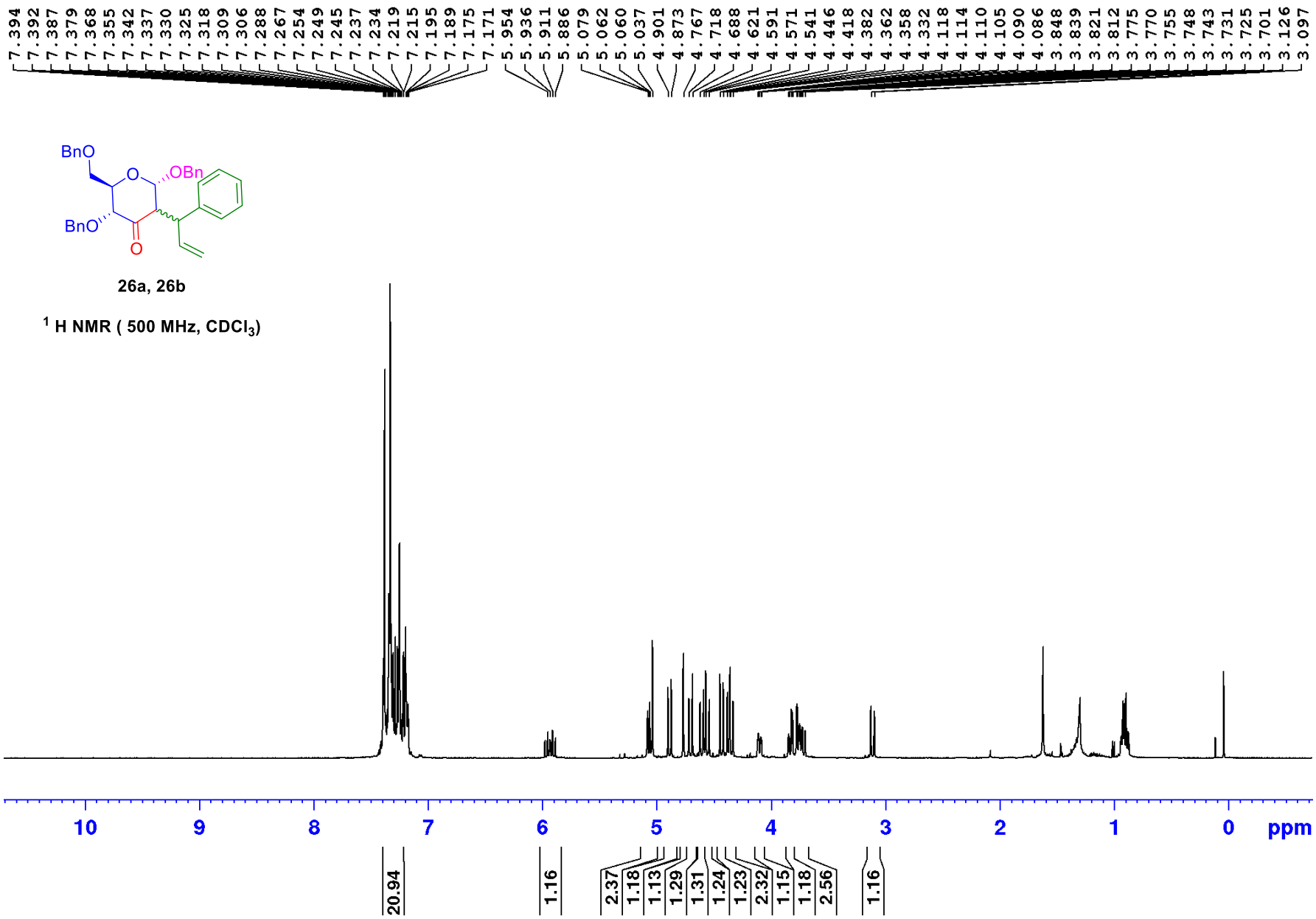
^{13} C NMR (125 MHz, $CDCl_3$)

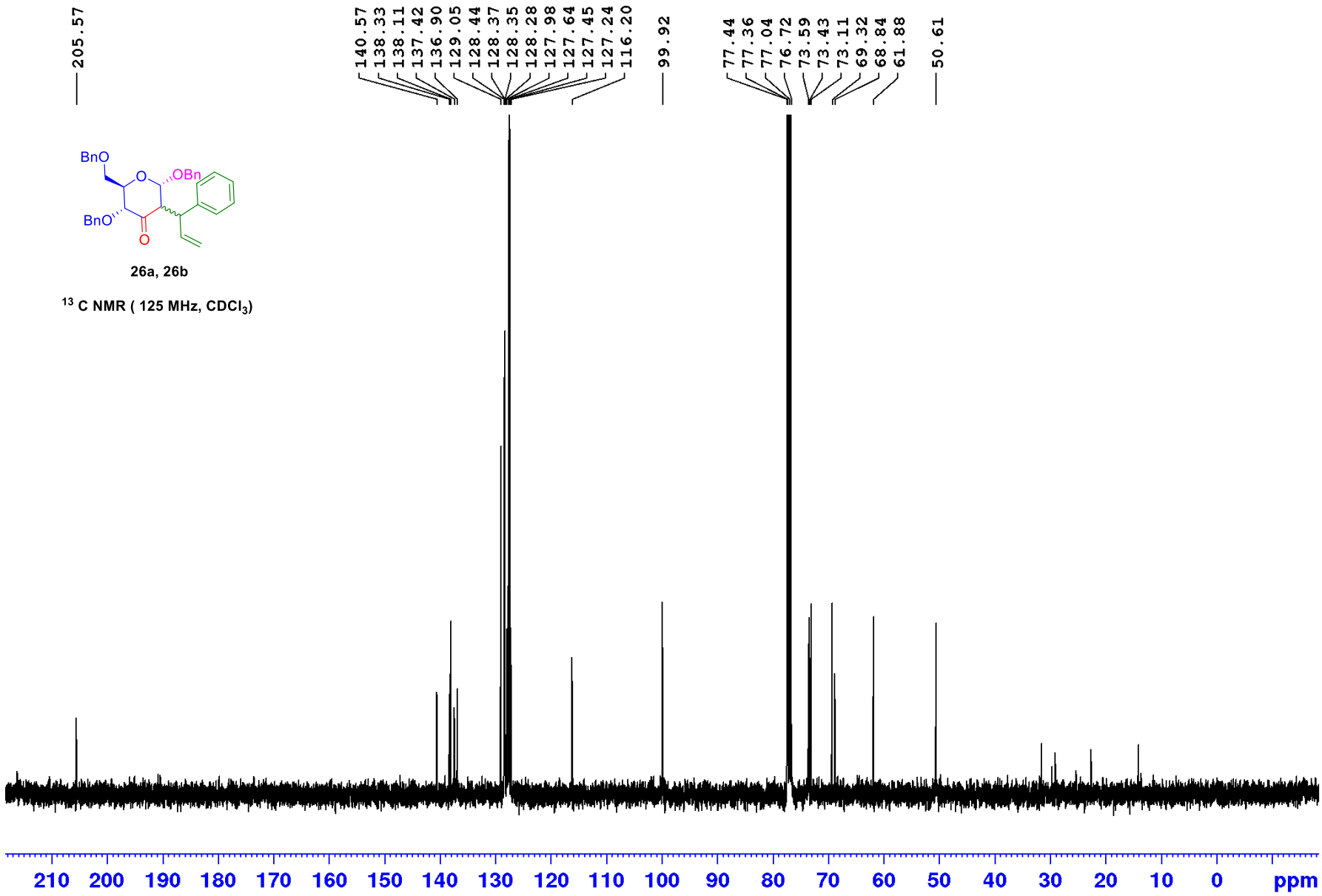

7.403
7.400
7.386
7.369
7.368
7.354
7.348
7.339
7.336
7.333
7.326
7.323
7.320
7.316
7.307
7.300
7.296
7.293
7.290
7.282
7.280
7.272
7.258
6.709
6.677
6.370
6.338
6.343
5.336
5.139
4.937
4.914
4.887
4.880
4.817
4.794
4.665
4.640
4.622
4.599
4.541
4.532
4.529
4.523
4.516
4.508
4.505
4.499
4.494
4.459
4.457
4.447
4.445
4.313
4.294
4.223
4.219
4.215
4.212
4.200
4.197
3.737
3.729
3.716
3.708
3.641
3.637
3.620
3.615
OBn
O
OBn
BnO
O
25
1H NMR (500 MHz, CDCl3)
10
9
8
7
6
5
4
3
2
1
ppm
20.81
1.00
1.01
1.09
1.10
1.06
1.14
1.11
1.10
1.03
1.16
0.86
1.11
1.25
1.35
1.02
1.04

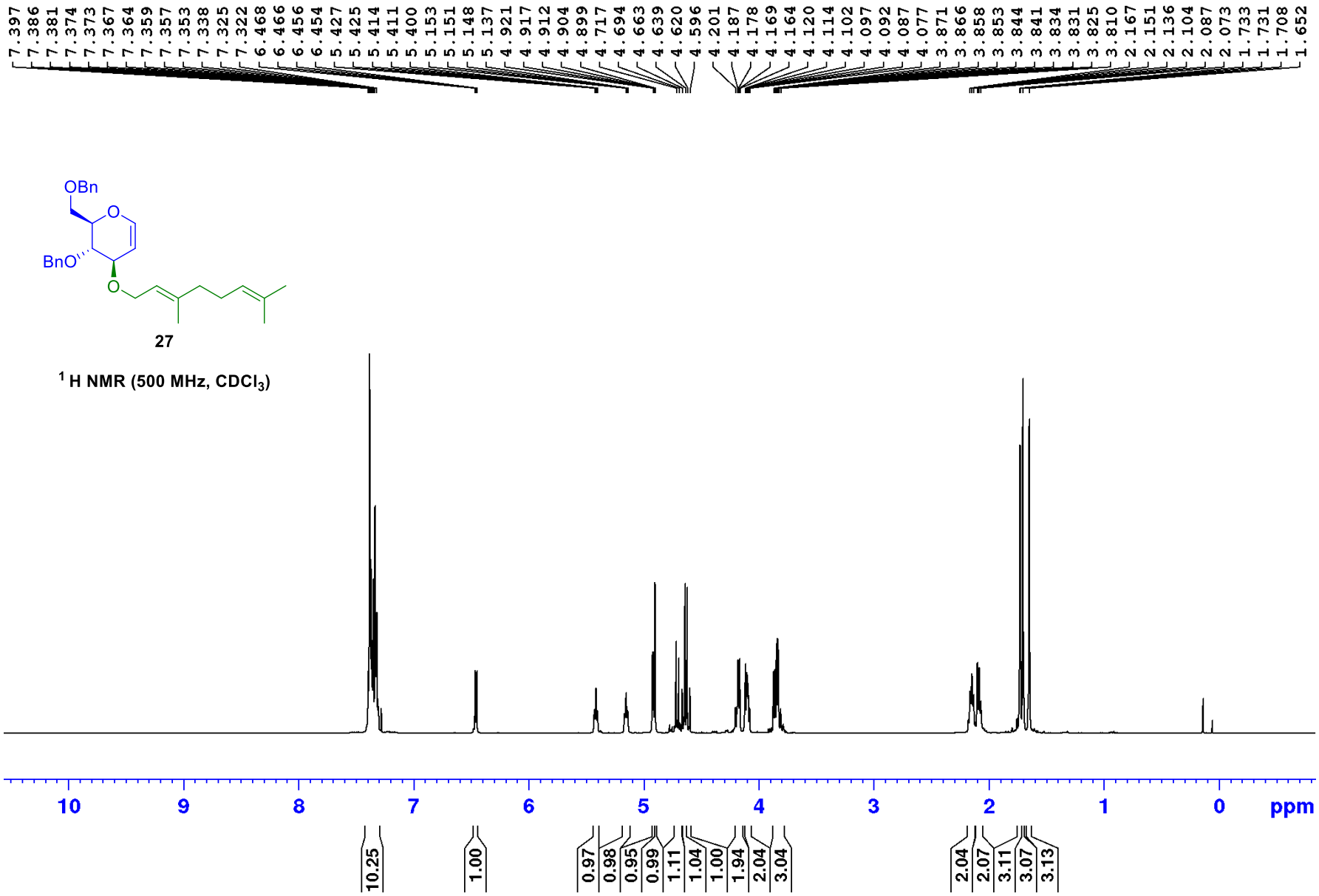


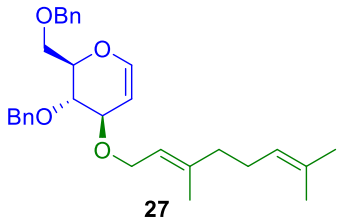
25

^{13} C NMR (125 MHz, $CDCl_3$)


7.394
7.392
7.387
7.379
7.368
7.355
7.342
7.337
7.330
7.325
7.318
7.309
7.306
7.288
7.267
7.254
7.249
7.245
7.237
7.234
7.219
7.215
7.195
7.189
7.175
7.171
5.954
5.936
5.911
5.886
5.079
5.062
5.060
5.037
4.901
4.873
4.767
4.718
4.688
4.621
4.591
4.571
4.541
4.446
4.418
4.382
4.362
4.358
4.332
4.118
4.114
4.110
4.105
4.090
4.086
3.848
3.839
3.821
3.812
3.775
3.770
3.755
3.748
3.743
3.731
3.725
3.701
3.126
3.097
BnO
O
OBn
BnO
O
26a, 26b
1 H NMR (500 MHz, CDCl3)
10
9
8
7
6
5
4
3
2
1
0
ppm
20.94
1.16
2.37
1.18
1.13
1.29
1.31
1.24
1.23
2.32
1.15
1.18
2.56
1.16


205.57
140.57
138.33
138.11
137.42
136.90
129.05
128.44
128.37
128.35
128.28
127.98
127.64
127.45
127.24
116.20
99.92
77.44
77.36
77.04
76.72
73.59
73.43
73.11
69.32
68.84
61.88
50.61
BnO
OBn
BnO
O
O
26a, 26b
13 C NMR (125 MHz, CDCl3)
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm

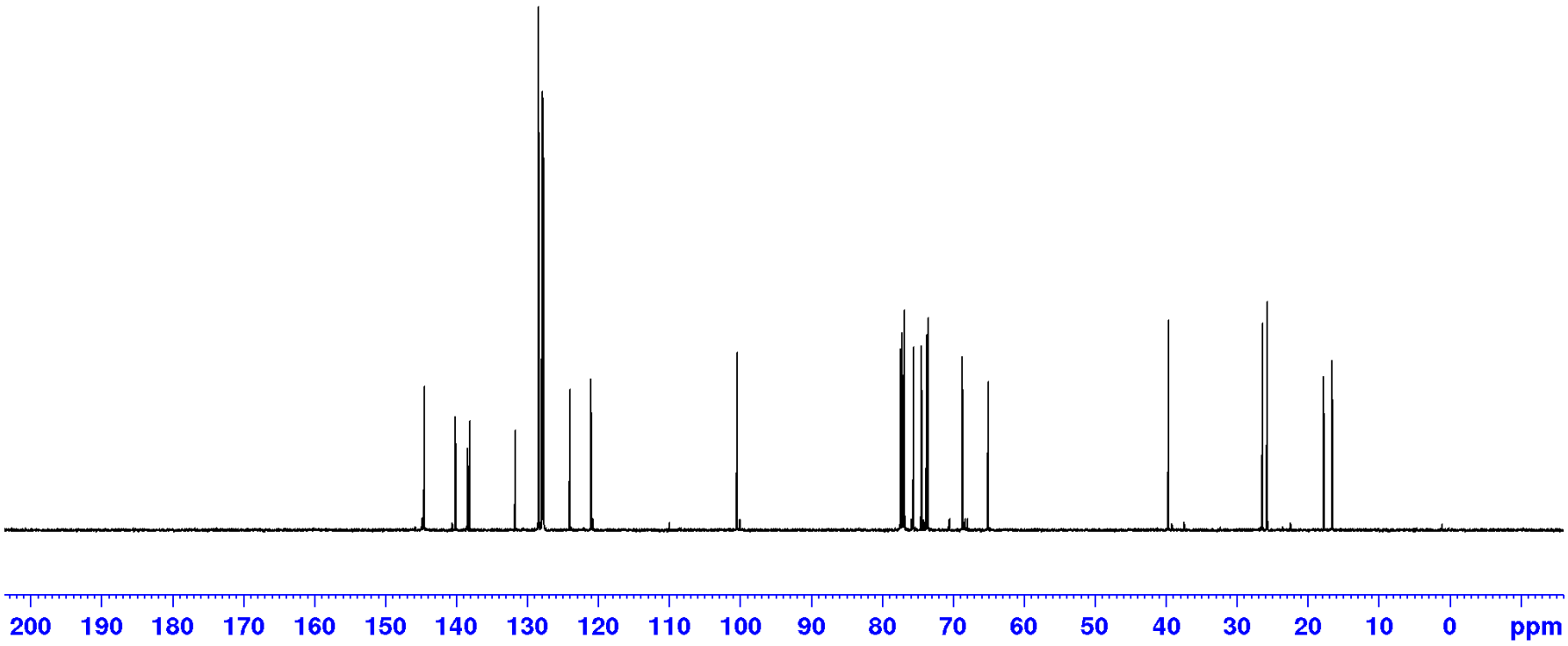

7.397
7.386
7.381
7.374
7.373
7.367
7.364
7.359
7.357
7.353
7.338
7.325
7.322
6.468
6.466
6.456
6.454
5.427
5.425
5.414
5.411
5.400
5.153
5.151
5.148
5.137
4.921
4.917
4.912
4.904
4.899
4.717
4.694
4.663
4.639
4.620
4.596
4.201
4.187
4.178
4.169
4.164
4.120
4.114
4.102
4.097
4.092
4.087
4.077
3.871
3.866
3.858
3.853
3.844
3.841
3.834
3.831
3.825
3.810
2.167
2.151
2.136
2.104
2.087
2.073
1.733
1.731
1.708
1.652
OBn
O
BnO
O
27
1 H NMR (500 MHz, CDCl3)
10
9
8
7
6
5
4
3
2
1
0
ppm
10.25
1.00
0.97
0.98
0.95
0.99
1.11
1.04
1.00
1.94
2.04
3.04
2.04
2.07
3.11
3.07
3.13

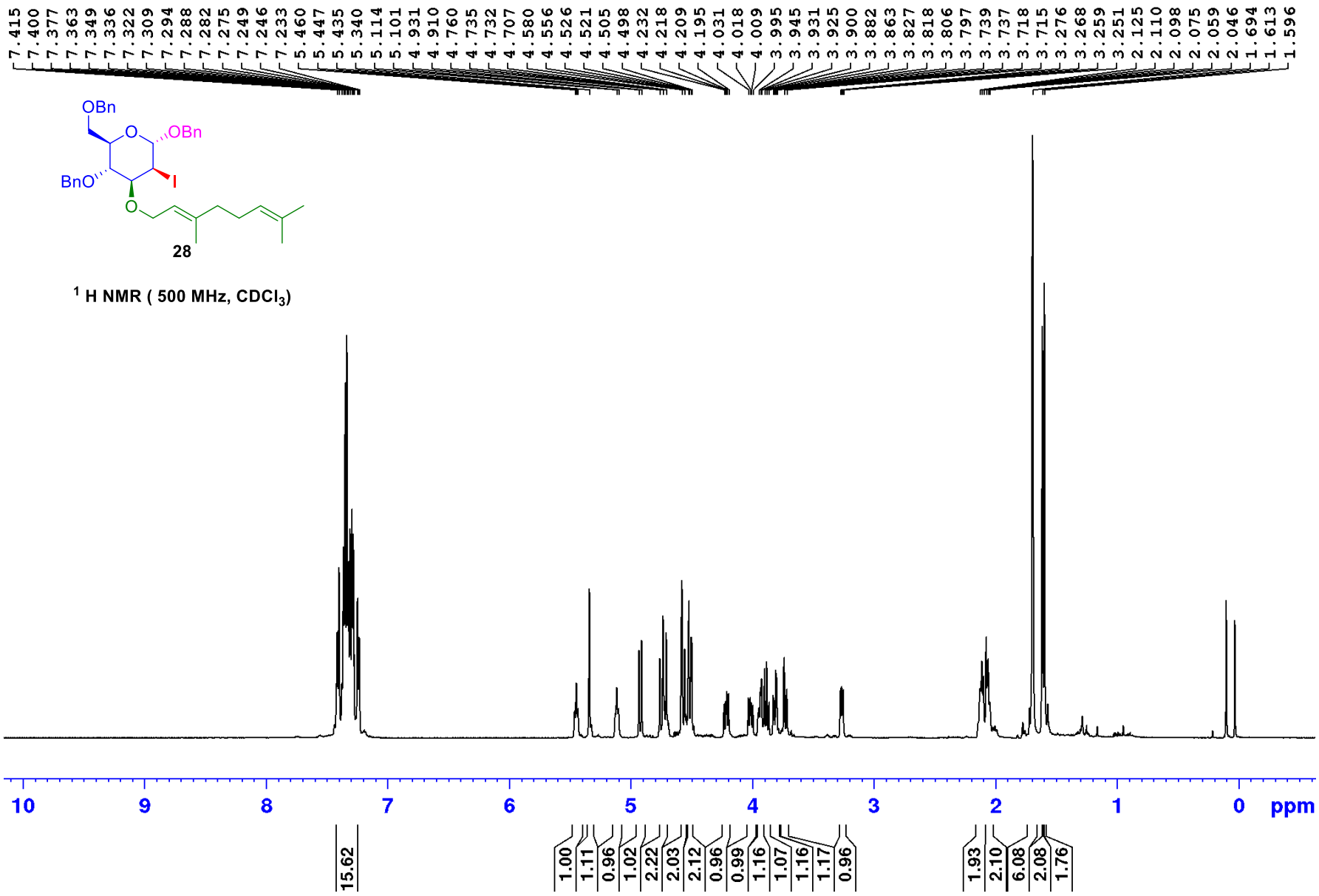


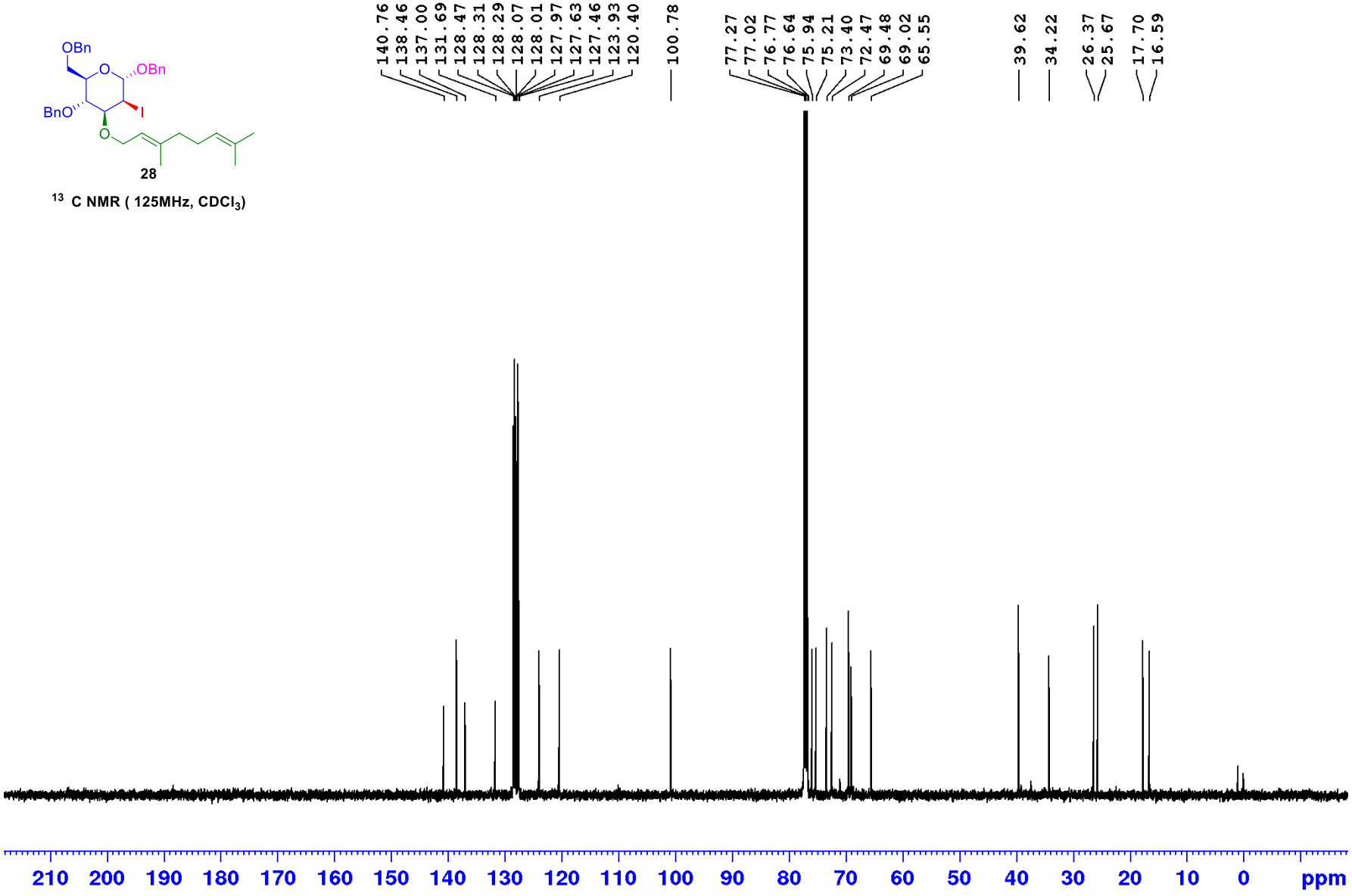
27

^{13}C NMR (500 MHz, $CDCl_3$)

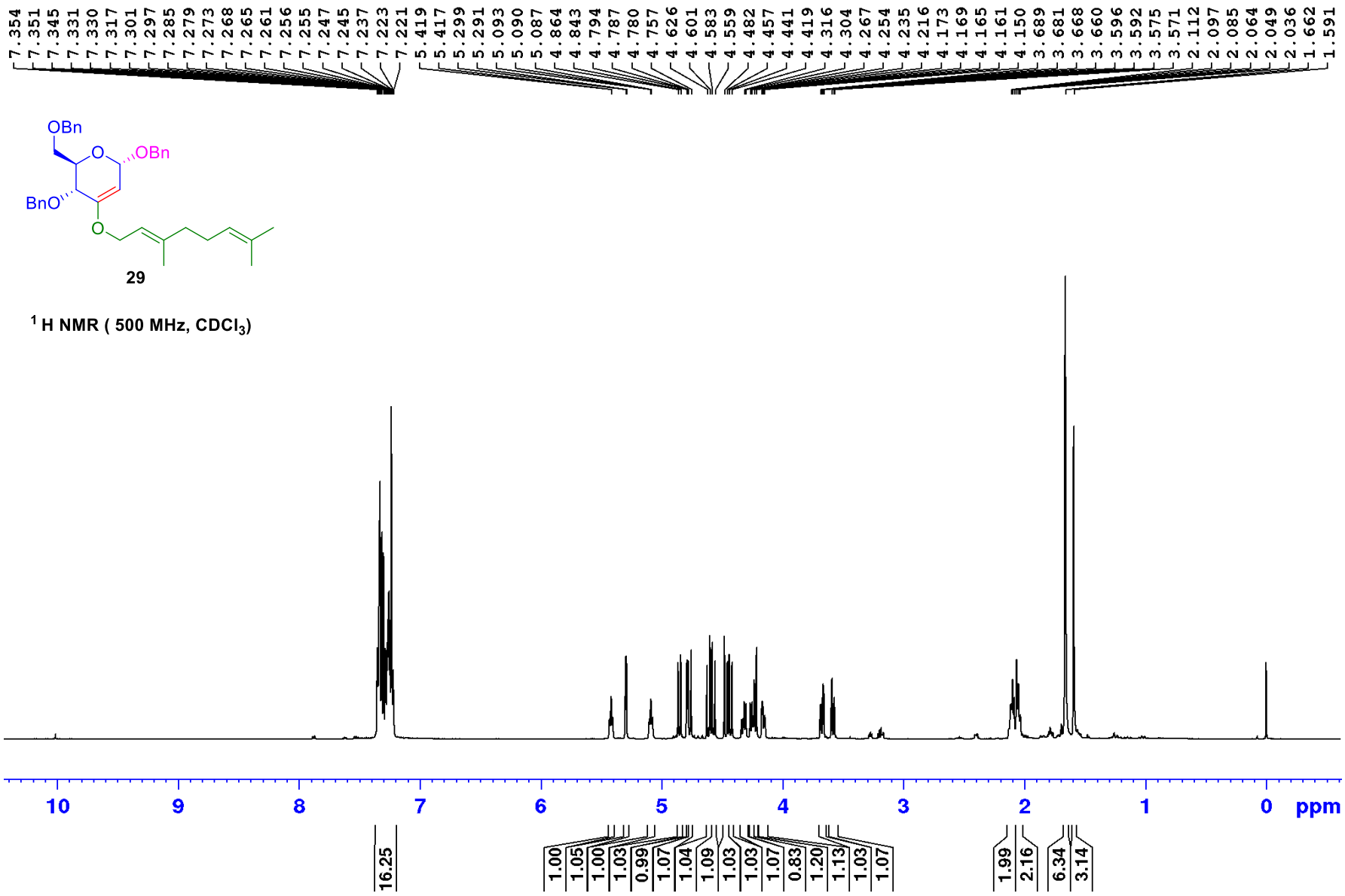
144.52
140.12
138.38
138.10
131.70
128.41
128.40
127.93
127.80
127.72
127.66
124.00
121.01
100.45
77.40
77.14
76.89
76.83
75.57
74.44
73.73
73.52
68.67
65.07
39.63
26.40
25.76
17.76
16.55

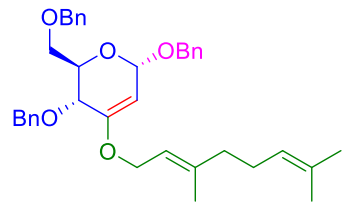



7.415 7.400 7.377 7.363 7.349 7.336 7.322 7.309 7.294 7.288 7.282 7.275 7.249 7.246 7.233 5.460 5.447 5.435 5.340 5.114 5.101 4.931 4.910 4.760 4.735 4.732 4.707 4.580 4.556 4.526 4.521 4.505 4.498 4.232 4.218 4.209 4.195 4.031 4.018 4.009 3.995 3.945 3.931 3.925 3.900 3.882 3.863 3.827 3.818 3.806 3.797 3.739 3.737 3.718 3.715 3.276 3.268 3.259 3.251 2.125 2.110 2.098 2.075 2.059 2.046 1.694 1.613 1.596
OBn
O
OBn
BnO
I
O
28
1 H NMR (500 MHz, CDCl3)
10 9 8 7 6 5 4 3 2 1 0 ppm
15.62
1.00 1.11 0.96 1.02 2.22 2.03 2.12 0.96 0.99 1.16 1.07 1.16 1.17 0.96
1.93 2.10 6.08 2.08 1.76



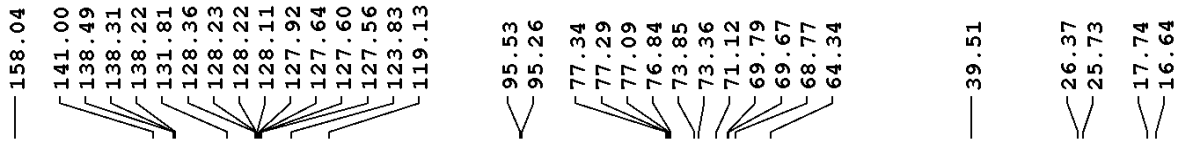
^{13} C NMR (125MHz, $CDCl_3$)

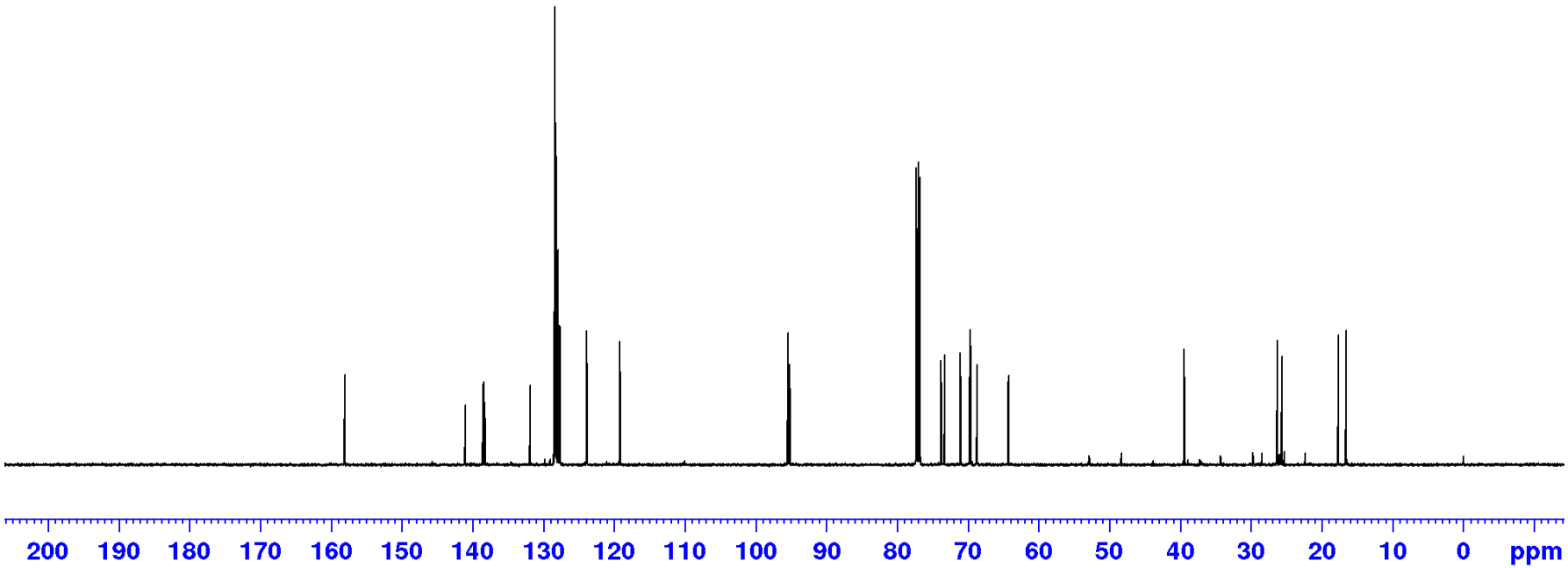

7.354
7.351
7.345
7.331
7.330
7.317
7.301
7.297
7.285
7.279
7.273
7.268
7.265
7.261
7.256
7.255
7.247
7.245
7.237
7.223
7.221
5.419
5.417
5.299
5.291
5.093
5.090
5.087
4.864
4.843
4.794
4.787
4.780
4.757
4.626
4.601
4.583
4.559
4.482
4.457
4.441
4.419
4.316
4.304
4.267
4.254
4.235
4.216
4.173
4.169
4.165
4.161
4.150
3.689
3.681
3.668
3.660
3.596
3.592
3.575
3.571
2.112
2.097
2.085
2.064
2.049
2.036
1.662
1.591
OBn
OBn
BnO
O
O
29
1 H NMR (500 MHz, CDCl3)
10
9
8
7
6
5
4
3
2
1
0
ppm
16.25
1.00
1.05
1.00
1.03
0.99
1.07
1.04
1.09
1.03
1.03
1.07
0.83
1.20
1.13
1.03
1.07
1.99
2.16
6.34
3.14

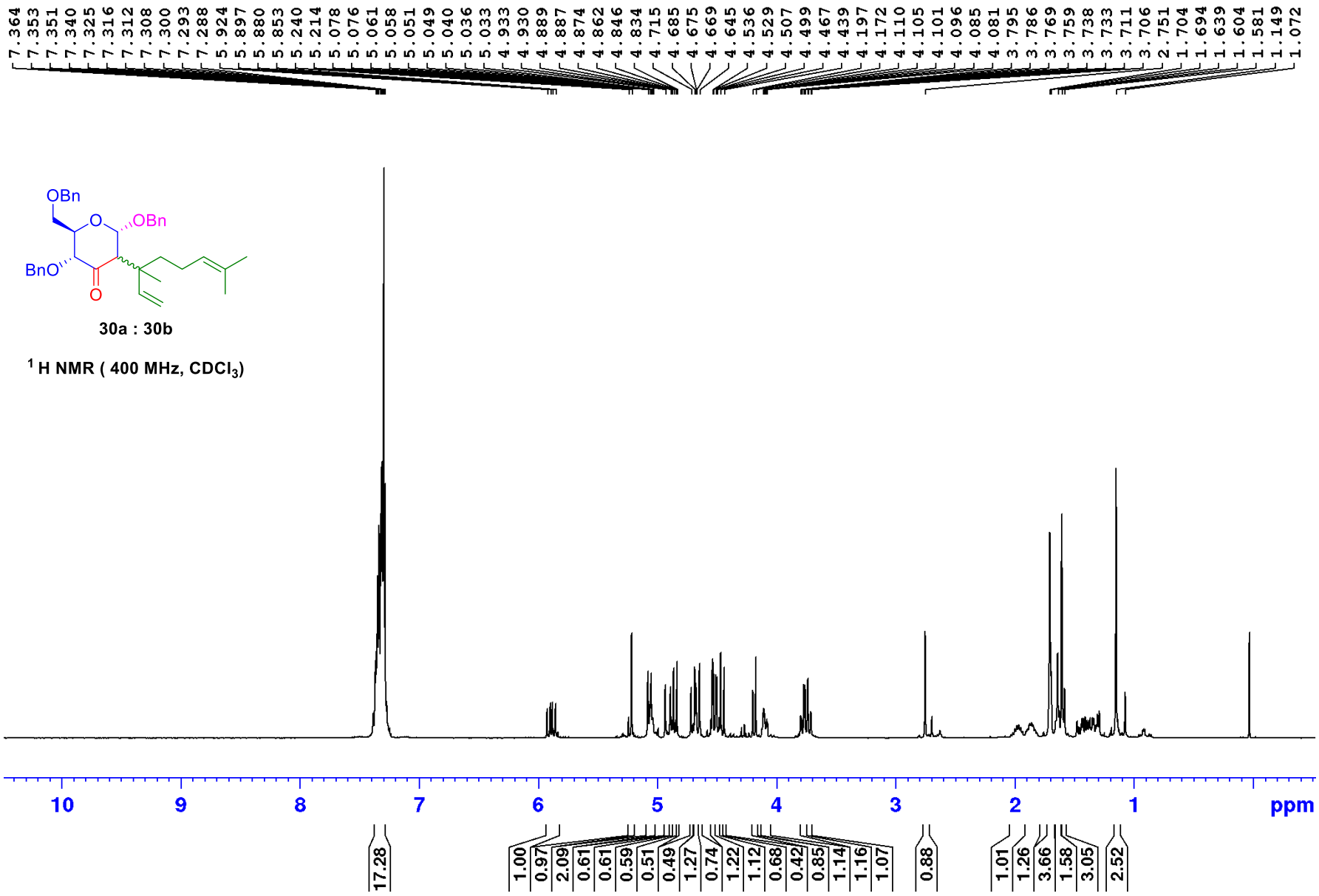


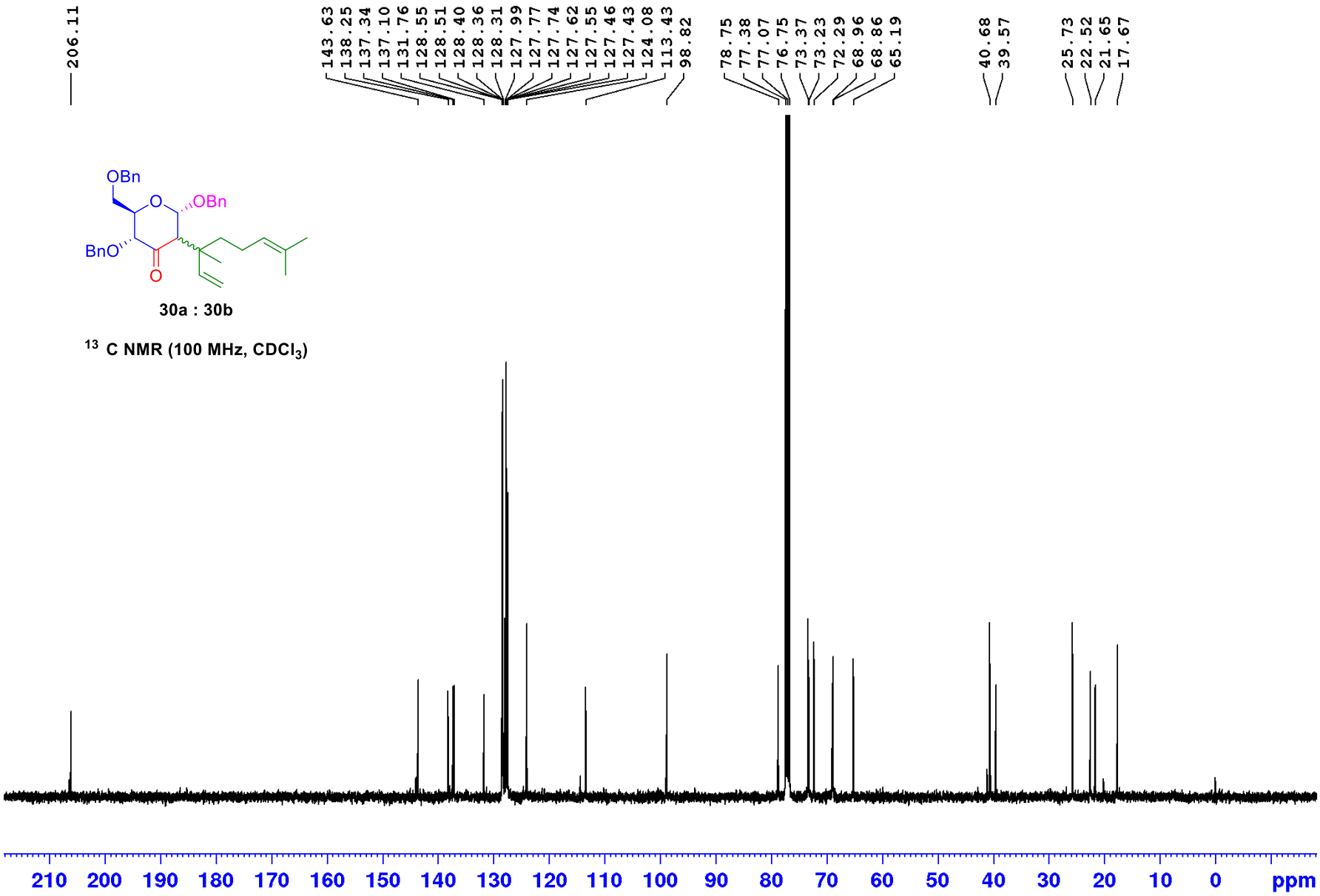
29

^{13}C NMR (125 MHz, CDCl)



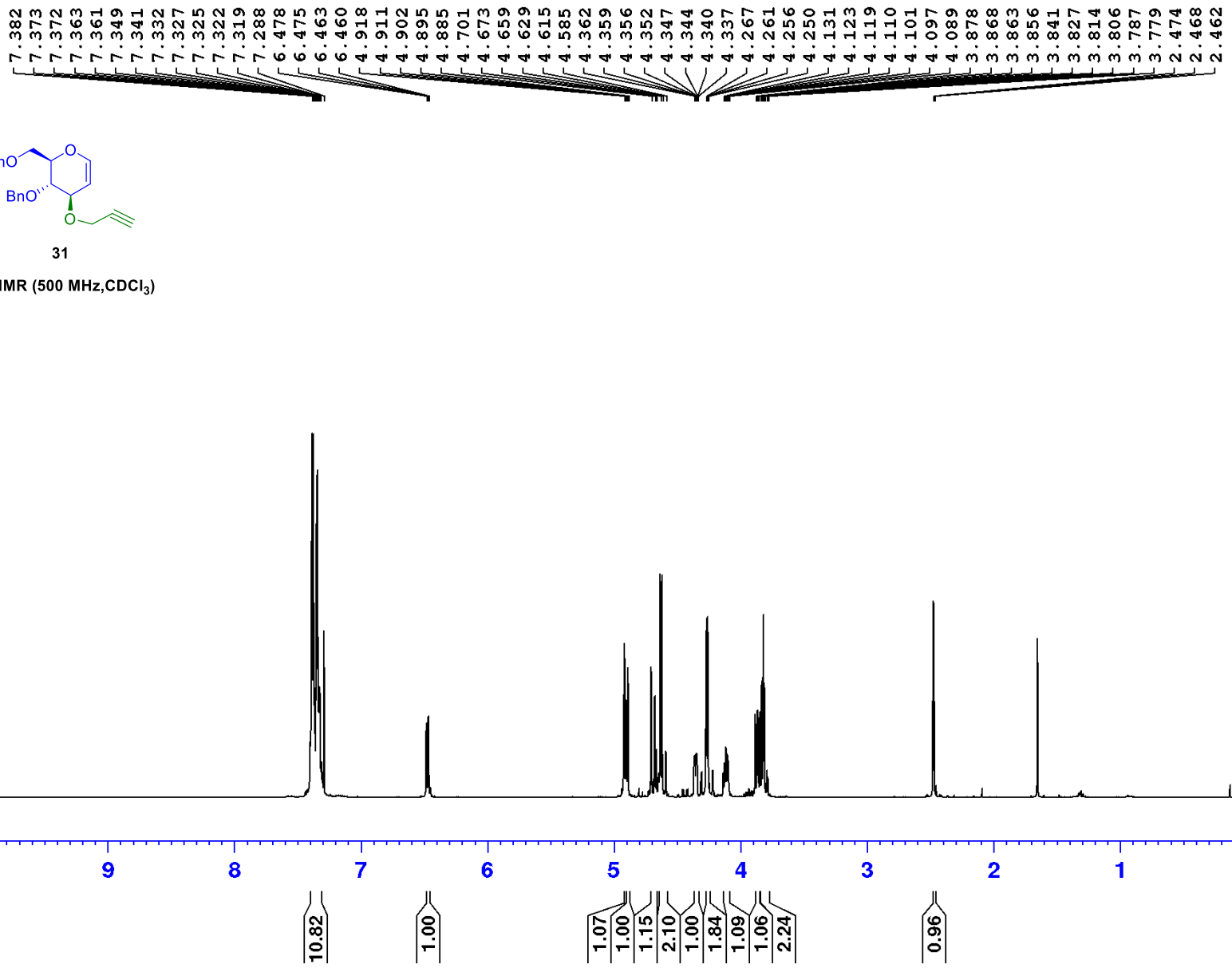


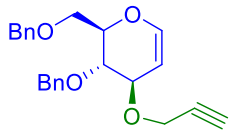

7.364
7.353
7.351
7.340
7.325
7.316
7.312
7.308
7.300
7.293
7.288
5.924
5.897
5.880
5.853
5.240
5.214
5.078
5.076
5.061
5.058
5.051
5.049
5.040
5.036
5.033
4.933
4.930
4.889
4.887
4.874
4.862
4.846
4.834
4.715
4.685
4.675
4.669
4.645
4.536
4.529
4.507
4.499
4.467
4.439
4.197
4.172
4.110
4.105
4.101
4.096
4.085
4.081
3.795
3.786
3.769
3.759
3.738
3.733
3.711
3.706
2.751
1.704
1.694
1.639
1.604
1.581
1.149
1.072
OBn
O
OBn
BnO
O
30a : 30b
1 H NMR (400 MHz, CDCl3)
10
9
8
7
6
5
4
3
2
1
ppm
17.28
1.00
0.97
2.09
0.61
0.61
0.59
0.51
0.49
1.27
0.74
1.22
1.12
0.68
0.42
0.85
1.14
1.16
1.07
0.88
1.01
1.26
3.66
1.58
3.05
2.52



30a : 30b

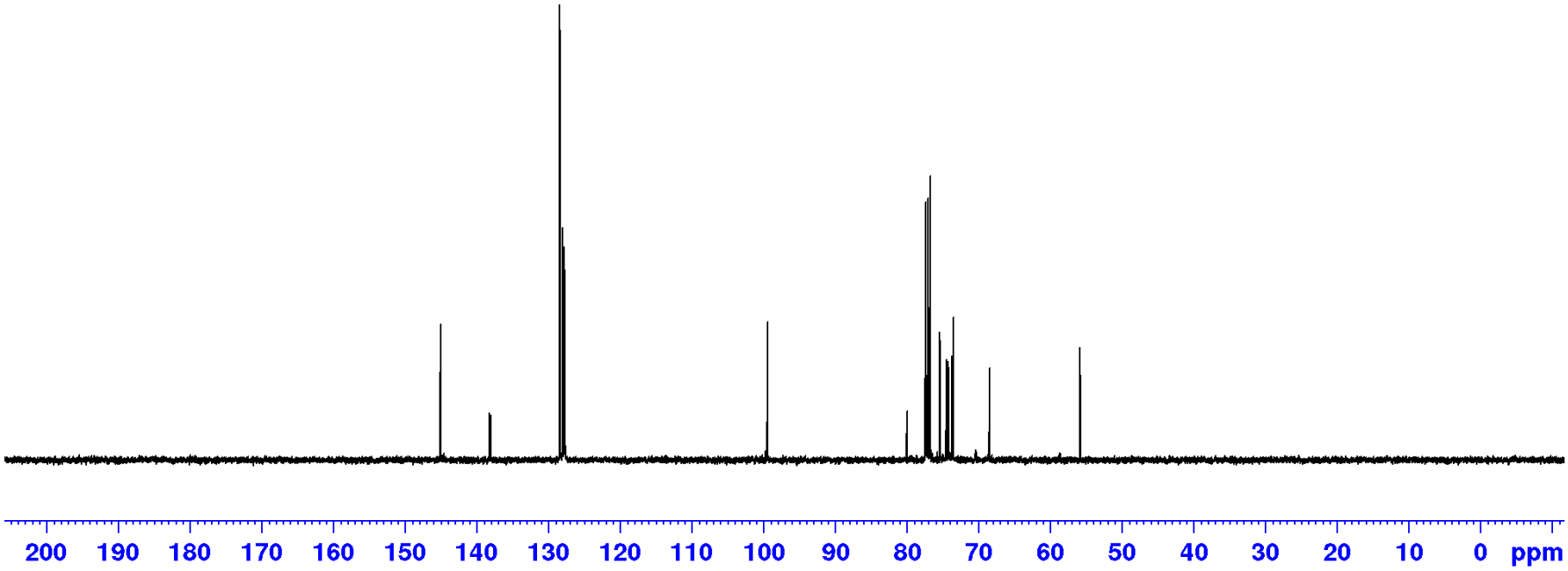
^{13} C NMR (100 MHz, $CDCl_3$)

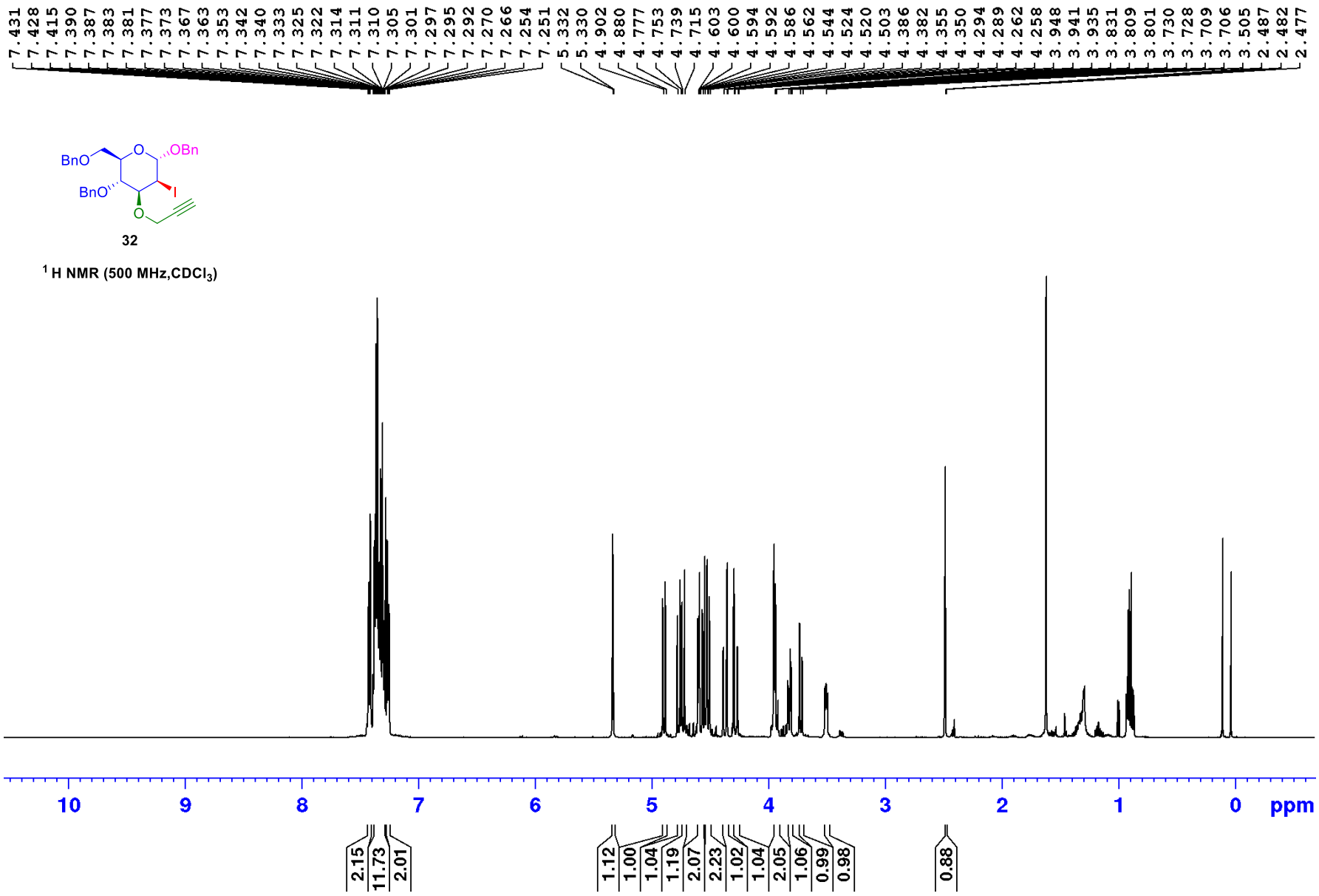

7.382
7.373
7.372
7.363
7.361
7.349
7.341
7.332
7.327
7.325
7.322
7.319
7.288
6.478
6.475
6.463
6.460
4.918
4.911
4.902
4.895
4.885
4.701
4.673
4.659
4.629
4.615
4.585
4.362
4.359
4.356
4.352
4.347
4.344
4.340
4.337
4.267
4.261
4.256
4.250
4.131
4.123
4.119
4.110
4.101
4.097
4.089
3.878
3.868
3.863
3.856
3.841
3.827
3.814
3.806
3.787
3.779
2.474
2.468
2.462
BnO
BnO
O
O
31
1 H NMR (500 MHz,CDCl3)
10
9
8
7
6
5
4
3
2
1
0
ppm
10.82
1.00
1.07
1.00
1.15
2.10
1.00
1.84
1.09
1.06
2.24
0.96

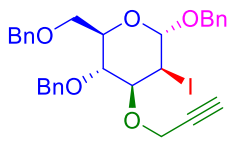


31

^{13} C NMR (125 MHz,$CDCl_3$)

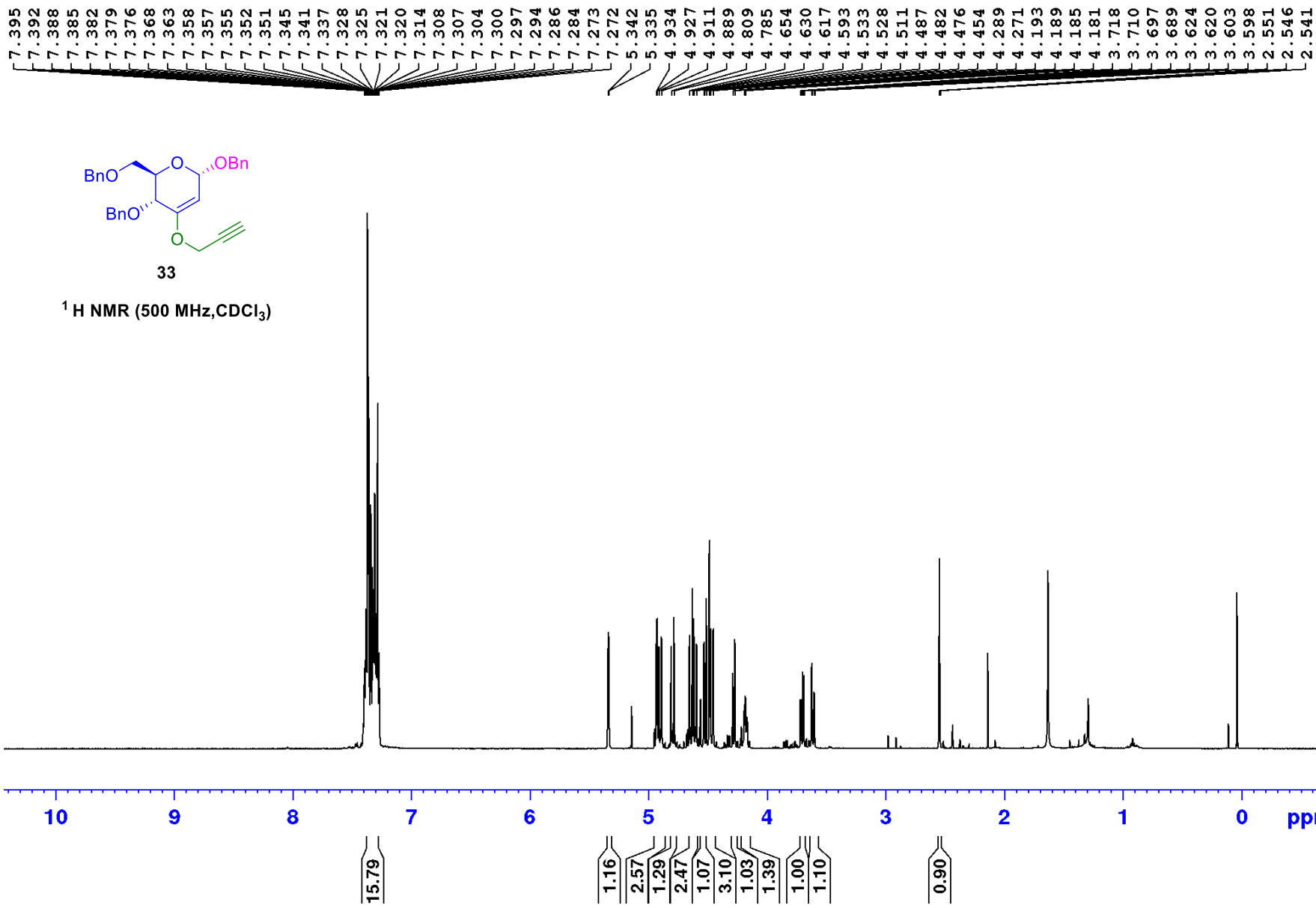


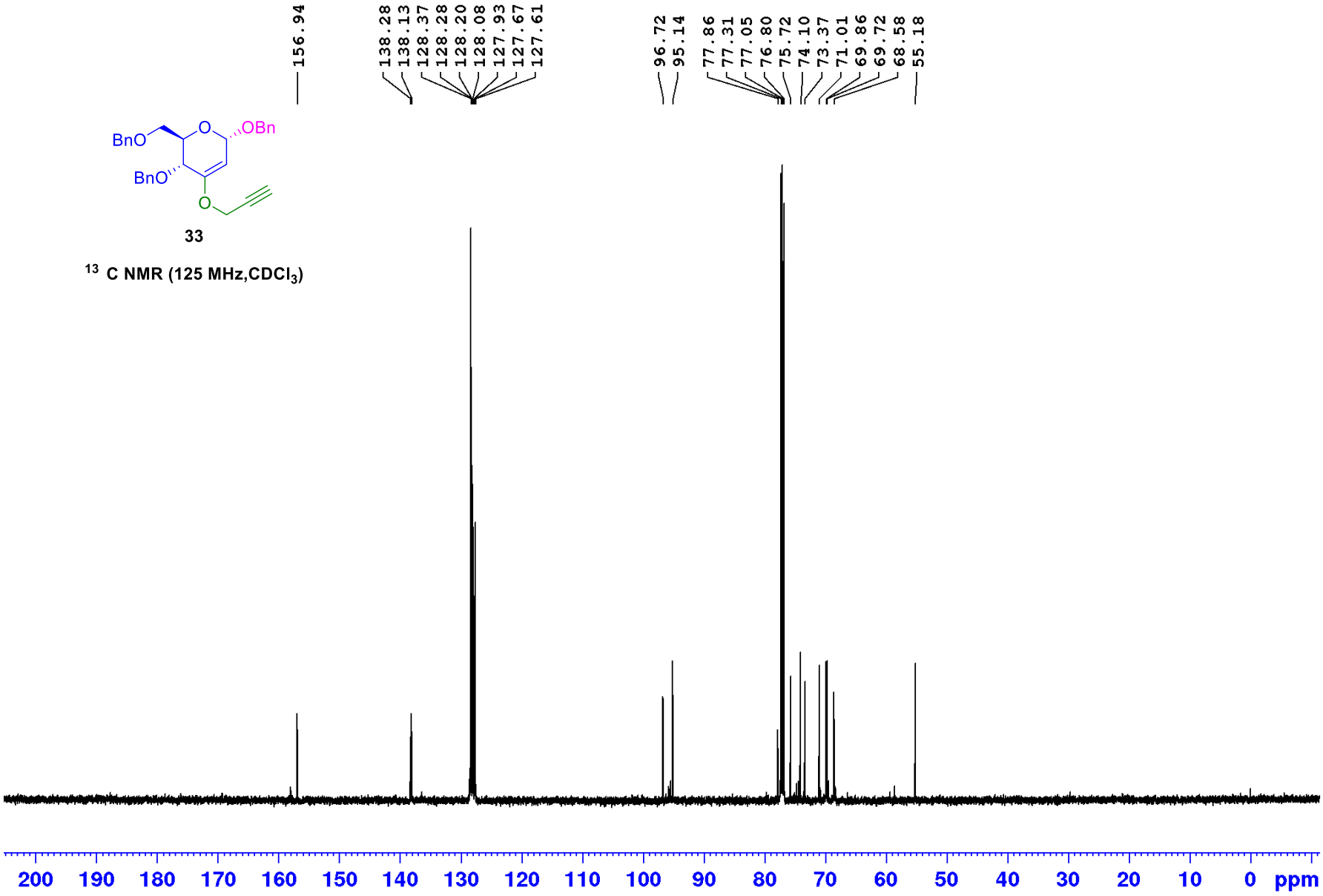

7.431
7.428
7.415
7.390
7.387
7.383
7.381
7.377
7.373
7.367
7.363
7.353
7.342
7.340
7.333
7.325
7.322
7.314
7.311
7.310
7.305
7.301
7.297
7.295
7.292
7.270
7.266
7.254
7.251
5.332
5.330
4.902
4.880
4.777
4.753
4.739
4.715
4.603
4.600
4.594
4.592
4.586
4.562
4.544
4.524
4.520
4.503
4.386
4.382
4.355
4.350
4.294
4.289
4.262
4.258
3.948
3.941
3.935
3.831
3.809
3.801
3.730
3.728
3.709
3.706
3.505
2.487
2.482
2.477
BnO
OBn
BnO
I
O
O
32
1 H NMR (500 MHz,CDCl3)
10
9
8
7
6
5
4
3
2
1
0
ppm
2.15
11.73
2.01
1.12
1.00
1.04
1.19
2.07
2.23
1.02
1.04
2.05
1.06
0.99
0.98
0.88



32

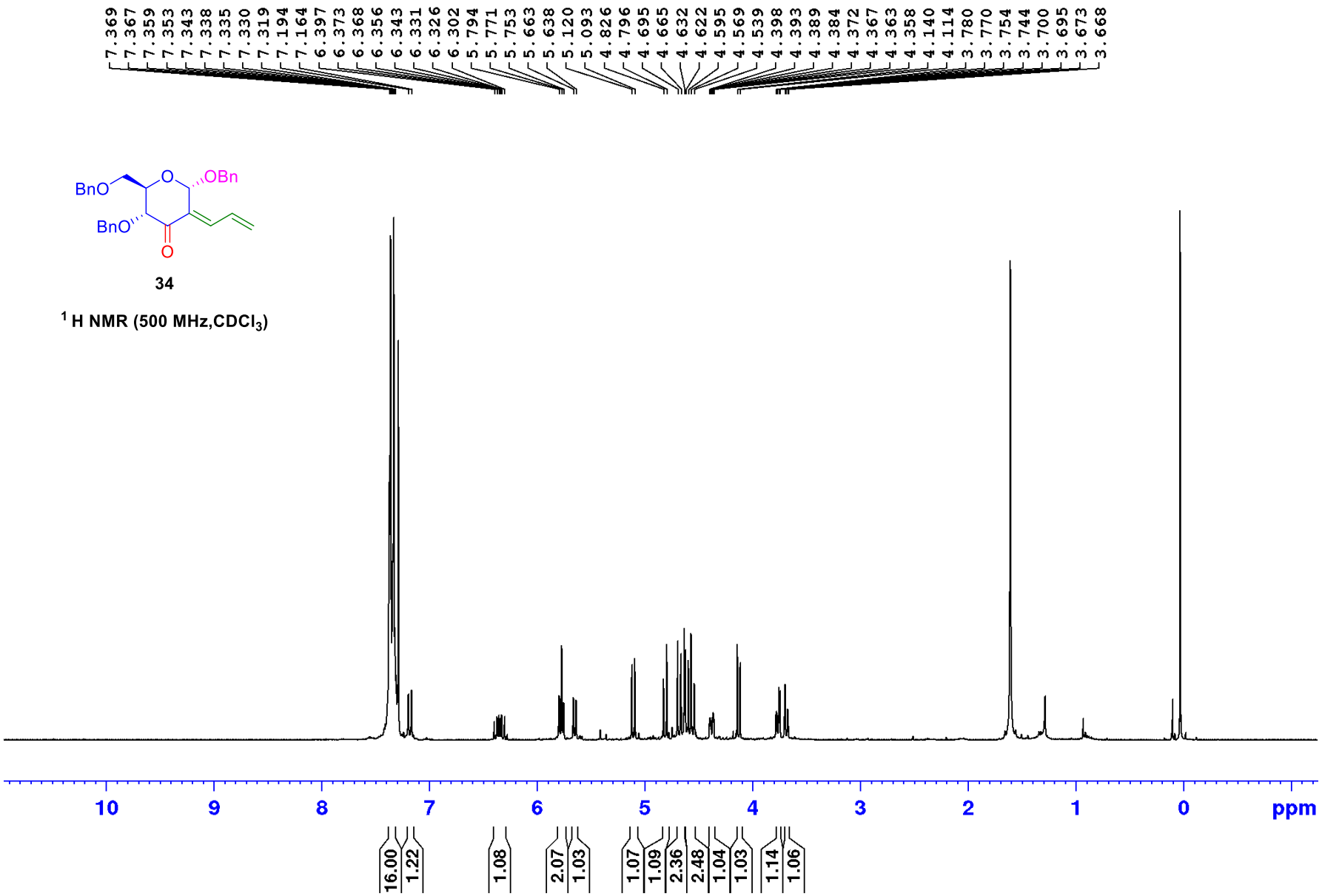
^{13} C NMR (125 MHz,$CDCl_3$)

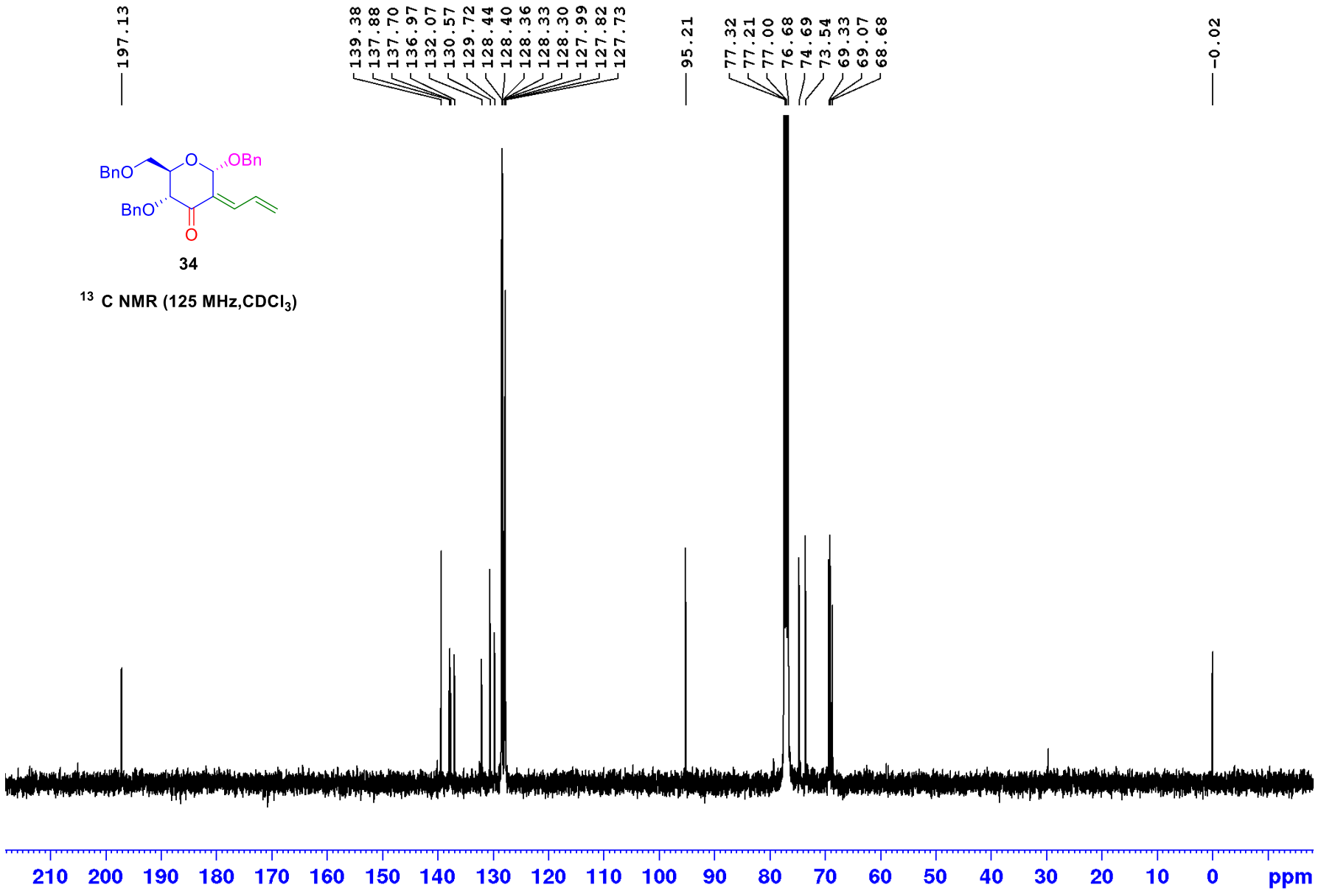

7.395
7.392
7.388
7.385
7.382
7.379
7.376
7.368
7.363
7.358
7.357
7.355
7.352
7.351
7.345
7.341
7.337
7.328
7.325
7.321
7.320
7.314
7.308
7.307
7.304
7.300
7.297
7.294
7.286
7.284
7.273
7.272
5.342
5.335
4.934
4.927
4.911
4.889
4.809
4.785
4.654
4.630
4.617
4.593
4.533
4.528
4.511
4.487
4.482
4.476
4.454
4.289
4.271
4.193
4.189
4.185
4.181
3.718
3.710
3.697
3.689
3.624
3.620
3.603
3.598
2.551
2.546
2.541
BnO
O
OBn
BnO
O
33
1 H NMR (500 MHz,CDCl3)
10
9
8
7
6
5
4
3
2
1
0
ppm
15.79
1.16
2.57
1.29
2.47
1.07
3.10
1.03
1.39
1.00
1.10
0.90

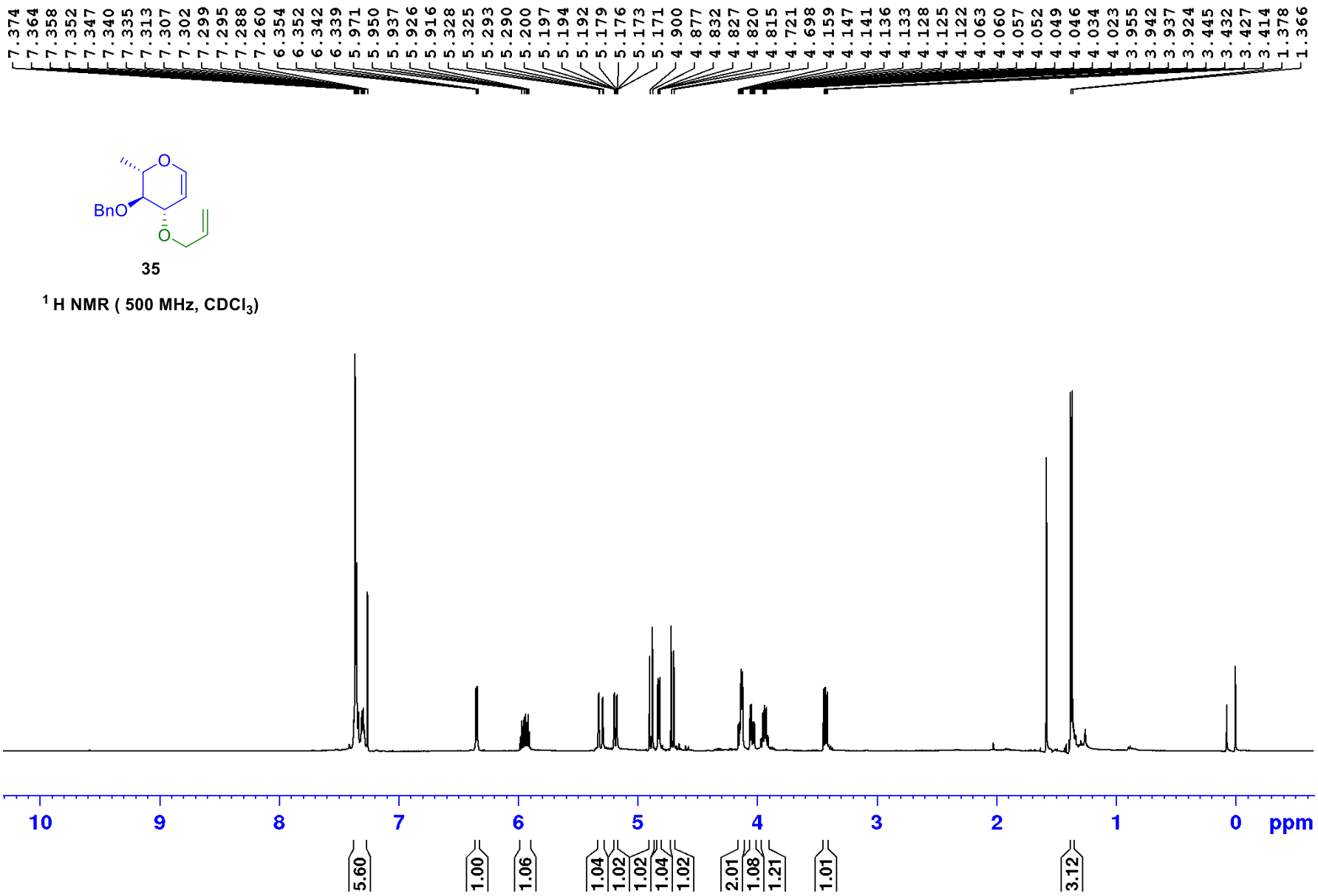


33

^{13} C NMR (125 MHz,$CDCl_3$)

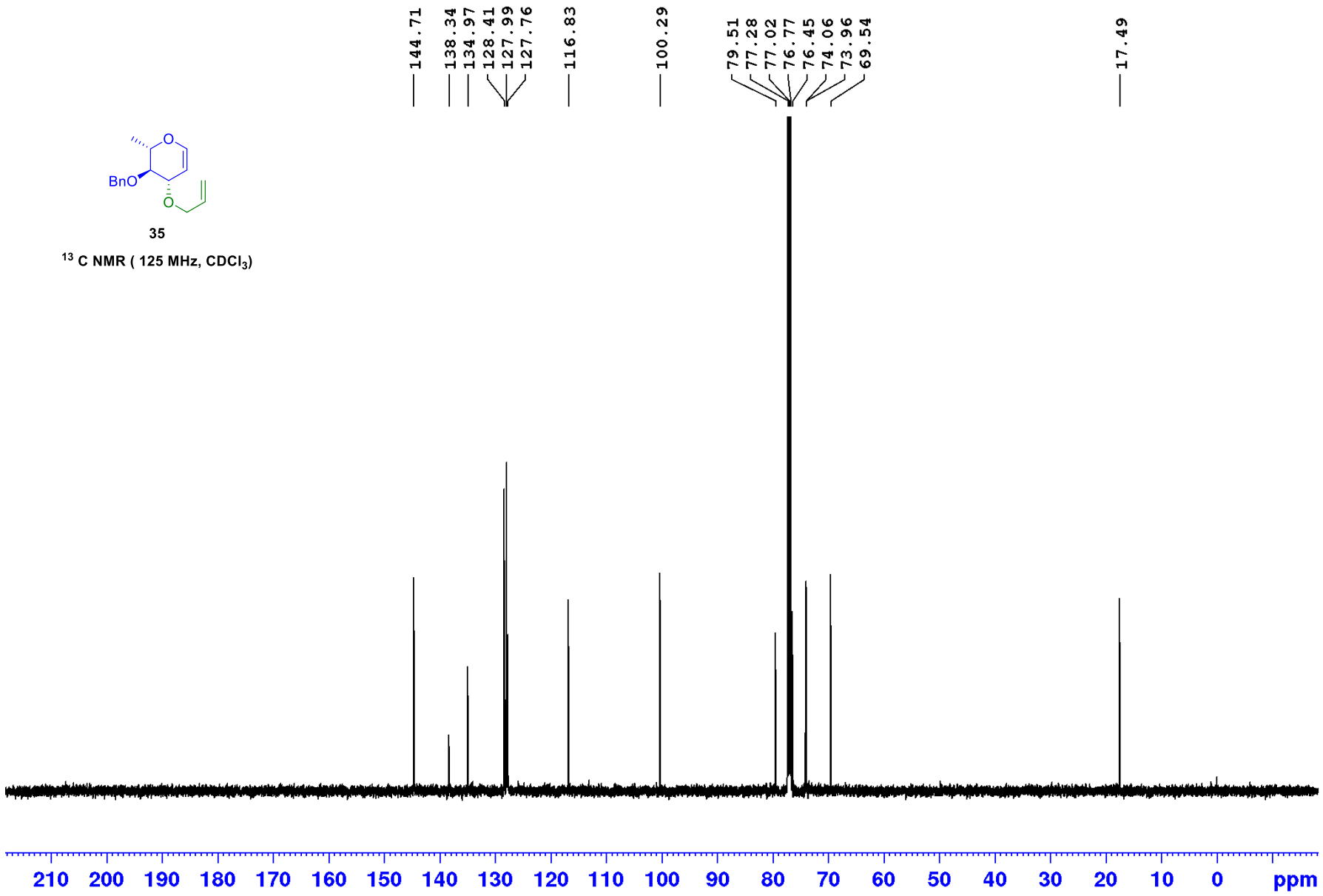

7.369
7.367
7.359
7.353
7.343
7.338
7.335
7.330
7.319
7.194
7.164
6.397
6.373
6.368
6.356
6.343
6.331
6.326
6.302
5.794
5.771
5.753
5.663
5.638
5.120
5.093
4.826
4.796
4.695
4.665
4.632
4.622
4.595
4.569
4.539
4.398
4.393
4.389
4.384
4.372
4.367
4.363
4.358
4.140
4.114
3.780
3.770
3.754
3.744
3.700
3.695
3.673
3.668
BnO
OBn
BnO
O
O
34
1 H NMR (500 MHz,CDCl3)
10
9
8
7
6
5
4
3
2
1
0
ppm
16.00
1.22
1.08
2.07
1.03
1.07
1.09
2.36
2.48
1.04
1.03
1.14
1.06


197.13
139.38
137.88
137.70
136.97
132.07
130.57
129.72
128.44
128.40
128.36
128.33
128.30
127.99
127.82
127.73
95.21
77.32
77.21
77.00
76.68
74.69
73.54
69.33
69.07
68.68
-0.02
BnO
O
OBn
BnO
O
34
13 C NMR (125 MHz,CDCl3)
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm



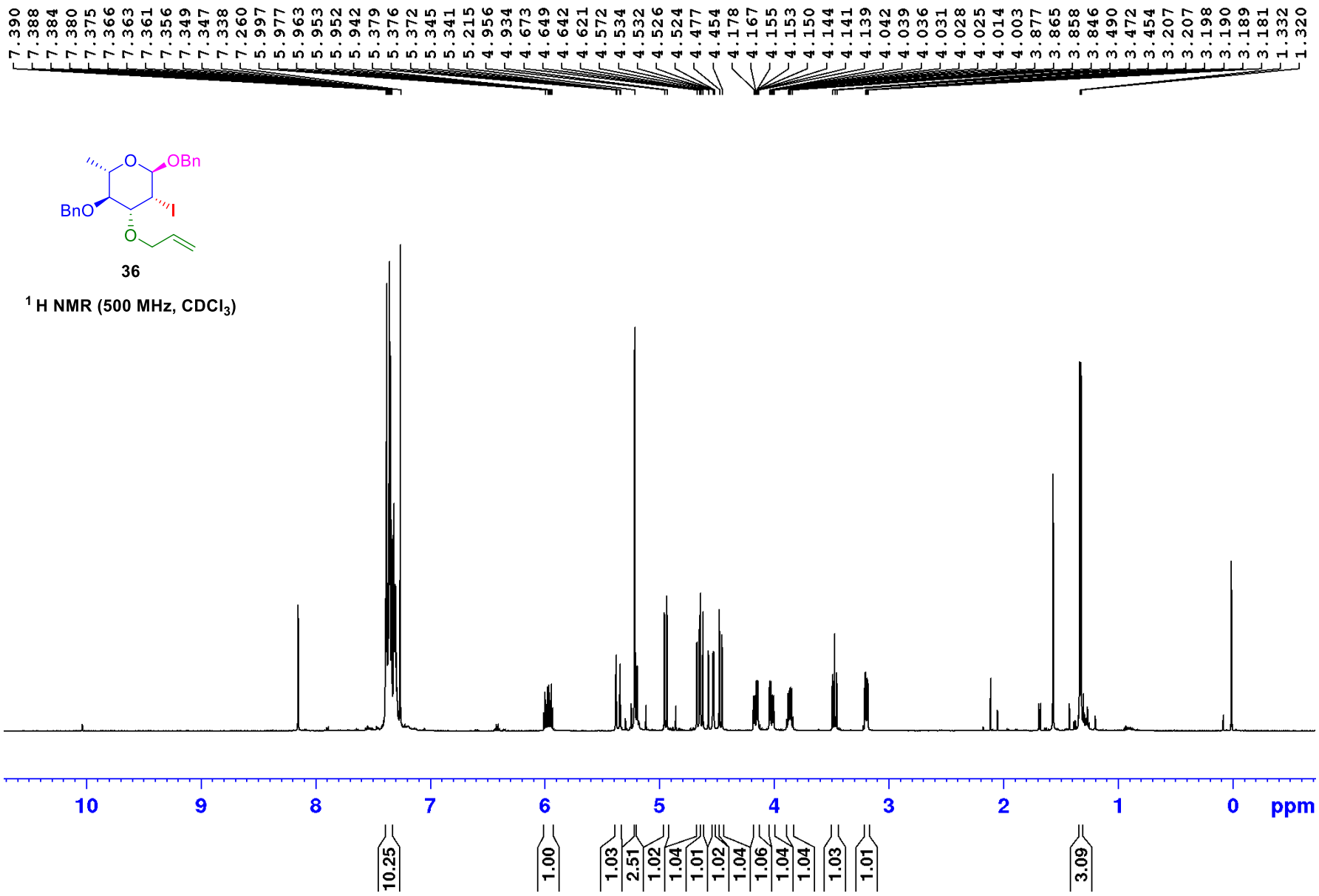
35

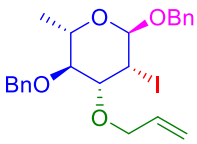
^{1}H NMR (500 MHz, $CDCl_3$)



35

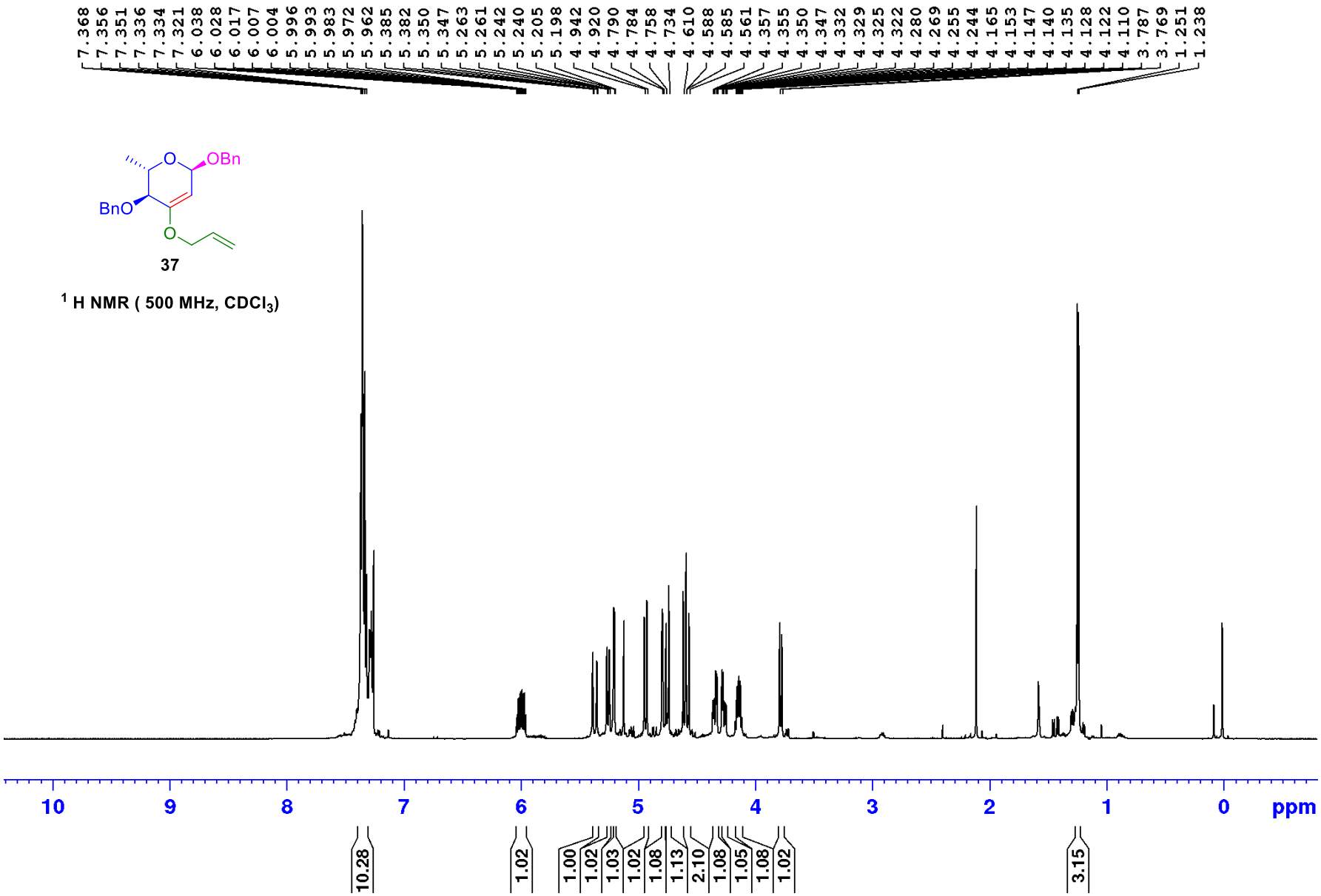
^{13}C NMR (125 MHz, $CDCl_3$)

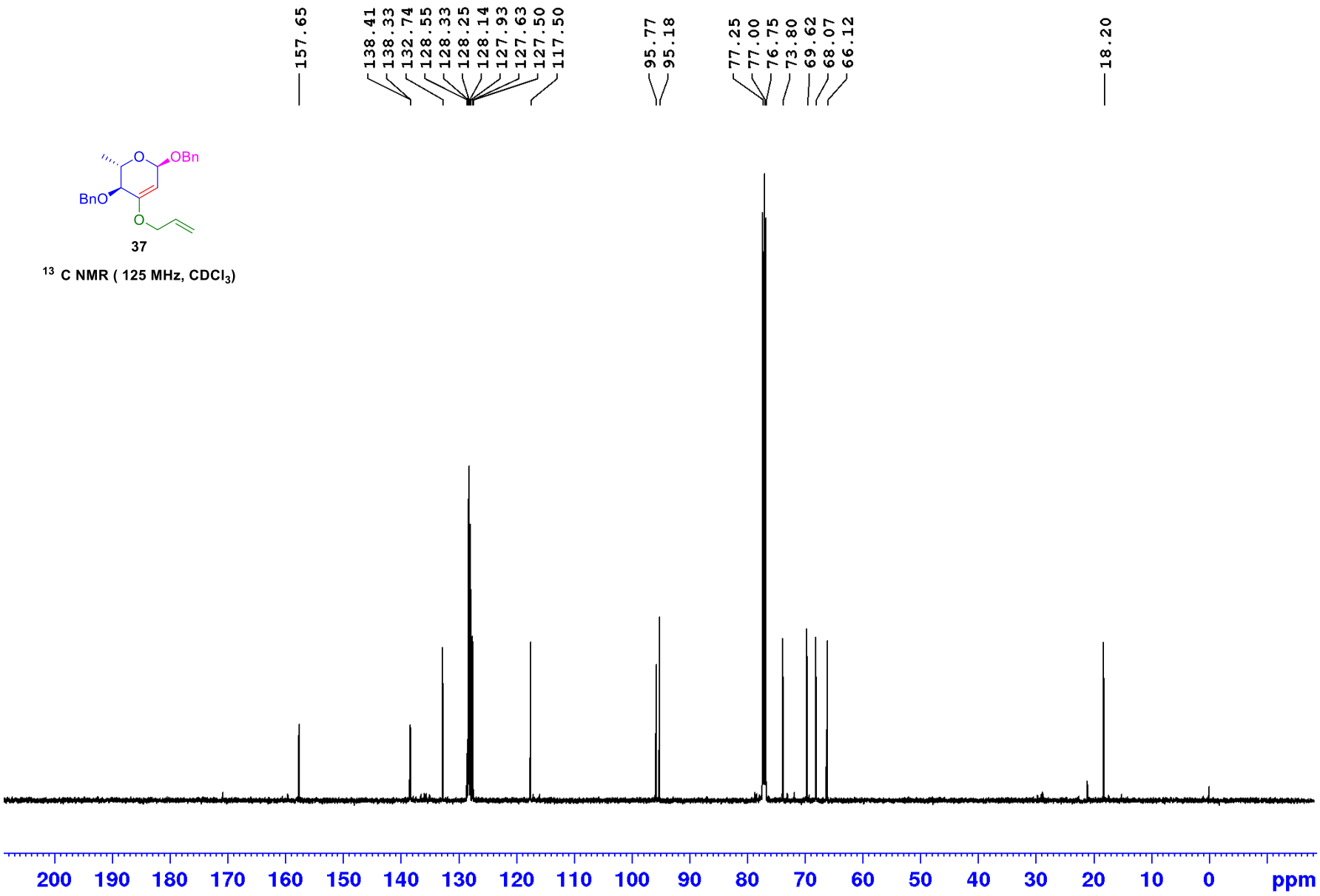

7.390
7.388
7.384
7.380
7.375
7.366
7.363
7.361
7.356
7.349
7.347
7.338
7.260
5.997
5.977
5.963
5.953
5.952
5.942
5.379
5.376
5.372
5.345
5.341
5.215
4.956
4.934
4.673
4.649
4.642
4.621
4.572
4.534
4.532
4.526
4.524
4.477
4.454
4.178
4.167
4.155
4.153
4.150
4.144
4.141
4.139
4.042
4.039
4.036
4.031
4.028
4.025
4.014
4.003
3.877
3.865
3.858
3.846
3.490
3.472
3.454
3.207
3.207
3.198
3.190
3.189
3.181
1.332
1.320
OBn
BnO
I
O
O
36
1 H NMR (500 MHz, CDCl3)
10
9
8
7
6
5
4
3
2
1
0
ppm
10.25
1.00
1.03
2.51
1.02
1.04
1.01
1.02
1.04
1.06
1.04
1.04
1.03
1.01
3.09

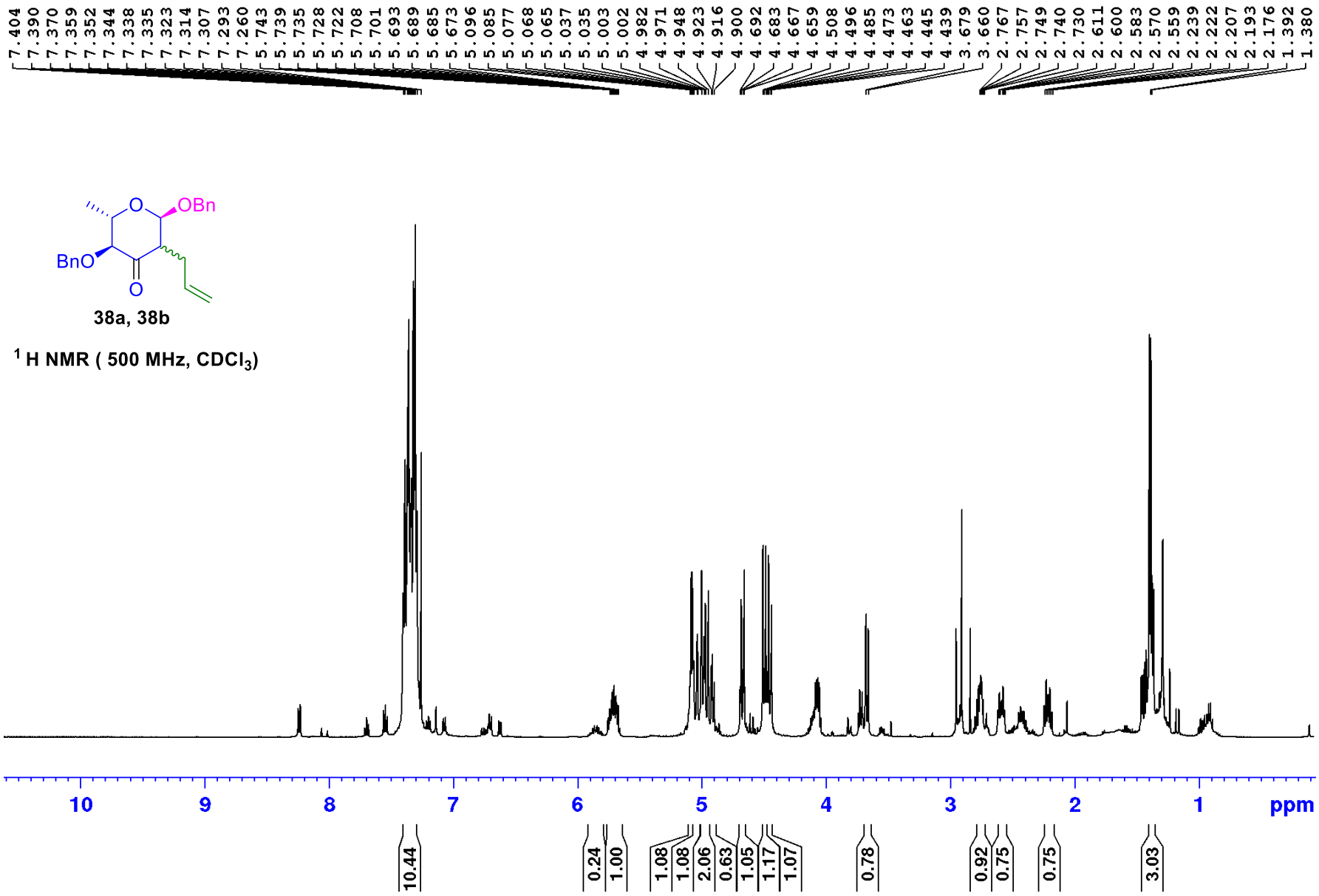


36

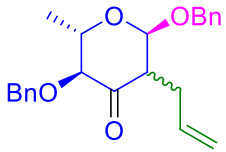
^{13} C NMR (125 MHz, $CDCl_3$)


7.368
7.356
7.351
7.336
7.334
7.321
6.038
6.028
6.017
6.007
6.004
5.996
5.993
5.983
5.972
5.962
5.385
5.382
5.350
5.347
5.263
5.261
5.242
5.240
5.205
5.198
4.942
4.920
4.790
4.784
4.758
4.734
4.610
4.588
4.585
4.561
4.357
4.355
4.350
4.347
4.332
4.329
4.325
4.322
4.280
4.269
4.255
4.244
4.165
4.153
4.147
4.140
4.135
4.128
4.122
4.110
3.787
3.769
1.251
1.238
OBn
BnO
O
O
37
1 H NMR (500 MHz, CDCl3)
10
9
8
7
6
5
4
3
2
1
0
ppm
10.28
1.02
1.00
1.02
1.03
1.02
1.08
1.13
2.10
1.08
1.05
1.08
1.02
3.15


157.65
138.41
138.33
132.74
128.55
128.33
128.25
128.14
127.93
127.63
127.50
117.50
95.77
95.18
77.25
77.00
76.75
73.80
69.62
68.07
66.12
18.20
OBn
BnO
O
O
37
13 C NMR (125 MHz, CDCl3)
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
ppm

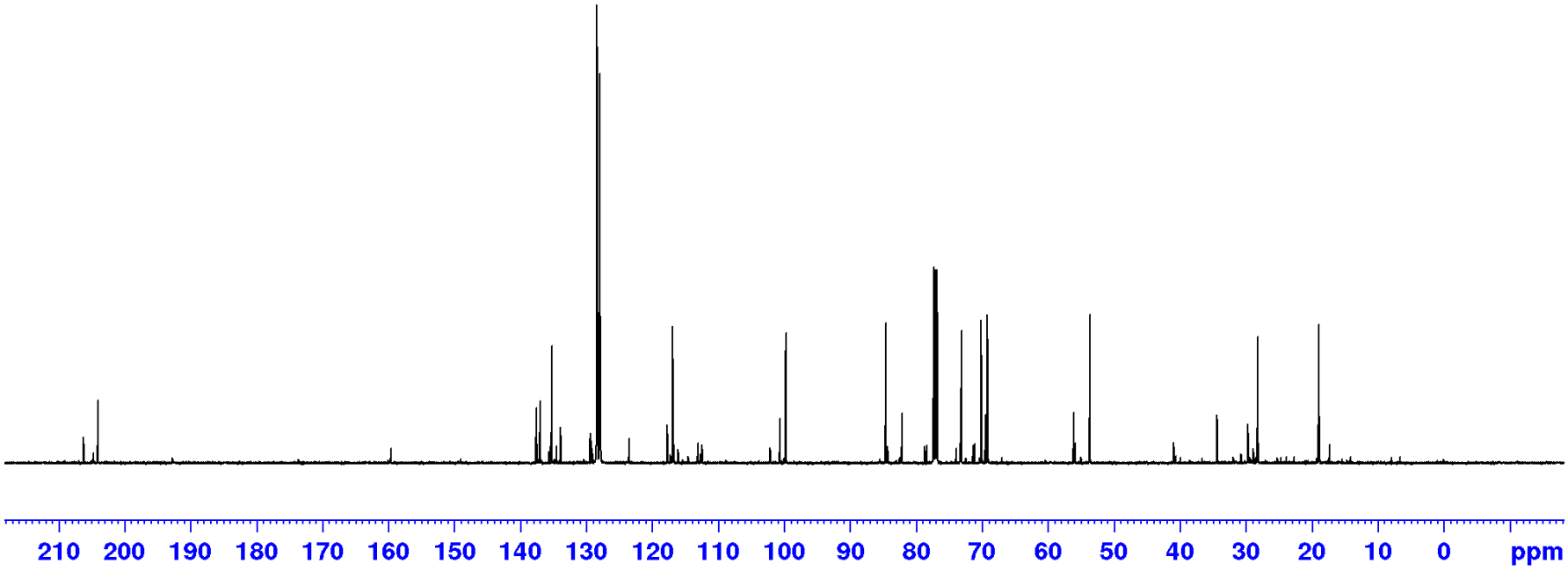

7.404
7.390
7.370
7.359
7.352
7.344
7.338
7.335
7.323
7.314
7.307
7.293
7.260
5.743
5.739
5.735
5.728
5.722
5.708
5.701
5.693
5.689
5.685
5.673
5.096
5.085
5.077
5.068
5.065
5.037
5.035
5.003
5.002
4.982
4.971
4.948
4.923
4.916
4.900
4.692
4.683
4.667
4.659
4.508
4.496
4.485
4.473
4.463
4.445
4.439
3.679
3.660
2.767
2.757
2.749
2.740
2.730
2.611
2.600
2.583
2.570
2.559
2.239
2.222
2.207
2.193
2.176
1.392
1.380
OBn
BnO
O
O
38a, 38b
1 H NMR (500 MHz, CDCl3)
10
9
8
7
6
5
4
3
2
1
ppm
10.44
0.24
1.00
1.08
1.08
2.06
0.63
1.05
1.17
1.07
0.78
0.92
0.75
0.75
3.03

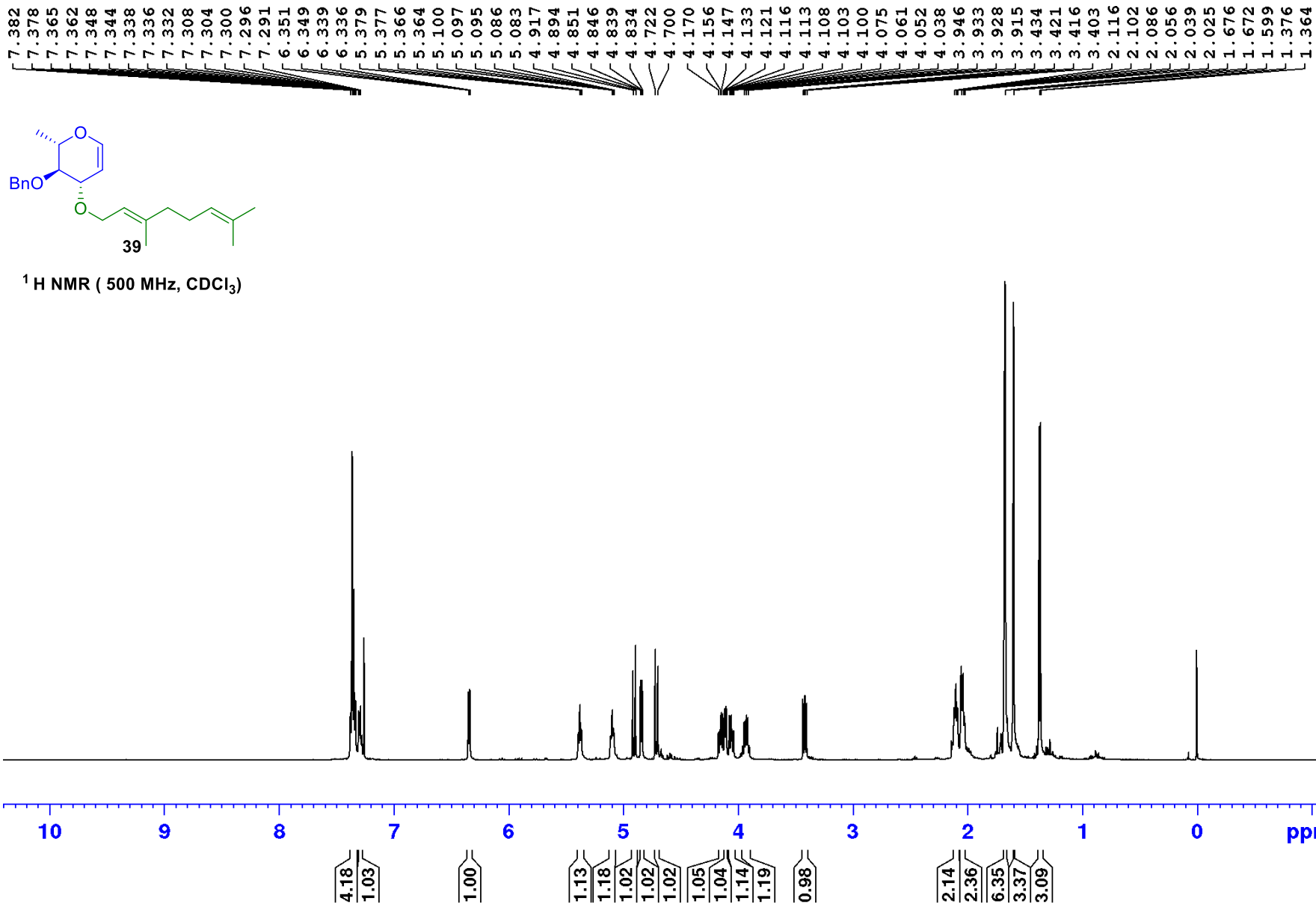
206.26
204.05
137.61
136.97
135.23
128.42
128.39
128.28
127.95
116.93
99.77
84.60
77.33
77.08
76.83
73.14
70.16
69.19
53.67
28.22
18.96

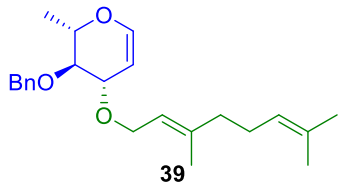


38a,38b

^{13}C NMR (125 MHz, $CDCl_3$)



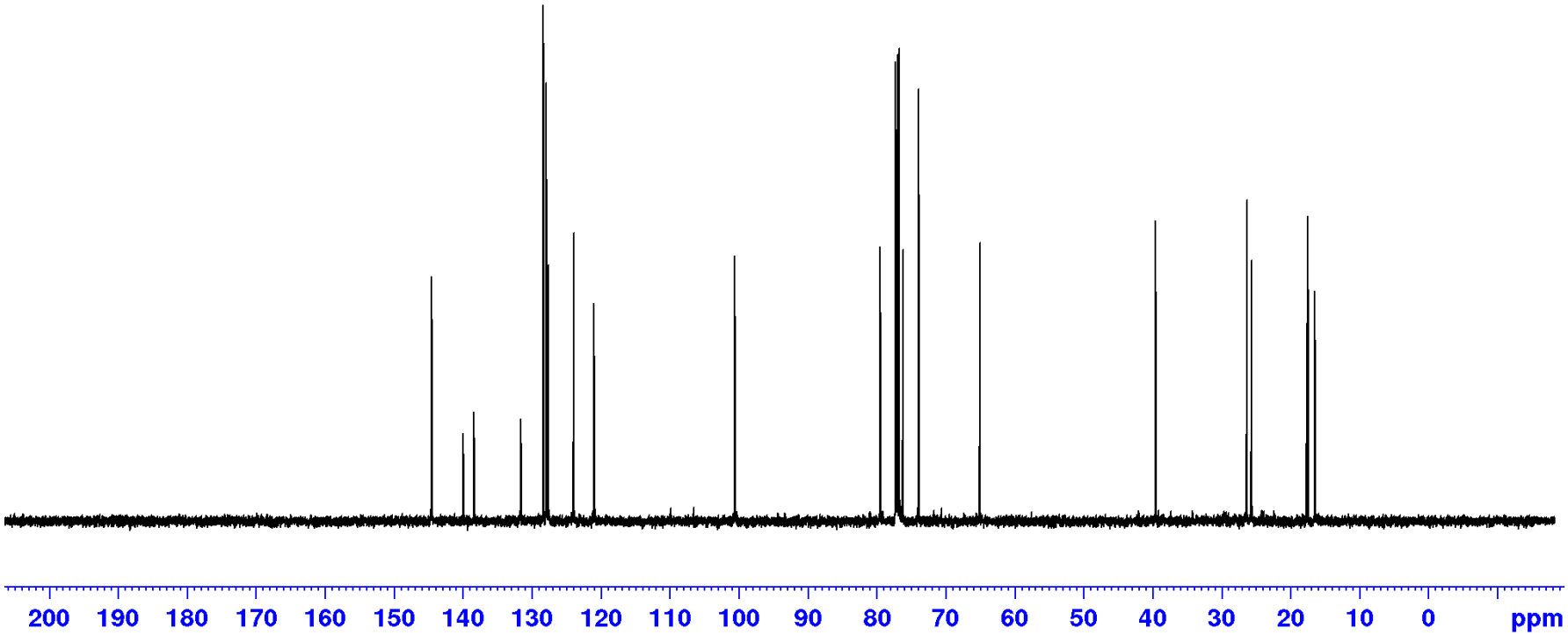

7.382
7.378
7.365
7.362
7.348
7.344
7.338
7.336
7.332
7.308
7.304
7.300
7.296
7.291
6.351
6.349
6.339
6.336
5.379
5.377
5.366
5.364
5.100
5.097
5.095
5.086
5.083
4.917
4.894
4.851
4.846
4.839
4.834
4.722
4.700
4.170
4.156
4.147
4.133
4.121
4.116
4.113
4.108
4.103
4.100
4.075
4.061
4.052
4.038
3.946
3.933
3.928
3.915
3.434
3.421
3.416
3.403
2.116
2.102
2.086
2.056
2.039
2.025
1.676
1.672
1.599
1.376
1.364
BnO
O
O
39
1 H NMR (500 MHz, CDCl3)
10
9
8
7
6
5
4
3
2
1
0
ppm
4.18
1.03
1.00
1.13
1.18
1.02
1.02
1.02
1.05
1.04
1.14
1.19
0.98
2.14
2.36
6.35
3.37
3.09

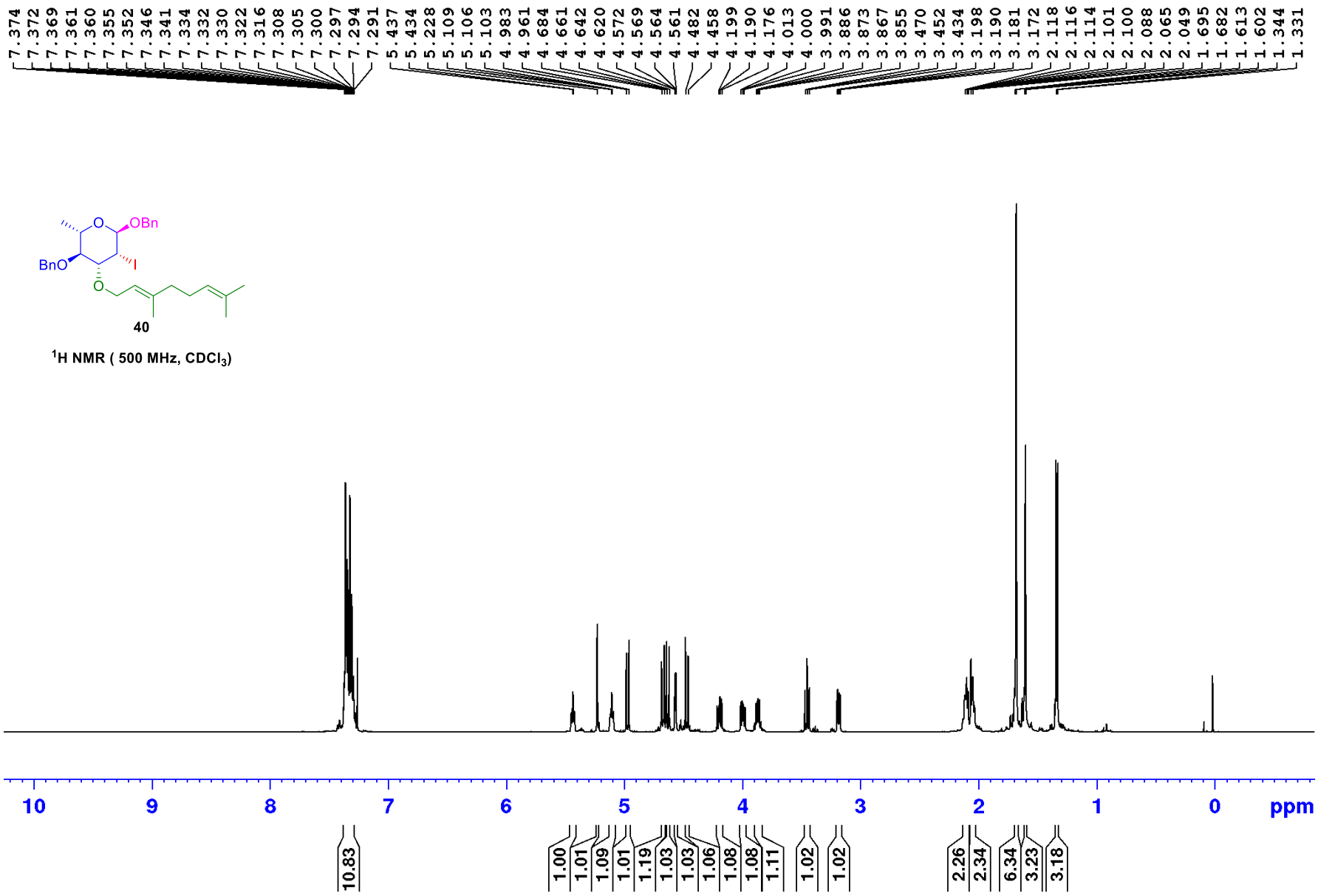


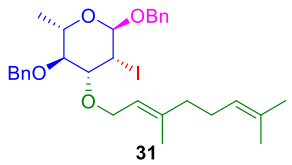
39

^{13}C NMR (125 MHz, CDCl)

144.52
139.97
138.41
131.62
128.33
127.91
127.65
123.92
121.01
100.58
79.52
77.25
77.00
76.75
76.21
73.94
65.04
39.56
26.33
25.65
17.65
17.49
16.46

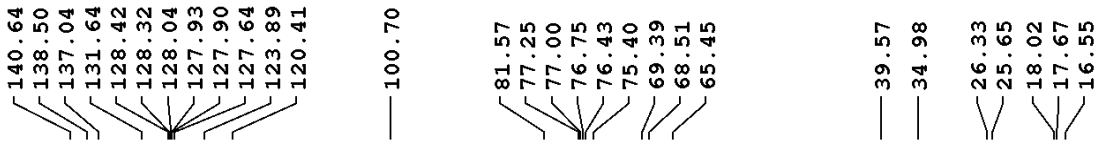


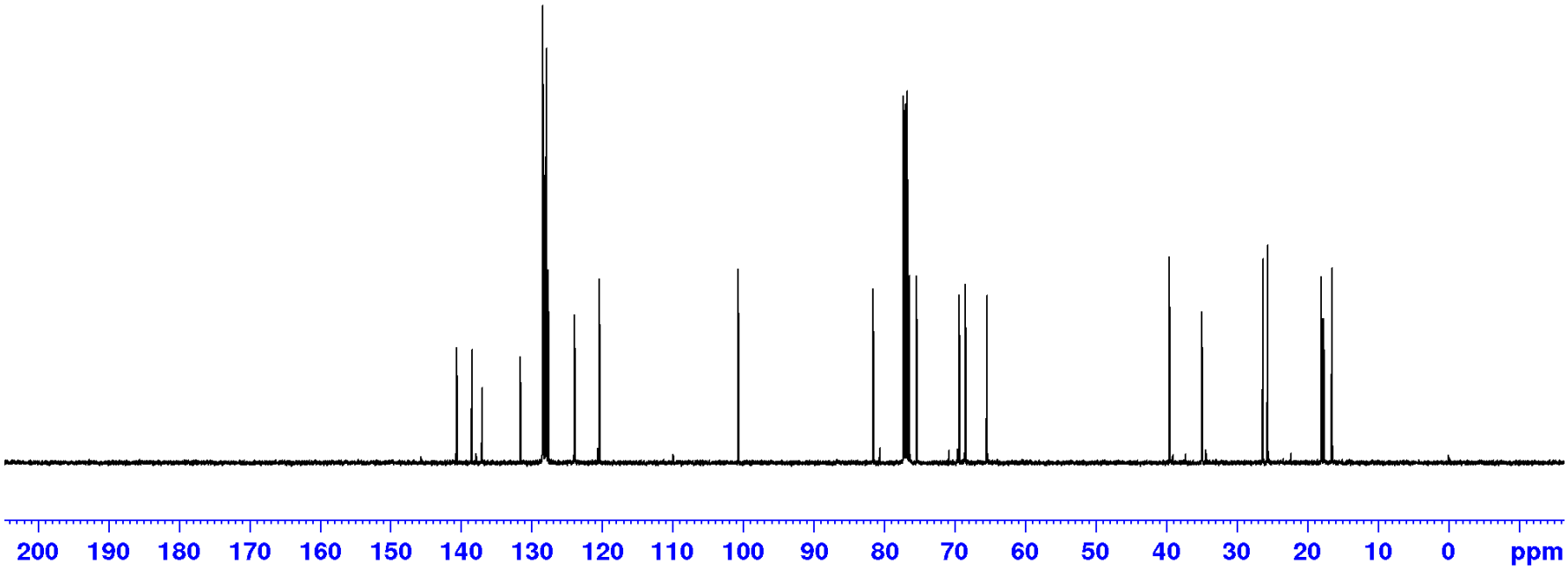

7.374
7.372
7.369
7.361
7.360
7.355
7.352
7.346
7.341
7.334
7.332
7.330
7.322
7.316
7.308
7.305
7.300
7.297
7.294
7.291
5.437
5.434
5.228
5.109
5.106
5.103
4.983
4.961
4.684
4.661
4.642
4.620
4.572
4.569
4.564
4.561
4.482
4.458
4.199
4.190
4.176
4.013
4.000
3.991
3.886
3.873
3.867
3.855
3.470
3.452
3.434
3.198
3.190
3.181
3.172
2.118
2.116
2.114
2.101
2.100
2.088
2.065
2.049
1.695
1.682
1.613
1.602
1.344
1.331
OBn
BnO
I
O
40
1H NMR (500 MHz, CDCl3)
10
9
8
7
6
5
4
3
2
1
0
ppm
10.83
1.00
1.01
1.09
1.01
1.19
1.03
1.03
1.06
1.08
1.08
1.11
1.02
1.02
2.26
2.34
6.34
3.23
3.18

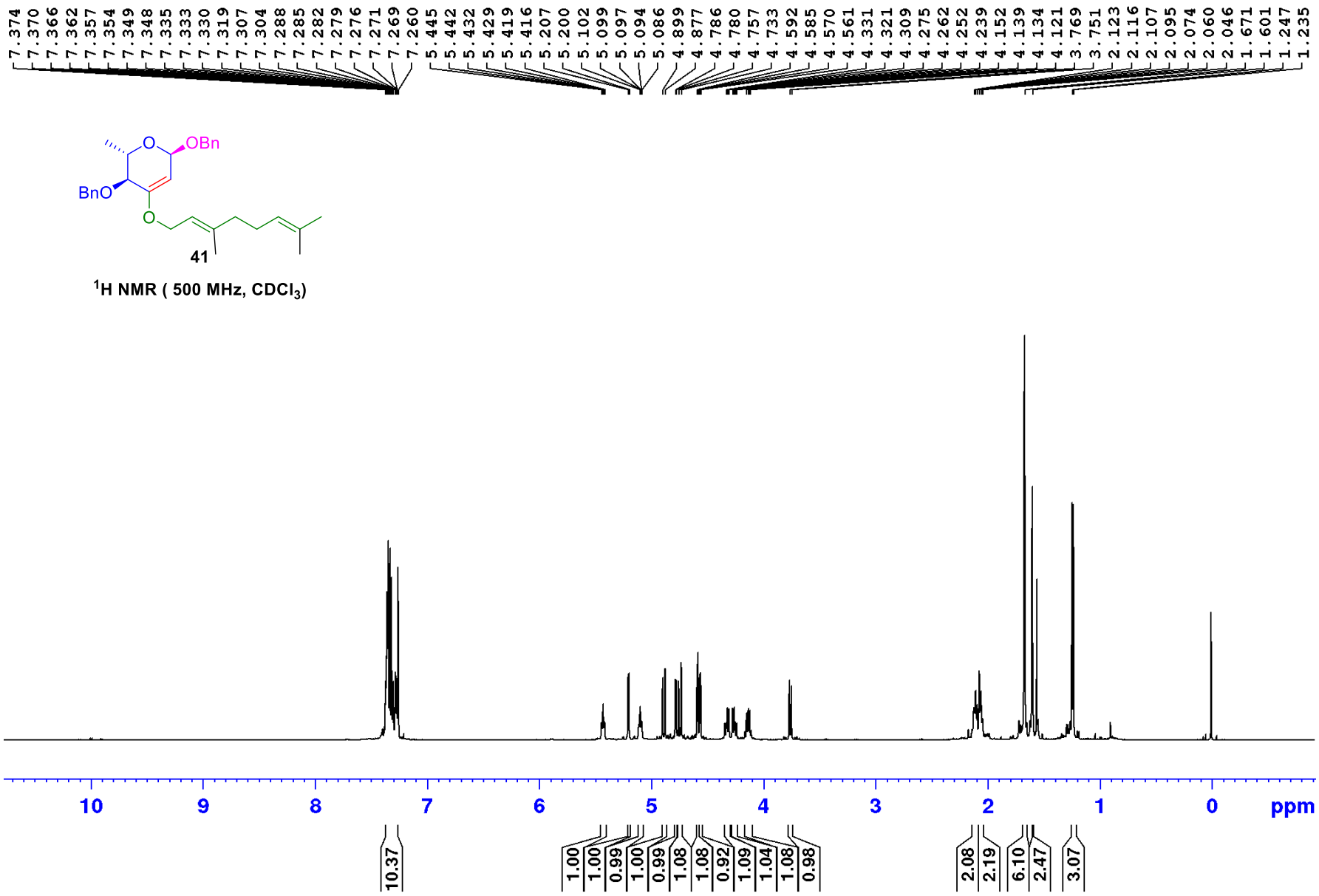


31

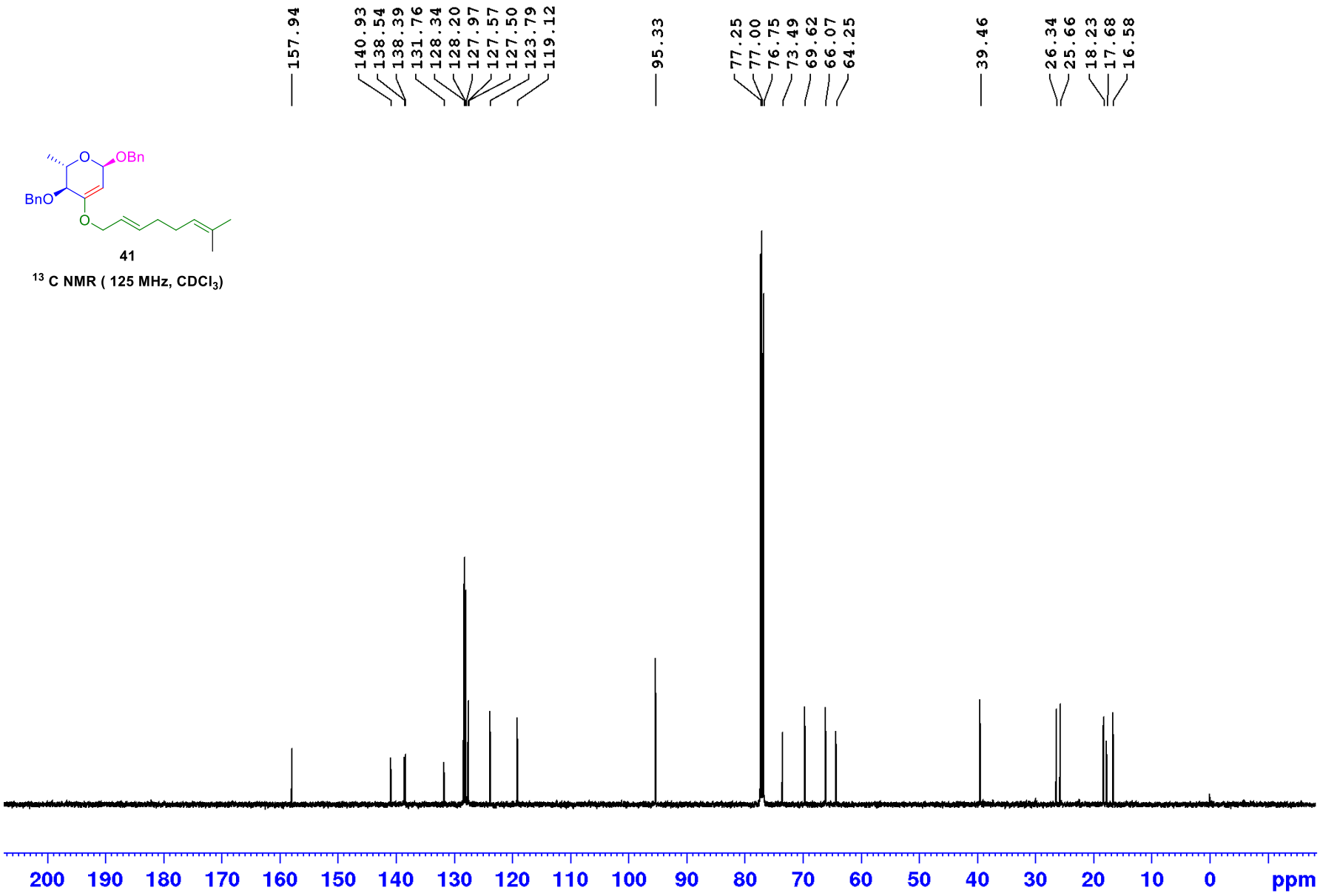
^{13} C NMR (125 MHz, $CDCl_3$)

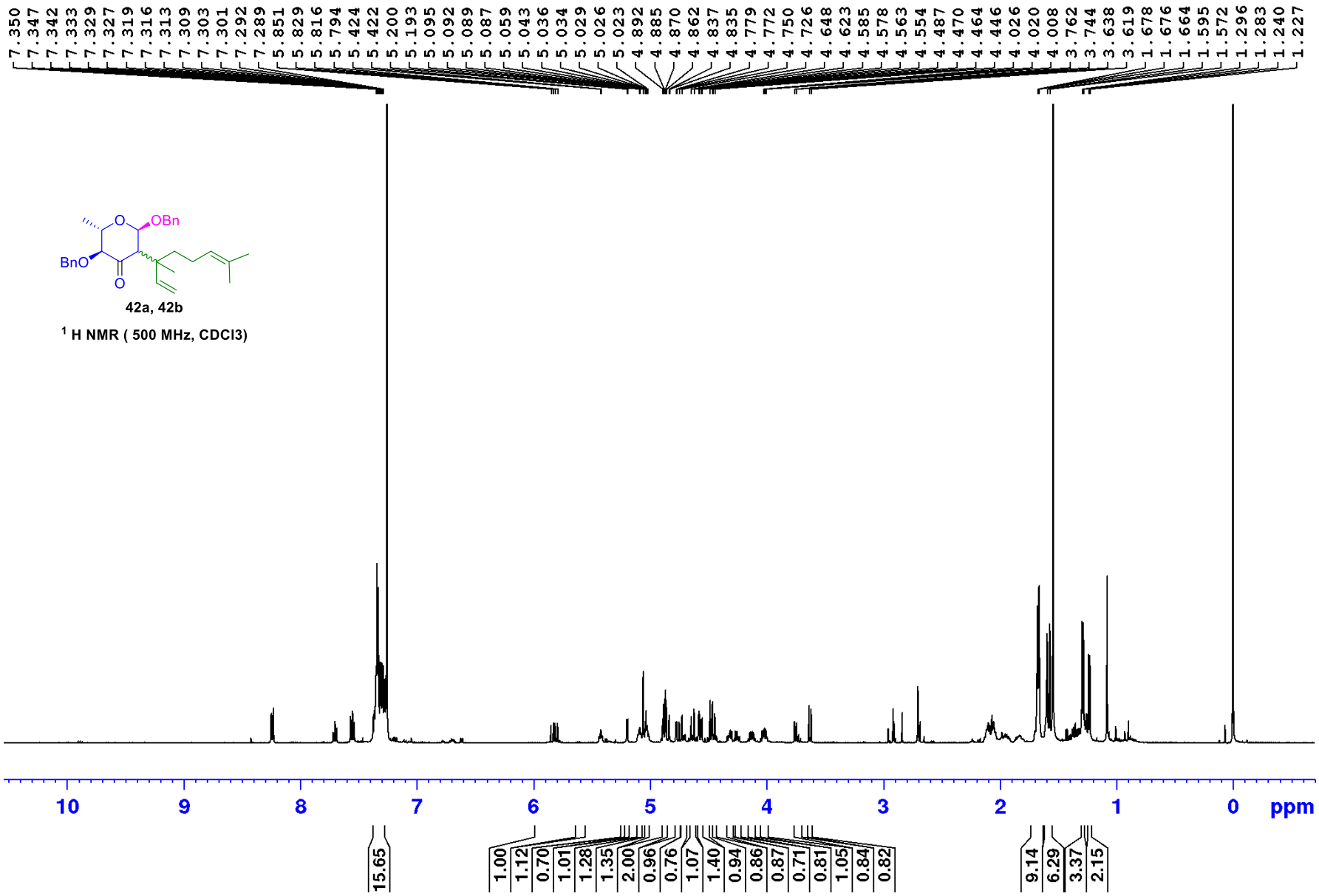


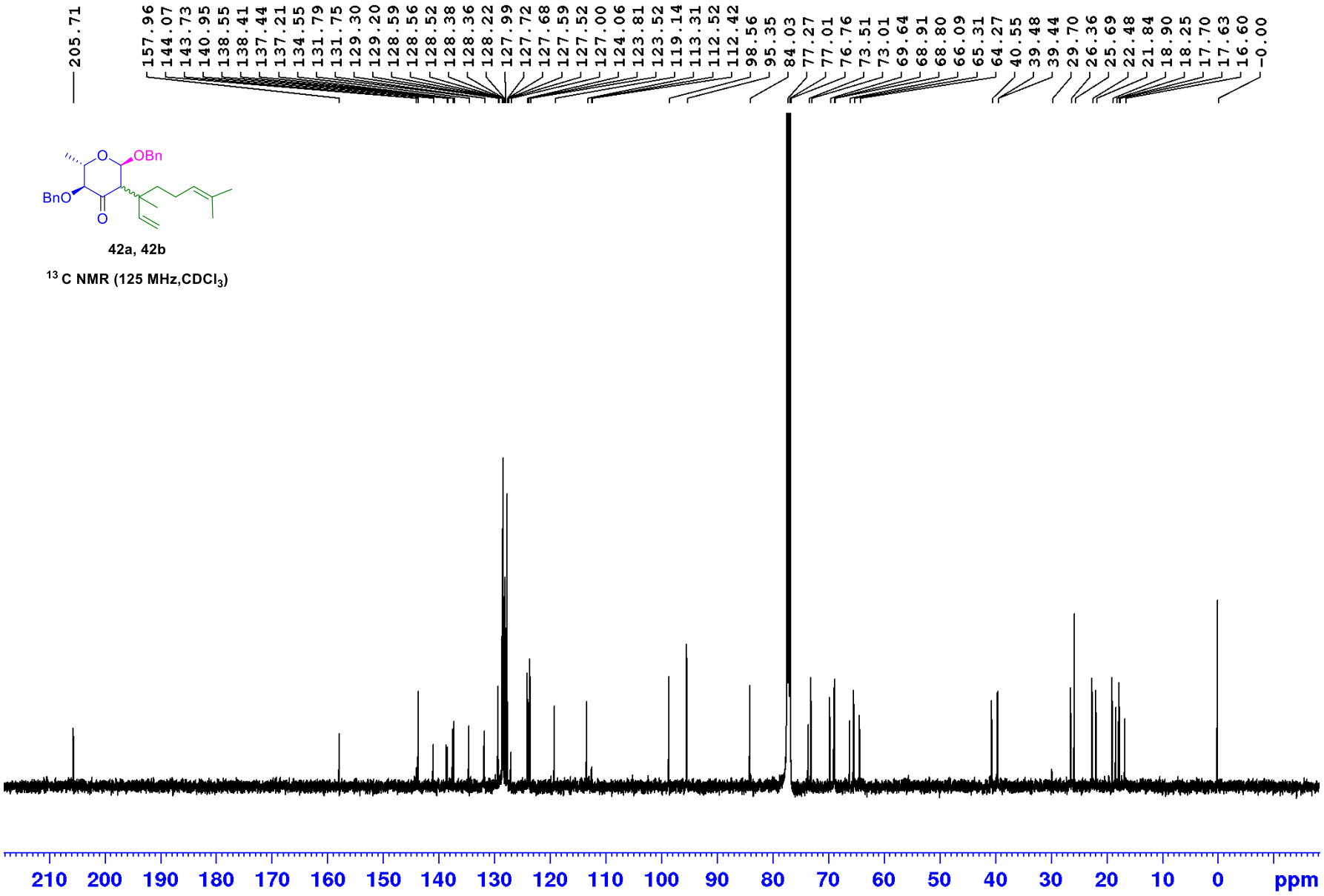




^{1}H NMR (500 MHz, $CDCl_3$)

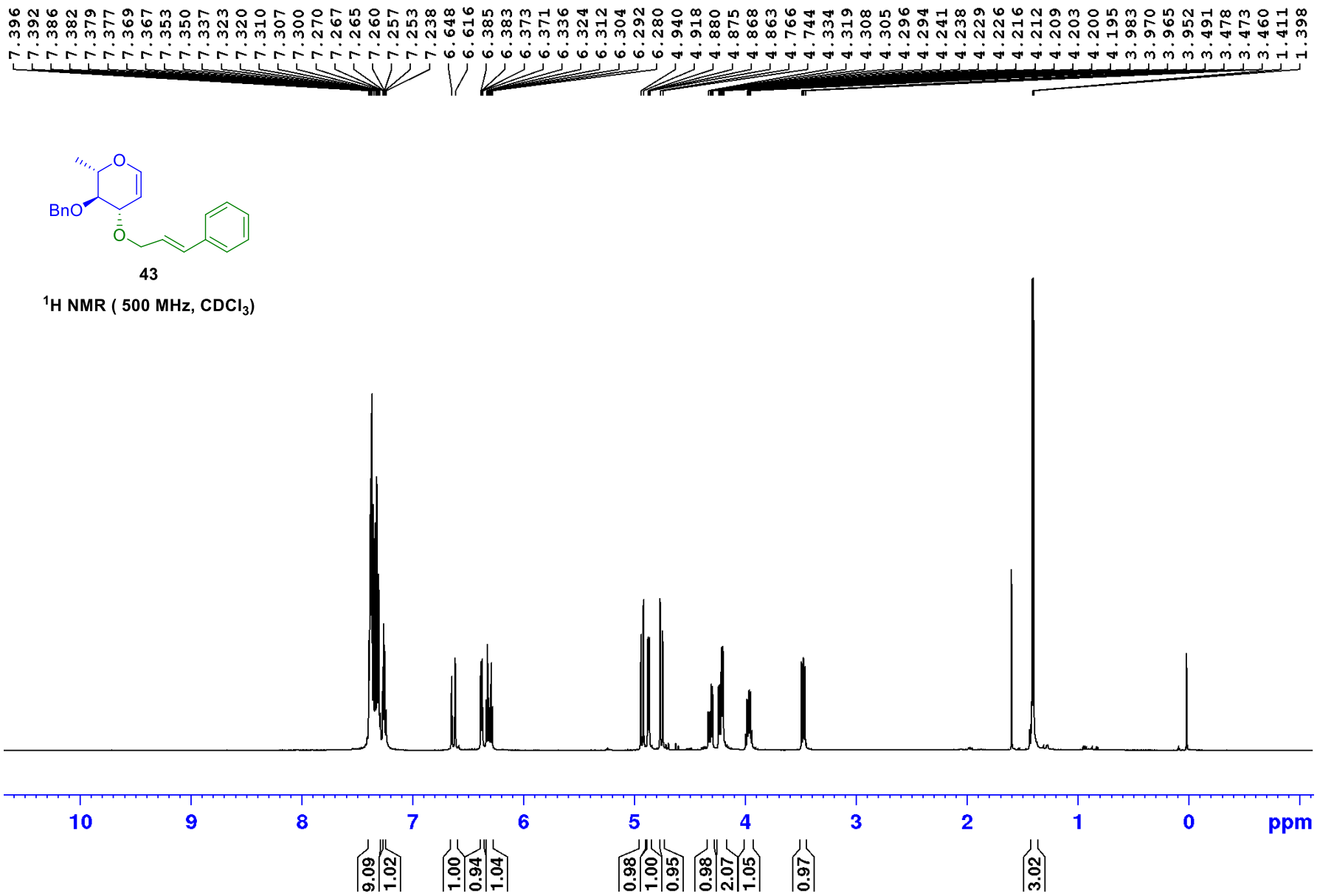

157.94
140.93
138.54
138.39
131.76
128.34
128.20
127.97
127.57
127.50
123.79
119.12
95.33
77.25
77.00
76.75
73.49
69.62
66.07
64.25
39.46
26.34
25.66
18.23
17.68
16.58
OBn
BnO
O
O
41
13 C NMR (125 MHz, CDCl3)
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
ppm

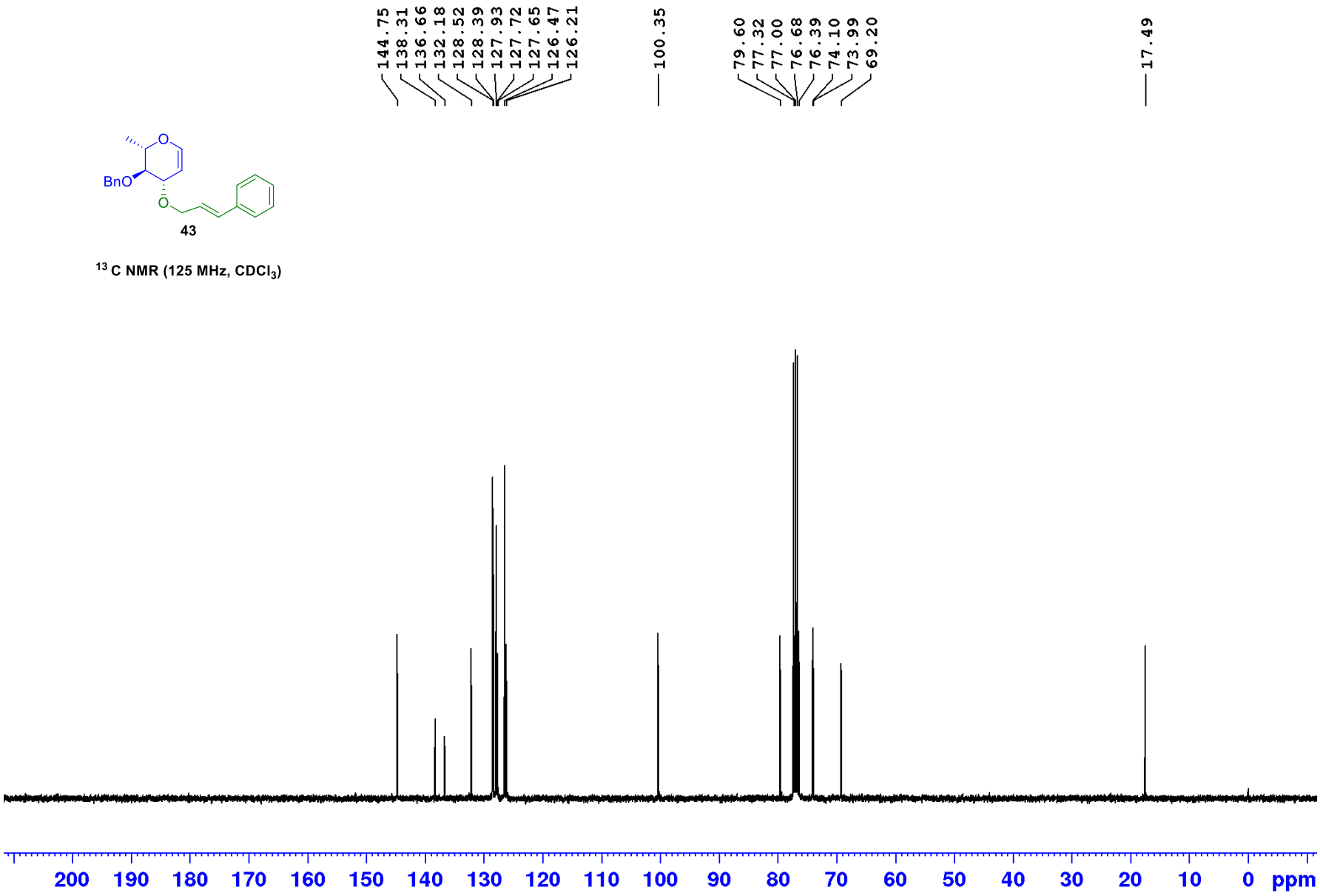

7.350
7.347
7.342
7.333
7.329
7.327
7.319
7.316
7.313
7.309
7.303
7.301
7.292
7.289
5.851
5.829
5.816
5.794
5.424
5.422
5.200
5.193
5.095
5.092
5.089
5.087
5.059
5.043
5.036
5.034
5.029
5.026
5.023
4.892
4.885
4.870
4.862
4.837
4.835
4.779
4.772
4.750
4.726
4.648
4.623
4.585
4.578
4.563
4.554
4.487
4.470
4.464
4.446
4.026
4.020
4.008
3.762
3.744
3.638
3.619
1.678
1.676
1.664
1.595
1.572
1.296
1.283
1.240
1.227
OBn
BnO
O
O
42a, 42b
1 H NMR (500 MHz, CDCl3)
10
9
8
7
6
5
4
3
2
1
0
ppm
15.65
1.00
1.12
0.70
1.01
1.28
1.35
2.00
0.96
0.76
1.07
1.40
0.94
0.86
0.87
0.71
0.81
1.05
0.84
0.82
9.14
6.29
3.37
2.15



42a, 42b

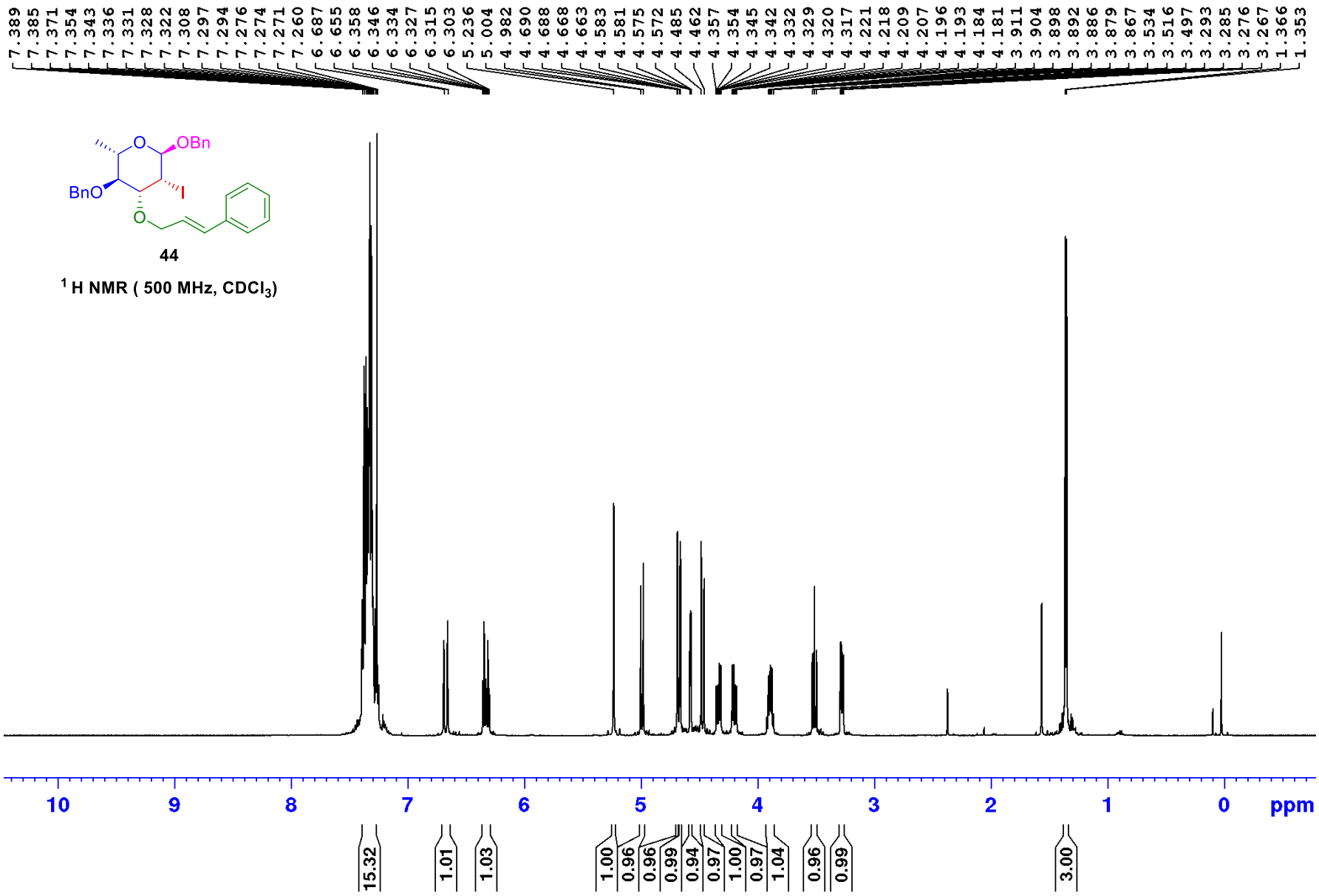
^{13}C NMR (125 MHz,$CDCl_3$)

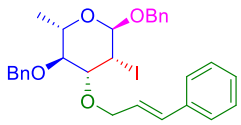

7.396
7.392
7.386
7.382
7.379
7.377
7.369
7.367
7.353
7.350
7.337
7.323
7.320
7.310
7.307
7.300
7.270
7.267
7.265
7.260
7.257
7.253
7.238
6.648
6.616
6.385
6.383
6.373
6.371
6.336
6.324
6.312
6.304
6.292
6.280
4.940
4.918
4.880
4.875
4.868
4.863
4.766
4.744
4.334
4.319
4.308
4.305
4.296
4.294
4.241
4.238
4.229
4.226
4.216
4.212
4.209
4.203
4.200
4.195
3.983
3.970
3.965
3.952
3.491
3.478
3.473
3.460
1.411
1.398
BnO
O
O
43
1H NMR (500 MHz, CDCl3)
10
9
8
7
6
5
4
3
2
1
0
ppm
9.09
1.02
1.00
0.94
1.04
0.98
1.00
0.95
0.98
2.07
1.05
0.97
3.02



43

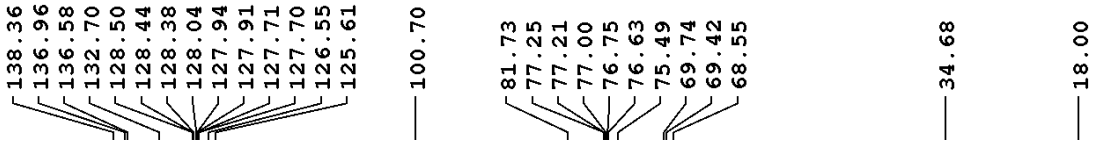
^{13}C NMR (125 MHz, $CDCl_3$)

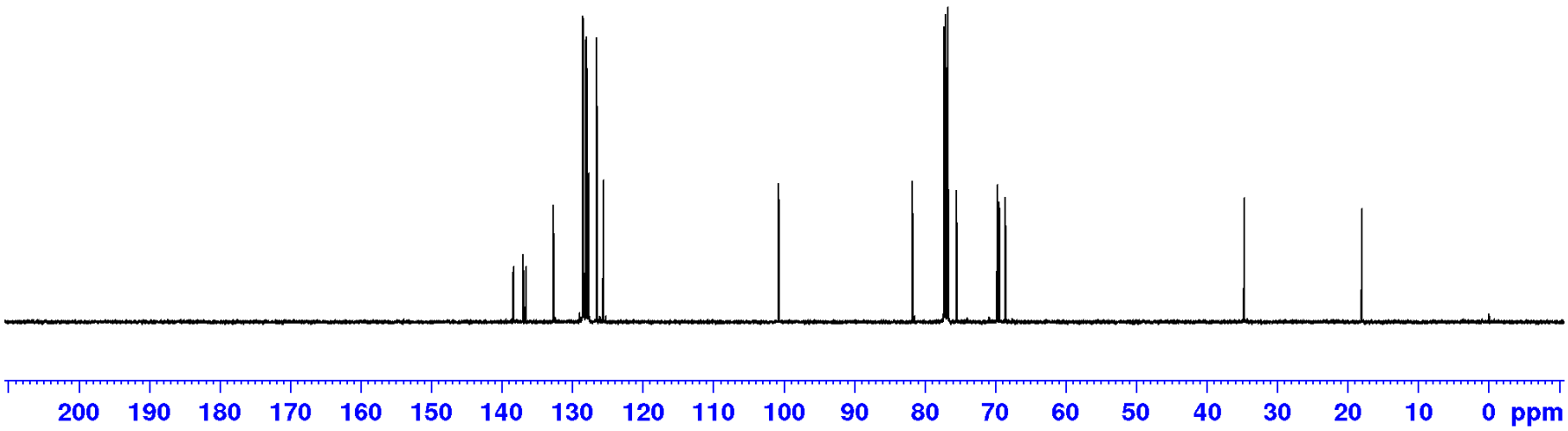

7.389
7.385
7.371
7.354
7.343
7.336
7.331
7.328
7.322
7.308
7.297
7.294
7.276
7.274
7.271
7.260
6.687
6.655
6.358
6.346
6.334
6.327
6.315
6.303
5.236
5.004
4.982
4.690
4.688
4.668
4.663
4.583
4.581
4.575
4.572
4.485
4.462
4.357
4.354
4.345
4.342
4.332
4.329
4.320
4.317
4.221
4.218
4.209
4.207
4.196
4.193
4.184
4.181
3.911
3.904
3.898
3.892
3.886
3.879
3.867
3.534
3.516
3.497
3.293
3.285
3.276
3.267
1.366
1.353
OBn
BnO
I
O
44
1 H NMR (500 MHz, CDCl3)
10
9
8
7
6
5
4
3
2
1
0
ppm
15.32
1.01
1.03
1.00
0.96
0.96
0.99
0.94
0.97
1.00
0.97
1.04
0.96
0.99
3.00

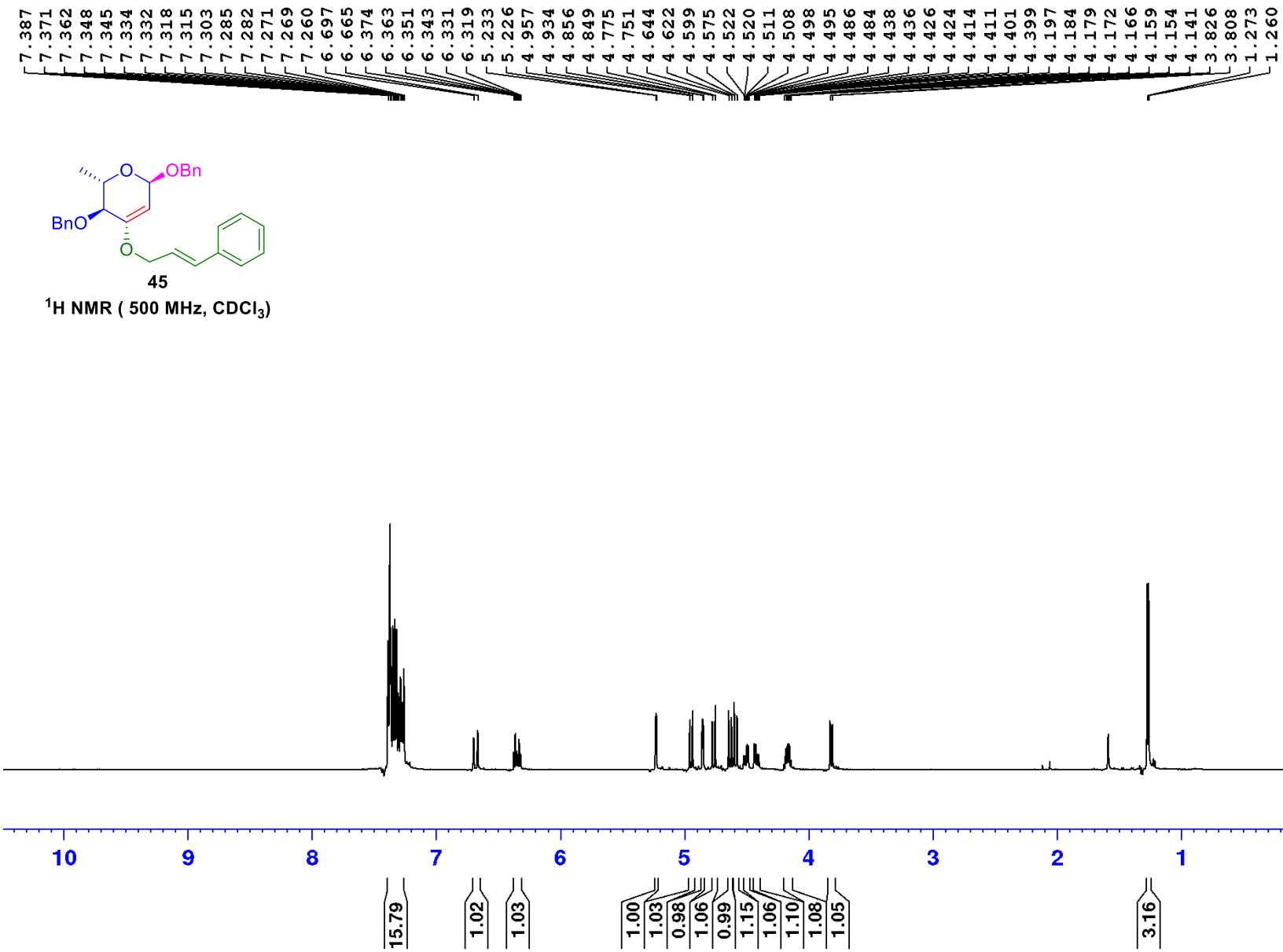


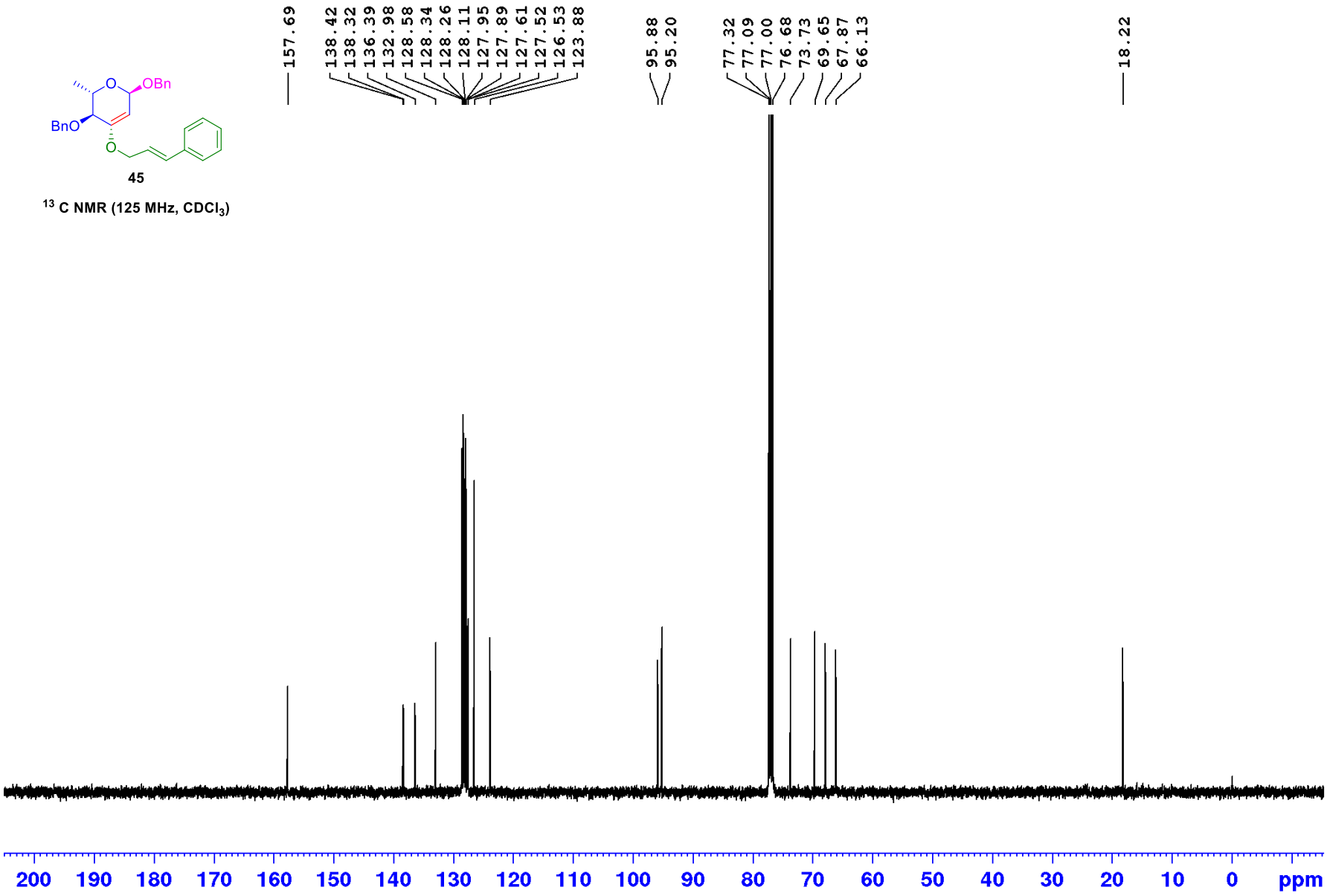
44

^{13} C NMR (125 MHz, $CDCl_3$)



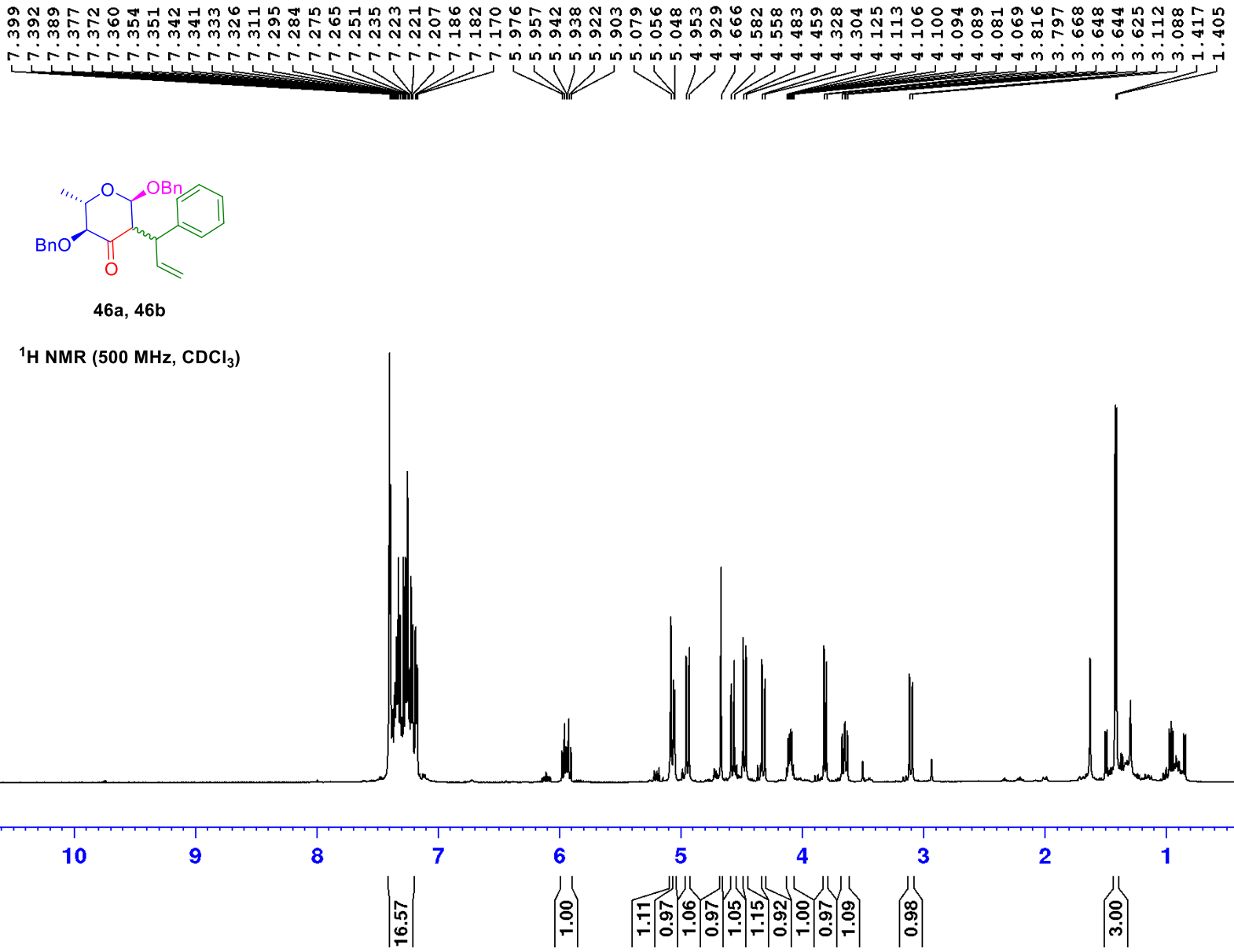


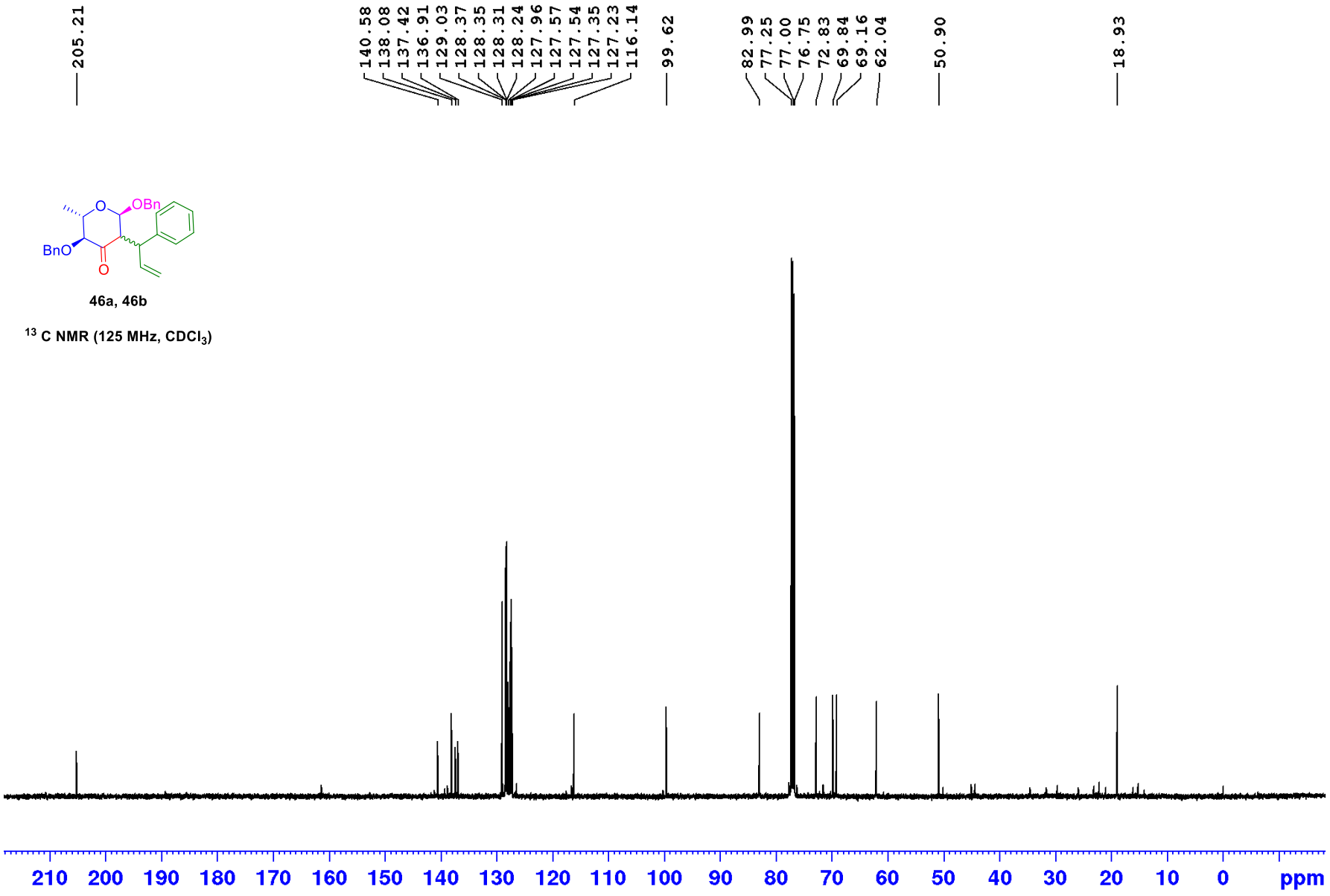

7.387
7.371
7.362
7.348
7.345
7.334
7.332
7.318
7.315
7.303
7.285
7.282
7.271
7.269
7.260
6.697
6.665
6.374
6.363
6.351
6.343
6.331
6.319
5.233
5.226
4.957
4.934
4.856
4.849
4.775
4.751
4.644
4.622
4.599
4.575
4.522
4.520
4.511
4.508
4.498
4.495
4.486
4.484
4.438
4.436
4.426
4.424
4.414
4.411
4.401
4.399
4.197
4.184
4.179
4.172
4.166
4.159
4.154
4.141
3.826
3.808
1.273
1.260
O
OBn
BnO
O
45
1H NMR (500 MHz, CDCl3)
10
9
8
7
6
5
4
3
2
1
0
ppm
15.79
1.02
1.03
1.00
1.03
0.98
1.06
0.99
1.15
1.06
1.10
1.08
1.05
3.16

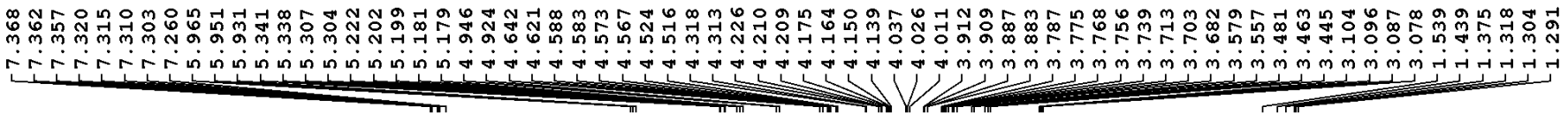


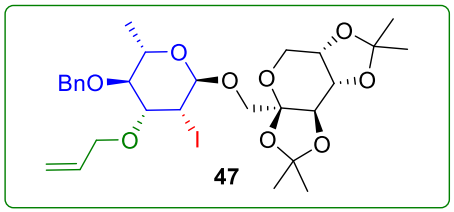
45

^{13}C NMR (125 MHz, $CDCl_3$)


7.399
7.392
7.389
7.377
7.372
7.360
7.354
7.351
7.342
7.341
7.333
7.326
7.311
7.295
7.284
7.275
7.265
7.251
7.235
7.223
7.221
7.207
7.186
7.182
7.170
5.976
5.957
5.942
5.938
5.922
5.903
5.079
5.056
5.048
4.953
4.929
4.666
4.582
4.558
4.483
4.459
4.328
4.304
4.125
4.113
4.106
4.100
4.094
4.089
4.081
4.069
3.816
3.797
3.668
3.648
3.644
3.625
3.112
3.088
1.417
1.405
O
OBn
BnO
O
46a, 46b
1H NMR (500 MHz, CDCl3)
10
9
8
7
6
5
4
3
2
1
0
ppm
16.57
1.00
1.11
0.97
1.06
0.97
1.05
1.15
0.92
1.00
0.97
1.09
0.98
3.00

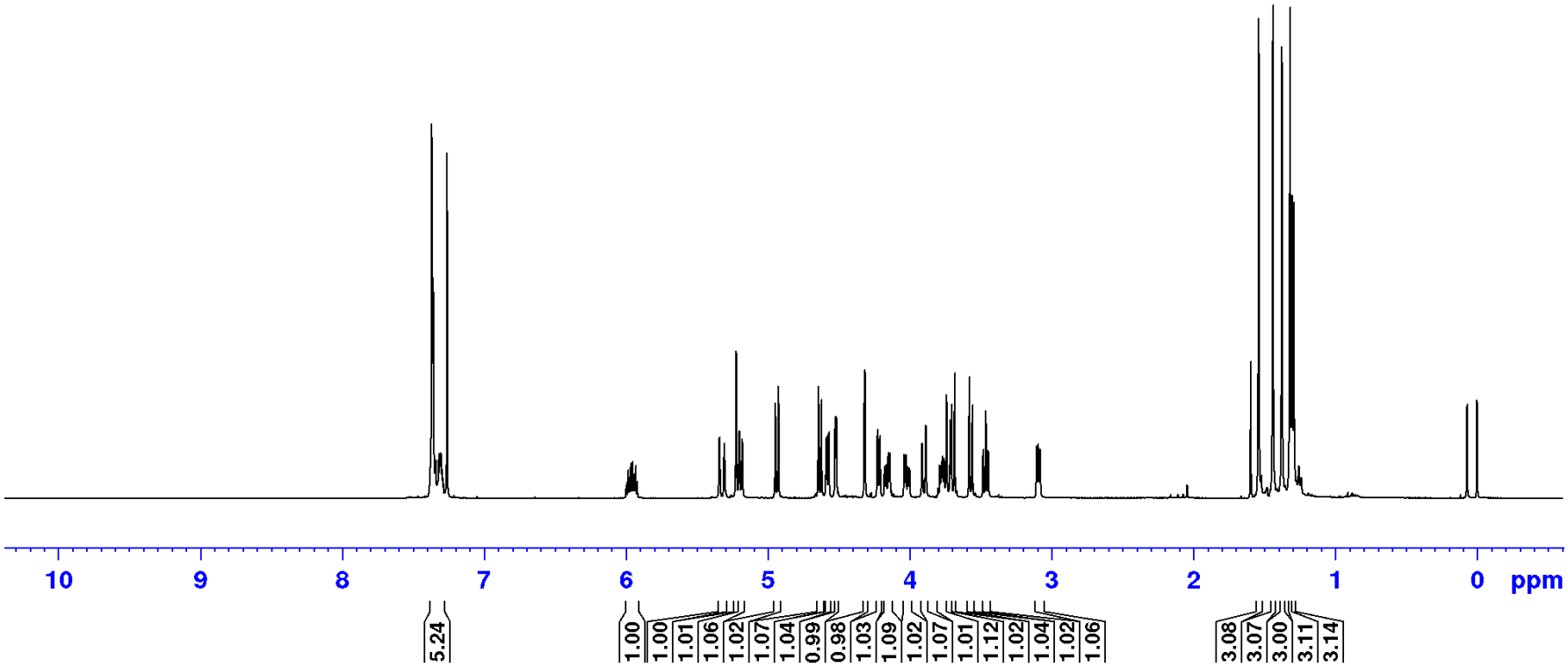

205.21
140.58
138.08
137.42
136.91
129.03
128.37
128.35
128.31
128.24
127.96
127.57
127.54
127.35
127.23
116.14
99.62
82.99
77.25
77.00
76.75
72.83
69.84
69.16
62.04
50.90
18.93
OBn
BnO
O
O
46a, 46b
13 C NMR (125 MHz, CDCl3)
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
ppm

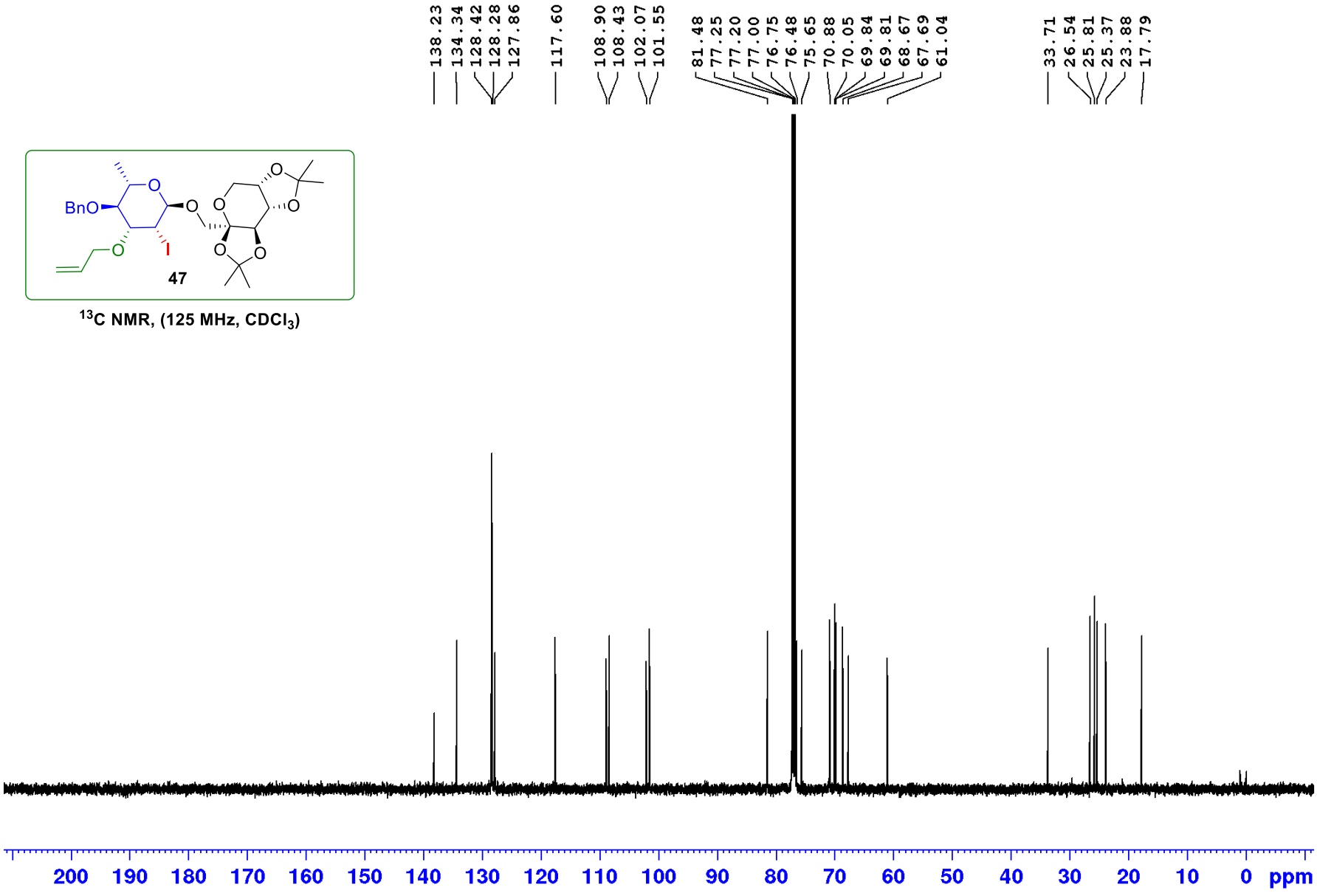




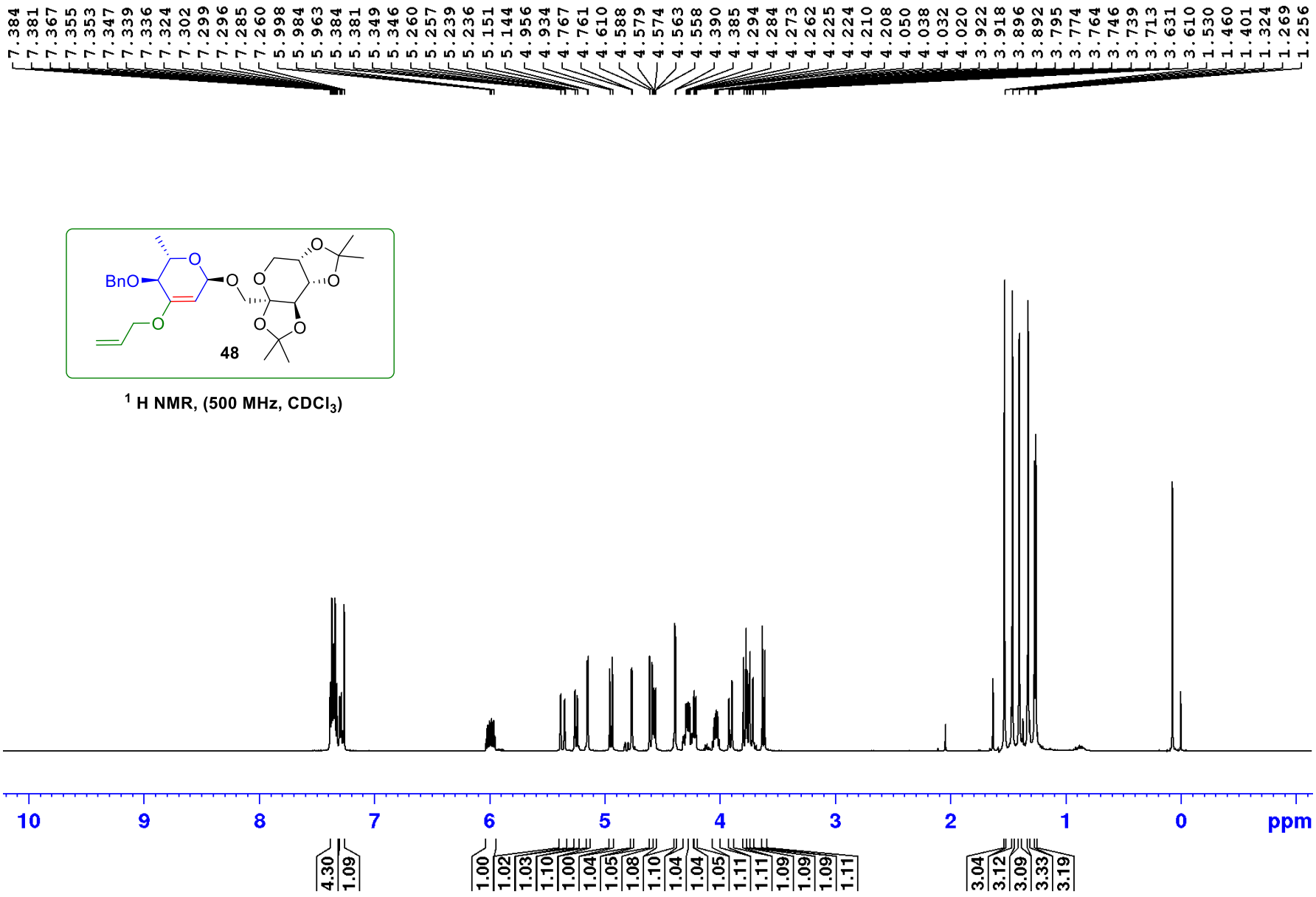
47

^{1}H NMR, (500 MHz, $CDCl_3$)

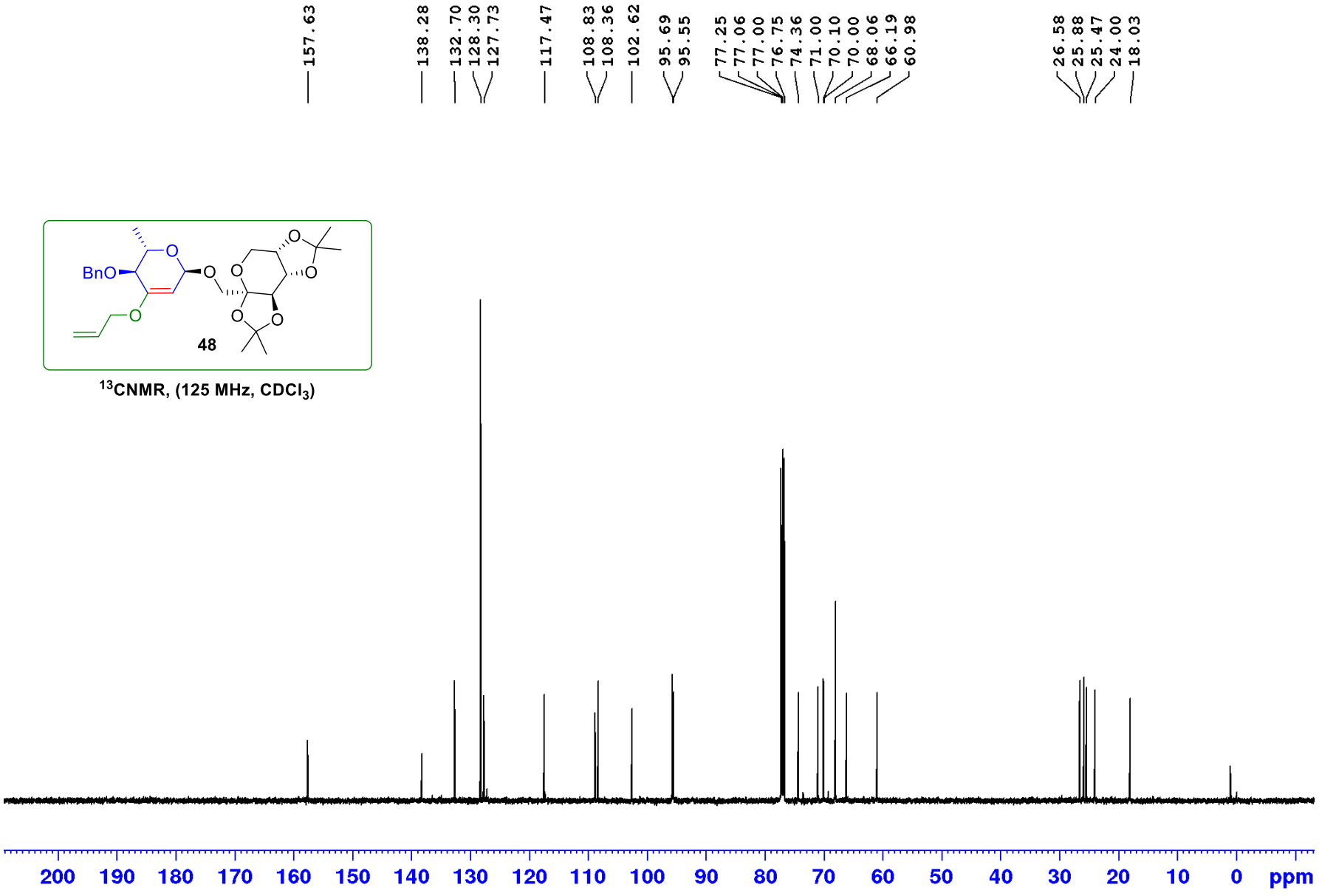




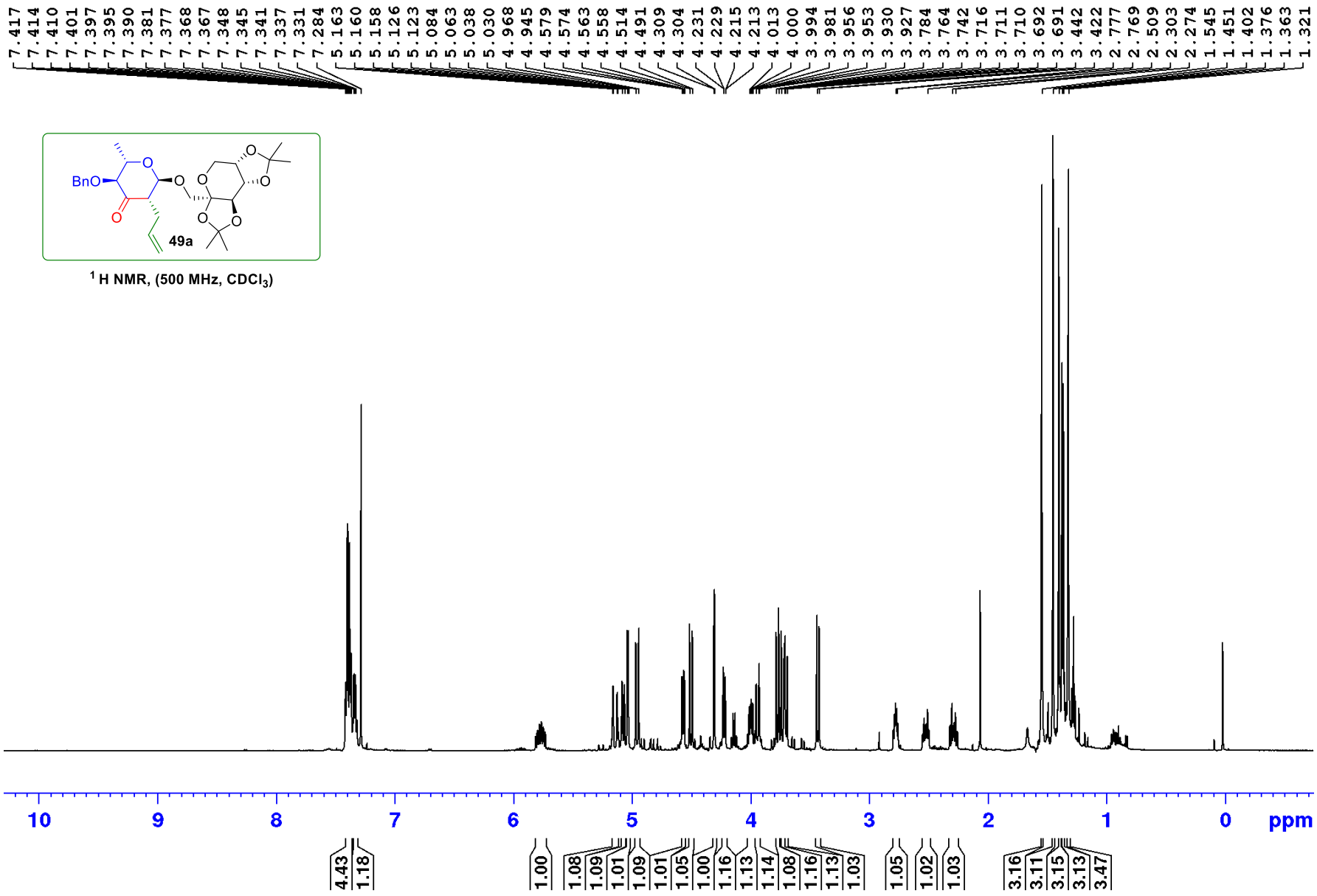
^{13}C NMR, (125 MHz, $CDCl_3$)



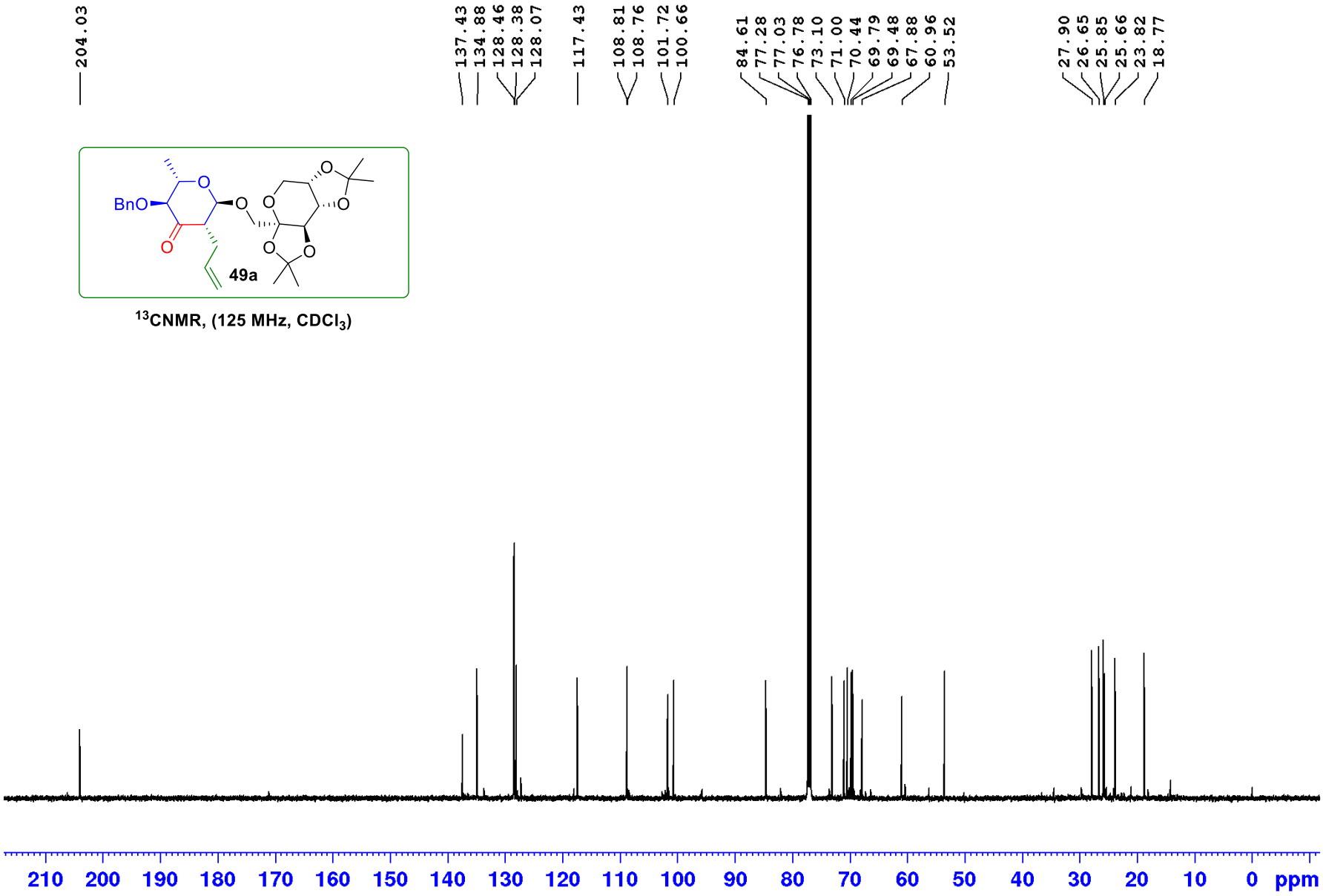
^{1} H NMR, (500 MHz, $CDCl_3$)



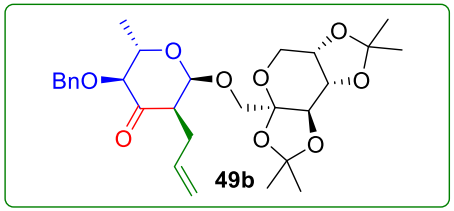
^{13}CNMR, (125 MHz, $CDCl_3$)



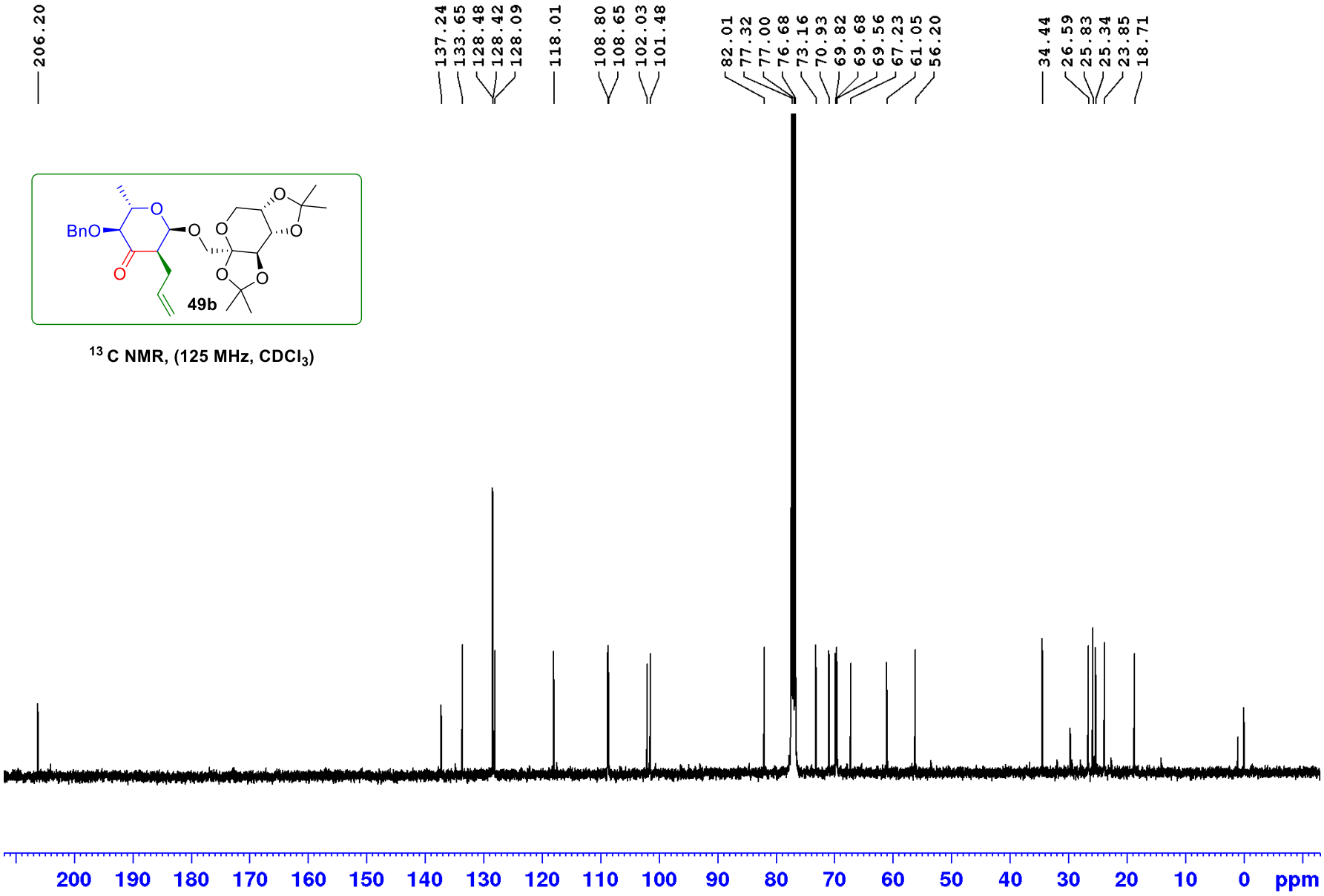
^{1}H NMR, (500 MHz, $CDCl_3$)



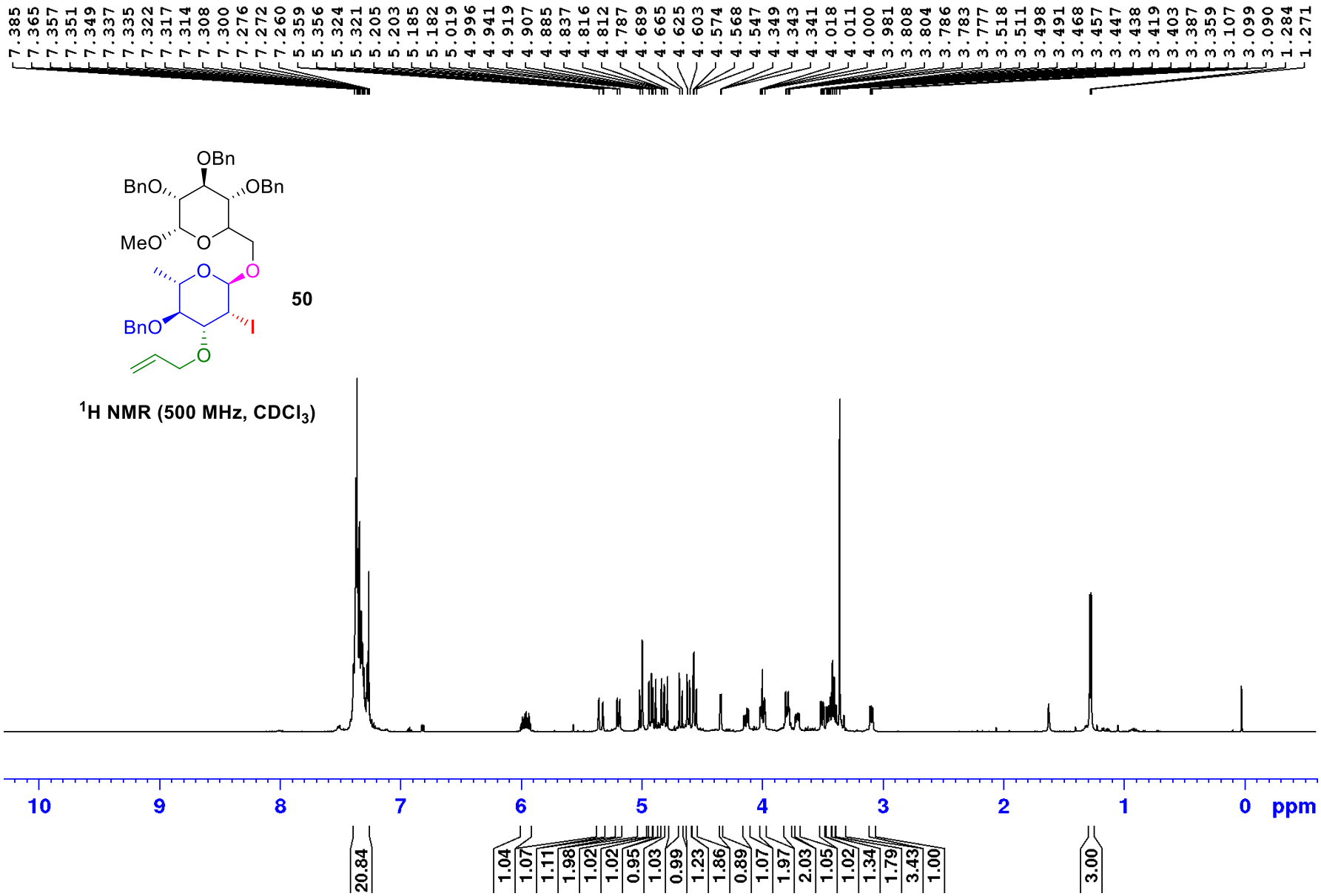
^{13}CNMR, (125 MHz, $CDCl_3$)

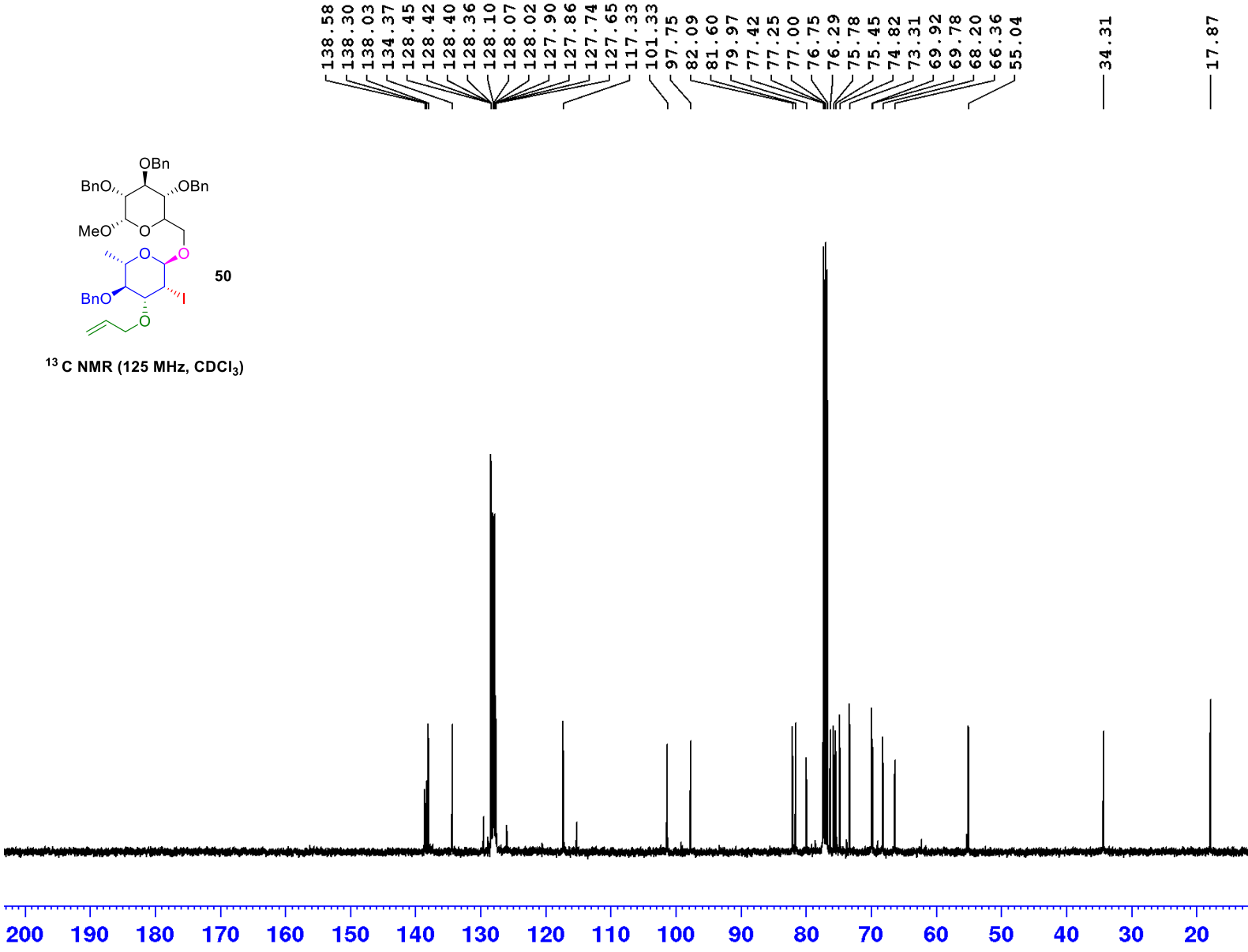


^{1}H NMR, (500 MHz, $CDCl_3$)

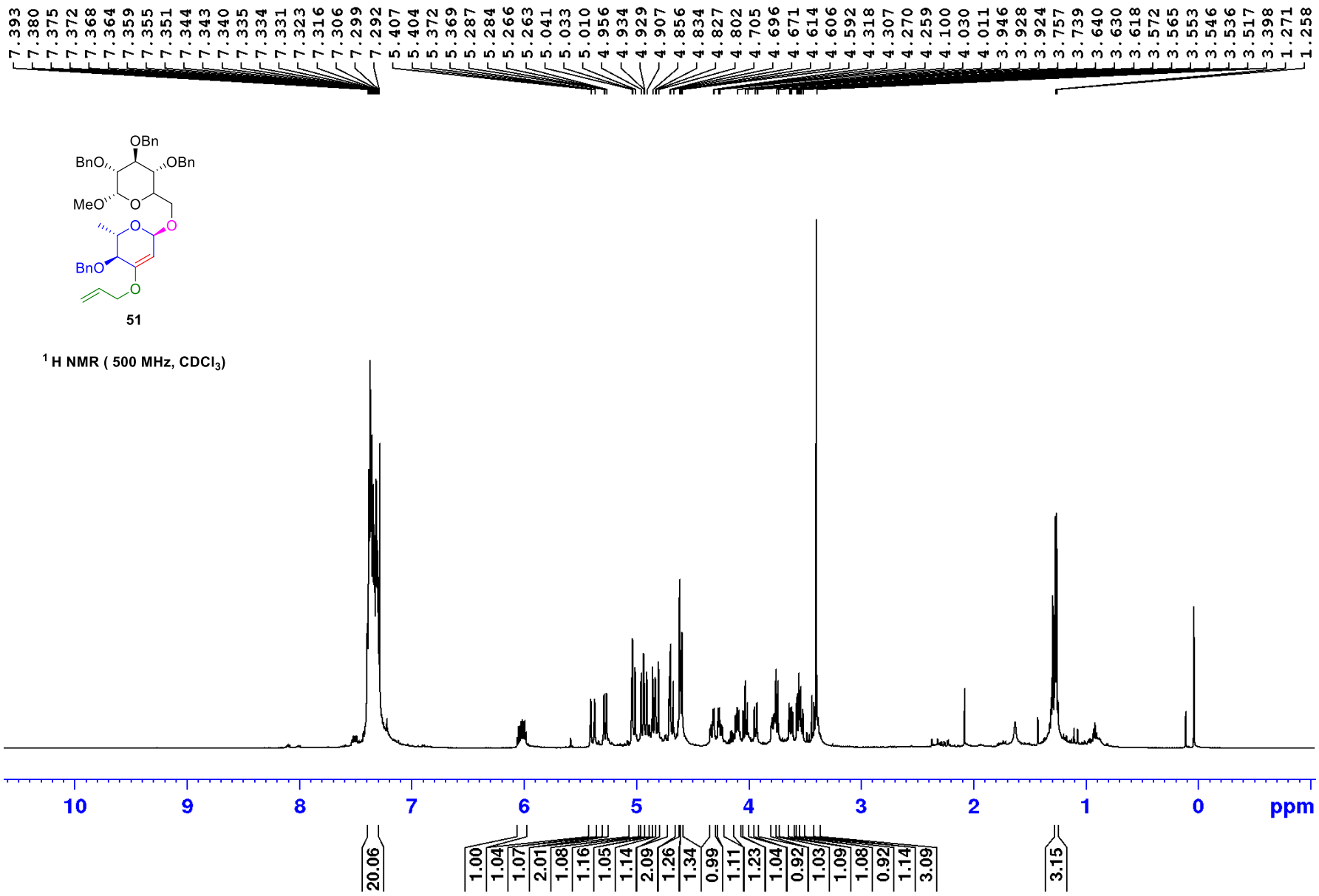


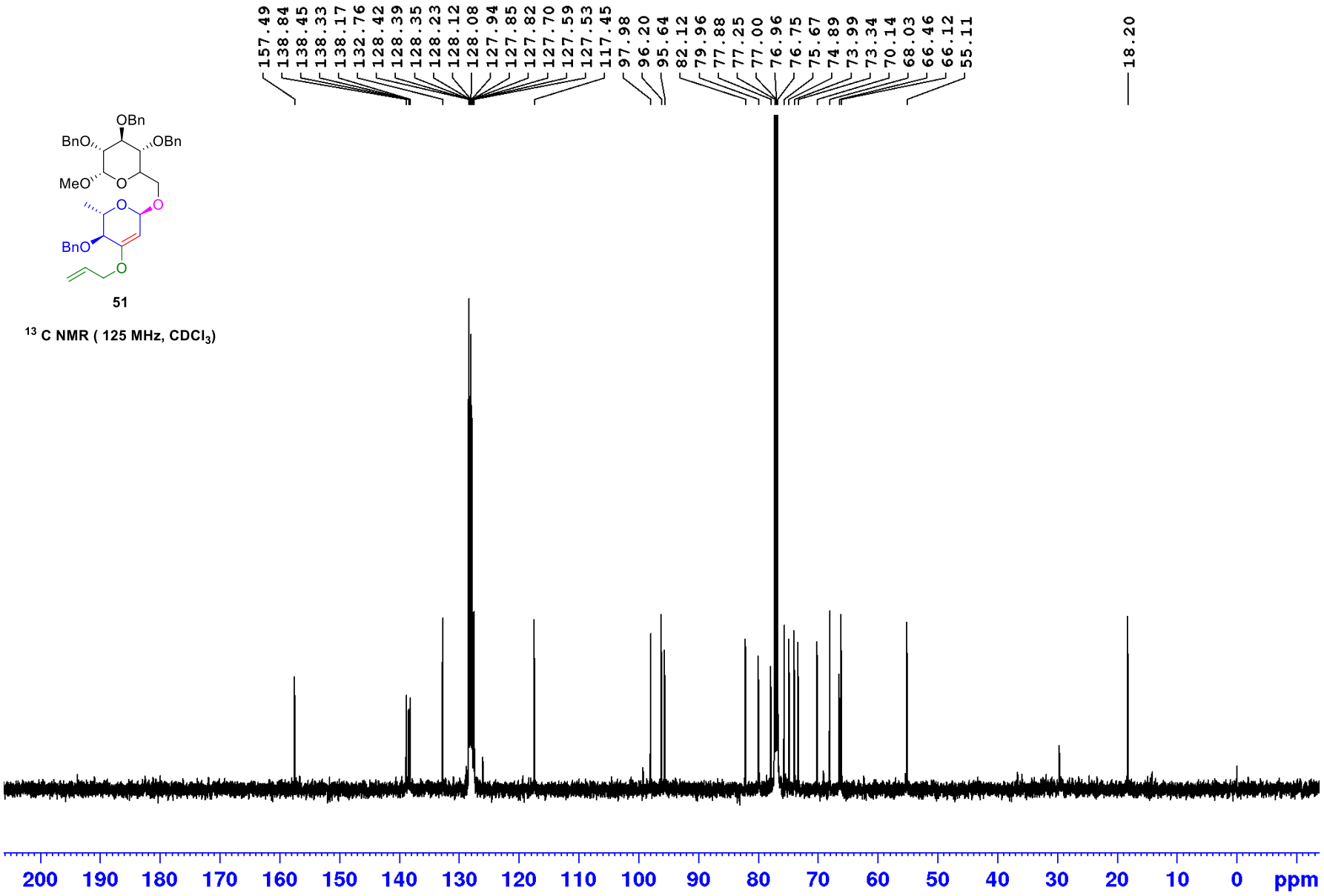
^{13}C NMR, (125 MHz, $CDCl_3$)


7.385
7.365
7.357
7.351
7.349
7.337
7.335
7.322
7.317
7.314
7.308
7.300
7.276
7.272
7.260
5.359
5.356
5.324
5.321
5.205
5.203
5.185
5.182
5.019
4.996
4.941
4.919
4.907
4.885
4.837
4.816
4.812
4.787
4.689
4.665
4.625
4.603
4.574
4.568
4.547
4.349
4.343
4.341
4.018
4.011
4.000
3.981
3.808
3.804
3.786
3.783
3.777
3.518
3.511
3.498
3.491
3.468
3.457
3.447
3.438
3.419
3.403
3.387
3.359
3.107
3.099
3.090
1.284
1.271
OBn
BnO
OBn
MeO
O
O
O
BnO
I
O
50
1H NMR (500 MHz, CDCl3)
10
9
8
7
6
5
4
3
2
1
0
ppm
20.84
1.04
1.07
1.11
1.98
1.02
1.02
1.02
0.95
1.03
0.99
1.23
1.86
0.89
1.07
1.97
2.03
1.05
1.02
1.34
1.79
3.43
1.00
3.00



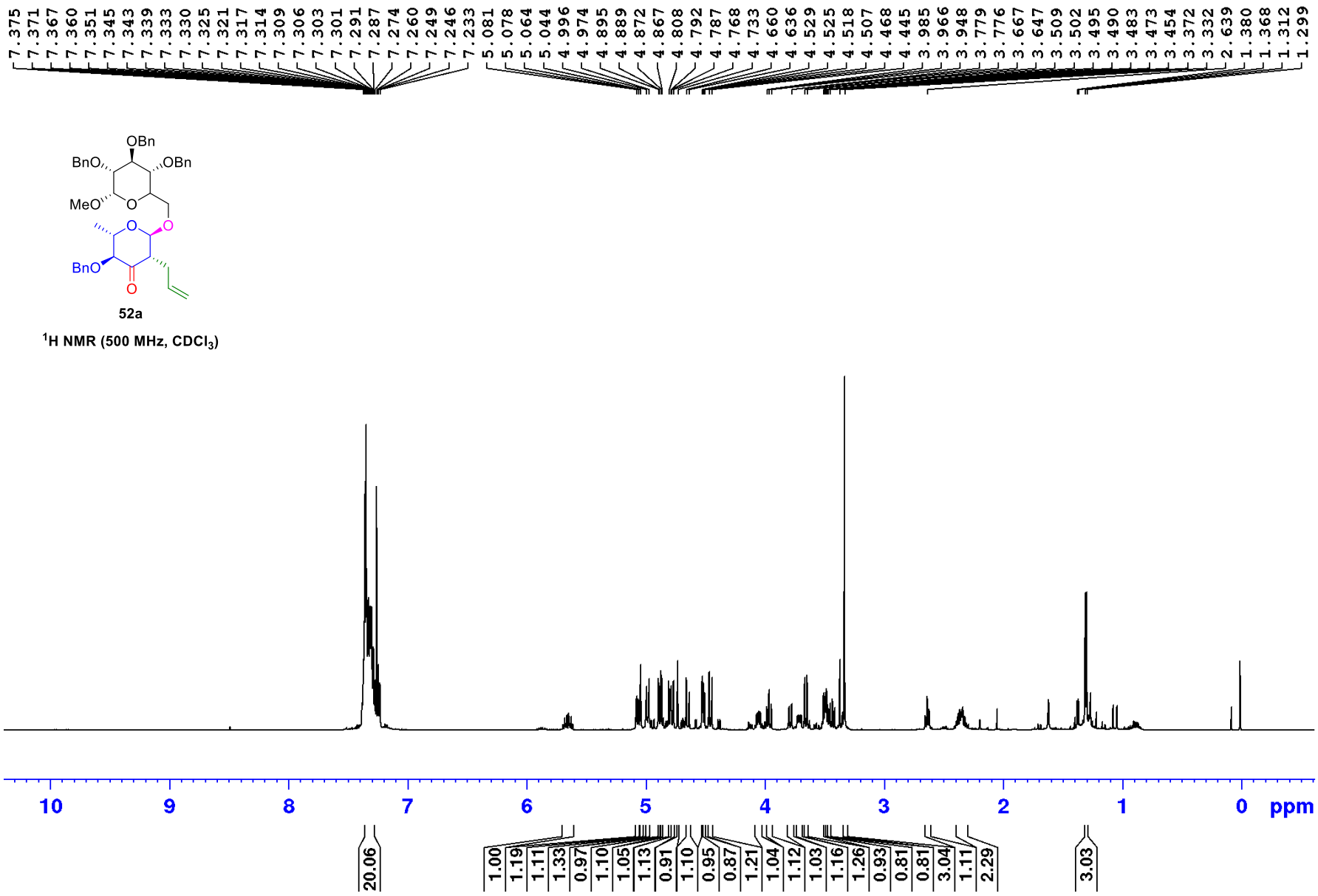
^{13}C NMR (125 MHz, $CDCl_3$)

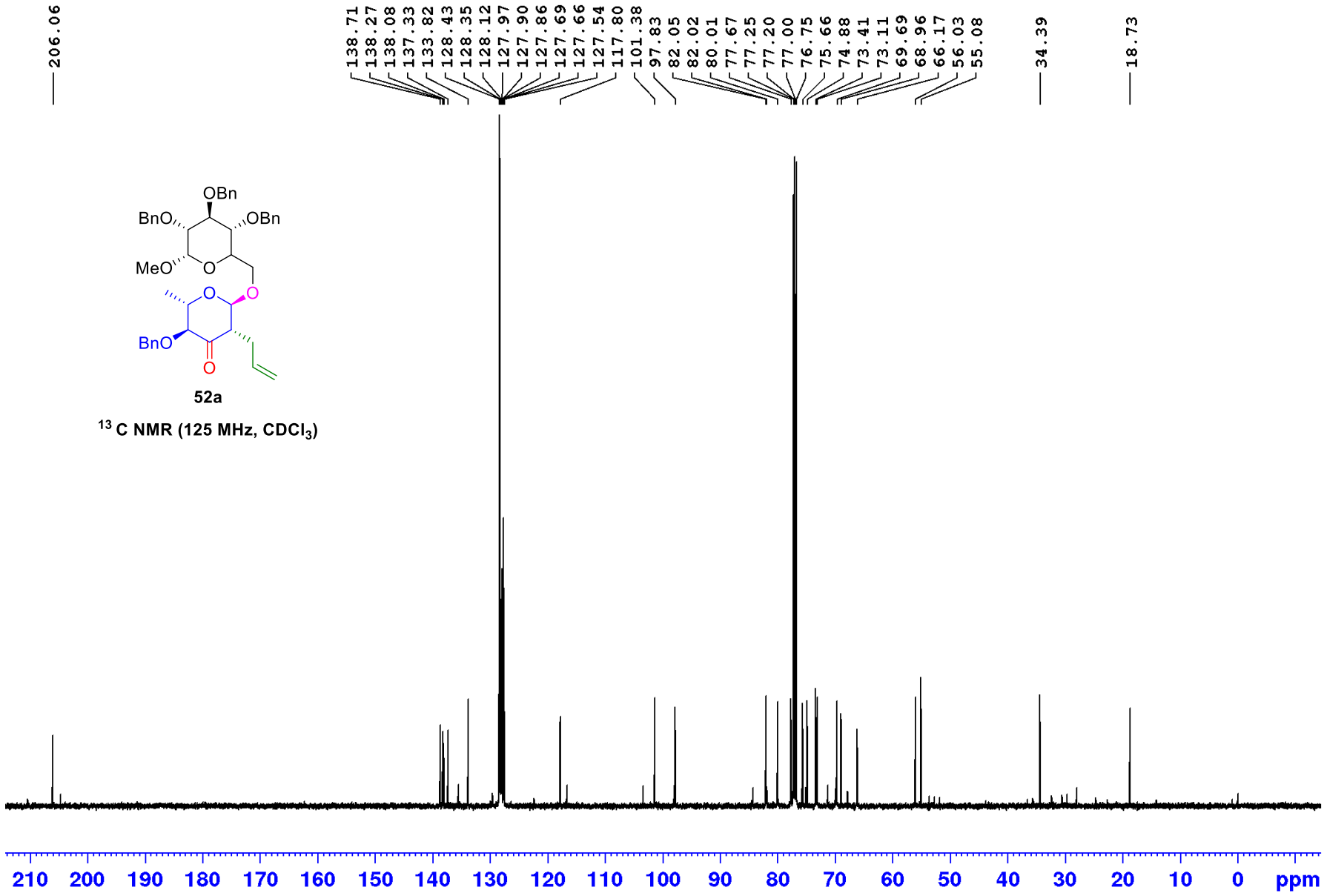

7.393
7.380
7.375
7.372
7.368
7.364
7.359
7.355
7.351
7.344
7.343
7.340
7.335
7.334
7.331
7.323
7.316
7.306
7.299
7.292
5.407
5.404
5.372
5.369
5.287
5.284
5.266
5.263
5.041
5.033
5.010
4.956
4.934
4.929
4.907
4.856
4.834
4.827
4.802
4.705
4.696
4.671
4.614
4.606
4.592
4.318
4.307
4.270
4.259
4.100
4.030
4.011
3.946
3.928
3.924
3.757
3.739
3.640
3.630
3.618
3.572
3.565
3.553
3.546
3.536
3.517
3.398
1.271
1.258
OBn
BnO
OBn
MeO
O
O
O
BnO
O
51
1 H NMR (500 MHz, CDCl3)
10
9
8
7
6
5
4
3
2
1
0
ppm
20.06
1.00
1.04
1.07
2.01
1.08
1.16
1.05
1.14
2.09
1.26
1.34
0.99
1.11
1.23
1.04
0.92
1.03
1.09
1.08
0.92
1.14
3.09
3.15

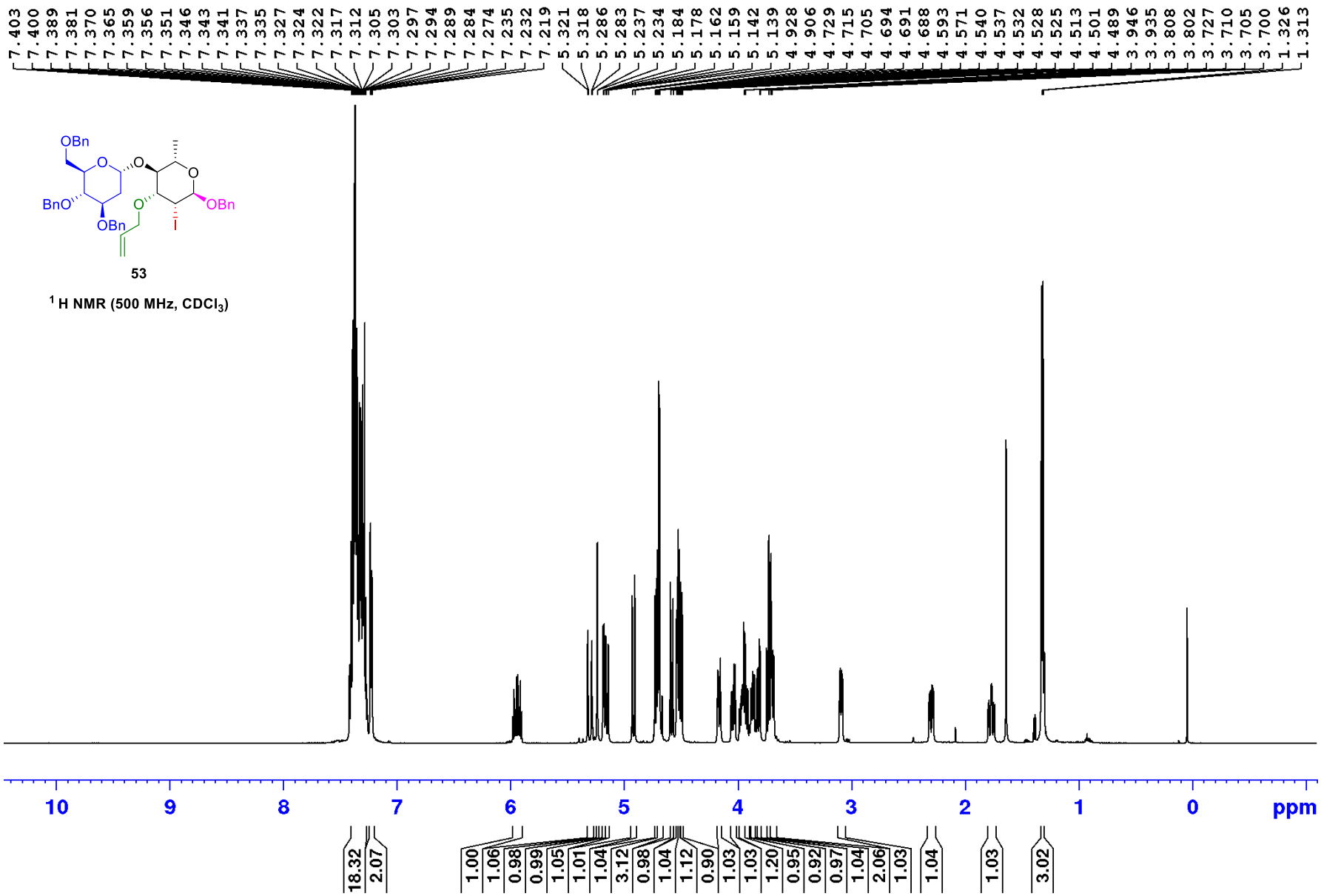


51

^{13}C NMR (125 MHz, $CDCl_3$)

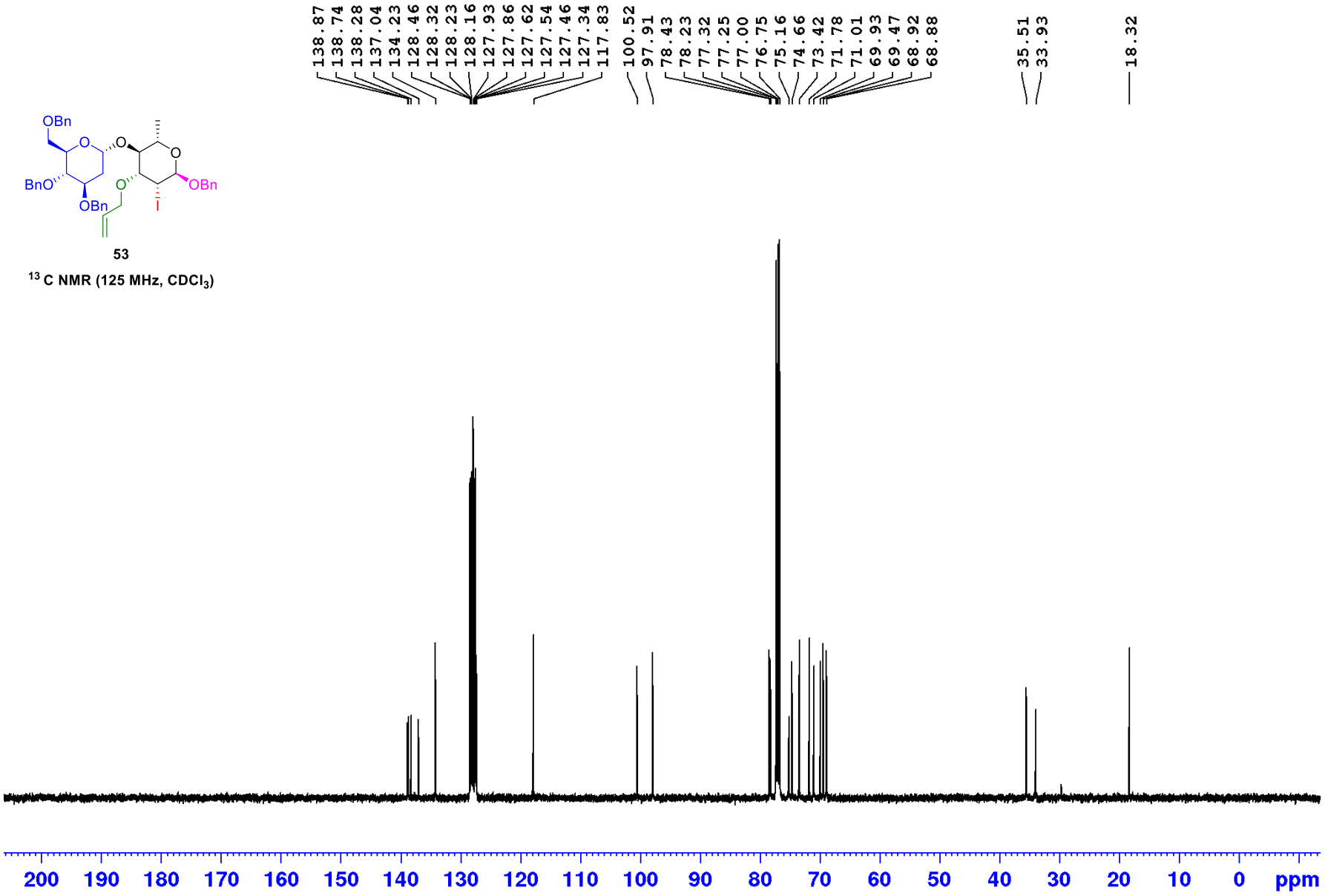

7.375
7.371
7.367
7.360
7.351
7.345
7.343
7.339
7.333
7.330
7.325
7.321
7.317
7.314
7.309
7.306
7.303
7.301
7.291
7.287
7.274
7.260
7.249
7.246
7.233
5.081
5.078
5.064
5.044
4.996
4.974
4.895
4.889
4.872
4.867
4.808
4.792
4.787
4.768
4.733
4.660
4.636
4.529
4.525
4.518
4.507
4.468
4.445
3.985
3.966
3.948
3.779
3.776
3.667
3.647
3.509
3.502
3.495
3.490
3.483
3.473
3.454
3.372
3.332
2.639
1.380
1.368
1.312
1.299
OBn
BnO
OBn
MeO
O
O
O
BnO
O
52a
1H NMR (500 MHz, CDCl3)
10
9
8
7
6
5
4
3
2
1
0
ppm
20.06
1.00
1.19
1.11
1.33
0.97
1.10
1.05
1.13
0.91
1.10
0.95
0.87
1.21
1.04
1.12
1.03
1.16
1.26
0.93
0.81
0.81
3.04
1.11
2.29
3.03


206.06
138.71
138.27
138.08
137.33
133.82
128.43
128.35
128.12
127.97
127.90
127.86
127.69
127.66
127.54
117.80
101.38
97.83
82.05
82.02
80.01
77.67
77.25
77.20
77.00
76.75
75.66
74.88
73.41
73.11
69.69
68.96
66.17
56.03
55.08
34.39
18.73
OBn
BnO
OBn
MeO
O
O
O
BnO
O
52a
13 C NMR (125 MHz, CDCl3)
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
ppm



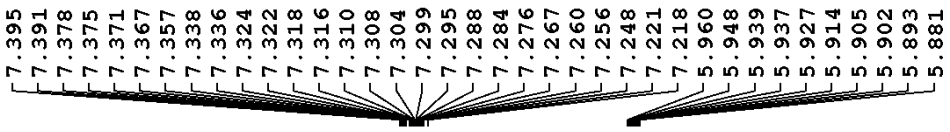
53

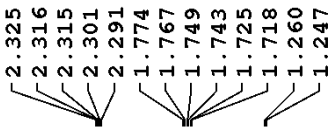
^{1}H NMR (500 MHz, $CDCl_3$)

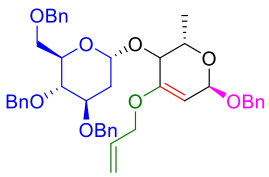


53

^{13}C NMR (125 MHz, $CDCl_3$)

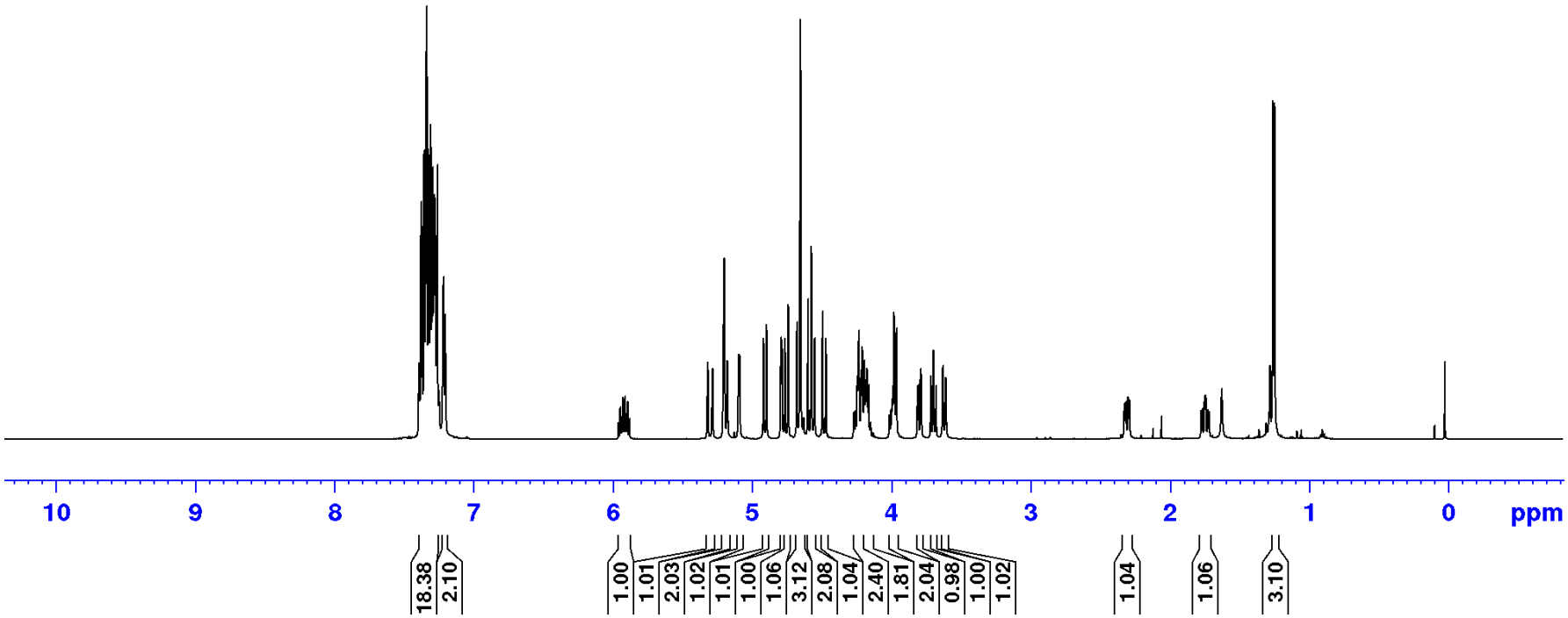


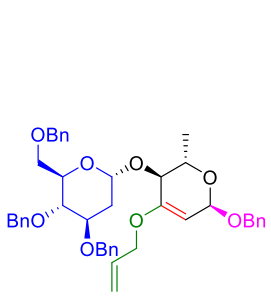




54

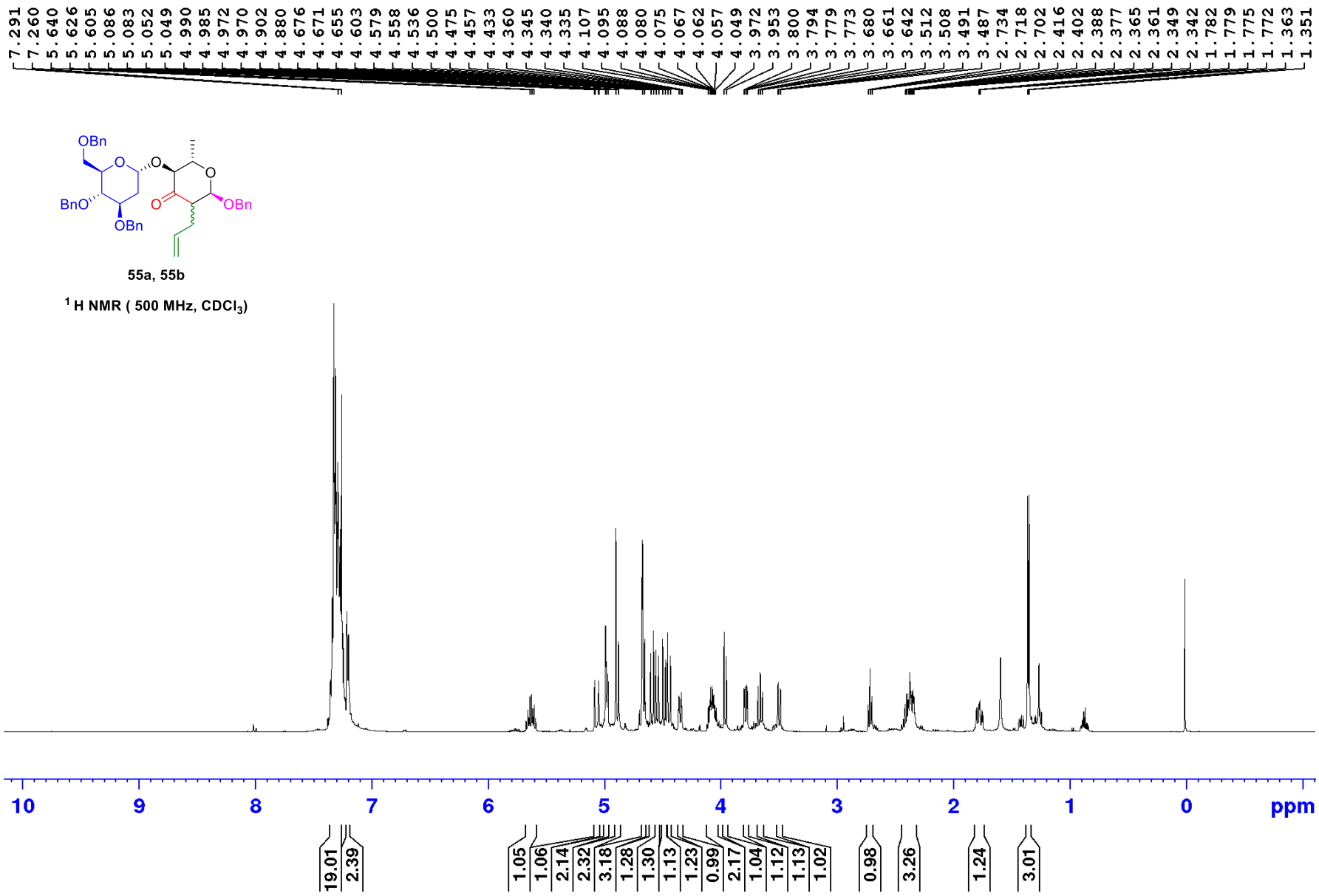
^{1}H NMR (500 MHz, $CDCl_3$)

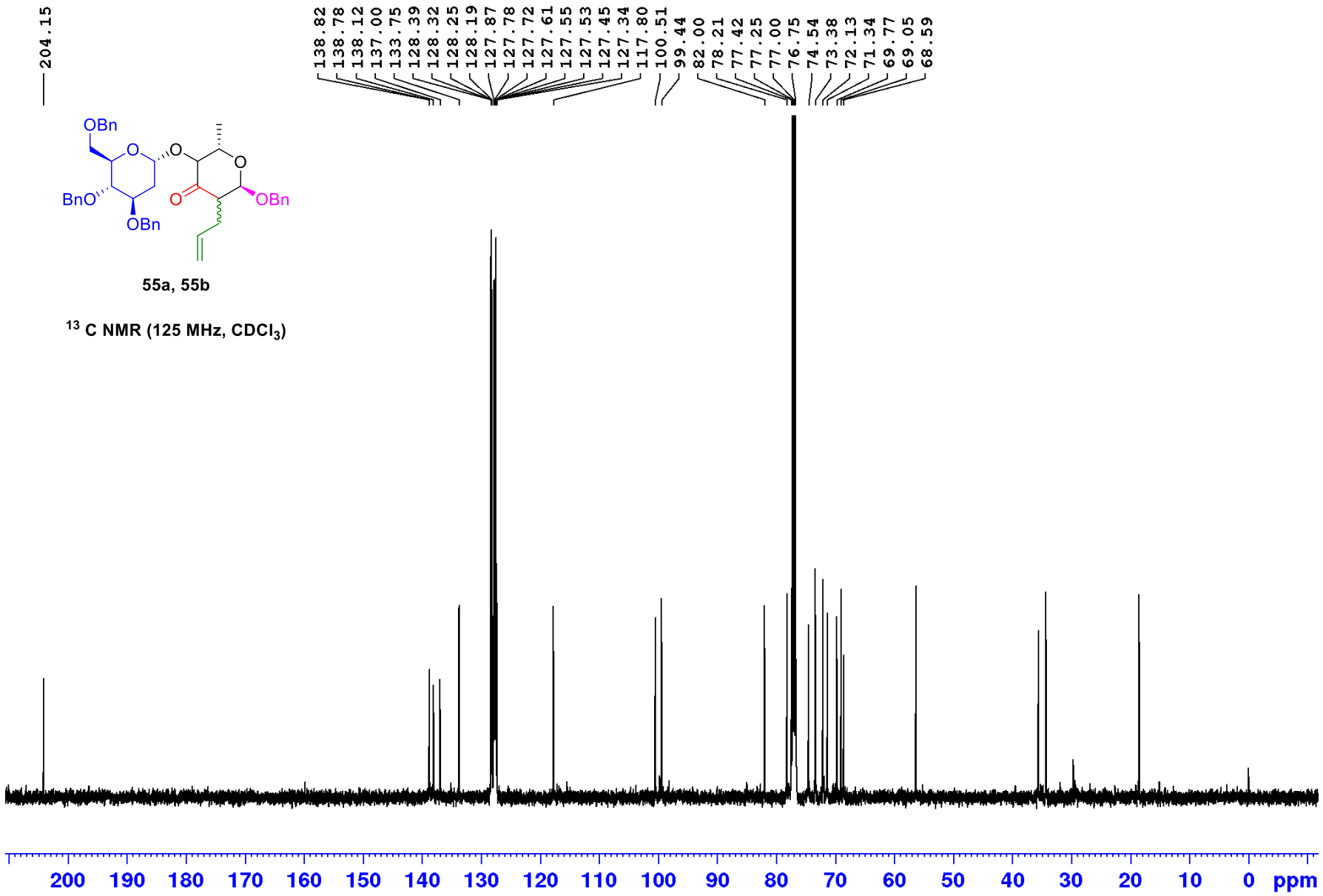




54

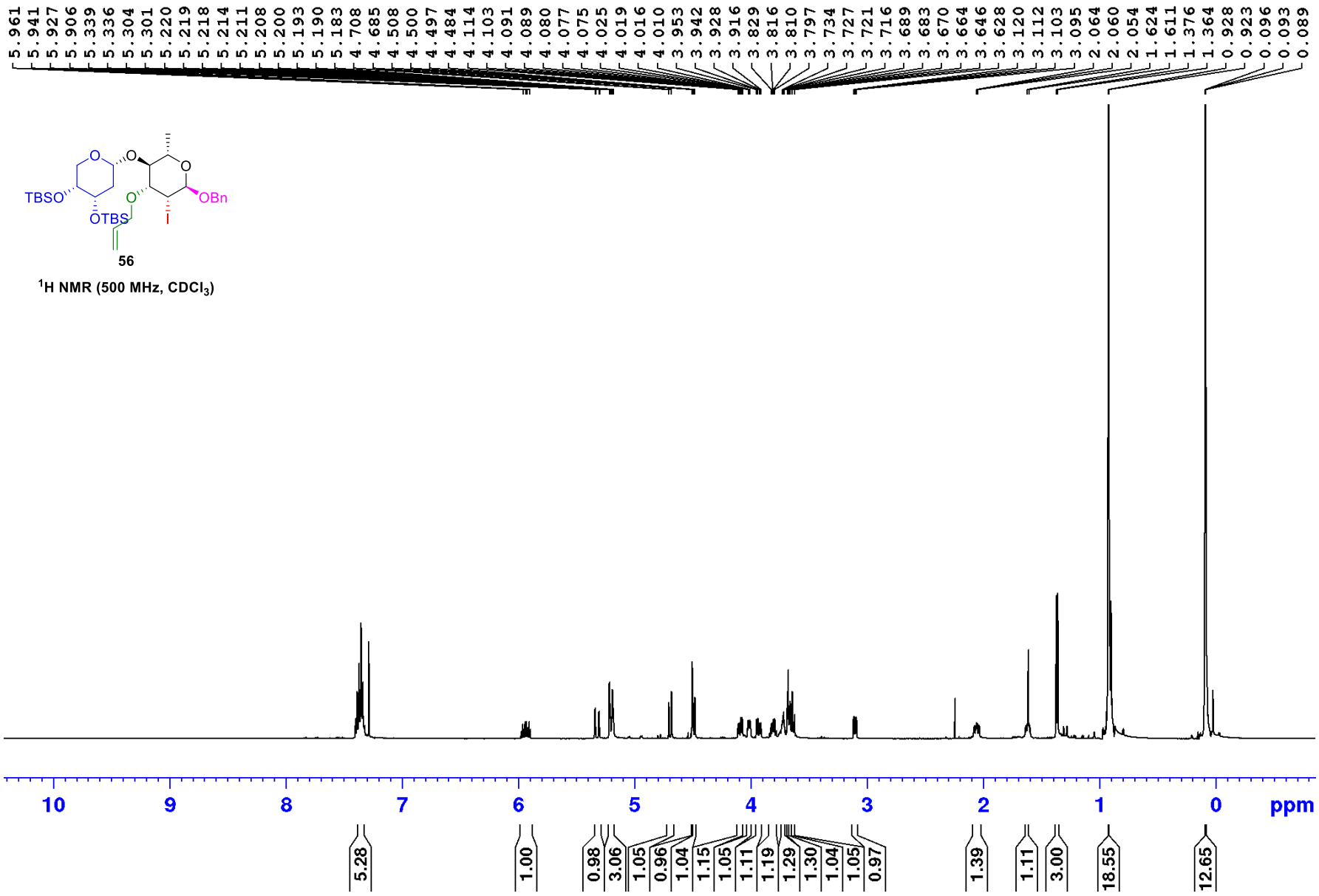
^{13}C NMR (125 MHz, $CDCl_3$)


7.291
7.260
5.640
5.626
5.605
5.086
5.083
5.052
5.049
4.990
4.985
4.972
4.970
4.902
4.880
4.676
4.671
4.655
4.603
4.579
4.558
4.536
4.500
4.475
4.457
4.433
4.360
4.345
4.340
4.335
4.107
4.095
4.088
4.080
4.075
4.067
4.062
4.057
4.049
3.972
3.953
3.800
3.794
3.779
3.773
3.680
3.661
3.642
3.512
3.508
3.491
3.487
2.734
2.718
2.702
2.416
2.402
2.388
2.377
2.365
2.361
2.349
2.342
1.782
1.779
1.775
1.772
1.363
1.351
OBn
BnO
OBn
O
O
O
OBn
55a, 55b
1 H NMR (500 MHz, CDCl3)
10
9
8
7
6
5
4
3
2
1
0
ppm
19.01
2.39
1.05
1.06
2.14
2.32
3.18
1.28
1.30
1.13
1.23
0.99
2.17
1.04
1.12
1.13
1.02
0.98
3.26
1.24
3.01

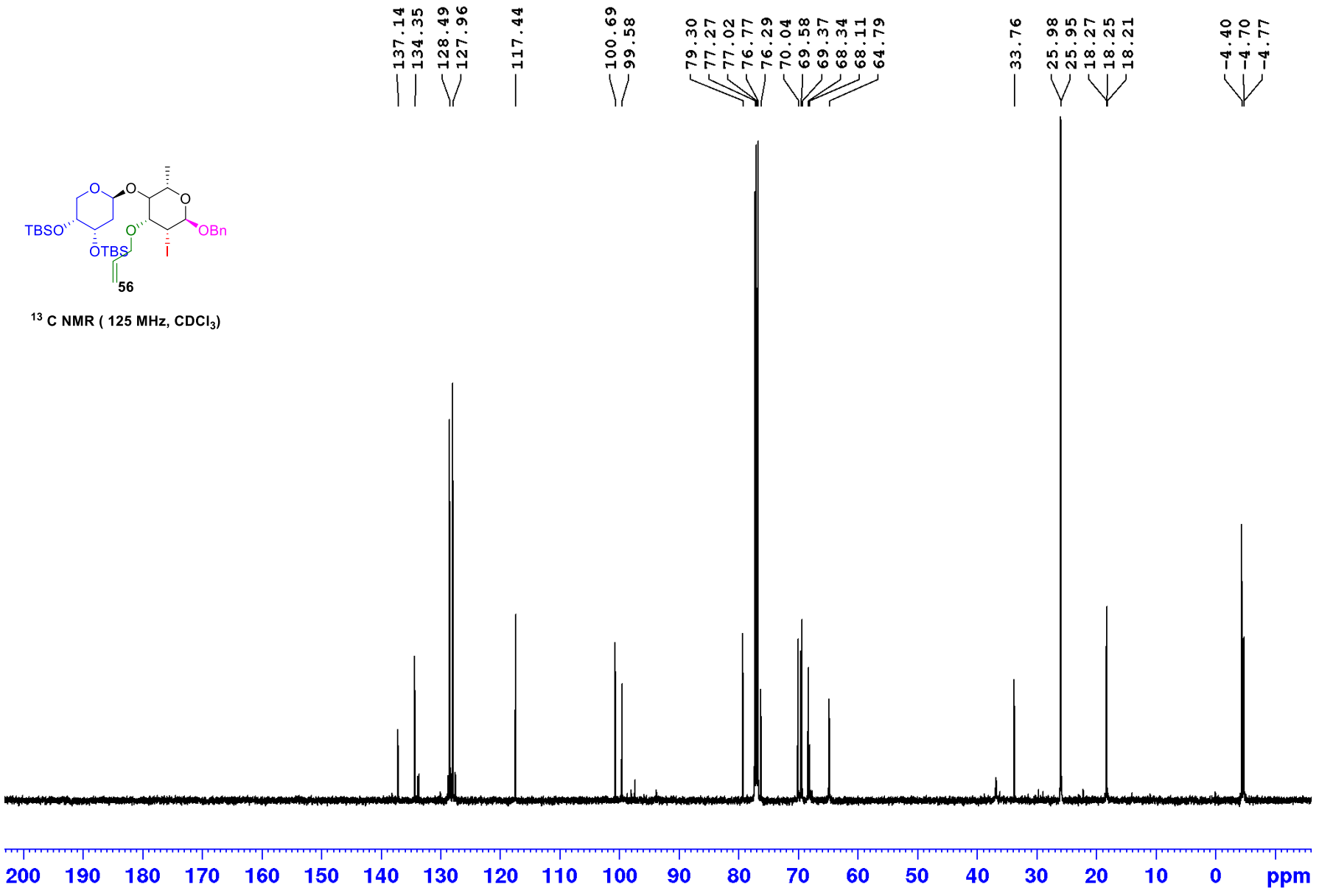


55a, 55b

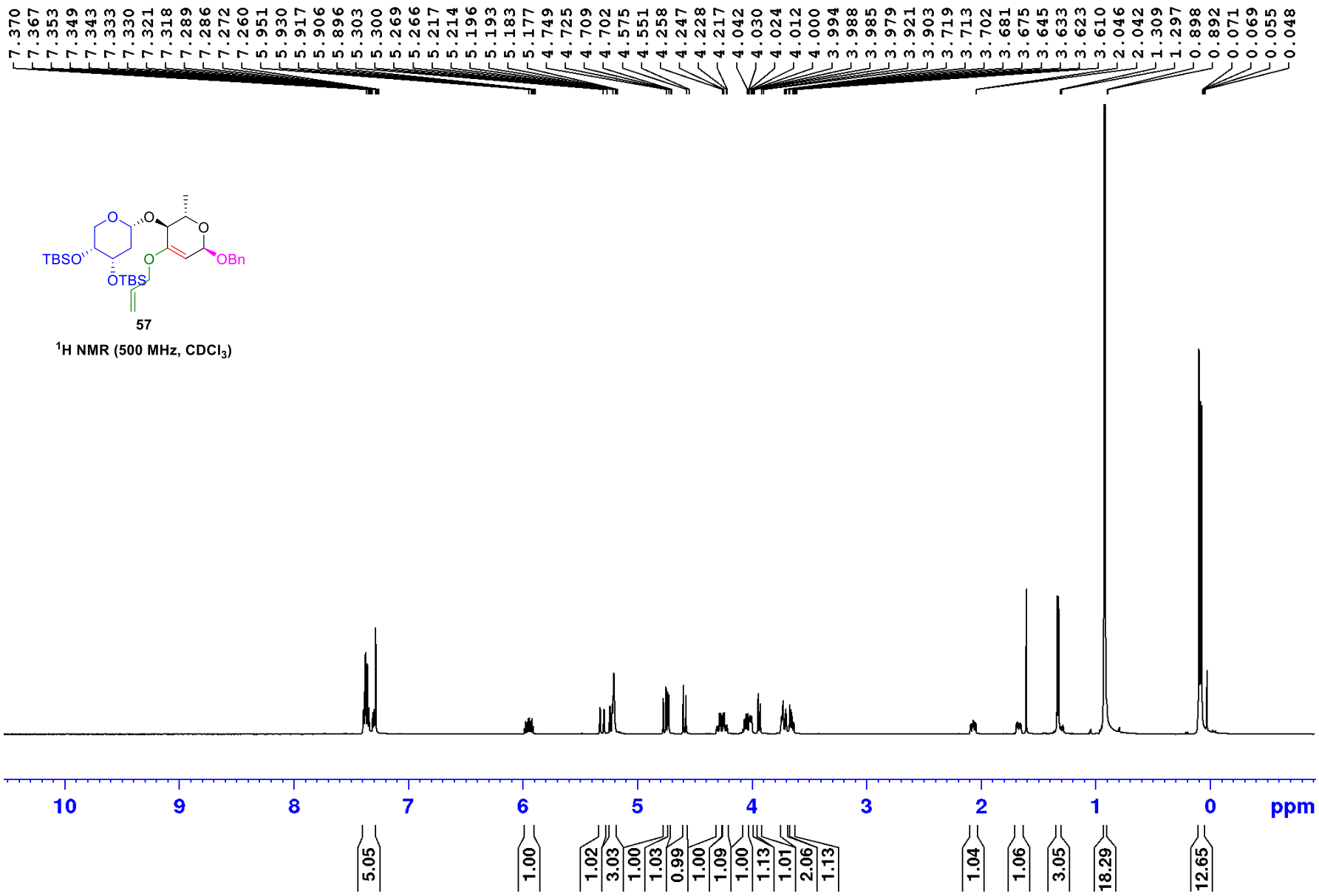
^{13}C NMR (125 MHz, $CDCl_3$)

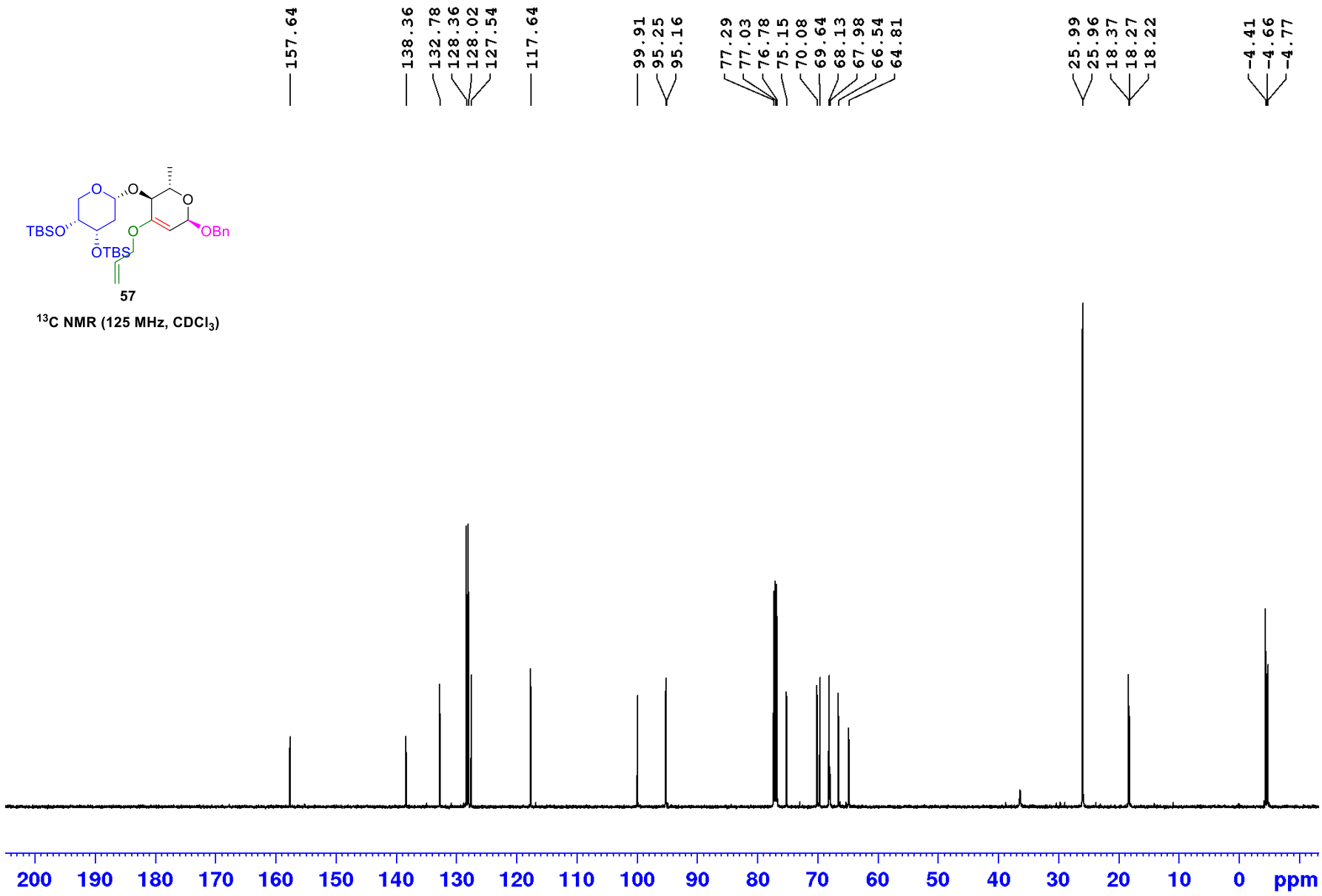


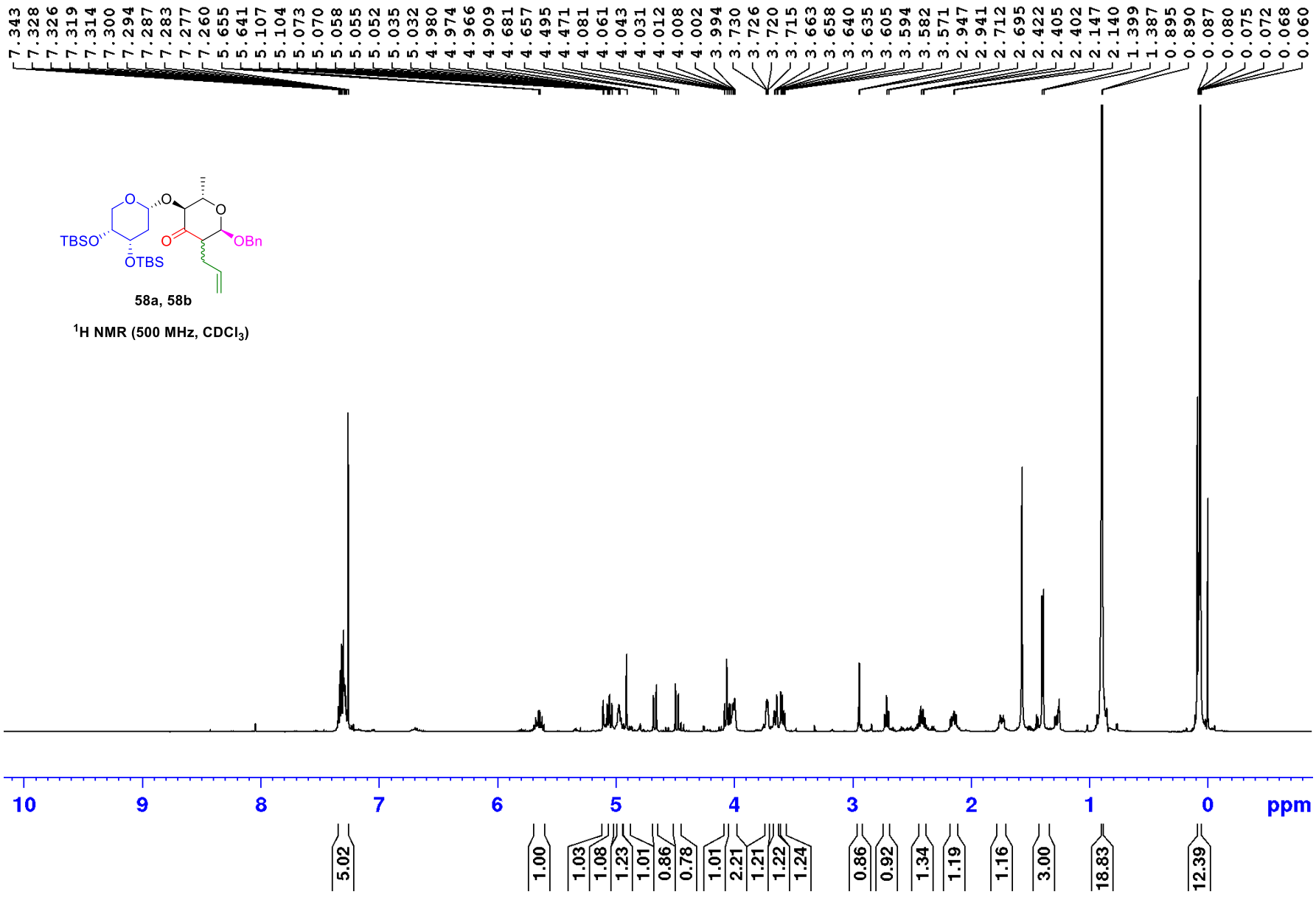
^{1}H NMR (500 MHz, $CDCl_3$)

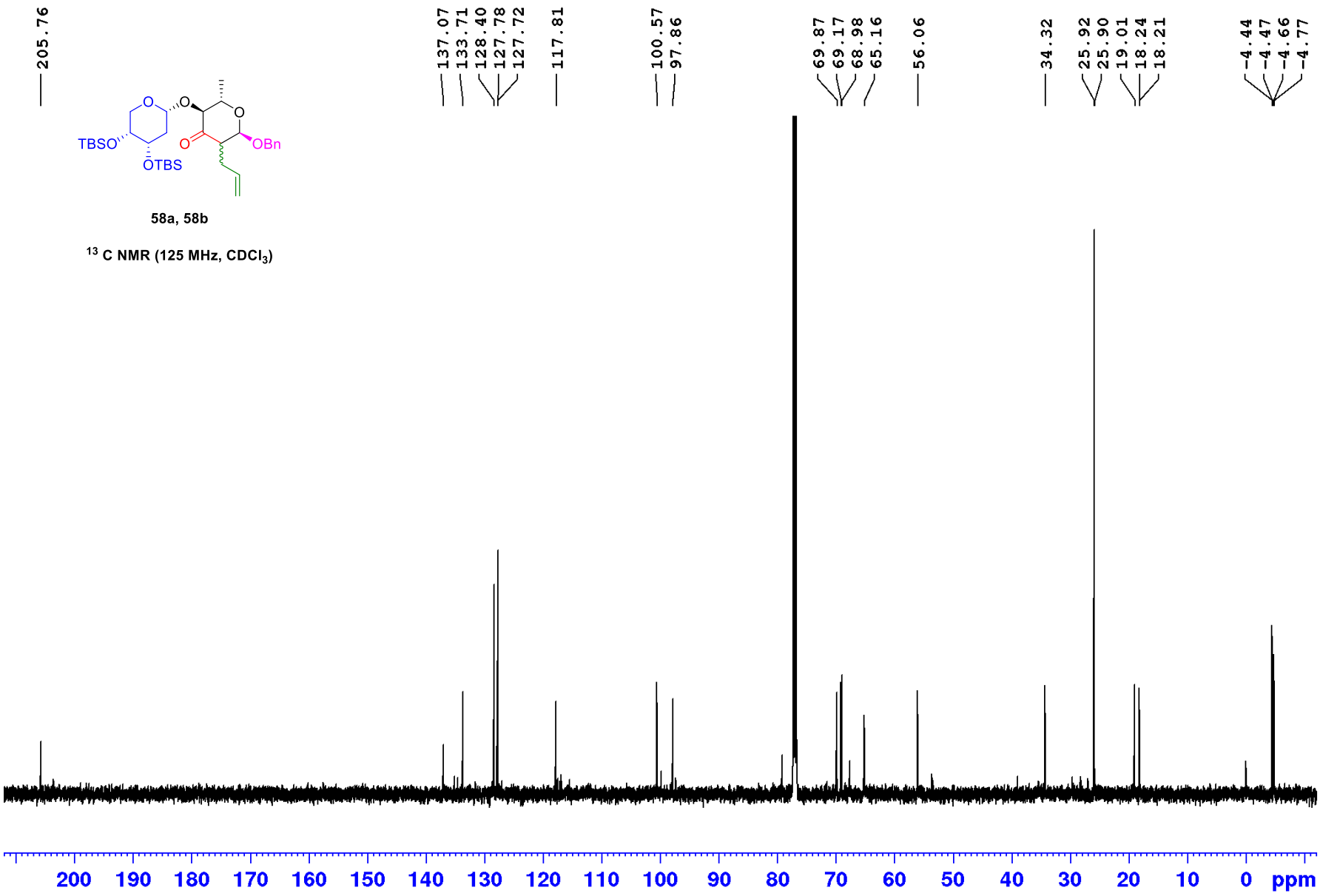


^{13} C NMR (125 MHz, $CDCl_3$)


7.370
7.367
7.353
7.349
7.343
7.333
7.330
7.321
7.318
7.289
7.286
7.272
7.260
5.951
5.930
5.917
5.906
5.896
5.303
5.300
5.269
5.266
5.217
5.214
5.196
5.193
5.183
5.177
4.749
4.725
4.709
4.702
4.575
4.551
4.258
4.247
4.228
4.217
4.042
4.030
4.024
4.012
4.000
3.994
3.988
3.985
3.979
3.921
3.903
3.719
3.713
3.702
3.681
3.675
3.645
3.633
3.623
3.610
2.046
2.042
1.309
1.297
0.898
0.892
0.071
0.069
0.055
0.048
TBSO
OTBS
O
OBn
57
1H NMR (500 MHz, CDCl3)
10
9
8
7
6
5
4
3
2
1
0
ppm
5.05
1.00
1.02
3.03
1.00
1.03
0.99
1.00
1.09
1.00
1.13
1.01
2.06
1.13
1.04
1.06
3.05
18.29
12.65


157.64
138.36
132.78
128.36
128.02
127.54
117.64
99.91
95.25
95.16
77.29
77.03
76.78
75.15
70.08
69.64
68.13
67.98
66.54
64.81
25.99
25.96
18.37
18.27
18.22
-4.41
-4.66
-4.77
TBSO
OTBS
OBn
57
^{13}C NMR (125 MHz, CDCl$_3$)
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
ppm


7.343
7.328
7.326
7.319
7.314
7.300
7.294
7.287
7.283
7.277
7.260
5.655
5.641
5.107
5.104
5.073
5.070
5.058
5.055
5.052
5.035
5.032
4.980
4.974
4.966
4.909
4.681
4.657
4.495
4.471
4.081
4.061
4.043
4.031
4.012
4.008
4.002
3.994
3.730
3.726
3.720
3.715
3.663
3.658
3.640
3.635
3.605
3.594
3.582
3.571
2.947
2.941
2.712
2.695
2.422
2.405
2.402
2.147
2.140
1.399
1.387
0.895
0.890
0.087
0.080
0.075
0.072
0.068
0.060
TBSO
OTBS
O
OBn
58a, 58b
1H NMR (500 MHz, CDCl3)
10
9
8
7
6
5
4
3
2
1
0
ppm
5.02
1.00
1.03
1.08
1.23
1.01
0.86
0.78
1.01
2.21
1.21
1.22
1.24
0.86
0.92
1.34
1.19
1.16
3.00
18.83
12.39

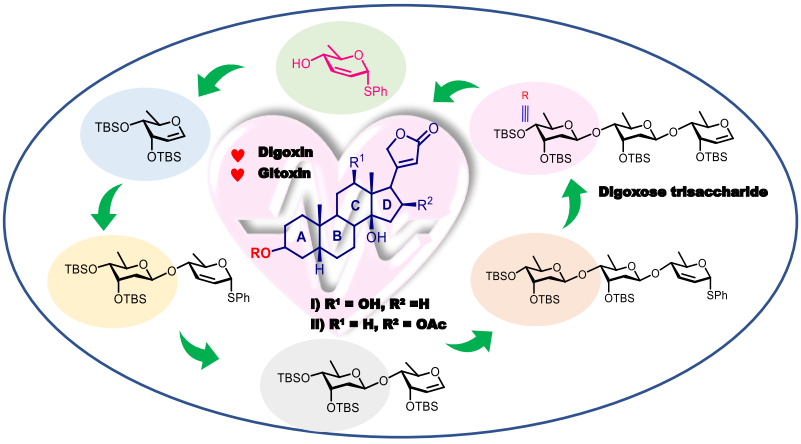


58a, 58b

^{13}C NMR (125 MHz, $CDCl_3$)

Chapter 4

An Efficient Method for the Synthesis of Digoxose Trisaccharide Glycal Donor via Mislow-Evans Rearrangement



Abstract

The Mislow-Evans rearrangement was used as a key reaction to construct digitoxose-derived glycal. The same rearrangement was iteratively performed on di- and tri-saccharides to form the digoxose glycal donor component present in cardenolides digitoxin, digoxin and gitoxin. The scalability of the trisaccharide synthesis was shown by carrying out the reactions on a multigram scale. Glycosylation reactions were also performed between the synthesized digoxin glycal donor and aglycons, digoxigenin and gitoxigenin, to synthesize novel cardenolide derivatives.

4.1 Introduction

Oligosaccharides possessing deoxy sugar subunits are integral part of various pharmacologically relevant antibiotics, vaccines, and anticancer medications.[1] Among these natural products, cardiac glycosides (CGs), a family of the steroid glycosides, attracted considerable attention due to their importance in treating congestive heart failure and cardiac arrhythmias for over last 300 years. CGs exert their predominant action through inhibition of the enzyme Na^+/K^+-ATPase resulting in improved concentration of intracellular Ca^{2+} that leads to faster and powerful contraction of heart muscles. While increasing the cardiac output, CGs also help in reducing the heart rate without abnormal blood pressure which allows them to be used as a medication for cardiac arrhythmias.[2] Structurally, a couple of cardiac glycosides, digitoxin (**1**), digoxin (**2**) and gitoxin (**3**) etc.,[3] possess a common trisaccharide unit called digoxose that is linked with the aglycone digitoxigenin, digoxigenin and gitoxigenin, respectively (Figure 1). In terms of the structure-activity relationship (SAR), cardiac glycosides provide a great illustration of the interaction between the steroidal aglycone, a pharmacophore that is generally inactive without the attachment of the digoxose sugar moiety.[3]

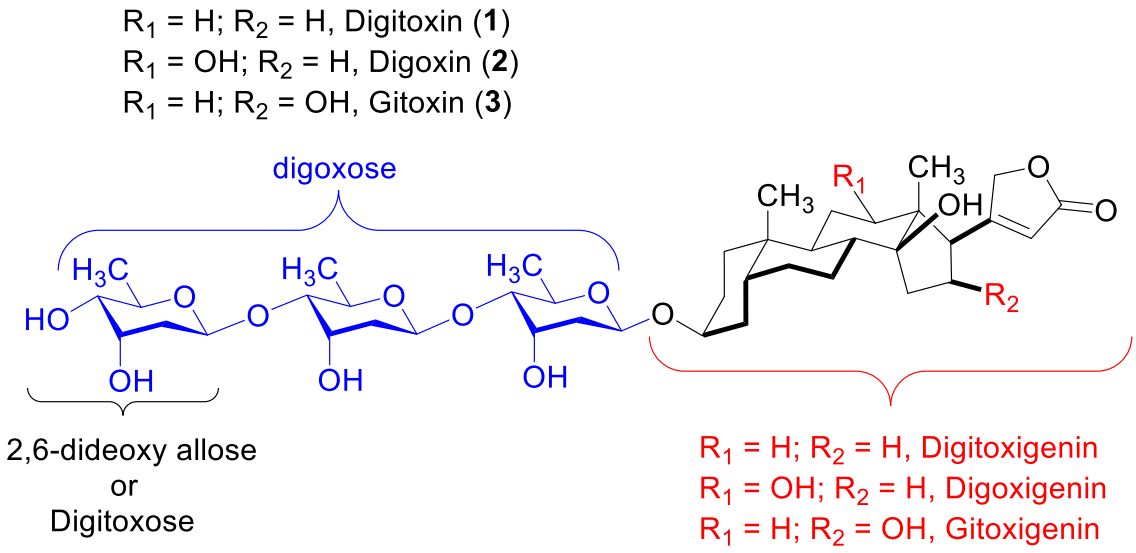


Figure 1. Representative structures of digitoxin, digoxin and gitoxin

To date, there are very few reports on the synthesis of cardiotonic glycosides (1-3),[4] its analogues[5] and neoglycosides.[6] These protocols involve the featured linear construction of the natural product

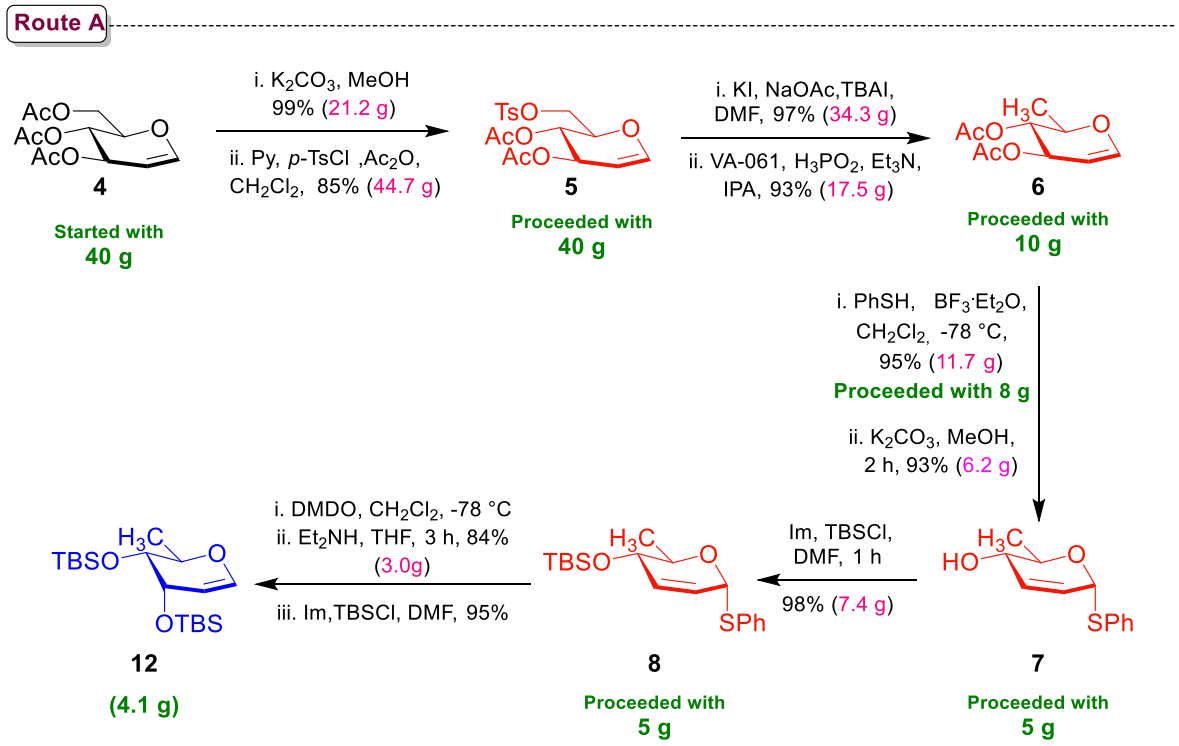
by sequential glycosylation of aglycon or its derivative with protected-digitoxose monosaccharide glycosyl donors. Despite the remarkable accomplishments, there are only two convergent syntheses protocol reported for the synthesis of digoxose trisaccharide, a common glycan unit present in a couple of CGs.[7-8] Eventually the synthesized trisaccharide was coupled with the digitoxigenin to synthesize the natural CG digitoxin **1.** Firstly, McDonald and co-workers[7] reported the synthesis of 6-deoxy-D-allal derivative and digoxose trisaccharide glycal donor involving tungsten carbonyl catalyzed endo-selective cycloisomerization of an appropriate alkynol substrate as the key step. Secondly, Jianglong Zhu and co-workers[8] reported the Re(V)-catalyzed stereoselective β-glycosylation as the key step to synthesize β-D-digoxosides from 6-deoxy-D-allal derivative as glycal donor. In this view, it was envisioned that 6-deoxy-D-allal derivative could also play an important role as a donor in the synthesis of several other natural products. It was found that compound 6-deoxy 3,4-di-*O*-*tert*-butyldimethylsilyl D-allal **12**[9] served as a key precursor in the total synthesis of altromycin B disaccharide[10] and α-lipomycin.[9b] In view of the importance of 6-deoxy-D-allal derivative, a thorough investigation was conducted on the previously developed methods for its synthesis. Following our observations, the Mislow-Evans rearrangement[11] was found to be fruitfully applied by Danishefsky's group[12] in the synthesis of D-allal derivative from D-glucal derived anomeric sulfoxide. Furthermore, this rearrangement has been used very often for the synthesis of prostaglandins, bioactive natural products and steroids and projects evidence for a good transfer of stereochemical information through an ordered transition state.[13] However, the rearrangement was not evaluated by any research group for the synthesis of oligosaccharides.

Major interests of our group include the development of new techniques for the construction and synthesis of natural products and application in carbohydrate chemistry.[14] Hence, in continuation with our previous research work, we decided to focus our attention towards the synthesis of 6-deoxy-D-allal-derivative. Herein we report the synthesis of 6-deoxy 3,4-di-*O*-*tert*-butyldimethylsilyl D-allal via the [2,3]-sigmatropic rearrangement of sugar derived-allylic anomeric sulfoxides. Additionally, the same methodology is extended for the synthesis of di- and trisaccharide. The orthogonally protected digoxose trisaccharide is synthesized in a multigram scale with smaller number of steps and high yield. It is worth mentioning that this is the first report to perform the Mislow-Evans [2,3]-sigmatropic rearrangement on a higher order oligosaccharide

till date. Also, this methodology has been successfully extended for convergent synthesis of orthogonally protected digoxin and gitoxin.

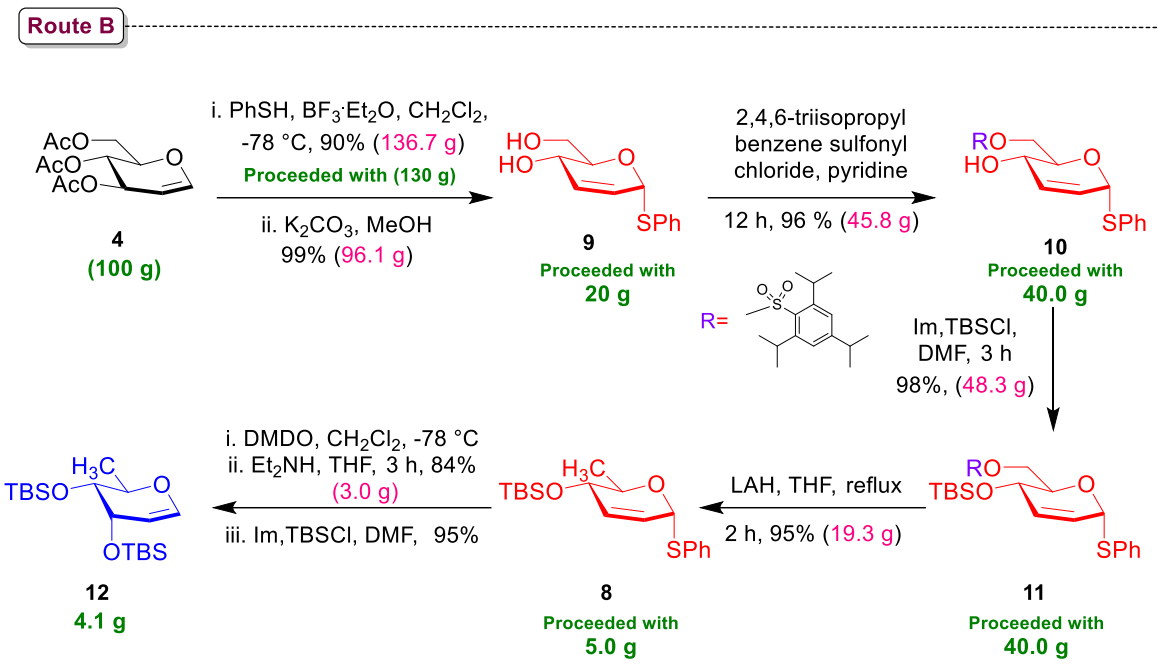
4.2 Results and Discussion

In this view, the investigation started with the study of choosing a more reliable and convenient protocol for synthesizing digoxose monosaccharide donor **12** from readily available starting materials and inexpensive reagents. Hence, two new methods were investigated to prepare compound **12** starting from the commercially inexpensive 3,4,6-tri-*O*-acetyl-D-glucal **4**. In route A (Scheme 1), compound **4** was deacetylated in the presence of K_2CO_3 and MeOH as solvent to obtain the D-glucal. This triol was subjected to primary hydroxyl tosylation followed by secondary hydroxyls acetylation reaction in a sequential one-pot manner to give compound **5**[15] in excellent yield over two steps. Substitution of the tosylate with iodide by using potassium iodide followed by deiodination using VA-061 as radical initiator and hypophosphorous acid (H_3PO_2) as the reducing agent provided the 6-deoxy 4,5-di-*O*-acetyl D-glucal **6** in excellent yield. Ferrier rearrangement of **6** with thiophenol and hydrolysis of the obtained mono-acetate resulted the 2,3-unsaturated thio-glycoside **7**. The TBS protection of the free hydroxyl group of this thioglycoside gave compound **8** in 98% yield. In the due course, it was predicted that, **8** could be an appropriate substrate to be subjected to Danishefsky's application of the Mislow−Evans rearrangement to prepare 6-deoxy D-allal derivative. Also, it was anticipated that dimethyl dioxirane (DMDO) will be the more appropriate oxidant for the controlled oxidation of **8** to the corresponding sulfoxide. Hence, **8** was subjected to DMDO mediated oxidation at -78 ℃ to form the allylic sulfoxide which subsequently underwent [2,3]-sigmatropic rearrangement resulting C3 sulfenate ester. Cleavage of the O−S bond in this ester with the thiophilic nucleophile diethylamine,[16] provided 6-deoxy 4-*O*-*tert*-butyldimethylsilyl D-allal in 84% yield. Ultimately, the route A ended with the TBS protection of the 3-OH to give the 6-deoxy 3,4-di-*O*-*tert*-butyldimethylsilyl D-allal, compound **12,** in 95% yield. This route accounted for the overall yield of 52.4% over 9 steps (Scheme 1, route A).



Scheme 1. Synthesis of 6-deoxy 3,4-di-*O*-*tert*-butyldimethylsilyl D-allal donor 12 -route A

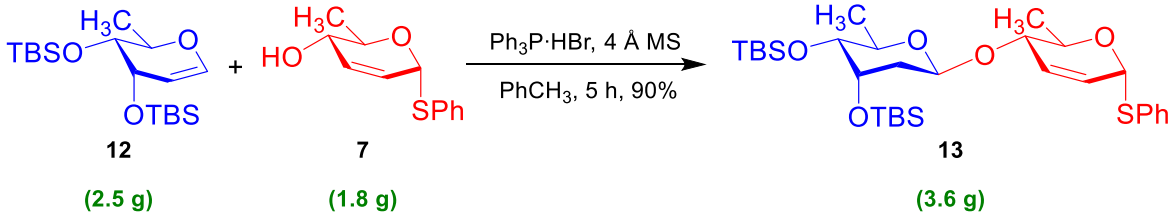
In route B (scheme 2), **4** was subjected to Ferrier rearrangement with thiophenol and the obtained diester was hydrolysed with K_2CO_3 to give 2,3-unsaturated thio-glycoside **9**. Selective sulfonylation of the primary alcohol with 2,4,6-triisopropylbenzene sulfonyl chloride provided the compound **10** in 96% yield. The 4-OH was protected with TBS to give **11** and then subjecting it to $LiAlH_4$ reduction provided the compound **8**. Finally, compound **12** was obtained in excellent yield via oxidative rearrangement followed by TBS protection of 3-OH (Scheme 2, route B). Consequently, it is worth to mention a multigram scale synthesis of compound **12** was successfully accomplished using this protocol with 63.5% overall yield over 7 steps.



Scheme 2. Synthesis of 6-deoxy 3,4-di-*O*-*tert*-butyldimethylsilyl D-allal donor 12 -route B.

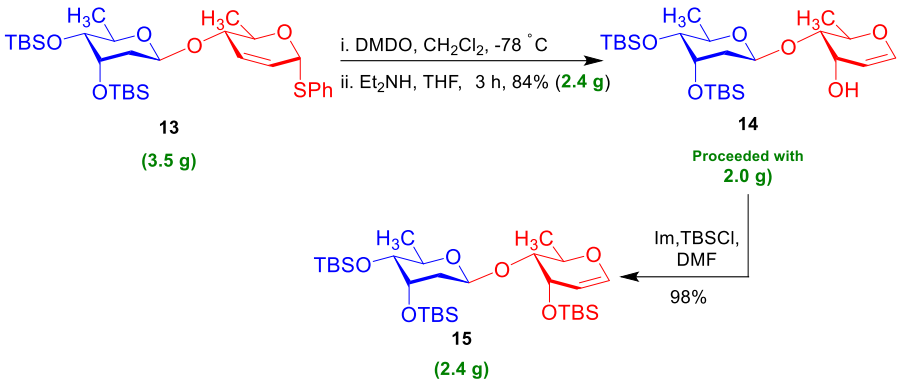
The design of both the strategies deserves to be highlighted equally because both the donor **12** and the acceptot **7** can be synthesised from one of the very common glucose derived glycal **4**.

According to our objective, the scope of the protocol was extended and focus was drawn towards the application of Mislow-Evans rearrangement on the disaccharide. Alongside, considerable efforts were done for the synthesis of the digoxose trisaccharide glycal unit using this protocol. Having obtained donor **12**, PPh_3·HBr mediated glycosylation of the C-4 secondary alcohol of acceptor **7** with donor **12** was performed following our previous method,[17] which afforded the disaccharide **13** with excellent β-selectivity and 90% yield (Scheme 3).



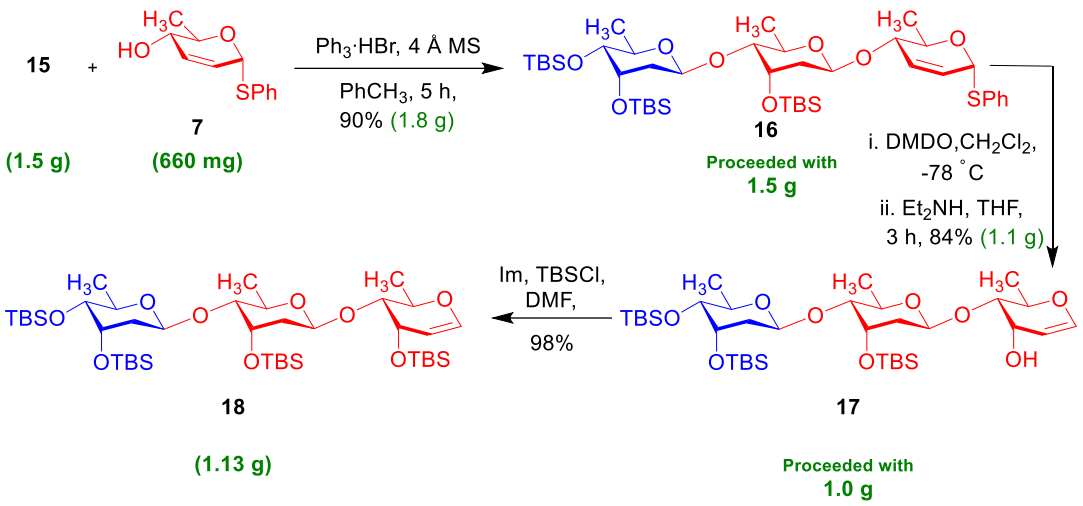
Scheme 3. First stereoselective glycosylation of donor 12 and acceptor thioglycoside **7**.

The real challenge of the methodology was then undertaken and compound **13** was subjected to the DMDO mediated oxidation, followed by rearrangement reaction. To our delight, the desired compound, glycal **14**, was successfully obtained in 84% yield. Further, protection of the hydroxyl of **14** with TBS provided the protected C-4 glycosylated disaccharide donor **15**[9a] in 98% yield (Scheme 4).



Scheme 4. Synthesis of TBS protected digoxose disaccharide via [2,3]-sigmatropic rearrangement

Inspired by the excellent outcome during the disaccharide synthesis, we turned our attention towards the synthesis of trisaccharide. In this regard, $PPh_3 \cdot HBr$ mediated glycosylation of **15** with **7** was performed, to obtain thio-glycoside trisaccharide **16** in 90% yield and yet again an excellent anomeric β-selectivity. Subsequently, subjecting **16** to Mislow−Evans rearrangement provided the trisaccharide glycal derivative **17**. Eventually, the digoxin trisaccharide glycal donor **18** was obtained by the protection of the free hydroxyl group of **17** with TBS (scheme 5).



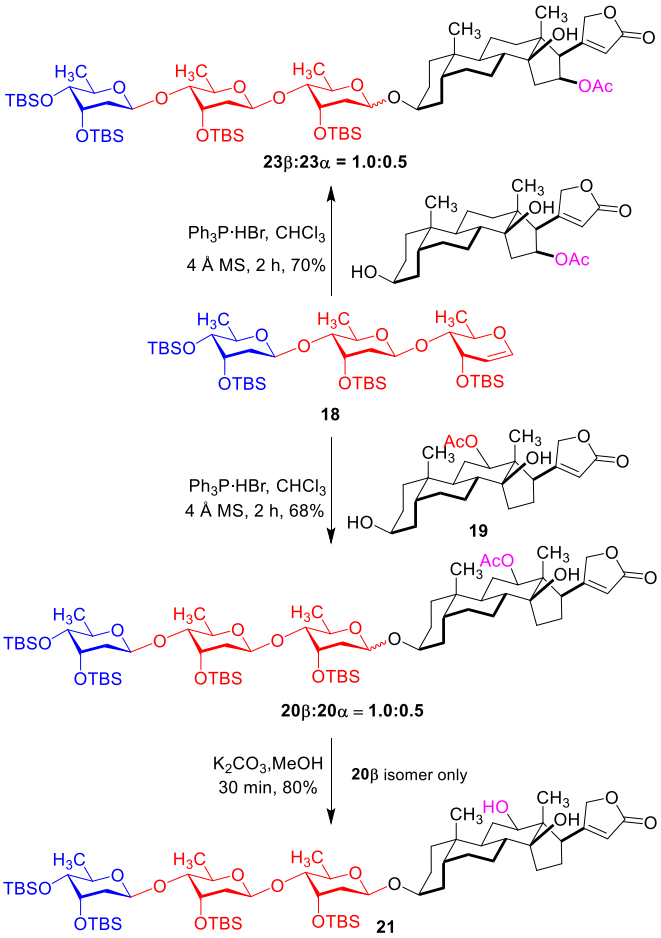
Scheme 5. An iterative process for the construction of TBS-protected digoxose trisaccharide glycal donor.

Towards the end, it is appropriate to note that the oxidative rearrangement was perfectly compatible, and this [2,3]-sigmatropic rearrangement was efficaciously applied on the higher order oligosaccharides. This synthetic method emerged as an excellent complimentary route for the synthesis of digoxose trisaccharide glycal donor with highly compatible donor-acceptor coupling synthons. And to our delight, we were able to successfully scale up the production of the appropriately protected digoxose trisaccharide up to the gram scale by adopting this effective protocol.

Having established the efficient synthetic protocol for constructing the digoxose trisaccharide glycal donor **18**, the direct synthesis of digoxin and gitoxin derivative via stereoselective glycosylation reaction was conducted as a part of post synthetic application. Initially we performed the PPh_3.HBr-catalyzed glycosylation of the trisaccharide glycal donor **18** with acetylated digoxigenin aglycone **19** in toluene solvent. However, due to the insolubility of aglycone in toluene, the reaction did not proceed and there was no product formation (Table 1, entry 1) observed. When the solvent was changed to 1,2-dichlorobenzene, product formation was initiated but it suffered from poor yield of 50% (Table 1, entry 2).

Entry	Solvent	Catalyst	β:α Ratio	20β + 20α (%)
1	Toluene	PPh_3·HBr	NR	NR
2	1,2dichlorobenzene	PPh_3·HBr	1:0.5	50%
3	DCM	PPh_3·HBr	1:1	55%
4	$CHCl_3$	PPh_3·HBr	1:0.5	68%

Table 1. Glycosylation of TBS protected digoxose trisaccharide glycal **18** with Digoxigenin **19**.



Scheme 6. Synthesis of orthogonally protected aglycone and glycan portion of the cardenolides: digoxin and gitoxin.

Hence, instead of nonpolar solvents, polar aprotic solvent like dichloromethane was chosen for this acid catalysed glycosylation and it afforded the desired product in 55% yield (Table 1, entry 3). However, employing $CHCl_3$ as solvent, the glycosylation reaction proceeded smoothly and provided the desired product **20**β + **20**α in 68% yield in 1:0.5 ratio, respectively, (Table 1, entry 4). The formation of β-glycoside as major stereoisomer is probably due to the predominant 1,3-diaxial interaction between the C-3 *O*-TBS and the incoming nucleophile over anomeric effect. We were fortunate to be able to separate **20**β during column chromatographic purification. Afterward, compound **20**β was subjected to deacetylation to give the orthogonally protected glycan portion of cardenolide digoxin **21** in 80% yield. Having optimized conditions, the synthesis of another CG, gitoxin was attempted in addition. In this section, the trisaccharide donor **18** was glycosylated with aglycone gitoxigenin **22** in presence of catalytic amount of PPh_3·HBr in $CHCl_3$. As expected, we obtained the orthogonally protected gitoxin cardenolide derivative **23**β and **23**α in 70% yield as an inseparable mixture of anomers in 1:0.5 ratio, respectively (Scheme 6).

4.3 Conclusion

In conclusion, a simple yet influential reaction, Mislow-Evans rearrangement, was efficiently adopted for the synthesis of 6-deoxy 3,4-di-*O*-*tert*-butyldimethylsilyl D-allal. Also, the [2,3]-sigmatropic rearrangement reaction was explored for the first time on a disaccharide as well as on a trisaccharide precursors. The developed synthetic protocol features an iterative gram scale synthesis of digoxose trisaccharide glycal moiety. As a part of post synthetic application, the stereoselective synthesis of two main CG derivatives, digoxin and gitoxin were accomplished. Furthermore, protocol for the global deprotection of TBS groups, application of this strategy in synthesis of digitoxin, its analogues bearing diverse sugar subunits, modified aglycone unit and investigations of their biological activity are ongoing and will be reported in due course.

4.4 EXPERIMENTAL SECTION

4.4.1 General information

1. General Considerations

Materials and chemicals: All the chemicals were purchased from Sigma-Aldrich Chemicals Company and local suppliers. Solvents used in the reactions were dried and distilled over dehydrating agents. Silica-gel (100-200 mesh) was used for column chromatography.

Experimental details: All the reactions were carried out under nitrogen or argon atmosphere and monitored by thin layer chromatography (TLC) using silica gel GF254 plates with detection by charring with 5% (v/v) H_2SO_4 in methanol or by phosphomolybdic acid (PMA) stain or by ultra violet (UV) detection. Known starting materials were prepared according to previously known literature procedures.

Compound characterization: ^{1}H, ^{13}C, DEPT 135 spectra were recorded on Bruker 500 MHz and 400 MHz spectrometer in $CDCl_3$ at 296 K. ^{1}H NMR chemical shifts were reported in ppm (δ) respect to solvent (^{1}H: $CDCl_3$, δ = 7.26 ppm). Splitting patterns are designated as s, singlet; d, doublet; t, triplet; q, quadruplet; m, multiplet; dd, double doublet; dt, double triplet. Coupling constants (*J*) are given in Hertz (Hz). ^{13}C NMR were reported in chemical shifts with solvent reference ($CDCl_3$, δ 77.00). High resolution mass spectra (HRMS) were obtained in the Bruker maXis ESI-TOF spectrometer. Structural assignments were made with additional information from gCOSY, gNOESY experiments.

4.4.2 General Experimental Procedures:

General Procedure A for TBS protection of alcohols

To a stirred solution of alcohol in anhydrous DMF (2 mL/mmol) under inert atmosphere was added imidazole (1.2 eq for each hydroxyl group) followed by TBSCl (1.1 eq for each hydroxyl group) at 0 ˚C room temperature and stirring was continued for overnight at room temperature. The reaction was quenched with slow addition of cold water and extracted with diethyl ether, dried over anhydrous Na_2SO_4 and concentrated under reduced pressure to obtain crude product. Purification of the crude product by column chromatography over silica gel using hexanes and ethyl acetate provided pure *O*-TBS protected sugar derivatives.

General procedure B for DMDO mediated oxidation followed by [2,3]-sigmatropic rearrangement:

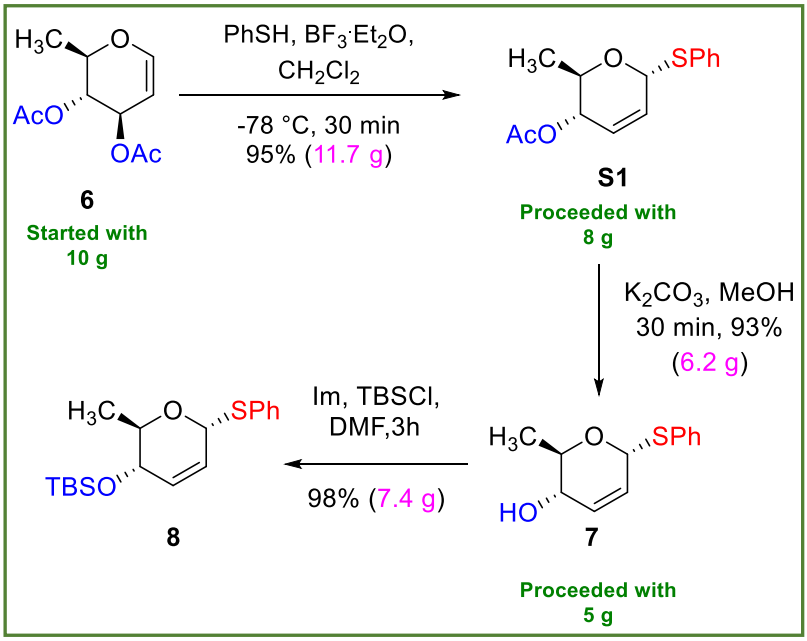
The stirred solution of Thio-glycoside (2.97 mmol) in dry dichloromethane under inert atmosphere was cooled to -78 ˚C. To the above solution was added DMDO in acetone (60 mL) in 3 portions. The reaction was monitored by TLC. After the completion of reaction, the solvent was removed under vacuum at 0 ˚C water bath to obtain the crude sugar-sulphoxide. The crude was immediately dissolved in dry THF (10 mL) and added diethyl amine (2 mL). The reaction was stirred for 3 hours at room temperature. After completion of reaction, the solvent was evaporated to obtain the crude product which was purified by silica gel column chromatography using ethyl acetate-hexane solvents.

General procedure C for HBr·PPh_3 mediated Glycosylation:

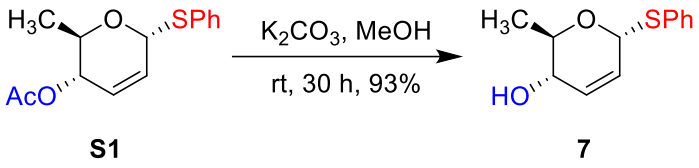
To a stirred solution of donor sugar (1 mmol) and acceptor sugar (1.2 mmol) in anhydrous Toluene (10 mL/mmol) under inert atmosphere was added 4Å molecular sieves and stirred for 1 hour. HBr·PPh_3 (0.2 mmol, 0.2 Equvi) was added to the above stirred solution and continued stirring for 5 hours. After complete conversion of starting material, solvent was concentrated under reduced pressure to obtain crude product which was purified using column chromatography to obtain the glycosylated product.

Synthesis of TBS-protected Thio-digitoxoside 8:

Route A:



Compound **S1** was synthesized from **6**[18] by following the previous literature procedure.[19]



S1 **7**

(2*R*,3*S*,6*R*)-2-methyl-6-(phenylthio)-3,6-dihydro-2*H*-pyran-3-ol (7):

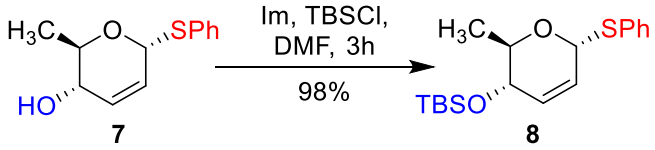
Compound **S1** (8 g, 30.2 mmol) was dissolved in 15 mL of dry methanol. To this solution, potassium carbonate (416 mg, 3.0 mmol, 0.1 Equiv) was added and stirred for complete conversion of starting material. The solvent was removed by rotary evaporator to obtain the crude and the crude was purified by silica gel column chromatography to obtain the pure compound **7**. Yield: 6.2 g (93%, 28.1 mmol); R*f* : 0.4 (20% EtOAc/hexane); White solid.

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.54-7.56 (m, 2H), 7.31-7.35 (m, 2H), 7.26-7.30 (m, 1H), 5.97-5.60 (m, 1H), 5.91 (dt, 1H, *J* = 1.5 Hz, *J* = 10.0 Hz), 5.72-5.73 (m, 1H), 4.03-4.08 (m, 1H), 3.95-3.97 (m, 1H), 2.38 (bs, 1H), 1.40 (d, 3H, *J* = 6.0 Hz).

^{13}C NMR (125 MHz, $CDCl_3$): δ 135.5, 131.7, 131.3, 128.8, 127.3, 127.2, 83.5, 69.3, 68.6, 17.9.

HRMS (ESI-TOF) *m/z*: $[M+Na]^+$ calcd for $C_{12}H_{22}O_2SNa$ 245.0612, found 245.0612.

IR(neat): 3397, 2935, 2924 cm^{-1}.



7 **8**

***tert*-butyldimethyl(((2*R*,3*S*,6*R*)-2-methyl-6-(phenylthio)-3,6-dihydro-2*H*-pyran-3-yl)oxy)silane (8):**

Compound **8** was synthesized from **7** (5 g, 22.4 mmol) by following general procedure A. Yield: 7.4 g (98%, 21.98 mmol); R*f* : 0.5 (5% EtOAc/hexane);White solid.

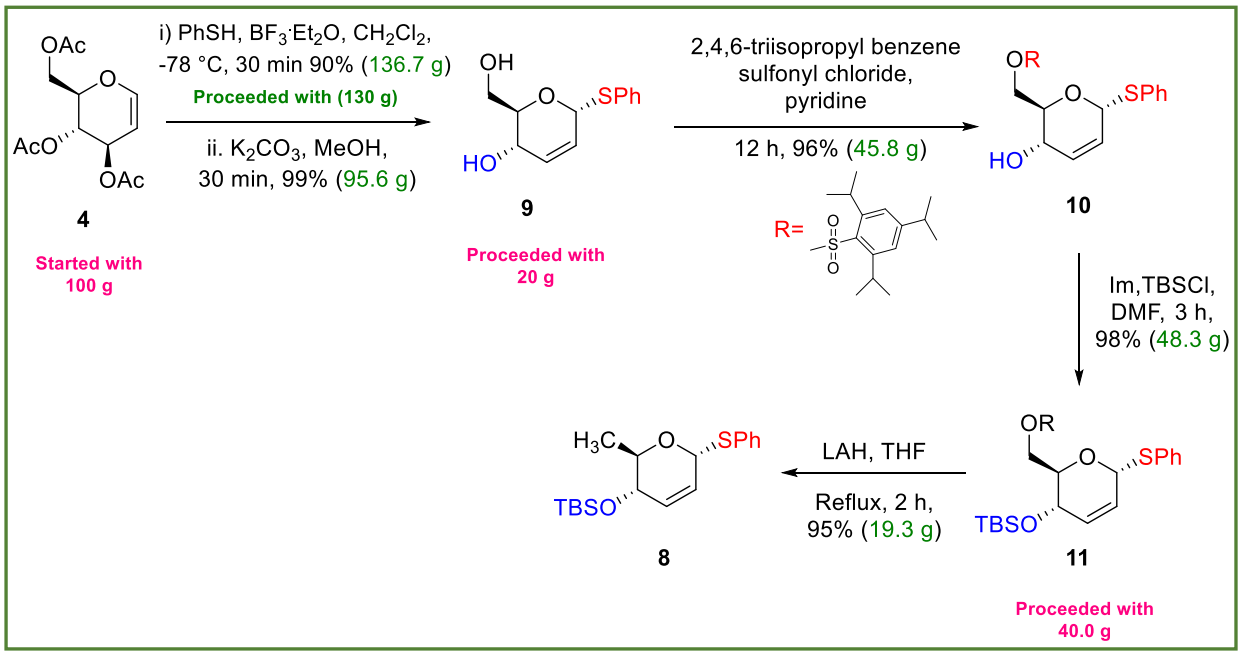
^{1}H NMR (500 MHz, $CDCl_3$): δ 7.38-7.41 (m, 2H), 7.14-7.18 (m, 2H), 7.09-7.12 (m, 1H), 5.74-5.77 (m, 1H), 5.68 (dt, 1H, *J* = 1.5 Hz, *J* = 10.0 Hz), 5.55-5.57 (m, 1H), 3.89-3.94 (m, 1H), 3.84-3.87 (m, 1H), 1.17 (d, 3H, *J* = 6.0 Hz), 0.80 (s, 9H), 0.009 (d, 6H, *J* = 4.5 Hz).

^{13}C NMR (125 MHz, $CDCl_3$): δ 136.1, 133.0, 131.3, 128.8, 127.1, 126.2, 84.0, 70.2, 68.5, 25.8, 18.2, 18.0, -4.1, -4.6.

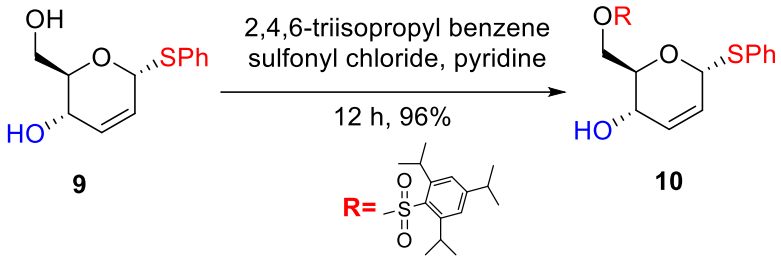
HRMS (ESI-TOF) *m/z*: $[M+Na]^+$ calcd for $C_{18}H_{28}O_2SSiNa$ 359.1477, found 359.1472.

IR(neat): 2953, 2927, 2854 cm^{-1}.

Route B:



Compound **9** was synthesized from **4** by following previous literature procedure.[19]



((2*R*,3*S*,6*R*)-3-hydroxy-6-(phenylthio)-3,6-dihydro-2*H*-pyran-2-yl)methyl 2,4,6-triisopropylbenzenesulfonate (10):

Compound **9** (20 g 83.9 mmol) was dissolved in 200 mL of dry pyridine. To this solution, 2,4,6-Triisopropylbenzenesulfonyl chloride (25.4 g, 84.0 mmol, 1 Equiv) was added and stirred for

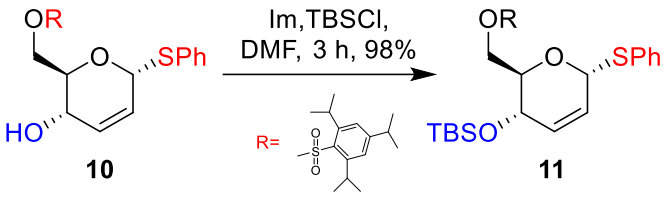
complete conversion of starting material. The solvent was removed by rotary evaporator to obtain the crude and the crude was purified by silica gel column chromatography to obtain the pure compound **10**. Yield: 43.9 g (96%, 80.0 mmol); R*f* : 0.6 (20% EtOAc/hexane); White solid.

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.47-7.48 (m, 2H), 7.18-7.21 (m, 5H), 5.90-5.96 (m, 2H), 5.67 (s, 1H), 4.39 (dd, 1H, *J* = 5 Hz, *J* = 11 Hz), 4.29-4.32 (m, 1H), 4.22-4.28 (m, 2H), 4.10-4.16 (m, 2H), 2.88-2.93 (m, 1H), 2.49 (bs, 1H), 1.26 (s, 3H), 1.24 (s, 6H), 1.23 (s, 3H), 1.22 (s, 3H), 1.21 (s, 3H),

^{13}C NMR (125 MHz, $CDCl_3$): δ 153.8, 150.9, 134.8, 131.8(2), 131.3, 129.0(3), 128.8,127.3, 127.0, 123.8(2), 83.7, 70.1, 68.0, 63.0, 34.1, 29.6(3), 24.6(3), 23.5(2).

HRMS (ESI-TOF) *m/z*: $[M+NH_4]^+$ calcd for $C_{27}H_{36}O_5S_2NH_4$ 522.2348, found 522.2244

IR(neat): 3488, 2958, 2935, 2869 cm^{-1}.



((2*R*,3*S*,6*R*)-3-((*tert*-butyldimethylsilyl)oxy)-6-(phenylthio)-3,6-dihydro-2*H*-pyran-2-yl)methyl 2,4,6-triisopropylbenzenesulfonate (11):

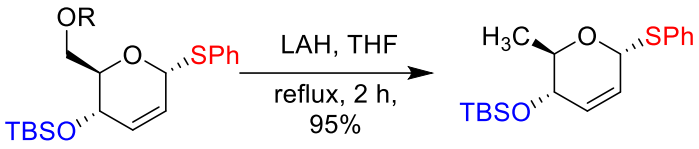
Compound **11** was synthesized from **10** (40 g, 73.1 mmol) by following general procedure A. Yield: 47.3 g (98%, 71.5 mmol); R*f* : 0.8 (10% EtOAc/hexane); White solid.

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.49-7.51 (m, 2H), 7.17-7.23 (m, 5H), 5.88-5.91 (m, 1H), 5.79 (dt, 1H, *J* = 1.5 Hz, *J* = 10 Hz), 5.60-5.62 (m, 1H), 4.21-4.27 (m, 3H), 4.1-4.18 (m, 3H), 2.88-2.93 (m, 1H), 1.26 (s, 3H), 1.25 (s, 3H), 1.23 (s, 3H), 1.22 (s, 3H), 1.21 (s, 3H) 1.19 (s, 3H), 0.85 (s, 9H), 0.09 (s, 3H), 0.05 (s, 3H).

^{13}C NMR (125 MHz, $CDCl_3$): δ 153.6, 151.1(2), 134.8, 132.4(2), 131.9, 129.0(2), 128.8(2) 127.6(2), 126.3, 123.7(2), 83.9, 70.0, 67.8, 64.0, 34.3, 29.6(2), 25.7(3), 24.7(2), 23.6(2), 17.8, -4.0, -4.8.

HRMS (ESI-TOF) *m/z*: $[M+NH_4]^+$ calcd for $C_{33}H_{50}O_5S_2SiNH_4$ 636.3213, found 636.3211.

IR(neat): 2955, 2929, 2859 cm^{-1}.



11 **8**

***tert*-butyldimethyl(((2*R*,3*S*,6*R*)-2-methyl-6-(phenylthio)-3,6-dihydro-2*H*-pyran-3-yl)oxy)silane (8):**

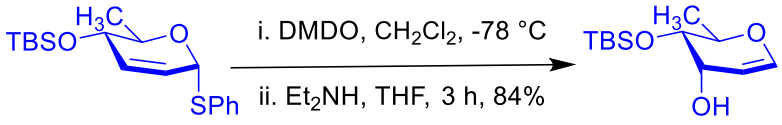
Compound **11** (40 g, 60.5 mmol) was dissolved in 250 mL of dry THF. The solution was cooled to 0 °C and lithium aluminium hydride (LAH) (12.2 g, 98.8 mmol, 5 Equiv) was added portion wise for 20 minutes. The reaction was allowed to room temperature and further refluxed for 3 hours. After complete conversion of starting material, the reaction was quenched by saturated ammonium chloride solution and filtered through celite. The organic layer was diluted with ethyl acetate, washed with brine and dried over sodium sulphate. The solvent was removed by rotary evaporator to obtain the crude and the crude was purified by silica gel column chromatography to obtain the pure compound **8**. Yield: 19.3 g (95%, 57.46 mmol); R*f* : 0.5 (10% EtOAc/hexane);White solid.

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.38-7.41 (m, 2H), 7.14-7.18 (m, 2H), 7.09-7.12 (m, 1H), 5.74-5.77 (m, 1H), 5.68 (dt, 1H, *J* = 1.5 Hz, *J* = 10.0 Hz), 5.55-5.57 (m, 1H), 3.89-3.94 (m, 1H), 3.84-3.87 (m, 1H), 1.17 (d, 3H, *J* = 6.0 Hz), 0.80 (s, 9H), 0.009 (d, 6H, *J* = 4.5 Hz).

^{13}C NMR (125 MHz, $CDCl_3$): δ 136.1, 133.0, 131.3, 128.8, 127.1, 126.2, 84.0, 70.2, 68.5, 25.8, 18.2, 18.0, -4.1, -4.6.

HRMS (ESI-TOF) *m/z*: $[M+Na]^+$ calcd for $C_{18}H_{28}O_2SSiNa$ 359.1477, found 359.1472.

IR(neat): 2953, 2927, 2854 cm^{-1}.



8 **12a**

(2*R*,3*S*,4*S*)-3-((*tert*-butyldimethylsilyl)oxy)-2-methyl-3,4-dihydro-2*H*-pyran-4-ol (12a):

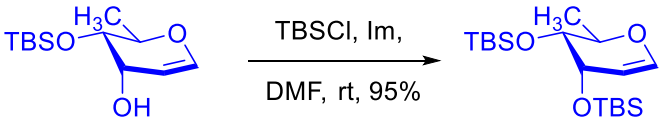
Compound **12a** was synthesized from **8** (5.0 g, 14.8 mmol) by following general procedure B. Yield: 3.0 g (84%, 12.2 mmol); R*f* : 0.5 (10% EtOAc/hexane); Colorless gel.

^{1}H NMR (500 MHz, $CDCl_3$): δ 6.41 (d, 1H, *J* = 6.0 Hz), 4.92 (t, 1H, *J* = 5.5 Hz), 3.98 (t, 1H, *J* = 4.5 Hz), 3.92-3.96 (m, 1H), 3.56 (dd, 1H, *J* = 3.5 Hz, *J* = 9.5 Hz), 2.67 (bs, 1H), 1.29 (d, 3H, *J* = 6.0 Hz), 0.93 (s, 9H), 0.13 (d, 6H, *J* = 2.0 Hz).

^{13}C NMR (125 MHz, $CDCl_3$): δ 146.6, 100.4, 73.5, 70.1, 62.8, 25.7, 18.0, 17.5, -4.4, -4.7.

HRMS (ESI-TOF) *m/z*: $[M+Na]^+$ calcd for $C_{12}H_{24}O_3SiNa$ 267.1392, found 267.1390.

IR(neat): 3554, 3062, 2952, 2929, 2886, 1644 cm^{-1}.



12a **12**

(((*2R*,3*R*,4*S*)-2-methyl-3,4-dihydro-2*H*-pyran-3,4-diyl)bis(oxy))bis(*tert*-butyldimethylsilane) (12):

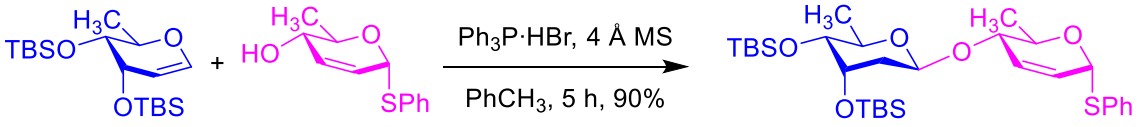
Compound **12** was synthesized from **12a** (3.0 g, 12.2 mmol) by following general procedure A. Yield: 4.1 g (95%, 7.5 mmol); R*f* : 0.5 (10% EtOAc/hexane); crystalline solid.

^{1}H NMR (500 MHz, $CDCl_3$): δ 6.28 (d, 1H, *J* = 6.0 Hz), 4.76 (t, 1H, *J* = 6.0 Hz), 4.09-4.14 (m, 1H), 3.99 (dd, 1H, *J* = 3.0 Hz, *J* = 5.5 Hz), 3.49 (dd, 1H, *J* = 3.5 Hz, *J* = 9.5 Hz), 1.27 (d, 3H, *J* = 6.5 Hz), 0.91 (s, 9H), 0.88 (s, 9H), 0.07 (s, 6H), 0.063-0.067 (m, 6H).

^{13}C NMR (125 MHz, $CDCl_3$): δ 145.1, 102.3, 73.8, 70.5, 64.4, 25.9, 18.1, 18.0, 17.9, -3.4, -3.8, -4.2, -4.8.

HRMS (ESI-TOF) *m/z*: $[M+Na]^+$ calcd for $C_{18}H_{38}O_3Si_2Na$ 381.2257, found 381.2255.

IR(neat): 2928, 2856,1640 cm^{-1}.



12 **7** **13**

(((2*R*,3*R*,4*S*,6*S*)-2-methyl-6-(((2*R*,3*S*,6*R*)-2-methyl-6-(phenylthio)-3,6-dihydro-2*H*-pyran-3-yl)oxy)tetrahydro-2*H*-pyran-3,4-diyl)bis(oxy))bis(*tert*-butyldimethylsilane) (13):

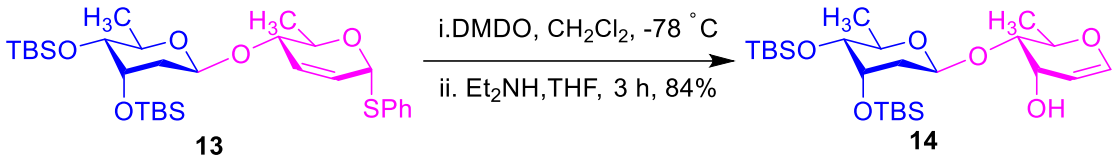
Compound **13** was synthesized from **12** (2.5 g, 6.9 mmol) and **7** (1.8 g, 8.3 mmol) by following general procedure C. Yield: 3.6 g (90%, 6.2 mmol); R*f* : 0.5 (5% EtOAc/hexane); Colorless gel.

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.52-7.54 (m, 2H), 7.29-7.33 (m, 2H), 7.24-7.28 (m, 1H), 6.11 (dt, 1H, *J* = 1.5 Hz, *J* = 10.0 Hz), 5.91-5.94 (m, 1H), 5.69-5.70 (m, 1H), 4.99 (dd, 1H, *J* = 2.0 Hz, *J* = 9.5 Hz), 4.16-4.21 (m, 1H), 4.02-4.04 (m, 1H), 3.90-3.95 (m, 2H), 3.31 (dd, 1H, *J* = 2.5 Hz, *J* = 9.0 Hz), 1.97-2.00 (m, 1H), 1.71-1.76 (m, 1H), 1.32 (d, 3H, *J* = 6.0 Hz), 1.22 (d, 3H, *J* = 6.5 Hz), 0.93 (d, 18H, *J* = 4.5 Hz), 0.10-0.11 (m, 9H), 0.08 (s, 3H).

^{13}C NMR (125 MHz, $CDCl_3$): δ 136.1, 131.7, 131.2, 128.8, 127.0, 126.7, 99.8, 83.8, 78.1, 75.1, 70.0, 69.5, 66.4, 40.0, 26.0, 25.8, 18.5, 18.1, 18.1, 18.0, -3.5, -4.4, -4.6, -4.7.

HRMS (ESI-TOF) *m/z*: $[M+Na]^+$ calcd for $C_{30}H_{52}O_5SSi_2Na$ 603.2972, found 603.2976.

IR(neat): 2952, 2928, 2888, 2855 cm^{-1}.



13 **14**

(2*R*,4*S*)-3-(((2*S*,4*S*,5*R*,6*R*)-4,5-bis((*tert*-butyldimethylsilyl)oxy)-6-methyltetrahydro-2*H*-pyran-2-yl)oxy)-2-methyl-3,4-dihydro-2*H*-pyran-4-ol (14):

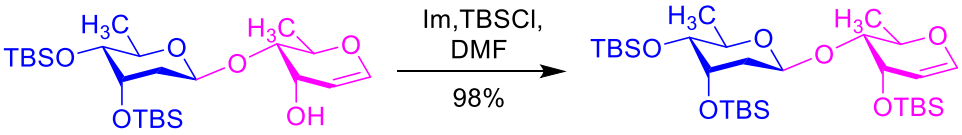
Compound **14** was synthesized from **13** (3.5 g, 6.0 mmol) by following general procedure B. Yield: 2.4 g (84%, 5.0 mmol); R*f* : 0.8 (20% EtOAc/hexane); Colorless gel.

^{1}H NMR (500 MHz, $CDCl_3$): δ 6.41 (d, 1H, *J* = 6.0 Hz), 4.95 (dd, 1H, *J* = 2.0 Hz, *J* = 9.5 Hz), 4.91 (t, 1H, *J* = 6.0 Hz), 4.23-4.25 (m, 1H), 3.91-4.00 (m, 3H), 3.40 (dd, 1H, *J* = 4.0 Hz, *J* = 10.0 Hz), 3.32 (d, 1H, *J* = 3.0 Hz), 3.26 (dd, 1H, *J* = 2.5 Hz, *J* = 9.0 Hz), 1.93-1.97 (m, 1H), 1.73 (ddd, 1H, *J* = 2.0 Hz, *J* = 9.5 Hz, *J* = 13.0 Hz), 1.31 (d, 3H, *J* = 6.0 Hz), 1.18 (d, 3H, *J* = 6.0 Hz), 0.89 (d, 18H, *J* = 1.5 Hz), 0.05-0.07 (m, 12H).

^{13}C NMR (125 MHz, $CDCl_3$): δ 146.4, 100.2, 99.1, 82.2, 74.9, 69.9, 69.8, 68.8, 61.5, 39.9, 26.0, 25.8, 18.5, 18.1 , 18.0, 17.2, -3.5, -4.4, -4.6, -4.7.

HRMS (ESI-TOF) *m/z*: $[M+Na]^+$ calcd for $C_{24}H_{48}O_6Si_2Na$ 511.2887, found 511.2887.

IR(neat): 3503, 2952, 2929, 2890, 2856, 1646 cm^{-1}.



14 **15**

(((2*R*,3*R*,4*S*,6*S*)-6-(((2*R*,3*R*,4*S*)-4-((*tert*-butyldimethylsilyl)oxy)-2-methyl-3,4-dihydro-2*H*-pyran-3-yl)oxy)-2-methyltetrahydro-2*H*-pyran-3,4-diyl)bis(oxy))bis(*tert*-butyldimethylsilane) (15):

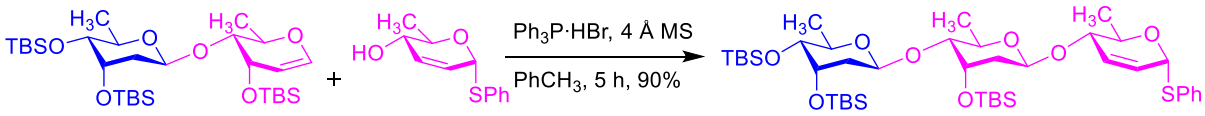
Compound **15** was synthesized from **14** (2.0 g, 4.09 mmol) by following general procedure A. Yield: 2.4 g (98%, 4.00 mmol); R*f* : 0.8 (5% EtOAc/hexane); White solid.

^{1}H NMR (500 MHz, $CDCl_3$): δ 6.28 (d, 1H, *J* = 6.0 Hz), 4.92 (dd, 1H, *J* = 2.0 Hz, *J* = 9.5 Hz), 4.77 (t, 1H, *J* = 5.5 Hz), 4.21 (dd, 1H, *J* = 3.5 Hz, *J* = 5.5), 4.07-4.13 (m, 1H), 3.98-3.99 (m, 1H), 3.80-3.86 (m, 1H), 3.42 (dd, 1H, *J* = 3.5 Hz, *J* = 10.5 Hz), 3.19 (dd, 1H, *J* = 2.0 Hz, *J* = 8.5 Hz), 1.95-1.99 (m, 1H), 1.62-1.67 (m, 1H), 1.28 (d, 3H, *J* = 6.5 Hz), 1.15 (d, 3H, *J* = 6.0 Hz), 0.89-0.90 (m, 27H), 0.06-0.09 (m, 18H).

^{13}C NMR (125 MHz, $CDCl_3$): δ 144.8, 103.0, 99.6, 80.6, 75.5, 70.0, 69.3, 69.2, 64.2, 39.6, 26.1, 26.0, 25.8, 18.6, 18.4, 18.1, 18.1, 17.3, -3.5,-4.2, -4.3, -4.6, -4.7, -4.8.

HRMS (ESI-TOF) *m/z*: $[M+Na]^+$ calcd for $C_{30}H_{62}O_6Si_3Na$ 625.3752, found 625.3752.

IR(neat): 2953, 2929, 2889, 2856 cm^{-1}.



15 **7** **16**

(((2*R*,3*R*,4*S*,6*S*)-6-(((2*R*,4*S*,6*S*)-4-((*tert*-butyldimethylsilyl)oxy)-2-methyl-6-(((2*R*,6*R*)-2-methyl-6-(phenylthio)-3,6-dihydro-2*H*-pyran-3-yl)oxy)tetrahydro-2*H*-pyran-3-yl)oxy)-2-methyltetrahydro-2*H*-pyran-3,4-diyl)bis(oxy))bis(*tert*-butyldimethylsilane) (16):

Compound **16** was synthesized from **15** (1.5 g, 2.4 mmol) and **7** (660.8 mg, 2.9 mmol) by following general procedure C. Yield: 1.8 g (90%, 2.1 mmol); R*f*: 0.6 (5% EtOAc/hexane); Colorless gel.

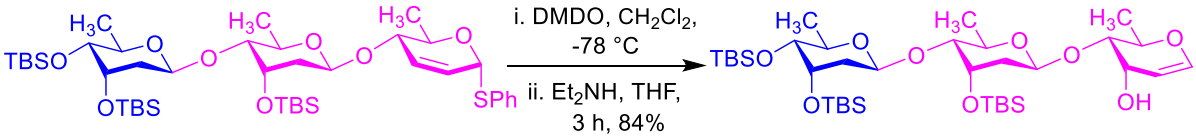
^{1}H NMR (500 MHz, $CDCl_3$): δ 7.52-7.54 (m, 2H), 7.26-7.33 (m, 3H), 6.09-6.11 (m, 1H), 5.90-5.93 (m, 1H), 5.69-5.70 (m, 1H), 4.97 (dd, 1H, *J* = 1.5 Hz, *J* = 9.5 Hz), 4.89 (dd, 1H, *J* = 1.5 Hz, *J* = 9.5 Hz), 4.30-4.31 (m, 1H), 4.15-4.21 (m, 1H), 3.99-4.00 (m, 1H), 3.92-3.95 (m, 1H), 3.83-3.90 (m, 2H), 3.18 (dd, 1H, *J* = 2.5 Hz, *J* = 9.0 Hz), 3.15 (dd, 1H, *J* = 2.5 Hz, *J* = 9.5 Hz), 1.90-

1.97 (m, 2H), 1.71-1.76 (m, 1H), 1.61-1.66 (m, 1H), 1.32 (d, 3H, *J* = 6.5 Hz) 1.21 (d, 3H, *J* = 6.5 Hz), 1.17 (d, 3H, *J* = 6.5 Hz), 0.92-0.93 (m, 27H), 0.08-0.11 (m, 18H).

^{13}C NMR (125 MHz, $CDCl_3$): δ 136.1, 131.9, 131.3, 128.8, 127.0, 126.6, 99.9, 99.8, 83.9, 82.3, 77.8, 75.5, 70.0, 69.4, 69.2, 68.4, 66.5, 39.9, 39.7, 26.0, 25.9, 25.8, 18.7, 18.2, 18.1, 18.1, 18.0, 17.9, -3.5, -4.2, -4.3, -4.6, -4.8, -5.4.

HRMS (ESI-TOF) *m/z*: $[M+NH_4]^+$ calcd for $C_{42}H_{76}O_8NH_4$ 842.4912, found 842.4906.

IR(neat): 2928, 2888, 2855 cm^{-1}.



16 **17**

(2*R*,4*S*)-3-(((2*S*,4*S*,6*R*)-5-(((2*S*,4*S*,5*R*,6*R*)-4,5-bis((*tert*-butyldimethylsilyl)oxy)-6-methyltetrahydro-2*H*-pyran-2-yl)oxy)-4-((*tert*-butyldimethylsilyl)oxy)-6-methyltetrahydro-2*H*-pyran-2-yl)oxy)-2-methyl-3,4-dihydro-2*H*-pyran-4-ol (17):

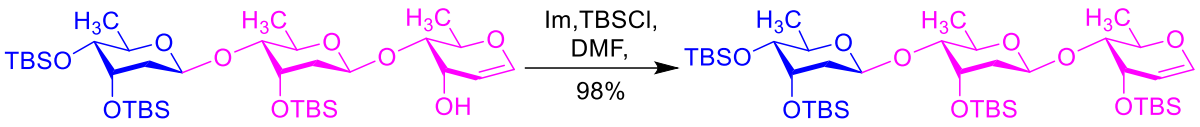
Compound **17** was synthesized from **16** (1.5 g, 1.8 mmol) by following general procedure B. Yield: 1.1 g (84%, 1.5 mmol); R*f* : 0.6 (10% EtOAc/hexane); Colorless gel.

^{1}H NMR (500 MHz, $CDCl_3$): δ 6.41 (d, 1H, *J* = 6.0 Hz), 4.93 (dd, 1H, *J* = 2.0 Hz, *J* = 9.5 Hz), 4.90 (t, 1H, *J* = 6.0 Hz), 4.86 (dd, 1H, *J* = 2.0 Hz, *J* = 9.5 Hz), 4.24-4.27 (m, 2H), 3.94-3.99 (m, 2H), 3.85-3.91 (m, 1H), 3.80-3.85 (m, 1H), 3.41 (dd, 1H, *J* = 3.5 Hz, *J* = 9.5 Hz), 3.33 (bs, 1H), 3.15 (dd, 1H, *J* = 2.5 Hz, *J* = 9.5 Hz), 3.12 (dd, 1H, *J* = 2.5 Hz, *J* = 9.5 Hz), 1.86-1.93 (m, 2H), 1.71-1.76 (m, 1H), 1.57-1.62 (m, 1H), 1.31 (d, 3H, *J* = 6.5 Hz), 1.18 (d, 3H, *J* = 6.5 Hz), 1.13 (d, 3H, *J* = 6.5 Hz), 0.88-0.89 (m, 27H), 0.05-0.08 (m, 18H).

^{13}C NMR (125 MHz, $CDCl_3$): δ 146.4, 100.2, 99.8, 99.2, 82.1, 81.9, 75.4, 69.9, 69.3, 69.2, 68.9, 68.7, 61.5, 39.7, 39.7, 26.0, 25.9, 25.8, 18.6, 18.2, 18.1, 18.1, 17.9, 17.2, -3.5, -4.2, -4.4, -4.6, -4.8, -5.4.

HRMS (ESI-TOF) *m/z*: $[M+Na]^+$ calcd for $C_{36}H_{72}O_9Si_3Na$ 755.4382, found 755.4384.

IR(neat): 3532, 2952, 2929, 2855, 1646 cm^{-1}.



17 18

(((2*R*,3*R*,4*S*,6*S*)-6-(((2*R*,4*S*,6*S*)-4-((*tert*-butyldimethylsilyl)oxy)-6-(((2*R*,4*S*)-4-((*tert*-butyldimethylsilyl)oxy)-2-methyl-3,4-dihydro-2*H*-pyran-3-yl)oxy)-2-methyltetrahydro-2*H*-pyran-3-yl)oxy)-2-methyltetrahydro-2*H*-pyran-3,4-diyl)bis(oxy))bis(*tert*-butyldimethylsilane) (18):

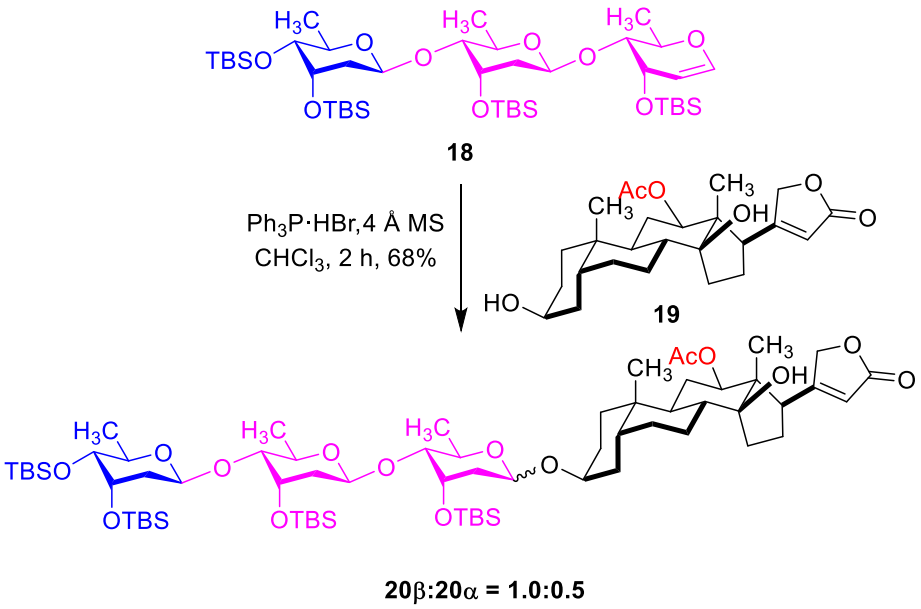
Compound **18** was synthesized from **17** (1.0 g, 1.36 mmol) by following general procedure A. Yield: 1.1 g (98%, 1.33 mmol); R*f* : 0.8 (5% EtOAc/hexane); White cotton.

^{1}H NMR (500 MHz, $CDCl_3$): δ 6.28 (d, 1H, *J* = 6.0 Hz), 4.85-4.91 (m, 2H), 4.77 (t, 1H, *J* = 5.5 Hz), 4.25-4.26 (m, 1H), 4.19 (dd, 1H, *J* = 3.5 Hz, *J* = 6.0 Hz), 4.07-4.13 (m, 1H), 3.96-3.97 (m, 1H), 3.81-3.85 (m, 1H), 3.75-3.78 (m, 1H), 3.43 (dd, 1H, *J* = 3.5 Hz, *J* = 10.5 Hz), 3.16 (dd, 1H, *J* = 2.0 Hz, *J* = 9.0 Hz), 3.04 (dd, 1H, *J* = 2.5 Hz, *J* = 9.5 Hz), 1.86-1.95 (m, 2H), 1.60-1.69 (m, 2H), 1.27-1.28 (m, 3H), 1.13-1.15 (m, 6H), 0.87-0.90 (m, 36H), 0.09 (s, 6H), 0.05-0.07(m, 18H).

^{13}C NMR (125 MHz, $CDCl_3$): δ 143.8, 101.9, 98.7, 98.7, 81.5, 79.4, 74.4, 69.0, 68.4, 68.4, 68.0, 67.3, 63.2, 38.8, 38.4, 25.0, 25.0, 24.8(2), 17.6, 17.3, 17.1, 17.1, 17.1, 17.0, 16.2, -4.5, -5.2, -5.2, -5.4, -5.6, -5.7, -5.8, -6.5.

HRMS (ESI-TOF) *m/z*: $[M+Na]^+$ calcd for $C_{42}H_{86}O_9Si_4Na$ 869.5247, found 869.5249.

IR (neat): 2952, 2929, 2891, 2855 cm^{-1}.



(5*R*,10*S*,12*R*,13*S*,14*S*)-3-(((2*R*,4*S*,6*R*)-5-(((2*S*,4*S*,6*R*)-5-(((2*S*,4*S*,5*R*,6*R*)-4,5-bis((*tert*-butyldimethylsilyl)oxy)-6-methyltetrahydro-2*H*-pyran-2-yl)oxy)-4-((*tert*-butyldimethylsilyl)oxy)-6-methyltetrahydro-2*H*-pyran-2-yl)oxy)-4-((*tert*-butyldimethylsilyl)oxy)-6-methyltetrahydro-2*H*-pyran-2-yl)oxy)-14-hydroxy-10,13-dimethyl-17-(5-oxo-2,5-dihydrofuran-3-yl)hexadecahydro-1*H*-cyclopenta[a]phenanthren-12-yl acetate (20β):

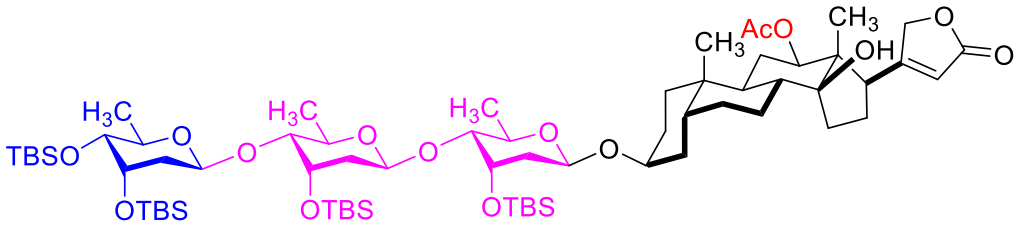
Compound **20β:20*α*** was synthesized from **18** (50 mg, 0.059 mmol) and **19** (28.0 mg, 0.06 mmol) by following general procedure C **(solvent used dry chloroform instead of toluene)** . Yield: 51.35 mg (68%, 0.040 mmol); R*f*: 0.4 (30% EtOAc/hexane); Colorless gel.

20β: δ 5.84 (s, 1H), 4.89 (d, 1H, *J* = 1.5 Hz), 4.82-4.86 (m, 3H), 4.77 (dd, 1H, *J* = 1.5 Hz, *J* = 18.0 Hz), 4.62 (dd, 1H, *J* = 4.0 Hz, *J* = 12.0 Hz), 4.23 (s, 2H), 4.10 (s, 1H), 3.96 (s, 1H), 3.73-23.85 (m, 3H), 3.15 (dd, 1H, *J* = 2.5 Hz, *J* = 9.0 Hz), 3.11 (dd, 1H, *J* = 2.5 Hz, *J* = 9.5 Hz), 3.01 (dd, 1H, *J* = 2.5 Hz, *J* = 9.5 Hz), 2.89 (dd, 1H, *J* = 6.5 Hz, *J* = 9.0 Hz), 2.13 – 2.19 (m, 1H), 2.08 (s, 3H), 1.97-2.01 (m, 1H), 1.90-1.94 (m, 2H), 1.82-1.87 (m, 3H), 1.74-1.78 (m, 2H), 1.63-1.71 (m, 7H), 1.58 (s, 9H), 1.49 (d, 2H, *J* = 10.0 Hz), 1.21-1.29 (m, 7H), 1.16 (d, 3H, *J* = 6.5 Hz), 1.13 (d, 3H, *J* = 6.0 Hz), 1.12 (d, 3H, *J* = 6.0 Hz), 0.86-0.92 (m, 40H), 0.08 (s, 3H), 0.07 (s, 3H), 0.06 (s, 3H), 0.06 (s, 3H), 0.05 (s, 3H), 0.04 (s, 3H).

^{13}C NMR (125 MHz, $CDCl_3$): δ 174.3, 173.3, 170.8, 118.0, 100.0, 99.7, 95.4, 85.9, 82.4, 82.4, 77.4, 75.4, 73.3, 72.2, 70.0, 69.5, 69.4, 69.0, 68.5, 68.2, 53.9, 45.9, 41.5, 40.2, 39.8, 39.6, 36.3, 35.2, 33.2, 32.4, 30.2, 29.8, 27.2, 26.6, 26.5, 26.0, 25.9, 25.8, 25.8, 23.5, 21.7, 21.3, 18.6, 18.2, 18.1, 18.1, 18.1, 17.9, 10.3, -3.5, -4.1, -4.2, -4.4, -4.6, -4.8, -5.5, -5.5.

HRMS (ESI-TOF) *m/z*: $[M+Na]^+$ calcd for $C_{67}H_{122}O_{15}Si_4Na$ 1301.7758, found 1301.7752.

IR(neat): 3475, 2928, 2886, 2855, 2359, 1738 cm^{-1}.



20β

K_2CO_3, MeOH,
30 min, 80%

21

4-((5*R*,10*S*,12*R*,13*S*,14*S*)-3-(((2*R*,4*S*,6*R*)-5-(((2*S*,4*S*,6*R*)-5-(((2*S*,4*S*,5*R*,6*R*)-4,5-bis((*tert*-butyldimethylsilyl)oxy)-6-methyltetrahydro-2*H*-pyran-2-yl)oxy)-4-((*tert*-butyldimethylsilyl)oxy)-6-methyltetrahydro-2*H*-pyran-2-yl)oxy)-4-((*tert*-butyldimethylsilyl)oxy)-6-methyltetrahydro-2*H*-pyran-2-yl)oxy)-12,14-dihydroxy-10,13-dimethylhexadecahydro-1*H*-cyclopenta[a]phenanthren-17-yl)furan-2(5*H*)-one (21):

Compound **20β** (25 mg, 0.019 mmol) was dissolved in 5 mL of dry methanol. To this solution, potassium carbonate (0.5 mg, 0.004 mmol, 0.2 Equiv) was added and stirred for complete conversion of starting material. The solvent was removed by rotary evaporator to obtain the crude and the crude was purified by silica gel column chromatography to obtain the pure compound **21.** Yield: 19.33 mg (80%, 0.015 mmol); R*f* : 0.4 (30% EtOAc/hexane); White powder.

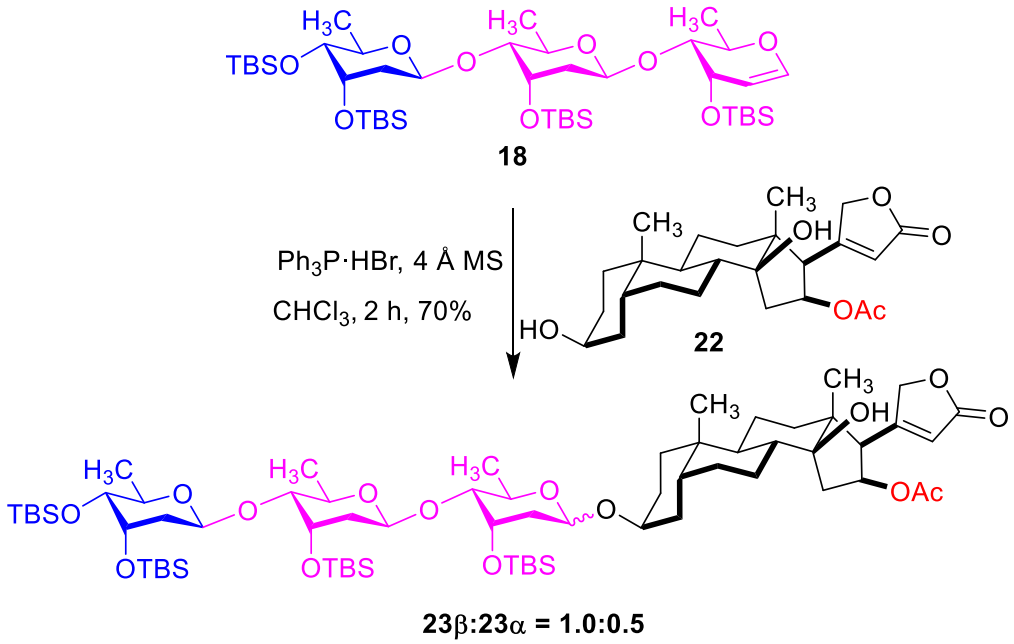
^{1}H NMR (500 MHz, $CDCl_3$): δ 5.93 (s, 1H), 4.90-4.91 (m, 1H), 4.87-4.89 (m, 1H), 4.84-4.86 (m, 1H), 4.79-4.83 (m, 2H), 4.23 (s, 2H), 4.00 (s, 1H), 3.96 (s, 1H), 3.74-3.84 (m, 3H), 3.37-3.39 (m, 1H), 3.30-3.34 (m, 1H), 3.15 (dd, 1H, *J* = 2.0 Hz, *J* = 9.0 Hz), 3.10-3.13 (m, 1H), 3.02 (dd,

1H, *J* = 3.0 Hz, *J* = 9.5 Hz), 1.16 (d, 3H, *J* = 6.5 Hz), 1.12-1.13 (m, 6H), 1.91-1.94 (m, 2H), 1.83-1.86 (m, 2H), 1.73-1.76 (m, 2H), 1.61-1.71 (m, 7H), 1.41-1.48 (m, 6H), 1.32-1.33 (m, 2H), 1.22-1.27 (m, 6H), 0.92 (s, 3H), 0.86-0.90 (m, 36H), 0.80 (s, 3H), 0.04-008 (m, 24H).

^{13}C NMR (125 MHz, $CDCl_3$): δ 174.5, 174.3, 117.7, 100.0, 99.7, 95.4, 85.9, 82.4, 82.4, 75.4, 75.1, 73.6, 72.1, 70.0, 69.5, 69.4, 69.0, 68.5, 68.2, 55.4, 45.6, 41.5, 40.2, 39.8, 39.6, 36.3, 35.0, 33.2, 32.6, 30.4, 30.1, 29.8, 29.7, 27.4, 26.7, 26.5, 26.0, 25.9, 25,8, 25.8, 23.5, 21.7, ,18.6, 18.2, 18.1, 18.1, 18.1, 17.9, 8.9, -3.5, -4.1, -4.2, -4.3, -4.6, -4.8, -5.5, -5.5

HRMS (ESI-TOF) *m/z*: $[M+NH_4]^+$ calcd for $C_{65}H_{120}O_{14}Si_4NH_4$ 1254.8099, found 1254.8099.

IR(neat): 3399, 2929, 2887, 2856, 1741 cm^{-1}.



(5*R*,10*S*,13*R*,14*S*,16*S*)-3-(((2*R*,4*S*,6*R*)-5-(((2*S*,4*S*,6*R*)-5-(((2*S*,4*S*,5*R*,6*R*)-4,5-bis((*tert*-butyldimethylsilyl)oxy)-6-methyltetrahydro-2*H*-pyran-2-yl)oxy)-4-((*tert*-butyldimethylsilyl)oxy)-6-methyltetrahydro-2*H*-pyran-2-yl)oxy)-4-((*tert*-butyldimethylsilyl)oxy)-6-methyltetrahydro-2*H*-pyran-2-yl)oxy)-14-hydroxy-10,13-dimethyl-17-(5-oxo-2,5-dihydrofuran-3-yl)hexadecahydro-1*H*-cyclopenta[a]phenanthren-16-yl acetate(23β:23α):

Compound **23β:23α** was synthesized as inseparable mixture from **18** (50 mg, 0.059 mmol) and **22** (30.63 mg, 0.070 mmol) by following general procedure C (**solvent used dry chloroform**

instead of toluene). Yield: 52.80 mg (70%, 0.040 mmol, **23β:23α**=1.0:0.5); R*f* : 0.5 (30% EtOAc/hexane); Colorless gel.

^{13}C NMR for 23β:23α mixture

^{13}C NMR (125 MHz, $CDCl_3$): δ 174.0, 170.4, 167.8, 167.8, 121.3, 99.9, 99.8, 99.6, 95.4, 94.6, 84.3, 84.3, 82.4, 82.4, 82.3, 82.1, 75.6, 73.9, 72.2, 71.2, 70.8, 69.5, 69.4, 69.3, 68.9, 68.4, 68.2, 68.1, 68.0, 62.0, 56.2, 56.1, 49.9, 41.8, 41.2, 41.1, 40.2, 39.8, 39.5, 39.4, 39.2, 37.9, 36.2, 35.7, 35.5, 35.1, 35.0, 32.1, 31.9, 30.1, 30.0, 29.8, 29.7, 26.7, 26.4, 26.3, 26.0, 26.0, 25.9, 25.8, 24.2, 23.6, 23.5, 21.0, 20.9, 20.8, 18.6, 18.3, 18.2, 18.1, 18.1, 18.0, 17.8, 17.5, 15.9, 15.9, -3.5, -4.1, -4.2, -4.4, -4.6, -4.8, -5.1, -5.5, -5.5, -5.5,

HRMS (ESI-TOF) *m/z*: $[M+Na]^+$ calcd for $C_{67}H_{122}O_{15}Si_4Na$ 1301.7758, found 1301.7761.

IR(neat): 3498, 2928, 2891, 2855, 2361, 1741 cm^{-1}.

4.5 References

1) Kirschning, A.; Bechthold, A. F.-W.; Rohr, J. Chemical and biochemical aspects of deoxysugars and deoxysugar oligosaccharides. *Top. Curr. Chem.* **1997**, *188*, 1-84.
2) (a) Schmiedeberg, J. E. O. Untersuchungen tiber die pharmakolog'iseh wirksamen*),Bestandtheile der Digitalis purpurea L. *Arch. Exp. Pathol. Pharmakol.* **1875**, *3*, 16-43. (b) Greeff, K.; Schadewaldt, H.; Cardiac Glycosides Part I: Experimental Pharmacology. In Handbook of Experimental Pharmacology; Greeff, K., Ed.; Springer-Verlag: Berlin, **1981**; Vol. 56, p1−12. (c) Hauptman, P. J.; Kelly, R. A. Digitalis. *Circulation.* **1999,** *99*, 1265−1270.
3) (a) Albrecht, H. P.; Cardiac glycosides. In Naturally Occurring Glycosides; Ikan, R., Ed.; John Wiley & Sons Ltd.: New York, **1999**; p 83. (b) D. Deepak, S. Sirsvastava, N. K. Khare, A. Khare, Cardiac Glycosides. *Fortschr. Chem. Org. Naturst.* **1996**, *69*, 71-156.
4) (a) Zhou, M.; O'Doherty, G. A. De Novo Approach to 2-Deoxy-β-glycosides: Asymmetric Syntheses of Digoxose and Digitoxin1. J. *Org. Chem.* **2007**, *72*, 2485-2493. (b) Ma, Y.; Shi, Z. Li. He.; Zhang, J.; Yu, B. Assembly of Digitoxin by Gold(I)-Catalyzed Glycosidation of Glycosyl O-Alkynylbenzoates. *J. Org. Chem.* **2011**, *76*, 9748−9756. (c) Zhou, M.; O'Doherty, G. A. A stereoselective synthesis of digitoxin and digitoxigen mono-

and bisdigitoxoside from digitoxigenin via a palladium-catalyzed glycosylation. *Org. Lett*. **2006**, *8*, 4339-4342.

5) (a) Beale, T. M.; Taylo, M. S. Synthesis of cardiac glycoside analogs by catalyst-controlled, regioselective glycosylation of digitoxin. *Org. Lett*. **2013**, *15*, 1358–1361. (b) Wang, H. L.; Xin, W.; Zhou, M. Stereochemical survey of digitoxin monosaccharides. *ACS Med. Chem. Lett.* **2011**, *2*, 73–78. (c) Zeng, J.; Sun, G.; Wang, R.; Zhang, S.; Teng, S.; Liao, Z.; Menga, L.; Wan, Q. Gold-catalyzed diversified synthesis of 3-aminosugar analogues of digitoxin and digoxin. *Org. Chem. Front.* **2017**, *4*, 2450-2454. (d) Zhang, M.; Chen, H.W.; Liu, Q. Q.; Gao, F.T.; Li, Y.X.; Hu, X.G.; Yu, C.Y. De Novo Synthesis of Orthogonally-Protected C2-Fluoro Digitoxoses and Cymaroses: Development and Application for the Synthesis of Fluorinated Digoxin. *J. Org. Chem.* **2022**, *87*, 1272−1284. (e) Hua-Yu, L.; Wang, B.; Wu, Q.; Zhang, S.; Kang, W.; Rojanasakul, Y.; O'Doherty, G. A. C5′-Alkyl Substitution Effects on Digitoxigenin α-l-Glycoside Cancer Cytotoxicity. *ACS Med. Chem. Lett.* **2011**, *2*, 259–263.

6) Iyer, A. K. V.; Zhou, M.; Azad, N.; Elbaz, H.; Wang, L.; Rogalsky, D. K.; Rojanasakul, Y.; O'Doherty, G. A.; Langenhan, J. M. A Direct Comparison of the Anticancer Activities of Digitoxin MeON-Neoglycosides and *O*-Glycosides. *ACS Med. Chem. Lett.* **2010**, *1*, 326–330.

7) McDonald, F. E.; Reddy, K. S. Convergent Synthesis of Digitoxin: Stereoselective Synthesis and Glycosylation of the Digoxin Trisaccharide Glycal. *Angew. Chem. Int. Ed.* **2001**, *40*, 3653-3655.

8) Baryal, K. N.; Adhikari, S.; Zhu, J. Catalytic Stereoselective Synthesis of β-Digitoxosides: Direct Synthesis of Digitoxin and C1′-epi-Digitoxin. *J. Org. Chem.* **2013**, *78*, 12469−12476.

9) (a) McDonald, F. E.; Reddy, K. S.; Diaz, Y. Stereoselective glycosylations of a family of 6-deoxy-1, 2-glycals generated by catalytic alkynol cycloisomerization. *J. Am. Chem. Soc.* **2000**, *122*, 4304-4309. (b) Hofferberth, M. L.; Brückner, R. α-and β-Lipomycin: Total Syntheses by Sequential Stille Couplings and Assignment of the Absolute Configuration of All Stereogenic Centers. *Angew. Chem. Int. Ed.* **2014,** *53*, 7328-7334.

10) Koo, B.; McDonald, F. E. Fischer carbene catalysis of alkynol cycloisomerization: Application to the synthesis of the altromycin B disaccharide. *Org. Lett.* **2007,** *9*, 1737-1740.

11) (a) Evans, D. A.; Andrews, G. C. Allylic sulfoxides. Useful intermediates in organic synthesis. *Acc. Chem. Res.* **1974**, *7,* 147−155. (b) Rojas, C. M.; Rojas, C. M. Molecular Rearrangements in Organic Synthesis. Ed.; John Wiley & Sons: Hoboken, NJ, **2016**; pp 569−62514.

12) Wittman, M. D.; Halcomb, R. L.; Danishefsky, S. J.; Golik, J.; Vyas, D. *J. Org. Chem.* **1990,** *55*, 1979−1981.

13) Colomer, I.; Velado, M.; Pradilla, R. F.; Viso, A. From Allylic Sulfoxides to Allylic Sulfenates: Fifty Years of a Never-Ending [2,3]-Sigmatropic Rearrangement. *Chem. Rev*. **2017**, *117*, 14201–14243.

14) (a) Sridhar, P. R.; Rao, B. U.; Drisya, C. S. [1,2]- vs [2,3]-Wittig Rearrangement in Carbohydrate Derived Alkenyl Systems. *Org. Lett.* **2021**, *23*, 3850-3853. (b) Sridhar, P. R.; Venukumar, P. A Ring Expansion Glycosylation Strategy toward the Synthesis of Septano-oligosaccharides. *Org. Lett.* **2012**, *14*, 5558−5561. (c) Reddy, G. M.; Sridhar, P. R. The first stereoselective total synthesis of neosemburin and isoneosemburin. ***Org. Biomol. Chem.*** **2014**, ***12***, 8408-8414. (d) Venukumar, P.; Sudharani, C.; Sridhar, P. R. A one-pot septanoside formation and glycosylation of acyclic dithioacetals derived from 1, 2-cyclopropanated sugars. ***Chem. Commun.*** **2014**, ***50***, 2218-2221. (e) Kamala Lakshmi, M. V.; Ali, I., Perali, R. S. A Ring Expansion-Stereoselective Cycloaddition of Carbohydrate-Derived Donor–Acceptor Cyclopropanes: Synthesis of Bridged Oxepanone–Indole Hybrids. *J. Org. Chem.* **2022**, *87*, 12370–12385.

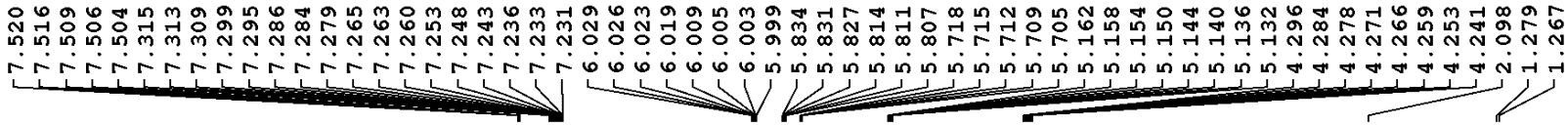
15) Hattori, H.; Roesslein, J. Caspers, P.; Zerbe, K.; Miyatake-Ondozabal, H.; Ritz, D.; Rueedi, G.; Gademann, K. Total synthesis and biological evaluation of the glycosylated macrocyclic antibiotic mangrolide A. *Angew. Chem. Int. Ed.* **2018**, *57*, 11020-11024.

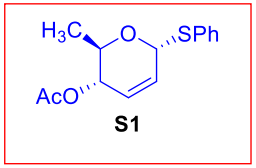
16) Buttar, S.; Caine, J.; Goné, E.; Harris, R.; Gillman, J.; Atienza, R.; Gupta, R.; Sogi, K. M.; Jain, L.; Abascal, N. C.; Levine, Y.; Repka, L. M.; Rojas, C. M. Glycal metallanitrenes for 2-amino sugar synthesis: amidoglycosylation of gulal-, allal-, glucal-, and galactal 3-carbamates. *J. Org. Chem.* **2018**, *83*, 8054–8080.

17) Sridhar, P. R.; Ali, I.; Kamala Lakshmi, M. V. Synthesis of Hexenuloses and a Library of Disaccharides Possessing 3-oxo-glycal Unit. *J. Org. Chem.* **2022,** *87*, 8939–8955.

18) Zeng, J.; Sun, G.; Yao, W.; Zhu, Y.; Wang, R.; Cai, L.; Liu, K.; Zhang, Q.; Liu, X.-W.; Wan, Q. 3-Aminodeoxypyranoses in Glycosylation: Diversity-Oriented Synthesis and Assembly in Oligosaccharides. *Angew. Chem. Int. Ed.* **2017**, *56*, 5227-5231.

19) Durantie, E.; Bucher, C.; Gilmour, R. Fluorine-Directed β-Galactosylation: Chemical Glycosylation Development by Molecular Editing. *Chem. Eur. J.* **2012,** *18,* 8208-8215. Note: Compound **S1** was synthesized by following the same protocol as used for triacetyl-D-glucal in the above-mentioned reference.

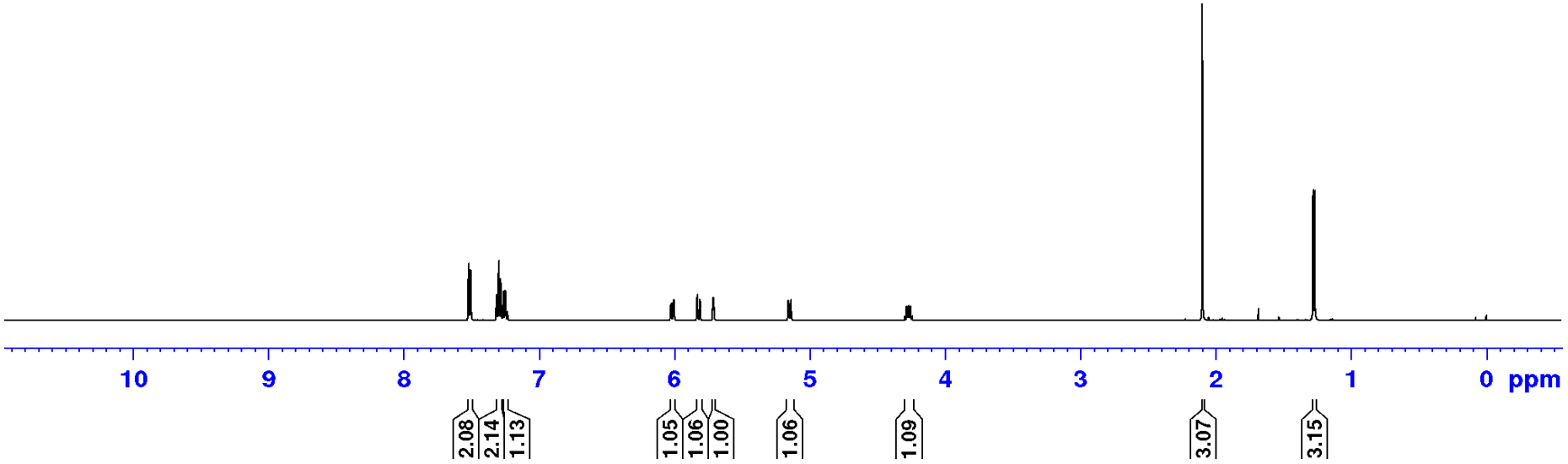


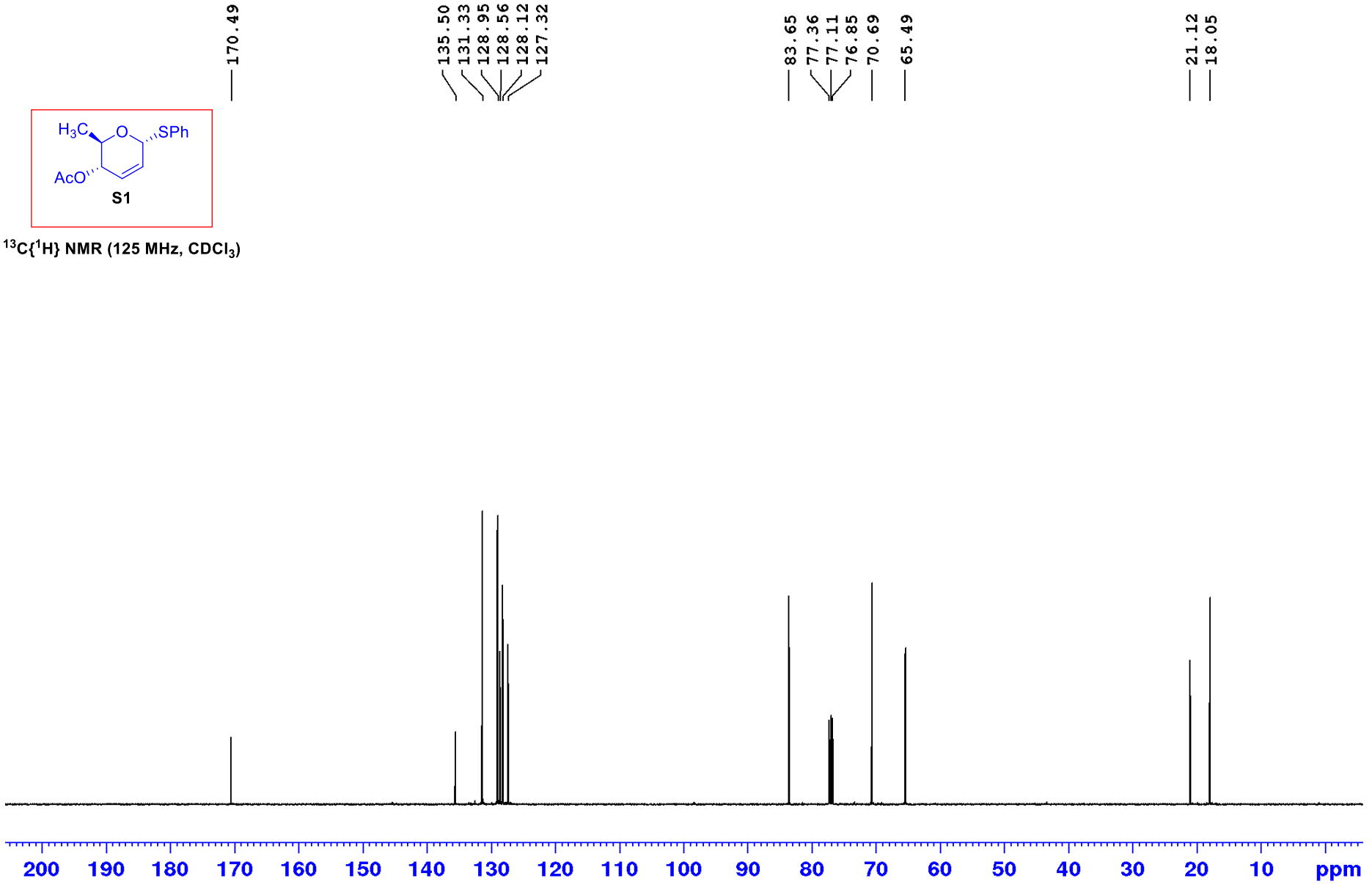


S1

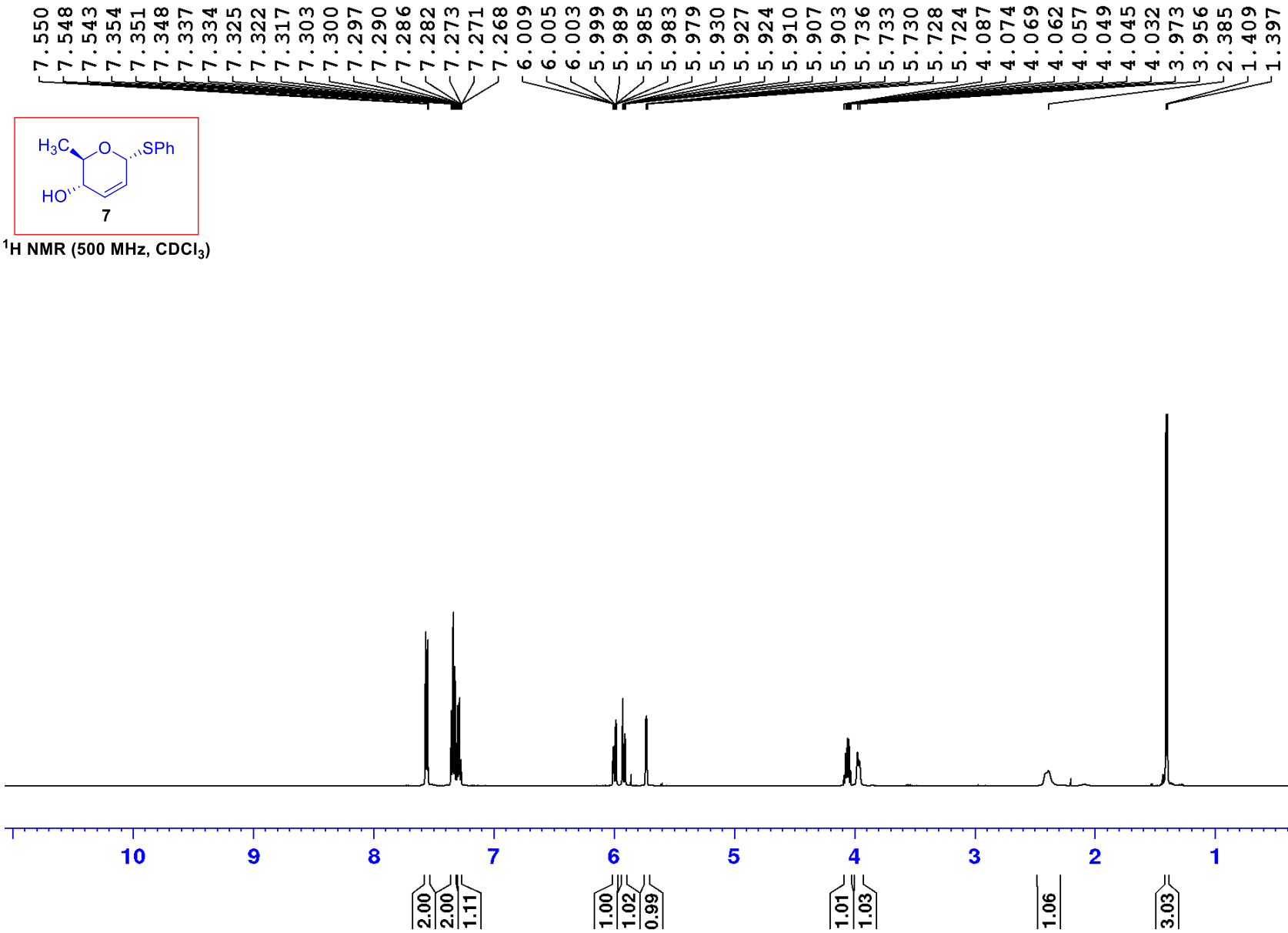
4.6 NMR Spectra

^{1}H NMR (500 MHz, $CDCl_3$)

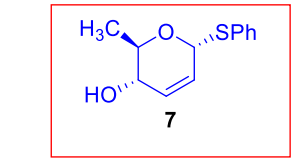




$^{13}C\{^{1}H\}$ NMR (125 MHz, $CDCl_3$)

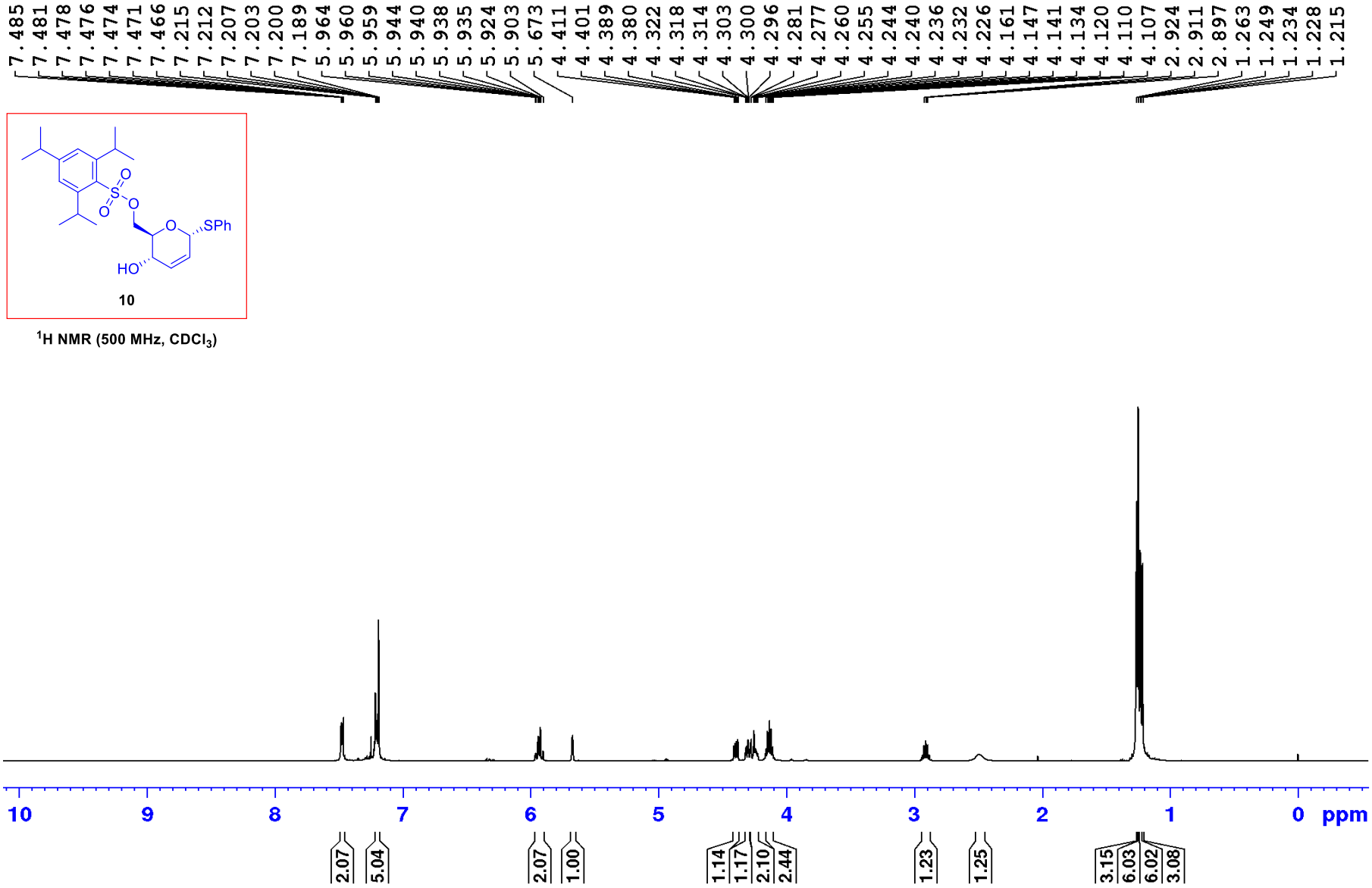


^{1}H NMR (500 MHz, $CDCl_3$)

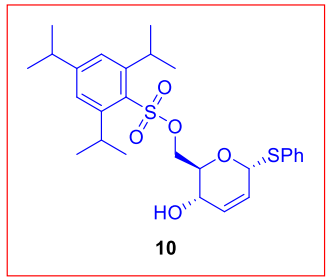


7

$^{13}C\{^{1}H\}$ NMR (125 MHz, $CDCl_3$)



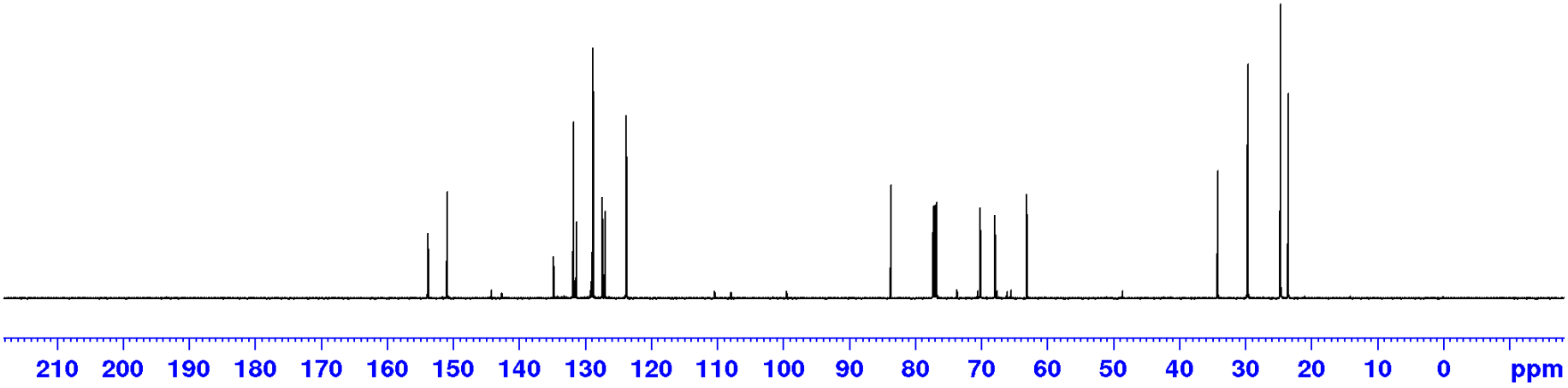
^{1}H NMR (500 MHz, $CDCl_3$)

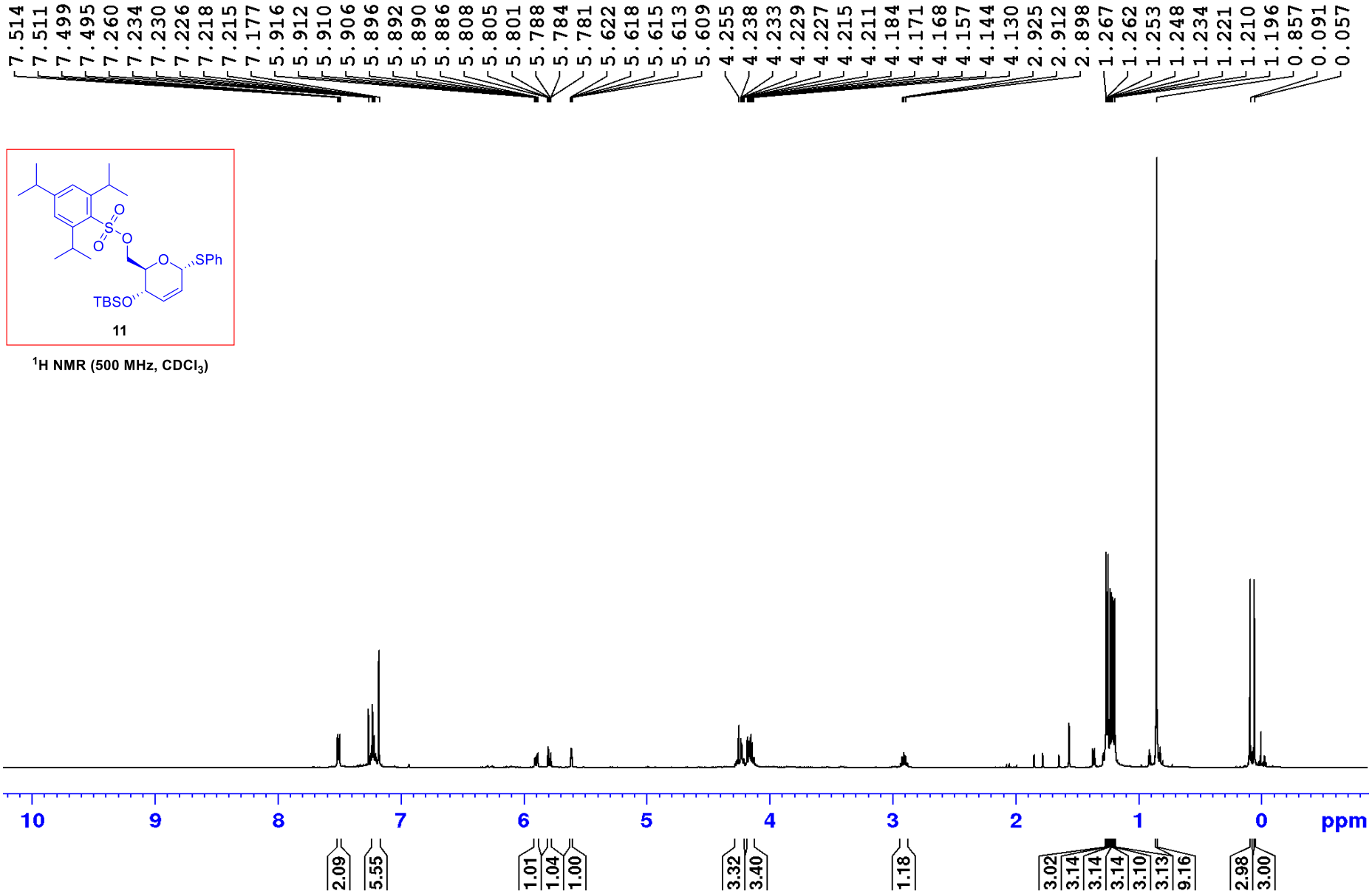


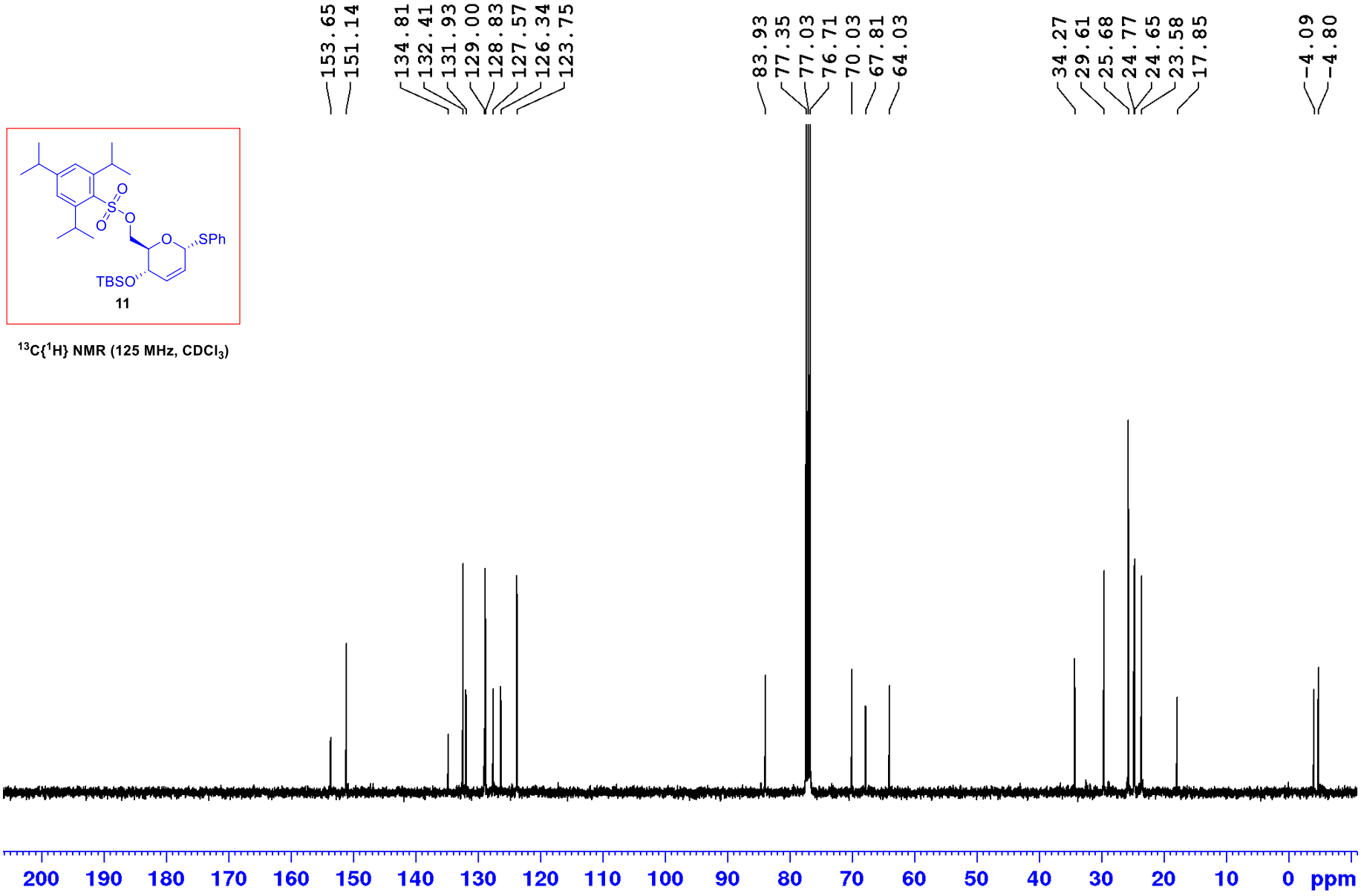
10

$^{13}C\{^{1}H\}$ NMR (125 MHz, $CDCl_3$)

153.82
150.93
134.79
131.77
131.31
128.97
128.77
127.37
126.97
123.77
83.67
77.25
77.00
76.75
70.16
67.91
63.07
34.19
29.62
24.64
24.63
23.47

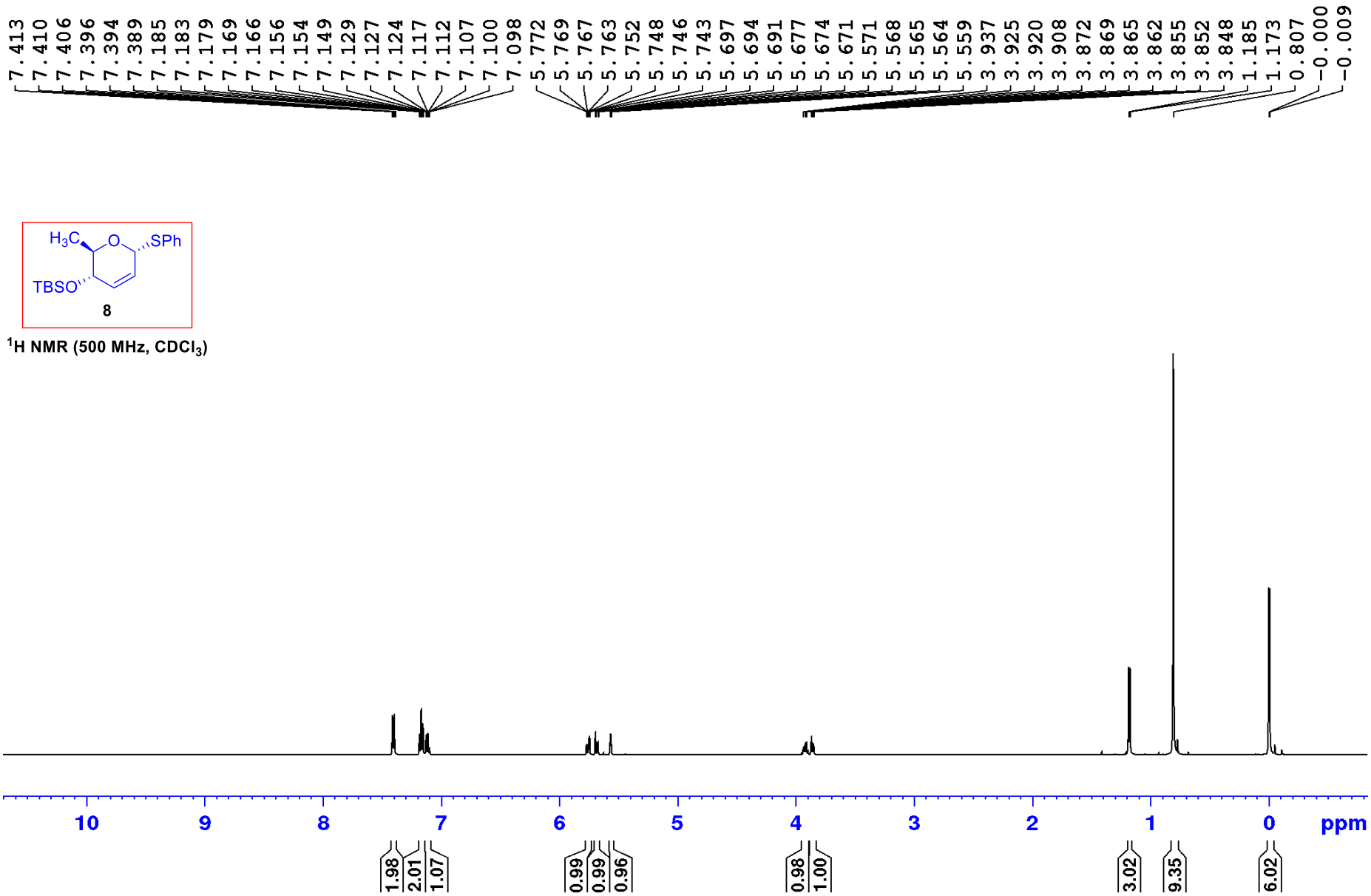



7.514
7.511
7.499
7.495
7.260
7.234
7.230
7.226
7.218
7.215
7.177
5.916
5.912
5.910
5.906
5.896
5.892
5.890
5.886
5.808
5.805
5.801
5.788
5.784
5.781
5.622
5.618
5.615
5.613
5.609
4.255
4.238
4.233
4.229
4.227
4.215
4.211
4.184
4.171
4.168
4.157
4.144
4.130
2.925
2.912
2.898
1.267
1.262
1.253
1.248
1.234
1.221
1.210
1.196
0.857
0.091
0.057
SPh
TBSO
11
1H NMR (500 MHz, CDCl3)
10
9
8
7
6
5
4
3
2
1
0
ppm
2.09
5.55
1.01
1.04
1.00
3.32
3.40
1.18
3.02
3.14
3.14
3.14
3.10
3.13
9.16
2.98
3.00

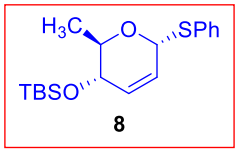


11

$^{13}C\{^{1}H\}$ NMR (125 MHz, $CDCl_3$)



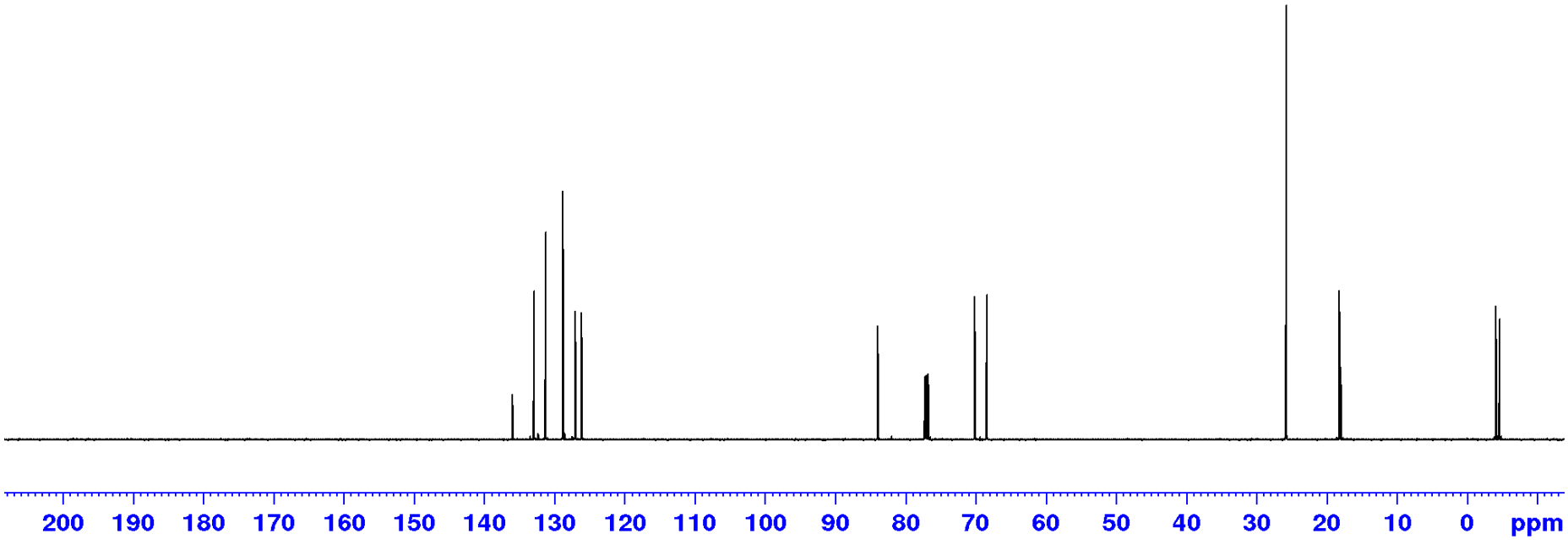
^{1}H NMR (500 MHz, $CDCl_3$)

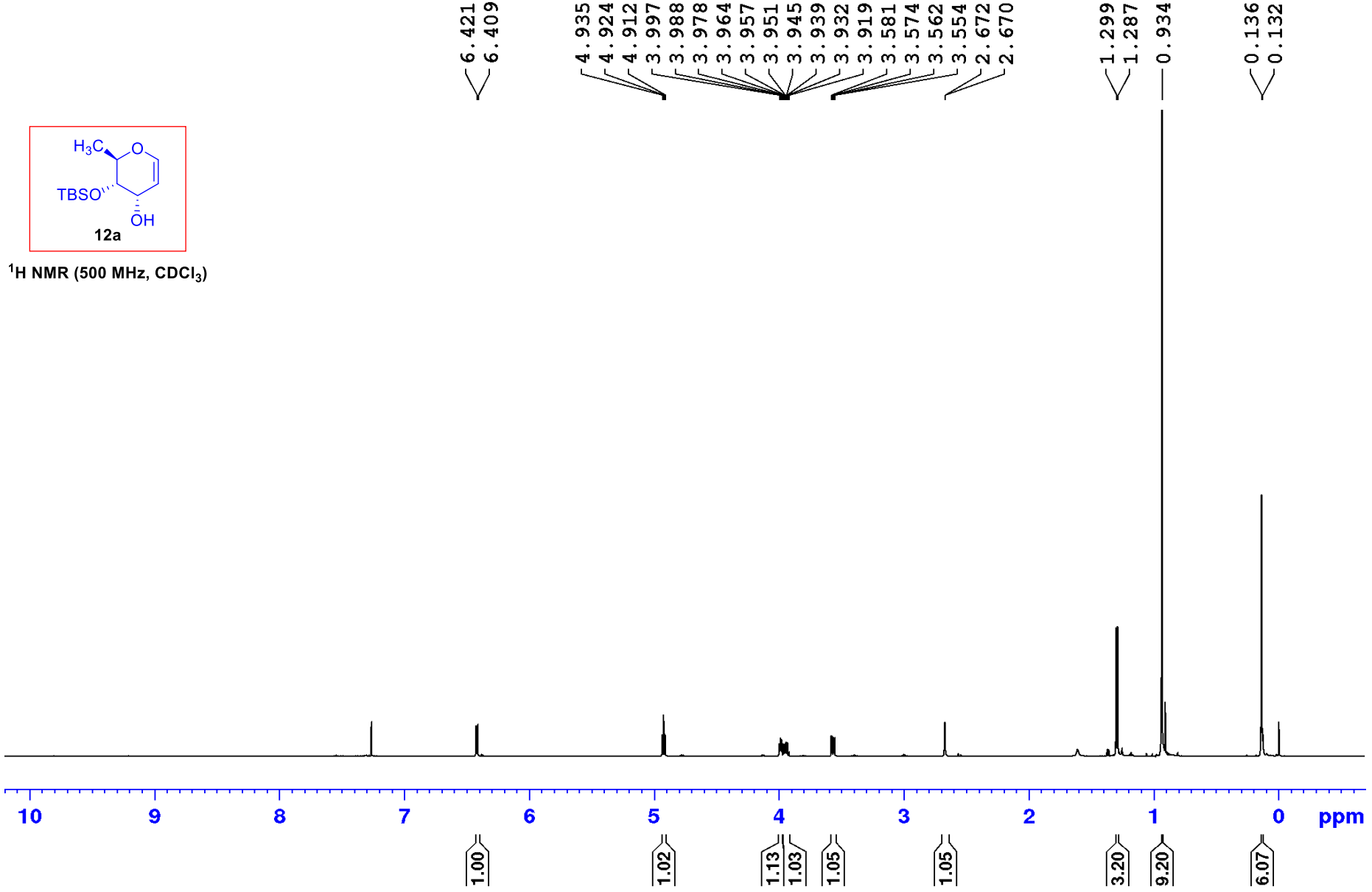


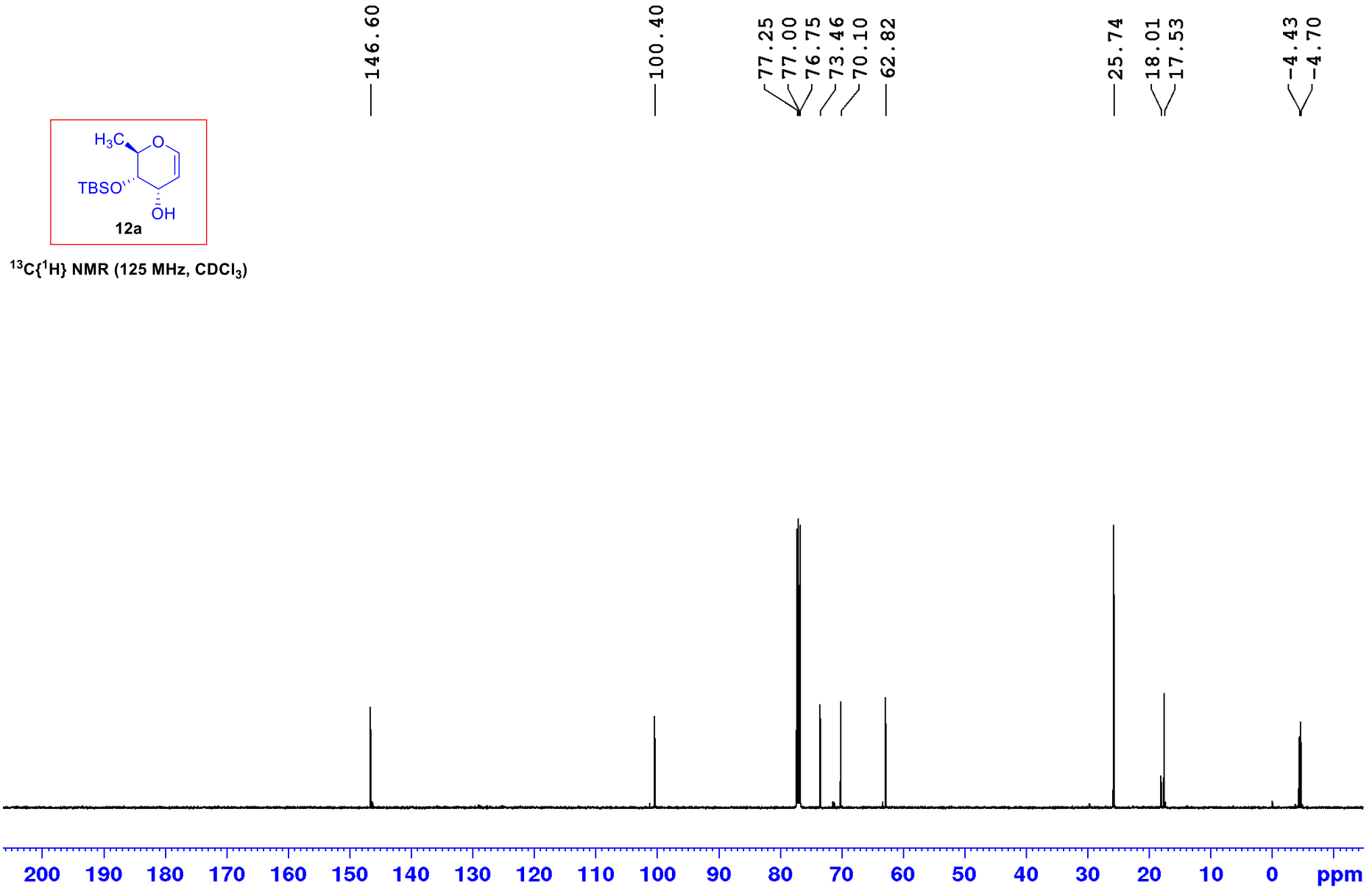
8

$^{13}C\{^{1}H\}$ NMR (125 MHz, $CDCl_3$)

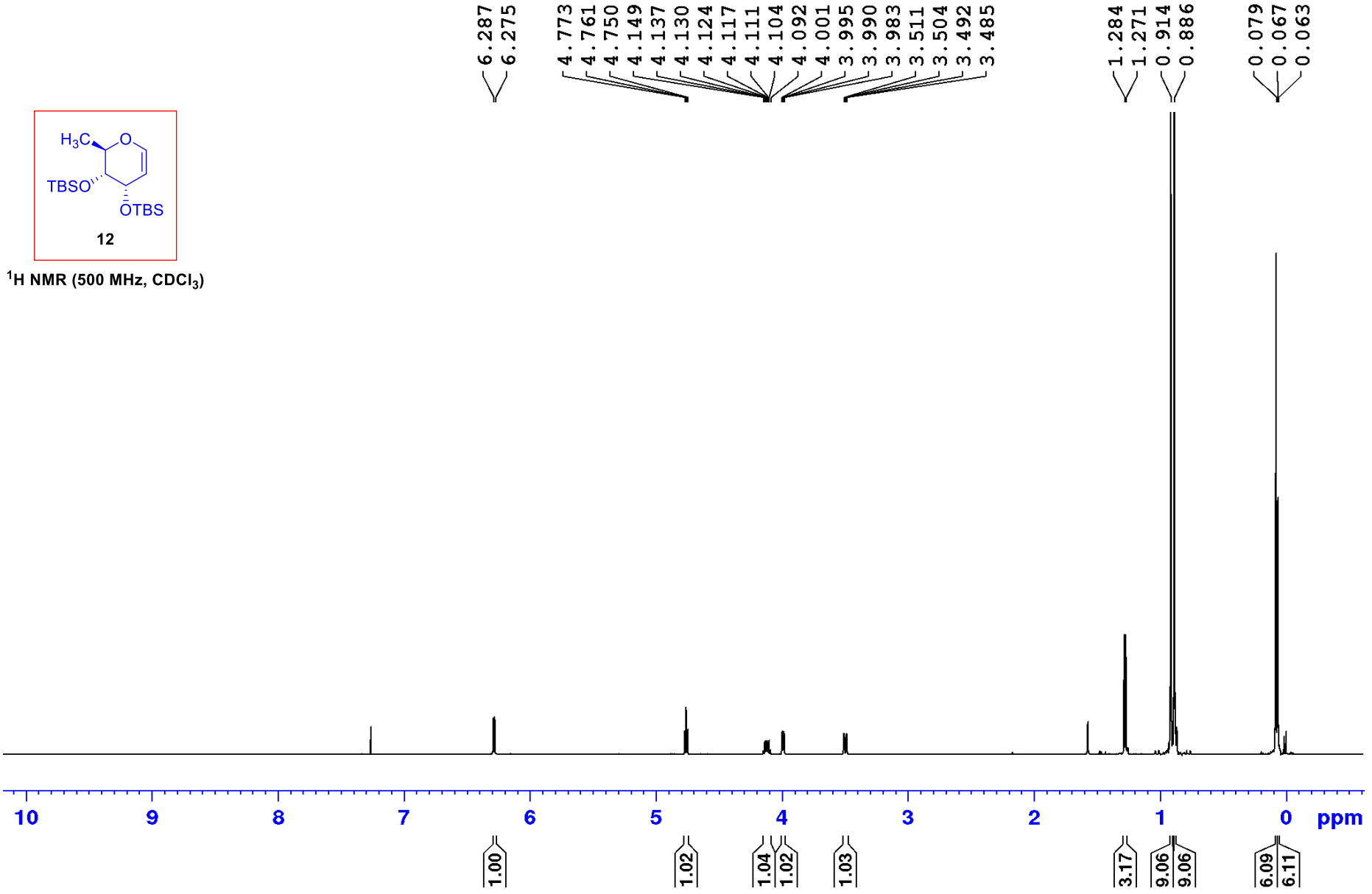
136.02
132.95
131.30
128.80
127.04
126.14
83.95
77.25
77.00
76.75
70.15
68.44
25.76
18.18
17.98
-4.11
-4.60



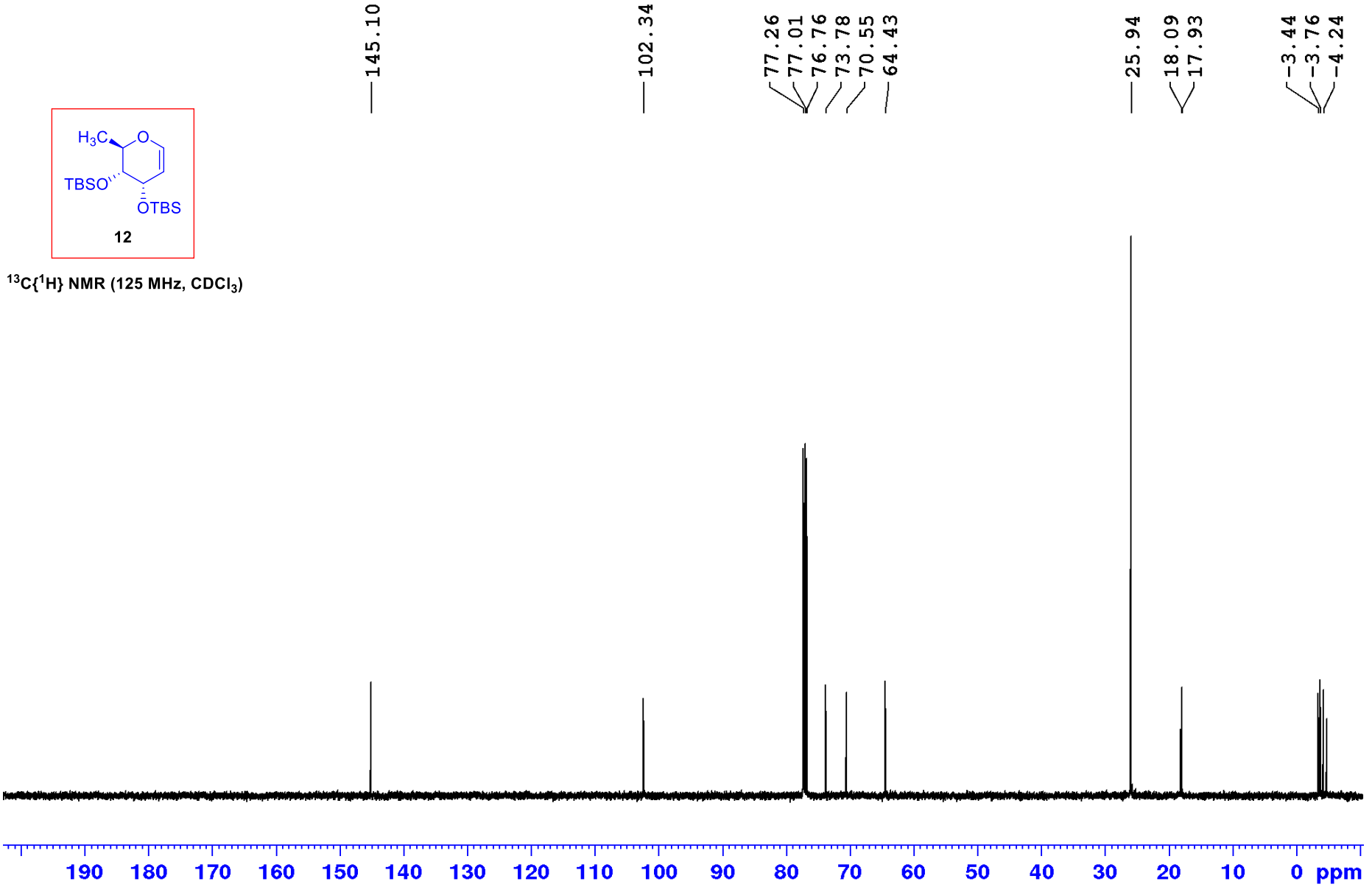

6.421
6.409
4.935
4.924
4.912
3.997
3.988
3.978
3.964
3.957
3.951
3.945
3.939
3.932
3.919
3.581
3.574
3.562
3.554
2.672
2.670
1.299
1.287
0.934
0.136
0.132
H3C
O
TBSO
OH
12a
1H NMR (500 MHz, CDCl3)
10
9
8
7
6
5
4
3
2
1
0
ppm
1.00
1.02
1.13
1.03
1.05
1.05
3.20
9.20
6.07



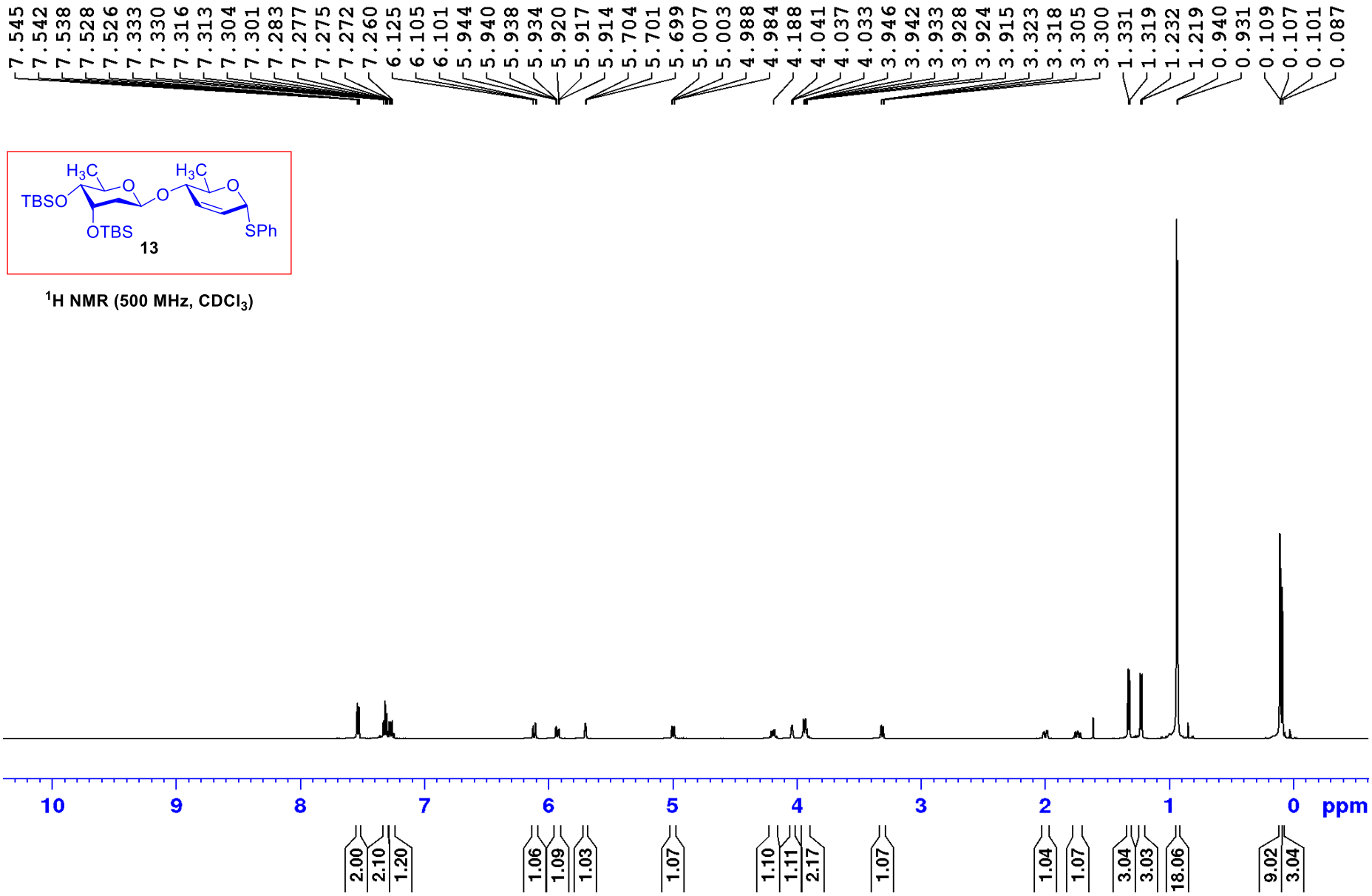
$^{13}C\{^{1}H\}$ NMR (125 MHz, $CDCl_3$)

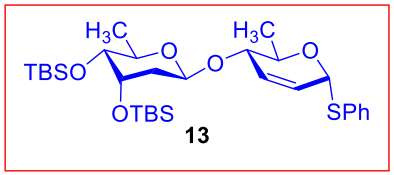


^{1}H NMR (500 MHz, $CDCl_3$)



$^{13}C\{^{1}H\}$ NMR (125 MHz, $CDCl_3$)

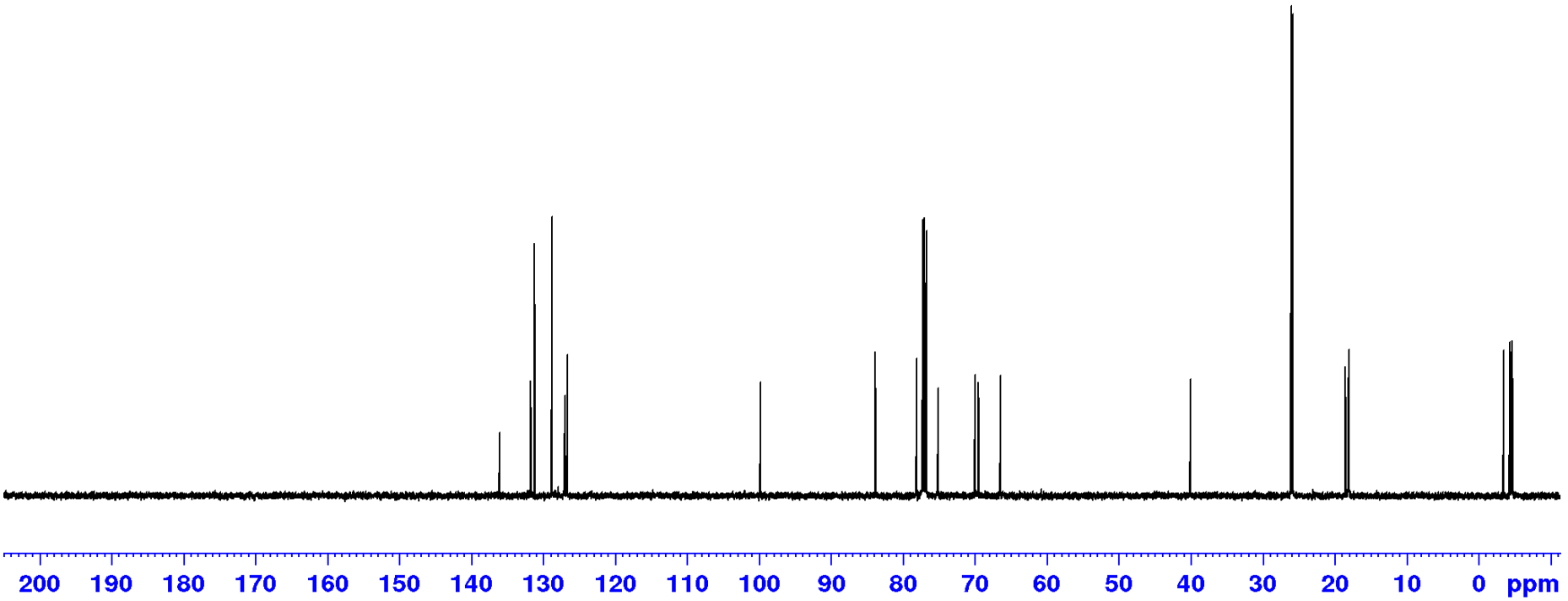

7.545
7.542
7.538
7.528
7.526
7.333
7.330
7.316
7.313
7.304
7.301
7.283
7.277
7.275
7.272
7.260
6.125
6.105
6.101
5.944
5.940
5.938
5.934
5.920
5.917
5.914
5.704
5.701
5.699
5.007
5.003
4.988
4.984
4.188
4.041
4.037
4.033
3.946
3.942
3.933
3.928
3.924
3.915
3.323
3.318
3.305
3.300
1.331
1.319
1.232
1.219
0.940
0.931
0.109
0.107
0.101
0.087
H3C
H3C
TBSO
OTBS
SPh
13
1H NMR (500 MHz, CDCl3)
10
9
8
7
6
5
4
3
2
1
0
ppm
2.00
2.10
1.20
1.06
1.09
1.03
1.07
1.10
1.11
2.17
1.07
1.04
1.07
3.04
3.03
18.06
9.02
3.04

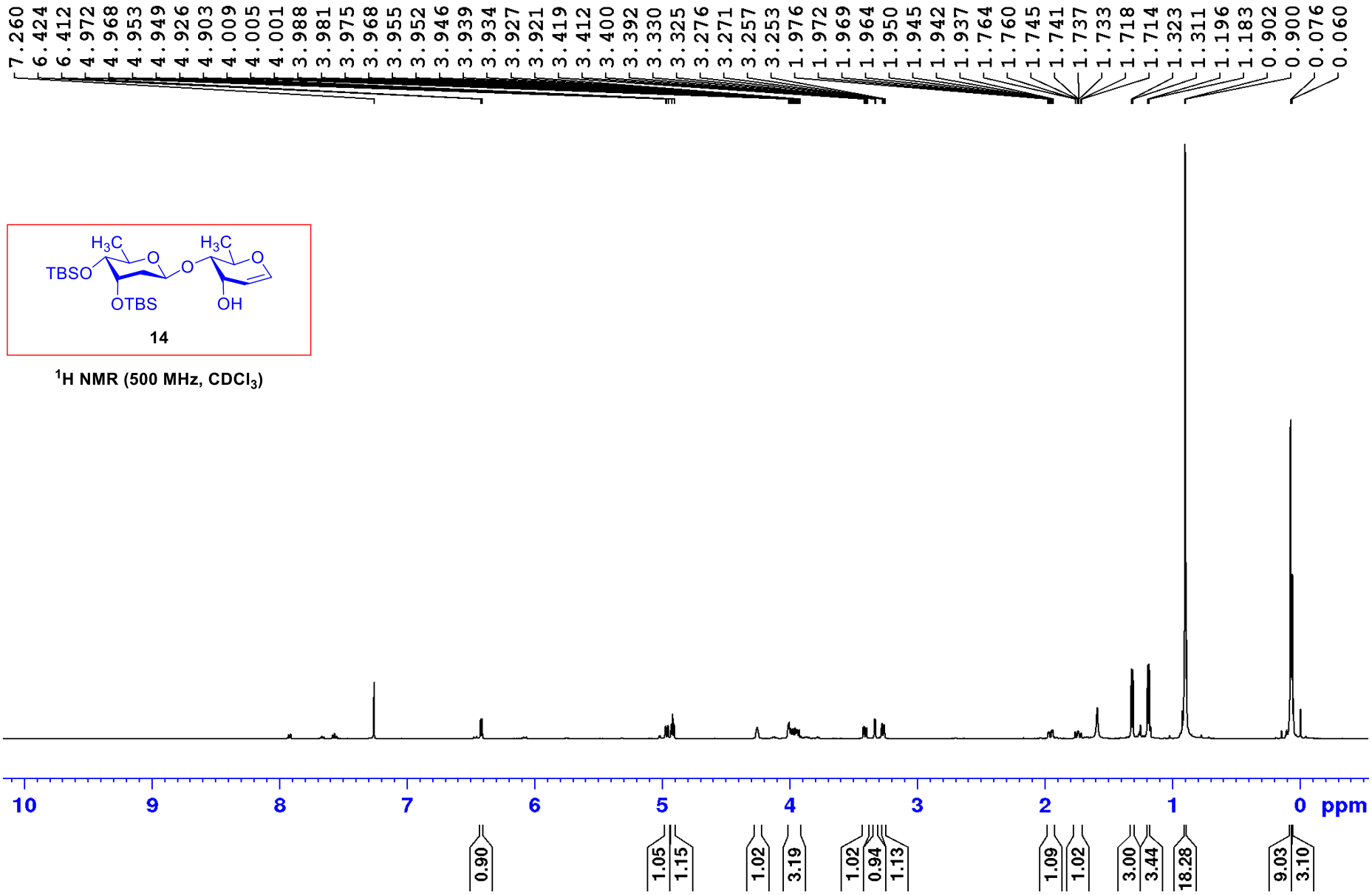


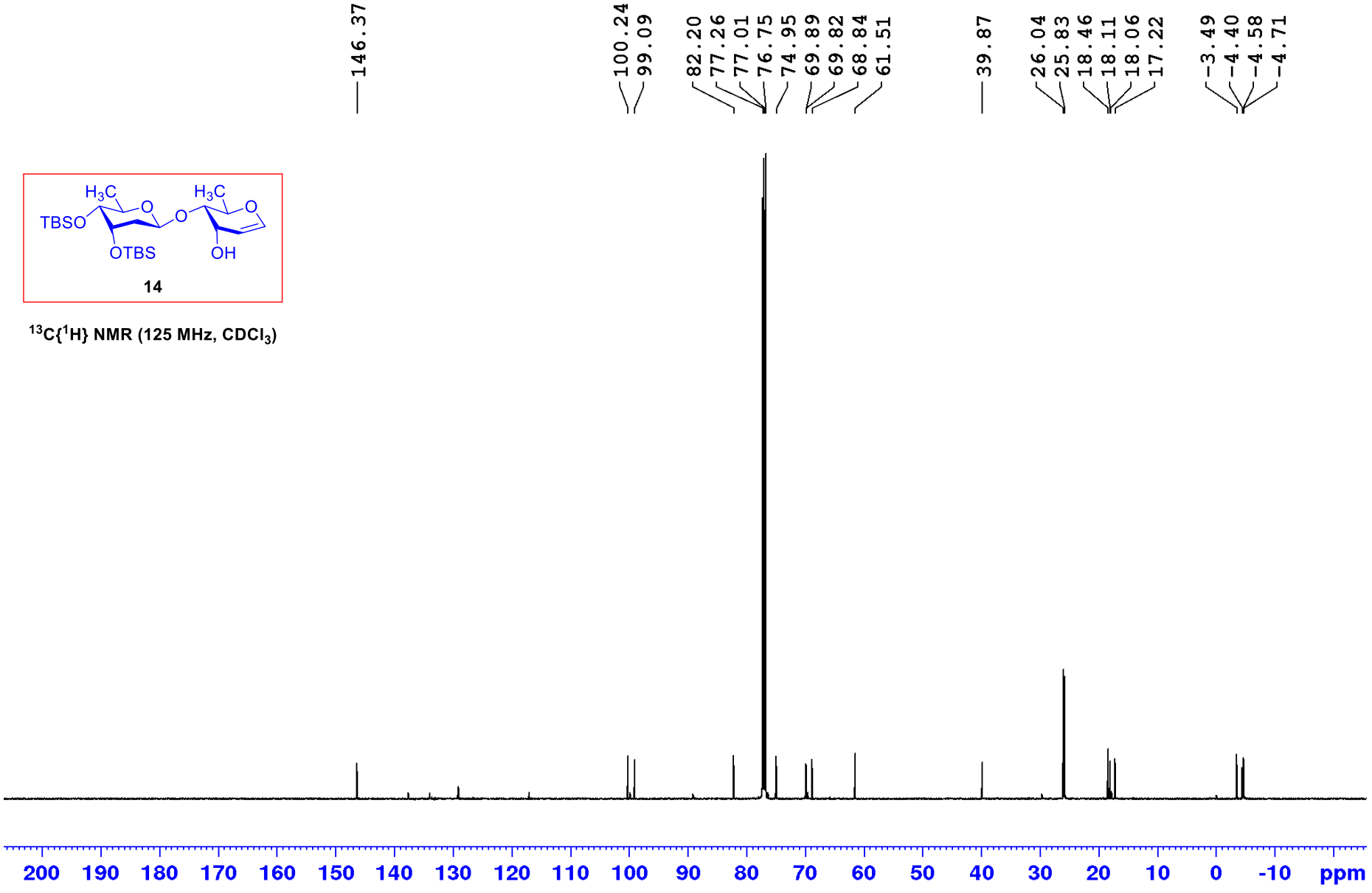
13

$^{13}C\{^{1}H\}$ NMR (125 MHz, $CDCl_3$)

136.10
131.74
131.21
128.81
127.01
126.66
99.80
83.83
78.10
77.25
77.00
76.75
75.13
70.00
69.49
66.42
40.02
26.05
25.82
18.49
18.11
18.06
17.99
-3.50
-4.37
-4.58

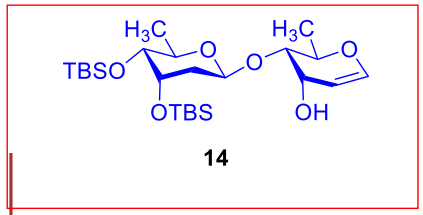



7.260
6.424
6.412
4.972
4.968
4.953
4.949
4.926
4.903
4.009
4.005
4.001
3.988
3.981
3.975
3.968
3.955
3.952
3.946
3.939
3.934
3.927
3.921
3.419
3.412
3.400
3.392
3.330
3.325
3.276
3.271
3.257
3.253
1.976
1.972
1.969
1.964
1.950
1.945
1.942
1.937
1.764
1.760
1.745
1.741
1.737
1.733
1.718
1.714
1.323
1.311
1.196
1.183
0.902
0.900
0.076
0.060
H3C
O
TBSO
O
H3C
O
OTBS
OH
14
1H NMR (500 MHz, CDCl3)
10
9
8
7
6
5
4
3
2
1
0
ppm
0.90
1.05
1.15
1.02
3.19
1.02
0.94
1.13
1.09
1.02
3.00
3.44
18.28
9.03
3.10

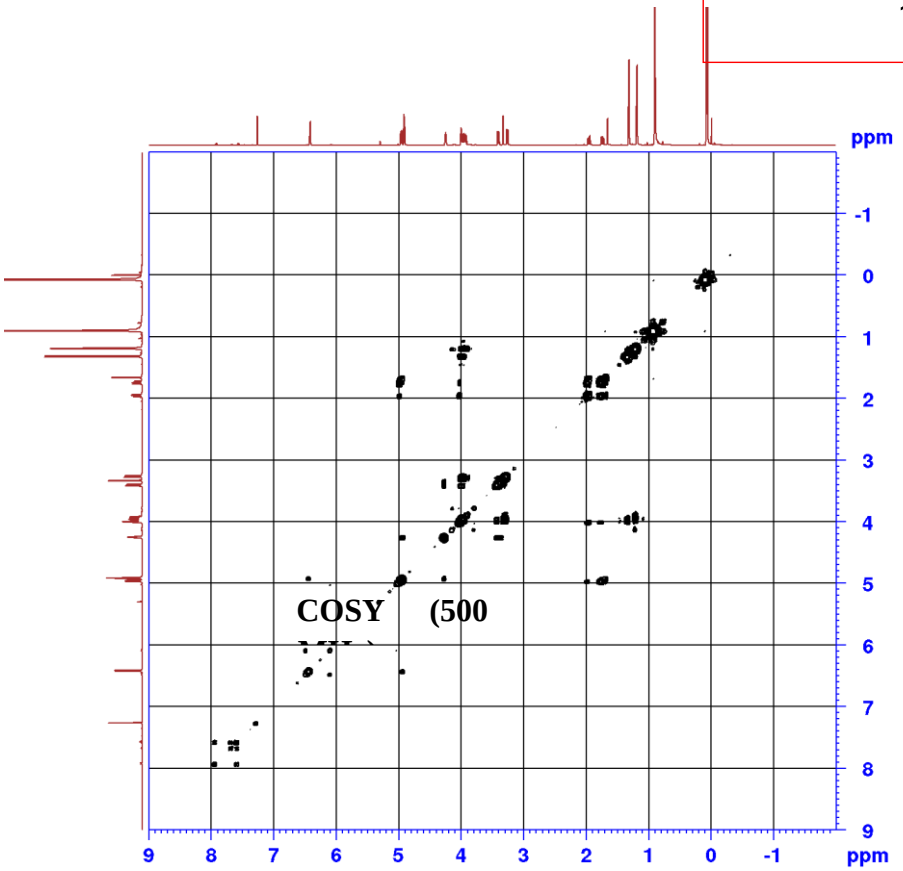


14

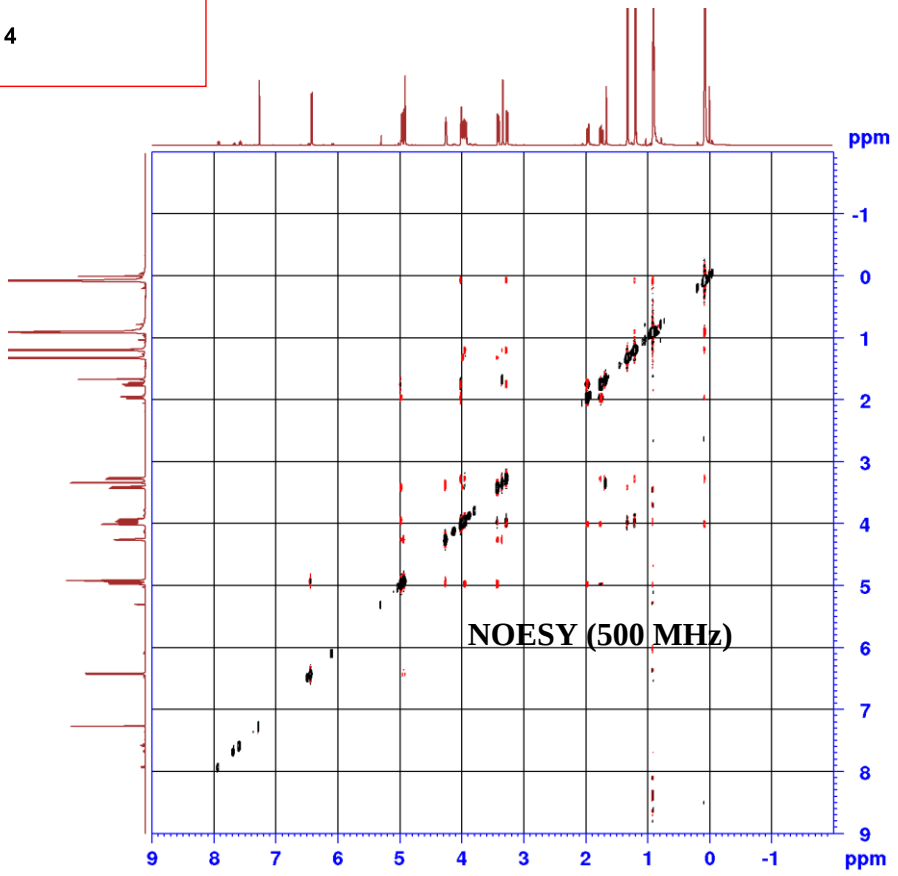
$^{13}C\{^{1}H\}$ NMR (125 MHz, $CDCl_3$)



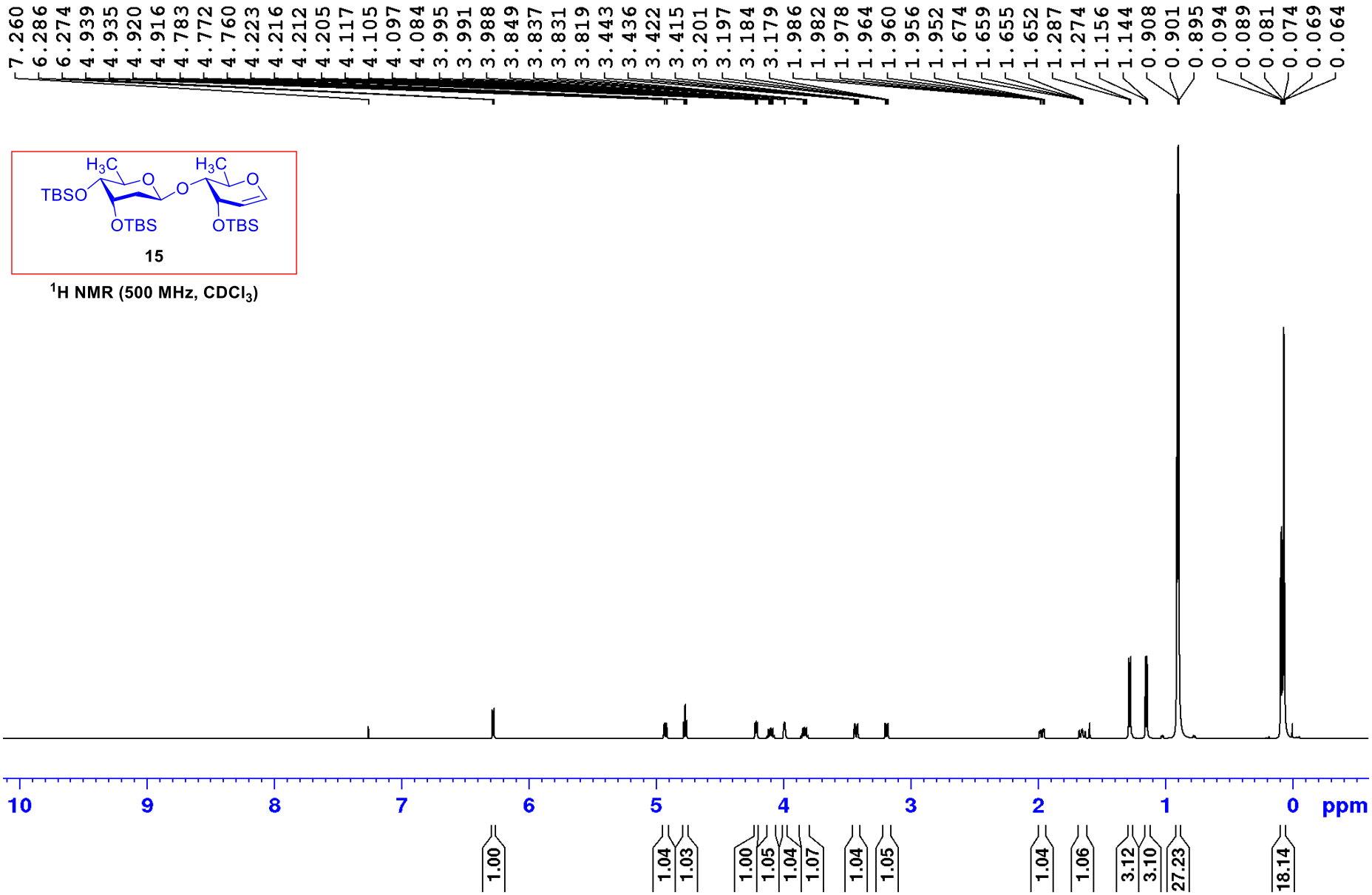
14

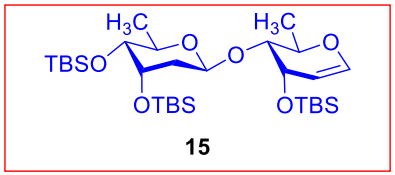


COSY (500



NOESY (500 MHz)


7.260
6.286
6.274
4.939
4.935
4.920
4.916
4.783
4.772
4.760
4.223
4.216
4.212
4.205
4.117
4.105
4.097
4.084
3.995
3.991
3.988
3.849
3.837
3.831
3.819
3.443
3.436
3.422
3.415
3.201
3.197
3.184
3.179
1.986
1.982
1.978
1.964
1.960
1.956
1.952
1.674
1.659
1.655
1.652
1.287
1.274
1.156
1.144
0.908
0.901
0.895
0.094
0.089
0.081
0.074
0.069
0.064
H3C
TBSO
O
O
H3C
O
OTBS
OTBS
15
1H NMR (500 MHz, CDCl3)
10
9
8
7
6
5
4
3
2
1
0
ppm
1.00
1.04
1.03
1.00
1.05
1.04
1.07
1.04
1.05
1.04
1.06
3.12
3.10
27.23
18.14

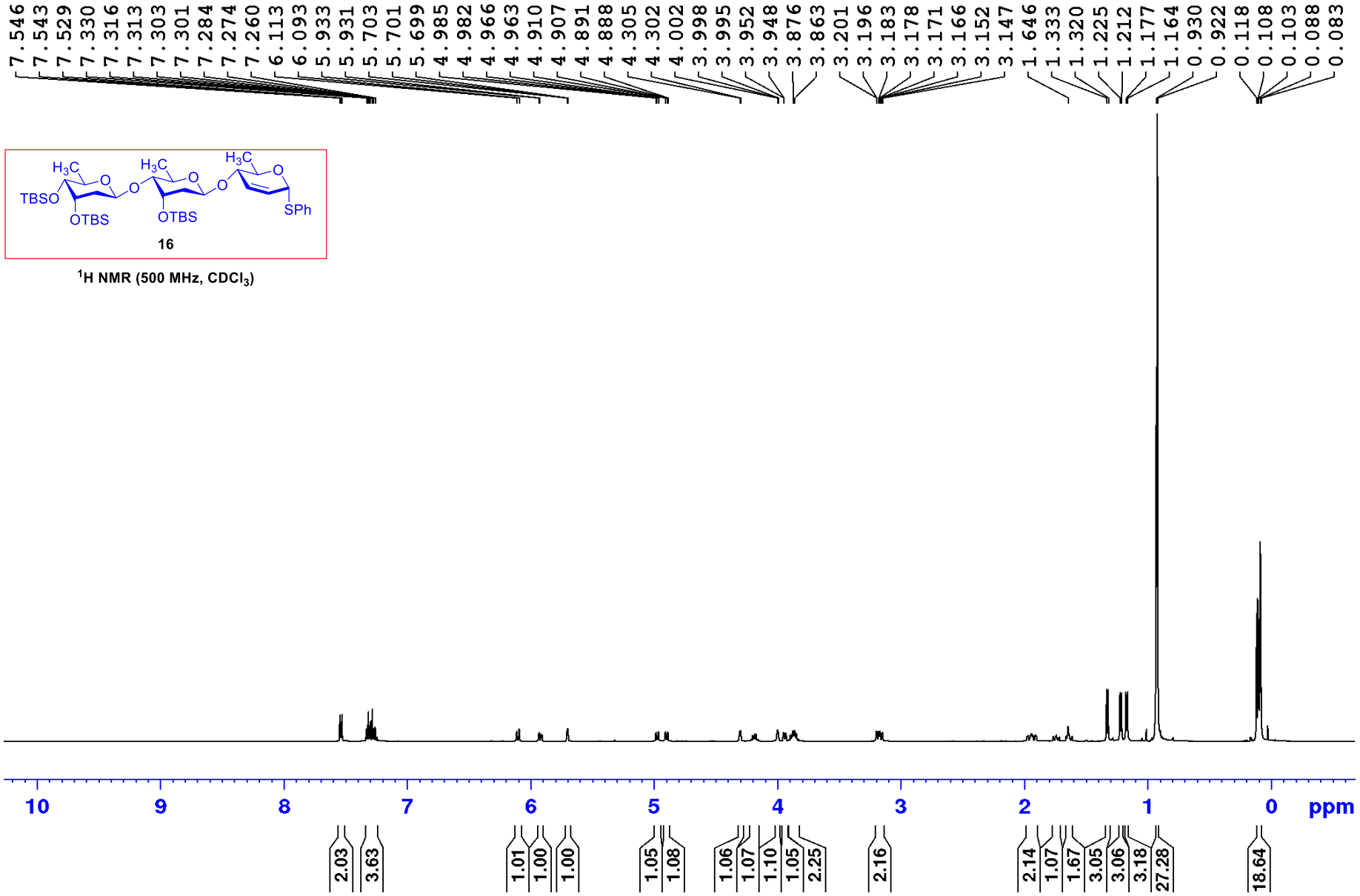


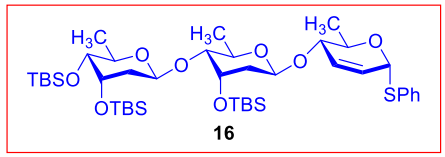
15

$^{13}C\{^{1}H\}$ NMR (125 MHz, $CDCl_3$)

144.76
102.96
99.59
80.57
77.25
77.00
76.75
75.49
70.02
69.26
69.20
64.21
39.61
26.05
26.00
25.82
18.61
18.35
18.11
18.07
17.32
-3.50
-4.20
-4.34
-4.61

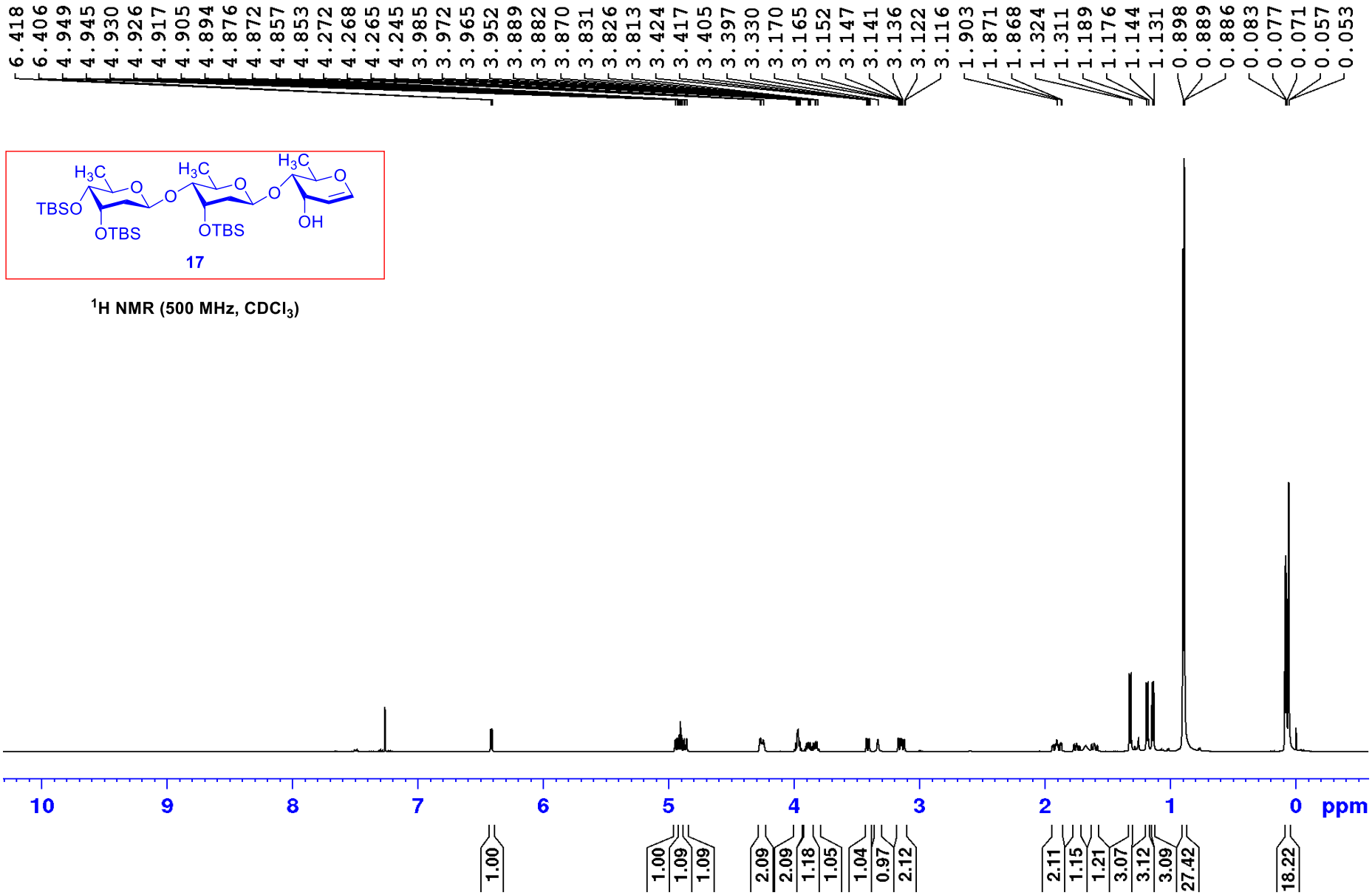
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm


7.546
7.543
7.529
7.330
7.316
7.313
7.303
7.301
7.284
7.274
7.260
6.113
6.093
5.933
5.931
5.703
5.701
5.699
4.985
4.982
4.966
4.963
4.910
4.907
4.891
4.888
4.305
4.302
4.002
3.998
3.995
3.952
3.948
3.876
3.863
3.201
3.196
3.183
3.178
3.171
3.166
3.152
3.147
1.646
1.333
1.320
1.225
1.212
1.177
1.164
0.930
0.922
0.118
0.108
0.103
0.088
0.083
H3C
TBSO
OTBS
OTBS
SPh
16
1H NMR (500 MHz, CDCl3)
10
9
8
7
6
5
4
3
2
1
0
ppm
2.03
3.63
1.01
1.00
1.00
1.05
1.08
1.06
1.07
1.10
1.05
2.25
2.16
2.14
1.07
1.67
3.05
3.06
3.18
27.28
18.64

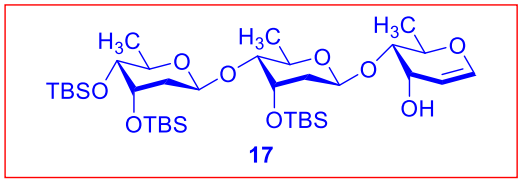


16

$^{13}C\{^{1}H\}$ NMR (125 MHz, $CDCl_3$)

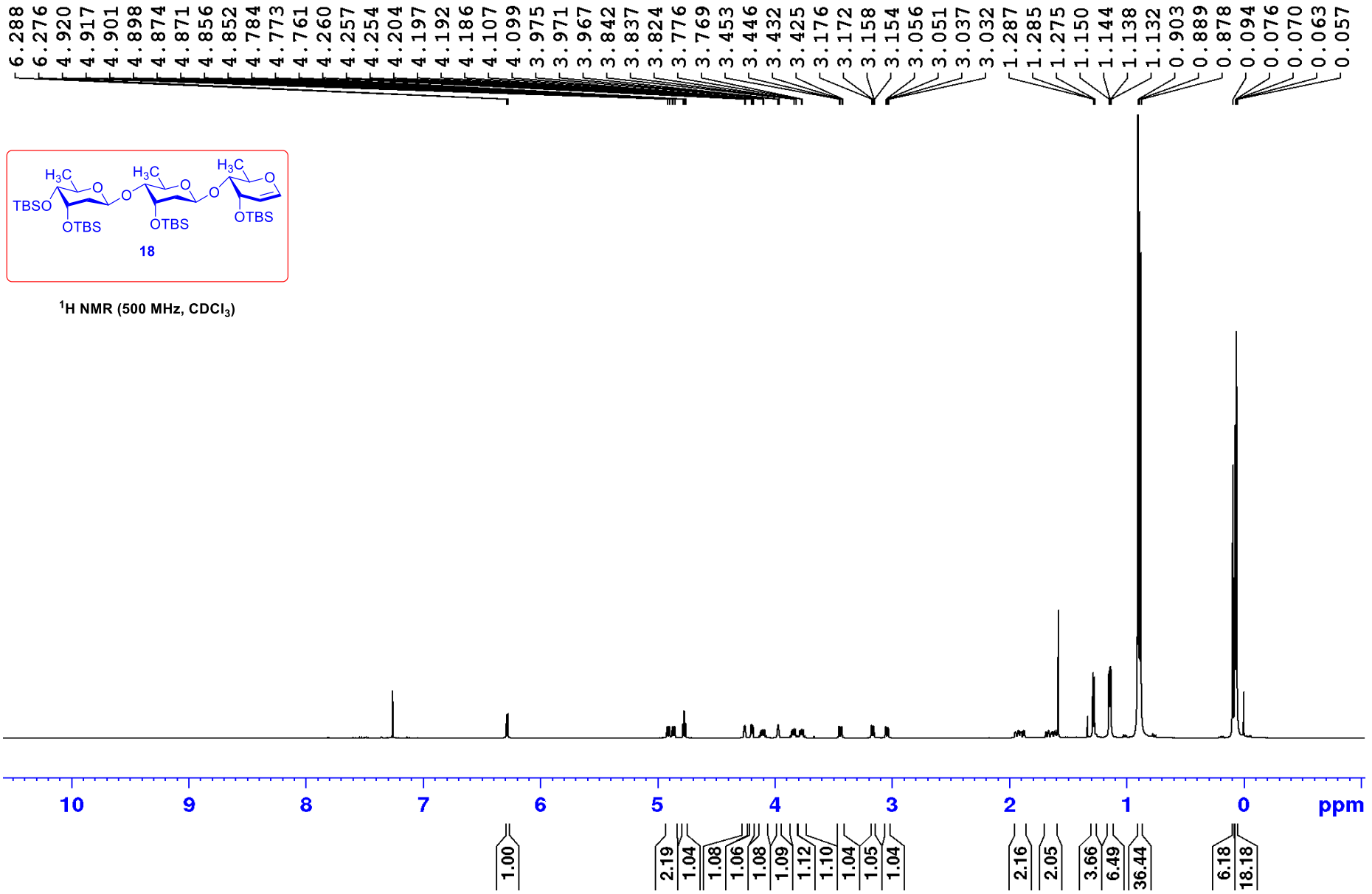


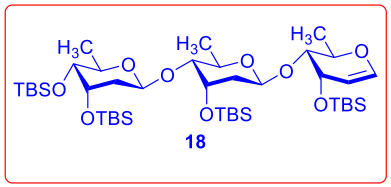
^{1}H NMR (500 MHz, $CDCl_3$)



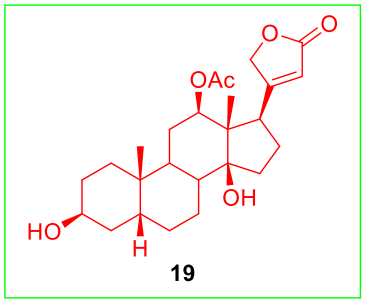
17

$^{13}C\{^{1}H\}$ NMR (125 MHz, $CDCl_3$)


6.288
6.276
4.920
4.917
4.901
4.898
4.874
4.871
4.856
4.852
4.784
4.773
4.761
4.260
4.257
4.254
4.204
4.197
4.192
4.186
4.107
4.099
3.975
3.971
3.967
3.842
3.837
3.824
3.776
3.769
3.453
3.446
3.432
3.425
3.176
3.172
3.158
3.154
3.056
3.051
3.037
3.032
1.287
1.285
1.275
1.150
1.144
1.138
1.132
0.903
0.889
0.878
0.094
0.076
0.070
0.063
0.057
H3C
TBSO
OTBS
OTBS
OTBS
18
1H NMR (500 MHz, CDCl3)
10
9
8
7
6
5
4
3
2
1
0
ppm
1.00
2.19
1.04
1.08
1.06
1.08
1.09
1.12
1.10
1.04
1.05
1.04
2.16
2.05
3.66
6.49
36.44
6.18
18.18

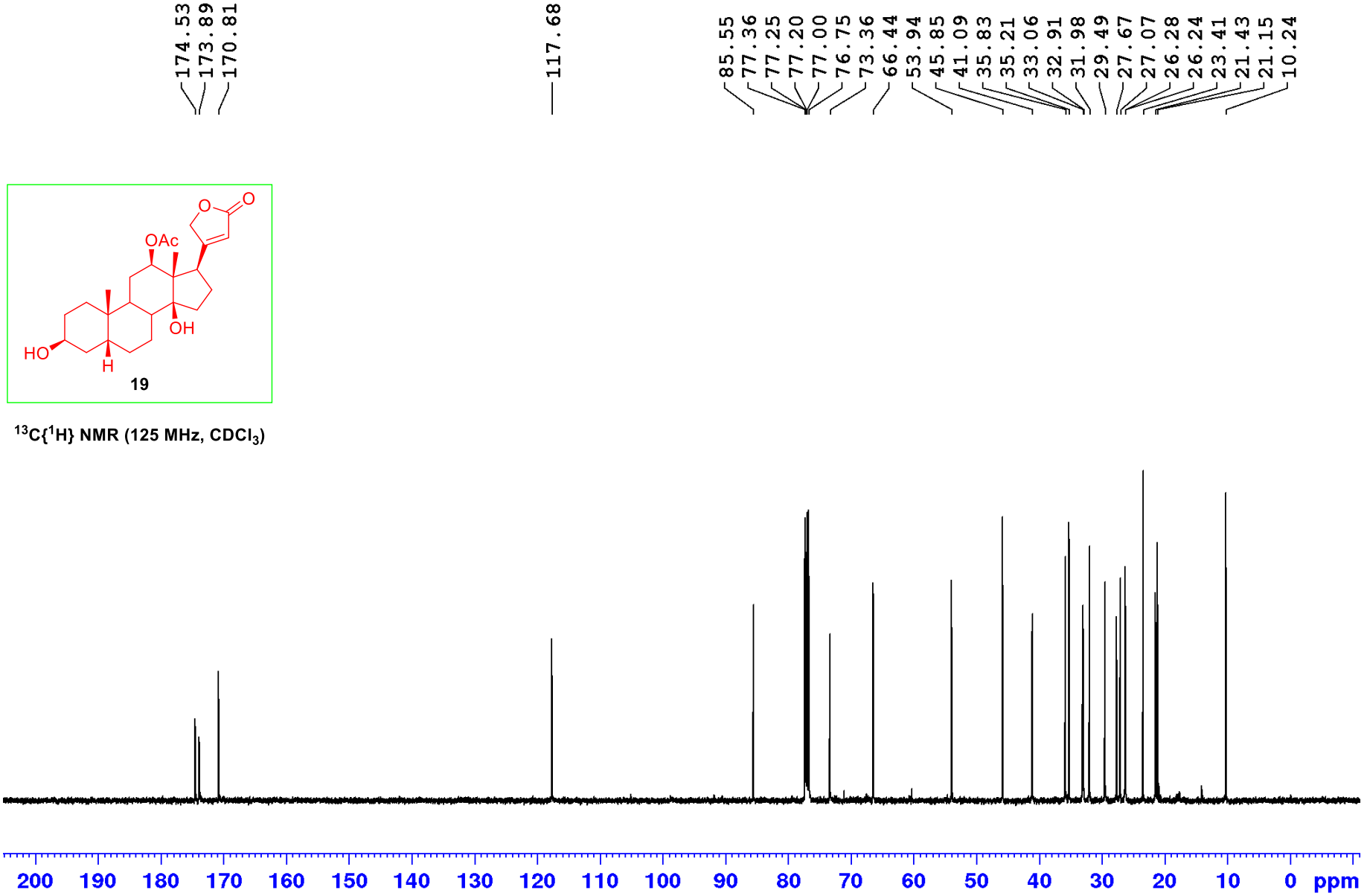


$^{13}C\{^{1}H\}$ NMR (125 MHz, $CDCl_3$)

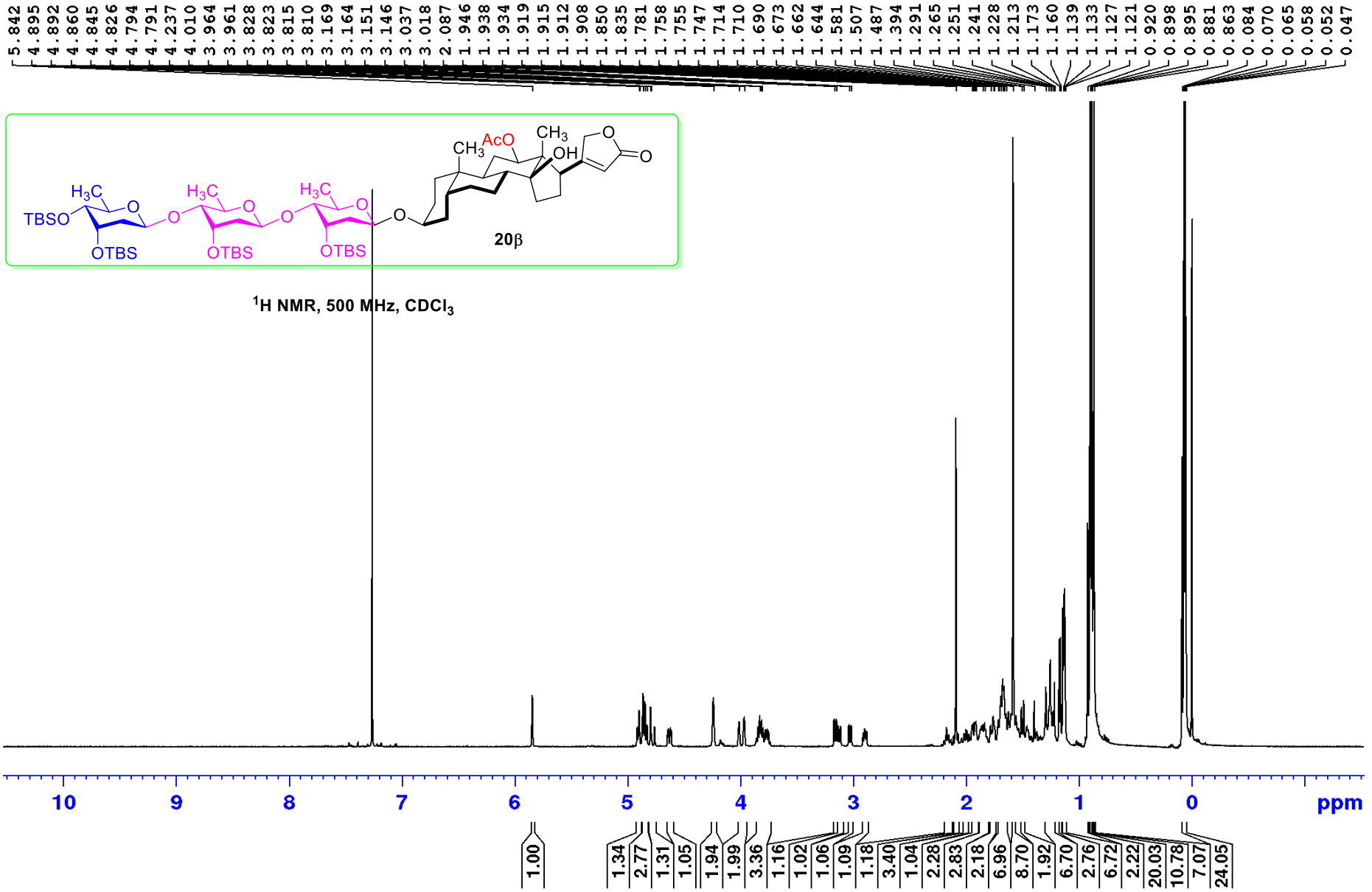


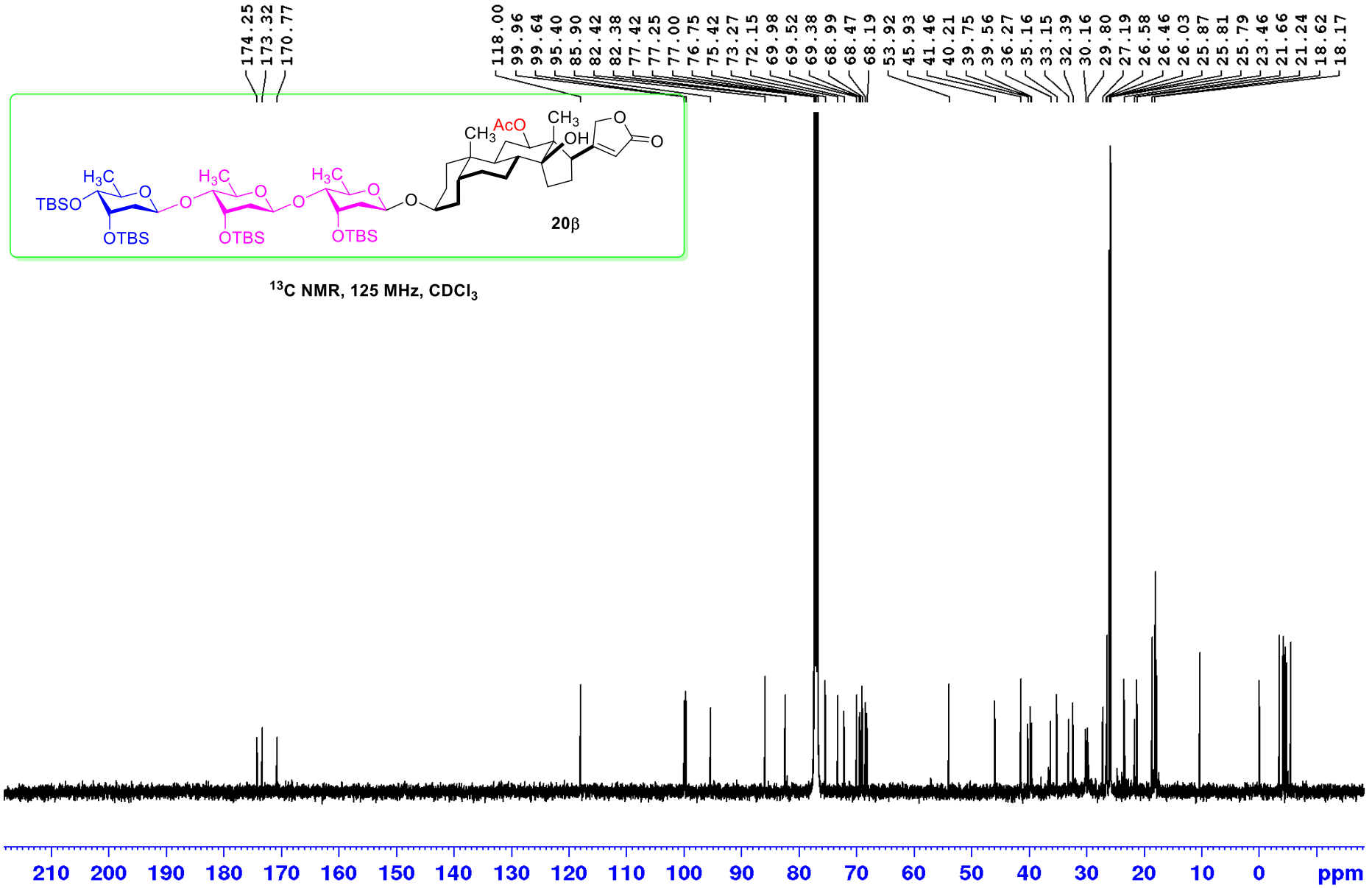
19

^{1}H NMR (500 MHz, $CDCl_3$)



$^{13}C\{^{1}H\}$ NMR (125 MHz, $CDCl_3$)


5.842
4.895
4.892
4.860
4.845
4.826
4.794
4.791
4.237
4.010
3.964
3.961
3.828
3.823
3.815
3.810
3.169
3.164
3.151
3.146
3.037
3.018
2.087
1.946
1.938
1.934
1.919
1.915
1.912
1.908
1.850
1.835
1.781
1.758
1.755
1.747
1.714
1.710
1.690
1.673
1.662
1.644
1.581
1.507
1.487
1.394
1.291
1.265
1.251
1.241
1.228
1.213
1.173
1.160
1.139
1.133
1.127
1.121
0.920
0.898
0.895
0.881
0.863
0.084
0.070
0.065
0.058
0.052
0.047
TBSO
OTBS
OTBS
OTBS
AcO
OH
20β
1H NMR, 500 MHz, CDCl3
10
9
8
7
6
5
4
3
2
1
0
ppm
1.00
1.34
2.77
1.31
1.05
1.94
1.99
3.36
1.16
1.02
1.06
1.09
1.18
3.40
1.04
2.28
2.83
2.18
6.96
8.70
1.92
6.70
2.76
6.72
2.22
20.03
10.78
7.07
24.05



^{13}C NMR, 125 MHz, $CDCl_3$

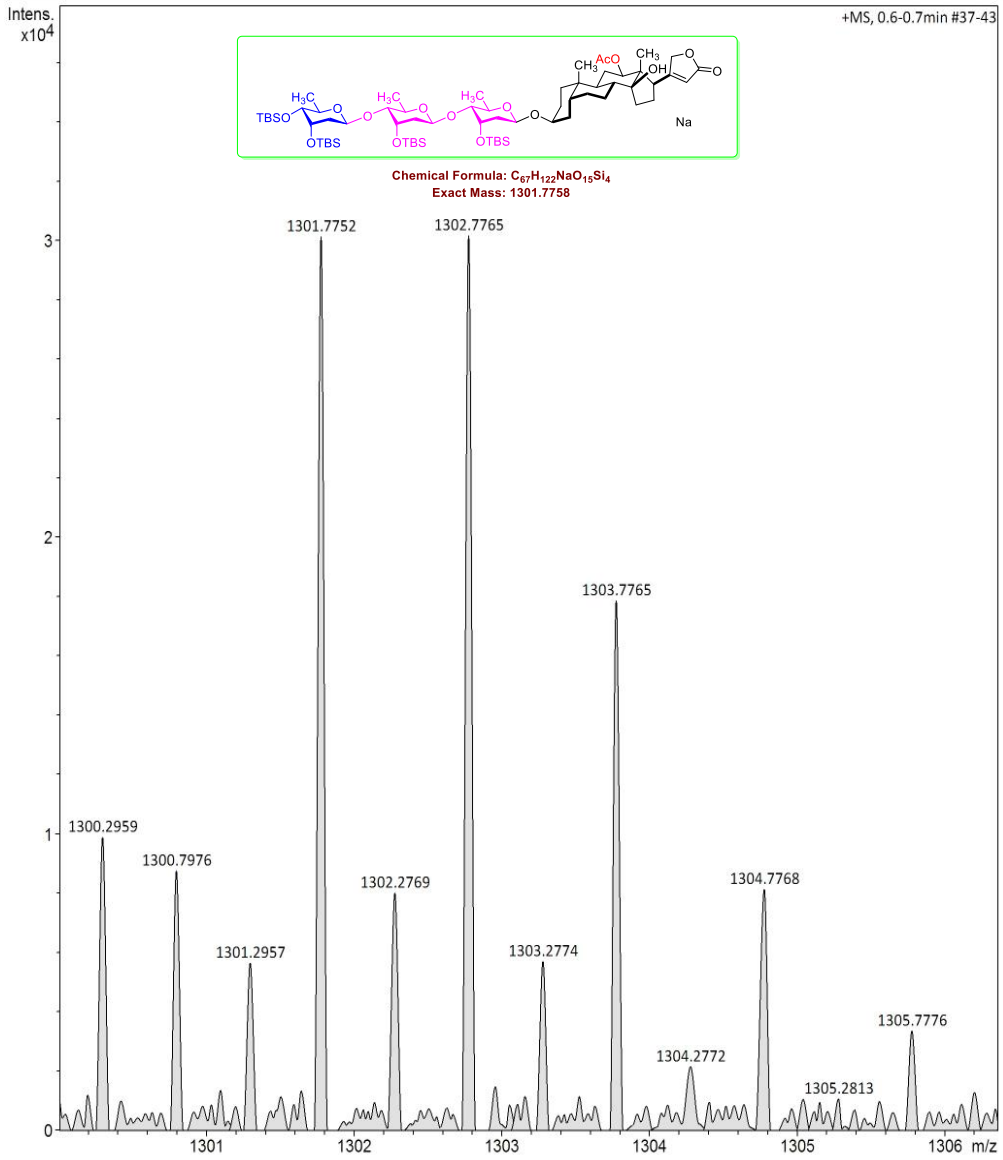
Display Report

Analysis Info

Analysis Name	E:\2022-Data\PROF .PRS\SEPT\ALI-PRS-03-57-1.d	Acquisition Date	29-09-2022 12:57:23
Method	tune_low.m	Operator	UOH
Sample Name	ALI-PRS-03-57-1	Instrument	maXis 255552.10138
Comment			

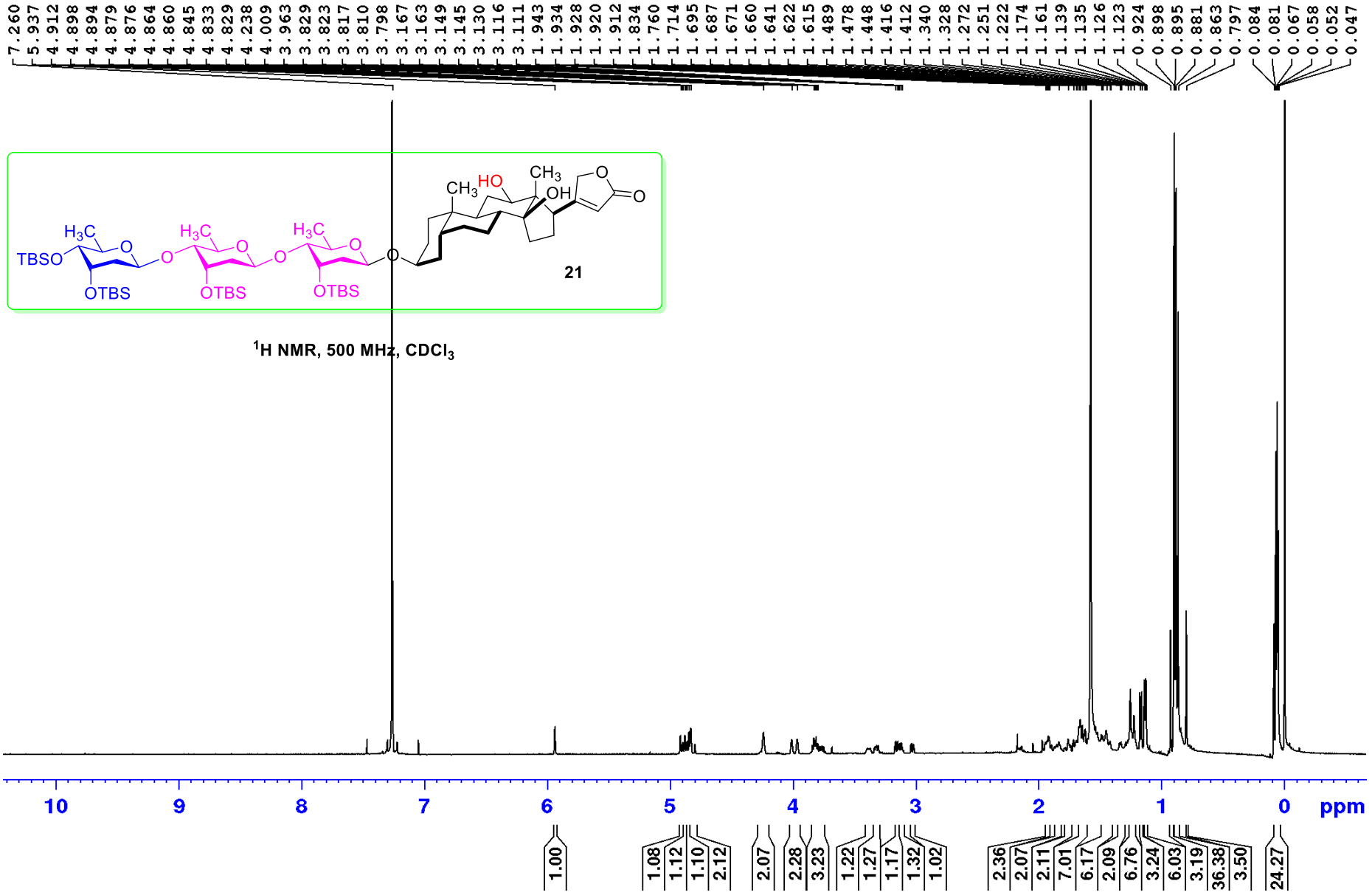
Acquisition Parameter

Source Type	ESI	Ion Polarity	Positive	Set Nebulizer	0.3 Bar
Focus	Not active	Set Capillary	3000 V	Set Dry Heater	180 °C
Scan Begin	50 m/z	Set End Plate Offset	-500 V	Set Dry Gas	4.0 l/min
Scan End	1500 m/z	Set Charging Voltage	0 V	Set Divert Valve	Waste
		Set Corona	0 nA	Set APCI Heater	0 °C

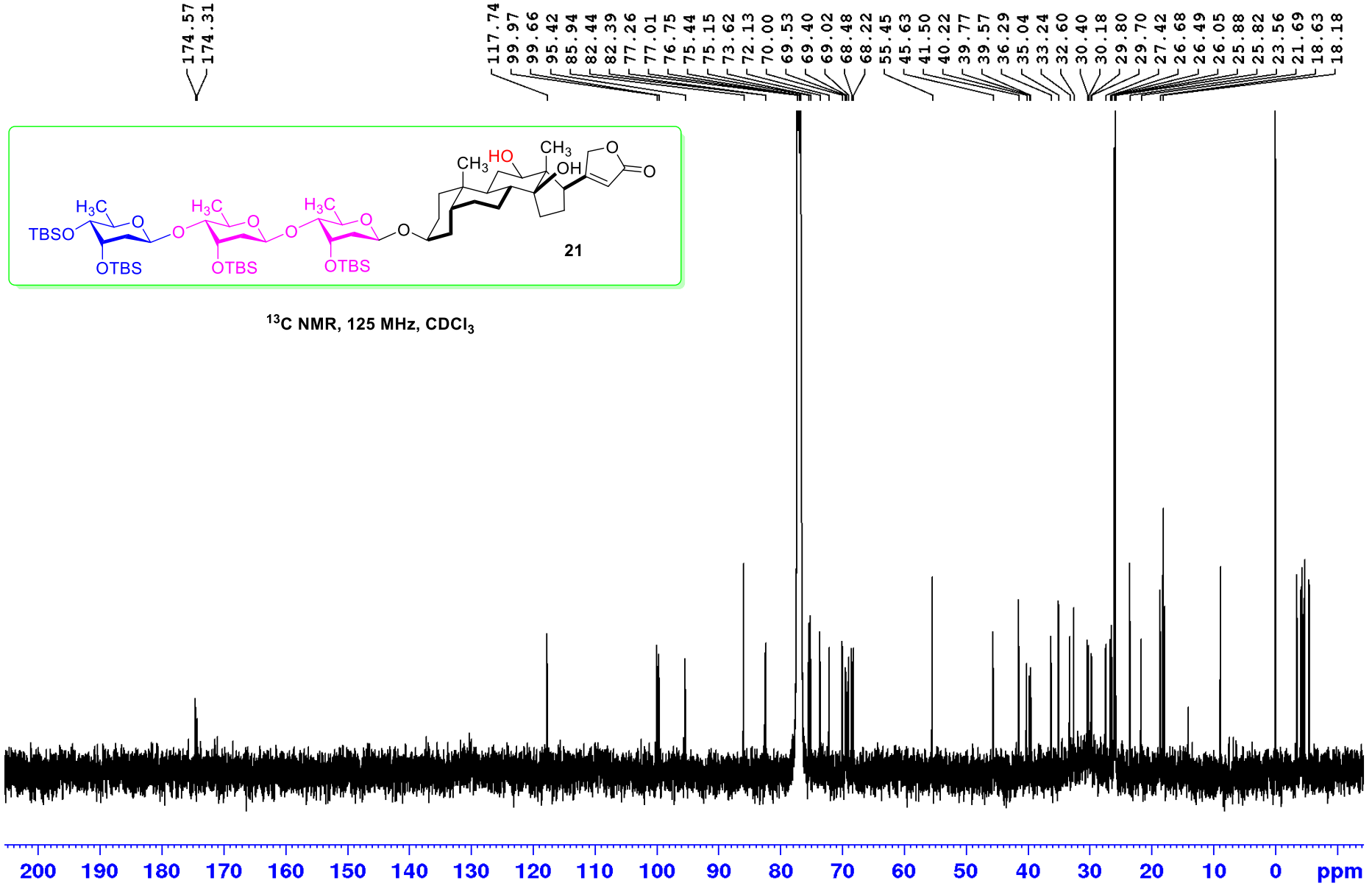


ALI-PRS-03-57-1.d

Bruker Compass DataAnalysis 4.2 printed: 13-03-2023 10:32:04 by: UOH Page 1 of 1



^{1}H NMR, 500 MHz, $CDCl_3$



^{13}C NMR, 125 MHz, $CDCl_3$

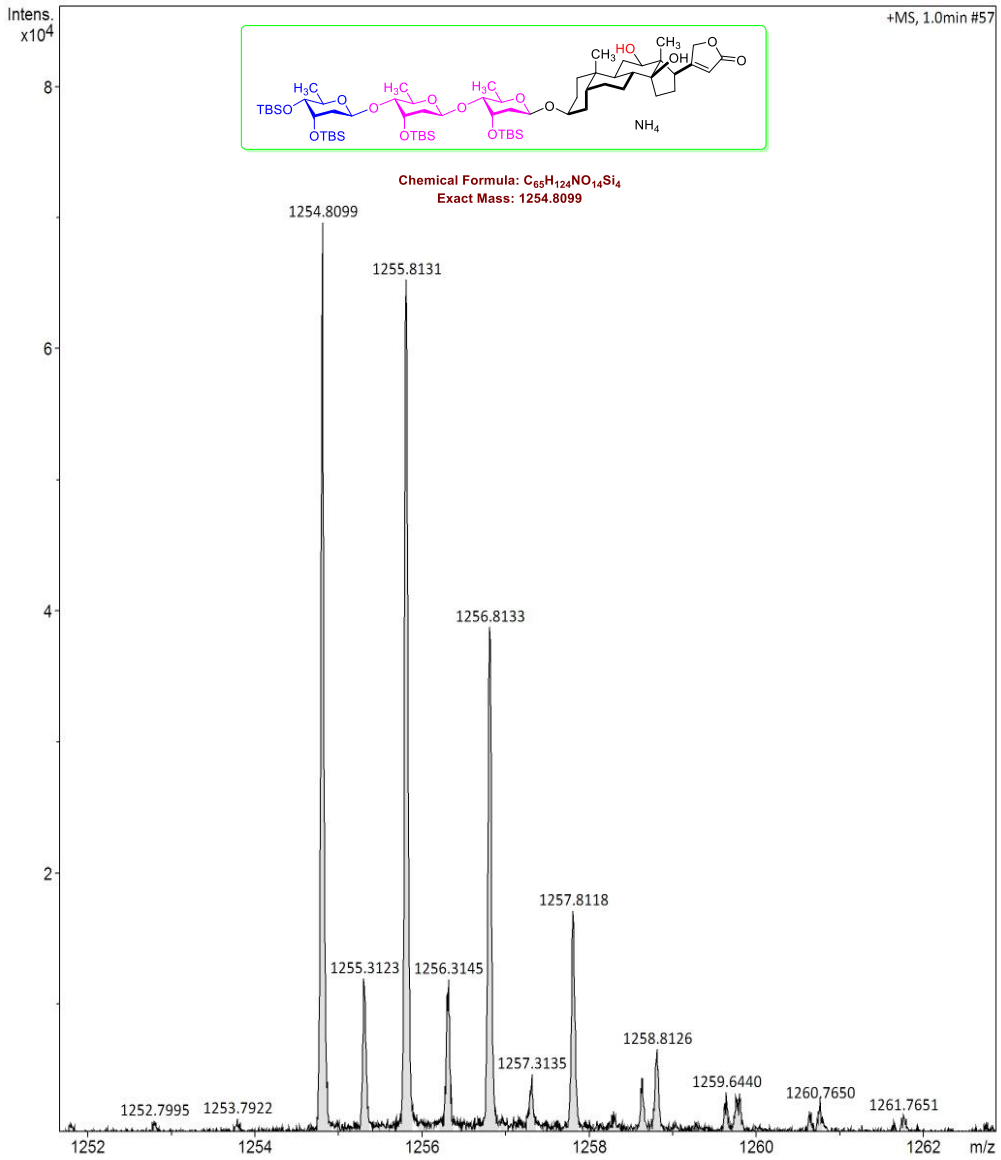
Display Report

Analysis Info

Analysis Name	E:\2022-Data\PROF .PRS\OCT\ALI-PRS-03-59-1.d	Acquisition Date	07-10-2022 15:22:53
Method	tune_low.m	Operator	UOH
Sample Name	ALI-PRS-03-59-1	Instrument	maXis 255552.10138
Comment			

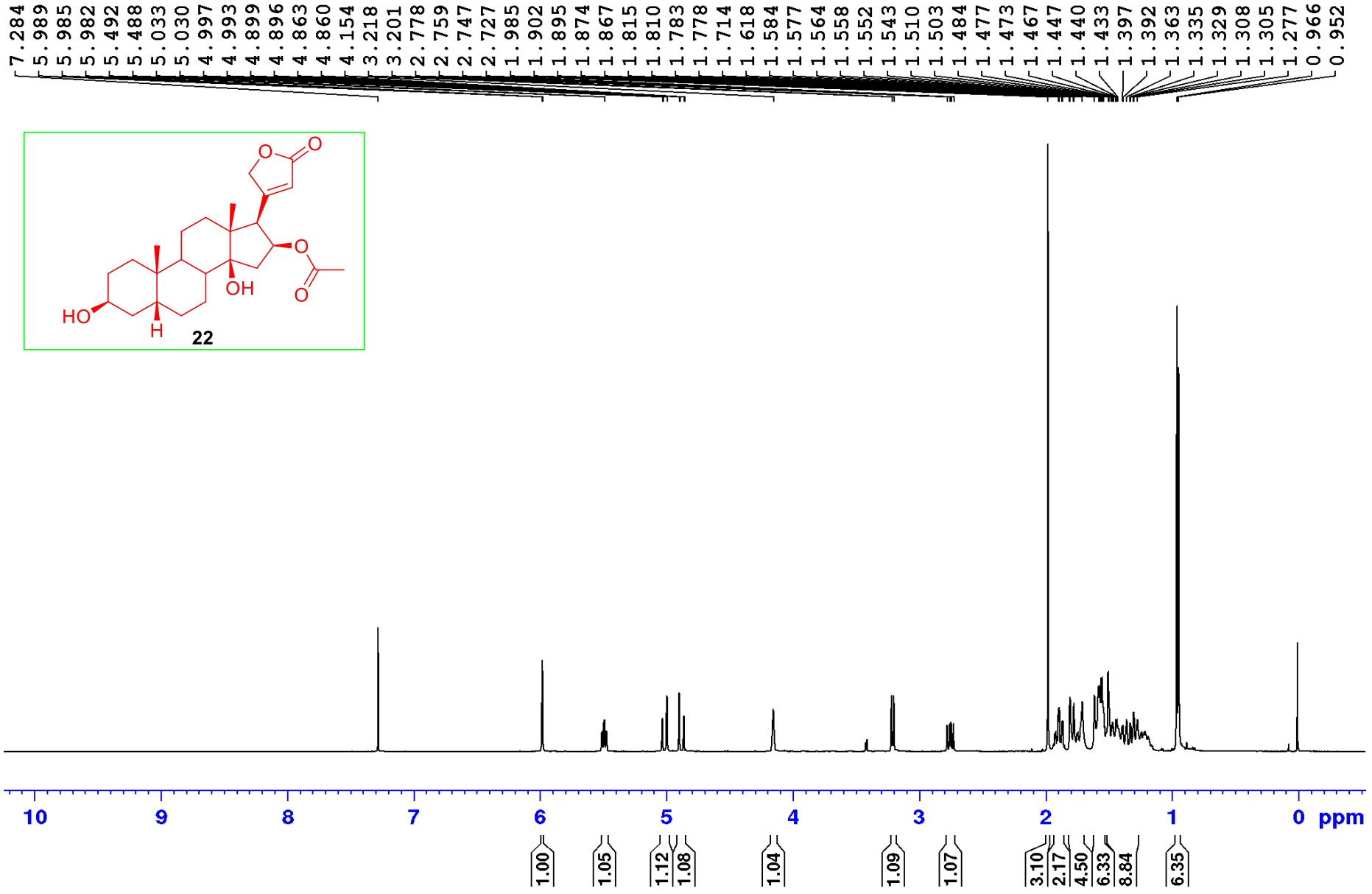
Acquisition Parameter

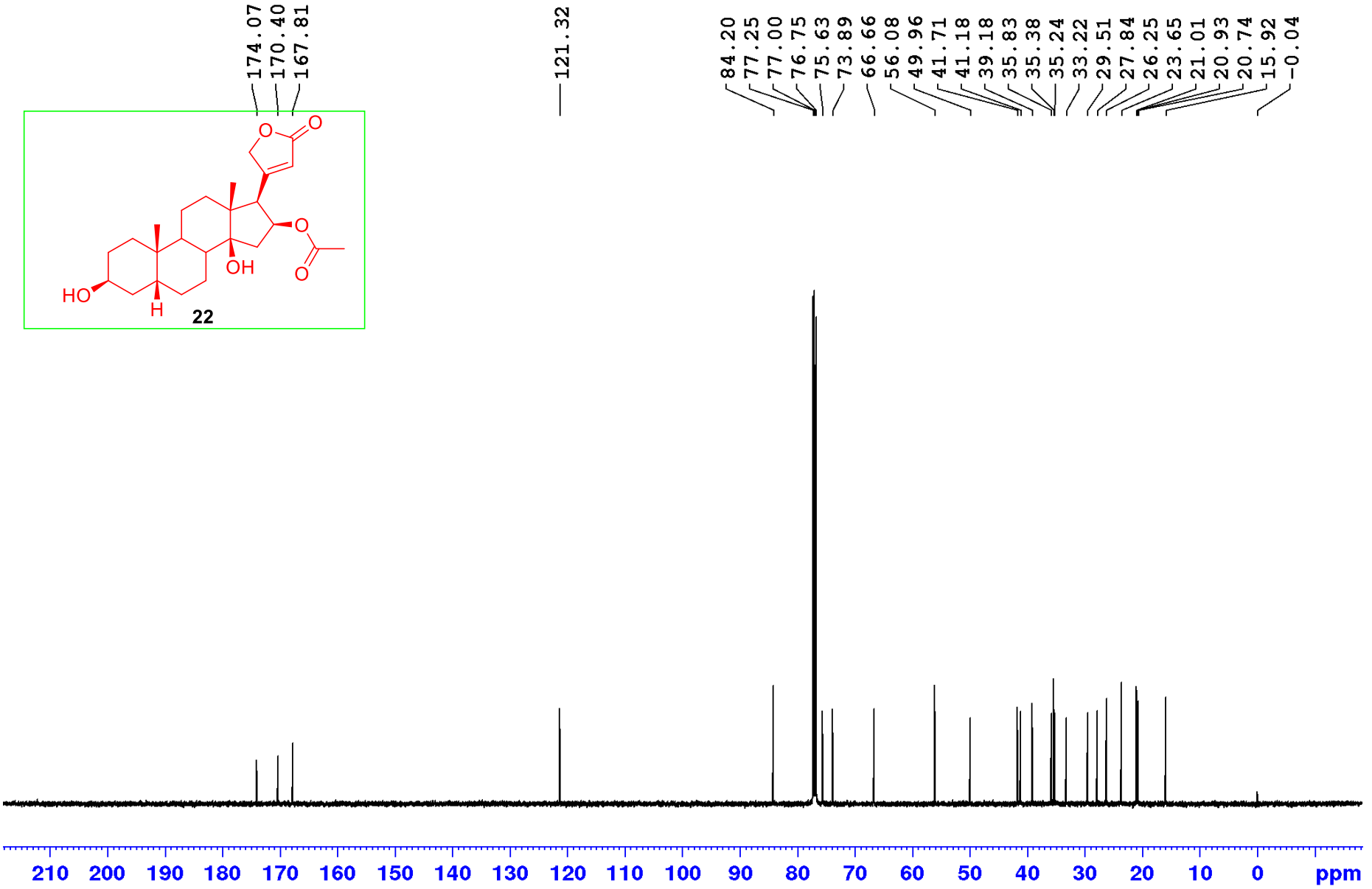
Source Type	ESI	Ion Polarity	Positive	Set Nebulizer	0.3 Bar
Focus	Not active	Set Capillary	4500 V	Set Dry Heater	180 °C
Scan Begin	50 m/z	Set End Plate Offset	-500 V	Set Dry Gas	4.0 l/min
Scan End	2000 m/z	Set Charging Voltage	0 V	Set Divert Valve	Waste
		Set Corona	0 nA	Set APCI Heater	0 °C

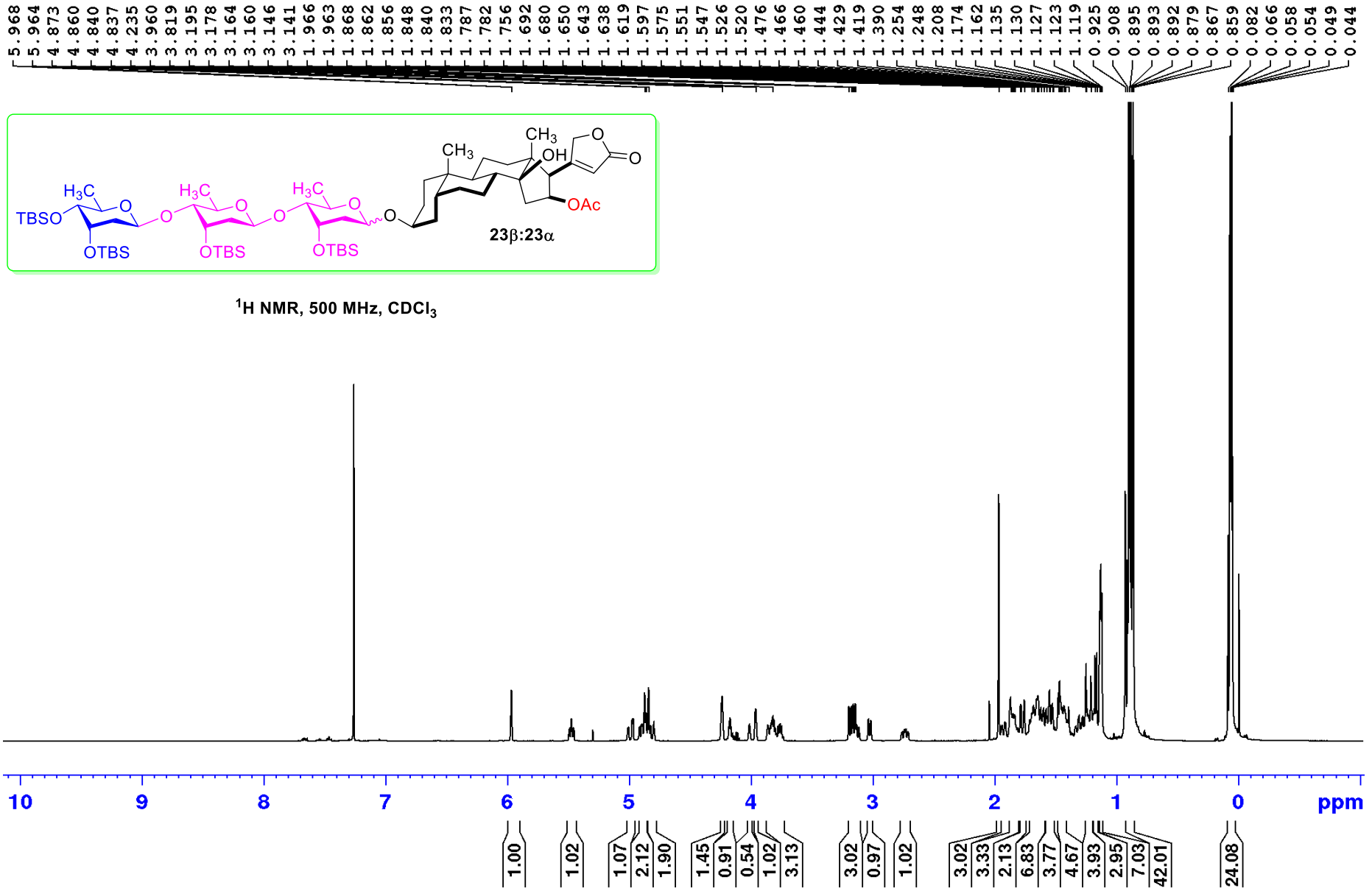


ALI-PRS-03-59-1.d

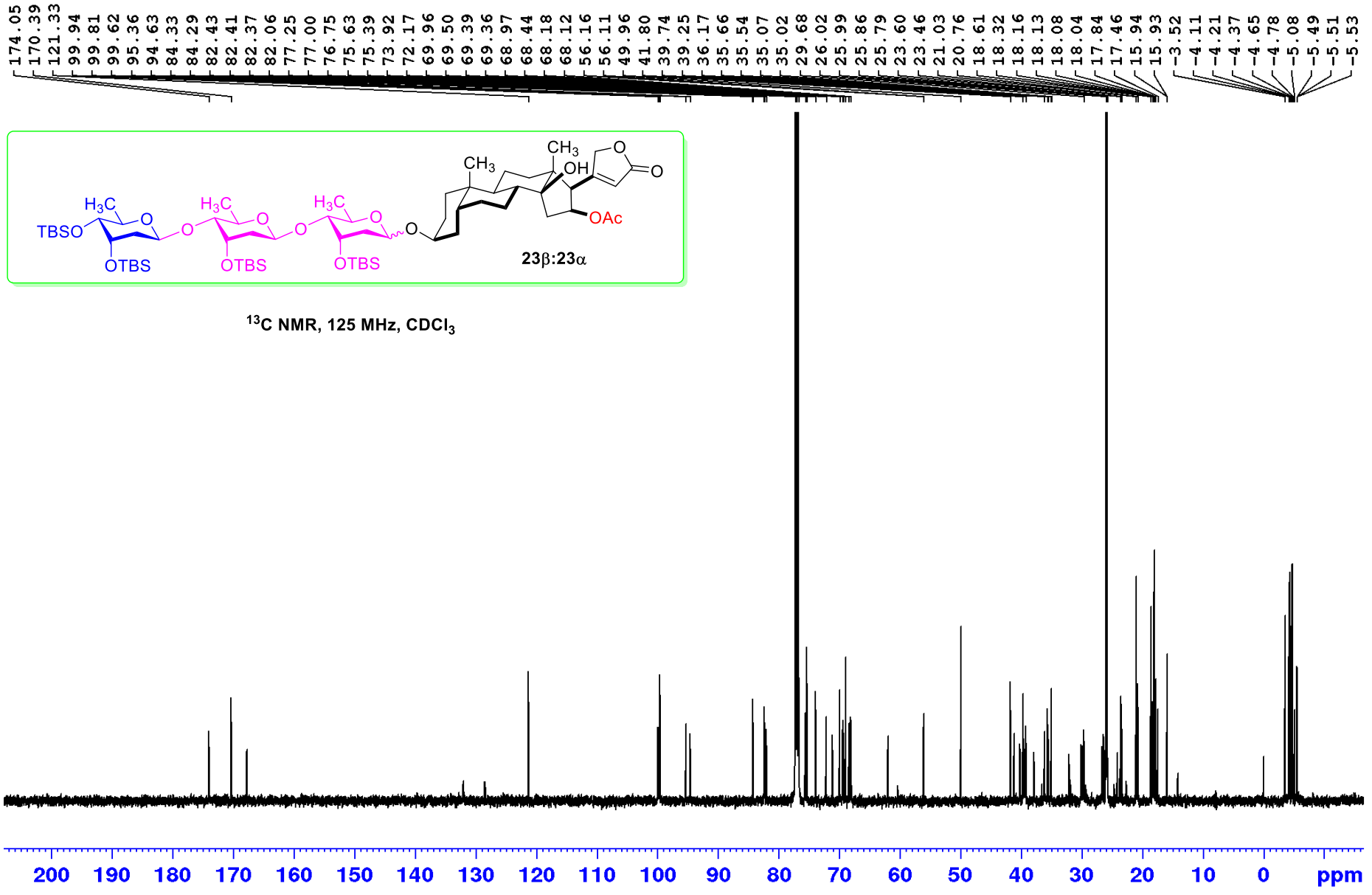
Bruker Compass DataAnalysis 4.2 printed: 13-03-2023 10:35:54 by: UOH Page 1 of 1


7.284
5.989
5.985
5.982
5.492
5.488
5.033
5.030
4.997
4.993
4.899
4.896
4.863
4.860
4.154
3.218
3.201
2.778
2.759
2.747
2.727
1.985
1.902
1.895
1.874
1.867
1.815
1.810
1.783
1.778
1.714
1.618
1.584
1.577
1.564
1.558
1.552
1.543
1.510
1.503
1.484
1.477
1.473
1.467
1.447
1.440
1.433
1.397
1.392
1.363
1.335
1.329
1.308
1.305
1.277
0.966
0.952
HO
H
OH
O
O
O
O
22
10
9
8
7
6
5
4
3
2
1
0
ppm
1.00
1.05
1.12
1.08
1.04
1.09
1.07
3.10
2.17
4.50
6.33
8.84
6.35


174.07
170.40
167.81
121.32
84.20
77.25
77.00
76.75
75.63
73.89
66.66
56.08
49.96
41.71
41.18
39.18
35.83
35.38
35.24
33.22
29.51
27.84
26.25
23.65
21.01
20.93
20.74
15.92
-0.04
O
O
O
O
OH
HO
H
22
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
ppm



^{1}H NMR, 500 MHz, $CDCl_3$



^{13}C NMR, 125 MHz, $CDCl_3$

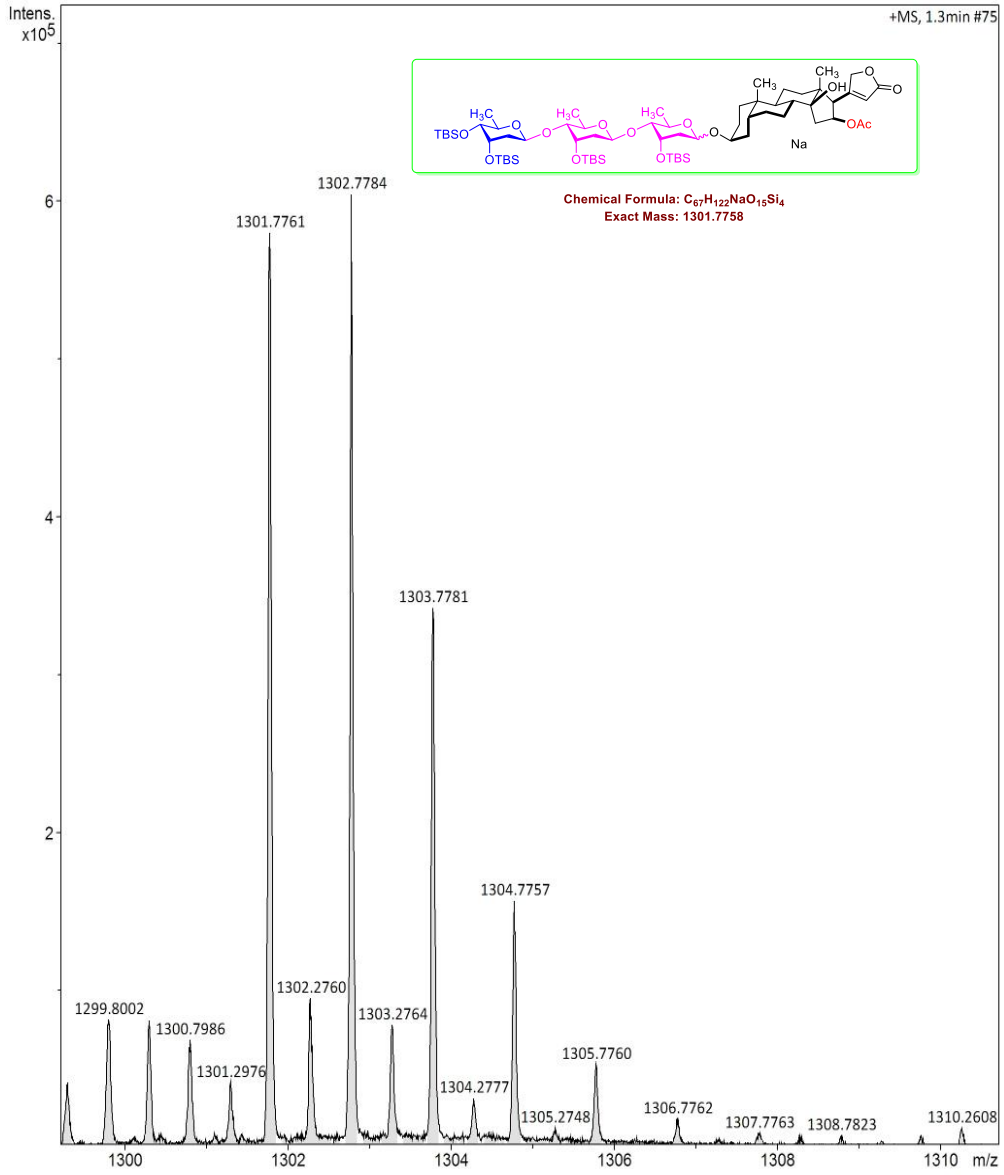
Display Report

Analysis Info

Analysis Name	E:\2022-Data\PROF .PRS\OCT\ALI-PRS-03-61-SPOT 1.d	Acquisition Date	26-10-2022 11:42:37
Method	TL-P.m	Operator	UOH
Sample Name	ALI-PRS-03-61-SPOT 1	Instrument	maXis 255552.10138
Comment			

Acquisition Parameter

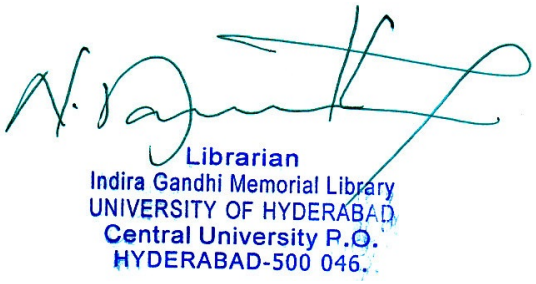
Source Type	ESI	Ion Polarity	Positive	Set Nebulizer	0.3 Bar
Focus	Not active	Set Capillary	3000 V	Set Dry Heater	180 °C
Scan Begin	50 m/z	Set End Plate Offset	-500 V	Set Dry Gas	4.0 l/min
Scan End	2500 m/z	Set Charging Voltage	0 V	Set Divert Valve	Waste
		Set Corona	0 nA	Set APCI Heater	0 °C



ALI-PRS-03-61-SPOT 1.d

Novel Transformations of 2,3-Unsaturated Sugars

by Intzar Ali



Submission date: 22-Jun-2023 04:09PM (UTC+0530)
Submission ID: 2120819780
File name: Ali_thesis_for_Plagarism_check.docx (2.23M)
Word count: 8334
Character count: 52058

Novel Transformations of 2,3-Unsaturated Sugars

ORIGINALITY REPORT

31%	6%	28%	3%
SIMILARITY INDEX	INTERNET SOURCES	PUBLICATIONS	STUDENT PAPERS

PRIMARY SOURCES

1	Perali Ramu Sridhar, Intzar Ali, M V Kamala Lakshmi. "Synthesis of Hexenuloses and a Library of Disaccharides Possessing 3-oxo-glycal Unit", The Journal of Organic Chemistry, 2022 Publication	20%
2	Submitted to University of Hyderabad, Hyderabad Student Paper	3%
3	hdl.handle.net Internet Source	2%
4	www.mdpi.com Internet Source	1%
5	"Coupling and Decoupling of Diverse Molecular Units in Glycosciences", Springer Science and Business Media LLC, 2018 Publication	1%
6	d-nb.info Internet Source	1%

P. Ramu Sridhar
Dr. P. Ramu Sridhar
Professor
School of Chemistry
University of Hyderabad
Hyderabad-500 046, India.

P. Ramu Sridhar
Dr. P. Ramu Sridhar
Professor
School of Chemistry
University of Hyderabad
Hyderabad-500 046, India

7	Vankar, Yashwant D., and Torsten Linker. "Recent Developments in the Synthesis of 2-C -Branched and 1,2-Annulated Carbohydrates : Synthesis of 2-C -Branched and 1,2-Annulated Carbohydrates", European Journal of Organic Chemistry, 2015. Publication	1 %
8	www.researchgate.net Internet Source	<1 %
9	Kedar N. Baryal, Surya Adhikari, Jianglong Zhu. "Catalytic Stereoselective Synthesis of β-Digitoxosides: Direct Synthesis of Digitoxin and C1'-epi-Digitoxin", The Journal of Organic Chemistry, 2013 Publication	<1 %
10	"Glycoscience: Chemistry and Chemical Biology I–III", Springer Science and Business Media LLC, 2001 Publication	<1 %
11	Perali Ramu Sridhar, Chalapala Sudharani. "Stereoselective synthesis of C-2-methylene and C-2-methyl-C-glycosides by Claisen rearrangement of 2-vinyloxymethyl glycals", RSC Advances, 2012 Publication	<1 %
12	"The Claisen Rearrangement", Wiley, 2007 Publication	<1 %

13	Ana Aljarilla, J. Cristóbal López, Joaquín Plumet. "Metathesis Reactions of Carbohydrates: Recent Highlights in Cross-Metathesis", European Journal of Organic Chemistry, 2010 Publication	<1%
14	Michael Martin Nielsen, Christian Marcus Pedersen. "Catalytic Glycosylations in Oligosaccharide Synthesis", Chemical Reviews, 2018 Publication	<1%
15	Frank E. McDonald, K. Subba Reddy. "Convergent Synthesis of Digitoxin: Stereoselective Synthesis and Glycosylation of the Digoxin Trisaccharide Glycal This research was supported by the U.S. National Institutes of Health (CA-59703). F.E.M. also thanks Novartis Pharmaceuticals for unrestricted additional funding (Grant Program for the Support of Academic Research in Synthetic Organic Chemistry).", Angewandte Chemie International Edition, 2001 Publication	<1%
16	epdf.pub Internet Source	<1%
17	Ande Chennaiah, Ashish Kumar Verma, Yashwant D. Vankar. " TEMPO-Catalyzed Oxidation of 3- -Benzylated/Silylated Glycals	<1%

to the Corresponding Enones Using a PIFA–Water Reagent System ", The Journal of Organic Chemistry, 2018
Publication

18	Naoyoshi Maezaki, Naoto Kojima, Hiroaki Tominaga, Minori Yanai, Tetsuaki Tanaka. "Systematic Synthesis of Bis-THF Ring Cores in Annonaceous Acetogenins", Organic Letters, 2003 Publication	<1 %
19	Perali Ramu Sridhar, Patteti Venukumar. "A Ring Expansion–Glycosylation Strategy toward the Synthesis of Septano-oligosaccharides", Organic Letters, 2012 Publication	<1 %
20	pubag.nal.usda.gov Internet Source	<1 %

Exclude quotes On
Exclude bibliography On
Exclude matches < 14 words