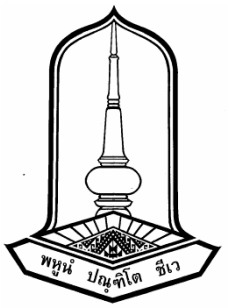

PALLADIUM- AND GOLD-CATALYZED HYDROAMINATION OF *C*- (TETRA-*O*-ACETYL-*β*-D-GALACTOPYRANOSYL) ALLENE

CHALEOWSAK KHAMWONG

A thesis submitted in partial fulfillment of the requirements for
the degree of Master of Science degree in Chemistry
Mahasarakham University
May 2012

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The examining committee has unanimously approved this thesis, submitted by Mr. Chaleowsak Khamwong, as a partial fulfillment of the requirements for the Master of Science degree in Chemistry, Mahasarakham University.

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(Prof. La-orsri Sanoamuang, Ph.D.)	(Prof. Pradit Terdtoon, Ph.D.)
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May, 29 2012

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Chaleowsak Khamwong

ชื่อเรื่อง แพลเลเดียม และทองคำที่เร่งปฏิกิริยาไฮโดรอะมิเนชันของ *C*-(tetra-*O*-acetyl-*β*-D-galactopyranosyl)allene

ผู้วิจัย นายเฉลียวศักดิ์ คำวงษ์

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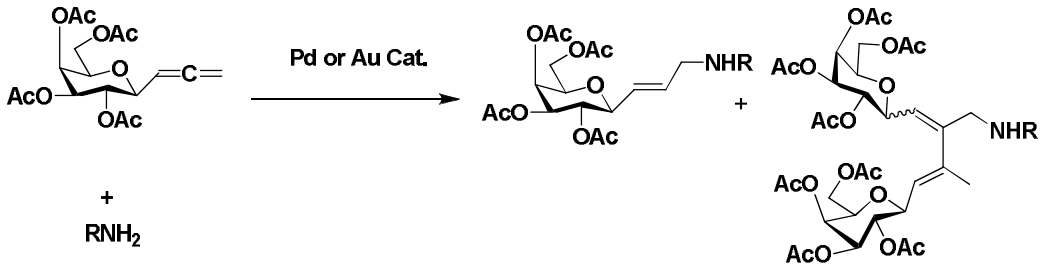
บทคัดย่อ

การพัฒนาของวิธิการทั่วไปและวิธีการที่มีประสิทธิภาพสำหรับการเติมของพันธะ N—H ไปยังพันธะ C—C ที่ไม่อิ่มตัว คือปฏิกิริยาไฮโดรอะมิเนชันแสดงให้เห็นถึงความสำคัญและความท้าทายทั้งในเคมีอินทรีย์สังเคราะห์ และการเร่งปฏิกิริยาที่เป็นเนื้อเดียวกัน การเร่งปฏิกิริยาของแพลเลเดียมและทองคำในปฏิกิริยาไฮโดรอะมิเนชันมีให้เห็นอย่างมากมาย และได้นำไปสู่ระเบียบวิธีวิทยาใหม่ๆ ในการสังเคราะห์โมเลกุลที่ประกอบด้วยพันธะ C—N

ทั้งวิธีการที่ใช้แพลเลเดียม และทองคำสำหรับการเร่งปฏิกิริยาไฮโดรอะมิเนชันของ *C*-(tetra-*O*-acetyl-*β*-D-galactopyranosyl) allene กับอะโรมาติกอะมีนต่างๆ ได้รับการพัฒนาจนประสบผลสำเร็จ



คำสำคัญ : ไฮโดรอะมิเนชัน ; อะมีน ; แพลเลเดียม ; ทองคำ ; แอลลีน ; กาแลคโตไพราโนซิล

TITLE Palladium- and Gold-catalyzed Hydroamination of *C*-(tetra-*O*-acetyl-*β*-D-galactopyranosyl)allene

CANDIDATE Mr. Chaleowsak Khamwong

DEGREE Master of Science degree in Chemistry

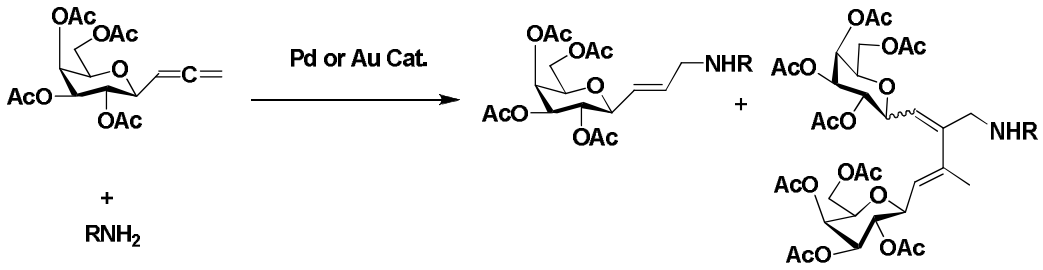
ADVISORS Asst. Prof. Uthai Sakee, Ph.D. and Senee Kruanetr, Ph.D.

UNIVERSITY Mahasarakham University **YEAR** 2012

ABSTRACT

The development of general and efficient methods for the addition of N—H bond across a C—C multiple bond, hydroamination represent a significant challenge in both organic synthesis and homogeneous catalysis. Palladium- and gold-catalyzed hydroamination has seen an explosion of activity and has led to new methodologies in the synthesis of C—N containing molecule.

Both palladium and gold methods for catalyzed hydroamination of *C*-(tetra-*O*-acetyl-*β*-D-galactopyranosyl)allene with a variety of aromatic amines have been successfully developed.



Key Words : Hydroamination ; Amine ; Palladium ; Gold ; Allene ; Galactopyranosyl

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LIST OF ABBREVIATIONS

br	Broad
c	Concentration
calcd	Calculate
Cat.	Catalyst
$CDCl_3$	Chloroform- D_1
δ	Chemical shift
DCM	Dichloromethane
equiv.	Equivalent
FT-IR	Fourier-Transform Infrared Spectroscopy
HRMS	High resolution mass spectrometers
OAc	Acetyl
PPh_3	Triphenylphosphin
rt	Room temperature
Sat.	Saturated
TFP	Tri(2-furyl)phosphin
THF	Tetrahydrofuran
TLC	Tin layer chromatography
TMS	Tetramethylsilande
^{1}H-NMR	Proton nuclear magnetic resonance
^{13}C-NMR	Carbon 13 nuclear magnetic resonance

CHAPTER 1

INTRODUCTION

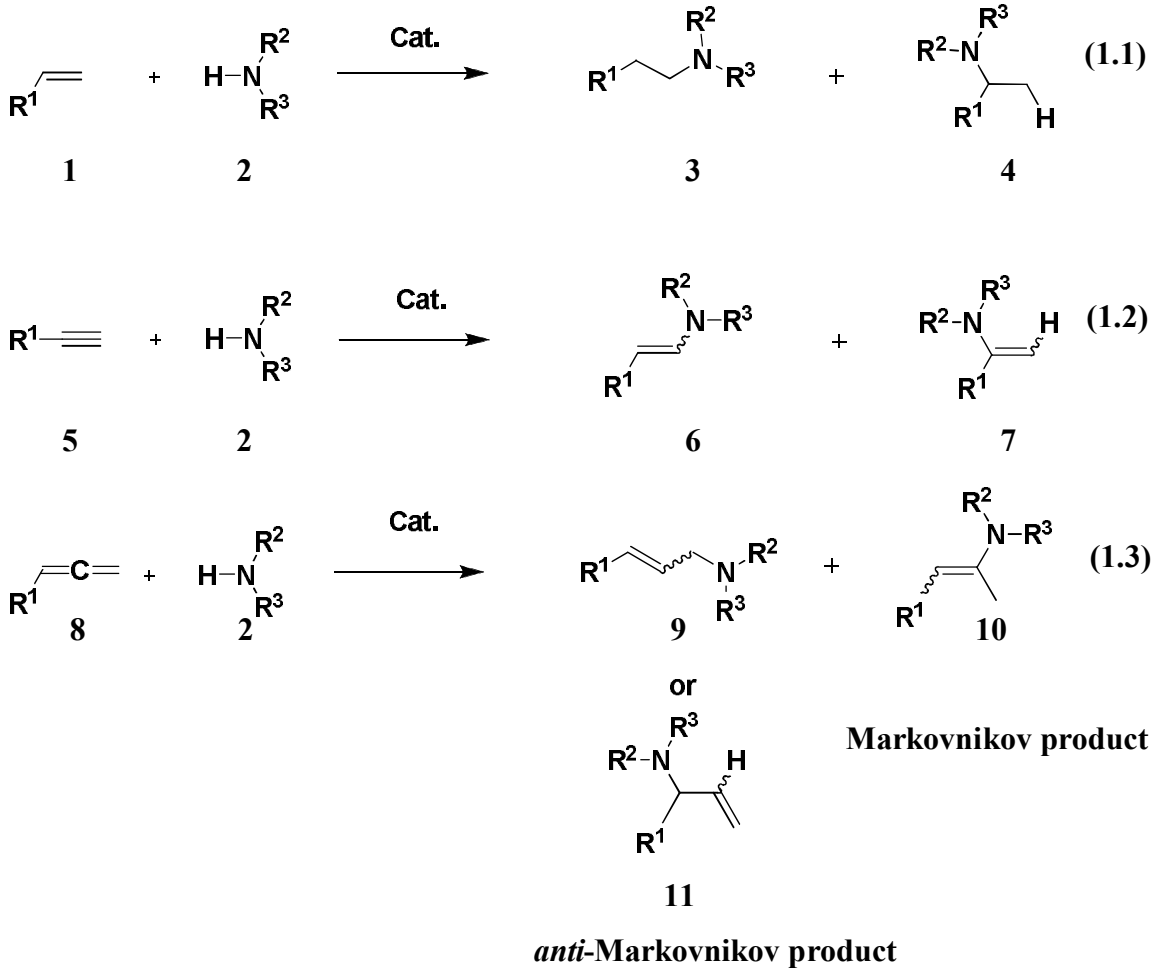
Carbohydrate-based starting materials are widely used in target-oriented syntheses of optically active compounds [1]. The important role of carbohydrates in many biological processes is evident, and tailored derivatives are discussed as promising leads for efficient pharmaceuticals [2]. Sugars or saccharides are the most abundant bio-molecule on the planet. They are important in a number of biological roles. Most obviously you will know them as a major component of your diet [3]. Sugars are essential feedstocks in biological systems and are useful substances because they are inexpensive, highly water-soluble, optically active materials. These properties can be exploited to prepare bioactive materials, chiral auxiliaries in asymmetric synthesis, and for functionalization of hydrophobic materials [4].

1.1 Hydroamination

The hydroamination is a highly atom economical process in which an amine N-H bond is added to an unsaturated carbon-carbon bond (Scheme 1.1). This reaction is a great potential interest for the waste-free synthesis of basic and fine chemicals, pharmaceuticals and other industrially relevant building blocks starting from inexpensive precursors (alkenes, alkynes, or allenes) [5-9]. The intermolecular hydroamination reaction of an amine with an unsymmetrical unsaturated carbon-carbon bond can be lead to either the Markovnikov or *anti*-Markovnikov product. The hydroamination of alkene or alkyne are providing a higher substituted amine or enamine, respectively (Scheme 1.1; Equation 1.1, 1.2), while hydroamination of unsymmetrical allene are providing allylic amines or enamine as products (Scheme 1.1; Equation 1.3).

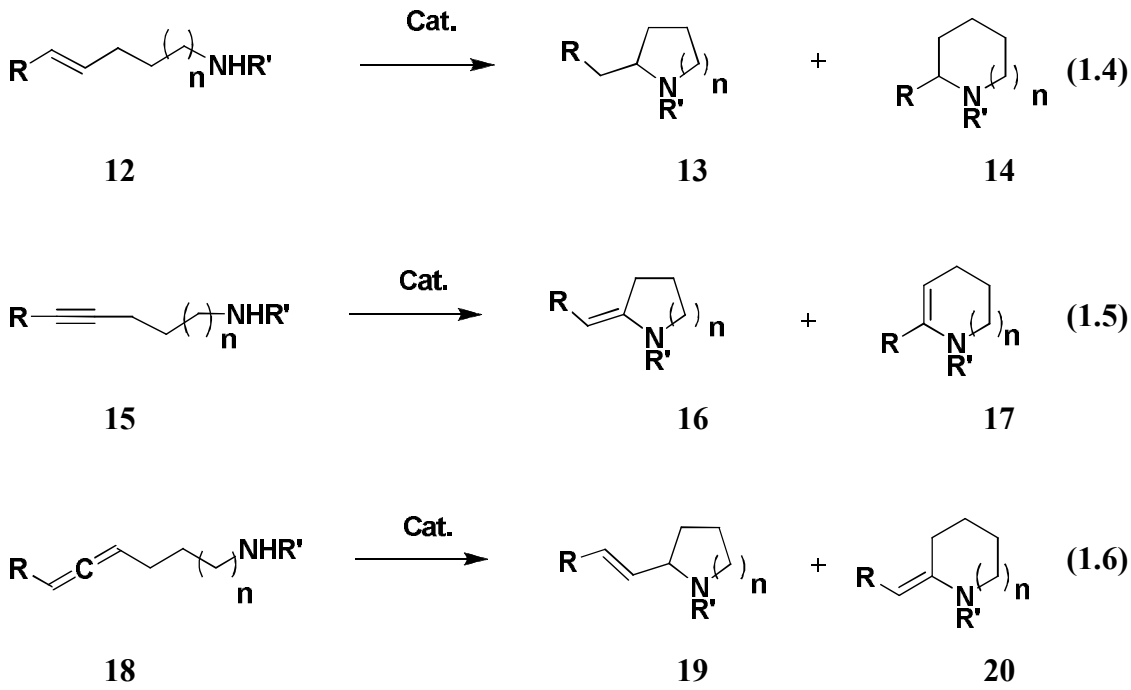
The intramolecular hydroamination of unsaturated carbon—carbon bond, is simply the addition of N—H across a C=C bond in an intramolecular fashion, illustrated in Scheme 1.2 [6]. The hydroamination/cyclization of an aminoolefin and aminoalkyne substrate leads to the cyclic amines and cyclic enamines product (Scheme 1.2 Equation

1.4, 1.5), while the aminoallene substrate can be the formation of allylic cyclic amine or cyclic enamine as products (Scheme 1.2 Equation 1.6).



Scheme 1.1 Hydroamination of unsaturated carbon-carbon bond

In generally, hydroamination reactions are hindered by two major problems: 1) a high activation barrier for the direct addition of amines across carbon-carbon multiple bonds exists which arises from electrostatic repulsion between the electron lone pair at the nitrogen atom and the electron-rich π-bond, and 2) the general negative reaction entropy $\Delta S°$ of the reaction is responsible for the fact that the equilibrium of hydroamination reaction is shifted towards the starting materials at the higher temperatures that are necessary to overcome the activation barrier [7].



Scheme 1.2 Intramolecular hydroamination of unsaturated carbon-carbon bond

Hence, there is a catalyst required to open an alternative, low-energy pathway by activating one or both of the reaction partners. The hydroamination can be assisted or catalyzed by alkali metal ions, lanthanide complexes, or transition metal, which allow the processes to be performed under milder conditions [6].

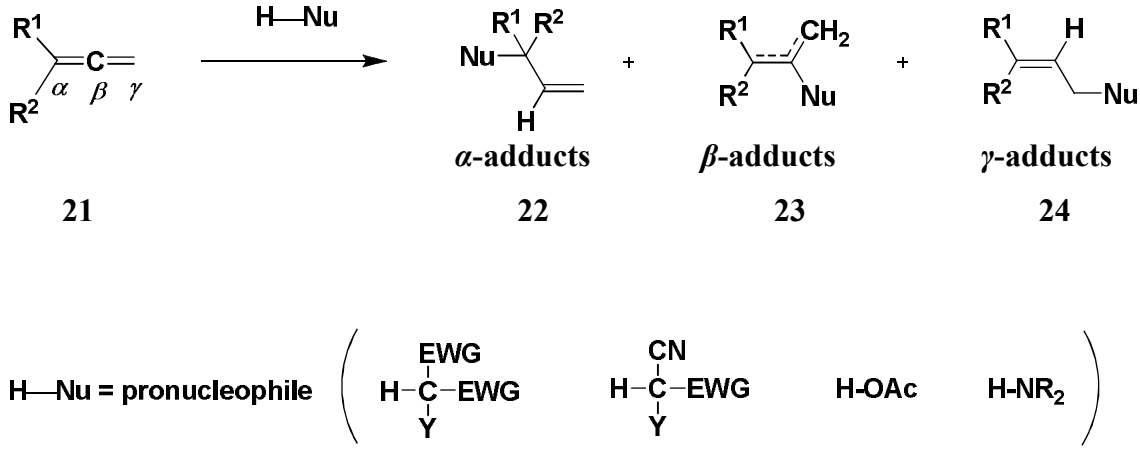
1.2 Palladium catalyzed reaction of allenes

Allenes are three-carbon functional groups possessing a 1,2-diene moiety and serve as potential precursors in the synthesis of highly complex and strained target molecules of biological and industrial importance [10]. The first synthetic allene can be dated back to as early as 1887, and its structure was confirmed in 1954. Allenes can also be found in many natural sources. Due to the nature that these compounds would be thermally unstable, for a long period of time, their chemistry and synthetic routes had not been well established. However, due to the presence of the unique cumulated diene structural unit, allenes are a class of compounds with the following interesting properties: (1) with up to four substituents, methodologies starting from allenes provide synthetic diversity; (2) the electron density and the reactivity of each carbon atom of allene unit can be tuned by the substituent effect; (3) the inherent axial chirality

provides a challenge for the highly stereoselective synthesis of optically active allenes and the transfer of the chirality of the allenes into final products [11].

Palladium-catalyzed reaction of allenes with carbon and heteroatom nucleophiles leading to the formation of carbon—carbon and carbon-heteroatom bonds generally proceed with the involvement of a π-allylpalladium intermediates, which plays an ever increasing role in organic synthesis [10]. The first report on Pd-catalyzed reaction of allenes with amines and malonate was given by Coulson in 1973 [12].

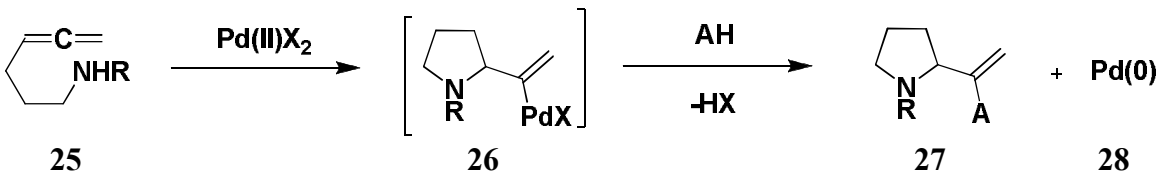
A nucleophilic addition on allene can occur on three carbon atoms depending on the substituents at the terminals. All three possible regioisomers can be selectively produced by properly substituting the allene at its terminals (steric and electronic effect) (Scheme 1.3) [10,13].



Scheme 1.3 Palladium-catalyzed addition of pronucleophiles to allenes

It was observed that alkoxy (aryloxy) allenes afford α-adducts, arylallenes bearing an electron-withdrawing group at the *para*-position afford β-adducts, and dialkyl-substituted allenes afford γ-adducts [10].

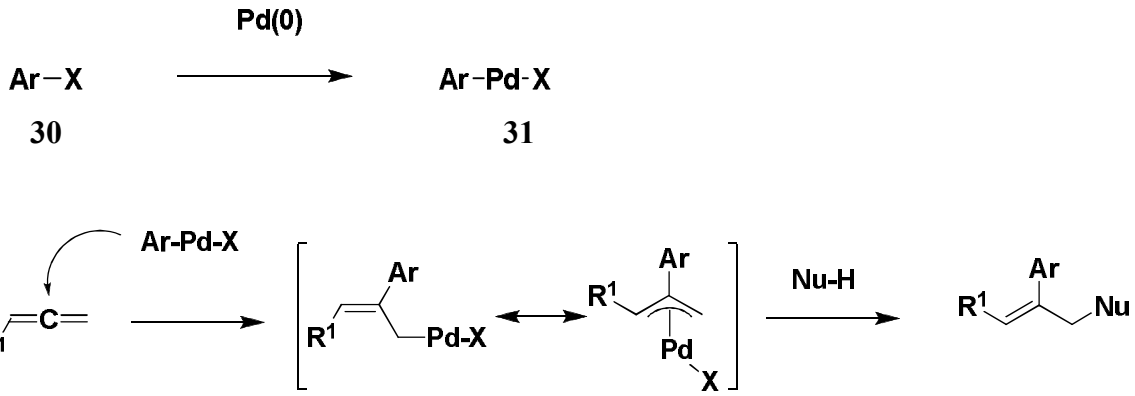
Pd-catalyzed and promoted reactions of allenes can be classified into three groups. The first one is promoted by Pd(II). For example, aminopalladation of hexa-1,2-dienyl-6-amine with Pd(II) generates the alkenylpalladium intermediate **26**, which is converted to functionalized alkene **27** with generation of Pd(0). In order to make the reaction catalytic, Pd(0) has to be oxidized to Pd(II) with some oxidants [13].



25 26 27 28

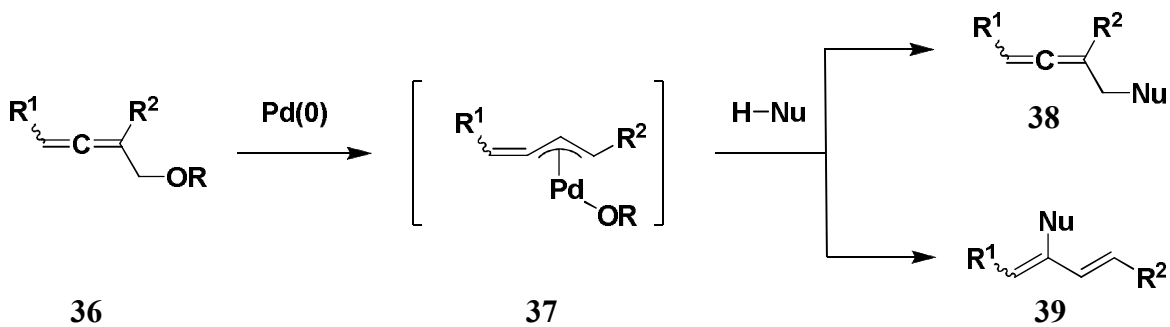
28 29

In the Pd(0)-catalyzed reaction of allene **32** with aryl halide, carbopalladation of allene with Ar—Pd—X takes place to give the π-allylpalladium intermediate **34**, which is attacked by a pronucleophile to give **35**. The catalytic reactions of this type have been extensively studied [13].



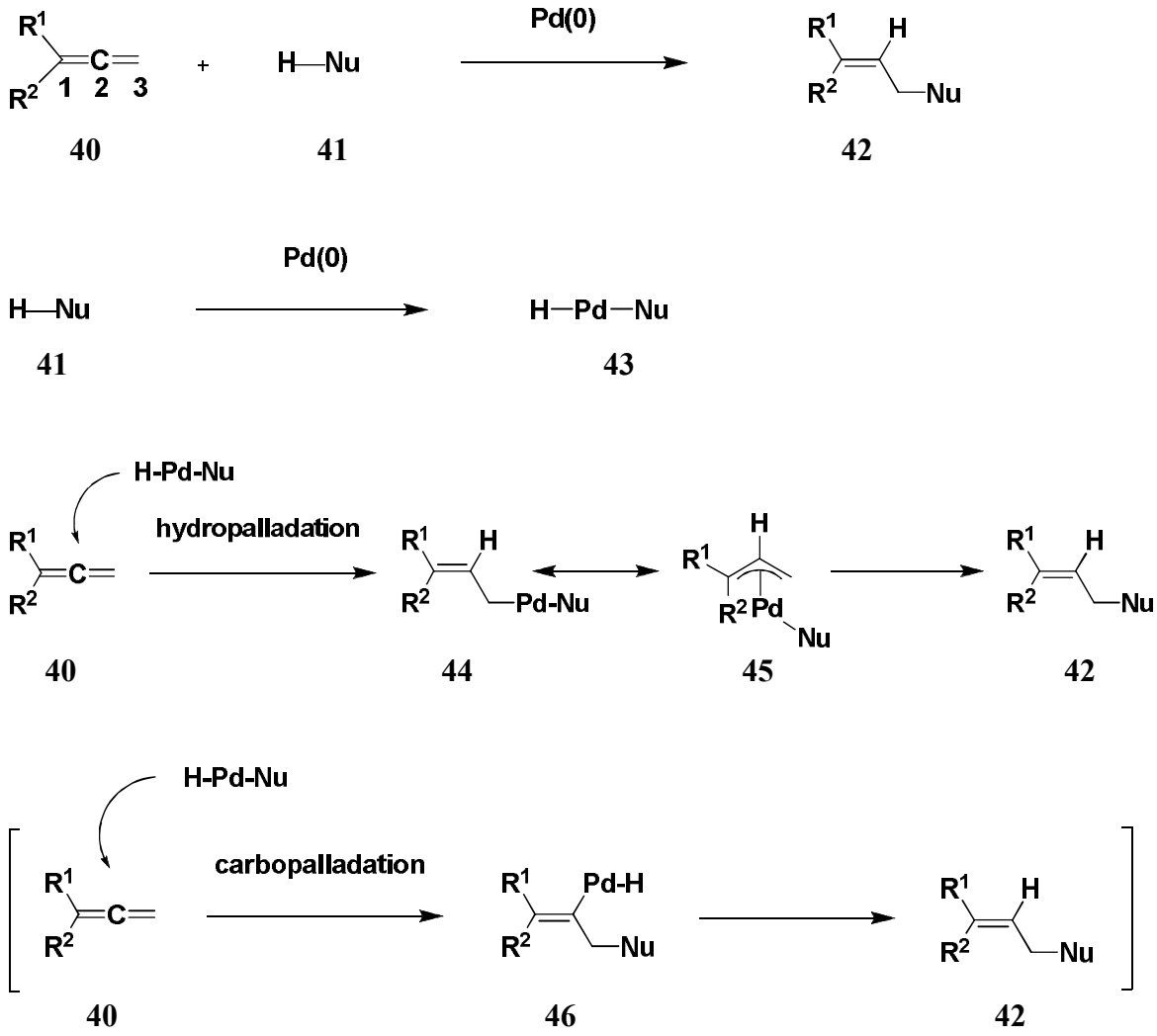
30 31 32 33 34 35

Facile Pd(0)-catalyzed reactions of 2,3-alkadienyl derivatives **36** with nucleophiles occur via the formation of methylene-π-allylpalladium intermediates **37**, from which 1,2- and 1,3-dienes **38** and **39** are formed depending on the nature of the pronucleophiles [13].



36 37 38 39

While, the Pd(0)-catalyzed reaction of allenes with pronucleophile are clearly different mechanistically from the reactions explained in the above. Attack of nucleophiles may occur at C−1, C−2, and C−3 carbons of the allenes **40**. Among them, attack at C−3 to give **42** is predominant. Most importantly, reactions of allenes with pronucleophiles start by the oxidative addition of pronucleophiles to Pd(0) to generate H—Pd—Nu **43**. The formation of **42** by hydrocarbonation can be explained in two ways in the case where Nu—H is the carbon pronucleophile. As one possibility, hydropalladation of one of the two double bonds occurs to afford the terminal palladium intermediate **44**, which is stabilized by the formation of π-allyl complex **45**, and reductive elimination provides the C−3 adduct **42**. Another possibility is carbopalladation to generate **46**, and subsequent reductive elimination provides **42**. Of these two possibilities, the hydropalladation mechanism is preferable [13].



1.3 Gold catalyzed organic transformation

Gold has accompanied mankind from the very early days; no name of a chemist is associated with the discovery of the element gold. It is probably the only chemical element that literally every adult has heard about. A highly positive normal potential is responsible for a low reactivity and allows gold to occur in nature in elemental form, for example, as nuggets. Some of the oldest and some of the most beautiful ancient art is made of gold, and this stresses the impressive durability of this metal. It has always been precious, which is nicely reflected by the Greek myth of king Midas. Monetary systems based on the rare gold and consequently the desire to possess gold has been the driving force for all kinds of activities such as gold rushes to even the most hostile regions of earth, wars, the conquering of whole continents, and, to come to the more positive effects, for the early development of science and chemistry. Besides the alchemists, famous names like Archimedes and Rutherford are connected with gold [14].

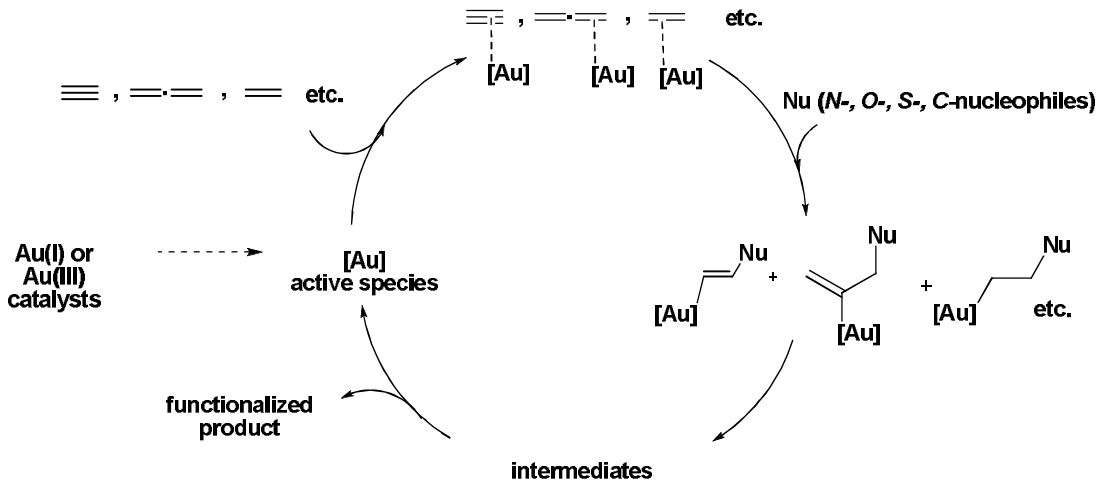
The frequent use of gold in dental medicine, applications in the treatment of arthritis and recent investigations of the anticancer activity have proven that, unlike, for example, with nickel, no problems of allergic reactions are associated with gold. Metallic gold is highly biocompatible, but gold in ionic form is toxic. While the stoichiometric chemistry of gold has intensively and continuously been investigated, this close relationship between gold and chemical applications got lost during the development of catalysis reactions. The periodic table with 81 stable, nonradioactive elements offers only a limited number of building blocks to the chemists exploring catalysis. Therefore, they can hardly afford to skip one of the elements, but they indeed heavily neglected it. Probably a low catalytic activity was mistakenly deduced from the inertness of elemental gold that only dissolves in aqua regia or oxidants such as air, the latter only in the presence of strong ligands such as cyanide [14].

Out of the different oxidation states possible for gold, in the presence of organic substrates, gold(0), gold(I), and gold(III) are possible. In aqueous solution, in the absence of stabilizing ligands, gold(I) spontaneously disproportionate to gold(III) and gold(0). From stoichiometric chemistry and theoretical considerations for gold(I), it is known that the fragment R_3PAu^+ is isolobal to H^+ and LHg_2^+. Relativistic effects

reach their maximum in the periodic table with gold [14]; significant for catalysis is, for example, that in complexes gold(I) can be smaller than silver(I) [15]. Gold has only one isotope and thus lacks a characteristic isotope pattern in mass spectrometry [16]. The nuclear spin of gold is 3/2, but because of a very low sensitivity and a quadropole moment, only a few 79Au spectra in a highly symmetric environment have been reported. The diamagnetic character of both gold(I) and gold(III) conveniently allows the monitoring of catalysis reactions by NMR. Mössbauer spectroscopy can deliver information about the oxidation state. Ligand exchange processes, which are essential for catalysis, have been investigated. There is only little data on Au(I), which favors an associative mechanism. Au(III) also favors an associative mechanism; the reaction rate was reported to be higher than in the corresponding palladium and platinum but lower than in the nickel complexes [14].

Although there are many types of transformations catalyzed by gold complexes, a vast majority of them proceed through some very similar mechanistic steps and involve the activation of a π-system (typically an alkyne or an allene, but sometimes even an alkene moiety) towards the attack of a nucleophile. A general pathway for these transformations is given in Scheme 1.4 [14,17]. The first step is always the formation of the catalyst's active species. The next step is the selective coordination of [Au] on the π-system, which renders this moiety more electrophilic and activates it for the nucleophilic attack.

The nucleophilic group can be nitrogenated (amines, imines etc.), oxygenated (alcohols, ethers, epoxides, aldehydes, ketones, esters etc.), sulfurated (thiols etc.) or carbonated (alkenes, alkynes, aryls, enols, enamines etc.). It can attack either in an inter- or in an intramolecular fashion. Given the excellent propensity of gold to undergo η^2 to η^1 migrations, the attack will result in the formation of two new C—[Au] and respectively C—Nu bonds.



Scheme 1.4 General mechanism of gold-catalyzed transformations

The final step is always the regeneration of the active species and the formation of final products. This happens usually by protodemetallation from the organogold intermediates, although alternatively other electrophiles can be used to trap these derivatives or direct eliminations can take place.

1.4 Research objectives

To developed methods for hydroamination of *C*-(tetra-*O*-acetyl-*β*-D-galactopyranosyl)allene using palladium and gold catalyst

1.5 Scope of research

1. The sugar allene, *C*-(tetra-*O*-acetyl-*β*-D-galactopyranosyl)allene was used as a starting material.

2. Aliphatic and aromatic amine derivatives were used as nucleophiles.

2.1 Aromatic amines: aniline, *o*-anisidine, *m*-anisidine, *p*-anisidine, *m*-toluidine, *p*-toluidine, 3-nitroaniline, 4-nitroaniline, 2,4-dinitroaniline, 1-napthylamine, 4-aminoacetophenone

2.2 Aliphatic amines: morpholine, *n*-butylamine, *n*-octhylamine, benzylamine, and phenylhydrazine.

3. Gold and palladium were used as catalysts.

1.6 Expected results of research

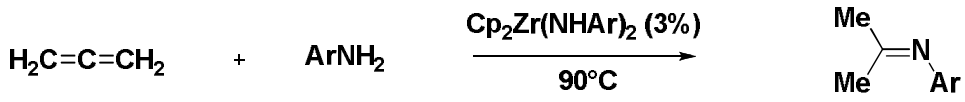
This research may find wide use in the laboratory for functionalization of *C*-glycoside.

CHAPTER 2

LITERATURE REVIEW

2.1 Intermolecular hydroamination of allenes

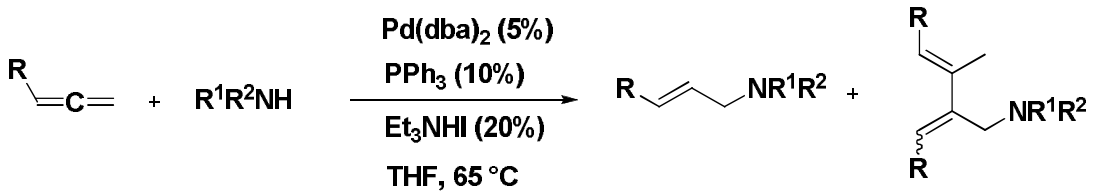
In 1992, Walsh and co-workers used zirconium bisamides $Cp_2Zr(NHAr)_2$ for the hydroamination of allene **47** to give the *anti*-Markovnikov addition product **49** (Scheme 2.1) [18]. In 1995, Besson and co-workers used palladium complex/Brønsted acid combinations for catalyzed hydroamination of mono-substituted allenes **49** with secondary amines to give a mixture of allylic amines **51** (hydroamination product) and **52** in the presence of a $Pd(dba)_2/PPh_3/Et_3NHI$ catalytic system (dba = dibenzylidene-acetone) (Scheme 2.2) [19]. These reactions have been improved (yields, reaction rates, and selectivity) to give only allylic amines by using 1, 1′-bis(diphenylphosphino)-ferrocene and acetic acid instead of PPh_3 and Et_3NHI, respectively (Scheme 2.3) [20].



47 **48** **49**

Ar = 2,6-dimethylphenyl

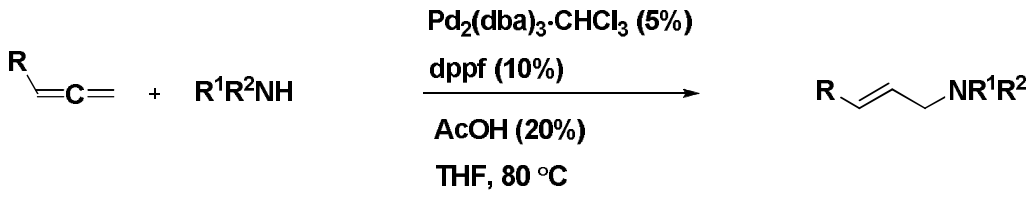
Scheme 2.1 Zirconium-catalyzed conversion of allenes to imines



49 **50** **51** **52**

R = *n*-C_7H_{15}, Ph; R^1R^2NH = Et_2NH, pyrrolidine, piperidine

Scheme 2.2 Palladium-catalyzed hydroamination of mono-substituted allenes

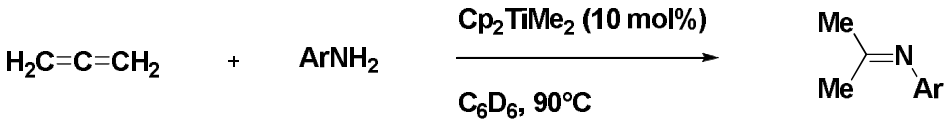


53 **54** **55**

R = Ph, *p*-MeC_6H_4, *p*-$CF_3OC_6H_4$; $R^1 = R^2$ = Bn, Ph; R^1 = Ph, R^2 = 2-naphtyl

Scheme 2.3 Synthesis of allylic amines from mono-substituted allenes

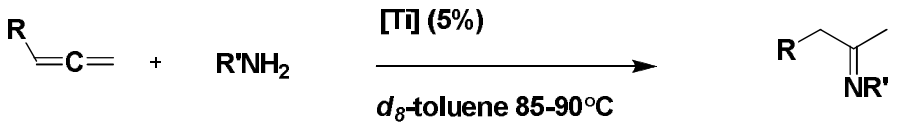
In 2001, Johnson and Bergman used imidotitanium complexes (Cp_2TiMe_2) catalyzed hydroamination of allene **47** with amine **48** in C_6D_6 at 90 °C to give the *anti*-Markovnikov addition product **49** (Scheme 2.4) [21]. In 2006, Schafer group and co-worker used a bis(amidate)-bis(amido) titanium complex as a precatalyst for the intermolecular hydroamination of allenes **56** with amines **57** to give imines **58**, which must be reduce by $LiAlH_4/Et_2O$ to give substituted amines (Scheme 2.5) [22].



47 **48** **49**

Ar = 2,6-dimethylphenyl

Scheme 2.4 Imidoitanium -catalyzed conversion of allenes to imines

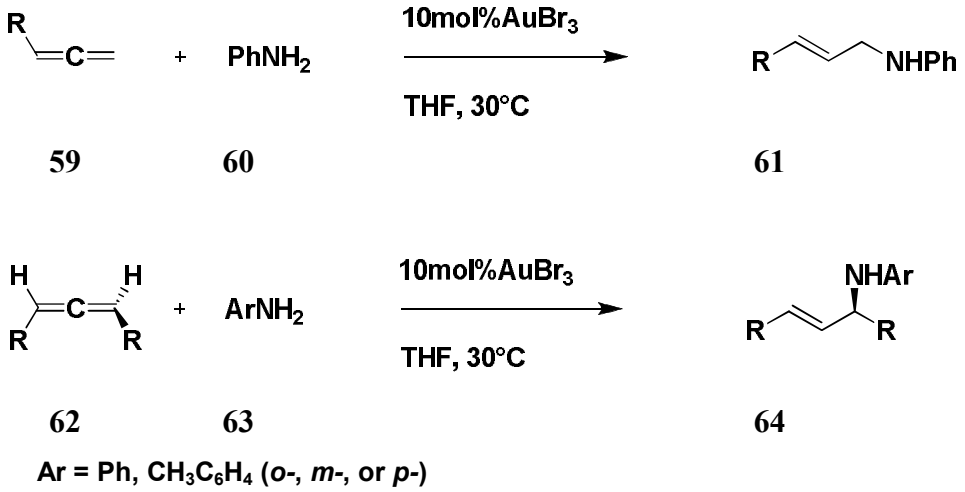


56 **57** **58**

R = Ph; R´ = Ph, 2,6-dimethylphenyl

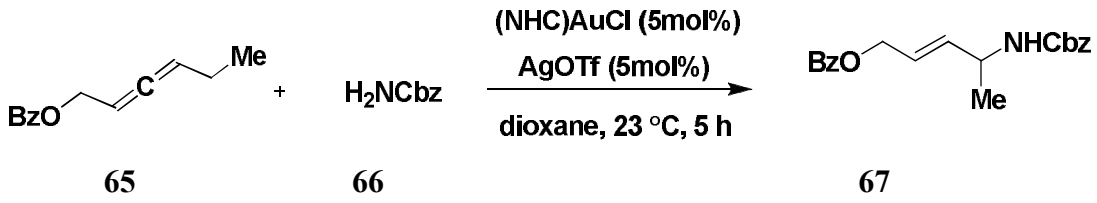
Scheme 2.5 Bis(amidate)-bis(amido) titanium -catalyzed conversion of allenes to imines

In the same year, Nishina and Yamamoto reported the intermolecular hydroamination of allenes **59** with aniline **60** takes place with gold(III) catalyst at ambient temperature in tetrahydrofuran to give corresponding allylic amine **61** in good to high yield. Furthermore, the axial chirality of allenes **62** can be transferred with very high *ee* values to the product **64** (Scheme 2.6) [23].



Scheme 2.6 Gold-catalyzed hydroamination of allenes with arylamine

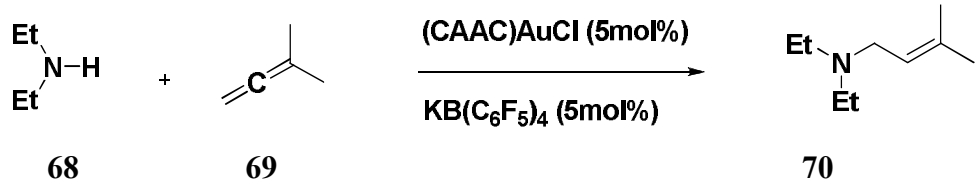
Kinder and co-workers reported intermolecular hydroamination of 2,3-pentadienyl benzoate **65** with benzyl carbamate in the presence of a 1:1 mixture of (NHC)AuCl and AgOTf at 23 °C to give (*E*)-4-(benzyloxycarbonylamino)-2-pentenyl benzoate **67** in good yield as a single regio- and diastereomerallylic (Scheme 2.7) [24].



Scheme 2.7 Synthesis of allylic carbamates from allenes

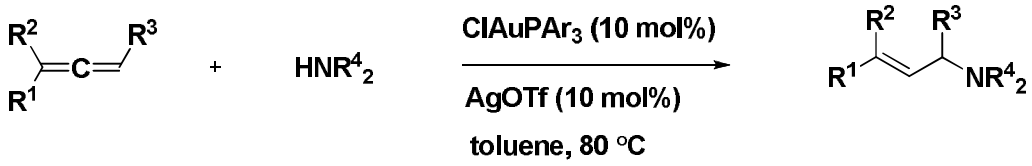
In another set of experiments, Zeng and co-workers reported intermolecular hydroamination of allene **68** with amine **69** in the presence of cationic (CAAC)gold(I)

complex afforded allylic amine **70** (Scheme 2.8) [25]. In the same year, Nishina and Yamamoto reported hydrofunctionalization of allene **71** with amine **72** in the presence of gold catalyst lead to formation of allylic amine **73** (Scheme 2.9) [26].



68 **69** **70**

Scheme 2.8 Synthesis of allylic amines from hydroamination of allenes

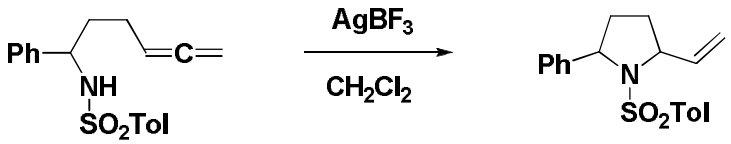


71 **72** **73**

Scheme 2.9 Hydrofunctionlization of allenes with amines

2.2 Intramolecular hydroamintion of allenes

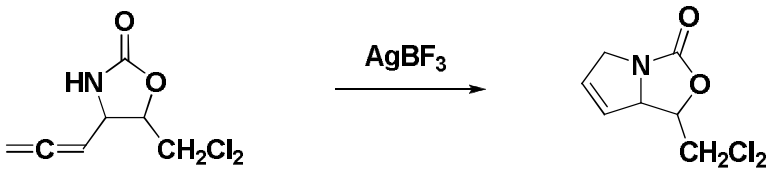
In 1991, Gallagher and co-workers synthesized of 2,4-disustituted pyrrolidine **75** from cyclization of allene **74** using silver tetrafluoroborate ($AgBF_4$) as a catalyst (Scheme 2.10) [27].



74 **75**

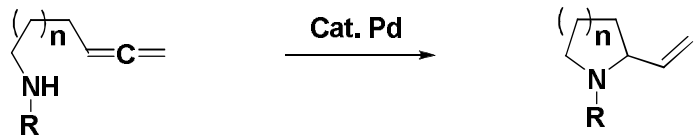
Scheme 2.10 Synthesis of 2,4-disubstituted pyrrolidine

In 1998, Schierle and co-workers used silver tetrafluoroborate ($AgBF_4$) for catalysed hydroamination/cyclization of allene **76** to give **77** in high yield (Scheme 2.11) [28]. In the same year, Meguro and Yamamoto reported a method for synthesis of nitrogen heteroatom via palladium catalyzed intramolecular hydroamination of allenes (Scheme 2.12) [29].



76 **77**

Scheme 2.11 Synthesis of pyrrolidine sugar precursor

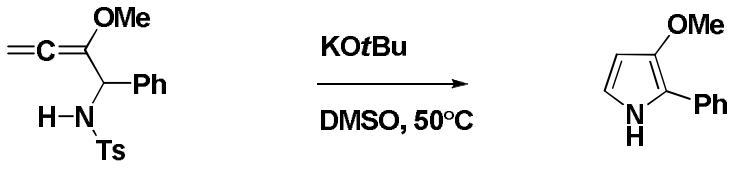


78 **79**

R= H, Ts, Tf

Scheme 2.12 Palladium catalyzed intramolecular hydroamination of allenes

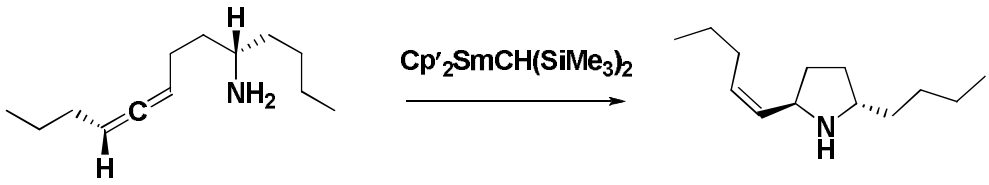
In 1999, Amombo and co-workers synthesized of pyrrole derivatives by cyclization of allene **80** using KO*t*Bu in DMSO at 50 °C (Scheme 2.13) [30].



80 **81**

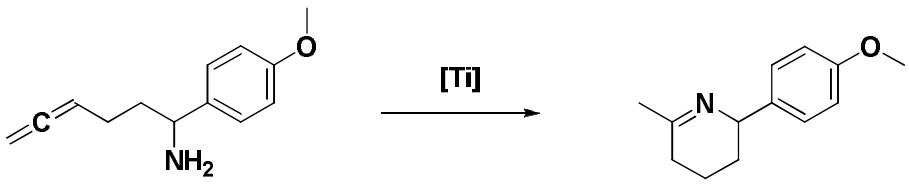
Scheme 2.13 Synthesis of pyrrole derivatives from allene

In the same year, Arredondo and co-workers reported intramolecular hydroamination/cyclization of 1,3-disubstituted aminoallene **82** using organo-lanthanide ($Cp'_2SmCH(SiMe_3)_2$) as a catalyst (Scheme 2.14) [31]. In 2003, Ackermann and co-workers used titanium complex for catalysed hydroamination of allene **84** to give imine **85** as major product (Scheme 2.15) [32].



82 **83**

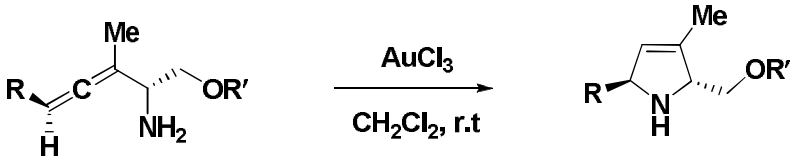
Scheme 2.14 Hydroamination of 1,3-disubstituted aminoallenes



84 **85**

Scheme 2.15 Titanium complex catalyzed hydroamination of allenes

In 2004, Morita and Krause synthesized of 3-pyrroline **87** from cyclo-isomerization of α-aminoallene **86** in the presence gold(III) chloride ($AuCl_3$) in CH_2Cl_2 at room temperature (Scheme 2.16) [33].

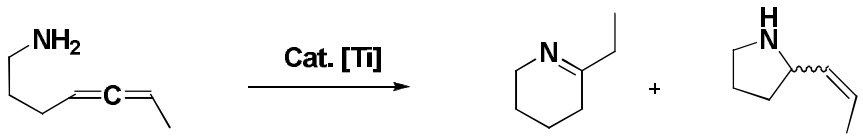


86 **87**

R = Me, *n*-hexyl, Ph; R′= Bn, TBS

Scheme 2.16 Gold(III) chloride-catalyzed hydroamination of allenes

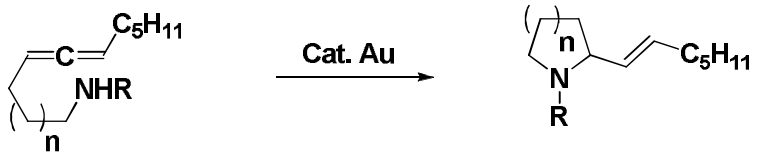
In the same year, Hoover and co-workers reported hydroamination of substituted aminoallene **88** catalyzed by chiral titanium amino-alcohol complex to give **89** and **90** (Scheme 2.17) [34].



88 **89** **90**

Scheme 2.17 Intramolecular hydroamination of substituted aminoallenes

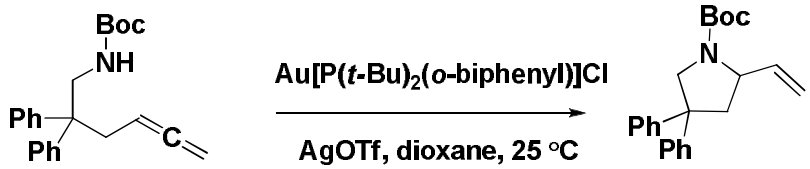
In 2006, Patil and co-workers synthesized of five and six membered nitrogen heterocycles from intramolecular hydroamination of allenes **91** in the presence of gold catalyst (Scheme 2.18) [35]. In the same year, Zhang and co-workers reported intramolecular hydroamination of *N*-allenyl carbamate **93** catalyzed by Au[P(*t*-Bu)$_2$(*o*-biphenyl)]Cl and AgOTf in dioxane at 25 °C to give amine **94** (Scheme 2.19) [36]. In 2007, Lalonde and co-workers reported hydroamination of allene **95** using gold(I) as a catalyst to give **96** in high yield (Scheme 2.20) [37].



91 **92**

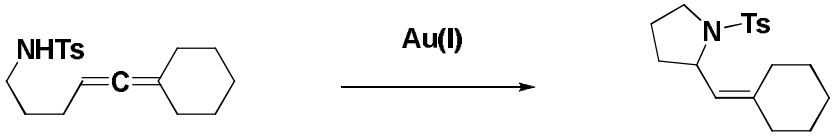
R=Ts, COOEt, Cbz, Bn, Nf

Scheme 2.18 Synthesis of five and six membered nitrogen heterocycles from intramolecular hydroamination of allenes



93 **94**

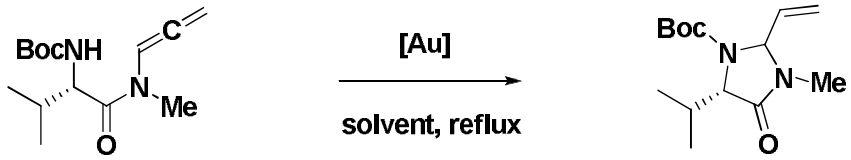
Scheme 2.19 Intramolecular hydroamination of *N*-allenyl carbamates



95 **96**

Scheme 2.20 Gold(I)-catalyzed hydroamination of allenes

In 2009, Manzo and co-workers reported intramolecular hydroamination of α-amino allenemide **97** using gold as a catalyst to give 2-vinylimidazolidinone **98** (Scheme 2.21) [38].



97 **98**

Scheme 2.21 Preparation of 2-vinylimidazolidinones

CHAPTER 3

RESEARCH METHODOLOGY

3.1 Materials

3.1.1 Instrumentation

Nuclear magnetic resonance (^{1}H NMR and ^{13}C NMR) spectra were determined on Varian Mercury Plus 400 spectrometer (400 MHz) at Department of Chemistry, Khon Kaen University. Deuterochloroform ($CDCl_3$) was used as solvent. Chemical shifts were given in parts per million (ppm) downfield from tetramethylsilane (TMS) at 0.00 ppm. Coupling constants (*J*) were reported in Hertz (Hz). Splitting patterns were designated as follows: s (singlet), d (doublet), t (triplet), q (quartet), m (multiplet), br (broad), dd (double doublet), dt (double triplet), app. t (apparent triplet).

High resolution mass spectra (HRMS) were obtained with LC/Mass spectrometer (LC WATERS, PDA) and (Bruker Daltonics, micrOTOF) at Department of Chemistry, Chiang Mai University and Mahidol University, respectively.

Optical rotations were measured with ADP 220 Polarimeter and the infrared (IR) spectra were recorded on a FTIR Perkin-Elmar Spectrum 1 spectrophotometer. IR spectra were recorded as a thin film on sodium chloride plates at the Central Instrumentation Unit, Faculty of Science, Mahasarakham University.

3.1.2 Chromatographic systems

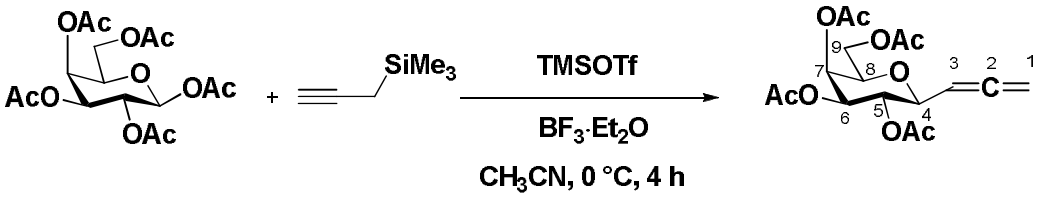
Thin layer chromatography (TLC) was performed on silica gel 60 F_{254} aluminum sheets. Flash column chromatography was used for purification some of products. Merck's silica gels (40-60 mesh) were employed. Using a glass column dry-packed silica gel according to the method of W. Clark Still (1978) [39].

3.1.3 Chemical reagents

All commercially available reagents and solvents were used as received from Merck, Fluka and Aldrich Chemical and where appropriate anhydrous quality material was purchased.

3.2. Methods

3.2.1 Synthesis of *C*-(tetra-*O*-acetyl-*β*-D-galactopyranosyl)allene 101



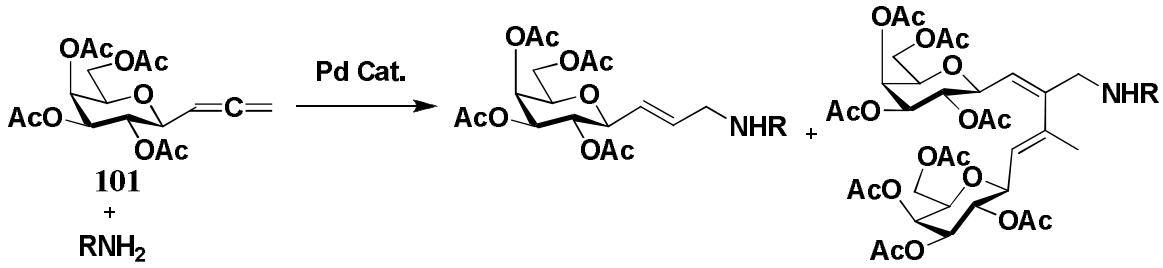
99 **100** **101**

The *C*-(tetra-*O*-acetyl-*β*-D-galactopyranose tetraacetate **101** was prepared according to the literature method [2,40,41]. Trimethylsilyl trifluoromethane sulfonate (TMSOTf) (14.8 mL, 82.0 mmol) and boron trifluoride dietherate (15.2 mL, 123.0 mmol) were sequentially added dropwise over 15 min to a solution of *β*-D-galactopyranose pentaacetate **99** (16.0 g, 41.0 mmol) and propargyl trimethylsilane (PTMS) **100** (16.0 g, 131.2 mmol) in anhydrous MeCN (200 mL). The reaction mixture was stirred for 4 h. at 0 °C, diluted with CH_2Cl_2 (200 mL), quenched with 1 M HCl (80 mL) and then saturated beine (100 mL). The organic layer was separated. Dried (Na_2SO_4), filtered and filtrate was evaporated. Purification of the residue by column chromatography, eluting with 2:1 v/v hexane-diethyl ether, gave the product (10.6g, 28.7 mmol, 71%) as colorless plates, mp 62-64 °C (diethyl ether).

^{1}H NMR (400 MHz, $CDCl_3$): δ 5.43 (2H, d, J = 1.7, 1-H), 5.35 (1H, dd, J = 5.6 Hz, 7-H), 5.23-5.27 (2H, m, 5-H, 6-H), 4.92 (2H, 2d, J = 5.6, 9.2 Hz, 9-H), 4.24 (1H, d, J = 6.7 Hz, 5-H), 4.06-4.14 (2H, m, 4-H, 8-H), 2.05, 2.04, 2.03, 2.00 (12H, 4xs, 4xOCOMe).

3.2.2 Palladium-catalyzed hydroamination of *C*-(tetra-*O*-acetyl-*β*-D-galactopyranosyl)allene 101 with amines

3.2.2.1 General procedure A



All reactions were performed under an atmosphere of air. A reaction tube was charged with the *C*-(tetra-*O*-acetyl-*β*-D-galactopyranosyl)allene **101** (1 equiv.), amines (3 equiv.), Pd salts (catalyst, 5-10 mol %), PPh_3 (ligand, 5 mol%), carboxylic acid (10-100 mol%), LiCl or LiBr (additive, 5 mol%), and solvent (0.5 mL). The mixture was either stirred at room temperature or heated at 60 °C for 24 h, then the solvent was evaporated under reduced pressure, and the residue was purified by flash column chromatography on silica gel to give the products.

3.2.2.1.1 Palladium-catalyzed hydroamination of *C*-(tetra-*O*-acetyl-*β*-D-galactopyranosyl)allene with aniline

According to the general procedure A, a mixture of *C*-(tetra-*O*-acetyl-*β*-D-galactopyranosyl)allene **101** (100 mg, 0.27 mmol), aniline **102** (0.81 mmol), $Pd_2(dba)_3{\cdot}CHCl_3$ (5 mol%), PPh_3(10 mol%), CH_3COOH (20 mol%) in tetrahydrofuran (THF) (0.5 mL) was stirred at 60 ºC for 24 h, then the solvent was evaporated under reduced pressure, and the residue was purified by flash column chromatography on silica gel, eluting with 2:1 v/v hexane-ethyl acetate, gave the mixtures of diallylated acetate **124** and diallylated amine **125** in 35% and 10% yields, respectively, along with trace amounts desired allylic amine **114**.

According to the general procedure A, a mixture of *C*-(tetra-*O*-acetyl-*β*-D-galactopyranosyl)allene **101** (100 mg, 0.27 mmol), aniline **102** (0.81 mmol), $Pd(OAc)_2$ (5 mol%), trifluoroacetic acid (TFA) (20 mol%) in tetrahydrofuran (THF) (0.5 mL) was stirred at room temperature for 24 h, then the solvent was evaporated

under reduced pressure, and the residue was purified by flash column chromatography on silica gel, eluting with 2:1 v/v hexane-ethyl acetate, gave the mixtures of desired allylic amine **114** (42%) and diallylated amine **125** (12%) as a byproduct.

3.2.2.1.2 Palladium-catalyzed hydroamination of *C*-(tetra-*O*-acetyl-*β*-D-galactopyranosyl)allene with *p*-anisidine

According to the general procedure A, a mixture of *C*-(tetra-*O*-acetyl-*β*-D-galactopyranosyl)allene **101** (100 mg, 0.27 mmol), *p*-anisidine **103** (0.81 mmol), $Pd(OAc)_2$ (5 mol%), trifluoroacetic acid (TFA) (20 mol%) in tetrahydrofuran (THF) (0.5 mL) was stirred at room temperature for 24 h, then the solvent was evaporated under reduced pressure, and the residue was purified by flash column chromatography on silica gel, eluting with 2:1 v/v hexane-ethyl acetate, gave the desired allylic amine **115** (16%).

3.2.2.1.3 Palladium-catalyzed hydroamination of *C*-(tetra-*O*-acetyl-*β*-D-galactopyranosyl)allene with *p*-nitroaniline

According to the general procedure A, a mixture of *C*-(tetra-*O*-acetyl-*β*-D-galactopyranosyl)allene **101** (100 mg, 0.27 mmol), *p*-nitroaniline **104** (0.81 mmol), $Pd(OAc)_2$ (5 mol%), trifluoroacetic acid (TFA) (20 mol%) in tetrahydrofuran (THF) (0.5 mL) was stirred at room temperature for 24 h, then the solvent was evaporated under reduced pressure, and the residue was purified by flash column chromatography on silica gel, eluting with 2:1 v/v hexane-ethyl acetate, gave the desired allylic amine **116** (22%).

3.2.2.1.4 Palladium-catalyzed hydroamination of *C*-(tetra-*O*-acetyl-*β*-D-galactopyranosyl)allene with *m*-nitroaniline

According to the general procedure A, a mixture of *C*-(tetra-*O*-acetyl-*β*-D-galactopyranosyl)allene **101** (100 mg, 0.27 mmol), *m*-nitroaniline **105** (0.81 mmol), $Pd(OAc)_2$ (5 mol%), trifluoroacetic acid (TFA) (20 mol%) in tetrahydrofuran (THF) (0.5 mL) was stirred at room temperature for 24 h, then the solvent was evaporated under reduced pressure, and the residue was purified by flash column chromatography on silica gel, eluting with 2:1 v/v hexane-ethyl acetate, gave the mixtures of desired allylic amine **117** (25%) and diallylated amine **126** (3%) as a byproduct.

3.2.2.1.5 Palladium-catalyzed hydroamination of *C*-(tetra-*O*-acetyl-*β*-D-galactopyranosyl)allene with 1-naphthylamine

According to the general procedure A, a mixture of *C*-(tetra-*O*-acetyl-*β*-D-galactopyranosyl)allene **101** (100 mg, 0.27 mmol), 1-naphthylamine **106** (0.81 mmol), $Pd(OAc)_2$ (5 mol%), trifluoroacetic acid (TFA) (20 mol%) in tetrahydrofuran (THF) (0.5 mL) was stirred at room temperature for 24 h, then the solvent was evaporated under reduced pressure, and the residue was purified by flash column chromatography on silica gel, eluting with 2:1 v/v hexane-ethyl acetate, gave the mixtures of desired allylic amine **118** (17%) and diallylated amine **127** (6%) as a byproduct.

3.2.3 Gold-catalyzed hydroamination of *C*-(tetra-*O*-acetyl-*β*-D-galactopyranosyl)allene

3.2.3.1 General procedure B

101 **amines** **allylic amines**

All reactions were performed under an inert atmosphere of nitrogen (balloon). A reaction tube was charged with the *C*-(tetra-*O*-acetyl-*β*-D-galactopyranosyl)allene **101** (1 equiv.), amines (3 equiv.), gold-catalyst (10-20 mol%) and solvent (0.5 mL). The mixture was stirred at room temperature for 1-3 day, then the solvent was evaporated under reduced pressure, and the residue was purified by flash column chromatography on silica gel to give the product. The conditions for the highest yield for gold-catalyzed hydroamination of *C*-(tetra-*O*-acetyl-*β*-D-galactopyranosyl)allene with several amines are reported below.

3.2.3.1.1 Gold-catalyzed hydroamination of *C*-(tetra-*O*-acetyl-*β*-D-galactopyranosyl)allene with aniline

According to the general procedure B, a mixture of *C*-(tetra-*O*-acetyl-*β*-D-galactopyranosyl)allene **101** (100 mg, 0.27 mmol), aniline **102** (0.81 mmol), $AuBr_3$ (10 mol%) in tetrahydrofuran (THF) (0.5 mL) was stirred at room temperature for 3

day, then the solvent was evaporated under reduced pressure, and the residue was purified by flash column chromatography on silica gel, eluting with 2:1 v/v hexane-ethyl acetate, gave the desired allylic amine **114** (82%).

3.2.3.1.2 Gold-catalyzed hydroamination of *C*-(tetra-*O*-acetyl-*β*-D-galactopyranosyl)allene with *p*-anisidine

According to the general procedure B, a mixture of *C*-(tetra-*O*-acetyl-*β*-D-galactopyranosyl)allene **101** (100 mg, 0.27 mmol), *p*-anisidine **103** (0.81 mmol), $AuBr_3$ (10 mol%) in tetrahydrofuran (THF) (0.5 mL) was stirred at room temperature for 3 day, then the solvent was evaporated under reduced pressure, and the residue was purified by flash column chromatography on silica gel, eluting with 2:1 v/v hexane-ethyl acetate, gave the desired allylic amine **115** (61%).

3.2.3.1.3 Gold-catalyzed hydroamination of *C*-(tetra-*O*-acetyl-*β*-D-galactopyranosyl)allene with *p*-nitroaniline

According to the general procedure B, a mixture of *C*-(tetra-*O*-acetyl-*β*-D-galactopyranosyl)allene **101** (100 mg, 0.27 mmol), *p*-nitroaniline **104** (0.81 mmol), $AuBr_3$ (10 mol%) in tetrahydrofuran (THF) (0.5 mL) was stirred at room temperature for 3 day, then the solvent was evaporated under reduced pressure, and the residue was purified by flash column chromatography on silica gel, eluting with 2:1 v/v hexane-ethyl acetate, gave the desired allylic amine **116** (47%).

3.2.3.1.4 Gold-catalyzed hydroamination of *C*-(tetra-*O*-acetyl-*β*-D-galactopyranosyl)allene with *m*-nitroaniline

According to the general procedure B, a mixture of *C*-(tetra-*O*-acetyl-*β*-D-galactopyranosyl)allene **101** (100 mg, 0.27 mmol), *m*-nitroaniline **105** (0.81 mmol), $AuBr_3$ (10 mol%) in tetrahydrofuran (THF) (0.5 mL) was stirred at room temperature for 3 day, then the solvent was evaporated under reduced pressure, and the residue was purified by flash column chromatography on silica gel, eluting with 2:1 v/v hexane-ethyl acetate, gave the desired allylic amine **117** (65%).

3.2.3.1.5 Gold-catalyzed hydroamination of *C*-(tetra-*O*-acetyl-*β*-D-galactopyranosyl)allene with 1-naphthylamine

According to the general procedure B, a mixture of *C*-(tetra-*O*-acetyl-*β*-D-galactopyranosyl)allene **101** (100 mg, 0.27 mmol), 1-naphthylamine **106** (0.81 mmol), $AuBr_3$ (10 mol%) in tetrahydrofuran (THF) (0.5 mL) was stirred at room

temperature for 3 day, then the solvent was evaporated under reduced pressure, and the residue was purified by flash column chromatography on silica gel, eluting with 2:1 v/v hexane-ethyl acetate, gave the desired allylic amine **118** (36%).

3.2.3.1.6 Gold-catalyzed hydroamination of *C*-(tetra-*O*-acetyl-*β*-D-galactopyranosyl)allene with *m*-anisidine

According to the general procedure B, a mixture of *C*-(tetra-*O*-acetyl-*β*-D-galactopyranosyl)allene **101** (100 mg, 0.27 mmol), *m*-anisidine **107** (0.81 mmol), $AuBr_3$ (10 mol%) in tetrahydrofuran (THF) (0.5 mL) was stirred at room temperature for 3 day, then the solvent was evaporated under reduced pressure, and the residue was purified by flash column chromatography on silica gel, eluting with 2:1 v/v hexane-ethyl acetate, gave the desired allylic amine **119** (56%).

3.2.3.1.7 Gold-catalyzed hydroamination of *C*-(tetra-*O*-acetyl-*β*-D-galactopyranosyl)allene with *o*-anisidine

According to the general procedure B, a mixture of *C*-(tetra-*O*-acetyl-*β*-D-galactopyranosyl)allene **101** (100 mg, 0.27 mmol), *o*-anisidine **108** (0.81 mmol), $AuBr_3$ (10 mol%) in tetrahydrofuran (THF) (0.5 mL) was stirred at room temperature for 3 day, then the solvent was evaporated under reduced pressure, and the residue was purified by flash column chromatography on silica gel, eluting with 2:1 v/v hexane-ethyl acetate, gave the desired allylic amine **120** (52%).

3.2.3.1.8 Gold-catalyzed hydroamination of *C*-(tetra-*O*-acetyl-*β*-D-galactopyranosyl)allene with *m*-toluidine

According to the general procedure B, a mixture of *C*-(tetra-*O*-acetyl-*β*-D-galactopyranosyl)allene **101** (100 mg, 0.27 mmol), *m*-toluidine **109** (0.81 mmol), $AuBr_3$ (10 mol%) in tetrahydrofuran (THF) (0.5 mL) was stirred at room temperature for 3 day, then the solvent was evaporated under reduced pressure, and the residue was purified by flash column chromatography on silica gel, eluting with 2:1 v/v hexane-ethyl acetate, gave the desired allylic amine **121** (39%).

3.2.3.1.9 Gold-catalyzed hydroamination of *C*-(tetra-*O*-acetyl-*β*-D-galactopyranosyl)allene with *p*-toluidine

According to the general procedure B, a mixture of *C*-(tetra-*O*-acetyl-*β*-D-galactopyranosyl)allene **101** (100 mg, 0.27 mmol), *p*-toluidine **110** (0.81 mmol), $AuBr_3$ (10 mol%) in tetrahydrofuran (THF) (0.5 mL) was stirred at room temperature

for 3 day, then the solvent was evaporated under reduced pressure, and the residue was purified by flash column chromatography on silica gel, eluting with 2:1 v/v hexane-ethyl acetate, gave the desired allylic amine **122** (39%).

3.2.3.1.10 Gold-catalyzed hydroamination of *C*-(tetra-*O*-acetyl-*β*-D-galactopyranosyl)allene with 4-aminoacetophenone

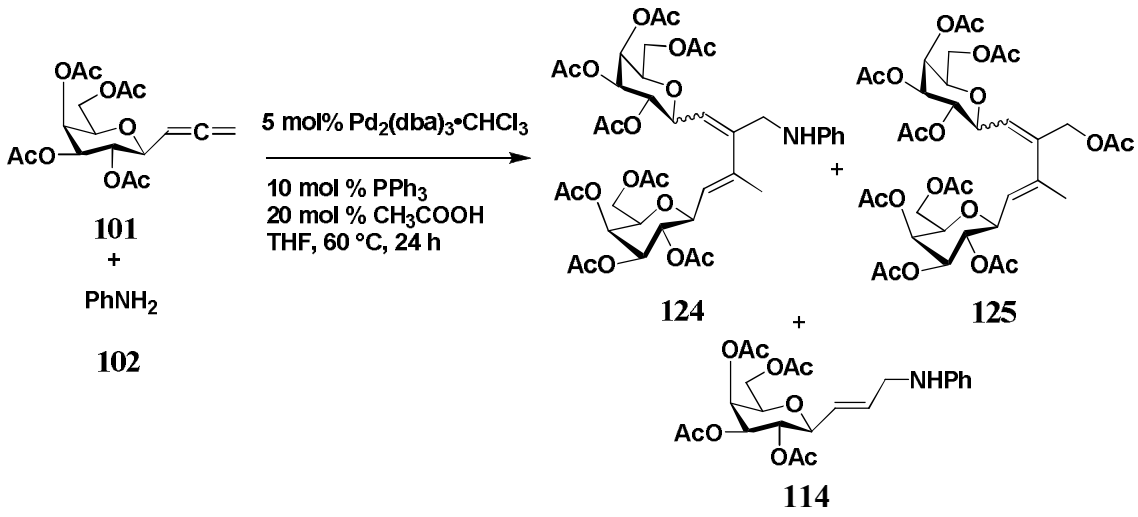
According to the general procedure B, a mixture of *C*-(tetra-*O*-acetyl-*β*-D-galactopyranosyl)allene **101** (100 mg, 0.27 mmol), 4-aminoacetophenone **111** (0.81 mmol), $AuBr_3$ (10 mol%) in tetrahydrofuran (THF) (0.5 mL) was stirred at room temperature for 3 day, then the solvent was evaporated under reduced pressure, and the residue was purified by flash column chromatography on silica gel, eluting with 2:1 v/v hexane-ethyl acetate, gave the desired allylic amine **123** (70%).

CHAPTER 4

RESULTS AND DISCUSSION

4.1 Palladium-catalyzed hydroamination of *C*-(tetra-*O*-acetyl-*β*-D-galactopyranosyl)allene

Initially the reaction of *C*-(tetra-*O*-acetyl-*β*-D-galactopyranosyl)allene **101** with aniline **102** using Yamamoto's conditions (5 mol% $Pd_2(dba)_3{\cdot}CHCl_3$, 10 mol% PPh_3, 20 mol% CH_3COOH in THF at 60 °C for 24 h) was studied [20]. Quite unexpectedly, a mixture of diallylated acetate **124** and diallylated amine **125** was obtained in 35% and 10% yields, respectively, along with trace amounts of **114** (Scheme 4.1). When the same reaction was carried out in the presence of trifluoroacetic acid (TFA), the mixture of desired allylic amine **114** (29%) and a minor amount (18%) of dienic amine **125** was obtained (entry 2 in Table 4.1).



Scheme 4.1 Palladium-catalyzed hydroamination of *C*-(tetra-*O*-acetyl-*β*-D-galactopyranosyl)allene

The reaction conditions were adjusted to find a suitable catalyst-ligand-solvent-carboxylic acid system for the desired transformation. The results are summarized in

Table 4.1. These results suggested that both Pd(0) and Pd(II) catalysts and carboxylic acid play a dramatic part on the yields of the desired allylic amine **114**. In addition, a profound solvent effect on the reaction was observed. THF was found to be the best solvent (Table 4.1, entry 20).

Table 4.1 Effect of reaction parameters on palladium-catalyzed hydroamination of *C*-(tetra-*O*-acetyl-*β*-D-galactopyranosyl)allene **101** with aniline **102** [a]

Entry	Palladium salt and ligand (mol %)	Carboxylic acid and additive (mol %)	Solvent	Temperature (°C)	% Yield[b]	
					114	**125**
1	$Pd_2(dba)_3.CHCl_3$ (5), Ph_3P (10)	CH_3COOH	THF	60	3	10
2	$Pd_2(dba)_3.CHCl_3$ (5), Ph_3P (10)	TFA (20)	THF	60	29	18
3	$Pd_2(dba)_3.CHCl_3$ (5), Ph_3P (10)	TFA (20)	THF	rt	10	46
4	$Pd_2(dba)_3$ (5), Ph_3P (10)	TFA (20)	THF	60	15	42
5	$Pd_2(dba)_3$ (5), Ph_3P (10)	TFA (20)	THF	rt	13	42
6	$Pd_2(dba)_3$ (5), TFP (10)	TFA (20)	THF	rt	6	47
7	$Pd_2(dba)_3$ (5), Ph_3P (10)	formic acid (20)	THF	rt	ND	14
8	$Pd_2(dba)_3$ (5), Ph_3P (10)	benzoic acid (20)	THF	rt	ND	17
9	$Pd(OAc)_2$(5), Ph_3P (20)	TFA (20)	THF	rt	6	48

[a] All reactions were carried out with conditions: *C*-(tetra-*O*-acetyl-*β*-D-galactopyranosyl)allene **101** (0.27 mmol) and aniline **102** (0.81mmol) in 0.5 mL of solvent for 24 h. [b] Isolated yields. ND = Not detected.

Table 4.1 (Continued) Effect of reaction parameters on palladium-catalyzed hydroamination of *C*-(tetra-*O*-acetyl-*β*-D-galactopyranosyl)allene **101** with aniline **102** [a]

Entry	Palladium salt and ligand (mol %)	Carboxylic acid and additive (mol %)	Solvent	Temperature (°C)	% Yield[b]	
					114	**125**
10	$Pd_2(dba)_3$ (5)	TFA (20)	THF	rt	21	12
11	$Pd_2(dba)_3$ (5)	TFA (20)	THF	60	23	12
12[c]	$Pd_2(dba)_3$ (5)	TFA (20)	THF	60	14	26
13	$Pd_2(dba)_3$ (5)	TFA (50)	THF	rt	25	13
14	$Pd_2(dba)_3$ (5)	TFA (100)	THF	rt	22	10
15	$Pd_2(dba)_3$ (5)	TFA (10)	THF	rt	13	7
16	$Pd_2(dba)_3$ (5)	TFA (5)	THF	rt	15	13
17	$Pd_2(dba)_3$ (5)	TFA (5)	DMF	rt	ND	17
18	$Pd_2(dba)_3$ (5)	TFA (5)	CH_3CN	rt	8	14
19	$Pd_2(dba)_3$ (5)	TFA (5)	Toluene	rt	2	5
20	$Pd(OAc)_2$(5)	TFA (20)	THF	rt	42	12
21	$Pd(OAc)_2$(5)	TFA (20)	THF	60	32	9
22	$Pd(OAc)_2$(5)	acetic acid (20)	THF	rt	25	9
23	$Pd(OAc)_2$(5)	-	THF	rt	17	3
24	$Pd(OAc)_2$(5)	-	THF	60	12	5
25[c]	$Pd(OAc)_2$(5)	TFA (20)	THF	rt	21	13
26	$Pd(OAc)_2$(5)	TFA (20), $K_2S_2O_8$(250)	THF	rt	25	19

[a] All reactions were carried out with conditions: *C*-(tetra-*O*-acetyl-*β*-D-galactopyranosyl)allene **101** (0.27 mmol) and aniline **102** (0.81mmol) in 0.5 mL of solvent for 24 h. [b] Isolated yields. [c] Catalyst 10 mol%. ND = Not detected.

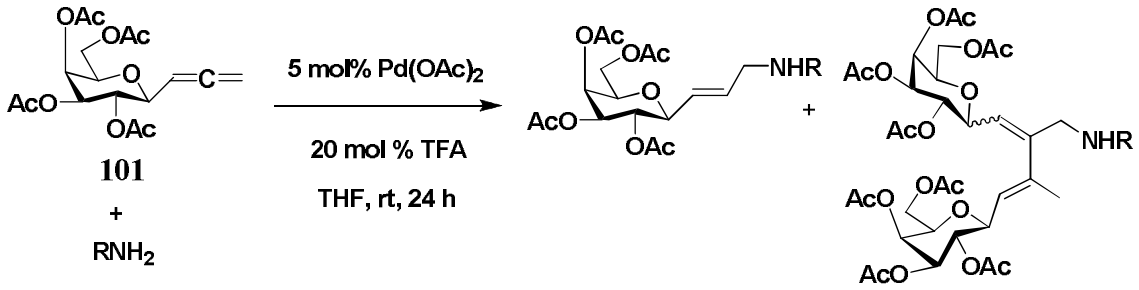
Table 4.1 (Continued) Effect of reaction parameters on palladium-catalyzed hydroamination of *C*-(tetra-*O*-acetyl-*β*-D-galactopyranosyl)allene **101** with aniline **102** [a]

Entry	Palladium salt and ligand (mol %)	Carboxylic acid and additive (mol %)	Solvent	Temperature (°C)	% Yield[b]	
					114	**125**
27	$Pd(OAc)_2$(5)	TFA (20), $K_2S_2O_8$(100)	THF	rt	17	12
28	$Pd(OAc)_2$(5)	TFA (20), LiCl (200)	THF	rt	31	ND
29	$Pd(OAc)_2$(5)	LiCl (200)	THF	rt	32	ND
30	$Pd(OAc)_2$(5)	TFA(50)	THF	rt	31	16
31	$Pd(OAc)_2$(5)	TFA(50)	THF	rt	32	15
32	$Pd(OAc)_2$(5)	TFA (20)	DCM	rt	30	14
33	$Pd(OAc)_2$(5)	TFA (20)	CH_3CN	rt	33	14
34	$Pd(OAc)_2$(5)	TFA (20)	Toluene	rt	24	15
35	$Pd(OAc)_2$(5)	TFA (20)	Dioxane	rt	14	9
36	-	TFA (20)	THF	rt-60°C	ND	ND

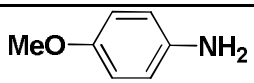
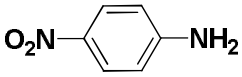
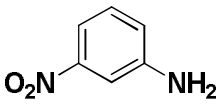
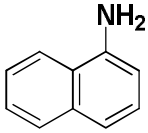
[a] All reactions were carried out with conditions: *C*-(tetra-*O*-acetyl-*β*-D-galactopyranosyl)allene **101** (0.27 mmol) and aniline **102** (0.81mmol) in 0.5 mL of solvent for 24 h. [b] Isolated yields. ND = Not detected.

The scope of the palladium-catalyzed hydroamination of *C*-(tetra-*O*-acetyl-*β*-D-galactopyranosyl)allene **101** with amines under the optimized condition is summarized in Table 4.2. From the results, it was found that in the presence of 5 mol% $Pd(OAc)_2$, 20 mol% TFA in THF, the reaction of *C*-(tetra-*O*-acetyl-*β*-D-galactopyranosyl)allene **101** with *p*-anisidine **103** and *p*-nitroaniline **104** gave the desire allylic amines **115** and **116** in moderate of yields without the byproduct (Table 4.2, entry 1 and 2, respectively).

Table 4.2 Palladium-catalyzed hydroamination of *C*-(tetra-*O*-acetyl-*β*-D-galactopyranosyl)allene **101** with amines [a]



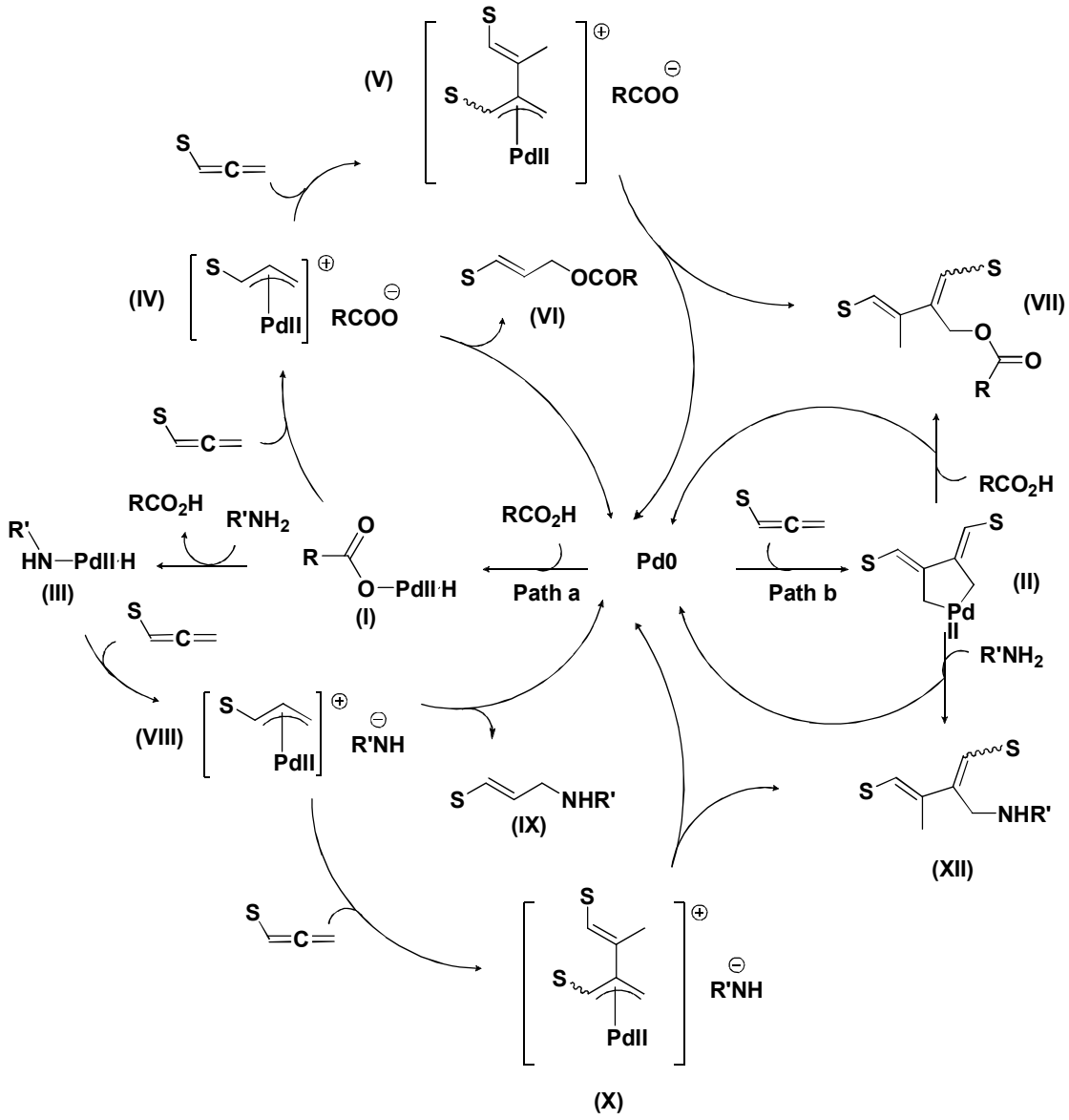
101 + **106-109** → **117-120** + **126-127**

Entry	Amine	Product Yield[b] (%)	
1	 **103**	**115** (16)	(ND)
2	 **104**	**116** (22)	(ND)
3	 **105**	**117** (25)	**126** (3)
4	 **106**	**118** (17)	**127** (6)

[a] Reaction condition: *C*-(tetra-*O*-acetyl-*β*-D-galactopyranosyl)allene **101** (0.27 mmol); amine (0.81 mmole); $Pd(OAc)_2$(5 mol %); TFA (20 mol %); THF (0.5 mL); room temperature for 24 h. [b] Isolated yields. ND = Not detected.

In the case of using *m*-nitroaniline **105** and 1-naphthylamine **106** obtained allylic amines **117** and **118** in moderate of yields along with trace amounts of diallylated amines **126** and **127** (Table 4.2, entry 3 and 4, respectively). Other amines, such as

morpholine, *n*-butylamine, *n*-octylamine, and benzylamine were no reaction occurred after testing.

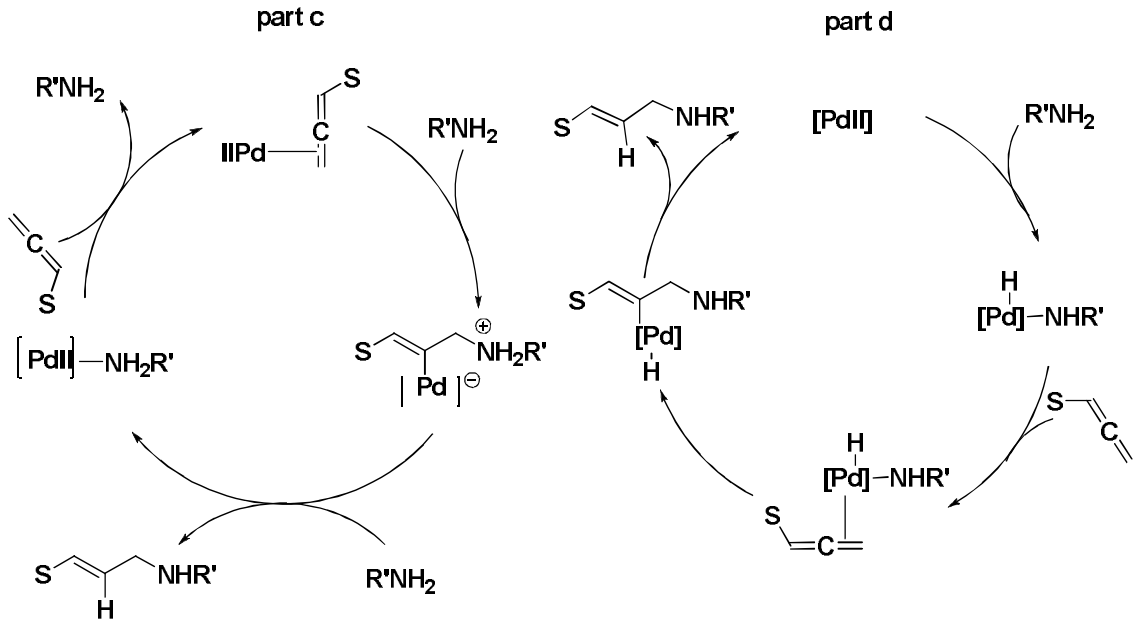


S = *C*-(tetra-*O*-acetyl-*β*-D-galactopyranosyl)-

Scheme 4.2 Proposed mechanistic pathways for Pd(0)-catalyzed hydroamination of *C*-(tetra-*O*-acetyl-*β*-D-galactopyranosyl)allene

A possible reaction pathway for Pd(0)-catalyzed hydroamination is shown in Scheme 4.2. The two principal mechanistic pathways to be considered for hydroamination involve either activation of the amine (path a) or palladacycle formation

(path b). The oxidative addition of carboxylic acid to Pd(0) produced hydropalladium(II) intermediate species (**I**), which on reaction with amine would give intermediate (**III**) and carboxylic acid. Species **III** would form the π-allylpalladium intermediate (**VIII**) with *C*-(tetra-*O*-acetyl-β-D-galactopyranosyl)allene **101** which, after reductive elimination, would give the hydroamination product (**IX**). The formation of diallylated acetate (**VII**) and diallylated amine (**XII**) could arise by a combination of either path a or path b, intermediate (**V, X**) (Scheme 4.2, path a) and intermediate (**II**) (Scheme 4.2, path b).



S = *C*-(tetra-*O*-acetyl-β-D-galactopyranosyl)-

Scheme 4.3 Proposed mechanistic pathways for Pd(II)-catalyzed hydroamination of *C*-(tetra-*O*-acetyl-β-D-galactopyranosyl)allene

On the other hand, hydroamination of *C*-(tetra-*O*-acetyl-β-D-galacto-pyranosyl)allene **101** gave a yield of 42% allylic amine **114** using $Pd(OAc)_2$ and TFA in THF (Table 4.1, entry 20). The two possible mechanistic pathways to be considered for hydroamination involve either activation of the amine or activation of the allene. In the allene activation (Scheme 4.3, path c) the CH_2═C double bond of allene is activated by coordination to the palladium, and the C—N bond is formed by nucleophilic attack of amine on the coordinate allene. To liberate the product, the palladium—carbon bond in

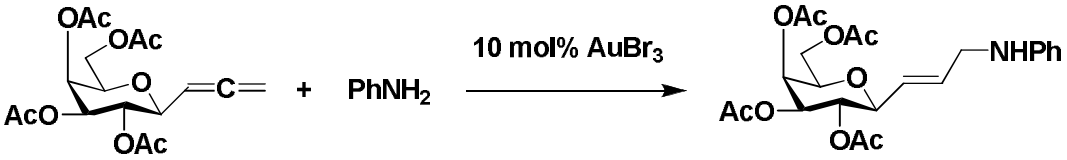
the resulting ammonioallyl complex has to be cleaved. This can be brought about either by direct protonolysis or by protonation at the palladium with subsequent C—H reductive elimination. Amine activation (Scheme 4.3, path d) proceeds via oxidative addition of the amine N—H bond to the coordinatively unsaturated palladium center, forming the amidohydrido complex, followed by allene coordination, insertion of the allene into the palladium—nitrogen bond, and finally C—H reductive elimination, liberating the product and closing the catalytic cycle.

In summary, the palladium(0)- and palladium(II)-catalyzed methods for hydroamination of *C*-(tetra-*O*-acetyl-*β*-D-galactopyranosyl)allene **101** with a variety of aromatic amines were successfully developed.

4.2 Gold-catalyzed hydroamination of *C*-(tetra-*O*-acetyl-*β*-D-galactopyranosyl)allene

In the initial experiment, the hydroamination of *C*-(tetra-*O*-acetyl-*β*-D-galacto-pyranosyl)allene **101** with aniline **102** in the presence of catalytic amount of $AuBr_3$ or $(PPh_3)AuCl$ was examined. Further optimization led to find that the reaction of *C*-(tetra-*O*-acetyl-*β*-D-galactopyranosyl)allene **101** and aniline **102** in THF proceeded smoothly at ambient temperature in the presence of 10 mol % of $AuBr_3$ and the corresponding allylic amine**114** was obtained in 82% yield after 3 day (Table 4.3, entry 3).

Table 4.3 Effect of reaction parameters on gold-catalyzed hydroamination of *C*-(tetra-*O*-acetyl-*β*-D-galactopyranosyl)allene **101** with aniline **102** [a]



101 **102** **114**

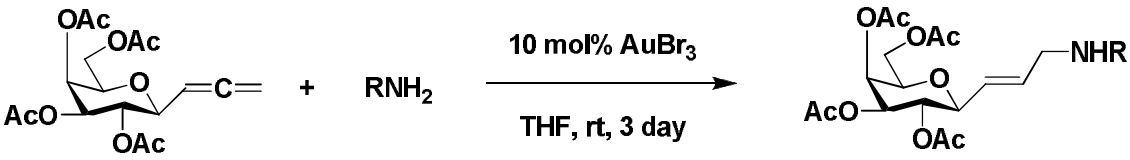
Entry	Reaction time (day)	Catalyst (10 mol %)	Solvent (0.5 mL)	Product[b] (%) 114
1	1	$AuBr_3$	THF	52
2	2	$AuBr_3$	THF	79
3	3	$AuBr_3$	THF	82
4	3	$AuBr_3$	DCM	18
5	3	$AuBr_3$	CH_3CN	27
6	3	$AuBr_3$	Toluene	31
7	1	$(PPh_3)AuCl$	THF	ND

[a] Reaction conditions: *C*-(tetra-*O*-acetyl-*β*-D-galactopyranosyl)allene **101** (0.27 mmol); amine (0.81 mmol); $AuBr_3$ (10 mol %) in 0.5 mL of solvent at room temperature. [b] Isolated yields. ND = Not detected.

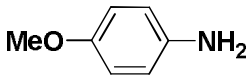
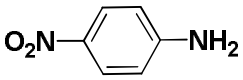
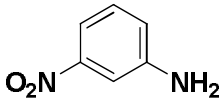
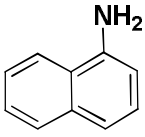
The reaction under this optimized condition gave **114** in 18% yield in DCM, 27% yield in CH_3CN and 31% yield in toluene. Other catalyst, such as $(PPh_3)AuCl$, did not promote the hydroamination of *C*-(tetra-*O*-acetyl-*β*-D-galactopyranosyl)allene **101**.

The scope of the gold-catalyzed hydroamination of *C*-(tetra-*O*-acetyl-*β*-D-galactopyranosyl)allene **101** with amines under the optimized condition is summarized in Table 4.4.

Table 4.4 Gold-catalyzed hydroamination of *C*-(tetra-*O*-acetyl-*β*-D-galactopyranosyl)allene **101** with amines [a]

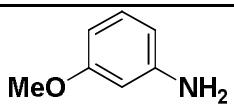
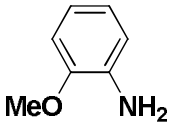
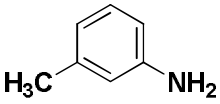
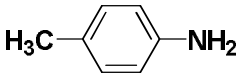
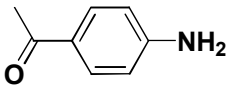
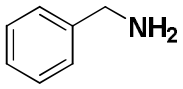
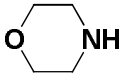


101 **103-113** **115-123**

Entry	Amine	Product[b] (%)
1	 **103**	**115** (61)
2	 **104**	**116** (47)
3	 **105**	**117** (65)
4	 **106**	**118** (36)

[a] Reaction conditions: *C*-(tetra-*O*-acetyl-*β*-D-galactopyranosyl)allene **101** (0.27 mmol); amine (0.81 mmol); $AuBr_3$ (10 mol %); THF (0.5 mL); room temperature for 3 day. [b] Isolated yields. ND = Not detected

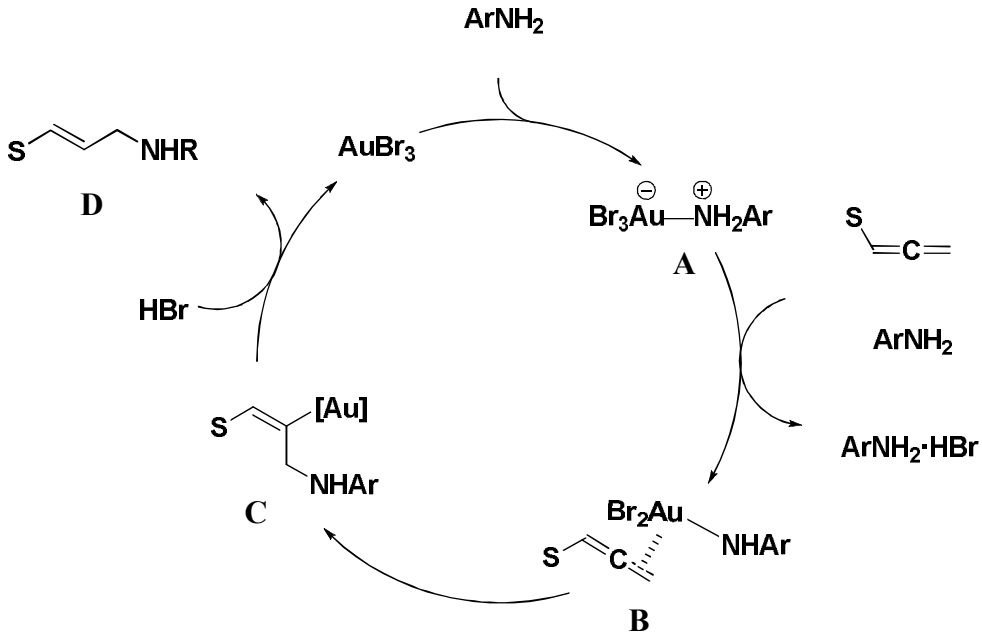
Table 4.4 (Continued) Gold-catalyzed hydroamination of *C*-(tetra-*O*-acetyl-*β*-D-galactopyranosyl)allene **101** with amines [a]

Entry	Amine	Product[b] (%)
5	 **107**	**119** (56)
6	 **108**	**120** (52)
7	 **109**	**121** (39)
8	 **110**	**122** (39)
9	 **111**	**123** (70)
10	 **112**	(ND)
11	 **113**	(ND)

[a] Reaction conditions: *C*-(tetra-*O*-acetyl-*β*-D-galactopyranosyl)allene **101** (0.27 mmol); amine (0.81 mmol); $AuBr_3$ (10 mol %); THF (0.5 mL); room temperature for 3 day. [b] Isolated yields. ND = Not detected.

As shown in Table 4.4, the intermolecular hydroamination with aliphatic amines is rather difficult compared to that with aromatic amines, although the intermolecular version with aliphatic amines is known [23]. The $AuBr_3$ catalysis system described above did not work with the aliphatic amines at all [23,26].

A mechanism for $AuBr_3$-catalyzed hydroamination of allene with aromatic amines has been reported by Yamamoto *et. al*. in 2009 (Scheme 4.4) [26].

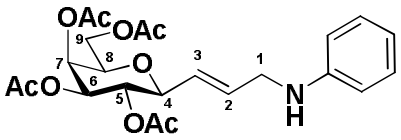


S = *C*-(tetra-*O*-acetyl-*β*-D-galactopyranosyl)-

Scheme 4.4 A mechanism for the $AuBr_3$-catalyzed hydroamination of *C*-(tetra-*O*-acetyl-*β*-D-galactopyranosyl)allene **101**

The catalytic cycle is most probably initially by the coordination of the allene to the gold-amine complex **A** to afford the intermediate **B**. Perhaps the amino-auration takes place through **B** to give the gold-alkenyl intermediate **C**, which produces **D** and $AuBr_3$ upon protonation by HBr.

4.3 Physical data



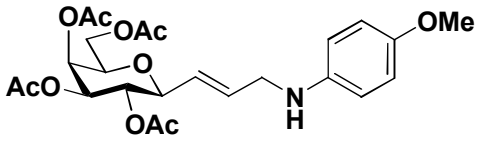
114

IR (film) cm^{-1}: 3418, 2361, 1746, 1633, 1604, 1507, 1371, 1226, 105

^{1}H-NMR (400 MHz, $CDCl_3$): δ 7.17 (2H, app. t, *J* 8.4 and 7.2, Ar□H), 6.71 (1H, app. t, *J* 8.4 and 7.2, Ar□H), 6.60 (2H, d, *J* 7.6, Ar□H), 5.98 (1H, dt, *J* 15.6 and 5.2, 2□H), 5.82 (1H, q, *J* 15.6 and 5.2, 3□H), 5.37 (1H, d, *J* 3.2, 6□H), 5.28 (1H, dd, *J* 10.4 and 5.6, 7□H), 5.10 (1H, dd, *J* 10.4 and 3.2, 5□H), 4.80 (1H, t, *J* 3.2, 4□H), 4.00–4.14 (3H, m, 8□H and 2x9□H), 3.84 (2H, d, *J* 5.2, 1□H), 1.90–2.10 (12H, 4xs, 4xOCOMe)

^{13}C-NMR (100 MHz, $CDCl_3$): δ 170.52, 170.19, 170.06, 169.87, 147.64, 134.47, 129.27, 123.49, 117.87, 113.14, 72.53, 68.31, 68.29, 68.01, 61.83, 45.62, 20.73, 20.69, 20.66

HRMS: calcd for $C_{23}H_{30}NO_9$ (M+H): m/z 464.1921; found: m/z 464.1968



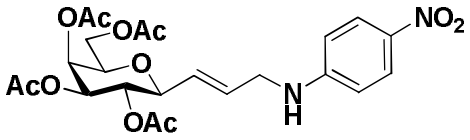
115

IR (film) cm^{-1}: 3442, 2362, 1747, 1638, 1515, 1372, 1231, 1023

^{1}H-NMR (400 MHz,$CDCl_3$): δ 6.79 (2H, d, *J* 8.8, Ar□H), 6.60 (2H, d, *J* 8.8, Ar□H), 5.97 (1H, dt, *J* 15.6 and 5.2, 2□H), 5.85 (1H, q, *J* 15.6 and 5.2, 3□H), 5.42 (1H, d, *J* 3.2, 6□H), 5.29 (1H, dd, *J* 10.4 and 5.6, 7□H), 5.12 (1H, dd, *J* 10.4 and 3.2, 5□H), 4.79 (1H, t, *J* 3.2, 4□H), 4.00–4.10 (3H, m, 8□H and 2x9□H), 3.80 (2H, d, *J* 5.2, 1□H), 1.90–2.10 (15H, 5xs, 5xOCOMe)

^{13}C-NMR (100 MHz, $CDCl_3$): δ 170.53, 170.23, 170.13, 170.08, 152.44, 141.82, 134.79, 123.41, 114.92, 114.57, 72.50, 68.40, 68.33, 68.04, 68.01, 61.87, 45.94, 20.72, 20.70, 20.66

HRMS: calcd for $C_{24}H_{31}NO_{10}Na$ (M+Na): m/z 516.1846; found: m/z 516.2006



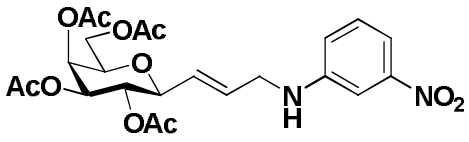
116

IR (film) cm^{-1}: 3439, 2362, 1747, 1636, 1604, 1474, 1372, 1312, 1228, 1113, 1048

^{1}H-NMR (400 MHz, $CDCl_3$): δ 8.09 (2H, d, *J* 8.8, Ar□H), 6.58 (2H, d, *J* 9.2, Ar□H), 5.96 (1H, dt, *J* 15.6 and 5.2, 2□H), 5.88 (1H, q, *J* 15.6 and 5.2, 3□H), 5.40 (1H, d, *J* 3.2, 6□H), 5.30 (1H, dd, *J* 10.4 and 5.6, 7□H), 5.10 (1H, dd, *J* 10.4 and 3.2, 5□H), 4.82 (1H, t, *J* 3.2, 4□H), 4.01–4.18 (3H, m, 8□H and 2x9□H), 3.95 (2H, d, *J* 5.2, 1□H), 1.93–2.14 (12H, 4xs, 4xOCOMe)

^{13}C NMR (100 MHz, $CDCl_3$): δ 170.64, 170.17, 170.08, 169.77, 152.98, 138.32, 132.15, 126.36, 124.85, 111.39, 72.24, 68.45, 68.23, 67.95, 67.82, 61.73, 44.89, 20.73, 20.69, 20.64

HRMS: calcd for $C_{23}H_{28}N_2O_{11}Na$ (M+Na): m/z 531.1591; found: m/z 531.1670



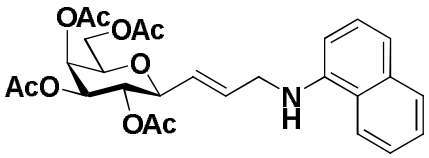
117

IR (film) cm^{-1}: 3398, 2926, 1748, 1622, 1532, 1351, 1228, 1050, 738

^{1}H-NMR (400 MHz, $CDCl_3$): δ 7.55 (1H, d, *J* 7.6, Ar□H), 7.40 (1H, s, Ar□H), 7.32 (1H, t, *J* 8.4, Ar□H), 6.90 (1H, d, *J* 1.2, Ar□H), 5.99 (1H, dt, *J* 15.6 and 5.2, 2□H), 5.92 (1H, q, *J* 15.6 and 5.2, 3□H), 5.39 (1H, d, *J* 3.2, 6□H), 5.33 (1H, dd, *J* 10.4 and 5.6, 7□H), 5.11 (1H, dd, *J* 10.4 and 3.2, 5□H), 4.82 (1H, t, *J* 3.2, 4□H), 4.02–4.15 (3H, m, 8□H and 2x9□H), 3.93 (2H, d, *J* 5.2, 1□H), 1.97–2.14 (12H, 4xs, 4xOCOMe)

^{13}C-NMR (100 MHz, $CDCl_3$): δ 170.61, 170.18, 170.07, 169.85, 149.44, 148.44, 132.92, 129.81, 124.40, 119.04, 112.38, 106.52, 72.39, 68.35, 68.25, 67.92, 61.73, 45.31, 20.72, 20.69, 20.66

HRMS: calcd for $C_{23}H_{28}N_2O_{11}Na$ (M+Na): m/z 531.1591; found: m/z 531.1668



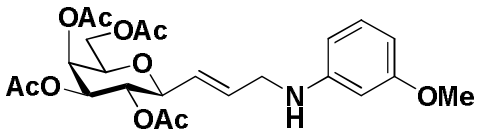
118

IR (film) cm^{-1}: 3440, 2361, 1748, 1584, 1533, 1372, 1228, 1050, 773

^{1}H-NMR (400 MHz, $CDCl_3$): δ 7.83–7.86 (1H, m, Ar□H), 7.77–7.82 (1H, m, Ar□H), 7.45–7.53 (2H, m, Ar□H), 7.36 (1H, d, *J* 7.6, Ar□H), 7.30 (1H, d, *J* 6.8, Ar□H), 6.61 (1H, d, *J* 7.2, Ar□H), 6.12 (1H, dt, *J* 15.6 and 5.2, 2□H), 5.93 (1H, q, *J* 15.6 and 5.2, 3□H), 5.38 (1H, d, *J* 3.2, 6□H), 5.33 (1H, dd, *J* 10.4 and 5.6, 7□H), 5.14 (1H, dd, *J* 10.4 and 3.2, 5□H), 4.83 (1H, t, *J* 3.2, 4□H), 4.07–4.15 (3H, m, 8□H and 2x9□H), 4.05 (2H, d, *J* 5.2, 1□H), 1.90–2.13 (12H, 4xs, 4xOCOMe)

^{13}C-NMR (100 MHz, $CDCl_3$): δ 170.58, 170.20, 170.05, 169.88, 142.73, 134.34, 133.99, 128.71, 126.45, 125.79, 124.86, 123.99, 123.53, 119.84, 117.95, 105.02, 72.50, 68.39, 68.33, 68.04, 68.01, 61.87, 45.94, 20.72, 20.70, 20.66

HRMS: calcd for $C_{27}H_{31}NO_9Na$ (M+Na): m/z 536.1897; found: m/z 536.1963



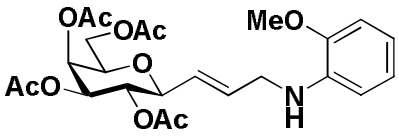
119

IR (film) cm^{-1}: 3738, 3399, 2941, 2362, 1747, 1685, 1614, 1509, 1458, 1372, 1226, 1164, 1049, 762, 689

^{1}H-NMR (400 MHz, $CDCl_3$): δ 7.09 (1H, app. t, *J* 8.4 and 8.0, Ar□H), 6.28 (1H, d, *J* 8.0, Ar□H), 6.23 (1H, d, *J* 7.6, Ar□H), 6.16 (1H, s, Ar□H), 6.00 (1H, dt, *J* 15.6 and 5.2, 2□H), 5.87 (1H, q, *J* 15.6 and 5.6, 3□H), 5.38 (1H, d, *J* 3.2, 6□H), 5.31 (1H, dd, *J* 10.0 and 5.6, 7□H), 5.13 (1H, dd, *J* 10.4 and 3.2, 5□H), 4.81 (1H, t, *J* 5.6, 4□H), 4.04-4.11 (3H, m, 8□H and 2x9□H), 3.83 (2H, d, *J* 5.2, 1□H), 3.75 (3H, s, OMe), 1.97-2.15 (12H, 4xs, 4xOCOMe)

^{13}C-NMR (100 MHz, $CDCl_3$): δ 170.53, 170.20, 170.04, 169.89, 160.84, 149.10, 134.52, 130.04, 123.49, 106.18, 102.82, 99.28, 72.52, 68.29, 68.07, 68.00, 61.86, 55.01, 45.61, 20.73, 20.68, 20.63

HRMS: calcd for $C_{24}H_{31}NO_{10}Na$ (M+Na): m/z 516.1846; found: m/z 516.1824



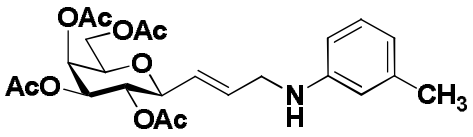
120

IR (film) cm^{-1}: 3738, 3677, 3651, 3423, 2938, 2362, 1748, 1685, 1603, 1511, 1458, 1372, 1225, 1125, 1051, 742

^{1}H-NMR (400 MHz, $CDCl_3$): δ 6.87 (1H, t, *J* 7.6, Ar□H), 6.78 (1H, d, *J* 8.0, Ar□H), 6.69 (1H, t, *J* 7.6, Ar□H), 6.58 (1H, d, *J* 8.0, Ar□H), 6.01 (1H, dt, *J* 15.6 and 5.2, 2□H), 5.87 (1H, q, *J* 15.6 and 5.2, 3□H), 5.37 (1H, d, *J* 3.2, 6□H), 5.31 (1H, dd, *J* 10.4 and 6.0, 7□H), 5.137 (1H, dd, *J* 10.4 and 3.6, 5□H), 4.82 (1H, t, *J* 5.6, 4□H), 4.01-4.12 (3H, m, 8□H and 2x9□H), 3.87 (2H, d, *J* 5.2, 1□H), 3.85 (3H, s, OMe), 1.98-2.13 (12H, 4xs, 4xOCOMe)

^{13}C-NMR (100 MHz, $CDCl_3$): δ 170.47, 170.20, 170.04, 169.88, 146.95, 137.59, 134.84, 123.30, 121.23, 117.01, 109.57, 72.62, 68.29, 68.09, 68.05, 61.88, 55.41, 45.47, 20.75, 20.72, 20.68, 20.65

HRMS: calcd for $C_{24}H_{31}NO_{10}Na$ (M+Na): m/z 516.1846; found: m/z 516.1835



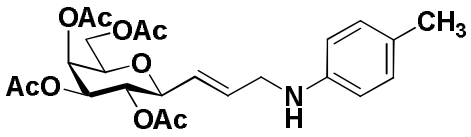
121

IR (film) cm^{-1}: 3738, 3398, 2924, 2362, 1748, 1685, 1608, 1509, 1492, 1435, 1372, 1227, 1050, 775, 695, 602, 427

^{1}H-NMR (400 MHz, $CDCl_3$): δ 7.06 (1H, t, *J* 7.6, Ar□H), 6.55 (1H, d, *J* 7.6, Ar□H), 6.44 (1H, d, *J* 8.0, Ar□H), 6.40 (1H, d, *J* 8.0, Ar□H), 6.01 (1H, dt, , *J* 15.6 and 5.2, 2□H), 5.87 (1H, q, *J* 15.6 and 5.2, 3□H), 5.38 (1H, d, *J* 3.2, 6□H), 5.31 (1H, dd, *J* 10.8 and 5.6, 7□H), 5.13 (1H, dd, *J* 10.0 and 3.2, 5□H), 4.81 (1H, t, *J* 5.2, 4□H), 4.03-4.20 (3H, m, 8□H and 2x9□H), 3.84 (2H, d, *J* 5.2, 1□H), 2.27 (3H, s, CH_3), 1.97-2.14 (12H, 4xs, 4xOCOMe)

^{13}C-NMR (100 MHz, $CDCl_3$): δ 170.48, 170.16, 170.01, 169.83, 147.67, 138.98, 134.61, 129.13, 123.31, 118.75, 113.88, 110.19, 72.57, 68.26, 68.02, 67.96, 61.80, 45.65, 21.54, 20.70, 20.65

HRMS: calcd for $C_{24}H_{32}NO_9$ (M+H): m/z 478.2077; found: m/z 478.2067



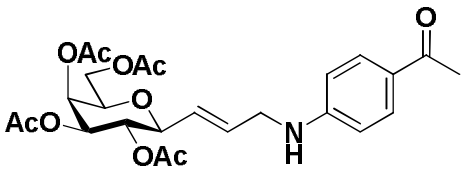
122

IR (film) cm^{-1}: 3737, 3394, 2923, 2361, 1747, 1684, 1618, 1521, 1458, 1371, 1226, 1049, 814

^{1}H-NMR (400 MHz, $CDCl_3$): δ 6.99 (2H, d, *J* 8.4, Ar□H), 6.55 (2H, d, *J* 8.4, Ar□H), 6.00 (1H, dt, , *J* 15.6 and 5.2, 2□H), 5.86 (1H, q, *J* 15.6 and 5.2, 3□H), 5.37 (1H, d, *J* 3.2, 6□H), 5.31(1H, dd, *J* 10.4 and 5.6, 7□H), 5.12 (1H, dd, *J* 10.4 and 3.2, 5□H), 4.81 (1H, t, *J* 5.6, 4□H), 4.03-4.11 (3H, m, 8□H and 2x9□H), 3.82 (2H, d *J* 5.6, 1□H), 2.22 (3H, s, CH_3), 1.99-2.13 (12H, 4xs, 4xOCOMe)

^{13}C-NMR (100 MHz, $CDCl_3$): δ 170.50, 170.19, 170.04, 169.86, 145.37, 134.73, 129.76, 127.09, 123.34, 113.35, 72.59, 68.24, 68.05, 68.00, 61.83, 46.03, 20.70, 20.67, 20.34

HRMS: calcd for $C_{24}H_{32}NO_9$ (M+H): m/z 478.2077; found: m/z 478.2064



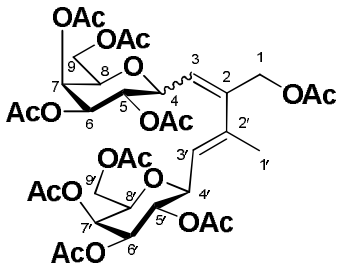
123

IR (film) cm^{-1}: 3738, 3394, 2362, 1747, 1685, 1599, 1539, 1458, 1369, 1227, 1052, 429

^{1}H-NMR (400 MHz, $CDCl_3$): δ 7.84 (2H, d, *J* 8.8, Ar□H), 6.59 (2H, d *J* 8.8, Ar□H), 6.12 (1H, dt, *J* 15.6 and 5.2, 2□H), 5.93 (1H, q, *J* 15.6 and 5.2, 3□H), 5.38 (1H, d, *J* 3.2, 6□H), 5.31 (1H, dd, *J* 10.0 and 5.6, 7□H), 5.12 (1H, dd, *J* 1.0 and 3.2, 5□H), 4.81 (1H, t, *J* 3.2, 4□H), 4.02-4.16 (3H, m, 8□H and 2x9□H), 3.93 (2H, d, *J* 4.8, 1□H), 2.50 (3H, s, $OCOCH_3$), 1.96-2.16 (12H, 4xs, 4xOCOMe)

^{13}C-NMR (100 MHz, $CDCl_3$): δ 196.43, 170.53, 170.15, 170.03, 169.78, 151.74, 133.05, 130.78, 130.73, 127.01, 124.12, 111.73, 111.66, 72.32, 68.35, 67.92, 67.85, 61.74, 44.83, 25.98, 20.70, 20.65, 20.60

HRMS: calcd for $C_{25}H_{31}NO_{10}Na$ (M+Na): m/z 528.1846; found: m/z 528.1820



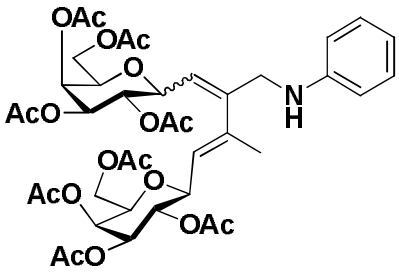
124

IR (film) cm^{-1}: 3477, 2964, 1747, 1436, 1372, 1229, 1119, 1049

^{1}H NMR (400 MHz, $CDCl_3$): δ 5.92 (1H, d, *J* 6.4, 3□H), 5.80 (1H, d, *J* 6.0, 3′□H), 5.41–5.45 (2H, m, 6 and 6′□H), 5.31–5.36 (2H, m, 7 and 7′□H), 5.24 (1H, t, *J* 2.4, 5□H), 5.21 (1H, t, *J* 3.6, 5′□H), 5.15(1H, t, *J* 6.4, 4□H), 5.03–5.06 (2H, m, 1□H), 4.82 (1H, d, *J* 13.2, 4′□H), 4.02–4.20 (6H, m, 2x(8,8′□H) and 4x(9,9′□H)), 1.90–2.20 (30H, 10xs, 9xOCOMe and 1′□CH_3)

^{13}C NMR (100 MHz, $CDCl_3$): δ 170.42, 170.32, 170.29, 170.15, 170.11, 170.01, 169.96, 169.82, 169.57, 145.01, 143.28, 123.86, 120.77, 69.62, 68.88, 68.76, 68.40, 68.24, 68.20, 67.98, 67.85, 67.82, 67.44, 61.67, 61.32, 59.27, 20.70, 20.66, 20.64, 20.60, 15.61

HRMS: calcd for $C_{36}H_{48}O_{20}Na$ (M+Na): m/z 823.2637; found: m/z 823.2566



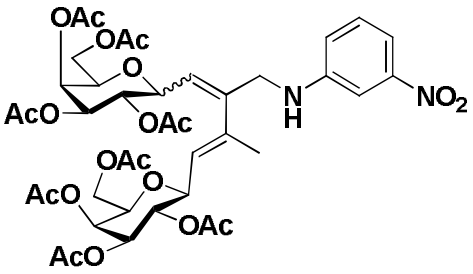
125

IR (film) cm^{-1}: 3440, 2361, 1747, 1637, 1372, 1226, 1023

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.16 (2H, app. t, *J* 8 and 7.6, Ar□H), 6.68–6.72 (1H, m, Ar□H), 6.58 (2H, d, *J* 8.4, Ar□H), 5.83 (1H, d, *J* 6.8, 3□H), 5.75 (1H, d, *J* 6.4, 3′□H), 5.41–5.45 (2H, m, 6 and 6′□H), 5.28–5.34 (2H, m, 7 and 7′□H), 5.21–5.26 (2H, m, 5 and 5′□H), 5.10–5.14 (3H, m, 2x(1□H) and 4□H), 5.00 (1H, app. t, *J* 6.4 and 5.6, 4′□H), 4.00–4.20 (6H, m, 8,8′□H and 4x(9,9′□H)), 1.80–2.10 (27H, 9xs, 8xOCOMe and 1′□CH_3)

^{13}C NMR (100 MHz, $CDCl_3$): δ 170.54, 170.41, 170.13, 170.09, 169.98, 169.90, 169.83, 169.81, 147.84, 144.58, 129.34, 129.24, 121.82, 120.62, 117.82, 112.75, 69.48, 69.06, 68.77, 68.36, 68.26, 68.10, 67.99, 67.91, 67.52, 61.82, 61.51, 42.14, 20.78, 20.75, 20.73, 20.67, 20.65, 15.87

HRMS: calcd for $C_{40}H_{51}NO_{18}Na$ (M+Na): m/z 856.3004; found: m/z 856.3036



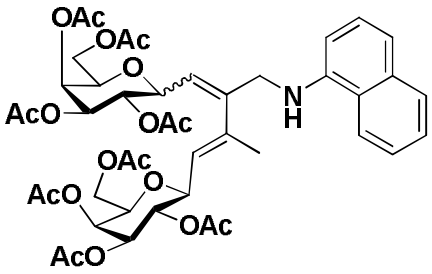
126

IR (film) cm^{-1}: 3736, 2362, 1744, 1540, 1370, 1225, 1023

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.53 (1H, d, *J* 6.4, Ar□H), 7.41 (1H, app. t, *J* 2.4 and 2.0, Ar□H), 7.27 (1H, s, Ar□H), 6.89 (1H, d, *J* 2.0, Ar□H), 5.91 (1H, d, *J* 7.2, 3□H), 5.40–5.46 (3H, m, 2x(6,6′□H) and 3′□H), 5.27–5.31 (2H, m, 7 and 7′□H), 5.22–5.26 (2H, m, 5 and 5′□H) 5.12–5.18 (4H, m, 2x(1□H) and 2x(4,4′□H)), 4.01–4.15 (6H, m, 2x(8,8′□H) and 4x(9,9′□H)), 2.00–2.13 (27H, 9xs, 8xOCOMe and 1′□CH_3)

^{13}C NMR (100 MHz, $CDCl_3$): δ 170.61, 170.52, 170.44, 170.19, 170.05, 170.01, 169.96, 169.91, 149.44, 148.82, 144.33, 142.93, 129.74, 123.26, 118.69, 117.18, 112.09, 106.16, 70.07, 69.06, 69.02, 68.16, 67.96, 67.73, 67.59, 61.85, 61.63, 42.34, 20.80, 20.75, 20.70, 20.65, 14.12

HRMS: calcd for $C_{40}H_{50}N_2O_{20}Na$ (M+Na): m/z 901.2855; found: m/z 901.2904



127

IR (film) cm^{-1}: 3442, 2362, 2066, 1746, 1638, 1372, 1227, 1048

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.83 (1H, d, *J* 8.8, Ar□H), 7.77 (1H, d, *J* 7.6, Ar□H), 7.35–7.46 (2H, m, Ar□H), 7.33 (1H, d, *J* 7.6, Ar□H), 7.24 (1H, d, *J* 8.4, Ar□H), 6.59 (1H, d, *J* 7.6, Ar□H), 5.94 (1H, d, *J* 7.2, 3□H), 5.40–5.45 (3H, m, 2x(6,6′□H) and 3′□H), 5.31–5.36 (3H, m, 2x(7,7′□H) and 4□H), 5.22–5.30 (2H, m, 5 and 5′□H), 5.16–5.21 (3H, m, 2x(1□H) and 4′□H), 4.02–4.25 (6H, m, 2x(8,8′□H) and 4x(9,9′□H)), 1.90–2.10 (27H, 9xs, 8xOCOMe and 1′□CH_3)

^{13}C NMR (100 MHz, $CDCl_3$): δ 170.64, 170.56, 170.51, 170.47, 170.23, 170.20, 170.12, 170.03, 145.22, 143.30, 134.36, 134.26, 129.29, 128.99, 128.67, 128.48, 126.54, 125.84, 122.82, 120.39, 117.79, 104.13, 69.60, 69.14, 69.07, 68.56, 68.40, 68.28, 67.90, 67.86, 67.70, 61.68, 61.64, 61.14, 43.52, 20.69, 20.67, 20.63, 14.12

HRMS: calcd for $C_{44}H_{53}NO_{18}Na$ (M+Na): m/z 906.3160; found: m/z 906.3220

CHAPTER 5

CONCLUSION

We have found that Pd(0), Pd(II), or Au(III) catalysts promote a highly efficient intermolecular hydroamination of *C*-(tetra-*O*-acetyl-*β*-D-galactopyranosyl)-allene under very mild conditions. The addition of aromatic amines proceeded smoothly at ambient temperature using commercially available palladium and gold complexes to give the desire allylic amine in moderate to good yield.

Both palladium and gold methods for catalyzed hydroamination of *C*-(tetra-*O*-acetyl-*β*-D-galactopyranosyl)allene with a variety of aromatic amines have been successfully developed

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REFERENCES

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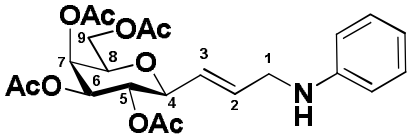
APPENDICES

Appendix A



Spectral data of compound 114

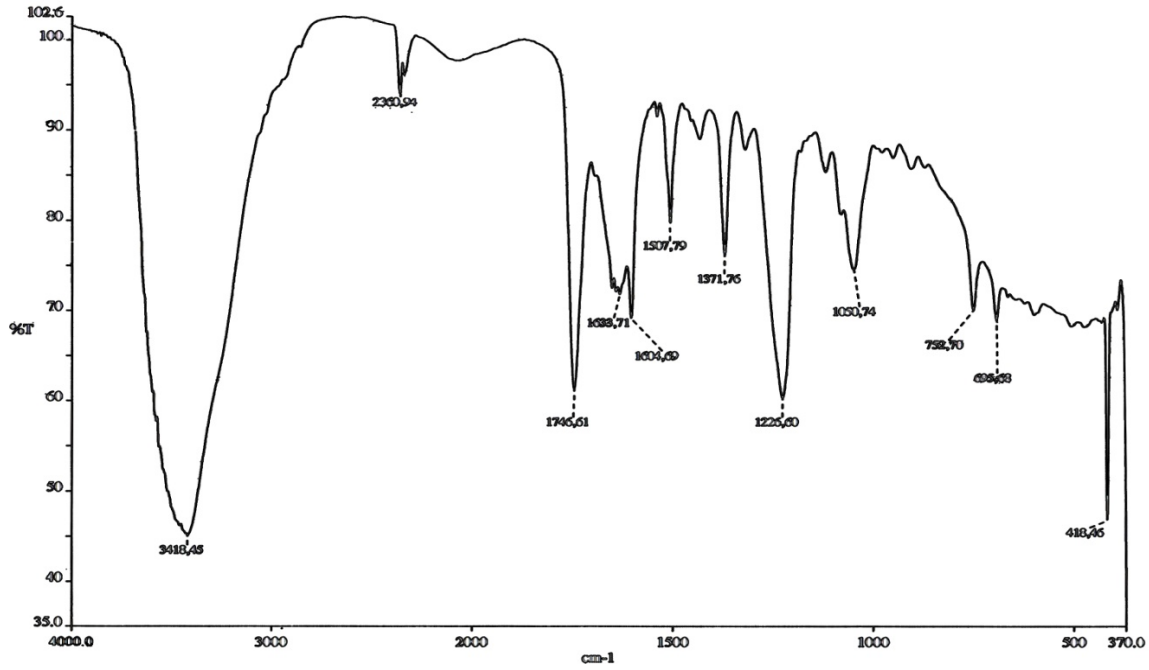


Figure 1 IR spectrum of compound **114**

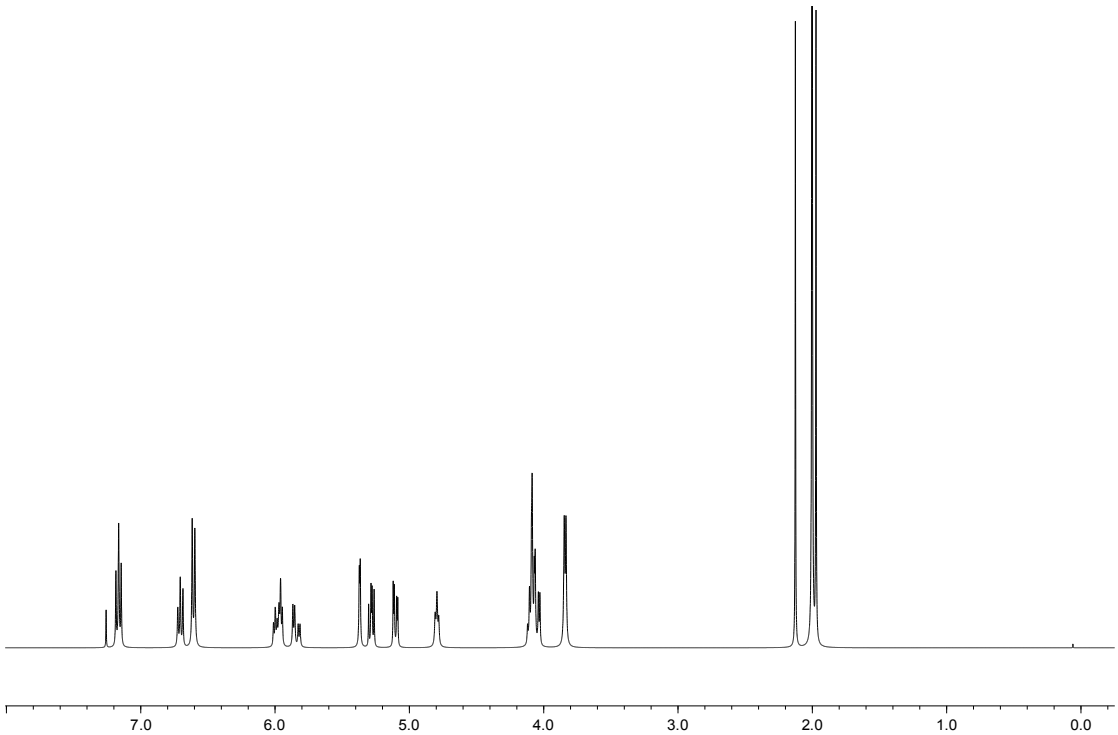


Figure 2 ^{1}H-NMR (400 MHz, $CDCl_3$) spectrum of compound **114**

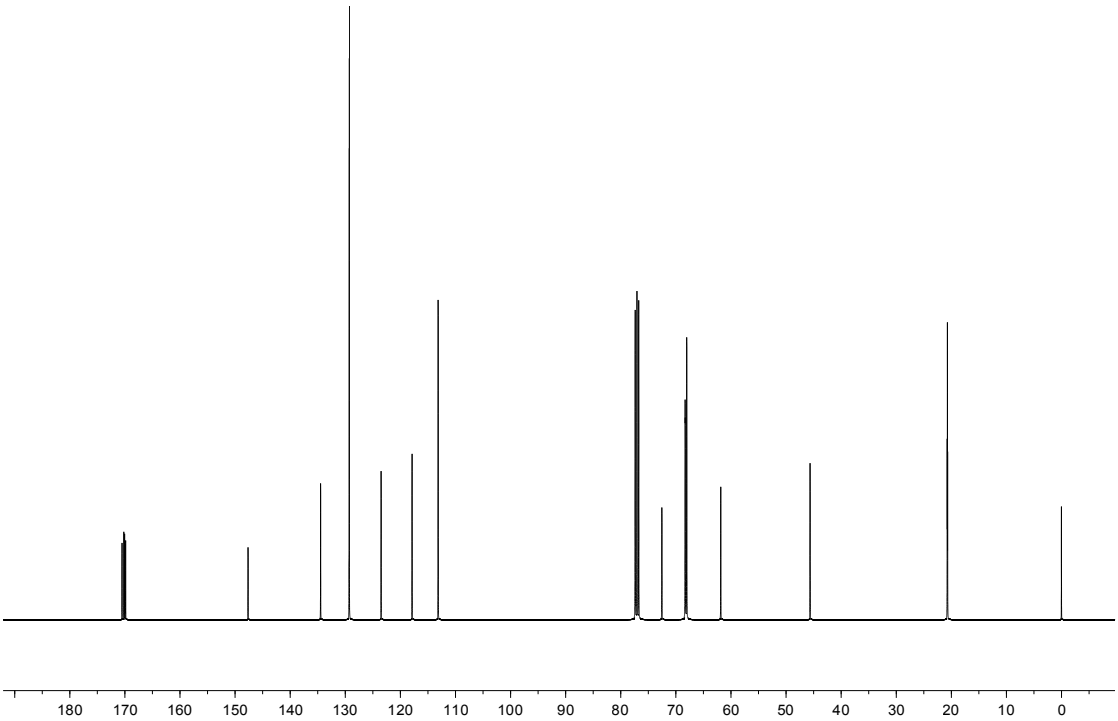


Figure 3 ^{13}C-NMR (100 MHz, $CDCl_3$) spectrum of compound **114**

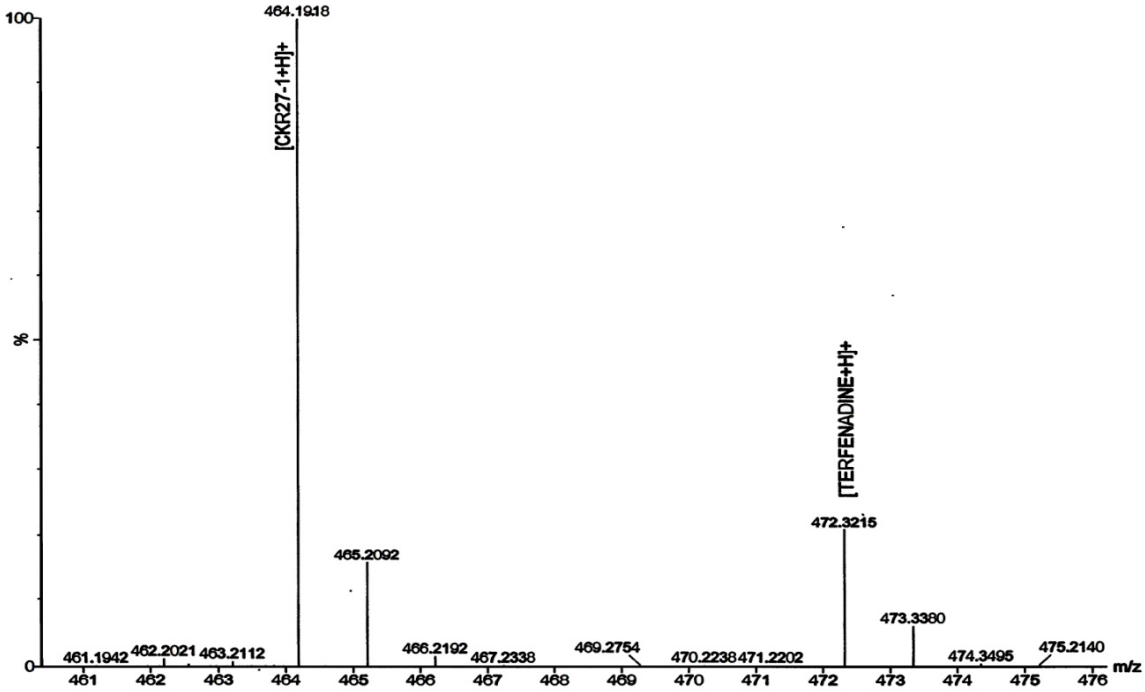
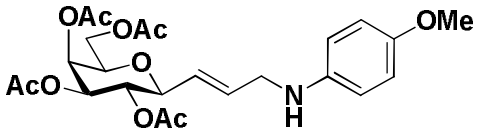


Figure 4 High resolution mass spectrum of compound **114**

Appendix B



Spectral data of compound 115

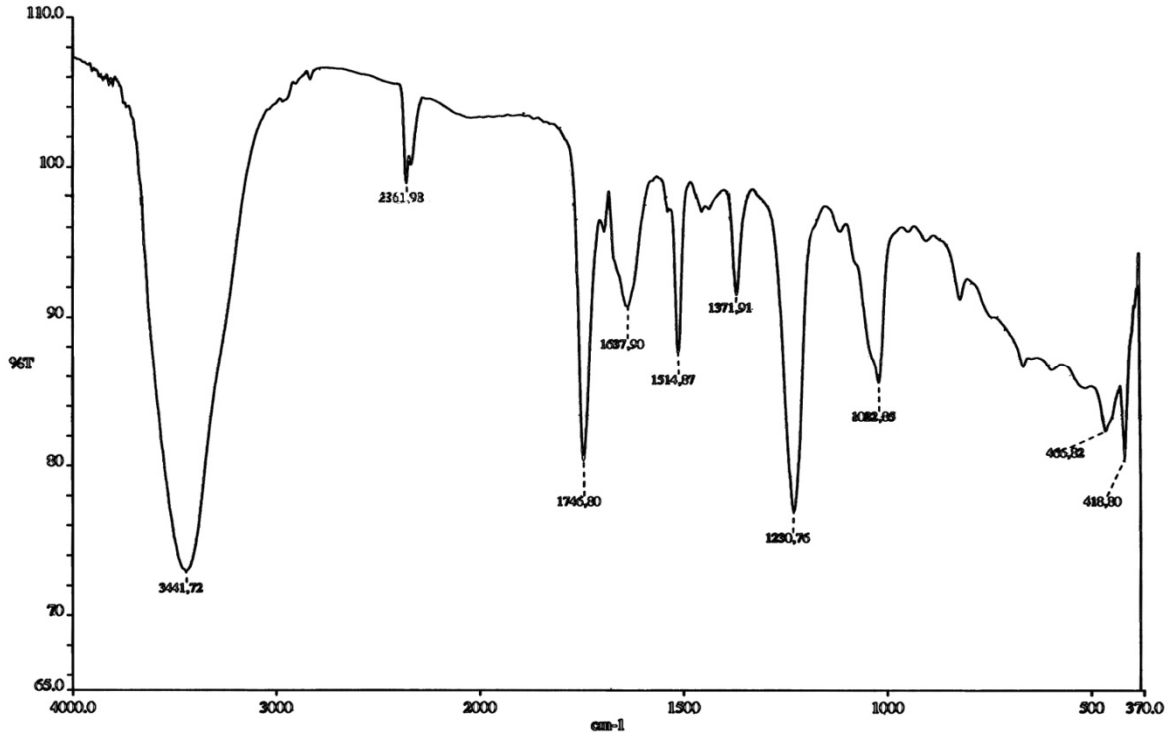


Figure 5 IR spectrum of compound **115**

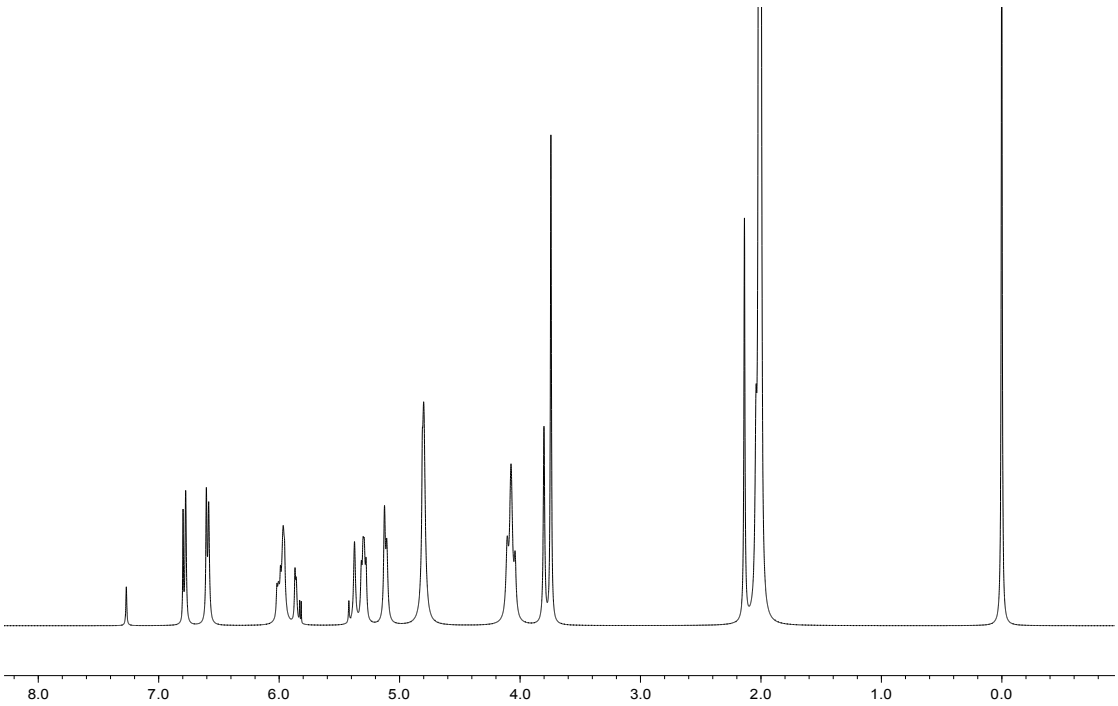


Figure 6 ^{1}H-NMR (400 MHz, $CDCl_3$) spectrum of compound **115**

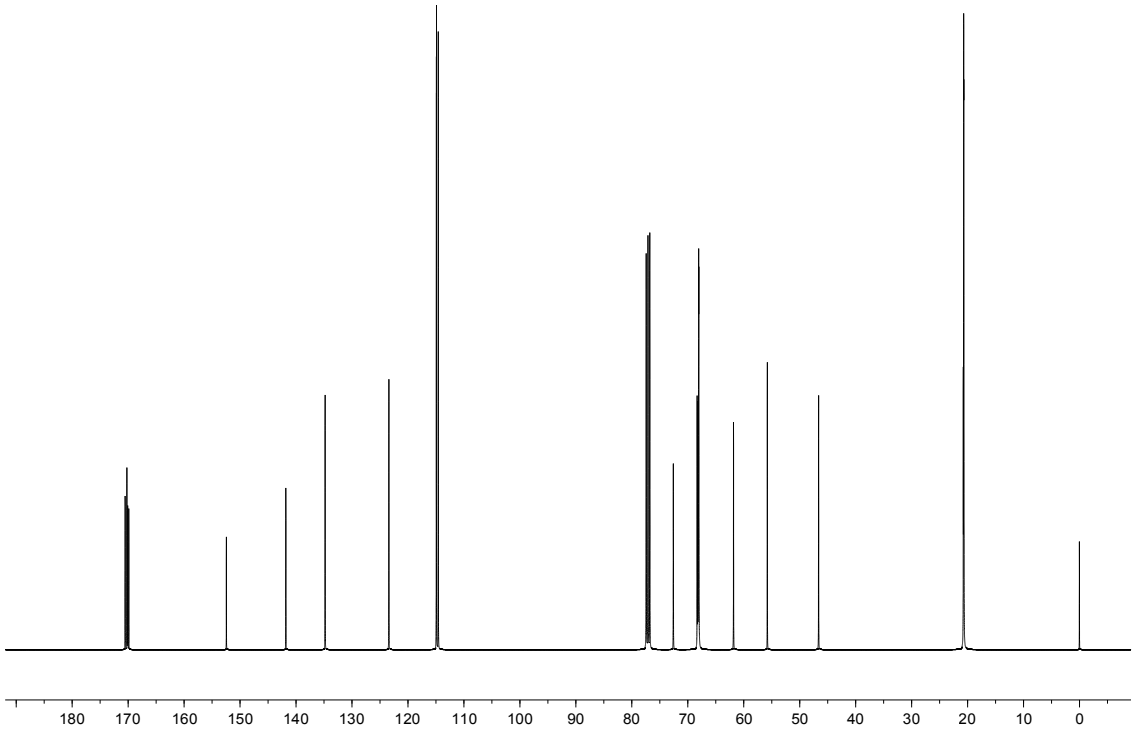


Figure 7 ^{13}C-NMR (100 MHz, $CDCl_3$) spectrum of compound **115**

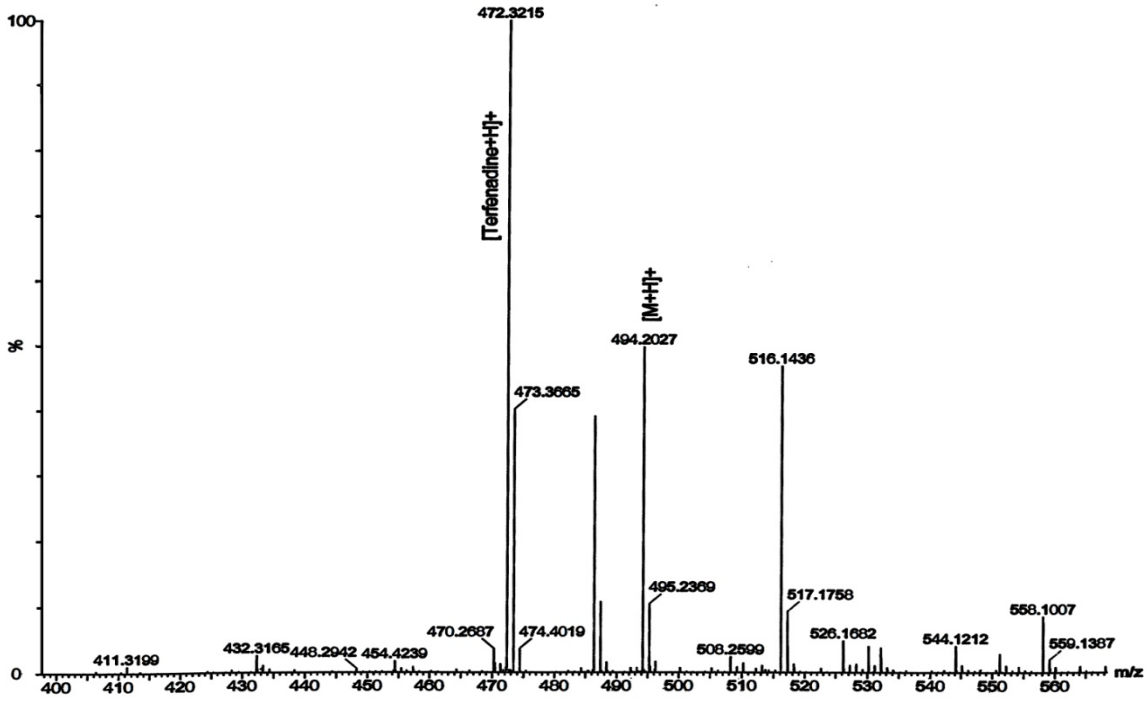
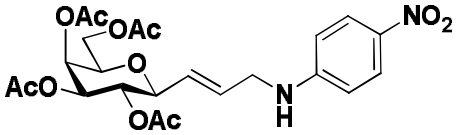


Figure 8 High resolution mass spectrum of compound **115**

Appendix C



Spectral data of compound 116

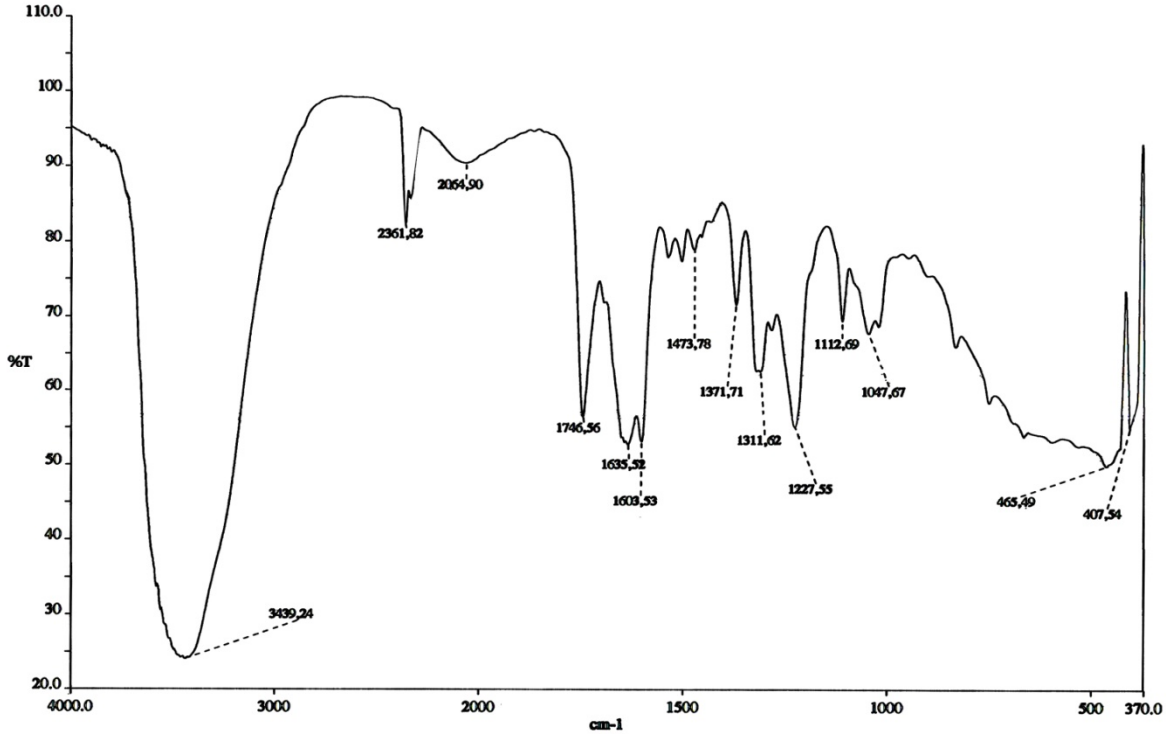


Figure 9 IR spectrum of compound **116**

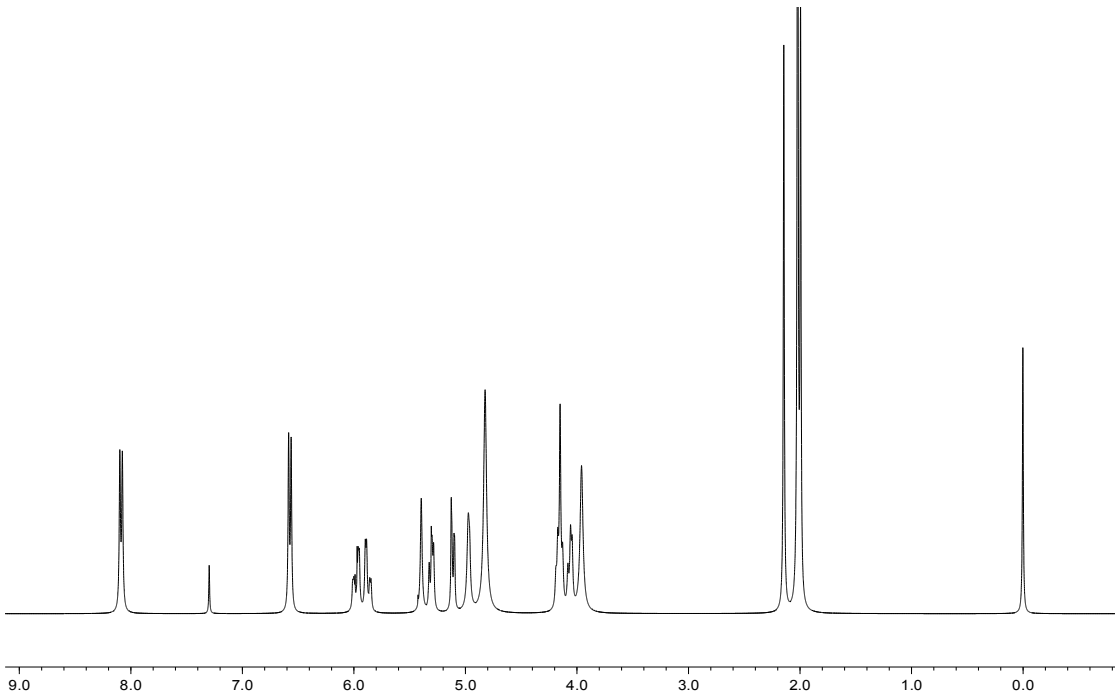


Figure 10 ^{1}H-NMR (400 MHz, $CDCl_3$) spectrum of compound **116**

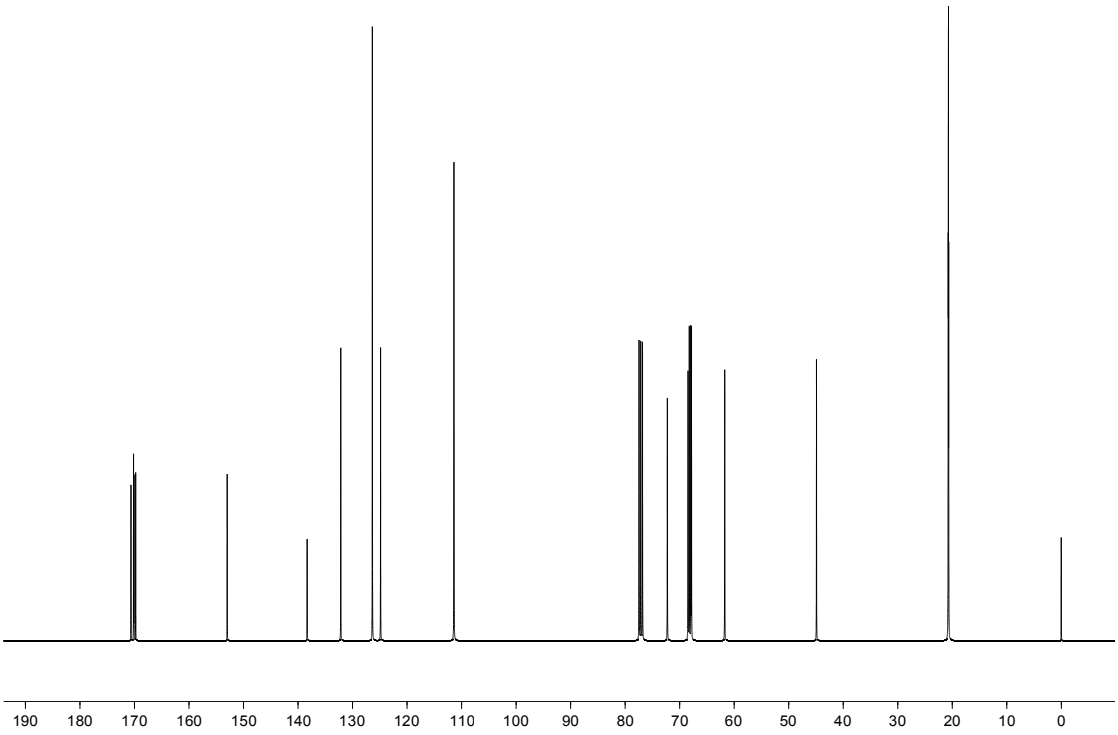


Figure 11 ^{13}C-NMR (100 MHz, $CDCl_3$) spectrum of compound **116**

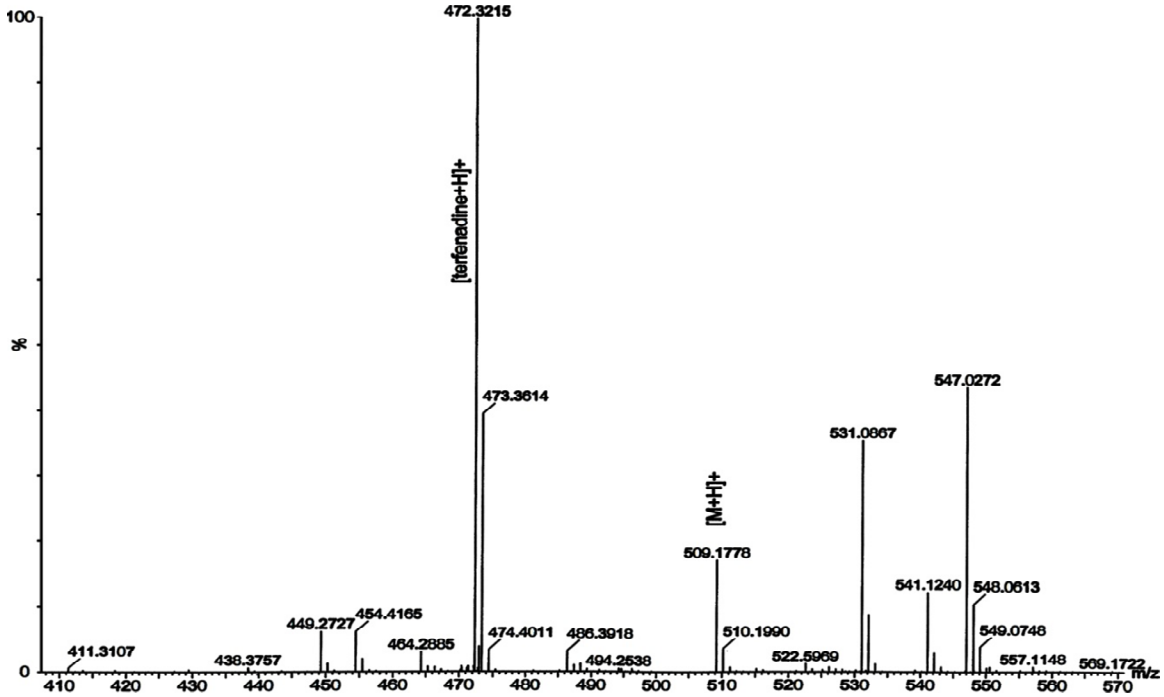
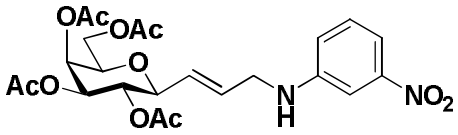


Figure 12 High resolution mass spectrum of compound **116**

Appendix D



Spectral data of compound 117

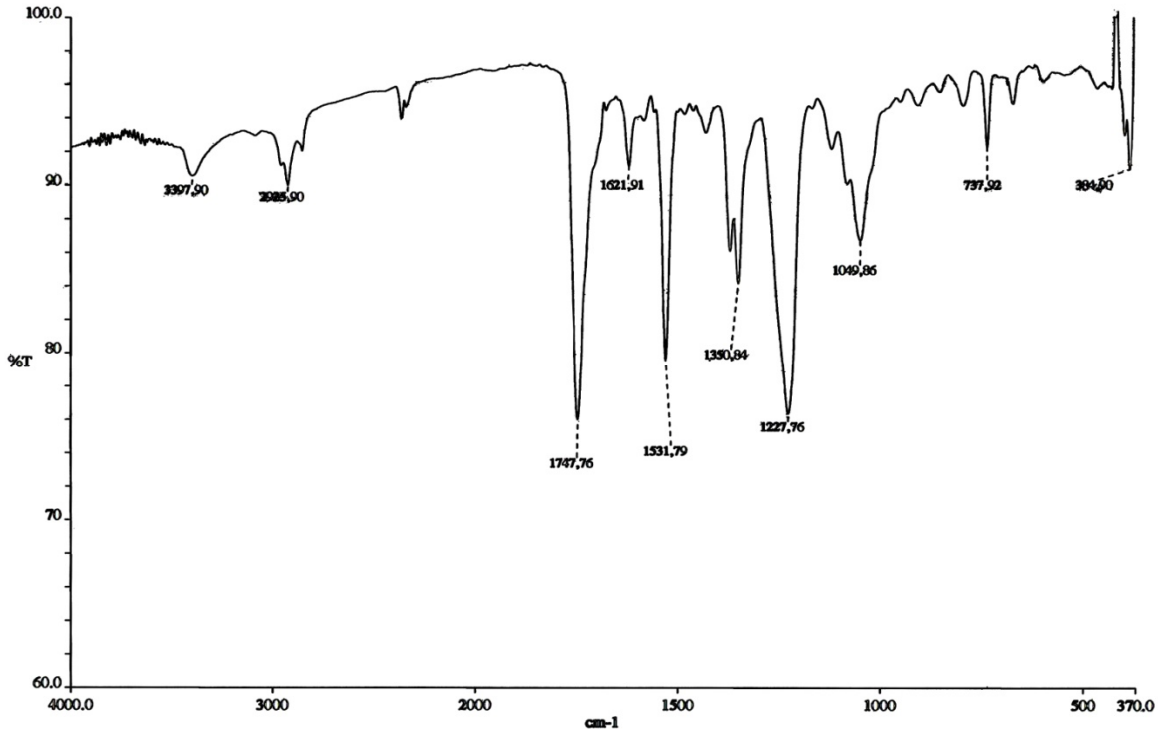


Figure 13 IR spectrum of compound **117**

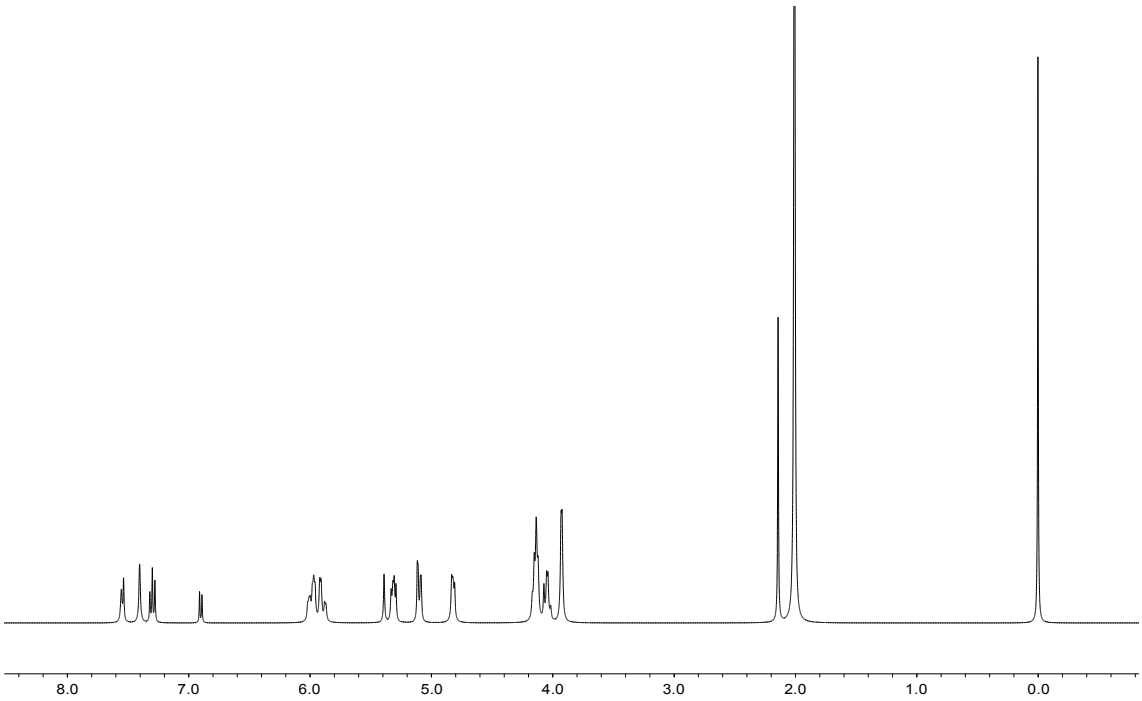


Figure 14 ^{1}H-NMR (400 MHz, $CDCl_3$) spectrum of compound **117**

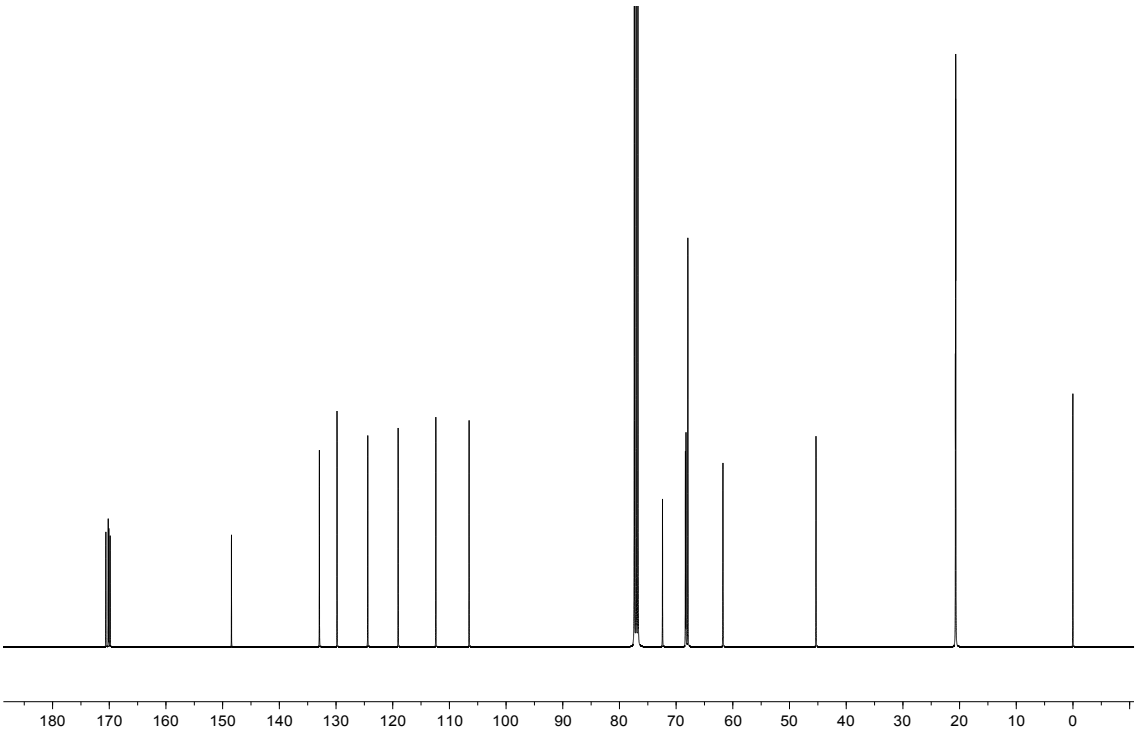


Figure 15 ^{13}C-NMR (100 MHz, $CDCl_3$) spectrum of compound **117**

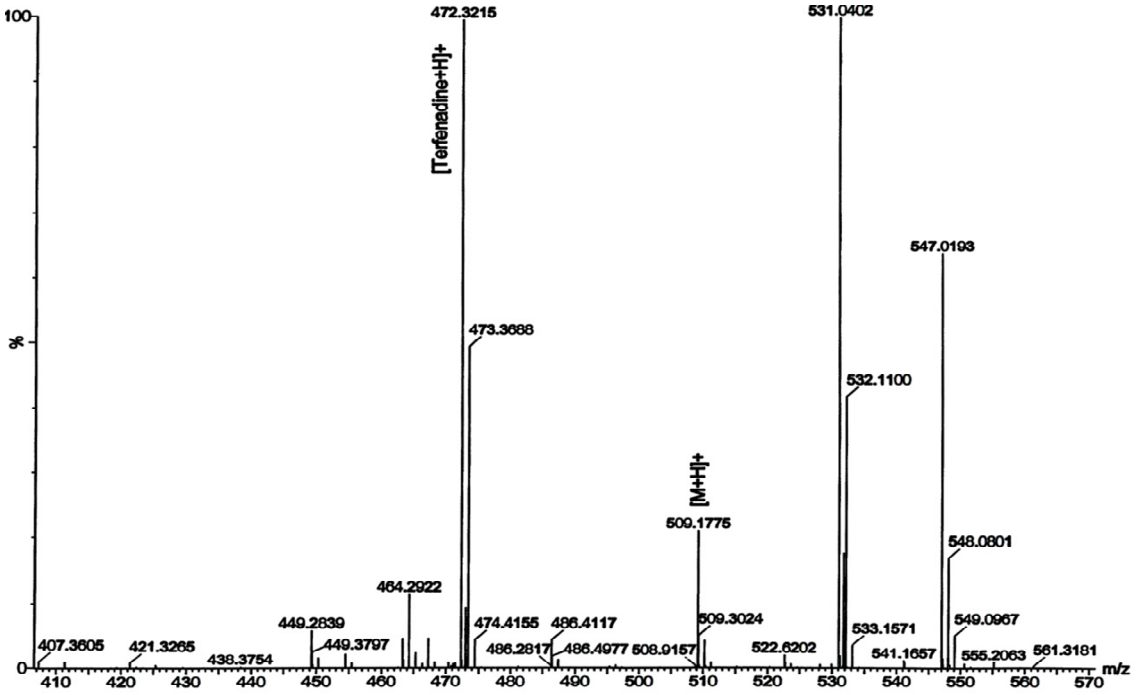
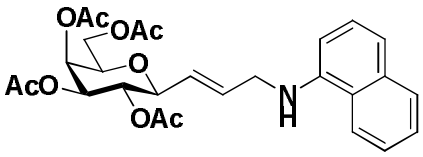


Figure 16 High resolution mass spectrum of compound **117**

Appendix E



Spectral data of compound 118

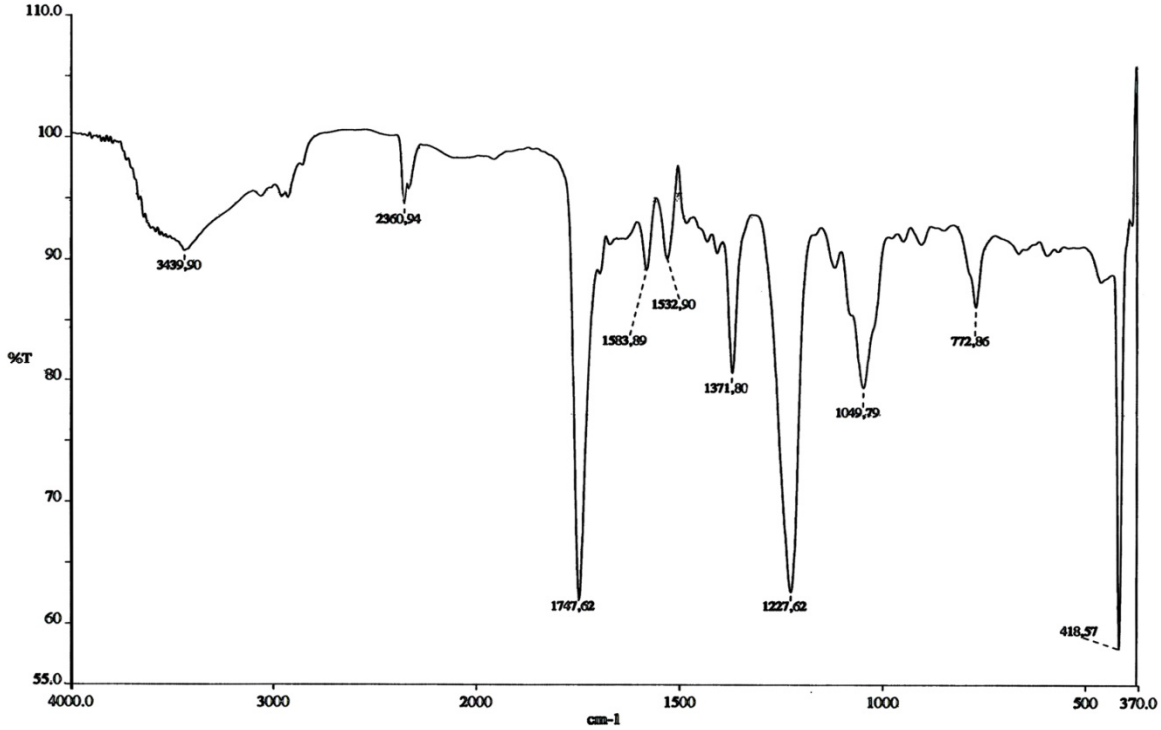


Figure 17 IR spectrum of compound **118**

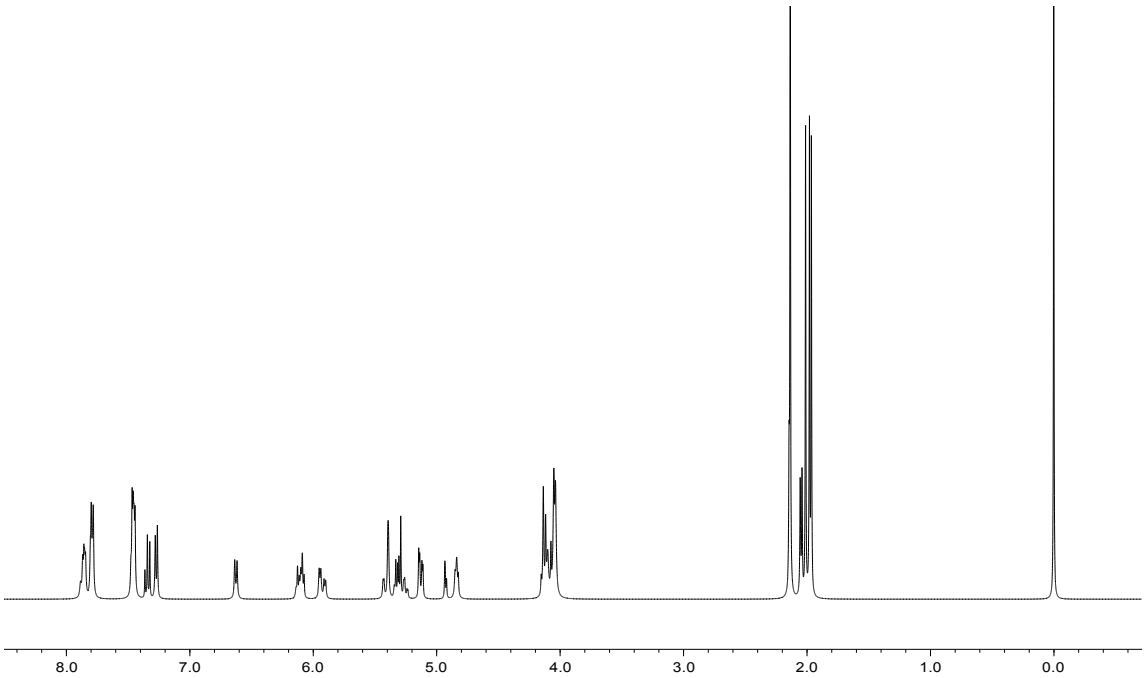


Figure 18 ^{1}H-NMR (400 MHz, $CDCl_3$) spectrum of compound **118**

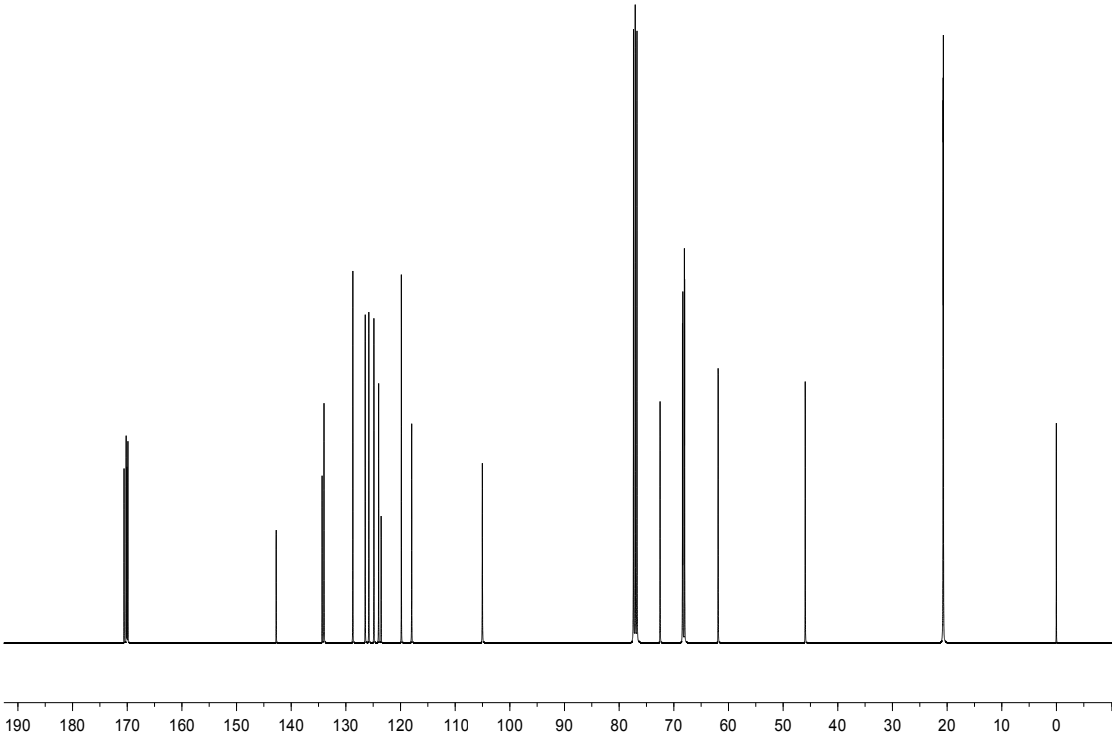


Figure 19 ^{13}C-NMR (100 MHz, $CDCl_3$) spectrum of compound **118**

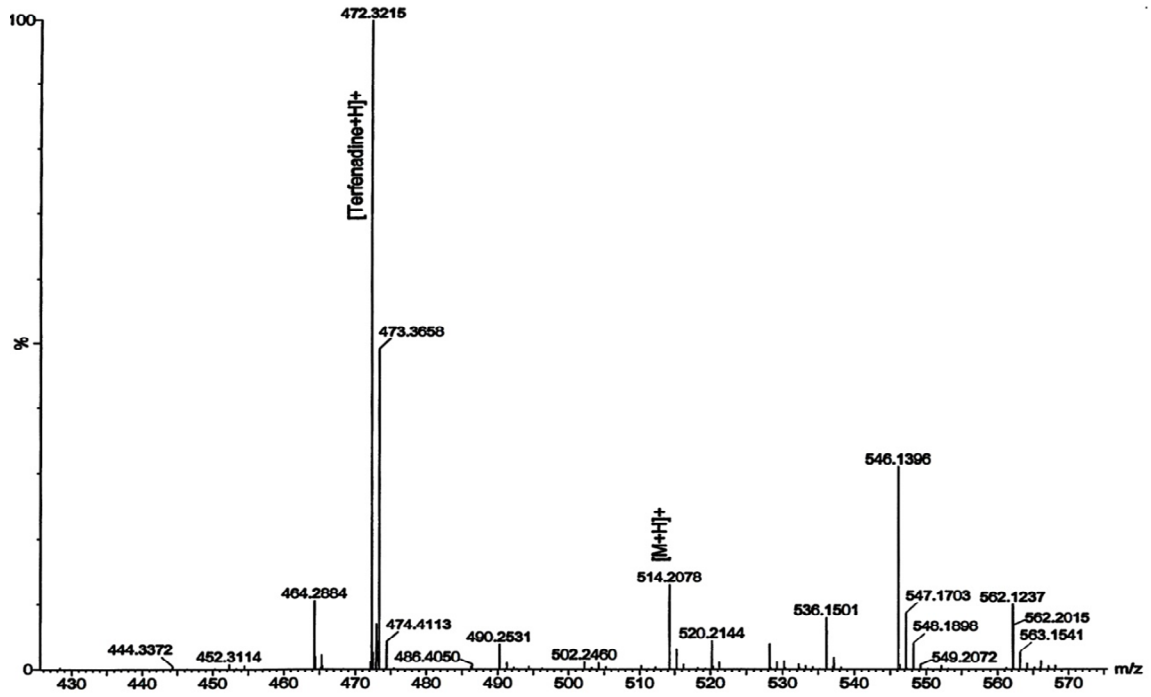
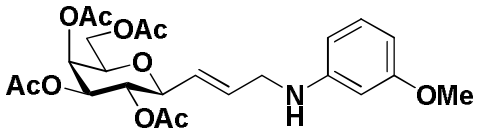


Figure 20 High resolution mass spectrum of compound **118**

Appendix F



Spectral data of compound 119

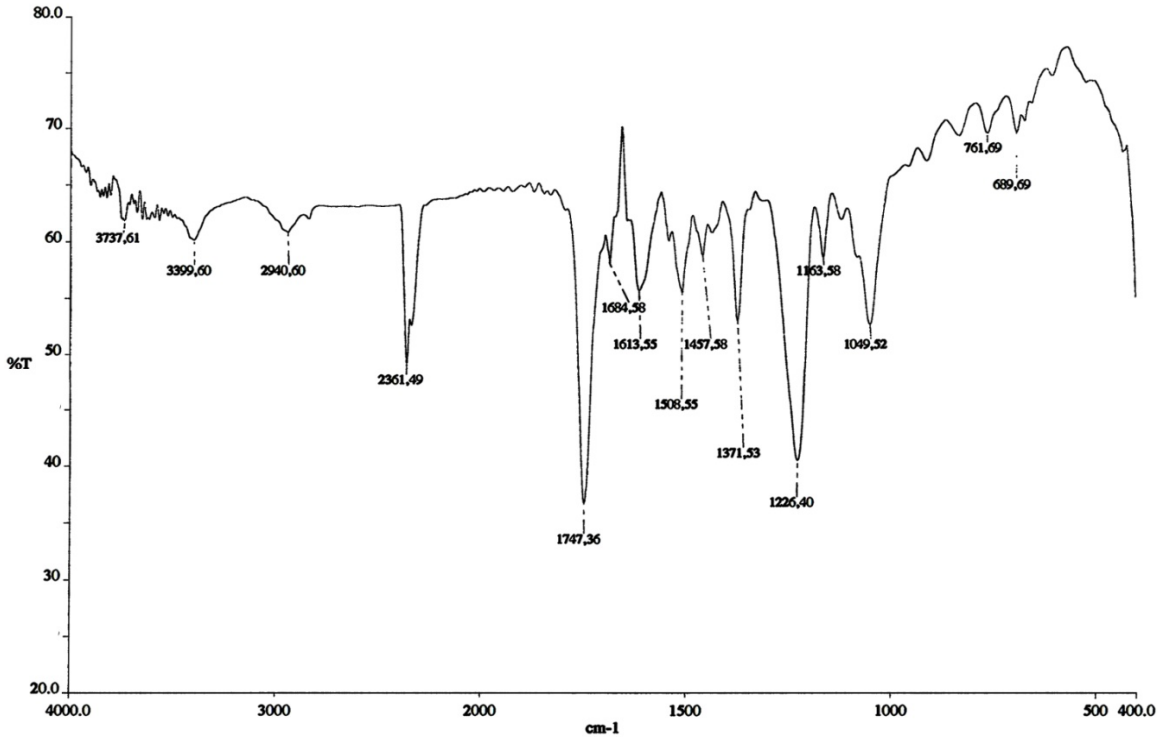


Figure 21 IR spectrum of compound **119**

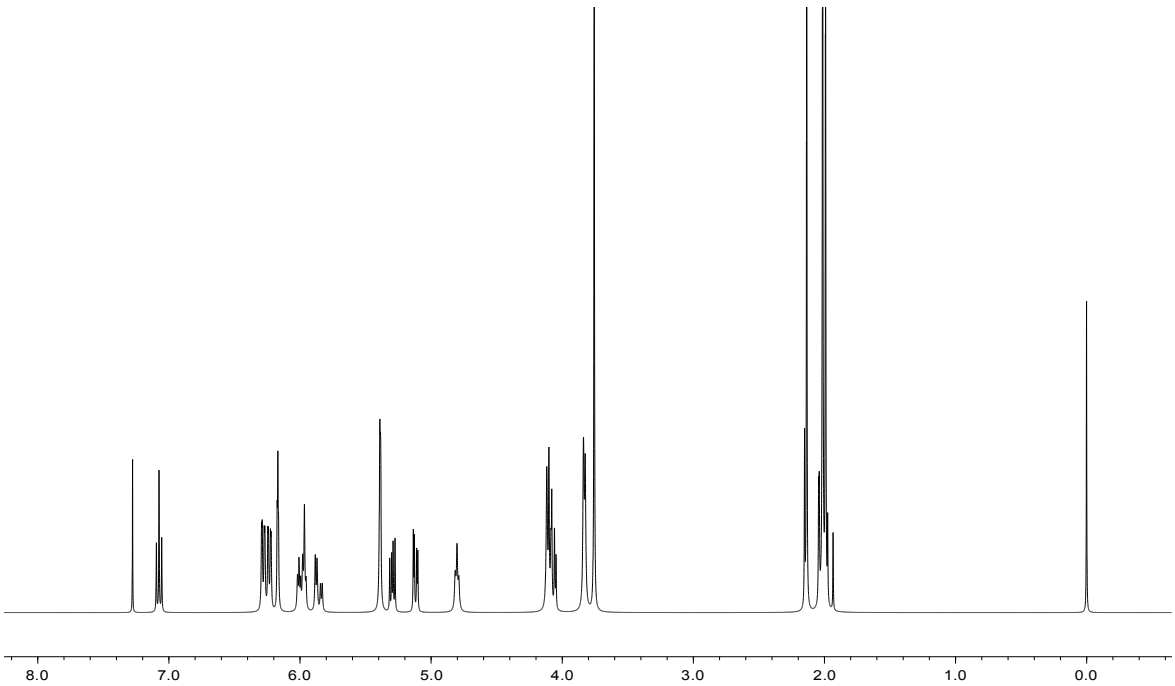


Figure 22 ^{1}H-NMR (400 MHz, $CDCl_3$) spectrum of compound **119**

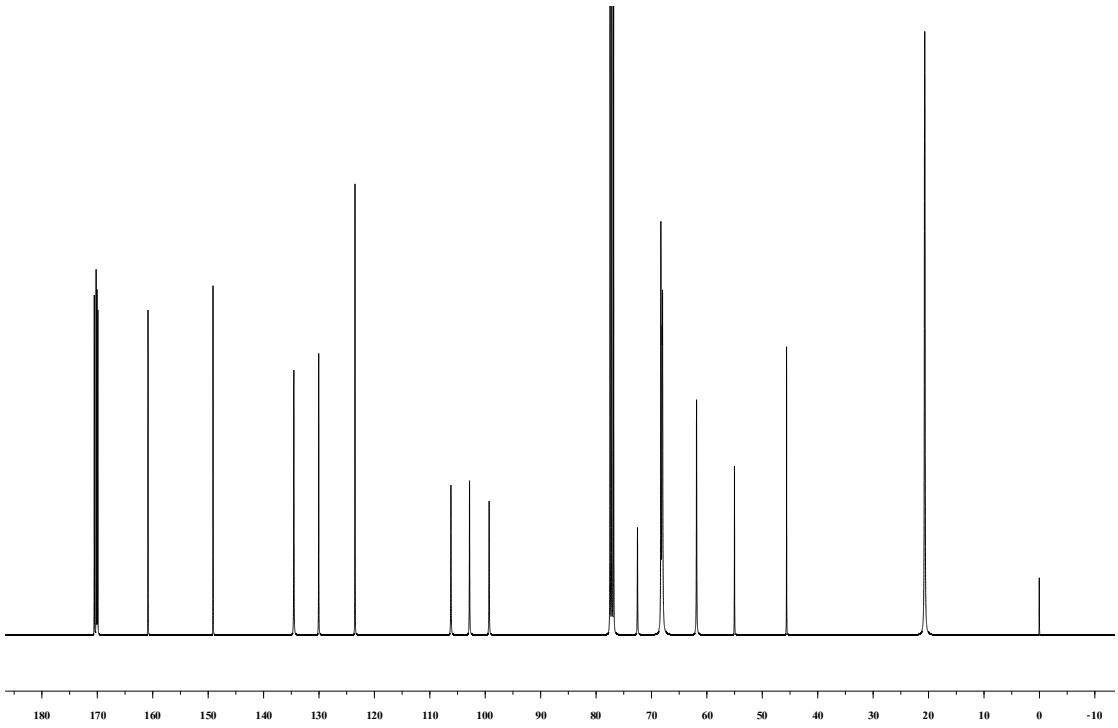


Figure 23 ^{13}C-NMR (100 MHz, $CDCl_3$) spectrum of compound **119**

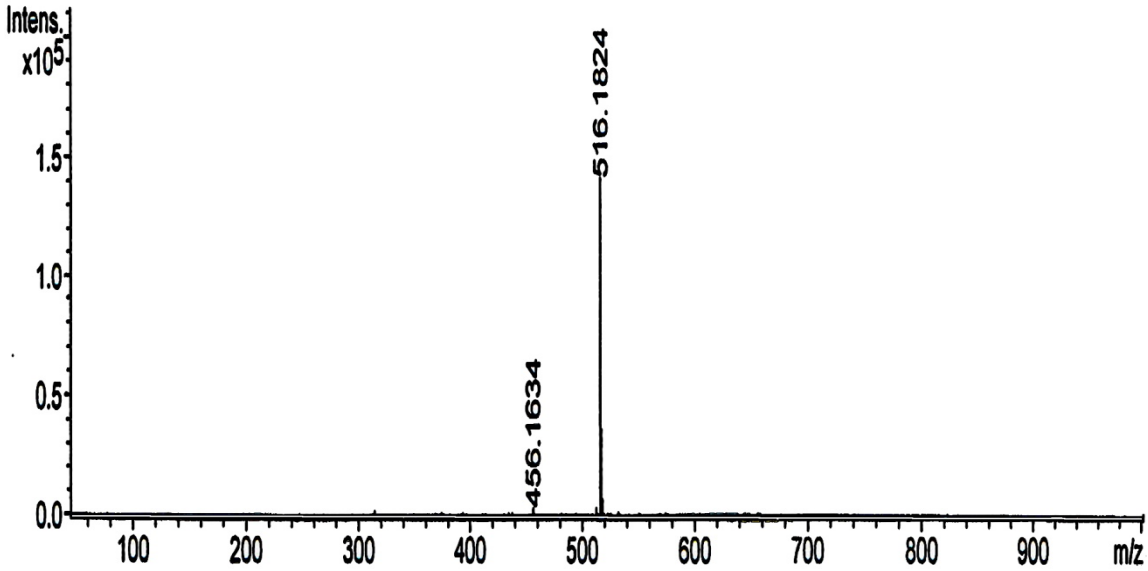
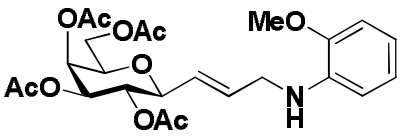


Figure 24 High resolution mass spectrum of compound **119**

Appendix G



Spectral data of compound 120

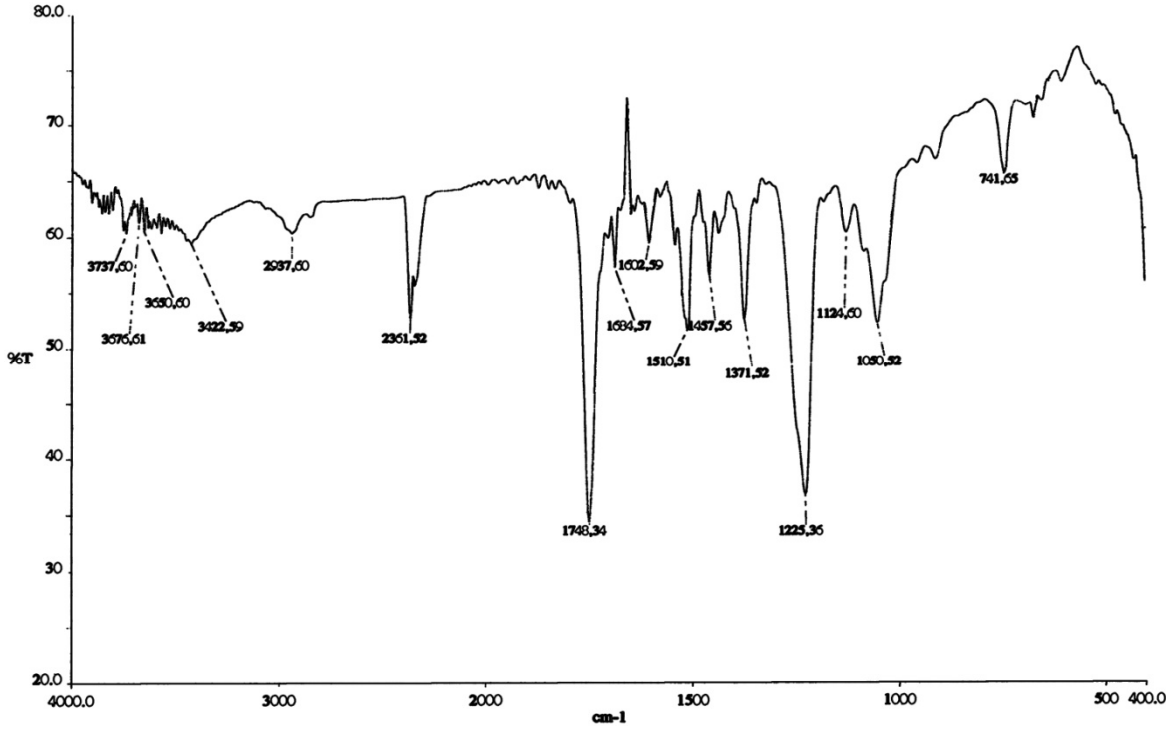


Figure 26 IR spectrum of compound **120**

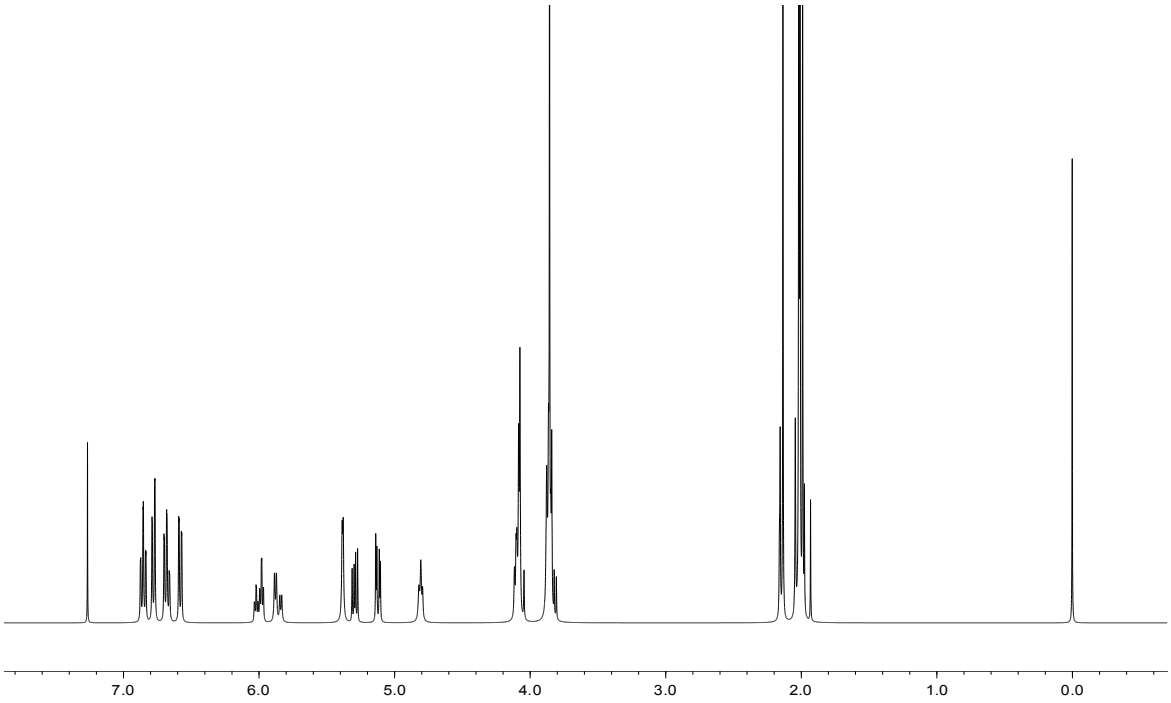


Figure 27 ^{1}H-NMR (400 MHz, $CDCl_3$) spectrum of compound **120**

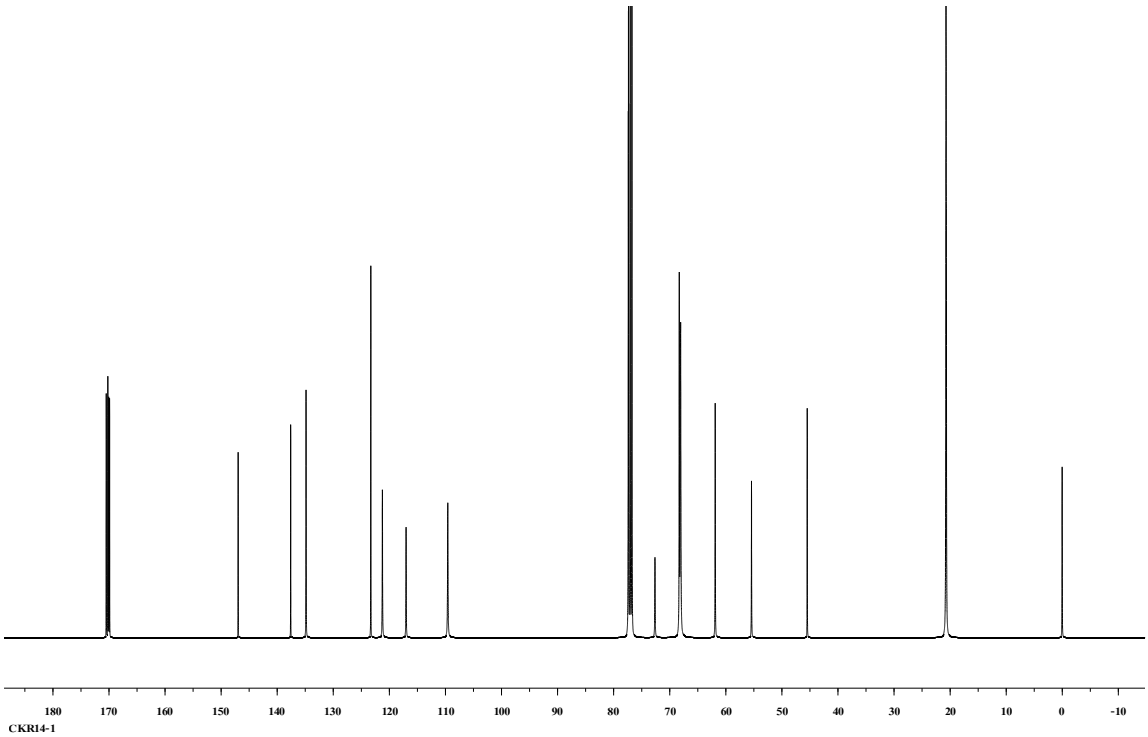


Figure 28 ^{13}C-NMR (100 MHz, $CDCl_3$) spectrum of compound **120**

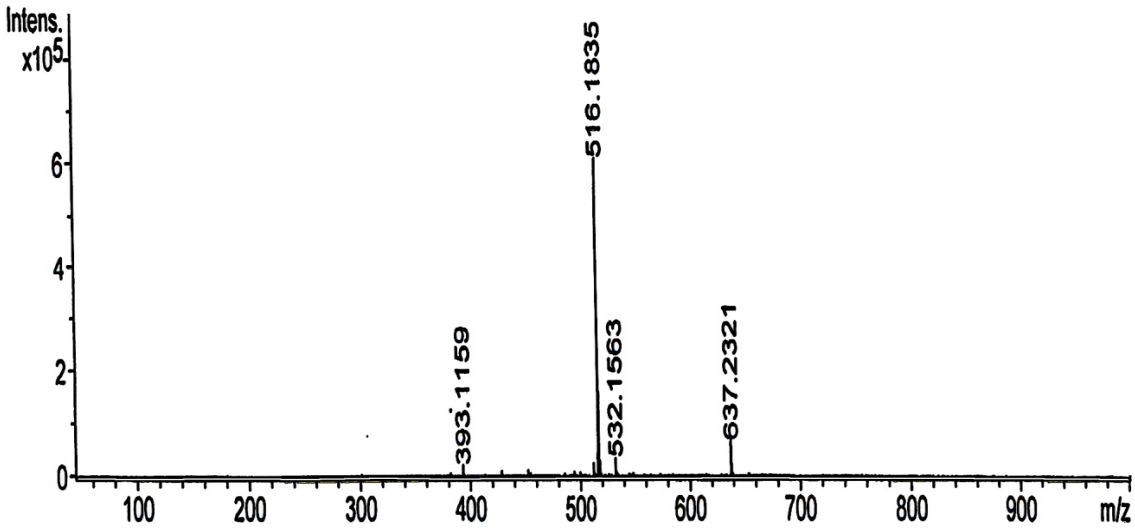
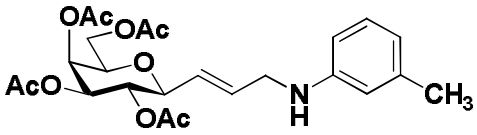


Figure 29 High resolution mass spectrum of compound **120**

Appendix H



Spectral data of compound 121

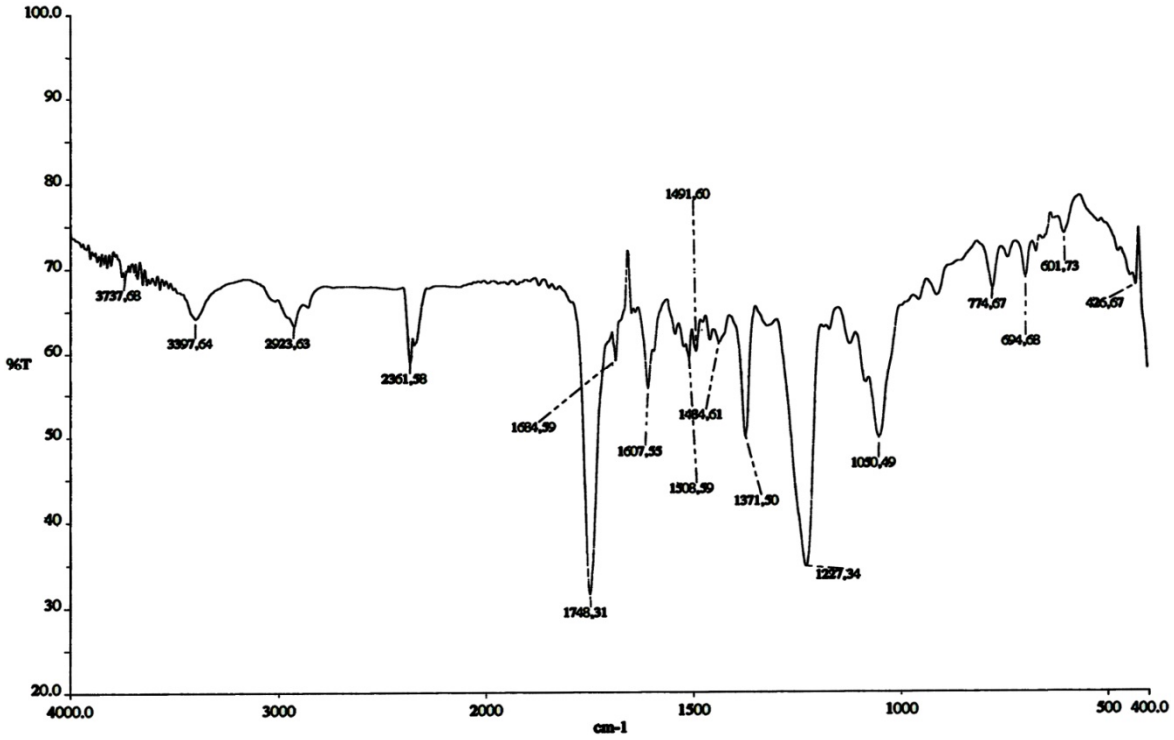


Figure 30 IR spectrum of compound **121**

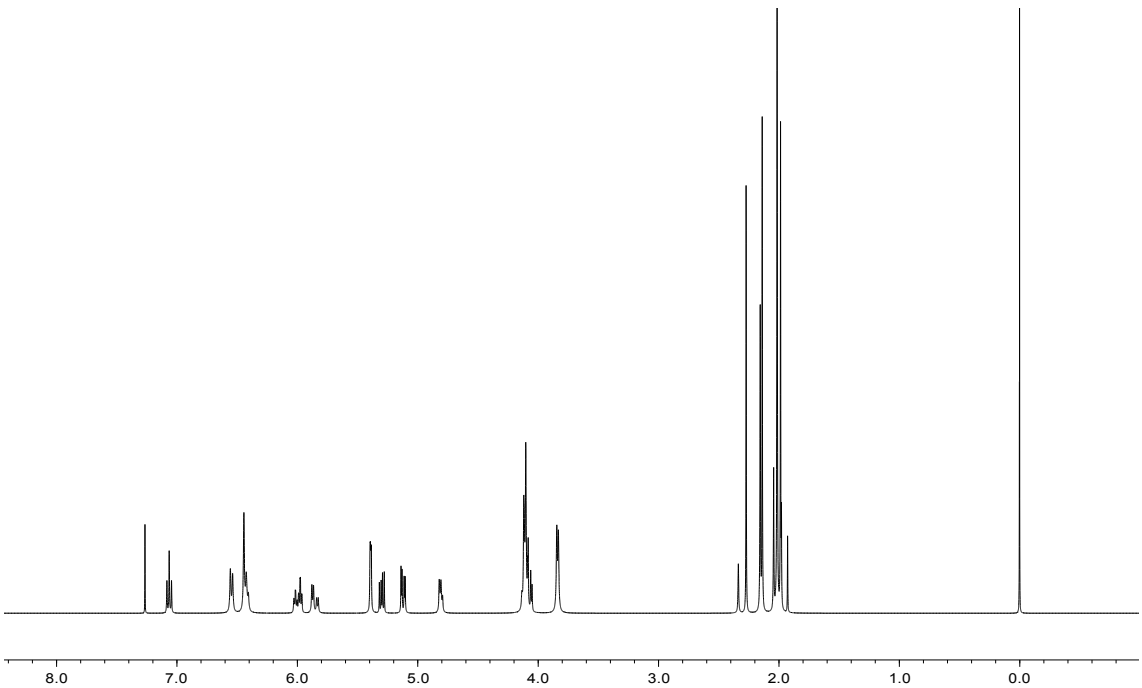


Figure 31 ^{1}H-NMR (400 MHz, $CDCl_3$) spectrum of compound **121**

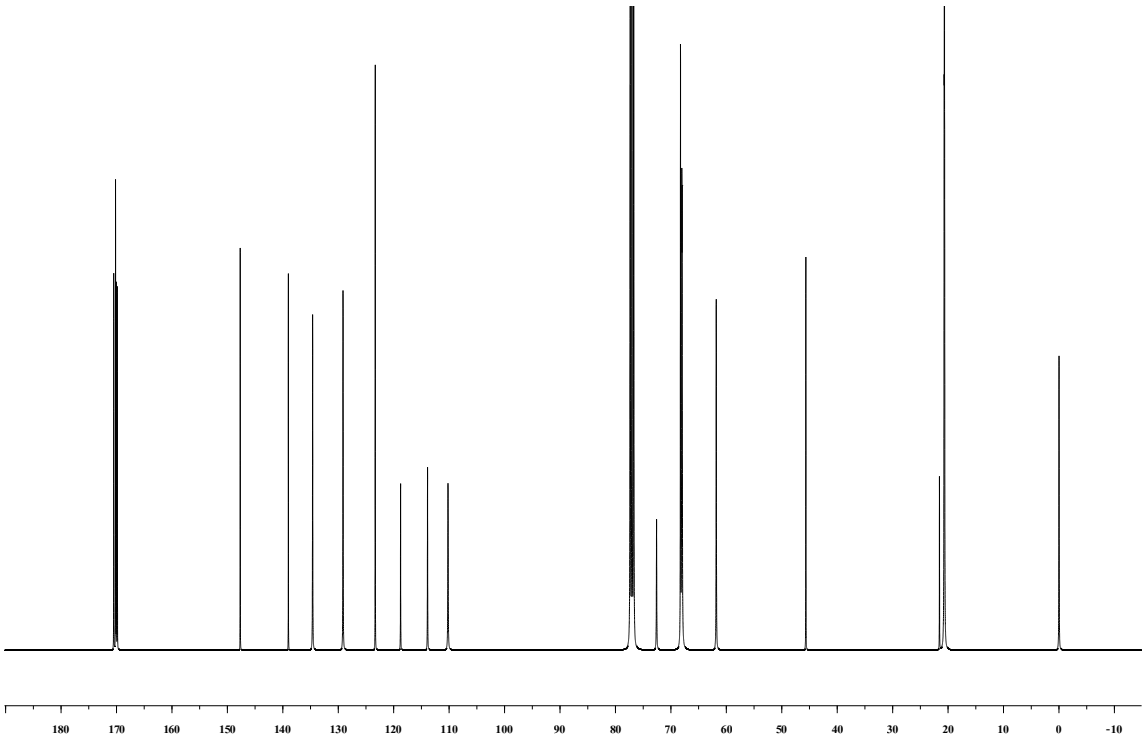


Figure 32 ^{13}C-NMR (100 MHz, $CDCl_3$) spectrum of compound **121**

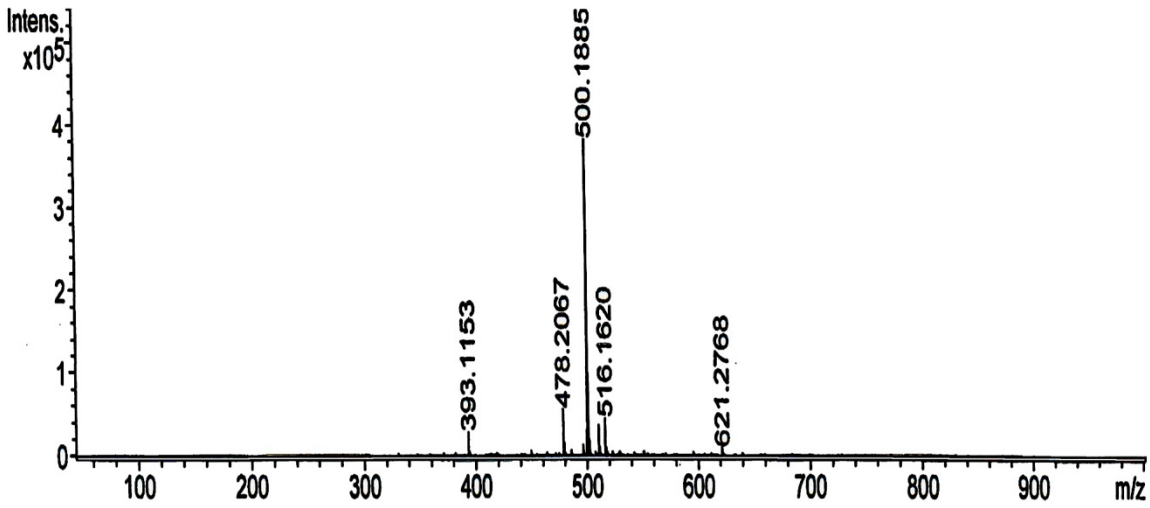
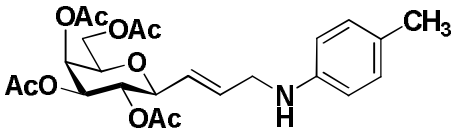


Figure 33 High resolution mass spectrum of compound **121**

Appendix I



Spectral data of compound 122

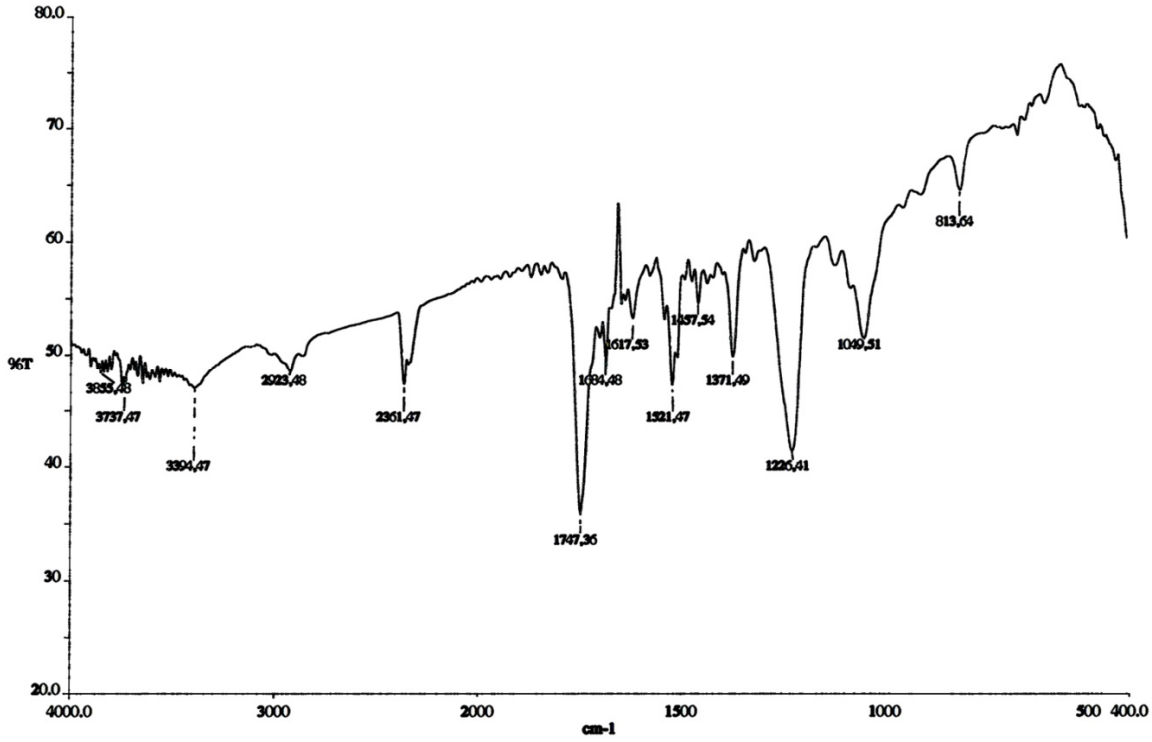


Figure 34 IR spectrum of compound **122**

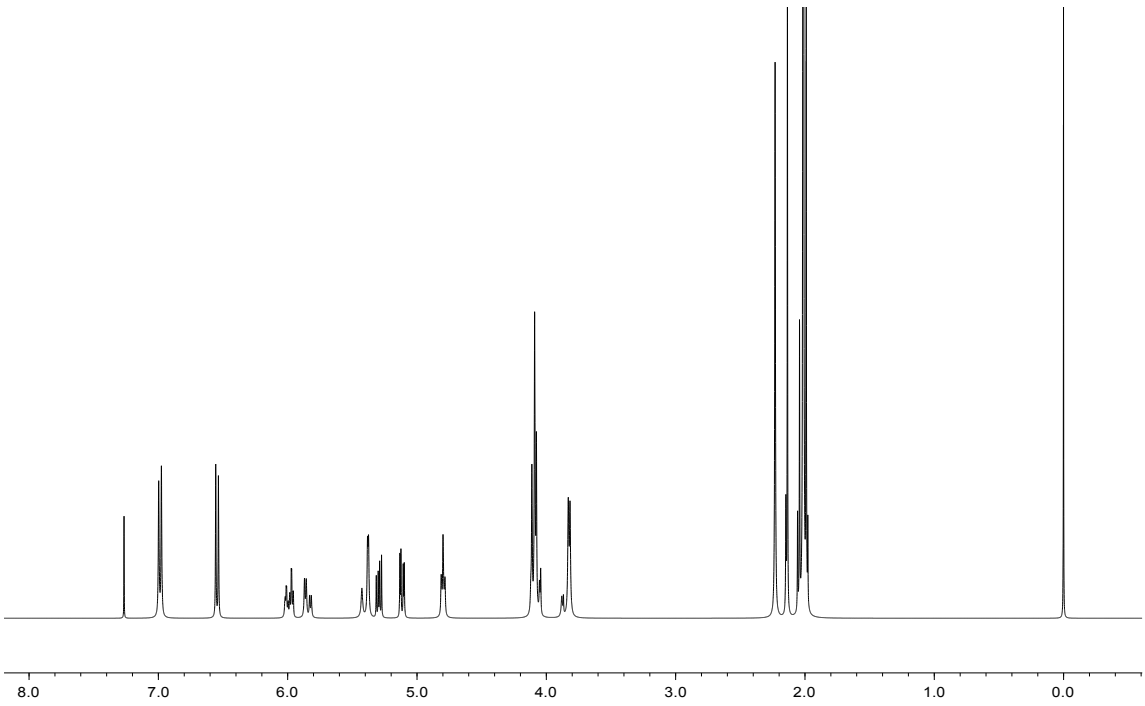


Figure 35 ^{1}H-NMR (400 MHz, $CDCl_3$) spectrum of compound **122**

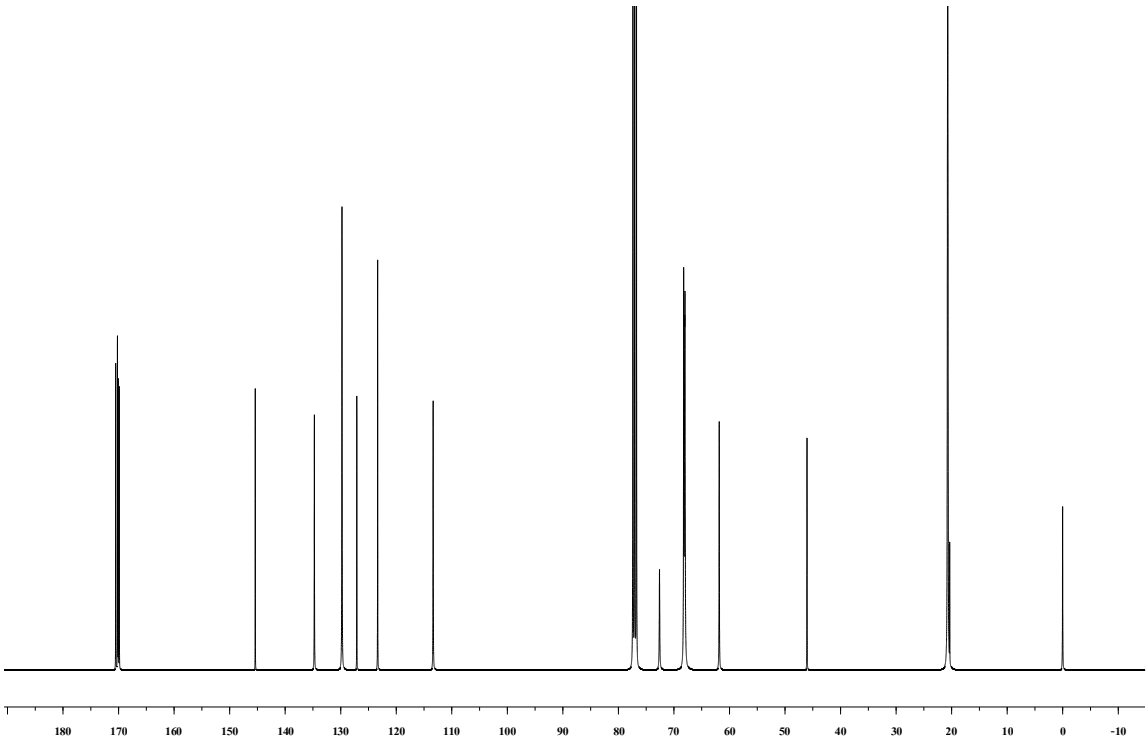


Figure 36 ^{13}C-NMR (100 MHz, $CDCl_3$) spectrum of compound **122**

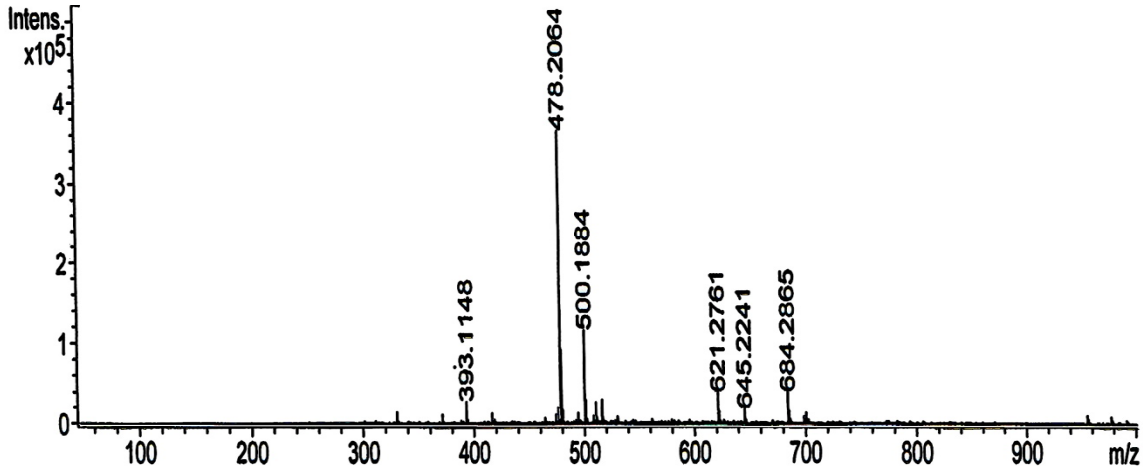
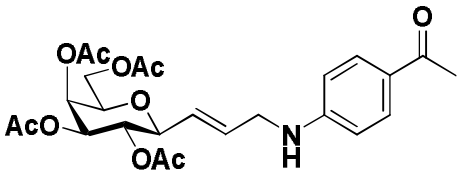


Figure 37 High resolution mass spectrum of compound **122**

Appendix J



Spectral data of compound 123

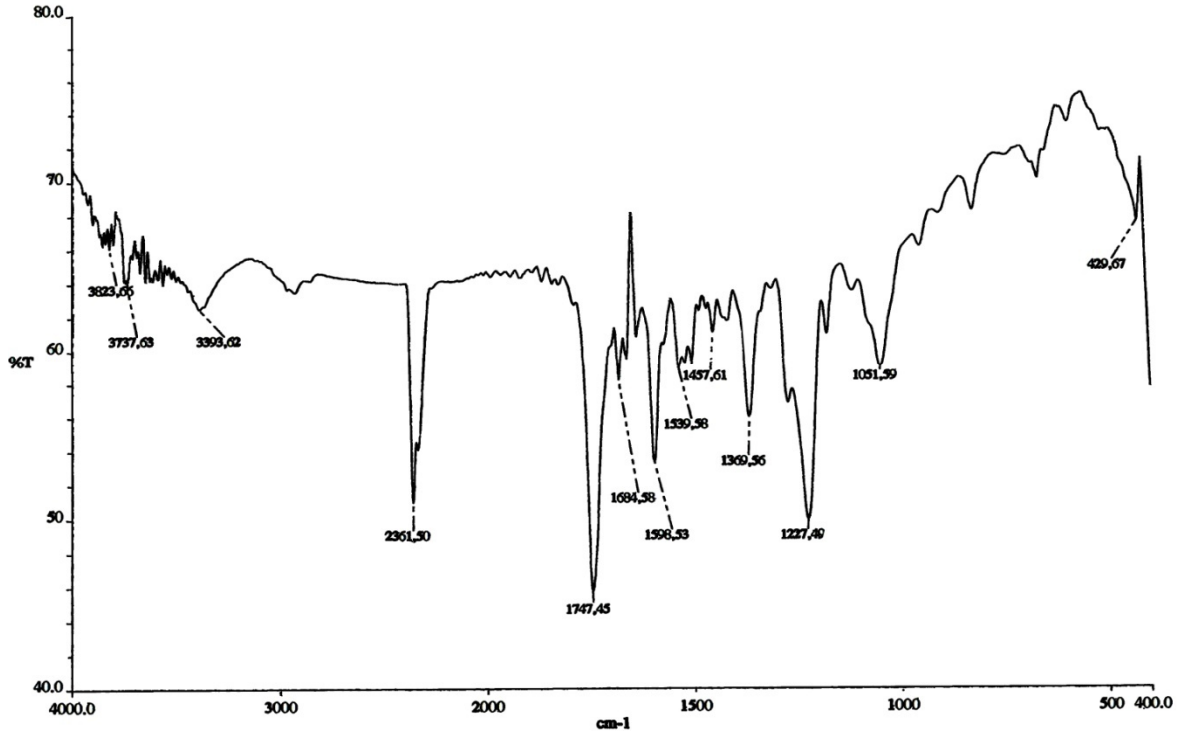


Figure 38 IR spectrum of compound **123**

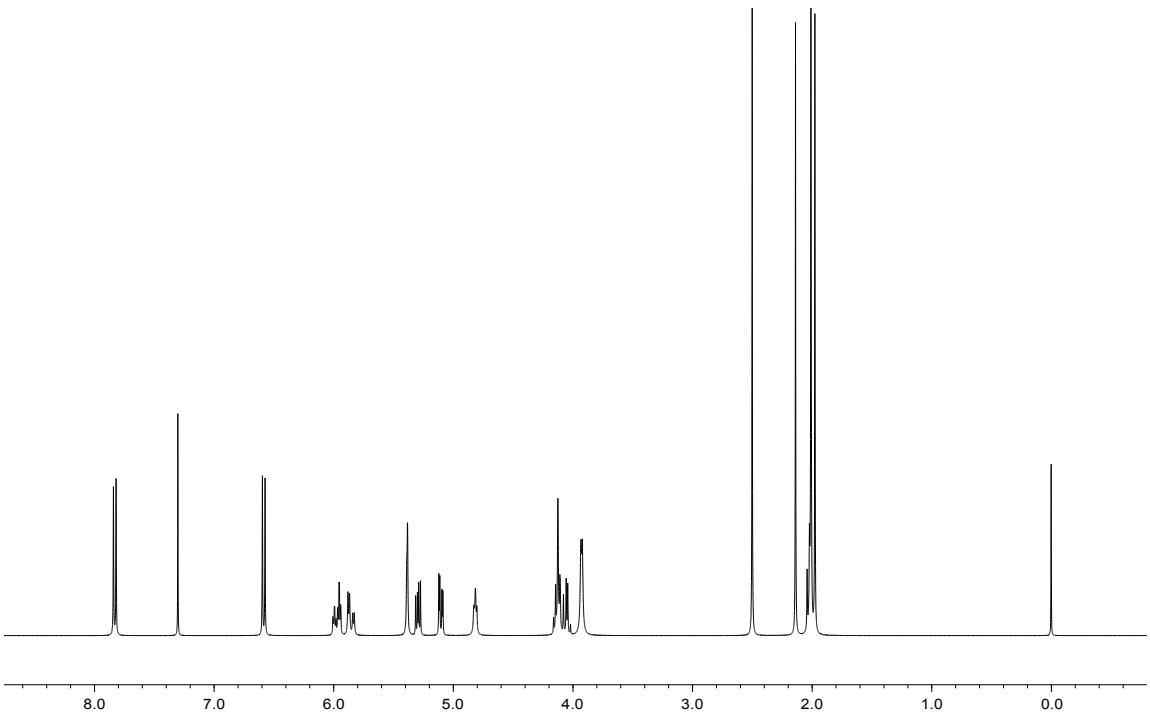


Figure 39 ^{1}H-NMR (400 MHz, $CDCl_3$) spectrum of compound **123**

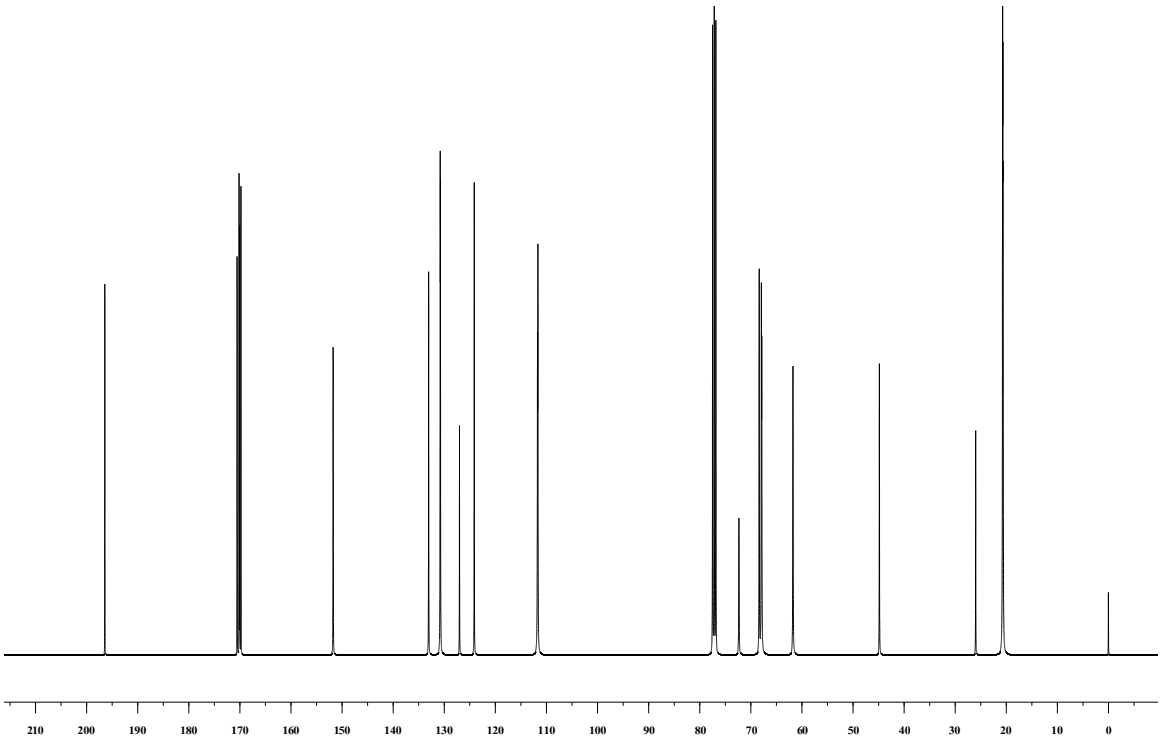


Figure 40 ^{13}C-NMR (100 MHz, $CDCl_3$) spectrum of compound **123**

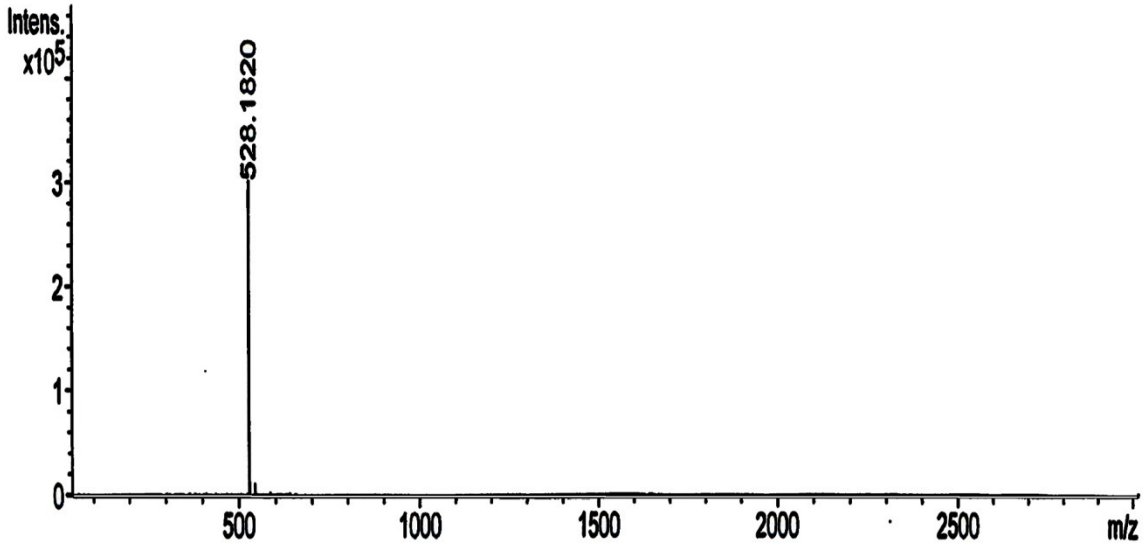
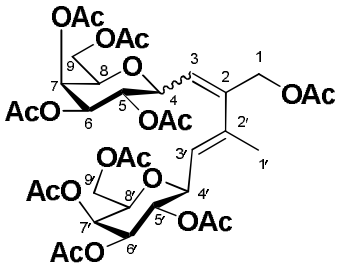


Figure 41 High resolution mass spectrum of compound **123**

Appendix K



Spectral data of compound 124

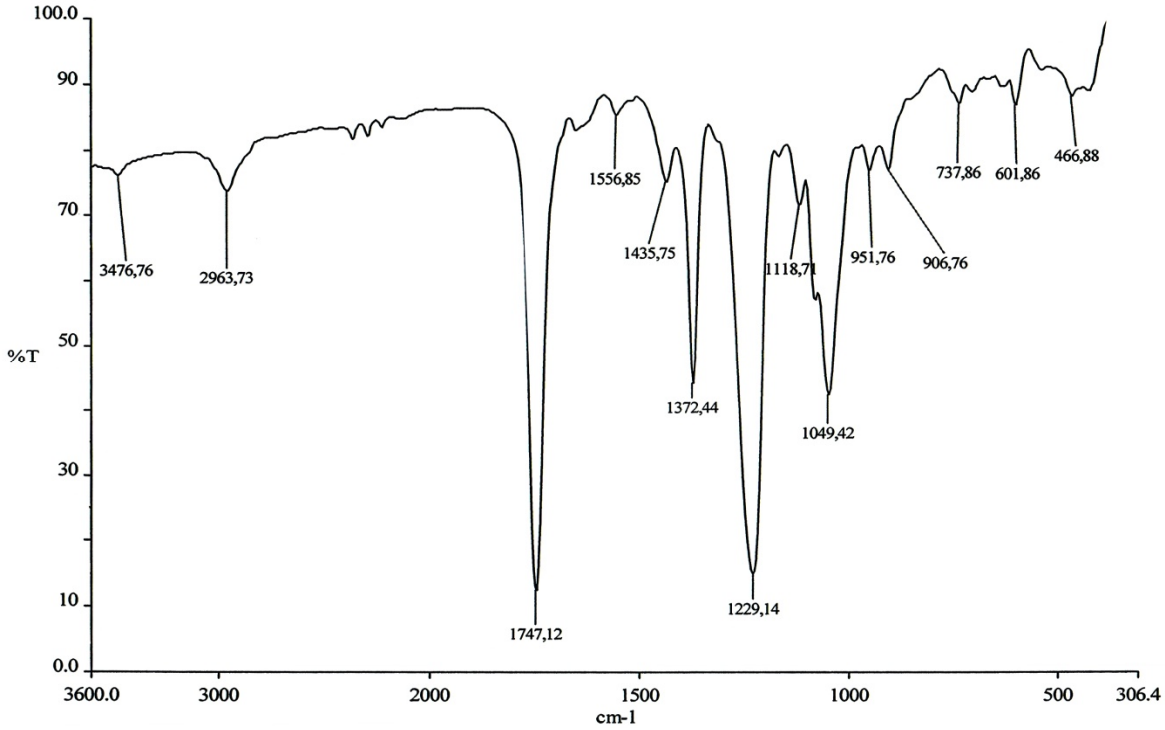


Figure 42 IR spectrum of compound **124**

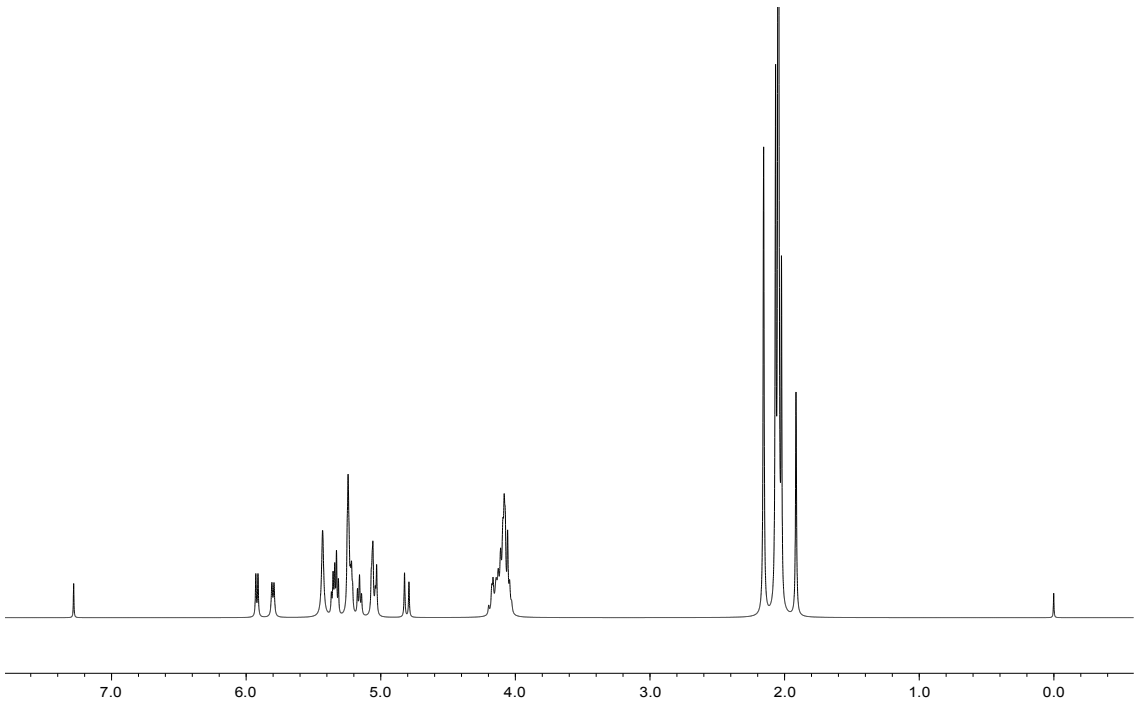


Figure 43 ^{1}H-NMR (400 MHz, $CDCl_3$) spectrum of compound **124**

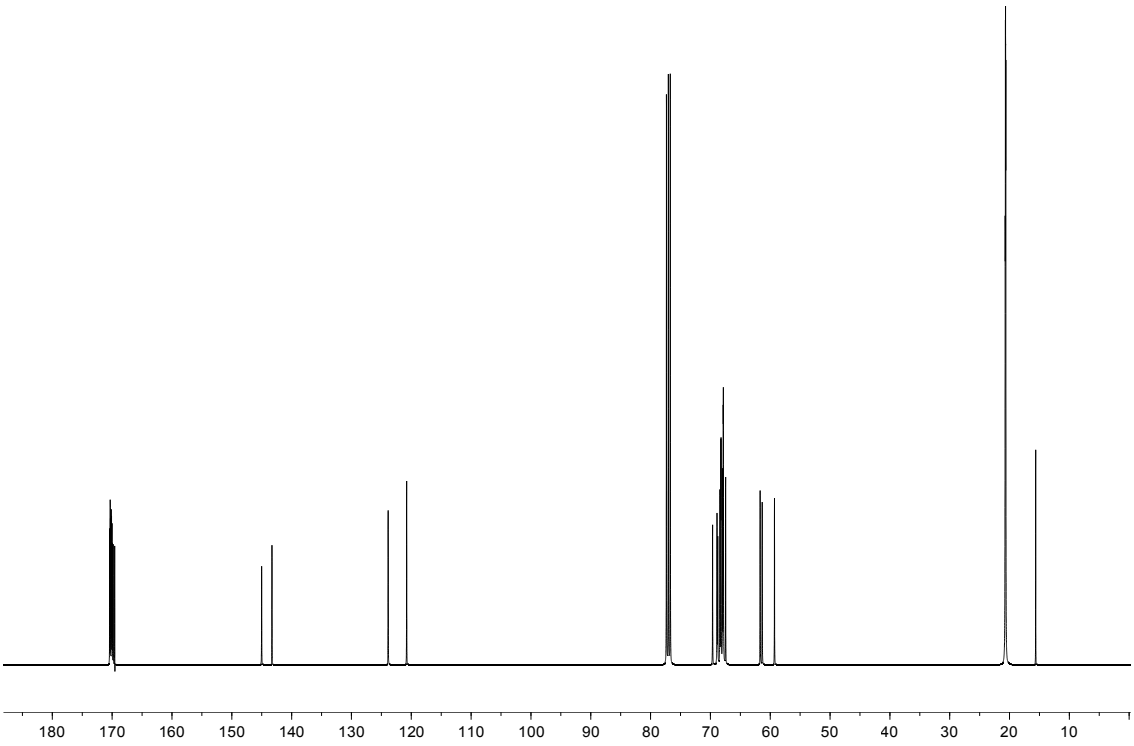


Figure 44 ^{13}C-NMR (100 MHz, $CDCl_3$) spectrum of compound **124**

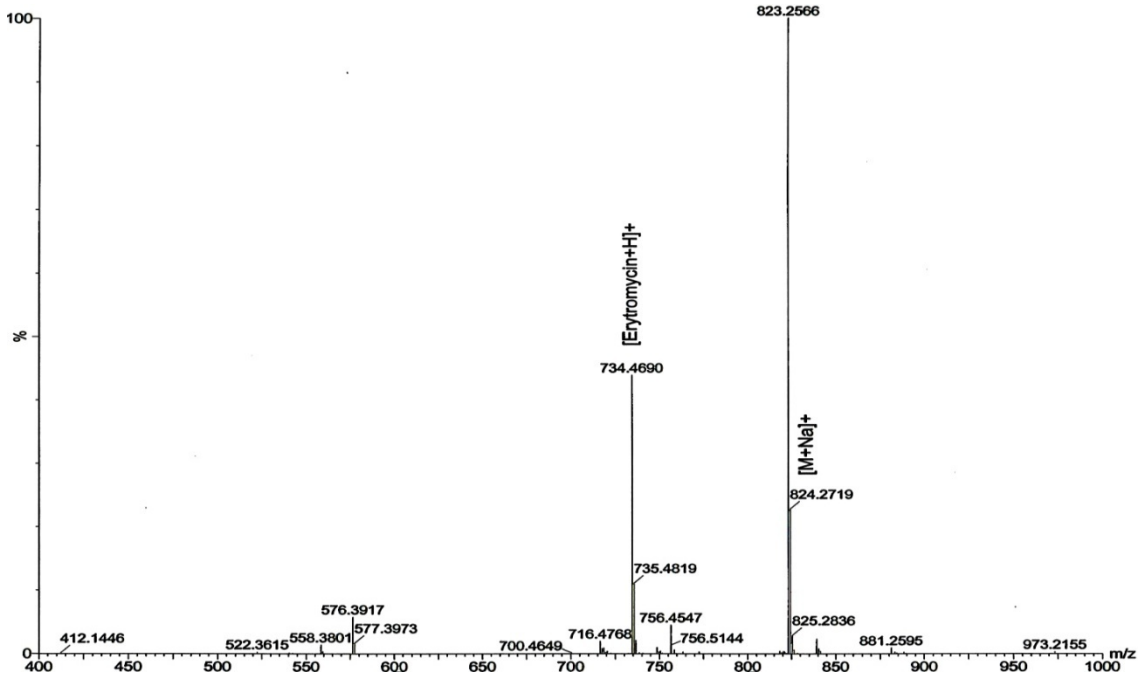
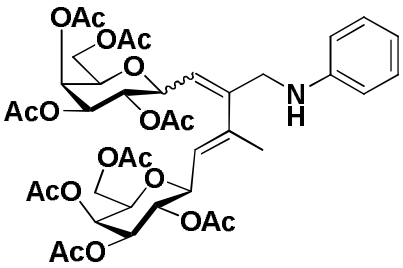


Figure 45 High resolution mass spectrum of compound **124**

Appendix L



Spectral data of compound 125

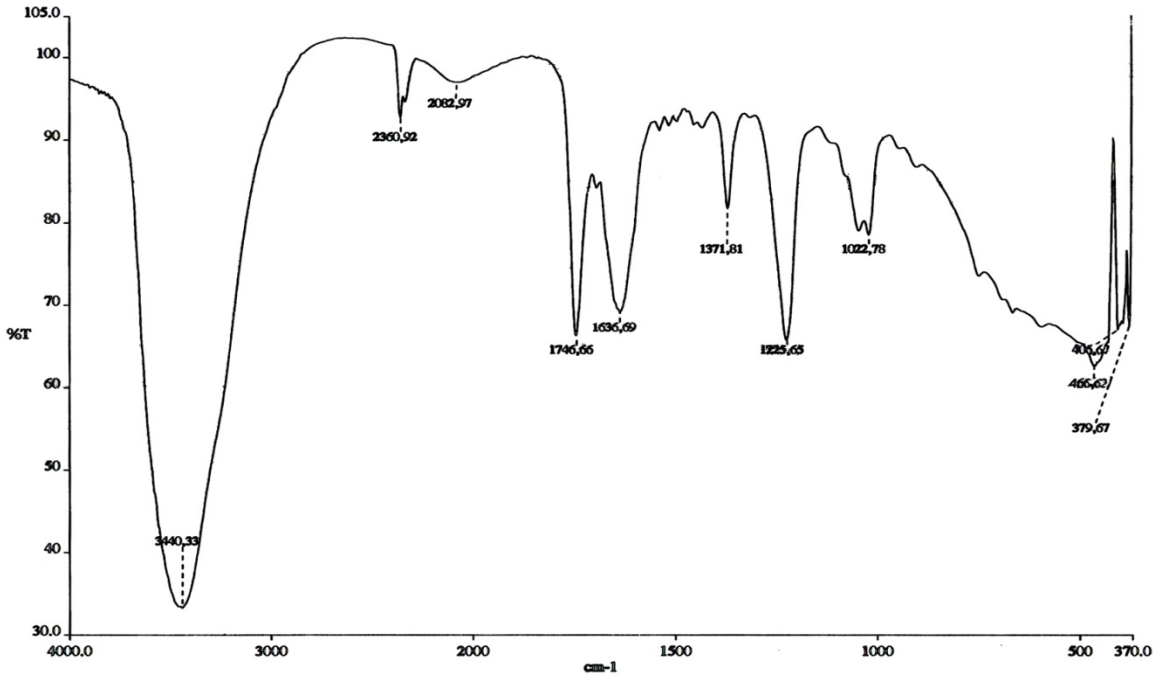


Figure 46 IR spectrum of compound **125**

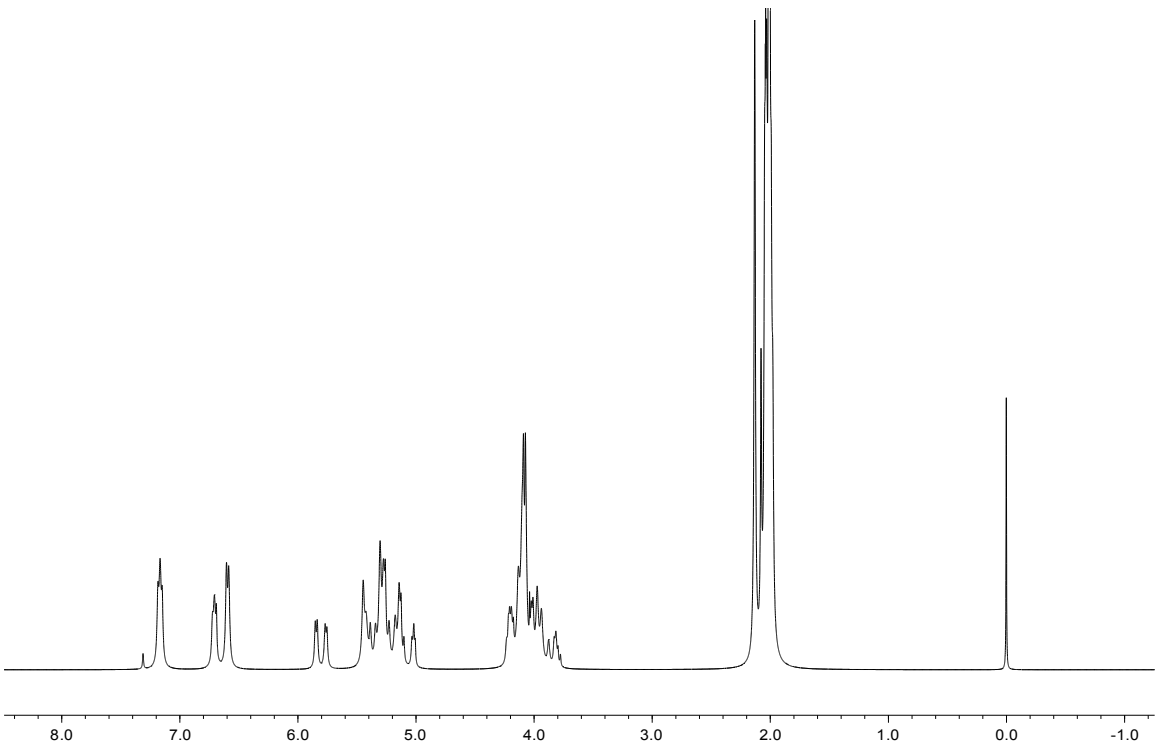


Figure 47 ^{1}H-NMR (400 MHz, $CDCl_3$) spectrum of compound **125**

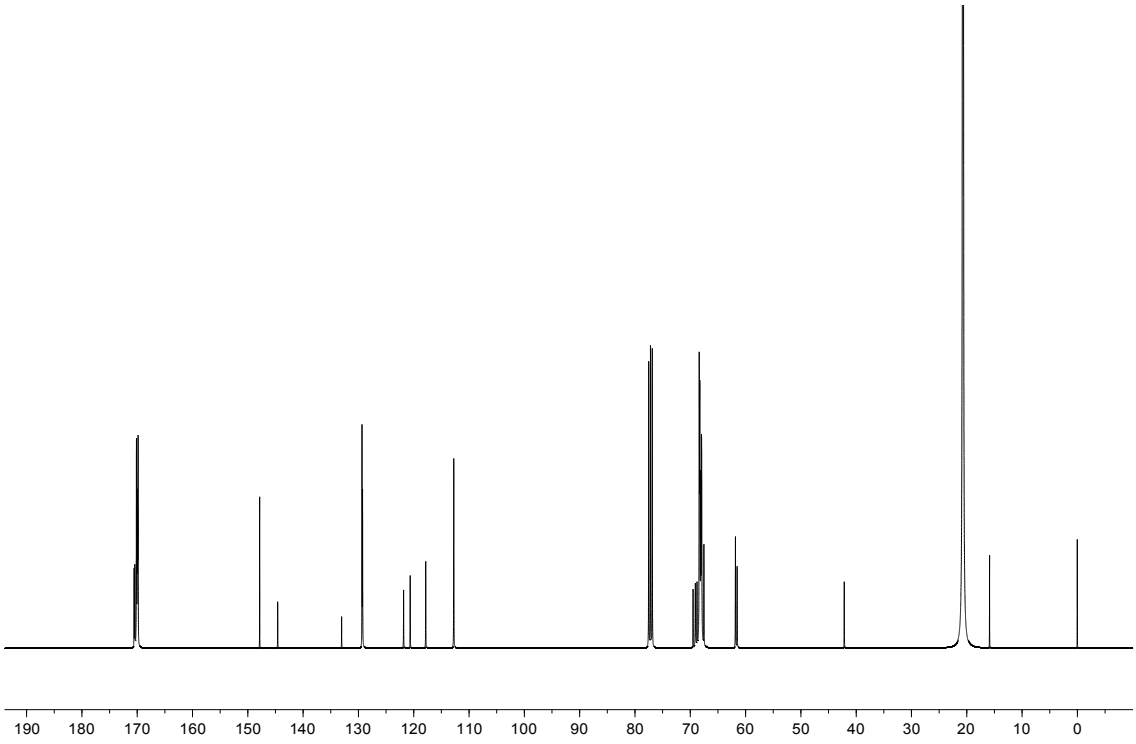


Figure 48 ^{13}C-NMR (100 MHz, $CDCl_3$) spectrum of compound **125**

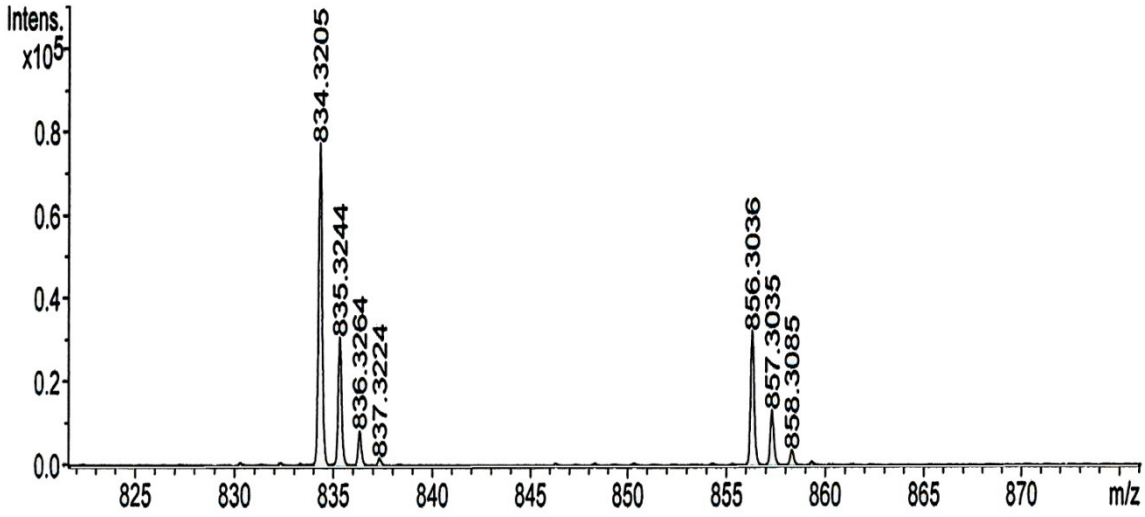
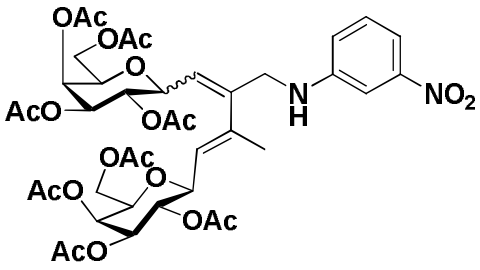


Figure 49 High resolution mass spectrum of compound **125**

Appendix M



Spectral data of compound 126

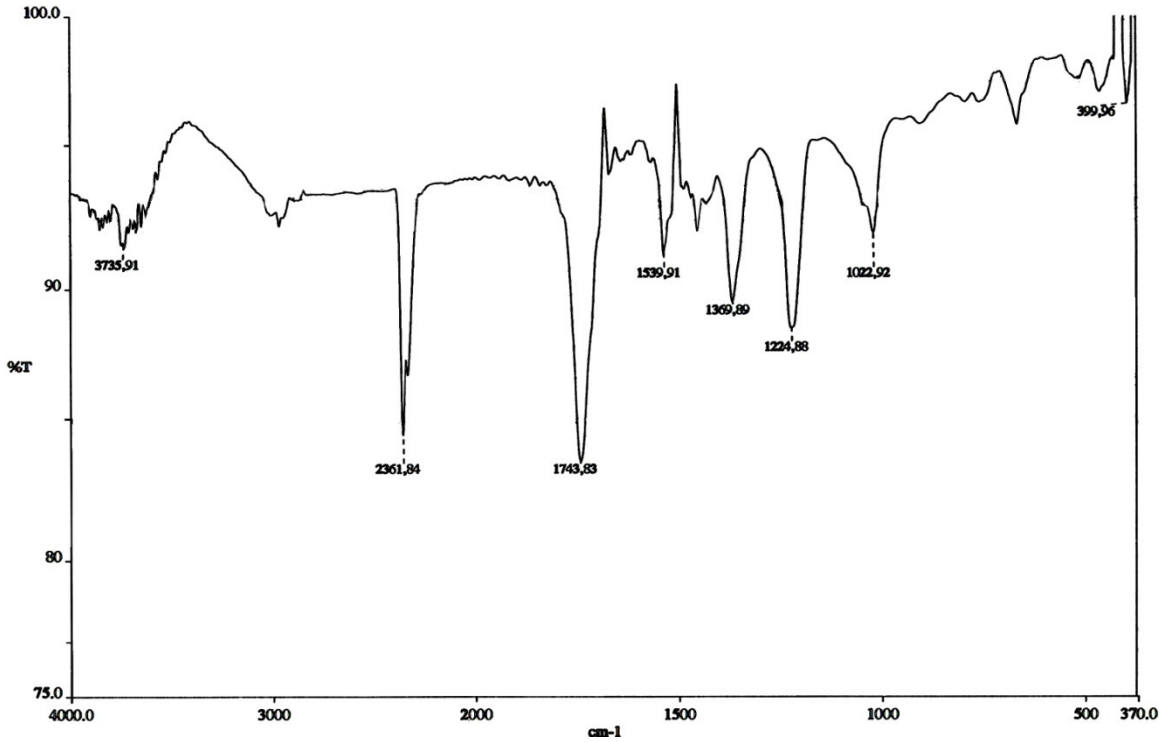


Figure 50 Infrared spectrum (thin film/NaCl) of compound **126**

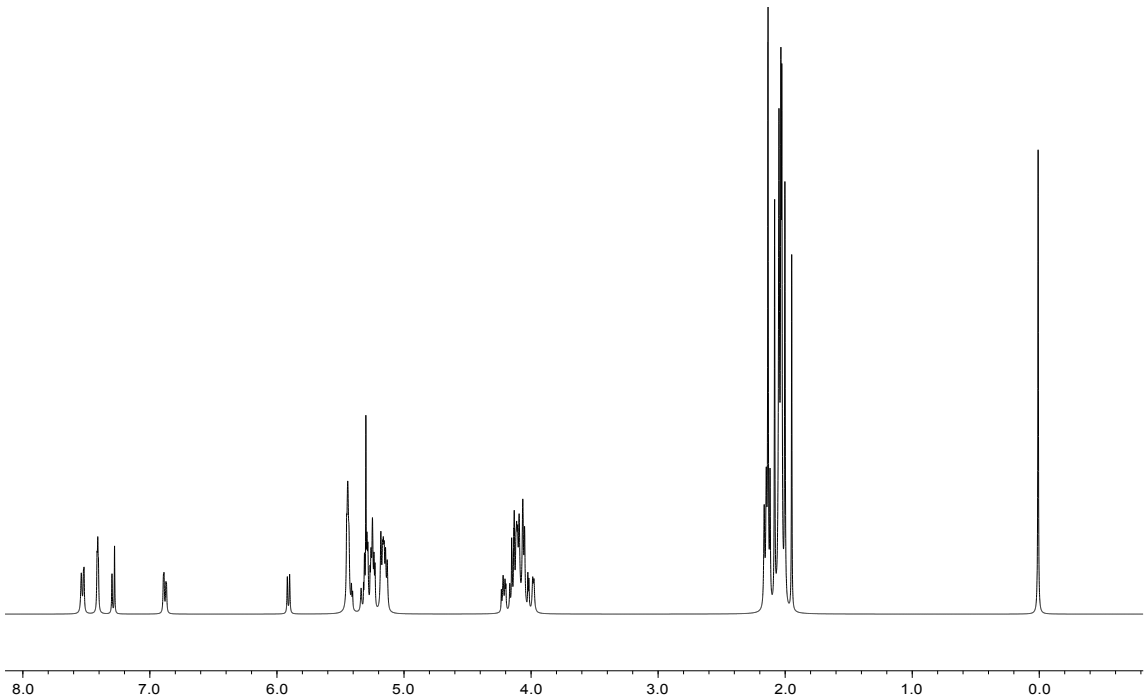


Figure 51 ^{1}H-NMR (400 MHz, $CDCl_3$) spectrum of compound **126**

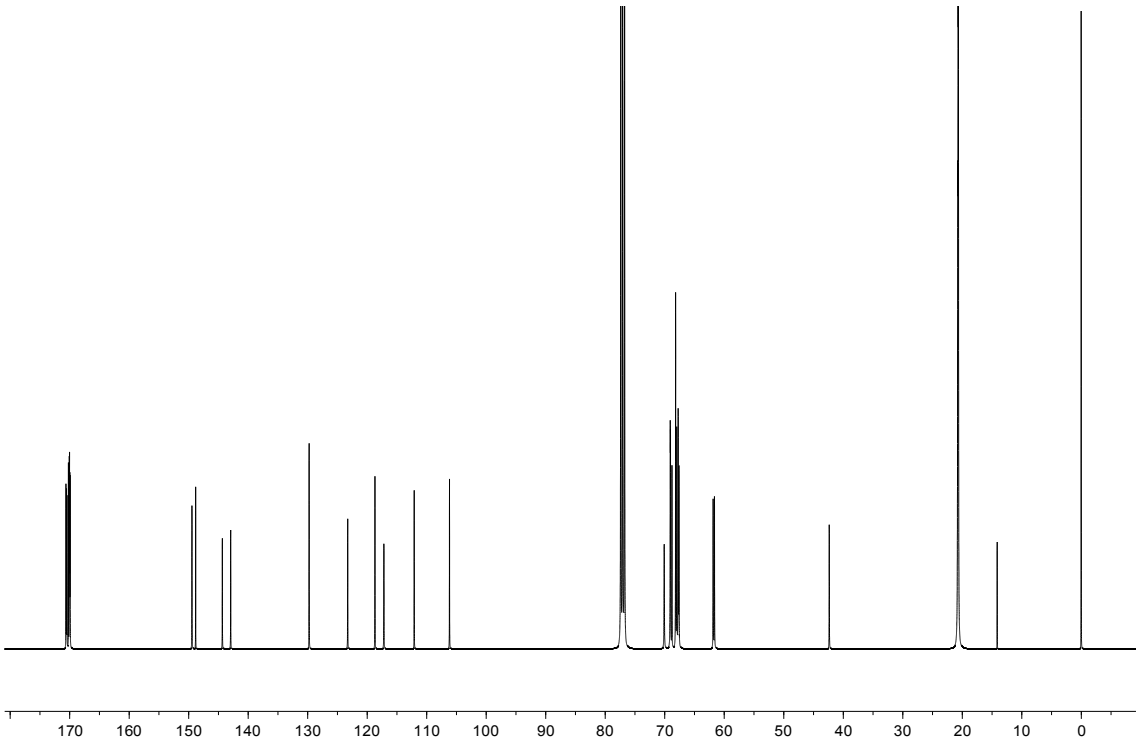


Figure 52 ^{13}C-NMR (100 MHz, $CDCl_3$) spectrum of compound **126**

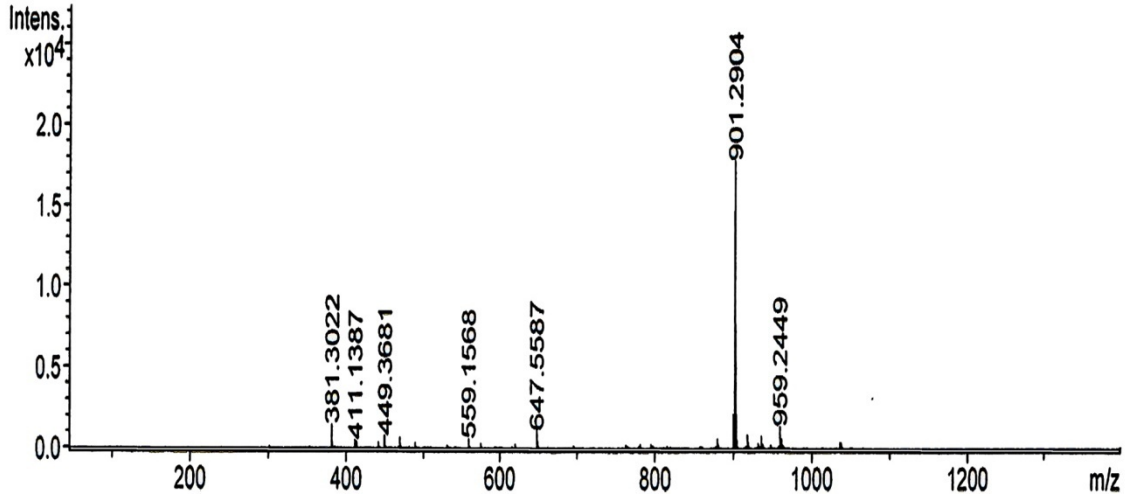
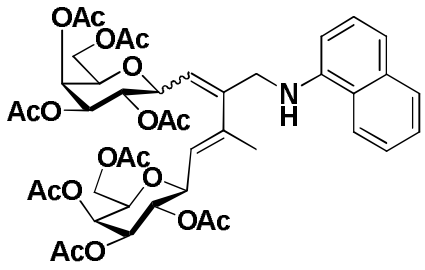


Figure 53 High resolution mass spectrum of compound **126**

Appendix N



Spectral data of compound 127

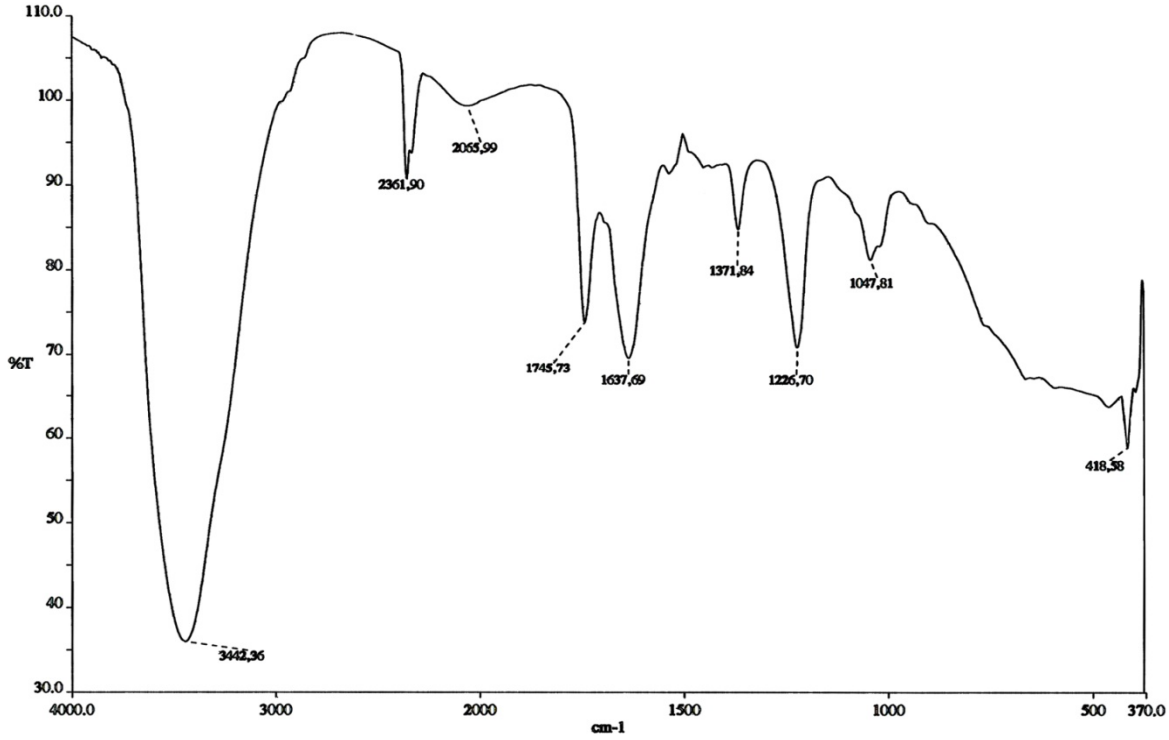


Figure 54 Infrared spectrum (thin film/NaCl) of compound **127**

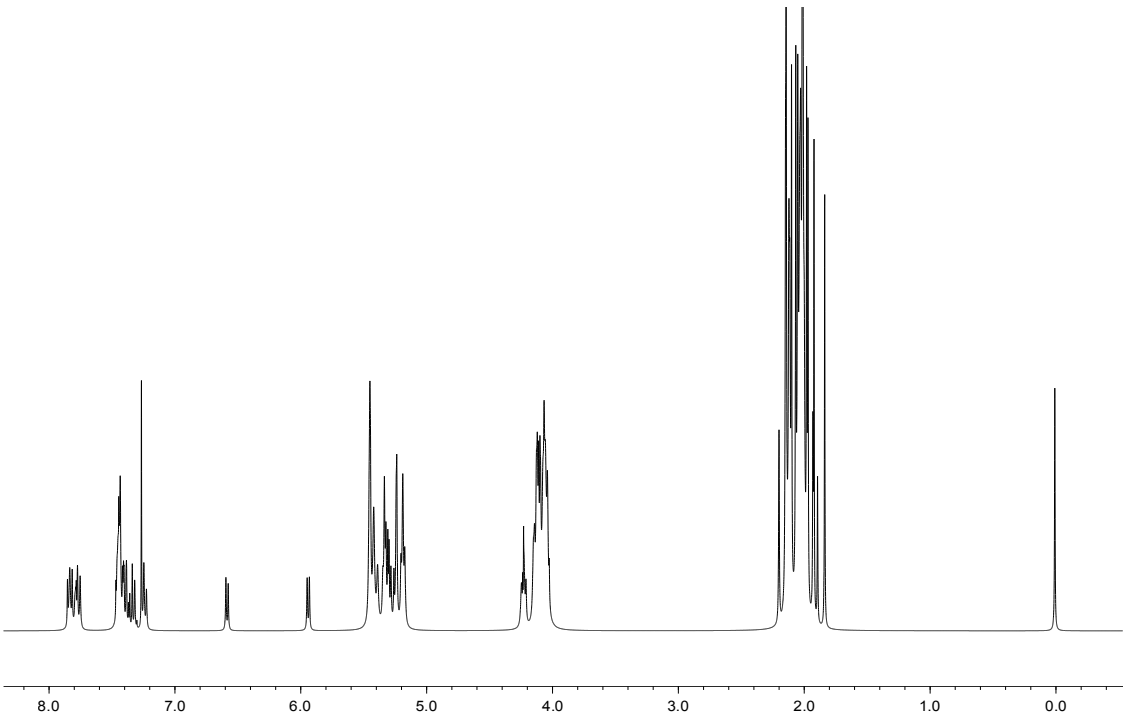


Figure 55 ^{1}H-NMR (400 MHz, $CDCl_3$) spectrum of compound **127**

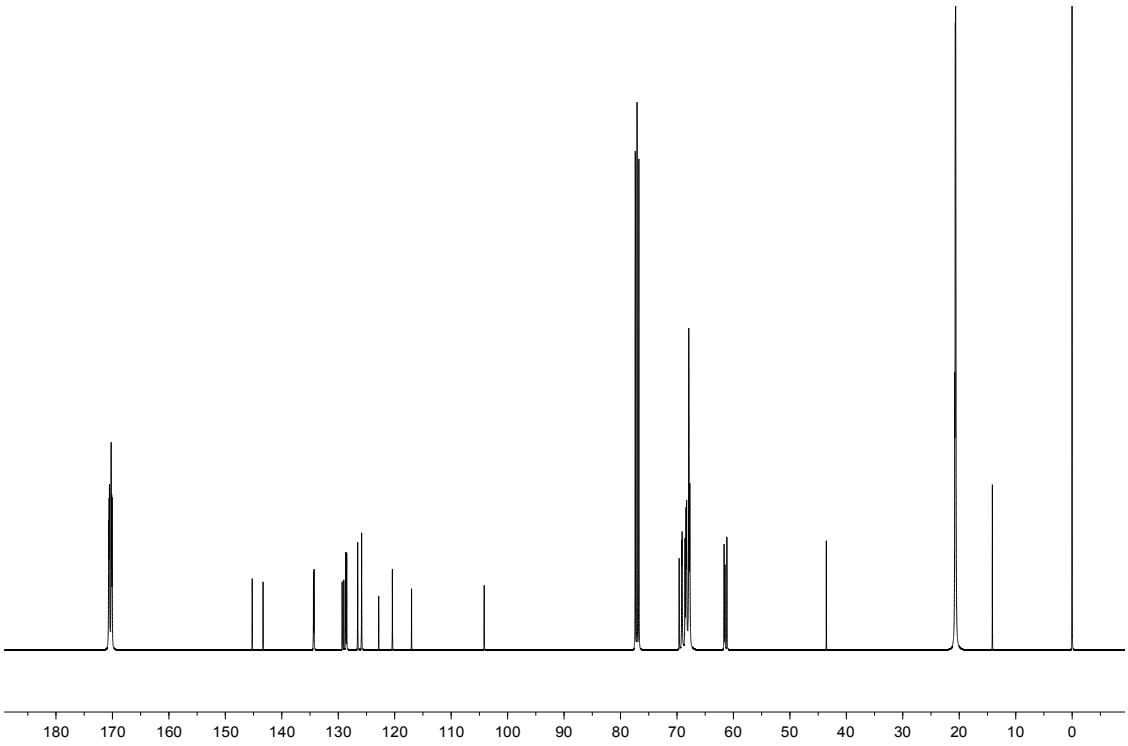


Figure 56 ^{13}C-NMR (100 MHz, $CDCl_3$) spectrum of compound **127**

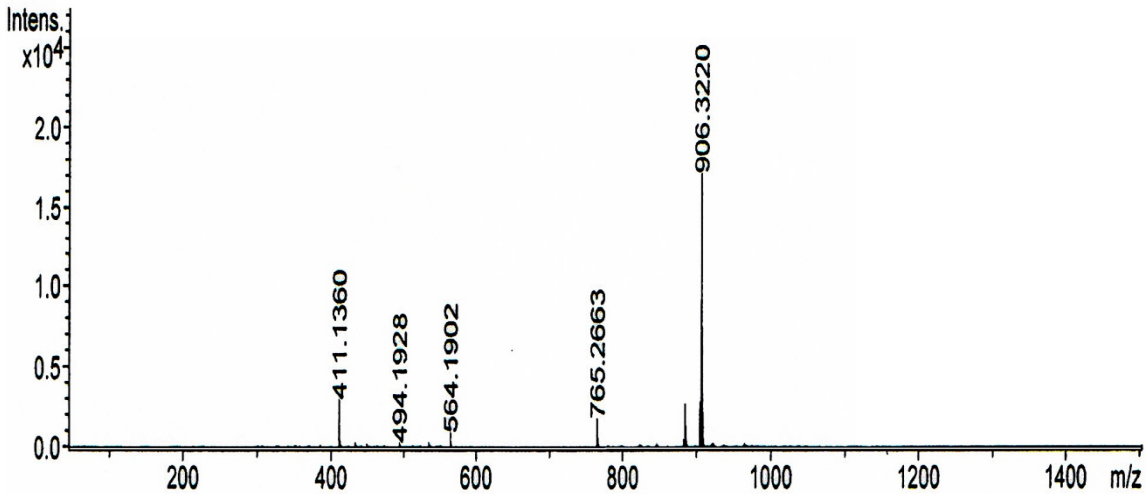


Figure 57 High resolution mass spectrum of compound **127**

BIOGRAPHY

BIOGRAPHY

NAME	Mr. Chaleowsak Khamwong
DATE OF BIRTH	October 3rd, 1986
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INSTITUTIONS ATTENDED	Bachelor of Science degree in Chemistry: Mahasarakham University, Thailand, 2005-2009 Master of Science degree in Chemistry: Mahasarakham University, Thailand, 2009-2012
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RESEARCH GRANTS & AWARDS

Center of Excellence for Innovation in Chemistry (PERCH-CIC)

RESEARCH OUTPUT

Publication:

- **Khamwong, C.** & Sakee, U. (2011) Palladium-catalyzed hydroamination of *C*-(tetra-*O*-acetyl-*β*-D-galactopyranosyl)allene. *Carbohydrate Research*, 346, 334-339.

Poster:

- Sakee, U. & **Khamwong, C.** Palladium-Catalyzed Hydroamination of Sugar Allene. *35th Congress on Science and Technology of Thailand (STT 35)*, 15th-17th October, 2009, Tide Resort (Bangsan Beach), Chonburi, Thailand.

Oral presentation:

- **Khamwong, C.**, Promthong, N., Kruanetr, S. & Sakee, U. Palladium- and Gold-catalyzed hydroamination of *C*-(tetra-*O*-acetyl-*β*-D-galactopyrano-syl)allene. *7th Congress on Center of Excellence for Innovation in Chemistry (PERCH-CIC VII)*, 4th-7th May 2011, Jomtien Palm Beach Hotel & Resort Pattaya, Chonburi, Thailand. p. 68.