تفاعل الإضافة ثنائية القطب الحلقية- ٣,١ لازيدات كاربوهيدراتية مع مشتقات كاربوهيدراتية تحتوي مجموعة غير مشبعة

أطروحة مقدمة إلى

مجلس كلية العلوم – جامعة بابل

وهي جزء من متطلبات نيل درجة الدكتوراه فلسفة علوم

في علوم الكيمياء / كيمياء عضوية

من

نبيل عبد عبد الرضا

تشرين الثاني – ٢٠٠٦ شوال - ١٤٢٦

بسم الله الرحمن الرحيم

يرفع الله الذين آمنوا منكم و الذين أوتوا العلم درجات و الله بما تعملون خبير

صدق الله العلي العظيم

(المجادلة :١١)

الإهداء

إلى الذي أحرق سنين عمره .... لينير لي الطريق

إلى الذي حلم أن يرى هذا اليوم ...

إلى الذي شجعني للوصول إلى الهدف ....

إلى الذي له كل هذا ...

والدي العزيز يرحمه الله و يسكنه فسيح جناته ..

إلى نبع الحنان الدافئ والدتي العزيزة أدام الله في عمرها

إلى الذين شدوا أزري و هيئوا لي الظروف أخوتي و أخواتي ..

إلى سندي و ساعدي في الحياة زوجتي .... أولادي ..

إلى كل الطيبين الذين ساعدوني ...

لهم هذا .....

نبيل عبد

الخلاصة

يتضمن البحث تحضير مشتقات كاربوهيدراتية جديدة تتميز بارتباط سكرين أحاديين بواسطة حلقة غير متجانسه اروماتية أو غيراروماتية ,اذ يرتبط السكر الأول بـ نتروجين الحلقة, و يرتبط السكر الثاني بذرة كاربون C-٥ أو C-٤ لنفس الحلقة.

و للحصول على هذه الأنواع من المركبات تطلب الأمر وضع استراتيجية تيسر الوصول إلى الهدف ، اذ قسمت إلى أربعة اتجاهات ، الاتجاه الأول منها هو تحضير مشتقات سكرية تحتوي في تركيبها على آصرة كاربون – كاربون مزدوجة أو ثلاثية و في مواقع مختلفة من السكر, اذ تم تحضير مشتقات الليلية او بروبرجيلة لسكر الفركتوزو الكلوكوز باستخدام طرائق عمل مختلفة معتمدة على نوع التقنية و نوع العامل المساعد المستخدم و قد حصلنا على المشتقات الآتيه :

[١١٥] ، [١١٦] ، [١١٧] ، [١١٨] ، [١١٩] ، [١٢٠] ، [١٢١] ، [١٢٢]

[١٢٣] ، [١٢٤] ، [١٢٥] ، [١٢٦] ، [١٢٧] ، [١٢٨] ، [١٢٩] ، [١٣٠]

[١٣١] ، [١٣٢] ، [١٣٣] ، [١٣٤] . الجدول(٧-٣) يوضح تراكيب و بعض خواص هذه المشتقات .

واما المرحلة الثانية فهي تحضير مشتقات سكرية تحتوي على مجموعة أزيد أيضاً في مواقع مختلفة من السكر باستخدام طرق عمل مختلفة و مخططات التفاعل اذحصلنا على المشتقات الإزيدية ، [١٣٧] ، [١٣٩] ، [١٤١] ، [١٤٢] [١٤٣] ، [١٤٤] ، [١٤٥] .

واما المرحلة الثالثة فقد تمثلت في تحضير نوعيين من السكريات غير المشبعة التي تحتوي على آصرة كاربون- كاربون مزدوجة داخل الحلقة و هي ٦,٤,٣ – ثلاثي استيتات كلوكال [١٤٦a] و ٥,٤,٣,١ – رباعي بنزويل فروكتال [١٤٧] .

واما المرحلة الأخيرة من الدراسة فهى بعد حصولنا على متطلبات تفاعلات الإضافة ثنائية القطب ٣,١ الحلقية ، اذا تم إجراء هذا النوع من التفاعلات باستخدام ظروف تفاعل مختلفة منها الطريقة الحرارية الاعتيادية حيث تطلب الآمر وقتا أطول و حرارة مرتفعة .

وكذلك أجريت بعض التفاعلات باستخدام تقنية الأنبوب المغلق . و لغرض التقليل من وقت التفاعل ودرجة الحرارة , اختيرت تقنية المايكروويف في إجراء هذا النوع من التفاعلات باستخدام عامل مساعد sod. ascorbate / $CuSO_4.5H_2O$ او استخدام العامل المساعد $CuBr.(PPh_3)_4$. وتم الحصول عل المشتقات (ترايزو سكريات ثنائية) Triazoyldisaccharide) جدول(٥-٣) جديدة تمتاز بكونها ذات فائدة حياتية جيدة اذ ان هذه المركبات هي سكريات ثنائية مرتبطة بحلقة ترايزولينيل او ترايزونليل و ليس أرتباط كلايكوسيدي اوكسجيني وهذا ما يجعلها مقاومة في بعض الأحيان للتحلل الكيميائي و الأنزيمي و تستخدم ايضا كعوامل مثبطات انزيمية و فعالية صيدلانية .

وشخصت جميع المركبات أعلاه باستخدام الطرائق الطيفية (طيف الأشعة تحت الحمراء و كذلك طيف الرنين النووي المغناطيسي و كذلك تحاليل العناصر بالإضافة الى دراسة بعض الخواص الفيزيائية للمشتقات المحضرة .

Dipolarcycloaddition reaction of Carbohydrate azides ١,٣ – with Carbohydrate Derivatives containing unsaturated groups

A Thesis

Submitted to the Council of College of Science

University of Babylon In Partial Fulfillment of the Requirements for the Award of the Degree of Doctor of Philosophy in Chemistry-Organic Chemistry

By

Nabeel Abed Abed AL-Radha

June- ٢٠٠٦ *Jamadi AL-A'awel* ١٤٢٦

Certification

I certify that this thesis was carried out under my supervision at the Department of Chemistry , College of Science , University of Babylon as partial requirements for the degree of Doctor of Philosophy in Organic Chemistry.

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Signature :

Name : Dr.Mousa Al-Samadi

Jordan/Unv.of Science and Technology

In the view of the available recommendation , I forward this thesis for debate by the Examining Committee .

Signature :

Name :

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ABSTRACT

The compounds of the present study are synthesized of disaccharides where the link between the two carbohydrate groups via a ١,٢,٣,-triazole or triazoline groups where the N-١ nitrogen atom of the triazole ring is linked to the first saccharide group and the ٤-carbon or ٥-carbon atom of the triazole ring is bound to a second saccharide groups which is named triazoyldisaccharides .

The key steps in this approach are divided into four parts .The first part is the synthesis of some carbohydrates containing the alkyne or alkene group in different position of the sugar moieties with different reagents affording compounds [١٢٢] ,[١٢١] , [١٢٠] , [١١٩] , [١١٨] , [١١٧] , [١١٦] , [١١٥] , [١٢٣] , [١٢٤] , [١٢٥] , [١٢٦] , [١٢٧] , [١٢٨] , [١٢٩] , [١٣٠] , [١٣١] , [١٣٢] , [١٣٣] , [١٣٤] .

The second part , is applying different methods to the synthesis of glycosyl azides derivatives in good yield affording compounds [١٣٧] , [١٣٩] , [١٤١] , [١٤٢], [١٤٣] , [١٤٤] , [١٤٥] s.

The third part of this work, includes preparation of unsaturated sugars which contained carbon carbon double bond inside the ring , like ٣,٤,٦ – tri acetyl glucal [١٤٦a] and ١,٣,٤,٦,-tetra benzoyl fructal [١٤٧] .

The last part of this study, applied ١,٣ -dipolar cycloaddition reaction after obtaining the azide derivatives and the alkynes or alkenes derivatives to the synthesis of triazolyl or triazolinyl sugar derivatives.

Several methods can be employed for the preparation of triazoles and triazolines derivatives , depending on the type of technique used (thermal , microwave , sealed tube ,one-pot synthesis reaction) and type of catalyst like CuBr. $(PPh_3)_4$, $CuSO_4.5H_2O$/sodium ascorbate .

The structures of all the products obtained have been identified by spectral (IR , H^1 – NMR) , elemental (C,H,N) analyses and by some physical properties .

These compounds are expected to show an importance in organic synthesis and expected to be more stable to enzymatic and chemical hydrolysis . They may find utility as enzyme inhibitor agents and potentially as pharmaceuticals .

List of Symbols and Abbreviations

DMF	*N,N* - Dimethyl formamide
TBAB	Tetrabutyl ammonium Bromide
NMR	Nuclear magnetic resonance
IR	Infra red
FT-IR	Fourier Transform-Infrared
α	Alpha (position w.r.t carbonyl group)
β	Beta (Position w.r.t carbonyl group)

Å	Angstrom
A	Arrhenius constant
Ac	Acetyl (CH_3CO-)

aq	Aqueous
Bz	benzoyl
DBU	١,٨-diazobicyclo{ ٥.٤.٠} undec-٧-ene
DCM	dichloromethane
EtOAc	Ethyl acetate
hr	hour
m.p	melting - point
min	minute
Ms	mesylate
ppm	Part per million
rt	Room temperature
TLC	Thin-Layer Chromatography
R_f	Factor of retention
Boc	*N*-tert-butoxy carbonyl
DMSO	Dimehyl sulfoxide
eq	equivalents
Me	Methyl
Tf	triflate
Ts	tosylate

NIS	N-iodosuccinimide
TfOH	trifluoromethane sulfonic acid (traffic acid)
TMS	trimethylsilyl
TMS-N_3	trimethylysilyl azide
TBAF	Tetrabutyl ammonium fluoride
ph	phenyl
TBAT	Tetrabutylammonium triflat
TG	١,١,٣,٣ tetramethylguanidinium azide
ZnN_6.pyr	Zinc azide bis pyridine
١,٣ DC	١,٣-dipolar cycloaddition reaction
CAN	Ceric (IV) ammoniumnitrate
BF_3.Et_2O	Boron trifluoro etherate
TMSOTF	Trifluromethanesulfonic triflate

HMPA	Hexamethylphosphoramide
MAOS	Microwave assisted organic synthesis
PTC	Phase transfer catalyst
NMP	N-methyl pyrrolidinone
ε	Dielectric constant
Bn	Benzyl
DEAD	Diethyl azodicarboxylate
BOP	Benzoyl peroxide
DIAD	Diisopropyl azodicarboxylate
DC	Dipolar Cycloaddition
THF	Tetrahydrofuran

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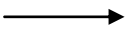

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CHAPTER ONE

١-٠ Introduction

One of the most abundant classes of organic and biological molecules found in nature are carbohydrates which over ٣٠ years have become a growing area in chemical and biochemical researches.[١] Carbohydrates have formula $C_x(H_2O)_y$, and are usually defined as poly - hydroxy aldehydes and ketones[٢]. They are divided into three types, monosaccharides which cannot be hydrolyzed into simple compounds and can be found in two forms : aldoses and ketoses.[٣],

They may be represented in different projections.

Figure ١.١ Different projections of D - glucopyranose

A monomer of a carbohydrate typically consists of a ٣ – ٩ carbon chain with several hydroxyl groups . These hydroxyl group can be modified into carboxylic acid , amine, phosphate , sulphonates , azides , acetate or can be removed , so it is called deoxy-sugars .

Figure ١.٢ Some important modified carbohydrates

Second type is oligosaccharides which when hydrolyzed yield (٢-١٠) molecules of monosaccharide. The third type is called polysaccharides , that yields a large number of monosaccharide molecules (more than ١٠) .

The linear chains of the carbohydrates can be cyclized into either five-member ring (furanoses) or six-membered ring (pyranoses) via an hemiacetal or ketal formation .

This ring closure can occur from one or both sides of the carbonyl group giving a new asymmetric centre and therefore results into two possible isomers[٤] α and β .

Scheme ١.١ Different forms of D- glucose

Carbohydrates are found ubiquitously as sources of metabolic energy and as key components feverous intercellular recognition processes including infection, inflammation, metastasis differentiation, development and regulation of signalling [٥].

For a long time, carbohydrates and peptides were considered as separate classes of natural products. However, it is now well established that most proteins of eukaryotic cells are glycoproteins ; they are covalently linked to saccharide portions [١,٤]. Carbohydrates are implicated in wide range of processes [٦] such as cell-cell recognition, fertilisation, embryogenesis, neuronal development, hormone activities, the proliferation of cells and their organisation into specific tissues, viral and bacterial infections and tumour cells metastases [٧].

Carbohydrates are involved in a whole range of biological processes which provide both the desire to develop new methods for carbohydrates synthesis [٨] and the investigation of carbohydrates as therapeutic agents [٩]. So carbohydrates analogues have also been identified as useful glycosidase inhibitors and as such have proved to be of use in therapeutic strategies for the treatment of cancers, aid and diabetes [١٠]. It is now well established that in the living cell, carbohydrates play key roles in many different processes[١١].

The chemists consider complex carbohydrates to be difficult to synthesize and manipulate, and their biological functions are often not well defined.

The biologists don't have useful tools to study carbohydrates. The medicinal chemists consider complex carbohydrates as an uninteresting class of molecules for drug development [١٢].

In addition to the manufacture of sucrose and paper, which are today important industries, carbohydrates play a major role in a number of other industries. These include; {a} food industry {b} textile industry {c} pharmaceutical industry {d} chemical industry .Carbohydrates also play a key role in the process of life [١٣].

١-١ Protecting Groups

The need for highly selective functional group manipulations must be regarded as one of the general problems in carbohydrate chemistry. Since carbohydrates are polyfunctional compounds, they are usually displaying several different reactive hydroxyl groups in combination with various other functionalities.

The planning of protecting group strategies is therefore a crucial step in carbohydrate chemistry and specially in the beginning of any carbohydrate synthesis [١٤].

For carbohydrates, the classical protecting groups are used most frequently (ester, ether) for the blocking of single hydroxyls as the benzylidene and

isopropylidene acetals for pairs of hydroxyls.

Figure ١.٣ Protecting groups commonly used in carbohydrate chemistry

Examples for the applications of these protecting groups are legions and several review articles which deal with general aspects of this topic [١٦-٢٤].

The protecting group is needed to block the functional group that is not to

participate in the coupling reaction .

A protecting group has to fulfil several important criteria i) it should be easy to introduce . ii) it should be stable under several reaction conditions, and iii) it should be easily removed .

١-١-١ protecting of the anomeric centre

Protecting of the anomeric centre in monosaccharides can most easily be achieved by the conversion into a simple alkyl glycoside which can be used as the starting material for further blocking reaction. The classical Fischer method still provides the simplest entry to alkyl α-D -glycosides and is often the first step in a complex protecting group protocol [١٥].

Figure ١.٤ : Commonly used glycosidation reagents in anomeric center

The stereoselectivity of the formation of an *O*-glycosidic linkage is strongly dependent on the nature of the protecting groups applied . A primary contribution comes from the protecting group attached to C-٢ of the glycoslyl donor [٢٥].

١-٢ *O*-glycosides

O - Glycosides and other bioactive oxygenated natural products are important because the polar hydroxyl function aids both water solubility and molecular recognition by directed hydrogen- bond interactions that convey biological specificity .

There are two independent approaches to produce hydroxylated compounds : oxidative functionalization of activated precursors and framework construction from building blocks with concomitant development of functionalities . [٢٦]

Glycosides are abundant in nature and many biologically important molecules contain glycosidic linkages [٢٤].

Treatment of monosaccharide hemiacetal with alcohol and an acid catalyst

yields an acetal in which the anomeric-OH has been replaced by an-OR group.

The pioneering works in the chemical synthesis of carbohydrate derivatives were performed by Michael (١٨٧٩), Fischer (١٨٩٣), Koenigs and Knorr (١٩٠١), Helferich and Olst (١٩٦٢), Lemieux at al.(١٩٧٥), Paulsen (١٩٨٢), and have contributed substantially to a better understanding of the strereospecific formation of the *O*-glycosides linkage [١٥].

The preparation of the fragments of *O*-glycosides requires a highly convergent synthetic strategy [٢٧].

The most synthetic effort is directed toward the preparation of the monomeric glycosyl donor and acceptors. The anomeric substituent of a saccharide building block should be sufficiently stable to withstand protecting group manipulation (acts as a protecting group), but also has an adequate reactivity to permit the use as a glycols donor (acts as a leaving group) [٢٨]. Thioglycosides [٢٩] and n-pentyl glycosides [٣٠] have been shown to possess these features figure(١-٤) .

Among the most spectacular achievements are the promising developments of solid – phase oligosaccharides syntheses [٣١] and the programmable one-pot glycosylation methods[٣٢] , the latter being an extensive advancement of the so-called " armed – disarmed " principle . The concept of armed and disarmed glycosyl donors refers to the increased reactivity of benzoylation over benzoylated glycosyl donors , a phenomenon was observed early by Paulsen [١٧] and which was originated from the greater electron – withdrawing capability of ester blocking group over ether blocking groups .

Fraser – Reid and Co- workers [٣٣,٣٤] were the first to name and exploit the armed- disarmed principle , synthetically showing that donors bearing ether protecting groups, [١] , could be activated chemoselectively over donors bearing ester groups [٣٢] [٢] allowing one-pot synthesis a trisaccharide via the *O*-pentenyl method .

[١] [٢]

١-٢-١ Glycosidation procedures

The present array of glycosidation procedures have been divided into two categories depending on the flexibility of the anomeric leaving group:-

١-The " labile " glycosyl donors which contain anomeric leaving groups that are not or are to a very limited extent stable towards standard protecting group manipulations .

٢-Grouping includes the "stable" glycosyl donors which contain anomeric functionalities that are stable towards standard protecting group manipulation but can be activated when desired [١٥] . The crucial consideration here is that must be able to activate the anomeric leaving group of glycosyl donor and prefer the nucleophilic substitution reaction[٣٥].

The effectiveness of the glycosylation depends upon the nature of the leaving group at the anomeric center and its activation with a Lewis acid or another activator .

Some of the most useful leaving groups include trichloroacetimidate[٣٦]

show in (scheme ١-٢) .

Scheme:١-٢The mechanism of glycosidation include

trichloroacetimidate .

Glycosyl donors could be " armed " or "disarmed" by a C-٢ ester or ether group which is electron – withdrawing effect of the ester [٣٧] .

The outcome of a glycosylation event in terms of yield and steroselectivity depends on solvent systems , temperature, the nature of the donor and acceptor and the applied protective group strategy .[٣٨]

The classical Fischer synthesis is a valuable method for the direct formation of glycosides from fully unprotected carbohydrates and simple alcohol .The method is useful despite the long reaction times required .[٣٩,٤٠] .

١-٢-٢ **Acid – catalyzed of *O*- glycosidation**

Partially protected sugars having a free hydroxyl group at the anomeric

center have been converted to glycosides using Lewis acids with excellent yields (٨٠ – ٩٥ %) and good α - selectivity was obtained .[٤١] The reaction required strong acid such as hydrochloric acid , trifloromethansulfonic acid or ferric chloride .

As a rule , furanoside predominate in the early stages of Fisher glycosidation,where as at equilibrium the pyranose is the dominant product.

Relatively strong acidic conditions favor thermodynamically controlled reaction [٤١] .

١–٢-٣ **Base – catalyzed of *O*- glycosidation**

Simple *O*- glycosides may be obtained via base – promoted reaction of

unprotected sugars with alkyl halides or dialkyl sulphates .

The ٢,٣,٤,٦- tetra –*O*- benzyl- D – glucopyranose (Scheme ١-٣) reacts efficiently with various primary alkyl bromides and triflates in the presence

of sodium hydride or potassium tert-butoxide in THF to give predominantly β- glycosides . [٤٢]

Scheme : ١-٣ Base – catalyzed of *O*-glycosidation

١ – ٣ Allyl ethers

Allyl protection of the anomeric position is common in carbohydrate chemistry [٤٣ , ٤٤] and it is a useful terminal functionality in the course of the preparation of glycoconjugates and gluco-polymers [٤٥- ٤٦] because it is easily cleaved via isomeric propen-١-yl intermediates, in addition to other methods [٤٨]. Furthermore stereoselective chemical modification of the alkene leads to interesting functionalized derivatives [٤٩,٥٠] . Allyl alcohol would be ideal allylating agent because of their availability and stability .[٥١]

Allyl groups have been found to be of general use as temporary hydroxyl – protection groups in sugar chemistry [٥٢] . The successful

application of the allyl group in carbohydrate chemistry is mainly due to its relative stability during glycosidation or deblocking procedures which lead to the removal of other protecting groups.[٥٢]

One – pot synthesis of glycosides or often referred to as a reactivity- based one – pot method in which glycosyl donors with decreasing anomeric reactivates are allowed to react sequentially in the same flask . This procedure , although is highly convenient because it reduces the number of steps considerably, has the inconvenience that the donor reactivates have to be carefully adjusted which implies extensive protecting group manipulations .

A neutral one – step allylation procedure involving alcohol [١٠] , especially carbohydrate, was possible using allyl ethyl carbononate[١١]as the allylating reagent in the presence of a catalytic amount of palladium(٠) .[٥٤,٥٥]

Zhong – Wu Guo and Co-workers[٥٦] prepared allyl glycosides with free C-٢ hydroxyl groups [١٥]and[١٦] by a one- step reaction .

In ١٩٨٨ *n*- pentenyl glycosides have proved valuable for the syntheses of oligosaccharides [٣٠] and enantiopure compounds [٥٧] for mechanistic studies of glycosides hydrolysis [٥٨,٥٩], electrophilic additions [٦٠] and for determining the relative reactivates of differently protected saccharides [٣٣]. The olefinic moiety should allow for ready transformation into spacer functionalities as has been exemplified by Vliegenthart and Co-workers.[٦١-٦٣]

The substituted allyl glycoside [١٩], was readily prepared from the corresponding tetra acetyl bromide[١٧] and ٣- butene- ٢ – ol [١٨] ,

deacetylation of [١٩] under Zemplen conditions, followed by benzylation with benzyl bromide and sodium hydride in DMF gave the fully benzylated allyl glycoside[٢٠] .[٦٤,٦٥] .

Recent developments showed that *O* –allyl , *O* – pentenyl , C- vinyl and C- allyl glycopyranosides [٢١] can undergo efficient homodimerization in refluxing dichloromethane in the presence of either Grubb ‘s or Schrock ‘s catalyst .[٦٦]

Allylation of ١,٢:٥,٦ – di-*O*- isopropylidene glucofuranose [١٣a] in the presence of strong base, very short reaction times were needed and excellent yield of products was obtained . [٦٧]

٢-*O*- Allyl protected glycosyl donors may be employed for the synthesis of a variety of *cis* –١, ٢-glycosides. Isomeriation of [٢٣] proceeded efficiently to yield the enol ethers [٢٤] which were subsequently examined as substrates for tethering and glycosylation . Conditions which are initially employed for the one-pot reactions of [٢٣] involve NIS mediated tethering with cyclohexanol and subsequent glycosylation by the additional reaction to produce the corresponding β-mannoside [٢٥] as single anomers [٦٨] .

Glycosylation of allyl ٢- acetamido ٤,٦-*O*- benzylidene -٢-deoxy-α-

D-glycopyranoside [٢٦] with bulky substituted glycosyl donors [٢٧] leads to the formation of derivatives of the disaccharide[٦٩] [٢٨].

The ٤- *n* -penten -١ -yl glycosides may be as glycosyl donors for further coupling with various alcohols in the presence of activators. The corresponding ٢-allyloxyethyl [٢٩] coupling with the known D – glucopyranosyl ٦-OH [٣٠] using NIS/ TfOH combination at ٠°C furnished the desired α- mannoside[٣١][٧٠].

Carbohydrates that are selectively protective at the anomeric position are useful building blocks , provided that the protecting groups are easily removable as is the case with benzyl and allyl glycosides. Encouraged by the microwave irradiation , by using a small range of starting materials (D-glucose , D- fructose) in methanol , allyl alcohol , to prepare the corresponding glycosides . Appling the microwave irradiation technique to conventional Fisher glycosylation resulting in an impressive acceleration of the reaction with good α – glycoside product selectivity. [٧١]

١ – ٤ Azido -Sugars

Glycosyl azides constitute an accessible class of sugar derivatives which is receiving considerable attention due to the versatile reactivity of the azido group[٧٢,٧٣] serving as valuable carbohydrate building blocks especially as precursors for the synthesis of glycosylamines [٧٢,٧٤,٧٥] , N- glycopeptides[٧٦] and glycosyl heterocyclic derivatives such as ١,٢,٣ – triazoles . [٧٧ - ٨٠]

The general formula of organic azides[٨١] is R- N_3, R = Alkyl , Aryl , sugars . Glycosyl azides are generally safe compounds , easily prepared in high yield and the azido group can react with both nucleophilic and electrophilic reagent [٨٢-٨٤] . The existing methods for the preparation of glycosyl azides are classified into the following classes :-

١- From glycosyl halides ,the most classical method uses metal azides LiN_3 ,NaN_3, AgN_3 under homogeneous conditions [٨٥-٨٧] . This method generally affords moderate yields . High boiling solvents (eg. HMPA or DMF) and heating sometimes is required . [٨٨]

٢- From glycosyl esters , this newer method utilizes trimethylsilyl azide and a Lewis acid catalyst (eg. $BF_3.OEt_2$ $SnCl_4$,TBATf) . The preparation of glycosyl azides in a catalytic and sterecontrolled manner azidosolicate provides a viable alternate rout for the preparation of glycosyl azides . [٨٩ ,٩٠]

٣-Most recently phase transfer reactions have been used for the efficient synthesis of a wide range of a glycosyl azides . This two –phase system required a full equivalent of phase transfer reagent (tetra butyl ammonium hydrogen sulphate or aliquat(٣٣٦) and ٣-٥ equivalents of sodium azide [٩١,٩٢]

٤-By the additional reaction to the double bond in glycals, starting from tri-*O*-acetyl-D-glucal[٣٨] the mixture ٤,٦-di-*O*-acetyl-٣-azido ٢,٣-dideoxy

hexopyranose[٣٩-٤٢] was synthesized in one – pot reaction . Those compound are great of interest as they may be used as precursors of different bio-active substance [٩٣,٩٤].

The azidation of substituted unsaturated carbohydrates[٤٣]may be accomplished by using pd $(PPh_3)_4$ as catalyst and sodium azide as the nucleophile , affording a mixture of three unsaturated azides [٤٦-٤٨] [٩٥]

Scheme ١- ٤ Azidation of unsaturated carbohydrates .

Fuchs et al[٩٦] have reported a convenient and high yielding synthesis of glycosyl azides from glylcosyl halides and ١,١,٣,٣-tetramethylguanidinium azide (TMGA) in the case of glucosyl azide .

Several Lewis acid catalysts were screened by taking a reaction of١,٢,٣,٤,٦-penta –*O*-acetyl- *β*-D-glucopyranose [٥٠] with trimethylsilyl azide[٨٤] . The best result was obtained when the catalyst was generated in situ from $SnCl_4$ and $AgClO_4$ was employed,and dichloromethane was used as solvent, the desired glycosyl azide was obtained in good yield .[٩٨]

Azidolysis of bromide [٥١] in DMF gave methyl ٦-azido-٤-*O*- benzoyl-٢,٦-dideoxy-٣-*O*-methyl-α-D-ribohexopyranoside [٥٢] in good yield [٩٢].

Treatment of primary and secondary alcohols[٥٣] with zinc azide bis-pyridine complex (١.٥ eq), triphenylphosphine(٢eq)and diisopropyl azodicarboxylate(٢eq) in toluene smoothly afford the corresponding azides[٥٤] , in good yields [٩٩]

Using ١,١-dimethoxyhexane[٥٥] and $TMSN_3$ as model substrates, azidation reaction was conducted in the presence of ١ mol% $In(OTf)_3$

as Lewis acids at room temperature within ٧ hr. to give α-azide ether [٥٦] along with the formation of a small a mount of *gem*-diazide [٥٧] .[١٠٠]

In order to avoid the use of excess acetic anhydride and other toxic catalysts such as pyridine and to shorten the synthetic efforts involved in the preparation of glycosyl azides, F. D. Tropper and co worker [١٠١] describe an efficient generalized one- pot phase-transfer reaction approach for the preparation of per-*O*- acetylated glycosyl bromide [١٧] directly from a free sugars [٣٠] and subsequent phase-transfer catalyze anomeric azidolysis in one-pot fashion[١٠٢] .

١- ٥ Unsaturated Sugars

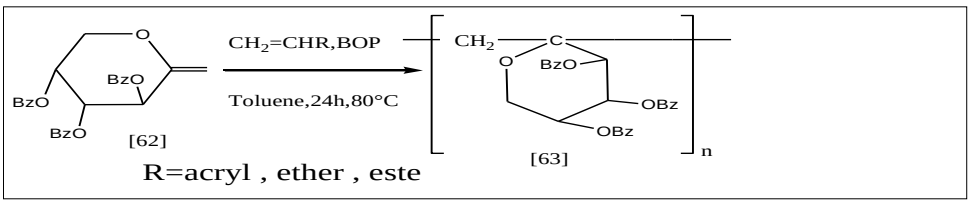
Many stable , discrete carbohydrate derivatives possessing a double bond in the carbon skeleton are now known .The double bond can be produced by the dehydration of a monosaccharide . This olefenic double bond can be in *endo* (inside the sugar ring)[٥٩] or *exo* (outside the sugar ring)[٦٠], cyclic position of the pyranoid six – member ether ring or furanoid five member ether ring structure of the monosaccharide derivatives involving several positions of the sugars ring[١٠٣,١٠٤]

Scheme ١-٥ Type structures of glucal

Unsaturated sugar monomers are useful building blocks for the synthesis

copolymers with special properties like biocompatibility , biodegradability

hydrophilicity / hydrophobicity balance and skin compatibility [١٠٥]. Unsaturated sugar monomers have been prepared on the basis of monosaccharides such as D- ribose[١٠٦] , D-glucose and D-fructose[١٠٧] . The polymerization group can be *exo*- or *endo*- cyclic involving several positions of the sugar ring . Different saccharide polymers [٦٣] based on unsaturated protected sugars have been synthesized[١٠٨]



١-٥-١ Glycal Sugars

Glycals are cyclic compounds having a double bond between C-١ (anomeric carbon) and C-٢ (the adjaceement carbon atom), are vinyl ethers and consequently can take part in a wide variety of selective addition reactions because they have highly electron – rich position . Pyranoid and furanoid members are known and the esters of each also undergo rearrangement to give ٢,٣-unsaturated product .

Glycals are among the most versatile chiral building blocks in the synthesis of various biomolecules[١١٠,١١١]. Due to their enol ether structure, they demonstrate high and versatile reactivates and are among the most transformable monosaccharide derivatives . *Exo*- glycals can be widely utilized with the same great potential as *endo*-glucals .[١١٢]

١-٥-٢ Preparation of Glycals

The glycals were discovered by Fischer and Zach in ١٩١٣ and later

extensively investigated by Bergman and Schotte [١١٣];their chemistry has been reviewed by Helferich[١١٤] .

Glycals are prepared by reductive removal of a halogen and neighbouring acetate group from an acetylated glycosyl halide followed by deacetylation[١١٥] . There are different methods that enable the rapid preparation of variously and specifically hydroxyl group- protected glycals . [١١٦]

The mechanism of reaction [١١٧] (Scheme ١-٦) can be started by a single electron transfer (SET) from Zn (٠) to ١ or ٣ to give the ***GBrA*** intermediate which can then lose a bromide ion resulting in ***GR***. Radical ***GR*** can then further reduced by Zn(٠) to give the electron rich intermediate ***GZn(١)*** or may combine with Zn(١) to give ***GZn(II)*** , an equivalent of ***GA*** in a non chain process . SET from ***GZn(I)*** to ١ or ٣ to give ***GBrA*** builds up the cycle for the chain while the organic zinc intermediate of anionic character ***(GZn(II))*** produces ٢ or ٤ by losing acetate [١١٧].

Scheme ١-٦ : Mechanism of synthesis of glucal

١-٥-٣ Glycosidation of Glycals

Because of that glycals can be ideally employed in the synthesis of carbohydrate derivatives as well as many other natural products, glycals have been used in various addition , rearrangement and substitution reactions which amazingly versatile properties . The very important transformation involves Lewis acid induced rearrangements , cycloaddition oxidation or epoxidation[١١٨,١١٩, ١٢٠].(scheme ١-٧)

Scheme ١-٧ : Some examples of reaction starting from glycals .

The most important reaction of glycals is the rearrangement by using a

Lewis acid catalyst in the presence of an alcohol ; this reaction is known as the Ferrier rearrangement , which is an excellent method for the preparation of ٢,٣- unsaturated glycosides .[١٠٥]

A variety of reagents are employed to effect this transformation including Lewis acids [١٢١,١٢٢];some of these methods involve stioichimoetric amount of catalyst , strongly acidic condition , long reaction time , unsatisfactory yield . In recent years , ceric(IV)ammonium nitrate (CAN) has been used [١٢٣].

The use of microwaves irradiation in the Ferrier reaction by using ٣٠٪ of $InCl_3$ as catalyst gave α - anomeric selectivity .[١٢١, ١٢٤]

Recently niobium (V)chloride has emerged as Lewis acid[١٢٥]

١-٥-٤ Fructal

Ness and Fletcher[١٢٦] noted that in view the wealth of synthetic

uses which have been found for the ordinary aldopyranose related glycals,it is somewhat surprising that more attention has not been paid to ketoses related glycals [١٢٧] . This situation still prevails mainly because the reductive elimination in acylated ketohexosyl chlorides of [٧٢] inducible by Fischer-Zach conditions (Zn/ HOAc) [١١٥] , can occur with formation of *exo*-D-fructals [٧٣], by elimination of the ١-*O*-acyl group, or alternately by placement of the double bond into the pyranoid ring to yield *endo*- D- fructals [٧٤] .[١٠٩]

Scheme ١-٨ : preparation of *exo* and *endo* acetyl fructal

Recently , the preparation of fructal via the dehydrohalogenation of benzobromo fructose [٧٦] is readily prepared from the parent ketose in a two –step one – pot procedure[١٠٦] , may proceed either toward the *exo* – or *endo*- product, depending on whether abstraction of an exocyclic or a pyranoid ring hydrogen is involved .[١٢٨]

Scheme ١-٩ : Preparation of *exo*-and *endo* –hydroxyfructal esters .

١ - ٦ ١,٣- Dipolar Cycloaddition Reactions

The addition of a ١,٣- dipole to a carbon- carbon double and triple bond leads to the synthesis of both aromatic and non- aromatic five- membered ring heterocyclic is a classic reaction in organic chemistry[١٢٩]. The ١,٣- dipolar cycloaddition (١,٣-DC) reaction is used for the preparation of molecules of fundamental importance for both academia and industry [١٣٠]. ١,٣-DC reaction like the Diels –Alder reaction are ($\pi^4s + \pi^2s$) reactions proceed through a ٦π-electron " aromatic " transition state but they differ from Diels –Alder reaction in the ٤π- electron component like the allyl anion contains only three atoms at least one of which is a hetero-atom [١٣٠].

A ١,٣- dipolar is defined as an a – b – c structure that undergoes ١,٣-DC reactions .

Basically, ١,٣-dipoles can be divided into two different types: the allyl anion type and the propargyl / allenyl anion type [١٣٢].

Figure ١-٥: The basic resonance structure of ١,٣-dipoles .

The ١,٣-DC reaction of parent ١,٣-dipoles, with alkenes and alkynes involves ٤ π electrons from the dipole and ٢ π electrons from the alkenes . If the ١,٣-DC reaction proceeds via a concerted mechanism it is thermally allowed with the description ($\pi^{4}s + \pi^{2}s$) according to the Woodward – Hoffmann rules. [١٣٣]

The ١,٣- DC of alkynes and azides has emerged as a highly useful connection method in both uncatalyzed [١٣٤] and catalyzed[١٣٥]forms .The practical importance of the process derives from the fact that it is the only facile ١,٣-DC reaction which uses chemically stable components[١٣٦].

١- ٦ - ١ ١,٢,٣- Triazoles

The reaction between an alkyne (dipolarophile)[٨٠] and azide (dipole) [٧٩]affords a ١,٢,٣ – triazole and the regioselectivitiy of reaction are generally low and thus, if the alkyne is unsymmetrical , two regioisomers will be formed [٨١,٨٢] in an approximately ١:١ ratio[١٣٧] . The procedure is known as the Huisgen reaction [١٣٨].

The triazole ring system is composed of five atoms, two carbon and three nitrogen atoms, which can be arranged in two combinations to give either ١,٢,٣-triazole [٨٣] or ١,٢,٤-triazole [١٣٨][٨٤] .

١,٢,٣- Triazoles are an important class of compounds because of their wide rang of applications [١٣٩] ; they have biological activity and are seen in many drugs[١٤٠ ١٤١], also have broad use in industrial applications[١٤٢] such as:-

dyes and brighteners for fibres; corrosion inhibitors for many metals and alloys; light stabilizers for organic materials and polymers ,and agrochemicals as herbicides, fungicides, and antibacterial

agent. Because of their potent usefulness, several synthetic methods have been developed for the construction of triazole frameworks .

١ –٦ –٢ Thermal cycloaddition reaction

The reaction is often conducted at high temperatures for a prolonged time , this type causes problem with regard to the regioselectivity of the derived triazoles; a mixture of ١,٤-substiuted and ١,٥-substituted – ١,٢,٣-triazoles is produced by heating with solvent , heating without solvent , heating in presence of catalysts .

The thermal cycloaddition reaction is a traditional procedure for the preparation triazoles, but there are several drawbacks inherent in this protocol [١٤٣] . The major problem arises due to the low reactivity of the substrates , therefore, the installation of an electron withdrawing group is usually required to activate the alkynes[١٣٠] . The recent investigations on the copper-catalyzed cycloadditoin reaction made it possible to use unactivated terminal alkynes as a starting material and terminal alkynes are activated by forming a copper- acetylide species[١٤٤-١٤٧].

Full conversion and high purity were observed for the copper(I)- catalyzed ١,٣-DC in the following tested solvents : acetonitrle , dichloromethane , tetrahydrofuran , toluene , *N,N* – dimethylformaamide[١٤٤] .Various attempts to control the regioselectivity have been reported without much success until the discovery of the copper (I) –catalyzed reaction in ٢٠٠٢, which exclusively yields the ١,٤ – disubstituted ١,٢,٣- triazoles [١٤٤,١٤٩] . Several copper (١) salt such as CuI and CuOTf -$C_٦H_٦$ can be employed but the reaction generally must be run with acetonitrile as co-solvent , require a nitrogen base , and sometimes generate unwanted diacetylene and bis-triazole by –products [١٤٩] .The use of $CuSO_{٤.٥}H_٢O$ with sodium ascorbate in aqueous solvents allows the

formation of ١,٤- triazoles at room temperature in high yield .[١٥٠] Recently discovered that copper(١) – catalysis of this transformation, which accelerates the reaction up to $١٠^{٧}$ times has placed it in class of its own and has enabled many novel applications .[١٥١]

The thermal reaction leads to the formation of two disubstituted triazole isomers while the copper (I) – catalyzed reaction selectively produces the ١,٤ – isomer in ٩١% yield after ٨ hours [١٥١].

The proposed mechanism has been for copper- catalyzed reaction[١٤٩,١٥٠]

as illustrated in scheme(١-١٠) .

Scheme ١-١٠ : The proposed mechanism for copper –catalysed reaction

The copper-acetylide species (A) would be formed from the alkyne **(١)** and CuCl with extrusion of TMSCl at the initial stage of catalytic cycle . At this point two pathways are conceivable to reach the final product **(٣)** .In path (a), [٣ + ٢] cycloaddition between the copper- acetylide [A] and the π – allyl palladiun azide complex [B] , which is generated in situ from Pd(٠), allyl carbonate , and $TMSN_3$ would give the intermediate [C] . The cross-coupling reaction between the vinyl copper derivative [C] and the π – allyl palladium(II) methoxide [D] would form the triazole[٣] with regeneration of the pd(٠)- Cu(I) bimetallic catalyst . In path (b) , [٣ + ٢] cycloaddition would take place between (A) and allyl azide [E] which is formed by reductive- elimination of [B] , two give the intermediate [F]. The successive cross-coupling reaction between [F]and[D] would affored the triazole **(٣)** .

٢- Azidoethyl ٢,٣,٤,٦ tetraacetyl- β-D-galactopyranoside [٩٠] react with alkyne [٩١] in microtiter plate technique to produce [٩٢] in ٨٩٪ .[١٤٥]

The construction of multivalent structures such as sugar heterodimers is designed by using ١,٣-DC, compound [٩٣] to react with ١,٢-ethanediazide [٩٤] leading to a mixture of the bis (triazole) sugar dimer [٩٥] .[١٣٦]

The coupling of glucosyl azide [٤٩] and acetylenes (R)-*N* –Boc –propargyl glycine methyl ester [٩٦] is successfully accomplished using the modified Sharpless conditions to give the corresponding adduct[١٥٢] [٩٧].

١ - ٧ Microwave assisted organic synthesis (MAOS)

In the electromagnetic spectrum of the microwave radiation (MW) region

is located between infrared radiation and radio waves . Microwave have wavelengths of ١ mm-١m corresponding to frequencies between^{١٥٣} ٠-٣ and

٣٠٠ GHz .In inorganic chemistry , mw technology has been used since the late ١٩٧٠ , while it has only been implemented in organic chemistry since the mid -١٩٨٠.Since the mid -١٩٩٠, the number of publication have increase significantly .The main reasons for this increase include the availability of commercial microwave equipment intended for organic chemistry and the development of the solvent free technique , which has improved the safety aspects , but are mostly due to an increased interest in shorter reaction times .

In general most organic reactions have been heated, using traditional heat transfer equipment such as oil baths ,sand baths and heating jackets . These heating techniques are, however , rather slow and a temperature gradient can develop within the sample . In addition , local oven heating can lead to product substrate and reagent decomposition. In m.w dielectric heating , the mw energy is introduced into the chemical reactor remotel and direct access by the energy source to the reaction vessel is obtained .

The mw radiation passes through the wall of the vessel and heats only the reactant and solvent , not the reaction vessel itself . There are two specific

mechanisms of interaction between materials and m.w :

١- dipole interaction

٢- Ionic conduction

Both mechanisms require effective coupling between components of the target material and the rapid oscillating electrical field of the mw. The main advantage of using mw assisted organic synthesis is the shorter reaction time . The rate of the reaction can be described by the Arrhenius Eq. :-

$K = A e^{-\Delta G/RT}$

The mw can increase the molecular vibration and it has been proposed that this factor (A)can be effected .MW irradiation produces an alteration in the exponential factor by affecting the free energy of activation[١٥٣] ΔG. Chemical reactions are performed using MAOS technique which are mainly rapid because the reaction are performed at higher temperature than their conventional counter parts .The modern mw based synthesizer can achieve temperature of up to ٢٥٠ ºC and pressure of up to ٢٠ bars allowing reaction to be carried out at higher temperature than their reflux counterparts[١٥٤] .

١- ٧ –١ Microwave application in organic synthesis

P.Pelle Lidstrom gave a detailed survey of mw assisted synthesis from the literature published from ١٩٩٤-٢٠٠٠ . It seems that all of the previously conventionally heated reaction could be performed ,using this technique. According to the sample preparation , several methods have been developed for operating mw reactions[١٥٥] :

١- In the presence of solvent .

a. reaction can be performed in solution phase

b. reaction can be performed in polymer -supported solid phase

٢-In the solvent free synthesis .

a. reaction with neat reactants

b. reaction under phase -transfer catalysis (PTC)

c. reaction mixtures absorbed into mw active inorganic supports

By exposure to mw , the thermal effects undergone by materials exhibit an increased magnitude with the polarity increase of the substrate. These effects can appear in liquid systems and in the solid state as well , where structural modifications can also occur concomitantly .In the pressure of polar solvents , organic reaction required closed Teflon vessels to avoid volatilization . The resultant advantage in comparison to classical heating are especially spectacular .Reaction are very rapid and usually complete after a few minutes , as a result of both temperature and pressure effects and supposed specific effects of the reaction such as improved homogeneity in temperature a faster temperature rise and possible modification of activation parameters ΔH^* and ΔS^* .

It is also generally observed that the purity of products is improved due to the shorter reaction period at high temperature and the absence of local overheating on the reaction walls which occurs under conventional heating[١٥٦].

١-٧-٢ Domestic household ovens

Most of the published chemistry has been performed using domestic mw ovens .The key reasons for using a device intended for heating food items the perform syntheses are that they are readily a available and inexpensive .

The lack of control in domestic microwave oven when performing mw assisted synthesis has to a vase number of incidents including explosions , being reported . One method for avoiding this problem has been to omit the solvent from reaction and perform the reaction on solid support such as various clays aluminium oxide and silica . [١٥٦]

One disadvantage of domestic mw oven is that the variable power levels are produced by simply switching the magnetron on and off this may be problematic if reaction mixtures cool downs rapidly. Modfiction of commercial mw equipment can be hazardous because of the possible leakage of microwave radiation .

١-٧ –٣ Vessels

M.w assisted reaction can under the appropriate conditions ,use conventional vessels Pyrex,Teflon or polystyrene. However, if reactions are to be carried out under pressure in sealed systems the major concern is the

ability of the vessel to withstand the changes in pressure and temperature associated with the particular transformation. Simple procedure suitable for small scale experiments is to seal the reactions in Pyrex vials, surround them in vermiculite and irradiate with mw. The preferred reaction vessel is a tall beaker with a loose cover of much larger capacity than the volume of the reaction mixture. A large Elenmeyer flask with a funnel as a loose top can be used in place of the beaker[١٥٧].

١-٧-٤ Solvents in m.w

All types of solvent can be used in MAOS .polar solvents, such as DMF,

NMP,ethanol are good mw absorbers and will heat efficiently , less polar or non-polar solvents such as toluene ,dioxane and THF are more less transparent the mw irradiation and will not heat in the pure form. However , most chemical reactions contain enough polar or ionic substances to efficiently absorb mw energy and generate heat [١٥٨].

Energy transfer between the polar molecules that couple with microwave

radiation and the non -polar solvent bulk is rapid and often provides an efficient means of using non-polar solvents for synthesis using mw irradiation .

An excellent energy-transfer for many types of reaction in a domestic mw oven is *N,N*-dimethylformamide (DMF): a good solvent with high b .p (١٦٠ ºC)and high dielectric constant (Є = ٣٦.٧). This solvent can retain water formed in a reaction, thus operating the need for water separator.The reaction temperature can be raised to about ١٤٠ ºC without noticeable vaporization .

The energy input is controlled so that solvent and for the reaction mixture is not allowed to approach the boiling point too closely .Thereby , the amount of vaporization is kept low and no reflux condenser is needed . [١٥٩,١٦٠]

The ١,٣-CD reaction becomes even more powerful under microwave irradiation where a one- pot synthesis of various ١,٢,٣- triazoles was completed in less than ١٥minutes[١٥٩] R.J. Pieters and co – workers[١٦٠] synthesised glycodendrimers using optimised microwave- assisted protocols by Cu(١) – catalysed ; the reactions were highly selective and efficient .

Benzyl bromide [١٠١] and phenylacetylene [١٠٢] in the presence of NaN_3 where suspended in a ١:١ mixture of *t*-BuOH and water , together with the catalyst . After ١٠ min of irradiation , the triazole product ١-benzyl-٤-phenyl-١*H*- ١,٢,٣- triazole [١٠٣] has been isolated in ٩٣٪ yield .[١٥٩]

١- ٨ Cycloaddation Reaction of Glycals

As the appreciation of the biological importance of carbohydrates has increased , so have efforts to develop methods for the synthesis of biologically relevant oligosaccahrides, glycoconjugates,aminoglycosides[١٦٠] are typically synthesized by modification of glucose or glucosamine [١٦١] or introduction of a nitrogen substituted into a glycal derivative[١٦٢-١٦٤] .

Glycal with electron –withdrawing protecting groups are found to undergo efficient cycloaddition with electron –rich azides .

Tri – *O*- acetyl –D- glucal [٦٥] readily engages in dipolar cycloaddition with benzyl azide [١٠٤] at elevated temperature to the ١,٢,٣ – triazoline [١٦٥] [١٠٥] , isolated in good yield with little or no purification .

Tri-*O*-acetyl-D-galactal [١٠٦] undergoes ready cycloaddition with benzyl azide [١٠٤] to form triazoline [١٠٦] subsequent photolysis and ring opening efficiently provides the corresponding methyl glycoside [١٦٥]. [١٠٧] in ٩٤٪ yield .

١- ٩ Triazole or Triazoline linked carbohydrates

The field of glycobiololgy and supramolecular chemistry required multivalent ligands[١٦٥] which could increase the weak interaction to biologically relevant levels [١٦٦]. The ١,٣-DC reactions are an efficient and highly versatile tool for the construction of multivalent structures such as sugars heterodimers , glycoclusters , calix-sugars and glycocyclodextrins .

Triazolyldisaccharides are compounds having monosaccharides where the link between them is via a ١,٢,٣- triazole group; where the nitrogen atom(N-١)of the triazole ring is linked to the first sugar and the C-٤ atom or C-٥ atom of the same ring linked other sugar .

The normally disaccharides are linked between the two sugars by ether oxygen linkage . This ether oxygen linkage is difficult to construct chemically , because the ether oxygen linking group is susceptible to hydrolysis by glycosyl hydrolases and non- enzymatic chemical hydrolysis. These compounds play as potential enzyme inhibitors , and as acetylenic intermediate compounds [١٦٧] .

Triazolyldisaccharides are expected to be synthesized by more general methods which use ١,٣-DC reactions where the glycosyl azides and the alkynes are prepared by different methods .

Scheme ١-١١ Structure of Triazolyldisaccarides

Thermal ١,٣-DC leads to the isolation of a mixture of the different possible regoisomers and long reaction times are required . A major advance has recently been achieved parallel to our investigation through the use of copper (I) –catalyzed reactions [١٦٨] which lead only to the ١,٤-disubstitued ١,٢,٣-triazole and short reactions times. The use of copper compounds$(Ph_3P)_3$.CuBr [١٦٩],$(EtO)_3P$.CuI [١٧٠] is due to their air stability and easy and inexpensive preparation . The reaction time could also be shorter by the use of microwave irradiation [١٧١] .

The cycloaddition of benzyl azide [١٠٩] with acetylenic amides [١٠٨] under microwave reaction with solvent-free condition at ٥٥°C for ٣٠ min resulted in complete conversion of the reaction into *N*- substituted

١,٢,٣- triazole [١١٠], without the formation of side products [١٧٠].

The construction of the multivalent neoglyconjugates can easily and effectively preformod by using the cycloaddition reaction , of propargyl mannoside [١١١] and polyazides [١١٢] when using the copper complexes $(Ph_3P)_3.CuBr$ as organic soluble catalysts , with assistance of the microwave irradiation which is shortens the reaction times considerably to formation the ١,٢,٣-triazole [١١٣] in good yield [١٧١] .

The aim of study

١- This study concerns triazolylodisaccharides compounds

having two monosaccharides wherein the bonding between

them is triazol or triazoline group .

٢- This compounds are expected to be more stable to enzymetic and chemical hydrolysis .

٣- This compounds are useful as potential enzyme inhibiters of glycosidase activity and/ or are expected to be resistant to glycosidase hydrolysis activity .

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CHAPTER TWO

٢ - Experimental

٢.١ General

١-Melting points (mp) were determined by Electro thermal ١A ٩٠٠٠ Digital –series , and uncorrected .

٢-Infrared (IR) spectra were recorded using a NICOLET ٤١٠ FT-IR spectrometer(Jordan) and perkin -Elmer L١١٠- ٠٦٢٧ , ٢٠٠١(France). (in $cm^{-١}$)

٣-Nuclear magnetic resonance (H-NMR) spectral were registered at perkin –Elmer ٢٠٠ MHz(France) and Topsin ١-٢ /BRVKER ٤٠٠ MHz(Jordan). Using tetramethyl silane (TMS) as an internal standard, and $CDCl_٣$ as solvents.

٤- Microwave reactions were preformed on apparatus Discover system CEM,٢٤٥٥ MHz (scheme ٢-١) , and some reaction on Domestic microwave oven in a ascre-cap close Pyrex vials (simith tube)in (France).

٥- Evaporating of solvent by using Buchi vacuum rotary evaporator type ١٦٠ .

٦-TLC was performed on pre-coated sheets with ٠.٢٥ mm layer of silica Gel G/UV ٢٥٤ of the Merck company , the detection was followed by UV-lamp or through coloring with iodine vapor or $H_٢SO_٤$ in ethanol ٦٠٪ , followed by heating .

٧- The Elemental analyses were performed in the analytical Laboratory of AL-al – bayt University (Jordan) .

٨- The chromatography separation carried out using Merck silica gel (٦٠-٢٣٠ mesh) .The ratio of the solvents and mixed mobile phase were given in volume ratios .

Scheme (٢-١) Microwave oven type Discover

* A CEM Discover microwave was used in this study . This system is a circular microwave single-mode cavity and can accommodate a single ١٠mL٢٥bar pressure rated sealed reaction vial . The system incorporates both temperature and pressure feedback system for control of the reaction conciliations .

The temperature feedback system uses an infrared temperature sensor positioned below the reaction vessel to permit reproducible temperature control . Reactions were quenched following heating by forced gas cooling with nitrogen gas .

٢.٢ Materials and Methods

All materials , unless otherwise noted , were obtained from commercial suppliers (table ٢-١) and used as provided .

Dichloromethane and Chloroform were dried and distilled over anhydrous calcium chloride . Ethanol and methanol were dried and distilled over magnesium . Acetone was dried and distilled prior to use from phosphorus pentoxide (P_2O_5) . Pyridine was distilled from calcium hydride under nitrogen . Dimethyl formamide dried and distillation after that stored over molecular sieves . Dry CH_3CN is distilled from CaH_2.

Table(٢-١)Chemicals and Company Supplied

Company	Compound	Purity
ACROS	D B U	٩٨٪
	Chlorotrimethyl Silane	٩٩٪
	Amberlite Resin IR – ١٢٠	
	Silica/gel ٢٠٠ mm	p.a
	Ammoniumcerium(iv) nitrate	stabilized ٩٨٪
		٩٩٪

	Allyl chloride .	
Schuchardt	٤ – Toluene sulfonyl chloride	٩٥٪
Scharlau	Benzene Methanol Molecular sieve ٤Aº, ٢.٣ mm Zinc-powder Tetrahydrofuran n.Hexane	٩٩.٧٪ ٩٩.٩٨ % extra pure extra pure ٩٩ % ٩٦ %
Lonover Laboratory chemicals	Chloroform	Pure ٩٩ %
Merck	Celite ٥٤٥ ٠.٠٢-٠-١ mm Aluminum oxide٨٠ active(neutral)	٧٠- ٢٣٠ mesh for syntheses

	Benzoyl chloride	٩٨ %
Gcc	Dichloromethane	٩٩.٥ %
	Acetonitrile	٩٩ %
	Xylene	٩٨ %
	Toluene	٩٩ %
	Acetic acid glacial	٩٩.٩٪
	Acetic acid	٩٨٪
Lancaster	Sodium carbonate	٩٨ %
	Sodium hydrogen carbonate	٩٩ %
	Phosphorous pentoxide	٩٨ %
	N,N-Dimethyl formamide	٩٩ %
Fluka	Triethylorthoformate	٩٨ %
	Cyclohexanone	٩٩٪
	Tetrabutylammonium bromide	٩٨٪
Chemex	Ferric chloride anhydrous	٩٩ %
BDH	D -Glucose	٦٠-٦٢٪

	D - Fructose	٤٠-٦٠ ºc
	Perchloric acid	٦٢ %
	Petroleum spirit ٤٠-٦٠ ْc	P .a
	Tin(IV) chloride anhydrous	٩٨ %
	Silver perchlorate	٩٩ %
	Triphenyl phosphine	٩٩.٩ %
	Sod. ascorbate	٩٨ %
Danssen Chemical	Acetyl chloride	٩٨ %
	Aliquat ٣٣٦	٩٨٪
	Cupper sulfate pentahydrate	٩٩٪

Lab.scan	١,٤- Dioxan	٩٩ %
	Acetone	٩٩ %
	Propargyl bromide	٩٩ %
Panreace ps sinthesis	Allyl alcohol	For synthesis

Laboratory Rasayan	Ethyl acetate	٩٩ %
	Ether Solvent	Stabilized
	Charcoal , activated	٠.٣٥ – ٠.٨٥ mm
Aldrich	Trimethylsilyl trifluromethansulfonate .	٩٩ %
	Boron triflouride etherate .	٩٩٪
	Sodium hydride .	٩٥ %
	Silver carbonate .	٩٩ %
	Diisopropyl azodicarboxylate.	٩٥ %
	Sulfuric acid .	cone
	Calcium chloride .	٩٩.٩٩ %
	Bromine.	٩٨ %
	Sodium acetate .	٩٨ %

٢-٣ General Remark

١- Zinc dust was activated with ١٠٪ HCl followed by consecutive night drying over P_2O_5 at ١٥٠°C

٢-When preparation of ١,٣,٤,٥-tetra-*O*-benzoyl-*β*-D-fructopyranosyl bromide, we can use the HBr saturated with dichloromethane not HBr saturated with acetic acid because the latter contains ٠.٢٥ -٠.٣ mol of acetic acid, which is extremely difficult to remove.

٣- The addition of a crown ether would further increase the effective concentration of azide anion and hence accelerate the reaction .

٤- Anhydrous benzene and toluene were obtained by isotropic removal of water .

٥- Caution should always be used when heating solution of azides .

٦- When crown ether is present , steric hindrance prohibits the formation of the *β*-glycoside .

٧- For the preparation of oligosaccharide , the regioselectivity is generally controlled by the use of suitably protected glycosyl acceptors .

٨- NaH can be freshly washed with anhydrous hexane ٢٠ ml.

٩- The use of a cation exchange resin(H^+) gives clear products and higher yields .

١٠- Phase transfer technique is simple procedure for regioselective alkylation of carbohydrates and could use the nucleophiles such as t-bu-ammonium halide , cesium fluoride , N-methyl imidazole

١١- Sodium iodide was ground into a fine powder , and then dried on a sand bath (approx. ٢٥٠ ° C) overnight in vacuum before use .

١٢ -The stereoselectivity in *O*-glycosidation was completely reversed in the presence of $LiClO_4$

١٣- ٢,٣,٤ , ٦ tetra -*O*- acetyl - α- D-glycosyl bromide is a reasonably stable compound which can be stored for a considerable period of time but *O*- benzylated derivative will decompose within several hours after preparation .

١٤- Glycosyl bromide is more reactive than glycosyl chloride but is also more stable .

١٥- The more stable α-anomer is usually obtained in high yield.

١٦ - ١-butyl-٣- methylimidazolium$(Bmim)^+$ is cation , and has high polar and strong ability to dissolve organic or inorganic compounds ; it could dissolve most of the $NaN_٣$ so the reaction was accelerated .

١٧- Cycloaddition reaction performed with same power input (٦٠w)lead to complex mixture of products , with (١٠ w) power and some what longer reaction time providing a more satisfying outcome .

١٨- Caution : it is important to note that when carrying out microwave heated reaction in closed vessel ,and quite large pressures may build up ; therefore, it is imperative that an appropriate septum is utilized as a pressure relief device

١٩- Caution: Ammonium azide , which might sublimate in reactions with sodium azide ammonium chloride is in dry form explosive at temperatures above ١٣٦ ^{o}C .

٢٠- In the procedure for preparation of *O*-glycoside by using $Ag_٢CO_٣$ the yields are often good without being quantitative and they are improved by removing the water liberated during the reaction by the addition of drying agent (Molecules sieves).

٢١- The excess of sodium hydride was destroyed by addition of a few drops of methanol and additional stirring for (١ hr) .

٢٢-The Cycloaddition reaction in benzene and toluene at reflux had little effect on stereoselectivity and the use of dichloromethane and acetonitrile at reflux did not afford the products .The same reaction in the absence of solvent was complete in ٤ h .

٢٣- Usually the addition of azides to terminal alkynes needs one week to finish in toluene catalyzed by copper(I) salts and the yields are not high while in ionic liquid without any other catalyst action as completed within three days at room temperature .

٢٤- We believe that the acid and base liability of the triazoline lead to the requirement for triethyl orthoformate as a non- basic acid scavenging solvent .

٢٥ -The powdered (fructose or glucose) should be dried in a vacuum desiccators over phosphorus pentoxide not in an oven which apparently causes changes on the surface of the sugars particles which render them un reactive .

٢٦ - The perchloric acid -acetic anhydride catalyst could be prepared by adding ١.٠ gm of ٦٠ % perchloric acid to ٢.٣ gm at acetic anhydride maintained at ٠° C .

٢٧- Zinc chloride is extremely deliquescent and it most therefore be introduced into the flask as rapidly as possible place a small stick of zinc chloride in glass mortar powder rapidly , and weight out the required amount .

٢٨- In benzoylation of sugar when the experiment is performed without effective cooling i.e , if the temperature rises to ٤٠-٥٠ °C , a mixture of anomers is obtained which cannot be separated by simple recrystallisation it is advisable to replace the ice-salt bath with one of acetone- cardice to ensure good temp . control.

٢٩- Universal indicator paper moistened with distilled water gives a satisfactory indication of neutralization

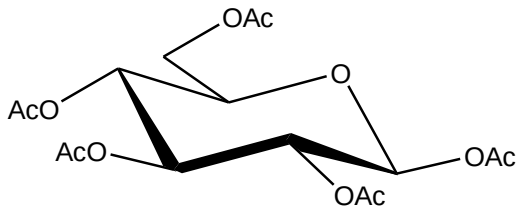
٣٠ - In all sulphonylations , allowing the mixture of *p*- toluene sulphonyl chloride in pyridine to stand for a bout half an hour before the addition of the material to be sulphonylated has been found to be beneficial .

٣٢- Direct anomeric *O*-alkylation of *O*-unprotected sugars seems to be rather difficult because not only α- and β-pyronsides but also α- and β -furanoside can expect additionally , all the other hydroxyl groups are readily accessible to *O* -allylation .

٢ – ٤ Methods

٢-٤-١ Synthesis of allyl and propargyl sugars.

١,٢,٣,٤,٦- penta-*O*- acetyl β -D- glucopyranose [١٧٢] [١١٤]



$C_{16}H_{22}O_{11}$

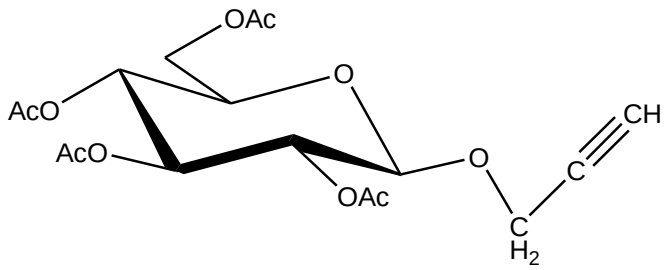
١٠ g , ٥٥.٥ mmol of anhydrous D-glucose was added slowly with stirring to ٧٠ ml of acetic anhydride and ٠.٥ ml of ٦٠ % perchloric acid , over a period of ٣٠ min, the temperature of reaction keep between ٣٠º C and ٤٠ º C . The

stiring continued for ٣٠ min , and mixture was poured into ٣٠٠ ml of ice and water .After two hours , the solid acetate was filtered by suction , washed with water , and dried at ٤٥ºC , recrystalization from ethanol to give [١١٤] (٦ g , ٦٠ % yield) m.p=١٣٠ – ١٣١° C , lit[١٧٢]

١٣٠ – ١٢٩°C .

Rf = ٠.٥ (Benzen : Methanol, ٨:٢) , IR (KBr disc) ١٧٦٠ cm^{-1} for (C=O) Fig (٣-٦) .

١-*O*-Propargyl ٢,٣,٤,٦ tetra-*O*-acetyl-β-D-glucopyranoside [٥٦,٦٢] [١١٥]



$C_{17}H_{22}O_{10}$

Method A

To a solution of D- glucose pentacetate [١١٤](١g , ٥.٥ mmol) in anhydrous dichloromethane (٢٠ ml) was stirred for ٢ hr with molecular sieves ٠.٤ nm(٣ g) under nitrogen atmosphere . Then the solution was treated with BF_3 . Et_2O, (٠.٣١٤ml, ٢.٥ mmol) and immediately after the propargyl alcohol(٠.١٨٧ml , ٢.٧ mmol) was dissolved in anhydrous dichloromethane (١٠ ml) was added at ٠ºC .After ١٦ hr , the mixture was poured into saturated sodium hydrogen carbonate solution (٥٠ ml) , the organic layer separated , the aqueous phase extracted with dichloromethane (٤ × ١٠ ml) , the combined organic phase washed twice with water (٢ × ٢٠ ml) , filtered over celite and evaporated in vacuum .The resulting syrup was purified by column chromatography: petroleum ether: EtOA

(٨ : ٢) , to produced [١١٥] (٠.٧٩ g) (٥٧ %) m.p ١١٥ – ١١٧ºC , lit[٥٦]

١١٤-١١٦ ºC *Rf* = ٠.٤٤ (Benzen : Methanol, ٨:٢) .

calculated for $C_{17}H_{22}O_{10}$ C, ٥٢.٨٤ ; H,٥.٦٩

found C,٥٣.٠٠ ; H,٤.٩٨

IR (KBr-disc) ٢١٢٠ cm^{-1} (C ≡ C) , ٣٢٧٤ cm^{-1} (≡ CH) ,١٧٥٠ cm^{-1} for (C=O) , Fig (٣-٧) .

Method B

Glucose pentacetate [١١٤] (٥ g , ٢٧.٧٥ mmol) was dissolved in CH_2Cl_2 ٢٥ ml under nitrogen atmosphere .A ٣٠ % solution of HBr in CH_2Cl_2(١٠m)

was added to the flask , and the mixture was stirred under darkness at r.t over night .The reaction mixtur was diluted with CH_2Cl_2 (٤٠ ml) and poured over ice . The organic layer was then extracted with cold H_2O

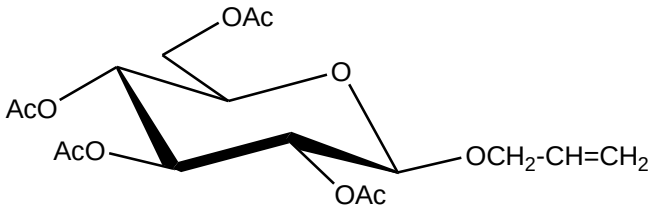
(٣ ×٢٠ ml), cold saturated $NaHCO_3$ (٢ × ٧٥ ml) and brine (٢ × ٥٠ ml). The

organic layer was dried over (Na_2SO_4) filtered , and concentrated to give tetra -*O*- acetyl α−D-glucopyranoside bromide . A portion this material (٢g) and the propargyl alcohol (٠.٨ml, ١٠٣mmol) were dissolved in CH_2Cl_2 (١٥ ml) under nitrogen atom and stirred with freshly activated powdered ٤A° molecular sieves(٢g) for ٣٠min . Silver carbonate(٢.٢٢g ,٧.٩٧mmol)was then added and the reaction mixture was stirred for ٦٠ hr at room temperature under darkness. The reaction mixture was then diluted with CH_2Cl_2 (٦٠ ml), filtered through a wet celite pad , and washed consecutively with saturated $NaHCO_3$ (٣٠ ml) and brine

(٣٠ ml) .The organic layer was dried over Na_2SO_4 . Filtered, concentrated , and purified by flash Chromatography (petroleum ether: EtOAc)

(٦٠ : ٤٠) to give the product [١١٥] as white solid (٠.٨ g) in ٤٠٪ yield .

١-*O*-Allyl ٢,٣,٤,٦-tetra-*O*-acetyl- β-D-glucopyransoide [١١٦]



$C_{17}H_{24}O_{10}$

To a solution of pentacetate D-glucose [١١٤] (٢.٧٣g , ٧mmol) in dry CH_2Cl_2 (٢٠ml) were added oven – dried ٤Aº molecular sieves , allyl alcohol (٠.٨٣ml , ١٢mmol) and trimethylsily triflate (TMSOTf)

(٢.٥٣ml , ١٤mmol) were added slowly at ٠Cº . The reaction was quenched by addition of a saturated solution of $NaHCO_3$ and filtered through a celite pad . The organic layer was washed twice with water , dried over

Na_2SO_4 , filtered and evaporated under reduced pressure .Purified by flash chromatography eluted with

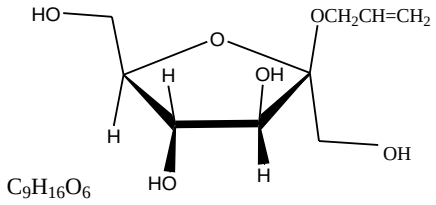
(petroleum ether : ethyl acetate) (٦: ٤ ⟶ ٥:) a syrup material of [١١٦] was obtained (١.٦٣g,٦٠٪yield) *Rf*=٠.٤٣ (Benzene : Methanol, ٨:٢).

IR (film): (٣٤٨٢ , ١٧٤٨ ,١٣٦٩ , ١٢٤٥ , ١٠٥٠) cm^{-1} fig (٣-٨)

Calculated for $C_{١٧}H_{٢٤}O_{١٠}$ C,٥٢.٥٧ ; H , ٦.١٨

found C,٥١.٥٦ ; H, ٦.١٧

O- Allyl –D-fructofuranoside [٧١,١٨٣] [١١٧]



Two methods were explored for allylation of D-fructose :-

Method A :

Dried D-Fructose (٥g, ٢.٢٧ mmol) was dissolved in dry Allyl alcohol (١٠٠ ml) . Ion exchange resin (Amberilte , $١٢٠H^+$) (٢g) was added as the acid catalyst. The mixture was heated under reflux with stirring for half an - hour at ٣٠ºC .

After this the resin was neutralized by adding sodium hydroxide dissolved in allyl alcohols . Removal the solvent under vacuum, gave syrup product[١١٧] (٤.٠ g) ٨٠٪ yield *Rf*=٠.٢٨ (Benzene : Methanol, ٨:٢) , IR (film) ٣٣٥٧cm^{-1} (OH) , ١٦٤١ cm^{-1} (C=CH_2) , ١٠٥٤ cm^{-1} (C-O-C) Fig (٣-٩)

calculated for $C_9H_{16}O_6$ C,٤٩.٠٩ ; H,٧.٢٧

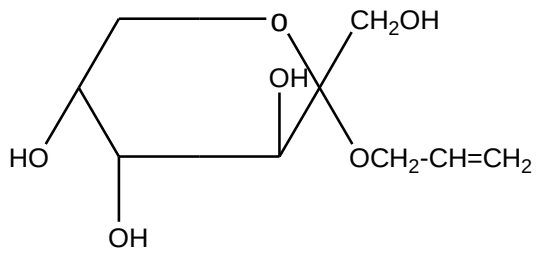
found C,٤٩.٠٠ ; H , ٧.٠١

Method B

General experimental procedure for microwave–accelerated Fischer glycosylation .

All reactions were carried out in a pressure tube , sealed with a Teflon septum . Reactions contained the sugar substrate (٠.١g) , Amberlite IRN ١٢٠H^+ resin (٠.١g) and alcohol (١ml) . The pressure tube was introduced to the center of a CEM Discover microwave oven and then heated to the desired temperature for the appropriate time . On completion of the heating cycle, an aliquot was removed from the reaction mixture concentrated to produce a syrup of derivatives [١١٧] [١١٨] [١١٩] [١٢٠] whose properties are given in table (٣-١) and IR spectrum showed in, Fig(٣-٩)(٣-١٠) (٣-١١)(٣-١٢) respectively .

***O*- Allyl –D- fructopyranoside [١١٨]**



$C_9H_{16}O_6$

A solution of ٠.٥٪ hydrochloric acid was prepared by dissolving acetyl chloride (١ml) in dry allyl alcohol (١٠٦ ml) and dried D-fructose (٥.٧ g) was added .

The mixture was heating with reflux at (٧٠-٨٠ºC) for ٣ hr. TLC (Benzene : Menthol) (٨:٢) indicated the completed of the reaction . The solution was then neutralized by drop wise addition of sod. hydroxide dissolved in allyl alcohol . The solvent was then removed under vacuum and a syrup product (٤.٢٢g) of [١١٨] .

was obtained , ٧٤٪ yield *Rf*=٠.٣ (Benzene : Methanol, ٨:٢)

IR (film) ٣٤٢٥ cm^{-1} (OH) , ١٦٧٨ cm^{-1} ($C=CH_2$) , ١٠٧٣ cm^{-1} (C-O-C)

Fig(٣-١٠) .

١,٢ : ٤,٥-Di-*O*-cyclohexylidene – D- fructopyranose[١٧٤] [١٢١]

(٥g, ٢.٢٧mmol) of finely powdered dry D-fructose was added with vigorous stirring to (١١ ml, ١١٢.٢mmol) of ice-cooled cyclohexanon containing (٠.٧٥ ml) of concentrated sulphuric acid , the reaction mixture becomes solid within ٣٠ minutes . The mixture was left overnight at room temperature . The product was dissolved in (٥ ml) of chloroform and the solution was washed with dilute aqueous sodium hydroxide , dilute hydrochoric acid and water and finally dried nuder Na_2SO_4 and evaporated. The residue was solidified by trituration with hexane and recrystllize from hexane to give pure product , (٣.٥٥ g , ٧١ %yield) m.p=١٤٣ –١٤٤ C , lit.[١٧٤] (١٤٥-١٤٦)ºC

IR(KBr) , ٣٤٧٥ cm^{-1} (OH) Fig (٣-١٣) .

Typical procedure for the preparation of ٣-*O*- allyl or ٣-*O*-propargyl ١,٢:٤,٥-di-*O*- cyclohexyldiene-D- fructopyranose [١٢٢] [١٢٣].

In a round bottom flask connected to a condenser derivative [١٢١] (٢g , ٥.٨٨ mmol) was dissolved in benzene (٢٠ml) , then propagyl or allyl bromide (١٠ mmol) was added dropwise after that ٢٠٪ sodium hydroxide and tetrabutyl ammonium bromide (TBAB) (٠.١g , ٠.٥٦ mmol)were added with continuous stirring and refluxed for ١٨hr, TLC (Benzene: Methanol) (٩: ١) indicted the completion of the reaction . The mixture was diluted with water and extracted with benzene (٣×١٥ ml) and the benzene layer was dried with $MgSO_4$ and the solvent was evaporated to leave a liquid layer which was purified on a silica –gel column , to produce the product [١٢٢] .

٣-*O*-allyl ١,٢ : ٤,٥ – Di-*O*- cyclohexyldiene-D- fructopyranose

syrup(١.٢٤ g , ٦٢ %) . IR (film) ١٤٢٢ cm^{-1} (C =CH_2),and ١٠٥٠ cm^{-1} for (C-O-C) , Fig(٣-١٤)

calculated for $C_{21}H_{32}O_6$ C,٦٦.٣١ ; H,٨.٤٢

Found C, ٦٦.٦٠ ; H,٨.٢٢

٣-*O*-Propargyl ١,٢: ٤,٥ –Di-*O*-cyclohexyldiene-D-fructopyranose[١٢٣] as syrup (١.٢٨ g ٦٤ % yield) .

IR Film ٣٢٨٦ cm^{-1}(≡ CH) , ٢١٢٨ cm^{-1} for (C ≡ C),Fig(٣-١٥)

Calculated for $C_{12}H_{31}O_6$ C,٦٦.٦٦ ; H,٧.٩٣

Found C, ٦٦.٨٠ ; H,٧.٦٣

Method B :

Microwave Method

Allyl bromide (٤٩ *µl*, ٠.٥٨ mmol) and sodium hydride(٠.٢٣mg,٠.٥٨ mmol) were added to solution of [١٢١] (١٠٠mg ,٠.٢٩ mmol) in MeCN (٥ ml) . Irradiation of the sample in mw oven was performed for ١٠ min at ١٤٠ ºC . The mixture was diluted with MeOH ,concentrated and purified to give[١٢٢](٠.١٥ mg) ٦٨ % . yield .

١,٢: ٥,٦ -Di-*O*-isopropylidene - α- D-glucofuranoside[١٧٥] [١٢٤]

To an efficiently stirred suspension of anhydrous D-glucose (٥ g, ٣٠.٥ mmol) in anhydrous acetone (٣٣.٣ ml) was added powdered anhydrous zinc chloride (٤ g) followed by (٠.٢٤ g) of ٨٥٪ phosphoric acid .This mixture was stirred for ٣٠ hours at r.t . The undissolved D-glucose was filtered and washed with acetone .The filtrate was made slightly alkaline with NaOH solution at ٠º C .The insoluble material was removed and the filtrate was concentrated to a syrup , which was extracted with CH_2Cl_2: water .The organic phase was dried and concentrated to white crystalline residue of

[١٢٤] (٤ g ,٨٠٪ yield) *Rf* = ٠.٤ (Benzene : Methanol, ٨:٢), m.p ١٠٩ – ١١٠º C Lit[١٧٥]: (١٠٨ –١٠٩) ºC

IR (KBr)٣٣٩٨ cm^{-1} (OH) , (٢٧٠٠ – ٢٩٠٠) cm^{-1} (isopropylidene)

Fig (٣-١٦) .

٣-*O*-Allyl-١,٢ : ٥,٦ -di -isopropylidene -α -D-glucofuranose[١٢٥]

Ally bromide (٤٩ *µl* , ١٠.٥mmol)and sodium hydride (٠.٢٣ g, ٠.٥٨mmol) were added to a solution of ١,٢ :٥,٦ di-*O* -isopropylidene - α −D− glucofuranose [١٢٤] (١ g , ٣.٨ mmol) in MeCN (٢ml) .Irradiation of the sample was performed for ٥ min at ٨٠ C º.

The mixture was diluted with MeOH , concentrated , and purified on a silica – gel column (petrolum ether :EtOAc) as an eluent to give the derivative [١٢٥] (٠.٨ g , ٦٠ % yield)

Rf : ٠.٣٨ (Benzene : Methanol, ٨:٢)

Calculated for $C_{١٥}H_{٢٤}O_{٦}$ C,٦٠.٠٠ ; H,٨.٠٠

C, ٥٩.٨٩ ; H,٧.٨٩

IR (film) disappearance of (OH) band , (٢٧٠٠-٢٩٠٠) $cm^{-١}$ for isopropylidene , ١٦٥٠ $cm^{-١}$ ($C=CH_{٢}$) Fig (٣-١٧)

٣-*O*-Propargyl- ١,٢;٥,٦-di-isopropylidene- α -D-glucofuranose[١٢٦]

R = Propargyl group

Sodium hydride powder (٠.٧٢ g , ٣٠.٤ mmol) was added to a solution ١,٢:٥,٦ di-isopropylidene α-glucofuranose [١٢٤](٢g , ٧.٦ mmol) in DMF and the suspension was stirred for ٢min .Then added with cooling ٠ ºC propargyl bromide (٥ .٨٢ ml, ٤٧ mmol). The reaction mixture was set aside at room

temperature for ٤٨ h . The reaction was monitored by TLC CH_2Cl_2 : EtOAc, ٧ : ٣). Methanol (١٠ ml) was added to the resulting clear solution , the solution was concentrated to dryness .The residue was partitioned between chloroform (٥٠ ml) and water (٥٠ ml) , and the separated organic layer was further washed with water (٣× ٢٠ ml) ,dried with $MgSO_4$, filtered and concentrated to yield brown solid that was purified by column chromatography(petroleum ether: EtOAc)(٧ :٣) to

(١ :١) to produce a brown syrup (١.٨ g , ٩٠ %) *Rf*=٠.٣٦ (Benzene : Methanol, ٨:٢)

IR (film) ٣٢٧٠ cm^{-1} (≡CH) , ٢٧٠٠-٢٩٠٠ cm^{-1} (isopropylidene band) , ٢١١٨ cm^{-1} (C ≡ C) , Fig (٣-١٨)

calculated for $C_{١٥}H_{٢٢}O_6$ C, ٦٠.٤٠ ; H , ٧.٨٣

found C , ٦٠.٢١ ; H , ٧.٥٢ .

٢,٣ : ٤ ,٥ –Di-*O*- isopropylidene-β-D- fructopyranose [١٧٦] [١٢٧]

In a conical flask (with a stopper) anhydrous fructose (١٥ g , ٨٣ mmol) was dissolved in dry acetone (٥٠٠ml) and stirred for ١٥ mints .To the resulting mixture anhydrous ferric chloride (٤.٥ g , ٢٨ mmol) was added and stirred continuous for ١٠ hrs , at ٣٦ ºC .The acidity of the mixture was neutralized by using ١٠ % potassium carbonate solution (١٥ g in ١٥٠ ml of water) and the solvent was evaporated under reduced pressure .The pale yellow oily residue was extracted from the aqueous layer with (٣ × ٥٠ ml) of chloroform .

The organic layer was washed with water , dried with anhydrous magnesium sulphate and the solvent was reduced to ١٥ ml . After cooling, white crystals precipitated which were recrystallized from chloroform : hexane (١: ٢) then from petroleum ether to give the pure product[١٢٧] (١٣ g , ٦٠ % yield) m.p ٩٤ – ٩٥º C , lit[١٧٦] : ٩٥ – ٩٦º C

IR (KBr disc) ٣٢٥٠ cm^{-1} (OH) , ٢٧٠٠ – ٢٩٠٠ cm^{-1} for isopropylidene

Fig (٣-١٩) .

١-*O*-Allyl or ١-*O*-propargyl ٢,٣:٤,٥ –Di-*O*-isopropylidene β-D-fructopyranose [١٢٨][١٢٩]

In a round bottomed flask connected to a condenser, compound, [١٢٧]

(٢ g , ٧.٦٩ mmol) was dissolved in benzene (٧٥ml) , then allyl bromide (٠.٨١٤ ml ,٩.٤٥ mmol) was added dropwise, after that ٢٪ sod. hydroxde solution and tetrabutyl ammonium bromide (٠.١٠ g ,٠.٥٦mmol) were added with continuous stirring and refluxed for ١٢ hr . TLC (Benzene : Methanol) (٩:١)(v:v) indicated the completion of the reaction .

The mixture was diluted with water and extracted with benzene (٣x١٥ml) The benzene layer was dried with anhydrous $MgSO_4$ and the solvent was evaporated to leave a liquid layer which was purified on a silica - gel column . The column was eluted with (Benzene : Methanol) (٩:١) a syrup material of [١٢٨] was obtained (١. ٤ g , ٧٠٪ yield)

calculated for $C_{١٥}H_{٢٤}O_٦$ C, ٦٠.٠٠ ; H,٨.٠٠

found C,٦١.١٢ ; H,٧.٨٥

IR (film) (٢٧٠٠-٢٩٠٠ $cm^{-١}$) (isopropylidene) ١٦١٦ $cm^{-١}$ (C = $CH_٢$) , ١٠٧٠ $cm^{-١}$ for (C-O-C) , Fig(٣-٢٠) .

Similar procedure was followed for preparation of propargyl derivative [١٢٩] was obtained (١.٣٩ g , ٦٥٪ yield)

Calculated for $C_{١٥}H_{٢٢}O_٦$ C, ٦٠.٤٠ H, ٧.٣٨

C, ٦٠.١٤ H, ٦.١٣

IR(film), ٣٠٥٥$cm^{-١}$for (≡CH), ٢١٩٦$cm^{-١}$ for (C≡C) , ١٠٦٩ $cm^{-١}$ for (C-O-C) , Fig (٣-٢١) .

١,٣,٤,٥ Tetra-*O*-benzoyl β-D- fructopyranose[١٧٩,١٨٩] [١٣٠] .

Anhydrous D-fructose (٢ g , ١١.١١ mmo١) was suspended in anyluar dry $CH_٢Cl_٢$ (٢٥ ml) and pyridine (٥ ml) .To this mixture benzoyl bromide (٧ ml)

was added , the mixture was stirred at (-١٥ºC) overnight and the reaction was monitored by TLC(CH_2Cl_2:MeOH) (٨ : ٢) (v:v).

The mixture was poured over ice-water , then was extracted with CH_2Cl_2 (٣×١٥ ml) . The combined organic phase was washed with

(١٠ ml) of ١N HCl solution and then with (١٠ ml) of (١N) Na_2CO_3 solution , the organic phase was dried over anhydrous $CaCl_2$ and filtered, the filtrate was evaporated to dryness in vacuum to give a syrup , that was crystallized from absolute carbon tetrachloride and ethanol alcohol to give white crystals of [١٣٠] , (١.٢ g , ٦٠ % yield) .

Rf= ٠.٨ (CH_2Cl_2: MeOH) (٨ : ٢) (v:v)

m.p=١٧٣-١٧٤ º C, Lit[١٧٩]: (١٧٤-١٧٥º C)

IR (KBr) ٣٤٣٢ cm^{-1} (OH) , ٣٠٥٥ cm^{-1} (C- H)aromatic ١٧٢٨ cm^{-1}

(C=O) , ١٦٠٢ $cm^{-1}$for C=C aromatic . Fig (٣-٢٢)

٢-*O*-Propargyl ١,٢,٣,٥ – tetra –*O*-benzoyl β-D-fructopyranose [١٣١]

$C_{٣٧}H_{٣٠}O_{١٠}$.

To a solution of tetra *O*- benzoyl - β - D –fructopyranose [١٣٠] (١.١٩٢ g, ٢ mmol) in dry DMF (١٠ ml) was added NaH (٦٠ % w/w in mineral oil) (٠.٠٤٨ g , ٢mmol) at ٠° C with frequent venting .After stirring for ٢٠ min propargyl bromide (٠.٣٤٤ml) , ٤ mmol) was added slowly and the mixture was maintained at rt for ١٢ h . TLC indicated the disappearance of the starting material .The reaction mixture was cooled to ٠ ºC and MeOH (١٠ ml) was added .The solvents were removed under reduced pressure .The residue was suspended in water (١٠ml) and extracted with ethyl acetate (٣ × ١٥ ml) . The combined organic layer was washed with saturated aqueous NaCl (٢٠ ml) , dried over anhydrous $Na_٢SO_٤$, filtered and concentrated to give a syrup which was purified by silica-gel chromatography (petroleum ether : EtOAc) to give the product [١٣١]

(٠.٩٥ g, ٨٠٪ yield) .

IR(film) ٣٢٦٧ $cm^{-١}$ (C ≡CH), ٢٩٨٣ $cm^{-١}$ (C≡C), ١٧٥٠ for (C=O),١٦٠٢

$cm^{-١}$, (C=C) aromatic , Fig (٣-٢٣)

calculated for $C_{٣٧}H_{٣٠}O_{١٠}$, C, ٧٠.٠٣ ; H,٤.٧٣

found C, ٦٩.٧٥ ; H,٤.١١

١,٣,٤,٦-Tetra-*O*- benzoyl- α -D- fructofuranoside [١٣٢a]

Benzoyl chloride (٢٠ml , mmol) was added to a solution of D- fructose (٦ g, ٣٣. ٣٣ mmol) in pyridine (١٠٠ ml) at such a rate that the temperature of the mixture did not exceed ٦٥ºC . The solution was then kept for ١٥min , water (٣ ml) was added and then the mixture was cooled to room temp. , diluted with chloroform (١٥٠ ml) , washed successively with(٣ × ١٠٠) ٣٪ sulfuric acid and (٣×١٠٠) of water, saturated aqueous sod. hydrogen carbonate (١٠٠ ml) , and water (١٠٠ ml) , then dried by ($CaCl_2$) and concentrated . The residue was crystallized from methanol (٥٠ ml) to give (٤.٦٢ g) ,٧٧ % yield , m.p = ١٢٢–١٢٣ ºC lit[١٨٠], m.p = ١٢١ – ١٢٣ ºC .

IR(KBr) , ٣٤١٤ cm^{-1} for (OH) , ١٧٢٥cm^{-1} for (C=O) and ١٦٠٠ cm^{-1} for C=C aromatic .Fig (٣- ٤٠b) .

٢-*O*-Allyl ١,٣,٤, ٦-tetra benzoyl β -D-fructofuranoside[١٣٢b]

Allyl bromide (٠.٠٦٦ml , ٠.٧٦٧ mmol) and sodium hydride (٠.٠٣٠g , ١.٢٥ mmol) were added to a solution of tetra-*O*-benzoyl - β -D – fructofuranose [١٣٢a] (٠.٣g , ٠.٥٠٣ mmol) in MeCN (٥ ml) .

Irradiation of the sample by microwave oven was performed for ٥ min at ١٧٠ C .The mixture was diluted with MeOH, concentrated and purified to give the product [١٣٢b](٠.٠٢٤ g , ٨٢٪ yield) .

IR(Film) = ١٧٢٣ $cm^{-1}$for (C=O) , ١٦٠٢ cm^{-1} for ($C=CH_2$) ١١١٠ $cm^{-1}$for

(C-O-C) , Fig (٣-٢٤) .

calculated for $C_{37}H_{32}O_{10}$, C, ٦٩.٨١ ; H,٥.٠٣

found C,٦٩.١٣ ; H,٤.٨٩

٢-٤-٢ Synthesis of *O*-glycoside of glucal sugar

١-*O*-Propargyl- ٤,٦- di-*O*-acetyl glucal [١٣٣] [١٨٣,١٢٣]

method A :

Tri – *O* –acetyl – D – glucal[١٠٩] (٢.٥ g , ٩.١mmo١) was dissolved in (٢٥ ml) toluene containing propargyl alcohol (٠.٥٩٨ ml ,١٠.٢ mmol) under nitrogen . Anhydrous zinc chloride (١.٧٩ g , ١٣.١ mmo١) was added in one portion to the mechanically stirred solution .

A purple color

developed after ٢٥ mins , the supernatant was decanted from the gelatinous solid , neutralized with solid sodium bicarbonate , filtered and concentrated to give the product[١٣٣] as a yellow syrup (١.٦٦g , ٦٩٪ yield) *Rf* = ٠.٢٥ (CH_2Cl_2 : MeOH) (٨ : ٢) (v:v)

IR (film) (٣٢٧٧ , ٢٩٢٠ , ٢١١٨ , ١٧٤٠ , ١٣٧٠ , ١٢٧٠ , ١٢٣٧ , ١٠٦٠ , ٩١٢ , ٧٣٣)cm^{-1} , Fig (٣-٢٥)

calculated for $C_{12}H_{16}O_6$, C, ٥٨.٢٠ ; H, ٥.٩٧

found C,٥٨.٠٠ ; H, ٥.٢٢

Method B

To a stirred solution of ٣,٤,٦ tri-D-glucal [١٤٦a] (٢.٥g ,٩.١mmo١) in dry toluene (٢٥ ml) were added propargyl alcohol (٠.٥ml ,٠.٢mmo١) and a catalytic amount of $BF_3.Et_2O$ (٠.٤ml , ٣.٢٥ mmo١) , the mixture was allowed to react for ١ h and then neutralized by addition of Na_2CO_3 (٢g) . After the solution had been stirred for ٣٠ min , the solids were filtered off and the filtrate was successively washed with a saturated aqueous solution of $NaHCO_3$ and dist. water . After drying with anhydrous Na_2SO_4 , the solvent was evaporated on a rotary evaporator under vacuum affording a syrup. The

residue was purified by dry flash chromatography (petroleum ether : ethylacetate) (٢ : ١) (v:v) (٠.٨٧ g , ٣٧ % yield) .

Method C:

A mixture of ٣,٤,٦-tri –D– acetyl –D–glucal (١.٣٦ g , ٥ mmol) , propargyl alcohol (٠,٤٠٨ml , ٧ mmol) and ceric ammonium nitrate (٠.٢٧٤ g , ٠.٥ mmol) in acetonitrile (١٥ ml) was stirring under reflux for ٦ hr . After completion of the reaction as indicated by TLC, the reaction mixture was quenched with water (١٠ ml) and extracted with ethyl acetate (٣ ×١٠ml) .The combined layers were dried over anhydrous $Na_٢SO_٤$, concentrated in vacuum and purified by column chromatography on silica-gel (petroleum ether : ethyl acetate ٨ : ٢) to produced [١٣٣]

(١.٠٧٤ g, ٧٨ %).

١-*O*-Allyl- ٤,٦- di-*O*-acetyl glucal [١٣٤]

Similar procedure was followed which was used in preparation compound [١٣٣] but using allyl alcohol (٠.٤٧٨ ml , ٧ mmo١) instead of propargyl alcohol ,to produce [١٣٤] as a syrup (١.٥٧ g ٦٣ % yield) .

Rf = ٠.٢٤ (CH_2Cl_2: MeOH) (٨ : ٢) (v:v)

IR (film) ١٧٦٠ cm^{-1} (C=O) , ١٦٥١ cm^{-1} (C = CH_2) ,١٠٤٤ cm^{-1} (C-O-C) Fig (٣-٢٦)

Calculated for $C_{13}H_{18}O_6$ C,٥٧.٧٧ ; H , ٦.٦٦

C,٥٧.٠١ ; H , ٦.١٣

٢-٤-٣ Synthesis of glycosyl azide

O-Methyl D- fructofuranoside[١٨٤]. [١٣٥]

Two methods were explored for methanolysis of D- fructose .

A- Dried D- fructose (٥ g , ٢.٢٧ mmol) was dissolved in dry methanol (١٠٠ml) . Ion exchange resin (Amberlite ١٢٠ H^+) (٢ g) was added as the acidic catalyst .The mixture was heated under reflux with stirring for half –an-hour at ٥٠ - ٥٥ºC .The resin was removed by filtration and the solution was neutralized by adding sodium methoxide .Removal of methanol under vacuum gave syrup product (٤.٦ g , ٩٢٪ yield).

B- A solution of ٠.٥ % hydrochloride acid was prepared by dissolving acetyl chloride (١ ml) in dry methanol (١٠٦ ml) and dried D-fructose (٥.٧g) was added .The reaction mixture was left for three hours at room temperature .The solution was then neutralized by drop wise addition of sodium hydroxide in methanol . The solvent was then removed at ٣٠ºC and a syrup product (٤.٩٩g) was obtained .

٨٢ % yield , *Rf* = ٠.٤ (CH_2Cl_2: MeOH) (٨ : ٢) (v:v)

IR (film) ٣٣٧٦ cm^{-1} (OH) , ١٠٥٤ cm^{-1} (C-O-C),Fig (٣-٢٧)

O-Methyl ١ , ٦- Di –*O*-toluene sulfonyl –D-fructofuranoside [٢٤] [١٣٦]

In a conical flask with a stopper , derivative [١٣٥] (٣ g , ١٥.٤ mmol) was dissolved in pyridine (٢٠ ml) and cooled to ٠ ºC . *p*-Toluene sulfonyl chloride (٢.٩٤٨ g ,١٥.٤٦mmol) was dissolved in (١٠ ml) cold pyridine and added at room temperature to above solution drop by drop and left for ٢٤hr, with stirring .TLC (Benzene : Methanol) (٨ : ٢) (v:v) showed the completion of the reaction .

The mixture was poured on crushed ice , then extracted by chloroform

(٥ ×١٥m) , the chloroform layer was dried by $MgSO_4$, filtered and evaporated under vacuum to give a syrup (٢.١٨ g) in ٧٢ % yield .

R f = ٠.٥٩ (CH_2Cl_2: MeOH) (٨ : ٢) (v:v)

IR= (film) ٣٢٠٠ cm^{-1} (OH) , ١٥٨١cm^{-1} (aromatic) ,(١١٧٧ , ٩٩٠) cm^{-1} (SO_2) , ١٠٣٠ cm^{-1} (C-O-C) . Fig (٣-٢٨)

Methyl-٦-deoxy-٦-azido –١-*O*- *p*-toluene sulfonyl – D-fructofuranoside[٢٤] , [١٣٧]

In a two – necked round bottomed flask connected to a reflux condenser and thermometer , the derivative [١٣٦] (٣ g) was dissolved in DMF (١٥ ml), and sodium azide (١.٠٩ g , ٢٠.٦ mmol) was added with continuous stirring at ٦٠ ºC for ١٩ hr .TLC ($CH_٢Cl_٢$:Methanol) (٨ : ٢) (v:v) showed the completion of the reaction .The mixture was diluted with water and extracted with chloroform (٣× ٢٠ ml) then dried with anhydrous $MgSO_٤$. The chlorofrom layer was evaporated in vacuum to give syrup [١٣٧] (١.٨٣ g ,٦١ % yield) .

Rf = ٠.٧٧ ($CH_٢Cl_٢$: MeOH) (٨ : ٢) (v:v)

IR (film) ٢١٠٠ $cm^{-١}$ ($N_٣$) . Fig (٣-٢٩)

٢,٣: ٤ ,٥ –Di-*O*- isopropylidene-١-*O*- *p*- toluene sulfonyl – β-D-fructopyranose[١٨٥] [١٣٨] .

In a conical flask (with stopper) ٢,٣: ٤,٥ –di-*O*- isopropylidene- β-D-fructopyranose [١٢٧](٥ g , ١٩ mmol) was dissolved in dry pyridine

(٢٠ml)and cooled to ٠ ºC . *p*-Toluene sulfonyl chloride (٢ g, ١٠.٤٨ mmol)

was dissolved in ١٠ ml dry pyridine and then added to solution at room temperature and left for ٢٠ hr.with stirring .TLC (Benzene : Methanol) (٩:١) (v:v) showed the completion of reaction .The mixture was poured on crushed ice to give brown precipitate , which was decolorized and recrystalized from ethanol to give white crystal [١٣٨] (٤ g , ٦٠ % yield) m.p ١٢٥- ١٢٦ ºC, lit[١٨٥]: ١٢٥- ١٢٦ ºC

IR(KBr) : (٩٦٨ and ١١٧٧) cm^{-1} (SO_2) Fig(٣-٣٠)

١-Azido – ١ – deoxy – ٢ , ٣ : ٤ , ٥ di –*O*-isopropylidene – β -D-fructo pyranose [١٣٩]

Method A

In a two –necked round bottomed flask connected to a reflux condenser and thermometer , ٢,٣ : ٤,٥ di –*O*-isopropylidene-١-*O*- toluene sulfonyl–β-D-fructopyranose [١٣٨] (٢.٥g ,٧.٣ mmol) was dissolved in DMF (٢٠ ml) and sodium azide (٠.٦ g , ٩.٢ mmol) and teratbulty ammonium bromide (٠.١g , ٠.٥٦mmol) were added with continuous stirring at ١٤٠ºC for ٢ days .TLC(Benzene : Methanol) (٩ :١) (v : v) showed the completion of the reaction . The mixture was diluted with water and extracted with chloroform (٥ × ٥) then dried with anhydrous $MgSO_4$ .The chloroform was evaporated to give [١٣٩](١.٥ g) as a syrup , ٧١ % yield .

IR(film) ٢١٠٠ cm^{-1} (N_3) Fig (٣-٣١)

Method B

Trimethylsilyl azid (٨٠μl , ٠.٦٠ mmol) and TBAF (٦٠٠ μl , ٠.٦٢ mmol) were added to an argon – blanketed solution of tosylate [١٣٨] (٠.١٤٢g , ٠.٢١٧ mmol) in ٨ml of CH_3CN .

The reaction was heated at reflux for ٦hr. The mixture was allowed to return to room temperature and ٢٠ml of water was added . The product was extracted with ethyl acetate , (٣×١٥ml) . The organic extracts were combined , dried over $MgSO_4$, and filtered . Solvent was removed in vacuum to afforded a yellow oil . The oil was purified by column chromatography (pet. ether: EtOAc) (٢ :١) to yield (٠.٨٢g , ٨٦ %) of azide [١٣٩] .

١,٢:٤,٥-Di-*O*-cyclohexylidene-٣-*O*-*p*-toluene sulfonoyl -β- D-fructopyranose[١٤٠]

$C_{٢٠}H_{٣٤}O_{٨}S$

In a conical flask with stopper, (٣ g ,٨.٨٢ mmol) from derivative [١٢١] was dissolved in dry pyridine ٣٠ml and cooled to ٠ ºC . *p*-Toluene sulfonyl chloride (١.٦٢g ,٨.٤٨ mmol) was dissolved in ١٠ml dry cold pyridine and then added to solution at room temperature and left for ٣ days in refrigerator . TLC (Benzene : methanol) (٩:١)(v:v) showed the completion of reaction . The mixture was poured on crushed ice to give precipitate which was recrystalized from ethanol to give crystals [١٤٠] (١.٨٧g , ٦٢٪ yield)

IR = (KBr) , (١١٧٧ , ٩٩٠) cm^{-1} ($-SO_2$) , Fig (٣-٣٢)

Calculated for $C_{٢٥}H_{٣٤}O_8S$ C, ٦٠.٧٢ : H, ٦.٨٨

Found C, ٦٠.١٥ : H , ٦.٢٢

٣-Azido-٣-deoxy- ١,٢:٤,٥-Di-*O*-cyclohexylidene-β- D-fructopyranose[٢٤] [١٤١]

In a two- neeked round bottomed flask connected to a reflux condenser and a thermometer ,derivative [١٤٠] (٢ g , ٤.٠٤ mmol)was dissolved in DMF (١٠ ml) , sodium azide (٢.٤ g , ١٥.٣ mmol) and tetrabutyl ammonium bromide (٠.٤ g , ٢.٢٤ mmol) were added with continuous stirring at ١٤٠ ºC for ٢٤ hr .The reaction was monitored with TLC (Benzene : Methanol) (٩ : ٢) (v:v) .The mixture was diluted with water and extracted with chloroform(٥×١٥ml) then dried with anhydrous magnesium sulphate , evaporated in vacuum to give (١ g , ٥٠ % yield)from [١٤١] as a syrup.

IR(film) ٢١٠٠ $cm^{-١}$ ($N_٣$) Fig (٣-٣٣)

Calculated for $C_{١٨}H_{٢٧}O_٥N_٣$ C , ٥٩.١٧ ; H,٧.٣٩ ; N,١١.٥٠

Found **C,** ٥٨.٨٦ **; H,** ٧.١٢ **; N ,**١٠.٨٩

٢-Azido-٢-deoxy- ١,٣,٤,٥-tetra-*O*- benzoyl- *β*-D-fructopyranose [١٤٢]

To a solution of [١٢٩] (٠.٨٣٨ g, ٦.٤ mmol) and pyridine (٠.٠٩٦ml ١٠.٣ mmol) in a anhydrous CH_2Cl_2 (١٠ml) at ٠ºC. Trifluromethane sulfonic anhydride(Tf_2O) (٠.١٦٦ml , ٩.٠mmol) was added slowly . After being stirred for ٥٠ min , the reaction mixture was diluted with CH_2Cl_2 washed with water , saturated $NaHCO_3$, and brine and dried over $MgSO_4$. The solution was filtered through celite and transferred into a solution of excess NaN_3 and DMF . The reaction mixture was stirred overnight . After completion of the reaction , the reaction mixture was filtered through celite . The residue was washed with EtOAc. The combined solutions were concentrated and purified with column chromatography (petroleum ether : EtOAc , ٩:١ to ٤:٦) to produce syrup (٠.٦٨ g , ٨٢٪ yield)

IR (film) ٢١٢٩ cm^{-1} (N_3) Fig (٣-٣٤)

Calculated for $C_{34}H_{27}O_9N_3$ C, ٦٥.٧٠ ; H, ٤.٣٤ ; N, ٦.٧٦

C, ٦٤.٠٢ ; H,٣.٧٨ ; N, ٦.١١

٣-Azido-٣-deoxy ١,٢: ٥,٦ –di-*O*-isopropylidene-D-glucofuranose [١٤٣]

$C_{١٢}H_{١٩}O_{٩}N_{٣}$

By using the similar procedure in preparation derivative [١٤٢]. The derivative [١٢٤] was converted to derivative [١٤٣] as a syrup in ٨٣٪ yield .

IR:Film (٢١١٠) $cm^{-١}$ ($N_{٣}$) , Fig (٣-٣٥)

Calculated for $C_{١٢}H_{١٩}O_{٥}N_{٣}$ C, ٥٠.٥٢ ; H, ٦.٦٦ ; N, ١٤.٧٣

Found C, ٤٩.٧٧ ; H, ٦.١٣ ; N, ١٣.٨٦

١-azido-١-dexy- ٢,٣,٤,٦-tetra-*O*-acetyl -β-D-glucopyranose[١٨٧] [١٤٤]

A solution of $SnCl_4$ (٠.٠١٥ ml , ٠.٠١ mmol) in toluene (٢ml) was added to a stirred suspension of $AgClO_4$ (٠.٠٣٣g , ٠.٠١mmol) in dichloromethane (٥ ml) at room temperature , and the mixture was shielded from a light and stirred for ١ hr .

To this mixture was added a soultion of penta acetate β -D-glucopyranose [١١٤] (١g , ٠.٢mmol) and trimethylsilyl azide (٠.٤٧ml,٠.٢٤mmol) in dichloromethane (٢ ml) at room temperature . After stirring the mixture for ٢٠ hr, aqueous sodium hydrogen carbonate was added .The mixture was extracted with CH_2Cl_2 (٣ × ١٥ ml) ,dried with $MgSO_4$ and evaporated under vacuum ,yellow syrup was product, after cooling , amorphous solid was obtained (٠.٧٨ g , ٧٨٪ yield)

m.p = (١١٦-١١٨ °C) Li[١٨٧]t:١١٧-١١٨ °C

IR(KBr) ٢١٢٠ cm^{-1} ($-N_3$) Fig(٣-٣٦)

Preparation of Zinc azide bis pyridine($ZnN_6 . 2py$)[99]

To a stirred ٢M aq. solution of $Zn(NO_3)_2$ (٦٠ ml , ١٢٠mmol) was added dropwise a ٢M aqueous solution of NaN_3 (١٢٠ml , ٢٤٠mmol). The white suspension is brought to ٥٠ºC , then a slight excess of pyridine (٢٠ml , ٢٤٧mmol) is added drop wise forming a dense white precipitate . Stirring is continued while the mixture is slowly cooled to rt . The salt is filtered , washed with ice cold water and dried in vacuum to give a white crystalline powder , yield ٣٠ g (٨١٪) .

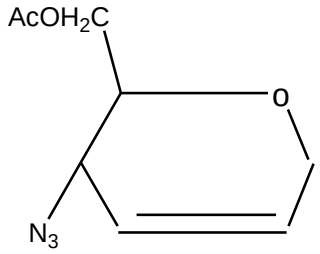
General procedure for preparation of azido sugars by using $Zn N_6 . 2py$.

$Zn N_6 . 2py$ (٠.٤٦ g , ١.٥ mmol) is suspended in a solution of the alcohol (٢mmol) and Ph_3P (١.٠٥g , ٤mmol) in anhydrous toluene (١٠ml)

To this stirred mixture at r.t, diisopopyl azodicabxylate (٠.٨ml , ٤ mmol) is added drop wise , causing a slightly exothermal reaction . Stirring is continued until complete consumption , (TLC)

monitoring of the product is observed . The heterogeneous mixture is filtered over a celite pad , concentrated in vacuum and purified by column chromatography over ٧٠-٢٣٠ mesh silica gel eluents (pet . ether: EtOAc) to afforded the pure azide .

٦-*O*-Acetyl-٤-azido ٢,٣,٤-trideoxy-α –D-erythro –hex-٢-ene pyranoside [١٤٥][٩٥]



$C_8H_{11}O_2N_3$

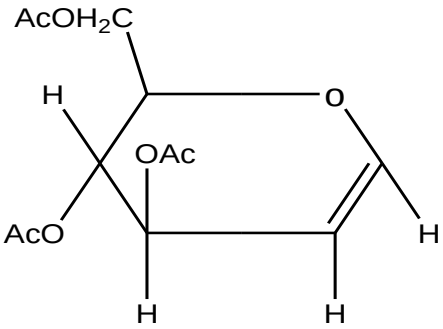
The catalytic system was prepared by stirring for ١h in a schlenk tube under argon the palladium complex $Pd(PPh_3)_4$ (٣ %) in (٣ml) tetrahydrofuran . This solution was added under argon to a schlenk tube containing the (١.٠٨٨g , ١mmol) tri-acetyl glucal[١٤٦a] , and sodium azide (٠.٢٨٦g , ١.١mmol) in a mixture(THF: water) (٣ml :٢ml). The mixture was stirred at ٥٠ºC for ١h , and then extracted with ether (٣×١٠ml) and the combined extracts were washed successively with ١M HCl (٣٠ml), saturated $NaHCO_3$ (٣٠ml) and brine (٣٠ml). The organic layer was dried over $MgSO_4$. Removal of the solvent under reduced pressure gave a residue that was submitted to column chromatagraphy on silica gel using petroleum ether : EtOAc as the eluent to afford the product as a syrup .

(٠.٤١ g) ٦٢ % yield, *Rf* = ٠.٥٦ (CH_2Cl_2: MeOH) (٨ : ٢) (v:v)

IR(film) ٢١٠٦ cm^{-1} ($-N_3$) Fig (٣-٣٧)

٢-٤-٤ Synthesis of ١,٢-unsaturated sugars

٢-٤-٤-١ Synthesis of ٣ , ٤, ٦-Tri-acetyl glucal[١٠٩] [١٤٦a]



$C_{12}H_{16}O_4$

Part : ١

D – Glucose (٥.٥ g ,٣٠.٥ mol) was added to a mixture of acetic anhydride (٢٠ml) and ٠.١٥ ml , ٦٢ % perchloric acid at ٤٠ºC during one hours . After the addition of red- phosphorus (١.٥ g ,٤٨.٤ mmo١) . The round bottom flask was cooled in ice-salt mixture , and bromine (٢.٩ ml , ٣٩.٠٣mmo١) was added dropwise with continued stirring at such a rate as to keep the internal temp. below ٢٠ºC (١ hours) . In the same way , ٥ ml of water was added during a course of ٣٠ min with careful control of temp . The vessel was closed by stopper and kept ٣ hr at room tempt . The mixture was filtered and the filter paper washed with little acetic acid . The filtrate contained tetra *–O–* acetyl-D - glycopyranosyl bromide .

Part : ٢

A solution of sodium acetate (٢٠ g , ٢٤٣mmo١) in water (٢٩ ml) and glacial acetic acid (٢٠ml) was prepared . After the solution was cooled in an ice-salt mixture , zinc dust (١١g, ١٦٨mmo١) and cupric sulfate

(١.١ g , ٦.٩mmo١) in water (٤ ml) were added to this solution . When the blue color had disappeared , the solution of above mentioned bromide was added graduaily during ١ hr , keeping the temperature between

(– ١٠ º C and – ٢٠ º C).

Efficient stirring was necessary and was continued for ٣ hr at ٠ ºC the mixture was filtered , and the filter paper was washed with ٥٠٪ acetic acid . Water (٥٠ml) was added to the combined filtrates at ٠ ºC and the solution was extracted with chloroform (٥×١٠٠ml) . The combined chloroform extracts were washed with iced-water ,saturated sodium carbonate solution, and again with cold water. The solution was dried by addition of calcium chloride , decanted , and evaporated under reduced pressure . The resulting syrup was dissolved in diethyl ether and petroleum ether was added to solution to

opalescence . After a few hours with the aid of seeding crystallization provided pure [١٤٦a] .

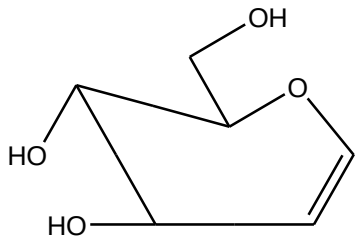
(٥g , ٦٠ % yield m.p ٥٣-٥٤ ºC lit[١٠٩] : ٥٤-٥٥ ºC

IR(KBr) ١٧٤٤ cm^{-1} (C=O), ١٦٥٠ cm^{-1} (C=C) Fig (٣-٣٨)

Calculated for $C_{١٢}H_{١٦}O_{٧}$ C: ٥٢.٩٤ H:٥.٨٨

C: ٥١.٩٤ H:٥.٨١

٢-٤-٤-٢ Synthesis of glucal [١٤٦b]



$C_6H_{10}O_4$

To a stirred solution of tri – *O*- acetyl-D- glucal[١٤٦a] , (٢ g) in dry methanol (٣٢ml) was added methanolic solution of sodium methoxide (prepared by dissolving ٠.٢٥٠ mg of sodium in ٢ ml methanol) and the solution was left at room temp. for ٢ days . Evaporation of the solution gave crystaline [١٤٦b] (١.٢ g , ٦٠٪) m.p ٥٦-٥٨ ºC lit.[٢١] m.p ٥٧-٥٩ ºC

IR(KBr) ٣٣٧٠ $cm^{-١}$ (OH) , ١٦٥٣ $cm^{-١}$ (C=C) Fig(٣-٣٩)

٢-٤-٤-٣ Synthesis of Fructal[١٢٨] [١٤٧]

٣,٤,٥- Tri (benzoyloxy) –١-benzoyloxymehyl –٣,٤- dihydro-٢H-pyran (*endo* –fructal)

To a stirred solution of tetra benzoate fructosyl bromide (٢.٠ g , ٣ mmol) and freshly desiccated molecular sieves (٤A º) in anhydrous acetone (٥٠ ml) , sodium iodide (٠.٧ g ٤.٧ mmol) was added and the mixture kept at ambient temp . for (١٠ h) .The resulting suspension was filtered through a layer of silica gel , followed by the removal of the solvent in vacuo at a bath temp. not exceeding ٢٥ ºC .The syrup thus obtained was taken up in boiling xylem (٥٠ ml) and the solution stirred at ١٤٠ º C for ٢ hr .The mixture was then allowed to return to room temp. where after water (٢٠ml) was added (to hydrolyze residual fructosyl iodide) , followed by filtration of the brown solution through a layer of silica gel and removal of the solvent in vacuo .The resulting residue was dissolved in $CHCl_3$ (٥٠ml) and the solution successively washed with water , $NaHCO_3$ solution and again with water (٢٥ ml each) . Drying over $MgSO_4$, and concentration in vacuo gave a syrup consisting mixture of *exo*- and *endo*-fructal separation has an effected on a silica gel column volume (٤ × ٤٠ ml) by elution with ١٠:١ toluene :EtOAc . Removal of the solvents from the fraction eluted as a syrup (٠.٩ g ,٣٣ %) *Rf* = ٠.٣١(CH_2Cl_2: MeOH) (٨ : ٢) (v:v)

IR (film) showed ١٧٥٠ cm^{-1} for (C=O) and ١٦٢٠ cm^{-1} For (C=C),

fig(٣-٤٠).

٢-٤-٥ Synthesis of Triazoyl linked Carbohydrate(Triazoyldisaccahride)

General procedures for Triazole and Triazoline formation under :-

٢-٤-٥-١ Microwave Irradiation Method.

a- A solution of the alkyne or alkene derivative (١.١mmol) and the azide derivative (١mmol) , DBU (٣mmol) and the copper catalyst $(Ph_3P)_3$.Cu Br (١٠-٢٠ mmol %)in toluene (٥ml) was irradiated at ٧٥٠ w in a microwave oven for period of ٢ min . The solution is allowed to cool during heating intervals , until TLC or the IR spectra of the reaction mixture showed complete disappearance of the starting materials .

The reaction mixture was evaporated and the crude product is purified in short flash column chromatography to yield the ١,٢,٣ triazole or triazoline derivative

b- A mixture of azide derivatives (٣mmol) and the alkyne or alkene derivatives(٤.٨ mmol) in a fine Pyrex tube of ١cm diameter was introduced in the microwave oven until TLC or the IR spectra of the reaction mixture showed complete disappearance of the starting material , CH_2Cl_2 (٢٠ ml) was then added .

The reaction mixture was purified in a short flash column chromatography to yield the ١,٢,٣ -triazole or triazoline derivative .

c- The alkenes or alkynes (٣٠-١٠٠ mmol) and the azido carbohydrates (١.٥ equiv.) ,$CuSO_4 . 5H_2O$(٣٠mol%) and sodium ascorbate(٦٠ mol%), were dissolved in DMF (١-١.٥ ml)containing several drops of H_2O . The solution was exposed to microwave irradiation at ٨٠ºC for periods of ٢٠ min, until TLC or the IR spectra of the reaction mixture showed complete disappearance of the starting material . Then it was concentrated and purified on a silica column first with (CH_2Cl_2:EtOAc) (٦:١) to recover the excess of starting azido carbohydrate followed by elution with CH_2Cl_2:MeOH(٦:١) .

٢-٤-٥-٢ Heating with solvent .

To a solution of azid derivative (٣ mmol) in toluene (١٠ml) was added dropwise with stirring the solution of alkynes or alkenes derivatives (٣mmol) .The reaction mixture was stirred under reflux at tempt.١١٠ ºC for the specified time (as in table ٣-٥),until the TLC or the IR- spectra of the reaction showed the end of reaction, then cooled, concentration under vacuum ,to gave the product which is isolated by flash chromatography eluting with petroleum ether: EtOAc (٦:٣) to yield the triazole or triazoline derivative.

٢-٤-٥-٣ Sealed tube method

Tri -*O*- acetyl -D- glucal[١٤٦a] (٢٠٠mg , ٠.٧٣ mmol) or fructal and azide derivative(١٢٦ mg ,٠.٩٥ mmol) were heated at ١٢٠ºC in ٣ ml trimethylorthoformate (sealed tube) for (٥٤ hr.) . Evaporation and chromatography on silica gel (hexane, ethyl acetate) (٢ :١) (v:v) gave the product .

٢-٤-٥-٤ One – pot reaction method

A solution of D- glucose pentaacetate[١١٤] (١ g)and HBr (٣٣٪ solution in CH_2Cl_2 ١.٥ ml) in dry chloroform (١٠ml) was stirred under nitrogen for ١٢ h at room temperature , until the completing of the reaction as monitored by TLC .The following reagents were added in order of : chloroform (١٠ ml), saturated sodium bicarbonate solution ٥ ml , sodium azide (٠.١٤٩g ,٢٢ mmol) , tetrabutylammonium hydrogen sulfate (٠.٥ g, ١.٥ mmol),

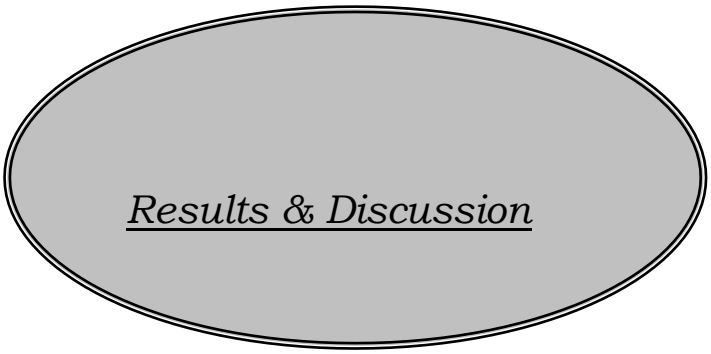
allyl or propargyl sugars (٠.١٥g, ١.٥ mmol), copper sulfate pentahydrate (١٢mg , ١٠.٠٥ mmol), sodium ascorbate (٣٠ mg , ٠.١٥ mmol) and ethanol(٥ml) . The reaction mixture was stirred at room temperature for about ١٨ h. The solvent was removed, and

the residue was cooled , chromatography on silica gel (hexane , ethyl acetate) (٢ :١) (v:v) to afford the product in ٨١٪ yield .

Table (٣-٥) explains the properties of the coupling reaction , and table

(٣-٦) explains the spectral data of some product derivatives .

CHAPTER THREE


Results & Discussion

٣-Results and Discussion

In search of the synthesis of new carbohydrate compounds , we thought that ١,٣ – dipolarcycloaddition reaction (١,٣-DC) could be used as

an efficient tool allowing for the simultaneous building up of aromatic or non-aromatic heterocyclic systems .

٣-١- Synthesis of allyl or propargyl ethers

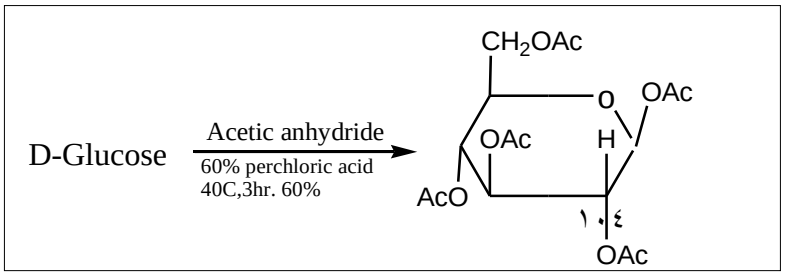
The first approach of our goal was the construction of sugar, containing alkyne or alkene group derivatives .

Several methods have been described for synthesis of these types

of sugars derivatives . The multistep synthesis of carbohydrate derivatives is difficult and requires many purification steps . The difficulty in synthesizing these derivatives stems from the similar reactivity of the hydroxyl group and any glycosidic linkages that need to be formed . For these reasons alternative approaches have been sought .

٣-١-١: Synthesis of glucose pentaacetate :

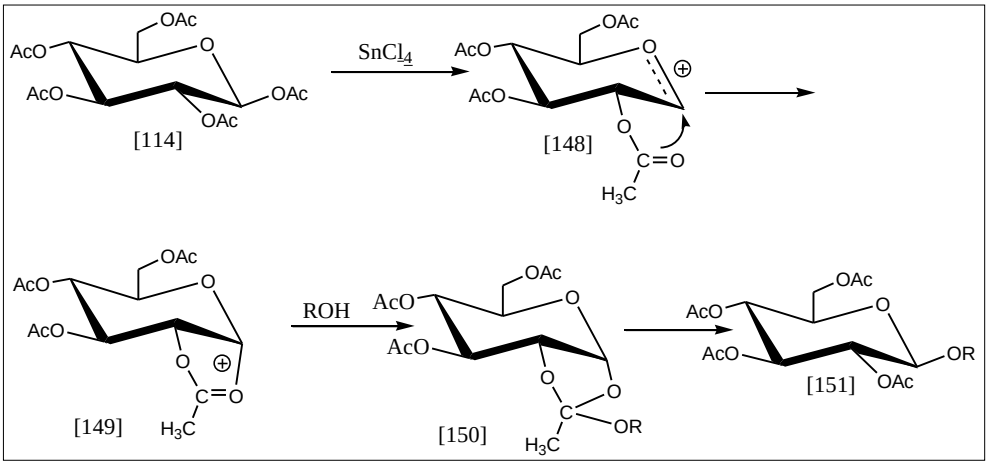
The glucose pentaacetate derivative is readily prepared in crystalline form in the α-or β – anomeric form depending on the procedure being used. The hydroxyl group of glucose react readily with acetic anhydride in the presence of an acid catalyst such as perchloric acid . The cyclic acetate formed by the acetylation procedures is normally in the pyranoid form .



The glucose pentaacetate was characterized by its IR spectrum and m.p which was identical with the literature[٢١,١٧٢]. The IR spectrum (Fig ٣-٦)
showed stretching band at ١٧٦٠ cm^{-1} for carbonyl acetate .

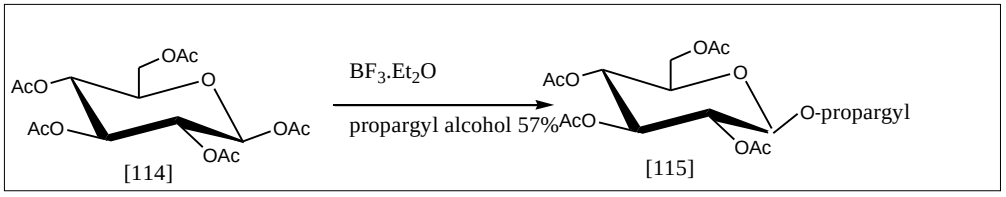
٣-١-٢ : Synthesis of allyl or propargyl glucose pentaacetate

The glucose pentaacetate [١١٤] is ether employed to prepare unsaturated *O*-glycoside, for example , when D-glucopyranose pentaacetate [١١٤] is dissolved in dichloromethane , containing one molar equivalent of tin(IV) chloride and treated with allyl or propargyl alcohol the addition take place at room temperature under anhydrous conditions to give the glycoside[١٥١] via ١,٢- acetoxinium ion [١٤٩][١٩١] .



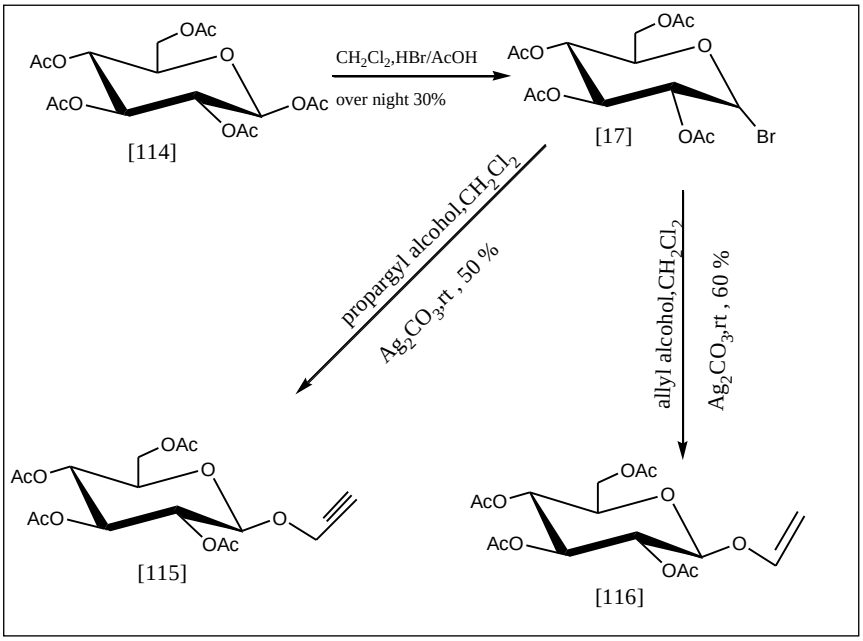
Scheme ٣-١ Mechanism of *O*-glycosidation

Similar glycoside formation is achieved when β-D-glucopyranose pentaacetate [١١٤] is treated with an excess of propargyl alcohol in the presence of a $BF_3.Et_2O$ as a Lewis acid , to produced[١١٥] in ٥٧٪ yield .

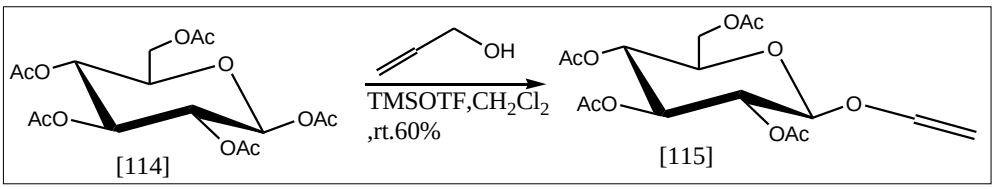


R.Rodebaujh and Fraser - Reid[٦٢] recently reported that *O*-allyl and

O-propargyl glycosides could be prepared by dissolving glucose pentaacetate [١١٤] in CH_2Cl_2 under argon in presence of ٣٠٪ solution of HBr in AcOH to convert glucose pentaacetate into α-D-glucopyranoside bromide[١٧].Moreover when a portion of this material[١٧] was allowed to react with allyl and propargyl alcohol dissolved in CH_2Cl_2 under argon in the presence of silver carbonate , peracetylated proparygl glucose[١١٥] was obtained in ٤٠٪ yield .



Best results were obtained when the reaction was performed with pentaacetat β-glucopyranos and (٢eq.) of allyl alcohol in dichloromethane in presence of trimethylsilyl triflate (TMSOTF)at rt, for ٢h.



The *O*-allyl tetraacetate[١١٥]showed stretching band at (١٧٤٨,١٣٦٩,١٢٤٥,١٠٥٠)cm^{-1} Fig(٣-٨) , and *O*-propargyl tetraacetate[١١٦]

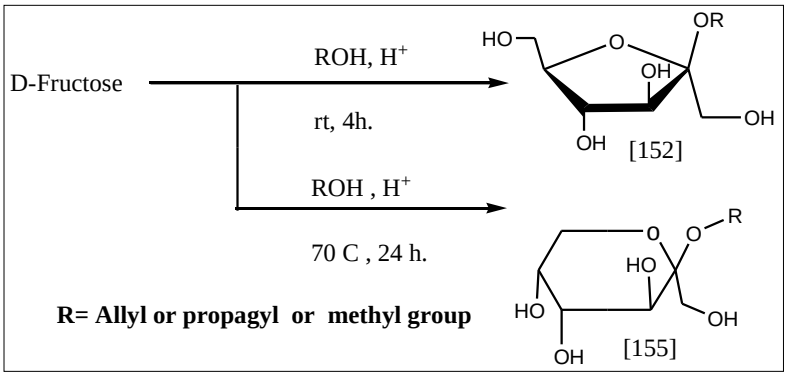
showed stretching band at (٢١٢٠, ١٧٥٠)cm^{-1} Fig(٣-٧).

٣-٢: Direct glycosylation of D-fructose and D-glucose

Fischer glycosylation of the anomeric hydroxyl group of a sugar takes place upon refluxing with an alcohol in the presence of acid catalyst . Using amberlite resin IR-١٢٠H^+ as acid catalyst adopted for the preparation of the desired glycosides . The use of an acid resin as catalyst offers advantages since the catalyst can be removed by simple filtration , avoiding the need for neutralization and giving cleaner products with higher

yields [١١٥] .

When fine powder of D-fructose was treated with allyl or propargyl or methyl alcohol in presence of amberlite resin IR-١٢٠H^+ for ٤h. allyl or propargyl D-fructofuranoside was obtained , but allyl and propargyl D-fructopyranoside was formed when thermodynamically controlled condition was used , ٧٠ ºC and long reaction time ١٨h .



In general , the glycoside products were characterized by its IR spectrum which showed stretching band at ١٠٠٠ – ١١٠٠ cm^{-1} for C – O – C band as in table(٣-١) which shown some properties of the reactions and IR- spectrum showed in figures[(٣-٩)(٣-١٠)(٣-١١)(٣-١٢)(٣-٢٧)] .

٣-٢-١ : Microwave – accelerated Fischer glycosylation

Fischer glycosylation of the anomerric hydroxyl of a sugar occurs upon reflux with an alcohol in the presence of acid catalyst and mixture of α - and β- glycosidic product is formed . The main deficiency of this reaction is the long reaction time required [١٩٥]. When microwave irradiation was applied to conventional Fischer glycosylation an impressive acceleration of reaction (few minutes compared to several hours) was noticed with good α-glycoside product selectivity .

Table ٣-١ Condition and some properties of Fischer glycosylation reaction

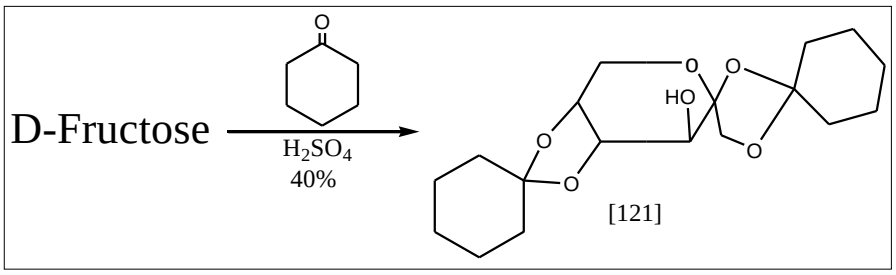
En.	*solvent*	*starting material*	me *min*	*Temp. ºC*	*IR Spectrum cm^{-1}*
١	Methanol	Glucose	١٠	٩٠	١٠٥٤ (C-O-C)
٢	Allyl alcohol	Glucose	١٠	١٢٠	١٦٥٠ (C=C)
٣	Propargyl alcohol	Glucose	١٠	١٢٠	٣٤٨٢,٢١٢٠ C≡C C≡CH
٤	Methanol	Fructose	١٥	٩٠	١٠٠٠-١١٠٠(C-O-C)
٥	Allyl alcohol	Fructose	١٥	١٢٠	١٦٠٠-١٧٠٠ C=CH$_2$
٦	Propargyl alcohol	Fructose	١٥	١٢٠	٣٤٠٠,٢١٩٠ C≡C C≡CH

٣-٣ : Synthesis of sugars derivatives containing an olefin group in different positionS

The other aims of the present study are to prepare sugars derivatives containing an olefenic ether group at position other than the anomeric position . For this approach , it required the protection of all the sugar hydroxyl groups leaving only the hydroxyl group for etherification free .

٣-٣-١ : Synthesis of ١,٢:٤, ٥ –Di – *O* – cyclohexyldiene – D-fructopyranose [١٢١]

When fine powder of D-fructose was treated with cyclohexanone in presence of concentrated H_2SO_4 , it gave a crystalline cyclohexylidene derivative [١٢١]which was further purified from heptane to give (٣.٥٥ g) in ٧١٪ m.p=١٤٣-١٤٤ ºC .



[121]

Compound [١٢١] is characterized by IR and C-H-N analysis , it's IR spectrum showed a stretching band at ٣٤٧٥cm^{-1} for hydroxyl group Fig (٣-١٣) .

The spectroscopic and other physical data agree with (Ref.١٧٤) reported for [١٢١] .

٣-٣-٢ : Synthesis of ٣-*O*- allyl ١,٢:٤,٥ Di-*O*- cyclohexylidene.

D-fructopyranose [١٢٢]

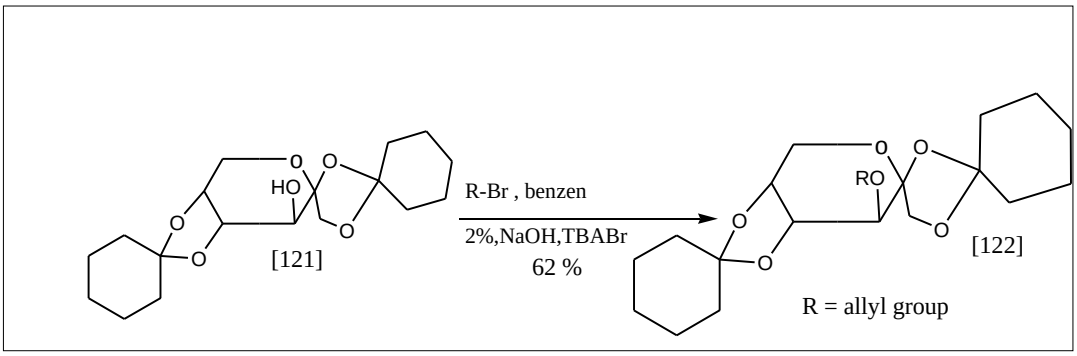
For the synthesis of the ٣- substituted – oxy derivatives [١٢٢].

The first step in the proposed reaction scheme was the etherification of the hydroxyl group at C-٣ of [١٢١]with allyl bromide .

Treatment of [١٢١]in benzene with allyl bromide using terabutyl

ammonium bromide[١٩٧] (TBAB) as phase transfer catalyst and (٢٪) sodium hydroxide solution for ١٨h gave the derivative [١٢٢]in

٦٢ % yield .

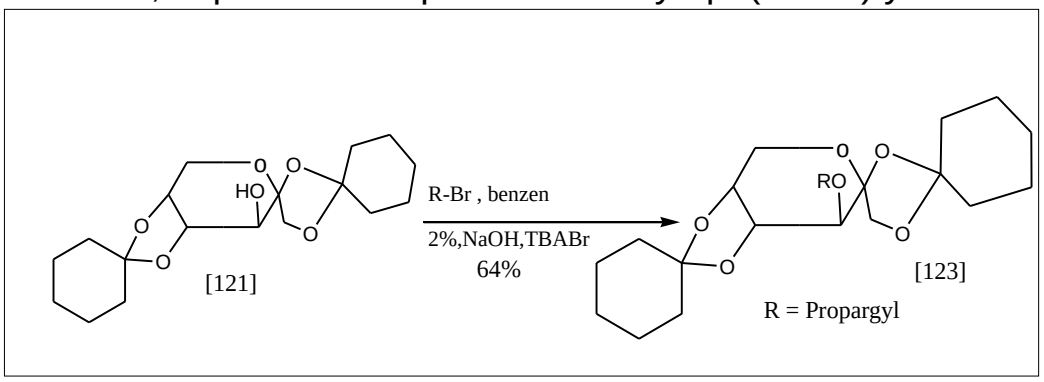


The allyl ether derivative [١٢٢]showed in the IR spectrum the characteristic bands for the (C = CH_2) at ١٤٢٢ cm^{-1} and ١١١٠ cm^{-1} for (C-O-C) bond Fig (٣-١٤) .

٣-٣-٣ : Synthesis of ٣-*O*- propargyl ١,٢:٤,٥ Di-*O*- cyclohexylidene

D-fructopyranose [١٢٣]

In a similar manner , the derivative [١٢٣]was prepared via a method described for derivative [١٢٢],by using propargyl bromide instead of allyl bromide , to produce the product as a syrup (٦٤ %) yield .



IR spectrum showed , the characteristic bands for the (C ≡ CH) at ٣٢٨٦cm$^{-١}$ and ٢١٢٨ cm$^{-١}$ for (C ≡ C) stretching band (Fig ٣-١٥) .

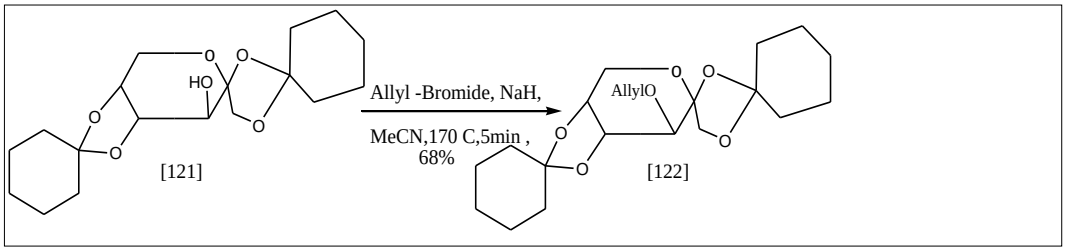
٣-٤ : Etherification of sugar derivatives by using microwave technique

Microwave heating has been shown to be the most useful method to assist protection group manipulation reaction on saccharide [١٩٨]. Short reaction times and large rate enhancements as compared to conventional methods are observed . Yields are comparable or better than when using conventional methods , and sometimes much higher in reactions where the short reaction time prevents

decomposition [٦٧].

٣-٤-١ : Synthesis of ٣-*O*- allyl ١,٢: ٤,٥ Di-*O*- cyclohexylidene D-fructopyranose by using microwave technique [١٢٢] .

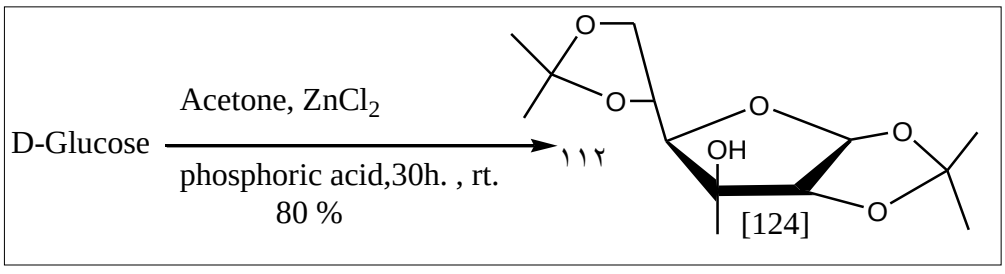
Using microwave (mw) technique in the reaction of [١٢١]and allyl alcohol in the presence of strong base (NaH), very short time gave good yields of products [١٢٢] in. ٦٨٪ yield .



٣-٤-٢ : Synthesis of ٣-*O*-allyl and ٣-*O*-propargyl ١,٢: ٥,٦ - Di-*O*- isoporpylidene - α -D-glucafuranose [١٢٥][١٢٦]

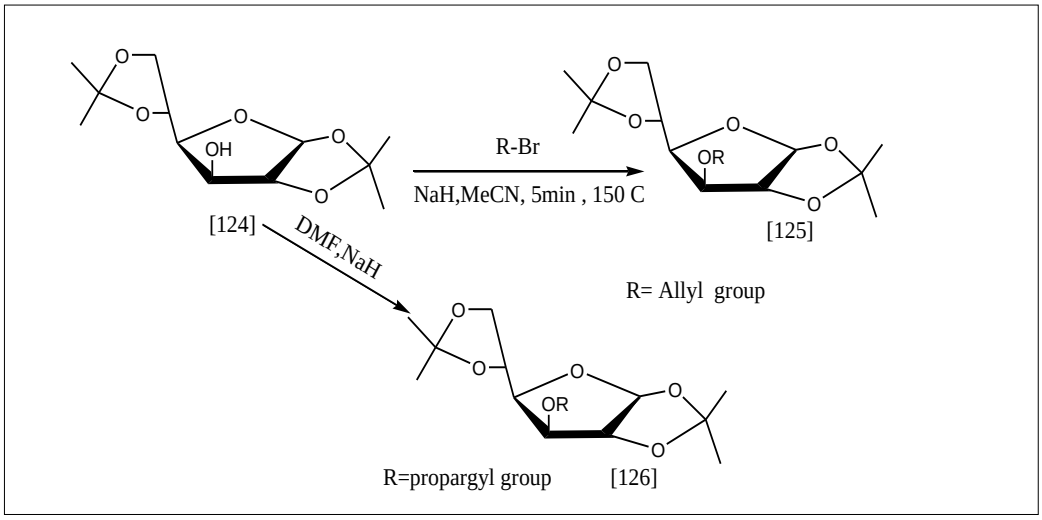
Acetonation (isopropylidennation) is the most widely used reaction for the initial step of carbohydrate derivates and many methods are known to accomplish this reaction [٢٠٢].

In order to obtain [١٢٥] and [١٢٦], D-glucose was first converted to ١,٢:٥,٦–di–*O*–isopropyliedene - α -D- glucofuranose[١٢٤] which was prepared in a similar manner method described in the literature (Ref . ١٧٥) . Treatment of D-glucose with acetone in the presence of $ZnCl_2$ gave [١٢٤] in ٨٠٪ yield after recrystalization from chloroform - hexane , m.p = ١٠٩ – ١١٠ ºC, Lit[١٧٥] :١٠٨-١٠٩ ºC .



IR spectrum showed stretching band at ٣٣٩٨ cm^{-1} for OH group and for isopropylidene group at ٢٧٠٠ –٢٩٠٠ cm^{-1} .Fig (٣-١٦)

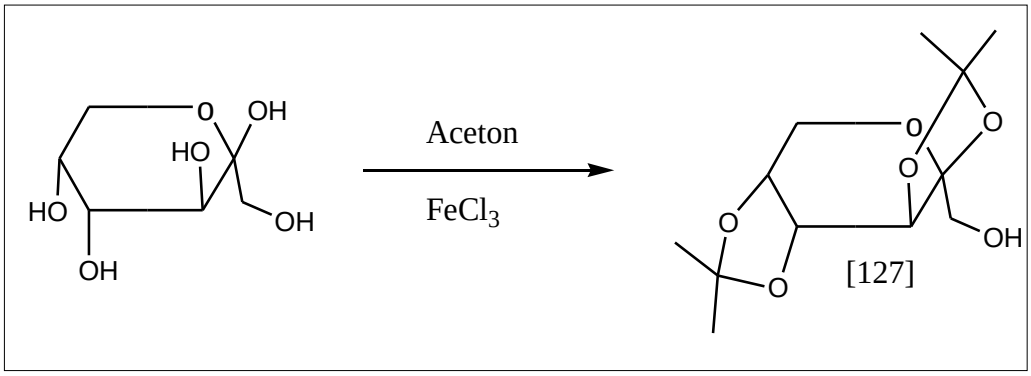
When [١٢٤] was reacted with allyl alcohol in presence of (NaH) in microwave oven , ١٥٠ºC , ٤٠٠ w , for ٥min it gave the corresponding ethers [١٢٥] (٨٠٪)yield . The IR spectra showed the stretching band at ١٦٥٠ cm^{-1} for $C=CH_2$, fig (٣-١٧) .
The derivative[١٢٤] was converted to [١٢٦] by reaction with propargyl bromide in presence of strong base(NaH)in dry DMF as solvent at rt for ٤٨ hr to produce the products as a brown syrup in ٩٠٪ yield .



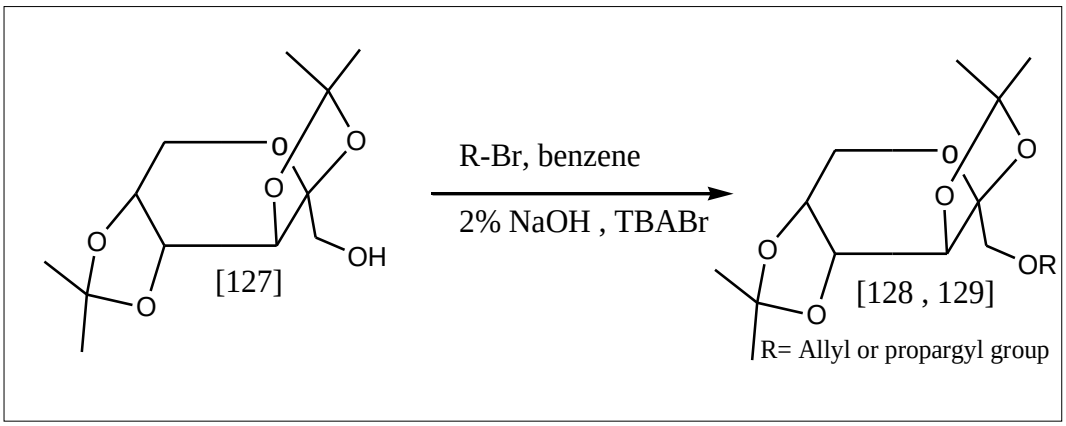
٣- ٥ : Synthesis of ١- allyl or propargyl ٢,٣:٤,٥ Di-*O*- isopropyliden

- D-fructopyranose [١٢٨] [١٢٩]

The strategy used for the synthesis [١٢٨]and [١٢٩] is by converting the D-fructose to ٢,٣:٤,٥-Di-*O*- isopropylidene -β–D- fructopyranose which was prepared from D-Fructose and acetone using anhydrous ferric chloride[١٩٩] as Lewis acid catalyst.



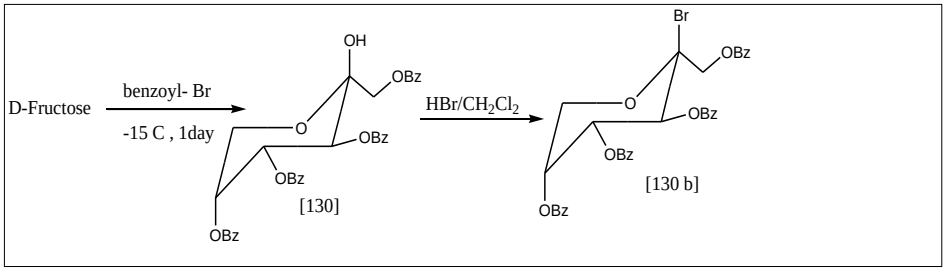
After that, the derivative [١٢٧] was converted to the ether derivates allyl or propargyl *O*-glycoside in a similar procedure which was used to prepare derivative [١٢٢]and [١٢٣] giving [١٢٨][١٢٩] in ٧٠٪ and ٦٥٪ yield respectively .The products characterized by IR spectrum which showed for derivative [١٢٨] a stretching band at ٢٧٠٠-٢٩٠٠ cm^{-1} for isopropylidene , ١٦١٦ cm^{-1} for $C=CH_2$, Fig (٣-٢٠) , and derivatives [١٢٩]showed stretching band at٣٠٥٥ cm^{-1} for C ≡ CH and ٢١٩٦ cm^{-1} for C ≡ C and, Fig (٣ - ٢١) .



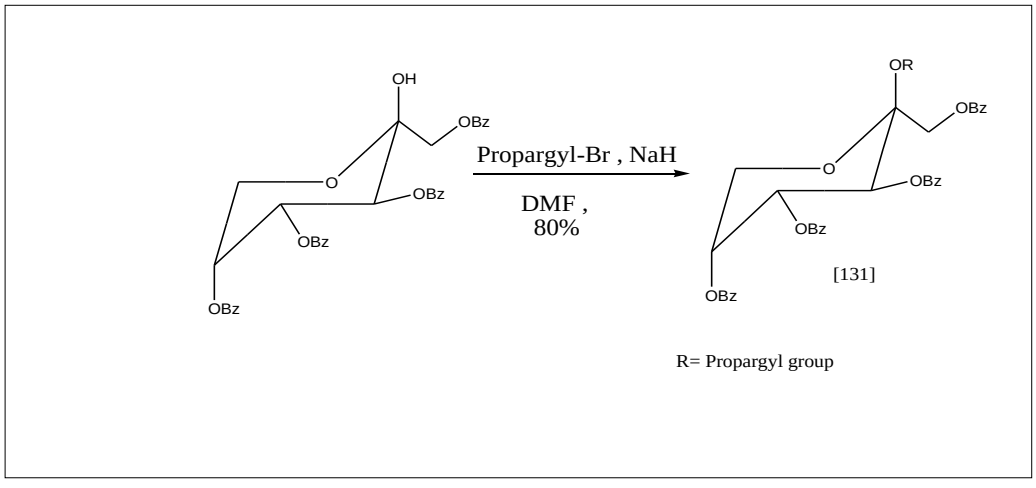
٣- ٥-١ Synthesis of ٢-*O*-propargyl tetra -*O*- benzoyl –*β*-D-fructopyranose . [١٣١]

To prepare derivative [١٣١], we need to convert the D-fructose to tetra–*O*-benzoyl - *β* -D-fructopyranose , the reason is to protect the hydroxyl group with a benzoate which is known to be stable toward acid conditions [٢٠٠]. ١,٣,٤,٥–Tetra–*O*- benzoyl – *β*-D- fructopyranose was obtained when D-fructose was treated with benzoyl bromide , using pyridine as a catalyst in carbon

tetrachloride at (-١٥ºC) for ٢٤ hr . This method was chosen[٢٠١] because it gives [١٣٠]in good yield (٦٠٪) and high purity after recrystlization from ethanol .



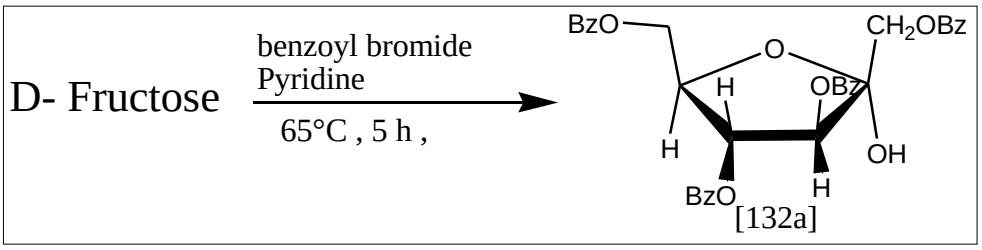
The derivative[١٣٠]was characterized by IR spectrum Fig(٣-٢٢) and elemental analysis .IR showed stretching band at ٣٤٣٢ cm^{-1} for hydroxyl, stretching band at ١٧٢٨ cm^{-1} for (C = O) of ester group and ١٦٠٢ cm^{-1} for the (C =C) aromatic bands . The derivative [١٣٠]was converted to [١٣١]by reaction with propargyl bromide in presence of strong base (NaH) in dry DMF solvent at ٠ºC .TLC indicated the disappearance of the starting material . The product was purified by silica-gel chromatography to give the product syrup in (٨٠ %) yield .



IR spectrum showed the disappearance of the band of hydroxyl group and showed the stretching band at for C ≡ CH and ٣٢٦٧ cm^{-1} ٢١٢٨ cm^{-1} for C ≡ C ,Fig (٣ – ٢٣) .

٣-٥-٢ Synthesis of ١-*O*-ally tetra–*O*-benzoyl-β-D-fructofuranoside

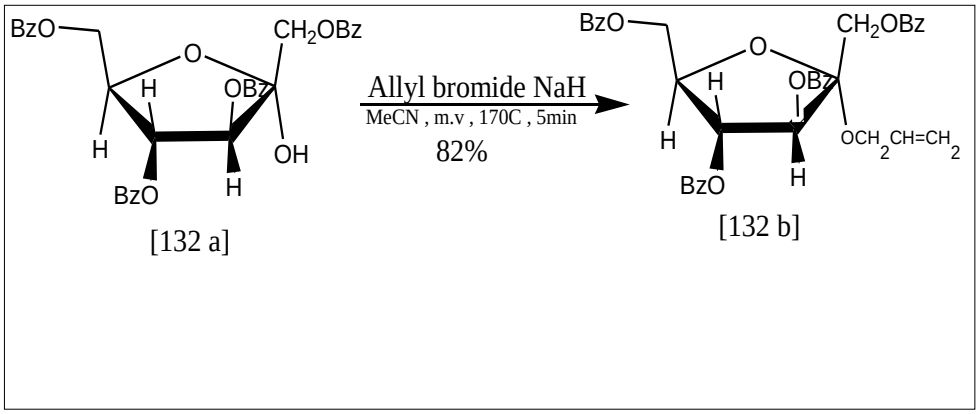
For the synthesis of derivatives [١٣٢b], D-fructose was first converted to ١,٣,٤,٦- tetra -*O*-benzoyl-β -D-fructofuranose [١٣٢a] , to leave the hydroxyl group at C-٢ free for the required chemical modification derivatives which was obtained when D-fructose was treated with benzoyl chloride, using pyridine as a catalyst .



[132a]

The product was characterized by its IR spectrum and elemental analysis . The IR spectrum showed a stretching band at ٣٤١٤ $cm^{-١}$ for

the OH group, ١٧٢٥ $cm^{-١}$ for C=O , and at ١٦٠٠ $cm^{-١}$ for aromatic C=C Fig(٣-٤٠b) . Allyl bromide and sodium hydride were added to a solution of ١,٣,٤,٦-tetra-benzoyl–β-D-fructofuranoside in MeCN and irradiation of the mixture by microwave oven for ٥min at ١٧٠°C gave product derivative [١٣٢b]in ٨٢٪ yield .



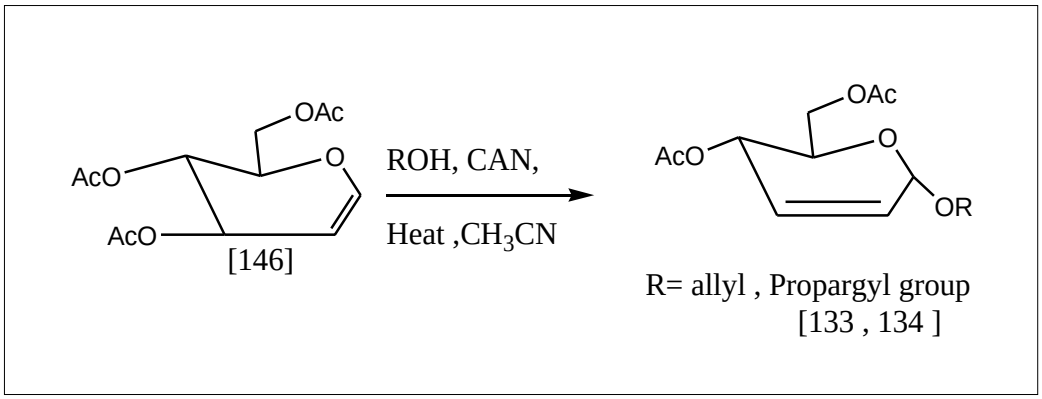
[132 a] [132 b]

The derivative [١٣٢b] was characterized by IR spectrum stretching band at ١٧٢٣ cm^{-1} for (C = O) , ١٦٠٢ cm^{-1} for (C = CH_2) ١١١٠ cm^{-1} for C– O –C . Fig (٣-٢٤) .

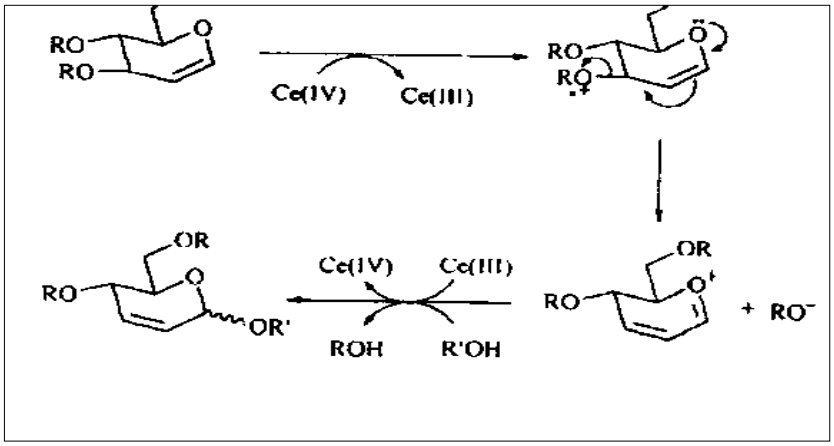
٣- ٦ : Glycosylation of glucal

٢, ٣- Unsaturated glycosides are versatile chiral building blocks in the synthesis of several natural products . Ferrier rearrangement was used to prepare glycoside from the glucal using a variety of Lewis acid reagents in the presence of alcohos[٢٠٣] such as ($BF_3.Et_2O$, $SnCl_4$, $AlCl_3$,$InCl_3$,$NbCl_5$) .

In this work Ceric(IV) ammonium nitrate (CAN) has been used , which is mild and efficient reagent for the glycosidation .



Treatment of ٣,٤,٦-tri-*O*-acetyl-D-glucal [١٤٦] with allyl and propargyl alcohol in the presence of ١٠ mol % ceric ammonium nitrate (CAN) in refluxing acetonitrile gave the corresponding *O*-allyl and *O*-propargyl ٢,٣- unsaturated glycoside in ٦٣٪ and ٧٤٪ respectively.The SN_2 mechanism of the reaction illustrated below[١٢٣] .



R= allyl , poropargyl , cinnamyl

scheme ٣-٢ Mechanism of glycosidation of glucal

Pure ٢,٣ - unsaturated glycoside was afforded by purifing in column chromatography on silica- gel (ethylacetate – petroleum ether ٢:٨)to produce the product [١٣٣]in ٧٤٪ yield , IR spectrum for compound[١٣٣] showed stretching band which were identical as described in (Ref ١٨٣,١٢٣) (٣٢٧٧, ٢٩٢٠ , ٢١١٨ ,١٧٤٠, ١٣٧٠ , ١٢٧٠ , ١٢٣٧ , ١٠٦٠ , ٩١٢ , ٧٣٣) cm^{-1} Fig (٣-٢٥) ,

And product [١٣٤] allyl derivative showed stretching band at (١٧٦٠, ١٦٥١ , ١٣٧٢ , ١٢٣١ , ١٠٤٤) cm^{-1} , Fig (٣-٢٦) .

٣- ٧ : Synthesis of azido – sugar derivatives

The second approach of this work was the construction of sugars –containing azido group at different positions of the sugar molecule .

Glycosyl azides are important derivatives in carbohydrate chemistry , so that several methods have been reported ; one important approach have been efficiently synthesized by Lewis acid catalyzed reaction . The detailed synthesis of azide glycosyl can be found below :-

٣- ٧-١ : Azidation of sulfonly sugar derivative

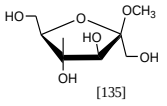
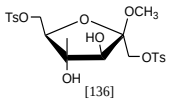
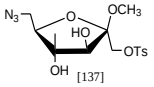
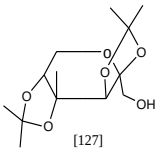
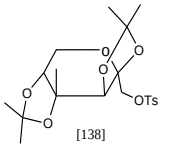
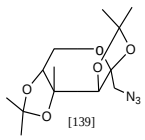
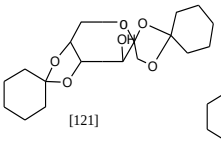
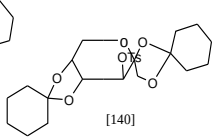
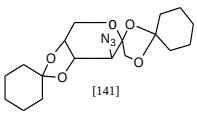
To synthesize the azido-sugars [١٣٧][١٣٩] [١٤١] ,

one strategy was the replacement of the hydroxyl group at different positions with azide group. This was a accomplished by converting it first to a good leaving group , such as the sulphonate ester , then its replacement via SN_2 displacement reaction with azide group .

Thus treatment of [١٣٥] [١٢٧] [١٢١] with *p*-toluene sulfonyl

chloride in pyridine at room temperature gave, after work up , the desired sulfonate esters [١٣٦] [١٣٨] [١٤٠] which were characterized by IR spectroscopy, CHN-analysis and some physical properties (table ٣-٢) . IR spectra show clearly the (SO_2) stretching band at (١١٧٥and ٩٨٠)cm^{-1} , and the disappearance of the hydroxyl stretching band at ٣٣٥٠cm^{-1} , Figures (٣- ٢٨),(٣-٣٠),(٣-٣٢).

Table(٣-٢) Conditions and some properties for preparation of azides derivatives

Entry	OH-Comp.	sulfonyl Comp.	azido Comp.	Time	Temp.C	IRcm^{-1} ($-N_3$)
1	 [135]	 [136]	 [137]	19hr	60	2100
2	 [127]	 [138]	 [139]	30 hr	140	2108
3	 [121]	 [140]	 [141]	24 hr	140	2100

The primary sulphonyloxy group is usually replaced by an azide ion in dipolar aportic solvent but the secondary sulfonate replacement needs more drastic conditions: high boiling aportic solvent and long reaction time .

The displacement of ١- sulfonate ester by (- N_3) ion is hindered for reason that this condition resemble a noepentyl type hindrance . Therefore, to increase the efficiency of a reaction Ali et al [٢٠٤] have used tetrabutyl ammonium bromide as catalyst to increase the polarity of the – $COSO_2$ bond .

The azido derivative [١٣٧][١٣٩][١٤١]were obtained in good yield and were characterized by IR spectroscopy . The spectrum clearly showed an (-N_3) stretching band at (٢١٠٠ -٢٢٠٠) cm^{-1} and disappearance of the (- SO_2) group stretching band ,Figures (٣-٢٩) (٣-٣١)(٣-٣٣).

٣-٧-٢ : Azidation of alcohols by one-pot method

We also used zinc azide in its more stable form bis-pyridine complex[٢٠٥]for the one-pot conversion of alcohol into azides. Treatment of derivatives [١٣٥][١٢١][١٢٤] with zinc azide bis-pyridine complex (١.٥ eq.) (prepared as described in reference [٩٩])

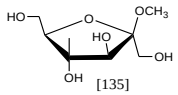
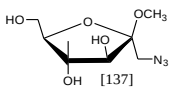
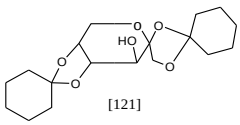
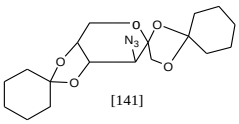
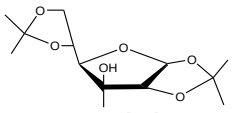
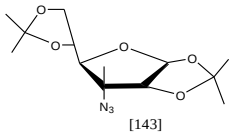
triphenyl phosphine (١.٥eq) and diisopropyl azodicarboxylat (DIAD)

(٢eq) in toluene or DMF smoothly afforded the corresponding azides [١٣٧] ١٤١][١٤٣] , table (٣-٣) .

These products were characterized by their IR spectrum and some physical properties which were identical with the literature .

The FT –IR spectrum clearly showed stretching band at ٢١٠٠ – ٢١٥٠ cm^{-1} for (-N_3) group

Table(٣-٣):Conditions and some properties for preparation azide derivatives

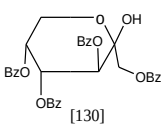
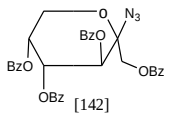
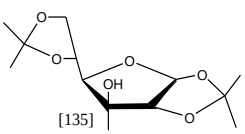
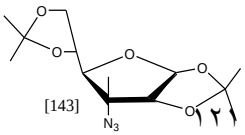
Entry	substrate	product	solvent	time	temp.	IRcm^{-1} ($-N_3$)
1	 [135]	 [137]	DMF	4h.	rt	2100
2	 [121]	 [141]	toluene	12h.	rt	2100
3	 [124]	 [143]	toluene	6h.	rt	2110

٣-٧-٣ Synthesis of some azido – sugar by using trifluoromethane sulfonic anhydride .

The azide - sugar [١٤٢] [١٤٣]were prepared from the hydroxyl sugar precursors using the method described by Sabesan[١٦٧] . Compounds [١٣٠] and [١٣٥]were dissolved in pyridine at ٠ºC . Tirfluoromethanesulfonic anhydride was added in drops under nitrogen atmosphere , after that the product of the first reaction was dissolved in anhydrous DMF and treated with sodium azide . The corresponding azides [١٤٢][١٤٣] were produced in good yields , which were characterized by IR spectroscopy .

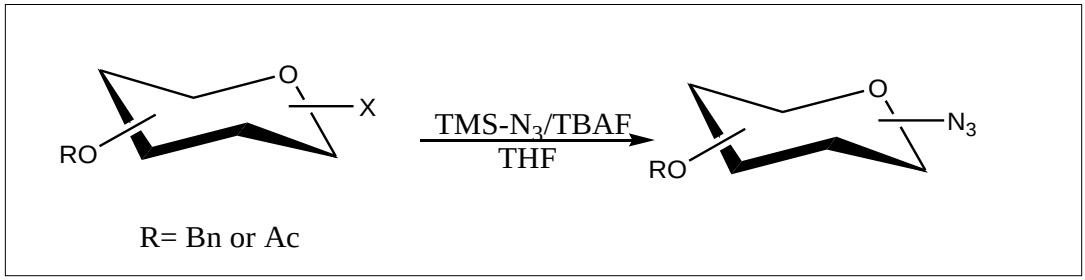
The FT-IR spectrum Fig (٣-٣٤) (٣-٣٥) clearly showed stretching band at (٢١٠٠-٢٢٠٠) cm $^{-١}$ for – $N_٣$ group and disappearance of stretching band of hydroxyl **g**roup **.**

Table (٣-٤) Condition and some properties for preparation of azide derivatives

Entry	substrat	product	solvent	time	temp C	IRcm^{-1} ($-N_3$)
1	 [130]	 [142]	DMF	42h	rt	2129
2	 [135]	 [143]	DMF	24h	rt	2110

٣-٧-٤ Synthesis of azido – sugar by using trimethylsily azide

The general transformation for azide displacement is outlined as below and involved nucleophic displacement of bromide , chloride , triflate , tosylate and trichloromidate (X) .



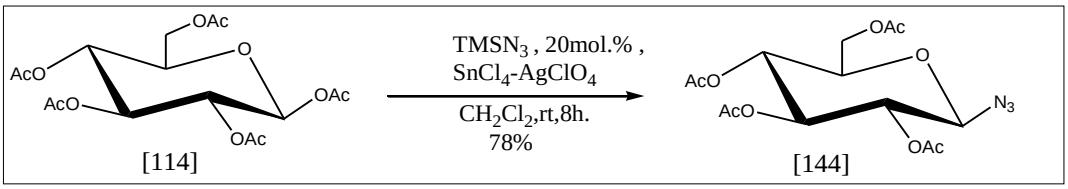
Several Lewis acid catalysts were screened by taking a reaction of ١,٢,٣,٤,٦-penta-*O*-acetyl- β-D-glucopyranose with trimethylsilyl azide TMS-N_3 (which prepared as reports in reference (٢٠٦).

K K.Matsubara and co- workers[٢٠٧,٢٠٨] found that the best result was obtained when the catalyst generated in situ from $SnCl_4$ and $AgClO_4$ was employed .The glycosyl donors with TMS-N_3 using the Sn(IV)catalyst having perchlorate anion a catalytic cycle is more efficiently made up to afford the desired glycosyl azide in nearly quantitative yield . Glycosyl azide was obtained in good yield when dichloromethane was used . This method was successfully carried out just starting from ١-*O*-acetyl -sugars without necessity of converting the sugars into glycosyl halides .

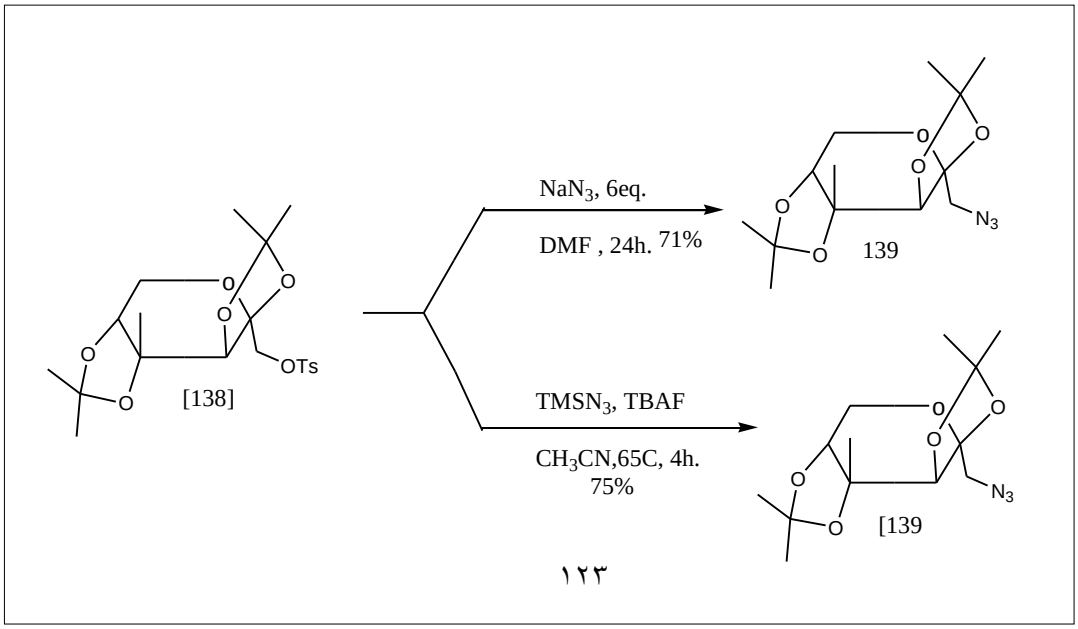
Reaction of ١,٢,٣,٤,٦-penta acetyl- β-D-glucopyranose with TMS-N_3 in presence of mixture of $SnCl_4$ (٠.٠١mmol) in toluene and suspension of $AgClO_4$ (٠.٠ ١ mmol) in CH_2Cl_2 at room temperature .After stirring the mixture for ٢٠ hrs, usual work up and the product separation by column

chromatography on silica gel afforded the desired glycosy azide [١٤٤] in ٧٨٪ yield m.p=١١٦-١١٨ºC .

The product is characterized by its IR spectrum and m.p which was identical with the literature[٢٠٧] .The IR showed stretching band at ٢١٢٠ cm^{-1} for ($-N_3$) Fig (٣-٣٦) .



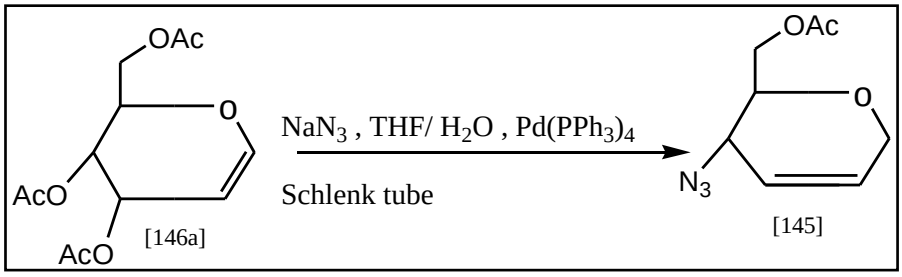
To prepare ١-azido-١-deoxy ٢,٣:٤,٥-di-*O*-isopropylidene-β-D-fructopyranose [١٣٨,١٣٩] we noticed that when using the typical azido displacement conditions were required (٢٤hr.) and (٦eq.) of sodium azide in warm DMF , but when tosylate derivative [١٣٨] was treated with TMS-N_3 / TBAT the displacement proceeds in good improved yield and short reaction time [٩٠] (٤h) .



٣-٧-٥ : Synthe

sis of glucal azide

The azidation of ٣,٤,٦ – tri-acetyl glucal[١٤٦a] was first examined by using $Pd(PPh_3)_4$ (prepared as describe in Ref ٢٠٩)as the catalyst and sodium azide as the nucleophile, the reaction being preformed in a THF/H_2O mixture at ٥٠ºC, the azidation occurred in ٦٢٪ yield from derivative ٦-O-acetyl-٤-azido-٢,٣,٤-tri-deoxy-D-erythro-hex-٢-ene-pyranoside[١٤٥] .



The IR spectrum clearly showed Fig(٣-٣٧) stretching band at ٢١٠٦

cm^{-1} for (N_3) and ١٧٦٠ cm^{-1} for C=O of acetyl group.

٣-٨ : Synthesis of unsaturated sugars

The double bond can be introduced by dehydration of monosaccharide to give the so-called unsaturated sugars .Those unsaturated sugars have different structures from the well-known vinyl sugar monomers .
E.Fischer [١١٣] reported the preparation of glycal by reduction of the per -*O*-acetyl glycopyranosyl halides using zinc dust and acetic acid to the corresponding acetylated glycals .

Glycal when prepared from glycosyl halide can give products in good yield and in high purity without the need for purification and

has been applied to different sugars protected with a variety of esters .

٣-٨-١ : Synthesis of ٣,٤,٦- triacetyl glucal

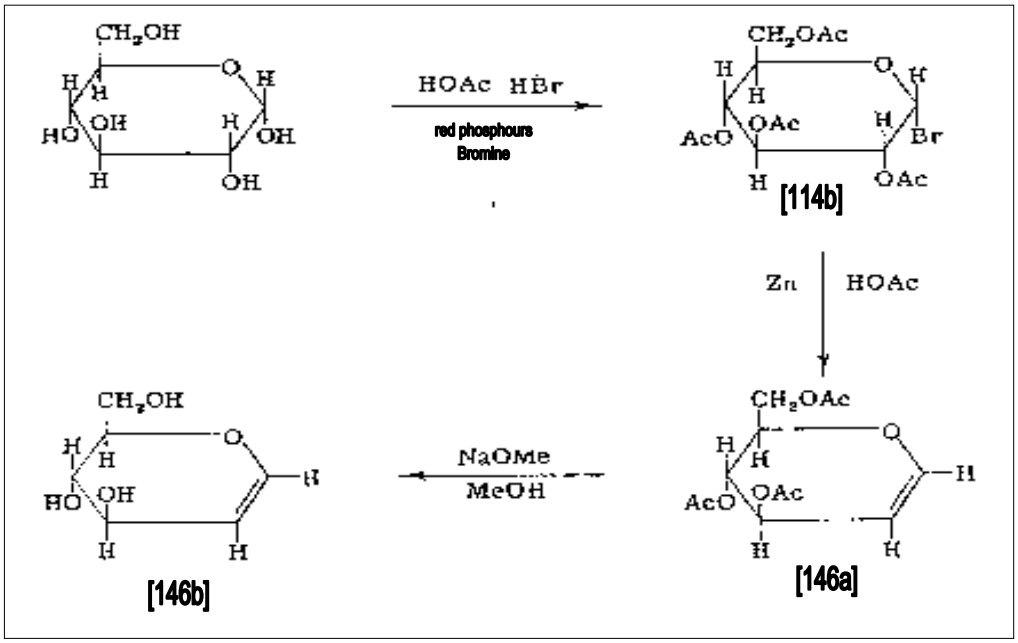
The best studied of the glycals is the tri-acetyl-D-glucal [١٤٦a]derived from D-glucose . The strategy used for the synthesis of glucal [١٤٦a]was started with D-glucose in a series of reaction shown in (scheme ٣-٣) .

In order to obtain the targeted compound ١,٢,٣,٤,٥-penta-*O*- acetyl -β-D-glucopyranose [١١٤] was prepared from D-glucose (as describe in page٥٣) The second reaction sequence was the bromination of [١١٤] with red phosphorus and bromine for ٤hrs at room temperature after filtration ,the filtrate contains tetra-*O*-acetylα-D-gucopyranosyl bromide[١١٤b] .

W.Lichtenthaler [١٨٢] preferred to use the HBr/CH_2Cl_2 in place of HBr/HOAc since acetic acid was extremely difficult to remove and severely interferes with ensuing reaction by concomitant formation at the anomerric acetate [٢٩٨, ٩٦]

The final step was a reductive elimination of the derivative [١١٤b]

with zinc dust to afforded the *endo*-glucal [١٤٦a]. By different trying with the aid of seeding the residual syrup crystallizes. By recrystallization from petroleum ether and ether, the pure compound can be produced yield is ٦٠٪ . m.p ٥٥-٥٦ ºC, lit[١٠٩] : ٥٤-٥٥ ºC



Scheme (٣-٣) Preparation of tri-acetyl glucal

The ٣,٤,٦-tri acetyl –glucal could be converted easily to glucal [١٤٦b] by deactylation process with a methanolic solution containing catalytic amounts of sodium.

The ٣,٤,٦-tri-*O*-acetyl glucal was characterized by IR spectrum and m.p which was identical with the literatures . The FT .IR spectrum Fig(٣-٣٨) showed band at ١٧٤٠ cm^{-1} for (C=O) .

And for glucal [١٤٦b] , band of OH group appeared clearly at ٣٤٧٥cm^{-1} Fig (٣-٣٩) .

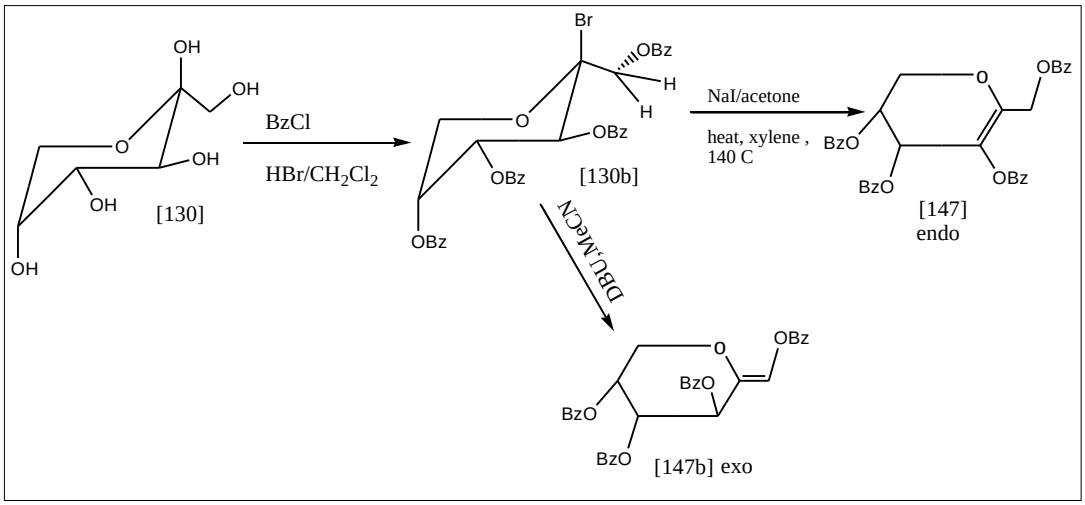
٣-٨-٢- Synthesis of *endo*-fructal

A proper substrate to study the reductive elimination was tetra-*O*-benzoyl- β-D-fructopyronosyl bromide [١٣٠ b] readily accessible from D-fructose by benzoylation to the tetrabenzoate [١٣٠] subsequent treatment with HBr / CH_2Cl_2 .

The primary ١-*O*-Bz is more readily expelled than the secondary ٣-*O*-Bz the leaving group capacity of the latter had to be increased to direct the displacement reaction towards *endo*-position .

The practical protocols have been developed to a stirred solution of fructosyl bromide [١٣٠b] in anhydrous acetone and sodium iodide. The syrup was taken up in boiling xylene (١٤٠ºC) for ٢hr. to produce sugar consisting of three compounds [١٣٠b] [١٤٧][١٤٧b]

Separation was effected on a silica gel column by elution with toluene : EtOAc (١٠: ١) to yield *endo*-hydroxy fructal ester [١٤٧] as an syrup , ٣٣٪ yield which was characterized by IR spectrum, CHN – analyses ,m.p and some other physical properties which was identical with literature , table (٣-٧)



The IR spectrum showed stretching band at ١٧٥٠ cm^{-1} for (C=O) ,١٦٢٠ cm^{-1} for (C=C) aromatic Fig (٣-٤٠) .

٣-٩ : Triazole linked carbohydrates

The main aim of this research is the bonding between the saccharide groups via a triazole group and may be found different methods for their preparation. Further disclosed was the use of their compounds as potential enzyme inhibitors , and acetylenic intermediate compound [١٦٧] .

Azido and alkyne are easy to introduce into organic compounds by both nucleophilic and electrophillic processes , and the cyloaddition reaction of azides and alkynes or alkenes are thermodynamically favorable [١٦٤] .

The ١,٣ –DC reaction of the parent ١,٣-dipoles , with alkenes , and alkynes involves ٤ π electron from the dipole and ٢ π electrons from the alkene or alkyne . If the ١,٣-DC reaction proceeds via a concerted mechanism it is thermally allowed with the description ($\pi_4 s + \pi_2 s$) according to the Wood ward – Hoffman rules[١٣٣]

Our objective was to prepare the triazole and triazoline under different conditions [١٢٧] .

The compounds of the present work are expected to be synthesized by more general methods .

٣-٩-١ Thermal reaction

The first approach was the use of thermal coupling reaction of allyl ether derivatives or propargyl ether derivatives [١٣٣] [١١٥][١٢٦][١٤٦a] with azido sugar derivatives [١٣٧] [١٣٧][١٤٤][١٤١] .

The standard condation for the construction of the triazole ring involves refluxing the two components in an organic solvent (often toluene) to afford compounds [cop١] [cop٢][cop٧][cop١٠]respectively for four compounds , in low yield and as expected as a mixture of regioisomers (١,٤ and ١,٥ –regioisomers) .

٣-٩-٢ Microwave reaction in presence of Copper – catalyzed reaction

A major advance has recently been achieved parallel to investigations through the use of copper – catalyzed reaction . This only yielded a slow conversion to the monocoupled products . A number of copper(I) sources can be used directly ,and found that the catalyst is better prepared in situ by reduction of Cu(II) salts , which are less costly and often pure than Cu(I) salt [٢١١] ($CuSO_{٤}.^{٥}H_{٢}O$ serves well)[٢١٢] . As the reductant , ascorbic acid or sodium ascorbate proved to be excellent[٢١٣] .The ١,٤-triazole products were obtained in high yields and high purity at ٠.٢٥ – ٢ mol catalyst loading . The use of an excess (١-٥ equiv) of the azido carbohydrate drove the reaction to completion while the excess could be readily recovered by column chromatography[٢١٤] .

The use of the microwave irradiation significantly reduced the time of the reaction . As the starting point of our exploration , we chose the reaction between allyl or propargyl sugars [١١٥] [١٢٨] [١٢٩] [١١٧][١٢٦][١١٦][١٢٠] and azides sugars [١٤٤] [١٣٩] [١٣٩][١٣٧][١٤٤] [١٤٤][١٣٩] to produce the coupling reaction [cop٣][cop٤] [cop٥] [cop٦] [cop٧][cop٨][cop١٣] respectively for seven compounds .

٣-٩-٣ : Sealed tube reaction

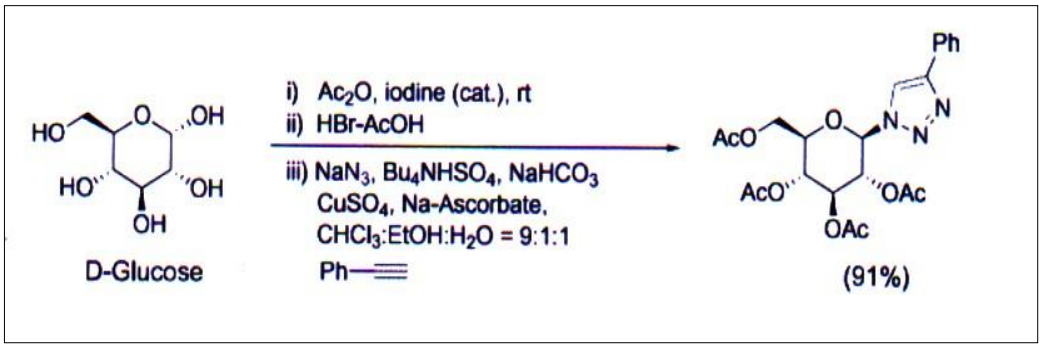
we have found that glucals with electron-withdrawing protecting groups undergo efficient cycloaddition with glycosyl azides . Tri-*O*-acetyl-D-glucal [١٤٦a] readily engage in ١,٣-DC with glycosyl azides [١٣٩] [١٤١] at elevated temperature (١٢٠ ºC) ,to produce [cop٩][cop١٠][cop١١] , the reaction is carried out in solvent of high boiling point like triethylorthoformate because the unstable triazoline intermediate can be isolated in good yield with little or no purification . In all other solvents the triazoline undergoes elimination to afford the corresponding triazole[٢١٥].

In smilar procedure *endo*-Fructal [١٤٧] react with azide sugar [١٤٤]to produced [cop١٤], in presence of CuBr.(Ph_3P) as catalyst .

In the other hand we used schlenk tube to make ١,٣ DC for allyl or propargyl ethers [١٤٦a] [١٣٣] [١٤٧] and glysoyl azied [١٤٤] [١٤٥] [١٤٥] in presence of CuBr.(Ph_3P) as a copper catalyst to produce the coupling products [cop١١] [cop١٢][cop١٦] respectively for three compounds .

٣-٩-٤ :The One –Pot reaction

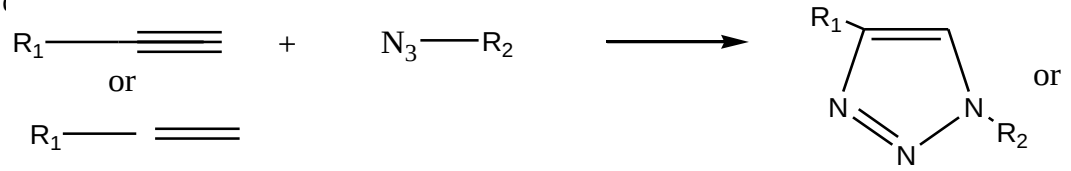
As shown below , unprotected D-glucose was acetylated with acetic anhydride as catalyzed with trace amount of iodine , followed by brominolysis of the anomeric acetate . After removal of all volatiles a subsequent azide conversion and in situ Cu (١) catalyzed ١,٣-dipolar fusion reaction with allyl sugars , to link the two carbohydrates and only ١,٣-triazoles were produced , the isolated yield was [٢١٦] ٩١ %

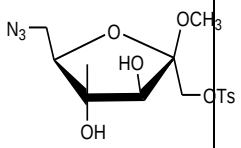
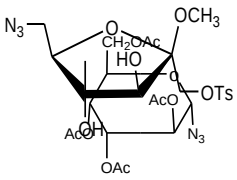
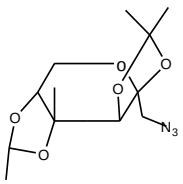


Saccharide acetate can also be used as substrates for this reaction . As shown in Table (٣-١١) , the acetate of D-glucose has been employed as starting materials , with a similar brominolysis procedure followed by the in situ generation of glycosylazide and ١,٣-dipolar cycloaddition, triazolyl glyconjugates were synthesized when the *O*-propargyl D-fructopyranoside [١١٨] react with azide acetate [١٤٤] to produce [cop١٥] in satisfactory yield (٨١٪) .

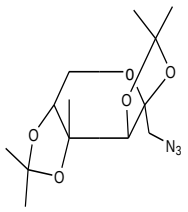
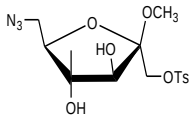
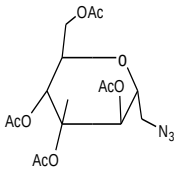
Table (٣-٥)(٣-٦) showed clearly some properties and spectral data for the products .The IR spectra are shown in Fig (٣-٥٣) to Fig (٣-٦٨) and H-NMR spectra are reproduced in Fig (٣-٦٩) to Fig (٣-٧٦). Due to the efficient transformation of the reaction it can also be used in synthesis of polyvalent glycomolecules such as [illegible].[٢١]

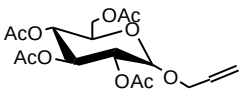
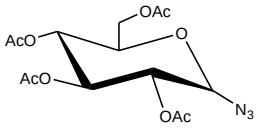
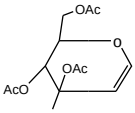
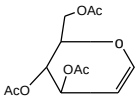
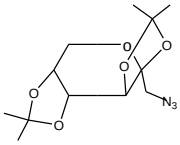
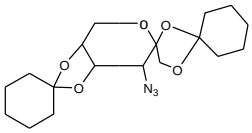
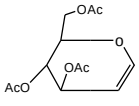
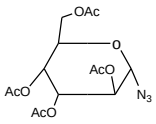
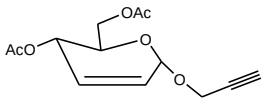
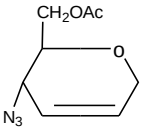
Table (3-5) Conditions for preparation of triazole and triazoli



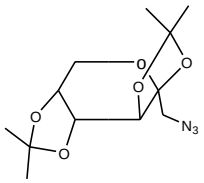
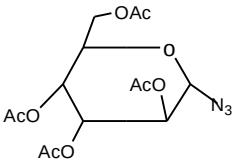
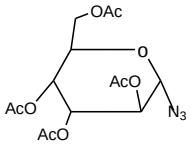
	R٢	Product	Conditions	Time (h/min)	Yield %
		Cop١	**Thermal condition** **Dioxane , ٦٠°C**	١٩٢	٦٠
		Cop٢	Schlenk tube Trimethylortho formate , ١٢٠ °C	٥٦	٨٢
		Cop٣	m.w,DBU, (Ph٣P)٣. CuBr	٧٠	٨٢
H=CH2				٩٠	٨٢

		Cop٤	M.W, toluene $CuBr.(Ph_3P)_3$ ١٢٠ °C		
	R^2	**Product**	**Conditions**	**Time (h/min)**	**Yield %**

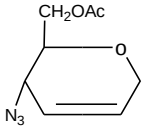
entry	R^1	R^2	Product	Conditio`ns	
		Cop٥	M.W , toluene ,CuBr.$(PPh_3)_3$,١٢٥°C	٦٠	٨٦
		Cop٦	M.W , toluene ,CuBr.$(PPh_3)_3$,١٢٥°C	٨٠	٧٦
		Cop٧	١-Thermal methode ,tolune,١١٠C°	١٢٠	٧٠
			٢. in prsence of $CuBr(PPh_3$	٨٠	٧٢
			٣-Microwave, ٨٠°C, ١٠٠W, DMF, $CuBr(PPh_3)_3$	٢	٨٢

٨			Cop٨	M.W. DBU,CuBr $(PPh_3)_3$ toluene , ١٢٥°C .
٩			Cop٩	seald tube trimethylortho formte,١٢٠°C
١٠		 	Cop١٠	seald tube trimethylortho formed,١٢٠°C ١.Schlenk tube tirmethlortho fromate ٢.$CuBr(PPh_3)_3$
١١			Cop١١	
١٢			Cop١٢	Schlenk tube trimethylortho formte ١٢٠°C $CuBr(PPh_3)_3$

	R^{2}	Product	Conditions	Time (h/min)	Yield %

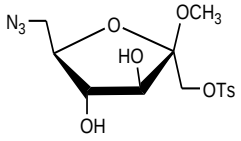
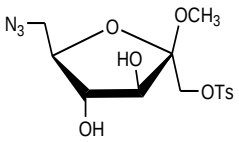
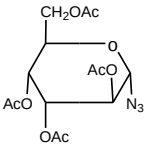
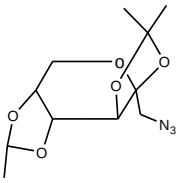
	Cop١٣	Microwave DBU,CuBr $(PPh_3)_3$ ١٢٥°C DMF solvent	١.١٠	٨٦
	Cop١٤	Schleuk tube trimethylorthe formate $CuBr(PPh_3)_3$	٦٠	٦٥
	Cop١٥	One - pot syn١hesis ١.$HBr.CH_2Cl_2$ ٢.NaN_3,$BuNHSO_4$ $NaHCO_3$ ٣.CuS,O_4 Na-ascorbate ٤.CH_3Cl:EtOH,rt	٣٦	٨١

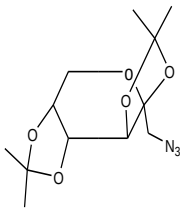
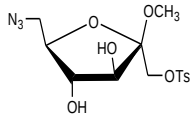
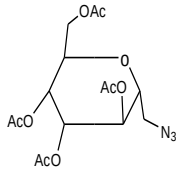
	R^2	Product	Conditions	Time (h/min)	Yield %

	Cop١٦	Schlenk tube trimethyl ortho formate $CuBr.(PPh_3)_3$	٩٦	٦٠	

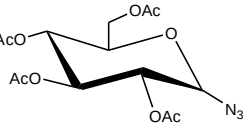
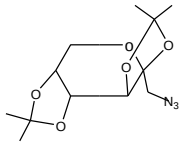
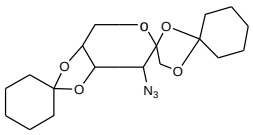
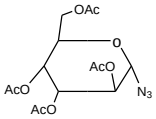
Tabel (3-6) IR & H1-MNR Spectra data for triazole

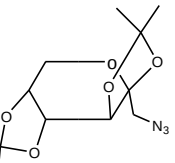
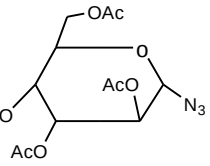
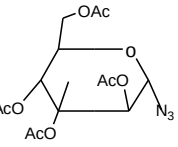
	R^2	Remarks of IR, cm^{-1}	Remarks of NMR

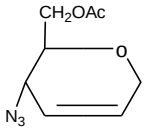
	R^2	Remarks of IR, cm^{-1}	Remarks of NMR
		Clearly disappearance of $-N_3$ band at (٢١٠٠ –٢٢٠٠) cm^{-1} ,٣٥٣٠ cm^{-1} OH group , ١٠٩٤ cm^{-1} (C-O-C)	σ = ٧.٢ (H of trizole ring) ٥.٥١ (H, CH_2 = CH) , ٤.٢ (٢H, mathylene) ٣.٨ –٣.٦ (H of the ring) ٢.٣ (H,CH_3) , ١.٦ (H , ring)
			
		Clearly disappearance of $-N_3$ band at (٢١٠٠ –٢٢٠٠) cm^{-1} ,٣٥٢٨ cm^{-1} OH	σ = ٧.٢ (H of trizole ring) , ٥.٢ –٥.٦ (H of the ring) ٤.٤ –٤.١ (٢H mathylene) , ٢.٠١ (١٢H , ٤ CH_3CO , ١.٦ ٢H, CH_2OSO_2
		Clearly disappearance of $-N_3$ band at (٢١٠٠ –٢٢٠٠) cm^{-1} , ١٧٥٤ cm^{-1}	σ = ٦.٤ (IH , H-٥) , ٥.٦ - ٥.٤ (٦H) , ٤.٨٨ (١H) ٤.٦٤ (٢H, CH_2N) , ٣.٩١ (OCH_2CH_2N) ٢.٢-١.٩٧ (٢٤H,٨CH_3CO)
		Clearly disappearance of $-N_3$ band at (٢١٠٠ –٢٢٠٠) cm^{-1} ٢٩٦٦ cm^{-1} ٢٩٦٦ cm^{-1} isopropylidene	σ = ٧.٨ –٧.٥ (H , trizole ring), ٤.٢ (H , ring) ١.٤ – ١.١ (٢٤ H , ٦ CH_3 of isopropylidene) ٢.٢ (٢H of methylene)

≡CH		Clearly disappearance of $-N_3$ band at(٢١٠٠ –٢٢٠٠) cm^{-1} ٢٩٧٩ cm^{-1} isopropylidene	σ = ٧.٨- ٧.٢ (H , triazole ring) , ٤.٢-٣.٧ (H,ring) ٢.٢(١H methylene) , ١.٥-١.١ (١٢H, ٤ isopropylidene)
=CH_2			
		Clearly disappearance of $-N_3$ band at(٢١٠٠ –٢٢٠٠) cm^{-1} ،٣٤١٨ cm^{-1} (OH) , ١٠٤٠ cm^{-1} (C-O-C)	σ = ٧.٣(٥H, aromatic ring) , ٧.٢(H, trizole ring) ٤.٢ (H, OH , sugar ring) , ٣.٨ –٣.٠١ (٢H , methylene) ٢.١ (٣H, OCH_3)
		Clearly disappearance of $-N_3$ band at(٢١٠٠ –٢٢٠٠) cm^{-1} ٢٩٦٥ cm^{-1} isopropylidene, ١٧٥٠ cm^{-1} acetate	σ = ٧.٢ (H , trizole ring) , ٣.٨ (H , proton sugar) ٢.٢ (١٢H , ٤CH_3CO) , ١.٤ (١٢ H of ٢ isopropylidene)

R^2	Remarks of IR, cm^{-1}	Remarks of NMR

R٢	Remarks of IR, cm -١	Remarks of NMR
	Clearly disappearance of –N٣ band at (٢١٠٠ –٢٢٠٠) cm −١ ١٧٥٠ cm −١ acetate	σ =٥.٢-٤.٢(H, proton ring) , ٢.٢ (٢H, ٢ methylene group , ١.٨-٢.٢ (٢٤H for ٨ CH_3O)
	Clearly disappearance of –N٣ band at (٢١٠٠ –٢٢٠٠) cm −١ ١٧٤٠ cm −١ Acetate	
	Clearly disappearance of –N٣ band at (٢١٠٠ –٢٢٠٠) cm −١ ١٧٤١ cm −١ acetate	
	Clearly disappearance of –N٣ band at (٢١٠٠ –٢٢٠٠) cm −١ ١٧٤٨ cm −١ acetate	
	Clearly disappearance of –N٣ band at (٢١٠٠ –٢٢٠٠) cm −١ ١٧٤٨ cm −١ acetate, ١٦٥٢ cm −١ (C=C)	

	Clearly disappearance of $-N_3$ band at ($2100-2200$) cm^{-1} 3494 cm^{-1} (OH) 2931 cm^{-1} isopropylidene	
	Clearly disappearance of $-N_3$ band at ($2100-2200$) cm^{-1} 1750 cm^{-1} (C=O) 3056 (C=C) aromatic	
	Clearly disappearance of $-N_3$ band at ($2100-2200$) cm^{-1} 1755 cm^{-1} acetate	

R^{2}	Remarks of IR, cm^{-1}	Remarks of NMR
	Clearly disappearance of $-N_3$ band at ($2100-2200$) cm^{-1} 3425 cm^{-1} (OH)	

Conclusions

1-The applied of microwave irradiation to conventional Fischer glycosylation resulting in an impressive acceleration of reaction time with good - α . glycoside .

٢- The reaction of allylation of sugars are not recommended to be carried out in a multimode domestic microwave oven due to uniform irradiation and temperature control and the reactions are run in a closed vessel .

3- With light- yielding wear synthesis of glycosyl azides was successfully carried out star from 1-O-zcetyl sugar and trimethylsilyl azide using a catalyst generated from $SnCl_4$ and $AgClO_4$ without converting the sugars into glycosyl halides .

4- It was found that the HBr saturated in dichloromethane not HBr saturated in acetic acid because the ;latter contains some mol of acetic acid which is extremely difficult to remove .

5- In acid glycosylation of unprotected sugars we can use the cation exchange resin (H^+) to give clear products and higher yields .

6- We have introduced a convenient and general method for preparation of substituted triazoles and triazolines sugars derivatives by 1,3-dipolarcycloaddittion of a variety of organic azides with olefenic or acetylenic sugars under thermal or microwave reaction-conditions .

7- It has been established that the construction of Triazoyldissacharied by using 1,3-DC reaction when using the copper complexes CuBr. $(Ph_3P)_3$ as organic soluble catalyst .

8-The one-pot procedure does not require isolation of the azide intermediate and should prove to be especially useful when unstable low-molecular weight and polyvalent azides are needed .

9- The preparation compounds are expected to be more stable to enzymatic and chemical hydrolysis .

10- Microwave – heating has been shown to be most useful method in organic synthesis because the short reaction time prevents decomposition .

11-Endo-glycale were applied for the stereoselective alcohol additions to afford unsaturated glycosides .

Future Studies :

The future studies , if any , had better comprise three main axes :-

١- Synthesis of multivalent alkynes or alkenes sugars and multivalent azides sugars to prepare a triazole glycodendrimers or heterodimers .

٢-Studying the thermal and photochemical reactivity of these compounds.

٣- Studying the biological activity of the new prepared products .

Appendixes

Table (٣-٧) Some Physical properties for the allyl and propargyl sugars

No.	Number of compound	Name of Compound	State of Compound	Percentage % yield	molecular formula	The C.H.N analysis		
						C %	H %	N %

١	١١٤	١,٢, ٣,٤, ٦ -penta-*O*-acetyl-*β*-D-glucopyranose	Solid mp= ١٣٠-١٣١ºC	٦٠٪	$C_{١٦}H_{٢٢}O_{١١}$			
٢	١١٥	١-*O*-propargyl ٢,٣,٤,٦-tetra-*O*-acetyl- *β* -D-glucopyranoside	Solid ١١٥-١١٧ºC	٥٧٪	$C_{١٧}H_{٢٢}O_{١٠}$	٥٢.٨٤ ٥٣.٠٠	٥.٦٩ ٤.٩٨	
٣	١١٦	١-*O*-allyl٢,٣,٤,٦-tetra-*O*-acetyl - *β* -D-glucopyranoside	Syrup	٦٠٪	$C_{١٧}H_{٢٤}O_{١٠}$	٥٢.٥٧ ٥١.٥٦	٦.١٨ ٦.١٧	
٤	١١٧	*O*-allyl – D-fructofurnoside	Syrup	٨٠٪	$C_{٩}H_{١٦}O_{٦}$	٤٩.٠٩ ٤٩.٠٠	٧.٢٧ ٧.٠١	
٥	١١٨	*O*-allyl-D-fructopyranoside	Syrup	٧٤٪	$C_{٩}H_{١٦}O_{٦}$			

No.	Number of compound	Name of Compound	State of Compound	Percentage % yield

٦	١١٩	*O*-propargyl-D- fructopyranosid	Syrup	٦٩٪
٧	١٢٠	*O*-propargyl-D-glucopyranoside	Syrup	٧٠٪
٨	١٢١	١,٢:٤,٥ – Di – *O*-cylohexylidene –D-fructopyranose	Solid m.p=١٤٣ – ٤٤ºC	٧١٪
٩	١٢٢	٣-*O*-allyl ١,٢:٤,٥-Di-*O*-cyclohexylidene – D-fructopyranose	Syrup	٦٢٪
١٠	١٢٣	٣-*O*- propargyl ١,٢:٤,٥-Di-*O*-cyclohexylidene –D-fructopyranose	Syrup	٦٤ %
١١	١٢٤	١,٢:٥,٦- Di-*O*- isopropylidene - α -D-glucofuranose	Solid m.p=١٠٩-١١٠ ºC	٨٠ %

No.	Number of compound	Name of Compound	State of Compound	Percent yield%
١٢	١٢٥	٣-*O*-allyl-١,٢:٥,٦-di-*O*-isopopylidene - *α* -D- glucofuranose .	Syrup	٦٠٪
١٣	١٢٦	٣- *O*-propargyl-١,٢:٥,٦-di-*O*-isopopylidene - *α* -D-glucofuranose	Syrup	٩٠٪

١٤	١٢٧	٢,٣:٤,٥-di-*O*-isopropylidene - *β* -D-fructopyranos	Solid m.p=٩٤ - ٩٥ºC	٦٠٪
١٥	١٢٨	١-*O*- allyl ٢,٣:٤,٥-di-*O*-isopopylidene - *β* -D- fructopyranose	Syrup	٧٠٪
١٦	١٢٩	١-*O*- propargyl ٢,٣:٤,٥-di-*O*-isopopylidene - *β* -D- fructopyranose	Syrup	٦٥ %
١٧	١٣٠	١,٢,٤,٥-tetra –*O*-benzoyl-*β*-D-fructopyranose	Solid m.p. = ١٧٣ - ١٧٤ºC	٦٠ %

No.	Number of compound	Name of Compound	State of Compound	Percentage % Yield
١٨	١٣١	٢- *O*-propargyl ١,٢,٤,٥- tetra-*O*-benzoyl-*β* -D-fructopyranoside	Syrup	٨٠٪
١٩	١٣٢a	١,٣,٤,٦- tetra-*O*-benzoyl-*B*-D-fructofuranose	Solid m.p=١٢٢-١٢٣ºC	٧٧٪
٢٠	١٣٢b	٢- *O*-allyl tetra-*O*-benzoyl-*B*-D-fructofuranoside	Syrup	٨٢٪
٢١	١٣٣	١- *O*- propargyl-٤,٦-di- *O*-acetyl glucal	Syrup	٧٤٪

٢٢	١٣٤	١- *O*- alyll-٤,٦-di- *O*-acetyl glucal	Syrup	٦٣٪

Table (٣-٨) Some Physical properties for azido sugars

No.	Number of compound	Name of Compound	State of Compound	Percentage %	molecular formula	The C.H.N analysis		
						C %	H %	N %
١	١٣٥	Methyl-D-fructofuranosid	Syrup	٩٢٪	$C_{٧}H_{١٤}O_{٦}$			
٢	١٣٦	Methyl ١, ٦ –di –*O*-*p*-toluene sulfonyl-D-fructofuranoside .	Syrup	٧٢٪	$C_{٩}H_{١٨}O_{١٠}S_{٢}$			
٣	١٣٧	Methyl-٦-deoxy –٦-azido –١-*O*-b toluene sulfonyl-D-fructofuranoside .	Syrup	٦١٪	$C_{٨}H_{١٥}O_{٧}N_{٣}S$			

٤	١٣٨	٢,٣ : ٤ , ٥ – di –*O*-isopropylidene –١-*O*-*p*-toluene sulfonyl-*β*-D-fructopyranose .	Solid m.p= ١٢٥-١٢٦ºC	٦٠٪	$C_{١٣}H_{٢٢}O_{٨}S$			
٥	١٣٩	١-Azido –١-deoxy – ٢,٣ : ٤, ٥ – di – *O*-isopropylidene – *β* -D fructopyranose .	Syrup	٧١٪	$C_{١٢}H_{١٩}N_{٣}O_{٥}$	٥٠.٥٢ ٥٠.١	٦.٦٦ ٦.٠	١٤.٧٣ ١٤.٢٢
٦	١٤٠	١.٢:٤, ٥ – Di –*O*-cyclohexylidene –٣-*O*-*p*-toluene sulfonyl- *β* -D-fructopyranose	Solid m.p=٩٦-٩٨ºC	٦٢٪	$C_{٢٥}H_{٣٤}O_{٨}S$	٦٠.٧٢ ٦٠.١٥	٦.٨٨ ٦.٢٢	

No.	Number of compound	Name of Compound	State of Compound	Percentage %	molecular formula	The C.H.N analysis		
						C %	H %	N %
٧	١٤١	٣-Azido – ٣-deoxy – ١,٢:٤,٥-di-*O*-cyclohexylidene- *β* -D-fructopyranose .	Syrup	٥٠٪	$C_{١٨}H_{٢٧}O_{٥}N_{٣}$	٥٩.١٧ ٥٨.٨٦	٧.٣٩ ٧.١٢	١١.٥٠ ١٠.٨٩

٨	١٤٢	٢-Azido-٢-deoxy-١,٣,٤,٥-tetra-*O*-benzoyl fructopyranose	Syrup	٨٢٪	$C_{٣٤}H_{٢٧}O_{٩}N_{٣}$	٦٥.٧٠ ٦٤.٠٢	٤.٣٤ ٣.٧٨	٦.٧٦ ٦.١١
٩	١٤٣	٣-Azido-٣-deoxy-١,٢:٥,٦-di-*O*-isporpylidene- *β* -D-glucofuranose .	Syrup	٨٣٪	$C_{١٢}H_{١٩}O_{٩}N_{٣}$	٥٠.٥٢ ٤٩.٧٧	٦.٦٦ ٦.١٣	١٤.٧٣ ١٣.٨٦
١٠	١٤٤	١-Azido-١-deoxy – ٢,٣,٤,٦. tetra –*O*-acetyl -β-D- gluco pyranose .	Solid m.p ١١٦-١١٨ºC	٧٨٪	$C_{١٤}H_{١٩}O_{٩}N_{٣}$			
١١	١٤٥	٦ - *O* – Acetyl – ٤-azido ٢,٣,٤-trideoxy –α-D-erythro – hex-٢-ene-pyranoside	Syrup	٦٢٪	$C_{٨}H_{١١}O_{٣}N_{٣}$			

Table (٣-٩) Some Physical properties for Unsaturated sugars

No.	Number of compound	Name of Compound	State of Compound	Percentage % Yield	molecular formula	The C.H.N analysis		
						C %	H %	N %
١	١٤٦ a	٣,٤,٦-Tri acetyl glucal	Solid m.p٥٣-٥٤ºC	٦٠ %	$C_{١٢}H_{١٦}O_{٧}$	٥٢.٩٤ ٥١.٩٤	٥.٨٨ ٥.٨١	
٢	١٤٦ b	Glucal	Solid m.p ٥٦-٥٨ºC	٦٠ %	$C_{٦}H_{١٠}O_{٤}$			
٣	١٤٧	Endo- fructal	Syrup	٣٣ %	$C_{٣٤}H_{٢٦}O_{٩}$	٧٠.٥٨ ٧٠.١٠	٤.٤٩ ٤.٦١	

Table (٣-١٠) IR and NMR Spectral data for the allyl and propargyl sugars

No.	Number of compound	Name of Compound	Remarks of IR, $cm^{-١}$	Remarks of NMR
١	١١٤	١,٢, ٣,٤, ٦ - penta-*O*-acetyl-*β*-D-glucopyranose	IR (KBr) υ ١٧٦٠ (C=O),١٠٠٠-١١٠٠(C-O-C)	δ- ٥.٧٧(IH,m,$H_{٣}$),٥.٣٠ (IH,d,$H_{١\alpha}$) ,٥.١٦(١H,t$J_{H٣-H٤}$=٩.٥٧HZ),٤.٣١(١H,dd$J_{H١-H٢}$=٣.٣٠HZ)٤.٢٩-٤.١ (٣H,m,$H_{٥}$,$H_{٦}$,$H_{٧}$),٢.١٥-٢.٠(١٢H,m,٤AcO)

٢	١١٥	١- *O*-propargyl ٢,٣,٤,٦-tetra-*O*-acetyl- *β* -D-glucopyranoside	IR (film) υ ٢١٢٠cm$^{-١}$ (C≡C) ٣٢٧٤ cm$^{-١}$ (≡ CH) ١٧٥٠ cm$^{-١}$ (C = O)	δ٥ .٢٦-٥ .٠(m,٤H), ٤.٨ (d,٢H,J=٢.٥HZ) ٤.٤١-٤.٢٧(m٢H),٤.٢(m,١H),٢.٥ (t,١H,J=٢.٥HZ),٢.٤-٢.٠(١٢H)٤AcO
٣	١١٦	١-*O*-allyl٢,٣,٤,٦-tetra-*O*-acctyl -*β* -D-glucopyranoside	IR (film) υ ٣٤٨٢ , ١٧٤٨ , ١٣٦٩ , ١٢٤٥ , ١٠٥٠	δ٥.٢٩(m,١H(CH=CH$_{٢}$),٥.١٣,٥.٠٩(٢mCH=CH$_{٢}$) ٥.٠(dd,١H),٤.٨(dd,١H),٤.٢٩(m,١H,OCH$_{٢}$-CH=),٣.٧١(ddd,١H,H-٥)٢.٠٥-٢.٠٤(٣S,٣H each ٣AcO)
٤	١١٧	*O*-allyl – D-fructofurnoside	IR (film) υ ٣٣٥٧, (OH), ١٦٤١ (C=C) , ١٠٥٤ (C-O-C)	
٥	١١٨	*O*-allyl-D-fructopyranoside	IR (film) υ ٣٤٢٥(OH) , ١٦٧٨ (C=C) , ١٠٧٣ (C-O-C)	

No.	Number of compound	Name of Compound	Remarks of IR, cm $^{-1}$
٦	١١٩	*O*-propargyl-D- fructopyranosid	IR (film) υ ٣٤٢٣(OH),٣٢٨٦(≡CH),٢١١٧(C≡C),١٠٧٣ (C-O-C)
٧	١٢٠	*O*-propargyl-D-glucopyranoside	IR (film) υ ٣٤٢٣ (OH) , ٣٢٨٦ (C≡CH) , ٢١١٨ (C≡C) ١٠٨٠ (C-O-C)
٨	١٢١	١,٢:٤,٥ – Di – *O*-cylohexylidene –D-fructopyranose	IR (KBr) υ ٣٤٧٥(OH)
٩	١٢٢	٣- *O*-allyl ١,٢:٤,٥-Di-*O*-cyclohexylidene –D-fructopyranose	IR (film) υ , ٢٩٣٩ (C=C) ١١١٠ (C-O-C)
١٠	١٢٣	٣- *O*- propargyl ١,٢:٤,٥-Di-*O*-cyclohexylidene –D-fructopyranose	IR (film) υ ٣٢٨٦ (C ≡ CH) , ٢١٢٨ (C ≡ C)
١١	١٢٤	١,٢:٥,٦- Di-*O*- isopropylidene - α -D-glucofuranose	IR (KBr) υ ٣٣٩٨ (OH) , (٢٧٠٠ –٢٩٠٠) isopropyliden

No.	Number of compound	Name of Compound	Remarks of IR, cm $^{-1}$
١٢	١٢٥	٣-*O*-allyl-١;٢:٥,٦-di-*O*-isopopylidene - *β* -D-gluco furanose .	IR (KBr) υ ١٦٥٠ cm^{-1} (C=CH$_2$)
١٣	١٢٦	٣-propargyl-١,٢:٥,٦-di-*O*-isopopylidene - *β* -D-glucofuranose	IR (film) υ ٣٢٧٠ (≡CH) (٢٧٠٠-٢٩٠٠) isopropylidene ٢١١٨ (C ≡ C) .
١٤	١٢٧	٢,٣:٤,٥-di-*O*-isopropylidene - *β* -D-fructopyranos	IR (KBr disc) : ٣٢٩٦ for (OH) , ١٠٦٠ –١١٥٠ for (C-O-C), ٢٩٣٠ fo isopropylidene
١٥	١٢٨	١- *O*- allyl ٢,٣:٤,٥-*O*-isopopylidene - *β* -D-fructopyranose	IR (film) : ١٦١٦(C = C) , ١٠٦٥ (C O-C)
١٦	١٢٩	١- *O*- propargyl ٢,٣:٤,٥-*O*-isopopylidene - *β* -D- fructopyranose	IR (film) : ٣٠٥٥(≡ CH),٢١٩٦ (C≡ C),١٠٦٩ (C-O-C)
١٧	١٣٠	١,٢,٤,٥-tetra –*O*-benzoyl- *β* -D-fructopyranose	IR (KBr disc) ٣٤٣٢ (OH) ٣٠٥٥ (C H) aromatic ١٧٢٨(C=O), ١٦٠٢ fo (C=C) aromatic .

No.	Number of	Name of Compound	Remarks of IR, cm $^{-1}$

	compound		
١٨	١٣١	٢- *O*-propargyl ١,٢,٣,٥- tetra-O-benzoyl- *β* -D-fructopyransoide	IR (film) , ٣٢٦٧ of (C≡C) ,٢١٢٨ (≡CH), ١٧٥٠ (C=O) , ١٦٠٢ (C=C) aromatic .
١٩	١٣٢a	١,٣,٤,٦- tetra-*O*-benzoyl- *β* -D-fructofuranoside	IR KBr : ٣٤١٤ (OH) , ١٧٢٥(C=O),١٦٠٠(C=C aromatic)
٢٠	١٣٢b	٢-*O*-allyl ١,٣,٤,٦-tetra-*O*-benzoyl- *β* -D-fructofuranoside	IR Film : ٣٠٥٥ (CH aromatic) , ١٧٢٣(C=O),١٦٠٢(C=C aromatic) ١١١٠ (C-O-C)
٢١	١٣٣	١- *O*-Propargyl – ٤,٦-di - *O*- acetyl glucal	IR (film) : ٣٢٧٧ , ٢٩٢٠ , ٢١١٨ , ١٧٤٠ , ١٣٧٠,١٢٣٧,١٠٦٠,٩١٢,٧٣
٢٢	١٣٤	١- *O*-Allyl – ٤,٦-di - *O*- acetyl glucal	IR(film) : ٣٤٦٢ , ١٧٦٠ , ١٦٦٥ , ١٣٧٢ , ١٢٣١ , ١٠٤٤

Table (٣-١١) IR and NMR Spectral data for azide sugars

No.	Number of compound	Name of Compound	Remarks of IR, cm^{-1}	Remarks of NMR
١	١٣٥	Methyl-D-fructofuranosid	IR (Film) ٣٣٧٦ (OH) ١٠٥٤(C-O-C)	
٢	١٣٦	Methyl ١, ٦ –Di –*O*-*p*-toluene sulfonyl-D-fructofuranoside .	IR (film) ٣٢٠٠ (OH) ١٥٨١ (C=C aromatic) ١١٧٧,٩٩٠ ($-SO_2$) ١٠٣٠ (C-O-C)	
٣	١٣٧	Methyl-٦-deoxy –٦-azido –١-*O*- *p*- toluene sulfonyl-D-fructofuranoside .	IR (Film) ٢١٠٠ (N_3)	
٤	١٣٨	٢,٣ : ٤ , ٥ – di –*O*-isopropylidene –١-*O*-*p*-toluene sulfonyl- *β* -D-fructopyranose .	IR (KBr) ١١٧٧ , ٩٦٨ (SO_4)	
٥	١٣٩	١-Azido –١-deoxy – ٢,٣ : ٤, ٥ – di – *O*-isopropylidene – *β* -D fructopyranose .	IR (film) ٢١٠٠ (N_3)	
٦	١٤٠	١.٢:٤, ٥ – Di –*O*-cyclohexylidene –٣-*O*-*p*-toluene sulfonyl- *β* -D-fructopyranose .	IR (KBr) ٩٩٠,١١٧٧ (SO_2)	

No.	Number of compound	Name of Compound	Remarks of IR, cm^{-1}	Remarks of NMR
٧	١٤١	٣-Azido – ٣-deoxy – ١,٢:٤,٥-di-*O*-cyclohexylidene- *β* -D-fructopyranose .	IR (film) ٢١٠٠ (N_3)	
٨	١٤٢	٢-Azido-٣-deoxy-١,٢,٣,٤-tetra-*O*-benzoyl fructopyranose	IR (Film) ٢١٢٩ (N_3)	
٩	١٤٣	٣-Azido-٢-deoxy-١,٢:٥,٦-di-*O*-isporpylidene- *β* -D-glucofuranose .	IR (KBr) ٢١٠٠ (N_3)	δ ٥.٣٠,(d,H-١) , ٤.٥٦ (d,H-٢) ٣.٩-٤.١٤ (groups (H^3,H-٤,H-٥) ١.٢٤ –١.٥ (t for isopropylidene)
١٠	١٤٤	١-Azido-١-deoxy – ٢,٣,٤,٦. tetra –*O*-acetyl -β- D- gluco pyranose .	IR (KBr) ٢١٢٠ (N_3)	Δ ٢.٠١ – ٢.١ for ١٢ H of ٤ AcO
١١	١٤٥	٦ - *O* – Acetyl – ٤-azido ٢,٣,٤-trideoxy –α-D-erythro – hex-٢-enopyranoside	IR (Film) ٢١٠٦ (N_3)	

Table (٣-١٢) IR and NMR Spectral data for Unsaturated sugars

No.	Number of compound	Name of Compound	Remarks of IR, cm $^{-١}$	Remarks of NMR
١	١٤٦ a	٣,٤,٥-Tri acetyl glucal	IR (KBr) ١٧٤٤ (C=O) ١٦٥٠ (C=C)	
٢	١٤٦b	Glucal	IR (KBr) ٣٣٧٠ (OH) , ١٦٥٣(C=C)	
٣	١٤٧	Endo- fructal	IR (film) ١٧٥٠ (C=O) ١٦٢٠ (C=C)	٤.١٠ dd(١H , H-٢a) ٤.١٦ dd (١H,H-٢b) ٤.٥٩ ,٥.٣٣(two,$CH_{٢}$- OBZ ٥.٩ (١H , H-٣) , ٦.٣٣ (dd,H,H٤) ٧.١٥ – ٧.٩٩ = m ٢٠H , $٤C_{٦}H_{٥}$

Table (٣- ١٣) Proton nuclear magnetic resonance spectra

The structures of some of the prepared compounds (starting material) were confirmed by H^{1}MNR as shown in table (٣-١٤) .

It was obvious from figures (٣-٤١ to ٣-٥٣) that the anomeric proton H-١ appeared as a doublet in the region δ ٥.٣ – ٥.٦ while the signal for the H-٢ appeared as a doublet in the region δ ٤.٦-٥.٤ the H^{1}MNR spectrum demon started the H-٤ as doublet at δ ٤.٥ , H-٥ at ٣-٥٥ and H٦ at ٣.٨٥ – ٣.٢٨ .

The signal at δ ٣.٥٤-٣.٥٢ was attributed to the proton of the hydroxyl group H-٤ and H-٥ appeared as multiplets in the region δ ٤.٦٦-٣.٥٢ .

The signal at δ ٧.٢ –٨ was attributed to the proton of triazole ring . The appearance of the sharp singlet at δ ٢.١٤ – ٢.٠٧ in the spectrum was attributed to the acetate groups .The aromatic proton appeared at δ ٨.٠٨-٧.٤١ .

The signal at δ ١.٢٥ – ١.١ was attributed to the proton of the methyl in the isopropylidene groups .

Table (٣-١٤) : H^1 NMR chemical shifts data (in δ values) for compound ١١٤ , ١١٥ , ١١٦ , ١٢٠ , ١٢١ , ١٢٦

Compound	*H-١*	*H-٢*	*H-٣*	*H-٤*	*H-٥*	*H-٦*	*HC=CH*	*Others*
١١٤	٥.٧	٥.٢	٥.١	٣.٧		٤.٥	---------	٢.٠٥-٢.١٥ (٣H of five acetate

								group)
١١٥	٦.٥	٥.٠	٤.٥			٤.٥	----------	٢.٠٤ – ٢.١٢ (٣H of four acetate group)
								٦.٢٥(١ H of Acetylinic group)
								٣.٨٢ (٢H of methylene group CH_2-C=CH
١١٦	٥.٥	٥.٠				٤.٥	٥.٢٥	٢.٠٣-٢.٢١ (٣H of four acetate group)
١٢٠	٥.٥	٤.٧				٣.٧	٥.٢٧	٣.٥ (٢H of methylene group)
								٣.٥٩ (١H of hydroxyl group)
١٢١	٣.٩٨	----	٤.٠٨	٤.٠٨٣	٤.٢٢	٤.٠٥	-------	١.٦٤ (١٠ H of two cyclohexyl group .
								٣.٩٤ (٤ H of two methylene group)
١٤٤	٥.٦					٣.٧	--------	٢.٠١-٢.١ (١٢ H of four acetate

group)								
١٢) ١.٣١ – ١.٤٢	٥.٢٥	٣.٧					٤.٨	١٢٨
H of the four CH_3 in the isopropylidene group)								

Table (٣-١٤): H ^{1} NMR chemical shifts date (in δ values) for compound ١١٤ , ١١٥ , ١١٦ , ١٢٠ , ١٢١ , ١٢٦

Compound	*H-١*	*H-٢*	*H-٣*	*H-٤*	*H-٥*	*H-٦*	*HC=CH*	*Others*
١٣٤	٥.٣٨	-----	-----	٤.٢	٥		٥.٢٦	٢.١ (٦ H of the two acetate group)
١٤٧	------	------	٤.٢			٤.٤	٥٣	٧. ٣٣ – ٧. ٤ (٥ H of four benzene groups)

Table (٣-١٥) : H ^{١} NMR chemical shifts data (in δ values) for compound ١٢٥ , ١٢٦ , ١٣٧ , ١٤٣ , ١٣٩

Compound	*H-١*	*H-٢*	*H-٣*	*H-٤*	*H-٥*	*H-٦*	*HC=CH*	*Others*
١٢٥	٥.٨	٤.٥				٤.١	٥.٢٥	١.٤٨ – ١.٢٥ (١٢ H of the four CH_3 in the isopropylidene groups). ٤.١(٢H of methylene group CH_2-C=C)
١٢٦	٤.٦٧	٤.٣٢				٣.٩٨	----	١.٥٣ – ١.٢٥ (١٢ H of the four CH_3 in

								isopropylidene groups) ٤.١٧ (٢ H of methylene group) ٥.٩ – ٥.٨٨ (١ H of the Acetylenic group)
١٣٧	----	٤.٢٧	←			٤.١٦	------	→٧. ٥٣ – ٧. ٦٥ (٤ H of benzene groups) ٤.١٦ – ٤.٢٧ (٣H of methyl group)
١٤٣	٥.٢٥	٤.٢	←			٣.٧	------	→١.٤٢ – ١.٢٥ (١٢ H of the four CH_3 in the isopropylidene group

Appendixes

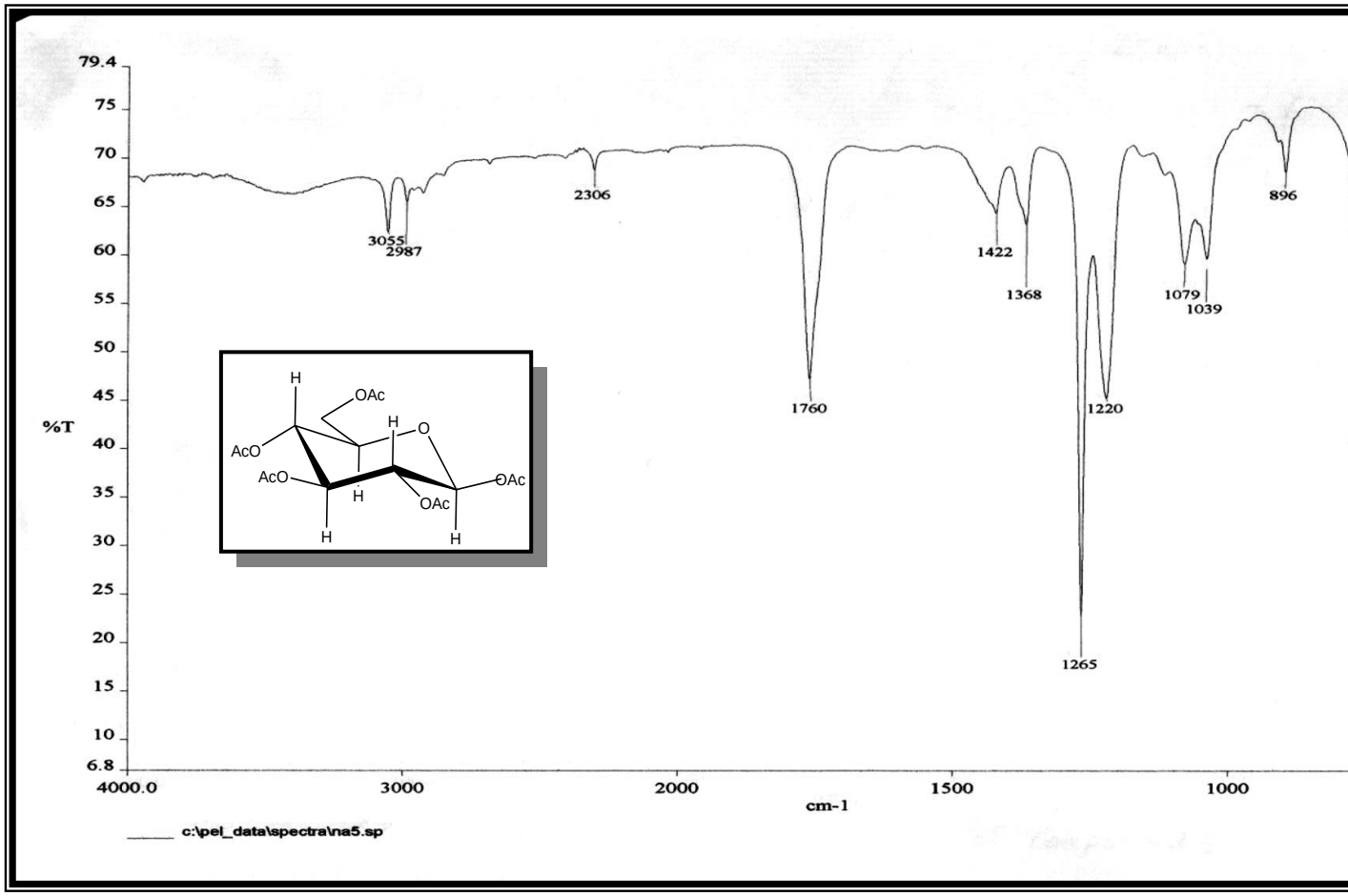


Figure (٣-٦) : IR Spectrum of compound [١١٤]

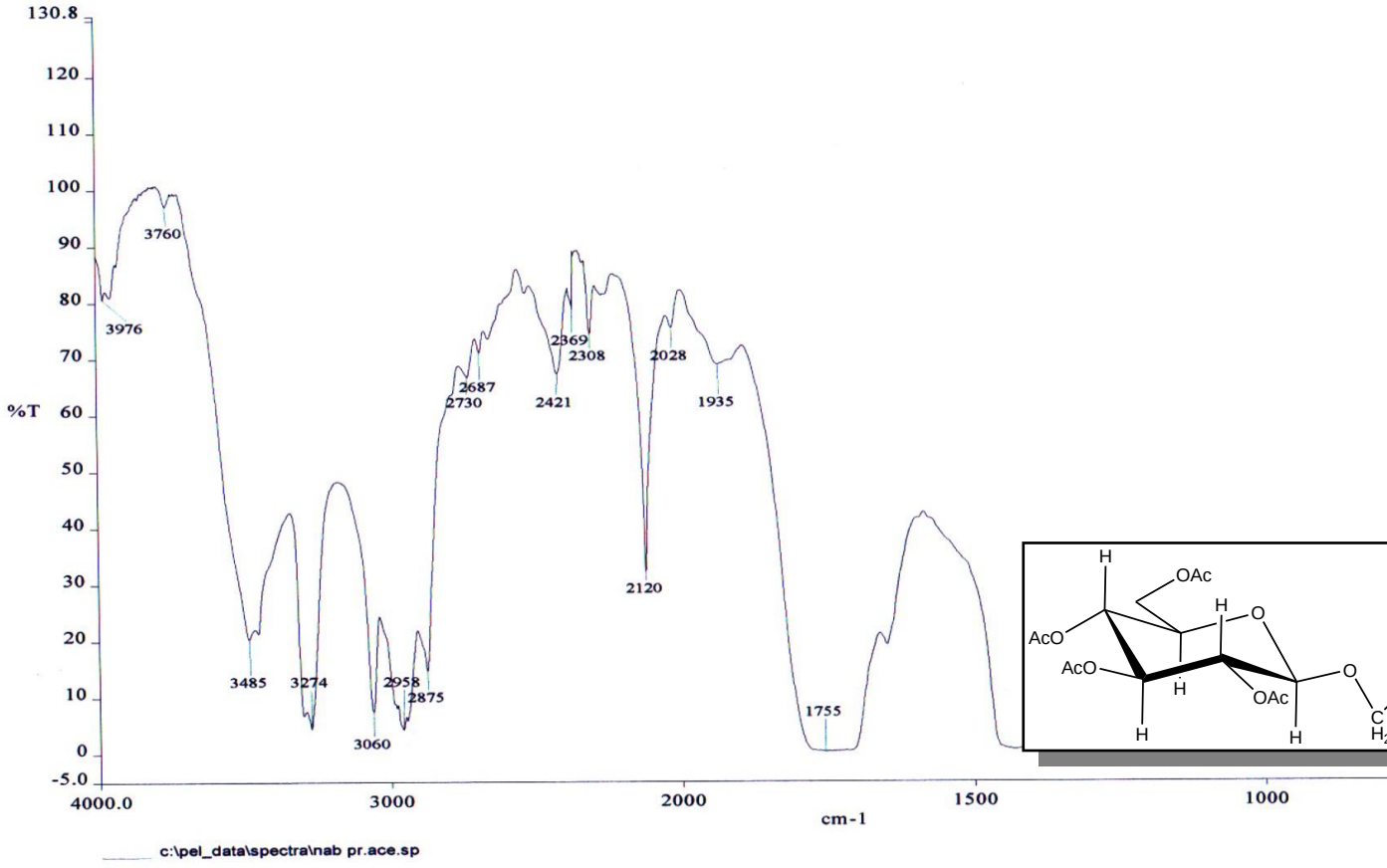
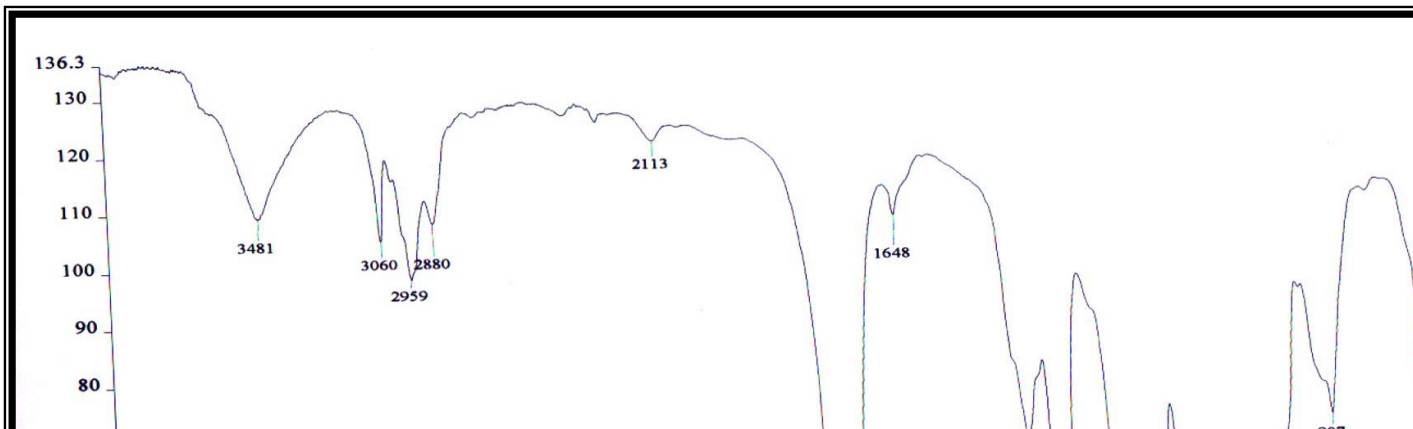


Figure (٣-٧) : IR Spectrum of compound [١١٥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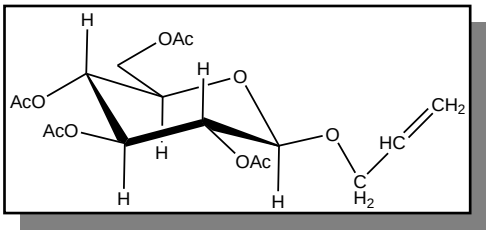
120
110
100
90
80
3481
3060
2880
2959
2113
1648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OAc
H
O
AcO
AcO
H
OAc
O
HC
CH2
C
H2
H
H

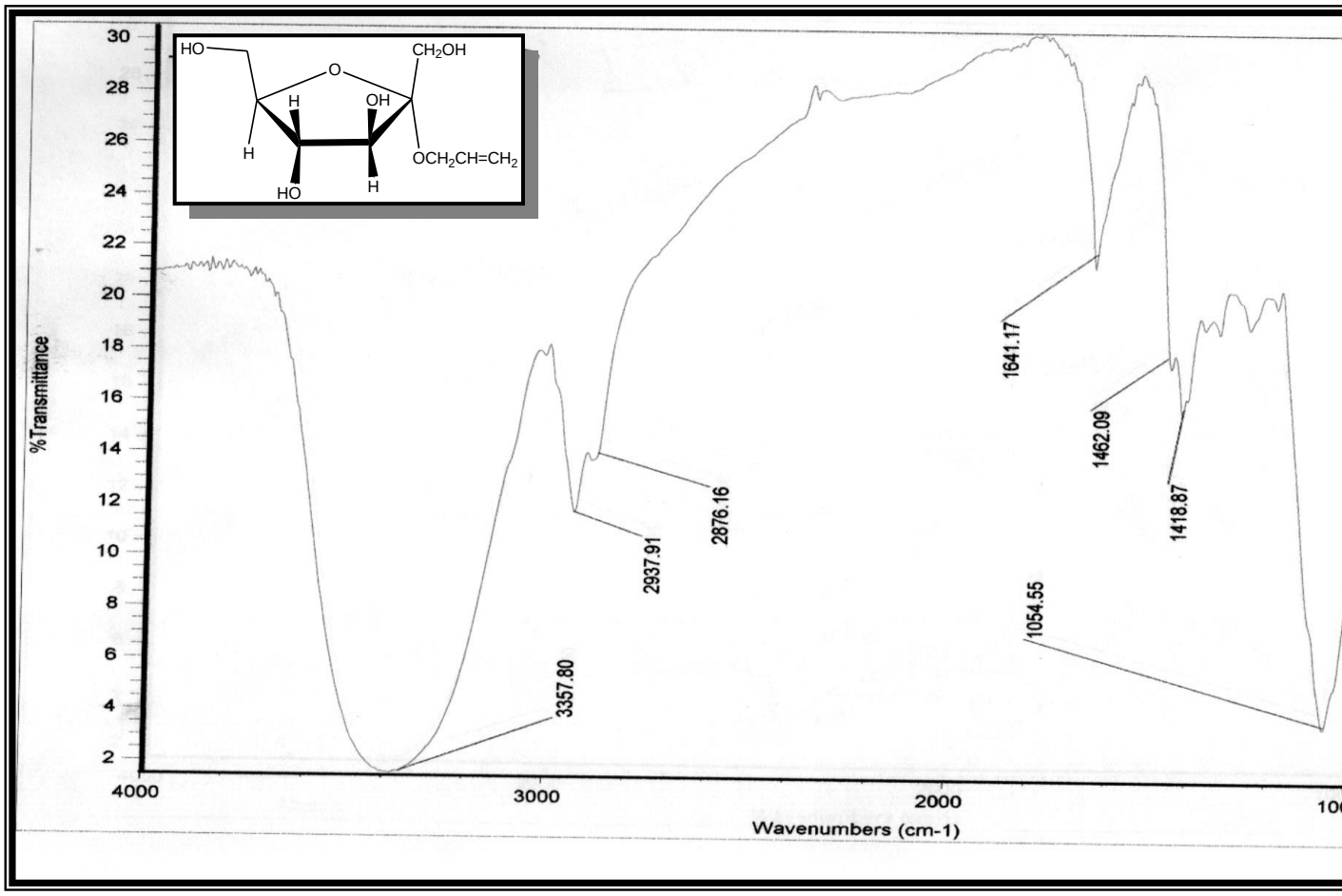
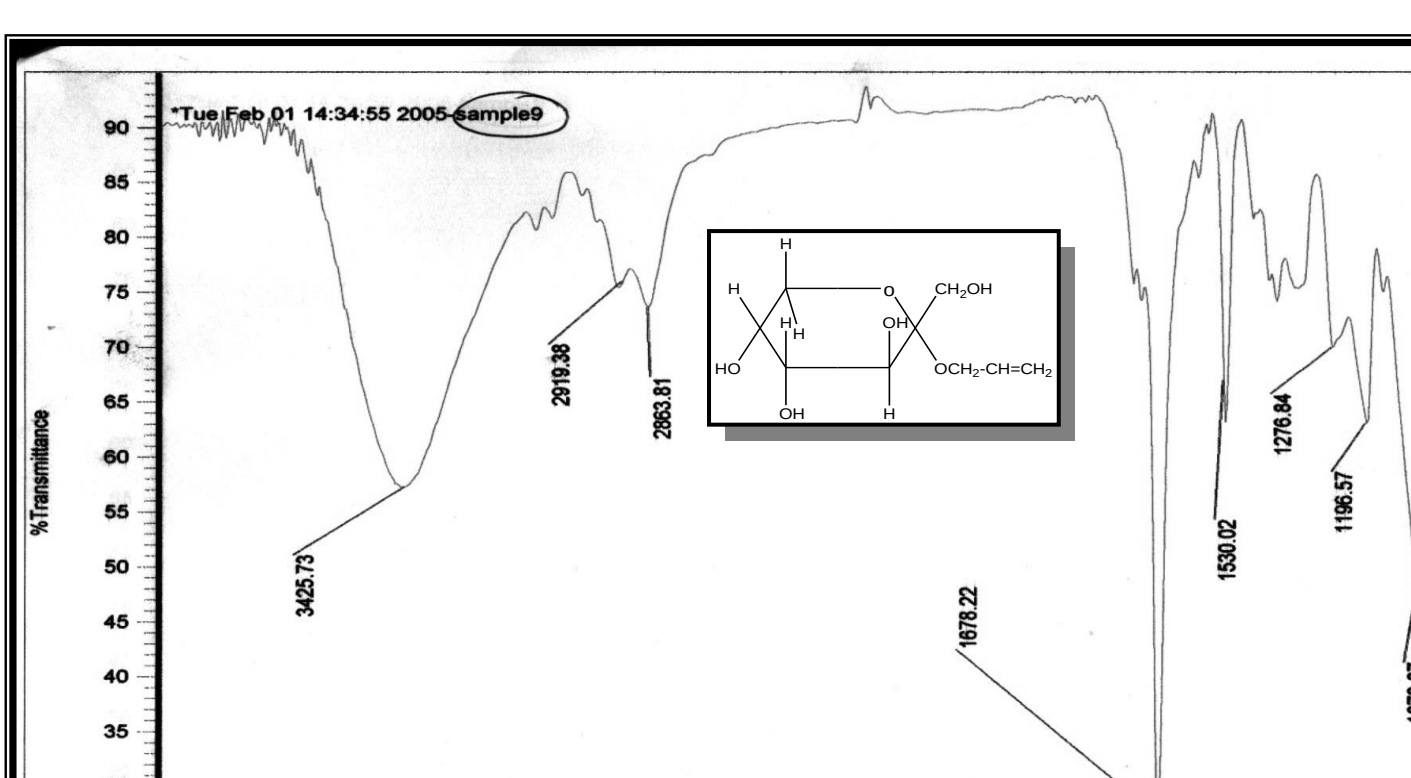


Figure (٣-٩) : IR Spectrum of compound [١١٧]


*Tue Feb 01 14:34:55 2005 sample9
%Transmittance
90
85
80
75
70
65
60
55
50
45
40
35
3425.73
2919.38
2863.81
1678.22
1530.02
1276.84
1196.57
H
H
O
CH2OH
H
H
OH
HO
OCH2-CH=CH2
OH
H

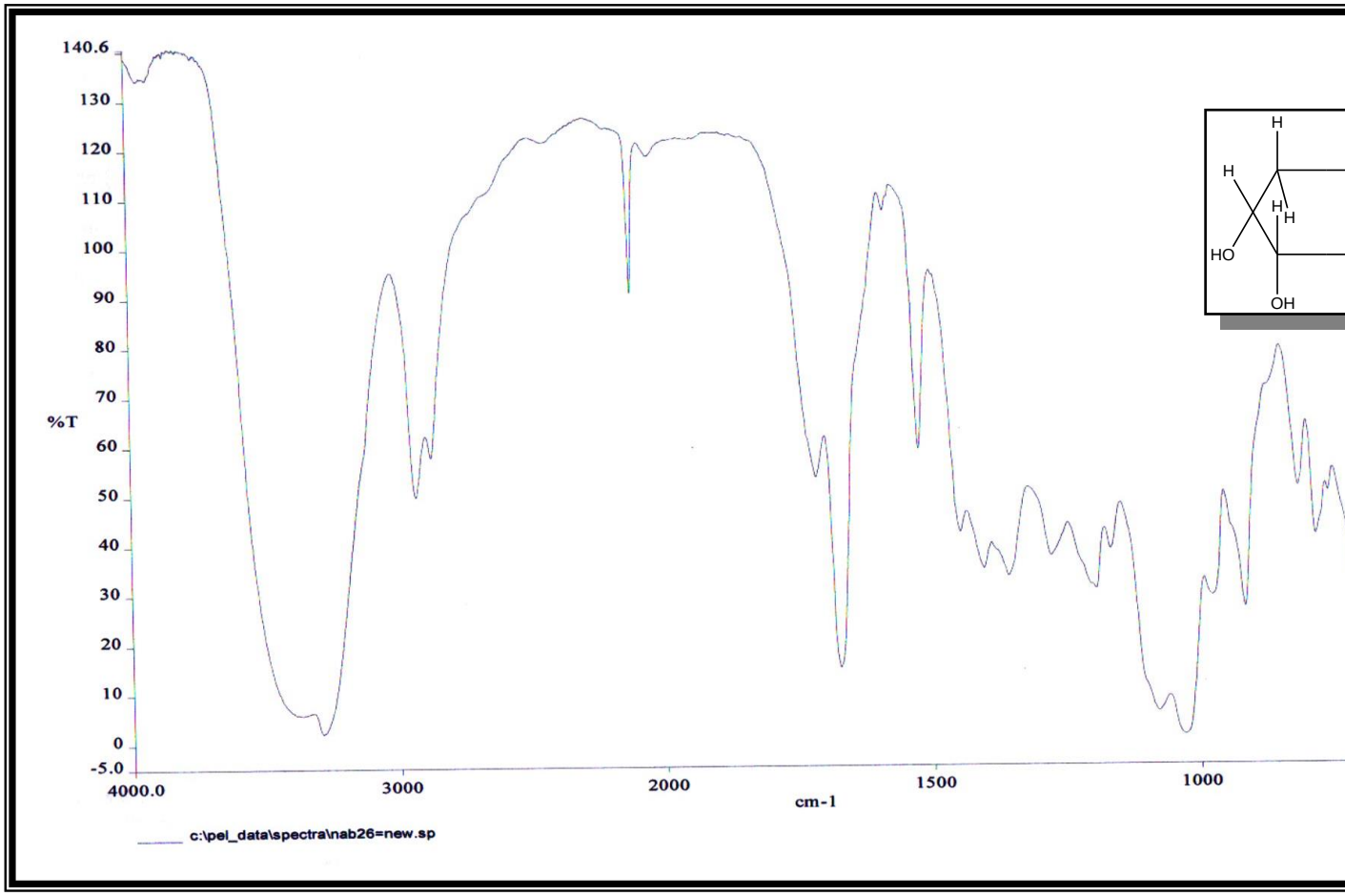


Figure (٣-١١) : IR Spectrum of compound [١١٩]

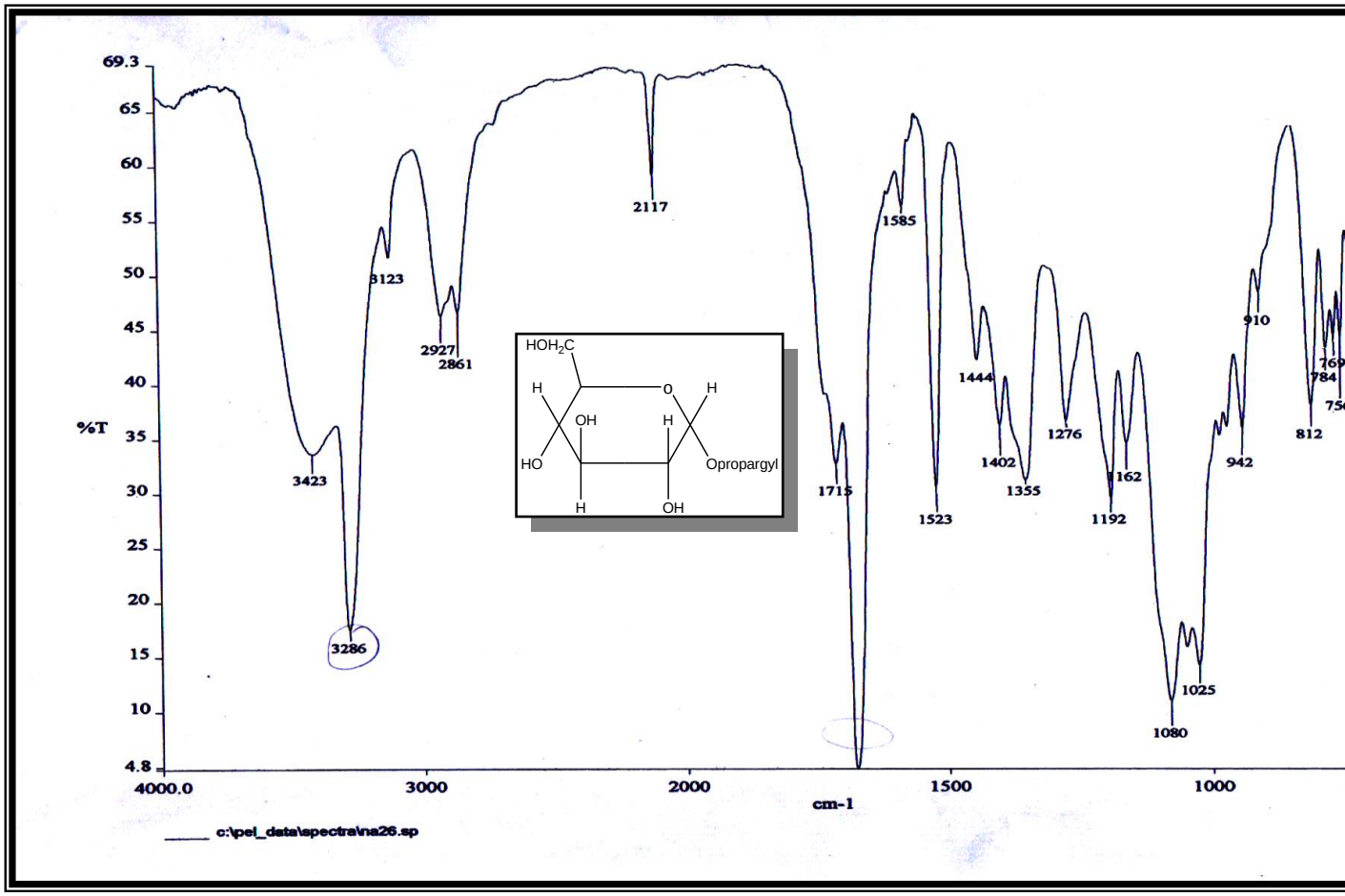
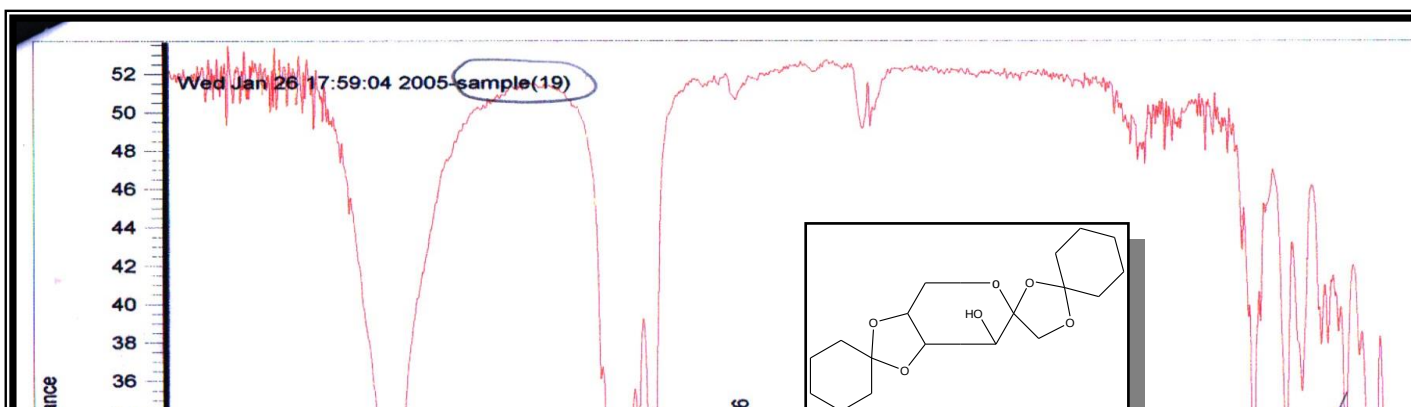


Figure (٣-١٢) : IR Spectrum of compound [١٢٠]


Wed Jan 26 17:59:04 2005 sample(19)
52
50
48
46
44
42
40
38
36
HO
O
O
O
O
O

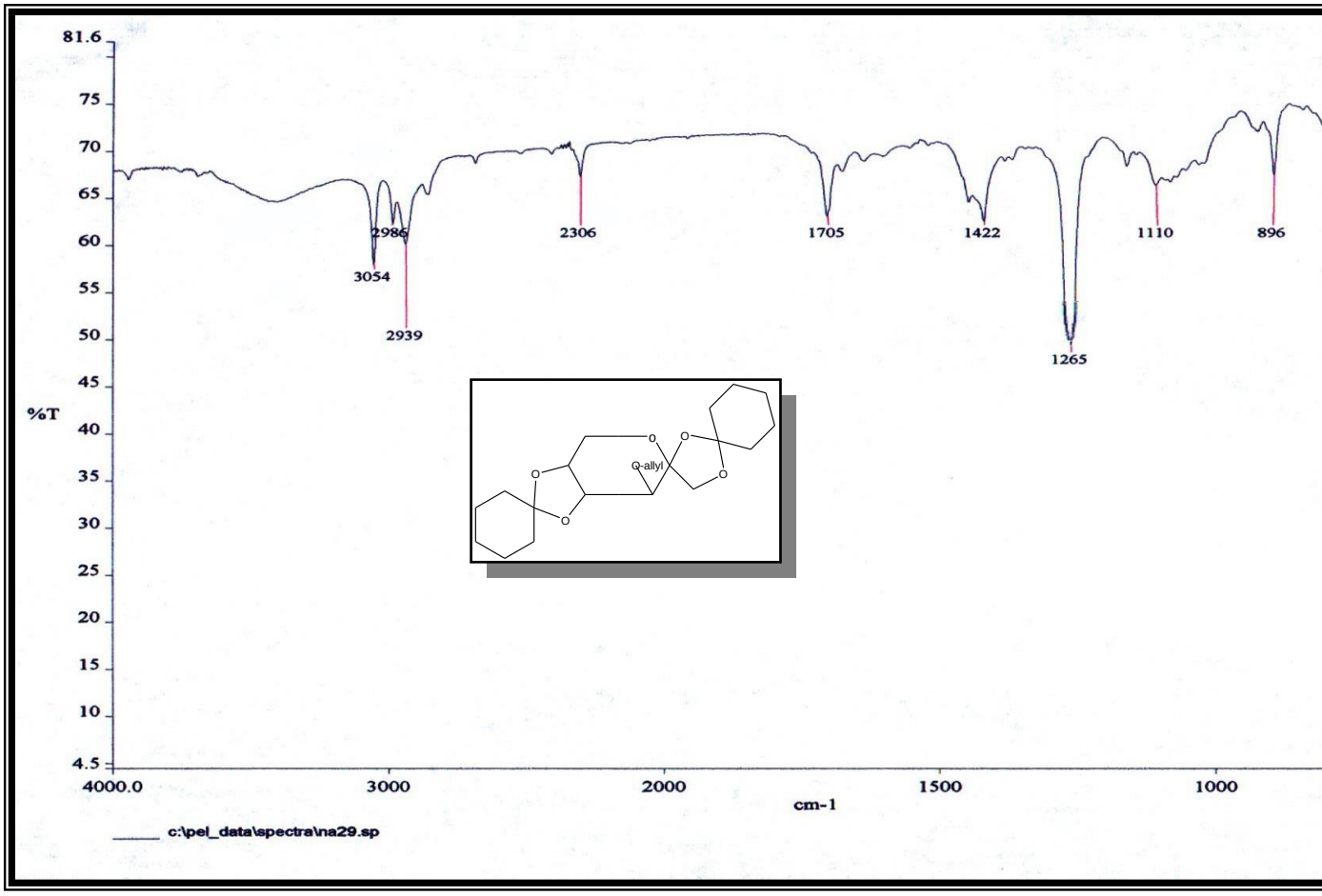


Figure (٣-١٤) : IR Spectrum of compound [١٢٢]

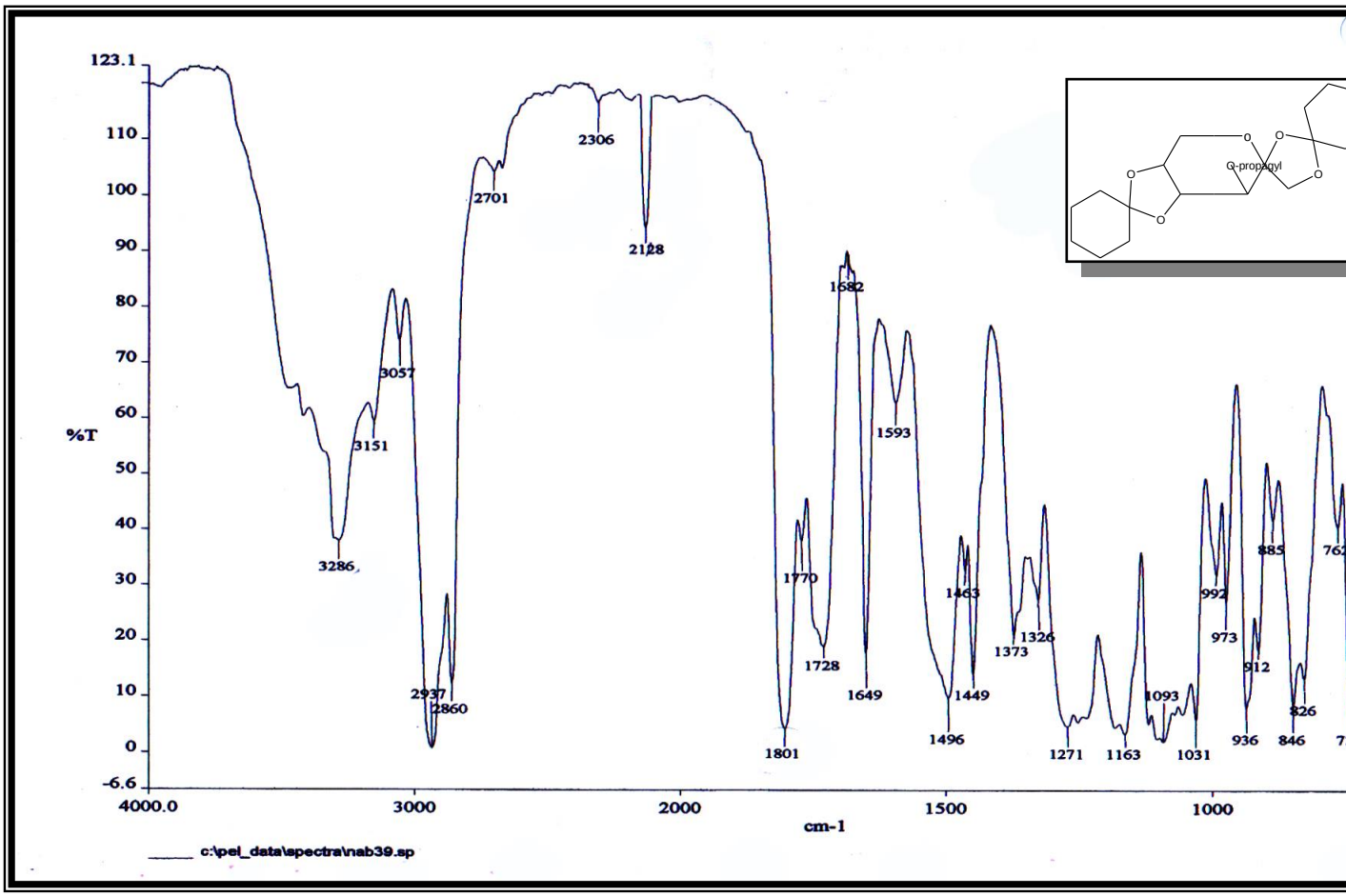


Figure (٣-١٥) : IR Spectrum of compound [١٢٣]

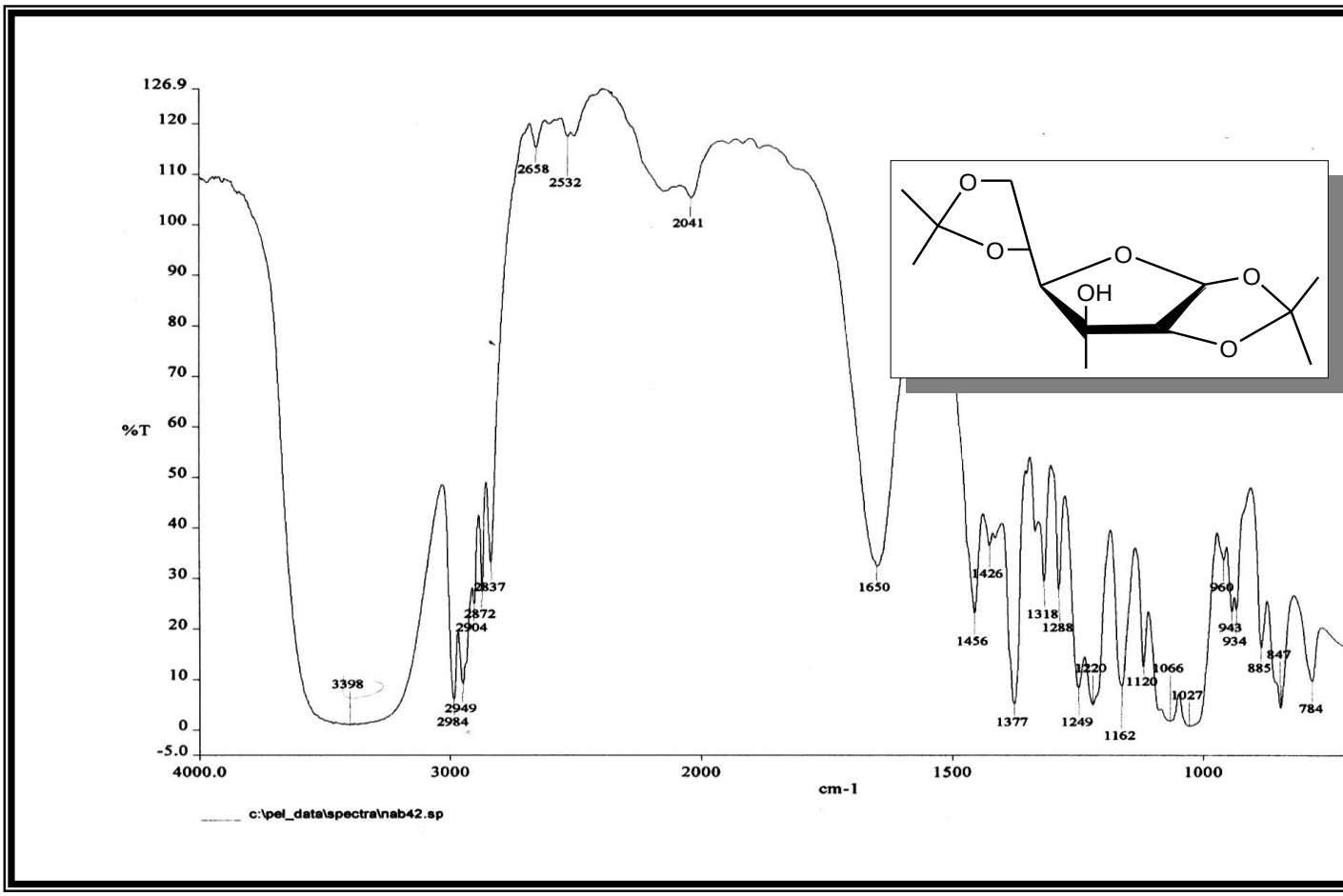
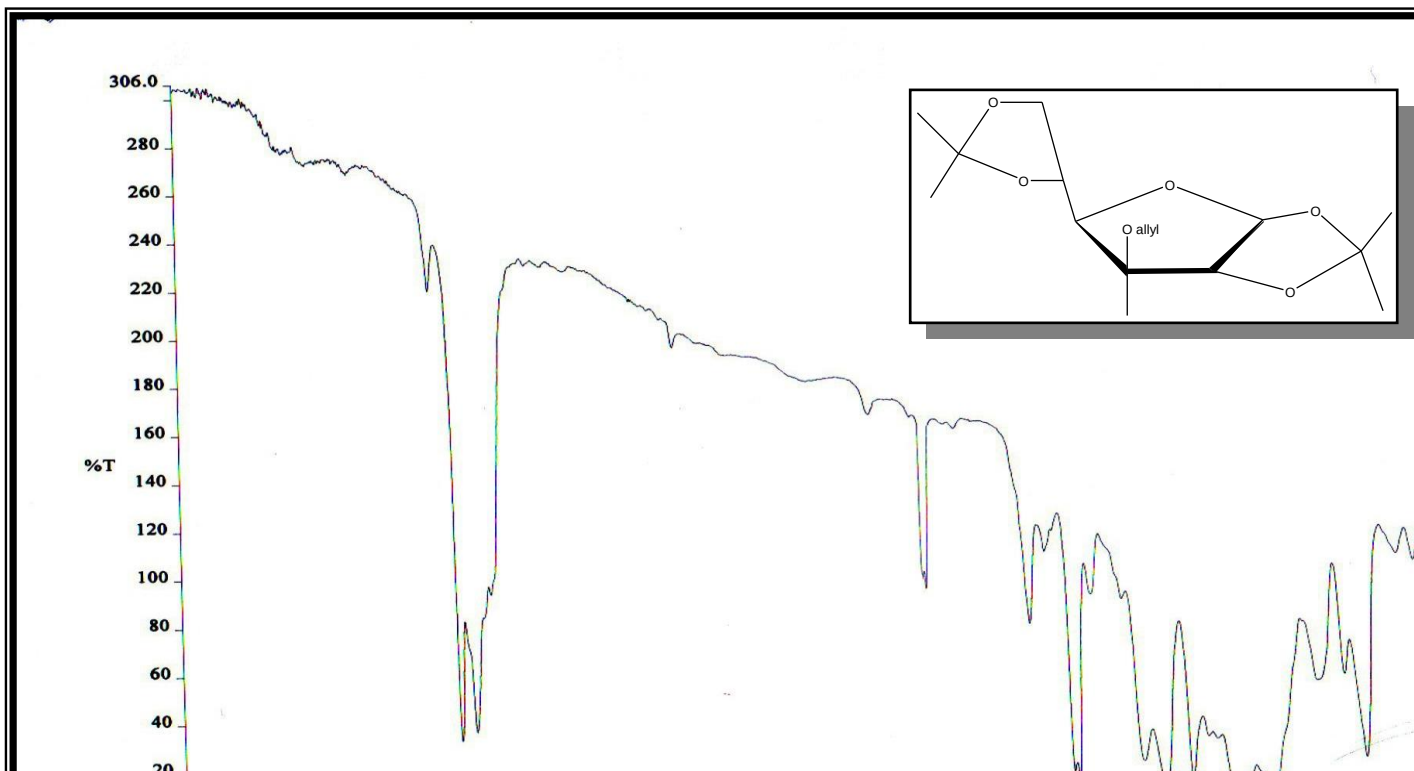
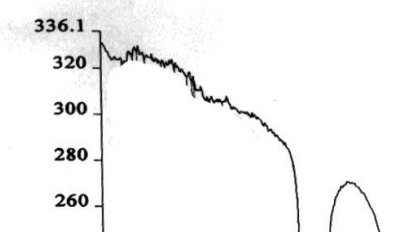
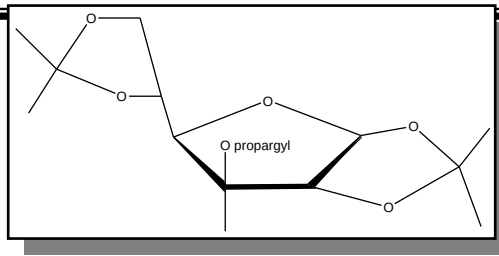


Figure (٣-١٦) : IR Spectrum of compound [١٢٤]


306.0
280
260
240
220
200
180
160
%T
140
120
100
80
60
40
20
O allyl


336.1
320
300
280
260


O
O
O
O
O
O propargyl

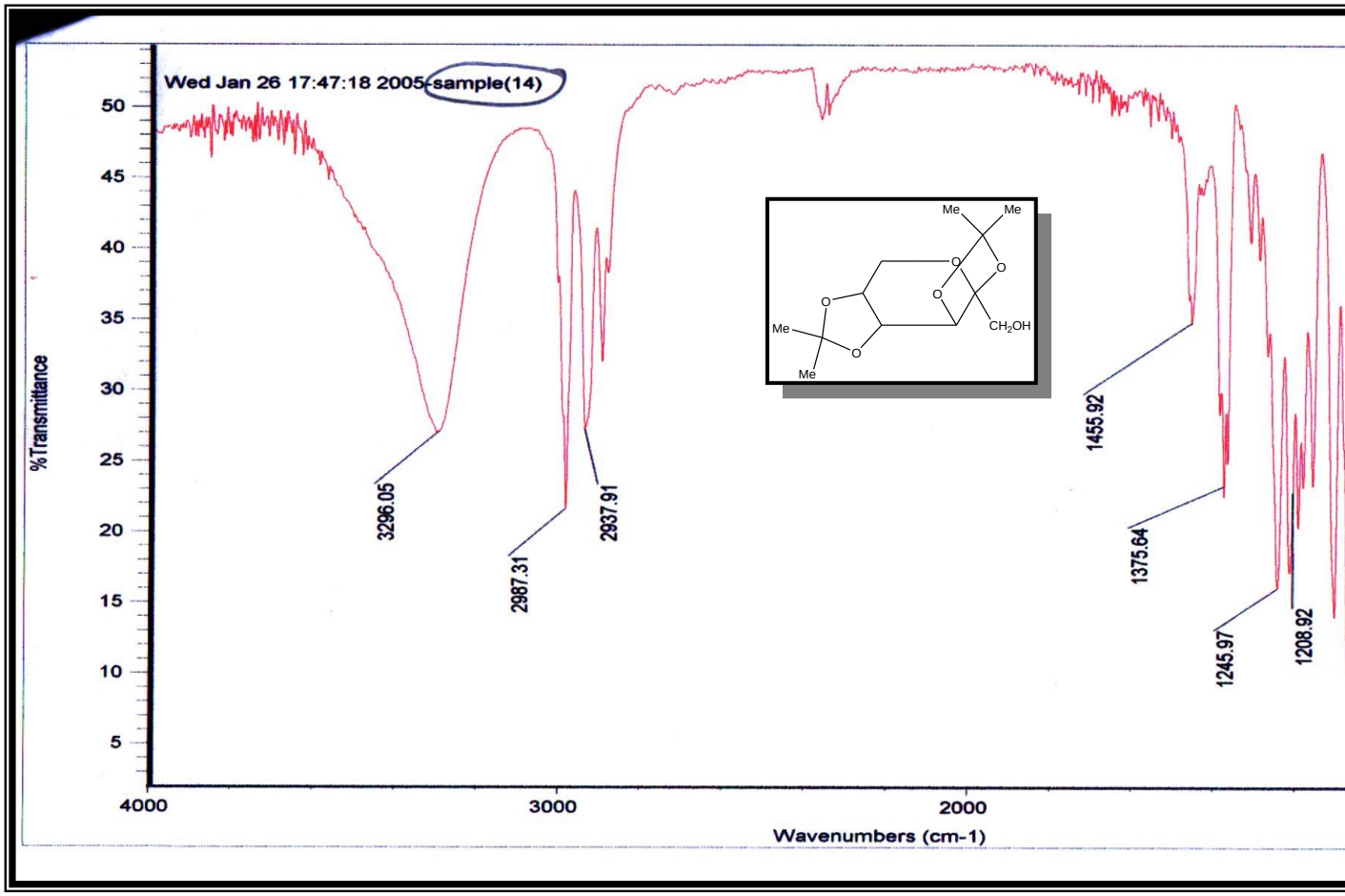


Figure (٣-١٩) : IR Spectrum of compound [١٢٧]

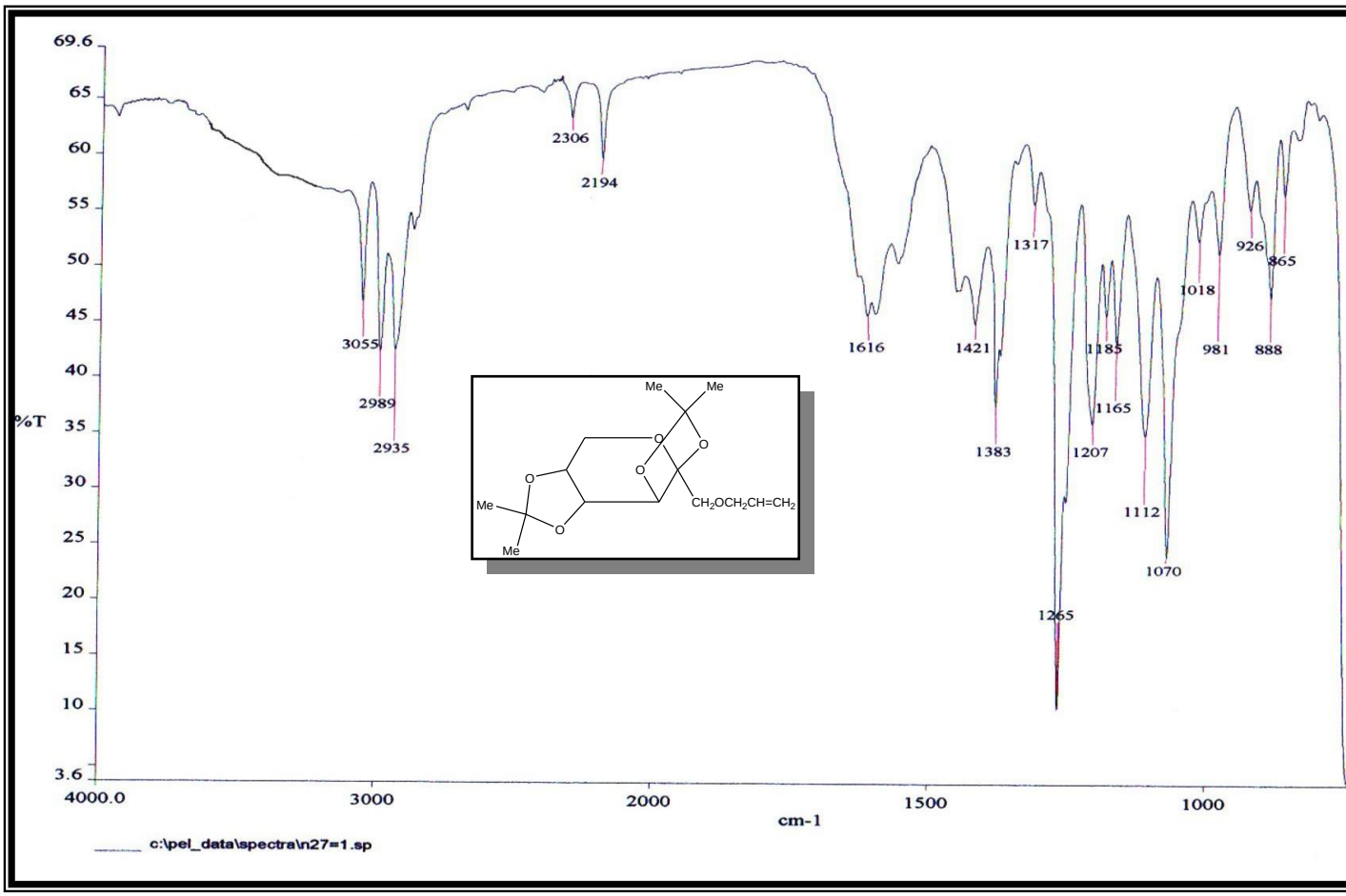


Figure (٣-٢٠) : IR Spectrum of compound [١٢٨]

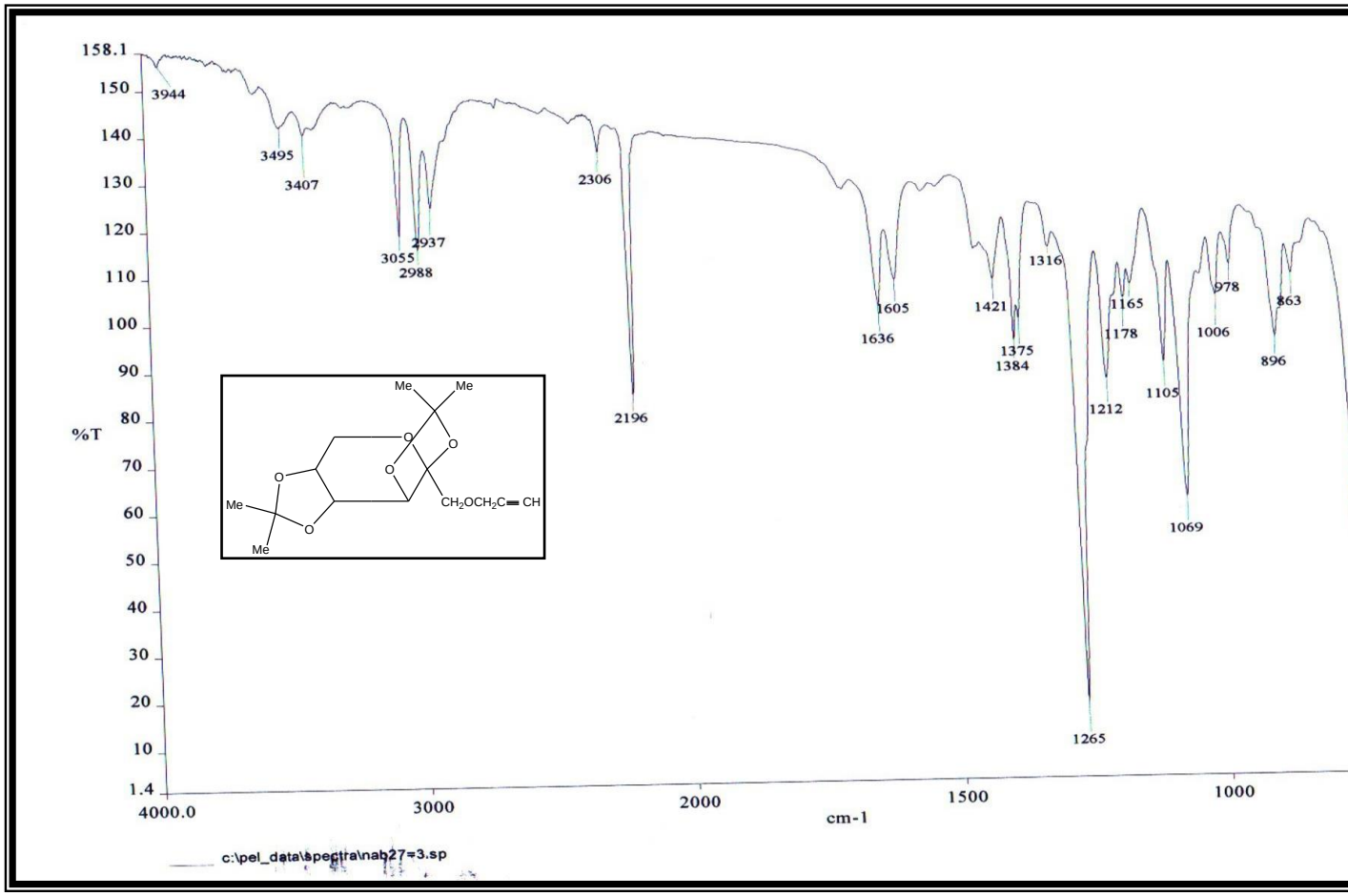
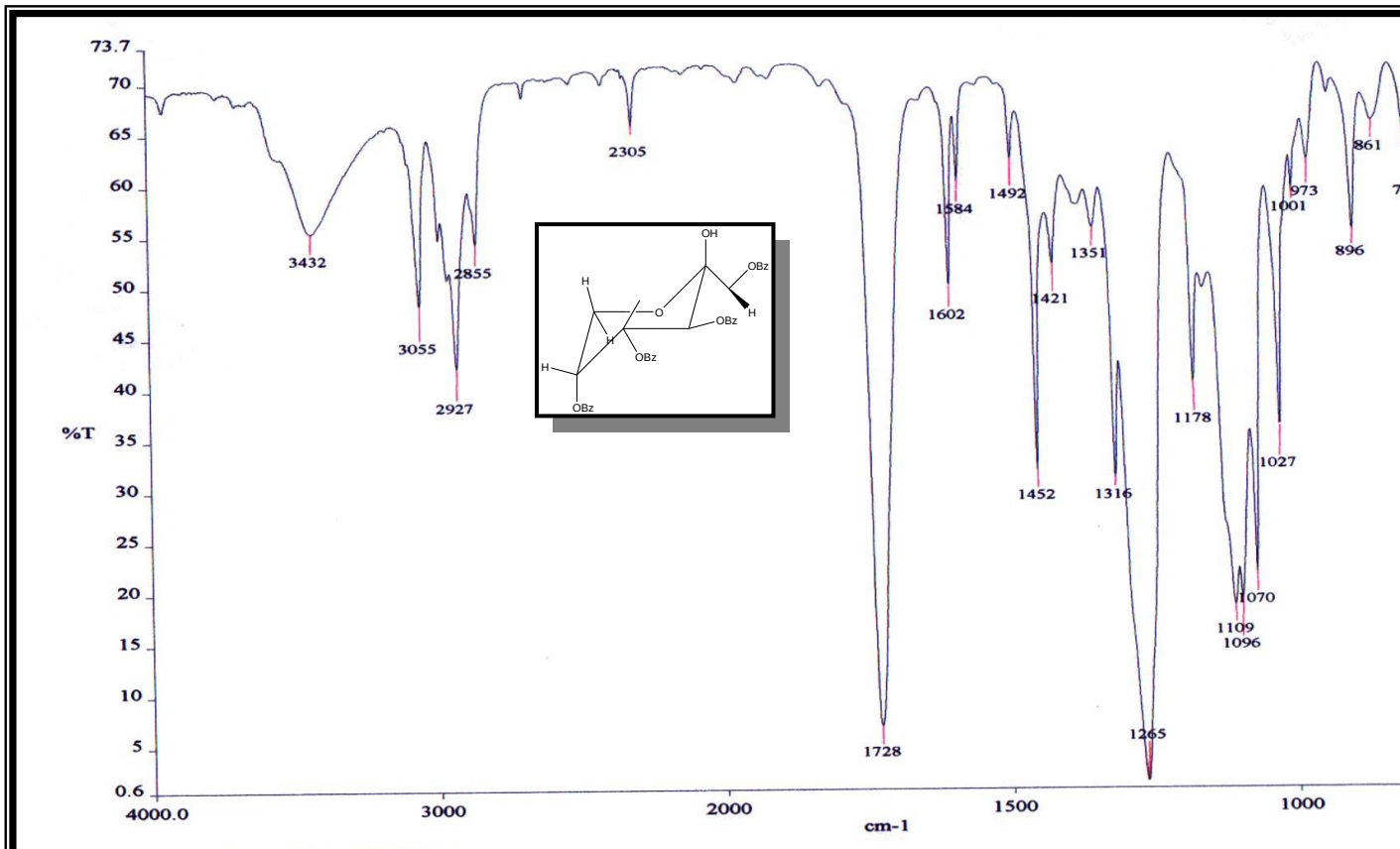


Figure (٣-٢١) : IR Spectrum of compound [١٢٩]


%T
cm-1
4000.0
3000
2000
1500
1000
73.7
70
65
60
55
50
45
40
35
30
25
20
15
10
5
0.6
3432
3055
2927
2855
2305
1728
1602
1584
1492
1452
1421
1351
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1265
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1096
1070
1027
1001
973
896
861
OH
OBz
H
O

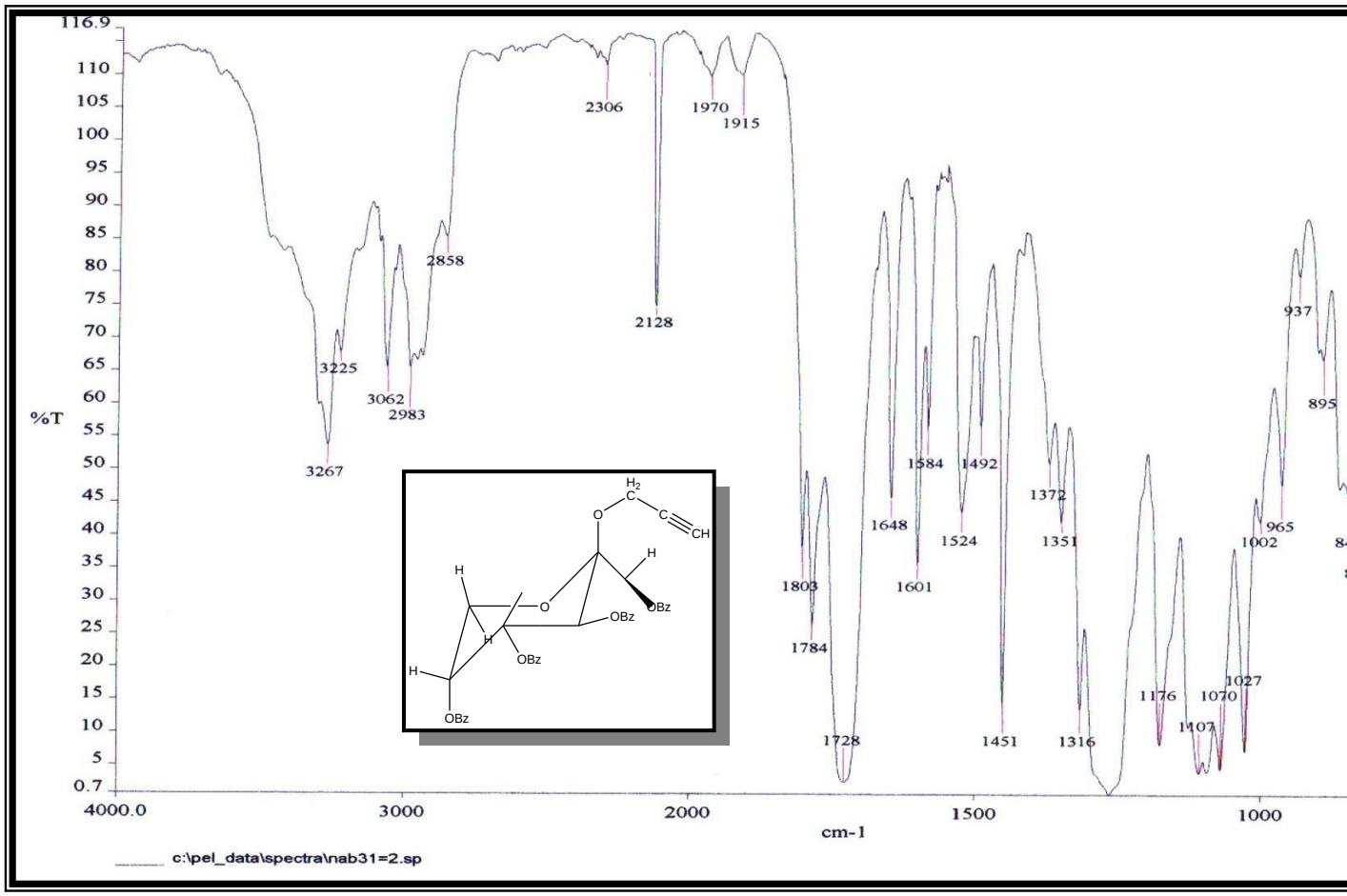


Figure (٣-٢٣) : IR Spectrum of compound [١٣١]

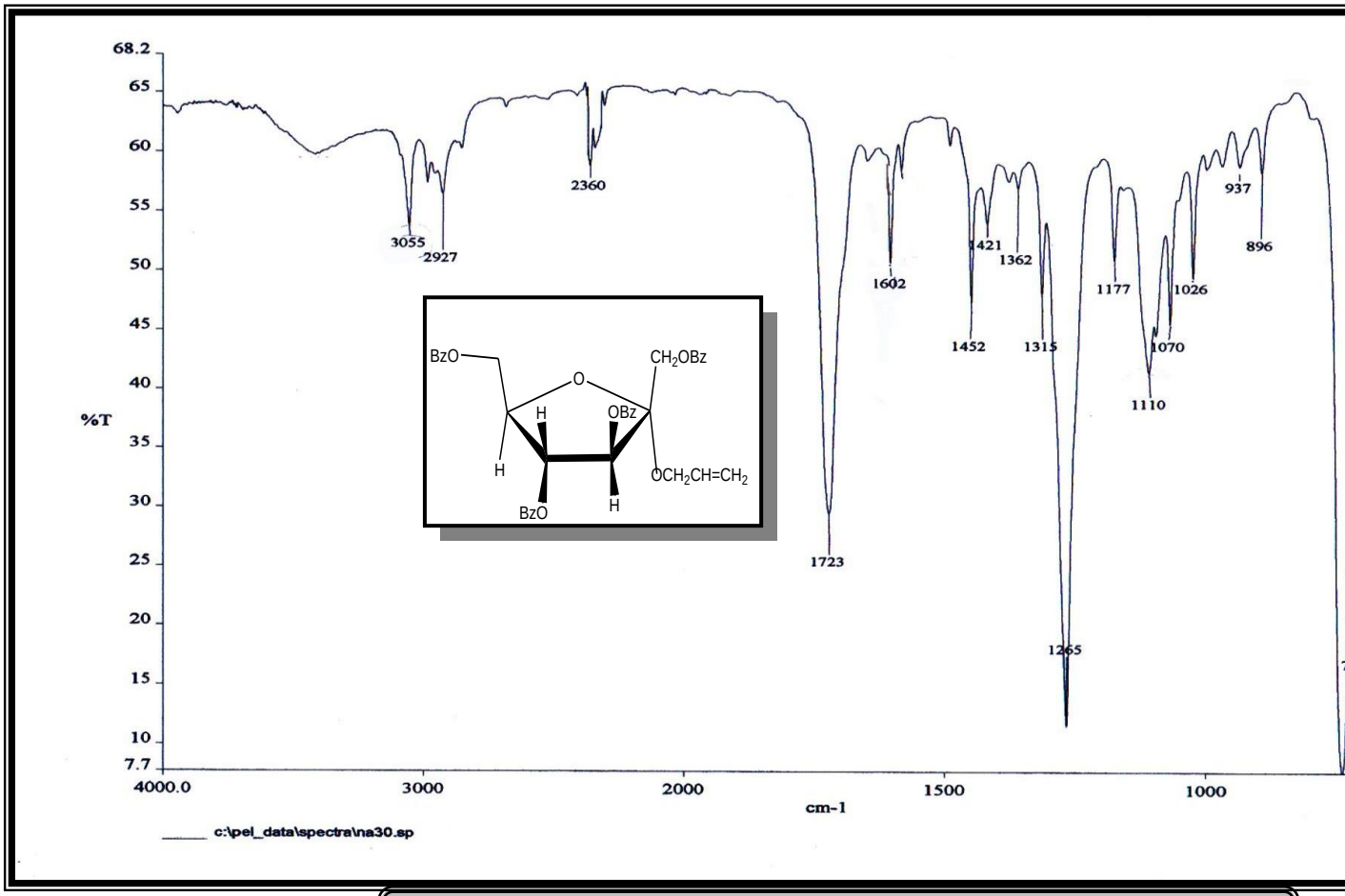
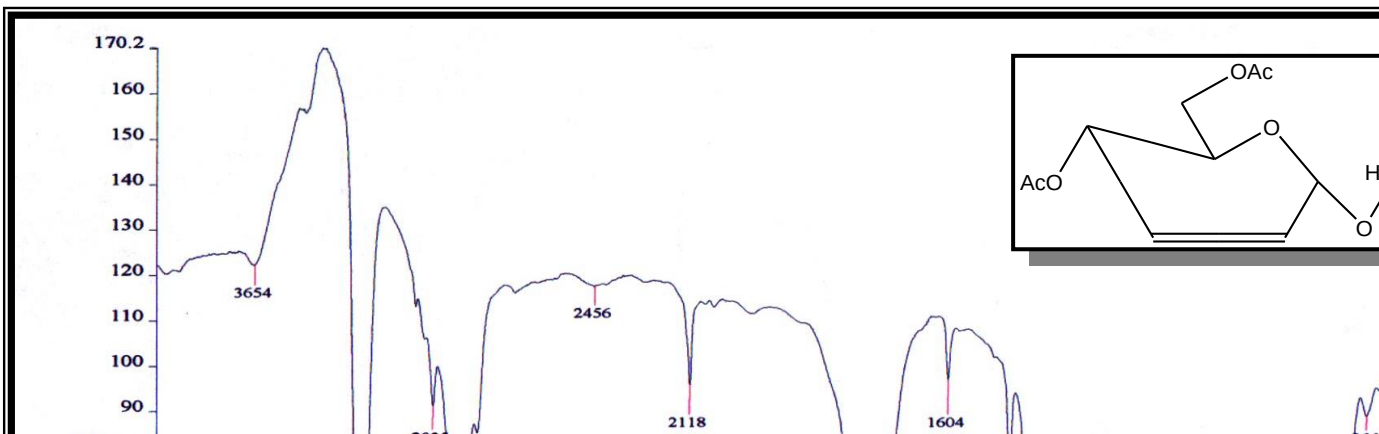


Figure (٣-٢٤) : IR Spectrum of compound[١٣٢b


170.2
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130
120
110
100
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2456
2118
1604
OAc
O
AcO
H
O

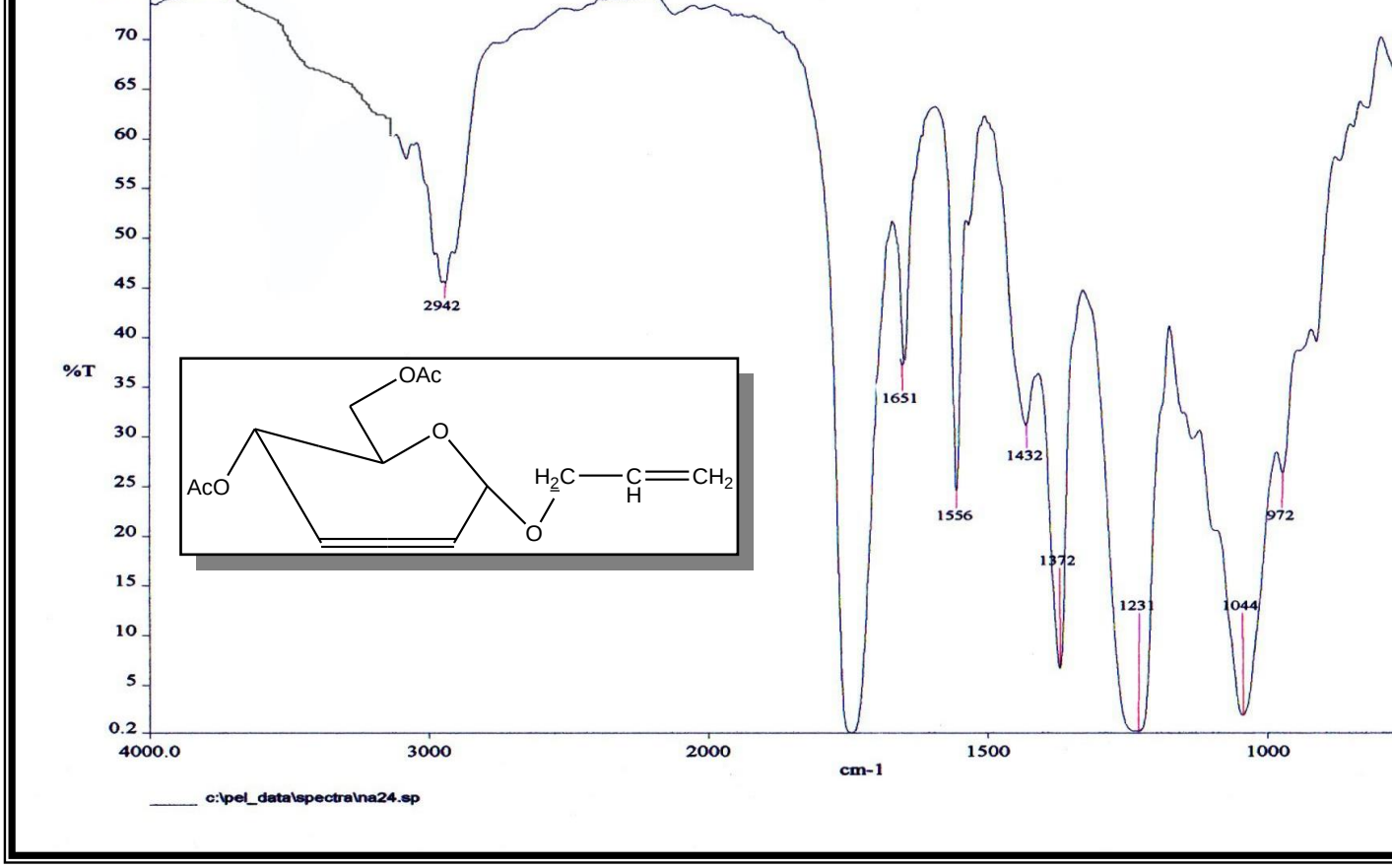
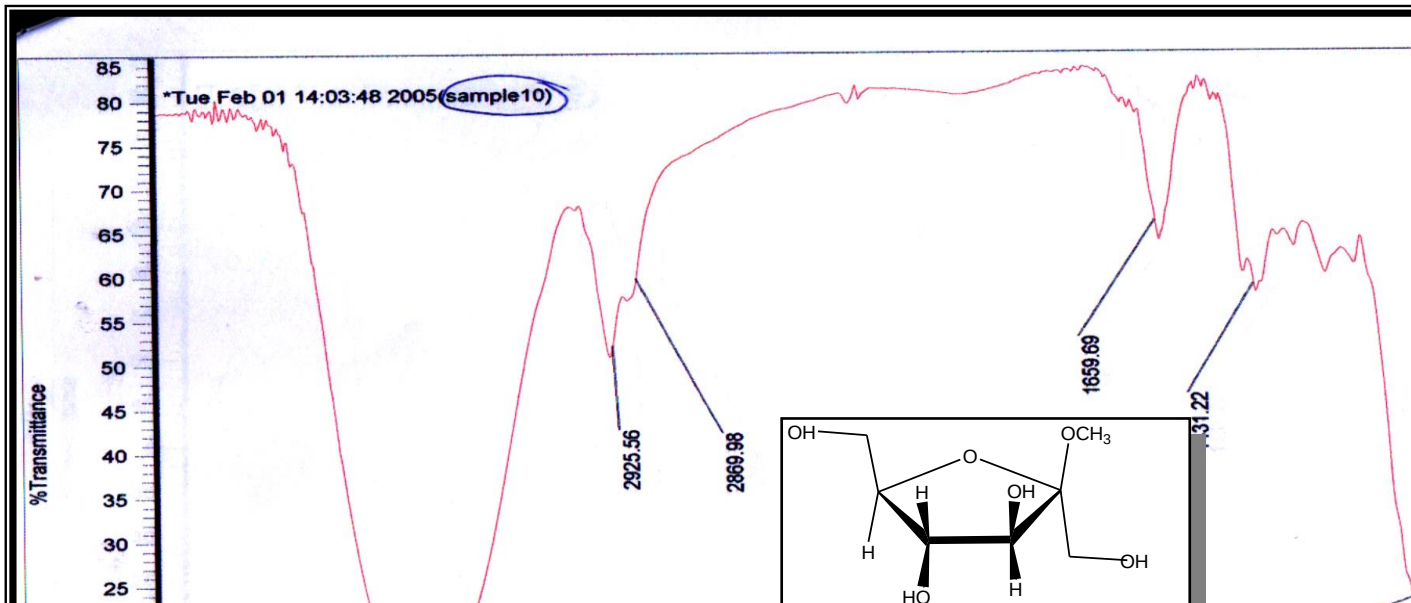


Figure (٣-٢٦) : IR Spectrum of compound [



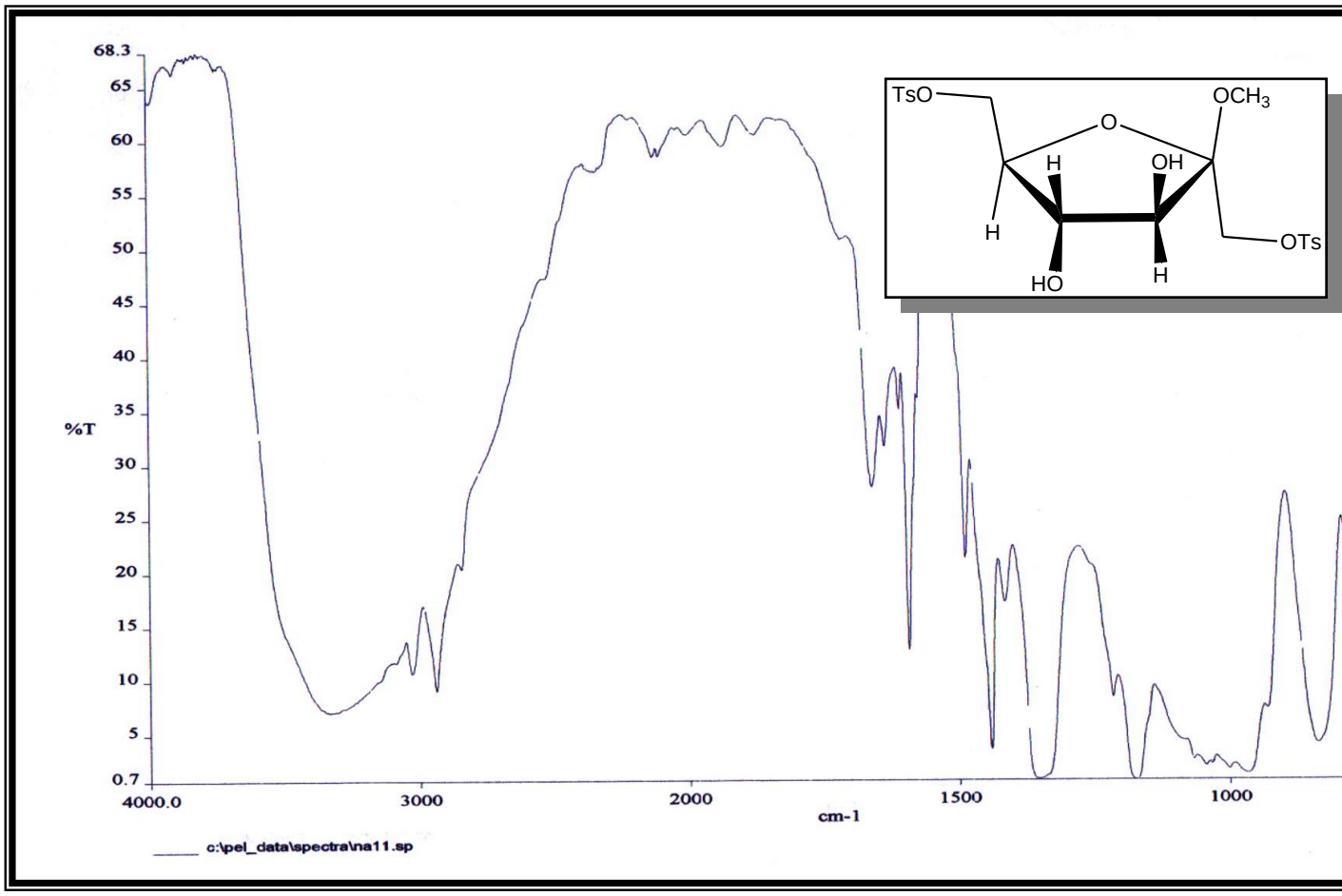


Figure (٣-٢٨) : IR Spectrum of compound [١٣٦]

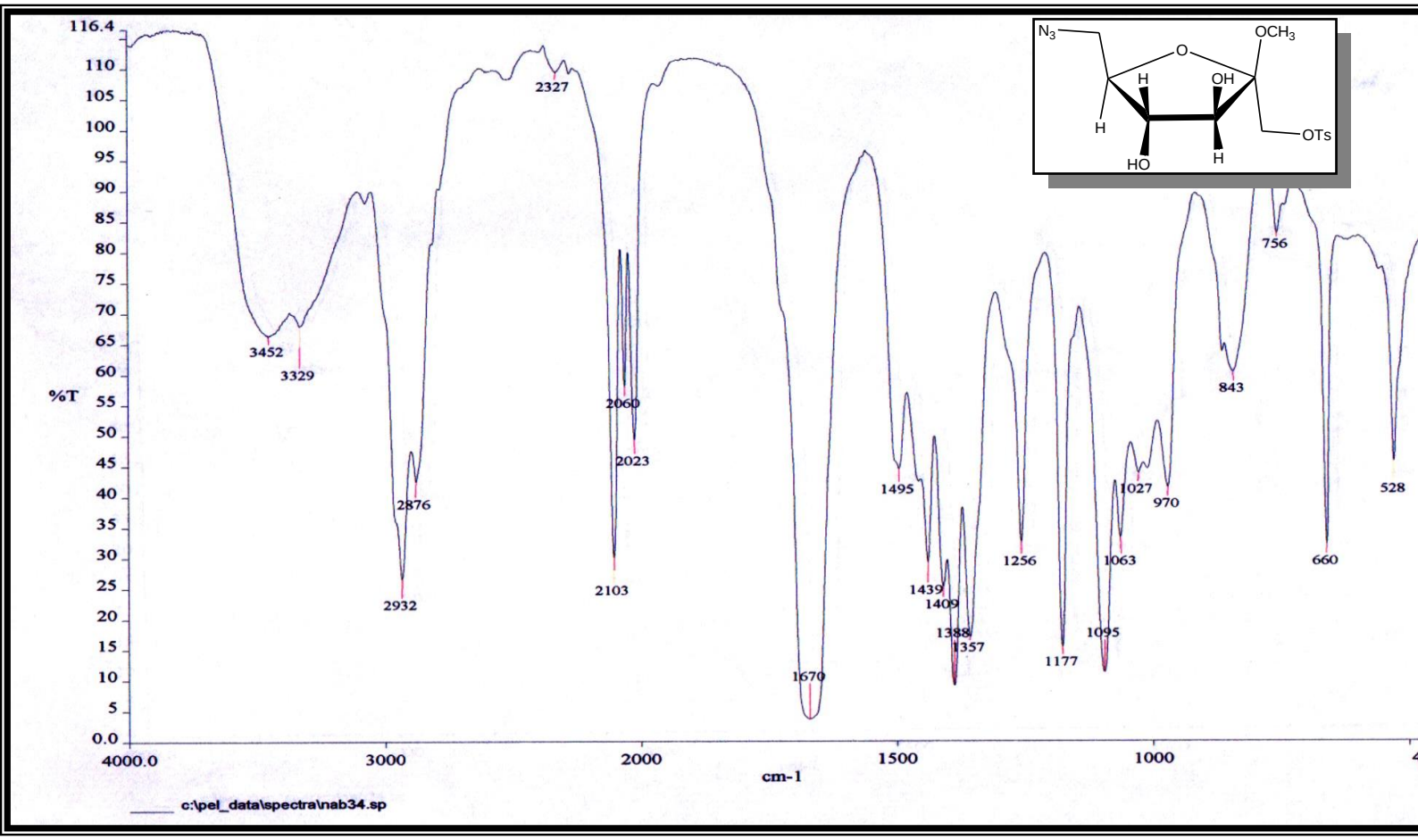
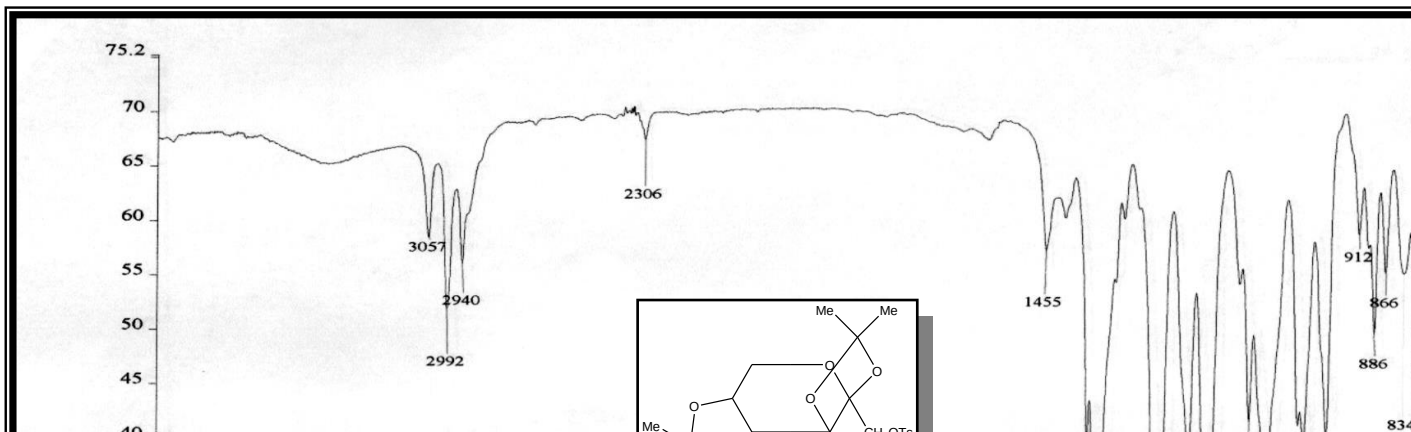


Figure (٣-٢٩) : IR Spectrum of compound [١٣٧]



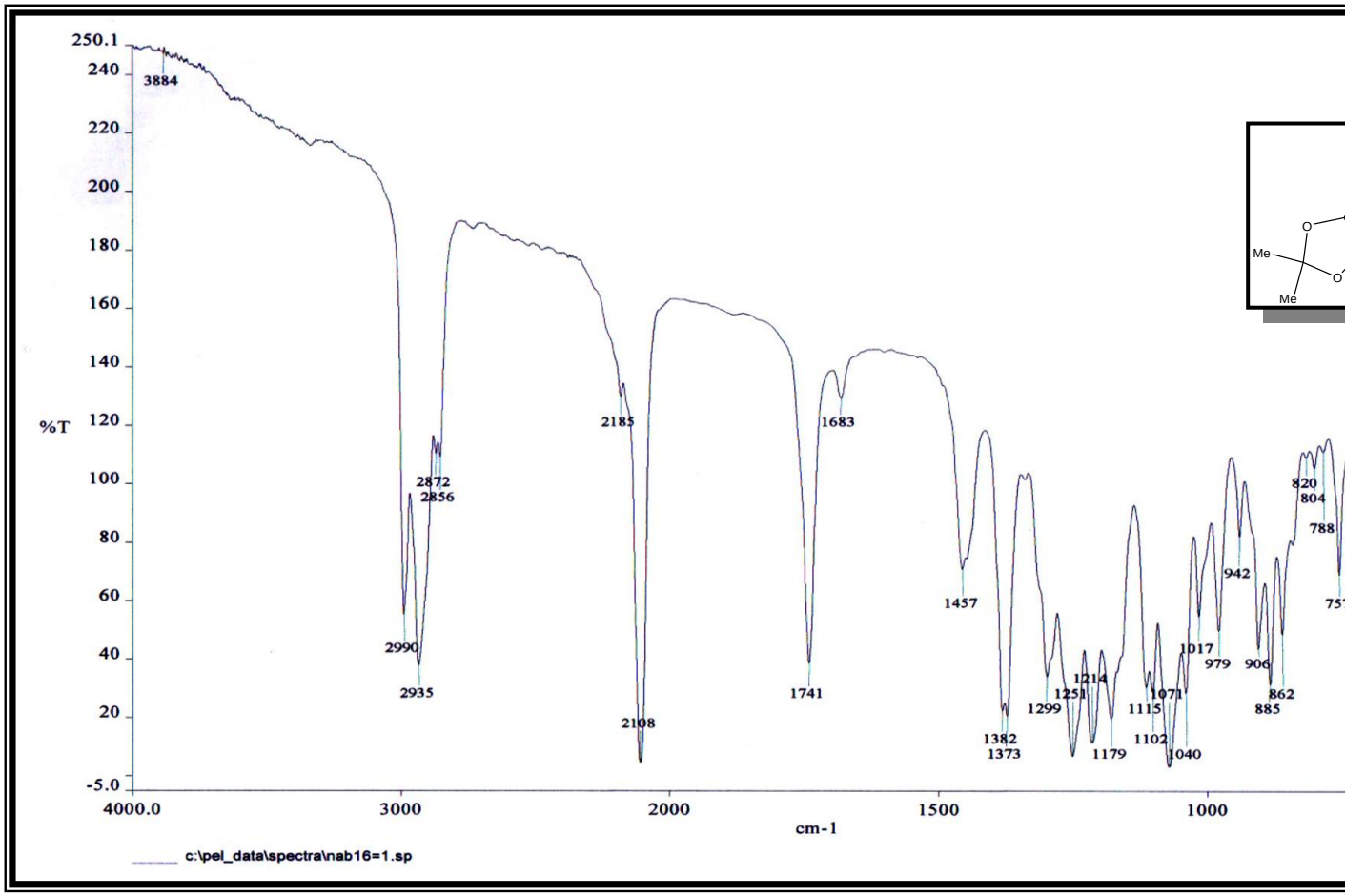
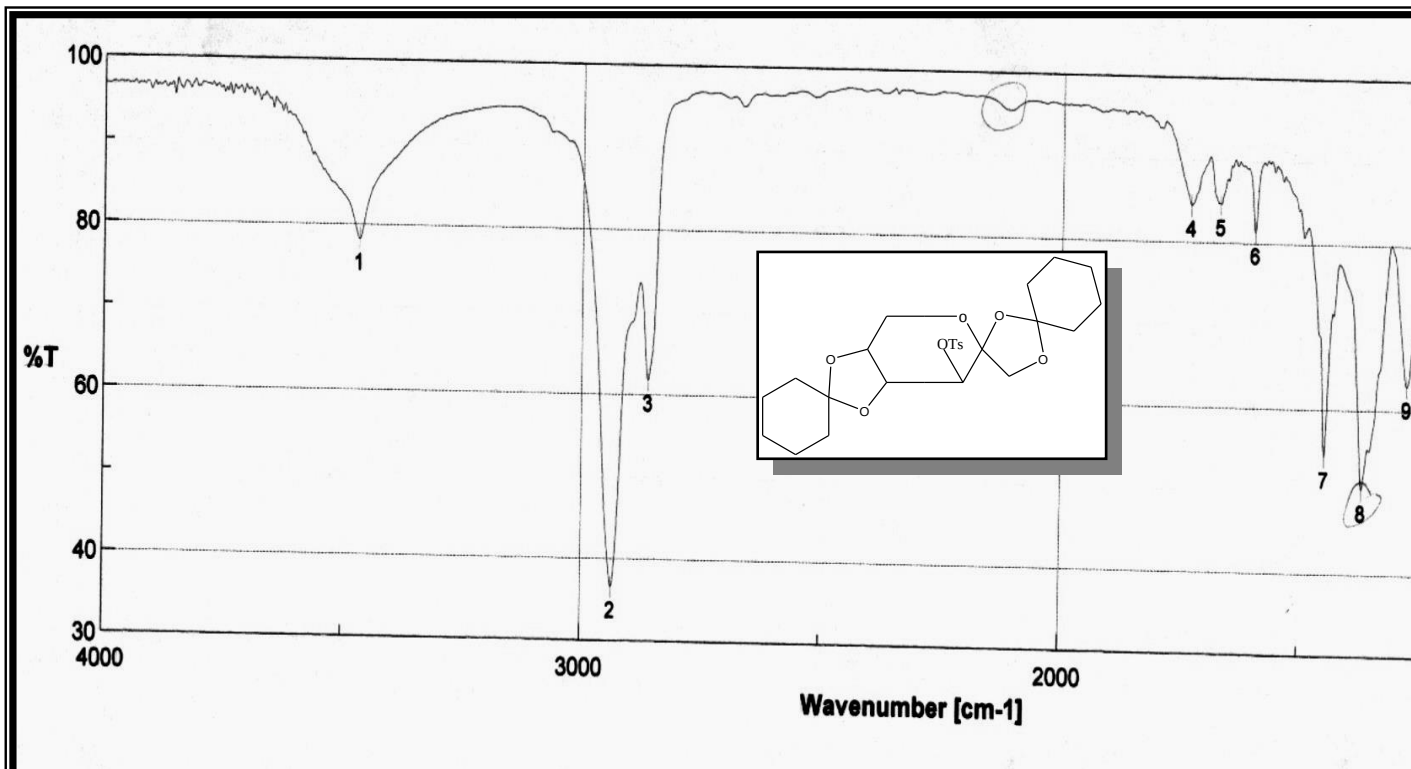


Figure (٣-٣١) : IR Spectrum of compound [١٣٩]


100
80
60
40
30
%T
4000
3000
2000
Wavenumber [cm-1]
1
2
3
4
5
6
7
8
9
QTs
O
O
O
O
O

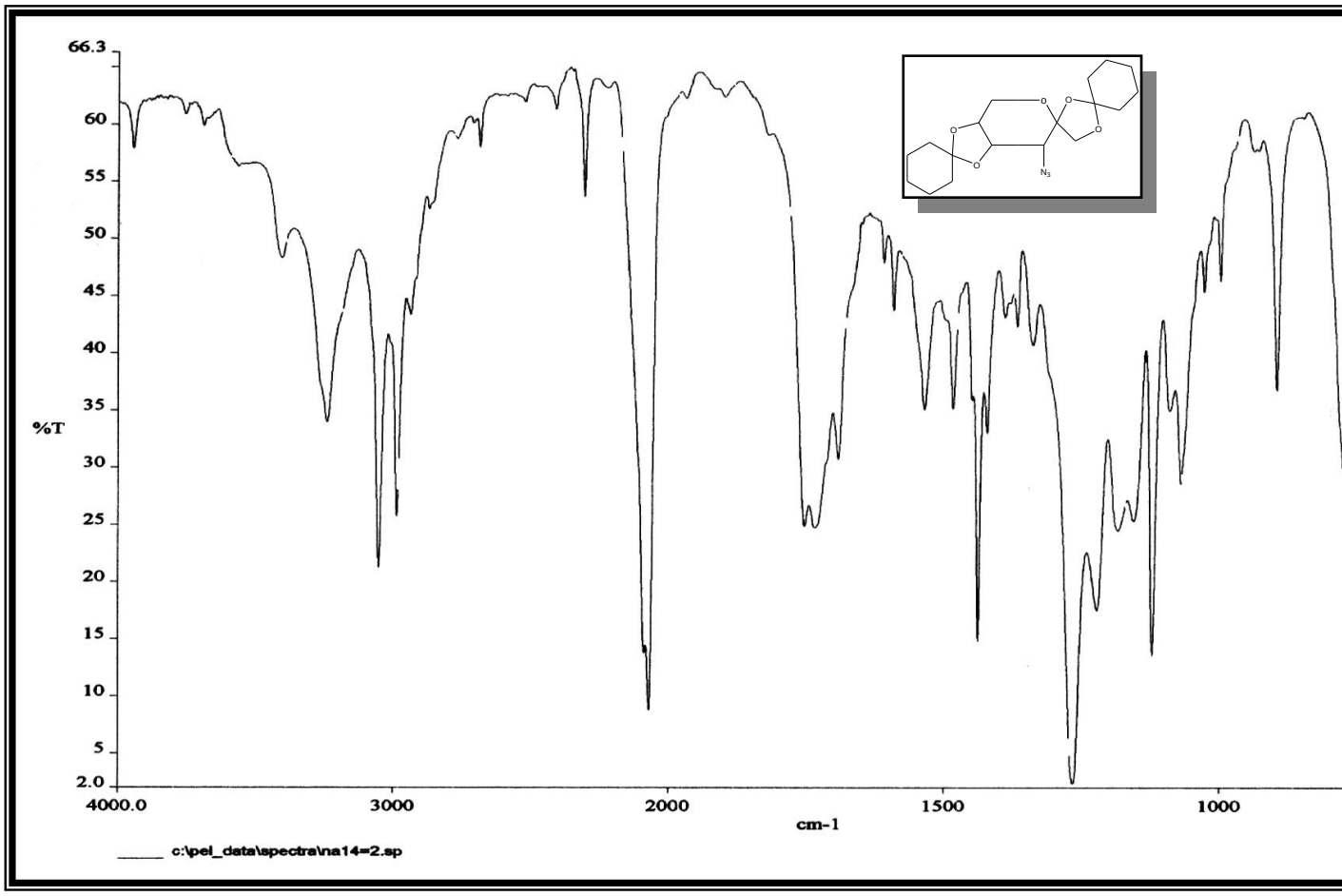
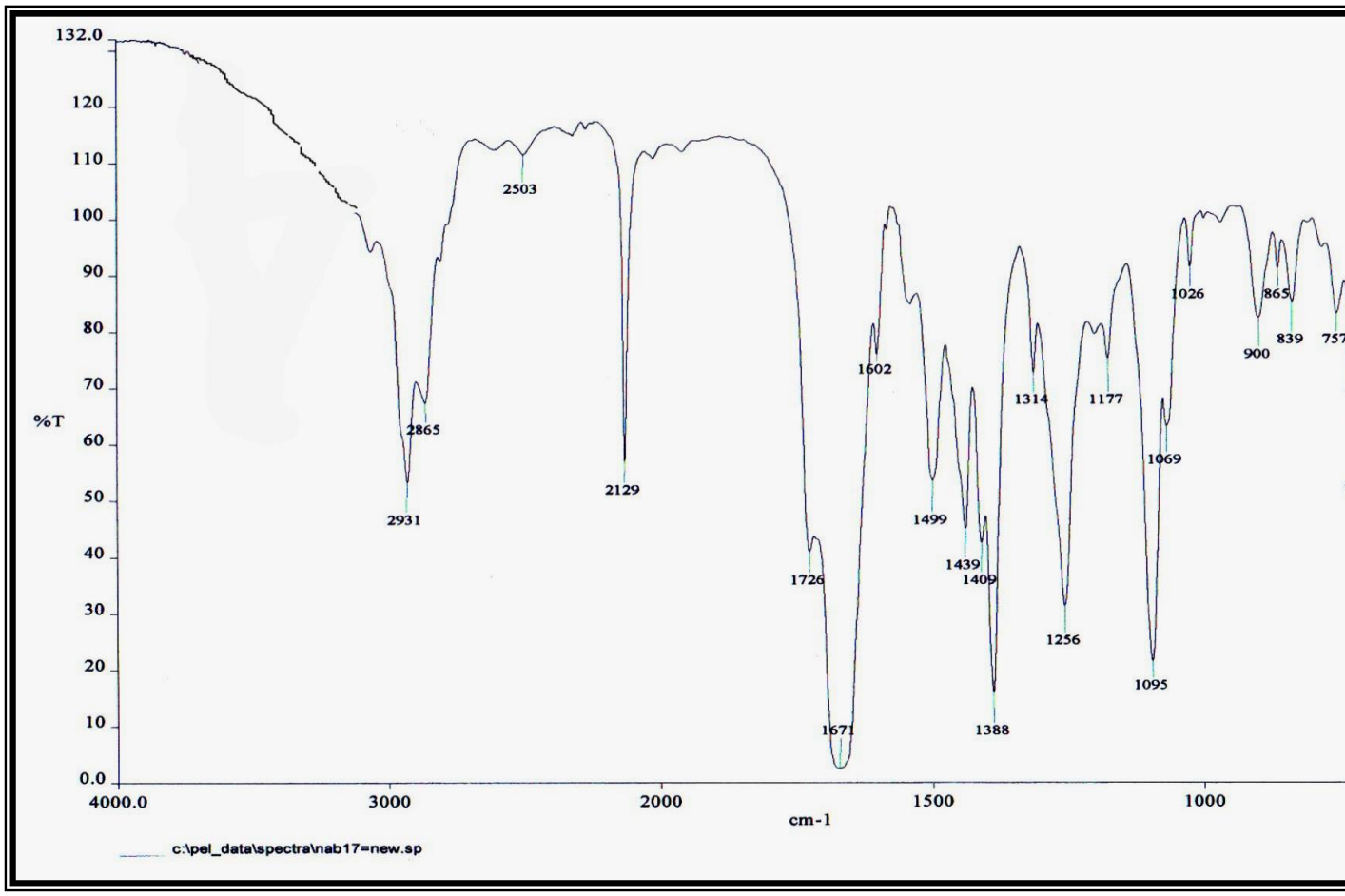


Figure (٣-٣٣) : IR Spectrum of compound [١٤١]


132.0
120
110
100
90
80
70
60
50
40
30
20
10
0.0
%T
4000.0
3000
2000
1500
1000
cm-1
2931
2865
2503
2129
1726
1671
1602
1499
1439
1409
1388
1314
1256
1177
1095
1069
1026
900
865
839
c:\pel_data\spectra\nab17=new.sp

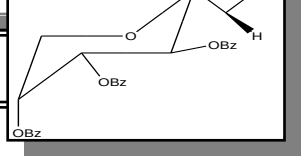
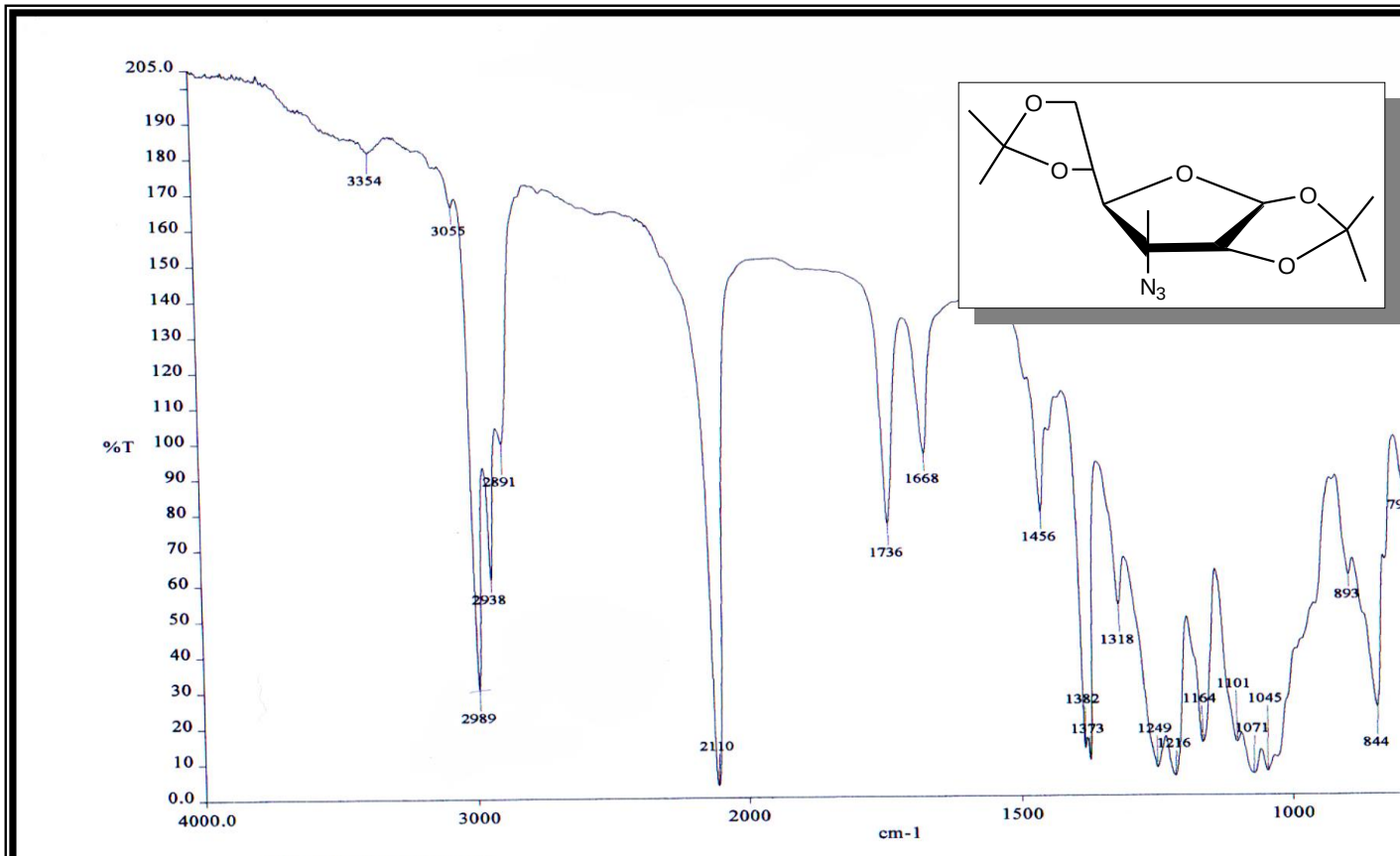


Figure (٣-٣٤) : IR Spectrum of compound [١٤٢]




104.4
100
95
90
85
80
75
70
65
3485
2945
1436
953
903
721
AcOH2C
H
O
H
OAc
H

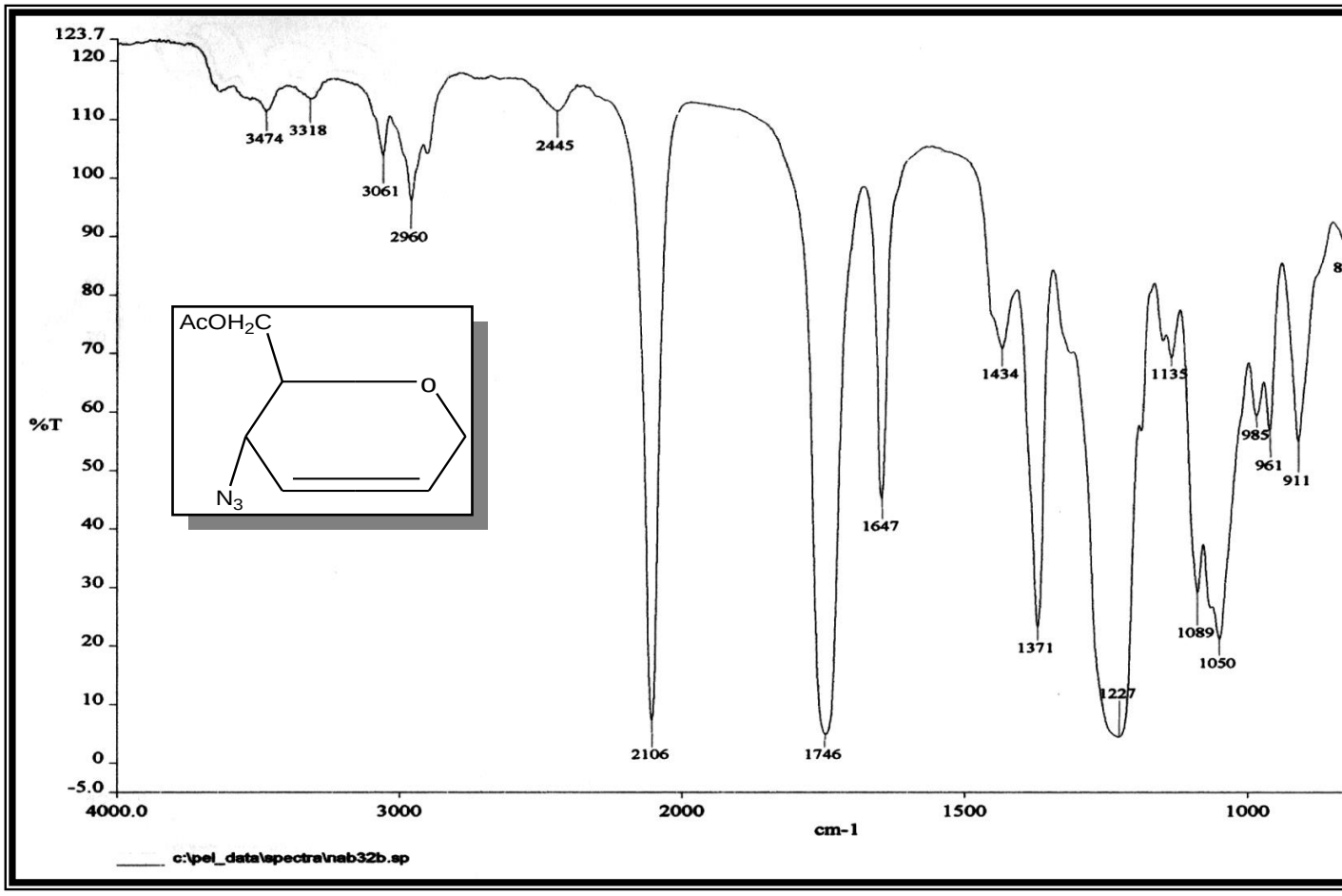


Figure (٣-٣٧) : IR Spectrum of compound [

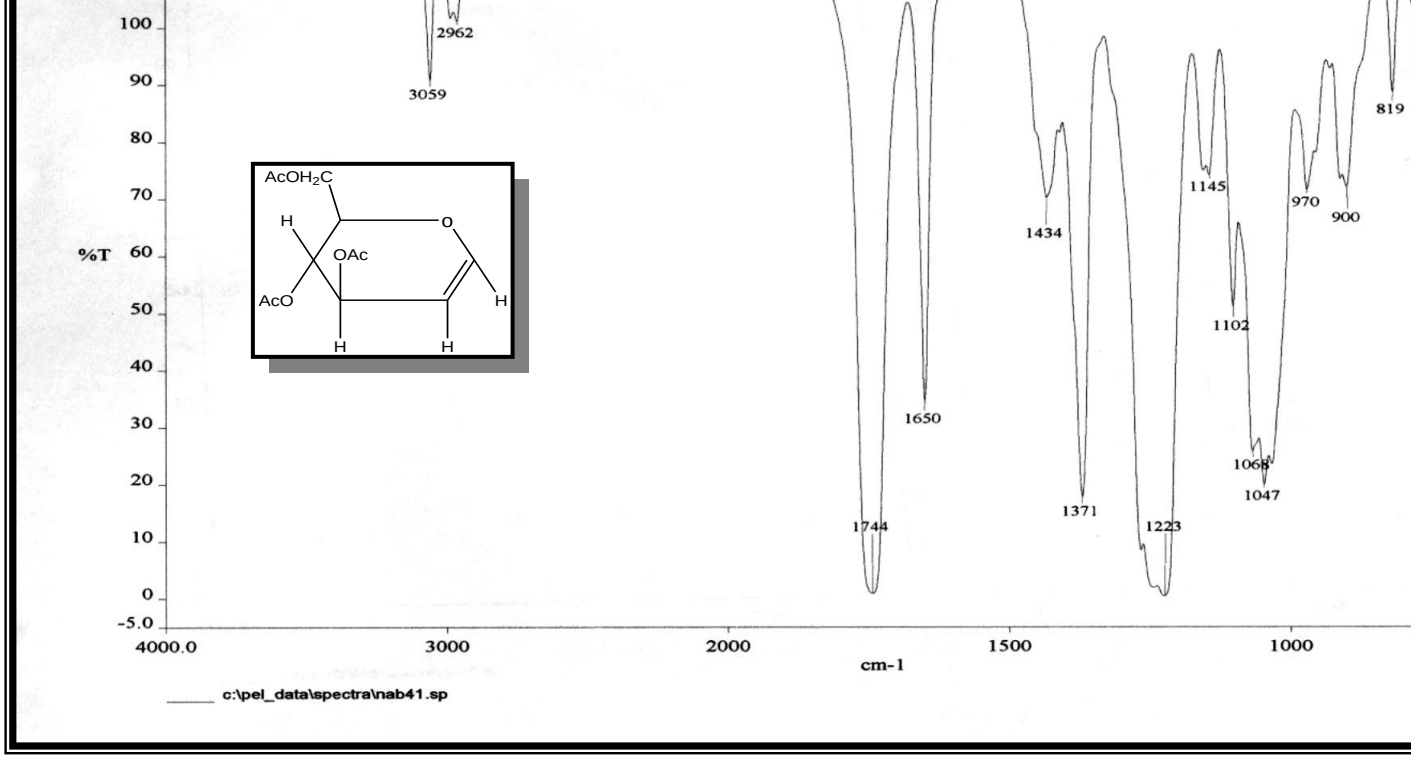
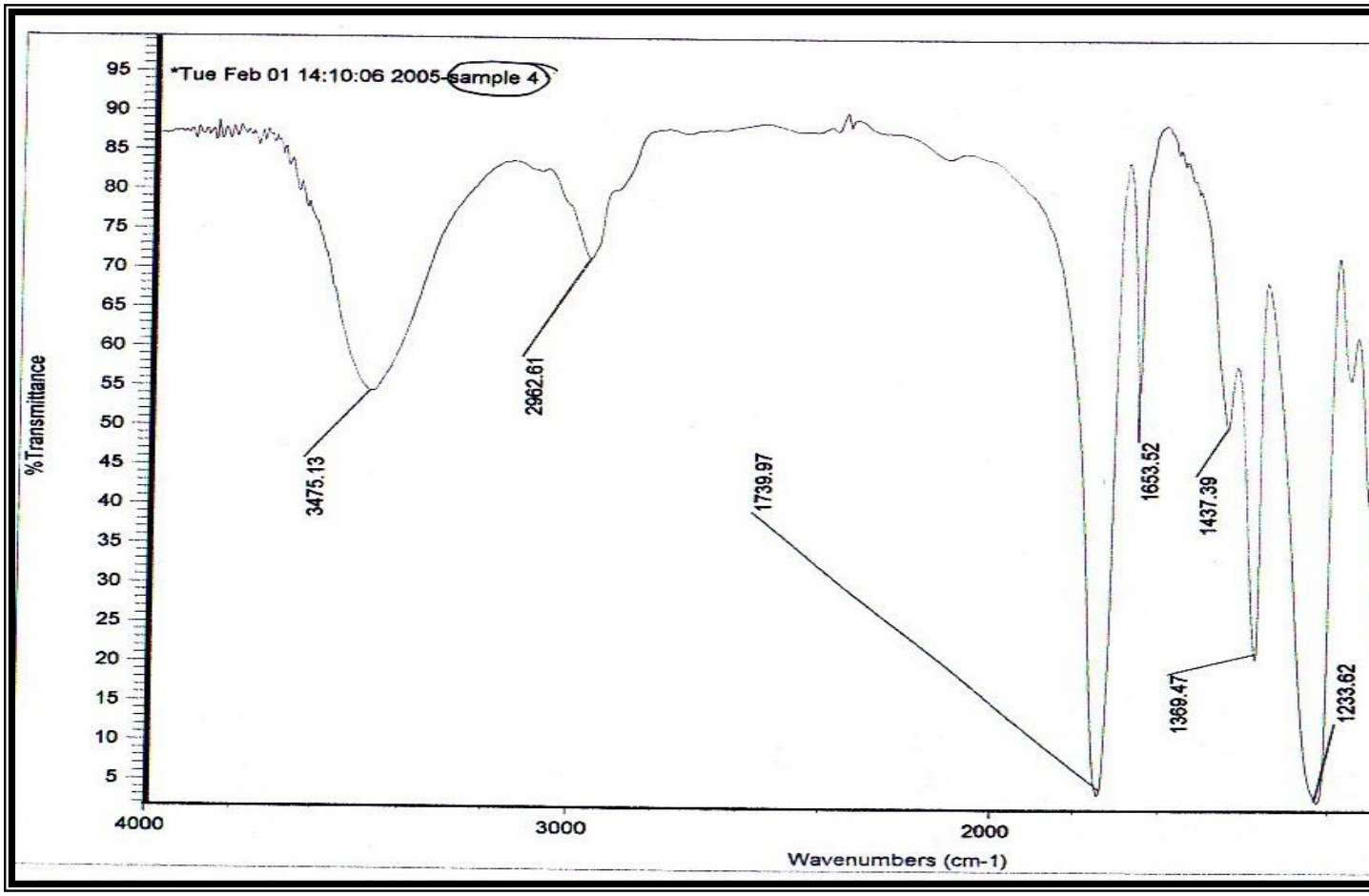


Figure (٣-٣٨) : IR Spectrum of compound [١٤٦]



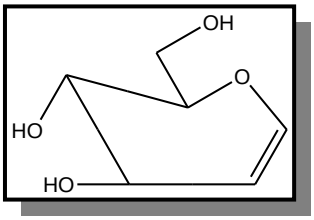
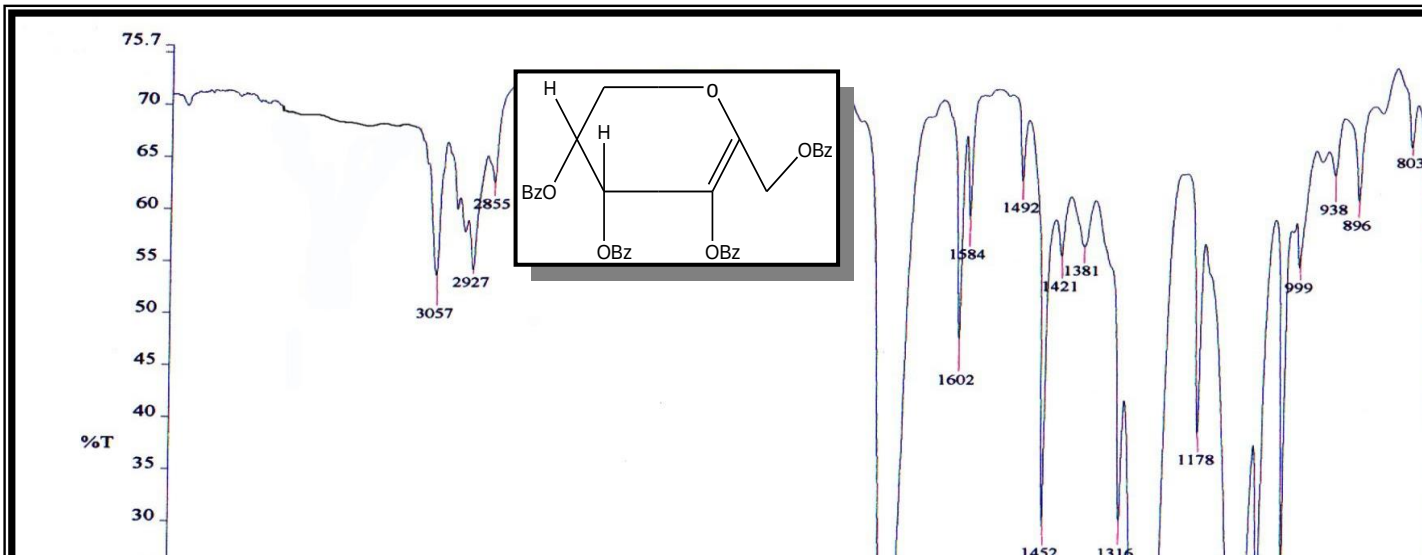


Figure (٣-٣٩): IR Spectrum of compound [١٤٦b]



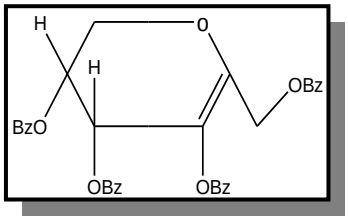
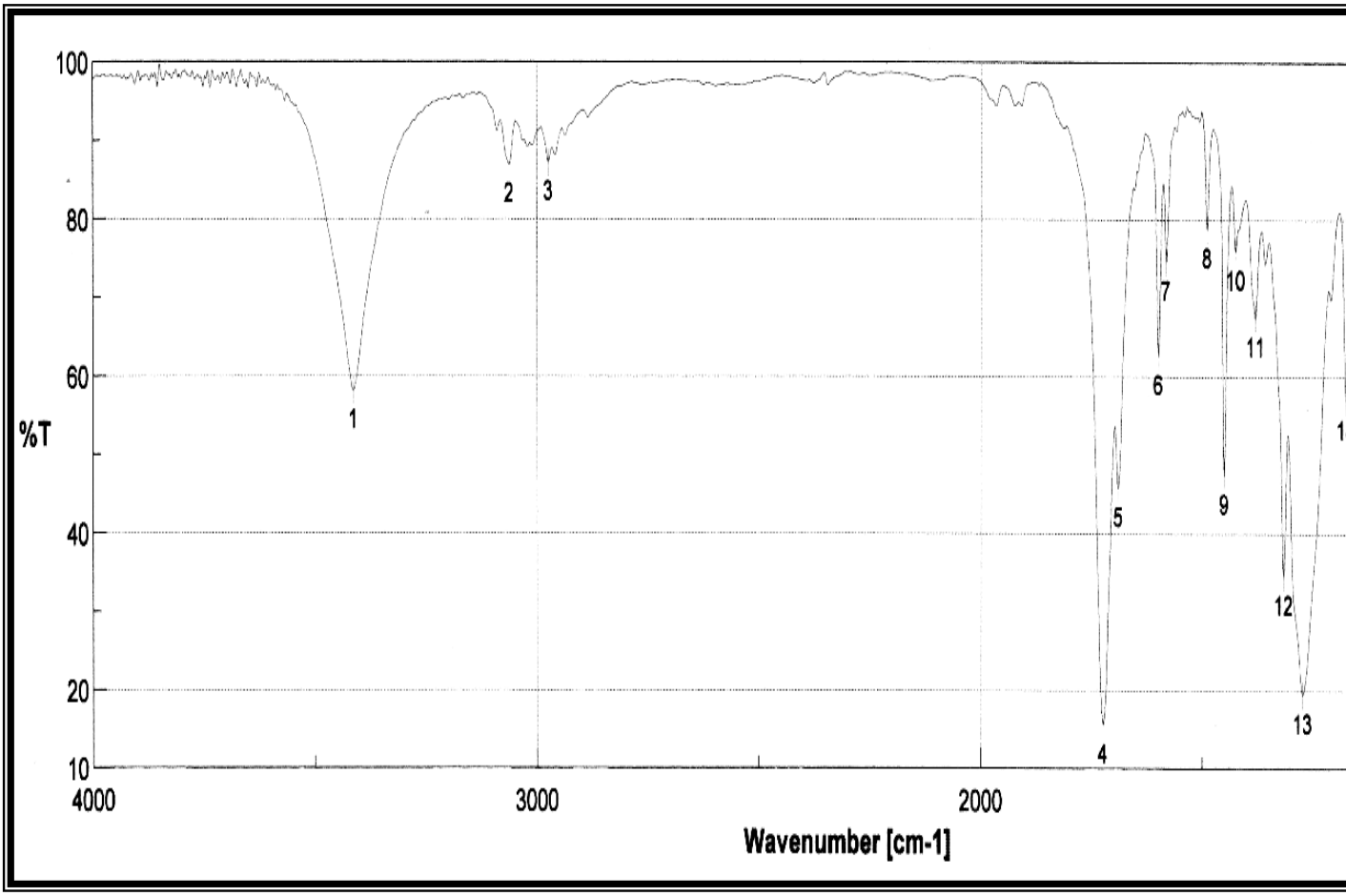
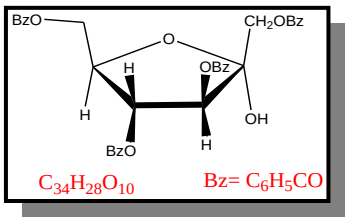


Figure (٣-٤٠): IR Spectrum of compound [١٤٧]





$C_{34}H_{28}O_{10}$ Bz= C_6H_5CO

Figure (٣-٤٠b): IR Spectrum of compound [١٣٢a]

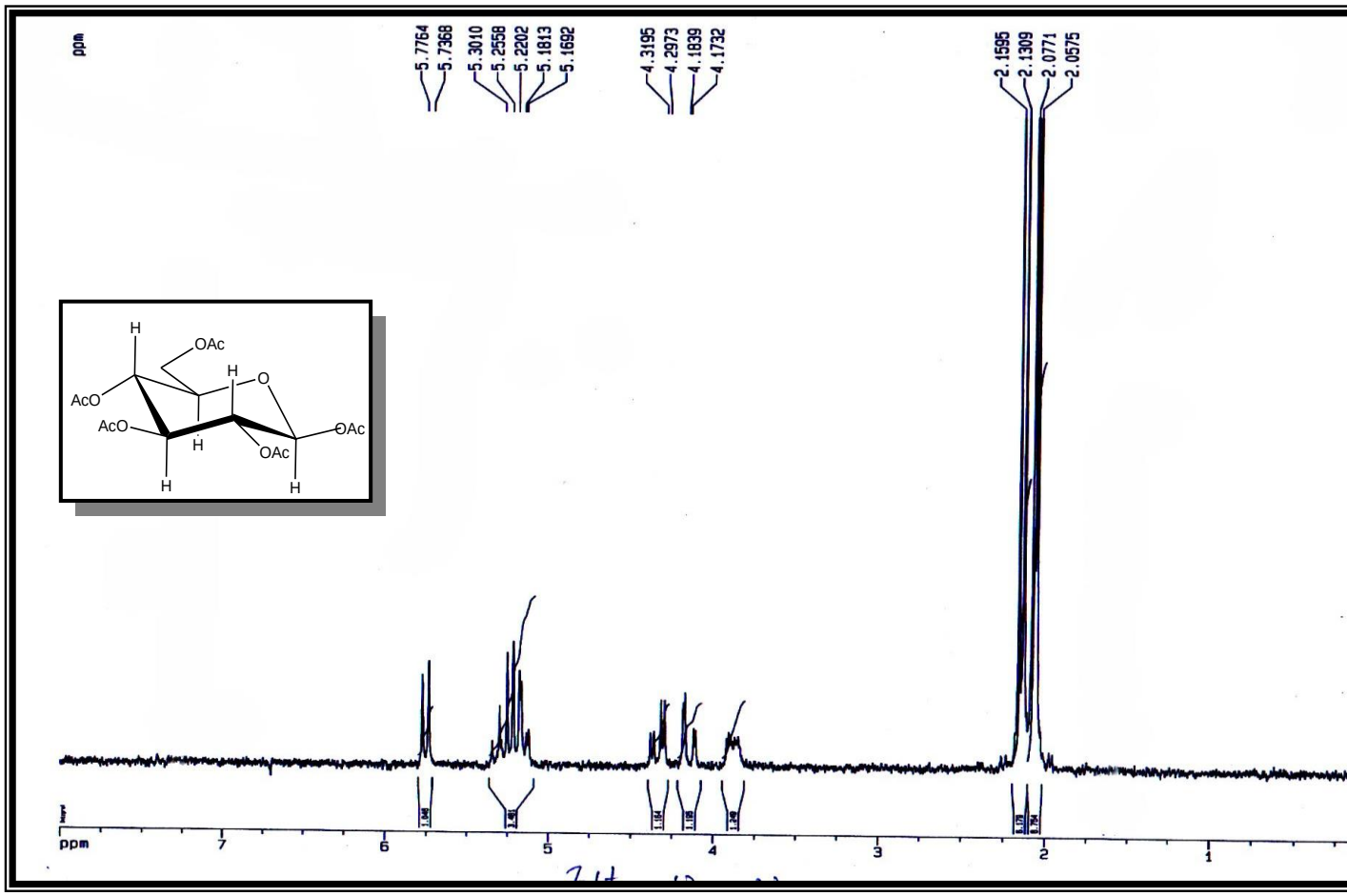


Figure (٣-٤١) : ^{1}H-MNR Spectrum of compound [

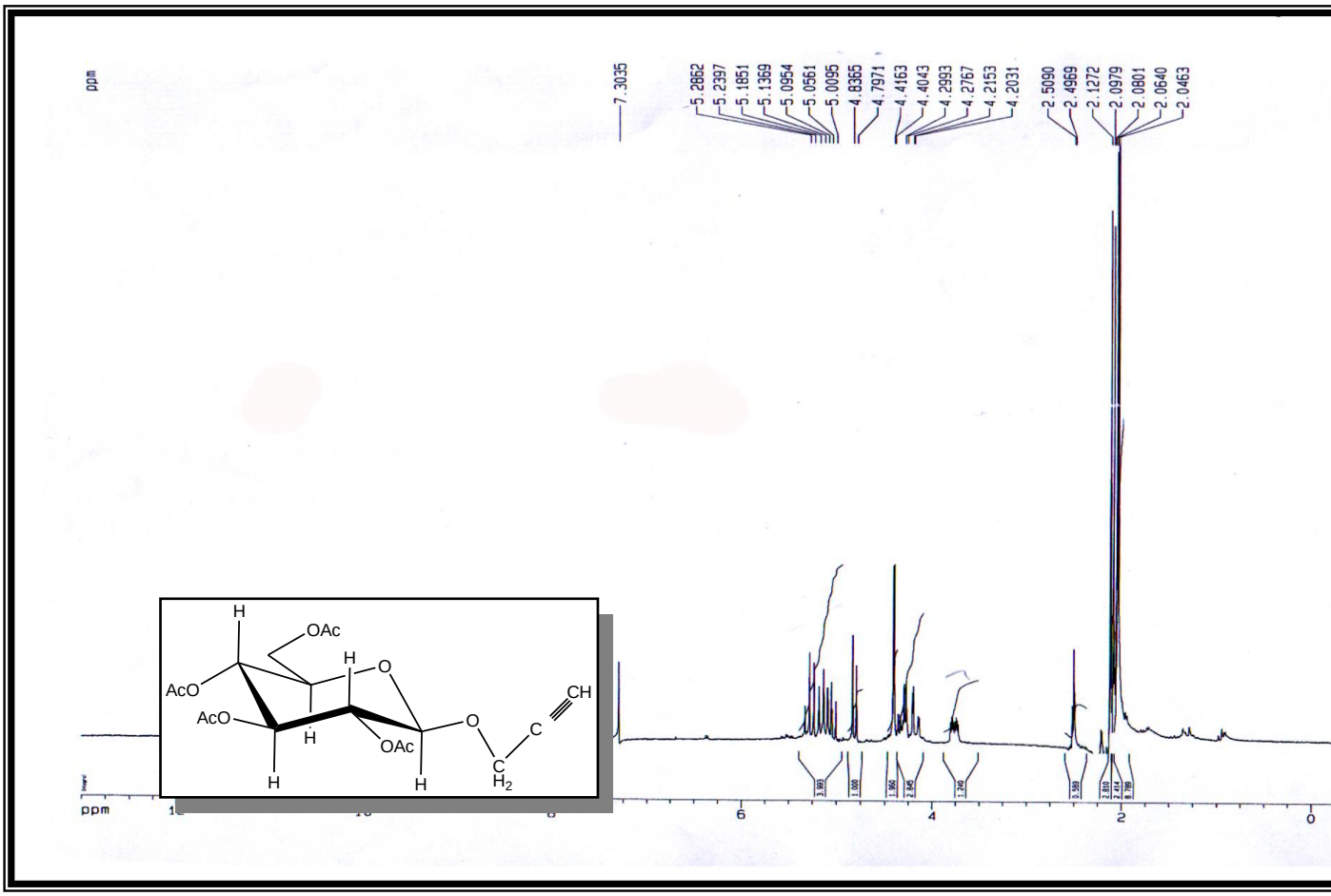
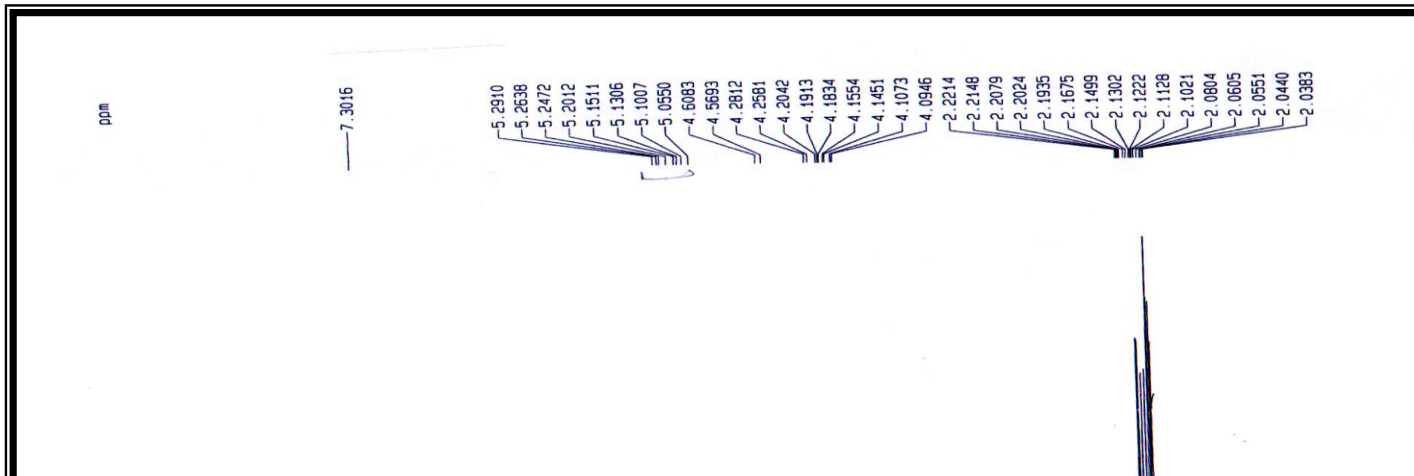
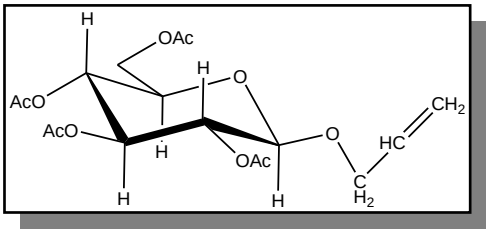

ppm
7.3035
5.2862
5.2397
5.1851
5.1369
5.0954
5.0561
5.0095
4.8365
4.7971
4.4163
4.4043
4.2993
4.2767
4.2153
4.2031
2.5090
2.4969
2.1272
2.0979
2.0801
2.0640
2.0463
H
OAc
H
O
AcO
CH
AcO
O
C
H
OAc
C
H
H
H
H2
ppm
6
4
2
0

Figure (٣-٤٢) : ^{1}H-MNR Spectrum of compound [١١٥]




H
OAc
H
O
AcO
CH2
AcO
O
HC
H
OAc
C
H2
H
H

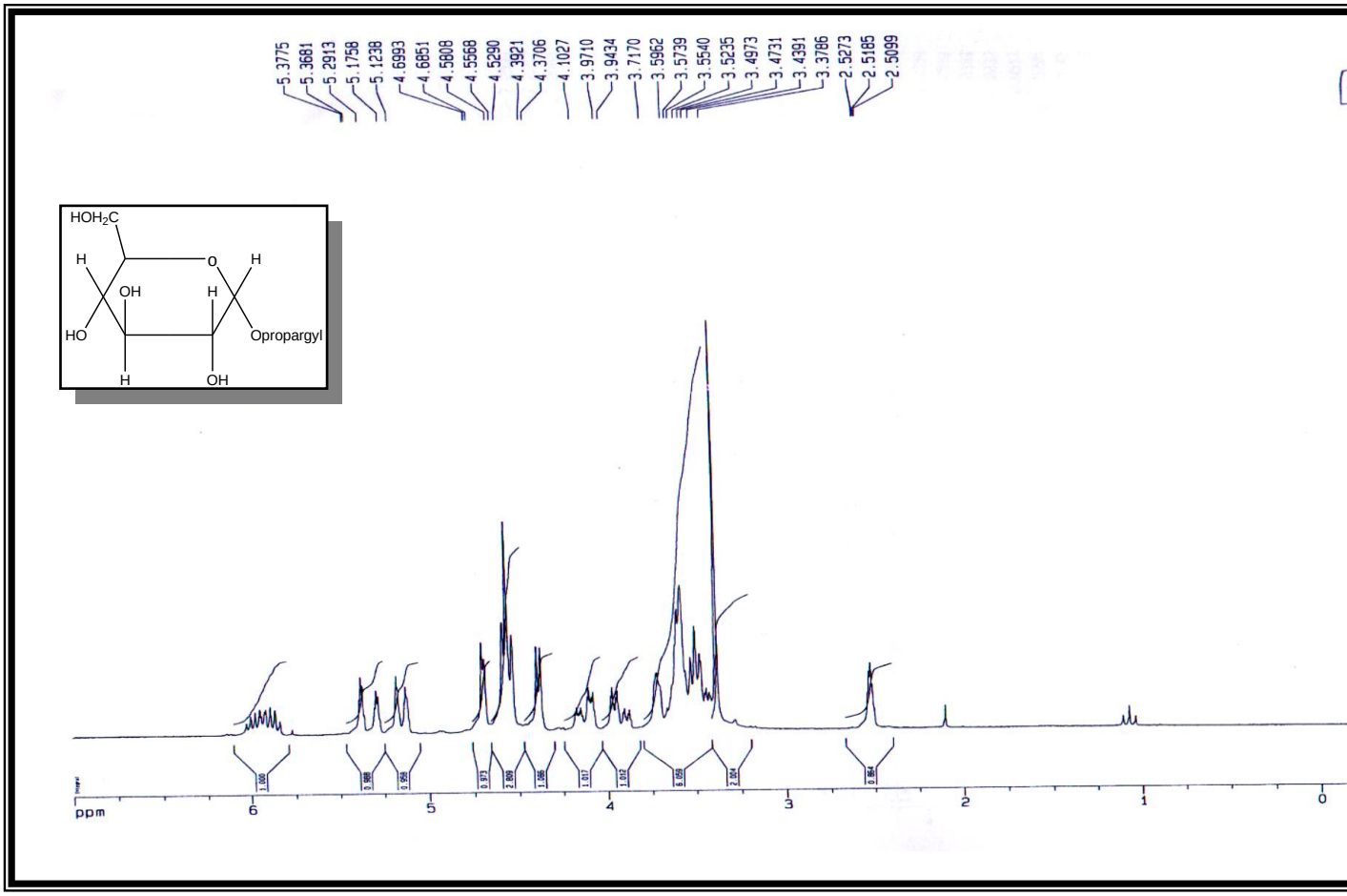
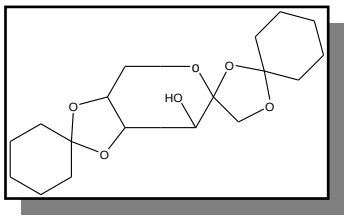


Figure (٣-٤٤) : ^{1}H-MNR Spectrum of compound [١٢


O
O
HO
O
O
O

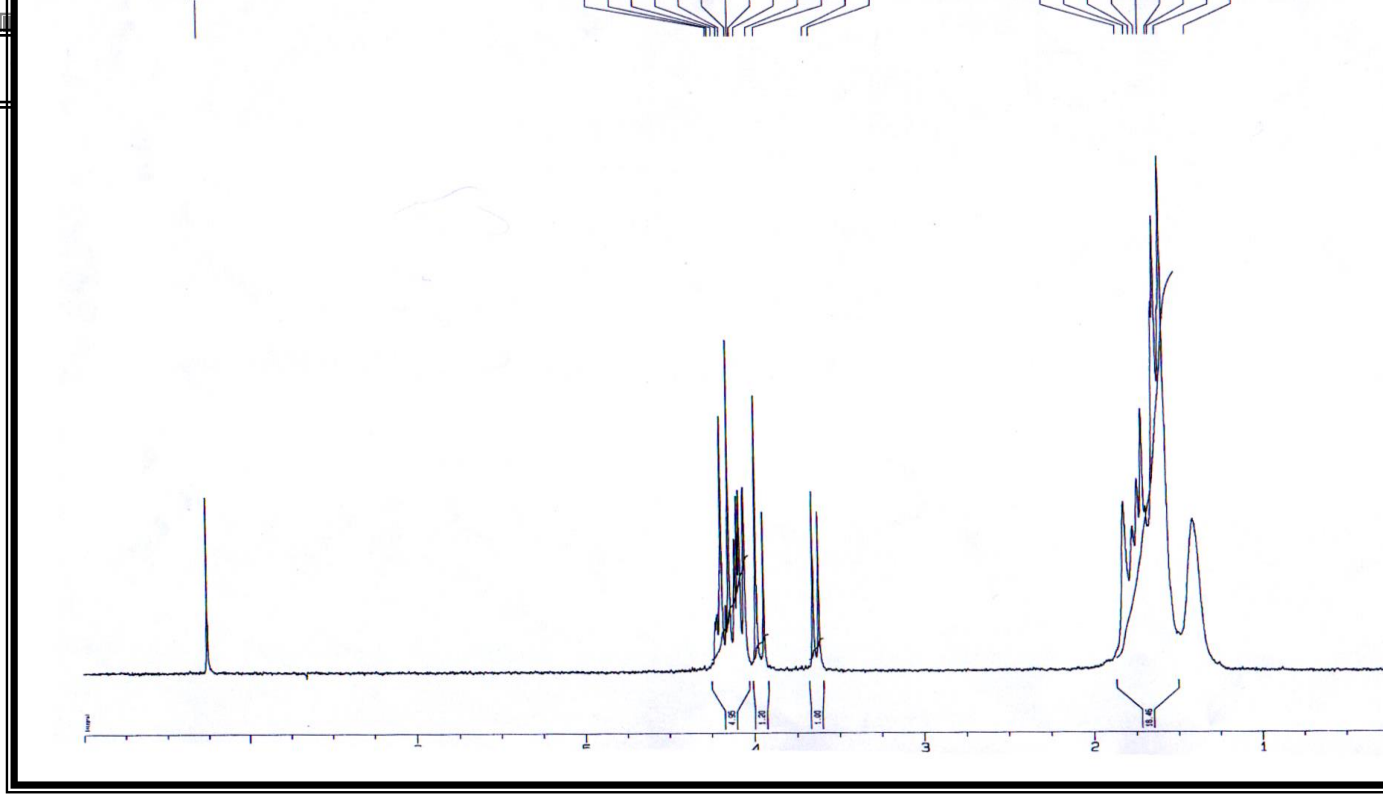


Figure (٣-٤٥) : ^{1}H-MNR Spectrum of compound [١٢١

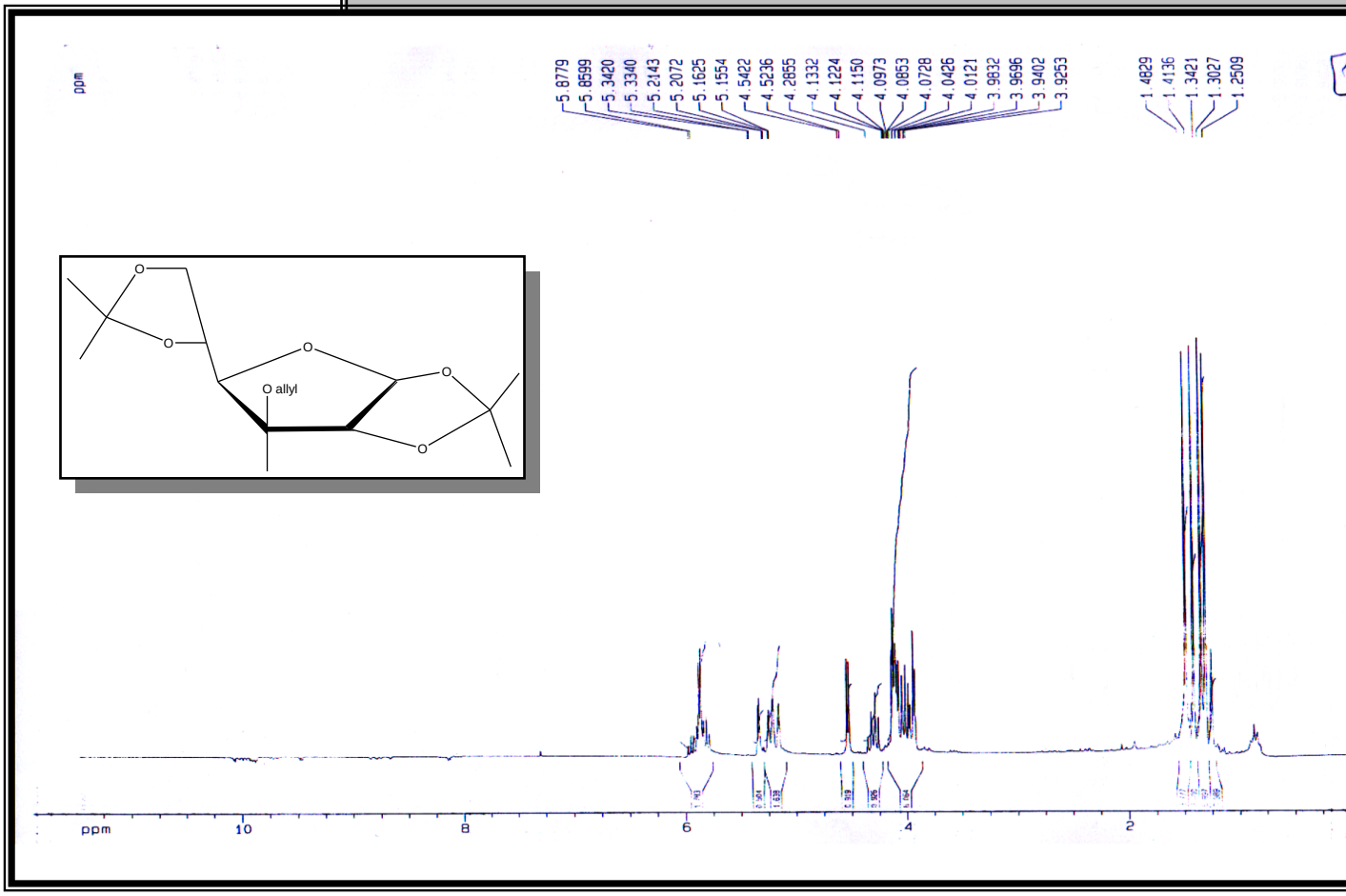
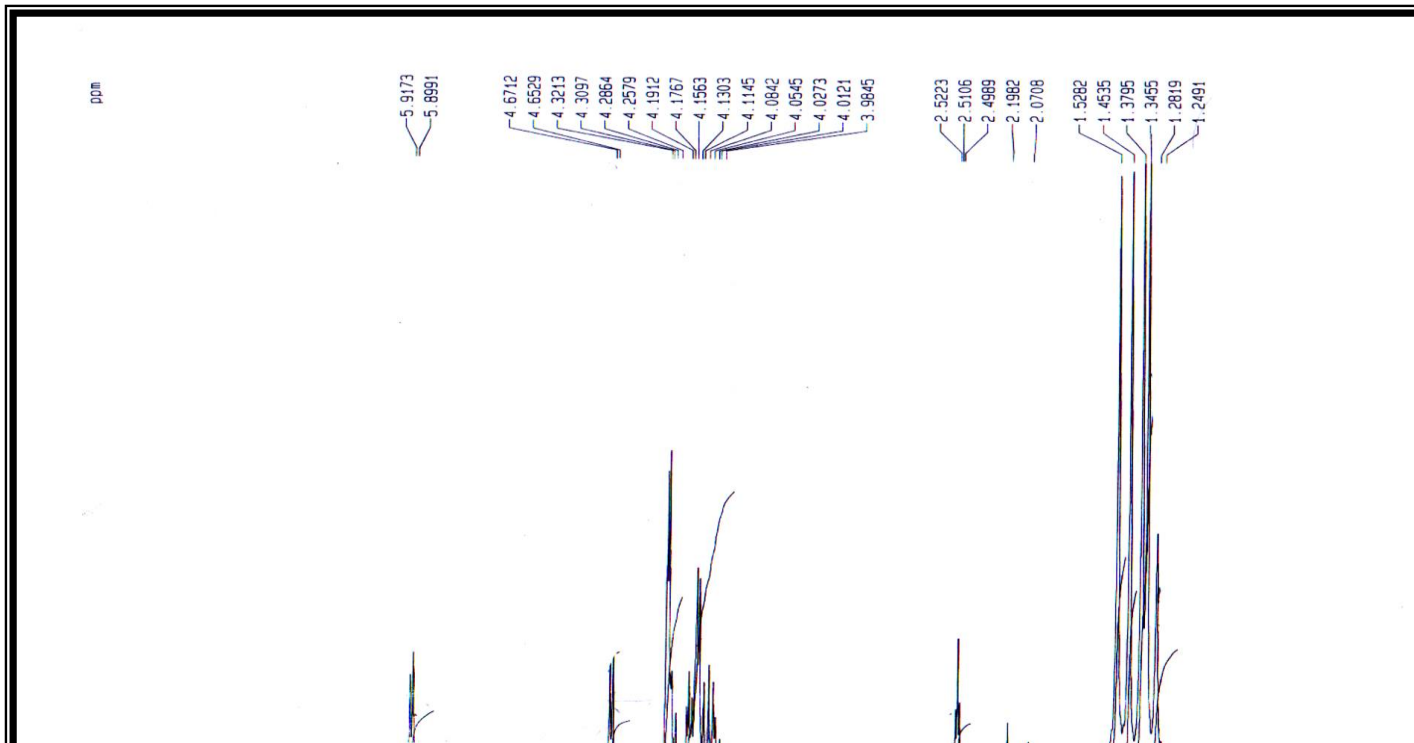
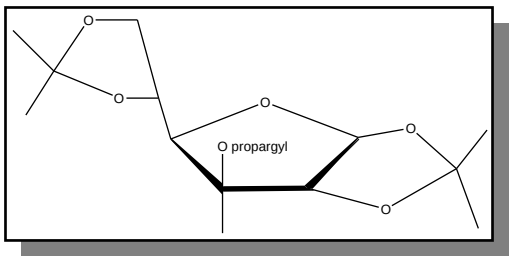


Figure (٣-٤٦) : ^{1}H-MNR Spectrum of compound [١٢٥




O
O
O
O propargyl
O
O

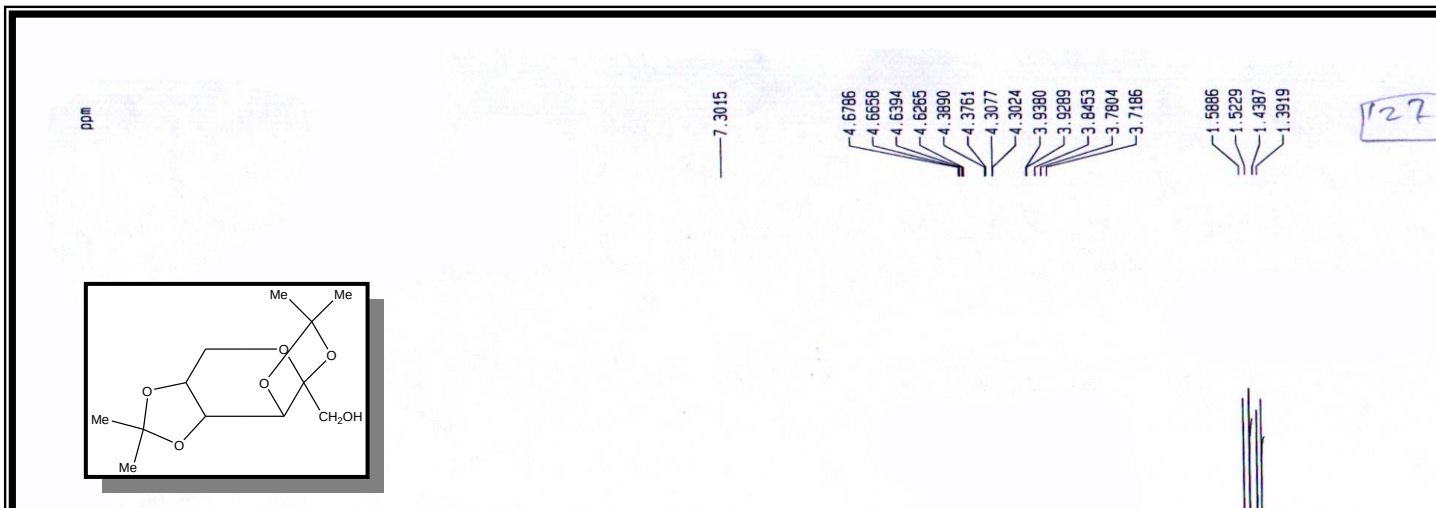
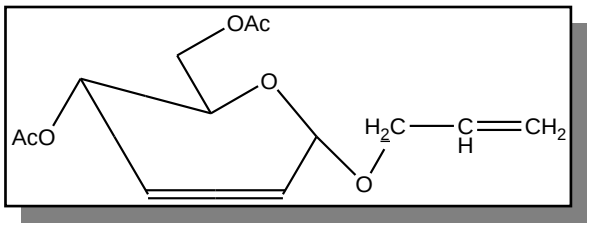

ppm
7.3015
4.6786
4.6658
4.6394
4.6265
4.3890
4.3761
4.3077
4.3024
3.9380
3.9289
3.8453
3.7804
3.7186
1.5886
1.5229
1.4387
1.3919
127
Me
Me
O
O
O
O
Me
O
CH2OH
Me

Figure (٣-٤٨) : ^{١}H-MNR Spectrum of compound [١٢٧]


OAc
O
AcO
H2C
C
H
CH2
O

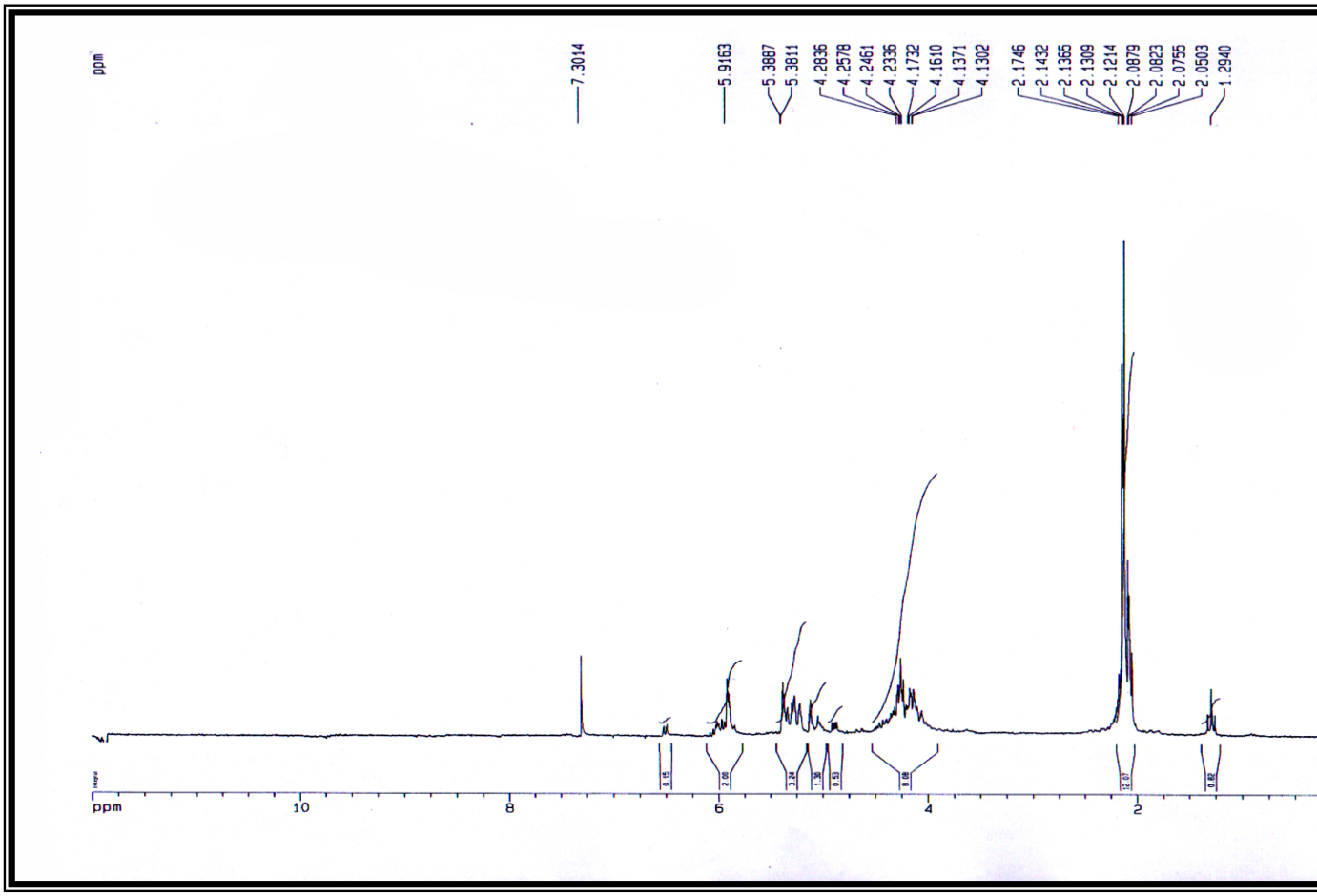


Figure (٣-٤٩) : ^{1}H-MNR Spectrum of compound [

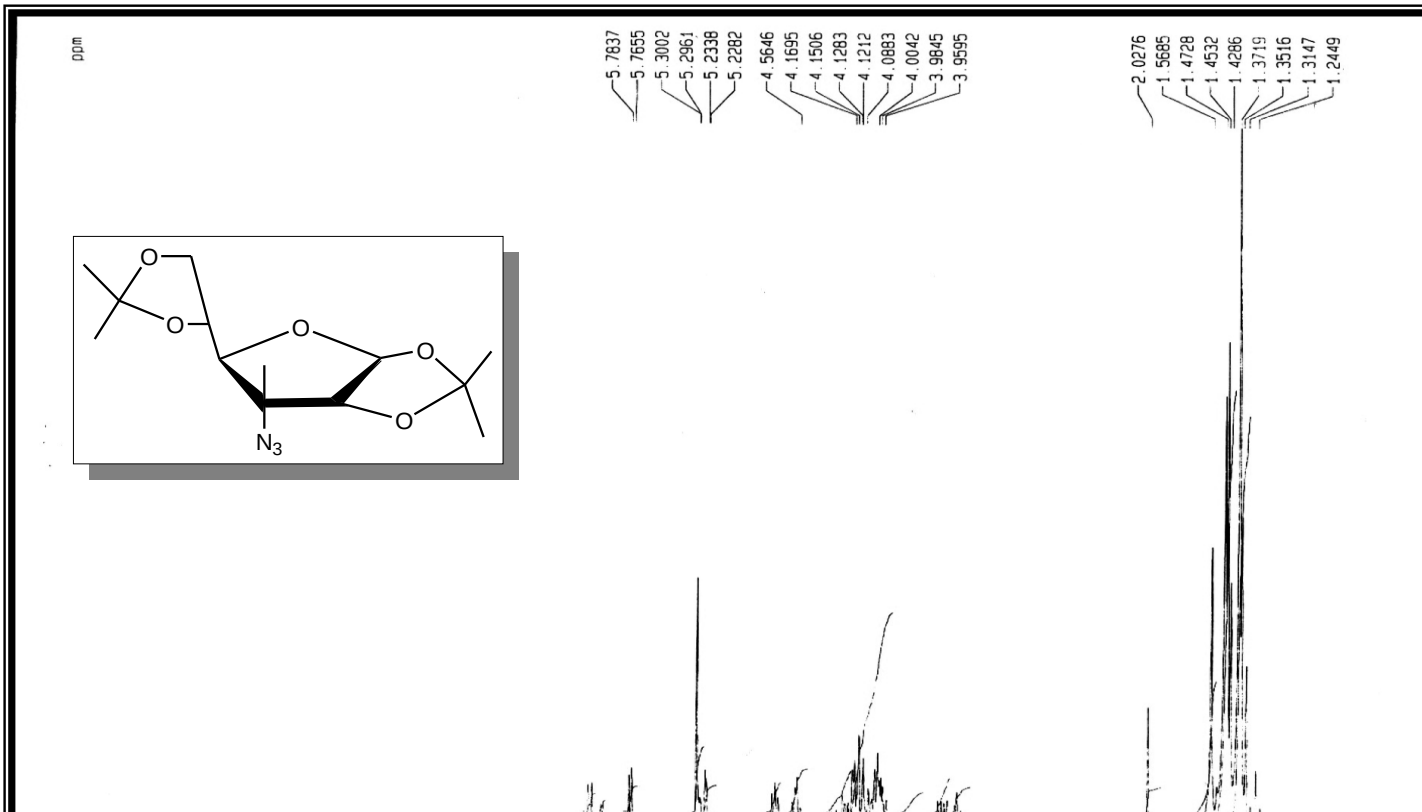


Figure (٣-٥٠) : ^{1}H-MNR Spectrum of compound [١٤٣]

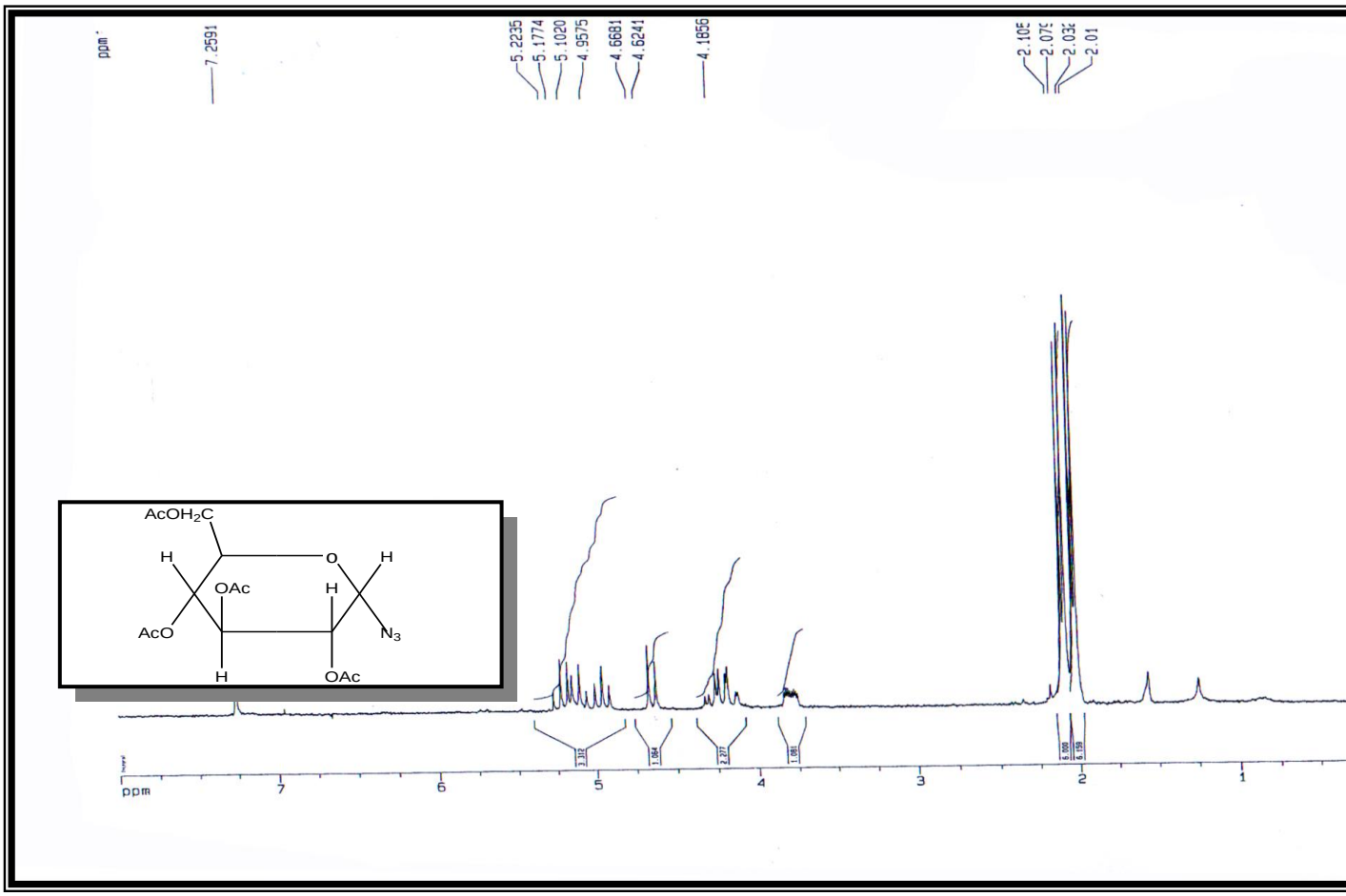


Figure (٣-٥١) : ^{1}H-MNR Spectrum of compound [١٤٤]

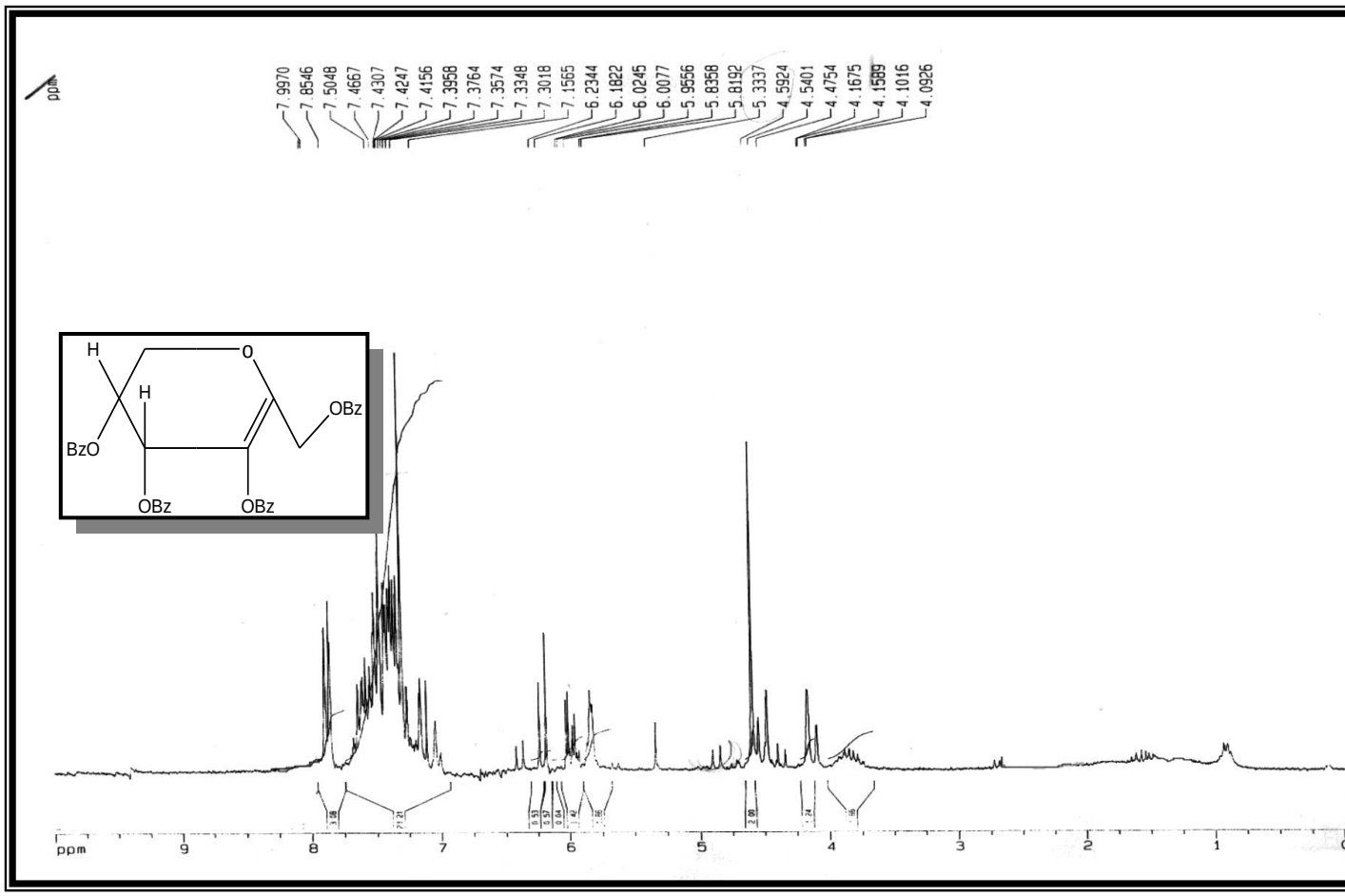

ppm
7.9970
7.8546
7.5048
7.4667
7.4307
7.4247
7.4156
7.3958
7.3764
7.3574
7.3348
7.3018
7.1565
6.2344
6.1822
6.0245
6.0077
5.9556
5.8358
5.8192
5.3337
4.5924
4.5401
4.4754
4.1675
4.1589
4.1016
4.0926
H
O
H
OBz
BzO
OBz
OBz
ppm
9
8
7
6
5
4
3
2
1

Figure (٣-٥٢) : ^{١}H-MNR Spectrum of compound [١٤٧]

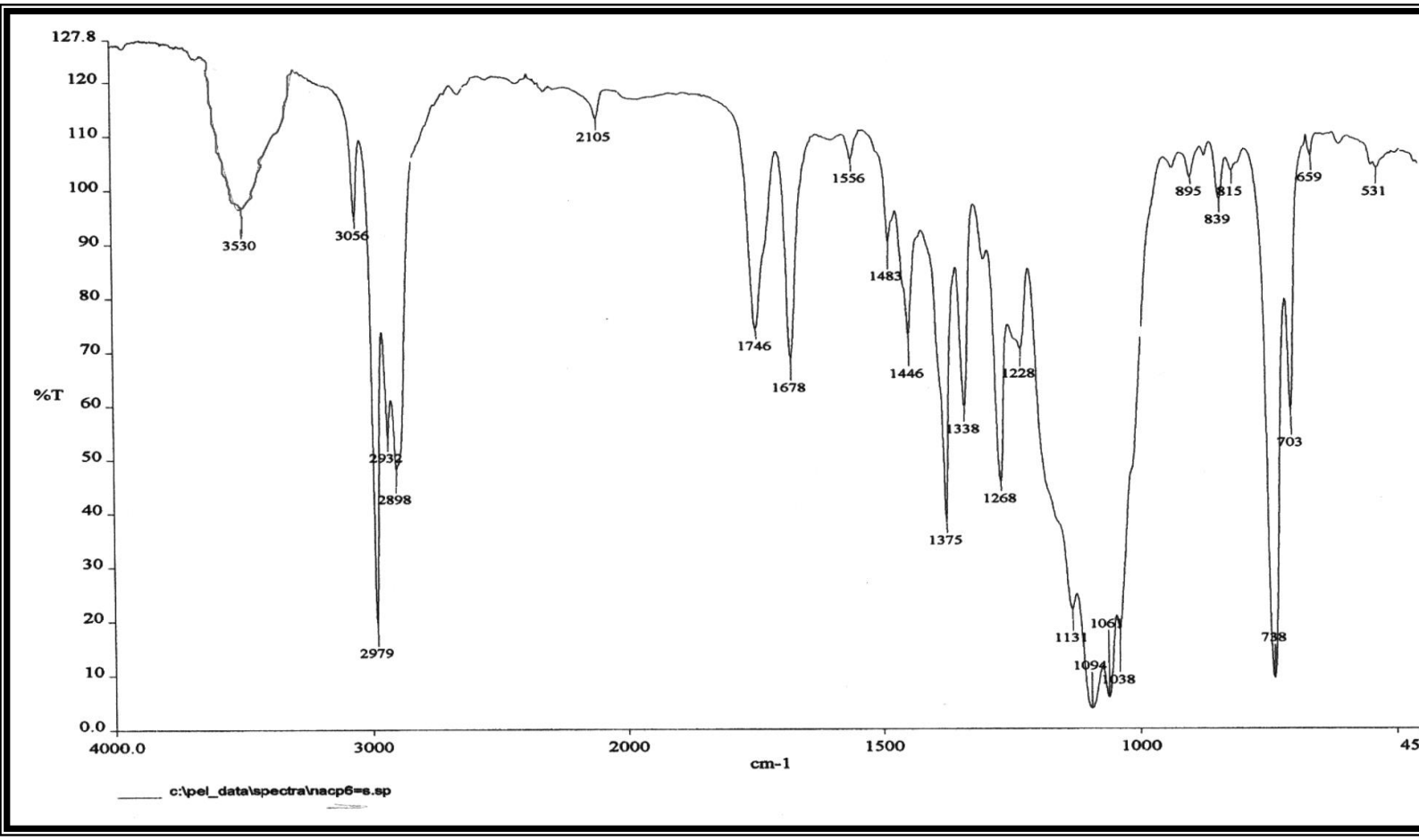
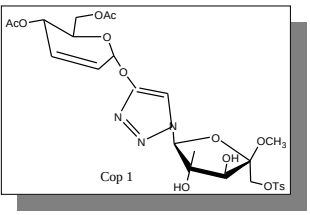
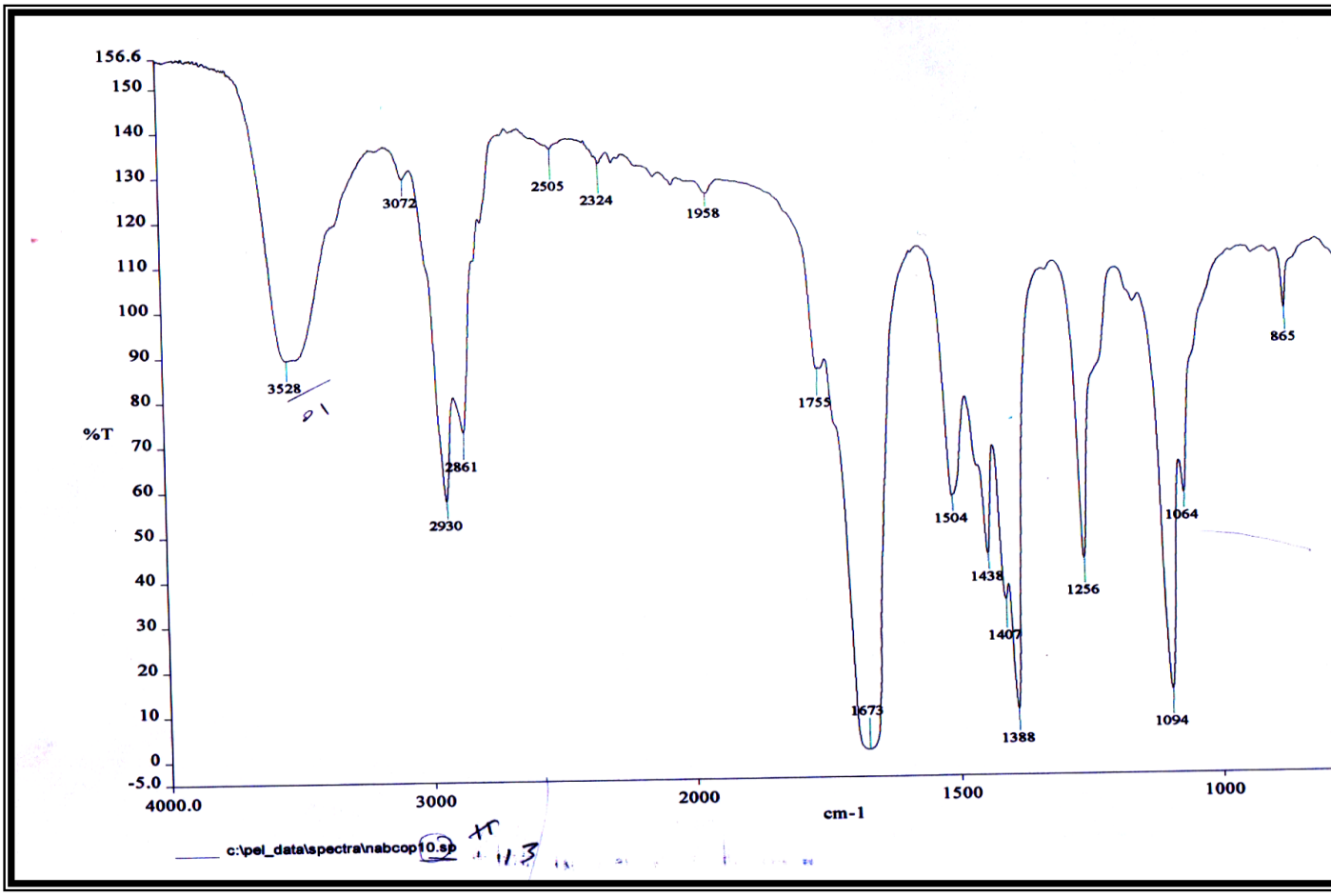


Figure (٣-٥٣) : IR Spectrum of compound [cop١]



Cop 1


156.6
150
140
130
120
110
100
90
80
%T
70
60
50
40
30
20
10
0
-5.0
4000.0
3000
2000
1500
1000
cm-1
3528
3072
2930
2861
2505
2324
1958
1755
1673
1504
1438
1407
1388
1256
1094
1064
865
c:\pel_data\spectra\nabcop10.sp

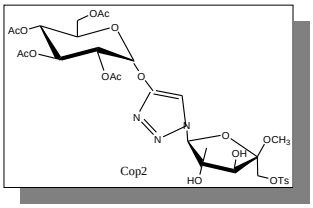
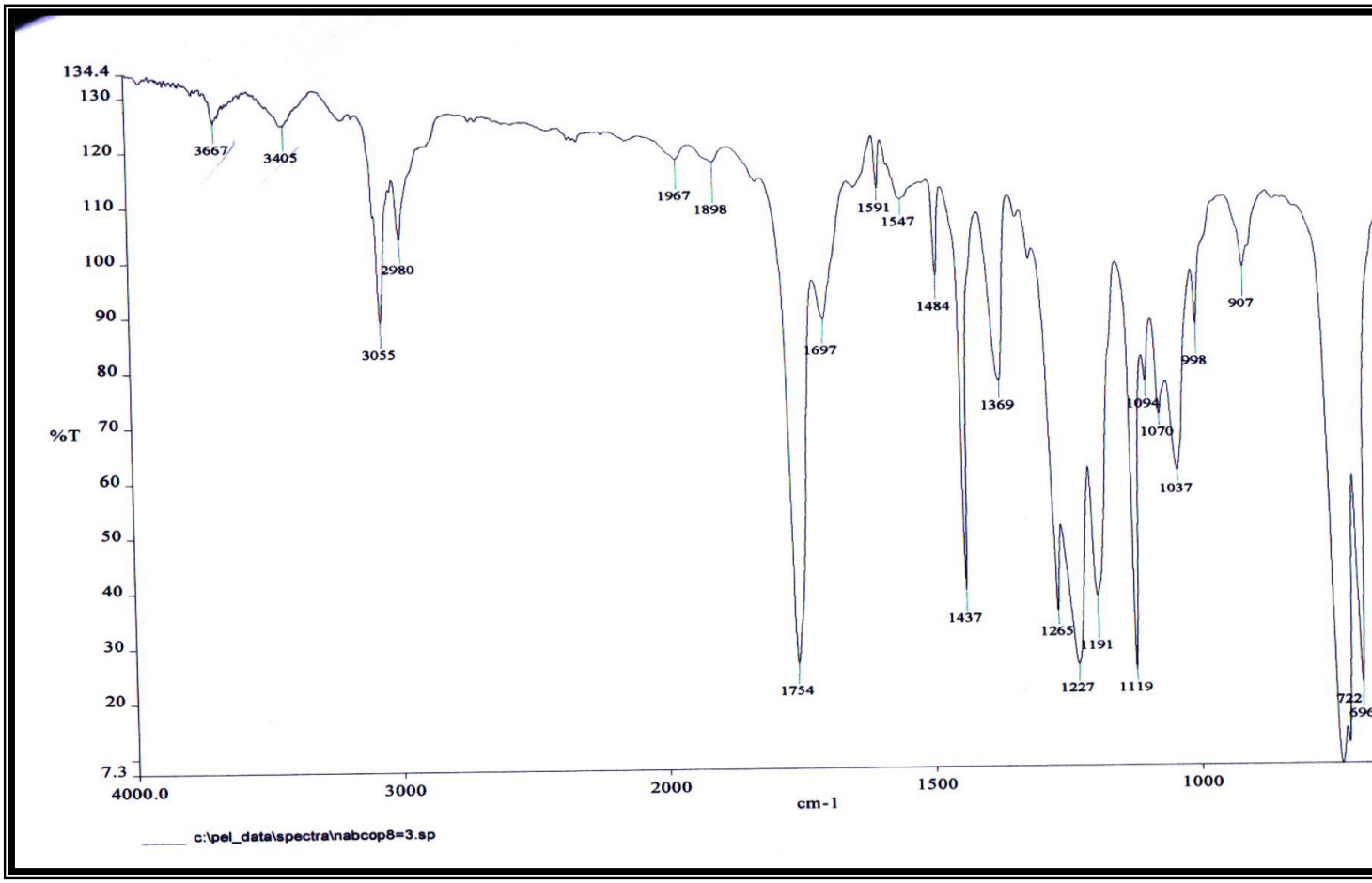

OAc
AcO
AcO
OAc
O
N
N
O
OCH3
OH
HO
OTs
Cop2

Figure (٣-٥٤) : IR Spectrum of compound [cop٢]



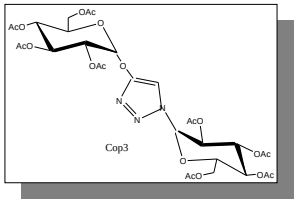
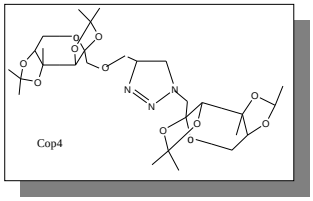


Figure (٣-٥٥) : IR Spectrum of compound [cop٣]



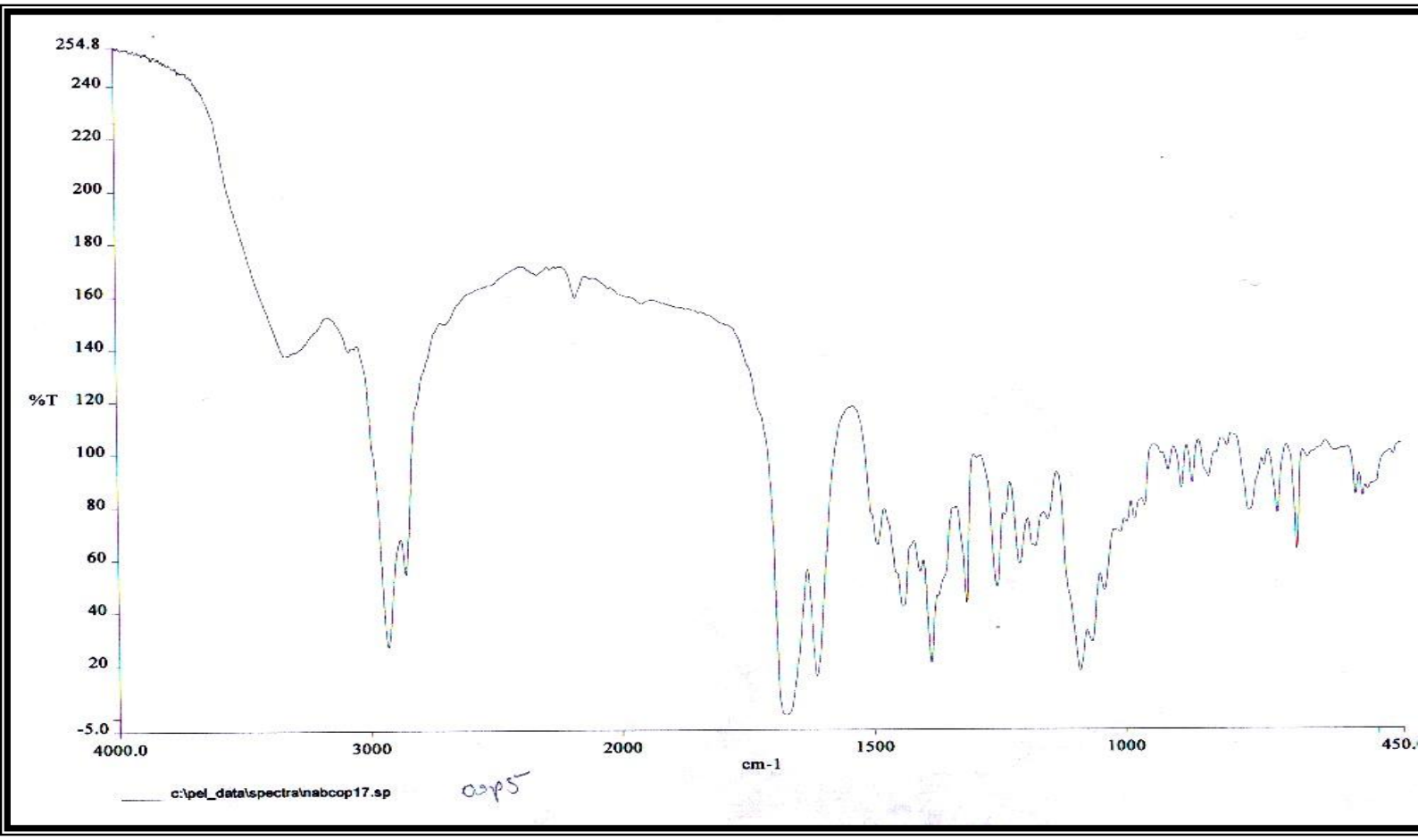
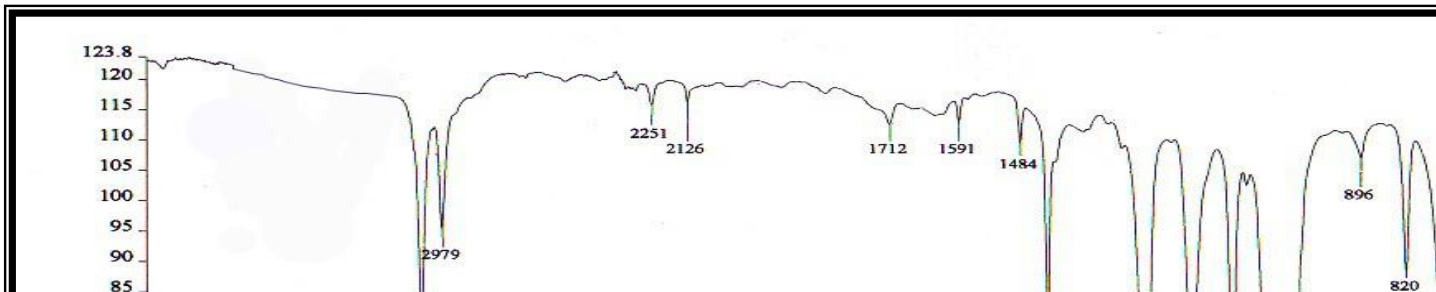
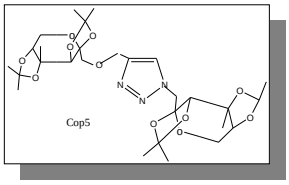


Figure (٣-٥٦) : IR Spectrum of compound [cop٤]





Cop5

Figure (٣-٥٧) : IR Spectrum of compound [cop٥]

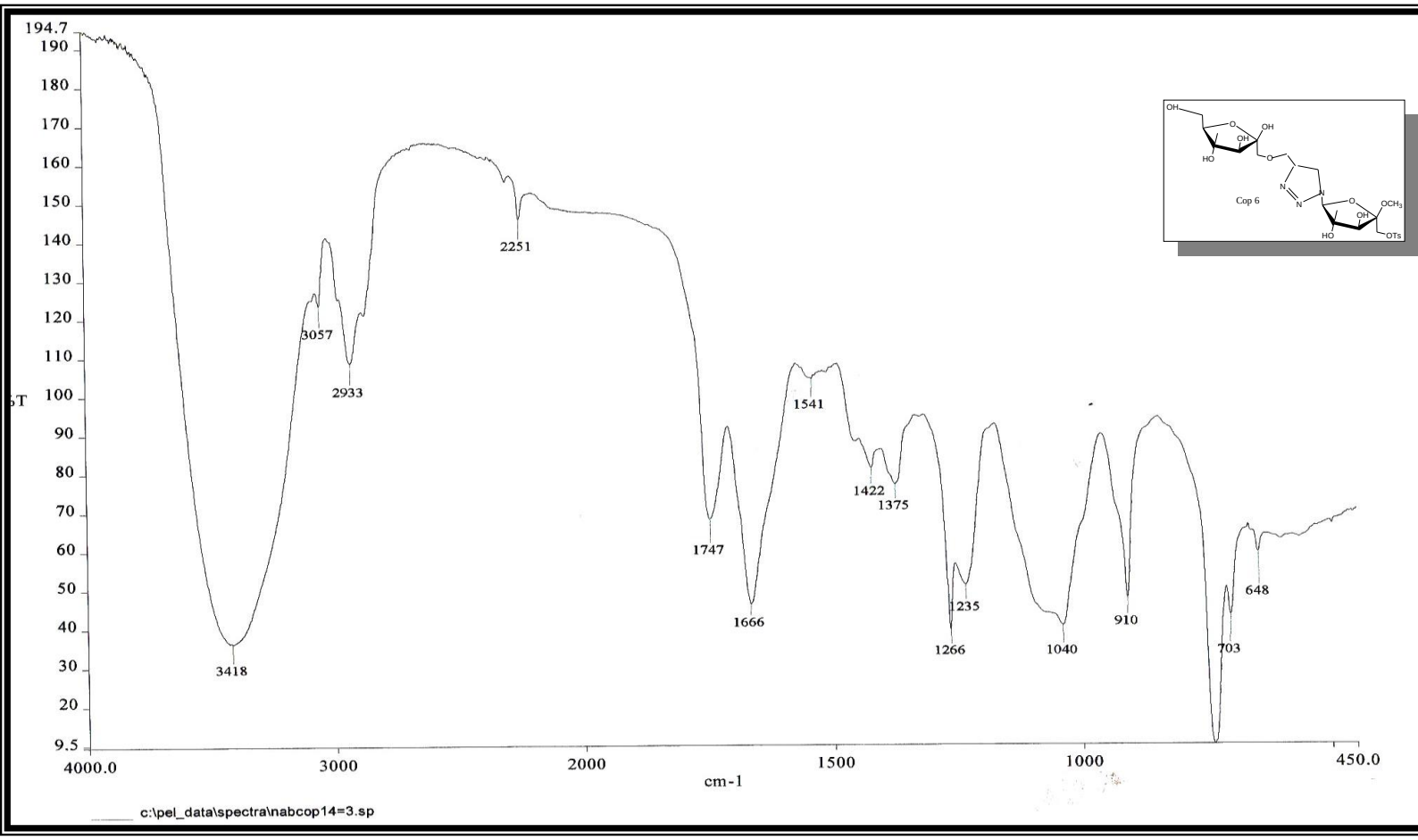


Figure (٣-٥٨) : IR Spectrum of compound [cop٦]

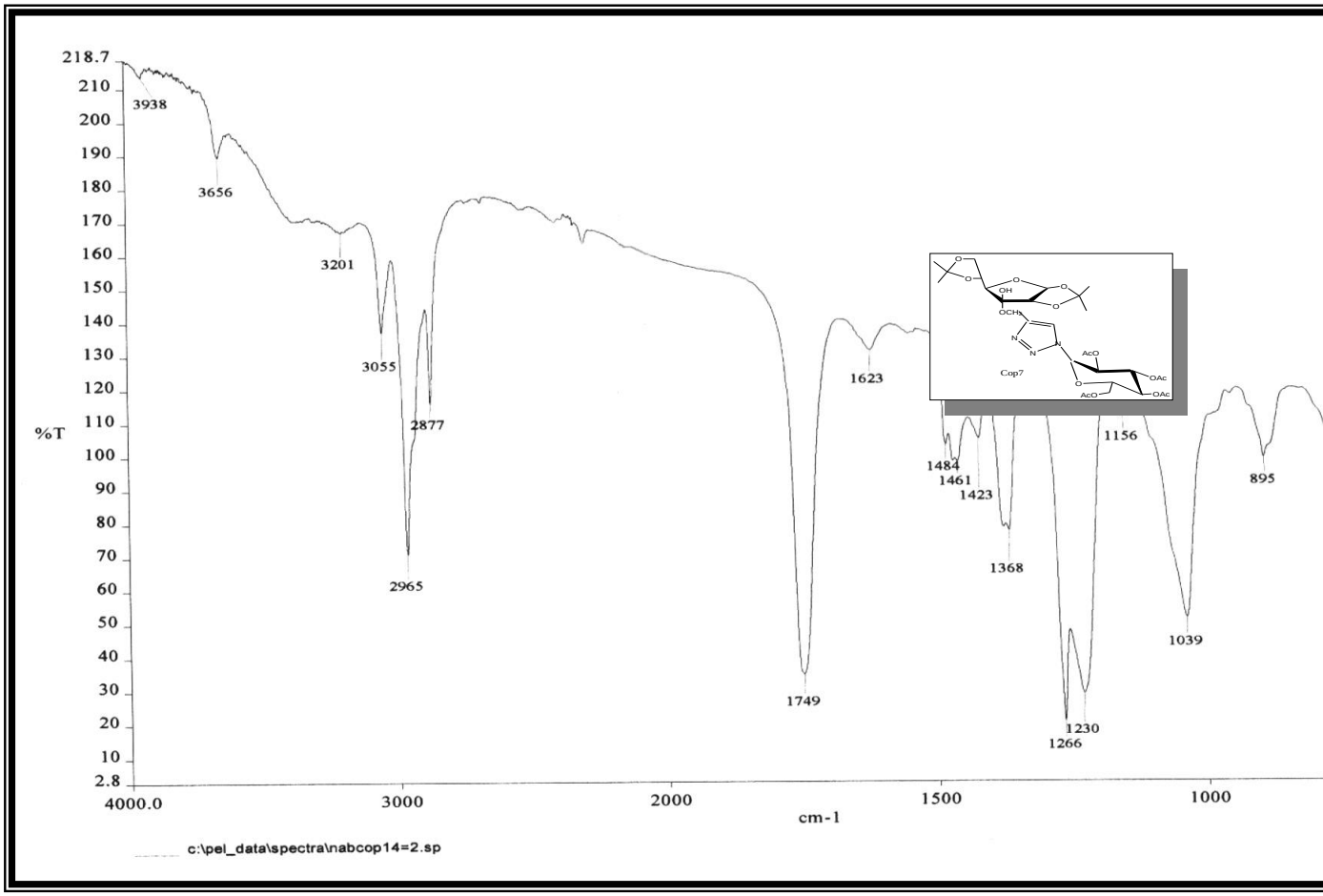


Figure (٣-٥٩) : IR Spectrum of compound[cop٧]

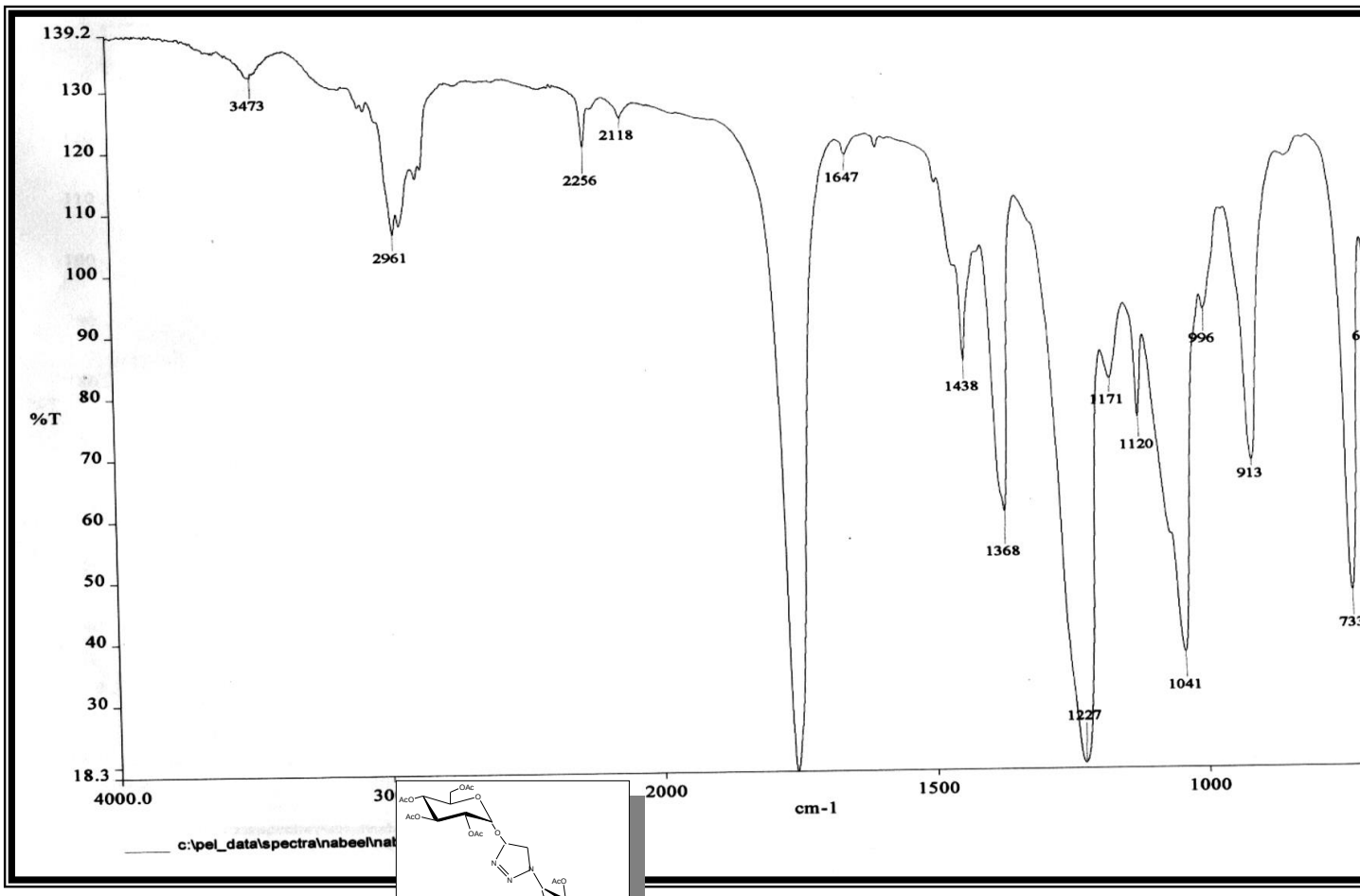
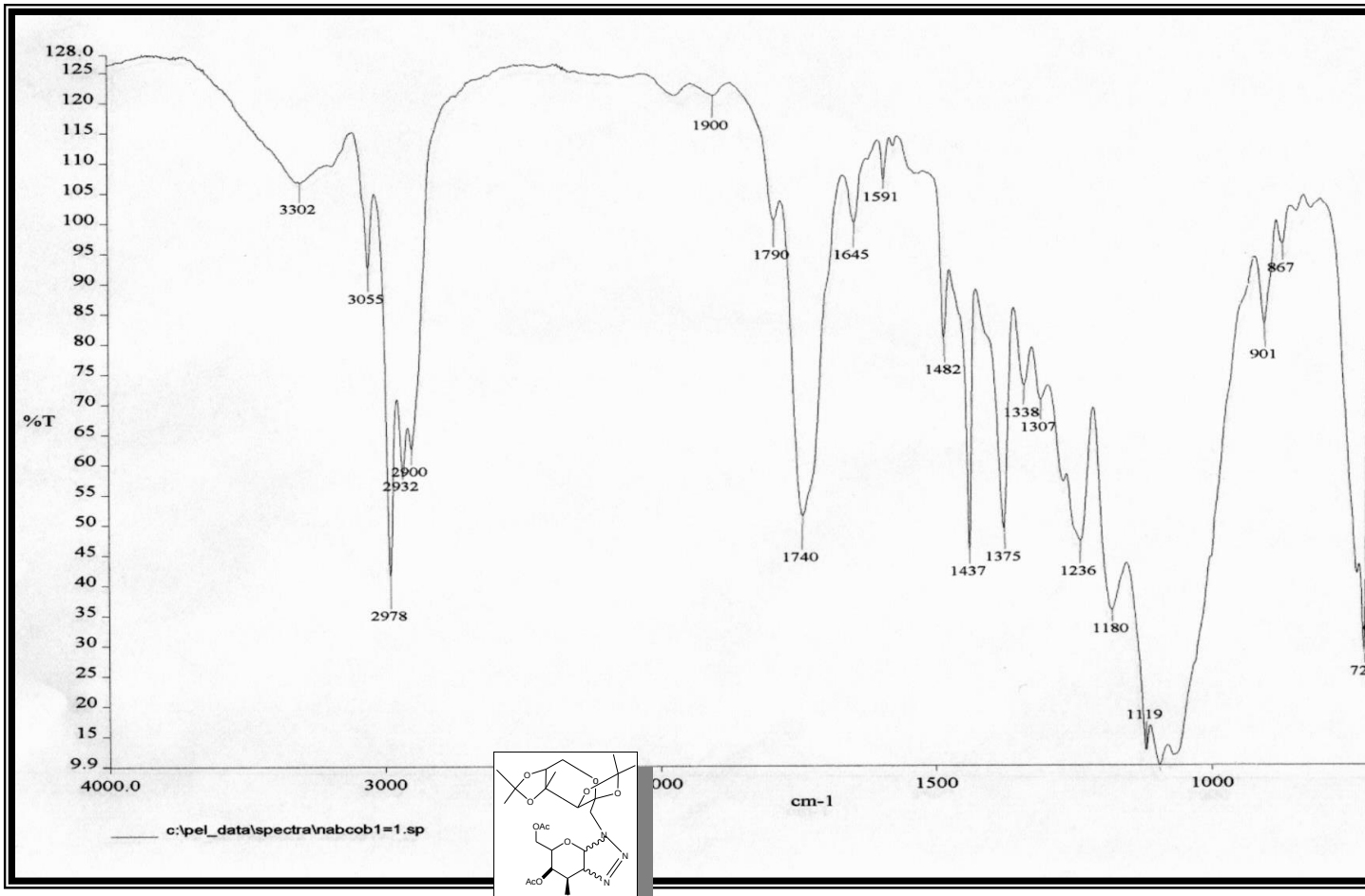

139.2
130
120
110
100
90
80
70
60
50
40
30
18.3
%T
3473
2961
2256
2118
1647
1438
1368
1227
1171
1120
1041
996
913
4000.0
2000
1500
1000
cm-1
c:\pel_data\spectra\nabeel\nat
Cop8

Figure (٣-٦٠) : IR Spectrum of compound [cop٨]


128.0
125
120
115
110
105
100
95
90
85
80
75
70
65
60
55
50
45
40
35
30
25
20
15
9.9
%T
4000.0
3000
1500
1000
cm-1
3302
3055
2900
2932
2978
1900
1790
1740
1645
1591
1482
1437
1375
1338
1307
1236
1180
1119
901
867
c:\pel_data\spectra\nabcob1=1.sp
OAc
AcO
OAc
Cop9

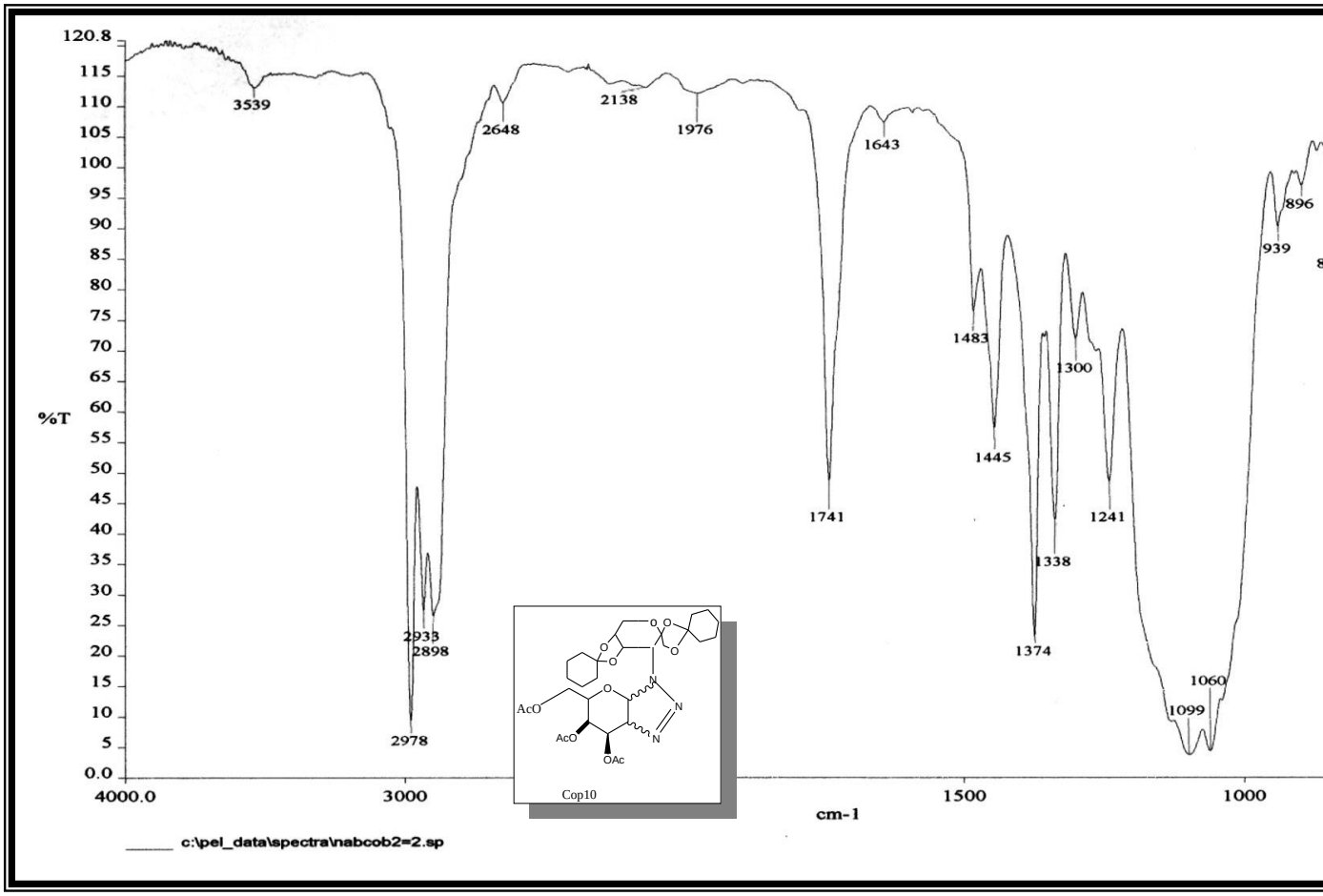
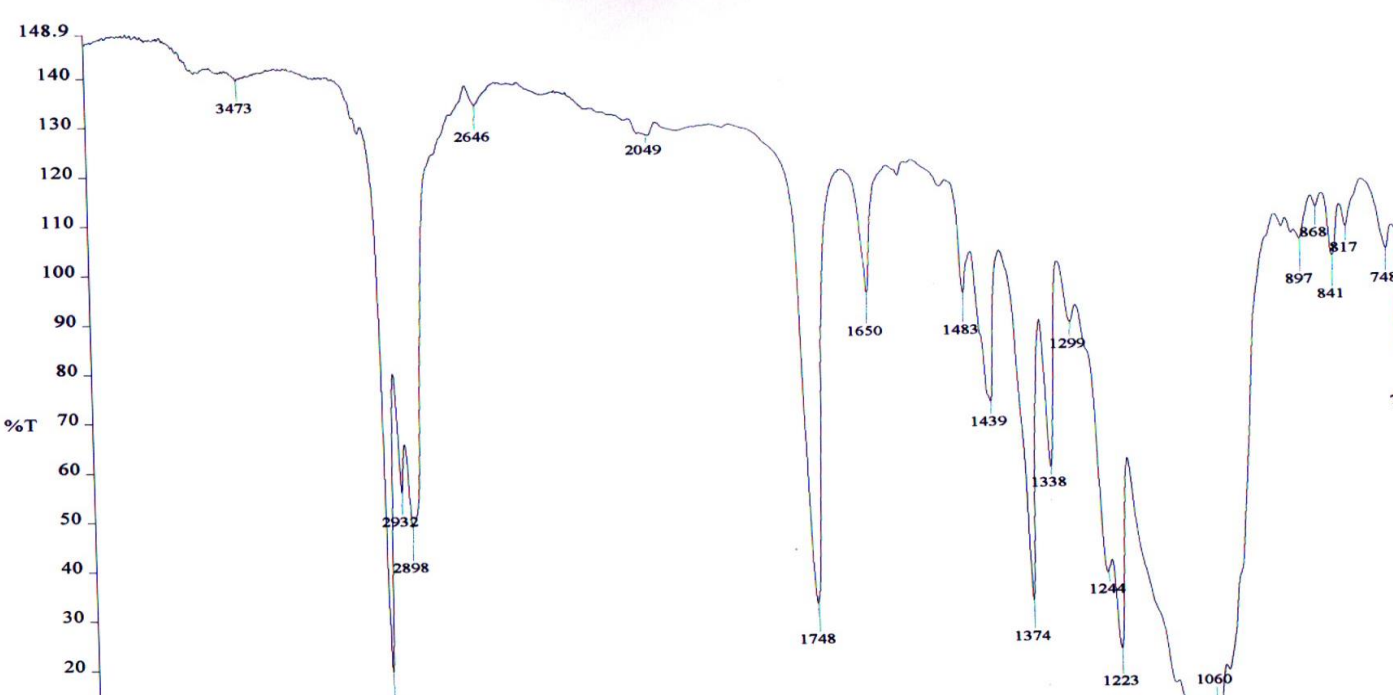

120.8
115
110
105
100
95
90
85
80
75
70
65
60
55
50
45
40
35
30
25
20
15
10
5
0.0
%T
4000.0
3000
1500
1000
cm-1
3539
2648
2138
1976
1643
1741
1483
1445
1374
1338
1300
1241
939
896
2933
2898
2978
1099
1060
AcO
AcO
OAc
Cop10
_____ c:\pel_data\spectra\nabcob2=2.sp

Figure (٣- ٦٢) : IR Spectrum of compound [cop١٠]



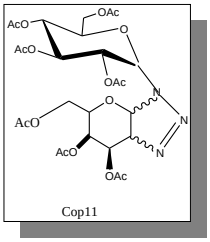


Figure (٣-٦٣) : IR Spectrum of compound [cop١١

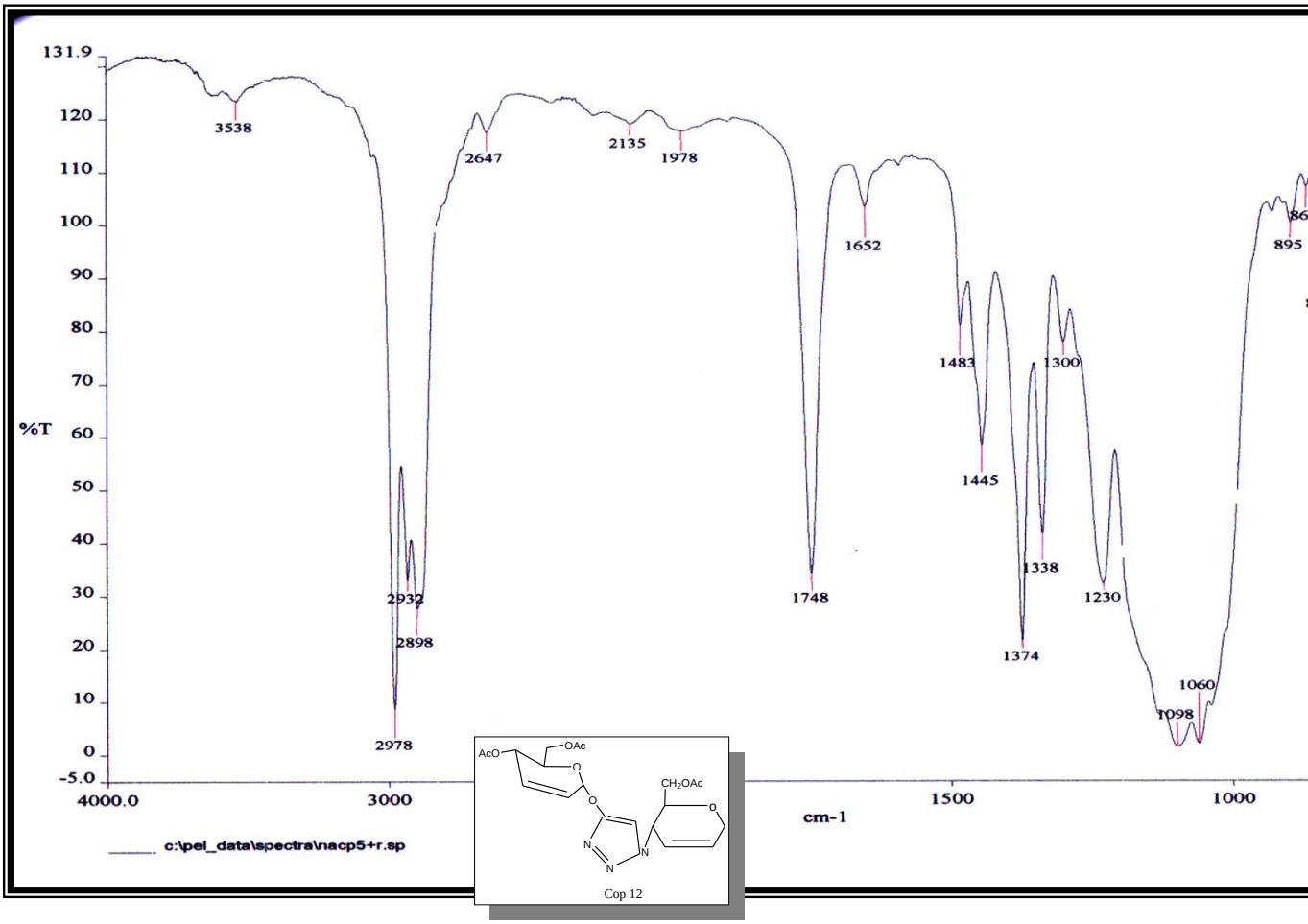
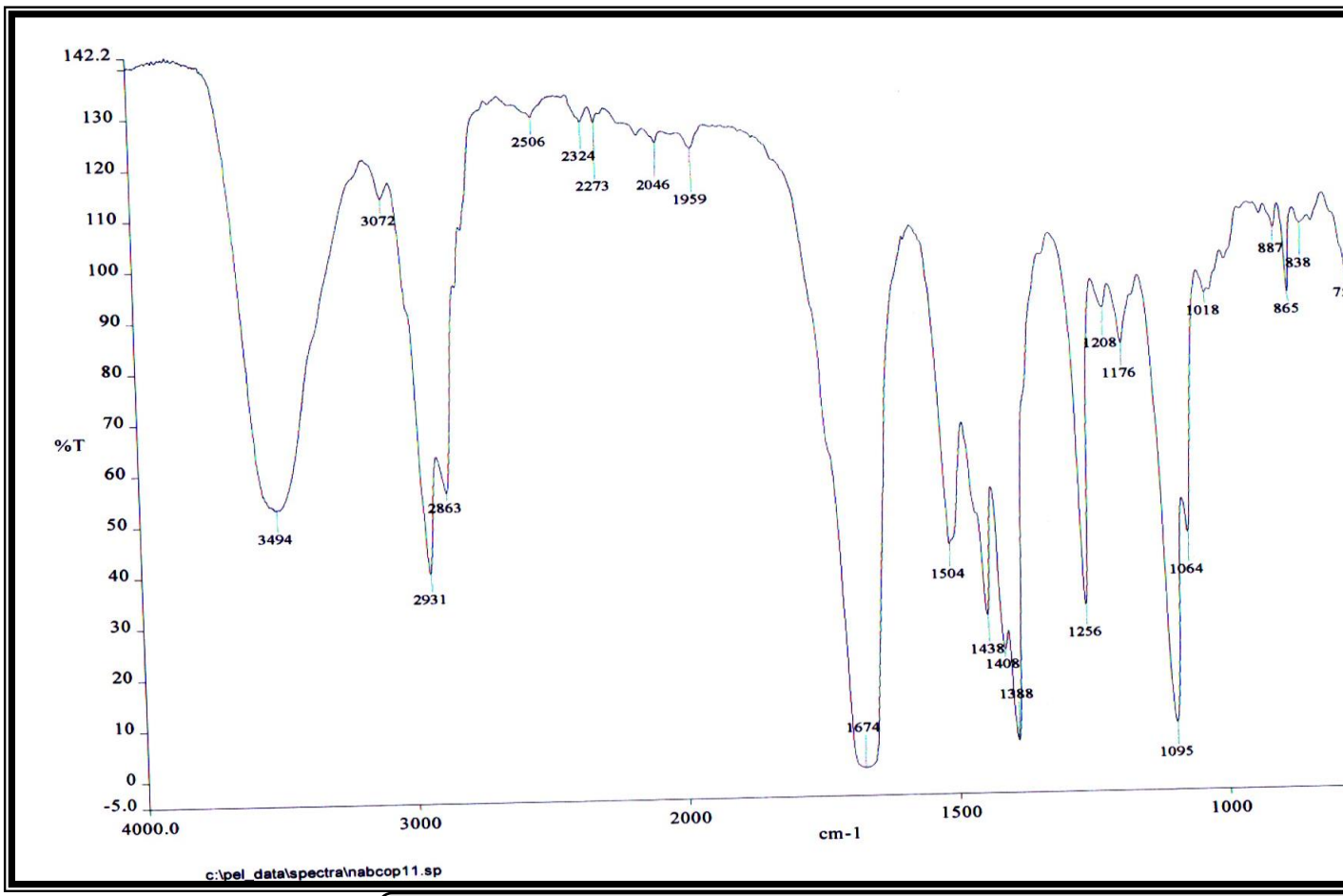


Figure (٣-٦٤) : IR Spectrum of compound [cop١٢]

Figure (٣-٦٤) : IR Spectrum of compound [cop١٢]



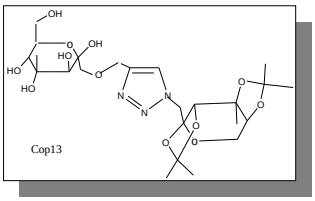
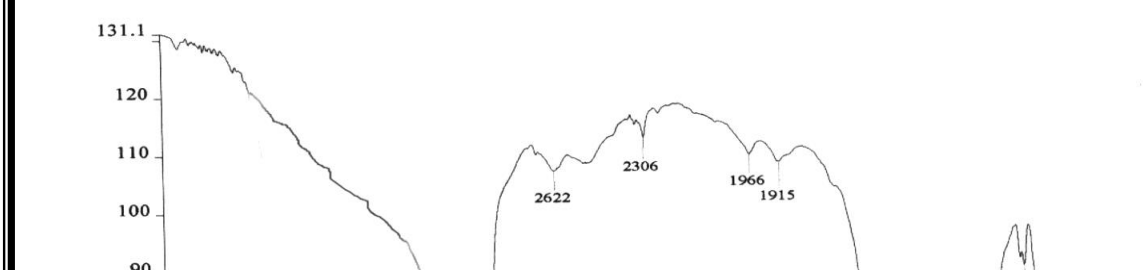
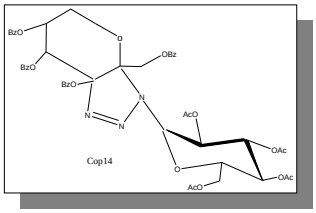


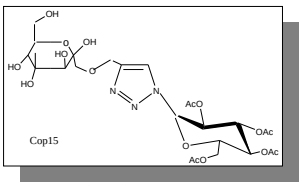
Figure (٣-٦٥) : IR Spectrum of compound [cop١٣]





Cop14

Figure (٣-٦٦) : IR Spectrum of compound [cop١٤]



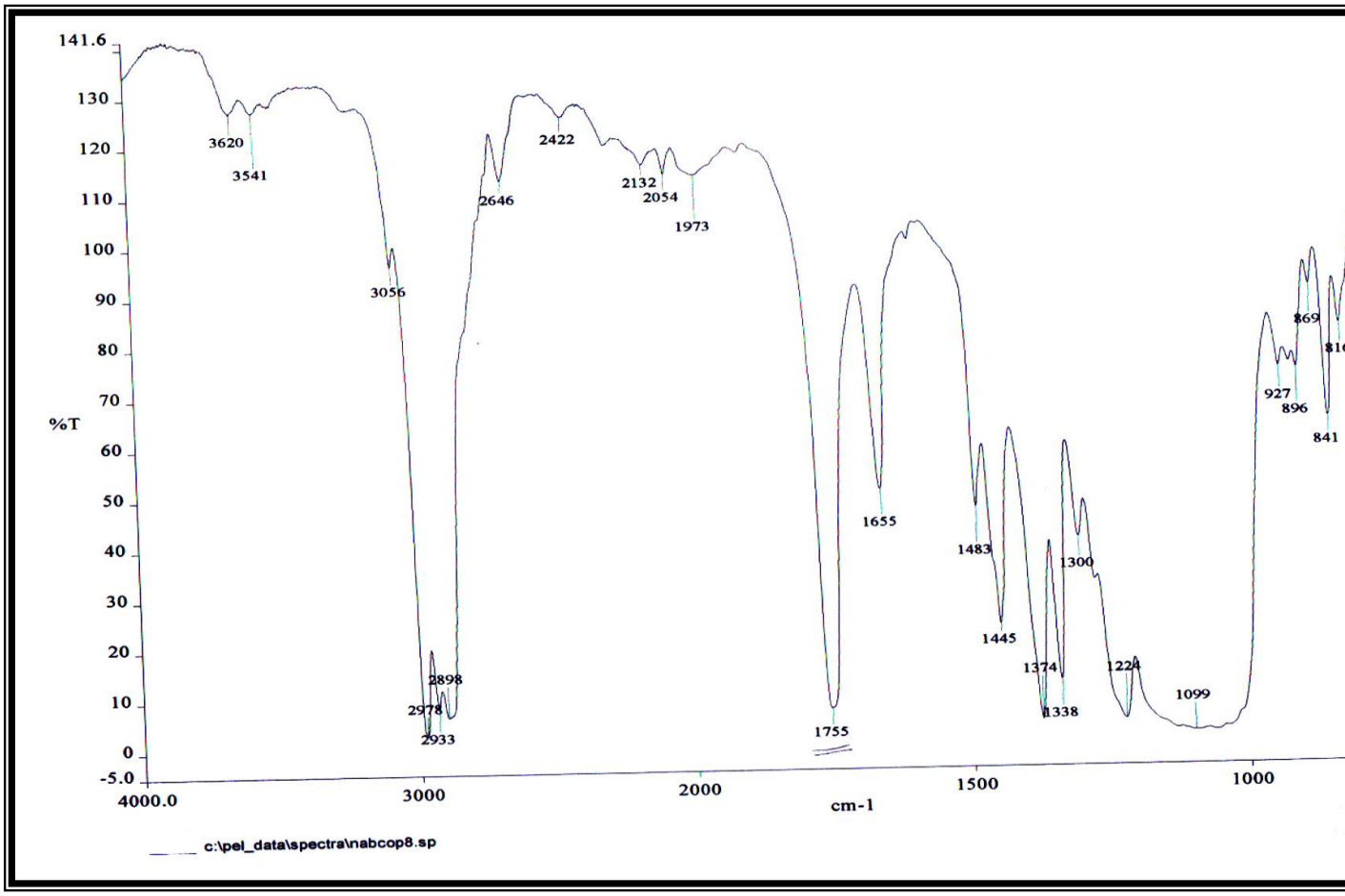
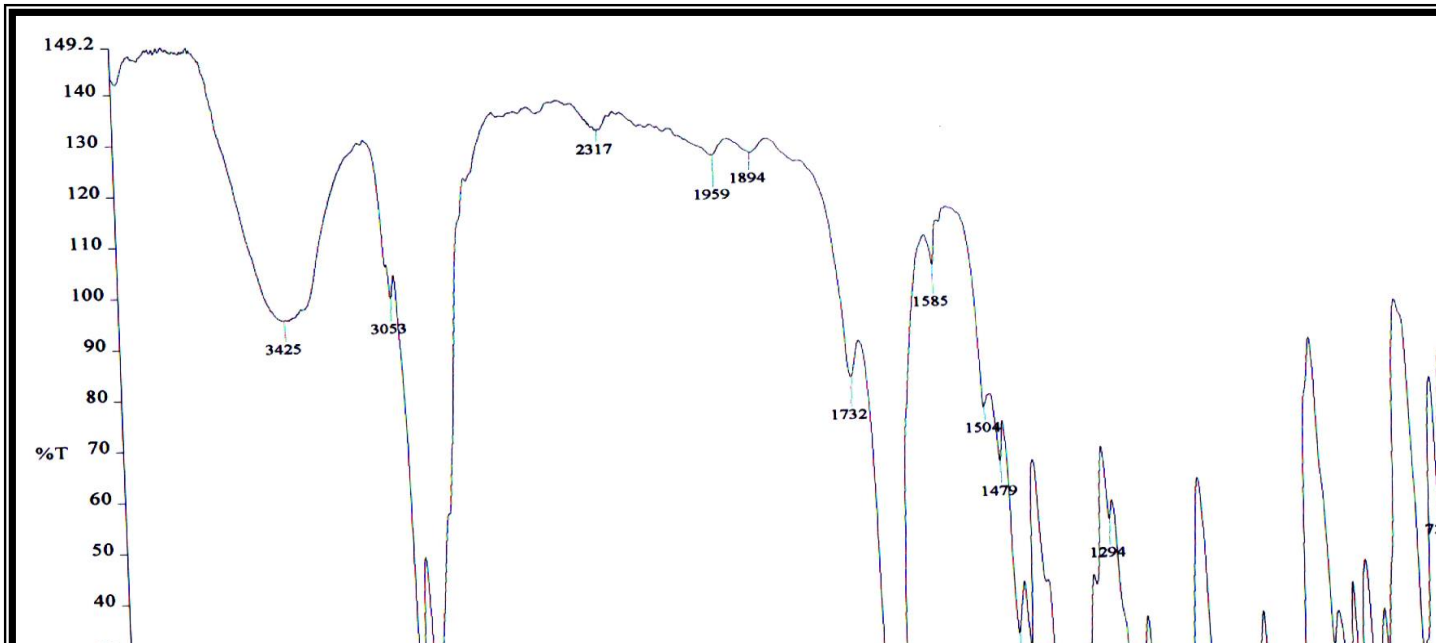


Figure (٣-٦٧) : IR Spectrum of compound [cop١٥]



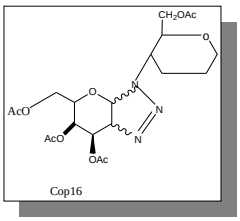
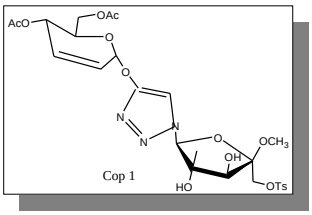


Figure (٣-٦٨) : IR Spectrum of compound [cop١٦]



Cop 1

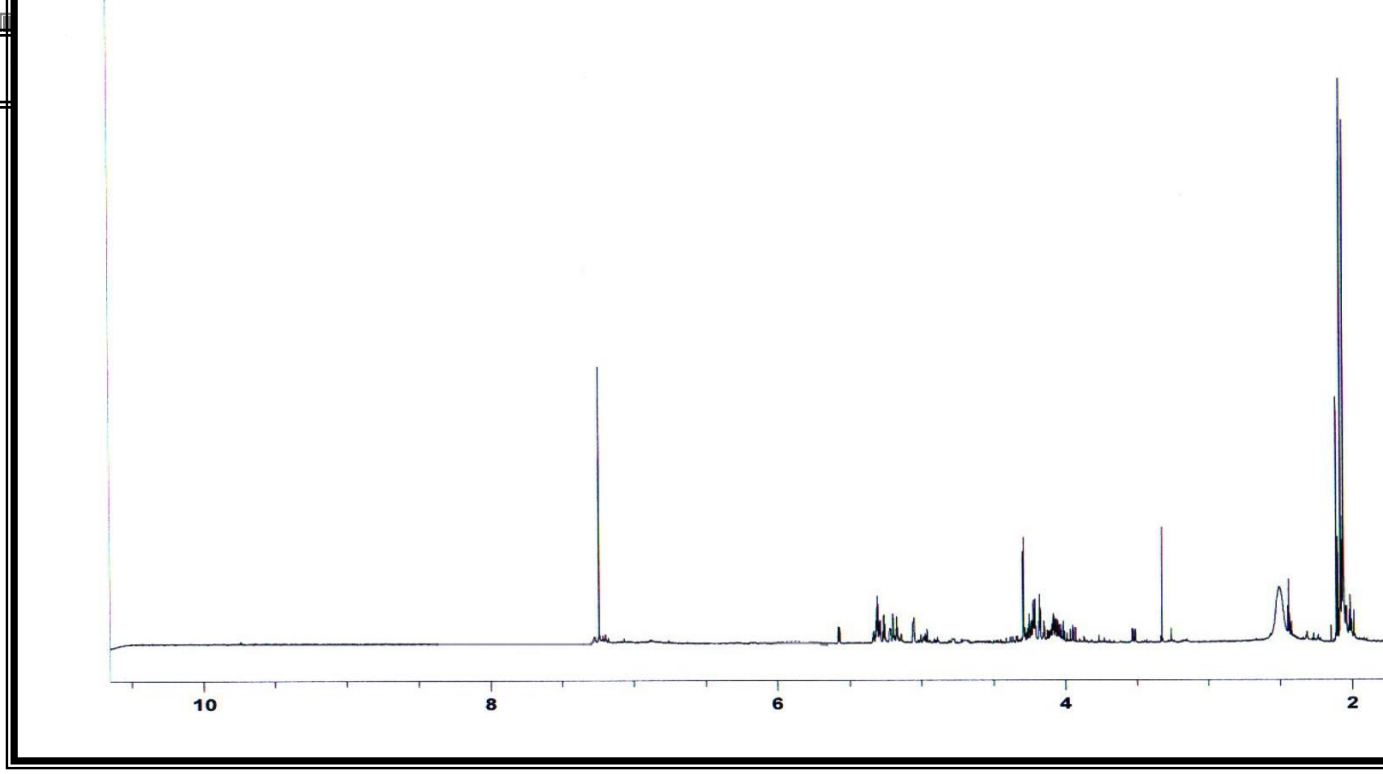


Figure (٣-٦٩) : ^{1}H-MNR Spectrum of compound [cop١]

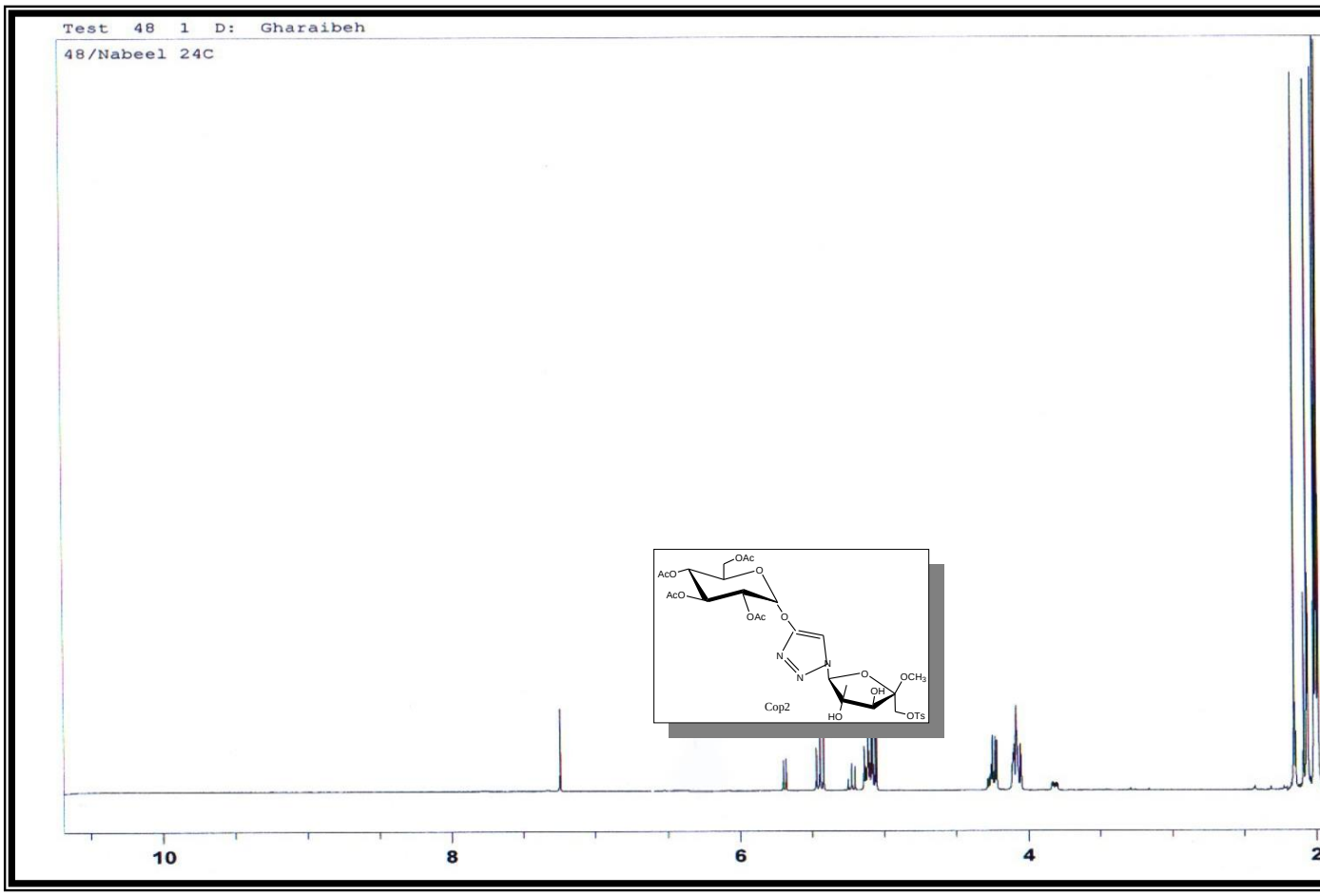
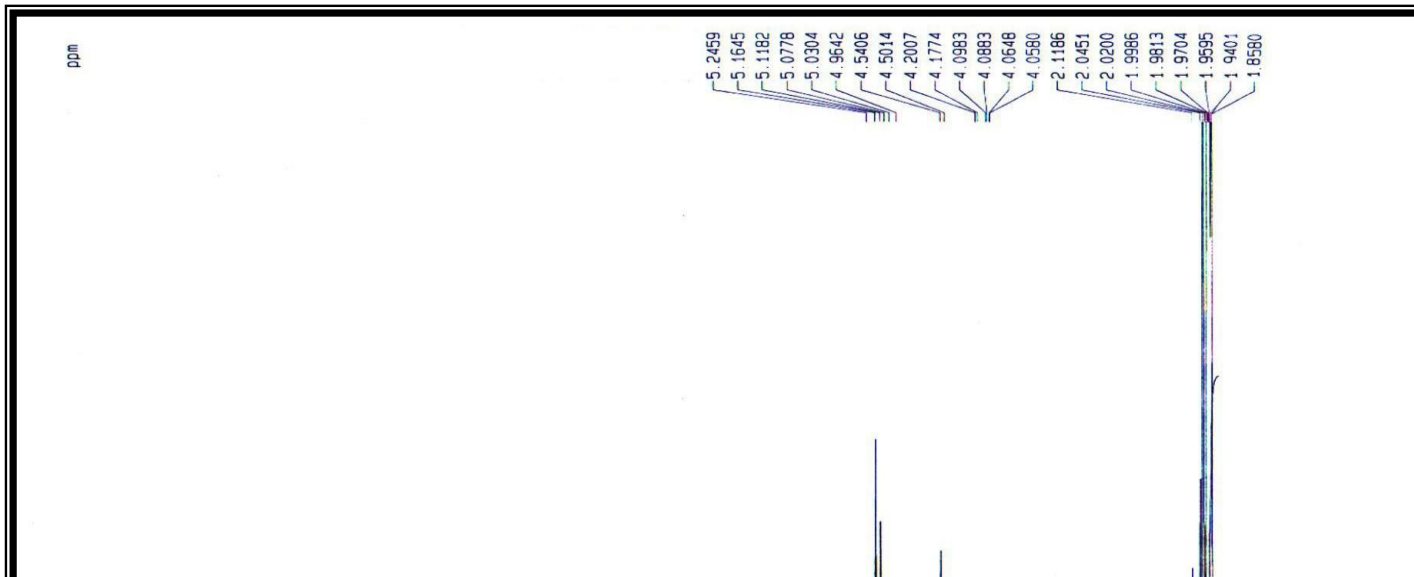
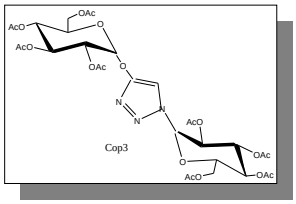


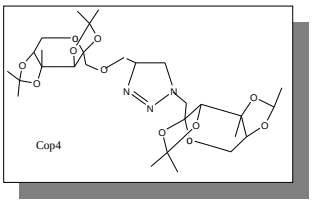
Figure (٣-٧٠) : ^{1}H-MNR Spectrum of compound [cpo٢





Test 36 1 D: Gharaibeh

36/Nabeel 13C



Cop4

Figure (٣-٧٢) : ^{1}H-MNR Spectrum of compound [cpo٤]

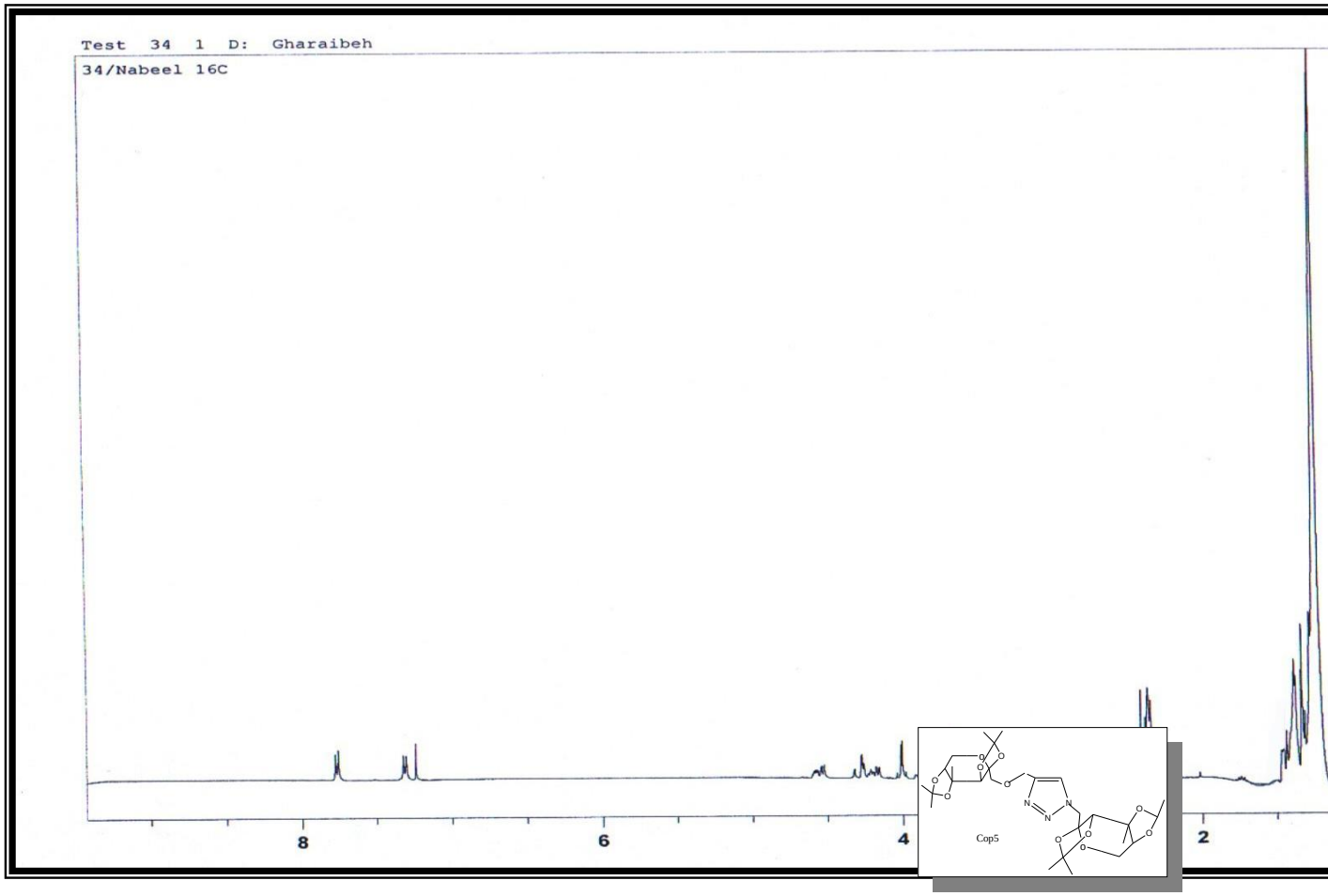


Figure (٣-٧٣) : ^{1}H-MNR Spectrum of compound [cpo

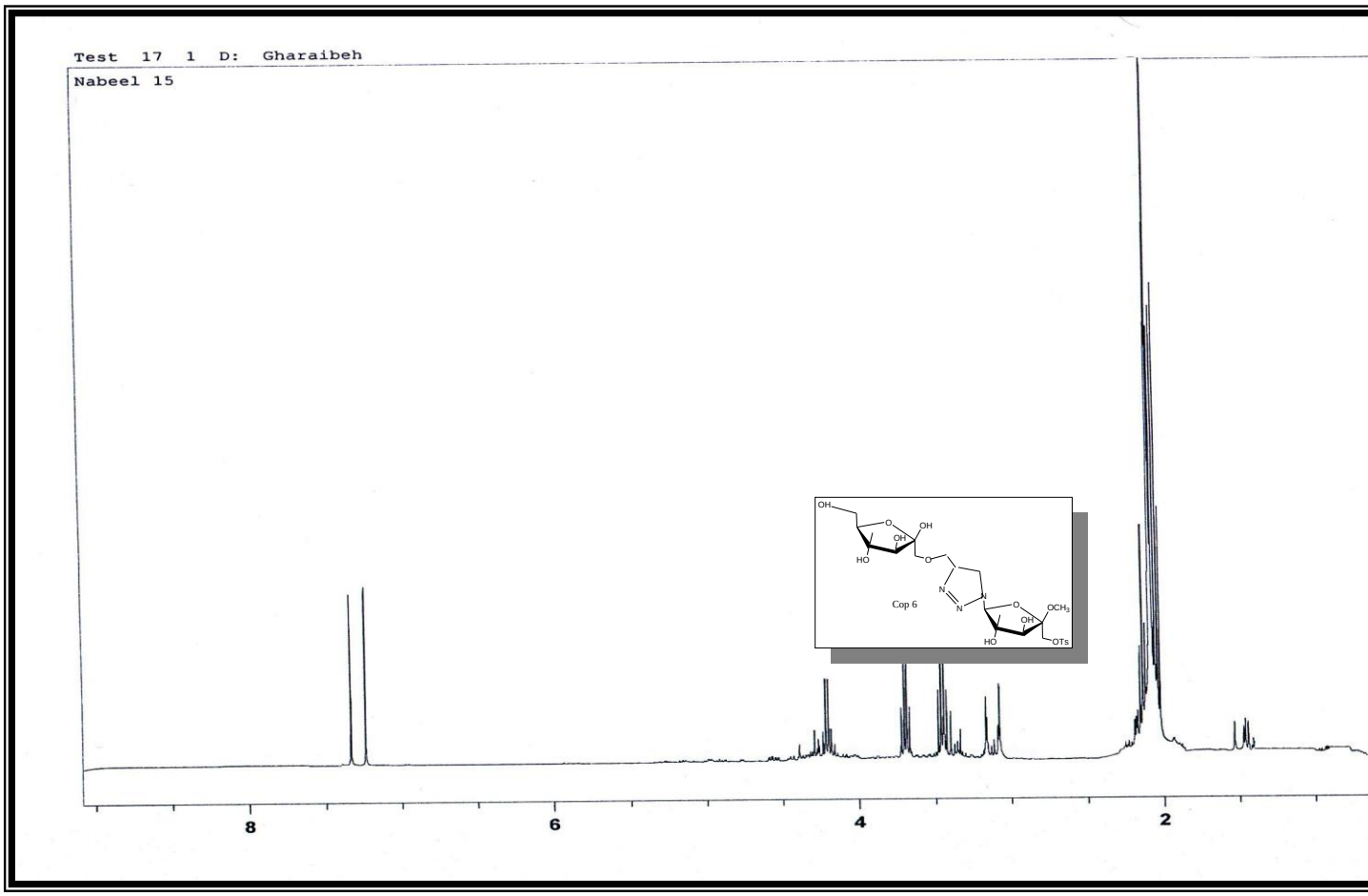
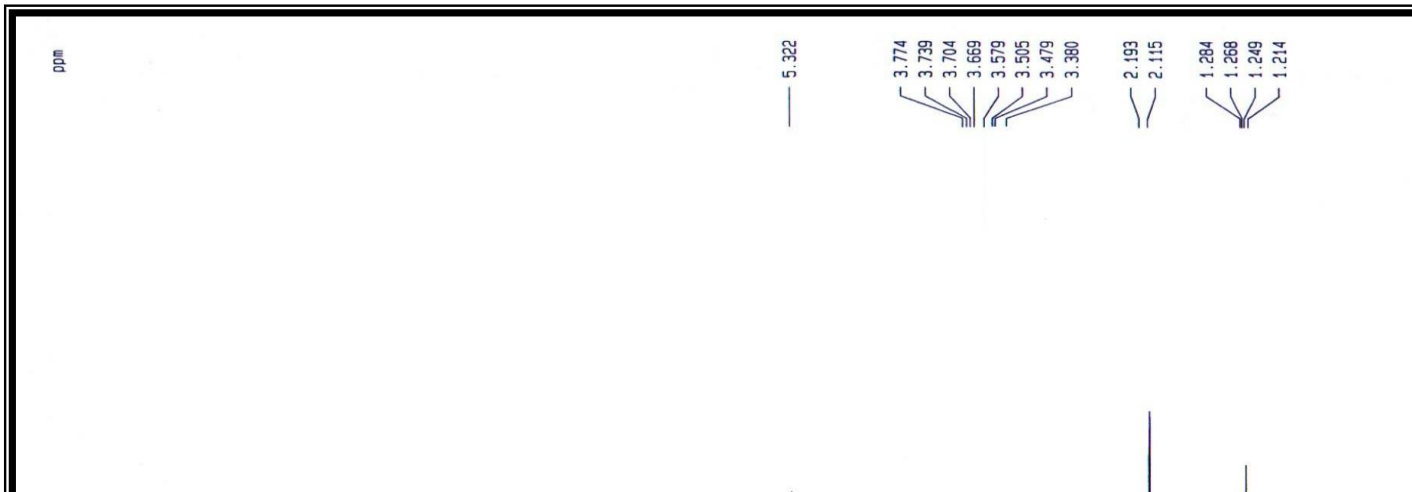
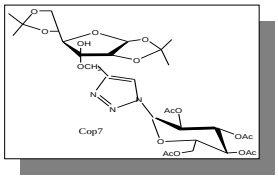

Test 17 1 D: Gharaibeh
Nabeel 15
Cop 6
8
6
4
2

Figure (٣-٧٤) : ^{1}H-MNR Spectrum of compound [cpo٦]




O
O
OH
O
O
O
OCH3
N
N
N
AcO
Cop7
O
OAc
AcO
OAc

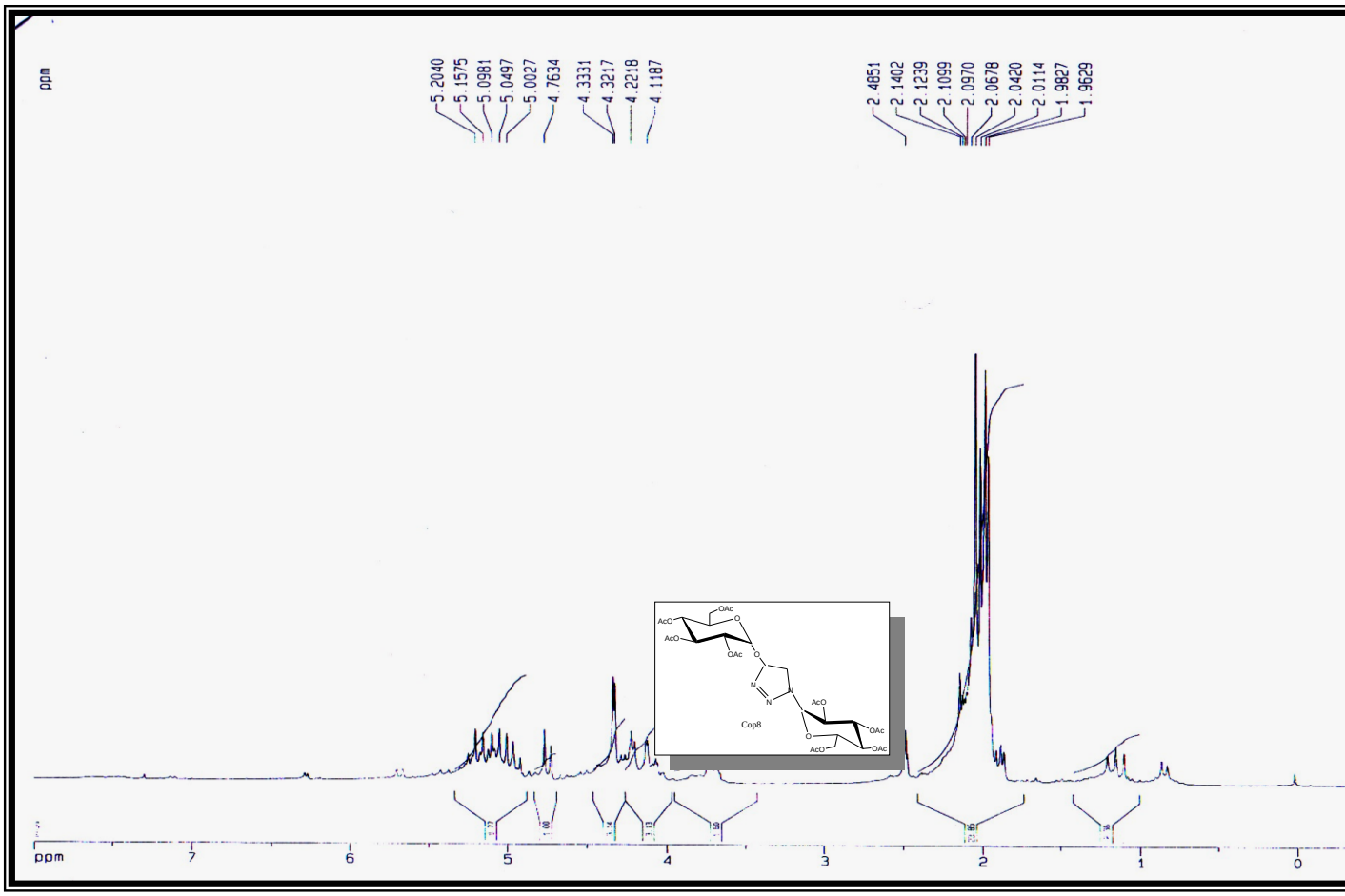
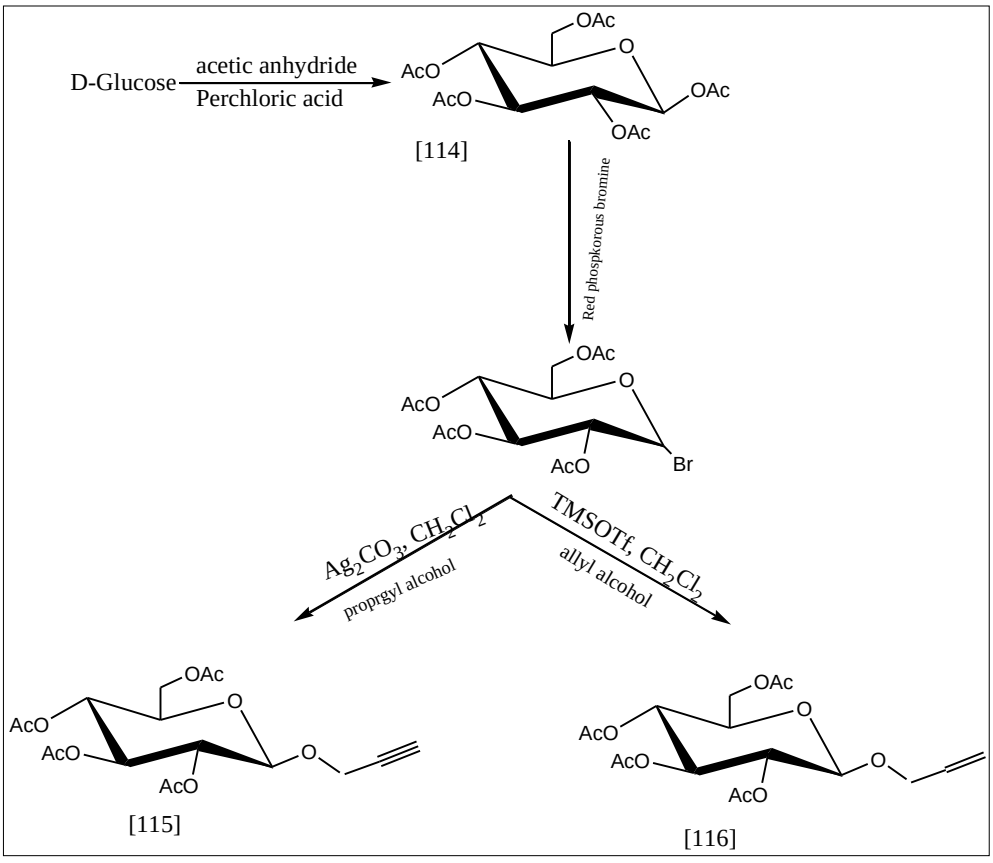
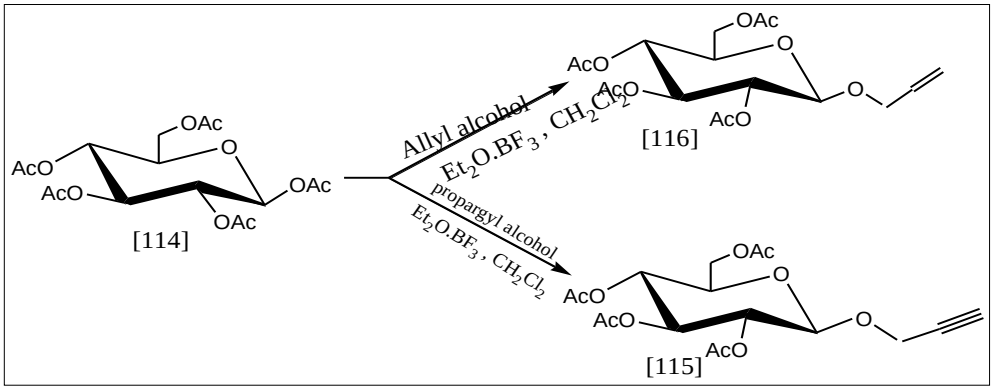

ppm
5.2040
5.1575
5.0981
5.0497
5.0027
4.7634
4.3331
4.3217
4.2218
4.1187
2.4851
2.1402
2.1239
2.1099
2.0970
2.0678
2.0420
2.0114
1.9827
1.9629
Cop8
ppm
7
6
5
4
3
2
1
0

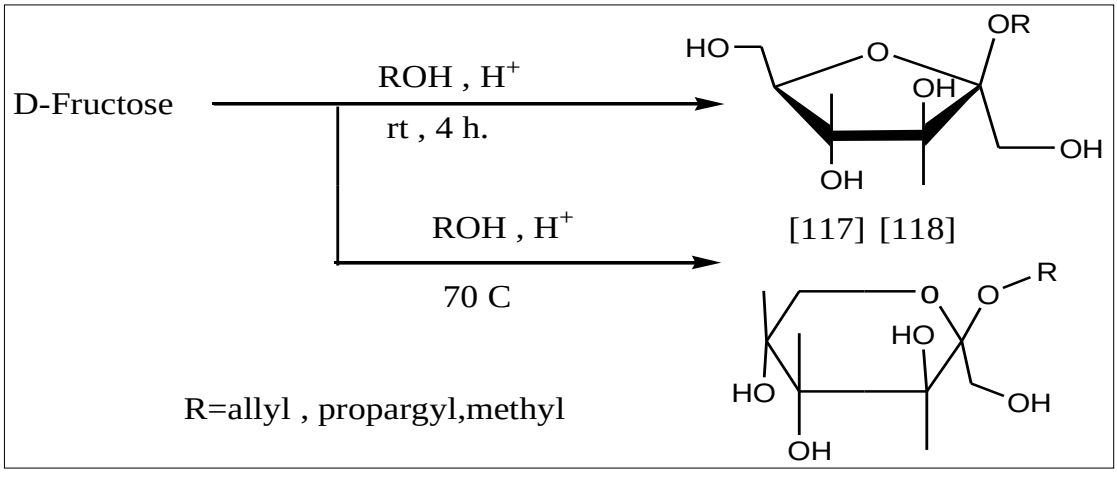
Figure (٣-٧٦) : ^{1}H-MNR Spectrum of compound [cop٨

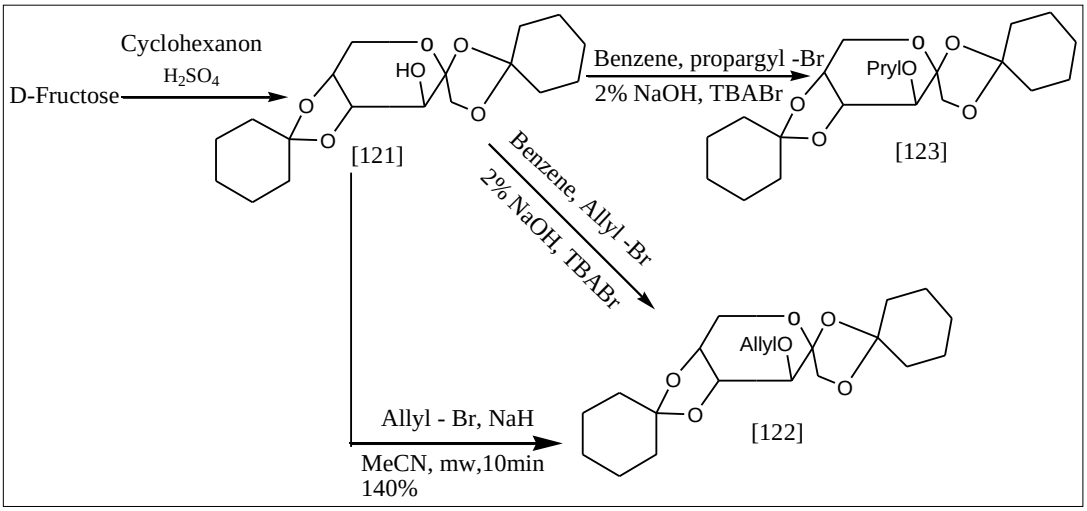
References

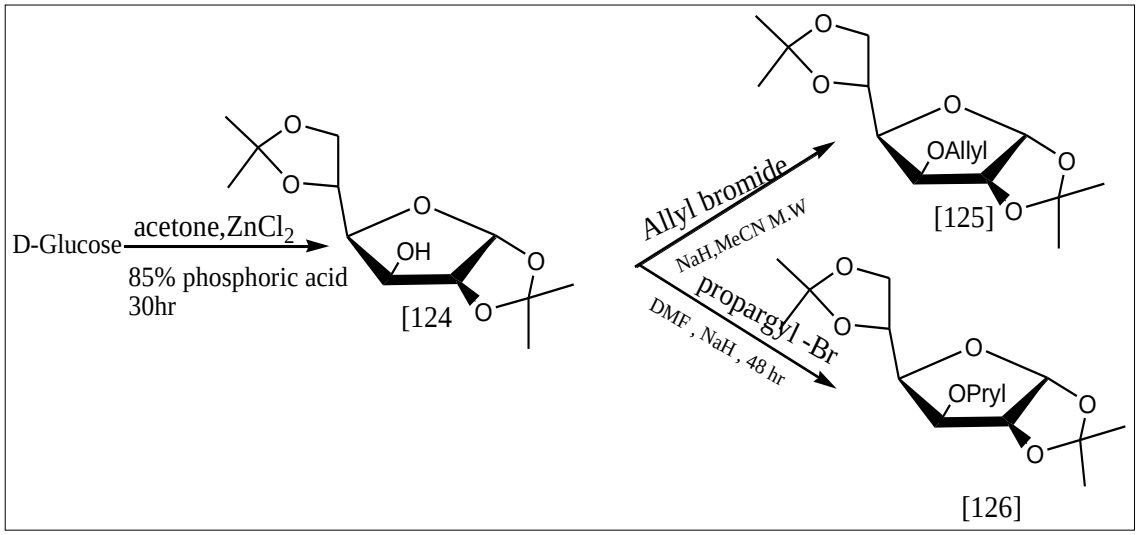
Reaction Scheme (٣-٤) Synthesis of some propargyl and allyl sugars

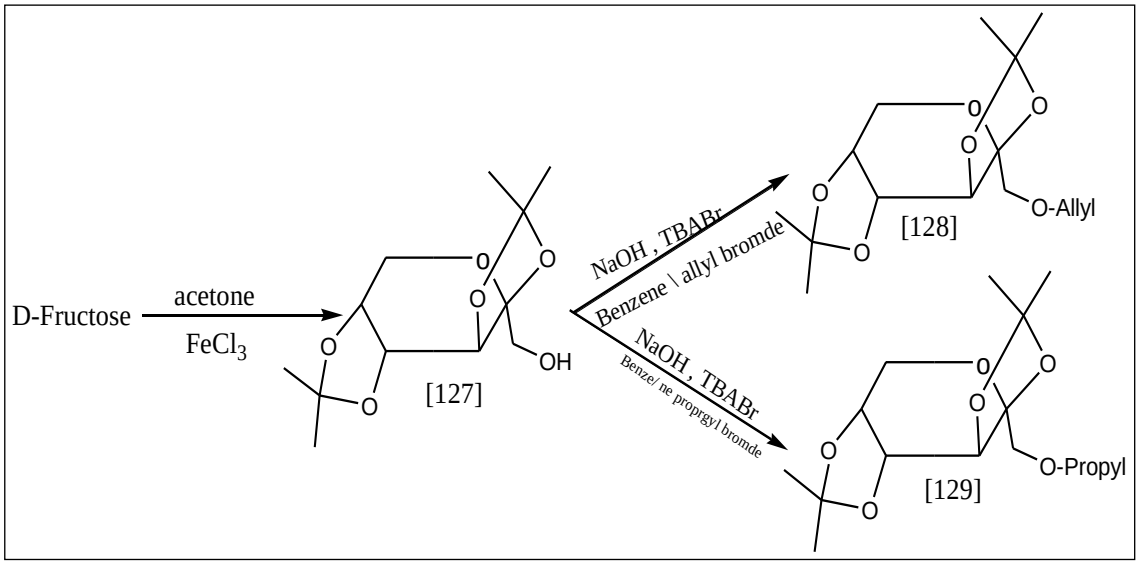


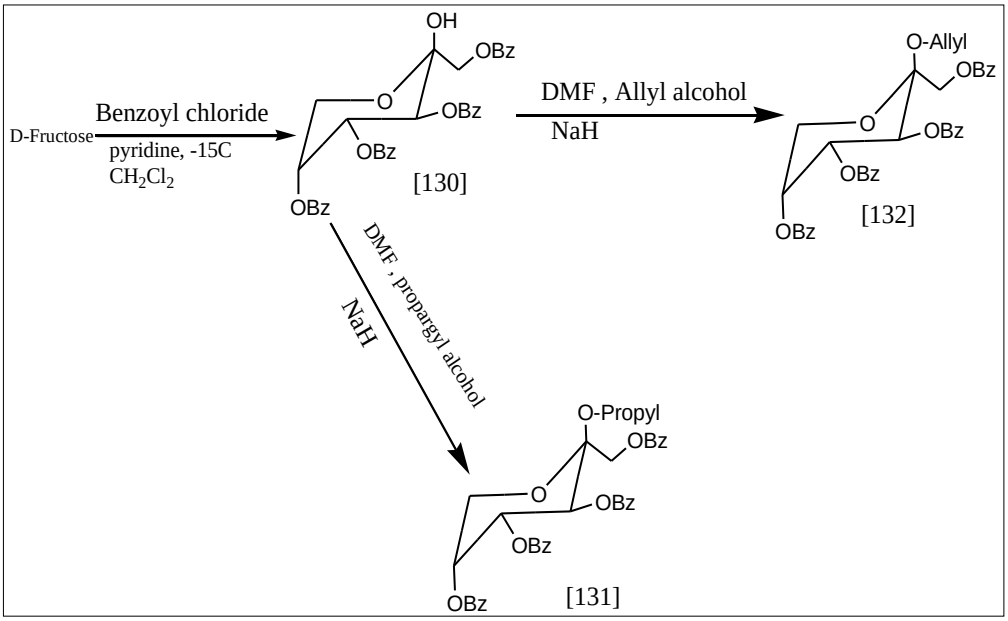

OAc
AcO
AcO
O
OAc
OAc
[114]
Allyl alcohol
$Et_2O.BF_3$, CH_2Cl_2
propargyl alcohol
$Et_2O.BF_3$, CH_2Cl_2
[116]
[115]

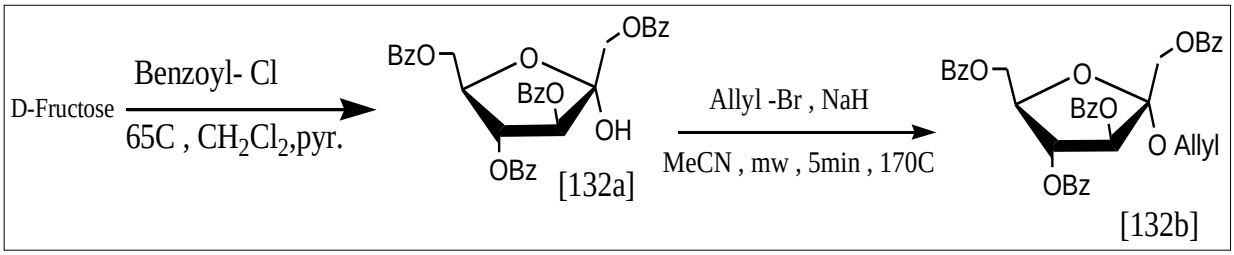

D-Fructose
ROH , H+
rt , 4 h.
ROH , H+
70 C
R=allyl , propargyl,methyl
HO
O
OR
OH
OH
OH
[117] [118]
O
O
R
HO
HO
OH
OH

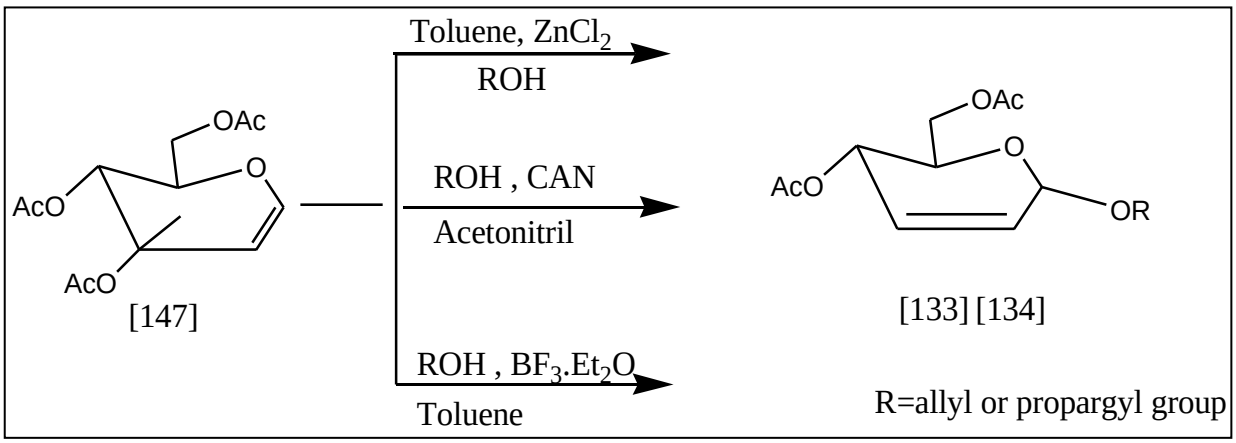

Cyclohexanon
H_2SO_4
D-Fructose
HO
[121]
Benzene, propargyl -Br
2% NaOH, TBABr
PrylO
[123]
Benzene, Allyl -Br
2% NaOH, TBABr
AllylO
[122]
Allyl - Br, NaH
MeCN, mw,10min
140%


D-Glucose
acetone,ZnCl2
85% phosphoric acid
30hr
OH
[124
Allyl bromide
NaH,MeCN M.W
OAllyl
[125]
propargyl -Br
DMF , NaH , 48 hr
OPryl
[126]

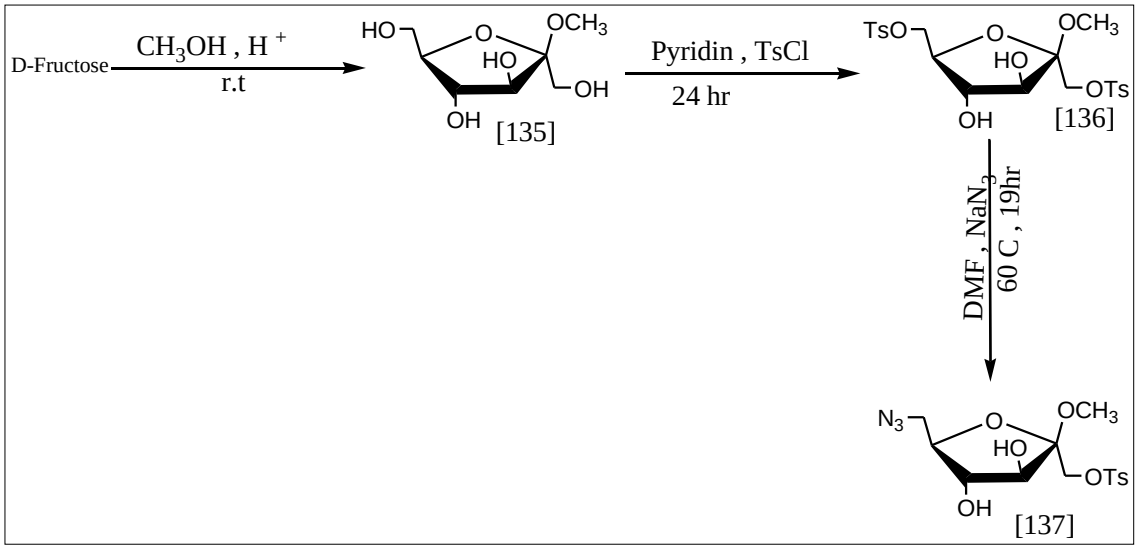

D-Fructose
acetone
FeCl3
[127]
OH
NaOH , TBABr
Benzene \ allyl bromde
[128]
O-Allyl
NaOH , TBABr
Benze/ ne propргyl bromde
[129]
O-Propyl

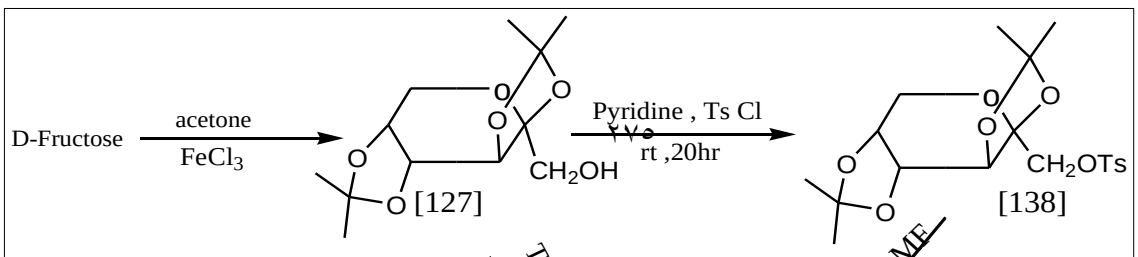

D-Fructose
Benzoyl chloride
pyridine, -15C
CH_2Cl_2
OH
OBz
O
OBz
OBz
OBz
[130]
DMF , Allyl alcohol
NaH
O-Allyl
OBz
O
OBz
OBz
OBz
[132]
NaH
DMF , propargyl alcohol
O-Propyl
OBz
O
OBz
OBz
OBz
[131]

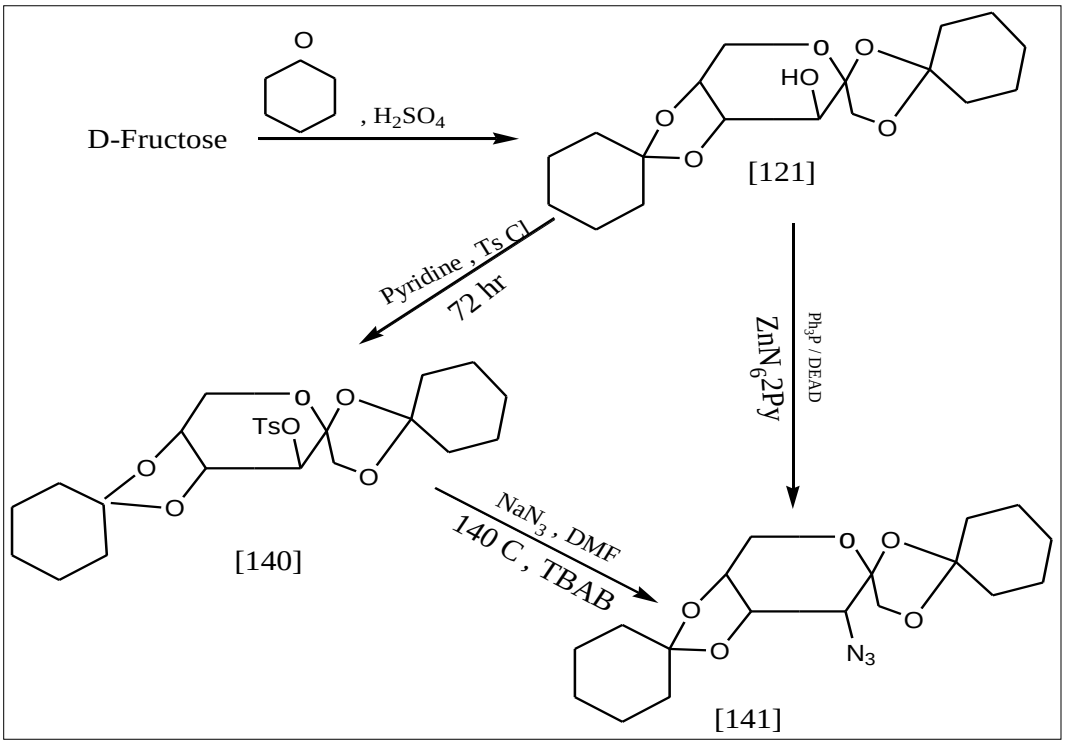

D-Fructose
Benzoyl- Cl
65C , CH2Cl2,pyr.
BzO
OBz
O
BzO
OH
OBz
[132a]
Allyl -Br , NaH
MeCN , mw , 5min , 170C
BzO
OBz
O
BzO
O Allyl
OBz
[132b]

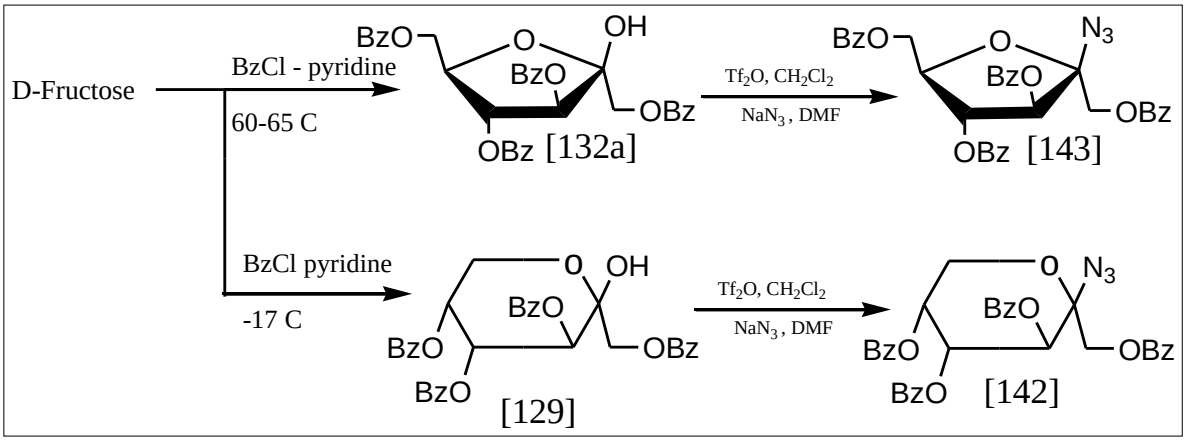

Toluene, ZnCl2
ROH
ROH , CAN
Acetonitril
ROH , BF3.Et2O
Toluene
OAc
O
AcO
AcO
[147]
OAc
O
AcO
OR
[133] [134]
R=allyl or propargyl group

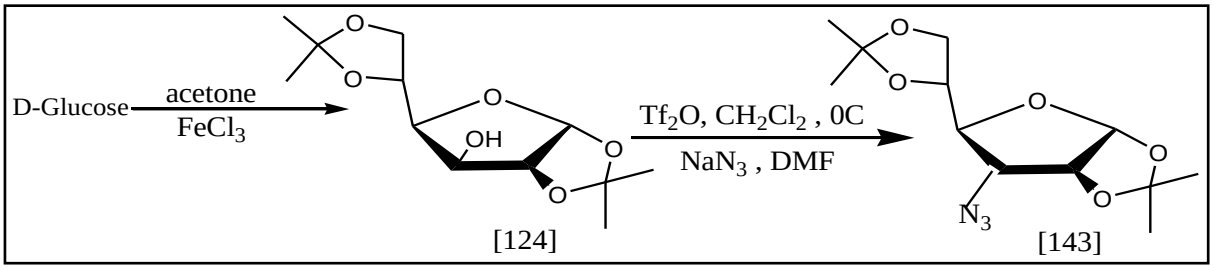
Reaction Scheme (٣-٥) Synthesis of some azides sugar



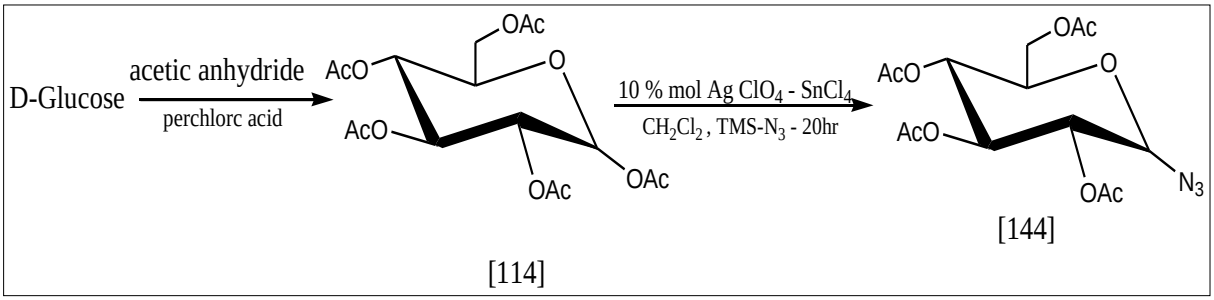



D-Fructose
, H_2SO_4
[121]
Pyridine , Ts Cl
72 hr
$ZnN_6$2Py
Ph_3P / DEAD
[140]
NaN_3 , DMF
140 C , TBAB
[141]

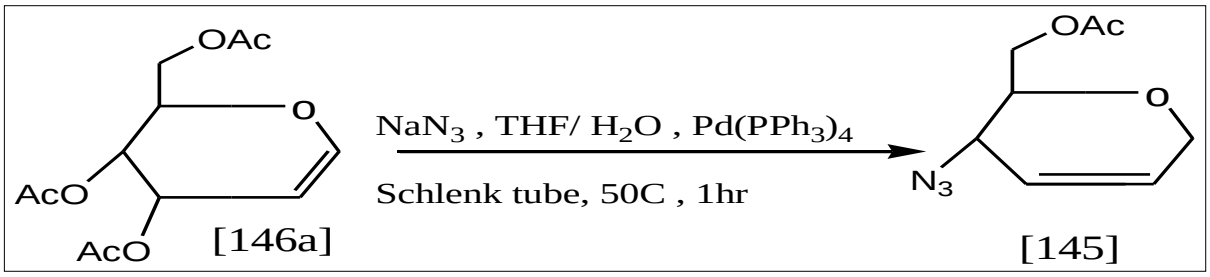

D-Fructose
BzCl - pyridine
60-65 C
BzO
O
OH
BzO
OBz
OBz
[132a]
Tf2O, CH2Cl2
NaN3 , DMF
BzO
O
N3
BzO
OBz
OBz
[143]
BzCl pyridine
-17 C
O
OH
BzO
BzO
OBz
BzO
[129]
Tf2O, CH2Cl2
NaN3 , DMF
O
N3
BzO
BzO
OBz
BzO
[142]



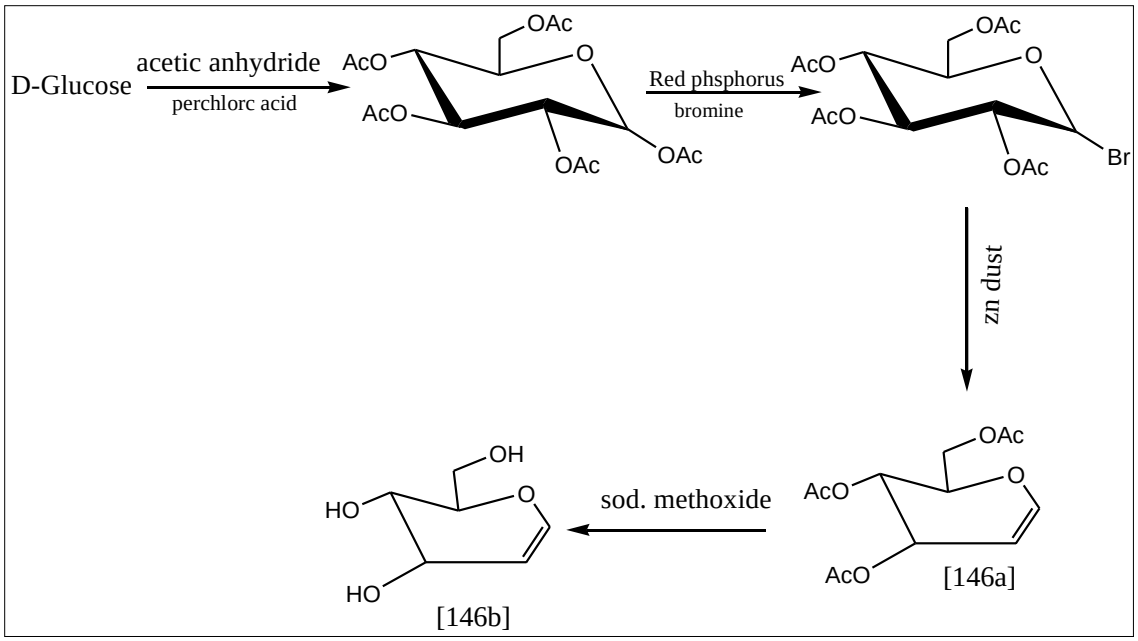
[124] [143]

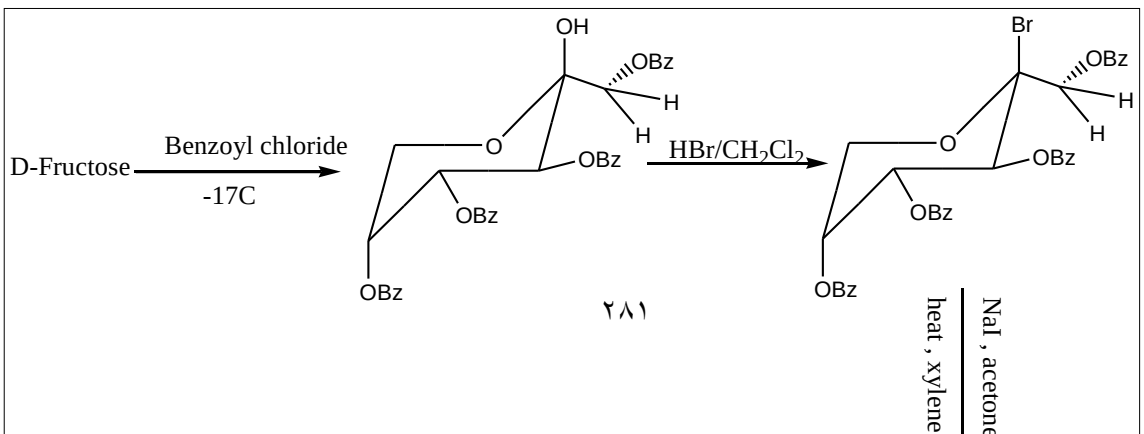


[114] [144]



Reaction Scheme (٣-٦) Synthesis of unsaturated sugaes


D-Glucose
acetic anhydride
perchlorc acid
Red phsphorus
bromine
zn dust
sod. methoxide
[146a]
[146b]


D-Fructose
Benzoyl chloride
-17C
HBr/CH2Cl2
heat , xylene
NaI , acetone

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