Republic of Iraq
Ministry of Higher Education
and Scientific Research
University of Baghdad
College of Education For Pure Science /Ibn Al-Haitham
Department of Chemistry

Synthesis, characterization and biological activity

Evaluation of some new D-fructose derivatives containing isoxazole,1,2,3 triazole and benzimidazole rings

A thesis

Submitted to the Council of College of Education For Pure Science ,Ibn-Al-Haitham , University of Baghdad , in Partial Fulfillment of the Requirements for the Degree of Doctor of Philosophy in Chemistry

By

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1441AH *2019 AC*

بِسم اللهِ الرَّحمنِ الرَّحيمِ

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Dedication

To my big family…..

with my great love

Ahmed

Acknowledgment

Praise be to Allah, and Allah's blessing and peace be upen our prophet Mohammed who rescued mankind from darkness to light**.** It is with great pleasure that I place my deep sense of gratitude and heartfelt thanks to my supervisor **Prof. Dr. Khalid F. Ali** for suggesting the proposal , kind support and constant encouragement throughout the progress of the dissertation work .

My great thanks to the Deanery of the college of education for pure science (Ibn-Al-Haitham) and to the staff of the department of chemistry, especially the head of the department **Prof. Dr**. **Mohamad Jaber Al-Jeboori** for the guidance and advice they gave me during the study period.

I would also express my appreciation to the staff of Central Service Laboratory /College of Education for Pure Science (Ibn-Al- Haitham) . Special thanks to **Prof. Dr. Jumbad H. Tomma** for her help .

Ahmed

Abstract

The present work involves the synthesis of new beta-D-fructopyranose derivatives containing heterocyclic ring. These derivatives are divided into the following parts:

1. The first part involves the synthesis and characterization of new D-fructopyranose derivatives containing isoxazole ring (compounds $[V]_{a-e}$,$[VI]_{a-e}$, $[VII]_{a-e}$, $[VIII]_{a-e}$ and [$IX]_{a-e}$) using the following steps (Scheme1):

a. Synthesis of 3-(4-or 3-substituted phenyl)-5-{(2,3,4,5-di-*O*-isopropylidene-beta-D-fructopyranose-O-yl)methyl}1H-isoxazole compounds $[V]_{a-e}$ by the reaction of Alkynyl sugar compound [IV] with N-hydroxy-4-or-3- substituted benzimidoyl chloride $[II]_{a-e}$ in DMSO via 1,3-dipolar cycloaddition reaction using $CuSO_4.5H_2O$ as a catalyst.

b. The compounds $[VI]_{a-e}$ 3-(4- or 3-substituted phenyl)-5-{(beta-D-fructopyranos-O-yl)methyl}1H-isoxazole were synthesized through the deprotected for isopropylidene group of compounds $[V]_{a-e}$ by using mixture of diluted acetic acid and absolute methanol under reflux.

c. Synthesis of new ester compounds $[VII]_{a-e}$, $[VIII]_{a-e}$, and $[IX]_{a-e}$ by reacting the hydroxyl groups of compounds $[VI]_{a-e}$ with different acid chloride in mixture of tetrahydrofuran (THF) and dimethylformamide (DMF) using triethylamine(Et_3N) as a catalyst at 0-4^{0}C.

2- The second part involves the synthesis and characterization of new D-fructopyranose derivatives containing 1,2,3-triazole ring compounds [XI], [XII],$[XIII]_{a-c}$ and $[XIV]_{a-c}$ by the following steps (Scheme2):

a. Synthesis of 1-((1H-benzo[d]imidazol-2-yl)methyl)-4-{(2,3,4,5-di-O-isopropylidene-beta-D-fructopyranose-O-yl)methyl}1H-1,2,3-triazole compound [XI] by the reaction of Alkynyl sugar compound [IV] with 2-

(azidomethyl)-1*H*-benzo[*d*]imidazole compound [X] and reflux at 65-70^{0}C in DMSO as a solvent using CuAAC protocol.

b. Synthesis of 1-((1H-benzo[d]imidazol-2-yl)methyl)-4-{(beta-D-fructopyranose-O-yl)methyl}1H-1,2,3-triazole [XII] by reacting compound [XI] with mixture of diluted acetic acid and absolute methanol under reflux .

c. Synthesis of new series of ester compounds $[XIII]_{a-c}$ by reacting hydroxyl groups of compound [XII] with three types of acid chloride in mixture of tetrahydrofuran THF and dimethylformamide DMF using triethylamine (Et_3N) as a catalyst at 0-4 ^{0}C**.**

d. Synthesis of new ether compounds $[XIV]_{a-c}$ by the reaction of hydroxyl groups of compound [XII] with excess of different alkyl bromide in absolute ethanol and potassium hydroxide KOH as a catalyst.

3. The third part involves the synthesis and characterization of new series of D- fructopyranose derivatives containing bis-triazole rings compounds [XV], [XVI], [XVII], $[XVIII]_{a-c}$, and $[XIX]_{a-c}$ as follows(Scheme3):

a. Synthesis of 1-((1-(prop-2-yn-1-yl)-1H-benzo[d]imidazol-2-yl) methyl)-4-{(2,3,4,5-di-O-isopropylidene-beta-D-fructopyranose-O-yl)methyl } 1H-1,2,3-triazole [XV] by the reaction of compound [XI] with propargyl bromide in methyl cyanide MeCN and potassium carbonate K_2CO_3 as a catalyst.

b. Synthesis of bis-triazole compound [XVI] 1-((1-((1-((-1Hbenzo[d] imidazol-2-yl)methyl)triazol-4-yl)methyl)-1H-benzo[d]imidazol-2-yl) methyl)-4-{(2,3,4,5-di-O-isopropylidene-beta-D-fructopyranose-O-yl) methyl1H-1,2,3-triazole using the same method of CuAAC protocol.

c. Synthesis of 1-((1-((1-((-1H benz[d] imidazol-2-yl)methyl)triazol-4-yl) methyl)-1H-benzo[d]imidazol-2-yl) methyl)-4-{(beta-D-fructopyranose -O-yl)methyl}1H-1,2,3-triazole [XVII] the same method reaction for deprotected of Isopropylidene group.

d. Synthesis of new ester derivatives containing bis-triazole compounds $[XVIII]_{a-c}$ by the same method used for the synthesis of ester compounds $[XIII]_{a-c}$ in paragraph (second part**).**

e. Synthesis of new ether derivatives contains bis-triazole compounds $[XIX]_{a-c}$ by the same method used for the synthesis of ether compounds $[XIV]_{a-c}$ (second part**).**

4- The fourth part involves the synthesis and characterization of new series of D- fructopyranose derivatives containing both triazole and isoxazole rings compounds $[XX]_{a-e}$, $[XXI]_{a-e}$ $[XXII]_{a-e}$,$[XXIII]_{a-e}$ and$[XXIV]_{a-e}$ as follows (Scheme 4):

a. Synthesis of 2,3,4,5-di-*O*-isopropylidene-beta-D-fructopyranose that contains both triazole and isoxazole rings compounds$[XX]_{a-e}$ using $CuSO_4.5H_2O$ and sodium ascorbate as a catalysts via1,3-dipolar cycloaddition reaction of compound [XV] with N-hydroxy-4-or-3-substituted benzimidoyl chloride $[II]_{a-e}$ under reflux.

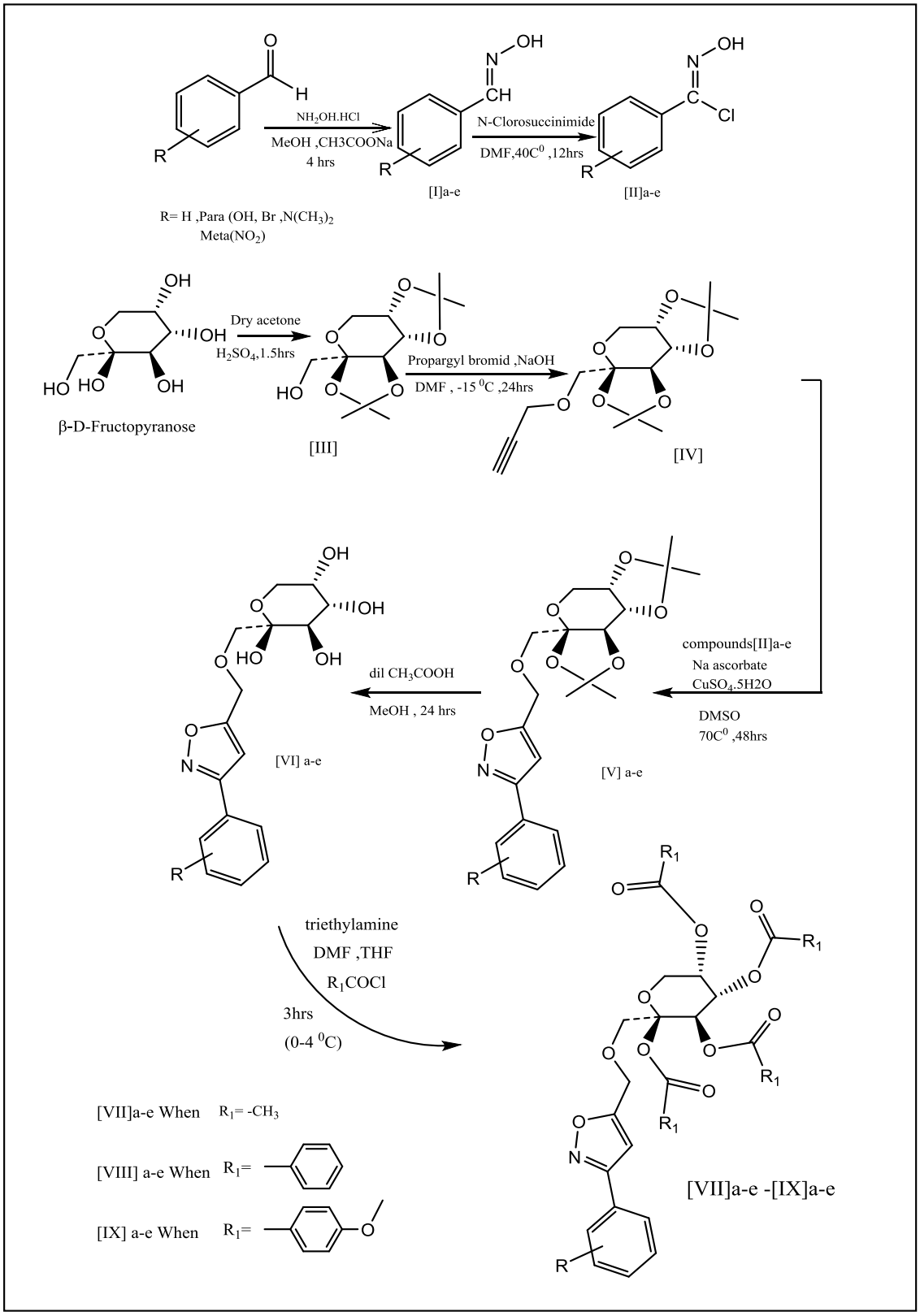
b. Synthesis of 1-((1-((3-(4- or 3-substituted phenyl)isoxazol-5-yl) methyl)-1H-benzo[d]imidazol-2-yl)methyl)-4-{ (beta-D-fructopyranose -O-yl)methyl}1H-1,2,3-triazole $[XXI]_{a-e}$ using compounds$[XX]_{a-e}$ with mixture of diluted acetic acid and absolute methanol under reflux.

c. Synthesis of ester derivatives containing both triazole and isoxazole rings compounds$[XXII]_{a-e}$,$[XXIII]_{a-e}$ and$[XXIV]_{a-e}$ by reacting hydroxyl groups of compounds $[XXI]_{a-e}$ with different acid chloride in mixture of tetrahydrofuran (THF) and dimethylformamide (DMF) using triethylamine (Et_3N) as a catalyst at 0-4^{0}C.

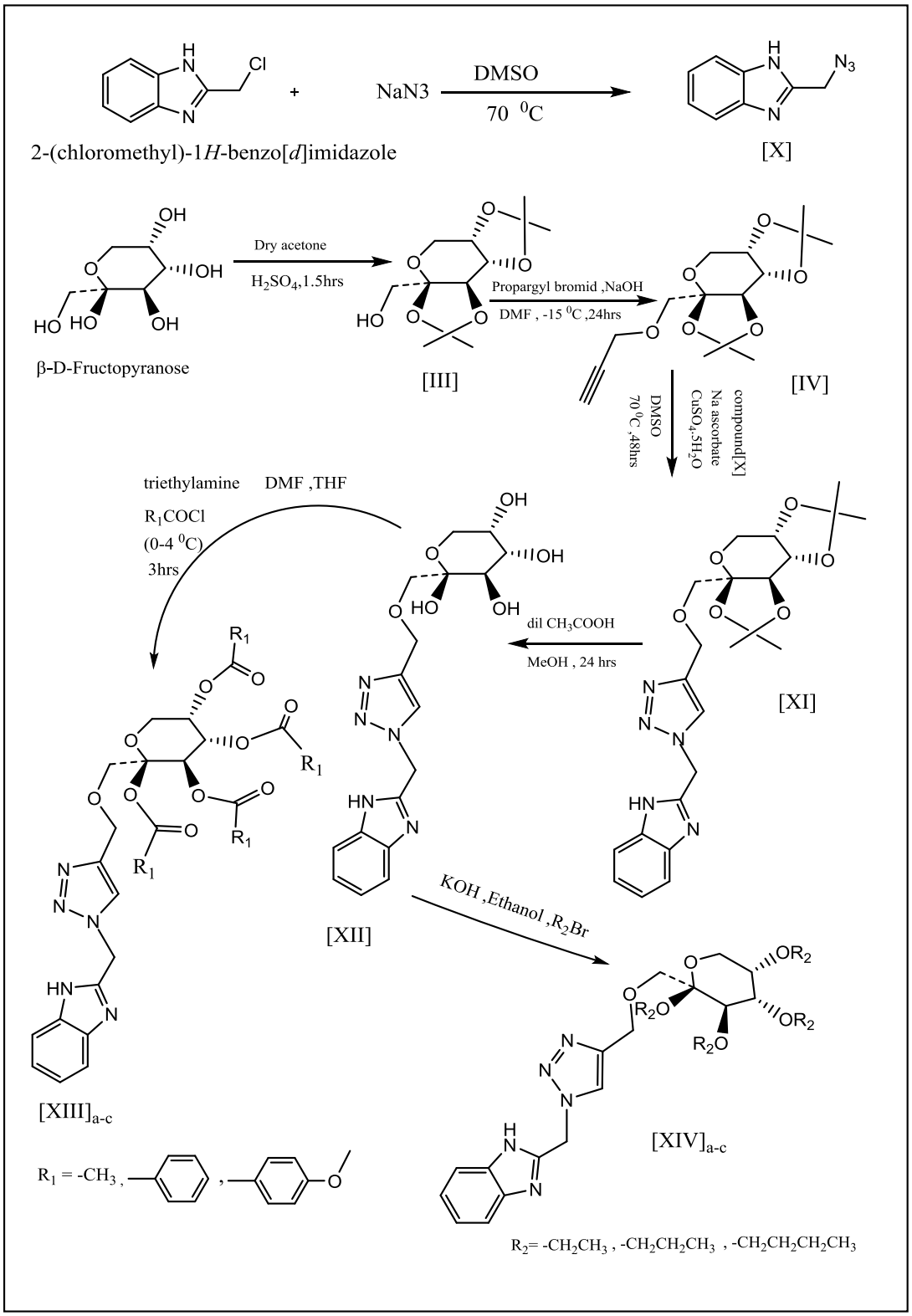
The synthesized compounds were characterized by their melting points, and by their spectral data such as FTIR, and ^{1}HNMR,^{13}C-NMR, Mass spectroscopy (for some of the compounds).

All newly synthesized compounds were tested against antibacterial activity; *Staphlocococs aureus* gram (+), *Bacillus subtitis* gram (+) and *E.coli* gram (-) bacteria and also on *candida albicans* fungal. Some compounds gave good biological activity and others did not show any biological activities.

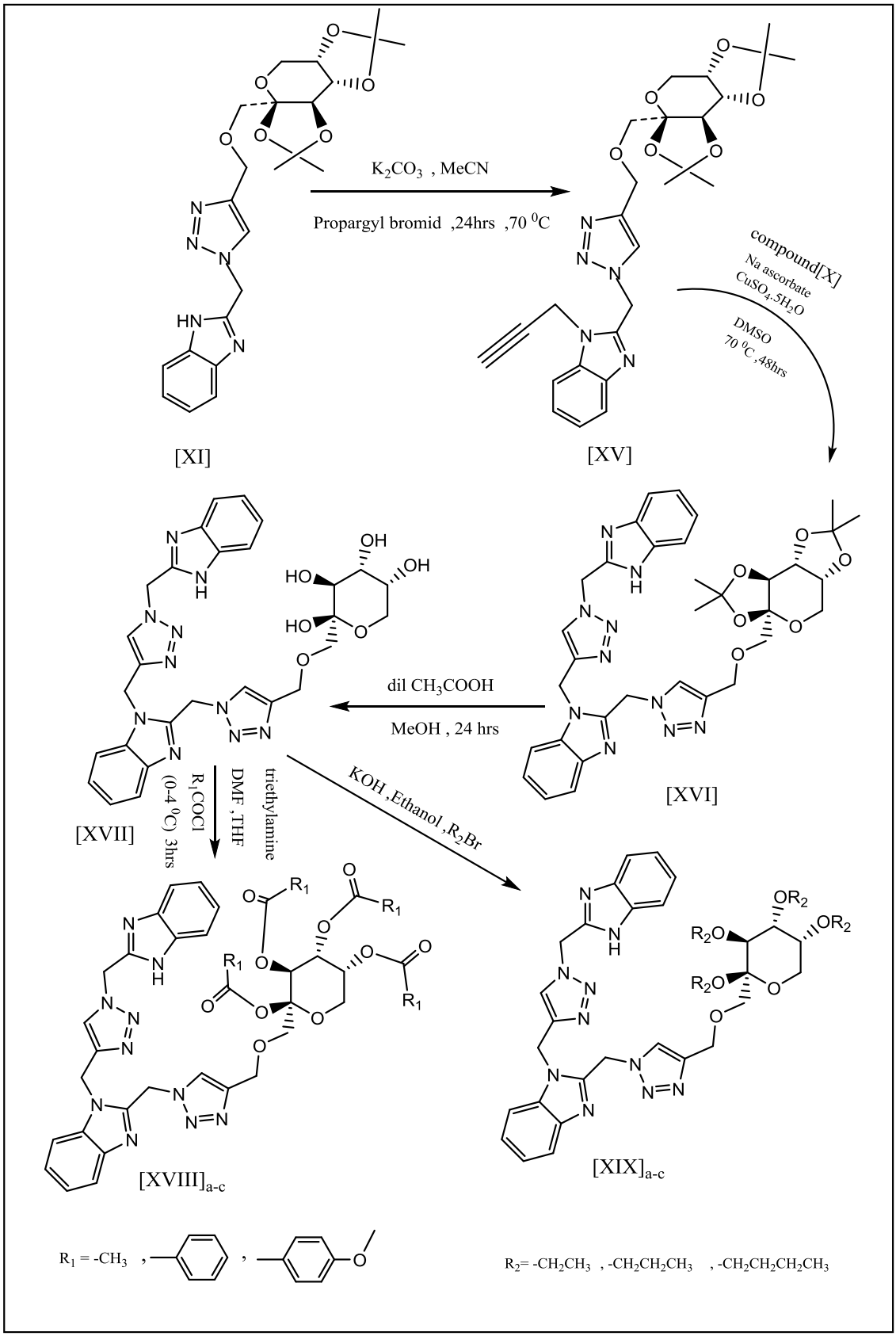
This work can be summarized by the following Schemes(1,2,3and4):



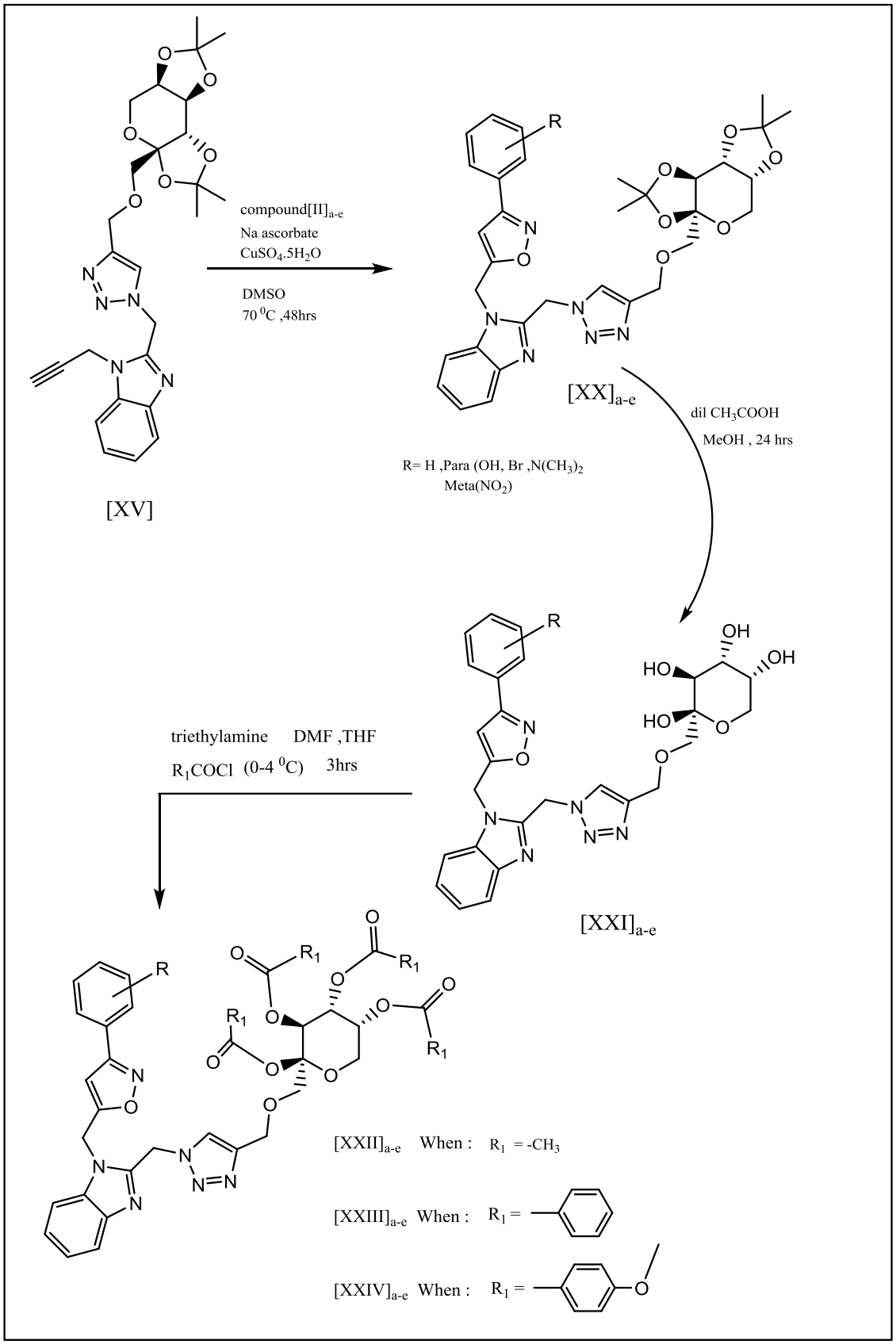
Schemes (1)


NaN3
DMSO
70 0C
2-(chloromethyl)-1H-benzo[d]imidazole
[X]
Dry acetone
H2SO4,1.5hrs
β-D-Fructopyranose
[III]
Propargyl bromid ,NaOH
DMF , -15 0C ,24hrs
[IV]
DMSO
70 0C ,48hrs
compound[X]
Na ascorbate
CuSO4,5H2O
triethylamine DMF ,THF
R1COCl
(0-4 0C)
3hrs
dil CH3COOH
MeOH , 24 hrs
[XI]
[XII]
KOH ,Ethanol ,R2Br
[XIII]a-c
R1 = -CH3 ,
[XIV]a-c
R2= -CH2CH3 , -CH2CH2CH3 , -CH2CH2CH2CH3

Schemes (2)


K2CO3 , MeCN
Propargyl bromid ,24hrs ,70 0C
compound[X]
Na ascorbate
CuSO4.5H2O
DMSO
70 0C ,48hrs
[XI]
[XV]
dil CH3COOH
MeOH , 24 hrs
[XVI]
[XVII]
R1COCl
(0-4 0C) 3hrs
DMF ,THF
triethylamine
KOH ,Ethanol ,R2Br
[XVIII]a-c
[XIX]a-c
R1 = -CH3 ,
R2= -CH2CH3 , -CH2CH2CH3 , -CH2CH2CH2CH3

Schemes (3)


compound[II]a-e
Na ascorbate
CuSO4.5H2O
DMSO
70 0C ,48hrs
[XV]
R= H ,Para (OH, Br ,N(CH3)2
Meta(NO2)
[XX]a-e
dil CH3COOH
MeOH , 24 hrs
[XXI]a-e
triethylamine DMF ,THF
R1COCl (0-4 0C) 3hrs
[XXII]a-e When : R1 = -CH3
[XXIII]a-e When : R1 =
[XXIV]a-e When : R1 =

Schemes (4)

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List of abbreviations

DNA	Deoxyribonucleic acid
LDL	Low- density lipoprotein
HDL	High-density lipoprotein
EFSA	European Food Safety Authority
β	Beta
α	Alfa
TsOH	Tosyl hydroxide
TsCl	Tosyl chloride
EtOH	Ethanol
DCM	Dichloro methane
DFA	Di fructose di anhydrides
BnBr	Benzyl bromide

TfOH	Trifluoromethanesulfonic acid
PDC	pyridinium dichromate
Fmoc	Fluorenylmethyloxycarbonyl
Fmoc-OSu	9-Fluorenylmethylsuccinimidyl carbonate
RePO	Refine process
MTBE	Methyl *tert*-butyl ether
MO	Molecular orbital
HOMO	highest occupied molecule orbital
LUMO	lowest un-occupied molecular orbital
FMO	Frontier molecular orbital
EWG	Electron withdrawing group
Bn	Benzyl
DABCO	1,4-diazabicyclo [2.2.2] octane
DBU	1,8-DiazaBicyclo[5.4.0]Undec-7-ene
MCPBA	Meta-Chloroperoxybenzoic acid
CuAAC	Copper-Catalyzed Azide-Alkyne Cycloaddition
DIPEA	N,N-Diisopropylethylamine
MCR	Multicomponent reaction
TBTA	Tris((1-benzyl-4-triazolyl)methyl)amine
NHC	N,N-ditertiarybutylimidazolium chloride
HIV	Human immunodeficiency virus
Et_3N	triethylamine
COX-2	Cyclooxygenase-2

NaAsc	Sodium-ascorbate
DMF	N,N- dimethyl formamide
THF	Tetrahydrofuran
TEA	Triethylamine
TLC	Thin layer chromatography
py	pyridine
Et_2O	Diethyl ether
hrs	hours
MWI	Microwave irradiation
DMSO-d_6	Dimethyl sulfoxide deuterated
Conc.	Concentration
abs.	Absolute
gm	Gram
mL	Milliliter
m p	Melting point
^{o} C	Degree centigrade
^{1}H-NMR	Proton Nuclear Magnetic Resonance
^{13}C-NMR	Carbon Nuclear Magnetic Resonance
FT-I R	Fourier Transform Infrared
cm^{-1}	Wave number
asym .	Asymmetry
sym	Symmetry
δ	Chemical shift
ppm	Part per million

s	Singlet
d	Doublet
t	Triplet
q	Quartet

1. Introduction

1.1Carbohydrate

A carbohydrate is any kind of neutral compound consist carbon (C), oxygen (O) and hydrogen (H) atoms, in which the ratio of hydrogen atom to oxygen atom is 2:1 with the empirical formula $C_m(H_2O)_n$ [(1)]. This formula is true for monosaccharide with exceptions of deoxy ribose, a sugar component of DNA[(2)] has an empirical formula $C_5H_{10}O_4$[(3)]. The carbohydrates are technically hydrates of carbon[(4)], structurally it is more precise to view them as aldoses and ketoses[(5)].

Carbohydrates are also known as saccharides, (saccharides derived from Greek word σάκχαρον (sakkharon), meaning sugar). They are classified on the basis of number of sugar units present in their structure[(6,7)] as follows:

1- Monosaccharide.

2- Disaccharides.

3- Oligosaccharides.

4- Polysaccharides.

All common monosaccharide and disaccharides have ending with the suffix -ose. Example of monosaccharide include glucose, fructose and galactose. Monosaccharide are the building blocks of disaccharides such as sucrose and lactose. Glycogen is a large, branched polysaccharides that it the main storage from of glucose in humans and animals. It is found in the liver and muscles (glycogen make up 6-10% of the liver by weight and 1-2% muscles by weight). cellulose, a complex carbohydrates or polysaccharides .The basic

structural component of plant cell .It is a source of human nutrition dietary fiber[8,9].

1.1.2 D-Fructose

D- Fructose is a monosaccharide that is found in sweet fruits and it is bonded to glucose to form the disaccharide , sucrose. The dietary monosaccharide include glucose , fructose and galactose. Dietary monosaccharide absorbed directly into blood during digestion [10-12].It was discovered in 1847 by Augustien-Piere Dubrunfaut [13,14] (french chemist). William Allen Mellir[15,16] was the first to use word fructose in 1857. Pure crystalline fructose is a white sweetener and odorless. It is the most water-soluble of all the sugars[17] . Fructose is sugar that found naturally in fruits, fruit juices, some vegetables, and honey.

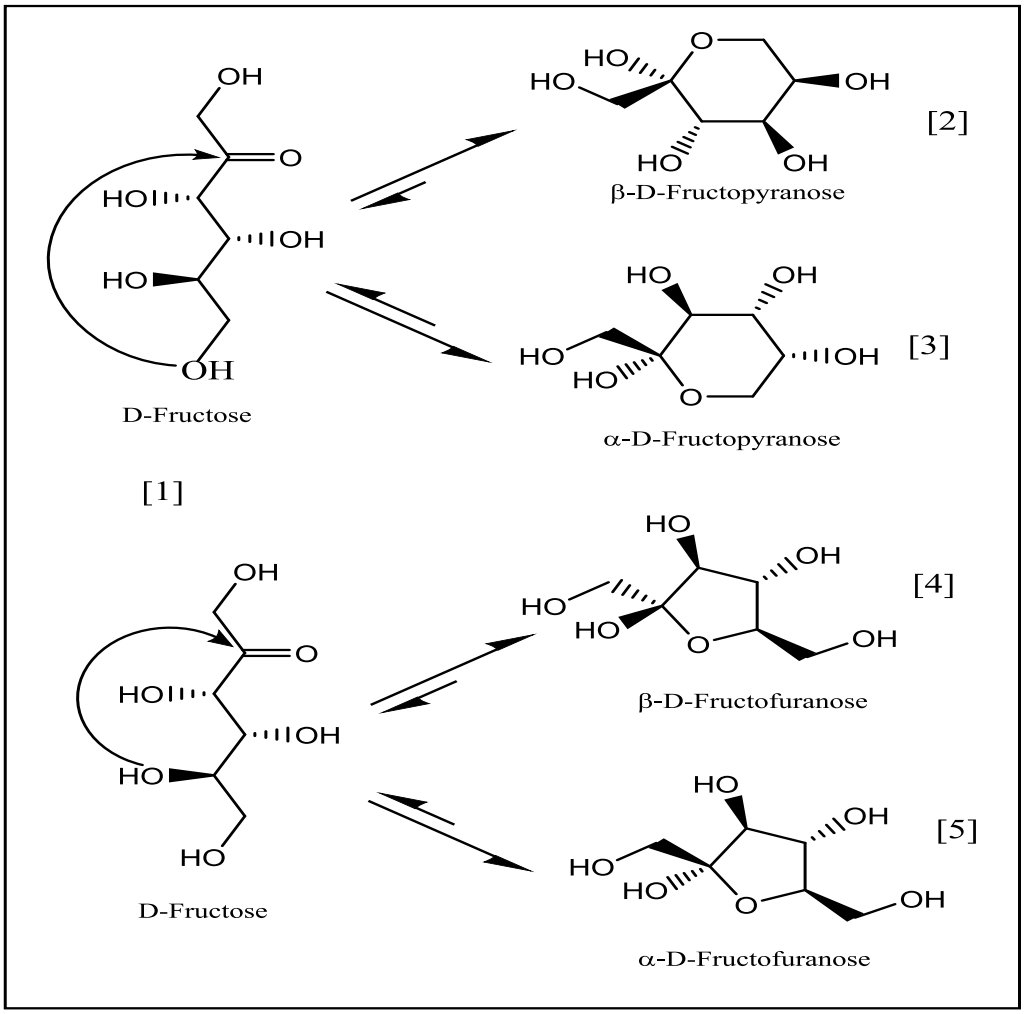
The main commercially sources of fructose are sugar cane, sugar beets, and maize. Corn syrup is one of several natural sweetener derived from corn starch. It is a mixture of glucose and fructose as monosaccharides . Sucrose is a non reducing disaccharides composed of glucose and fructose linked via their anomeric carbons. Fructose of fruits

and juices is usually added to foods and drinks for enhancing taste. Nearly 240,000 tonnes of crystalline fructose are produced per year[18].

Excessive consumption of fructose cause insulin resistance , which can lead to obesity, and type II diabetes. Fructose does not supress appetite as much as glucose docs. But it might promote overeating. Excessive fructose consumption may leptin resistance, disturbing body fat regulation, elevated LDL, HDL, cholesterol and triglycerides, leading to metabolic syndrome[19], and cardiovascular disease[20]. European Food Safety Authority (EFSA) mentioned that fructose consumption in foods or beverages compared with sucrose and glucose is preferable because of its lower effect on postprandial blood sugar levels, and also noted that "high intakes of fructose may lead to metabolic complications such as dyslipidaemia, insulin resistance, and increased visceral adiposity[21]. Further, the UK's Scientific Advisory Committee on Nutrition in 2015 disputed the claims of fructose causing metabolic disorders, stating that "there is insufficient evidence to demonstrate that fructose intake leads to adverse health outcomes independent of any effects related to its presence as a component of total and free sugars" [22].

1.1.3 Chemistry of D-Fructose

D- fructose is a 6-carbon polyhydroxy ketone[1]with a chemical formula of $C_6H_{12}O_6$. Crystalline fructose is a cyclic six-membered structure which leads to the stability of its hemiketal and internal hydrogen-bonding. This form is formally called β-D-fructopyranose (Scheme 1-1)form [23].



Scheme(1-1): Equilibrium in solution between the acyclic and the cyclic isomers of fructose

At equilibrium, in solution at 20 ºC, β-D-fructopyranose [2] is the preponderant tautomer of fructose comprising 69.1% of the total, followed by β-D-fructofuranose [4] (21.4%), α-D-fructofuranose [5] (6.1%), α-D-fructopyranose [3] (2.8%) and the linear keto form of fructose (0.6%)[24]. The mutarotation to achieve equilibrium is complicated by varying rates of transformation. The pyranose to pyranose transformation occurs between two stable chair conformations and is consequently slow [23,25,26]. In contrast, the transformation between pyranose and furanose forms is quick [22] and the furanose to furanose transformation occurs effectively instantaneously between high energy envelope and twist forms [27-30]. Despite this complexity, the mutarotation

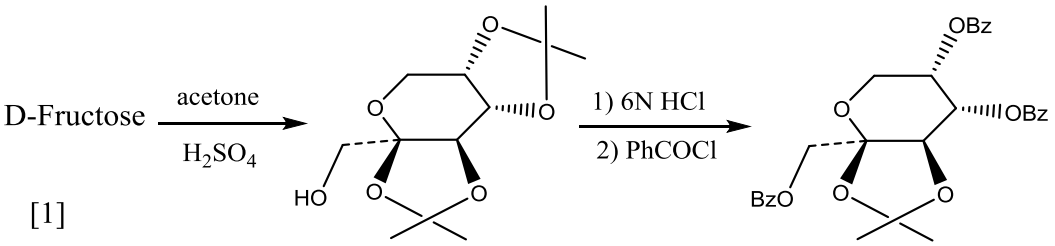
of fructose can usually be approximated as a simple first-order process [23], with the kinetics represented by the conversion of β-pyranose to the furanose forms [31]. Using this kinetic assumption the mutarotation of fructose has recently been demonstrated to have an activation energy of 62.6 kJ.mol^{-1}[24].

1.

2. 1.1.4 Reactions of D-Fructose

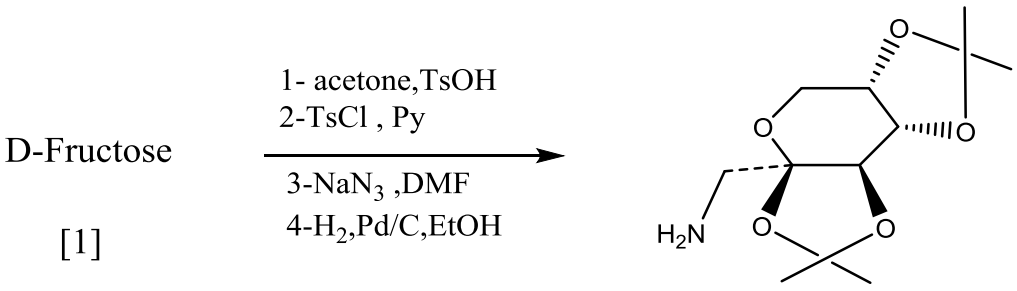
3.

Nortey et al[32]. Synthesized 1, 4, 5 - tri - O - benzoyl- 2, 3 - O - isopropylidene - β - D –Fructopyranose[7] from D-fructose in only three steps. Steps one acetonation of β -D-fructose using acetone and sulfuric acid H_2SO_4 as catalysts to produce 2,3:4,5-di-O-isopropylidene-D-fructopyranose [6]. Steps two is hydrolysis of compound[6] using 6N HCl. Steps three is the esterification of hydroxyl groups with benzoyl chloride.



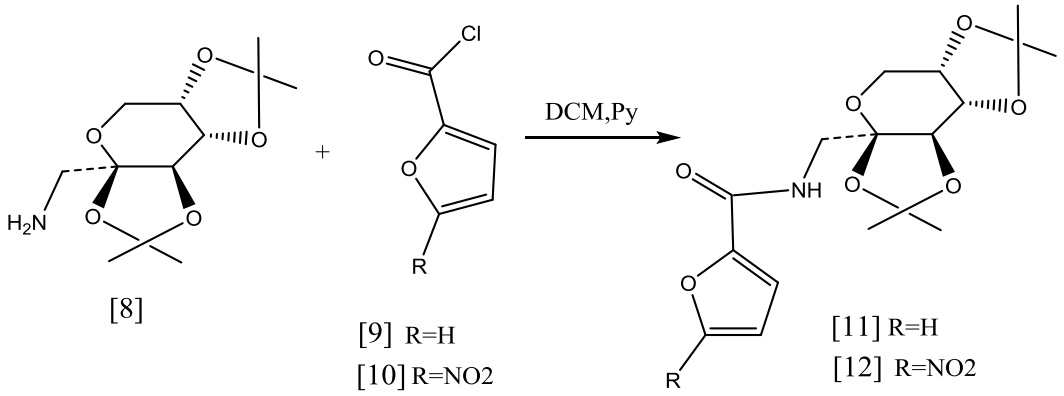
[1] [6] [7]

On the other hand, Mauro et al[33]. prepared of aminosugar [8] from D-fructose[1] under blow reagents.



[1] [8]

The treated amino sugar [8] reacted with furoyl chloride [9] 5-nitrofuroyl chloride [10], in dichloromethane in the presence of pyridine, leading to compounds [11],[12].

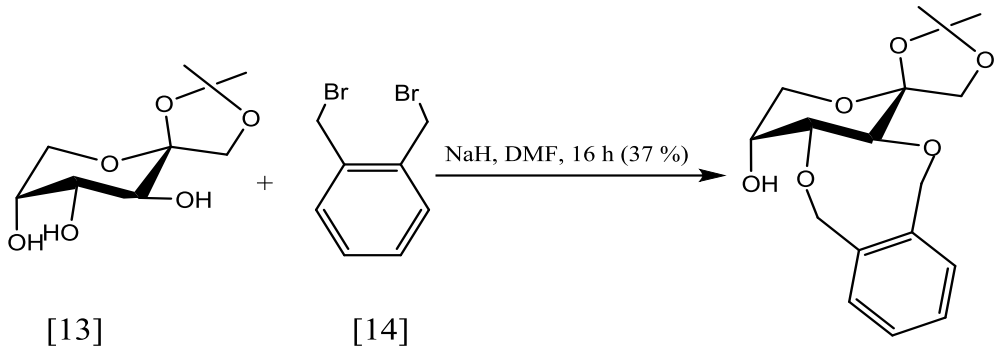


[8]

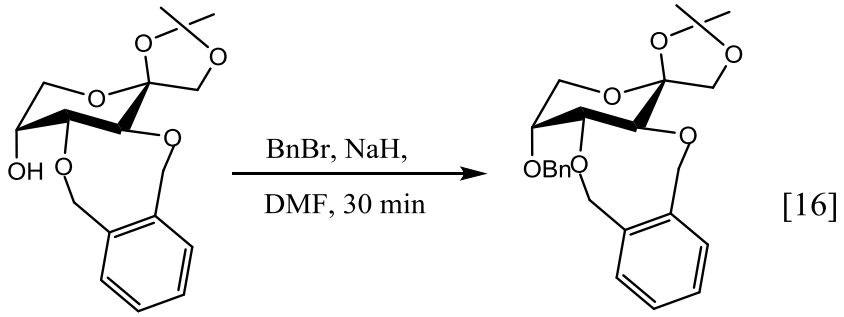
[9] R=H
[10] R=NO2

[11] R=H
[12] R=NO2

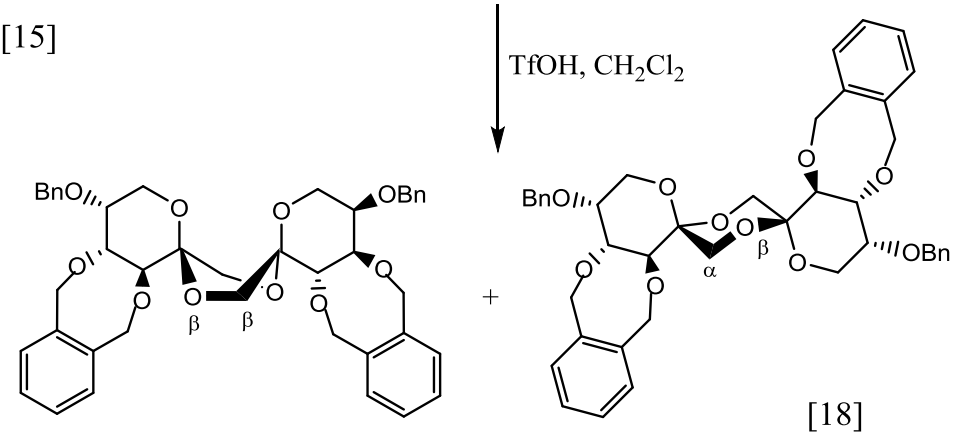
While, Alejandro et al[34]. Prepared difructose dianhydrides DFA [19] and [20] using a four-step reaction. Step one is the reaction of triol derivative[13] with α,α_-dibromo-*o*-xylene[35] [14] in the presence of sodium hydride to produce compound [15]. In step two, benzylation of the remaining hydroxy group (5-OH) in compound[15] using benzyl bromide (BnBr) in the presence of sodium hydride (NaH) in dimethylformamide (DMF) gave compound [16]. And subsequent TfOH-promoted dimerisation/spirocyclisation produce a mixture of the two dipyranose β,β - and α,β -DFAs [17] and [18]. Finlly hydrogenolysis of the benzyl and cyclic *o*-xylylene groups compounds [17],[18] with Pd/C in the presence of formic acid proceeded smoothly to give the difructose dianhydrides DFA [19],[20].



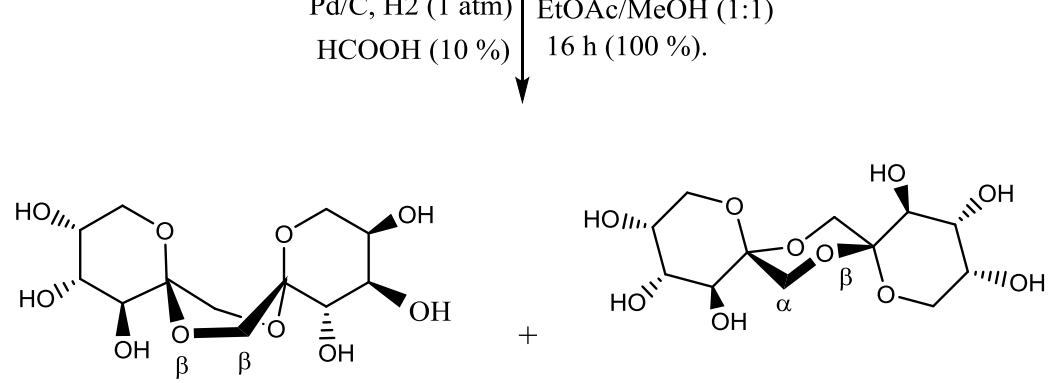
[13] [14] [15]



[15] [16]

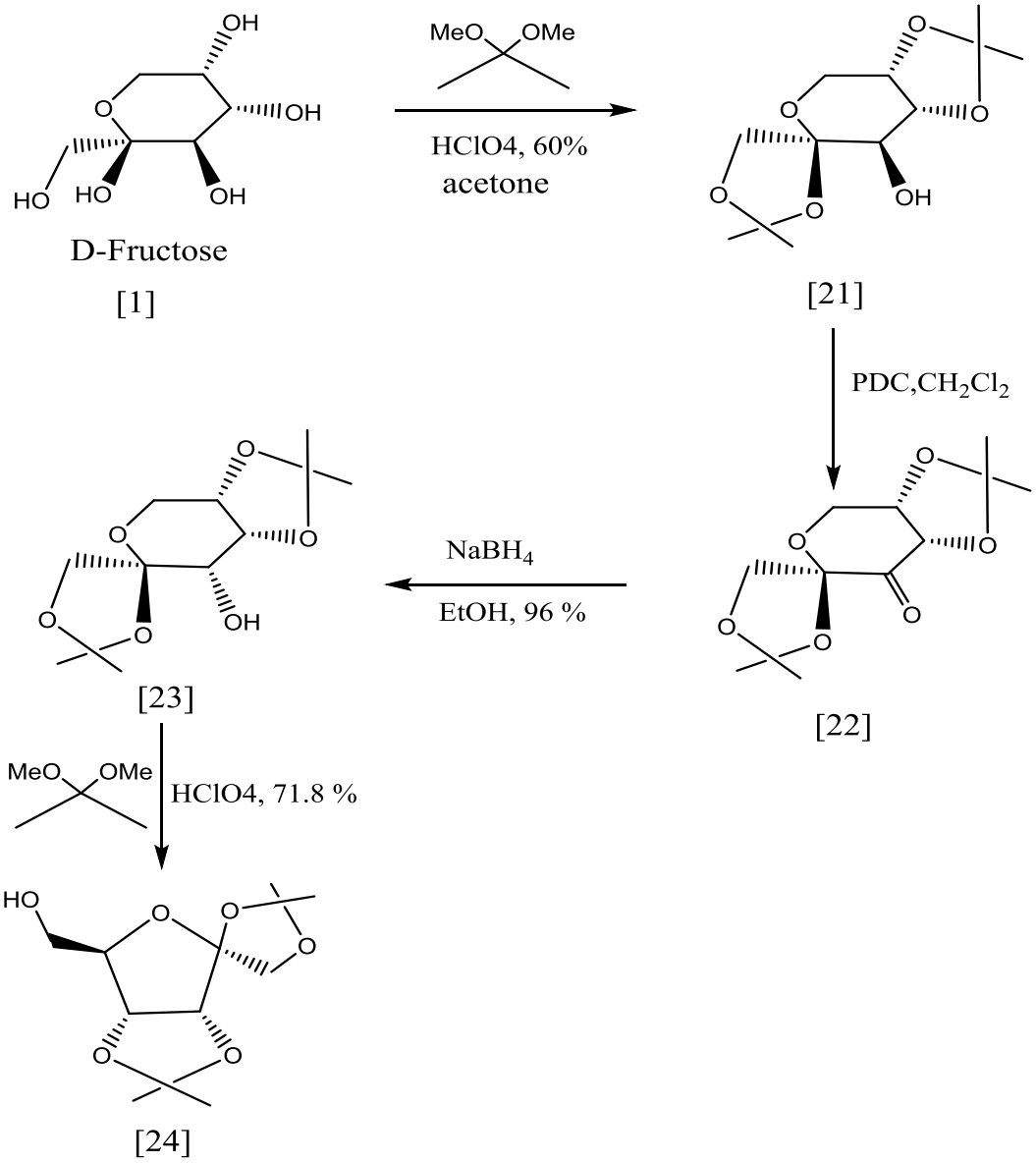


[17] [18]



[19] [20]

D-fructopyranose [1] was converted to 1,2:4,5-di-O-isopropylidene-D-fructopyranose [21] by Perali[36] et al. Via mediated oxidation of compound [21] using pyridinium dichromate to give 1,2:4,5-di-O-isopropylidene-D-erythro-2,3-hexodiulo-2,6-pyranose [22] followed by stereoselective reduction produce 1,2:4,5-di-O-isopropylidene-D-psicopyranose [23]. Isomerization of pyranose [23] to its furanose isomer 1,2:3,4-di-O-isopropylidene-D-psicofuranose [24] was accomplished using catalytic $HClO_4$ in acetone and 2,2- dimethoxy propane.



D-Fructose

[1]

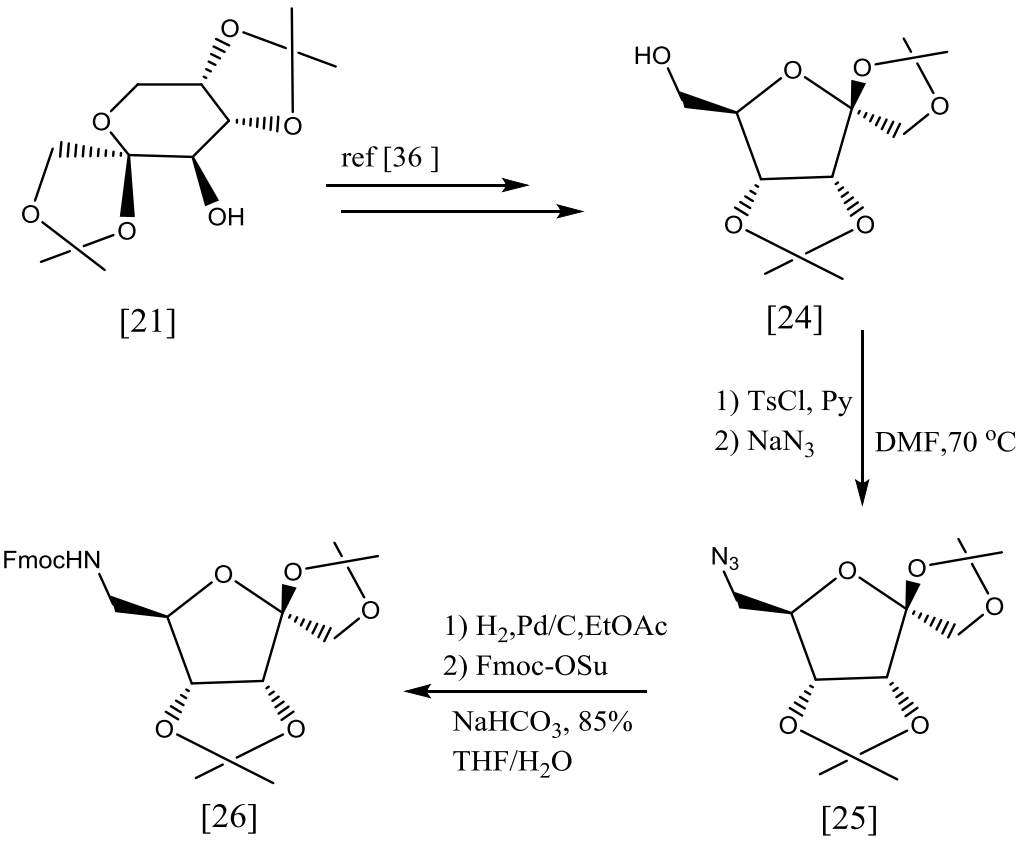
[21]

[22]

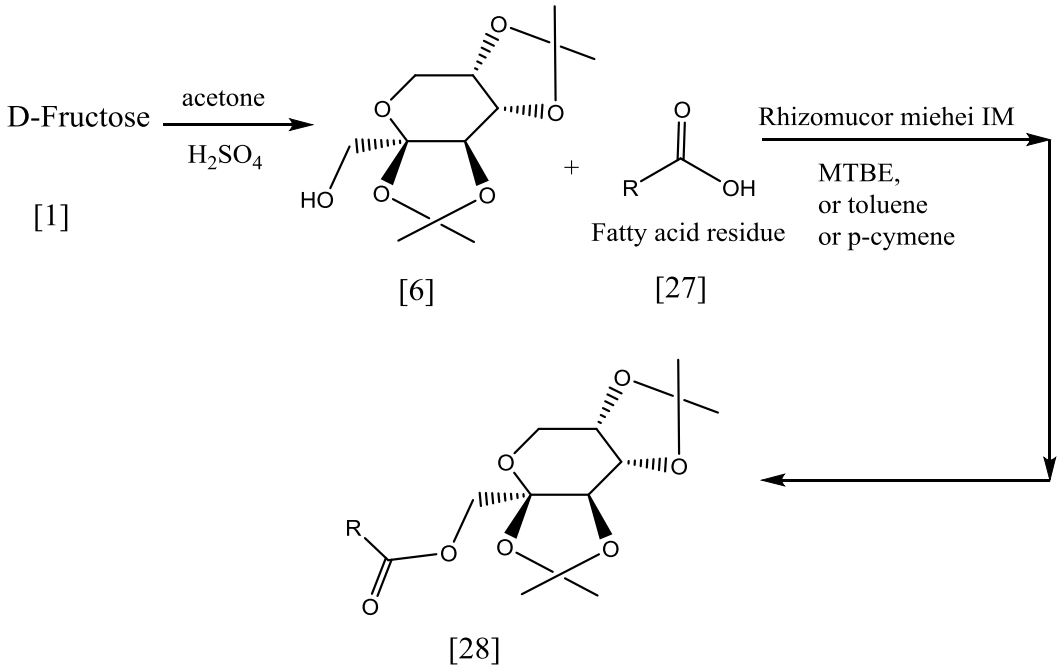
[23]

[24]

Madhuri et al[37]. prepared of 6-NHFmoc-6-deoxy-1,2;3,4-di-*O*-isopropylidene- β-D-psicofuranose [26]. They used 1,2;4,5-di-*O*-isopropylidene-β-D-fructopyranos [21] converted to 1,2:3,4-di-O-isopropylidene-D-psicofuranose [24] in three steps as noted in the previous paragraph. In the next step, reaction of compound [24] with sodium azide (NaN_3) in DMF via C6-*O*-tosyl intermediate to yield 6-azido-6-deoxy-1,2;3,4-di-*O*-isopropylidene- β-D-psicofuranose [25]. Finally, hydrogenation of the azide with 10% Pd/C in EtOAc gave the primary amine[38], which was protected using Fmoc-OSu/$NaHCO_3$ in THF/H_2O to yield [26].



Under continuous-flow conditions, at increasing concentrations (0.1, 0.3 and 0.5 M), using the commercial Rhizomucor miehei im - mobilized lipase (bio-catalyzed), Felipe[39] et al. prepared ester compound [28] by reacting 2,3:4,5-di-O-isopropylidene - β-D-fructopyranose [6] with acidic residue of palm oil refine process (RePO) [40] [27]in different solvent(MTBE, toluene or p-cymene) .



1.2. 1,3-Dipolar or[3+2] Cycloaddition Reactions

One of the classic reactions in organic chemistry is the preparation of 5- membered heterocyclic rings by the addition of 1,3-dipoles to an alkene or alkyne. Diazoacetic esters were the first 1,3-dipolar discovered by Curtius in 1883. [41] His collaegue Buchner later studied the reactions of these diazoacetic esters with *α,β*-unsaturated esters, which were the first 1,3-dipolar cycloaddition reactions[42] .

The general concepts of 1,3-dipolar cycloadditions were developed by Huisgen in 1960[43,44],and the concept of preservation of orbital symmetry developed by Woodward and Hoffmann at the same time were crucial for understanding the mechanism of concerted cycloaddition reactions[45)]. A 1,3-dipolar cycloaddition reaction results

in the formation of a five-membered ring due to the reaction of a 1,3-dipole, a three-atom subsistence which is a 4π component and a dipolarophile which is a 2π, two atom entity. All of the 1,3-dipoles have four electrons in three over lapping π orbitals. On observing the resonance structures of any dipole can be deduce that dipoles have both nucleophilic and electrophilic characteristics. To understand the reactivity of 1,3-dipolarophile it is fundamental that this ambivalence is understood. 1,3-Dipolar cycloaddition reactions are stereoselective syn additions with respect to the dipolarophiles[46].

1,3-dipoles may be defined as species which are represented by zwitterionic resonance structures,which undergoes1,3-cycloadditions to a multiple bond system, the dipolarophile[47] (Figure 1-1).

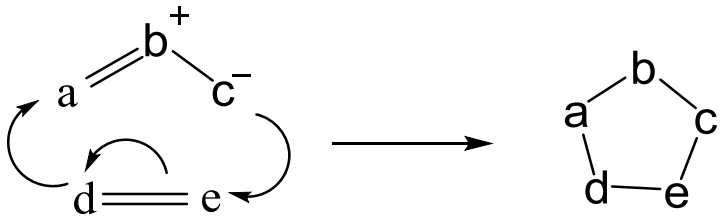


Figure (1-1) The reaction of 1,3-dipoles with dipolarophile

1,3-Dipoles of the kind where an additional bond in the plane vertical to the allyl anion, molecular orbital (MO) provides an element of diversity. The additional π-bond in the allyl type makes them bent, whereas propargyl- allenyl type is linear[48,49] (Figure 1-2).

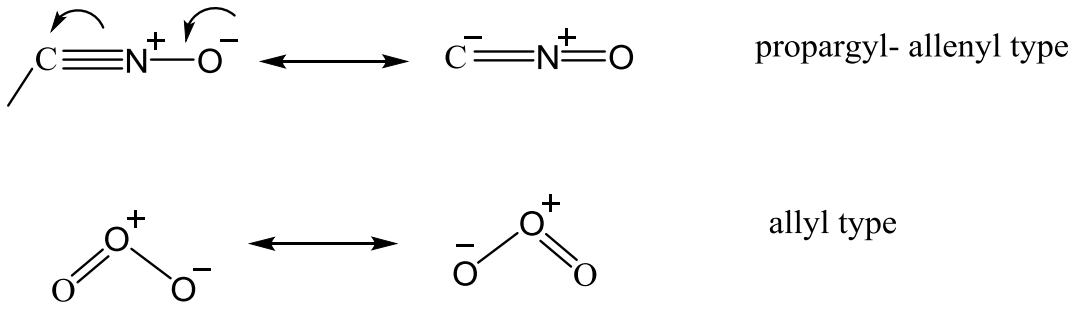
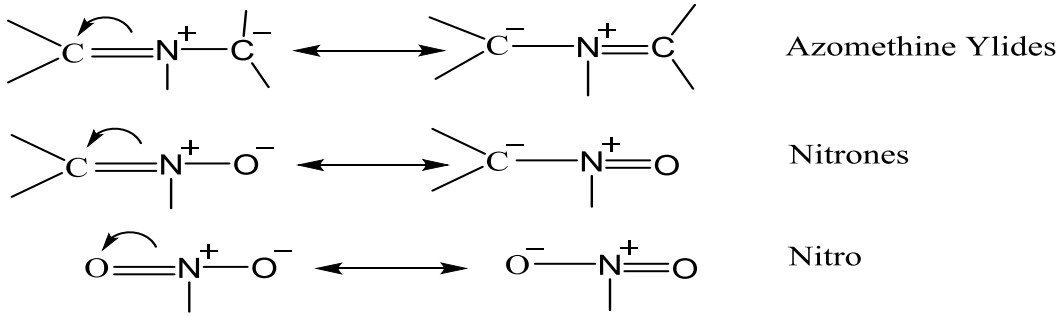


Figure (1- 2) The *π*-bond of allyl type and propargyl allenyl type

Some examples for 1,3-dipoles are given in below [47,50] (Figure 1-3).

I. Allyl Type



II. Propargyl- Allenyl type

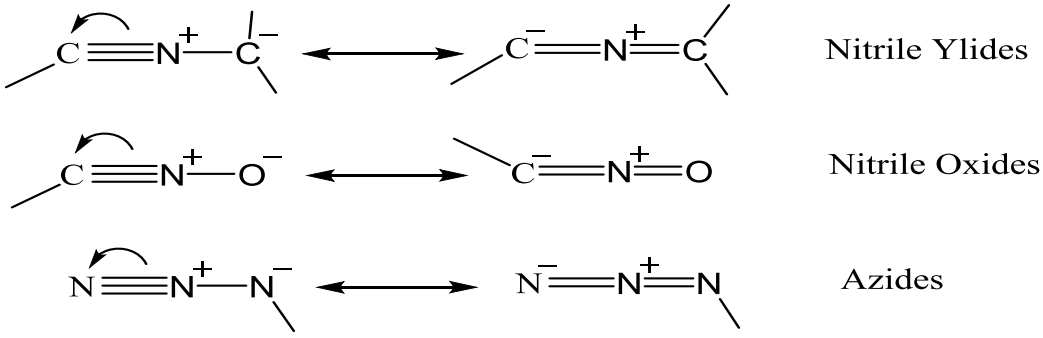


Figure (1- 3)Some of allyl type and propargyl allenyl type

Inclusive phosphorus and sulfur atoms as centers increases the diversity of 1,3- dipoles.

1.2.1. Mechanism of 1,3-dipolar cycloaddition reactions

Many experiments[48,51] which were carried out supported the concerted mechanism for 1,3-dipolar cycloaddition and it is accepted as the pathway through which the interaction accurs. It is defined as an orbital symmetry allowed [π4s + π2s] cycloaddition wherein the 4π reactant is the 1,3 dipole and the 2π reactant is the dipolarophile[52].

It was also observed that the correlation diagram of molecular orbital symmetry 1,3-dipolar cycloaddition bears a significant degree of resemblance with that of Diels-Alder reaction. It has also been described that the concertedness of the reaction is impute to the Huckel aromatic type molecular orbital (MO) of the transition state[53].

The reaction rates were found to be independent of solvent polarity; the negative entropy of activation the stereo selectivity and region selectivity all indicate to the formation of a highly ordered transition state. While Huisgen supported the concerted mechanism[54],Firestone supported the di radical mechanism[55]. Experimental evidence concerning the highly stereospecific nature of the reaction highly confirm the reaction being concerted analogous to the Diels-Alder reaction[56].

1.2.2.Orbital Symmetry analysis for 1,3-dipolar cycloaddition reactions:

We know that, in a 1,3-dipolar cycloaddition reaction, two new sigma bonds are formed at the expense of pi-electrons from the reactants. The overlap of orbitals from one molecule, with the orbitals of the other , orbitals of dipole with dipolarophile. If we concentrate on the HOMO, we see that the HOMO of both the dipole and dipolarophile are fully occupied[57]. Thus we conclude that HOMO-HOMO interaction is not possible. Bond formation is possible only if each HOMO overlaps with

an empty orbital, namely the most stable of the empty orbitals , LUMO[58].

The transition states of 1,3-dipolar cycloadditions are stabilized by the overlap of the HOMO of one reactant (dipole or dipolarophile) with the LUMO of the other (dipolarophile or dipole) in bonding fashion[58] (Figure1-4).

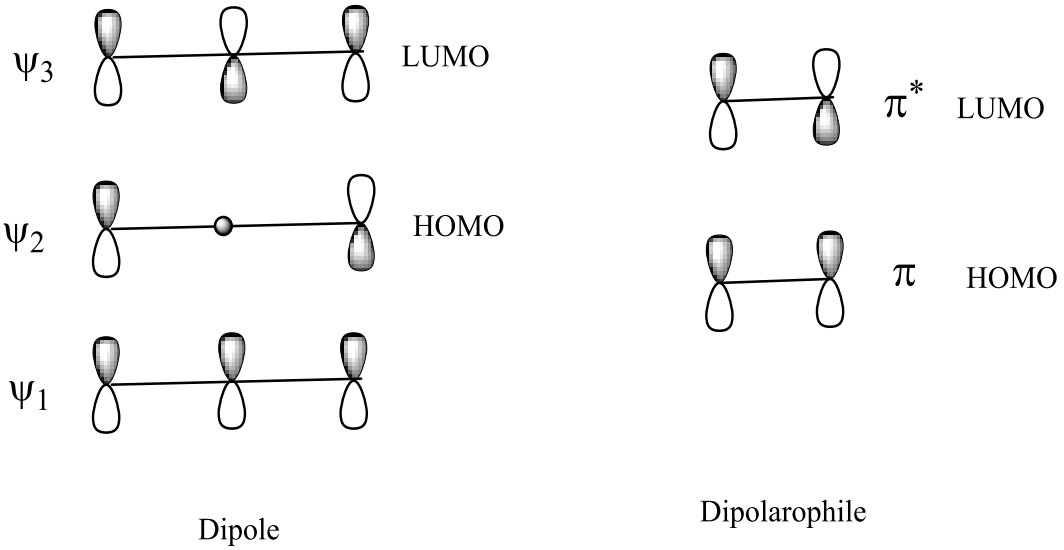


Figure (1-4) The HOMO and LUMO orbitals

The bonding interactions can be observe either by considering the LUMO of 1,3- dipole and the HOMO of the dipolarophile[59] (Figure 1-5). Or by considering the LUMO of dipolarophile and the HOMO of the 1,3-dipole (Figure1-6).

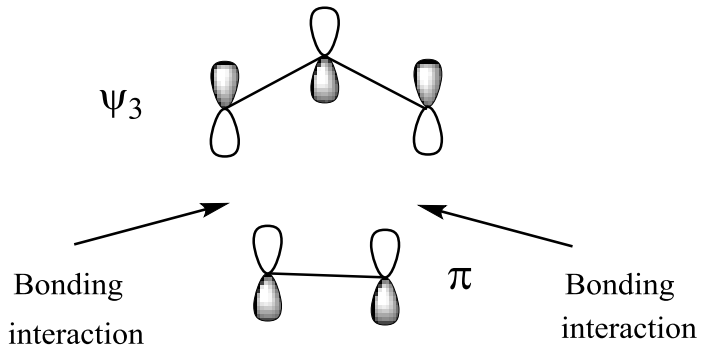
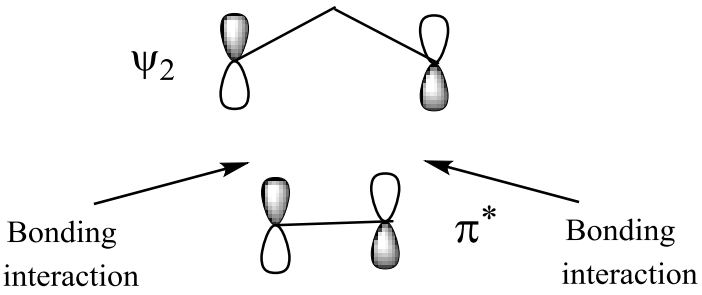


Figure (1-5)The bonding interactions by LUMO of 1,3- dipole and the HOMO of the dipolarophile



Figure(1-6) The bonding interactions by LUMO of dipolarophile and the HOMO of the 1,3-dipole

As seen in the above frontier molecular orbital interactions these reactions are thermally allowed. It is also observed that the nature of substituents on the double bond will influence the regiochemistry of the cycloaddition, whether 4-substituted or 5-substituted products are formed[(60)].

If on the other hand these reactions were photochemical we have to consider the HOMO of the excited state of one of the reactant (dipole/dipolarophile) and the LUMO in the ground state of another (dipolarophile/dipole).HOMO of the excited state of the1,3-dipole is ψ3 and the LUMO of the ground state of the dipolarophile is π (Figure 1-7) [(60)].

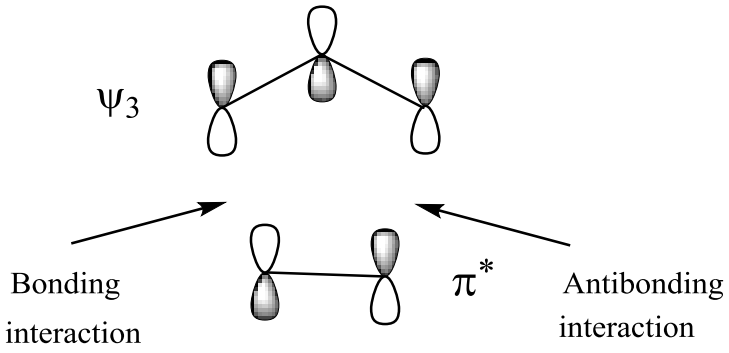
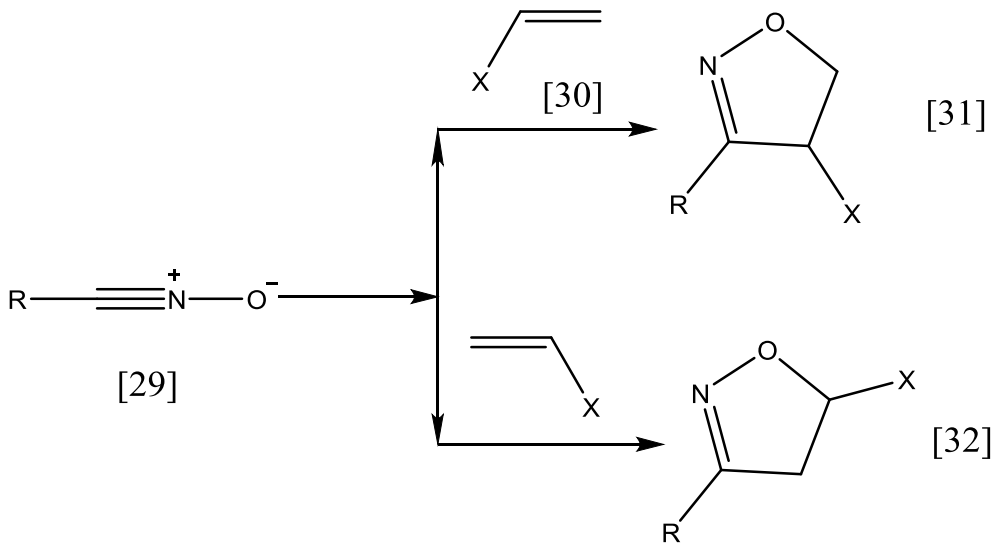


Figure (1-7) The antibonding interactions

On examining the frontier molecular orbital (FMO) interactions we conclude that since there is antibonding situation on one side there is no product formed. Therefore [π4s + π2s] is forbidden in photochemical conditions[61]

1.2.3. Regio- and Stereochemistry of 1,3-Dipolar Cycloaddition Reactions

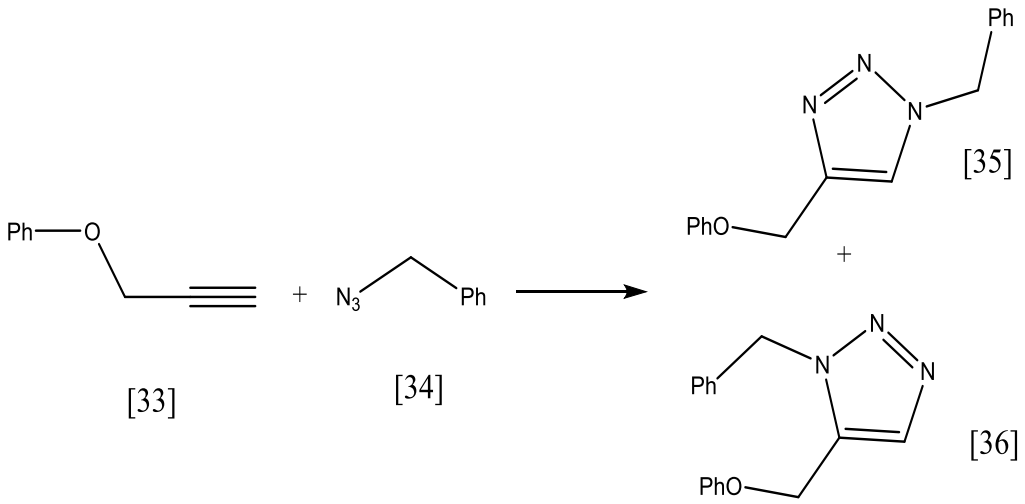
1,3-dipolar cycloaddition reactions are stereospecific syn additions with respect to the dienophile[62] and can be thus say that the stereochemistry of the dienophile is preserved in the product. Some of the dipoles listed react with dipolarophiles to give diastereomers because of two differing orientations of the reactant molecules. This is illustrated in Scheme 1-2 where due to the orientation of the dipolarophile [30], two diastereomeric products [31],[32] are possible[63].



Scheme (1-2) The stereospecific of two diastereomers

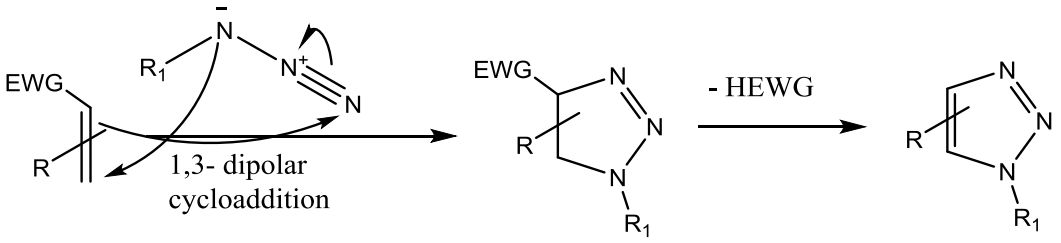
The interaction between the frontier molecular orbital (FMO) of 1,3-dipole and dipolarophile is used to explain the regioselectivity[(64)]. In the case of dipolarophiles with electron attracting groups, the interaction between HOMO of the dipole and LUMO of the dipolarophile is dominant. It is reverse for the dipolarophiles with electron donating groups. There are also cases of HOMO-LUMO interactions of comparable magnitude. As the principle of maximum overlap states, the preferred isomers of each interaction can be predicted by the union of two sites of the reactants having the largest coefficient value[(64)].

In this instance can be seen that the addition of alkynes[33] to azides[34] and leads to the formation of regioisomers [35], [36] in unequal amount[(66)].



1.2.4. Synthetic&Application of 1,3-dipolar cycloaddition

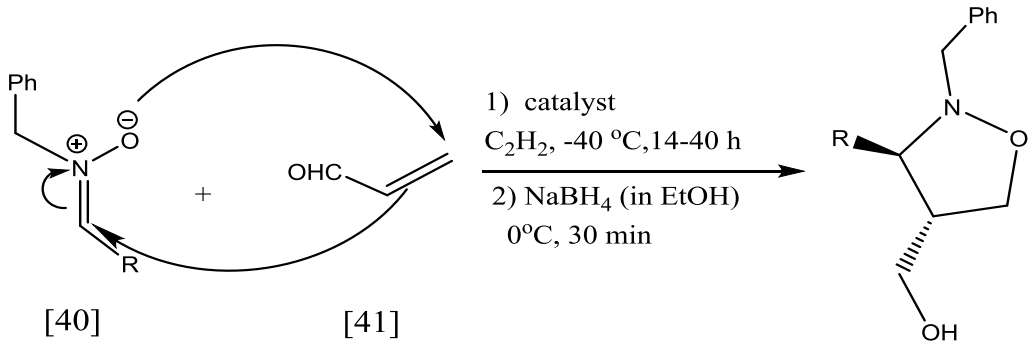
Amantini et al[67]. synthesized 1,2,3-triazole [38] derivatives using sharpless and Fokin groups , which is no longer a classic Huisgen cycloaddition. Another approach prefers the use of a directing electron withdrawing group[37], which is removable later to give compound [39]



R= alkyl, Bn

R_1= Ph, CO_2H

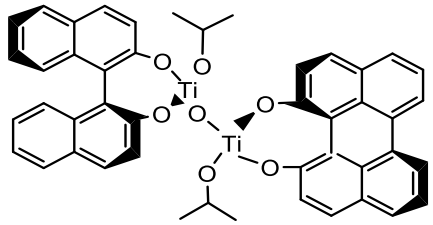
Kano et al[68]. synthesized isoxazeliden derivatives [42] by 1,3-dipolar cycloaddition reaction of nitrones[40] and acrolein[41] with a bis-Titanium catalyst as Lewis acid



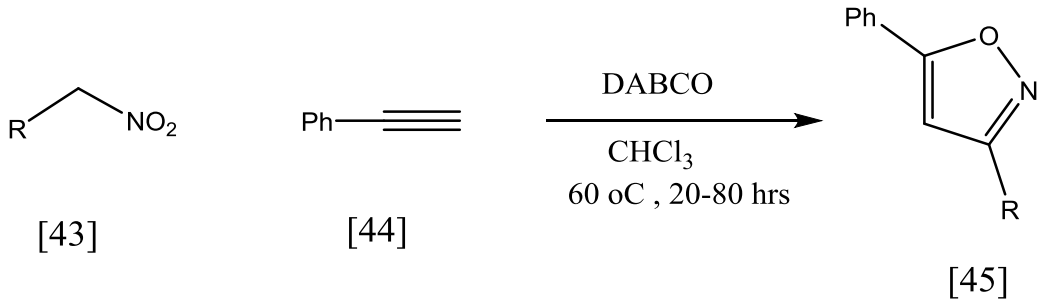
[40] [41] [42]

R= Aryl ,Alkyl

catalyst =



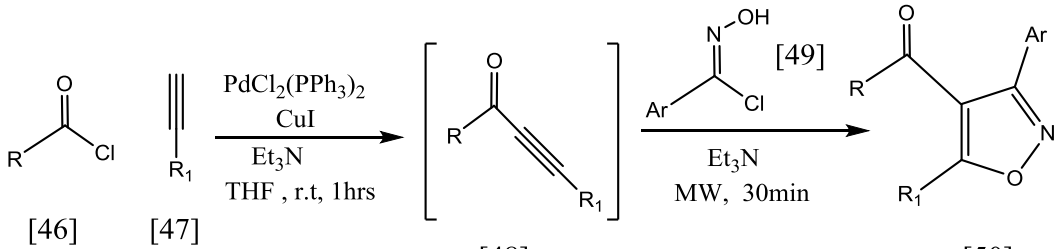
On the other hand, Cecchi et al[(69)] . used 1,4-diazabicyclo [2.2.2] octane (DABCO) as an efficient reagent for the synthesized of isoxazole derivatives [45] from primary nitro compounds dipole[43] and propargyl compound dipolarophiles[44].



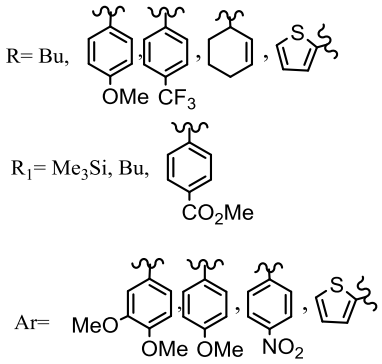
[43] [44] [45]

R= PhCO, $PhSO_2$, Ph

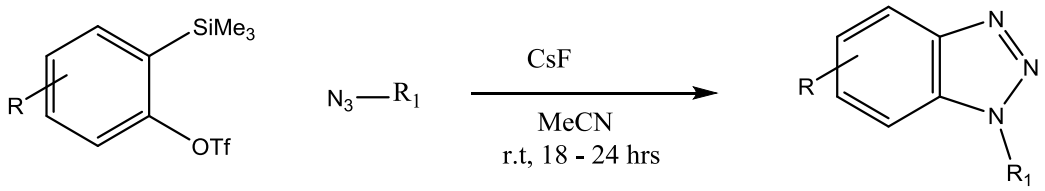
While , Willy et al[(70)]. synthesized isoxazoles [50] by a three-component coupling - cycloaddition sequence using Microwave-Assisted One-Pot, by reacting acid chlorides [46]with terminal alkyne compound [47] and the intermediate compound [48] treat with nitrile oxides of in situ generated from hydroximinoyl chlorides [49].



[46] [47] [48] [50]



Using click chemistry method, Shi et al[71]. synthesized new benzotriazoles [53] from compound[51] and azides[52] by using CsF as a catalyst.

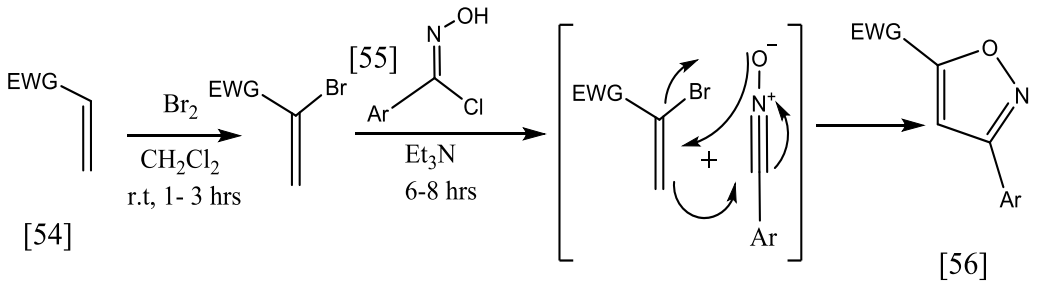


[51] [52] [53]

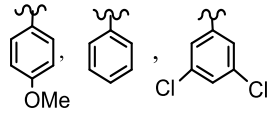
R= 4,5-Me_2 , 4,5-$(OMe)_2$, F_2

R_1= Bn, Ph, 2,5-$(OMe)_2C_6H_3$, 3,5-$Me_2C_6H_3$, 2,5-$Cl_2C_6H_3$

Xu and Hamme [72] reported the synthesis of isoxazoles [56] from alkenes[54] hydroximinoyl chlorides [55] via1,3-dipolar cycloaddition reaction, as follows:

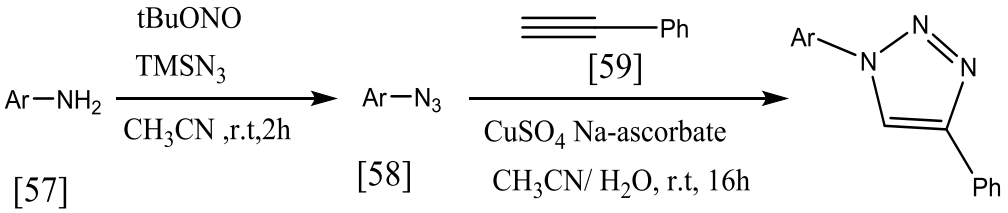


[54] [56]

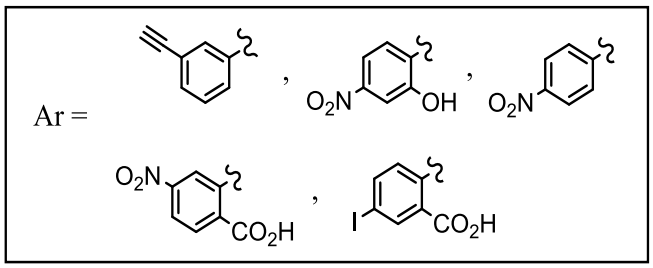
Ar = 

EWG= CHO, CO_2Me, COMe, $PhSO_2$

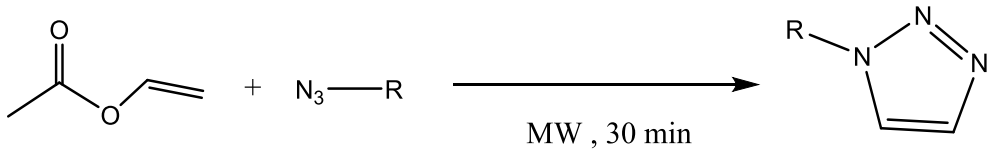
Barral et al [73]. efficiently converted aromatic amines[57] into azides[58] using terminal alkyne[59] to obtain triazoles [60] .



[57] [58] [60]



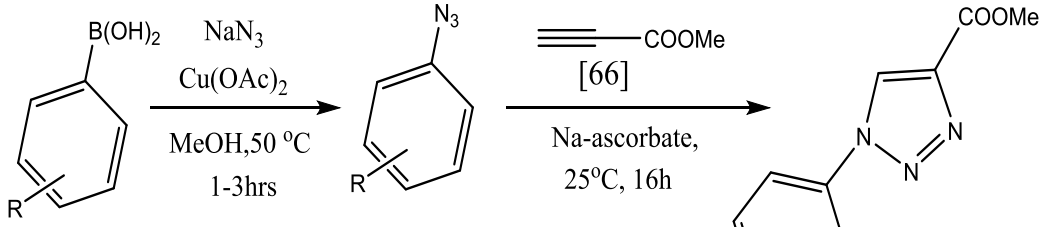
Hansen and Jensen [74] synthesized un substituted *N*-Linked 1,2,3-triazoles[63] from vinyl acetate[61] and azides [62] by microwave irradiation method.



[61] [62] [63]

R= benzyl, alkyl

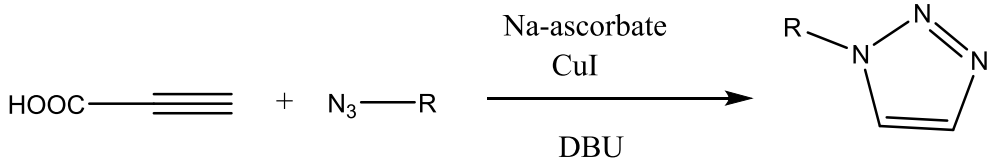
Grimes et al[75]. synthesized triazole derivatives [67] from converted heteroaryl boronic acids[64], into the accordant azides [65] with terminal alkyne compound [66] via using copper acetate and Na-ascorbate as a catalyst .



[64] [65] [67]

R= H, 4-OMe, 4-OPh, 4-Ph, 4-CH2OH,4- SMe
,4- CONH2, 4-CHO, 4-I, 4-Br, 4-Cl, 4-F

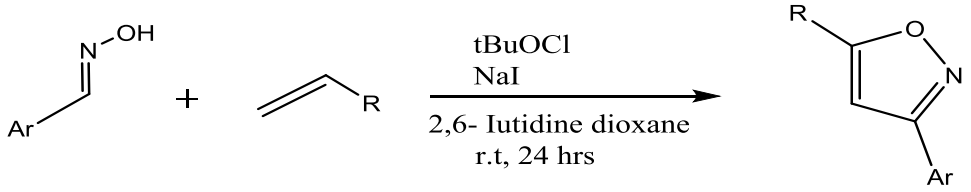
Also, M. Xu et al[76]. synthesized 1,2,3-triazole derivatives[70] by reacting azides[69] with terminal alkyne[68] using copper(I) as a catalyst .



[68] [69] [70]

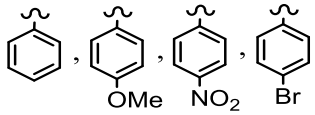
R= Ar, Vinyl

Minakata, et al[77]. synthesized Isoxazoles derivatives [73] by generating nitrile oxides from oximes[71] using *t*-BuOCI and treat with alkene compound[72] followed by cycloaddition reaction.

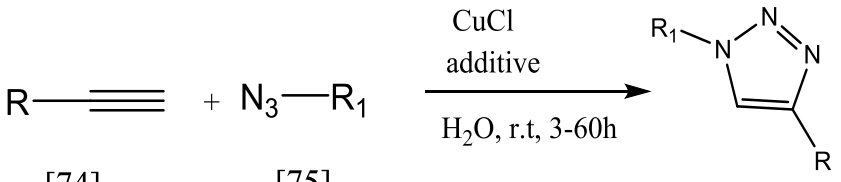


[71] [72] [73]

R= Ph, C_6H_{13}, CO_2Me

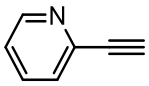
Ar= 

Hiroki et al[78]. synthesized triazole derivatives [76] by using copper (I) chloride as catalyst; alkyne[74]-azide[75] cycloaddition was carried out in water.



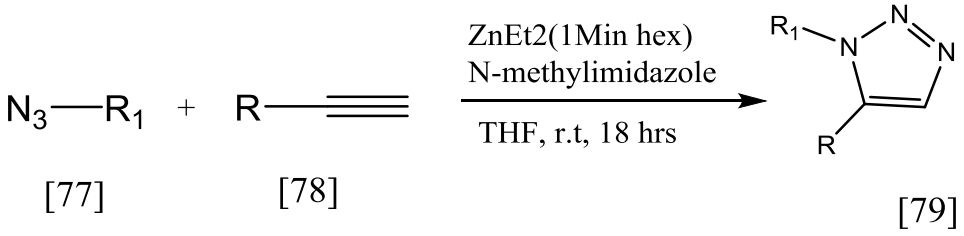
[74] [75] [76]

R= Ar, alkyl,COOMe,CH_2OH
R_1= Bn,C_8H_{17},Ph

Additive= 

Smith and Greaney [79] synthesized 1,5- substituted 1,2,3-triazoles [79]by using zinc mediated($ZnEt_2$ in hexane) azide[77]-alkyne[78]

ligation.

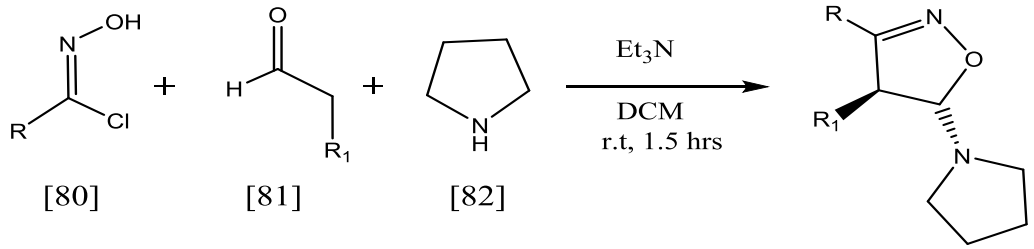


[77] [78] [79]

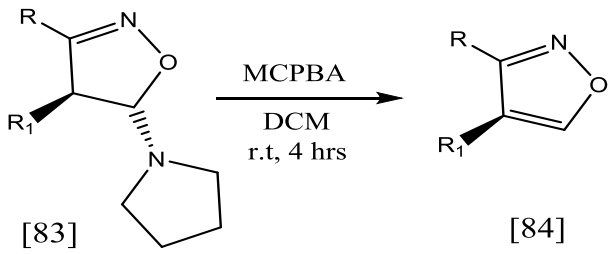
R = alkyl, Ph, vinyl

R_1 = Ar, Bn

Jia et al[80]. synthesized 3,4, -disubsituted Isoxazoles[84] via Enamine 3,4,5-trisubstituted 5-(pyrrolidinyl)-4,5-dihydroisoxazoles [83], [3+2] cycloaddition reactions, using *N*-hydroximidoyl chlorides [80], aldehydes [81] and pyrrolidinyl [82] in the presence of triethylamine.



[80] [81] [82] [83]



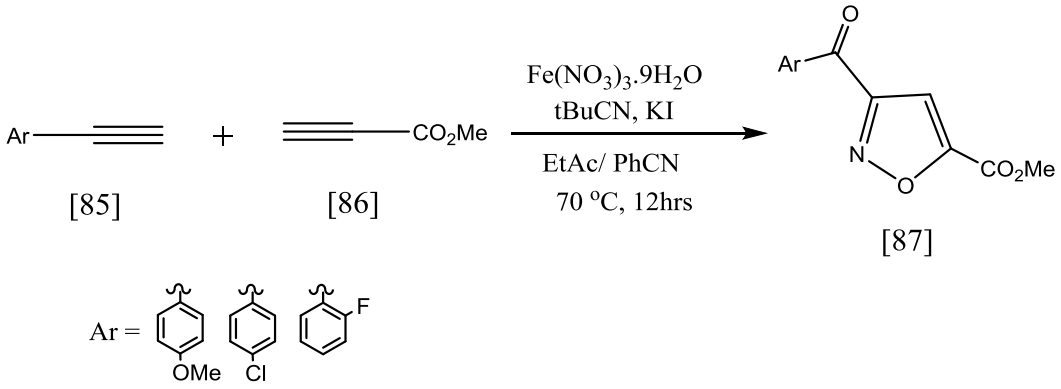
[83] [84]

R = Ar, Cy

R_1= Ph, alkyl , iPr,H

By using iron(III) nitrate as the nitration and cyclization reagent and KI as an additive, Lai et al[81]. synthesized of new isoxazoles[87] from alkynes[85], [86]. Both self-coupling and cross-coupling products could be successfully prepared. In the cross-coupling and cyclizing of

two different alkynes, the iron-mediated system shows a good chemoselectivity.



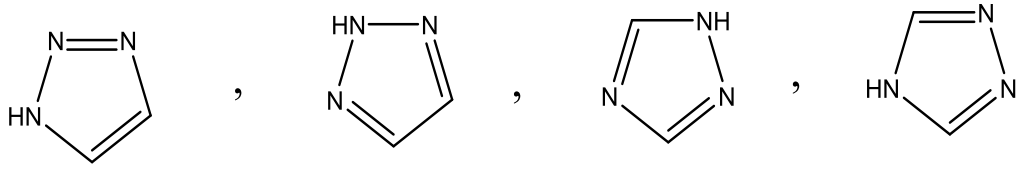
1.3. Heterocyclic Compounds

A heterocyclic compound is one which possesses a cyclic structure with at least one different kind of an atom in the ring. Nitrogen, oxygen and sulfur are considered the most hetero atoms known[82-84].

The heterocyclic compounds usually possess a stable ring structure while the three and four-membered heterocyclic rings are more strained and reactive compared to five and six membered rings [85-88]. Heterocyclic compounds occur widely in nature and in a variety of non-naturally compounds, large number of heterocyclic compounds are essential to life such as alkaloids, antibiotics, essential amino acids, vitamins, hemoglobin, hormones, and the large number of synthetic drugs and dyes [89-91]. Heterocyclic chemistry is one of the most complex and intriguing branch of organic chemistry and constitutes the largest and most varied family of organic compounds [92,93].The heterocyclic compounds are very important part of medicinal chemistry. They have a broad spectrum of pharmacological activities[94] such as anticancer [95,96], antibacterial [97,98] , antifungal activity [99], antioxidant[100,101], antimicrobial[102],anti-inflammatory [103]

1.3.1 Triazoles

Triazole is five membered ring systems contain three nitrogen heteroatoms, defines an interesting class of compounds. The triazoles[104] have two isomeric types of triazole: 1,2,3-triazoles (Vicinal triazole) [88], [89] and 1,2,4-triazole(Symmetrical triazole)[105] [90], [91] (Figure 1-8).



4. [88] [89] [90] [91]

Figure (1-8) The isomers of triazoles

5. Triazole ring is plannar with 6 π-electron aromatic system with distortion of the π-system induced by the annular nitrogen atoms[106].

The 1,2,3-Triazoles is an important class of nitrogen containing aromatic heterocyclic compounds not found in nature, and have attracted a great deal of interest in the fields of organic chemistry and medical chemistry because of their various biological activities[107-109] such as antiviral[110,111], antibacterial[112,113], antifungal[114-116], antiprotozoal[117], anticancer[118,119], anti-HIV [120], carbonic anhydrase inhibitor [121] anti-proliferative and anti-inflammatory [122]. The 1,2,3- triazole ring is stable against acidic or basic hydrolysis, oxidative, and reductive conditions, reflecting a high aromatic stabilization and relative resistance to metabolic degradation [123] .

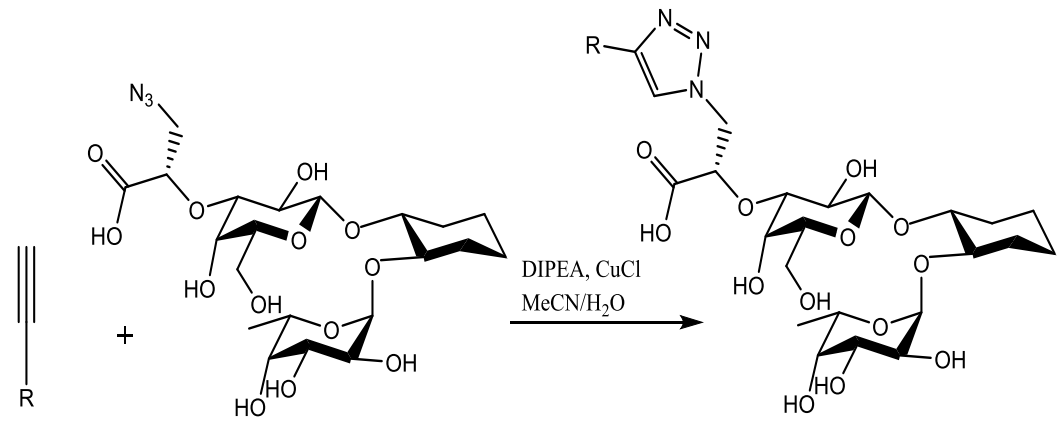
1.3.2.Synthesis of 1,2,3-triazoles derivatives.

1,2,3-triazoles is aromatic heterocyclic ring and many workers synthesized 1,2,3-triazoles using the following methods:

The common methods for the synthesis of 1,2,3-triazoles derivatives via cyclization reaction of thermal 1,3-dipolar cycloaddition of azides to alkynes :

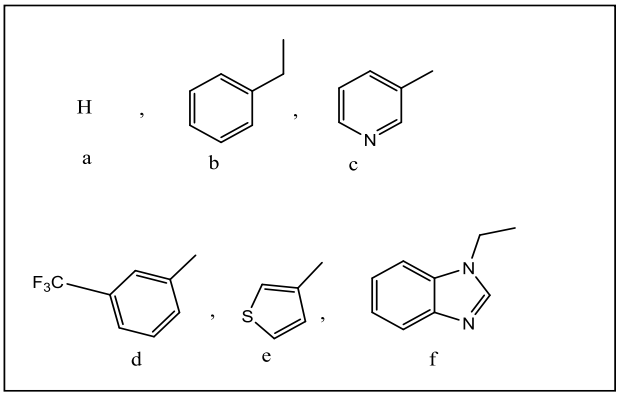
.

By regioselective using CuAAC protocol, Ernst et al[124]. synthesized a series of sugar-based triazole derivatives[94]$_{a-f}$ via the click reaction of series alkynes[92]$_{a-f}$ and azidosugar[93].

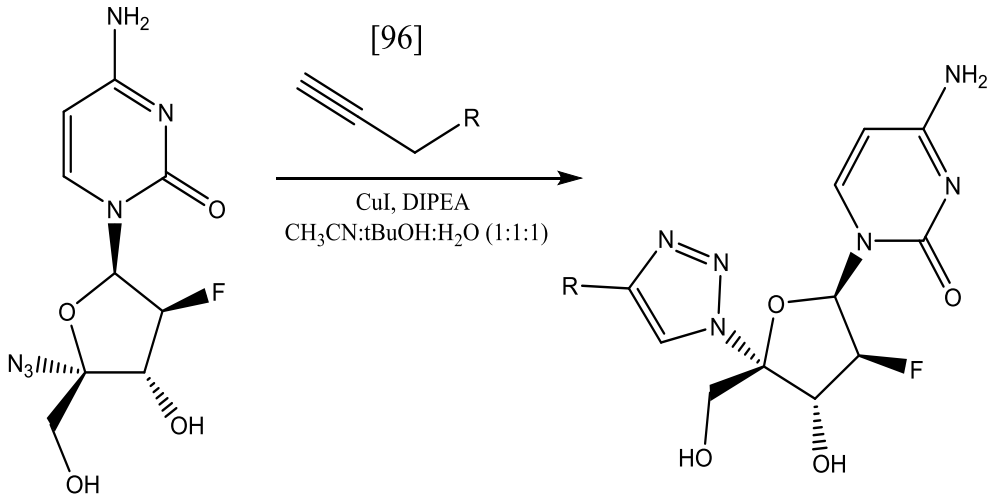


[92]$_{a-f}$ [93] [94]$_{a-f}$

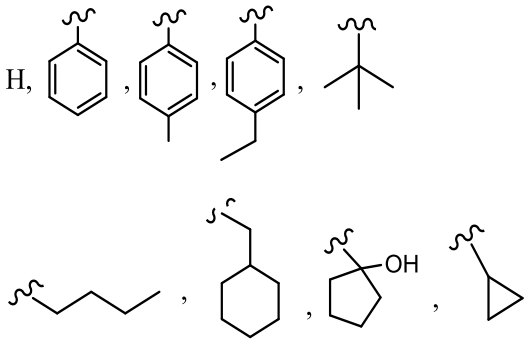
R =



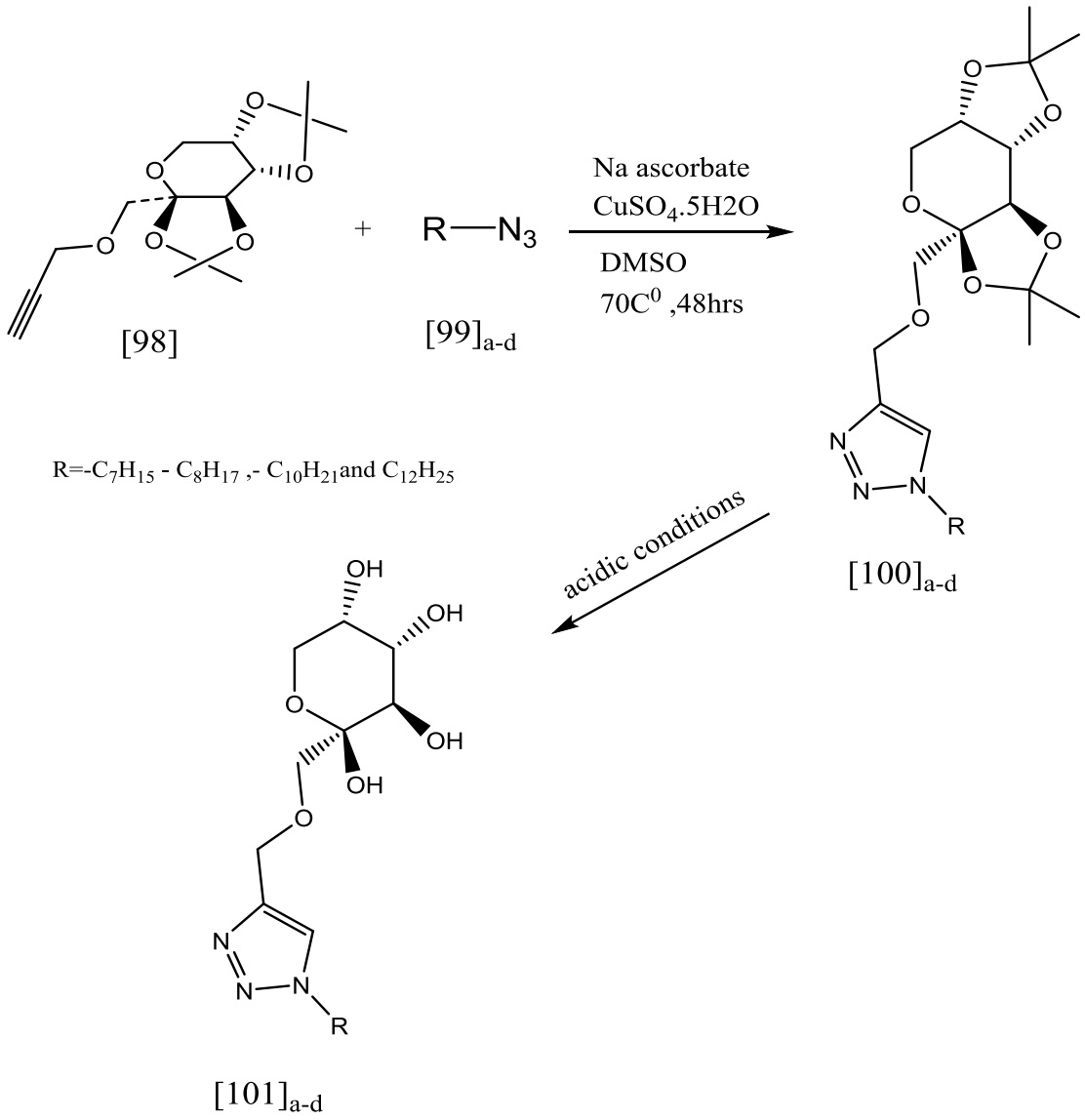
While Wu et al[125]. synthesized 4-(1,2,3-triazol-1-yl)-2-deoxy-2_-fluoro-β-d-arabinofuranosyl-cytosine [97] through CuAAC reactions between 4-azido-arabinofuranosyl-cytosines [95]and appropriate alkynes [96], which is described in below:



R=

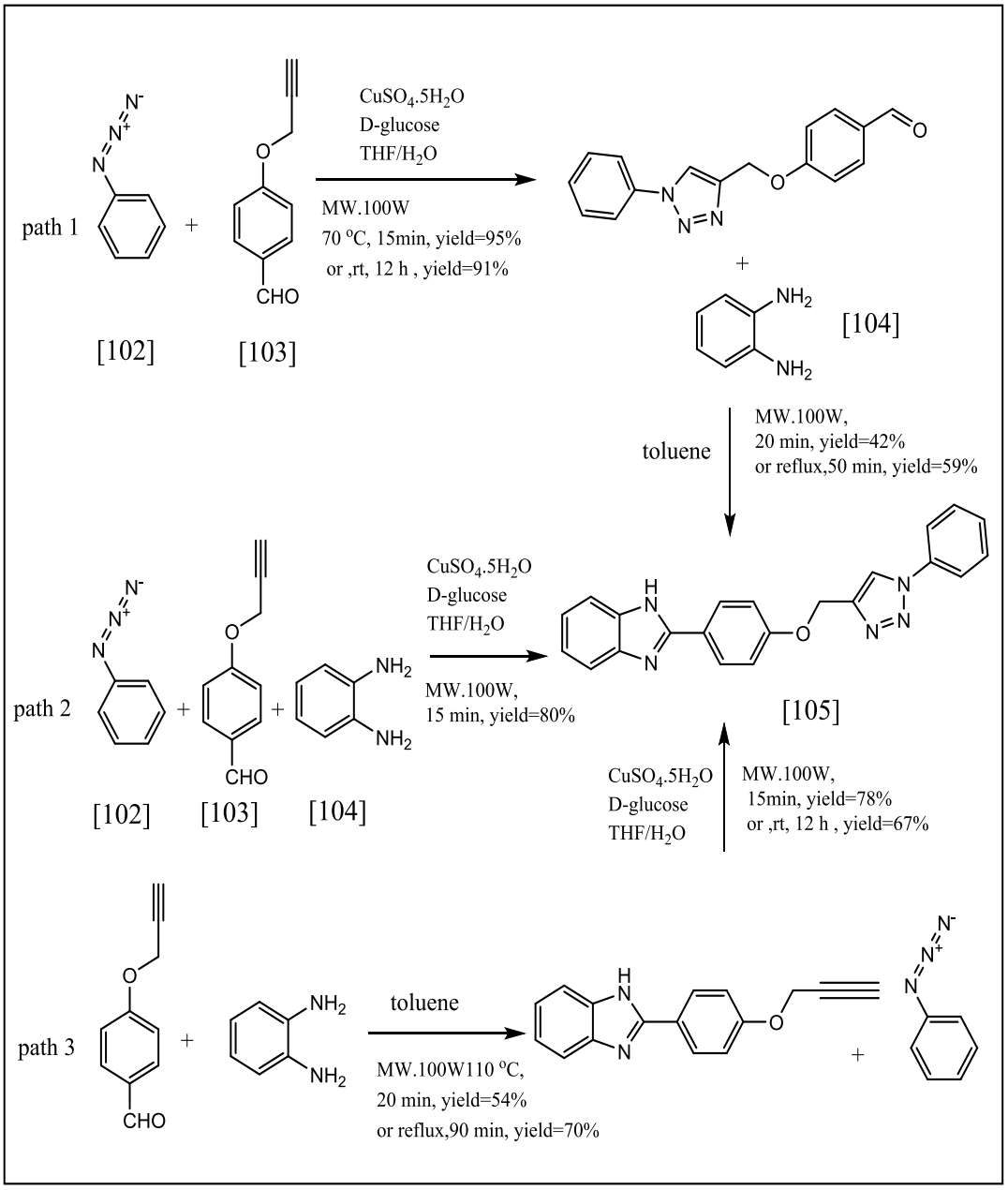


On the other hand , Adnan et al[126]. synthesized new 1-Alkyl-4-[(2,3,4,5-di-*O*- isopropylidene -β-D-fructopyranos-O-yl) methyl]1*H*-1,2,3-triazole$[100]_{a-d}$ from 1-O-propargyl-2,3,4,5-Di-*O*-isopropylidene-beta-D-fructopyranose [98] and number of *n*-alkyl azides$[99]_{a-d}$ *via* cycloaddition reaction using Cu(I) as a catalyst The acetal groups of triazoles $[100]_{a-d}$ were removed under acidic conditions to give the 1-alkyl -4-[(β -D-fructopyranos-O-yl) methyl]1H-1,2,3-triazole $[101]_{a-d}$



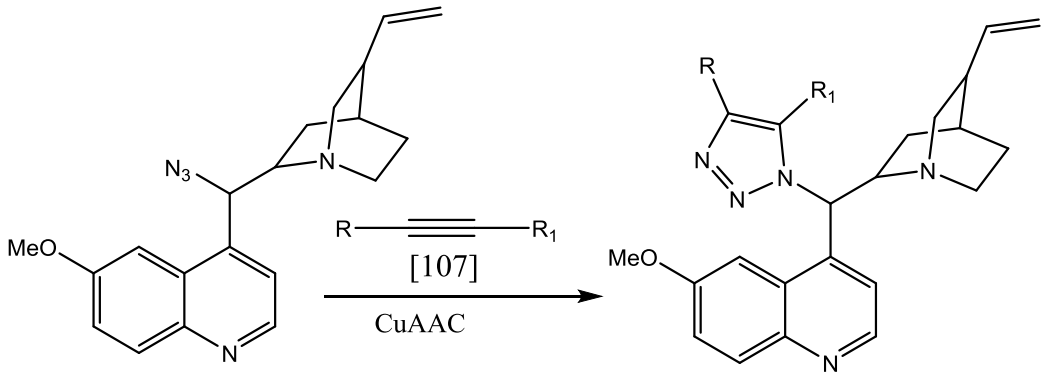
[98] [99]$_{a-d}$ [100]$_{a-d}$ [101]$_{a-d}$

By microwave-assisted is it reaction, Kumar et al[(127)]. synthesized 2- (4- ((1 - phenyl- 1*H*- 1,2,3-triazol - 4- yl) methoxy) phenyl) -1*H* – benzo [*d*] imidazoles [105] from a phenylazid[102], propargyloxy benzaldehyde[103] and a 1,2-diaminobenzene[104] is proposed in three different approaches which are illustrated in (Scheme 1-3). In a two-step process the triazole and imidazole ring are synthesized consecutively (Scheme 1-3, path 1 and 3). However, we reasoned that the desired adduct could also be formed in a one-pot fashion (Scheme 1-4, path 2) as a multicomponent reaction (MCR).



Scheme 1-3 proposed of three different approaches for synthesizedof triazole

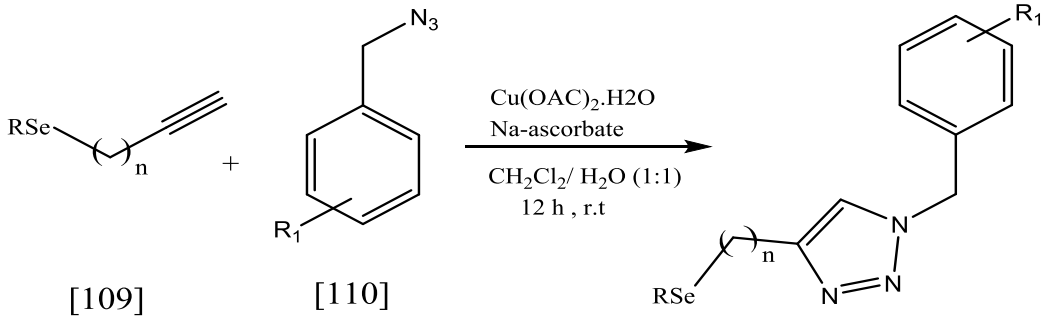
On the other hand , Porta et al[(128)] . synthesized 9-(1,2,3-Triazole)-substituted cinchona alkaloids[108] by the reaction of 9-azido cinchona derivatives[106] with commercially available alkynes[107] and using the standard CuAAC protocol. High yields and easy isolation of the products (in some cases by the precipitation with water).



[106] [108]

R = COOMe, CH_2OAc, CH_2OH,Ph
R_1= H, COOMe

By click reaction , Heravi et al[129]. achieved and reported the synthesis of organoselenium-functionalized triazoles [111]from the reaction between alkynyl seleniumand[109] and benzyl azides [110] in the presence of copper(II) acetate and sodium ascorbate



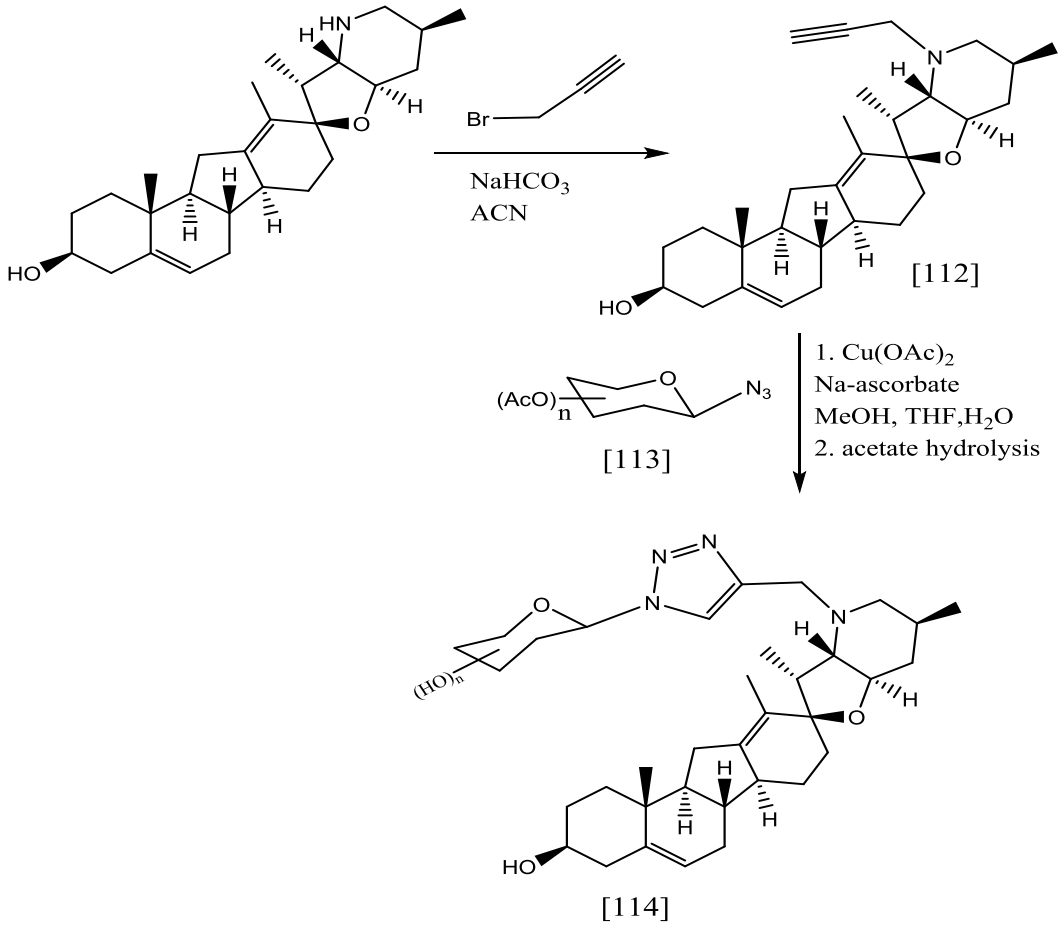
[109] [110] [111]

R= Aryl

R_1 = H , Me, OMe, Cl, CF_3

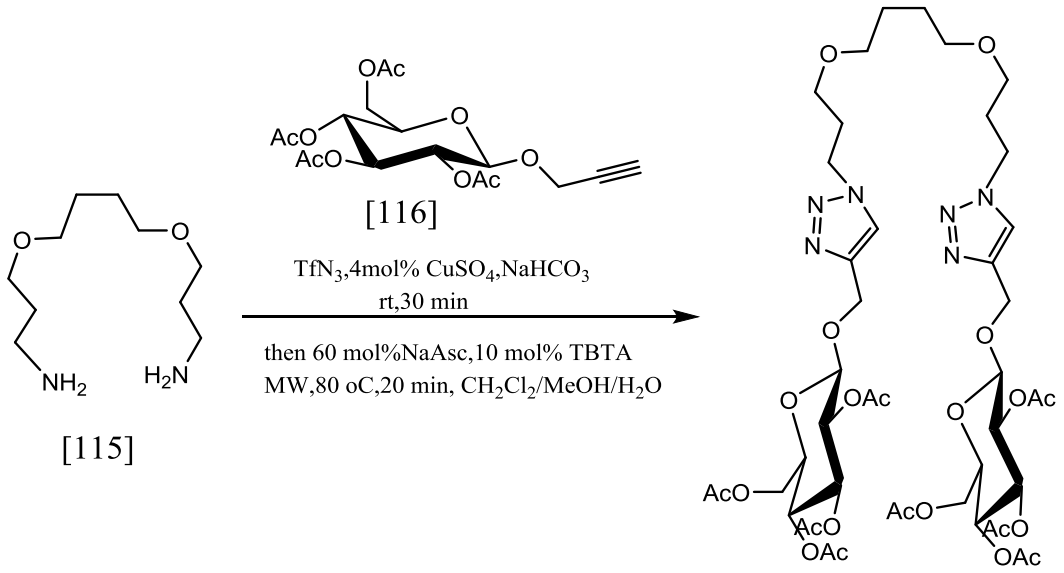
n = 0 , 1, 2, 3

In 2016, Kacprzak et al[130]. synthesized of 1,2,3-Triazole – substituted glycoconjugates [114] using the CuAAC reaction. N-propargylcyclopamine served as an alkyn[112] and reacted with azidosugars[113].



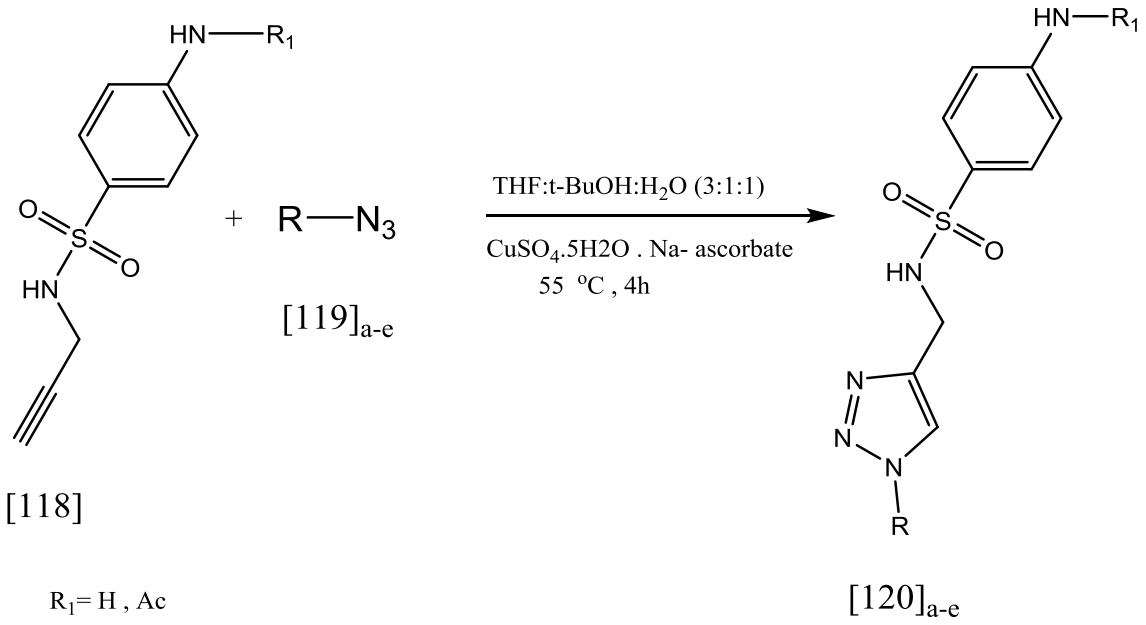
[114]

Under microwave induced click conditions, Vinod et al [131]. synthesized of bistriazolyl glycoconjugate [117] from diamines without the need for isolation of the azide intermediates. Reaction of diamine [115] with glycosyl alkyne[116] in the presence of TfN_3, $CuSO_4$, and $NaHCO_3$ at room temperature for 30 min followed by addition of NaAsc and TBTA.



[115] [116] [117]

On the other hand ,in 2017. Kadir Ay et al [(132)]. synthesized sulfanilamidomethyl glycoconjugates $[120]_{a-e}$ containing 1,2,3-triazole bridge from reaction of terminal alkyne group in compound [118] with azide$[119]_{a-e}$ derivatives of D-glucose, D-galactose ,D-mannose and D-fructose via 1,3-dipolar cycloaddition reaction using Cu(I) as a catalyst.

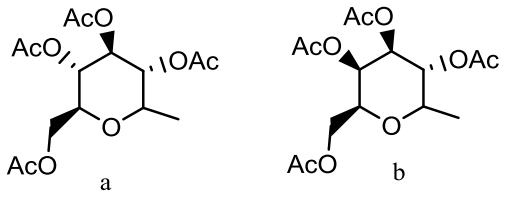


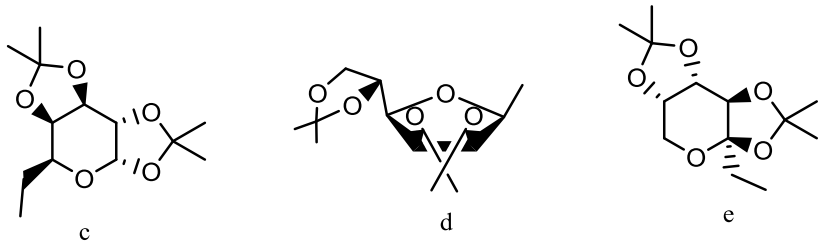
[118]

R_1= H , Ac

[120]$_{a-e}$

R=

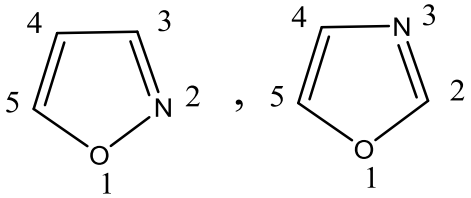




1.3.3 Isoxazoles

Isoxazoles [121] are unsaturated aromatic heterocyclic compounds containing a ring with three carbon atoms, one oxygen atom and one nitrogen atom [(133)]. The trivial name for the title five-membered fully unsaturated heterocycles as (isoxazole) was originally proposed by Hantszch as it was the isomer (oxazole) discovered first. The trivial name follows the Hantszch Widmen system of nomenclature: The prefix (iso) represents isomer, (oxa) represents the oxygen atom, (aza) represents the nitrogen atom, and the suffix (ole) denotes the ring size as

five-membered; altogether the derived name is (isoxazole) [134,135]. This name has been accepted in IUPAC and has been used in chemical abstracts. In chemical abstracts, the other systematic name 1,2-oxazole[136] is also used. There are two types of isomers



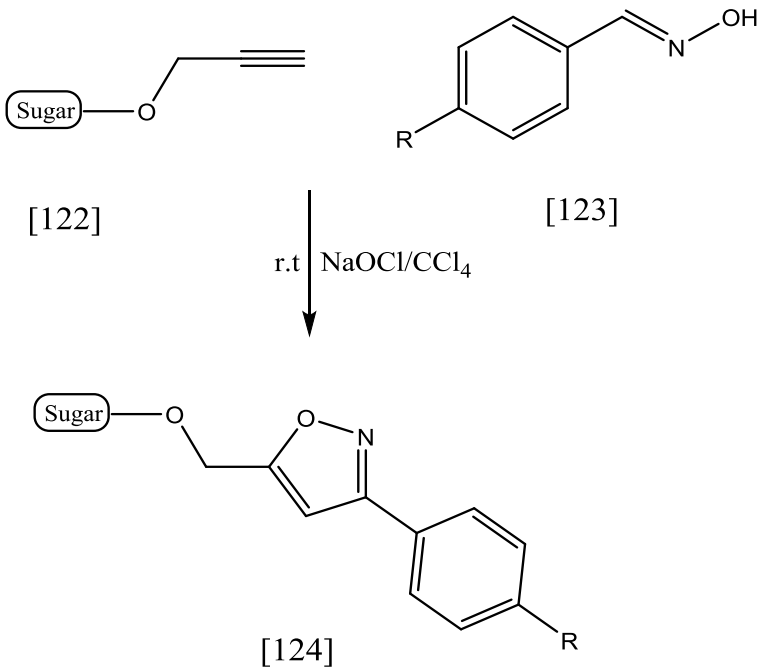
[121]

Isoxazoles constitute an important family of five membered heterocycles ring in view of their use in many natural products synthesis and occurrence in pharmaceutical agents viz., COX-2 inhibitor[137,138], and which are largely employed in the area of pharmaceuticals[139] and therapeutics such as insecticidal[140,141], antibacterial[142-144], antibiotic[145,146],antitumour[147-149],antifungal[150-152] , antituberculosis[153], anti-inflammatory[154-156], anticancer[157-159] antidepressant[160,161], antiviral,[162] antinocicept,[163] analgesic[164] and Herbicidal. [165]

1.3.4. Synthesis of Isoxazoles derivatives

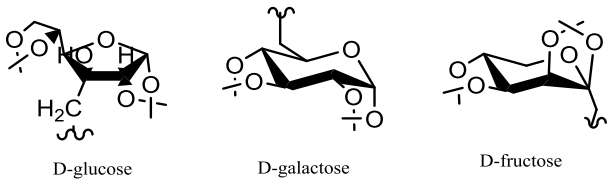
There are many derivatives of isoxazoles and many methods for synthesizing them. For that, The 1,3-dipolar cycloaddition between oximes and terminal alkynes one of these methods will be presented in this section:

Via 1,3-dipolarcycloaddition reaction between a series of propargyl sugars(dipolarophiles) [122], and the in situ generated aryl nitrile oxide (dipoles)[123] was carried out in carbon tetrachloride at room temperature, Gaamoussi [166] et al synthesized a new series of glycosyl-3,5-isoxazoles[124].

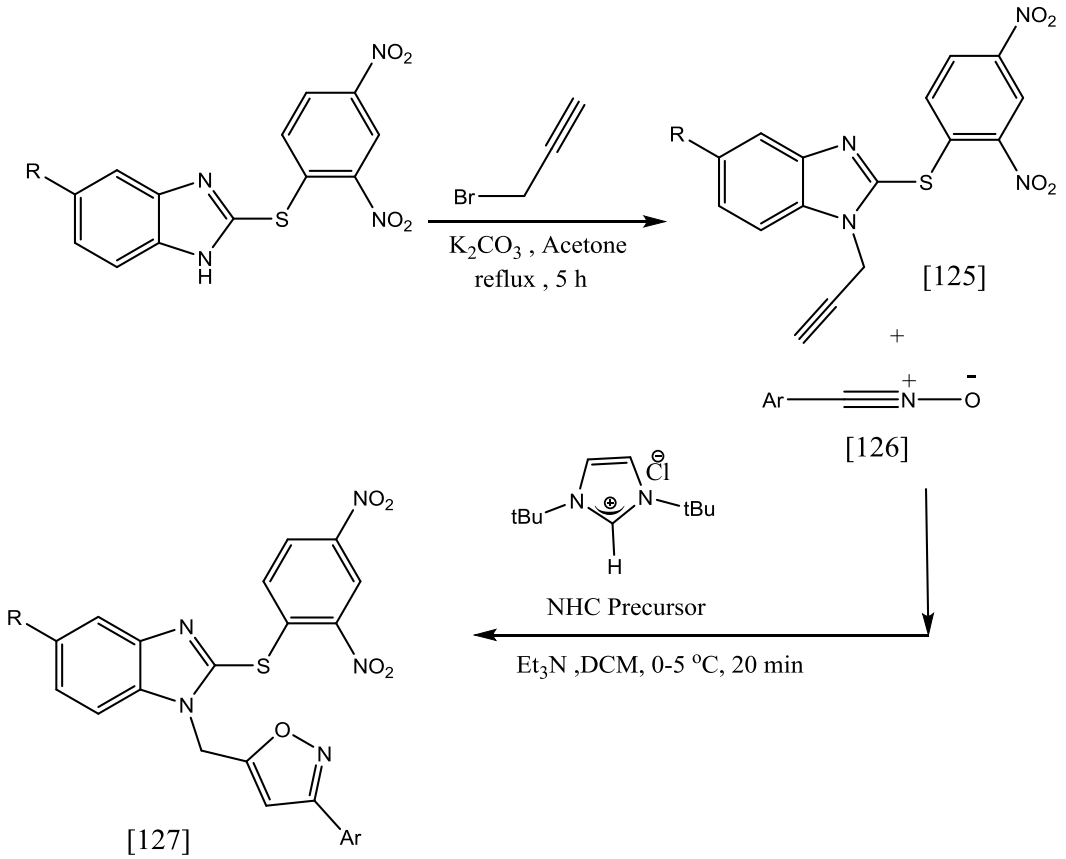


R= Cl, NO_2

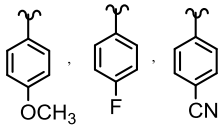
Sugar =



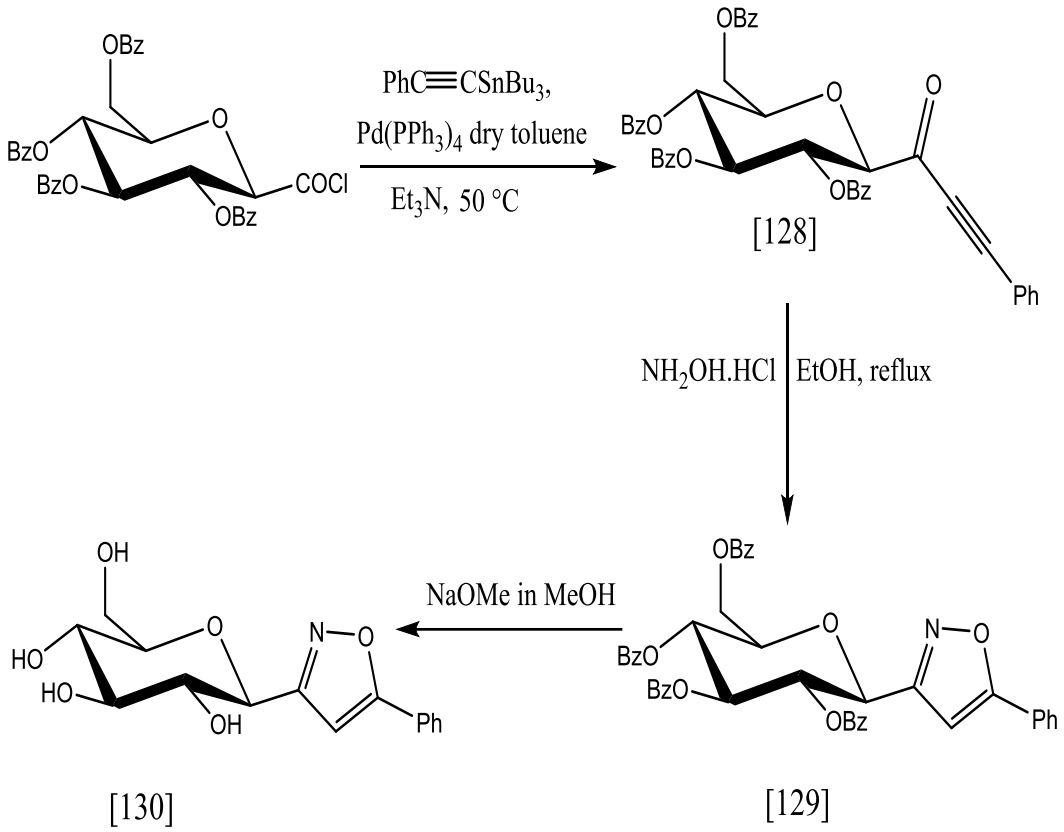
As well , in 2013, Kankala et al[167]. synthesized new 2-mercaptobenzimidazole containing 3,5-disubstituted isoxazole compounds [127] by cycloaddition reaction between N-propargyl-2-mercaptobenzimidazoles(terminal alkynes) [125] and aryl nitrile oxides[126] in the presence of an organo-N-heterocyclic carbene (NHC) (N,N-ditertiarybutylimidazolium chloride) as a catalyst.



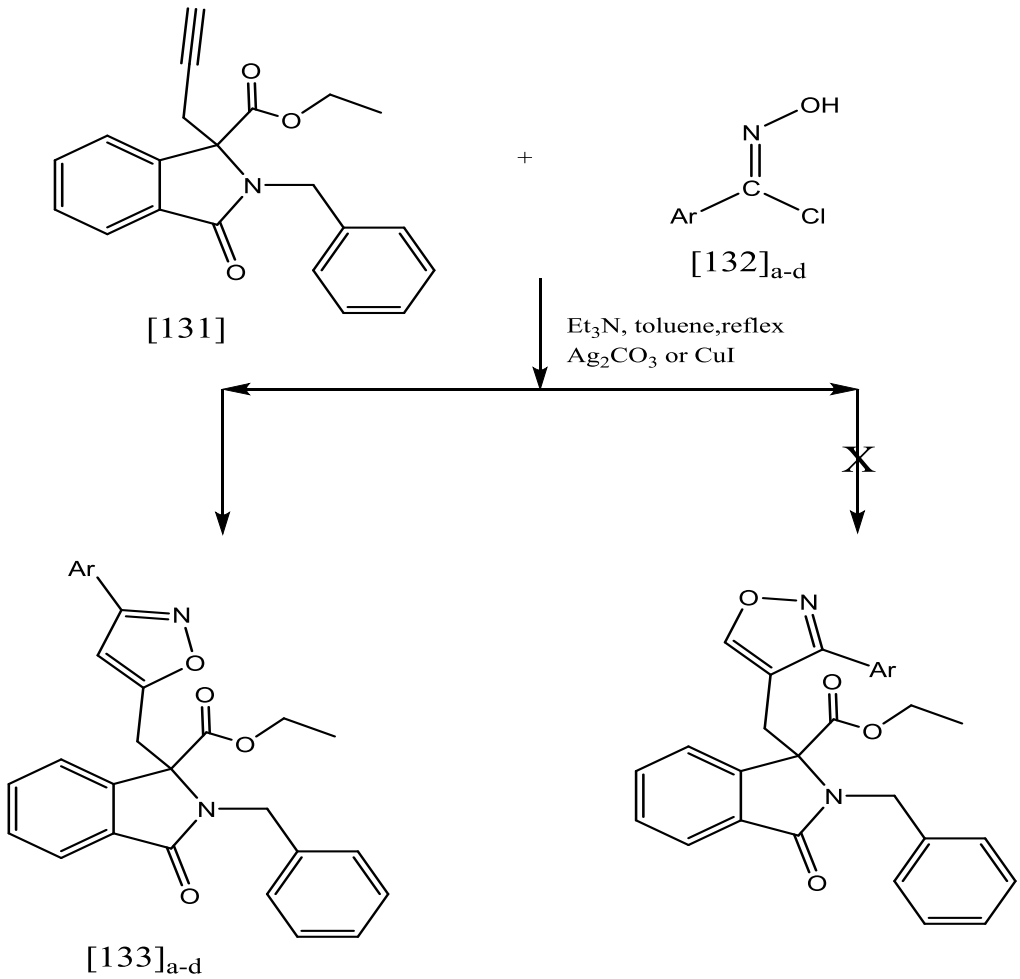
R= H , Br , OCH_3 , NO_2

Ar = 

On the other hand , Bokor et al[(168)]. synthesized 3-(β-D-Glucopyranosyl) 5- phenyl-isoxazole [130] by cycloaddition reaction of *C*-glycosyl nitrile-oxides with alkynes[128] in the same molecule given the Glycopyranosyl- isoxazoles derivatives[129] . Hydrolysis of this product produces compound[130].

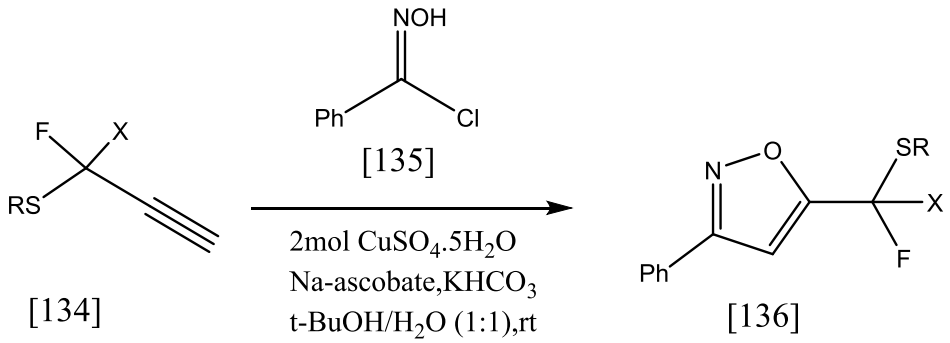


By [3+2] cycloadditions reaction involving dipole and dipolarophile, Rammah et al[169]. synthesized isoxazoles derivatives $[133]_{a\text{-}d}$ from reacting of propargyl-substituted dihydroisoindolin-1-one [131] with aryl nitrile oxides$[132]_{a\text{-}d}$, generated in situ from aromatic oximes precursors ,using Ag_2CO_3-catalyzed. The reaction times could be further shortened when using CuI as a catalyst.



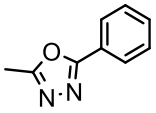
Ar = a: C_6H_5, b: p-MeC_6H_4, c: p-$OMeC_6H_4$, d: p-ClC_6H_4

Finally, by copper-catalyzed, Kuribayashi et al[170]. synthesized isoxazoles derivatives[136] via1,3-dipolar cycloaddition from the reaction of mono-/ di-fluorinated propargylic thioethers [134] with nitrile oxides derived[135] from an imidoyl chloride.



[134] [136]

X = F , H

R = Ph ,  , 

The aim of the work

Since both D-fructose and most heterocyclic compounds exhibited a wide range of biological activities, natural product and medical fields and have wide spectrum of applications, the aim of the present work directed towards synthesis of new D-fructose derivatives containing other different hetero rings. The main line of this work includes different synthesis pathways:-

1- Synthesis and characterization of new D-fructose derivatives containing isoxazole ring.

2- Synthesis and characterization of new D-fructose derivatives containing both1,2,3-triazole and benzo[*d*]imidazole rings.

3- Synthesis and characterization of new D-fructose derivatives containing 1,2,3-triazole, isoxazole and benzo[*d*]imidazole rings.

4- Study the anti-bacterial and antifungal activity of the synthesized compounds.

2.Chemicals and techniques

2.1.Chemicals

All chemicals and solvents used in this work and their suppliers are .listed in Table 2-1. They were used without further purification

Table (2-1): Chemicals and their manufactures.

Chemicals	Purity %	Supplied from
1-Bromo butane	99	Fluka
1-Bromo ethane	99	Fluka
1-Bromo propane	99	BDH
2-(chloromethyl)-1H-benzimidazole	97	Aldrich
3-Nitrobenzaldehyde	98	Aldrich
4-(Dimethylamino)benzaldehyde	99.5	Aldrich
4-Bromobenzaldehyde	99	Aldrich
4-Hydroxy benzaldehyde	99	Aldrich
Acetone	99	Fluka
Acetonitrile	99.7	HIMEDIA
Acetyl chloride	99	Fluka
Anhydrous potassium carbonate	99	Aldrich
Anisoyl chloride	99.5	Fluka
Benzaldehyde	99	Aldrich
Benzene	99.5	Aldrich
Benzoyl chloride	99	Fluka
Chloroform	99.5	Scharlau
Dichloro methane (DCM)	99	GCC
Diethyl ether	99.5	Aldrich
Dimethyl formamide (DMF)	99	Aldrich
Dimethyl sulphoxide (DMSO)	99.8	Fluka
Ethanol (absolute)	99.8	Aldrich
Ethyl acetate	99	BDH
Glacial acetic acid	99.8	Riedal-deHaën
Hydrochloric acid	37	Riedal-deHaën

Methanol	99.8	Aldrich
Petroleum ether	98	BDH
Potassium hydroxide	98	ROMIL
propargyl bromide	97	TCI
Sodium acetate	98	BDH
sodium ascorbate	98	Aldrich
Sodium azide	99	Merck
Sodium carbonate	99.5	Aldrich
Sodium hydroxide	97	Fluka
Sodium sulfate	99	Merck
Sulfuric acid	98	Fluka
Tetrahydrofuran (THF)	99	BDH

2.2.Techniques

2. 2.1. Spectroscopy

a) Fourier transform infrared spectrophotometer (FT-IR)

FTIR spectra were recorded using potassium bromide discs by a SHIMADZU (IR Affinity-1) FTIR spectroscopy. College of Education for Pure Science (Ibn-Al-Haitham), University of Baghdad. . And Central Service Laboratory College of Education for Pure Science (Ibn-Al-Haitham), University of Baghdad.

(b) Nuclear magnetic resonance spectrometer (^{1}HNMR and ^{13}CNMR)

^{1}H and ^{13}C-NMR spectra were carried out by: Ultra Shield 300 MHz, Bruker , Switzerland at Gazi University College of Science (in Ankara, Turkey) also some spectra were carried out Ultra Shield 400 MHz, Bruker, Center Lab.(in Iran) University of Tehran , are reported in ppm(δ), DMSO-d_6 was used as a solvent with TMS as an internal standard.

c- Mass spectroscopy

The mass spectra recorded by MS model: 5975c VL MSD with Tripe-Axis Detector University of Tehran, Center Lab. (in Iran).

2.2.2. Melting point measurements

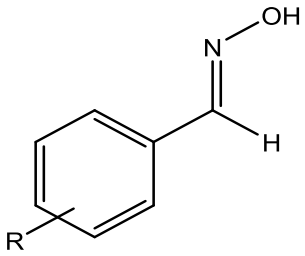
Uncorrected melting points were determined by using hot-stage, Gallen Kamp melting point apparatus.

2.2.3. Biological activity screening

Biological activity screening were determined in center laboratory College of Education for Pure Science (Ibn-Al-Haitham), University of Baghdad. The synthesized compounds were dissolved in DMSO (which was used as a solvent and as control) to give concentration 10^{-3}M. The three types of the bacteria were activated in a nutrient growth medium at 37 ^{0}C for 24 hrs, then examined after 24 hrs and 48 hrs for antifungal activities. The zones of inhibition formed were measured in millimeter

2.3. Synthetic procedures

2.3.1. General preparation of 4- or 3-substituted benzaldoximes $[I]_{a-e}$:



$[I]_{a-e}$

R = H , 4- OH , 4-Br , 4-$N(CH_3)_2$
3- NO_2

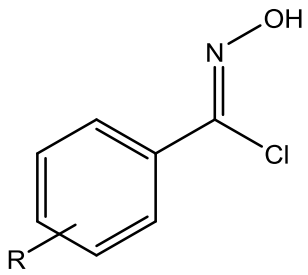
In a round-bottomed flask (50 mL) equipped with a condenser, benzaldehyde or substituted benzaldehyde (10mmol), $NH_2OH{\cdot}HCl$ (10 mmol) and sodium acetate (10 mmol) in methyl alcohol (10 ml) were prepared. The mixture was stirred under reflux conditions for 4hrs . The progress of the reaction was monitored by TLC (cyclohexane / ethyl acetate 8:2). After completion of the reaction, H_2O (15 mL) was added and the reaction mixture was continued to stirring for 5 min. The product has been extracted with dichloromethane DCM (3x15 mL).The mixture was dried over anhydrous Na_2SO_4.Filtered then evaporation of the solvent to give compounds (I_{a-e})[171] . The physical properties were corresponding to the literatures and listed in Table 2-2 .

Table (2-2): The physical properties of compounds $[I]_{a-e}$

Comp. No	M.P ^oC	color	Yield%
$[I]_a$	31-33 Lit [33-35 [172]]	Yellow	80
$[I]_b$	71-72 Lit [72-74[173]]	Red	82

$[I]_c$	112-114 Lit [110-113[174]].	White	78
$[I]_d$	142-144 Lit [141-143[173]]	Pale yellow	79
$[I]_e$	120-121 Lit [121-123[171]].	yellow	79

2.3.2. General Preparation of N-hydroxy-4-or-3- substituted benzimidoyl chloride $[II]_{a-e}$



$[II]_{a-e}$

R = H , 4-OH ,4- Br ,4- $N(CH_3)_2$
3-NO_2

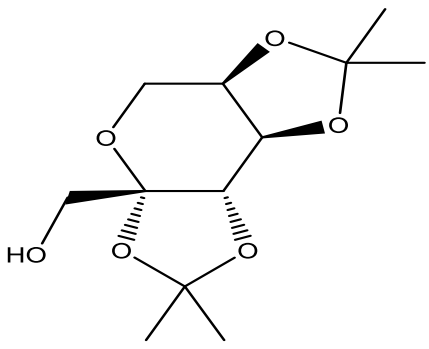
The 4- or 3-substituted benzaldoximes $[I]_{a-e}$ (30 mmol) were dissolved in DMF (50 mL) with stirring, and N-chlorosucceinimide (30 mmol) was added in two portions at room temperature. Initiation of the reaction was accelerated by use of a slight increase in the temperature to (40 ^{0}C for 20 min) . The reaction was monitored by TLC (cyclohexane / ethyl acetate 8:2). After about 12 hrs , the reaction was complete, an ice/ water mixture was added and extracted twice with diethyl ether. The organic phases was washed twice with ice/ water. The organic phases were dried over Na_2SO_4, and

concentrated to give compounds $[II]_{a-e}$. The physical properties were corresponding to the literatures[175] and listed in Table 2-3.

Table (2-3): The physical properties of compounds $[II]_{a-e}$

Comp. No	M.P ^{o}C	color	Yield%
$[II]_a$	46-49 Lit [48-52[176]]	Pale yellow	82
$[II]_b$	90-92 Lit [93-95[175]]	Deep red	79
$[II]_c$	80-82 Lit [79-82[177]]	White	83
$[II]_d$	158-160 Lit [161-162[178]]	Deep yellow	78
$[II]_e$	103-105 Lit [105-107[179]]	Deep yellow	80

2.3.3. Preparation of 2,3,4,5-di-O-isopropylidene-beta-D-fructopyranose [III]

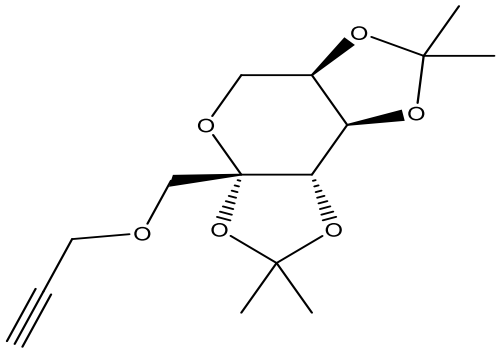


[III]

D-Fructose (3.6g, 20 mmol) was dissolved in acetone (70 mL) and concentrated H_2SO_4 (3.5 mL) was added. The reaction was stirred for (90 min) and then cooled in ice-salt bath to 0 ^{0}C . NaOH

(11g in 50 mLH_2O) was then gradually added with stirring. The solution was then concentrated and extracted with CH_2Cl_2(3 x 20 mL). The combined organic layers were then washed with distilled water (2 x 10 mL). The organic phases was dried over Na_2SO_4, and concentrated . The resulting crude product was dissolved in hot ethyl ether Et_2O (5 mL) and n-pentane was added to precipitate the desired bis – acetal as a crystalline solid recrystallization from ethanolEt_2OH : n-hexane 1:1 (25 mL) to give compound[III] as a white crystals(55%), m.p.116 -118 ^{0}C, lit (118-120 ^{0}C) (126)

2.3.4. Preparation of 1-*O*-propargyl- 2,3,4,5-di-O-isopropylidene-beta-D-fructopyranose [IV]

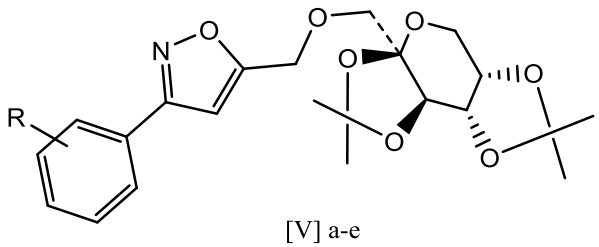


[IV]

Compound [III] (1 gm,4 mmol) was dissolved in DMF (15 mL) and NaOH pellets (15 mmol) were added. The mixture was cooled in ice-salt bath to (-15 ^{0}C) and the contents was stirred for (10 min) and then propargyl bromide (0.4 mL, 4.3 mmol) was added drop wise. The heterogeneous reaction mixture was stirred for (24 hrs), slowly warming to room temperature. The mixture was filtered and H_2O (50 mL) was added and the product was extracted with Et_2O (3 x 50 mL). The organic phases were combined and washed sequentially with 5% HCl (2 x 50 mL) and distilled water (50 mL). The organic phases was dried over Na_2SO_4, filtered and the solvent was evaporated to dryness

under reduced pressure to yield compound [IV] (75%) as pale yellow oil[126] .

2.3.5. Synthesis of 3-(4-or 3-substituted phenyl)-5-{(2,3,4,5-di-*O*-isopropylidene-beta-D-fructopyranose-O-yl)methyl}1H-isoxazole $[V]_{a-e}$

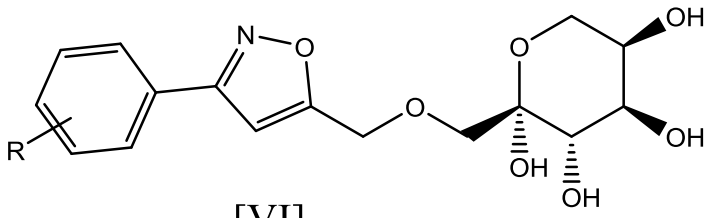


[V] a-e

R = H , 4- (OH , Br , $N(CH_3)_2$)
3- (NO_2)

Alkynyl sugar compound [IV] (0.28gm, 1mmol) and N-hydroxy-4-or-3- substituted benzimidoyl chloride $[II]_{a-e}$ (1 mmol) was added to a suspension of sodium ascorbate (0.018g, 0.09 mmol) and $CuSO_4.5H_2O$ (0.011g, 0.045 mmol) in DMSO (5mL) . The mixture was heated to 70 ^{0}C and stirred for (48 hrs) . The reaction mixture was diluted with water (30 mL) and extracted with EtOAc (3 x 30 mL) . Dried over Na_2SO_4 then filtered and evaporated to dryness under reduced pressure to yield oily compounds $[V]_{a-e}$. The nomenclature structural formula, molecular formula, yields and physical properties were listed in Table 2-4.

2.3.6. Synthesis of 3-(4- or 3-substituted phenyl)-5-{(beta-D-fructopyranose-O-yl)methyl}1H-isoxazole $[VI]_{a-e}$

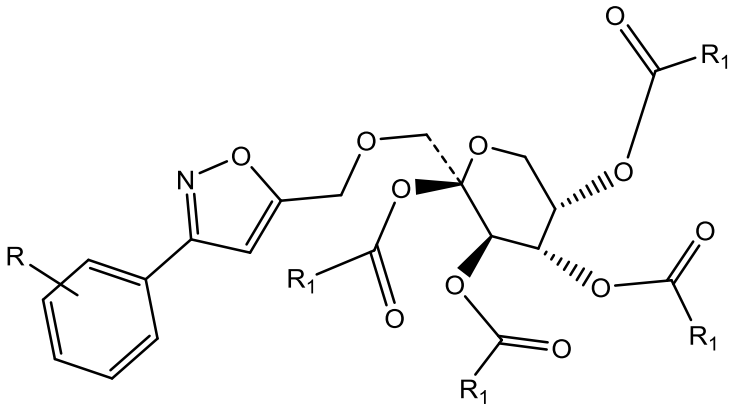


$[VI]_{a-e}$

R= H, 4- OH, 4-Br, 4-$N(CH_3)_2$
3- NO_2

The compounds $[VI]_{a-e}$ were synthesized by dissolving compounds $[V]_{a-e}$ (2.36 mmol) in mixture of dilute acetic acid (3 mL) and absolute methanol (1 mL) and stirred for (48 hrs) at room temperature. The TLC showed that the reaction was complete (benzene : methanol, 6:4). To the resulting solution a benzene (4 mL) , was added and evaporated (this process repeated four times). The residue recrystallized from chloroform. The nomenclature structural formula, molecular formula, yields and physical properties were listed in Table 2-5.

2.3.7. Synthesis of ester compounds $[VII]_{a-e}$, $[VIII]_{a-e}$, $[IX]_{a-e}$



R= H ,4-OH,4- Br ,4-$N(CH_3)_2$
3-NO_2

$[VII]_{a-e}$ When : R_1 = $-CH_3$

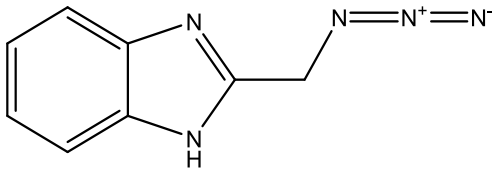
$[VIII]_{a-e}$ When : R_1 =

$[IX]_{a-e}$ When : R_1 =

To a stirred solution of compounds $[VI]_{a-e}$ (1 mmol) in triethylamine (8 mmol) and dried mixture of (5 mL DMF : 10 mL THF), was added dropwise a acid chloride (4 mmol) at (0-4 ^{0}C) . After the addition had been completed the resulting suspension was stirred at the same temperature for (3hrs). The triethylaminhydrochloride salt was precipitate. It was filtered and the filtrate was poured with stirring onto (100 mL) ice- water then the mixture was extracted with Et_2O (3 x 50 mL). The ether solvent was evaporated to give a residue which was recrystallized from ethanol / water . The nomenclature structural formula, molecular formula,

yields and physical properties were listed in Table 2-6. All compounds in paragraph (2.3.7.) are synthesized by the same way except for the three compounds [VII_b, $VIII_b$, IX_b] because they contain another one hydroxyl group, so you will need another one mole of the base and the acid chloride.

2.3.8. Preparation of 2-(azidomethyl)-1*H*-benzo[*d*]imidazole [X]:

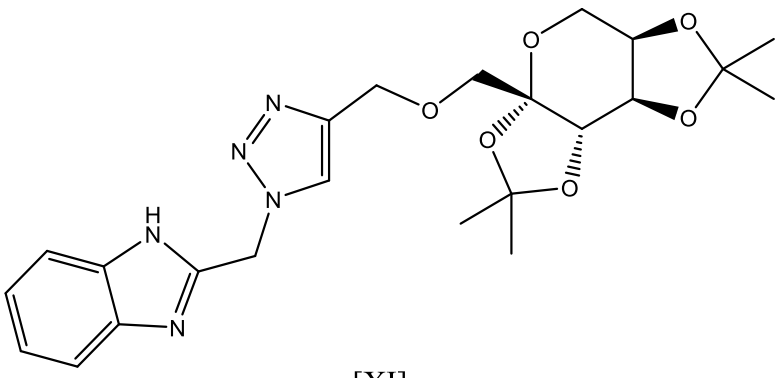


[X]

Substituted 2-(azidomethyl)-1*H*-benzo[*d*]imidazole was prepared according to the literature procedure. 2-(chloromethyl)-1*H*-benzo [*d*] imidazole (8.3gm,50mmol) and NaN_3 (3.6gm,55mmol) was dissolved in DMSO (40 mL) was stirred at room temperature. The reaction was monitored by TLC (cyclohexane / ethyl acetate 8:2). After completion, diluted with 100 mL of water and extracted with diethyl ether (10 mL x 3). The combined organic extracts were washed with brine, and dried over anhydrous Na_2SO_4. Filtered after that the organic solvent was removed under reduced pressure, the residue which was recrystallized from ethanol (50 mL) to give title compound.

Off-white solid, 75%, m.p. 120-121 °C lit (119-122 ^{0}C)[180]

2.3.9. Synthesis of 1-((1H-benzo[d]imidazol-2-yl)methyl)-4-{(2,3,4,5-di-O-isopropylidene-beta-D-fructopyranose-O-yl)methyl}1H-1,2,3-triazole [XI]

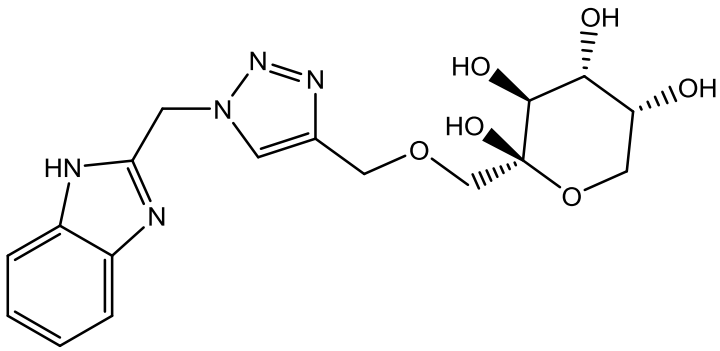


[XI]

1-*O*-propargyl- 2,3,4,5-di-O -isopropylidene –beta – D -fructopyranose compound [IV] (0.28gm,1mmol) and 2-(azidomethyl)-1*H* benzo[*d*]imidazole[X] (0.17gm,1mmol) was added to a suspension of sodium ascorbate (0.018g, 0.09 mmol) and $CuSO_4.5H_2O$ (0.011g, 0.045 mmol) in DMSO (5mL) . The mixture was heated to 70 ^{0}C and stirred for 48 hrs . The reaction mixture was diluted with water (30 mL) . extracted with EtOAc (3 x 30 mL) . Dried over Na_2SO_4 filtered and evaporated to dryness under reduced pressure , the residue which was recrystallized from ethanol (50 mL) to yield compounds [XI] .

The nomenclature structural formula, molecular formula, yields and physical properties were listed in Table 2-7.

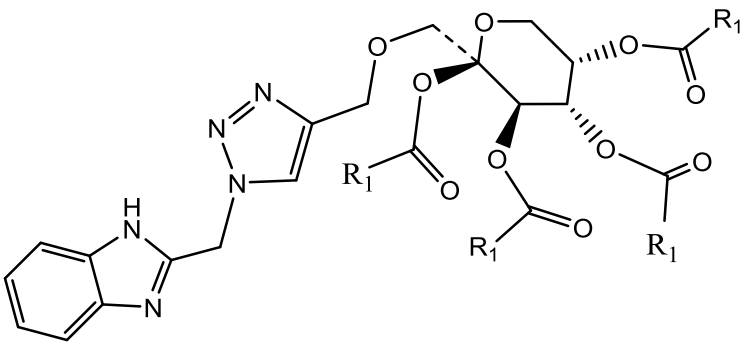
2.3.10. Synthesis of 1-((1H-benzo[d]imidazol-2-yl)methyl)-4-{(beta-D-fructopyranose-O-yl)methyl}1H-1,2,3-triazole [XII]



[XII]

The compound [XII] was synthesized by the same method used for the synthesis of compound$[VI]_{a-e}$ in paragraph (2.3.6.). Except using compound [XI] instead of compound $[V]_{a-e}$. The nomenclature structural formula, molecular formula, yields and physical properties were listed in Table 2-7.

2.3.11. Synthesis of ester compounds $[XIII]_{a-c}$.

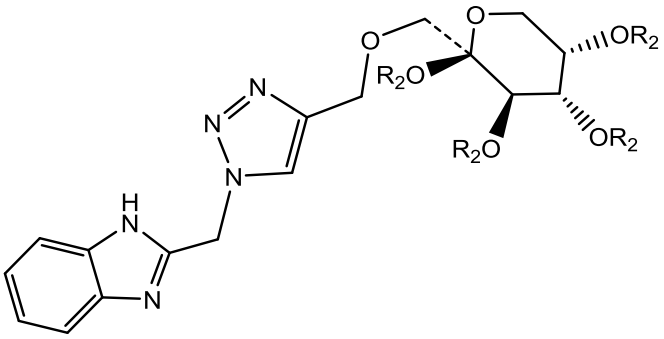


$[XIII]_{a-c}$

R_1 = -CH_3 , , O

The compounds $[XIII]_{a-c}$ was synthesized by the same method used for the synthesis of compounds$[VII]_{a-e}$, $[VIII]_{a-e}$, $[IX]_{a-e}$ in paragraph (2.3.7.). Except using compound [XII] instead of compounds$[VI]_{a-e}$. The nomenclature structural formula, molecular formula, yields and physical properties were listed in Table 2-8.

2.3.12. Synthesis of ether compounds $[XIV]_{a-c}$



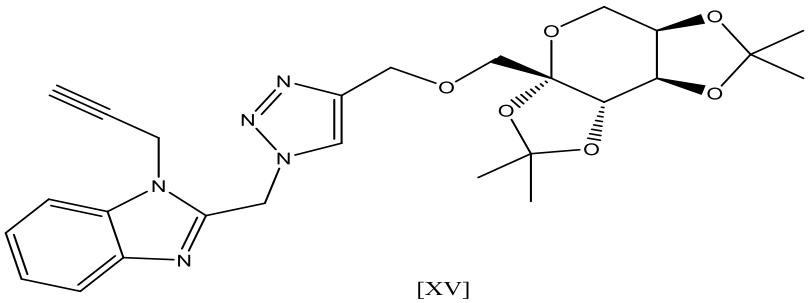
$[XIV]_{a-c}$

R_2= -CH_2CH_3, -$CH_2CH_2CH_3$, -$CH_2CH_2CH_2CH_3$

To a solution of potassium hydroxide (1.9gm,34.8 mmol) in absolute ethanol (20 mL) , 1-((1H-benzo[d]imidazol-2-yl)methyl)-4-{(beta-D-fructopyranose-O-yl)methyl}1H-1,2,3-triazole [XII] (3.4gm, 8.7 mmol) and n-alkyl bromide (52 mmol) were added , the reaction

mixture was refluxed for 6 hrs ,and potassium bromide was precipitate , It was filtered and the filtrate was poured with stirring onto (50 mL) water then the mixture was extracted with Et_2O (3 x 50 mL). The organic phases were combined and washed sequentially with 10% sodium hydroxide solution and distilled water (50 mL). The organic phases was dried over Na_2SO_4, filtered and the solvent was evaporated to dryness under reduced pressure to yield as a crystalline solid recrystallization from ethanol (25 mL). The nomenclature structural formula, molecular formula, yields and physical properties were listed in Table 2-9.

2.3.13. Synthesis of 1-((1-(prop-2-yn-1-yl)-1H-benzo[d]imidazol-2-yl)methyl)-4-{(2,3,4,5-di-O-isopropylidene-beta-D-fructopyranose-O- yl)methyl}1H-1,2,3-triazole [XV]

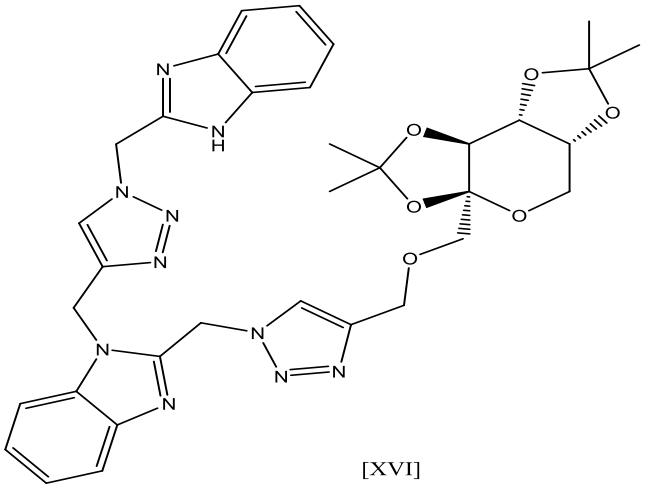


[XV]

Compound [XI] (1.9gm,4mmol) was dissolved in MeCN (15mL) and K_2CO_3 (1.1gm,8 mmol) was added. The mixture was stirred for (10 min) and then propargyl bromide (0.4 mL, 4.3 mmol) was added drop wise. The reaction mixture was heated to 70 ^{0}C and stirred for 24 hrs, and then cooled to room temperature. The mixture was filtered and H_2O (50 mL) was added and the product was extracted with Et_2O (3 x 50 mL). The organic phases were combined and washed sequentially with 5% HCl (2 x 50 mL) and distilled water

(50 mL). The organic phases was dried over Na_2SO_4, filtered and the solvent was evaporated to dryness under reduced pressure to yield as a crystalline solid, recrystallization from ethanol(EtOH) to give compound [XV] as a light brown crystals(80%), m.p.200 -202 ^{0}C

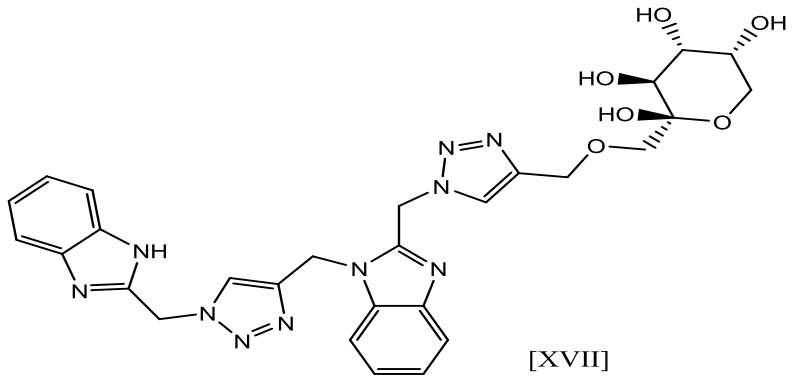
2.3.14. Synthesis of 1-((1-((1-((-1H-benzo [d] imidazole -2-yl)methyl)triazol-4-yl)methyl)-1H-benzo[d]imidazol-2-yl)methyl)-4-{(2,3,4,5-di-O-isopropylidene-beta-D-fructopyranose-O-yl)methyl}1H-1,2,3-triazole [XVI]



[XVI]

The compound [XVI] was synthesized by the same method used for the synthesis of compound [XI] in paragraph (2.3.9.), except using compound [XV] instead of compound [IV]. The nomenclature structural formula, molecular formula, yields and physical properties were listed in Table 2-10.

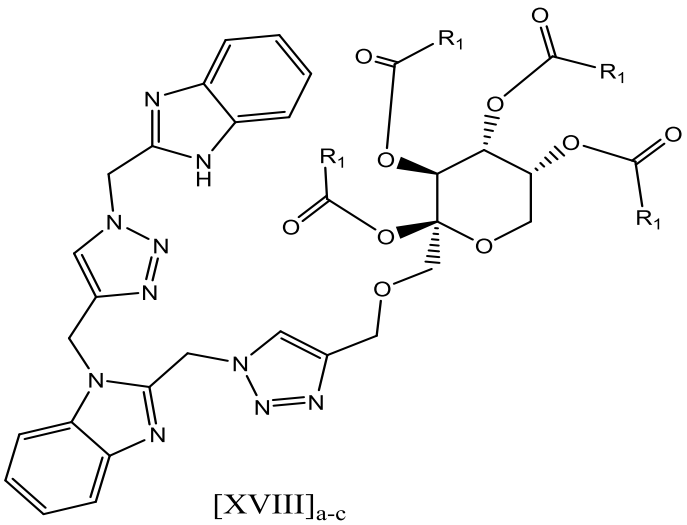
2.3.15. Synthesis of 1-((1-((1-((-1H-benzo[d]imidazol-2-yl)methyl) triazol-4-yl)methyl)-1H-benzo[d]imidazol-2-yl)methyl)-4-{(beta-D-fructopyranose-O-yl)methyl}1H-1,2,3-triazole[XVII]



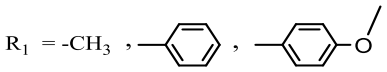
[XVII]

The compound [XVII] was synthesized by the same method used for the synthesis of compound$[VI]_{a-e}$ in paragraph(2.3.6.), except using compound [XVI] instead of compound $[V]_{a-e}$. The nomenclature structural formula, molecular formula, yields and physical properties were listed in Table 2-10.

2.3.16. Synthesis of ester compounds $[XVIII]_{a-c}$

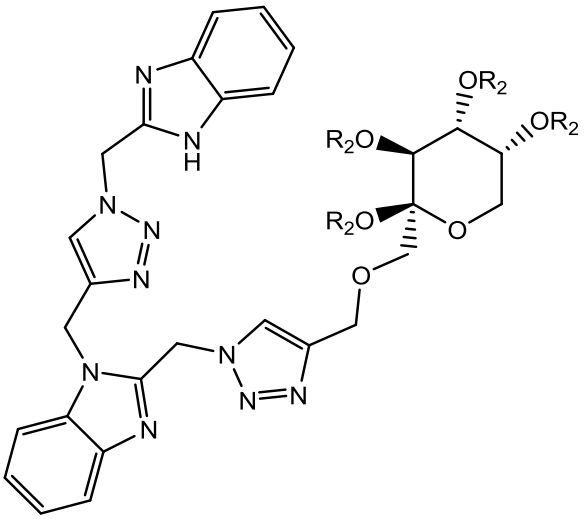


$[XVIII]_{a-c}$



The compounds $[XVIII]_{a-c}$ was synthesized by the same method used for the synthesis of compounds$[VII]_{a-e}$, $[VIII]_{a-e}$, and $[IX]_{a-e}$ in paragraph (2.3.7.), except using compound [XVII] instead of compounds$[VI]_{a-e}$. The nomenclature structural formula, molecular formula, yields and physical properties were listed in Table 2-11.

2.3.17. Synthesis of ether compounds $[X\ IX]_{a-c}$

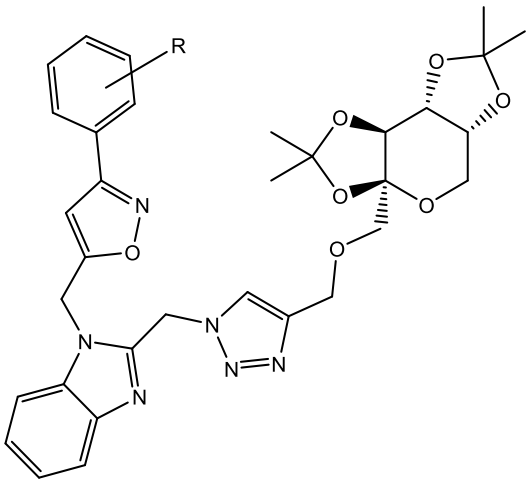


$[XIX]_{a-c}$

R_2= $-CH_2CH_3$ $-CH_2CH_2CH_3$, $-CH_2CH_2CH_2CH_3$

The compounds $[XIX]_{a-c}$ was synthesized by the same method used for the synthesis of compounds$[XIV]_{a-c}$ in paragraph (2.3.12.), except using compound [XVII] instead of compounds[XII]. The nomenclature structural formula, molecular formula, yields and physical properties were listed in Table 2-12.

2.3.18. Synthesis of 1-((1-((3-(4-or 3-substituted phenyl)isoxazol-5-yl)methyl)-1H-benzo[d]imidazol-2-yl)methyl)-4-{(2,3,4,5-di-O-isopropylidene-beta-D-fructopyranose-O-yl)methyl}1H-1,2,3-triazole[XX]$_{a-e}$

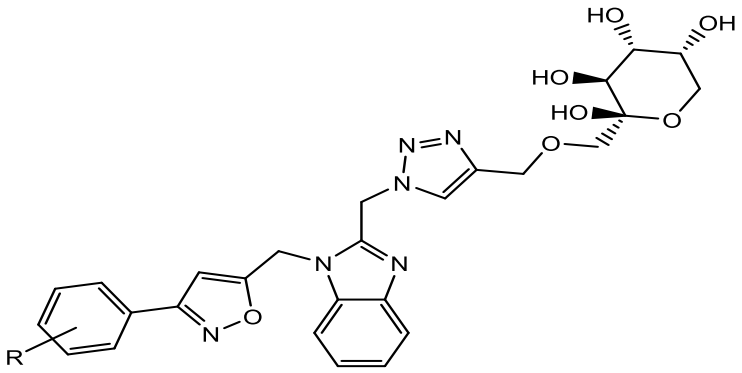


[XX]$_{a-e}$

R= H ,4- OH, 4-Br ,4-N$(CH_3)_2$
3-NO_2

The compounds [X X]$_{a-e}$ was synthesized by the same method used for the synthesis of compounds[V]$_{a-e}$ in paragraph (2.3.5.), except using compound [XV] instead of compounds[IV]. The nomenclature structural formula, molecular formula, yields and physical properties were listed in Table 2-13.

2.3.19. Synthesis of 1-((1-((3-(4- or 3-substituted phenyl)isoxazol-5-yl)methyl)-1H-benzo[d]imidazol-2-yl)methyl)-4-{(beta-D-fructo pyranose -O-yl)methyl}1H-1,2,3-triazole[XXI]$_{a-e}$.



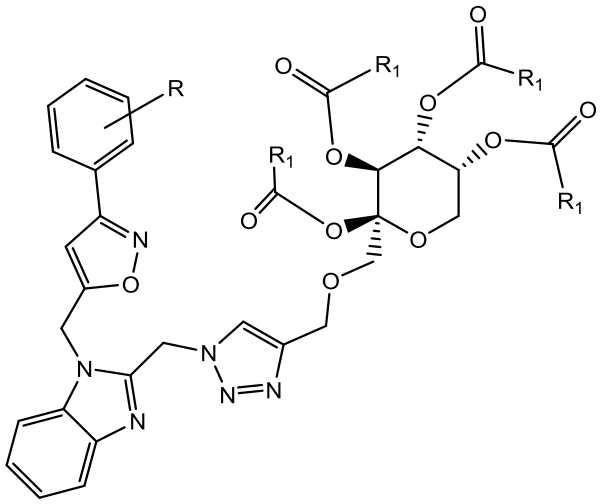
[XXI]$_{a-e}$

R= H, 4- (OH, Br, $N(CH_3)_2$)

3- (NO_2)

The compounds [XXI]$_{a-e}$ was synthesized by the same method used for the synthesis of compounds[VI]$_{a-e}$ in paragraph (2.3.6.), except using compounds [XX]$_{a-e}$ instead of compounds[V]$_{a-e}$. The nomenclature structural formula, molecular formula, yields and physical properties were listed in Table 2-14.

2.3.20. Synthesis of ester compounds $[XXII]_{a-e}$, $[XXIII]_{a-e}$ and $[XXIV]_{a-e}$



R= H ,4-OH,4- Br ,4-$N(CH_3)_2$
3-NO_2

$[XXII]_{a-e}$ When : R_1 = $-CH_3$

$[XXIII]_{a-e}$ When : R_1 =

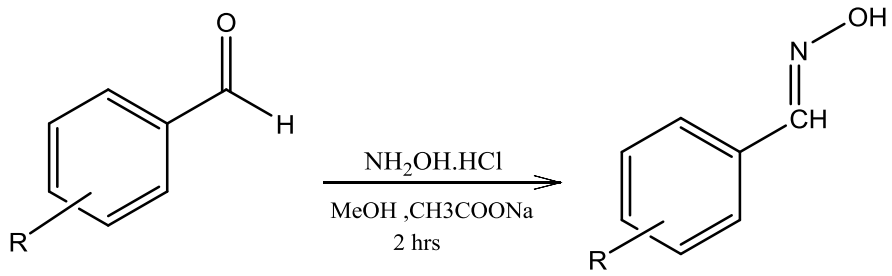
$[XXIV]_{a-e}$ When : R_1 =

The compounds$[XXII]_{a-e}$,$[XXIII]_{a-e}$ and$[XXIV]_{a-e}$ was synthesized by the same method used for the synthesis of compounds$[VII]_{a-e}$, $[VIII]_{a-e}$, and [$IX]_{a-e}$ in paragraph (2.3.7.), except using compound $[XXI]_{a-e}$ instead of compounds$[VI]_{a-e}$. The nomenclature structural formula, molecular formula, yields and physical properties were listed in Table 2-15.

3.1. Results and discussion

3.1.1. Preparation and characterization of 4- or 3-substituted benzaldoximes $[I]_{a-e}$

Benzaldoxime and their substituted $[I]_{a-e}$ were prepared via addition-elimination reaction between aromatic aldehyde and hydroxylamine hydrochloride in methyl alcohol in presence of sodium acetate as a catalyst .



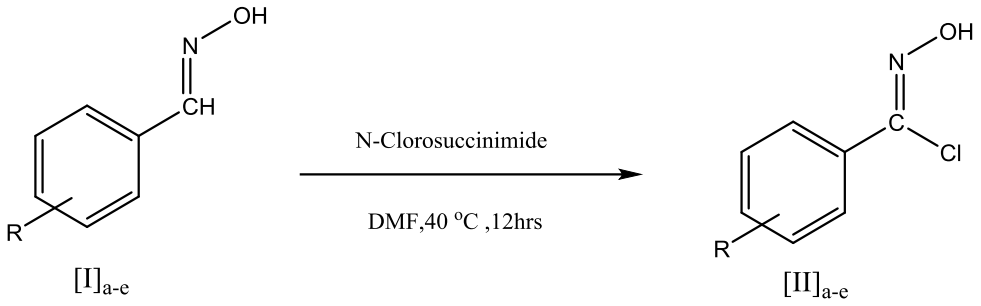
$[I]_{a-e}$

R= H ,4- OH,4- Br ,4-$N(CH_3)_2$
3-NO_2

The compounds $[I]_{a-e}$ were characterized by melting point and FT-IR spectroscopy. The FT-IR spectrum of compound $[I]_e$, (Figure 3-1) shows the disappearance of stretching vibration bands for C=O and NH_2 groups of the starting materials. It is also showed appearanceof the strong absorption band at 3265cm^{-1}which is due to OH of oxime group in addition to the appearance the stretching absorption band at 1643 cm^{-1} which attributed to the new imine group C=N .

3.1.2.Preparation and characterization of N-hydroxy-4-or-3-substituted benzimidoyl chloride $[II]_{a-e}$

Chlorination of compounds $[I]_{a-e}$ by N-chlorosucceinimide in DMF to get the N-hydroxy-4-or-3- substituted benzimidoyl chloride $[II]_{a-e}$ was used.



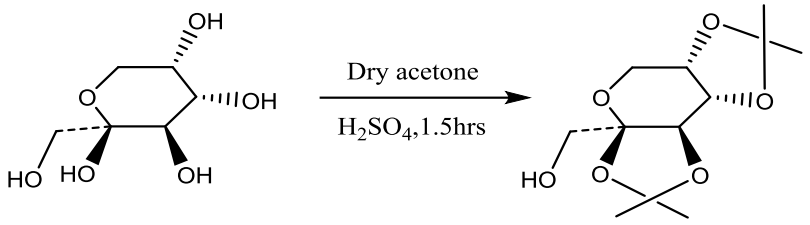
$[I]_{a-e}$ $[II]_{a-e}$

R= H ,4- OH,4- Br ,4-$N(CH_3)_2$
3-NO_2

The compounds $[II]_{a-e}$ were characterized by melting point and FT-IR spectroscopy. The FT-IR spectrum of compound $[II]_d$, (Figure 3-2) shows the strong absorption band at 3280 cm^{-1}, due to OH group,3061 cm^{-1},2983,2893 cm^{-1} due to CH aromatic and CH aliphatic (asym. and sym.), respectively. Band at 1631 cm^{-1} for (υ, C ═ N) was also appeared in addition to the appearance of strong absorption band at 867 cm^{-1} due to C-Cl.

3.1.3.Preparation and characterization of 2,3,4,5-di-O-isopropylidene -beta-D-fructopyranose [III].

The acetal of beta -D-fructopyranose compound[III] was prepared from reacting acetone with β -D-fructose in the presence of concentrated H_2SO_4 as a catalyst[126].

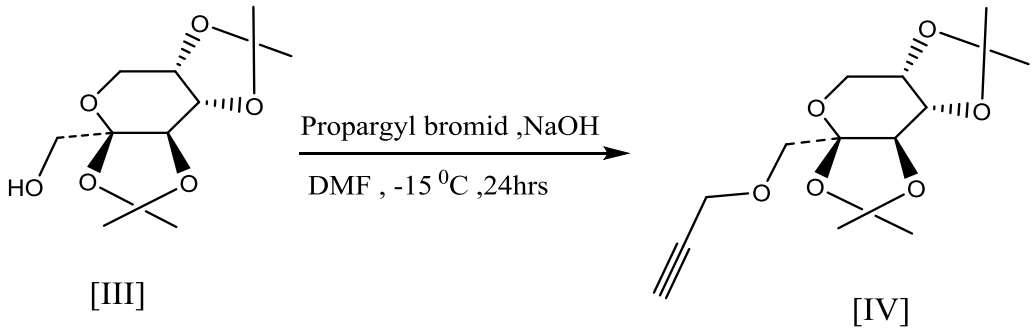


β-D-Fructopyranose [III]

The compound [III] was characterized by melting point and FT-IR spectroscopy. The FT-IR spectrum of compound [III], (Figure 3-3) shows a strong absorption band at 3271 cm^{-1} which attributed to OH group and 2983-2897 cm^{-1} for C-H aliphatic group. The appearance of absorption band at 1242cm^{-1} is attributed to C-O ether bond.

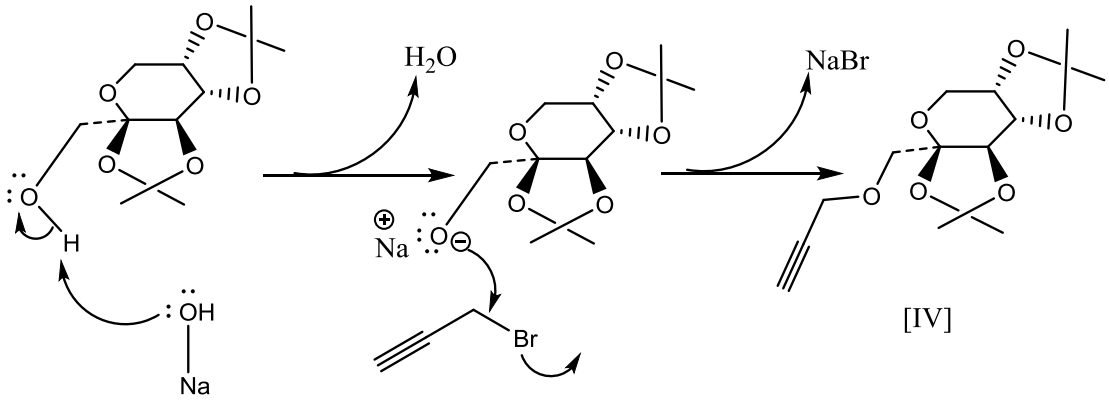
3.1.4.Preparation and characterization of 1-*O*-propargyl- 2,3,4,5-di-O-isopropylidene-beta-D-fructopyranose [IV]

The reaction of propargyl bromide with 2,3,4,5-di-O-isopropylidene-beta-D-fructopyranose compound [III] was occurred under basic conditions to produce compound [IV], via Williamson ether synthesis.



[III] [IV]

The path way mechanism[181] of this reaction may be outline in Scheme 3-1.

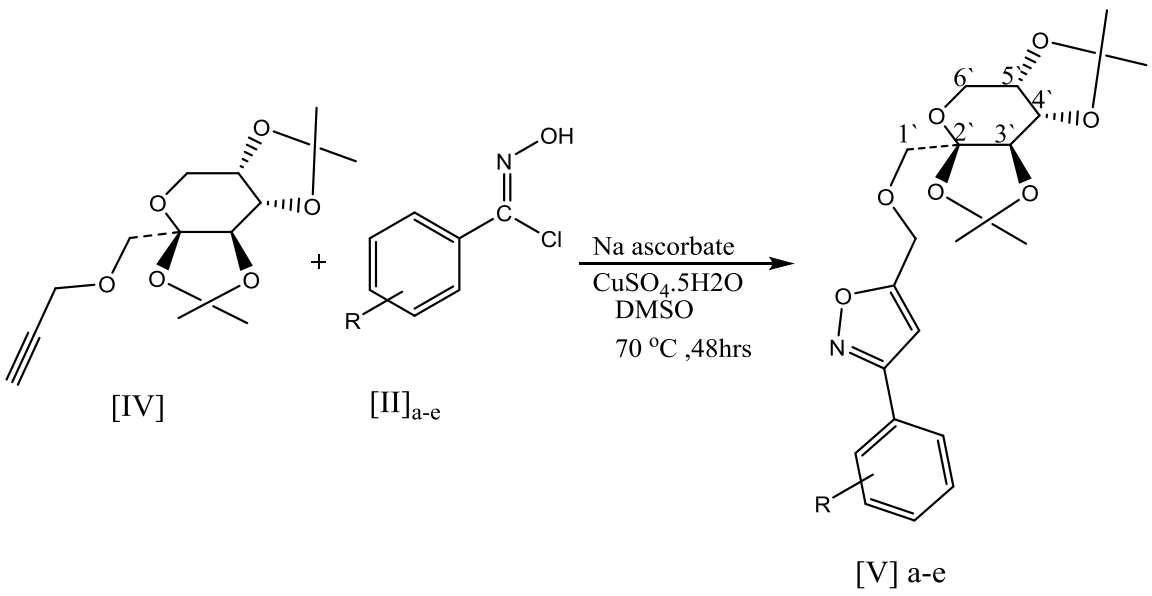


Scheme (3-1) The reaction mechanism of compound [IV]

The physical properties and FT-IR spectroscopy were corresponding to the literatures[126] . The compound [IV] was characterized by FT-IR spectroscopy. The FT-IR spectrum of compound [IV], (Figure 3-4) shows disappearance of stretching vibration band of OH group of the starting materials and appearance of strong absorption band at 3273cm^{-1} due to terminal alkyne (≡C-H). Band at 2119 cm^{-1} is attributed to new alkyne group (C≡C) which gave a very good proof for the formation of compound [IV].

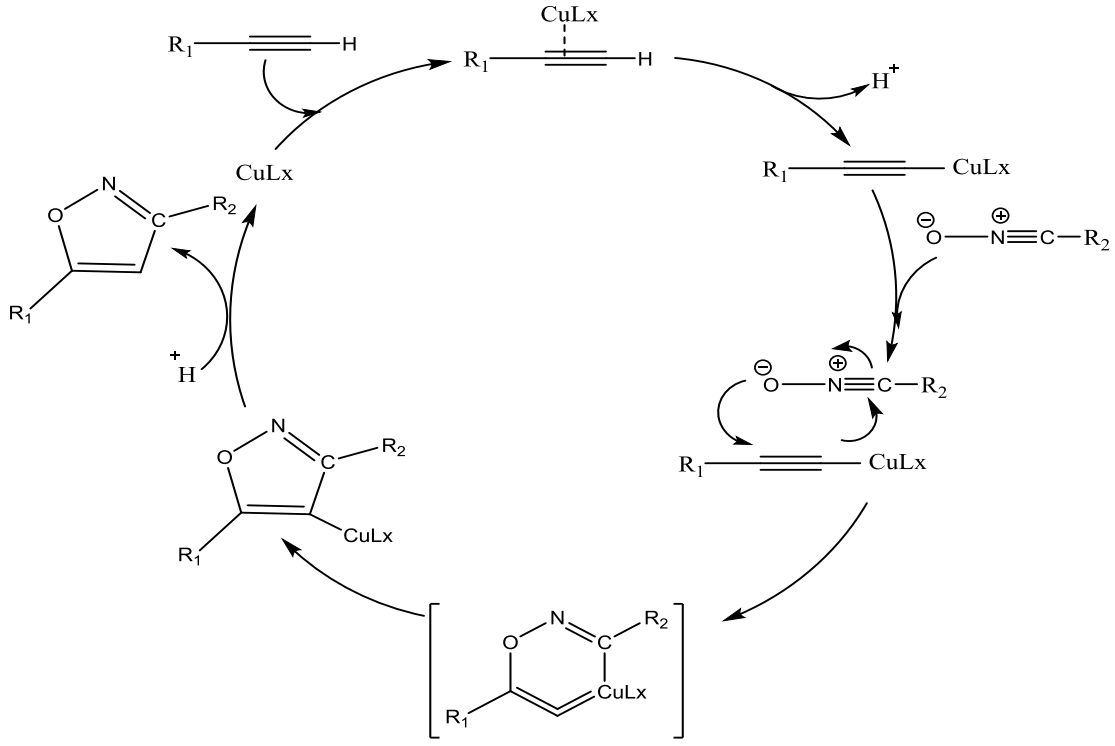
3.1.5.Synthesis and characterization of 3-(4- or 3-substituted phenyl) -5-{(2,3,4,5-di-*O*-isopropylidene-beta-D-fructopyranose-O-yl)methyl } 1H-isoxazole [V]$_{a-e}$

By using $CuSO_4.5H_2O$ as a catalyzed (1,3-dipolar cycloaddition) reaction under reflux of compound [IV] with N-hydroxy-4-or-3-substituted benzimidoyl chloride [II]$_{a-e}$ yielded the β -D-fructose based isoxazoles [V]$_{a-e}$.



[IV] [II]$_{a-e}$ [V] a-e

The mechanism[182] of 1,3-dipolar cycloaddition was outline in Scheme 3-2.



R_1= D-Fructose moeity
R_2= Aryl group

Scheme (3-2) The reaction mechanism of β -D-fructose based isoxazoles [V]$_{a-e}$.

The β-D-fructose based isoxazoles compounds $[V]_{a-e}$, were identified by FT-IR and ^{1}HNMR, ^{13}C-NMR, Mass spectroscopy (of some of them) , The FT-IR spectrum of compound $[V]_c$ (Figure 3-5) shows disappearance of stretching vibration band of OH group of N-hydroxy-4-or-3- substituted benzimidoyl chloride compounds $[II]_{a-e}$ and (≡C-H), C≡C groups of terminal alkyne suger compound [IV] of the starting materials together the appearance of absorption band at 1645 cm^{-1} is attributed to C ═ N for isoxazole moiety and that is good indicator for the ring closure of isoxazole. In addition the appearance of absorption bands at 3095 cm^{-1} and 2983,2935 cm^{-1} due to CH aromatic and CH aliphatic (asym. and sym.), respectively. The characteristic FT-IR absorption bands of β -D-fructose based isoxazoles compounds $[V]_{a-e}$ were listed in Table 3-1.

The FT-IR spectrum of compound $[V]_b$ (Figure 3-6) shows the following bands: 3292 cm^{-1}(υ,-OH), 3066 cm^{-1}(υ,C-H aromatic), 2991 ,2937 cm^{-1}(υ, C-H aliphatic),1647 cm^{-1}(υ, C ═ N),1593 cm^{-1}(υ, C ═ C).

^{1}H-NMR spectrum (in DMSO-d_6 as a solvent) of compound $[V]_b$ (Figure 3-7) shows two singlet signals at δ (1.10 and 1.17) ppm due to twelve protons of CH_3 for isopropylidene moiety. A doublet signal at δ (3.49-3.51) ppm is due to one proton for - C3`H-Ogroup. The singlet signal at δ 3.53 ppm could be attributed to the two protons for Fru-$CH_2$-O group. Besides to a quartet signal at δ ( 3.74 - 3.76) ppm due to one proton for -C5`H-O group. Also a doublet signal at δ (3.80 - 3.82) ppm due to two protons for -C6`$H_2$-O group. A triplet signal at δ (4.24- 4.28) ppm could be attributed to the one proton of -C4`H-O group. A singlet signal at δ 4.61 ppm due to two protons for het-CH_2-O group and

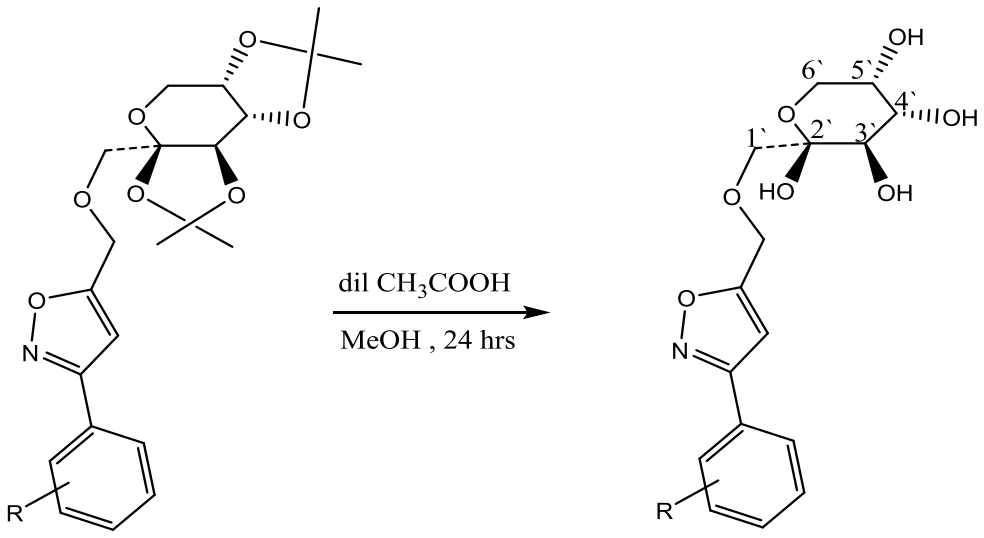
appearance of singlet signal at δ 6.79 ppm due to one proton for isoxazole moiety. Besides to a multiple signal in the region δ (7.53 - 7.63) ppm that could be attributed to the four aromatic protons. Finally a singlet signal at δ 9.70 ppm is due to one proton for OH phenolic group.

^{13}C-NMR spectrum (75 MHz, DMSO-d6) of compound $[V]_b$, (Figure3-8) displays the signals corresponding to carbon atoms as follows : two signals at δ 29.0, 29.5 ppm could be attributed to four carbon atoms of four CH_3 isopropylidenegroup. Another signals appeared at δ 62.4, 70.7,73.0 ppm could be assigned to three carbon for -CH_2-Ogroups ,and signals at δ 70.7,75.7,77.5 ppm due to three carbon for -CH-O groups. Signal at δ 100.0 ppm may be attributed to one carbon of O-C-O ,so that signal at δ 116.4 ppm due to two carbon for $C(CH_3)_2$ isopropylidene group . Also many signals in the region δ(127.1-140.4) ppm for aromatic carbon atoms. Finally, a good signal at δ156.5 ppm may be related to carbon of C ═ N group.

The mass spectrum of compound $[V]_b$, showed the a parent ion at m/z=433 and the base peak at m/z = 191 and the peaks at (m/z =260,202, 172, 144,126,114)[183] gave a good evidence to the presence the 2,3,4 ,5-di-O-isopropylidene - β -D-fructopyranose moiety (Figure 3-9) . In addition the two peaks at (67, 43) refers to the presence of isoxazole ring [184].

3.1.6.Synthesis and characterization of 3-(4- or 3-substituted phenyl)-5-{(beta-D-fructopyranose-O-yl)methyl}1H-isoxazole $[VI]_{a-e}$

Isopropylidene group of compound $[V]_{a-e}$ were deprotected by using diluted CH_3COOH. The a broad band around (3278-3429)cm^{-1} which attributed to the O-H stretching is a very good evidence of the deprotection and formation of compounds $[VI]_{a-e}$.



[V] $_{a-e}$ [VI] $_{a-e}$

These compounds were identified by FT-IR , ^{1}HNMR ,^{13}C-NMR and Mass spectroscopy (of some of them) and these data give good indicators to formation of compounds $[VI]_{a-e}$. The FT-IR spectrum of compound $[VI]_a$ (Figure 3-10) shows appearance the strong absorption band at 3402 cm^{-1}due to OH of D-fructose moiety, In addition the appearance of absorption bands at 3060 $cm^{-1}$and 2987-2873 cm^{-1} is due to CH aromatic and CH aliphatic (asym. and sym.) respectively. So that the strong absorption band at 1624 cm^{-1}, 1570 cm^{-1} is attributed to C ═ N,and C ═ C groups, respectively.

^{1}H-NMR spectrum (in DMSO-d_6 as a solvent) of compound $[VI]_a$, (Figure3-11) shows the appearance of four singlet signal at δ (4.36 , 4.54, 4.84,4.90) ppm that could be attributed to the four protons of OH groups for D-fructose moiety . A doublet signal at δ (3.11-3.13) ppm due to two proton for -C6`$H_2$-O group. Also a doublet signal at δ ( 3.28 - 3.31) ppm due to one proton for - C3`H-O group. So that a singlet signal at δ 3.60 ppm that could be attributed to the two protons for Fru-CH_2-O group.

Besides to a quartet signal at δ (3.70 - 3.72) ppm due to one proton for -C5`H-O group. A triplet signal at δ (3.84- 3.86) ppm could be attributed to the one proton of -C4`H-O group. A singlet signal at δ 4.60 ppm due to two protons for het-CH_2-O group and the appearance a singlet signal at δ 6.74 ppm due to one proton for isoxazole moiety. Finally, a multiple signals in the region δ (7.36 - 7.74) ppm that could be attributed to the five aromatic protons. The disappearance of singlet signal for twelve protons of CH_3 for isopropylidene groups with appearance of four singlet signal due to OH groups for D-fructose moiety which gives a good evidence of deprotection and formation of compounds $[VI]_{a-e}$.

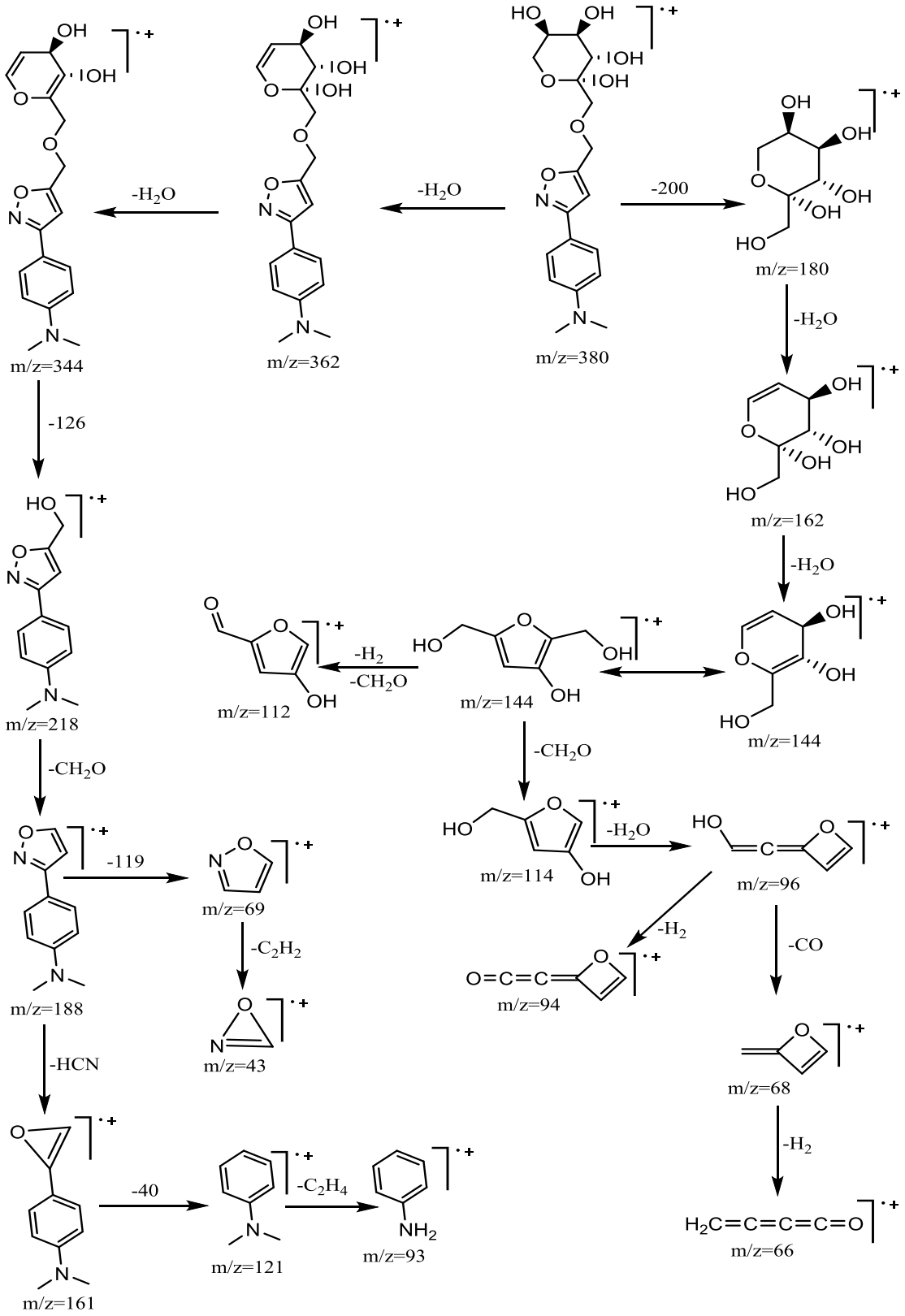
The FT-IR spectrum of 3-(4-N,N-dimethylamino phenyl)-5-{(beta-D-fructopyranose-O-yl)methyl}1H-isoxazole compound $[VI]_d$ (Figure 3-12) shows the following bands:3429 cm^{-1}(υ,-OH), 3065 cm^{-1} (υ, C-H aromatic), 2987 ,2927 cm^{-1}(υ, C-H aliphatic),1664 cm^{-1}(υ, C ═ N) and1612cm^{-1}(υ, C ═ C). All the spectral data for other compounds are listed in Table 3-2 .

^{1}H-NMR spectrum of compound $[VI]_d$ in (Figure 3-13) shows the following characteristic chemical shifts (DMSO-d_6, ppm): 3.10 (s, 6H, -N(CH_3)$_2$), (3.62-3.64) (d,1H, - C3`H-O), 3.65 (s, 2H, Fru -$CH_2$-O),(3.69-3.72) (q,1H, - C5`H-O)(3.82-3.84) (d, 2H, -C6`$H_2$-O), (3.87 - 3.91) (t,1H, -C4`H-O) 4.63 (s, 2H, het -CH_2-O), 4.32,4.51,4.74,4.77 (s, 4H, -OH D-fructose), 6.59 (s, 1H, Ar-H isoxazole) and 6.98-7.28 (m, 4H, Ar-H).

^{13}C-NMR spectrum (75 MHz, DMSO-d6) δ, of compound $[VI]_d$ in (Figure 3-14) displays the signals corresponding to carbon atoms as follows: δ 40.1 ppm (2C, -N(CH_3)$_2$), δ 65.1,68.2,70.4 ppm (3C, -CH_2-O),

δ 70.2,71.4,73.5 ppm (3C, -CH-OH), δ 115.3 ppm (1C, O-C-OH), δ 102.06,115.2, 118.1,129.2,145.2,150.3,160.4 ppm (6C, C-Ar) and (3C, C-isoxazole).

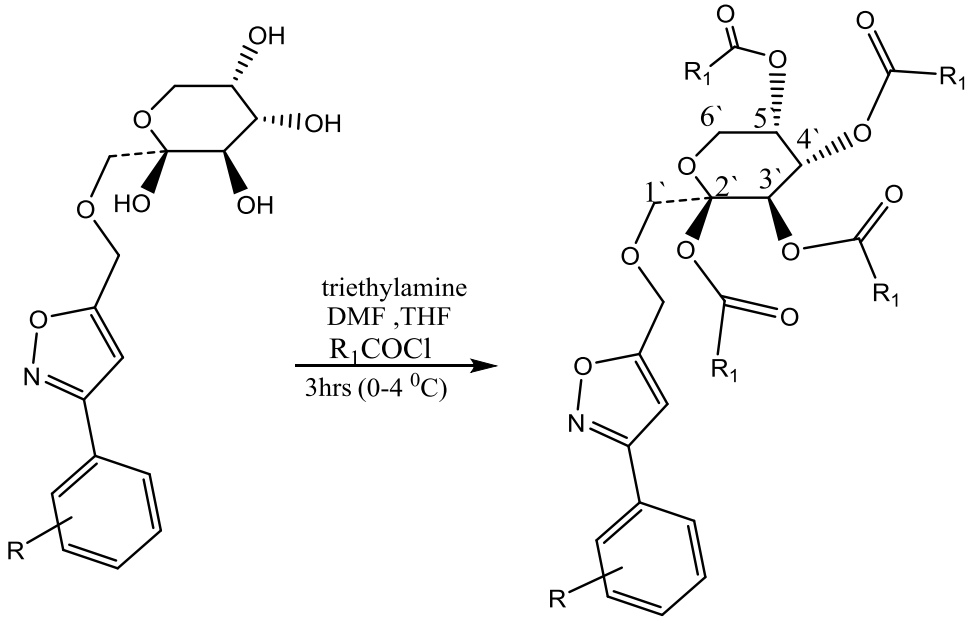
The mass spectrum of compound $[VI]_d$. (Figure 3-15), shows a parent ion at m/z= 380 and the main peak at m/z = 188 and the peaks at (m/z =180,162, 144, 114,112, 96, 94,68 and 66)[185] which give a good evidence to the presence of β -D-fructopyranose moiety. In addition the two peaks at (69, 43) refers to the presence of isoxazole ring. The most characteristic fragments of this compound were illustrated in Scheme 3-3.



Scheme(3-3) The mass fragmentation pattern of compound[IV]$_d$.

3.1.7. Synthesis and characterization of ester compounds $[VII]_{a-e}$, $[VIII]_{a-e}$ and $[IX]_{a-e}$

The esterification reaction of hydroxyl groups of compounds $[VI]_{a-e}$ with different acid chloride in mixture of THF and DMF using triethylamine as a catalyst at 0-4^{0}C give new esters compounds .



[VI] a-e

[VII]a-e -[IX]a-e

[VII]a-e When R_1= -CH_3

[VIII] a-e When R_1=

[IX] a-e When R_1=

These compounds were identified by FT-IR and ^{1}H-NMR , ^{13}C-NMR , Mass spectroscopy (of some of them) and these data gave good evidence to the formation of new ester compounds. The FT-IR spectrum of compounds $[VII]_{a-e}$, $[VIII]_{a-e}$ and $[IX]_{a-e}$. shows disappearance the stretching vibration band of OH group in the region of (3278-3429) cm^{-1}. The appearance of strong absorption stretching band at(1738 - 1712) cm^{-}

[1] due to C=O and C-O around (1267-1238) cm^{-1} of ester group is a very good evidence of the formation of ester compounds.

The FT-IR spectrum of compound $[VII]_d$, shows the appearance new stretching bands at 1736 cm^{-1} , (Figure 3-16). which could be attributed to C=O group the appearance of strong absorption stretching band at 1263 cm^{-1} is due to C-O of ester group, and the disappearance of strong absorption stretching band of OH group, In addition the appearance absorption bands at 3035 $cm^{-1}$and 2971-2845cm^{-1} is due to CH aromatic and CH aliphatic (asym. and sym.), respectively.

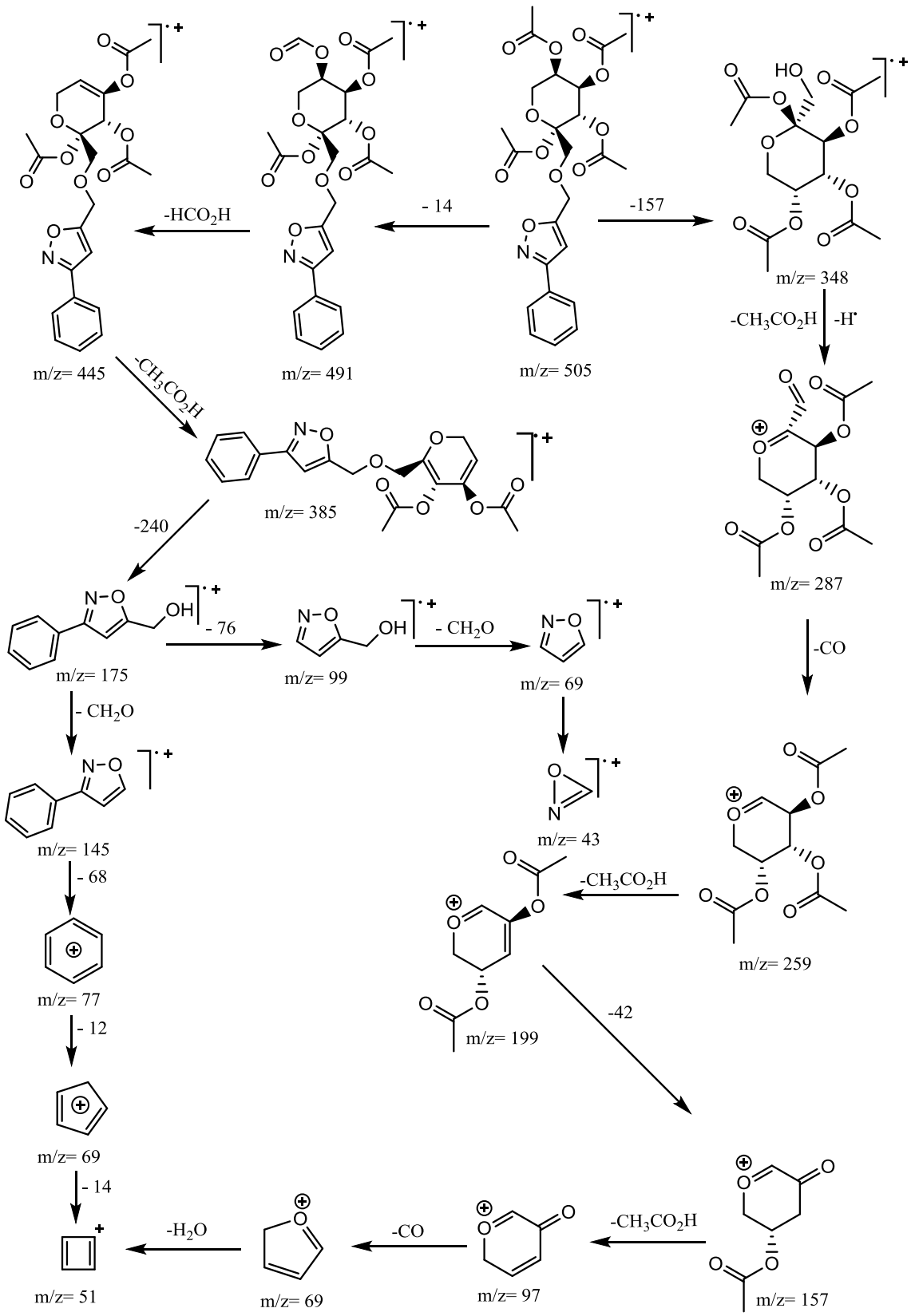
FT-IR spectrum of 3-phenyl-5-{(2,3,4,5-tetra-O-acetyl-beta-D-fructopyranose -O-yl)methyl}1H-isoxazole compound $[VII]_a$ (Figure 3-17) shows the following bands:3093 cm^{-1}(υ, C-H aromatic), 2997-2904cm^{-1}(υ, C-H aliphatic), 1738cm^{-1} (υ,- C=O)1614 cm^{-1}(υ, C ═ N),1585 cm^{-1}(υ, C ═ C) and (1070,1265)cm^{-1} (υ,- C-O)**.** The FT-IR absorption bands data of these compounds $[VII]_{a-e}$ were listed in Table 3-3.

^{1}H-NMR spectrum (400 MHz, DMSO-d_6) of compound $[VII]_a$, (Figure 3-18) shows the disappearance of four singlet signals belong to the four protons of OH groups for D-fructose moiety, with the appearance of singlet signal at δ 2.24 ppm which is due to twelve protons for CH_3 of ester groups . A doublet signal at δ 3.01 ppm is due to one proton for -C3`H-O group. So that a singlet signal at δ 3.79 ppm that could be attributed to the two protons for Fru-$CH_2$-O group. Also a doublet signals at δ ( 4.53 - 4.55) ppm are due to two protons for-C6`H_2-O group. A singlet signal at δ 4.68 ppm due to two protons for het-CH_2-O group. A triplet signal at δ (5.30- 5.32) ppm could be attributed to the one proton of -C4`H-O group. Besides to a quartet signal at δ (5.49- 5.57)

ppm due to one proton for -C5`H-O group, and the appearance of singlet signal at δ 6.73 ppm is due to one proton for isoxazole moiety. Finally, a multiple signals in the region δ (7.42 - 7.79) ppm that could be attributed to the five aromatic protons.

^{13}C-NMR spectrum (75 MHz, DMSO-d6) of compound $[VII]_a$, (Figure 3-19) displayed the signals corresponding to carbon atoms as follows : signal at δ 30.0 ppm could be attributed to four carbon atoms of four CH_3 acetyl groups, also another signals appeared at δ 60.1, 67.2,70.3 ppm could be assigned to three carbons for -CH_2-O groups, and signals at δ 69.2,71.4,72.6 ppm are due to three carbons for -CH-O groups, signal at δ 98.2 ppm may be attributed to one carbon of O-C-O ,so that many signals in the region δ(112.5-150.4) ppm for carbons of aromatic moiety. Also a signal at δ160.4 ppm may be related to carbon of C ═ N group. Finally, two signals at δ 177.5and 179.9 ppm are due to four carbons of C=O for ester moiety.

The mass spectrum of compound $[VII]_a$ as in (Figure 3-20) which showed the base peak at (m/z= 175) and the parent ion at m/z 505 corresponding to the molecular weight of this compound, Also exhibited many peaks at (m/z= 348,287,259,199,157, and 97)[186] refers to presence 2,3,4,5-tetra-O-acetyl-beta-D-fructopyranose moeity. In addition the two peaks at (69 and 43) refers to presence the isoxazole ring. The peaks at (m/z 77, 65 and 51)[187] are characteristic of benzene rings. The most characteristic fragments of this compound were illustrated in Scheme3-4.



Scheme (3-4) The mass fragmentation pattern of compound[VII]$_a$

The F-TIR spectrum of compound $[VIII]_d$, shows the disappearance of strong absorption stretching band of OH group , with appearance new stretching bands at 1712 cm^{-1}, which could be attributed to C=O group beside appearance the strong absorption stretching band at (1257) cm^{-1}due to C-O of ester group. In addition the appearance absorption bands at 3074 $cm^{-1}$and 2983,2936 cm^{-1} are due to CH aromatic and CH aliphatic (asym. and sym.) respectively, (Figure 3-21).

FT-IR spectrum of 3-(4-bromo phenyl)-5-{(2,3,4,5-tetra-O-benzoyl-beta-D-fructopyranose-O-yl)methl}1H-isoxazole compound $[VIII]_c$ shows the following bands:,3095 cm^{-1}(υ, C-H aromatic) ,2987,2935 cm^{-1}(υ, C-H aliphatic), 1714cm^{-1} (υ,- C=O)1674 cm^{-1}(υ, C ═ N),1616cm^{-1} (υ, C ═ C) ,(1263) cm^{-1} (υ,- C-O), (Figure 3-22) **.** The FT-IR absorption bands data of these compounds $[VIII]_{a-e}$ were listed in Table 3-3.

^{1}H-NMR spectrum (400 MHz, DMSO-d_6) of compound $[VIII]_c$, (Figure3-23) shows disappearance a singlet signal to the four protons of OH groups for D-fructose moiety, appearance a doublet signal at δ (3.72 - 3.75) ppm due to two protons for-C6`$H_2$-O group. So that a singlet signal at δ 3.85 ppm that could be attributed to the two protons for Fru-$CH_2$-O group. A doublet signal at δ( 4.02 -4.05 ) ppm due to one proton for -C3`H-O group. Also a singlet signal at δ 4.63 ppm due to two protons for het-CH_2-O group. Besides to a quartet signal at δ (5.40- 5.54) ppm due to one proton for -C5`H-O group. A triplet signal at δ 5.83 ppm could be attributed to the one proton of -C4`H-O group. and appearance a singlet signal at δ 6.43 ppm due to one proton for isoxazole moiety. Finally, a multiple signals in the region δ (6.50 - 7.83) ppm that could be attributed to the twenty four aromatic protons.

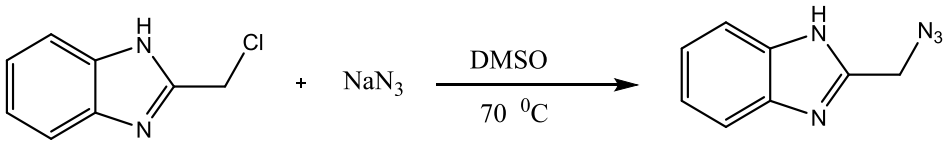
The F-TIR spectrum of compound $[IX]_a$, shows the disappearance of strong absorption stretching band of OH groups ,with appearance new stretching bands at 1724 cm^{-1} , which could be attributed to C=O group, beside appearance the strong absorption stretching band at (1263) cm^{-1}due to C-O of ester group. Also appearance the absorption stretching band at 1642 cm^{-1},1618cm^{-1}due to C ═ N and C ═ C groups .In addition the appearance absorption bands at 3089$cm^{-1}$and 2981,2933cm^{-1} due to CH aromatic and CH aliphatic (asym. and sym.) respectively, (Figure 3-24).

FT-IR spectrum of 3-(4-N,N-dimethylamino phenyl)-5-{(2,3, 4,5-tetra-O-paramethoxybenzoyl-beta-D-fructopyranose-O-yl)methyl} 1H-isoxazole compound $[IX]_d$, shows the following bands:,3074 cm^{-1}(υ, C-H aromatic),2983,2881 cm^{-1}(υ, C-H aliphatic), 1727cm^{-1} (υ,- C=O)1668 cm^{-1}(υ, C ═ N),1583cm^{-1} (υ, C ═ C),(1259) cm^{-1} (υ,- C-O) (Figure 3-25) **.** The FT-IR absorption bands data of these compounds $[IX]_{a-e}$ were listed in Table 3-3.

^{1}H-NMR spectrum (400 MHz, DMSO-d_6) of compound $[IX]_d$ (Figure 3-26), shows the following characteristic chemical shifts: δ 3.03 ppm (s, 6H, -N(CH_3)$_2$), δ 3.72 ppm (s, 12H, -OCH_3), δ (4.03 -4.05) ppm (d,1H, - C3`H-O), δ 4.15 ppm (s, 2H, Fru -$CH_2$-O), δ 4.66 ppm (s, 2H, het -$CH_2$-O), δ (5.44- 5.46) ppm (q,1H, - C5`H-O), δ 5.72 ppm (t,1H, - C4`H-O), δ 5.88 ppm (d, 2H, -C6`H_2-O), δ 6.72 ppm (s, 1H, Ar-H isoxazole), δ (7.17-7.82) ppm (m, 20H, Ar-H).

3.1.8.Preparation and characterization of 2-(azidomethyl)-1*H*-benzo[*d*]imidazole [X]

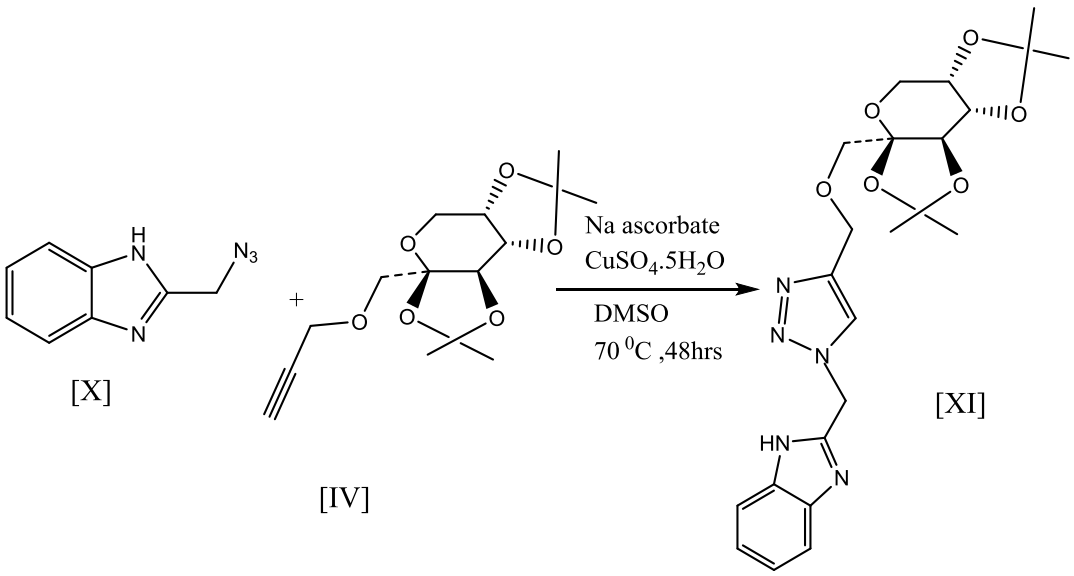
The compound 2-(azidomethyl)-1*H*-benzo[*d*]imidazole [X] was prepared (in very good yields) from the reaction of 2-(chloromethyl)-1*H*-benzo[*d*]imidazole and sodium azide in traditional SN^2 reaction. FT-IR spectrm of 2-(azidomethyl)-1*H*-benzo[*d*]imidazole, (Figure 3-27) shows the significant $-N_3$ band at 2100 cm^{-1} as a good indicator of formation of the mentioned azide. In addition the appearance absorption bands at 3360 cm^{-1} due to NH for benzo[d]imidazol moiety. The physical properties and FT-IR spectroscopy were corresponding to the literatures[180]



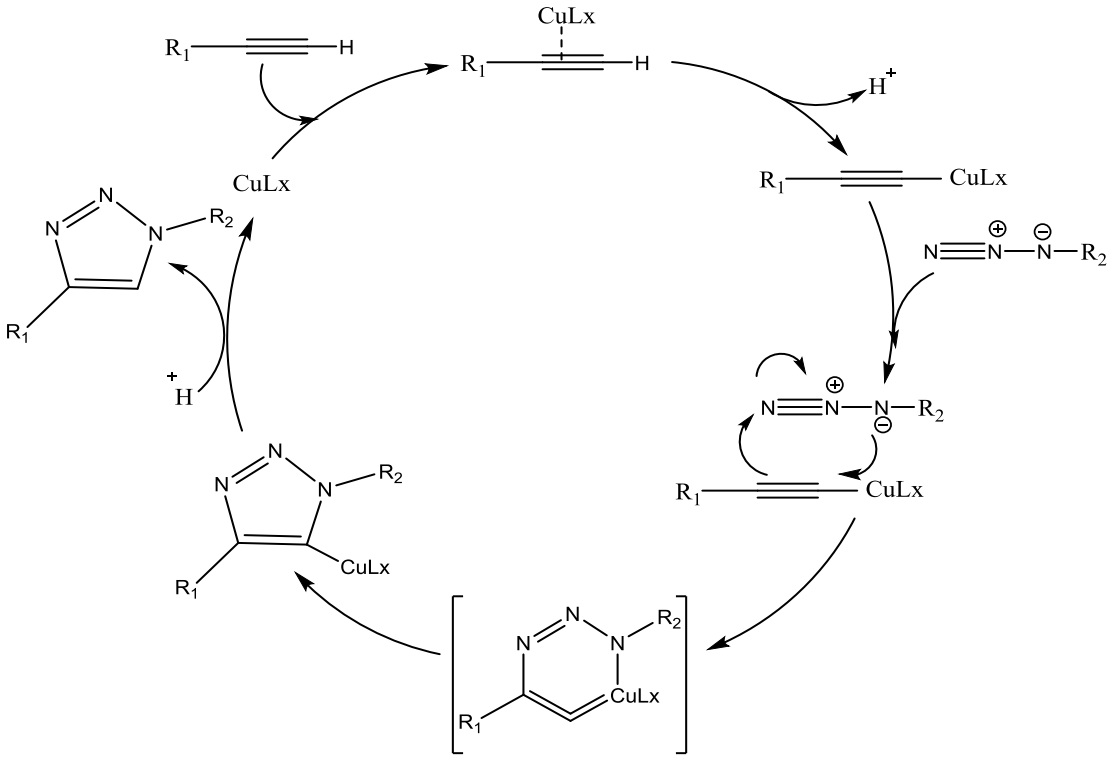
2-(chloromethyl)-1*H*-benzo[*d*]imidazole [X]

3.1.9.Synthesis and characterization of 1-((1H-benzo[d]imidazol-2-yl)methyl)-4-{(2,3,4,5-di-O-isopropylidene-beta-D-fructopyranose-O-yl)methyl}1H-1,2,3-triazole[XI].

The compound [XI] was synthesized by the same method used for the synthesis of compounds$[V]_{a-e}$ in paragraph (3.1.5.), except using 2-(azidomethyl)-1*H*-benzo[*d*]imidazole compound [X] instead of compounds$[II]_{a-e}$.



The mechanism[188] of 1,3-dipolar cycloaddition was outline in Scheme (3-5).



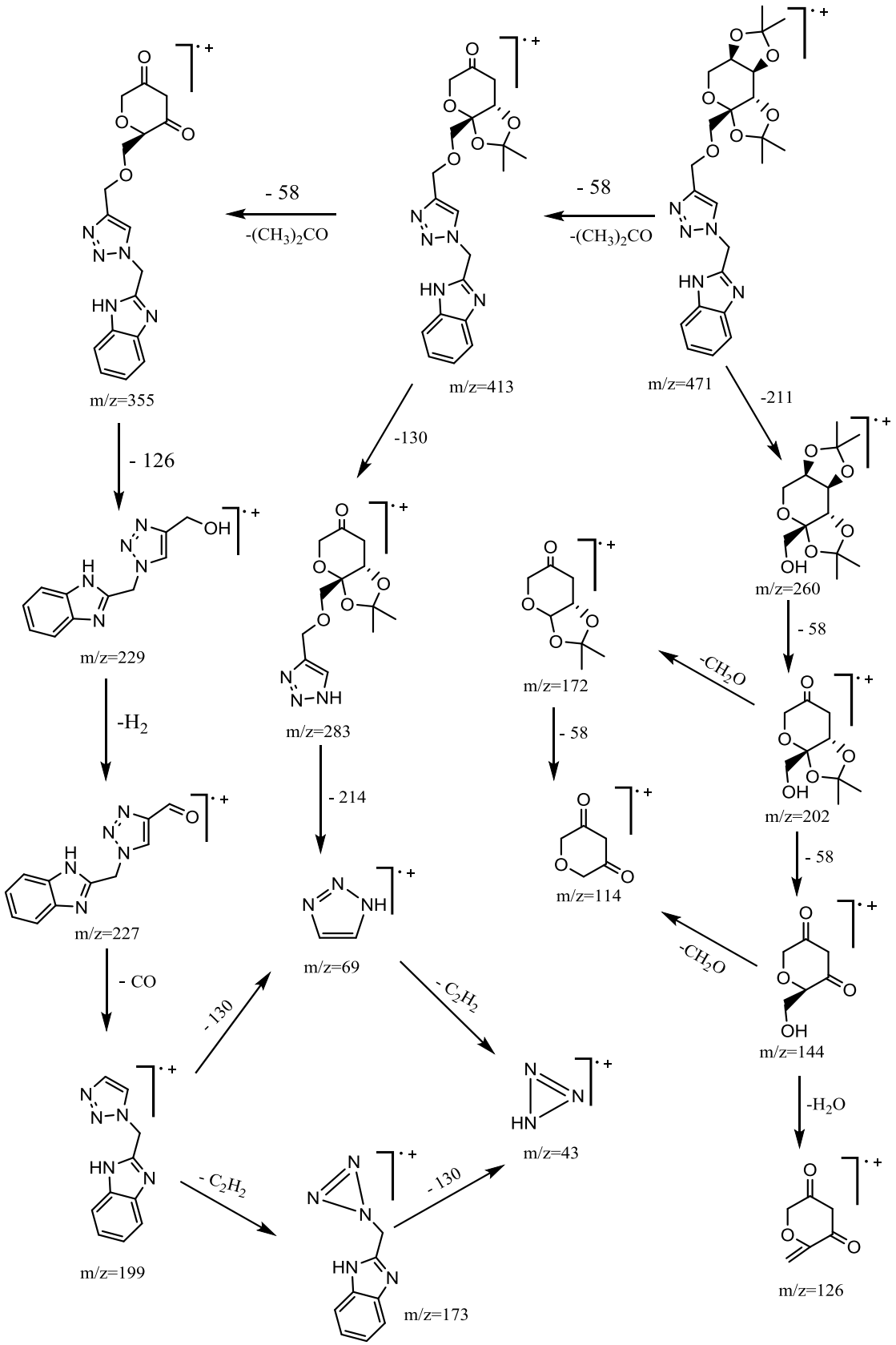
Scheme (3-5). The reaction mechanism of 1,2,3-triazole derivatives compound [XI].

The structure of the compound [XI] was studied by F-TIR, ^{1}HNMR,^{13}C-NMR and Mass spectroscopy. The F-TIR spectrum of compound [XI], (Figure3-28) shows the disappearance of strong absorption stretching band of $-N_3$ for azide group of compound [X], and ≡C-H , C≡C groups of terminal alkyne suger compound [IV] of the starting materials together that is good indicator for the ring closure of triazole. beside appearance the strong absorption stretching band at 3255 cm^{-1} is due to secondary amine NH for benzo[d]imidazol moiety .Also appearance the absorption stretching band at 1667 cm^{-1},1614cm^{-1} are due to C ═ N and C ═ C groups .In addition the appearance absorption bands at 3089 $cm^{-1}$and 2981-2830 cm^{-1} due to CH aromatic and CH aliphatic (asym. and sym.), respectively.

^{1}H-NMR spectrum (in DMSO-d_6 as a solvent) of compound [XI], (Figure3-29) shows two a singlet signal at δ (1.26, 1.28) ppm due to twelve protons of CH_3 for isopropylidene moiety. So that a singlet signal at δ 3.70 ppm that could be attributed to the two protons for Fru-CH_2-O group.A doublet signal at δ (3.80 - 3.82) ppm due to two protons for -C6`$H_2$-O group. Besides to a quartet signal at δ ( 3.90 - 3.92) ppm due to one proton for -C5`H-O group. A triplet signal at δ (4.10- 4.14) ppm could be attributed to the one proton of -C4`H-O group. Also a doublet signal at δ (4.22- 4.24) ppm due to one proton for - C3`H-O group. A singlet signal at δ 4.70ppm due to two protons for het-CH_2-O group. A singlet signal at δ 5.10ppm due to two protons for -CH_2-N-triazole[189] group. Besides to a multiple signal in the region δ (7.31-7.74) ppm that could be attributed to the four aromatic protons of benzene ring and appearance a singlet signal at δ 8.35 ppm due to one proton for triazole ring Finally a singlet signal at δ 12.04 ppm due to one proton for N-H[190,191] benzo[d]imidazol group.

^{13}C-NMR spectrum (75 MHz, DMSO-d6) of compound [XI], (Figure3-30) displays the signals corresponding to carbon atoms as follows : two signals at δ 26.5, 27.1 ppm could be attributed from four carbon atoms of four CH_3 isopropylidene group and one signal at δ 55.0 due to one carbon for -CH_2-N group also another signals appeared at δ 64.0, 67.5,71.4 ppm could be assigned of three carbons for -CH_2-O group,and signals at δ 74.5,76.5,77.9 ppm due to three carbons for -CH-O group, signal at δ 111.5 ppm may be attributed to one carbon of O-C-O ,so that signal at δ 112.0, 115.7 ppm due to two carbons for $C(CH_3)_2$. Finally , many signals in the region δ (116.1-146.2) ppm for aromatic ten carbons of benzo[d]imidazole and triazole rings.

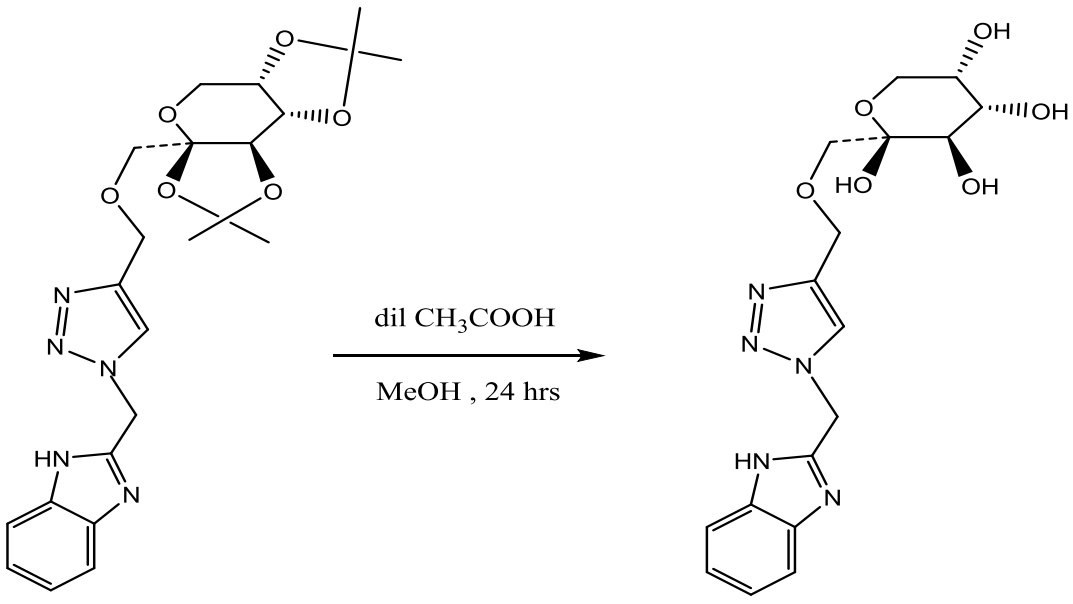
The mass spectrum of compound[XI] , is shown in (Figure 3-31). The peaks at m/z =260, 202, 172, 144, 126, and 114 are produced because of the characteristic fragmentation of the 2,3,4,5-di-O-isopropylidene-beta-D-fructopyranose. While the fragments at m/z = 69 and 43 refer to presence of 1, 2, 3-triazole ring. Also the interesting peaks at m/z = 199(100%) (Base peak) due to both the triazole and benzo[d]imidazole rings. And the parent ion at m/z 471corresponding to the molecular weight of this compound . The other important fragments given in Scheme 3-6.



Scheme (3-6) The mass fragmentation pattern of compound[XI].

3.1.10.Synthesis and characterization of 1-((1H-benzo[d]imidazol-2-yl)methyl)-4-{(beta-D-fructopyranose-O-yl)methyl}1H-1,2,3-triazole [XII] .

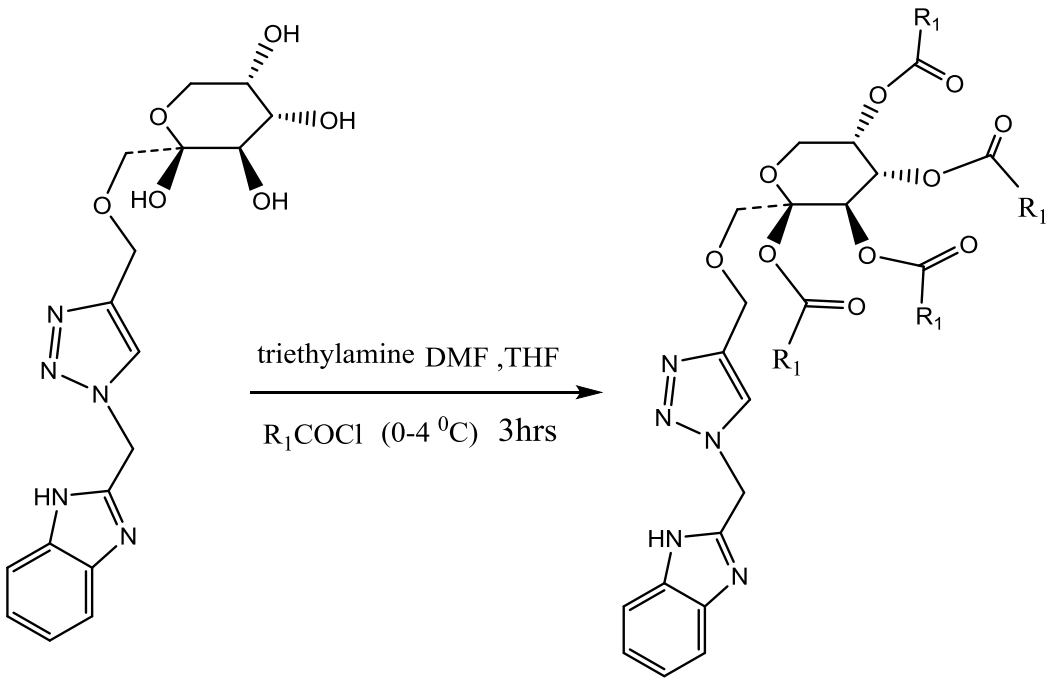
Hydrolysis of isopropylidene group for compound [XI] occur by using dil CH_3COOH. The F-TIR spectrum of compound [XII], (Figure 3-32) shows the appearance of strong absorption stretching broad band at 3428cm^{-1} which attributed to the O-H for d-fructopyranose moiety is a very good evidence of the deprotection and formation of compound [XII] . So that appearance the strong absorption stretching band at 3252 cm^{-1} due to secondary amine NH for benzo[d]imidazol moiety, beside appearance the absorption stretching band at 1660 cm^{-1},1604$cm^{-1}$are due to C ═ N and C ═ C groups. In addition the appearance absorption bands at 3009 $cm^{-1}$and 2958-2900 cm^{-1} are due to CH aromatic and CH aliphatic (asym. and sym.), respectively.



[XI] [XII]

3.1.11. Synthesis and characterization of ester compounds $[XIII]_{a-c}$.

The reaction of hydroxyl groups of compound [XII]with different acid chloride in mixture of tetrahydrofuran THF and dimethylformamide DMF using triethylamine(Et_3N) as a catalyst at 0-4^{0}C to give new ester compounds[XIII] **a-c**.



[XII] [XIII]$_{a-c}$

R_1 = -CH_3 , , O

The compounds[XIII]$_{a-c}$, were identified by FT-IR and ^{1}H-NMR, ^{13}C-NMR, Mass spectra (of some of them). The FT-IR spectra of compounds [XIII] **a-c** , shows the disappearance of stretching vibration band of OH group so that appearance the strong absorption stretching band at (1740- 1713) cm^{-1} due to C=O beside to C-O around(1265-1249) cm^{-1} of ester groups is a good evidence for the formation new ester compounds.

The FT-IR spectrum of compound $[XIII]_b$, shows the appearance of new stretching bands at 1713 cm^{-1}, (Figure3-33). which could be attributed to C=O group beside appearance the strong absorption stretching band at (1249) cm^{-1}due to C-O of ester group. Also appearance the strong absorption stretching band at 3250 cm^{-1} is due to NH for benzo[d]imidazol moiety. So that disappearance the strong absorption stretching band of OH group, In addition the appearance absorption bands at 3035 $cm^{-1}$and 2987-2870 cm^{-1} are due to CH aromatic and CH aliphatic (asym. and sym.), respectively.

The FT-IR spectrum of compound $[XIII]_c$ 1-((1H-benzo [d]imidazol-2-yl)methyl)-4-{(2,3,4,5-tetra-O-para methoxy benzoyl -beta-D-fructopyranose-O-yl)methyl}1H-1,2,3-triazole, Figure (3-34) showed the following bands: 3273 cm^{-1}(υ,-NH), 3072 cm^{-1}(υ, C-H aromatic), 2995,2860 cm^{-1}(υ, C-H aliphatic), 1726cm^{-1}(υ,- C=O),1668 cm^{-1}(υ, C ═ N),1620 cm^{-1}(υ, C ═ C)**.** The FT-IR absorption bands data of these compounds $[XIII]_{a-c}$ were listed in Table (3-4).

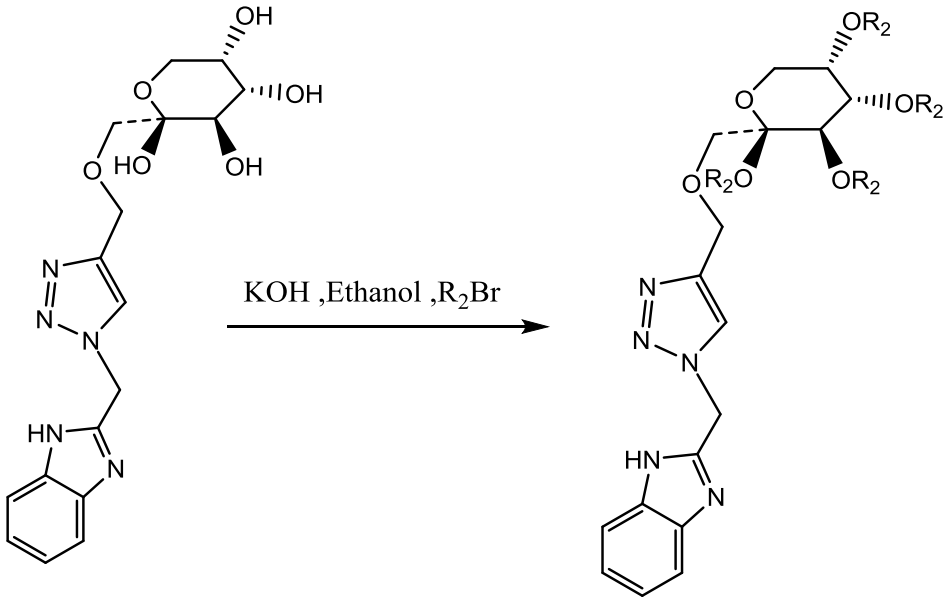
^{1}H-NMR spectrum (in DMSO-d_6 as a solvent) of compound $[XIII]_c$, (Figure3-35) shows a doublet signal at δ (3.71 - 3.72) ppm due to two protons for -C6`H_2-O group.A singlet signal at δ 3.78 ppm due to twelve protons of -OCH_3 groups. So that a singlet signal at δ 3.89 ppm that could be attributed to the two protons for Fru-CH_2-O group. A singlet signal at δ 4.68ppm due to two protons for het-CH_2-O group. Also a singlet signal at δ 5.02 ppm due to two protons for -CH_2-N-triazole group. Besides to a quartet signal at δ (5.42 - 5.47) ppm due to one proton for -C5`H-O group. Also a doublet signal at δ (5.70- 5.71) ppm due to one proton for - C3`H-O group. A triplet signal at δ (5.88 - 5.90) ppm could be attributed to the one proton of -C4`H-O group. Besides to a multiple signal in the region δ (7.10-8.17) ppm that could be

attributed to the twenty one, aromatic protons for benzene and triazole rings. Finally, a singlet signal at δ 12.06 ppm is due to one proton for N-H benzo[d]imidazol group.

The mass spectrum of compound[XIII]$_a$, shows the a parent ion at m/z=559 and the base peak at m/z = 43, (Figure 3-36).The characteristic fragmentation at (m/z =348, 287, 259,157) and (m/z = 229, 199,106) were related to the 2,3,4,5-tetra-O-acetyl-beta-D-fructopyranose moeity and (both the triazole and benzo[d]imidazole rings) , respectively. The peaks at (m/z 77, 65 and 51) this fragment characteristic of benzene rings.

3.1.12. Synthesis and characterization of ether compounds [XIV]$_{a-c}$.

On the other hand compound [XII] was converted to new ether compounds [XIV]$_{a-c}$ using different alkyl bromide in ethanol and potassium hydroxide KOH as a catalyst .



[XII] [XIV]$_{a-c}$

R_2= -CH_2CH_3 , -$CH_2CH_2CH_3$, -$CH_2CH_2CH_2CH_3$

The structure of the compounds [XIV]$_{\mathbf{a-c}}$ were studied by F-TIR and ^{1}HNMR,^{13}C-NMR, Mass spectroscopy (of some of them). The FT-IR spectra of compounds [XIV]$_{\mathbf{a-c}}$ shows the disappearance of stretching vibration band of OH group is a good evidence of the formation of new ether compounds .

The FT-IR spectrum of compound [XIV]$_c$, (Figure 3-37) shows the appearance of new stretching bands at 1109 cm^{-1}due to C-O of ether group. beside disappearance the strong absorption stretching band of OH group, Also appearance the strong absorption stretching band at3292 cm^{-1} due to NH for benzo[d]imidazol moiety. Also appearance the absorption stretching band at 1647 cm^{-1},1610cm^{-1} are due to C = N and C = C groups . In addition the appearance absorption bands at 3066 cm^{-1}and 2986,2922cm^{-1} are due to CH aromatic and CH aliphatic (asym. and

sym.) respectively. All the spectral data for other compounds are listed in Table 3-5.

The FT-IR spectrum of compound $[XIV]_a$ 1-((1H-benzo [d] imidazol -2-yl)methyl)-4-{(2,3,4,5-tetra-O-ethyl-beta-D-fructopyranose-O-yl) methyl}1H-1,2,3-triazole, (Figure 3-38) shows the following bands : 3273cm^{-1}(υ,-NH),3072 cm^{-1}(υ, C-H aromatic),2995,2940 cm^{-1}(υ, C-H aliphatic) ,1668cm^{-1}(υ, C ═ N),1620 cm^{-1}(υ, C ═ C) 1101 cm^{-1}(υ, C-O).

^{1}H-NMR spectrum (in DMSO-d_6 as a solvent) of compound $[XIV]_a$, (Figure3-39) shows two a triplet signal appeared at δ (1.09- 1.24) ppm due to twelve protons of -CH_3 groups for ether moiety. So that showed two a quartet signal at δ (3.25,3.42) ppm that could be attributed to the eight protons for O-$\underline{CH_2}CH_3$ groups. Besides to a quartet signal at δ (3.60 - 3.65) ppm due to one proton for -C5`H-O group. A triplet signal at δ (3.71 - 3.75) ppm could be attributed to the one proton of (-C4`H-O) group. Also a doublet signal at δ (3.81 - 3.83) ppm due to one proton for - C3`H-O group. So that a sharp singlet signal at δ 3.95 ppm that could be attributed to the two protons for Fru-$CH_2$-O group. A doublet signal at δ (3.97 - 3.99) ppm due to two protons for -C6`H_2-O group. A singlet signal at δ 4.70ppm due to two protons for het-CH_2-O group. Also a singlet signal at δ 5.08 ppm due to two protons for -CH_2-N-triazole group. Besides to a multiple signal in the region δ (7.41-7.61) ppm that could be attributed to the five aromatic protons for benzene and triazole rings .Finally, a singlet signal at δ 12.11 ppm due to one proton for N-H benzo[d]imidazol group.

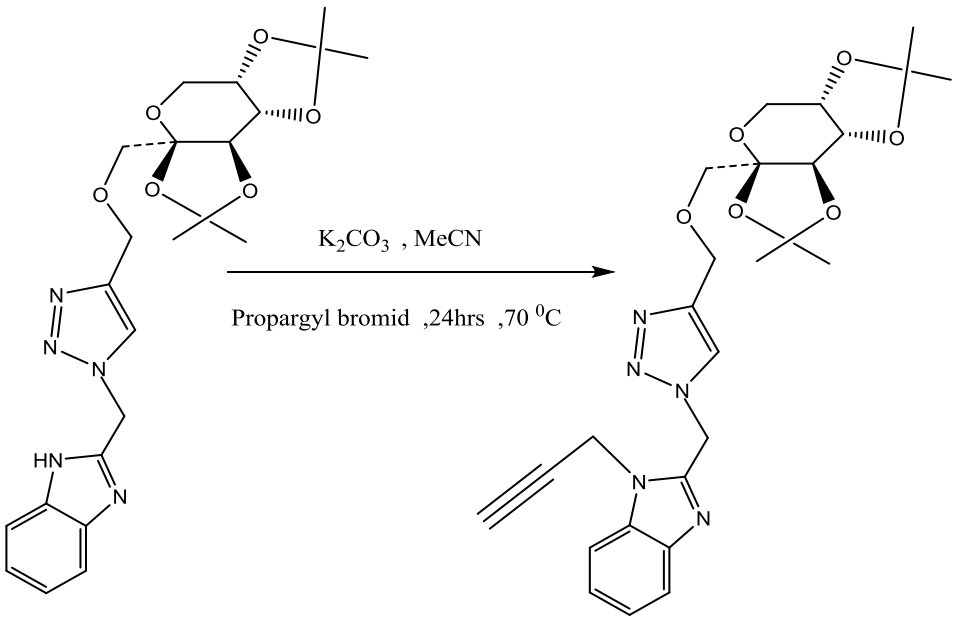
^{13}C-NMR spectrum (75 MHz, DMSO-d6) of compound $[XIV]_a$, (Figure3-40) displays the signals corresponding to carbon atoms as follows : two signals at δ 12.0,12.5 ppm could be attributed from four

carbon atoms of four CH_3 groups for ether moiety and one signal at δ 52.1 due to one carbon for -CH_2-N group, also another signals appeared at δ 55.2,62.4,65.9,66.5,67.5ppm could be assigned of seven carbons for -CH_2-O group and showed appeared many signals at δ 73.1 ,75.7 , 77.0 ppm could be assigned of three carbons for -CH-O group , signal at δ 110.1 ppm may be attributed to one carbon of O-C-O. Finally , many signals in the region δ(116.4.2-142.3) ppm for aromatic ten carbons of benzo[d]imidazo and triazole rings.

The mass spectrum of compound $[XIV]_a$, exhibited a molecular ion at m/z=503 and the base peak at m/z = 180, also showed a characteristic fragmentation of 2,3,4,5-tetra-O-ethyl-beta-D-fructopyranose moiety at m/z =(292, 264, 236, 208 and 144), Figure(3-41). Besides to appeared many peaks at m/z=(229,199,173,69 and 43) to give a good evidence for the formation of this compound .

3.1.13. Synthesis and characterization of 1-((1-(prop-2-yn-1-yl)-1H-benzo[d]imidazol-2-yl)methyl)-4-{(2,3,4,5-di-O-isopropylidene-beta-D-fructopyranose-O-yl)methyl}1H-1,2,3-triazole[XV].

The reaction of compound [XI] with propargyl bromide in methyl cyanide MeCN and potassium carbonate K_2CO_3 as a catalyst[192] afforded the compound [XV].



[XI] [XV]

The structure of the compound [XV] was studied by F-TIR, ^{1}HNMR,^{13}C-NMR and mass spectroscopy. Disappearance the absorption stretching vibration bands of secondary amine NH for benzo[d]imidazol moiety of the starting materials and appearance the sharp absorption stretching band at 3220cm^{-1} of ≡C-H , 2106 cm^{-1} C≡C for terminal alkyne group . The FT-IR spectrum (Figure 3-42) give a very good proof for the formation of compound [XV] beside appearance the absorption stretching band at 1665 cm^{-1}and 1620cm^{-1}are due to C ═ N and C ═ C groups. In addition the appearance absorption bands at 3097 cm^{-1}and 2981,2925 cm^{-1} due to CH aromatic and CH aliphatic (asym. and sym.) respectively.

^{1}H-NMR spectrum (in DMSO-d_6 as a solvent) of compound [XV] 1-((1-(prop-2-yn-1-yl)-1H-benzo[d]imidazol-2-yl)methyl)-4-{(2,3,4,5-di-O-isopropylidene-beta-D-fructopyranose-O-yl)methyl}1H-1,2,3-triazole. Shows disappearance a singlet signal to the one proton of NH for benzo[d] imidazol moiety, with appearance a singlet signal at δ 3.32 ppm

due to one protons of ≡C-H, for terminal alkyne group. give a good evidence formation of compound [XV]. ^{1}H-NMR spectrum(400 MHz, DMSO-d_6) in (Figure3-43), shows the following characteristic chemical shifts: 3.32 ppm (s, 1H, ≡C-H),1.11, 1.21 ppm (s, 12H, -CH_3, isopropylidene), 3.40 ppm (s, 2H, Fru-CH_2-O), 3.64 ppm (d, 2H, -C6`$H_2$-O), 3.92 ppm (q,1H, - C5`H-O), 4.02 ppm (t,1H, C4`H-O) , 4.18 ppm (d,1H, - C3`H-O), 4.50 ppm (s, 2H, -CH_2-N), 4.60 ppm (s, 2H, -het-CH_2-O), 4.91 ppm (s, 2H, -CH_2-N-triazole), 7.60-7.95 ppm (m, 4H, Ar-H), 7.99 ppm (s, 1H, Ar-H triazole).

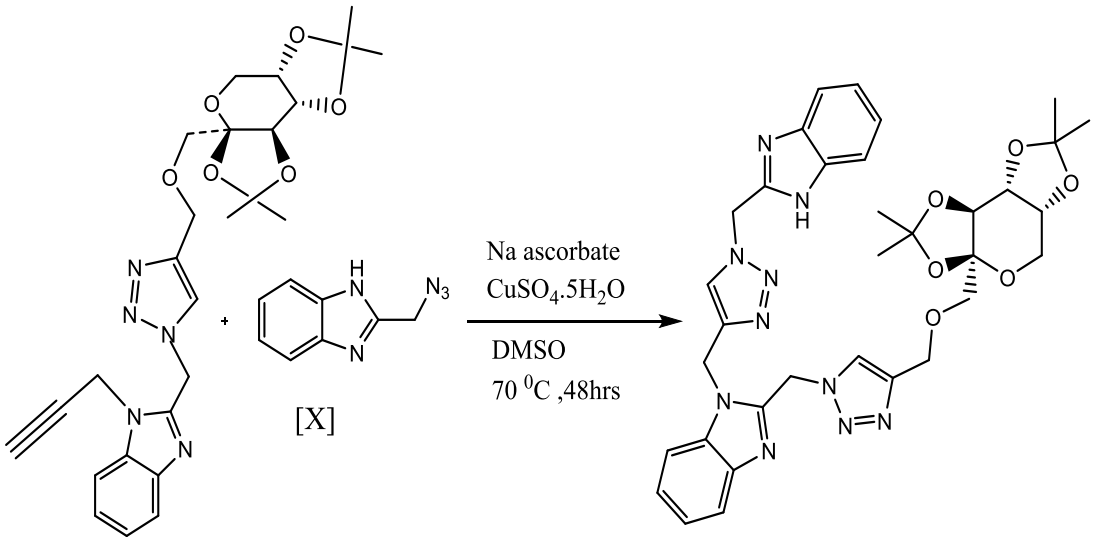
^{13}C-NMR spectrum (75 MHz, DMSO-d6) of compound [XV]. (Figure 3-44) displayed the signals corresponding to carbon atoms as follows,; δ 26.7, 27.6 ppm (4C, CH_3 isopropylidene), δ 47.6,60.7 ppm (2C, C≡C) δ 68.1 ppm (1C, -CH_2-N), δ 68.2,69.8,70.1 ppm (3C, -CH_2-O), δ 70.8,74.2 ,77.7 ppm (3C, -CH-O), δ 108.5,110.2 ppm (2C, $C(CH_3)_2$ isopropylidene), δ 116.3 ppm (1C, O-C-O), δ 119.2,121.3,128.6, 134.7,142.2,145.0,147.1 ppm (9C, C- triazole and benzo[d] imidazol).

The mass spectrum of compound [XV]. (Figure 3-45), shows the a parent ion at m/z=509 and the base peak at m/z = 199 and the peaks at (m/z =283,267, 260,239,202, 199,173,144 and 69) were give good evidence to presence the 2,3,4,5-di-O-isopropylidene-beta-D-fructopyranose, triazole and benzo[d] imidazol) rings.

3.1.14.Synthesis and characterizationof bis-triazole compound [XVI]

1-((1-((1-((-1Hbenzo[d]imidazol-2-yl)methyl)triazol-4-yl)methyl)-1H-benzo[d]imidazol-2-yl)methyl)-4-{(2,3,4,5-di-O-isopropylidene-beta-D-fructopyranose-O-yl)methyl1H-1,2,3-triazole .

By CuAAC protocol using $CuSO_4.5H_2O$ and sodium ascorbate as a catalyzed via1,3-dipolar cycloaddition reaction of 1-((1-(prop-2-yn-1-yl)-1H-benzo[d]imidazol-2-yl)methyl)-4-{(2,3,4,5-di-O-isopropylidene-beta-D-fructopyranose-O-yl)methyl}1H-1,2,3-triazole compound [XV] with 2-(azidomethyl)-1*H*-benzo[*d*]imidazole [X] under reflux yielded the bis-triazole compound [XVI].



[XV] [X] [XVI]

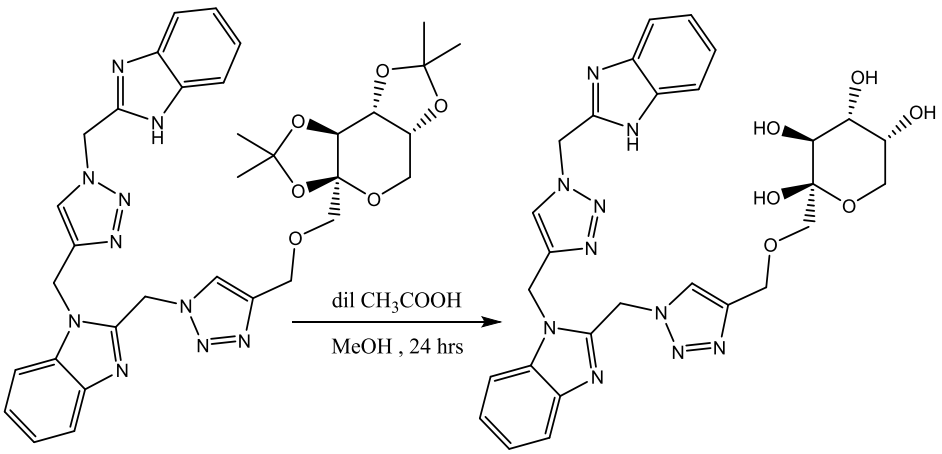
The structure of the compound [XVI]was studied by FT-IR and mass spectroscopy. The F-TIR spectrum in (Figure3-46) shows the disappearance of strong absorption stretching band of $–N_3$ for azide group of compound [X], and ≡C-H , C≡C groups of terminal alkyne compound [XV]of the starting materials together that is good indicator for the ring closure of bis triazole. beside appearance the strong absorption stretching

band at 3275 cm^{-1} due to secondary amine NH for benzo[d]imidazol moiety .Also appearance the absorption stretching band at 1657 cm^{-1} , 1630cm^{-1}due to C ═ N and C ═ C groups .In addition the appearance absorption bands at 3018 $cm^{-1}$and 2981-2830 cm^{-1} due to CH aromatic and CH aliphatic (asym. and sym.) respectively.

The mass spectrum of compound [XVI], exhibited a characteristic fragmentations formation at m/z= (the a parent ion 682 and 624, 566,552, 471, 283,260, 229, 202, 199, 184,173,161, 138,132,118,91,69 and 43) and that gave indicated to the formation of this compound, (Figure 3-47).

3.1.15. Synthesis and characterization of 1-((1-((1-((-1H benz[d] imidazol-2-yl)methyl)triazol-4-yl)methyl)-1H-benzo[d]imidazol-2-yl) methyl)-4-{(beta-D-fructopyranose-O-yl)methyl}1H-1,2,3-triazole [XVII].

Hydrolysis of isopropylidene group for compound [XVI] occur by using diluted CH_3COOH. The band (3398) cm^{-1} which attributed to the O-H stretching is a very good evidence of the deprotection and formation of compound [XVII] .



[XVI] [XVII]

The synthesized compound is characterized by FT-IR, ^{1}HNMR and ^{13}C-NMR spectroscopy. The F-TIR spectrum of compound [XVII], (Figure 3-48) shows the appearance of strong absorption stretching broad band at 3398cm^{-1} which attributed to the O-H for d-fructopyranose moiety . So that appearance the strong absorption stretching band at 3278 cm^{-1} due to secondary amine NH for benzo[d]imidazol moiety . beside appearance the absorption stretching band at 1660 cm^{-1},1589cm^{-1} are due to C ═ N and C ═ C groups .In addition the appearance absorption bands at 3095 cm^{-1}and 2935,2899 cm^{-1} are due to CH aromatic and CH aliphatic (asym. and sym.), respectively.

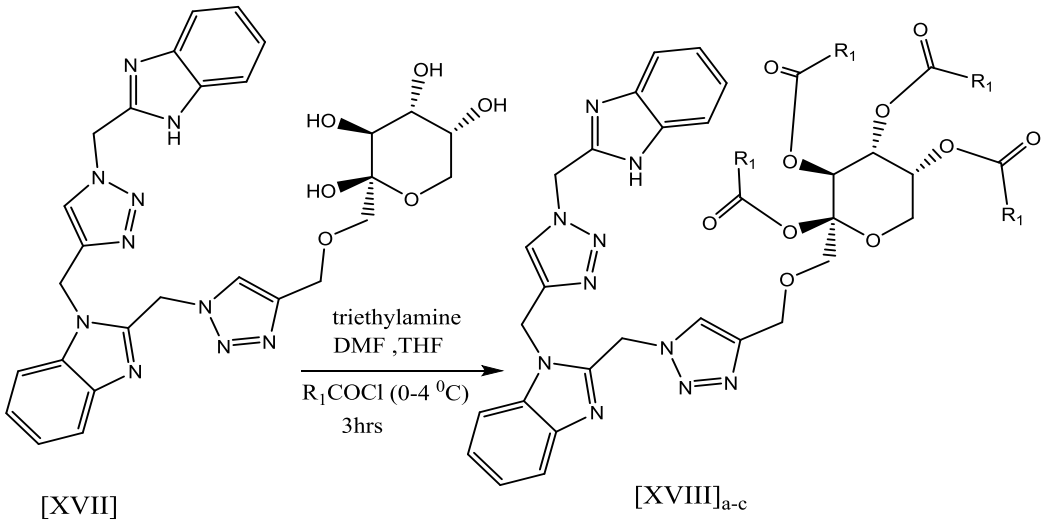
^{1}H-NMR spectrum (in DMSO-d_6 as a solvent) of compound [XVII], (Figure 3-49) shows appearance a quartet signal at δ (3.63 - 3.66) ppm due to one proton for (-C5`H-O) group. Also a doublet signal at δ ( 3.69 - 3.70) ppm due to two proton for -C6`H_2-O group. A triplet signal at δ (3.72- 3.74) ppm could be attributed to the one proton of -C4`H-O group. So that a singlet signal at δ 3.88 ppm that could be attributed to the two protons for Fru-$CH_2$-O group. Besides to a doublet signal at δ ( 3.93-3.95) ppm due to one proton for-C3`H-O group and showed appearance four a singlet signal at δ (4.49 ,4.50 ,4.70 ,4.75) ppm that could be attributed to the four protons of OH groups for D-fructose

moiety. A singlet signal at δ 4.65 ppm due to two protons for het-CH_2-O group. Also a singlet signal at δ 5.17 ppm due to six protons for -CH_2-N-bis-triazole groups. Besides to a multiple signal in the region δ (7.40-7.79) ppm that could be attributed to the ten aromatic protons for benzene and bis triazole rings .Finally, a singlet signal at δ 12.20 ppm due to one proton for N-H benzo[d]imidazol group.

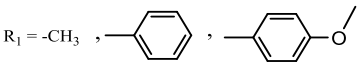
^{13}C-NMR spectrum (75 MHz, DMSO-d6) of compound [XVII], (Figure3-50) displays the signals corresponding to carbon atoms as follows : two signals at δ 49.4 , 51.1 ppm could be attributed of three carbon atoms from -CH_2-N groups also another signals appeared at δ 65.1 ,68.4 ,69.1 ppm could be assigned of three carbons for -CH_2-O groups, and signals at δ 70.5 ,71.1,71.9 ppm due to three carbons for -CH-OH groups, signal at δ 105.5 ppm may be attributed to one carbon of O-C-OH group. Finally , many signals in the region δ(111.9-150.7) ppm for aromatic eighteen carbons of benzo[d]imidazo and bistriazole rings.

3.1.16. Synthesis and characterization of ester derivatives contains bis-triazole compounds[XVIII]$_{a-c}$.

The reaction of hydroxyl groups of compound [XVII] with different acid chloride in mixture of tetrahydrofuran THF and dimethylformamide DMF using triethylamine Et_3N as a catalyst at 0-4^{0}C give new esters compounds[XVIII]$_{a-c}$.



[XVII] [XVIII]$_{a-c}$



These compounds were identified by FTIR and ^{1}HNMR,^{13}C-NMR spectroscopy (of some of them) and these data give good evidence to formation the new ester compounds. The FT-IR spectrum of compounds [XVIII]$_{a-c}$. shows the disappearance of stretching vibration band of OH group, so that appearance the strong absorption stretching band at(1737-1715) cm^{-1} due to C=O beside to C-O around (1265-1253) cm^{-1} of ester group is a very good evidence of the formation for ester compounds.

While, the FT-IR spectrum of compound [XVIII]$_{a}$, shows the appearance of strong absorption stretching band at 3217 cm^{-1} due to secondary amine NH for benzo[d]imidazol moiety and appearance new stretching bands at 1737 cm^{-1}, (Figure 3-51). which could be attributed to C=O group beside appearance the strong absorption stretching band at (1257) cm^{-1}due to C-O of ester group. So that disappearance the strong absorption stretching band of OH groups, In addition the appearance

absorption bands at 3049 $cm^{-1}$and 2947,2872cm^{-1} due to CH aromatic and CH aliphatic (asym. and sym.), respectively.

^{1}H-NMR spectrum (300 MHz, DMSO-d_6) of compound [XVIII]$_a$, (Figure3-52) shows disappearance four a singlet signal to the four protons of OH groups for D-fructose moiety, with appearance two a singlet signal at δ2.07,2.12 ppm due to twelve protons for CH_3ester groups . Also a doublet signal at δ (3.89 - 3.90) ppm due to two protons for-C6`H_2-O group. A singlet signal at δ 3.92 ppm that could be attributed to the two protons for Fru-CH_2-O group. So that a singlet signal at δ 4.76 ppm due to two protons for het-CH_2-O group and showed appearance two a singlet signal at δ 5.00,5.01ppm due to six protons for -CH_2-N-bis-triazole groups. Besides to a quartet signal at δ (5.32- 5.41) ppm due to one proton for -C5`H-O group. A triplet signal at δ (5.52- 5.55) ppm could be attributed to the one proton of -C4`H-O group. So that a doublet signal at δ (5.78-5.79) ppm due to one proton for -C3`H-O group. Besides to a multiple signal in the region δ (7.08-7.59) ppm that could be attributed to the ten aromatic protons for benzene and bis- triazole rings .Finally, a singlet signal at δ 12.13 ppm due to one proton for N-H benzo[d]imidazol group.

^{13}C-NMR spectrum (75 MHz, DMSO-d6) of compound [XVIII]$_f$, (Figure3-53) displays the signals corresponding to carbon atoms as follows :two signals at δ 21.1,21.9 ppm could be attributed from four carbon atoms of four CH_3 acetyl groups, two a signals at δ 49.9 , 51.6 ppm could be attributed of three carbon atoms from -CH_2-N groups also another signals appeared at δ 60.1,65.1,67.4 ppm could be assigned of three carbons for -CH_2-O groups, and signals at δ68.4,69.4 ppm due to three carbon for -CH-O groups, signal at δ 106.6 ppm may be attributed to one carbon of O-C-O, so that many signals in the region δ (111.7-

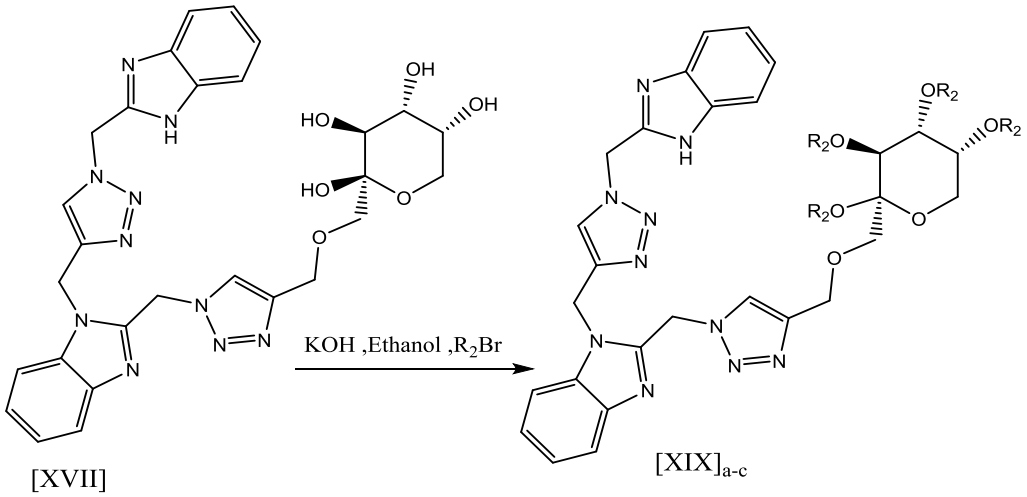
150.5) ppm for aromatic eighteen carbons of benzo[d]imidazo and bistriazole rings. Finally,two signals at δ 168.4, 170.0 ppm due to four carbon of C=O for ester moiety.

The FT-IR spectrum of compound $[XVIII]_c$.(Figure 3-54) shows the following bands: 3273cm^{-1}(υ,-NH),3093 cm^{-1}(υ, C-H aromatic), 2999,2904 cm^{-1}(υ, C-H aliphatic), 1715cm^{-1} (υ,- C=O)1672 cm^{-1}(υ, C ═ N),1616 cm^{-1}(υ, C ═ C) ,(1265)cm^{-1} (υ,- C-O) **.** The FT-IR absorption bands data of compounds $[XVIII]_{a-c}$ were listed in Table 3-6.

^{1}H-NMR spectrum (300 MHz, DMSO-d_6) of compound $[XVIII]_c$. (Figure 3-55) shows the following characteristic chemical shifts (ppm): 3.39 (s, 12H, --OCH_3,ester)3.66 (d, 2H, -C6`$H_2$-O), 4.13 (s, 2H, Fru-$CH_2$-O), 4.70 (s, 2H, het-$CH_2$-O), 5.13(s, 6H, -$CH_2$-N-triazole), 5.42 (q,1H, -C5`H-O), 5.70 (t,1H, -C4`H-O), 5.90 (d,1H, -C3`H-O), 7.00-8.09 (d-d and m, 26H, Ar-H), 12.12 (s, 1H, N-H benzo[d]imidazol).

3.1.17. Synthesis and characterization of ether derivatives contains bis-triazole compounds $[XIX]_{a-c}$.

On the other hand compound [XII] was converted to new ether compounds $[XIX]_{a-c}$ using different alkyl bromide in ethanol and potassium hydroxide KOH as a catalyst .



[XVII] $[XIX]_{a-c}$

R_2= $-CH_2CH_3$, $-CH_2CH_2CH_3$, $-CH_2CH_2CH_2CH_3$

The structure of the compounds $[XIX]_{a-c}$ were studied by F-TIR and ^{1}H-NMR spectroscopy (of some of them). The FT-IR spectra of compounds $[XIX]_{a-c}$ showed disappearance the stretching vibration band of OH group .

The FT-IR spectrum of compound $[XIX]_b$, (Figure 3-56) shows the appearance of new stretching bands at 1130 cm^{-1}due to C-O of ether group. beside disappearance the strong absorption stretching band of OH group, Also appearance the strong absorption stretching band at 3254 cm^{-1} is due to NH for benzo[d]imidazol moiety. Also appearance the absorption stretching band at 1661 $cm^{-1}$and 1606cm^{-1} are due to C ═ N and C ═ C groups . In addition the appearance absorption bands at 3084 $cm^{-1}$and 2987,2907cm^{-1} due to (CH) aromatic and (CH) aliphatic (asym. and sym.) respectively. All the spectral data for other compounds are listed in Table (3-7).

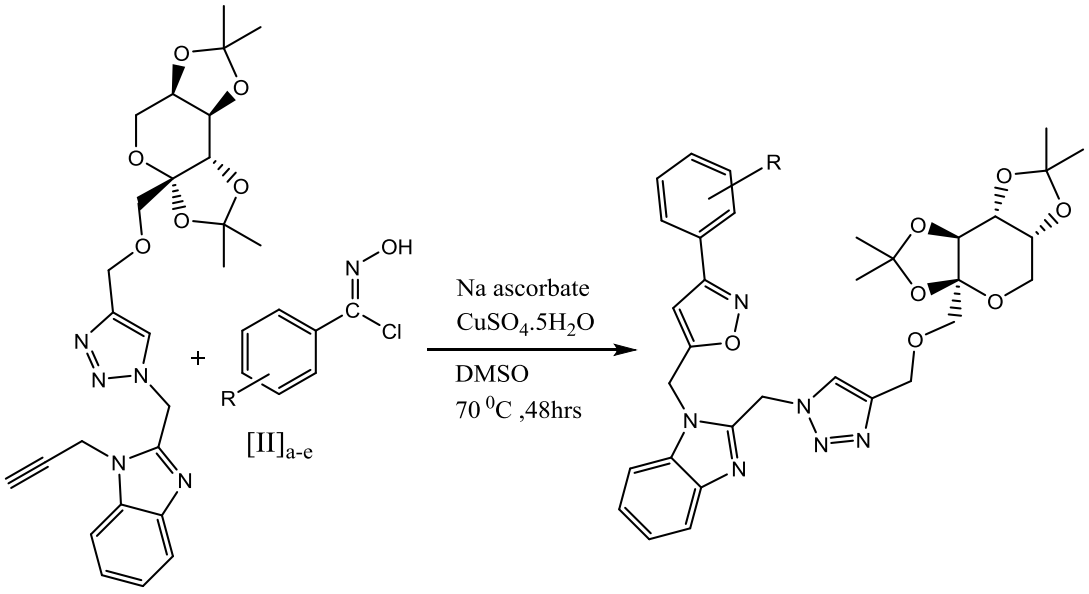
The FT-IR spectrum of compound $[XIX]_a$, (Figure 3-57) shows the following bands : 3244cm^{-1}(υ,-NH),3070 cm^{-1}(υ, C-H aromatic),

2985,2910 cm^{-1}(υ, C-H aliphatic) ,1641cm^{-1}(υ, C ═ N),1610 cm^{-1}(υ, C ═ C) 1126 cm^{-1}(υ, C-O).

^{1}H-NMR spectrum (in DMSO-d_6 as a solvent) of compound $[XIX]_a$, (Figure3-58) shows a pair of triplet signal appeared at δ (1.01-1.24) ppm due to twelve protons of -CH_3 groups for ether moiety. So that showed two a quartet signal at δ (3.19,3.50) ppm that could be attributed to the eight protons for O-$\underline{CH_2}CH_3$ groups. Also a doublet signal at δ (3.59 - 3.61) ppm due to one proton for -C3`H-O group. A triplet signal at δ (3.71 - 3.76) ppm could be attributed to the one proton of -C4`H-O group. So that a sharp singlet signal at δ 3.82 ppm that could be attributed to the two protons for Fru-CH_2-O group. A doublet signal at δ (3.96 - 3.99) ppm due to two protons for -C6`$H_2$-O group. Besides to a quartet signal at δ (4.11- 4.14) ppm due to one proton for -C5`H-O group. A singlet signal at δ 4.77ppm due to two protons for het-CH_2-O group. Also two a singlet signal at δ 5.19,5.21 ppm due to six protons for -CH_2-N-triazole group. Besides to a multiple signal in the region δ (7.00-7.74) ppm that could be attributed to the ten aromatic protons for benzene and bis-triazole rings .Finally, a singlet signal at δ 12.10 ppm due to one proton for N-H benzo[d]imidazol group.

3.1.18. Synthesis and characterization of 2,3,4,5-di-*O*-isopropylidene-beta-D-fructopyranose contains both triazole and isoxazole rings compounds[XX]$_{a-e}$

By using $CuSO_4.5H_2O$ and sodium ascorbate as a catalyzed via1,3-dipolar cycloaddition reaction of 1-((1-(prop-2-yn-1-yl)-1H-benzo[d]imidazol-2-yl)methyl)-4-{(2,3,4,5-di-O-isopropylidene-beta-D-fructopyranose-O-yl)methyl}1H-1,2,3-triazole compound [XV] with N-hydroxy-4-or-3- substituted benzimidoyl chloride [II]$_{a-e}$ under reflux to yielded the compounds [XX]$_{a-e}$.



[II]$_{a-e}$

[XV]

[XX]$_{a-e}$

R= H ,4- (OH, Br ,$N(CH_3)_2$
3-(NO_2)

The compounds[XX]$_{a-e}$, were identified by FT-IR and ^{1}HNMR spectroscopy (of some of them), The FT-IR spectrum of compound [XX]$_a$, (Figure 3-59) shows the disappearance of stretching vibration bands of OH and C-Cl groups of N-hydroxy-4-or-3- substituted benzimidoyl chloride compounds [II]$_{a-e}$ and ≡C-H , C≡C groups of

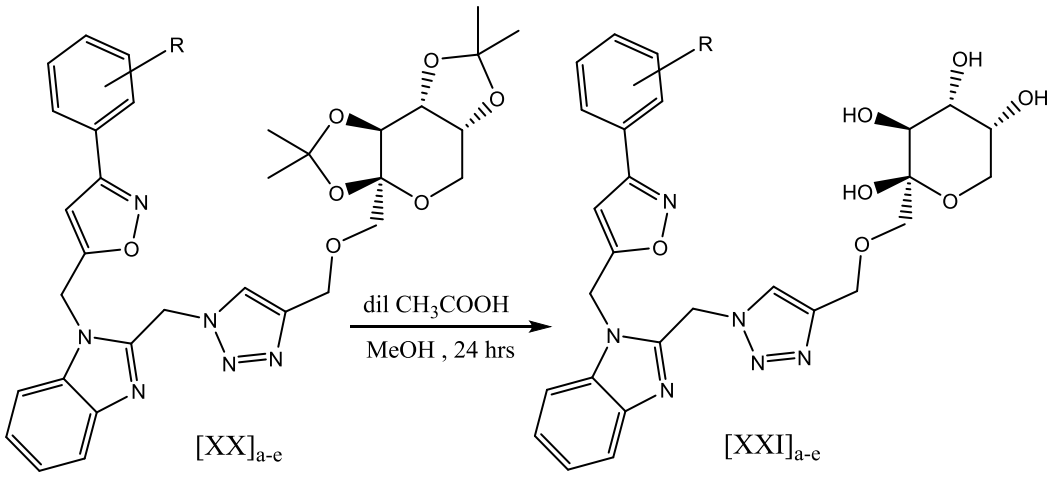
terminal alkyne compound [XV]of the starting materials together, that is good indicator for the ring closure of isoxazole. Also appearance the absorption stretching band at 1631 cm^{-1}and1600cm^{-1} are due to C ═ N and C ═ C groups . In addition the appearance absorption bands at 3061 cm^{-1} and 2983,2893cm^{-1} due to CH aromatic and CH aliphatic (asym. and sym.), respectively. The characteristic FT-IR absorption bands of compounds $[XX]_{a-e}$ were listed in Table 3-8.

The FT-IR spectrum of compound $[XX]_d$, (Figure 3-60) shows the following bands: 3010 cm^{-1}(υ,C-H aromatic) , 2958 ,2900cm^{-1}(υ, C-H aliphatic),1662 cm^{-1}(υ, C ═ N),1604 cm^{-1}(υ, C ═ C).

^{1}H-NMR spectrum (in DMSO-d_6 as a solvent) of compound $[XX]_d$, (Figure 3-61) shows two a singlet signal at δ (1.23, 1.35) ppm due to twelve protons of CH_3 for isopropylidene moiety. A singlet signal at δ 2.99 ppm due to six protons for $N(CH_3)_2$ group. Also a doublet signal at δ (4.18 – 4.20) ppm due to two protons for -C6`H_2-O group. A singlet signal at δ 4.50 ppm that could be attributed to the two protons for Fru-CH_2-O group. So that a singlet signal at δ 4.72 ppm that could be attributed to the two protons for het-CH_2-O group. Also a singlet signal at δ 4.95 ppm due to four protons for -CH_2-N group. Besides to a quartet signal at δ (5.42 - 5.52) ppm due to one proton for -C5`H-O group .A triplet signal at δ (5.42- 5.74) ppm could be attributed to the one proton of -C4`H-O group. A doublet signal at δ (5.92-5.93) ppm due to one proton for -C3`H-O group. Finally, a multiple signal in the region δ (6.82 - 7.95) ppm that could be attributed to the ten aromatic protons.

3.1.19. Synthesis and characterization of1-((1-((3-(4- or 3-substituted phenyl)isoxazol-5-yl)methyl)-1H-benzo[d]imidazol-2-yl)methyl)-4-{ (beta-D-fructopyranose-O-yl)methyl}1H-1,2,3-triazole $[XXI]_{a-e}$

Isopropylidene group of compound $[XX]_{a-e}$ were deprotected by using diluted CH_3COOH. The a broad band around (3295-3240)cm^{-1} which attributed to the O-H stretching is a very good evidence of the deprotection and formation of compounds $[XXI]_{a-e}$.



R= H ,4- (OH, Br ,$N(CH_3)_2$, 3-(NO_2)

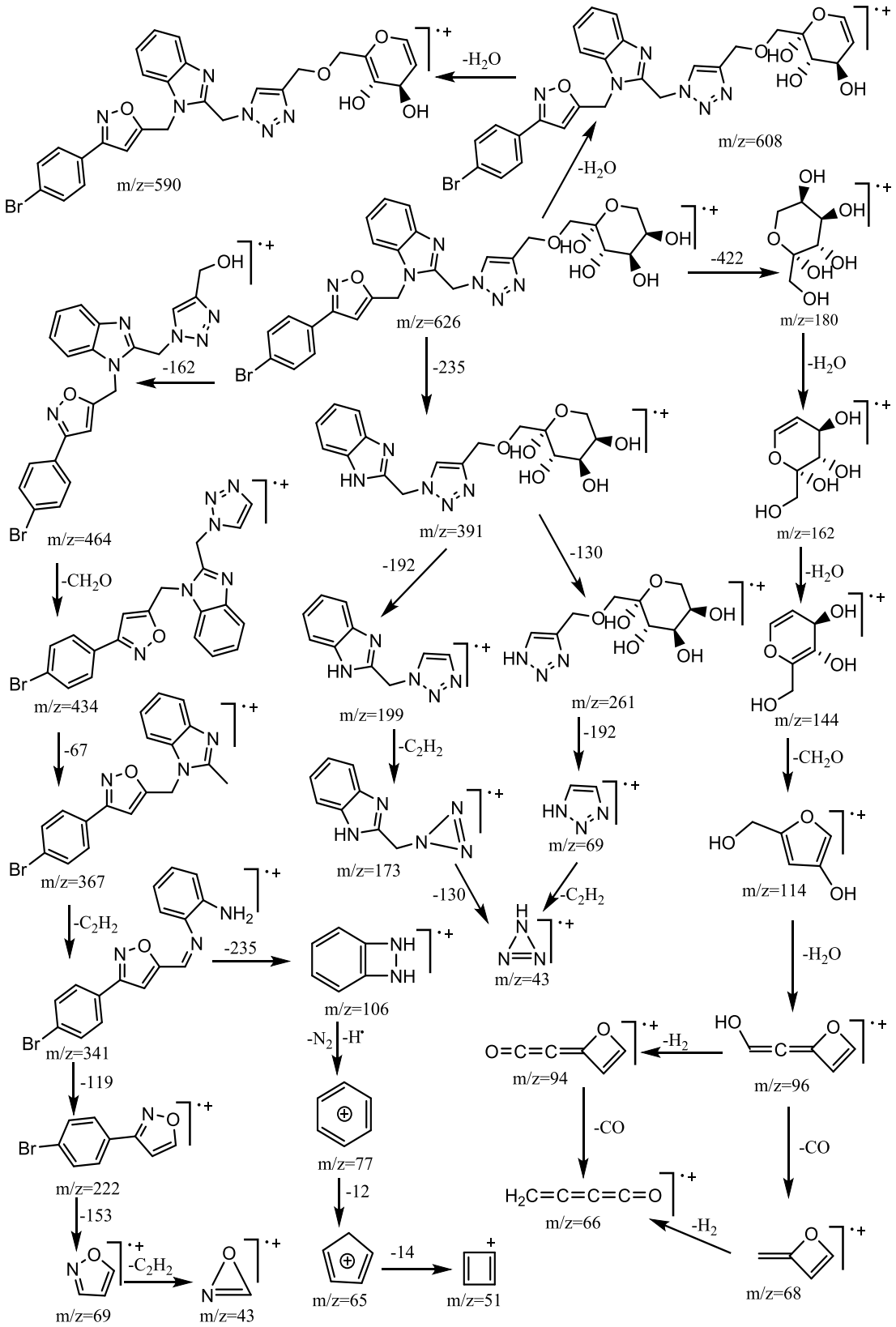
These compounds were identified by FT-IR and ^{1}H-NMR, ^{13}C-NMR, Mass spectroscopy (of some of them) and these data give good indicators to formation of compounds $[XXI]_{a-e}$. The FT-IR spectrum of compound $[XXI]_{c,}$ (Figure 3-62) shows the appearance of strong absorption band at 3240 cm^{-1}due to OH of D-fructose moiety, In addition the appearance absorption bands at 3095 $cm^{-1}$and 2935,2877 cm^{-1} are due to CH aromatic and CH aliphatic (asym. and sym.), respectively. So that the strong absorption band at 1672, 1651 and 1602 cm^{-1} attributed to C ═ N, and C ═ C groups . All the spectral data for other compounds are listed in Table 3-9.

^{1}H-NMR spectrum (in DMSO-d_6 as a solvent) of compound[XXI]$_c$, (Figure3-63) shows appearance four a singlet signal at δ (4.32 , 4.51, 4.75,4.77) ppm that could be attributed to the four protons of OH groups for D-fructose moiety. A doublet signal at δ (3.68-3.70) ppm due to two proton for -C6`$H_2$-O group. Also a doublet signal at δ ( 3.80 - 3.81) ppm due to one proton for -C3`H-O group. Besides to a quartet signal at δ (3.82 - 3.85) ppm due to one proton for -C5`H-O group. A triplet signal at δ (3.90- 3.92) ppm could be attributed to the one proton of -C4`H-O group. So that a singlet signal at δ 4.06 ppm that could be attributed to the two protons for Fruc-CH_2-O group. A singlet signal at δ 4.73 ppm due to two protons for het-CH_2-O group. Also a singlet signal at δ 5.02 ppm due to four protons for -CH_2-N group. Finally, a multiple signals in the region δ (6.40 - 7.41) ppm that could be attributed to the ten aromatic protons. The disappearance a singlet signal for twelve protons of CH_3 for isopropylidene groups with appearance four a singlet signal due to OH groups for D-fructose moiety give a good evidence to the deprotection and formation of compounds [XXI]$_{a-e}$

^{13}C-NMR spectrum (75 MHz, DMSO-d6) δ, of compound [XXI]$_c$ in (Figure 3-64) displays the signals corresponding to carbon atoms as follows: : two signals at δ 45.0 , 49.2 ppm could be attributed of two carbon atoms from -CH_2-N groups also another signals appeared at δ 63.1 ,68.2 ,69.1 ppm could be assigned of three carbons for -CH_2-O groups,and signals at δ 69.7 ,70.6,71.9 ppm due to three carbons for -CH-OH groups, signal at δ 101.2 ppm may be attributed to one carbon

of O-C-OH group. Finally , many signals in the region δ(107.3-166.9) ppm for aromatic eighteen carbons of benzene, benzo[d]imidazo and both triazole, isoxazole rings.

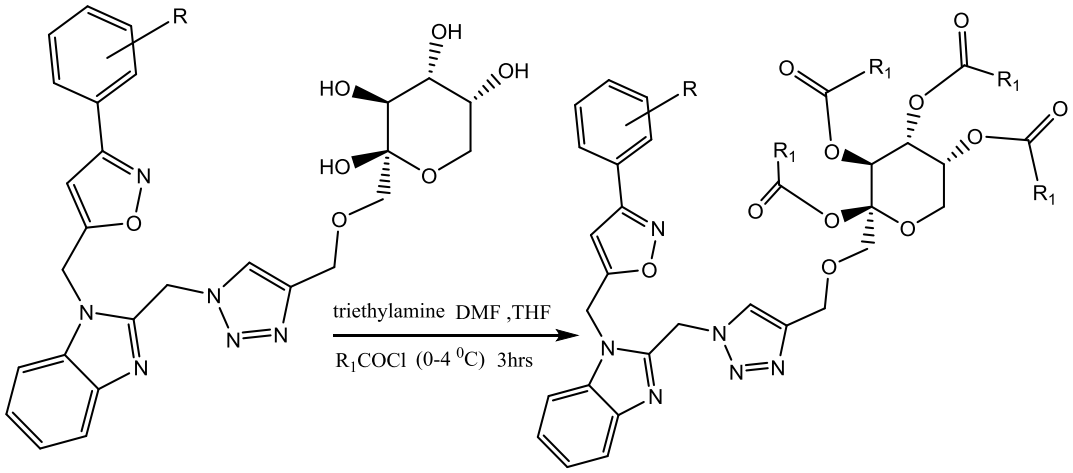
The mass spectrum of compound [XXI]c, (Figure 3-65) given molecular ion at m/z = 626,628(M^+,M^{+2}) which corresponds to the molecular weight of structures suggested for this compound. The results obtained from the mass spectrum suggested that fission was more easily accomplished at the carbon-nitrogen and carbon-oxygen bonds rather than at the carbon-carbon bond such as fragments at m/z = 590, 464,434 and 367 and the peaks at (m/z =180,162, 144, 114,112, 96, 94,68 and 66)[193] were give good evidence to presence the beta-D-fructopyranose moiety. This spectrum showed the base peak at m/z = 69 due to the triazole and isoxazole rings . The other important fragments given in Scheme 3-7.



Scheme (3-7). The mass fragmentation pattern of compound[XXI]c

3.1.20. Synthesis and characterization of ester derivatives contains both triazole and isoxazole rings compounds[XXII]$_{a-e}$,[XXIII]$_{a-e}$ and[XXIV]$_{a-e}$.

To a stirred for 3hrs reaction hydroxyl groups of compounds [XXI]$_{a-e}$ with different acid chloride in mixture of tetrahydrofuran THF and dimethylformamide DMF using triethylamineEt_3N as a catalyst at 0-4^{0}C give new esters compounds[XXII]$_{a-e}$, [XXIII]$_{a-e}$ and[XXIV]$_{a-e}$.



[XXI]$_{a-e}$

R= H ,4- (OH, Br ,$N(CH_3)_2$
3-(NO_2)

[XXII]$_{a-e}$ When : R_1 = -CH_3

[XXIII]$_{a-e}$ When : R_1 =

[XXIV]$_{a-e}$ When : R_1 =

These compounds were identified by FT-IR and ^{1}H-NMR^{13}C-NMR, Mass spectroscopy (of some of them) and these data give good evidence to formation the new ester compounds. The FT-IR spectra of compounds [XXII]$_{a-e}$, [XXIII]$_{a-e}$ and [XXIV]$_{a-e}$, showed disappearance the stretching vibration band of OH group so that appearance the strong absorption stretching band at (1740- 1711) cm^{-1} due to C=O beside to

C-O around (1217-1263) cm^{-1} of ester group is a good evidence of the formation of ester compounds.

The FT-IR spectrum of compound $[XXII]_b$, shows the appearance of new stretching bands at 1735 cm^{-1}, which could be attributed to C=O group beside appearance the strong absorption stretching band at (1219) cm^{-1}due to C-O of ester group. So that disappearance the strong absorption stretching band of OH groups, In addition the appearance absorption bands at 3061 $cm^{-1}$and 2978,2955cm^{-1} due to CH aromatic and CH aliphatic (asym. and sym.) respectively, (Figure3-66).

^{1}H-NMR spectrum (300 MHz, DMSO-d_6) of compound $[XXII]_b$, (Figure3-67) shows disappearance four a singlet signal to the four protons of (OH)groups for D-fructose moiety and disappearance(OH)group of phenol , with appearance three a singlet signal at δ 2.09, 2.25 ,2.32 ppm due to fifteen protons for CH_3 ester groups . So that a singlet signal at δ 3.80 ppm that could be attributed to the two protons for Fru-CH_2-O group. A doublet signal at δ (3.92 – 3.93) ppm due to two protons for -C6`$H_2$-O group. Also a singlet signal at δ 4.60 ppm due to two protons for het-$CH_2$-O group. And a singlet signal at δ 5.03 ppm due to four protons for -$CH_2$-N group. A triplet signal at δ (5.37- 5.39) ppm could be attributed to the one proton of -C4`H-O group. So that a doublet signal at δ (5.59- 5.61) ppm due to one proton for -C3`H- group. Besides to a quartet signal at δ (5.87- 5.91) ppm due to one proton for -C5`H-O group, Finally, a multiple signals in the region δ (6.62 - 7.32) ppm that could be attributed to the ten aromatic protons.

^{13}C-NMR spectrum (75 MHz, DMSO-d6) of compound $[XXII]_b$, (Figure3-68) displays the signals corresponding to carbon atoms as follows :three signals at δ 22.8, 23.1, 24.3 ppm could be attributed to five

carbon atoms of five CH_3 acetyl groups. Two signals at δ 42.5 , 47.6 ppm could be attributed of two carbon atoms from -CH_2-N groups, also another signals appeared at δ 58.7, 65.1, 65.8 ppm could be assigned of three carbons for -CH_2-Ogroups, and signals at δ 67.5,68.1,68.8 ppm due to three carbons for -CH-O groups, signal at δ 100.7 ppm may be attributed to one carbon of O-C-O ,so that many signals in the region δ(110.2-165.4) ppm could be attributed of eighteen aromatic carbons. Finally, three signals at δ (168.0-171.6) ppm due to five carbons of C=O group for ester moiety.

FT-IR spectrum of 1-((1-((3-(3-nitrophenyl)isoxazol-5-yl) methyl) -1H-benzo[d]imidazol-2-yl)methyl)-4-{(2,3,4,5-tetra-O-acetyl-beta-D-fructopyranose-O-yl)methyl}1H-1,2,3-triazole compound $[XXII]_e$ (Figure 3-69)shows the following bands:,3093 cm^{-1}(υ, C-H aromatic) , 2995,2935 cm^{-1}(υ, C-H aliphatic), 1738cm^{-1} (υ,- C=O)1660 cm^{-1}(υ, C ═ N),1620 cm^{-1}(υ, C ═ C), (1257)cm^{-1} (υ,- C-O) **.** The FT-IR absorption bands data of these compounds $[XXII]_{a-e}$, $[XXIII]_{a-e}$ and$[XXIV]_{a-e}$. were listed in Table 3-10.

^{1}H-NMR spectrum(300 MHz, DMSO-d_6) of compound $[XXII]_e$ (Figure 3-70), shows the following characteristic chemical shifts: δ 2.09, 2.28ppm (s, 12H, -CH_3), δ (3.65 -3.77) ppm (d, 2H, (-C6`$H_2$-O), δ 4.02 ppm (s, 2H, Fru -$CH_2$-O), δ 4.44 ppm (s, 2H, het -$CH_2$-O), δ 4.95 ppm (s, 4H, -$CH_2$-N), δ (5.39 -5.49) ppm (d,1H, -C3`H-O), δ (5.79 -5.83) ppm (t,1H, -C4`H-O), δ (5.90- 5.94) ppm (q,1H, -C5`H-O), δ (6.59-7.90) ppm (m, 10H, Ar-H).

The FT-IR spectrum of compound $[XXIII]_a$. (Figure 3-71), shows the appearance of new stretching bands at 1718 cm^{-1},which could be attributed to C=O group, beside appearance the strong absorption

stretching band at (1252) cm^{-1}due to C-O of ester group. So that disappearance the strong absorption stretching band of OH group, In addition the appearance absorption bands at 3059 $cm^{-1}$and 2941,2844cm^{-1} due to CH aromatic and CH aliphatic (asym. and sym.), respectively.

^{1}H-NMR spectrum (300 MHz, DMSO-d_6) of compound $[XXIII]_a$, (Figure3-72) shows disappearance four a singlet signal to the four protons of OH groups for D-fructose moiety . So that appearance a singlet signal at δ 3.88 ppm that could be attributed to the two protons for Fru-CH_2-O group. A doublet signal at δ (4.33 – 4.35) ppm due to two protons for -C6`$H_2$-O group. Also a singlet signal at δ 4.77 ppm due to two protons for het-$CH_2$-O group. And a singlet signal at δ 4.91 ppm due to four protons for -$CH_2$-N group. A triplet signal at δ (5.20- 5.24) ppm could be attributed to the one proton of -C4`H-O) group. Besides to a quartet signal at δ (5.51- 5.55) ppm due to one proton for -C5`H-O group. So that a doublet signal at δ (5.91- 5.92) ppm due to one proton for -C3`H-O group. Finally, a multiple signals in the region δ (6.75 – 8.17) ppm that could be attributed to the thirty one aromatic protons.

FT-IR spectrum of compound $[XXIV]_c$, shows the appearance of new stretching bands at 1728 cm^{-1}, (Figure 3-73). which could be attributed to C=O group, beside appearance the strong absorption stretching band at (1261) cm^{-1}due to C-O of ester group. So that disappearance the strong absorption stretching band of OH group, In addition the appearance absorption bands at 3089 $cm^{-1}$and 2945,2845cm^{-1} due to CH aromatic and CH aliphatic (asym. and sym.), respectively.

^{1}H-NMR spectrum (in DMSO-d_6 as a solvent) of compound $[XXIV]_c$, (Figure3-74) shows disappearance four a singlet signal to the four protons of OH groups for D-fructose moiety, with appearance two a

singlet signal at δ 3.43 ,3.45 ppm due to twelve protons for -OCH_3 groups . So that a singlet signal at δ 4.11 ppm that could be attributed to the two protons for Fru-CH_2-O group. A doublet signal at δ (4.35 – 4.37) ppm due to two protons for -C6`$H_2$-O group. Also a singlet signal at δ 4.70 ppm due to two protons for het-$CH_2$-O group. And a singlet signal at δ 4.92 ppm due to four protons for -$CH_2$-N group. A quartet signal at δ (5.30- 5.34) ppm due to one proton for -C5`H-O group. Besides to a triplet signal at δ (5.53- 5.55) ppm could be attributed to the one proton of -C4`H-O group. So that a doublet signal at δ (5.75- 5.77) ppm due to one proton for -C3`H-O group. Finally, a multiple signals in the region δ (7.44 – 8.03) ppm that could be attributed to the twenty two aromatic protons.

3.2.Biological Activity

Heterocyclic rings and carbohydrate considered an important class of compounds having a wide spectrum of biological activity, and their antimicrobial activity[194]. The synthesized isoxazoles and triazoles derivatives in this work are expected to possess biological activity thus preliminary evaluation of anti-bacterial and antifungal activity for many synthesized compounds were performed. The antibacterial and antifungal activity of the synthesized compounds performed using agar diffusion method [195,196], on three types of pathological bacteria: the *Escherichia coli (G-), Staphylococcus aureus (G+)* and *Bacillus substilis(G+)* and one type of pathological fungal (*Candida albicans*) .

The results were discuss as follows:

1)The first line (D-fructose derivatives based isoxazole ring.) showed:-

a) All the 3-(4-or 3-substituted phenyl)-5-{(2,3,4,5-di-*O*-isopropylidene-beta-D-fructopyranose-O-yl)methyl}1H-isoxazole compounds $[V]_{a-e}$

showed good biological activity against *Staphlocococs aureus, bacillus subtitis* and *E.coli* . On the other hand, compounds $[V]_{a-e}$ did not show any antifungal activity (*candida albicans*) except compound$[V]_{c}$.

b) 3-(4- or 3-substituted phenyl)-5-{(beta-D-fructopyranose-O-yl)methyl}1H-isoxazole compounds $[VI]_{a-e}$ exhibited good activity against three type of bacteria . The compounds $[VI]_{c,e}$ showed antifungal activity, while the other compounds $[VI]_{a,b,d}$ did not showed antifungal activity.

c) On the other hand, the ester derivatives compounds $[VII]_{a-e}$, $[VIII]_{a-e}$ and $[IX]_{a-e}$ showed different activity against three type of bacteria and did not show antifungal activity except compounds$[VII]_{e}$, $[VIII]_{a,b}$ and $[IX]_{a-c,e}$ .The antibacterial and antifungal data of the compounds$[VI]_{a-e}$, $[VII]_{a-e}$, $[VIII]_{a-e}$and $[IX]_{a-e}$ were listed in Table 3-11.

2) The second line (D-fructose derivatives based 1,2,3-triazole ring) showed, the following data which were listed in Table 3-12.

a) The 2,3,4,5-di-*O*-isopropylidene-beta-D-fructopyranose based triazole compound [XI], showed good biological activity against *E.coli* gram (-) and *bacillus subtitis*, *Staphlocococs aureus* gram (+) and antifungal activity .

b) Beta-D-fructopyranose based triazole compound[XII] exhibited good biological activity towards bacteria and fungal types .

c) The ester derivative compounds $[XIII]_{a-c}$ showed different inhibition zones against bacterial and antifungal activity excepted compound $[XIII]_b$ did not show antifungal activity.

d) The ether derivative compounds $[XIV]_{a-c}$ showed antibacterial activity and some of them showed antifungal activity.

3) The third line (D-fructose derivatives based bis-1,2,3-triazole rings) showed the following data which were listed in Table 3-13.

a) The 1-((1-(prop-2-yn-1-yl)-1H-benzo[d]imidazol-2-yl)methyl)-4-{(2,3,4,5-di-O-isopropylidene-beta-D-fructopyranose-O- yl)methyl}1H-1,2,3-triazole [XV] showed good biological activity against *bacillus subtitis*, *Staphlocococs aureus* gram (+) and antifungal activity while did not showed activity towards *E.coli* gram (-).

b) On the other hand, beta-D-fructopyranose based bis triazole compounds[XVI], [XVII], showed good biological activity against *E.coli* gram (-) and *bacillus subtitis*, *Staphlocococs aureus* gram (+) and antifungal activity .

c) The ester derivatives compounds $[XVIII]_{a-c}$ showed different (between good to high) activity against fungal activity and a good activity against bacterial.

d) The ether derivatives compounds $[XIX]_{a-c}$ exhibited good data against bacterial and antifungal activity, but the compound $[XIX]_a$ showed only antifungal activaty.

4) The fourth line (D-fructose derivatives based both1,2,3-triazoleand isoxazole rings) showed:-

a) All the 1-((1-((3-(4-or 3-substituted phenyl)isoxazol-5-yl)methyl)-1H-benzo[d]imidazol-2-yl)methyl)-4-{(2,3,4,5-di-O-isopropylidene-beta-D-fructopyranose- O - yl) methyl} 1H-1,2,3-triazole compounds $[XX]_{a-e}$ showed good biological activity against *Staphlocococs aureus, bacillus subtitis* and *E.coli* and some of them showed antifungal activity

b) On the other hand, 1-((1-((3-(4- or 3-substituted phenyl)isoxazol-5-yl)methyl)-1H-benzo[d]imidazol-2-yl)methyl)-4-{(beta-D-fructo pyranose -O-yl)methyl}1H-1,2,3-triazole compounds $[XXI]_{a-e}$ exhibited good activity against three type of bacteria . The compounds$[XXI]_{d,e}$ showed antifungal activity, while the other compounds $[XXI]_{a-c}$, did not showed antifungal activity.

c) The ester derivative compounds$[XXII]_{a-e}$, $[XXIII]_{a-e}$ and $[XXIV]_{a-e}$ showed different activity against three types of bacteria and some of them showed antifungal activity. The antibacterial and antifungal data of the compounds$[XX]_{a-c}$, $[XXI]_{a-c}$, $[XXII]_{a-e}$, $[XXIII]_{a-e}$ and $[XXIV]_{a-e}$ were listed in Table 3-14.

The results in general showed that most of the tested compounds possess biological activity against the three types of the bacteria and one type of pathological fungal . The biological activity of the synthesized compounds, which were exhibited high, moderate,low or no inhibition zones. The antimicrobial activity can be attributed on one hand to the isoxazoles , 1*H*-benzo[*d*]imidazole and triazoles moiety which active in different biological field. On the other hand, the chirality of sugar moiety is an important reason for the inhibition as well as the overall synthesized molecules are mimics to the glycolipids because they contains both hydrophilic and lipophilic parts. Figures(3-75),(3-76), (3-77), (3-78)

and(3-79) showed the effect of these compounds on three types of bacteria and one type of antifungal.

Conclusions

In this work new derivatives 2,3,4,5-di-O-isopropylidene-beta-D-fructopyranose, beta-D-fructopyranose, esters, ether and their heterocyclic compounds derivatives synthesized and characterized. The following conclusions could be drawn as below :-

1-The 3-(4-or 3-substituted phenyl)-5-{(2,3,4,5-di-*O*-isopropylidene-beta-D-fructopyranose-O-yl)methyl}1H-isoxazole compounds $[V]_{a-e}$ were synthesized by reaction of Alkynyl sugar compound [IV] with N-hydroxy-4-or-3- substituted benzimidoyl chloride $[II]_{a-e}$ by refluxed for a long time between (40-48) hrs. with moderate yields.

2- New triazole derivative 1-((1H-benzo[d]imidazol-2-yl)methyl)-4-{(2,3,4,5-di-O-isopropylidene-beta-D-fructopyranose-O-yl)methyl}1H-1,2,3-triazole compound [XI] was synthesized by the reaction of Alkynyl sugar compound [IV] with 2-(azidomethyl)-1*H*-benzo[*d*]imidazole compound [X] by refluxed at 65-70 ^{0}C temperature for a long time between 40-48 hrs. with low yields.

3- Beta-D-fructopyranose derivative compounds $[VI]_{a-e}$**,** [XII], [XVII] and$[XXI]_{a-e}$ were synthesized through the deprotected for Isopropylidene group of compounds $[V]_{a-e}$, [XI], [XVI] and$[XX]_{a-e}$ by using diluted CH_3COOH in moderate yield by simple method.

4- Ester compounds $[VII]_{a-e}$, $[VIII]_{a-e}$, $[IX]_{a-e}$, $[XIII]_{a-c}$. $[XVIII]_{a-c}$, $[XXII]_{a-e}$, $[XXIII]_{a-e}$ and $[XXIV]_{a-e}$ were synthesized in simple method and short time by reaction of hydroxyl groups of compounds $[VI]_{a-e}$**,** [XII], [XVII] and $[XXI]_{a-e}$ with different acid chloride in mixture

of tetrahydrofuran THF and dimethylformamide DMF using triethylamine Et_3N as a catalyst at 0-4^{0}C .

5- Ether compounds $[XIV]_{a-c}$ and $[X\ IX]_{a-c}$ were obtained in good yield by reaction of compounds[XII], [XVII] with different alkyl bromide in ethanol and potassium hydroxide KOH as a catalyst

6-The physical properties and spectral data (FT-IR and ^{1}H-NMR^{13}C-NMR , Mass spectroscopy) give good information and indication of the suggested structure for the new synthesized compounds.

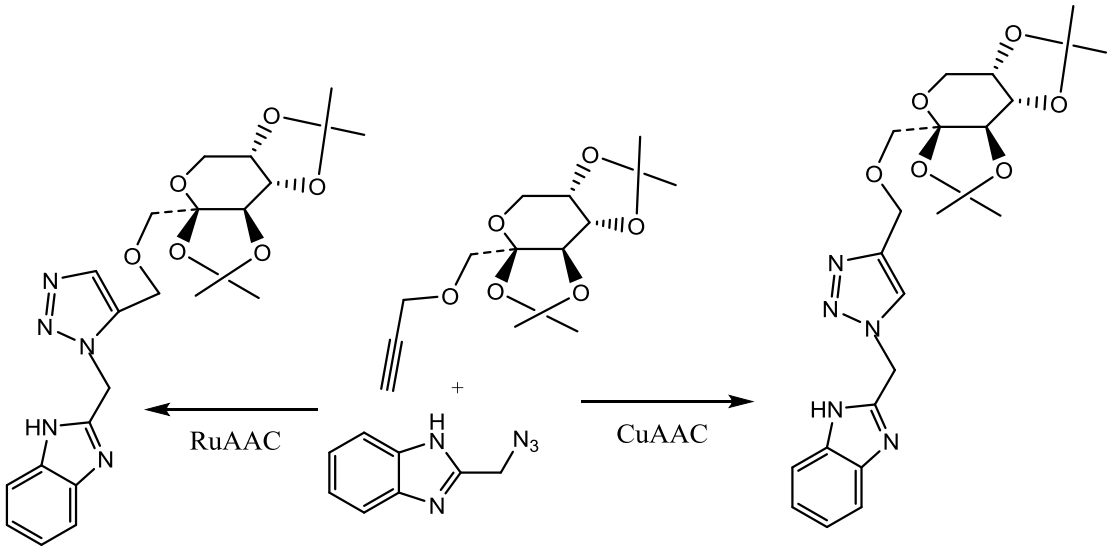
7- The antimicrobial of all compounds of these derivatives studied against of Gram-positive bacteria (*Staphylococcus aureus*, *Bacillus substilis*) and Gram-negative bacteria (*Escherichia coli*) and pathological fungal(*Candida albicans*). Many synthesized compounds gave good biological activity and other did not showed any biological activities. That may be related to the functional groups and the chemical structure for the examined compounds.

Suggestion of future work

1-Synthhesis new tris and tetrakis triazoles from the new triazoles derivative (were synthesized in this work).

2-Convert the OH group in 3-(4- or 3-substituted phenyl)-5-{(beta-D-fructopyranose-O-yl)methyl}1H-isoxazole to ether compounds .

3-Changing the catalytic conditions (Regioselective) leads to the formation of new isomers that vary in link locations

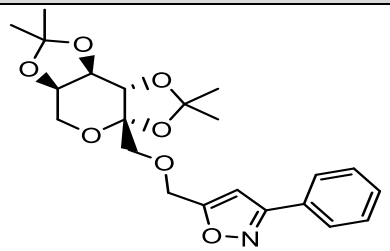
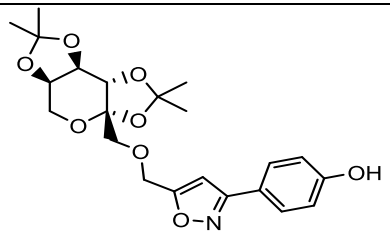
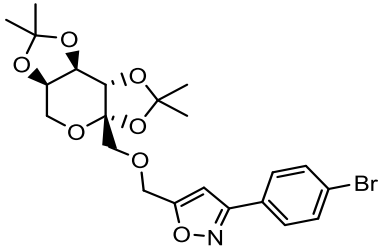


1,5-regioisomer 1,4-regioisomer

4-Study the anticancer activity of the synthesized compounds.

5-Study the liquid crystalline properties of the synthesized compounds.

Table 2-4:The nomenclature, structural formula, molecular formula and physical properties of compounds $[V]_{a-e}$

Comp No	Nomenclature	Structural formula	Molecular formula	M. P ºC	Yield %	color
$[V]_a$	3-phenyl-5-{(2,3,4,5-di-O-isopropylidene-beta-D-fructopyranose-O-yl)methyl}1H-isoxazole		$C_{22}H_{27}N_1O_7$	Oily	67	Deep yellow
$[V]_b$	3-(4-Hydroxyl phenyl)-5-{(2,3,4,5-di-O-isopropylidene-beta-D-fructopyranose-O-yl)methyl}1H-isoxazole		$C_{22}H_{27}N_1O_8$	Oily	70	Red
$[V]_c$	3-(4-bromo phenyl)-5-{(2,3,4,5-di-O-isopropylidene-beta-D-fructopyranose-O-yl)methyl}1H-isoxazole		$C_{22}H_{26}N_1O_7Br$	Oily	75	Brown

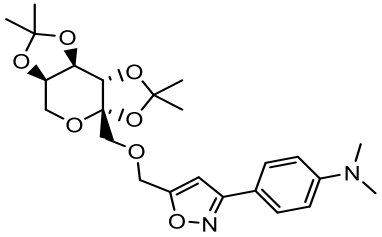
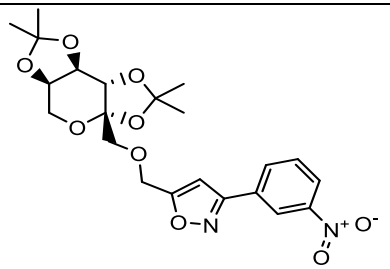
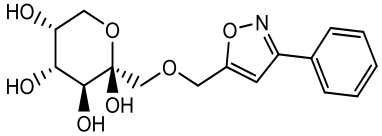
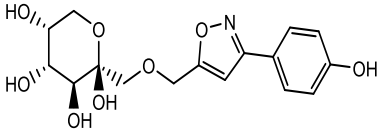
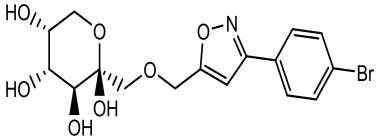
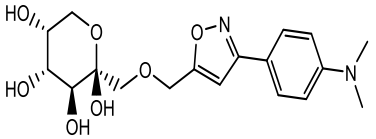
$[V]_d$	3-(4-N,N-dimethylamino phenyl)-5-{(2,3,4,5-di-O-isopropylidene-beta-D-fructopyranose-O-yl)methyl}1H-isoxazole		$C_{24}H_{32}N_2O_7$	Oily	63	White
$[V]_e$	3-(3-nitro phenyl)-5-{(2,3,4,5-di-O-isopropylidene-beta-D-fructopyranose-O-yl)methyl}1H-isoxazole		$C_{22}H_{26}N_2O_9$	Oily	60	Deep Brown

Table 2-5:The nomenclature, structural formula, molecular formula and physical properties of compounds $[VI]_{a-e}$

Comp No	Nomenclature	Structural formula	Molecular formula	M. P °C	Yield %	color
$[VI]_a$	3- phenyl-5-{(beta-D-fructopyranose-O-yl) methyl}1H-isoxazole		$C_{16}H_{19}N_1O_7$	80-82	77	Pale yellow
$[VI]_b$	3-(4-Hydroxyl phenyl)-5-{(beta-D-fructopyranose-O-yl) methyl}1H-isoxazole		$C_{16}H_{19}N_1O_8$	140-142	82	Red
$[VI]_c$	3-(4-bromo phenyl)-5-{(beta-D-fructopyranose-O-yl) methyl}1H-isoxazole		$C_{16}H_{18}N_1O_7Br$	136-138	80	Brown
$[VI]_d$	3-(4-N,N-dimethylamino phenyl)-5-{(beta-D-fructopyranose-O-yl) methyl}1H-isoxazole		$C_{18}H_{24}N_2O_7$	160-162	73	White

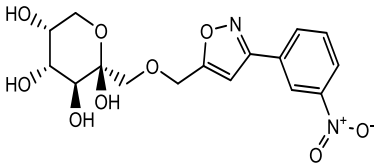
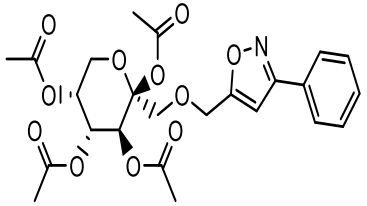
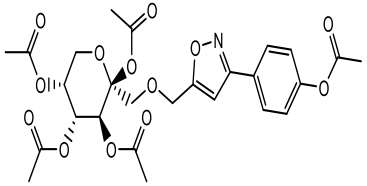
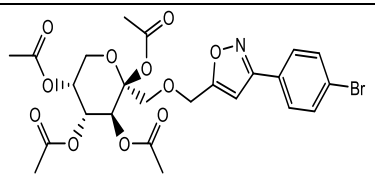
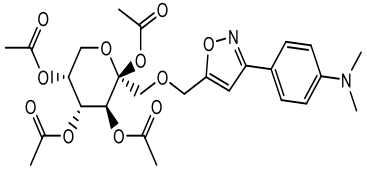
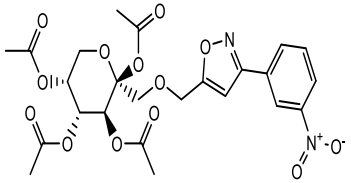
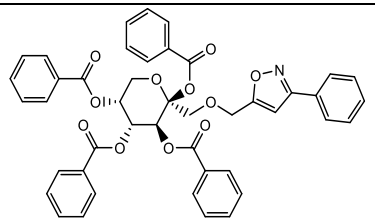
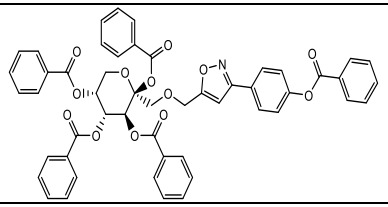
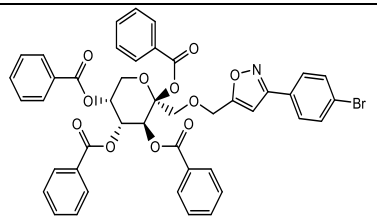
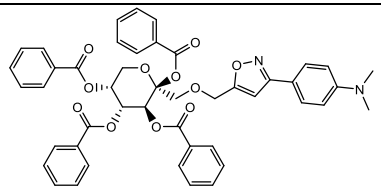
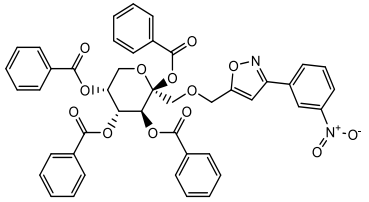
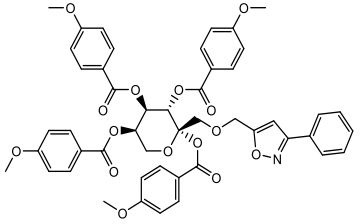
$[VI]_e$	3-(3-nitro phenyl)-5-{(beta-D-fructopyranose-O-yl) methyl}1H-isoxazole		$C_{16}H_{18}N_2O_9$	166-168	71	Brown

Table 2- 6: The nomenclature , structural formula, molecular formula and physical properties of esters compounds[VII]a-e, [VIII]a-e and [IX]a-e

Comp No	Nomenclature	Structural formula	Molecular formula	M. P ºC	Yield %	color
$[VII]_a$	3-phenyl-5-{(2,3,4,5-tetra-O-acetyl-beta-D-fructopyranose-O-yl)methyl}1H-isoxazole		$C_{24}H_{27}N_1O_{11}$	158-160	60	Yellow
$[VII]_b$	3-(4-acetyloxy phenyl)-5-{(2,3,4,5-tetra-O-acetyl-beta-D-fructopyranose-O-yl)methyl}1H-isoxazole		$C_{26}H_{29}N_1O_{13}$	190-192	65	Brown

$[VII]_c$	3-(4-bromo phenyl)-5-{(2,3,4,5-tetra-O-acetyl-beta-D-fructopyranose-O-yl)methyl}1H-isoxazole		$C_{24}H_{26}N_1O_{11}Br$	170-172	67	Pale brown
$[VII]_d$	3-(4-N,N-dimethylamino phenyl)-5-{(2,3,4,5-tetra-O-acetyl-beta-D-fructopyranose-O-yl)methyl}1H-isoxazole		$C_{26}H_{32}N_2O_{11}$	181-183	58	Yellow
$[VII]_e$	3-(3-nitro phenyl)-5-{(2,3,4,5-tetra-O-acetyl-beta-D-fructopyranose-O-yl)methyl}1H-isoxazole		$C_{24}H_{26}N_2O_{13}$	177-179	61	Deep yellow
$[VIII]_a$	3- phenyl-5-{(2,3,4,5-tetra-O-benzoyl-beta-D-fructopyranose-O-yl)methyl}1H-isoxazole		$C_{44}H_{35}N_1O_{11}$	161-163	62	Deep yellow
$[VIII]_b$	3-(4-benzoyloxy phenyl)-5-{(2,3,4,5-tetra-O-benzoyl-beta-D-fructopyranose-O-yl)methyl}1H-isoxazole		$C_{44}H_{27}N_1O_{11}$	197-199	66	Deep pink

$[VIII]_c$	3-(4-bromo phenyl)-5-{(2,3,4,5-tetra-O-benzoyl-beta-D-fructopyranose-O-yl)methyl}1H-isoxazole		$C_{44}H_{34}N_1O_{11}Br$	176-178	67	Brown
$[VIII]_d$	3-(4-N,N-dimethylamino phenyl)-5-{(2,3,4,5-tetra-O-benzoyl-beta-D-fructopyranose-O-yl)methyl}1H-isoxazole		$C_{46}H_{40}N_2O_{11}$	189-192	60	Yellow
$[VIII]_e$	3-(3-nitro phenyl)-5-{(2,3,4,5-tetra-O-benzoyl-beta-D-fructopyranose-O-yl)methyl}1H-isoxazole		$C_{44}H_{34}N_2O_{13}$	181-183	62	Yellow
$[IX]_a$	3-phenyl-5-{(2,3,4,5-tetra-O-para methoxybenzoyl-beta-D-fructopyranose-O-yl)methyl}1H-isoxazole		$C_{48}H_{27}N_1O_{15}$	165-167	58	Pale yellow

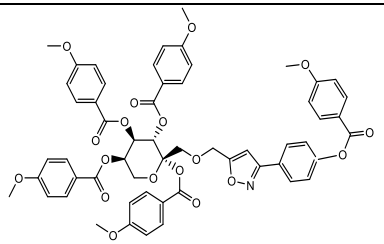
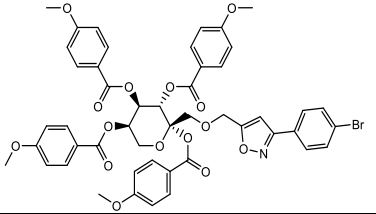
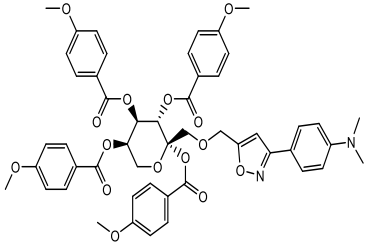
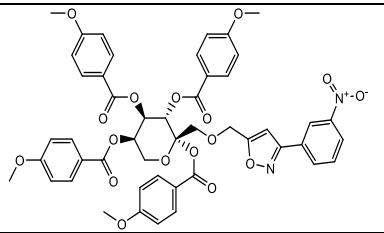
$[IX]_b$	3-(4- methoxybenzoyloxy phenyl)-5-{(2,3,4,5-tetra-O-para methoxybenzoyl-beta-D-fructopyranose -O-yl)methyl}1H-isoxazole		$C_{56}H_{33}N_1O_{18}$	205-207	60	Red
$[IX]_c$	3-(4-bromo phenyl)-5-{(2,3,4,5-tetra-O-para methoxybenzoyl-beta-D-fructopyranose -O-yl)methyl}1H-isoxazole		$C_{48}H_{26}N_1O_{15}Br$	199-201	57	Brown
$[IX]_d$	3-(4-N,N-dimethylamino phenyl)-5-{(2,3,4,5-tetra-O-para methoxybenzoyl-beta-D-fructopyranose-O-yl)methyl}1H-isoxazole		$C_{50}H_{32}N_2O_{15}$	211-213	59	Pale yellow
$[IX]_e$	3-(3-nitro phenyl)-5-{(2,3,4,5-tetra-O-para methoxybenzoyl-beta-D-fructopyranose-O-yl)methyl}1H-isoxazole		$C_{48}H_{26}N_2O_{17}$	200-202	55	Yellow

Table 2- 7: The nomenclature , structural formula, molecular formula and physical properties of compounds [XI]and [XII].

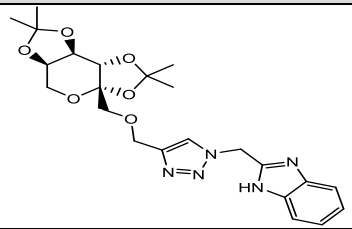
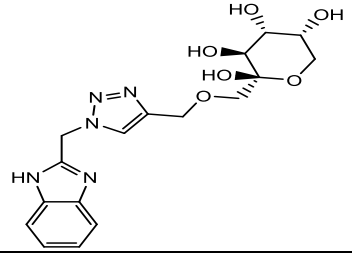
Comp No	Nomenclature	Structural formula	Molecular formula	M. P ºC	Yield %	color
[XI]	1-((1H-benzo[d]imidazol-2-yl)methyl)-4-{(2,3,4,5-di-O-isopropylidene-beta-D-fructopyranose-O-yl)methyl}1H-1,2,3-triazole		$C_{23}H_{29}N_5O_6$	160-162	68	Deep brown
[XII]	1-((1H-benzo[d]imidazol-2-yl)methyl)-4-{(beta-D-fructopyranose-O-yl)methyl}1H-1,2,3-triazole		$C_{17}H_{21}N_5O_6$	190 -192	71	brown

Table 2- 8: The nomenclature , structural formula, molecular formula and physical properties of esters compounds[XIII]$_{a-c}$

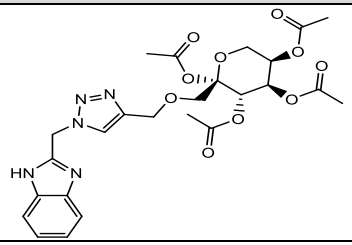
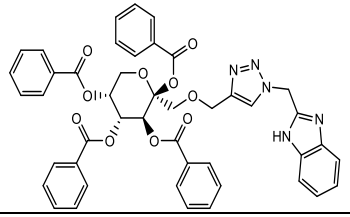
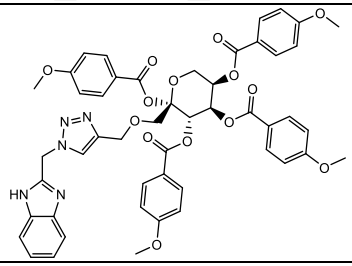
Comp No	Nomenclature	Structural formula	Molecular formula	M. P ºC	Yield %	color
[XIII]$_a$	1-((1H-benzo[d]imidazol-2-yl)methyl)-4-{(2,3,4,5-tetra-O-acetyl-beta-D-fructopyranose-O-yl)methyl}1H-1,2,3-triazole		$C_{25}H_{29}N_5O_{10}$	185 -187	82	Deep green
[XIII]$_b$	1-((1H-benzo[d]imidazol-2-yl)methyl)-4-{(2,3,4,5-tetra-O-benzoyl-beta-D-fructopyranose-O-yl)methyl}1H-1,2,3-triazole		$C_{45}H_{37}N_5O_{10}$	193 -195	70	Deep yellow
[XIII]$_c$	1-((1H-benzo[d]imidazol-2-yl)methyl)-4-{(2,3,4,5-tetra-O-para methoxy benzoyl-beta-D-fructopyranose-O-yl)methyl}1H-1,2,3-triazole		$C_{49}H_{45}N_5O_{14}$	201 -203	65	Yellow

Table 2- 9: The nomenclature , structural formula, molecular formula and physical properties of ethers compounds[XIV]$_{a-c}$

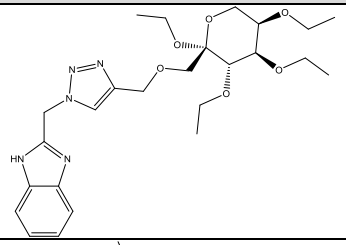
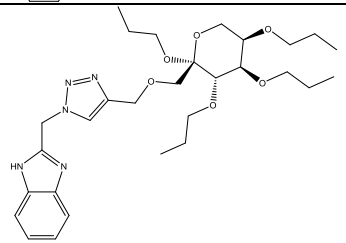
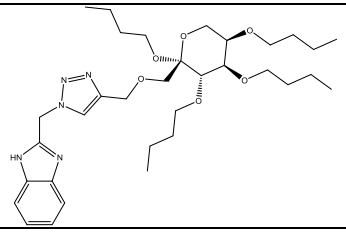
Comp No	Nomenclature	Structural formula	Molecular formula	M. P ºC	Yield %	color
[XIV]$_a$	1-((1H-benzo[d]imidazol-2-yl)methyl)-4-{(2,3,4,5-tetra-O-ethyl-beta-D-fructopyranose-O-yl)methyl}1H-1,2,3-triazole		$C_{25}H_{37}N_5O_6$	Oily	77	Green
[XIV]$_b$	1-((1H-benzo[d]imidazol-2-yl)methyl)-4-{(2,3,4,5-tetra-O-propyl-beta-D-fructopyranose-O-yl)methyl}1H-1,2,3-triazole		$C_{29}H_{45}N_5O_6$	110 -112	73	Yellow
[XIV]$_c$	1-((1H-benzo[d]imidazol-2-yl)methyl)-4-{(2,3,4,5-tetra-O-butyl-beta-D-fructopyranose-O-yl)methyl}1H-1,2,3-triazole		$C_{33}H_{53}N_5O_6$	116 -118	62	Brown

Table 2- 10: The nomenclature , structural formula, molecular formula and physical properties of compounds [XV], [XVI] and [XVII]

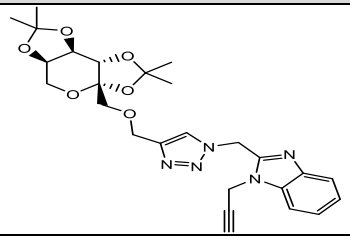
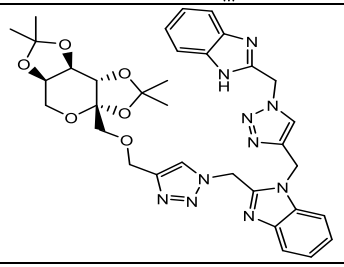
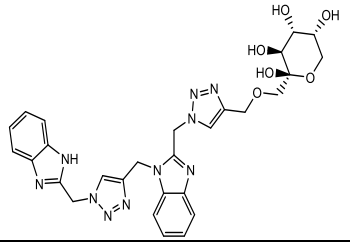
Comp No	Nomenclature	Structural formula	Molecular formula	M. P ºC	Yield %	color
[XV]	1-((1-(prop-2-yn-1-yl)-1H-benzo[d]imidazol-2-yl)methyl)-4-{(2,3,4,5-di-O-isopropylidene-beta-D-fructopyranose-O-yl)methyl}1H-1,2,3-triazole		$C_{26}H_{31}N_5O_6$	200 -202	80	Light brown
[XVI]	1-((1-((1-((-1H-benzo[d]imidazol-2-yl)methyl)triazol-4-yl)methyl)-1H-benzo[d]imidazol-2-yl)methyl)-4-{(2,3,4,5-di-O-isopropylidene-beta-D-fructopyranose-O-yl)methyl}1H-1,2,3-triazole		$C_{34}H_{38}N_{10}O_6$	225 -227	66	Orang
[XVII]	1-((1-((1-((-1H-benzo[d]imidazol-2-yl)methyl)triazol-4-yl)methyl)-1H-benzo[d]imidazol-2-yl) methyl)-4-{(beta-D-fructo pyranose -O-yl)methyl}1H-1,2,3-triazole		$C_{28}H_{30}N_{10}O_6$	241 -243	75	Deep yellow

Table 2- 11: The nomenclature , structural formula, molecular formula and physical properties of esters compounds[XVIII]$_{a-c}$

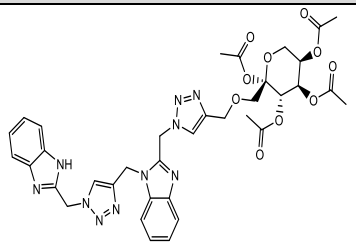
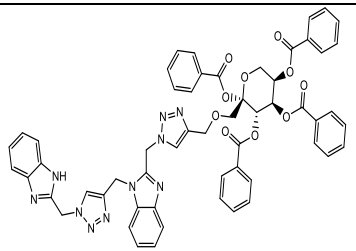
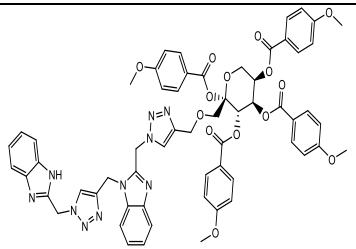
Comp No	Nomenclature	Structural formula	Molecular formula	M. P ºC	Yield %	color
[XVIII]$_a$	1-((1-((1-((-1H-benzo[d]imidazol-2-yl)methyl)triazol-4-yl)methyl)-1H-benzo[d]imidazol-2-yl)methyl)-4-{(2,3 ,4,5-tetra-O-acetyl-beta-D-fructopy ranose-O-yl)methyl}1H-1,2,3-triazole		$C_{36}H_{38}N_{10}O_{10}$	198 -200	76	Light brown
[XVIII]$_b$	1-((1-((1-((-1H-benzo[d]imidazol-2-yl)methyl)triazol-4-yl)methyl)-1H-benzo[d]imidazol-2-yl)methyl)-4-{(2,3 ,4,5-tetra-O-benzoyl-beta-D-fructopyr anose-O-yl)methyl}1H-1,2,3-triazole		$C_{56}H_{46}N_{10}O_{10}$	Dec 242	71	Brown
[XVIII]$_c$	1-((1-((1-((-1H-benzo[d]imidazol-2 -yl)methyl)triazol-4-yl)methyl)-1H-benzo[d]imidazol-2-yl)methyl)-4-{ (2,3,4,5-tetra-O-para methoxy benzoyl-beta-D-fructopyranose-O-yl)methyl}1H-1,2,3-triazole		$C_{60}H_{54}N_{10}O_{14}$	Dec 235	67	Orang

Table 2- 12: The nomenclature , structural formula, molecular formula and physical properties of ethers compounds[XIX]$_{a-c}$

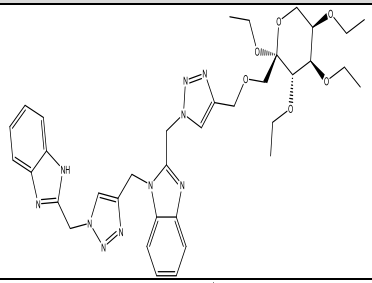
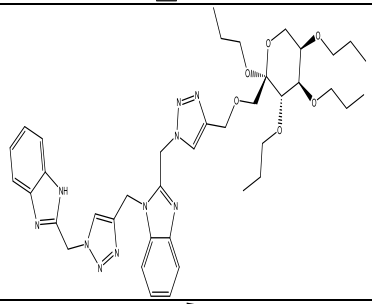
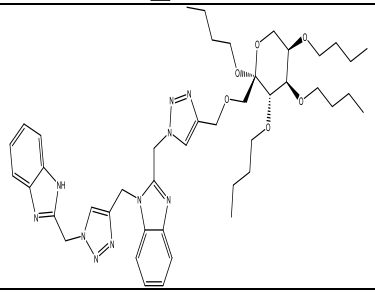
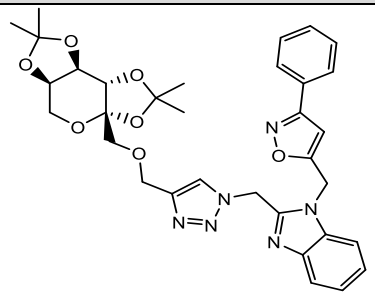
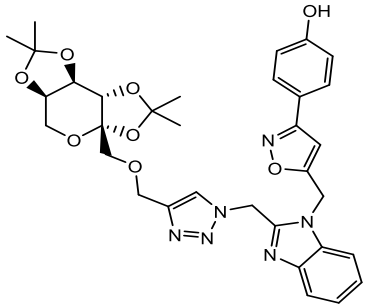
Comp No	Nomenclature	Structural formula	Molecular formula	M. P ºC	Yield %	color
[XIX]$_a$	1-((1-((1-((-1H-benzo[d]imidazol-2-yl)methyl)triazol-4-yl)methyl)-1H-benzo[d]imidazol-2-yl)methyl)-4-{(2,3,4,5-tetra-O-ethyl-beta-D-fructopyranose-O-yl)methyl}1H-1,2,3-triazole		$C_{36}H_{46}N_{10}O_6$	Oily	84	Deep brown
[XIX]$_b$	1-((1-((1-((-1H-benzo[d]imidazol-2-yl)methyl)triazol-4-yl)methyl)-1H-benzo[d]imidazol-2-yl)methyl)-4-{(2,3,4,5-tetra-O-propyl-beta-D-fructopyranose-O-yl)methyl}1H-1,2,3-triazole		$C_{40}H_{54}N_{10}O_6$	125 -127	75	Light brown
[XIX]$_c$	1-((1-((1-((-1H-benzo[d]imidazol-2-yl)methyl)triazol-4-yl)methyl)-1H-benzo[d]imidazol-2-yl)methyl)-4-{(2,3,4,5-tetra-O-butyl-beta-D-fructopyranose-O-yl)methyl}1H-1,2,3-triazole		$C_{44}H_{62}N_{10}O_6$	131 -133	64	Deep yellow

Table 2-13: The nomenclature , structural formula, molecular formula and physical properties of compounds[XX]$_{a-e}$.

Comp No	Nomenclature	Structural formula	Molecular formula	M. P ºC	Yield %	color
[XX]$_a$	1-((1-((3-phenylisoxazol-5-yl)methyl)-1H-benzo[d]imidazol-2-yl)methyl)-4-{(2,3,4,5-di-O-isopropylidene-beta-D-fructopyranose-O-yl)methyl}1H-1,2,3-triazole		$C_{33}H_{36}N_6O_7$	143-145	61	Deep yellow
[XX]$_b$	1-((1-((3-(4-Hydroxyl phenyl)isoxazol-5-yl)methyl)-1H-benzo[d]imidazol-2-yl)methyl)-4-{(2,3,4,5-di-O-isopropylidene-beta-D-fructopyranose-O-yl)methyl}1H-1,2,3-triazole		$C_{33}H_{36}N_6O_8$	177-179	70	Brown

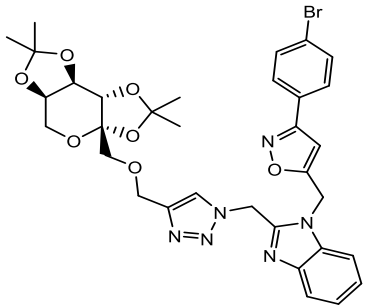
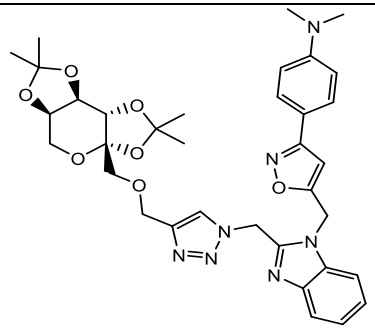
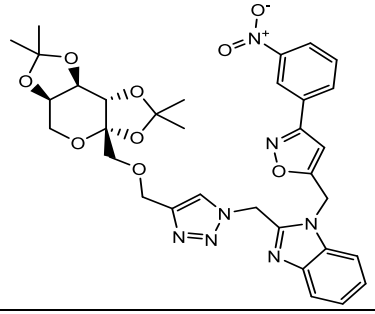
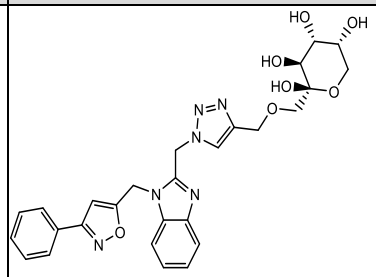
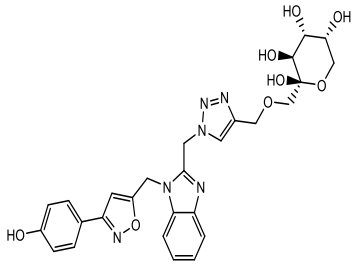
$[XX]_c$	1-((1-((3-(4-bromophenyl)isoxazol-5-yl)methyl)-1H-benzo[d]imidazol-2-yl)methyl)-4-{(2,3,4,5-di-O-isopropylidene-beta-D-fructopyranose-O-yl)methyl}1H-1,2,3-triazole		$C_{33}H_{35}N_6O_7Br$	151-153	69	Brown
$[XX]_d$	1-((1-((3-(4-N,N-dimethylaminophenyl)isoxazol-5-yl)methyl)-1H-benzo[d]imidazol-2-yl)methyl)-4-{(2,3,4,5-di-O-isopropylidene-beta-D-fructopyranose-O-yl)methyl}1H-1,2,3-triazole		$C_{35}H_{41}N_7O_7$	145-147	72	Deep yellow
$[XX]_e$	1-((1-((3-(3-nitrophenyl)isoxazol-5-yl)methyl)-1H-benzo[d]imidazol-2-yl)methyl)-4-{(2,3,4,5-di-O-isopropylidene-beta-D-fructopyranose-O-yl)methyl}1H-1,2,3-triazole		$C_{33}H_{35}N_7O_9$	161-164	65	Yellow

Table 2- 14: The nomenclature , structural formula, molecular formula and physical properties of compounds[XXI]$_{a-e}$.

Comp No	Nomenclature	Structural formula	Molecular formula	M. P ºC	Yield %	color
[XXI]$_a$	1-((1-((3-phenylisoxazol-5-yl)methyl)-1H-benzo[d]imidazol-2-yl)methyl)-4-{(beta-D-fructopyranose-O-yl)methyl}1H-1,2,3-triazole		$C_{27}H_{28}N_6O_7$	159-161	78	Yellow
[XXI]$_b$	1-((1-((3-(4-Hydroxyl phenyl)isoxazol-5-yl)methyl)-1H-benzo[d]imidazol-2-yl)methyl)-4-{(beta-D-fructopyranose-O-yl)methyl}1H-1,2,3-triazole		$C_{27}H_{28}N_6O_8$	181-183	75	Brown

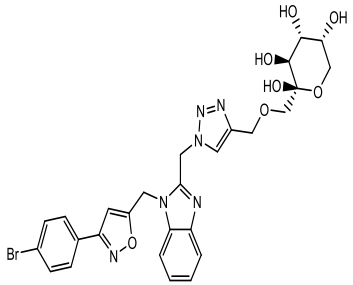
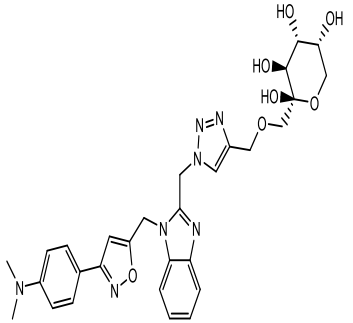
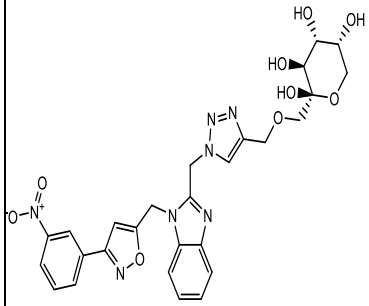
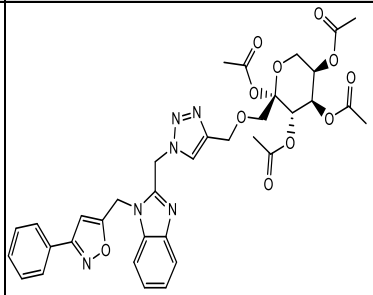
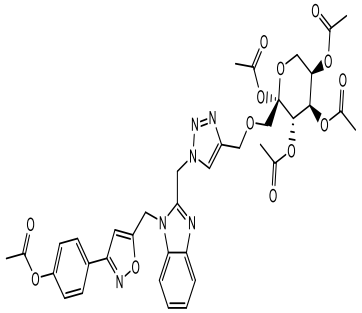
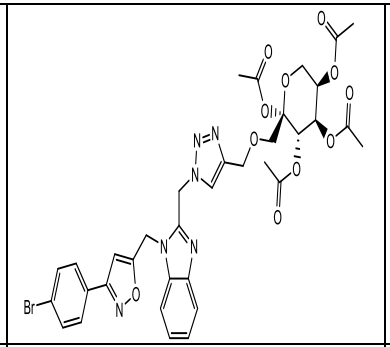
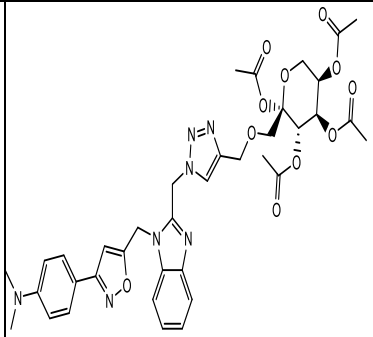
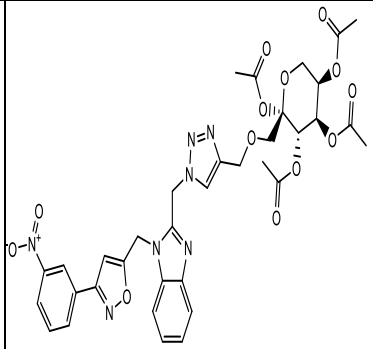
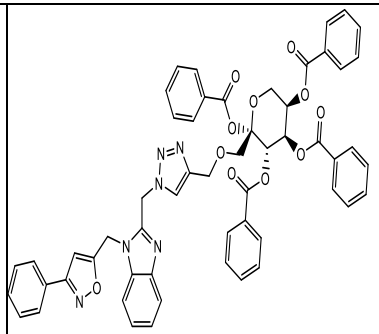
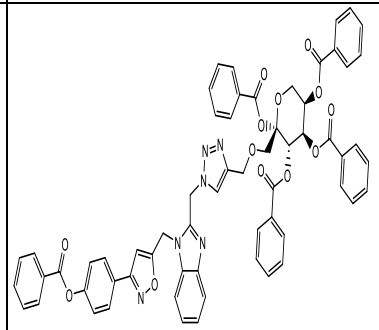
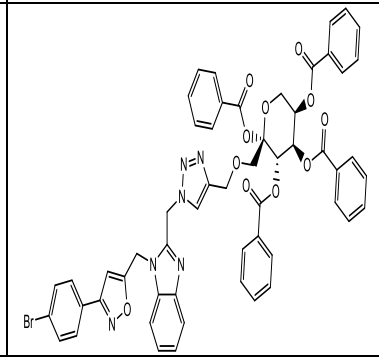
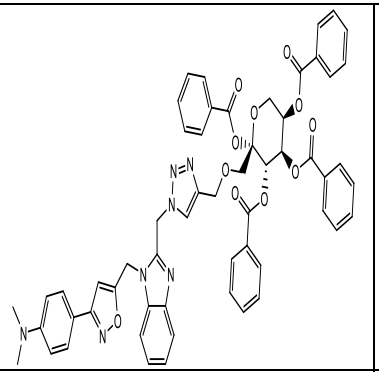
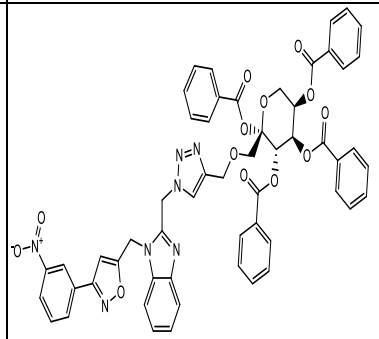
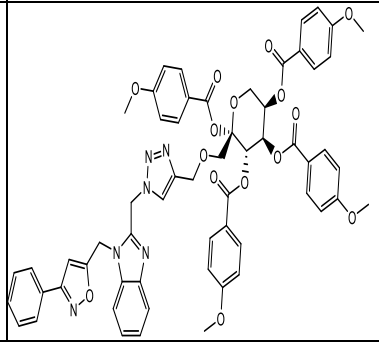
$[XXI]_c$	1-((1-((3-(4-bromophenyl)isoxazol-5-yl)methyl)-1H-benzo[d]imidazol-2-yl)methyl)-4-{(beta-D-fructopyranose-O-yl)methyl}1H-1,2,3-triazole		$C_{27}H_{27}N_6O_7Br$	173-175	80	Yellow
$[XXI]_d$	1-((1-((3-(4-N,N-dimethylaminophenyl)isoxazol-5-yl)methyl)-1H-benzo[d]imidazol-2-yl)methyl)-4-{(beta-D-fructopyranose-O-yl)methyl}1H-1,2,3-triazole		$C_{29}H_{33}N_7O_7$	182-185	82	Brown
$[XXI]_e$	1-((1-((3-(3-nitrophenyl)isoxazol-5-yl)methyl)-1H-benzo[d]imidazol-2-yl)methyl)-4-{(beta-D-fructopyranose-O-yl)methyl}1H-1,2,3-triazole		$C_{27}H_{27}N_7O_9$	163-165	74	Deep yellow

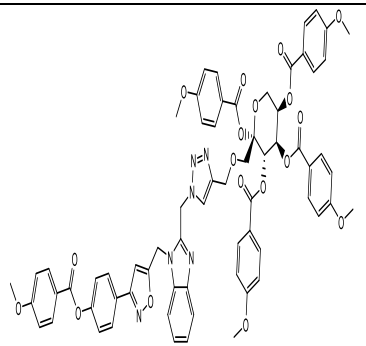
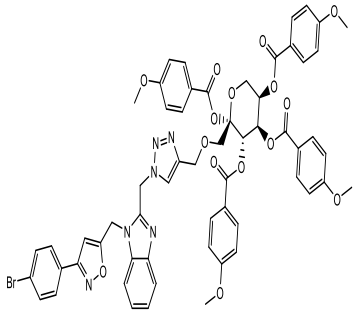
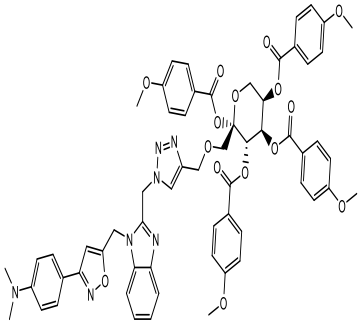
Table 2- 15: The nomenclature , structural formula, molecular formula and physical properties of esters compounds[XXII]$_{a-e}$, [XXIII]$_{a-e}$ and [XX IV]$_{a-e}$

Comp No	Nomenclature	Structural formula	Molecular formula	M. P ºC	Yield %	color
[XXII]$_a$	1-((1-((3-phenylisoxazol-5-yl)methyl)-1H-benzo[d]imidazol-2-yl)methyl)-4-{(2,3,4,5-tetra-O-acetyl-beta-D-fructopyranose-O-yl)methyl}1H-1,2,3-triazole		$C_{35}H_{36}N_6O_{11}$	154-157	79	Yellow
[XXII]$_b$	1-((1-((3-(4-(acetoxy)phenyl)isoxazol-5-yl)methyl)-1H-benzo[d]imidazol-2-yl)methyl)-4-{(2,3,4,5-tetra-O-acetyl-beta-D-fructopyranose-O-yl)methyl}1H-1,2,3-triazole		$C_{37}H_{38}N_6O_{13}$	220-222	84	Brown

$[XXII]_c$	1-((1-((3-(4-bromophenyl)isoxazol-5-yl)methyl)-1*H*-benzo[*d*]imidazol-2-yl)methyl)-4-{(2,3,4,5-tetra-*O*-acetyl-beta-D-fructopyranose-O-yl)methyl}1*H*-1,2,3-triazole		$C_{35}H_{35}N_6O_{11}Br$	203-205	76	Light brown
$[XXII]_d$	1-((1-((3-(4-N,N-dimethylaminophenyl)isoxazol-5-yl)methyl)-1H-benzo[d]imidazol-2-yl)methyl)-4-{(2,3,4,5-tetra-O-acetyl-beta-D-fructopyranose-O-yl)methyl}1H-1,2,3-triazole		$C_{37}H_{41}N_7O_{11}$	211-213	81	Yellow
$[XXII]_e$	1-((1-((3-(3-nitrophenyl)isoxazol-5-yl)methyl)-1H-benzo[d]imidazol-2-yl)methyl)-4-{(2,3,4,5-tetra-O-acetyl-beta-D-fructopyranose-O-yl)methyl}1H-1,2,3-triazole		$C_{35}H_{35}N_7O_{13}$	216-219	72	Deep yellow

$[XXIII]_a$	1-((1-((3-phenylisoxazol-5-yl)methyl)-1H-benzo[d]imidazol-2-yl)methyl)-4-{(2,3,4,5-tetra-O-benzoyl-beta-D-fructopyranose-O-yl)methyl}1H-1,2,3-triazole		$C_{55}H_{44}N_6O_{11}$	167-169	69	Deep yellow
$[XXIII]_b$	1-((1-((3-(4-(benzoyloxy)phenyl)isoxazol-5-yl)methyl)-1*H*-benzo[*d*]imidazol-2-yl)methyl)-4-{(2,3,4,5-tetra-*O*-benzoyl-beta-D-fructopyranose-O-yl)methyl}1*H*-1,2,3-triazole		$C_{62}H_{48}N_6O_{13}$	209-211	78	Brown
$[XXIII]_c$	1-((1-((3-(4-bromophenyl)isoxazol-5-yl)methyl)-1*H*-benzo[*d*]imidazol-2-yl)methyl)-4-{(2,3,4,5-tetra-*O*-benzoyl-beta-D-fructopyranose-O-yl)methyl}1*H*-1,2,3-triazole		$C_{55}H_{43}N_6O_{11}Br$	191-193	71	Yellow

$[XXIII]_d$	1-((1-((3-(4-N,N-dimethylaminophenyl)isoxazol-5-yl)methyl)-1*H*-benzo[*d*]imidazol-2-yl)methyl)-4-{(2,3,4,5-tetra-*O*-benzoyl-beta-D-fructopyranose-O-yl)methyl}1H-1,2,3-triazole		$C_{57}H_{49}N_7O_{11}$	230-233	68	Light brown
$[XXIII]_e$	1-((1-((3-(3-nitrophenyl)isoxazol-5-yl)methyl)-1*H*-benzo[*d*]imidazol-2-yl)methyl)-4-{(2,3,4,5-tetra-*O*-benzoyl-beta-D-fructopyranose-O-yl)methyl}1*H*-1,2,3-triazole		$C_{55}H_{43}N_7O_{13}$	216-218	70	Yellow
$[XXIV]_a$	1-((1-((3-phenylisoxazol-5-yl)methyl)-1H-benzo[d]imidazol-2-yl)methyl)-4-{(2,3,4,5-tetra-O-para methoxybenzoyl-beta-D-fructopyranose-O-yl)methyl}1H-1,2,3-triazole		$C_{59}H_{52}N_6O_{15}$	187-190	76	Brown

$[XXIV]_b$	1-((1-((3-(4-(para methoxybenzoyloxy)phenyl)isoxazol-5-yl)methyl)-1H-benzo[d]imidazol-2-yl)methyl)-4-{(2,3,4,5-tetra-O-para methoxybenzoyl-beta-D-fructopyranose-O-yl)methyl}1H-1,2,3-triazole		$C_{67}H_{58}N_6O_{18}$	239-241	78	Light brown
$[XXIV]_c$	1-((1-((3-(4-bromophenyl)isoxazol-5-yl)methyl)-1H-benzo[d]imidazol-2-yl)methyl)-4-{(2,3,4,5-tetra-O-para methoxybenzoyl-beta-D-fructopyranose-O-yl)methyl}1H-1,2,3-triazole		$C_{59}H_{51}N_6O_{15}Br$	226-228	69	Orang
$[XXIV]_d$	1-((1-((3-(4-N,N-dimethylaminophenyl)isoxazol-5-yl)methyl)-1H-benzo[d]imidazol-2-yl)methyl)-4-{(2,3,4,5-tetra-O-para methoxybenzoyl-beta-D-fructopyranose-O-yl)methyl}1H-1,2,3-triazole		$C_{61}H_{57}N_7O_{15}$	246-248	66	Deep yellow

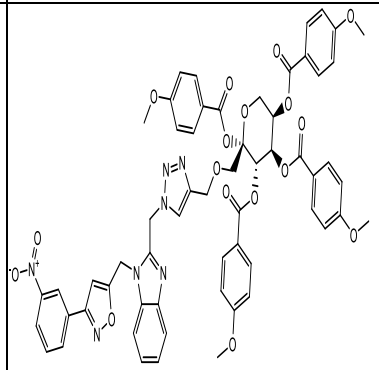
$[XXIV]_e$	1-((1-((3-(3-nitrophenyl)isoxazol-5-yl)methyl)-1H-benzo[d]imidazol-2-yl)methyl)-4-{(2,3,4,5-tetra-O-para methoxybenzoyl-beta-D-fructopyranose-O-yl)methyl}1H-1,2,3-triazole		$C_{59}H_{51}N_7O_{17}$	219-221	71	Brown

Table 3- 1: Characteristic FTIR spectral data of compounds$[V]_{a-e}$

Comp. No.	υ(C-H) aromatic cm^{-1}	υ(C-H) Aliphatic cm^{-1}	υ(C=N) cm^{-1}	υ(C=C) cm^{-1}	Others bands cm^{-1}
$[V]_a$	3034	2974,2933	1647	1606	υ(C-O) 1240,1068
$[V]_b$	3066	2991,2937	1647	1593	υ(OH) 3292 υ(C-O) 1248,1072
$[V]_c$	3095	2983,2935	1645	1585	υ(C-O) 1269,1072 υ(C-Br) 713
$[V]_d$	3038	2983,2893	1633	1577	υ $N(Me)_2$ 1301,1157 υ(C-O) 1240,1074
$[V]_e$	3037	2980,2927	1641	1560	υ(NO_2)1517, 1361 υ(C-O) 1256,1074

Table 3- 2: Characteristic FTIR spectral data of compounds[VI]$_{a-e}$

Comp. No.	υ(OH) cm^{-1}	υ(C-H) aromatic cm^{-1}	υ(C-H) Aliphatic cm^{-1}	υ(C=N) cm^{-1}	υ(C=C) cm^{-1}	Others bands cm^{-1}
$[VI]_a$	3402	3060	2987,2933	1624	1570	υ(C-O) 1211,1070
$[VI]_b$	3278	3062	2987,2931	1664	1577	υ(C-O) 1209,1074
$[VI]_c$	3379	3061	2987,2935	1622	1555	υ(C-Br) 720 υ(C-O) 1212,1070
$[VI]_d$	3429	3065	2987,2927	1664	1612	υ $N(Me)_2$ 1331,1165 υ(C-O) 1214,1071
$[VI]_e$	3290	3068	2968,2905	1649	1580	υ(NO_2) 1531, 1348 υ(C-O) 1215,1076

Table 3- 3: Characteristic FTIR spectral data of esters compounds [VII]$_{a-e}$, [VIII]$_{a-e}$ and [IX]$_{a-e}$

Comp. No.	υ(C-H) aromatic cm^{-1}	υ(C-H) Aliphatic cm^{-1}	υ(C=O) cm^{-1}	υ(C=N) cm^{-1}	υ(C=C) cm^{-1}	Others bands cm^{-1}
$[VII]_a$	3093	2997, 2945	1738	1614	1585	υ(C-O) 1265 ,1070
$[VII]_b$	3057	2983, 2916	1735	1641	1539	υ(C-O) 1251,1066
$[VII]_c$	3095	2999, 2962	1734	1641	1585	υ(C-Br) 713 υ(C-O) 1267,1070
$[VII]_d$	3035	2971, 2845	1736	1661	1604	υ $N(Me)_2$ 1319,1157 υ(C-O) 1263,1045

$[VII]_e$	3003	2966, 2936	1735	1645	1579	υ(NO_2) 1533, 1348 υ(C-O) 1260,1076
$[VIII]_a$	3093	2960, 2861	1712	1660	1581	υ(C-O) 12651072
$[VIII]_b$	3091	2941, 2833	1712	1678	1587	υ(C-O) 1253,1067
$[VIII]_c$	3095	2987, 2935	1714	1674	1616	υ(C-Br) 667 υ(C-O) 1263,1068
$[VIII]_d$	3074	2983, 2936	1712	1649	1597	υ $N(Me)_2$ 1311,1153 υ(C-O) 1257,1068
$[VIII]_e$	3064	2983, 2872	1714	1679	1599	υ(NO_2) 1521, 1359 υ(C-O) 1257,1066
$[IX]_a$	3089	2981, 2933	1724	1642	1618	υ(C-O) 1263,1070
$[IX]_b$	3089	2983, 2935	1726	1676	1585	υ(C-O) 1249,1066
$[IX]_c$	3093	2960, 2837	1730	1678	1591	υ(C-Br) 713 υ(C-O) 1238,1069
$[IX]_d$	3074	2983, 2881	1727	1668	1583	υ $N(Me)_2$ 1319,1168 υ(C-O) 1265,1074
$[IX]_e$	3091	2992, 2956	1721	1680	1557	υ(NO_2) 1539, 1371 υ(C-O) 1259,1068

Table 3-4: Characteristic FTIR spectral data of esters compounds [XIII]$_{a-c}$

Comp. No.	υ(NH) cm^{-1}	υ(C-H) aromatic cm^{-1}	υ(C-H) Aliphatic cm^{-1}	υ(C=O) cm^{-1}	υ(C=N) cm^{-1}	υ(C=C) cm^{-1}	υ(C-O) cm^{-1}
[XIII]$_a$	3244	3062	2985,2922	1740	1680	1620	1249, 1066
[XIII]$_b$	3250	3035	2987,2870	1713	1664	1618	1249, 1066
[XIII]$_c$	3273	3072	2995,2860	1726	1668	1620	1263, 1076

Table 3-5: Characteristic FTIR spectral data of ether compounds [XIV]$_{a-c}$

Comp. No.	υ(NH) cm^{-1}	υ(C-H) aromatic cm^{-1}	υ(C-H) Aliphatic cm^{-1}	υ(C=N) cm^{-1}	υ(C-O) cm^{-1}	υ(C=C) cm^{-1}
[XIV]$_a$	3273	3072	2995, 2940	1668	1101	1620
[XIV]$_b$	3246	3062	2954, 2843	1665	1093	1625
[XIV]$_c$	3292	3066	2986, 2922	1647	1109	1610

Table3-6: Characteristic FTIR spectral data of esters compounds $[XVIII]_{a-c}$

Comp. No.	υ(NH) cm^{-1}	υ(C-H) aromatic cm^{-1}	υ(C-H) Aliphatic cm^{-1}	υ(C=O) cm^{-1}	υ(C=N) cm^{-1}	Others bands cm^{-1}
$[XVIII]_a$	3217	3049	2947,2872	1737	1655	υ(C-O) 1257,1066 υ(C=C) 1600
$[XVIII]_b$	3260	3066	2991,2937	1726	1658	υ(C-O) 1253,1053 υ(C=C) 1616
$[XVIII]_c$	3273	3093	2999,2904	1715	1672	υ(C-O) 1265,1072 υ(C=C) 1616

Table3-7: Characteristic FTIR spectral data of ether compounds$[XIX]_{a-c}$

Comp. No.	υ(NH) cm^{-1}	υ(C-H) aromatic cm^{-1}	υ(C-H) Aliphatic cm^{-1}	υ(C=N) cm^{-1}	υ(C-O) cm^{-1}	Others bands cm^{-1}
$[XIX]_a$	3244	3070	2985, 2910	1641	1126	υ(C=C)1610
$[XIX]_b$	3254	3084	2987, 2907	1661	1130	υ(C=C)1606
$[XIX]_c$	3289	3051	2960, 2852	1652	1111	υ(C=C)1612

Table 3-8: Characteristic FTIR spectral data of compounds[XX]$_{a-e}$

Comp. No.	υ(C-H) aromatic cm^{-1}	υ(C-H) Aliphatic cm^{-1}	υ(C=N) cm^{-1}	υ(C=C) cm^{-1}	Others bands cm^{-1}
$[XX]_a$	3061	2983,2893	1631	1600	υ(C-O) 1209,1074
$[XX]_b$	3064	2987,2877	1653	1606	υ(OH) 3251 υ(C-O) 1221,1057
$[XX]_c$	3065	2983,2935	1645	1605	υ(C-O) 1213,1064 υ(C-Br) 663
$[XX]_d$	3010	2958,2900	1662	1604	υ $N(Me)_2$ 1334,1147 υ(C-O) 1232,1076
$[XX]_e$	3060	2924,2916	1662	1620	υ(NO_2)1579, 1342 υ(C-O) 1251,1076

Table 3-9: Characteristic FTIR spectral data of compounds[XXI]$_{a-e}$

Comp. No.	υ(OH) cm^{-1}	υ(C-H) aromatic cm^{-1}	υ(C-H) Aliphatic cm^{-1}	υ(C=N) cm^{-1}	υ(C=C) cm^{-1}	Others bands cm^{-1}
$[XXI]_a$	3294	3066	2987,2935	1647	1612	υ(C-O) 1252,1070
$[XXI]_b$	3273	3062	2993,2939	1649	1608	υ(C-O) 1250,1072
$[XXI]_c$	3240	3095	2935,2877	1651	1602	υ(C-Br) 673 υ(C-O) 1244,1065
$[XXI]_d$	3295	3065	2987,2902	1643	1602	υ $N(Me)_2$ 1330,1150 υ(C-O) 1245,1074
$[XXI]_e$	3290	3055	2935,2885	1645	1601	υ(NO_2) 1557, 1367 υ(C-O) 1244,1071

Table 3-10 : Characteristic FTIR spectral data of esters compounds[XXII]$_{a-e}$, [XXIII]$_{a-e}$ and [XXIV]$_{a-e}$

Comp. No.	υ(C-H) aromatic cm^{-1}	υ(C-H) Aliphatic cm^{-1}	υ(C=O) cm^{-1}	υ(C=N) cm^{-1}	υ(C=C) cm^{-1}	Others bands cm^{-1}
$[XXII]_a$	3016	2985, 2877	1737	1639	1606	υ(C-O) 1265 ,1070
$[XXII]_b$	3061	2978, 2955	1735	1649	1602	υ(C-O) 1219,1097
$[XXII]_c$	3066	2970, 2855	1733	1645	1602	υ(C-Br) 669 υ(C-O) 1217,1078
$[XXII]_d$	3071	2989, 2930	1740	1650	1601	υ $N(Me)_2$ 1350,1160 υ(C-O) 1222,1061
$[XXII]_e$	3093	2995, 2935	1738	1660	1620	υ(NO_2) 1537, 1363 υ(C-O) 1257,1066
$[XXIII]_a$	3059	2941, 2844	1718	1622	1589	υ(C-O) 1252,1072
$[XXIII]_b$	3060	2979, 2890	1715	1649	1601	υ(C-O) 1239,1071
$[XXIII]_c$	3030	2993, 2937	1716	1666	1610	υ(C-Br) 677 υ(C-O) 1263,1068
$[XXIII]_d$	3035	2983, 2933	1711	1654	1604	υ $N(Me)_2$ 1319,1197 υ(C-O) 1263,1070

$[XXIII]_e$	3058	2972, 2840	1714	1641	1589	$\upsilon(NO_2)$ 1531, 1361 υ(C-O) 1230,1078
$[XXIV]_a$	3049	2960, 2920	1727	1643	1601	υ(C-O) 1223,1063
$[XXIV]_b$	3060	2955, 2880	1726	1650	1606	υ(C-O) 1220,1070
$[XXIV]_c$	3089	2945, 2845	1728	1635	1591	υ(C-Br) 684 υ(C-O) 1261,1049
$[XXIV]_d$	3037	2970, 2833	1724	1644	1604	υ $N(Me)_2$ 1323,1196 υ(C-O) 1238,1045
$[XXIV]_e$	3050	2981, 2919	1728	1651	1605	$\upsilon(NO_2)$ 1551, 1340 υ(C-O) 1221,1066

Table 3-11: antimicrobial activity of compounds $[V]_{a-e}$, $[VI]_{a-e}$,$[VII]_{a-e}$, $[VIII]_{a-e}$ and $[IX]_{a-e}$

Compound	*E. coli- mm*	*S. aureus- mm*	*B. substilis-mm*	*C. albicans -mm*
	Gram negative(-)	Gram Positive(+)	Gram Positive(+)	
DMSO	Nil	Nil	Nil	Nil
$[V]_a$	30	30	25	0
$[V]_b$	19	22	20	4
$[V]_c$	15	34	20	12
$[V]_d$	0	14	12	0
$[V]_e$	21	27	21	8
$[VI]_a$	20	25	18	0
$[VI]_b$	19	32	10	6
$[VI]_c$	24	30	22	12
$[VI]_d$	20	15	16	0
$[VI]_e$	22	30	20	14
$[VII]_a$	20	25	28	4
$[VII]_b$	28	22	25	8
$[VII]_c$	9	19	8	6
$[VII]_d$	16	15	12	4
$[VII]_e$	28	32	26	16
$[VIII]_a$	28	30	24	15
$[VIII]_b$	20	28	19	13
$[VIII]_c$	22	28	20	10
$[VIII]_d$	21	15	10	0
$[VIII]_e$	29	24	18	7
$[IX]_a$	30	26	22	15
$[IX]_b$	32	30	20	16
$[IX]_c$	26	22	20	12
$[IX]_d$	25	20	20	4
$[IX]_e$	28	22	25	20

Table 3-12: antimicrobial activity of compounds [XI] , [XII] , $[XIII]_{a-c}$ and$[XIV]_{a-c}$

Compound	*E. coli- mm*	*S. aureus- mm*	*B. substilis-mm*	*C. albicans -mm*
	Gram negative(-)	Gram Positive(+)	Gram Positive(+)	
DMSO	Nil	Nil	Nil	Nil
[XI]	12	15	10	30
[XII]	29	32	33	29
$[XIII]_a$	15	14	19	33
$[XIII]_b$	0	0	6	4
$[XIII]_c$	11	21	22	34
$[XIV]_a$	0	15	20	22
$[XIV]_b$	9	12	22	30
$[XIV]_c$	24	10	18	28

Table3-13: antimicrobial activity of compounds [XV] , [XVI] , [XVII], $[XVIII]_{a-c}$ and$[XIX]_{a-c}$

Compound	*E. coli- mm*	*S. aureus- mm*	*B. substilis-mm*	*C. albicans -mm*
	Gram negative(-)	Gram Positive(+)	Gram Positive(+)	
DMSO	Nil	Nil	Nil	Nil
[XV]	0	25	26	23
[XVI]	22	20	22	34
[XVII]	23	25	31	32
$[XVIII]_a$	8	22	11	29
$[XVIII]_b$	9	19	20	32
$[XVIII]_c$	12	15	17	27
$[XIX]_a$	0	2	0	33
$[XIX]_b$	21	23	25	34
$[XIX]_c$	20	24	21	31

Table 3-14: antimicrobial activity of compounds $[XX]_{a-e}$, $[XXI]_{a-e}$,$[XXII]_{a-e}$, $[XXIII]_{a-e}$ and $[XXIV]_{a-e}$

Compound	*E. coli- mm*	*S. aureus- mm*	*B. substilis-mm*	*C. albicans -mm*
	Gram negative(-)	Gram Positive(+)	Gram Positive(+)	
DMSO	Nil	Nil	Nil	Nil
$[XX]_a$	30	30	25	18
$[XX]_b$	19	22	20	4
$[XX]_c$	15	34	20	0
$[XX]_d$	0	14	12	0
$[XX]_e$	21	27	21	12
$[XXI]_a$	20	25	18	0
$[XXI]_b$	19	32	10	4
$[XXI]_c$	24	30	22	0
$[XXI]_d$	20	15	16	22
$[XXI]_e$	22	30	20	18
$[XXII]_a$	20	25	28	0
$[XXII]_b$	28	22	25	8
$[XXII]_c$	9	19	8	16
$[XXII]_d$	16	15	12	0
$[XXII]_e$	28	32	26	26
$[XXIII]_a$	28	30	24	18
$[XXIII]_b$	20	28	19	16
$[XXIII]_c$	22	28	20	0
$[XXIII]_d$	21	15	10	10
$[XXIII]_e$	29	24	18	4
$[XXIV]_a$	30	26	22	18
$[XXIV]_b$	32	30	20	20
$[XXIV]_c$	26	22	20	10
$[XXIV]_d$	25	20	20	4
$[XXIV]_e$	28	22	25	28

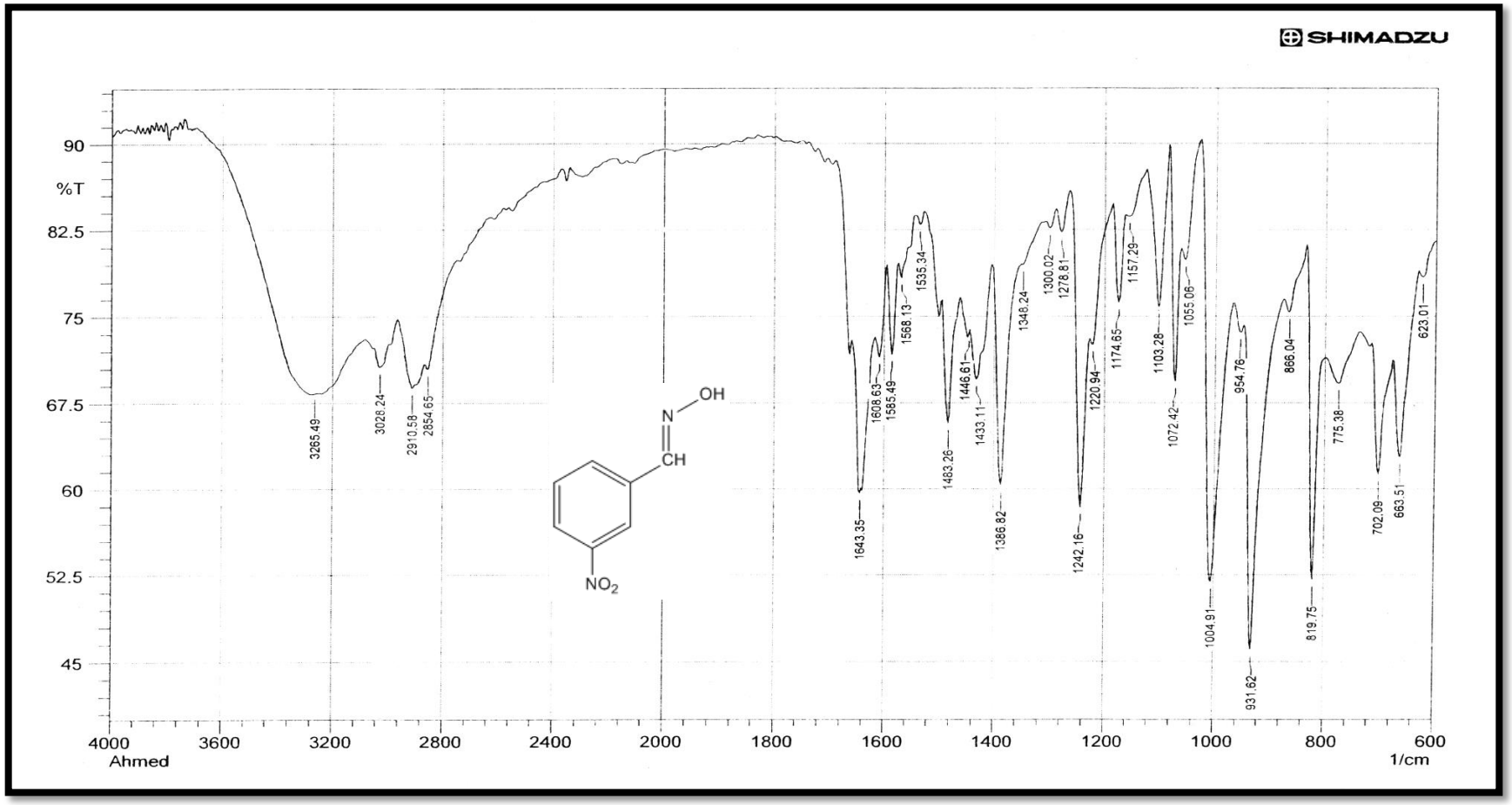


Figure (3-1) FT-IR –spectrum of compound [I]e

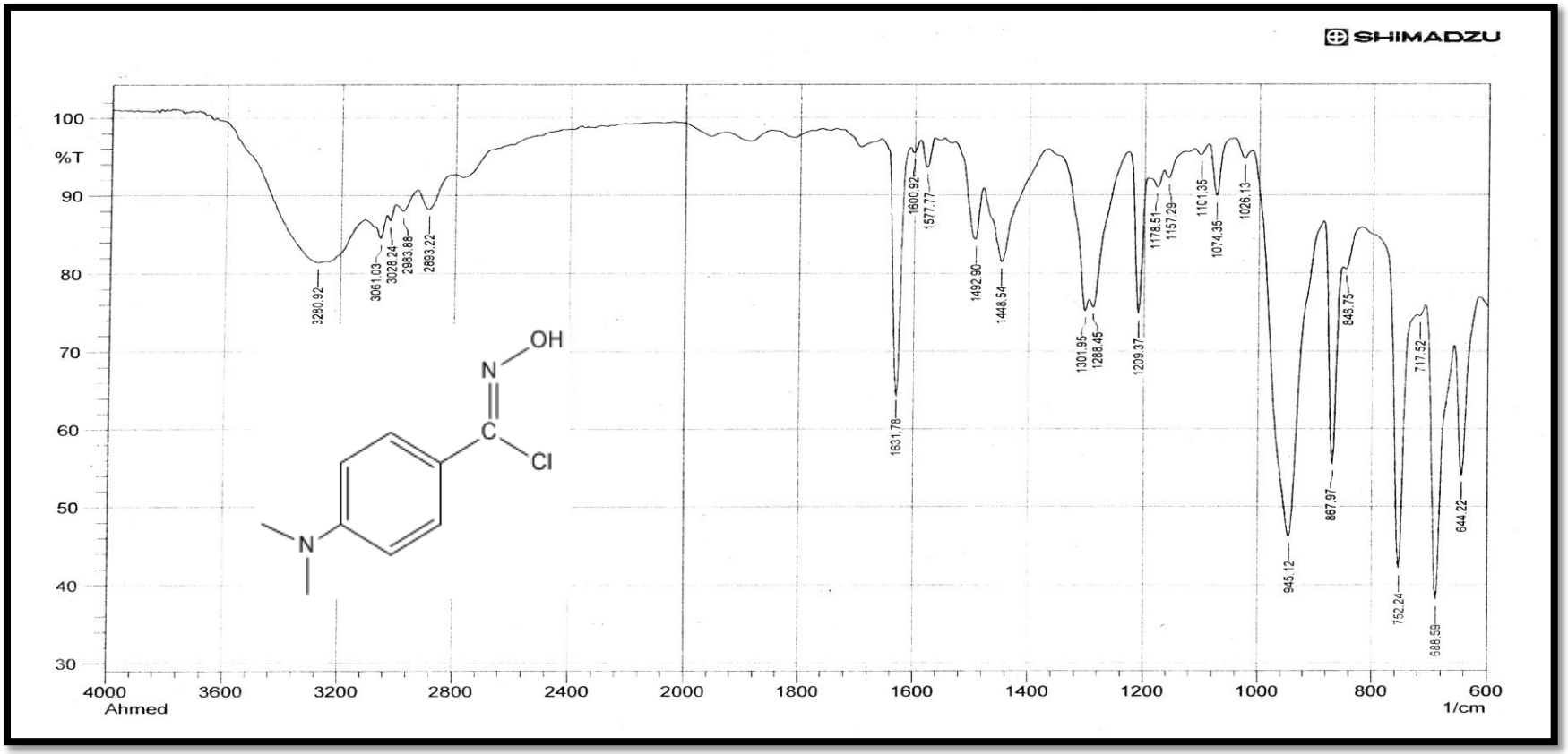


Figure (3-2) FTIR –spectrum of compound $[II]_d$

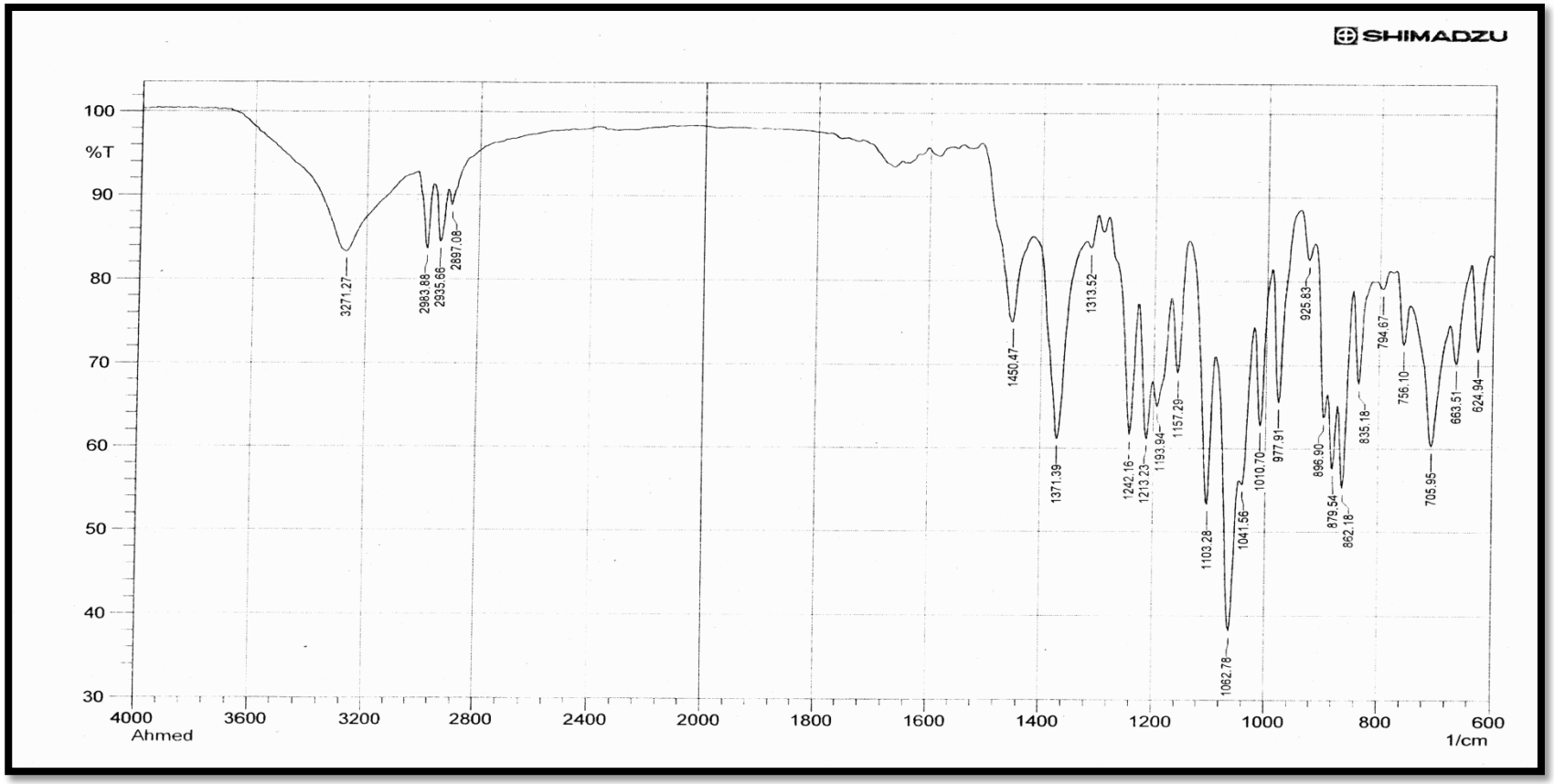


Figure (3-3) FTIR –spectrum of compound [III]

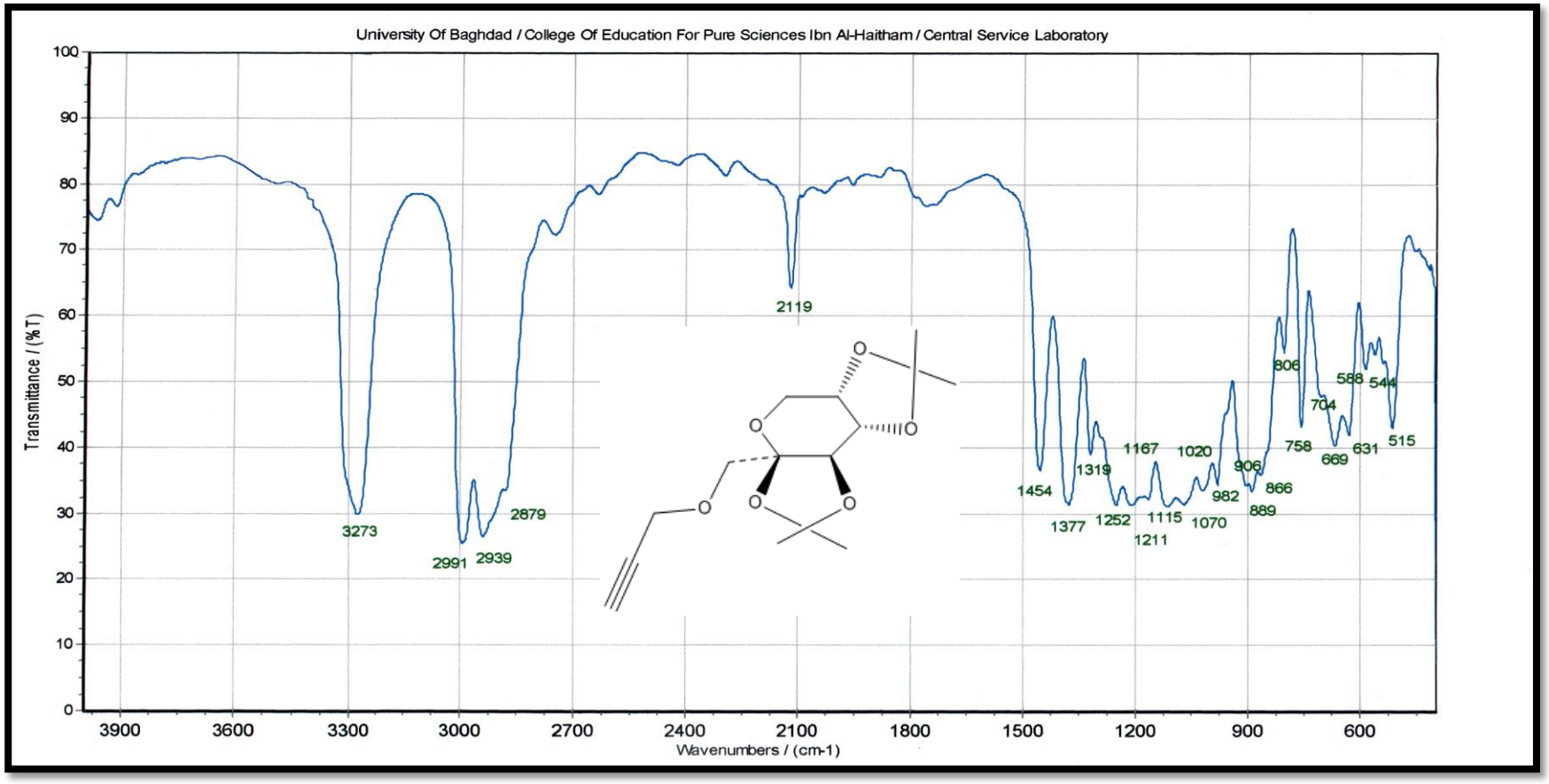


Figure (3-4) FTIR –spectrum of compound [IV]

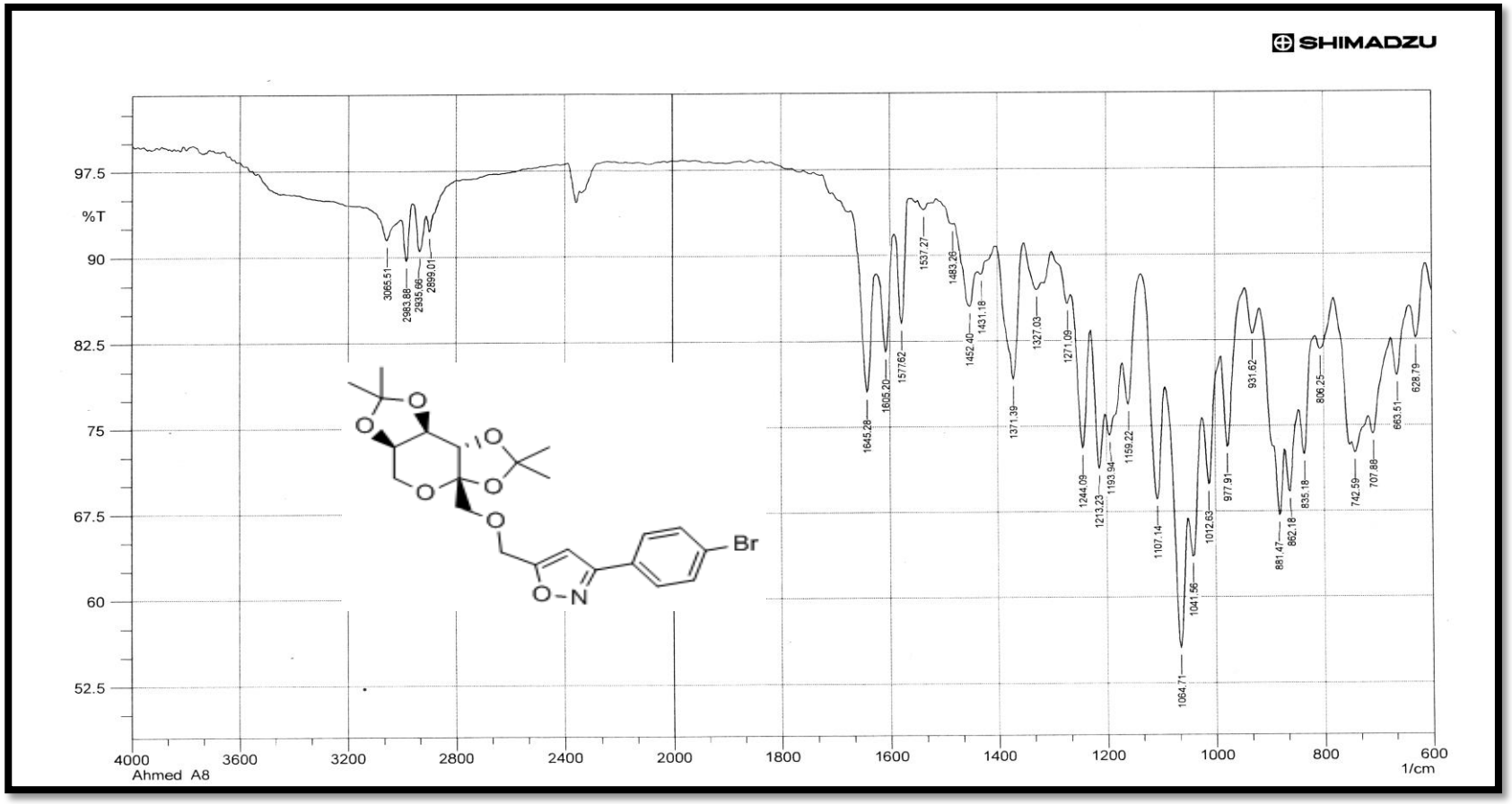


Figure (3-5) FT-IR –spectrum of compound $[V]_c$

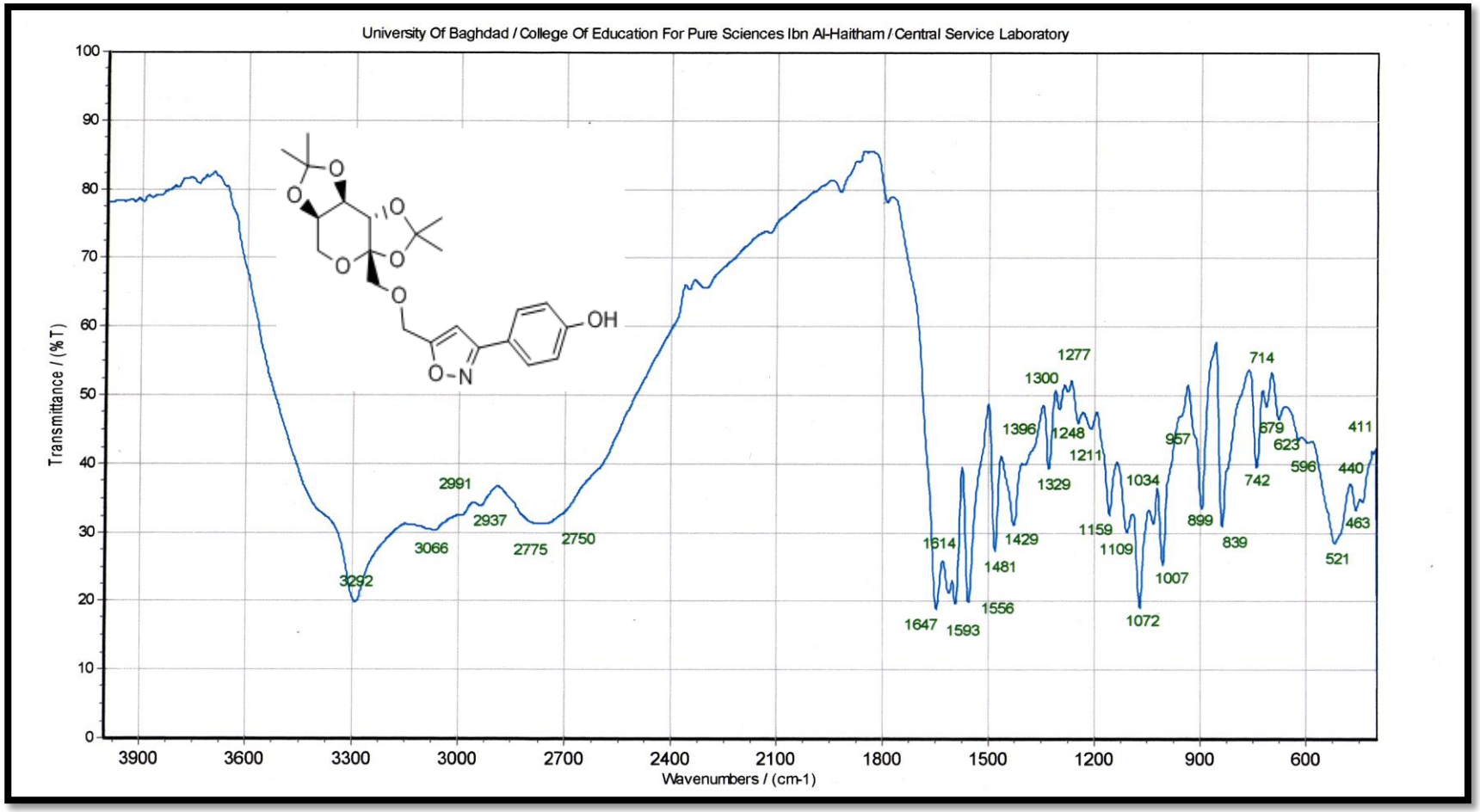


Figure (3-6) FTIR –spectrum of compound $[V]_b$

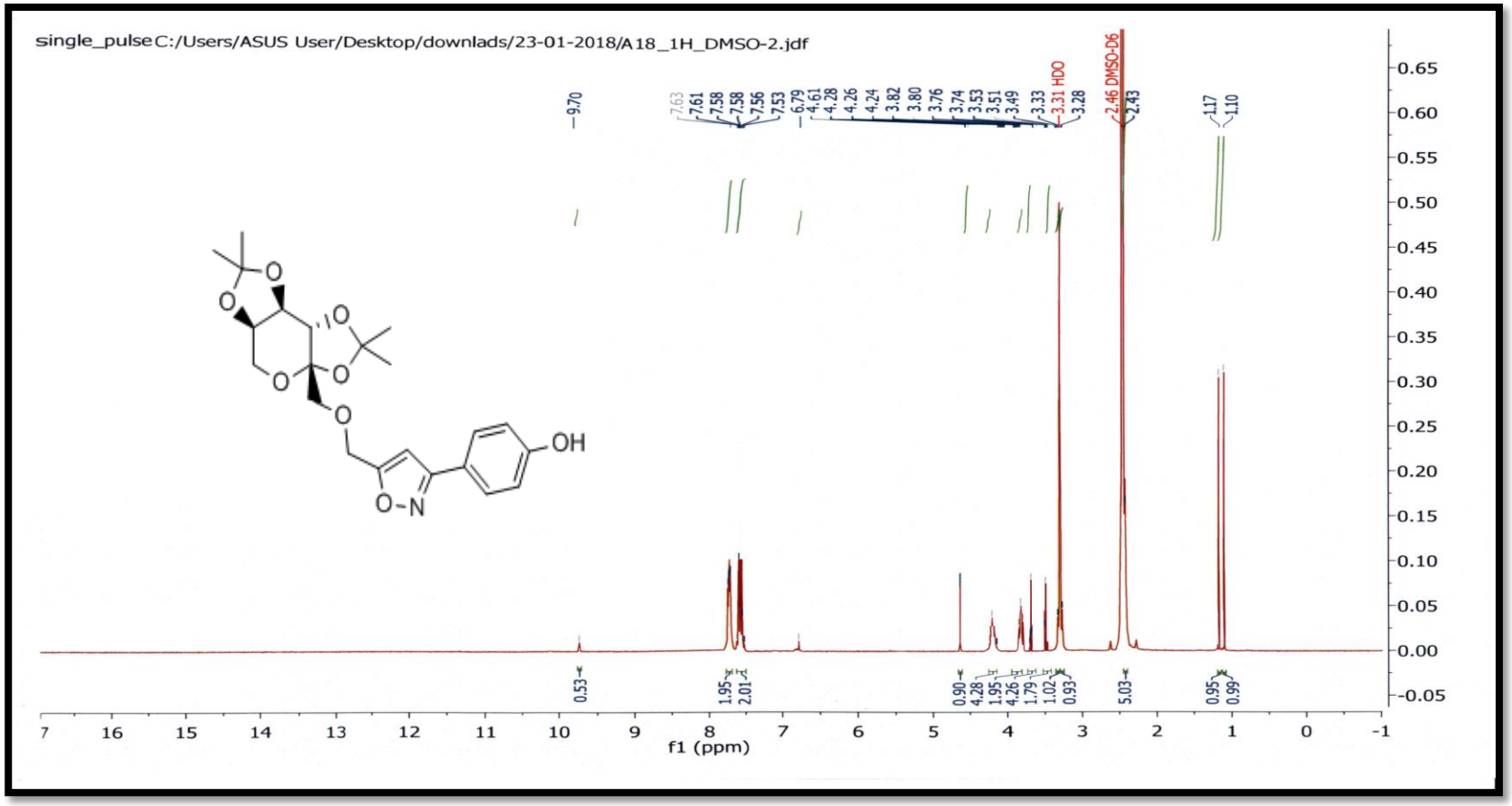


Figure (3-7) ^{1}H-NMR –spectrum of compound $[V]_b$

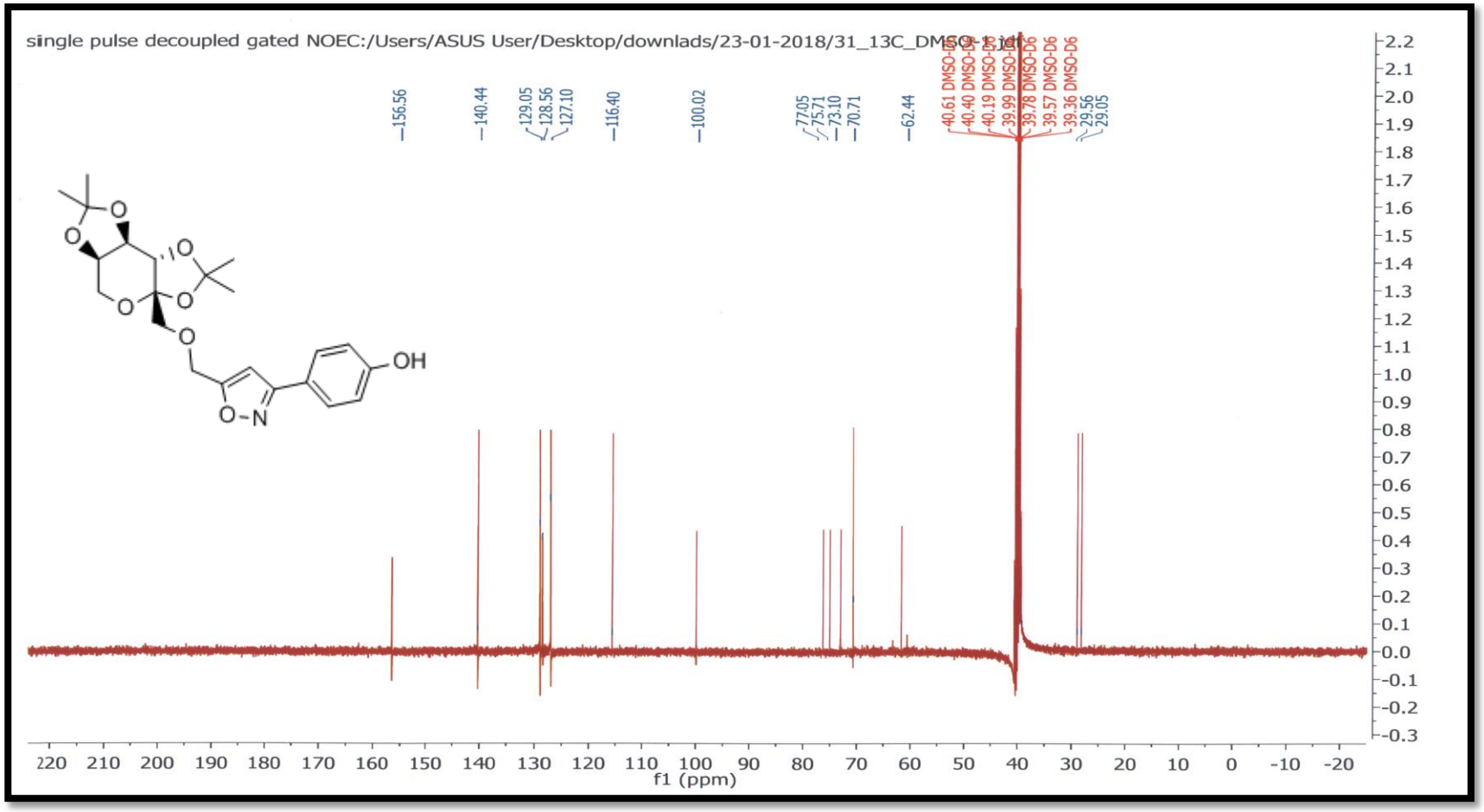


Figure (3-8)^{13}C-NMR –spectrum of compound $[V]_b$

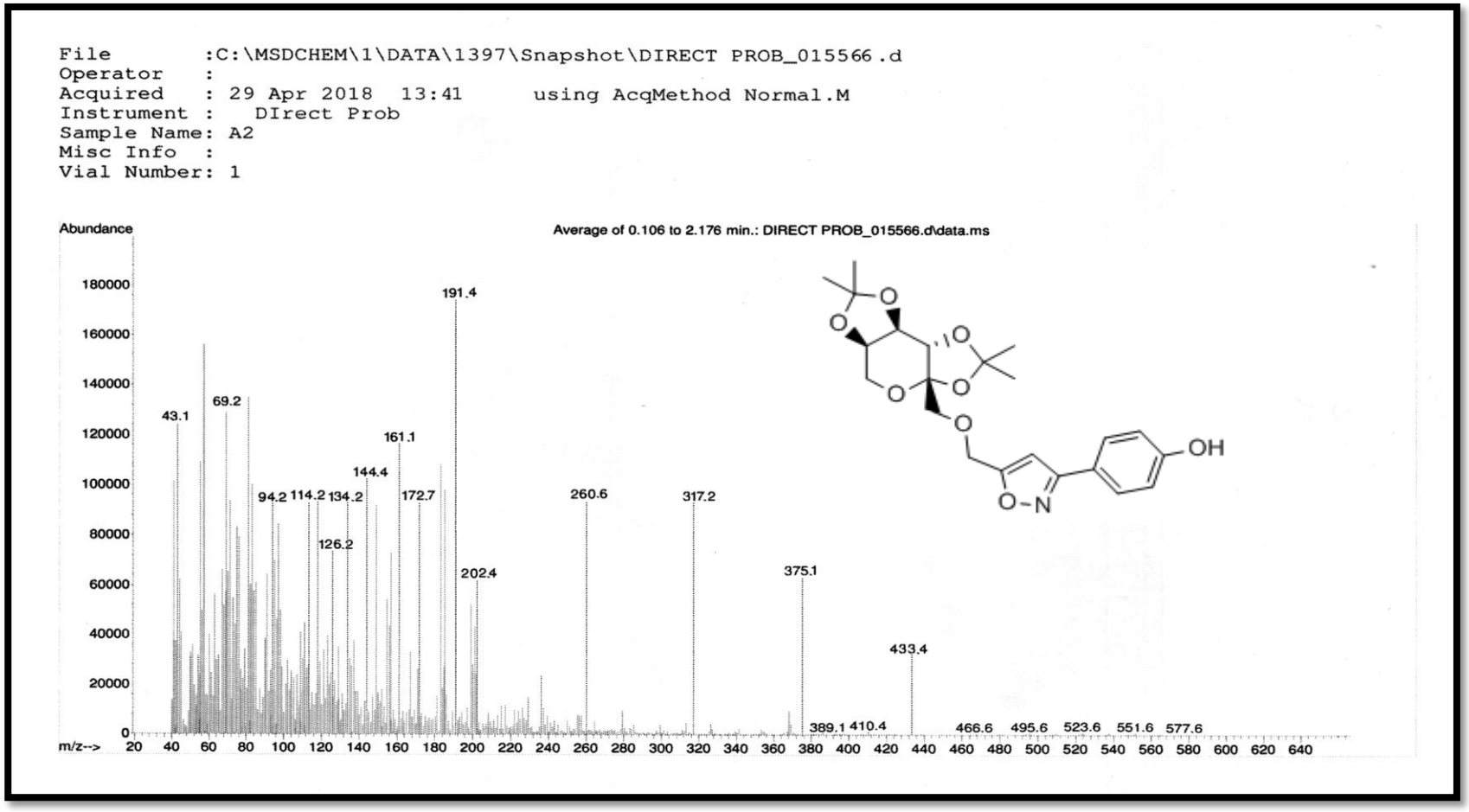


Figure (3-9)The mass spectrum of compound[V]$_{b}$

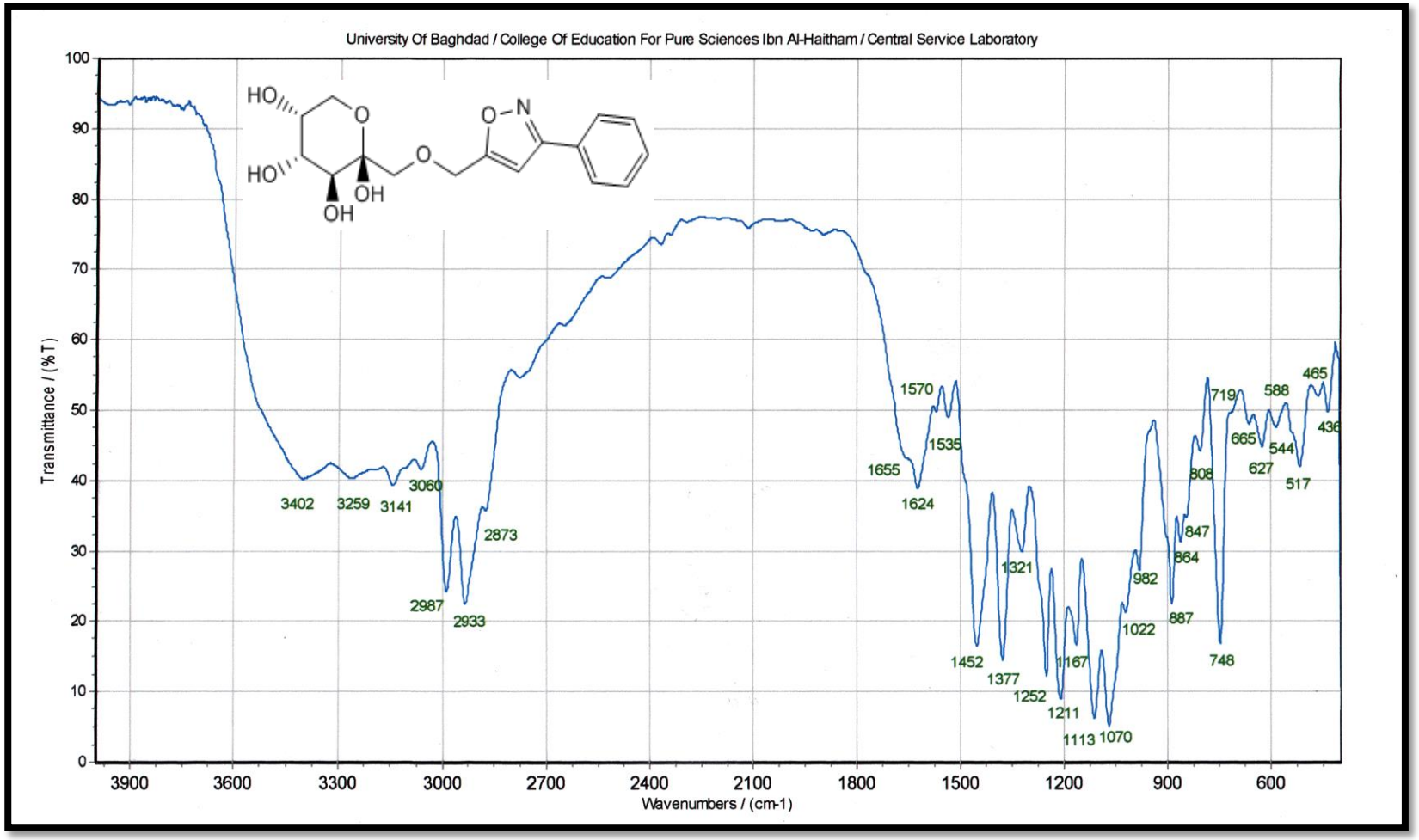


Figure (3-10) FTIR –spectrum of compound $[VI]_a$

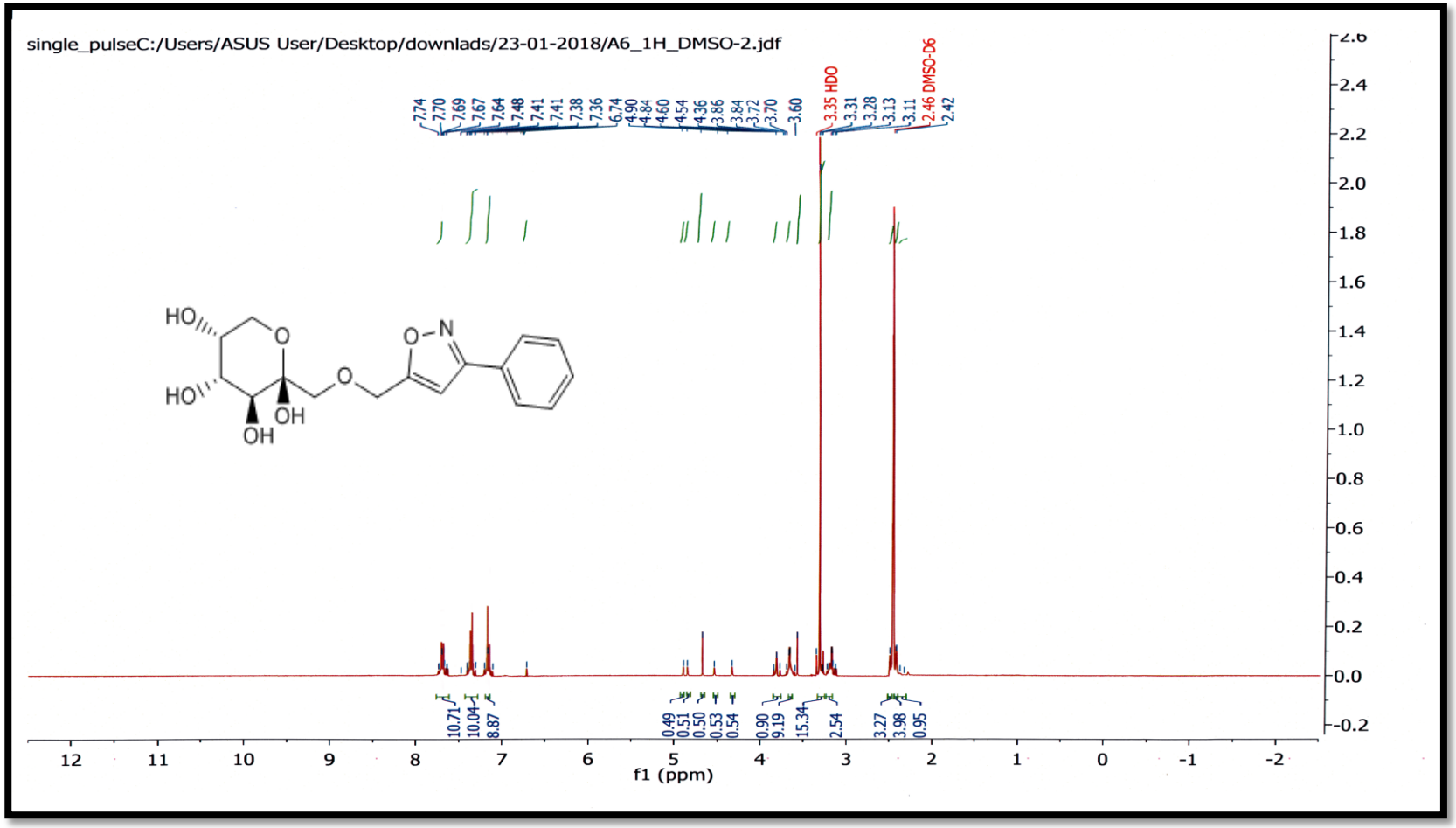


Figure (3-11) ^{1}H-NMR –spectrum of compound $[VI]_a$

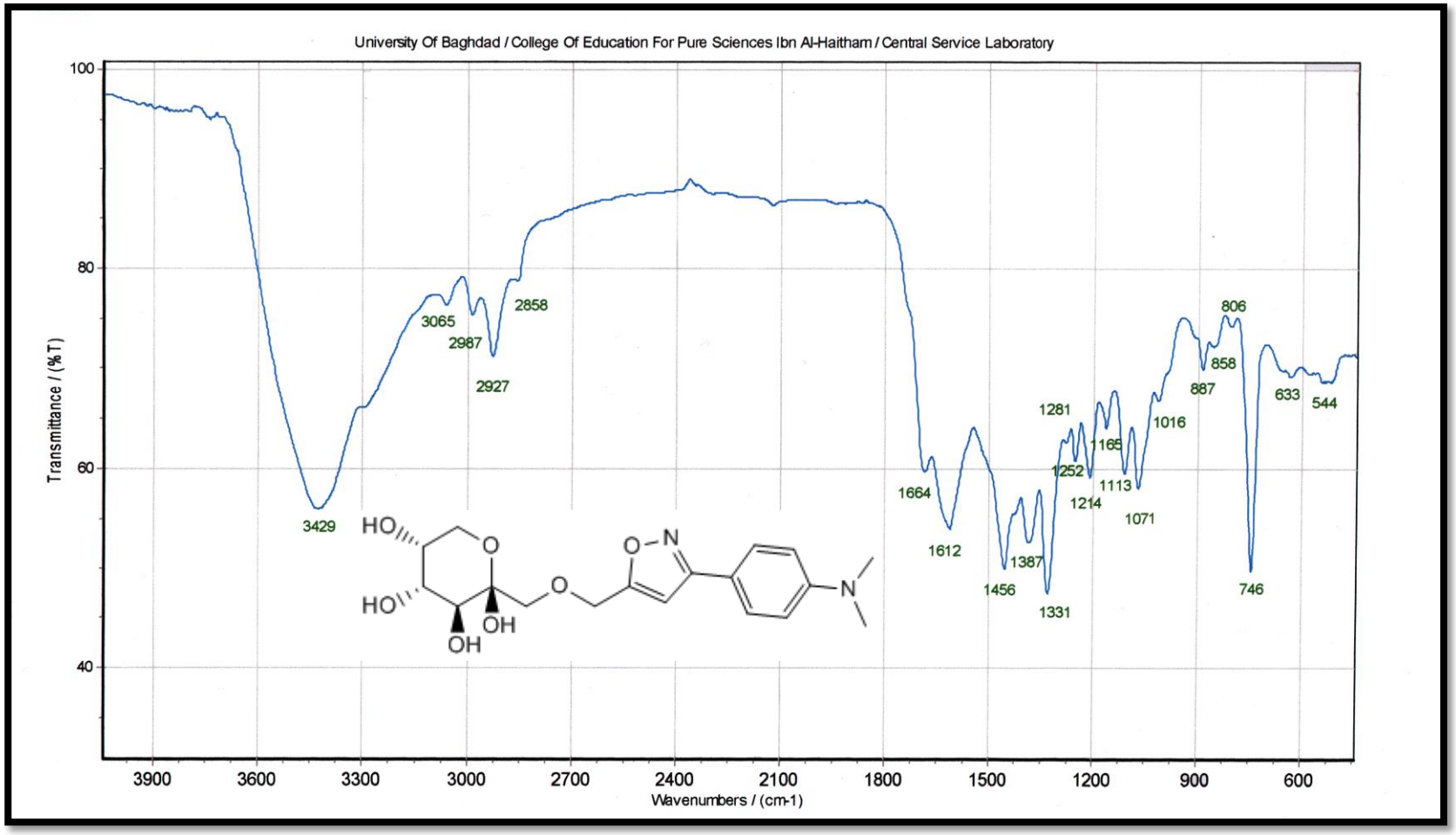


Figure (3-12) FT-IR –spectrum of compound $[VI]_d$

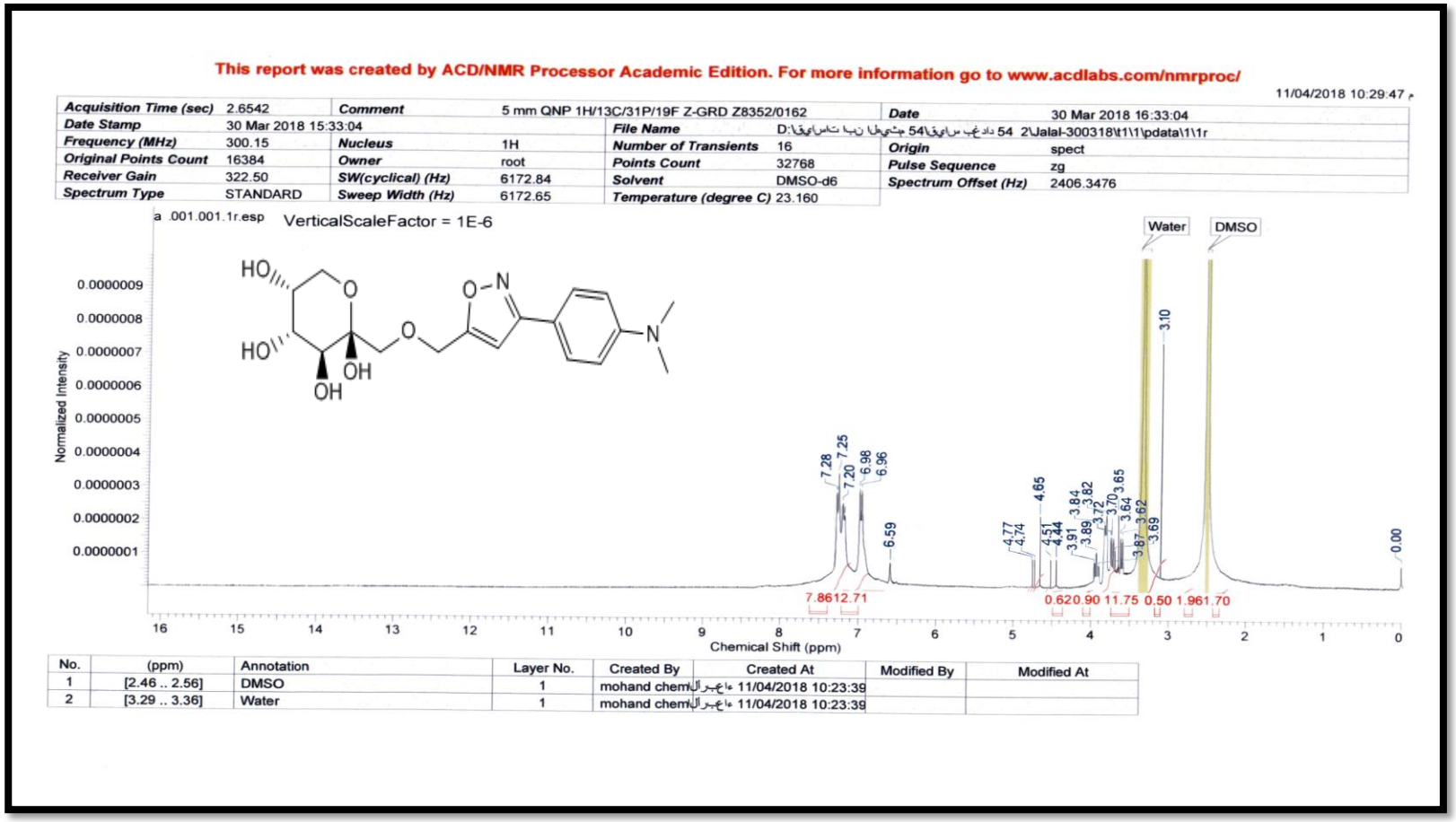


Figure (3-13) ^{1}H-NMR –spectrum of compound $[VI]_d$

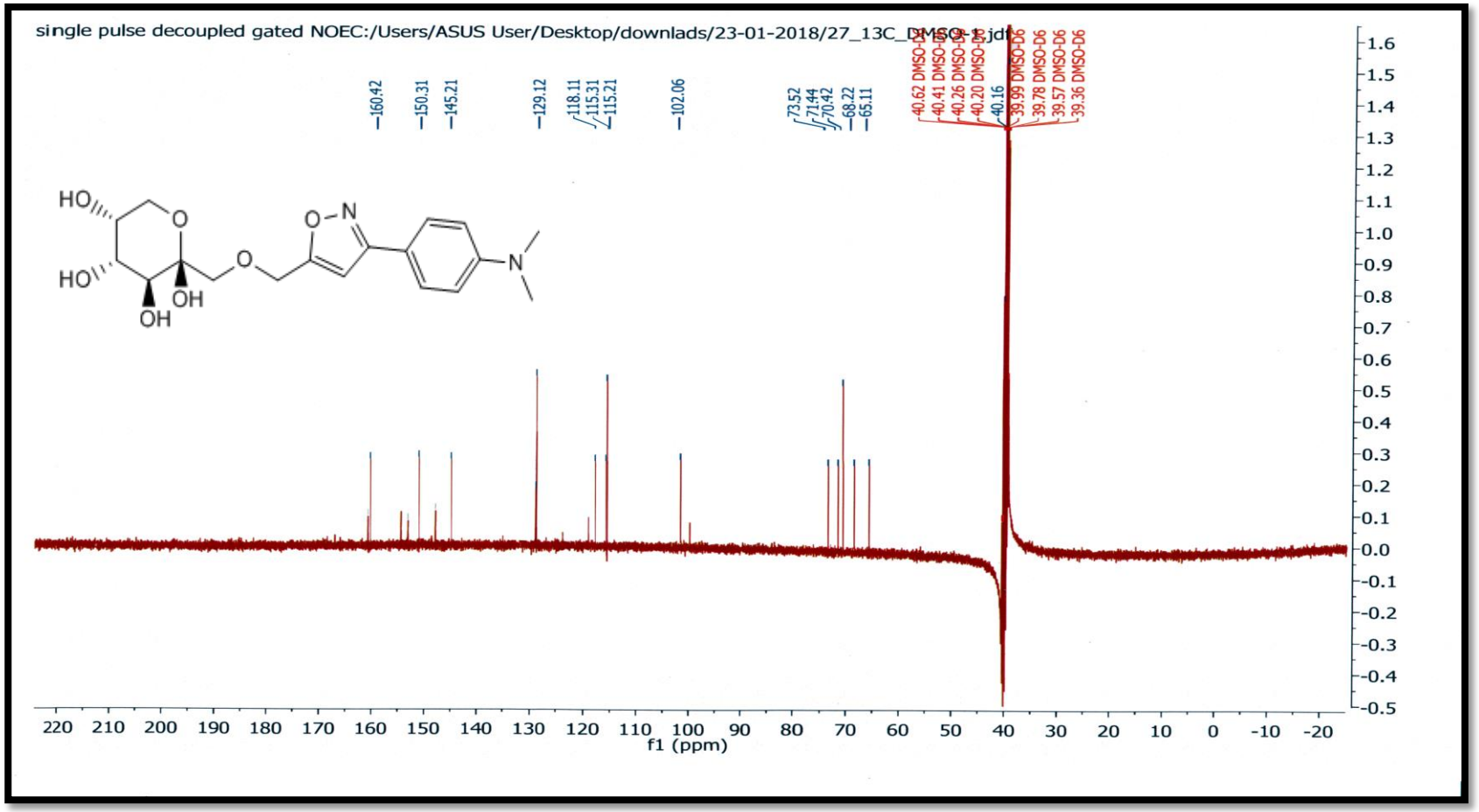


Figure (3-14)^{13}C-NMR –spectrum of compound $[VI]_d$

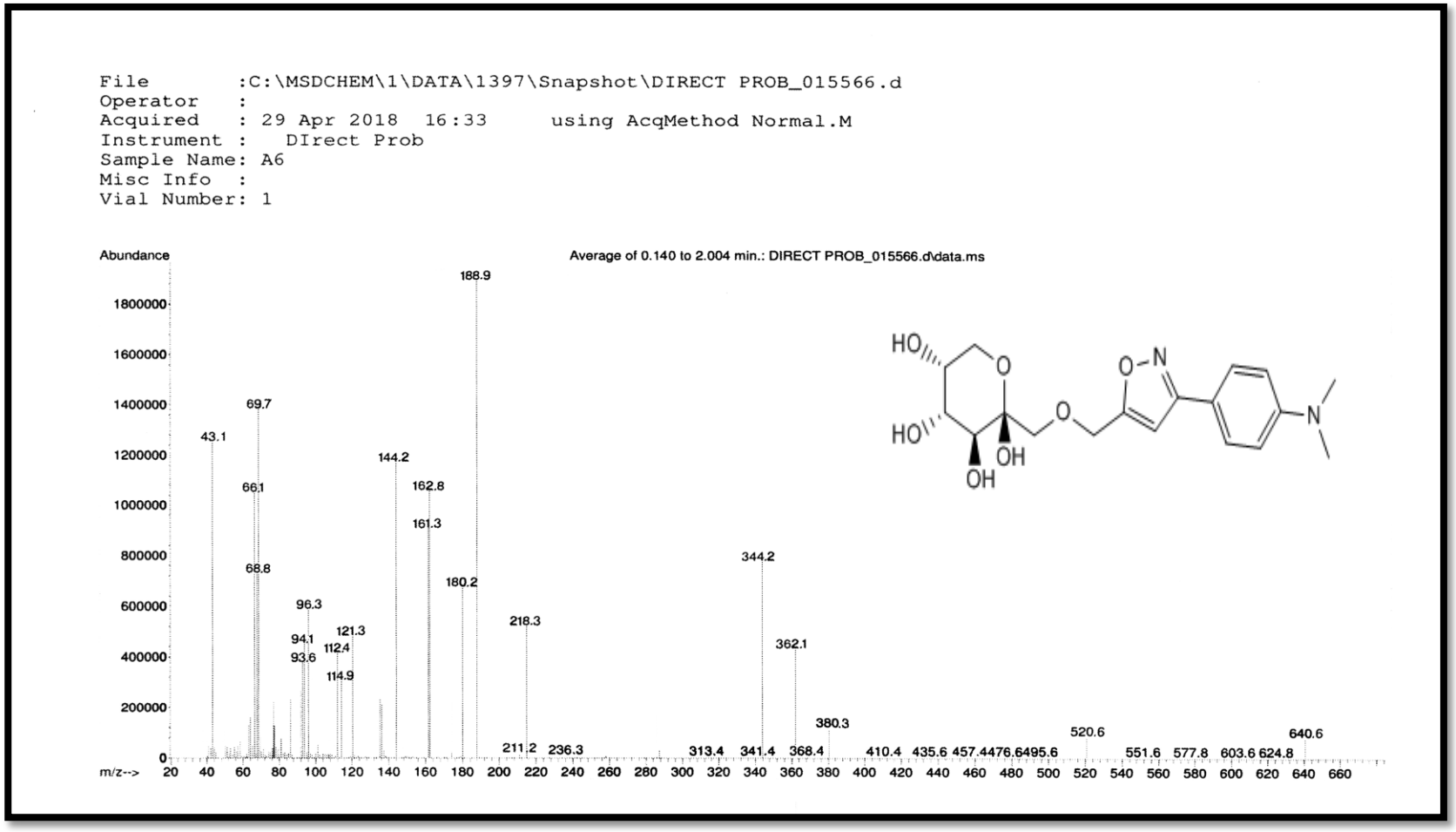


Figure (3-15)The mass spectrum of compound[VI]$_{d}$

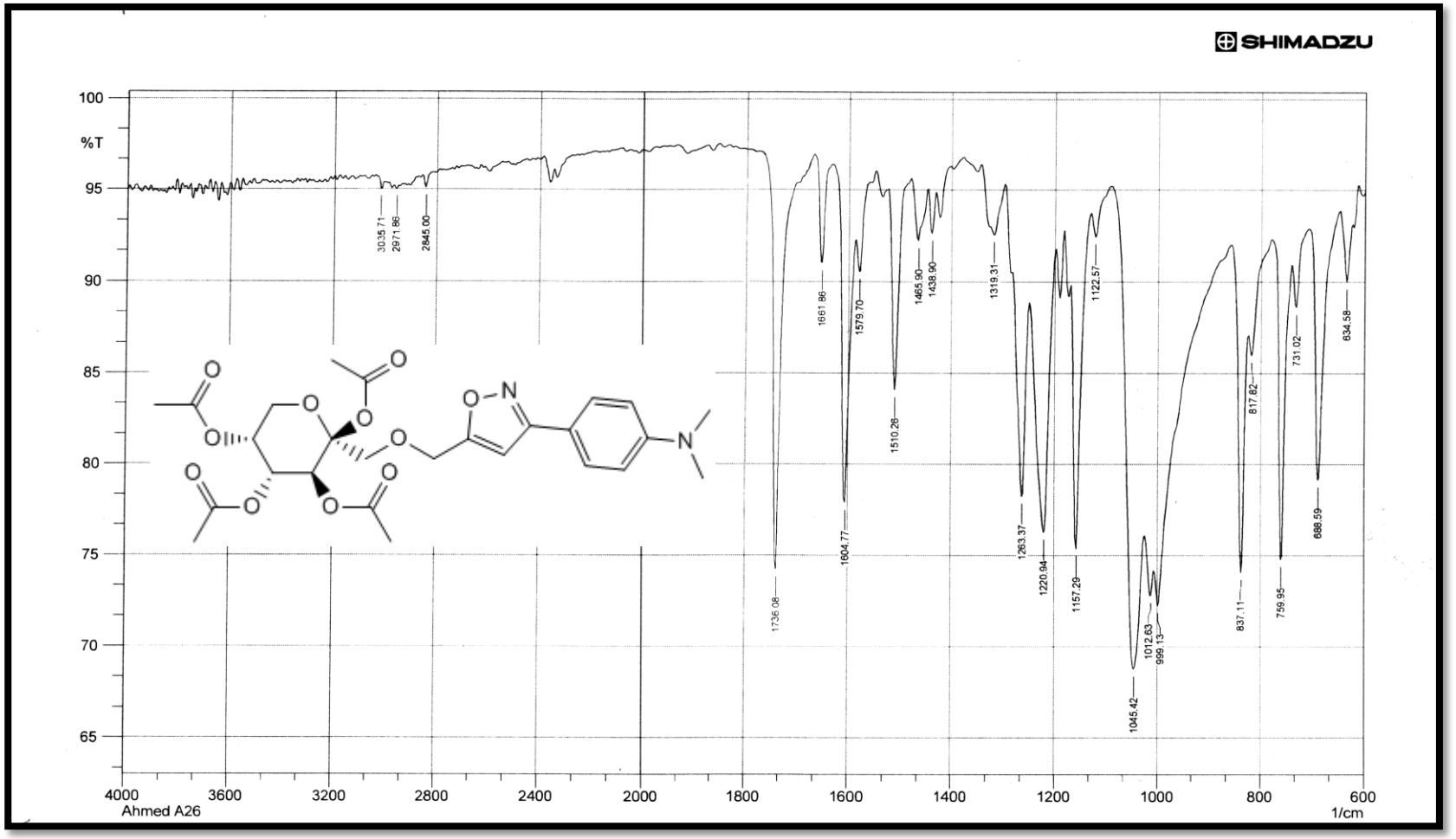


Figure (3-16) FT-IR –spectrum of compound $[VII]_d$

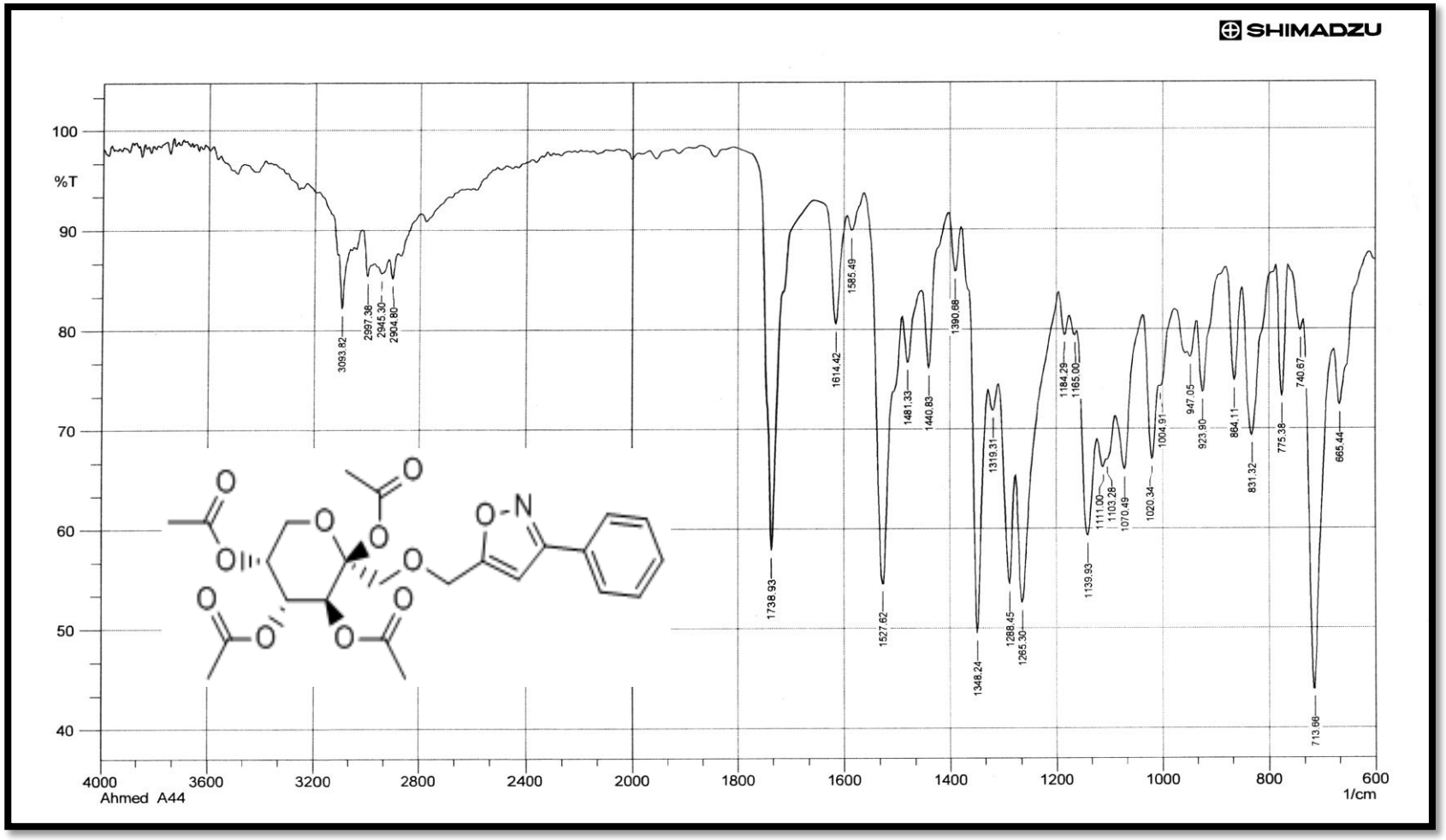


Figure (3-17) FT-IR –spectrum of compound $[VII]_a$

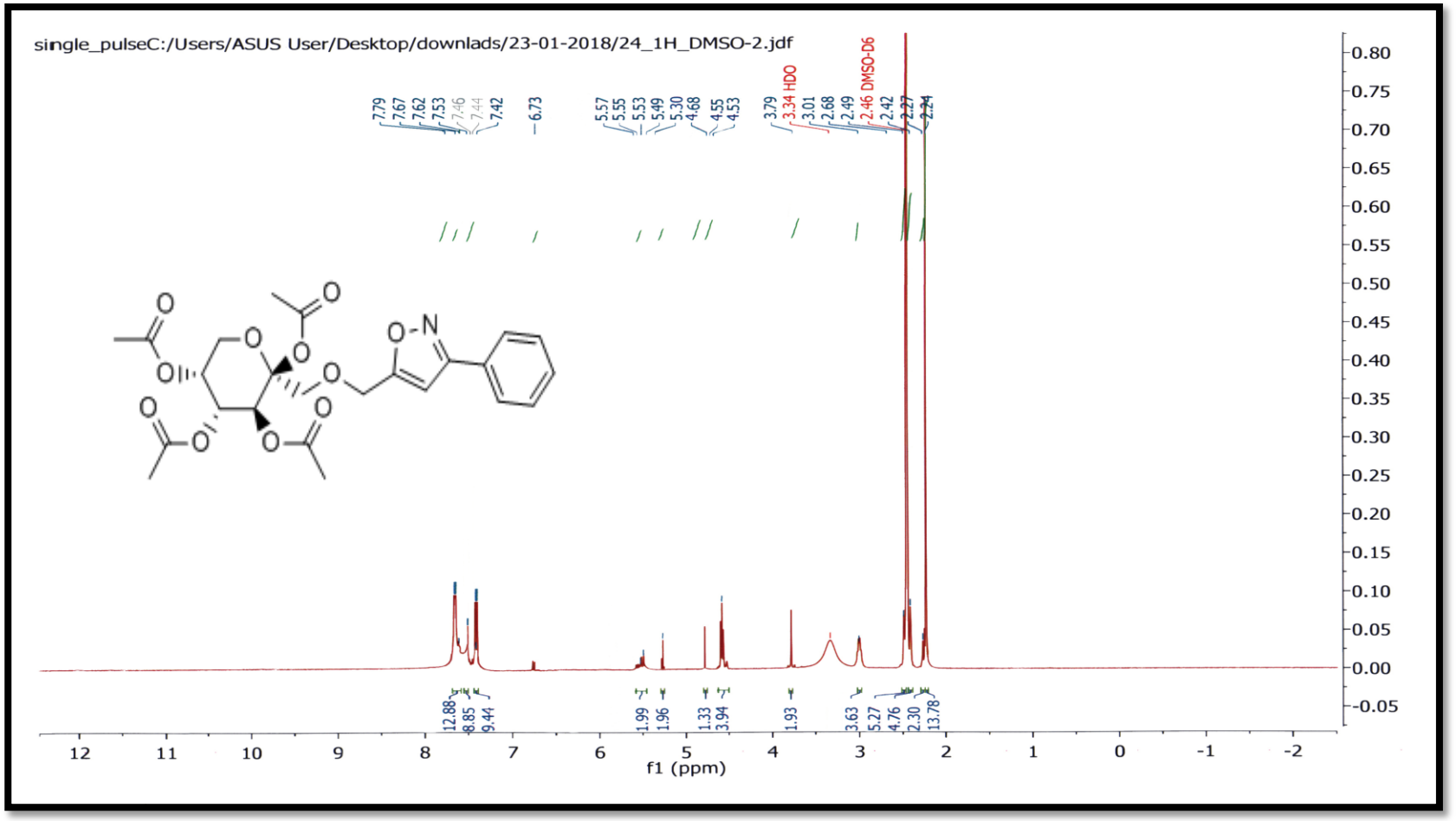


Figure (3-18) ^{1}H-NMR –spectrum of compound [VII]$_a$

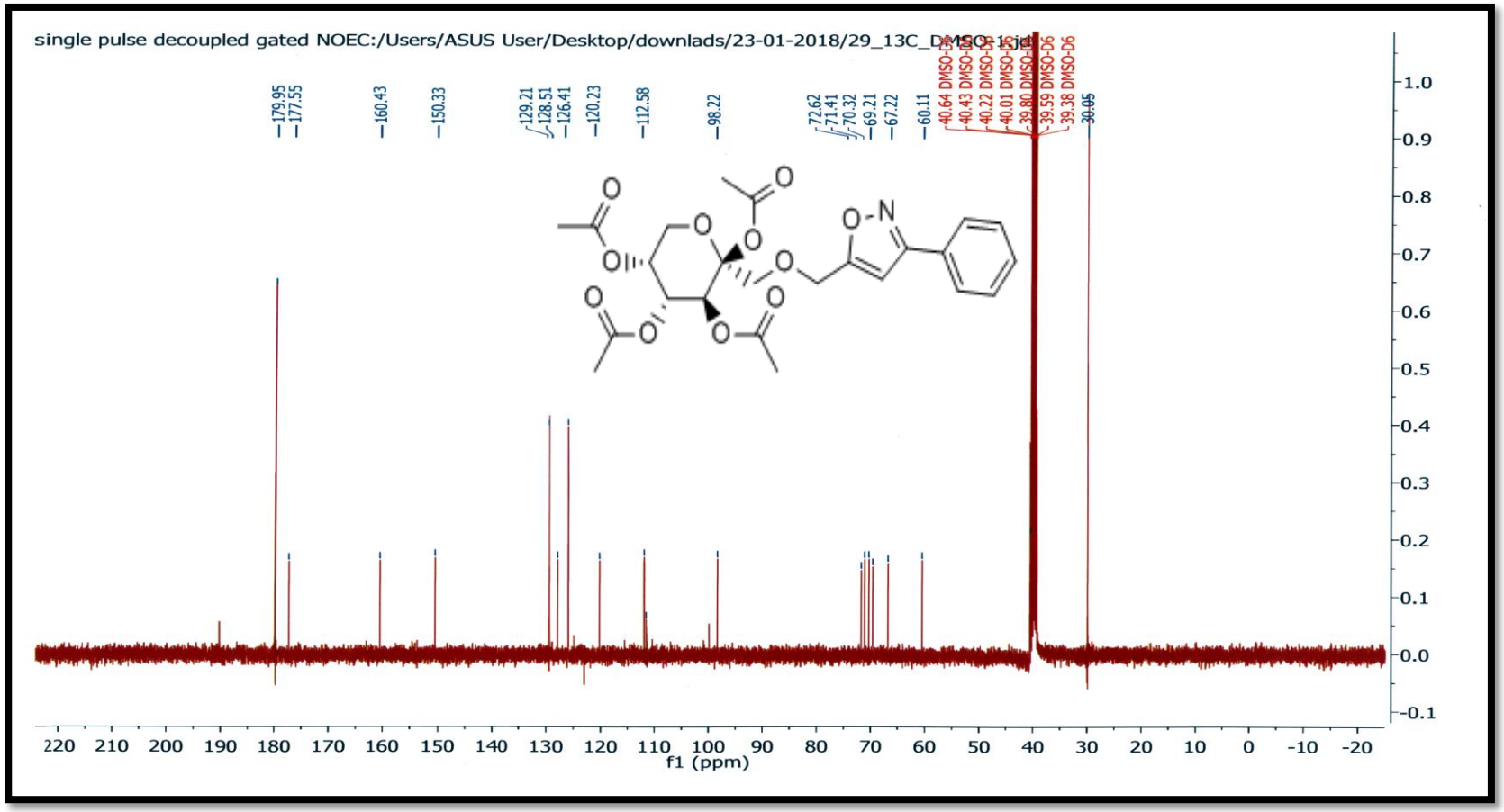


Figure (3-19)^{13}C-NMR –spectrum of compound $[VII]_a$

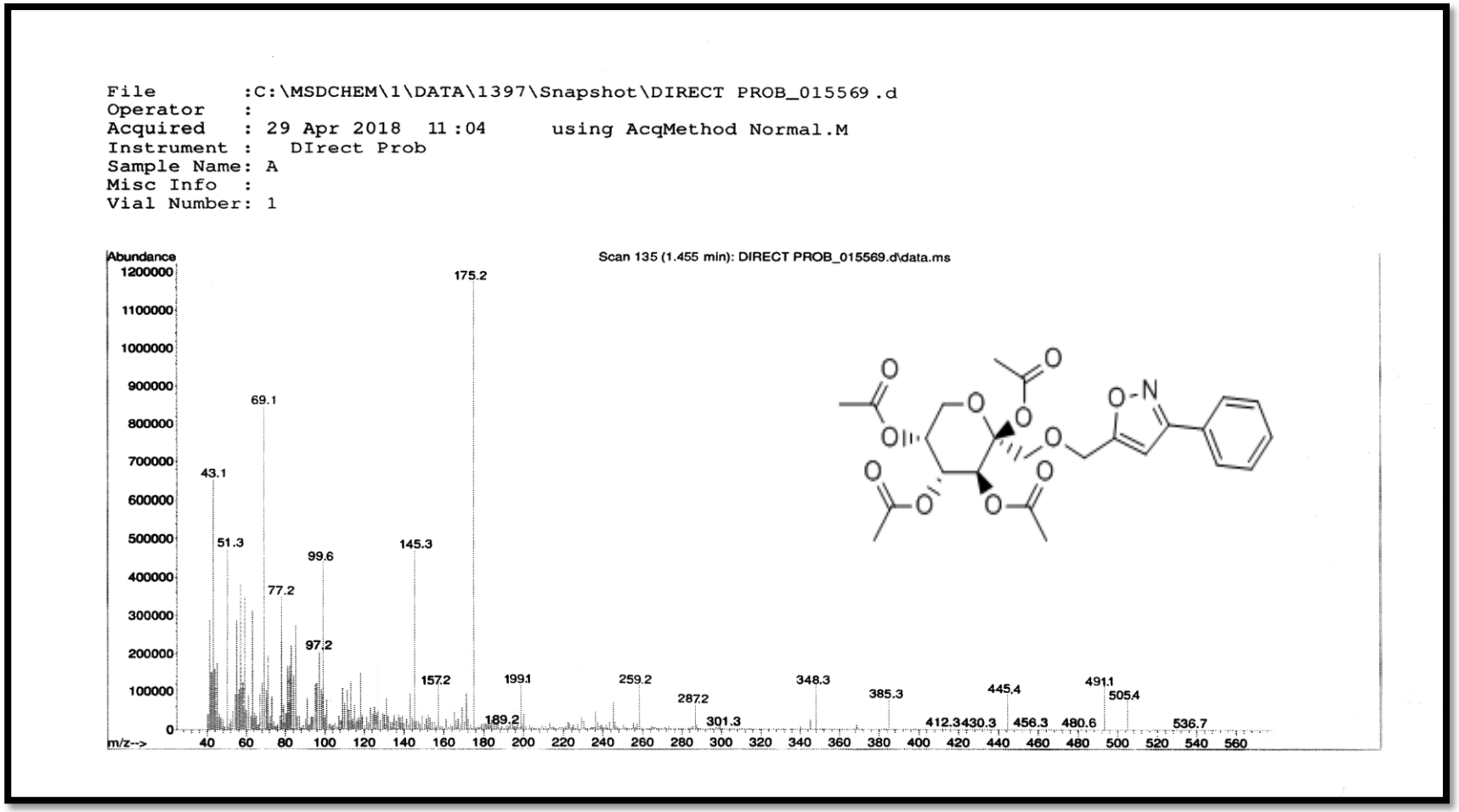


Figure (3-20)The mass spectrum of compound[VII] **a**

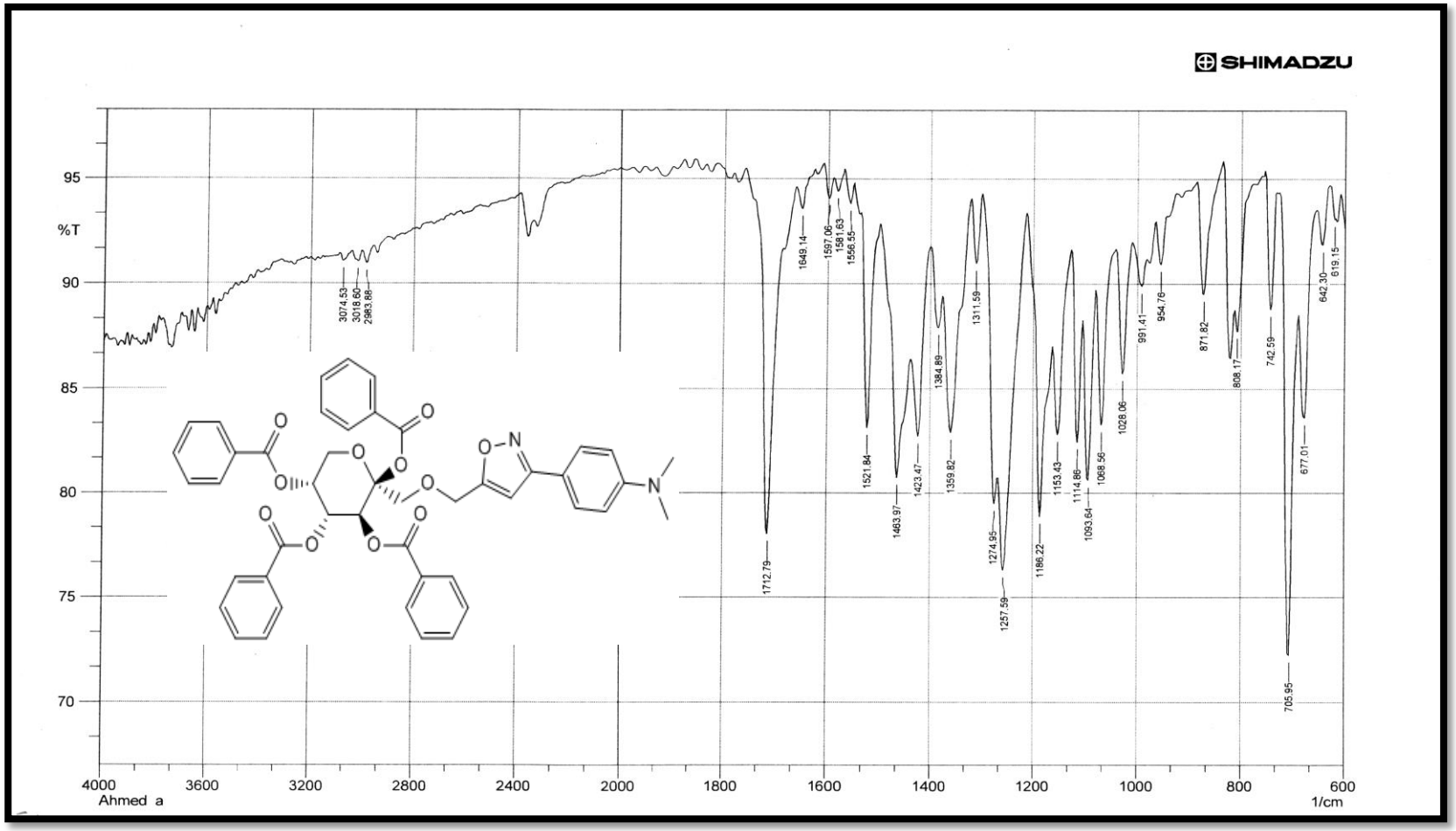


Figure (3-21) FT-IR –spectrum of compound $[VIII]_d$

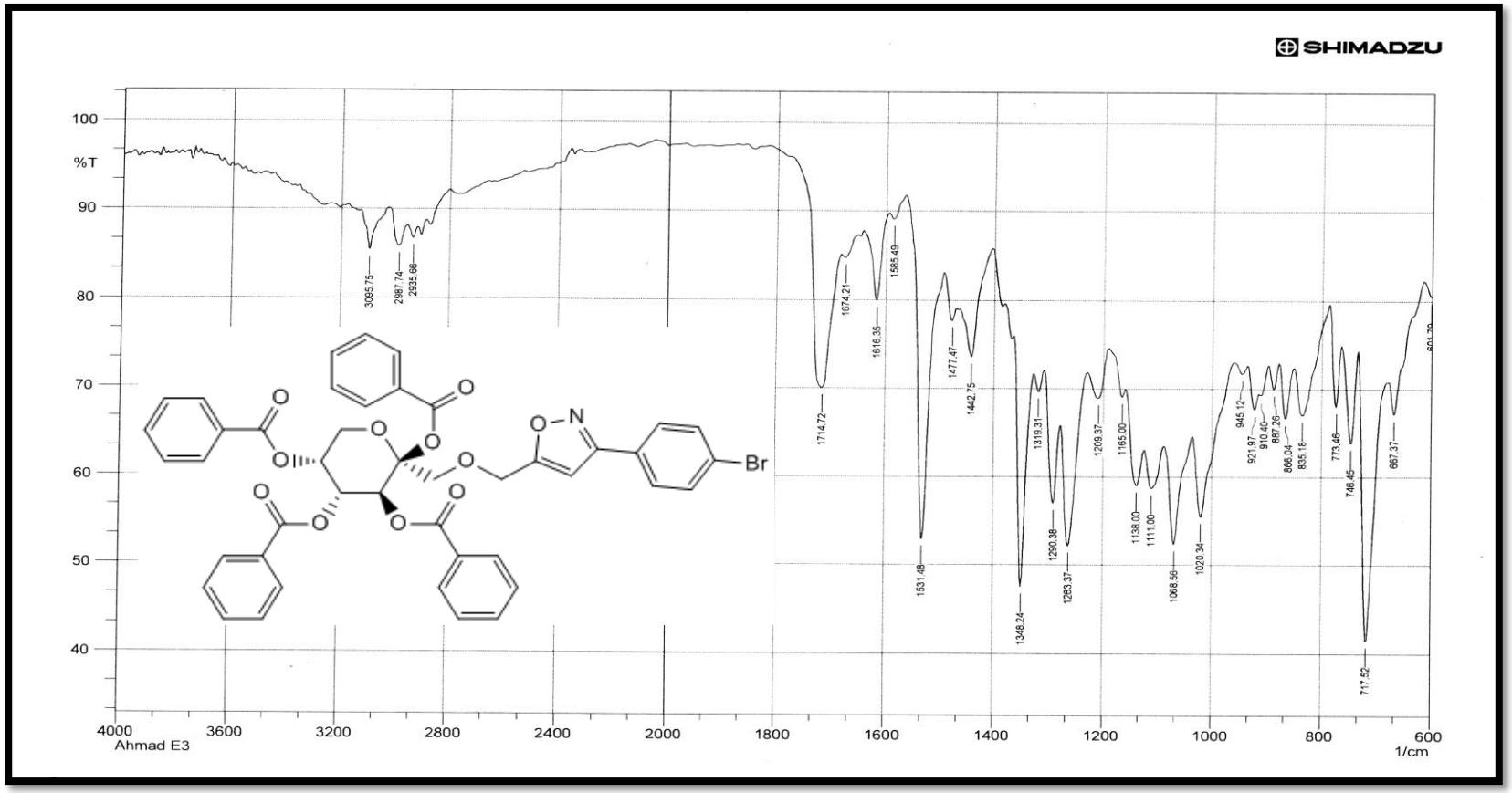


Figure (3-22) FT-IR –spectrum of compound $[VIII]_c$

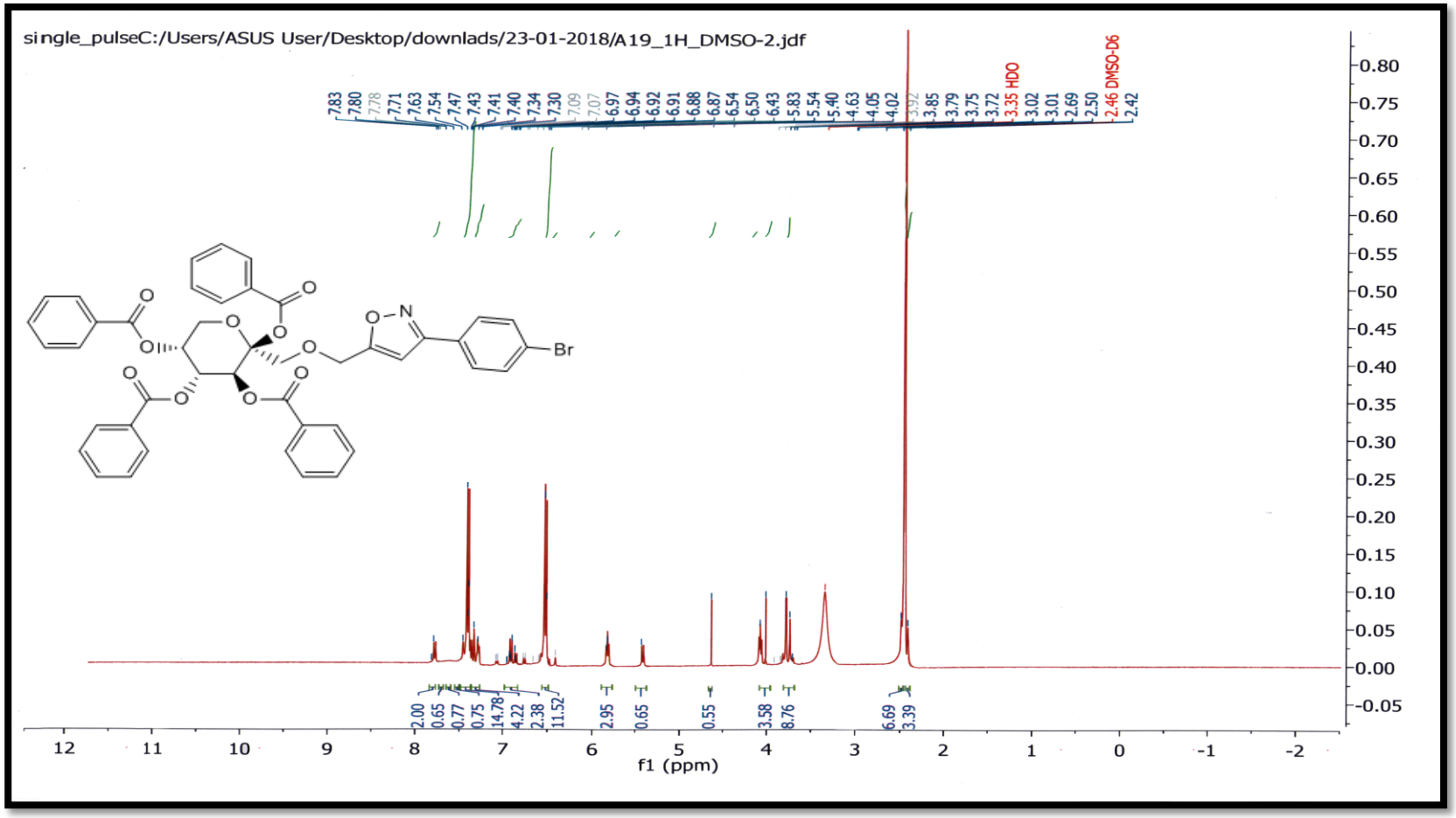


Figure (3-23) ^{1}H-NMR –spectrum of compound [VIII]$_c$

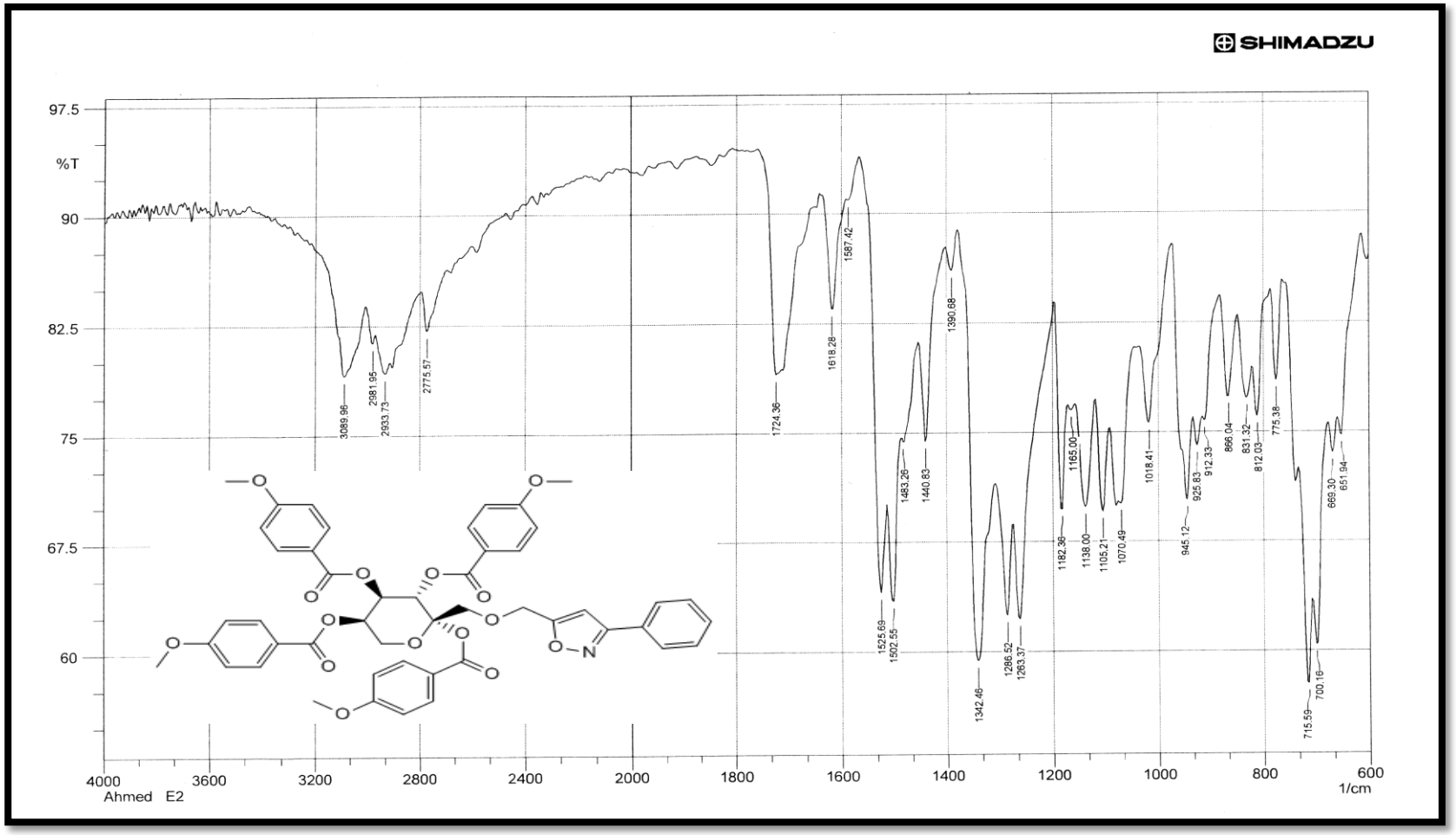


Figure (3-24) FT-IR –spectrum of compound $[IX]_a$

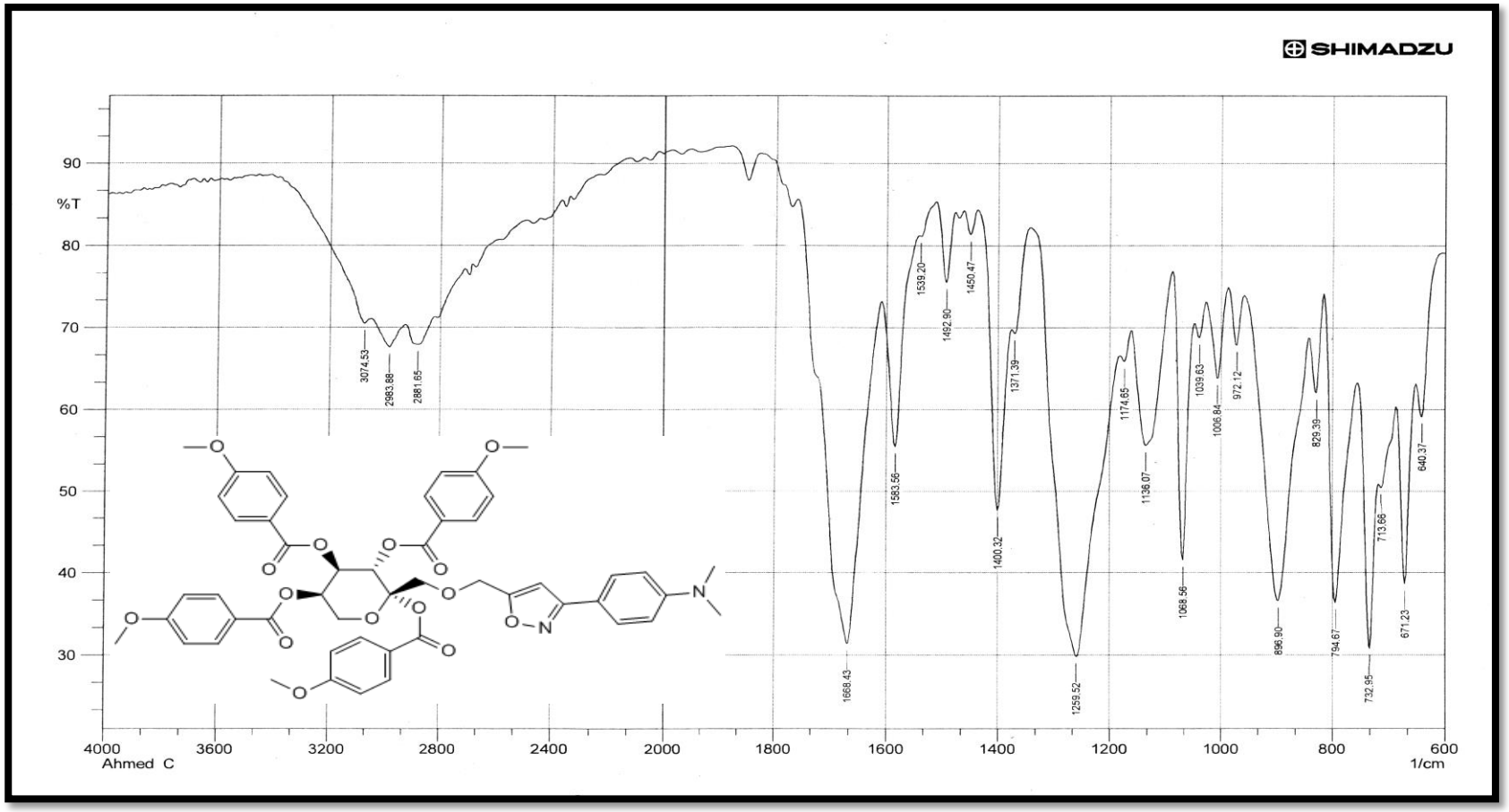


Figure (3-25) FT-IR –spectrum of compound $[IX]_d$

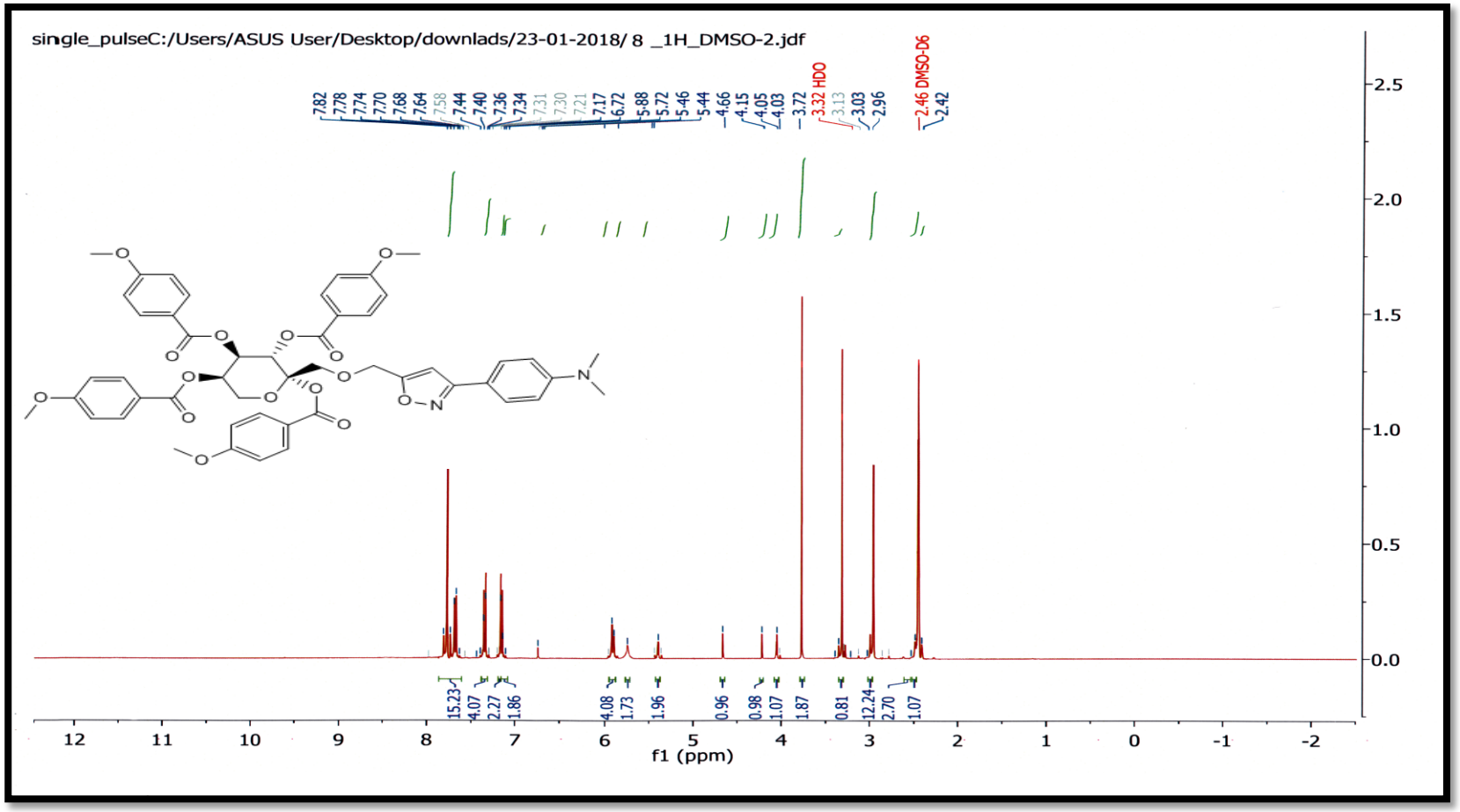


Figure (3-26) ^{1}H-NMR –spectrum of compound $[IX]_d$

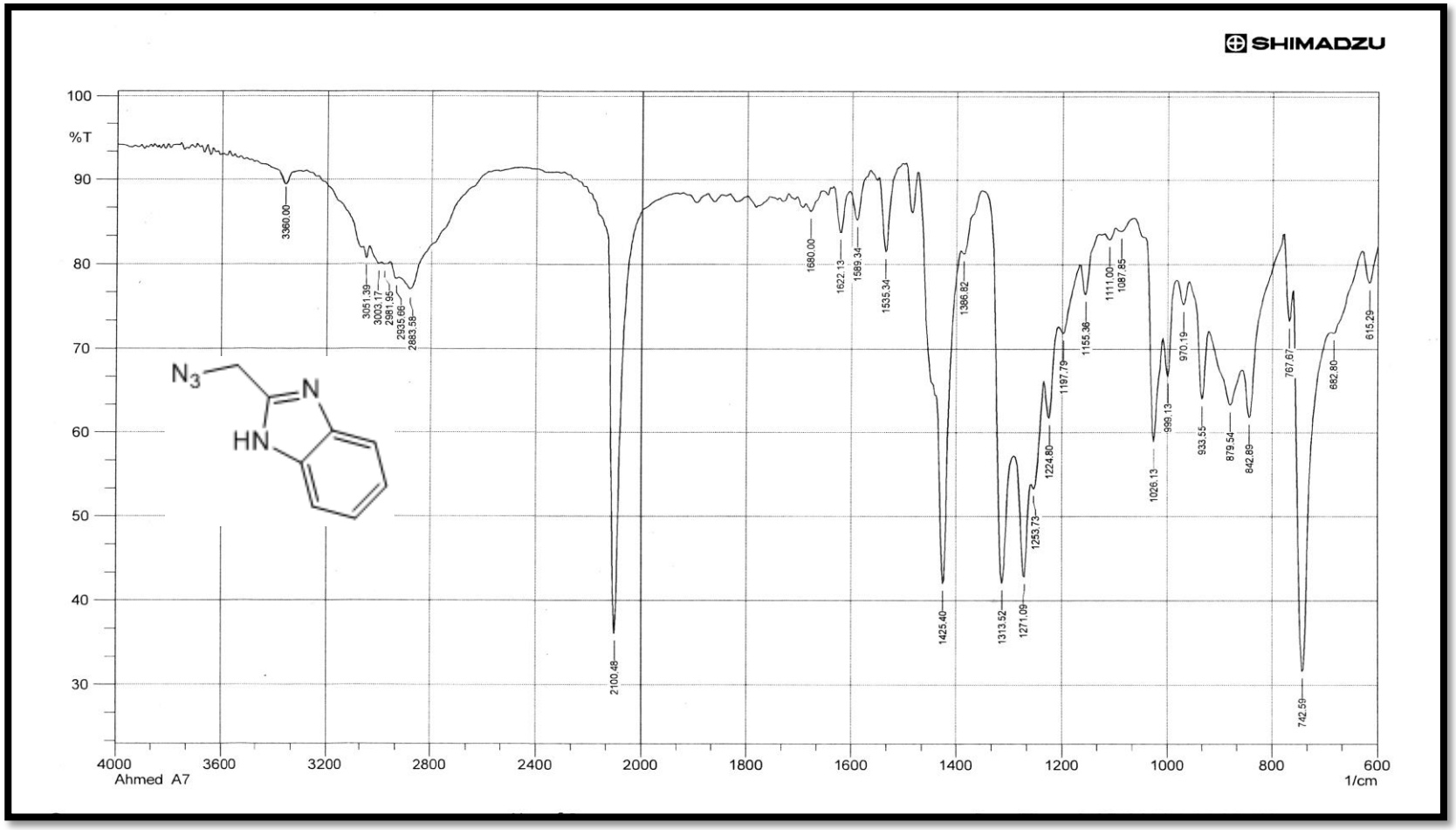


Figure (3-27) FT-IR –spectrum of compound [X]

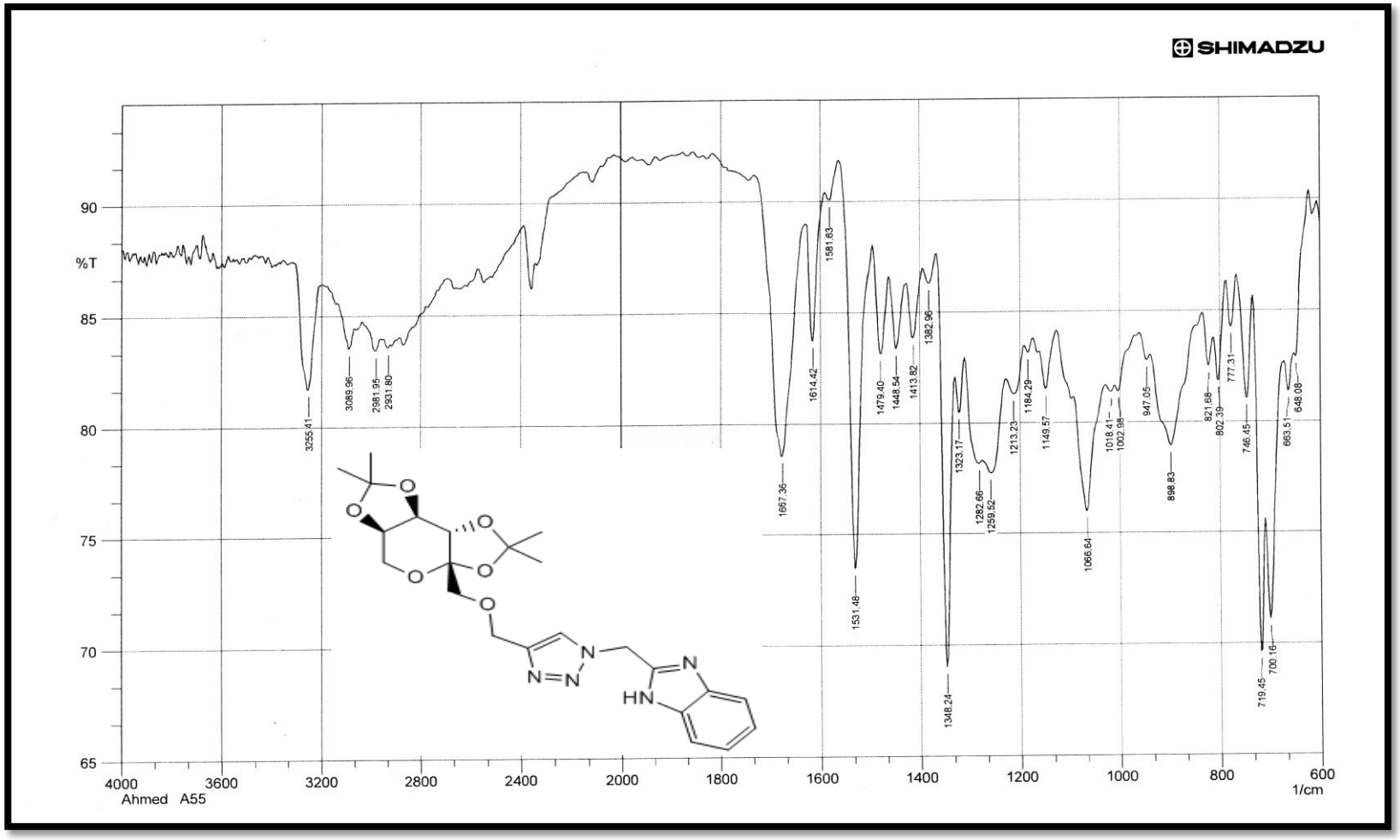


Figure (3-28) FT-IR –spectrum of compound [XI]

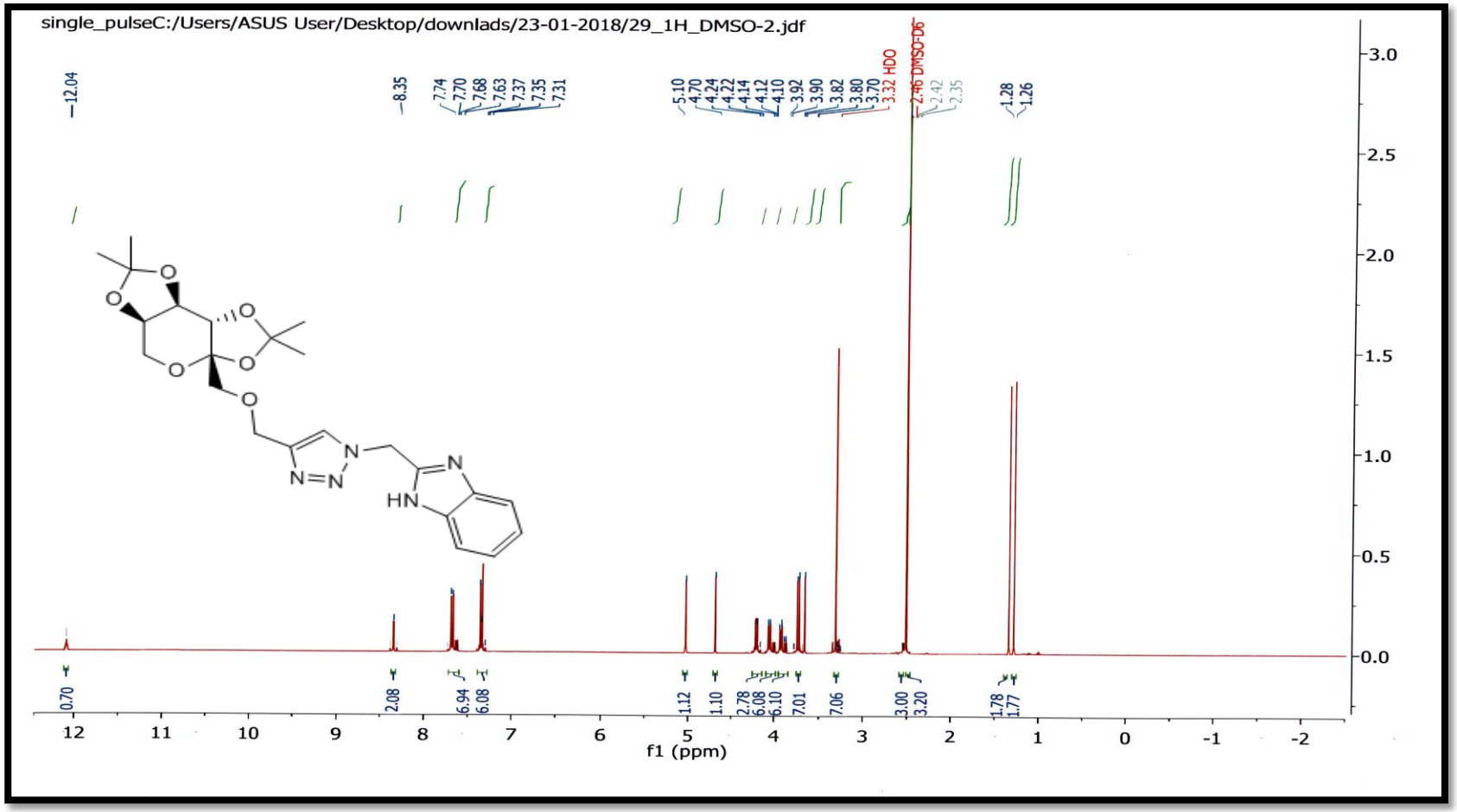


Figure (3-29) ^{1}H-NMR –spectrum of compound [XI]

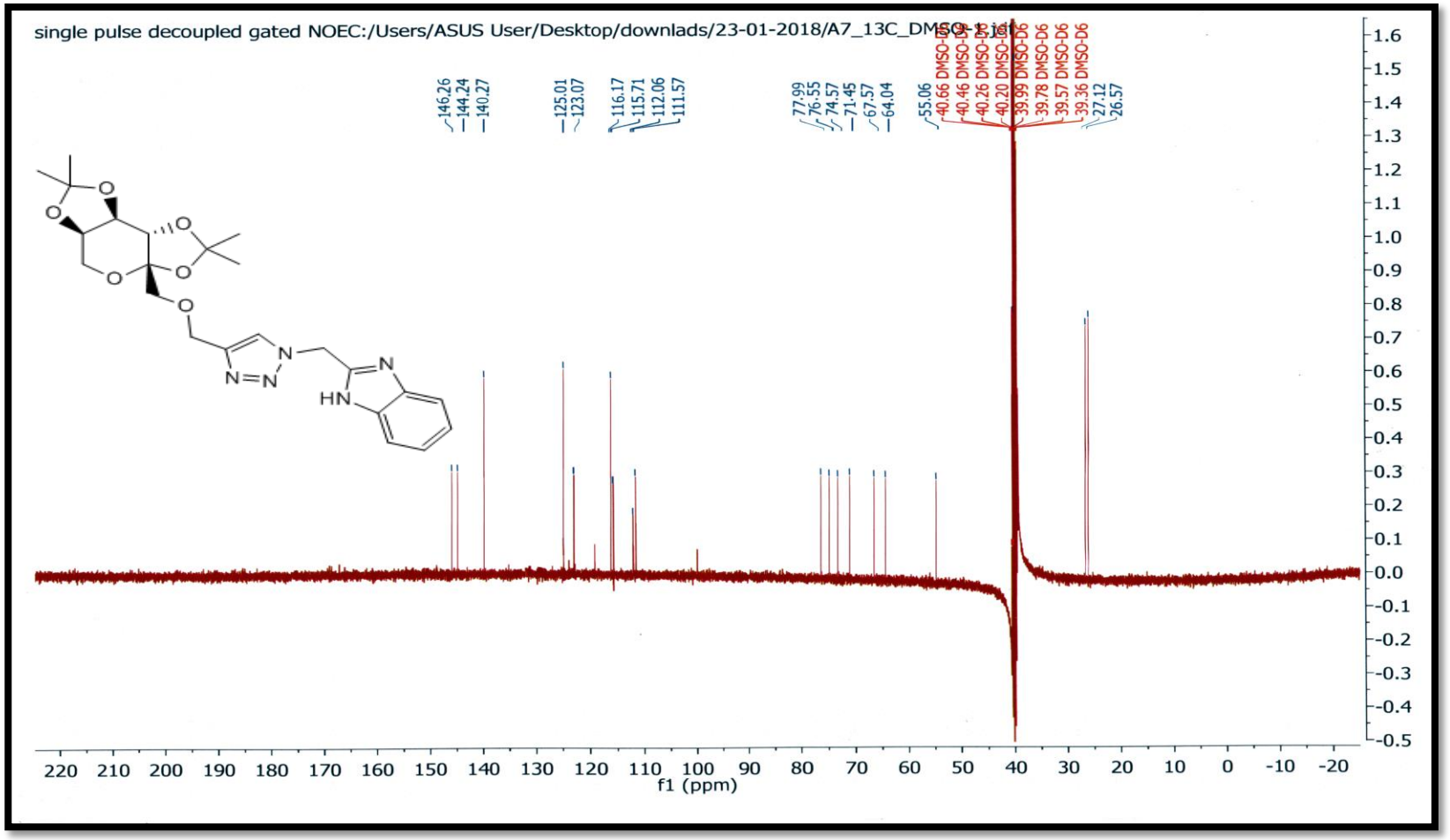


Figure (3-30)^{13}C-NMR –spectrum of compound [XI]

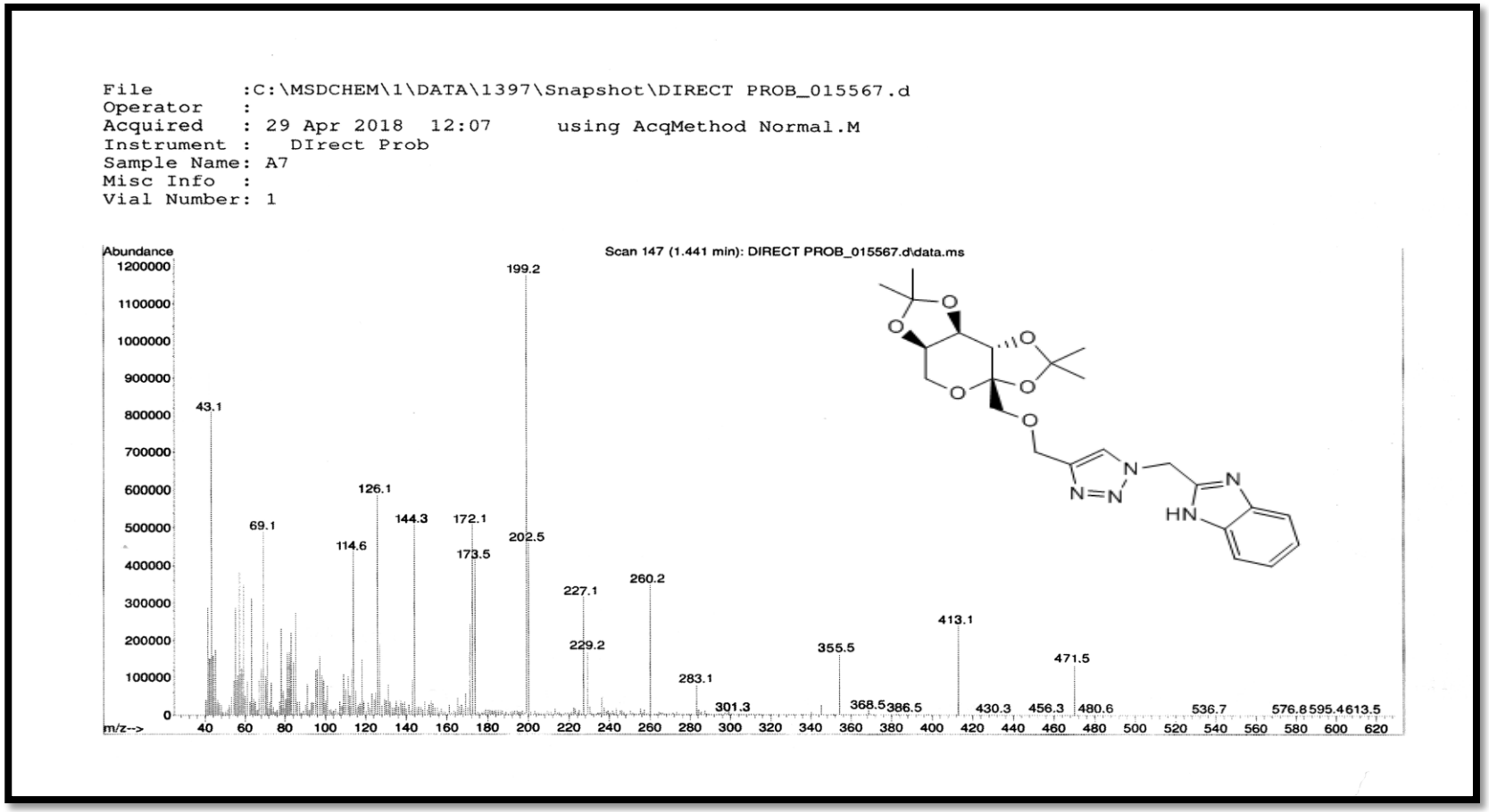


Figure (3-31)The mass spectrum of compound [XI

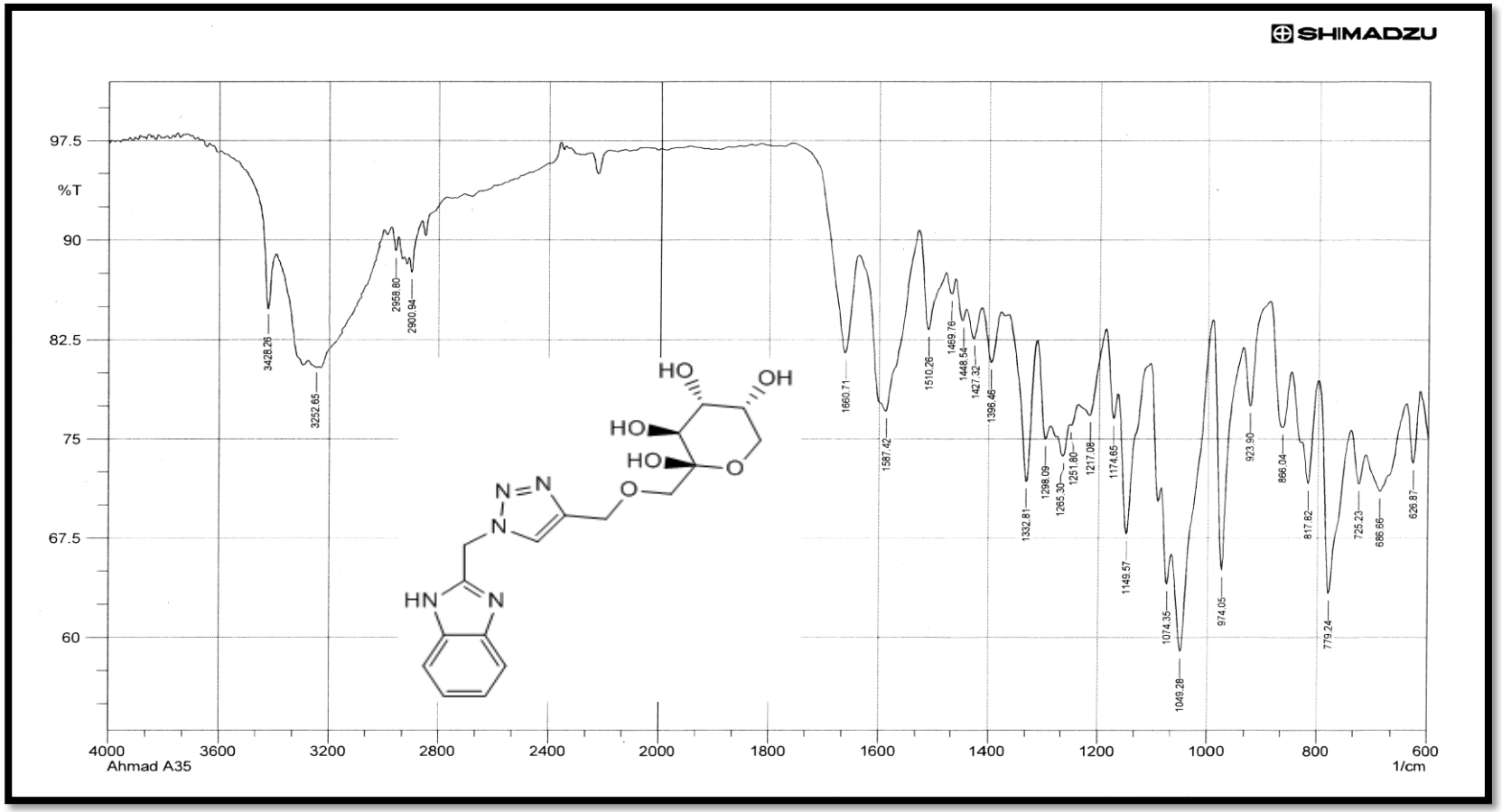


Figure (3-32) FT-IR –spectrum of compound [XII]

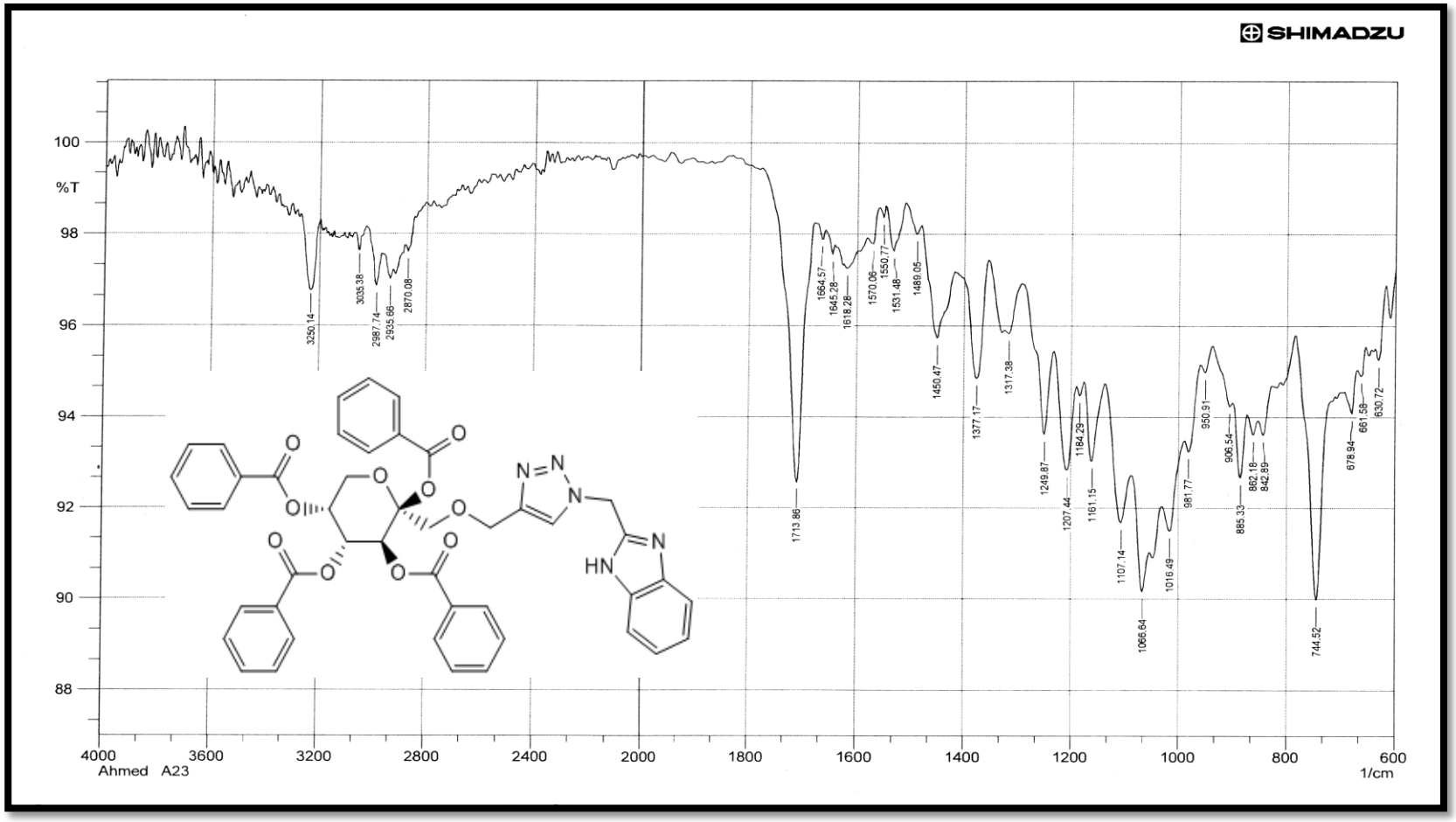


Figure (3-33) FT-IR –spectrum of compound $[XIII]_b$

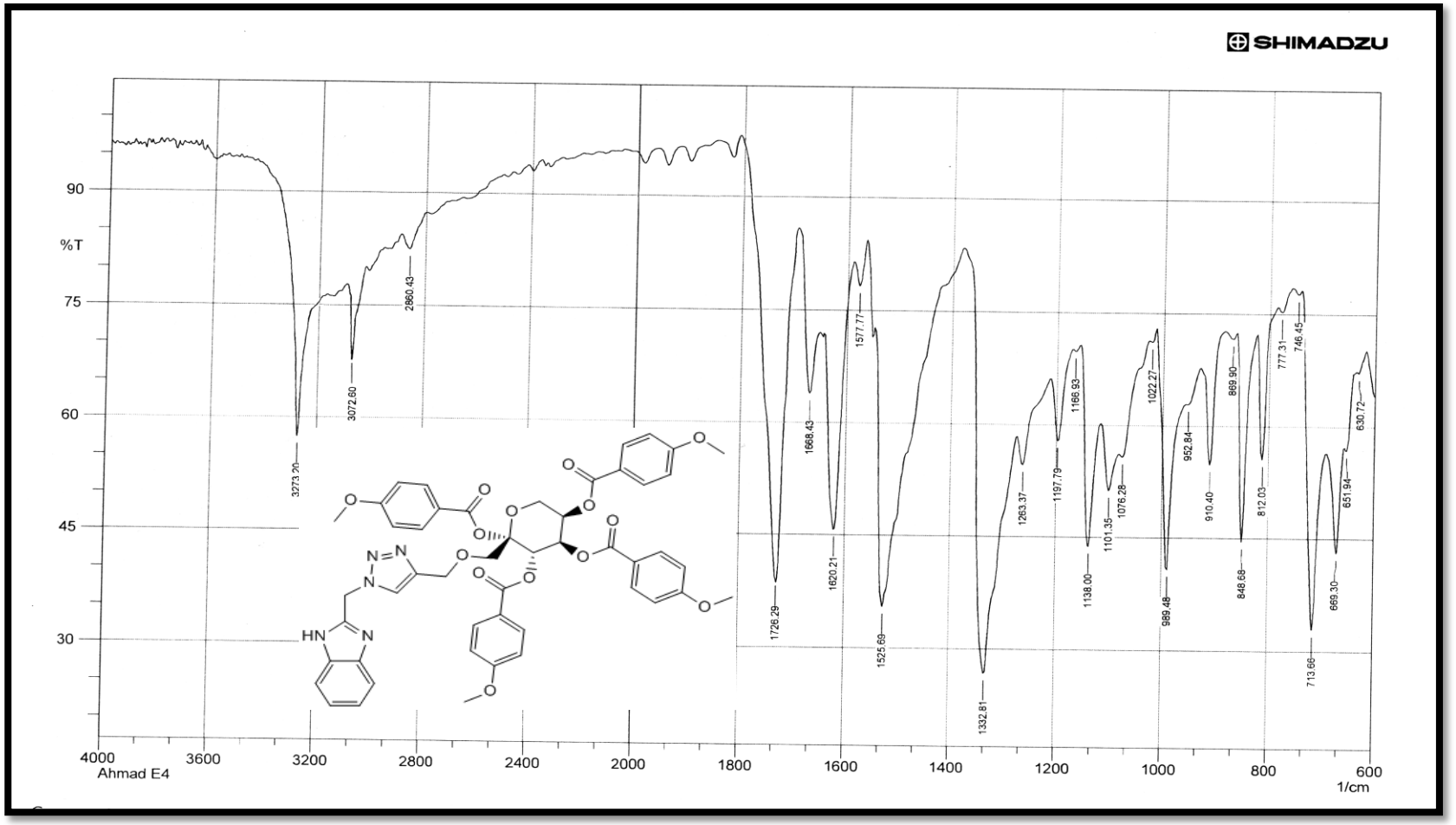


Figure (3-34) FT-IR –spectrum of compound $[XIII]_c$

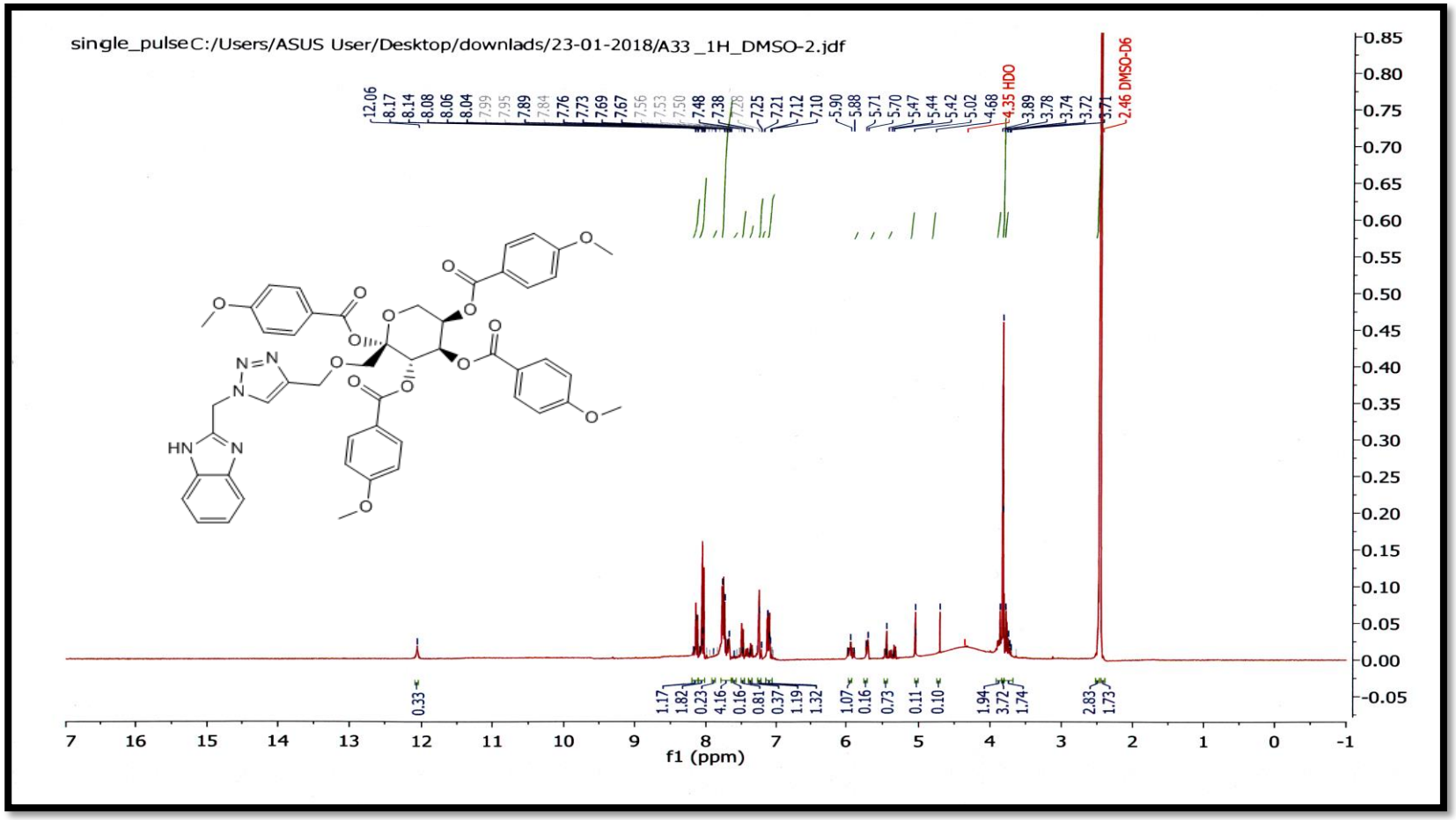


Figure (3-35) ^{1}H-NMR –spectrum of compound $[XIII]_c$

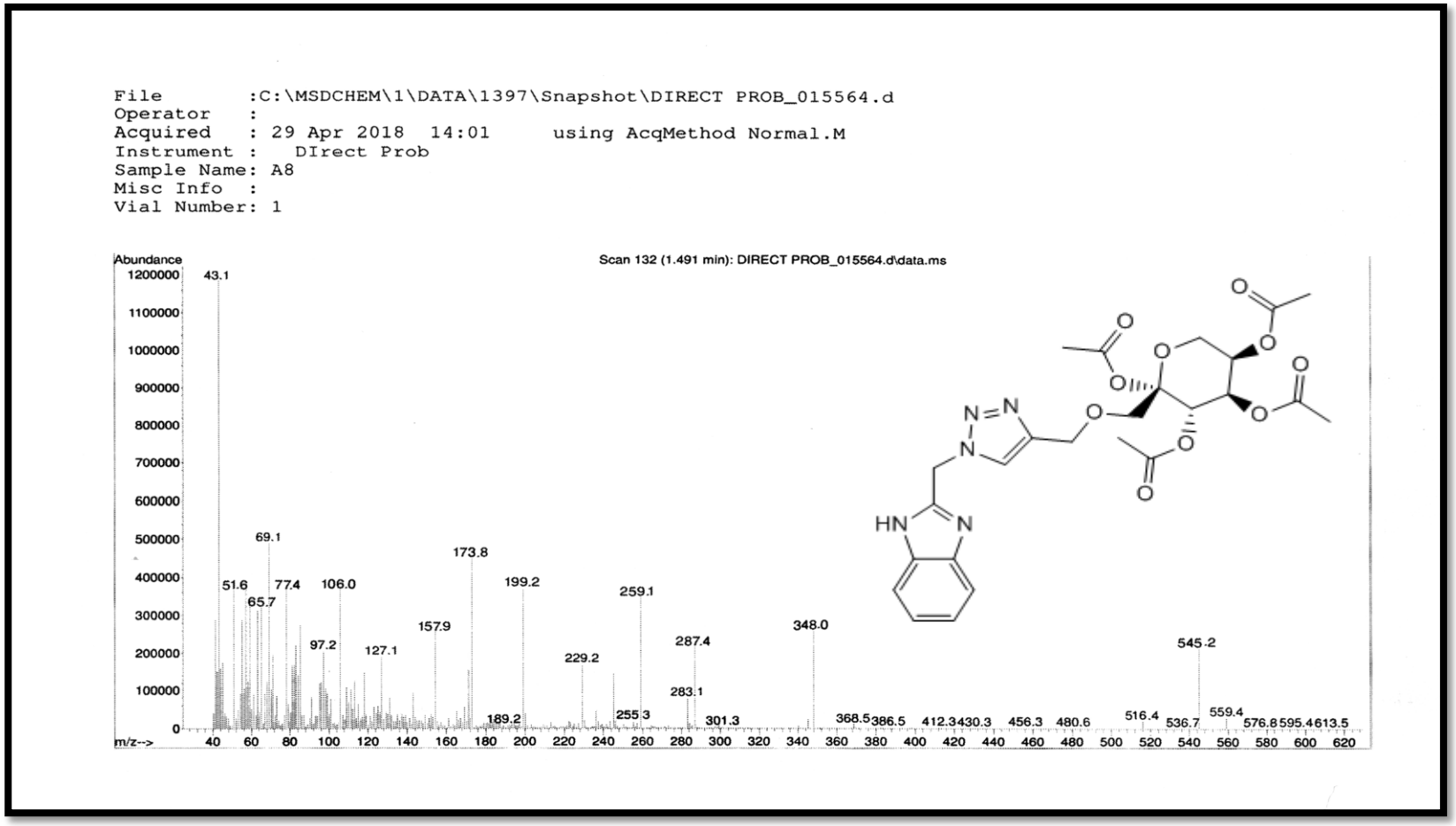


Figure (3-36)The mass spectrum of compound[XIII] a

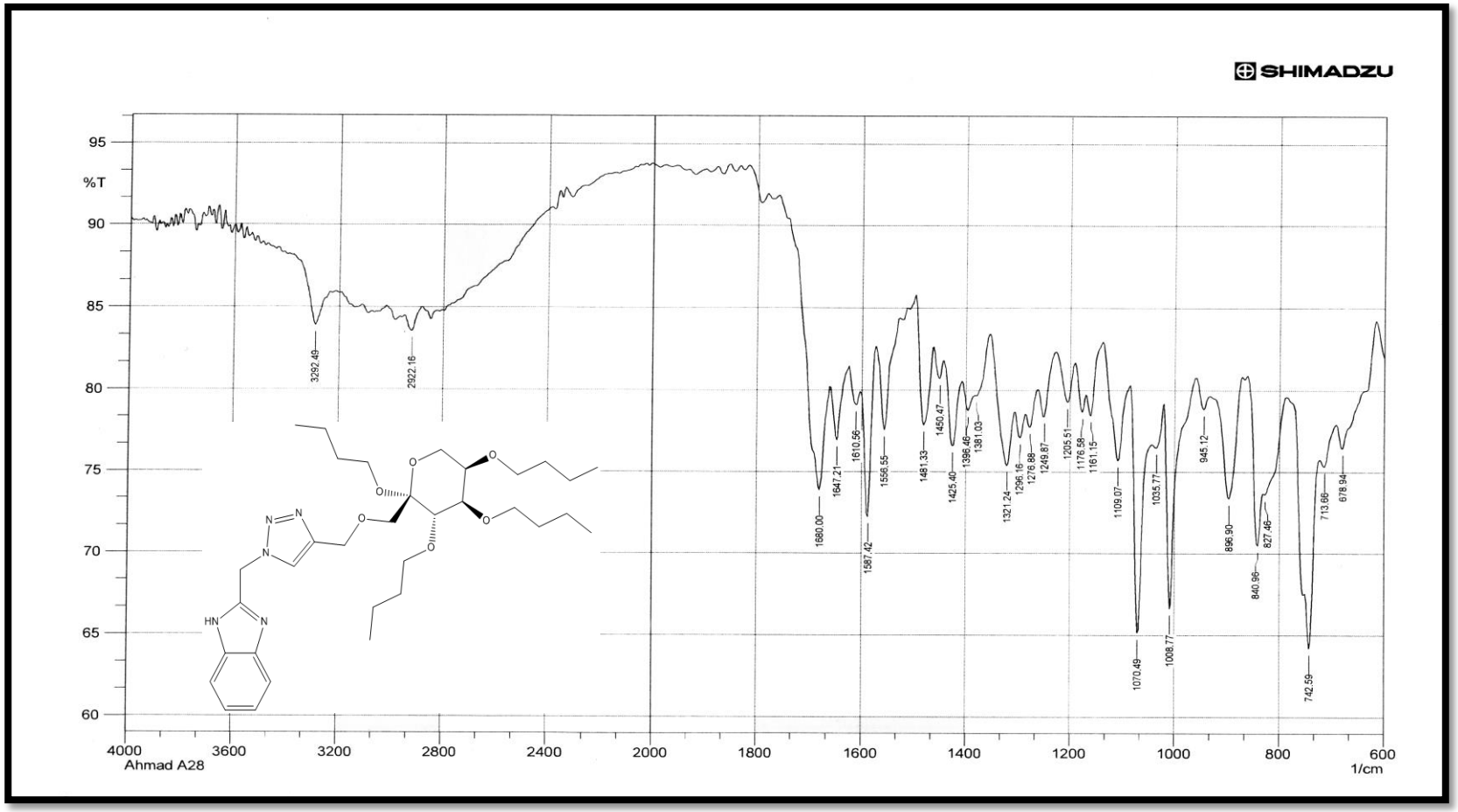


Figure (3-37) FT-IR –spectrum of compound $[XIV]_c$

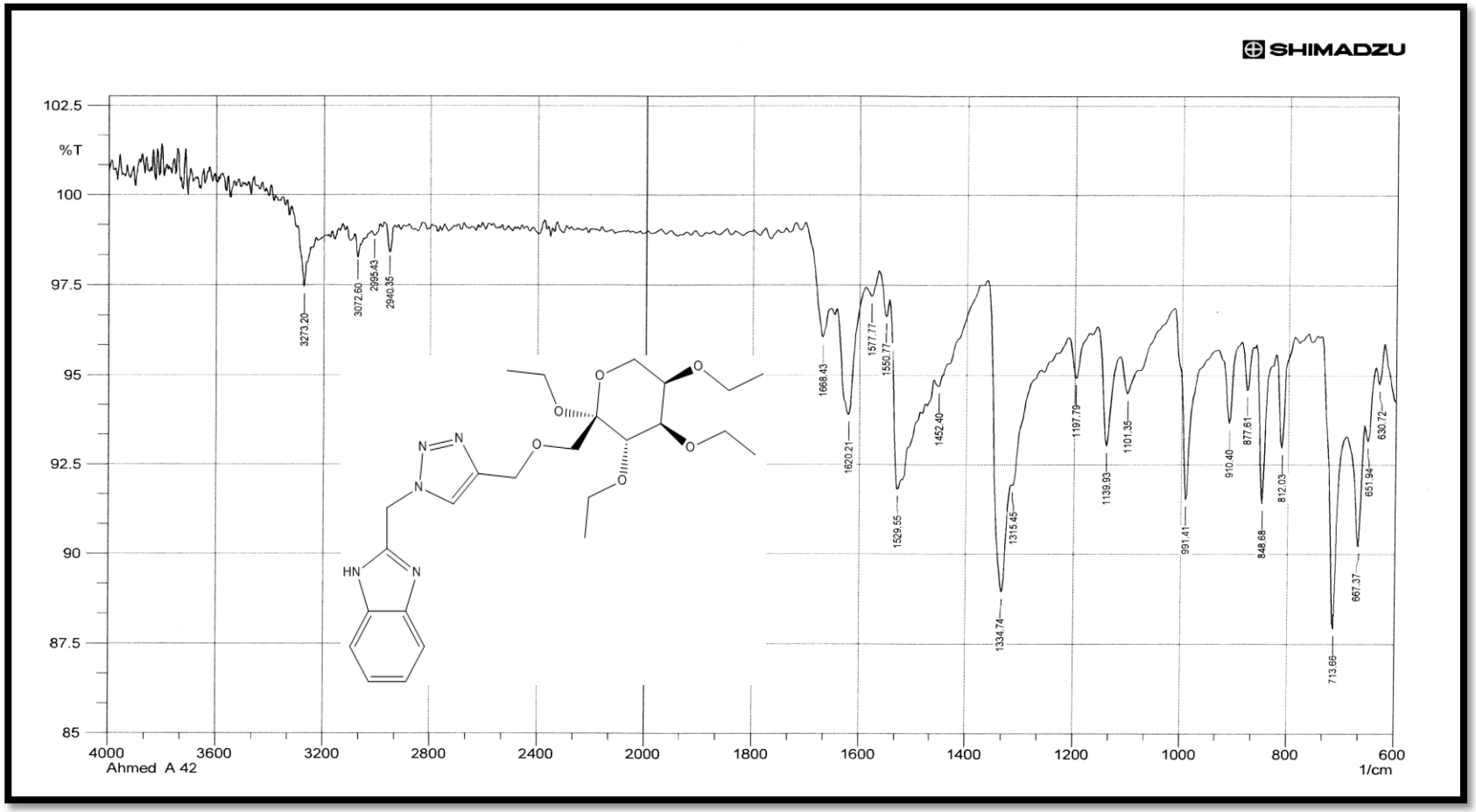


Figure (3-38) FT-IR –spectrum of compound $[XIV]_a$

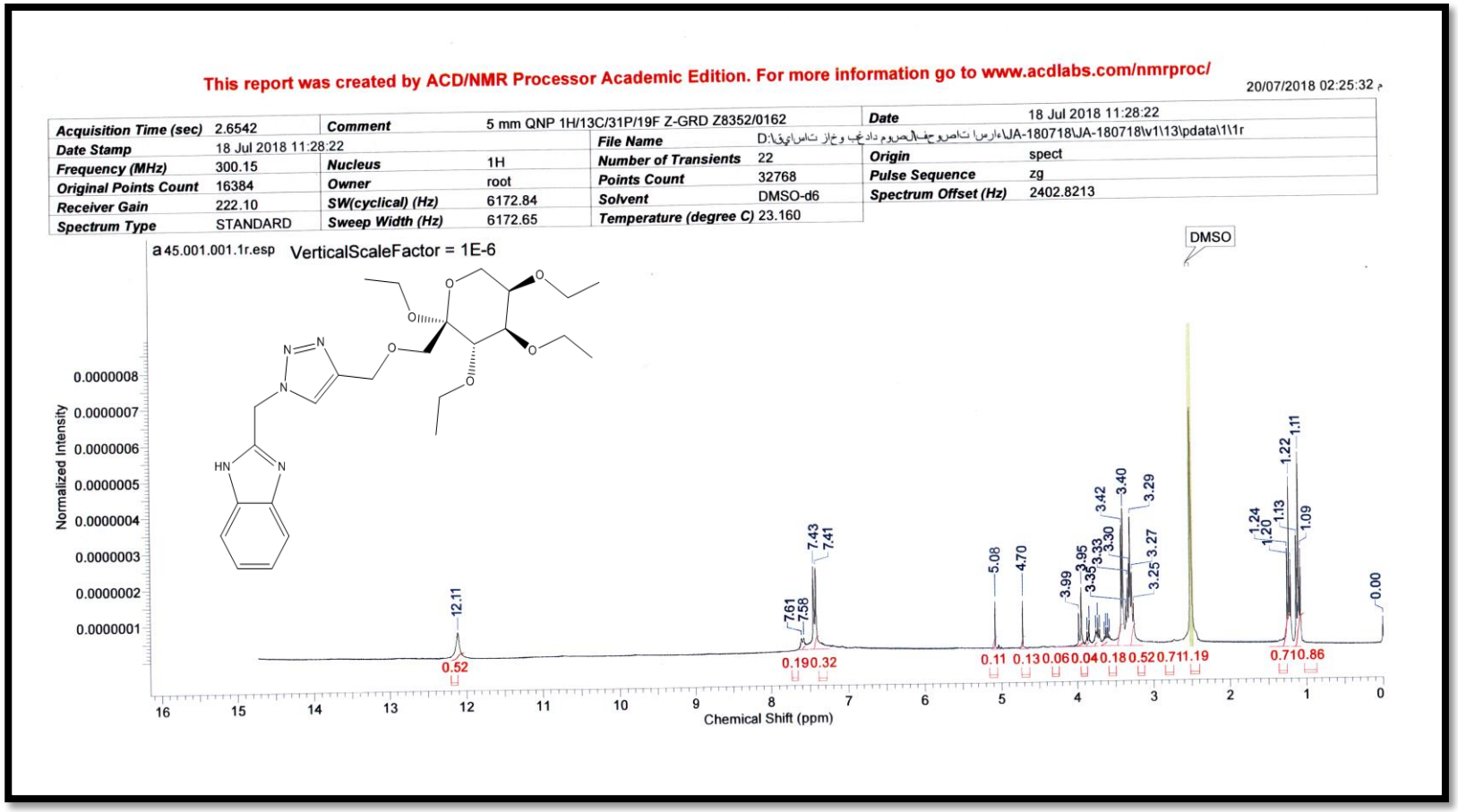


Figure (3-39) ^{1}H-NMR –spectrum of compound [XIV]$_a$

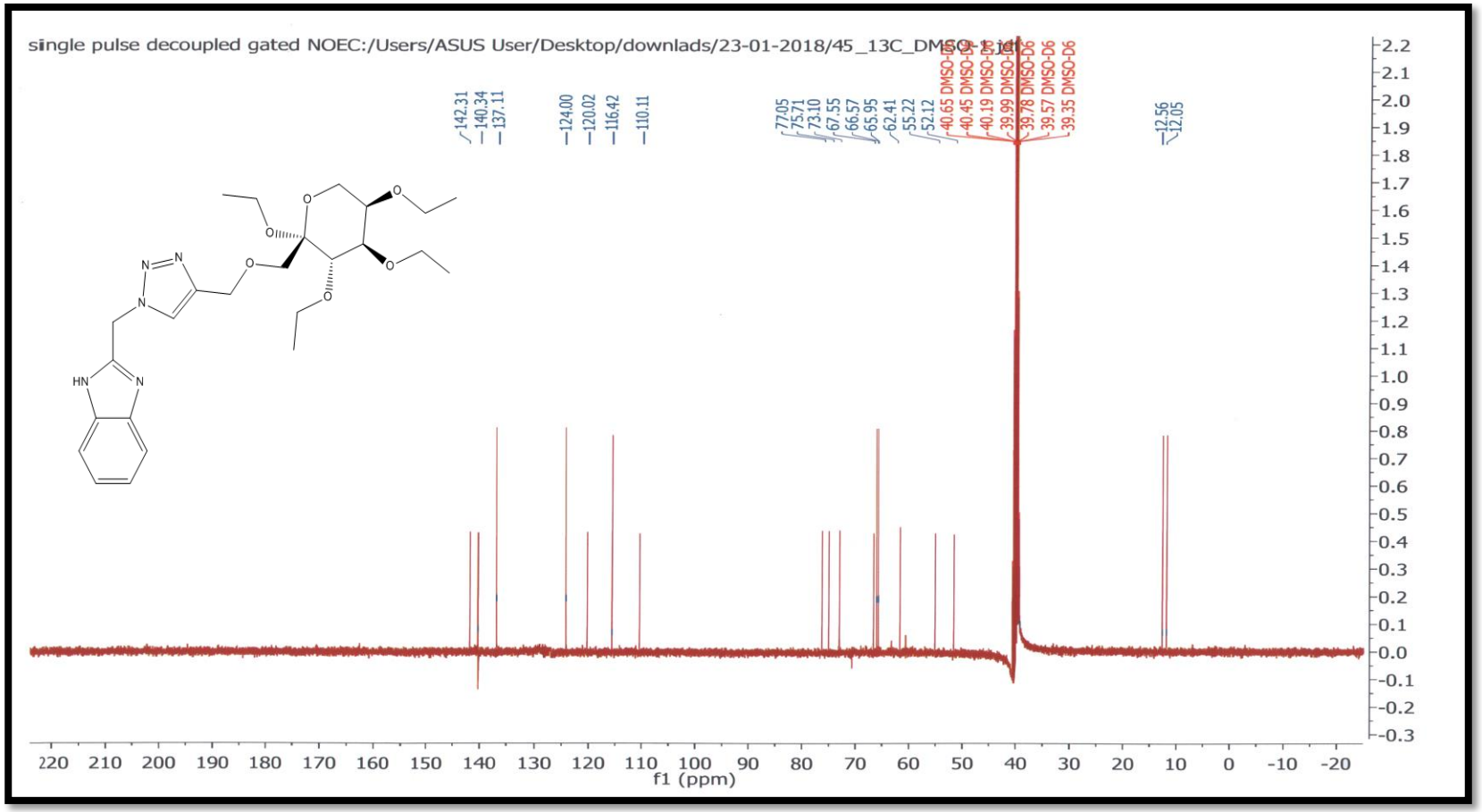


Figure (3-40)^{13}C-NMR –spectrum of compound [XIV]$_a$

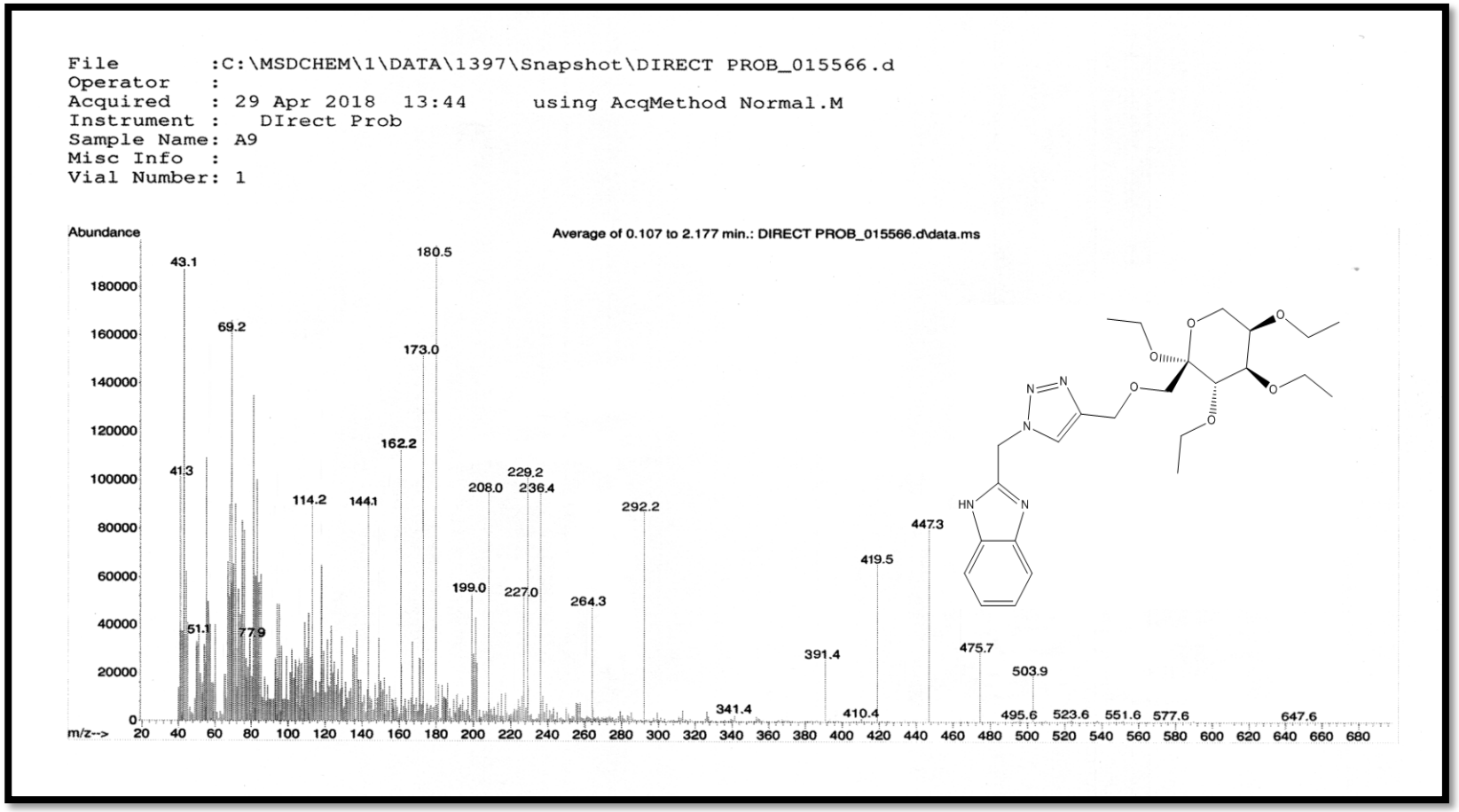


Figure (3-41)The mass spectrum of compound[XIV]$_a$

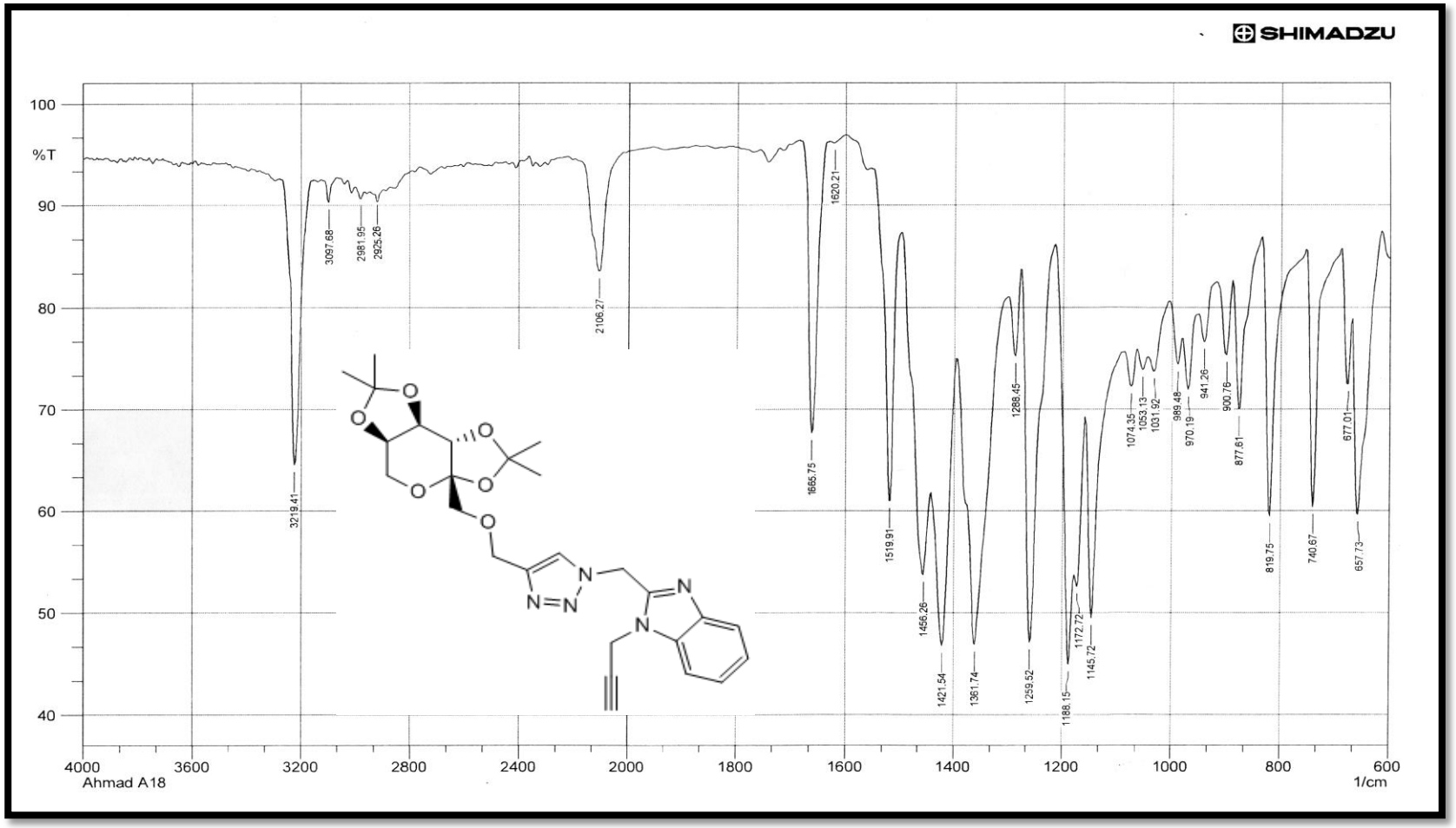


Figure (3-42) FT-IR –spectrum of compound [XV]

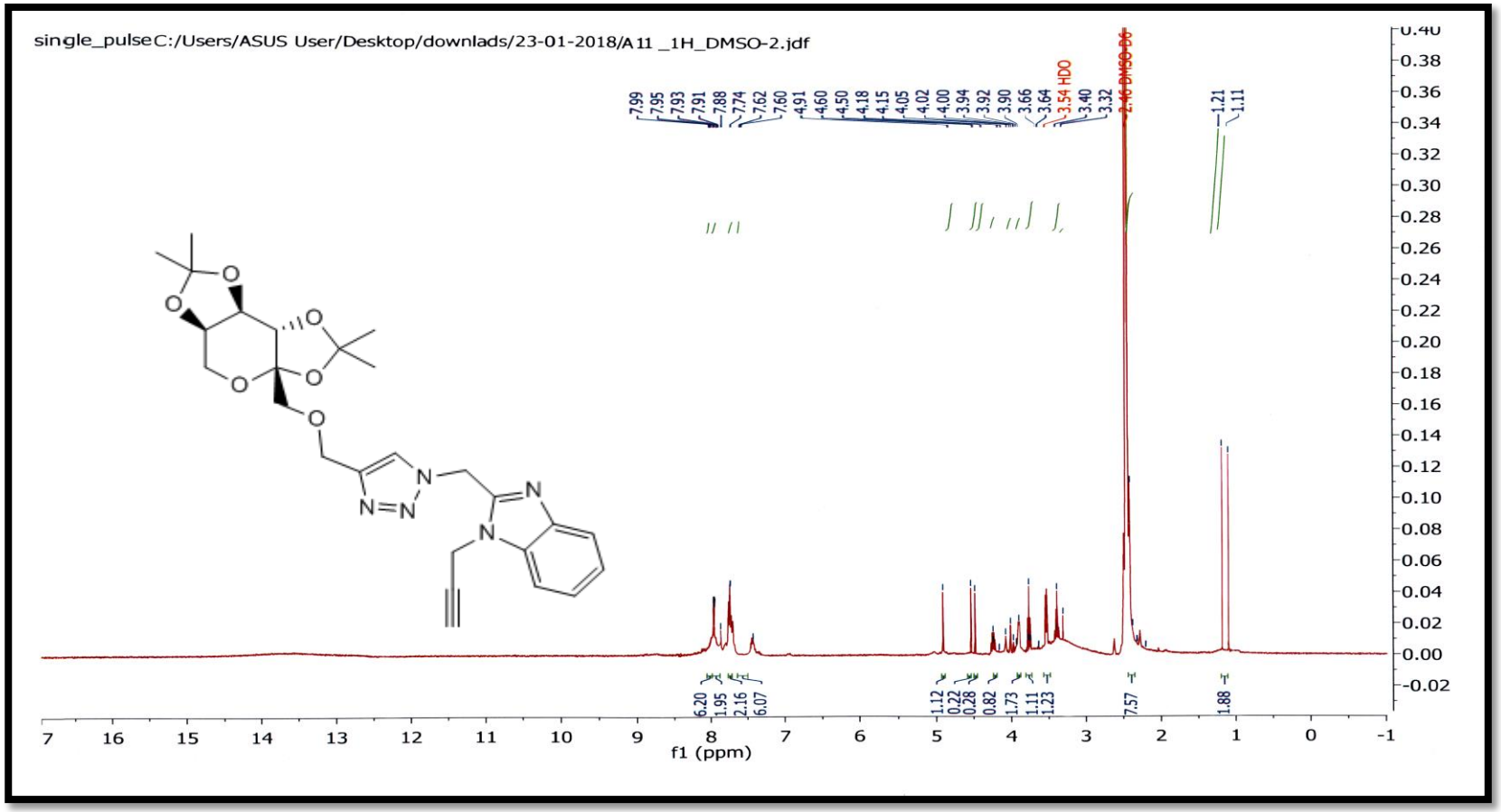


Figure (3-43) ^{1}H-NMR –spectrum of compound [XV]

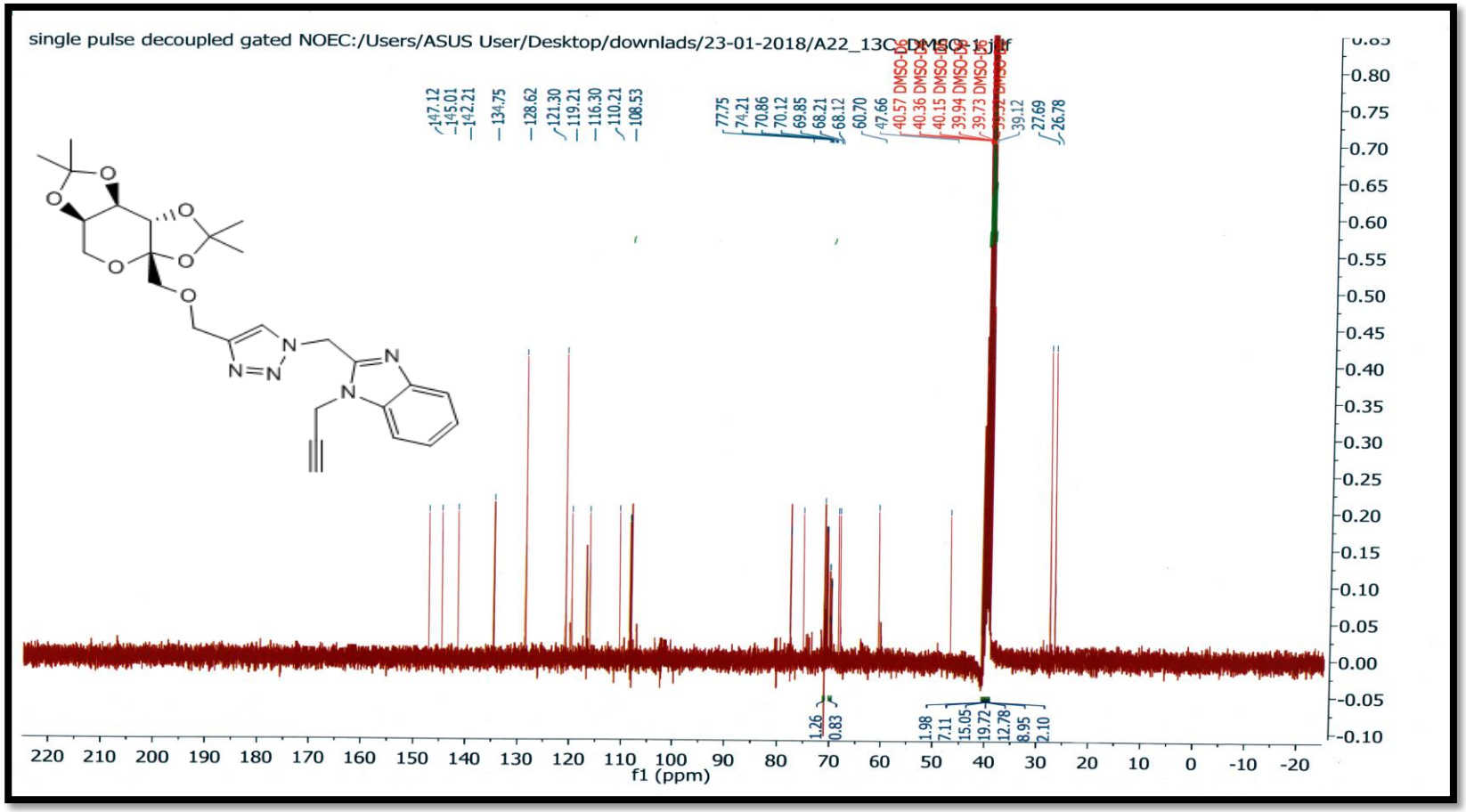


Figure (3-44)^{13}C-NMR –spectrum of compound [XV]

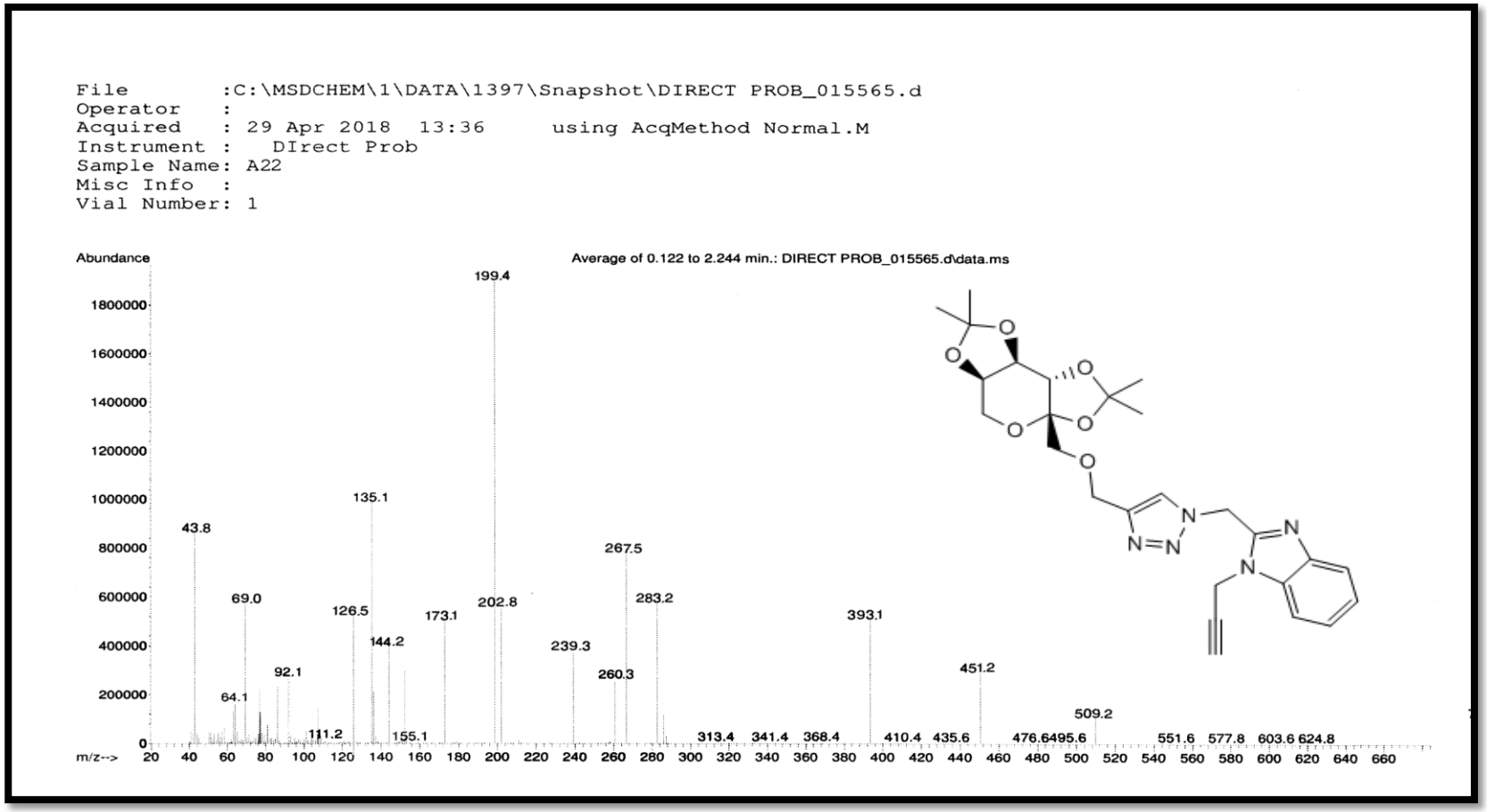


Figure (3-45)The mass spectrum of compound[XV]

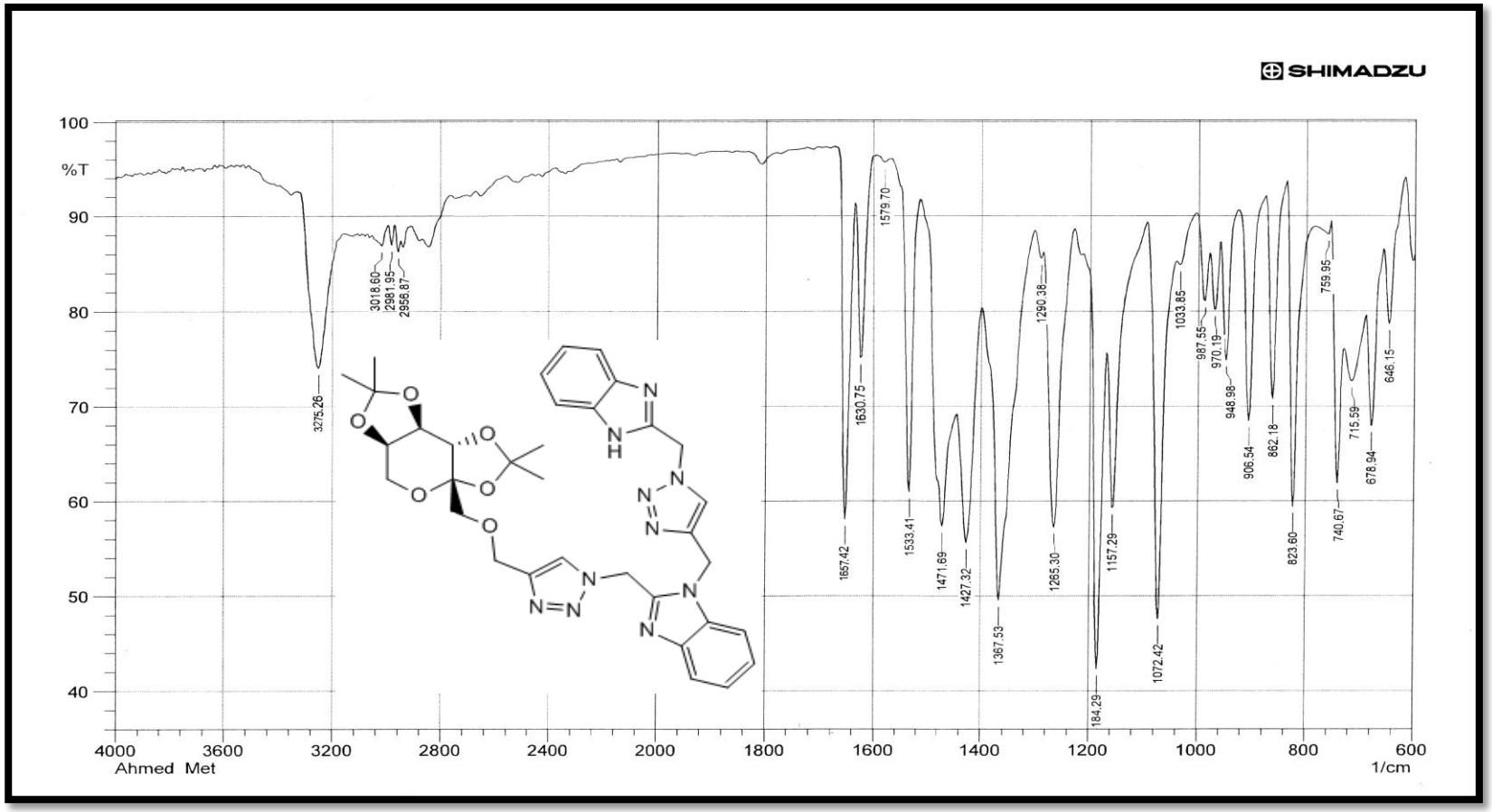


Figure (3-46) FT-IR –spectrum of compound [XVI]

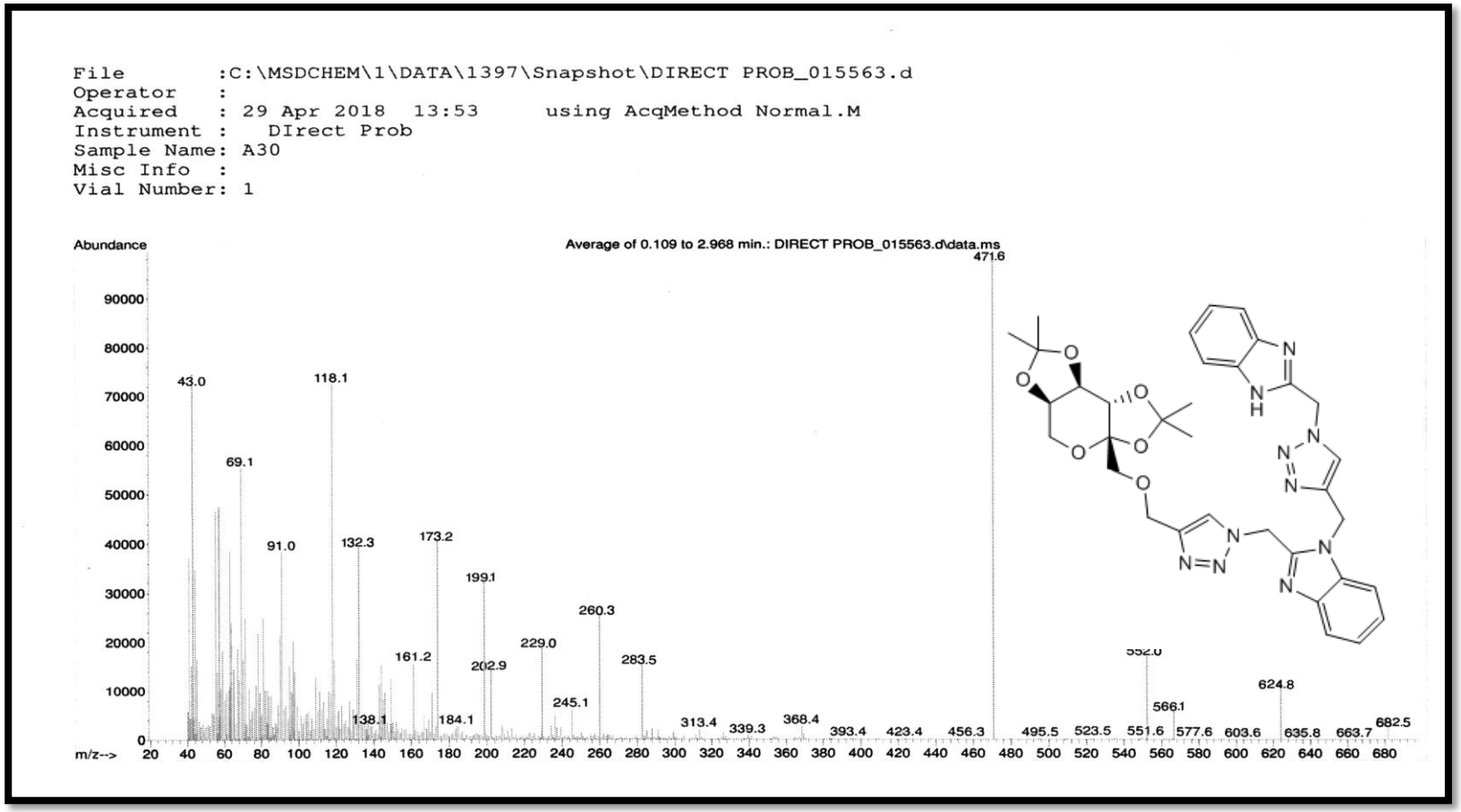


Figure (3-47)The mass spectrum of compound[XVI]

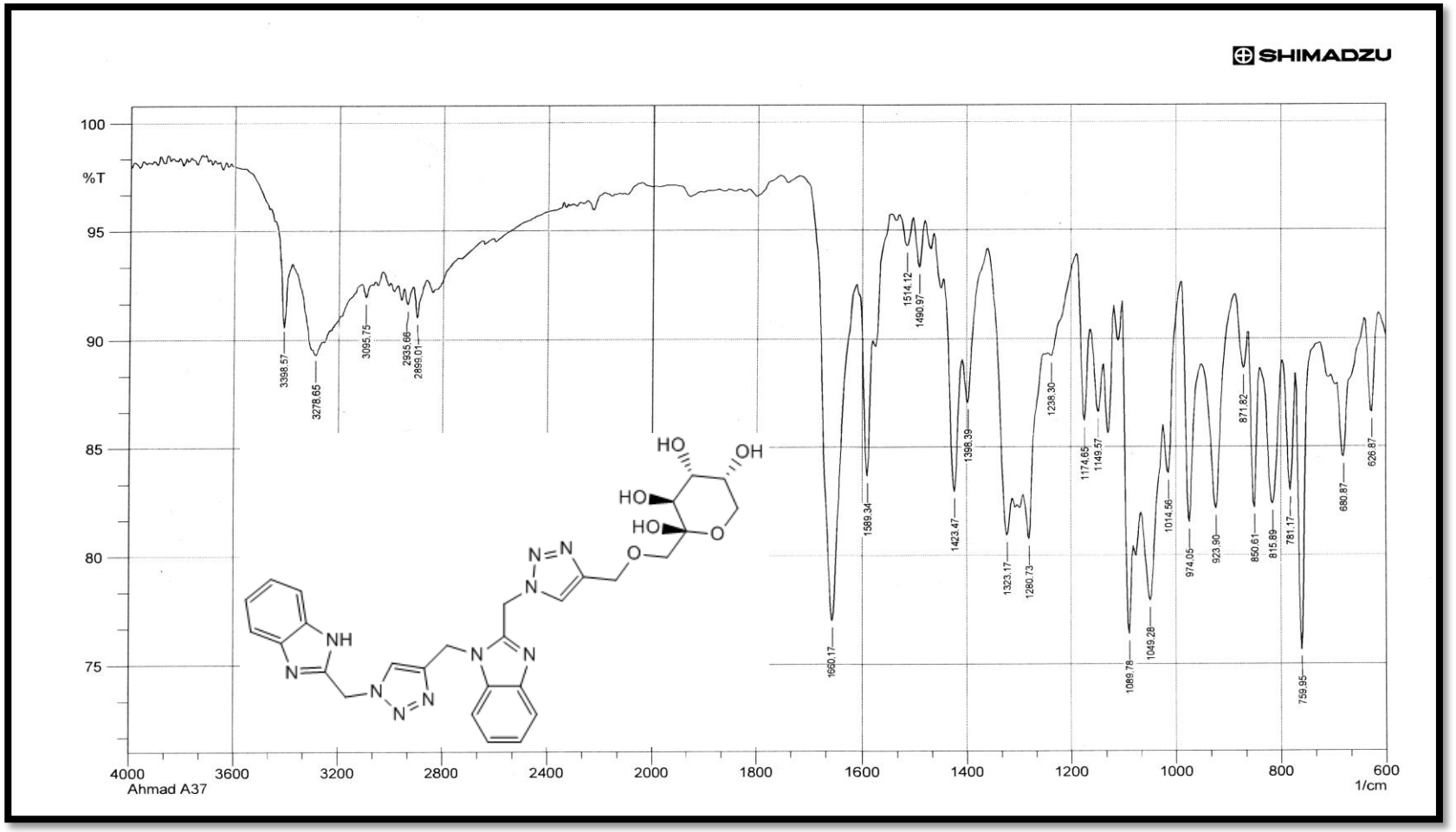


Figure (3-48) FT-IR –spectrum of compound [XVII]

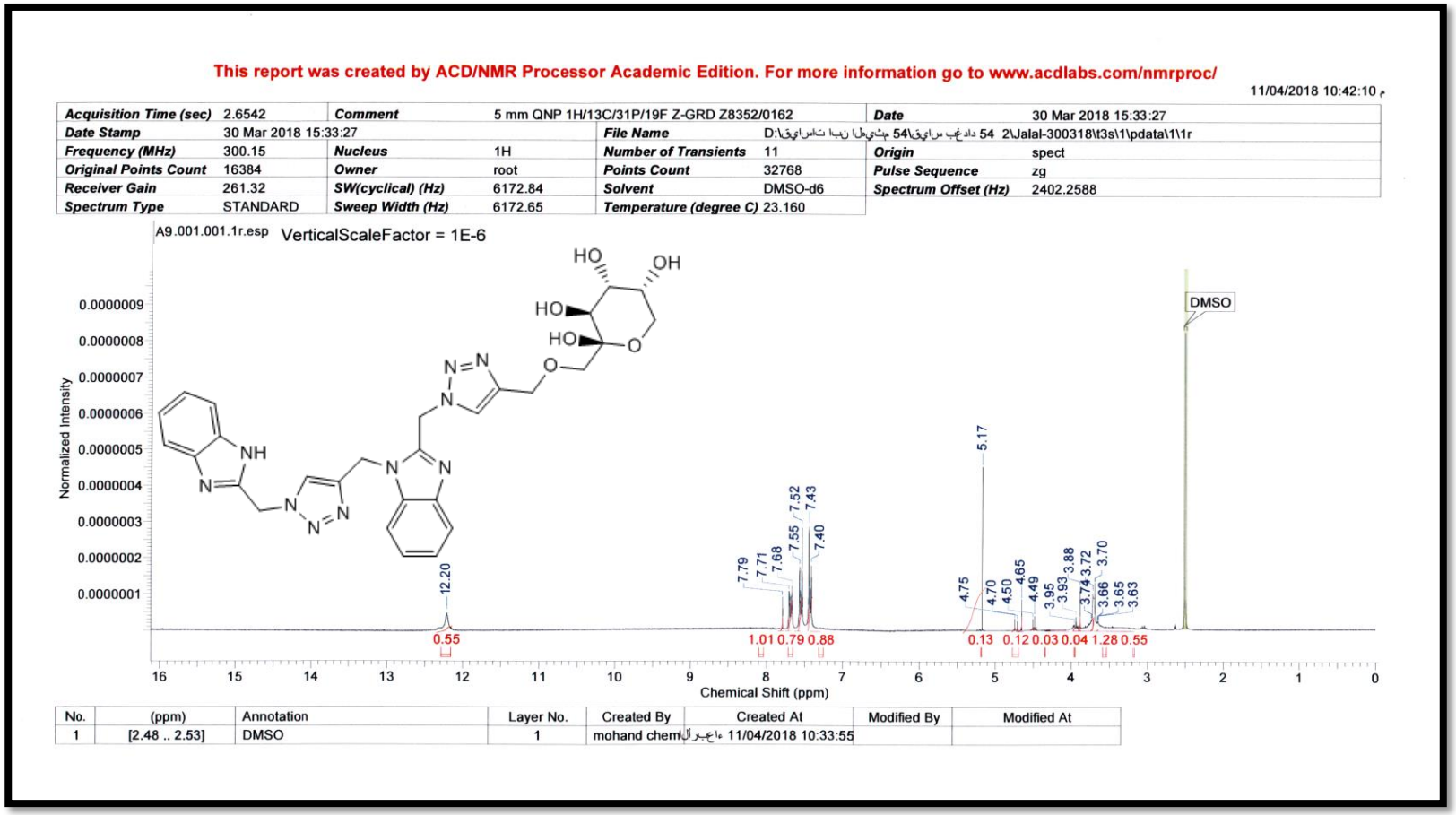


Figure (3-49) ^{1}H-NMR –spectrum of compound[XVII]

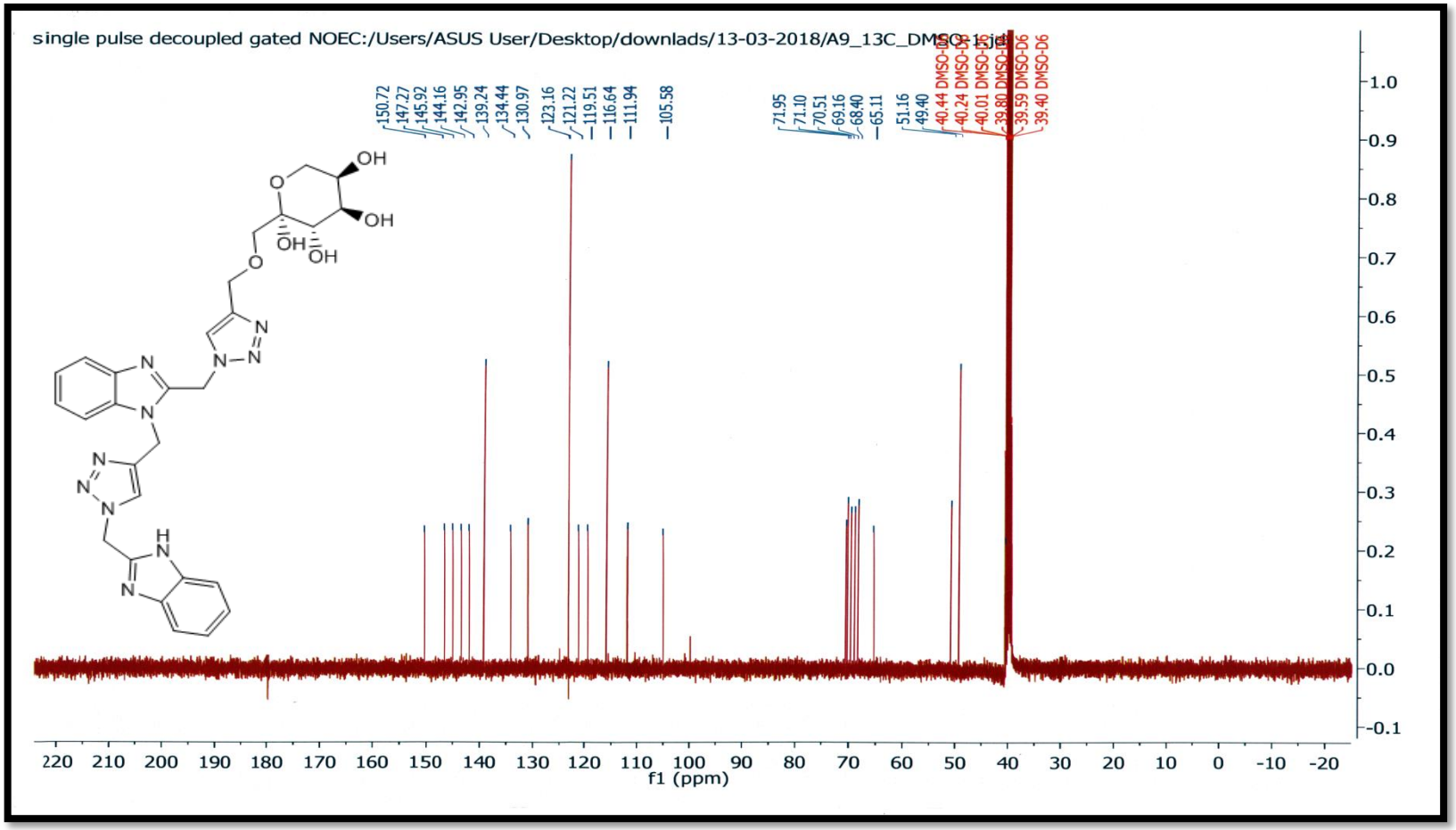


Figure (3-50)^{13}C-NMR –spectrum of compound [XVII]

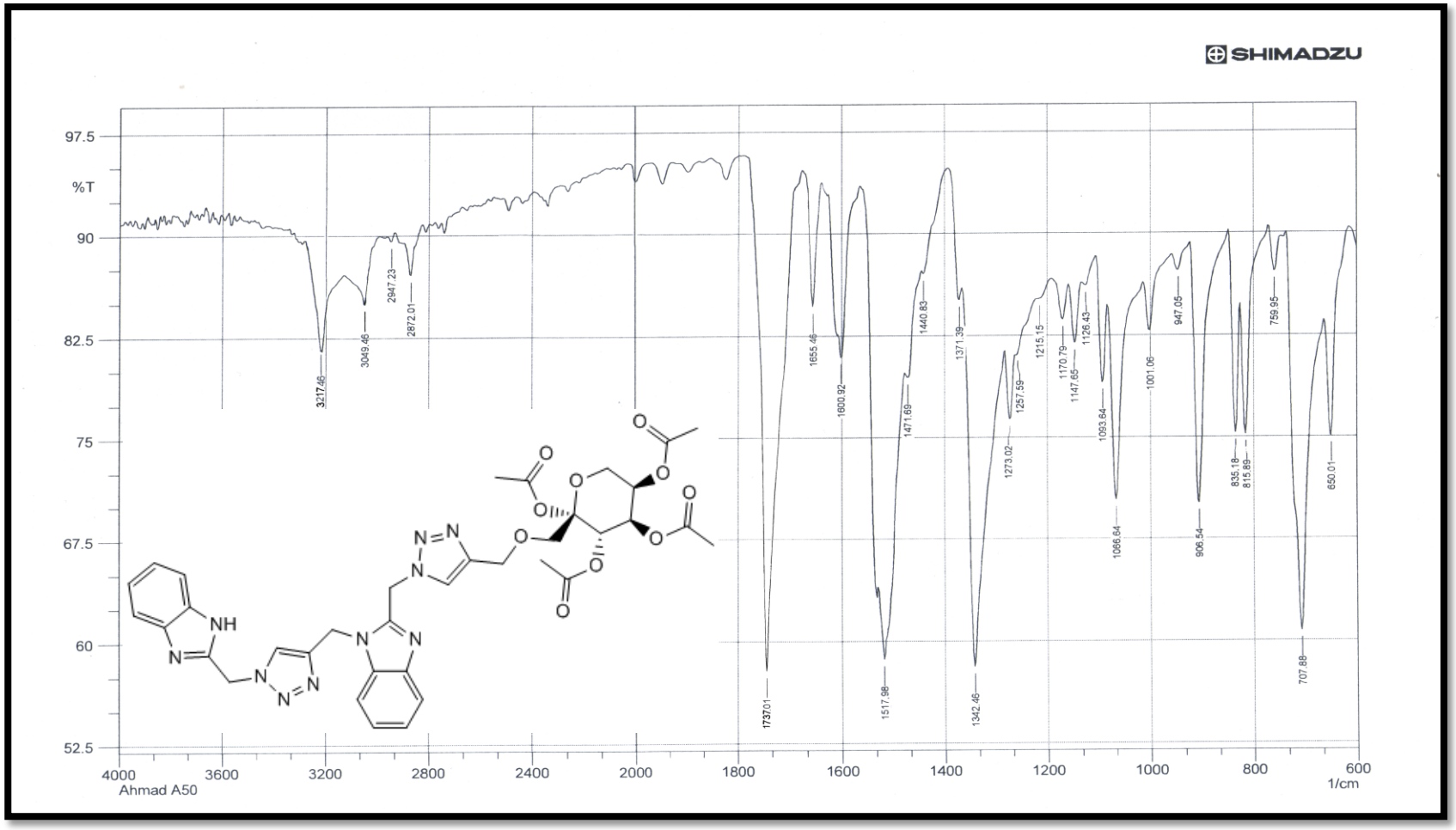


Figure (3-51) FT-IR –spectrum of compound $[XVIII]_a$

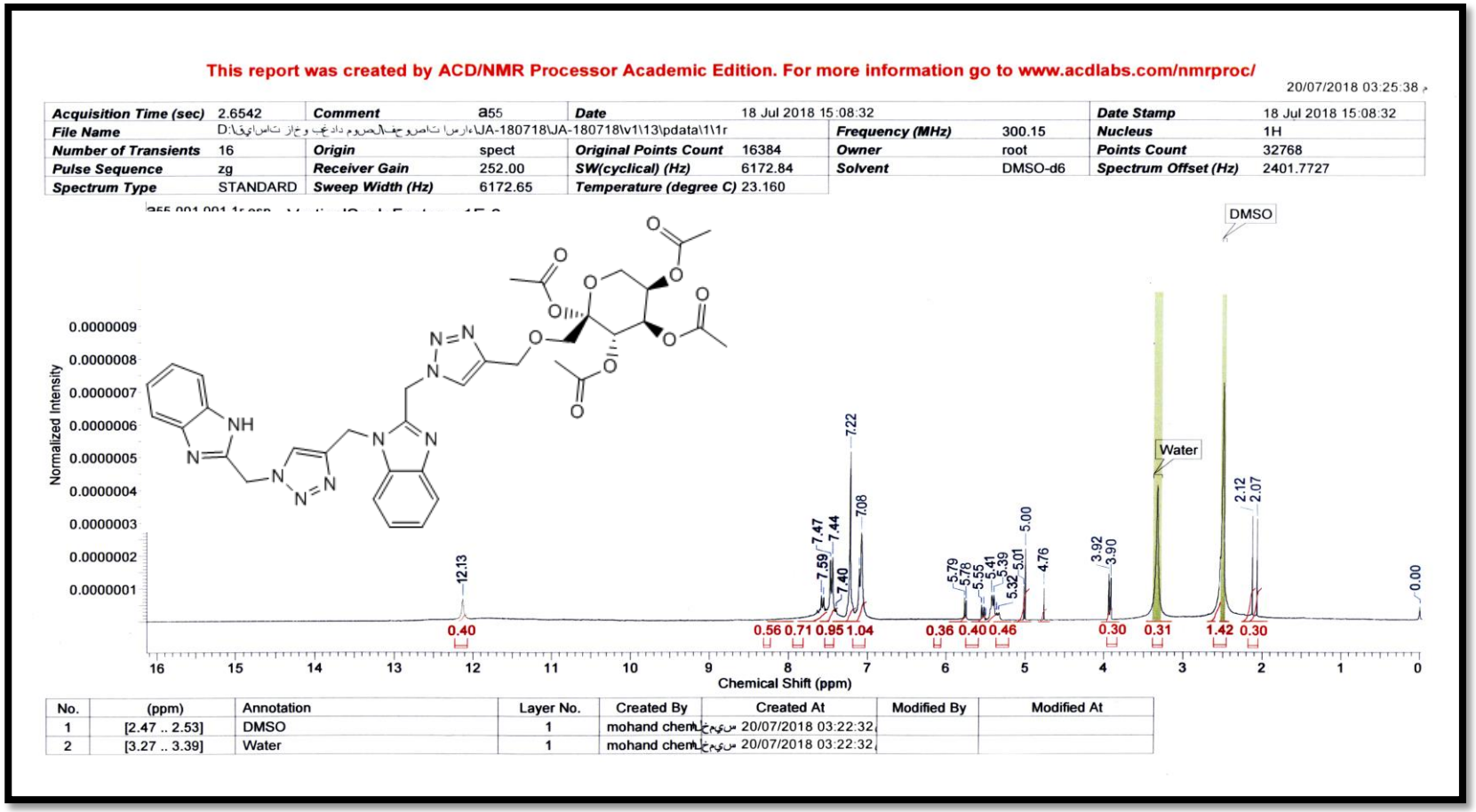


Figure (3-52) ^{1}H-NMR –spectrum of compound[XVIII]$_a$

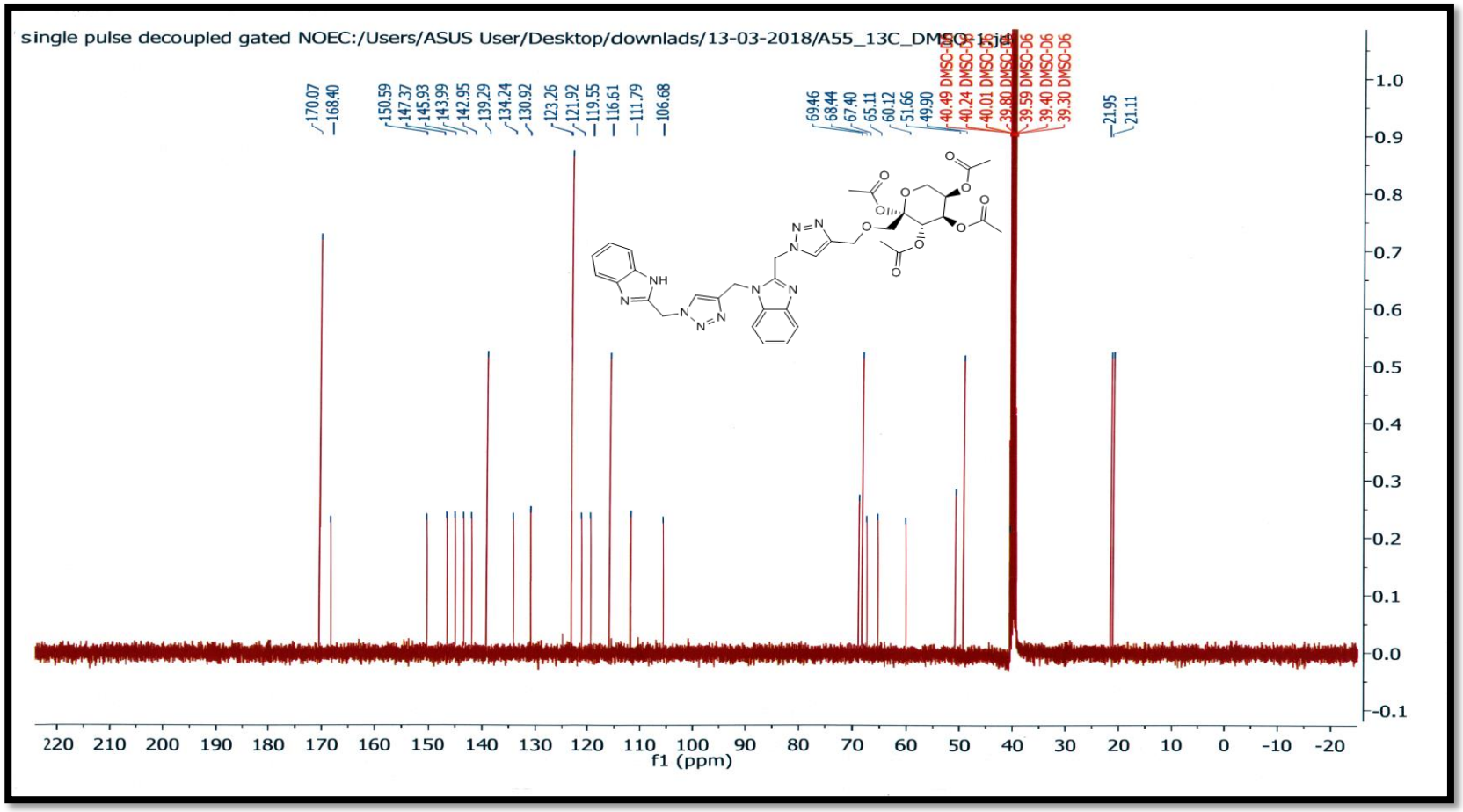


Figure (3-53)^{13}C-NMR –spectrum of compound [XVIII]$_a$

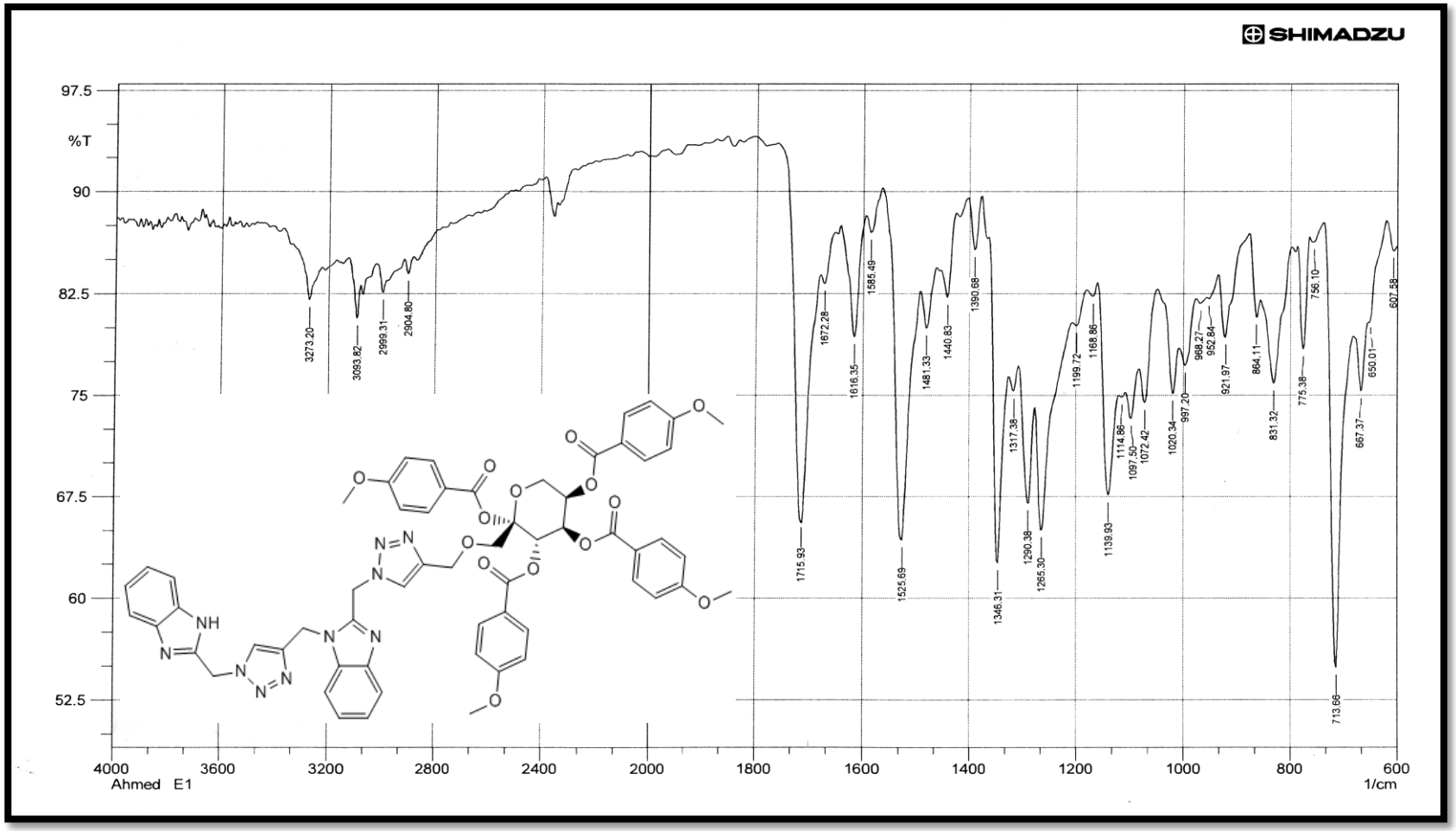


Figure (3-54) FT-IR –spectrum of compound $[XVIII]_c$

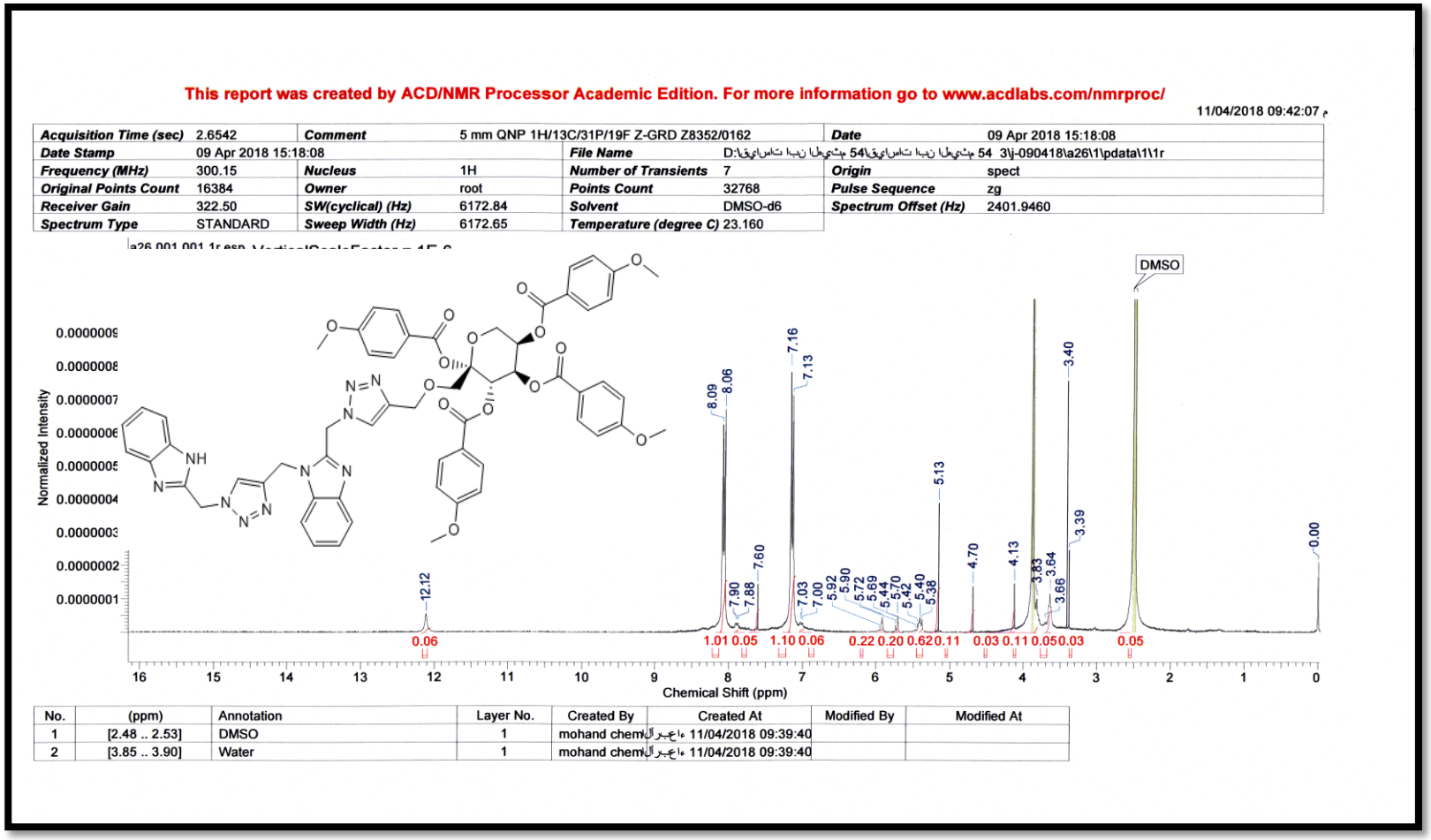


Figure (3-55) ^{1}H-NMR –spectrum of compound[XVIII]$_c$

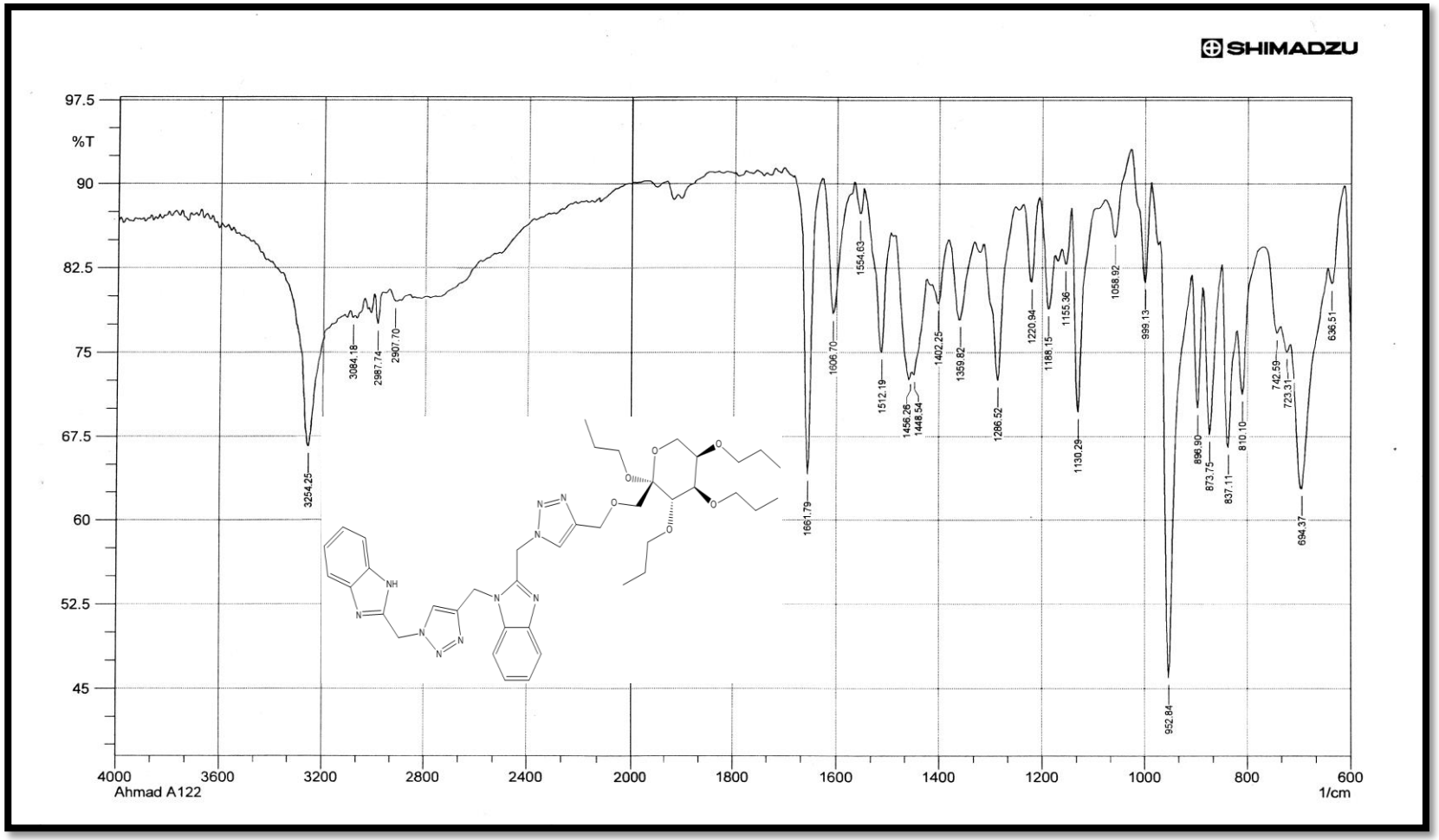


Figure (3-56) FT-IR –spectrum of compound $[XIX]_b$

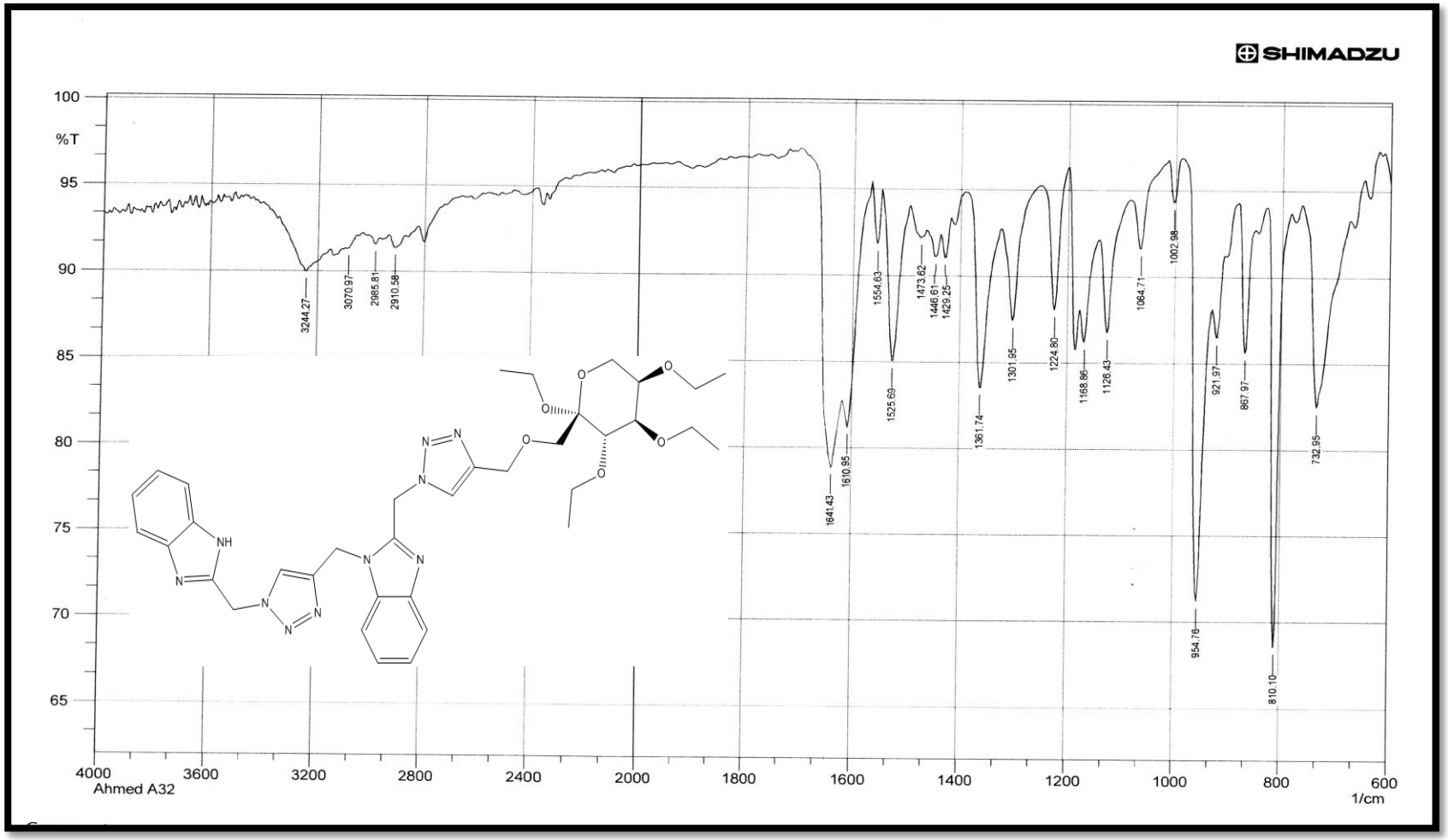


Figure (3-57) FT-IR –spectrum of compound $[XIX]_a$

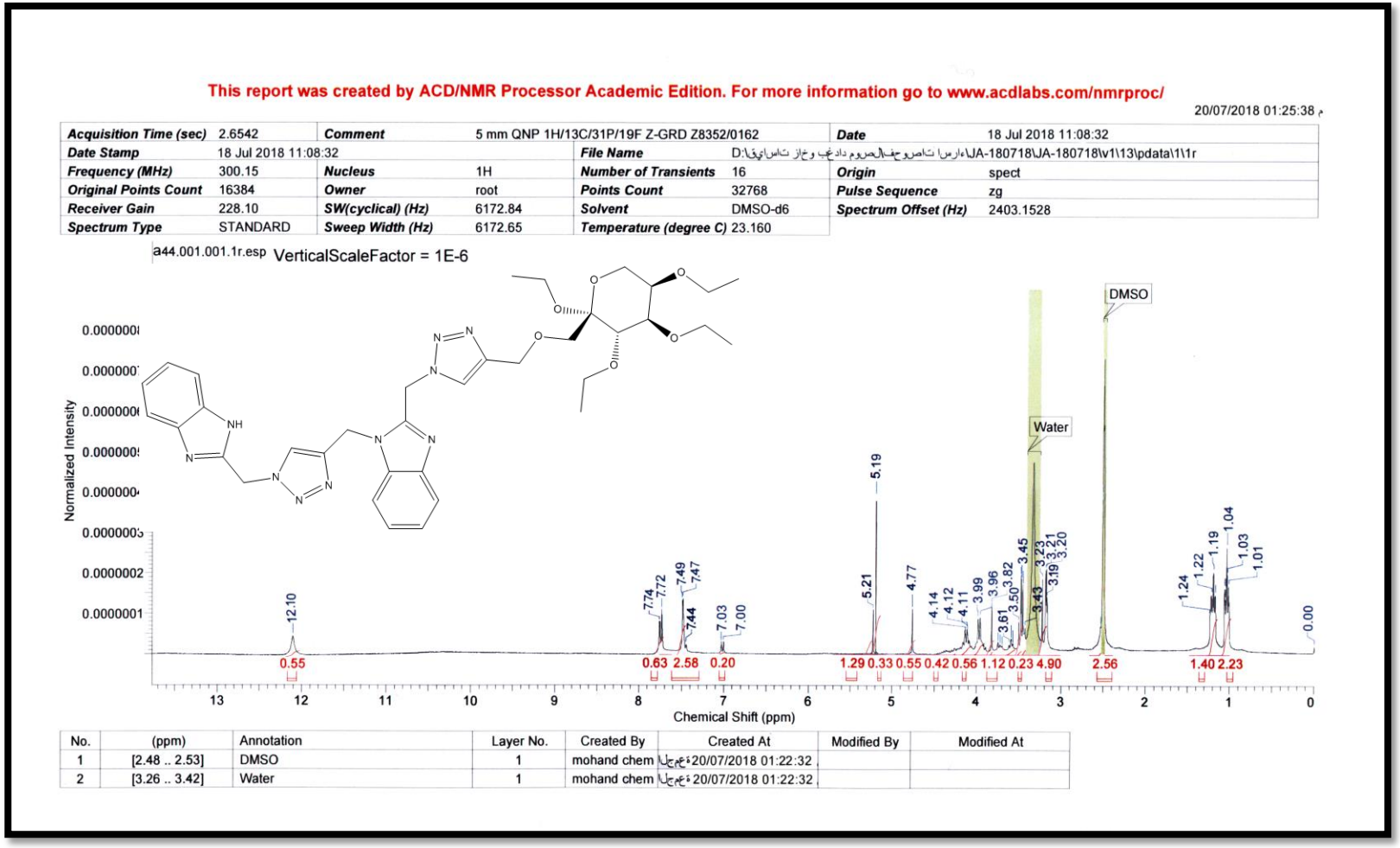


Figure (3-58) ^{1}H-NMR –spectrum of compound $[XIX]_a$

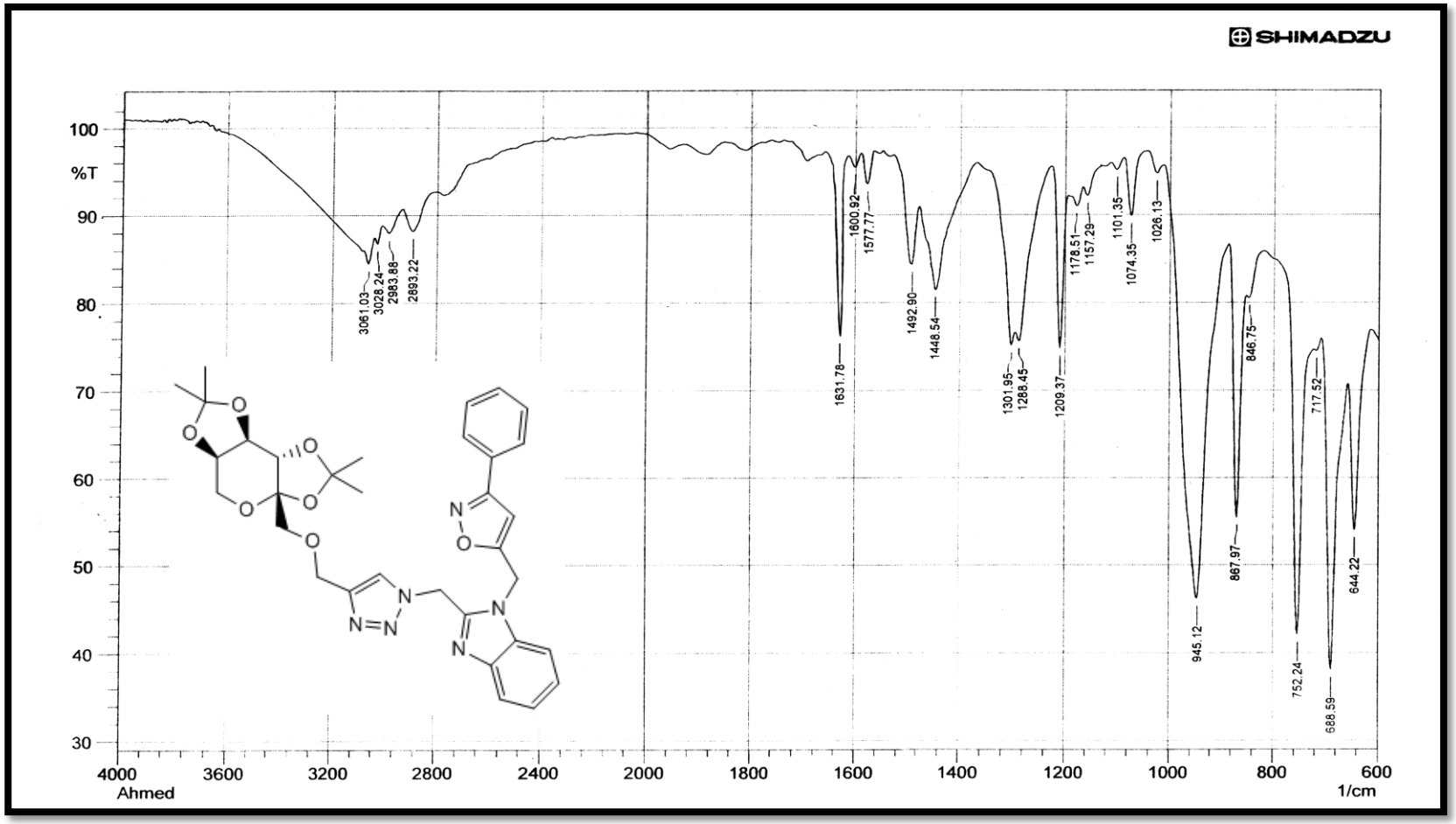


Figure (3-59) FT-IR –spectrum of compound $[XX]_a$

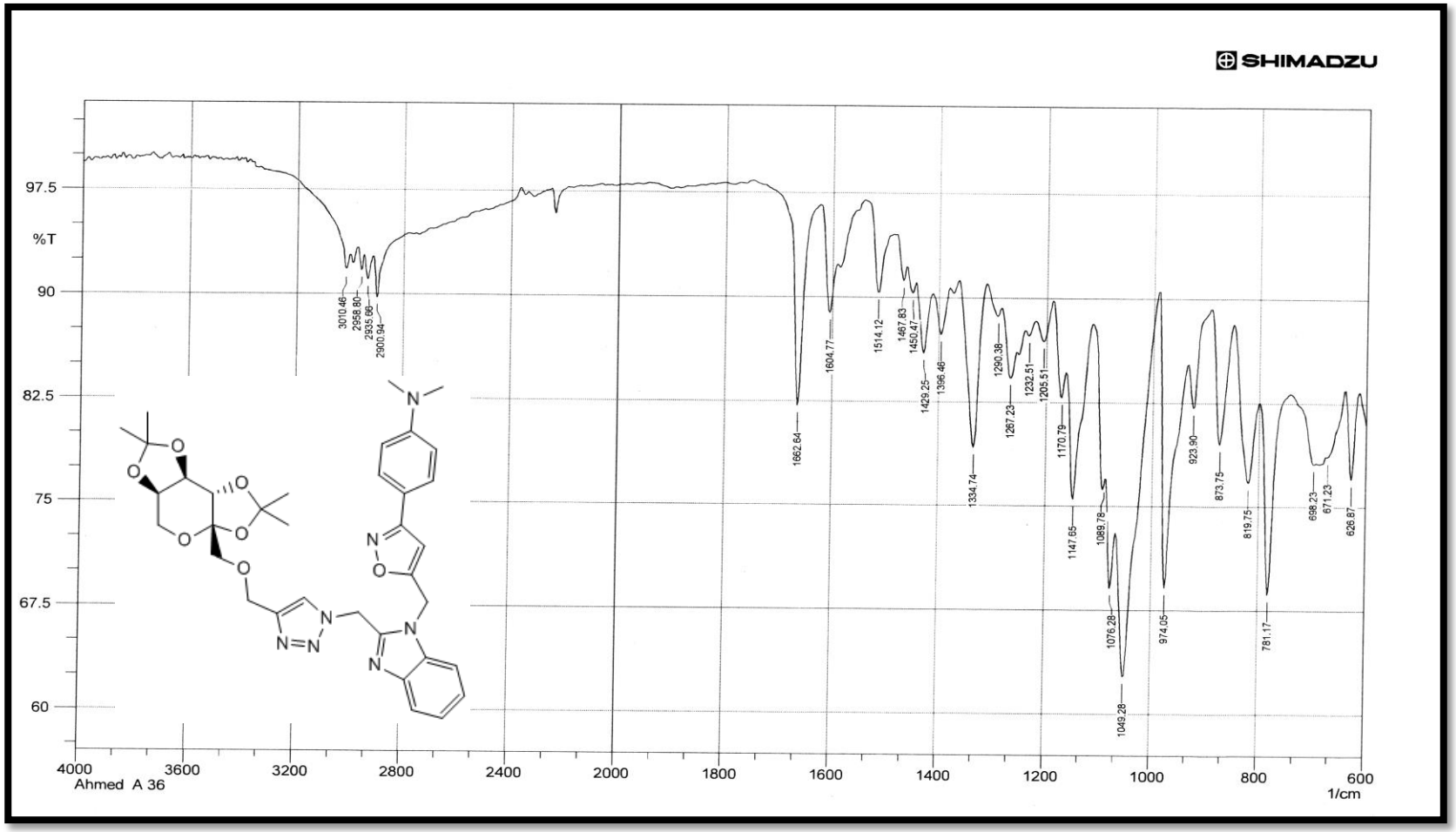


Figure (3-60) FT-IR –spectrum of compound $[XX]_d$

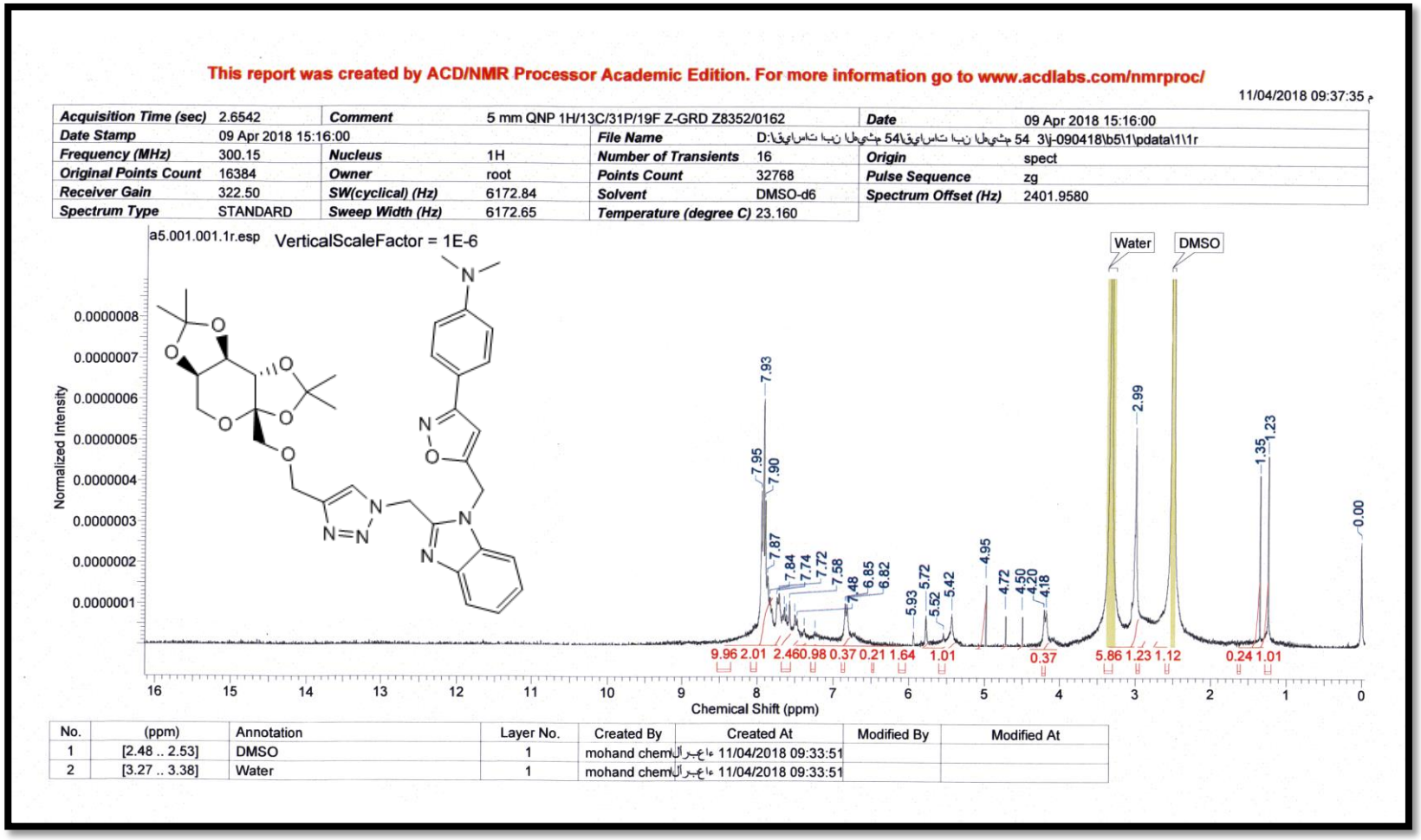


Figure (3-61) ^{1}H-NMR –spectrum of compound $[XX]_d$

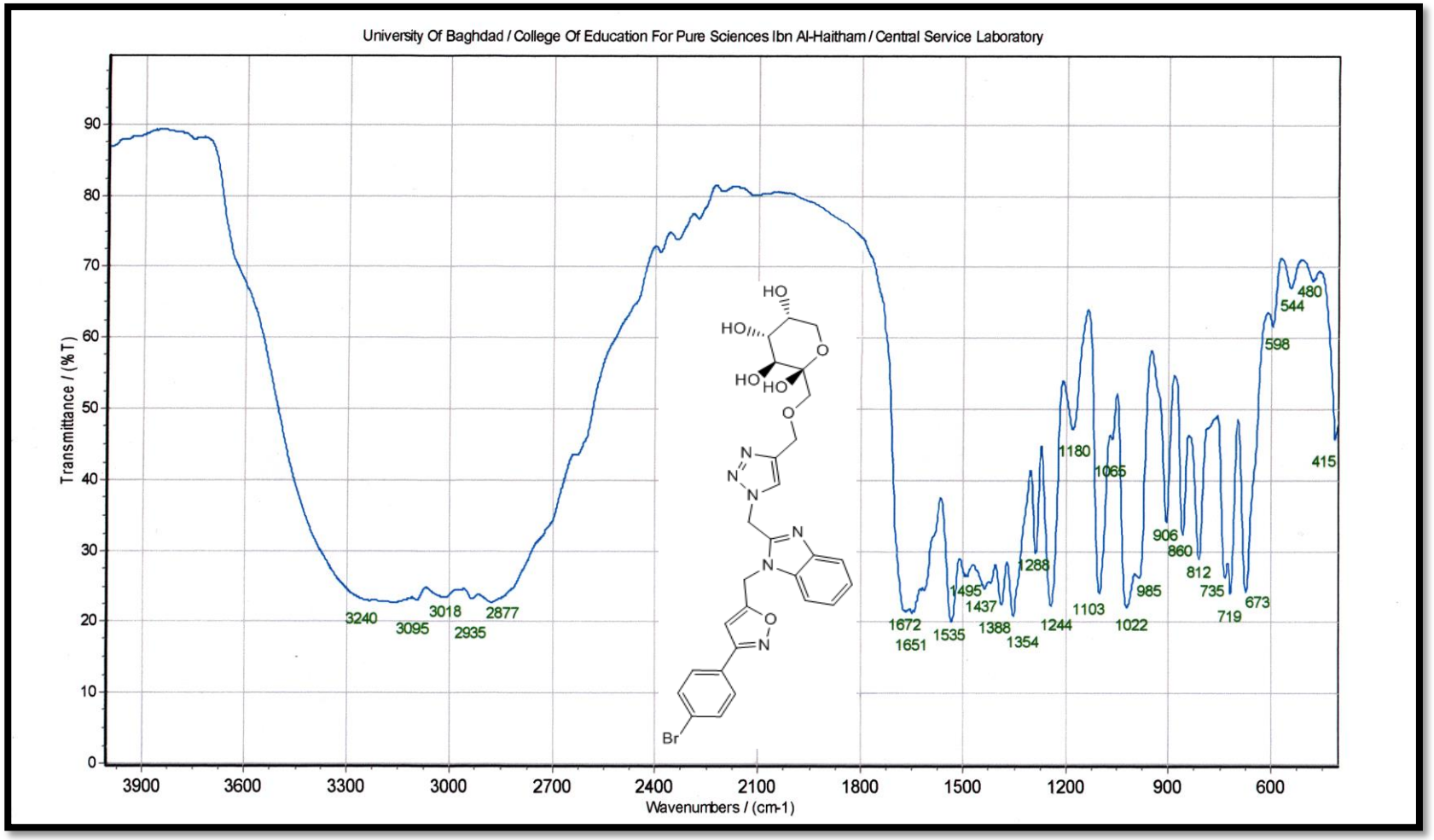


Figure (3-62) FT-IR –spectrum of compound $[XXI]_c$

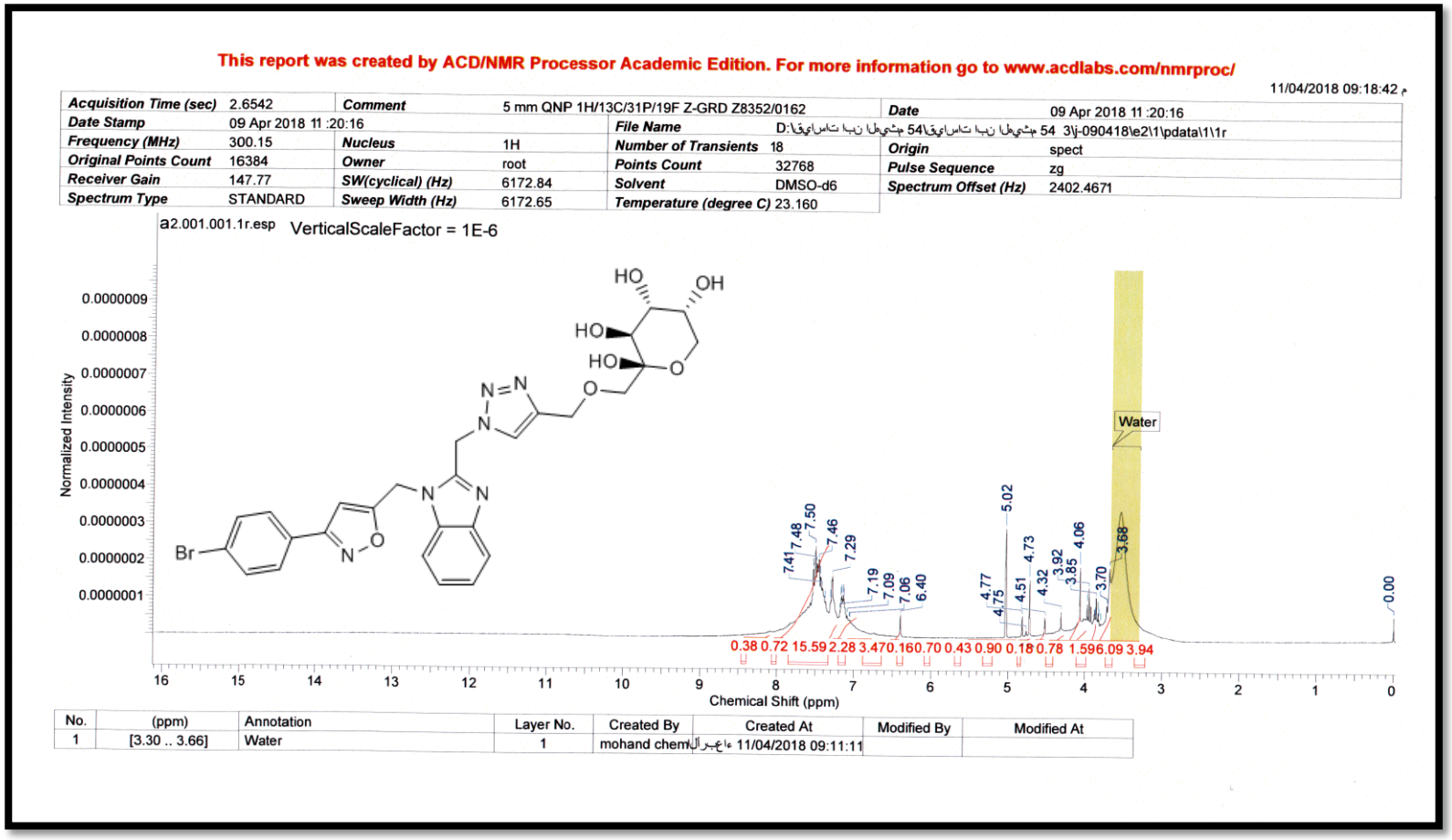


Figure (3-63) ^{1}H-NMR –spectrum of compound [XXI]$_c$

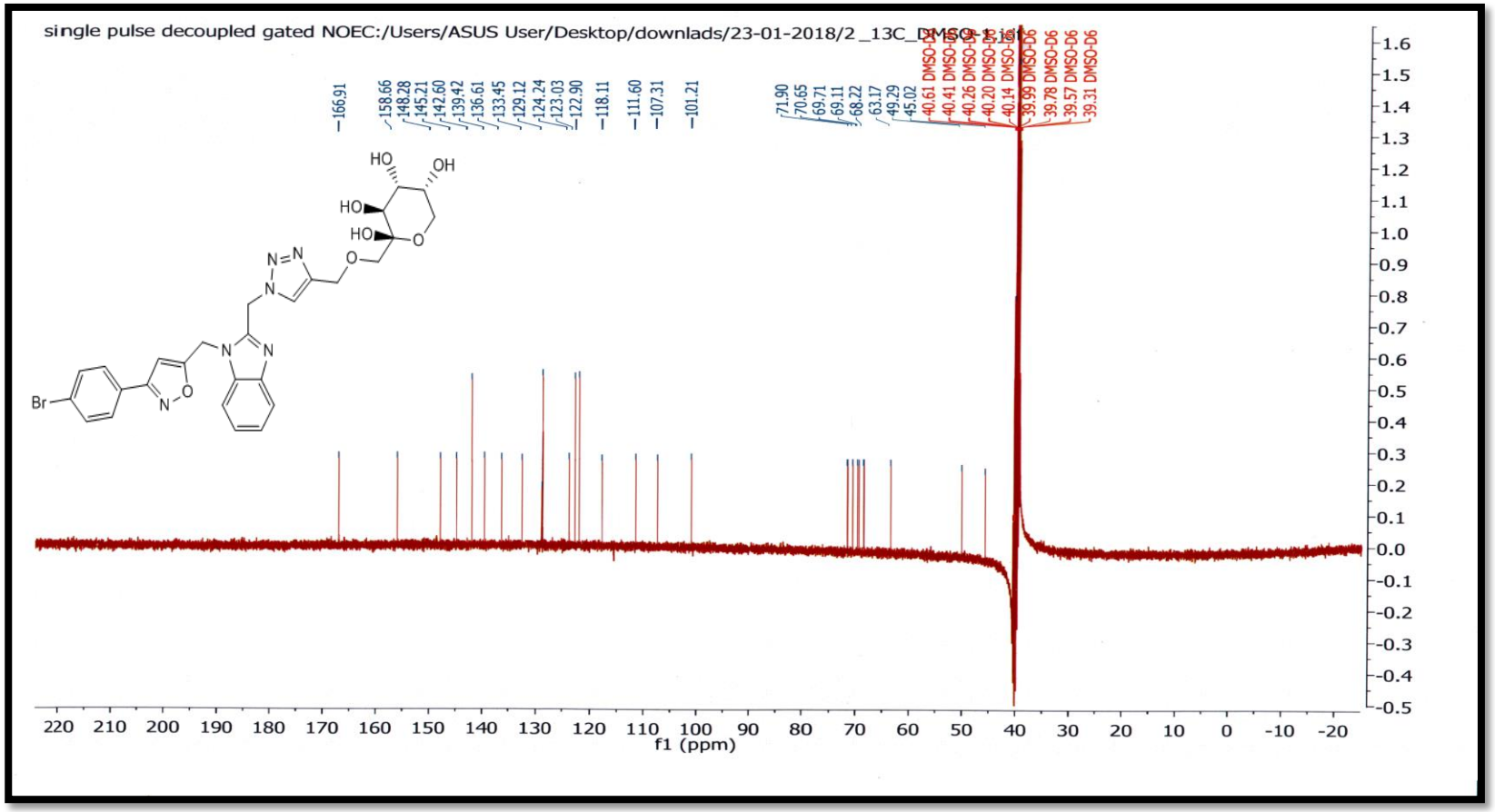


Figure (3-64)^{13}C-NMR –spectrum of compound [XXI]$_c$

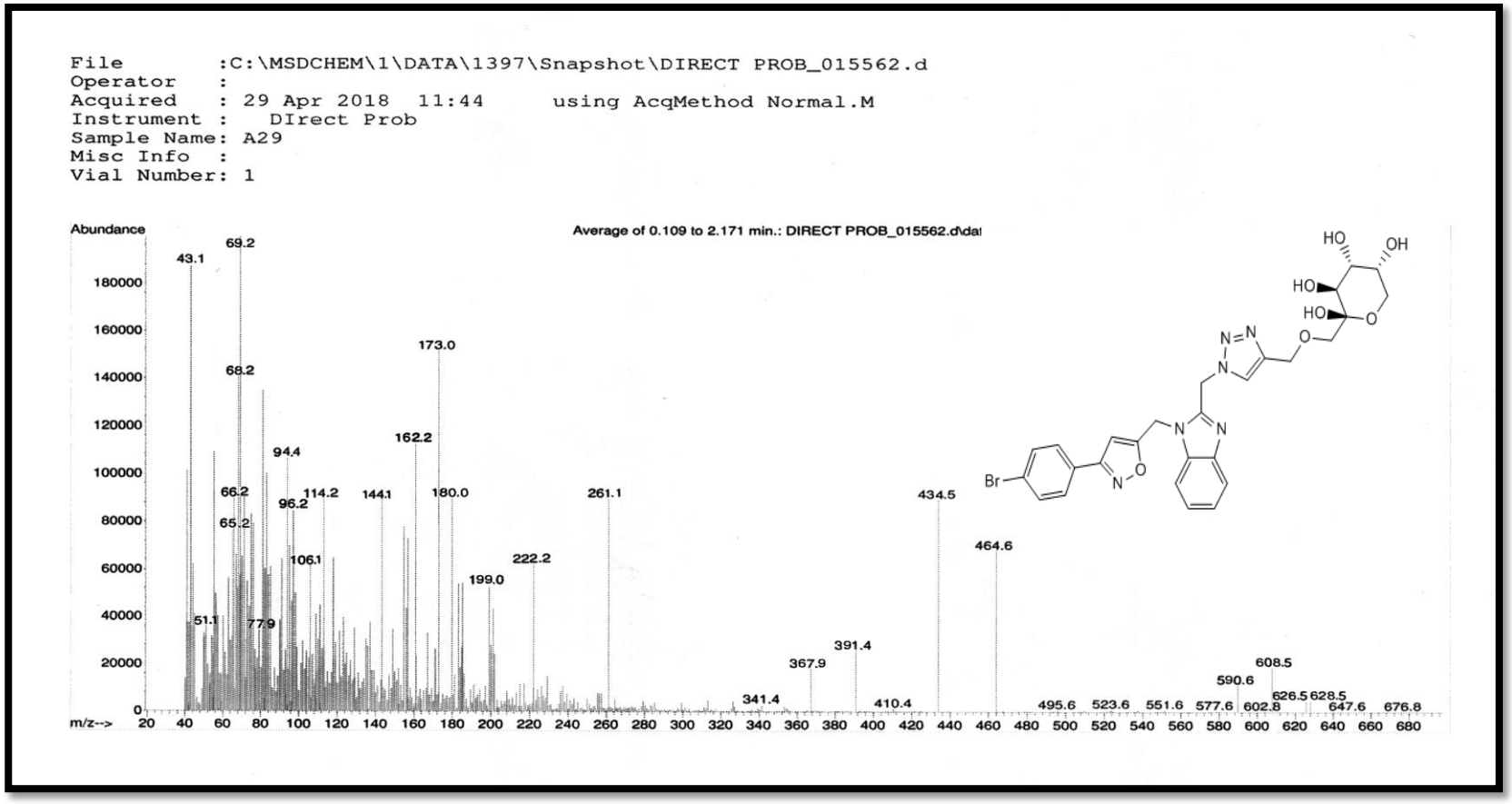


Figure (3-65)The mass spectrum of compound[XXI]$_c$

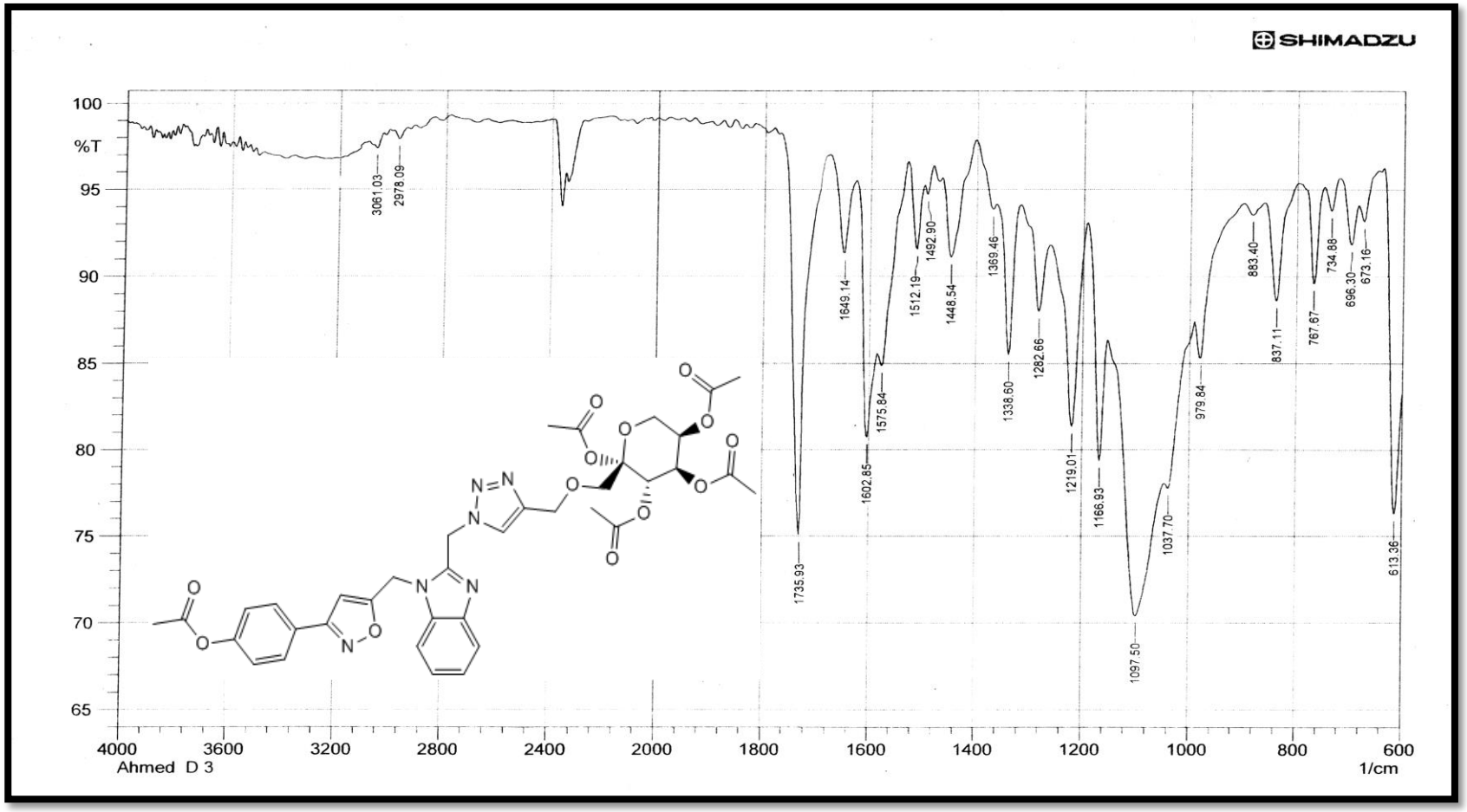


Figure (3-66) FT-IR –spectrum of compound $[XXII]_b$

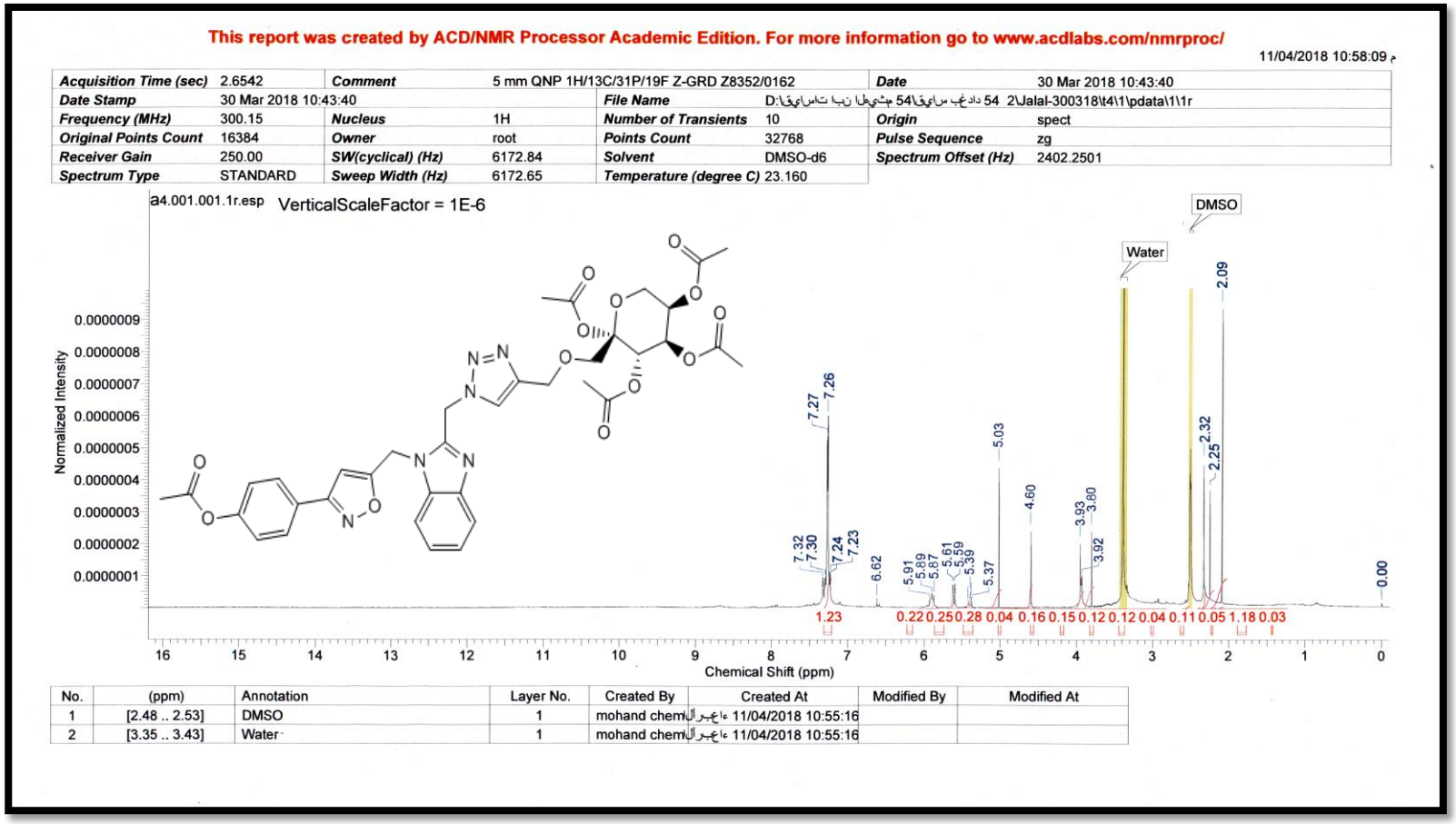


Figure (3-67) ^{1}H-NMR –spectrum of compound $[XXII]_b$

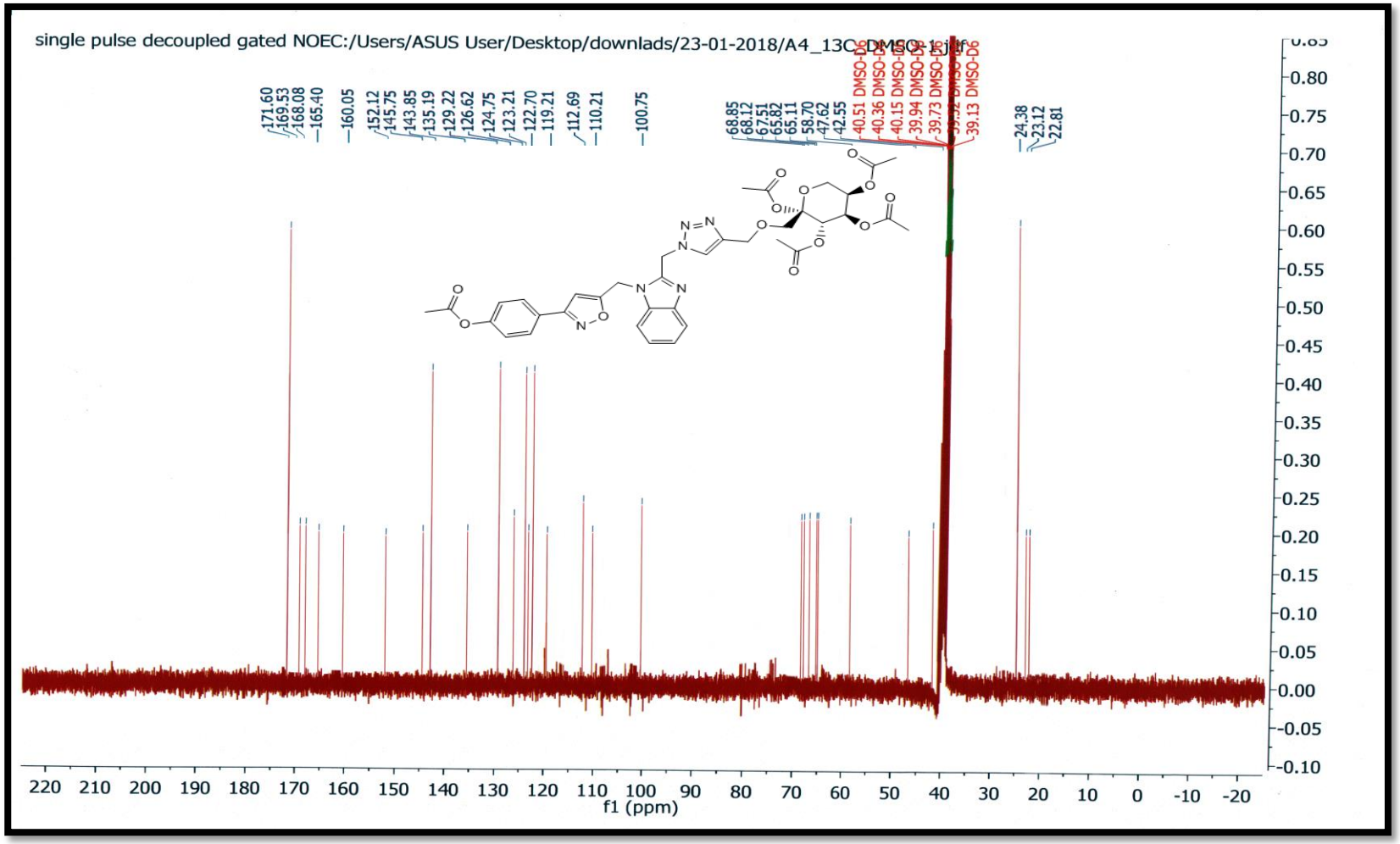


Figure (3-68)^{13}C-NMR –spectrum of compound $[XXII]_b$

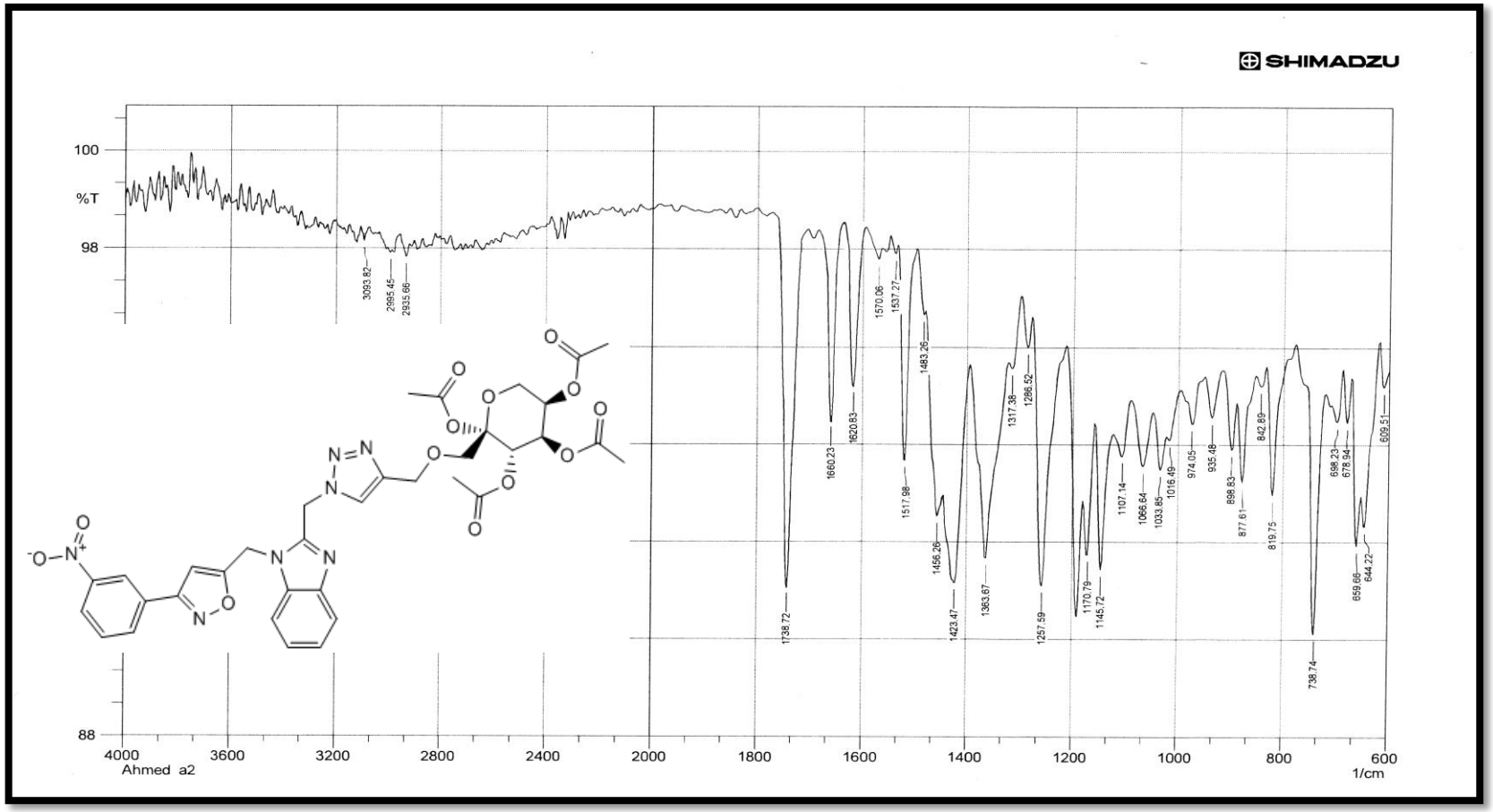


Figure (3-69) FT-IR –spectrum of compound [XXII]$_e$

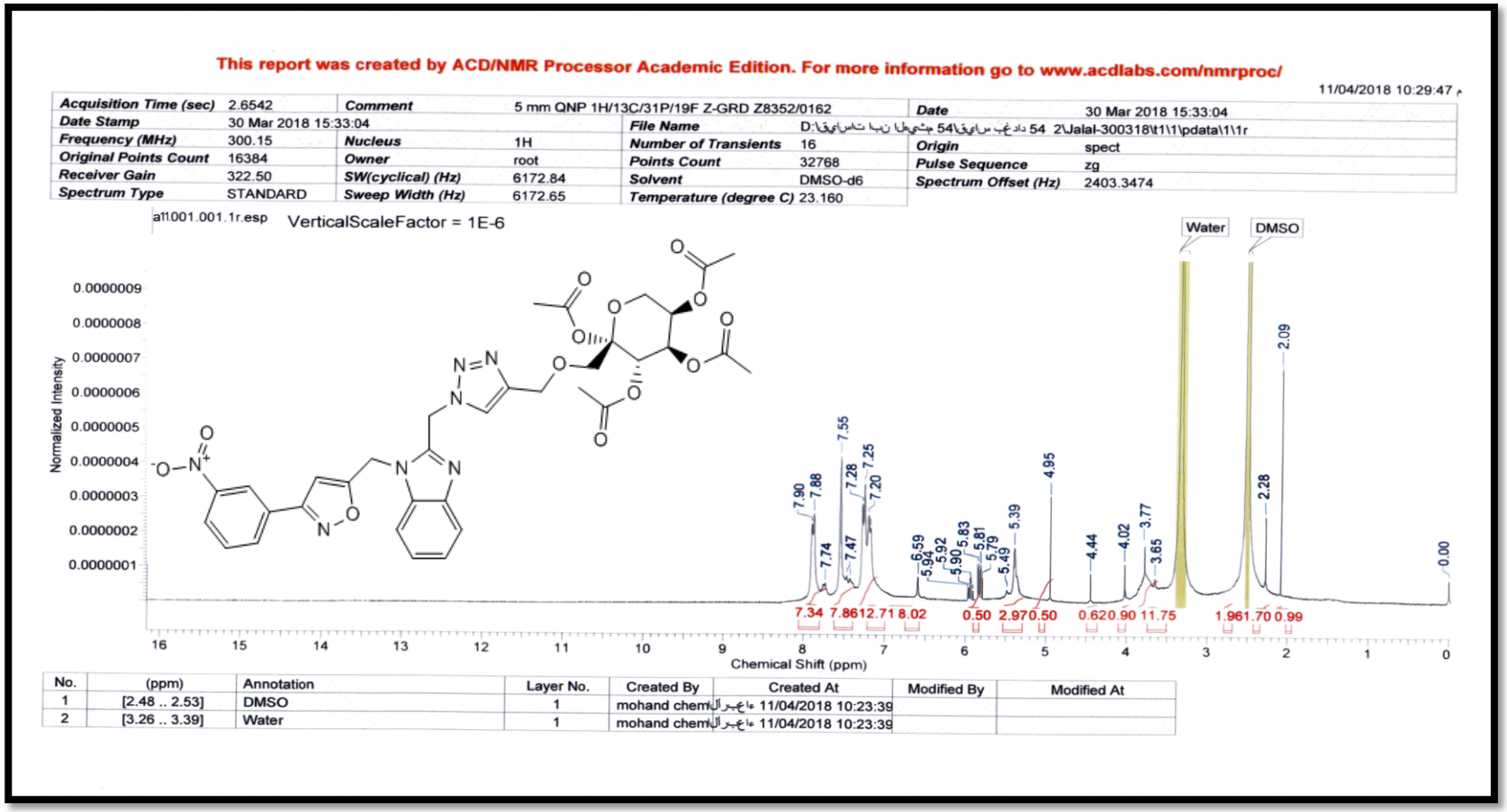


Figure (3-70) ^{1}H-NMR –spectrum of compound $[XXII]_e$

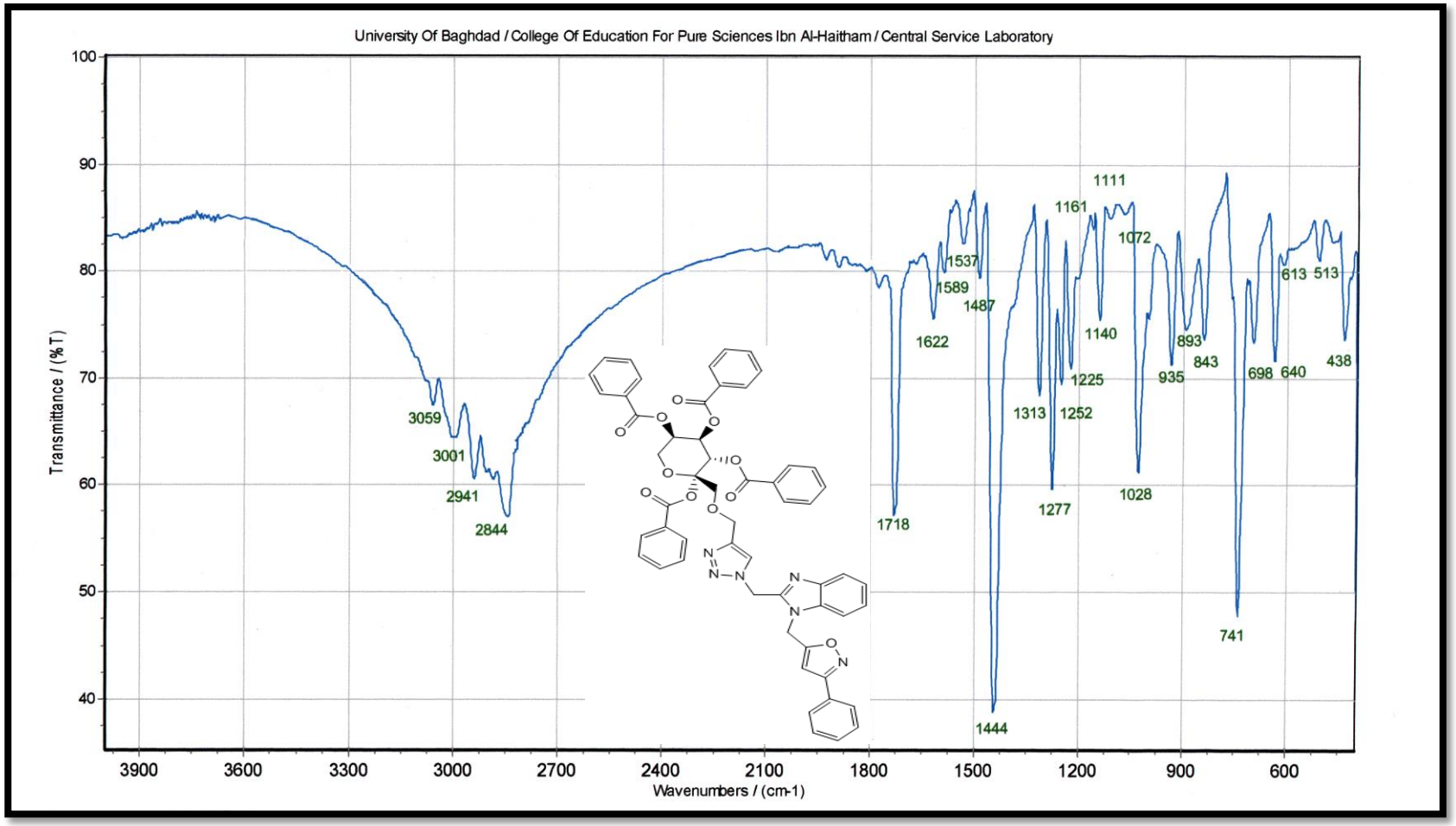


Figure (3-71) FT-IR –spectrum of compound [XXIII]$_a$

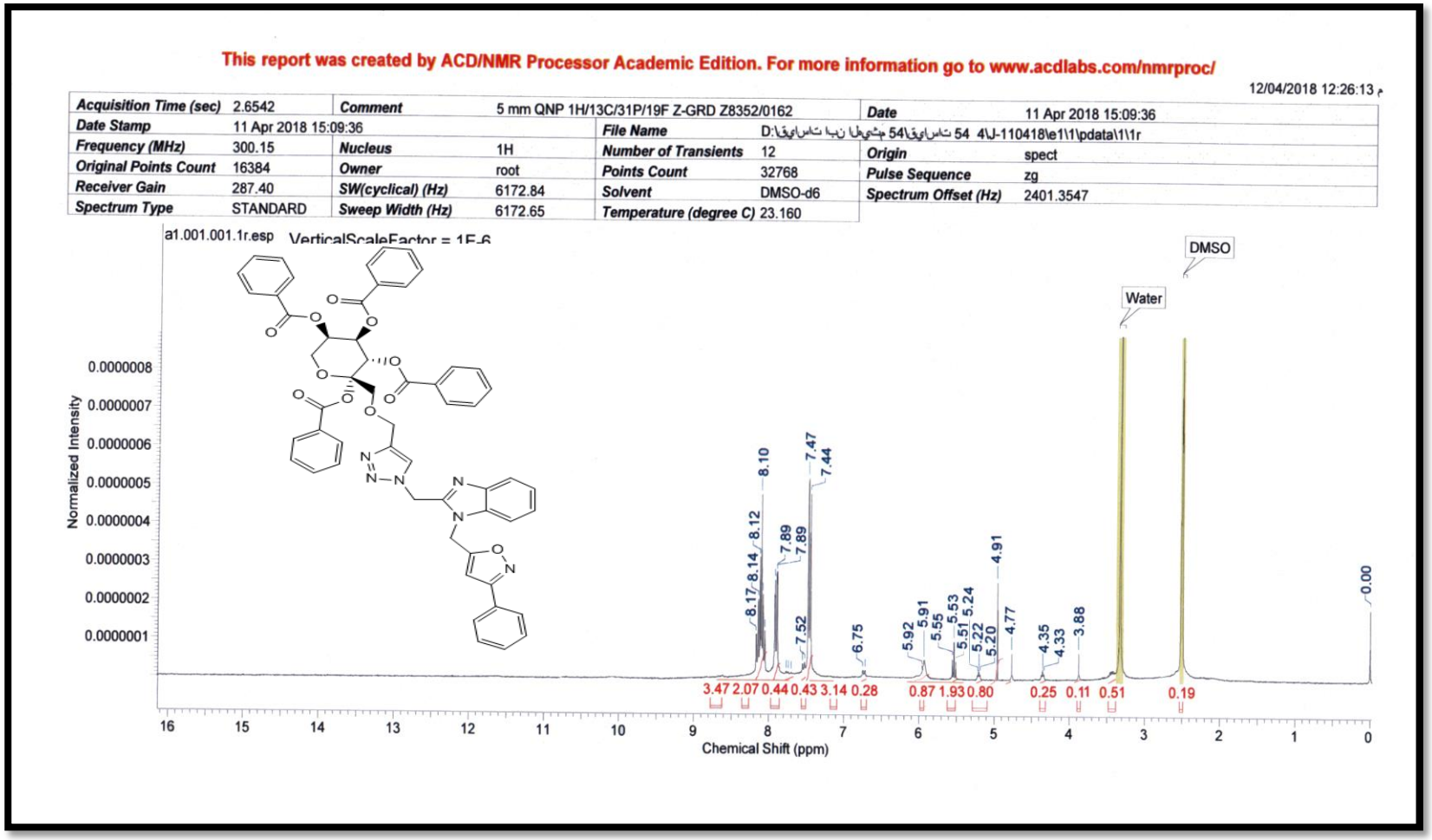


Figure (3-72) ^{1}H-NMR –spectrum of compound [XXIII]$_a$

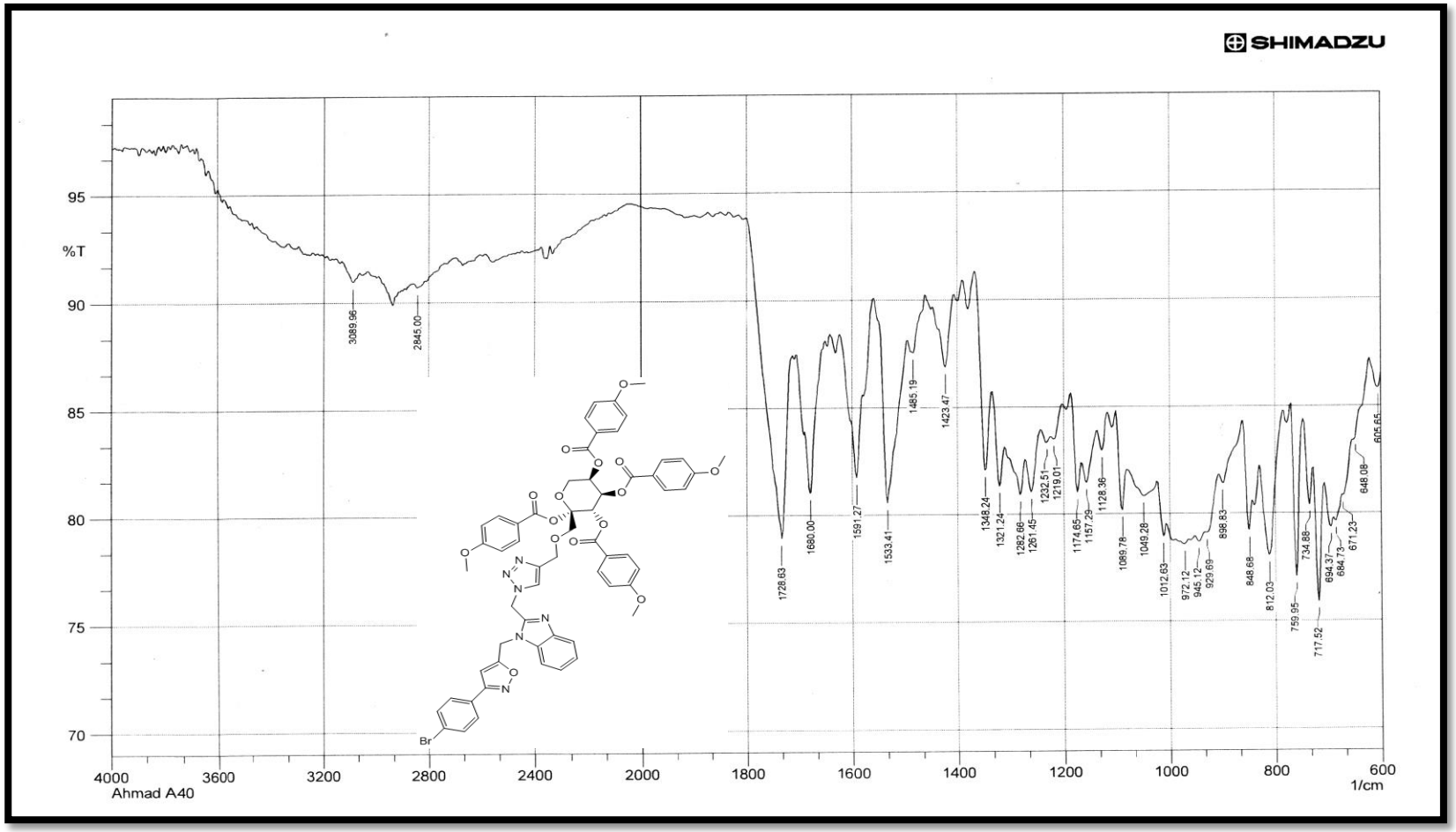


Figure (3-73) FT-IR –spectrum of compound $[XXIV]_c$

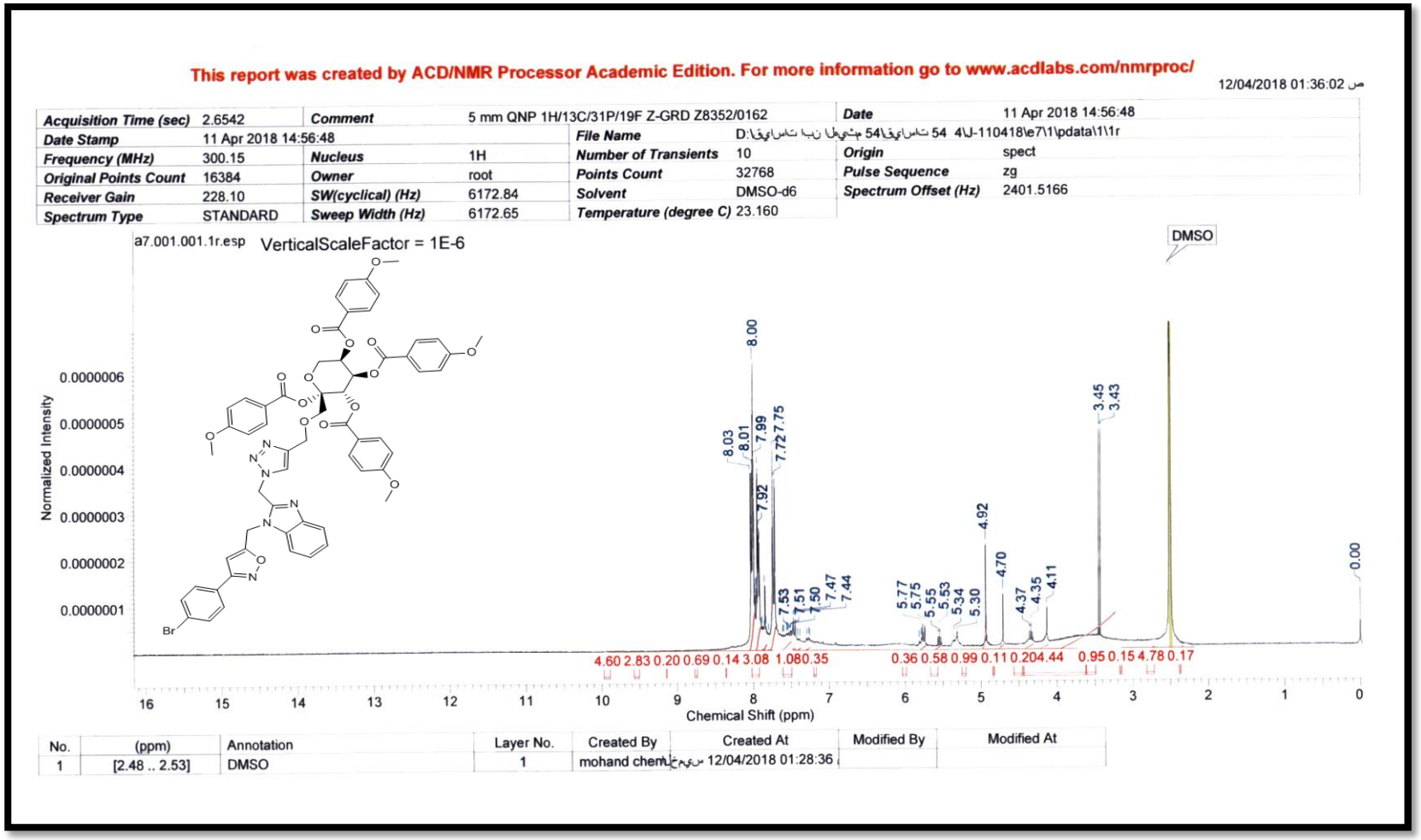


Figure (3-74) ^{1}H-NMR –spectrum of compound $[XXIV]_c$

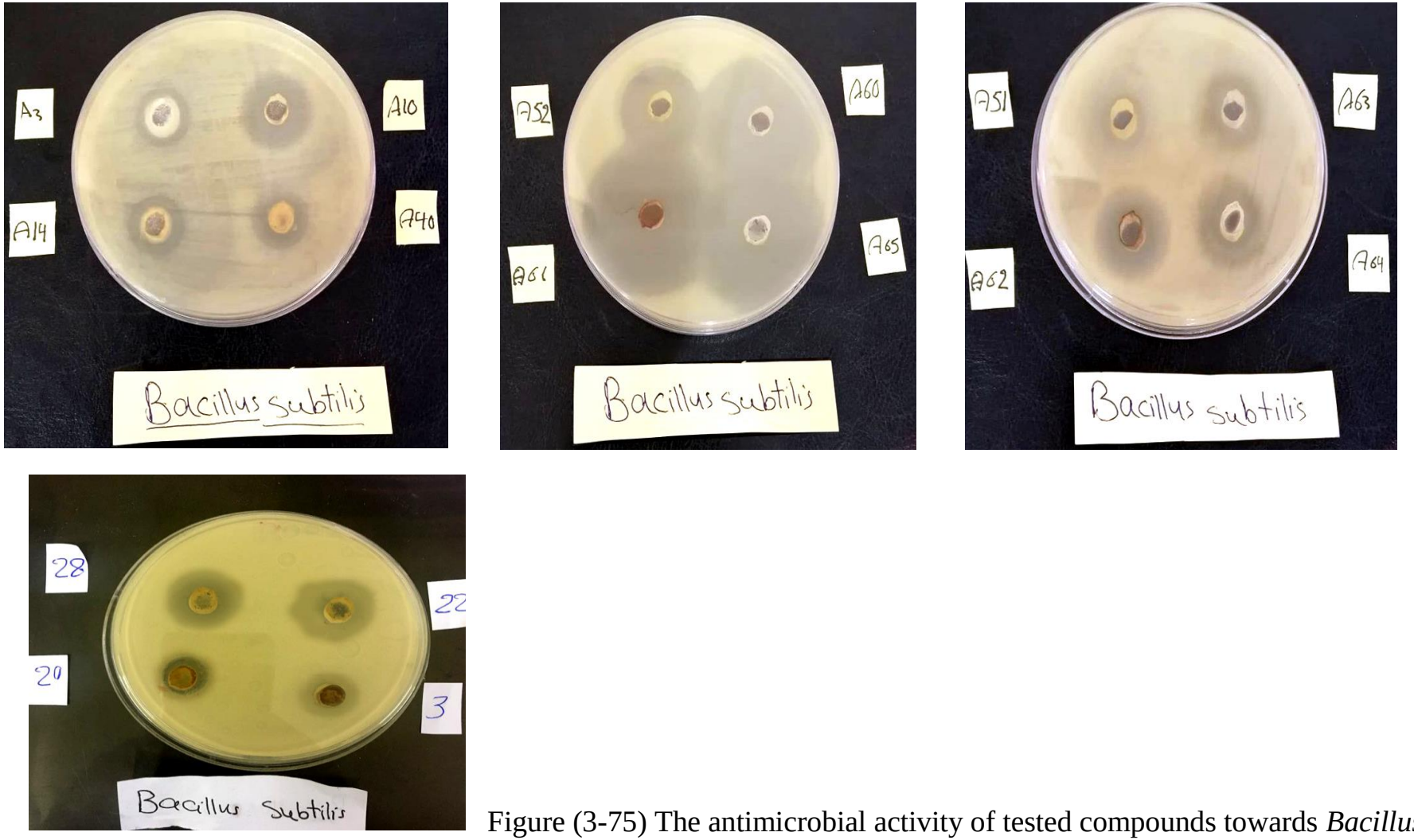


Figure (3-75) The antimicrobial activity of tested compounds towards *Bacillus subtitis* gram(+)

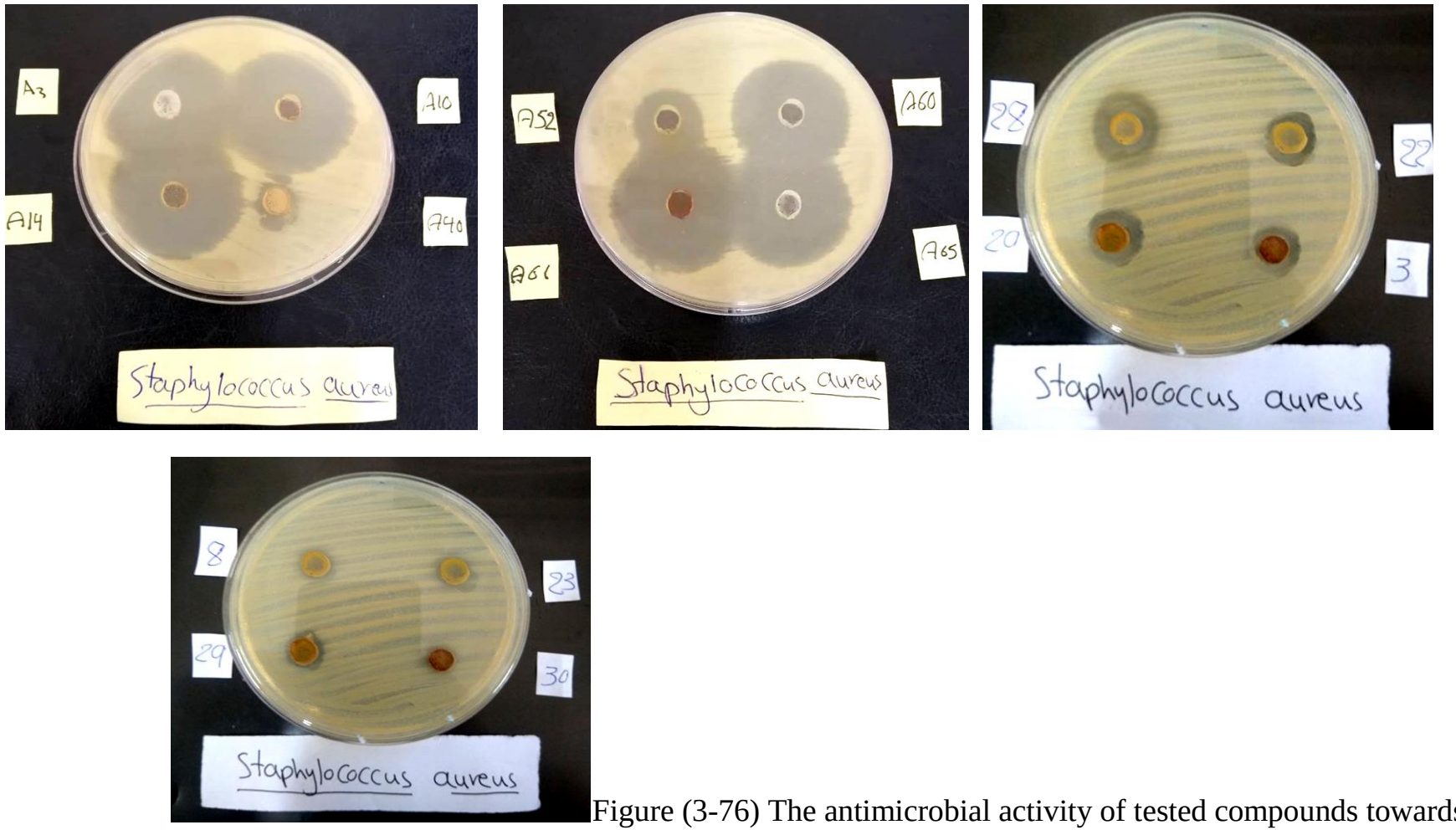


Figure (3-76) The antimicrobial activity of tested compounds towards *Staphlococococs aureus* gram(+)

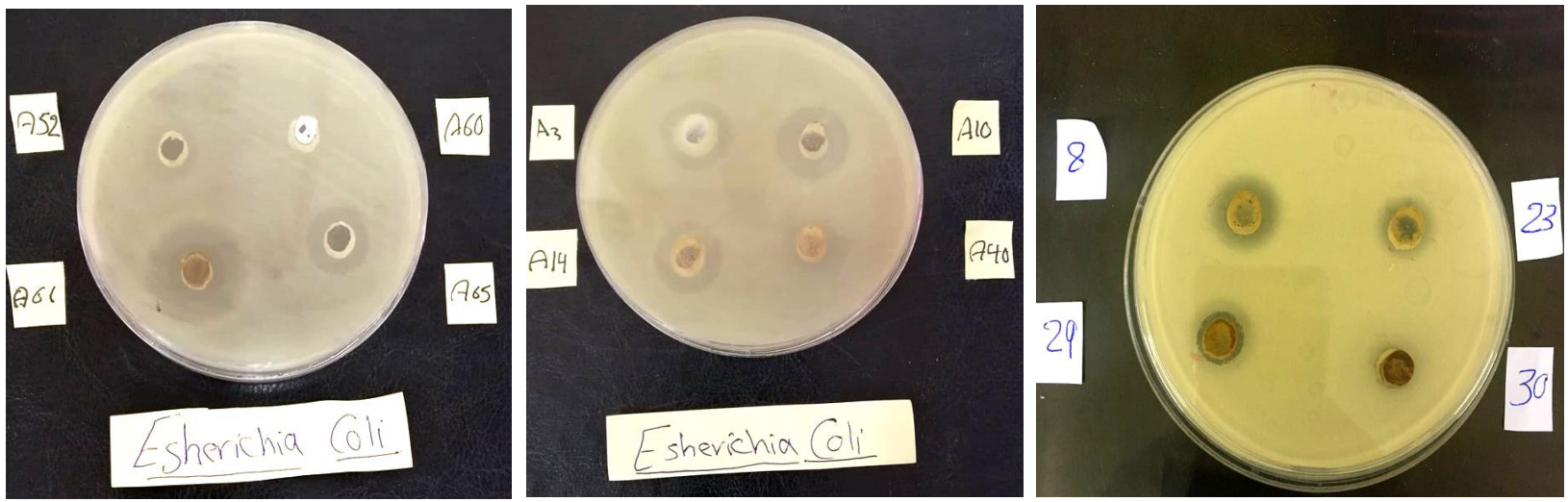


Figure (3-77) The antimicrobial activity of tested compounds towards *E.coli* gram(-)

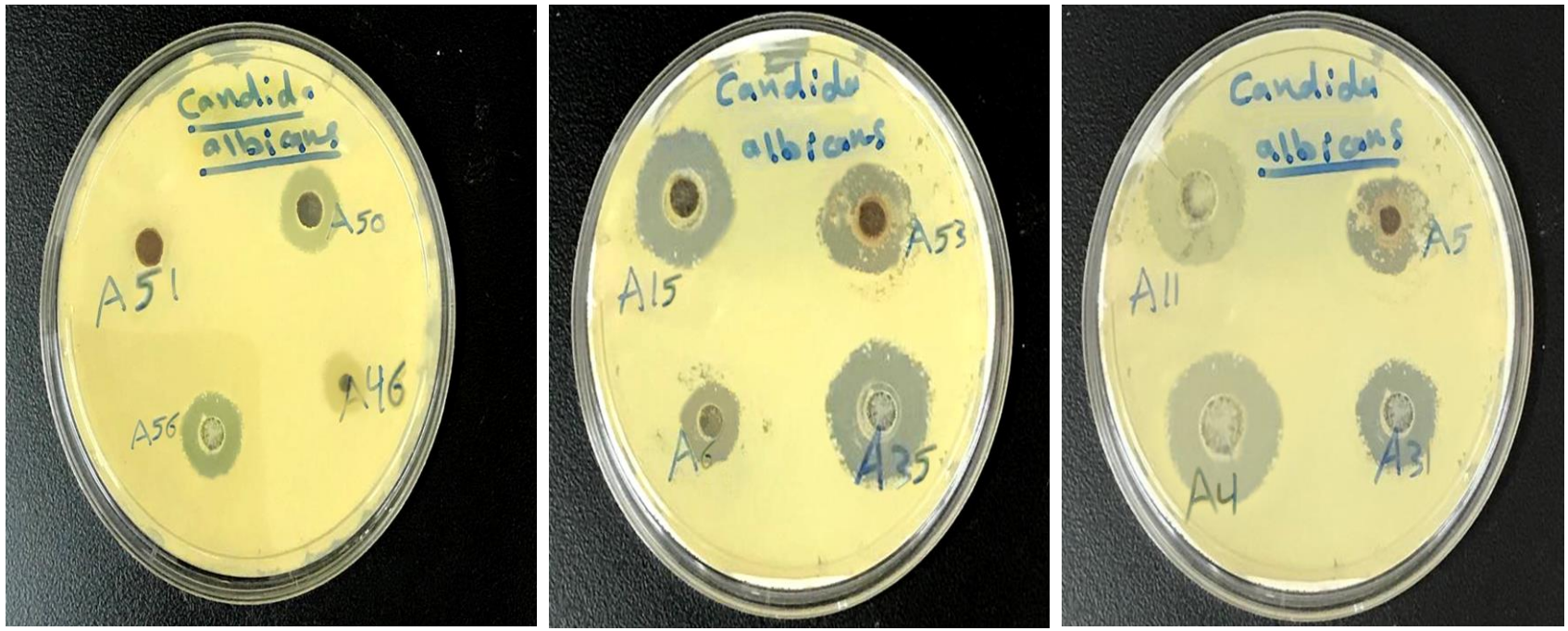


Figure (3-78) The antimicrobial activity of tested compounds towards *candida albicans*

Figure (3-79)The antimicrobial activity of tested compounds towards *candida albicans*

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الخلاصة

يتضمن هذا البحث تحضير مشتقات جد يدة ل(بيتا -D- قركتوزسداسي الحلقه) تحتوي حلقات غير متجانسة متنو عة ولغرض تحقيق هذا الهدف تم تحضير وتشخيص المركبات الآتية:

أولا يتضمن الجزء الأول تحضير وتشخيص مشتقات بيتا -D- قركتوزسداسي الحلقه تحتوي على حلقة الايزواوكسازول.المركبات $[IX]_{a-e}$, $[VIII]_{a-e}$, $[VII]_{a-e}$, $[VI]_{a-e}$, $[V]_{a-e}$ بأتباع الخطوات التالية : (مخطط ١)

أ- تحضير ٣-(٤- او ٣- فنيل معوض)- ٥- [(٣،٢:٤،٥-ثنائي-O-ايزوبروبايلدين- بيتا- D- فركتوبايرانوز -O- يل) مثيل]H1-ا يزواوكسازول. المركبات $[V]_{a-e}$ هذه المركبات حضرت من تفاعل الكاين سكر مركب [IV] مع N- هيدروكسي -٤- او ٣- كلوريد البنزايميدويل المعوض $[II]_{a-e}$ في ثنائي مثيل سلفوكسيد عن طريق تفاعل التحليق ٣،١ ثنائي القطب باستخدام كبرتات النحاس المائيه $CuSO_4.5H_2O$ كعامل مساعد .

ب- المركبات $[VI]_{a-e}$ ٣-(٤- او ٣- فنيل معوض)- ٥- [(بيتا- D- فركتوبايرانوز -O- يل) مثيل- H1[ا يزواوكسازول حضرت من خلال ازالة مجاميع ايزوبروبايلدين للمركبات $[V]_{a-e}$ بواسطة استخدام مزيج من حامض الخليك المخفف والميثانول النقي تحت التصعيد.

ج- تحضير مركبات الاستر الجديده $[VII]_{a-e}$ ، $[VIII]_{a-e}$ و $[IX]_{a- e}$ بواسطة تفاعل مجاميع الهيدروكسيل للمركبات $[VI]_{a-e}$ مع مجموعه من كلوريدات الحامض المختلفه في مزيج من رباعي هيدروفيوران (THF) وثنائي مثيل فورماميد (DMF) باستخدام ثلاثى اثيل امين (Et_3N) كعامل مساعد في درجة حراره ^0C(4-0) .

ثانيا اما الجزء الثاني فيتضمن تحضير وتشخيص مشتقات بيتا -D- قركتوزسداسي الحلقه تحتوي على حلقة ٣،٢،١- ترايازول.المركبات[XI] ,[XII] , $[XIII]_{a-c}$, $[XIV]_{a-c}$ بأتباع الخطوات التالية : (مخطط ٢)

أ- تحضير المر كب 1-((H1- بنزو[d] ايميدازول- ٢- يل)مثيل) - ٤- [(٣،٢:٤،٥-ثنائي-O- ايزوبروبايلدين- بيتا- D- فركتوبايرانوز -O- يل) مثيل]H1-٣،٢،١- ترايازول. المركب [XI]

بواسطة تفاعل الكاين سكر مركب [IV] مع ٢-(ازيدو مثيل) H1- بنزو[d] ايميدازول المركب [X] تحت التصعيدعند درجة حرارة ^0C(70-65) في ثنائي مثيل سلفوكسيد DMSO كمذيب بواسطة

استخدام طريقة CuAAC .

ب- تحضير 1 -((H1- بنزو[d] ايميدازول- ٢- يل)مثيل) - ٤- [(- بيتا- D- فركتوبايرانوز -O- يل) مثيل]H1-٣،٢،١- ترايازول. المركب [XII] بواسطة تفاعل مركب [XI] مع مزيج من حامض الخليك المخفف و الميثانول النقي تحت التصعيد.

ج- تحضيرسلسله من مركبات الاستر الجديده $[XIII]_{a-c}$ بواسطة تفاعل مجاميع الهيدروكسيل للمركب [XII] مع ثلاث انواع من كلوريد الحامض في مزيج من رباعي هيدروفيوران (THF)وثنائي مثيل فورماميد (DMF) باستخدام ثلاثى اثيل امين (Et_3N) كعامل مساعد عند درجة حراره $(0-4)^0C$

د- تحضير مركبات الايثر الجديده $[XIIV]_{a-c}$ بواسطة تفاعل مجاميع الهيدروكسيل للمركب [XII]مع زياده من مجموعه مختلفه من بروميد الالكيل في الايثانول النقي واستخدام هيدروكسيد البوتاسيومKOH كعامل مساعد .

ثالثا الجزء الثالث يتضمن تحضير وتشخيص مجموعه جديده من مشتقات بيتا -D- قركتوزسداسي الحلقه تحتوي على حلقتي ٣،٢،١- ترايازول.المركبات $[XVIII]_{a-c}$, [XVII], [XVI], [XV] $[XIX]_{a-c}$ بأتباع الخطوات التالية : (مخطط ٣)

أ- تحضير 1-((١-(بروب-٢-ين-١-يل) -H1- بنزو[d] ايميدازول- ٢- يل)مثيل) - ٤- [(٣،٢:٤،٥-ثنائي-O-ايزوبروبايلدين- بيتا- D- فركتوبايرانوز -O- يل) مثيل]H1-٣،٢،١- ترايازول. المركب [XV] بواسطة تفاعل مركب [XI] مع بروميد البروبرجيل في سيانيد المثيل واستخدام كاربونات البوتاسيوم K_2CO_3 كعامل مساعد .

ب- تحضيرمركب ثنائي الترايازول [XVI] 1 -((1-((1-((H1- بنزو[d] ايميدازول- ٢- يل)مثيل) ترايازول - ٤- يل) مثيل) -H1- بنزو[d] ايميدازول- ٢- يل)مثيل) - ٤- [(٣،٢:٤،٥-ثنائي-O-ايزوبروبايلدين- بيتا- D- فركتوبايرانوز -O- يل) مثيل]H1-٣،٢،١- ترايازول. باستخدام نفس طريقة(CuAAC).

ج- تحضير 1-((1-((1-((H1- بنزو[d] ايميدازول- ٢- يل)مثيل) ترايازول - ٤- يل) مثيل) -H1- بنزو[d] ايميدازول- ٢- يل)مثيل) - ٤- [(- بيتا- D- فركتوبايرانوز -O- يل) مثيل]H1-٣،٢،١- ترايازول.بواسطة استخدام نفس طريقة تفاعل ازالة مجموعة ايزوبروبايلدين

د- تحضير مشتقات استر جديده تحتوي على حلقتين من الترايازول مركبات$_{a-c}$[XVIII] بواسطة نفس الطريقة المستخدمه في تحضير مركبات الاستر$_{a-c}$[XIII] في فقرة (الجزء الثاني) .

ح- تحضير مشتقات ايثر جديده تحتوي على حلقتين من الترايازول مركبات $_{a-c}$[XIX] بواسطة نفس الطريقة المستخدمه في تحضير مركبات الايثر $_{a-c}$[XIV] في فقرة (الجزء الثاني) .

رابعا الجزء الرابع يتضمن تحضير وتشخيص سلسله جديده من مشتقات بيتا -D- قركتوزسداسي الحلقه تحتوي على حلقتي الترايازول و الايزواوكسازول معا .المركبات , $_{a-e}$[XXI] , $_{a-e}$[XX] $_{a-e}$[XXIV], $_{a-e}$[XXIII], $_{a-e}$[XXII] بأتباع الخطوات التالية : (مخطط ٤)

أ- تحضير ٢،٣:٤،٥-ثنائي-O-ايزوبروبايلدين- بيتا– D فركتوبايرانوز التي تحتوي على حلقتي الترايازول و الايزواوكسازول معا . المركبات $_{a-e}$[XX] باستخدام كبرتات النحاس المائيه $CuSO_4.5H_2O$ كعامل مساعد عن طريق تفاعل التحليق ٣،١ ثنائي القطب للمركب[XV] مع N- هيدروكسي -٤- او ٣- كلوريد البنزايميدويل المعوض$_{a-e}$[II] تحت التصعيد.

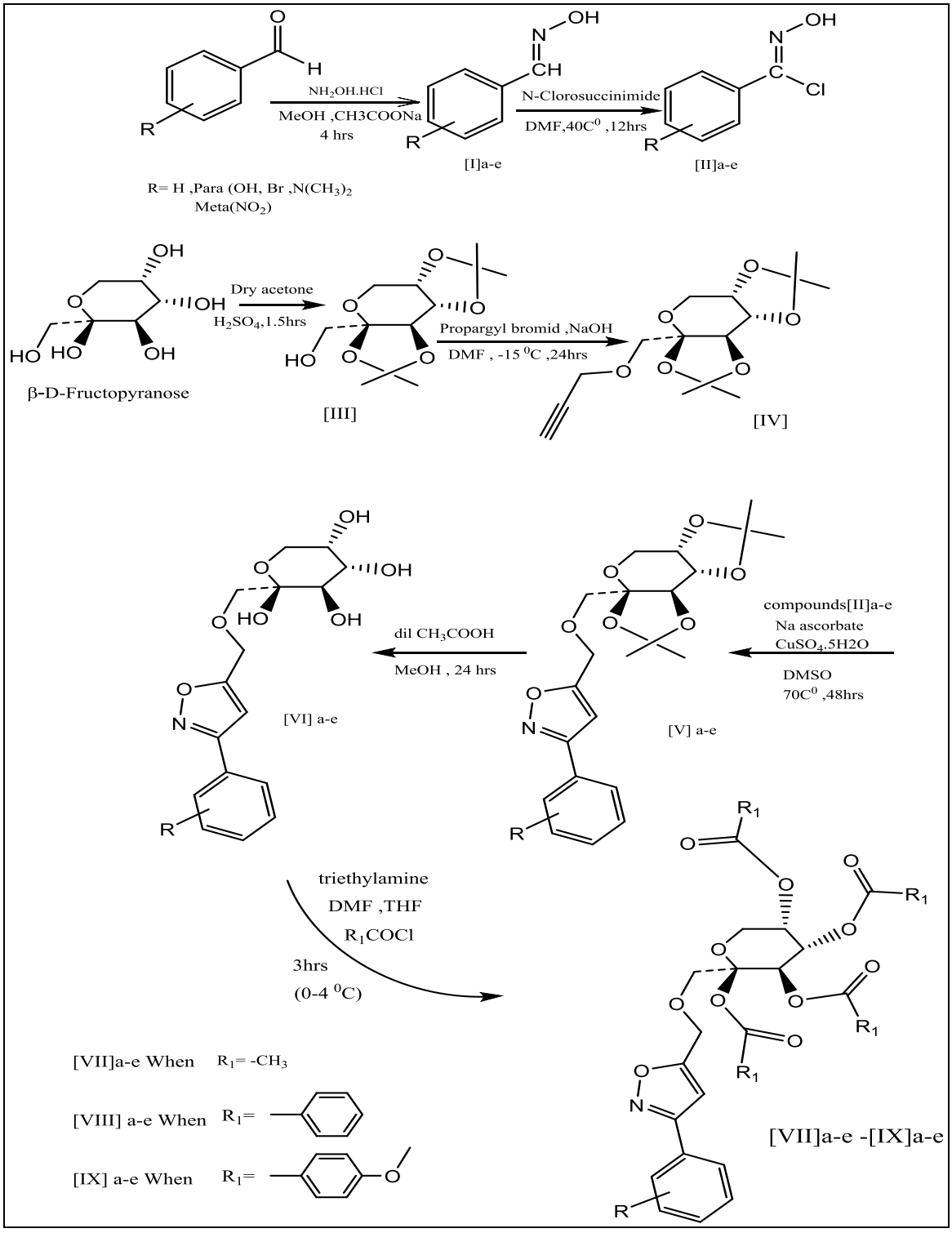
ب- تحضير1-((1-((٣-(٤- او ٣- فنيل معوض)ايزواوكسازول- ٥- يل) مثيل) -H1- بنزو[d] ايميدازول- ٢- يل)مثيل) - ٤- [(- بيتا- D- فركتوبايرانوز -O- يل) مثيل]H1-١،٢،٣- ترايازول$_{a-e}$[XXI] بواسطة تفاعل مركب [XX] مع مزيج من حامض الخليك المخفف و الميثانول النقي تحت التصعيد.

ج- تحضير مشتقات الاستر الجديده التي تحتوي على حلقتي الترايازول و الايزواوكسازول معا. المركبات $_{a-e}$[XXIV], $_{a-e}$[XXIII], $_{a-e}$[XXII] بواسطة تفاعل مجاميع الهيدروكسيل للمركبات$_{a-e}$[XXI] مع مجموعه من كلوريدات الحامض المختلفه في مزيج من رباعي هيدروفيوران (THF) وثنائي مثيل فورماميد (DMF) باستخدام ثلاثى اثيل امين (Et_3N) كعامل مساعد في درجة حراره ^0C(0-4).

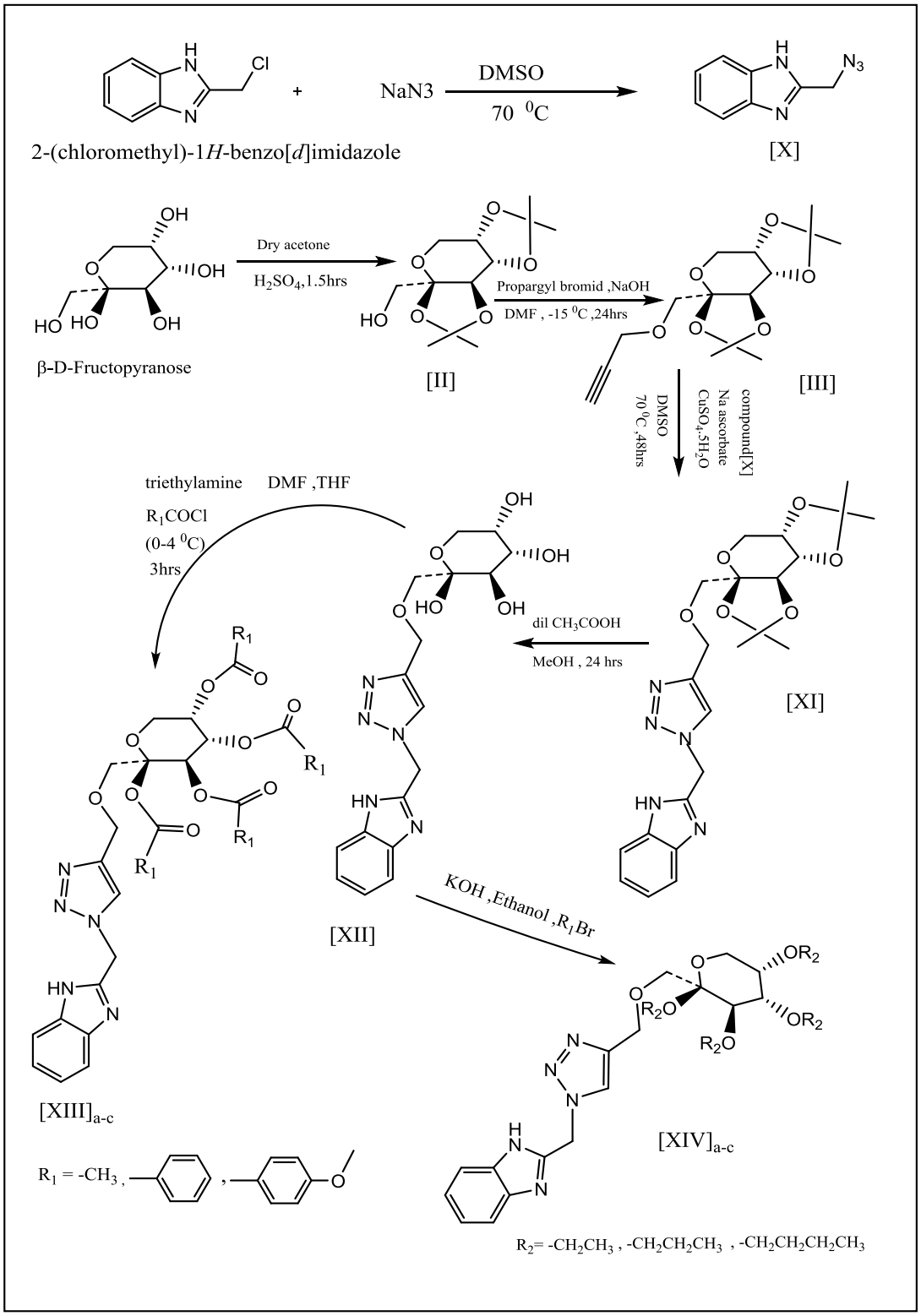
شخصت جميع المركبات المحضرة اعلاه بواسطة درجة الانصهارواطياف الاشعة تحت الحمراء وطيف الرنين النووي المغناطيسي ^1HNMR, ^{13}C-NMR وطيف الكتلة (للبعض منها) .

درست الفعالية البيولوجية للمركبات المحضرة باستخدام ثلاث انوع من البكتريا *Staphlococcs aureus* gram (+) *Bacillus subtitis*(gram+) و *E.coli* (gram-) ونوع واحد من الفطريات *candida albicans*.

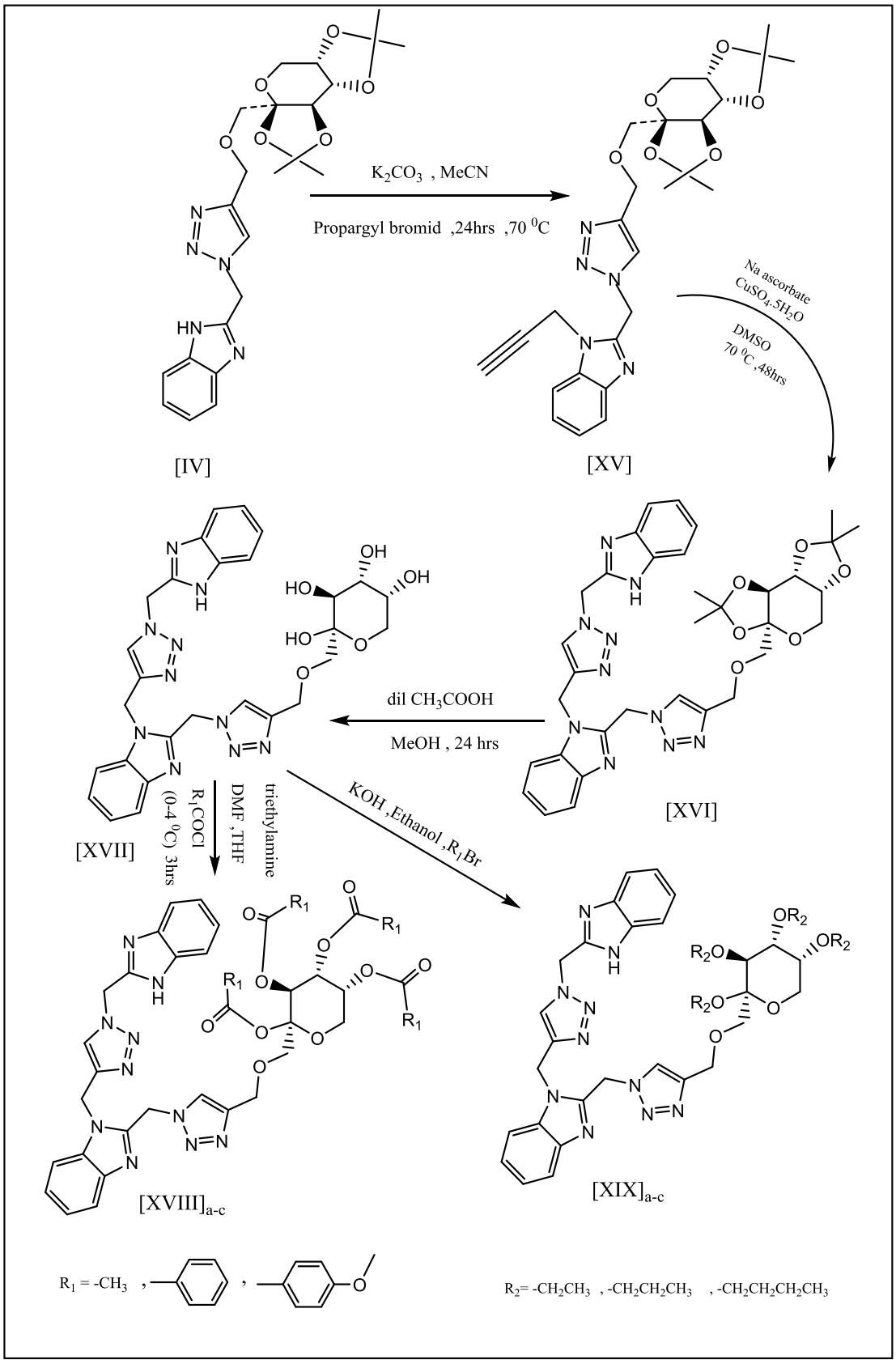
بعض المركبات اعطت فعالية جيدة والبعض الاخر لم يعطي اي فعالية بيولوجية تجاه البكتريا والفطريات. هذا العمل لخص بالمخططات الاربعه التاليه (١،٢،٣ و ٤)



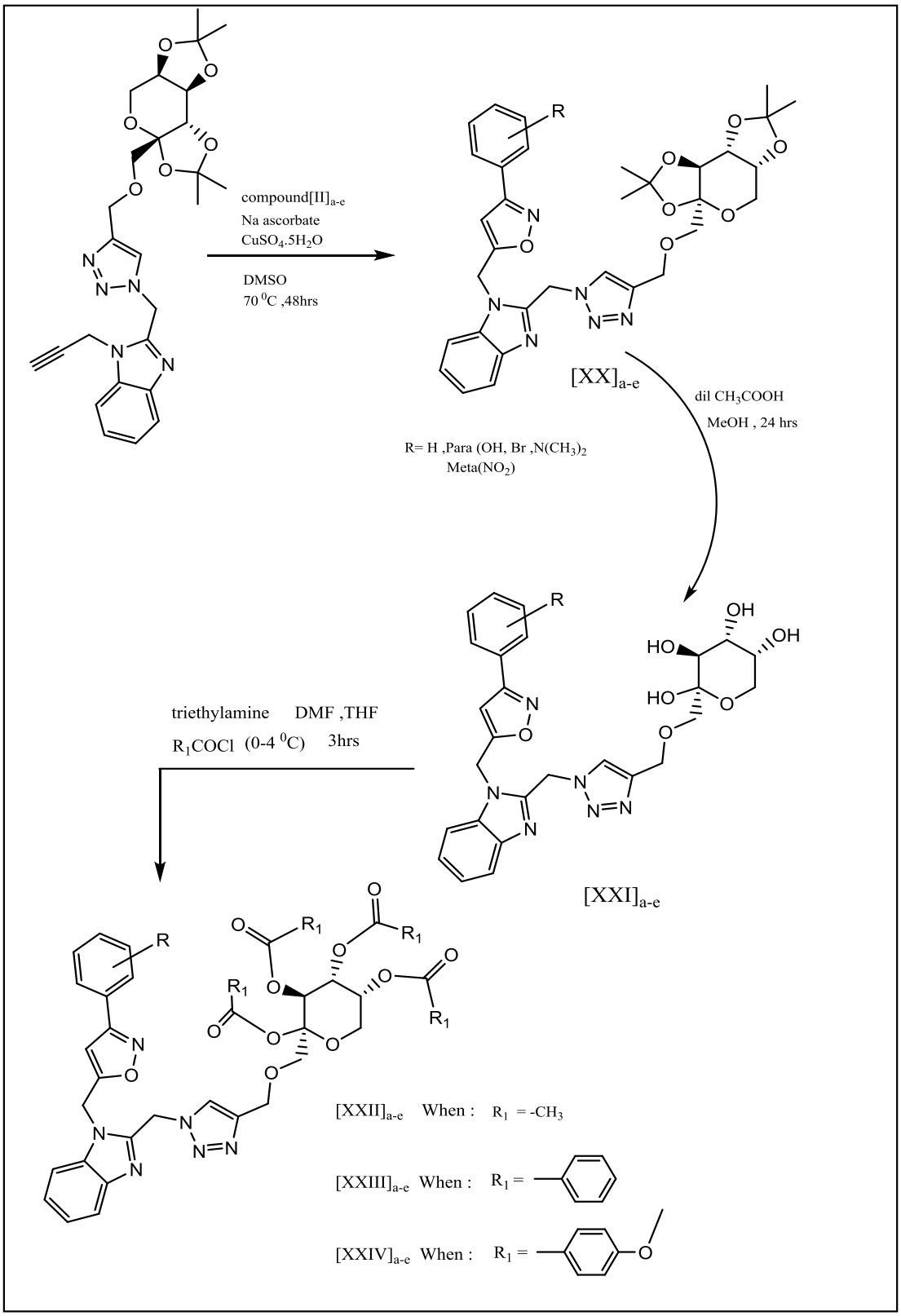
مخطط -١-


NaN3
DMSO
70 0C
2-(chloromethyl)-1H-benzo[d]imidazole
[X]
Dry acetone
H2SO4,1.5hrs
β-D-Fructopyranose
[II]
Propargyl bromid ,NaOH
DMF , -15 0C ,24hrs
[III]
compound[X]
Na ascorbate
CuSO4,5H2O
DMSO
70 0C ,48hrs
triethylamine
DMF ,THF
R1COCl
(0-4 0C)
3hrs
dil CH3COOH
MeOH , 24 hrs
[XI]
[XII]
KOH ,Ethanol ,R1Br
[XIII]a-c
R1 = -CH3 ,
[XIV]a-c
R2= -CH2CH3 , -CH2CH2CH3 , -CH2CH2CH2CH3

مخطط -٢-


K2CO3 , MeCN
Propargyl bromid ,24hrs ,70 0C
Na ascorbate
CuSO4.5H2O
DMSO
70 0C ,48hrs
[IV]
[XV]
dil CH3COOH
MeOH , 24 hrs
[XVI]
[XVII]
R1COCl
(0-4 0C) 3hrs
DMF ,THF
triethylamine
KOH ,Ethanol ,R1Br
[XVIII]a-c
[XIX]a-c
R1 = -CH3 ,
R2= -CH2CH3 , -CH2CH2CH3 , -CH2CH2CH2CH3

مخطط -٣-


compound[II]a-e
Na ascorbate
CuSO4.5H2O
DMSO
70 0C ,48hrs
[XX]a-e
R= H ,Para (OH, Br ,N(CH3)2
Meta(NO2)
dil CH3COOH
MeOH , 24 hrs
triethylamine DMF ,THF
R1COCl (0-4 0C) 3hrs
[XXI]a-e
[XXII]a-e When : R1 = -CH3
[XXIII]a-e When : R1 =
[XXIV]a-e When : R1 =

مخطط -٤-

جمهورية العراق

وزارة التعليم العالي والبحث العلمي

جامعة بغداد

كلية التربية للعلوم الصرفة/ إبن الهيثم

قسم الكيمياء

تحضيروتشخيص وتقييم الفعاليه الحيويه لبعض المشتقات الجديده للفركتوز تحتوي على حلقات ايزوكسازول و ١،٢،٣- ترايازول والبنزايميدازول

رسالة مقدمة إلى

مجلس كلية التربية للعلوم الصرفة - إبن الهيثم/ جامعة بغداد كجزء من متطلبات نيل درجة فلسفة دكتوراه في الكيمياء

من قبل

احمد عبيد جاسم

بكلوريوس علوم في الكيمياء-١٩٨٩

ماجستير علوم في الكيمياء-٢٠٠٩

باشراف

أ.د. خالد فهد الجبوري

١٤٤١ هـ **٢٠١٩ م**