T.R.

EGE UNIVERSITY

Graduate School of Applied and Natural Science

SYNTHESIS OF NEW MONOMERS BASED ON CHLORALOSE

Selin YILDIRAN EVREN

Supervisor : Assoc. Prof. Dr. A.Yeşim SALMAN

Chemistry Departmant

Organic Chemistry

İzmir

2019

Selin YILDIRAN EVREN tarafından **yüksek lisans** tezi olarak sunulan **"Kloraloz Esaslı Yeni Monomerlerin Sentezleri"** başlıklı bu çalışma EÜ Lisansüstü Eğitim ve Öğretim Yönetmeliği ile EÜ Fen Bilimleri Enstitüsü Eğitim ve Öğretim Yönergesi'nin ilgili hükümleri uyarınca tarafımızdan değerlendirilerek savunmaya değer bulunmuş ve 09/09/2019 tarihinde yapılan tez savunma sınavında aday oybirliği/oyçokluğu ile başarılı bulunmuştur.

Jüri Üyeleri:		**İmza**
Jüri Başkanı	: Doç.Dr. A. Yeşim Salman	
Raportör Üye	: Prof.Dr. Yurdanur Akgöl	
Üye	: Prof. Dr. Haluk Oruç	

EGE ÜNİVERSİTESİ FEN BİLİMLERİ ENSTİTÜSÜ

ETİK KURALLARA UYGUNLUK BEYANI

EÜ Lisansüstü Eğitim ve Öğretim Yönetmeliğinin ilgili hükümleri uyarınca Yüksek Lisans Tezi olarak sunduğum **"Kloraloz Esaslı Yeni Monomerlerin Sentezleri"** başlıklı bu tezin kendi çalışmam olduğunu, sunduğum tüm sonuç, doküman, bilgi ve belgeleri bizzat ve bu tez çalışması kapsamında elde ettiğimi, bu tez çalışmasıyla elde edilmeyen bütün bilgi ve yorumlara atıf yaptığımı ve bunları kaynaklar listesinde usulüne uygun olarak verdiğimi, tez çalışması ve yazımı sırasında patent ve telif haklarını ihlal edici bir davranışımın olmadığını, bu tezin herhangi bir bölümünü bu üniversite veya diğer bir üniversitede başka bir tez çalışması içinde sunmadığımı, bu tezin planlanmasından yazımına kadar bütün safhalarda bilimsel etik kurallarına uygun olarak davrandığımı ve aksinin ortaya çıkması durumunda her türlü yasal sonucu kabul edeceğimi beyan ederim.

09 / 09 / 2019

Selin YILDIRAN EVREN

ÖZET

KLORALOZ ESASLI YENİ

MONOMERLERİN SENTEZLERİ

YILDIRAN EVREN, Selin

Yüksek Lisans Tezi, Kimya Bölümü

Tez Danışmanı: Doç. Dr. A. Yeşim Salman

Eylül 2019 ,82 pages

Bu araştırmada D-mannoz, D-galaktoz ve D-glukoz başlangıç şekerleri olarak kullanıldı. Bu monosakkaritlerden yola çıkılarak yeni akrilik ve metakrilik polimerlerin sentezi ve karakterizasyonu üzerine çalışılmıştır.

D-galaktoz'un susuz kloralle tepkimesi sonucu 1,2-*O*-trikloroetiliden-α-D-galaktofuranoz elde edildi. 1,2-*O*-trikloroetiliden-α-D-galaktofuranoz ile 2,2-dimetoksipropan tepkimeye sokularak 5,6-*O*-izopropiliden-1,2-*O*-trikloroetiliden-α-D-galaktofuranoz oluşturuldu. Bir sonraki basamakta 5,6-*O*-izopropiliden-1,2-*O*-trikloroetiliden-α-D-galaktofuranoz'un epiklorohidrin ile tepkimesi sonucu 3 numaralı karbona epoksi halkası bağlandı. Epoksi halkasının bazik ortamdaki açılma tepkimesinin özelliğinden faydalanarak akrilik ve metakrilik asitler ile halka açılma tepkimesi gerçekleştirildi.

Benzer şekilde D-glukoz ve D-mannoz' dan başlayarak sırasıyla 5,6-*O*-izopropiliden-1,2-*O*-trikloroetiliden-α-D-glukofuranoz ve 5,6-*O*-izopropiliden-1,2-*O*-trikloroetiliden-α-D-mannofuranoz oluşturuldu. D-galaktoz'un reaksiyon basamakları bu şekerler için de aynen tekrarlandı.

Anahtar Kelimeler: Kloraloz, Trikloroetiliden asetal, Epoksi şeker, Şeker bazlı polimer

ABSTRACT

SYNTHESIS OF NEW MONOMERS

BASED ON CHLORALOSE

YILDIRAN EVREN, Selin

MSc in Department of Chemistry
Supervisor: Assoc. Prof. Dr. A. Yeşim SALMAN
September 2019, 82 pages

In this research, D-mannose, D-galactose and D-glucose were used as starting sugars. Starting from these monosaccharides, the synthesis and characterization of acrylic and methacrylic polymers were investigated.

As a result of anhydrous chloral and D-galactose reaction, 1,2-*O*-trichloroethylidene-α-D-galactofuranose was obtained. 5,6-*O*-isopropylidene-1,2-*O*-trichloroethylidene-α-D-galactofuranose was obtained, 2-*O*- trichloroethylidene -α-D-galactofuranose and 2,2-dimethoxypropane. In the next stage, 5,6-*O*-isopropylidene-1,2-*O*-trichloroethylidene-α-D-galactofuranose and epichlorohydrine were reacted and the result of this reaction epoxy ring was added to number 3 carbon. Epoxy rings may be opened with the base catalyst. The use of this property was performed ring opening reactions with acrylic and methacrylic acid. In this way, sugar-based monomers were obtained and investigated.

Likewise D-glucose and D-mannose were used as starting sugar.5,6-*O*-isopropylidene-1,2-*O*-trichloroethylidene-α-D-glucofuranose and 5,6-*O*-isopropylidene-1,2-*O*-trichloroethylidene-α-D-mannofuranose were obtained. The steps of D-galactose reaction were repeated for other sugars.

Key Words: Chloralose, Trichloroethylidene acetals, Epoxy sugar, sugar based polymer

PREFACE

In this research, D-mannose, D-galactose and D-glucose were used as starting sugars. Starting from these monosaccharides, the synthesis and characterization of 8 new acrylic and methacrylic polymers were investigated.

All hydroxyl groups except for the OH group on carbon 3 were protected. The epoxy ring was added to carbon 3 as a result of the reaction of epichlorohydrin with sugar. Epoxy rings may be opened with the base catalyst. The use of this property was performed ring opening reactions with acrylic and methacrylic acid. In this way, sugar-based monomers were obtained and investigated.

The products obtained were purified by Column Chromatography. The structures of all synthesized compounds were determined by H-NMR, 13C-NMR and IR spectroscopic methods.

Some parts of the results of this thesis were published in the journal eXPRESS Polymer Letters 11(10), 799-808.

İZMİR

09/09/2019

Selin YILDIRAN EVREN

CONTENTS

Page

ÖZET ..... **vii**
ABSTRACT ..... **ix**
PREFACE ..... **xi**
LIST OF FIGURES ..... **xviii**
LIST OF TABLE ..... **xix**
ABBREVIATIONS ..... **xxi**
GRAPHICAL ABSTRACT ..... **xxv**
1.INTRODUCTION **1**
1.1 Carbohydrates 1
1.2 Types of Carbohydrates 1
1.3 Stereochemistry of Monosaccharides 2
1.4 Optical Properties of Sugars 4
2.LITERATURE SURVEY **4**
2.1 Protecting Groups 4
2.2 Epoxy Gropus 6
2.3 Ring Opening of the Epoxides 7
2.3.1 Acid Catalysed Ring Opening Reactions of Epoxides 7
2.3.2 Base Catalysed Ring Opening Reactions of Epoxides 8
2.4 Sugar Based Polymers 8
2.5 Polymerization of Vinyl Sugar Monomers to Obtain Poly(vinylsaccharide)s 11
3.MEHTOD AND MATERIAL **13**
3.1.General Methods 13
3.2. EXPERİMENTS 14
3.2.1. Preparation of anhydrous chloral 14

CONTENTS (continue)

Page

3.2.2. Synthesis of 1,2-*O*-(S)-Trichloroethylidene-α-D-galactofuranose (1).....14

3.2.3. Synthesis of 5,6-*O*-Isopropylidene-1,2-*O*-(S)-trichloroethylidene-α-D-galactofuranose (2).....15

3.2.4. Synthesis of 3-*O*-(2',3'-Epoxypropan-1'-yl)-5,6-*O*-isopropylidene-1,2-*O*-(S)-trichloroethylidene-α-D-galactofuranose (3).....15

3.2.5. Synthesis of 3-*O*-(2'-Hydroxy-3'-acryloyloxypropyl)-5,6-*O*-isopropylidene-1,2-*O*-(S)-trichloroethylidene-α-D-galactofuranose (4).....16

3.2.6. Synthesis of 3-*O*-(2'-Hydroxy-3'-methacryloyloxypropyl)-5,6-*O*-isopropylidene-1,2-*O*-(S)- trichloroethylidene-α-D-galactofuranose (5).....16

3.2.7. Synthesis of 1,2-*O*-(S)-Trichloroethylidene-α-D-mannofuranose (6).....17

3.2.8. Synthesis of 5,6-*O*-Isopropylidene-1,2-*O*-trichloroethylidene-β-D-mannofuranose (7).....17

3.2.9. Synthesis of 3-*O*-(2',3'-Epoxypropan-1'-yl)-5,6-*O*-isopropylidene-1,2-*O*-(S)-trichloroethylidene-α-D-mannofuranose (8).....18

3.2.10. Synthesis of 3-*O*-(2'-Hydroxy-3'-acryloyloxypropyl)-5,6-*O*-isopropylidene-1,2-*O*-(S)-trichloroethylidene-α-D-mannofuranose (9).....18

3.2.11. Synthesis of 3-*O*-(2'-Hydroxy-3'-methacryloyloxypropyl)-5,6-*O*-isopropylidene-1,2-*O*-(S)-trichloroethylidene-α-D-mannofuranose (10)...19

3.2.13. Synthesis of 5,6-*O*-Isopropylidene-1,2-*O*-(S)-trichloroethylidene-α-D-glucofuranose (13).....20

3.2.14. Synthesis of 3-*O*-(2',3'-epoxypropan-1'-yl)-5,6-*O*-isopropylidene-1,2-*O*-(S)-trichloroethylidene-α-D-glucofuranose (14).....20

3.2.15. Synthesis of 3-*O*-(2'-Hydroxy-3'-acryloyloxypropyl)-5,6-*O*-isopropylidene-1,2-*O*-(S)-trichloroethylidene-α-D-glucofuranose (15).....21

3.2.16. Synthesis of 3-*O*-(2'-Hydroxy-3'-methacryloyloxypropyl)-5,6-*O*-isopropylidene-1,2-*O*-(S)-trichloroethylidene-α-D-glucofuranose (16).....21

3.2.18. Synthesis of 5,6-*O*-Isopropylidene-1,2-*O*-(S)-trichloroethylidene-β-D-glucofuranose (17).....22

CONTENTS (continue)

Page

3.2.19. Synthesis of 3-*O*-(2',3'-Epoxypropan-1'-yl)-5,6-*O*-isopropylidene-1,2-*O*-(S)-trichloroethylidene-β-D-glucofuranose (18) 22

3.2.20. Synthesis of 3-*O*-(2'-hydroxy-3'-acryloyloxypropyl)-5,6-*O*-isopropylidene-1,2-*O*-(S)-trichloroethylidene-β-D-glucofuranose (19) 23

3.2.21. Synthesis of 3-*O*-(2'-hydroxy-3'-methacryloyloxypropyl)-5,6-*O*-isopropylidene-1,2-*O*-(S)-trichloroethylidene-β-D-glucofuranose (20) 24

4. RESULTS AND DISCUSSIONS 25

4.1 Synthesis of Acrylic and Methacrylic Monomers 26

4.2 Structural Characterization of the Compounds 28

4.3. 3-O-(2'-Hydroxy-3'-acryloyloxypropyl)-5,6-O-isopropylidene-1,2-O-(S)-trichloroethylidene-α-D-galactofuranose (4)……..... 28

4.4. 3-O-(2'-Hydroxy-3'-methacryloyloxypropyl)-5,6-O-isopropylidene-1,2-O-(S)- trichloroethylidene-α-D-galactofuranose (5)……...…. 29

4.5. 3-*O*-(2'-Hydroxy-3'-acryloyloxypropyl)-5,6-*O*-isopropylidene-1,2-*O*-(S)-trichloroethylidene-α-D-mannofuranose (10)……... 29

4.6. 3-*O*-(2'-Hydroxy-3'-methacryloyloxypropyl)-5,6-*O*-isopropylidene-1,2-*O*-(S)-trichloroethylidene-α-D-mannofuranose (11)…….. 30

4.7. 3-O-(2'-Hydroxy-3'-acryloyloxypropyl)-5,6-O-isopropylidene-1,2-O-(S)-trichloroethylidene-α-D-glucofuranose (15)……... 30

4.8. 3-*O*-(2'-Hydroxy-3'-methacryloyloxypropyl)-5,6-*O*-isopropylidene-1,2-*O*-(S)-trichloroethylidene-α-D-glucofuranose (16)……...……..... 30

4.9. 3-O-(2'-hydroxy-3'-acryloyloxypropyl)-5,6-O-isopropylidene-1,2-O-(S)-trichloroethylidene-β-D-glucofuranose (19)……...……. 31

4.10. 3-*O*-(2'-hydroxy-3'-methacryloyloxypropyl)-5,6-*O*-isopropylidene-1,2-*O*-(S)-trichloroethylidene-β-D-glucofuranose (20)……..…… 31

REFERENCES 33
ACKNOWLEDGEMENT 37
CURRICULUM VITAE 38

LIST OF FIGURES

Figure **Page**

1.1 The configuration of Fisher projection of acyclic polyhydroxy aldehydes and ketones 2

1.2 Configuration of D- and L-sugars 3

1.3 Haworth Projections 3

2.1 Distillation of chloral hydrate 4

2.2 Acetanation reactions of D-glucose, D-mannose and D-galactose with 5

2.3 Reaction of D-glucose, D-mannose and D-galactose with acetone 6

2.4 A small part of biosynthesis of cholesterol (ring opening reaction of epoxides) 7

2.5 Typical ring opening epoxide reaction with acid catalysed 7

2.6 In the unsymmetrical epoxide; acid-catalyzed ring opening reactio 8

2.7 In the unsymmetrical epoxide; base-catalyzed ring opening reaction 8

2.8 Poly(methacryloyl-D-glucose) 9

2.9 Poly(3-*O*-methacryloyl-1,2:5,6-di-*O*-isopropylidene-D-glucofuranose) 10

4.1 Etheric Bonding 25

4.2 Epoxy ring opening 25

4.3 The steps of for D-galactose synthesis of acrylic and methacrylic monomer 26

LIST OF FIGURES (continued)

Figure **Page**

4.4 Protective group……..……27

4.5 Collective representation of FTIR spectra of synthesized monomers).....28

LIST OF TABLE

Table Pages

1.1 Types of Carbohydrates 2

4.1 FTIR data (cm^{-1}) of the compound **4**……...…….28

4.2 ^{1}H-NMR spectral data of the compound **4**..... 29

4.3 FTIR data (cm^{-1}) of the compound **5**…….....29

4.4 ^{1}H-NMR spectral data of the compound **5** …….....29

4.5 FTIR data (cm^{-1}) of the compound **10**……...…29

4.6 ^{1}H-NMR spectral data of the compound **10**…….....29

4.7 FTIR data (cm^{-1}) of the compound **11**…….……....30

4.8 ^{1}H-NMR spectral data of the compound **11**…….....30

4.9 FTIR data (cm^{-1}) of the compound **15**……...…..30

4.10 ^{1}H-NMR spectral data of the compound **15**……...….30

4.11 FTIR data (cm^{-1}) of the compound **16**…….....…….31

4.12 ^{1}H-NMR spectral data of the compound **16**……...……31

4.13 FTIR data (cm^{-1}) of the compound **19**……...……31

4.14 ^{1}H-NMR spectral data of the compound **19**…...……..31

4.15 FTIR data (cm^{-1}) of the compound **20**……...……...31

4.16 ^{1}H-NMR spectral data of the compound **20**…...……..31

ABBREVIATIONS

Abbreviation	Explanation
bp	Boiling point
d	Doublet
DCM	Dichloromethane
dd	Doublet of doublet
ddd	Doublet of doublet of doublet
DMF	*N*,*N*-Dimethyl formamide
DMP	*2*,*2*-Dimethoxypropane
dt	Doublet of triplet
EtOAc	Ethylacetate
EtOH	Ethanol
Fig	Figure
g	Gram
IR	Infrared Spectroscopy

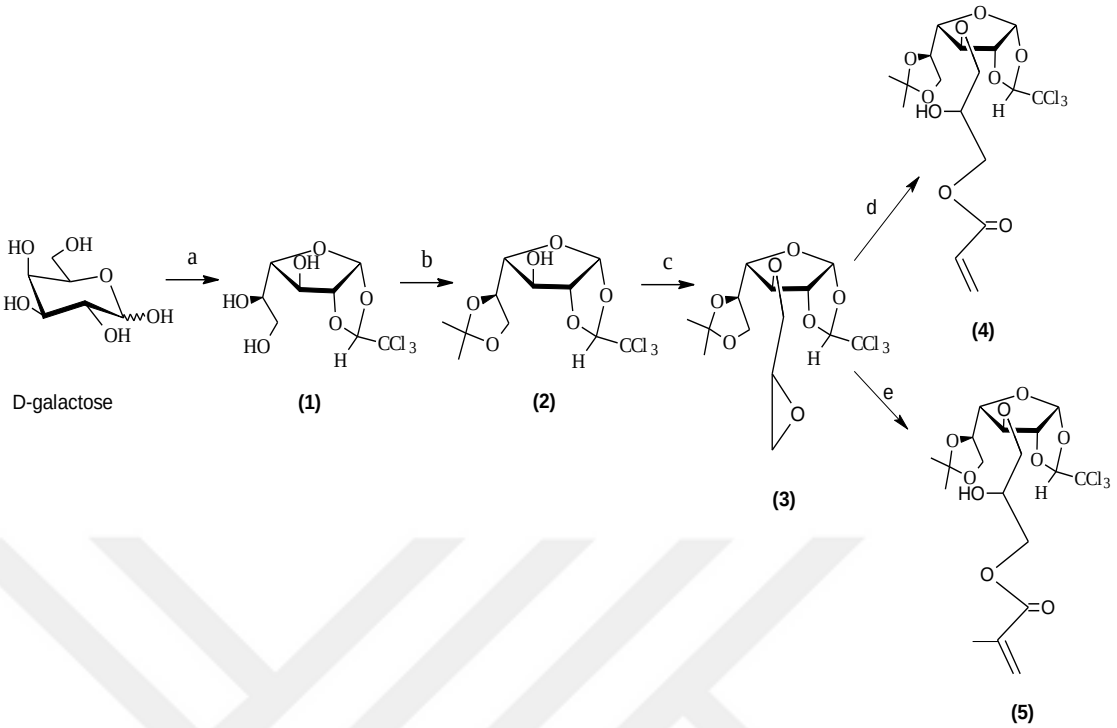
ABBREVIATIONS (continued)

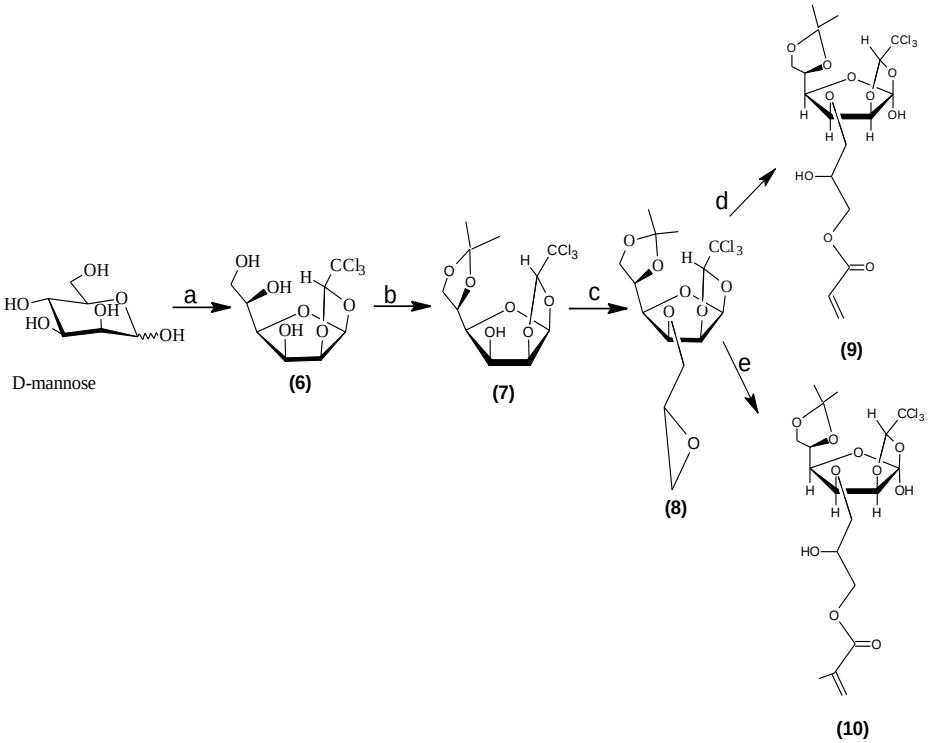
Abbreviation	Explanation
h	Hours
H_2SO_4	Sulfuric acid
m	Multiplet
mg	Milligram
mp	Melting point
Me	Methyl
MeOH	Methanol
ml	Milliliters
min	Minute
mol	Mole
mmol	Millimole
NMR	Nuclear Magnetic Resonance Spectroscopy
PTSA	*p*-Toluenesülfonic Acit

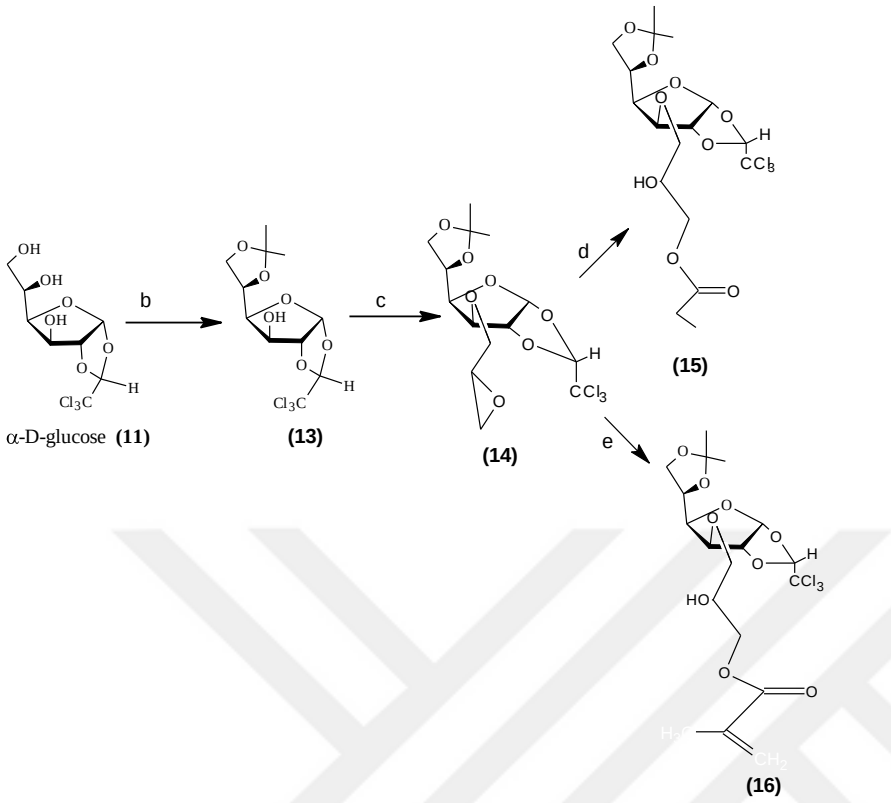
ABBREVIATIONS (continued)

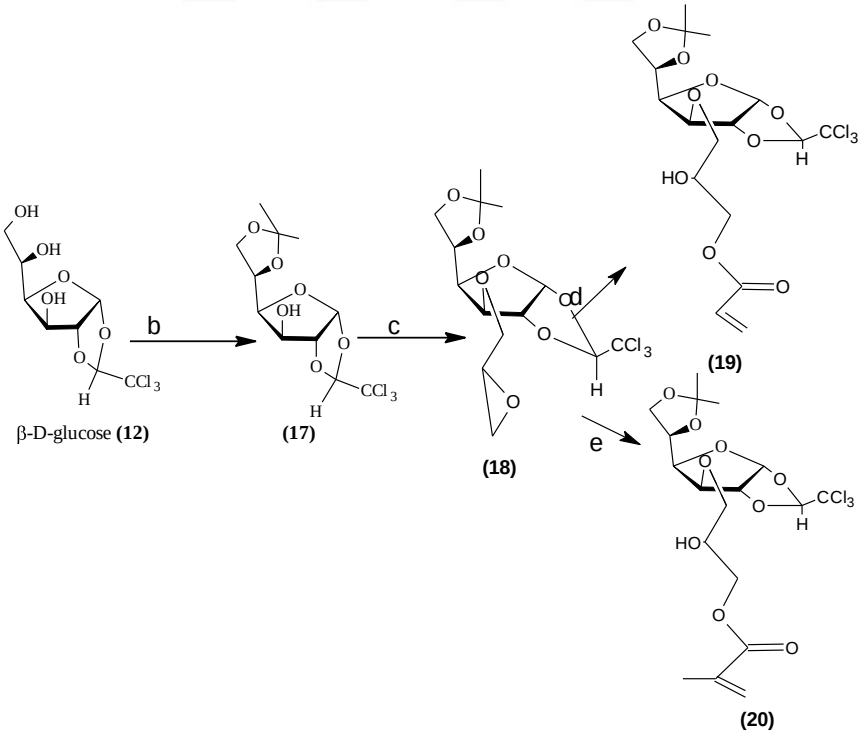
Abbreviation	Explanation
Pyr	Pyridine
s	Singlet
t	Triplet
TBAB	Tetrabutyl ammonium bromide
TEA	Triethylamine
TLC	Thin Layer Chromatography
Tol	Toluene

GRAPHICAL ABSTRACT









a) Chloral, H_2SO_4, b)DMP, PTSA, DMF, c)Epichlorohydrine, NaOH, TBAB, d)Acrylic acid, TEA, DMF e)Methacrylic acid, TEA, DMF

1. INTRODUCTION

1.1 Carbohydrates

Carbohydrates occur carbon, oxygen, hydrogen, and other modification atoms. They provide up to 40% of the energy the human body needs. In addition, many physiological and pathological effects are known. These effects; fertilization, biological functions, reproductive system, immune system and effects on viruses.

Carbon atoms have four valence electrons. so that it be bound with four different atoms. Since the end of the nineteenth century, chemists have directed their work to these characteristics. The study of carbohydrates began with the work of Emil Fischer. The researches started in those years, have reached very important stages today.

1.2 Types of Carbohydrates

Carbohydrates are classified into four types monosaccharides, disaccharides, polysaccharides, oligosaccharides. Monosaccharides can not be hydrolyzed further into simpler form of carbohydrates. All disaccharides and polysaccharides are ultimately converted to monosaccharides. Disaccharides are composed of two sugars bound by a glycosidic bond. This glycosidic linkage is formed by a condensation reaction between two sugar units and causes the loss of one hydrogen atom from one monosaccharide and one hydroxyl group from the other. Oligosaccharides are polymeric carbohydrate structures consisting of between 3-9 repeating units (mono or disaccharides) joined by glycosidic bonds. Polysaccharides are polymeric carbohydrate structures consisting of more than 10 repeating units (mono or disaccharides) joined by glycosidic bonds.

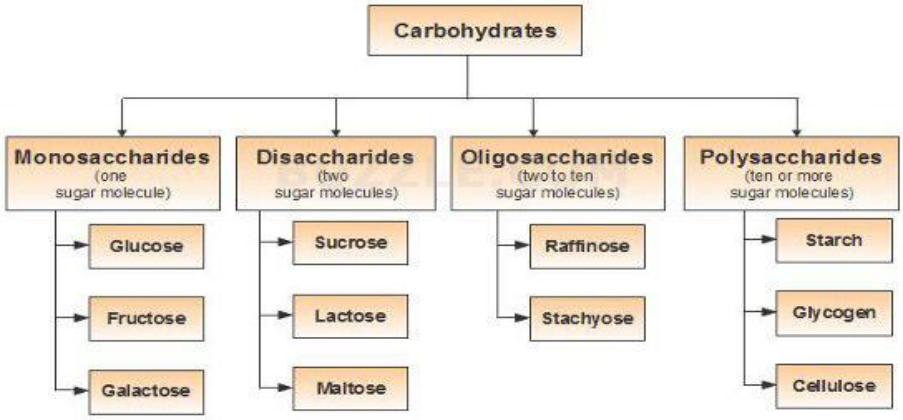


Table 1.1 Types of Carbohydrates

1.3 Stereochemistry of Monosaccharides

Monosaccharide known as polyhydroxy aldehydes or ketones. Monosaccharides's general formul is CnH_2nOn or $Cn(H_2O)n$. The carbon chains have 4 or 9 carbons and a hydroxyl group. This structure is known as the Fisher structure. The location of carbonyl groups in monosaccharides is important. They are referred to as aldehyde or ketone relative to the carbonyl group.

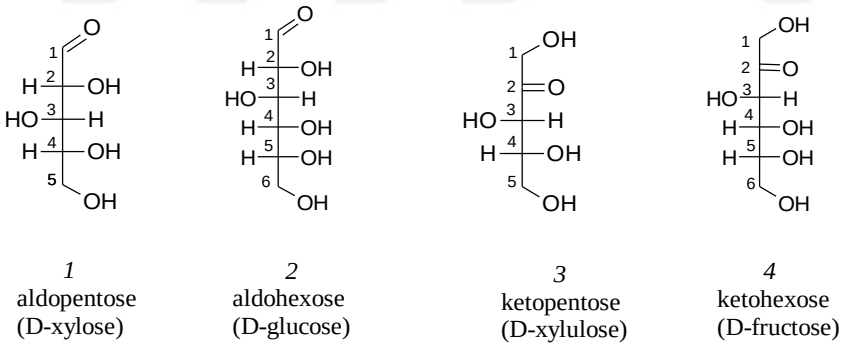


Figure 1.1 The configuration of Fischer projection of acyclic polyhydroxy aldehydes and ketones

A Fischer projection used to represent carbohydrates shows chiral carbons, shows -H or -OH groups on the horizontal intersecting line and places the CH_2OH groups. In a Fischer projection, the isomer L or D is determined by the direction of the hydroxyl group bound to the C atom farthest away from the carbonyl group It is indicated by the letter L on the left and the letter D on the

right. The carbonyl carbon has always the lowest possible number in monosaccharide chain.

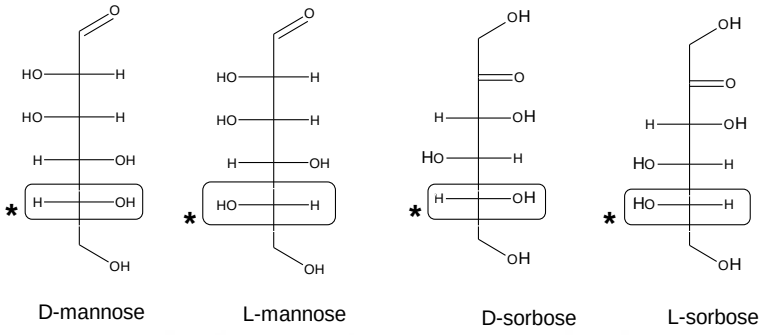


Figure 1.2 Configuration of D- and L- sugars

Some of the monosaccharide chemistry could not be explained by the open chain structure. Emile Fischer explained the structure of the monosaccharides by an open chain. However, the open chain formula cannot accurately represent the actual structure. Haworth developed the ring structure. These cyclic structures are named according to the number of C they contain. The 4-carbon ring furanose is called, the 5-carbon ring pyranose. OH groups attached to carbonyl carbon indicate alpha and beta forms. It is called alpha, if the OH groups below the structure. If the group OH is above the ring, it is called beta. These two structures are diastereoisomers of each other.

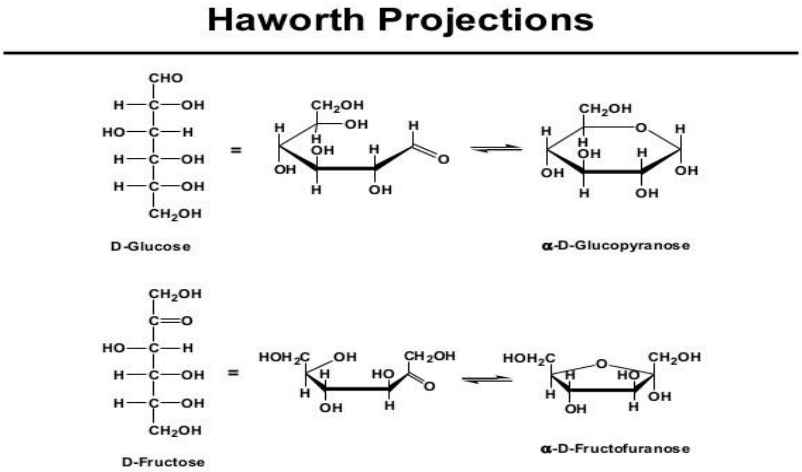


Figure 1.3 Haworth Projections

1.4 Optical Properties of Sugars

The ability of an object to deflect polarized light from its plane is called optically activity. Only sugars with different OH groups belonging to asymmetric carbon are mirror images of each other. Such substances are called optically active enantiomers. The physical and chemical properties are the same. Being optically active is an important feature for the food industry. Turning the polarized light to the right is indicated by "D" (dextro) or "+" and turning to the left is indicated by "L" (Levo) or "-".

2. LITERATURE SURVEY

2.1 Protecting Groups

Protecting of hydroxyl groups play an important role in carbohydrate chemistry (Wuts and Greene, 2007). This process is often used to temporarily mask a functional group that may interfere with a particular reaction.

The use of acetals and ketones as protecting groups for hydroxyl is very common. Because these derivatives can be readily hydrolyzed with dilute acids and no changes in the configuration of the carbon atom are observed (Yüceer, 1978).

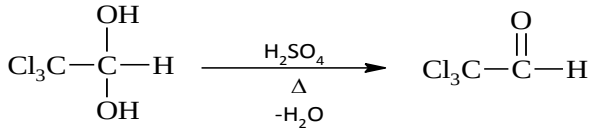


Figure 2.1 Distillation of chloral hydrate.

Chloral was obtained by distillation of chloral hyrate and sulphuric acid. Chloraloses were first synthesized by Hefter with condensation of trichloroacetaldehyde with free glucose in the presence of acid catalyst (Lunitskii, 1975; Dutka et al, 1992).

Trichloroethylidene acetals are highly resistant to acidic effects. But there are not enough studies for trichloroethyliden acetals of monosaccarides in the literature. Because trichloroethylidene acetals are not easy to isolate. Two diastereomers from D-glucose were obtained in the protection with trichloroethylidene acetals. These are α-chloralose and β-chloralose. These symbols determine the configuration of the acetal carbon.

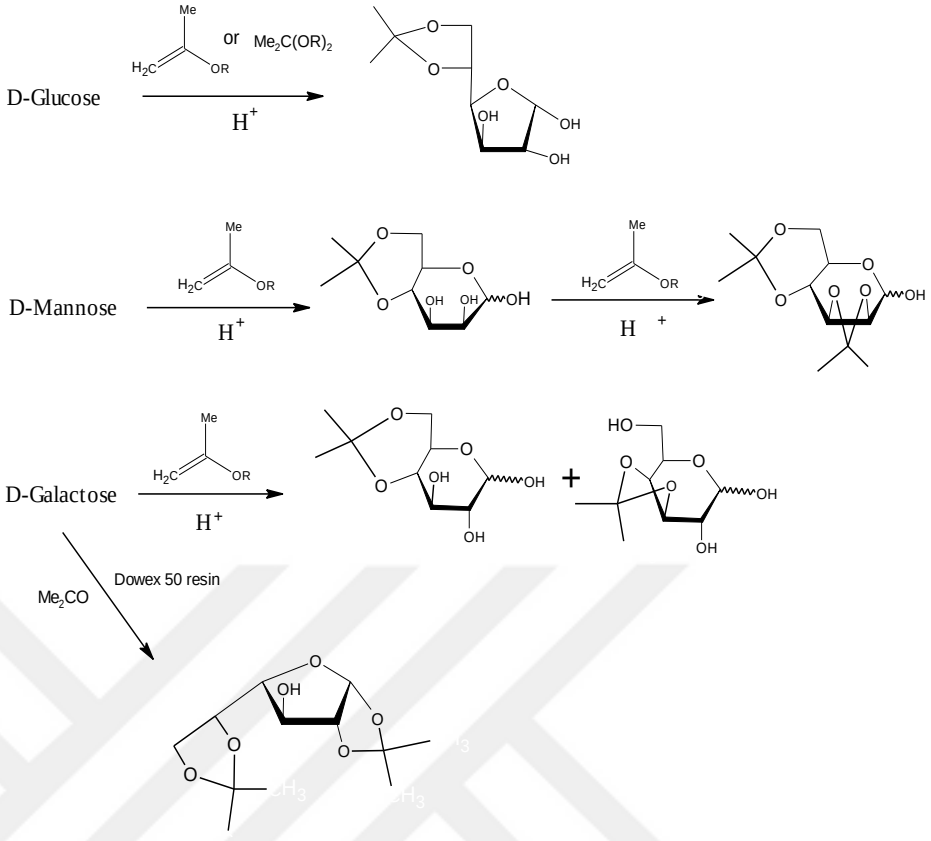


Figure 2.2 Acetonation reactions of D-glucose, D-mannose and D-galactose with

Trichloroethylidene acetals are biologically potentially active compounds. α-chloralose is used as an anesthetic agent on laboratory animals (Metz et al, 1996). Used as a commercial drug α-chloralose is also properly used in bird repellent, rodenticide, veterinary medicine and neuroscience for loss of sensation named sedative and anesthetic (Forsen et al., 1965; Zosimo-Landolfo et al., 1999).

O-isopropylidene and *O*-benzylidene sugars as a protecting sugars are the most important derivatives in carbohydrate chemistry. Many methods of synthesizing *O*-isopropylidene derivatives are known in the literature. Traditional method comprises condensing the diol in the anhydrous state in the presence of acetone and a catalyst.

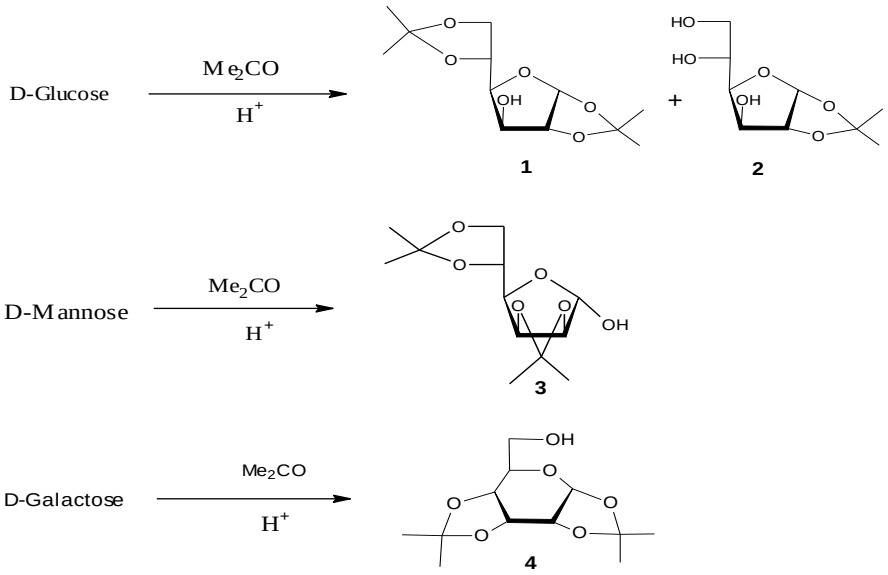


Figure 2.3 Reaction of D-glucose, D-mannose and D-galactose with acetone

Reaction of D-glucose with acetone and acid gives the 1,2: 5,6-di-*O*-isopropylidene-α-D-glucofuranose and monoacetone glucose. The use of 2,2-DMP or 2-methoxypropene increases the proportion of monoacetone glucose (Hannessian,1997).

2.2 Epoxy Groups

The epoxide structure, also known as oxirane, is a three-membered ring. The ring members are an oxygen and two carbons. It's three-membered ring makes it more susceptible to nucleophilic attacks (Solomons and Fryhle, 2007).

Epoxides are building blocks commonly used in the synthesis of complex organic compounds. Their use as valuable intermediates was further extended by the synthesis of asymmetric catalytic processes.

Epoxides are important substances for organic synthesis laboratories. With the emergence of asymmetric methods for synthesis, their value has increased further. It is also present as an intermediate in some biosynthetic reactions.

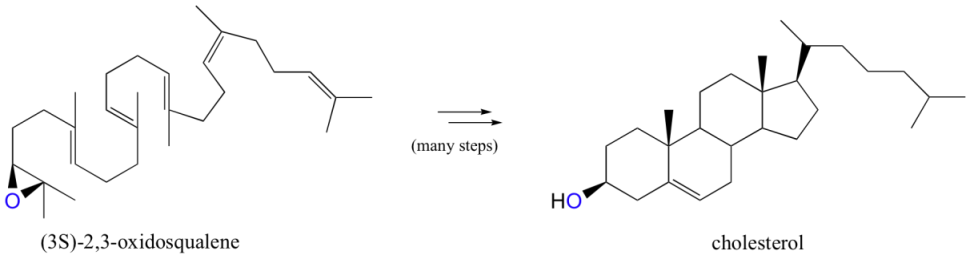


Figure 2.4 A small part of biosynthesis of cholesterol (ring opening reaction of epoxides)

2.3 Ring Opening of the Epoxides

The opening reactions of the epoxy ring are very important for organic synthesis. The most important feature of epoxides is that they are more sensitive to nucleophilic attacks than simple ethers. Thus, they react rapidly even with nucleophiles in which other ethers are ineffective.

2.3.1 Acid Catalysed Ring Opening Reactions of Epoxides

In the typical reaction of epoxide with acid catalyst as a nucleophile; acid catalysis helps to open the epoxide ring provided that it forms a better leaving group (alcohol) at the carbon atom undergoing the nucleophilic attack (Fig.2.5). This catalysis is more important when the nucleophile is water or alcohol (Solomons and Fryhle, 2007).

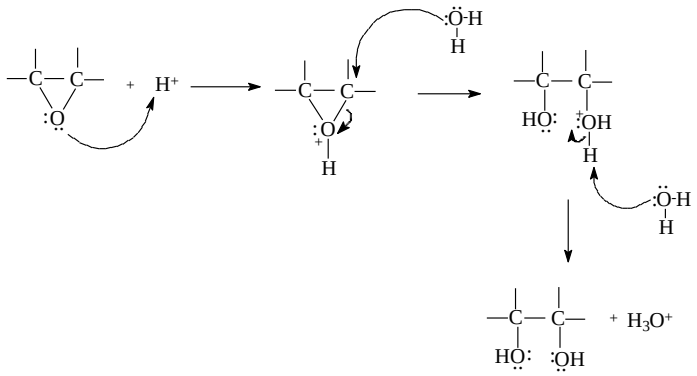


Figure 2.5 Typical ring opening epoxide reaction with acid catalysed

As a result of their reaction, the acid forms a protonated epoxide. The protonated epoxide structure reacts with a weak nucleophile such as water to form

protonated glycol. The protonated glycol after that transfers a proton to water to form a hydronium ion and a glycol.

İf the epoxide structure is not symmetrical in acid catalyzed ring openings, the nucleophile attacks the more substituted carbon atom.

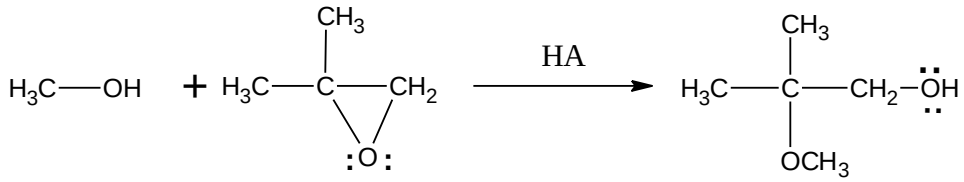


Figure 2.6 In the unsymmetrical epoxide; acid-catalyzed ring opening reaction

2.3.2 Base Catalysed Ring Opening Reactions of Epoxides

The epoxides may also give a base catalyst ring opening reaction. Such reactions do not be formed with all ethers. However, it is possible with epoxides (due to ring tension) on condition that the attacking nucleophile is a strong base.

Opening an epoxide ring with a strong nucleophile proceeds like an S_N2 reaction.

If the epoxide structure is not symmetrical in base catalyzed ring openings, the nucleophile attacks the less substituted carbon atom.

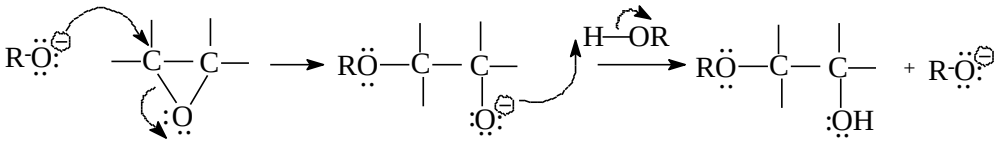


Figure 2.7 In the unsymmetrical epoxide; base-catalyzed ring opening reaction

2.4 Sugar Based Polymers

Plants and microorganisms produce billions of tons of carbohydrates every year. Therefore, carbohydrates are the most plenty group of products in

nature. At the beginning of the 20th century, many trials were made to use carbohydrates as crude materials in the chemical industry, especially for producing polymers. The industrially high purity of carbohydrates increased the interest in these substances. The chemical bonding of the sugar moieties to the synthetic material increased their functionality. In addition, high hydrophilic character, compatibility with skin and other biological surfaces increased interest in their use. Sugars are a good food source for microorganisms. Thus, many poly(vinylsaccharide)s are biodegradable polymers.

These sugar polymers, have an important field of study that is of interest to scientists today. Synthesis of polyvinylsaccharides started with Reppe in the early 1930s. He is known as the first person to synthesize vinyl saccharide monomers. But in the last 30-40 years, sugars have begun to attract more attention. Intensive researches are carried out by the researchers for their application areas.

In 1945, Nichols and Yanovsky reported that glucose was prepared as a sugar monomer. GPM (pentamethacrylate) monomer was formed by direct addition of methacrylic hydride to D-glucose at 65 ° C for 3.5 hours. This monomer was dissolved in most of the organic solvents. Thus, the first cross-linked polymer containing pentamethacrylate and glucose monomer group was synthesized in carbohydrate chemistry.

In 1946, Haworth, Gregory, and Wiggins polymerized acrylate and methacrylate-containing carbohydrates to produce hard products. The first linear and water-soluble poly(vinylsaccharide) was reported in 1960 by Bird, Black, Dewar and Rutherford. the same substance was synthesized in 1961 by Kimura and Imoto as copolymers.

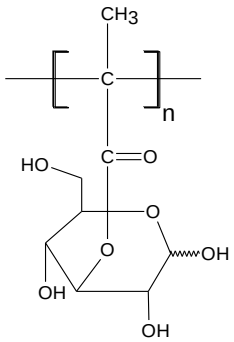


Figure 2.8 Poly(methacryloyl-D-glucose)

Poly(3-*O*-methacryloyl 1,2:5,6 di-*O*-isopropylidene-D-glucofuranose) structure was formed by polymerizing structure 1,2:5,6 di-*O*-isopropylidene-D-glucofuranose methyl methacrylate by free radical polymerization.

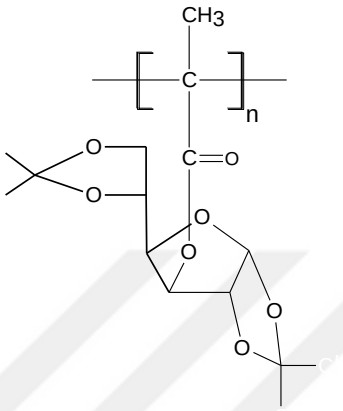


Figure 2.9 Poly(3-*O*-methacryloyl-1,2:5,6-di-*O*-isopropylidene-D-glucofuranose)

In 1976, polymeric derivatives of methacrylic acid containing aromatic synthesized glycopronoside side chains were first reported by Carpino, Ringsdorf and Ritter.

There are four general methods of synthesizing synthetic polysaccharides:

- vinyl sugars polymerization (polyvinylsaccharide)s
- anhydro-sugar polymerization (polyanhydrosugar)s
- synthesis of enzyme-mediated carbohydrate polymers
- synthetic polymers functionalized by polymer-like reactions.

In addition, olefin metathesis reactions were used for the synthesis of poly(vinylsaccharide)s.

The most preferred methods of poly(vinylsaccharide)s synthesis are homopolymerization of vinyl sugars or copolymerization with other polymerizable monomers.

It is also possible to obtain poly(vinylsaccharide)s from ring opening polymerization of anhydro sugars using macromolecular halides (Uryu et al.,1981). In the 1990s, many articles emphasized the importance of polyvinyl saccharides in the biological system. In 1994a Kaboyashi et al. Synthesized poly (N- (p-vinyl benzyl) -4-*O*-β-D-galactopyranosyl D-gluconamide) as a substrate for hepatocyte culture. Pinilla et al. synthesized poly (ester amide) based on arabinose, which may be an AIDS drug carrying a carbohydrate fragment (Pinilla et al., 2002).

2.5 Polymerization of Vinyl Sugar Monomers to Obtain Poly(vinylsaccharide)s

These monomers are prepared by linking an unsaturated component to a carbohydrate derivative via an ether, ester or amido linkage. Such carbohydrate-based polymers are the most extensively studied. Synthesis of pure vinyl sugar monomers is an important step in polymer synthesis.

Homopolymerization of vinyl sugar or copolymerization of poly(vinylsaccharide)s with polymerizable vinyl monomers are more commonly used synthesis methods. Vinyl sugar syntheses can be listed as follows;

- addition of acrylic ester to a sugar moiety and homopolymerization
- copolymerize the presence of radical catalyst with acrylate (Patil et al., 1991).
- an alkyl isosionate is condensed with a sugar molecule followed by free radical polymerization with a urea bond (Zhou et al., 1999).
- The sugars converted to the glycosyl amine are then converted to the N-acryloyl derivative by radical polymerization (Kallin et al., 1989).

The free radical polymerization of vinyl sugars is the most common synthesis method of poly(vinylsaccharide)s. A sugar is added to a polymeric backbone by means of ether (Furuike et al., 1995; Nishimura et al., 1991), amide (Fraser & Grubbs, 1995; Kobayashi et al., 1986; Nishimura et al., 1994a, b) or ester (Chen et al., 1995) linkages.

Free radical polymerizations were performed in both aqueous and non-aqueous media. Previous studies have included the polymerization of vinyl sugars

in non-aqueous media using the AIBN (Carpino et al., 1976; Emmerling & Pfannemuller, 1983; Kimura & Hirai, 1962; Ouchi et al, 1984; Rios & Bertorello, 1997) or benzoyl peroxide radical initiator (Bird et al, 1960; Rios & Bertorello, 1997).

The sugar unit in the structure of a vinyl sugar may be a mono, di or oligosaccharide containing a protecting group. These sugars can be separated from their protecting groups after polymerization.

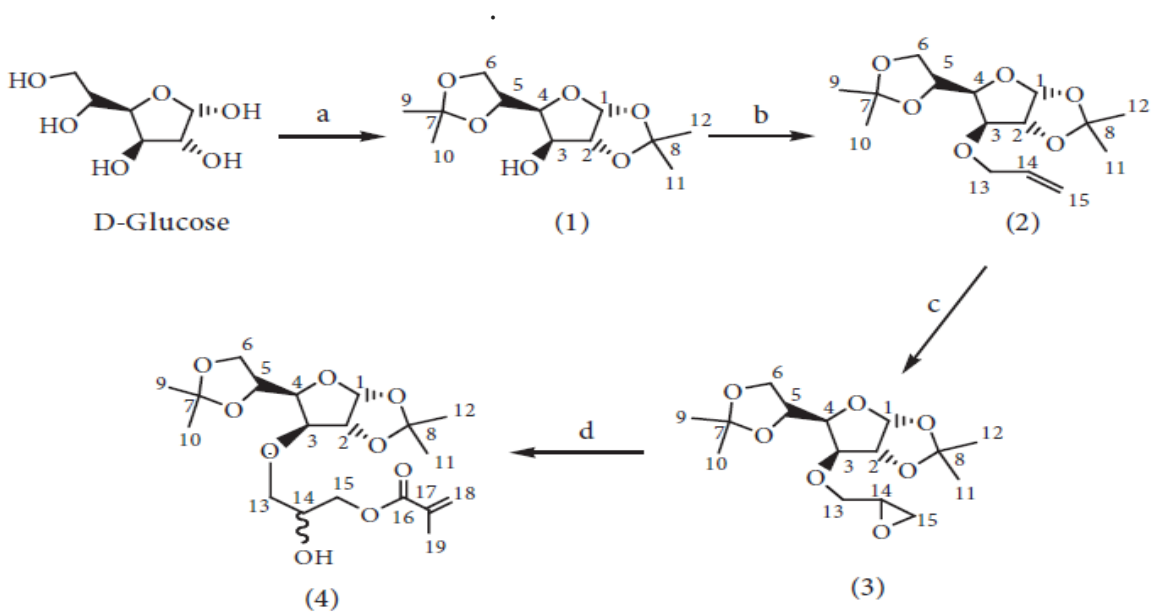


Figure 2.10 Preparation of D-glucose monomer; (a)acetone, H_2SO_4 ; (b)AllCl, NaH, DMF; (c)MCPBA, $CHCl_3$; (d)methacrylic acid, TEA.

The easiest way of protecting sugar compounds with all but one hydroxyl groups is to prepare isopropylidene derivatives in many cases. The starting compound (acetone) is inexpensive, yields are generally good, and isopropylidene groups can be easily removed if desired. In the literature, vinyl sugar monomers (acrylate, methacrylate, etc.) with isopropylidene derivatives protected can be seen.

Trichlorethylene acetals are basically not used as protecting groups. However, they are subject to studies due to their biological activities. Trichloroethylidene acetals are potential active compounds in biologically. Therefore, examples of this method are also seen in the literature. There are sugars commercially available as well as sugars formed with anhydrous chloral in the presence of sulfuric acid.

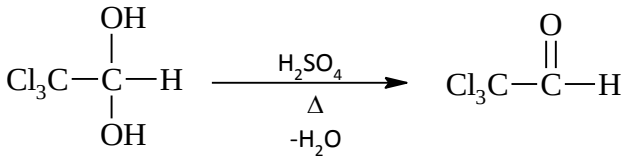
3. METHOD AND MATERIAL

3.1 General Methods

- Melting point was measured by Gallenkamp electrothermal melting point device.
- Reactions were monitored by TLC (Merc 5554) and purified by silica gel G-60 (Merc 7734 and Merc 9385) column chromatography. Stains of TLC were observed by spraying 5% sulfuric acid and heating the plates above 120^0 C.
- Starting products were purchased from Merck and Sigma Aldrich. Solvents (Hexane, Methanol, Dichloromethane) were purified from industrial grade solvents.
- Solvents were dried with molecular sieve (4Å and 3Å).
- Water remaining in the solvent were filtered with anhydrous sodium sulphate.
- All of the solvent were evapored by Rotary evaporator.
- IR spectra were obtained by Perkin Elmer Spectrum 100 FTIR Spectrometer.
- ^{1}H-NMR and ^{13}C-NMR (400 MHz) spectra were recorded on an Oxford NMR 400 MHz spectrometer using TMS as the internal standard d-values (in ppm) and coupling constants (in Hz). $CDCl_3$ peak were used as reference in ^{1}H-NMR (7.26 ppm) and ^{13}C-NMR (77.36 ppm) respectively.
- Optical rotation measurements were done with Rudolph Autopol-1 Automatic Polarimeter

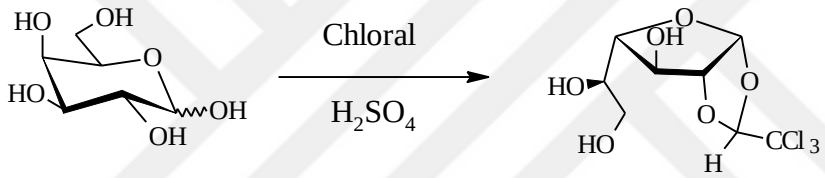
3.2 EXPERIMENTS

3.2.1 Preparation of anhydrous chloral



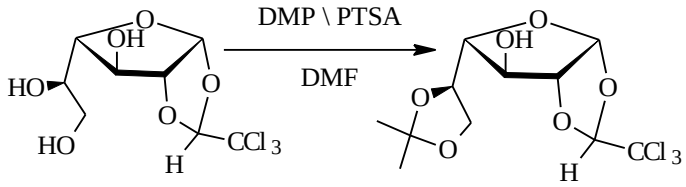
At room temperature concentrated H_2SO_4 (180 mL, d=1.84 g/cm^3) was slowly added on chloral hydrate (320g, 1.9 mol). The resulting solution was allowed to stir for 2 hours at 98^0 C. As a result of this reaction, anhydrous chloral was obtained in 91% yield. (171 mL, d=1.512 g/cm^3)

3.2.2 Synthesis of 1,2-*O*-(S)-Trichloroethylidene-α-D-galactofuranose (1)



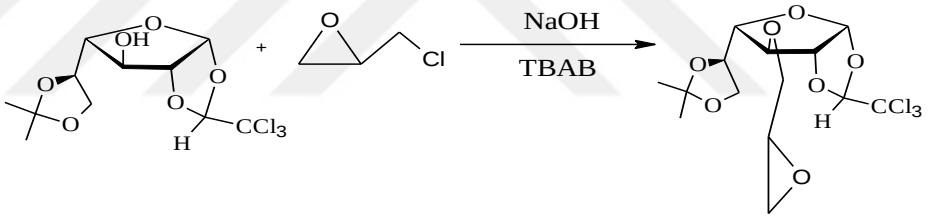
Anhydrous chloral (170 mL, d=1.512 g/cm^3, 259g) was added on D-galactose (50g, 0.28mol) on the magnetic stirrier. Then concentrated H_2SO_4 (180 mL, d=1.84 g/cm^3) was added on the same mixture. The mixture was refluxed during 3 hours. After the excess chloral has been evaporated, black syrup was obtained. 350ml of methanol was added to the black syrup and it has been dissolved. Dissolved syrup was heating and added active carbon. Thus, the color removal process was made. The mixture was filtered and crystalized with methanol. (62 g, 72%), mp: 205-207 ^{o}C, $[\alpha]_D^{22}$: -30^o (c: 0.5 in MeOH).

3.2.3 Synthesis of 5,6-*O*-Isopropylidene-1,2-*O*-(S)-trichloroethylidene-α-D-galactofuranose (2)



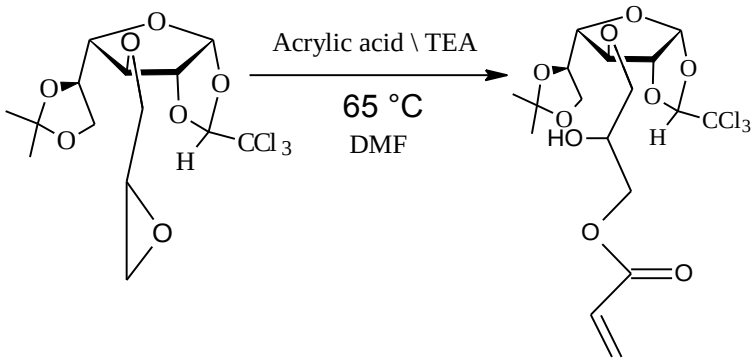
Product **1** (10 g, 0.032 mol), was solved with DMF (50 mL). To this solution was added on DMP(10 mL, d=0.85 g/cm^3, 8.5 g) and anhydrous PTSA(10 mg, 0.058 mmol). The mixture was stirred during 24 hours and was notralized with $NaHCO_3$. DMF was evaporated. The product was crystalized with methanol. The resulting product was obtained as colorless crystal. (9.1 g, 81%), mp: 216-219^{o}C, $[\alpha]_D^{22}$: +17.0^o (c: 5.0 in pyr).

3.2.4 Synthesis of 3-*O*-(2',3'-Epoxypropan-1'-yl)-5,6-*O*-isopropylidene-1,2-*O*-(S)-trichloroethylidene-α-D-galactofuranose (3)



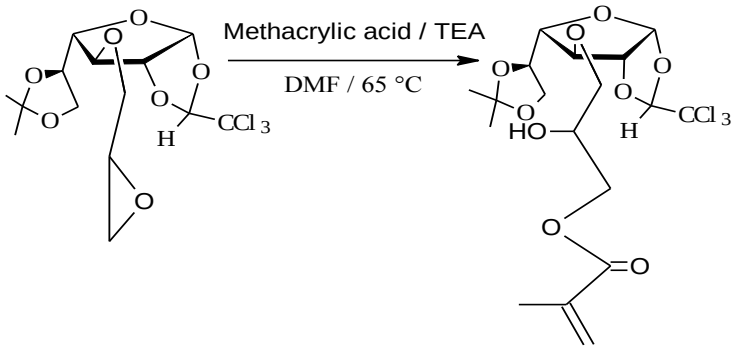
Epichlorohydrine (7.5 mL, 96 mmol), tetrabutyl ammonium bromide and solution of NaOH (50%, 15mL) was allowed to stir at room temperature for 30 minutes. To this mixture product **2** (3g, 8.6mmol) was slowly added at 5 °C. The reaction continued at the same temperature for 3 hours. The mixture was poured onto ice and extracted with EtOAC (4x15ml). The organic layer was washed with NH_4Cl (10%, 2x2.5 mL), dried with anhydrous Na_2SO_4 and filtered. The solvent was evaporated and the syrup was purified by column chromatography using Hexane / EtOAC (2/1). The resulting product was colorless crystal (2.58 g, yield 74 %), $[\alpha]^{21}{}_D$ -46 (c=1 in CH_2Cl_2).

3.2.5 Synthesis of 3-*O*-(2'-Hydroxy-3'-acryloyloxypropyl)-5,6-*O*-isopropylidene-1,2-*O*-(S)-trichloroethylidene-α-D-galactofuranose (4)



Product **3** (2,50g, 5.8mmol) was dissolved with DMF (13 ml). Triethylamine (0.87 mL, 0.64 g, 6.33 mmol) and acrylic acid (4.34 mL, 4.56 g, 63.24 mmol) was added drop by drop at room temperature.The mixture was stirred while heating to 65 oC. The reaction was continued at the same temperature for 24 hours. The product obtained was extracted with CH2Cl2 and the organic layer was washed with distilled cold water. The product was purified by Hexane/ EtOAC (2/1) column chromatography. Yellow transparent gel was obtained (1.94g, 70 % yield)

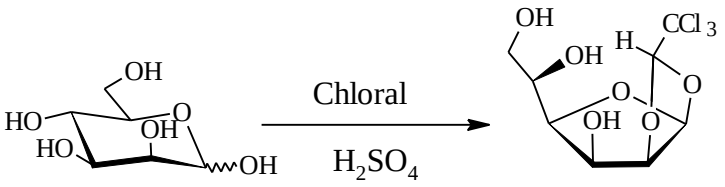
3.2.6 Synthesis of 3-*O*-(2'-Hydroxy-3'-methacryloyloxypropyl)-5,6-*O*-isopropylidene-1,2-*O*-(S)- trichloroethylidene-α-D-galactofuranose (5)



Product **3 (**1.94g, 4mmol) dissolved with DMF (6 ml). Triethylamine (0.68 mL, 0.49g, 4.9 mmol) and methacrylic acid (3.37 mL, 3.54 g, 49.07 mmol) was added drop by drop at room temperature. The mixture was stirred while heating to 65 ^{o}C. The reaction was continued at the same temperature for 24 hours. The

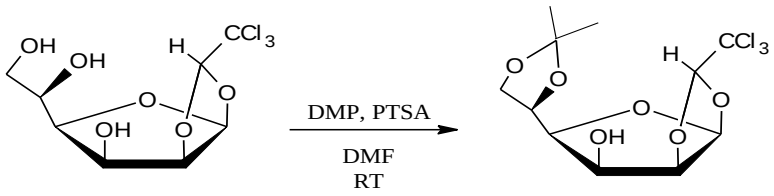
product obtained was extracted with CH_2Cl_2 and the organic layer was washed with distilled cold water. The product was purified by Hexane/ EtOAC (2/1) column chromatography. Yellow transparent gel was obtained (1.31 g, 67 % yield

3.2.7 Synthesis of 1,2-*O*-(S)-Trichloroethylidene-α-D-mannofuranose (6)



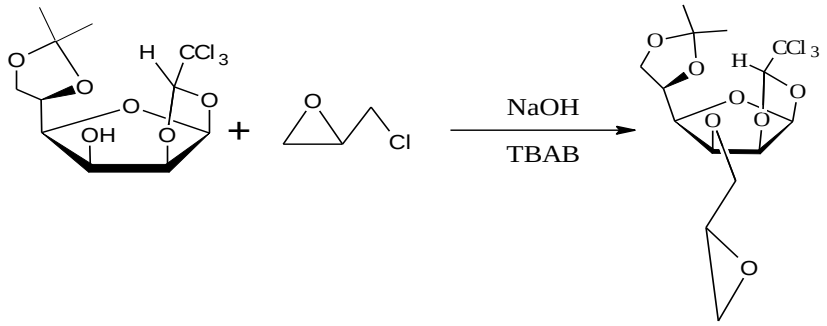
Anhydrous chloral (170 mL, d=1.512 g/cm^3, 259 g) was added on D-mannose (50 g, 0.28 mol) on the magnetic stirrier. Then concentrated sulphuric acid (1 mL, d=1.84 g/cm^3) was added on the same mixture. The mixture was refluxed during 3 hours. After the excess chloral has been evaporated, black syrup was obtained. 350 ml of methanol was added to the black syrup and it has been dissolved. Dissolved syrup was heating and added active carbon. Thus, the color removal process was made. The mixture was filtered and crystalized with methanol. (21.1 g, 39%), mp: 205-207^{o}C, $[\alpha]_D^{22}$: -15.0^o (c: 0.4 in MeOH).

3.2.8 Synthesis of 5,6-*O*-Isopropylidene-1,2-*O*-trichloroethylidene-β-D-mannofuranose (7)



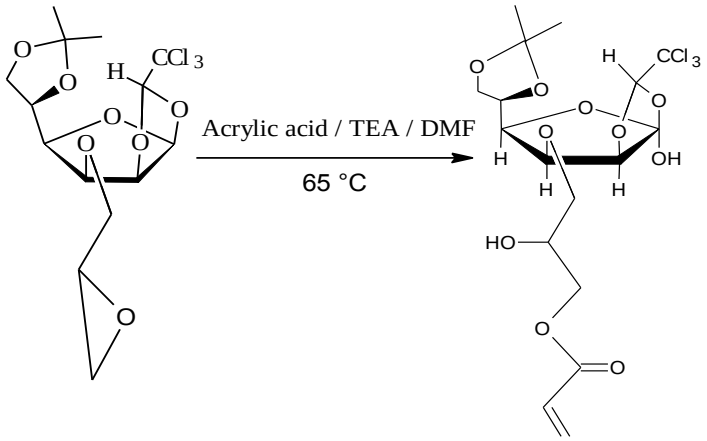
Product **6** (10 g, 0.032 mol), was solved with DMF (50 mL). To this solution was added on DMP (10 mL, d=0.85 g/cm^3, 8.5 g) and anhydrous PTSA (10 mg, 0.058 mmol). The mixture was stirred during 24 hours and was neutralized with $NaHCO_3$. DMF was evaporated. The product was crystalized with methanol. The resulting product was obtained as colorless crystal. (7.4 g, 72%), mp: 169-171^{o}C, $[\alpha]_D^{22}$: - 34.0^o (c: 0.25 in $CHCl_3$).

3.2.9 Synthesis of 3-*O*-(2',3'-Epoxypropan-1'-yl)-5,6-*O*-isopropylidene-1,2-*O*-(S)-trichloroethylidene-α-D-mannofuranose (8)



Epichlorohydrine (8 mL, 100 mmol), tetrabutyl ammonium bromide and solution of NaOH (50%, 15mL) was stirred at room temperature for 30 minutes. To this mixture product **7** (3g, 9mmol) was slowly added at 5 °C. The reaction continued at the same temperature for 3 hours. The mixture was poured onto ice and extracted with EtOAC (4x15ml). The organic layer was washed with NH_4Cl (10%, 2x2.5 mL), dried with anhydrous Na_2SO_4 and filtered. The solvent was evaporated and the syrup was purified by column chromatography using Hexane / EtOAC (2/1). The resulting product was colorless crystal (2.48 g, yield 68 %), $[\alpha]^{21}_D$ -46 (c=1 in CH_2Cl_2).

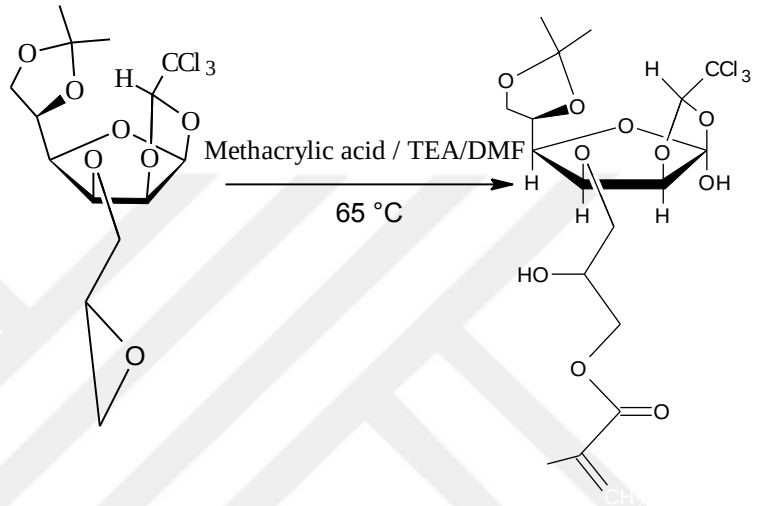
3.2.10 Synthesis of 3-*O*-(2'-Hydroxy-3'-acryloyloxypropyl)-5,6-*O*-isopropylidene-1,2-*O*-(S)-trichloroethylidene-α-D-mannofuranose (9)



Product **8** (2g, 5mmol) dissolved with DMF (10 ml). Triethylamine (0.6 mL, 0.44 g, 4.36 mmol) and acrylic acid (2.99 mL, 3.15 g, 43.61 mmol) was added drop by drop at room temperature. The mixture was stirred while heating to 65 ^oC. The reaction was continued at the same temperature for 24 hours. The

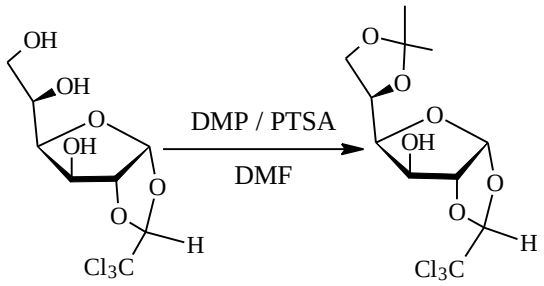
product obtained was extracted with CH_2Cl_2 and the organic layer was washed with distilled cold water. The product was purified by Hexane/ EtOAC (2/1) column chromatography. Yellow transparent gel was obtained (1.46 g, 67 % yield)

3.2.11 Synthesis of 3-*O*-(2'-Hydroxy-3'-methacryloyloxypropyl)-5,6-*O*-isopropylidene-1,2-*O*-(S)-trichloroethylidene-α-D-mannofuranose (10)



Product **8 (**2g, 5mmol) dissolved with DMF (10 ml). Triethylamine (0.87 mL, 0.64 g, 6.32 mmol) and methacrylic acid (4.21 mL, 4.43 g, 58.83 mmol) was added drop by drop at room temperature. The mixture was stirred while heating to 65 ^{o}C. The reaction was continued at the sama temperature for 24 hours. The product obtained was extracted with CH_2Cl_2 and the organic layer was washed with distilled cold water. The product was purified by Hexane/ EtOAC (2/1) column chromatography. Yellow transparent gel was obtained (1.56 g, 65 % yield)

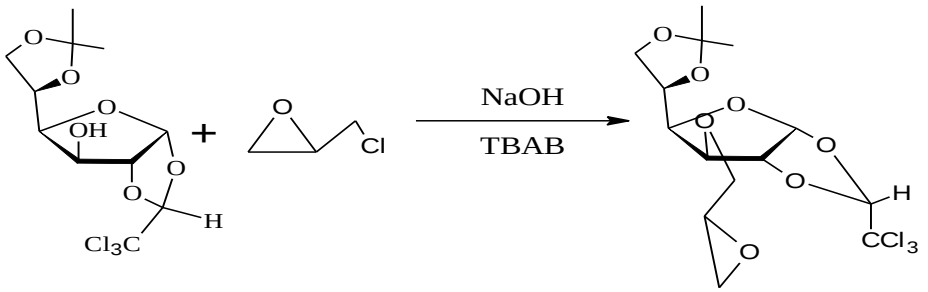
3.2.13 Synthesis of 5,6-*O*-Isopropylidene-1,2-*O*-(S)-trichloroethylidene-α-D-glucofuranose (13)



(11)

Commercially available α-D-glucose (10 g, 0.032 mol), was solved with DMF (50 mL). To this solution was added on DMP (10 mL, d=0.85 g/cm^3, 8.5 g) and anhydrous PTSA(10 mg, 0.058 mmol). The mixture was stirred during 24 hours and was neutralized with $NaHCO_3$. DMF was evaporated. The product was crystalized with methanol. The resulting product was obtained as colorless crystal. (8.2 g, 75%), mp: 169-171^{o}C, $[\alpha]_D^{22}$: - 34.0^o (c: 0.25 in $CHCl_3$).

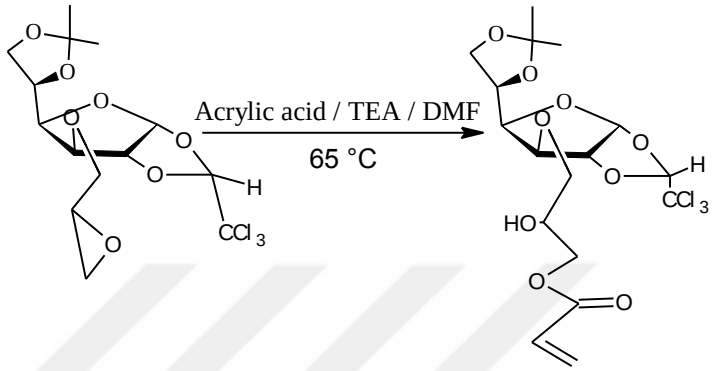
3.2.14 Synthesis of 3-*O*-(2',3'-epoxypropan-1'-yl)-5,6-*O*-isopropylidene-1,2-*O*-(S)-trichloroethylidene-α-D-glucofuranose (14)



Epichlorohydrine (7 mL, 88 mmol), tetrabutyl ammonium bromide and solution of NaOH (50%, 15mL) was stirred at room temperature for 30 minutes. To this mixture product **13** (3g, 8mmol) was slowly added at 5 °C. The reaction continued at the same temperature for 3 hours. The mixture was poured onto ice and extracted with EtOAC (4x15ml). The organic layer was washed with NH_4Cl (10%, 2x2.5 mL), dried with anhydrous Na_2SO_4 and filtered. The solvent was evaporated and the syrup was purified by column chromatography using Hexane /

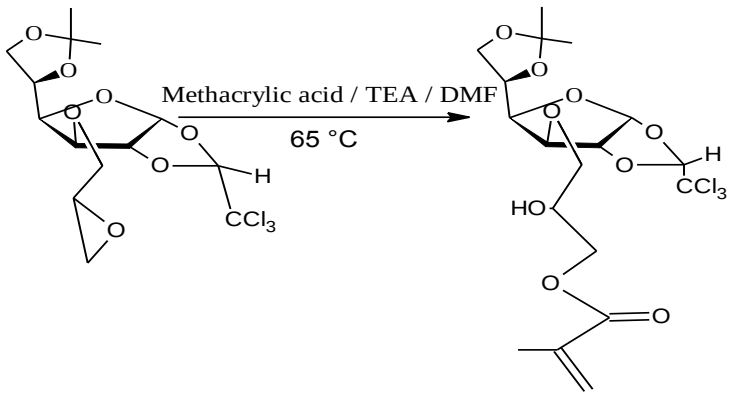
EtOAC (2/1). The resulting product was colorless cyrstal (1.27 g, yield 70 %), $[\alpha]^{21}_{D}$ -46 (c=1 in CH_2Cl_2).

3.2.15 Synthesis of 3-*O*-(2'-Hydroxy-3'-acryloyloxypropyl)-5,6-*O*-isopropylidene-1,2-*O*-(S)-trichloroethylidene-α-D-glucofuranose (15)



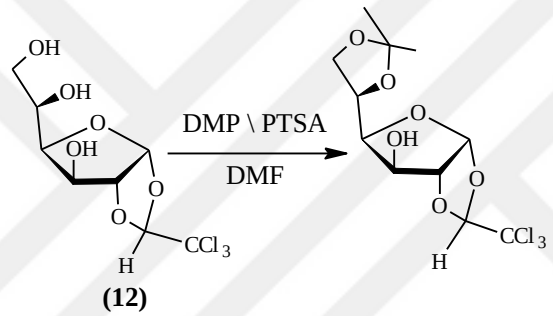
Product **14** (1.27g, 3mmol), dissolved with DMF (10 ml). Triethylamine (0.36 mL, 0.26 g, 2.6 mmol) and acrylic acid (1.79 mL, 1.89 g, 2.17 mmol) was added drop by drop at room temperature. The mixture was stirred while heating to 65 ^{o}C. The reaction was continued at the same temperature for 24 hours. The product obtained was extracted with CH_2Cl_2 and the organic layer was washed with distilled cold water. The product was purified by Hexane/ EtOAC (2/1) column chromatography. Transparent gel was obtained. (1 g, 72 % yield)

3.2.16 Synthesis of 3-*O*-(2'-Hydroxy-3'-methacryloyloxypropyl)-5,6-*O*-isopropylidene-1,2-*O*-(S)-trichloroethylidene-α-D-glucofuranose (16)



Product **14** (1.27g, 3mmol) , dissolved with DMF (10 ml). Triethylamine (0.52 mL, 0.31 g, 3.03 mmol) and methacrylic acid (2.53 mL, 2.63 g, 35.30 mmol) was added drop by drop at room temperature. The mixture was stirred while heating to 65 ^{o}C. The reaction was continued at the same temperature for 24 hours. The product obtained was extracted with CH_2Cl_2 and the organic layer was washed with distilled cold water. The product was purified by Hexane/ EtOAC (2/1) column chromatography. Yellow transparent gel was obtained (1.65 g, 67 % yield)

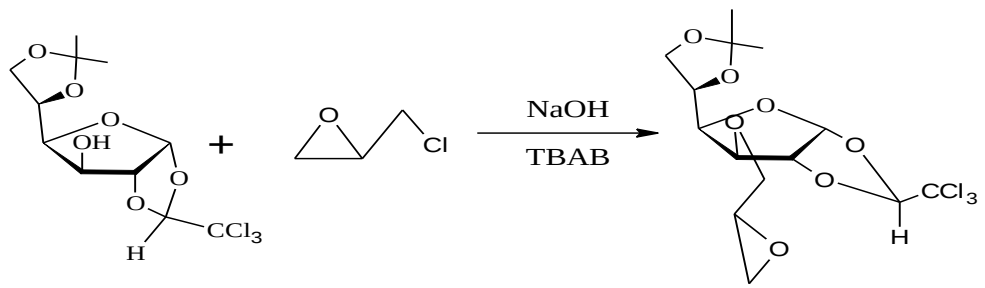
3.2.18 Synthesis of 5,6-*O*-Isopropylidene-1,2-*O*-(S)-trichloroethylidene-β-D-glucofuranose (17)



(12)

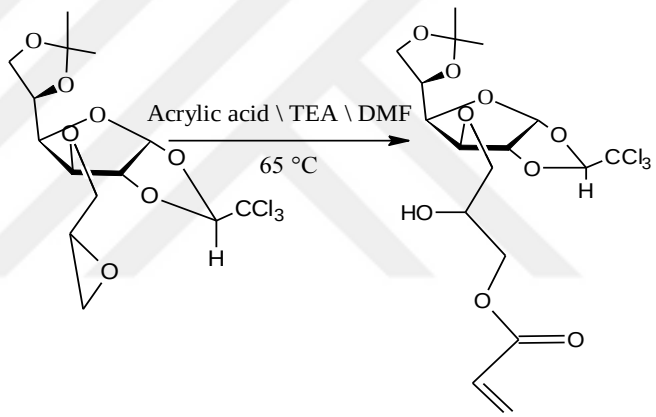
Commercially available β-D-glucose (10 g, 0.032 mol), was solved with DMF (50 mL). To this solution was added on DMP (10 mL, d=0.85 g/cm^3, 8.5 g) and anhydrous PTSA (10 mg, 0.058 mmol). The mixture was stirred during 24 hours and was neutralized with $NaHCO_3$. DMF was evaporated. The product was crystalized with methanol. The resulting product was obtained as colorless crystal. (8.2 g, 72%), mp: 169-171^{o}C, $[\alpha]_D^{22}$: - 34.0^{o} (c: 0.25 in $CHCl_3$).

3.2.19 Synthesis of 3-*O*-(2',3'-Epoxypropan-1'-yl)-5,6-*O*-isopropylidene-1,2-*O*-(S)-trichloroethylidene-β-D-glucofuranose (18)



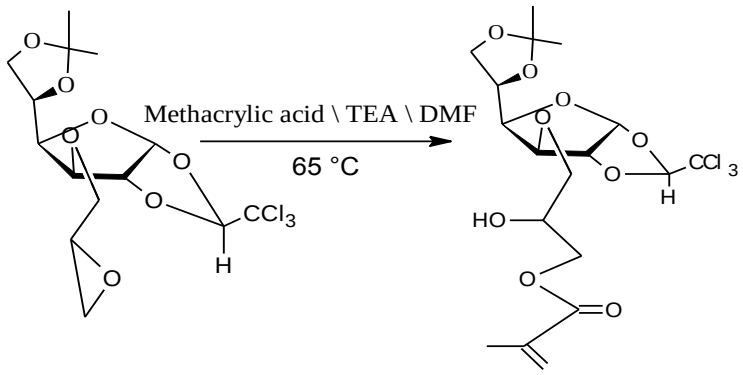
Epichlorohydrine (7 mL, 88 mmol), tetrabutyl ammonium bromide and solution of NaOH (50%, 15mL) was stirred at room temperature for 30 minutes. To this mixture product **17** (3g,8mmol) was slowly added at 5 °C. The reaction continued at the same temperature for 3 hours. The mixture was poured onto ice and extracted with EtOAC (4x15ml). The organic layer was washed with NH_4Cl (10%, 2x2.5 mL), dried with anhydrous Na_2SO_4 and filtered. The solvent was evaporated and the syrup was purified by column chromatography using Hexane / EtOAC (2/1). The resulting product was colorless crystal (2.20 g, yield 68 %), $[\alpha]^{21}_D$ -46 (c=1 in CH_2Cl_2).

3.2.20 Synthesis of 3-*O*-(2'-hydroxy-3'-acryloyloxypropyl)-5,6-*O*-isopropylidene-1,2-*O*-(S)-trichloroethylidene-β-D-glucofuranose (19)



Product **18** (2.20g, 5mmol) dissolved with DMF (15 ml). Triethylamine (0.87 mL, 0.64 g, 6.32 mmol) and acrylic acid (4.21 mL, 4.43 g, 58.83 mmol) was added drop by drop at room temperature.The mixture was stirred while heating to 65 ^oC. The reaction was continued at the same temperature for 24 hours. The product obtained was extracted with CH_2Cl_2 and the organic layer was washed with distilled cold water. The product was purified by Hexane/ EtOAC (2/1) column chromatography. Transparent gel was obtained (1.62 g, 70 % yield)

3.2.21 Synthesis of 3-*O*-(2'-hydroxy-3'-methacryloyloxypropyl)-5,6-*O*-isopropylidene-1,2-*O*-(S)-trichloroethylidene-β-D-glucofuranose (20)



Product **18** (2.20g, 5mmol) , dissolved with DMF (10 ml). Triethylamine (0.87 mL, 0.64 g, 6.32 mmol) and methacrylic acid (4.21 mL, 4.43 g, 58.83 mmol) was added drop by drop at room temperature.The mixture was stirred while heating to 65 ^{o}C. The reaction was continued at the same temperature for 24 hours. The product obtained was extracted with CH_2Cl_2 and the organic layer was washed with distilled cold water. The product was purified by Hexane/ EtOAC (2/1) column chromatography. Transparent gel was obtained (1.63 g, 68 % yield)

4. RESULTS AND DISCUSSIONS

With the current development in glucose science, the design and synthesis of sugar based materials, especially glycopolymers, has become a important topic. Glycopolymers are a good example of biodegradable polymers. They are also of great importance as they have many biological, biochemical and biomedical applications.

The synthesis of our sugar-based monomers synthesized in the presented project consists of three stages;

- Synthesis of protected sugar structures to release the hydroxyl groups number three (**2,7,13,17**)
- Etheric bonding of epichlorohydrin to free hydroxyl of sugar (**3,8,14,18**)

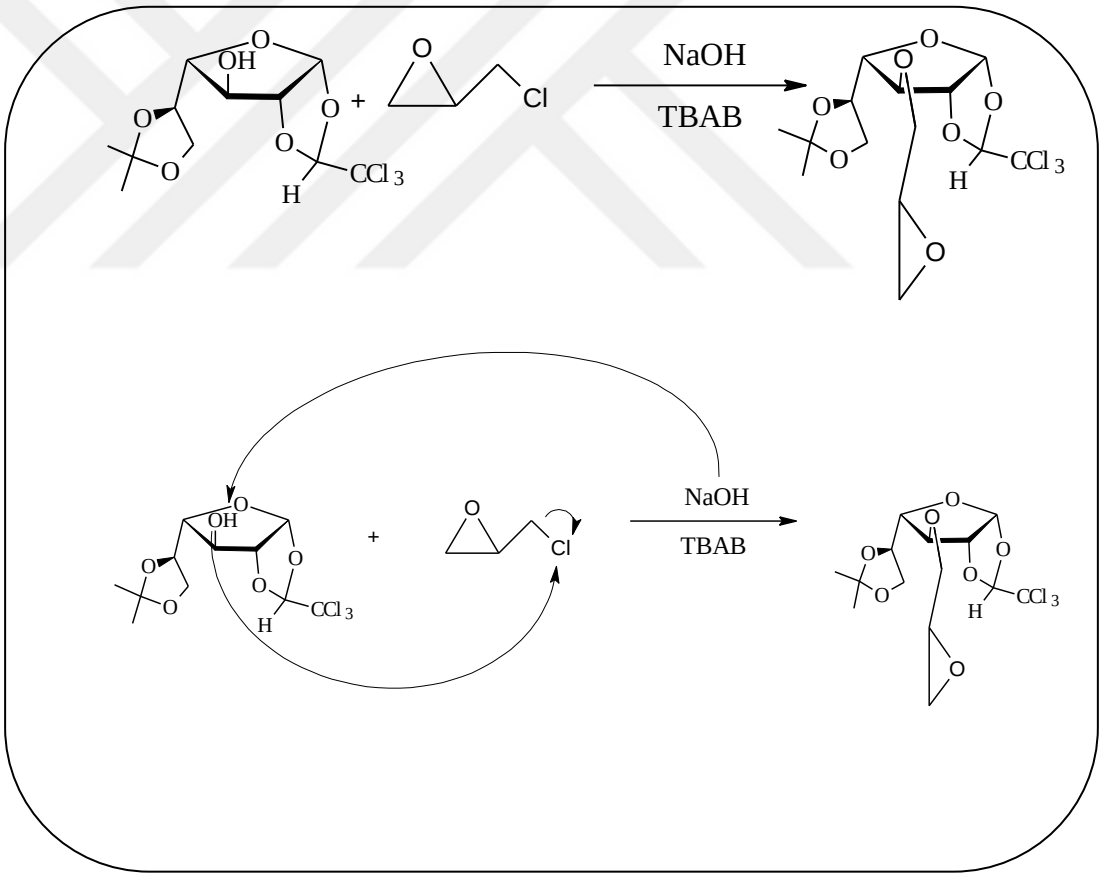


Figure 4.1 Etheric Bonding

- Opening of epoxy ring with methacrylic acid and acrylic acid (**4, 5, 9, 10, 15, 16, 19, 20**)

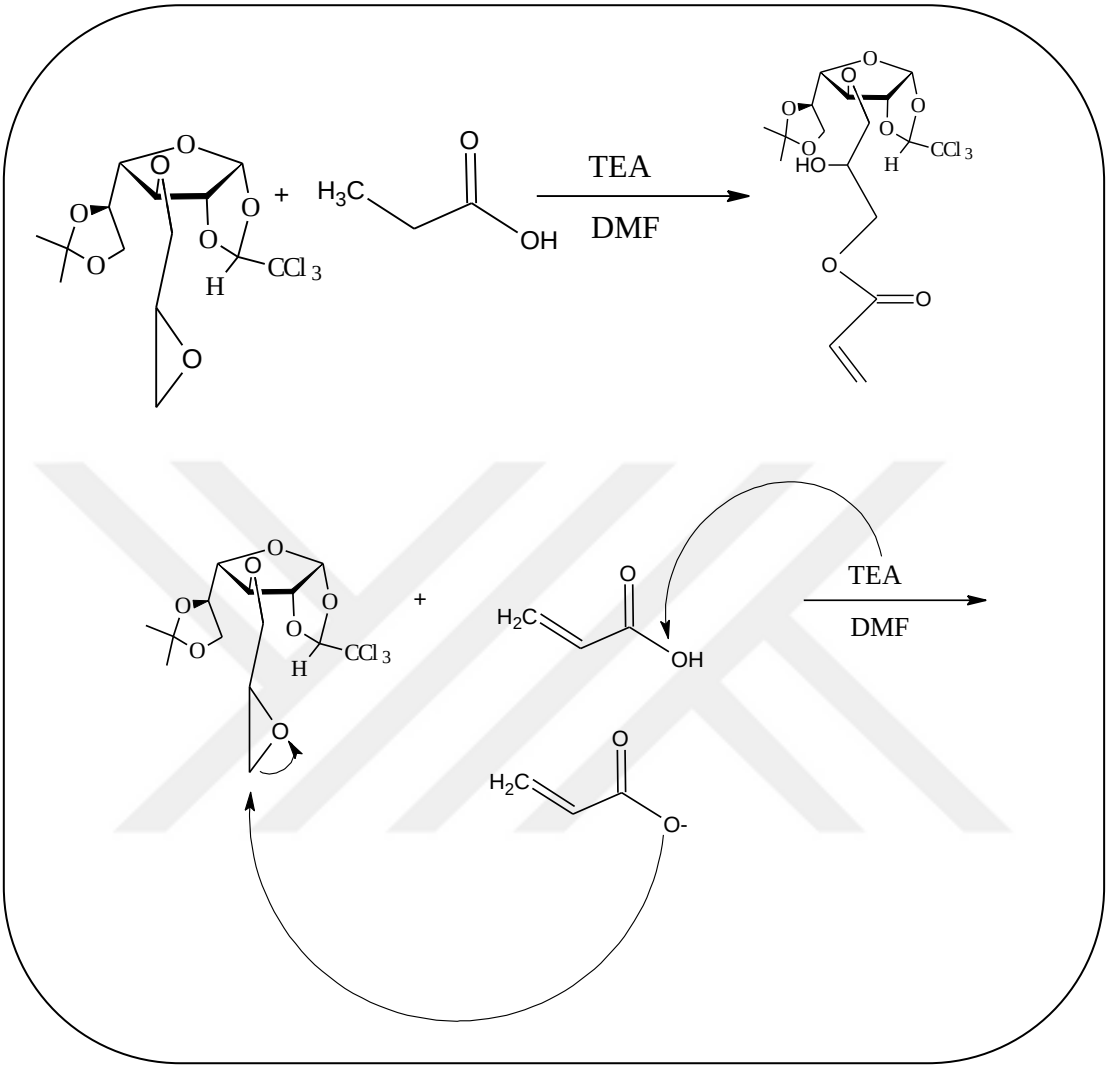


Figure 4.2 Epoxy ring opening

4.1. Synthesis of Acrylic and Methacrylic Monomers

The steps of for D-galactose synthesis of acrylic and methacrylic monomer are shown in the diagram. The other steps were repeated in the same manner for D-glucose and D-mannose.

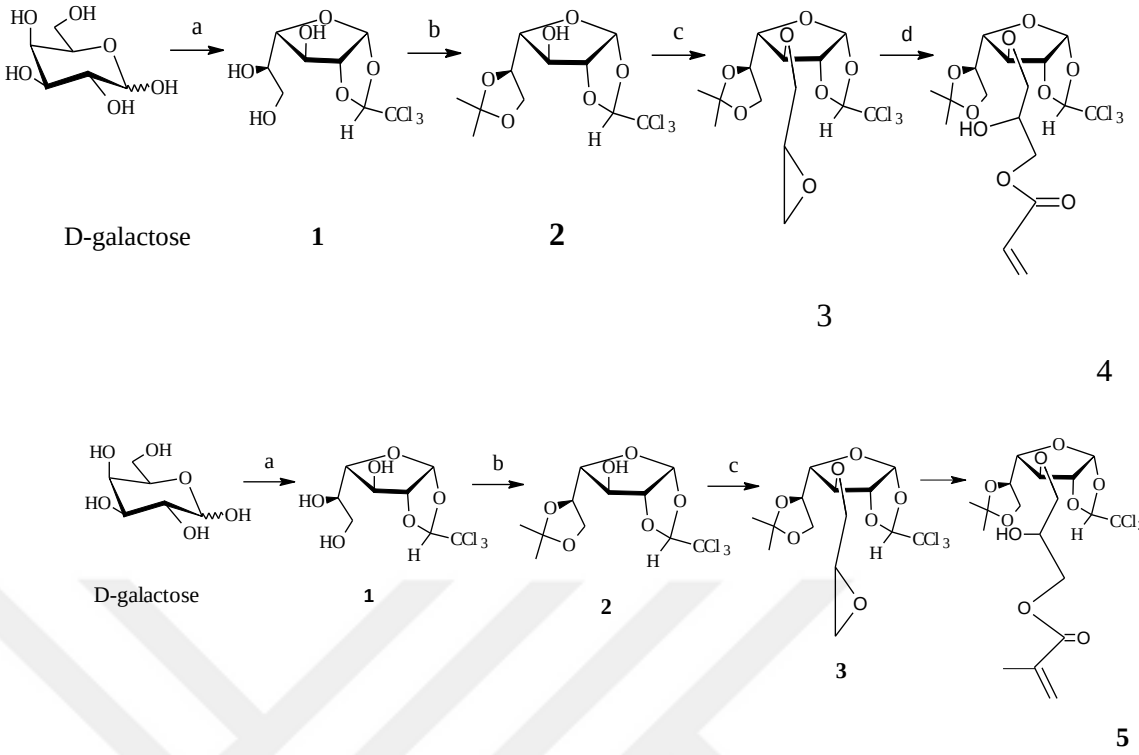


Figure 4.3 The steps of for D-galactose synthesis of acrylic and methacrylic monomer

Compounds **1, 2, 3, 6, 7, 8, 13, 14, 17** and **18** were synthesized according to the methods in the literature (Anıl and Yüceer, 1983; Salman et al 2004; Kök et al 2010; Kök and Salman, 2012; Kök et al 2014, Koruyucu et al, 2016). Experimental datas were including identical to literature for compounds. Starting sugar D-galactose, D-glucose and D-mannose are commercially available and purified.

The 1-OH and 2-OH groups protected with chloral using the Chloral / H_2SO_4. The 5-OH and 6-OH groups protected with isopropylidene group using the conventional DMP/PTSA/DMF procedure (Salman et al, 2004).

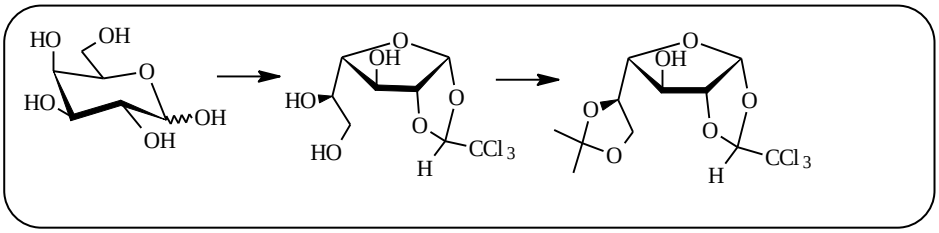


Figure 4.4 Protective groups

4.2 Structural Characterization of the Compounds

Various spectroscopic methods for acrylic and methacrylic sugar-based monomers were applied.

Characteristic ^{1}H-NMR chemical shifts of sugar-based methacrylic monomers are shown in the Table 4.4, Table 4.8, Table 4.12, Table 4.16.

Acetal proton single peaks at 5.60, 5.64, 5.30 and 5.66 ppm are consistent with literature data (Anıl and Yüceer, 1983; Salman et al 2004; Kök et al 2010; Kök and Salman, 2012; Kök et al 2014, Koruyucu et al, 2016). Furthermore, H-1 protons and J 1.2 coupling constants (4 Hz) at 6.21, 5.92, 6.10 and 6.19 ppm of the corresponding monomers are also consistent with the literature data (Anıl and Yüceer, 1983; Salman et al, 2004; Kök et al, 2010; Kök and Salman, 2012; Kök et al, 2014, Koruyucu et al, 2016).

Similarly characteristic ^{1}H-NMR chemical shifts of sugar-based acrylic monomers are shown in the Table 4.2, Table 4.6, Table 4.10, Table 4.14.

In addition, the specific adsorbance values of FTIR spectra of carbohydrate based monomers synthesized are shown in Table 4.1, Table 4.3, Table 4.5, Table 4.7, Table 4.9, Table 4.11, Table 4.13, Table 4.15.

Accordingly, the wide OH peaks of hydroxyl groups formed by epoxy ring opening of monomers are about 3450 cm^{-1}, C-H peaks around 2930 cm^{-1}, the peak of the C = O bond in the (meth) acrylic section is about 1710 cm^{-1} and the C=C peak of the carbon-carbon double bond in the (meth) acrylic portion was also observed at 1610 cm -1. In addition, peaks of the etheric C-O-C bond are around 1175 cm^{-1} and peaks of the C-Cl bonds in the trichloroethylidene group are around 720 cm^{-1}.

All these results show that the synthesis of acrylic and methacrylic sugar based monomers has been accomplished successfully.

4.3. 3-O-(2'-Hydroxy-3'-acryloyloxypropyl)-5,6-O-isopropylidene-1,2-O-(S)-trichloroethylidene-α-D-galactofuranose (4)

Table 4.1 FTIR data (cm^{-1}) of the compound **4**

Functional Groups	(cm^{-1})
O-H	3479
C-H	2986
C=O	1728
C=C	1635

Table 4.2 ^{1}H-NMR spectral data of the compound **4**

Proton type	**^{1}H-NMR chemical shifts**
H-**1**	6.20 (d), J = 4 Hz
>C**H**CCl_3	5.65 (s)
H-C=C$\mathbf{H_2}$	6.43, 6.14, 5.89
H-**2**	4.93 (d)
>C(C$\mathbf{H_3}$)$_2$	1.39 (s), 1.47 (s)

4.4. 3-O-(2'-Hydroxy-3'-methacryloyloxypropyl)-5,6-O-isopropylidene-1,2-O-(S)-trichloroethylidene-α-D-galactofuranose (5)

Table 4.3 FTIR data (cm^{-1}) of the compound **5**

Functional Groups	**(cm^{-1})**
O-H	3480
C-H	2985
C=O	1716
C=C	1637

Table 4.4 ^{1}H-NMR spectral data of the compound **5**

Proton type	**^{1}H-NMR chemical shifts**
H-**1**	6.19 (d), J = 4 Hz
>C**H**CCl_3	5.64 (s)
$\mathbf{H_2}$C=C<	6.13, 5.60
H-**2**	4.93 (d)
=C-C$\mathbf{H_3}$	1.95 (s)
>C(C$\mathbf{H_3}$)$_2$	1.37 (s), 1.46 (s)

4.5. 3-*O*-(2'-Hydroxy-3'-acryloyloxypropyl)-5,6-*O*-isopropylidene-1,2-*O*-(S)-trichloroethylidene-α-D-mannofuranose (10)

Table 4.5 FTIR data (cm^{-1}) of the compound **10**

Functional Groups	**(cm^{-1})**
O-H	3456
C-H	2925
C=O	1727
C=C	1634

Table 4.6 ^{1}H-NMR spectral data of the compound **10**

Proton type	**^{1}H-NMR chemical shifts**
H-**1**	5.94 (two dublet), J = 4 Hz
>C**H**CCl_3	5.66 (two singlet)
H-C=C$\mathbf{H_2}$	6..44, 6.12, 5.86
H-**2**	4.93 (d)
>C(C$\mathbf{H_3}$)$_2$	1.39 (s), 1.45 (s)

4.6. 3-*O*-(2'-Hydroxy-3'-methacryloyloxypropyl)-5,6-*O*-isopropylidene-1,2-*O*-(S)-trichloroethylidene-α-D-mannofuranose (11)

Table 4.7 FTIR data (cm^{-1}) of the compound **11**

Functional Groups	**(cm^{-1})**
O-H	3442
C-H	2987
C=O	1716
C=C	1638

Table 4.8 ^{1}H-NMR spectral data of the compound **11**

Proton type	**^{1}H-NMR chemical shifts**
H-1	5.92, two set of dublet J = 4 Hz
>C**H**CCl_3	62 and 5.65 two set of singlet
H_2C=C<	6.13, 5.57
H-2	5.07 two set of dublet
=C-C**H_3**	1.93 (s)
>C(C**H_3**)$_2$	1.37 (s), 1.40 (s)

4.7. 3-O-(2'-Hydroxy-3'-acryloyloxypropyl)-5,6-O-isopropylidene-1,2-O-(S)-trichloroethylidene-α-D-glucofuranose (15)

Table 4.9 FTIR data (cm^{-1}) of the compound **15**

Functional Groups	**(cm^{-1})**
O-H	3455
C-H	2987
C=O	1726
C=C	1636

Table 4.10 ^{1}H-NMR spectral data of the compound **15**

Proton type	**^{1}H-NMR chemical shifts**
H-**1**	6.07
>C**H**CCl_3	5.29 (two singlet)
H-C=CH_2	6..41, 6.12, 5.86
H-**2**	4.71
>C(C**H_3**)$_2$	1.34 (s), 1.40 (s)

4.8. 3-*O*-(2'-Hydroxy-3'-methacryloyloxypropyl)-5,6-*O*-isopropylidene-1,2-*O*-(S)-trichloroethylidene-α-D-glucofuranose (16)

Table 4.11 FTIR data (cm^{-1}) of the compound **16**

Functional Groups	**(cm^{-1})**
O-H	3460
C-H	2987
C=O	1717
C=C	1638

Table 4.12 ^{1}H-NMR spectral data of the compound **16**

Proton type	**^{1}H-NMR chemical shifts**
H-**1**	6.08 (d), J = 4 Hz
>C**H**CCl_3	5.29 (s)
H_2C=C<	6.12, 5.58
H-**2**	4.71 (d)
=C-C**H_3**	1.94 (s)
>C(C**H_3**)$_2$	1.34 (s), 1.40 (s)

4.9. 3-O-(2'-hydroxy-3'-acryloyloxypropyl)-5,6-O-isopropylidene-1,2-O-(S)-trichloroethylidene-β-D-glucofuranose (19)

Table 4.13 FTIR data (cm^{-1}) of the compound **19**

Functional Groups	**(cm^{-1})**
O-H	3454
C-H	2989
C=O	1725
C=C	1635

Table 4.14 ^{1}H-NMR spectral data of the compound **19**

Proton type	**^{1}H-NMR chemical shifts**
H-**1**	5.94 (two dublet)
>C**H**CCl_3	5.66 (two singlet)
H-C=C**H_2**	6..40, 6.15, 5.85
H-**2**	4.90 J = 3.6 Hz
>C(C**H_3**)$_2$	1.35 (s), 1.43 (s)

4.10. 3-*O*-(2'-hydroxy-3'-methacryloyloxypropyl)-5,6-*O*-isopropylidene-1,2-*O*-(S)-trichloroethylidene-β-D-glucofuranose (20)

Table 4.15 FTIR data (cm^{-1}) of the compound **20**

Functional Groups	**(cm^{-1})**
O-H	3455
C-H	2956
C=O	1719
C=C	1638

Table 4.16 ^{1}H-NMR spectral data of the compound **20**

Proton type	**^{1}H-NMR chemical shifts**
H-**1**	6.21 (d), J = 4 Hz
>C**H**CCl_3	5.60 (s)
H_2C=C<	6.13, 5.59
H-**2**	4.92 (d)
=C-C**H_3**	1.95 (s)
>C(C**H_3**)$_2$	1.36 (s), 1.44 (s)

REFERENCES

Ambrosi, M., Cameron, N. R. ve Davis, B. G., 2005, Lectins: Tools for the Molecular Understanding of the Glycocode, Organic and Biomolecular Chemistry, 3, 1593–1608pp.

Anıl, H. ve Yüceer, L., 1983, Effects of the trichloromethyl group in displacement reactions of some 3-O-tosyl-1,2-O-trichloroethylidene-α-D-galacto- and -gluco-furanose derivatives. Carbohydrate Research, 123, 315-319pp.

Bahulekar, R., Tokiwa, T., Kano, J., Matsumura, T., Kojima, I. and Kodama, M., 1998b, Polyacrylamides containing sugar residues: synthesis, characterization and hepatocyte attachment studies, Biotechnology Techniques, 12(10):721-724pp.

Belgacem M. N., Gandini A., 2008, Monomers, Polymers and Coenosites from Renewable Resources, Elsevier, Oxford,

Bertozzi, C. R. ve Kiessling, L. L., 2001, Chemical glycobiology, Science, 291(5512):2357–2364pp.

Carpino, L. A., Ringsdorf, H., ve Ritter, H., 1976, Pharmacologically active polymers, 10. Preparation and polymerization of 1-O-(4-methacryloylaminophenyl)-β-D-glucopyranoside, Macromolecular Chemistry, 177:1631–1635pp.

Choi., S. K., Mammen, M., Whitesides, G. M., 1997, Generation and in Situ Evaluation of Poly(acrylic acid) Presenting Sialosides as Side Chains as Polyvalent Inhibitors of Influenza-Mediated Hemagglutination, J. Am. Chem. Soc.

Freudenberg, K., Hochstetter, H.v. ve Engels, H., 1925, 58B:666-671pp.

Graham Solomons., T. W,. Fryhle, C., 2007, Organic Chemistry Ninth Edition

Kiessling, L. L., Gestwicki, J. E. ve Strong, L. E., 2000, Synthetic multivalent ligands in the exploration of cell-surface interactions, Current Opinion in Chemical Biology, 4:696–703pp.

REFERENCES (continued)

Koruyucu, M., Saltan, F., Kök, G, Akat, H., Salman, Y., 2016, Synthesis, characterization and polymerization of novel sugars based on methacrylate, Iranian Polymer Journal, DOI 10.1007/s13726-016-0437-5.

Kök, G. and Salman, Y., 2012, A Convenient Synthesis of a Cardiac Sugar: "D-Digitalose". Journal of Carbohydrate Chemistry,. 31, 1–9pp.

Kök, G., Ay, K., Ay, E., Doğan, F., Kaya, İ., 2014, "Synthesis, characterization and non-isothermal decoenosition kinetic of a new galactochloralose based polymer". Carbohydrate Polymers, 101, 324-331pp.

Ladmiral, V., Melia E. ve Haddleton, D. M., 2004, Synthetic glycopolymers: an overview, European Polymer Journal, 40(3):431–449pp.

Lin, J. W.-P. ve Schuerch, C., 1972, Synthesis and properties of stereoregular 2,3,4-tri-O-acetyl-[1 .far. 6]-α-D-gluco-, -manno-, and -galactopyranans, Journal of Polymer Science, Part A-1: Polymer Chemistry, 10(7):2045p.

Pinilla, I. M., Martinez, M. B., Mata, F. Z., ve Galbis, J. A., 2002, Carbohydrate-Based Copolymers. Hydrolysis of Copoly(ester amide)s Containing L-Arabinose Units, Macromolecules, 35(8):2977–2984pp.

Ruckel, E. R. ve Schuerch, C., 1966, Preparation of high polymers from 1,6-anhydro-2,3,4-tri-Osubstituted β-D-glucopyranose, Journal of Organic Chemistry, 31(7):2233p.

Ruckel, E. R., ve Schuerch, C., 1966, Chemical synthesis of a stereoregular linear polysaccharide, Journal of American Chemical Society, 88(11):2605-2606pp.

Salman, Y., Kök, G. ve Yüceer, L., 2004, Tricyclic furanoid dichloroacetyl orthoesters of D-mannose from 1,2-O-trichloroethylidene-β-D-mannofuranose. Carbohydrate Research, 339, 1739-1745pp.

REFERENCES (continued)

Spaltenstein A., Whitesides., G. M., 1991, Polyacrylamides bearing pendant alpha-sialoside groups strongly inhibit agglutination of erythrosytes by influenza virüs, J. Am. Chem. Soc.

Spain, S. G., Gibson, M. I. and Cameron, N. R., 2007, Recent advances in the synthesis of well-defined glycopolymers, Journal of Polymer Science Part A: Polymer Chemistry, 45(11):2059–2072pp.

Ting, S. R. S., Chen G. and Stenzel, M. H., 2010, Polymer Chemistry, 1: 1392-1412pp.

Yoshida, T., Akasaka., T., Y. Choi., K. Hattori., B. Yu., T. Mimura., Y. Kaneko., H. Nakashima., E. Aragaki., M. Premanathan., N. Yamamoto T. Uryu., 1999, AIDS, J. Polym. Sci. Part A: Polym. Chem.

Uryu, T., Kitano, K., Ito, K., Yamanouchi, J., and Matsuzaki, K., 1981, Selective ring-opening polymerization of 1,4-anhydro-α-D-ribopyranose derivatives and synthesis of stereoregular (1→4)-β-D-ribopyranan, Macromolecules, 14(1):1–9pp.

Uryu, T., Libert, H., Zachoval, J., & Schuerch, C., 1970. Chemical synthesis and properties of stereoregular poly-α-(1.far.6′)-anhydro-D-galactopyranose, Macromolecules, 3(3):345p.

Uryu, T., Yamanouchi, J., Kato, T., Higuchi, S., and Matsuzaki, K., 1983, Selective ring-opening polymerization of di-O-methylated and di-O-benzylated 1,4-anhydro-α-D-ribopyranoses and structure proof of synthetic cellulose-type poly, Journal of American Chemical Society, 105(23):6865-6871pp

Wulff, G., Schmid, J. and Venhoff, T., 1996, The synthesis of polymerizable vinyl sugars, Macromolecular Chemistry and Physics, 191:259-274pp.

Y. Miura., K. Yasuda., K. Yamamoto., M. Koike., Y. Nishida., K. Kobayashi., 2007, Alzheimer, Biomacromolecules.

REFERENCES (continued)

Zachoval, J. and Schuerch, C., 1969, Steric control in the polymerization of 1,6-anhydro-β-D-glucopyranose derivatives, Journal of American Chemical Society, 91(5):1165pp.

ACKNOWLEDGEMENT

My biggest thanks to my supervisor Assoc. Prof. Dr. A. Yeşim SALMAN, for valuable advice, support, patience, significant contribution and supervision. I am so thankful to Assoc. Prof. Dr. Gökhan KÖK. This thesis would not have been possible without their help. I learned everything from them on behalf of my thesis.

I would also like to thank all my group friends, my laboratory friends and teachers for their contribution to my life.

I would like to thank my dear mother, father and husband for their support in every aspect of my life.

Finally thank you to my little son for choosing me as a mother…

Eylül 2019

Selin YILDIRAN EVREN

CURRİCULUM VİTAE

Name and Surname **:** Selin YILDIRAN EVREN

Date/Place of Birth **:** 07.08.1990 / İZMİR

Nationality **:** Turkish

Phone Number **:** +0905062110570

E-mail **:** yildiran.selinn@gmail.com

Educational Backround

2009-2013 Bsc. in Chemistry, Ege University, Faculty of Science

2013-2019 MSc. in Organic Chemistry, Graduate School of Natural and Applied Sciences, Ege University

APPENDIX

Appendix 1 **^{1}H-NMR spectrum of the compound 4**

Appendix 2 **FTIR specrtum of the compound 4**

Appendix 3 **^{1}H-NMR spectrum of the compound 5**

Appendix 4 **FTIR spectrum of the compound 5**

Apendix 5 **1H-NMR specrtum of the compound 10**

Appendix 6 **FTIR spectrum of the compound 10**

Appendix 7 **1 H-NMR spectrum of the compound 11**

Appendix 8 **FTIR spectrum of the compound 11**

Appendix 9 **1H-NMR spectrum of the compound 15**

Appendix 10 **FTIR spectrum of the compound 15**

Appendix 11 **1 H-NMR spectrum of the compound 16**

Appendix 12 **FTIR spectrum of the compound 16**

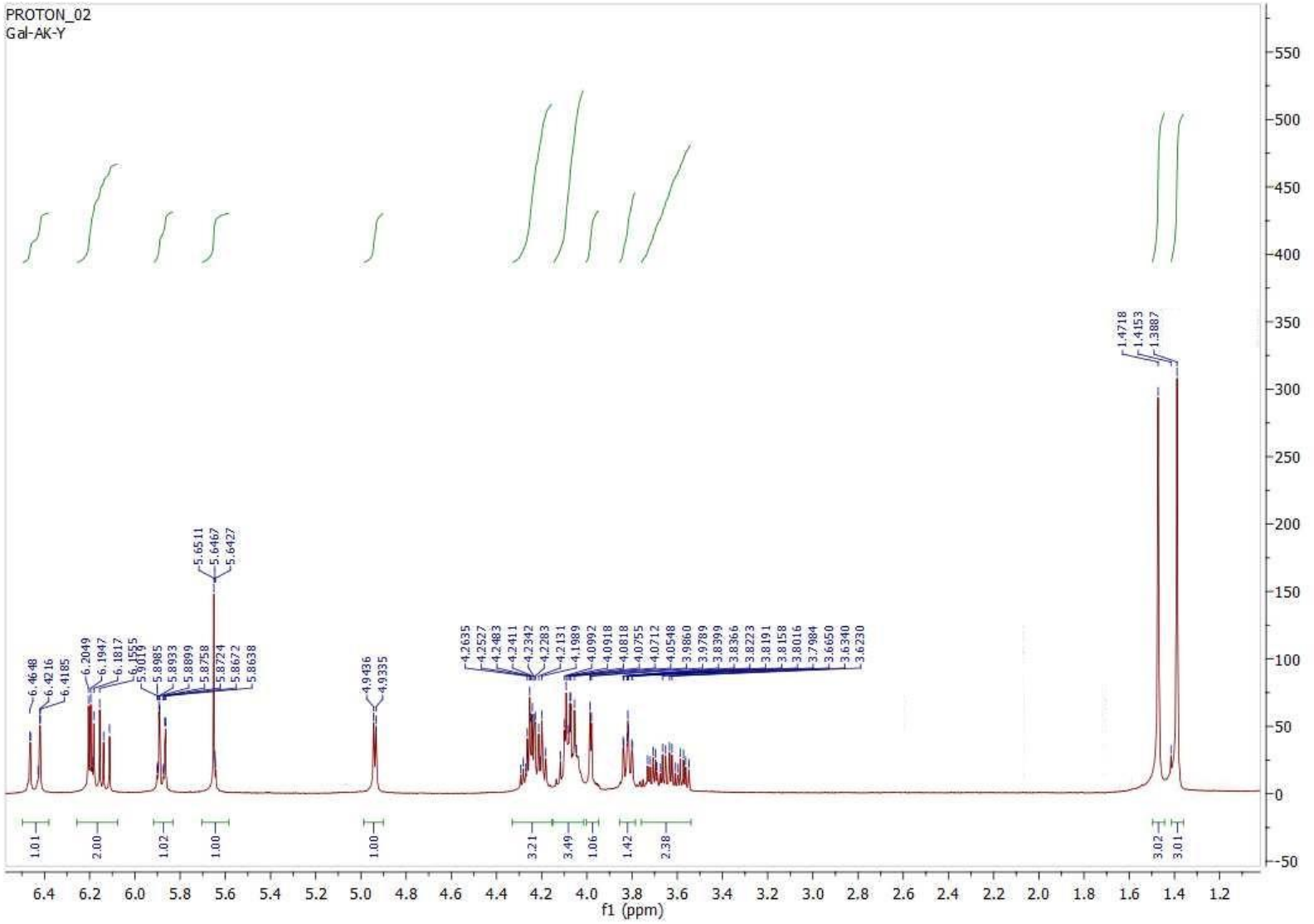
Appendix 13 **1H-NMR spectrum of the compound 19**

Appendix 14 **FTIR spectrum of the compound 19**

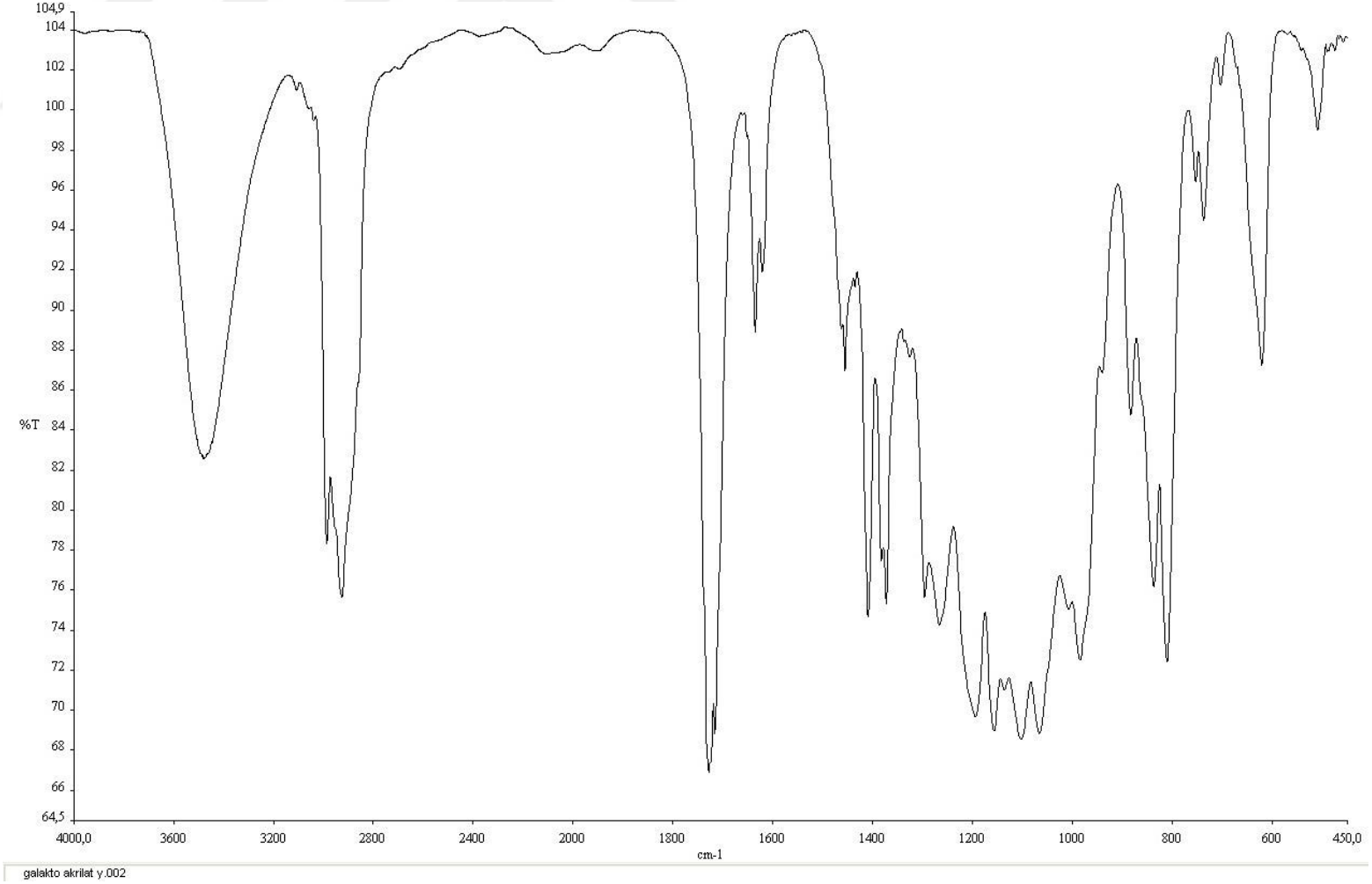
Apendix 15 **1 H-NMR spectrum of the compound 20**

Appendix 16 **FTIR spectrum of the compound 20**

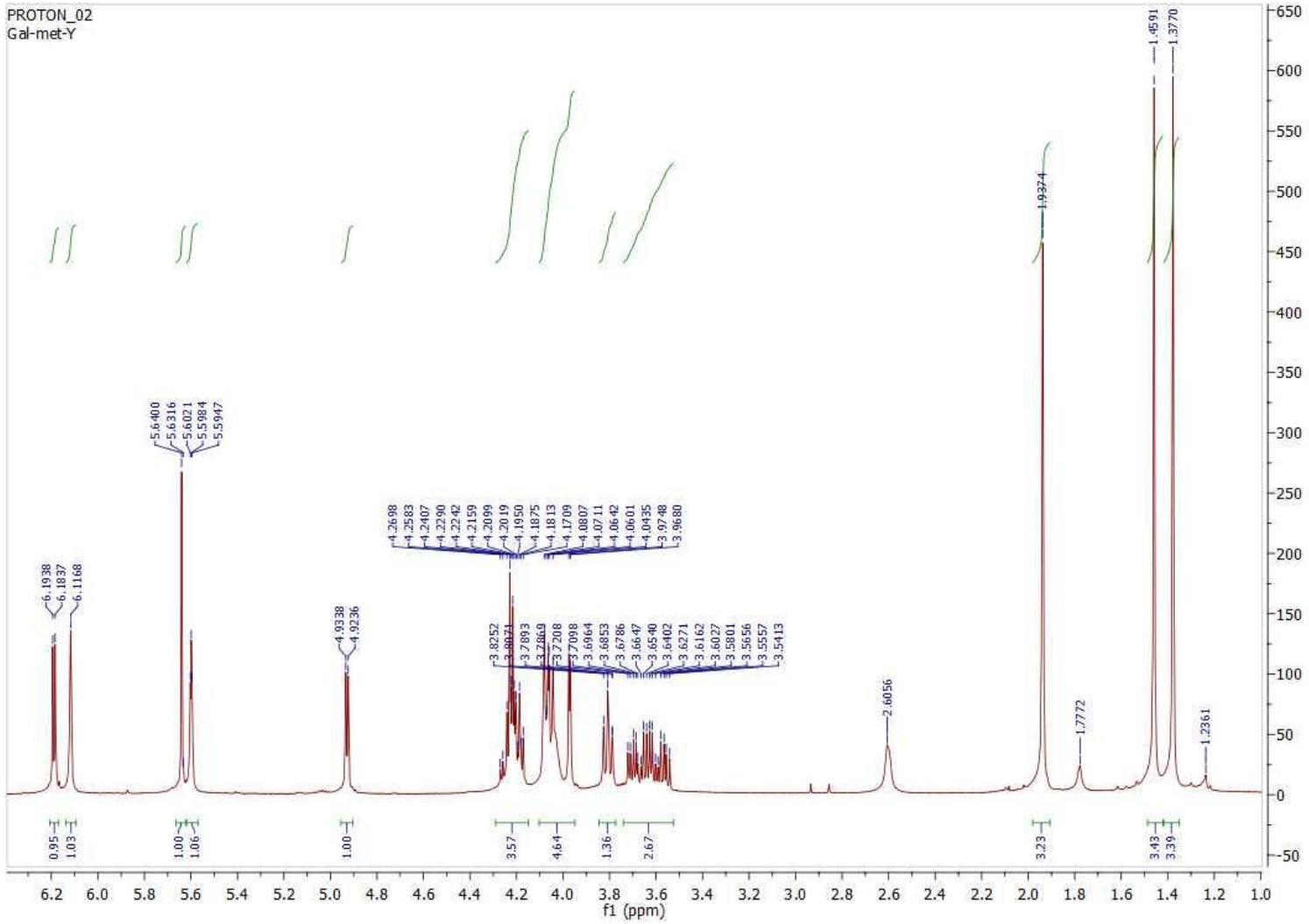
Appendix 1 [1] H-NMR spectrum of the 3-*O*-(2-hydroxy-3-acrylopropyl)-5,6-*O*-isopropylidene-1,2-*O*-(S)- trichloroethylidene-α-D-galactofuranose (compound **4)**



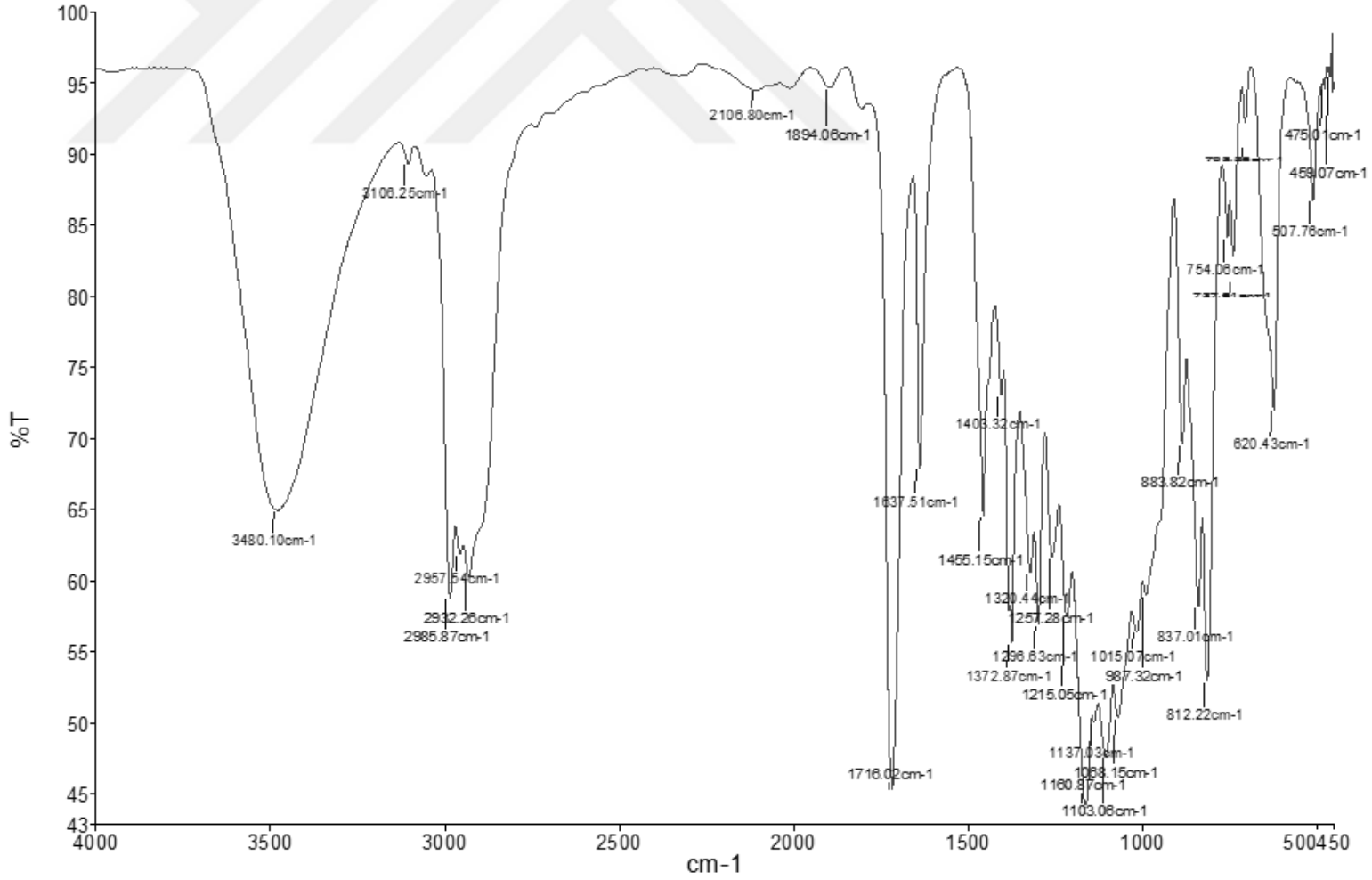
Appendix 2 FTIR spectrum of 3-*O*-(2-hydroxy-3-acrylopropyl)-5,6-*O*-isopropylidene-1,2-*O*-(S)- trichloroethylidene-α-D-galactofuranose (compound **4)**



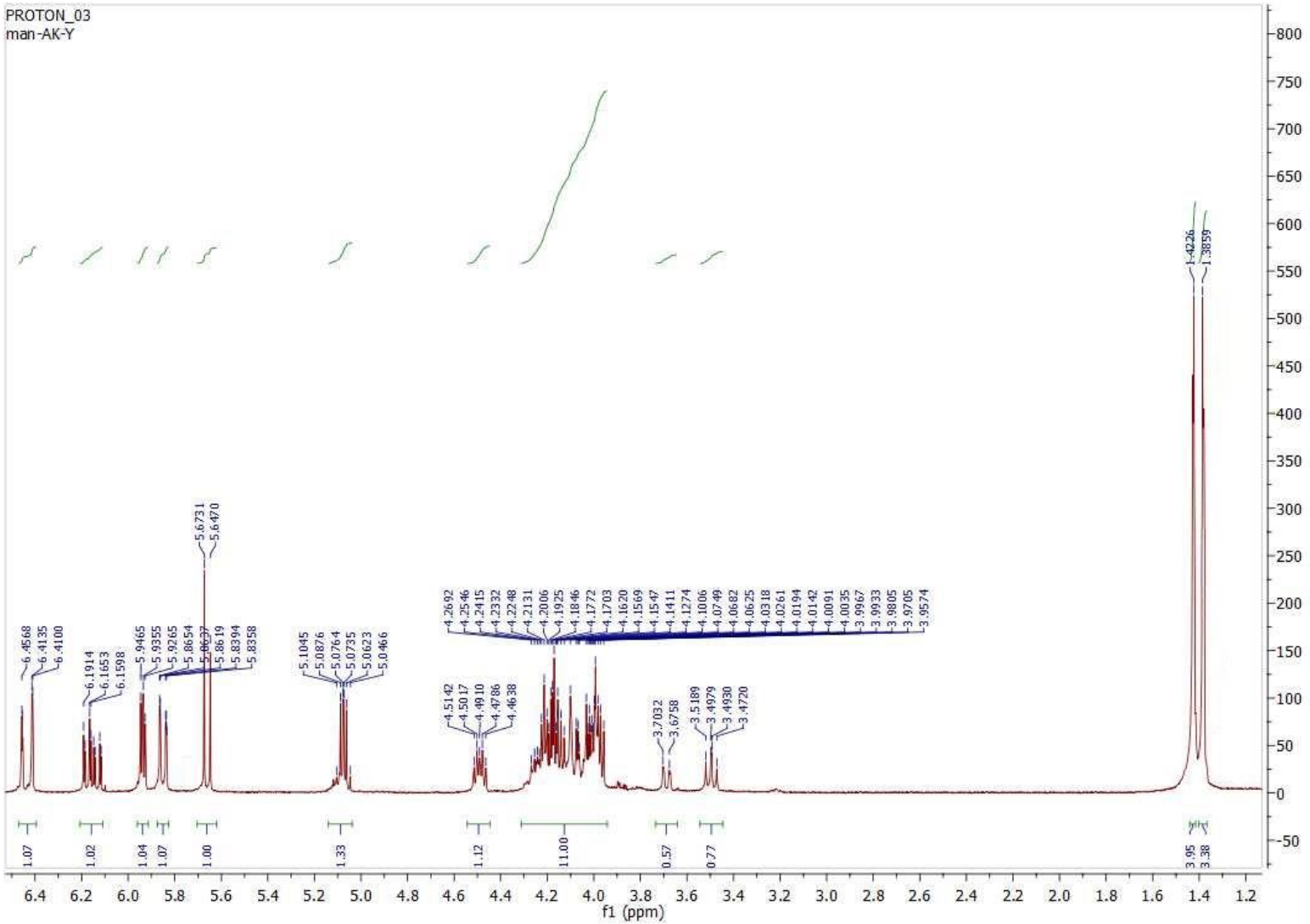
Appendix 3 [1] H-NMR spectrum of 3-*O*-(2-hydroxy-3-methacrylopropyl)-5,6-*O*-isopropylidene-1,2-*O*-(S)- trichloroethylidene-α-D-galactofuranose (compound **5)**



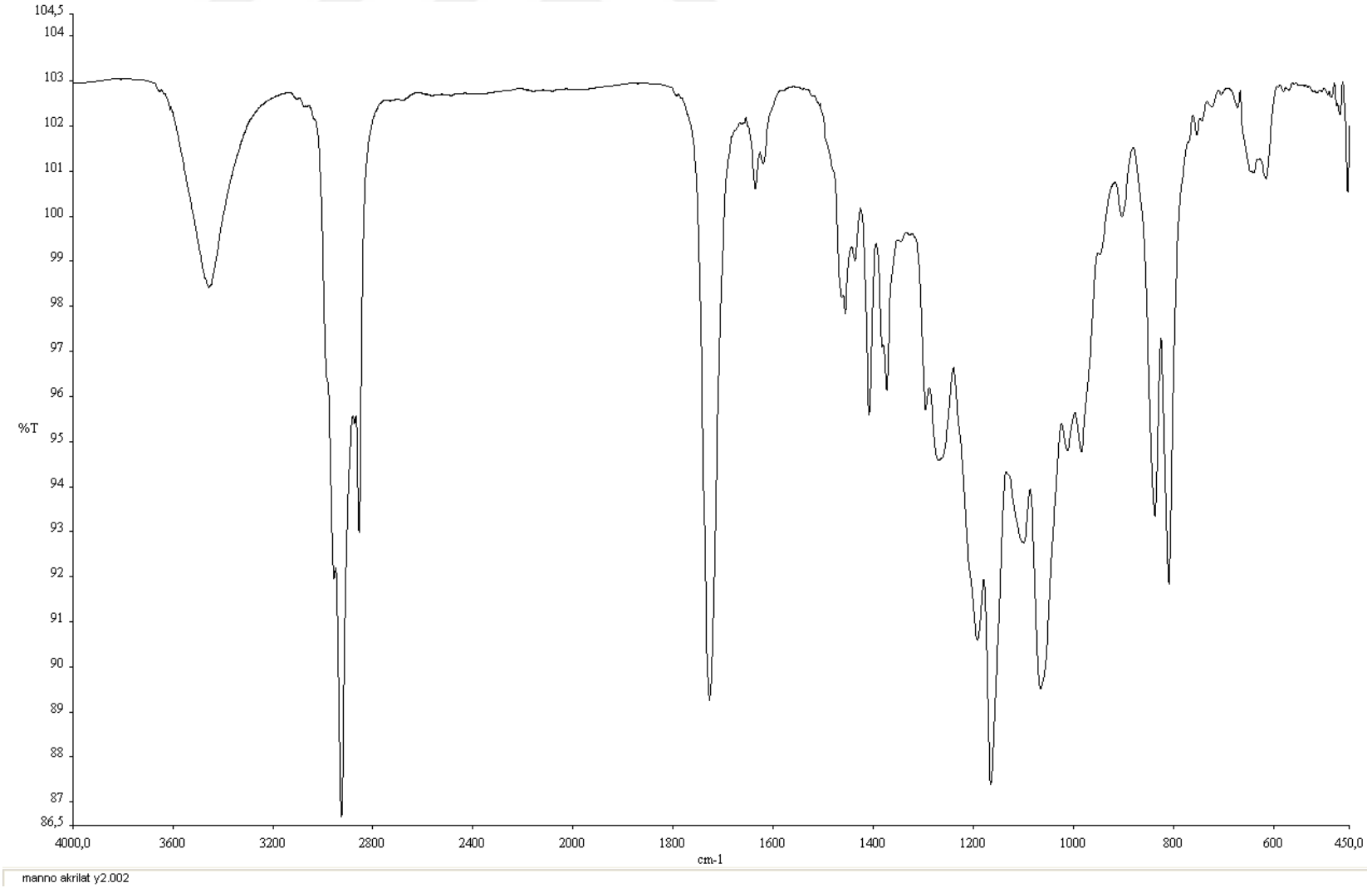
Appendix 4 FTIR spectrum of 3-*O*-(2-hydroxy-3-methacrylopropyl)-5,6-*O*-isopropylidene-1,2-*O*-(S)- trichloroethylidene-α-D-galactofuranose (compound **5)**



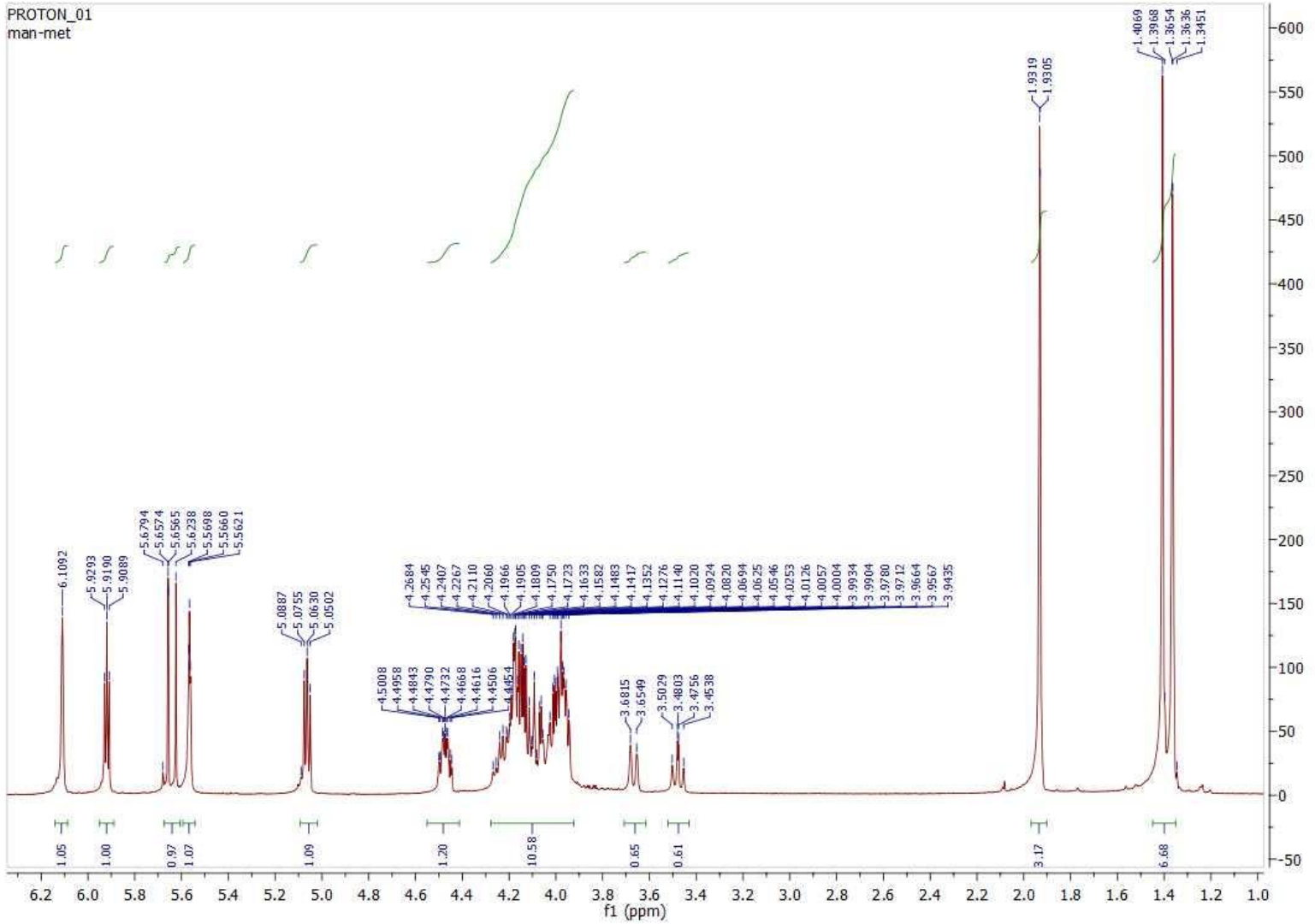
Appendix 5 [1] H-NMR spectrum of 3-*O*-(2-hydroxy-3-acrylopropyl)-5,6-*O-isopropylidene-1,2-O*-(S)-trichloroethylidene-α-D-mannofuranose (compound **10)**



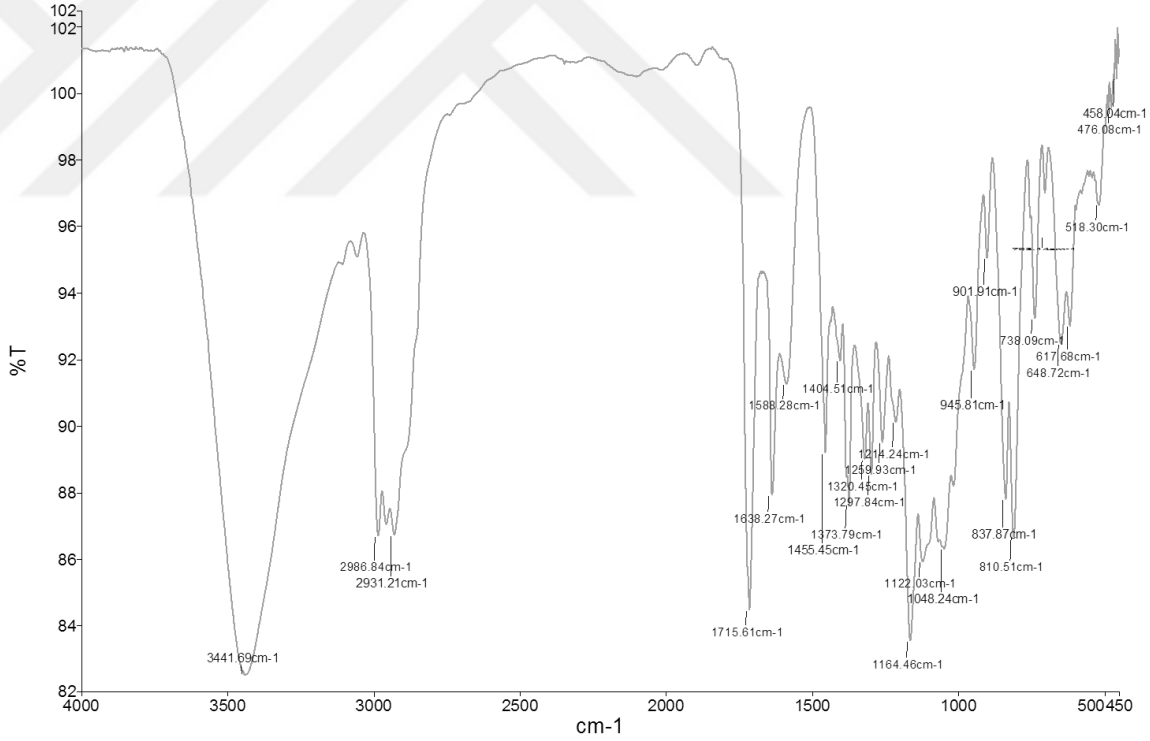
Appendix 6 FTIR spectrum of 3-*O*-(2-hydroxy-3-acrylopropyl)-5,6-*O*-isopropylidene-1,2-*O*-(S)-trichloroethylidene-α-D-mannofuranose (compound **10)**



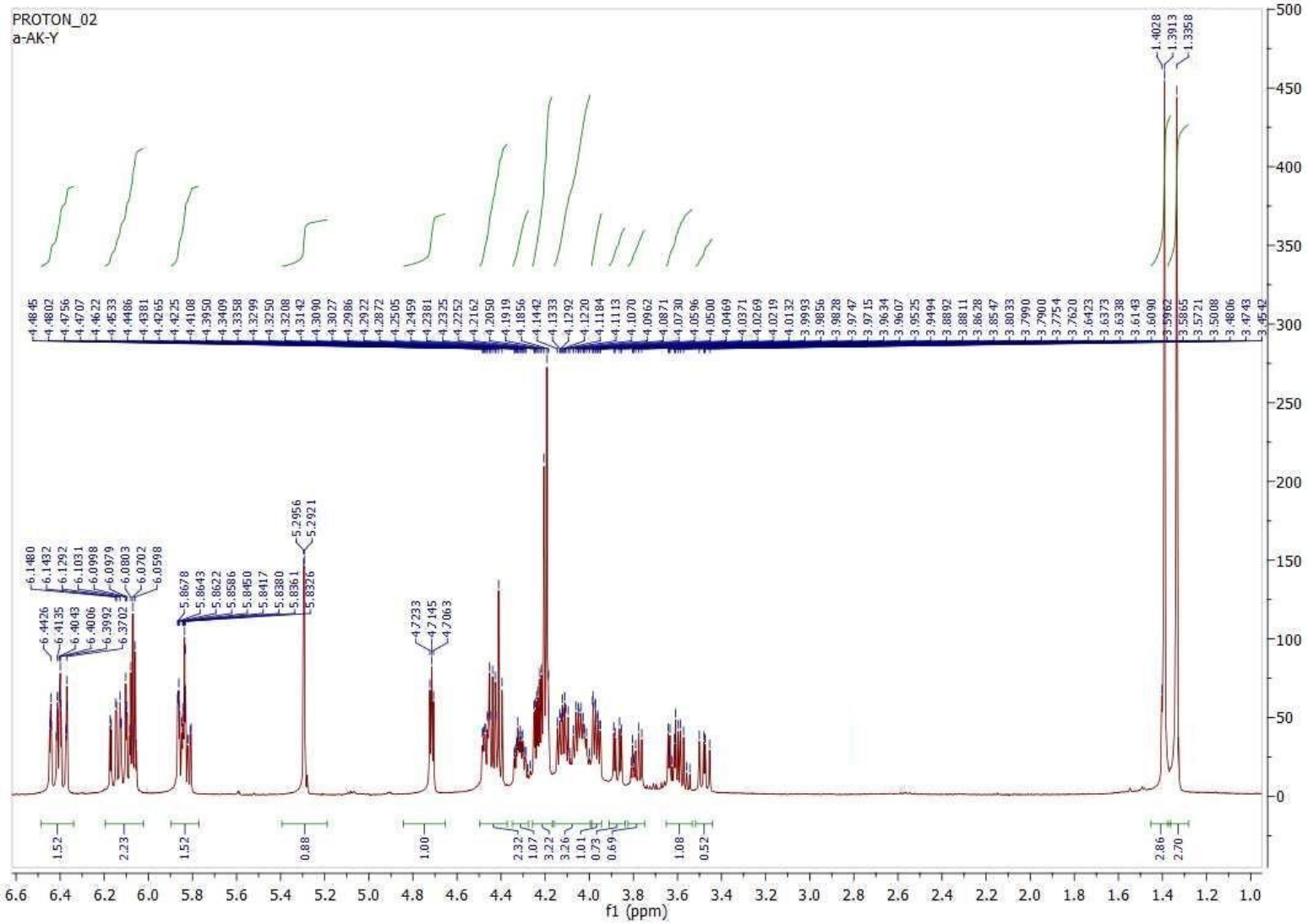
Appendix 7 [1] H-NMR spectrum of 3-*O*-(2-hydroxy-3-methacrylopropyl)-5,6-*O*-isopropylidene-1,2-*O*-(S)-trichloroethylidene-α-D-mannofuranose (compound **11**)



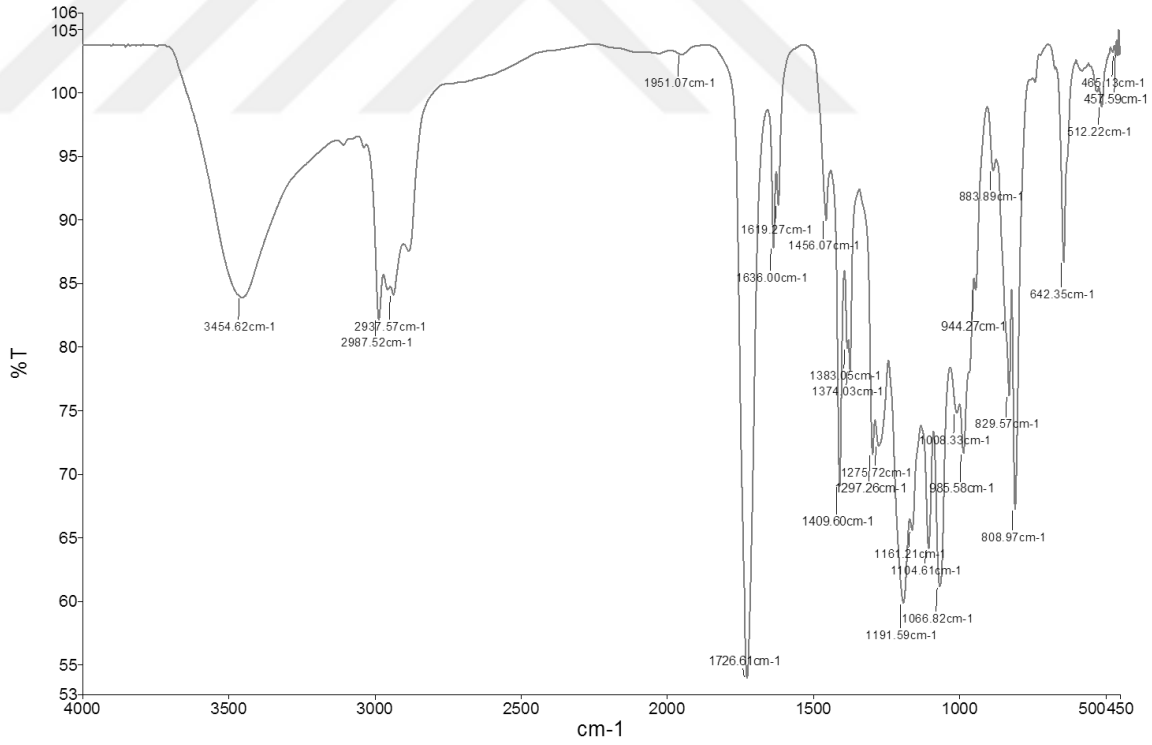
Appendix 8 FTIR spectrum of 3-*O*-(2-hydroxy-3-methacrylopropyl)-5,6-*O*-isopropylidene-1,2-*O*-(S)-trichloroethylidene-α-D-mannofuranose (compound **11**)



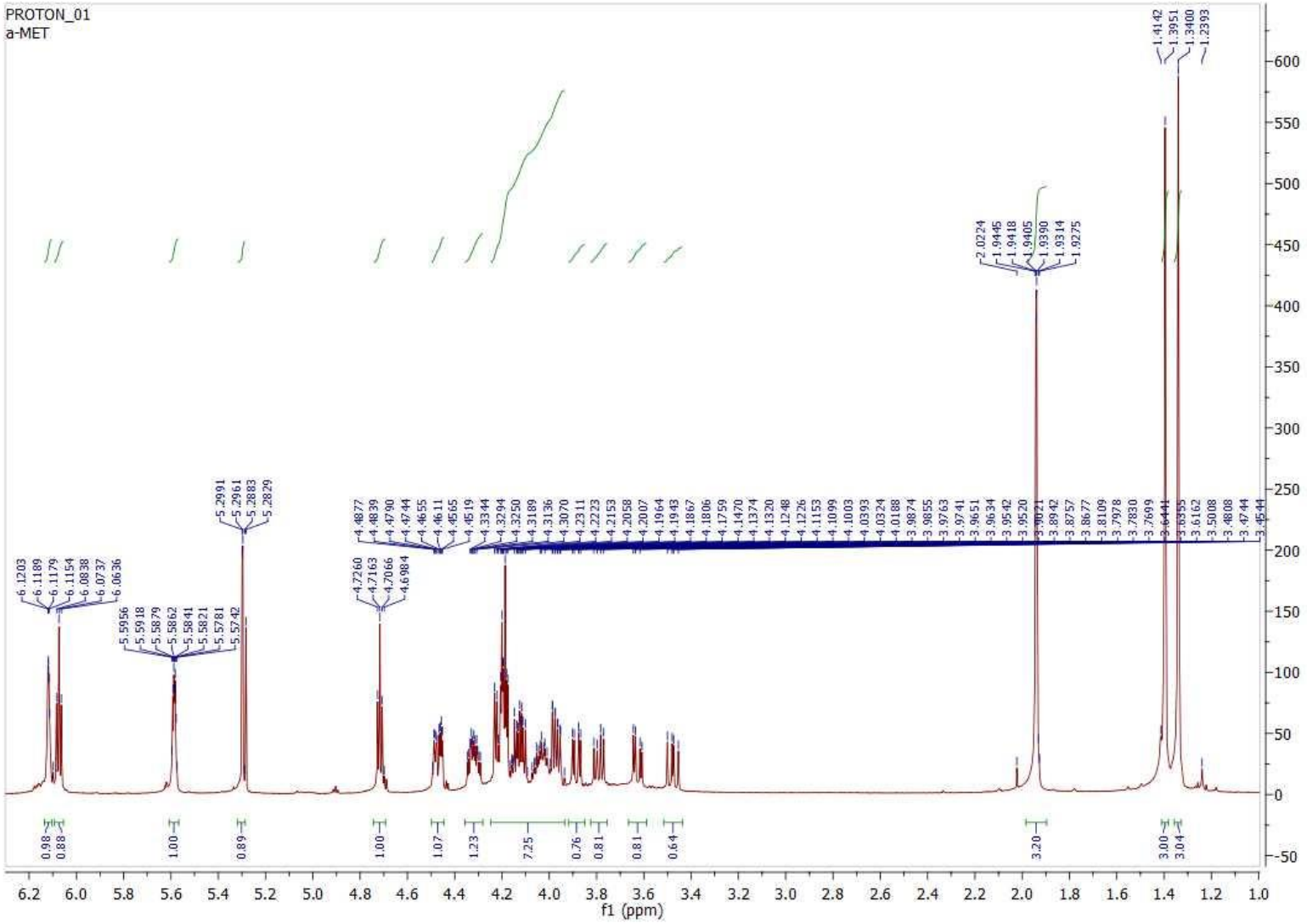
Appendix 9 ^{1}H-NMR spectrum of 3-*O*-(2-hydroxy-3-acrylopropyl)-5,6-*O*-isopropylidene-1,2-*O*-(S)-trichloroethylidene-α-D-glucofuranose (compound **15**)



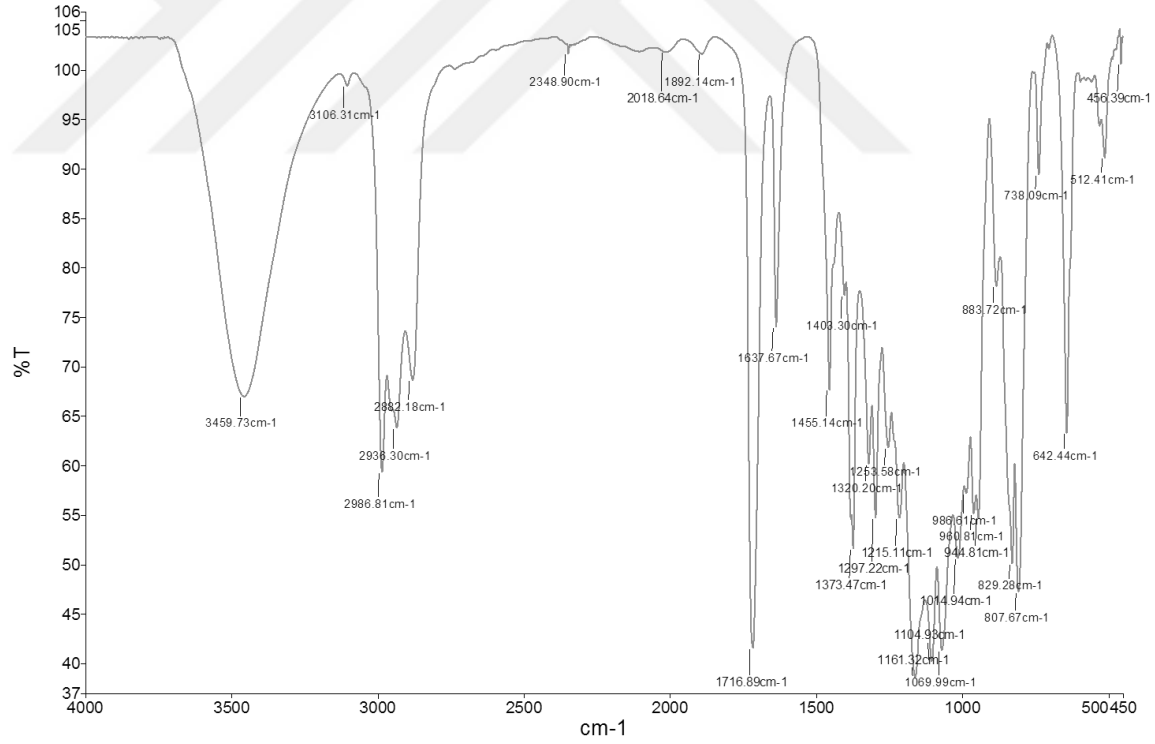
Appendix 10 FTIR spectrum of 3-*O*-(2-hydroxy-3-acrylopropyl)-5,6-*O*-isopropylidene-1,2-*O*-(S)-trichloroethylidene-α-D-glucofuranose (compound **15**)



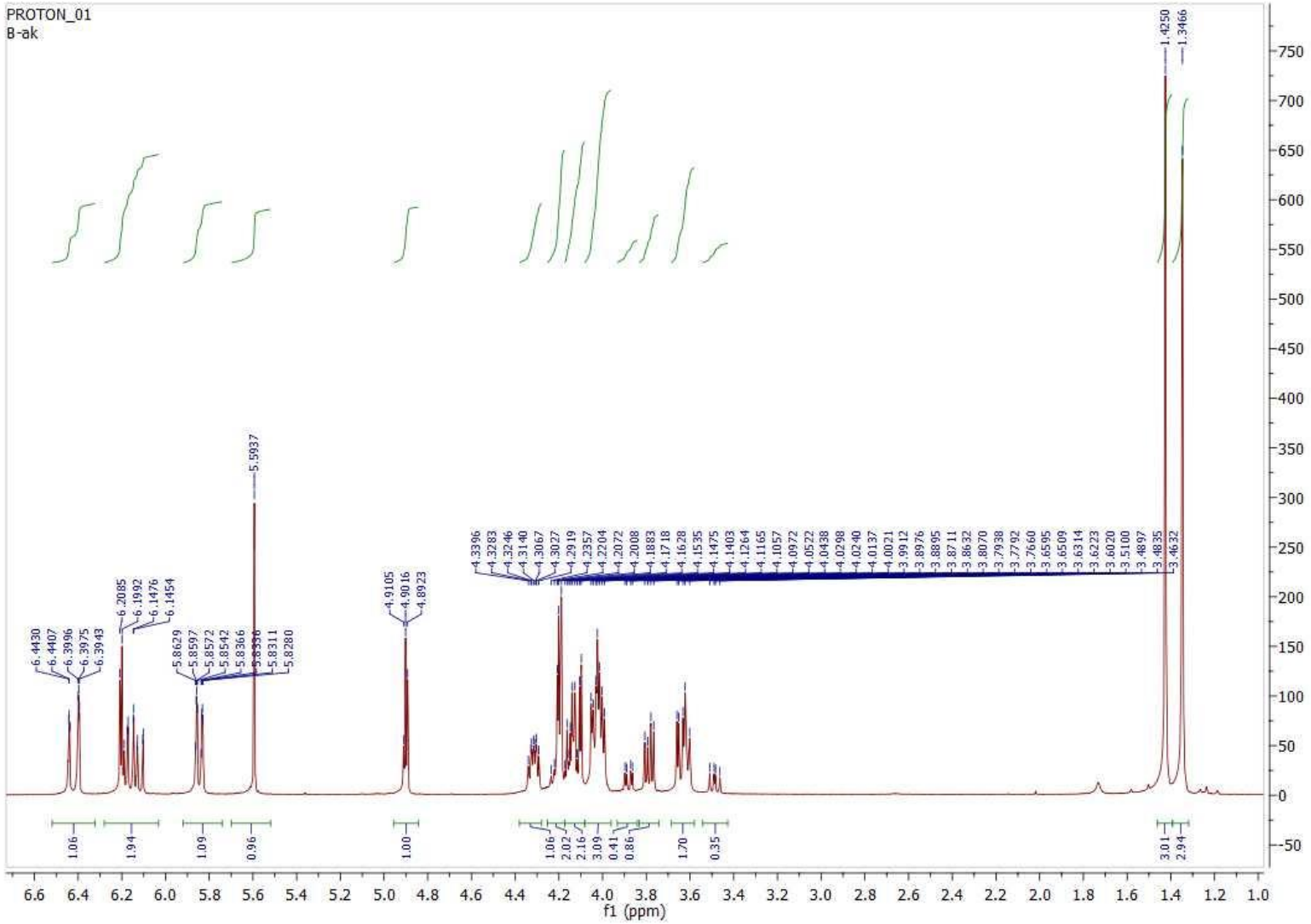
Appendix 11 [1] H-NMR spectrum of 3-*O*-(2-hydroxy-3-methacrylopropyl)-5,6-*O*-isopropylidene-1,2-*O*-(S)- trichloroethylidene-α-D-glucofuranose (compound **16**)



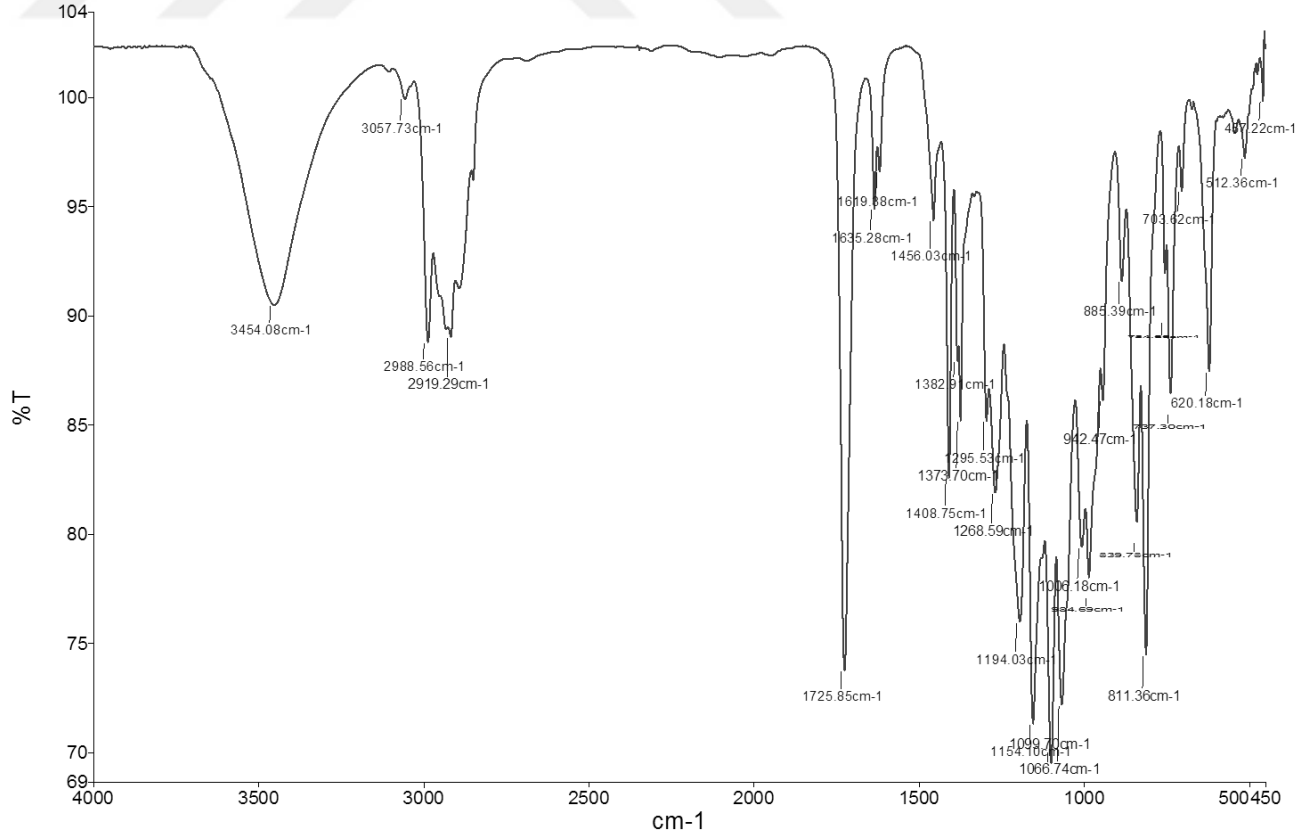
Appendix 12 FTIR spectrum 3-*O*-(2-hydroxy-3-methacrylopropyl)-5,6-*O*-isopropylidene-1,2-*O*-(S)- trichloroethylidene-α-D-glucofuranose (compound **16**)



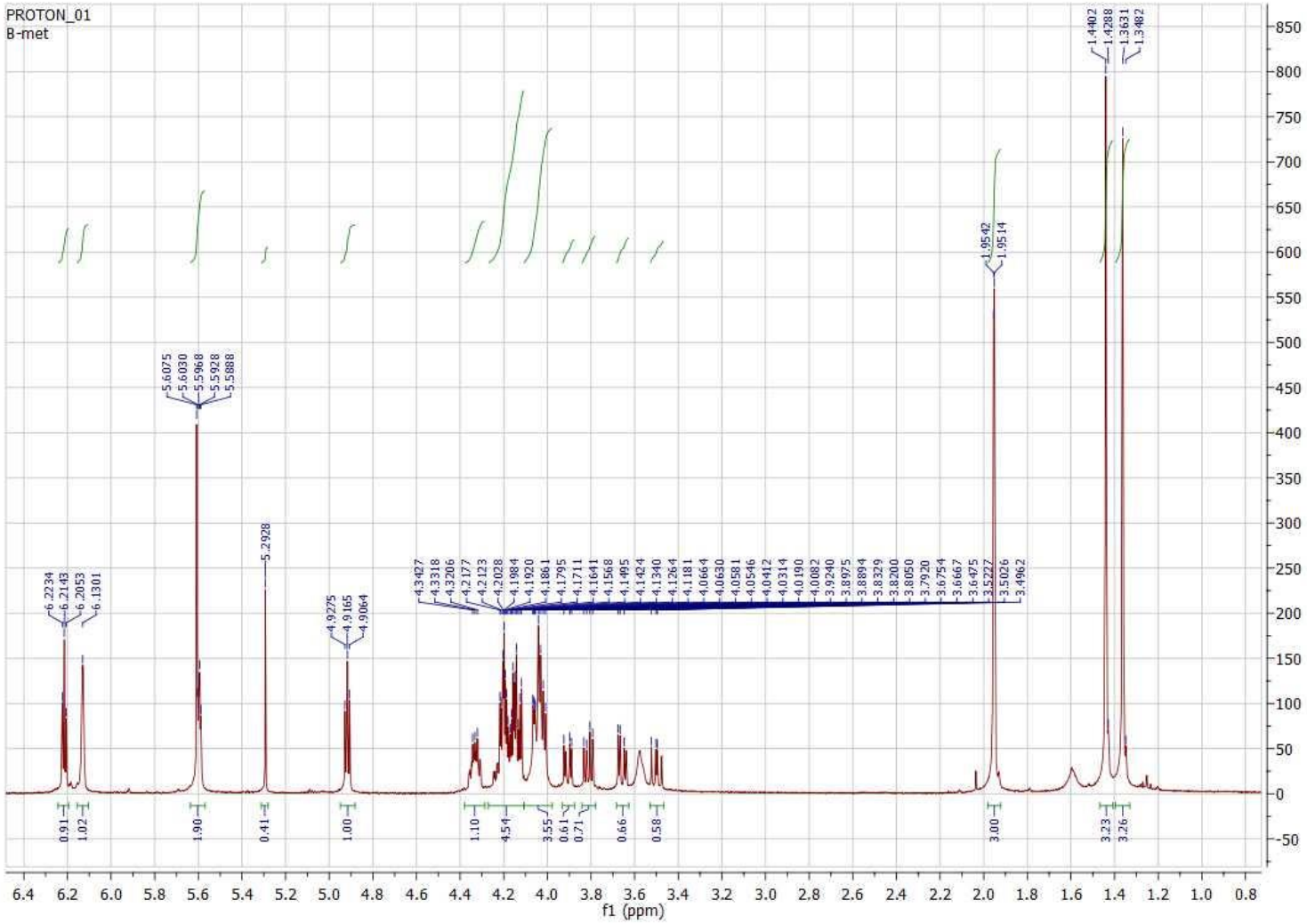
Appendix 13 ^{1}H-NMR spectrum of 3-*O*-(2-hydroxy-3-acrylopropyl)-5,6-*O*-isopropylidene-1,2-*O*-(S)-trichloroethylidene-β-D-glucofuranose (compound **19**)



Appendix 14 FTIR spectrum of 3-*O*-(2-hydroxy-3-acrylopropyl)-5,6-*O*-isopropylidene-1,2-*O*-(S)-trichloroethylidene-β-D-glucofuranose (compound **19**)



Appendix 15 ^{1}H-NMR spectrum of 3-*O*-(2-hydroxy-3-acryloyloxypropyl)-5,6-*O*-isopropylidene -1,2-*O*-(S)-trichloroethylidene-β-D-glucofuranose (compound **20**)



Appenix 16 FTIR spectrum of the 3-*O*-(2-hydroxy-3-acryloyloxypropyl)-5,6-*O*-isopropylidene -1,2-*O*-(S)-trichloroethylidene-β-D-glucofuranose (compound **20**)