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(MASTER OF SCIENCE THESIS)

NOVEL TRICYCLIC GLYCOSYL DONORS AND THEIR APPLICATIONS TO GLYCOSYLATION REACTIONS

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.... / .... / 2015

İmzası

Başak Nurçin AK

ÖZET

YENİ TRİSİKLİK GLİKOZİL DONÖRLER VE GLİKOZİLASYON REAKSİYONLARINA UYGULAMALARI

AK, Başak Nurçin

Yüksek Lisans Tezi, Kimya Anabilim Dalı
Tez Danışmanı: Doç. Dr. Yeşim GÜL SALMAN
Ekim 2015, 49 sayfa

Bu araştırmada D-mannoz, D-galaktoz ve D-glukoz başlangıç şekerleri olarak kullanıldı. Deneysel araştırmalar bu temel şekerlerin yeni glikozil donörleri ve glikozilasyon reaksiyonları uygulamaları üzerine oldu.

D-mannoz'un susuz kloralle tepkimesi sonucu 1,2-*O*-trikloroetiliden-α-D-mannofuranoz elde edildi. 1,2-*O*-trikloroetiliden-α-D-mannofuranoz ile 2,2-dimetoksipropan tepkimeye sokularak 5,6-*O*-izopropiliden-1,2-*O*-trikloroetiliden-α-D-mannofuranoz oluşturuldu. Bir sonraki basamakta 5,6-*O*-izopropiliden-1,2-*O*-trikloroetiliden-α-D-mannofuranoz potasyum tersiyer bütoksit ile tepkimesi sonucu trisiklik bir glikozil donör olan 1,2,3-*O*-dikloroetiliden-5,6-*O*-izopropiliden-α-D-mannofuranoz oluşturuldu. Bu trisiklik glikozil donöre lewis asidi yardımıyla metanol ve oktanol ile glikozilasyon reaksiyonu uygulaması yapıldı.

Benzer şekilde D-glukoz ve D-galaktozdan başlayarak sırasıyla 5,6-*O*-izopropiliden-1,2-*O*-trikloroetiliden-α-D-glukofuranoz ve 5,6-*O*-izopropiliden-1,2-*O*-trikloroetiliden-α-D-galaktofuranoz oluşturuldu. D-mannoz'un reaksiyon basamaklarına ek olarak, bu iki üründe trisiklik glikozil donörün oluşturulabilmesi için önce piridinyum dikromat ile yükseltgeme yapıldı. Bir sonraki basamakta sodyumborhidrür kullanılarak indirgeme yapılıp trisiklik glikozil donör oluşturmaya elverişli olan 1,2,3-*O*-dikloroetiliden-5,6-*O*-izopropiliden-α-D-allofuranoz ve 1,2,3-*O*-dikloroetiliden-5,6-*O*-izopropiliden-α-D-gulofuranoz elde edildi. Sonraki basamaklarda benzer şekilde glikozil donörler ve glikozilasyon reaksiyonları uygulamaları yapıldı.

Anahtar Kelimeler: Kloraloz, Trikloroetiliden asetal, Trisiklik glikozil donör, Glikozilasyon, Ortoester.

ABSTRACT

NOVEL TRICYCLIC GLYCOSYL DONORS AND THEIR APPLICATIONS TO GLYCOSYLATION REACTIONS

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In this research, D-mannose, D-galactose and D-glucose were used as starting sugars. These experimental researches were based upon glycosyl donors and glycosylation reactions of these basic sugars.

As the result of the reaction of D-mannose and anhydrous chloral, 1,2-*O*-trichloroethylidene-α-D-mannofuranose was obtained. 1,2-*O*-trichloroethylidene-α-D-mannofuranose was reacted with 2,2-dimethoxypropane to afford 5,6-*O*-isopropylidene-1,2-*O*-trichloroethylidene-α-D-mannofuranose. In a further step, as the result of the reaction between 5,6-*O*-isopropylidene-1,2-*O*-trichloroethylidene-α-D-mannofuranose with potassium tert-butoxide 1,2,3-*O*-dichloroethylidene-5,6-*O*-isopropylidene-α-D-mannofuranose which was a tricyclic glycosyl donor was obtained. This tricyclic glycosyl donor was applied to a glycosylation reaction with methanol and octanol in the presence of a Lewis acid.

Similarly, beginning with D-glucose and D-galactose, respectively 5,6-*O*-isopropylidene-1,2-*O*-trichloroethylidene-α-D-glucofuranose and 5,6-*O*-isopropylidene-1,2-*O*-trichloroethylidene-α-D-galactofuranose were prepared. In addition to D-mannose's sequence of reactions in order to obtain a tricyclic glycosyl donor, these two products were oxidized with pyridinium dichromate. In the next sequence, reduction with sodium borohydride afforded 1,2,3-*O*-dichloroethylidene-5,6-*O*-isopropropylidene-α-D-allofuranose and 1,2,3-*O*-dichloroethylidene-5,6-*O*-isopropropylidene-α-D-gulofuranose. These products were used to form a tricyclic glycosyl donor. In the next steps glycosyl donors and glycosylation reactions were applied using the same process.

Key Words: Chloralose, Trichloroethylidene acetals, Tricyclic glycosyl donor, Glycosylation, orthoesters.

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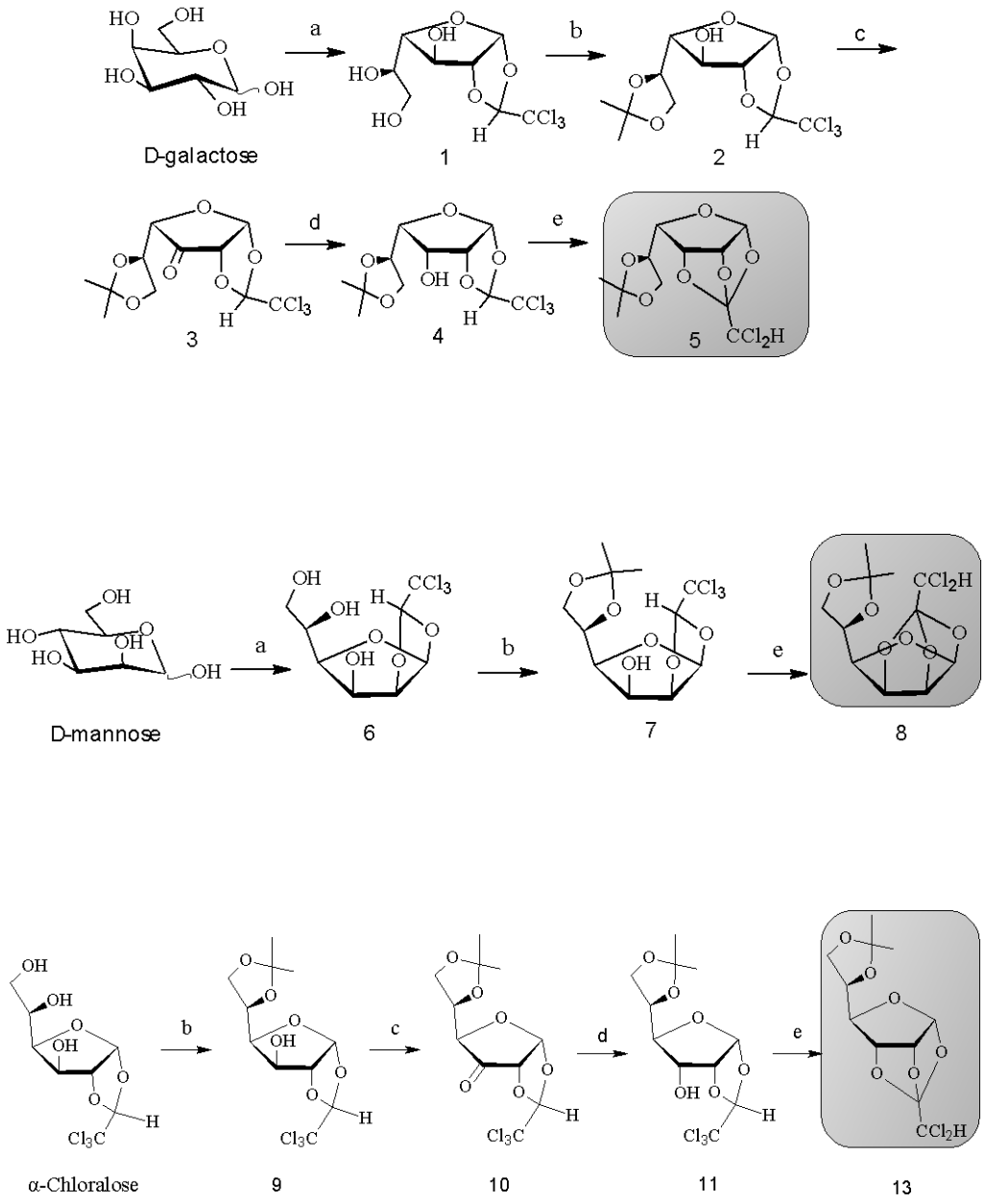


a) TCA, H_2SO_4, b) DMP, PTSA c) PDC d) $NaBH_4$ e) K^+t-BuO^-

ABBREVIATIONS

Abbreviation	Explanation
Ac	Acetyl
Ac_2O	Acetic anhydride
AcOH	Acetic acid
bp	Boiling point
BF_3Et_2O	Boron trifluoride diethyl etherate
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
equ	Equivalent
EtOH	Ethanol
Fig	Figure
g	Gram
IR	Infrared Spectroscopy

ABBREVIATIONS
(continued)

Abbreviation	Explanation
h	Hours
H_2SO_4	Sulfuric acid
K^+ t-BuO^-	Potassium tert-butoxide
m	Multiplet
mg	Milligram
mp	Melting point
Me	Methyl
MeOH	Methanol
mL	Milliliters
Min	Minute
mol	Mole
mmol	Millimole
$NaBH_4$	Sodium borohydride
NMR	Nuclear Magnetic Resonance Spectroscopy
PCC	Pyridinium Chlorochromate

ABBREVIATIONS (continued)

PTSA	*p*-Toluenesulfonic Acid
Pyr	Pyridine
s	Singlet
$SnCl_4$	Tin (IV) chloride
t	Triplet
TCA	Trichloroacetaldehyde
TLC	Thin Layer Chromatography
THF	Tetrahydrofurane
Tol	Toluene

1. INTRODUCTION

The most abundant molecules on earth are Carbohydrates. Although the information regarding these molecules and compounds is not complete, we already know that there are crucial aspects in the involvement of carbohydrates in the cure of bacterial and viral infections, development and growth of tumors and their metastasis, and deadly diseases that cause septic shock such as aids, cancer, septicemia and meningitis by damaging the cellular processes of aforementioned diseases. The medicinal potential of these glycostructures has already been acknowledged and proven through development of synthetic carbohydrate based vaccines and therapeutics. However, the involvement of carbohydrate in these disease progression mechanisms and the elucidation thereof could be further improved if there were a detailed and reliable knowledge of structure, conformation and properties of carbohydrate molecules. It has become critical for the field of glycosciences that a development of effective methods for isolating and synthesizing these complex carbohydrates is performed. Although improvements have emerged of glycoside and oligosaccharide synthesis, that are of great significance for this field of study, a variety of challenging glycosidic linkages cannot yet be accessed directly.

The majority of active carbohydrates that are of biological and therapeutical significance exist as polysaccharides (e.g. Cellulose, starch, chitin) or complex glycoconjugates (e.g. glycolipids, glycopeptides, glycoproteins) in which the monosaccharides units are joined using glycosidic bonds. (Demchenko, 2008)

Carbohydrate chemistry was regarded as a separate minor branch of organic chemistry until the middle of the 20th century despite the importance of carbohydrates in nutrition, food industry, biology and medicine, and as raw organic materials. The reason for this was; many organic chemists were doubtful regarding carbohydrates, because the sugars are not soluble in organic solvents, only in water.

After the middle of the 20th century this view has changed greatly. Renowned organic chemists have extended the range of applications for carbohydrates and in turn the carbohydrates are now being widely used as starting materials for the synthesis of many organic compounds, especially chiral compounds. The research and development of carbohydrate chemistry is rapidly

growing and has great potential due to the importance of carbohydrates in biochemistry and biology. (Stütz, 2001)

Some protein-carbohydrate interactions constitute the underlying aspects of some important processes such as; cell differentiation, cell adhesion, immune response, trafficking and tumor metastasis, which occur through glycoprotein, glycolipid, and polysaccharide entities at cell surfaces, lectins, proteins with carbohydrate-binding domains (Fig. 1.1). The most widely used anticoagulant heparin, which is used in antibiotics, and vaccines is a carbohydrate. To facilitate advancements in science and medicine the contributions of carbohydrates to cell biology should be uncovered. However, carbohydrates and their functions in biology have not been studied extensively due to the more complex structure of oligosaccharides and the lack of the general method or methods for the synthesis and analysis of these molecules. (Donk, 2006)

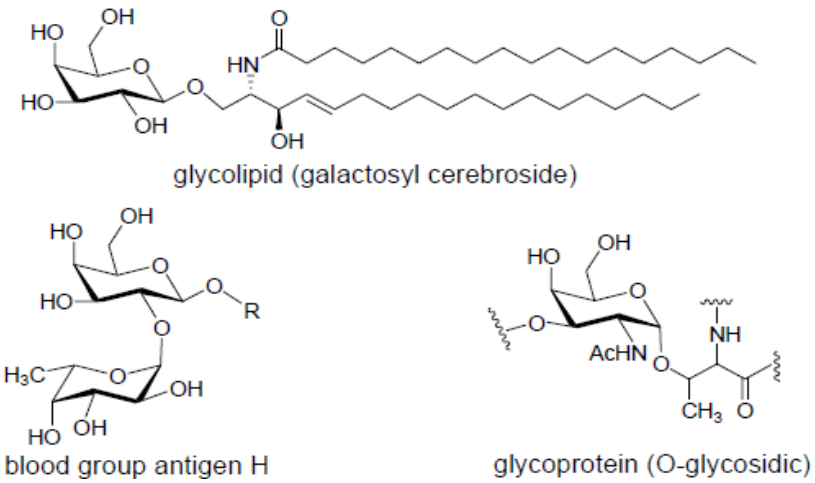


Figure 1.1. Natural carbohydrate containing entities.

Vaccines in the past were based on preparation of organisms or toxins isolated from different bacteria. After a better understanding of the structure and chemical composition of bacteria was obtained, vaccines are now being produced so that type specific protection against particular infections is possible.

A different way for producing desired polysaccharide antigens is chemical synthesis of said antigens. In addition to this, this approach should also be widened to include more than just bacterial infections, but also the more deadly diseases of the 20th century such as deadly cancers.

The globo-H tumor antigen (Fig.1.2) has been identified on the surface of both prostate and breast-cancer cells. (Stick, 2001)

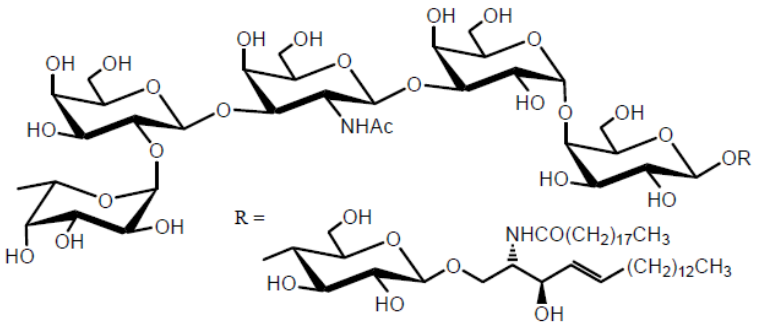


Figure1.2. The globo-H tumor antigen.

1.1 Carbohydrate-Based Antibiotics

After the discovery of streptomycin in 1944, aminoglycosides have been used widely in antibacterial drug treatment (Fig.1.3). The advances made in biochemistry and carbohydrate chemistry, coupled with technological advances in nucleic acid synthesis, biochemistry and structure analysis; an increase in aminoglycoside research among chemists and biochemists has occurred.

Although the first antibiotic was penicillin which is a fungal product that was isolated a few years earlier, the discovery of streptomycin was a landmark in antibiotic history because of its effectiveness in the therapy of tuberculosis; which is a disease that had terrorized humanity for centuries due to its high morbidity and mortality. It is the first noteworthy aminoglycoside that was identified and characterized as a useful antibiotic isolated from a bacterial source. (Arya, 2007)

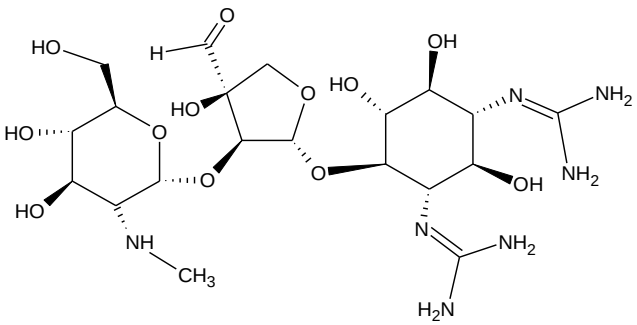


Figure 1.3. Streptomycin.

Antibiotics are known for being bacterial and fungal products that inhibit growth of microorganisms. But beside this definition a much broader definition has been proposed that defines antibiotics as chemical compounds derived from or produced by living organisms which in small concentrations are capable to inhibit vital processes of microorganisms. However this definition does not include the vast number of synthetic / semi-synthetic antibiotics. Antibiotics can be isolated from bacteria, yeast, molds, algae, lichens and plants.

Besides the antibiotics isolated from plants, there are even many more modified natural antibiotics that have been modified to increase activity, improve selectivity and decrease the side effects. Antibiotics, in chemistry, belong to many classes of organic compounds, but in this case we are only interested in antibiotics that are related to carbohydrates.

In a general way, there are three types of antibiotics that are carbohydrate related. Namely “antibiotics that are linked to cyclitols or amino cyclitols using a glycosidical link” (e.g. streptomycin, kanamycin, amikacin), “antibiotics consisting of oligosaccharides in which monosaccharides are linked both glycosidically and with one or more orthoester linkages” (e.g. orthosomycins), “antibiotics where the carbohydrates are glycosidically linked to non-carbohydrate parts of an antibiotic” (e.g. erythromycins, nystatin which are macrolide antibiotics). (Fig. 1.4, Fig. 1.5) (Miljkovic, 2009)

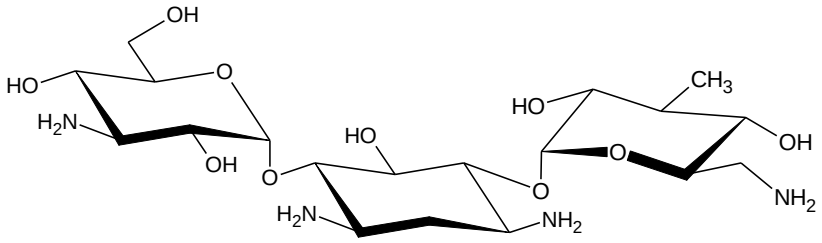


Figure 1.4. Kanamycin.

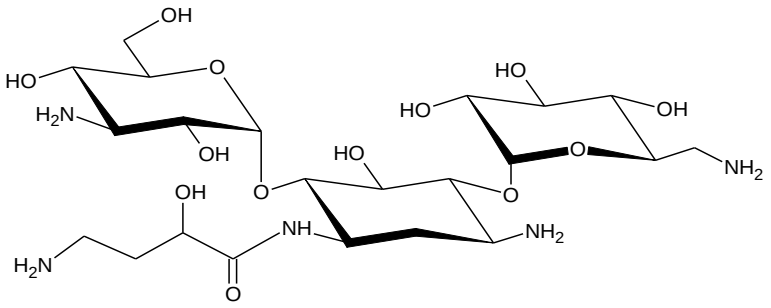


Figure 1.5. Amikacin.

1.2 Structure of Carbohydrates

The three most important components of living cells are carbohydrates, amino acids, and lipids To understand the biochemical behavior of carbohydrates one must understand their chemistry and reactivity by understanding how this chemistry and reactivity is controlled by their steric and electronic factors.

Anomeric effect, a very important electronics effect first discovered in studies of carbohydrates and later found to be of general importance in many other organic molecules, glycosidic bond hydrolysis, isomerization of free carbohydrates in aqueous solution, relative reactivity of hydroxyl groups in a carbohydrate molecule, nucleophilic displacement with or without change of configuration at the reacting carbon atom, addition of nucleophiles to glycopyranosiduloses, etc… are all to a various extend related to stereoelectronic effects that exist in carbohydrate structures.

Cyclic acetals, ketals and anhydrosugars are important intermediates in carbohydrate chemistry, being used as protecting hydroxyl groups that will not further partake in other chemical reactions and are being used as intermediates in synthetic carbohydrate chemistry because of the fact that they can serve as starting materials for the synthesis of many different carbohydrate derivatives (e.g. amino sugars, branched chain sugars, oligosaccharides). Of these carbohydrate derivatives, namely amino sugars, are important components of many biomolecules such as glycosaminoglycans, heparin but also many natural sugar based antibiotics.

There is great attention given to the mechanisms of various carbohydrate reactions, as well as the role of the stereoelectronic effects that they have in the reactivity of carbohydrates and the stereochemical outcomes of various carbohydrate reactions. (Miljkovic, 2009)

1.3 Glycosidation

Because of its great importance and the important role it plays in living organisms, carbohydrates and their chemistry consist of many reactions of which hydrolysis and glycosidic bonding are the most important ones . As important as amino acids are in the synthesis of peptides and proteins in living organisms, monosaccharides are important for the synthesis of oligosaccharide,

polysaccharides, and glycoconjugants (e.g. glycoproteins, glycosaminoglycans, glycolipids, proteoglycans). The synthesis of these oligo-, poly-saccharides, glycoconjugants requires formation of glycosidic bonds. But differing from the synthesis of peptides and proteins from amino acids, the synthesis of oligo-, poly-saccharides represents a much greater challenge for synthetic chemists due to the structural complexity of monosaccharides in contrast to amino acids. (Miljkovic, 2009)

Since the beginning of the twentieth century, where the first attempts were made, great progress has been made in the area of the chemical synthesis of glycosides. But the scientific world has witnessed a dramatic improvement of the methods used for glycosylation reactions only in the past 3 decades. Development of newer classes of glycosyl donor (e.g. glycosyl halides, thioglycosides, n-pentenyl glycosides, glycals, trichloroacetimidate method) has further allowed us to access novel types of glycosydic linkages but also led to discovery of convenient and rapid synthesis of oligosaccharides

1.4 Strategies in Glycoside Synthesis

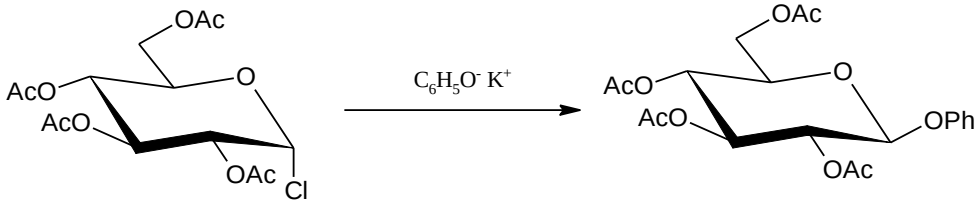
If you were to enquire about the best way of constructing a particular glycosidic linkage, the answer would depend on the person being asked:

David Gin	‘a hemiacetal’
Hans Paulsen	‘ use a glycosil halide’
Ray Lemieux	‘halide-catalaysis, of course’
K. C. Nicolaou and Teruaki Mukaiyama	‘ a glycosil fluoride’
Richard Schmidt	‘trichloroacetimidates’
Per Gareg or David Crich	‘a thioglycoside’
Dan Kahne	‘ a glycosyl sulfoxide’
Sam Danishefsky	‘glycal assembly’
Bert Frase-Reid	‘NPG activation’

All offer good advice; in fact, there is no one method of glycosidation that is general an reliable enough to guarantee success (Stick and Williams, 2009).

1.5 Glycoside Synthesis

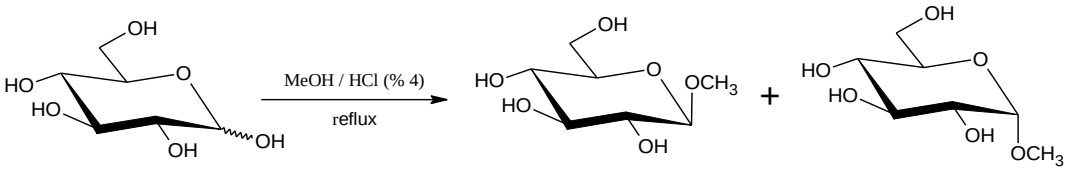
The first synthesis of an *O*-glycoside was carried out by Michael (Michael, 1879; Michael, 1885; Michael, 1879) by reacting the 2,3,4,6-tetra-*O*-acetyl-α-D-glucopyranosyl chloride with potassium phenoxide (Scheme 1.1)



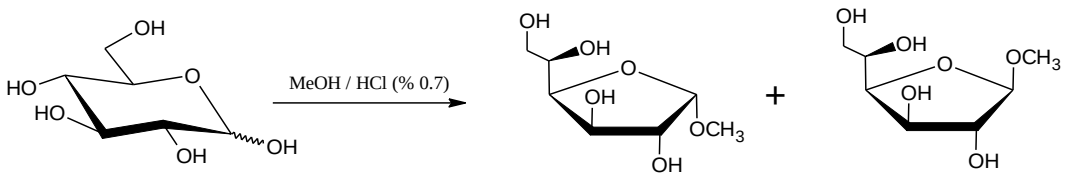
Scheme 1.1. The first synthesis of an *O*-glycoside by Michael.

1.5.1 Fischer glycosidation

In 1883 E. Fischer (Fischer, 1893; Fischer, 1895) developed a synthesis of glycosides of lower alcohols by refluxing a monosaccharide with an alcohol in the presence of an anhydrous mineral acid. If the concentration of mineral acid is several percent,α- and β-glycopyranosides are obtained(scheme 1.2). However, if the concentration of mineral acid is low and if the reaction is conducted at room temperature, the reaction of D-glucose with anhydrous methanol affords a mixture of methyl α- and β-glucofuranosides in good yield (Scheme1.3).



Scheme 1.2. Fischer's method for pyranosidic *O*-glycoside synthesis.

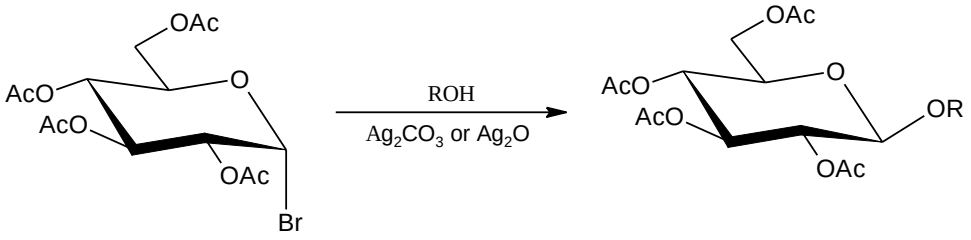


Scheme 1.3. Fischer's method for furanosidic *O*-glycoside synthesis.

1.5.2 Königs-Knorr synthesis

In 1901 Königs and Knorr (Königs and Knorr, 1901) developed a new method for the synthesis of glycosides which was immediately recognized as the more general and useful preparative method than Fisher method and which is still used today. The Königs-Knorr method consist of reacting a fully acetylated glycosyl halide with an alcohol or with a hydroxyl group of another sugar (dissolved in a dry inert solvent) in the presence of silver carbonate or silver oxide as promoter and acid acceptor (Scheme 1.4)

O-Acylglycosyl halides (excluding fluorides) react with alcohols also directly (in absence of silver carbonate or silver oxide) to yield glycosides.

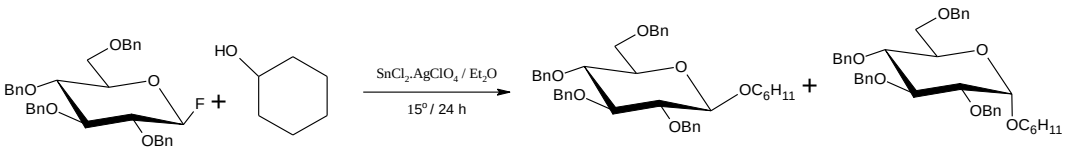


Scheme 1.4. Königs-Knorr Synthesis.

1.5.3 Glycosyl fluorides in glycosydation

Glycosyl fluorides have now been widely and effectively used for *O*-glycosidation reaction, because of their much higher thermal and chemical stability as compared to the low stability of other glycosyl halides, such as glycosyl chlorides and bromides. Thus, for example, the glycosyl fluorides can be purified by distillation and even by column chromatogaphy on silica gel. There are several good reviews on glycosyl fluorides as glycosyl donors. (Toshima, 2000; Shimizu et al, 1998)

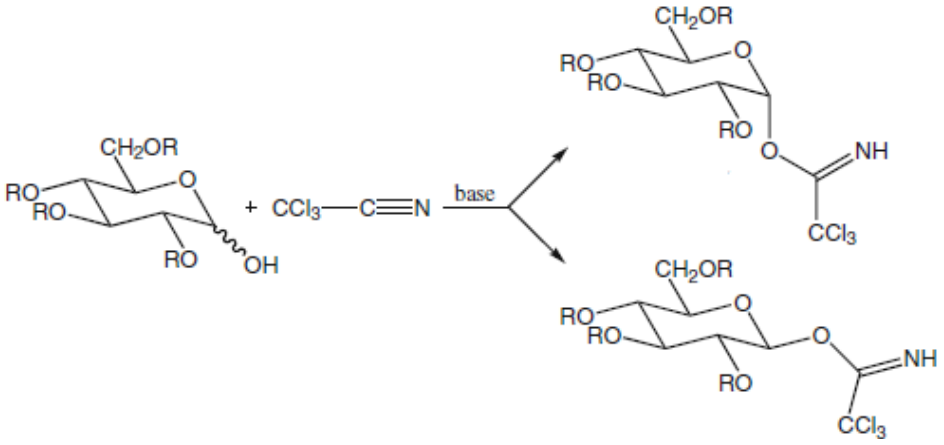
The use of glycosyl fluorides as glycosyl donors war firs developed by Mukaiyama et al (Mukaiyama et al, 1981). Thus 2,3,4,6-tetra-*O*-benzyl-β-D-glycopyranosyfluoride was reacted with cyclohexanol in ether, at -15^{o}C, in the presence 4Å molecular sieves (to maintain the anhydrous conditions) and silver perchlorate-stannous chloride as fluorophilic activators. A mixture of anomeric cyclohexyl 2,3,4,6-tetra-*O*-benzyl-α- and β-D-glucopyranosides was obtained with 88% yield in which the α-anomer predominated in almost 5:1 ratio (Scheme 1.5)



Scheme 1.5 Using of glycosyl fluorides in glycosydation by Mukaiyama.

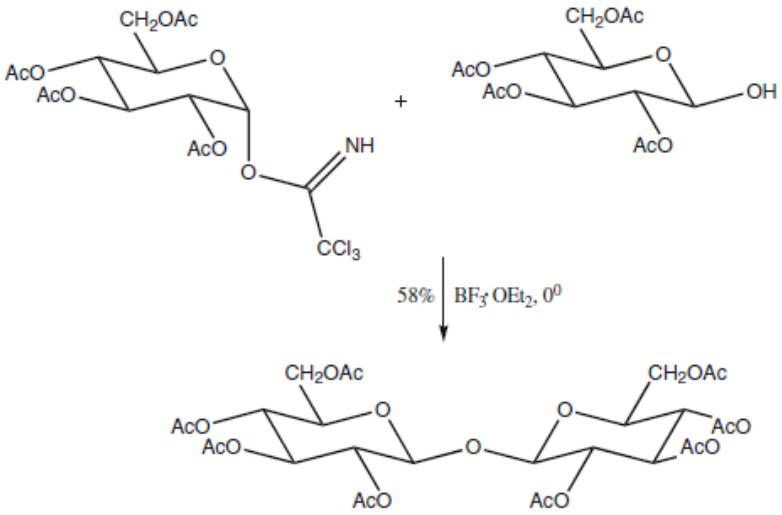
1.5.4 Trichloroacetimidate method of glycosidation

Electron-deficient nitriles, such as trichloro- or trifluoroacetonitriles (scheme 1.6) are known to undergo direct and reversible base-catalyzed addition of alcohols giving *O*-alkyltrichloroacetimidates. (Schmidt, 1986; Schmidt, 1987; Schmidt, 1989; Schmidt and Michel, 1984)



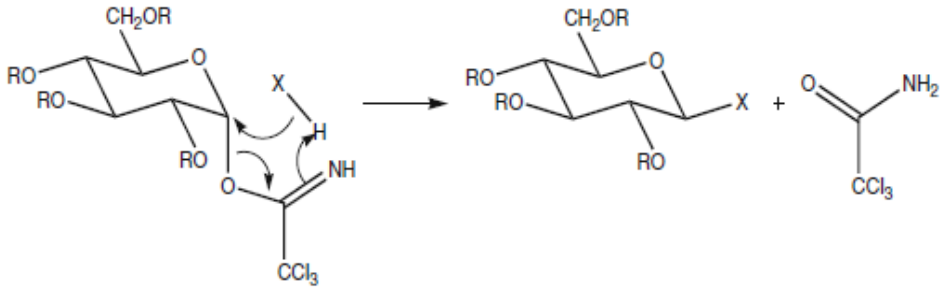
Scheme 1.6. Synthesis of *O*-alkyltrichloroacetimidates.

The reaction of glycosyl acceptors (alcohols or sugars having one unprotected hydroxyl group) with *O*-glycosyl trichloroacetimidate donor requires the presence of an acid catalyst (Scheme 1.7)



Scheme 1.7. Trichloroacetimidate method of glycosidation by Schmidt.

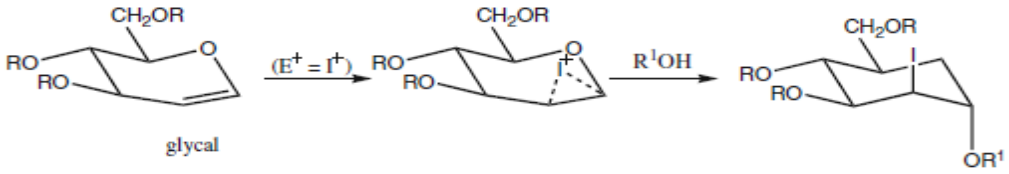
For the reaction of alcohols (or other monosaccharides) with *O*-glycosyl trichloroacetimidates the Brønsted acids are not suitable. The glycosyl trichloroacetimidate reacts readily at room temperature with Brønsted acids to give in high yields the corresponding glycosyl derivatives of anions of Brønsted acid (Scheme 1.8) (Miljkovic, 2009).



Scheme 1.8. Using of mineral acid in trichloroacetimidate method.

1.5.5 Glycals as glycosyl donors

Utilizing glycals as glycosyl donors in disaccharide by halonium-catalyzed coupling to suitably protected acceptors had been pioneered by Lemieux (Lemieux and Levine, 1964; Lemieux and Fraser-Reid, 1965) and Tiem (Tiem and Karl, 1978; Tiem and Ossowski, 1984; Tiem and Klaffke, 1989). The Lemieux-Thiem methods has thus far found its most useful application in the synthesis of 2-deoxyglycosides (Tiem and Karl, 1978; Tiem and Ossowski, 1984; Tiem and Klaffke, 1989; Lemieux and Morgan, 1965)



Scheme 1.9 Using of glycals as glycosyl donors

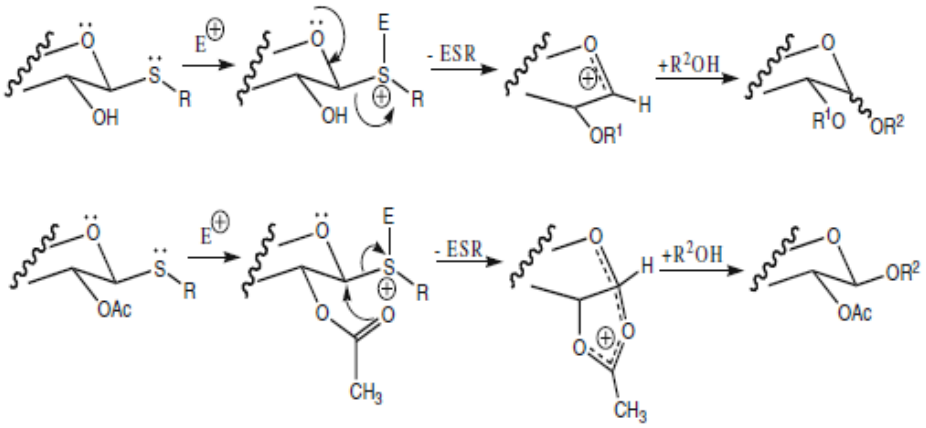
Iodoglycosylation is carried out with glycal serving as a glycosyl donor. The glycal linkage is attacked by an "I^+ equivalent" reagent, such as *N*-iodosuccinimide and the intermediate obtained is attacked by a nonglycal acceptor that is also present in the solution; the anomeric carbon of glycosyl acceptor has to be appropriately protected. The stereochemistry of glycosylation is controlled by *trans*-diaxial addition and the α-linked disaccharide is obtained (Scheme 1.9).

1.5.6 Thioglycosides as glycoside donors

Ethyl 1-thio-α and β-glucopyranosides, on treatment with bromine and silver carbonate in methanol, gave methyl β - and α -D-glucopyranosides, respectively, in high yield apparently by a way bromosulfonium ion intermediate (Weygand and Ziemmann, 1962).

This pioneering study attracted widespread attention for 1-thioglycosides as glycosyl donors because 1-thioglycosides are stable compounds that are readily available, the 1-sulfur atom could be activated with a wide range of electrophilic activators, and the glycosylation reaction seems to proceed with a high anomeric stereoselectivity.

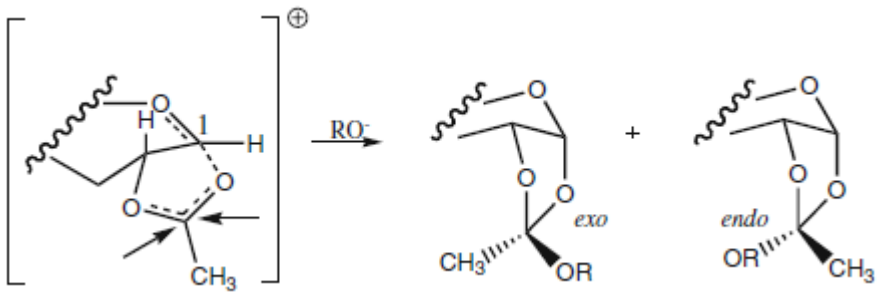
If the C2 carbon is protected with a nonparticipating substituent (e.g., benzyl) a mixture of anomers is obtained, whereas if the C2 substituent is a participating one (e.g., acetate) the glycoside obtained is 1,2-*trans* (β) (Scheme 1.10) (Miljkovic, 2009).



Scheme 1.10. Participating and nonparticipating substituent effect in glycosylation.

1.5.7 Orthoester method of glycosidation

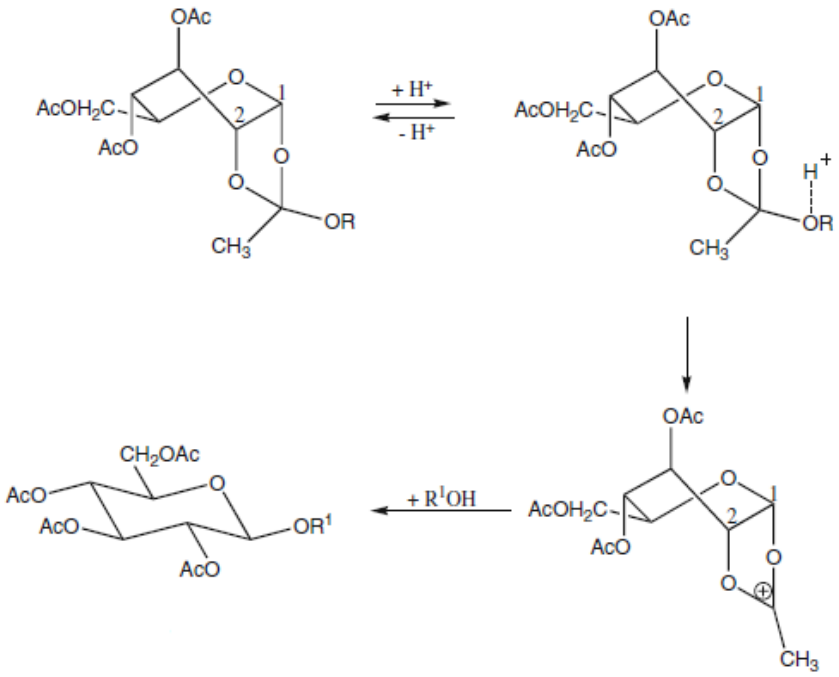
It has already been mentioned that the attack of a nucleophile on oxocarbonium ion obtain as a result of neighboring group participation of the C2 acetoxy group in the solvolysis of the glycosyl halides does not always have to the place at the C1 carbon. A nucleophile can also attack the carbonyl carbon of the C2 acetate giving one or both diastereomeric orthoesters (Scheme 1.11). Hence the orthoesters formation is closely related to the Königs-Knorr reaction, because by a slight change in experimental conditions the formation of orthoesters can be made to become the major pathway of Königs-Knorr reaction.



Scheme 1.11. Diastereomeric orthoesters measure

The orthoester method produces stereoselectivity 1,2-*trans*-glycosides and it is generally applicable to the synthesis of both pyranosides an furanosides of pentoses and hexoses.

The protonation of the exocyclic oxygen of orthoester followed by elimination of alcohol will result in the formation of 1,2-cyclic acetoxonium ion, which can be attacked by an alcohol (the same part of the orthoester, or another alcohol) either at the carbonyl carbon of the acetyl group or at the C_1 carbon. In the first case, the same or the isomeric orthoester will be obtained (if the attacking alcohol is the one that was part of the orthoester). In the second case if the attack takes place at the C_1 carbon, the corresponding β-glycoside will be obtained in which at the aglycon can be either the alcohol that was part of the orthoester or the new one.(Scheme 1.12) (Miljkovic, 2009).

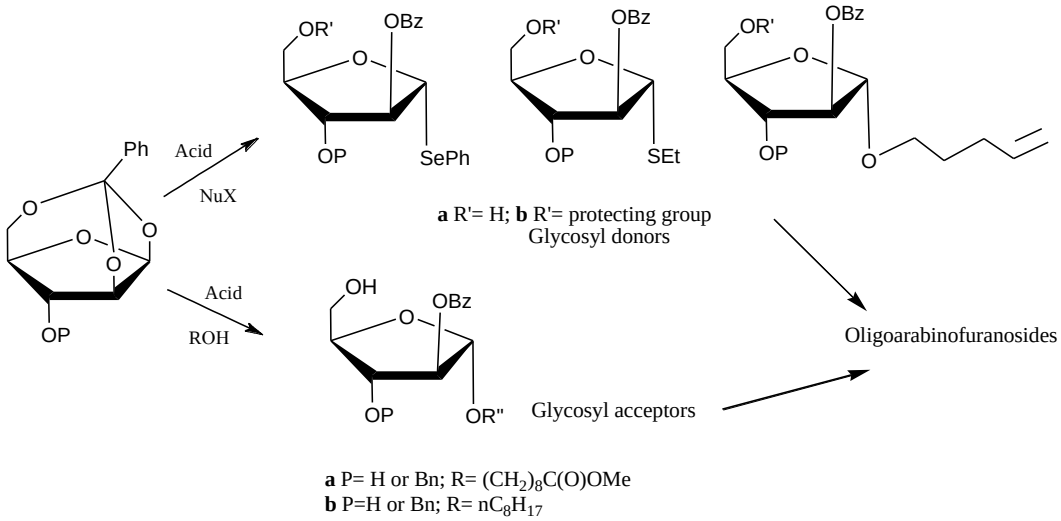


Scheme 1.12. 1,2-cyclic acetoxonium ion, which can be attacked by an alcohol

1.5.7.1 Internal orthoesters

Furanosides are commonly found in nature with many biologically significant roles, e.g. in the polysaccharides of bacteria, parasites, plant and fungi. An arabino galactan (a polymer of arabinofuranose and galactofuranos) and a lipoarabinomannan (a polymer of arabinofuranose and mannopyranose) major components of the mycobacterial cell wall, are targets for the treatment of diseases such as tuberculosis. It has been necessary to develop methods for the synthesis of furanosides, both to provide fragment oligosaccharides an to a develop inhibitors that interfere with assembly of the oligosaccharide.

Prandi and coworkers have described the use of D- arabinose 1,2,5-orthoesters, in a convergent-divergent strategy to oligoarabinofuranosides. Acid-catalyzed opening of orthoesters in the presence of selenophenol, thioethanol, 4-pentanol, followed by the protection of their 6-OH, gave raise to the corresponding selenyl-, thio- and *n*-pentnyl- glycosyl donors, whereas ring opening in the presence of alcohols furnished gycosyl acceptors. Protecting-group manipulation and glycosyl assembly of these building blocks thus permitted the synthesis of oligoarabinofuranosides. (scheme 1.13) (Demchenko, 2008)



Scheme 1.13. Prandi's strategy to oligoarabinofuranosides from internal orthoesters.

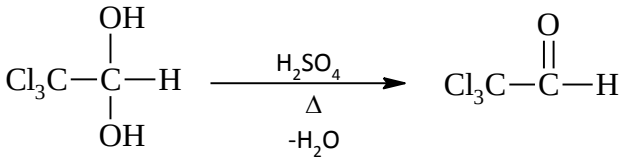
2. MATERIAL AND METHODS

2.1 General Technique

- Melting points were recorded with Gallenkamp electrothermal melting point apparatus in capillary.
- T.l.c and column chromatography were performed on precoated aluminum plates (Merck 5554) and silica gel G-60 (Merck 7734 and Merck 9385), respectively. The spots of t.l.c were developed by 20 % aqueous sulfuric acid and by heating the plates above 120 ^{o}C.
- Starting compound and reagents were obtained from Merck and Aldrich. Solvents like toluene, dichloromethane, methanol, ethylacetate, and hexane were obtained from industrial grade solvents which were further purified by distillation.
- Solvents were dried with molecular sieve (type 4Å and 3Å) and metallic sodium. Anhydrous sodium sulfate was also used for drying solvent especially after extraction of the product from water.
- All solvents were evaporated under reduced pressure with 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 carried out on a Rudolph Autopol-1 Automatic Polarimeter.

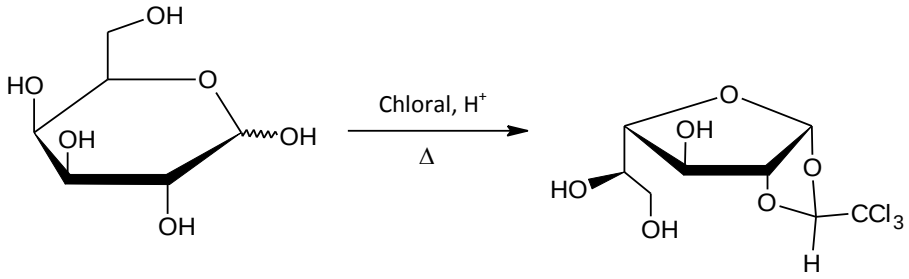
2.2 Experiments

2.2.1 Preparation of anhydrous chloral



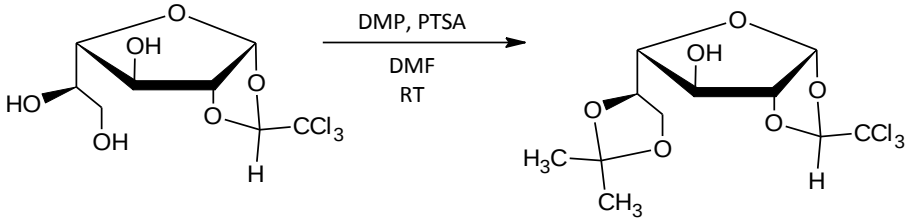
Concentrated H_2SO_4 (180 mL, d=1.84 g/cm^3) was added on chloral hydrate (320 g, 1.9 mol) and refluxed for about 2 hours at max 98 ^oC. Distillation gave pure anhydrous chloral (171 mL, d=1.512 g/cm^3) with 91% yield.

2.2.2 1,2-*O*-(S)-Trichloroethylidene-α-D-galactofuranose (1)



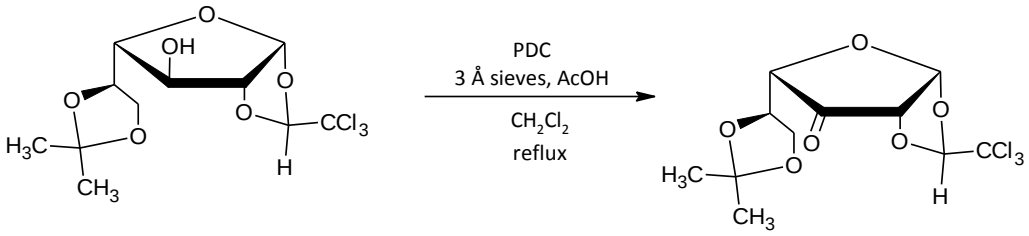
D-galactose (50 g, 0.28 mol) was added on anhydrous chloral (170 mL, d=1.512 g/cm^3, 259 g) under continuous stirring. Conc. Sulfuric acid (1 mL, d=1.84 g/cm^3) was added and the mixture was refluxed for 3 hours. Excess chloral was evaporated and the black coloured syrup was obtained. 350 mL methanol was added in order to dissolve all solidified material. Then, the solution was heated and decolorized with activated charcoal. The product was obtained as colourless crystals from methanol solution (62 g, 72%), mp: 205-207 ^oC, $[\alpha]_D^{22}$: -30^o (c: 0.5 in MeOH).

2.2.3 5,6-*O*-Isopropylidene-1,2-*O*-(S)-trichloroethylidene-α-D-galactofuranose (2)



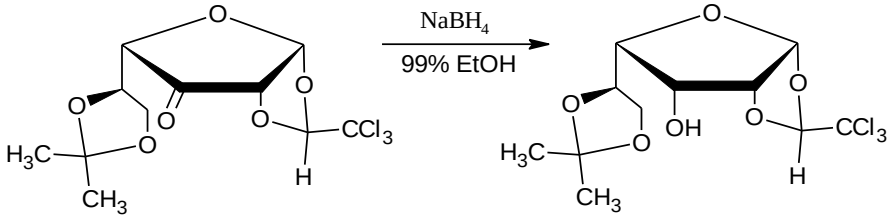
A solution of **1** (10 g, 0.032 mol) in dried DMF (50 mL) were added DMP (10 mL, d=0.85 g/cm^3, 8.5 g) and anhydrous PTSA (10 mg, 0.058 mmol). The mixture was stirring at room temperature for about 24 hours. After completion of reaction the mixture was neutralized with saturated $NaHCO_3$, then, DMF was evaporated. The product was obtained as colourless crystal from cold methanol solution (9.1 g, 81%), mp: 216-219^{o}C, $[\alpha]_D^{22}$: +17.0^o (c: 5.0 in pyr).

2.2.4 5,6-*O*-Isopropylidene-1,2-*O*-(S)-trichloroethylidene-α-D-galactofuranose-3-ulose (3)



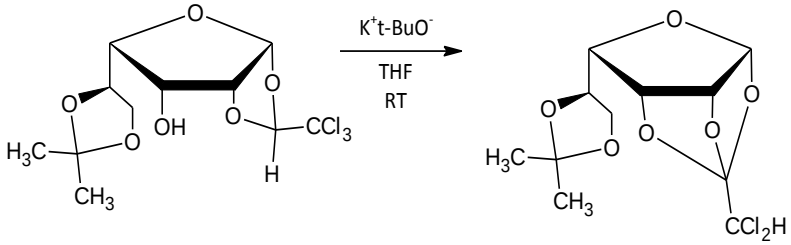
A solution of **2** (5 g, 14.3 mmol) in CH_2Cl_2 (50 mL) was treated with 3 Å powdered molecular sieves (1 g) and pyridinium dichromate (8.1 g, 21.5 mmol) followed by the addition of AcOH (0.5 mL). The mixture was heated and stirred for 3 hours. After completion of reaction the solution was evaporated to dark oil. A solution of the oil in diethyl ether (250 mL) was filtered through silica gel (100 g, 0.063–0.200 mm mesh) and the eluent was evaporated to give ketone (4.9 g, 13.7 mmol, 93%) as a white solid mp: 224-228 ^oC, $[\alpha]_D^{22}$: + 27.8^o (c: 2.0 in DCM).

2.2.5 5,6-*O*-Isopropylidene-1,2-*O*-(S)-trichloroethylidene-α-D-gulofuranose (4)



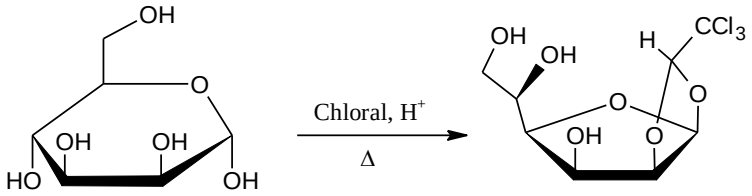
A solution of **3** (3 g, 8.6 mmol) in anhydrous ethanol (100 mL) was cooled to 0^{o}C. Sodium borohydride (0.13 g, 3.43 mmol) was added, and the mixture was stirred at 0 ^{o}C for 10 min. After 10 min the reaction was stirred for 45 min at room temperature. The organic layer was removed, and the aqueous layer was extracted with CH_2Cl_2 (3 x 50 mL). The combined organic layers were dried (over anhydrous Na_2SO_4) and concentrated to give (2.73 g, 7.8 mmol, 91%) of the secondary alcohol as a white solid, mp: 211-215 ^{o}C, $[\alpha]_D^{22}$: - 30.4^o (c: 1.37 in $CHCl_3$).

2.2.6 5,6-*O*-Isopropylidene-1,2,3-*O*-orthodichloroethylidene-α-D-gulofuranose (5)



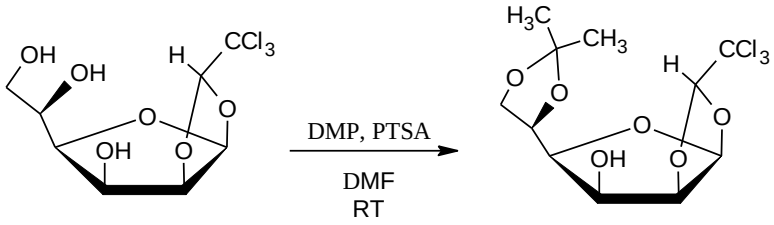
A solution of **4** (2 g, 5.72 mmol) in THF (30 mL) was added potassium tert-butoxide (1.97 g, 17.6 mmol) and stirred for 2 hours. After completion of reaction the solution was evaporated and the aqueous layer was extracted with CH_2Cl_2 (3 x 25 mL). The DCM solution was dried over anhydrous Na_2SO_4. TLC (Tol/MeOH; 9:1) revealed the presence of two carbohydrate components with a strong spot corresponding to our product. Then, the solution was evaporated under reducing pressure. The crude syrupy product was purified by column chromatography with CH_2Cl_2/MeOH as eluting system giving product as solid (1.51 g, 4.82 mmol, 84%), mp:134-136 ^oC, $[\alpha]_D^{22}$: -14.6^o (c: 0.011 in DCM).

2.2.7 1,2-*O*-(R)-Trichloroethylidene-β-D-mannofuranose (6)



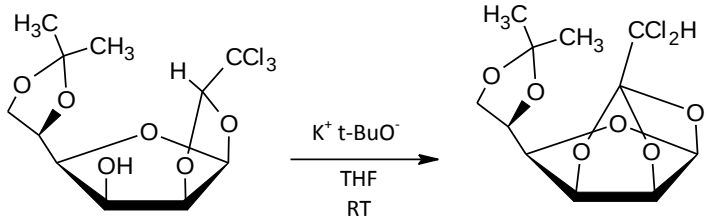
D-mannose (32 g, 0.178 mol) was added on anhydrous chloral (150 mL, d=1.512 g/cm^3, 226.8 g) under continuous stirring. Conc. sulfuric acid (1 mL, d=1.84 g/cm^3) was added and the mixture was refluxed for 3 hours. Excess chloral was evaporated and the black coloured syrup was obtained. 250 mL methanol was added in order to dissolve all solidified material. Then, the solution was heated and decolorized with activated charcoal. The product was obtained as colourless crystals from methanol solution (21.1 g, 39%), mp: 205-207^{o}C, $[\alpha]_D^{22}$: -15.0^o (c: 0.4 in MeOH).

2.2.8 5,6-*O*-Isopropylidene-1,2-*O*-trichloroethylidene-β-D-mannofuranose (7)



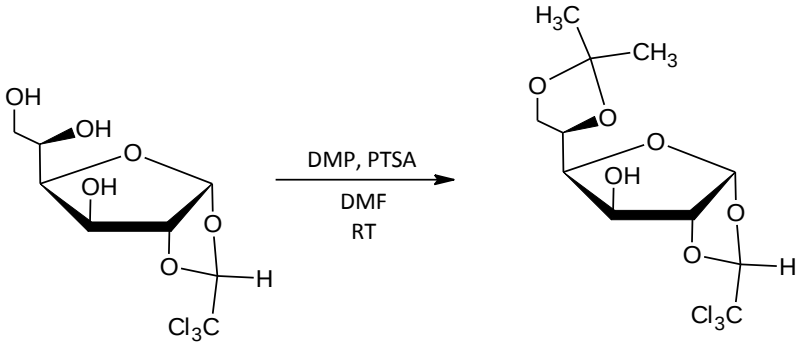
A solution of **6** (10 g, 0.032 mol) in dried DMF (50 mL) were added DMP (10 mL, d=0.85 g/cm^3, 8.5 g) and anhydrous PTSA (10 mg, 0.058 mmol). The mixture was stirring at room temperature for about 24 hours. After completion of reaction the mixture was neutralized with saturated $NaHCO_3$, then, DMF was evaporated. The product **7** was obtained as colourless crystal from cold methanol solution (8.2 g, 72%), mp: 169-171^{o}C, $[\alpha]_D^{22}$: - 34.0^o (c: 0.25 in $CHCl_3$).

2.2.9 5,6-*O*-Isopropylidene-1,2,3-*O*-orthodichloroethylidene-β-D-mannofuranose (8)



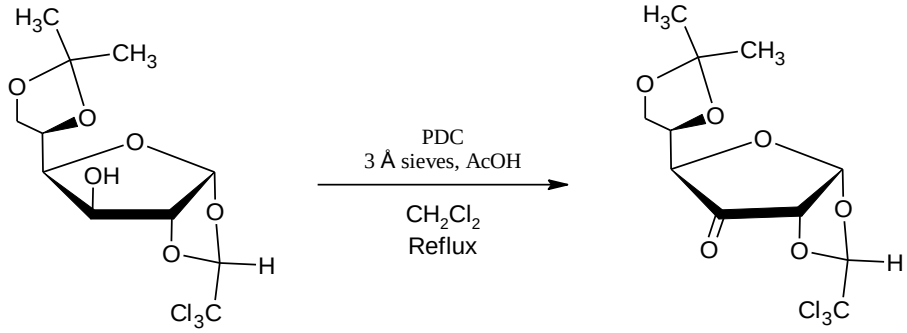
A solution of **7**(4 g, 11.44 mmol) in THF (50 mL) was added potassium tert-butoxide (3.94 g, 35.2 mmol) and stirred for 2 hours. After completion of reaction the solution was evaporated and the aqueous layer was extracted with CH_2Cl_2 (3 x 25 mL). The DCM solution was dried over anhydrous Na_2SO_4. TLC (Tol/MeOH; 9:1) revealed the presence of two carbohydrate components with a strong spot corresponding to our product. Then, the solution was evaporated under reducing pressure. The crude syrupy product was purified by column chromatography with CH_2Cl_2/MeOH as eluting system giving product as solid product (3.12 g, 9.96 mmol, 87%), mp: 130-133^{o}C, $[\alpha]_D^{22}$: -27.9^o (c: 0.35 in DCM).

2.2.10 5,6-*O*-Isopropylidene-1,2-*O*-(S)-trichloroethylidene-α-D-glucofuranose (9)



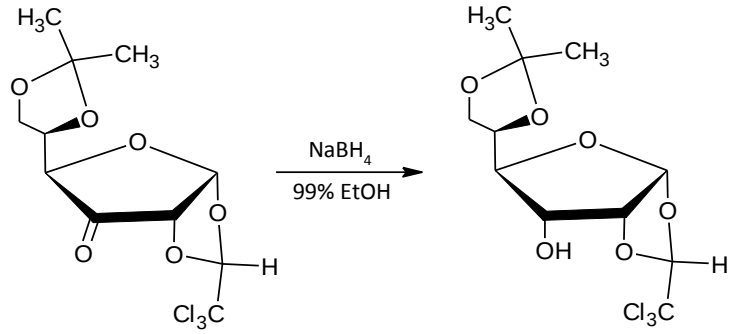
A solution of α-chloralose (10g, 0.032 mol) in dried DMF (50 mL) were added DMP (10 mL, d=0.85 g/cm^3, 8.5g) and anhydrous PTSA (10 mg, 0.058 mmol). The mixture was stirring at room temperature for about 24 hours. After completion of reaction the mixture was neutralized with saturated $NaHCO_3$, then, DMF was evaporated. The product was obtained as colourless crystals from methanol and water solution (8.9 g, 79%), mp: 124-127^{o}C, $[\alpha]_D^{22}$: + 47.8^o (c: 0.5 in DCM).

2.2.11 5,6-*O*-Isopropylidene-1,2-*O*-(S)-trichloroethylidene-α-D-glucofuranose-3-ulose (10)



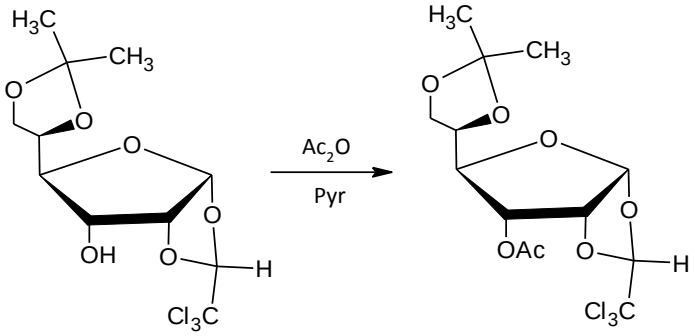
A solution of **9** (5 g, 14.3 mmol) in CH_2Cl_2 (50 mL) was treated with 3 Å powdered molecular sieves (1 g) and PDC (8.1 g, 21.5 mmol) followed by the addition of AcOH (0.5 mL). The mixture was heated and stirred for 3 hours. After completion of reaction the solution was evaporated to dark oil. A solution of the oil in diethyl ether (250 mL) was filtered through silica gel (100 g, 0.063–0.200 mm mesh) and the eluent was evaporated to give ketone (4.6 g, 13.2 mmol, 92%) as a white solid, mp:147-151^{o}C, $[\alpha]_D^{22}$: + 22.4^o (c: 1.3 in DCM).

2.2.12 5,6-*O*-Isopropylidene-1,2-*O*-(S)-trichloroethylidene-α-D-allofuranose (11)



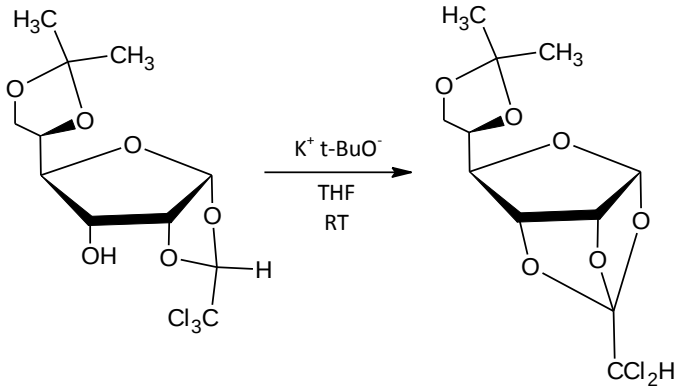
A solution of **10** (3 g, 8.6 mmol) in anhydrous ethanol (100 mL) was cooled to 0^0C. Sodium borohydride (0.13 g, 3.43 mmol) was added, and the mixture was stirred at 0 ^{o}C for 10 min. After 10 min the reaction was stirred for 45 min at room temperature. The organic layer was removed, and the aqueous layer was extracted with CH_2Cl_2 (3 x 50 mL). The combined organic layers were dried (over anhydrous Na_2SO_4) and concentrated to give (2.47 g, 7.1 mmol, 82.1%) of the secondary alcohol as a white solid, mp: 110-113 ^{o}C, $[\alpha]_D^{22}$: +42.1^o (c: 2.27 in $CHCl_3$).

2.2.13 3-*O*-Acetyl-5,6-*O*-isopropylidene-1,2-*O*-(S)-trichloroethylidene-α-D-allofuranose (12)



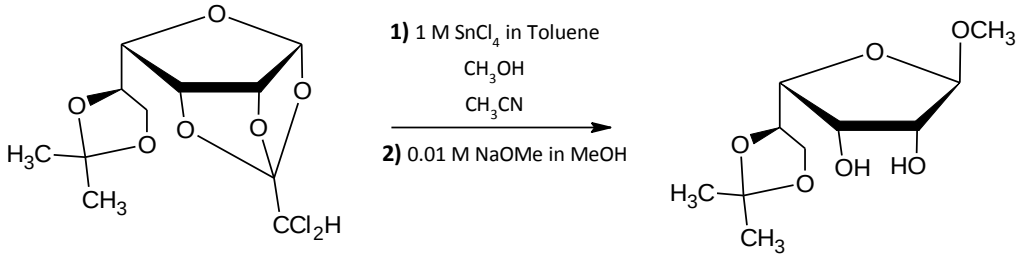
Acetylation of **11** (0.2 g, 0.572 mmol) in pyridine (2 mL) with Ac_2O (0.7 mL, 7.4 mmol). After completion of reaction the solution was evaporated and the aqueous layer was extracted with CH_2Cl_2 (3 x 10 mL). The DCM solution was dried over anhydrous Na_2SO_4 and concentrated to give of the product (0.203 g, 0.518 mmol, 91%), mp: 120-123^{o}C, $[\alpha]_D^{22}$: + 88.8^o (c: 2.67 in $CHCl_3$).

2.2.14 5,6-*O*-Isopropylidene-1,2,3-*O*-orthodichloroethylidene-α-D-allofuranose (13)



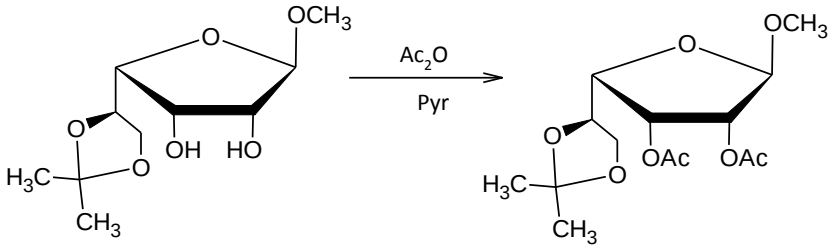
A solution of **12** (3 g, 8.58 mmol) in THF (40 mL) was added potassium tert-butoxide (2.96 g, 25.7 mmol) and stirred for 24 hours. After completion of reaction the solution was evaporated and the aqueous layer was extracted with CH_2Cl_2 (3 x 25 mL). The DCM solution was dried over anhydrous Na_2SO_4 and concentrated to give of product as a white solid (2.54 g, 8.11 mmol, 95%), mp: 114-116ºC, $[\alpha]_D^{22}$: +64º (c: 0.11 in DCM).

2.2.15 Methyl 5,6-*O*-isopropylidene-β-D-gulofuranoside (14)



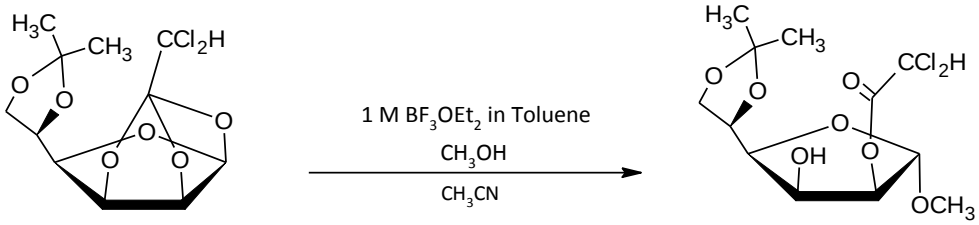
Compound **5** (0.1 g, 0.319 mmol) was dissolved in CH_3CN (1 mL) and treated at 0ºC with $SnCl_4$ (0.064 mL) of a 1 M solution in toluene, (0.064 mmol). After 10 min, methanol (0.013 mL, 0.32 mmol) was added and the mixture stirred for 24h at room temperature. After completion of reaction the mixture was neutralized with saturated $NaHCO_3$, then, the mixture filtered. The filtrate was washed DCM and solvent was evaporated. The residue was treated for 1 h at room temp with NaOMe (0.01 M solution in MeOH). Then, neutralized mixture was filtered and filtrate was evaporated to the dryness. Chromatographic purification of this residue with petroleum ether/ethyl acetate (3:7) gave the product as a colourless gel (0.039 g, 0.166 mmol, 52%), $[\alpha]_D^{22}$: - 52.9º (c: 0.35 in $CHCl_3$).

2.2.16 Methyl 2,3-*O*-diacetyl-5,6-*O*-isopropylidene-β-D-gulofuranoside (15)



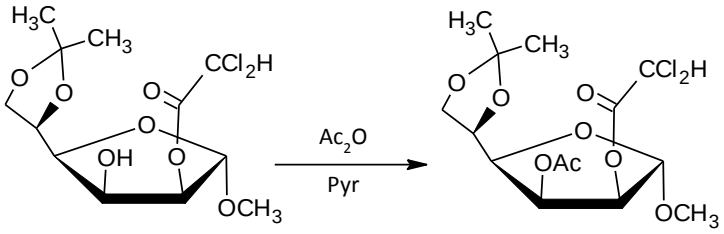
Acetylation of **14** (0.05 g, 0.213 mmol) in pyridine (1 mL) with Ac_2O (0.1 mL, 1.05 mmol). After completion of reaction the solution was evaporated and the aqueous layer was extracted with CH_2Cl_2 (3 x 5 mL). The organic phase was dried over anhydrous Na_2SO_4 and concentrated to give of the product as a colourless syrup (0.052 g, 0.162 mmol, 76%), $[\alpha]_D^{22}$: -188^o (c: 1.3 in $CHCl_3$).

2.2.17 Methyl 2-*O*-dichloroacetyl-5,6-*O*-isopropylidene-α-D-mannofuranoside (16)



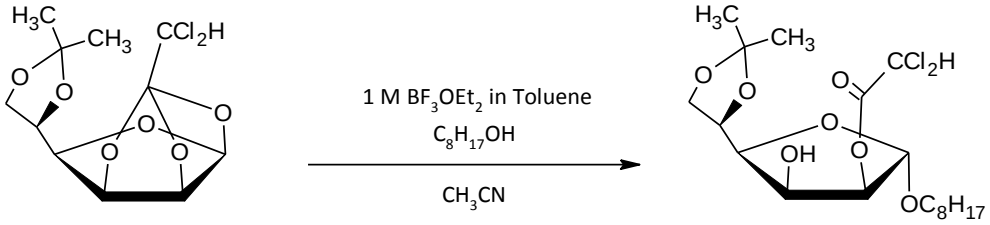
Compound **8** (0.1 g, 0.32 mmol) was dissolved in CH_3CN (1 mL) and treated at 0 ^{o}C with BF_3OEt_2 (0.32 mL of a 1 M solution in toluene, 0.032 mmol). After 10 min, methanol (0.013 mL, 0.032 mmol) was added and the mixture stirred for 24 h at room temperature. After completion of reaction the mixture was neutralized triethylamine, then solvent was evaporated. And chromatographic purification with petroleum ether/ethyl acetate (7:3) gave the product as a colourless gel (0.07 g, 0.201 mmol, 63%), $[\alpha]_D^{22}$: - 56.7^o (c: 1.4 in DCM).

2.2.18 Methyl 2-*O*-dichloroacetyl-3-*O*-acetyl-5,6-*O*-isopropylidene-α-D-mannofuranoside (17)



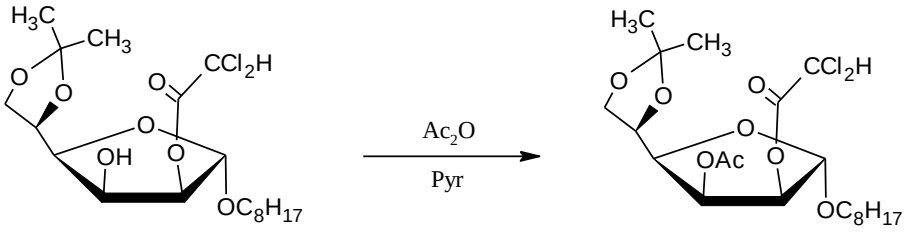
Acetylation of **16** (0.05 g, 0.15 mmol) in pyridine (1 mL) with Ac_2O (0.1 mL, 1.05 mmol) . After completion of reaction the solution was evaporated and the aqueous layer was extracted with CH_2Cl_2 (3 x 5 mL). The DCM phase was dried over anhydrous Na_2SO_4 and concentrated under reduced pressure to give of the product as a colourless syrup (0.053 g, 0.136 mmol, 94%), $[\alpha]_D^{22}$: +22.1^o (c: 1.4 in DCM).

2.2.19 Octyl 2-*O*-Dichloroacetyl-5,6-*O*-isopropylidene-α-D-mannofuranoside (18)



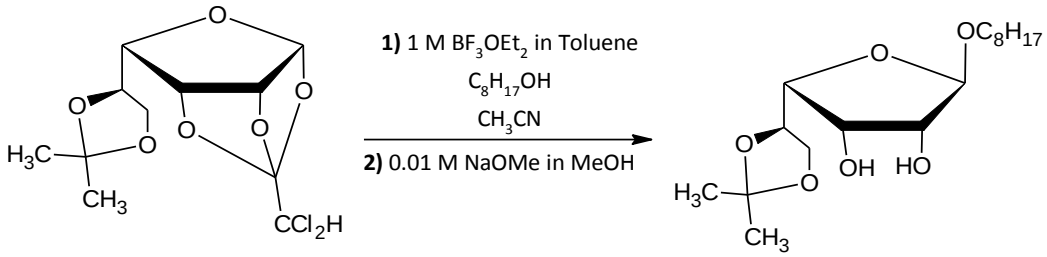
Compound **8** (0.1 g, 0.32 mmol) was dissolved in CH_3CN (1 mL) and treated at 0^{o}C with BF_3OEt_2 (0.064 mL of a 1 M solution in toluene, 0.064mmol). After 10 min, octanol (0.05 mL, 0.32 mmol) was added and the mixture stirred for 48 h at room temperature. After completion of reaction the mixture was neutralized triethylamine, then solvent was evaporated. Purification by column chromatography (Petroleum ether/ ethyl acetate; 7:3) resulted desired 0.08 g syrupy product with 58% yield. $[\alpha]_D^{22}$: -1.7^o (c: 2.33 in $CHCl_3$).

2.2.20 Octyl 2-*O*-dichloroacetyl-3-*O*-acetyl-5,6-*O*-isopropylidene-α-D-mannofuranoside (19)



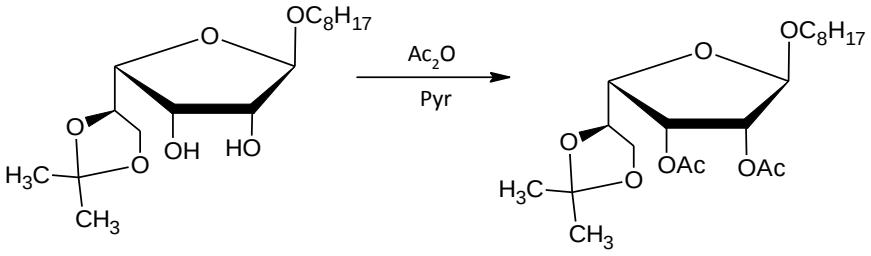
Acetylation of **18** (0.05 g, 0.113 mmol) in pyridine (1 mL) with Ac_2O (0.1 mL, 1.05 mmol) . After completion of reaction the solution was evaporated and the aqueous layer was extracted with CH_2Cl_2 (3 x 5 mL). The organic layer was dried over anhydrous Na_2SO_4 and concentrated under reduced pressure to give syrupy product (0.05 g, 0.1 mmol, 89%), $[\alpha]_D^{22}$: +16.5^o (c: 2.1 in $CHCl_3$).

2.2.21 Octyl 5,6-*O*-isopropylidene-β-D-gulofuranoside (20)



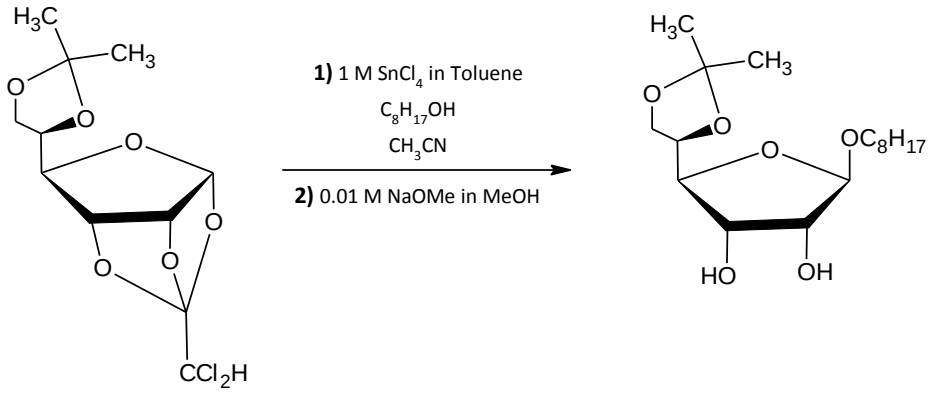
Compound **5** (0.1 g, 0.32 mmol) was dissolved in CH_3CN (1 mL) and treated at 0^{o}C with BF_3OEt_2 (0.032 mL of a 1 M solution in toluene, 0.032 mmol). After 10 min, octanol (0.05 mL, 0.32 mmol) was added and the mixture stirred for 48 h at room temperature. After completion of reaction the mixture was neutralized triethylamine, then solvent was evaporated. The residue was treated for 1 h at room temp with NaOMe (0.01 M solution in MeOH). Then, neutralized mixture was filtered and filtrate was evaporated to the dryness. Chromatographic purification of this residue with petroleum ether/ethyl acetate (9:1, 8:2, 7:3) gave the product as a colourless syrup (0.06 g, 0.18 mmol, 56%), $[\alpha]_D^{22}$: -52.9^o (c: 0.35 in $CHCl_3$).

2.2.22 Octyl 2-3-*O*-diacetyl-5,6-*O*-isopropylidene-β-D-gulofuranoside (21)



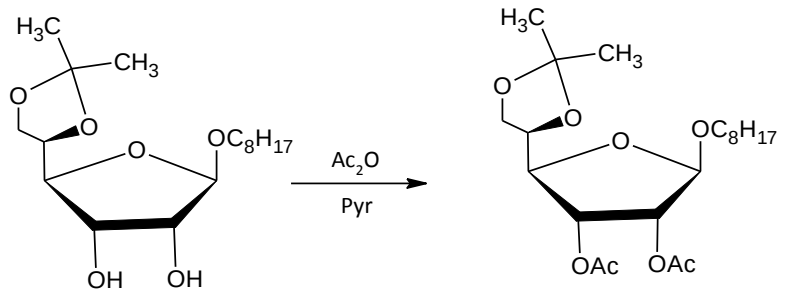
Acetylation of **20** (0.05 g, 0.15 mmol) in pyridine (1 mL) with Ac_2O (0.1 mL, 1,05 mmol). After completion of reaction the solution was evaporated and the aqueous layer was extracted with CH_2Cl_2 (3 x 5 mL). The organic phase was dried over anhydrous Na_2SO_4 and concentrated to give of the product as gel (0.051 g, 0.124 mmol, 81%), $[\alpha]_D^{22}$: - 87.9° (c: 0.67 in $CHCl_3$).

2.2.23 Octyl 5,6-*O*-isopropylidene-β-D-allofuranoside (22)



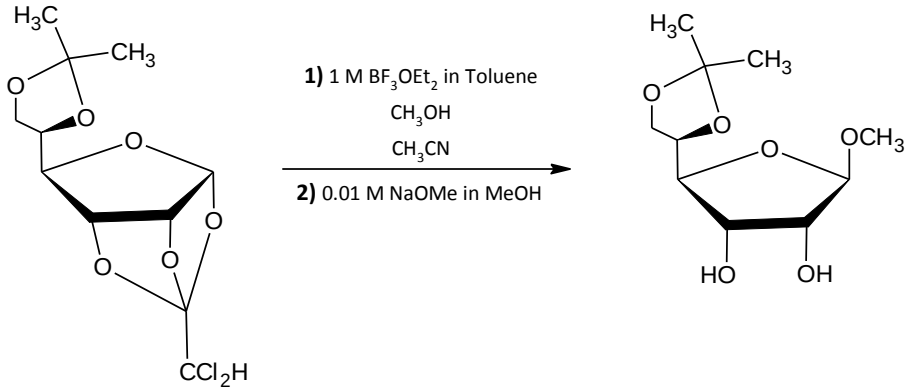
Compound **13** (0.1g, 0.32 mmol) was dissolved in CH_3CN (1 mL) and treated at 0°C with $SnCl_4$ (0.064 mL of a 1 M solution in toluene, 0.064 mmol). After 10 min, octanol (0.05 mL, 0.32 mmol) was added and the mixture stirred for 48 h at room temperature. After completion of reaction the mixture was neutralized with saturated $NaHCO_3$, then, the mixture filtered. The filtrate was washed DCM and solvent was evaporated. The residue was treated for 1 h at room temp with NaOMe (0.01 M solution in MeOH). The mixture was neutralized and filtered. Concentration of this filtrate under reduced pressure to dryness, and chromatographic purification with petroleum ether/ethyl acetate (8:2, 7:3, 6:4, 1:1) gave the product as a syrup (0.05 g, 0.16 mmol, 49%), $[\alpha]_D^{22}$: - 34.6° (c: 1.3 in DCM).

2.2.24 Octyl 2,3-*O*-diacetyl-5,6-*O*-isopropylidene-β-D-allofuranoside (23)



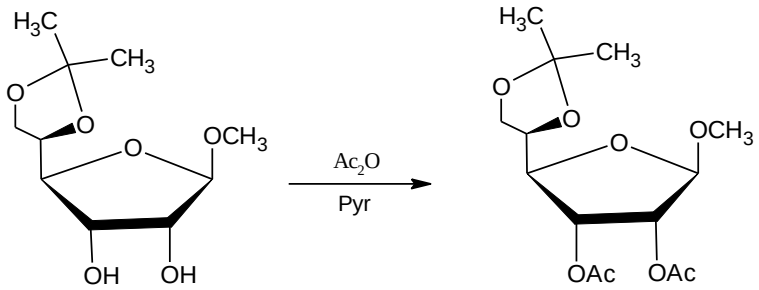
Acetylation of **22** (0.05 g, 0.15 mmol) in pyridine (1 mL) with Ac_2O (0.1 mL, 1.05 mmol). After completion of reaction the solution was evaporated and the aqueous layer was extracted with CH_2Cl_2 (3 x 5 mL). The organic layer was dried over anhydrous Na_2SO_4 and concentrated under reduced pressure to give of the product as gel (0.052 g, 0.125 mmol, 83%), $[\alpha]_D^{22}$: - 2.63^o (c: 0.76 in $CHCl_3$).

2.2.25 Methyl 5,6-*O*-isopropylidene-β-D-allofuranoside (24)



Compound **13** (0.1g, 0.32 mmol) was dissolved in CH_3CN (1 mL) and treated at 0^{o}C with BF_3OEt_2 (0.032 mL of a 1 M solution in toluene, 0.032 mmol). After 10 min, methanol (0.013 mL, 0.32 mmol) was added and the mixture stirred for 24 h at room temperature. After completion of reaction the mixture was neutralized triethylamine, then solvent was evaporated. The residue was treated for 1 h at room temp with NaOMe (0.01 M solution in MeOH). Then mixture was filtered and filtrate was evaporated to dryness. Chromatographic purification of this residue with Petroleum ether/ethyl acetate (7:3, 1:1, 3:7) gave the product as a colourless syrup (0.04 g, 0.18 mmol, 56%), $[\alpha]_D^{22}$: + 37.8^o (c: 0.74 in DCM).

2.2.26 Methyl 2,3-*O*-diacetyl-5,6-*O*-isopropylidene-β-D-allofuranoside (25)



Acetylation of **24** (0.05 g, 0.213 mmol) in pyridine (1 mL) with Ac_2O (0.1 mL, 1.05 mmol). After completion of reaction the solution was evaporated and the aqueous layer was extracted with CH_2Cl_2 (3 x 5 mL). The DCM solution was dried over anhydrous Na_2SO_4 and concentrated under reduced pressure to give syrupy product (0.054 g, 0.169 mmol, 80%), $[\alpha]_D^{22}$: -16.9^o (c: 1.53 in $CHCl_3$).

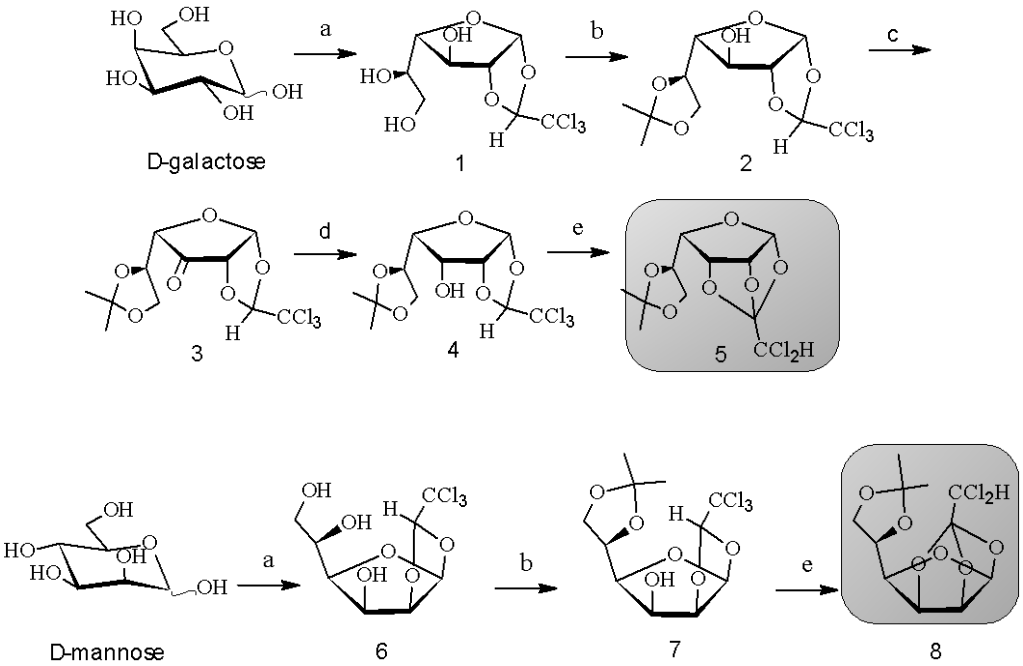
3. RESULTS AND DISCUSSIONS

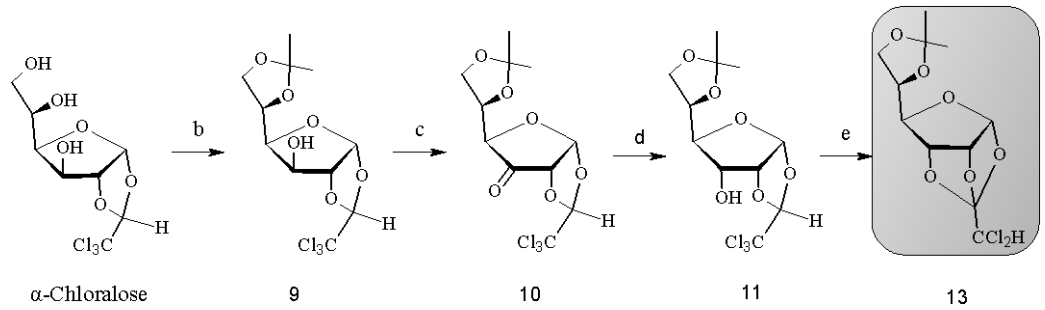
Efficient formation of glycosidic linkages has played an important role in the development of modern synthetic carbohydrate chemistry. Among the various types of donors that can be employed for the construction of glycosidic bonds, carbohydrate orthoesters have long been used (Bamhaoud et al, 2000; Hiranuma et al, 1999; Hori and Nakatsubo, 1999; Kong, 2006; Marotte et al, 2003; Podvalnyy et al, 2009 and 2011; Sanchez et al, 2002).

In this study three tricyclic glycosyl donors (**5, 8, 13**) were synthesized. **5** and **13** are new compounds. These donors have 1,2,3-orthoester group as leaving group. This novel tricyclic glycosyl donors were applied to glycosylation reactions with methanol and octanol by means of various Lewis acids.

3.1 Synthesis of Glycosyl Donors

Our synthetic approach for the preparation of new glycosyl donors is shown in Scheme 3.1.





Scheme 3.1. Synthesis of glycosyl donors, a) TCA, H_2SO_4, b) DMP, PTSA c) PDC d) $NaBH_4$ e) K^+t-BuO^-

Experimental data including melting point and angle of optically rotation were identical to literature for compounds **1** and **2** (Kök and Salman, 2012); **3** and **10** (Ay et al, 2007); **6, 7** and **8** (Salman et al, 2004). α-Chloralose was commercially available and purified by recrystallization from MeOH/H_2O.

The 5-OH and 6-OH groups of **1, 6** and α-chloralose were protected with isopropylidene group using the conventional DMP/PTSA/DMF procedure (Salman et al, 2004).

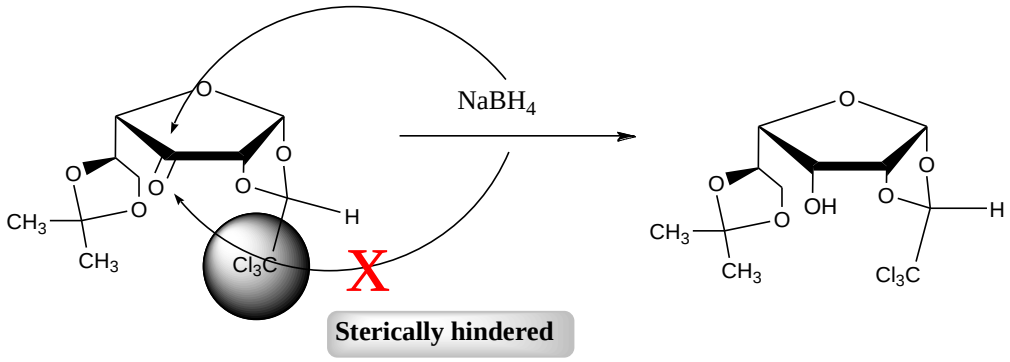
In order to obtain 3-keto derivatives (**3** and **10**) several conditions were examined (Ay et al, 2007; Burke and Danheiser, 2000; Soarez et al, 2013; Yenil and Yüceer, 2003) (Table 3.1). The best results were obtained when 1.5 equivalents of PDC was used with the catalytic amount of AcOH in DCM.

Table 3.1. Summary of the optimization results for oxidation reaction of 3-OH groups

Entry	Reagent (eq)	Solvent	Time	Product	Yield
2	PCC (3) , rt	DCM	4 days	3	50
9	PCC (3) , rt	DCM	4 days	10	54
2	PCC (3) , reflux	Toluene	3 days	3	51
2	PCC (3) , Ac_2O, reflux	Benzene	3 days	3	52
2	PCC (3) , Ac_2O, reflux	Toluene	1 day	3	-
2	PDC (1.5) , Ac_2O, reflux	DCM	3 h	3	-
2	PDC (1.5) , AcOH, reflux	DCM	3 h	3	93
9	PDC (1.5) , AcOH, reflux	DCM	3 h	10	92

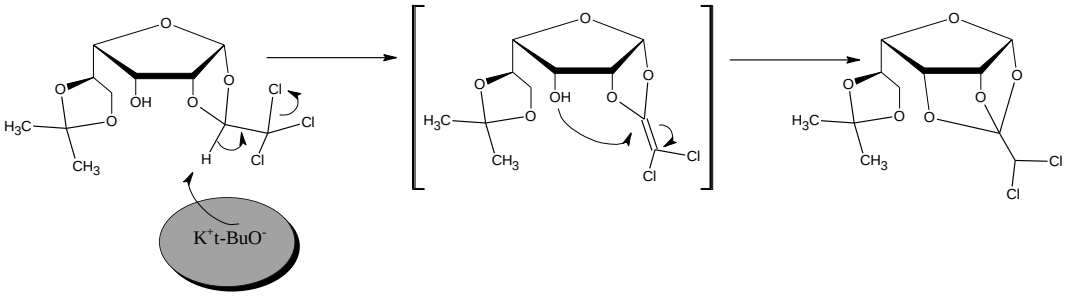
Stereoselective reduction of **3** and **10** with $NaBH_4$ was easily achieved (Bemiller and Whistler, 1972; Lucas et al, 2009). By means of sterical effect of

bulky trichloroethylidene group, 100% stereoselectivity can be obtained for both of **4** and **11** (Scheme 3.2).



Scheme 3.2. Stereoselective reduction of the ketone group for **2** with $NaBH_4$.

The syntheses of tricyclic furanoid 1,2,3-orthoesters as glycosyl donors were achieved according to the literature (Salman et al, 2004) with a slight modification. **4**, **7** and **11** were dissolved in dry THF and stirred with potassium tertiary butoxide at room temperature. According to proven (Salman et al, 2004; Ko et al, 2008) reaction mechanism; firstly ketene acetal derivatives were formed as an intermediate via dehydrochlorination on the trichloroethylidene group by a bulky base, potassium tertiary butoxide. After that, nucleophilic attack of 3-OH group to the double bond of ketene acetal intermediate resulted the formation of tricyclic orthoesters (Scheme 3.3).



Scheme 3.3. Tricyclic orthoester formation via the reaction of **4** with K^+t-BuO^-.

3.2 Analyzing the Effectiveness of Tricyclic Orthoesters as Glycosyl Donors

Usefulness of the glycosyl donors (**5, 8, 13**) in glycosylation reactions was examined via various reaction conditions; different temperatures (-20 ºC, 0 ºC, rt),

various Lewis acids (BF_3, $SnCl_4$) different acceptors (CH_3OH, $C_8H_{17}OH$) (Table 3.2).

Table 3.2. Optimum conditions for the glycosylation reactions of new glycosyl donors

Entry	Conditions	Product	Yield (%)
5	$SnCl_4$(0.2 eq), MeOH (1 eq), CH_3CN	14	52
8	BF_3(0.1 eq), MeOH (1 eq), CH_3CN	16	63
13	BF_3(0.1 eq), MeOH (1 eq), CH_3CN	24	56
5	BF_3(0.1 eq), OcOH (1 eq), CH_3CN	20	56
8	BF_3(0.2 eq), OcOH (1 eq), CH_3CN	18	58
13	BF_3(0.2 eq), OcOH (1 eq), CH_3CN	22	49

3.3 Structural Characterization of the Compounds

Compound **1** and **6** were synthesized according to literature (Salman et al, 2004 and Kök and Salman, 2012) and their experimental data including melting point and angle of optically rotation were identical.

On the other hand, structures of other new compounds (**4**, **5, 12**, **13, 15, 17, 19, 21, 23, 25**) were determined by the analyses of their spectral data including ^{1}H NMR, ^{13}C NMR, and COSY.

Characteristic ^{1}H NMR chemical shifts of acetal protons as singlets for **4** and **12** were 5.76 and 5.34 respectively. For compounds **5** and **13**, disappearing of the H-CCl_2 peaks and appearing of orthoester singlets as 6.02 and 6.01 in ^{1}H NMR spectra proved the formation of orthoester structures (Table 3.2).

Table 3.3. Characteristic ^{1}H NMR chemical shifts of compounds **4, 5, 12** and **13**.

Compound	4	5	12	13
^{1}H NMR Chemical shift value for H-C-CCl_3	5.76	-	5.34	-
^{1}H NMR Chemical shift value for H-CCl_2	-	6.02	-	6.01

Similarly, changing of characteristic chemical shifts of C-8 and C-9 for compounds **4, 5, 12, 13** in ^{13}C NMR spectra clearly indicated the formation of orthoester structures (Table 3.3).

Table 3.4. Characteristic ^{13}C NMR chemical shifts of compounds **4, 5, 12** and **13**.

Compound	4	5	12	13
^{13}C NMR Chemical shift value for C-8	108.3	117.8	110.1	117.8
^{13}C NMR Chemical shift value for C-9	100.3	65.7	97.0	66.0

Finally, formation of glycosidic bonds with CH_3OH for compounds **15**, **17** and **25** (Table 3.4); and with $C_8H_{17}OH$ for **19**, **21** and **23** (Table 3.5) can be seen in ^1H NMR spectra of related compounds. All spectral data of glycosidic compounds were in agreement with similar compounds in literature (Evans and Parrish, 1976; Bischofbberger et al, 1978; Dureau et al, 2010; Vill et al, 2008; Pathak et al, 2001)

Table 3.5. ^1H NMR chemical shifts of $-OCH_3$ group in compounds **15**, **17** and **25**.

Compounds	**$-OCH_3$ chemical shift in ^1H NMR spectra**
15	3.37 (s), 3H
17	3.42 (s), 3H
25	3.35 (s), 3H

Table 3.6. ^1H NMR chemical shifts of $–OC_8H_{17}$group in compounds **19**, **21** and **23**.

Compounds	**Chemical shifts in ^1H NMR spectra**			
	$-OC\underline{\mathbf{H}}_2CH_2(CH_2)_5CH_3$	$-OCH_2C\underline{\mathbf{H}}_2(CH_2)_5CH_3$	$-OCH_2CH_2(C\underline{\mathbf{H}}_2)_5CH_3$	$-OCH_2CH_2(CH_2)_5C\underline{\mathbf{H}}_3$
19	3.67 (t), 2H	1.53-1.61 (m), 2H	1.23-.1.34 (m), 10 H	0.87 (t), 3H
21	3.38 (dt), 1H 3.59 (dt), 1H	1.50-1.61 (m), 2H	1.21-.1.38 (m), 10 H	0.87 (t), 3H
23	3.37 (dt), 1H 3.65 (dt), 1H	1.50-1.61 (m), 2H	1.21-.1.38 (m), 10 H	0.87 (t), 3H

Consequently, application of novel donors to glycosidation reactions with methanol and octanol as representative glycosyl acceptors was resulted in the formation of expected 1,2-cis furanosidic glycosides in various yields.

3.4 Spectroscopic Data

3.4.1 5,6-*O*-Isopropylidene-1,2-*O*-(S)-trichloroethylidene-α-D- gulofuranose (compound 4)

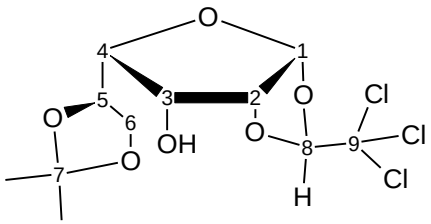


Table 3.7. ^{1}H-NMR spectral data (DMSO - D_6, 400MHz) of Compound **4**

Location of Atoms	^{1}HNMR (δ)	H and Coupling Constants (Hz)
H_1	5.97(d)	1H, $J_{1,2}$ =4.4
H_{OH-3}	5.56(d)	1H, J_{OH-3}= 5.6
H_{acetal}	5.76(s)	1H
H_2	4.89(dd)	1H, $J_{2,3}$= 5.6
H_3 + H_5	4.16-4.25(m)	2H,
H_{6a}	4.02(dd)	1H, $J_{5,6a}$= 6.6
H_4	3.90 (dd)	1H, $J_{3,4}$= 6.2 ,
H_{6b}	3.34(dd)	1H, $J_{5,6b}$= 7.0, $J_{6a,6b}$= 8.8
OH	2.5(bs)	1H
H_{isop}	1.27(s) and 1.30(s)	(3H) x 2

Table 3.8. ^{13}C-NMR spectral data (DMSO - D_6, 400MHz) of Compound **4**

Location of Atoms	^{13}CNMR (δ)
C_1	105.8
C_2	84.2
C_3	75.5
C_4	82.6
C_5	70.1
C_6	66.4
C_7	109.3
C_8	108.3
C_9	100.1
C_{isop}	27.1 and 25.8

3.4.2 5,6-*O*-Isopropylidene-1,2,3-*O*-orthodichloroethylidene-α-D-gulofuranose (compound 5)

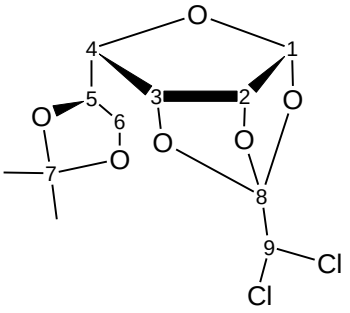


Table 3.9. ^{1}H-NMR spectral data ($CDCl_3$, 400MHz) of Compound **5**

Location of Atoms	**^{1}HNMR (δ)**	**H and Coupling Constants (Hz)**
H_{acetal}	6.02(s)	1H
H_1	5.17(s)	1H, $J_{1,2}$ = 2.4
H_2	5.36(dd)	1H, $J_{2,3}$ = 5.2
H_3	4.49(dd)	1H, $J_{3,4}$= 2.8
H_{6a}	4.36(dd)	1H, $J_{6a,6b}$= 14
H_4	4.23 (dd)	1H, $J_{4,5}$= 8.4
H_{6b}	4.19(dd)	1H, $J_{5,6b}$ = 6.8, $J_{6a\text{-}6b}$= 14
H_5	3.75(dd)	1H, $J_{5,6a}$= 6.8
H_{isop}	1.45(s) and 1.39(s)	(3H) x 2

Table 3.10. ^{13}C-NMR spectral data ($CDCl_3$, 400MHz) of Compound **5**

Location of Atoms	**^{13}CNMR (δ)**
C_1	102.9
C_2	83.5
C_3	80.6
C_4	76.1
C_5	74.1
C_6	64.5
C_7	110.3
C_8	117.8
C_9	65.7
C_{isop}	27.0 and 25.5

3.4.3 3-*O*-Acetyl-5,6-*O*-isopropylidene-1,2-*O*-(S)-trichloroethylidene-α-D-allofuranose (compound 12)

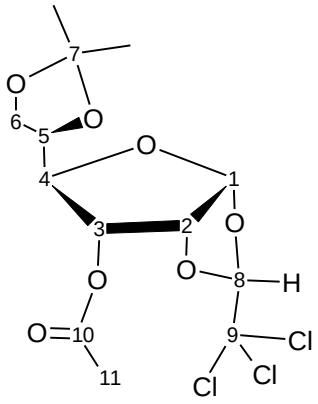


Table 3.11. ^{1}H-NMR spectral data ($CDCl_3$, 400MHz) of Compound **12**

Location of Atoms	^{1}HNMR (δ)	H and Coupling Constants (Hz)
H_1	6.02(d)	1H, $J_{1,2}$= 4.0
H_{acetal}	5.34(s)	1H
H_2	4.98(dd)	1H, $J_{2,3}$= 4.2
H_3	4.92(dd)	1H, $J_{3,4}$= 8.6
H_4	4.52(dd)	1H, $J_{4,5}$= 4.8
H_5	4.31 (m)	1H
H_{6a}	4.05(dd)	1H, $J_{5,6a}$= 8.2, $J_{6a,6b}$= 8.6
H_{6b}	3.87(dd)	1H
H_{acetyl}	2.11(s)	3H
H_{isop}	1.33(s) and 1.40(s)	(3H) x 2

Table 3.12. ^{13}C-NMR spectral data ($CDCl_3$, 400MHz) of Compound **12**

Location of Atoms	^{13}CNMR (δ)
C_1	105.0
C_2	79.4
C_3	74.7
C_4	79.0
C_5	72.3
C_6	65.5
C_7	107.7
C_8	110.1
C_9	97.0
C_{10}	170.0
C_{11}	20.5
C_{isop}	25.0 and 26.1

3.4.4 5,6-*O*-Isopropylidene-1,2,3-*O*-orthodichloroethylidene-α-D-allofuranose (compound 13)

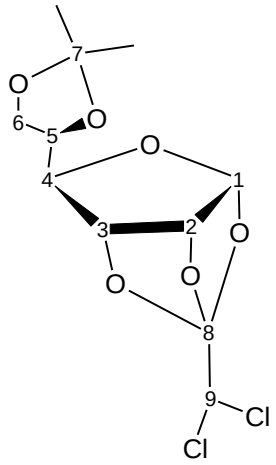


Table 3.13. ^{1}H-NMR spectral data ($CDCl_3$, 400MHz) of Compound **13**

Location of Atoms	^{1}HNMR (δ)	H and Coupling Constants (Hz)
H_1	5.71(d)	1H, J_{1-2}= 2.54
H_{acetal}	6.01(s)	1H
H_2	5.33(dd)	1H, $J_{2,3}$= 3.14
H_3	4.53(d)	1H, $J_{3,4}$ = 0
H_4	4.31(d)	1H, $J_{4,5}$ = 4.30
H_{6a} + H_5	4.17-4.10(m)	2H, $J_{6a,6b}$= 12.9
H_{6b}	3.81(dd)	1H, $J_{6a,6b}$= 12.9
H_{isop}	1.32(s) and 1.43(s)	(3H) x 2

Table 3.14. ^{13}C-NMR spectral data ($CDCl_3$, 400MHz) of Compound **13**

Location of Atoms	^{13}CNMR (δ)
C_1	102.3
C_2	84.3
C_3	79.5
C_4	74.5
C_5	76.8
C_6	64.3
C_7	110.3
C_8	117.7
C_9	66.1
C_{isop}	24.3 and 26.1

3.4.5 Methyl 2-3-*O*-diacetyl-5,6-*O*-isopropylidene-β-D-gulofuranoside (compound 15)

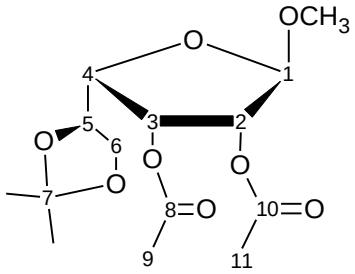


Table 3.15. ^{1}H-NMR spectral data ($CDCl_3$, 400MHz) of Compound **15**

Location of Atoms	^{1}HNMR (δ)	H and Coupling Constants (Hz)
H_1	4.97(d)	1H, $J_{1,2}$= 1.38
H_3	5.48(dd)	1H, $J_{3,4}$= 5.86
H_2	5.14(dd)	1H, $J_{2,3}$= 5.26
H_5	4.29(m)	1H, $J_{5,6a}$= 6.74, $J_{5,6b}$= 6.94
H_4	4.16 (dd)	1H, $J_{4,5}$= 8.4
H_{6a}	3.98(dd)	1H, $J_{6a,6b}$= 8.6
H_{6b}	3.57(dd)	1H
H_{acetyl}	2.02(s)	6H
H_{isop}	1.40(s) and 1.34(s)	(3H) x 2
-O$C\underline{H}_3$	3.37(s)	3H

Table 3.16. ^{13}C-NMR spectral data ($CDCl_3$, 400MHz) of Compound **15**

Location of Atoms	^{13}CNMR (δ)
C_1	105.7
C_2	79.5
C_3	76.2
C_4	75.4
C_5	65.8
C_6	71.2
C_7	109.5
C_8, C_{10}	169.1 and 169.3
O-CH_3	55.6
C_{isop}	25.2 and 26.6

3.4.6 Methyl 2-*O*-dichloroacetyl-3-*O*-acetyl-5,6-*O*-isopropylidene-α-D-mannofuranoside (compound 17)

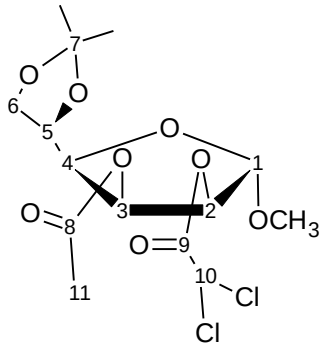


Table 3.17. ^{1}H-NMR spectral data ($CDCl_3$, 400MHz) of Compound **17**

Location of Atoms	**^{1}HNMR (δ)**	**H and Coupling Constants (Hz)**
H_1	6.26(s)	1H, $J_{1,2}$= 0
$H_{dichloroacetyl}$	5.70(s)	1H
H_3	5.17(dd)	1H, $J_{3,4}$= 3.12
H_2	5.00(d)	1H, $J_{2,3}$= 6.46
H_5	4.47 (ddd)	1H, $J_{5,6a}$= 3.52, $J_{5,6b}$= 6.06
H_{6b}	4.12(dd)	1H, $J_{6a\text{-}6b}$= 9
H_{6a}	4.02(dd)	1H,
H_4	3.95(dd)	1H, $J_{4,5}$= 9.36
H_{acetyl}	2.08(s)	3H
H_{isop}	1.45(s) and 1.37(s)	(3H) x 2
H-OCH_3	3.42(s)	3H

3.4.7 Octyl 2-*O*-dichloroacetyl-3-*O*-acetyl-5,6-*O*-isopropylidene-α-D-mannofuranoside (compound 19)

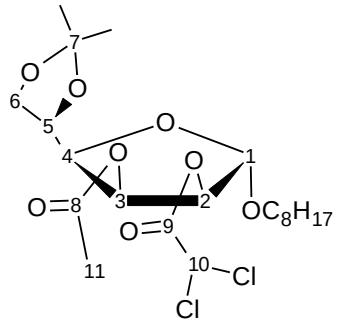


Table 3.18. ^{1}H-NMR spectral data ($CDCl_3$, 400MHz) of Compound **19**

Location of Atoms	^{1}HNMR (δ)	H and Coupling Constants (Hz)
H_1	6.23(s)	1H, $J_{1,2}$= 0
$H_{dichloroacetyl}$	5.70(s)	1H
H_3	5.15(dd)	1H, $J_{3,4}$= 3.12
H_2	4.99(d)	1H, $J_{2,3}$= 6.24
H_5	4.43 (ddd)	1H, $J_{5,6a}$= 5.84, $J_{5,6b}$= 3.90
H_{6a}	4.11(dd)	1H, $J_{6a\text{-}6b}$= 8.96
H_{6b}	4.02(dd)	1H,
H_4	3.94(dd)	1H, $J_{4,5}$= 9.2
H_{acetyl}	2.08(s)	3H
H_{isop}	1.45(s) and 1.37(s)	(3H) x 2
$OC\underline{H}_2$ (octanol)	3.67(t)	2H, J= 6.24
$OCH_2\text{-}C\underline{H}_2$	1.53-1.61(m)	2H
$OCH_2\text{-}CH_2\text{-}(C\underline{H}_2)_5$-	1.23-1.34(m)	10H
$OCH_2\text{-}CH_2\text{-}(CH_2)_5\text{-}C\underline{H}_3$	0.87(t)	3H, J= 6.64

Table 3.19. ^{13}C-NMR spectral data ($CDCl_3$, 400MHz) of Compound **19**

Location of Atoms	^{13}CNMR (δ)
C_1	99.7
C_2	87.1
C_3	82.1
C_4	82.5
C_5	73.6
C_6	67.2
C_7	109.9
C_8, C_9	169.0 and 163.2
C_{10}	63.1
$O\text{-}\underline{C}H_2$	72.0

3.4.8 Octyl 2,3-*O*-diacetyl-5,6-*O*-isopropylidene-β-D-gulofuranoside (compound 21)

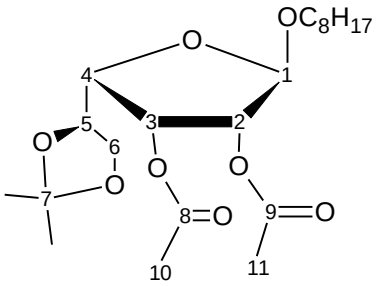


Table 3.20. ^{1}H-NMR spectral data ($CDCl_3$, 400MHz) of Compound **21**

Location of Atoms	^{1}HNMR (δ)	H and Coupling Constants (Hz)
H_1	4.99 (s)	1H, $J_{1,2}$= 0
H_3	5.49 (dd)	1H, $J_{3,4}$= 3.5
H_2	5.17 (d)	1H, $J_{2,3}$= 5.9
H_5	4.27 (ddd)	1H, $J_{5,6a}$= 2.7, $J_{5,6b}$= 4.6
H_{6a}	3.99 (dd)	1H, $J_{6a\text{-}6b}$= 12.4
H_{6b}	3.58 (dd)	1H
H_4	4.14 (dd)	1H, $J_{4,5}$= 8,5
H_{acetyl}	2.08 (s), 2.07 (s)	2 x 3H
H_{isop}	1.42 (s), 1.44 (s)	2 x 3H
$OC\underline{H}_2$ (octanol)	3.38 (dt) and 3.59 (dt)	2H, J= 6.24
$OCH_2\text{-}C\underline{H}_2$	1.50-1.61(m)	2H
$OCH_2\text{-}CH_2\text{-}(C\underline{H}_2)_5$-	1.21-1.38(m)	10H
$OCH_2\text{-}CH_2\text{-}(CH_2)_5\text{-}C\underline{H}_3$	0.87(t)	3H J= 6.64

Table 3.21. ^{13}C-NMR spectral data ($CDCl_3$, 400MHz) of Compound **21**

Location of Atoms	^{13}CNMR (δ)
C_1	106.0
C_2	85.3
C_3	79.5
C_4	78.0
C_5	70.7
C_6	67.0
C_7	112.7
C_8, C_9	169.0 and 170.2
$O\text{-}\underline{C}H_2$	67.5

3.4.9 Octyl 2,3-*O*-diacetyl-5,6-*O*-isopropylidene-β-D-allofuranoside (compound 23)

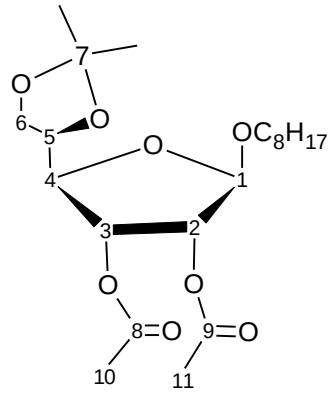


Table 3.22. ^{1}H-NMR spectral data ($CDCl_3$, 400MHz) of Compound **23**

Location of Atoms	^{1}HNMR (δ)	H and Coupling Constants (Hz)
H_1	4.95 (d)	1H, $J_{1,2}$= 1.16
H_3	5.42 (dd)	1H, $J_{3,4}$= 4.7
H_2	5.23 (dd)	1H, $J_{2,3}$= 5.1
$H_4 + H_5 + H_{6a}$	4.05-4.11 (m)	3H
H_{6b}	3.95-3.98 (m)	1H, J_{6a-6b}= 8,5
H_{acetyl}	2.08 (s), 2.04 (s)	2 x 3H
H_{isop}	1.32 (s), 1.40 (s)	2 x 3H
$OC\underline{H}_2$ (octanol)	3.37 (dt) and 3.65 (dt)	2H, J= 6.64
$OCH_2\text{-}C\underline{H}_2$	1.50-1.61(m)	2H
$OCH_2\text{-}CH_2\text{-}(C\underline{H}_2)_5\text{-}$	1.21-1.38(m)	10H
$OCH_2\text{-}CH_2\text{-}(CH_2)_5\text{-}C\underline{H}_3$	0.87(t)	3H J= 6.64

Table 3.23. ^{13}C-NMR spectral data ($CDCl_3$, 400MHz) of Compound **23**

Location of Atoms	^{13}CNMR (δ)
C_1	108.4
C_2	87.5
C_3	84.1
C_4	83.9
C_5	70.6
C_6	62.5
C_7	114.7
C_8, C_9	170.0 and 170.4
$O\text{-}\underline{C}H_2$	69.1

3.4.10 Methyl 2,3-*O*-diacetyl-5,6-*O*-isopropylidene-β-D-allofuranoside (compound 25)

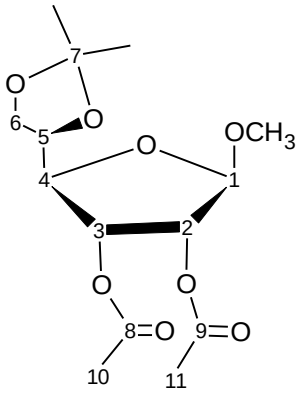


Table 3.24. ^{1}H-NMR spectral data ($CDCl_3$, 400MHz) of Compound **25**

Location of Atoms	**^{1}HNMR (δ)**	**H and Coupling Constants (Hz)**
H_1	4.87 (s)	1H,
H_3	5.38 (t)	1H, $J_{3,4}$= 5.1
H_2	5.22 (d)	1H, $J_{2,3}$= 5.1
$H_4 + H_5 + H_{6a}$	4.06-4.13 (m)	3H
H_{6b}	3.94-3.98 (m)	1H, J_{6a-6b}= 8,6
H_{acetyl}	2.08 (s), 2.03 (s)	2 x 3H
H_{isop}	1.31 (s), 1.41 (s)	2 x 3H
$OC\underline{H}_3$ (methanol)	3.35 (s)	3H

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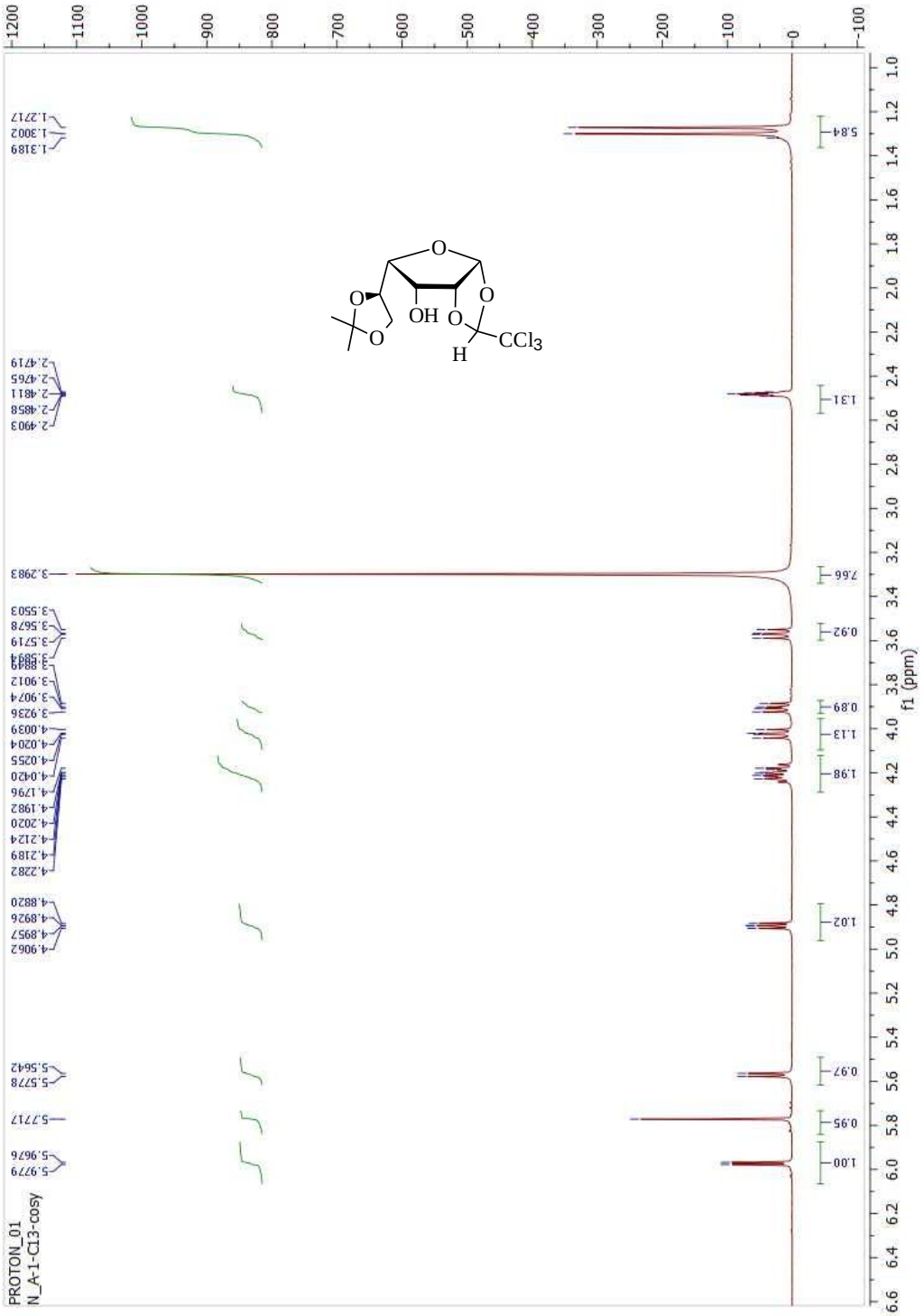
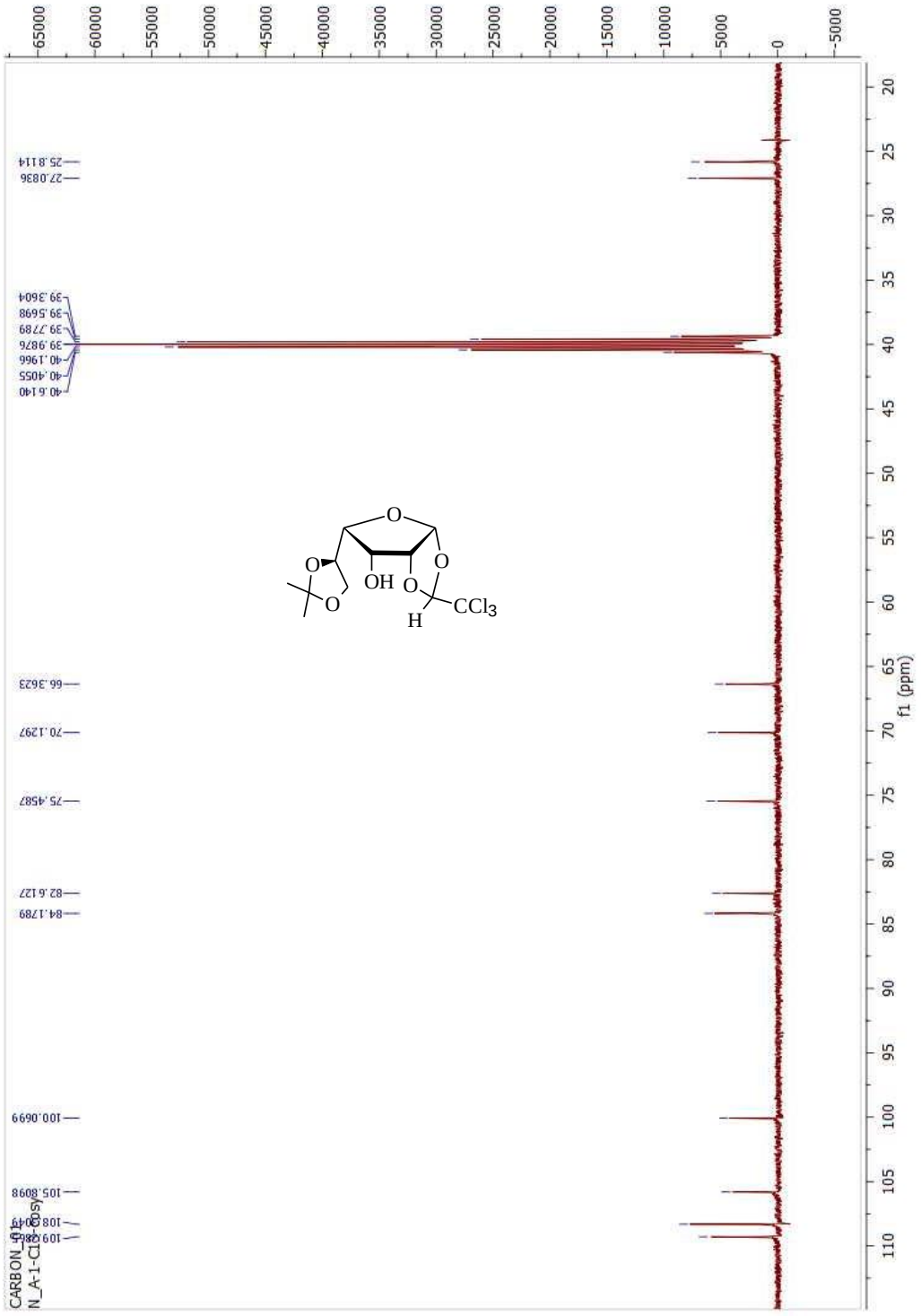
APPENDIX

APPENDIX

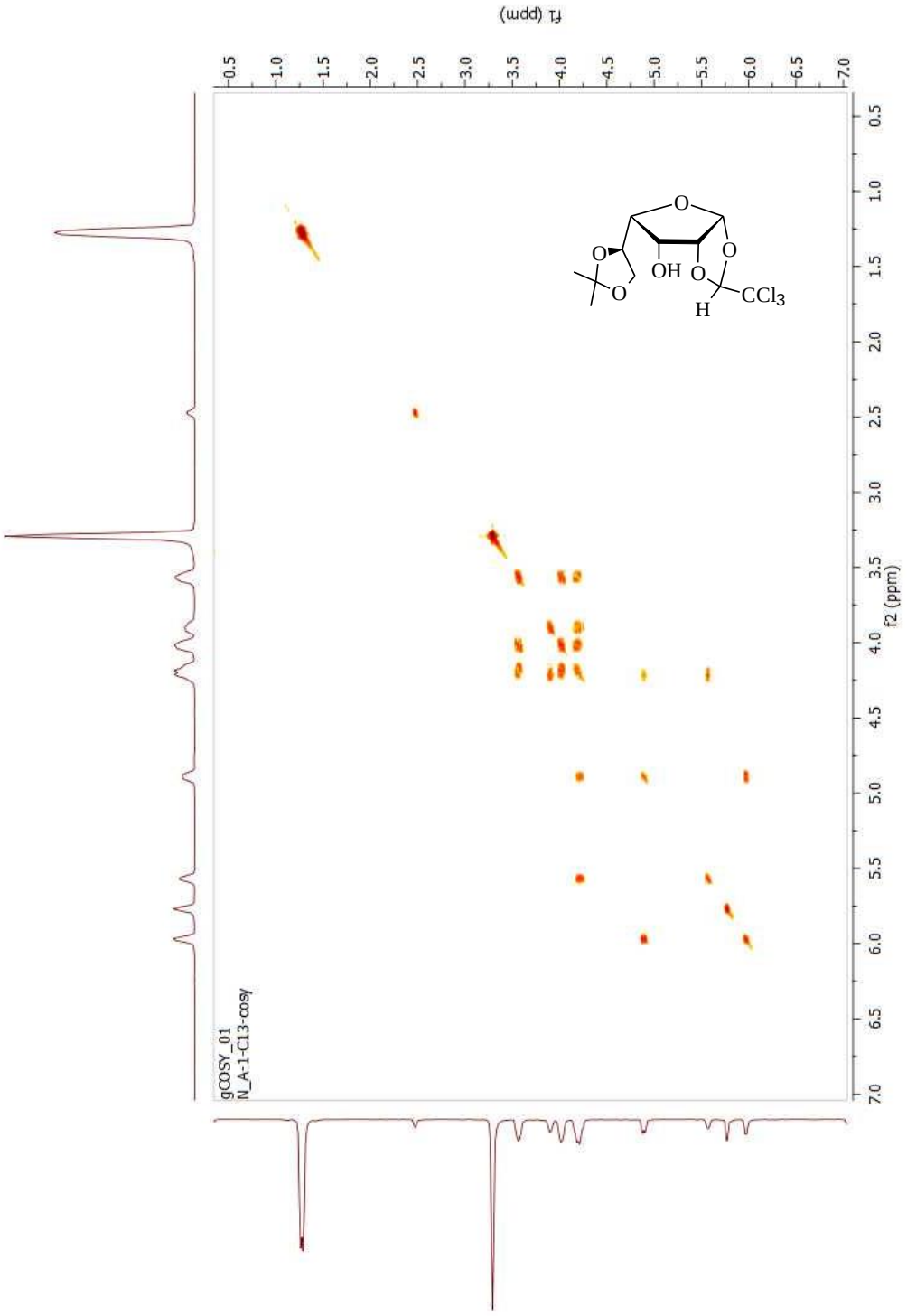
Appendix 1 [1]H-NMR spectrum of the 5,6-*O*-Isopropylidene-1,2-*O*-(S)-trichloroethylidene-α-D-gulofuranose (compound **4)**



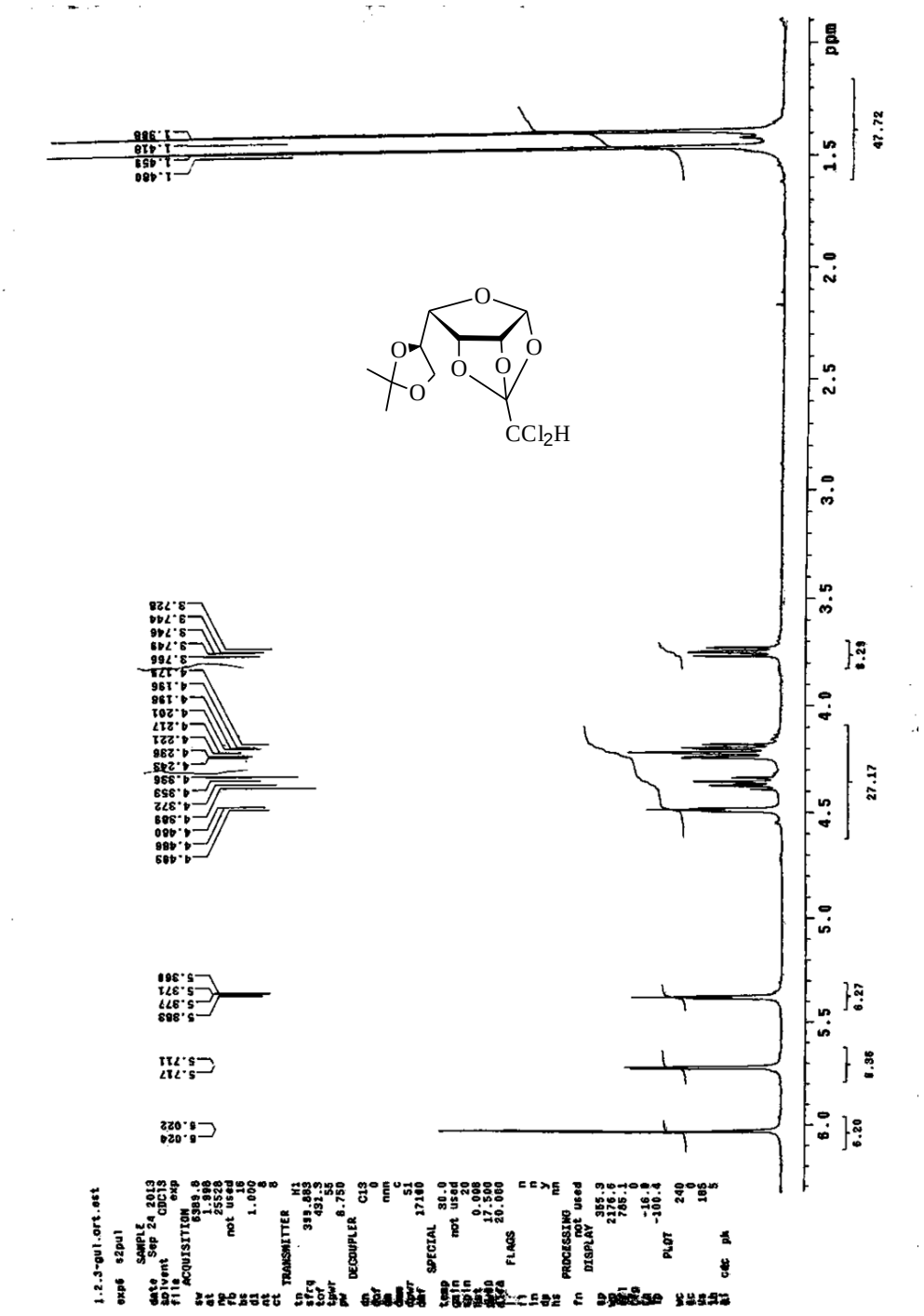
Appendix 2 ^{13}C-NMR spectrum of the 5,6-*O*-Isopropylidene-1,2-*O*-(S)-trichloroethylidene-α-D-gulofuranose (compound **4**)



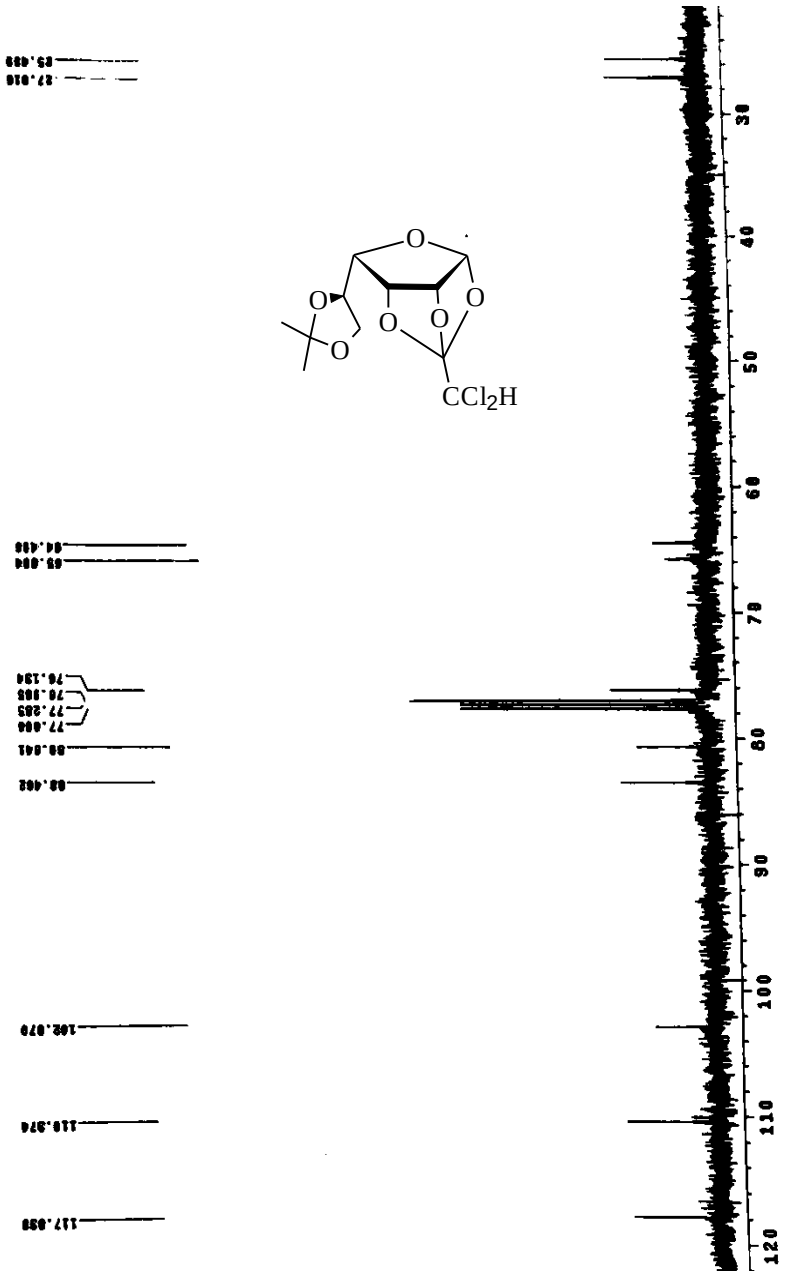
Appendix 3 COSY spectrum of the 5,6-*O*-Isopropylidene-1,2-*O*-(S)-trichloroethylidene-α-D-gulofuranose (compound **4**)



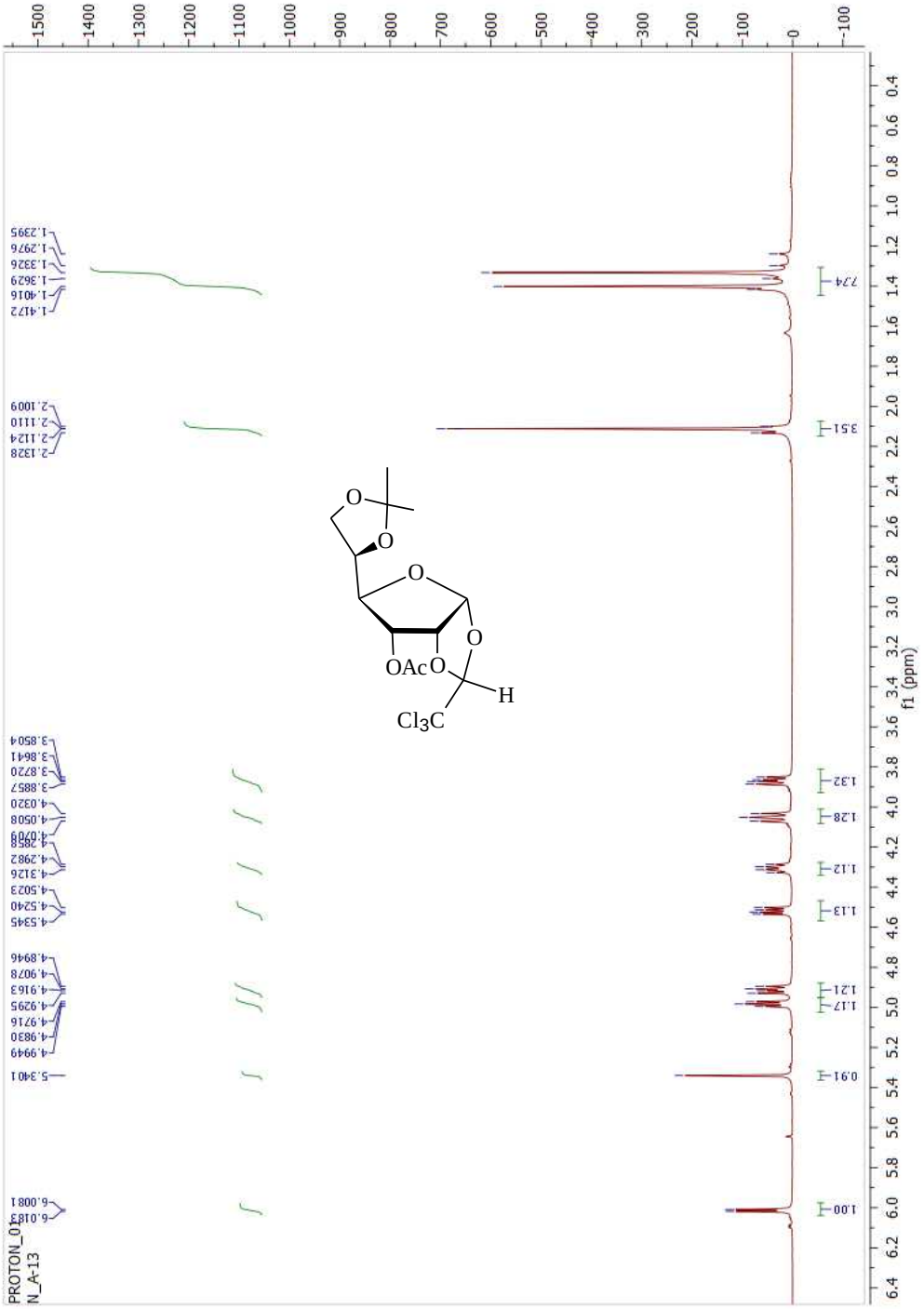
Appendix 4 ^{1}H-NMR spectrum of the 5,6-*O*-Isopropylidene-1,2,3-*O*-orthodichloroethylidene-α-D-gulofuranose (compound **5**)



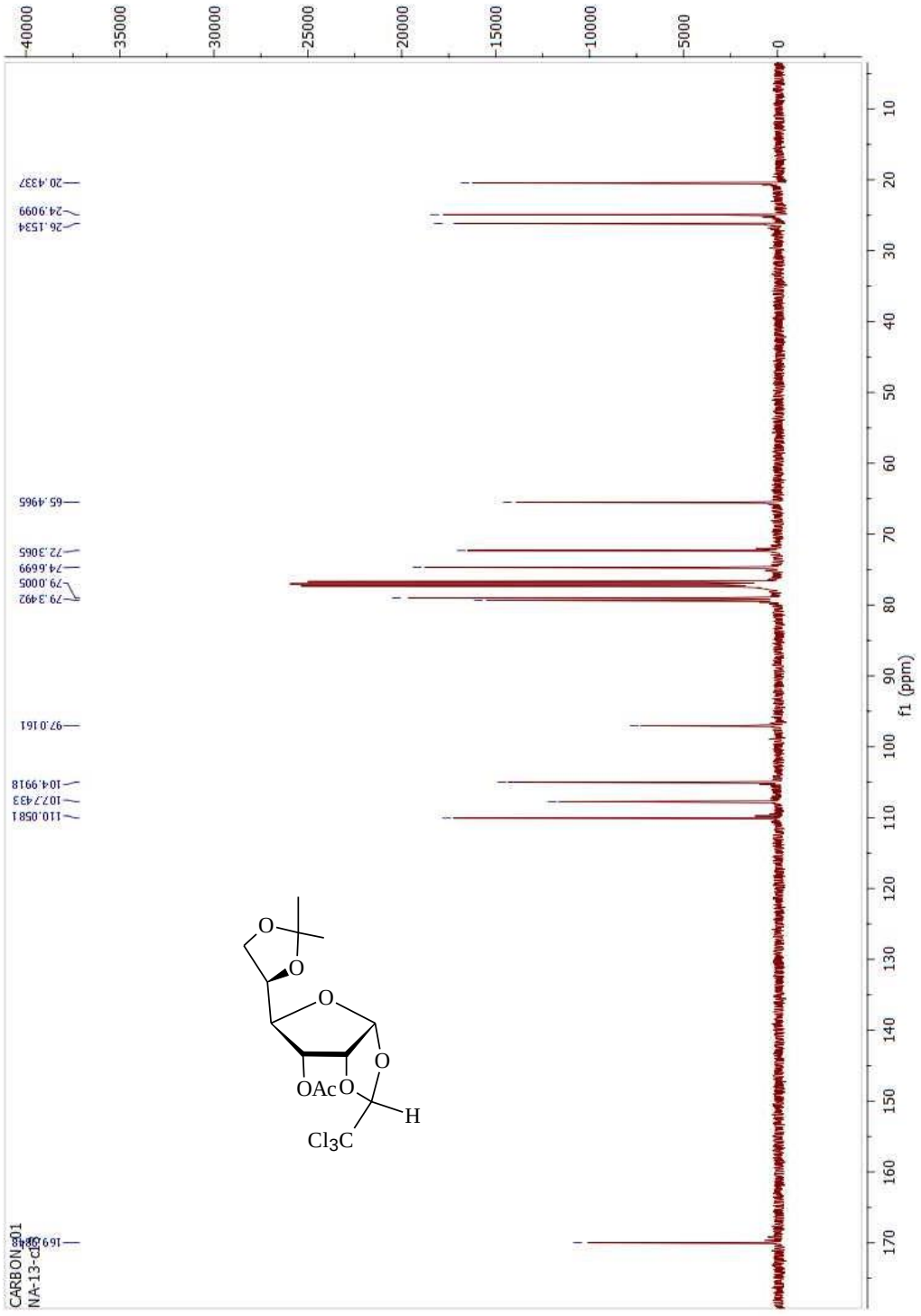
Appendix 5 ^{13}C-NMR spectrum of the 5,6-*O*-Isopropylidene-1,2,3-*O*-orthodichloroethylidene-α-D-gulofuranose (compound **5**)



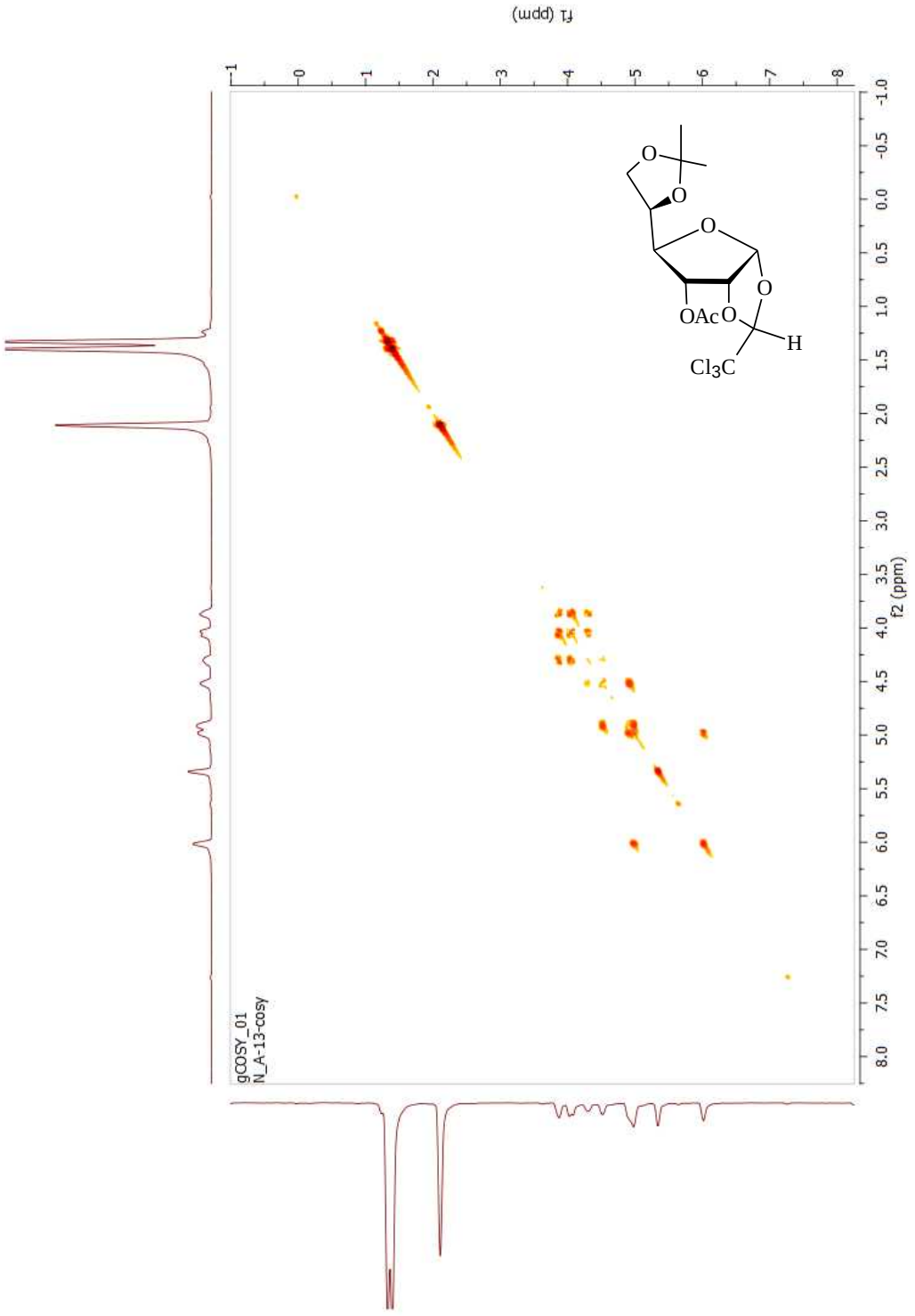
Appendix 6 ^{1}H-NMR spectrum of the 3-*O*-Acetyl-5,6-*O*-isopropylidene-1,2-*O*-(S)-trichloroethylidene-α-D-allofuranose (compound **12**)



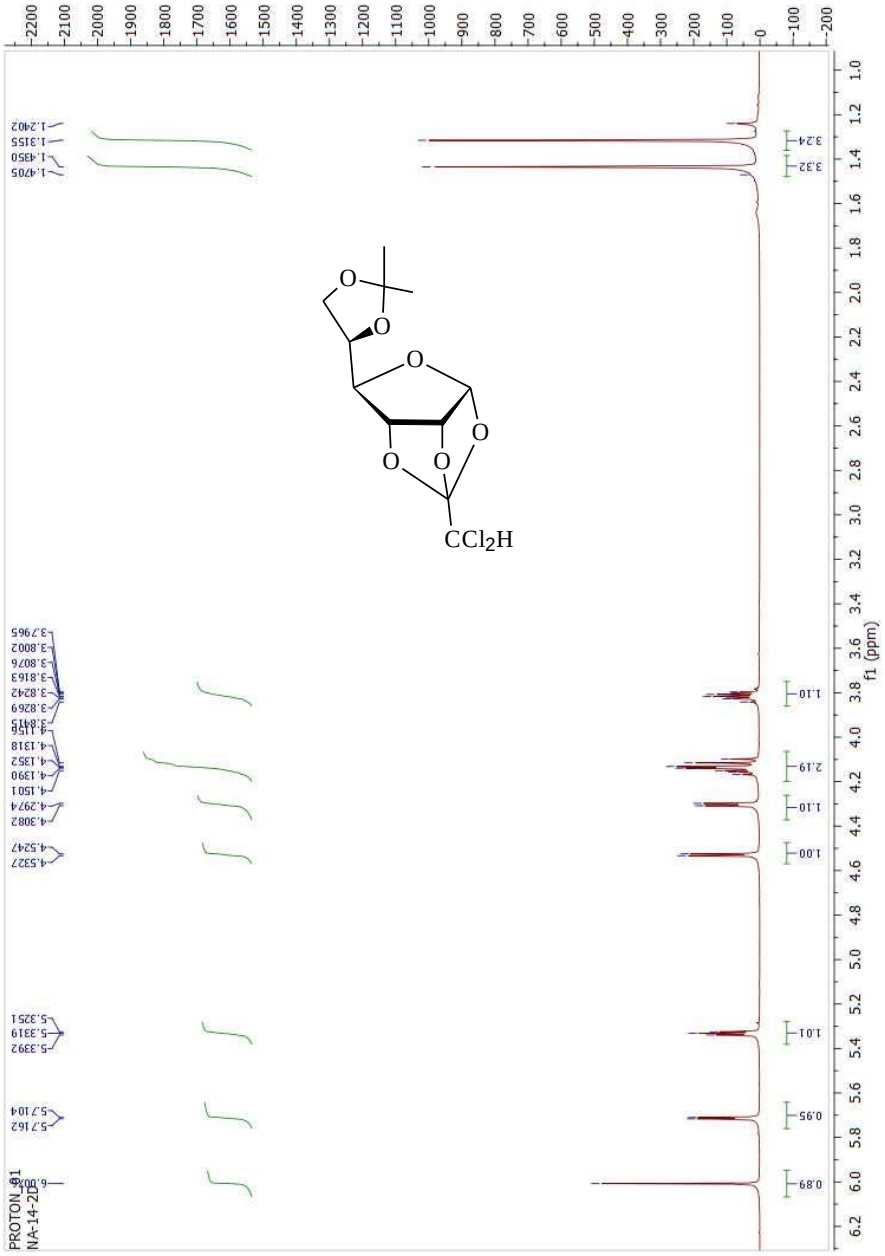
Appendix 7 ^{13}C-NMR spectrum of the 3-*O*-Acetyl-5,6-*O*-isopropylidene-1,2-*O*-(S)-trichloroethylidene-α-D-allofuranose (compound **12**)



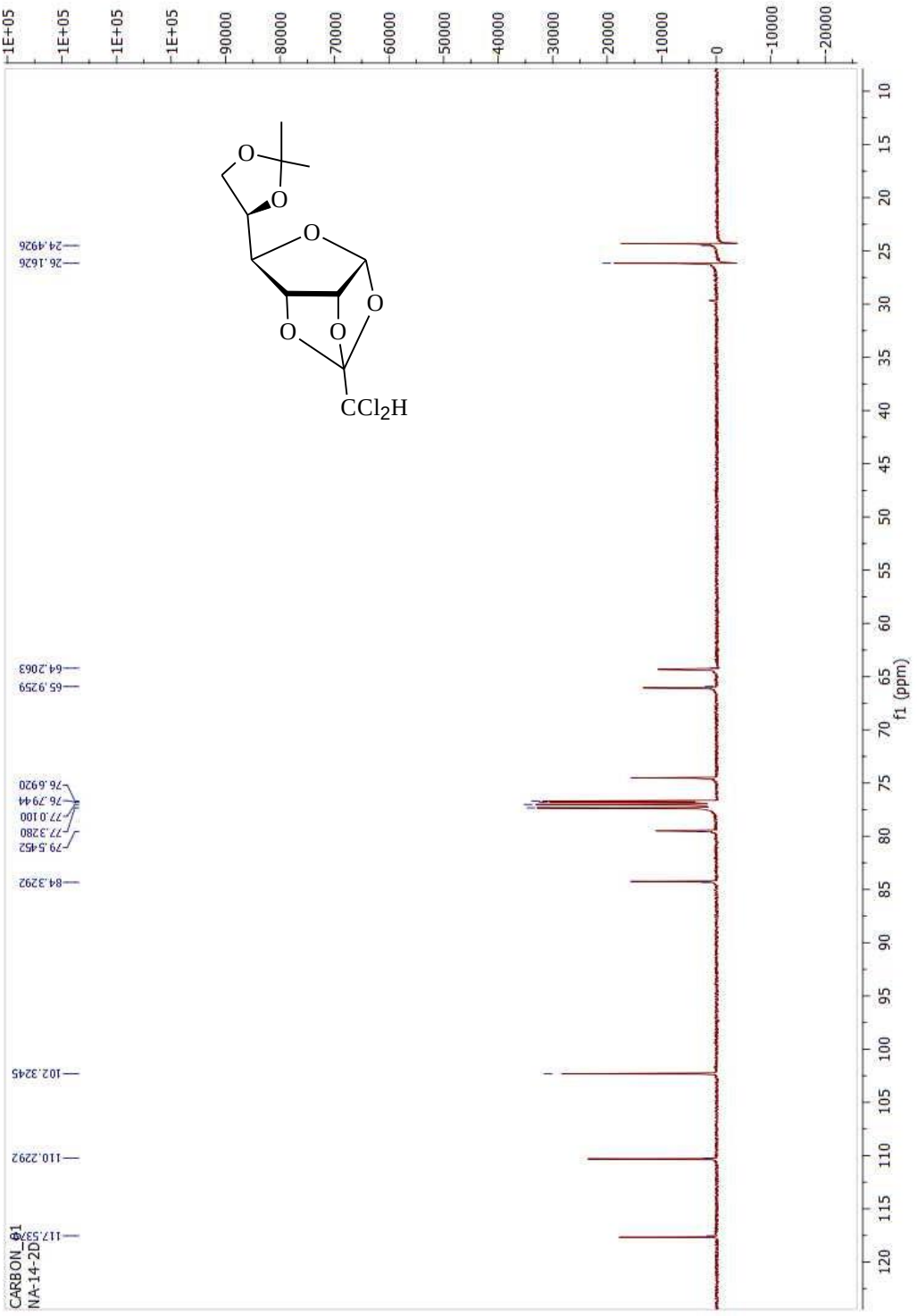
Appendix 8 COSY spectrum of the 3-*O*-Acetyl-5,6-*O*-isopropylidene-1,2-*O*-(S)-trichloroethylidene-α-D-allofuranose (compound **12**)



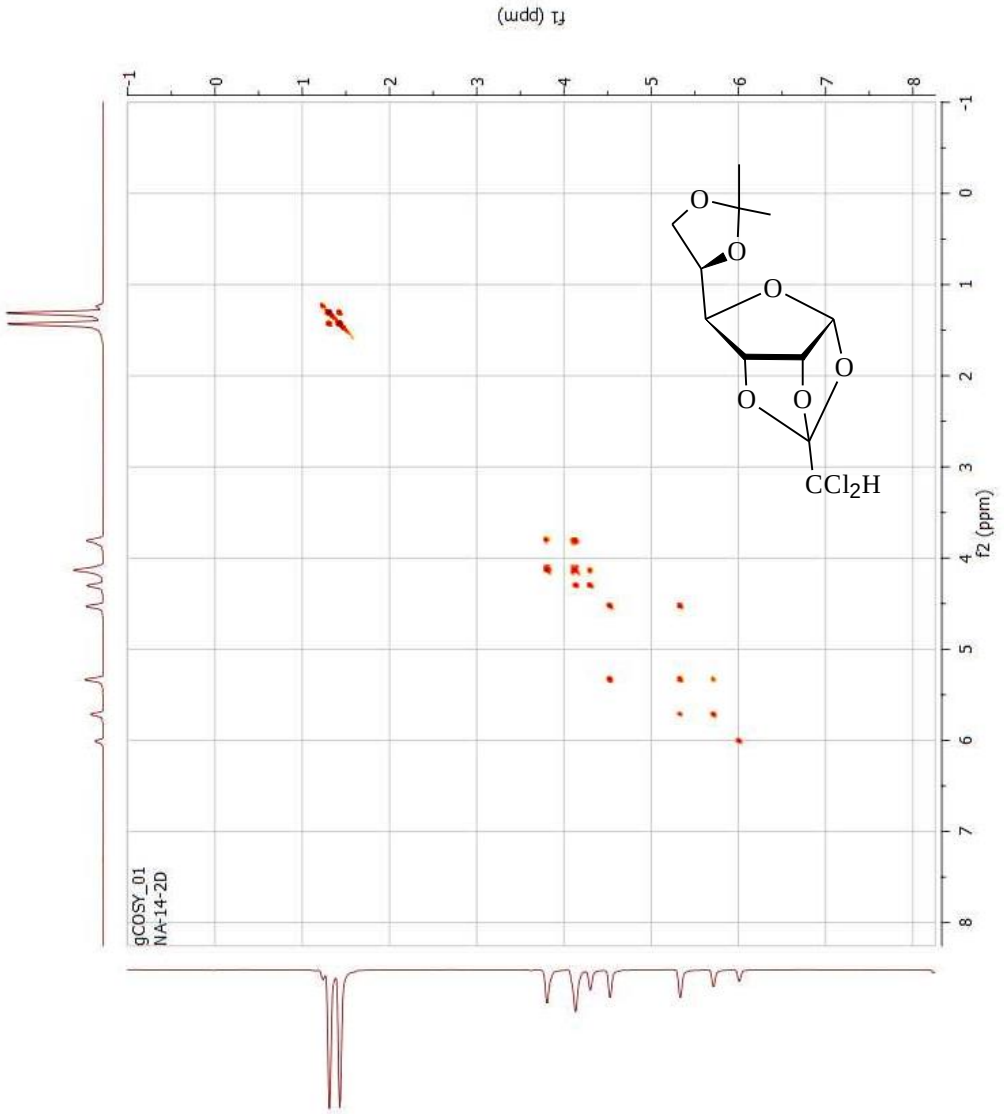
Appendix 9 ^{1}H-NMR spectrum of the 5,6-*O*-Isopropylidene-1,2,3-*O*-orthodichloroethylidene-α-D-allofuranose (compound **13**)



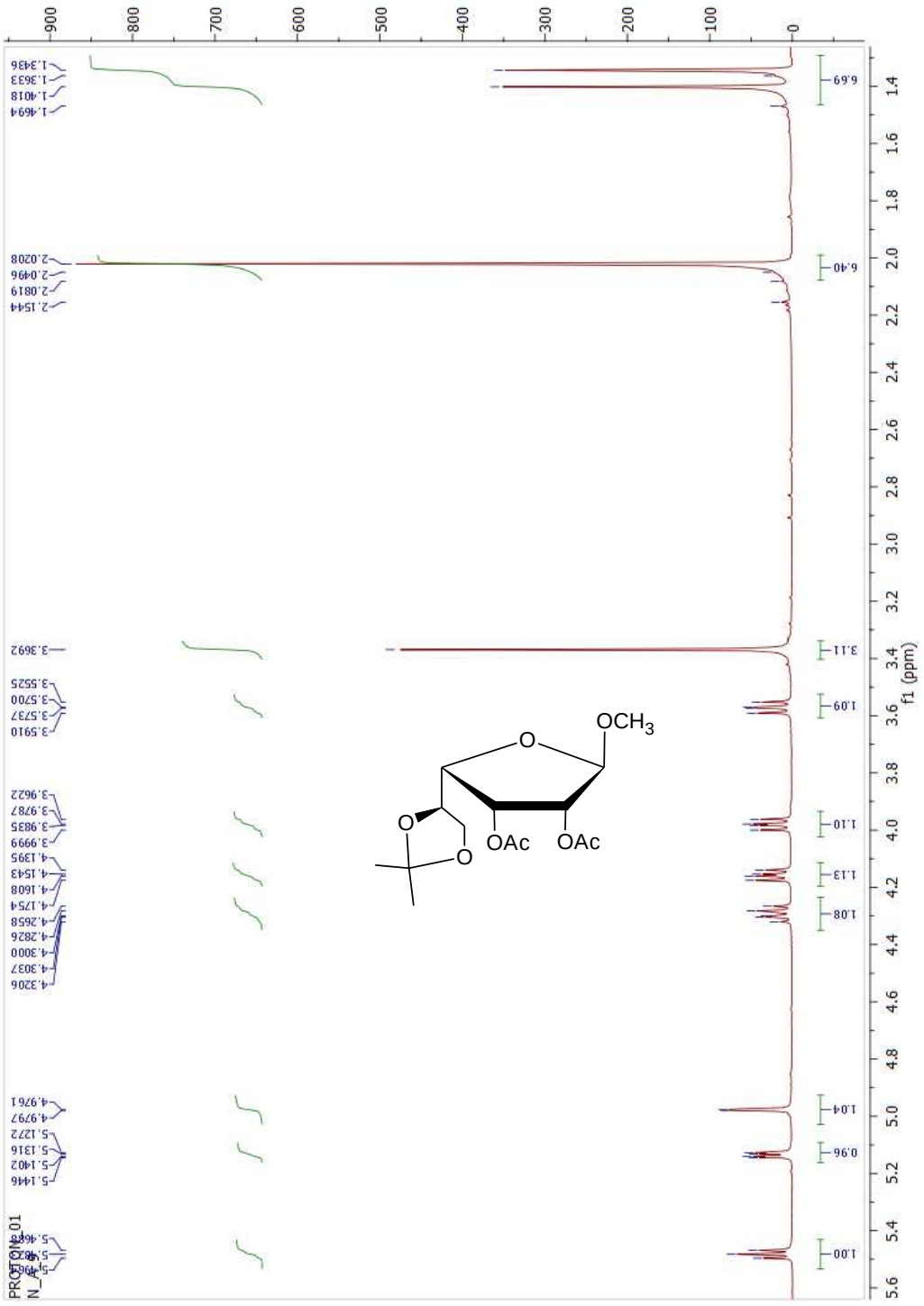
Appendix 10 ^{13}C-NMR spectrum of the 5,6-*O*-Isopropylidene-1,2,3-*O*-orthodichloroethylidene-α-D-allofuranose (compound **13**)



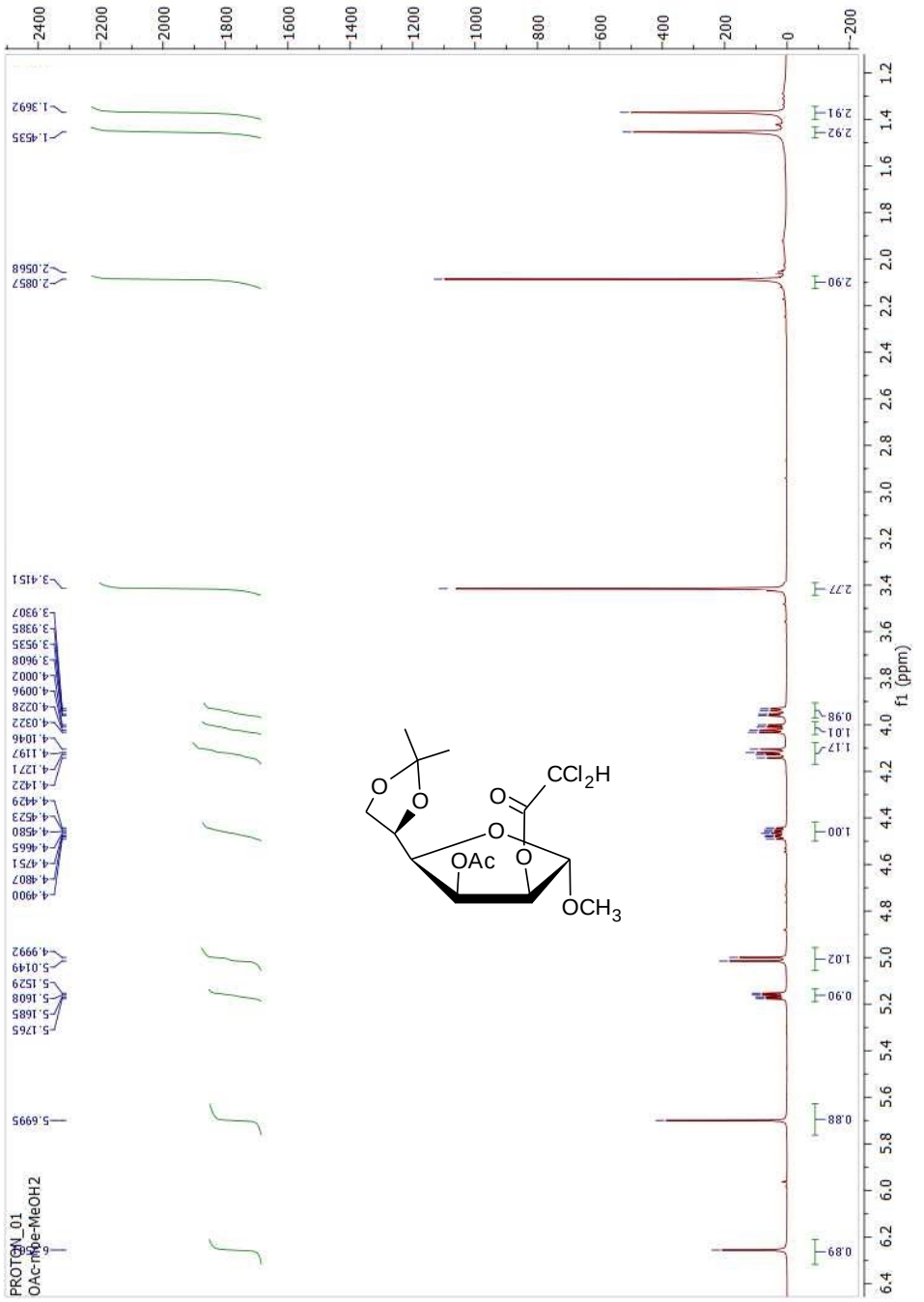
Appendix 11 COSY spectrum of the 5,6-*O*-Isopropylidene-1,2,3-*O*-orthodichloroethylidene-α-D-allofuranose (compound **13**)



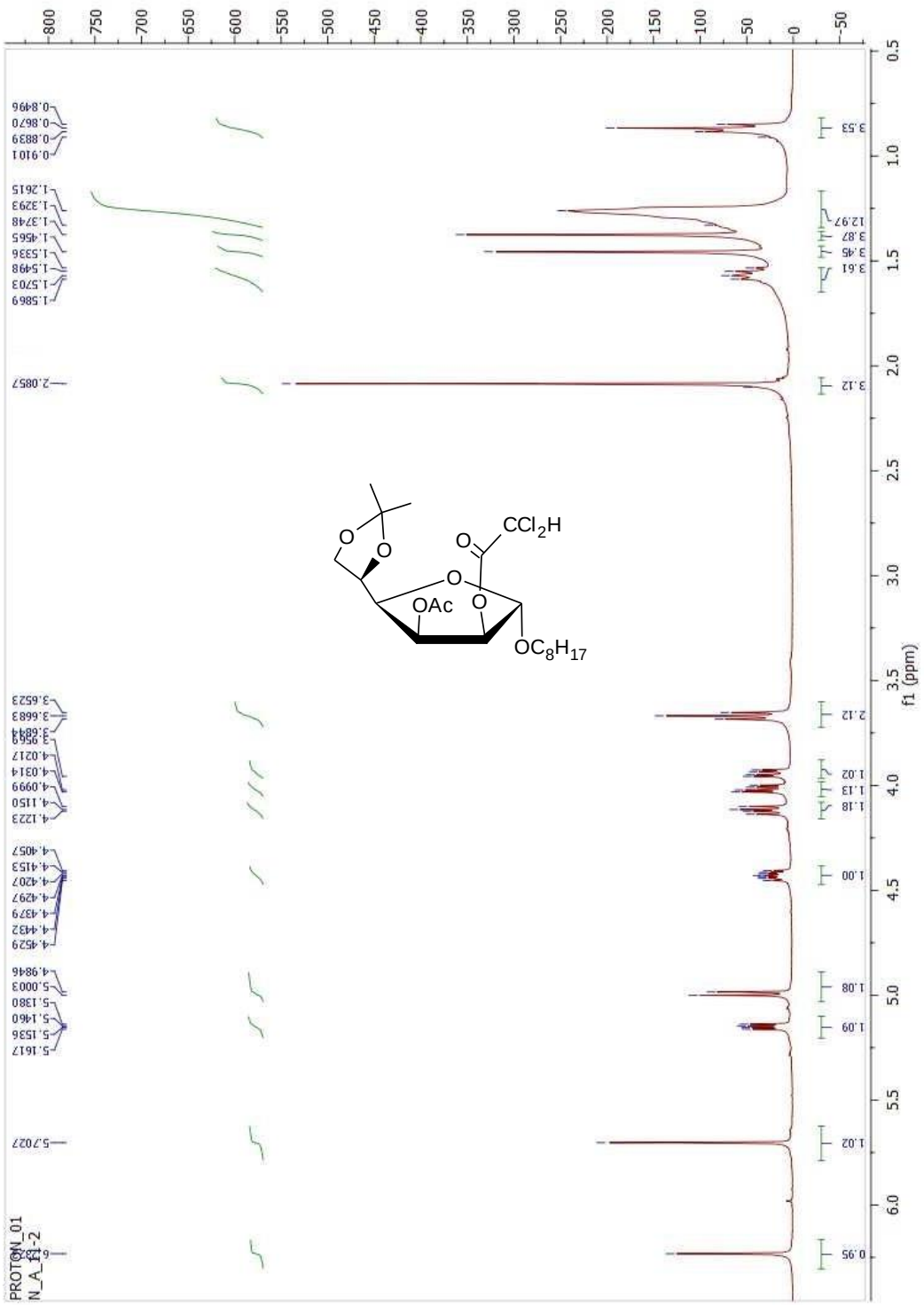
Appendix 12 ^{1}H-NMR spectrum of the Methyl 2,3-*O*-diacetyl-5,6-*O*-isopropylidene-β-D-gulofuranoside (compound **15**)



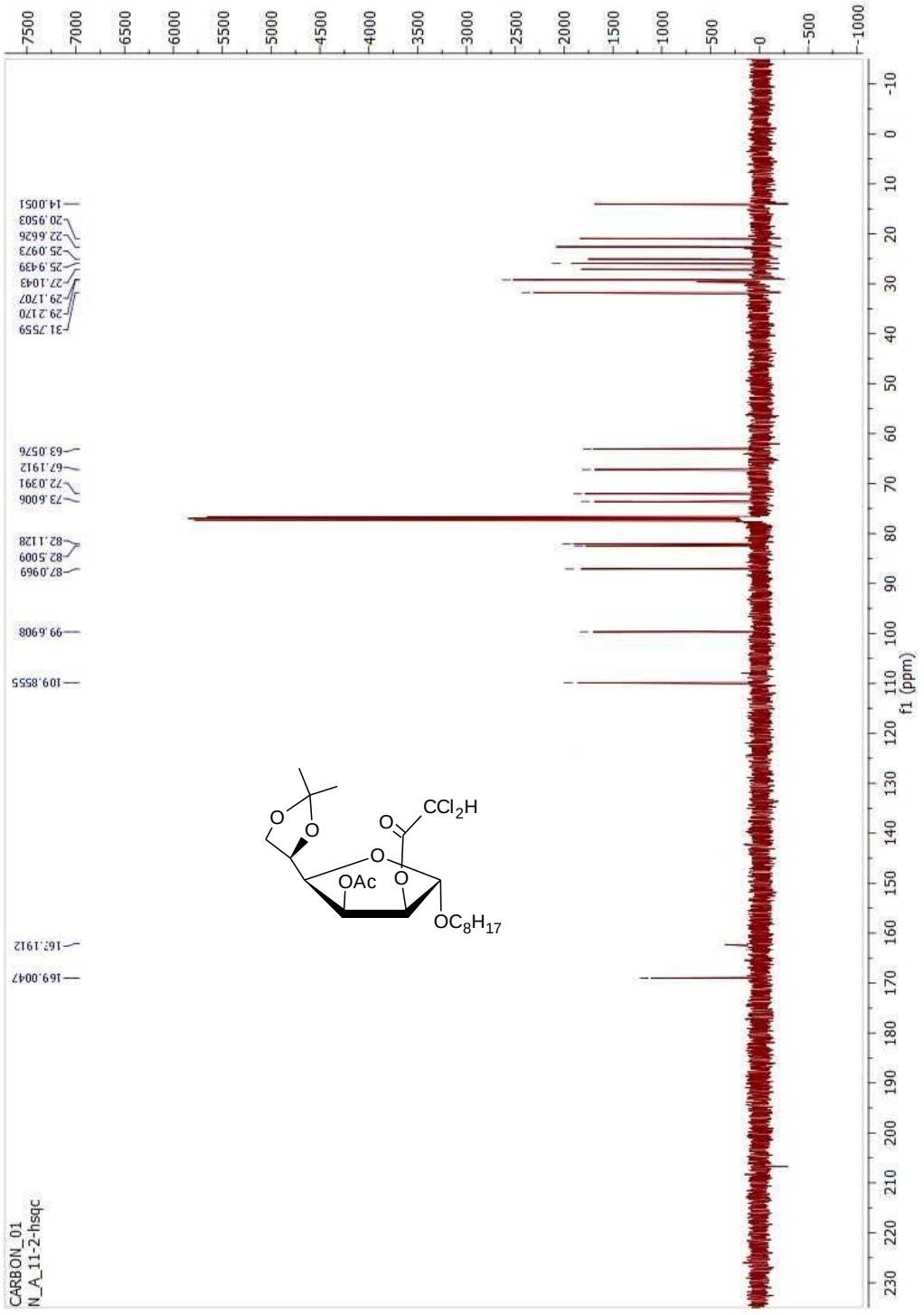
Appendix 13 [1]H-NMR spectrum of the Methyl 2-*O*-dichloroacetyl-3-*O*-acetyl-5,6-*O*-isopropylidene-α-D-mannofuranoside (compound **17**)



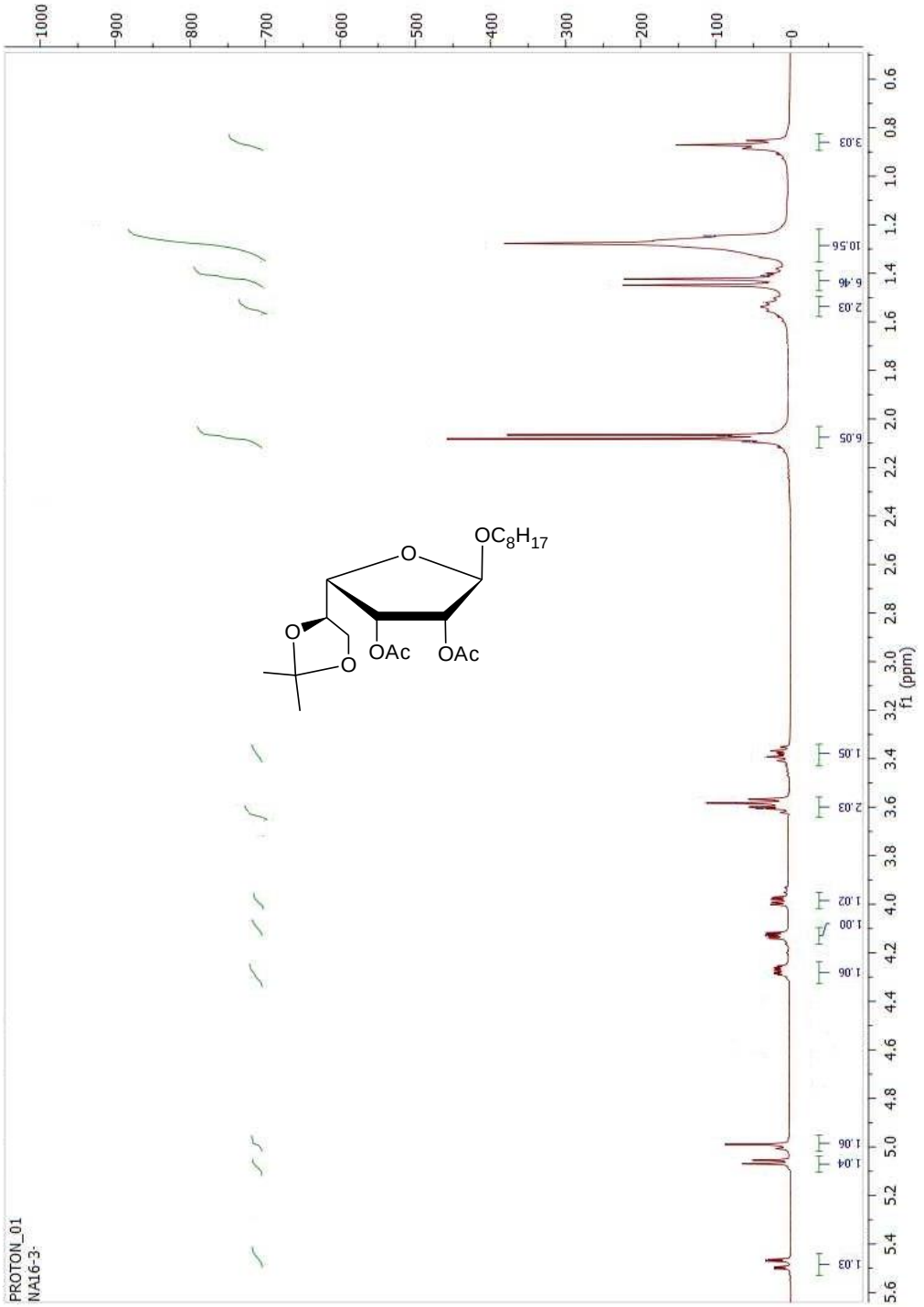
Appendix 14 ^{1}H-NMR spectrum of the Octyl 2-*O*-dichloroacetyl-3-*O*-acetyl-5,6-*O*-isopropylidene-α-D-mannofuranoside (compound **19**)



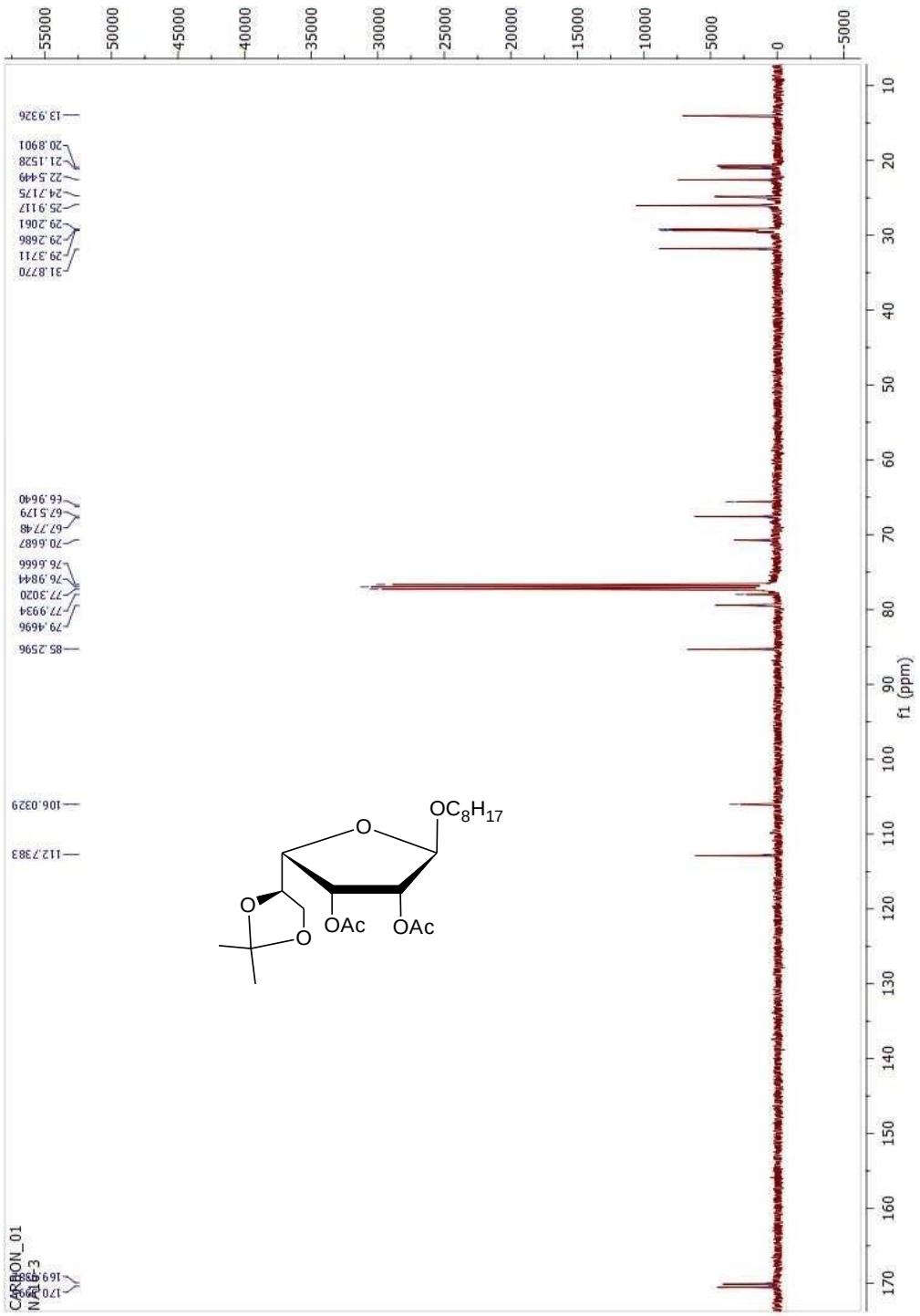
Appendix 15 ^{13}C-NMR spectrum of the Octyl 2-*O*-dichloroacetyl-3-*O*-acetyl-5,6-*O*-isopropylidene-α-D-mannofuranoside (compound **19**)



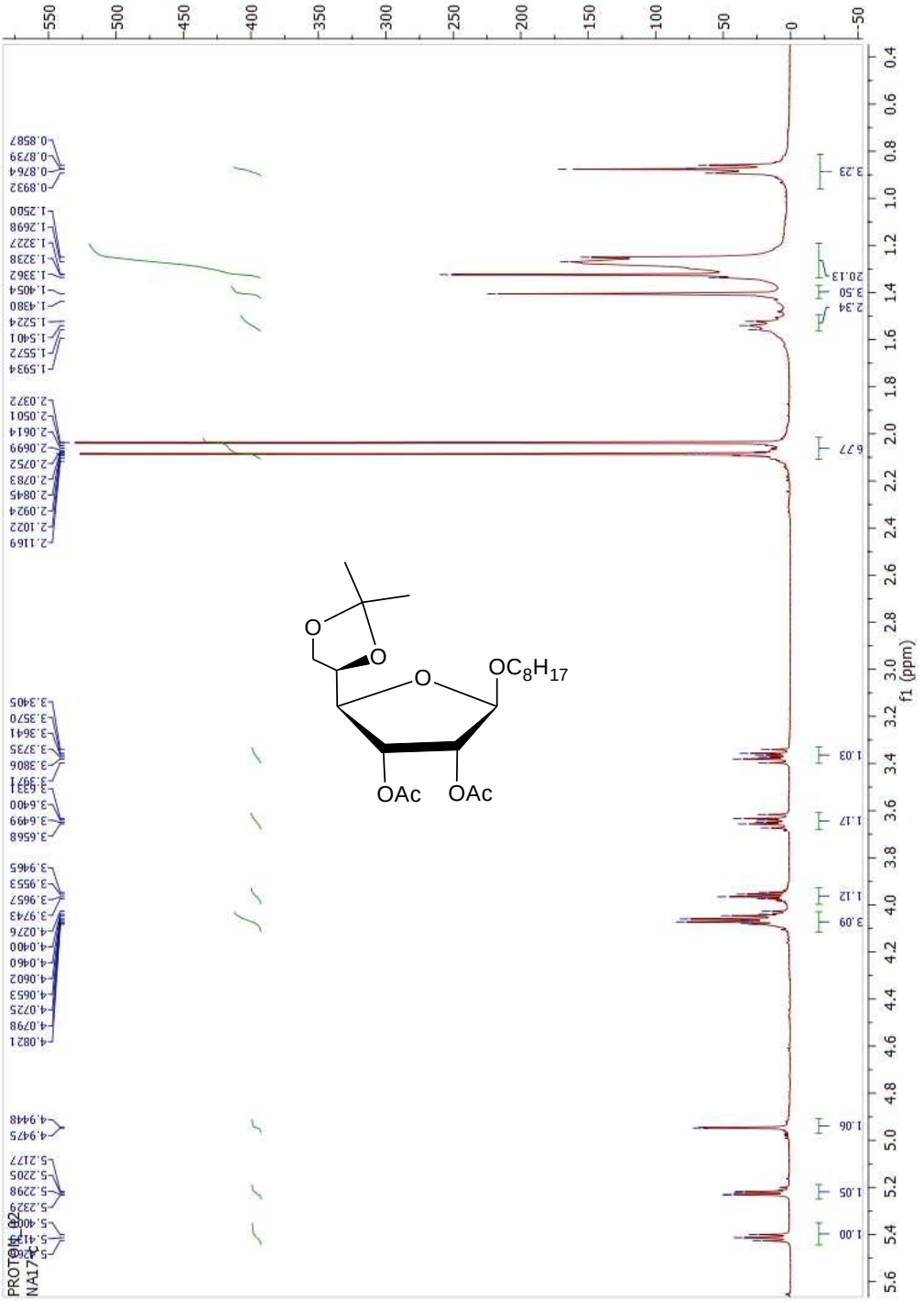
Appendix 16 ^{1}H-NMR spectrum of the Octyl 2,3-*O*-diacetyl-5,6-*O*-isopropylidene-β-D-gulofuranoside (compound **21**)



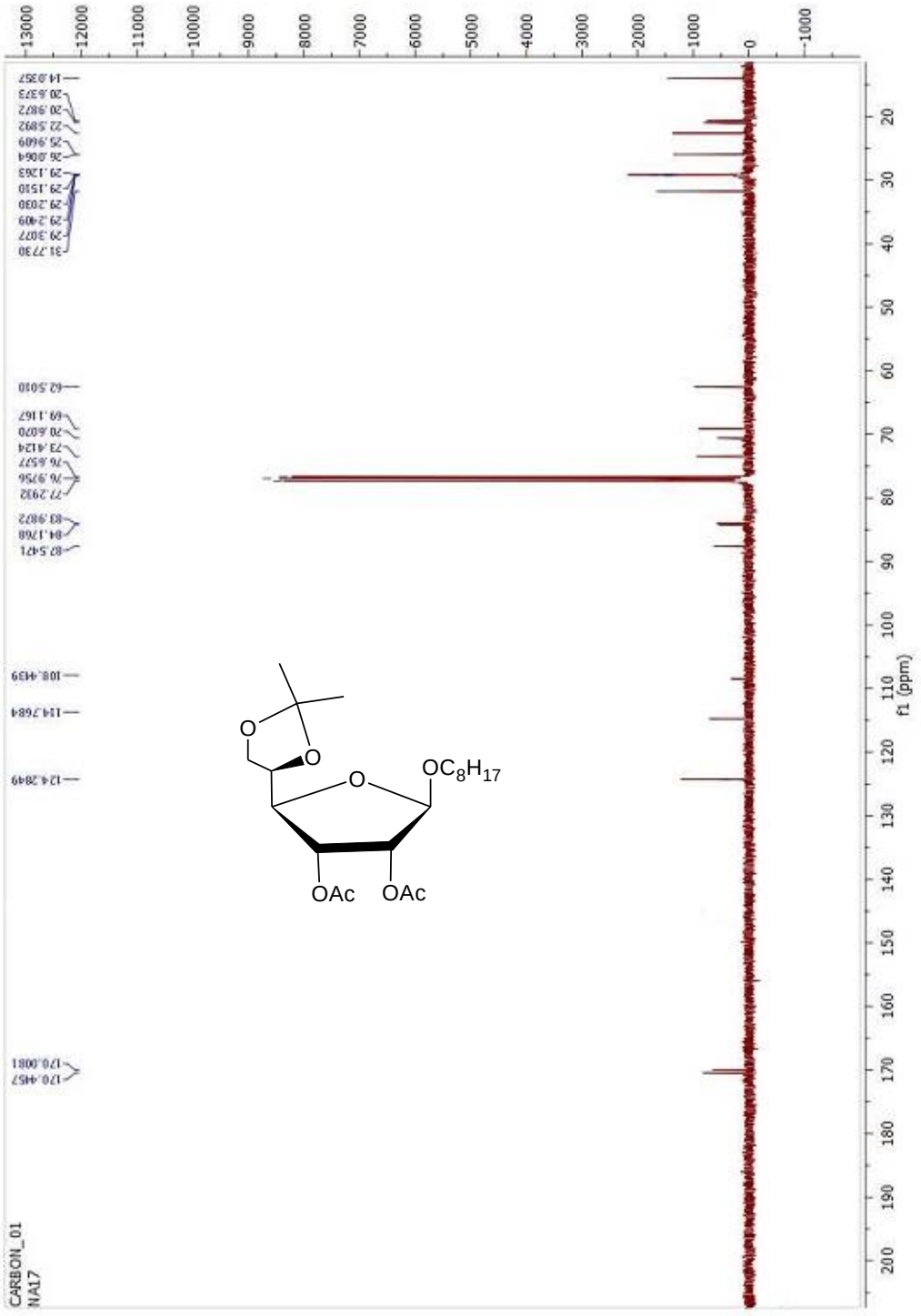
Appendix 17 ^{13}C-NMR spectrum of the Octyl 2,3-*O*-diacetyl-5,6-*O*-isopropylidene-β-D-gulofuranoside (compound **21**)



Appendix 18 [1]H-NMR spectrum of the Octyl 2,3-*O*-diacetyl-5,6-*O*-isopropylidene-β-D-allofuranoside (compound **23**)



Appendix 19 ^{13}C-NMR spectrum of the Octyl 2,3-*O*-diacetyl-5,6-*O*-isopropylidene-β-D-allofuranoside (compound **23**)



Appendix 20 [1]H-NMR spectrum of the Methyl 2,3-*O*-diacetyl-5,6-*O*-isopropylidene-β-D-allofuranoside (compound **25**)