EGE UNIVERSITY INSTITUTE OF NATURAL AND APPLIED SCIENCES

(MASTER OF SCIENCE THESIS)

THE SYNTHESIS OF SOME NITROGEN-CONTAINING SUGAR DERIVATIVES

Pierre Claver MPAWENAYO

Supervisor : Ass. Prof. Dr. Yeşim GÜL SALMAN

Co-Supervisor : Dr. Gökhan KÖK

Chemistry Department

Code of Discipline : 405.02.01
Presentation Date : January 15, 2013

Bornova-İZMİR

2013

Pierre Claver MPAWENAYO tarafından yüksek lisans tezi olarak sunulan "**The Synthesis of Some Nitrogen-Containing Sugar Derivatives**" başlıklı bu çalışma E.Ü. Lisansüstü Eğitim ve Öğretim Yönetmeliği ile E.Ü. Fen Bilimleri Enstitüsü Eğitim ve Öğretim Yönergesi'nin ilgili hükümleri uyarınca tarafımızdan değerlendirilerek savunmaya değer bulunmuş ve **15.01.2013** tarihinde yapılan tez savunma sınavında aday oybirliği/oyçokluğu ile başarılı bulunmuştur.

Jüri Üyeleri: **İmza**

Jüri Başkanı **: ....**

Üye **: ....**

Üye **: ....**

ÖZET

BAZI ŞEKERLERIN AZOT IÇEREN TÜREVLERİNİN SENTEZİ

MPAWENAYO, Pierre Claver

Yüksek Lisans Tezi, Kimya Anabilim Dalı

Tez Danışmanı : Yrd. Doç. Dr. Yeşim GÜL SALMAN

İkinci Danışman : Dr. Gökhan KÖK

Ocak 2013, 59 sayfa

Bu çalışmada D-galaktoz ve D-arabinoz, başlangıç şekerleri olarak kullanıldı. Deneysel çalışmalar, bu basit şekerlerin azot-içeren şeker türevlerinin sentezleri üzerinde oluşturuldu.

D-arabinoz'un susuz kloralle tepkimesi sonucu sırasıyla 1,2-*O*-trikloroetiliden-α-D-arabinofuranoz hazırlandı. 1,2-*O*-trikloroetiliden-α-D-arabinofuranoz'ile *p*-toluensülfonilklorürün tepkimeye sokulmasıyla 1,2-*O*-trikloroetiliden-α-D-arabinofuranoz'un tosil türevleri elde edildi ve daha sonra bu tosil türevleri nücleofilik yerdeğiştirme tepkimesi ile azit formuna dönüştürüldü. Elde edilen azit bileşikleri, ilgili amino-şeker türevlerini elde etmek için, indirgeyici reaktif olarak trifenilfosfin ile reaksiyona sokuldu.

Benzer bir şekilde, aynı sentez zincirinin kullanılmasıyla 1,2-*O*-trikloroetiliden-α-D-galaktoz'un amino şeker türevleri de elde edildi. Ek olarak, 1,2-*O*- trikloroetiliden-α-D-galaktofuranoz'un ditosil türevi ve diazit türevi de sentezlendi. Bu diazit türevinden diamino yapısının elde edilmesi için deneysel çalışmalar hala devam etmektedir.

Ayrıca trisiklik ortoamit yapısının oluşumu için 1,2-*O*-trikloroetiliden-α-D-arabinofuranoz'un amino türevinin halka kapanması reaksiyonu gerçekleştirildi.

Anahtar Kelimeler: Amino şekerler, Antimikrobiyal aktivite, Kloraloz, Trikloroetiliden asetal, Ortoamit.

ABSTRACT

THE SYNTHESIS OF SOME NITROGEN-CONTAINING SUGAR DERIVATIVES

MPAWENAYO, Pierre Claver

MSc in Department of Chemistry

Supervisor : Ass. Prof. Dr. Yeşim GÜL SALMAN

Co-Supervisor : Dr. Gökhan KÖK

January 2013, 59 pages

In this study, D-galactose and D-arabinose were used as starting sugars. The experimental works were constituted on the synthesis of nitrogen-containing sugar derivatives of these simple sugars.

1,2-*O*-trichloroethylidene-α-D-arabinofuranose was prepared from the reaction of D-arabinose and anhydrous chloral. Tosyl derivatives of 1,2-*O*-trichloroethylidene-α-D-arabinofuranose were obtained by the reaction of this compound with *p*-toluenesulfonylchloride and then, these tosyl derivatives were converted to the azide form by following nuclephilic substitution reaction. Obtained azide derivatives were reacted with triphenylphosphine as reducing agent in order to get the related amino-sugars derivatives.

Similarly, amino sugar derivatives of 1,2-*O*-trichloroethylidene-α-D-galactose were also obtained by using the same synthetic pathway. Additionally, ditosyl and diazide derivatives of 1,2-*O*- trichloroethylidene-α-D-galactofuranose were also synthesized. The experimental study is still going on in order to get the diamino structure formation from these diazide derivatives.

Furthermore, ring closure reaction of the amino derivative of 1,2-*O*-trichloroethylidene-α-D-arabinofuranose for the formation of tricyclic orthoamide structure was also accomplished.

Keywords: Amino sugars, Antimicrobial activity, Chloralose, Trichloroethylidene acetal, Orthoamide.

ACKNOWLEDGEMENT

I am heartily thankful to my supervisor, Ass. Prof. Dr. Yeşim GÜL SALMAN, whose encouragement guidance and considerable contributions were so valuable for me from the initial to the final level of the study. I learned from her what means the word "Carbohydrate". I am also grateful to Dr. Gökhan KÖK for enlightening me with his deep knowledge and experience. This thesis would not have been possible unless their precious suggestions and supports.

I offer my sincerest gratitude to Prof. Dr. Levent YÜCEER for his advices for interpretation of NMR spectra. He has supported me thought my thesis with his knowledge, informative contributions and suggestions.

I specially thank to PhD. student Meryem KORUYUCU for her great encouragement recommendations and patience have been invaluable for me.

I would like to thank Uzm. Salih GÜNNAZ for not only his support to obtain NMR spectroscopic data, but also his help. Words alone cannot express the thanks I owe to him for his valuable suggestions and encouragements.

I also wish to thank my dear wife Marie Thérèse HATEGEKİMANA for her patience, supportive behaviours, collaborations and assistance.

Finally, I would like to thank and present my gratitude to my family who have encouraged and supported me during my studies from the beginning to the end.

Pierre Claver MPAWENAYO

CONTENTS

Pages

CONTENTS (continued)

Pages

CONTENTS (continued)

Pages

LIST OF FIGURES

LIST OF FIGURES (continued)

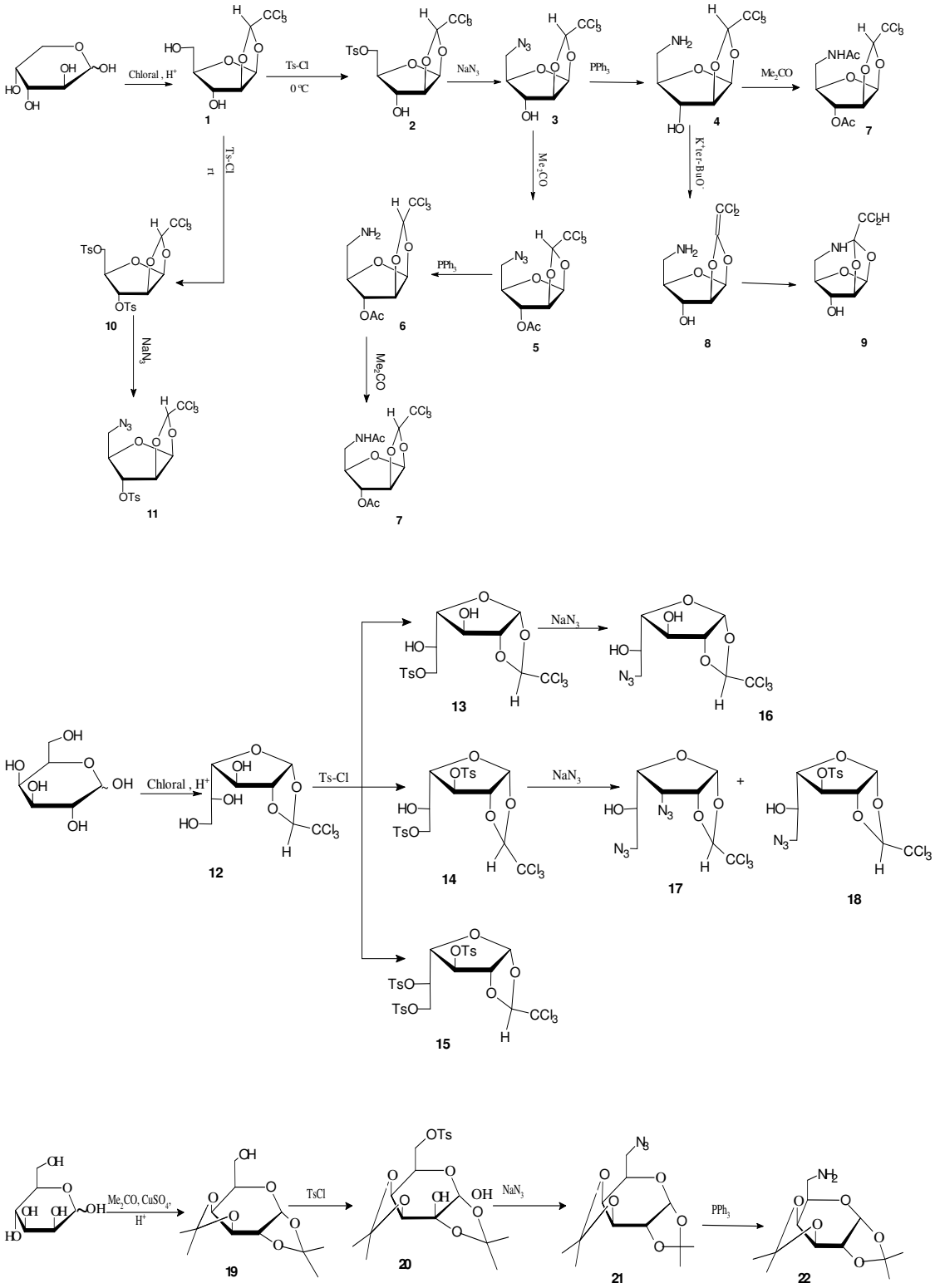
Figures Pages

LIST OF TABLES

LIST OF TABLES (continued)

LIST OF SCHEMES

GRAPHICAL ABSTRACT



ABBREVIATIONS

Abbreviation	Explanation
Ac	Acetyl
bp	Boiling point
DMF	*N,N*-Dimethylformamide
DMSO	Dimethylsulfoxide
equ	equivalent
Fig	Figure
IR	Infrared Spectroscopy
h	Hours
HMPA	Hexamethylphosphoramide
H_2SO_4	Sulfuric acid
mp	Melting point
Me	Methyl
mL	Millilitre
Min	Minute
mol	Mole
mmol	Millimole
MS	Molecular sieve
NaN_3	Sodium azide
NMR	Nuclear Magnetic Resonance Spectroscopy
Pyr	Pyridine
RT	Room temperature

TLC	Thin layer chromatograhy
THF	Tetrahydrofurane
PPh_3	Triphenylphosphine
Tol	Toluene
Ts	Para-toluene sulfonyl “tosyl”

1. INTRODUCTION

Nitrogen including derivatives of carbohydrates are very important since theses derivatives are not only useful by their biological activities but also as starting compounds in syntheses of many new products (Reist et al., 1960).

These derivatives bearing an amino substituent in different ring positions on the sugar skeleton are called amino sugars (Csuk, 1985; Ermolenko et al., 1999; Juan, 2003; Sun, 2006) and are known constituents of several bio-active compounds such as antibiotics and biopolymers (Williams, 1972; Takemoto, 2002; Nishiyama, 2005). On the cell surface, amino sugars play a key role as receptors for proteins and enzymes, and they have been shown to interact with either RNA or the backbone phosphate of DNA (Kim et al., 2002).

1.1 Amino Sugars

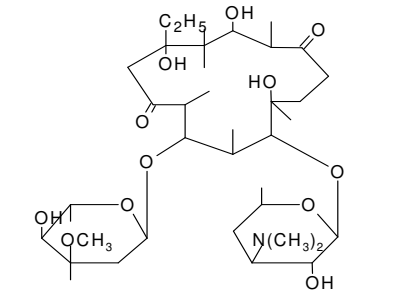
Amino sugars are aldoses or ketoses which have a hydroxyl group replaced by an amino group at any position other than the anomeric carbon. These glycosylamines are named from the sugar from which they are derived by use of the enumerated term “aminodeoxy” (Guthrie and Honeyman, 1968).

Figure 1.1 Some Aminodeoxy-Sugars

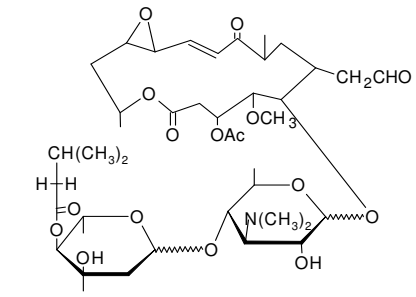
2-Amino-2-deoxy–D-glucose (D-glucosamine or chitosamine 1, R=H) is abundant in nature appearing in particular in the polysaccharide chitin as its *N*-acetyl derivative (1, R=Ac).

Several other 2-amino-2-deoxy-sugars also occur, 2-amino-2-deoxy-D-galactose (2) being one of the more common since it is a constituent monosaccharide unit of chondroitin sulphate, a polysaccharide found in mammalian tissue and cartilage.

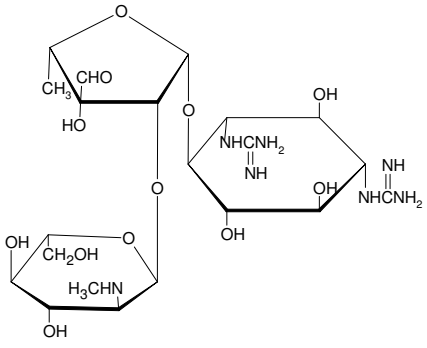
Many antibiotics, e.g. erythromycin (3) and carbomycin (magnamycin, 4), streptomycine (5), have amino-sugars as constituents, and at least one amino-sugar, nojirimycin (6), itself shows antibiotic activity (Guthrie and Honeyman, 1968).



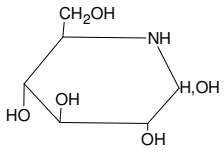
Erythromycin (3)



Carbomycin (magnamycin) (4)



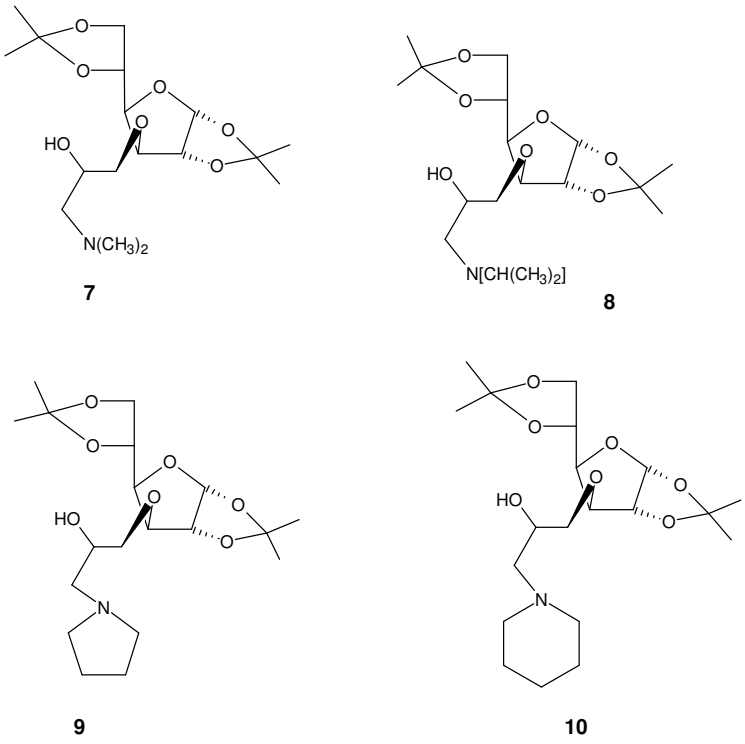
Streptomycin (5)



Nojirimycin (6)

Figure 1.2 Some Antibiotics Amino-Sugars

A number of synthesized aminoalkyl-sugars have also been reported in the literature. Some Indian researchers synthesized low molecular weight sugar derivatives with aminoalkyl appendages known as potent immunomodulators. One such compound, therafectin (7), a candidate drug for the rheumatoid arthritis, and its analogues are known to be associated with antifungal (8), antiparasitic (9) and antiviral (10) (Khan et al., 2001).



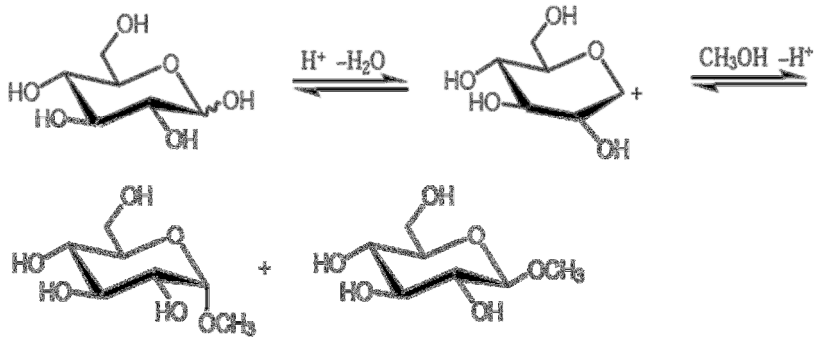
Figuure 1.3 Some Synthesized Aminoalkyl-Sugars

The synthesis of amino derivatives is generally achieved by a simple sequence involving protection of primary hydroxyl groups, nucleophic substitution and reductions.

1.2. Acetals

The study of carbohydrate acetals is based on the reactivity of the various hydroxyl groups within the sugar form.

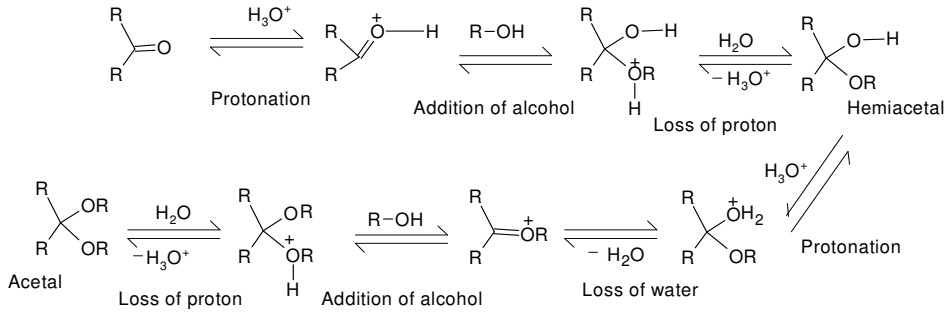
For D-glucopyranose for example, of the five hydroxyl groups, only the anomeric hydroxyl group is unique, being part of a hemiacetal structure. All of the other hydroxyl groups show the reactions typical of an alcohol (Fischer, 1893)



Scheme 1.1 Synthesis of -α-and β- Methyl Acetal Glucopyranoside

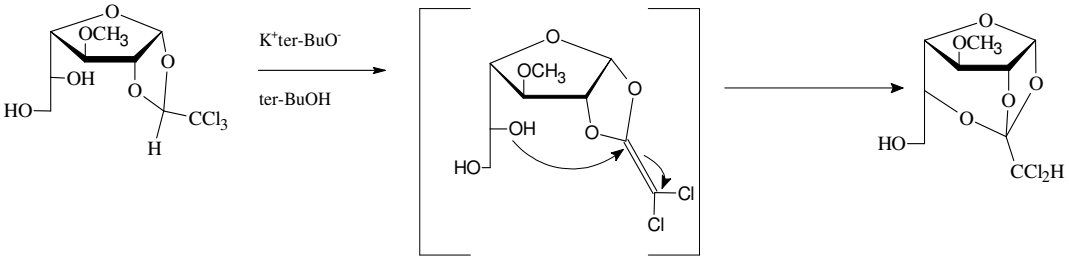
These methyl acetals, methyl-α-and β-glucopyranoside, offered a form of protection to the anomeric center and allowed for the useful synthesis of other products (Jarowicki and Kocienski, 2000).

Upon reaction of the carbonyl group within a free sugar with alchols in acidic conditions the hemiacetal forms and then this hemiacetal reacts with a second molar equivalent of the alcohol to produce an acetal. Acetals have two -OR groups attached to the same carbon atom (Solomons, 1996).



Scheme 1.2 Mechanism of Acetal Formation

Although acetals can be hydrolysed to aldehydes and ketones in aqueous acid, they are stable in basic conditions. During hydrolysis no changes are observed in the confugaration of carbon atom (Yüceer, 1978; Belder, 1965). Because of this properties, cyclic acetals are very important protecting groups for basic and neutral reaction conditions. However, under strongly basic conditions e.g potassium *tert*-butoxide, trichloroethylidene acetals can form ketene acetals and when the sugar stereochemistry permits, tricyclic orto esters can also be formed (Salman et al., 1994).



Scheme 1.3 Mechanism of Ortoesters Formation

1.3. Trichloroethlidene Acetals (chloraloses)

Chloraloses are furanose-type cyclic acetals of pentoses and hexoses containing to 1,2-*O*-trichloroethylidene ring. Heffter Arthur firstly synthesized chloralose in 1889 from the condensation of D-glucose and trichloroacetaldehyde (chloral) in the presence of an acid catalyst (Heffter, 1889).

A mixture of two diastereomers was obtained from glucose which *α*-glucochloralose (*α*-chloralose) and *β*-glucochloralose (*β*-chloralose). If the trichloromethyl (**CCl_3**) substituent has endo orientation, this compound is called *α*-chloralose and exo orientation is *β*-chloralose (**Fig.1. 4**). (*α*-) and (*β*-) terms show the configuration on the acetal carbon. Trichloroethylidene rings are highly stable in acidic and mildly basic conditions (Ay et al., 2007) but they are unstable in strongly basic condition such as potassium *tert*-butoxide. Cyclic ketene acetal occurred by HCl elimination from trichloroethylidene ring of chloralose with alkoxide (strong base) (Salman et al., 1994; Salman et al., 2004) and removing of

trichloroethylidene group can be accomplished by hydrogenation reaction using of Raney nickel, followed by acidic hydrolysis (Forsén et al., 1965).

Trichloroethylidene acetals are potential biologically active compounds; so *α*-chloralose (1,2-*O*-(*R*)-trichloroethylidene-*α*-D-glucofuranose) is a hypnotic drug has been used as an anesthetic agent in laboratory animals (Zosimo-Landolfo and Tronchet, 1999). It also was used in humans until the early part of the twentieth century (Krasowski, 2003). Used as a commercial drug *α*-chloralose is also widely used in bird repellent, rodenticide, neuroscience and veterinary medicine as an anesthetic and sedative (Forsén et al., 1965; Zosimo-Landolfo et al., 1999).

Surprisingly, Overton found that anesthetic differences between *α*-chloralose and its structural isomer *β*-chloralose were hard to explain. The phenomena of narcosis with *α*-chloralose are not very easy to interpret. *β*-chloralose, which is only very slightly soluble in water in most solutions, has no narcotic effect (**Fig.1.4**). It has been characterized as a molecule possessing potent central nervous system activity, and has been evaluated in human and animal models, for its therapeutic properties (Segev et al., 2006; Aburto-Luna et al., 2008).

α-Chloralose (anaesthetic) β-Chloralose (not anaesthetic)

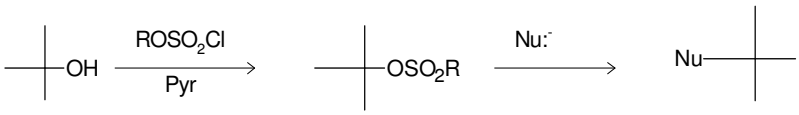
Figure 1.4 Molecular Structures of α-Chloralose and β-Chloralose

In addition, due to its well-known anesthesia effects, arabinochloralose has been used as an intermediate compound for the development of new anti-tuberculosis drugs in pharmaceutical research (Sanchez et al., 2000). *Spiro*-endoperoxide chloraloses were synthesized and investigated in regard to antimicrobial activity against some microorganisms (Yenil et al 2008; Çetin et al.,

2005). Then trichloroethylidene asetals are not used mainly as protecting group but because of their interesting biological activities.

1.4. Sulfonates

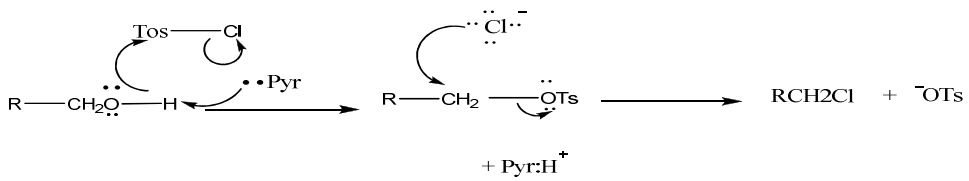
This group of esters is characterized not at all by its protection of hydroxyl group but, rather, by its activation of the group towards nucleophilic substitution i.e the very great importance of sulfonate esters in carbohydrate chemistry comes from the excellent "leaving properties" of sulphoxy goups in nucleophilic displacement reactions (Ferrier and Collins, 1972).



Scheme 1.4 Nucleophilic Substitution of Sulfonate Esters

Sullfonates are stable toward mild acids and mildly basic conditions, but are cleaved with aqueous alkali. The sulfonates are reconverted to the alcohols by treatment with sodium amalgam or Raney Nikel. Tosylate may be cleaved photolytically in the presence of methoxide to give alcohols (Ferrier and Collins, 1972).

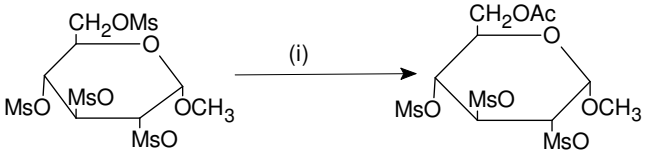
In this group, there are three common sulfonates: ***Tosylate***; (4-toluenesulfonate), ***Mesylate***; (methanesulfonate) and ***Triflate***; (trifluoromethanesulfonyl chloride and methanesulfonyl choride) or trifluoromethanesulfonic anhydride. Sulfonate esters of polyhydroxyl compounds give S_N2 reactions by nucleophiles:



Scheme 1.5 S_N2 Reactions of Sulfonate Esters

At lower temperatures, a tosylate is formed from the reaction of *p*-toluenesulphonyl chloride and an alcohol. The new bond is formed between the toluensulphonyl group and the oxygen of the alcohol. At higher temperatures, the chloride anion can displace the –OTs group, which is an excellent leaving group, to form an orgonochloride.

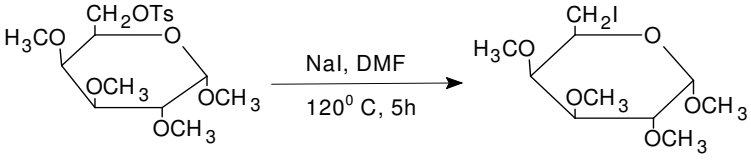
Sulfonates are usually prepared by use of acid chloride in cold pyridine and under these conditons the reagent show marked selectivity for primary hydroxyls group (Ferrier and Collins, 1972). But it could be said that because of stereochemistry of carbohydrates, steric effects are very important as much as the degree of hydroxyl groups of sugar. As an example 6-sulfonate ester can react with nucleophiles very easily (Rodd, 1967).



(i) KOAc, AcOH, Ac_2O, reflux, 1h 95%

Scheme 1.6 An Example of Nucleophilic Reaction of 6-Sulfonate Ester

However in the galactopyranose derivative, 6-sulfonates esters could not easily react in the S_N2 reactions because of the interaction of the substituents in the C-4 axial position. An axial substituent at C-4 is capable of exerting a rate-retarding effect upon the reaction, as is shown by the slow conversion of methyl 2,3,4-tri-*O*-mesyl-6-*O*-toluene-*p*-sulphonyl-α-D-galactopyranoside into its 6-deoxy-6-iodo-derivative (Nad Karni and Williams, 1965).



35% conversion

Scheme 1.7 C-6-OTs Nucleophilic Substitution Reaction of Galactopyranoside

In the galactopyranoside the approach path of nucleophile X^- will be collinear with the C-6-OTs bond and will be subjected to interference from group A. Since in the galacto-compound, this is a methoxy group, its interaction with X^- will be greater than it would be in its isomers gluco-series where it is a hydrogen atom (Nad Karni and Williams, 1965).

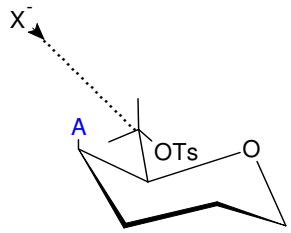
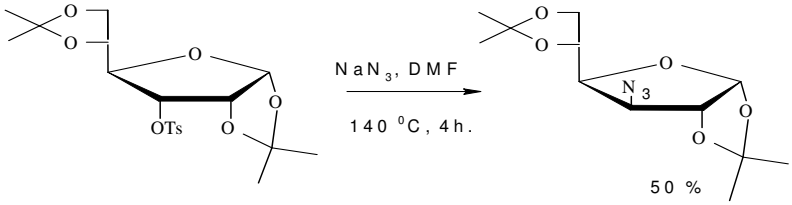


Figure 1.5 Displacement Reactions on Pyranoid rings

Generally displacement reactions on the pyranoid rings are more difficult than displacement reactions on the furanoid rings. At pyranoid rings, during the time from the ground state to the transition state, the great bending tension is observed among non bonding substituents in addition to unfavorable interactions. Whereas furanoid rings have a bending tension in any case but it is not observed extra tension in transion state. Because of this, the displacement reactions are more easily formed on furanoid rings.

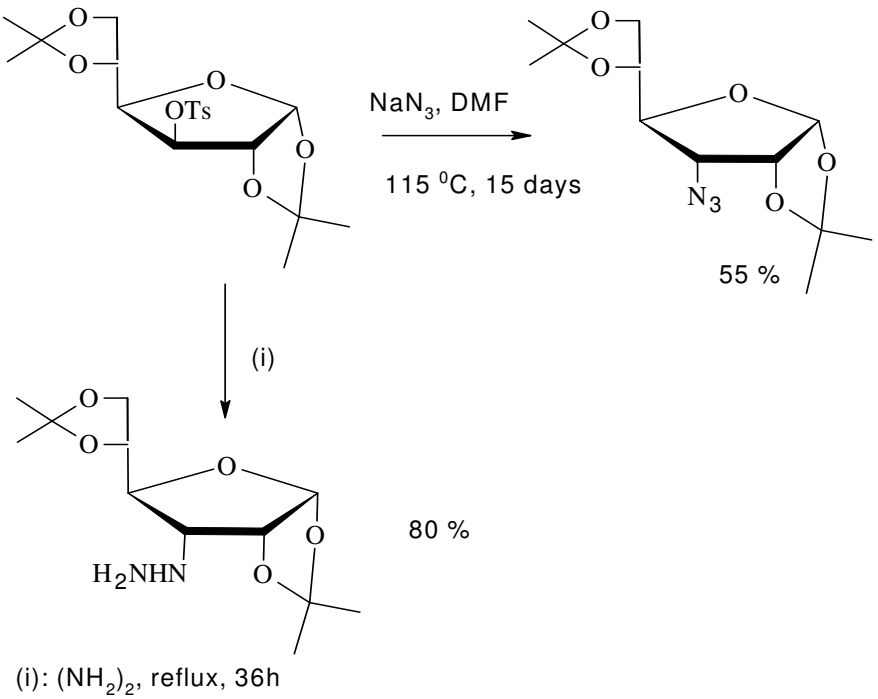
Displacement at C-2 and C-3 of furanoid rings is also possible. For example the conversion of 1,2:3,4-di-*O*-isopropylidene-3-*O*-toluene-*p*-sulfonyl-α-D-allofuranose led to the 3-azido-3-deoxyglucofuranose derivativative (Scheme 1.8).



Scheme 1.8 Displacement at C-3 of 1,2:3,4-di-*O*-isopropylidene-3-*O*-toluene-*p*-sulfonyl-α-D-allofuranose

However, with the gluco-toluene-*p*-sulfonate, where the leaving group occupies an exo position to the bicyclic system formed by two cis-fused five-membered rings, the displacement is more difficult in these conditions becaause of the difficulty of the nucleophile approaching C-3 from the endo direction (Ferrier and Collins, 1972).

It is possible however to displace the exo-sulphonate ester residue from this compound with uncharged nucleophiles such as hydrazine or amines more readily, probably because such uncharged species encounter a smaller electrostatic repulsion from the oxygen atoms at C-1 and C-2 than do charged nucleophiles. Hydazine has also been used to bring about displacement at C-3 in furanosyl derivatives even though this would be expected to be the least reactive position (Ferrier and Collins, 1972).



Scheme 1.9 Displacement of the Exo-sulphonate Ester by Hydrazine

1.5. The synthesis of Azides

The halide displacement by azide ion is the most commonly applied route especially to alkyl azides (Scriven and Turnboll, 1988; Sasaki et al., 1982). It is also applicable to acyl azide preparation by using sodium azide (NaN_3) and acyl chloride (Holden, 1984; Gmulka et al., 1985).

The displacement of sulfonates by azide ion is another important route to organic azides: Alkyl azides can be prepared from alcohols in a two step process involving conversion of alcohols to sulfonates and displacement of the sulfonate groups to azides. At high temperature in polar aprotic solvent for example in DMF, the azido compounds are prepared in good yields by the action of NaN_3 on tosylates or mesylates (Holden, 1984; Gmulka et al., 1985).

The displacement of primary sulfonyloxy groups by azide is usually facile in solvent such as acetone and butanone except in certain cases, D-galactopyranoses, where unfavorable steric and polar factors operate.

Replacement of seconder sulfonyloxy groups is more difficult and required the use of polar aprotic solvent, such as *N, N*-dimethylformamide, *N*-methylpyrrolidone, or hexamethylphosphoramide. The later is the most effective (Normant, 1967) solvent for these reactions. The factor is the greater solubility of sodium azide in HMPA (2.68 g per 100 mL) than in DMF (0.74 g per 100 mL at 120^{o}C) but its use is hampered by its high boiling point which makes it difficult to remove from the reaction product (Normant, 1967).

The epoxides can be also starting compound for preparation of azides but present disadvantage in case they lead to the formation of bifunctional group of azide and alcohol (Zambani and Rokach, 1984; Scriven and Turnboll, 1988). Carboxylic acids (Lemmens et al., 1984), alkenes (Hassner et al., 1984), nitro compounds (Noris et al., 1982) and amino or hydrazines (Kim et al., 1986) can be also used as starting compounds for synthesis of alkyl azides.

1.6. The synthesis of Amino Products

The most common approach for their preparation involves a three step protocol via:

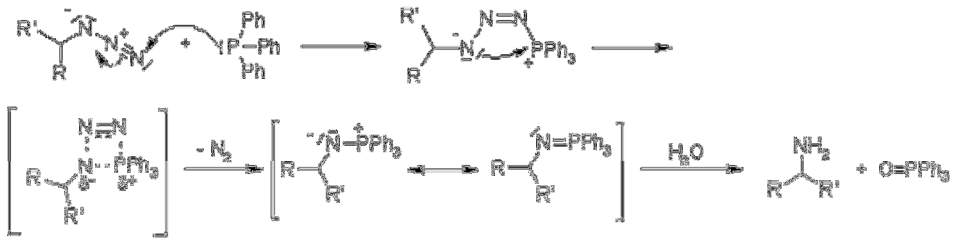
a) Conversion of alcohols to corresponding halides or sulfonates;

b) Nucleophilic substitution by azide anion and

c) Reduction of azide to amine by using various reagents.

The **Staudinger reaction** or **Staudinger reduction** is one of chemical reactions in which the combination of an azide with a phosphine or phosphite produces an iminophosphorane intermediate (Tian et al., 2004; Bergman et al., 2005). Combined with the hydrolysis of the aza-ylide to produce a phosphine oxide and an amine, this reaction is a mild method of reducing an azide to an amine. Triphenylphosphine is commonly used as the reducing agent, yielding triphenylphosphine oxide as the side product in addition to the amine.

Triphenylphosphine reacts with the azide to generate a phosphazide, which loses N_2 to form an iminophosphorane. Aqueous work up leads to the amine and the very stable phosphine oxide.



Scheme 1.10 An Example of a Staudinger Reduction

Alternatively they can be prepared by a two step methodology via:

a) Conversion of alcohol to azide by Mitsunobu reaction using hydrazoic acid, to which correspondence should be adressed triphenylphosphine and diethylazodicarboxylate (DEAD)

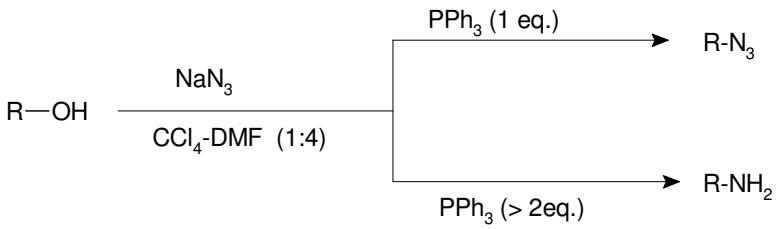
b) Reduction of azide to amine.

Although these methods work well, extra time is required to isolate intermediate products and leading to low overall yields, and involves the risk of handling explosive azides.

Herein, reported also an onepot protocol for the conversion of alcohols to azide and amines using NaN_3 and PPh_3 in $CC1_4$-DMF (1:4). Treatment of alcohols with NaN_3 and two equivalents of PPh_3 in $CC1_4$-DMF (1:4) at 90°C afforded amines in an excellent yield (85-95%).

Formation of amines may be visualized as the initial azide formed would react with second equivalent of PPh_3 giving the iminophosphorane which in turn converted to the amine upon treatment with water.

Treatment of alcohols with one molar equivalent of PPh_3 afforded azides exclusively in good yields. The reaction of primary alcohols was completed within 4-6 h, whereas secondary alcohols required longer time (8-10h).



Scheme 1.11 Onepot Protocol Conversion of Alcohols into Azide and Amines

Azides, which have proven to be useful precursors for amines in chemical syntheses, can be introduced by displacement of a suitable nucleofuge or direct conversion of an existing amine by a diazotransfer reaction. Furthermore, azides are resistant to many reaction conditions and can be easily reduced to amines either generally (hydrogenation metal hydrides, etc.) or orthogonally (Staudinger and Meyer, 1919).

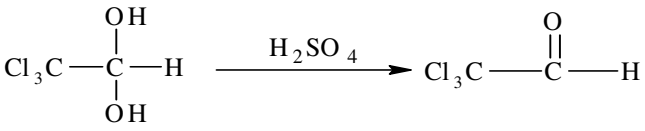
2. MATERIAL AND METHODS

2.1. General Techniques

- Melting points were recorded with Gallenkamp electrothermal melting point apparatus in capillary.
- T.l.c and column chromatography were performed on precoated aluminium plates (Merck 5554) and silicagel G-60 (Merck 7734), respectively. The spots of t.l.c were developed by spraying 20 % aqueous sulphuric acid and by heating the plates above 120 ºC.
- Starting compounds and reagents were obtained from Merck, Carlo Erba and Aldrich. Solvents like hexane, methanol, dichloromethane, and toluene were obtained from industrial grade solvents which were further purified by distillation.
- Solvents were dried with molecular sieve (type 4 ^{o}A). Anhydrous sodium sulphate 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 (400MHz) 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).
- Optical rotation measurements were carried out on a Rudolph Autopol-1 Automatic Polarimeter.

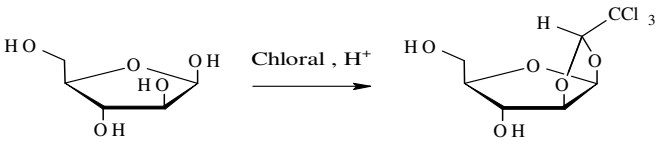
2.2. Experiments

2.2.1 Preparation of anhydrous chloral



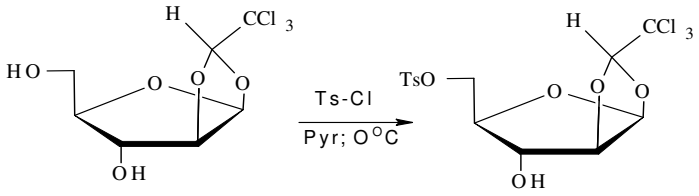
Concentrated H_2SO_4 (245 mL, d=1.84) was added on chloral hydrate (430 g, 2.6 mol) and refluxed for about 2 hours at max. 97°C. Distillation gave pure anhydrous chloral (216 mL, d=1,512; 327 g) with 92 % yield.

2.2.2 1,2-*O*-(*S*)-trichloroethylidene-α-D-arabinofuranose (1)



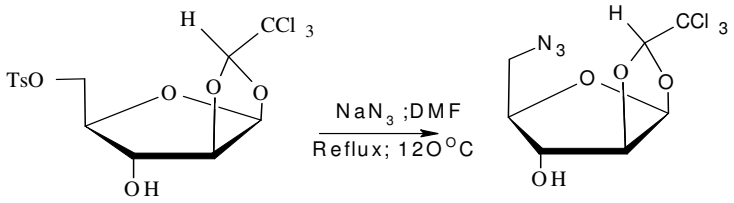
D-arabinose (40 g; 266 mmol) was added on anhydrous chloral (110 mL, d=1.512; 169 g) under continuous stirring. Conc. sulphuric acid (1 mL; d=1.84) was added and the mixture was refluxed for 2 h30min. The mixture was then poored into a flask. The remaining solide was taken with dichloromethane and added to the first portion untill all solid was taken. Excess chloral and dichloromethane were 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 decolourised with activated charcoal. The product **1** was obtained as colourless crystals from methanol solution (44 g; 60 %), mp 188-190 °C.

2.2.3 5-*O*-tosyl-1,2-*O*-(*S*)-trichloroetylidene-α-D-arabinofuranose (2)



A solution of **1** (10 g, 35.78 mol) in pyridine (80 mL) was cooled with ice bath and *p*-toluenesulfonyl chloride (8.2 g; 43 mmol) in pyridine (20 mL) was added dropwise and stirred for 4 h 30min. TLC (toluene-MeOH, 8:2) showed the completely disappearance of the starting sugar. The reaction mixture was concentrated to half volume by evaporation of the solution and poored into ice-water (300 mL). Then, it was extracted with CH_2Cl_2 (3x100 mL). The washed dichloromethane solution was dried over anhydrous Na_2SO_4. Filtered off, TLC (Tol-MeOH, 8-2) revealed the presence of two carbohydrate components with a very 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 **2** as solid product:(10.6 g; 68 %), mp 183-184 °C. $[\alpha]_D^{21}$:-0.5^0(c 0.6, MeOH).

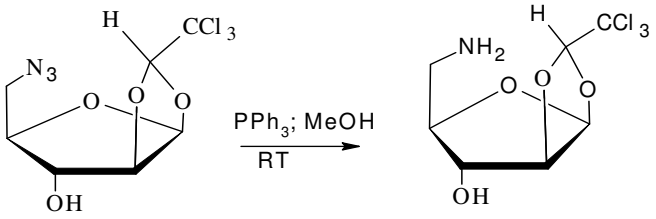
2.2.4 5-Azido-5-deoxy-1,2-*O*-(*S*)-trichloroethylidene-α-D-arabinofuranose (3)



To a solution of **2** (5 g; 11.5 mmol) in dried DMF (60 ml) was added NaN_3 (0.9 g, 14 mmol). The mixture was heated with stirring in an oil bath at 120 °C. After 5 h, TLC (toluene-MeOH, 8:2) showed completion of the reaction. The reaction mixture was evaporated under reduced pressure. 5.701 g of crude product

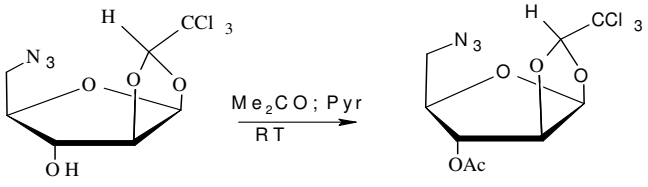
obtained was extracted with CH_2Cl_2-H_2O (100 mL x 2). The washed dichloromethane solution was dried over anhydrous Na_2SO_4 filtered off and evaporated gave colourless crystals as pure compound **3** (3.91 g, 98 %), mp 152-154 ^oC. $[\alpha]_D^{21}$:+33.5^0 (c 1, CH_2Cl_2).

2.2.5 5-Amino-5-deoxy-1,2-*O*-(*S*)-trichloroethylidene-α-D-arabinofuranose (4)



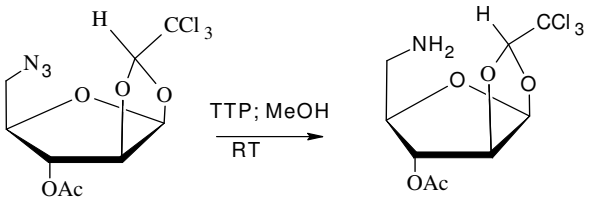
To a solution of **3** (3 g; 10.2 mmol) in MeOH (100 mL) was added triphenylphosphine (3.25 g; 1.24 mmol). The reaction mixture was stirred at room temperature for 3 h. TLC (toluene-MeOH, 8:2) showed the completed reaction with two products seen by thin layer chomatography. One corresponding to our product and another triphenylphosphineoxide. The reaction mixture was evaporated under reduced pressure and the crude residue afforded the title compound almost in pure form, which was passed through a short pad of silica gel with CH_2Cl_2/MeOH: 1/1 to give pure amine **4** as colourless crystals (2.3 g; 82.7 %), mp 154-156 ^oC, $[\alpha]_D^{21}$:+44^0 (c 1, MeOH).

2.2.6 5-Azido-5-deoxy-3-*O*-acetyl-1,2-*O*-(*S*)-trichloroethylidene-α-D-arabinofuranose (5)



A solution of **3** (1.30 g; 4.03 mmol) in pyridine (15 mL) was acetylated with Me_2O (1 mL); at room temperature for an overnight. Evaporated, extracted twice with CH_2Cl_2-H_2O and dried on anhydrous sodium sulfate Na_2SO_4 the solution the product **5** was obtained as colourless crystals (1.40 g; 95 %), mp 98-100 ^oC, $[\alpha]_D^{21}$:-60^0 (c 0.6, MeOH).

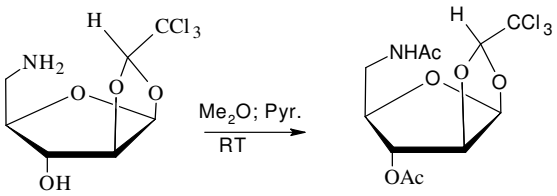
2.2.7 5-Amino-5-deoxy- 3-*O*-acetyl- 1,2-(*S*) trichloroethylidene-α-D-arabinofuranose (6)



To a solution of **5** (0.7 g; 2 mmol) in MeOH (20 mL) was added triphenylphosphine (0.65 g, 2.5 mmol). The reaction mixture was stirred at room temperature. After 3 h., TLC (toluene-MeOH, 8:2) showed the completion of the reaction. The solvent was evaporated under reduced pressure. The syrupy product was purified by column chromatography with CH_2Cl_2-MeOH as eluting system to give the product **6** as colourless crystals (0.510 g; 88.5 %); mp 134-136 ^oC, $[\alpha]_D^{21}$:+33^0 (c 0.6, MeOH).

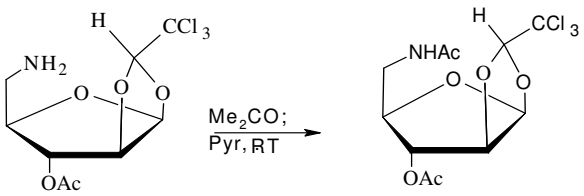
2.2.8. 5-acetamido-5-deoxy-3-*O*-acetyl-1,2-*O*-(*S*)-trichloroethylidene-α-D-arabinofuranose (7)

a) Starting from **4.**



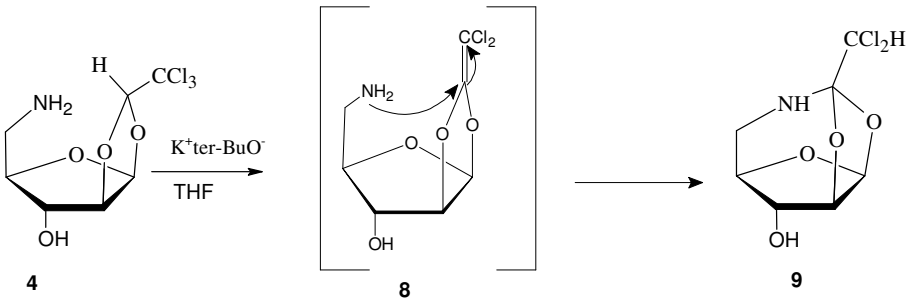
Compound **4** (1,2 g; 4,31 mmol) dissolved in pyridine (15 mL) was treated with Me_2O 1 mL and allowed to stand at room temperature for 24 h. Pyridine was removed by evaporation under reduced pressure. Purified on a silica gel column with CH_2Cl_2-MeOH (100:1) gave the oil product **7** (1 g; 64 %), $[\alpha]_D^{21}$:+6^0 (c 1, MeOH).

b) Starting from **6.**



Compound **6** (2 g; 6 mmol) dissolved in pyridine (12 mL) was treated with Me_2CO 1 mL and allowed to stand at room temperature for 18 h. Pyridine was removed by evaporation under reduced pressure. The same work-up and chromatographic purification as on a) led to compound **7** (1.46 g, 55 %) which showed the same physical and spectroscopic properties as the product reported in a).

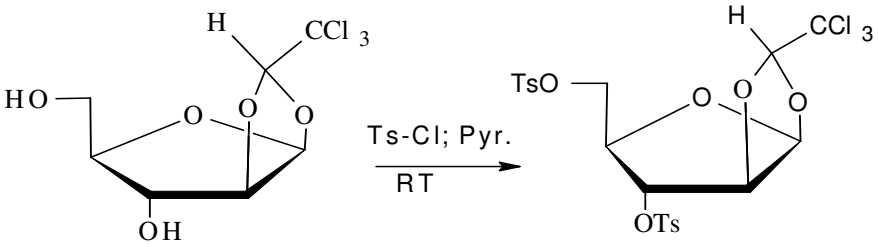
2.2.9 5-Amino-5-deoxy-1,2-*O*-dichloroethhylidene-α-D-arabinofuranose (8) and 5-Amido-5-deoxy-1,2-*O*-,5-*N*-orthodichloroacetyl-α-D-arabinofuranose (9)



A mixture of compound **4** (0.89 g, 3.2 mmol) and potassium *tert*-butoxide (0.77 g, 6.4 mmol, 2 equivalents), in **THF** (30 mL) was stirred at room temperature for 2 hour. The mixture was concentrated by evaporation and the silica gel was added to the resulting crude mixture. Then the THF was completely evaporated. Column chromatography (10:2 CH_2Cl_2-MeOH) afforded a yellow cristals; which was identified as compound **9** (0.26 g, 34 %), mp 120-122 ^oC, $[\alpha]_D^{21}$:+25^0 (*c* 0.64, MeOH).

Evaporation of the fractions which contained the more polar product led to the very colourless crystals which had been expected to be likely the ketene acetal derivative **8** (0.06 g, 8 %), mp 112-113.5 ^{o}C, $[\alpha]_D^{21}$:-18^0 (*c* 1, MeOH).

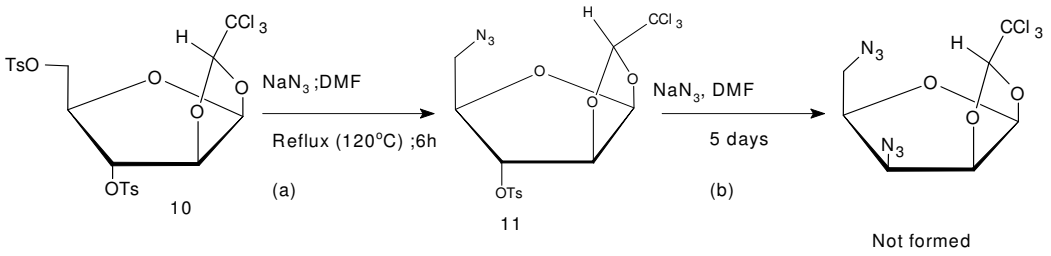
2.2.10 3,5-Ditosyl-1,2-*O*-(*S*)-trichloroetylidene-α-D-arabinofuranose (10)



To a solution of **1** (5 g, 17.89 mol) in pyridine (60 mL) was added *p*-toluenesulfonyl chloride (8.12 g; 42.6 mmol) in pyridine (15 mL) and stirred at room temperature for 6 h. TLC (toluene-MeOH, 8:2) showed the completely disappeared of the starting sugar with strong spot corresponding to monotosyl product. The reaction was allowed to stand overnight. Then, TLC showed that only a small spot remained as a by-product.

The reaction mixture was evaporated and to the crude product obtained was poored ice-water (300 mL). Then, it was extracted with CH_2Cl_2 (3x100 mL). The washed dichloromethane solution was dried over anhydrous Na_2SO_4. Filtered off, TLC Tol-MeOH reveled that the two components were in dichloromethane solution with a very stong spot corresponding to ditosyl product. Then, the solution was evaporated under reducing pressure. Monotosyl product was crystallized out from hot CH_2Cl_2-Hexane. Filtered of and evapated off and dried the product **10** was obtained as colourless crystals: (8.6 g; 81 %), mp 110-111 ^{o}C, $[\alpha]_D^{21}$:+18.4^0 (*c* 0.76, CH_2Cl_2).

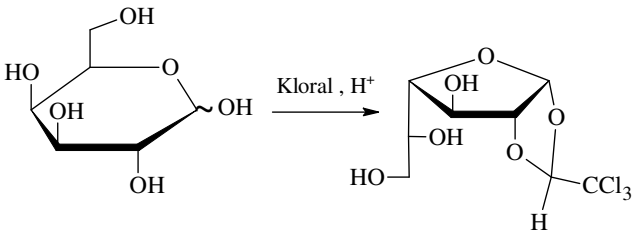
2.2.11 Attempt to synthesise 3,5-Diazido-3,5-dideoxy-1,2-*O*-(*S*)-trichloroethylidene -α-D-arabinofuranose



a) To 8.5 g; 14.46 mmol of **8** in dried DMF (60 mL) was added NaN_3 (2.25 g, 34.7 mmol). The mixture was heated with stirring in an oil bath at 120 ^oC for 6 h. TLC (toluene-MeOH, 8:2) showed completion of the reaction. The reaction mixture was evaporated under reduced pressure. The crude product obtained was extracted with CH_2Cl_2-H_2O (100 mL x 2). The washed dichloromethane solution was dried over anhydrous Na_2SO_4; filtered off and evaporated the filtrate gave 5.3 g as crude product which was purified on column chromatography (Tol-MeOH). Colourless crystals was obtained as pure compound. However, the spectroscopic data of that product revealed that only one tosyl-group was displaced **11** (4,325 g, 92 %, mp 96-97 ^oC), $[\alpha]_D^{21}$:+64^0 (*c* 1, MeOH).

b) To 0.85 g; 1.45 mmol of **11** dissolved in DMF was added 0.225 g; 3.47 mmol) and the mixture was stirred in conditions above for 5 days. However no change has been observed. The desired diazide derivative was not obtained.

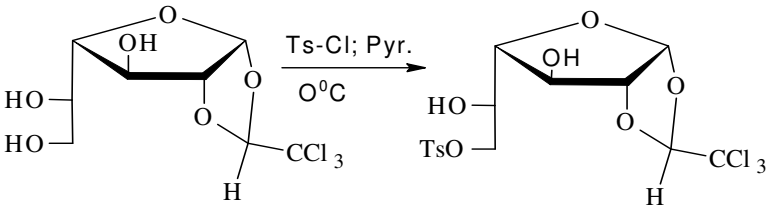
2.2.12 1,2-*O*-(*S*)-Trichloroethylidene-α-D-galactochloralose (12)



D-galactose (54.25 g; 300.4 mmol) was added on anhydrous chloral (166 mL; d=1.512; 250 g) under continuous stirring. Conc. sulphuric acid (1 mL) was added and the mixture was refluxed for 2 h 30min. The mixture was then poored into a flask. The remaining solide was taken with dichloromethane and added to the first portion untill all solid was taken. Excess chloral and dichloromethane

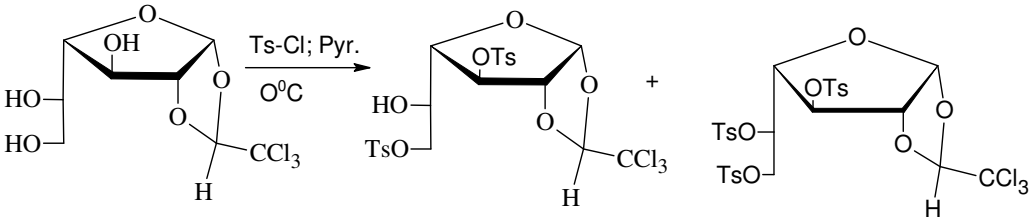
were evaporated and the black coloured syrup was obtained. Methanol (400 mL) was added in order to dissolve all solidified material. The solution was heated about 1h30min. and then decolourised with activated charcoal. After evaporation of solvent the product **12** was obtained as colourless crystals from hot methanol solution (93 g; 98 %); mp 207-209 ^{o}C, $[\alpha]_D^{21}$:-31.7^0 (*c* 1.07, MeOH).

2.2.13 6-*O*-Tosyl- 1,2-*O*-(*S*)-trichloroethylidene-α-D-galactochloralose (13)



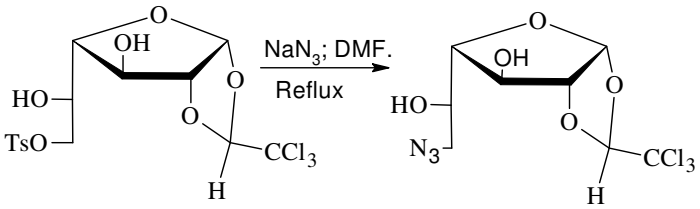
A solution of **12** (4.4g, 0.014 mol) in pyridine was cooled with ice bath and 1.2 equivalent of *p*-toluenesulfonyl chloride dissolved in pyridine was added dropwise. The reaction mixture stirred for 10 h at O ^{o}C; TLC (toluene-MeOH, 8:2) showed the completely disappeared of the starting sugar with two spots. The reaction mixture was concentrated to half volume by evaporation of the solution and poored into ice-water (200 mL). Then, it was extracted with CH_2Cl_2 (3x100 mL). Organic phase was washed with water and dried over anhydrous Na_2SO_4. Filtered off, evaporated under reducing pressure. The crude syrupy product was purified by column chromatography with CH_2Cl_2-MeOH as eluting system giving product **13** as colourless crystals product: (6.12 g; 74 %), mp 166-167 ^{o}C, $[\alpha]_D^{21}$:-16^0 (*c* 1, MeOH).

2.2.14 (3,6 Ditosyl-and 3,5,6-tritosil) 1,2-*O*-(*S*)-trichloroethylidene-α-D-galactochloralose (14 and 15)



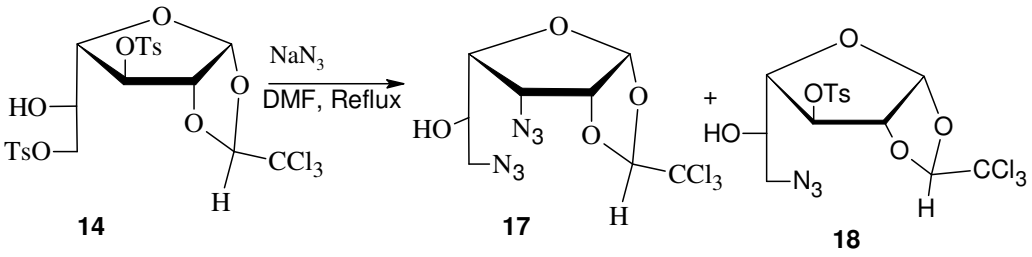
The procedure of the previous experiment was repeated using the same starting material as above. To the solution of **10** (1g, 3.2 mmol) in pyridine (20 mL) cooled with ice bath-water was added *p*-toluenesulfonyl chloride (2.2 g; 11.52 mol) in pyridine (10 mL). The reaction mixture was stirred at O ^{o}C. After 20 h; TLC (toluene-MeOH, 8:2) showed the completely disappearance of the starting sugar with 4 spots. Then, 1 equ. of *p*-toluenesulfonyl chloride was added to the reaction mixture and allowed to stand at room temperaure for a night. Then, TLC revealed that only two strong spots remained. After evaporation of the solvent, the crude product was extracted twice with CH_2Cl_2-H_2O. Dried over anhydrous Na_2SO_4; the organic phase was filtered off and evaporated. The crude syrupy product obtained was purified by column chromatography with CH_2Cl_2-MeOH as eluting system giving product **14** as colourless crystals product: (1.17 g; 49 %), mp 66-67 ^{o}C and a byproduct **15** :(0.871 g; 39 %), mp 61-63 ^{o}C, $[\alpha]_D^{21}$:-14^0 (*c* 2, CH_2Cl_2).

2.2.15 6-Azido-6-deoxy-1,2-*O*-*(S)*-trichloroethylidene -α-D-galactochloralose (16)



To 2.6 mmol (1.2g) of **9** dissolved in dried DMF (20 mL); was added NaN_3 (0.315 g, 5 mmol) and the mixture was refluxed at 100 ^{o}C for 6 h. Then, TLC (toluene-MeOH, 8:2) showed completion of the reaction with 1 product. The reaction was poured into ice-water (50 mL) and extracted twice with CH_2Cl_2-water. Dried over anhydrous Na_2SO_4 and filtered off; the organic phase was evaporated giving colourless crystals as pure compound **16** (0.75 g, 80 %), mp 159-161 ^{o}C, $[\alpha]_D^{21}$:-45.7^0 (*c* 0.7, MeOH).

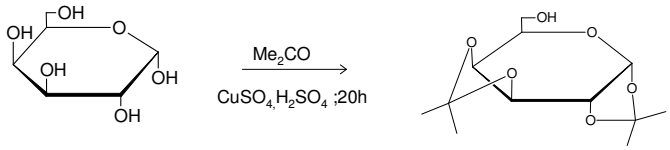
2.2.16 3,6-Diazido-5,6-deoxy- 1,2-*O*-(*S*)-trichloroethylidene -α-D-galactochloralose (17) and 6-azido- 6-deoxy-3-*O*-tosyl-3-deoxy-1,2-*O*-trichloroethylidene α-D-galactochloralose (18)



Sodium azide (0.1 g, 1.6 mmol) was added to a solution of the tosylate **14** (0.026 g, 0.4 mmol) in dry DMF (25 mL) and the suspension was heated at 110 °C for 8 h, when TLC showed two main spots and two very small spots (10:1 EtOAc-MeOH) and complete consumption of the starting material. Then the reaction mixture was heated with various temperatures 110-135 °C for a week. The solvent was evaporated, and the residue was extracted with CH_2Cl_2-H_2O, dried over Na_2SO_4, filtrated and evaporated, the crude product was applied to a Column chromatography (20:1 Tol-MeOH) afforded colourless crystals; which was identified as **17** (70 mg, 14 %), mp 90-91 ^oC, $[\alpha]_D^{21}$:+16^0 (*c* 0.5, MeOH).

Evaporation of the fractions which contained the more polar product led to the partially azited derivative **18** named 6-azido- 6-deoxy-3-*O*-tosyl-3-deoxy-1,2-*O*-trichloroethylidene α-D-galactochloralose (600 mg, 80 %); mp 82-83 ^oC.

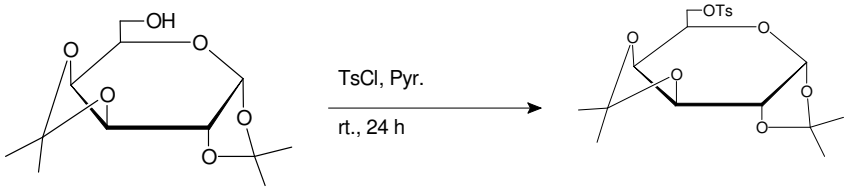
2.2.18 1,2:3,4-Di-*O*-isopropylidene-α-D-galactopyranose (19)



To 9 g (0.05 mol) of finely powdered anhydrous D-galactose was added 20 g (0.125 mol) of powdered anhydrous cupric sulfate, 1 mL of concentrated sulfuric acid, and 200 mL of anhydrous acetone. The mixture was allowed to

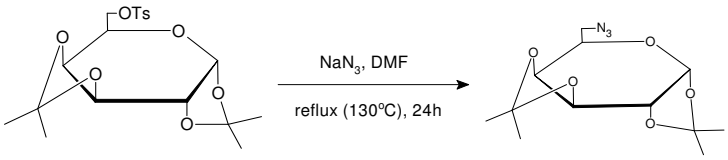
stand at room temperature with continous stirring for 20h. Then t.l.c showed the completely disappearance of the starting sugar. The cupric sulfate was removed by filtration and washed with anhydrous acetone; the washing were combined with the orginal filtrate. The combined washings and filtrate were neutralized by stirring with 9.4 g (0.127 mol) of powdered calcium hydroxide pH=7. The unreacted calcium hydroxide and calcium sulfate were filtrated, washed with dry acetone; and the solvent was evaporated under reduced pressure. The residual light yellow oil was the named product **20** 1,2:3,4-di-*O*-α-D-galactopyranose: yield (9.8 g, 76 %), $[\alpha]_D^{21}$:-57^0 (*c* 1.2, CH_2Cl_2).

2.2.19 6-*O*-Tosyl-1,2:3,4-di-*O*-isopropylidene-α-D-galactopyranose (20)



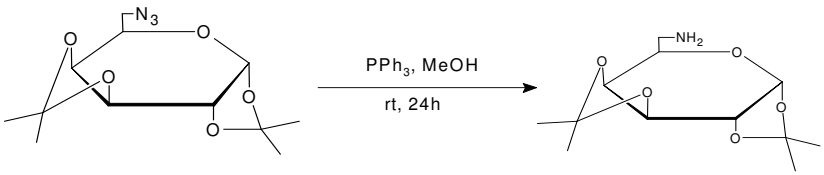
A solution of 1,2:3,4-Di-*O*-isopropylidene-α-D-galactopyranose (6 g, 0.023 mol) in pyridine (80 mL) and *p*-toluenesulfonyl chloride (7.6 g; 0.04 mol) in pyridine (30 mL) was added and stirred at room temperature for 24 h. TLC (toluene-MeOH, 8:1) showed the completely disappearance of the starting sugar. The reaction mixture was concentrated by evaporation of the solution and poored into ice-water (300 mL). Then, it was extracted with CH_2Cl_2 (3x100 mL). The washed dichloromethane solution was dried over anhydrous Na_2SO_4. Filtered off, evaporated; the product **21** was obtained as syrupy product: yield 7.7 g; 85 % $[\alpha]_D^{21}$ = -112^0 (*c* 1, CH_2Cl_2).

2.2.20 6-Azido-6-deoxy-1,2:3,4-di-*O*-isopropylidene-α-D-galactopyranose (21)



Starting from compound **21** (6 g, 15 mmol) dissolved in dry DMF was treated with sodium azide (3.7 g, 0.6 mol) at 110 ^{0}C. After 10 h the temperature was raised to 125 °C, and the heating was continued for an additional 10 h. TLC (toluene-MeOH, 9:1) showed completion of the reaction. The mixture was concentreted in vacum, and the residue was extracted with CH_2Cl_2-H_2O (100 mL x 3). The washed dichloromethane solutions were combined and dried over anhydrous Na_2SO_4. The filtrate was concentrated, and the resulting syrup was applied to a chromatographic column (Tol: MeOH 9.5:0.5) to afford oily **22** (3.5 g, 87.5 %); $[\alpha]_D^{21}$ = -107 (*c* 1.2, CH_2Cl_2).

2.2.21 6-Amino-6-deoxy- 1,2:3,4-di-*O*-isopropylidene-α-D-galactopyranose (22)



To a solution of **22** (2 g; 7 mmol) in MeOH (30 mL) was added triphenylphosphine (4 g; 1.4 mmol). The reaction mixture was stirred at room temperature for 5 h. TLC (toluene-MeOH, 9:1) showed the completed reaction. Evaporated, the reaction mixture afforded amine almost in pure form, which were passed through a short pad of silica gel with CH_2Cl_2/MeOH: 8/2 to give pure amine **23** as colourless crystals (1.71 g; 95 %), mp 74-75 ^{o}C; $[\alpha]_D^{21}$ = -50.6^0 (*c* 1, CH_2Cl_2).

3. SPECTROSCOPIC DATA

3.1 5-Azido-5-deoxy-1,2-*O*-trichloroethylidene-α-D-arabinofuranose (compound 3)

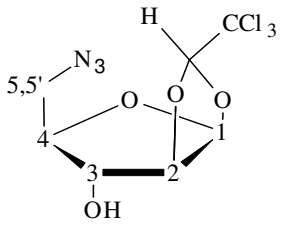


Table 3.1. a) IR Spectral Data (cm^{-1}) of the Compound 3

Functional Groups	cm^{-1}
OH	3470.1
C-H	2984.4 – 2927.7
N_3	2101.9
C-Cl	836.2 – 741.6

Table 3. 1. b) ^{1}H-NMR Spectral Data (DMSO - D_6, 400MHz) of Compound 3

Location of Atoms	^{1}HNMR (δ)	H and Coupling Constants (Hz)
H_1	6.30(d)	1H, $J_{1,2}$ =3.6
H_{acetal}	6.00(s)	1H
H_2	5.70(d)	1H, $J_{2,3}$ =0
H_3	4.79(d)	1H, $J_{3,4}$ =0
H_4	4.08(m)	1H, $J_{4,5}$ =9.2, $J_{4,5'}$ =5.2
H_5	3.52(dd)	1H, $J_{5,5'}$ =13.2
$H_{5'}$	3.34(dd)	1H
OH	2.5(bs)	1H

3.2 5-Amino-5-deoxy-1,2-*O*-trichloroethylidene-α-D-arabinofuranose (compound 4)

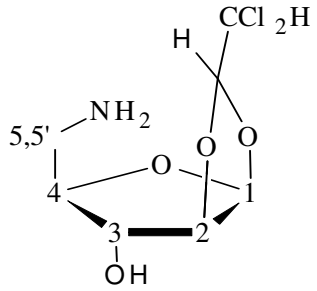


Table 3.2.a) IR Spectral Data (cm^{-1}) of the Compound 4

Functional Groups	cm^{-1}
N-H_2 and OH	3503.9 - 3123.7
C-H	2.975.7 - 2890.6
N-H	1598.9
C-Cl	838.0 - 751.8

Table 3.2.b) ^{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	6.23(d)	1H, $J_{1,2}$ =4
H_{acetal}	5.79(s)	1H
H_2	5.70(d)	1H
H_4	4.15(s)	1H, $J_{4,5}$ =3.6
H_3	3.90(t)	1H, $J_{2,3}$ =0; $J_{3,4}$ =0
$H_{5, 5'}$	2.67(d)	2H, $J_{4,5}$ =7.6
NH_2 and OH	3.25(br s)	3H

3.3 5-Azido-5-deoxy-3-*O*-aceto-1,2-*O*-trichloroethylidene-α-D-arabinofuranose (compound 5)

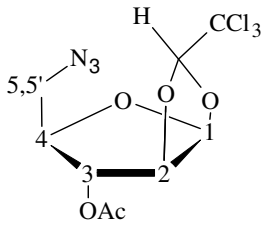


Table 3.3 ^{1}H-NMR Spectral Data ($CDCl_3$, 400MHz) of Compound 5

Location of Atoms	^{1}HNMR (δ)	H and Coupling Constants (Hz)
H_1	6.31(d)	1H, $J_{1,2}$ =4.0
H_{acetal}	5.69(s)	1H
H_3	5.12(s)	1H, $J_{2,3}$ =0; $J_{3,4'}$ =0
H_2	5.04(d)	1H
H_4	4.27(t)	1H
H_5	3.56(dd)	1H, $J_{4,5}$ =6.8; $J_{5,5'}$ =13.0
$H_{5'}$	3.46(dd)	1H, $J_{5',4}$ =5.6
H_{acetyl}	2.11(s)	3H

3.4 5-Amino-5-deoxy-3-*O*-acetyl-1,2-*O*-trichloroethylidene-α-D-arabinofuranose (compound 6)

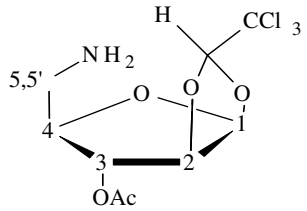


Table 3.4 ^{1}H-NMR Spectral Data (CD_3OD, 400MHz) of Compound 6

Location of Atoms	^{1}HNMR (δ)	H and Coupling Constants (Hz)
H_1	6.20(d)	1H, $J_{1,2}$ =4.0
H_{acetal}	5.75(s)	1H
H_2	4.73(d)	1H, $J_{2,3}$ =0
H_3	4.12(s)	1H, $J_{3,4}$ =0
H_4	3.85(t)	1H, $J_{4,5}$=7.2
$H_{5,5'}$	2.56-2.67(m)	2H, $J_{5,4}$=7.2; $J_{5,5'}$ =13.6
H_{acetyl} and NH_2	2.95(bs)	5H

3.5 5-Amino-5-deoxy-3-*O*-acetyl-1,2-*O*-trichloroethylidene-α-D-arabinofuranose (Deuterium Exchange) for the Compound 6

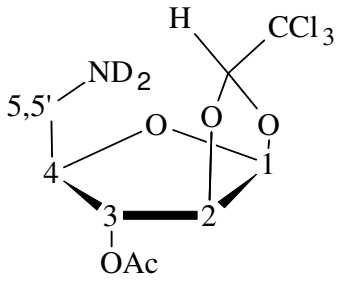


Table 3.5 Deuterium Exchange ^{1}H-NMR Spectral Data (CD_3OD, 400MHz) of the Compound 6

Location of Atoms	^{1}HNMR (δ)	H and Coupling Constants (Hz)
H_1	6.20(d)	1H, $J_{1,2}$ =4.0
H_{acetal}	5.75(s)	1H
H_2	4.73(d)	1H, $J_{2,3}$ =0
H_3	4.08(s)	1H, $J_{3,4}$ =0
H_4	3.85(t)	1H, $J_{4,5}$=7.2
H_{acetyl}	3.70(s)	3H
$H_{5,5'}$	2.58(d)	2H, $J_{5,4}$=7.2; $J_{5,5'}$ =13.6

3.6 5-acetamido-5-deoxy-3-*O*-acetyl-1,2-*O*-(*S*)-trichloroethylidene-α-D-arabinofuranose (7)

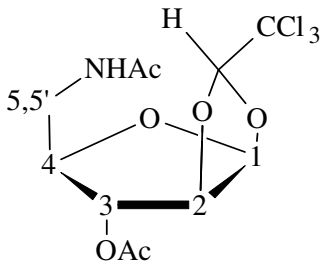


Table 3.6 IR Spectral Data (cm^{-1}) of the Compound 7

Functional Groups	cm^{-1}
N-H	3288.2
C-H	2.984.5- 2937.4
OAc (Ester)	1743.6
NHAc	1655.1
N-H	1550.2
C-Cl	814.1-773.7

3.7 5- Amino-5-deoxy-1,2-*O*-dichloroethylidene-α-D-arabinofuranose (8)

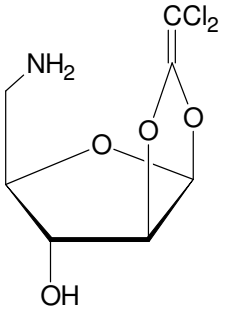


Table 3.7.a) IR Spectral Data (cm^{-1}) of the Compound 8

Functional Groups	cm^{-1}
N-H_2 and OH	3600 - 3200
C-H	2.924.5
C=C	1682.4
N-H	1540.3
C-O	1047.1
C-Cl	812.6 - 750.26

Table 3.7.b) ^{1}H-NMR Spectral Data (CD_3OD, 400MHz) of Compound 8

Location of Atoms	^{1}HNMR (δ)	H and Coupling Constants (Hz)
H_1	6.47(d)	1H, $J_{1,2}$ =4
H_2	5.09(d)	1H, $J_{2,3}$=0
H_4	4.48(m)	1H,
H_3	4.33(s)	1H, $J_{3,4}$=0
H_5	3.44(dd)	1H, $J_{4,5}$ =3.2; $J_{5,5'}$ =13.2
$H_{5'}$, OH and NH_2	2.72-2.78(m)	4H

3.8 5-Amido-5-deoxy-1,2-*O*-,5-*N*-orthodichloroacetyl-α -D-arabinofuranose (9)

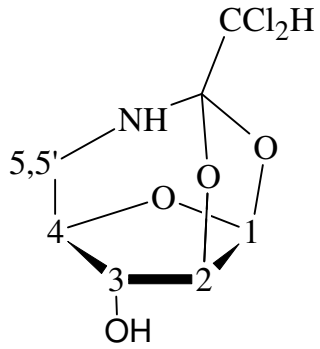


Table 3.8.a) IR Spectral Data (cm^{-1}) of the Compound 9

Functional Groups	cm^{-1}
N-H and OH	3600 - 3200
C-H	2.926.7
NH (amide)	1680.9
C-O	1275.8
C-Cl	750.2

Table 3.8.b) ^{1}H-NMR Spectral Data (CD_3OD, 400MHz) of Compound 9

Location of Atoms	^{1}HNMR (δ)	H and Coupling Constants (Hz)
H_1	6.02(d)	1H, $J_{1,2}$ =3.6
H_{acetal}	5.72(s)	1H
H_2	4.62(dd)	1H, $J_{2,4}$ =1.6 (w coupling)
H_4	4.08(d)	1H, $J_{4,5 \text{ and } 4,5'}$=3.2
H_3	4.34(s)	1H, $J_{2,3}$ =0, $J_{3,4}$ =0
H_5	3.28(dd)	1H, $J_{5,5'}$ =14.4
$H_{5'}$	3.09(dd)	1H
OH and NH	2.74-2.55(bs)	2H

3.9 3,5-*O*-Ditosyl-1,2-*O*-trichloroethylidene-α-D-arabinofuranose (10)

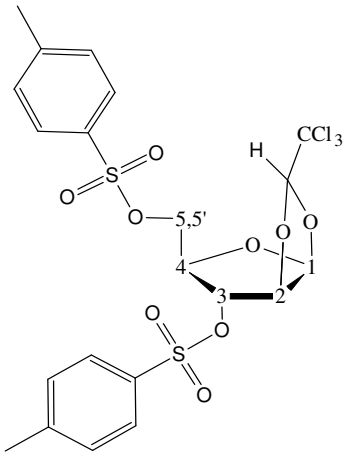


Table 3.9 ^{1}H-NMR Spectral Data ($CDCl_3$, 400MHz) of Compound 10

Location of Atoms	^{1}HNMR (δ)	H and Coupling Constants (Hz)
H_1	6.19(d)	1H, $J_{1,2}$ =4
H_{acetal}	5.36(s)	1H
H_2	4.98(d)	1H, $J_{2,3}$ =0
H_3	4.85(s)	1H, $J_{3,4}$ =0
H_4	4.35(t)	1H, $J_{4,5}$ =5.2, $J_{4,5'}$ =5.6
H_5	4.05 (dd)	1H, $J_{5,5'}$=11.2
$H_{5'}$	3.94 (dd)	1H
Ar-H	7.37-7.81(m)	8H

3.10 3-*O*-Tosyl-5-azido-5-deoxy-1,2-*O*-trichloroethylidene-α-D-arabinofuranose (11)

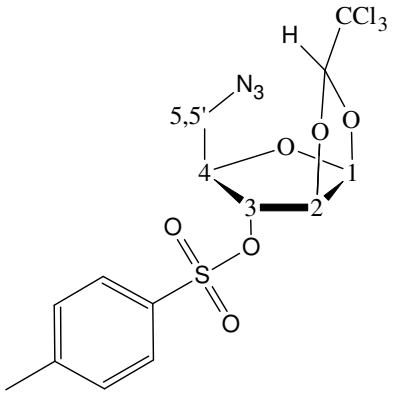


Table 3.10 ^{1}H-NMR Spectral Data ($CDCl_3$, 400MHz) of Compound 11

Location of Atoms	^{1}HNMR (δ)	H and Coupling Constants (Hz)
H_1	6.23(d)	1H, $J_{1,2}$ =4
H_{acetal}	5.62(s)	1H
H_2	5.0(d)	1H, $J_{2,3}$ =0
H_3	4.87(s)	1H, $J_{3,4}$ =0
H_4	4.29(m)	1H, $J_{4,5}$ =6.4, $J_{4,5'}$ =6.4
H_5	3.46 (dd)	1H, $J_{5,5'}$=13.0
$H_{5'}$	3.32 (dd)	1H
Ar-H	7.39-7.84(m)	4H
Ar-CH_3	2.48(s)	3H

3.11 3,6-*O*-Ditosyl-1,2-*O*-trichloroethylidene-α-D-galactofuranose (14)

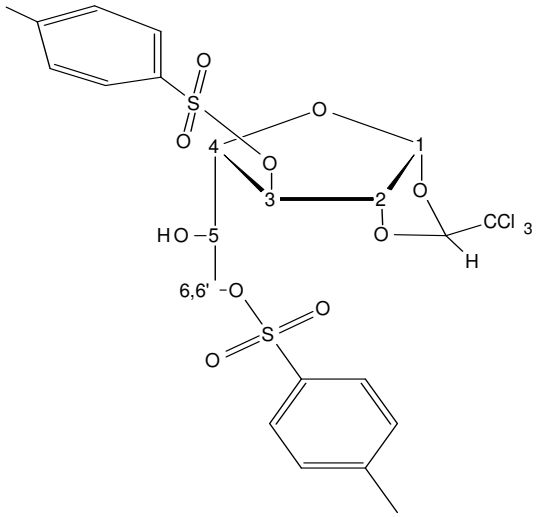


Table 3.11 ^{1}H-NMR Spectral Data ($CDCl_3$, 400MHz) of the Compound 14

Location of Atoms	^{1}HNMR (δ)	H and Coupling Constants (Hz)
H_1	6.16(d)	1H, $J_{1,2}$ =4.4
H_{acetal}	5.59(s)	1H
H_2	4.96(s)	1H, $J_{2,3}$ =0
H_3	5.01(s)	1H, $J_{3,4}$ =0
H_4	4.22(d)	1H
H_6+$H_{6'}$	4.00-4.09(m)	2H
H_5	3.89-3.92(m)	1H
Ar-H	7.32-7.83(m)	8H
2 x Ar-CH_3	2.45(s) and 2.47(s)	6H
OH	2.63(d)	1H, $J_{OH,H-5}$=5.6

3.12 3,5,6-*O*-Tritosyl-1,2-*O*-trichloroethylidene-α-D-galactofuranose (15)

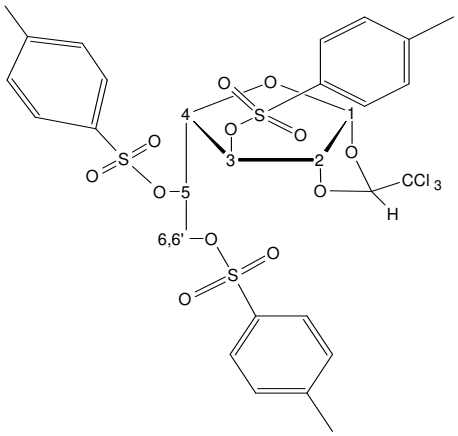


Table 3.12 ^{1}H-NMR Spectral Data ($CDCl_3$, 400MHz) of the Compound 15

Location of Atoms	^{1}HNMR (δ)	H and Coupling Constants (Hz)
H_1	6.12(d)	1H, $J_{1,2}$ =4
H_{acetal}	5.6(s)	1H
H_2	4.94(d)	1H, $J_{2,1}$ =4
H_3	4.85(s)	1H
H_4	4.32(bs)	1H
H_5	4.58-4.62(m)	1H
$H_{6 \text{ and } 6'}$	4.07(d)	2H, $J_{6,6'}$=6.8
Ar-H	7.34-7.84(m)	12H
Ar-CH_3	2.33(s) and 2.49(s)	9H

3.13 6-Azido-6-deoxy-1,2-*O*-trichloroethylidene-α-D-galactofuranose (16)

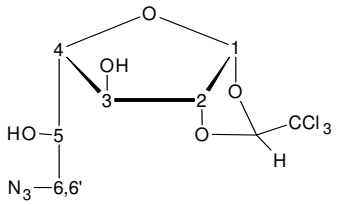


Table 3.13.a) IR Spectral Data (cm^{-1}) of the Compound 16

Functional Groups	cm^{-1}
OH	3477.1
C-H	2937.9
N_3	2099.0

Table 3.13.b) ^{1}H-NMR Spectral Data (DMSO - D_6, 400MHz) of the Compound 16

Location of Atoms	^{1}HNMR (δ)	H and Coupling Constants (Hz)
H_1	6.17(d)	1H, $J_{1,2}$ =4,4
H_{acetal}	5.73(s)	1H
OH	5.61(d) and 5.42(d)	2H
H_2	4.73(dd)	1H, $J_{2,3}$ =0.8
H_3	4.20(dd)	1H, $J_{3,4}$ =3.6
H_4	3.79(dd)	1H, $J_{4,5}$ =5.6
H_5	3.70-3.73(m)	1H
$H_{6 \text{ and } 6'}$	3.28-3.33(m)	2H

3.14 3,6-Diazido-3,6-deoxy-1,2-*O*-trichloroethylidene-α-D-galactofuranose (17)

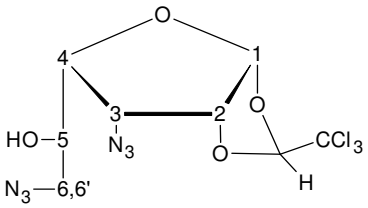


Table 3.14.a) IR Spectral Data (cm^{-1}) of the Compound 17

Functional Groups	cm^{-1}
O-H	3533.1
C-H	2927.3
N_3	2107.3
C-O	1047.1
C-Cl	812.7 - 740.5

Table 3.14.b) ^{1}H-NMR Spectral Data ($CDCl_3$, 400MHz) of the Compound 17

Location of Atoms	^{1}HNMR (δ)	H and Coupling Constants (Hz)
H_1	6.27(d)	1H, $J_{1,2}$ =4
H_{acetal}	5.60(s)	1H
H_2	4.99(d)	1H, $J_{2,3}$ =0
H_3	4.53(s)	1H, $J_{3,4}$ =0
H_4	3.93(d)	1H, $J_{4,5}$ =7.2
H_5	3.77-3.91(m)	1H
$H_{6,6'}$	3.52-3.59(m)	2H
-OH	2.2(bs)	1H

3.15 6-Azido-6-deoxy-1,2:3,4-di-*O*-isopropylidene-α-D-galactopyranose (21)

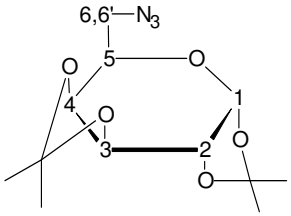


Table 3.15.a) IR Spectral Data (cm^{-1}) of the Compound 21

Functional Groups	cm^{-1}
C-H	2917.5
N_3	2100.1
C=O	1714.6
C-H	1378.8
C-O	1067.0

Table 3.15.b) ^{1}H-NMR Spectral Data ($CDCl_3$, 400MHz) of the Compound 21

Location of Atoms	^{1}HNMR (δ in ppm)	H and Coupling Constants (Hz)
H_1	5.54(d)	1H, $J_{1,2}$ =4.8
H_3	4.63(dd)	1H, $J_{2,3}$=2; $J_{3,4}$=8
H_2	4.33(d)	1H
H_4	4.19(d)	1H, $J_{4,5}$=7.6
H_5	3.92(t)	1H, $J_{5,6}$ =8; $J_{5,6'}$=5.2
H_6	3.52(dd)	1H, $J_{6,5}$=8; $J_{6,6'}$=12.4
$H_{6'}$	3.37(dd)	1H
2xCH_3	1.53-1.45	6H
2xCH_3	1.34	6H

3.16 6-Amino-6-deoxy-1,2:3,4-di-*O*-isopropylidene-α-D-galactopyranose (22)

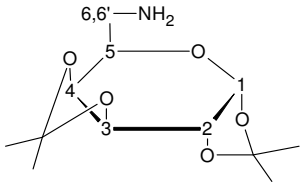


Table 3.16.a) IR Spectral Data (cm-1) of the Compound 22

Functional Groups	cm^{-1}
NH_2	3402.1
C-H	2986.5 - 2936.0
N-H	1614.5
CH_3	1384.6
C-O	1070.3

Table 3.16.b) ^{1}H-NMR Spectral Data ($CDCl_3$, 400MHz) of the Compound 22

Location of Atoms	^{1}HNMR (δ in ppm)	H and Coupling Constants (Hz)
H_1	5.56(d)	1H, $J_{1,2}$ =5.2
H_3	4.63(dd)	1H, $J_{2,3}$=2.4; $J_{3,4}$=8
H_2	4.34(dd)	1H
H_4	4.25(dd)	1H, $J_{4,5}$ =1.6
H_5	3.92(ddd)	1H, $J_{5,6}$ =9.6; $J_{5,6}$=5.2
H_6	3.52(dd)	1H, $J_{6',5}$=9.2; $J_{6,6'}$=13.2
$H_{6'}$	3.37(dd)	1H
-NH_2	2.16(sb)	2H
2xCH_3	1.53-1.45	6H
2xCH_3	1.34	6H

Table 3.17 ^{13}C-NMR Spectral Data (cm-1) of the Compound 8

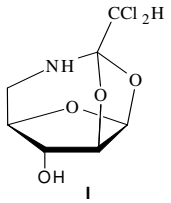
Location of atoms	**^{13}C-NMR (δ in ppm)**
Acetal carbon	155.92
Anomeric carbon	108.39
C_5	50.83
C_2, C_2, C_4 and CCl_2	85.37, 84.17, 75.46 and 77.83

Table 3.18 ^{13}C-NMR Spectral Data (cm-1) of the Compound 9

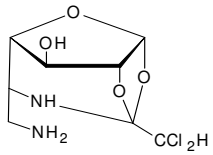
Location of atoms	**^{13}C-NMR (δ in ppm)**
Acetal carbon	137.14
Anomeric carbon	114.58
C_5	72.33
C_2, C_3, C_4 and CCl_2	104.87, 85.07, 76.95 and 84.69

4. RESULTS AND DISCUSSION

The aim of this project was to be able to prepare the compounds shown below:



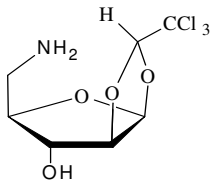
I



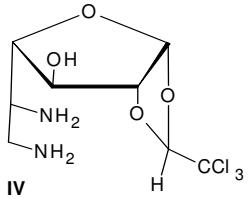
II

These compounds are novel and likely to be opened up by nucleophiles producing glycosides. Especially these compounds are important as they would give rise to the formation of amino sugar containing glycosides which are normally very difficult to obtain under acidic conditions since amino group binds the acid catalyst. However, in this case the acidification of amino group is expected to make it easier to leave and consequently break the N-C bond. Thus attack of the nucleophile is expected to be much easier.

A possible strategy for making the compound **I** is to reduce D-arabinochloralose into its amino derivative by replacing the primary –OH by tosyl group followed by S_N2 substitution of this group by azide and then the azido derivatives obtained reduced into its amino derivative by PPh_3 in MeOH solution. These derivatives called amino sugars are not only important as starting compounds in synthesis of different new products but also due to their biological activities (Csuk, 1985; Ermolenko et al., 1999; Juan Xie, 2003; Sun, 2006).

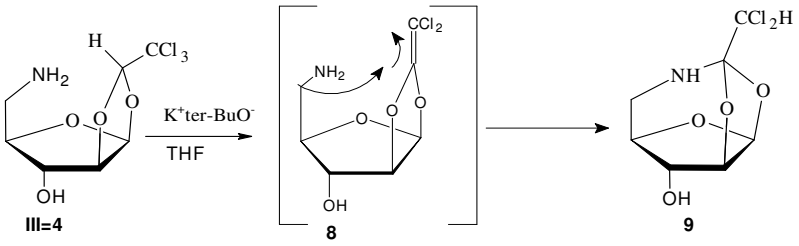


III



IV

The reaction of amino compound **III** with potassium *tert*-butoxide is expected to produce a dichloroethylidene ketene acetal **8**. Attack of the amine to the ketene acetal double bond would be expected to produce the compound **9**.



For the preparation of **9**, 5-amino 5-deoxy-D-arabinochloralose is needed as the starting compound. To introduce an amino group at position 5 of 1,2-*O*-(*S*)-trichloroethylidene-α-D-arabinofuranose **1**, the comercially available D-arabinose was employed as starting material. The initial plan for the synthesis of 5-Amino 5-deoxy-1,2-*O*-(*S*)-trichloroethylidene-α-D-arabinofuranose **4** scheduled homologation of a pentofuranose derivative by introduction of an azido group. For this purpose the free hydroxy group of the compound **1** available by reacting D-arabinose with chloral would be activated for nucleophilic substitution. Thus, the free hydroxyl group at C-5 of **1** was substituted by tosyl group by reaction of the compound **1** with *p*-toluenesulfonyl chloride in pyridine. The tosylate **2** reacted with NaN_3 afforded a single product **3**, 5-Azido 5-deoxy-1,2-*O*-(*S*)-trichloroethylidene-α-D-arabinofuranose in 98 % yield.

Treatment of **3** with a solution of PPh_3 in methanol, at room tempeture, caused the reduction of azido group into amino group. The t.l.c showed formation of two main products, which were separated by column chromatography. The more polar product was identified by IR and ^{1}H-NMR spectroscopy as the -amino **5**. Furthermore, the broad band-singlet at 2.37 ppm was assigned to the -NH_2 and -OH for these protons.

Alternatively, a synthesis of **6**, 5-Amino-5-deoxy- 3-*O*-acetyl- 1,2-(*S*) trichloroethylidene-α-D-arabinofuranose was designed to facilitate NMR analysis. The starting material was azide **3**, which was readily acetylated at the secondary hydroxyl group C-3 to afford the compound **5**; 5-azido-5-deoxy-3-*O*-acetyl- 1,2-*O*-(*S*)- trichloroethylidene-α-D-arabinofuranose. Treatment of **5** with a solution of PPh_3 in methanol, at room temperature, led to the amino **6,** 5-Amino-5-deoxy- 3-

O-acetyl- 1,2-(*S*)-trichloroethylidene-α-D-arabinofuranose in 88.5 % yield which was then acetylated to lead to the product **7,** 5-acetamido-5-deoxy-3-*O*-acetyl-1,2-*O*-(*S*)-trichloroethylidene α-D-arabinofuranose.

The structure of this product was confirmed by using spectral methods (IR, ^{1}H- NMR). In the IR spectrum of the new amino acetyl compound **7**, the bands corresponding to the $-NH_2$ and the carbonyl group are observed at 3,493 cm^{-1} and 1,737 cm-1, respectively. In the ^{1}H-NMR spectrum, the –NH and the carbonyl methyl group of this compound appeared as broad peak and a sharp singlet at 2.98 ppm and 2.90 ppm respectively.

The reaction of **4** with tert-butoxite at room temperature in THF or with warm heating in *tert*-butanol afforded a mixture chromatographed on silicagel with 10:2 CH_2Cl_2-MeOH as eluent, to give 2 main fractions **A** and **B** being totally 42 % in yield.

The fraction **A** (34 %) having higher mobility by t.l.c was characterized as 5-Amido-5-deoxy-1,2-O-,5-*N*-orthodichloroacetyl- α -D-arabinofuranose (**9**). The H-1 and acetal proton of this new compound appeared as a singlet at 6.04 and 5.72 ppm respectively in the ^{1}H-NMR spectrum. The coupling constant $J_{2,3}$ and $J_{3,4}$ are zero in the spectra of compounds **3, 4, 5, 6, 8** and **9**.

Molecular models indicate that the dihedral angle between H-2 and H-3; and between H-3 and H-4 are almost 90^0 which is consistent with the observed $J_{2,3}$ and $J_{3,4}$ values. These results clearly show the assigned structure (Figure 4.1 and Figure 4.2).

On the other hand, the coupling constant $J_{2,4}$ is 1.6 Hz in the spectra of compound **9**. Molecular model indicates that the dihedral angle between H-2 and H-4 is almost W which is consistent also with the observed coupling (Figure 4.3). In the ^{13}C-NMR spectrum, the C-1 and the acetal group peak appeared at 114.58 and 137.14 ppm respectively. These results clearly show the assigned structure.

In the IR spectrum of this new compound **9**, the bands corresponding to the –NH and CONH- are observed at 3,356 cm^{-1} and 1,6680 cm^{-1}, respectively.

The spectroscopic studies (IR, 1H and ^{13}C- NMR) of the fraction **B**; 8 % of yield, showed that the compound had the ketene acetal structure. In the IR

spectrum of this new amino ketene acetal **8**, the bands corresponding to the $-NH_2$ and C=C were observed at 3,332 cm^{-1} and 1,6682 cm^{-1}, respectively with a weak band at 1,540 cm^{-1} assigned to the NH- symetric vibration. The structure of this product was confirmed also by its ^{13}C-NMR spectrum. The C-1 and the acetal group peak appeared at 108.4 and 155.6 ppm respectively in the ^{13}C-NMR spectrum. The ^{1}H-NMR spectrum study confirmed that the compound had the ketene acetal structure: its ^{1}H-NMR spectrum clearly indicated the absence of the acetal proton singlet.

Surprisingly, using Tol: MeOH as solvent reversed the results: The fraction **A** was obtained almost in the same proportions but the ketene acetal compound **8** was not isolated.

These compounds were not stable compound and were extremely sensitive toward humidity. This has been reported in literature on orto-ester derivatives (Yesim et al., 1996). Probably the humidity sensitivity of these products would be the main reason of difficulties in NMR spectroscopic data analysis.

For the preparation of **II**; 5,6-diamino-5,6-dideoxy-D-galactofuranose was planned using the same conditions as we proceeded on **I**.

The sulfonates **13**, **14** and **15** were available by reaction of the compound **12** with *p*-toluenesulfonyl chlorine in pyridine. The reaction of compound **13** with NaN_3 afforded a single product azido derivate **16** in 80 % yield. The free hydroxyl protons at C-3 and C-5 appeared as doublets (J = 5.2 Hz for each) at 5.61 and 5.42 ppm, respectively in ^{1}H-NMR spectrum of this compound.

However, the reaction of **14** and **15** with NaN_3 failed to give their diazide and triazide derivatives. Several modifications were investigated including variation of the NaN_3-amount (1 to 6 equivalents), the solvent (e.g., acetone, DMF, HMPA), the reaction-time and the reaction temperature (up to 150 ^{o}C). Finally, the isolation of a small amount of the diazide **17** but the yield of this compound was lower (only 14 %) succeeded after heating the sulfonate **14** with 4 equivalent in DMF for 60h. The main amount of the isolated product (80 %) was the partially azited compound **18** identified as 6-azido- 6-deoxy-3-*O*-tosyl-3-deoxy-1,2-*O*-trichloroethylidene α-D-galactochloralose.

The nucleophilic substitution of the tosyl group of **14** and **15** would be easier using hexamethylphosphoramide (HMPA) as solvent instead of *N,N*-dimethylformamide (DMF) as revealed on t.l.c but isolation of the products was impossible. The high boiling point of the HMPA (235 ^{o}C) makes it very difficult to evaporate (Roy and James, 1972).

Obviously the nucleophilic substitution of the tosyl group of **14** and **15** in HMPA is due to its greater solubility of sodium azide in HMPA (2.68 g per 100 mL) than in DMF (0.74 g per 100 mL) at 120 ^{o}C (Normant, 1967).

The difficult displacement at C-3 in furanosyl derivatives, which is expected to be the least reactive position (Ferrier and Collins, 1972) accounts for the low yield of this derivative.

The structure of this nitrogen-containing sugar product **17** was confirmed by using spectral methods (IR, 1H-NMR). In the IR spectra of compound **17** a broad OH absorption (stretching) band 3,533 cm^{-1}, typical C=N absorption bands at 2,107 cm^{-1} appeared.

The structure of compound **17** was also confirmed by ^{1}H-NMR spectra. ^{1}H-NMR spectrum of this compound clearly indicated the complete absence of the Ar-H peaks seen at 7.8 and 7.4 ppm in the ^{1}H-NMR spectra of tosylates **14** which indicated the completely displacement of the tosyl groups.

Summed up, these spectral data proved the formation of this new azido – galactofuranose derivative **17.**

Furthermore, the 6-amino-6-deoxygalactopyranose, in literature obtained by $LiAlH_4$ reduction of the oxime, was resynthesised by us using the **Staudinger reaction** or **Staudinger reduction** in which the combination of an azide **21** with a phosphine afforded **22**, 6-Amino-6-deoxy- 1,2:3,4-di-*O*-isopropylidene-α-D-galactopyranose in high yield.

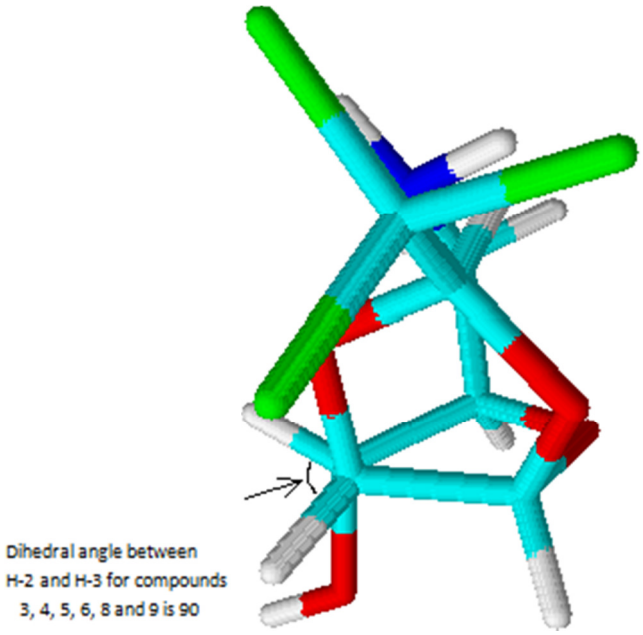


Figure 4.1. Dihedral Angle between H-2 and H-3 for Compounds 3, 4, 5, 6, 8 and 9.

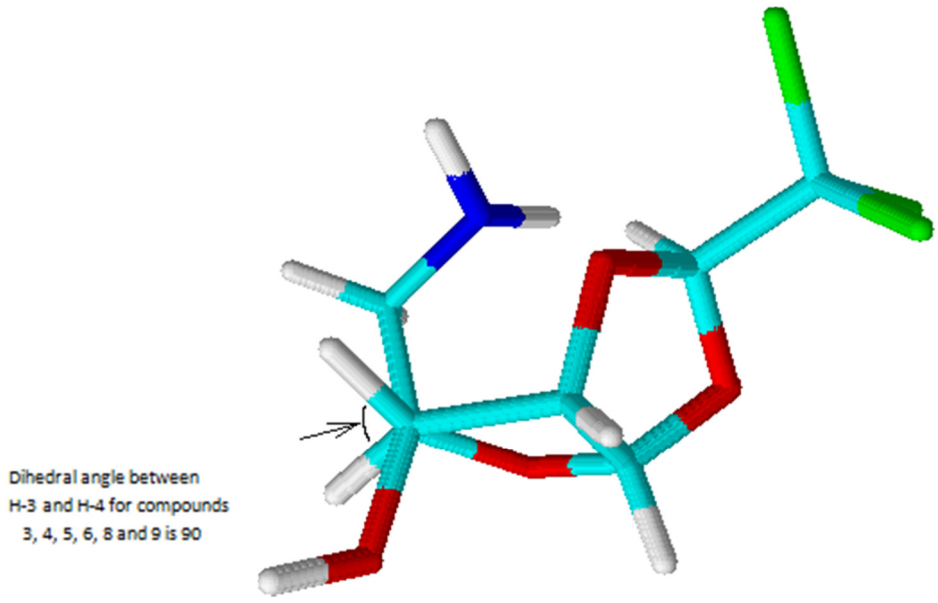


Figure 4.2. Dihedral Angle between H-3 and H-4 for Compounds 3, 4, 5, 6, 8 and 9.

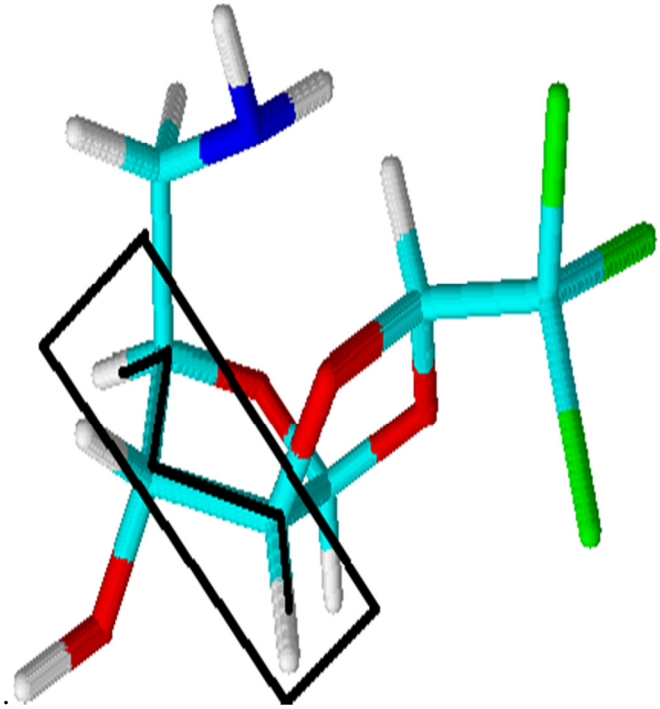


Figure 4.3 W- Coupling between H-2 and H-4 for Compound 9

REFERENCES

Aburto-Luna, V., Meza-Léon, R.L. and Bernes, S., 2008, Acta Cryst., E64, O1784.

Ay, K., Çetin, F. and Yüceer, L., 2007, Carbohyd. Res., 342 (8), 1091-1095,.

Bergman, R.G. and Bertozzi, C.R., 2005, J. Am. Chem. Soc, 127, 2686.

Csuk, R., 1985, Carbohydr. Res., 140, 167–168.

Çetin, F., Yenil, N. and Yüceer, L., 2005, Carbohyd. Res., 340 (17), 2583-2589.

De Belder, A.N., 1965, Cyclic acetals of the aldoses and aldosides, in Advances Carbohydr.Chem., 20, 219-302.

Ermolenko, L., Sasaki, N.A. and Potier, P., 1999, Tetrahedron Lett. 40, 5187–5190.

Ferrier, R.J. and Collins, P.M., 1972, Monosaccharides Chemistry , 1932, 318.

Fischer, E., 1893, Ber. Dtsch., Chem. Ges., 28, 1145.

Forsén, S., Lindberg, B. and Silvander, B.G., 1965, Acta Chem. Scand., 19, 359-369.

Gmulka, A., İbrahim, I.H. and Zbiqniew, B., 1985, Canadian Journal of Chemistry, 63,766.

Guthrie, R.D. and Honeyman, J., 1968, An introduction to the Chemistry of Carbohydrates, Clarendon Press, 3rd edn,.

Han, M.J., Yoo, K.S., Kim, Y.H. and Chang, J.Y., 2002, Tetrahedron Lett., 43, 5597–5600.

Hassner, A., Fibijer, R. and Andisik, D., 1984, Lewis acid catalyzed conversion of alkenes and alcohols to azides, Journal of Organic Chemistry, 49, 4237.

REFERENCES (continued)

Heffter, A., 1889, Ber. Dtsch. Chem. Ges., 22 (1), 1050-1051.

Holden, D.A., 1984, Synthesis and spreading behavior of some reactive derivatives of long chain alchols and carboxylic acids, Canadian Journal of Chemistry, 62,574.

Jarowicki, K. and Kocienski, P.J., 2000, Chem. Soc., Perkin Trans., 1,2495

Ji, X.M., Mo, J., Liu, H.M. and Sun, H.P., 2006, Carbohydr. Res., 341, 2312–2320.

Wang, J., Li, J., Tuttle, D., Takemoto, J.Y. and Chang, C.W.T., 2002, Org. Lett., 4, 3997–4000.

Juan Xie, J., 2003, Carboyhdrate. Res.; 338, 399–406.

Khan, A.R., Tripathi, R.P., Bhaduri, A.P., Puri, R.S.A., Tripathi, L.M. and Srivastava, V.M.L., 2001, Synthesis and immunomodulatory activity of 3-O-[2'-hydroxy-3'-N,N-disubstituted aminopropan-1'-yl]-α-D-glucofuranoses, European Journal of Medicinal Chemistry, 36, 435-445.

Kim, H.Y., Kim, K. and Goto, T., 1973, Facile synthesis of azides: conversion of hydrazines using dinitrogen tetroxides, Tetrahedron Letters, 27 (39), 4749.

Krasowski, M.D., 2003, Bulletin of Anesthesia History, 21 (3), 1-8.

Lemmens, J.M., Blommende, W.W.J.M. and Thijs, L., 1984, Synthesis of α,β-Epoxyacyl azides and their rearrangement to epoxy isocyanates and 3- and 4-oxazolin-2 ones, Journalof Organic Chemistry, 49,2231.

Nadkarni, S. and Williams, N.R., 1965, Journal of Chemical Society, 3496.

Nishiyama, T., Isobe, M. and Icikawa, Y., 2005, Angew. Chem., 117, 4446–4449.

REFERENCES (continued)

Normant, H., 1967, Angew.Chem.,**79**, 10929.

Norris, R.K. and Symith-King, R.J., 1982, The stereochemistry of the $S_{RN}1$ reaction in some cyclohexane derivatives, Tetrahedron, 38 (8), 1051.

Oskay, M., Yenil, N. and Ay, K., 2008, World Applied Sciences Journal, 4 (5), 720-723.

Reist, E.J., Spencer, R.R. and Baker, B.R., 1960, J. Am. Chem. Soc., 82, 2025–2029.

Roy, L.W. and James, N.B., 1972, Methods In Carbohydrate Chemistry, 1972.

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

Salman, Y.G., Makinabakan, Ö. and Yüceer, L., 1994, Tetrahedron Lett., 35 (49), 9233-9236.

Sanchez, S., Bamhaoud, T. and Prandi, J., 2000, Tetrahedron Lett., 41, 7447-7452.

Sasaki, T., Eguchi, S. and Hioki, T., 1982, Journal of Chemical Society, Perkin Trans I, 1953.

Scriven, E.F.V. and Turnball, K., 1988, Azides: Their preparation and synthetic uses, Chemical Review, 88, 298.

Segev, G., Yas-Natan, E., Shlosberg, A. and Aroch, I., 2006, The Veterinary Journal, 172, 109-113.

Solomons, T.W.G., 1996, Organic Chemistry, John Wiley & Sons, İnc., 1220.

REFERENCES (continued)

Staudinger, H. and Meyer, J., 1919, "Über neue organische Phosphorverbindungen III. Phosphinmethylenderivate und Phosphinimine", Helv. Chim. Acta **2** (1): 635.

Tian, W.Q. and Wang, Y.A., 2004, J. Org. Chem., 69, 4299

Werngs, W.D., Williams, D.H., Feeney, J., Brown, J.P. and King, R.W.J., 1972, Chem.Soc., Perkin Trans. 1, 443–446.

Yenil, N., Ay, E., Ay, K., Oskay, M. and Maddaluno, J., 2010, Carbohydrate Research, 345, 1617-1621.

Yücer, L., 1978, Galacto ve glukokloralozlar. Bazı tosıl türevlerinin nükleofilik sübstitüsyon reaksiyonlarında sterik ve polar etkenler, Doçentlik Tezi, Ege Üniversitesi, 121.

Zamboni, R. and Rokach, J., 1983, Synthesis of the aza analog of LTA_4, Tetrahedron Letters, 24, 331.

Zosimo-Landolfo, G. and Tronchet, J.M.J., 1999, Il Farmaco, 54, 852-853.

CURRICULUM VITAE

Personal Knowledge

Name and Surname **:** Pierre Claver MPAWENAYO

Date/Place of Birth **:** 01.01.1979 / Kiremba-Ngozi

Nationality **:** Burundian

Connexion Address **:** Burundi University / Bujumbura-Burundi

Phone Number **:** +25779945910 and +25779765443

E-mail **:** **mpapierros@yahoo.fr** and

mpierreclaver@ymail.com

Educational Backround

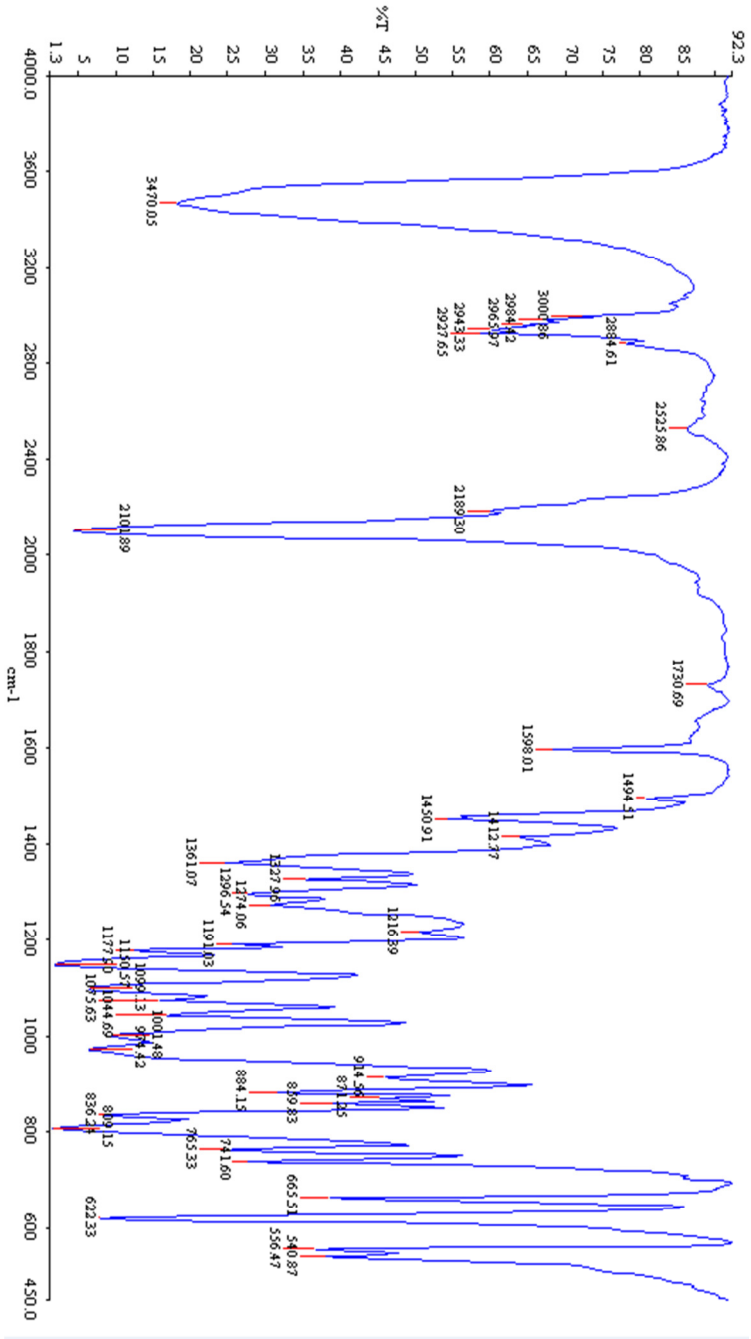
2003-2008 Bsc. in Chemistry, Burundi University, Faculty of Science

2008-2009 Assistant at Burundi University, Faculty of Science

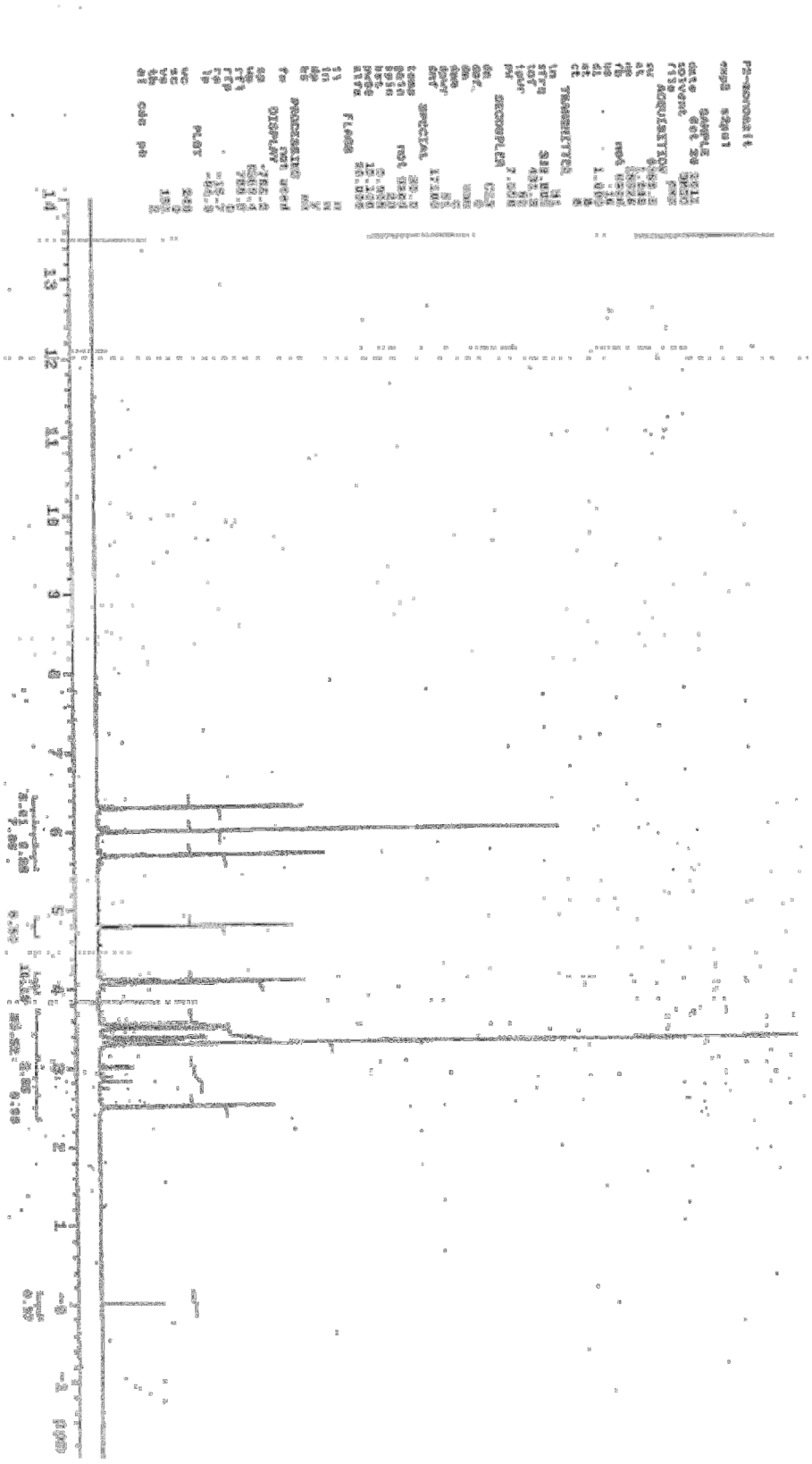
2010-20013 MSc. in Organic Chemistry, Graduate School of Natural and Applied Sciences, Ege University

APPENDIX

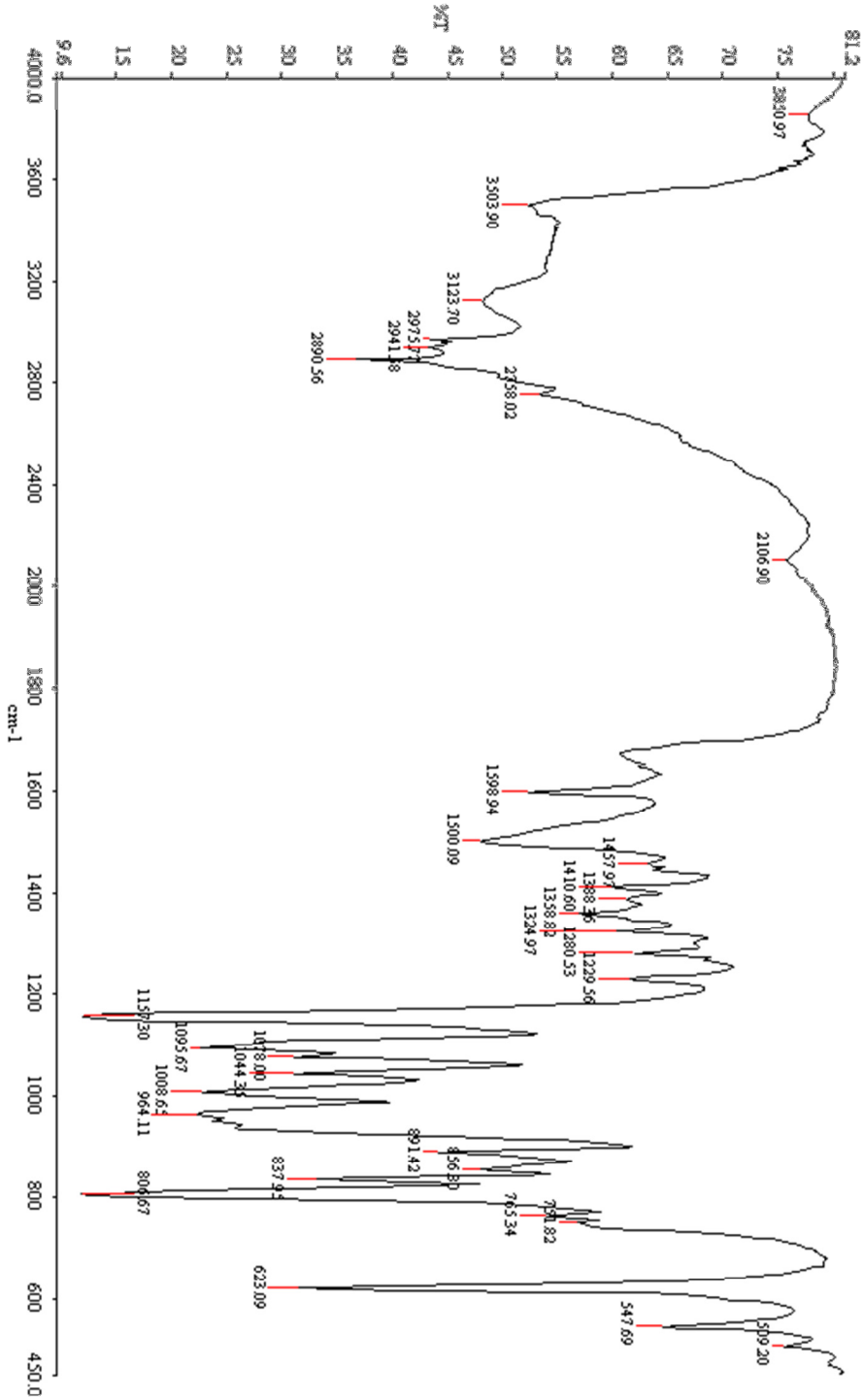
Appendix 1 FTIR Spectrum of the Compound 3



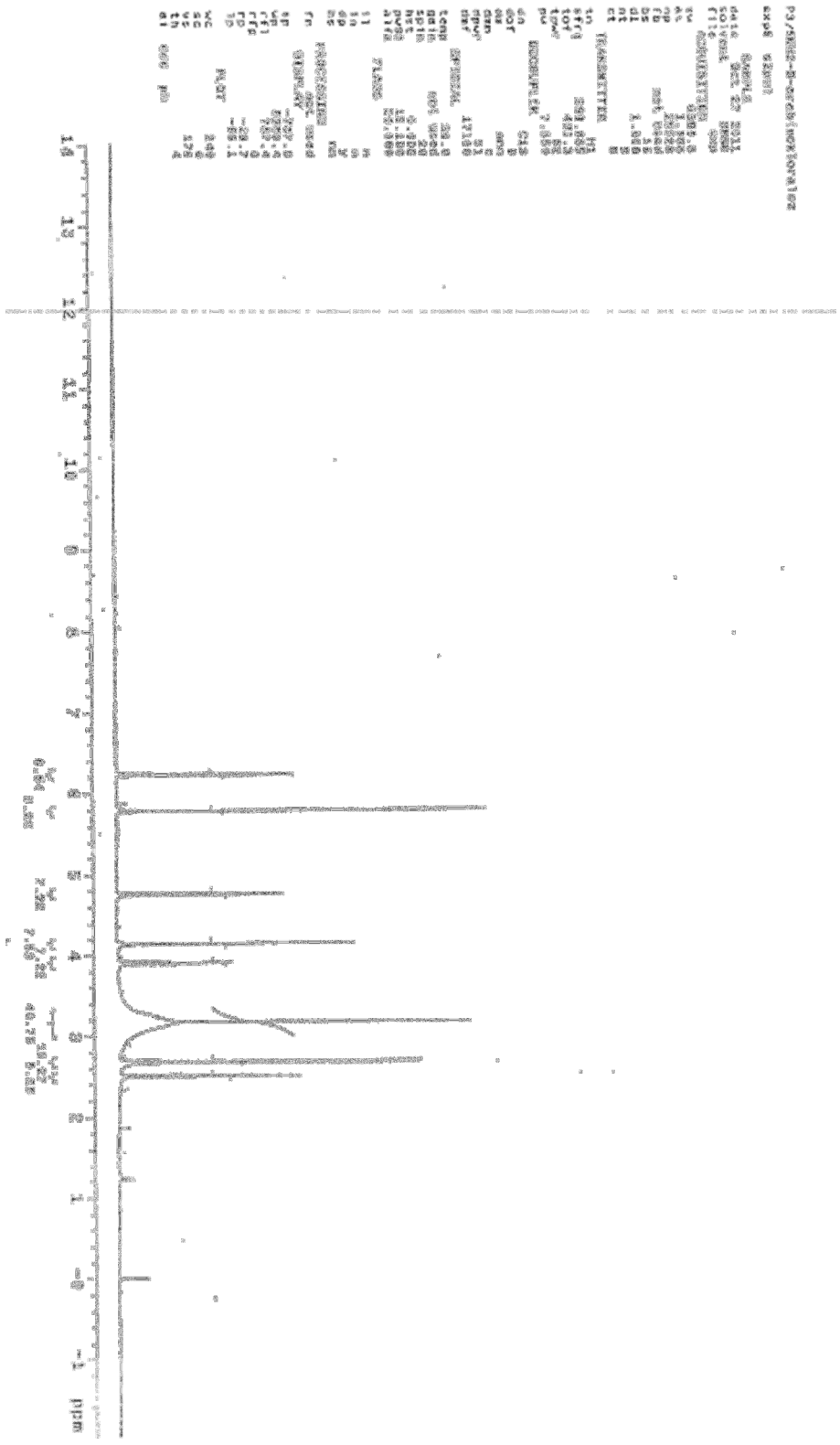
Appendix 2 ^{1}H-NMR Spectrum of the Compound 3



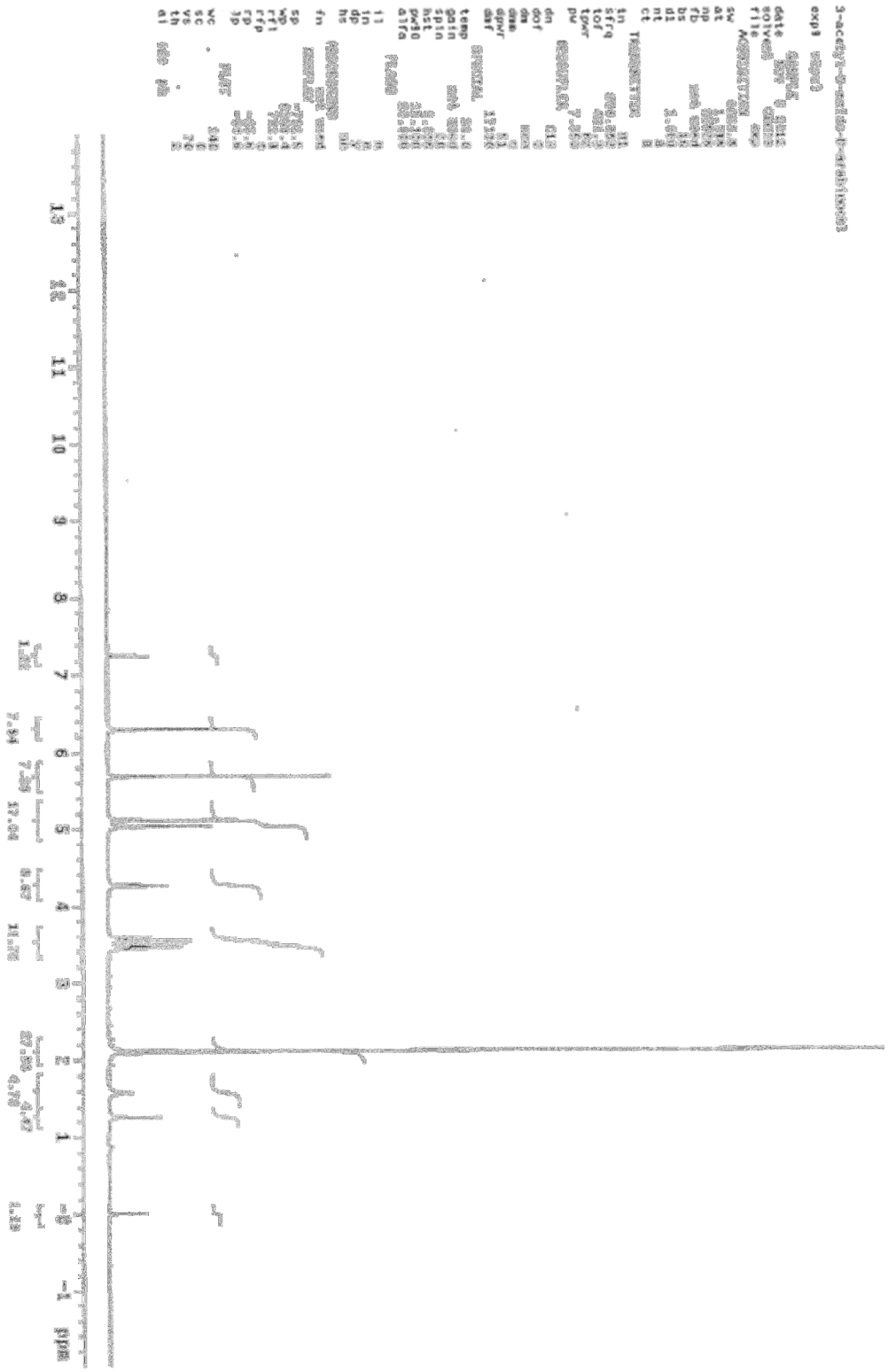
Appendix 3 FTIR Spectrum of the Compound 4



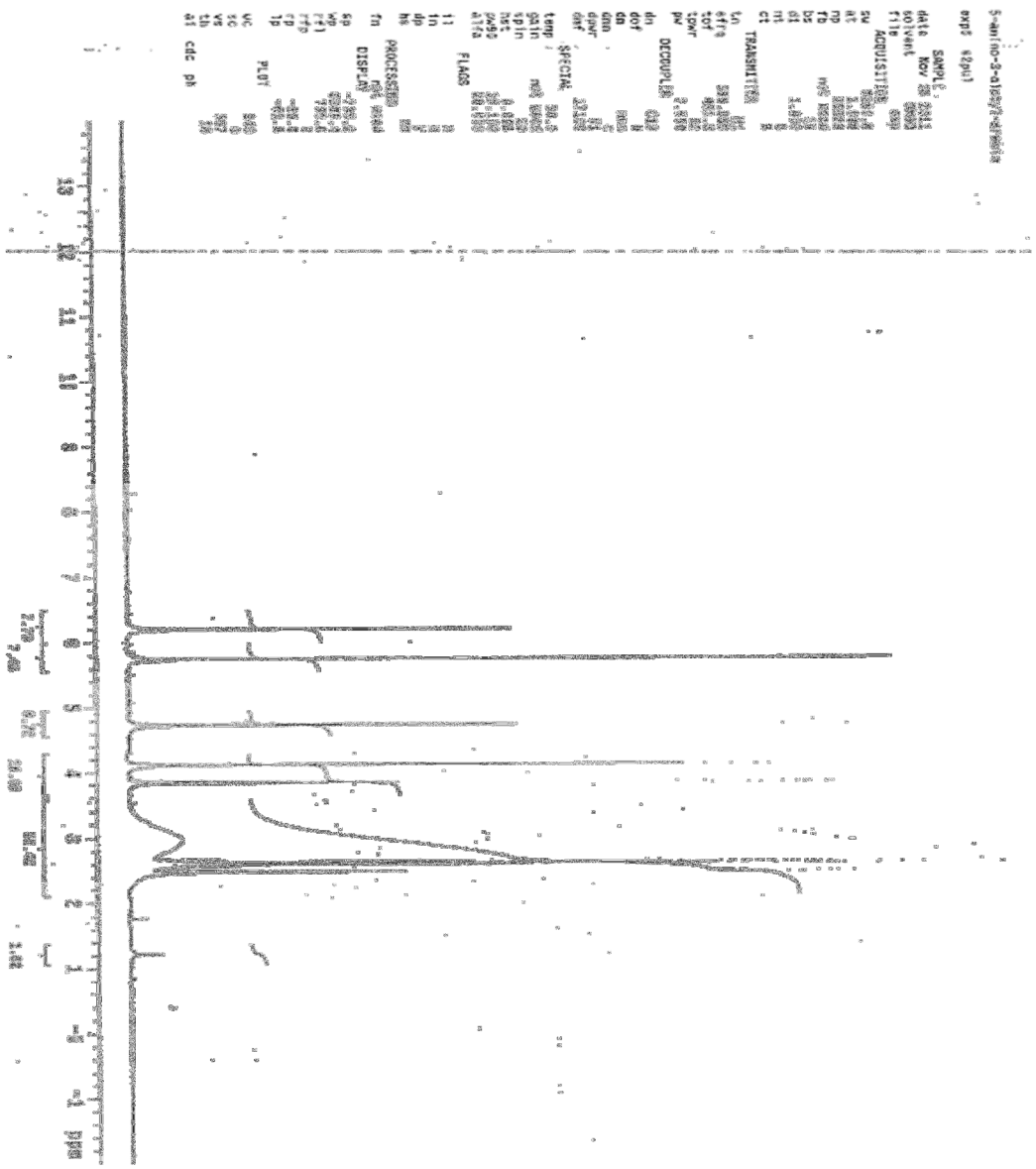
Appendix 4 ^{1}H-NMR Spectrum of the Compound 4



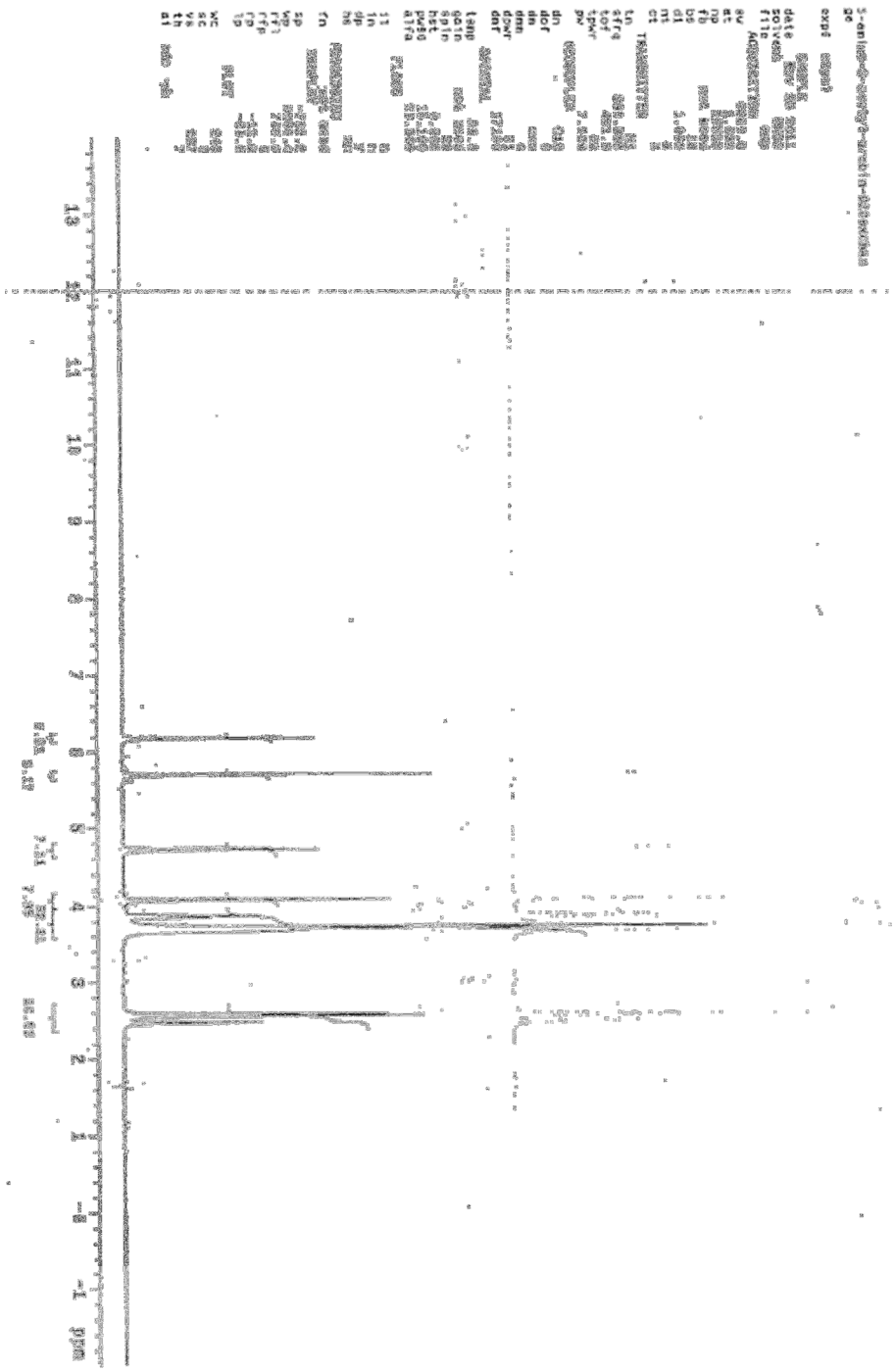
Appendix 5 ^{1}H-NMR Spectrum of the Compound 5



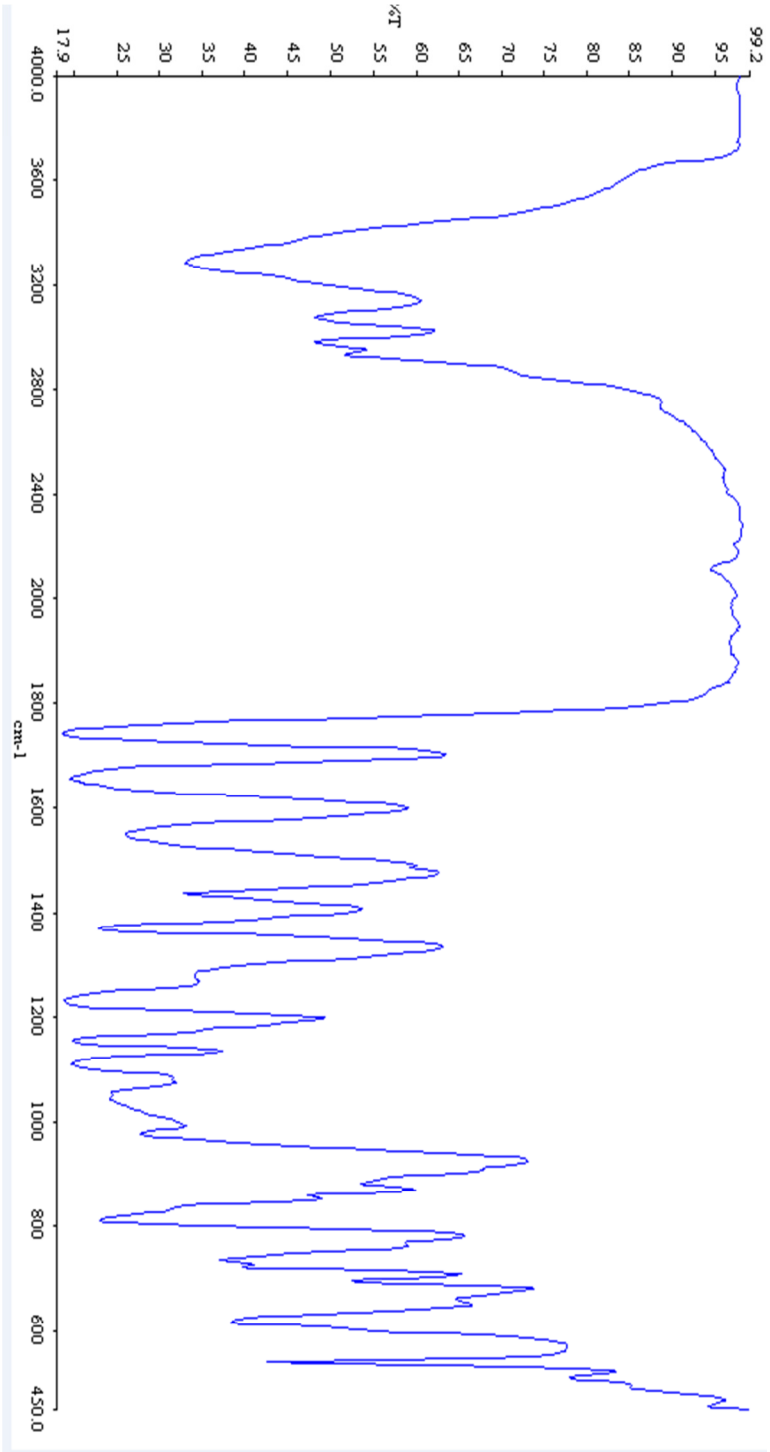
Appendix 6 ^{1}H-NMR Spectrum of the Compound 6



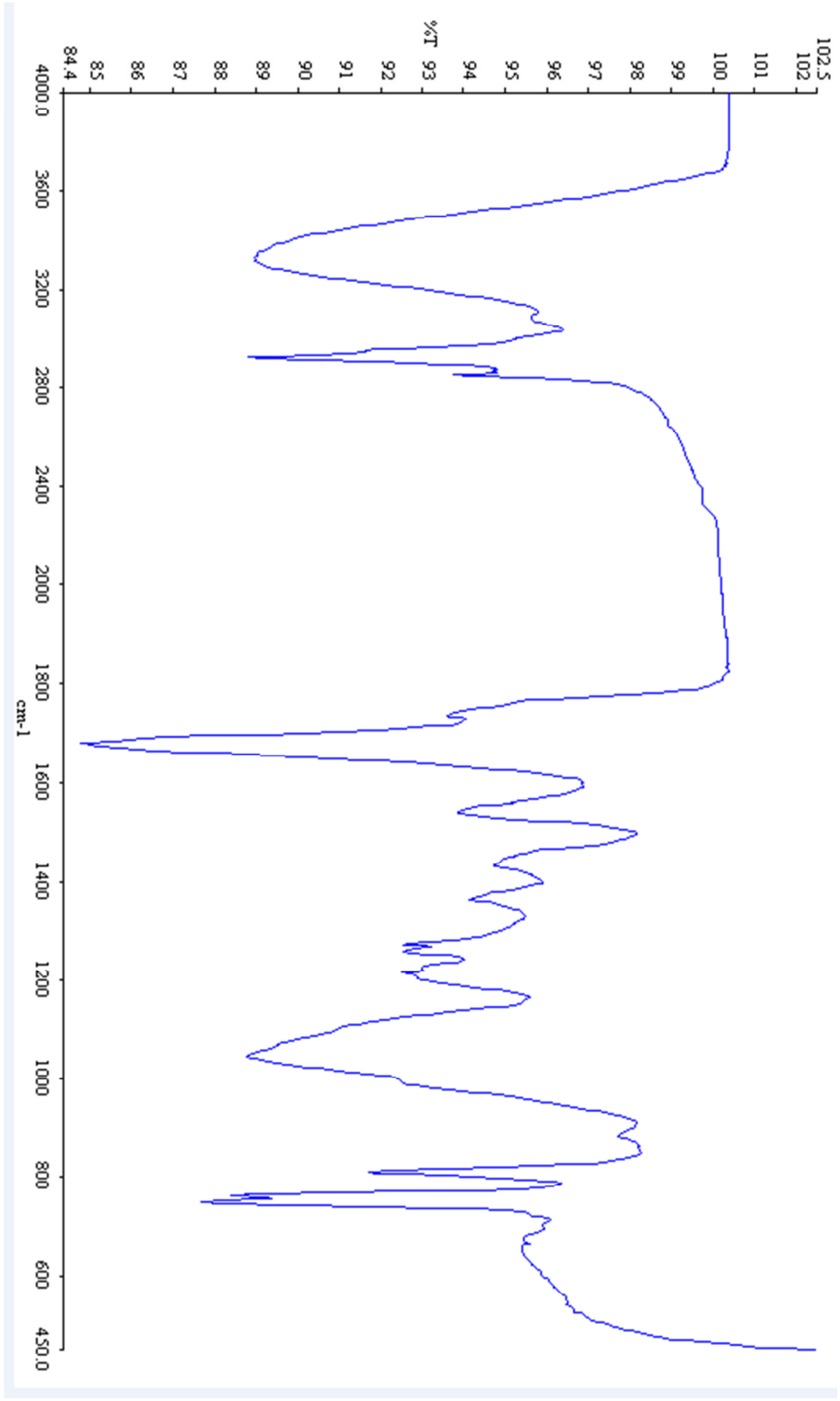
Appendix 7 Deuterium Exchange ^{1}H-NMR (DMSO-D_6, 400MHz) Spectral Data of the Compound 6



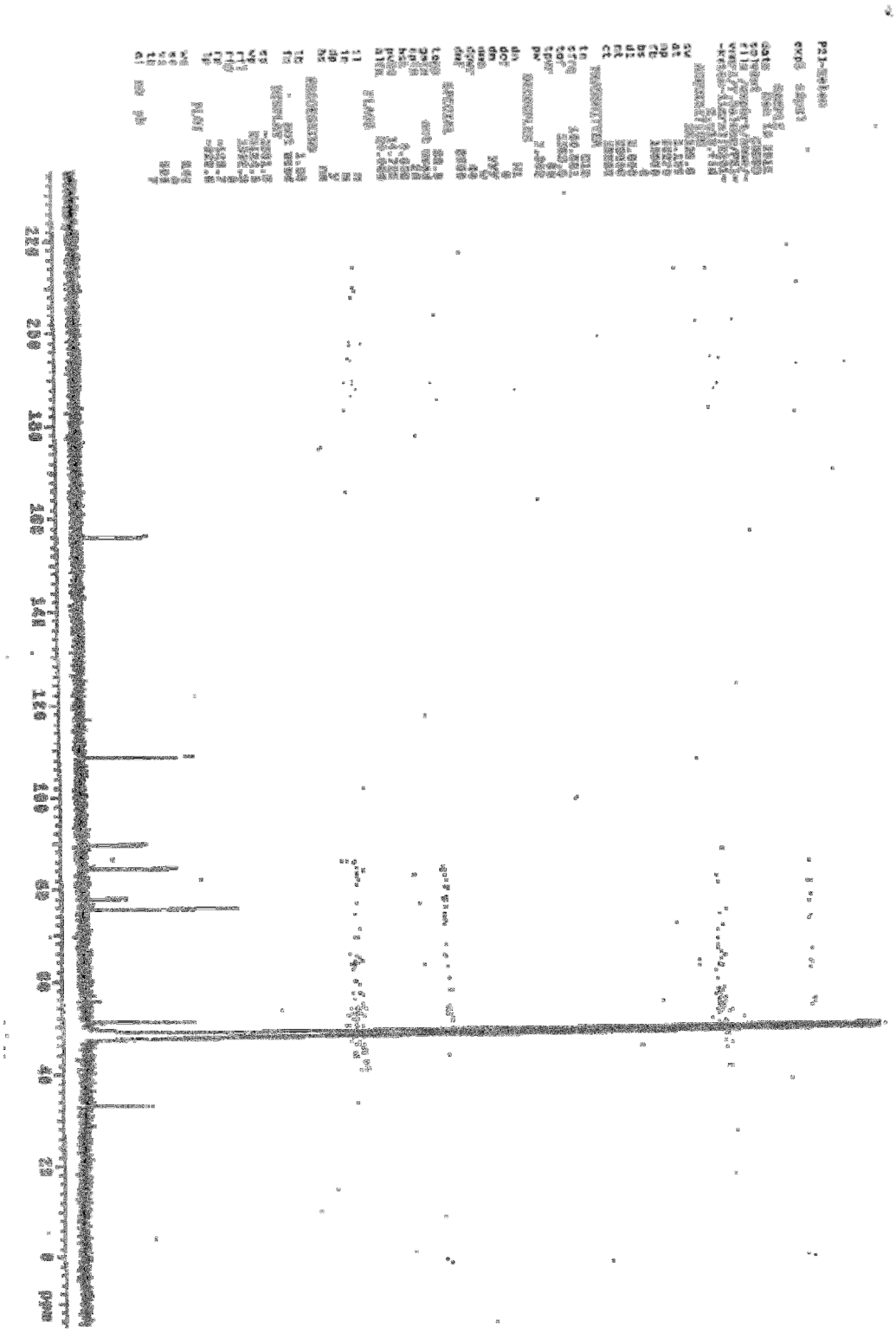
Appendix 8 FTIR Spectrum of the Compound 7



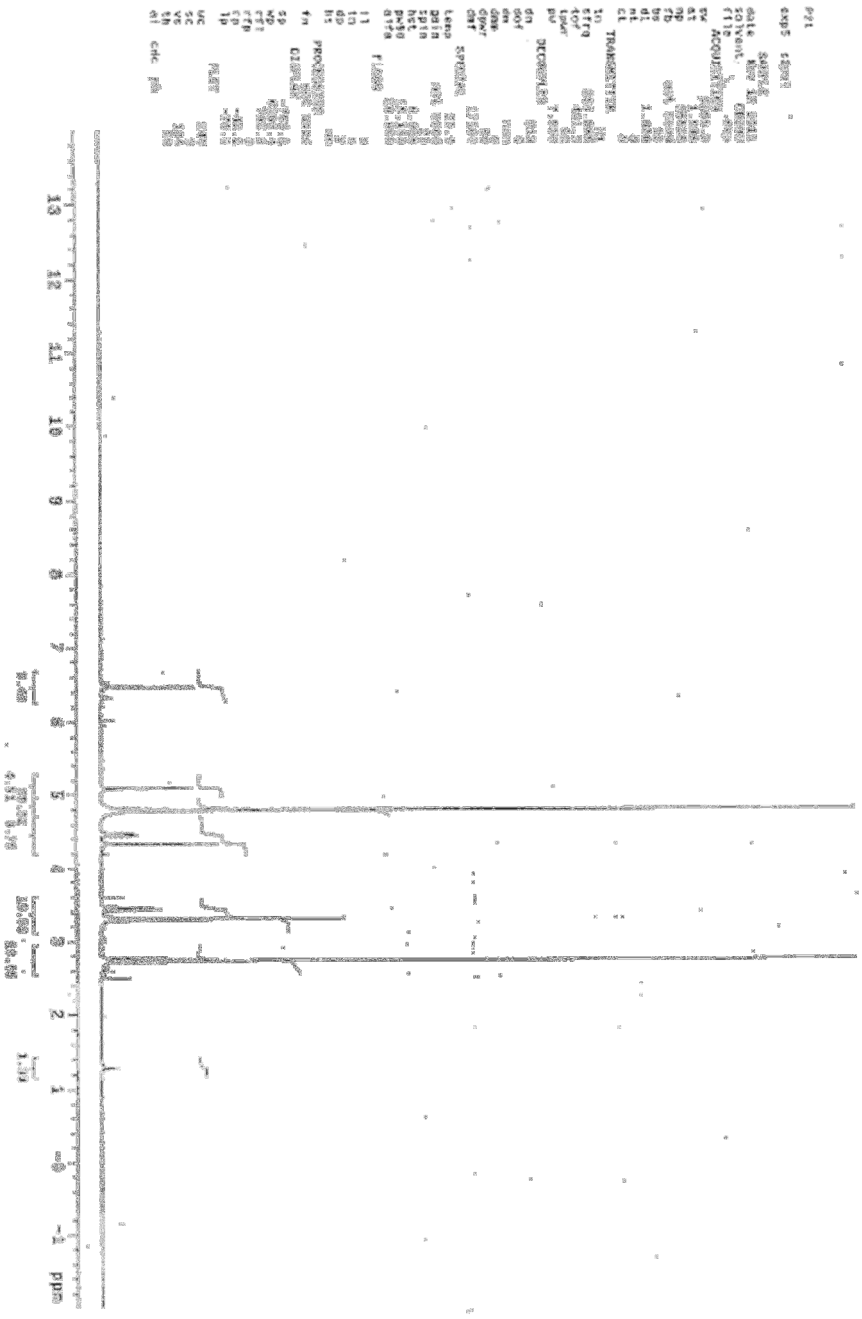
Appendix 9 FTIR Spectrum of the Compound 8



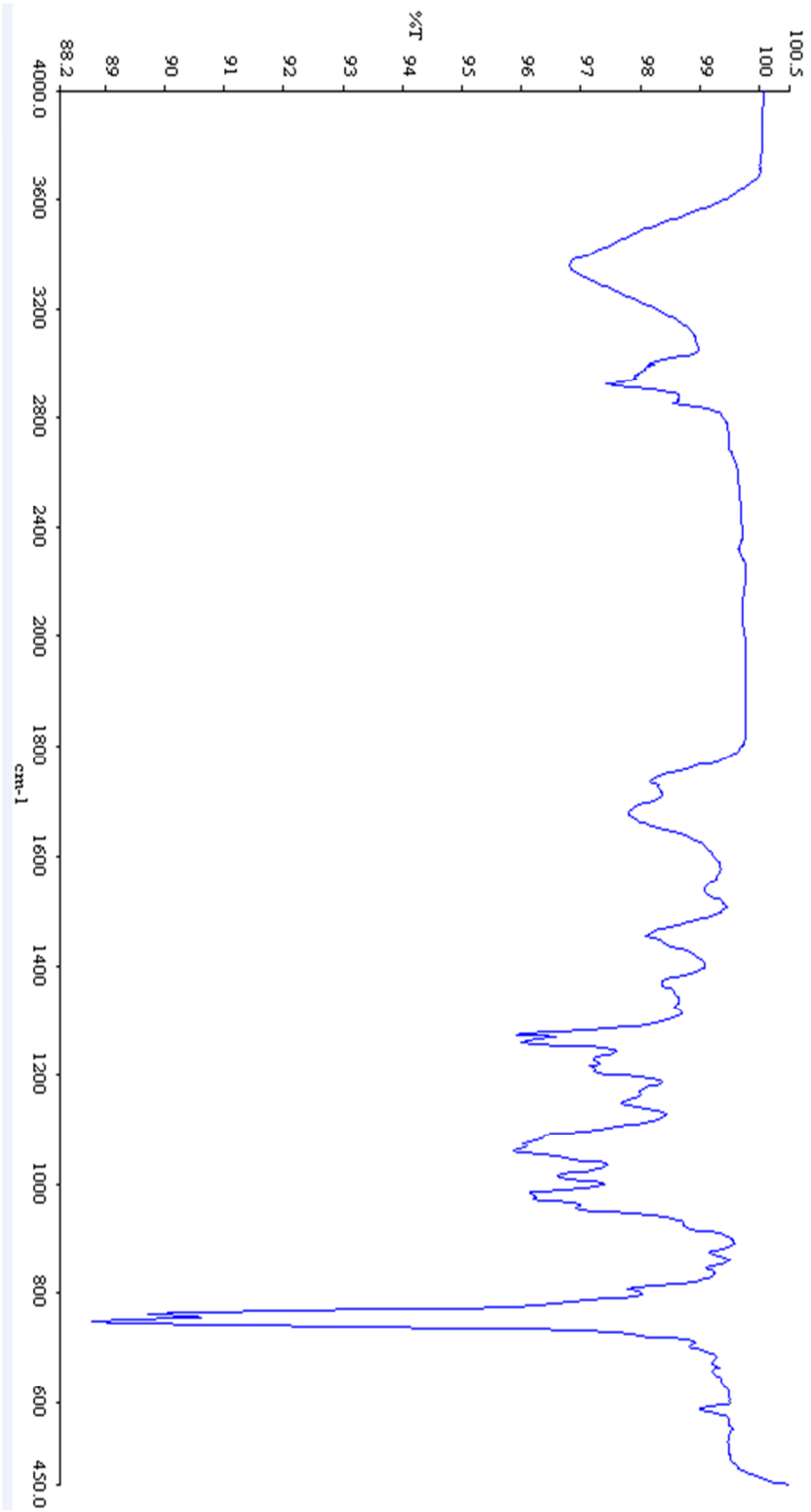
Appendix 10 ^{13}C-NMR Spectrum of the Compound 8



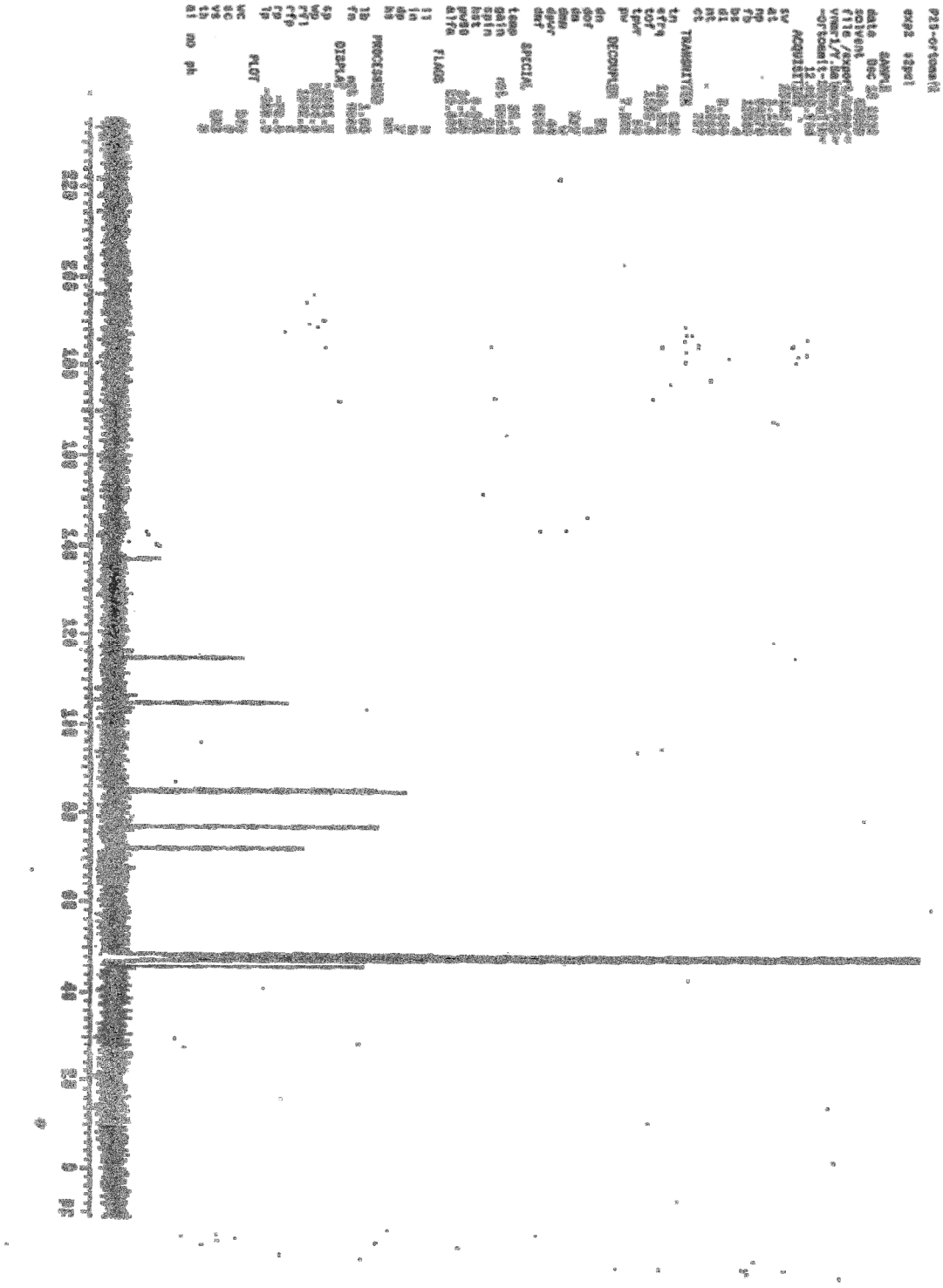
Appendix 11 ^{1}H-NMR Spectrum of the Compound 8



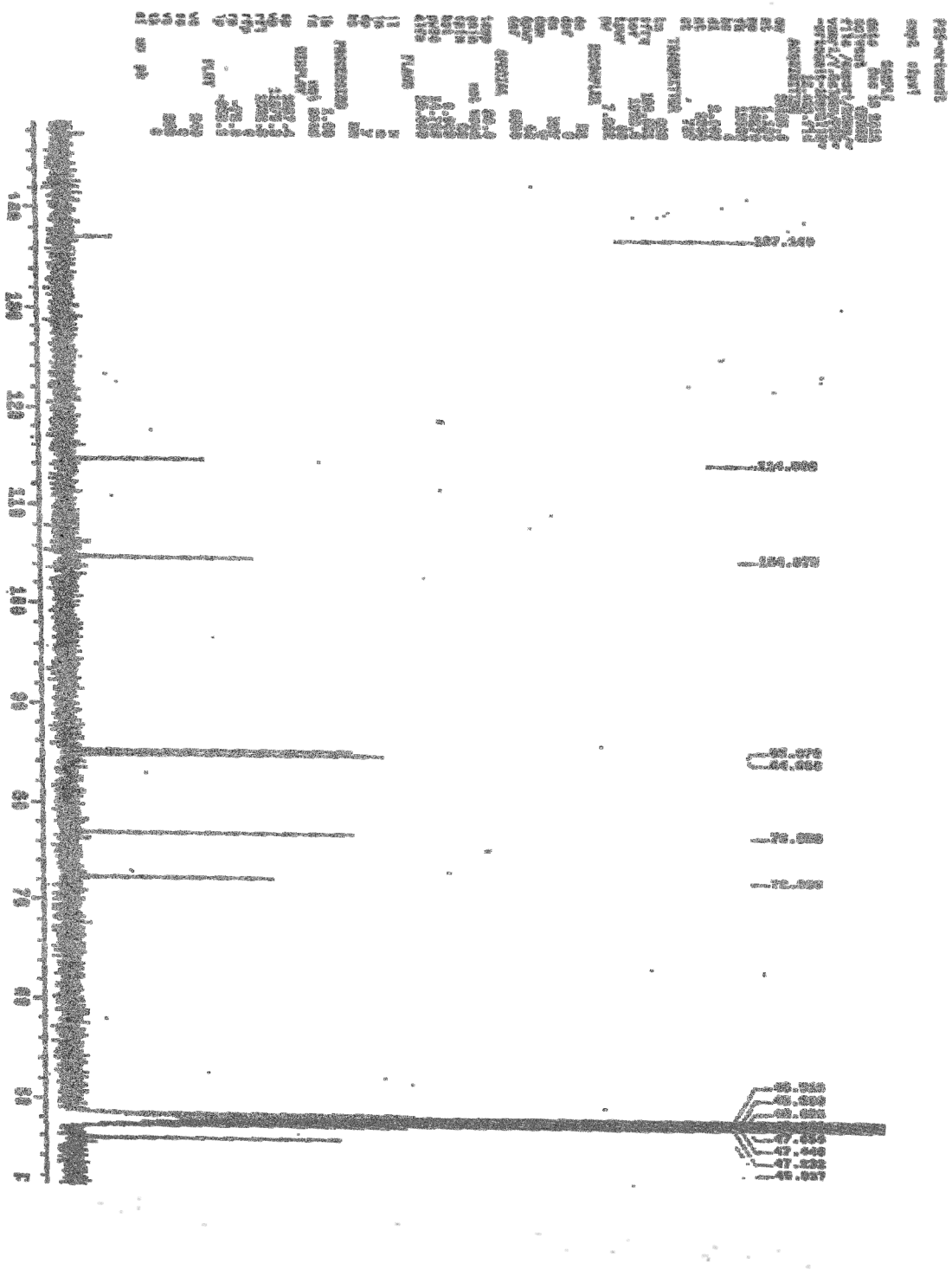
Appendix 12 FTIR Spectrum of the Compound 9



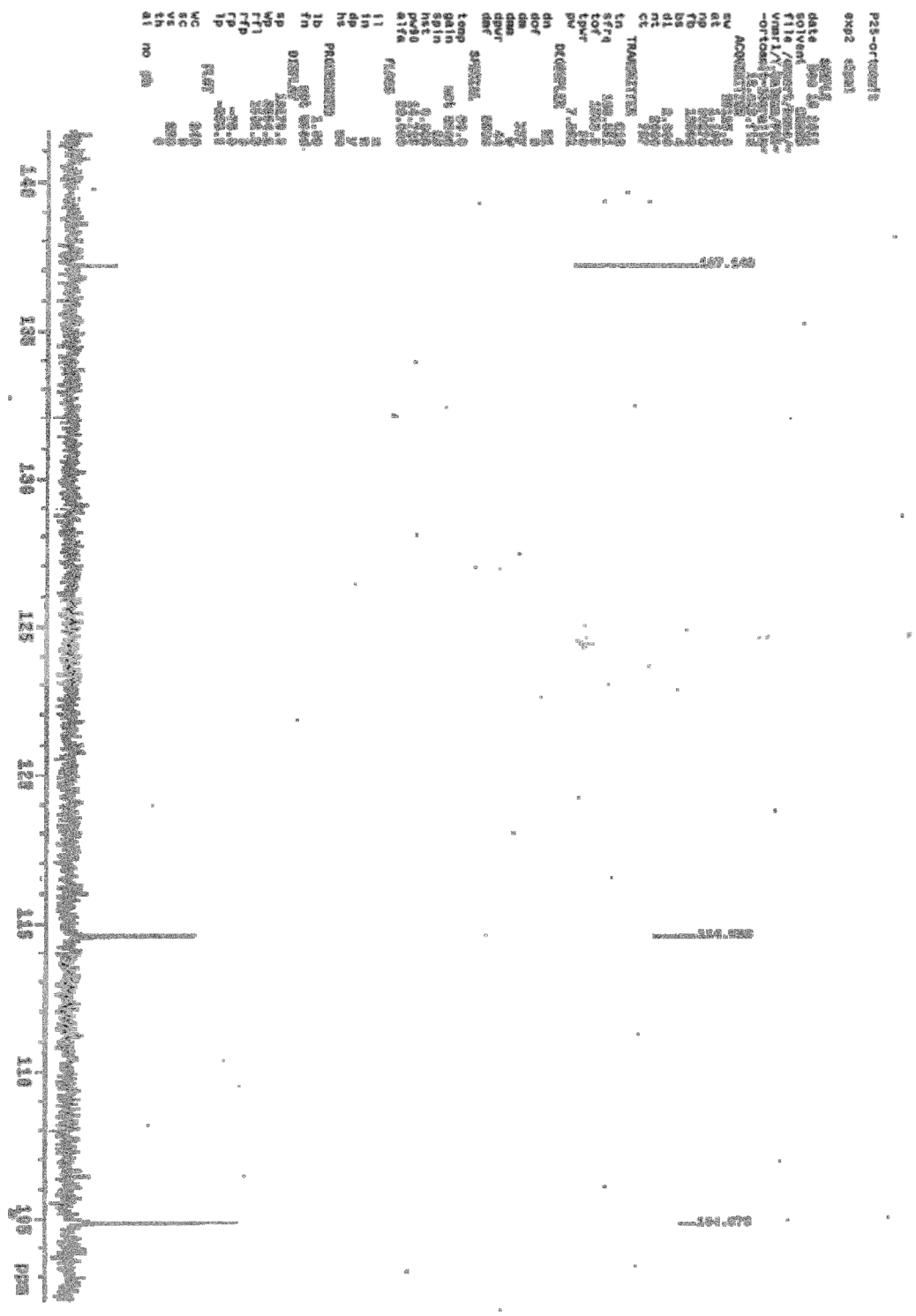
Appendix 13 Expansion of the ^{13}C-NMR Spectrum of the Compound 9



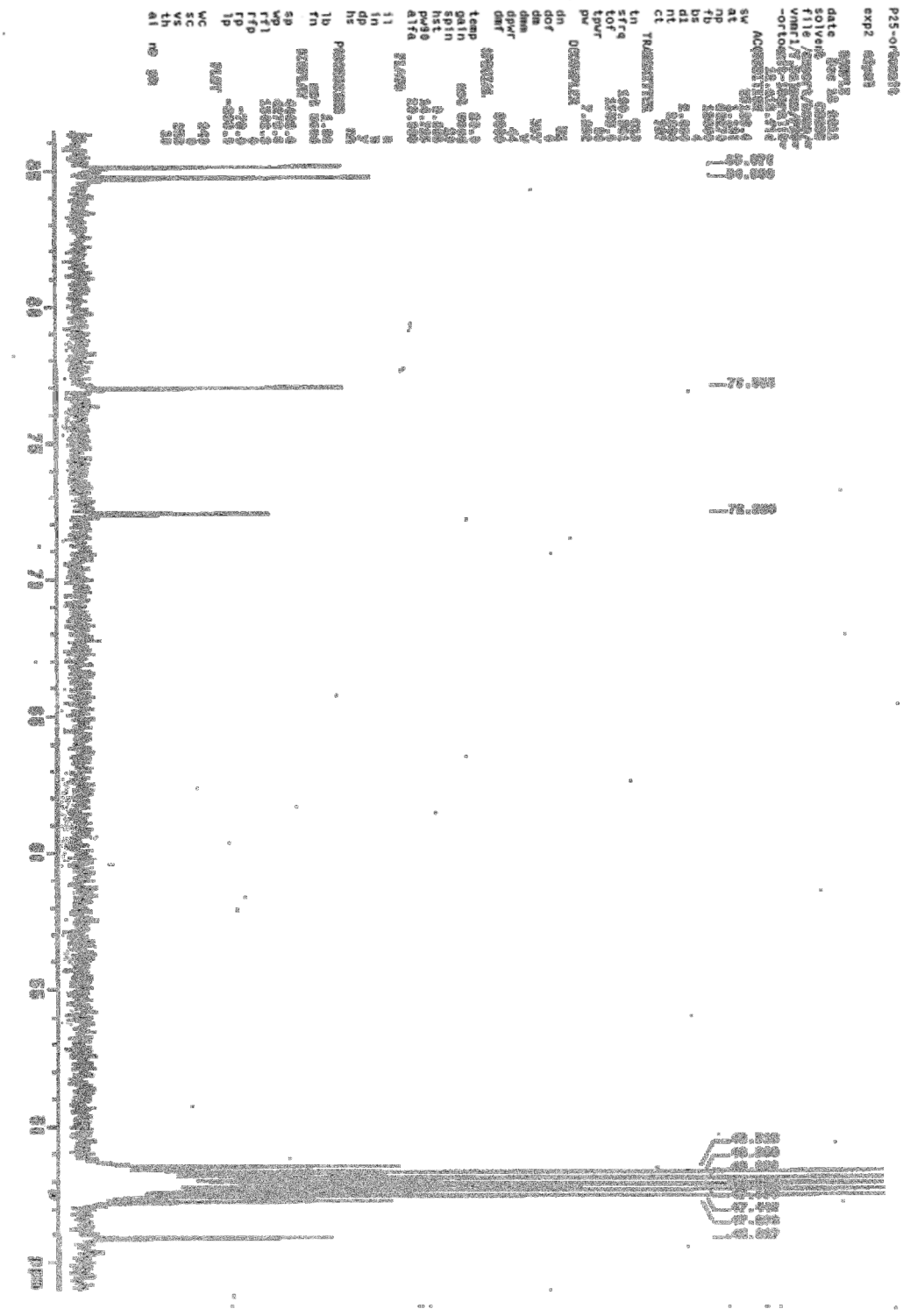
Appendix 14 Expansion of the ^{13}C-NMR Spectrum of the Compound 9



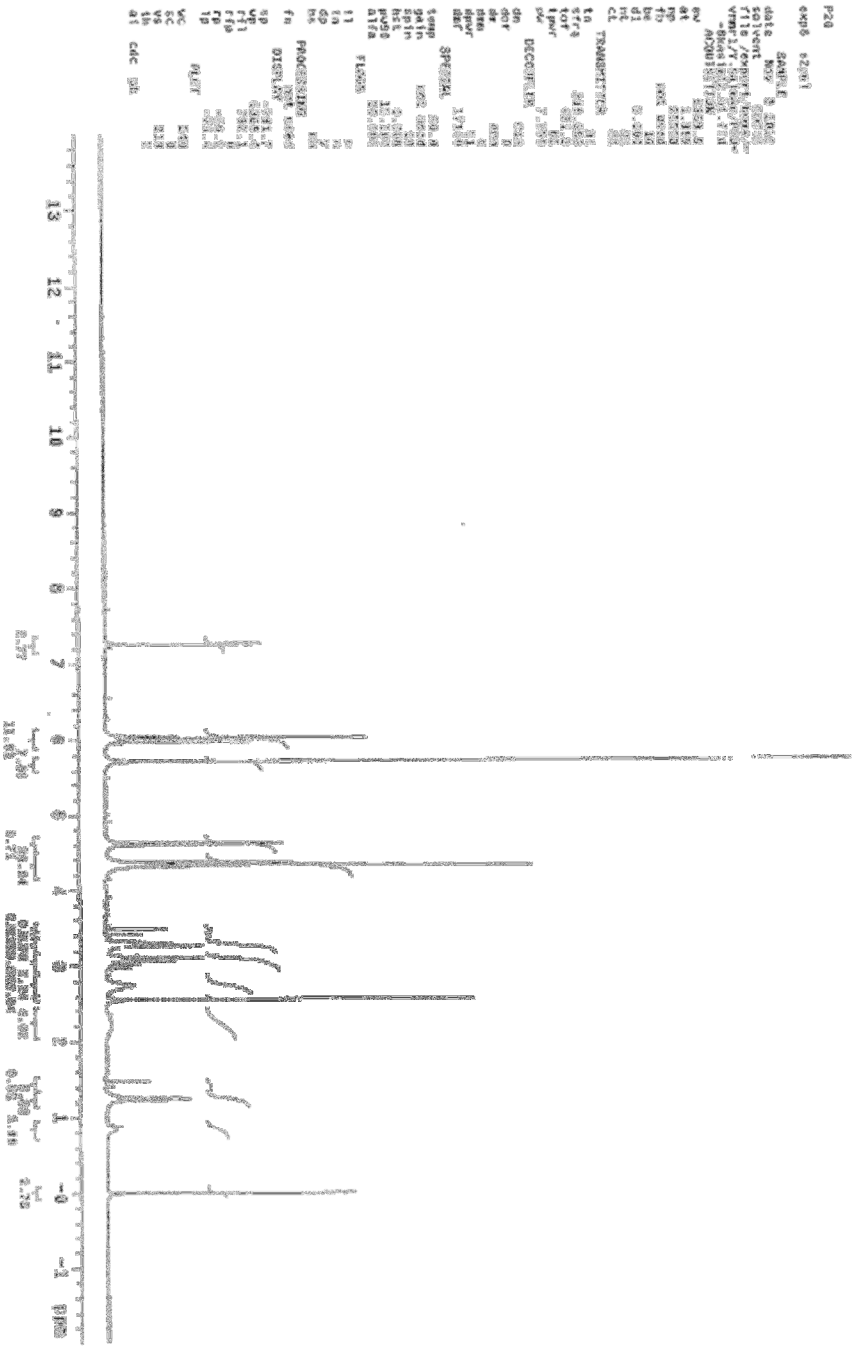
Appendix 15 Expansion of the ^{13}C-NMR Spectrum of the Compound 9



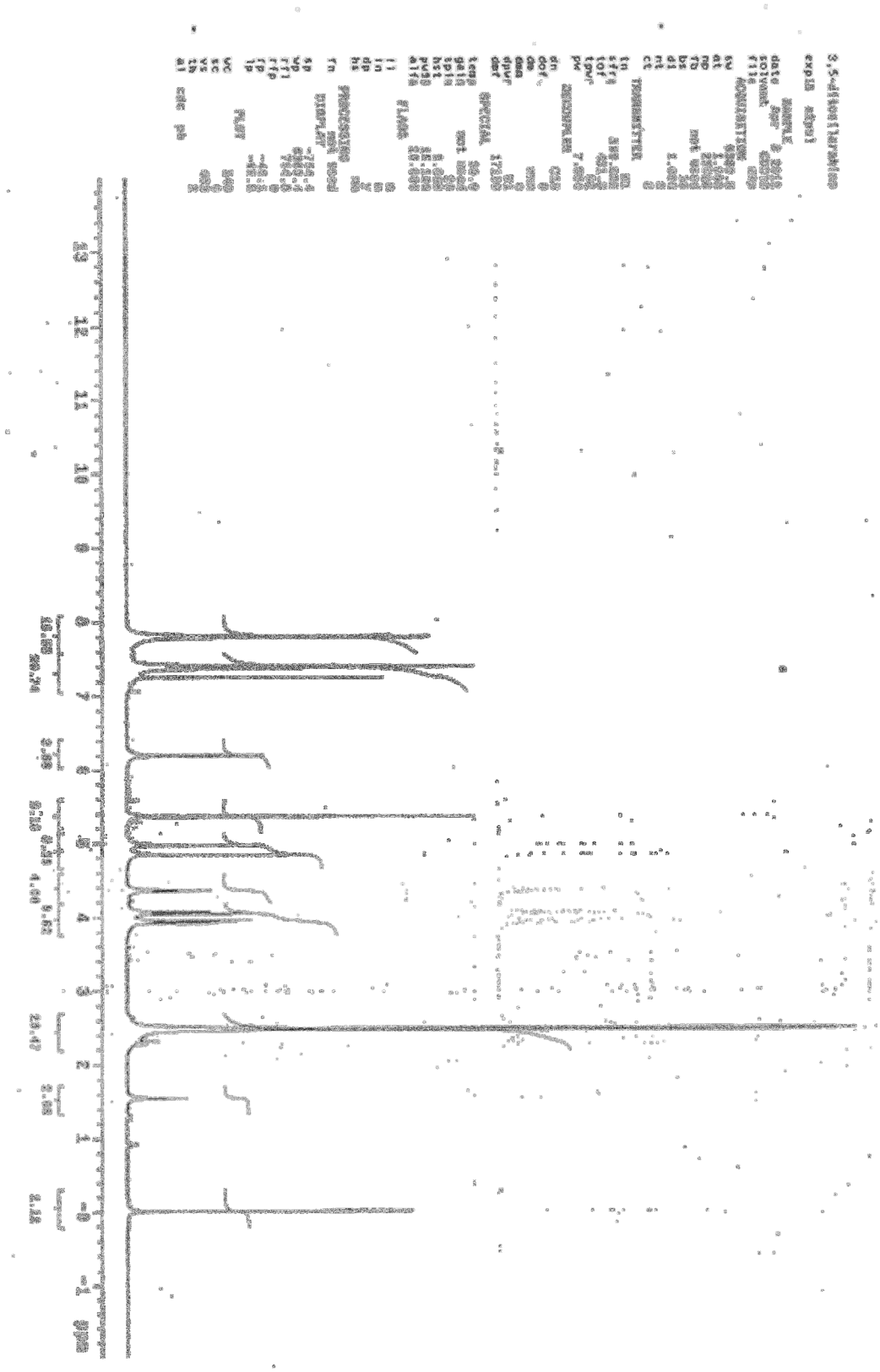
Appendix 16 Expansion of the ^{13}C-NMR Spectrum of the Compound 9



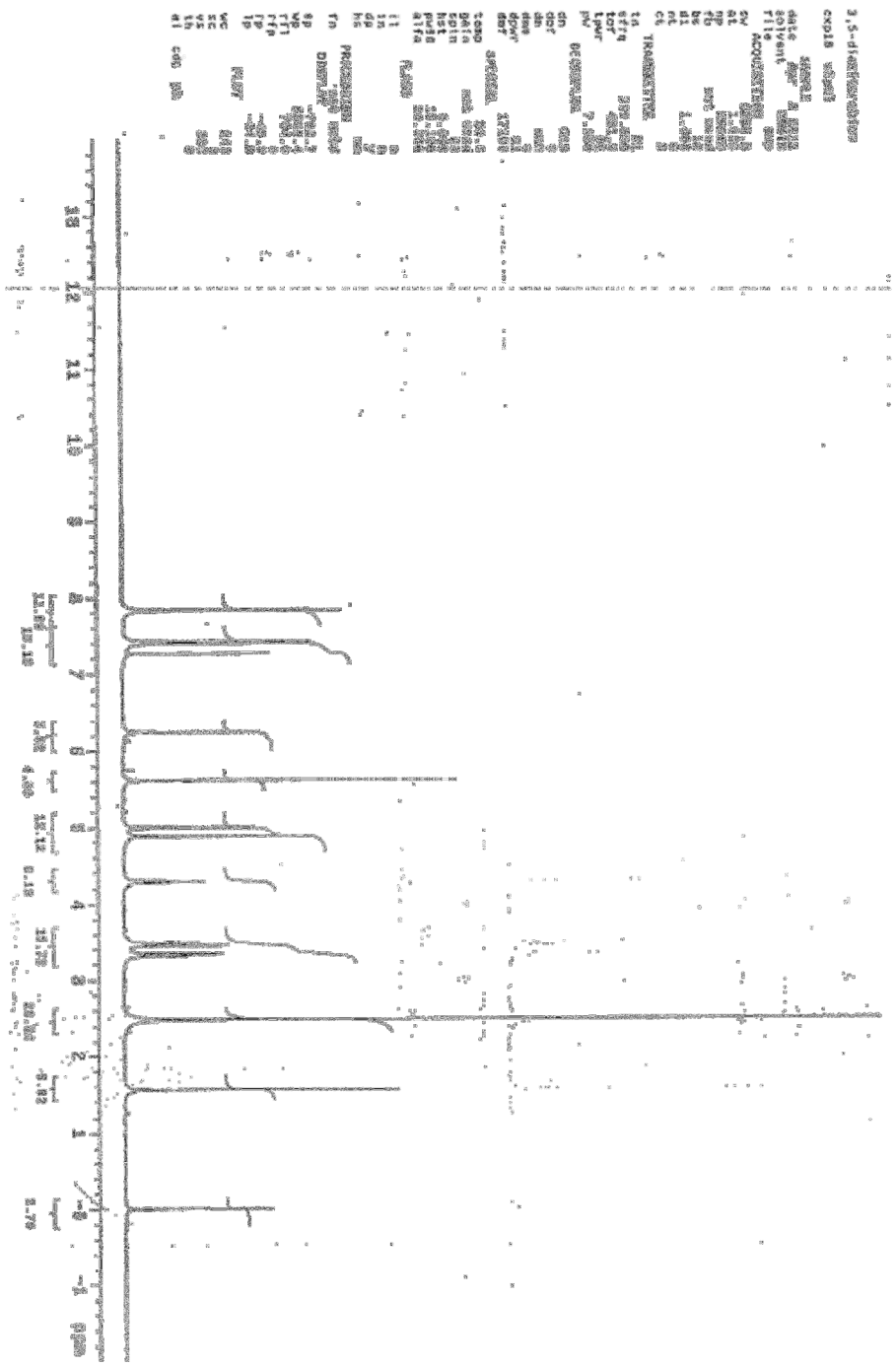
Appendix 17 ^{1}H-NMR Spectrum of the Compound 9



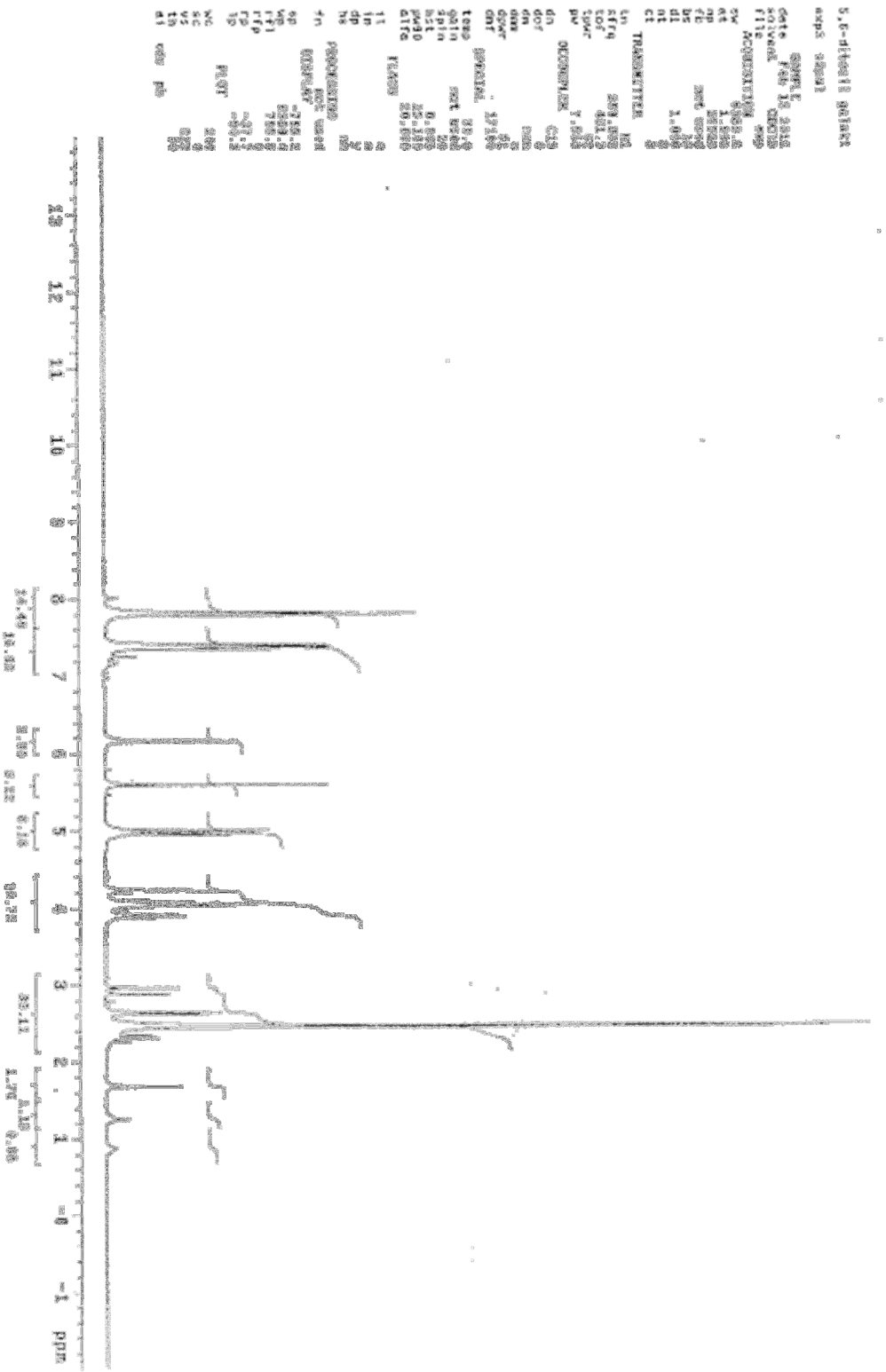
Appendix 18 ^{1}H-NMR Spectrum of the Compound 10



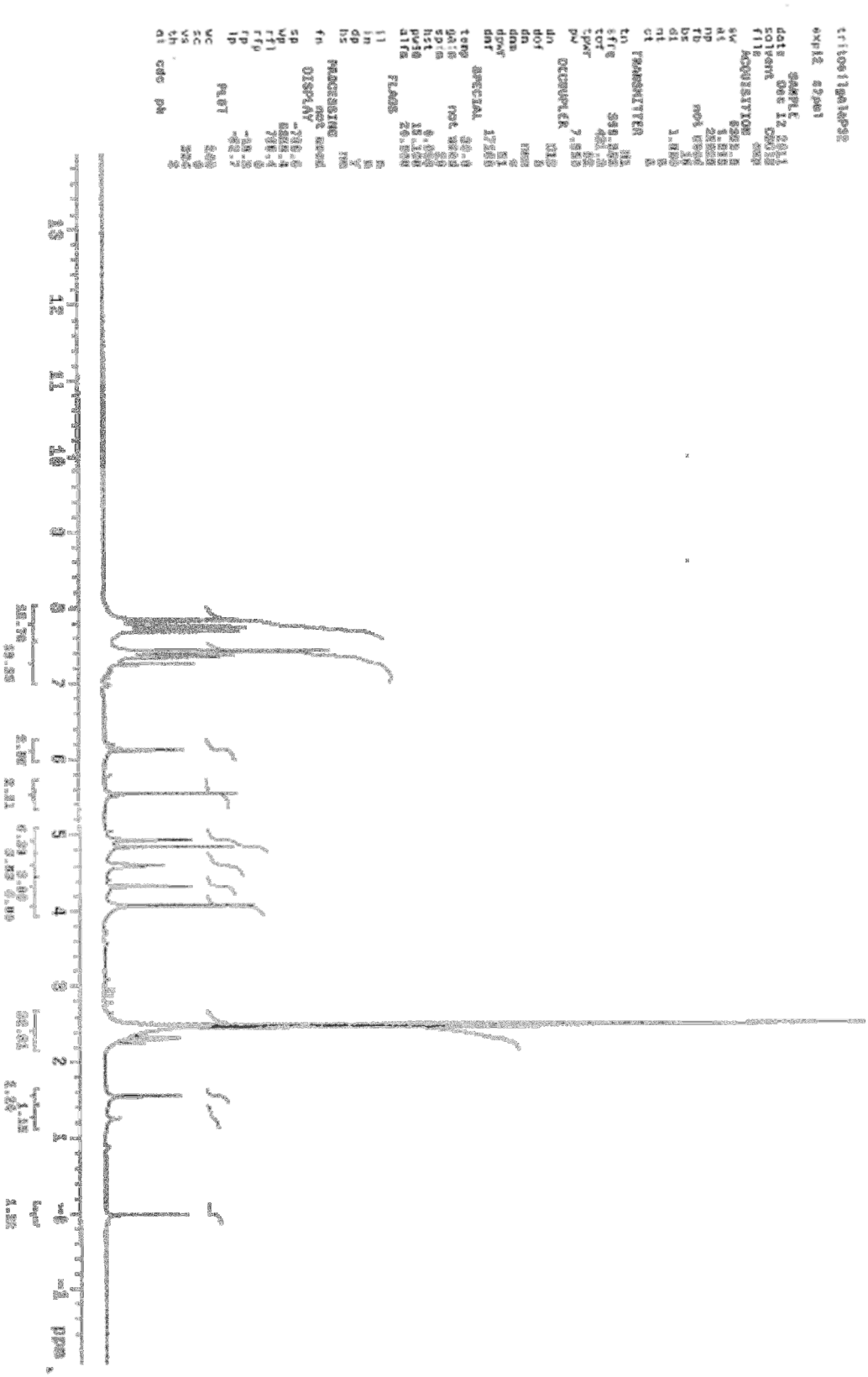
Appendix 19 ^{1}H-NMR Spectrum of the Compound 11



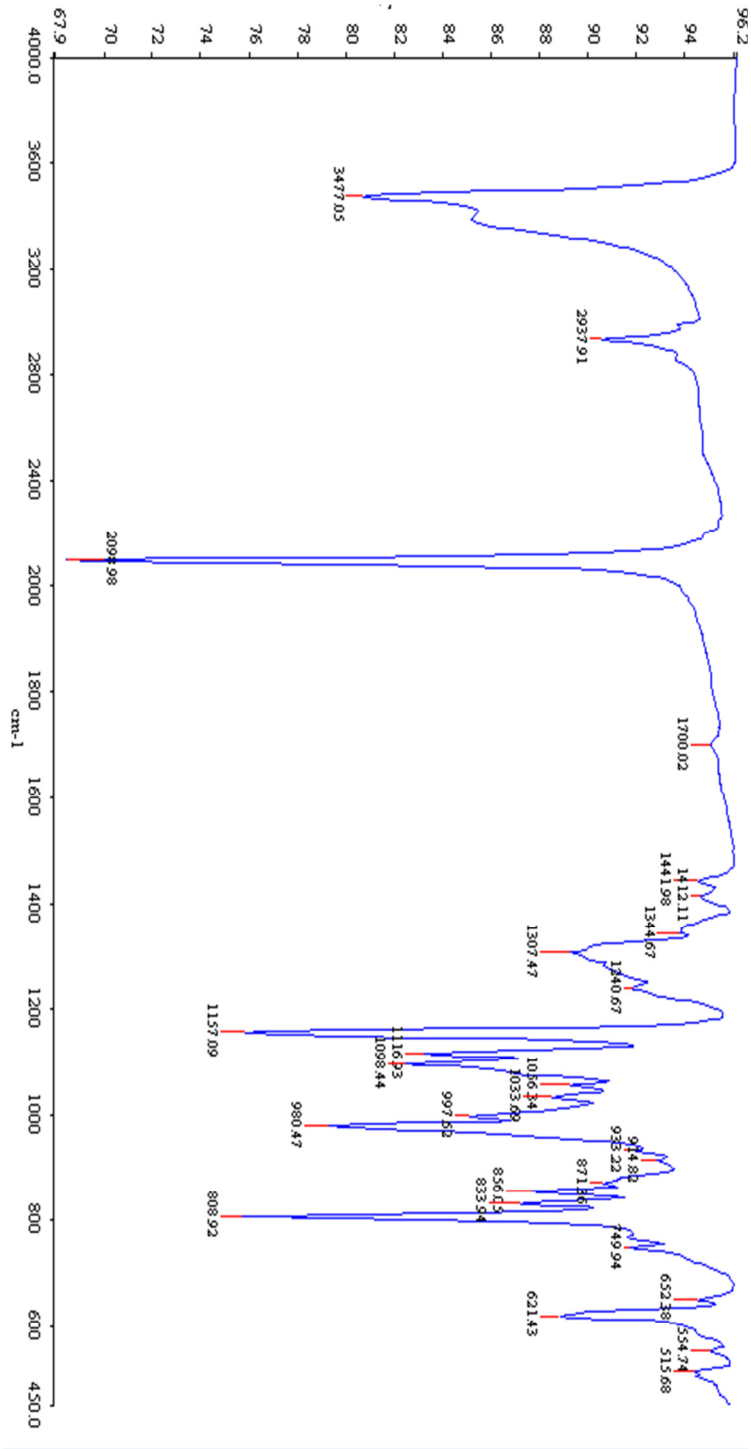
Appendix 20 ^{1}H-NMR Spectrum of the Compound 14



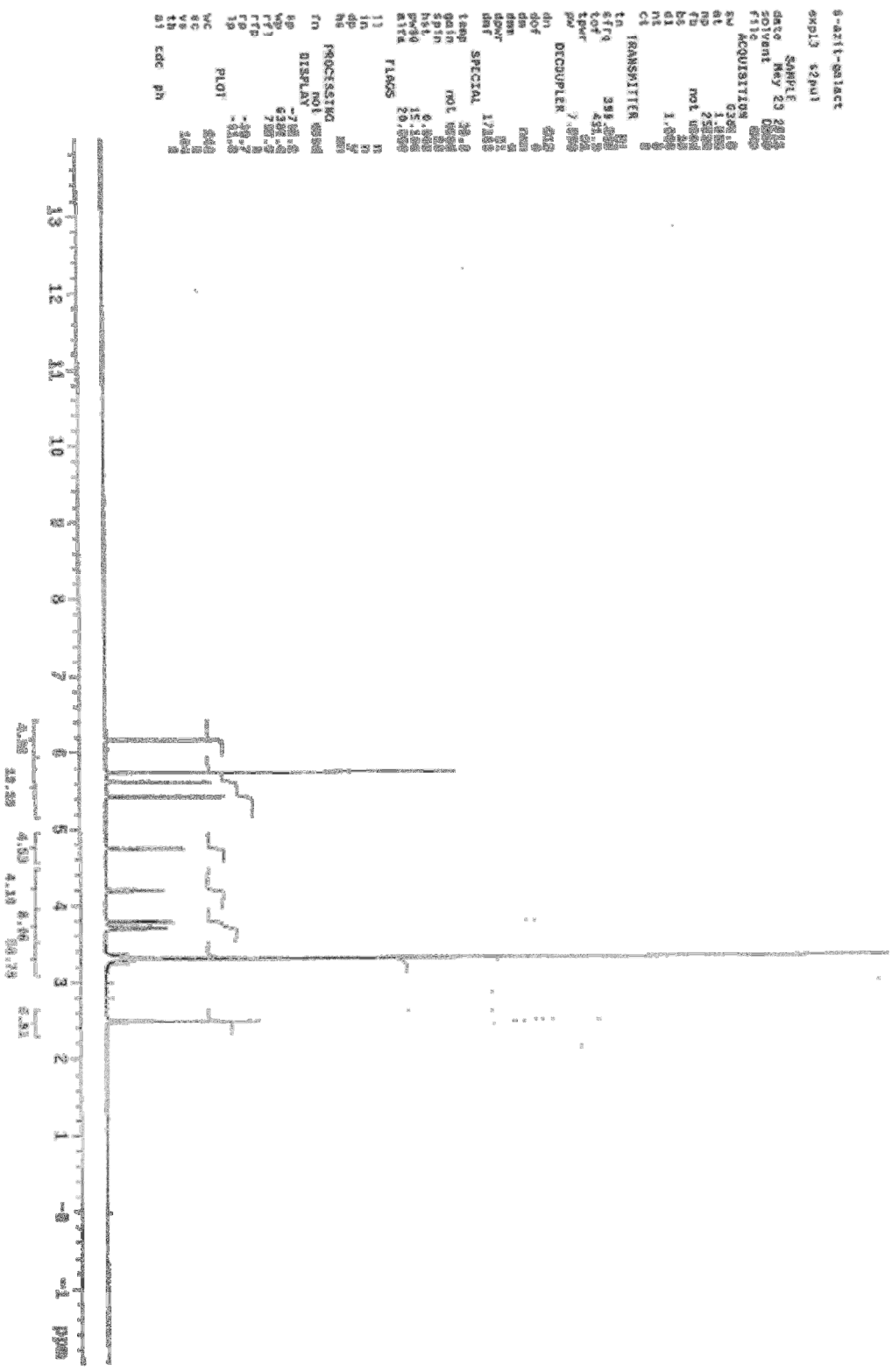
Appendix 21 ^{1}H-NMR Spectrum of the Compound 15



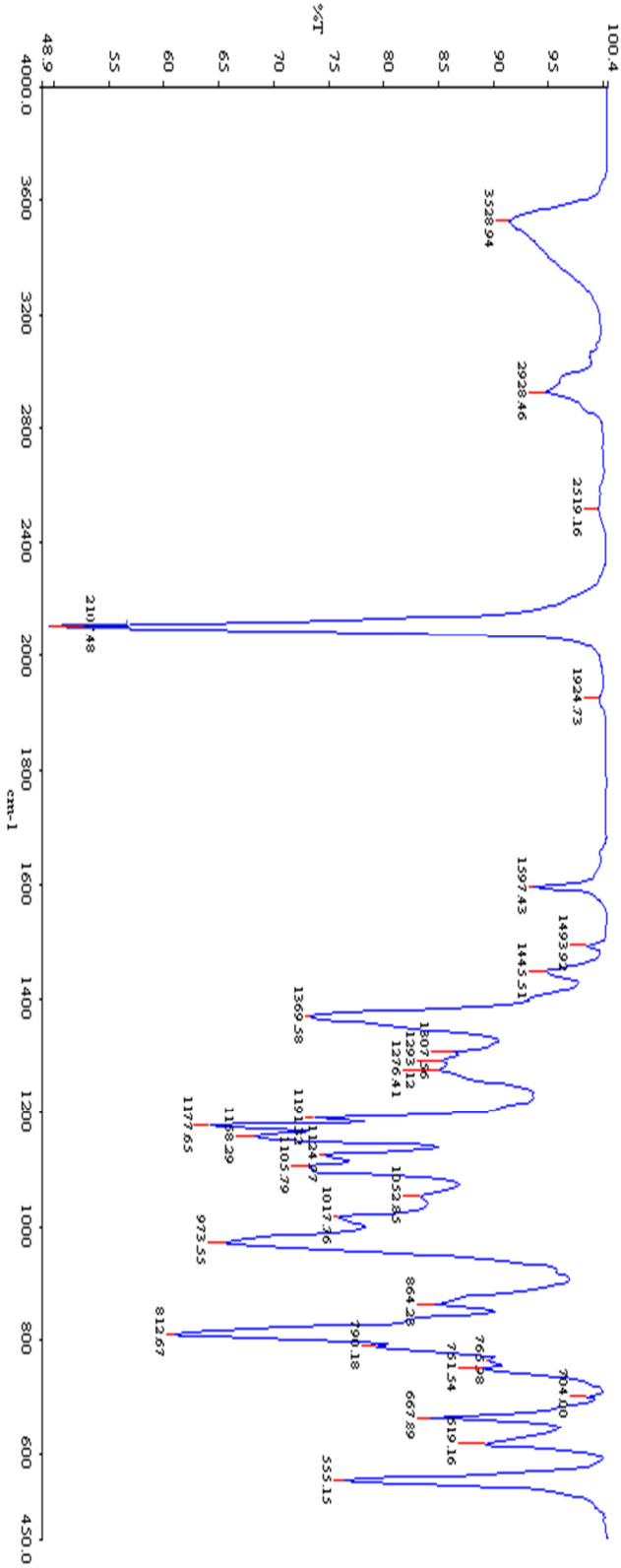
Appendix 22 FTIR Spectrum of the Compound 16



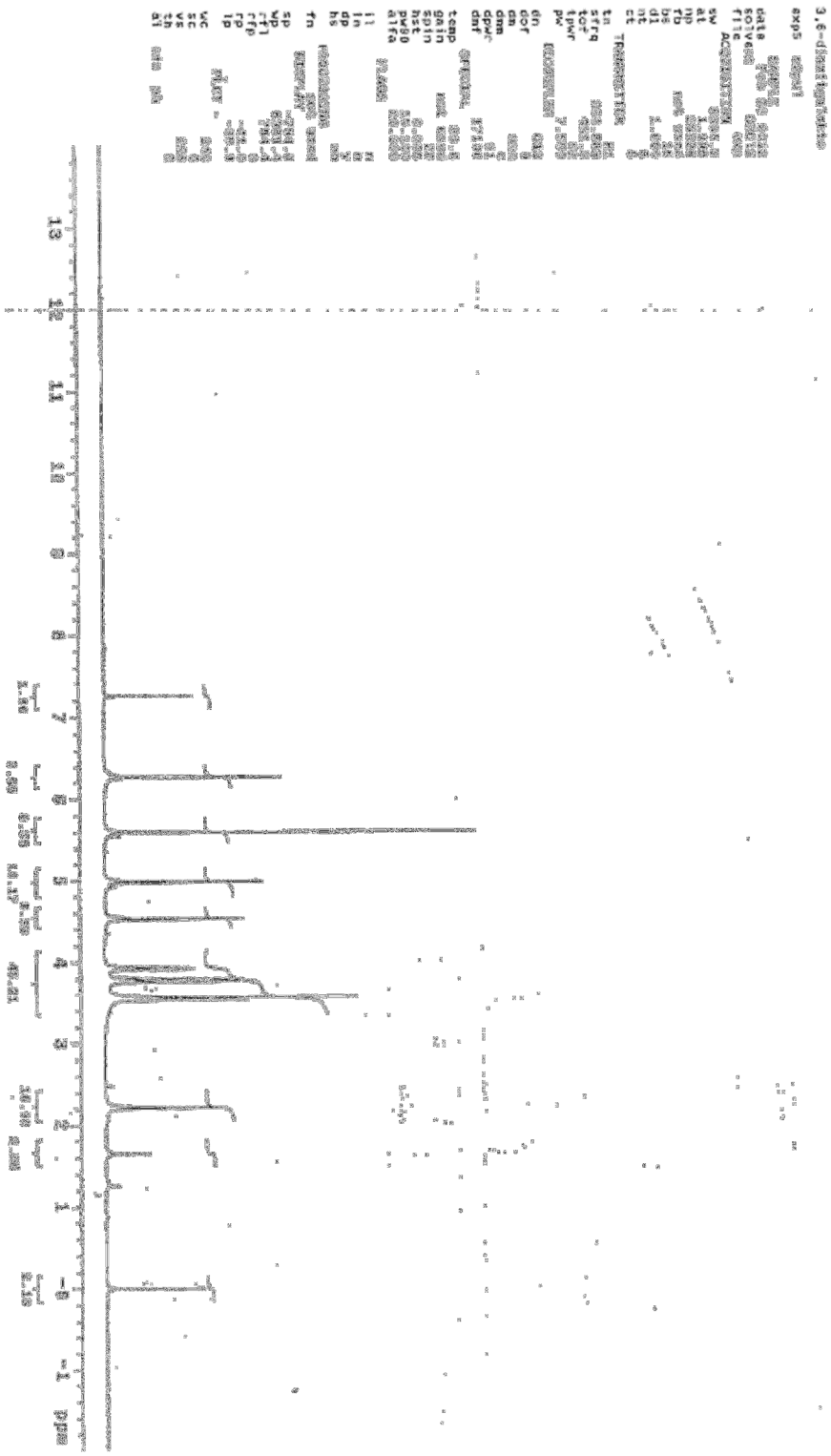
Appendix 23 ^{1}H-NMR Spectrum of the Compound 16



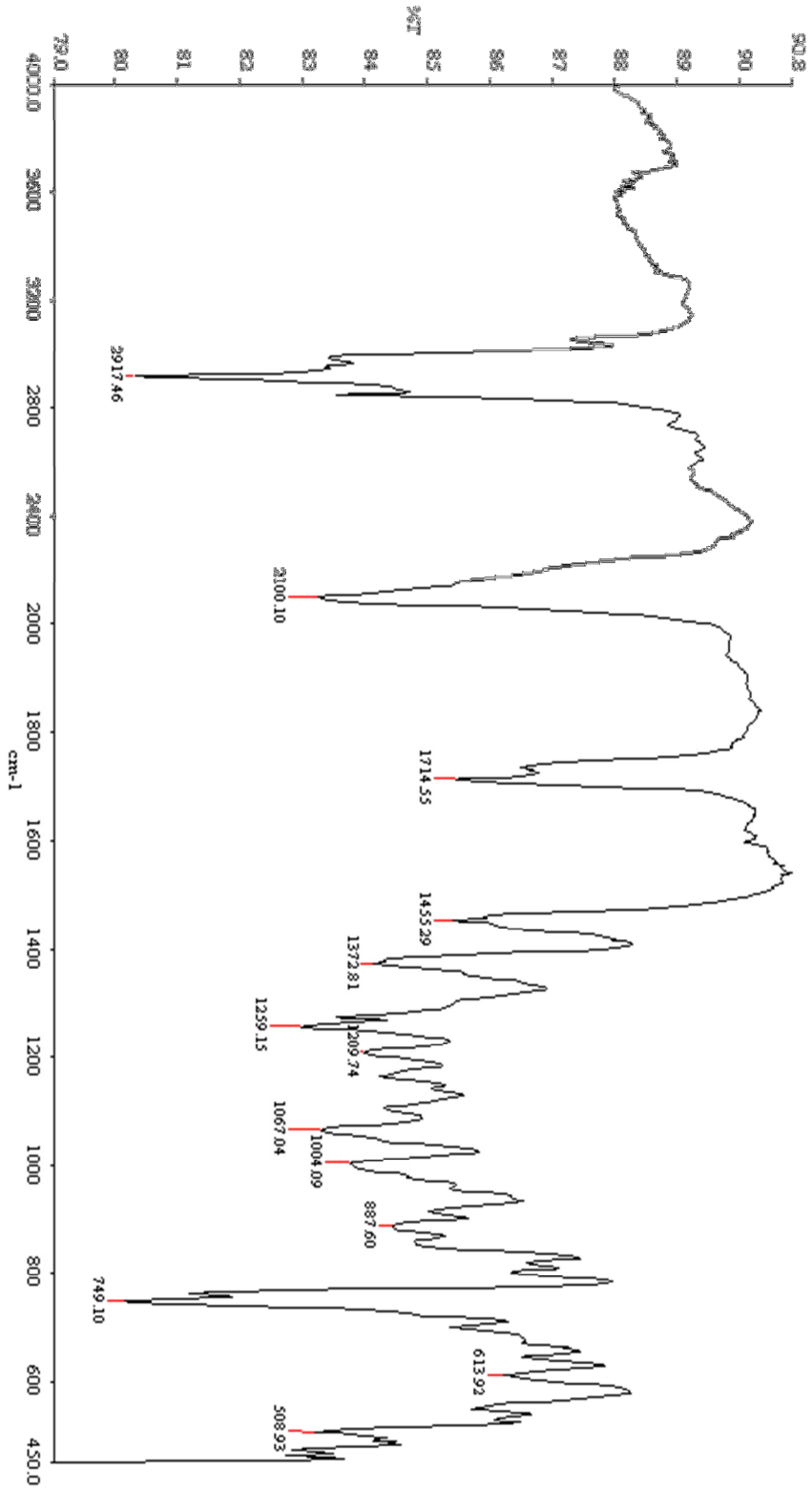
Appendix 24 FTIR Spectrum of the Compound 17



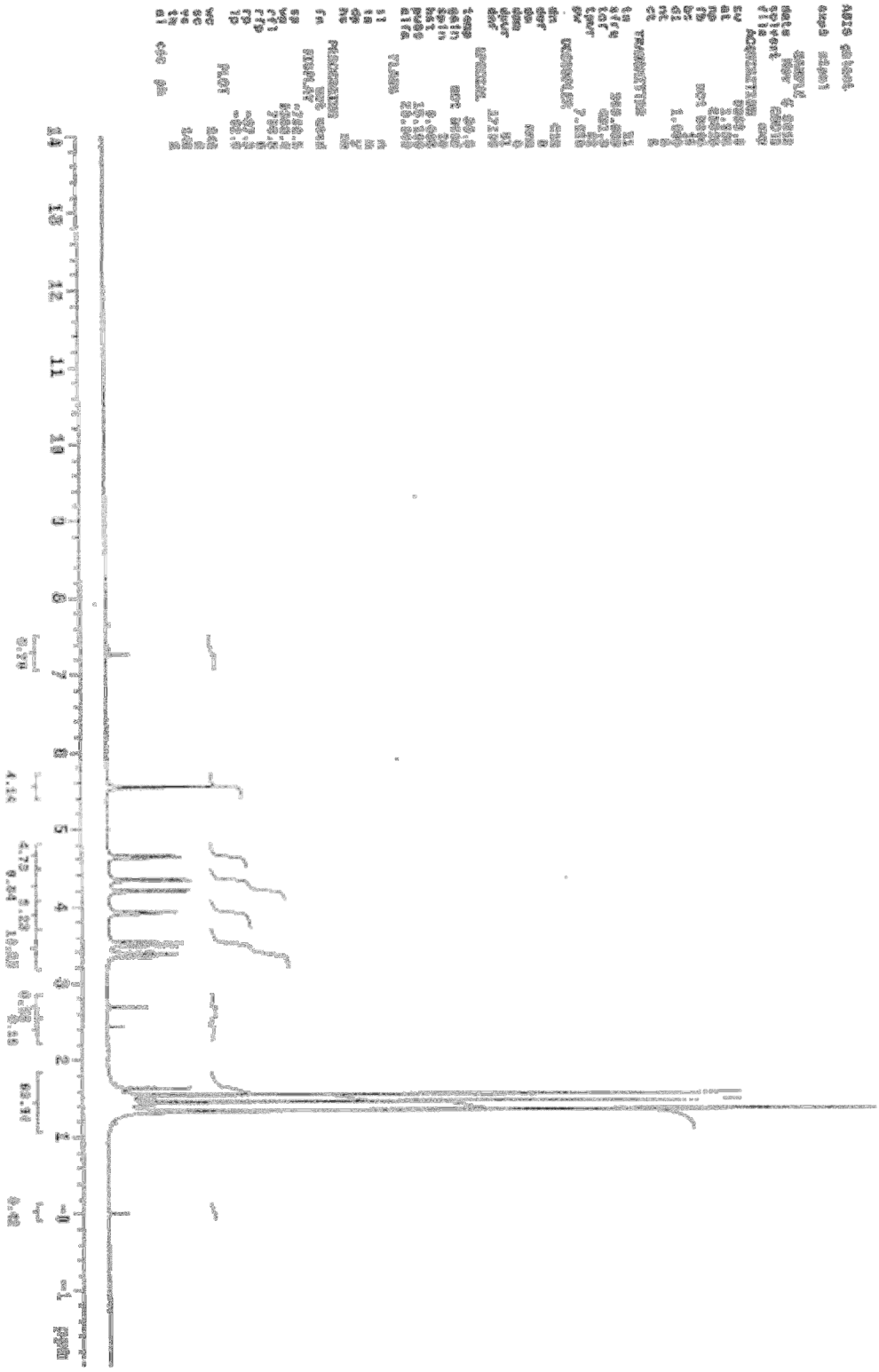
Appendix 25 ^{1}H-NMR Spectrum of the Compound 17



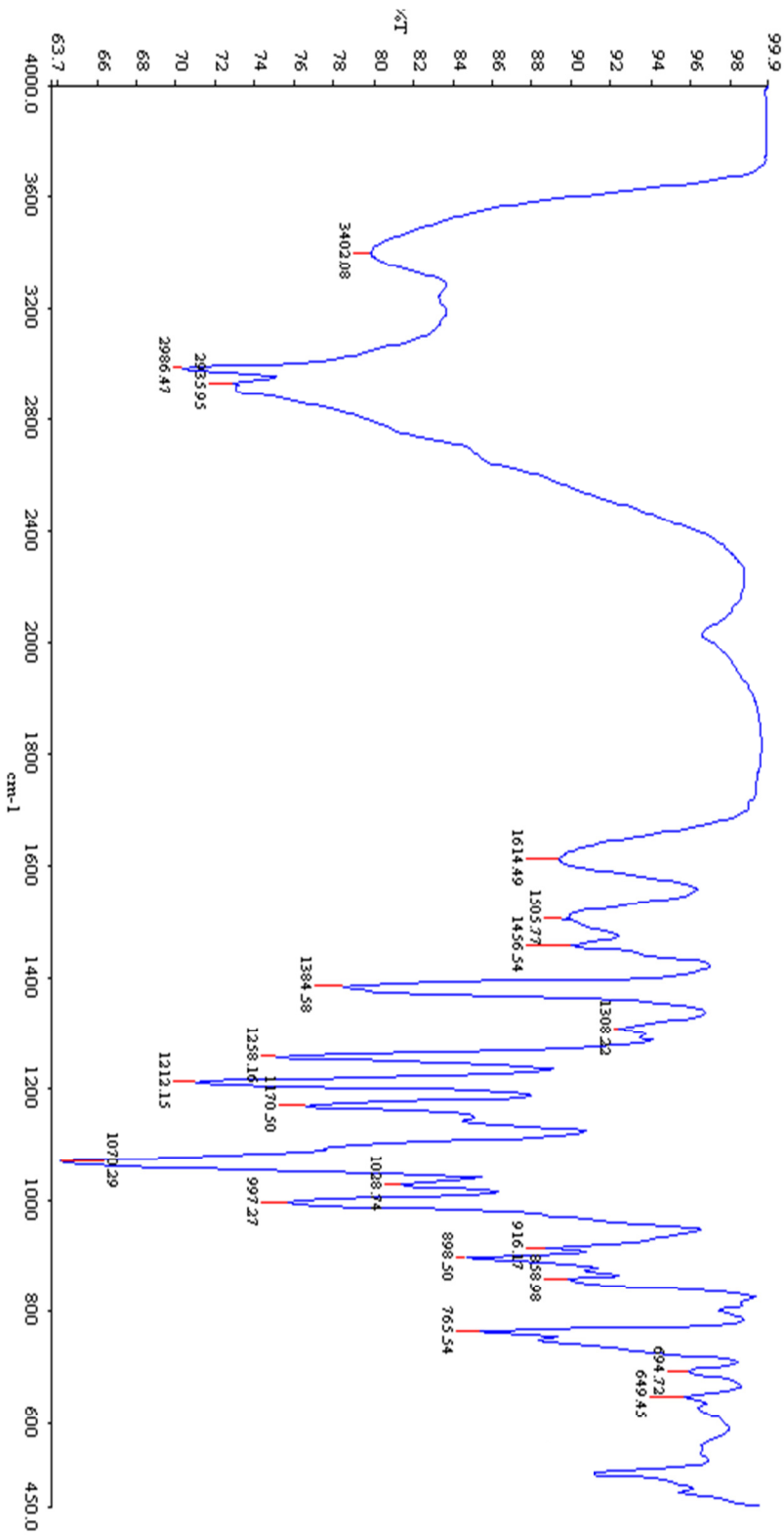
Appendix 26 FTIR Spectrum of the Compound 21



Appendix 27 ^{1}H-NMR Spectrum of the Compound 21



Appendix 28 FTIR Spectrum of the Compound 22



Appendix 29 ^{1}H-NMR Spectrum of the Compound 22