UNIVERSITY OF TARTU
FACULTY OF SCIENCE AND TECHNOLOGY

The stereoselective synthesis of 2,2,5-trisubstituted tetrahydrofurans, oriented to the preparation of lilac aldehydes and alcohols

MASTER THESIS

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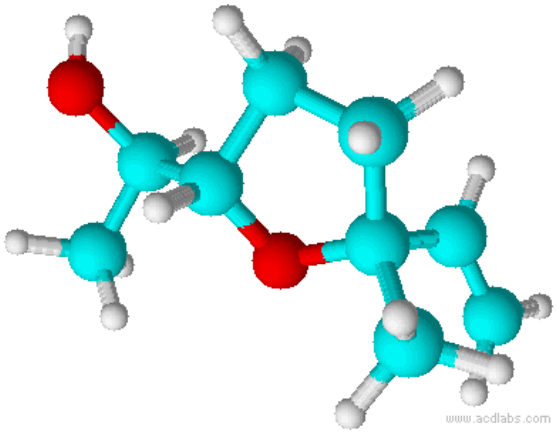

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1. List of abbreviations

AD – asymmetric dihydroxylation

DCM - dichloromethane

de – diastereomeric excess

dr – diastereomeric ratio

dept – distortionless enhancement by polarization transfer

$(DHQD)_2PHAL$ – hydroquinidine 1,4-phthalazinediyl diether

$(DHQ)_2PHAL$ – hydroquinine 1,4-phthalazinediyl diether

DIBAL – diisobutylaluminium hydride

DMAP - 4-(Dimethylamino)pyridine

DMF – dimethylformamide

ee – enantiomeric excess

er – enantiomeric ratio

Et_3N – triethylamine

EtOH – ethanol

FG – functional group

FT-IR – Fourier Transformation Infrared spectroscopy

GC – gas chromatography

HPFC – High-Performance Flash Chromatography

HPLC – High-Performance Liquid Chromatography

HSQC – heteronuclear single quantum coherence

IR – infrared

i-PrOH – *iso*-propanol

m-CPBA – 3-Chloroperbenzoic acid

MeOH – methanol

MsCl – mesylchloride

NMO – 4-Methylmorpholine *N*-oxide

NMR – Nuclear Magnetic Resonance Spectroscopy

PE – petroleum ether

PNO – pyridine *N*-oxide

Pd_2dba_3 – Tris(dibenzylideneacetone)dipalladium(0)

p-TsCl – *para*-tosylchloride

TBAF – Tetrabutylammonium fluoride hydrate

t-BuOH – *terc* - buthanol

THF – Tetrahydrofuran

TLC – Thin layer chromatography

TPAP – Tetrapropylammonium perruthenate

UV – Ultraviolet

UV-VIS – Ultraviolet–visible spectroscopy

2. Introduction

Lilac alcohols and aldehydes are chiral compounds which play an important role in chemical ecology mediating the chemical communication between plants and insects. Lilac compouds are among the most complicated chiral monoterpenoid components in flower volatiles. There are three stereogenic centers in lilac compounds, and therefore eight different alcohol and aldehyde enantiomers.

These compounds are widely present in many flowering plants and can attract the pollinators. It is not known if chirality influesces this attraction, it is therefore a great need to have a pure enantiomers of these compounds.

The stereoselective synthesis of lilac compounds has not been drawn out, and therefore the influence of each enantiomer to insect behaviour is not known. Knowledge that the content of lilac compouds in plants is species-specific reinforced by the view that these isomers have different biological properties.

Several studies like insects behavior, attraction, egg-laying, repellence and insects antennal responses could be made, when pure lilac alcohol and aldehyde enantiomers will be available.

The total stereoselective synthesis of lilac compounds is not published. The stereoselective synthesis of 2,2,5-trisubstituted tetrahydrofurans is not very well studied area, quite few publications are available.

The main goal for this thesis was to work out the new scheme for stereoselective synthesis of 2,2,5-trisubstituted tetrahydrofuran rings, which could form the basis for the preparation of the pure enantiomers of lilac compounds.

The present study is based on the pathway to enantiomerically pure THF-diols, which connects the establishment of stereogenic centers with the ring-forming reactions, namely the catalytic method for the stereocontrolled oxidative cyclization of dihydroxyalkenes to yield THF-diols in high enantiopurity and good yields. For the synthesis of dihydroxyalkenes the scheme starting from geraniol and including the stereoselectivity determing steps like catalytic Sharpless stereoselective dihydroxylation and Wittig reaction, was under investigation.

3. Literature overview

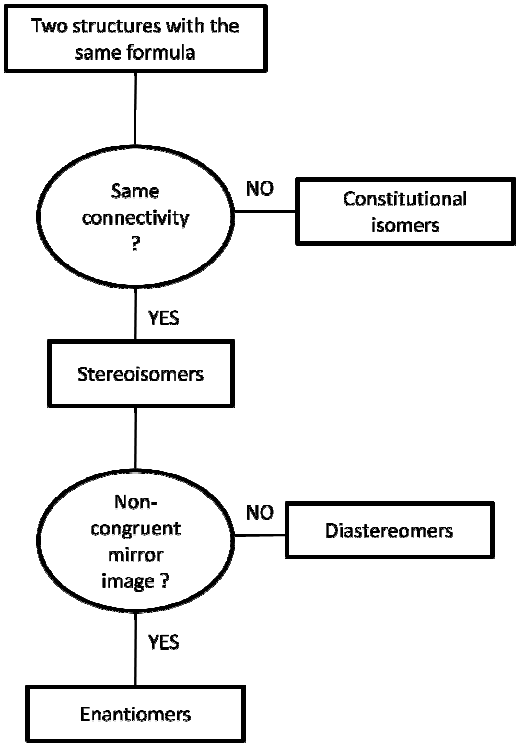
3.1. Theory of stereochemistry

3.1.1. Basic concepts and Terminology

Stereochemistry is the study of the static and dynamic aspects of the three-dimensional shapes of molecules. The most important component of stereochemistry is stereoisomers. Stereoisomers are molecules that have the same connectivity but differ in the arrangement of atoms in space, such as *cis*- and *trans*-2-butene. The constitution of a molecule is defined by the number and types of atoms and their connectivity, including bond multiplicity.

An historical distinction, but one that is not entirely clear cut, is that between configurational isomers and conformational isomers. Conformational isomers are interconvertible by rotations about single bonds, and the conformation of a molecule concerns features related to rotations about single bonds.

There are two types of isomers-geometrical isomers and optical isomers. Geometrical isomers are isomers that differ only in the way that atoms are oriented in space relative to each other. Optical isomers are molecules that differ three-dimensionally by the placement of substituents around one or more atoms in a molecule. There are two types of optical isomers: enantiomers and diastereomers.[1]



Scheme 1. Simple flowchart for classification of various kinds of isomers

According to scheme 1, enantiomers are molecules that are related as non-congruent mirror image, but diastereomers are stereoisomers that are not enantiomers. Any object that is nonsuperposable (noncongruent) with its mirror image is chiral. If an object is not chiral-that is, if its mirror image is congruent with the original-it is achiral.

Number of possible enantiomers can be calculated by formula 2^n, where *n* is number of stereogenic centers. Number of diastereomers can be calculated by formula 2^{n-1}, where *n* is amount of stereogenic centers. Enantiomerical excess (ee)-represents the percentage of one enantiomer in excess of the other. The ee of a

substance shows how pure it is. Ee can be calculated by formula:

$$ee\ \% = \frac{major\ enantiomer - minor\ enantiomer}{major\ enantiomer + minor\ enantiomer} \times 100$$

The term ee is coming from optical rotation and is introduced by Morrison and Moser in 1971. Nowadays is has been replaced by *er*, which is enantiomeric ratio (S:R) due to the other measurement techniques to determine the R and S directly. Diastereomeric excess de is changed to diastereomeric ratio *dr*.[2]

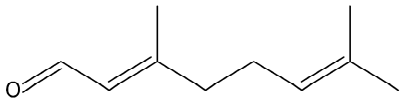
3.1.2. Stereochemical descriptors

Many of the descriptors for stereogenic units begin with assigning priorities to the attached ligands. Higher atomic number gets higher priority. If two atoms under comparison are isotops, the one with higher mass is assigned the higher priority. Ties are settled by moving out from the stereocenter until a distinction is made. In other words, when two attached atoms are the same, one examines the next atoms in the group, only looking for a winner by examining individual atomic number.

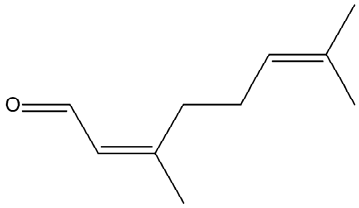
Multiple bonds are treated as multiple ligand; that is, C=O is treated as a C that is singly bonded to two oxygen with one oxygen bond to a C.

E, Z System

For olefins and related structures is used the same priority rules, but is devided the double bond in half and compare the two sides. For each carbon of an olefin, assign one ligand high priority and one low priority according to the rules above. If the two high priority ligands lie on the same side of the double bond, the system is *Z* (*Germ:* zusammen); if they are on opposite sides, the system is *E* (*Germ:* entgegen). If an H atom is on each carbon of the double bond, however, also could be used the traditional "cis" and "trans" descriptors. For example, citral, or 3,7-dimethyl-2,6-octadienal or lemonal, is either of, or a mixture of, a pair ofterpenoids with the molecular formula $C_{10}H_{16}O$. The two compounds are double bond isomers. The *E*-isomer is known as geranial or citral A. The *Z*-isomer is known as neral or citral B.



(2*E*)-3,7-dimethylocta-2,6-dienal



(2*Z*)-3,7-dimethylocta-2,6-dienal

Figure 1. *Cis* and *trans* positions of citral compound

R,S System

For tetracoordinate carbon and related structures is used the Cahn-Ingold-Prelog system. The highest priority group is given number 1, whereas the lowest priority group is given number 4. Sight down the bond from the stereocenter to the ligand of lowest priority behind. If moving from the highest (#1), to the second (#2), to the third (#3) priority ligand involves a clockwise direction, the center is termed *R*. A counterclockwise direction implies *S*. Figure 2 illustrates a Cahn-Ingolg-Prelog system.[3]

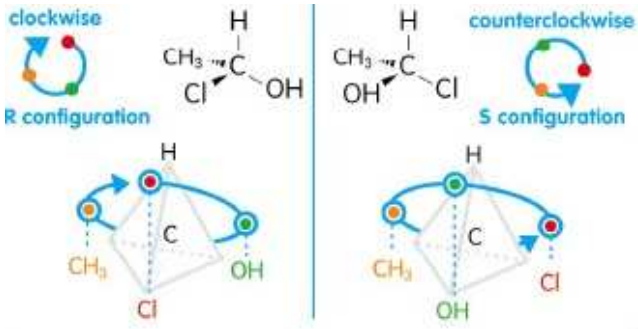


Figure 2. Ilustration of Cahn – Ingold – Prelog system

D and L

The descriptors D and L represent an older system for distinguishing enantiomers, relating the sense of chirality of any molecule in Fischer projection form introduced by Fischer in 1891. In a Fischer projection, the horizontal lines represent bonds coming out of the plane of the paper, while the vertical lines represent bonds projecting behind the plane of the paper. The D and L nomenclature system is fundamentally different than the R/S or E/Z systems. The D and L descriptors derive from only one stereogenic center in the molecule and are used to name the entire molecule.[4] Figure 3 illustrates a Fischer projection.[5]

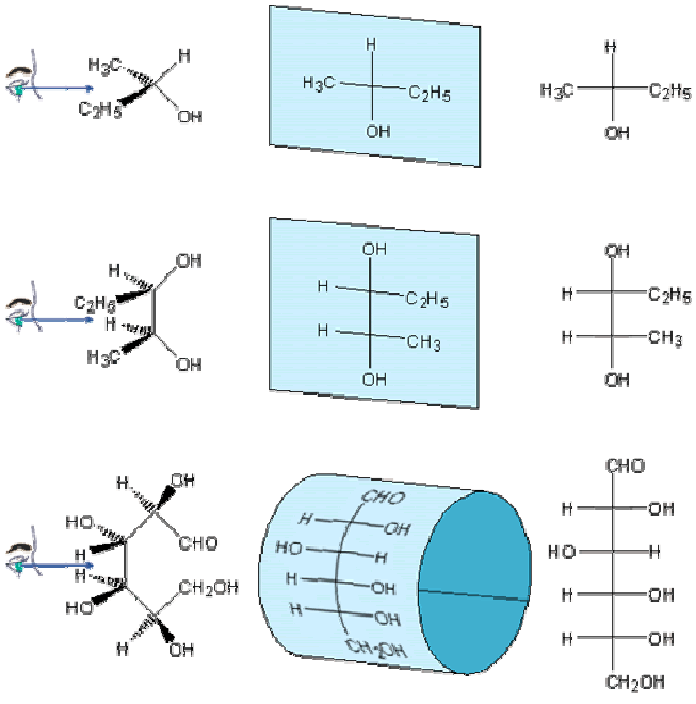


Figure 3. Ilustration of Fischer projection

These are three most widespread descriptors systems. There are also systems like Erythro and Threo, Helical Descriptors-M and P, Ent and Epi. In this work to describe different enantiomers R/S descriptor system is used.

3.1.3. Distinguishing enantiomers

Enantiomers are distinguishable if and only if they are placed in a chiral environment, and all methods to separate or characterize enantiomers are based on this principle. Chiral gas chromatography and chiral liquid chromatography are commonly used to separate and analyze enantiomers. A convenient technique to measure the ratio of enantiomers in a solution is to differentiate them using NMR spectroscopy by inserting a derivatizing agent that contains other nucleus than H or C. For example Mosher's acid, that contains -CF_3 group.

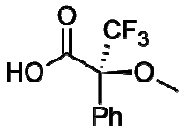


Figure 4. Mosher's acid

There are several methods for the determination of the structure of stereoisomers:

- ✓ Diftraction analysis (X-ray)
- ✓ Spectriscopic analysis (1 D NMR, 2 D NMR, IR)

3.1.4. Stereospecific and stereoselective reactions

In a stereospecific reaction one stereoisomer of reactant gives one stereoisomer of the product, while a different stereoisomer of the reactant gives a different stereoisomer of product. Hence, to determine whether a reaction is stereospecific, one has to examine the product ratio from the different stereoisomers of the reactant.

A stereoselective reaction is one in which a single reactant can give two or more stereoisomeric products, and one or more of these products are preferred over the others-even if the preference is very small. A reaction is also stereoselective when two stereoisomers of the starting material give the same ratio of stereoisomeric products, as long as the ratio is not 50:50. This just means that reaction is not stereospecific.[6]

3.2. Chemical ecology of lilac compounds

Lilac aldehydes and lilac alcohols have been first isolated from the lilac flower oil and described as characteristic monoterpenoids in *Syringa Vulgaris* L. (Oleraceae) flowers positively influencing the lilac odor quality.[7] Syringa (Lilac) is among the popular ornamental bushes and is cultivated in the middle latitude of Eurasia and North America. These flowers are white or purple in color and release the aroma compounds, which are very pleasant to the human sensor system.

The lilac compounds occur in plant spieces of many families, such as Caryophyllaceae (*Dianthus* spp., *Silene* spp.), Rosaceae (*Prunus padus*), Lamiaceae (*Origanum vulgare*), Onagraceae (*Gaura longiflora*), Orchidaceae (*Platanthera* spp.), Polemoniaceae (*Phlox paniculata*), Salicaceae (*Salix* spp.), Violaceae (*Viola etrusca*), Actinidiaceae (*Actinidia*), Rubiaceae (*Cephalanthus occidentalis*), Vitaceae (*Vitis vinifera* cv. Moscato bianco), Asteraceae (*Artemisia pallens*, *Eupatorium cannabinum*), Oleaceae (*Syringa vulgaris*), and are found in several honeys.[8] Lilac aldehydes are an important class of fragrance and flavor compounds in perfumery and ecology.[9]

Lilactype fragrance compounds are in high demand by the perfume industry because there are no natural lilac flower oils or concentrates commercially available and synthetic fragrance compounds are used to imitate the desired odour. Lilac aldehydes and lilac alcohols are very powerful fragrance compounds due to their exceptionally low odour thresholds of about 0.2-0.4 and 2-4 ng, respectively.[10]

The volatile compounds produced by plants are responsible for multiple interactions between plants and other organisms. Floral fragrances are characteristic for many insect – pollinated flowers and are involved in the attraction and guidance of pollinators to the reproductive organs. The scent of a flower together with its colour is considered to be the main signal attracting insects ensuring pollination.[11]

Floral odours are important signals for chemical communication between flowering plants and animal pollinators, and may be of importance for reproductive isolation among sympatric, closely related species. Scent is particularly important in night-blooming species when visual cues become inefficient due to darkness.

From pheromone studies it is known that chirality is an important factor in insect communication. In addition to pheromonal tests it is known from studies on plant-herbivore interaction that chirality is an important factor.[12]

It is unknown in most pollination systems whether or not chirality plays a role in pollination system. Among the most complicated chiral floral scent compounds are the oxygenated monoterpenoids lilac aldehydes and alcohols.[13] Each of these compounds has three stereogenic centers, and therefore eight different aldehyde and eight different alcohol enantiomers and four different aldehyde and four different alcohol diastereomers are possible. In figure 5 eight possible lilac alcohol enantiomers are illustrated. Lilac aldehydes have same stereocenters.

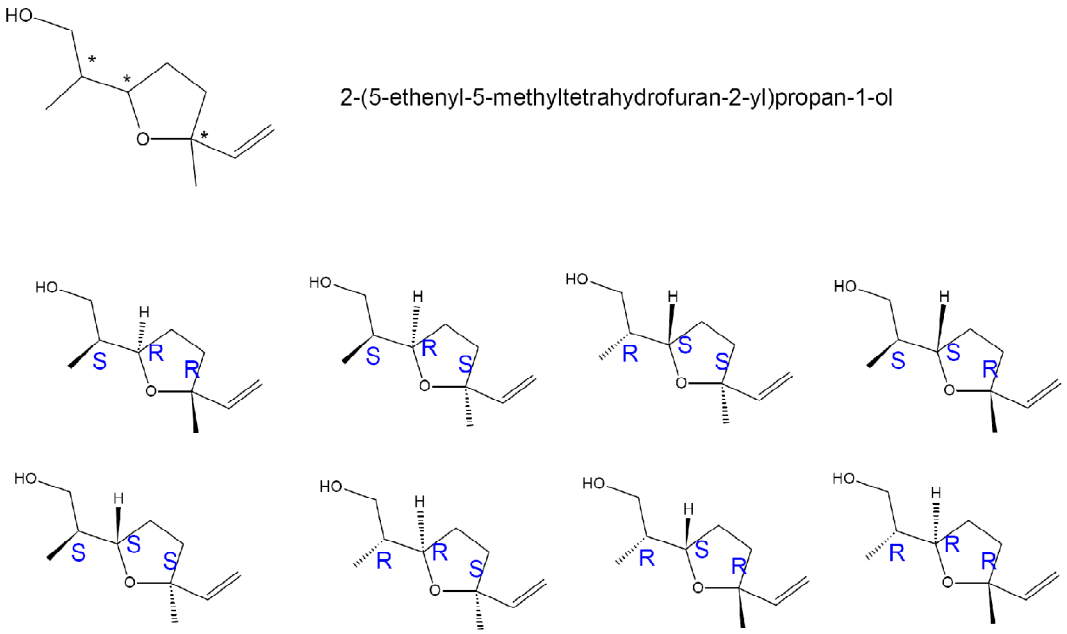


Figure 5. Lilac alcohol stereoisomers

Flowers emitting these compounds are mainly attracting butterflies and moths. There is not much known about which enantiomers in the blend of lilac compounds are the attractive ones, and it is unknown if the enantiomers of the alcohols and aldehydes have different functions or differently activate the antennal receptors of the insects.[14]

It is known that lilac aldehydes play an important role in the attraction of Lepidoptera (butterflies and moths) to flowers. Lilac compounds are known to attract noctuid moths alone, or together with other compounds, and are known as effective antennal stimulants in electroantennographic detections. Responses of *Autographa gamma* to a mixture of lilac aldehyde

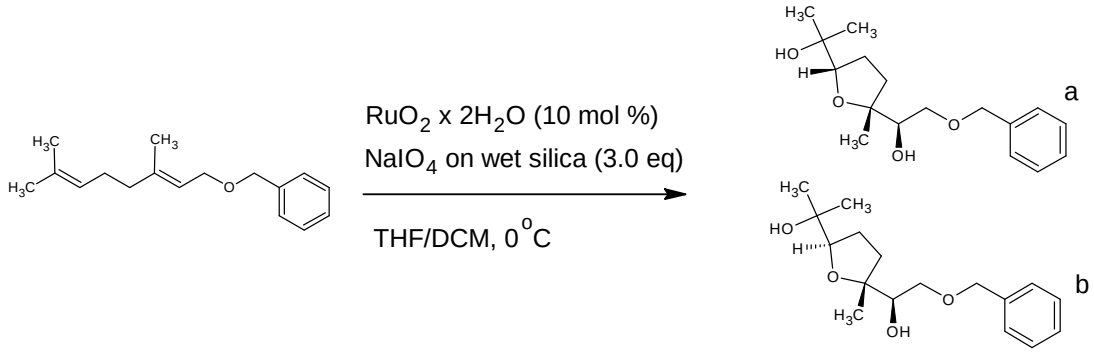
isomers were similar as to a mixture of in total 9 attractive compounds (including lilac aldehydes), and the lilac aldehydes elicited significantly more responses than any other compound tested. The lilac aldehydes were also proved to be the most attractive compounds for *Hadena bicruris*, the nursery pollinator of *Sagittaria latifolia*. However, it is not known if the single enantiomers differ in their biological activity.[15]

There is a great need for synthesis of these compounds as they are commonly occurring in many insect interactions and almost always occur in mixture. Studies on the behavior, attraction, egg laying, feeding, repellence and insect antennal responses, single receptor cell responses can be made, when there will be access to these pure enantiomers.

3.3. Suggestions for synthesis of 2,2,5-trisubstituted tetrahydrofurans

In this chapter several methods for 2,2,5-trisubstituted tetrahydrofuran synthesis are described.

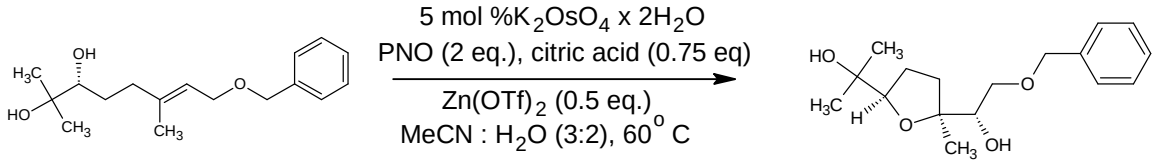
Method A – a single step formation using Ru catalyst (Scheme 2)



Scheme 2. A single step formation using Ru catalyst

Important factor of this reaction is avoiding water as a co-solvent. Water usually has to be added to dissolve sodium periodate, the terminal oxidizing agent. Therefore solid-supported terminal oxidant was chosen. Sodium periodate on wet silica as a solid supported terminal oxidant resulted in a smooth conversion of diene substrate. The starting material was almost quantitatively converted into the desired cyclization product. The yield of reaction is up to 90%. Diastereomeric ratio between two isomers *a* and *b* was 95:5 respectively. As catalyst in this reaction could be used also $RuCl_3$, TPAP, RuO_4 or $KMnO_4$.[16]

Method B – A Lewis acid promoted oxidative cyclization (Scheme 3)

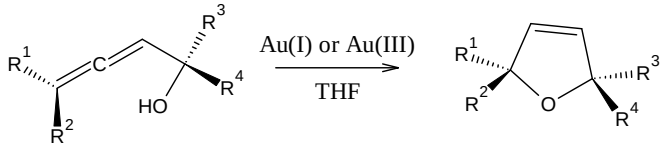


Scheme 3. Lewis acid promoted oxidative cyclization

The reaction mixture was heated to 60°C, resulting in an increase of the rate of reaction, with no loss in yield. $Cu(OTf)_2$ and $Zn(OTf)_2$ are cheaper, milder, and equally reliable alternatives to $Sc(OTf)_2$. Both $Cu(OTf)_2$ and $Zn(OTf)_2$ gave similar yields and are essentially interchangeable. Rates of reaction are much quicker, when more water was added. The pH of the Lewis acid-promoted cyclization was measured to be pH 2. In analogous reaction the Lewis acid was omitted

and the reaction adjusted to pH 2 by addition of TfOH. This approach was not working and significant amounts of decomposition were seen, with only a trace of desired THF recovered. The yield of reaction was 85 %. Diastereomeric ratio between two isomers was 97.5 : 2.5.[17]

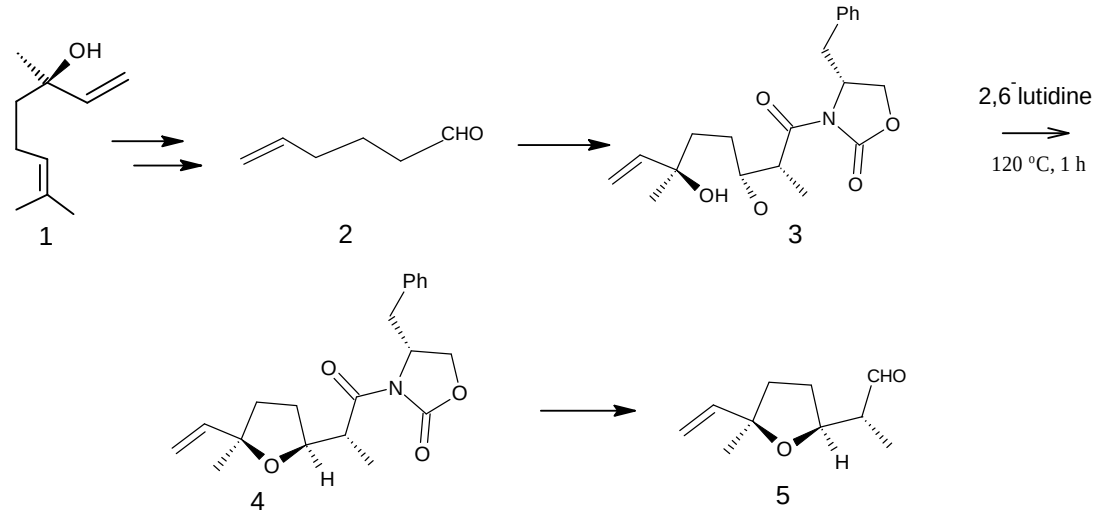
Method C – using gold catalyst (Scheme 4)



Scheme 4. Cyclization reaction using gold catalyst

The subsequent gold-catalyzed cycloisomerization was achieved in the presence of only 0.1 mol % $AuCl_3$ in THF, which gave the 2,5-dihydrofuran **2** with chemical yield (96%) as a single diastereomer, completing the key center-to-axis-to-center-chirality transfer. Only the hydroxyl group in α-position participates in the cyclization.[18]

Method D – cyclization reaction using 2,6-lutidine (Scheme 5)

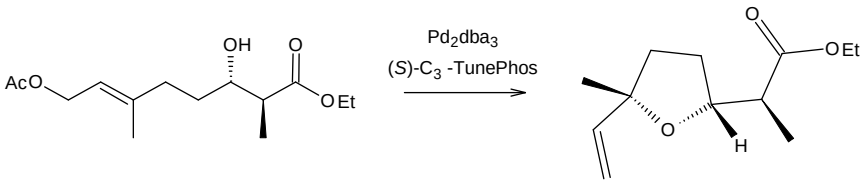


Scheme 5. Cyclization reaction using 2,6-lutidine

The synthesis scheme was started with (-)-linalool (**1**). Aldehyde (**2**) was subjected to the Evans *syn* aldol reaction with the enolate of chiral -*N*-propionyl oxazolidinone to furnish the aldol adduct with high diastereoselectivity (de 98 %) in 87 % yield. After several reaction steps on treatment with 2,6-lutidine at 120°C, **3** rapidly cyclised to the cyclic ether *anti*, *cis*-**4** as a single

isomer in 93 % yield through an S_N2-type substitution. Next step was cleavage of the oxazolidinone in **4** usind DIBAL-H provided aldehyde **5** in 88 % yield.[19]

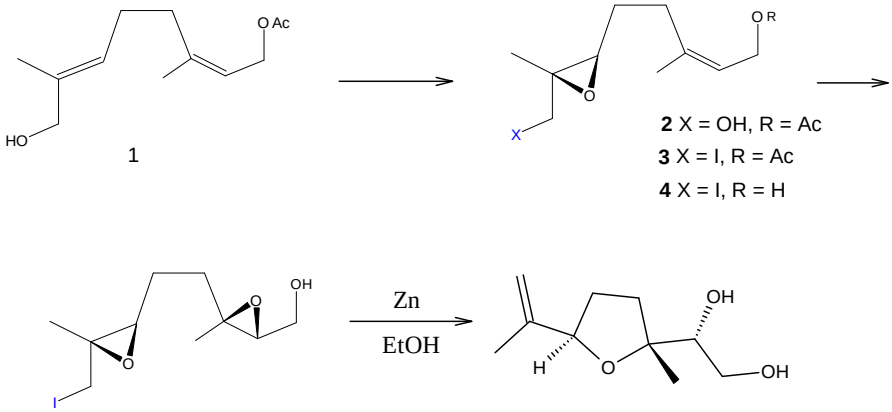
Method E – cyclization reaction using (*S*)-C_3 TunePhos (Scheme 6)



Scheme 6. Cyclization reaction using (*S*)-C_3TunePhos

In this synthesis of Davana acid ester ß-hydroxy ester was effectively provided in reaction with Bode's salt using a non-aldol approach. The decision was made that the inherent diastereofacial preference of ester would be to form *trans*-THP-ester rather than the desired *cis*-product. In this case Pd_2dba_3 with (*S*)-C_3TunePhos enabled to overcome the substrate's diastereofacial bias and favor *cis*-davana acid ethyl ester. (*R*)-C_3 TunePhos gave substantial (>12:1) selectivity for the undesired *trans*-product. THF was used as solvent for reaction, and reaction was heated to 87^{o}C over 72 h. Yield of reaction was 87 % and 2.5 : 1 *cis*/*trans* ratio was obtained.[20]

Method F – cyclization reaction using Zn in ethanol (Scheme 7)

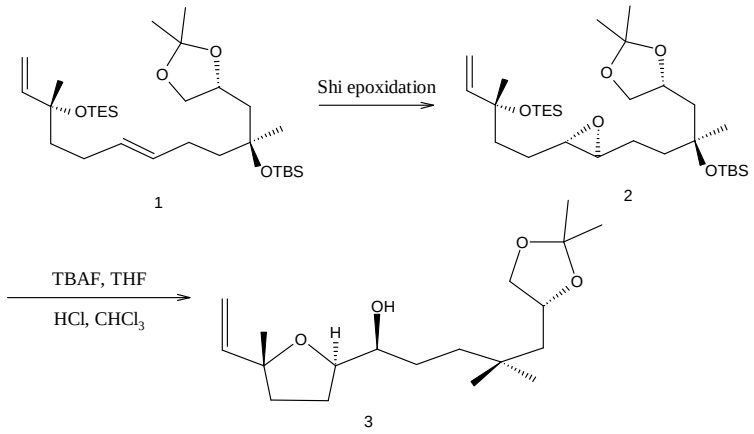


Scheme 7. Cyclization reaction using Zn in ethanol

Synthesis was started from allylic alcohol **1**, the SeO_2 oxidation product of neryl acetate, with epoxidation with the D-(-)-tartrate complex to yield the epoxy alcohol **2** as a 95 : 5 mixture of enantiomers. A second Sharpless epoxidation, carried out on allylic alcohol **3**, afforded an 85 : 15

mixture of diastereomers favoring **5**. This mixture, upon treatment with zinc in ethanol, gave tetrahydrofuran product **6** in high yield as an 85 : 15 mixture.[21]

Method G – cyclization reaction with TBAF (Scheme 8)



Scheme 8. Cyclization reaction using TBAF

First, hydroboration/Suzuki coupling defined a robust means of coupling the linalool derivatives after which Shi epoxidation of **1** provided **2** in 59 % yield (dr ≥ 20 : 1). Desilylation with TBAF, followed by treatment with HCl in $CHCl_3$ resulted in cyclization to deliver the stereodefined tetrahydrofuran **3** in 86 % yield.[22]

Method H will be described in paragraph *3.5.3. Oxidative cyclization reaction*

3.4. Description of used analytical methods

For analysis of all synthesized compounds several analytical methods such as infrared spectroscopy, nuclear magnetic resonance spectroscopy, gas-liquid chromatography, high-performance liquid chromatography, modular circular polarimetry has been used.

3.4.1. Infrared Spectroscopy

Infrared (IR) spectroscopy is one of the most useful spectroscopic techniques in organic chemistry. It is a rapid and effective method for identifying the presence or absence of simple functional groups. When infrared energy is passed through a sample of an organic compound, absorption bands are observed. The position of these IR absorption bands have been correlated with types of chemical bonds, which can provide key information about the nature of functional groups in the sample.

The mid infrared, extending from 4000 to 600 cm^{-1}, is the region of most interest to organic chemists. This is the region in which absorptions from typical organic compounds appear. When coupled with other spectroscopic techniques, such as nuclear magnetic resonance, IR spectroscopy allows organic chemists to systematically and confidently determine the molecular structures of organic compounds.

An IR spectrum has energy, measured as frequency or wavelength, plotted along the horizontal axis and intensity of the absorption plotted along the vertical axis.[23]

The atoms making up a molecule are in constant motion. The movements of the atom relative to each other can be described as vibrations, and IR spectroscopy has been called vibrational spectroscopy. The photons of IR radiation absorbed by an organic molecule have just the right amount of energy to stretch or bend its covalent bonds. The energy of IR radiation is on the order of 8-40 kJ/mole (2-10 kcal/mole). This amount is not enough energy to break a covalent bond, but it is enough to increase the amplitude of bond vibration.

An absorption band appears in an IR spectrum at a frequency where a molecule vibration occurs in the molecule. Energy levels of molecular vibrations are quantized, which means that only infrared energy with the same frequency as the molecular vibrations can be absorbed.[24]

3.4.2. Nuclear Magnetic Resonance Spectroscopy

Nuclear magnetic resonance (NMR) spectroscopy is one of the most important modern instrumental techniques used in the determination of molecular structure. For the past 50 years,

NMR has been in the forefront of the spectroscopic techniques that have completely revolutionized organic structure determination. Like other spectroscopic techniques, NMR depends on quantized energy changes that are induced in molecules when they interact with electromagnetic radiation. The energy needed for NMR is in the radio frequency range of the electromagnetic spectrum and is much lower energy than that needed by other spectroscopic techniques.[25]

The theoretical foundation for nuclear magnetic resonance arises from the spin, *I*, of atomic nucleus. The value of *I* is related to the atomic number and the mass number and may be 0, ½, 1, 3/2, 2, and so forth. Any isotope whose nucleus has a nonzero magnetic moment ($I > 0$) is in theory detectable by NMR spectroscopy. The most important nuclei for organic structure determination are ^{1}H and ^{13}C, both of which have spin of ½.[26]

The DEPT-135 experiment (Distortionless Enhancement by Polarization Transfer) may be applied as a powerful means for distinguishing CH_3, CH_2 and CH groups. This experiment uses a polarization transfer from protons to an X nucleus to increase the signal strength. The experiment may be performed with polarization transfer over one or more bonds, with or without ^{1}H decoupling. Important note is that no signals of quarternary carbon atoms appear.

The HSQC (Heteronuclear Single Quantum Coherence) experiment performs the H, C-correlation via the ^{13}C chemical shift evolution of a double-quantum coherence. The HSQC scheme is included as a building-block in many 3D sequences, especially for structural biology.[27]

3.4.3. Gas-Liquid Chromatography

Few techniques have altered the analysis of volatile organic chemicals as much as gas-liquid chromatography (GC). Before GC, that became widely available just over 50 years ago, organic chemists usually looked for ways to convert liquid compounds into solids in order to analyze them. Gas-liquid chromatography changed all that by providing a quick, easy way for both qualitative and quantitative analysis of volatile organic mixtures.

In GC the stationary phase consists of a nonvolatile liquid, usually a polymer, with high boiling point. A flow of inert gas, such as helium or nitrogen, serves as the mobile phase. When the mixture being separated is injected into the heated injection port, the components vaporize and are carried by the carrier gas into the column, where separation occurs. The compounds in the mixture partition themselves between the gas phase and the liquid phase in the column, in an equilibrium that depends on the temperature, the rate of gas flow, and the solubility of components in the liquid phase. A GC column has thousands of theoretical plates as a result of the huge surface

area on which the gas and liquid phases can interact. The partitioning of a substance between the liquid and gas phases depends both on its relative attraction for the liquid phase and on its vapor pressure. In general, lower-boiling-point compounds with higher vapor pressures travel through a GC column faster than higher-boiling compounds. Another factor which influences traveling speed of compounds through column is compounds polarity. Different functional groups change polarity of compound. More polar compounds travel faster through GC column.[28]

Chiral chromatography involves the separation of stereoisomers. In the case of enantiomers, these have no chemical or physical differences apart from being three-dimensional mirror images. Conventional chromatography or other separation processes are incapable of separating them. To enable chiral separations to take place, either the mobile phase or the stationary phase must themselves be made chiral, giving differing affinities between the analytes.[29]

A GC can have either capillary or packed columns. Capillary columns have an interior diameter of only 0.2-0.5 mm and a length of 10-100 m. A packed column typically has an interior diameter of 2-4 mm and a length of 2-3 m. Capillary columns usually give much better separation than do packed columns.

Two kinds of detectors are most often used in gas-liquid chromatography: flame ionization detector and thermal conductivity detectors. The function of a detector is to "sense" a material and convert the sensing into an electrical signal. Flame ionization is a highly sensitive detector system that is commonly used with capillary columns, where the amount of sample reaching the detector is substantially less than that emanating from a packed column. In a flame ionization detector, the organic substances leaving the column are burned in a hydrogen/air flame. The combustion process produces ions that alter the current output of the detector.[30]

3.4.4. High-Performance Liquid Chromatography

High-performance liquid chromatography (HPLC) allows separations and analysis to be completed quickly and with superior separation and sensitivity compared with other liquid chromatography techniques. However, like GC, HPLC generally utilizes small samples and is most often used for the analysis of mixtures rather than for preparative purposes. Unlike GC, HPLC can be used equally well with volatile and nonvolatile mixtures.

The stationary phase in an HPLC column has a particle size of only 3-10 µm. The enhanced separation and sensitivity of the column come from the increased surface area provided

by these very small particles. However, particles of this small size pack very tightly, a condition that severely restricts the flow of solvent through the column.

There are two main classes of column: "normal" and "reversed" phase. Normal phase columns are most usually packed with silica gel; they work in the partition/adsorption mode in the same manner as a normal silica gel column in conventional chromatography. Reversed phase chromatography, which is the most common form of HPLC, is a type of partition chromatography. Frequently, reversed phase columns are packed with a chemically bonded octadecylsilyl coated silica; such columns are referred to as C-18 and are very non-polar. Other popular bonded phase columns have octasilyl, cyanopropyl, or phenylsilyl packings.

The eluent used with reversed phase columns is relatively polar, e.g. MeOH/H_2O. Unlike normal phase chromatography, the more polar components of a mixture elute first, since these partition relatively unfavourably on the highly non-polar packing. Increasing the polarity of the solvent increases the retention time of a particular component.[31]

The detectors used for HPLC have a high sensitivity, usually in the microgram-to-nanogram range. The two most common types are ultraviolet (UV) and refractometer detectors. A UV detector is relatively inexpensive and can be used with gradient eluetion. It detects any organic compounds that absorbs in the UV region. The limitation of a UV detector precludes its use with solvents that themselves absorb in the UV region or with sample that do not have a suitable chromophore for UV absorption.[32]

HPLC chiral columns are packed with Chiral Stationary Phases-consisting of a silica support onto which the polymeric chiral selector (polysaccharide derivatives) has been immobilised. Immobilisation of the polysaccharide derivatives provides universal solvent compatibility on highly selective Chiral Stationary Phases.[33]

3.4.5. Polarimetry

The light beam approaching the polarizer has wave oscillations in all the planes perpendicular to the direction in which the beam is traveling. When the light beam hits the polarizer, which has ranks and files of molecules arranged in a highly ordered fashion, only the light whose oscillations are in one plane is transmitted through the polarizer. The light that gets through is called *plane-polarized light*. The remaining waves are refracted away or absorbed by the polarizer.

The analyzer is a second polarizer whose ranks and files of molecules must also be lined up for the polarized light waves to be transmitted. If the polarized light has been rotated by an optically active substance in the sample tube, the analyzer must be rotated the same amount to let the light through. The rotation is measured in degrees, indicated by α.

The magnitude of the optical rotation depends on the concentration of the optically active compound in the solution, the length of the light path through the solution, the wavelength of the light, the nature of the solvent, and the temperature. Inherent property of optically active compounds is *specific rotation*. The specific rotation is calculated from the observed angle of rotation:

Equation 1. Specific rotation calculation.

$$[\alpha]_{\lambda}^{T^o} = \frac{\alpha}{l \times c},$$

where α is the observed angle of rotation, l is the length of the light path through the sample in decimeters, and c is the concentration of the sample (g/mL).[34]

3.5. Theory of asymmetrical reactions in this work

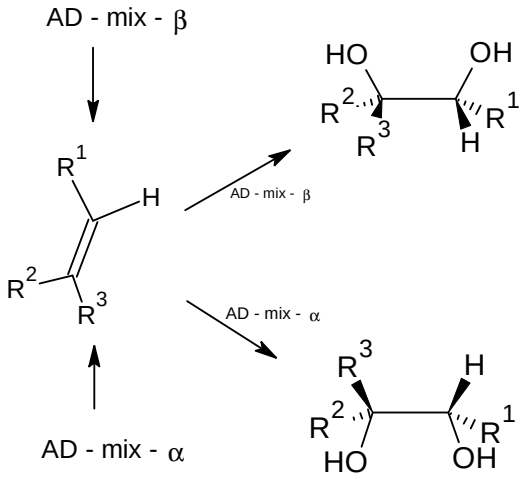
3.5.1. Sharpless catalytic asymmetric dihydroxylation

The Sharpless Dihydroxylation or Bishydroxylation is a method for the enantioselective preparation of 1,2-diols from prochiral olefins, by the reaction of an alkene with Os-catalyst in the presence of a chiral ligand. This procedure is performed with an osmium catalyst and a stoichiometric oxidant e.g. $K_3Fe(CN)_6$ or *N*-methylmorpholine oxide (NMO). The oxidant is regenerating the catalyst osmium tetroxide and therefore reduces the amount of highly toxic and very expensive osmium compound.

Reaction is carried out in a buffered solution to ensure a stable pH, since the reaction proceeds more rapidly under slightly basic conditions. Enantioselectivity is achieved through the addition of enantiomerically-enriched chiral ligands $(DHQD)_2PHAL$, $(DHQ)_2PHAL$ or their derivatives. These reagents are also available as stable, prepackaged mixtures (AD-mix α and AD-mix β, AD=asymmetric dihydroxylation) for either enantiopreferenc.[35] Methanesulfonamide enhance the rate of hydrolysis of the intermediate.[36]

Sharpless was awarded a share of the 2001 Nobel Prize in Chemistry.

AD-mix-α/ß:



Scheme 9. Brief scheme of Sharpless Asymmetric Dihydroxylation

The mixes contain:

- ✓ Potassium osmate $K_2OsO_2(OH)_4$-the source of osmium tetroxide OsO_4;
- ✓ Potassium ferricyanide $K_3Fe(CN)_6$-re-oxidant;
- ✓ Potassium carbonate K_2CO_3-slightly basic conditioner;
- ✓ Chiral ligands-$(DHQD)_2PHAL$ or $(DHQ)_2PHAL$.[37]

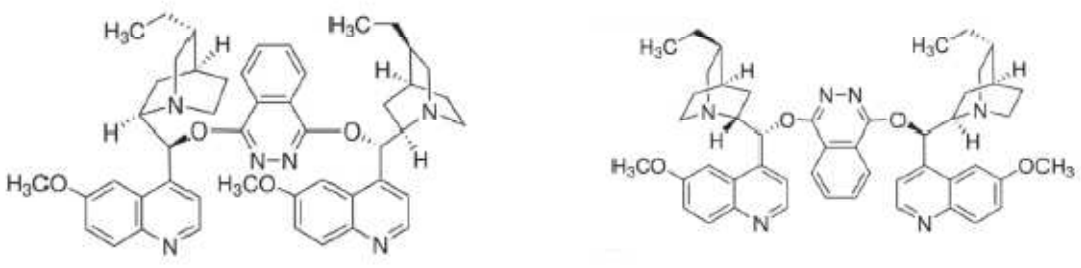
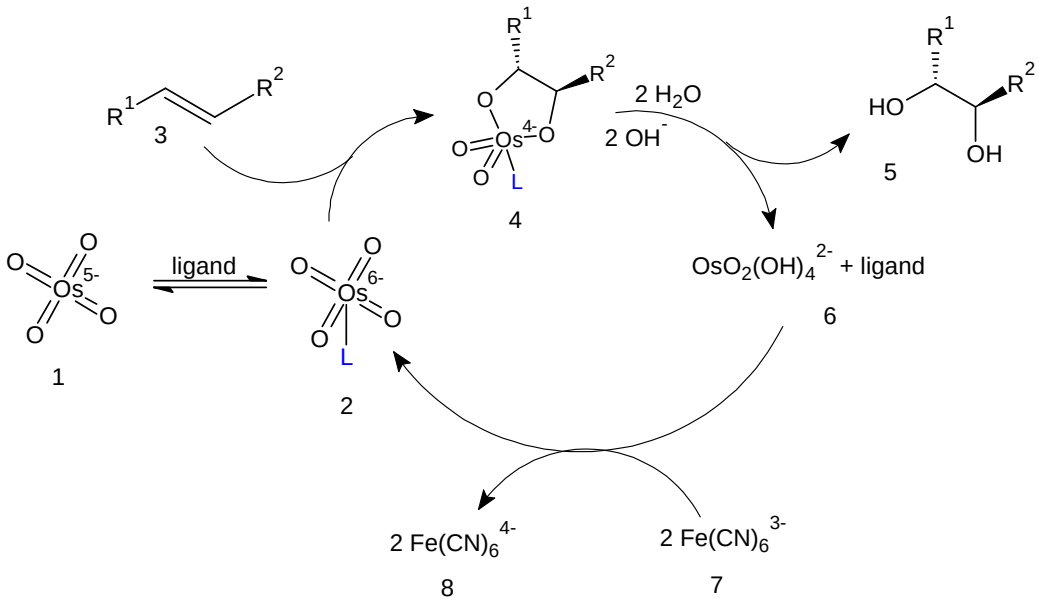


Figure 6. Structures of chiral ligands

Structure on the left side represents the chiral ligand $(DQHD)_2PHAL$ in AD-mix-ß. Structure on the right side represents the chiral ligand $(DHQ)_2PHAL$ in AD-mix-α.

Reaction mechanism:



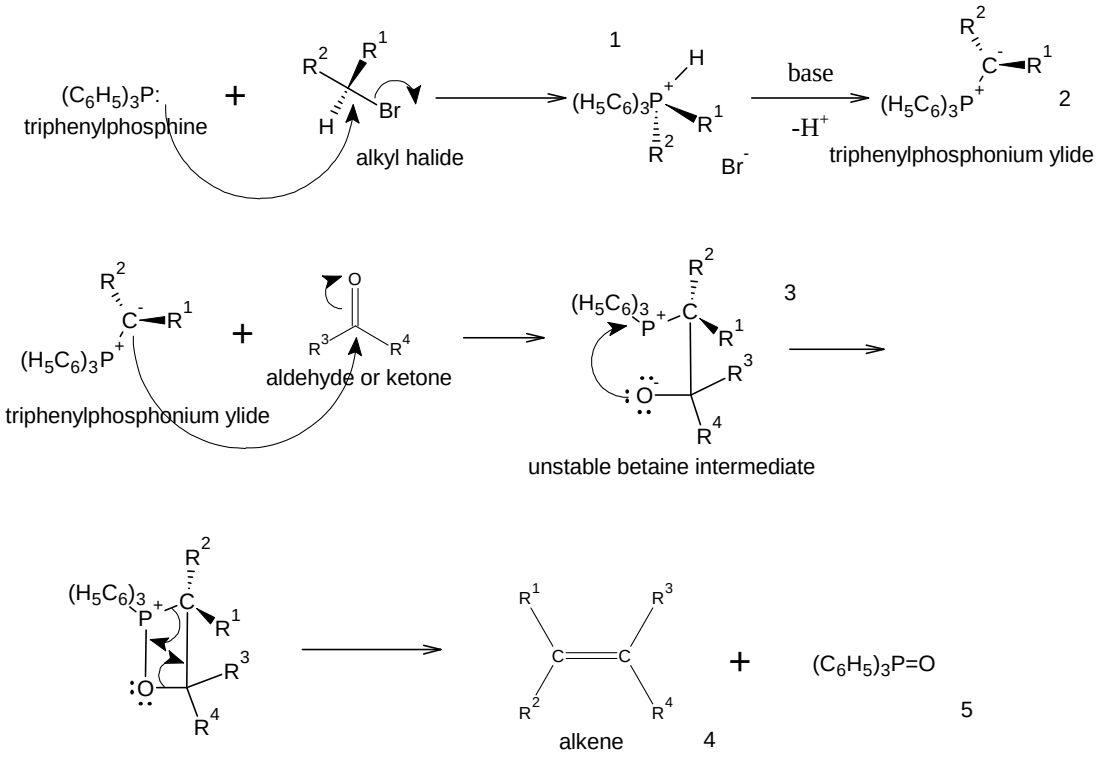
Scheme 10. Reaction mechanism of Sharpless catalytic asymmetric dihydroxylation

Reaction starts with the formation of the osmium tetroxide-ligand complex (**2**). Then a [3+2]-cycloaddition with the alkene (**3**) gives the cyclic intermediate (**4**). Basic hydrolysis liberates the diol (**5**) and the reduced osmate (**6**). The stoichiometric oxidant (**7**) regenerates the osmium tetroxide-ligand complex (**2**).[38]

3.5.2. Wittig reaction

The Wittig reaction allows the preparation of an alkene by the reaction of an aldehyde or ketone with the ylide generated from a phosphonium salt. This reaction was discovered by Georg

Wittig in 1954.[39] He was awarded by Nobel Prize in Chemistry in 1979. This reaction generates the C=C double bond in the place of C=O double bond. The ylide is also called as Wittig reagent and is usually prepared from phosphorium salt, which can be derived from triphenyl phosphine and alkyl halide. The geometry of the resulting alkene depends on reaction conditions-temperature and ratio between salt and base. Considering all necessary aspects of this reaction it is possible to obtain cis-isomer.[40]

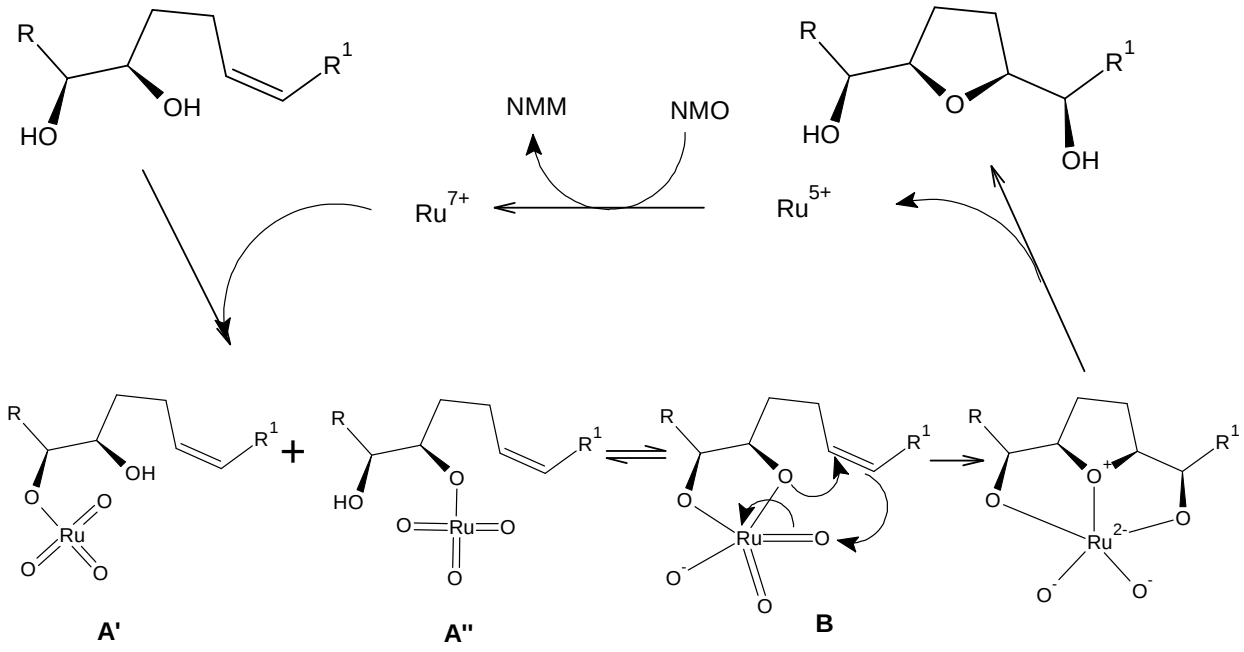


Scheme 11. Reaction mechanism of Wittig reaction

Reaction starts with preparation of Witting salt (**1**) which is derived from triphenyl phosphine and alkyl halide. Next step is Witting salt treating with base to prepare triphenylphosphium ylide (**2**). With carbonyl compound a betaine (**3**) is formed, which is unstable (a betaine is a dipolar substance with nonadjacent opposite charges.) Electron pair movement continues as oxygen departs its bond with carbon to bond with phosphorus. The two carbons of interest now possess a double bond between them. Reaction is completed and in a product mixture contains alkene (**4**) and triphenylphosphonium oxide (**5**).

3.5.3. Oxidative cyclization reaction

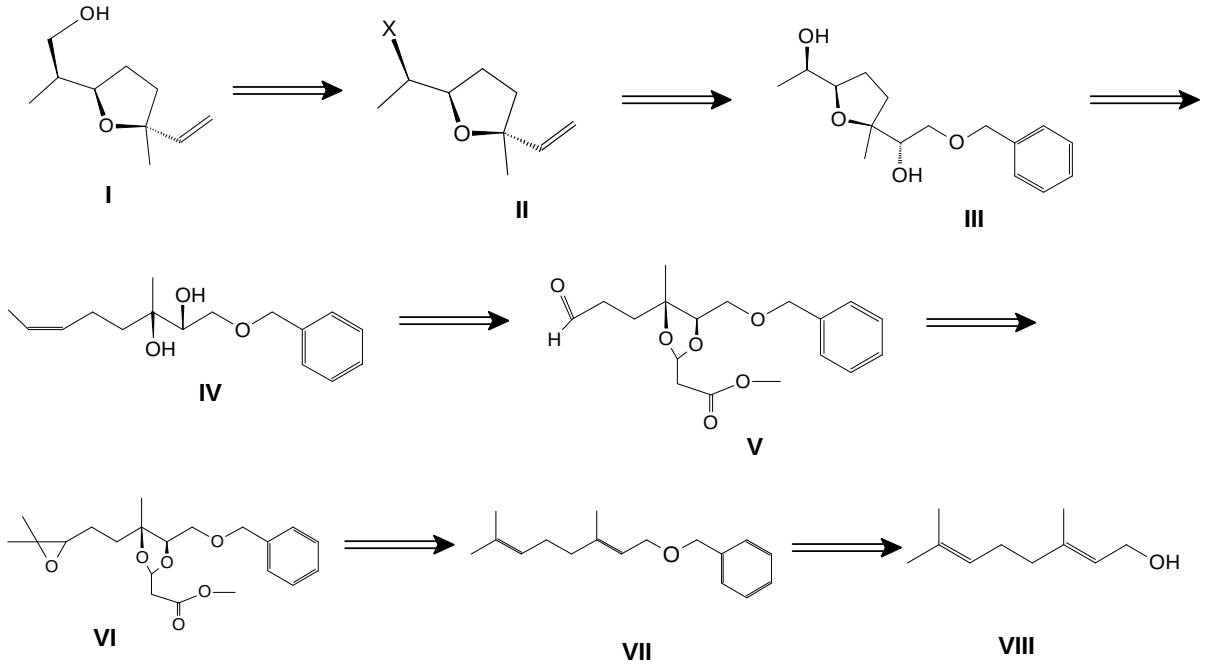
Using ruthenium (VII) catalyst (TPAP-Tetrapropylammonium perruthenate) for the oxidative cyclization of the vicinal diol, in the first step two regioisomeric intermediates A and A' (see reaction mechanism below) are conceivable, the ratio of which will primarily be controlled by steric factors. Instead of mediating an alcohol oxidation, the high Lewis acidity of the metal center is assumed to drive an intramolecular interaction with the neighboring hydroxyl group. Thus, both intermediates A and A' will rapidly be converted into the same cyclic ruthenium (VII) diester B (see reaction mechanism below). Within this key intermediate the doubly activated transition metal is now electrophilic and carbophilic enough to undergo a [3+2]-cycloaddition to the proximal C–C double bond. Finally, hydrolysis liberates the THF (tetrahydrofuran)-diol product and a ruthenium (V) species which is reoxidized with NMO (4-Methylmorpholine *N*-oxide) to the active catalyst.[41]



Scheme 12. Reaction mechanism of oxidative cyclization reaction

4. Results and discussion

4.1. Retrosynthetic scheme for lilac compound synthesis

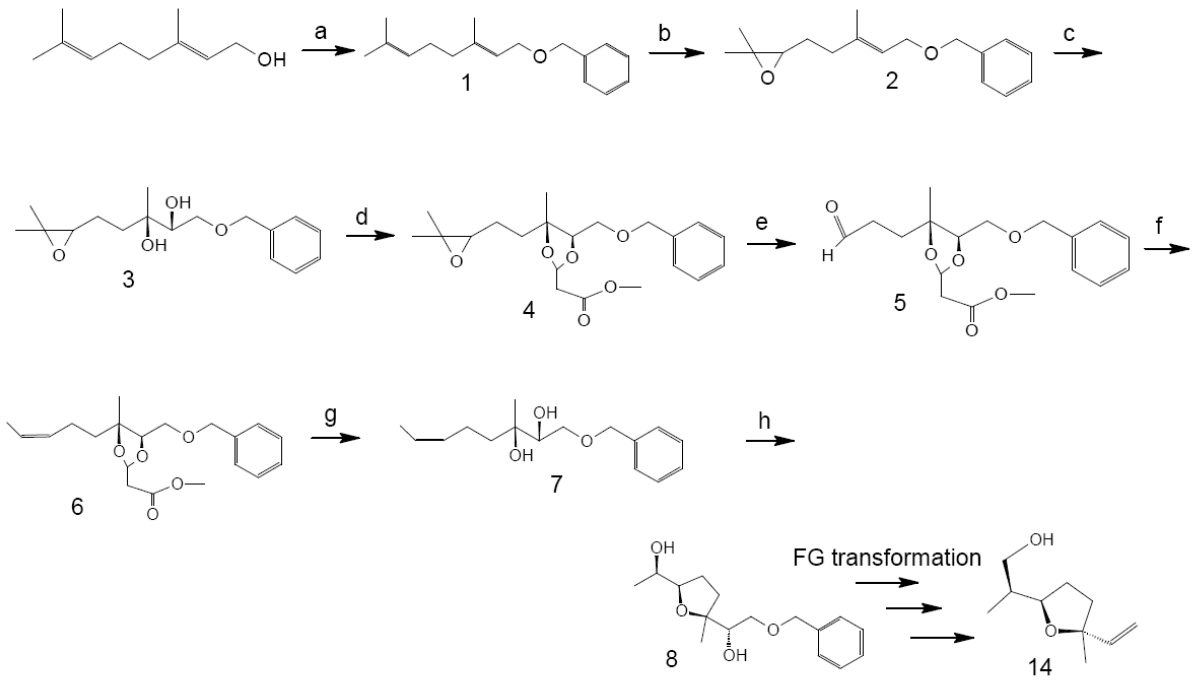


Scheme 13. Retrosynthetic scheme of lilac compounds

To obtain lilac compound series of reactions should be made. Suggested scheme contains three stereoselective reactions. To obtain compound **I** reaction of addition carbon should be made in place of leaving group X in compound **II**. This reaction can change conformation of C-X chiral center. It depends on reaction mechanism (S_N1 or S_N2). Compound **II** can be achieved after series of reactions including benzyl ether deprotection from compound **III**. Compound **III** is the product of oxidative cyclization reaction of compound **IV**. Compound **IV** is the product of Wittig reaction of compound **V**. To obtain compound **V** epoxide transformation to aldehyde should be made to compound **VI**. Compound **VI** is the product of epoxidation reaction of the furthest C=C double bond in compound **VII**. Compound **VII** can be obtained from commercially available geraniol by alcohol group protection reaction with benzyl bromide.

4.2. Used synthetic scheme

The synthetic strategy shown in Scheme 14 comprise the stereoselective construction of 2,2,5-trisubstituted tetrhydrofuran skeletons.



Scheme 14. Used synthetic scheme

[a] NaH, benzyl bromide, THF, 60 °C-rt, 6 h, 99%. [b] m-CPBA, DCM, 0 °C-rt, 4 h, 60%. [c] K_2CO_3, $K_3N(CN)_6$, $(DHQD)_2PHAL$, $K_2OsO_2(OH)_4$, $CH_3SO_2NH_2$, *t*-BuOH and H_2O, 0 °C, 12 h, 90%. [d] DMAP, methyl-propynoate in acetonitrile, rt, 2 h, 66%. [e] H_5IO_6, THF and H_2O, 0 °C-rt, 2 h, 71%. [f] $C_2H_5P(C_6H_5)_3 \cdot Br$, $((CH_3)_3Si)_2NNa$, THF, -78 °C-rt, 12 h, 70%. [g] Buthyllithium, pyrrolidine, THF, 0 °C-rt, 2 h, 53%. [h] NMO, TPAP, *t*-BuOH, rt, 24 h, 56%.

The commercially available geraniol was quantitatively converted into its benzyl ether **1** using sodium hydride and benzyl bromide in THF.[49]

The furthest double C=C bond in benzyl ether **1** was oxidized with m-CPBA in DCM yielding 60 % of racemic epoxide **2**.[50]

The first key intermediate diol **3** was prepared by stereoselective catalytic Sharpless dihydroxylation of allylic alcohol **2**.[51]

Three parallel reactions were run to make the diol **3**.

1) Sharpless catalytic dihydroxylation without any chiral ligand to get reference compounds for chiral HPLC analysis after reaction step **g**. For HPLC analysis Phenomenex LUX column was chosen, oven temp. was 30 °C, isocratic 10 % *i*-PrOH in hexane at flowrate 1.5 mL/min. Racemic mixture had ratio of isomers 50.2:49.8 [Appendix 31] after reaction **g**.

Allylic alcohol was dihydroxylated with potassium osmate (VI) dihydrate, potassium hexacyanoferrate(III), and potassium carbonate in *t*-BuOH-water (1:3) to yield racemic diol **3'** in 90 % yield.

2) For Sharpless catalytic stereoselective dihydroxylation a chiral ligand $(DHQD)_2PHAL$ (AD-mix β) was added to identical reaction mixture in aim to get pure enantiomer **3''**. Reaction yielded **3''** in 70 % yield and the ratio of enantiomers was determined by chiral HPLC as 22:78 after reaction **g** [Appendix 33]. For HPLC analysis Phenomenex LUX column was chosen, oven temp. was 30 °C, isocratic 10 % *i*-PrOH in hexane at flowrate 1.0 mL/min.

3) To obtain better enantiomeric ratio a co-solvent methanesulfonamide was added to the reaction mixture. This operation increased the enantiomeric ratio up to 2:98 (result after reaction **g**) [Appendix 32]. For HPLC analysis Phenomenex LUX column was chosen, oven temp. was 30 °C, isocratic 10 % *i*-PrOH in hexane at flowrate 1.5 mL/min.

Yield of diol **3'''** was 90 %.

Weakly acidic methanesulfoamide is a general acid catalyst that accelerates the rate-limiting hydrolysis step under the heterogeneous reaction conditions by protonating the intermediate osmate ester.[36]

First time the dihydroxylation reaction was made according to the procedure found from literature.[51] The authors used solvent mixture H_2O-*t*-BuOH (1:1). In our experiments solvents ratio 3:1 was improved the yield of reaction from 70 to 90% due to better solubility of inorganic salts ($K_3[Fe(CN)_6]$ and K_2CO_3) in the mixture that contained more water.

It is expected that using the other chiral ligand (AD-mix α) gives the other enantiomer with similar enantiomeric purity.

Before the chain extension via Wittig reaction, it was necessary to protect both OH-groups of diol **3**, because we didn't expect to achieve good yields after adding two extra equivalents of base that deprotonates the diol. Very popular way for protection of vicinal diol is to protect it as acetonide with 2,2-dimethoxypropane using catalytic amount of p-TsOH in dry DCM.[53] This reaction failed in our hands. Looking for alternative possibilities, relatively new and

little-used method was found. The diol **3** was protected in 66 % yield as cyclic mocdene acetal **4** by reacting diol with methyl propynoate in the presence of catalytic amount of DMAP in AcCN.[52]

In order to prepare the desired aldehyde for Wittig reaction, the epoxide **4** was oxidatively opened with periodic acid. A proposed mechanism of the epoxide opening with periodic acid involves a first step of epoxide hydrolysis to the corresponding 1,2-diol followed by oxidation to aldehyde. Reaction in Et_2O [54] yielded 45% of aldehyde **5**, whereas the yield was improved up to 71% by using THF-H_2O (1:1) as a solvent.

The second stereoselective step in this synthetic scheme was the two-carbons Wittig olefination. The reaction of aldehyde **5** with triphenylethylphosphorane under Bestmann's salt-free conditions where bis(trimethylsilyl)amide was used as a base to generate the phosphorane in THF furnished the *Z*-alkene **6** in 70 % yield.[55]

To obtain corresponding *E*-alkene, a different approach, the Kocienski variation of Julia olefination [42] should be used.

Mocdene acetal **6** was opened through a treatment with a base yielding diol **7** in 53 % yield. *n*-BuLi in THF was applied to produce the elimination that yielded the mocvinyl intermediate, which was cleaved in situ by a good nucleophile such as pyrrolidine via an addition-elimination mechanism.[56]

For racemic mixture **7'** and for pure enantiomer **7''** specific rotation was measured [Appendix 30]. Specific rotation for pure enantiomer was +6.44, but for racemic mixture it was -0.18. Racemic mixture had a ratio of isomers by HPLC 50.2:49.8, that explains non-zero value for optical rotation.

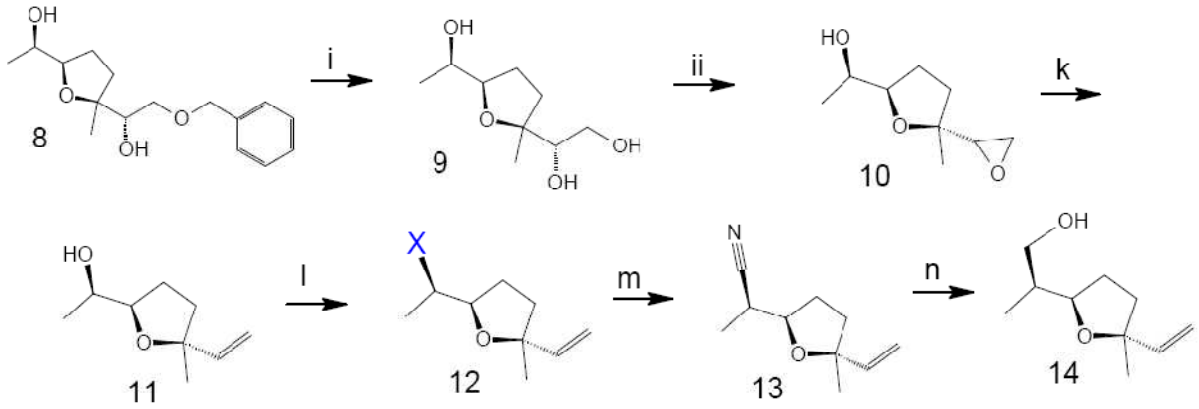
Diol **7** was subjected to stereocontrolled oxidative cyclization, the third stereoselective step in this scheme, in *t*-BuOH to yield the THF-diol **8** in 56 % yield. TPAP was used as a catalyst and NMO to re-oxidize the ruthenium (V) species.[57]

After cyclization reaction stereochemical purity of the product was checked by chiral HPLC. For racemic mixture **8'** ratio between isomers was 47:53 [Appendix 38]. Product **8''** showed the enantiomeric ratio of 2:98 [Appendix 39]. For HPLC analysis Chiralpak IA column was chosen, oven temp. was 30 °C, isocratic 10 % *i*-PrOH in hexane at flowrate 1.0 mL.min.

Functional groups transformations in order to prepare lilac alcohol **14** from THF-diol **8** are shown in Scheme 15.

For conversion the right side of the molecule, benzyl ether was deprotected via hydrogenation over Pd-catalyst in MeOH. Diol **9** was prepared in 78% yield.[58]

Tosylation of the diol **9** was performed under the conditions yielded the selective transformation of primary alcohol. Catalytic amount of Bu_2SnO, stoichiometric amount of p-TsCl and Et_3N were used.[59] Epoxidation of the crude tosylate achieved in slightly basic conditions by treatment with K_2CO_3 in MeOH. Epoxide **10** separated in 53% yield after two reactions.



Scheme 15. Reaction scheme of FG transformation

[i] 10% Pd-C, MeOH, rt, 48 h, 78%. [ii] 1. p-TsCl, Bu_2SnO, Et_3N, toluene, 0 °C-rt, 12 h. 2. K_2CO_3, DCM, rt, 12 h, 53%. [k] In-powder, bis(cyclopentadienyl)titanium(IV) dicloride, THF, 60 °C-rt, 30 min, 43%. [l] *N*-bromosuccinimide, Ph_3P, DMF, 0 °C-rt, 2 h, 42%.

Deoxygenation of epoxide **10** to olefin was performed using mild and efficient bis(cyclopentadienyl)titanium(IV)dichloride-indium system in THF.[60] This transformation yielded 43 % of alkene **11.**

To correct the left side of the molecule the prolongation of the chain from hydroxyl-group is necessary.

It was planned the strategy to activate the OH-site by introducing a good leaving group and to use it for one-carbon elongation of the chain via cyanation. Expected nitrile was planned to reduce by DIBAL to target lilac compound **14**.

A series of unsuccessful reactions were made.

We attempted to get tosylate, mesylate, and triflate from the secondary alcohol **11**.

Tosylation of the secondary alcohol **11** attempted in DCM using p-TsCl and Et_3N.[59] Maybe there was too big steric hindrance to get the reaction and prolongated heating can realize the goal.

Mesylation reaction is very moisture sensitive. In case of traces of water in reaction mixture the mesyl chloride can decompose to the corresponding acid and mesylation doesn't occur.[61]

Triflation attempted in DCM using trifluoromethanesulfonic acid anhydride as reagent and pyridine to trap acidic products.[62] It turned out that the resulted triflate was sensitive even towards weakly acidic media and decomposed during purification by silica gel chromatography. Because of that, the reaction repeated and the crude product obtained, used immediately for the next reaction.

The crude mixture of triflate was analyzed by ^{1}H NMR, ^{13}C NMR and IR-spectroscopy. Proton spectra showed double bond still present, in carbon spectra characteristic for C-F quartet was found in the range of 130-110 ppm. In IR spectra two sharp peaks (C-F) in the range of 1220-1200 cm^{-1}were seen while –OH peak at 3300 cm^{-1} had disappeared.

The crude triflate was subjected to the cyanation reaction with so-called "naked" anione ie. the reaction performed with 1:1 complex of KCN and 18-crown-6 in THF.[62] Reaction was unsuccessful, maybe insufficient purity of triflate used.[62]

Another attempt to substitute the alcohol functionality was tried via bromination with *N*-bromosuccinimide-triphenylphosphine in DMF.[63] Reaction was successful according to TLC-check and the product was purified and analyzed by NMR and IR. In IR-spectra –OH peak at 3300 cm^{-1} had disappeared and at a range of 534 cm^{-1} C-Br signal appeared. In ^{13}C NMR spectra C-Br carbon appeared at 27.5 ppm

The bromination reaction proceeds via S_N2 mechanism, therefore the configuration of the chiral center of formed alcohol was inverted.

The conversion of nitrile to lilac aldehyde was intended to realize via DIBAL reduction. Lilac alcohol is available via reduction of aldehyde with sodium borohydride ($NaBH_4$).

The attempted reactions conversions of the left side of the molecule need more investigations. It is planned in future to run the reactions in bigger scale to get more clear results. Obtained enantiomers will be analyzed by GC and results will be compared with reference material – mixture of 8 lilac alcohol enantiomers [Appendix 55].[43] The order of separated lilac alcohol enantiomers by GC is known from previous studies.

The main goal of present research work was successfully realized: the developed synthetic pathway enables to synthesize the 2,2,5-trisubstituted THF structure with enantiomeric purity of 98% using three stereoselectivity defining steps in the scheme. The total yield from geraniol was 3.3%. Table of used chemicals is located in Appendix 1.

4.3. Used equipment and analysis

4.3.1. Flash columns

Biotage® Isolera™ Flash Purification System

Instrument attributes:[44]

Solvent delivery: two constant (3 mL) electric HPFC pumps; *Flow rate*: 1-200 mL/min; *Pressure limit*: 145 psi (10 bar); *UV Detection*: choice of variable wavelength (200-400 nm), fixed (254 nm) or UV-VIS (200-800 nm) detectors; *Flow cell path length*: 0.3 mm; *UV collection modes*: Single/dual/?-All wavelengths (variable UV and UV-VIS); *Fractionation modes*: volume, threshold, threshold with volume, low slope, medium slope, custom slope; *Used cartridges*: 4 g, 12 g, 24 g, 48 g, 80 g, 120 g.

4.3.2. Nuclear Magnetic Resonance

1 D spectra: ^{1}H-proton spectra

^{13}C-carbon spectra

Dept-135 - carbon spectra which show CH/CH_3 carbons in postive side of baseline and CH_2 carbons in negative side of baseline. Quarteary carbons are not present in those spectra.

2D spectra: HSQCEDETGP–^{1}H with respect to ^{13}C

Characteristic data:[45]

Proton Frequency: 400 MHz; *Central Field*: 9.40 Tesla; *Magnetic Energy*: 28 kJoule; *Integral uncertainty*: 5 %.

4.3.3. High Performance Liquid Chromatography

Shimadzu Prominence Modular HPLC system:[46]

Used columns: Phenomenex LUX, No 530654-4, size: 250x4.60mm and Chiralpak IA, No IA00CE-L1056, size: 250x4.60mm; *System controller*: CBM-20A; *Solvent delivery*: LC-20A; *Auto sampler*: SIL-20A; *Column oven*: CTO-20A; *UV-VIS detector*: SPD-M20A.

4.3.4. Gas Chromatography

Chromatograph: Agilent Technology Gas-chromatography Agilent 7890A

Chiral capilary column ß-DEX 325 (Supelco, 30m x 0.25mm x 0.25μm)

Phase: non-bonded; 25% 2,3-di-O-methyl-6-0-TBDMS-β-cyclodextrin embedded in SPB-20 [poly(20% phenyl/80% dimethylsiloxane)]

Detector: FID

Signal intensity expressed in electric current (pA).

4.3.5. Fourier transformation Infrared spectroscopy

Shimadzu Fourier Transform Infrared spectrometer IRPrestige-21/IRAffinity-1/FTIR-8400S with MIRacle 10 attachment.

Instrument attributes:[47]

Signal-to-Noise Ratio: 20,000 : 1 (KRS-S window, 4 cm^{-1}, 1 minute, 2200 cm^{-1}, P-P; *Wavenumber Range*: 7800 to 350 cm^{-1}; *Wavenumber Resolution*: 0.85 cm^{-1}(max): Additional Specification: *Interferometer*: Michelson type with 30^{o} incident angel, dynamic alignment, sealed and desiccated; *Optical system*: single beam optics; *Beam splitter*: Germanium coated KBr plate; *Light source*: high brightness ceramic; *Detector*: temperature controlled high sensitivity detector (DLATGS detector); *Resolution*: 0.85, 1, 2, 4, 8, 16 cm^{-1}; *Mirror speed*: 3 steps, 2.8, 5, 9 mm/sec; Data sampling: He-Ne laser; *MIRACLE 10 crystal*: ZnSe.

4.3.6. Optical rotation

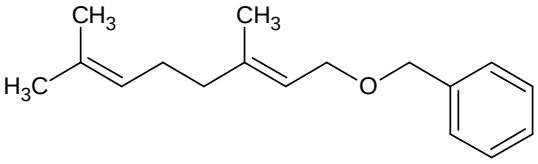
Modular Circular Polarimeter MCP 200

Instrument attributes for optical rotation at 589 nm:[48]

Measuring range: ± 89.9°; *Resolution*: 0.001°; *Accuracy*: ± 0.005°; *Repeatability*: ± 0.002°; *Response time*: 12 sec; *Sensitivity*: A light intensity control compensates attenuation up to an Optical Density (OD) of 4.0; *Light source*: Tungsten halogen lamp, 6V, 20 W, with average lifetime of 2000 h; Temperature interface: *Resolution*: 0.1°C; *Accuracy*: ± 0.2°C; *Temperature control*: Peltier system for automatic temperature control at 20 °C and 25 °C; *Sample cell*: ToolMaster™ - Automatic identification of the sample cell (Option); Sample cell path length from 2.5 mm to 200 mm.

4.4. Experimental description

4.4.1. Synthesis of E-2-(((3,7-dimethylocta-2,6-dien-1-yl)oxy)methyl)benzene (1)



To a stirred solution of sodium hydride (60% in mineral oils) (430.0 mmol, 17.1 g) in THF (200 mL) was added one half of geraniol (97.0 mmol, 15.0 g). Suspension became yellow. Mixture was maintained at 60^{o}C over 2 h. Then over 1 h period second half of alcohol (97.0 mmol, 15.0 g) was added dropwise. After warming 2 h benzyl-bromide (230.0 mmol, 39.9 g) was added dropwise over 20 min. Colour changed from yellow to light grey. The reaction mixture was allowed to cool down to room temperature stirred for additional 2 h, then diluted with water and extracted 3x with PE. The combined extracts were washed successively with water, 5 % NH_4OH, water and brine, dried with $MgSO_4$. Crude mixture was purified by silica gel column chromatography using 0.5 % EtOAc/PE as eluent. Yield of **1** was 47 g (99 %).[49]

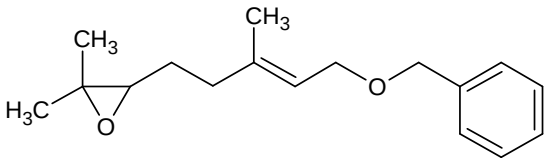
^{1}H NMR (400MHz, $CDCl_3$):δ= 7.44-7.28 (m, 5H, ArC*H*), 5.48 (qt, *J*=6.8, 1.3 Hz, 1H, C=C*H*-CH_2), 5.16 (tq, *J*= 6.8, 1.4 Hz, 1H, C=C*H*-CH_2), 4.55 (s, 2H, O-CH_2-Ar), 4.09 (dq, *J*=6.8, 0.8Hz, 2H, CH-CH_2-O), 2.22-2.07 (m, 4H, CH_2), 1.74 (q, *J*=1.3Hz, 3H, CH_3), 1.71-1.68(m, 3H, CH_3), 1.67-1.64(m, 3H, CH_3). [Appendix 2]

^{13}C NMR (400MHz, $CDCl_3$):δ= 140.4 (CH_3-*C*=CH), 138.7 (CH_3-*C*=CH), 128.9 (C*H*Ar), 128.4 (C*H*Ar), 127.6 (C*H*Ar), 127.9 (C*H*Ar), 124.1 (C=*C*H-CH_2), 120.9 (C=*C*H-CH_2), 71.9 (O-*C*H_2-Ar), 66.7 (*C*H_2-O-CH_2), 39.7 (*C*H_2), 26.7 (*C*H_2), 25.7 (*C*H_3), 17.7 (*C*H_3), 16.5 (*C*H_3). [Appendix 3]

^{1}H-^{13}C HSQC (400MHz, $CDCl_3$) [Appendix 4]

IR: 2922 cm^{-1} (C-H), 1452 cm^{-1} (C=C), 1066 cm^{-1} (C-O), 694 cm^{-1} (C-H). [Appendix 5]

4.4.2. Synthesis of 3-((3E)-5-(benzyloxy)-3-methylpent-3-en-1-yl)-2,2-dimethyloxirane (2)



Compound **1** (192.0 mmol, 47.0 g) was dissolved in CH_2Cl_2 (800 mL) and the mixture was cooled to 0^{o}C using ice-bath. m-CPBA (213 mmol, 47.9 g) was added in four portions every 30-min. After stirring for 2 h at room temp. the reaction mixture was concentrated under vacuum and diluted with sat. aq. $NaHCO_3$ (100 mL). Aqueous layer was extracted with PE (2x100mL). The combined organic layers were washed with sat. aq. $NaHCO_3$ (2x100mL), brine (2x100mL), dried

with $MgSO_4$. Crude mixture was purified by silica gel column chromatography using 10 % EtOAc/PE as eluent. Yield of **2** was 30 g (60 %).[50]

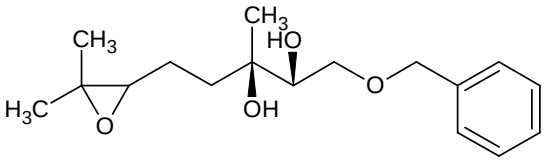
^{1}H NMR (400MHz, $CDCl_3$):δ= 7.36-7.24 (m, 5H, ArC*H*), 5.46 (qt, *J*=6.8, 1.3 Hz, 1H, C=C*H*-CH_2), 4.51 (s, 2H, O-C*H*$_2$-Ar), 4.03 (dq, *J*=6.8, 0.8Hz, 2H, CH-C*H*$_2$-O), 2.71 (t, *J*=12.5, 6.2 Hz, 1H, C-C*H*-O), 2.27-2.09 (m, 2H, C*H*$_2$), 1.72-1.63 (m, 5H, C*H*$_2$-C*H*$_3$), 1.31-1.29 (s, 3H, C*H*$_3$), 1.27-1.25 (s, 3H, C*H*$_3$). [Appendix 6]

^{13}C NMR (400MHz, $CDCl_3$):δ= 139.3 (CH_3-*C*-O), 138.6 (CH_3-*C*=CH), 128.4 (*C*HAr), 127.8 (*C*HAr), 127.7 (*C*HAr), 127.5 (*C*HAr), 121.6 (C=*C*H-CH_2), 72.1 (O-*C*H_2-Ar), 66.6 (*C*H_2-O-CH_2), 63.9 (CH_3-C-O-*C*H), 36.3 (*C*H_2), 27.2 (*C*H_2), 24.9 (*C*H_3), 18.8 (*C*H_3), 16.5 (*C*H_3). [Appendix 7]

^{1}H-^{13}C HSQC (400MHz, $CDCl_3$) [Appendix 8]

IR: 2924 cm^{-1} (C-H), 1452 cm^{-1} (C=C), 1377 cm^{-1} (C-H), 1068 cm^{-1} (C-O), 696 cm^{-1} (C-H). [Appendix 9]

4.4.3. Synthesis of 1-(benzyloxy)-5-(3,3-dimethyloxiran-2-yl)-3-methylpentane-2,3-diol (3) Sharpless catalytic asymmetric dihydroxylation



Mixture of potassium carbonate (345.6 mmol, 48.3 g), potassium hexacyanoferrate (III) (345.6 mmol, 114.9 g), $(DHQD)_2PHAL$ (1.2 mmol, 0.9 g) and $CH_3SO_2NH_2$ (115.0 mmol, 11.3 g) was dissolved in H_2O-*t*-BuOH (3 : 1, 400 mL). $K_2OsO_2(OH)_4$ (0.5 mmol, 0.2 g) was added and reaction mixture was stirred at room temperature for 30 min. Mixture was cooled to 0^{o}C using ice-bath and stirring was continued for 30 minutes. Compound **2** (115 mmol, 30.0 g) in *t*-BuOH (30 mL) was added under ice-cooling and stirring was continued at the same temp. for 12 h. Reaction quenched with Na_2SO_3, extracted with EtOAc, combined organic layers were washed with H_2O, dried with $MgSO_4$. Crude mixture was purified by silica gel column chromatography using 10 % MeOH/CH_2Cl_2 as eluent. Yield of **3** was 28.2 g (90%).[51]

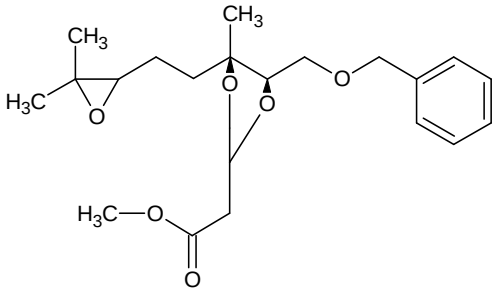
^{1}H NMR (400MHz, $CDCl_3$):δ= 7.38-7.24 (m, 5H, ArC*H*), 5.46 (qt, *J*=6.8, 1.3 Hz, 1H, C-C*H*-OH), 4.50 (s, 2H, O-C*H*$_2$-Ar), 4.03 (dq, *J*=6.8, 0.8Hz, 2H, CH-C*H*$_2$-O), 2.72 (t, *J*=12.5, 6.2 Hz, 1H, C-C*H*-O), 1.79-1.52 (m, 4H, C*H*$_2$), 1.28 (s, 3H, C*H*$_3$), 1.25 (d, *J*=1.48 Hz, 3H, C*H*$_3$), 1.10 (d, *J*=3.57 Hz, 3H, C*H*$_3$) [Appendix 10]

^{13}C NMR (400MHz, $CDCl_3$):δ= 139.6 (CH_3-*C*-O), 128.5 (*C*HAr), 127.9 (*C*HAr), 127.8 (*C*HAr), 127.7 (*C*HAr), 74.4 (C-*C*H-OH), 73.7 (O-*C*H_2-Ar), 71.4 (*C*H_2-O-CH_2), 64.5 (CH_3-C-O-*C*H), 58.6 (CH_3-*C*-OH), 35.4 (*C*H_2), 24.9 (*C*H_3), 23.3 (*C*H_2), 22.3 (*C*H_3), 18.7 (*C*H_3). [Appendix 11]

^{1}H-^{13}C HSQC (400MHz, $CDCl_3$) [Appendix 12]

IR: 3442 cm^{-1} (O-H), 2924 cm^{-1} (C-H), 1454 cm^{-1} (C=C), 1377 cm^{-1} (C-H), 1070 cm^{-1} (C-O), 734 cm^{-1} (C-H). [Appendix 13]

4.4.4. Synthesis of methyl {(5R,6R)-5-[2-(3,3-dimethyloxiran-2-yl)ethyl]-6-[(benzyloxy)methyl]-5-methyl-1,4-dioxan-2-yl}acetate (4)



Prepared solution I of compound **3** (96.0 mmol, 28.2 g), DMAP (48.0 mmol, 5.8 g) in acetonitrile (15 mL) and solution II of methyl-propynoate (115 mmol, 9.7 g) in acetonitrile (12 mL). Solution II was added dropwise to solution I at room temperature. The colour changed from colourless to dark brown. Reaction mixture was stirred for 2 h at room temp. and then quenched with MeOH. Crude mixture was purified by silica gel column chromatography using 30 % EtOAc/PE as eluent. Yield of **4** was 23.7 g (66%).[52]

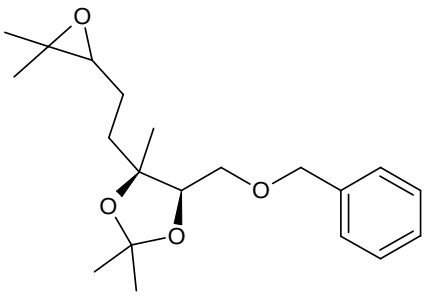
^{1}H NMR (400MHz, $CDCl_3$):δ= 7.35-7.27 (m, 5H, ArC*H*), 5.31 (qt, *J*=6.8, 1.3 Hz, 1H, C-C*H*-O), 4.59 (d, *J*= 12.1Hz, 1H, O-CH_2-Ar), 4.51 (dd, *J*= 12.1, 1.0 Hz, 1H, O-CH_2-Ar), 3.93 (dddd, *J*=6.6, 5.4, 4.5Hz, 1H, O-C*H*-CH_2), 3.69 (s, 3H, COO-CH_3), 3.64 - 3.57 (m, 1H, CH-CH_2-COO), 3.52-3.47 (m, 1H, CH-CH_2-COO), 2.71 (m, 1H, C-C*H*-O), 2.69-2.65 (m, 2H, CH-CH_2-O), 1.89-1.54 (m, 4H, CH_2-CH_2), 1.31-1.28 (s, 3H, CH_3), 1.26-1.24 (d, *J*=2.9 Hz, 3H, CH_3), 1.14-1.11 (d, *J*=3.5Hz, 3H, CH_3). [Appendix 14]

^{13}C NMR (400MHz, $CDCl_3$):δ= 169.7 (CH_2-*C*OOCH_3), 137.7 (CH_3-*C*-CHO), 128.4 (*C*HAr), 128.2 (*C*HAr), 127.8 (*C*HAr), 127.7 (*C*HAr), 99.6 (C-*C*H-O), 81.7 (O-*C*H-CH_2), 73.6 (O-CH_2-Ar), 68.9 (CH_2-O-CH_2), 64.2 (C-*C*H-O), 58.4 (CH_3-*C*-O), 51.8 (COO-*C*H_3), 40.8 (CH-*C*H_2-C=O), 35.4 (*C*H_2), 25.1 (*C*H_3), 23.4 (*C*H_2), 20.4 (*C*H_3), 18.7 (*C*H_3). [Appendix 15]

^{1}H-^{13}C HSQC (400MHz, $CDCl_3$) [Appendix 16]

IR: 2926 cm^{-1} (C-H), 1739 cm^{-1} (C=O), 1454 cm^{-1} (C=C), 1377 cm^{-1} (C-H), 1128 cm^{-1} (C-O), 732 cm^{-1} (C-H). [Appendix 17]

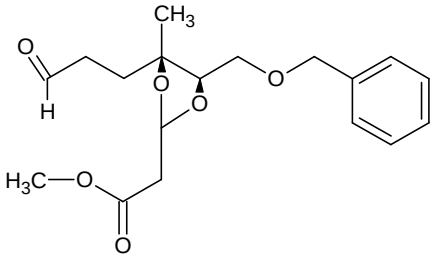
4.4.5. Attempted synthesis of 5-[(benzyloxy)methyl]-4-[2-(3,3-dimethyloxirane-2-yl)ethyl]-2,2,4-trimethyl-1,3-dioxolane



To a stirred solution of **3** (1.0 mmol, 300.0 mg) in anhyd. CH_2Cl_2 (5mL) p-Toluenesulfonic acid (0.1 mmol, 7.7 mg) was added. Reaction mixture was cooled to 0 ^oC using ice-bath and 2,2-dimethoxypropane (3.31 mmol, 345 mg) was added dropwise.[53]

Reaction was monitored via TLC during 7 days. No changes were observed neither TLC nor NMR.

4.4.6. Synthesis of methyl {5-[(benzyloxy)methyl]-4-methyl-4-(3-oxopropyl)-1,3-dioxolan-2-yl}acetate (5)



Compound **4** (62.6 mmol, 23.7 g) was dissolved in 50 mL of THF and H_2O (1 : 1), cooled to 0^oC using an ice-bath and a solution of H_5IO_6 (81.4 mmol, 18.6 g) in 50 mL of THF and H_2O (1 : 1) was added dropwise over 30 min period. Reaction was stirred for 2 h at 0^oC. Reaction mixture was poured into water and extracted with EtOAc. Organic phase was washed with brine and dried with $MgSO_4$. Crude mixture was purified by silica gel column chromatography using 35 % EtOAc/PE as eluent. Yield of **5** was 14 g (71 %).[54]

^1H NMR (400MHz, $CDCl_3$):δ= 9.75 (t, *J*=3.7, 1.5 Hz, 1H, *H*-C=O), 7.36-7.28 (m, 5H, ArC*H*), 5.30 (t, *J*=10.3, 5.3 Hz, 1H, C-C*H*-OH), 4.54 (dd, J= 30.4, 11.9 Hz, 2H, O-CH_2-Ar), 3.91 (t, *J*=12.2, 6.0 Hz, 1H, O-C*H*-CH_2), 3.68 (s, 3H, COO-CH_3), 3.62 (dd, *J*=10.1, 3.7 Hz,1H, CH_2-O-CH_2), 3.49 (dd, *J*=10.1, 3.7 Hz,1H, CH_2-O-CH_2), 2.69-2.63 (m, 2H, O-CH-CH_2), 2.59-2.54 (m, 2H, COH-CH_2-CH_2), 2.01-1.86 (m, 2H, CH_2-CH_2-C), 1.11 (s, 3H, CH_3). [Appendix 18]

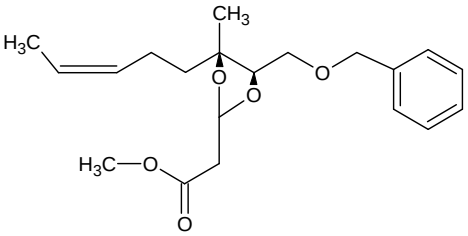
^{13}C NMR (400MHz, $CDCl_3$):δ= 201.6 (H-*C*=O), 169.7 (CH_2-*C*OOCH_3), 137.7 (CH_2-*C*-CHO), 128.5 (*C*HAr), 128.4 (*C*HAr), 127.7 (*C*HAr), 127.0 (*C*HAr), 99.5 (C-*C*H-CH_2), 82.0 (O-*C*H-CH_2), 73.7 (O-*C*H_2-Ar), 68.49 (*C*H_2-O-CH_2), 51.8 (COO-*C*H_3), 40.7 (CH-*C*H_2-O), 38.4 (CH_2), 30.76 (*C*H_2), 20.83 (*C*H_3). [Appendix 19]

^1H-^{13}C HSQC (400MHz, $CDCl_3$) [Appendix 20]

IR: 2900 cm^{-1} (C-H), 1735 cm^{-1} (C=O), 1454 cm^{-1} (C=C), 1126 cm^{-1} (C-O), 698 cm^{-1} (C-H). [Appendix 21]

4.4.7. Synthesis of methyl {(4R,5R)-5-[(benzyloxy)methyl]-4-methyl-4-[(3Z)-pent-3-en-1-yl]-1,3-dioxolan-2-yl}acetate (6)

Wittig reaction



Ethyl(triphenyl)phosphonium bromide (62.5 mmol, 23.2 g) was suspended in THF (120 mL) under inert atmosphere. The solution was cooled to 0^{o}C using ice-bath. $((CH_3)_3Si)_2NNa$ (56.0 mmol, 5.6 mL) was added dropwise. Reaction colour was bright orange. Reaction mixture was cooled to -78^{o}C using a dry-ice bath and after 30 min aldehyde **5** (20.8 mmol, 7.0 g) in THF (25 mL) was added dropwise. Reaction was allowed to warm up to room temp. and stirring continued for 12 h. Reaction mixture was concentrated under vacuum. Crude mixture was purified by silica gel column chromatography using 15 % EtOAc/PE as eluent. Yield of **6** was 5 g (70%).[55]

^{1}H NMR (400MHz, $CDCl_3$):δ=7.37-7.28 (m, 5H, ArC*H*), 5.60-5.34 (m, 3H, CH_3-C*H*=C*H*; O-C*H*-O), 4.61 (d, J=11.9Hz, 1H, O-CH_2-Ar), 4.52 (dd, J=12.1, 3.15 Hz, 1H, O-CH_2-Ar), 3.99-3.93 (m, 1H, C-C*H*-CH_2), 3.69 (s, 3H, COOCH_3), 3.64-3.56 (m, 1H, CH-CH_2-O), 3.54-3.46 (m, 1H, CH-CH_2-O), 2.72-2.61 (m, 2H, CH_2-C=O), 2.13-2.12 (m, 2H, CH_3-CH=), 1.64-1.57 (m, 4H, CH-CH_2-CH_2), 1.26-1.24 (m, 1H, CH_3-CH=), 1.14 (s, 3H, CH_3-C). [Appendix 22]

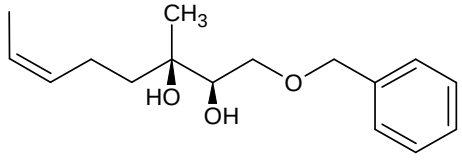
^{13}C NMR (400MHz, $CDCl_3$):δ= 169.9 (CH_2-*C*=O), 137.8 (CH_2-*C*-CHO), 129.9 (CH_3-*C*H=CH), 128.4 (*C*HAr), 127.74 (*C*HAr), 127.72 (*C*HAr), 127.70 (*C*HAr), 124.3 (CH_3-CH=*C*H), 99.3 (O-*C*H-O), 82.1 (CH_3-*C*-O), 73.6 (O-*C*H_2-Ar), 69.0 (*C*H_2-O-CH_2), 51.8 (*C*H_3-O), 40.8 (CH-*C*H_2-C=O), 38.6 (CH_2), 21.3 (CH_2), 20.7 (*C*H_3), 18.4 (*C*H_3). [Appendix 23]

^{1}H-^{13}C HSQC (400MHz, $CDCl_3$) [Appendix 24]

IR: 2918 cm^{-1} (C-H), 1739 cm^{-1} (C=O), 1454 cm^{-1} (C=C), 1128 cm^{-1} (C-O), 732 cm^{-1} (C-H). [Appendix 25]

4.4.8. Synthesis of 1-(benzyloxy)-3-methyloct-6-ene-2,3-diol (7)

Deprotection reaction



Buthyllithium (35.9 mmol, 2.3 g) was added dropwise to a solution of pyrrolidine (71.8 mmol, 5.1 g) in THF (30 mL) under Ar atmosphere at -78^{o}C. Temperature allowed to raise to 0^{o}C and reaction mixture was stirred for additional 30 min. This mixture was transferred to a pre-cooled (0^{o}C) solution of compound **6**

(14.4 mmol, 5.0 g) in THF (10 mL) via cannula. Reaction mixture was stirred for 2 h and solvent was partly removed under reduced pressure. 1M HCl was added until the pH of the solution reached to 2. Reaction mixture was poured into water and extracted with EtOAc (2x50 mL). The combined organic phase was washed with brine and dried with $MgSO_4$. Crude mixture was purified by silica gel column chromatography using 10 to 20 % EtOAc/PE as eluent. Yield of **7** was 1.6 g (53%).[52]

^{1}H NMR (400MHz, $CDCl_3$):δ=7.40-7.27 (m, 5H, ArC*H*), 5.50-5.33 (m, 2H, CH_3-C*H*=C*H*), 4.56-4.55 (m, 2H, O-CH_2-Ar), 3.71-3.58 (m, 3H, C-C*H*; CH_2-O), 2.79 (s, 1H, O*H*), 2.61 (s, 1H, O*H*), 2.17-2.07 (m, 2H, CH_2-CH_2-C), 1.63-1.56 (m, 5H, CH_3-CH=; =CH-CH_2), 1.15 (s, 3H, CH_3-C). [Appendix 26]

^{13}C NMR (400MHz, $CDCl_3$):δ=137.6 (CH_3-*C*-OH), 130.5 (CH_3-*C*H=CH), 128.5 (*C*HAr), 127.9 (*C*HAr), 127.8 (*C*HAr), 127.79 (*C*HAr), 124.0 (CH_3-CH=*C*H), 74.1 (C-*C*H-OH), 73.7 (O-CH_2-Ar), 71.4 (*C*H_2-O-CH_2), 38.7 (CH_2-*C*H_2-C), 22.2 (*C*H_3), 21.2 (CH_2), 12.7 (*C*H_3). [Appendix 27]

^{1}H-^{13}C HSQC (400MHz, $CDCl_3$) [Appendix 28]

IR: 3444 cm^{-1} (O-H), 2918 cm^{-1} (C-H), 1454 cm^{-1} (C=C), 1365cm^{-1} (C-H), 1070 cm^{-1} (C-O), 696 cm^{-1} (C-H). [Appendix 29]

Optical rotation: for reference material **7b** specific rotation equals -0.18 ± 0.03

for product **7a** specific rotation equals +6.44 ± 0.03

Optical rotation calculations are in Appendix 30

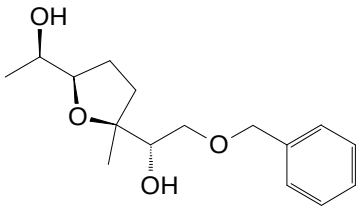
HPLC analyses were made after this reaction.

For reference material (**7b**): ratio of isomers was 50.2 : 49.8 [Appendix 31]

For product **7a**: ratio of isomers was 2.3 : 97.7 [Appendix 32];

4.4.9. Synthesis of (1S)-2-(benzyloxy)-1-{(2S,5R)-5-[(1R)-1-hydroxyethyl]-2-methyltetrahydrofuran-2-yl}ethanol (8)

Cyclization reaction



A solution of compound **7** (6.3 mmol, 1.7 g) in *t*-BuOH (30 mL) was treated with NMO (7.6 mmol, 0.9 g) followed by TPAP (0.3 mmol, 0.1 g). Reaction mixture was stirred at room temperature for 24 h and *i*-PrOH (5 mL) was added to quench the reaction. Solvent was removed under vacuum. Crude mixture was purified by silica gel column chromatography using 40 to 70 % EtOAc/PE as eluent. Yield of **8** was 0.8 g (56 %).[56]

^{1}H NMR (400MHz, $CDCl_3$):δ= 7.38-7.27 (m, 5H, ArC*H*), 4.56 (q, *J*=11.82 Hz, 2H, O-CH_2-Ar), 4.01-3.94 (m, 2H, CH_3-C*H*-OH, CH-C*H*-CH_2), 3.76 (dd, *J*=3.3 Hz, 1H, CH_2-O-CH_2), 3.74 (dd, J=3.3 Hz, 1H, CH_2-O-CH_2), 3.59-3.53 (m, 1H, O-CH_2-C*H*), 2.91 (s, 2H, OH), 2.27-2.19 (m, 1H, CH-CH-CH_2), 2.09-1.99 (m, 1H, CH-CH-CH_2), 1.91-1.81 (m, 1H, CH-CH_2-CH_2), 1.67-1.59 (m, 1H, CH-CH-CH_2), 1.15 (s, 3H, CH_3-C-CH_2), 1.08 (d, J=6.44 Hz, 3H, CH_3-CH-OH). [Appendix 34]

^{13}C NMR (400MHz, $CDCl_3$):δ = 137.8 (CH_2-*C*-CH_3), 129.2 (*C*HAr), 128.4 (*C*HAr), 127.7 (*C*HAr), 125.5 (*C*HAr), 83.5 (CH-*C*H-CH_2), 75.6 (O-CH_2-*C*H), 73.7 (O-*C*H_2-Ar), 71.0 (*C*H_2-O-CH_2), 68.9 (CH_3-*C*H-OH), 35.4 (CH-CH-*C*H_2), 24.6 (CH-CH-*C*H_2), 23.5 (*C*H_3), 18.4 (*C*H_3). [Appendix 35]

^{1}H-^{13}C HSQC (400MHz, $CDCl_3$). [Appendix 36]

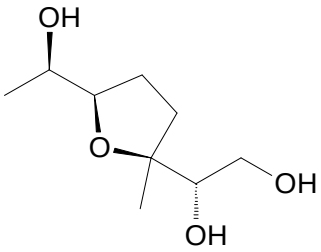
IR: 3402 cm^{-1} (O-H), 2920 cm^{-1} (C-H), 1454 cm^{-1} (C=C), 1373 cm^{-1} (C-H), 1060 cm^{-1} (C-O), 906 cm^{-1} (C-H), 698 cm^{-1} (C-H). [Appendix 37]

HPLC analyses were made after this reaction.

For reference material (**8b**): ratio of isomers was 47.3 : 52.7 [Appendix 38]

For product **8a**: ratio of isomers was 2.1 : 97.9 [Appendix 39]

4.4.10. Synthesis of (1S)-1-{(2S,5R)-5-[(1R)-1-hydroxyethyl]-2-methyltetrahydrofuran-2-yl}ethane-1,2-diol (9)



Compound **8** (750 mg) was dissolved in MeOH (25 mL) and catalyst 10 % Pd-C (250 mg) was added. Reaction was stirred for 48 h at room temp. Catalyst was removed by filtration through celite. Solvent was removed under vacuum. Yield of **9** was 0.4 g (78 %).[57]

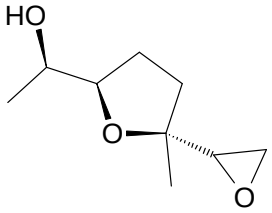
^{1}H NMR (400MHz, $CDCl_3$):δ = 4.06-3.94 (m, 2H, CH_3-C*H*-OH, CH-C*H*-CH_2), 3.79-3.67 (m, 2H, CH-CH_2-OH), 3.57-3.50 (m, 1H, OH-C*H*-C), 2.27-2.16 (m, 1H, CH-CH-CH_2), 2.09-1.98 (m, 1H, CH-CH-CH_2), 1.91-1.79 (m, 1H, CH-CH_2-CH_2), 1.72-1.58 (m, 1H, CH-CH_2-CH_2), 1.18 (s, 3H, CH_3-C-CH_2), 1.08 (d, J=6.49 Hz, 3H, CH_3-CH-OH). [Appendix 40]

^{13}C NMR (400MHz, $CDCl_3$):δ = 85.1 (CH_2-*C*-CH_3), 83.2 (CH_3-*C*H-OH), 76.7 (OH-*C*H-C), 68.1 (CH_3-CH-*C*H), 63.6 (CH-*C*H_2-OH), 35.9 (CH-CH-*C*H_2), 24.3 (CH-CH_2-*C*H_2), 23.6 (*C*H_3), 18.7 (*C*H_3). [Appendix 41]

^{1}H-^{13}C HSQC (400MHz, $CDCl_3$). [Appendix 42]

IR: 3433 cm^{-1} (O-H), 2972 cm^{-1} (C-H), 1450 cm^{-1} (C-H), 1369 cm^{-1} (C-H), 1049 cm^{-1} (C-O), 896 cm^{-1} (C-H). [Appendix 43]

4.4.11. Synthesis of (1R)-1-{(2R)-5-methyl-5-[(2S)-oxiran-2-yl]tetrahydrofuran-2-yl}ethanol (10)



To an ice-cooled solution of **9** (2.1 mmol, 396.7 mg) in toluene (15 mL) p-TsCl (2.2 mmol, 418.0 mg) and Bu_2SnO (0.08 mmol, 20.8 mg) were added followed by dropwise addition of Et_3N (2.7 mmol, 274.7 mg). The reaction mixture was allowed to warm to room temp. and stirring continued for 12 h. Reaction mixture was poured into water and extracted with EtOAc (2 x 20 mL). The combined organic phase was washed with brine, dried with $MgSO_4$, and concentrated under reduced pressure.[58]

Crude intermediate product (2.2 mmol, 772.0 mg) was dissolved in MeOH-CH_2Cl_2 (1 : 1, 40 mL) and K_2CO_3 (3.4 mmol, 465.0 mg) was added. Reaction was stirred for 12 h at room temp. After being filtrated through celite, the reaction mixture was concentrated under reduced pressure. Crude mixture was purified by silica gel column chromatography using 5 to 10 % MeOH/CH_2Cl_2 as eluent. Yield of **10** was 258.7 mg (53 %).

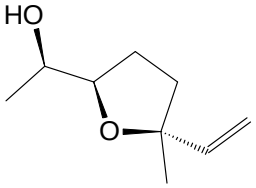
^{1}H NMR (400MHz, $CDCl_3$):δ = 4.00-3.93 (m, 2H, CH_3-C*H*-OH, CH-C*H*-CH_2), 3.70 (s, 1H, OH), 2.99 (dd, *J*=2.87, 4.22 Hz, 1H, O-C*H*-C), 2.87 (dd, *J*=2.95, 5.23Hz, 1H, O-CH_2-CH), 2.71 (dd, J=2.95, 5.27 Hz, 1H, O-CH_2-CH), 2.27-2.15 (m, 1H, CH-CH-CH_2), 2.13-2.04 (m, 1H, CH-CH-CH_2), 1.88-1.78 (m, 2H, CH-CH_2-CH_2), 1.29 (s, 3H, CH_3-C-CH_2), 1.04 (d, J=6.39 Hz, 3H, CH_3-CH-OH). [Appendix 44]

^{13}C NMR (400MHz, $CDCl_3$):δ= 84.3 (CH_3-*C*H-OH), 79.1 (CH_2-*C*-CH_3), 68.5 (CH_3-CH-*C*H), 58.2 (O-*C*H-C), 43.8 (O-*C*H_2-CH), 36.8 (CH-CH-*C*H_2), 24.9 (*C*H_3), 23.8 (CH-CH_2-*C*H_2), 18.4 (*C*H_3). [Appendix 45]

^{1}H-^{13}C HSQC (400MHz, $CDCl_3$). [Appendix 46]

IR: 3433 cm^{-1} (O-H), 2972 cm^{-1} (C-H), 1450 cm^{-1} (C-H), 1369 cm^{-1} (C-H), 1049 cm^{-1} (C-O), 896 cm^{-1} (C-H). [Appendix 47]

4.4.12. Synthesis of (1R)-1-[(2R)-5-ethenyl-5-methyltetrahydrofuran-2-yl]ethanol (11)



Indium powder (3.0 mmol, 345.0 mg) and bis (cyclopentadienyl)titanium (IV) dichloride (6.0 mmol, 1498 mg) were mixed in THF (10 mL) under Ar atmosphere and the resulting mixture was stirred at reflux for 30 min. Resulted mixture was cooled to room temp. and compound **10** (1.5 mmol, 258.7 mg) in THF (1 mL) was added dropwise. Reaction was stirred for 30 min. After filtration through celite the reaction mixture was concentrated under vacuum. Crude mixture was purified by silica gel column chromatography using 10 to 30 % EtOAc/PE as eluent. Yield of **11** was 80 mg (43 %).[59]

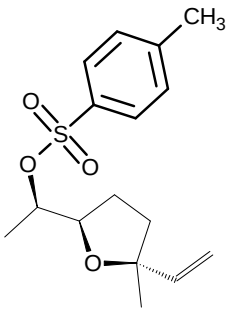
^{1}H NMR (400MHz, $CDCl_3$):δ= 5.96 (q, *J*=10.72Hz, 1H, CH_2=C*H*), 5.21;5.17 (2d, *J*=1.30Hz, 2H, C*H*$_2$=CH), 5.02;5.00 (2d, *J*=1.30Hz, 2H, C*H*$_2$=CH), 3.97-3.90 (m, 2H, CH_3-C*H*-OH, CH-C*H*-CH_2), 2.05 (s, 1H, OH), 1.96-1.75 (m, 4H, CH-C*H*$_2$-C*H*$_2$), 1.31 (s, 3H, C*H*$_3$-C-CH_2), 1.14 (d, J=6.35 Hz, 3H, C*H*$_3$-CH-OH). [Appendix 48]

^{13}C NMR (400MHz, $CDCl_3$):δ= 125.5 (CH_2=*C*H), 111.5 (*C*H_2=CH), 82.9 (CH_3-*C*H-OH), 68.1 (CH-*C*H-CH_2), 37.8 (CH-*C*H_2-CH_2), 25.9 (*C*H_3-C-CH_2), 24.9 (CH-CH_2-*C*H_2), 18.4 (*C*H_3). [Appendix 49]

^{1}H-^{13}C HSQC (400MHz, $CDCl_3$). [Appendix 50]

IR: 3381 cm^{-1} (O-H), 2926 cm^{-1} (C-H), 1458 cm^{-1} (C-C), 1365 cm^{-1} (C-H), 1049 cm^{-1} (C-O), 916 cm^{-1} (C-H). [Appendix 51]

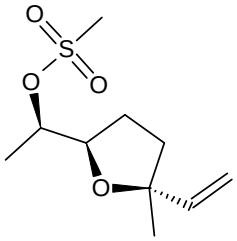
4.4.13. Attempted synthesis of (1R)-1-[(2R)-5-ethenyl-5-methyltetrahydrofuran-2-yl]ethyl-4 - methylbenzenesulfonate



Compound **11** (2.0 mmol, 396.7 mg) was dissolved in toluene (15 mL) and was cooled to 0 ^{o}C using ice-bath. p-TsCl (2.2 mmol, 418.0 mg) was added followed by dropwise addition of Et_3N (2.7 mmol, 275 mg).[58]

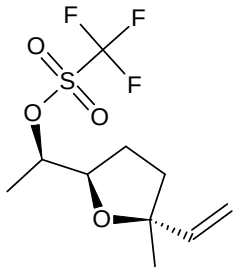
The resulted mixture was stirred for 48 h. No changes were observed neither by TLC nor NMR.

4.4.14. Attempted synthesis of (1R)-1-[(2R)-5-ethenyl-5-methyltetrahydrofuran-2-yl]ethyl methanesulfonate



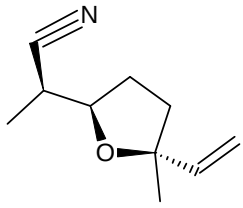
To a stirred solution of compound **11** (0.3 mmol, 4.0 mg) in dry, alcohol free CH_2Cl_2 (0.1 mL) Et_3N (0.5 mmol, 7.3 μL) was added. Reaction mixture was cooled to 0^oC using ice-bath and methanesulfonyl chloride (0.3 mmol, 2.7 μL) was added dropwise[60] Reaction was stirred for 48 h. No changes were observed neither by TLC nor NMR.

4.4.15. Attempted synthesis of (1R)-1-[(2R)-5-ethenyl-5-methyltetrahydrofuran-2-yl]ethyl trifluoromethanesulfonate



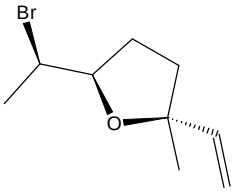
To a stirred solution of compound **11** (0.1 mmol, 20 mg) in CH_2Cl_2 (1 mL) pyridine (0.3 mmol, 0.7 mL) was added. Reaction mixture was cooled to -10^oC and trifluoromethanesulfonic anhydride (0.3 mmol, 1.4 mL) was added dropwise.[61] Reaction mixture was extracted with EtOAc, dried with $MgSO_4$ and concentrated under vacuum. Crude mixture was used as such in next step.

4.4.16. Attempted synthesis of (1R)-1-[(2R)-5-ethenyl-5-methyltetrahydrofuran-2-yl] propanenitrile



18-crown-6 (0.1 mmol, 33.1 mg) and KCN (0.1 mmol, 8.1 mg) were dissolved in THF (0.5 mL) and cooled to -15 ^oC. Compound **12** (0.05 mmol, 16.4 mg) was dissolved in THF (0.2 mL) and was added dropwise to reaction flask.[61] Reaction was stirred for 48 h at room temp. No changes were observed neither by TLC, NMR nor IR.

4.4.17. Synthesis of (5R)-5[(1R)-1-bromoethyl]-2-ethyl-2 methyltetrahydrofuran



Compound **11** (0.2 mmol, 36.4 mg) in DMF (1 mL) was dropwise added to a pre-cooled solution of *N*-bromosuccinimid (0.3 mmol, 54.0 mg) and triphenylphosphine (0.3 mmol, 85.7 mg) in DMF (1 mL). Reaction mixture was allowed to warm to room temp. and stirred for 2 h. Reaction

mixture was poured into water and extracted with EtOAc. The combined organic layers were dried with $MgSO_4$ and concentrated under reduced pressure. Crude mixture was purified by silica gel column chromatography using 1 to 10% EtOAc/PE as eluent. Yield of **11** was 21 mg (42 %).[62]

^{1}H NMR (400MHz, $CDCl_3$):δ= 5.90 (dd, *J*=10.7, 17.11 Hz, 1H, CH_2=C*H*), 5.18; 5.14 (2d, *J*=1.47 Hz, 1 H, CH_2=CH), 4.98; 4.96 (2d, *J*=1.47 Hz, 1 H, CH_2=CH), 4.30-4.15(m, 1H, Br-CH-C*H*), 4.01-4.00 (m, 1H, C*H*-Br), 1.89-1.70 (m, 4 H, CH_2-CH_2), 1.41 (s, 3H, CH_3-C), 1.29 (d, *J*=2.74 Hz, 3 H, CH_3-CH). [Appendix 52]

^{13}C NMR (400MHz, $CDCl_3$):δ= 143.9 (CH_2=*C*H), 111.7 (*C*H_2=CH), 83.5 (*C*H_3-C), 80.5 (CH_3-*C*), 72.2 (*C*H_3-CH-Br), 31.4 (CH-*C*H-CH_2), 29.6 (CH-*C*H_2-CH_2), 27.5 (*C*H-Br), 16.4 (CH-CH_2-*C*H_2). [Appendix 53]

IR: 2924 cm^{-1} (C-H), 1458 cm^{-1} (C=C), 1373 cm^{-1} (C-H), 1180 cm^{-1} (C-O), 921 cm^{-1} (C-H), 543 cm^{-1} (C-Br). [Appendix 54]

5. Summary

Main goal of this master thesis was to work out the synthetic scheme for the stereoselective synthesis of 2,2,5-trisubstituted tetrahydrofurans that leads to lilac compounds: alcohols and corresponding aldehydes. Lilac compounds are widely found in nature bioactive compounds that play important role in plant-insect interactions, especially in pollination chemistry. Lilac compounds have three stereocenters and therefore there are 8 possible enantiomers and 4 possible pairs of diastereomers of alcohols and aldehydes.

There is not found any scheme for the stereoselective total synthesis of the pure enantiomers of lilac compounds in literature. Relatively few syntheses are found for the synthesis of similar structures.

In this thesis is presented a new method for the stereoselective synthesis of lilac compounds. The synthetic pathway starting from geraniol and containing three stereoisomeric purity defining key steps: Sharpless catalytic asymmetric dihydroxylation, Wittig olefination and Ru(VII)-catalyzed stereocontrolled oxidative cyclization, was built up.

The synthesis has been accomplished in a highly stereoselective manner: the enantiomeric purity of the synthesized 2,2,5-trisubstituted tetrahydrofurane was 98%.

In a future it is planned to solve the functional group transformations leading from the synthesized enantiopure substituted tetrahydrofurans to the lilac compounds structures.

The synthesized compounds were characterized by NMR, IR, HPLC and optical rotation analysis.

6. Summary in Estonian

Käesoleva magsitritöö peamiseks eesmärgiks oli välja töötada stereoselektiivne 2,2,5-kolmasendatud tetrahüdrofuraanide sünteesiskeem, mis sobiks sirelalkoholide ja vastavate aldehüüdide saamiseks. Sirelühendid on laialdase loodusliku levikuga bioaktiivsed ained, millel on tähtis roll taimede ja putukate vahelises keemilises suhtlemises, eriti tolmeldajate meelitamisel õitele.

Sirelühenditel on kolm stereotsentrit ning järelikult on võimalikud 8 enantiomeeri ja 4 paari diastereomeere nii alkoholidel kui ka aldehüüdidel.

Kirjanduses ei ole avaldatud ühtegi täielikku sirelühendite puhaste enantiomeeride sünteesiskeemi, vähe on avaldatud sarnaste tetrahüdrofuraanide stereoselektiivse sünteesi kohta üldse.

Käesolevas töös kirjeldatakse uut meetodit sirelühendite stereoselektiivseks sünteesiks. Väljatöötatud sünteesiskeem sisaldab kolm võtmeetappi, mis määravad produkti stereoisomeerse puhtuse: Sharplessi katalüütiline asümmeetriline dihüdroksüleerimine, Wittigi reaktsioon ja Ru(VII)-katalüütiline stereokontrollitud oksüdatiivne tsükliseerimine.

Sünteesiskeem õnnestus realiseerida väga kõrgel stereoselektiivsuse tasemel, saadud 2,2,5-kolmasendatud tetrahüdrofuraani enantiomeerne puhtus oli 98%.

Edaspidi on kavas lahendada lõplikult sünteesitud enantiopuhaste tetrahüdrofuraanide külgahelate muutmine sellisteks nagu need on sirelühendites.

Sünteesitud ühendid on iseloomustatud NMR, IR, HPLC ja optilise rotatsiooni mõõtmise andmete abil.

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Hereby, I would like to express my sincere gratitude to all the persons who have helped during my studies in Estonia.

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Last, but not the least, I would like to thank my family and especially my husband for support, understanding and true motivation during hard time.

And I would like to thank the person who invented the acknowledgment page in master's thesis. It feels so awesome to write whatever I want without knowing that it will be scrutinized.

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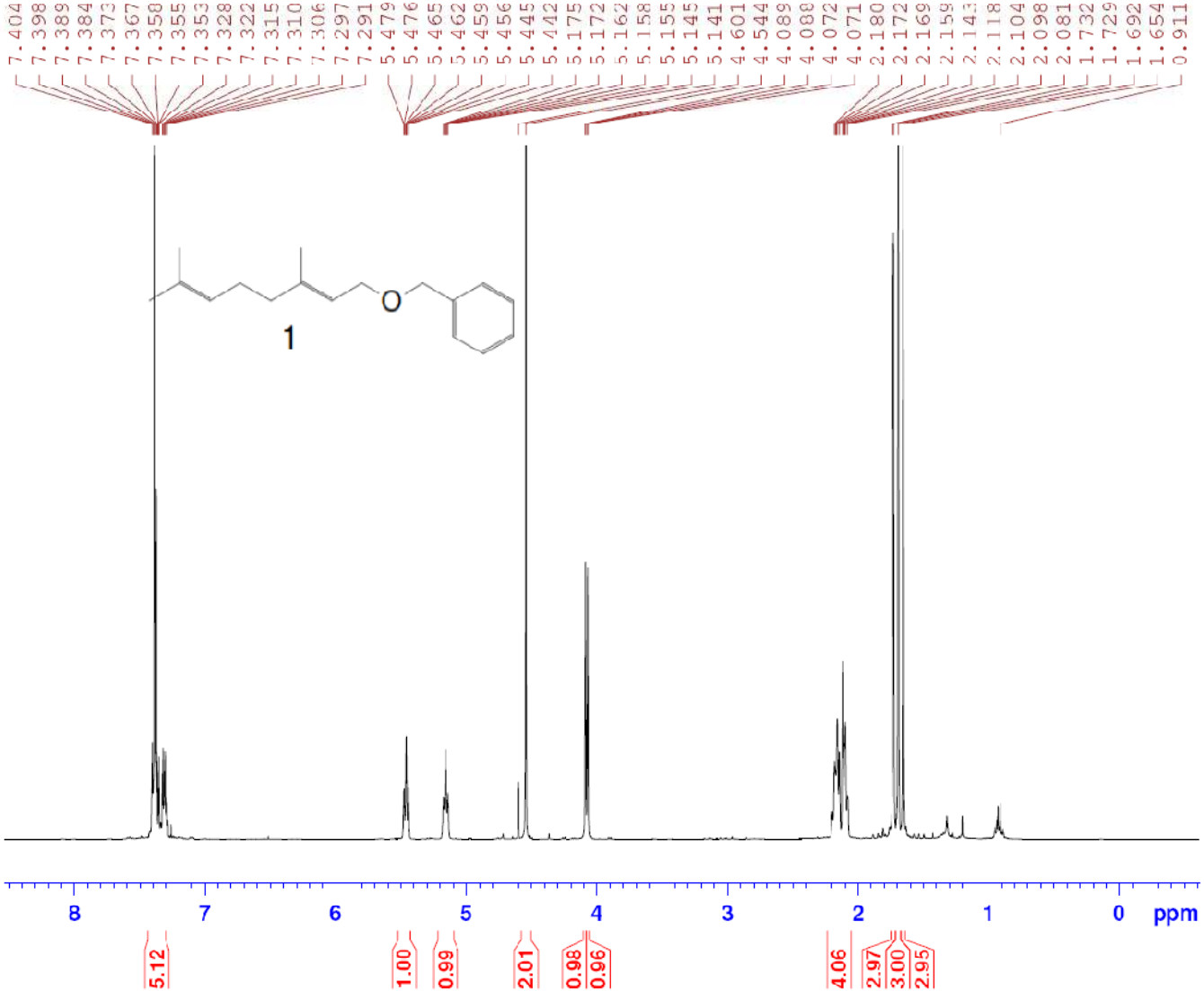
9. Appendices

Appendix 1. Table of used chemicals

Name of compound	Molecular formula	Mol. weight	CAS number	Company	Purity
Geraniol	$C_{10}H_{18}O$	154.25	106-24-1	Alfa Aesar	97.0 %
Sodium hydride	HNa	24.00	7646-69-7	Fluka	55-65 %
Tetrahydrofuran	C_4H_8O	72.11	109-99-9	Fluka	> 99.5 % (GC)
Benzyl bromide	C_7H_7Br	171.03	100-39-0	Aldrich	Reagent grade, 98 %
Magnesium sulfate	$MgSO_4$	120.37	7487-88-9	Lach-Ner	Anhydrous
Ammonia					
Hexane	C_6H_{14}	86.18	110-54-3	Rathburn	HPLC grade, 97.0 %
Ethyl acetate	$C_4H_8O_2$	88.11	141-78-6	Merck	Min 99.8 %
Petroleum ether			8032-32-4	Caldig	Tehnical grade
Dichloromethane	CH_2Cl_2	84.93	75-09-2	Fluka	> 99.5 % (GC)
3-Chloroperoxybenzoic acid	$C_7H_5ClO_3$	172.57	937-14-4	Aldrich	77.0 % max
Potassium carbonate	K_2CO_3	138.20	584-08-7	BioTop	Analytical grade
Potassium hexacyanoferrate (III)	$C_6N_6FeK_3$	329.24	13746-66-2	Alfa Aesar	99+ %
Potassium osmate (VI) dihydrate	$K_2OsO_2(OH)_4$	368.45	10022-66-9	Aldrich	Not indicated
$(DHQD)_2PHAL$	$C_{48}H_{54}N_6O_4$	778.98	140853-	Aldrich	95+ %

			10-7		
tert-Butanol	$C_4H_{10}O$	74.12	75-65-0	Sigma-Aldrich	> 99.3 %
Methanol	CH_4O	32.04	67-56-1	Rathburn	HPLC grade
Cloroform-d	$CDCl_3$	120.38	865-49-6	Aldrich/ Deutero	99.8 % D
Methyl-propynoate	$C_4H_4O_2$	84.07	922-67-8	Aldrich	99.0 %
4-Dimethylaminopyridine	$C_7H_{10}N_2$	122.17	1122-58-3	Fluka	> 98.0 % (NT)
Acetonitrile	C_2H_3N	41.05	75-05-8	Scharlau	Min 99.9 %
Periodic acid	H_5IO_6	227.94	10450-60-9	Sigma-Aldrich	Reagent grade, 98 %
Ethyl(triphenyl)-phosphonium bromide	$C_2H_5P(C_6H_5)_3 \cdot Br$	371.26	1530-32-1	Aldrich	99.0 %
Sodium bis(trimethylsilyl)-amide	$((CH_3)_3Si)_2NNa$	183.37	1070-89-9	Aldrich	Not indicated
Pyrrolidine	C_4H_9N	71.12	123-75-1	Fluka	≥ 99.0 %
Buthyllithium	$CH_3(CH_2)_3Li$	64.06	109-72-8	Aldrich	
4-methylmorpholine-N-oxide	$C_5H_{11}NO_2$	117.15	7529-22-8	Fluka	≥ 95.0 %
Tetrapropylammonium perruthenate	$(CH_3CH_2CH_2)_4NRuO_4$	351.43	114615-82-6	Fluka	Purum
Methanesulfonamide	$CH_3SO_2NH_2$	95.12	3144-09-0	Aldrich	≥ 97.0 %
Palladium, 10wt% on active carbon	10 % Pd-C		7440-05-3	Aldrich	Not indicated
p-Toluenesulfonyl chloride	$C_7H_7ClO_2S$	190.65	98-59-9	Fluka	≥ 99.0 %
Di-n-butyltin oxide	$C_8H_{18}OSn$	248.94	818-08-6	AlfaAesar	98 %
Triethylamine	$C_6H_{15}N$	101.19	121-44-8	Sigma-Aldrich	≥ 99.0 %
Toluene	C_7H_8	92.14	108-88-3	Lach-ner	G.R

Indium powder	In	114.82	7440-74-6	Aldrich	99.99 %
Bis(cyclopentadienyl)-titanium(IV) dichloride	$C_{10}H_{10}Cl_2Ti$	248.96	1271-19-8	Aldrich	97.0 %
Trifluoromethanesulfonic anhydride	$C_2F_6O_5S_2$	282.14	358-23-6	Alfa Aesar	98 %
Pyridine					
18-crown- 6	$C_{12}H_{24}O_6$	264.32	17455-13-9	Fluka	≥ 99.0 %
Potassium cyanide	KCN	65.12	151-50-8	Fluka	≥ 97.0 %
Methanesulfonyl chloride	CH_3SO_2Cl	114.55	124-63-0	Sigma-Aldrich	≥ 99.7 %
Triphenylphosphine	$(C_6H_5)_3P$	262.29	603-35-0	Sigma-Aldrich	≥ 98.5 %
N-Bromosuccinimide	$C_4H_4BrNO_2$	177.98	128-08-5	Aldrich	99 %
N,*N*-Dimethylformamide	$HCON(CH_3)_2$	73.09	68-12-2	Fluka	99.8 %



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INSTITUTE OF TECHNOLOGY

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EXPNO                     4
PROCNO                    1

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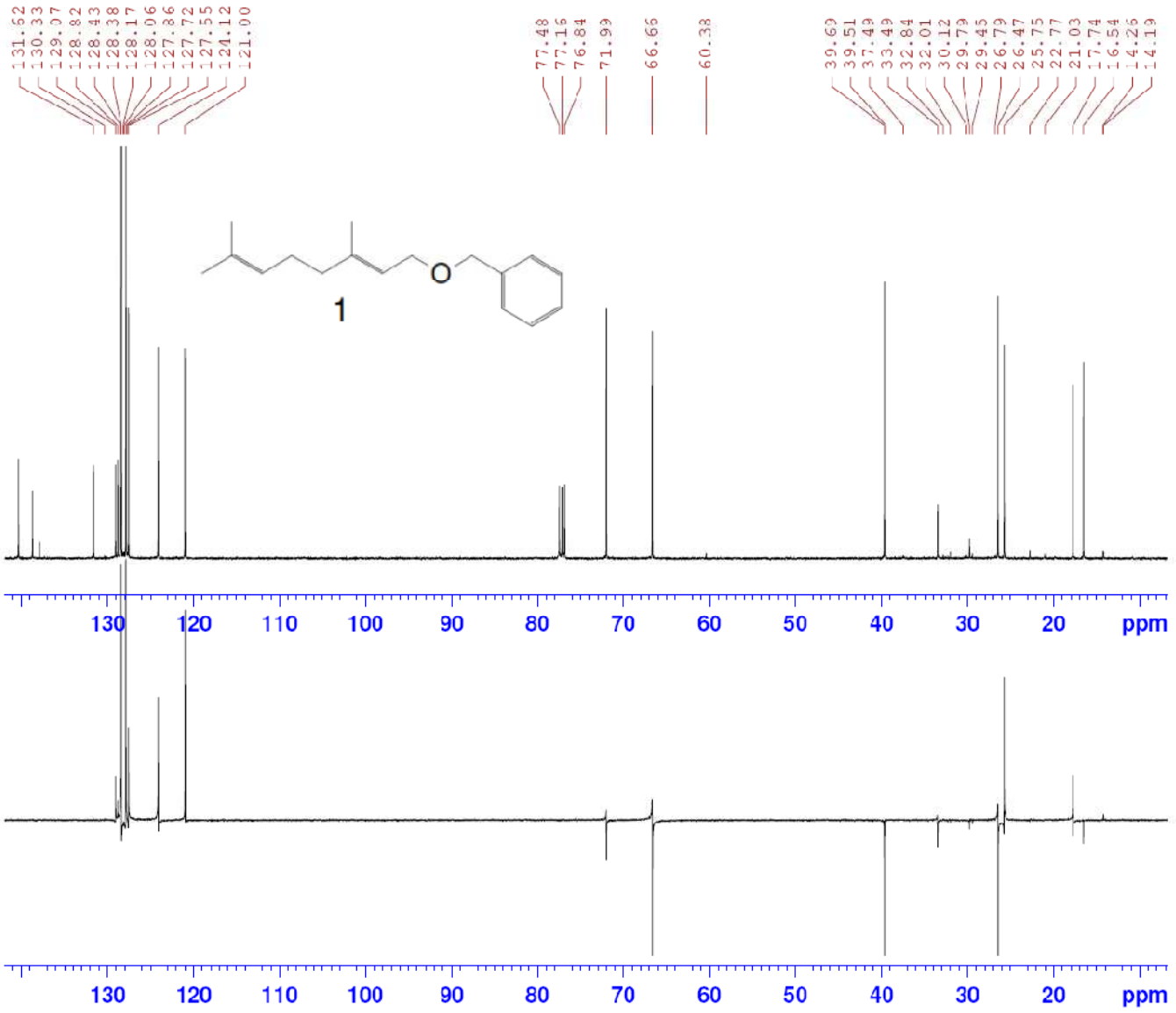
Time                 18.18
INSTRUM              spect
PROBHD    5 mm EBO BB-1H
PULPROG              zg30
TD                  32768
SOLVENT             CDCl3
NS                     32
DS                      0
SWH              6393.862 Hz
FIDRES           0.195125 Hz
AQ               2.5625076 sec
RG                   14.2
DW                 78.200 usec
DE                  6.00 usec
TE                298.2 K
D1             5.00000000 sec
TD0                     1

--------- CHANNEL f1 ---------
NUC1                   1H
P1                  14.35 usec
PL1                  0.00 dB
SFO1         400.1324710 MHz

F2 - Processing parameters
SI                  65536
SF           400.1300173 MHz
WDW                    EM
SSB                     0
LB                   0.30 Hz
GB                      0
PC                   1.00
```

Appendix2



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PROCNO	1	
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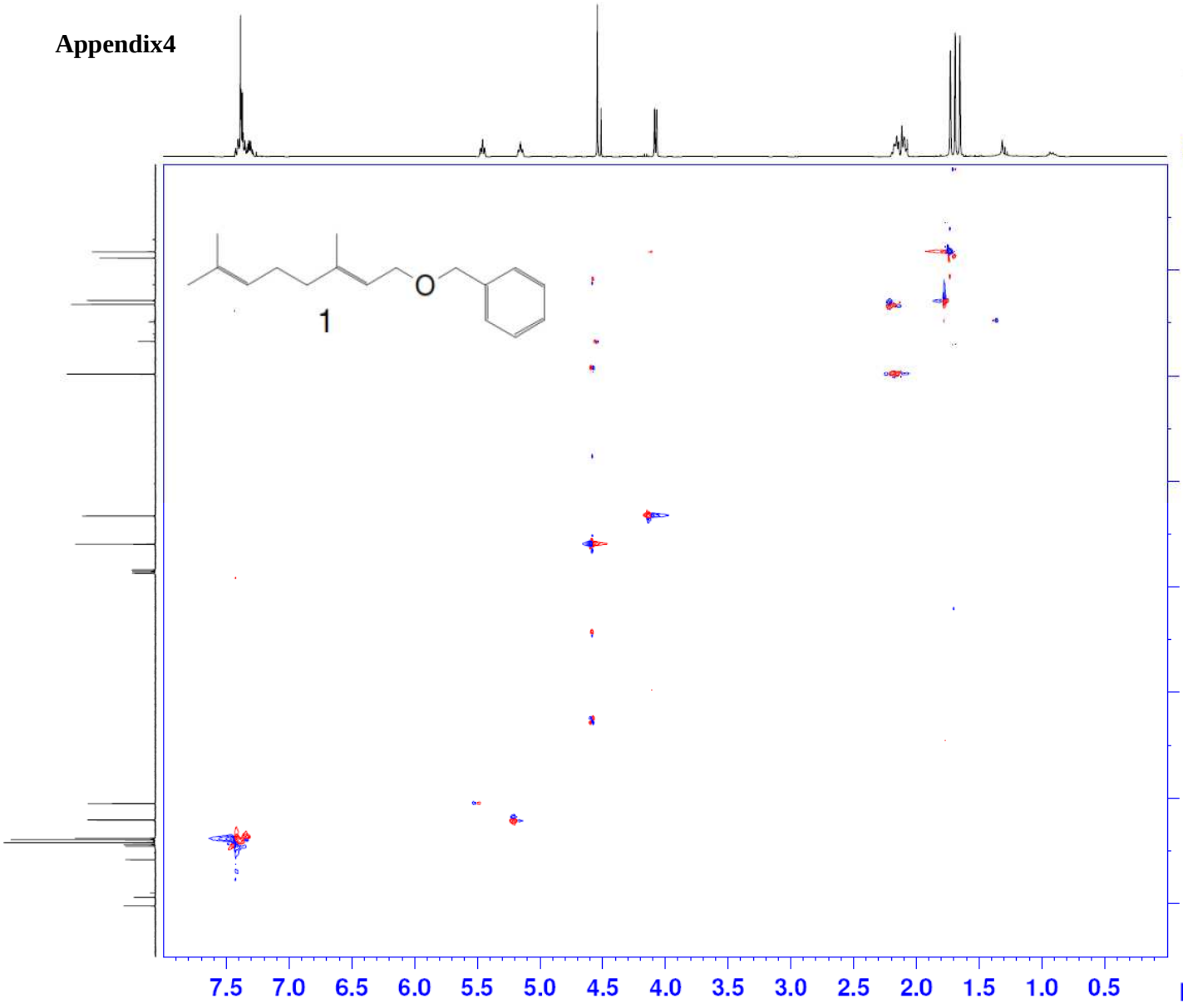
Time	18.07	
INSTRUM	spect	
PROBHD	5 mm BBO BB-1H	
PULPROG	dept135	
TD	65536	
SOLVENT	CDCl3	
NS	512	
DS	4	
SWH	24038.461	Hz
FIDRES	0.366798	Hz
AQ	1.3631989	sec
RG	32800	
DW	20.800	usec
DE	6.00	usec
TE	298.3	K
CNST2	145.0000000	
D1	2.00000000	sec
d12	0.00002000	sec
d2	0.00344828	sec
DELTA	0.00001210	sec
TD0	1	
======== CHANNEL f1 ========		
NUC1	13C	
P1	9.50	usec
p2	19.00	usec
PL1	-2.00	dB
SFO1	100.6228298	MHz
-------- CHANNEL f2 --------		
CPDPRG2	waltz16	
NUC2	1H	
P3	14.35	usec
p4	28.70	usec
PCPD2	70.00	usec
PL12	13.76	dB
PL2	0.00	dB
SFO2	400.1316005	MHz
F2 - Processing parameters		
SI	32768	
SF	100.6127690	MHz
WDW	EM	
SSB	0	
LB	1.00	Hz
GB	0	
PC	1.40	

Appendix3

Appendix4



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```
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NAME                  AA024
EXPNO                    15
PROCNO                    1

F2 - Acquisition Parameters
Date_              20120530
Time                  18.30
INSTRUM                spect
PROBHD   5 mm BBO BB-1H
PULPROG         hsqcedetgp
TD                      4096
SOLVENT                 CDCl3
NS                         2
DS                        16
SWH                3201.024 Hz
FIDRES             0.781500 Hz
AQ                 0.6398452 sec
RG                     18400
DW                   156.200 usec
DE                     6.00 usec
TE                   298.4 K
CNST2            145.0000000
d0                 0.00000300 sec
D1                 1.50000000 sec
d11                0.03000000 sec
d13                0.00000400 sec
D16                0.00020000 sec
D21                0.00345000 sec
d4                 0.00172414 sec
DELTA              0.00221530 sec
DELTA1             0.00071614 sec
IN0                0.00003315 sec
STICNT                   128
ZGOPTNS

-------- CHANNEL f1 --------
NUC1                      1H
P1                     14.35 usec
p2                     28.70 usec
P28                  2000.00 usec
PL1                    0.00 dB
SFO1          400.1316005 MHz

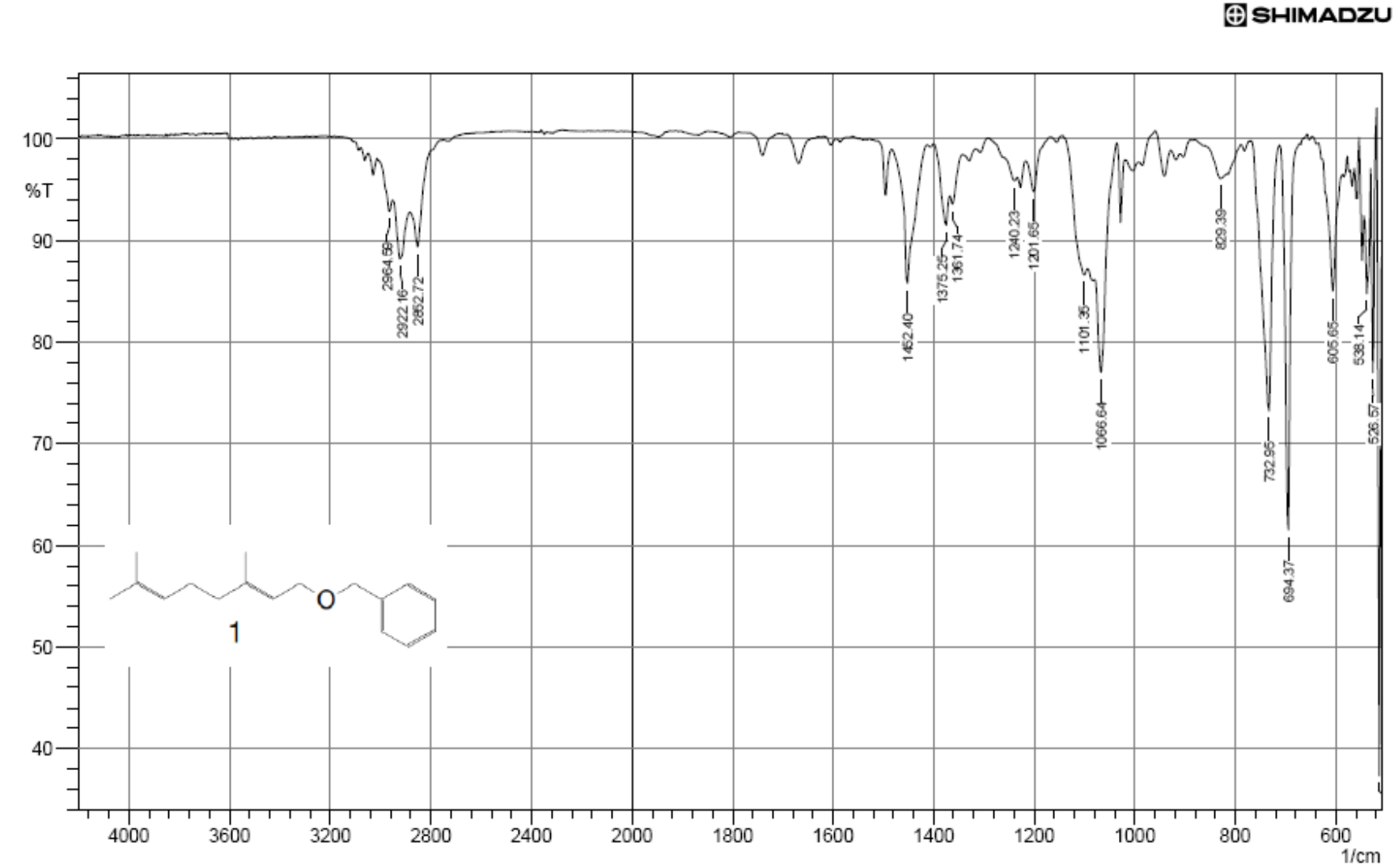
-------- CHANNEL f2 --------
CPDPRG2                 garp
NUC2                     13C
P3                     9.50 usec
p4                    19.00 usec
PCPD2                 60.00 usec
PL12                  13.00 dB
PL2                   -2.00 dB
SFO2          100.6203150 MHz

------ GRADIENT CHANNEL -----
GPNAM1             SINE.100
GPNAM2             SINE.100
GPZ1                  80.00 %
GPZ2                  20.10 %
P16                 1000.00 usec

F1 - Acquisition parameters
ND0                        2
TD                       256
SFO1            100.6203 MHz
FIDRES           58.917797 Hz
SW                149.900 ppm
FnMODE     Echo-Antiecho

F2 - Processing parameters
SI                      1024
SF            400.1300000 MHz
WDW                    QSINE
SSB                        2
LB                      0.00 Hz
GB                         0
PC                      1.40

F1 - Processing parameters
SI                      1024
MC2         echo-antiecho
SF            100.6127690 MHz
WDW                    QSINE
SSB                        2
LB                      0.00 Hz
GB                         0
```



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Appendix5

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Apodization;

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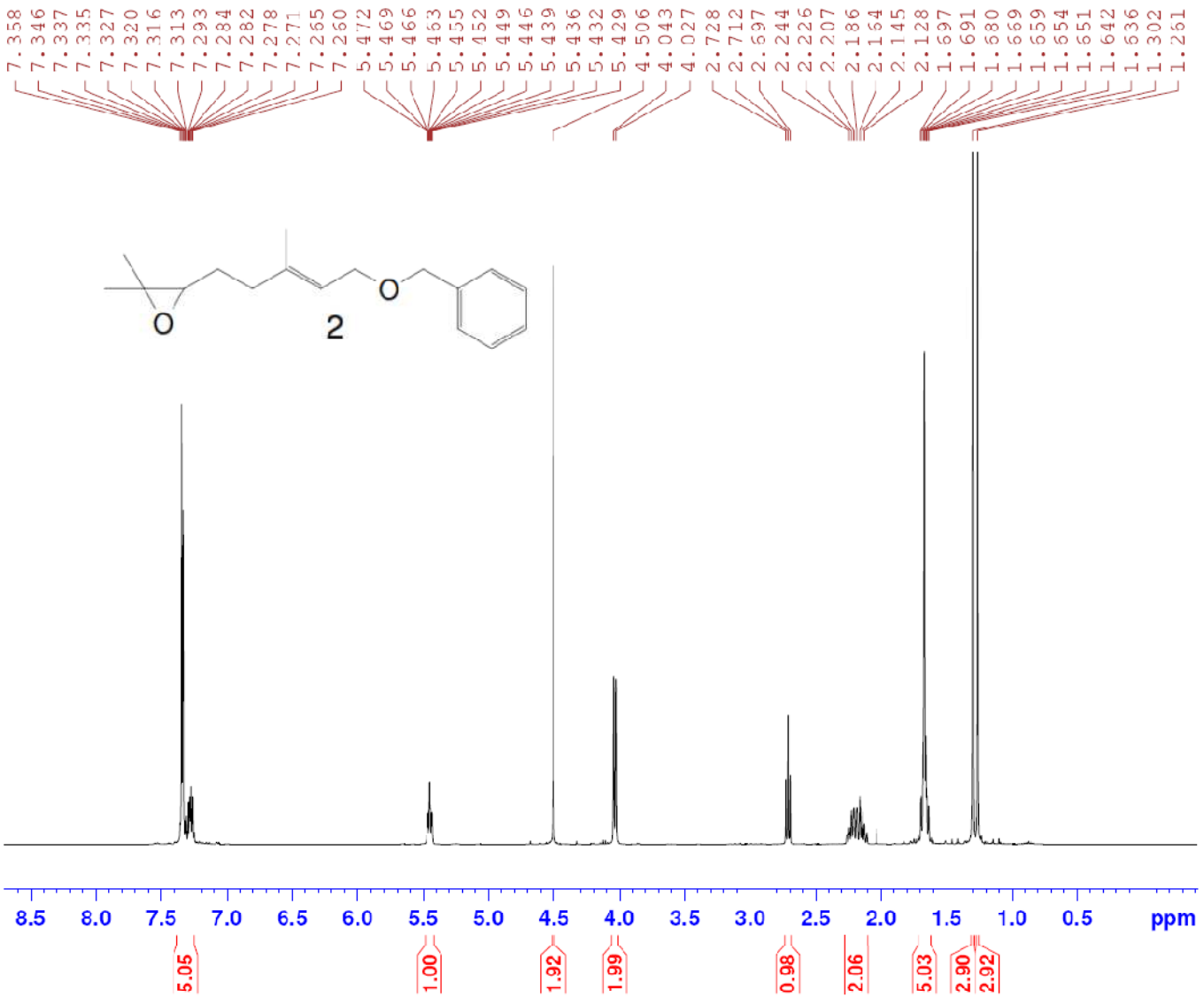

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Current Data Parameters
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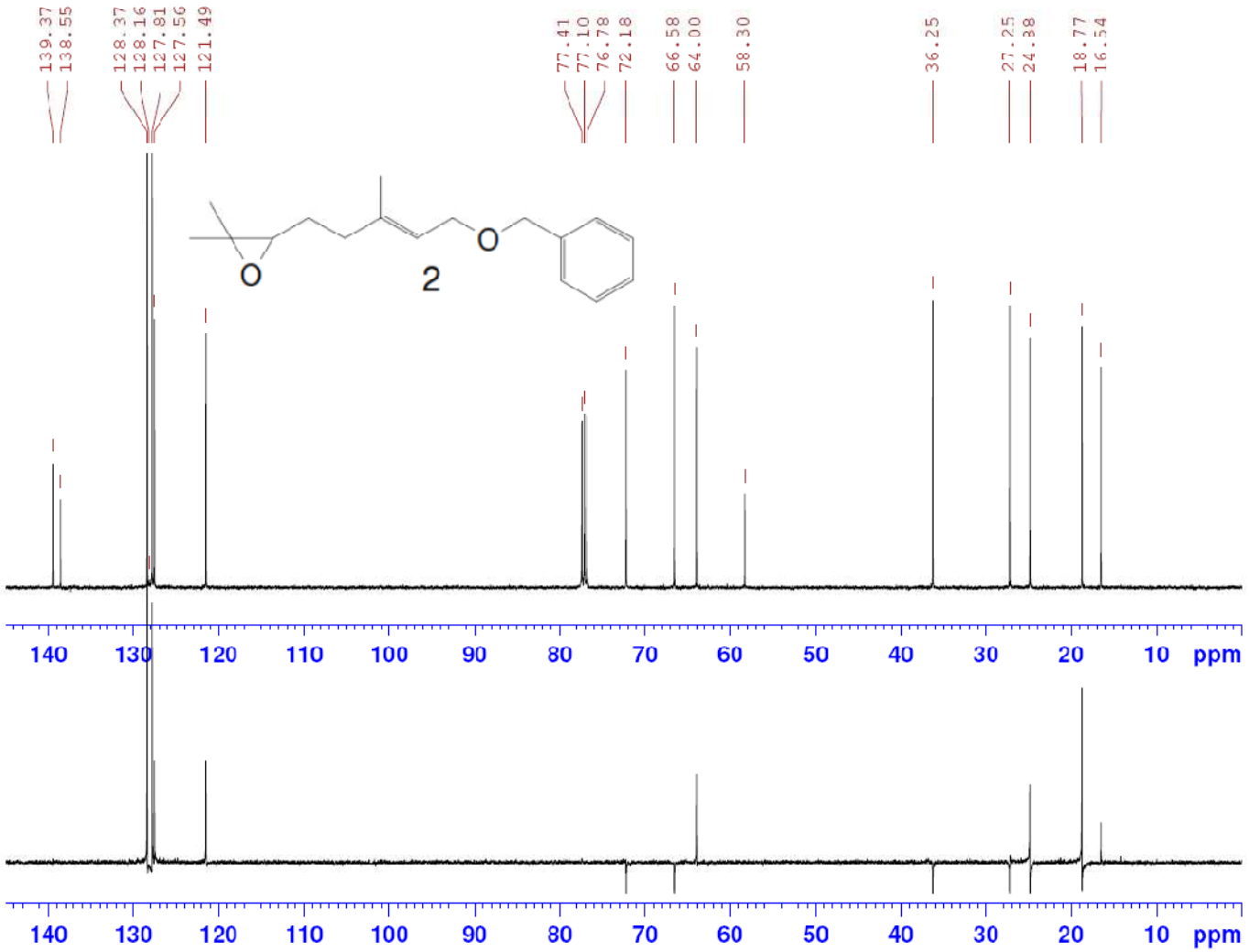
EXPNO                    11
PROCNO                    1

F2 - Acquisition Parameters
Date                20120314
Time                   12.00
INSTRUM                spect
PROBHD    5 mm BBO BB-1H
PULPROG                zg30
TD                    32768
SOLVENT               CDCl3
NS                       64
DS                        0
SWH                6393.862 Hz
FIDRES             0.195125 Hz
AQ                 2.5625076 sec
RG                      45.2
DW                   78.200 usec
DE                    6.00 usec
TE                   298.2 K
D1                5.00000000 sec
TD0                       1

======== CHANNEL f1 ========
NUC1                      1H
P1                    14.35 usec
PL1                    0.00 dB
SF01          400.1324710 MHz

F2 - Processing parameters
SI                        65536
SF          400.1300177 MHz
WDW                      EM
SSB                       0
LB                     0.30 Hz
GB                        0
PC                     1.00
```

Appendix6



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INSTITUTE OF TECHNOLOGY

```
Current Data Parameters
NAME                  AA025
EXPNO                    12
PROCNO                    1

F2 - Acquisition Parameters
Date_              20120314
Time                  12.11
INSTRUM               spect
PROBHD    5 mm BBO BB-1H
PULPROG            zgpg30
TD                  65536
SOLVENT             CDCl3
NS                    481
DS                      4
SWH           24038.461 Hz
FIDRES         0.366798 Hz
AQ             1.3631988 sec
RG                  32800
DW                 20.800 usec
DE                  6.00 usec
TE                298.2 K
D1             2.00000000 sec
d11            0.03000000 sec
DELTA          1.89999998 sec
TD0                     1

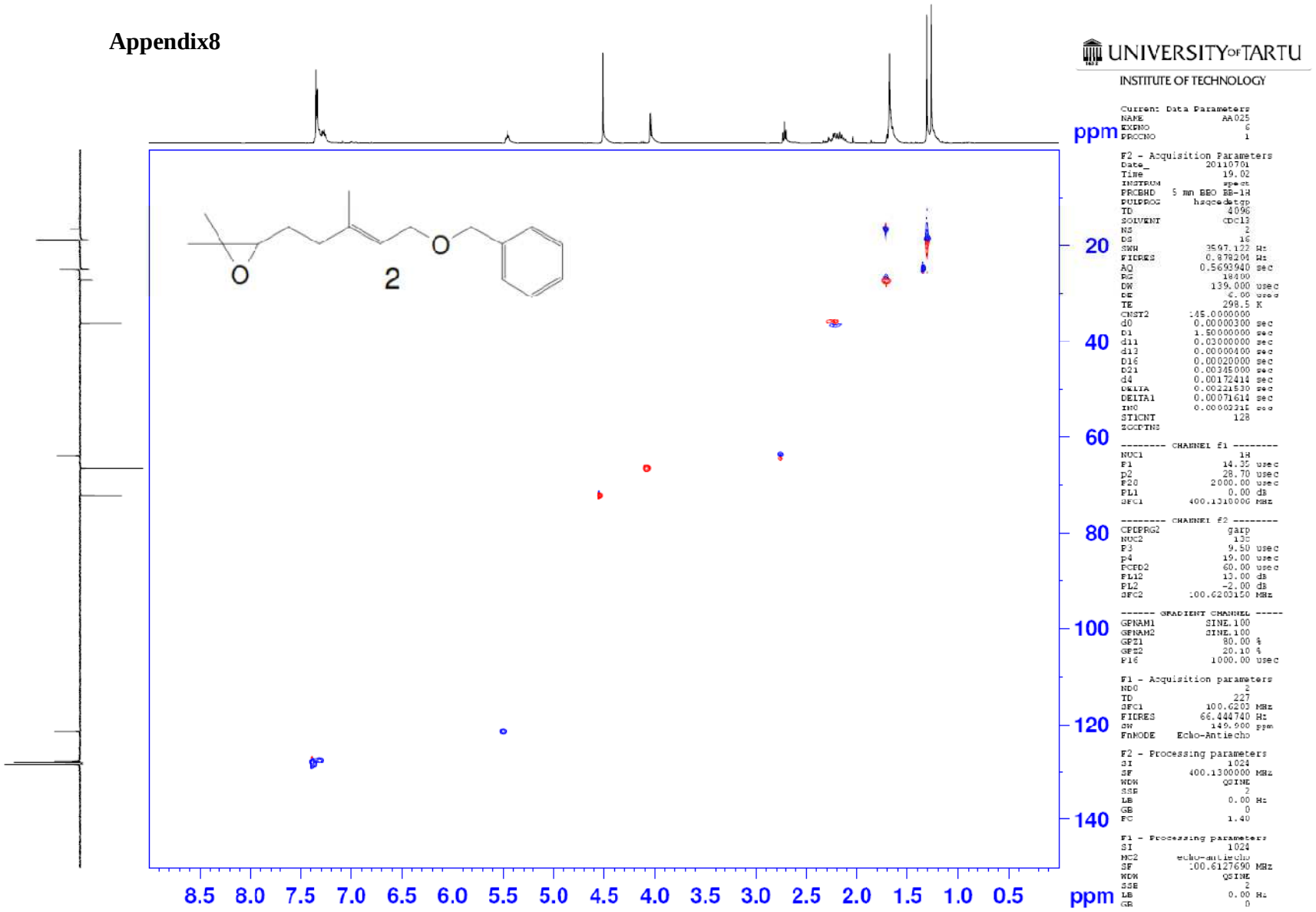
======== CHANNEL f1 ========
NUC1                  13C
P1                  9.50 usec
PL1                -2.00 dB
SFO1         100.6228298 MHz

-------- CHANNEL f2 --------
CPDPRG2           waltz16
NUC2                  1H
PCPD2              70.00 usec
PL12               13.76 dB
PL13               14.00 dB
PL2                 0.00 dB
SFO2         400.1316005 MHz

F2 - Processing parameters
SI                  32768
SF           100.6127690 MHz
WDW                    EM
SSB                     0
LB                  1.00 Hz
GB                      0
PC                   1.40
```

Appendix7

Appendix8



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```
Current Data Parameters
NAME                  AA025
EXPNO                     6
PROCNO                    1

F2 - Acquisition Parameters
Date_              20110701
Time                  19.02
INSTRUM                spect
PROBHD     5 mm BBO BB-1H
PULPROG       hsqcedetgp
TD                     4096
SOLVENT               CDCl3
NS                        2
DS                       16
SWH                3597.122 Hz
FIDRES             0.878204 Hz
AQ                 0.5693940 sec
RG                     18400
DW                   139.000 usec
DE                     6.00 usec
TE                   298.5 K
CNST2              145.0000000
d0                 0.00000300 sec
D1                 1.50000000 sec
d11                0.03000000 sec
d12                0.00000400 sec
D16                0.00020000 sec
D21                0.00345000 sec
d4                 0.00172414 sec
DELTA              0.00221630 sec
DELTA1             0.00071614 sec
IN0                0.00003215 sec
ST1CNT                   128
ZGOPTNS

-------- CHANNEL f1 --------
NUC1                      1H
P1                     14.30 usec
p2                     28.70 usec
P20                  2000.00 usec
PL1                     0.00 dB
SFO1           400.1310006 MHz

-------- CHANNEL f2 --------
CPDPRG2                garp
NUC2                      13C
P3                      9.50 usec
p4                     19.00 usec
PCPD2                  60.00 usec
PL12                   13.00 dB
PL2                    -2.00 dB
SFO2           100.6203150 MHz

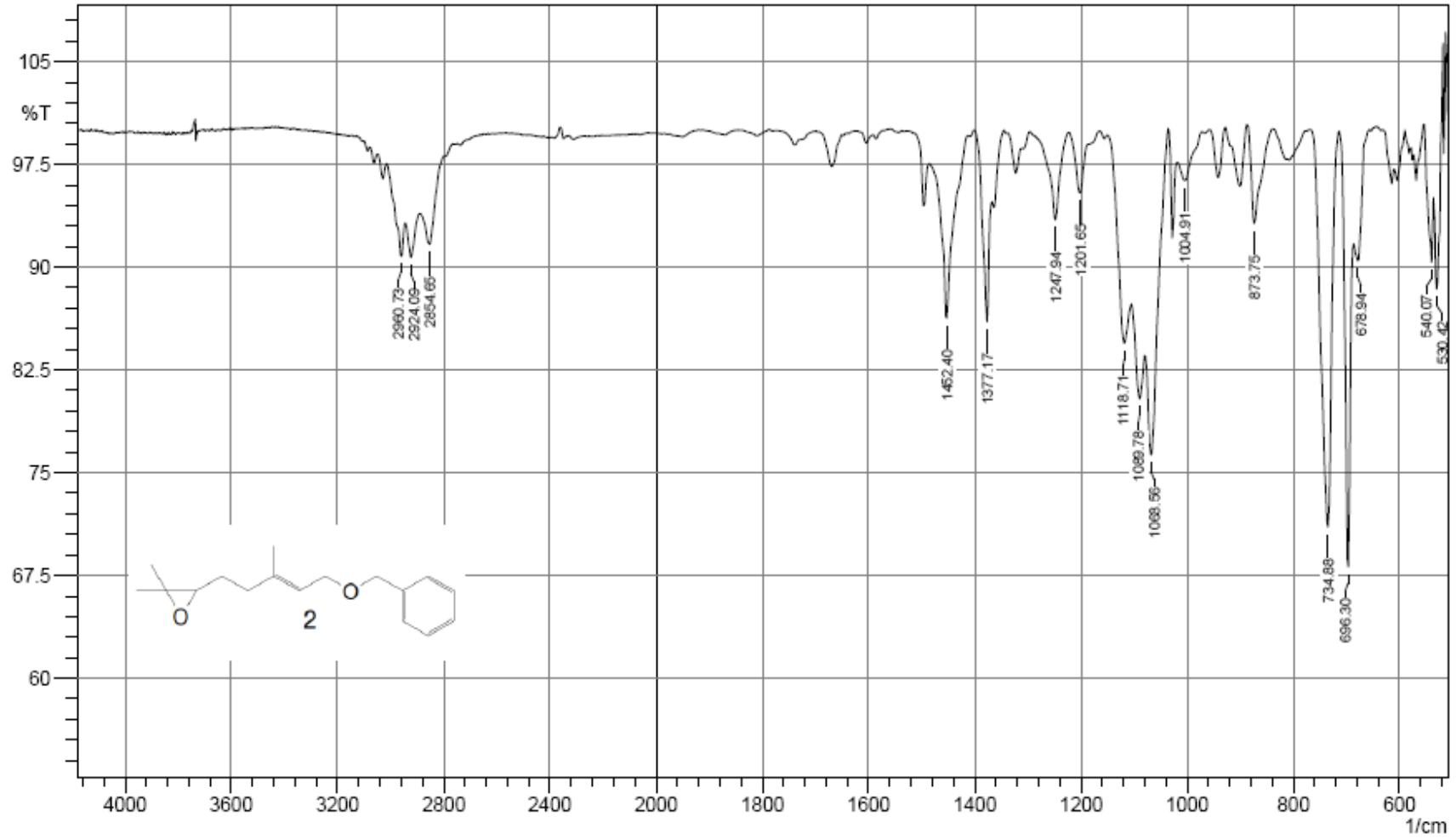
------ GRADIENT CHANNEL -----
GPNAM1              SINE.100
GPNAM2              SINE.100
GPZ1                   80.00 %
GPZ2                   20.10 %
P16                  1000.00 usec

F1 - Acquisition parameters
ND0                       2
TD                      227
SFO1           100.6203 MHz
FIDRES          66.444740 Hz
SW                149.900 ppm
FnMODE     Echo-Antiecho

F2 - Processing parameters
SI                     1024
SF             400.1300000 MHz
WDW                   QSINE
SSB                       2
LB                     0.00 Hz
GB                        0
PC                     1.40

F1 - Processing parameters
SI                     1024
MC2          echo-antiecho
SF             100.6127690 MHz
WDW                   QSINE
SSB                       2
LB                     0.00 Hz
GB                        0
```

SHIMADZU



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Appendix9

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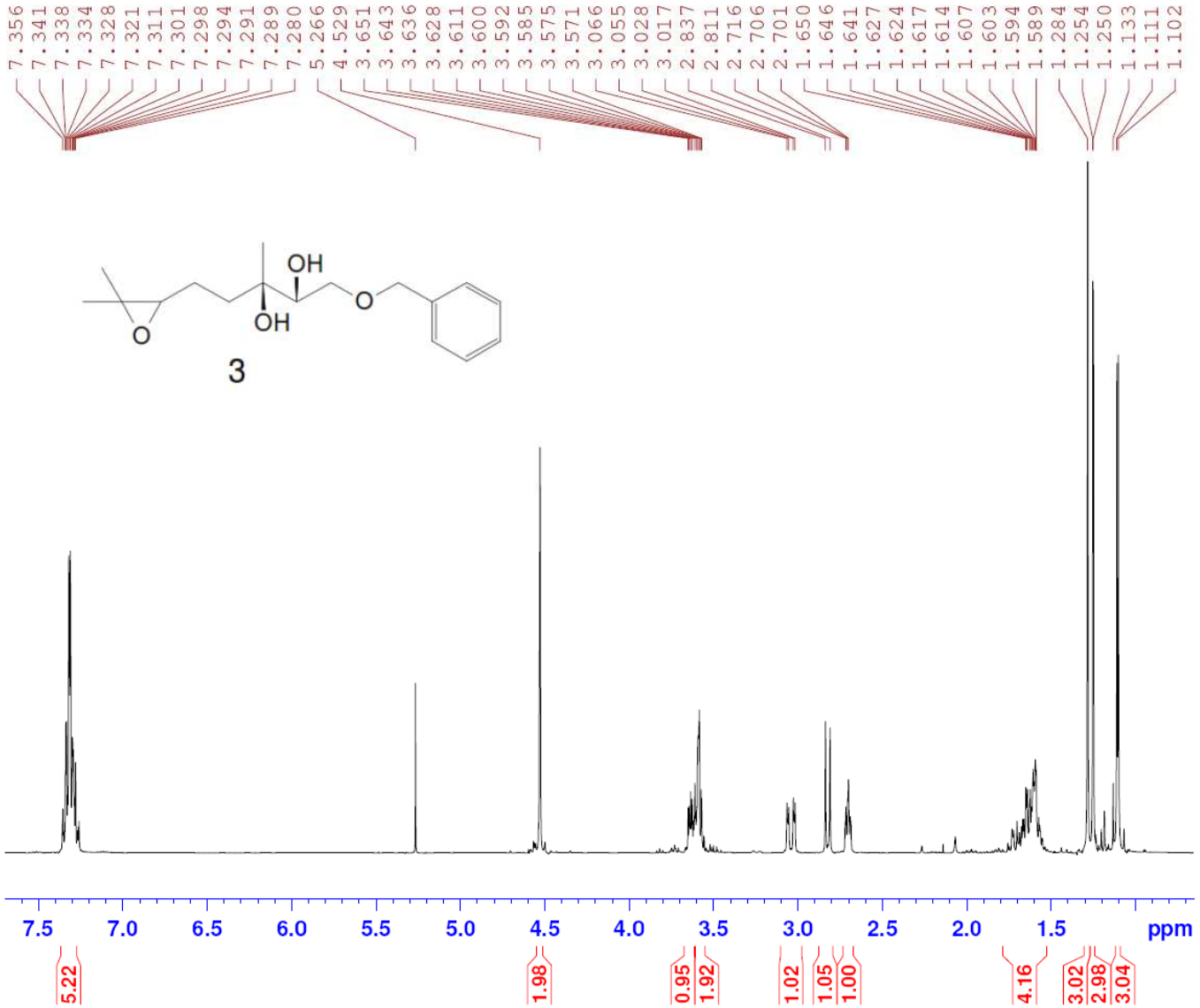

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INSTITUTE OF TECHNOLOGY

```
Current Data Parameters
NAME                  AA026
EXPNO                    16
PROCNO                    1

F2 - Acquisition Parameters
Date_              20110812
Time                  17.39
INSTRUM               spect
PROBHD    5 mm BBO BB-1H
PULPROG               zg30
TD                   32768
SOLVENT              CDCl3
NS                      32
DS                       0
SWH                6393.862 Hz
FIDRES            0.195125 Hz
AQ                2.5625076 sec
RG                     28.5
DW                   78.200 usec
DE                    6.00 usec
TE                   298.2 K
D1              5.00000000 sec
TD0                      1

======== CHANNEL f1 ========
NUC1                    1H
P1                   14.35 usec
PL1                   0.00 dB
SFO1          400.1324710 MHz

F2 - Processing parameters
SI                    65536
SF            400.1300174 MHz
WDW                      EM
SSB                      0
LB                    0.30 Hz
GB                       0
PC                    1.00
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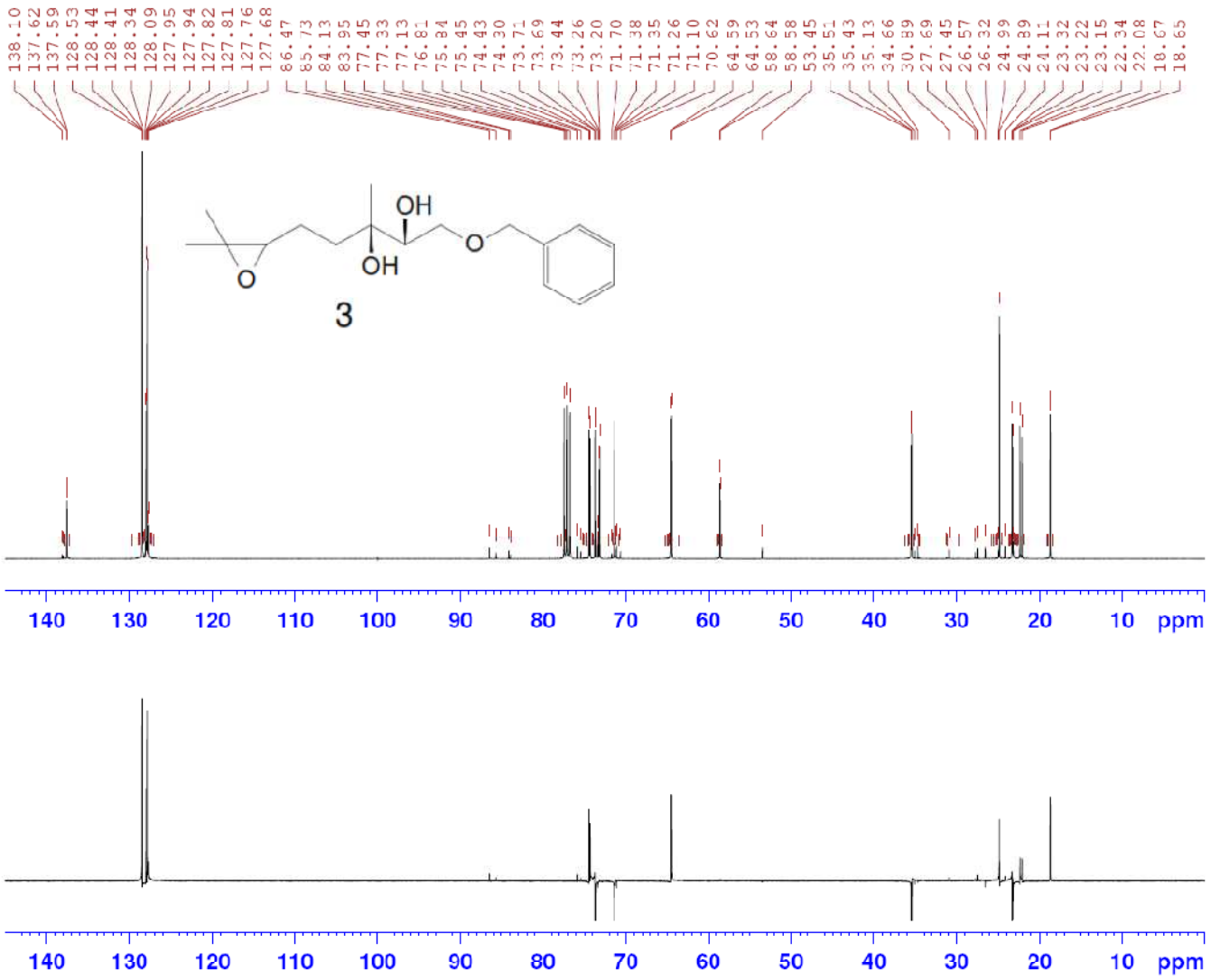
Appendix10



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```
Current Data Parameters
NAME                  AA026
EXPNO                    17
PROCNO                    1

F2 - Acquisition Parameters
Date_              20110814
Time                  16.35
INSTRUM               spect
PROBHD   5 mm BBO BB-1H
PULPROG           zgpg30
TD                 65536
SOLVENT            CDCl3
NS                 49152
DS                     4
SWH           24038.461 Hz
FIDRES         0.366798 Hz
AQ             1.3631988 sec
RG                 32800
DW                20.800 usec
DE                 6.00 usec
TE                298.1 K
D1            2.00000000 sec
d11           0.03000000 sec
DELTA         1.89999998 sec
TD0                    1

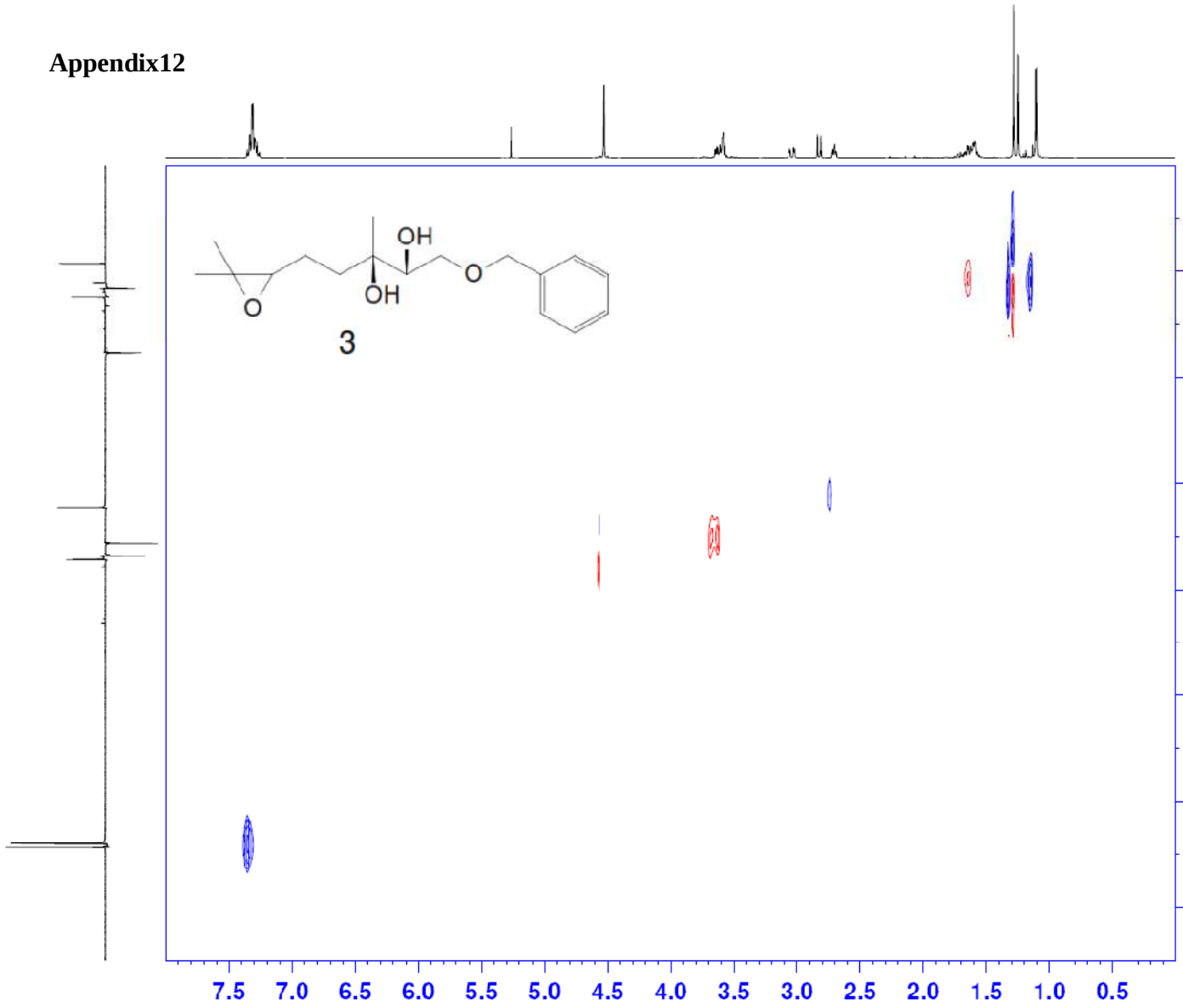
======== CHANNEL f1 ========
NUC1                  13C
P1                 9.50 usec
PL1               -2.00 dB
SFO1        100.6228298 MHz

======== CHANNEL f2 ========
CPDPRG2         waltz16
NUC2                  1H
PCPD2             70.00 usec
PL12              13.76 dB
PL13              14.00 dB
PL2                0.00 dB
SFO2        400.1316005 MHz

F2 - Processing parameters
SI                 32768
SF          100.6127690 MHz
WDW                   EM
SSB                    0
LB                 1.00 Hz
GB                     0
PC                  1.40
```

Appendix11

Appendix12



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```
Current Data Parameters
NAME                  AA026
EXPNO                     9
PROCNO                    1

F2 - Acquisition Parameters
Date_              20110815
Time                  13.58
INSTRUM                spect
PROBHD     5 mm BBO BB-1H
PULPROG       lsqueded1gp
TD                     4096
SOLVENT               CDCl3
NS                        2
DS                        6
SWH               3201.024 Hz
FIDRES            0.781500 Hz
AQ                0.6398452 sec
RG                    10400
DW                  156.280 usec
DE                    6.00 usec
TE                  298.5 K
CNST2          145.0000000
d0                0.00000300 sec
d1                1.50000000 sec
d11               0.03000000 sec
d13               0.00000400 sec
D16               0.00020000 sec
D21               0.00345000 sec
d4                0.001724.4 sec
DELTA             0.00221630 sec
DELTA1            0.000716.4 sec
IN0               0.000033.5 sec
ST1CNT                  128
ZGOPTNS

-------- CHANNEL f1 --------
NUC1                      1H
P1                     14.35 usec
P2                     28.70 usec
PL0                 2000.00 usec
PL1                    0.00 dB
SFO1           400.1316005 MHz

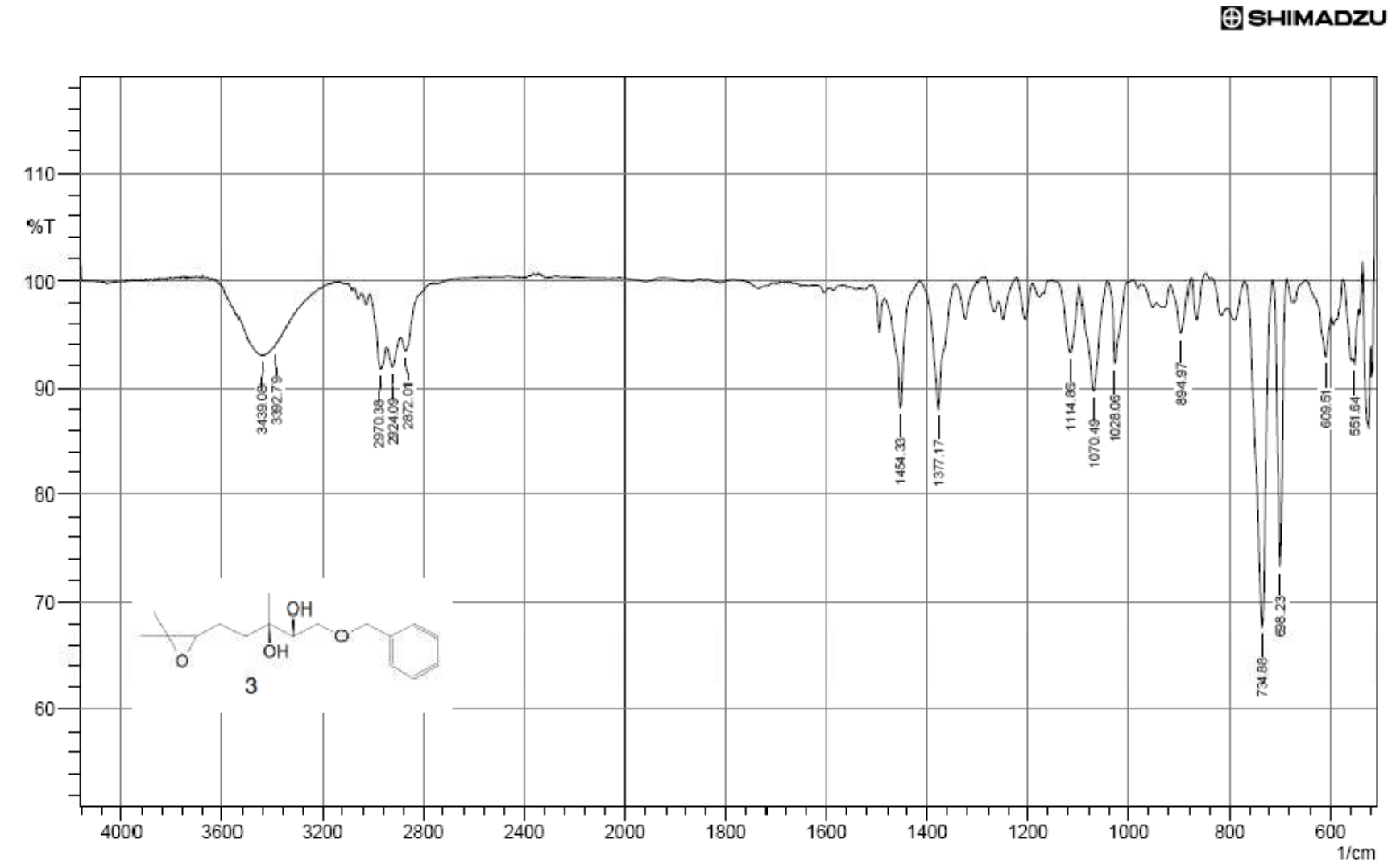
-------- CHANNEL f2 --------
CPDPRG2                garp
NUC2                    13C
P3                     9.50 usec
P4                    19.00 usec
PCPD2                 60.00 usec
PL12                  13.00 dB
PL2                   -2.00 dB
SFO2           100.6203150 MHz

------ GRADIENT CHANNEL -----
GPNAM1             SINE.100
GPNAM2             SINE.100
GPZ1                  80.00 %
GPZ2                  20.00 %
P16                 1000.00 usec

F1 - Acquisition parameters
NN0                       2
TD                      256
SFO1           100.6283 MHz
FIDRES          58.917797 Hz
SW                149.980 ppm
FnMODE     Echo-Antiecho

F2 - Processing parameters
SI                      1024
SF             400.1300000 MHz
WDW                   QSINE
SSB                       2
LB                    0.00 Hz
GB                        0
PC                    1.40

F1 - Processing parameters
SI                      1024
MC2          echo-antiecho
SF             100.6127690 MHz
WDW                   QSINE
SSB                       2
LB                    0.00 Hz
GB                        0
```



Comment;

Appendix13

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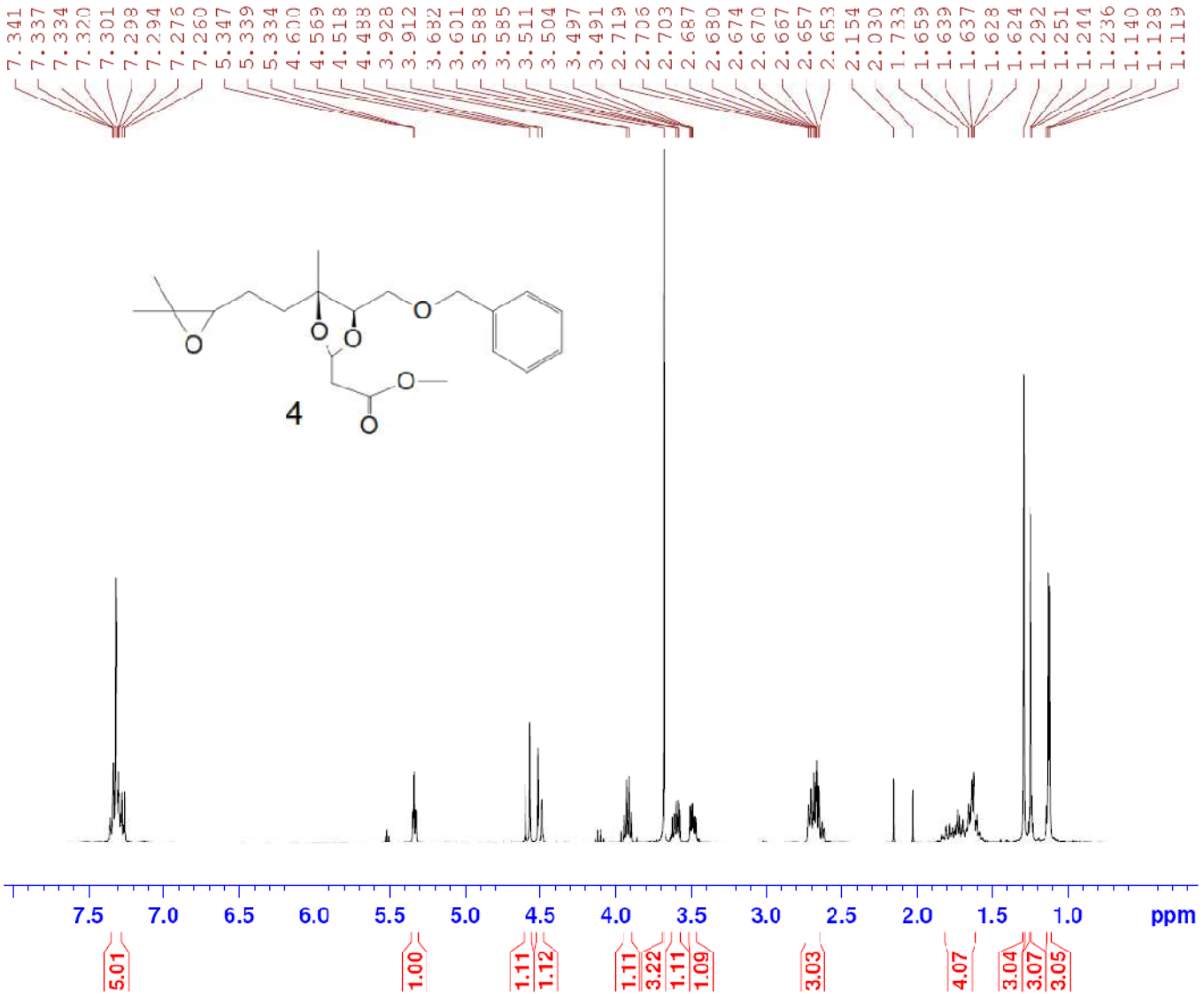
Date/Time; 3/13/2012 4:47:12 PM
User; Agilent



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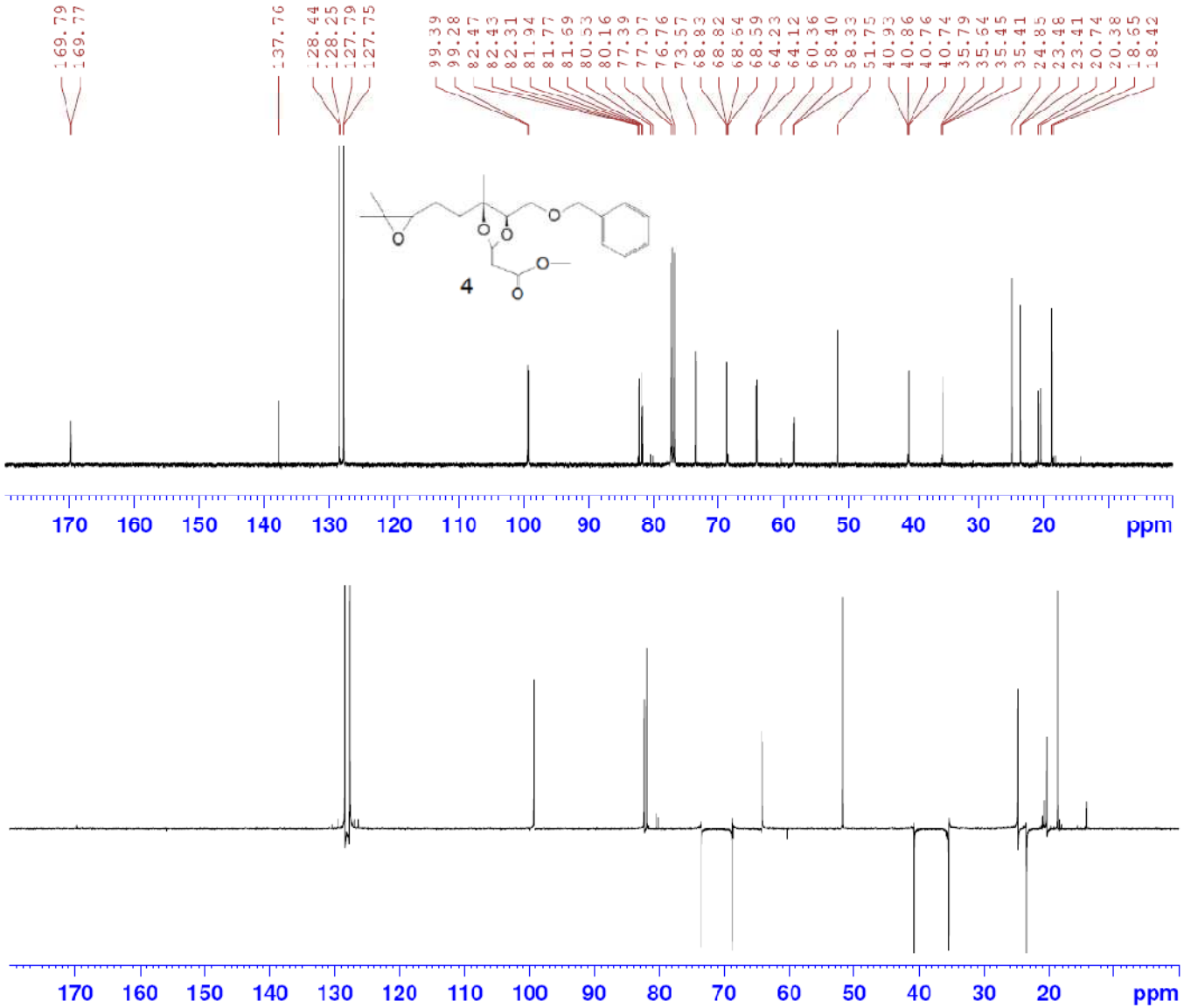
```
Current Data Parameters
NAME                  AA028
EXPNO                    16
PROCNO                    1

F2 - Acquisition Parameters
Date                20120319
Time                   12.09
INSTRUM                spect
PROBHD    5 mm BBO BB-1H
PULPROG                zg30
TD                    32768
SOLVENT               CDCl3
NS                       64
DS                        0
SWH                6393.862 Hz
FIDRES            0.195125 Hz
AQ                2.5625076 sec
RG                       57
DW                  78.200 usec
DE                   6.00 usec
TE                   298.2 K
D1                5.00000000 sec
TD0                       1

======== CHANNEL f1 ========
NUC1                     1H
P1                  14.35 usec
PL1                  0.00 dB
SFO1          400.1324710 MHz

F2 - Processing parameters
SI                    65536
SF          400.1300174 MHz
WDW                      EM
SSB                       0
LB                   0.30 Hz
GB                        0
PC                     1.00
```

Appendix14



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Current Data Parameters

NAME	AA028
EXPNO	17
PROCNO	1

F2 - Acquisition Parameters

Date_	20120319
Time	12.23
INSTRUM	spect
PROBHD	5 mm BBO BB-1H
PULPROG	zgpg30
TD	65536
SOLVENT	CDCl3
NS	469
DS	4
SWH	24038.461 Hz
FIDRES	0.366798 Hz
AQ	1.3631988 sec
RG	32800
DW	20.800 usec
DE	6.00 usec
TE	298.2 K
D1	2.00000000 sec
d11	0.03000000 sec
DELTA	1.89999998 sec
TD0	1

======== CHANNEL f1 ========

NUC1	13C
P1	9.50 usec
PL1	-2.00 dB
SFO1	100.6228298 MHz

======== CHANNEL f2 ========

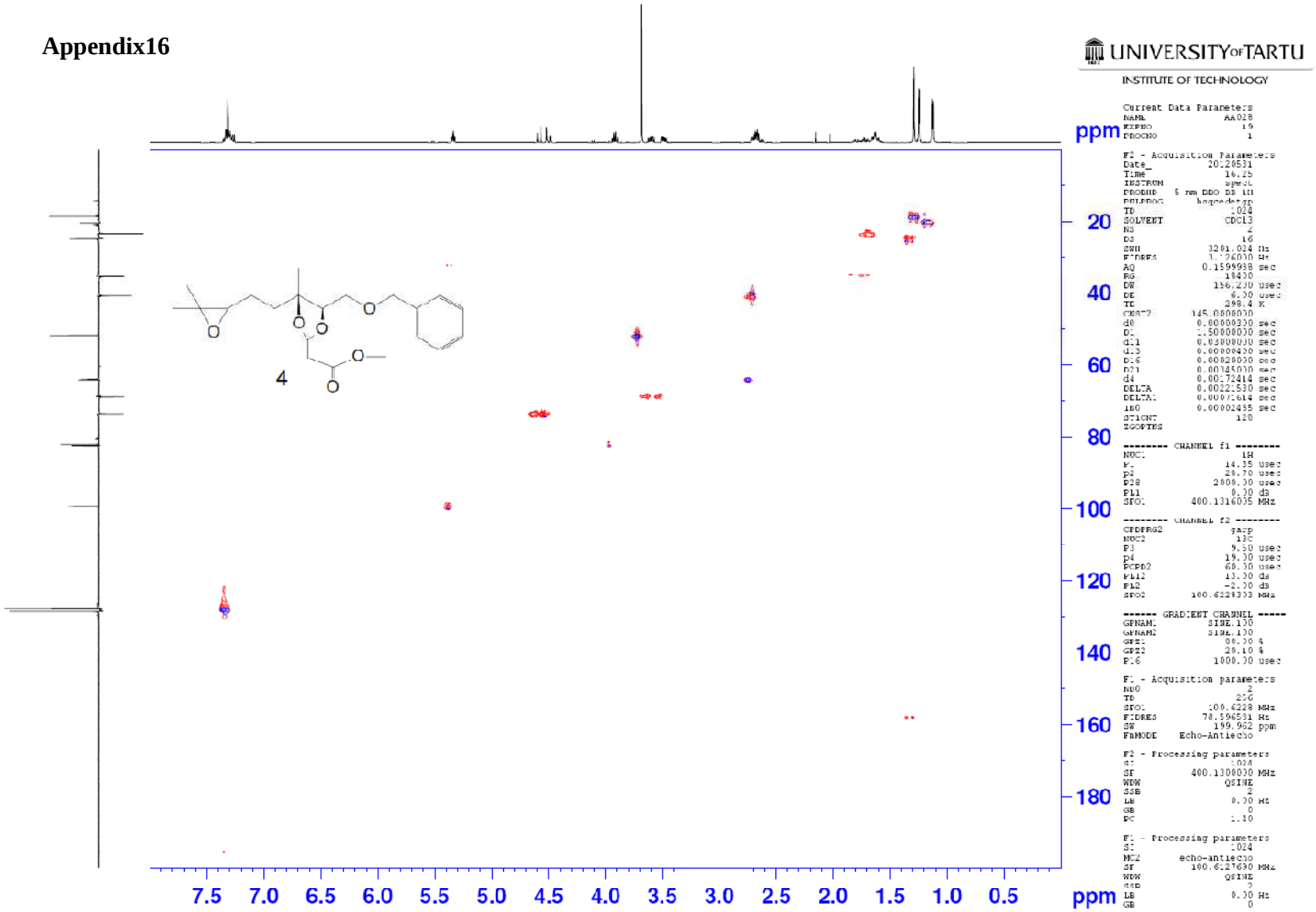
CPDPRG2	waltz16
NUC2	1H
PCPD2	70.00 usec
PL12	13.76 dB
PL13	14.00 dB
PL2	0.00 dB
SFO2	400.1316005 MHz

F2 - Processing parameters

SI	32768
SF	100.6127690 MHz
WDW	EM
SSB	0
LB	1.00 Hz
GB	0
PC	1.40

Appendix15

Appendix16



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```
Current Data Parameters
NAME                  AA028
EXPNO                     19
PROCNO                     1

F2 - Acquisition Parameters
Date_              20120531
Time                  16.25
INSTRUM                spect
PROBHD    5 mm BBO BB 1H
PULPROG          hsqcedetgp
TD                      1024
SOLVENT                 CDCl3
NS                         2
DS                        16
SWH               3201.024 Hz
FIDRES            3.126000 Hz
AQ                0.1599938 sec
RG                     18400
DW                   156.200 usec
DE                     6.50 usec
TE                   298.4 K
CNST2             145.0000000
d0                0.00000330 sec
D1                1.50000000 sec
d11               0.03000000 sec
d13               0.00000430 sec
D16               0.00020000 sec
D21               0.00345000 sec
d4                0.00172414 sec
DELTA             0.0022:530 sec
DELTA1            0.0007:614 sec
in0               0.00002435 sec
SFIGNT                   120
ZGOPTNS

-------- CHANNEL f1 --------
NUC1                     1H
P1                    14.35 usec
p2                    28.70 usec
P28                 2000.00 usec
PL1                    0.00 dB
SFO1          400.1316005 MHz

-------- CHANNEL f2 --------
CPDPRG2                garp
NUC2                    13C
PCPD2                  9.50 usec
p4                    19.00 usec
PCPD2                 60.00 usec
PL12                  13.00 dB
PL2                   -2.00 dB
SFO2          100.6228303 MHz

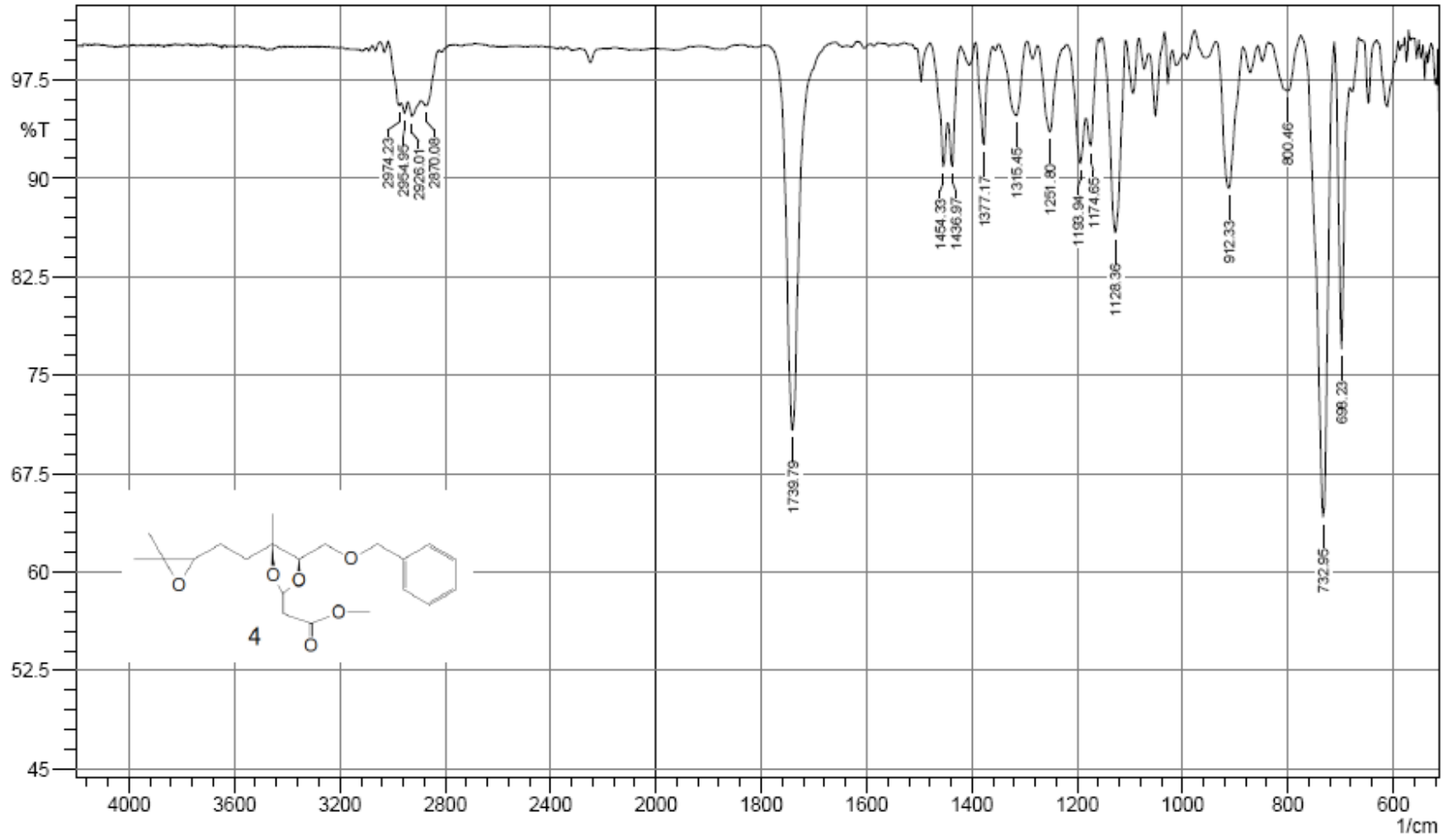
------ GRADIENT CHANNEL -----
GPNAM1             SINE.100
GPNAM2             SINE.100
GPZ1                  80.00 %
GPZ2                  20.10 %
P16                 1000.00 usec

F1 - Acquisition parameters
ND0                        2
TD                       256
SFO1          106.6228 MHz
FIDRES          78.596531 Hz
SW                199.962 ppm
FnMODE     Echo-Antiecho

F2 - Processing parameters
SI                      1024
SF            400.1300000 MHz
WDW                    QSINE
SSB                        2
LB                      0.00 Hz
GB                         0
PC                      1.40

F1 - Processing parameters
SI                      1024
MC2         echo-antiecho
SF            100.6127690 MHz
WDW                    QSINE
SSB                        2
LB                      0.00 Hz
GB                         0
```

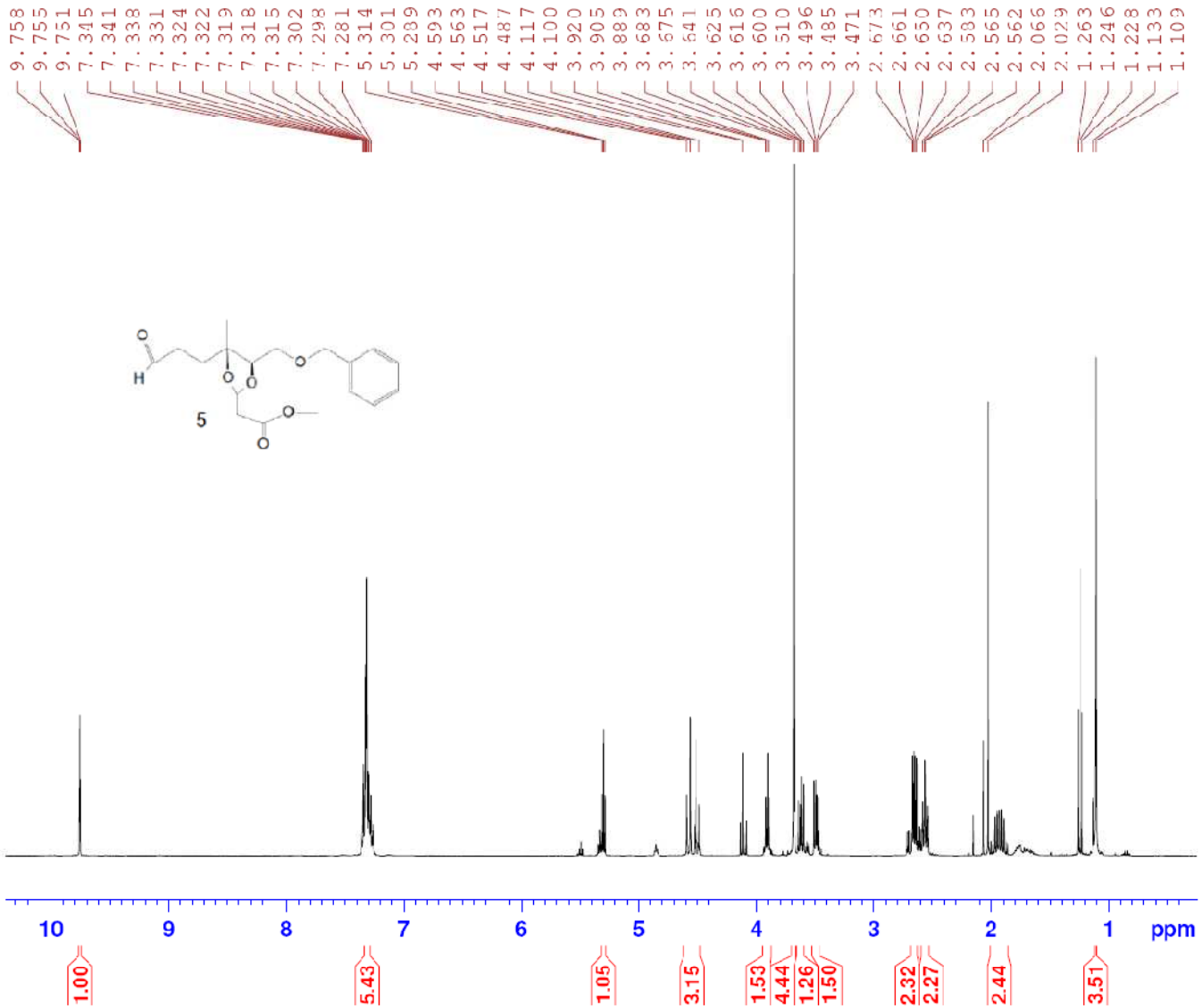
SHIMADZU



Comment; **Appendix17**

No. of Scans;
Resolution;
Apodization;

Date/Time; 5/8/2012 4:49:29 PM
User; Agilent



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Current Data Parameters

NAME	AA029
EXPNO	16
PROCNO	1

F2 - Acquisition Parameters

Date_	20120324
Time	16.25
INSTRUM	spect
PROBHD	5 mm BBO BB-1H
PULPROG	zg30
TD	32768
SOLVENT	CDCl3
NS	64
DS	0
SWH	6393.862 Hz
FIDRES	0.195125 Hz
AQ	2.5625076 sec
RG	64
DW	78.200 usec
DE	6.00 usec
TE	298.2 K
D1	5.00000000 sec
TD0	1

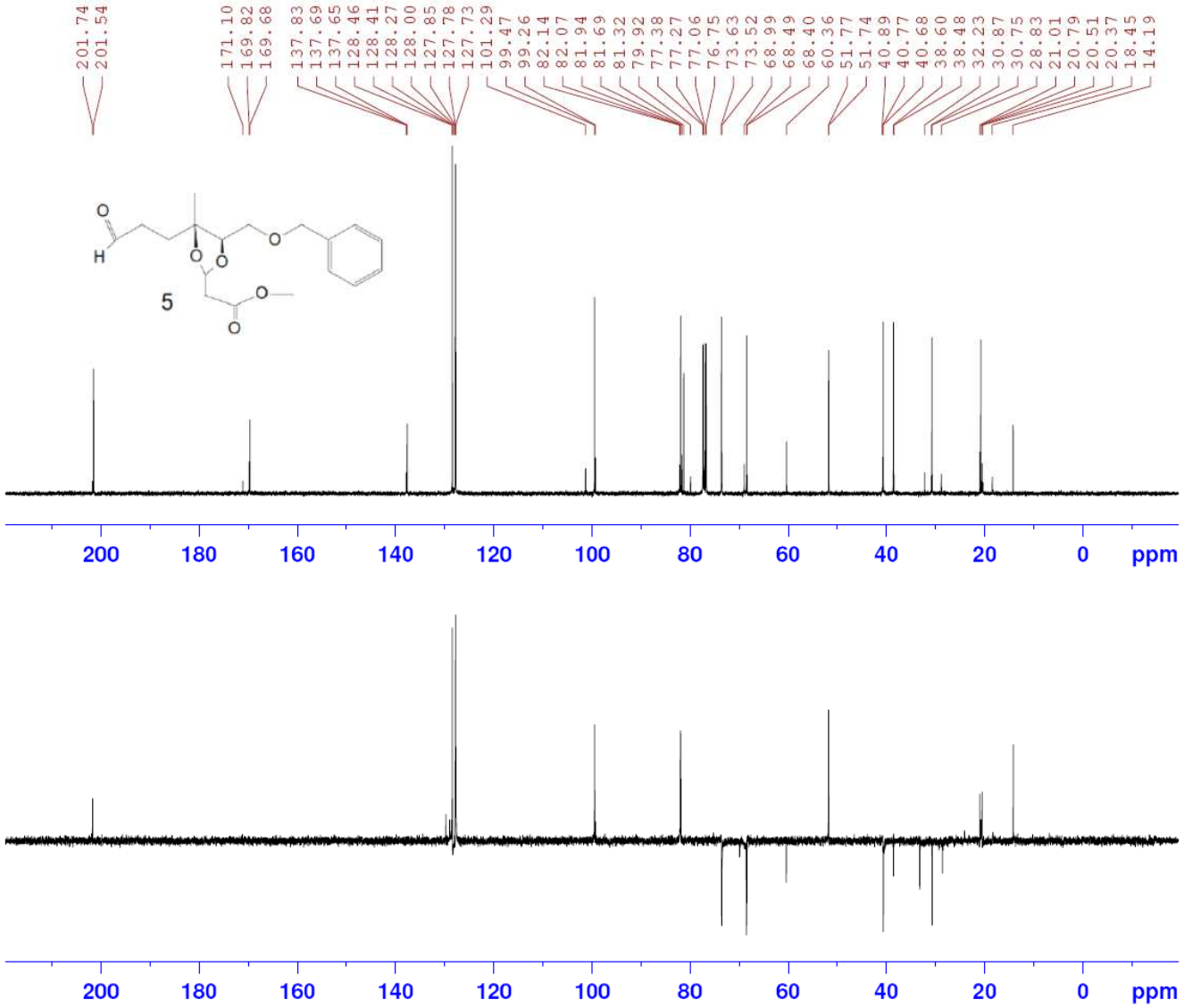
-------- CHANNEL f1 --------

NUC1	1H
P1	14.35 usec
PL1	0.00 dB
SFO1	400.1324710 MHz

F2 - Processing parameters

SI	65536
SF	400.1300173 MHz
WDW	EM
SSB	0
LB	0.30 Hz
GB	0
PC	1.00

Appendix18



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```
Current Data Parameters
NAME                  AA029
EXPNO                    17
PROCNO                    1

F2 - Acquisition Parameters
Date_              20120324
Time                  17.36
INSTRUM               spect
PROBHD    5 mm BBO BB-1H
PULPROG             zgpg30
TD                   65536
SOLVENT              CDCl3
NS                    1024
DS                       4
SWH             24038.461 Hz
FIDRES           0.366798 Hz
AQ               1.3631988 sec
RG                   32800
DW                  20.800 usec
DE                   6.00 usec
TE                  298.1 K
D1              2.00000000 sec
d11             0.03000000 sec
DELTA           1.89999998 sec
TD0                      1

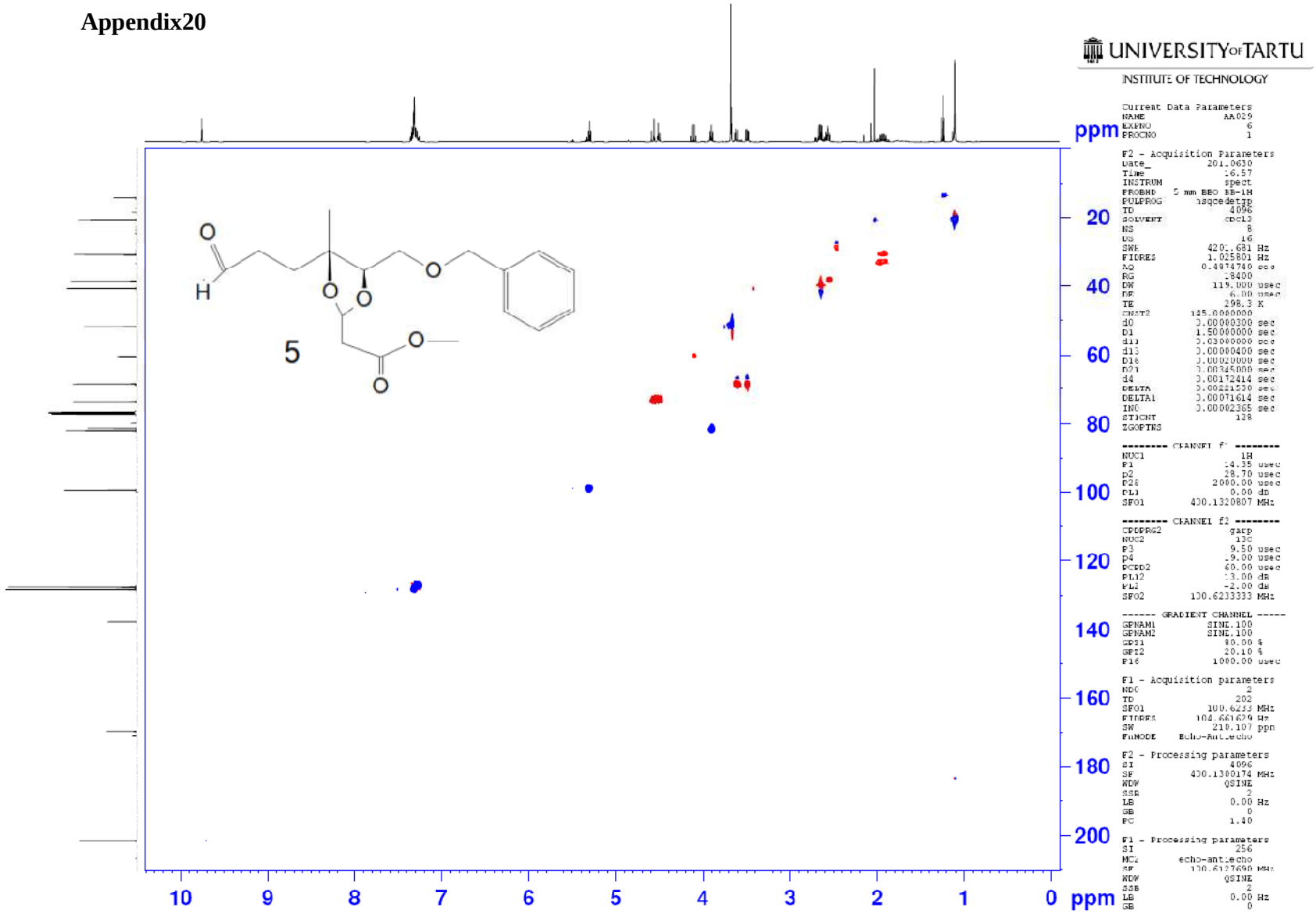
======== CHANNEL f1 ========
NUC1                   13C
P1                    9.50 usec
PL1                  -2.00 dB
SFO1          100.6228298 MHz

======== CHANNEL f2 ========
CPDPRG2            waltz16
NUC2                   1H
PCPD2                70.00 usec
PL12                 13.76 dB
PL13                 14.00 dB
PL2                   0.00 dB
SFO2          400.1316005 MHz

F2 - Processing parameters
SI                   65536
SF            100.6127690 MHz
WDW                    EM
SSB                     0
LB                   1.00 Hz
GB                      0
PC                    .40
```

Appendix19

Appendix20


UNIVERSITY OF TARTU
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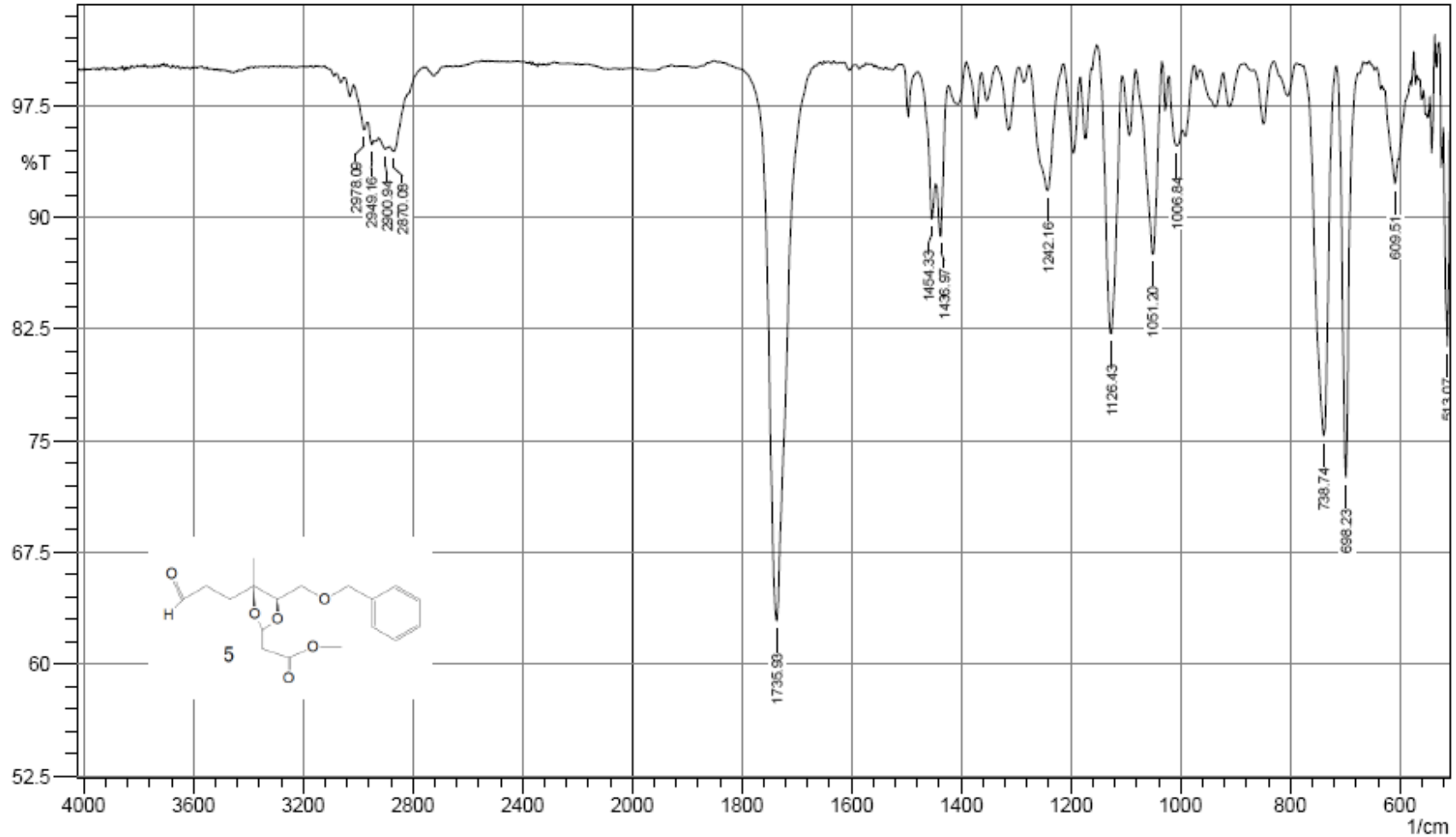
ppm
10
9
8
7
6
5
4
3
2
1
0
20
40
60
80
100
120
140
160
180
200
5

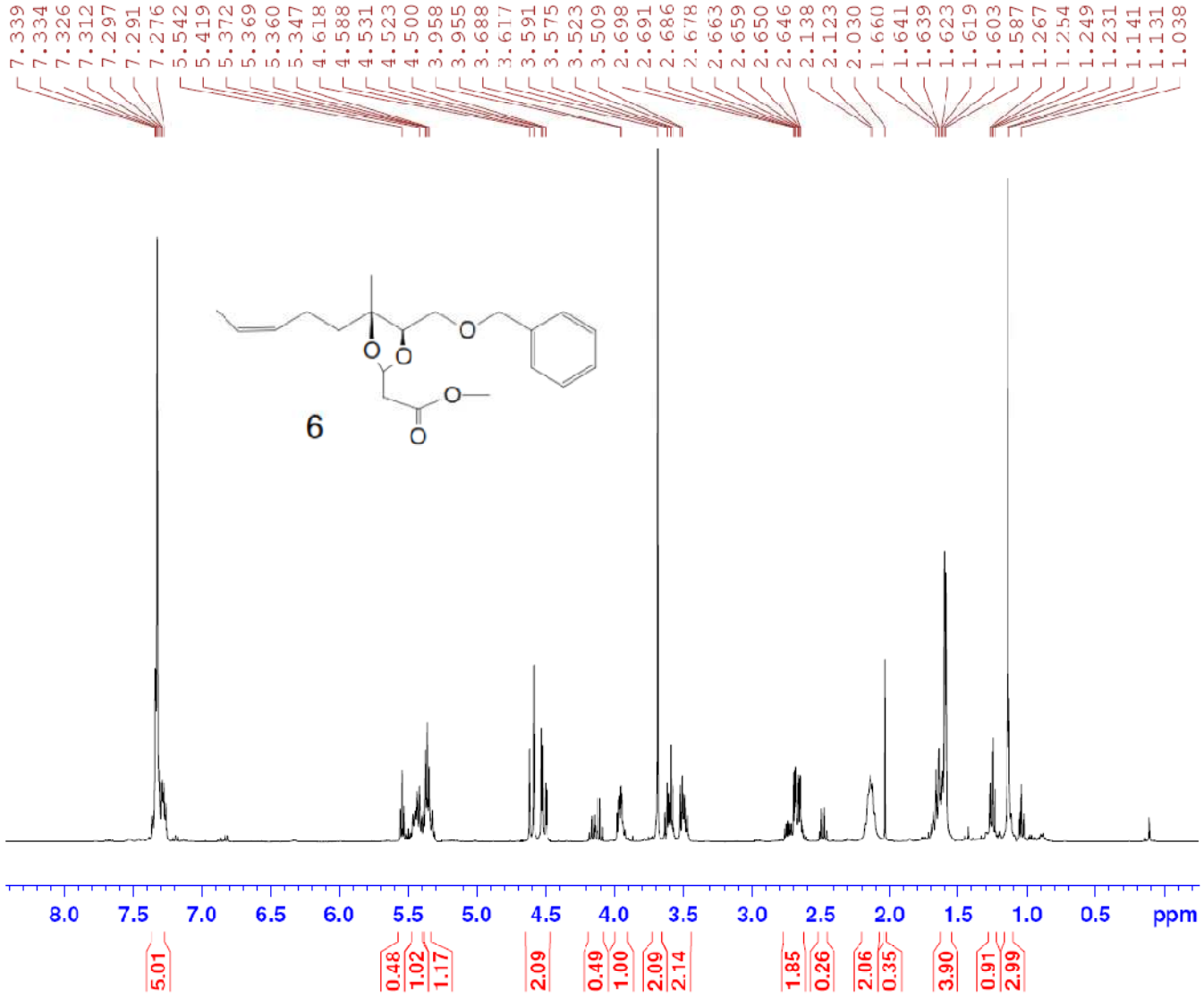
SHIMADZU



Comment; **Appendix21**

No. of Scans;
Resolution;
Apodization;

Date/Time; 3/30/2012 5:32:53 PM
User; Agilent



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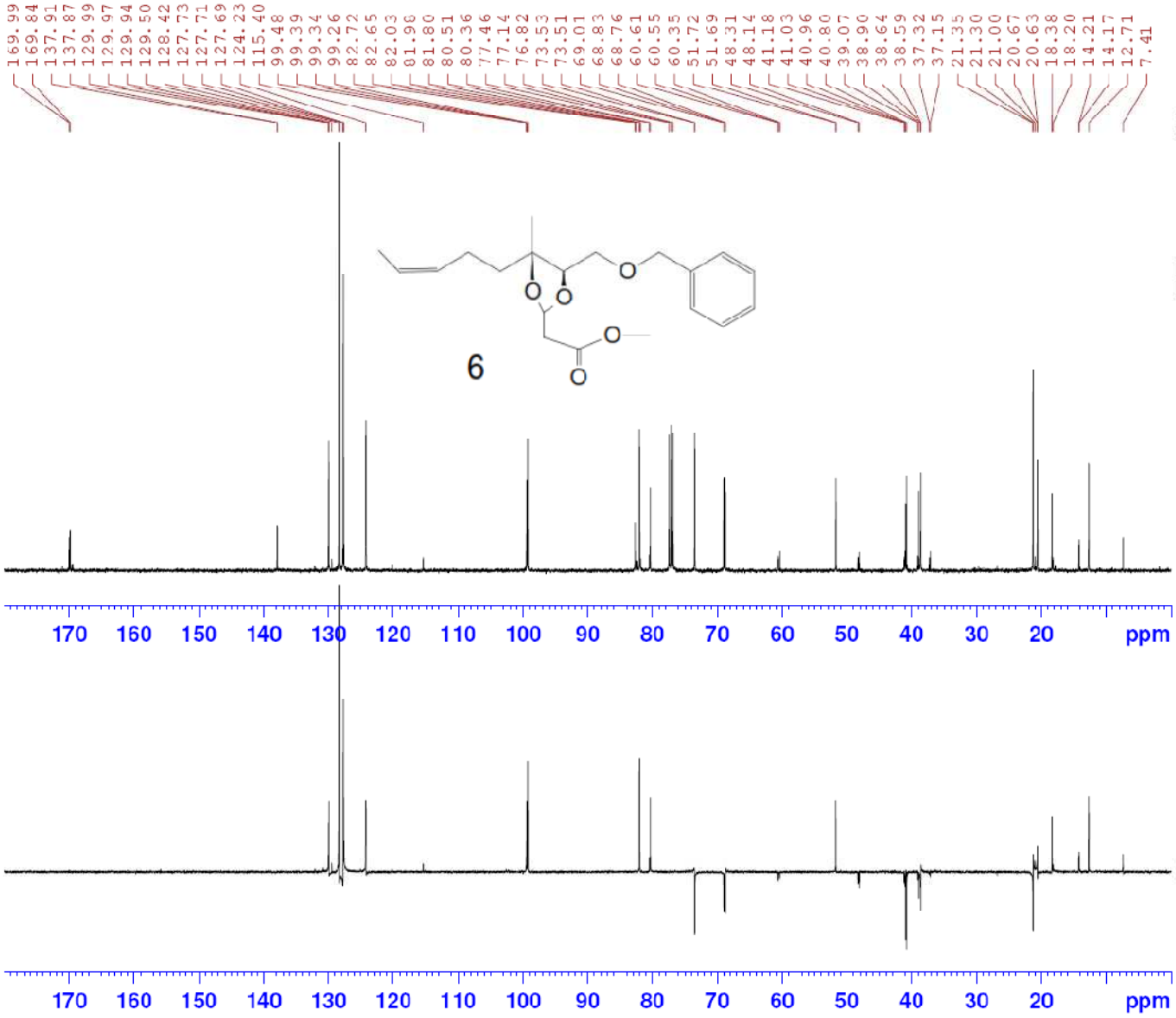
```
Current Data Parameters
NAME                  AA043
EXPNO                     5
PROCNO                    1

F2 - Acquisition Parameters
Date_              20111117
Time                  16.19
INSTRUM                spect
PROBHD    5 mm BBO BB-1H
PULPROG                zg30
TD                    32768
SOLVENT               CDCl3
NS                       64
DS                        0
SWH                6393.862 Hz
FIDRES             0.195125 Hz
AQ                 2.5625076 sec
RG                      22.6
DW                   78.200 usec
DE                    6.00 usec
TE                   298.2 K
D1                5.00000000 sec
TD0                       1

-------- CHANNEL f1 --------
NUC1                     1H
P1                    14.35 usec
PL1                    0.00 dB
SFO1          400.1324710 MHz

F2 - Processing parameters
SI                    65536
SF            400.1300174 MHz
WDW                      EM
SSB                       0
LB                     0.30 Hz
GB                        0
PC                     1.00
```

Appendix22



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INSTITUTE OF TECHNOLOGY

Current Data Parameters	
NAME	AA043
EXPNO	6
PROCNO	1

F2 - Acquisition Parameters	
Date_	20111117
Time	16.29
INSTRUM	spect
PROBHD	5 mm BBO BB-1H
PULPROG	zgpg30
TD	65536
SOLVENT	CDCl3
NS	352
DS	4
SWH	24038.461 Hz
FIDRES	0.366798 Hz
AQ	1.3631988 sec
RG	32800
DW	20.800 usec
DE	6.00 usec
TE	298.2 K
D1	2.00000000 sec
d11	0.03000000 sec
DELTA	1.89999998 sec
TD0	1

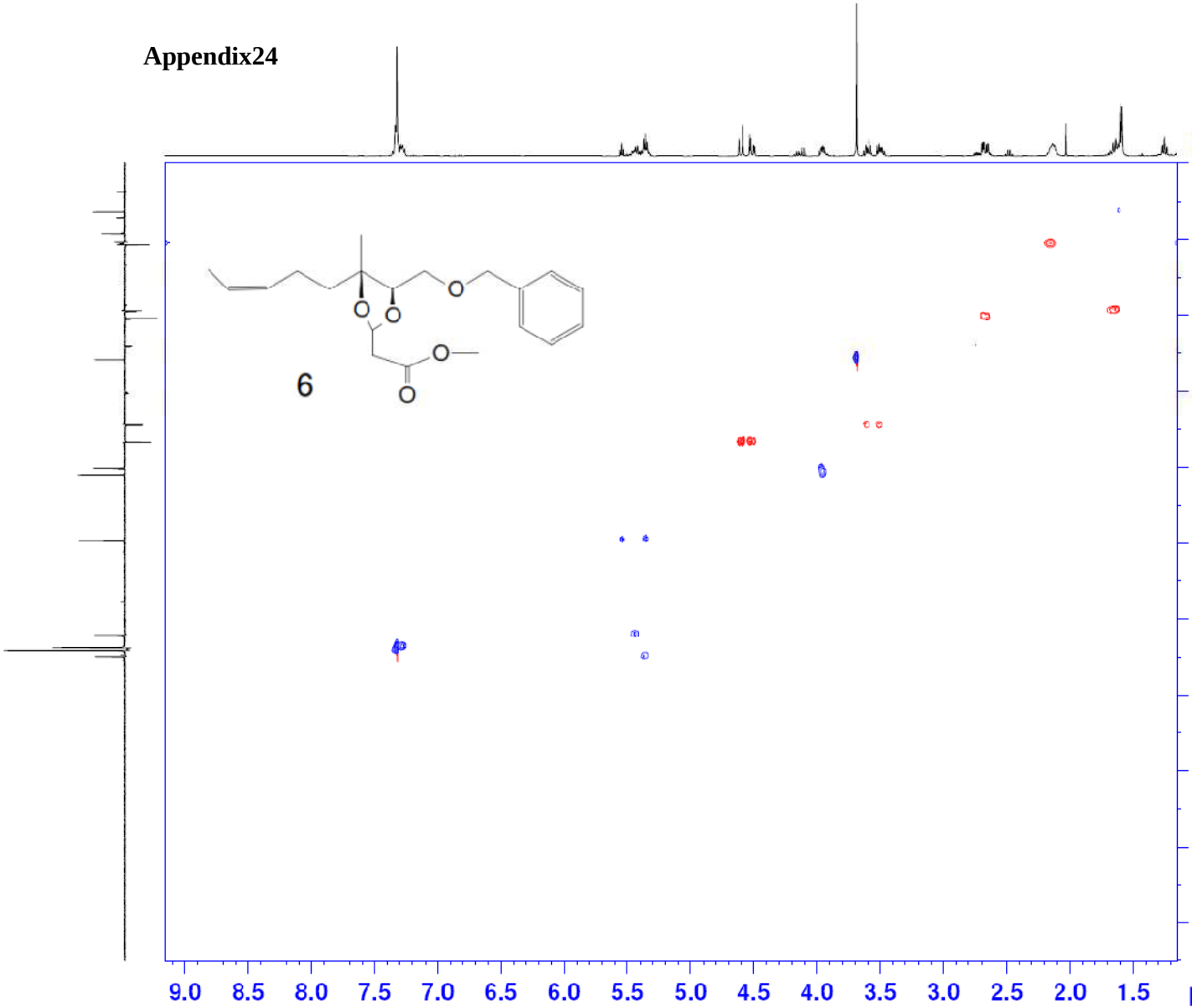
======== CHANNEL f1 ========	
NUC1	13C
P1	9.50 usec
PL1	-2.00 dB
SFO1	100.6228298 MHz

-------- CHANNEL f2 --------	
CPDPRG2	waltz16
NUC2	1H
PCPD2	70.00 usec
PL12	13.76 dB
PL13	14.00 dB
PL2	0.00 dB
SFO2	400.1316005 MHz

F2 - Processing parameters	
SI	32768
SF	100.6127690 MHz
WDW	EM
SSB	0
LB	1.00 Hz
GB	0
PC	1.40

Appendix23

Appendix24



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```
Current Data Parameters
NAME                  AA043
EXPNO                     8
PROCNO                    1

F2 - Acquisition Parameters
Date_              20111118
Time                  12.06
INSTRUM                spect
PROBHD     5 mm EBO BB-1H
PULPROG         hsqcedetgp
TD                     4096
SOLVENT                CDCl3
NS                        8
DS                       16
SWH                3201.024 Hz
FIDRES             0.781500 Hz
AQ                 0.6398452 sec
RG                     18400
DW                   156.200 usec
DE                     6.00 usec
TE                   298.5 K
CNST2              145.0000000
d0                 0.00000300 sec
D1                 1.50000000 sec
d11                0.03000000 sec
d13                0.00000400 sec
D16                0.00020000 sec
D21                0.00345000 sec
d4                 0.00172414 sec
DELTA              0.00221530 sec
DELTA1             0.00071614 sec
INU                0.00002365 sec
ST1CNT                   128
ZGOPTNS

-------- CHANNEL f1 --------
NUC1                      1H
P1                     14.35 usec
p2                     28.70 usec
P28                 2000.00 usec
PL1                    0.00 dB
SFO1            400.1320807 MHz

-------- CHANNEL f2 --------
CPDPRG2                garp
NUC2                    13C
P3                     9.50 usec
p4                    19.00 usec
PCPD2                 60.00 usec
PL12                  13.00 dB
PL2                   -2.00 dB
SFO2            100.6233333 MHz

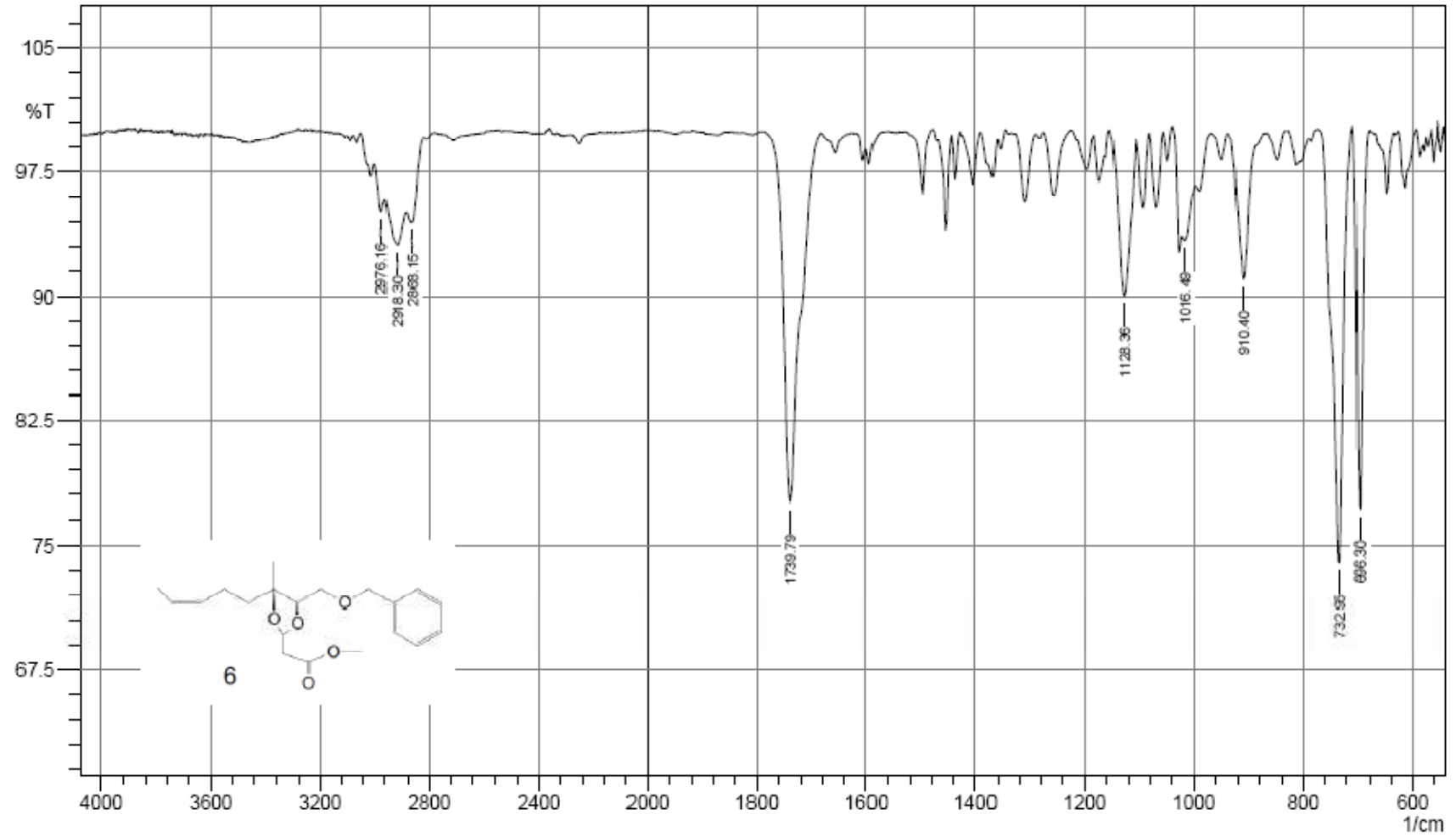
------ GRADIENT CHANNEL -----
GPNAM1              SINE.100
GPNAM2              SINE.100
GPZ1                  80.00 %
GPZ2                  20.10 %
P16                 1000.00 usec

F1 - Acquisition parameters
ND0                       2
TD                      147
SFO1            100.6233 MHz
FIDRES          143.820740 Hz
SW                 210.107 ppm
FnMODE     Echo-Antiecho

F2 - Processing parameters
SI                     4096
SF          400.1300174 MHz
WDW                   QSINE
SSB                       2
LB                     0.00 Hz
GB                        0
PC                     1.40

F1 - Processing parameters
SI                      256
MC2         echo-antiecho
SF            100.6127690 MHz
WDW                   QSINE
SSB                       2
LB                     0.00 Hz
GB                        0
```

SHIMADZU

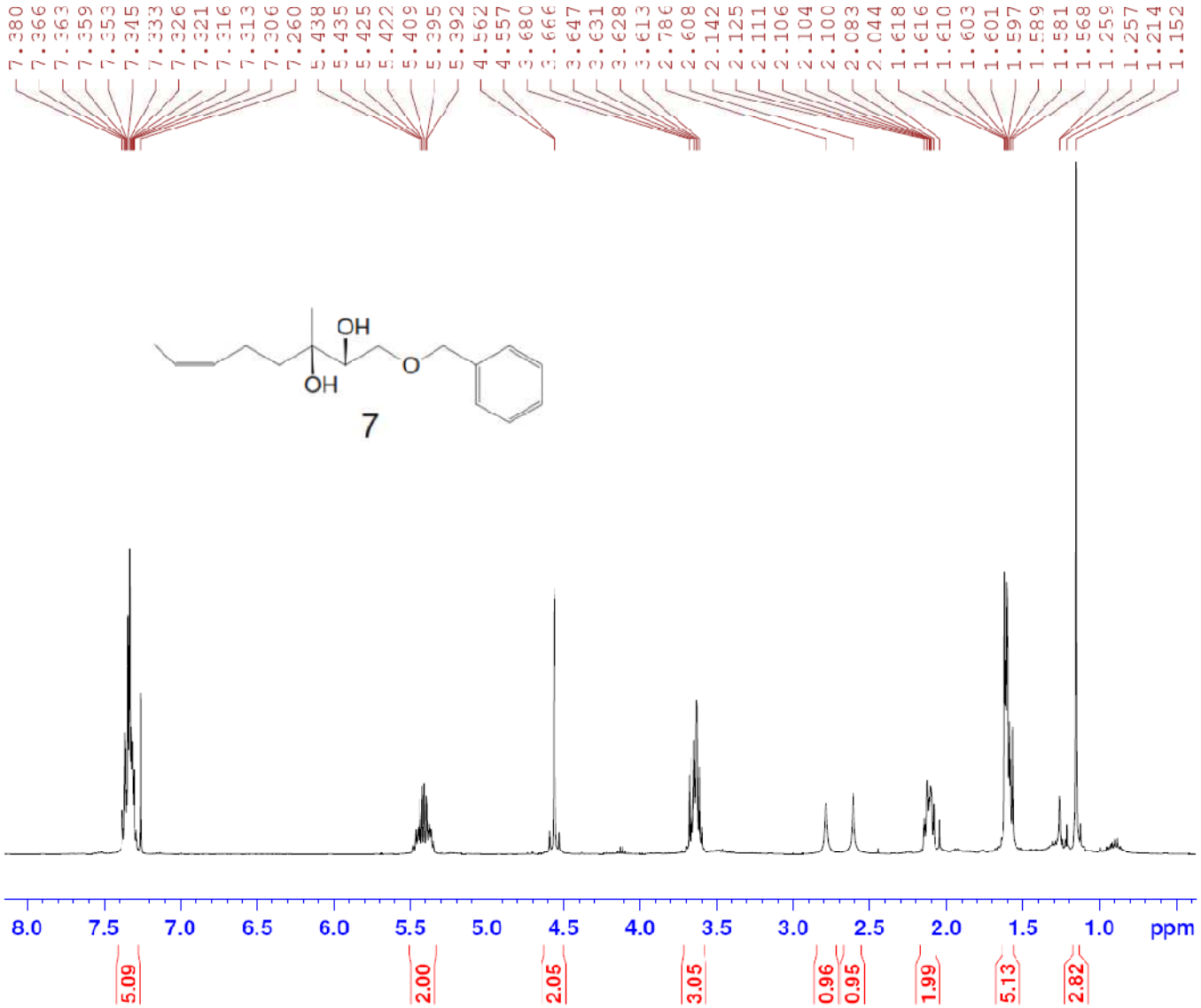


Comment:

Appendix25

No. of Scans:
Resolution:
Apodization:

Date/Time; 3/30/2012 5:40:19 PM
User: Agilent



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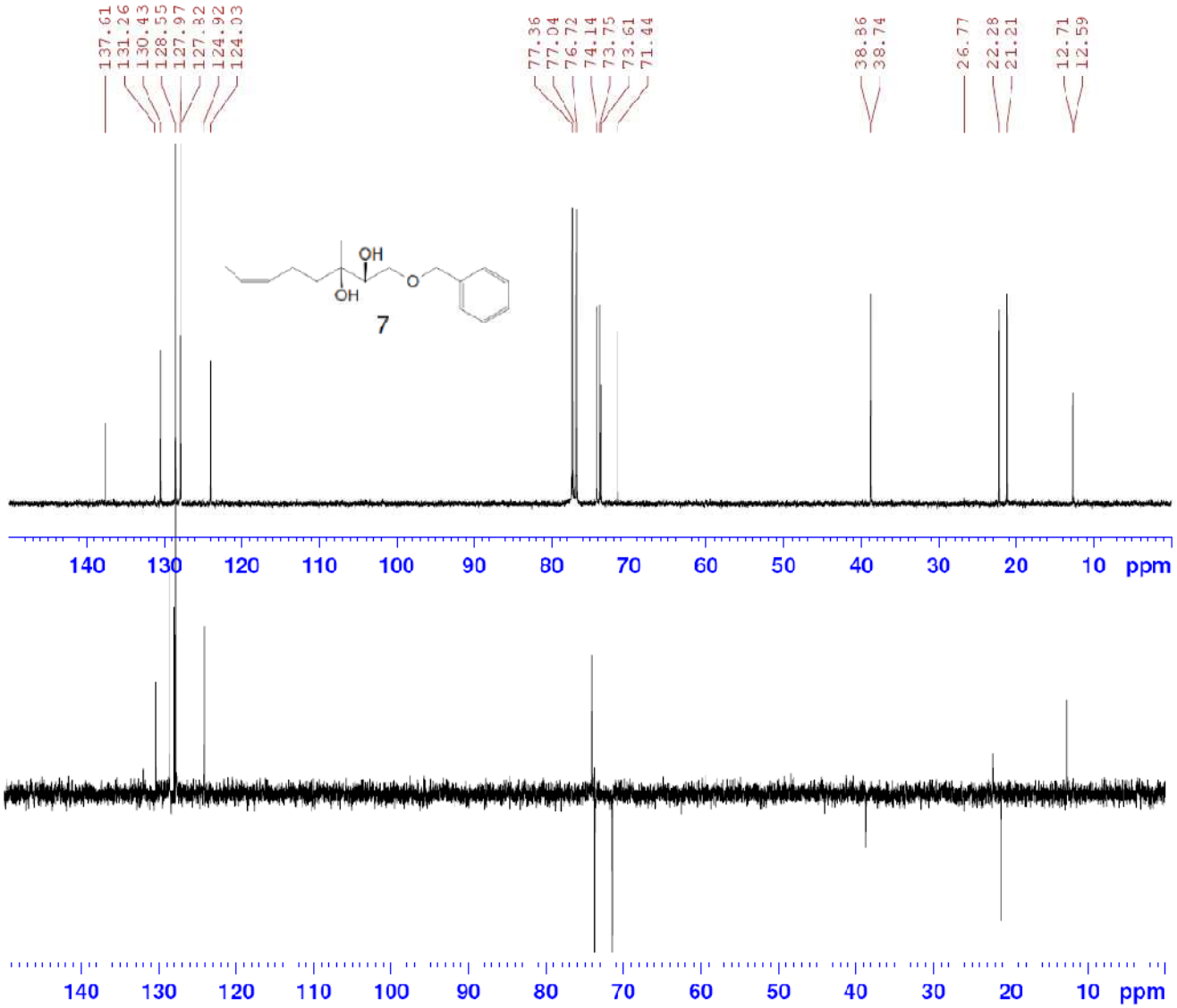
```
Current Data Parameters
NAME                  AA044
EXPNO                    15
PROCNO                    1

F2 - Acquisition Parameters
Date_              20111220
Time                  15.25
INSTRUM                spect
PROBHD    5 mm BBO BB-1H
PULPROG                zg30
TD                    32768
SOLVENT               CDCl3
NS                       64
DS                        0
SWH                6393.862 Hz
FIDRES            0.195125 Hz
AQ                2.5625076 sec
RG                      181
DW                   78.200 usec
DE                    6.00 usec
TE                  298.2 K
D1                5.00000000 sec
D0                        1

-------- CHANNEL f1 --------
NUC1                     1H
P1                    14.35 usec
PL1                    0.00 dB
SFO1          400.1324710 MHz

F2 - Processing parameters
SI                    65536
SF               400.1300176 MHz
WDW                      EM
SSB                       0
LB                     0.60 Hz
GB                        0
PC                     1.00
```

Appendix26



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```
Current Data Parameters
NAME                  AA044
EXPNO                    31
PROCNO                    1

F2 - Acquisition Parameters
Date_              20120402
Time                   14.20
INSTRUM                spect
PROBHD   5 mm BBO BB-1H
PULPROG             zgpg30
TD                   65536
SOLVENT              CDCl3
NS                     778
DS                       4
SWH              24038.461 Hz
FIDRES            0.366798 Hz
AQ                1.3631988 sec
RG                   32800
DW                  20.800 usec
DE                   6.00 usec
TE                  298.2 K
D1                2.00000000 sec
d11               0.03000000 sec
DELTA             1.89999998 sec
TD0                      1

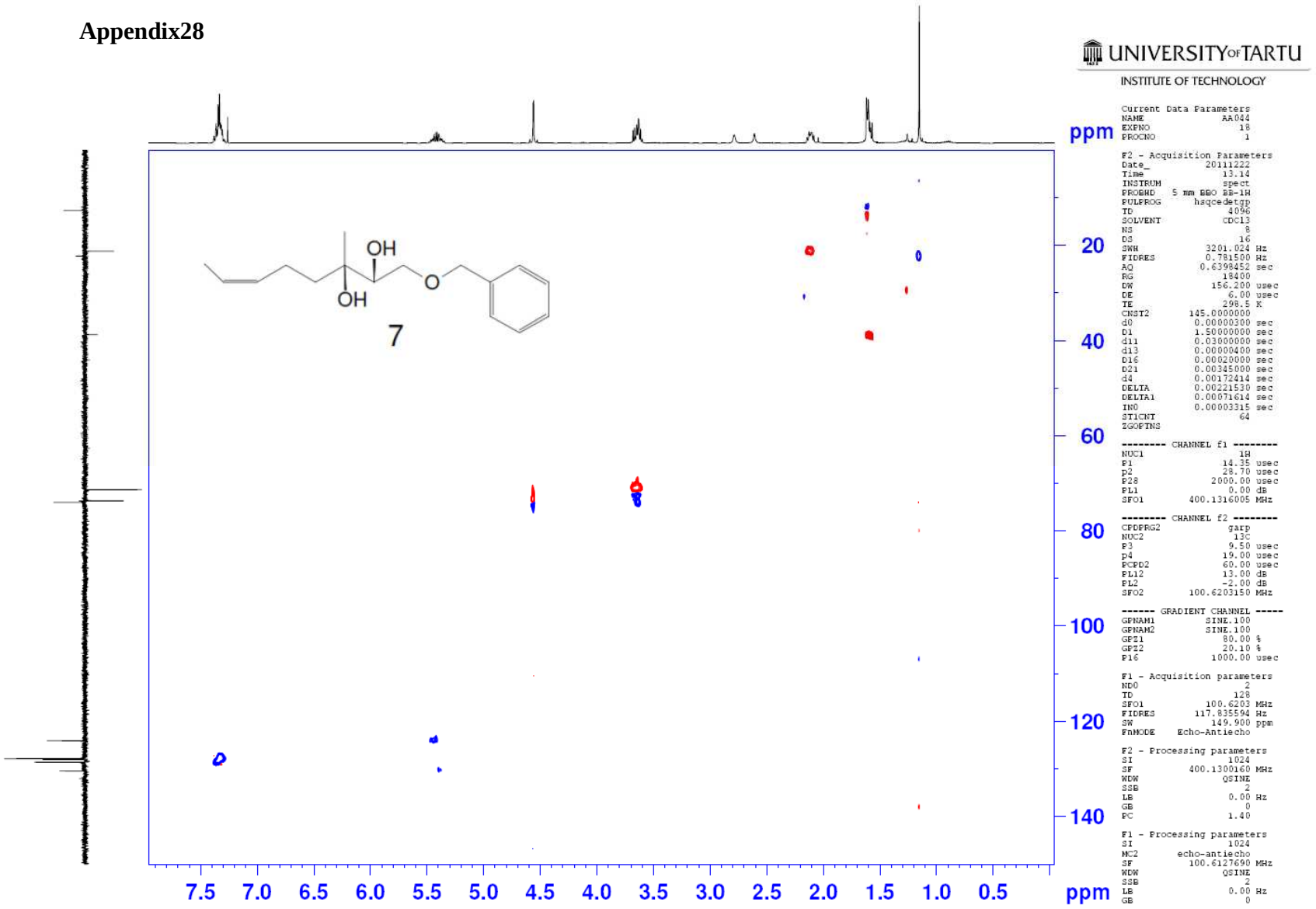
======== CHANNEL f1 ========
NUC1                   13C
P1                    9.50 usec
PL1                  -2.00 dB
SFO1          100.6228298 MHz

-------- CHANNEL f2 --------
CPDPRG2          waltz16
NUC2                   1H
PCPD2                70.00 usec
PL12                 13.76 dB
PL13                 24.00 dB
PL2                   0.00 dB
SFO2          400.1316005 MHz

F2 - Processing parameters
SI                    32768
SF            100.6127690 MHz
WDW                     EM
SSB                      0
LB                    1.00 Hz
GB                       0
PC                    1.40
```

Appendix27

Appendix28



UNIVERSITY OF TARTU
INSTITUTE OF TECHNOLOGY

```
Current Data Parameters
NAME                  AA044
EXPNO                    18
PROCNO                    1

F2 - Acquisition Parameters
Date_              20111222
Time                  13.14
INSTRUM                spect
PROBHD   5 mm BBO BB-1H
PULPROG          hsqcedetgp
TD                     4096
SOLVENT                CDCl3
NS                        8
DS                       16
SWH                3201.024 Hz
FIDRES             0.781500 Hz
AQ                 0.6398452 sec
RG                     18400
DW                   156.200 usec
DE                     6.00 usec
TE                   298.5 K
CNST2              145.0000000
d0                 0.00000300 sec
D1                 1.50000000 sec
d11                0.03000000 sec
d13                0.00000400 sec
D16                0.00020000 sec
D21                0.00345000 sec
d4                 0.00172414 sec
DELTA              0.00221530 sec
DELTA1             0.00071614 sec
IN0                0.00003315 sec
ST1CNT                   64
ZGOPTNS

-------- CHANNEL f1 --------
NUC1                     1H
P1                    14.35 usec
p2                    28.70 usec
P28                2000.00 usec
PL1                   0.00 dB
SFO1          400.1316005 MHz

-------- CHANNEL f2 --------
CPDPRG2                garp
NUC2                    13C
P3                     9.50 usec
p4                    19.00 usec
PCPD2                 60.00 usec
PL12                  13.00 dB
PL2                   -2.00 dB
SFO2          100.6203150 MHz

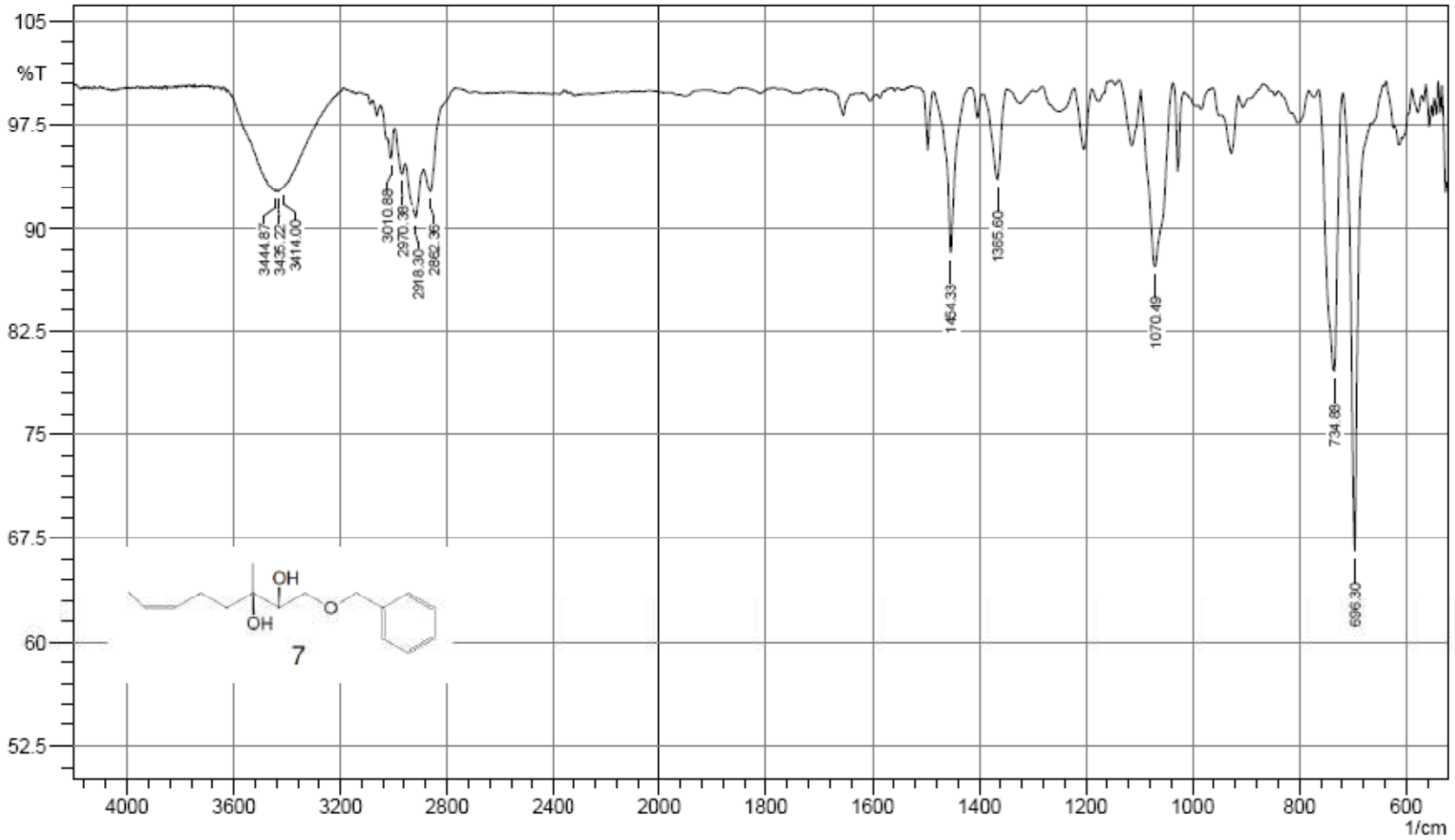
------ GRADIENT CHANNEL -----
GPNAM1             SINE.100
GPNAM2             SINE.100
GPZ1                  80.00 %
GPZ2                  20.10 %
P16                 1000.00 usec

F1 - Acquisition parameters
ND0                       2
TD                      128
SFO1          100.6203 MHz
FIDRES        117.835594 Hz
SW                149.900 ppm
FnMODE     Echo-Antiecho

F2 - Processing parameters
SI                     1024
SF            400.1300160 MHz
WDW                   QSINE
SSB                       2
LB                    0.00 Hz
GB                        0
PC                    1.40

F1 - Processing parameters
SI                     1024
MC2         echo-antiecho
SF            100.6127690 MHz
WDW                   QSINE
SSB                       2
LB                    0.00 Hz
GB                        0
```

SHIMADZU



Comment: **Appendix29**

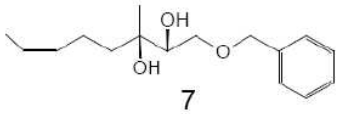
No. of Scans:
Resolution:
Apodization:

Date/Time: 3/30/2012 5:17:51 PM
User: Agilent

Appendix 30

Uncertainty budget for specific rotation for compound ***7***

1. Calibration of 5 mL volumetric flask



7

	Measurements: m_empty flask	m_ full flask*
	10.3435	15.3571
	10.3435	15.3569
	10.3437	15.3566
	10.3439	15.3566
	10.3437	15.3563
		15.3567
		15.3571
		15.3569
		15.3566
		15.3561
Average	10.34366	15.3567
stdev	0.000167	0.00032472

$$y = f(x_1, x_2, \ldots, x_n)$$

$$u^2(y) = \left(\frac{\partial y}{\partial x_1}\right)^2 u^2(x_1) + \left(\frac{\partial y}{\partial x_2}\right)^2 u^2(x_2) -$$

** H_2O is used for calibration of 5 mL volumetric flask*

parameter	value	STDEV	uncertainty		dV/dx	
m_empty	10.34366	0.000167	5.7735E-05	**0.000177**	14.38835	6.49E-06
m_full	15.3567	0.000325	5.7735E-05	**0.00033**	-9.36426	9.54E-06
density	0.9978	0				
V	5.024093					4.00E-03

$V_{5\ mL\ flask}$= (5.02 ± 0.01) ml *(k=2)*

2. Optical rotation measurements for compound **7**

a) racemic mixture - reference material (**7'**)

	Optical Rotation	Sample Cell t°
	°	°C
	-0.0050	27.30
	0.0000	27.20
	-0.0050	27.20
	0.0050	27.10
	-0.0050	27.10
	-0.0070	27.00
	0.0010	26.90
	0.0000	26.90
	-0.0040	26.80
	0.0070	26.80
average	-0.0013	27.03
stdev	0.005	0.177
b type	0.005	

b) one enantiomer (**7''**)

	Optical Rotation	Sample Cell t°
	°	°C
	0.0450	25.20
	0.0350	25.10
	0.0340	25.10
	0.0450	25.00
	0.0350	25.00
	0.0350	25.00
	0.0440	24.90
	0.0380	24.90
	0.0360	24.90
	0.0400	24.80
average	0.0387	24.99
stdev	0.004	0.12
b type	0.005	

3. Uncertainty calculations

a) racemic mixture - reference material (**7'**)

Parameter	Value	u		Unit
m flask	14.1364	0.000358		g
m flask+prod	14.1693	0.001659		g
m prod	0.0362	0.002018		g
V solution	5.02	0.014979	0.004	ml
Concentration	0.007211	0.015114		g/ml
Cell length	1.0			dm
Opt. Rotation	-0.001	0.006856		°
Specific rotation	-0.18028	0.016596		

			mean	stdev a	stdev b
m flask	14.1364	14.1369	14.13665	0.000354	5.77E-05
m flask+prod	14.1693	14.1671	14.1682	0.001556	0.000577

$[\alpha]^{27}_{D}$ = (**-0.18** ± **0.03**) ***(k=2)***

(*c* 0.007 t-BuOH)

b) one enantiomer (**7''**)

Parameter	Value	u		Unit
m flask	15.8793	0.002887		g
m flask+prod	15.9095	0.000582		g
m prod	0.0302	0.003468		g
V solution	5.02	0.014979	0.004	ml
Concentration	0.006011	0.015375		g/ml
Cell length	1.0			dm
Opt. Rotation	0.039	0.006709		°
Specific rotation	6.438159	0.016775		

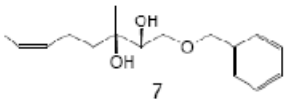
			mean	stdev a	stdev b
m flask	15.8793	15.8833	15.8813	0.002828	0.000577
m flask+prod	15.9095	15.9096	15.90955	7.07E-05	0.000577

$[\alpha]^{27}_{D}$ = (**6.44** ± **0.03**) ***(k=2)***

(*c* 0.006 t-BuOH)

==== Shimadzu LCMSsolution Analysis Report ====

Acquired by	: Admin
Sample Name	: AA_044_reference material
Sample ID	:
Vail #	: 76
Injection Volume	: 5 uL
Data File Name	: 20120217_R44_reference_material.lcd
Method File Name	: Kiraalne-LUX_Hexanes-2PrOH_20100525.lcm
Batch File Name	: 20120216_LV_1.lcb
Report File Name	: DefaultLCMS.lcr
Data Acquired	: 17.02.2012 17:49:03
Data Processed	: 17.02.2012 18:35:31



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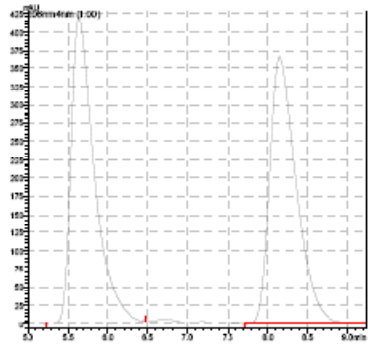
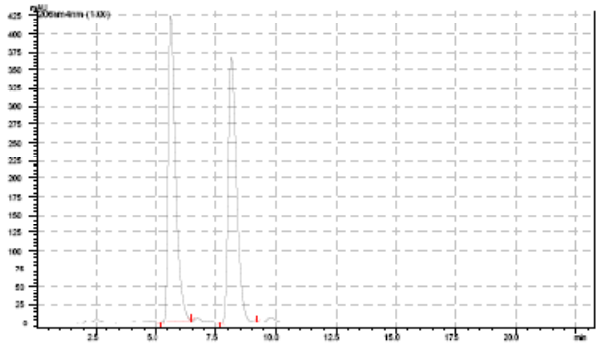
Appendix 31

<Chromatogram>





Method

<<Comment>>
<<System Controller>>
SCL Type :CBM-20A
Power On :ON
Event1 :OFF
Event2 :OFF
Event3 :OFF
Event4 :OFF

<<Data Acquisition>>
LC Stop Time :100.00 min
--ADJ Detector--
Name :ELSD
--PDA Detector--
Name :PDA
Sampling Frequency :1.5625 Hz
Start Time :0.00 min
End Time :100.00 min
Constant :0.640 sec

<<Option Box A>>

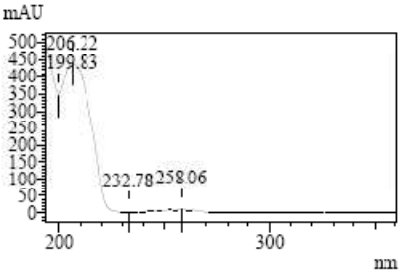
<<Option Box B>>

<<Pump>>
Pump Mode :Binary gradie
Pump A :LC-20AD
Pump B :LC-20AD
Total Flow :1.5000 mL/m
B.Conc :10.0 %
B.Curve :0
PressMax :100 bar
PressMin :0 bar

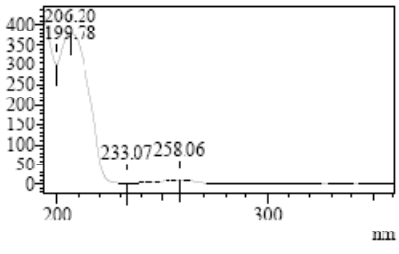
<<AutoSampler>>
AutoSampler :SIL
Use AutoSampler :Use
Sample Rack :Rac
Rinsing Volume :200
Needle Stroke :52
Control Vial Needle Stroke :52
Rinsing Speed :35

Spectrum

ID# : 1
Retention Time : 5.636
Compound Name : RT5.636
Spectrum Operation : None



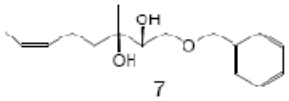
ID# : 2
Retention Time : 8.147
Compound Name : RT8.147
Spectrum Operation : None



Name	Time	Area	Area%
RT	5.636	8659958	50.183
RT	8.147	8596519	49.816

==== Shimadzu LCMSsolution Analysis Report ====

Acquired by	: Admin
Sample Name	: AA_44_cis isomer
Sample ID	:
Vail #	: 96
Injection Volume	: 10 uL
Data File Name	: 20120402_AA_R44_cis_isomer(3).lcd
Method File Name	: Kiraalne-LUX_Hexanes-2PrOH_20100525.lcm
Batch File Name	: 20120323_LV_8.lcb
Report File Name	: DefaultLCMS.lcr
Data Acquired	: 2.04.2012 14:55:50
Data Processed	: 2.04.2012 18:30:48



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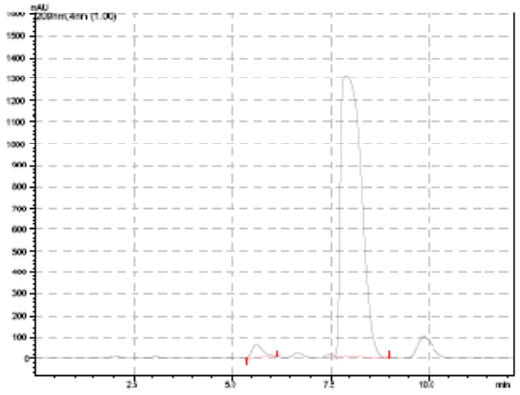
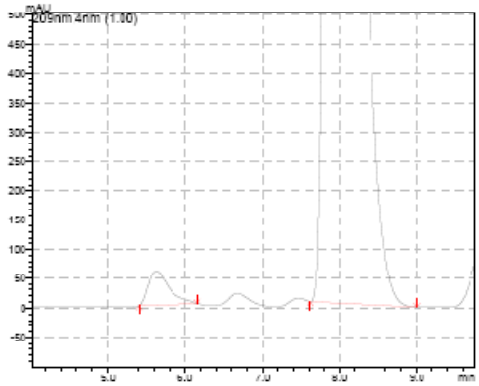
Appendix 32

<Chromatogram>





Method

<<Comment>>
<<System Controller>>

SCL Type	:CBM-20A
Power On	:ON
Event1	:OFF
Event2	:OFF
Event3	:OFF
Event4	:OFF

<<Data Acquisition>>

LC Stop Time	:60.00 min
--ADI Detector--	
Name	:ELSD
--PDA Detector--	
Name	:PDA
Sampling Frequency	:1.5625 Hz
Start Time	:0.00 min
End Time	:100.00 min
Constant	:0.640 sec

<<Option Box A>>

<<Option Box B>>

<<Pump>>

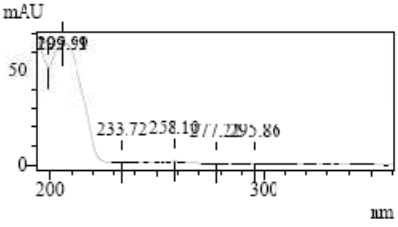
Pump Mode	:Binary gradient
Pump A	:LC-20AD
Pump B	:LC-20AD
Total Flow	:1.5000 mL/min
B.Conc	:10.0 %
B.Curve	:0
PressMax	:100 bar
PressMin	:0 bar

<<AutoSampler>>

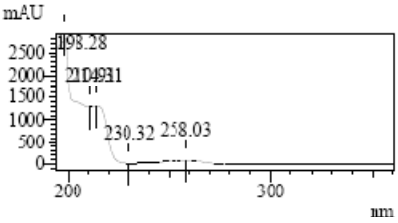
AutoSampler	:SIL-20A
Use AutoSampler	:Use
Sample Rack	:Rack 1.5mL
Rinsing Volume	:200 uL
Needle Stroke	:52 mm

Spectrum

ID# : 1
Retention Time : 5.622
Compound Name : RT5.622
Spectrum Operation : None



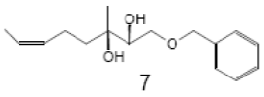
ID# : 2
Retention Time : 7.902
Compound Name : RT7.902
Spectrum Operation : None



Name	Time	Area	Area%
RT	5.622	1051957	2.2569
RT	7.902	45557881	97.7431

==== Shimadzu LCMSsolution Analysis Report ====

Acquired by	: Admin
Sample Name	: R44_1,2diol (cis one should be)
Sample ID	:
Vail #	: 49
Injection Volume	: 5 uL
Data File Name	: 20120118_AA_R44_one_isomer.lcd
Method File Name	: Kiraalne-LUX_Hexanes-2PrOH_20100525.lcm
Batch File Name	: LUX_20110601_KA007.2(3%).lcb
Report File Name	: DefaultLCMS.lcr
Data Acquired	: 18.01.2012 13:02:30
Data Processed	: 18.01.2012 14:06:30



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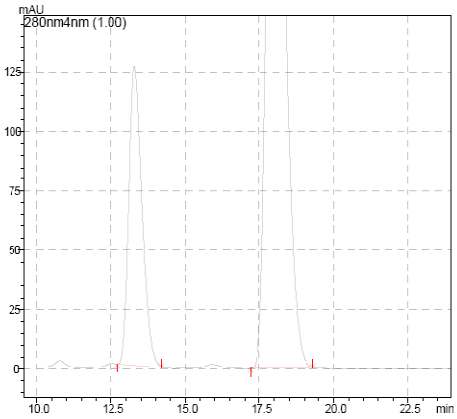
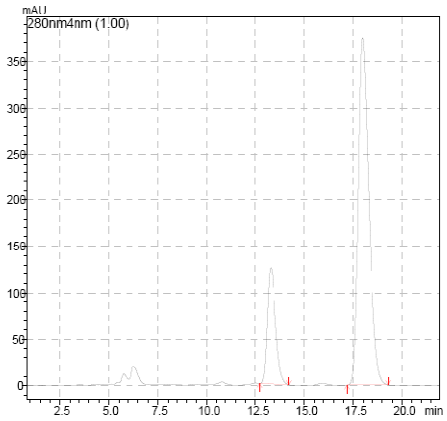
Appendix 33

<Chromatogram>





Method

<<Comment>>
<<System Controller>>
SCL Type :CBM-20A
Power On :ON
Event1 :OFF
Event2 :OFF
Event3 :OFF
Event4 :OFF

<<Data Acquisition>>
LC Stop Time :100.00 min
--AD2 Detector--
Name :ELSD
--PDA Detector--
Name :PDA
Sampling Frequency :1.5625 Hz
Start Time :0.00 min
End Time :100.00 min
Constant :0.640 sec

<<Option Box A>>

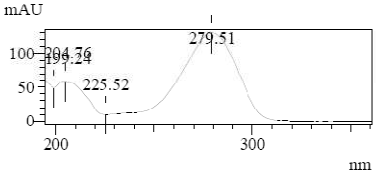
<<Option Box B>>

<<Pump>>
Pump Mode :Binary gradient
Pump A :LC-20AD
Pump B :LC-20AD
Total Flow :1.0000 mL/min
B.Conc :10.0 %
B.Curve :0
PressMax :100 bar
PressMin :0 bar

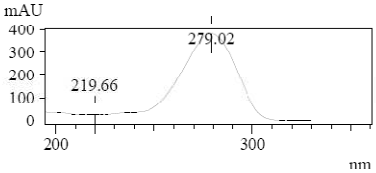
<<AutoSampler>>

Spectrum

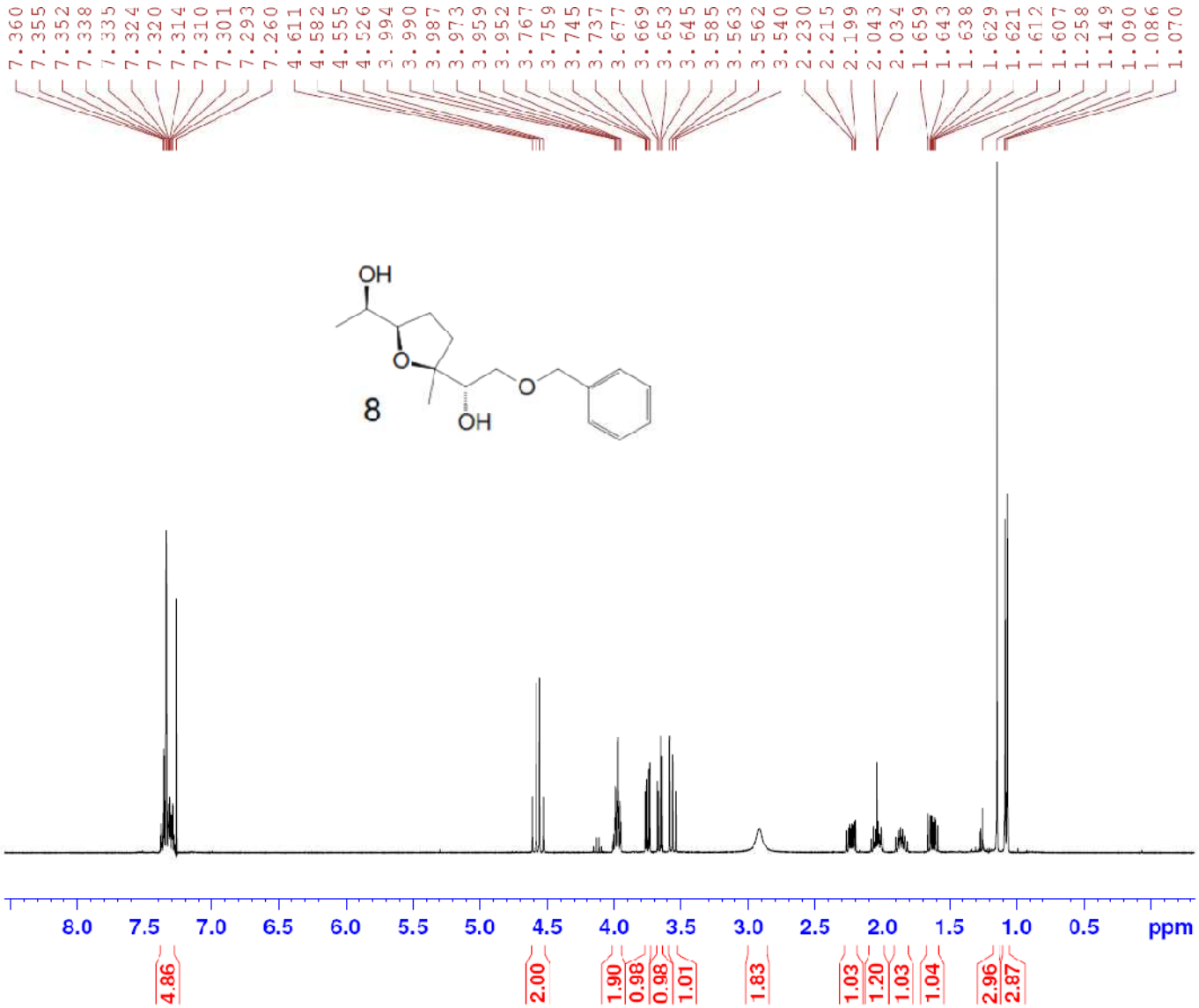
ID# : 1
Retention Time : 13.278
Compound Name : RT13.278
Spectrum Operation : None



ID# : 2
Retention Time : 17.967
Compound Name : RT17.967
Spectrum Operation : None



Name	Time	Area	Area%
RT	13.278	3810374	21.0022
RT	17.967	14332341	78.9978



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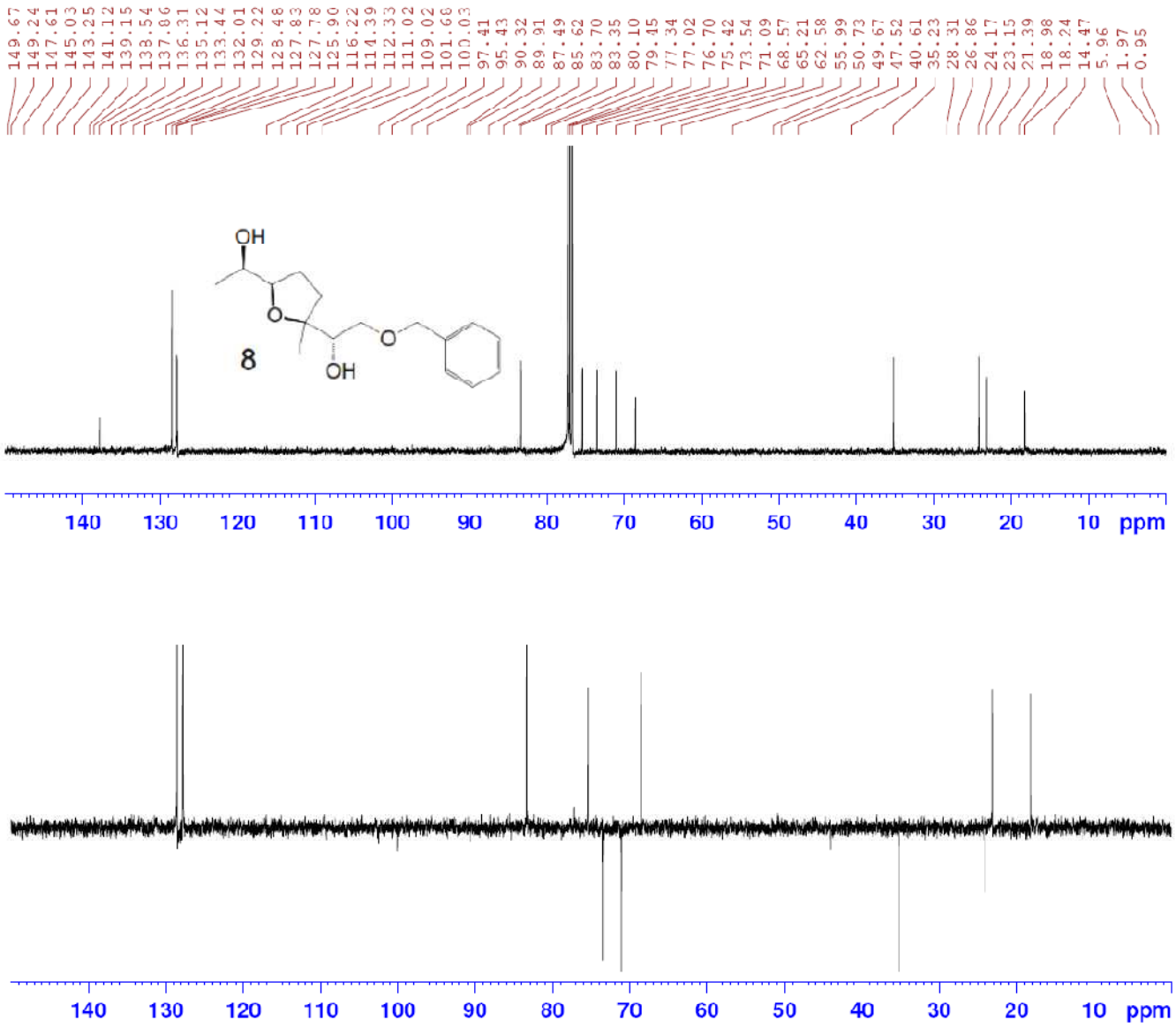
```
Current Data Parameters
NAME                  AA045
EXPNO                    36
PROCNO                    1

F2 - Acquisition Parameters
Date_              20120404
Time                  12.14
INSTRUM               spect
PROBHD    5 mm BBO BB-1H
PULPROG                zg30
TD                    32768
SOLVENT               CDCl3
NS                       64
DS                        0
SWH                6393.862 Hz
FIDRES            0.195125 Hz
AQ                2.5625076 sec
RG                      203
DW                   78.200 usec
DE                    6.00 usec
TE                   298.2 K
D1             5.00000000 sec
TD0                       1

-------- CHANNEL f1 --------
NUC1                     1H
P1                    14.35 usec
PL1                    0.00 dB
SFO1          400.1324710 MHz

F2 - Processing parameters
SI                    65536
SF            400.1300176 MHz
WDW                      EM
SSB                       0
LB                     0.30 Hz
GB                        0
PC                     1.00
```

Appendix 34



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INSTITUTE OF TECHNOLOGY

```
Current Data Parameters
NAME                  AA045
EXPNO                    37
PROCNO                    1

F2 - Acquisition Parameters
Date_              20120404
Time                  13.15
INSTRUM               spect
PROBHD    5 mm BBO BB-1H
PULPROG            zgpg30
TD                  65536
SOLVENT             CDCl3
NS                   1024
DS                      4
SWH           24038.461 Hz
FIDRES        0.366798 Hz
AQ            1.3631900 sec
RG                   32800
DW                20.800 usec
DE                 6.00 usec
TE                 298.1 K
D1            2.00000000 sec
d11           0.03000000 sec
DELTA         1.89999998 sec
TD0                       1

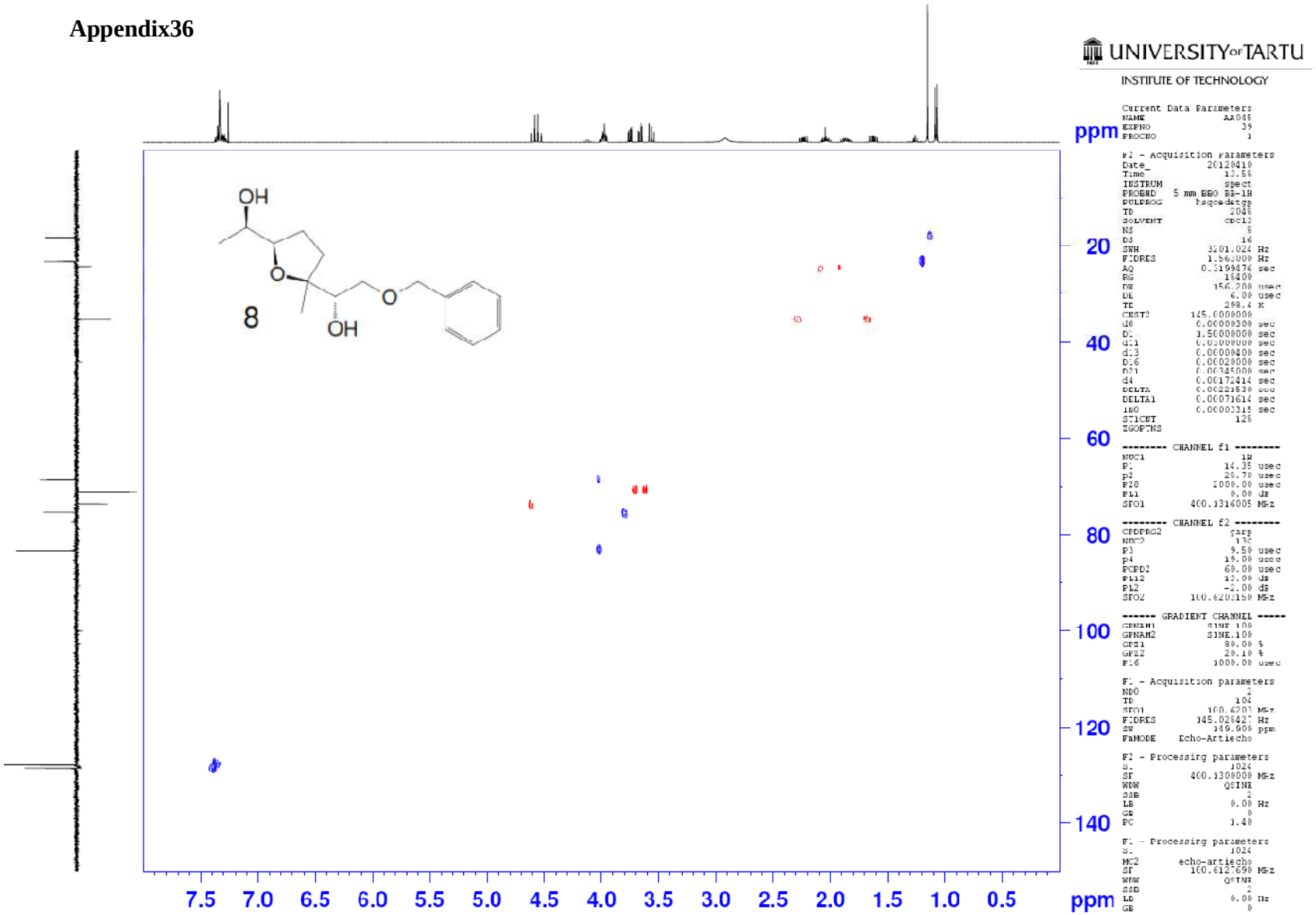
======== CHANNEL f1 ========
NUC1                   13C
P1                  9.50 usec
PL1                -2.00 dB
SFO1        100.6228298 MHz

======== CHANNEL f2 ========
CPDPRG2          waltz16
NUC2                   1H
PCPD2              70.00 usec
PL12               13.76 dB
PL13               14.00 dB
PL2                 0.00 dB
SFO2        400.1316005 MHz

F2 - Processing parameters
SI                  16384
SF          100.6127690 MHz
WDW                    EM
SSB                     0
LB                  1.00 Hz
GB                      0
PC                  1.40
```

Appendix35

Appendix36



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Current Data Parameters
NAME AA045
EXPNO 39
PROCNO 1

F2 - Acquisition Parameters
Date_ 20120410
Time 13.56
INSTRUM spect
PROBHD 5 mm BBO BB-1H
PULPROG hsqcedetgp
TD 2048
SOLVENT cdcl3
NS 8
DS 16
SWH 3201.024 Hz
FIDRES 1.562000 Hz
AQ 0.3199474 sec
RG 16400
DW 156.200 usec
DE 6.00 usec
TE 298.4 K
CNST2 145.0000000
D0 0.00000300 sec
D1 1.50000000 sec
D11 0.03000000 sec
d13 0.00004400 sec
D16 0.00020000 sec
D21 0.00345000 sec
d4 0.00172414 sec
DELTA 0.00221530 sec
DELTA1 0.00071614 sec
in0 0.00003315 sec
ST1CNT 126
ZGOPTNS

-------- CHANNEL f1 --------
NUC1 1H
P1 14.35 usec
p2 29.70 usec
P28 2000.00 usec
PL1 0.00 dB
SFO1 400.1316005 MHz

-------- CHANNEL f2 --------
CPDPRG2 garp
NUC2 13C
P3 9.50 usec
p4 19.00 usec
PCPD2 60.00 usec
PL12 13.00 dB
PL2 -2.00 dB
SFO2 100.6230150 MHz

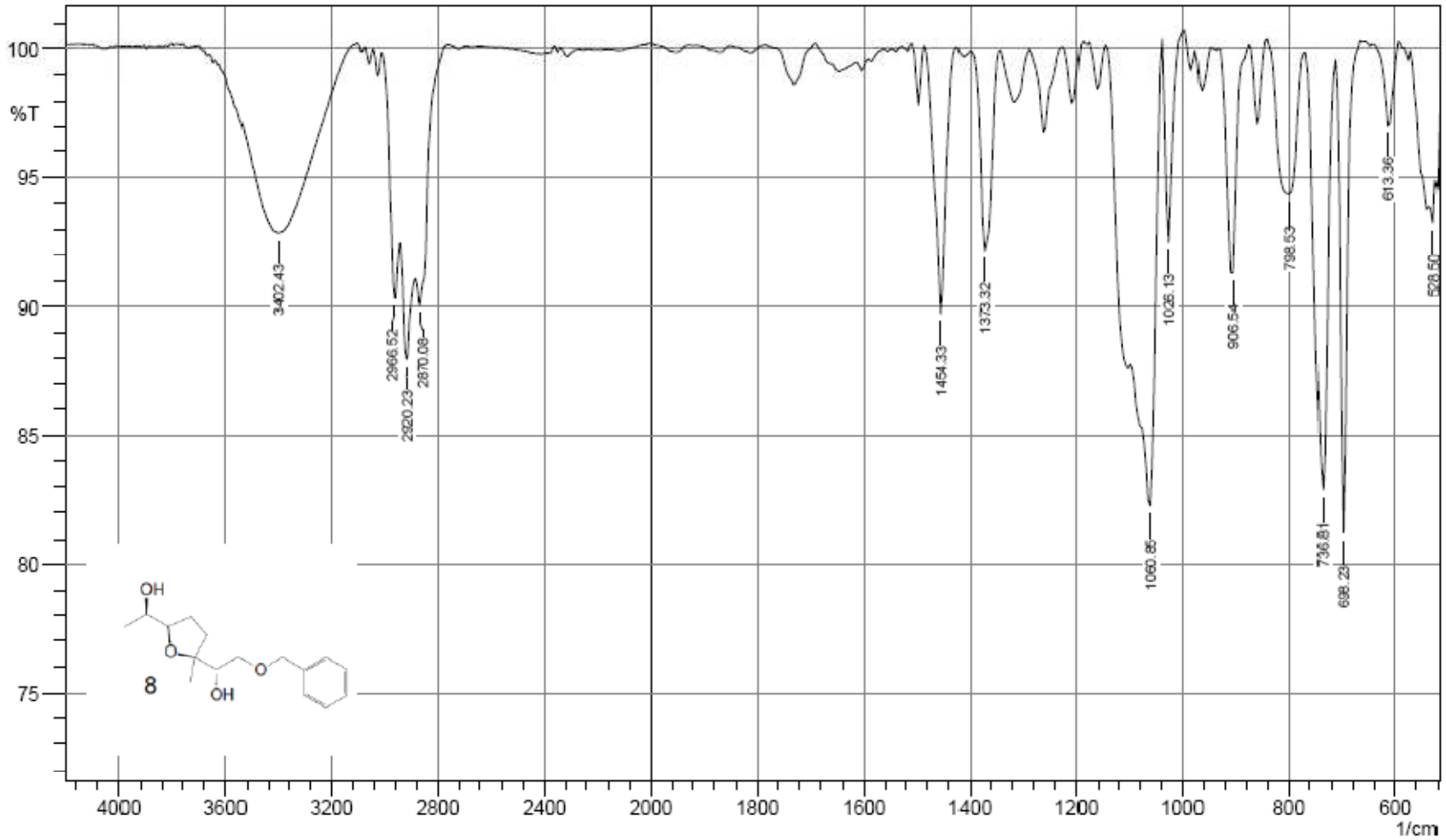
------ GRADIENT CHANNEL -----
GPNAM1 SINE.100
GPNAM2 SINE.100
GPZ1 80.00 %
GPZ2 20.10 %
P16 1000.00 usec

F1 - Acquisition parameters
ND0 2
TD 104
SFO1 100.6203 MHz
FIDRES 145.026427 Hz
SW 149.909 ppm
FnMODE Echo-Antiecho

F2 - Processing parameters
SI 1024
SF 400.1300000 MHz
WDW QSINE
SSB 2
LB 0.00 Hz
GB 0
PC 1.40

F1 - Processing parameters
SI 1024
MC2 echo-antiecho
SF 100.6127690 MHz
WDW QSINE
SSB 2
LB 0.00 Hz
GB 0

SHIMADZU



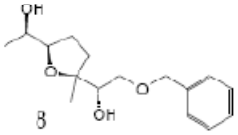
Comment: **Appendix37**

No. of Scans:
Resolution:
Apodization:

Date/Time: 5/31/2012 4:10:32 PM
User: Agilent

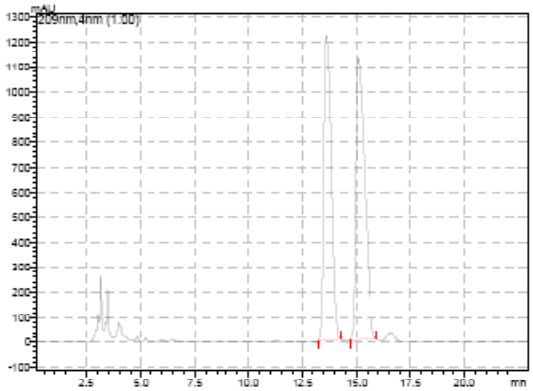
==== Shimadzu LCMSsolution Analysis Report ====

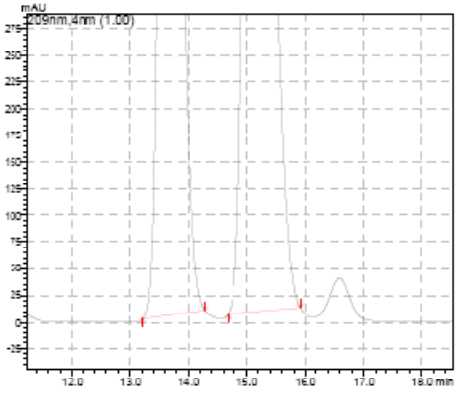
Acquired by	: Admin
Sample Name	: AA045_reference
Sample ID	:
Vail #	: 96
Injection Volume	: 10 uL
Data File Name	: 20120326_R45_reference6.lcd
Method File Name	: Kiraalne-LUX_Hexanes-2PrOH_20100525.lcm
Batch File Name	: 20120323_LV_8.lcb
Report File Name	: DefaultLCMS.lcr
Data Acquired	: 26.03.2012 14:00:43
Data Processed	: 3.05.2012 15:56:23



Appendix38

<Chromatogram>





Method

<<Comment>>
<<System Controller>>

SCL Type	:CBM-20A
Power On	:ON
Event1	:OFF
Event2	:OFF
Event3	:OFF
Event4	:OFF

<<Data Acquisition>>

LC Stop Time	:60.00 min
AD2 Detector	
Name	:ELSD
--FDA Detector--	
Name	:PDA
Sampling Frequency	:1.5625 Hz
Start Time	:0.00 min
End Time	:100.00 min
Constant	:0.640 sec

<<Option Box A>>

<<Option Box B>>

<<Pump>>

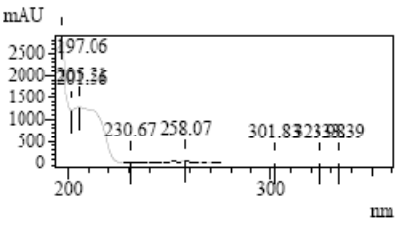
Pump Mode	:Binary gradient
Pump A	:LC-20AD
Pump B	:LC-20AD
Total Flow	:1.0000 mL/min
B.Conc	:10.0 %
B.Curve	:0
PressMax	:100 bar
PressMin	:0 bar

<<AutoSampler>>

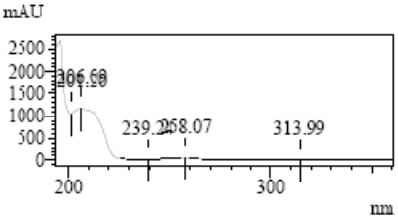
AutoSampler	:SIL-20A
Use AutoSampler	:Use
Sample Rack	:Rack 1.5mL
Rinsing Volume	:200 uL

Spectrum

ID# : 1
Retention Time : 13.599
Compound Name : RT13.599
Spectrum Operation : None



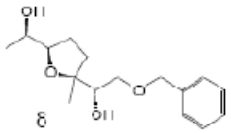
ID# : 2
Retention Time : 15.053
Compound Name : RT15.053
Spectrum Operation : None



Name	Time	Area	Area%
RT	13.599	29048738	47.2752
RT	15.053	32397338	52.7248

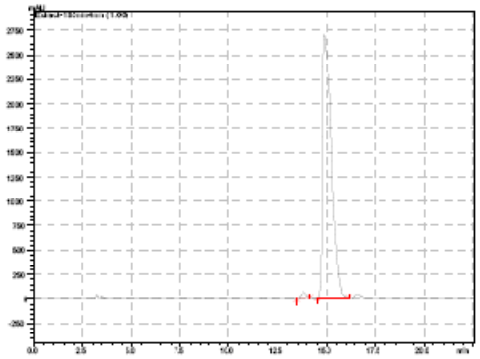
==== Shimadzu LCMSsolution Analysis Report ====

Acquired by	: Admin
Sample Name	: AA_45_cis isomer
Sample ID	:
Vail #	: 96
Injection Volume	: 10 uL
Data File Name	: 20120404_AA_R45_cis_isomer.lcd
Method File Name	: Kiraalne-LUX_Hexanes-2PrOH_20100525.lcm
Batch File Name	: 20120323_LV_8.lcb
Report File Name	: DefaultLCMS.lcr
Data Acquired	: 4.04.2012 11:58:13
Data Processed	: 3.05.2012 15:59:17

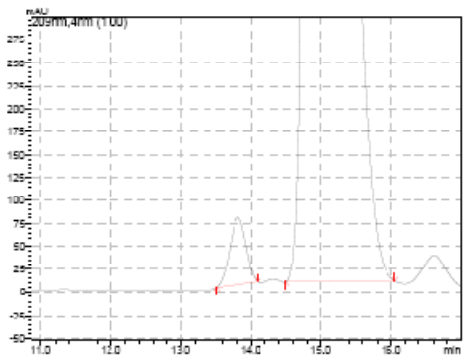


Appendix39

<Chromatogram>



Method



Spectrum

Name	Time	Area	Area%
RT	13.806	1138203	2.0530
RT	14.842	54302198	97.947(

<<Comment>>
<<System Controller>>

SCL Type	:CBM-20A
Power On	:ON
Event1	:OFF
Event2	:OFF
Event3	:OFF
Event4	:OFF

<<Data Acquisition>>

LC Stop Time	:60.00 min
--ADJ Detector--	
Name	:ELSD
--PDA Detector--	
Name	:PDA
Sampling Frequency	:1.5525 Hz
Start Time	:0.00 min
End Time	:100.00 min
Constant	:0.640 sec

<<Option Box A>>

<<Option Box B>>

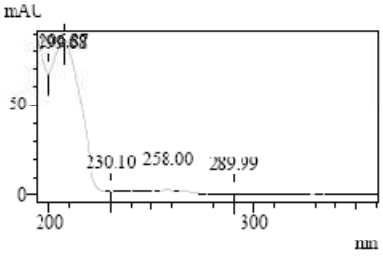
<<Pump>>

Pump Mode	:Binary gradient
Pump A	:LC-20AD
Pump B	:LC-20AD
Total Flow	:1.0000 mL/min
B.Conc	:10.0 %
B.Curve	:0
PressMax	:100 bar
PressMin	:0 bar

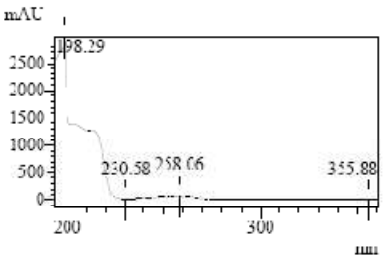
<<AutoSampler>>

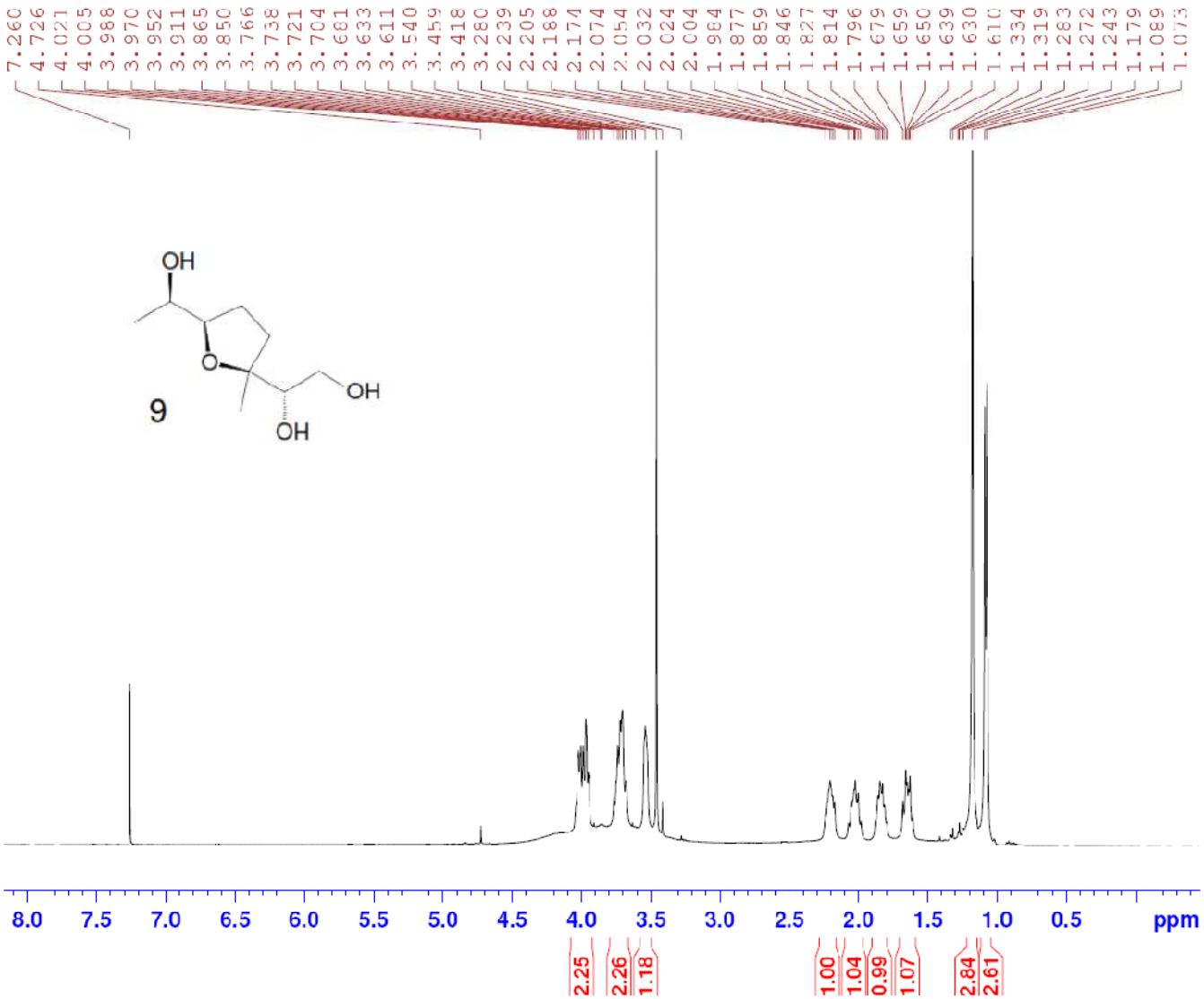
AutoSampler	:SIL-20A
Use AutoSampler	:Use
Sample Rack	:Rack 1.5mL 1(
Rinsing Volume	:200 uL
Needle Stroke	:52 mm
Control Vial Needle Stroke	:52 mm
Rinsing Speed	:35 uL/sec
Sampling Speed	:15 uL/sec

ID# : 1
Retention Time : 13.306
Compound Name : RT13.806
Spectrum Operation : None



ID# : 2
Retention Time : 14.842
Compound Name : RT14.842
Spectrum Operation : None





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INSTITUTE OF TECHNOLOGY

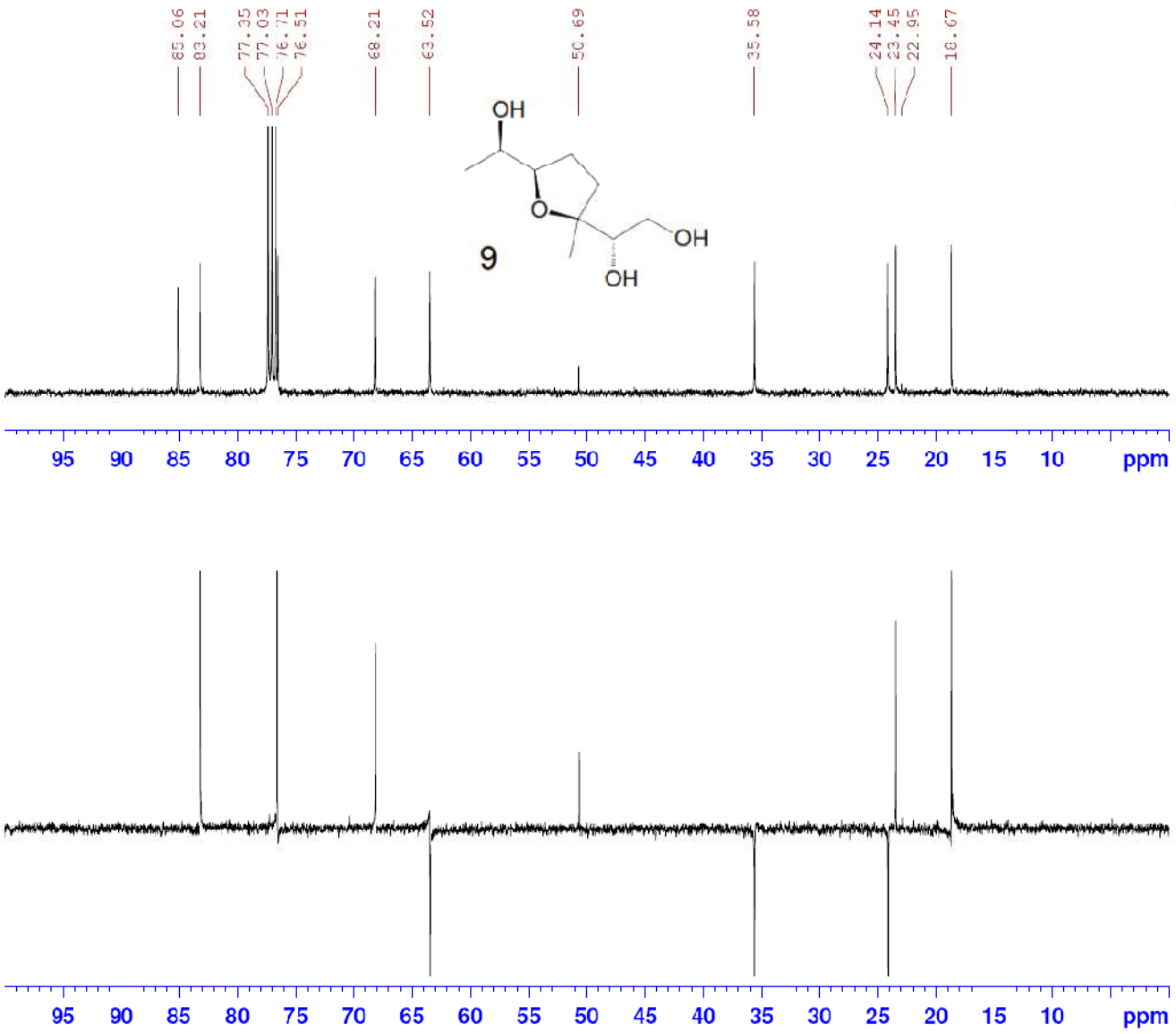
```
Current Data Parameters
NAME                  AA046
EXPNO                     2
PROCNO                    1

F2 - Acquisition Parameters
Date                20120417
Time                   15.30
INSTRUM                spect
PROBHD    5 mm BBO BB-1H
PULPROG                zg30
TD                    32768
SOLVENT               CDCl3
NS                       64
DS                        0
SWH                6393.862 Hz
FIDRES             0.195125 Hz
AQ                 2.5625076 sec
RG                      144
DW                  78.200 usec
DE                   6.00 usec
TE                  298.2 K
D1                5.00000000 sec
TD0                       1

======== CHANNEL f1 ========
NUC1                      1H
P1                   14.35 usec
PL1                   0.00 dB
SFO1          400.1324710 MHz

F2 - Processing parameters
SI                        65536
SF            400.1300175 MHz
WDW                      EM
SSB                       0
LB                    0.30 Hz
GB                        0
PC                    1.00
```

Appendix40



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Current Data Parameters

NAME	AA046
EXPNO	3
PROCNO	1

F2 - Acquisition Parameters

Date	20120417
Time	16.32
INSTRUM	spect
PROBHD	5 mm BBO BB-1H
PULPROG	zgpg30
TD	65536
SOLVENT	CDCl3
NS	1024
DS	4
SWH	24038.461 Hz
FIDRES	0.366798 Hz
AQ	1.3631988 sec
RG	32800
DW	20.800 usec
DE	6.00 usec
TE	298.1 K
D1	2.00000000 sec
d11	0.03000000 sec
DELTA	1.89999998 sec
TD0	1

======== CHANNEL f1 ========

NUC1	13C
P1	9.50 usec
PL1	2.00 dB
SFO1	100.6228298 MHz

======== CHANNEL f2 ========

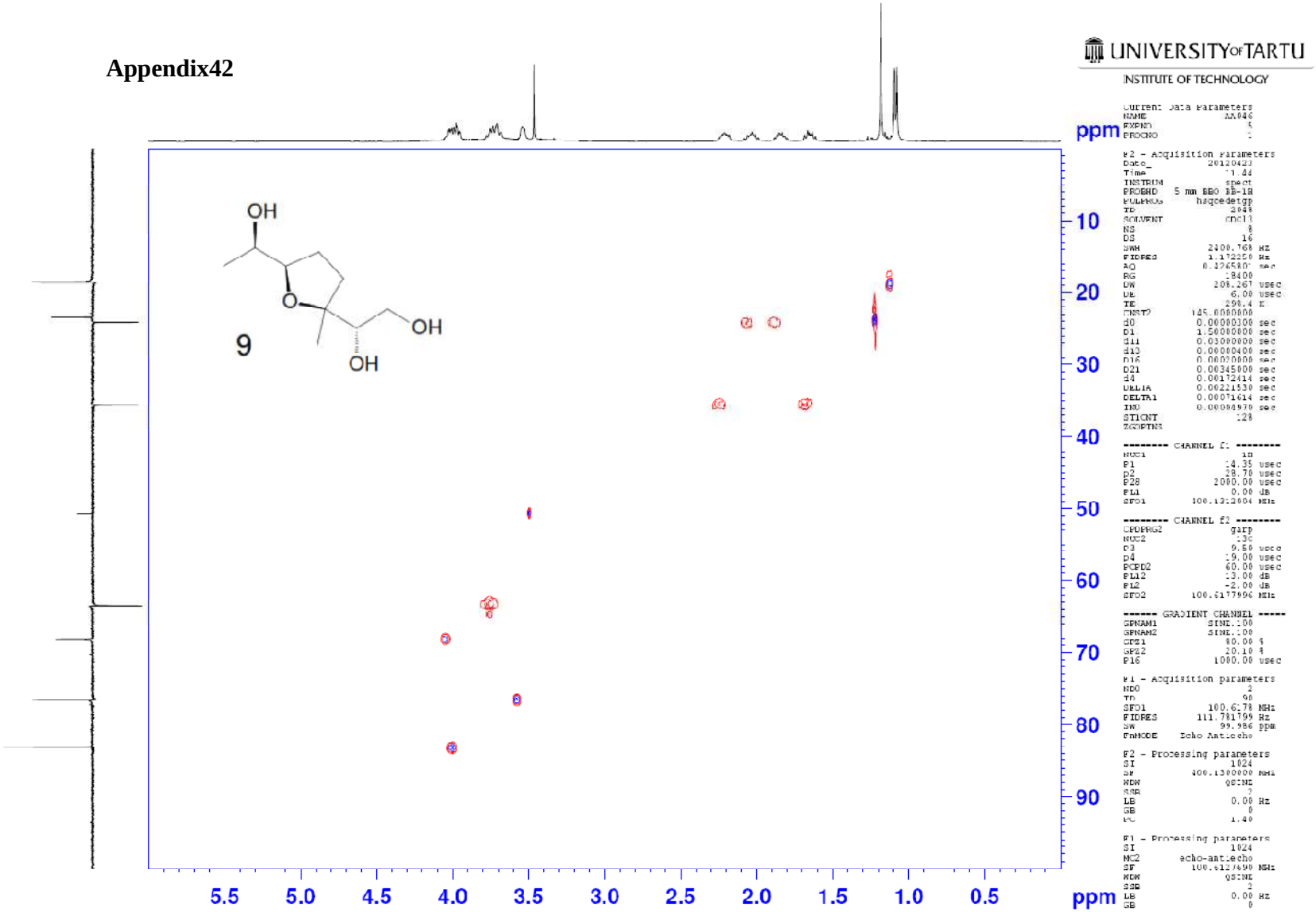
CPDPRG2	waltz16
NUC2	1H
PCPD2	70.00 usec
PL12	13.76 dB
PL13	14.00 dB
PL2	0.00 dB
SFO2	400.1316005 MHz

F2 - Processing parameters

SI	16384
SF	100.6127690 MHz
WDW	EM
SSB	0
LB	1.00 Hz
GB	0
PC	1.40

Appendix41

Appendix42



UNIVERSITY OF TARTU
INSTITUTE OF TECHNOLOGY

```
Current Data Parameters
NAME                  AA046
EXPNO                     5
PROCNO                    1

F2 - Acquisition Parameters
Date_              20120423
Time                  11.44
INSTRUM                spect
PROBHD   5 mm BBO BB-1H
PULPROG        hsqcedetgp
TD                     2048
SOLVENT               CDCl3
NS                        8
DS                       16
SWH                2400.768 Hz
FIDRES             1.172250 Hz
AQ                 0.1706480 sec
RG                      8400
DW                  208.267 usec
DE                    6.00 usec
TE                  298.4 K
CNST2              145.0000000
d0                 0.00000300 sec
D1                 1.50000000 sec
d11                0.03000000 sec
d13                0.00000400 sec
D16                0.00020000 sec
D21                0.00345000 sec
d4                 0.00172414 sec
DELTA1A            0.00221530 sec
DELTA1             0.00071614 sec
INO                0.00004970 sec
STSCNT                    128
ZGOPTNS

======== CHANNEL f1 ========
NUC1                      1H
P1                     14.35 usec
p2                     28.70 usec
P28                 2000.00 usec
PL1                    0.00 dB
SFO1            100.1212604 MHz

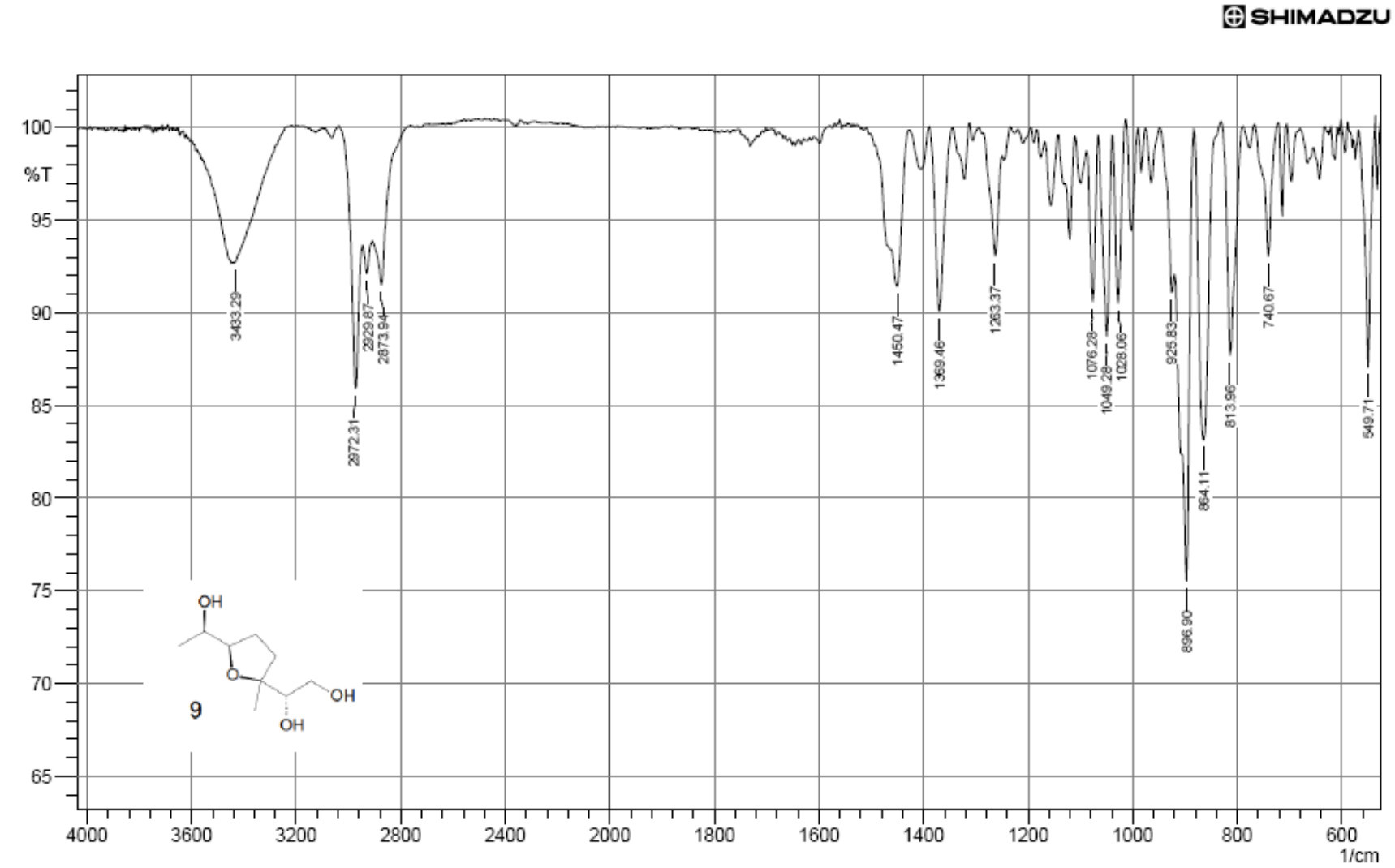
======== CHANNEL f2 ========
CPDPRG2                garp
NUC2                     13C
P3                     9.50 usec
p4                    19.00 usec
PCPD2                 80.00 usec
PL12                  13.00 dB
PL2                   -2.00 dB
SFO2            100.5177996 MHz

====== GRADIENT CHANNEL =====
GPNAM1               SINE.200
GPNAM2               SINE.100
GPZ1                  80.00 %
GPZ2                  20.10 %
P16                 1000.00 usec

F1 - Acquisition parameters
ND0                       2
TD                       96
SFO1            100.6278 MHz
FIDRES          111.781799 Hz
SW                 99.986 ppm
FnMODE     Echo Antiecho

F2 - Processing parameters
SI                     1024
SF              400.1300000 MHz
WDW                    QSINE
SSB                       2
LB                     0.00 Hz
GB                        0
PC                     1.40

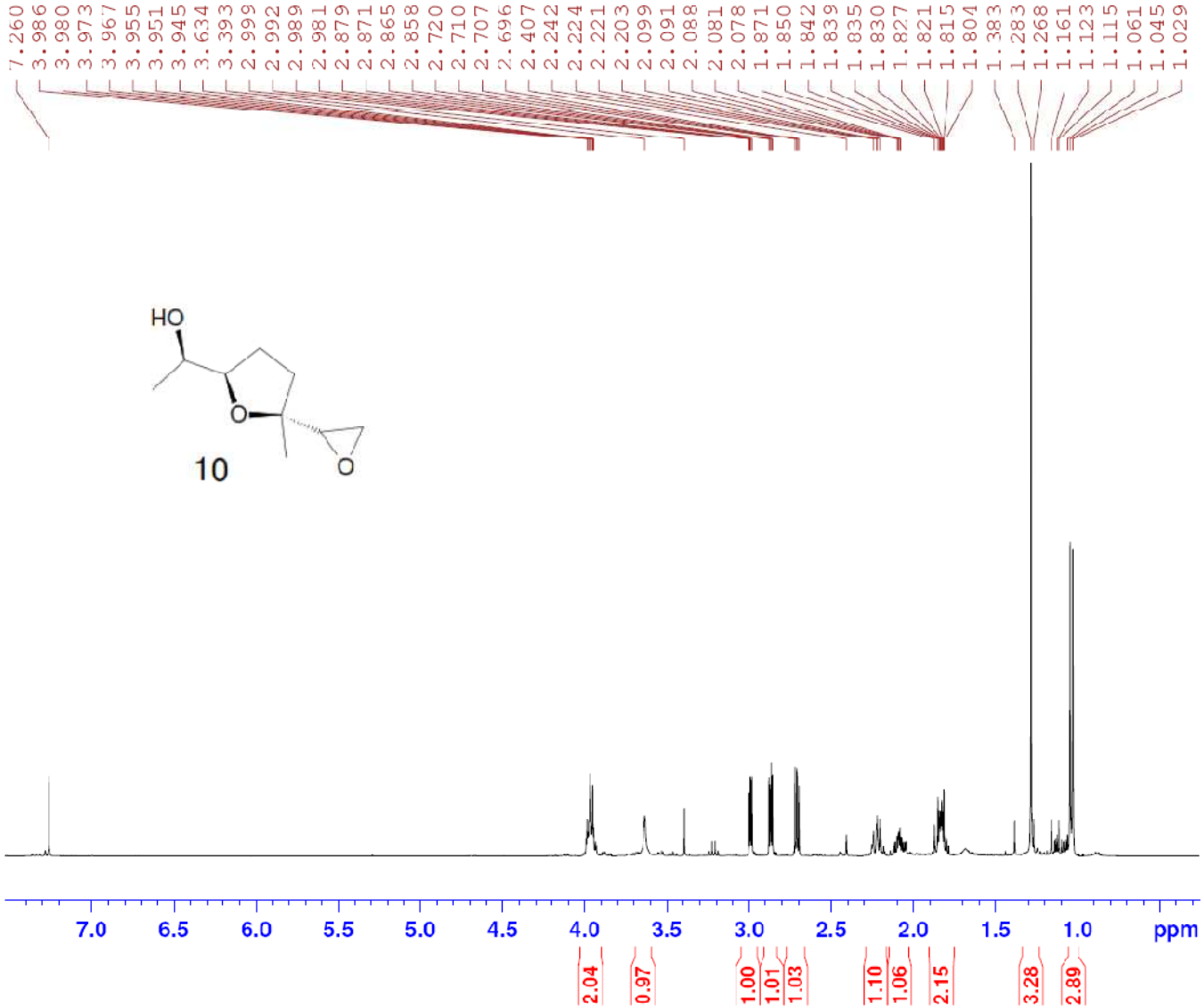
F1 - Processing parameters
SI                     1024
MC2          echo-antiecho
SF              100.6127690 MHz
WDW                    QSINE
SSB                       2
LB                     0.00 Hz
GB                        0
```



Comment; **Appendix43**

No. of Scans;
Resolution;
Apodization;

Date/Time; 4/23/2012 3:17:36 PM
User; Agilent



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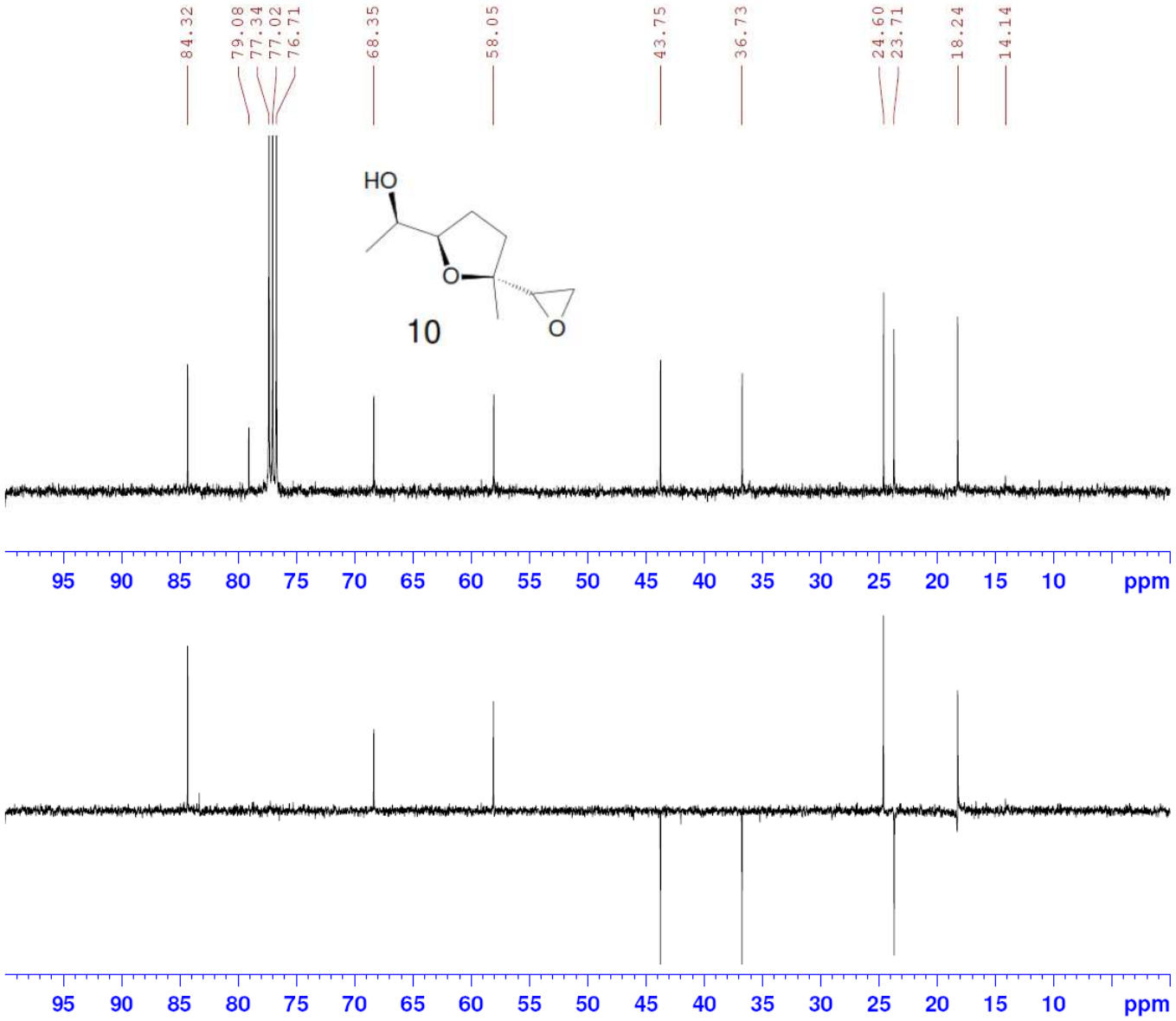
```
Current Data Parameters
NAME                  AA048
EXPNO                     2
PROCNO                    1

F2 - Acquisition Parameters
Date_              20120423
Time                  15.37
INSTRUM               spect
PROBHD    5 mm BBO BB-1H
PULPROG               zg30
TD                   32768
SOLVENT              CDCl3
NS                      64
DS                       0
SWH               6393.862 Hz
FIDRES           0.195125 Hz
AQ               2.5625076 sec
RG                     161
DW                78.200 usec
DE                 6.00 usec
TE                298.2 K
D1             5.00000000 sec
TD0                      1

======== CHANNEL f1 ========
NUC1                   1H
P1                 14.35 usec
PL1                 0.00 dB
SFO1          400.1324710 MHz

F2 - Processing parameters
SI                   65536
SF            400.1300175 MHz
WDW                     EM
SSB                      0
LB                  0.30 Hz
GB                       0
PC                    1.00
```

Appendix44



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```
Current Data Parameters
NAME                  AA048
EXPNO                     3
PROCNO                    1

F2 - Acquisition Parameters
Date_              20120424
Time                  10.47
INSTRUM               spect
PROBHD   5 mm BBO BB-1H
PULPROG             zgpg30
TD                   65536
SOLVENT              CDCl3
NS                     356
DS                       4
SWH             24038.461 Hz
FIDRES           0.366798 Hz
AQ               1.3631988 sec
RG                   32800
DW                  20.800 usec
DE                   6.00 usec
TE                  298.2 K
D1              2.00000000 sec
d11             0.03000000 sec
DELTA           1.89999998 sec
TD0                      1

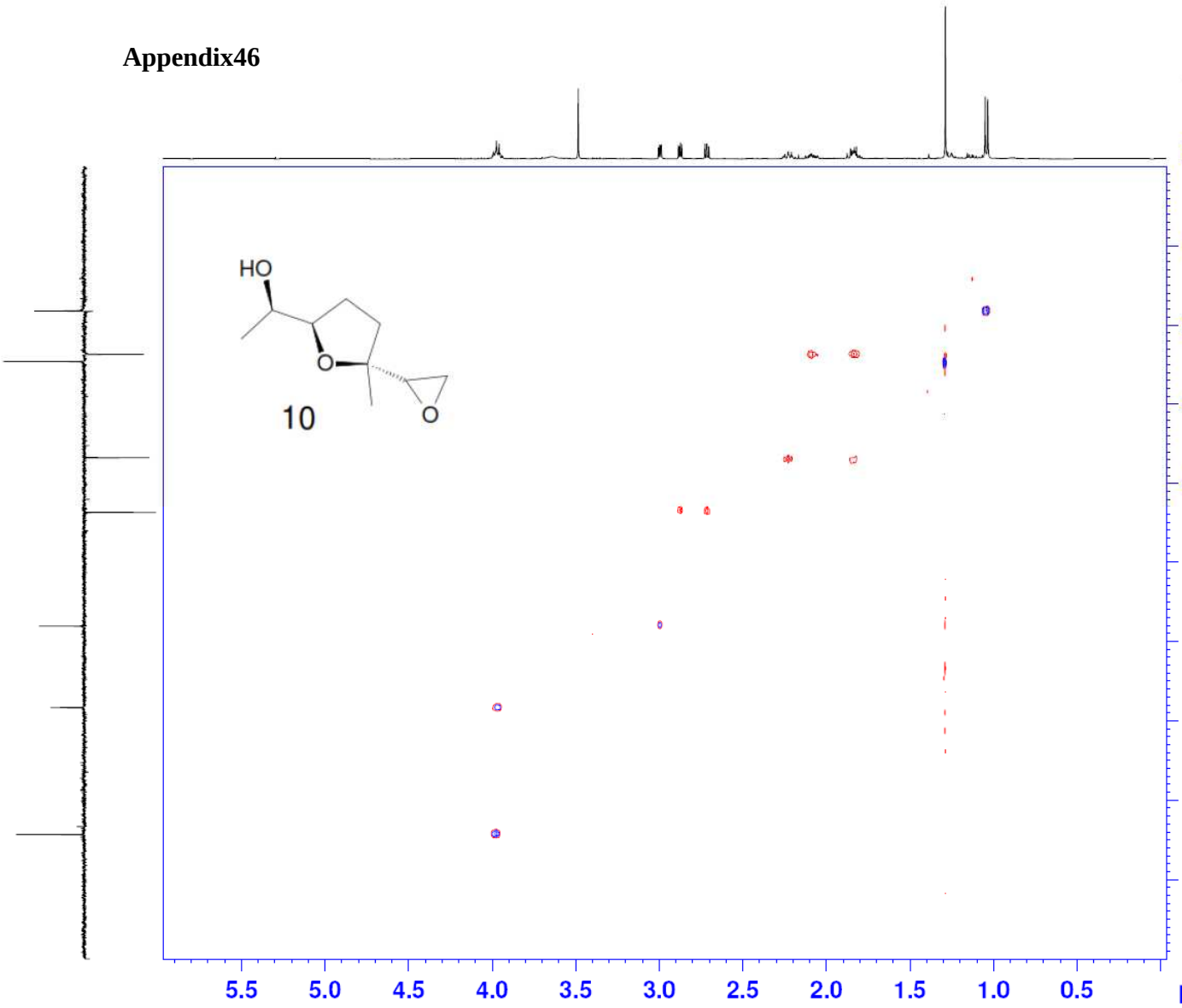
======== CHANNEL f1 ========
NUC1                   13C
P1                    9.50 usec
PL1                  -2.00 dB
SFO1          100.6228298 MHz

======== CHANNEL f2 ========
CPDPRG2          waltz16
NUC2                   1H
PCPD2                70.00 usec
PL12                 13.76 dB
PL13                 14.00 dB
PL2                   0.00 dB
SFO2          400.1316005 MHz

F2 - Processing parameters
SI                   16384
SF            100.6127690 MHz
WDW                     EM
SSB                      0
LB                    1.00 Hz
GB                       0
PC                    1.40
```

Appendix45

Appendix46



UNIVERSITY OF TARTU
INSTITUTE OF TECHNOLOGY

```
Current Data Parameters
NAME                  AA048
EXPNO                     5
PROCNO                    1

F2 - Acquisition Parameters
Date_              20120424
Time                  15.24
INSTRUM                spect
PROBHD   5 mm BBO BB-1H
PULPROG        hsqcedetgp
TD                     2048
SOLVENT                CDCl3
NS                        8
DS                       16
SWH               2400.768 Hz
FIDRES               1.172250 Hz
AQ                0.4265801 sec
RG                     18400
DW                  208.267 usec
DE                    6.00 usec
TE                  298.3 K
CNST2             145.0000000
d0                0.00000300 sec
D1                1.50000000 sec
d11               0.03000000 sec
d13               0.00000400 sec
D16               0.00020000 sec
D21               0.00345000 sec
d4                0.00172414 sec
DELTA             0.00221530 sec
DELTA1            0.00071614 sec
IN0               0.00004970 sec
ST1CNT                   128
ZGOPTNS

-------- CHANNEL f1 --------
NUC1                      1H
P1                     14.35 usec
p2                     28.70 usec
P28                  2000.00 usec
PL1                     0.00 dB
SFO1           400.1312004 MHz

-------- CHANNEL f2 --------
CPDPRG2                 garp
NUC2                      13C
P3                      9.50 usec
p4                     19.00 usec
PCPD2                  60.00 usec
PL12                   13.00 dB
PL2                    -2.00 dB
SFO2           100.6177996 MHz

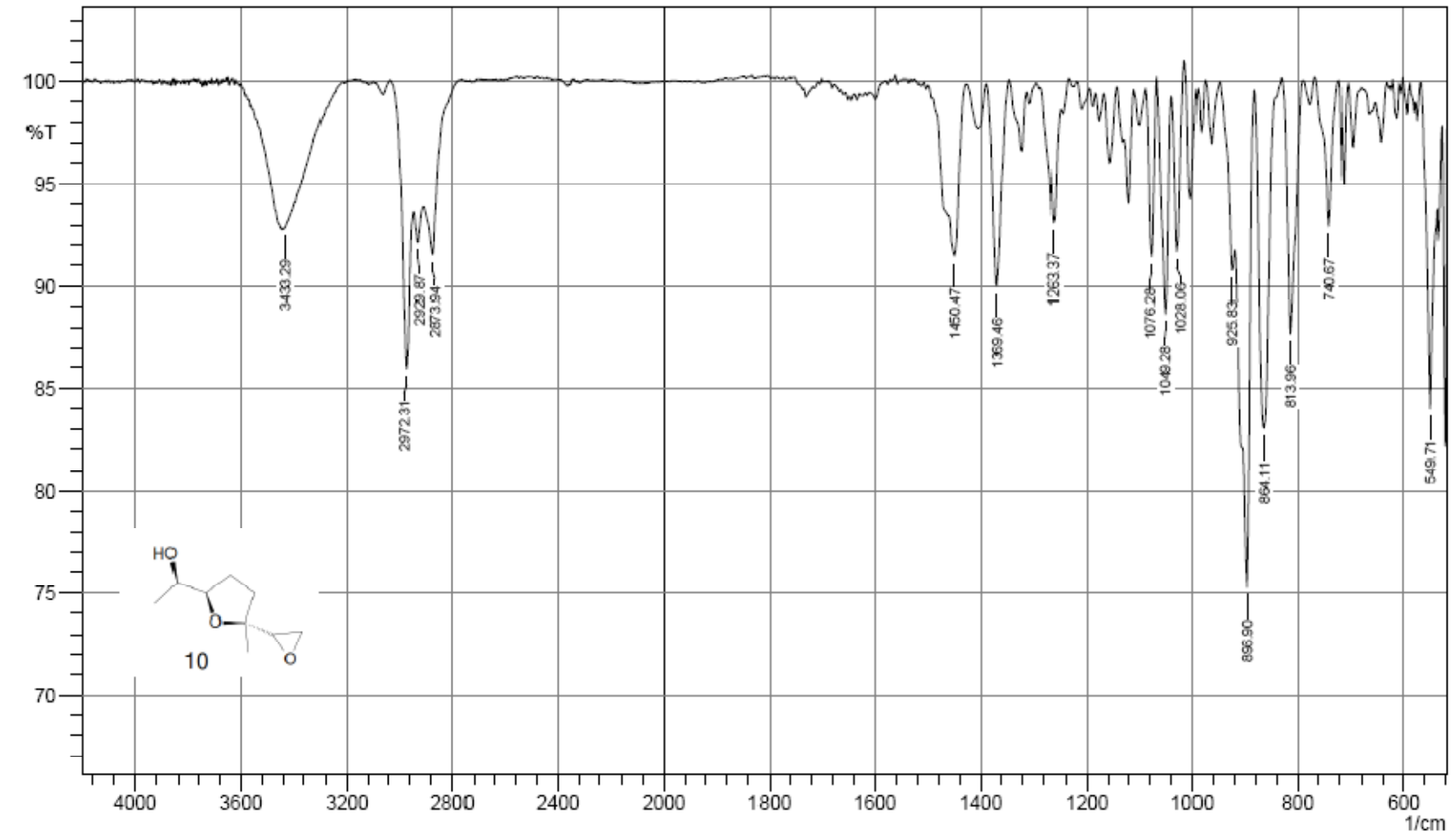
------ GRADIENT CHANNEL -----
GPNAM1               SINE.100
GPNAM2               SINE.100
GPZ1                   80.00 %
GPZ2                   20.10 %
P16                  1000.00 usec

F1 - Acquisition parameters
ND0                       2
TD                      128
SFO1             100.6178 MHz
FIDRES            78.596581 Hz
SW                   99.986 ppm
FnMODE     Echo-Antiecho

F2 - Processing parameters
SI                     1024
SF             400.1300132 MHz
WDW                   QSINE
SSB                       2
LB                     0.00 Hz
GB                        0
PC                     1.40

F1 - Processing parameters
SI                     1024
MC2          echo-antiecho
SF             100.6127690 MHz
WDW                   QSINE
SSB                       2
LB                     0.00 Hz
GB                        0
```

SHIMADZU

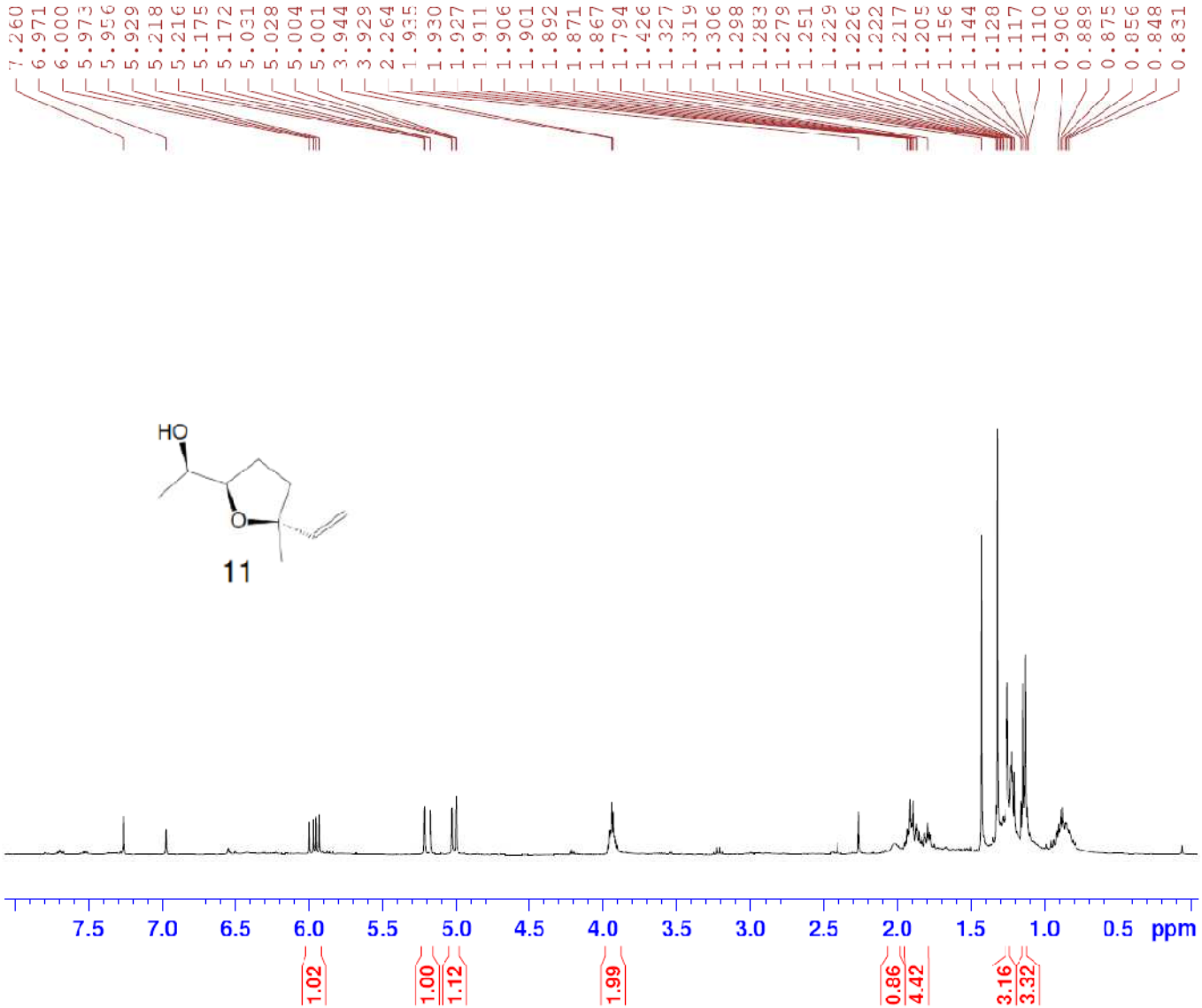


Comment;

Appendix47

No. of Scans;
Resolution;
Apodization;

Date/Time; 4/23/2012 3:17:36 PM
User; Agilent



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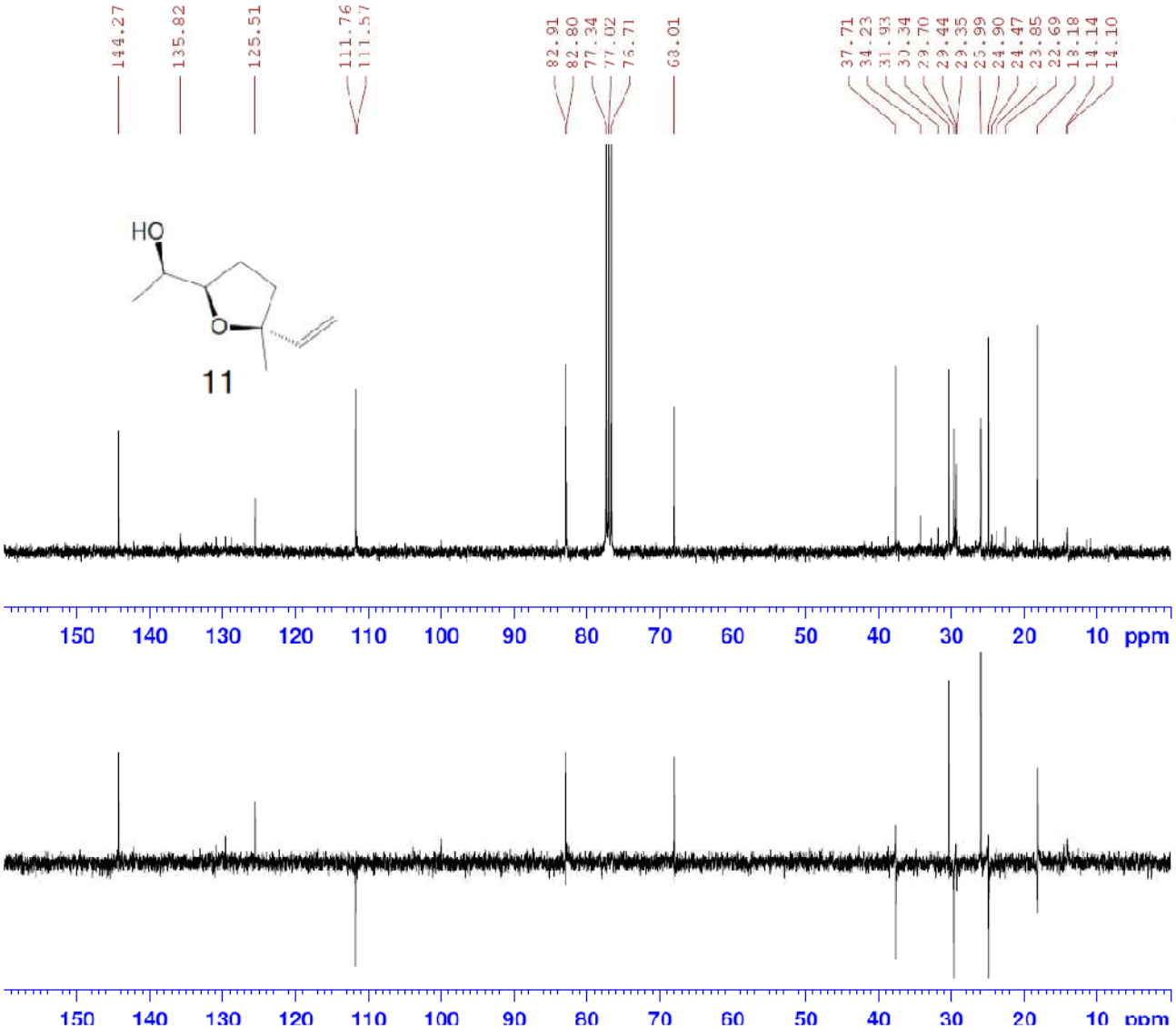
```
Current Data Parameters
NAME                  AA049
EXPNO                    10
PROCNO                    1

F2 - Acquisition Parameters
Date_              20120504
Time                  12.49
INSTRUM               spect
PROBHD    5 mm BBO BB-1H
PULPROG                zg30
TD                    32768
SOLVENT               CDCl3
NS                       64
DS                        0
SWH                6393.862 Hz
FIDRES            0.195125 Hz
AQ                2.5625076 sec
RG                     90.5
DW                  78.200 usec
DE                   6.00 usec
TE                  298.2 K
D1               5.00000000 sec
TD0                       1

======== CHANNEL f1 ========
NUC1                      1H
P1                   14.35 usec
PL1                   0.00 dB
SFO1          400.1324710 MHz

F2 - Processing parameters
SI                    65536
SF            400.1300176 MHz
WDW                      EM
SSB                       0
LB                    0.30 Hz
GB                        0
PC                     1.00
```

Appendix48



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Current Data Parameters

NAME	AA049
EXPNO	11
PROCNO	1

F2 - Acquisition Parameters

Date_	20120504
Time	13.02
INSTRUM	spect
PROBHD	5 mm BBO BB-1H
PULPROG	zgpg30
TD	65536
SOLVENT	CDCl3
NS	575
DS	4
SWH	24038.461 Hz
FIDRES	0.366798 Hz
AQ	1.3631988 sec
RG	32800
DW	20.800 usec
DE	6.00 usec
TE	298.2 K
D1	2.00000000 sec
d11	0.03000000 sec
DELTA	1.89999990 sec
TD0	1

======== CHANNEL f1 ========

NUC1	13C
P1	9.50 usec
PL1	-2.00 dB
SFO1	100.6228298 MHz

-------- CHANNEL f2 --------

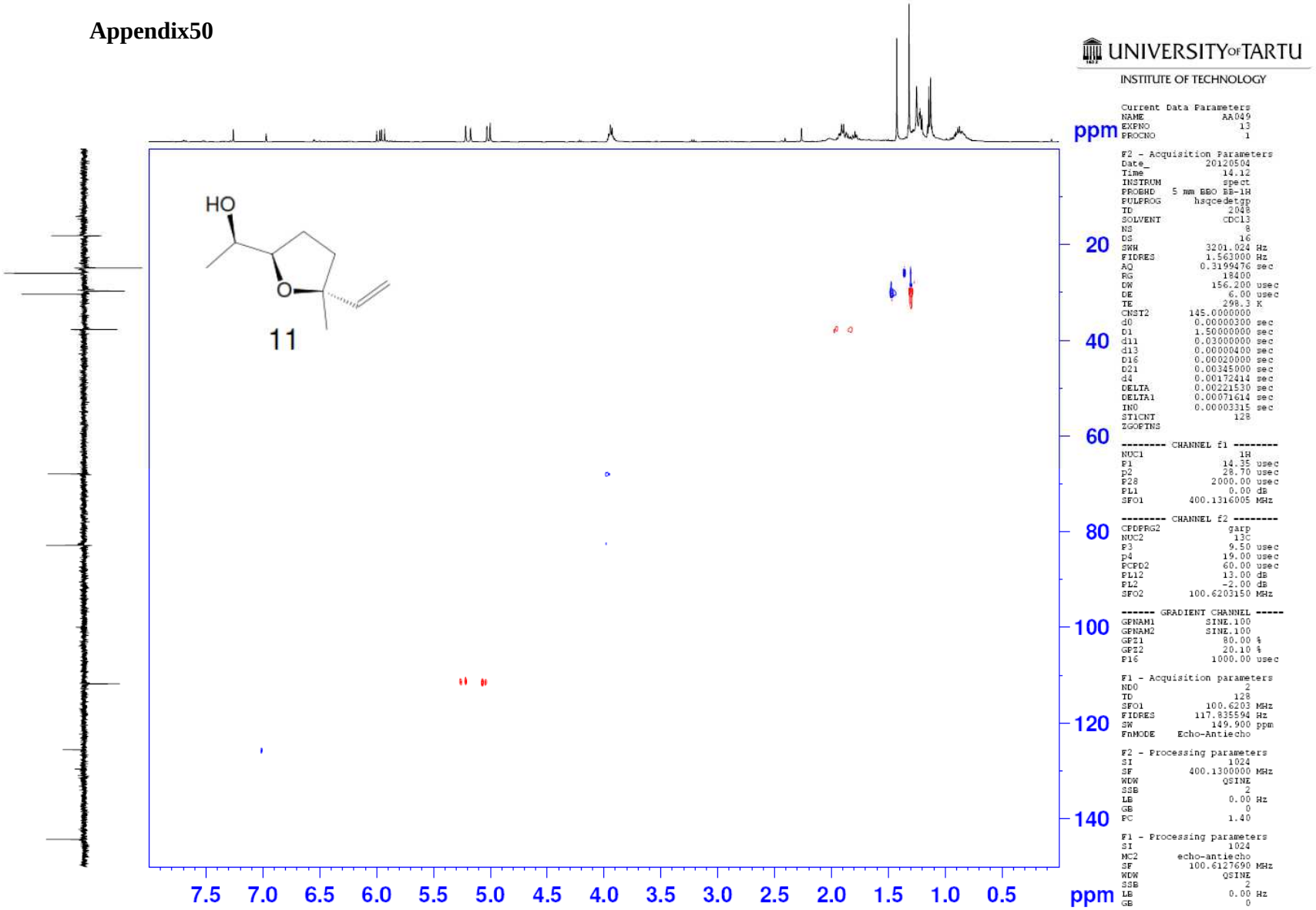
CPDPRG2	waltz16
NUC2	1H
PCPD2	70.00 usec
PL12	13.76 dB
PL13	14.00 dB
PL2	0.00 dB
SFO2	400.316005 MHz

F2 - Processing parameters

SI	16384
SF	100.6127690 MHz
WDW	EM
SSB	0
LB	1.00 Hz
GB	0
PC	1.40

Appendix49

Appendix50



UNIVERSITY OF TARTU
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```
Current Data Parameters
NAME                  AA049
EXPNO                    13
PROCNO                    1

F2 - Acquisition Parameters
Date_              20120504
Time                 14.12
INSTRUM              spect
PROBHD    5 mm BBO BB-1H
PULPROG       hsqcedetgp
TD                   2048
SOLVENT              CDCl3
NS                      8
DS                     16
SWH               3201.024 Hz
FIDRES            1.563000 Hz
AQ                0.3199476 sec
RG                   18400
DW                 156.200 usec
DE                   6.00 usec
TE                  298.3 K
CNST2         145.0000000
d0             0.00000300 sec
D1             1.50000000 sec
d11            0.03000000 sec
d13            0.00000400 sec
D16            0.00020000 sec
D21            0.00345000 sec
d4             0.00172414 sec
DELTA          0.00221530 sec
DELTA1         0.00071614 sec
IN0            0.00003315 sec
ST1CNT               128
ZGOPTNS

-------- CHANNEL f1 --------
NUC1                  1H
P1                 14.35 usec
p2                 28.70 usec
P28              2000.00 usec
PL1                0.00 dB
SFO1         400.1316005 MHz

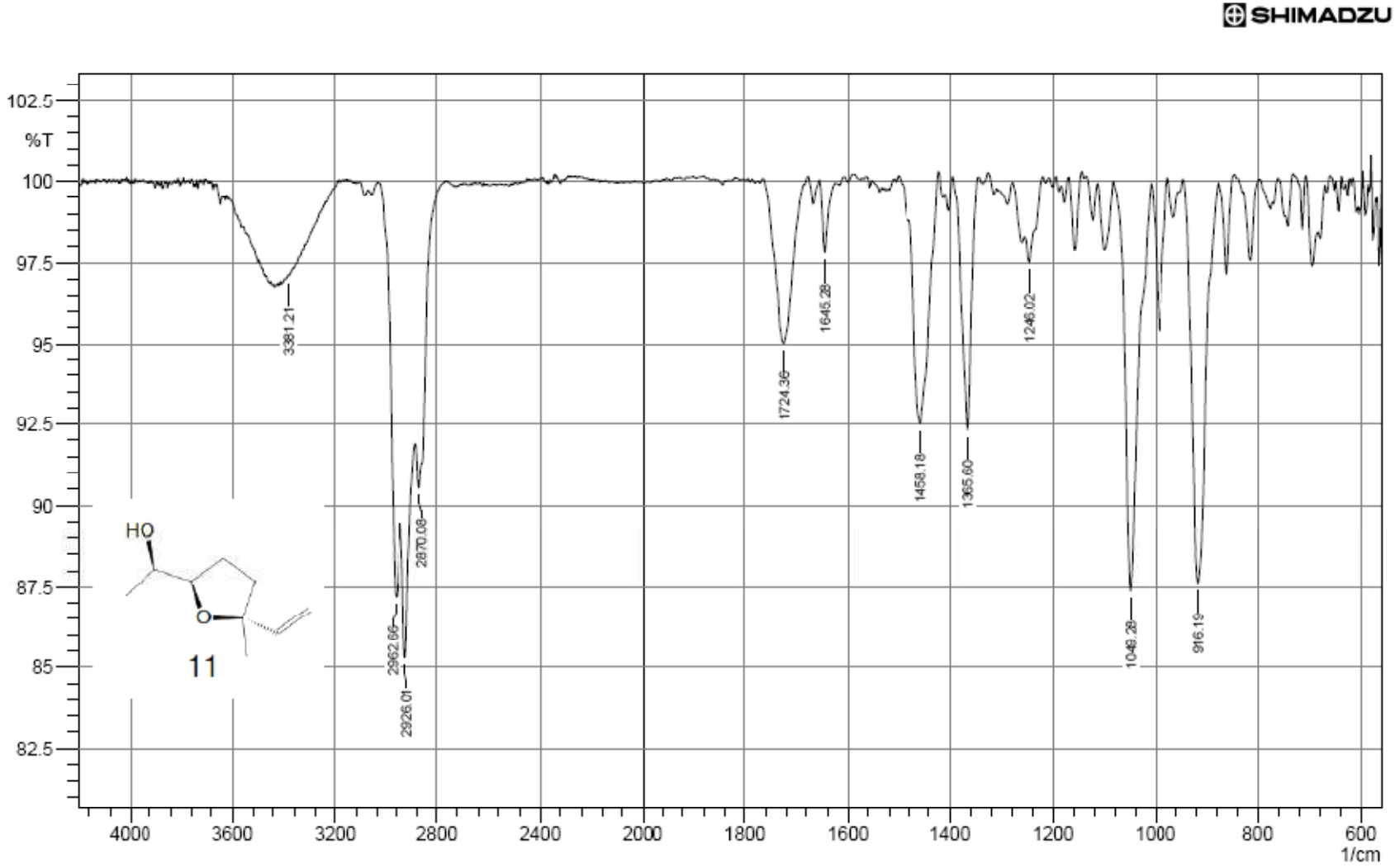
-------- CHANNEL f2 --------
CPDPRG2              garp
NUC2                  13C
P3                  9.50 usec
p4                 19.00 usec
PCPD2              60.00 usec
PL12               13.00 dB
PL2                -2.00 dB
SFO2         100.6203150 MHz

------ GRADIENT CHANNEL -----
GPNAM1          SINE.100
GPNAM2          SINE.100
GPZ1               80.00 %
GPZ2               20.10 %
P16              1000.00 usec

F1 - Acquisition parameters
ND0                    2
TD                   128
SFO1          100.6203 MHz
FIDRES        117.835594 Hz
SW               149.900 ppm
FnMODE    Echo-Antiecho

F2 - Processing parameters
SI                  1024
SF           400.1300000 MHz
WDW                QSINE
SSB                    2
LB                  0.00 Hz
GB                     0
PC                  1.40

F1 - Processing parameters
SI                  1024
MC2         echo-antiecho
SF           100.6127690 MHz
WDW                QSINE
SSB                    2
LB                  0.00 Hz
GB                     0
```

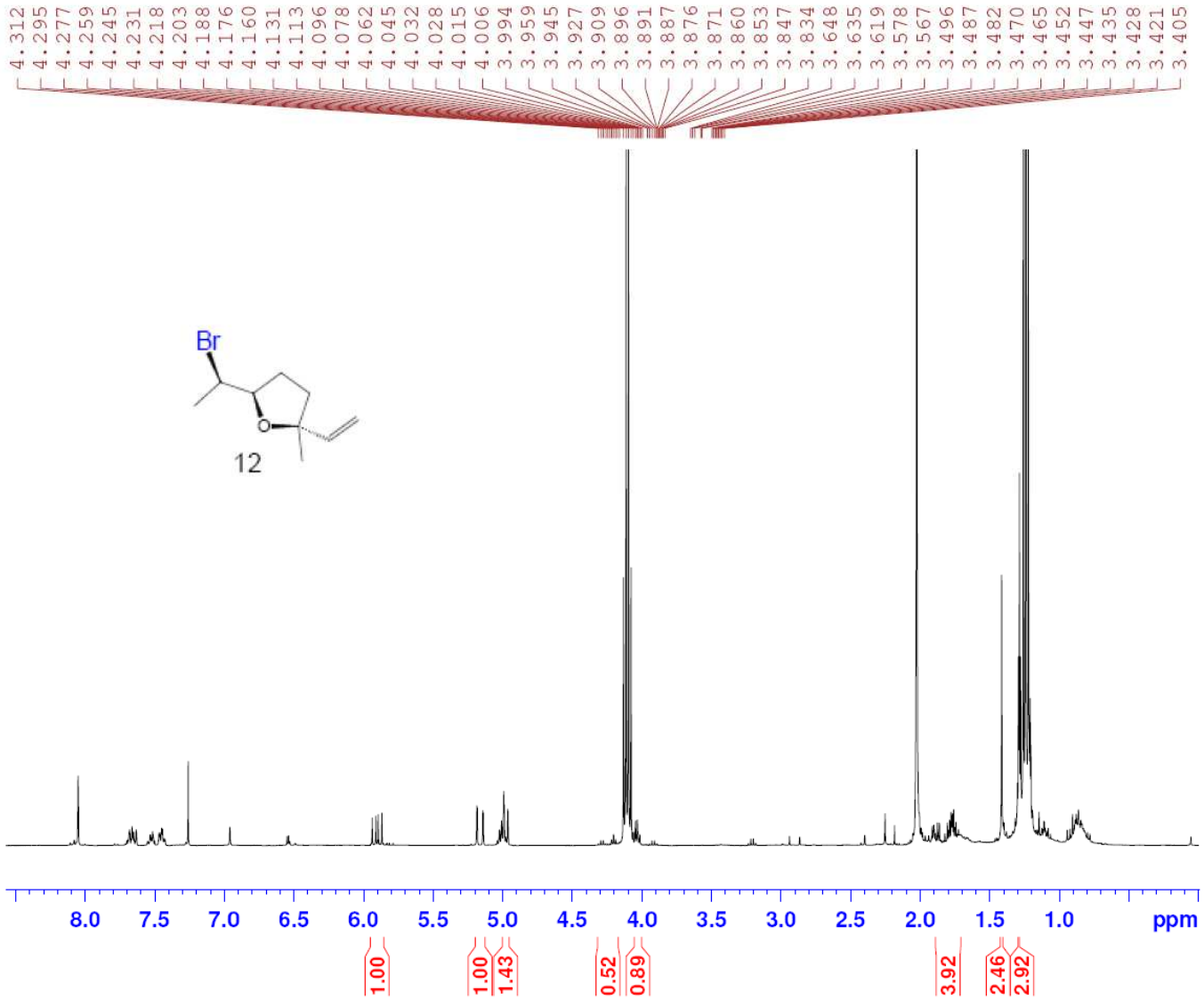


Comment;

Appendix51

No. of Scans;
Resolution;
Apodization;

Date/Time; 5/4/2012 1:59:41 PM
User; Agilent



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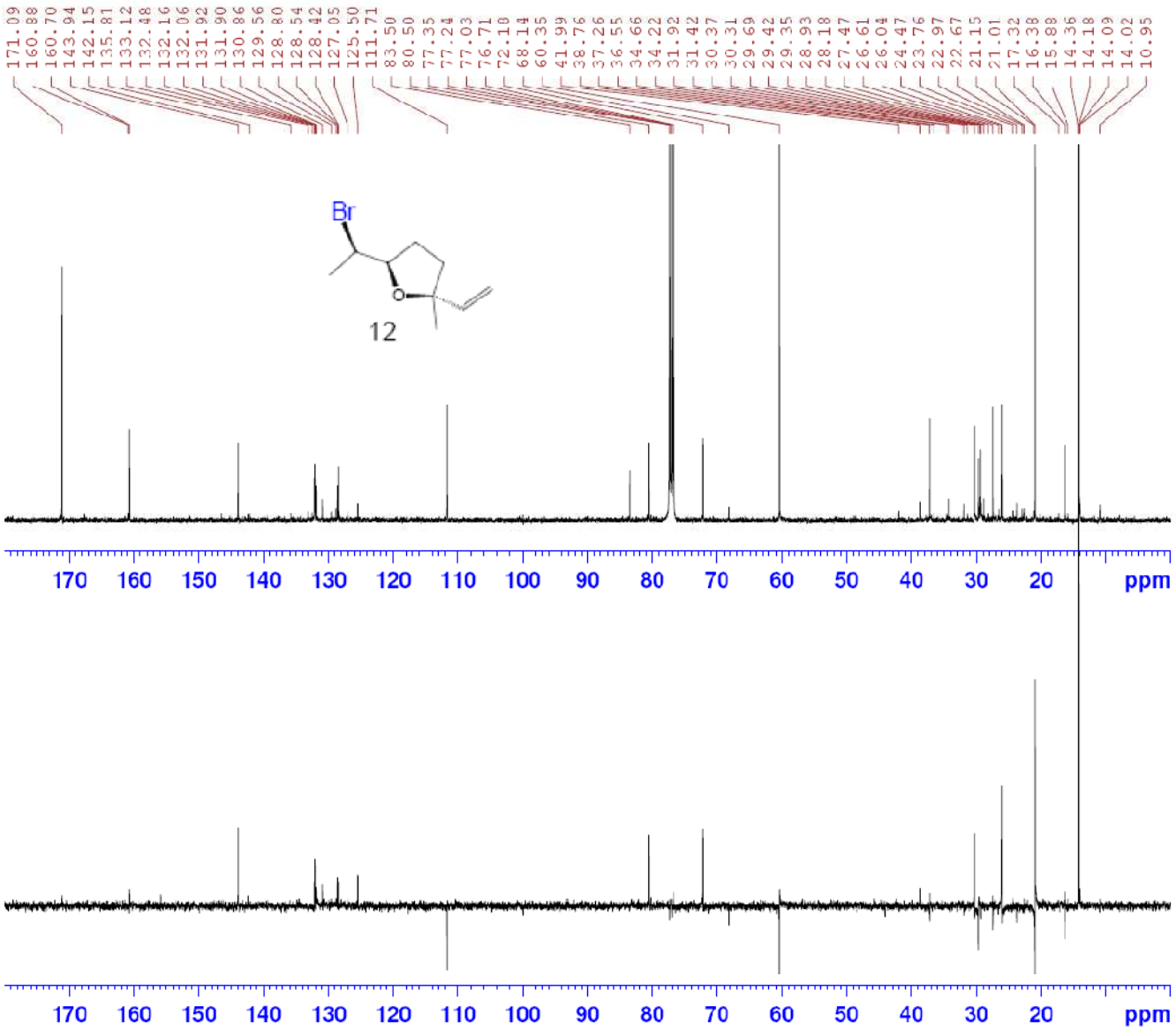
```
Current Data Parameters
NAME                  AA050
EXPNO                    11
PROCNO                    1

F2 - Acquisition Parameters
Date_              20120529
Time                  20.39
INSTRUM               spect
PROBHD    5 mm BBO BB-1H
PULPROG                zg30
TD                    32768
SOLVENT               CDCl3
NS                      256
DS                        0
SWH                6393.862 Hz
FIDRES            0.195125 Hz
AQ                2.5625076 sec
RG                     80.6
DW                   78.200 usec
DE                    6.00 usec
TE                   298.2 K
D1               5.00000000 sec
TD0                       1

======== CHANNEL f1 ========
NUC1                     1H
P1                   14.35 usec
PL1                   0.00 dB
SFO1           400.1324710 MHz

F2 - Processing parameters
SI                    65536
SF             400.1300175 MHz
WDW                      EM
SSB                       0
LB                    0.30 Hz
GB                        0
PC                    1.00
```

Appendix52



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```
Current Data Parameters
NAME                  AA050
EXPNO                    12
PROCNO                    1

F2 - Acquisition Parameters
Date                20120530
Time                    2.22
INSTRUM                spect
PROBHD    5 mm BBO BB-1H
PULPROG              zgpg30
TD                    65536
SOLVENT               CDCl3
NS                     6000
DS                        4
SWH               24038.461 Hz
FIDRES             0.366798 Hz
AQ                 1.3631930 sec
RG                     32800
DW                  20.800 usec
DE                   6.00 usec
TE                   298.1 K
D1                2.00000000 sec
d11               0.03000000 sec
DELTA             1.89999998 sec
TD0                       1

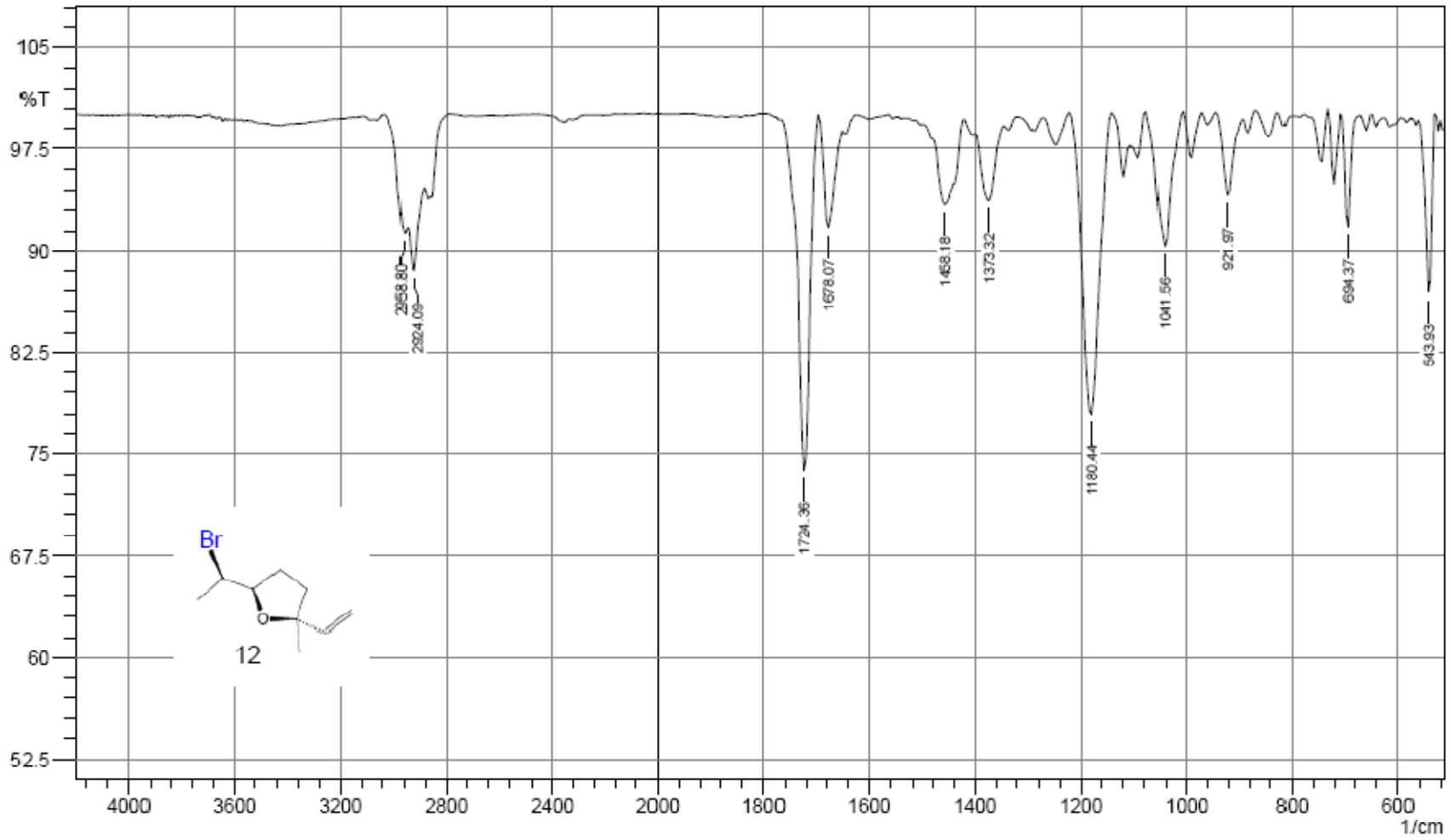
======== CHANNEL f1 ========
NUC1                     13C
P1                    9.50 usec
PL1                  -2.00 dB
SF01          100.6228298 MHz

======== CHANNEL f2 ========
CPDPRG2             waltz16
NUC2                    1H
PCPD2                70.00 usec
PL12                 13.76 dB
PL13                 14.00 dB
PL2                   0.00 dB
SF02          400.1316005 MHz

F2 - Processing parameters
SI                      16384
SF            100.6127690 MHz
WDW                        EM
SSB                         0
LB                       1.00 Hz
GB                          0
PC                       1.40
```

Appendix53

SHIMADZU



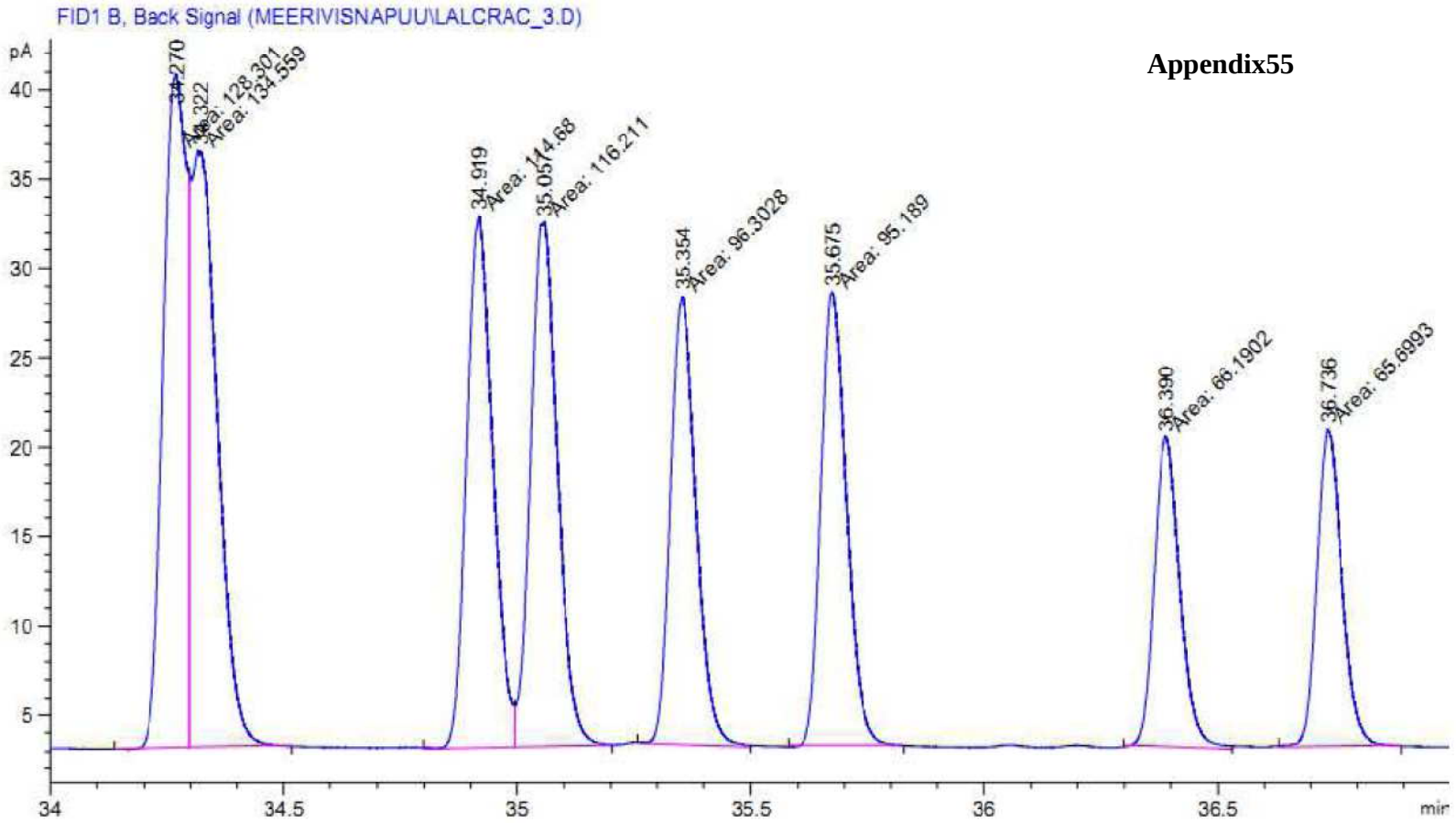
Comment;

Appendix54

No. of Scans;
Resolution;
Apodization;

Date/Time; 5/29/2012 7:40:20 PM
User; Agilent

Appendix55



Chromatogram of the racemic mixture of lilac alcohols. X-axis - retention times (minutes); y-axis – electric current (pA).