University of KwaZulu-Natal

Synthesis, Characterization & Antibacterial Evaluation of Novel Substituted Galactose Thiazolidin-4-ones

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Synthesis, Characterization & Antibacterial Evaluation of Novel Substituted Galactose Thiazolidin-4-ones

A Thesis

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MASTER OF SCIENCE

in the

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College of Agriculture, Engineering & Science

By

Christina Kannigadu

2014

Supervisor: Prof. N.A. Koorbanally

Preface

The experimental work described in this dissertation was carried out from August 2013 to November 2014 in the School of Chemistry and Physics, Westville campus, Durban, under the supervision of Prof N.A Koorbanally.

This study represents original work by the author and has not been submitted in any other form to another university. Where use was made of work of others it has been duly acknowledged in the text.

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Christina Kannigadu
BSc (Hons)

As the Candidate's supervisor, I have approved this dissertation for submission

Signed: _____

Prof N.A Koorbanally
Ph.D (Natal)

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2. This thesis has not been submitted for any degree or examination at any other university.
3. This thesis does not contain other persons' data, pictures, graphs or other information, unless specifically acknowledged as being sourced from other persons.
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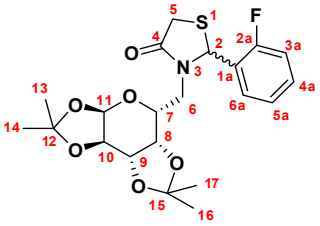
Structures of compounds synthesized



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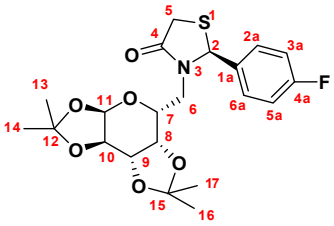

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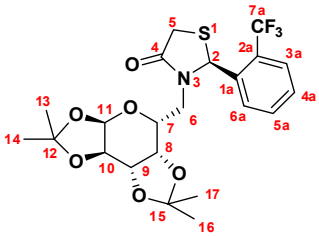

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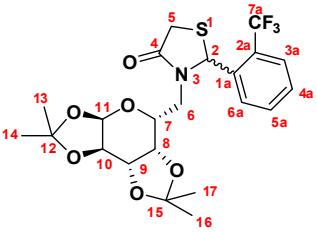

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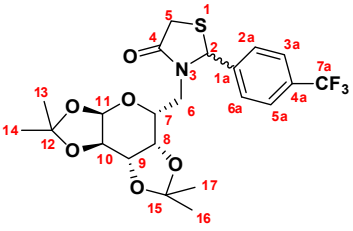

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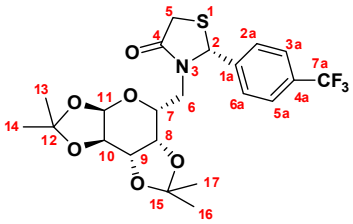

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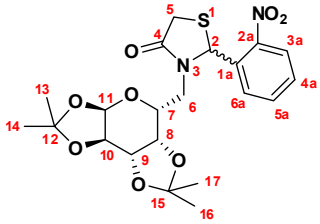

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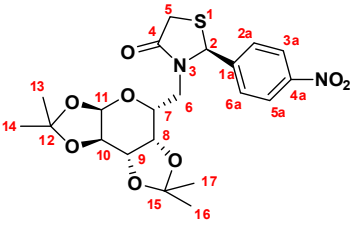

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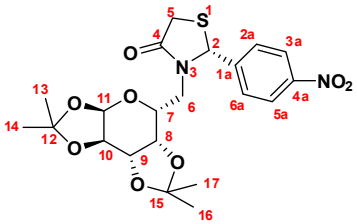

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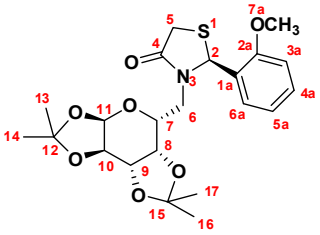

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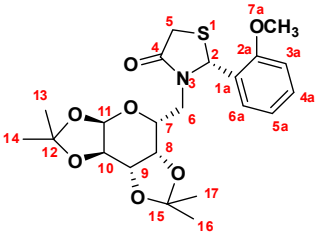

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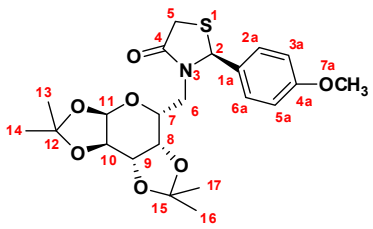

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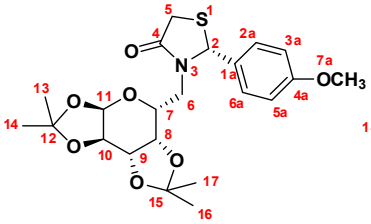

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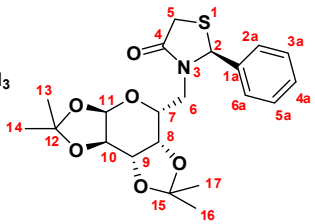

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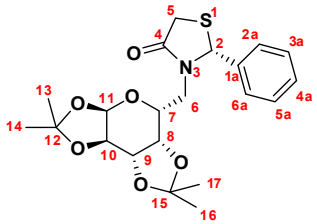

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List of Abbreviations

^{1}H NMR - Proton Nuclear Magnetic Resonance Spectroscopy

^{13}C NMR - Carbon-13 Nuclear Magnetic Resonance Spectroscopy

°C - Degrees Celsius

$CDCl_3$ - Deuterated Chloroform

$CHCl_3$ - Chloroform

COSY - Correlated Nuclear Magnetic Resonance Spectroscopy

d - Doublet

DCC - *N,N*-dicyclohexylcarbodiimide

DCM - Dichloromethane

dd - Double doublet

DMA - Dimethylacetal

DMAD - Dimethyl acetylenedicarboxylate

DMF - Dimethylformamide

DMSO - Dimethyl sulfoxide

dt - Doublet of triplets

EDC - *N*-(3-Dimethylaminopropyl)-*N*′-ethylcarbodiimide hydrochloride

EUCAST - European Committee on Antibiotic Susceptibility

EtOAc - Ethyl actetate

EtOH - Ethanol

FT- IR - Fourier Transform – Infrared Spectroscopy

GC-MS - Gas Chromatography - Mass Spectrometry

HBTU - 2-(1*H*-benzotriazo-1-yl)-1,1,3,3 tetramethyluranium hexafluorophospate

HCl - Hydrochloric acid

HMBC - Heteronuclear Multiple Bond Coherence

HOBt -1-Hydroxybenzotriazole

HPLC - High Pressure Liquid Chromatography

HRMS - High Resolution Mass Spectrometry

H_2SO_4 - Sulphuric acid

HSQC - Heteronuclear Multiple Quantum Coherence

Hz - Hertz

LiOH - Lithium hydroxide

m - Multiplet

MDR - Multi-drug resistant bacteria

MeOH - Methanol

MIC - Minimum Inhibitory Concentration

MS - Mass Spectrometry

NCCLS - National Committee for Clinical Laboratory Standards

R_f - Retention Factor

s - Singlet

t - Triplet

TBAB - Tetra-*N*-butylammonium bromide

td - Triplet of doublets

THF - Tetrahydrofuran

TLC - Thin Layer Chromatography

UV - Ultraviolet Spectroscopy

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Abstract

In this study, fifteen novel thiazolidinone derivatives were synthesized from galactose. In general it was observed that stereoselectivity for most of the *2R* diastereomers was better than the *2S* diastereomers. All compounds were characterized using NMR, melting point, optical rotation, FT-IR, UV, HPLC, GC-MS and HRMS. In order to unequivocally assign each of the proton and carbon resonances, HMBC, HSQC, COSY and NOESY were used for both the 2-methoxy substituted diastereomers. The assignments in all the other compounds with electron donating groups were confirmed based on this. For the 2-nitro and 4-nitro derivatives, with electron withdrawing substituents, HMBC was used to confirm the assignments of the protons on the phenyl ring. Similarly, the protons on the aromatic ring were also confirmed by HMBC correlations for the 4-methoxy *R* diastereomer. Single crystal XRD was performed on the 2-methoxy *R* diastereomer, which confirmed the *R* configuration of one of the diastereomers in each of the pairs. This enabled us to differentiate between the *R* and *S* configuration at C-2 on the thiazolidinone ring. The synthesized compounds showed antibacterial activity against methicillin resistant *Staphylococcus aureus*, *Klebsiella pneumonia,* and *Escherichia coli*.

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Chapter 1. Introduction

1.1 Introduction to antibiotics

The discovery of antibiotics has modernised our world to the point where infections that were once previously regarded as widely fatal can now be easily cured. Antibiotics have now become part of our daily times and are used to treat even the most trivial infections (Alanis, 2005). Growing antibiotic resistance due to the overuse of antibiotics has become a threat to human healthcare in the last five decades. This abuse has resulted in a widespread resistance of pathogenic bacteria to known antibiotics (Romero et al, 2011).

Extreme drug resistant strains are non-susceptible to all antibiotics, while multi-drug resistant bacteria (MDR) are susceptibility to one or more classes of antibiotics at the same time being non-susceptible to most antibiotics (Bassetti et al., 2013). Studies have indicated that bacteria have shown a remarkable ability to endure and adapt to their environment, thus resulting in many strains of bacteria becoming resistant to many pharmaceuticals. This is problematic as it renders our current market of antibiotics ineffective (Alanis, 2005). Since new bacterial resistance emerges on a continual basis, there is thus a need for the continual discovery of new drugs to fight these evolving bacteria, particularly multi-drug resistant gram negative bacteria (Vashishtha, 2010).

Many bacterial strains have developed resistance to antibiotics over the last century; starting from the sulfonamide and penicillin-resistant *Staphylococcus aureus* in the 1930's and 1940's, to the penicillin-resistant *Neisseria gonorrhoeae* (PPNG), the *β*-lactamase-producing *Haemophilus influenzae* in the 1970's, the methicillin resistant *Staphylococcus aureus* (MRSA) and multi-drug

resistant (MDR) *Mycobacterium tuberculosis* in the late 1970's and 1980's, and several resistant strains of common enteric and non-enteric gram-negative bacteria such as *Shigella* sp., *Salmonella* sp., *Vibrio cholerae*, *Eschirichia coli*, *Klebsiella pneumoniae*, *Actinetobacter baumanii* and *Pseudomonas aeruginosa*, some of these associated with the use of antimicrobials in animals grown for human food consumption in the 1980's and 1990's (Alanis, 2005; Lowy, 2003).

The future of modern medicine now depends on how effective the current market of antibiotics are against the growing population of bacterial species (Alanis, 2005). Modifying existing antibiotics can lead to several analogues which can be used to combat the growing resistance to these antibiotics (Coates et al., 2011). Between 1930 and 1962 there were 20 novel classes of antibiotics on the market, however these numbers have rapidly decreased due to multi-drug resistant bacteria, so called "superbugs". Since then, there have been numerous analogues of existing classes on the market, many of which have made it to clinical trials. However, in the last decade only two new classes of antibiotics (oxazolidinone and cyclic lipopetide) have been marketed (Coates et al., 2011).

The rate at which antibiotics are currently being produced cannot cope sufficiently with the worldwide emergence of bacterial resistance. If this continues, we may face a future without any effective antibiotics (Vashishtha, 2010). A potential way forward is combinational therapy, producing hybrid molecules. This method can be applied more widely for the treatment of pathogenic bacteria and may provide a more efficient and effective combination drug therapy than a drug comprising of a single compound (Coates et al., 2011).

1.2 The importance of hybrid molecules

Hybrid molecules where two or more compounds combined together is an effective and commonly used method in modern medicinal chemistry to produce novel drugs with widespread pharmaceutical applications (Havrylyuk et al., 2012; Meunier, 2008; Solomon et al., 2009). These hybrid molecules are normally derived from two or more different bioactive molecules that have complementary pharmacophoric functions or different mechanisms of action, which often display synergistic effects (Havrylyuk et al., 2012; Meunier, 2008; Solomon et al., 2009). An example of this is the antitumor activity of the 4-thiazolidinone derivatives coupled with varying heterocyclic fragments, such as the 4-thiazolidinone (**1**), 2,3-dihydro-1*H*-indol-2-ones (**2**), with pyrazole (**3**) or pyrazoline moieties (**4**) (**Figure 1**) (Havrylyuk et al., 2012; Meunier, 2008; Solomon et al., 2009).

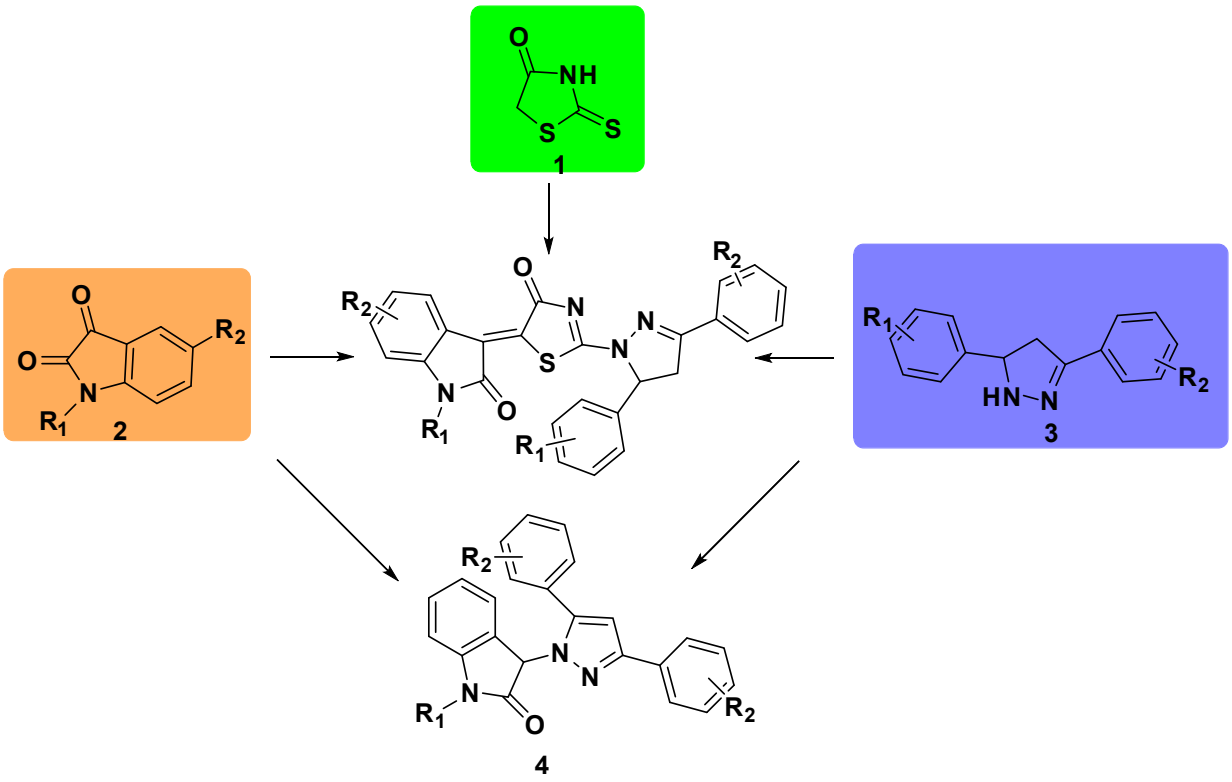

Figure 1. 4-Thiazolidinone, 2,3-dihydro-1*H*-indol-2-one and pyrazole or pyrazoline moieties

It was found that combinations of pyrazoline, 4-thiazolidinone, and 2,3-dihydro-1*H*-indol-2-one moieties in one molecule increased the antitumor cytotoxicity at the GI_{50} level (-5.5 to -7.5) activity range in comparison with pyrazole-indolin-2-one conjugates (-4.8 to -5.5) or pyrazoline−thiazolidinone analogous compounds (-4.1 to -5.6), which were previously reported (Havrylyuk et al., 2012; Meunier, 2008; Solomon et al., 2009).

1.3 Thiazolidinone derivatives

One of the main objectives of medicinal chemistry research and organic chemistry is to design and develop compounds that are easily accessible and show the desired biological activities (Behbehani et al., 2012). These compounds are then isolated from natural resources or synthesised in the laboratory. Thiazolidinones and their derivatives are an important class of heterocyclic compounds containing nitrogen and sulfur atoms and they possess a broad spectrum of antimicrobial (Suryavanshi et al., 2006), anti-inflammatory (Vigorita et al., 2003), anti-HIV (Rawal et al., 2005, Balzarini et al., 2009), anti-tubercular (Babaoglu et al., 2003), antibacterial (Bondock et al., 2007; Vicini et al., 2008), anticancer (Gududuru et al., 2004; Ottana et al., 2005), antihistaminic (Diurno et al., 1999), antifungal (Omar et al., 2010), antihyperglycemic (Raza et al., 2013) and anticonvulsant activities (Dwivedi et al., 1972; Parmar et al., 1972).

Thiazolidinones are a saturated form of thiazole with a carbonyl group. They are heterocycles that have a nitrogen atom at position 3 and a carbonyl group at either of positions 2, 4 or 5. Modification of the parent structure (**5**) can be done by varying substituents in the 2, 3 and 5 positions (**Figure 2**).

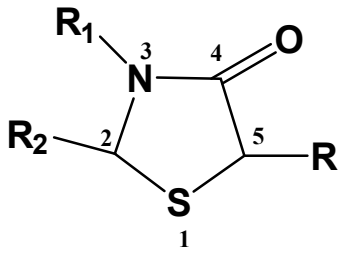

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Figure 2. Structure of thiazolidinone

However, research has indicated that substitution at C-2 (**6-9**) shows promising activity (**Figure 3**) (Tripathi et al., 2014; Brown, 1961; Singh et al., 1980)

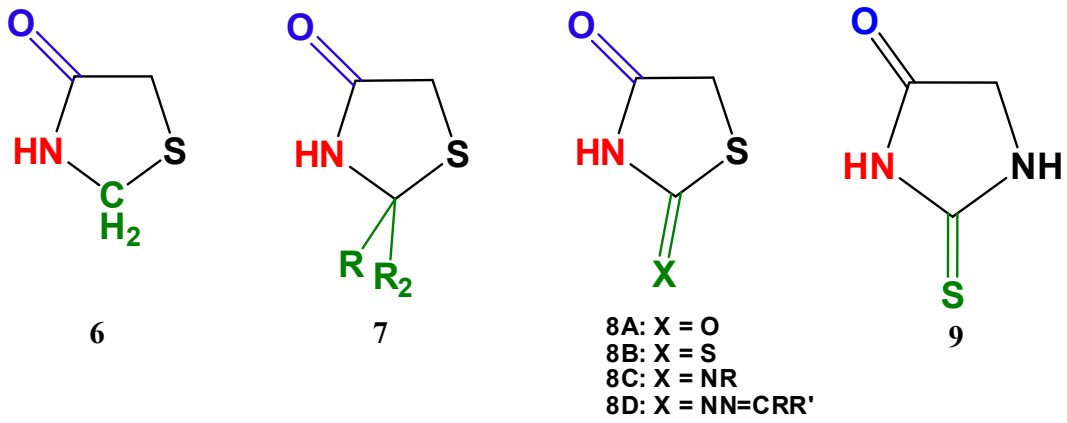

Figure 3. Structure of the 4-thiazolidinone nucleus with substituents at various positions

On structures **7** and **8**, it is possible to attach varying substituents on the nitrogen atom and the methylene carbon however the carbonyl group is highly unreactive but in some cases Lawesson's reagent has been successfully used to form the corresponding 4-thione derivative (Tripathi et al., 2014). However there was a considerable amount of confusion regarding the structure of thiazolidinone. Initially for rhodanine (**8B**) and pseudothiohydantoin (**8C**) derivatives, non- cyclic

formulas were proposed (Brown, 1961; Singh et al., 1981). An alternative cyclic formula for thiohydantoin (IV) was proposed for **8C** (R = H) (**Figure 3**), but upon recognition that thioglycolic acid is a primary product of the hydrolysis of 3-phenyl-2-phenylimino-4-thiazolidinone, formula IIIC was established as the correct structure instead of **9** for all the 2-imino derivatives (Brown, 1961; Singh et al., 1981).

1.3.1 Thioglycolic acid

Thioglycolic acid is an organic compound with a structural formula of $HSCH_2CO_2H$ (**Figure 4**). The structure consists of a thiol group and a carboxylic acid. It is very useful for addition, elimination and cyclization chemical reactions since the sulfur has a pair of electrons that can act as a nucleophile and the carboxyl group carbon can act as an electrophile. The sulfur group will react with bases to abstract the hydrogen of sulfur making it a better nucleophile. It reacts with acids, protonating the sulfur, and reacts with ketones and organic halides acting as a nucleophile. The carboxylic acid group will react with nucleophiles such as alcohols or amines. Sulfur is a better nucleophile than that of oxygen and therefore some nucleophilic reactions that are not possible with oxygen can be carried out with sulfur thus thioglycolic acid (**10**) is much more reactive than 2-hydroxyacetic acid as a nucleophile.

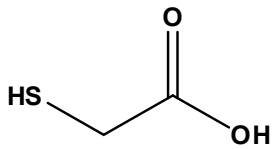

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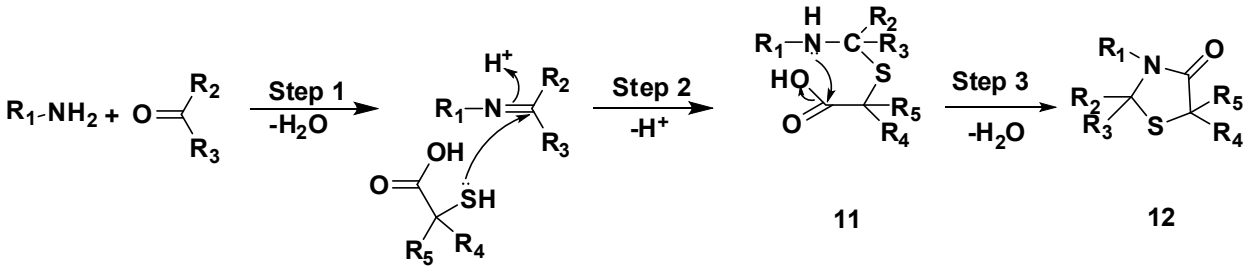
Figure 4. Thioglycolic acid

Current reviews indicate that 4-thiazolidinone derivatives are steadily gaining interest because of their diverse biological properties such as anti-inflammatory, anti-proliferative, anti-tubercular, antiviral, anticonvulsant, anti-diabetic, anti-hyperlipidemic, cardiovascular, antifungal, and antibacterial activity (Tripathi et al., 2014; Agrawal et al., 2013).

1.3.2 Synthesis of thiazolidinones

1.3.2.1 Synthesis with benzaldehydes and anilines *via* an imine intermediate using thioglycolic acid

There are several methods available for the synthesis of thiazolidinone derivatives. The most common of these is the reaction of aldehydes and amines forming an imino intermediate (**11**) which is subsequently converted to the thiazolidin-4-ones (**12**) with thioglycolic acid. A general mechanism for the synthesis of the thiazolidinone ring is shown below (**Scheme 1**) (Tripathi et al., 2014; Agrawal et al., 2013).



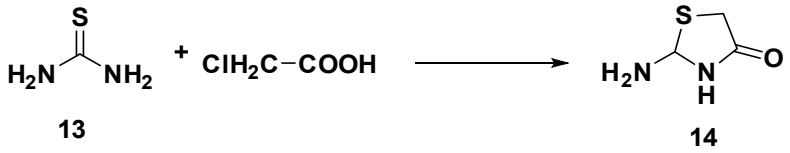
Scheme 1. General mechanism for the formation of 4-thiazolidinone

This reaction proceeds by initial formation of an imine, which undergoes an attack by the sulfur nucleophile, followed by intramolecular cyclization and the elimination of water (Tripathi et al.,

2014; Agrawal et al., 2013). The process can be done either *via* a one-pot three component condensation reaction or *via* a two-step process. However, the use of a dehydrating agent such as *N,N*-dicyclohexylcarbodiimide (DCC) or 2-(1*H*-benzotriazo-1-yl)-1,1,3,3 tetramethyluranium hexafluorophospate (HBTU) has been shown to improve yields and accelerate the rate of intramolecular cyclization (Verma et al., 2008).

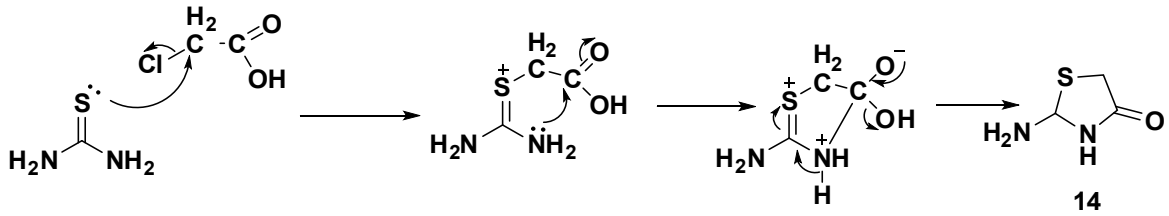
1.3.2.2 Synthesis *via* thiourea and chloroacetic acid

Thiourea (**13**) or thiourea derivatives can also be used for the cyclization of thiazolidin-4-ones with chloroacetic acid and sodium acetate according to the reaction below (**Figure 5**) (Avdieiev et al., 2014, da Silva et al., 2014, Ghorab et al., 2014). The mechanism for the reaction proceeds *via* a nucleophilic attack by the lone pair on sulfur on the electrophilic methylene group forming a S-CH_2 bond. Subsequent attack of the carboxyl carbonyl by the lone pair on nitrogen completes formation of the thiazoline ring. Electronic rearrangements then results in the 2-amino thiazolidin-4-one (**14**) (**Scheme 2**).



13 14

Figure 5. Reaction for the synthesis of 2-amino thiazolidin-4-ones using thiourea and chloroacetic acid



Scheme 2. Mechanism for the formation of 2-amino thiazolidin-4-ones with thiourea and chloroacetic acid

1.3.2.3 Synthesis of 4-thiazolidinones from dithiocarbamates & fumaronitrile or bis (alkylthio) maleonitrile

It was observed that reactions of dithiocarbamates with fumaronitrile or bis (alkylthio) maleonitrile gives intermediates (**15**) and (**16**) in **Figure 6**, which can further be treated with acid or methanol to form 4-thiazoldinones (**17-19**) (**Figure 6**) (Singh et al., 1981; Nagase, 1974).

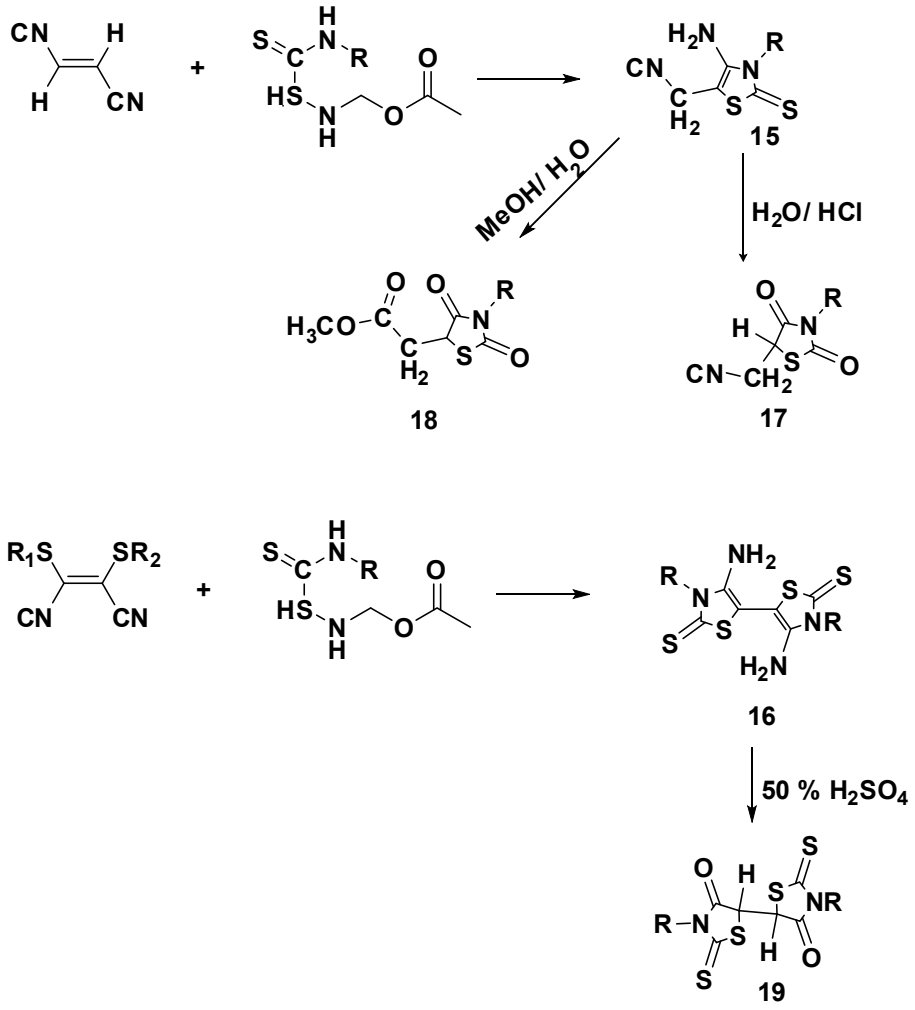


Figure 6. Formation of 4-thiazolidinone by acid treatment

1.3.2.4 Derivatisation of thiazolidin-4-ones

Many syntheses of 4-thiazolidinone have been carried out in the past. One of the most common is the aldol condensation between the methylene group at C-5 and various aldehydes. However, the degree of nucleophilic activity and the formation of the anion in the presence of a base is highly dependent upon the electron-withdrawing effect of the adjacent carbonyl group and other electron-withdrawing groups present at C-2. The product formed contains an *α-β* unsaturated carbonyl group. Different 2-thio-4-thiazoldinones (**20**) have synthesized using the aldol condensation with

a variety of aliphatic, aromatic and heterocyclic aldehydes (useful synthetic reagents) in good yields according to **Figure 7** (Singh et al., 1981).

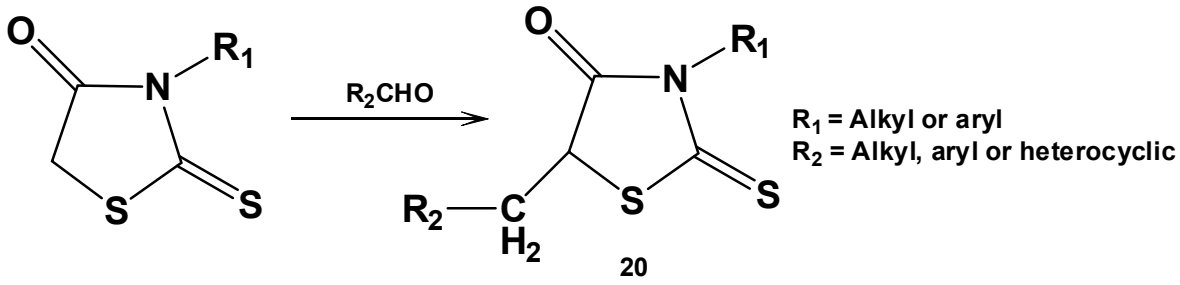


Figure 7. Aldol condensation of 4-thiazolidinone using various substituents

Depending on the substituted anilines that is used in the reaction to form the thiazolidinones, various substituents can be placed on the nitrogen. This could lead to many variations within the thiazolidinone backbone.

Variation at C-5 of the thiazolidinone ring is not as common as that at the nitrogen or C-2, however derivatives have been made at C-5 with pyrazoline and formaldehyde (Pujari et al., 2014) and with 2-methyl mercaptopropanoic acid (Singh et al., 2014b).

1.3.3 Structure elucidation

The characteristic ^{1}H NMR resonances in 5-substituted thiazolidinones is the H-2 proton reported to occur as a singlet in the range of 5-6 ppm and the two non-equivalent methylene protons, H-5i/5ii (**Figure 8**) which occurs as doublets in the range of 3.5 to 3.9 ppm (Verma et al., 2008; Singh et al., 1981). The actual chemical shifts depend on the substituents present on the nitrogen and C-

2. The carbonyl group at C-4 usually appears at approximately δ164 in the ^{13}C NMR spectrum (Singh et al, 1981; Verma et al., 2008; Nagase, 1973). The carbonyl absorption band is reported to occur between 1687-1725 cm^{-1} for similar compounds (Omar et al., 2010; Vicini et al., 2008).

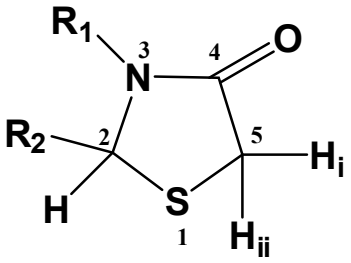
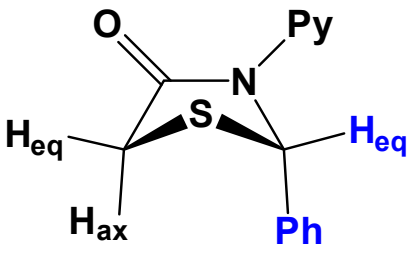


Figure 8. Structure of 4-thiazolidinone with substituents at the nitrogen and C-2

1.3.4 Conformational studies

Thiazolidinones substituted at the nitrogen and C-5 form two diastereomers (**21** and **22**) (**Figure 9**). Vigorita et al. (1979) reported that the preferred conformation is where H-2 and one of the methylene protons are in *cis* 1,3-diequatorial relationship (**21**). This formation is preferred due to the fact that the phenyl group will prefer the axial orientation to avoid steric crowding with the pyridyl group (Verma et al., 2008; Vigorita et al., 1979).



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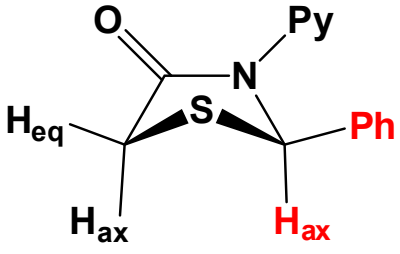


22

Figure 9. Stereochemical orientation of 4-thiazolidinone

1.3.5 Applications of thiazolidinones

Thiazolidinone compounds have been shown to have protein phosphatase inhibitory action. Over the last decade, thiazolidinone derivatives have been tested against protein phosphatases due to its structural resemblance to the natural peptide substrates of the enzymes and many have been very active, especially against PTP1B (Geronikaki et al., 2008).

Thiazolidinones can also be used as ligands for metal complexes. The 2-thiono-4-thiazolidinone and its 3-substituted derivatives were used as a ligand with copper (I), silver (I), gold (I), palladium (II), and platinum (II) (Singh et al., 1981). Upon studying molar conductivity, infrared and nuclear magnetic resonance, it is believed that coordination in these complexes takes place through the thiocarbonyl group of the ligand.

1.4 Introduction to antibacterial activity

Antimicrobial susceptibility testing is an important technique that is required to detect possible drug resistance in common pathogens and to assure the susceptibility of antimicrobial drugs to a particular infection (Powers, 2004).

The methods used for obtaining the Minimum Inhibitory Concentration (MIC) of the antibiotic to the organisms concerned currently include broth dilution, agar dilution and disc diffusion. Each method has its own advantages and disadvantages, and is chosen depending on the type of data required. The broth dilution method determines whether a compound has microbicidal or microbiostatic action at a particular concentration. This method is recommended for testing commercial antifungal drugs targeting yeasts using either the National Committee for Clinical

Laboratory Standards (NCCLS) reference procedure M27-A2 or EUCAST (European Committee on Antibiotic Susceptibility, 2002) (Pfaller, 2012, Jorgensen and Ferraro, 2009).

The broth dilution method involves a two-fold dilution of antibiotic drugs in a liquid growth medium dispensed in well plates of which can then be inoculated with a standardized bacterial suspension (**Figure 10**). They are then incubated at 35 °C overnight before they are examined for visible bacterial growth (turbidity). The MIC is reached when the lowest concentration of the drug that prevents microbial growth is reached. The broth dilution method is advantageous because it generates reproducible results and can assist in the generation of computerized reports if an automated 96 well plate reader is used (Jorgensen and Ferraro, 2009).

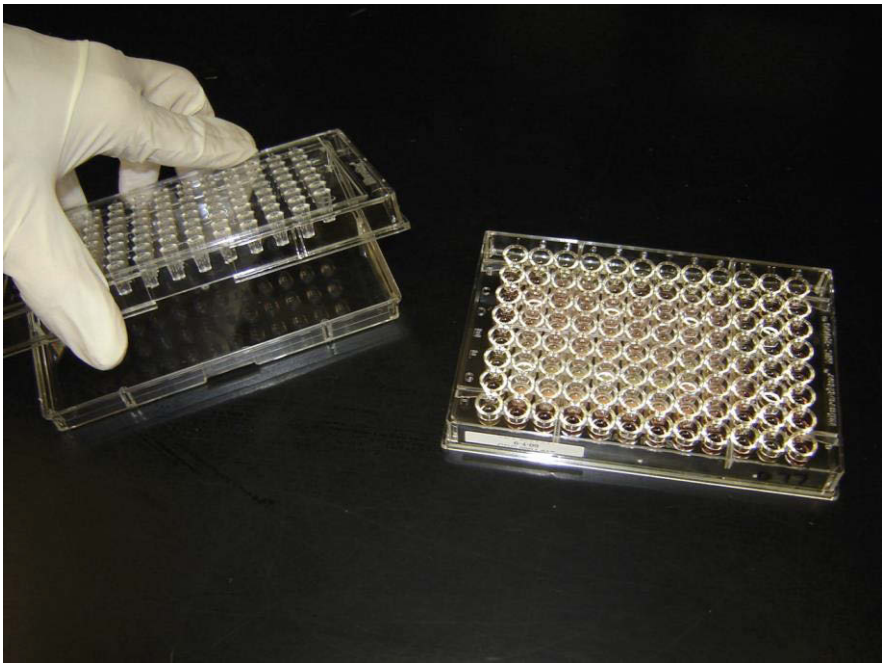


Figure 10. A broth microdilution susceptibility panel containing 98 reagent wells and a disposable tray inoculator

The disc diffusion susceptibility method is a well-recognized cost effective method that is widely used throughout laboratories. This method is very reliable, easy to interpret and requires no specialized equipment. However, it is limited by its inability to allow for a very accurate testing of all bacteria and fungi. This test can be conducted by applying absorbent discs containing various concentrations of the drug on agar growth medium that has been inoculated with bacteria and incubated for 16-24 hours at 35 °C (**Figure 11**). The diameter of the clear zone around the disc is measured at the end of the incubation period and compared with standard drugs (Jorgensen and Ferraro, 2009).

Figure 11. A *Staphylococcus aureus* isolate tested with the disc diffusion method

The current study was conducted to investigate the antimicrobial activity of the fifteen synthesized galactose substituted thiazolidin-4-one derivatives as they are known to be potential antibacterial agents. The susceptibility testing was evaluated by the broth micro-dilution method in accordance with the standardized protocol developed by the NCCLS.

1.5 Aims and objectives

Sugar based drugs are exceptionally good to be used as core structures since sugar interacts with and controls many proteins such as enzymes. New insights into the biology of sugars are constantly providing new targets so there is a huge potential for sugar based drugs for diverse diseases (Kalamkar, 2010). The thiazolidinone ring system comprises of a broad spectrum for a number of biologically active compounds and by incorporating a sugar based core and varying the aromatic or aliphatic aldehyde group attached to the thiazolidinone ring, it may result in better biological activity.

In this proposed study, the specific aim is centered on synthesizing, characterizing and evaluating the antibacterial activity of substituted sugar thiazolidinones derivatives.

Objectives of the study:

1. To synthesize a molecule with a thiazolidinone ring incorporated onto a galactose core structure.
2. To substitute different aromatic aldehyde groups onto the thiazolidinone ring, thereby creating a small library of compounds.
3. To compare the differences observed between the various groups in characterisation of the synthesized compounds.
4. To determine the antibacterial activity of the synthesized compounds.
5. To compare the effect that different substituents have at different positions on the phenyl ring with regard to bioactivity.

Chapter 2. A review of the recent literature

2.1 A review of the recent syntheses and bioactivity of thiazolidinones

To date there has been approximately two-thousand publications on the synthesis of thiazolidinones. There has also been a number of review articles for the synthesis and bioactivity of these molecules. Most recently, Tripathi et al. (2014) reviewed the synthesis and bioactivity of the thiazolidin-4-ones after 2006. In his review, he also contains information on the structural elucidation and conformation of these molecules (Tripathi et al., 2014). Due to the vast amount of literature on this topic, we have herein reviewed only the most recent journal articles published in 2014 with regard to the synthesis and bioactivity of thiazolidin-4-ones.

2.2 Synthesis of 4-thiazolidinones using Schiff base and thioglycolic acid

Amongst the articles reviewed, this was the most common method used to synthesize these molecules. Depending on the various anilines used, a variety of substituents was introduced at C-3 and the different aldehydes introduced variety at C-2. A number of these reactions published recently are discussed below. In all of these reactions, aldehydes and amines are reacted to first form imine intermediates, which are then cyclized with thioglycolic acid to form the thiazolidin-4-one ring.

A range of 3-(3,4-dichlorophenyl)-2-(3-substitued phenyl)thiazolidin-4-ones (**24**) with bromo, chloro, methoxy, nitro, methyl and dimethylamine groups were synthesized from 3,4-dicholoraniline and 3-substitued benzaldehydes through a benzenamine intermediate (**23**) (**Figure 12**). The compounds were subjected to docking studies against the DNA polymerase enzyme

bearing the PDB id-3MDA where the 3,4,5-trimethoxy and the unsubstitued derivatives were found to be the most active (Aanandhi et al., 2014).

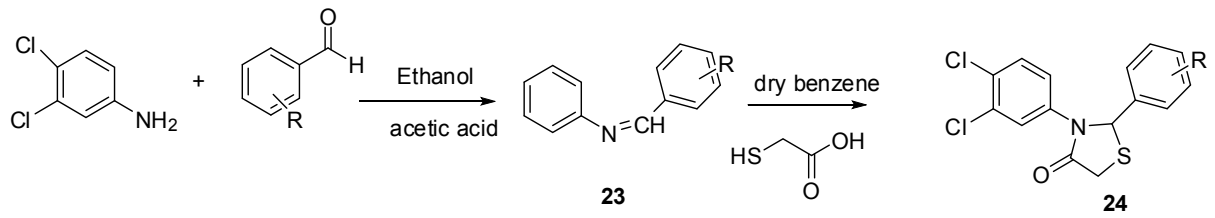


Figure 12. The synthesis of 3-(3,4-dichlorophenyl)-2-(3-substituted phenyl)thiazolidin-4-ones

Several 3-arylalkyl-2-phenylthiazolidin-4-ones (**25**) were synthesized from *N*-alkylamines and substituted arylaldehydes (**Figure 13**) (Amutha et al., 2014). The unsubstitued 3-arylalkyl-2-phenyl-thiazolidin-4-one was shown to reduce the enzymatic lipid peroxide levels in ISO administered rats, showing antioxidant activity.

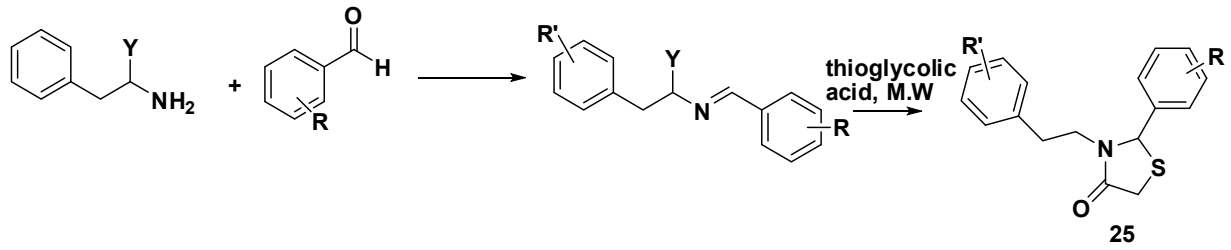


Figure 13. Synthesis of substituted 3-arylalkyl-2-phenyl-thiazolidin-4-ones

N-Aryl-1,4-(*o*-chlorobenzyloxy)-3-methoxyphenyl-1-yl-4-thiazolidinones (**27**) were formed from vanillin derivatised with *o*-chlorobenzylchloride (**26**) and aryl amines (**Figure 14**). All the synthesized compounds were found to be mild to moderately active against gram negative and gram positive bacteria (Dangar et al., 2014).

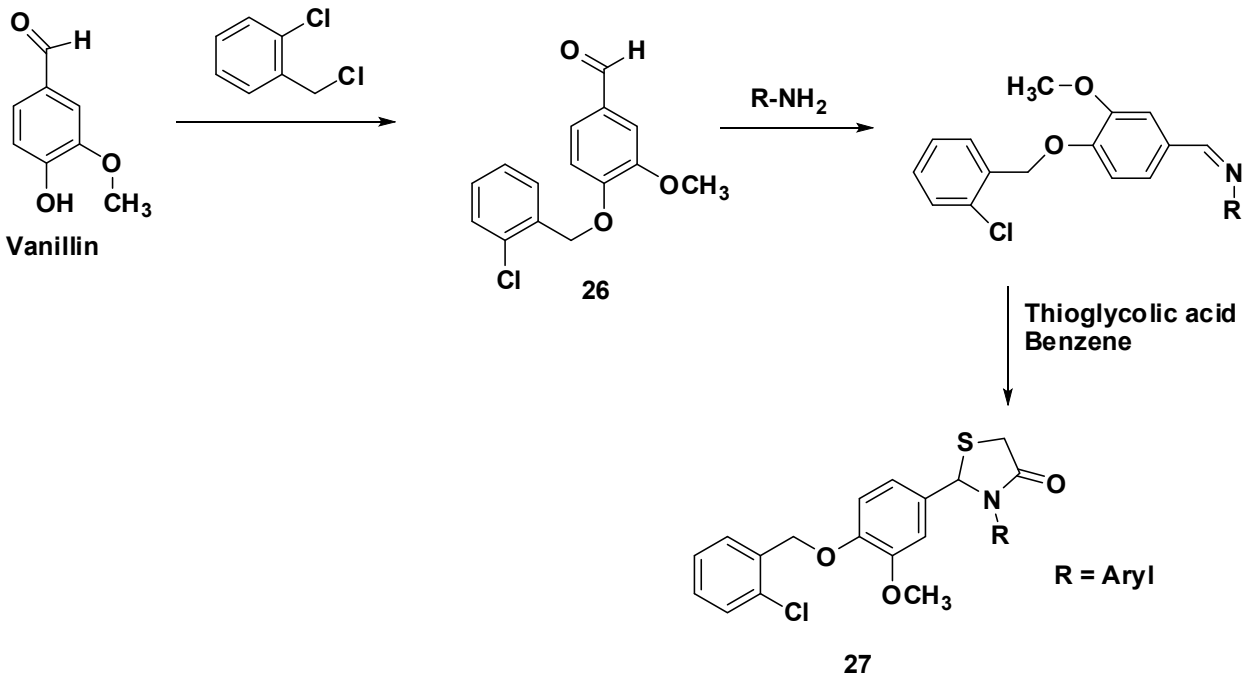


Figure 14. The synthesis of *N*-aryl-1,4-(*o*-chlorobenzyloxy)-3-methoxyphenyl-1-yl-4-thiazolidinones from vanillin derivatised with *o*-chlorobenzylchloride

A series of *N*'-(2-(4-oxo-2-thiazolidin-3-ylamino)quinazolin-4-yl)isonicotinohydrazide (**29**) was synthesized from (*E*)-*N*'-(2-(2-benzalidene)hydrazinyl)quinazolin-4-yl)isonicotinohydrazide (**28**) and thioglycolic acid with zinc chloride using DMF as a solvent (**Figure 15**). The 2-nitro and the 4-dimethylamine derivatives were the most active in the antibacterial assays from the series of compounds synthesized. These two compounds also showed good antifungal activity together with the 4-hydroxy-3-methoxy derivative towards *A. niger, A. clavatus* and *C. albicans* (Desai et al., 2014).

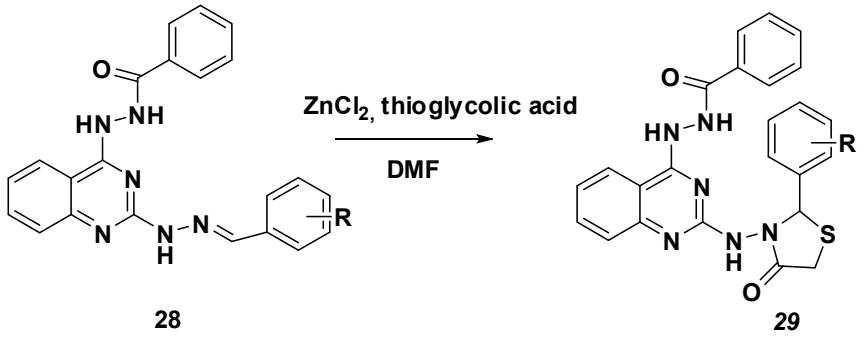


Figure 15. Synthesis of *N*'-(2-(4-oxo-2-substituted thiazolidin-3-ylamino)-quinazolin-4-yl)-isonicotinohydrazide

Quinoline based thiazolidinones (**31**) were formed from (*Z*)-3-((phenylimino)methyl)quinoline-2-thiol intermediates (**30**) with thioglycolic acid and zinc chloride in DMF. The imino-intermediate was formed from 2-mercaptoquinoline-3-carbaldehyde and substituted aromatic amines. The quinoline carbaldehydes were formed from acetanilide which was cyclized with phosphoryl chloride in DMF (**Figure 16**). Some of these compounds showed excellent antimicrobial activity and good activity against mycobacterium tuberculosis (Mistry et al., 2014).

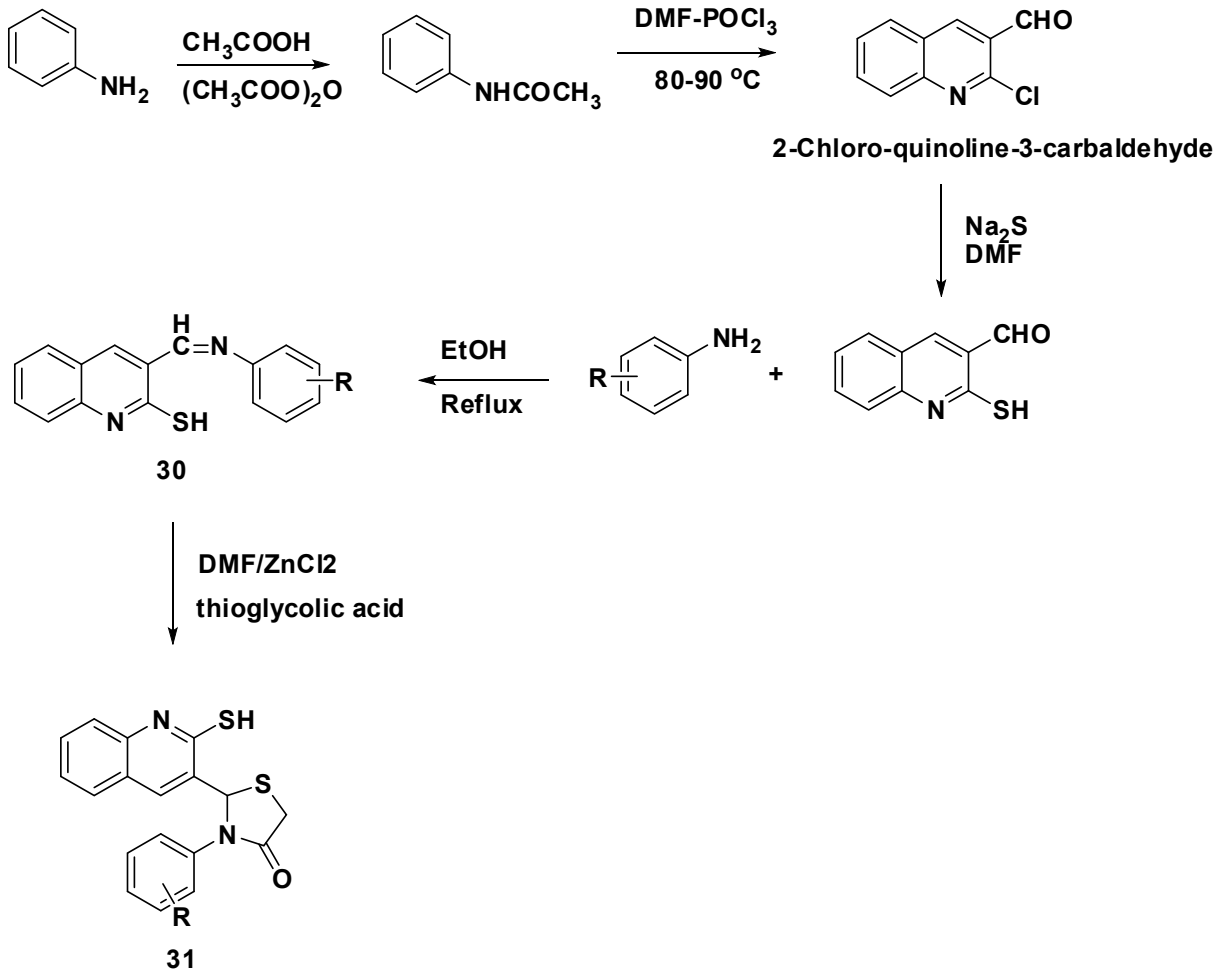


Figure 16. Synthesis of quinoline based thiazolidinones from (*Z*)-3-(phenyliminomethyl) quinoline-2-thiol intermediates

Substituted aryl thiazolidin-4-ones (**32-33**) with *N*-substituted benzeneamides, sulfonamides and anilines were synthesized from substituted anilines, tosylhydrazines or isonicotinohydrazide with thioglycolic acid and substituted aldehydes. Most of the synthesized compounds showed anti-HIV-1 activity with the 2-chloro-6-nitro-2-phenyl derivative containing a 3-substituted-4,6-dimethylpyridin-2-yl ring having the best activity (**Figure 17**) (Murugesan et al., 2013).

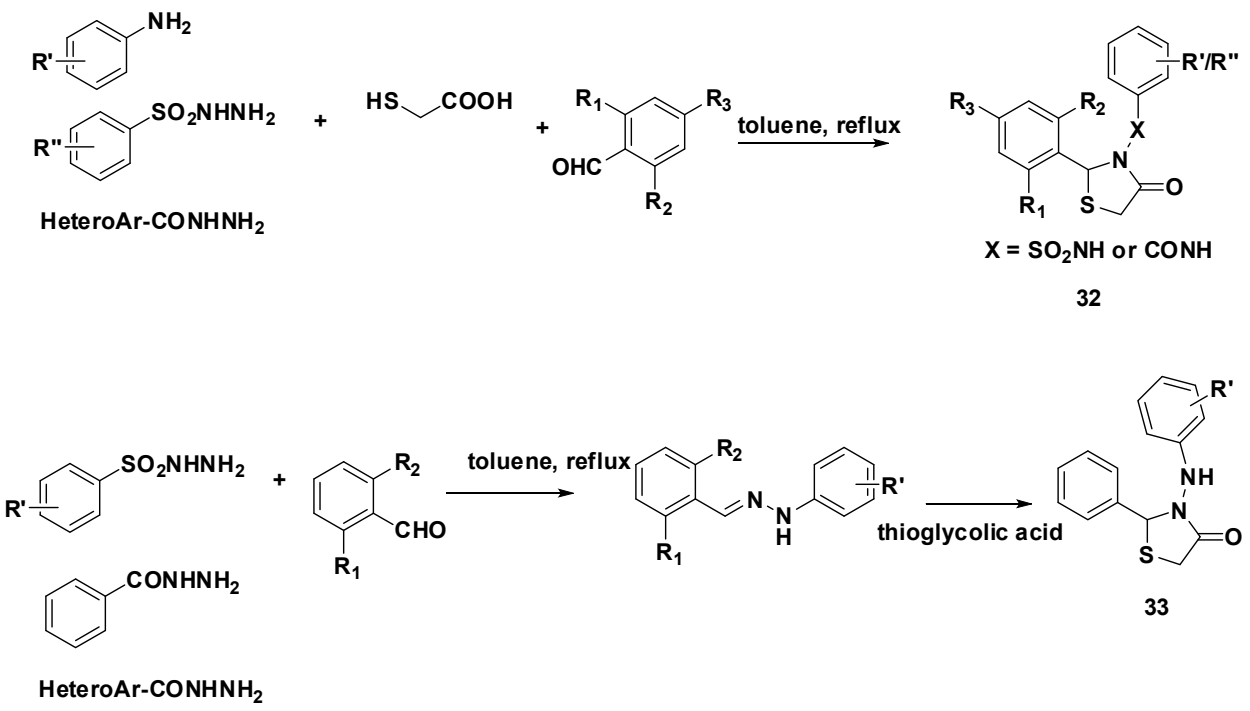


Figure 17. Synthesis of substituted aryl thiazolidin-4-ones with *N*-substituted benzeneamides, sulfonamides and anilines

A series of 3-(5-methyl-1,3-thiazol-2-yl)-2-phenyl-1,3-thiazolidin-4-ones (**35**) was synthesized from 5-methyl-*N*-((*E*)-phenylmethylidene)-1,3-thiazol-2-imines (**34**), thioglycolic acid and benzene. The thiazole-2-imines were formed from 2-amino thiazole and substituted benzaldehydes in benzene (**Figure 18**). Most of the synthesized compounds showed moderate activity against gram-positive and gram-negative bacteria (Patel et al., 2014a).

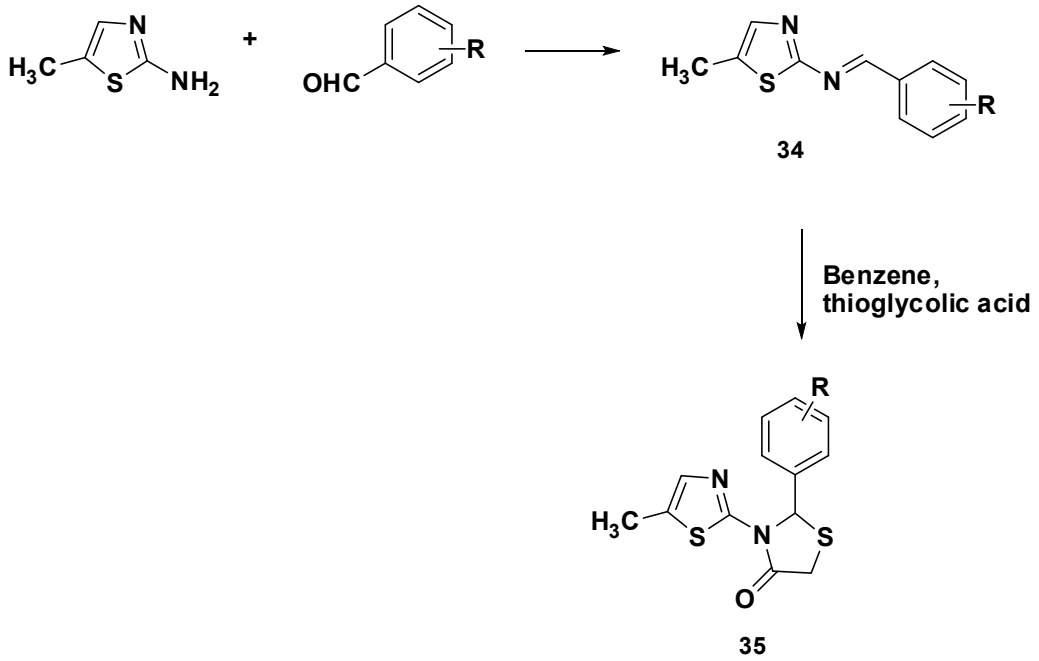


Figure 18. Synthesis of 3-(5-methyl-1,3-thiazol-2-yl)-2-phenyl-1,3-thiazolidin-4-ones

Several 2-phenyl-*N*-(5-cyclopropylthiadiazole)thiazolidin-4-ones (**36**) were prepared from the condensation of 2-amino-5-cyclopropylthiadiazoles and substituted benzaldehydes. The synthesized compounds showed good activity against gram positive *Staphylococcus aureus* and *Bacillus subtilis* and the gram negative *Escherichia coli* and *Pseudomonas aeruginosa* (**Figure 19**) (Patel et al., 2014b).

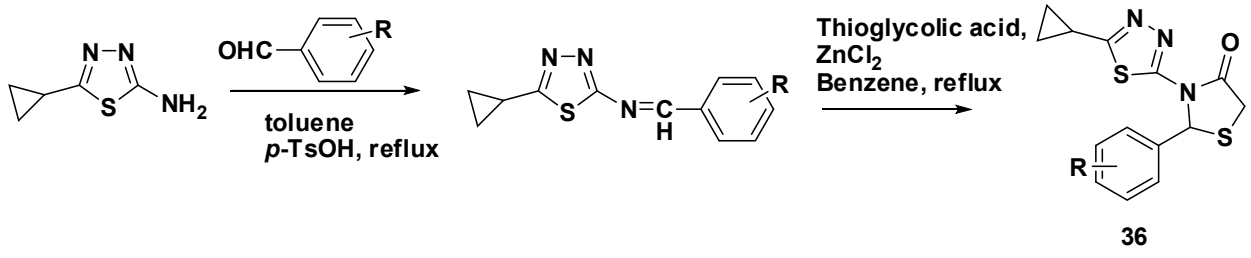


Figure 19. Synthesis of 2-phenyl-*N*-(5-cyclopropylthiadiazole)thiazolidin-4-ones

Compounds of the 2-piperidine-*N*-benzylthiazolylthiazolidin-4-one (**37-38**) type based on ciprofloxacin and norfloxacin were formed from their respective antibiotics. The *N*-benzylthiazolyl group (**38**) was synthesized by forming an *N*-formyl group on the piperidine substituent before condensing it with substituted benzylthiazolyls, which were formed from various amines and potassium thiocyanate (**Figure 20**). Some of the synthesized derivatives enhanced the activity of ciprofloxacin against *S. aureus*, *B. subtilis*, *E. coli* and *P. aeruginosa* (Patel et al., 2014c).

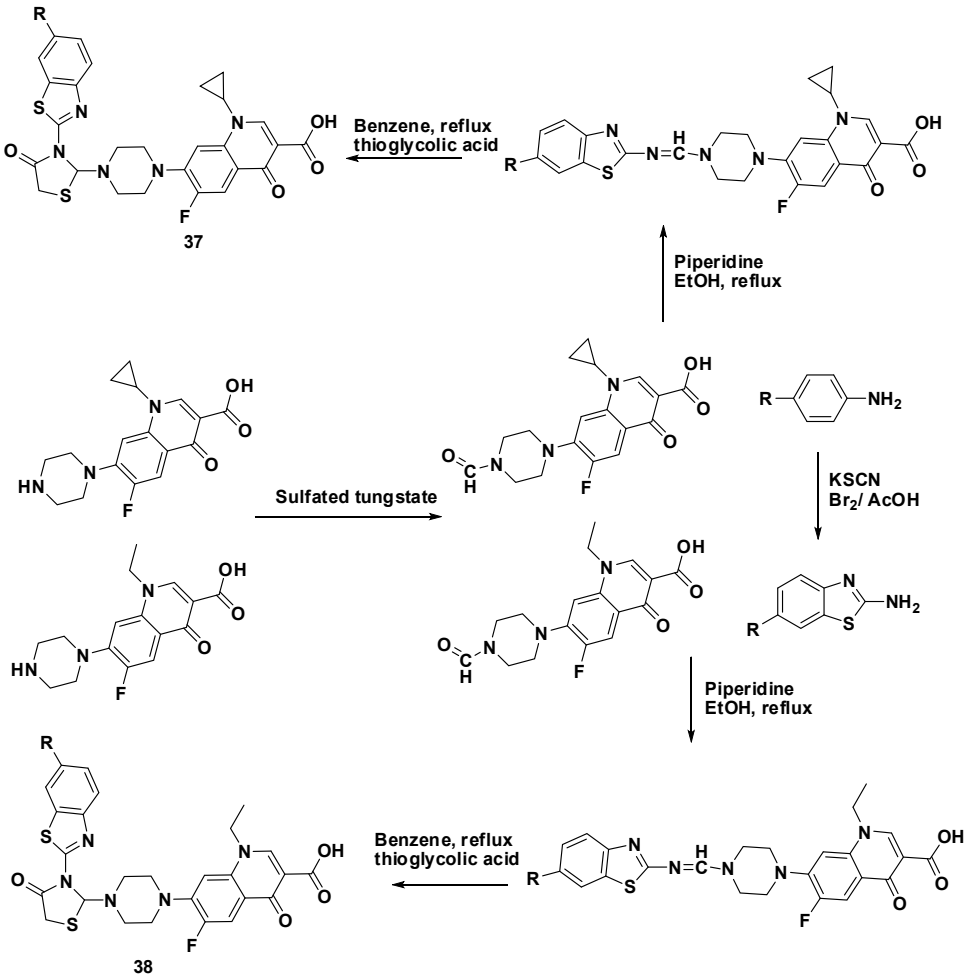


Figure 20. Synthesis of thiazolidin-4-one derivatives of fluoroquinolines

N-substituted pyrimidine thiazolidinones with substituted 2-phenyl groups and various substituted phenyl groups on the pyrimidine were synthesized by first forming the phenyl pyrimidines (**39**) with various benzaldehydes, urea/thiourea and ethyl acetoacetate and then forming hydrazines (**40**) which was then reacted with various benzaldehydes to form the imine intermediates (**41**). These imine intermediates were then reacted with thioglycolic acid and zinc chloride to form the pyrimidine thiazolidinones (**42**) (**Figure 21**). The derivatives with *meta* and *para* nitro groups on the phenyl ring of the pyrimidine showed antibacterial activity comparable to streptomycin against gram positive *S. aureus* and gram negative *E. coli*, whilst the rest of the compounds showed moderate activity (Piste and Kanase, 2014).

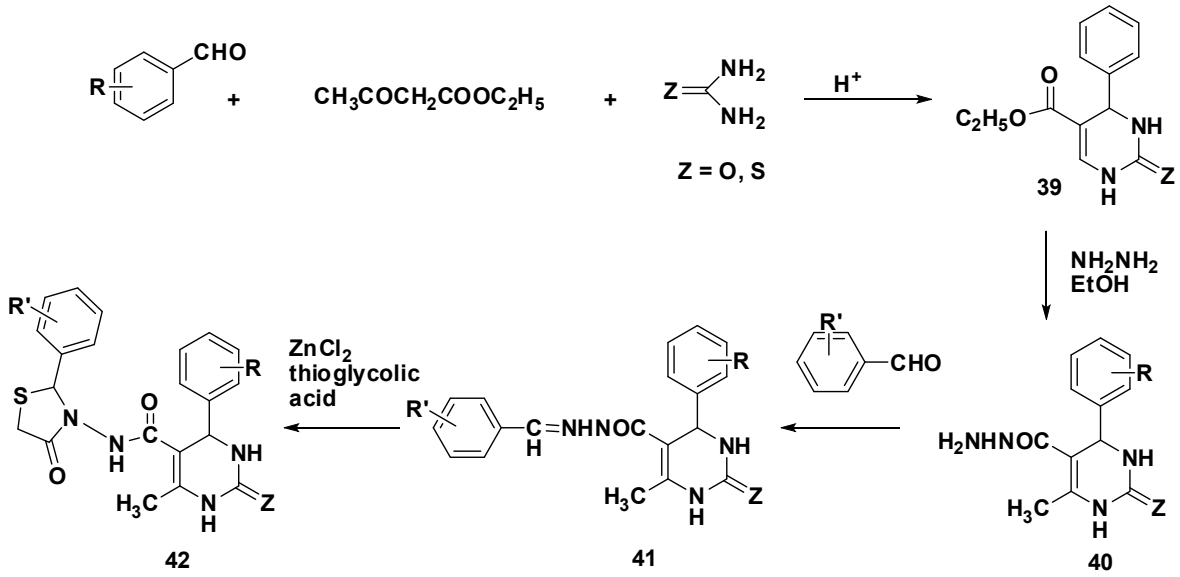


Figure 21. Synthesis of *N*-substituted pyrimidine thiazolidinones

Novel mannich bases of thiazolidinones (**45**) derived from pyrazolines (**44**) were synthesized by reacting the pyrazolines with thiazolidin-4-ones (**43**). These thiazolidin-4-ones were formed from sulfanilamides and benzaldehydes, forming the imines which were then converted to the

thiazolidin-4-ones with thioglycolic acid. The pyrazolines were formed through a chalcone intermediate using hydrazine (**Figure 22**) (Pujari et al., 2014).

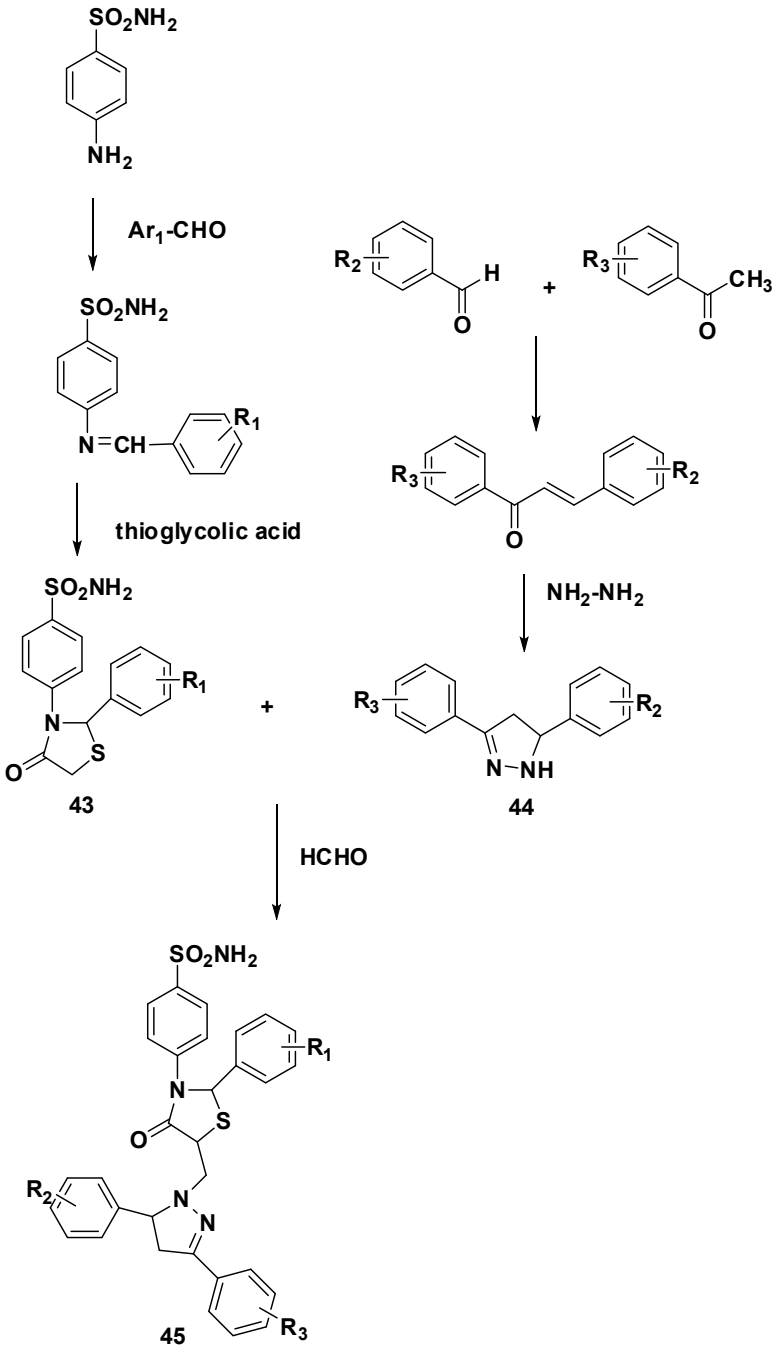


Figure 22. Synthesis of novel mannich bases of thiazolidinones derived from pyrazolines

Isoxazolyl-2-aminobenzamide thiazolidin-4-ones (**47**) were synthesized from isoxazolyl-2-aminobenzamides and substituted benzaldehydes in the usual fashion using thioglycolic acid through an imine intermediate (**46**). The isoxazolyl-2-aminobenzamides were formed through the condensation of amino-isoxazolyls and *ortho*-amino benzoic acid (**Figure 23**) (Rajanarendar et al., 2014).

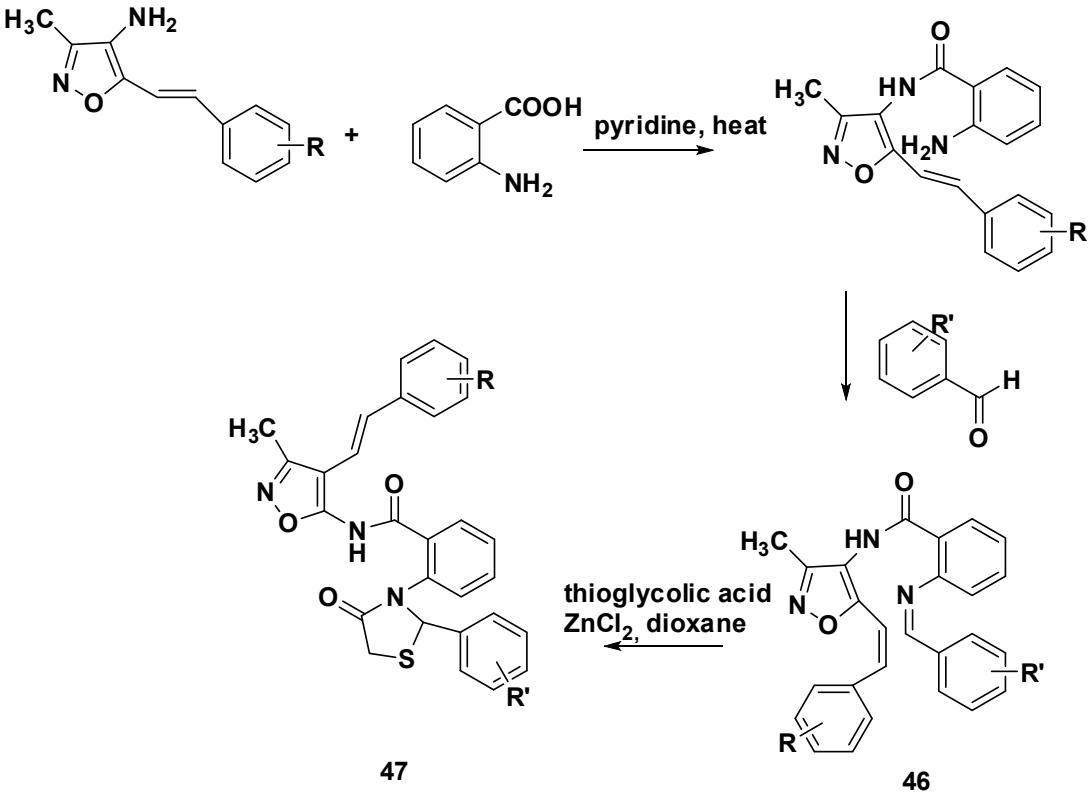


Figure 23. Synthesis of isoxazolyl-2-aminobenzamide thiazolidin-4-ones

The 4-thiazolidinone derivatives (**50**) of 2,6-dichloro-1-(*N*-substituted phenyl)-1,4-dihydropyridine-3,5-dicarbaldehydes were synthesized from the dicarbaldehydes (**48**) by a condensation reaction with substituted anilines to form the imines (**49**) at both the aldehydes, which were subsequently cyclized with thioglycolic acid to form thiazolidinones at both C-3 and

C-5. The diformylated intermediate was formed from glutaric acid converted to the glutarimides with thionyl chloride and substituted anilines (**Figure 24**). All the synthesized compounds showed moderate activity against the bacterial species *S. aureus*, *B. subtilis*, *E. coli* and *P. aeruginosa.* Some compounds showed comparable activity, whilst the other compounds showed better activity than the fungal strain, *Aspergillus niger* (Rajput and Girase, 2014).

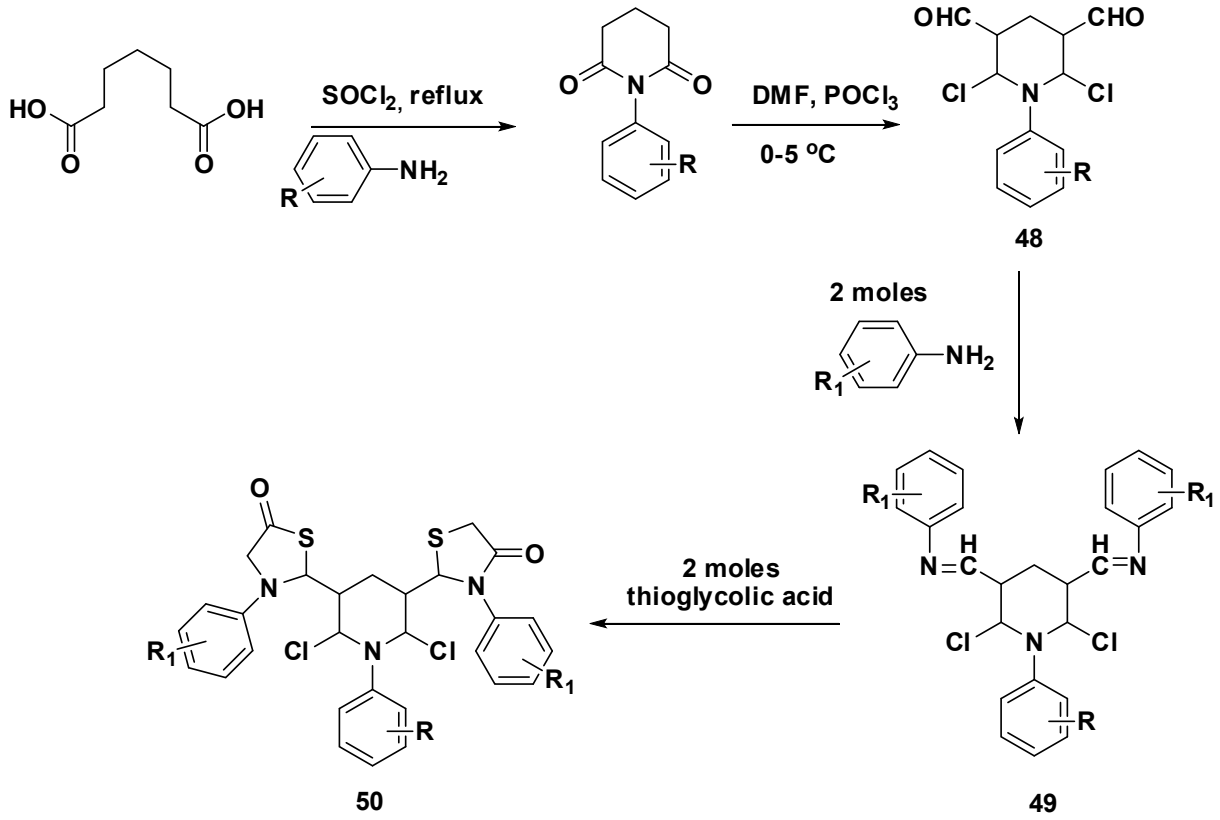


Figure 24. Synthesis of 4-thiazolidinone derivatives

The thiazolidinone quinoxaline-2,3-dione derivatives (**53**) were formed from sulphonamide quinoxalines by reacting these sulphonamides (**51**) with substituted benzaldehydes to form the imines (**52**) and then the thiazolidinones with thioglycolic acid. The quinoxaline-2,3-diones were

formed from 1,2-diaminobenzene and oxalic acid and subsequently reacted with *para*-aminobenzenesulfonamine to form the sulphonamide quinoxalines (**Figure 25**) (Sankari et al., 2013).

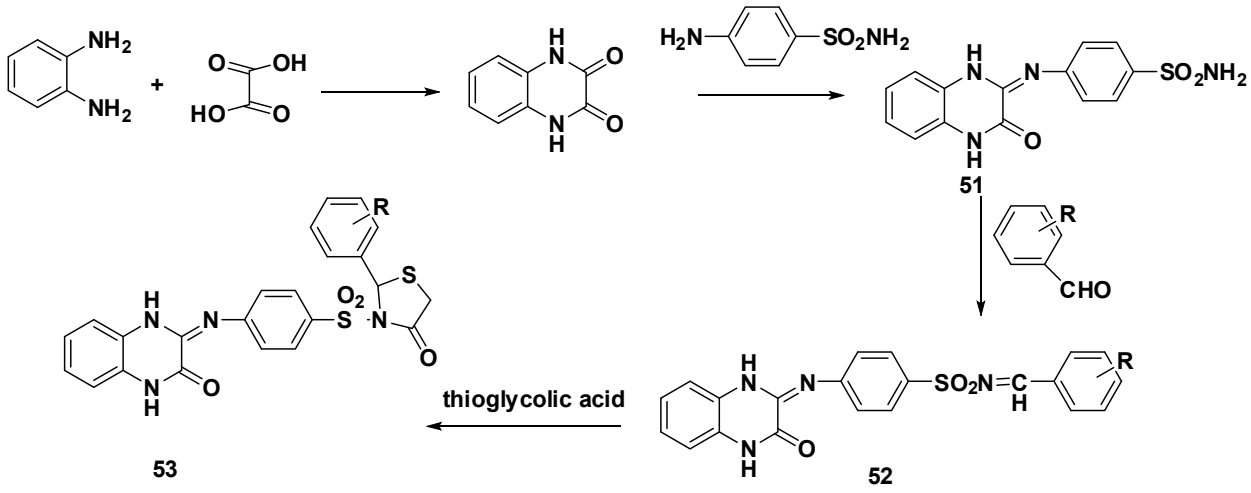


Figure 25. Synthesis of thiazolidinone quinoxaline-2,3-dione derivatives

The 1,2,4-triazolyl-thiazolidinones were formed from 3-amino-1,2,4-triazoles and substituted benzaldehydes, first forming the imines (**54**), which were cyclized either with thioglycolic acid or 2-mercaptopropanoic acid to form either the thiazolidinones (**55**) or the 5-methyl-thiazolidinones (**56**) (**Figure 26**) (Singh et al., 2014b).

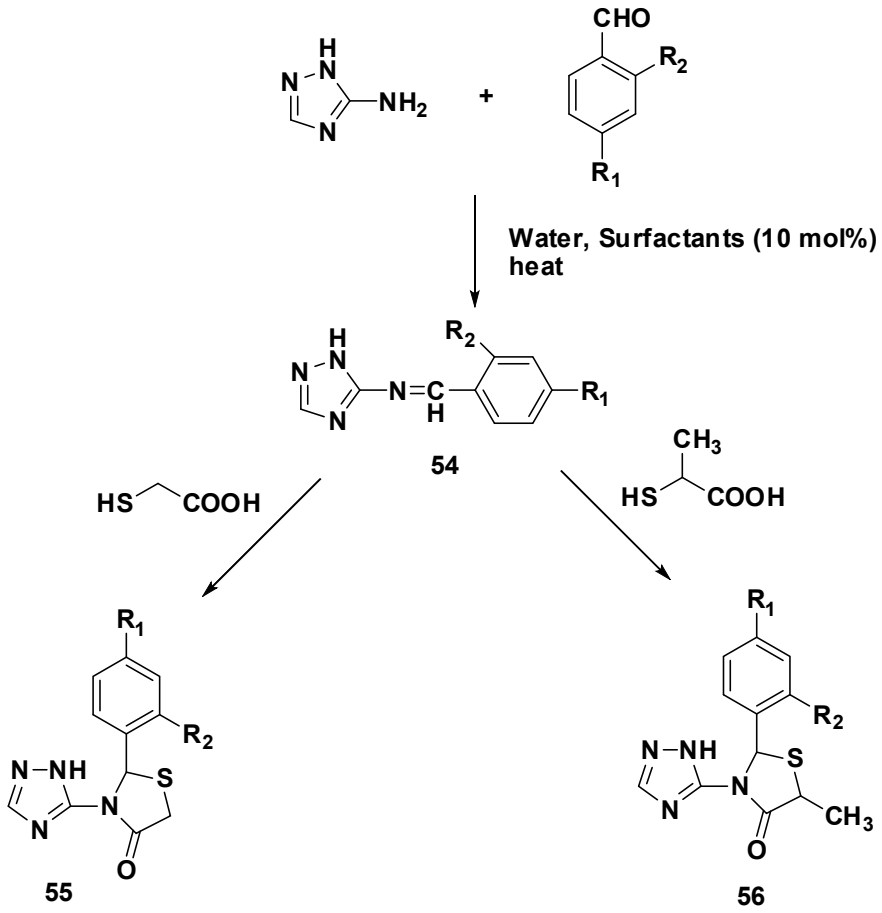


Figure 26. Synthesis of 1,2,4-triazolyl-thiazolidinones

Substituted anilines and aldehydes were reacted in alcohol and acid to produce Schiff bases (**57**) which were cyclized with thioglycolic acid to form the thiazolidinones (**58**) with substituted phenyl groups at the nitrogen and C-2. These derivatives were then reacted with morpholine and formaldehyde to form 5-substituted morpholine derivatives (**59**) (**Figure 27**). These compounds showed antitubercular activity against the *Mycobacterium tuberculosis* H37Rv strain (Thomas et al., 2014).

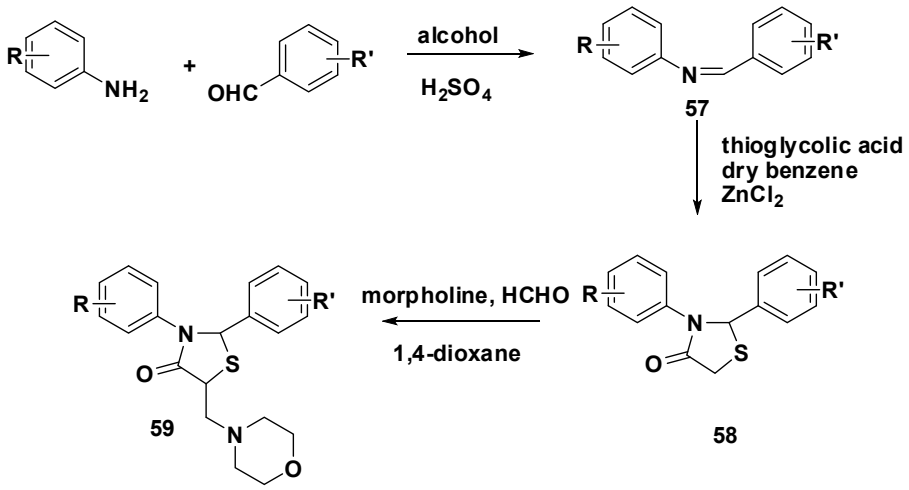


Figure 27. Synthesis of 5-substituted morpholine thiazolidinone derivatives

Indolo-2,3*b*-quinoxalines were derivatized with 2-phenyl-*N*-carboxyamide substituted thiazolidinones forming the Schiff bases (**60**) first with benzaldehydes and then cyclizing them with thioglycolic acid to form Indolo-2,3*b*-quinoxalines thiazolidinones (**61**) (**Figure 28**). This synthesis was a greener approach to previous methods carried out (Waghmode et al., 2014).

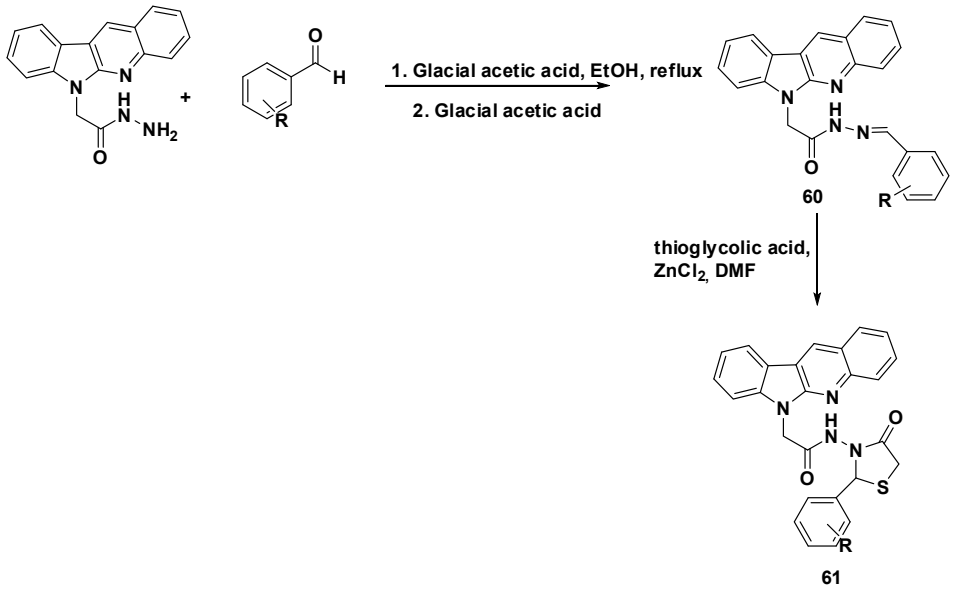


Figure 28. Synthesis of indolo-2,3*b*-quinoxalines thiazolidinones

Thiazolidinones with different phenyl substituents (**62**) at both C-2 and the nitrogen atom were synthesized in the usual way from benzaldehydes and anilines with thioglycolic acid. In another method, the benzaldehydes were first esterified with methanol and thionyl chloride and then reacted with 2-methoxyaniline and thioglycolic acid to produce the thiazolidin-4-ones (**63**) after which the ester was hydrolysed with LiOH to form the derivative **64**. The free carboxylic acids were then coupled with various amines using *N*-(3-dimethylaminopropyl)-*N*′-ethylcarbodiimide hydrochloride (EDC) and 1-hydroxy-benzotriazole (HOBt) to produce arylalkyl amino groups at C-2 of the thiazolidinones (**65**) (**Figure 29**). Most of the synthesized compounds had good anti-cancer activity against the A549 and MDA-MB-231 cell lines with the 4-bromophenylethylamine carboxyl derivative having the best activity (Wu et al., 2014).

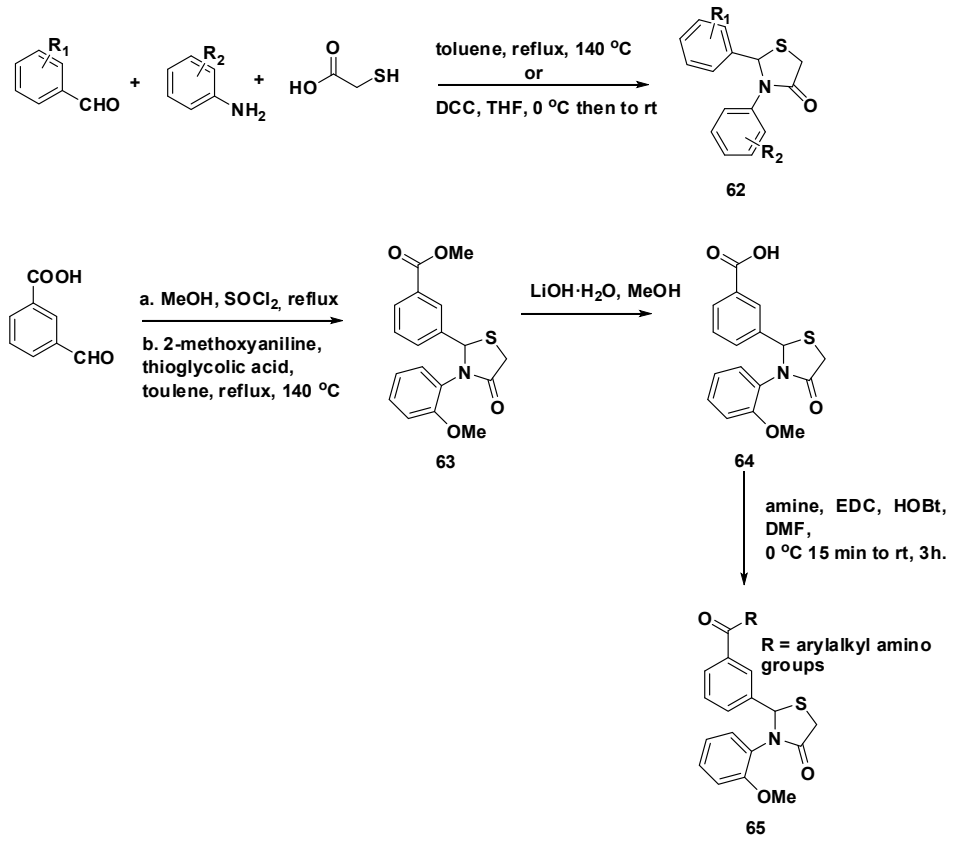


Figure 29. Synthesis of arylalkyl amino thiazolidinones

2.3 Formation of thiazolidinones using esters of thioglycolic acid and amines without the use of benzaldehydes

In most of the reactions with thioglycolic acid, both aldehydes and amines are needed to form the imines which are then converted to the thiazolidinones, however the reaction below shows an example of forming the thiazolidinones using thioglycolic acid derivatives together with the amines, without the use of aldehydes.

Pentachloro-2-nitro-1,3-butadiene was reacted with ethyl 2-mercaptoacetate to form ethyl 2-(1,3,4,4-tetrachloro-2-nitrobuta-1,3-dien-1-yl)thioacetate (**66**) as an intermediate. Similarly, pentachloro-2-nitro-1,3-butadiene was reacted with the methyl ester of 2-mercaptoacetate to form a mixture of methyl 2-(1,3,4,4-tetrachloro-2-nitrobuta-1,3-dien-1-yl)thioacetate and 1,1-bis(methoxycarbonylmethylthio)-2-nitro-3,4,4-trichlorobuta-1,3-diene (**67-68**). These intermediates were then reacted with various anilines to form (*Z)*-3-aryl-2-(2,3,3-trichloro-1-nitroallylidene) thiazolidin-4-ones (**69**). One of the chloro groups on the alkyl chain at C-2 of the thiazolidinone was then substituted with a *p*-toluyl thiophenol group to form (*Z*)-3-(4-tolyl)-2-(3,3-dichloro-1-nitro-2-[4-tolylthio]allylidene)thiazolidin-4-one (**70**) (**Figure 30**) (Zapolskii et al., 2014).

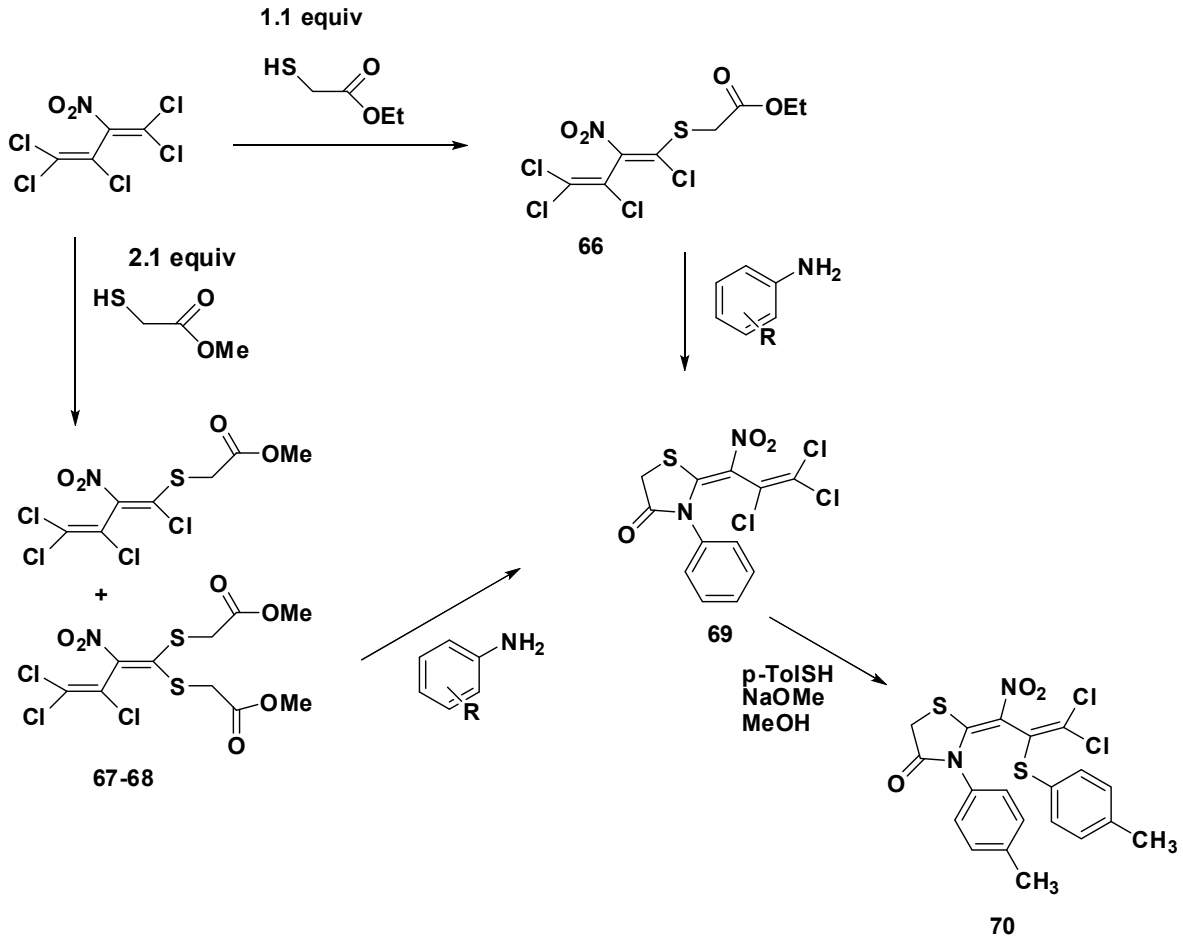


Figure 30. Synthesis of (*Z*)-3-aryl-2-(2,3,3-trichloro-1-nitroallylidene) thiazolidin-4-ones

2.4 Formation of thiazolidinones using thiourea, chloroacetic acid and sodium acetate

This method of synthesis is not as commonly used as that of condensation with aldehydes, anilines and thioglycolic acid. However, this is a good method to attach groups with a nitrogen (such as pyrazoles) at C-2. Some recent examples are given below.

The 5-benzylidene-2-arylamine thiazolidin-4-ones (**71**) and the pyrazoline-thiazolidinone-isatin conjugates (**72**) were synthesized according to the scheme in **Figure 31**. These compounds showed high toxicity toward a panel of 60 tumor cell lines (Avdieiev et al., 2014).

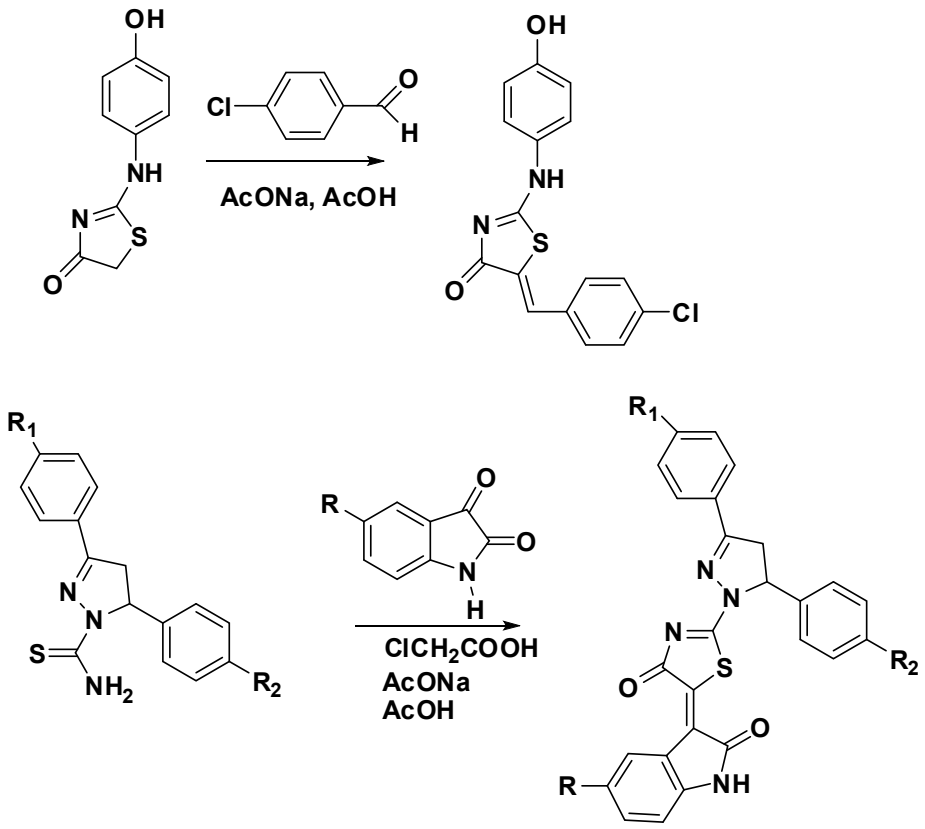


Figure 31. The synthesis of 5-benzylidene-2-arylamine thiazolidin-4-ones and pyrazoline-thiazolidinone-isatin conjugates

Two thiazolidinone derivatives (**74-75**) were prepared from *L*-norephedrine and ethyl isothiocyanate in chloroform with triethylamine to form 1-ethyl-3-(1-hydroxy-1-phenylpropan-2-yl)-thiourea (**73**) first before being condensed with chloroacetyl chloride in the presence of triethylamine to form the 2-imino-4-thiazolidinones (**Figure 32**) (Ghorab et al., 2014).

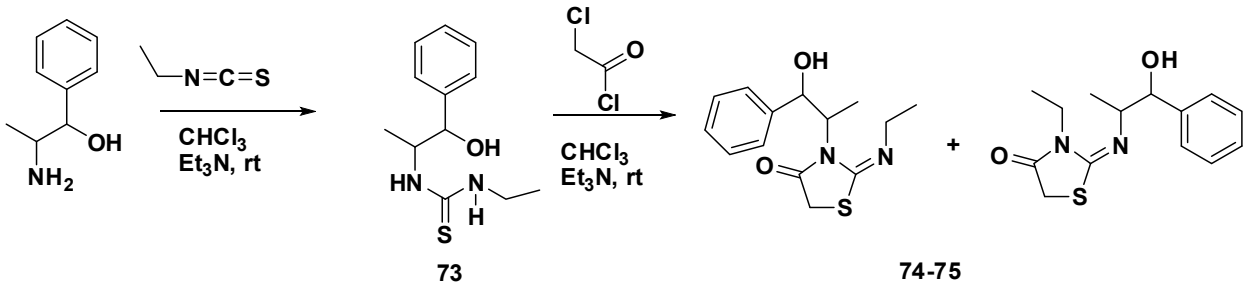


Figure 32. Synthesis of 2-imino-4-thiazolidinones from *L*-norephedrine and ethyl isothiocyanate

Compounds of the 5-arylidene-thiazolidine-2,4-diones (**76**) were synthesized in a two-step reaction involving monochloroacetic acid and thiourea in water to form the thiazolidin-2,4-diones which were then reacted with substituted benzaldehydes in ethanol and piperidine as shown in **Figure 33** (da Silva et al., 2014). All the synthesized compounds were tested for their antibacterial activity against both gram positive and gram negative bacteria. The 3-methoxy and 4-hydroxy derivatives were the most active against the gram positive bacteria whilst the 2,4-dichloro and 3,4-dichloro derivatives were the most active against the gram negative bacteria.

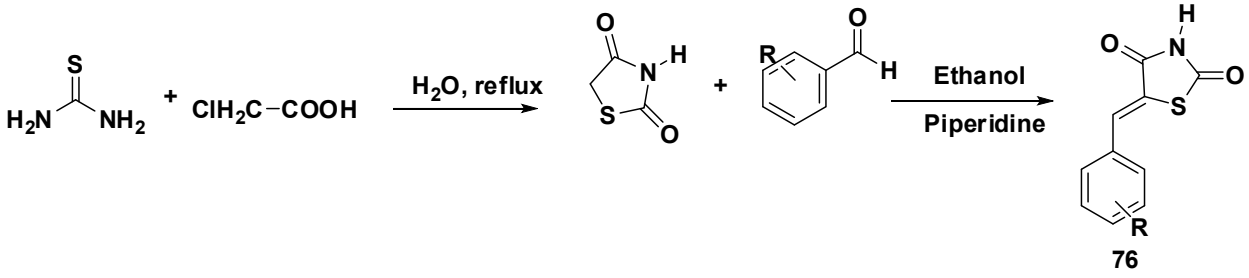


Figure 33. Synthesis of 5-arylidene-thiazolidine-2,4-diones from thiourea and monochloroacetic acid

2.5 The synthesis of thiazolidinones from thioamines and dimethyl acetylenedicarboxylate (DMAD)

The thiazolidinones (**78**) in **Figure 34** were formed from enamines and azaenamines containing a thioamide group and DMAD with triethylamine and methanol or chloroform through a dicarboxylate intermediate (**77**) (Belskaya et al., 2014).

2.6 Formation of thiazolidinones with 2-chloroacetamides and ammonium thiocyanate (NH_4SCN)

Derivatives of 5-aryliden-2-imino-4-thiazolidinones were synthesized from aniline and chloroacetyl chloride forming 2-chloro-*N*-etheroaryl acetamides which were then cyclized with ammonium thiocyanate forming the 5-aryliden-4-thiazolidinones (**79**). These were then condensed with benzaldehydes to form the 2-imino derivatives. These compounds showed good *in vivo* and *in vitro* anti-inflammatory activity (**Figure 35**) (Singh et al., 2014a).

2.7 Derivatisation of previously prepared thiazolidinones

The C-4 carbonyl of thiazolidinones can be converted to the thiocarbonyl group with Lawesson's reagent. This can then be further reacted to make a series of derivatives. The nitrogen can be derivatised with the bromo ester and aromatic substituents can be introduced at C-5 with benzaldehydes.

Enaminones of 4-thiazolidinones were reacted with a dimethylformide-dimethylacetal mixture (DMF-DMA) to form a methylene dimethylamine intermediate at C-5 before reacting it with Lawesson's reagent to convert the ketone to the sulfide and then using various hydrazines to form

the substituted dihydro-1*H*-pyrazolo-3,4*d*-thiazoles (**80**) (**Figure 36**) (Gautam and Chaudhary, 2014).

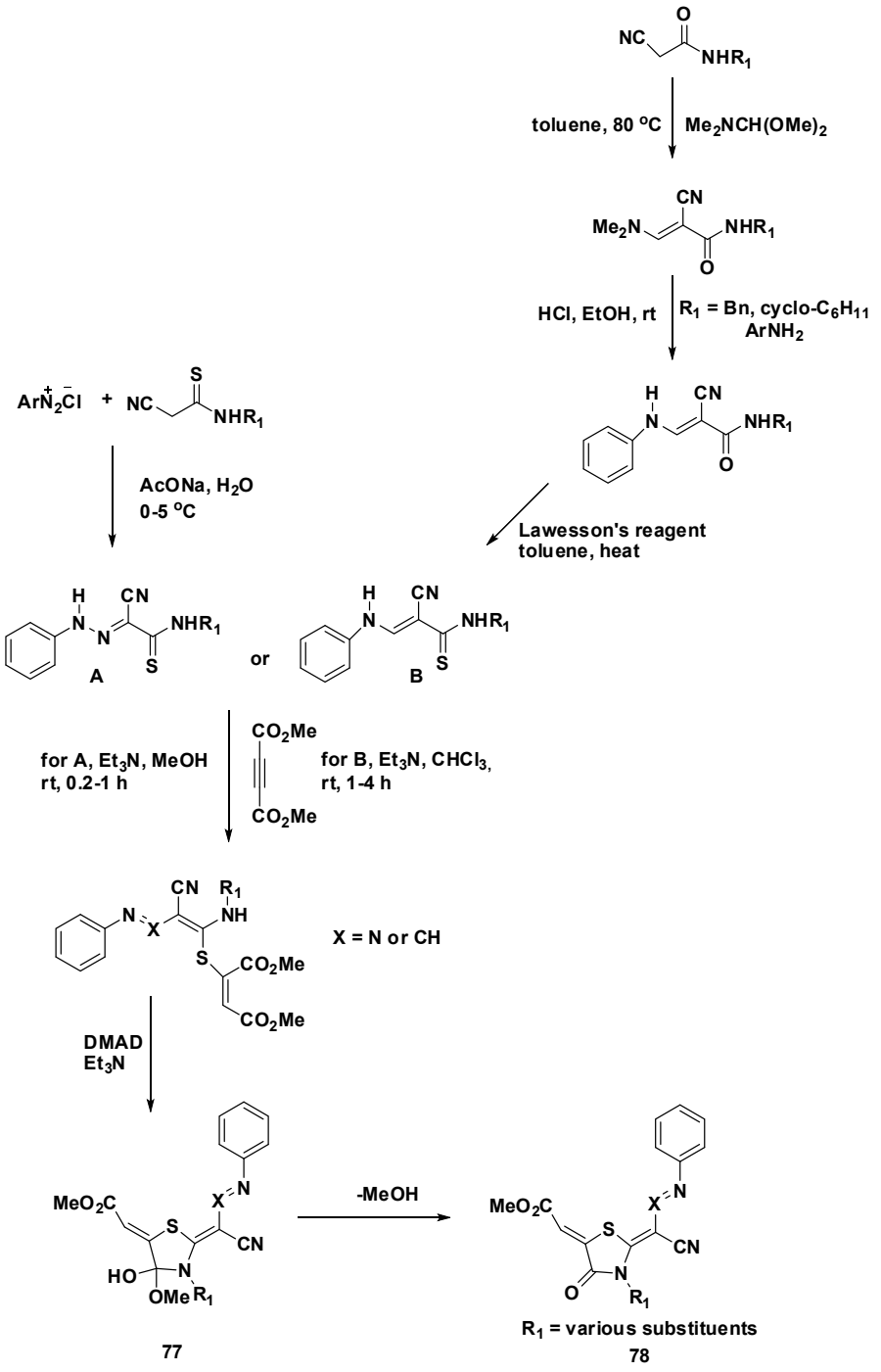


Figure 34. Thiazolidin-4-ones synthesized from enamines and azaenamines containing a thioamide group and dimethyl acetylenedicarboxylate

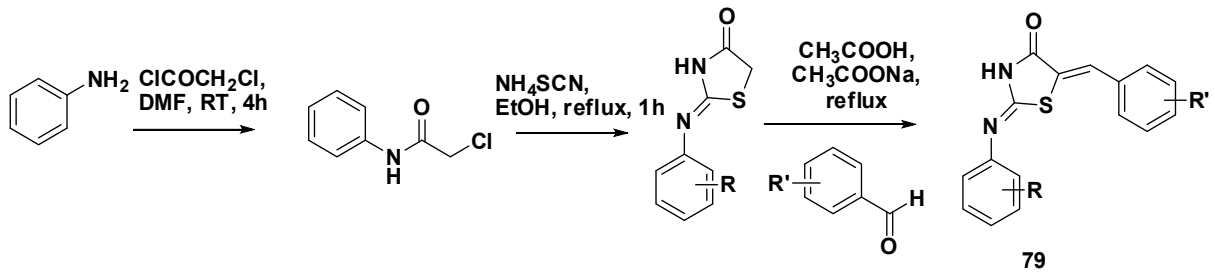


Figure 35. Synthesis of 5-aryliden-2-imino-4-thiazolidinones

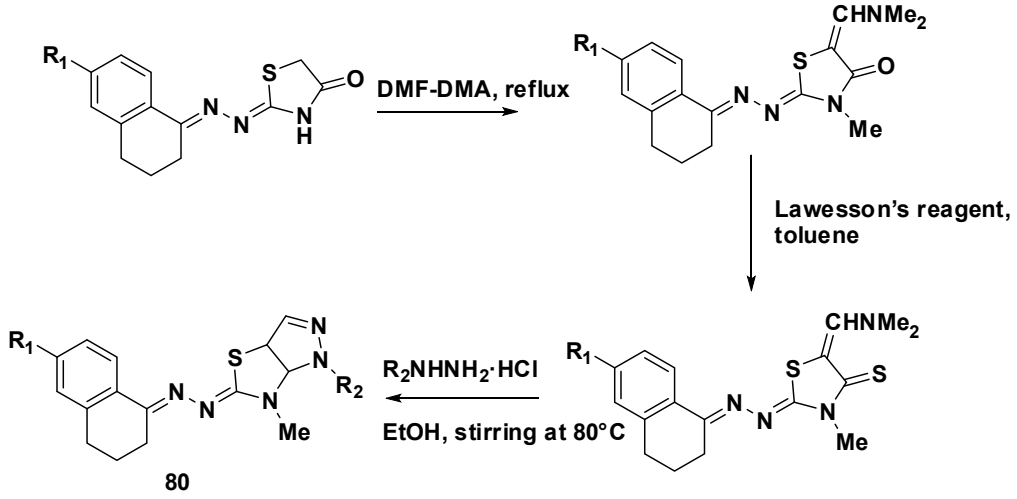


Figure 36. Synthesis of substituted dihydro-1*H*-pyrazolo(3,4*d*)thiazoles from enaminones of 4-thiazolidinones

Thiazolidinones (**81**) containing 2-oxo and 2-thioxo groups were formed from 2,4-dioxothiazolidines and various benzaldehydes (**Figure 37**) (Maccari et al., 2014). These compounds were found to have anti-inflammatory activity being active against the aldose reductase enzyme at submicromolar IC_{50} values.

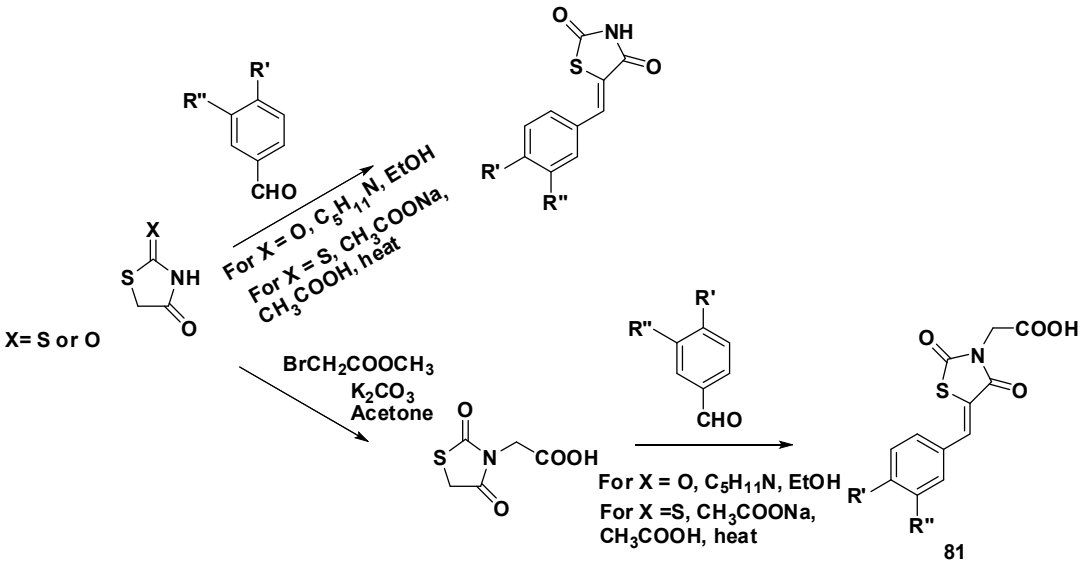


Figure 37. Synthesis of 2-oxo and 2-thioxo thiazolidinones from 2,4-dioxothiazolidines and various benzaldehydes

Chapter 3. Experimental

3.1 General procedures

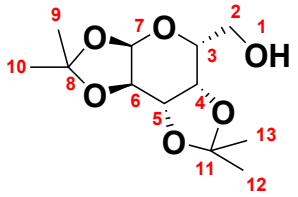
Nuclear magnetic resonance (NMR) spectra were recorded on Bruker AVANCE III 400 MHz spectrophotometer. ^{1}H and ^{13}C NMR data were recorded at 400 MHz and 100 MHz respectively, at room temperature with chemical shifts (δ) recorded in deuterated chloroform ($CDCl_3$) against the internal standard, tetramethylsilane (TMS). Thin layer chromatography (TLC) was performed using Merck Kieselgel 60 F_{254} plates. Column chromatography was carried out using silica gel 60 as the stationary phase and with different mobile phases consisting of various ratios of organic solvents. Infrared (FT-IR) spectra were recorded on a Perkin Elmer Spectrum 100 FT-IR spectrometer with universal ATR sampling accessory. Ultraviolet (UV) analyses were performed using a UV-VIS Shimadzu series 200 spectrophotometer in methanol. Melting point determinations were carried out using a Stuart Smart scientific melting point apparatus. Optical rotational values were obtained using a Perkin Elmer 341 Polarimeter at a concentration of 0.2% in chloroform at 589 nm. The purity of each compound was analyzed using a Shimadzu High Pressure Liquid Chromatography (HPLC) instrument equipped with an Agilent Eclipse XDB-C18 column (5.0 μm, 9.4 x 250 mm ID). Samples were dissolved in methanol and analysed with a mobile phase of acetonitrile with a formic acid buffer (0.1%) at a flow rate of 3 mL min^{-1}. Gas Chromatography Mass Spectrometry (GC-MS) data were acquired using an Agilent Technologies GC-MSD apparatus equipped with a DB-5SIL MS (30 m x 0.25 mm i.d., 0.25 μm film thickness) fused silica capillary column. Helium (2 mL min^{-1}) was used as a carrier gas and methanol was used to dissolve the samples. High Resolution mass data (HRMS) were obtained for selected compounds using a Bruker microTOF-Q II ESI instrument operating at ambient temperatures, with a sample concentration of 1 ppm.

3.2 Synthetic procedures

3.2.1 Acetonide protection of galactose (1)

Galactose (20.0 g, 0.111 mols) and anhydrous copper sulphate (19.7 g, 0.124 mols) were added to acetone (100 mL) and stirred at 0°C for 24 hours. Concentrated H_2SO_4 (1.00 mL) was then added dropwise to the mixture under nitrogen and the mixture allowed to stir for 20 hours at room temperature. The reaction progress was monitored by TLC. On completion, the mixture was made basic to pH 9 with a saturated solution of potassium carbonate, dissolved in 20.0 mL of water and the product extracted with dichloromethane (DCM). The organic layer was dried over magnesium sulphate and concentrated under reduced pressure to yield **compound 1** in 95% yield.

(2,2,7,7-Tetramethyltetrahydro-*bis*[1,3]dioxolo[4,5b;4',5'd]pyran-5-yl)-methanol (1)



Physical description: Colourless sticky solid

Molecular formula: $C_{12}H_{20}O_6$ (260.28 g mol^{-1})

Yield: 95%

Optical rotation: $[\alpha]_D^{25}$ -59.5° (*c* 0.077 MeOH)

^{1}H NMR data: (400 MHz, $CDCl_3$): δ 5.55 (d, 1H, *J* = 5.0 Hz, H-7), 4.60 (dd, 1H, *J* = 8.0, 2.4 Hz, H-5), 4.32 (dd, 1H, *J* = 5.0, 2.3 Hz, H-6), 4.26 (d, 1H, *J* = 7.9 Hz, H-4), 3.80-3.87 (m, 2H, H-2i/3),

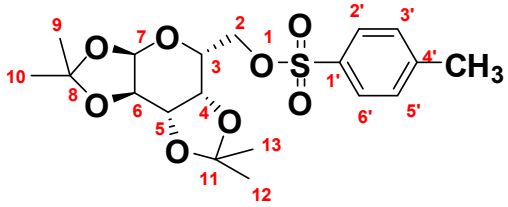
3.71-3.75 (m, 1H, H-2ii), 1.99 (d, 1H, J = 7.0 Hz, H-1), 1.51 (s, 3H, H-9), 1.44 (s, 3H, H-13), 1.32 (s, 6H, H-12/10).

^{13}C NMR Data: (100 MHz, $CDCl_3$): δ 109.5 (C-11), 108.7 (C-8), 96.3 (C-7), 71.6 (C-4), 70.8 (C-5), 70.6 (C-6), 68.1 (C-3), 62.3 (C-2), 26.0 (C-9), 25.9 (C-13), 24.9 (C-12), 24.3 (C-10).

3.2.2 Synthesis of toluene sulfonyl ester, toluene-4-sulfonic acid 2,2,7,7-tetramethyl tetrahydro-*bis*[1,3]dioxolo[4,5b;4',5'd]pyran-5-ylmethyl ester (2)

Compound 1 (13.0 g, 0.0500 mols) was dissolved in DCM (150 mL), cooled to 0°C and pyridine (19.7 g, 0.250 mols) and a tosyl chloride mixture in DCM (11.4 g, 0.0597 mols) was added to the reaction mixture under nitrogen and stirred at room temperature for 12 hours. The product was then cooled to 0°C and made neutral (pH 7) with dilute acid. The organic portion was then extracted with DCM, washed with water and sodium bicarbonate and dried over sodium sulphate. Evaporation of the solvent yielded **compound 2** in 85% yield.

Toluene-4-sulfonic acid 2,2,7,7-tetramethyltetrahydro-*bis*[1,3]dioxolo[4,5b;4',5'd]pyran-5-ylmethyl ester (2)



Physical description: White solid

Molecular formula: $C_{19}H_{26}O_8S$ (414.47 g mol^{-1})

Yield: 85%

Melting point: 118-120 °C

Optical rotation: $[\alpha]_D^{25}$ -52.8° (*c* 0.048 MeOH)

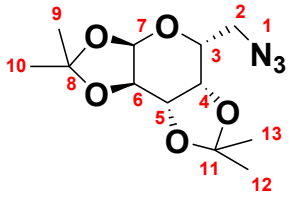
^{1}H NMR: (400 MHz, $CDCl_3$) δ 7.78 (d, 2H, *J* = 8.2 Hz, H-3'/5'), 7.30 (d, 2H, *J* = 8.2 Hz, H-2'/6'), 5.42 (d, 1H, *J* = 4.9 Hz, H-7), 4.56 (dd, 1H, *J* = 7.9, 2.4 Hz, H-5), 4.26 (dd, 1H, *J* = 4.9, 2.5 Hz, H-6), 4.15-4.19 (m, 2H, H-2i/4), 4.00-4.08 (m, 2H, H-2ii/3), 2.42 (s, 3H, H-7'), 1.47 (s, 3H, H-9), 1.32 (s, 3H, H-13), 1.29 (s, 3H, H-12), 1.26 (s, 3H, H-10).

^{13}C NMR: (100 MHz, $CDCl_3$) δ 144.8 (C-1'), 132.8 (C-4'), 129.7 (C-3'/5'), 128.1 (C-2'/6'), 109.6 (C-11), 108.9 (C-8), 96.1 (C-7), 70.5 (C-4), 70.4 (C-5), 70.4 (C-6), 68.2 (C-2), 65.9 (C-3), 26.0 (C-9), 25.8 (C-12), 24.9 (C-13), 24.3 (C-10), 21.6 (C-7').

3.2.3 Azide preparation of 5-azidomethyl-2,2,7,7-tetramethyltetrahydro-*bis* [1,3]dioxolo[4,5b;4',5'd]pyran (3)

Compound 2 (16.0 g, 0.0386 mols) was dissolved in dry DMF (100 mL) and stirred for 5 minutes. Sodium azide (7.54 g, 0.116 mols) and a catalytic amount of tetra-n-butylammonium bromide (TBAB) was added to the reaction mixture under nitrogen and left to stir at 110 °C for 12 hours. The product was extracted with ethyl acetate and brine, dried over sodium sulphate, the solvent evaporated and the compound purified by column chromatography using ethyl acetate: n-hexane (1:4). **Compound 3** was obtained in 95% yield.

5-Azidomethyl-2,2,7,7-tetramethyltetrahydro-*bis*[1,3]dioxolo[4,5b;4',5'd]pyran (3)



Physical description: Colourless sticky solid

Molecular formula: $C_{12}H_{19}N_3O_5$ (285.30 g mol^{-1})

Yield: 95%

Optical rotation: $[\alpha]_D^{25}$ 78.2° (*c* 0.070 MeOH)

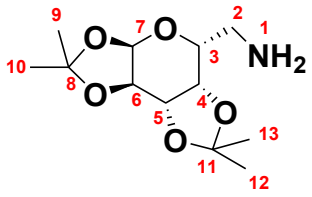
^{1}H NMR data: (400 MHz, $CDCl_3$): δ 5.47 (d, 1H, *J* = 5.0 Hz, H-7), 4.57 (dd, 1H, *J* = 7.9, 2.4 Hz, H-5), 4.27 (dd, 1H, *J* = 5.0, 2.4 Hz, H-6), 4.13 (dd, 1H, *J* = 7.9, 1.8 Hz, H-4), 3.82-3.86 (m, 1H, H-3), 3.46 (dd, 1H, *J* = 12.7, 7.9 Hz, H-2i), 3.31 (dd, 1H, *J* = 12.7, 5.3 Hz, H-2ii), 1.47 (s, 3H, H-9), 1.38 (s, 3H, H-13), 1.27 (s, 6H, H-10/12).

^{13}C NMR Data: (100 MHz, $CDCl_3$): δ 109.5 (C-11), 108.7 (C-8), 96.3 (C-7), 71.1 (C-4), 70.8 (C-5), 70.3 (C-6), 67.0 (C-3), 50.6 (C-2), 26.0 (C-9), 25.9 (C-13), 24.8 (C-12), 24.4 (C-10).

3.2.4 Reduction of the azide (3) to 2,2,7,7-tetramethyltetrahydro-*bis*[1,3]dioxolo [4,5b;4',5'd]pyran-5-yl)-methylamine (4)

Compound 3 (10.0 g, 0.0351 mols) was dissolved in DCM (60.0 mL) and transferred to a two necked round bottom flask containing a palladium catalyst (500 mg). Methanol (40.0 mL) was added to the flask and the reaction mixture left to stir at room temperature for 5 hours under an atmosphere of hydrogen. On completion, the product was filtered under vacuum and concentrated under reduced pressure to afford **compound 4** (100% yield).

2,2,7,7-Tetramethyltetrahydro-*bis*[1,3]dioxolo[4,5b;4',5'd]pyran-5-yl)-methylamine (4)



Physical description: Colourless sticky solid

Molecular formula: $C_{12}H_{21}NO_5$ (259.30 g mol^{-1})

Yield: 100%

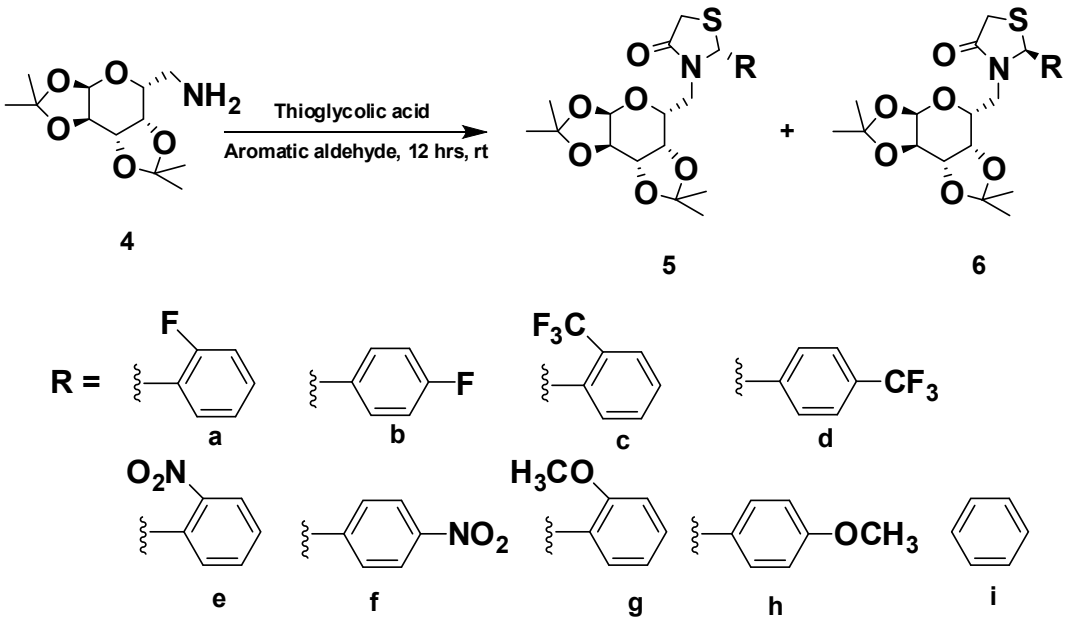
Optical rotation: $[\alpha]_D^{25}$ +61.3° (*c* 0.077 MeOH)

^{1}H NMR: (400 MHz, $CDCl_3$) δ 8.28 (s, 2H, NH_2), 5.55 (d, 1H, *J* = 5.0 Hz, H-7), 4.60 (dd, 1H, *J* = 7.6, 2.2 Hz, H-5), 4.31 (dd, 1H, *J* = 4.8, 2.3 Hz, H-6), 4.22 (d, 1H, *J* = 8.0 Hz, H-3), 4.17 (d, *J* = 7.6, H-4), 2.81 (s, 2H, H-2i/2ii), 1.62 (s, 3H, H-9), 1.40 (s, 3H, H-13), 1.29 (s, 6H, H-10/12).

^{13}C NMR: (100 MHz, $CDCl_3$) δ 109.8 (C-11), 109.5 (C-8), 95.9 (C-7), 71.1 (C-4), 70.6 (C-5), 70.3 (C-6), 64.5 (C-3), 40.3 (C-2), 26.1 (C-9), 25.9 (C-10), 24.9 (C-13), 24.3 (C-12).

3.2.5 Synthesis of the sugar thiazolidinone derivatives

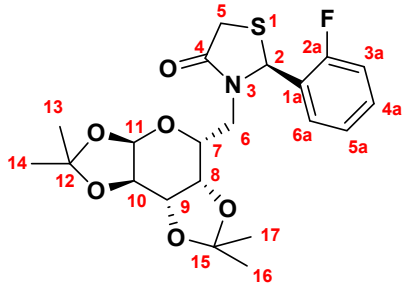
Compound 4 (800 mg, 0.00309 mols) was dissolved in dry THF (60.0 mL) and cooled to 0°C. Two equivalents of the aromatic aldehyde (0.00649 mols), thioglycolic acid (856 mg, 0.00927 mols), and EDC (957 mg, 0.00618 mols) was added to the reaction mixture and left to stir for 12 hours under nitrogen (**Scheme 3**). Once completed, the THF was removed under reduced pressure and the compound extracted using DCM and a sodium bicarbonate, washed with aqueous HCl, sodium bicarbonate, water and then dried over magnesium sulphate. The organic fraction was evaporated and further purified by column chromatography using acetone: n-hexane (10:90).



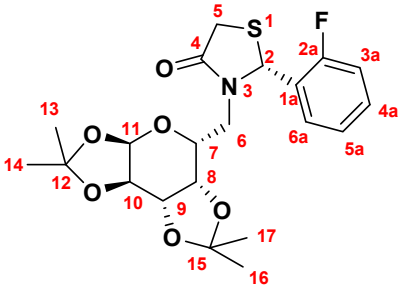
Scheme 3. Reaction for the synthesis of sugar thiazolidinone derivatives

3.3 Spectroscopic data

2-(2-Fluorophenyl)-3-(2,2,7,7-tetramethyltetrahydro-*bis*[1,3]dioxolo[4,5b;4',5'd]pyran-5-ylmethyl)thiazolidin-4-one (mixture of 5a and 6a)



5a



6a

Physical description: Light yellow gummy solid

Molecular formula: $C_{21}H_{26}FNO_6S$ (439.5 g mol^{-1})

Yield: 75.0%

UV: λ_{max} (nm) (log ε) 202 (4.32), 265 (3.25)

FT-IR: υ_{max} 1677 (C=O), 1209, 1064 cm^{-1}

Optical rotation: $[\alpha]_D^{25}$ -25.83° (*c* 0.046 $CHCl_3$)

^{1}H NMR: (400 MHz, $CDCl_3$) δ 7.24-7.30 (m, 2H, H-4a), 7.20 (t, 2H, *J* = 7.4 Hz, H-6a), 7.13 (t, 2H, *J* = 7.0 Hz, H-5a), 7.02 (t, 2H, *J* = 7.8 Hz, H-3a), 6.20* and 6.07* (s, 2H, H-2), 5.47* and 5.42* (d, 1H, *J* = 4.9 Hz, H-11), 4.57* and 4.52* (dd, 1H, *J* = 7.7, 2.2 Hz, H-9), 4.24-4.25 (m, 1H, H-10), 4.06-4.16 (m, 2H, H-7/8), 3.92 (dd, 1H, *J* = 13.4, 7.4 Hz, H-6i), 3.75* and 3.72* (d, 1H, *J* = 15.4 Hz, H-5i), 3.61 (d, 1H, *J* = 15.4 Hz, H-5ii), 2.84* and 2.80* (dd, 1H, *J* = 13.4, 6.3 Hz, H-6ii), 1.50* and 1.47* (s, 6H, H-13), 1.36* and 1.31* (s, 6H, H-17), 1.29* and 1.28* (s, 6H, H-16), 1.25* and 1.23* (s, 6H, H-14).

^{13}C NMR: (100 MHz, $CDCl_3$) δ 172.2* and 171.7* (C-4), 160.7* and 160.5* (d, *J* = 248.2 Hz, C-2a), 130.4* and 130.3* (d, *J* = 8.5 Hz, C-4a), 128.1* and 127.9* (d, *J* = 3.2 Hz, C-6a), 124.6* and 124.5* (d, *J* = 3.6 Hz, C-5a), 116.1* and 116.0* (d, *J* = 21.1, C-3a), 127.1* and 127.0* (d, *J* = 11.4 Hz, C-1a), 109.6* and 109.5* (C-15), 109.0* and 108.7* (C-12), 96.3* and 96.2* (C-11), 71.8* and 71.9* (C-8), 70.89* and 70.86* (C-9), 70.41* and 70.38* (C-10), 67.0* and 63.5* (C-7), 58.9* and 57.1* (d, *J* = 3.9 Hz, C-2), 43.7* and 43.1* (C-6), 32.4 (s, 2C, C-5), 26.0* and 25.92* (C-13), 25.90* and 25.7* (C-17), 25.0* and 24.9* (C-16), 24.5 (2C, C-14).

**One resonance for each diastereomer*

^{19}F NMR (376.4 MHz, $CDCl_3$): δ -118.2* and -118.9*

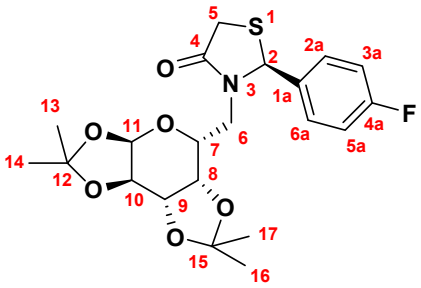
MS data: *m/z* (rel. int.):

Diastereomer 1: 439 (60) [M^+], 424 (23) [M^+ - CH_3], 366 (38), 268 (49), 196 (100), 109 (87)

Diastereomer 2: 439 (74) [M^+], 424(25) [M^+ - CH_3], 366 (33), 268 (38), 196 (100), 109 (96)

Purity (HPLC): 77.8% (9.5 min in acetonitrile with 0.1% formic acid buffer)

2-(4-Fluorophenyl)-3-(2,2,7,7-tetramethyltetrahydro-*bis*[1,3]dioxolo[4,5b;4',5'd]pyran-5-ylmethyl)thiazolidin-4-one (5b)



Physical description: White solid

Molecular formula: $C_{21}H_{26}FNO_6S$ (439.50 g mol^{-1})

Yield: 45.0%

Melting point: 110-113 °C

UV: λ_{max} (nm) (log ε) 202 (4.25), 263 (3.14)

FT-IR: υ_{max} 2992, 1681 (C=O), 1604, 1508, 1371, 1213 cm^{-1}

Optical rotation: $[\alpha]_D^{25}$ -14.17° (*c* 0.046 $CHCl_3$)

^{1}H NMR: (400 MHz, $CDCl_3$) δ 7.27 (dd, 2H, *J* = 8.8, 5.3 Hz, H-2a/6a), 7.03 (t, 2H, *J* = 8.8 Hz, H-3a/5a), 5.76 (1H, s, H-2), 5.45 (d, 1H, *J* = 5.0 Hz, H-11), 4.57 (dd, 1H, *J* = 7.9, 2.4 Hz, H-9), 4.26 (dd, 1H, *J* = 5.0, 2.4 Hz, H-10), 4.08 (dd, 1H, *J* = 7.9, 1.8 Hz, H-8), 4.04 (td, 1H, *J* = 7.4, 1.6 Hz, H-7), 3.90 (dd, 1H, *J* = 13.9, 7.3 Hz, H-6i), 3.74 (d, 1H, *J* = 15.6 Hz, H-5i), 3.66 (d, 1H, *J* = 15.6 Hz, H-5ii), 2.77 (dd, 1H, *J* = 13.9, 6.1 Hz, H-6ii), 1.56 (s, 3H, H-13), 1.53 (s, 3H, H-14), 1.33 (s, 3H, H-16), 1.30 (s, 3H, H-17).

^{13}C NMR: (100 MHz, $CDCl_3$) δ 171.9 (C-4), 163.0 (d, *J* = 246.8 Hz, C-4a), 135.3 (d, *J* = 3.1 Hz, C-1a), 129.2 (d, *J* = 8.3 Hz, C-2a/6a), 115.9 (d, *J* = 21.7 Hz, C-3a/5a), 109.5 (C-15), 108.7 (C-12), 96.4 (C-11), 71.1 (C-8), 71.0 (C-9), 70.4 (C-10), 63.5 (C-7), 62.9 (C-2), 42.8 (C-6), 32.7 (C-5), 26.1 (C-13), 26.0 (C-14), 24.9 (C-16), 24.7 (C-17).

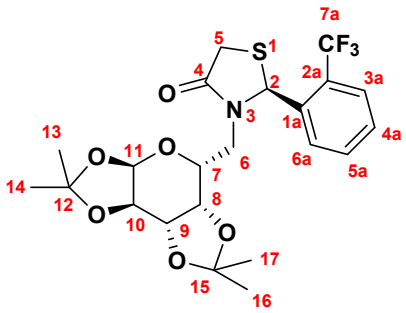
^{19}F NMR: (376.4 MHz, $CDCl_3$) δ -112.3

MS data: *m/z* (rel. int.): 439 (60) [M^+], 424 (24), 366 (38), 306 (23), 268 (43), 196 (95), 109 (100).

HRMS: M^+ at *m/z* 462.1352 (Calculated for $C_{21}H_{26}FNO_6SNa$, 462.1363)

Purity (HPLC): 99.8% (10.2 min in acetonitrile with 0.1% formic acid buffer)

3-(2,2,7,7-Tetramethyltetrahydro-*bis*[1,3]dioxolo[4,5b;4', 5'd]pyran-5-ylmethyl)-2-(2-trifluoromethylphenyl)thiazolidin-4-one (5c)



Physical description: White solid

Molecular formula: $C_{22}H_{26}F_3NO_6S$ (489.51 g mol^{-1})

Yield: 21.2%

Melting point: 120-123 °C

UV: λ_{max} (nm) (log ε) 201 (4.25), 276 (3.29)

FT-IR: υ_{max} 2988, 1686 (C=O), 1310, 1071 cm^{-1}

Optical rotation: $[\alpha]_D^{25}$ +71.50° (*c* 0.041 $CHCl_3$)

^{1}H NMR: (400 MHz, $CDCl_3$) δ 7.65 (d, 1H, *J* = 7.8 Hz, H-6a), 7.57 (t, 1H, *J* = 7.8 Hz, H-4a), 7.42 (t, 1H, *J* = 7.8 Hz, H-5a), 7.29 (d, 1H, *J* = 7.8 Hz, H-3a), 6.27 (s, 1H, H-2), 5.42 (d, 1H, *J* = 5.0 Hz, H-11), 4.60 (dd, 1H, *J* = 7.9, 2.4 Hz, H-9), 4.26 (dd, 1H, *J* = 5.0, 2.3 Hz, H-10), 4.16-4.21

(m, 2H, H-7/8), 3.88 (dd, 1H, *J* = 13.7, 6.4 Hz, H-6i), 3.74 (dd, 1H, *J* = 15.6, 1.7 Hz, H-5i), 3.59 (d, 1H, *J* = 15.6 Hz, H-5ii), 2.85 (dd, 1H, *J* = 13.8, 7.3 Hz, H-6ii), 1.53 (s, 3H, H-13), 1.36 (s, 3H, H-14), 1.32 (s, 3H, H-16), 1.29 (s, 3H, H-17).

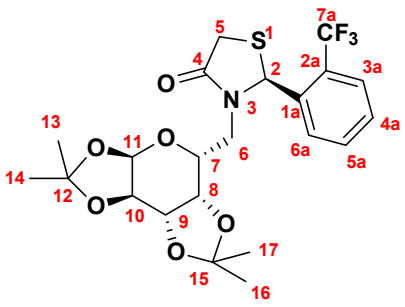
^{13}C NMR: (100 MHz, $CDCl_3$) δ 172.8 (C-4), 139.8 (C-2a), 133.0 (C-4a), 128.5 (C-6a), 126.4 (C-5a), 126.0 (s, C-3a), 124.1 (q, *J* = 272.8 Hz, CF_3), 109.6 (C-15), 108.8 (C-12), 96.3 (C-11), 70.8 (C-8), 70.7 (C-9), 70.6 (C-10), 63.7 (C-7), 59.1 (C-2), 44.0 (C-6), 31.7 (C-5), 26.0 (C-13), 25.7 (C-14), 25.0 (C-16), 24.3 (C-17).

^{19}F NMR (376.4 MHz, $CDCl_3$): δ: -57.93

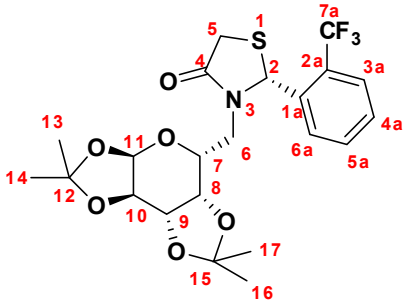
MS data: *m/z* (rel. int.): 489 (45) [M^+], 474 (16) [M - CH_3] $^+$; 416 (25), 246 (50), 159 (33), 100 (100)

Purity (HPLC): 96.3% (13.3 min in acetonitrile with 0.1% formic acid buffer)

3-(2,2,7,7-Tetramethyltetrahydro-*bis*[1,3]dioxolo[4,5b;4',5'd]pyran-5-ylmethyl)-2-(2 trifluoromethylphenyl) thiazolidin-4-one (mixture of 5c and 6c)



5c



6c

Physical description: Yellow gummy solid

Molecular formula: $C_{22}H_{26}F_3NO_6S$ (489.51 g mol^{-1})

Yield: 52.9%

UV: λ_{max} (nm) (log ε) 202 (4.07), 269 (3.19)

FT-IR: υ_{max}: 2987, 2920, 1680 (C=O), 1311, 1107, 1065 cm^{-1}

Optical rotation: $[\alpha]_D^{25}$ -22.33° (*c* 0.046 $CHCl_3$)

^{1}H NMR data: (400 MHz, $CDCl_3$): δ 7.64* and 7.62* (d, 2H, *J* = 7.7 Hz, H-6a), 7.56 (t, 2H, *J* = 7.7 Hz, H-4a), 7.37-7.41 (m, 3H, H-5a/3a$^{\#}$), and 7.28 (d, 1H, *J* = 7.9 Hz, H-3a$^{\#}$) 6.37* and 6.26* (s, 2H, H-2), 5.46* and 5.41* (d, 2H, *J* = 5.0 Hz, H-11), 4.58* and 4.54* (dd, 2H, *J* = 7.9, 2.3 Hz, H-9), 4.24-4.26 (m, 2H, H-10), 4.13-4.18 (m, 4H, H-7/8), 3.87 (dd, 1H, *J* = 13.8, 6.4 Hz, H-6i), 3.68-3.75 (m, 3H, H-5i, H-6i), 3.65* and 3.58* (d, 2H, *J* = 15.6 Hz, H-5ii), 2.80-2.86 (m, 2H, H-6ii), 1.52* and 1.48* (s, 6H, H-13), 1.35* and 1.31* (s, 6H, H-17), 1.30* and 1.29* (s, 6H, H-16), 1.23 (s, 6H, H-14).

$^{\#}$ *H-3a for the one diastereomer overlaps with the H-5a resonance*

^{13}C NMR: (100 MHz, $CDCl_3$) δ 172.8* and 172.1* (C-4), 139.7 (C-2a), 133.0* and 132.9* (C-4a), 128.5 (C-6a), 127.0* and 126.5* (C-5a), 126.0 (C-3a), 124.1* and 123.9* (q, *J* = 272.7 Hz, CF_3), 109.7* and 109.6* (C-15), 109.0* and 108.8* (C-12), 96.3* and 96.2* (C-11), 71.8* and 71.5* (C-8), 70.9* and 70.8* (C-9), 70.6* and 70.4* (C-10), 66.2* and 63.7* (C-7), 60.3* and 59.0* (C-2), 44.1* and 43.9* (C-6), 32.2* and 31.7* (C-5), 26.0* and 25.9* (C-13), 25.7* and 25.6* (C-17), 25.0* and 24.7* (C-16), 24.3* and 24.4* (C-14).

**One resonance for each diastereomer*

^{19}F NMR (376.4 MHz, $CDCl_3$): δ -58.13* and -57.94*

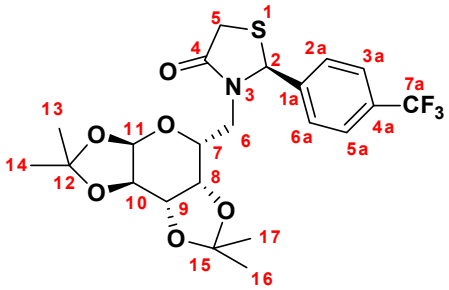
MS data: *m/z* (rel. int.):

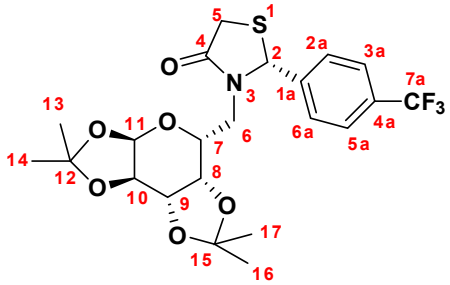
Diastereomer 1: 489 (72) [M^+], 474 [M-CH_3]$^+$ (24), 416 (32), 318 (42), 246 (100), 159(48), 100 (66).

Diastereomer 2: 489 (42) [M^+], 474 [M-CH_3]$^+$ (15), 416 (20), 318 (13), 246 (50), 159 (33), 100 (100).

Purity (HPLC): 48.9% (12.4 min), 39.9% (13.5 min) (in acetonitrile with 0.1% formic acid buffer)

3-(2,2,7,7-Tetramethyltetrahydro-*bis*[1,3]dioxolo[4,5b;4',5'd]pyran-5-ylmethyl)-2-(4-trifluoromethylphenyl)thiazolidin-4-one (mixture of 5d and 6d)





Physical description: Yellow gummy solid

Molecular formula: $C_{22}H_{26}F_3NO_6S$ (489.51 g mol^{-1})

Yield: 47.2%

Melting point: 135-138 °C

UV: λ_{max} (nm) (log ε) 202 (4.16), 263 (3.29)

FT-IR: υ_{max} 2988, 1680 (C=O), 1323, 1064 cm^{-1}

Optical rotation: $[\alpha]_D^{25}$ -39.17° (*c* 0.046 $CHCl_3$)

^{1}H NMR: (400 MHz, $CDCl_3$) δ 7.67* and 7.60* (d, 4H, *J* = 8.2 Hz, H-2a/6a), 7.45* and 7.42* (d, 4H, *J* = 8.3 Hz, H-5a/3a), 5.82* and 6.02* (s, 2H, H-2), 5.48* and 5.44* (d, 2H, *J* = 5.0 Hz, H-11), 4.57* and 4.54* (dd, 2H, *J* = 7.8, 2.5 Hz, H-9), 4.31* and 4.27* (dd, 2H, *J* = 5.0, 2.7 Hz, H-10), 3.91-4.21 (m, 3H, H-7/8/6i), 3.75* and 3.73* (dd, 2H, *J* = 15.6, 1.8, H-5i), 3.68* and 3.67* (d, 2H, *J* = 15.4 Hz, H-5ii), 2.79* and 2.78* (dd, 2H, *J* = 14.7, 9.8 Hz, H-6ii), 1.52* and 1.49* (s, 6H, H-13), 1.39* and 1.33* (s, 6H, H-17), 1.31* and 1.30* (s, 6H, H-16), 1.25* and 1.24* (s, 6H, H-14).

^{13}C NMR Data: (100 MHz, $CDCl_3$): δ 172.1* and 171.5* (C-4), 143.8* and 143.7* (C-4a), 128.3* and 127.9* (C-2a/6a), 127.6* and 125.6* (C-3a/5a), 123.8 (q, J = 270.5, CF_3), 109.6* and 109.5* (C-15), 109.1* and 108.7* (C-12), 96.4* and 96.3* (C-11), 71.1* and 71.0* (C-8), 70.80* and 70.76* (C-9), 70.43* and 70.39* (C-10), 67.1* and 66.7* (C-7), 63.7* and 62.9* (C-2), 43.6 *and 43.1* (C-6), 32.62* and 32.59* (C-5), 26.1* and 26.0* (C-13), 25.79* and 25.78* (C-17), 25.0* and 24.8* (C-16), 24.6* and 24.4* (C-14).

**One resonance for each diastereomer*

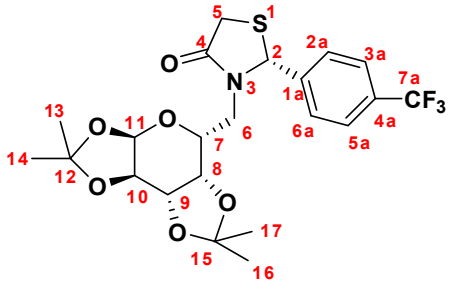
^{19}F NMR (400 MHz, $CDCl_3$): δ -62.71 (s, 3F)

MS data: *m/z* (rel. int.): 489 (70) [M^+], 416 (32), 318 (46), 246 (85), 159 (49), 100 (57), 81 (100), 85 (44), 59 (70)

HRMS: *[m/z]:* 512.1332 (Calculated mass for$C_{22}H_{26}F_3NO_6SNa$; 512.1331)

Purity (HPLC): 20.1% (12.7 min) and 56.9% (13.1 min) (in acetonitrile with 0.1% formic acid buffer)

3-(2,2,7,7-Tetramethyltetrahydro-*bis*[1,3]dioxolo[4,5b;4',5'd]pyran-5-ylmethyl)-2-(4-trifluoromethylphenyl)thiazolidin-4-one (6d)



Physical description: White solid

Molecular formula: $C_{22}H_{26}F_3NO_6S$ (489.51 g mol^{-1})

Yield: 23.6%

Melting point: 122-125 °C

UV: λ_{max} (nm) (log ε) 202 (4.37), 255 (3.37)

FT-IR: υ_{max} 2988, 1687 (C=O), 1322, 1110, 1064 cm^{-1}

Optical rotation: $[\alpha]_D^{25}$ -3.5° (*c* 0.046 $CHCl_3$)

^{1}H NMR: (400 MHz, $CDCl_3$) δ 7.59 (d, 2H, *J* = 8.2 Hz, H-2a/6a), 7.40 (d, 2H, *J* = 8.2 Hz, H-3a/5a), 5.82 (d, 1H, *J* = 1.0 Hz, H-2), 5.44 (d, 1H, *J* = 5.0 Hz, H-11), 4.57 (dd, 1H, *J* = 7.9, 2.4 Hz, H-9), 4.27 (dd, 1H, *J* = 5.0, 2.3 Hz, H-10), 4.12 (dd, 1H, *J* = 7.9, 1.8 Hz, H-8), 4.01-4.05 (m, 1H, H-7), 3.94 (dd,1H, *J* = 13.9, 7.2 Hz, H-6i), 3.77 (dd, 1H, *J* = 15.5, 1.7 Hz, H-5i), 3.67 (d, 1H, *J* = 15.5 Hz, H-5ii), 2.79 (dd, 1H, *J* = 13.8, 5.9 Hz, H-6ii), 1.52 (s, 3H, H-13), 1.38 (s, 3H, H-17), 1.33 (s, 3H, H-16), 1.30 (s, 3H, H-14).

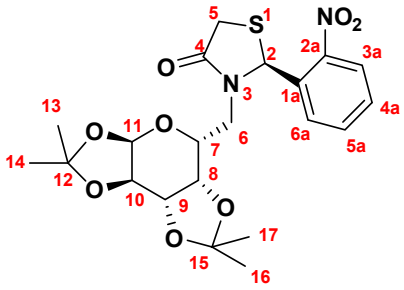
^{13}C NMR: (100 MHz, $CDCl_3$) δ 172.1 (C-4), 143.8 (C-4a), 127.6 (C-2a/6a), 126.0 (C-3a/5a), 109.51 (C-15), 108.7 (C-12), 96.4 (C-11), 71.1 (C-8), 71.0 (C-9), 70.4 (C-10), 63.7 (C-7), 62.9 (C-2), 43.1 (C-6), 32.6 (C-5), 26.1 (C-13), 26.0 (C-17), 24.9 (C-16), 24.6 (C-14).

^{19}F NMR: (376.4 MHz, $CDCl_3$) δ -62.71

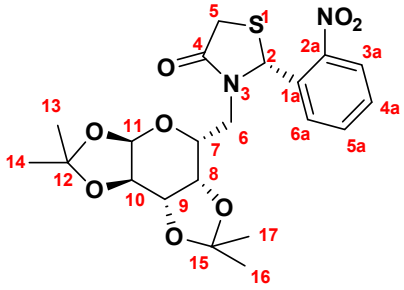
MS data: *m/z* (rel. int.): 489 (57) $[M^+]$, 474 (23) $[M\text{-}CH_3]^+$, 416 (26), 318 (25), 246 (65), 159 (46), 100 (100).

Purity (HPLC): 96.5% (12.7 min in acetonitrile with 0.1% formic acid buffer)

2-(2-Nitrophenyl)-3-(2,2,7,7-tetramethyltetrahydro-*bis*[1,3]dioxolo[4,5b;4',5'd]pyran-5-ylmethyl)thiazolidin-4-one (mixture of 5e and 6e)



5e



6e

Physical description: Brown gummy solid

Molecular formula: $C_{21}H_{26}N_2O_8S$ (466.50 g mol^{-1})

Yield: 60.0%

UV: λ_{max} (nm) (log ε) 204 (4.42), 305 (3.53)

FT-IR: υ_{max} 2987, 2932, 1678 (C=O), 1525, 1209, 1065 cm^{-1}

Optical rotation: $[\alpha]_D^{25}$ -38.3° (*c* 0.043 $CHCl_3$)

^{1}H NMR: (400 MHz, $CDCl_3$) δ 8.01* and 7.98* (d, 2H, *J* = 8.7 Hz, H-3a$^{\#}$), 7.61-7.66 (m, 2H, H-5a$^{\#\#}$), 7.45 (t, 2H, *J* = 7.60 Hz, H-4a$^{\#\#}$), 7.32* and 7.29* (d, 2H, *J* = 8.6, H-6a$^{\#}$), 6.49* and 6.43* (s, 2H, H-2), 5.37* and 5.36* (d, 1H, *J* = 5.1 Hz, H-11), 4.56* and 4.51* (dd, 2H, *J* = 7.9, 2.1 Hz, H-9), 4.20-4.24 (m, 2H, H-10), 4.13 (dd, 1H, *J* = 7.9, 1.4, H-8), 3.88-4.03 (m, 2H, H-7/6i), 3.70* and 3.66* (d, 2H, *J* = 15.8 Hz, H-5i), 3.59* and 3.58* (d, 2H, *J* = 15.8, H-5ii), 2.69-2.76 (m, 2H, H-6ii), 1.46* and 1.47* (s, 6H, H-13), 1.32* and 1.30* (s, 6H, H-17), 1.28* and 1.27* (s, 6H, H-16), 1.22 (s, 6H, H-14).

^{13}C NMR Data: (100 MHz, $CDCl_3$): δ 172.9* and 172.4* (C-4), 148.0* and 147.9* (C-2a), 136.5* and 136.4* (C-1a), 134.3* and 134.2* (C-3a), 129.2* and 129.1* (C-5a), 126.78* and 126.76* (C-4a), 125.5* and 125.3* (C-6a), 109.6* and 109.5* (C-15), 109.0* and 108.8* (C-12), 96.2* and 96.1* (C-11), 71.8* and 70.8* (C-8), 70.72* and 70.70* (C-9), 70.5* and 70.3* (C-10),

67.0* and 63.9* (C-7), 59.8* and 58.7* (C-2), 44.2* and 43.4* (C-6), 31.8* and 31.7* (C-5), 26.03* and 25.97* (C-13), 25.7* and 25.6* (C-17), 25.0* and 24.9* (C-16), 24.4* and 24.0* (C-14).

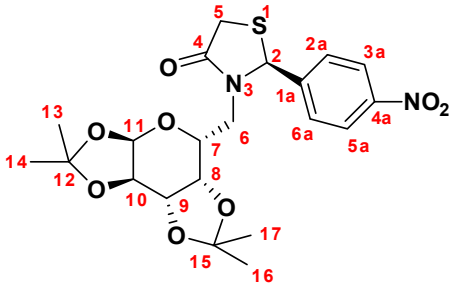
#, ## assignments may be interchanged

***One resonance for each diastereomer*

MS data: *m/z* (rel. int.): 503 (20) [M^+], 429 (35), 355 (63), 281 (38), 221 (46), 147 (51), 73 (100)

Purity (HPLC): 60.2% (8.4 min in acetonitrile with 0.1% formic acid buffer)

2-(4-Nitro-phenyl)-3-(2,2,7,7-tetramethyltetrahydro-*bis*[1,3]dioxolo[4,5b;4',5'd]pyran-5-ylmethyl)thiazolidin-4-one (5f)



Physical description: Brown gummy solid

Molecular formula: $C_{21}H_{26}N_2O_8S$ (466.50 g mol^{-1})

Yield: 23.9%

UV data: λ_{max} (nm) (log ε): 201 (4.05), 263 (3.57)

FT-IR data: ν_{max} (cm^{-1}): 2989, 1679 (C=O), 1608, 1209

Optical rotation: $[\alpha]_D^{25}$ -89.8° (*c* 0.043 $CHCl_3$)

^{1}H NMR data: (400 MHz, $CDCl_3$): δ 8.22 (d, 2H, *J* = 8.8 Hz, H-3a/5a), 7.47 (d, 2H, *J* = 8.8 Hz, H-2a/6a), 6.07 (s, 1H, H-2), 5.48 (d, 1H, *J* = 5.2 Hz, H-11), 4.56 (dd, 1H, *J* = 7.9, 2.5 Hz, H-9), 4.28 (dd, 1H, *J* = 5.0, 2.5 Hz, H-10), 4.15 (dd, 1H, *J* = 7.8, 1.7 Hz, H-8), 4.10 (dt, 1H, *J* = 9.7, 1.5

Hz, H-7), 3.78 (dd, 1H, *J* = 14.7, 1.7 Hz, H-6i), 3.76 (dd, 1H, *J* = 15.6, 1.7 Hz, H-5i), 3.69 (d, 1H, *J* = 15.4 Hz, H-5ii), 2.76 (dd, 1H, *J* = 14.6, 9.8 Hz, H-6ii), 1.49 (s, 3H, H-13), 1.32 (s, 3H, H-14), 1.25 (s, 3H, H-16), 1.24 (s, 3H, H-17).

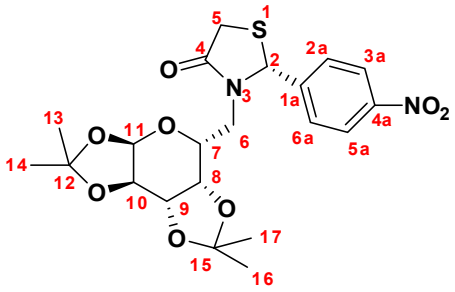
^{13}C NMR Data: (100 MHz, $CDCl_3$): δ 171.5 (C-4), 148.2 (C-4a), 147.0 (C-1a), 128.3 (C-3a/5a), 124.2 (C-6a/2a), 109.6 (C-15), 109.1 (C-12), 96.3 (C-11), 71.8 (C-8), 70.7 (C-9), 70.4 (C-10), 67.2 (C-7), 63.7 (C-2), 43.7 (C-6), 32.5 (C-5), 26.0 (C-13), 25.8 (C-14), 25.0 (C-16), 24.4 (C-17).

MS data: *m/z* (rel. int.): 466 (53) [M^+], 449 (90), 393 (23), 391 (25), 223 (42), 100 (48), 81 (100).

Purity (HPLC): 9.5 min (58.8% in acetonitrile with 0.1% formic acid buffer**)**

HRMS: *[m/z]:* 489.1307 (Calculated for $C_{21}H_{26}N_2O_8SNa$, 489.1308)

2-(4-Nitrophenyl)-3-(2,2,7,7-tetramethyltetrahydro-*bis*[1,3]dioxolo[4,5b;4',5'd]pyran-5-ylmethyl)thiazolidin-4-one (6f)



Physical description: Brown gummy solid

Molecular formula: $C_{21}H_{26}N_2O_8S$ (466.50 g mol^{-1})

Yield: 38.1%

UV data: λ_{max} (nm) (log ε): 201 (4.38), 266 (3.87)

FT-IR data: ν_{max} (cm^{-1}): 2986, 1681 (C=O), 1608, 1209

Optical rotation: $[\alpha]_D^{25}$ +22.7° (*c* 0.043 $CHCl_3$)

^{1}H NMR data: (400 MHz, $CDCl_3$): δ 8.21 (d, 2H, *J* = 8.8 Hz, H-3a/5a), 7.45 (d, 2H, *J* = 8.8 Hz, H-2a/6a), 5.86 (d, 1H, *J* = 1.3 Hz, H-2), 5.42 (d, 1H, *J* = 5.0 Hz, H-11), 4.57 (dd, 1H, J = 7.9, 2.4

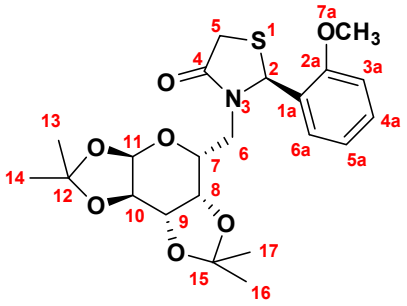
Hz, H-9), 4.26 (dd, 1H, *J* = 5.0, 2.4 Hz, H-10), 4.14 (dd, 1H, *J* = 7.8, 1.6 Hz, H-8), 4.03 (dt, 1H, *J* = 7.0, 1.5 Hz, H-7), 3.91 (dd, 1H, *J* = 14.0, 6.9 Hz, H-6i), 3.77 (dd, 1H, *J* = 15.5, 1.6 Hz, H-5i), 3.67 (d, 1H, *J* = 15.5 Hz, H-5ii), 2.86 (dd, 1H, *J* = 14.0, 5.8 Hz, H-6ii), 1.50 (s, 3H, H-13), 1.38 (s, 3H, H-17), 1.33 (s, 3H, H-16), 1.30 (s, 3H, H-14).

^{13}C NMR Data: (100 MHz, $CDCl_3$): δ 172.0 (C-4), 148.2 (C-4a), 147.1 (C-1a), 128.1 (C-3a/5a), 124.2 (C-2a/6a), 109.5 (C-15), 108.8 (C-12), 96.3 (C-11), 71.1 (C-8), 71.0 (C-9), 70.4 (C-10), 63.9 (C-7), 62.7 (C-2), 43.5 (C-6), 32.6 (C-5), 26.1 (C-13), 26.0 (C-17), 24.9 (C-16), 24.6 (C-14).

MS data: *m/z* (rel. int.): 466 (43) [M^+], 449 (65), 393 (18), 223 (31), 100 (100)

Purity (HPLC): 49.1% (12.5 min in acetonitrile with 0.1% formic acid buffer)

2-(2-Methoxyphenyl)-3-(2,2,7,7-tetramethyltetrahydro-*bis*[1,3]dioxolo[4,5b;4',5'd]pyran-5-ylmethyl)-thiazolidin-4-one (5g)



Physical description: Colourless solid

Molecular formula: $C_{22}H_{29}NO_7S$ (451.53 g mol^{-1})

Melting point: 122-125 °C

Yield: 39.2%

UV data: λ_{max} (nm) (log ε): 202 (4.43), 277 (3.26)

FT-IR data: ν_{max} (cm^{-1}): 2986, 1674 (C=O), 1600, 1208

Optical rotation: $[\alpha]_D^{25}$ -119.8° (*c* 0.044 $CHCl_3$)

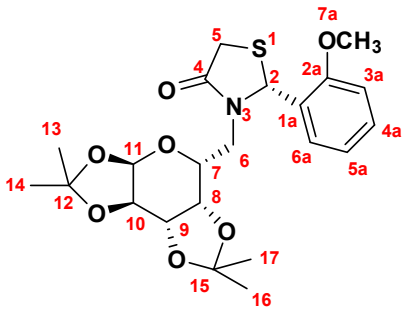
^{1}H NMR data: (400 MHz, $CDCl_3$):δ 7.26 (td, 1H, *J* = 7.9, 1.6 Hz, H-4a), 7.03 (dd, 1H, *J* = 7.5, 1.5 Hz, H-6a), 6.91 (td, 1H, *J* = 7.5, 0.6 Hz, H-5a), 6.89 (d, 1H, *J* = 8.1 Hz, H-3a), 6.17 (d, 1H, *J* = 1.7 Hz, H-2), 5.48 (d, 1H, *J* = 5.0 Hz, H-11), 4.56 (dd, 1H, *J* = 7.8, 2.4 Hz, H-9), 4.26 (dd, 1H, *J* = 5.0, 2.5 Hz, H-10), 4.14 (dd, 1H, *J* = 7.9, 1.8 Hz, H-8), 4.13 (dt, 1H, *J* = 9.5, 1.9 Hz, H-7), 3.83 (s, 3H, H-7a), 3.79 (dd, 1H, *J* = 14.4, 2.2 Hz, H-6i), 3.68 (dd, 1H, *J* = 15.3, 1.8 Hz, H-5i), 3.55 (d, 1H, *J* = 15.3 Hz, H-5ii), 2.93 (dd, 1H, *J* = 14.4, 9.5 Hz, H6ii), 1.50 (s, 3H, H-13), 1.31 (s, 3H, H-14), 1.30 (s, 3H, H-16), 1.26 (s, 3H, H-17).

^{13}C NMR Data: (100 MHz, $CDCl_3$):δ 172.4 (C-4), 157.1 (C-2a), 129.6 (s, C-4a), 128.3 (C-1a), 126.5 (C-6a), 120.7 (C-5a), 111.1 (C-3a), 109.5 (C-15), 108.9 (C-12), 96.2 (C-11), 71.9 (C-8), 70.9 (C-9), 70.5 (C-10), 67.1 (C-7), 60.3 (C-2), 55.6 (C-7a), 44.2 (C-6), 32.3 (C-5), 26.0 (C-13), 25.8 (C-14), 25.1 (C-16), 24.4 (C-17).

MS data: *m/z* (rel. int.): 451 (45) [M^+], 436 (15), 378 (30), 280 (37), 208 (100), 121 (44)

Purity (HPLC): 95.0% (9.4 min in acetonitrile with 0.1% formic acid buffer)

2-(2-Methoxyphenyl)-3-(2,2,7,7-tetramethyltetrahydro-*bis*[1,3]dioxolo[4,5b;4',5'd]pyran-5-ylmethyl)-thiazolidin-4-one (6g)



Physical description: White solid

Molecular formula: $C_{22}H_{29}NO_7S$ (451.53 g mol^{-1})

Melting point: 137-140 °C

Yield: 46.3%

UV data: λ_{max} (nm) (log ε): 202 (4.44), 277 (3.34)

FT-IR data: ν_{max} (cm^{-1}): 2986, 1680 (C=O), 1599, 1211

Optical rotation: $[\alpha]_D^{25}$ +85.5° (*c* 0.044 $CHCl_3$)

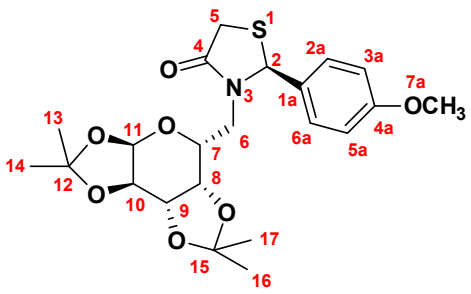
^{1}H NMR data: (400 MHz, $CDCl_3$):δ 7.27 (dt, 1H, *J* = 8.0, 1.6, H-4a), 7.06 (dd, 1H, *J* = 7.5, 1.6 Hz, H-6a), 6.92 (t, 1H, *J* = 7.5 Hz, H-5a), 6.92 (t, 1H, *J* = 8.0 Hz, H-3a), 6.07 (d, 1H, *J* = 1.5 Hz, H-2), 5.46 (d, 1H, J = 5.0 Hz, H-11), 4.58 (dd, 1H, *J* = 7.6, 2.3 Hz, H-9), 4.28 (dd, 1H, *J* = 5.0, 2.4 Hz, H-10), 4.07-4.10 (m, 2H, H-8/7), 3.97 (dd, 1H, *J* = 14.0, 7.7 Hz, H-6i), 3.82 (s, 3H, H-7a), 3.70 (dd, 1H, *J* = 15.3, 1.6 Hz, H-5i), 3.58 (d, 1H, *J* = 15.3 Hz, H-5ii), 2.82 (dd, 1H, *J* = 14.0, 6.1 Hz, H-6ii), 1.54 (s, 3H, H-13), 1.39 (s, 3H, H-17), 1.32 (s, 3H, H-16), 1.30 (s, 3H, H-14).

^{13}C NMR Data: (100 MHz, $CDCl_3$):δ 172.8 (C-4), 157.0 (C-2a), 129.8 (C-4a), 127.8 (C-1a), 126.8 (C-6a), 120.8 (C-5a), 111.1 (C-3a), 109.5 (C-15), 108.7 (C-12), 96.4 (C-11), 71.1 (C-8), 70.9 (C-9), 70.5 (C-10), 63.5 (C-7), 58.5 (C-2), 55.5 (C-7a), 43.1 (C-6), 32.5 (C-5), 26.0 (C-13), 25.9 (C-17), 24.9 (C-16), 24.6 (C-14).

MS data: *m/z* (rel. int.): 451 (42) [M^+], 436 (18), 378 (28), 280 (29), 208 (100), 121 (44)

Purity (HPLC): 99.6% (9.4 min in acetonitrile with 0.1% formic acid buffer)

2-(4-Methoxyphenyl)-3-(2,2,7,7-tetramethyltetrahydro-*bis*[1,3]dioxolo[4,5b;4',5'd]pyran-5-ylmethyl)thiazolidin-4-one (5h)



Physical description: White solid

Molecular formula: $C_{22}H_{29}NO_7S$ (451.53 g mol^{-1})

Melting point: 139-142 °C

Yield: 21.1%

UV data: λ_{max} (nm) (log ε): 202 (4.62), 234 (4.25), 275 (3.34)

FT-IR data: ν_{max} (cm^{-1}): 2979, 1666 (C=O), 1613, 1210

Optical rotation: $[\alpha]_D^{25}$ -51.8° (*c* 0.044 $CHCl_3$)

^{1}H NMR data: (400 MHz, $CDCl_3$):δ 7.25 (d, 2H, *J* = 8.7 Hz, H-2a/6a), 6.85 (d, 2H, *J* = 8.7 Hz, H-5a/3a), 5.92 (s, 1H, H-2), 5.49 (d, 1H, *J* = 5.0 Hz, H-11), 4.55 (dd, 1H, *J* = 7.6, 2.5 Hz, H-9), 4.27 (dd,1H, *J* = 5.0, 2.5 Hz, H-10), 4.15 (dd, 1H, *J* = 8.0, 1.8 Hz, H-8), 4.12 (dt, 1H, *J* = 11.9, 1.8 Hz, H-7), 3.78 (s, 3H, H-7a), 3.68-3.70 (m, 2H, H-6i/5i), 3.62 (dd, 1H, *J* = 14.9, 2.2 Hz, H-5ii), 2.87 (dd, 1H, *J* = 15.5, 9.8 Hz, H-6ii), 1.48 (s, 3H, H-13), 1.30 (s, 3H, H-14), 1.28 (s, 3H, H-16), 1.24 (s, 3H, H-17).

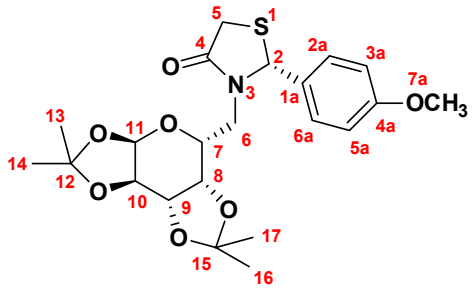
^{13}C NMR Data: (100 MHz, $CDCl_3$):δ 171.4 (C-4), 160.1 (C-4a), 131.1 (C-1a), 129.2 (C-2a/6a), 114.2 (C-3a/5a), 109.6 (C-15), 109.0 (C-12), 96.3 (C-11), 71.9 (C-8), 70.9 (C-9), 70.4 (C-10), 66.9 (C-7), 64.8 (C-2), 55.3 (C-7a), 43.3 (C-6), 32.8 (C-5), 26.0 (C-13), 25.9 (C-14), 25.1 (C-16), 24.6 (s, C-17).

MS data: *m/z* (rel. int.): 451 (40) [M^+], 436 (16), 378 (31), 280 (37), 208 (100), 121 (64)

Purity (HPLC): 99.1% (9.3 min in acetonitrile with 0.1% formic acid buffer)

HRMS: *[m/z]:* 474.1553 (Calculated for $C_{22}H_{29}NO_7SNa$, 474.1562)

2-(4-Methoxyphenyl)-3-(2,2,7,7-tetramethyltetrahydro-*bis*[1,3]dioxolo[4,5b;4',5'd]pyran-5-ylmethyl)thiazolidin-4-one (6h)



Physical description: White solid

Molecular formula: $C_{22}H_{29}NO_7S$ (451.53 g mol^{-1})

Melting point: 124-127 °C

Yield: 59.6%

UV data: λ_{max} (nm) (log ε): 202 (4.52), 234 (4.19), 276 (3.34)

FT-IR data: ν_{max} (cm^{-1}): 2970, 1683 (C=O), 1612, 1208

Optical rotation: $[\alpha]_D^{25}$ +9.5° (*c* 0.044 $CHCl_3$)

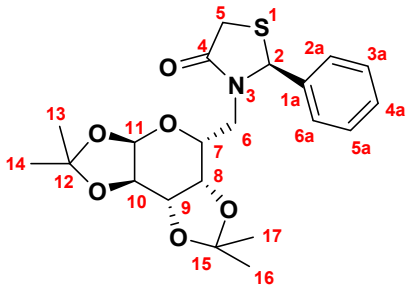
^{1}H NMR data: (400 MHz, $CDCl_3$):δ 7.27 (d, 2H, *J* = 8.7 Hz, H-2a/6a), 6.91 (d, 2H, *J* = 8.7 Hz, H-3a/5a), 5.78 (s, 1H, H-2), 5.51 (d, 1H, *J* = 5.1 Hz, H-11), 4.62 (dd, 1H, *J* = 7.8, 2.4 Hz, H-9), 4.31 (dd, 1H, *J* = 5.0, 2.4 Hz, H-10), 4.06-4.12 (m, 2H, H-7/8), 3.99 (dd, 1H, *J* = 13.9, 7.5 Hz, H-6i), 3.82 (s, 3H, H-7a), 3.78 (d, 1H, *J* = 15.7 Hz, H-5i), 3.70 (d, 1H, *J* = 15.7 Hz, H-5ii), 2.83 (dd, 1H, *J* = 13.8, 6.1 Hz, H-6ii), 1.58 (s, 3H, H-13), 1.45 (s, 3H, H-17), 1.37 (s, 3H, H-16), 1.35 (s, 3H, H-14).

^{13}C NMR Data: (100 MHz, $CDCl_3$): δ 171.9 (C-4), 160.1 (C-4a), 131.2 (C-1a), 128.6 (C-2a/6a), 114.3 (C-5a/3a), 109.5 (C-15), 108.6 (C-12), 96.4 (C-11), 71.03 (C-8), 70.96 (C-9), 70.4 (C-10), 63.4 (C-7), 63.1 (C-2), 55.4 (C-7a), 42.6 (C-6), 32.8 (C-5), 26.1 (C-13), 26.0 (C-17), 24.9 (C-16), 24.7 (C-14).

MS data: *m/z* (rel. int.): 451 (34) [M^+], 436 (14), 378 (28), 280 (32), 208 (100), 121 (65)

Purity (HPLC): 99.9% (9.6 min in acetonitrile with 0.1% formic acid buffer)

2-Phenyl-3-(2,2,7,7-tetramethyl-tetrahydro-bis[1,3]dioxolo[4,5-b;4',5'-d]pyran-5-ylmethyl)-thiazolidin-4-one (5i)



Physical description: Colourless gummy solid

Molecular formula: $C_{21}H_{27}NO_6S$ (421.51 g mol^{-1})

Yield: 34.6%

UV data: λ_{max} (nm) (log ε): 201 (4.13), 258 (3.00)

FT-IR data: ν_{max} (cm^{-1}): 2924, 1675 (C=O), 1456, 1209

Optical rotation: $[\alpha]_D^{25}$ -54.0° (*c* 0.047 $CHCl_3$)

^{1}H NMR data: (400 MHz, $CDCl_3$): δ: 7.29-7.33 (m, 5H, H-2a/3a/4a/5a/6a), 5.96 (s, 1H, H-2), 5.49 (d, 1H, *J* = 5.0 Hz, H-11), 4.54 (dd, 1H, *J* = 7.7, 2.5 Hz H-9), 4.27 (dd, 1H, *J* = 5.0, 2.5 Hz, H-10), 4.11-4.16 (m, 2H, H-8/7), 3.74 (dd, 1H, *J* = 15.5, 1.8 Hz, H-6i), 3.68 (d, 2H, *J* = 14.9 Hz, H-5i/5ii), 2.85 (dd, 1H, *J* = 14.6, 9.8 Hz, H-6ii), 1.49 (3H, s, H-13), 1.31 (s, 3H, H-14), 1.26 (s, 3H, H-16), 1.23 (s, 3H, H-17).

^{13}C NMR Data: (100 MHz, $CDCl_3$): δ 171.6 (C-4), 139.5 (C-1a), 128.94 (C-4a), 128.86 (C-2a/6a), 127.6 (C-3a/5a), 109.6 (C-15), 109.0 (C-12), 96.3 (C-11), 71.9 (C-8), 70.9 (C-9), 70.4 (C-

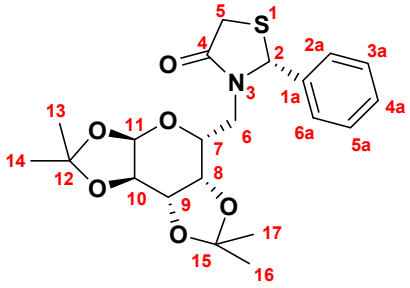
10), 67.0 (C-7), 65.1 (C-2), 43.5 (C-6), 32.8 (C-5), 26.0 (C-13), 25.8 (C-14), 25.1 (C-16), 24.6 (C-17)

MS data: *m/z* (rel. int.): 421 (63) [M^+], 406 (21), 348 (38), 250 (58), 178 (100), 91 (89)

Purity (HPLC): 63.6% (9.8 min in acetonitrile with 0.1% formic acid buffer)

HRMS: *[m/z]* 444.1440 (Calculated for $C_{21}H_{27}NO_6SNa$, 444.1457)

2-Phenyl-3-(2,2,7,7-tetramethyltetrahydro-*bis*[1,3]dioxolo[4,5b;4',5'd]pyran-5-ylmethyl)-thiazolidin-4-one (6i)



Physical description: Colourless gummy solid

Molecular formula: $C_{21}H_{27}NO_6S$ (421.51 g mol^{-1})

Yield: 22.3%

UV data: λ_{max} (nm) (log ε): 201 (4.13), 259 (2.92)

FT-IR data: ν_{max} (cm^{-1}): 2921, 1678 (C=O), 1456, 1209

Optical rotation: $[\alpha]_D^{25}$ -10.3° (*c* 0.047 $CHCl_3$)

^{1}H NMR data: (400 MHz, $CDCl_3$): δ: 7.30-7.35 (m, 3H, H-2a/4a/6a), 7.25-7.27 (m, 2H, H-3a/5a), 5.77 (d, 1H, *J* = 1.2 Hz, H-2), 5.46 (d, 1H, *J* = 5.1 Hz, H-11), 4.57 (dd, 1H, *J* = 7.8, 2.4 Hz, H-9), 4.27 (dd, 1H, *J* = 5.0, 2.4 Hz, H-10), 4.07 (dd, 1H, *J* = 7.7, 1.7 Hz, H-8), 4.04 (td, 1H, *J* = 7.6, 1.6 Hz, H-7), 3.96 (dd, 1H, *J* = 13.8, 7.5 Hz, H-6i), 3.76 (dd, 1H, *J* = 15.5, 1.7 Hz, H-5i), 3.66

(d, 1H, *J* = 15.5 Hz, H-5ii), 2.78 (dd, 1H, *J* = 13.8, 6.0 Hz, H-6ii), 1.54 (s, 3H, H-13), 1.40 (s, 3H, H-17), 1.33 (s, 3H, H-16), 1.30 (s, 3H, H-14).

^{13}C NMR Data: (100 MHz, $CDCl_3$): δ 172.1 (C-4), 139.5 (C-1a), 129.03 (C-4a), 129.00 (C-2a/6a), 127.1 (C-3a/5a), 109.5 (C-15), 108.7 (C-12), 96.4 (C-11), 71.0 (C-8), 70.9 (C-9), 70.4 (C-10), 63.41 (C-7), 63.36 (C-2), 42.7 (C-6), 32.7 (C-5), 26.1 (C-13), 26.0 (C-17), 24.9 (C-16), 24.7 (C-14).

MS data: *m/z* (rel. int.): (421 (58) [M^+], 406 (23), 348 (35), 250 (44), 178 (100), 91 (100), 71 (69), 59 (50)

HPLC data: 78.2% (9.4 min in acetonitrile with 0.1% formic acid buffer)

3.4 Antibacterial study

3.4.1 Microbial strains

The antimicrobial activities of the synthesized compounds **5a - 6i** were investigated against several representative pathogenic organisms, yeast (*Candida albicans* ATCC 10231), two gram positive bacteria (*Staphylococcus aureus* ATCC 25923, *Staphylococcus aureus* Rosenbach ATCC BAA-1683 (methicillin resistant *S. aureus*)) and three gram negative bacteria (*Pseudomonas aeruginosa* ATCC 27853, *Klebsiella pneumonia* ATCC 31488 and *Escherichia coli* ATCC 25922).

Fungal test organisms were grown on sabouraud dextrose agar (30 g L^{-1}), and bacterial test organisms on Mueller-Hinton agar (21 g L^{-1}) at 35-37 °C in a CO_2 incubator for 24 hours. Organisms were suspended in saline and the turbidity adjusted to 0.5 McFarland standard.

3.4.2 Disc diffusion method

The Mueller-Hinton agar plate was inoculated with the required strain of bacteria by streaking a swab over the entire sterile agar surface evenly after it has been firmly dipped into the adjusted suspension. Antibiotic assay discs were impregnated with 10 µL of each sample (10 mg, 1mL DMSO) and was then placed into the Mueller-Hinton plates, left to incubate for 16-18 hours at 37°C, thereafter the zones of inhibition was measured.

3.4.3 Broth dilution method

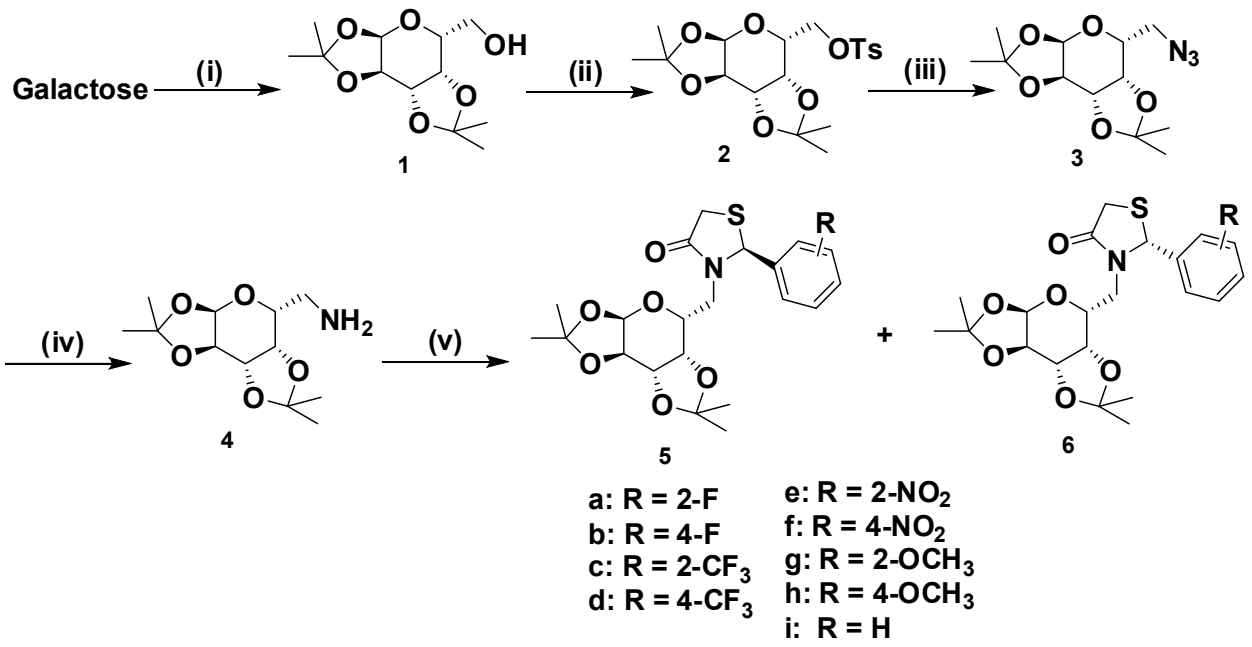
All compounds that exhibited activity during the disc diffusion preliminary tests were dissolved in DMSO (10 mg mL^{-1}), serially diluted over five dilutions with Mueller-Hinton broth, inoculated with bacterial cultures and then incubated at 37ºC for 18 hours. This was performed in duplicate. Thereafter, 10 µL from each concentration was then placed on Mueller-Hinton plates and incubated at 37ºC for 18 hours to determine the MBC (µg mL^{-1}). The MBC was the lowest concentration which showed no bacterial growth in the area in which the sample was placed.

Chapter 4. Results & Discussion

4.1 Thiazolidinone derivatives synthesized

4.1.1 Chemical Synthesis

We synthesized a series of thiazolidinone derivatives starting from galactose which was first protected with acetone (intermediate **1**) and tosyl chloride (intermediate **2**) to protect the hydroxyl groups. This was then converted to a primary amine (intermediate **4**) *via* the azide (intermediate **3**). The thiazolidinone derivatives were finally formed from the galactose amine intermediate **4**, thioglycolic acid and various substituted benzaldehydes to produce two diastereomers of the thiazolidinones (the *2S* **5** and *2R* **6** diastereomers) (**Scheme 4**). Acetone and n-hexane (15:85) was used to purify the reaction mixture and the two resultant diastereomers where possible. The 4-substituted derivatives were better resolved than the 2-substituted derivatives. For the acetonide protection to occur, the copper sulphate needed to be very dry. The galactose intermediate **4** was hygroscopic and needed to be kept dry before being used in subsequent steps. The coupling reaction also needed to be done under very dry conditions, using the coupling reagent *N*-(3-dimethylaminopropyl)-*N*'-ethylcarbodiimide hydrochloride (EDC).



Scheme 4. Synthetic scheme for synthesizing thiazolidinone galactoside derivatives; (i) anhydrous $CuSO_4$, acetone, H_2SO_4, 20 hrs, rt (ii) pyridine, tosyl chloride, 12hrs, rt (iii) NaN_3, DMF, 7-10hrs, reflux 110 °C (iv) methanol, 10% Pd/C, 5 hrs, rt. (v) thioglycolic acid, substituted aromatic aldehydes, EDC, 12 hrs, rt.

The 2-fluoro and 2-nitro thiazolidinone derivatives could not be separated at all after the reaction of thioglycolic acid. For the 2-trifluoromethyl and 4-trifluoromethyl thiazolidinone derivatives, only one diastereomer in each could be purified. For the 4-fluoro thiazolidinone derivative, only one diastereomer was synthesized with a 99% purity. The second isomer was unstable and decomposed whilst being purified. The trifluoromethyl thiazolidinone derivatives where the diastereomers were able to be separated had a purity of 96%. The 4-nitro thiazolidinone diastereomers were each synthesized with 58% and 49% purity. This low purity was a result of a by-product also being formed in the reaction. Similarly, the unsubstituted thiazolidinone diastereomers were also synthesized with 63% and 78% purity. By-products were also formed in

these reactions. The four methoxy thiazolidinone diastereomers were synthesized with a purity greater than 95%.

In this study, four of these thiazolidinone reactions formed mixtures that could not be separated with column chromatography. This contained a mixture of the two diastereomers which had a combined yield between 47-75%. The highest combined yield was shown by 2-F (75%), followed by the 2-NO_2 (60%) and then the 2- and 4-CF_3 derivatives with yields of approximately 50%. The *2R* 4-OCH_3 derivative had the highest yield of 59.6% from all the diastereomers that were possible to separate. The *2S* 4-F derivative was the only diastereomer that was separated from the *2R*/*2S* mixture as the other was unstable and decomposed whilst purifying. This pure compound had a yield of 45%. The *2R* 2-OCH_3 compound had a similar yield. The *2S* 2-CF_3 derivative had a yield of less than half of this value at 21.2%. The *2R* 4-CF_3, *2S* 4-NO_2, *2S* 4-OCH_3 and *2R* unsubstituted compounds had similar yields. The remaining *2R* 4-NO_2, *2S* 2-OCH_3, and *2S* unsubstituted compounds had yields between 34-40%.

Table 1. Melting point, optical rotation, yields and percent purity of thiazolidinone derivatives

Compound	Substitution	Melting point/°C*	$[\alpha]_D^{25}$/°	Yield/%	Purity/%
5a/6a	2-F	-	-25.8	75.0	77.8
5b	4-F	110-113	-14.2	45.0	99.8
5c	2-CF_3	120-123	+71.5	21.2	96.3
5c/6c	2-CF_3	-	-22.3	52.9	48.9 & 39.9
5d/6d	4-CF_3	135-138	-39.2	47.2	20.1 & 56.9
6d	4-CF_3	122-125	- 3.5	23.6	96.5
5e/6e	2-NO_2	-	- 38.3	60.0	60.2
5f	4-NO_2	-	-89.8	23.9	58.8
6f	4-NO_2	-	+22.7	38.1	49.1
5g	2-OCH_3	122-125	-119.8	39.2	95.0
6g	2-OCH_3	137-140	+85.5	46.3	99.6
5h	4-OCH_3	139-142	-51.8	21.1	99.1
6h	4-OCH_3	124-127	+9.5	59.6	99.9
5i	H	-	-54.0	34.6	63.6
6i	H	-	-10.3	22.3	78.2

**Melting points for compounds that were gums could not be obtained.*

4.1.2 Structure elucidation

The compounds were characterized using NMR, IR, MS and single crystal XRD. In the FT-IR spectrum, a characteristic carbonyl absorption was found at 1674 cm^{-1}. Using the 2-methoxy thiazolidinone derivative as an example, the aromatic protons appeared as a triplet of doublets for H-4a and H-5a at δ 6.91 (J = 7.5, 0.6 Hz) and δ 6.92 (J = 7.5 Hz) respectively, a double doublet for H-6a at δ 7.03 (J = 7.5, 1.5 Hz) and a doublet at δ 6.89 for H-3a (J = 8.1 Hz). The methoxy proton 7a appeared as a singlet at δ 3.83. The thiazolidinone proton at H-2 appeared as a doublet

at δ 6.17 with a small coupling constant of 1.7 Hz. H-11 appeared as a doublet at δ 5.48 with J = 5.0 Hz and H-9 and H-10 each appeared as double doublets at δ 4.56 (J = 7.8, 2.4 Hz) and δ 4.26 (J = 5.0, 2.5 Hz) respectively. The H-7 and H-8 protons appeared as a triplet of doublets at δ 4.13 (J = 9.5, 1.9 Hz) and double doublet at δ 4.14 (J = 7.9, 1.8 Hz) respectively. The methylene protons H-6i and H-6ii both appeared as double doublets at δ 3.79 (J = 14.4, 2.2 Hz) for H-6i and at δ 2.93 (J = 14.4, 9.5 Hz) for H-6ii. The thiazolidinone methylene protons H-5i and H-5ii appeared as a double doublet at δ 3.68 (J = 15.3, 1.8 Hz) and a doublet at δ 3.55 (J = 15.3 Hz) respectively. The acetonide methyl groups H-13, H-14, H-16 and H-17 each appeared as three proton singlets at δ 1.50, δ 1.31, δ 1.30 and δ 1.26 respectively. The corresponding carbon resonances were determined using the HSQC spectrum. In addition, the carbonyl resonance (C-4) from the thiazolidinone ring appeared at δ 172.4, the two acetonide singlet carbon resonances C-12 and C-15 appeared at δ 108.9 and δ 109.5 respectively.

Table 2. ^{1}H NMR shifts of the galactose thiazolidinone derivatives **5a-6d** (400 MHz, $CDCl_3$, *J* given in Hz)

Pos.	5a/6a	5b	5c	5c/6c	5d/6d	6d
H-2a	-	7.27 (dd, 8.8, 5.3)	-	-	7.67 and 7.60 (d, 8.2)	7. 59 (d, 8.2)
H-3a	7.02 (t,7.8)	7.03 (t, 8.8 Hz)	7.29 (d, 7.8)	7.37-7.41 (m)[#1] and 7.28 (d, 7.9)	7.45 and 7.42 (d, 8.3)	7.40 (d, 8.2)
H-4a	7.24 - 7.30 (m)	-	7.57 (t, 7.8)	7.56 (t, 7.7)	-	-
H-5a	7.13 (t,7.0)	7.03 (t, 8.8 Hz)	7.42 (t, 7.8)	7.37-7.41 (m)[#1]	7.45 and 7.42 (d, 8.3)	7.40 (d, 8.2)
H-6a	7.20 (t, 7.4)	7.27 (dd, 8.8, 5.3)	7.65 (d, 7.8)	7.64 and 7.62 (d, 7.7)	7.67 and 7.60 (d, 8.2)	7. 59 (d, 8.2)
H-2	6.20 and 6.07 (s)	5.76 (s)	6.27 (s)	6.37 and 6.26 (s)	5.82 and 6.02 (s)	5.82 (d)
H-5i	3.75 and 3.72 (d, 15.4)	3.74 (d, 15.6)	3.74 (dd, 15.6, 1.7)	3.68-3.75 (m)[#2]	3.75 and 3.73 (dd, 15.6, 1.8)	3.77 (dd, 15.5, 1.7)
H-5ii	3.61 (d, 15.4)	3.66 (d, 15.6)	3.59 (d, 15.6)	3.65 and 3.58 (d, 15.6)	3.68 and 3.67 (d, 15.4)	3.67 (d, 15.5)
H-6i	3.92 (dd, 13.4, 7.4)	3.90 (dd, 13.9, 7.3)	3.88 (dd, 13.7, 6.4)	3.87 (dd, 13.8, 6.4) and 3.68-3.75 (m)[#2]	4.21 (m)	3.94 (dd, 13.9, 7.2)
H-6ii	2.84 and 2.80 (dd, 13.4, 6.3)	2.77 (dd, 13.9, 6.1)	2.85 (dd, 13.8, 7.3)	2.80-2.86 (m)	2.79 and 2.78 (dd, 14.7, 9.8)	2.79 (dd, 13.8, 5.9)
H-7	4.06-4.16 (m)	4.04 (td, 7.4, 1.6)	4.16-4.21 (m)	4.13-4.18 (m)	4.21 (m)	4.01-4.05 (m)
H-8	4.06-4.16 (m)	4.08 (dd, 7.9, 1.8)	4.16-4.21 (m)	4.13-4.18 (m)	4.21 (m)	4.12 (dd, 7.9, 1.8)
H-9	4.57 and 4.52 (dd, 7.7, 2.2)	4.57 (dd, 7.9, 2.4)	4.60 (dd, 7.9, 2.4)	4.58 and 4.54 (dd, 7.9, 2.3)	4.57 and 4.54 (dd, 7.8, 2.5)	4.57 (dd, 7.9, 2.4)
H-10	4.24-4.25 (m)	4.26 (dd, 5.0, 2.4)	4.26 (dd, 5.0, 2.3)	4.24-4.26 (m)	4.31 and 4.27 (dd, 5.0, 2.7)	4.27 (dd, 5.0, 2.3)
H-11	5.47 and 5.42 (d, 4.9)	5.45 (d, 5.0)	5.42 (d, 5.0)	5.46 and 5.41 (d, 5.0)	5.48 and 5.44 (d, 5.0)	5.44 (d, 5.0)
H-13	1.50 and 1.47 (s)	1.56 (s)	1.53 (s)	1.52 and 1.48 (s)	1.52 and 1.49 (s)	1.52 (s)
H-14	1.25 and 1.23 (s)	1.53 (s)	1.36 (s)	1.23 (s)	1.25 and 1.24 (s)	1.30 (s)
H-16	1.29 and 1.28 (s)	1.33 (s)	1.32 (s)	1.30 and 1.29 (s)	1.31 and 1.30 (s)	1.33 (s)
H-17	1.36 and 1.31 (s)	1.30 (s)	1.29 (s)	1.35 and 1.31 (s)	1.39 and 1.33 (s)	1.38 (s)

[#1, #2] *resonances overlap*

Table 3. ^{1}H NMR shifts of the galactose thiazolidinone derivatives 5e-6i (400 MHz, $CDCl_3$, *J* given in Hz)

Pos.	5e/6e	5f	6f	5g	6g	5h	6h	5i	6i
H-2a	-	7.47 (d, 8.8)	7.45 (d, 8.8)	-	-	7.25 (d, 8.7)	7.27 (d, 8.7)	7.29-7.33 (m)	7.30-7.35 (m)
H-3a	8.01 and 7.98 (d, 8.7)[#2]	8.22 (d, 8.8)	8.21 (d, 8.8)	6.89 (d, 8.1)	6.92 (t, 8.0)	6.85 (d, 8.7)	6.91 (d, 8.7)	7.29-7.33 (m)	7.25-7.27 (m)
H-4a	7.45 (t, 7.60)[#1]	-	-	7.26 (td, 7.9, 1.6)	7.27 (dt, 8.0, 1.6)	-	-	7.29-7.33 (m)	7.30-7.35 (m)
H-5a	7.61-7.66 (m)[#1]	8.22 (d, 8.8)	8.21 (d, 8.8)	6.91 (td, 7.5, 0.6)	6.92 (t, 7.5)	6.85 (d, 8.7)	6.91 (d, 8.7)	7.29-7.33 (m)	7.25-7.27 (m)
H-6a	7.32 and 7.29 (d, 8.6)[#2]	7.47 (d, 8.8)	7.45 (d, 8.8)	7.03 (dd, 7.5, 1.5)	7.06 (dd, 7.5, 1.6)	7.25 (d, 8.7)	7.27 (d, 8.7)	7.29-7.33 (m)	7.30-7.35 (m)
H-7a	-	-		3.83 (s)	3.82 (s)	3.78 (s)	3.82 (s)	-	-
H-2	6.49 and 6.43 (s)	6.07 (s)	5.86 (d, 1.3)	6.17 (d, 1.7)	6.07 (d, 1.5)	5.92 (s)	5.78 (s)	5.96 (s)	5.77 (d, 1.2)
H-5i	3.70 and 3.66 (d, 15.8)	3.76 (dd, 15.6, 1.7)	3.77 (dd, 15.5, 1.6)	3.68 (dd, 15.3, 1.8)	3.70 (dd, 15.3, 1.6)	3.68-3.70 (m)	3.78 (d, 15.7)	3.68 (d, 14.9)	3.76 (dd, 15.5, 1.7)
H-5ii	3.59 and 3.58 (d, 15.8)	3.69 (d, 15.4)	3.67 (d, 15.5)	3.55 (d, 15.3)	3.58 (d, 15.3)	3.62 (dd, 14.9, 2.2)	3.70 (d, 15.7)	3.68 (d, 14.9)	3.66 (d, 15.5)
H-6i	3.88-4.03 (m)	3.78 (dd, 14.7, 1.7)	3.91 (dd, 14.0, 6.9)	3.79 (dd, 14.4, 2.2)	3.97 (dd, 14.0, 7.7)	3.68-3.70 (m)	3.99 (dd, 13.9, 7.5)	3.74 (dd, 15.5, 1.8)	3.96 (dd, 13.8, 7.5)
H-6ii	2.69-2.76 (m)	2.76 (dd, 14.6, 9.8)	2.86 (dd, 14.0, 5.8)	2.93 (dd, 14.4, 9.5)	2.82 (dd, 14.0, 6.1)	2.87 (dd, 15.5, 9.8)	2.83 (dd, 13.8, 6.1)	2.85 (dd, 14.6, 9.8)	2.78 (dd, 13.8, 6.0)
H-7	3.88-4.03 (m)	4.10 (dt, 9.7, 1.5)	4.03 (dt, 7.0, 1.5)	4.13 (dt, 9.5, 1.9)	4.07-4.10 (m)	4.12 (dt, 11.9, 1.8)	4.06-4.12 (m)	4.11-4.16 (m)	4.04 (td, 7.6, 1.6)
H-8	4.13 (dd, 7.9, 1.4)	4.15 (dd, 7.8, 1.7)	4.14 (dd, 7.8, 1.6)	4.14 (dd, 7.9, 1.8)	4.07-4.10 (m)	4.15 (dd, 8.0, 1.8)	4.06-4.12 (m)	4.11-4.16 (m)	4.07 (dd, 7.7, 1.7)
H-9	4.56 and 4.51 (dd, 7.9, 2.1)	4.56 (dd, 7.9, 2.5)	4.57 (dd, 7.9, 2.4)	4.56 (dd, 7.8, 2.4)	4.58 (dd, 7.6, 2.3)	4.55 (dd, 7.6, 2.5)	4.62 (dd, 7.8, 2.4)	4.54 (dd, 7.7, 2.5)	4.57 (dd, 7.8, 2.4)
H-10	4.20-4.24 (m)	4.28 (dd, 5.0, 2.5)	4.26 (dd, 5.0, 2.4)	4.26 (dd, 5.0, 2.5)	4.28 (dd, 5.0, 2.4)	4.27 (dd, 5.0, 2.5)	4.31 (dd, 5.0, 2.4)	4.27 (dd, 5.0, 2.5)	4.27 (dd, 5.0, 2.4)
H-11	5.37 and 5.36 (d, 5.1)	5.48 (d, 5.2)	5.42 (d, 5.0)	5.48 (d, 5.0)	5.46 (d, 5.0)	5.49 (d, 5.0)	5.51 (d, 5.1)	5.49 (d, 5.0)	5.46 (d, 5.1)
H-13	1.46 and 1.47 (s)	1.49 (s)	1.50 (s)	1.50 (s)	1.54 (s)	1.48 (s)	1.58 (s)	1.49 (s)	1.54 (s)
H-14	1.22 (s)	1.32 (s)	1.30 (s)	1.31 (s)	1.30 (s)	1.30 (s)	1.35 (s)	1.31 (s)	1.30 (s)
H-16	1.28 and 1.27 (s)	1.25 (s)	1.33 (s)	1.30 (s)	1.32 (s)	1.28 (s)	1.37 (s)	1.26 (s)	1.33 (s)
H-17	1.32 and 1.30 (s)	1.24 (s)	1.38 (s)	1.26 (s)	1.39 (s)	1.24 (s)	1.45 (s)	1.23 (s)	1.40 (s)

[#1, #2] *resonances overlap*

Table 4. ^{13}C NMR of galactose thiazolidinone derivatives **5a-6d** (100 MHz, $CDCl_3$, *J* given in Hz)

Pos.	5a/6a[*2]	5b	5c	5c/6c[*2]	5d/6d[*2]	6d
C-1a	127.1 and 127.0 (d, 11.4)	135.3 (d, 3.1)	*[1]	*[1]	*[1]	*[1]
C-2a	160.7 and 160.5 (d, 248.2)	129.2 (d, 8.3)	139.8	139.7	128.3 and 127.9	127.6
C-3a	116.1 and 116.0 (d, 21.1)	115.9 (d, 1.7)	126.0	126.0	127.6 and 125.6	126.0
C-4a	130.4 and 130.3 (d, 8.5)	163.0 (d, 246.8)	133.0	133.0 and 132.9	143.8 and 143.7	143.8
C-5a	124.6 and 124.5 (d, 3.6)	115.9 (d, 1.7)	126.4	127.0 and 126.5	127.6 and 125.6	126.0
C-6a	128.1 and 127.9 (d, 3.2)	129.2 (d, 8.3)	128.5	128.5	128.3 and 127.9	127.6
C-7a	-	-	124.1 (q, 272.8)	124.1 and 123.9 (q, 272.7)	123.8 (q, 270.5)	*[1]
C-2	58.9 and 57.1 (d, 3.9)	62.9	59.1	60.3 and 59.0	63.7 and 62.9	62.9
C-4	172.2 and 171.7	171.9	172.8	172.8 and 172.1	172.1 and 171.5	172.1
C-5	32.4	32.7	31.7	32.2 and 31.7	32.62 and 32.59	32.6
C-6	43.7 and 43.1	42.8	44.0	44.1 and 43.9	43.6 and 43.1	43.1
C-7	67.0 and 63.5	63.5	63.7	66.2 and 63.7	67.1 and 66.7	63.7
C-8	71.8 and 71.9	71.1	70.8	71.8 and 71.5	71.1 and 71.0	71.1
C-9	70.89 and 70.86	71.0	70.7	70.9 and 70.8	70.80 and 70.76	71.0
C-10	70.41 and 70.38	70.4	70.6	70.6 and 70.4	70.43 and 70.39	70.4
C-11	96.3 and 96.2	96.4	96.3	96.3 and 96.2	96.4 and 96.3	96.4
C-12	109.0 and 108.7	108.7	108.8	109.0 and 108.8	109.1 and 108.7	108.7
C-13	25.92	26.1	26.0	25.9 and 26.0	26.1 and 26.0	26.1
C-14	24.5	26.0	25.7	24.3 and 24.4	24.6 and 24.4	24.6
C-15	109.6 and 109.5	109.5	109.6	109.7 and 109.6	109.6 and 109.5	109.51
C-16	25.0 and 24.9	24.9	25.0	25.0 and 24.7	25.0 and 24.8	24.9
C-17	25.90 and 25.7	24.7	24.3	25.7 and 25.6	25.79 and 25.78	26.0

**[1] resonances too weak to be detected; *[2] where two resonances are given, these are for both of the diastereomers. Resonances reported to two decimal places are used to distinguish each of them*

Table 5. ^{13}C NMR of galactose thiazolidinone derivatives **5e-6i** (100 MHz, $CDCl_3$, *J* given in Hz)

Pos.	5e/6e[*1]	5f	6f	5g	6g	5h	6h	5i	6i
C-1a	136.5 and 136.4	147.0	147.1	128.3	127.8	131.1	131.2	139.5	139.5
C-2a	148.0 and 147.9	128.3	128.1	157.1	157.0	129.2	128.6	128.86	129.00
C-3a	134.3 and 134.2	124.2	124.2	111.1	111.1	114.2	114.3	127.6	127.1
C-4a	126.78 and 126.76	148.2	148.2	129.6	129.8	160.1	160.1	128.94	129.03
C-5a	129.2 and 129.1	124.2	124.2	120.7	120.8	114.2	114.3	127.6	127.1
C-6a	125.5 and 125.3	128.3	128.1	126.5	126.8	129.2	128.6	128.86	129.00
C-7a	-	-	-	55.6	55.5	55.3	55.4	-	-
C-2	59.8 and 58.7	63.7	62.7	60.3	58.5	64.8	63.1	65.1	63.36
C-4	172.9 and 172.4	171.5	172.0	172.4	172.8	171.4	171.9	171.6	172.1
C-5	31.8 and 31.7	32.5	32.6	32.3	32.5	32.8	32.8	32.8	32.7
C-6	44.2 and 43.4	43.7	43.5	44.2	43.1	43.3	42.6	43.5	42.7
C-7	67.0 and 63.9	67.2	63.9	67.1	63.5	66.9	63.4	67.0	63.41
C-8	71.8 and 70.8	71.8	71.1	71.9	71.1	71.9	71.03	71.9	71.0
C-9	70.72 and 70.70	70.7	71.0	70.9	70.9	70.9	70.96	70.9	70.9
C-10	70.5 and 70.3	70.4	70.4	70.5	70.5	70.4	70.4	70.4	70.4
C-11	96.2 and 96.1	96.3	96.3	96.2	96.4	96.3	96.4	96.3	96.4
C-12	109.0 and 108.8	109.1	108.8	108.9	108.7	109.0	108.6	109.0	108.7
C-13	26.03 and 25.97	26.0	26.1	26.0	26.0	26.0	26.1	26.0	26.1
C-14	24.4 and 24.0	25.8	24.6	25.8	24.6	25.9	24.7	25.8	24.7
C-15	109.6 and 109.5	109.6	109.5	109.5	109.5	109.6	109.5	109.6	109.5
C-16	25.0 and 24.9	25.0	24.9	25.1	24.9	25.1	24.9	25.1	24.9
C-17	25.7 and 25.6	24.4	26.0	24.4	25.9	24.6	26.0	24.6	26.0

*[*1] where two resonances are given, these are for both of the isomers. Resonances reported to two decimal places are used to distinguish each of them*

The assignments above were verified by the COSY spectrum where the following coupled systems were seen; H-6i, H-6ii and H-7; H-5i and H-5ii; H-8 and H-9; H-9 and H-10; and H-10 and H-11. Long range coupling between H-2 and H-5i were also seen. The aromatic protons H-3a, H-4a, H-5a, and H-6a were all also seen coupled to each other. The formation of the thiazolidinone ring and the attachment of the phenyl ring to C-2 was verified by the HMBC correlations from H-2 to the aromatic carbons C-6a, C-2a and the carbonyl resonance C-4. Furthermore, H-6ii shows HMBC correlations to C-2 and C-4 indicating that the sugar moiety is attached to the thiazolidinone ring. Within the galactose ring, H-11 shows HMBC correlations to C-7, C-9, and C-12, which allowed C-12 to be differentiated from C-15. The methyl protons were assigned as a result of HMBC correlations from H-13 and H-14, to C-12, and from H-16 and H-17 to C-15. The NOESY correlation between the methoxy H-7a and H-3a confirmed the position of the methoxy on the aromatic ring.

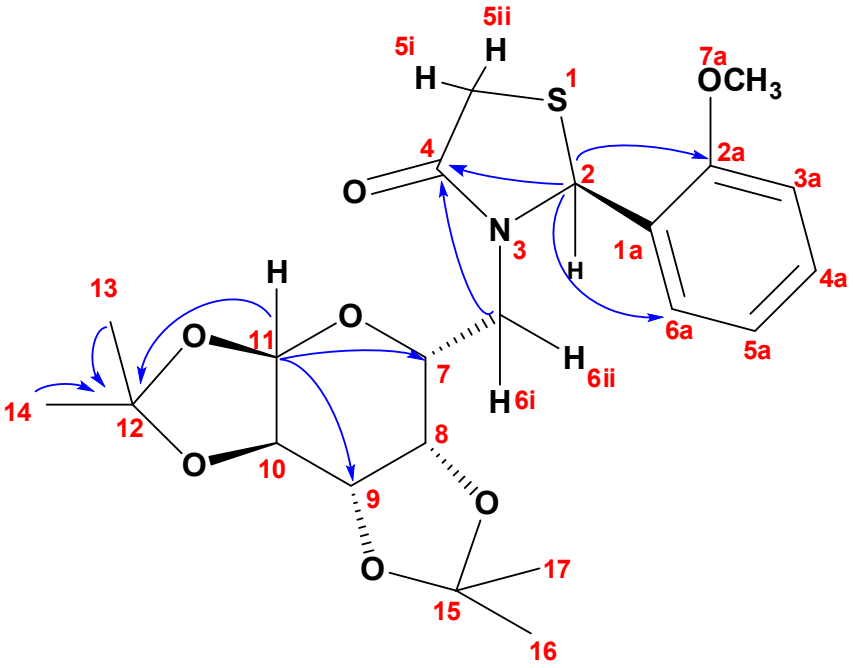


Figure 38. HMBC correlations of 2-methoxy thiazolidinone derivatives

In the NMR spectra of all the related derivatives, the galactose and the thiazolidinone were similar. The differences were seen in the phenyl ring attached to C-2 due to different substituents on the aromatic ring. For the 2-trifluoromethyl derivative, the proton resonances of H-3a to H-6a were all well resolved unlike the 2-methoxy derivative above, where the H-3a and H-5a resonances overlapped and the H-4a resonance overlapped with the solvent peak. In **5c** (2-trifluoromethyl derivative), *meta* coupling for H-4a, H-5a and H-6a was not observed unlike in **5g** (2-methoxy derivative). In **5c**, all the proton resonances are shifted downfield relative to those in **5g**. The H-3a resonance at δ 7.29 (d, J = 7.8 Hz) and H-5a at δ 7.42 (t, J = 7.8 Hz) are still the most shielded resonances. However, in **5c**, H-6a at δ 7.65 (d, J = 7.8 Hz) is now more deshielded than H-4a at δ 7.57 (t, J = 7.8 Hz) unlike in **5g** where H-4a is the most deshielded resonance.

The 2-nitro derivative was synthesized as a mixture of diastereomers. The H-6a and H-3a resonances for both the diastereomers overlap at δ 7.29 - δ 7.32 and δ 7.98 - δ 8.01. However, the doublets for each of these resonances can be distinguished with J = 8.6 Hz. In this case the H-4a and H-6a resonances are the most shielded since the nitro group is deactivating leaving the *meta* positioned H-3a and H-5a electron-rich. Thus, H-4a and H-6a resonate at δ 7.45 and δ 7.29 - δ 7.32 and H-3a and H-5a resonate at δ 7.98 – δ 8.01 and δ 7.61 - δ 7.66 respectively. An HMBC correlation from H-6a to C-2 confirms this assignment. Even though the H-4a resonances for both diastereomers overlap, this is observed as a triplet, however due to overlap of the H-5a resonances this appears as a multiplet.

In the 4-methoxy derivative, a pair of doublets is observed for the aromatic ring at δ 6.90 and δ 7.27 (J = 8.7 Hz). The more shielded resonance at δ 6.90 is attributed to H-3a/5a because of the

electron-donating methoxy group and the more deshielded resonance to H-2a/6a. This assignment was confirmed from a HMBC correlation from H-2a/6a to C-2. The same pattern occurs for the 4-trifluoromethyl derivative with the exception of these resonances being more deshielded at δ 7.39 and δ 7.59 (d, J = 8.2 Hz). For the 4-nitro derivative, the H-2a/6a doublet is now more shielded at δ 7.45 (J = 8.8 Hz) and the H-3a/5a doublet more deshielded at δ 8.21. The reversal of assignments in **6f** (4-nitro derivative) compared to **6h** and **6d** is due to the electron-withdrawing nitro group. This was supported by a HMBC correlation from H-2a/6a to C-2.

For the 4-fluorinated derivative, the H-3a and H-5a appear as a triplet at δ 7.03 since they are coupled by both the adjacent aromatic proton and fluorine atom, with the same coupling constant of 8.8 Hz. The H-2a/6a resonance appears as a double doublet at δ 7.27 with $J_{H,\,H}$ = 8.8 Hz and $J_{H,\,F}$ = 5.3 Hz. In the fluorinated aromatic ring C-3a/5a at δ 115.9 has the largest coupling constant with J = 21.7 Hz. C-2a/6a at δ129.2 is *meta* coupled to the fluorine atom with J = 8.3 Hz and C-1a is *para* coupled to the fluorine with J = 3.1 Hz. The carbon to which the fluorine is directly bonded is the most deshielded at δ 163.0 with a large coupling constant of 246.8 Hz.

The two diastereomers of the 2-fluoro thiazolidinone derivatives could not be separated and occurred as a mixture. This was evident since two resonances, one for each of H-2, H-11 and H-9 could clearly be seen in the ^{1}H NMR spectrum. For the protons on the fluorinated benzene ring, the H-6a, H-5a and the H-3a resonances at δ 7.20, δ 7.13, and δ 7.02 respectively all appears as triplets. This is due to both proton-proton and proton-fluorine coupling. The H-4a resonance however appears as a multiplet at δ 7.24 - δ 7.30. Eight methyl resonances were also observed at

δ 1.50, δ 1.47, δ 1.36, δ 1.31, δ 1.29, δ 1.28, δ 1.25 and δ 1.23, each three proton singlets which further indicated that a mixture of the two diastereomers were present.

All the carbon resonances on the fluorinated aromatic ring appear as doublets due to coupling with the fluorine. The C-2a resonance of each of the diastereomers could be seen at δ 160.7 and δ 160.5 with a large *J* value of 248.2 Hz confirming that the fluorine was directly bonded to the atom. The *ortho* coupled C-3a resonance was the most shielded at δ 116.1 and δ 116.0 (*J* = 21.1 Hz). The *para* coupled C-5a occurred at δ 124.5 and δ 124.6 with a small *J* value of 3.6 Hz. The *meta* coupled C-4a and C-6a occur at δ 130.4 and δ 130.3 (*J* = 8.5 Hz, C-4a) and at δ 128.1 and δ 127.9 (*J* = 3.2 Hz, C-6a). The C-6a *J* value was smaller since it was coupled to fluorine across the thiazolidinone substituent. The C-1a resonance could be seen at δ 127.1 and δ 127.0 with *J* = 11.4 Hz. Seven methyl resonances could be seen, two for each of C-13 (δ 26.0 and δ 25.92), C-17 (δ 25.90 and δ 25.7), and C-16 (δ 25.0 and δ 24.9) and one resonance at δ 24.5 for the two overlapping C-14 resonances.

In most of the spectra where the two diastereomers have been separated, the *S* diastereomer has H-2 more deshielded than the *R* diastereomer. For example, in the 2-methoxy diastereomers, the *S* diastereomer has H-2 at δ 6.17 and the *R* diastereomer has H-2 at δ 6.07.

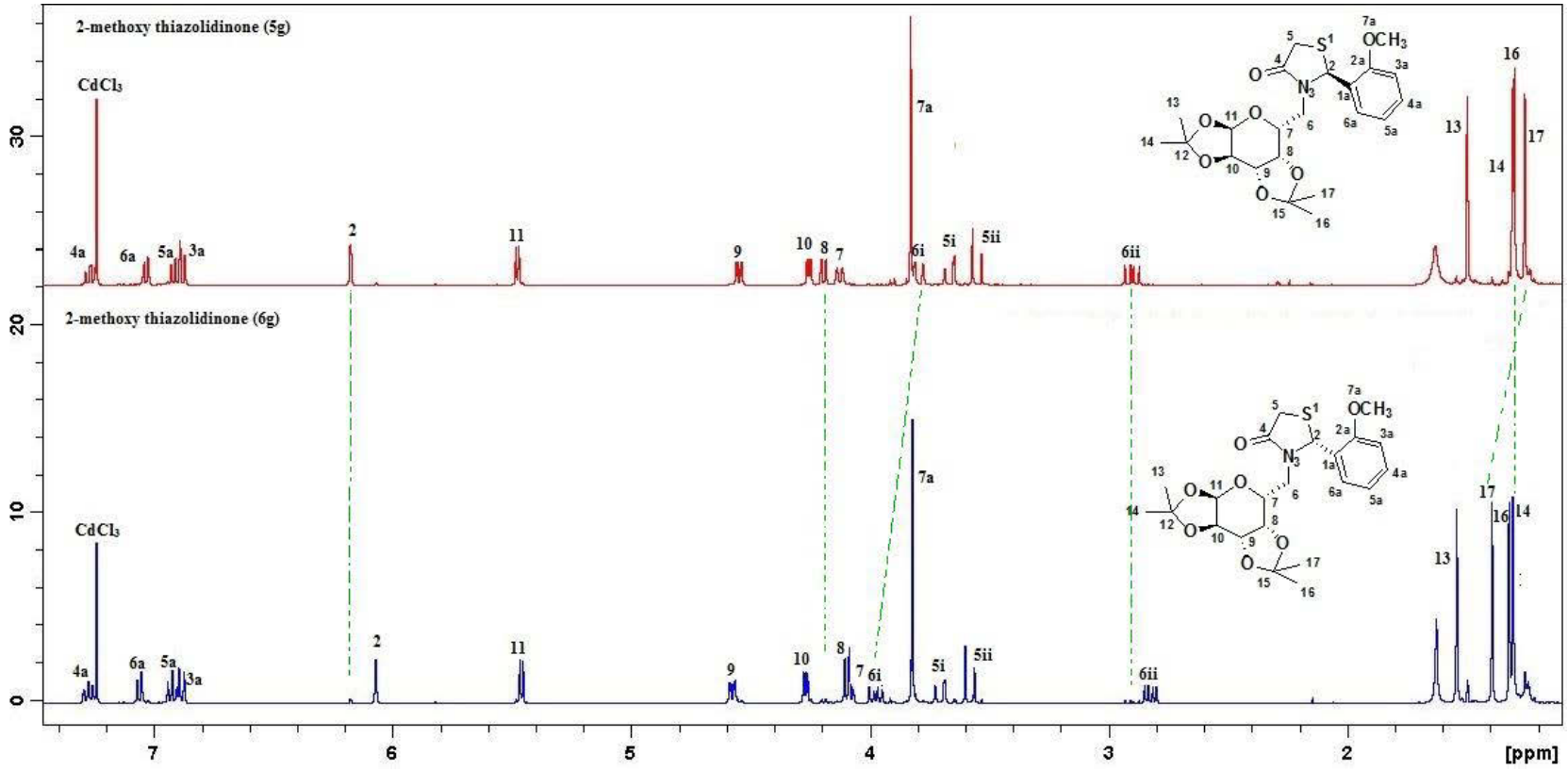


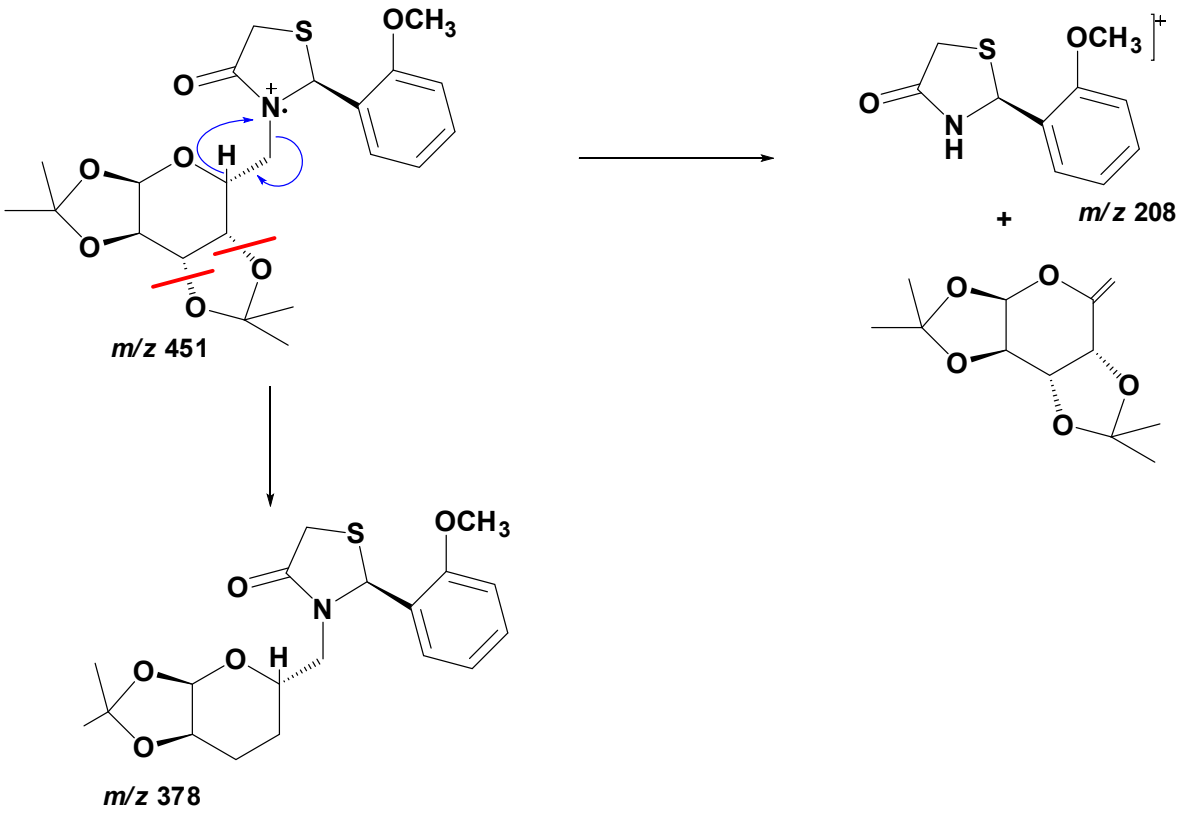
Figure 39. Overlapping ^{1}H NMR spectra of the *2R* and *2S* 2-methoxy diastereomers showing the differences between them

Likewise, the 4-methoxy diastereomers has H-2 at δ 5.92 and δ 5.78, H-2 in the 4-nitro diastereomers are at δ 6.07 and δ 5.86 and the unsubstituted diastereomers have H-2 at δ 5.96 and δ 5.77. In general, the H-11 resonance of the *S* diastereomer occurs at a slightly higher chemical shift (~δ 5.48) than the *R* diastereomer (δ 5.42 - 5.46) with the exception of the 4-methoxy derivative where the reverse was observed. The H-9 double doublet in each of the *S* diastereomers are more shielded at approximately δ 4.55 than the *R* diastereomer, and appears slightly more downfield between δ 4.57 - δ 4.61. In the *S* diastereomer, we assigned the order of the methyl protons from HMBC correlations to be H-13, H-14, H-16, and H-17 with H-13 being much more deshielded than the others. In the *R* diastereomer, C-12 was differentiated from C-15 by an HMBC correlation to H-11. This allowed us to assign H-13 and H-14 through HMBC correlations with C-12. Thus, H-13 and H-14 were the most and least deshielded of the methyl resonances at δ 1.54 and δ 1.30 respectively, whilst H-16 and H-17 were at δ 1.32 and δ 1.39. Their corresponding carbon resonances followed the same trend at δ 26.0, δ 24.6, δ 24.9, δ 25.9 for C-13 to C-17 respectively. In addition, H-2 in the *R* diastereomer showed a weak NOESY interaction with the methyl group H-13. This was not observed for the *S* diastereomer.

In the *2R* diastereomer, the H-2a/4a/6a resonances were separated from the H-3a/5a resonances. Both these resonances appeared as multiplets at δ 7.25 - δ 7.27 (H-3a/5a) and δ 7.30 - δ 7.35 (H-2a/4a/6a). In the *2S* diastereomer these proton resonances all overlap at δ 7.29 - δ 7.33. In the ^{13}C spectra, most of the resonances for each of the unsubstituted diastereomers are similar with the exception of C-8 which is more deshielded in the *2S* diastereomer which makes it easy to distinguish between the C-8 and C-9 resonances in this diastereomer. In the *2R* diastereomer, C-8

and C-9 almost overlap at δ 70.9 and δ 71.0. Likewise the same trend is observed for C-2 and C-7.

In all the molecules a molecular ion fragment is seen with an electron being bombarded from either the nitrogen or the sulfur atom. The fragment at *m/z* 208 results from a hydrogen migration possibly from the sugar to the nitrogen, with cleavage of the N-CH_2 bond. Cleavage of both the C-O bonds in the acetonide group result in the fragment at *m/z* 378. A plausible fragmentation pattern is shown in **Scheme 5**.



Scheme 5. Mass spectrometry fragmentation pattern of 2-methoxy thiazolidinone derivatives

For the 2-methoxy and 4-methoxy derivatives, which were obtained in reasonable purity the compounds with the *2R* were dextrorotatory and the compounds with a *2S* value were levorotatory. The 4-fluoro derivative with the *2S* value, was also obtained with reasonable purity was levorotatory. The 2-trifluoromethyl *2S* diastereomer was dextrorotatory and the 4-trifluoromethyl *2R* diastereomer was levorotatory. In the 4-nitro derivatives, the *2S* diasteromer was levorotatory and the *2R* diastereomer was dextrorotatory. Both the unsubstituted derivatives were levorotatory.

All the compounds synthesized were novel and therefore high resolution mass spectra (HRMS) were obtained for representative samples. In all the synthesized compounds, the same substituent was placed at either C-2a or C-4a in the phenyl ring. In addition, two diastereomers were formed for each of the C-2a and C-4a derivatives. HRMS was carried out on one of each of the F, CF_3, OCH_3, NO_2, and unsubstituted diastereomers. In each of the acquired spectra, a sodium adduct was obtained and therefore had 22.99 mass units higher than the expected molecular mass. For example, the 4-F derivative had an exact mass at *m/z* 462.1352 (calculated for $C_{21}H_{26}FNNaO_6S$, 462.1363). Similarly, the exact masses were obtained for each of the other derivatives within 5 ppm of the calculated mass (**Table 6**).

Table 6. High Resolution Mass Spectra of selected compounds

No.	Substitution	Molecular formula	Exact mass	Calculated mass
5b	F	$C_{21}H_{26}FNNaO_6S$	462.1352	462.1363
5d	CF_3	$C_{22}H_{26}F_3NNaO_6S$	512.1332	512.1331
5f	NO_2	$C_{21}H_{26}N_2NaO_8S$	489.1307	489.1308
5h	OCH_3	$C_{22}H_{29}NNaO_7S$	474.1553	474.1562
5i	H	$C_{21}H_{27}NNaO_6S$	444.1440	444.1457

4.2 Crystal structure

The crystal structure of compound **6g** shows an *2R* configuration at C(8) and C(12). The sugar moiety and the phenyl ring at C(8) point away from each other with a torsion angle C(11)-N(1)-C(8)-C(6) of 71.6(5)°. The phenyl ring is almost orthogonal to the thiazolidinone ring with a S(1)-C(8)-C(6)-C(5) torsion angle of -103.2(5)°. The two acetonide groups on the sugar moiety point in opposite directions to each other. In the five membered thiazolidinone ring, the sulfur atom was slightly out of the plane of the four other atoms. In this ring the shortest bond was the N(1)-C(10) bond with a bond length of 1.353(6) Å, followed by the N(1)-C(8) (1.450(6) Å). Both the S-C bonds were long with the S(1)-C(8) being the longest at 1.847(5) Å, followed by 1.792(7) Å. In the thiazolidinone ring, the largest bond angle was shown by C(10)-N(1)-C(8) (119.6(4)°), followed by N(1)-C(10)-C(9) (111.6(5)°). The smallest bond angle was shown by C(8)-S(1)-C(9) (92.6(3) Å).

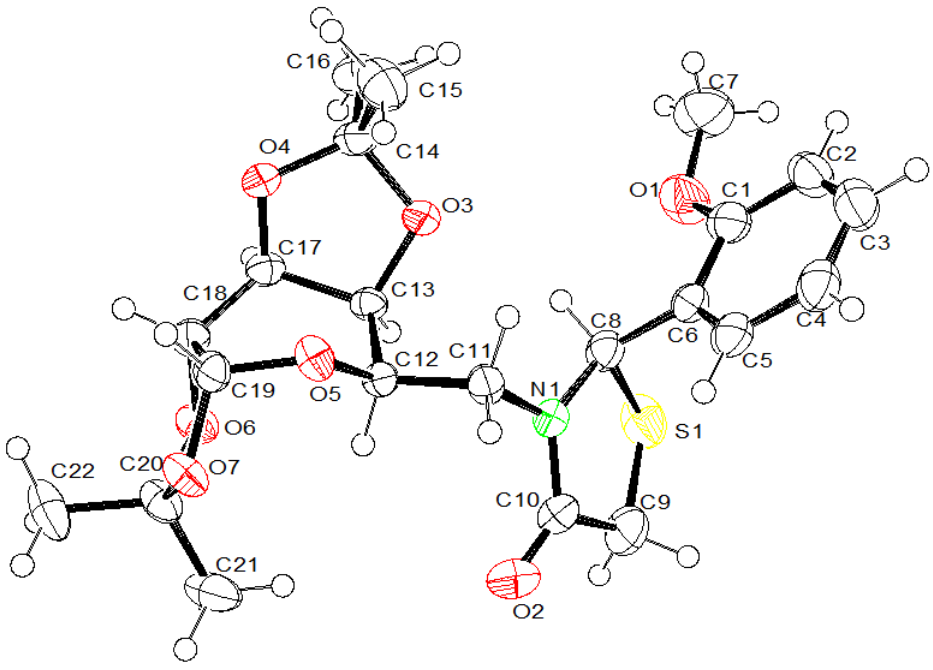


Figure 40. Crystal structure of 2-methoxy thiazolidinone (**6g)**

Table 7. Selected bond lengths/ **Å** and angles/**°**

	Bond lengths (Å)
S(1)-C(8)	1.847(5)
C(8)-N(1)	1.450(6)
N(1)-C(10)	1.353(6)
C(10)-C(9)	1.511(8)
C(9)-S(1)	1.792(7)
N(1)-C(11)	1.460(6)
C(11)-C(12)	1.515(6)
C(8)-C(6)	1.513(7)
	Bond angles (°)
N(1)-C(8)-S(1)	104.2(3)
C(8)-S(1)-C(9)	92.6(3)
N(1)-C(10)-C(9)	111.6(5)
C(10)-C(9)-S(1)	107.2(4)
C(8)-N(1)-C(10)	119.6(4)

Table 8. Crystal data and structure refinement parameters

Empirical formula	$C_{22}\ H_{29}\ N\ O_7\ S$	
Formula weight	451.52	
Temperature	173(2) K	
Wavelength	0.71073 Å	
Crystal system	Orthorhombic	
Space group	$P\ 2_1\ 2_1\ 2_1$	
Unit cell dimensions	a = 7.3677(6) Å	α = 90°
	b = 11.5857(9) Å	β = 90°
	c = 26.259(2) Å	γ = 90°
Volume	2241.4(3) $Å^3$	
Z	4	
Crystal size	0.505 x 0.337 x 0.252 mm^3	
Goodness-of-fit on F^2	1.317	
Final R indices [I>2sigma(I)]	R1 = 0.0597, wR2 = 0.1473	
R indices (all data)	R1 = 0.0775, wR2 = 0.1521	

4.3 Antibacterial study

In this study, five bacterial (two gram positive, *Staphylococcus aureus* ATCC 25923, *Staphylococcus aureus* Rosenbach ATCC BAA-1683 (methicillin resistant *S. aureus* (MRSA)) and three gram negative *Pseudomonas aeruginosa* ATCC 27853, *Klebsiella pneumonia* ATCC 31488 and *Escherichia coli* ATCC 25922) and one fungal strain (*Candida albicans* ATCC 10231) were used in the disc diffusion assay method to determine the antibacterial activity of the synthesized compounds. The disc diffusion was only used to detect antibacterial activity of the test compounds at a concentration of 10 mg mL^{-1} (20-24 mM). Hence, this was more of a qualitative rather than a quantitative test to be used for the MBC assay. The results indicated that the test compounds were only active against three of these strains, MRSA, *K. pneumonia* and *E. coli*. Further to this, only three of the test compounds, the **5c** (*2S* 2-CF_3), **6d** (*2R* 4-CF_3) and **6i** (*2R* unsubstituted) compounds showed activity against MRSA. Most of the test compounds showed some activity in the other two strains. However, **5c** (*2S* 2-CF_3), **6g** (*2R* 2-OCH_3), **5h** (*2S* 4-OCH_3) and **6h** (*2R* 4-OCH_3) did not exhibit any antibacterial activity against *K. pneumonia*. Test compounds **5g** (*2S* 2-OCH_3), **6h** (*2R* 4-OCH_3) and **6i** (*2R* H) were inactive against *E. coli*. All compounds that were inactive were recorded as having a MBC of 20-24 mM.

From the three test compounds that showed activity against MRSA, **5c** (*2S* 2-CF_3) and **6d** (*2R* 4-CF_3) had MBC values at the highest concentration prepared (20 mM). The **6i** (*2R* unsubstituted) compound had the best activity against MRSA at an MBC of 12 mM.

The fluorinated derivatives **5a/6a** (*2S/2R* 2-F), **5b** (*2S* 4-F), **5d/6d** (*2S/2R* 4-CF_3) and **5e/6e** (*2S/2R* 2-NO_2) showed the best activity against *E. coli* with MBCs between 10-11 mM. The rest of the

compounds tested in the MBC assay had activity at the highest concentration prepared at MBCs between 20-24 mM.

The test compounds showed the best activity with *K. pneumonia* with seven of the test compounds having MBCs between 10-12 mM. These were the **5c/6c** (*2S/2R* 2-CF_3), **5d/6d** (*2S/2R* 4-CF_3), **5e/6e** (*2S/2R* 2-NO_2), **5f** (*2S* 4-NO_2), **6f** (*2R* 4-NO_2), **5g** (*2S* 4-OCH_3) and **6i** (*2R* H) compounds. The other three compounds **5a/6a** (*2S/2R* 2-F), **5b** (*2S* 4-F) and **5i** (*2S* H) had MBCs at higher concentrations between 22-24 mM.

Table 9. Antibacterial activity of **5a-6i** using the disc diffusion assay (zones of inhibition (mm))

Compound	Substitution	MRSA	*K. pneumonia*	*E. coli*
5a/6a	2-F	-	3	5
5b	4-F	-	2	5
5c	2-CF_3	5	-	3
5c/6c	2-CF_3	-	6	2
5d/6d	4-CF_3	-	5	5
6d	4-CF_3	5	8	2
5e/6e	2-NO_2	-	6	6
5f	4-NO_2	-	8	2
6f	4-NO_2	-	6	3
5g	2-OCH_3	-	6	-
6g	2-OCH_3	-	-	2
5h	4-OCH_3	-	-	2
6h	4-OCH_3	-	-	-
5i	H	-	3	2
6i	H	12	5	-

*****_No activity was observed by all the test compounds against S. aureus, C. albicians and P. aeruginosa_

Table 10. Minimum Bactericidal Concentration (MBC in mM) of test compounds on thiazolidinone derivatives

Compound	Substitution	*S. aureus*	*C. albicans*	*P. aeruginosa*	MRSA	*K. pneumonia*	*E. coli*
5a/6a	2-F	> 22	> 22	> 22	> 22	22	11
5b	4-F	> 22	> 22	> 22	> 22	22	11
5c	2-CF_3	> 20	> 20	> 20	20	> 20	20
5c/6c	2-CF_3	> 20	> 20	> 20	> 20	10	20
5d/6d	4-CF_3	> 20	> 20	> 20	> 20	10	10
6d	4-CF_3	> 20	> 20	> 20	20	> 20	20
5e/6e	2-NO_2	> 21	> 21	> 21	> 21	11	11
5f	4-NO_2	> 21	> 21	> 21	> 21	11	21
6f	4-NO_2	> 21	> 21	> 21	> 21	11	21
5g	2-OCH_3	> 22	> 22	> 22	> 22	11	> 22
6g	2-OCH_3	> 22	> 22	> 22	> 22	> 22	22
5h	4-OCH_3	> 22	> 22	> 22	> 22	> 22	22
6h	4-OCH_3	> 22	> 22	> 22	> 22	> 22	> 22
5i	H	> 24	> 24	> 24	> 24	24	24
6i	H	> 24	> 24	> 24	12	12	> 24

In this bioassay study, the compounds that showed activity in more than one strain, being active against both *K. pneumonia* and *E. coli* at MBCs between 10-11 mM were **5d/6d** (*2S/2R* 4-CF_3) and **5e/6e** (*2S/2R* 2-NO_2). Compound **6i** (*2R* H) also showed activity against two strains, MRSA and *K. pneumonia* at MBCs of 12 mM.

Our results revealed that there must be some sort of synergistic effect between the *2S* and *2R* diastereomers containing a 4-trifluoromethyl group, since the pure *2R* 4-trifluoromethyl diastereomer was not as active as the *2S/2R* mixture. Unfortunately, we did not have pure *2R* or *2S* 2-nitro diastereomers to compare with the mixture. With regard to the unsubstituted compounds, the *2R* diastereomer was more active than the *2S* compound.

The common antibiotic, Ampicillin, had MIC values of 0.69 µM, 35.77 µM and 143.10 µM against *S. aureus*, *E. coli* and *P. aeruginosa* respectively (Patel et al., 2014b) and Vancomycin, which is used for the treatment of MRSA had MIC values in the range of 0.34 - 1.38 µM (Prakash et al., 2008). A commonly used antifungal, Nystatin, had MICs 0.54 - 1.08 µM against *C. albicans* (Arikan et al., 2002). In comparison to these frequently used antibiotics and antifungal, which had MIC values in the µM range our test compounds were not as active as they had MIC values in the mM range.

Chapter 5. Conclusion

We have successfully synthesized a small library of novel thiazolidin-4-ones using substituted aldehydes, thioglycolic acid and acetal protected galactosamine. The galactosamine was synthesized from galactose, which was first protected with acetone, then tosyl chloride after which it was converted to the azide and further reduced to an amine with a Pd/C catalyst under hydrogen conditions. In this way we have incorporated a galactose sugar onto the thiazolidinone core structure. Variation on the phenyl ring was introduced by substituting F, CF_3, NO_2 or OCH_3 at the *ortho* or *para* position.

In this reaction, it was possible to form both the *2R* and *2S* diastereomers. The 2-F, 2-CF_3, 4-CF_3 and 2-NO_2 diastereomers could not be separated. From these mixtures, the highest yield was observed by the 2-F (75%), followed by 2-NO_2 (60%) and 2- and 4-CF_3 (50%) derivatives. However, the *2R* and *2S* diastereomers in each of the other mixtures was separated by column chromatography with an acetone/n-hexane solvent system. In this way it was possible to synthesize eleven pure thiazolidin-4-ones. The *2R* 4-OCH_3 derivative had the best stereoselectivity with a yield of 59.6% and the *2S* 2-CF_3, *2R* 4-CF_3, *2S* 4-NO_2, *2S* 4-OCH_3 and *2R* unsubstituted compounds had the worst stereoselectivity with yields of approximately 20%.

All the synthesized compounds were characterized using NMR, FT-IR, single-crystal XRD, GC-MS, HRMS, HPLC, melting point, UV and optical rotation. The ^{1}H NMR spectrum of the *2S* diastereomer showed that the H-2, H-8, and H-6ii resonances had shifted slightly more downfield and H-6i shifted upfield in comparison to the *2R* diastereomer. In addition, the H-17 resonance

was more shielded than H-14. The ^{1}H and ^{13}C NMR spectra of the fluorinated derivatives were more complex due to fluorine splitting both the hydrogen and carbon. Thus in the ^{13}C NMR spectra of these compounds more carbon signals were observed due to C-F coupling. Similarly, in the ^{13}C NMR spectrum, a quartet was also observed for the CF_3 carbon. HRMS on selected compounds was used to confirm the structure of the synthesized thiazolidinones.

It was possible to obtain a crystal for one of the 2-methoxy diastereomers. In Thin Layer Chromatography (TLC), this particular diastereomer was observed to have a lower R_f value between the pair. Single crystal XRD was performed to determine its configuration. The configuration of this particular diastereomer was found to be *2R*. Therefore, the other diastereomer was concluded to be *2S*. On the basis of this criteria, we assigned all the other pure diastereomers synthesized, to be either of the *2R* or *2S* configuration.

In the antibacterial bioassay, six strains of bacteria were used but activity was only observed with three of these (*K. pneumonia*, *E. coli* and MRSA). The best antibacterial activity was shown by **5d/6d** (*2S/2R* 4-CF_3), **5e/6e** (*2S/2R* 2-NO_2) and **6i** (*2R* H). In comparison to amoxicillin, the activity of our compounds were much lower. However, it is possible that there may be some sort of synergistic effect between the *2S* and *2R* diastereomers containing a 4-trifluoromethyl group, since the pure *2R* 4-trifluoromethyl diastereomer was not as active as the *2S/2R* mixture.

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University of KwaZulu-Natal

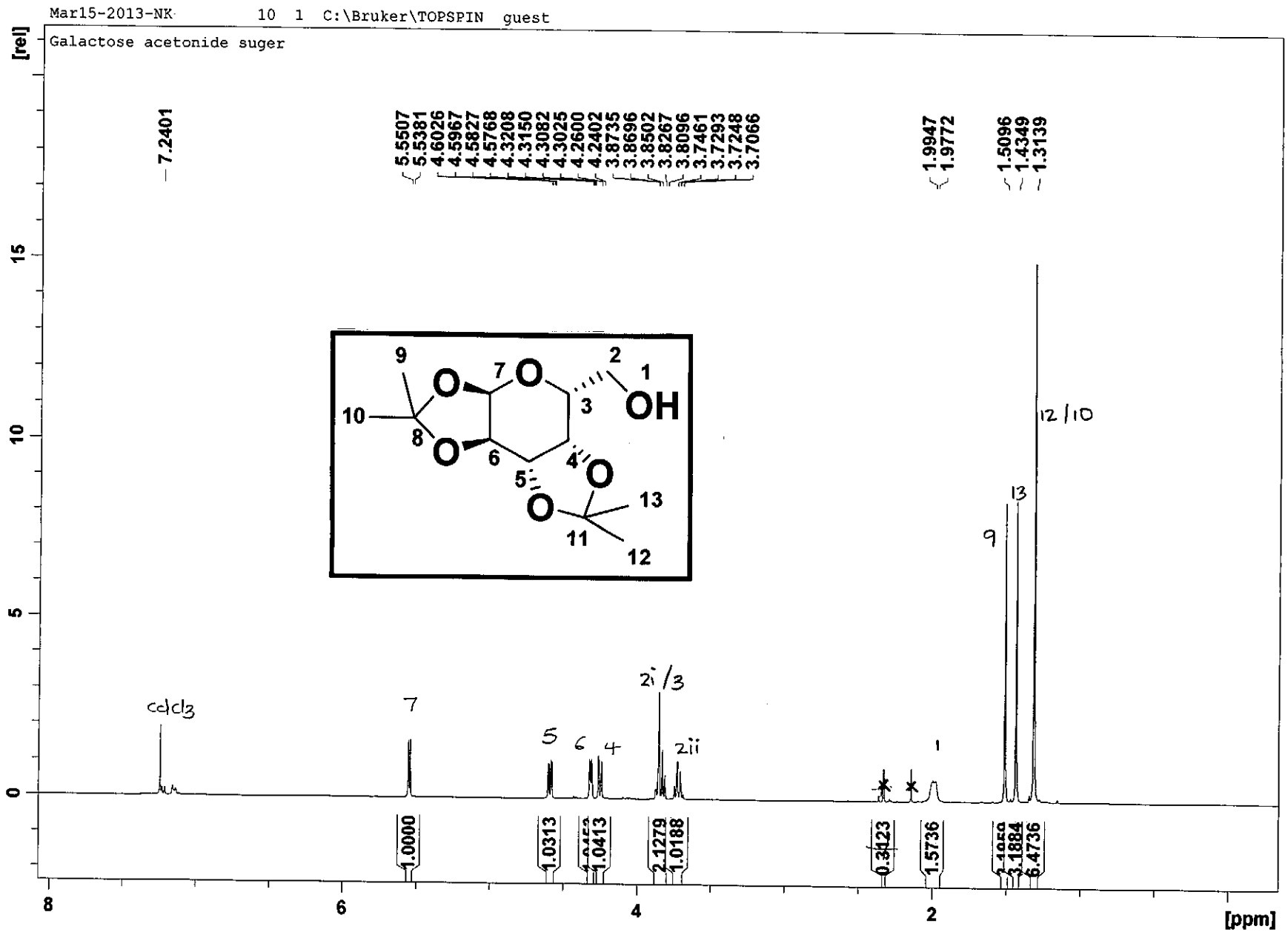
Synthesis, Characterization & Antibacterial Evaluation of Novel Substituted Galactose Thiazolidin-4-ones

Appendix A: Characterization data

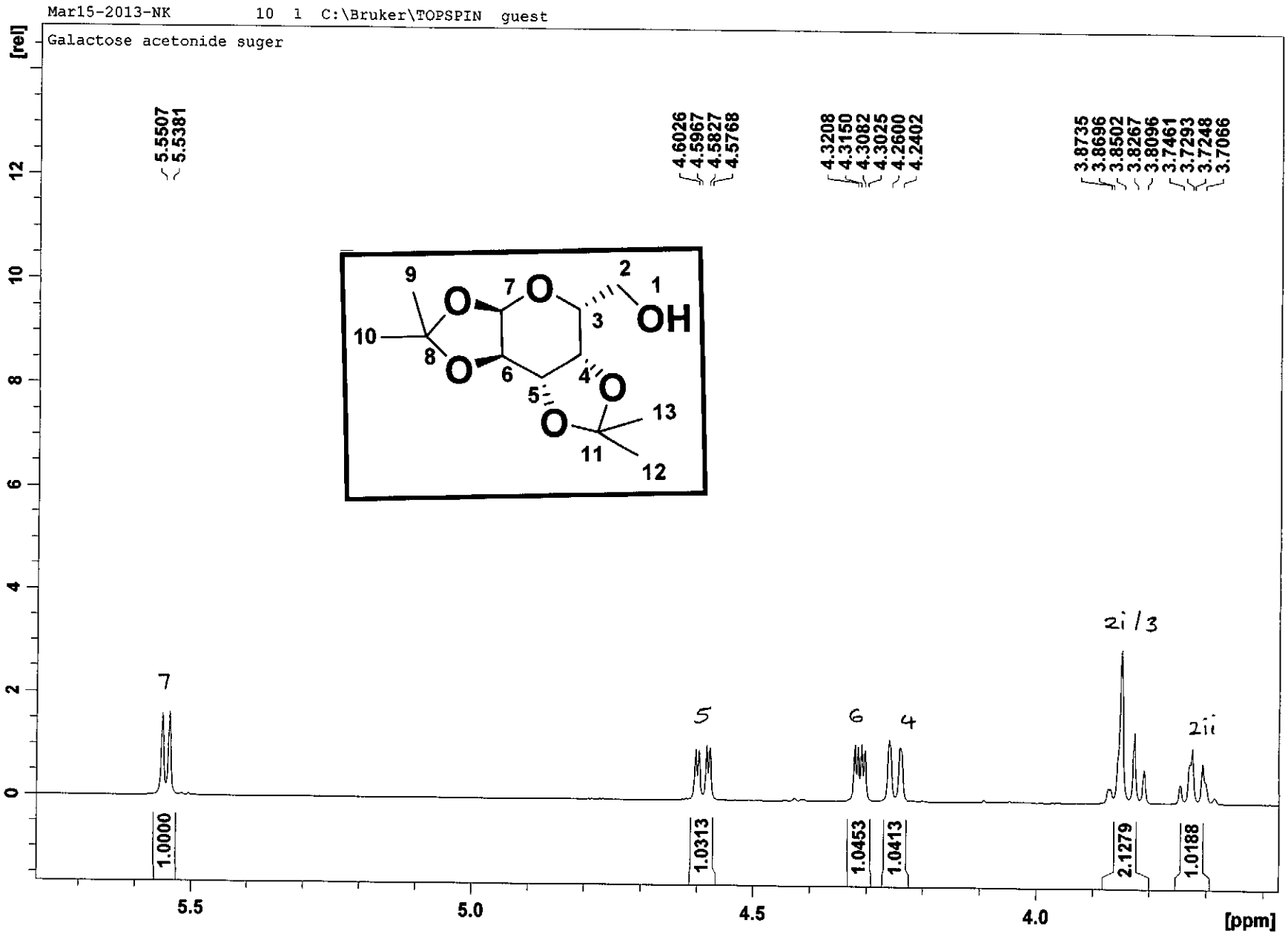
2014

Christina Kannigadu

Table of Contents



^{1}H Spectrum of Compound 1: 2,2,7,7-Tetramethyl-tetrahydro-bis[1,3]dioxolo[4,5-b;4',5'-d]pyran-5-yl)-methanol



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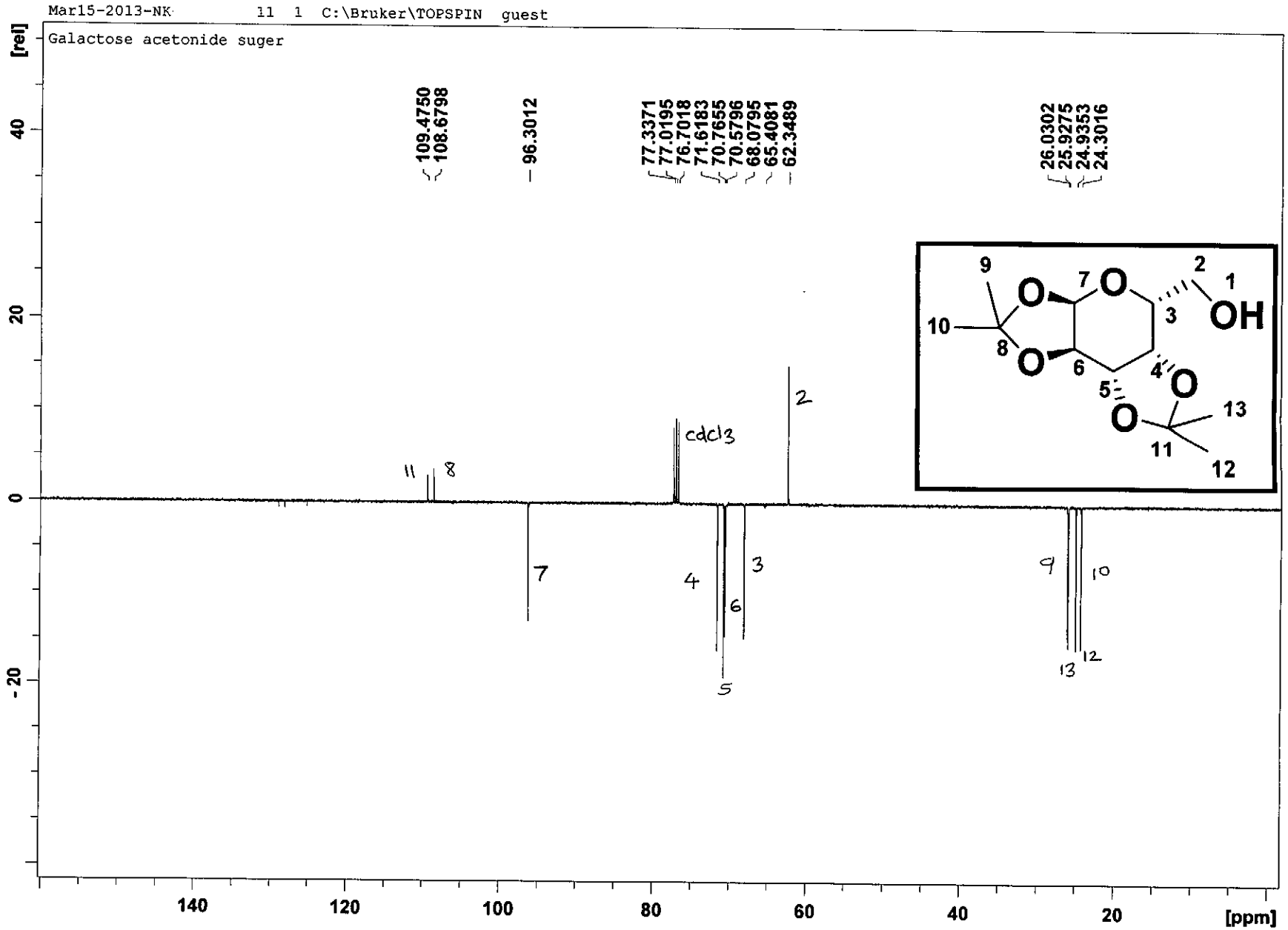

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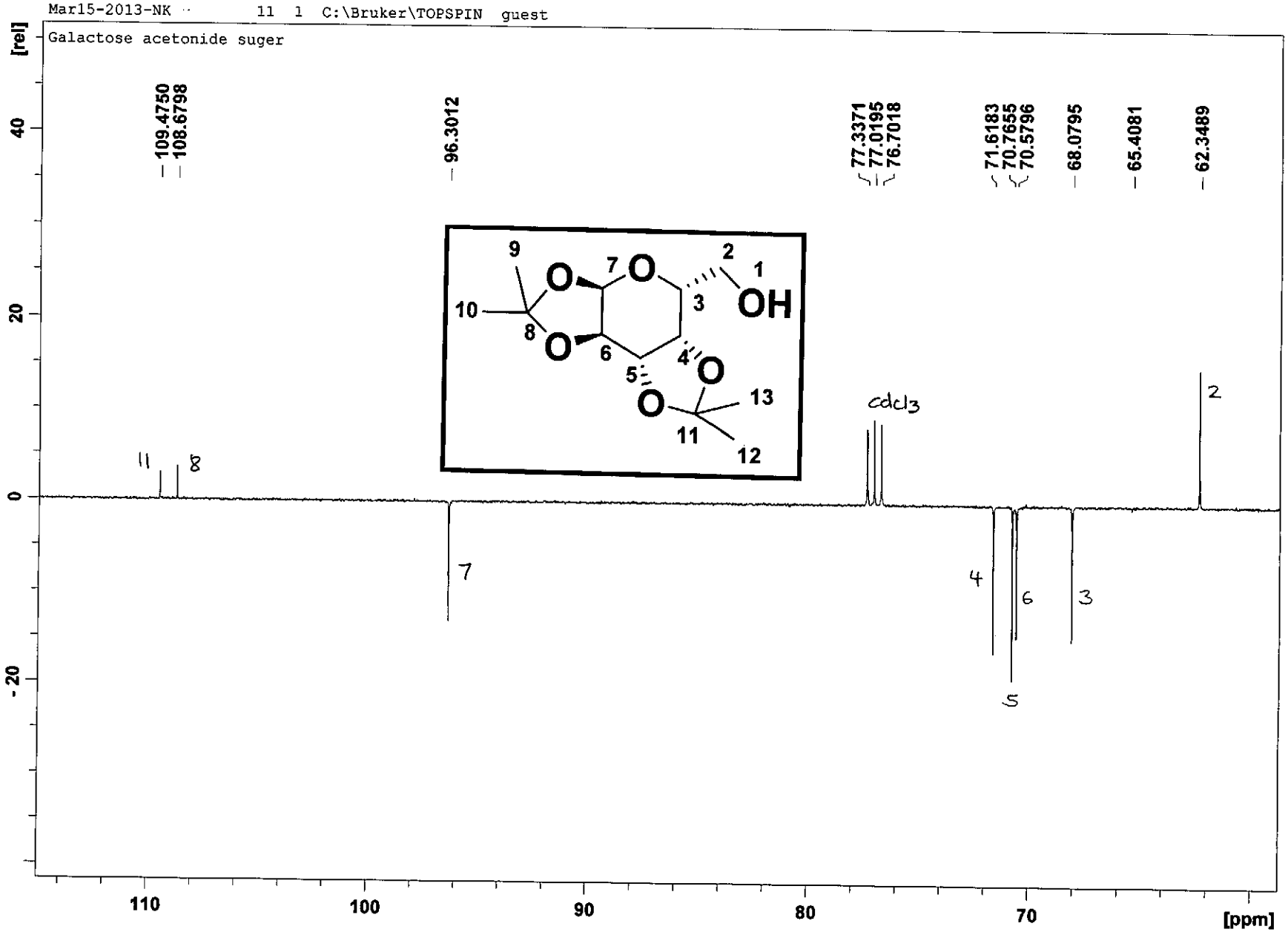
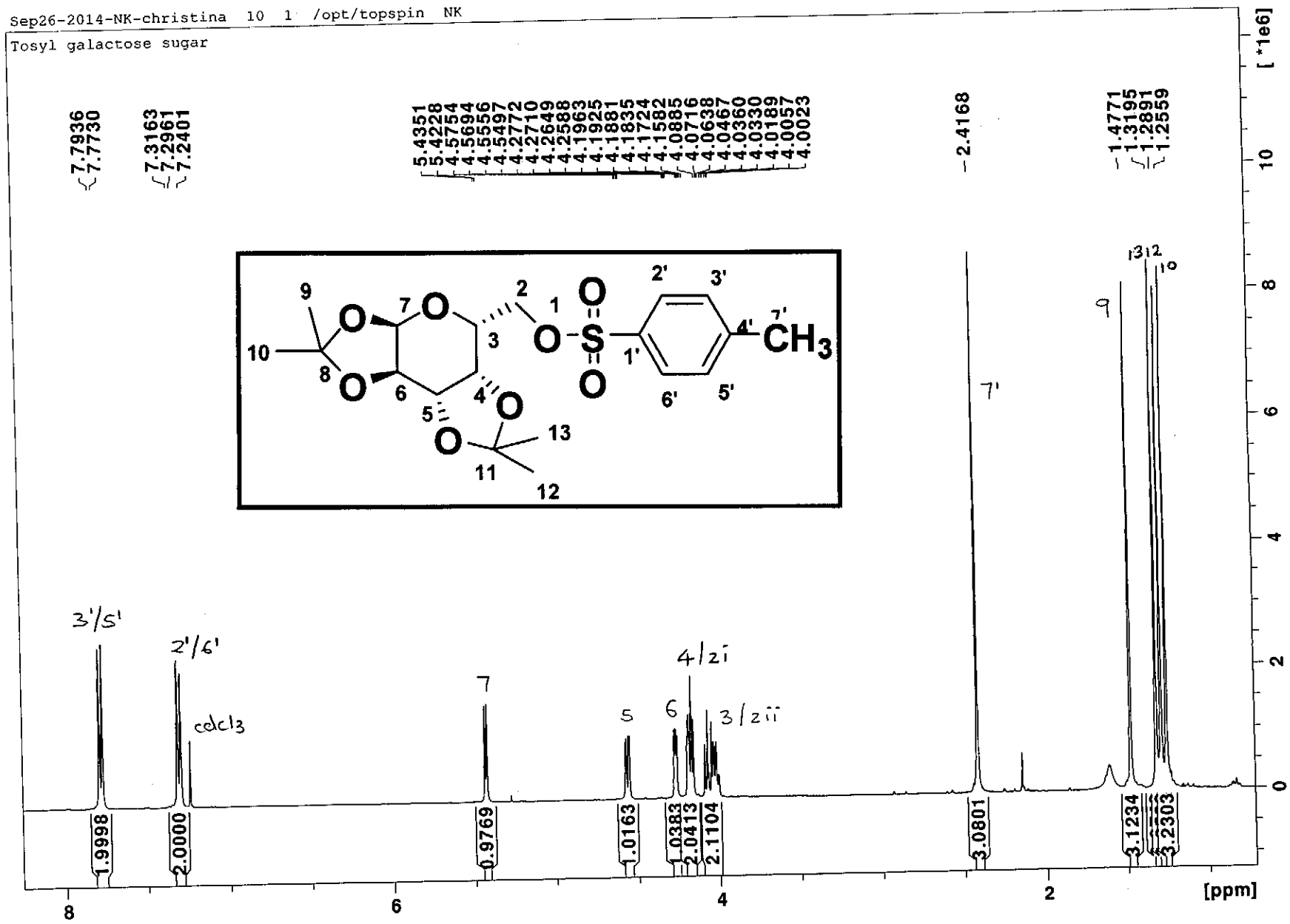
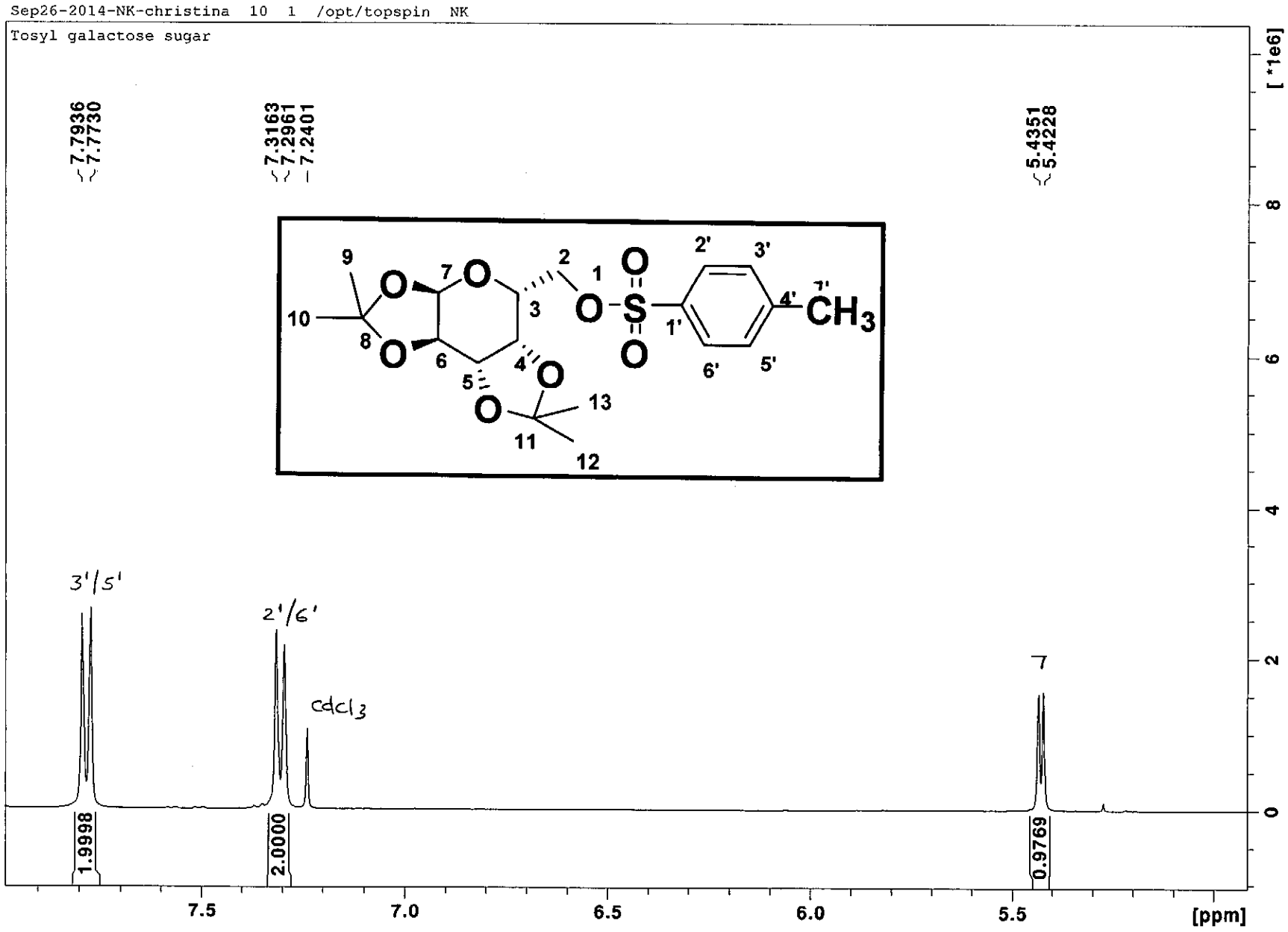


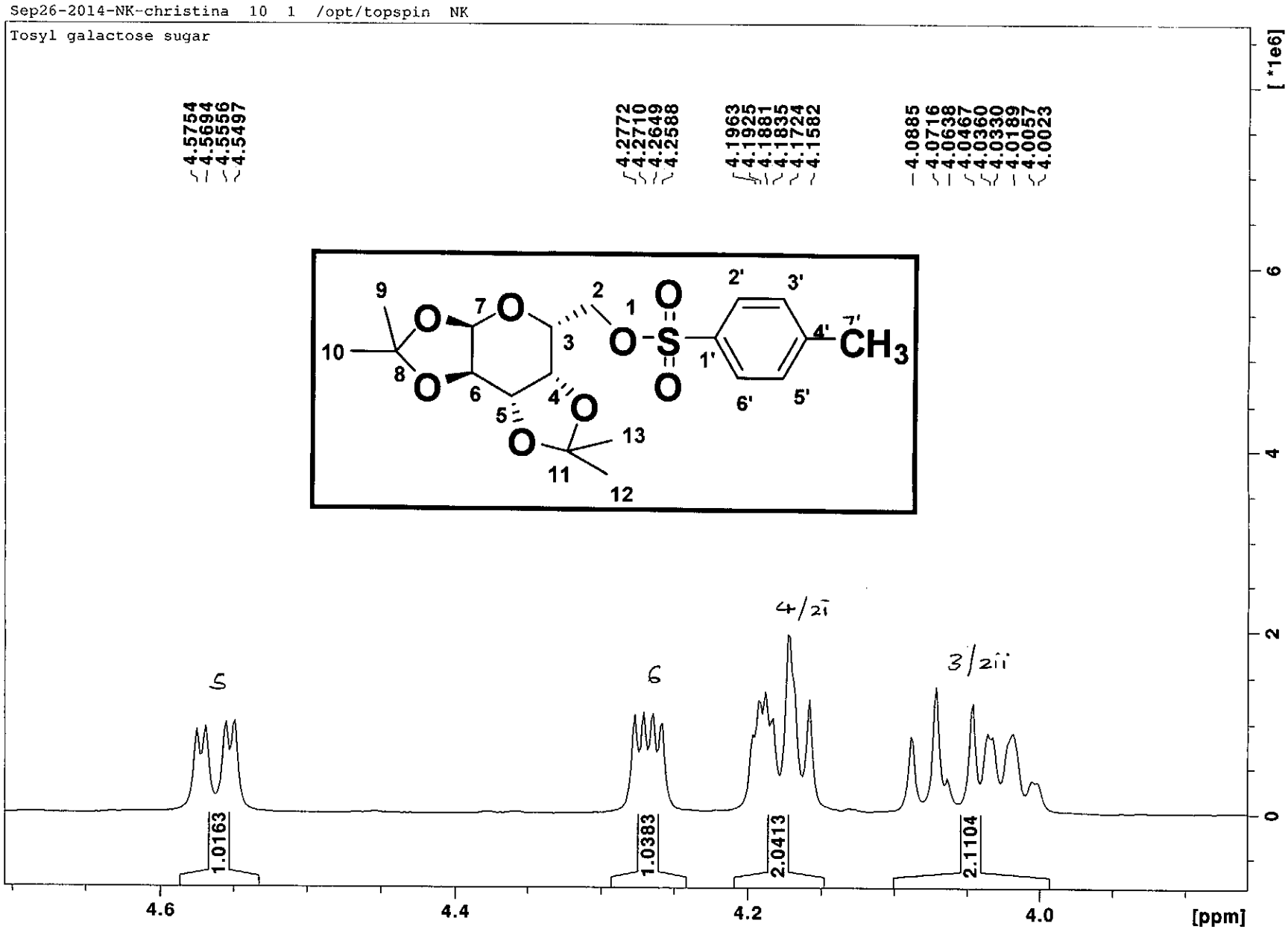
Expanded ^{13}C Spectrum of Compound 1: 2,2,7,7-Tetramethyl-tetrahydro-bis[1,3]dioxolo [4,5-b;4',5'-d]pyran-5-yl)-methanol



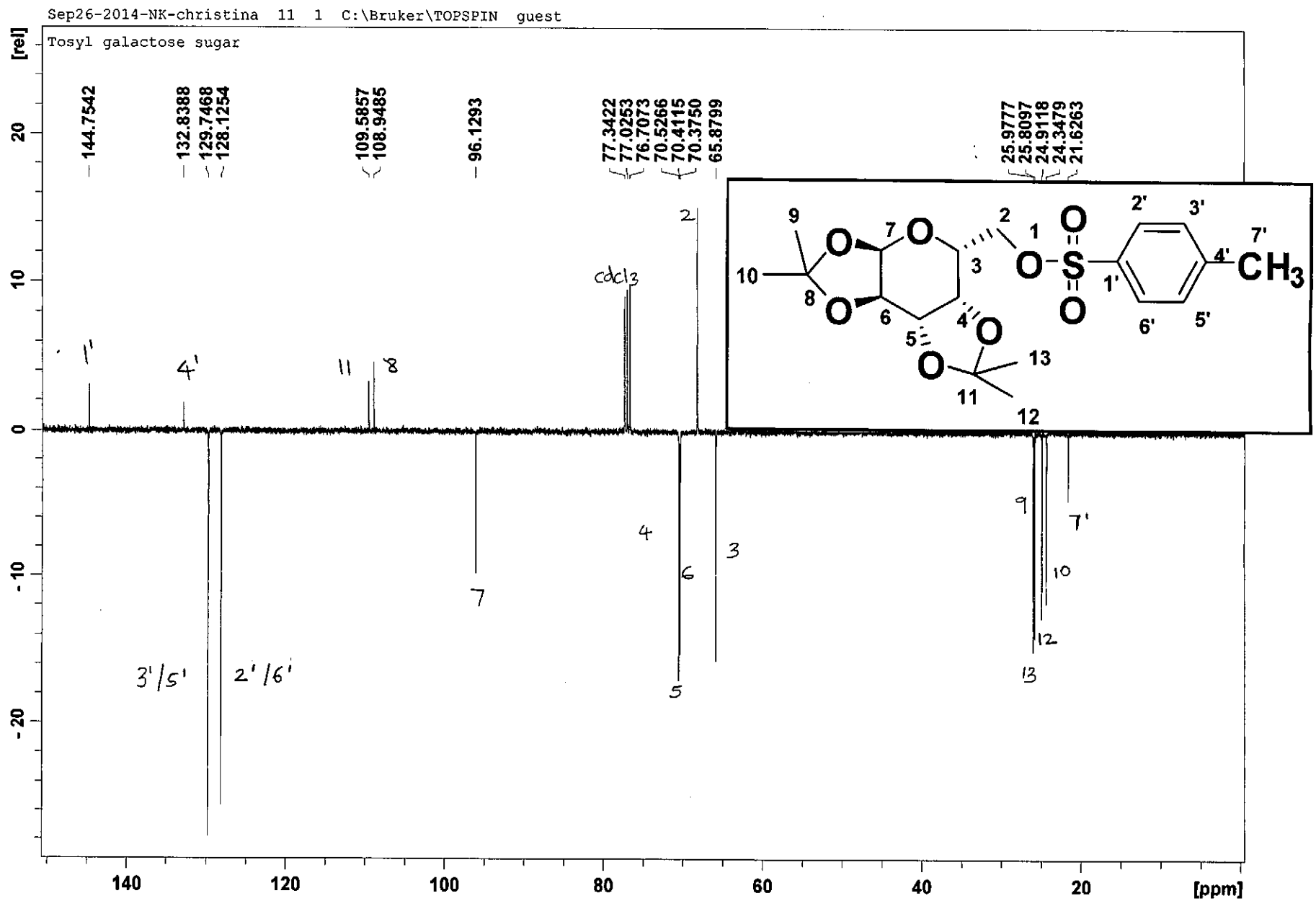
[1]H Spectrum of Compound 2: Toluene-4-sulfonic acid 2,2,7,7-tetramethyl-tetrahydro-bis[1,3]dioxolo[4,5-b;4',5'-d]pyran-5-ylmethyl ester



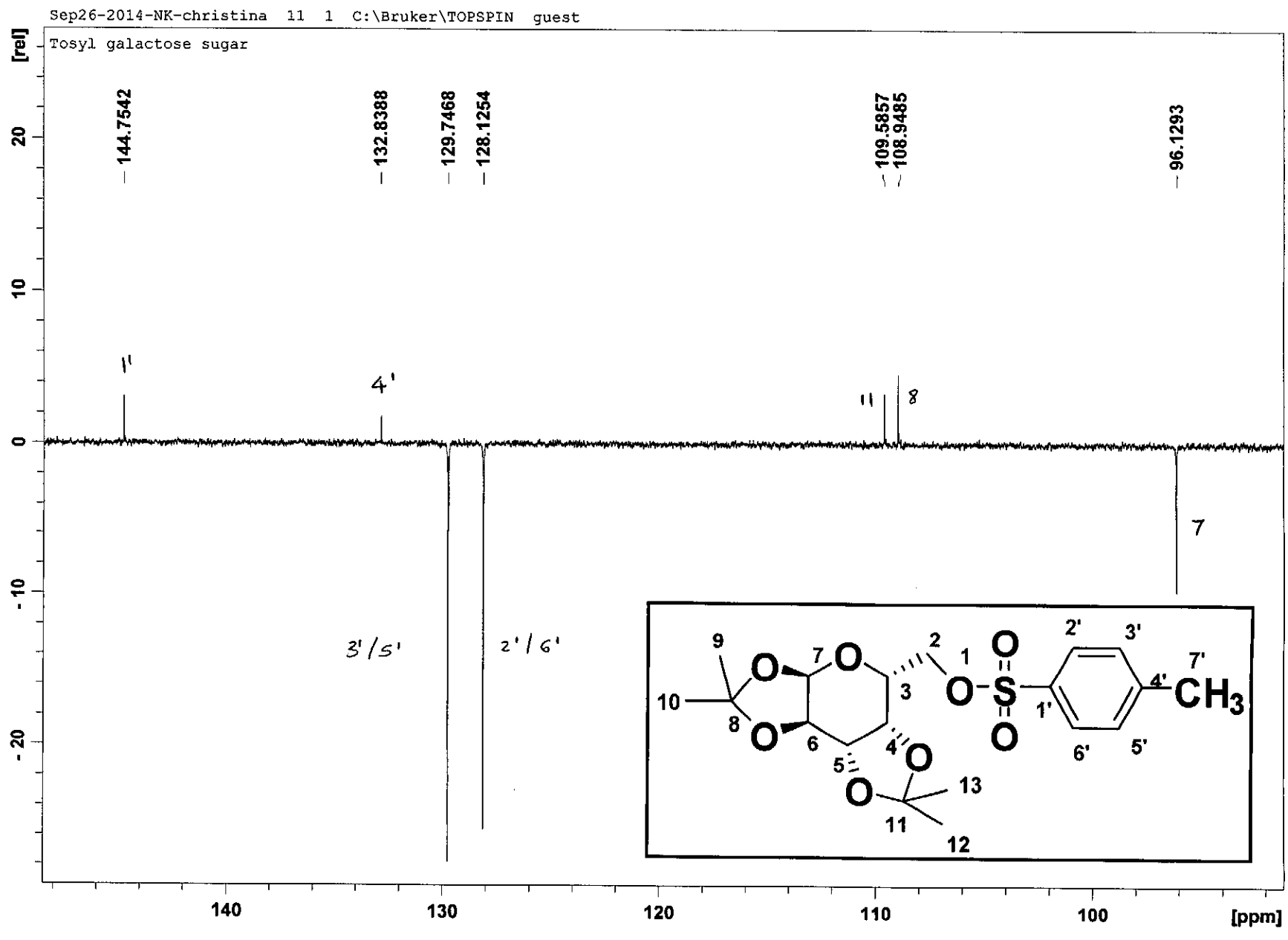
Expanded ^{1}H Spectrum of Compound 2: Toluene-4-sulfonic acid 2,2,7,7-tetramethyl-tetrahydro-bis[1,3]dioxolo[4,5-b;4',5'-d]pyran-5-ylmethyl ester



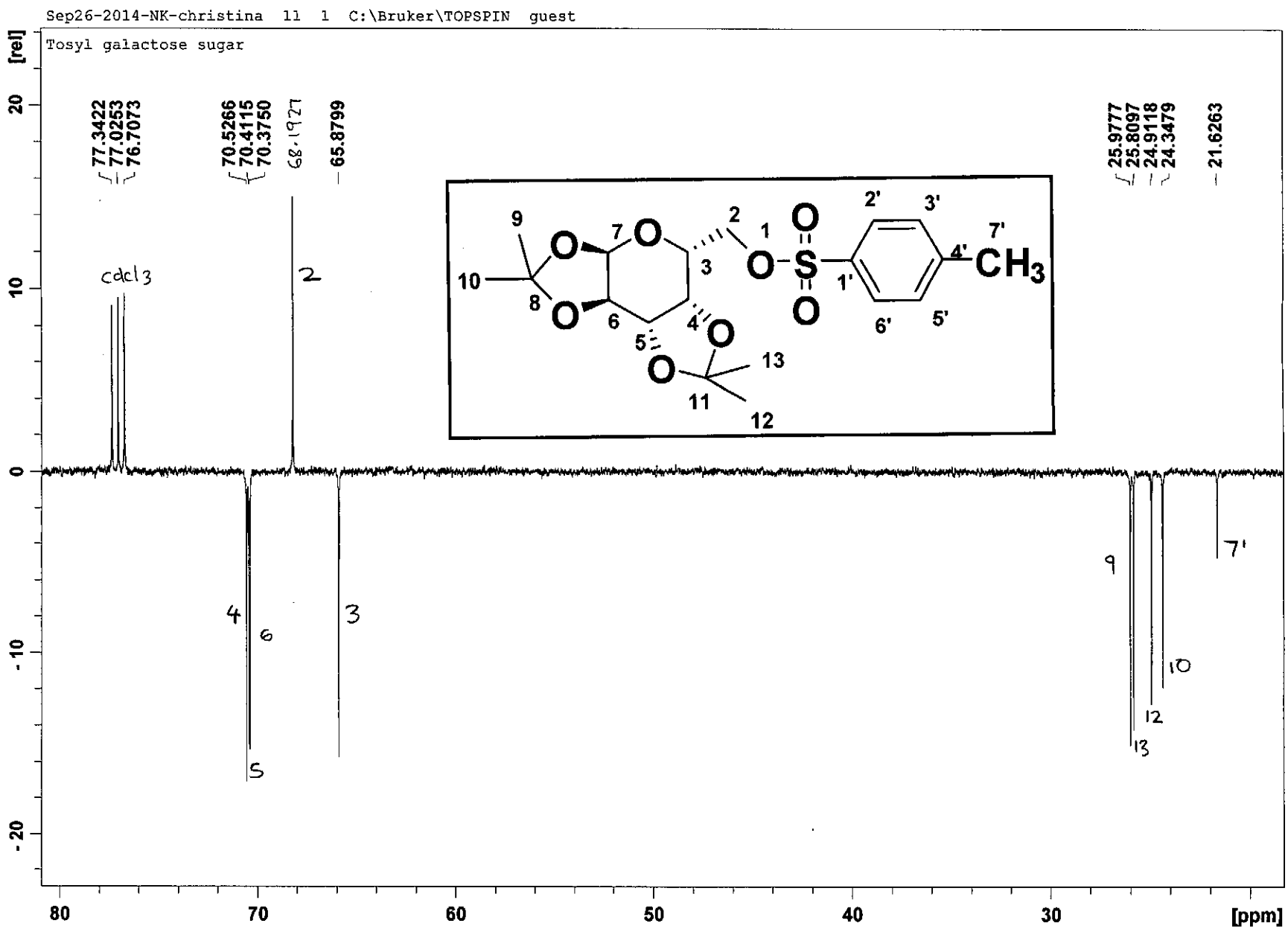
Expanded ^{1}H Spectrum of Compound 2: Toluene-4-sulfonic acid 2,2,7,7-tetramethyl-tetrahydro-bis[1,3]dioxolo[4,5-b;4',5'-d]pyran-5-ylmethyl ester



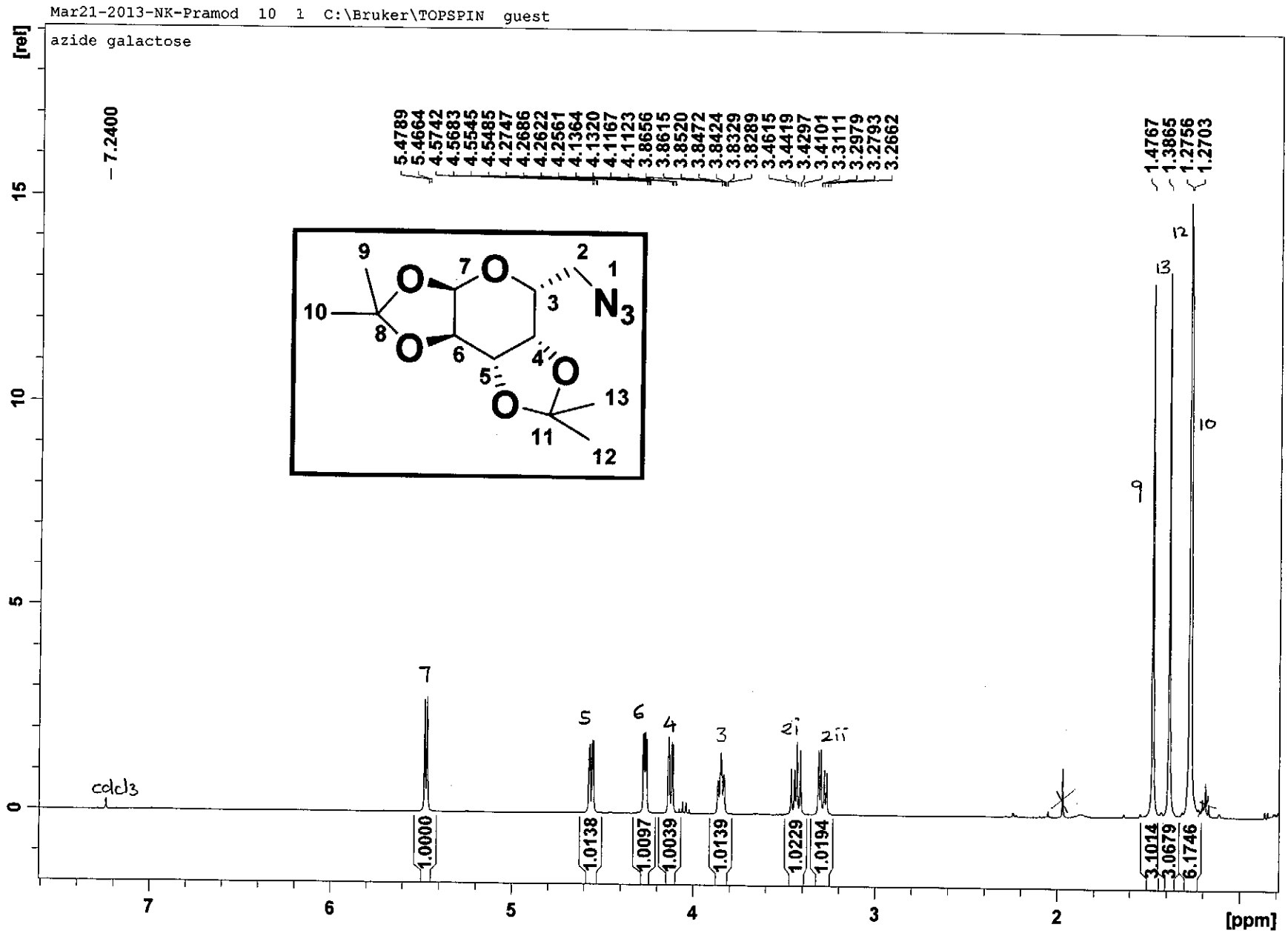
^{13}C Spectrum of Compound 2: Toluene-4-sulfonic acid 2,2,7,7-tetramethyl-tetrahydro-bis[1,3]dioxolo[4,5-b;4',5'-d]pyran-5-ylmethyl ester



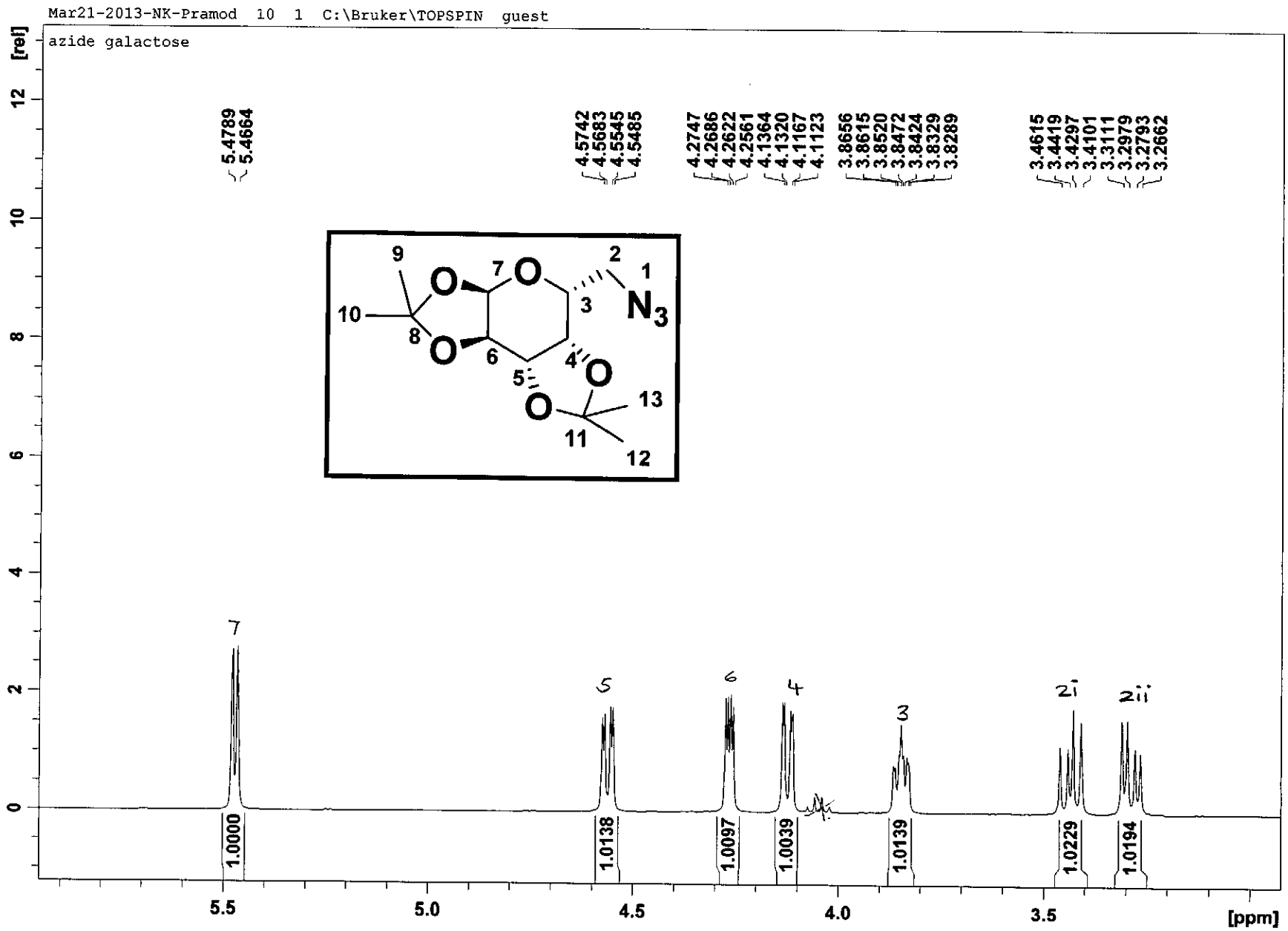
Expanded ^{13}C Spectrum of Compound 2: Toluene-4-sulfonic acid 2,2,7,7-tetramethyl-tetrahydro-bis[1,3]dioxolo[4,5-b;4',5'-d]pyran-5-ylmethyl ester



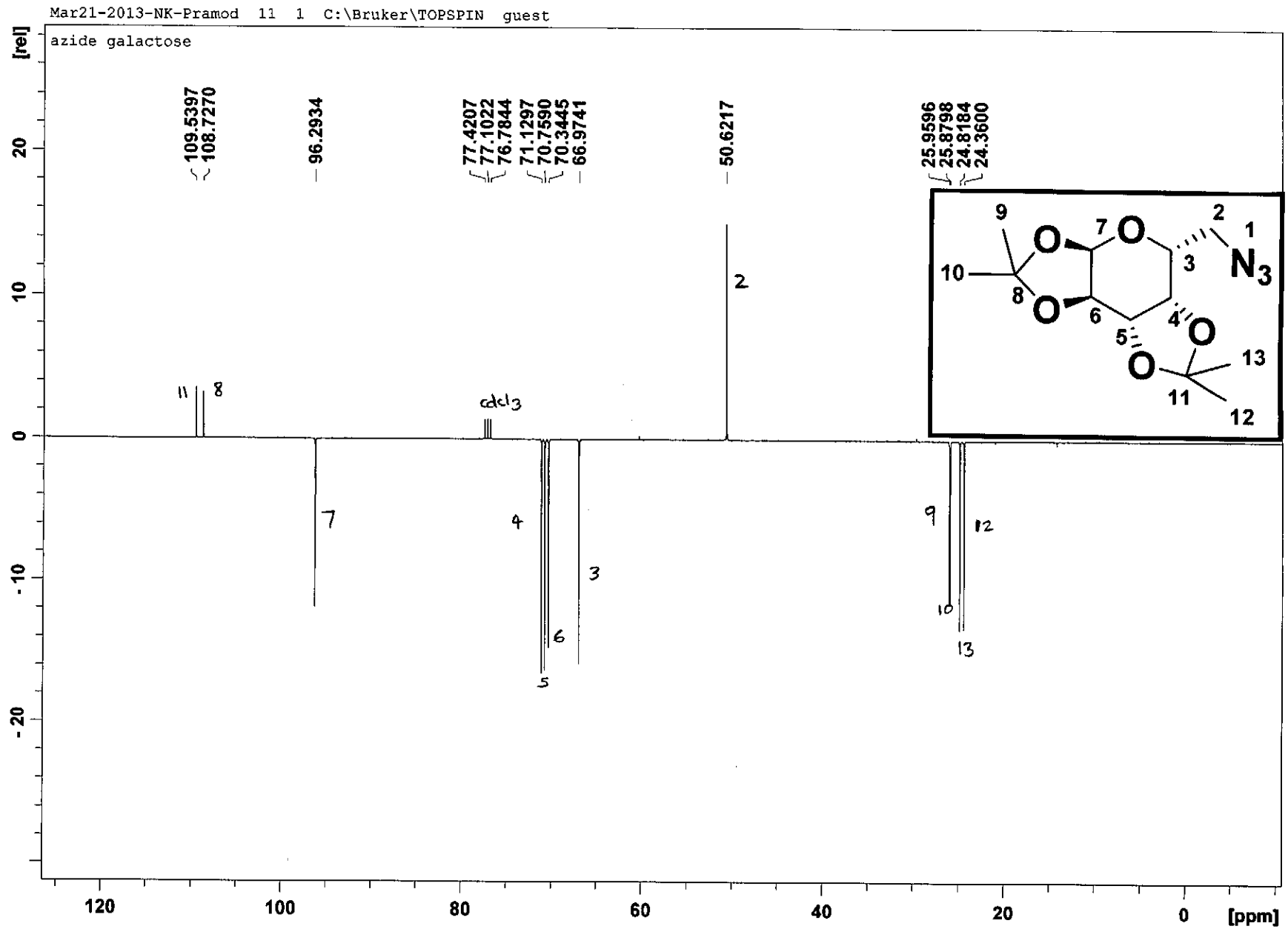
Expanded ^{13}C Spectrum of Compound 2: Toluene-4-sulfonic acid 2,2,7,7-tetramethyl-tetrahydro-bis[1,3]dioxolo[4,5-b;4',5'-d]pyran-5-ylmethyl ester



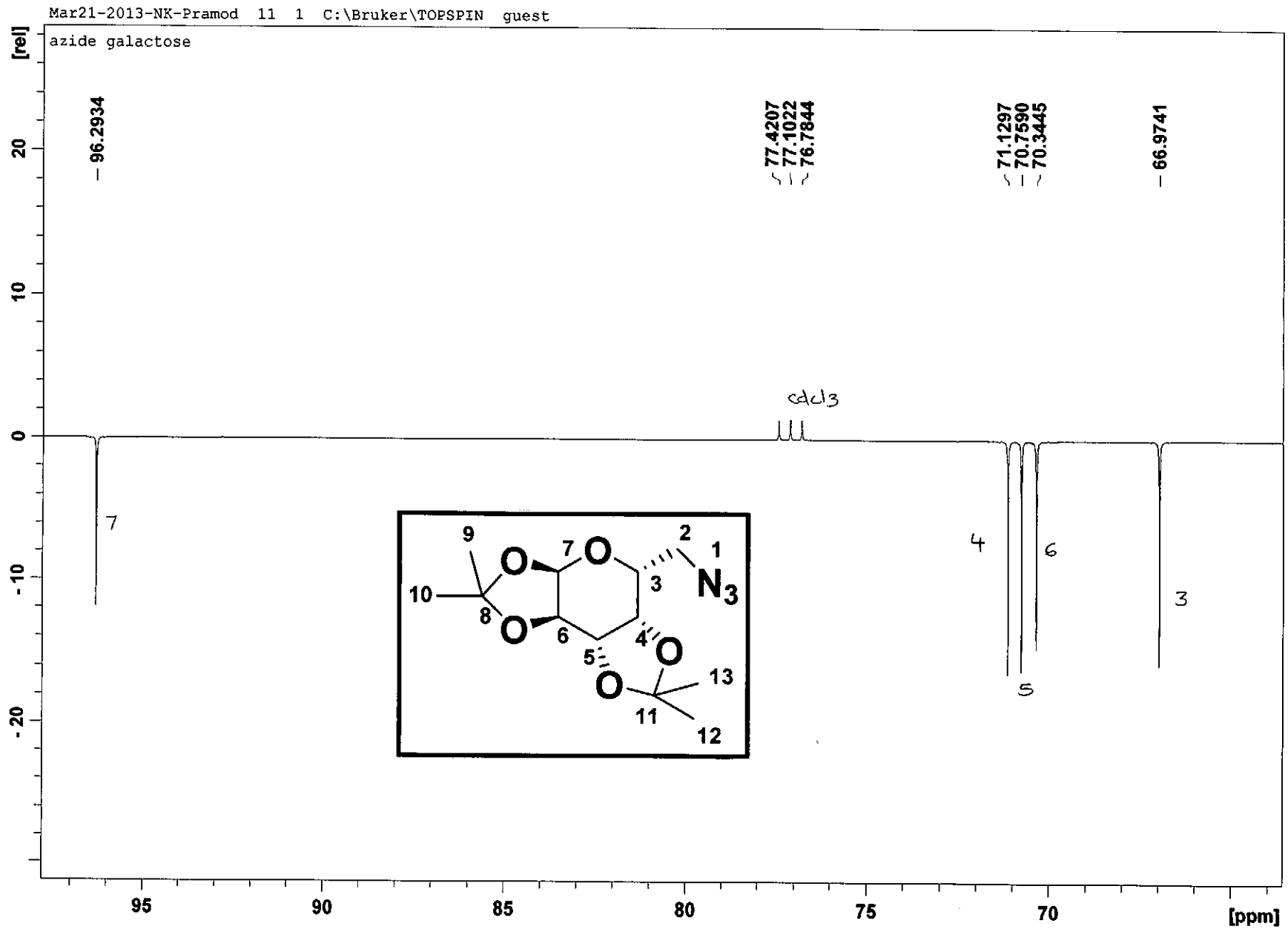
^{1}H Spectrum of Compound 3: 5-Azidomethyl-2,2,7,7-tetramethyl-tetrahydro-bis[1,3] dioxolo[4,5-b;4',5'-d]pyran



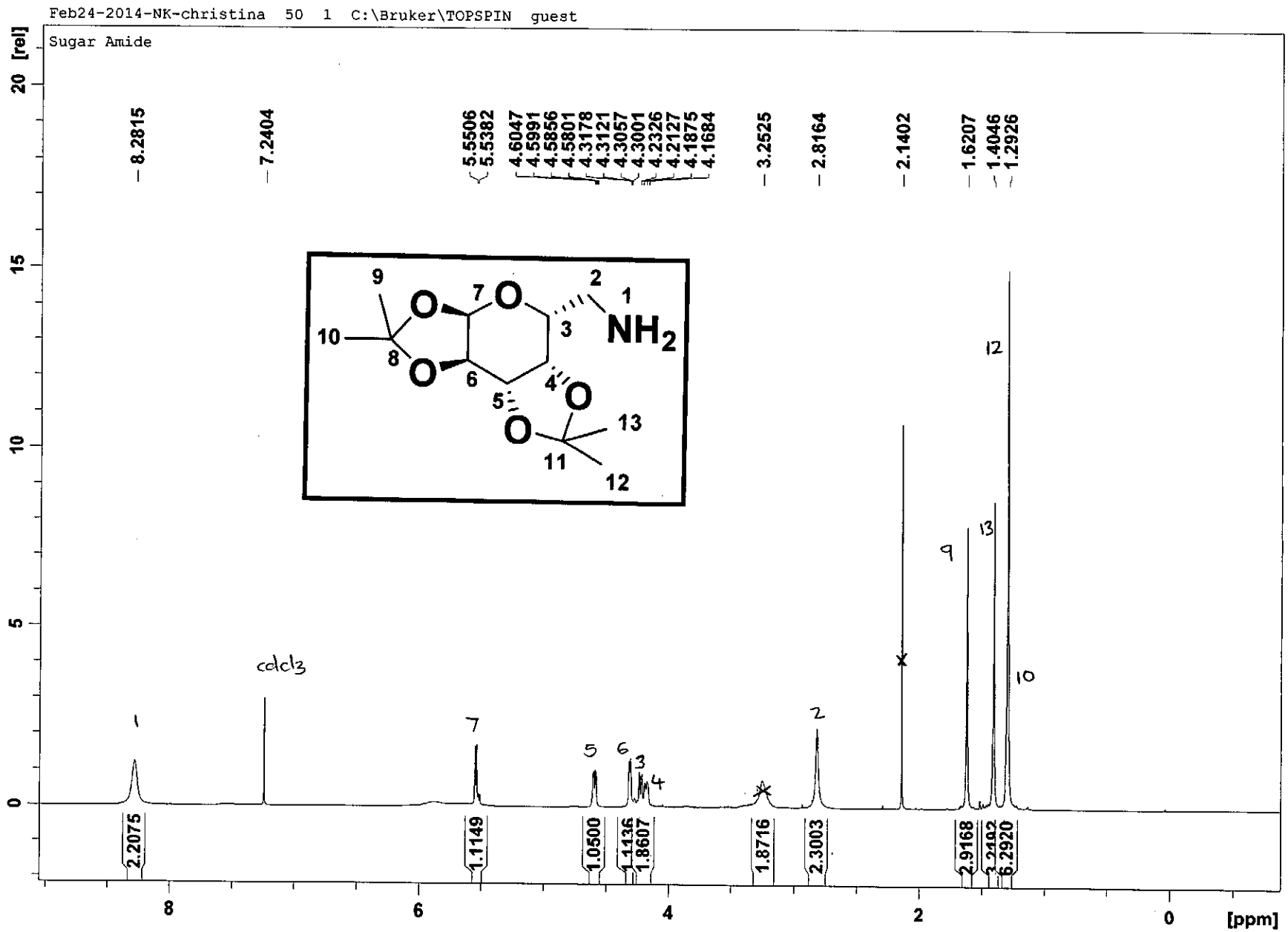
Expanded ^{1}H Spectrum of Compound 3: 5-Azidomethyl-2,2,7,7-tetramethyl-tetrahydro-bis[1,3]dioxolo[4,5-b;4',5'-d]pyran



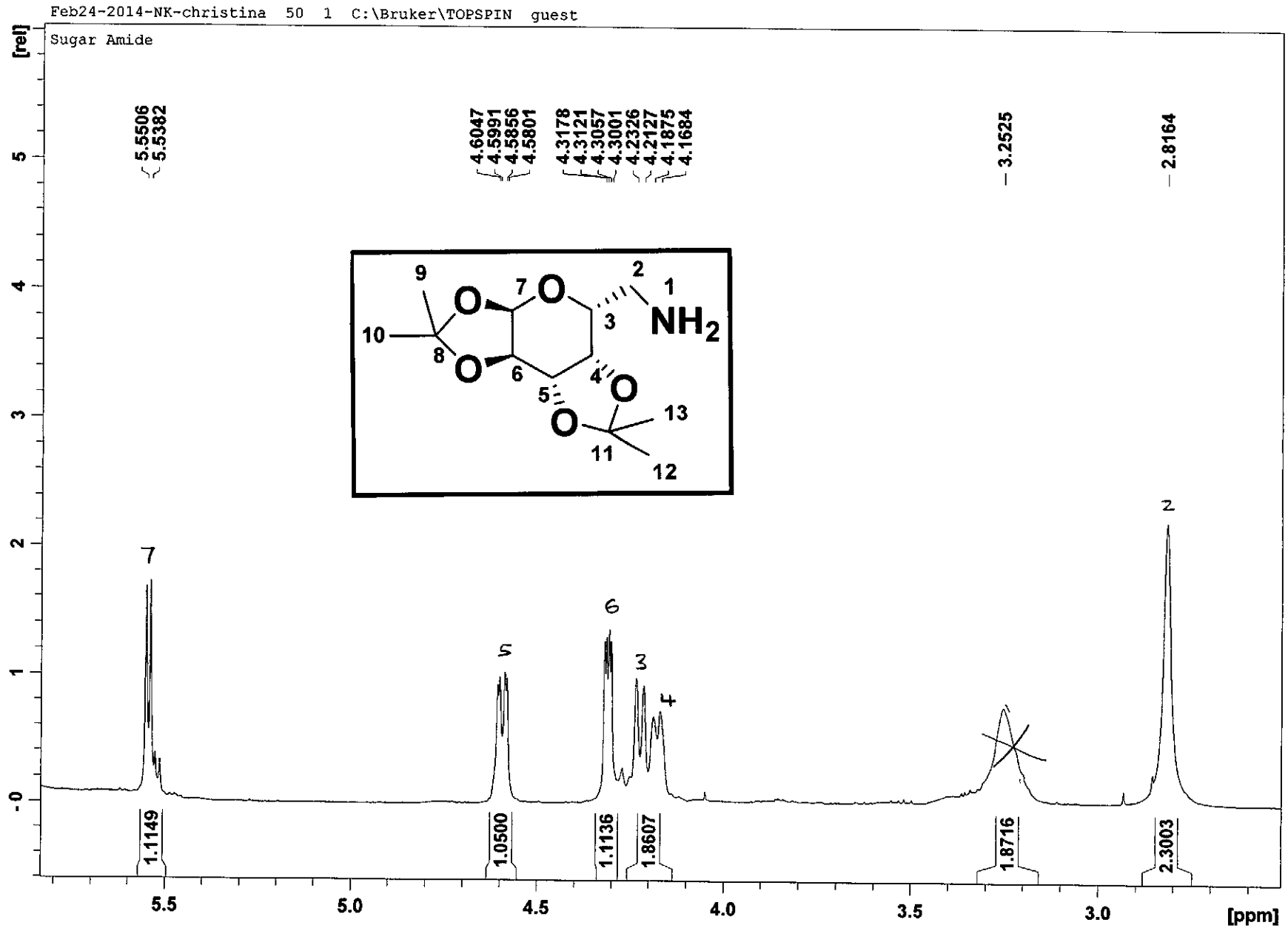
^{13}C Spectrum of Compound 3: 5-Azidomethyl-2,2,7,7-tetramethyl-tetrahydro-bis[1,3] dioxolo[4,5-b;4',5'-d]pyran



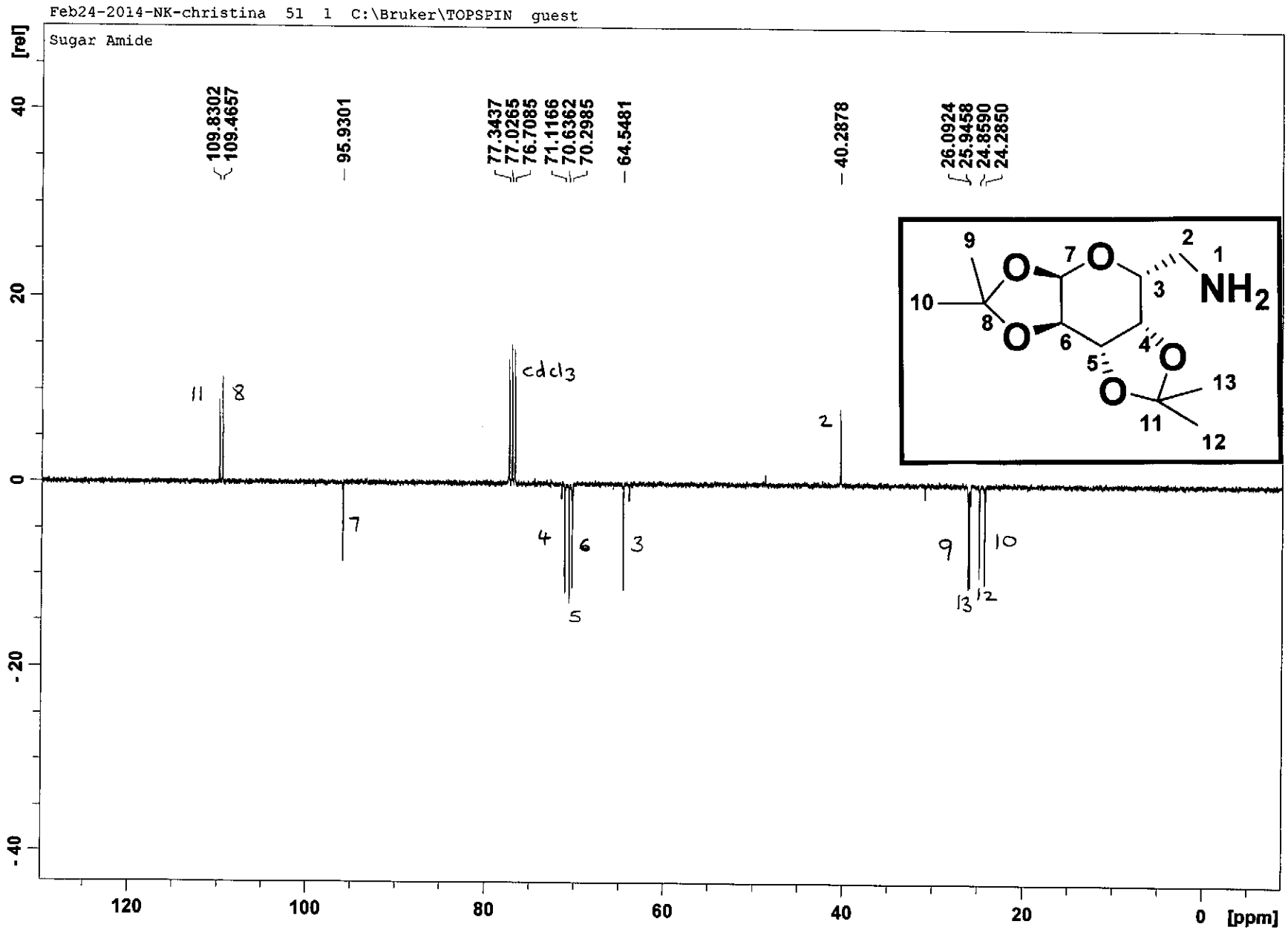
Expanded ^{13}C Spectrum of Compound 3: 5-Azidomethyl-2,2,7,7-tetramethyl-tetrahydro-bis[1,3]dioxolo[4,5-b;4',5'-d]pyran



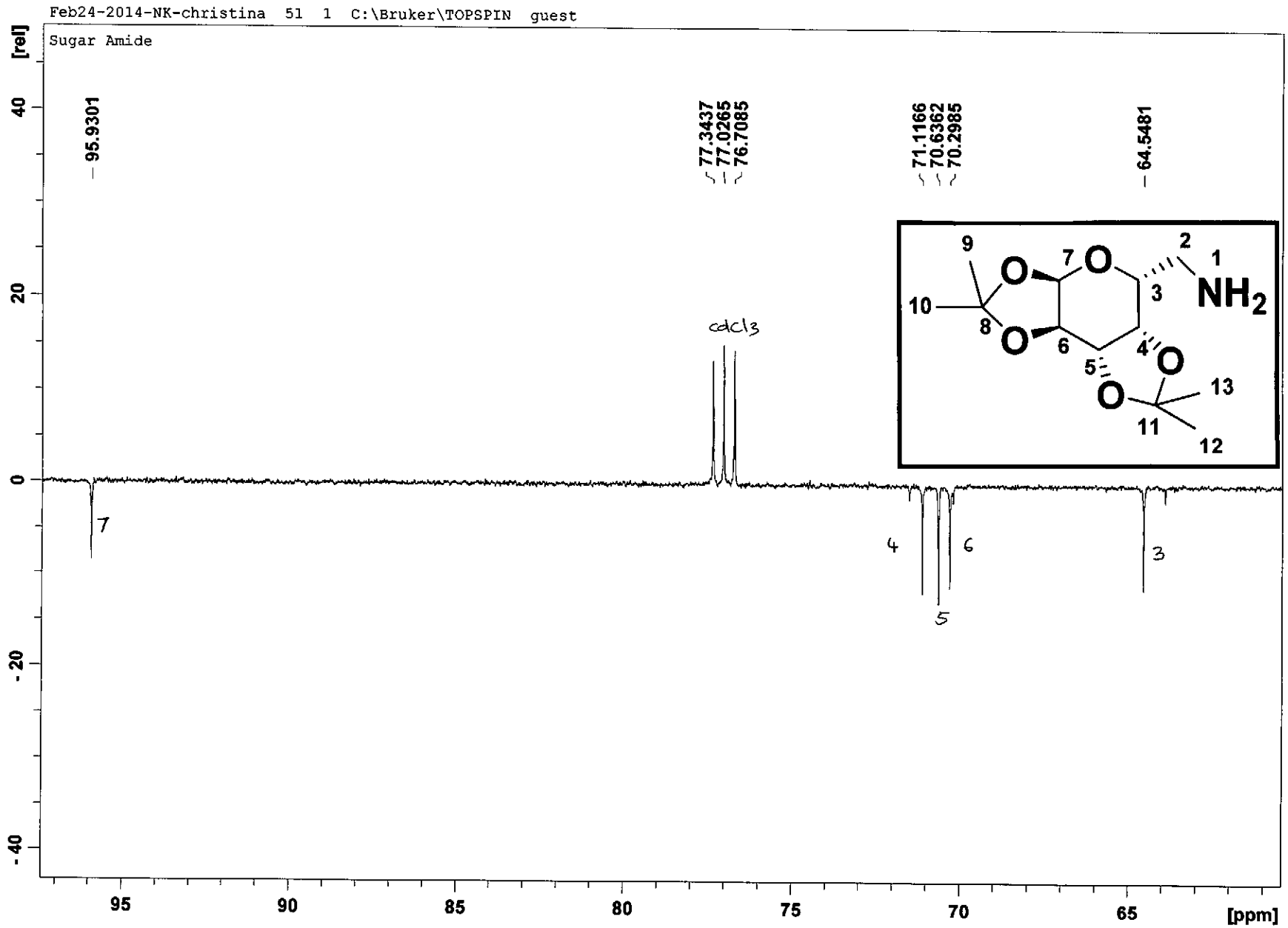
[1]H Spectrum of Compound 4: 2,2,7,7-Tetramethyl-tetrahydro-bis[1,3]dioxolo[4,5-b;4',5'-d]pyran-5-yl)-methylamine



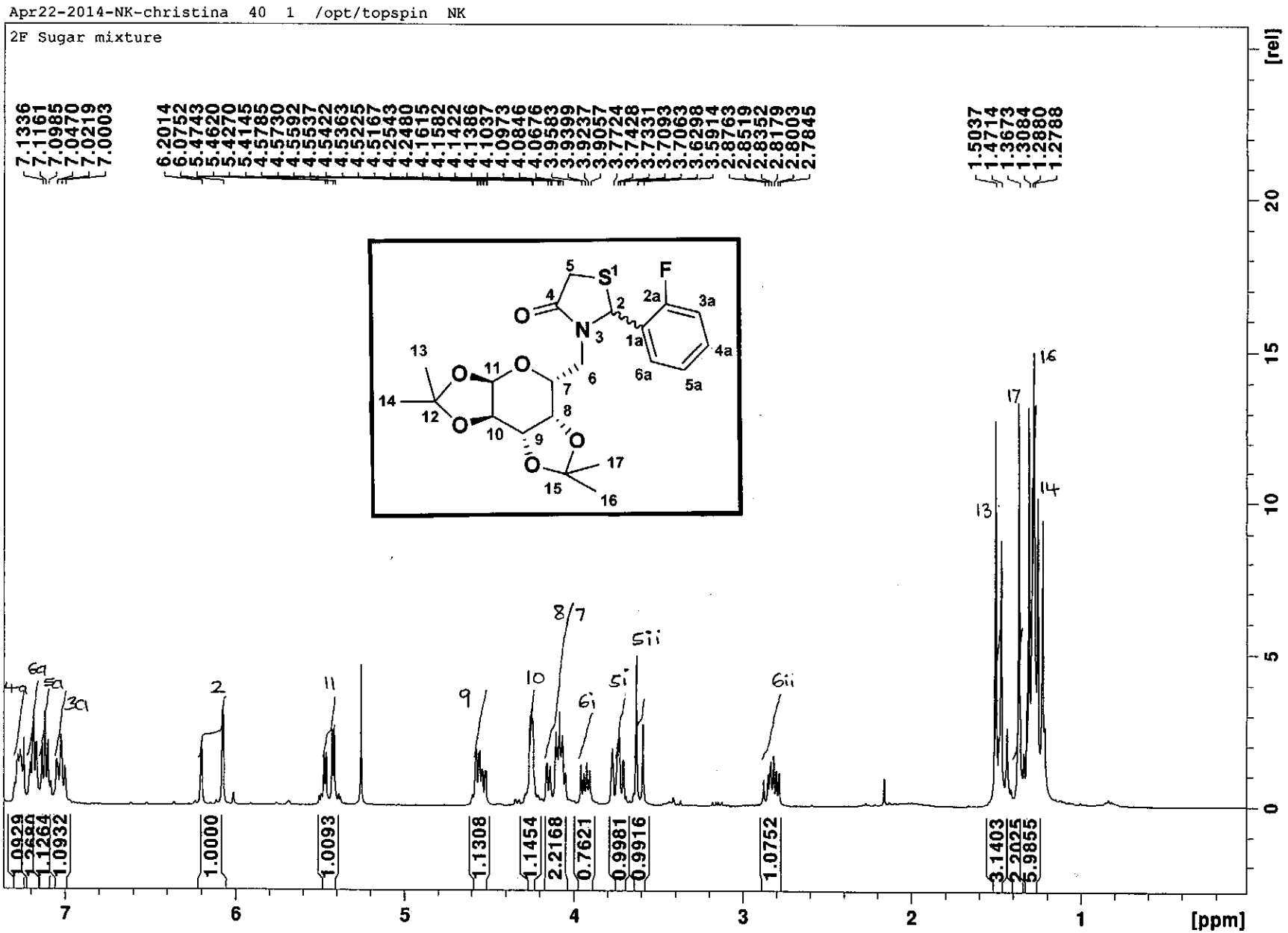
Expanded ^{1}H Spectrum of Compound 4: 2,2,7,7-Tetramethyl-tetrahydro-bis[1,3]dioxolo [4,5-b;4',5'-d]pyran-5-yl)-methylamine



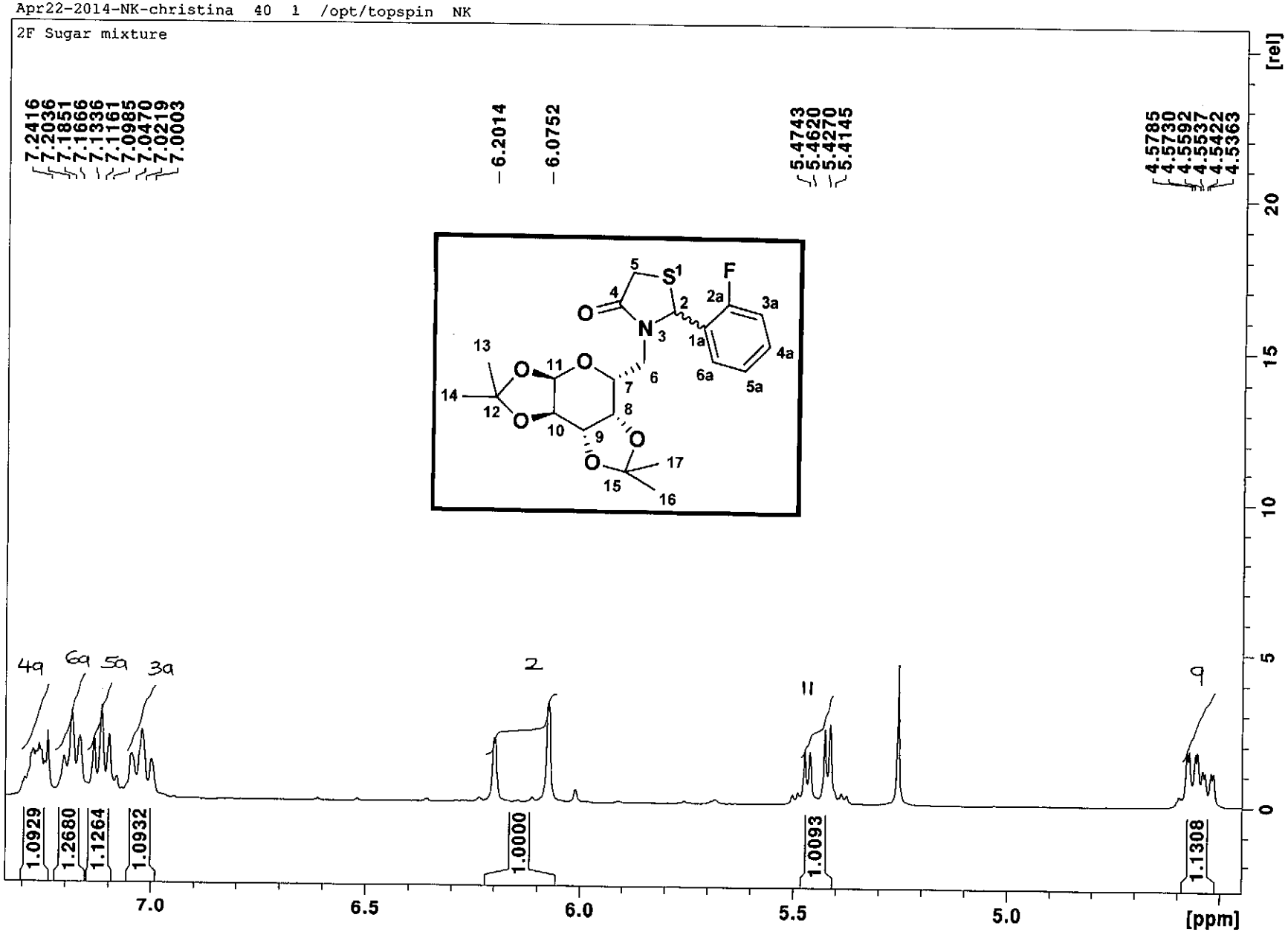
^{13}C Spectrum of Compound 4: 2,2,7,7-Tetramethyl-tetrahydro-bis[1,3]dioxolo[4,5-b;4',5'-d]pyran-5-yl)-methylamine



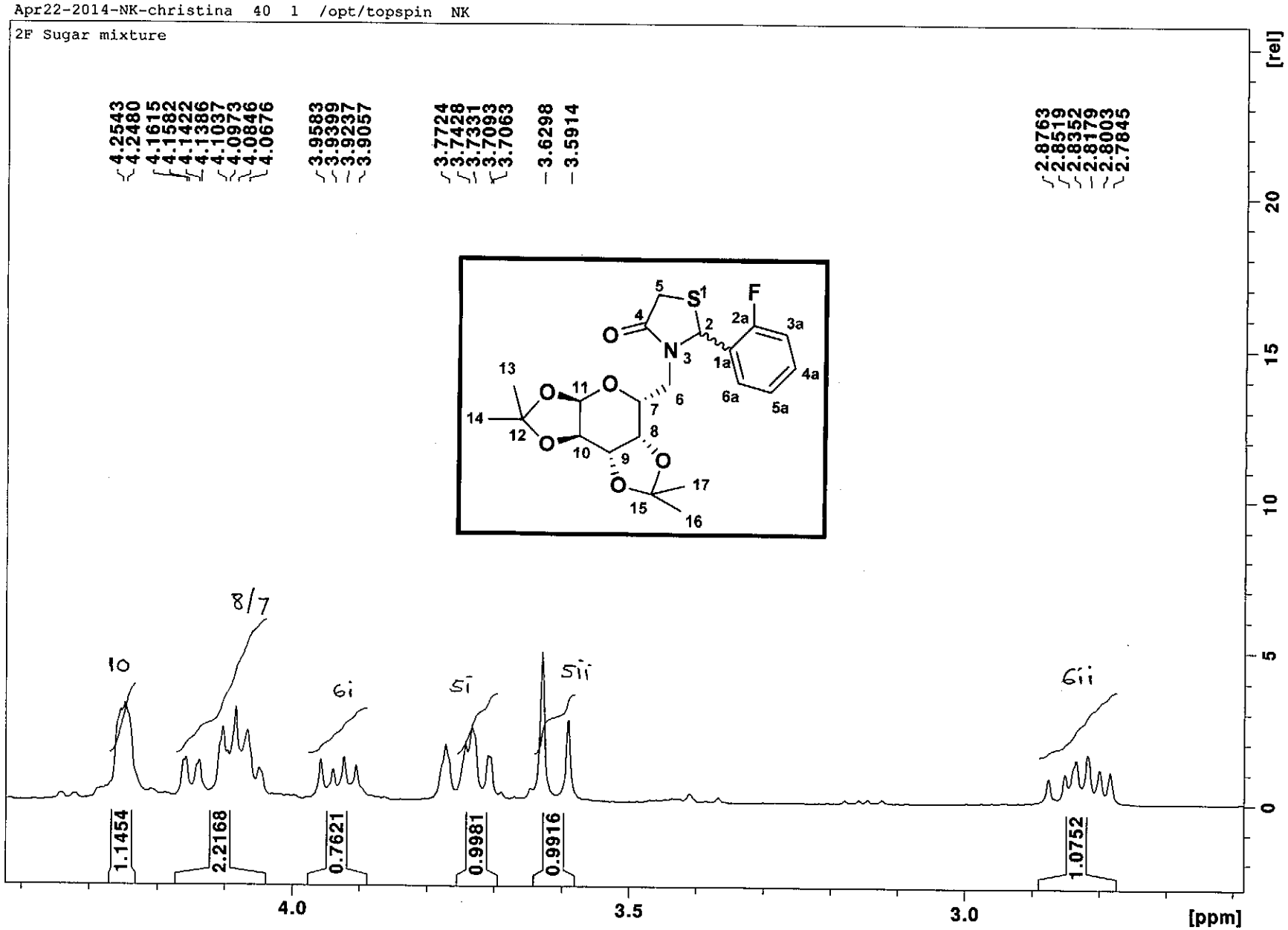
Expanded ^{13}C Spectrum of Compound 4: 2,2,7,7-Tetramethyl-tetrahydro-bis[1,3]dioxolo [4,5-b;4',5'-d]pyran-5-yl)-methylamine



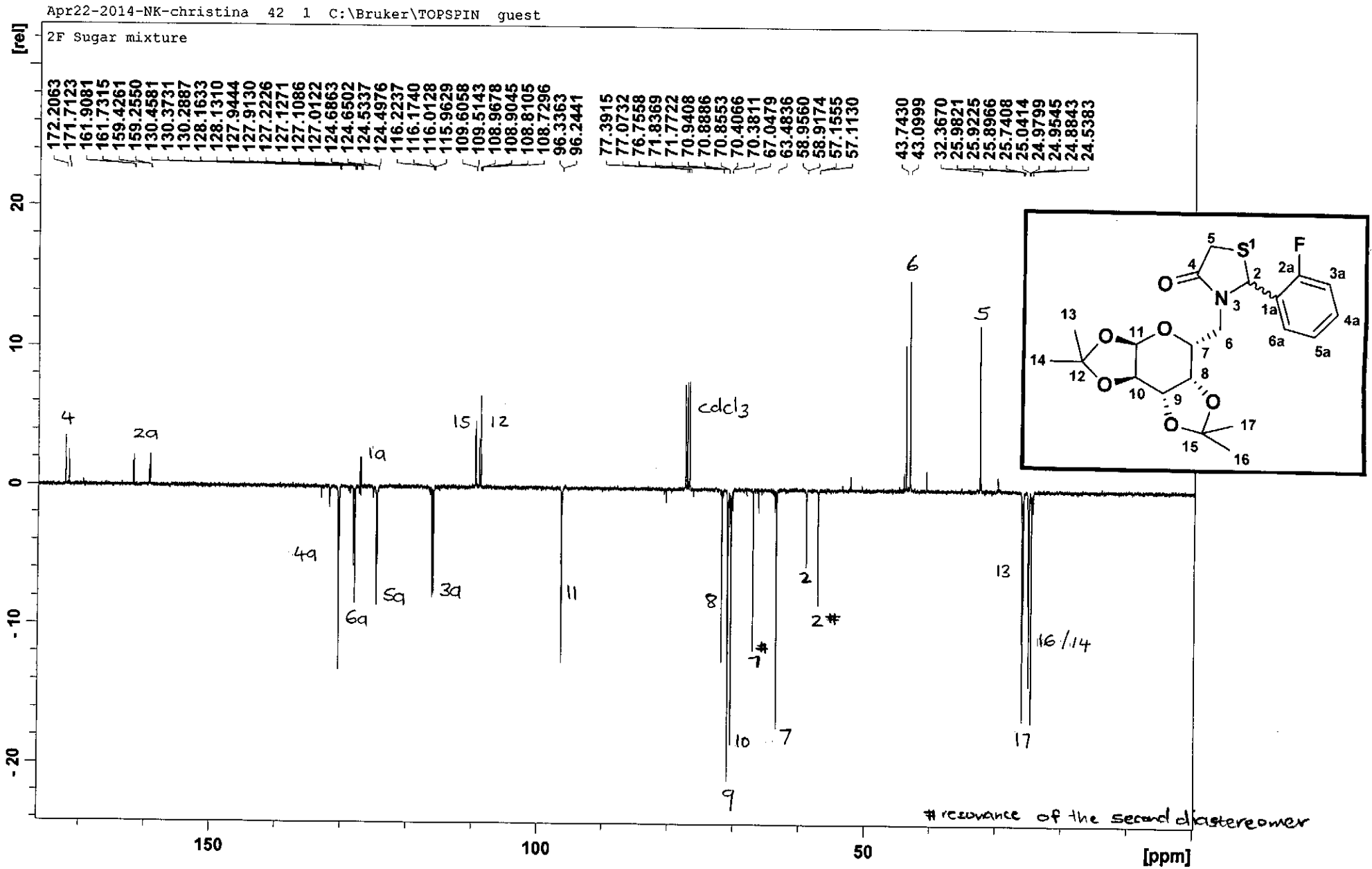
^{1}H Spectrum of Compound 5a and 6a: 2-(2-Fluorophenyl)-3-(2,2,7,7-tetramethyltetra hydro-bis[1,3]dioxolo[4,5-b;4',5'-d]pyran-5-ylmethyl)thiazolidin-4-one



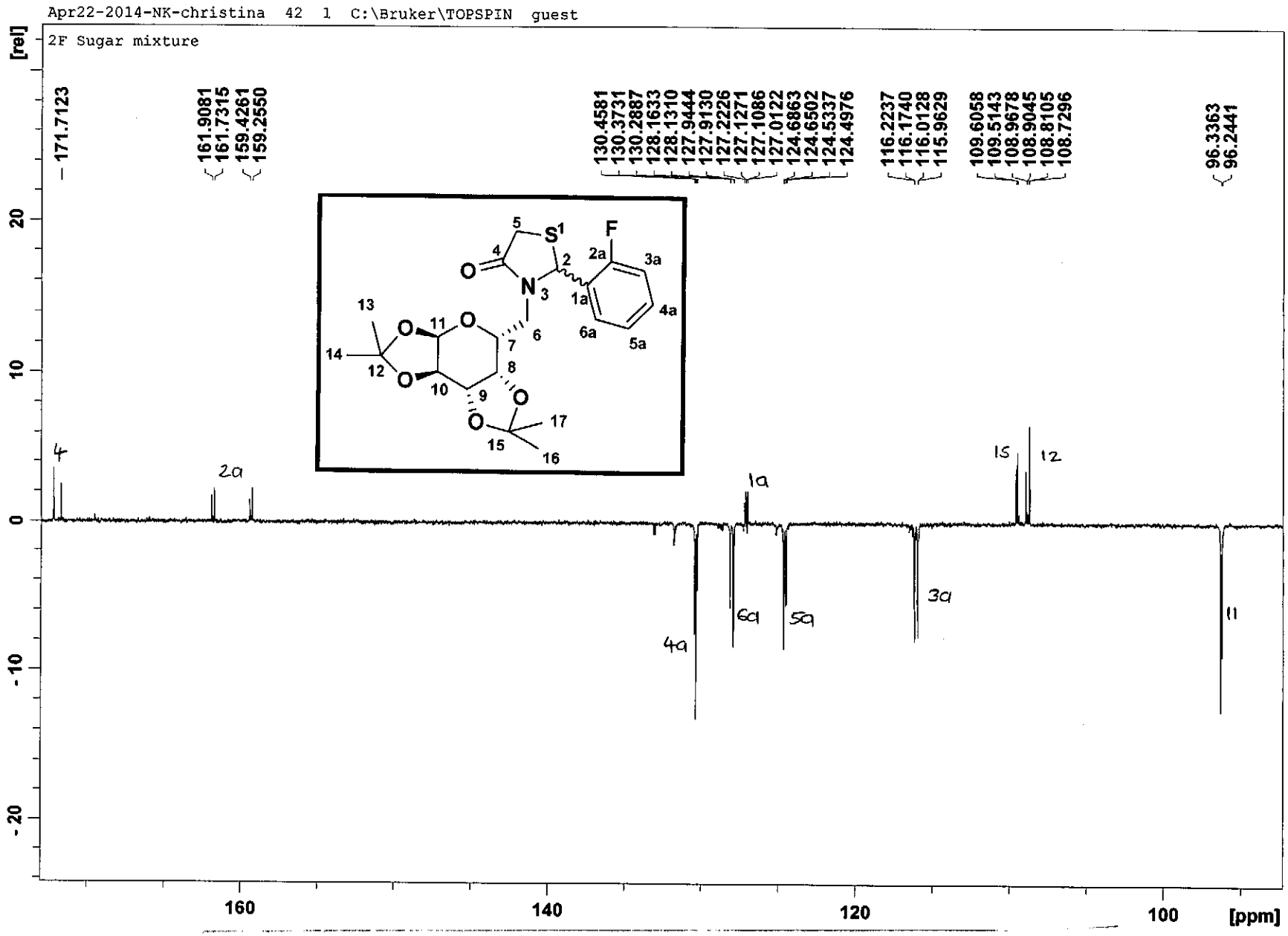
Expanded ^{1}H Spectrum of Compound 5a and 6a: 2-(2-Fluorophenyl)-3-(2,2,7,7-tetramethyltetra hydro-bis[1,3]dioxolo[4,5-b;4',5'-d]pyran-5-ylmethyl)thiazolidin-4-one



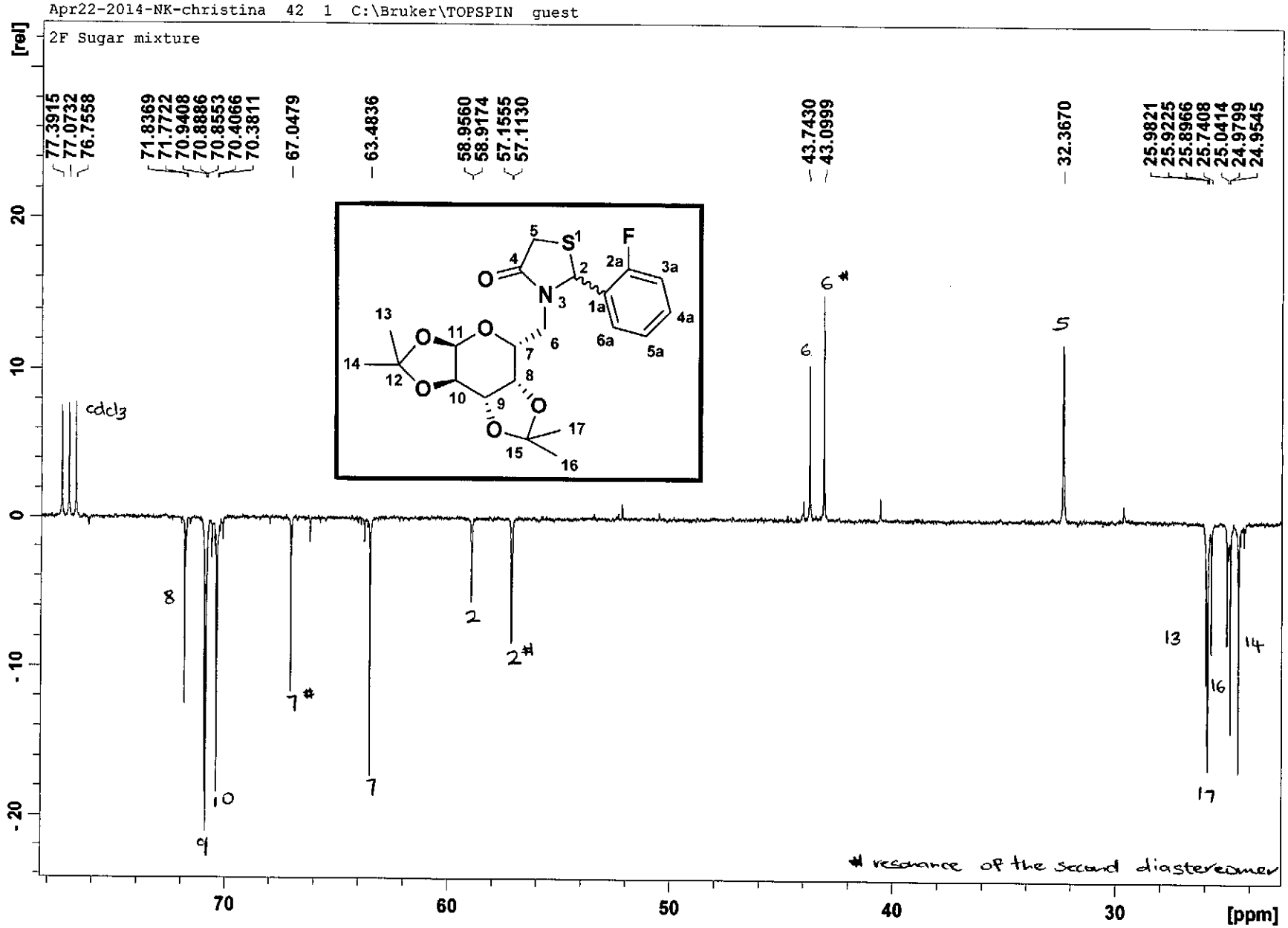
Expanded ^{1}H Spectrum of Compound 5a and 6a: 2-(2-Fluorophenyl)-3-(2,2,7,7-tetramethyltetra hydro-bis[1,3]dioxolo[4,5-b;4',5'-d]pyran-5-ylmethyl)thiazolidin-4-one



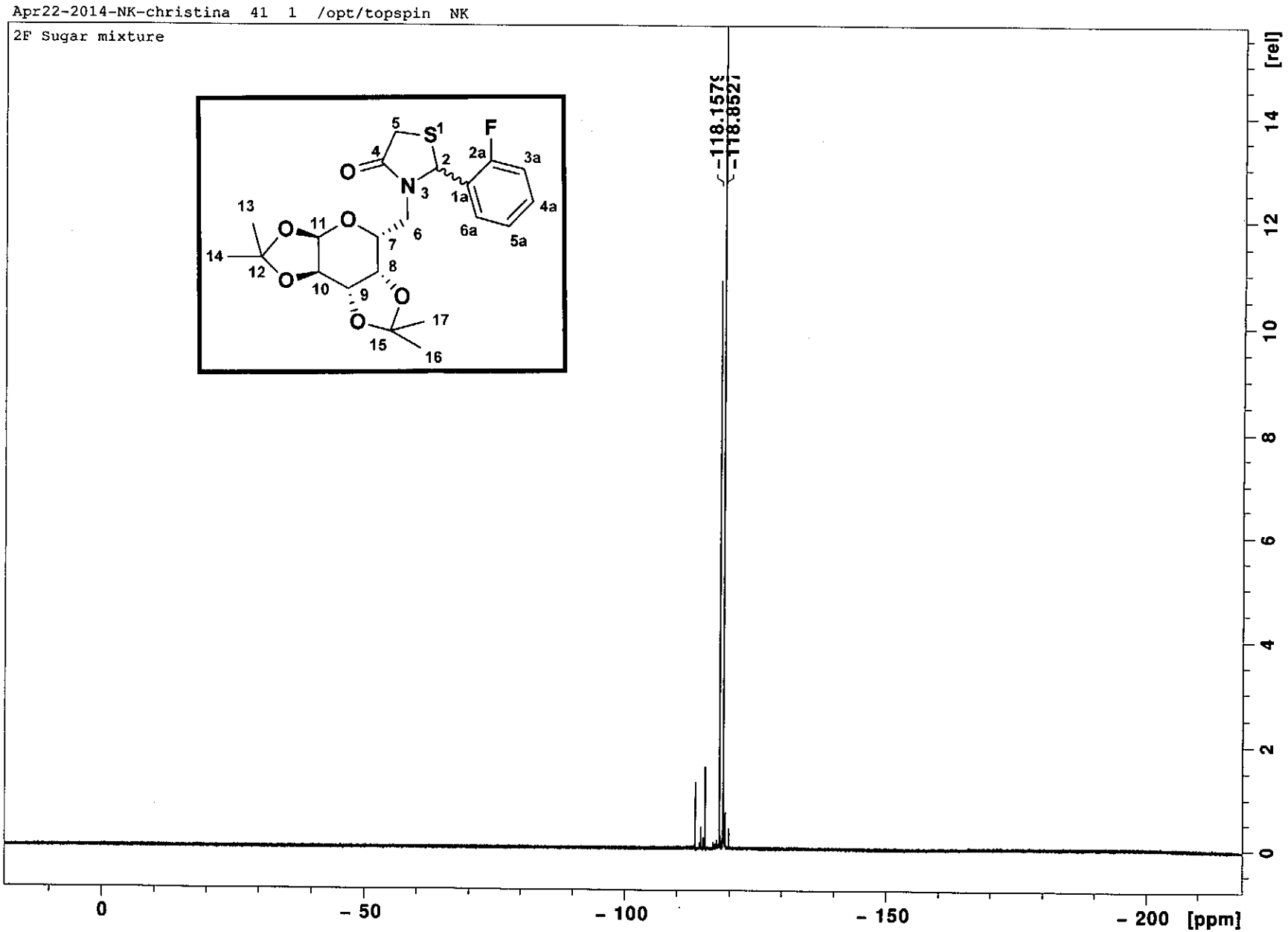
^{13}C Spectrum of Compound 5a and 6a: 2-(2-Fluorophenyl)-3-(2,2,7,7-tetra methyltetra hydro-bis[1,3]dioxolo[4,5-b;4',5'-d]pyran-5-ylmethyl)thiazolidin-4-one



Expanded ^{13}C Spectrum of Compound 5a and 6a: 2-(2-Fluorophenyl)-3-(2,2,7,7-tetra methyltetra hydro-bis[1,3]dioxolo[4,5-b;4',5'-d]pyran-5-ylmethyl)thiazolidin-4-one

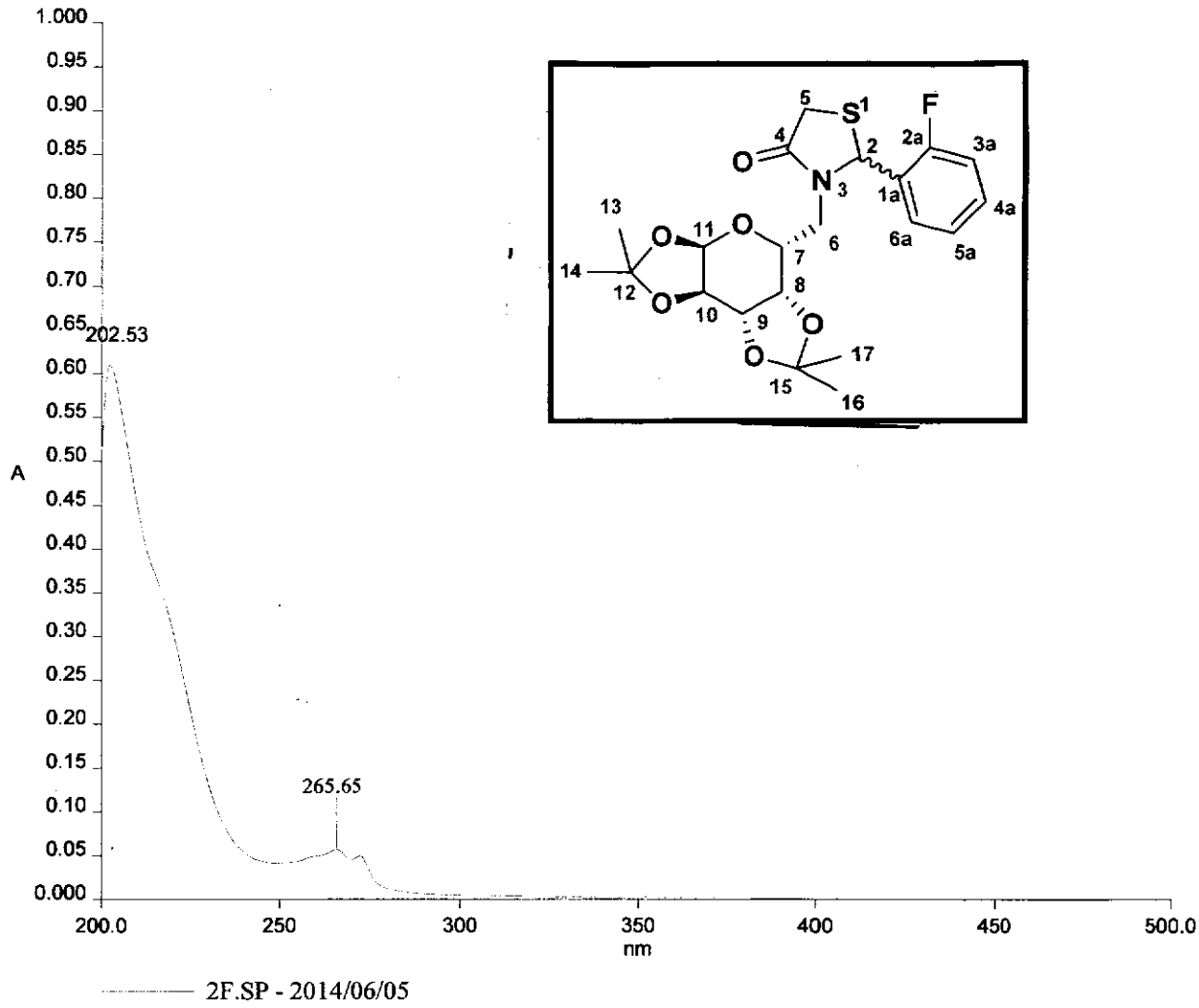


Expanded ^{13}C Spectrum of Compound 5a and 6a: 2-(2-Fluorophenyl)-3-(2,2,7,7-tetra methyltetra hydro-bis[1,3]dioxolo[4,5-b;4',5'-d]pyran-5-ylmethyl)thiazolidin-4-one

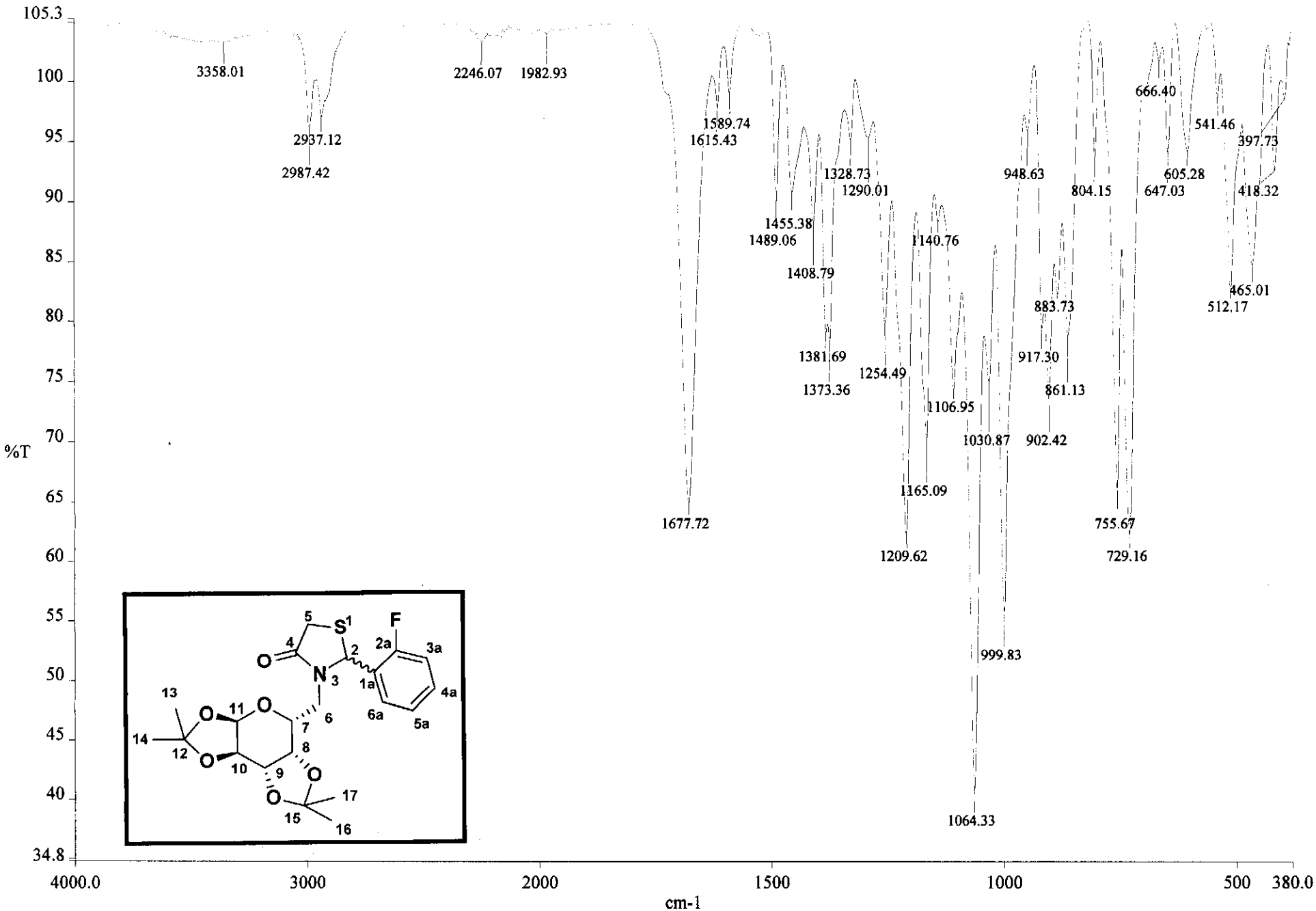


^{19}F Spectrum of Compound 5a and 6a: 2-(2-Fluorophenyl)-3-(2,2,7,7-tetramethyltetra hydro-bis[1,3]dioxolo[4,5-b;4',5'-d]pyran-5-ylmethyl)thiazolidin-4-one

Date: 2014/06/05 Time: 04:24:24 PM



Ultraviolet Spectrum of Compound 5a and 6a: 2-(2-Fluorophenyl)-3-(2,2,7,7-tetra methyltetra hydro-bis[1,3]dioxolo[4,5-b;4',5'-d]pyran-5-ylmethyl)thiazolidin-4-one

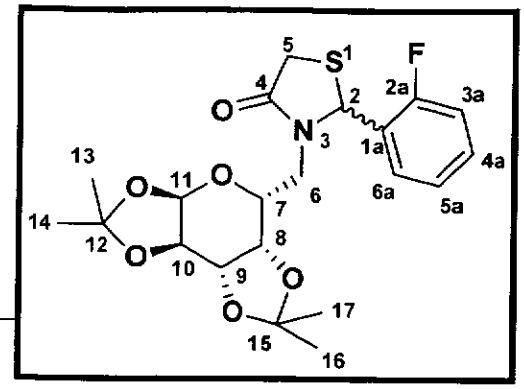


c:\pel_data\spectra\christina\2f mix.001

Infrared Spectrum of Compound 5a and 6a: 2-(2-Fluorophenyl)-3-(2,2,7,7-tetramethyl tetra hydro-bis[1,3]dioxolo[4,5-b;4',5'-d]pyran-5-ylmethyl)thiazolidin-4-one

==== Shimadzu LCsolution Analysis Report ====

Acquired by	: Admin
Sample Name	: 2f with formic buffer
Sample ID	: 2f with formic buffe
Vail #	: 2
Injection Volume	: 100 uL
Data File Name	: 2f with formic buffe.lcd
Method File Name	: Pramod 09jun 2014.lcm
Batch File Name	: 20_03_2014.lcb
Report File Name	: Default.lcr
Data Acquired	: 2014/06/23 10:36:25 AM
Data Processed	: 2014/06/23 11:16:27 AM



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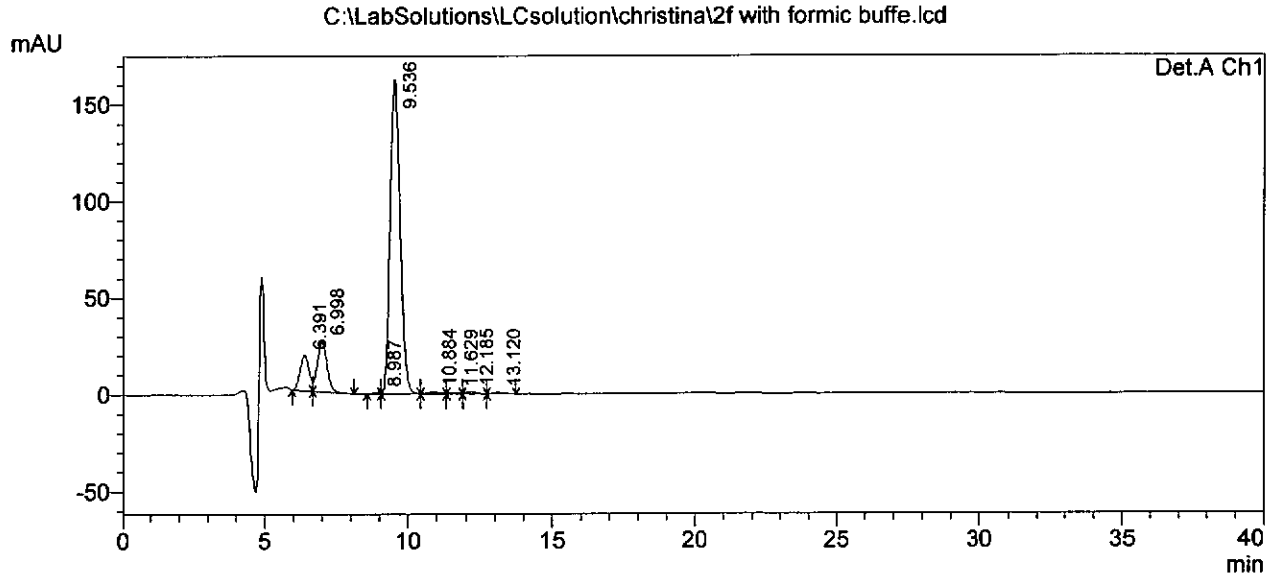


1Det.A Ch1/220nm

<Results>

PeakTable C:\LabSolutions\LCsolution\christina\2f with formic buffe.lcd

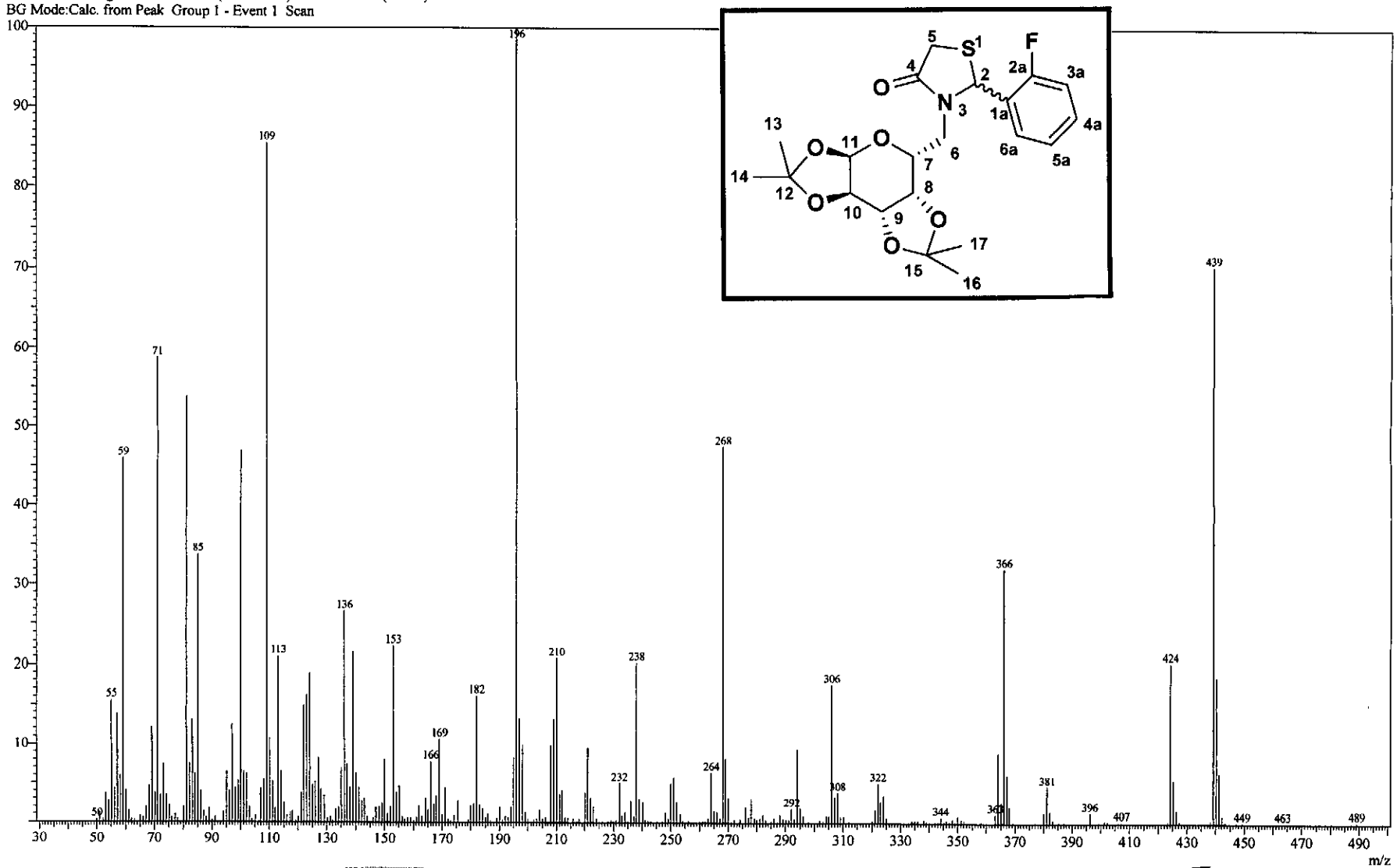
Detector A Ch1 220nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	6.391	394897	18396	7.815	8.678
2	6.998	618523	26450	12.241	12.478
3	8.987	12643	787	0.250	0.371
4	9.536	3931310	162710	77.801	76.760
5	10.884	28134	900	0.557	0.425
6	11.629	15860	710	0.314	0.335
7	12.185	30324	1170	0.600	0.552
8	13.120	21343	850	0.422	0.401
Total		5053034	211972	100.000	100.000

HPLC of Compound 5a and 6a: 2-(2-Fluorophenyl)-3-(2,2,7,7-tetramethyltetra hydro-bis[1,3]dioxolo[4,5-b;4',5'-d]pyran-5-ylmethyl)thiazolidin-4-one

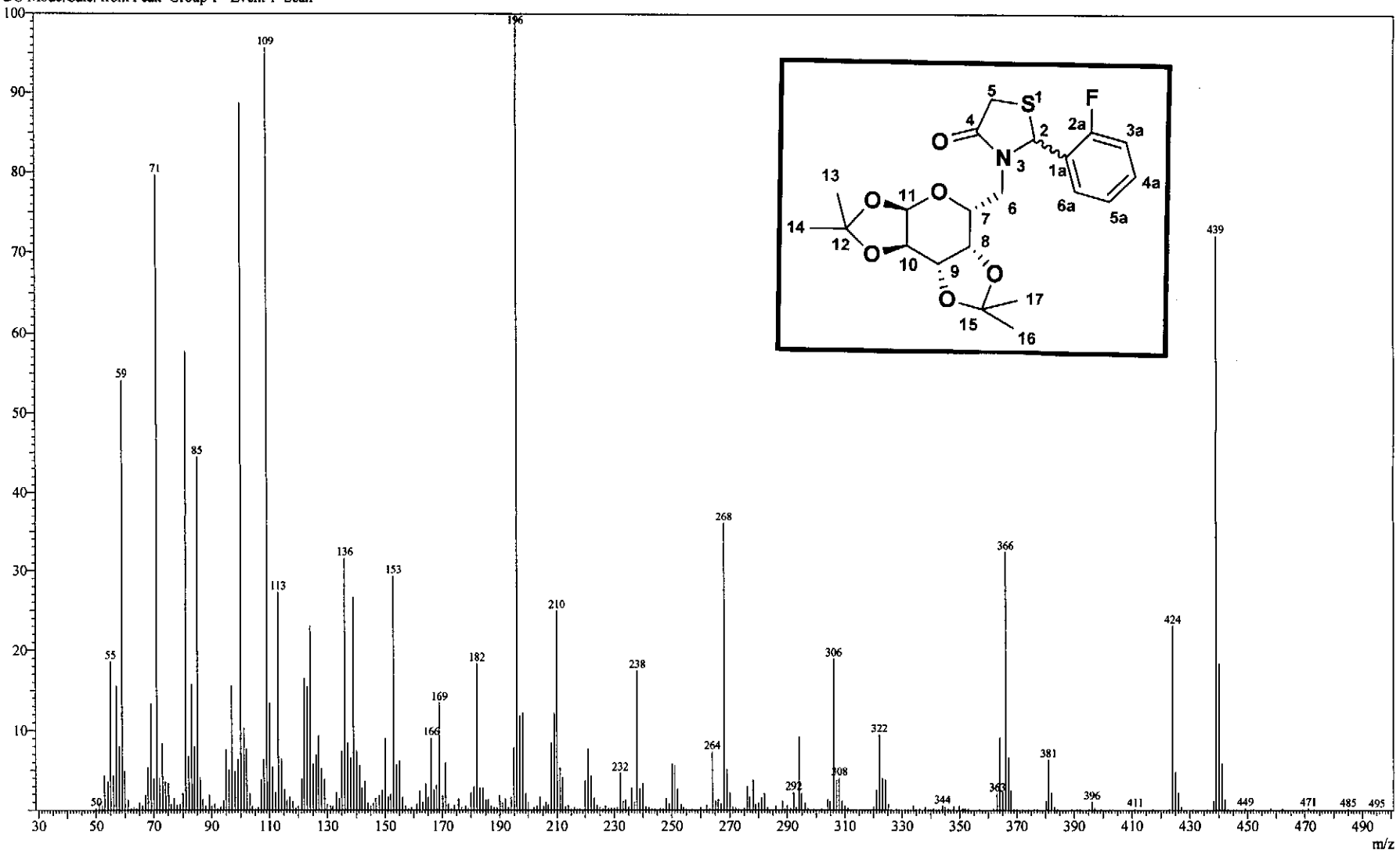
Spectrum

Line#:1 R.Time:15.835(Scan#:2368)
MassPeaks:503
RawMode:Averaged 15.830-15.840(2367-2369) BasePeak:196(41136)
BG Mode:Calc. from Peak Group 1 - Event 1 Scan

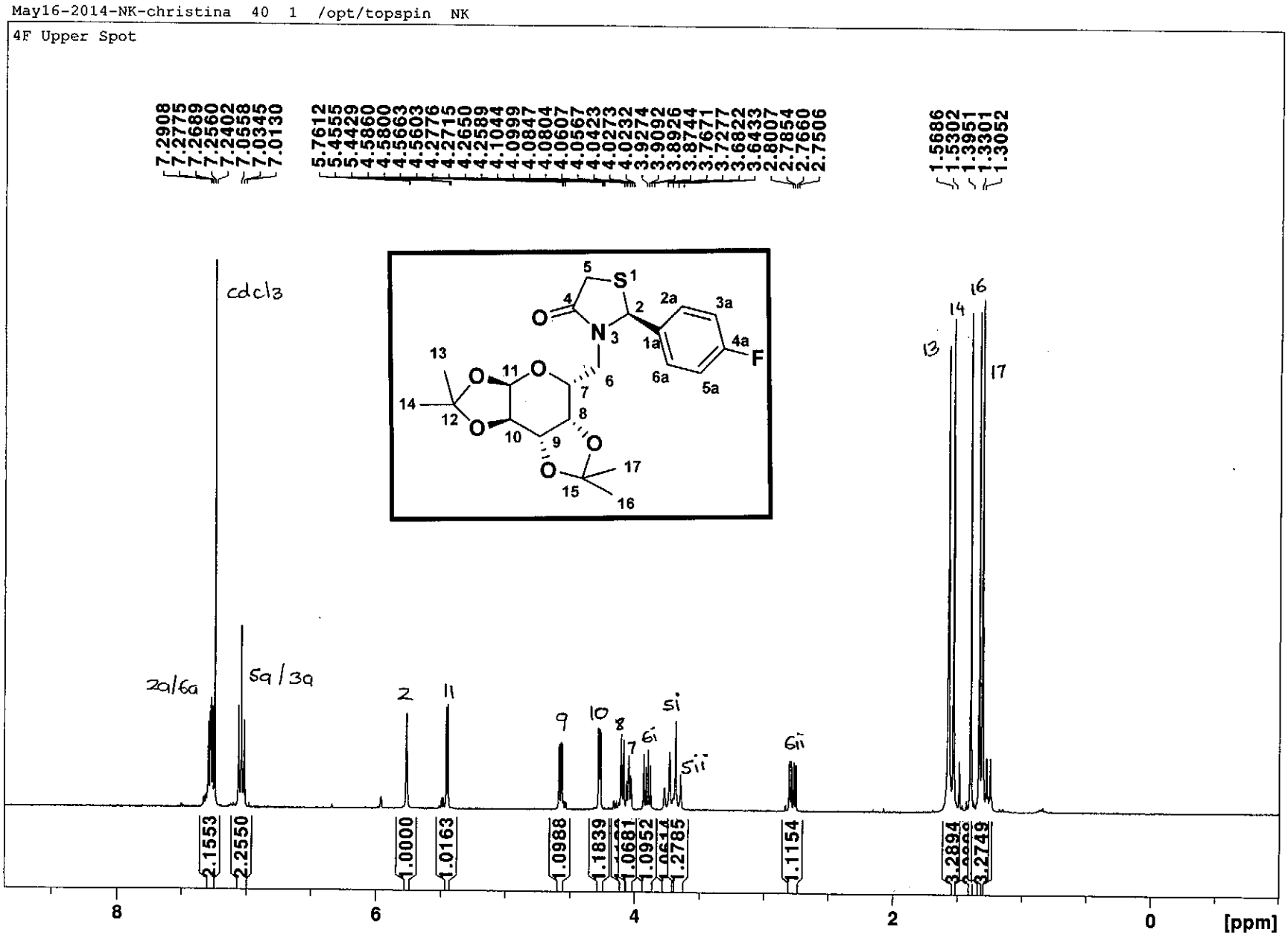


GC-MS of Compound 5a and 6a: 2-(2-Fluorophenyl)-3-(2,2,7,7-tetramethyltetra hydro-bis[1,3]dioxolo[4,5-b;4',5'-d]pyran-5-ylmethyl)thiazolidin-4-one

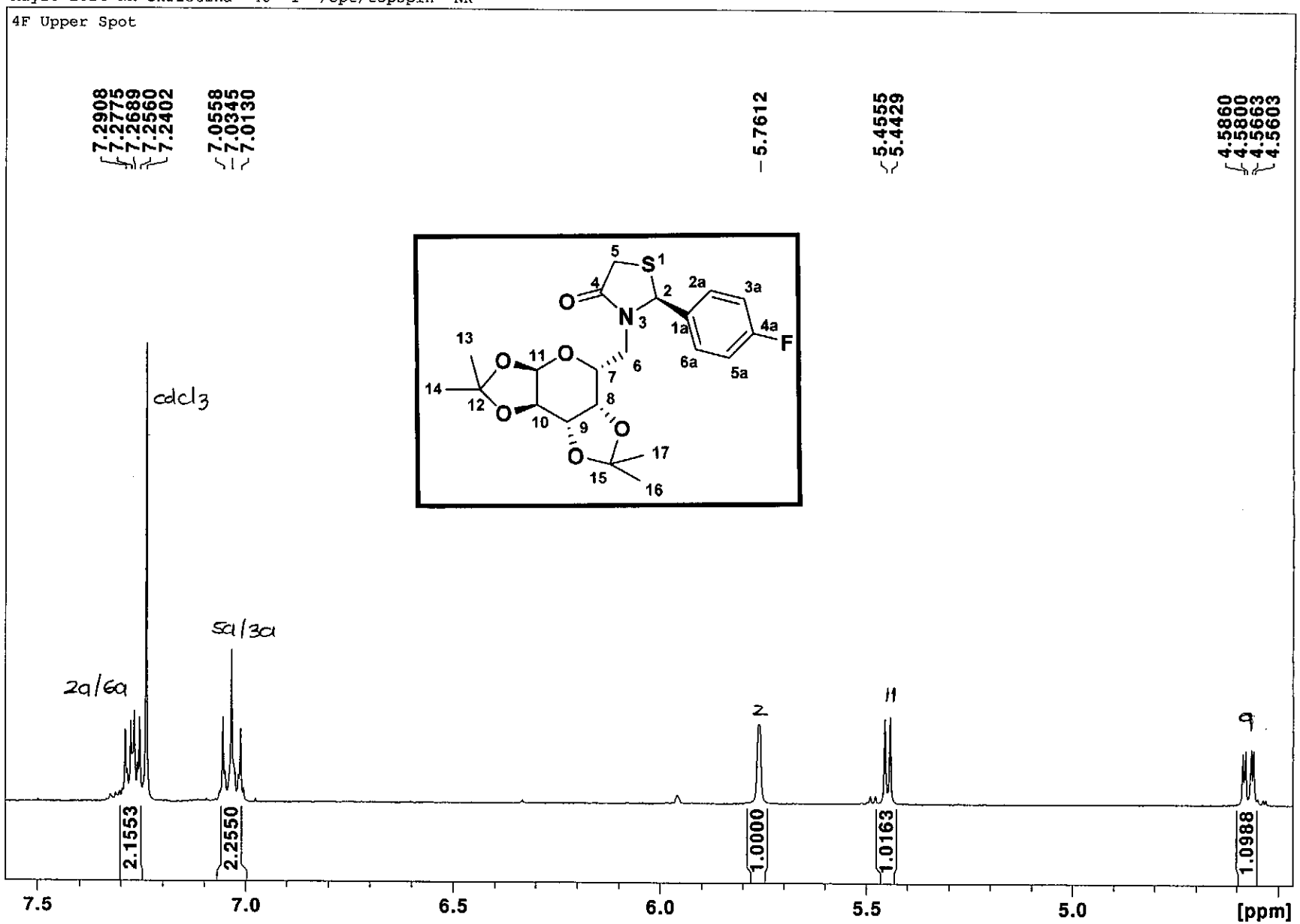
Line#:2 R.Time:16.210(Scan#:2443)
MassPeaks:532
RawMode:Averaged 16.205-16.215(2442-2444) BasePeak:196(48269)
BG Mode:Calc. from Peak Group 1 - Event 1 Scan



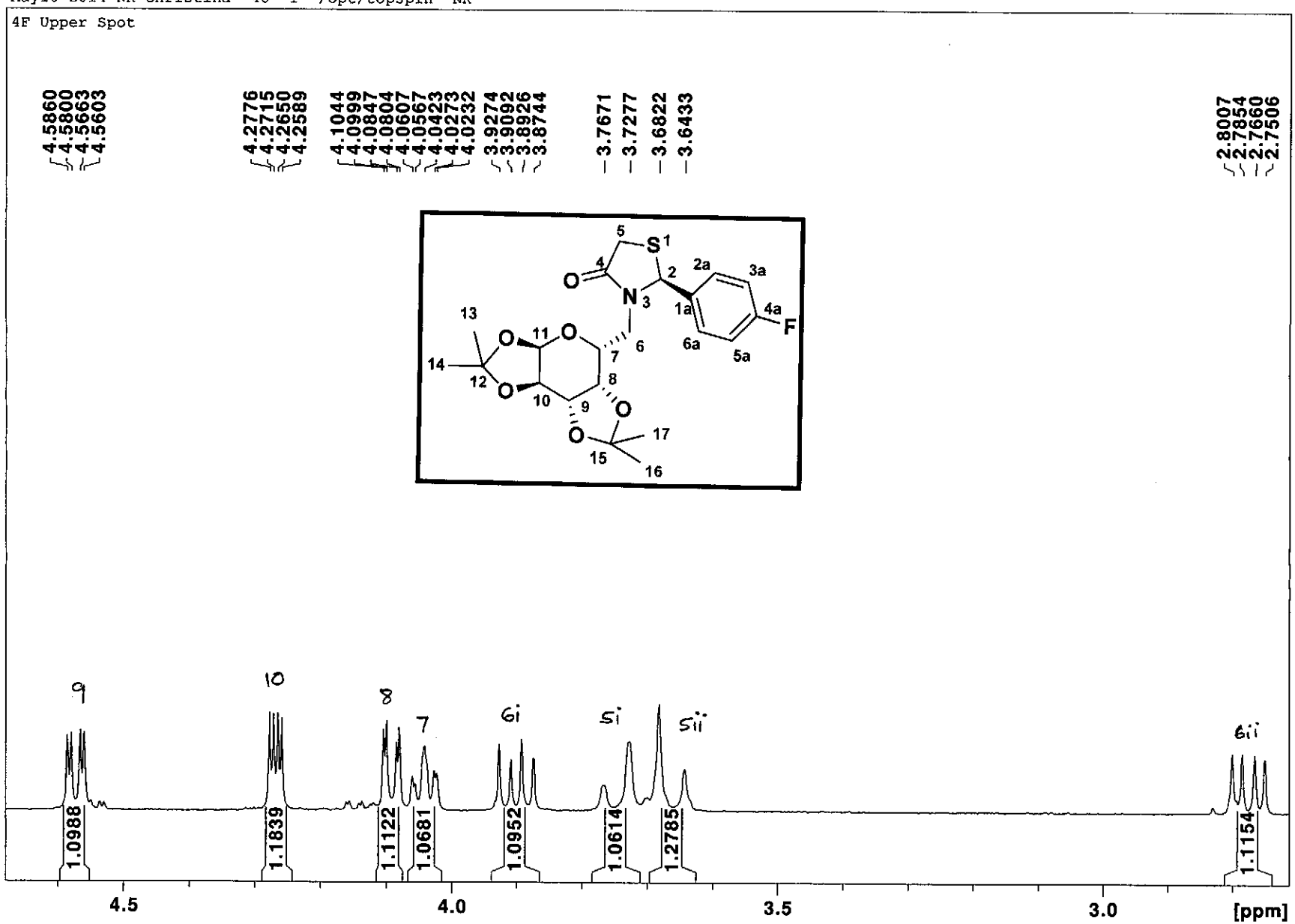
GC-MS of Compound 5a and 6a: 2-(2-Fluorophenyl)-3-(2,2,7,7-tetramethyltetra hydro-bis[1,3]dioxolo[4,5-b;4',5'-d]pyran-5-ylmethyl)thiazolidin-4-one



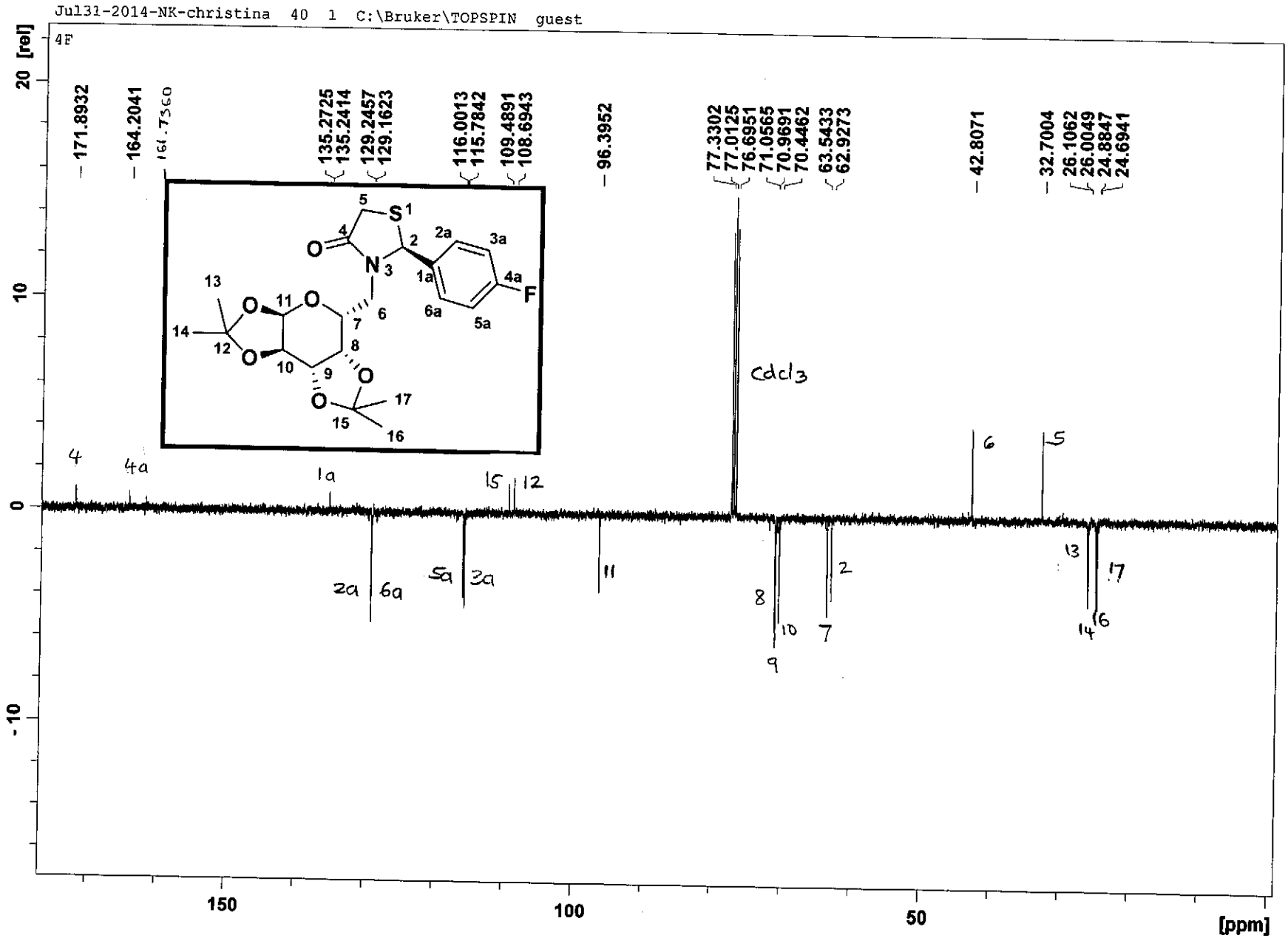
[1]H Spectrum of Compound 5b: 2-(4-Fluoro-phenyl)-3-(2,2,7,7-tetramethyl-tetrahydro-bis [1,3]dioxolo[4,5-b;4',5'-d]pyran-5-ylmethyl)-thiazolidin-4-one



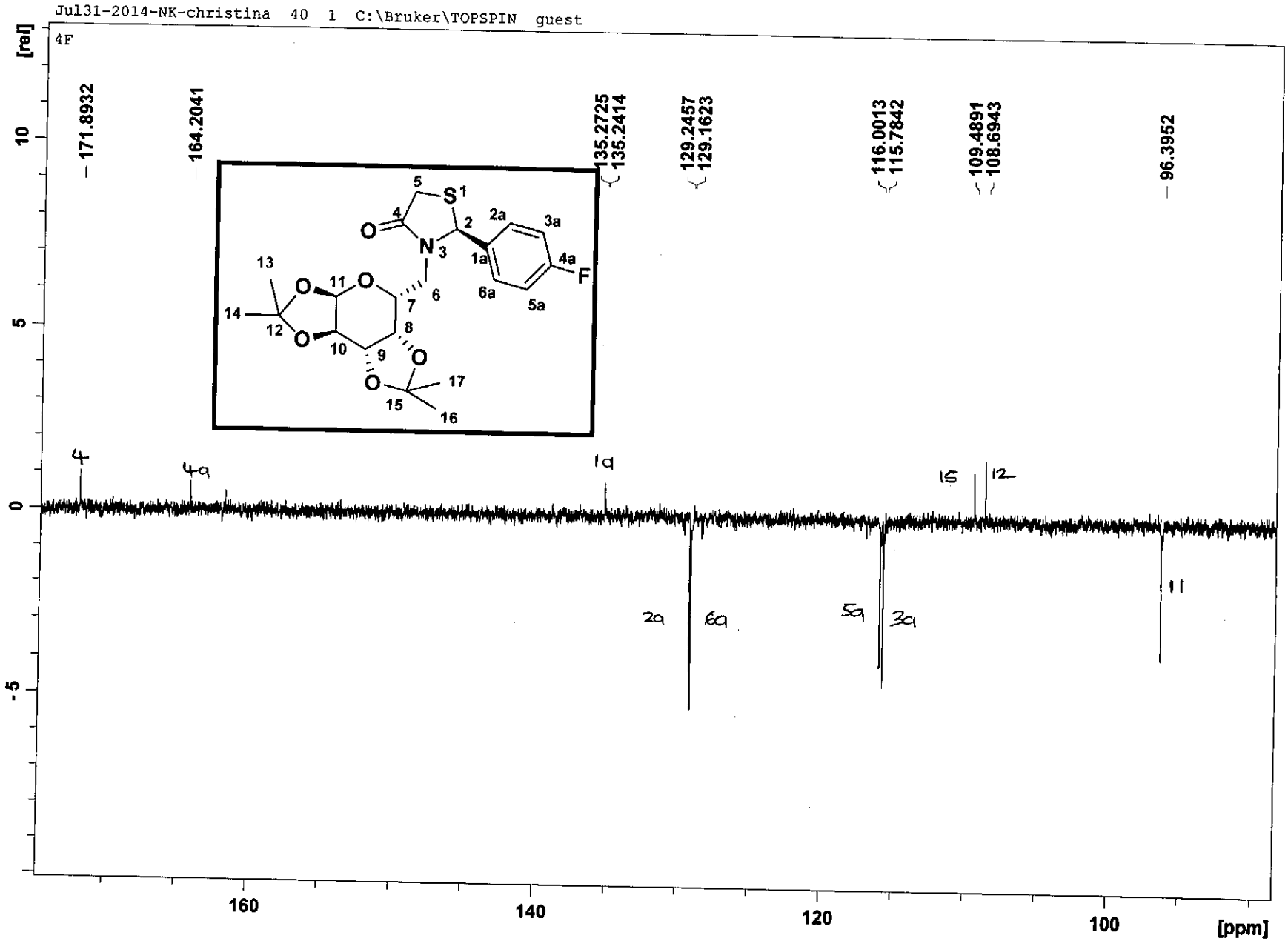
Expanded ^{1}H Spectrum of Compound 5b: 2-(4-Fluoro-phenyl)-3-(2,2,7,7-tetramethyl-tetrahydro-bis[1,3]dioxolo[4,5-b;4',5'-d]pyran-5-ylmethyl)-thiazolidin-4-one



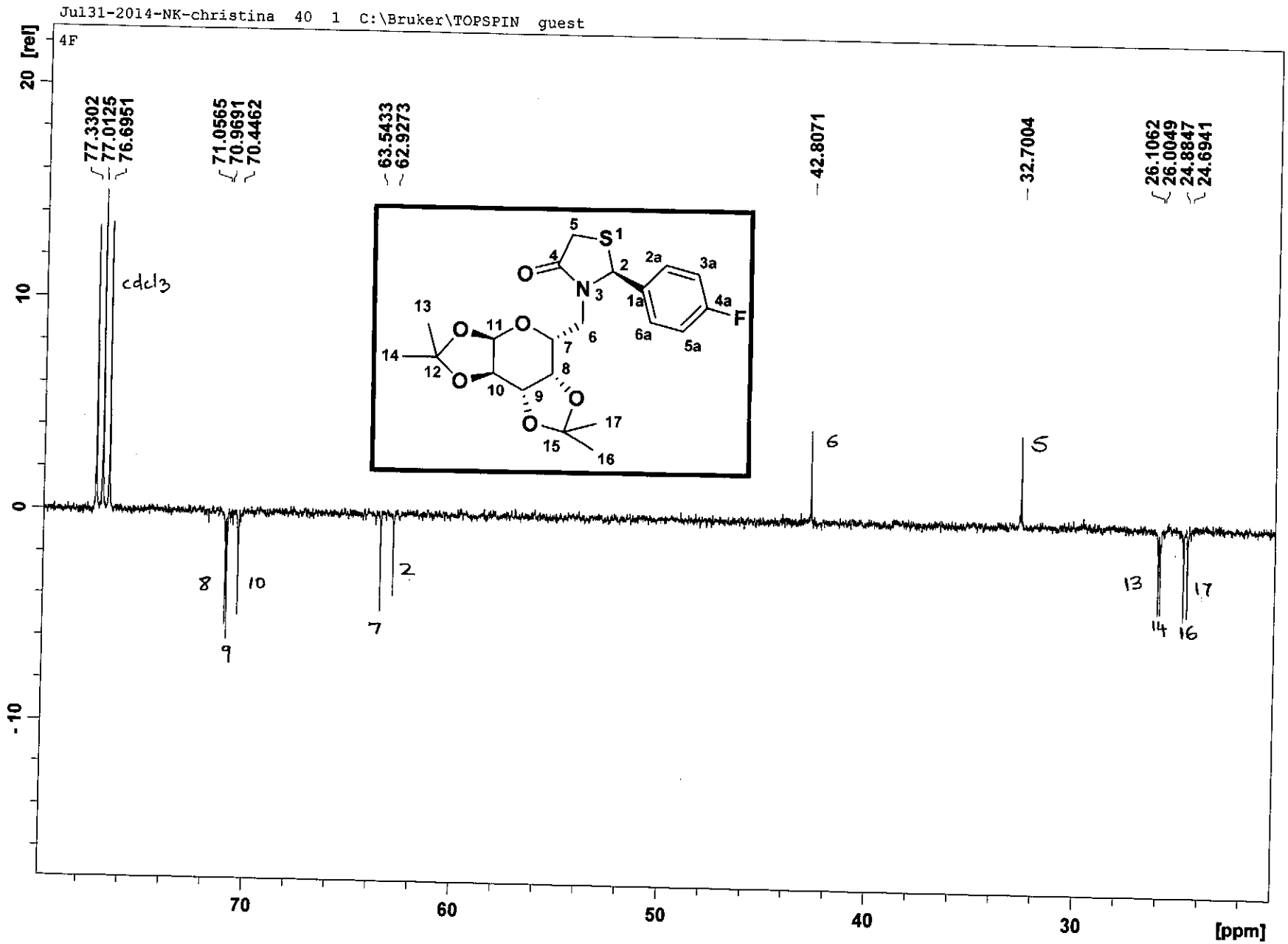
Expanded ^{1}H Spectrum of Compound 5b: 2-(4-Fluoro-phenyl)-3-(2,2,7,7-tetramethyl-tetrahydro-bis[1,3]dioxolo[4,5-b;4',5'-d]pyran-5-ylmethyl)-thiazolidin-4-one



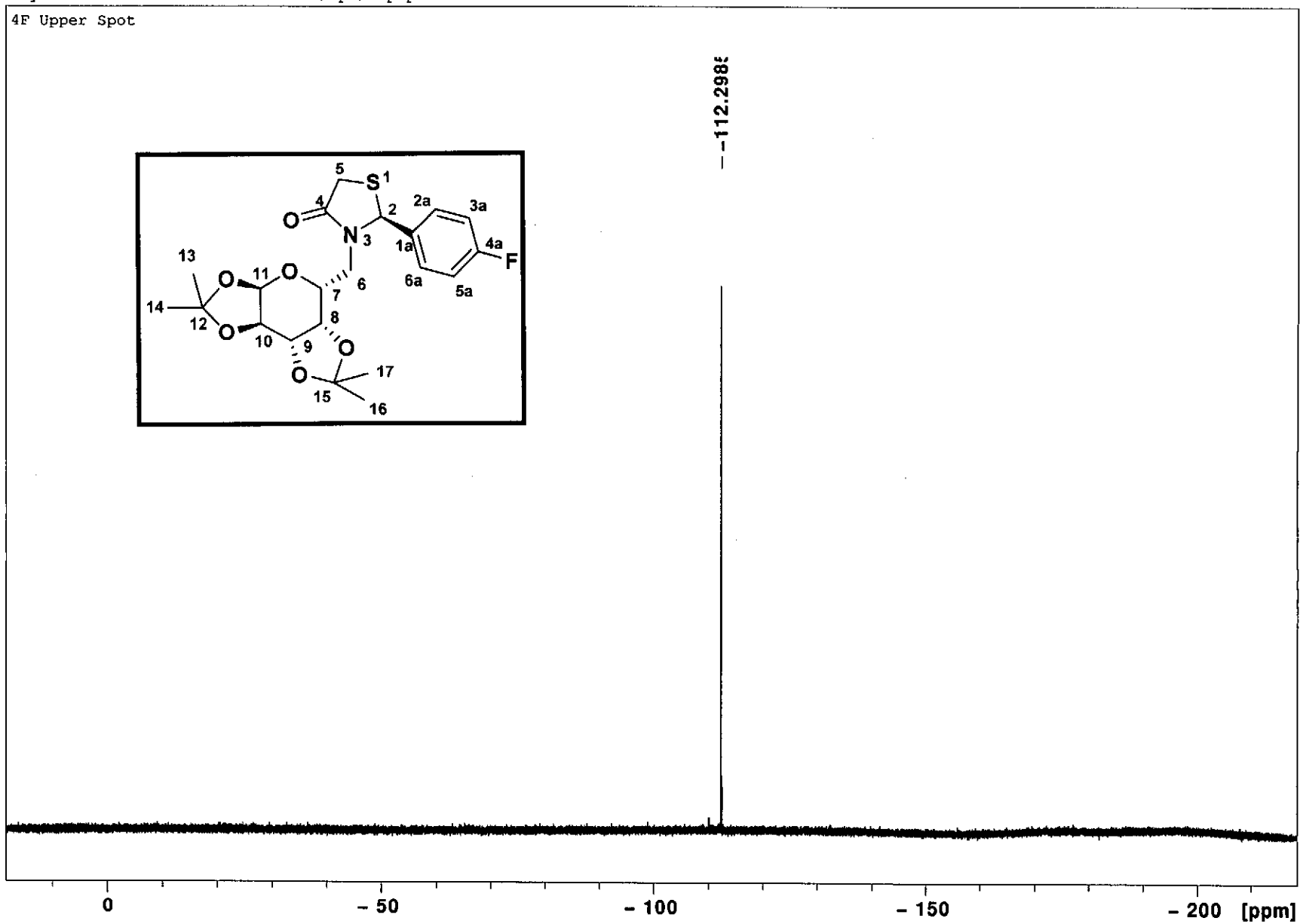
^{13}C Spectrum of Compound 5b: 2-(4-Fluoro-phenyl)-3-(2,2,7,7-tetramethyl-tetrahydro-bis [1,3]dioxolo[4,5-b;4',5'-d]pyran-5-ylmethyl)-thiazolidin-4-one



Expanded ^{13}C Spectrum of Compound 5b: 2-(4-Fluoro-phenyl)-3-(2,2,7,7-tetramethyl-tetrahydro-bis[1,3]dioxolo[4,5-b;4',5'-d]pyran-5-ylmethyl)-thiazolidin-4-one

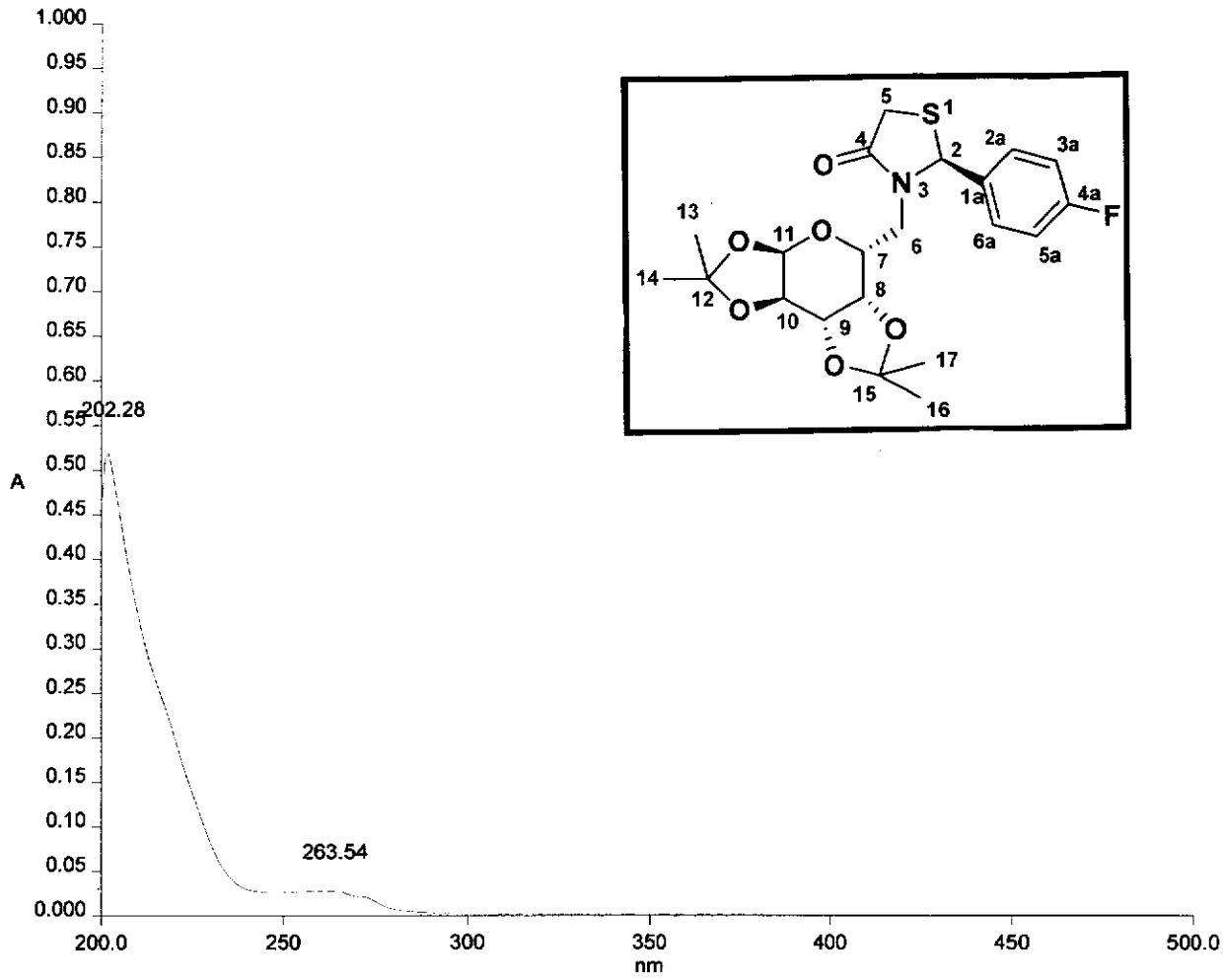


Expanded ^{13}C Spectrum of Compound 5b: 2-(4-Fluoro-phenyl)-3-(2,2,7,7-tetramethyl-tetrahydro-bis[1,3]dioxolo[4,5-b;4',5'-d]pyran-5-ylmethyl)-thiazolidin-4-one

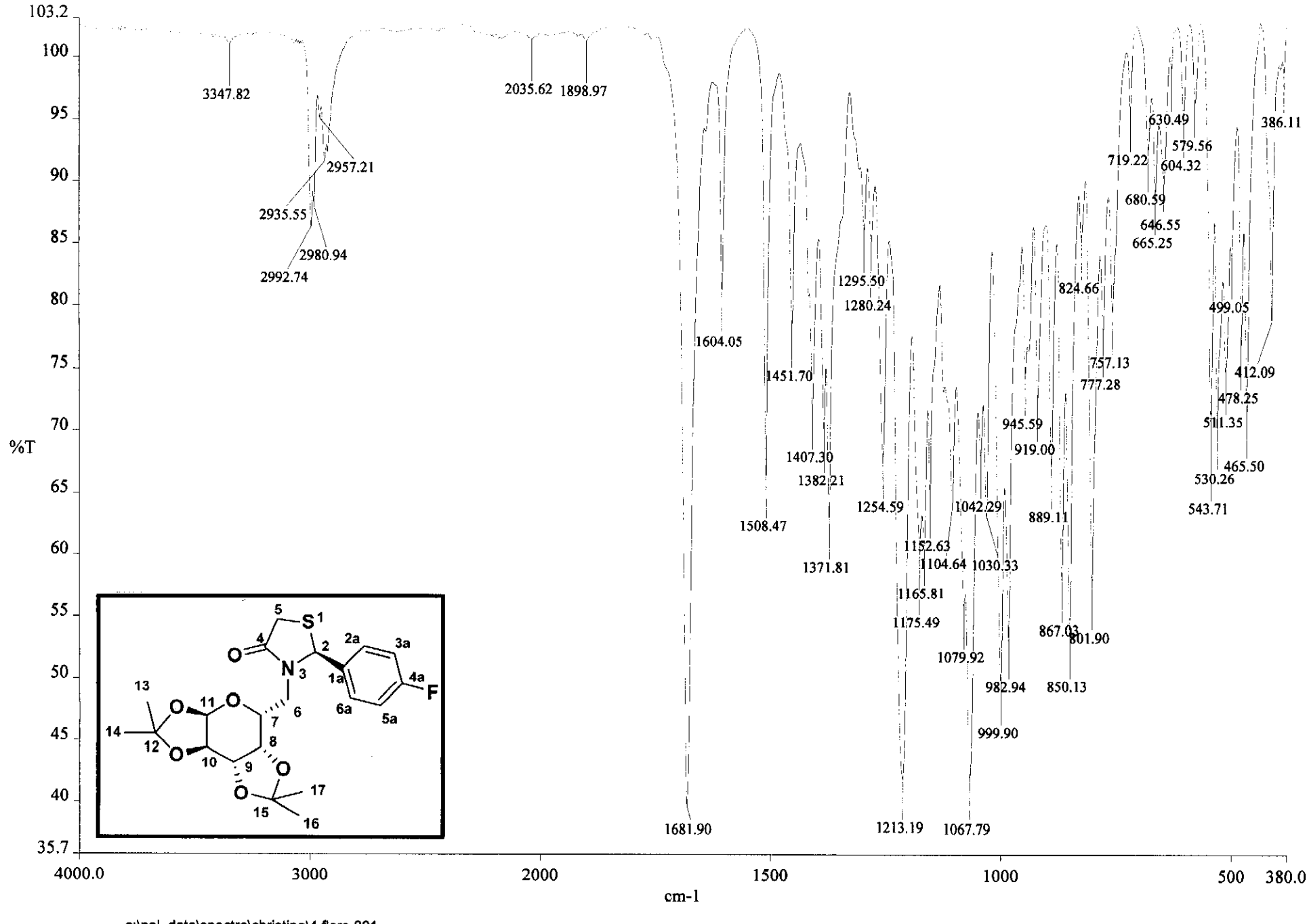


^{19}F Spectrum of Compound 5b: 2-(4-Fluoro-phenyl)-3-(2,2,7,7-tetramethyl-tetrahydro-bis [1,3]dioxolo[4,5-b;4',5'-d]pyran-5-ylmethyl)-thiazolidin-4-one

Date: 2014/06/05 Time: 04:35:25 PM



Ultraviolet Spectrum of Compound 5b: 2-(4-Fluoro-phenyl)-3-(2,2,7,7-tetramethyl-tetrahydro-bis[1,3]dioxolo[4,5-b;4',5'-d]pyran-5-ylmethyl)-thiazolidin-4-one

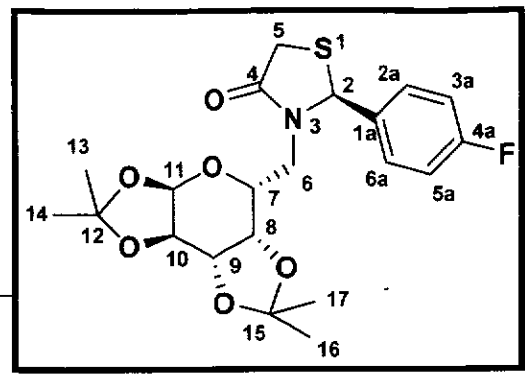


c:\pel_data\spectra\christina\4-floro.001

Infrared Spectrum of Compound 5b: 2-(4-Fluoro-phenyl)-3-(2,2,7,7-tetramethyl-tetrahydro-bis[1,3]dioxolo[4,5-b;4',5'-d]pyran-5-ylmethyl)-thiazolidin-4-one

==== Shimadzu LCsolution Analysis Report ====

Acquired by	: Admin
Sample Name	: 4f formic buffer
Sample ID	: 4f formic buffer
Vail #	: 1
Injection Volume	: 100 uL
Data File Name	: 4f formic buffer.lcd
Method File Name	: Pramod 09jun 2014.lcm
Batch File Name	: suger thiozolidinon.lcb
Report File Name	: Default.lcr
Data Acquired	: 2014/06/18 09:14:54 AM
Data Processed	: 2014/06/18 09:54:56 AM



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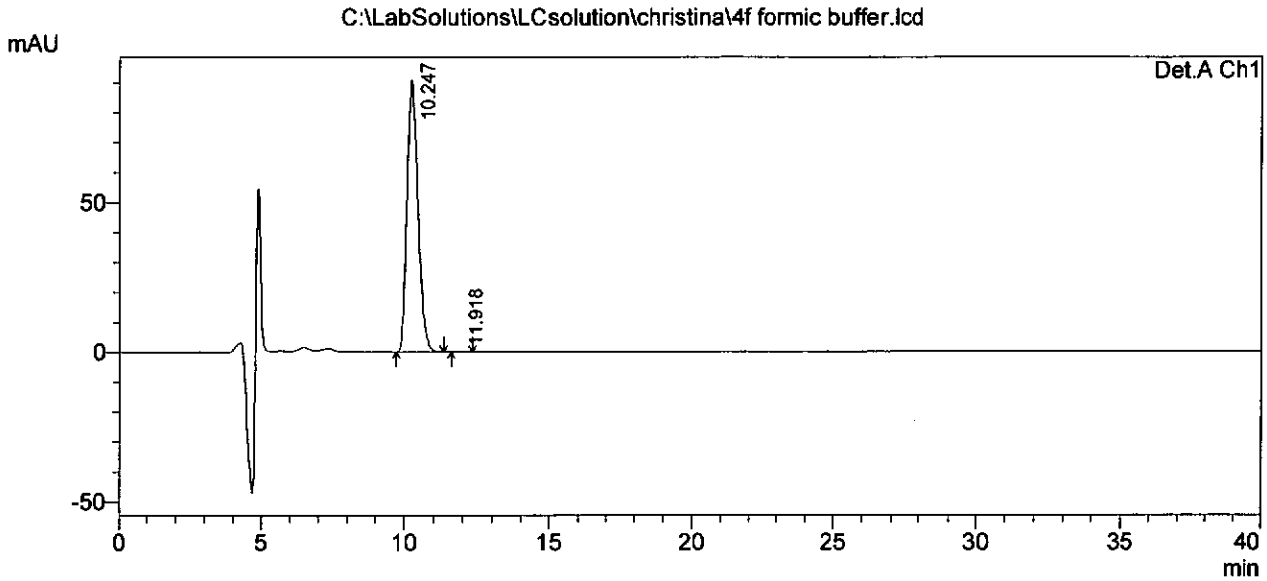

1 Det.A Ch1/220nm

<Results>

PeakTable C:\LabSolutions\LCsolution\christina\4f formic buffer.lcd

Detector A Ch1 220nm

Peak#	Ret. Time	Area	Height	Area %	Height %
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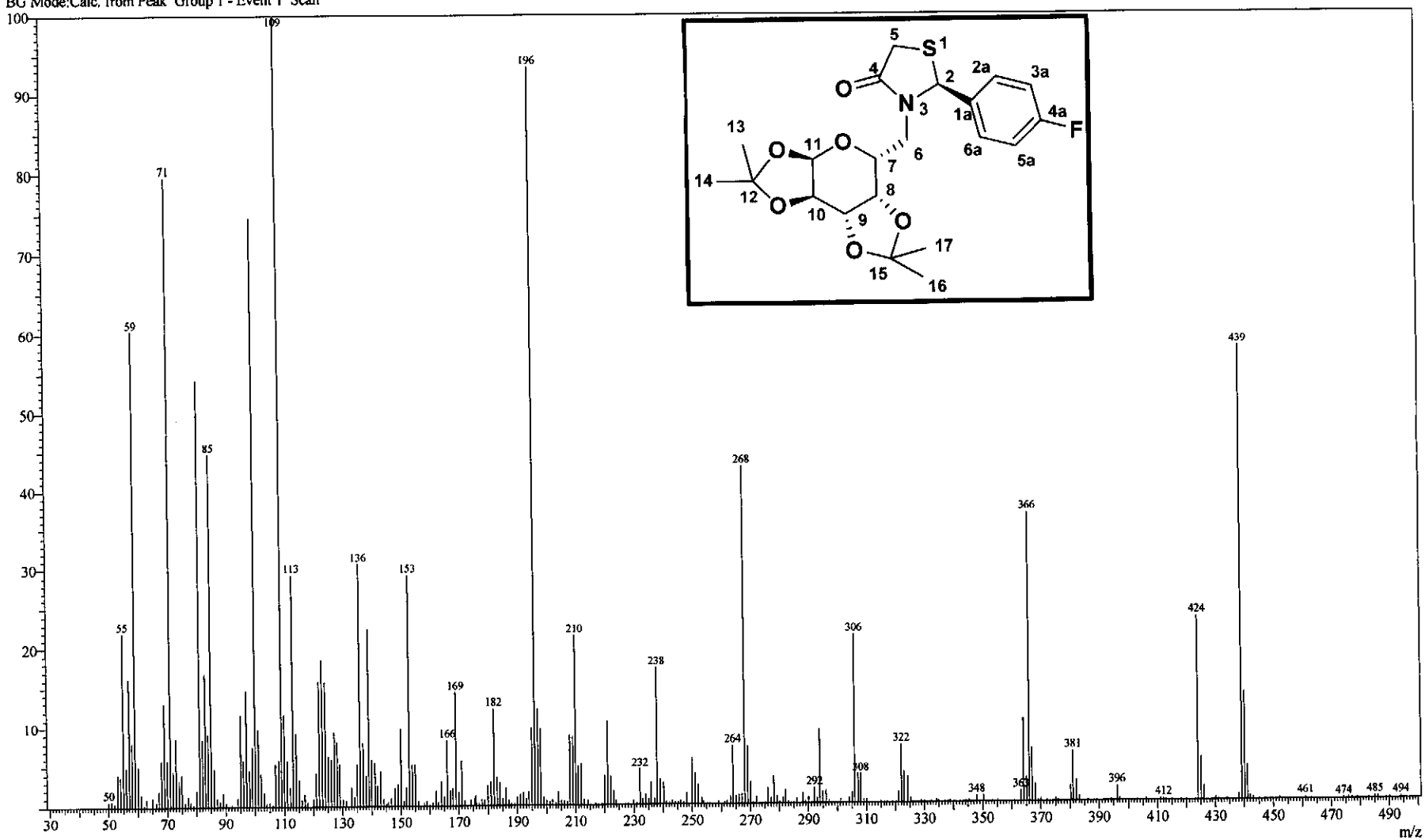
2	11.918	3521	149	0.151	0.163
Total		2338671	91077	100.000	100.000

HPLC of Compound 5b: 2-(4-Fluoro-phenyl)-3-(2,2,7,7-tetramethyl-tetrahydro-bis[1,3] dioxolo[4,5-b;4',5'-d]pyran-5-ylmethyl)-thiazolidin-4-one

Spectrum

Line#:1 R.Time:16.035(Scan#:2408)
MassPeaks:545
RawMode:Averaged 16.030-16.040(2407-2409) BasePeak:109(29728)
BG Mode:Calc. from Peak Group 1 - Event 1 Scan



GC-MS of Compound 5b: 2-(4-Fluoro-phenyl)-3-(2,2,7,7-tetramethyl-tetrahydro -bis[1,3] dioxolo[4,5-b;4',5'-d]pyran-5-ylmethyl)-thiazolidin-4-one

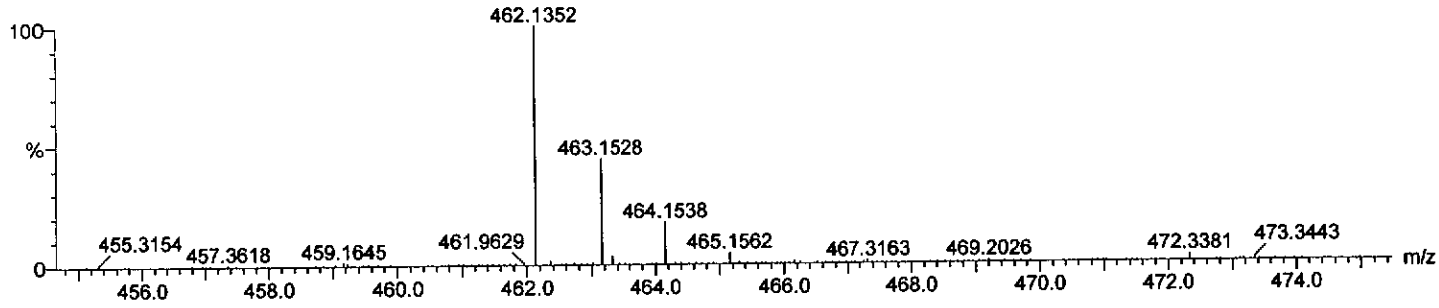
Elemental Composition Report

Single Mass Analysis
Tolerance = 5.0 PPM / DBE: min = -1.5, max = 100.0
Element prediction: Off
Number of isotope peaks used for i-FIT = 3

Monoisotopic Mass, Even Electron Ions
69 formula(e) evaluated with 1 results within limits (up to 20 best isotopic matches for each mass)
Elements Used:
C: 20-25 H: 25-30 N: 0-5 O: 5-10 F: 1-1 Na: 0-1 S: 0-1

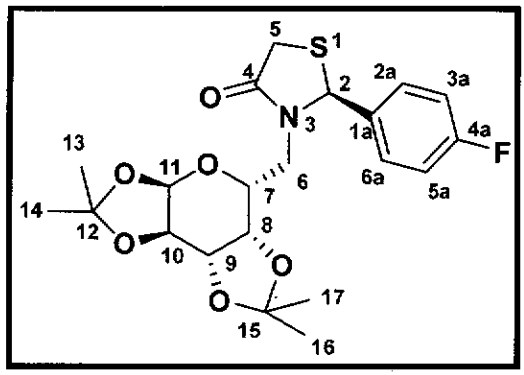
3 58 (1.922)
TOF MS ES+

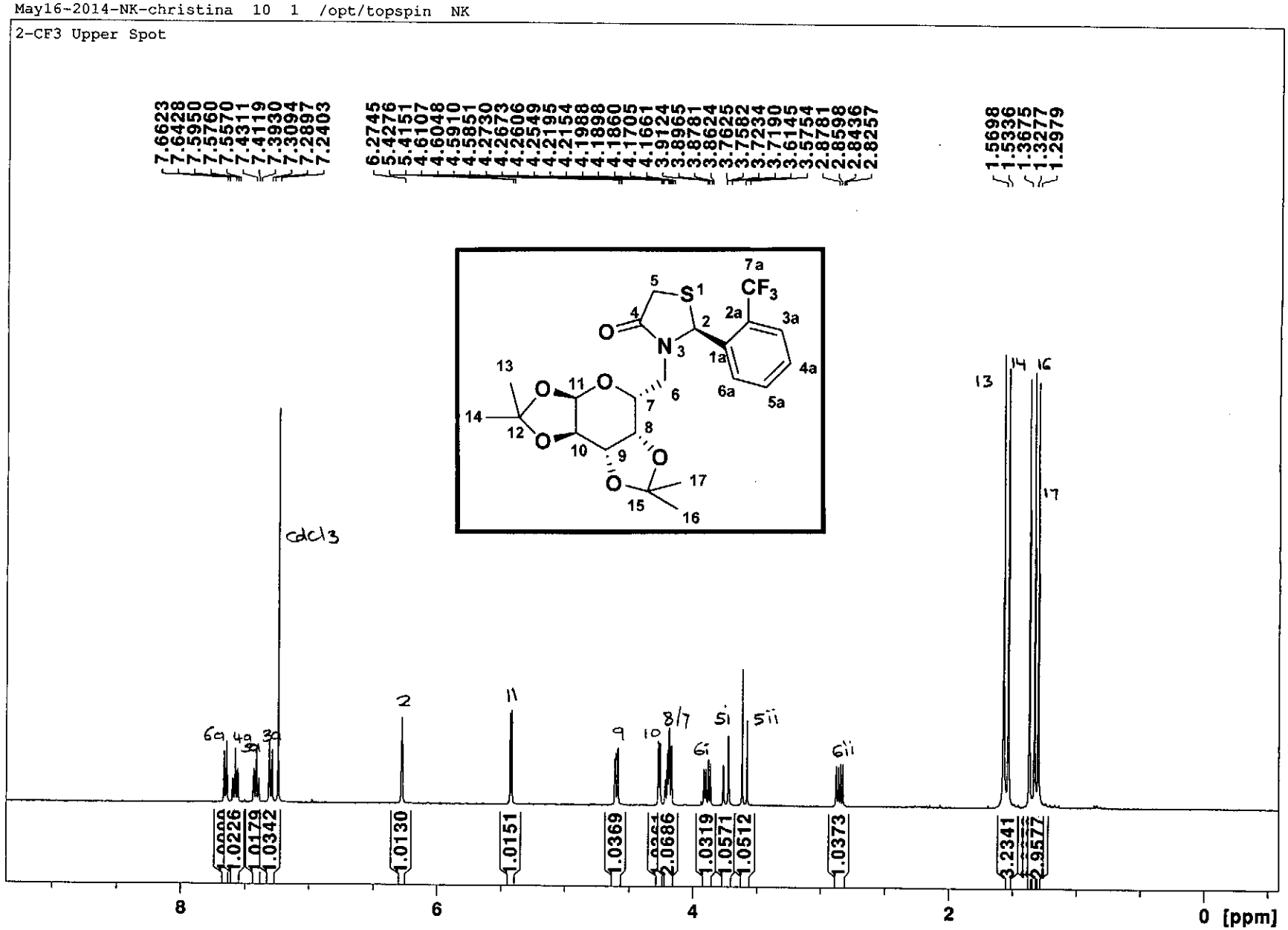
3.94e+003



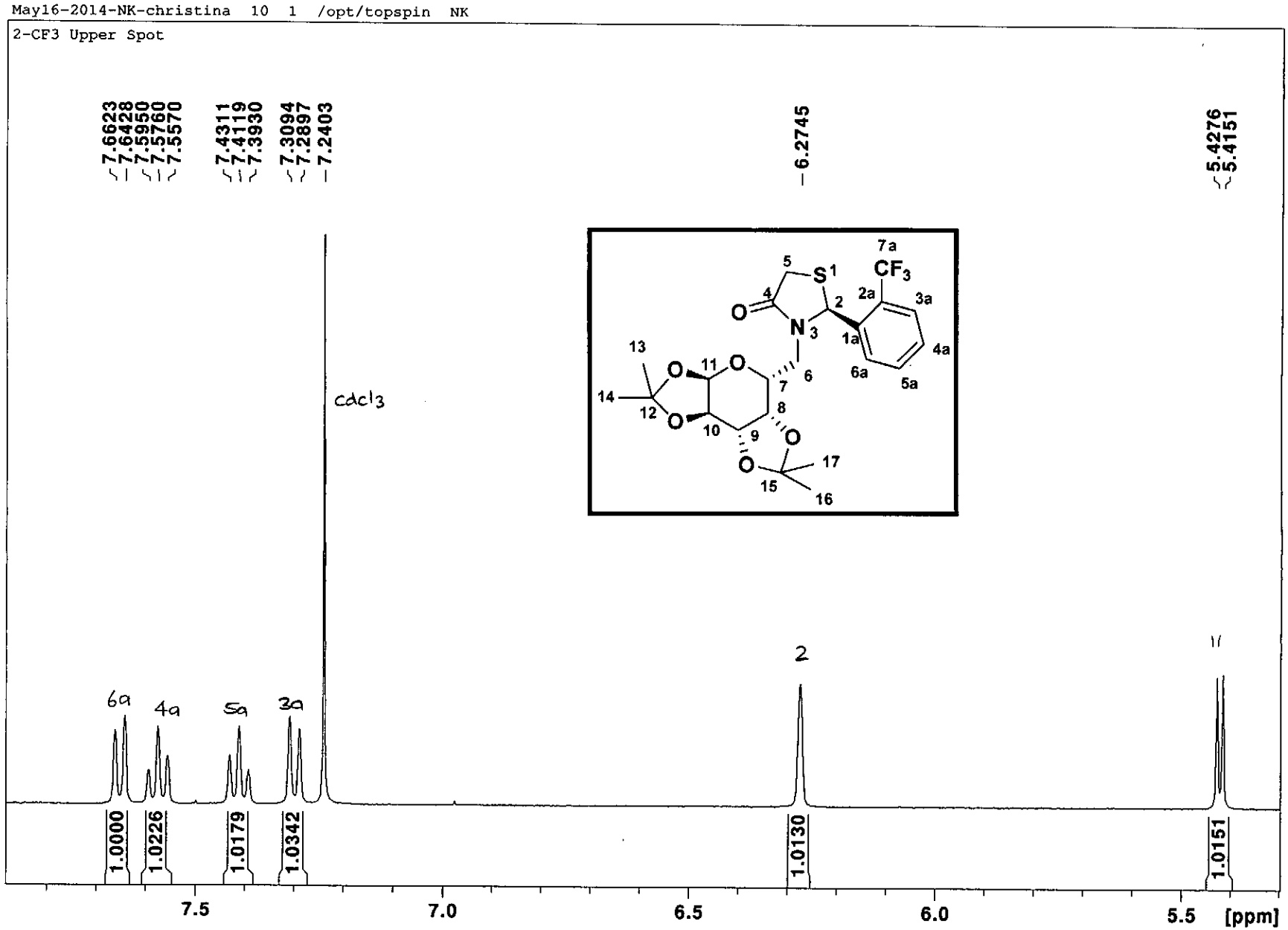
Minimum:				-1.5			
Maximum:		5.0	5.0	100.0			
Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	i-FIT (Norm)	Formula
462.1352	462.1363	-1.1	-2.4	8.5	122.3	0.0	C21 H26 N O6 F Na S

HRMS of Compound 5b: 2-(4-Fluoro-phenyl)-3-(2,2,7,7-tetramethyl-tetrahydro-bis[1,3] dioxolo[4,5-b;4',5'-d]pyran-5-ylmethyl)-thiazolidin-4-one

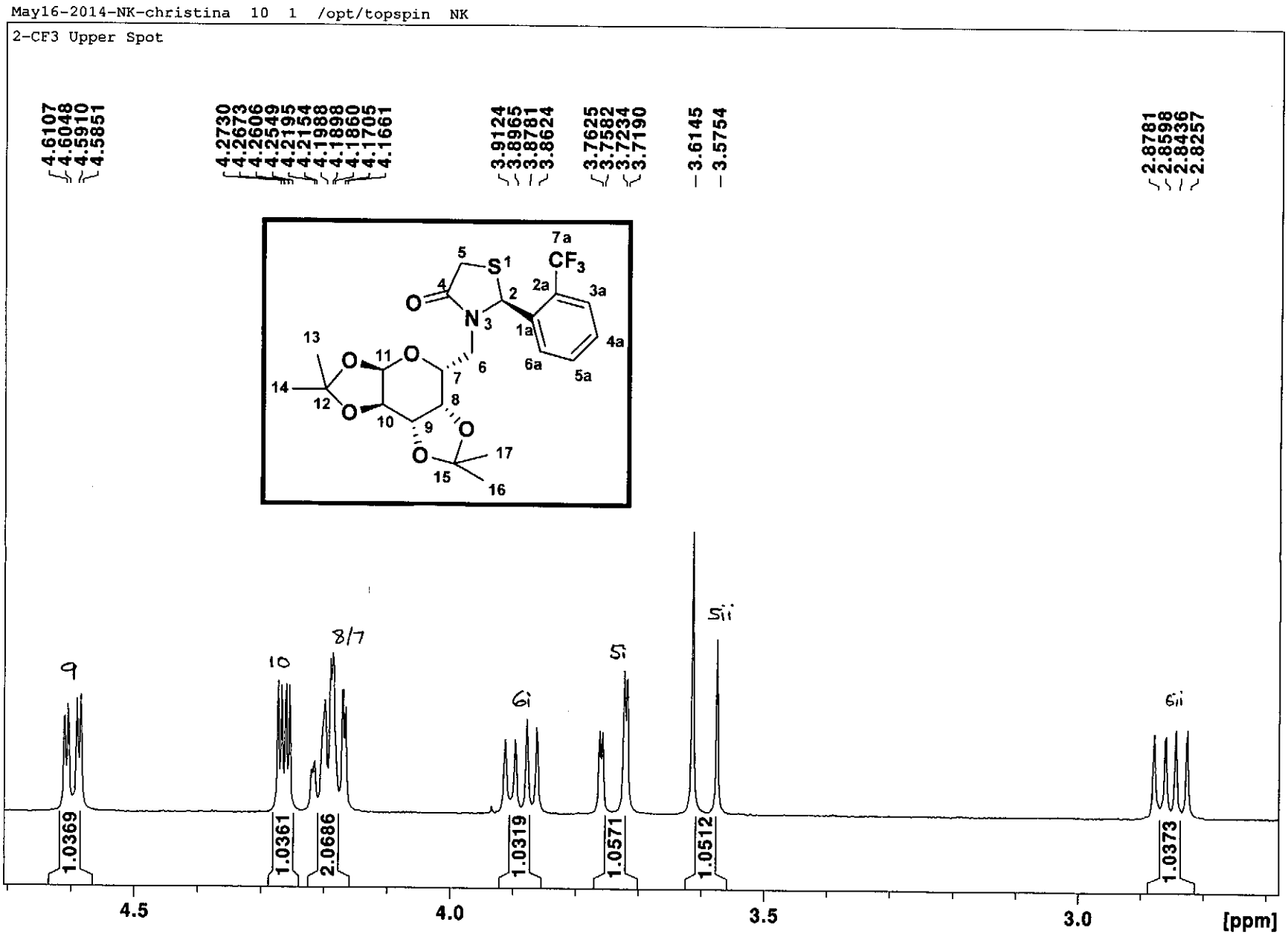




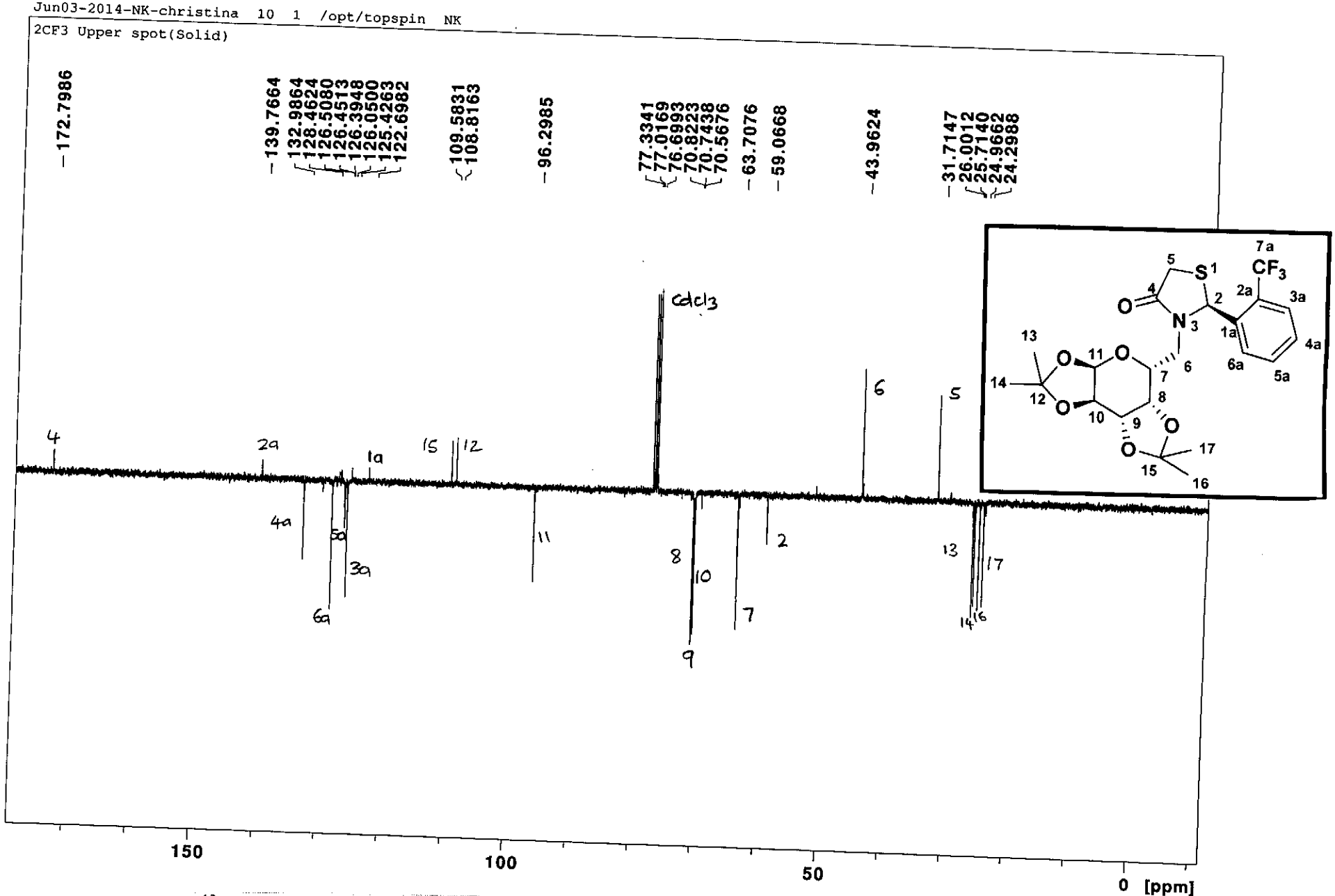
[1]H Spectrum of Compound 5c: 3-(2,2,7,7-Tetramethyl-tetrahydro-bis[1,3]dioxolo[4,5-b;4', 5'-d]pyran-5-ylmethyl)-2-(2-trifluoromethyl-phenyl)-thiazolidin-4-one



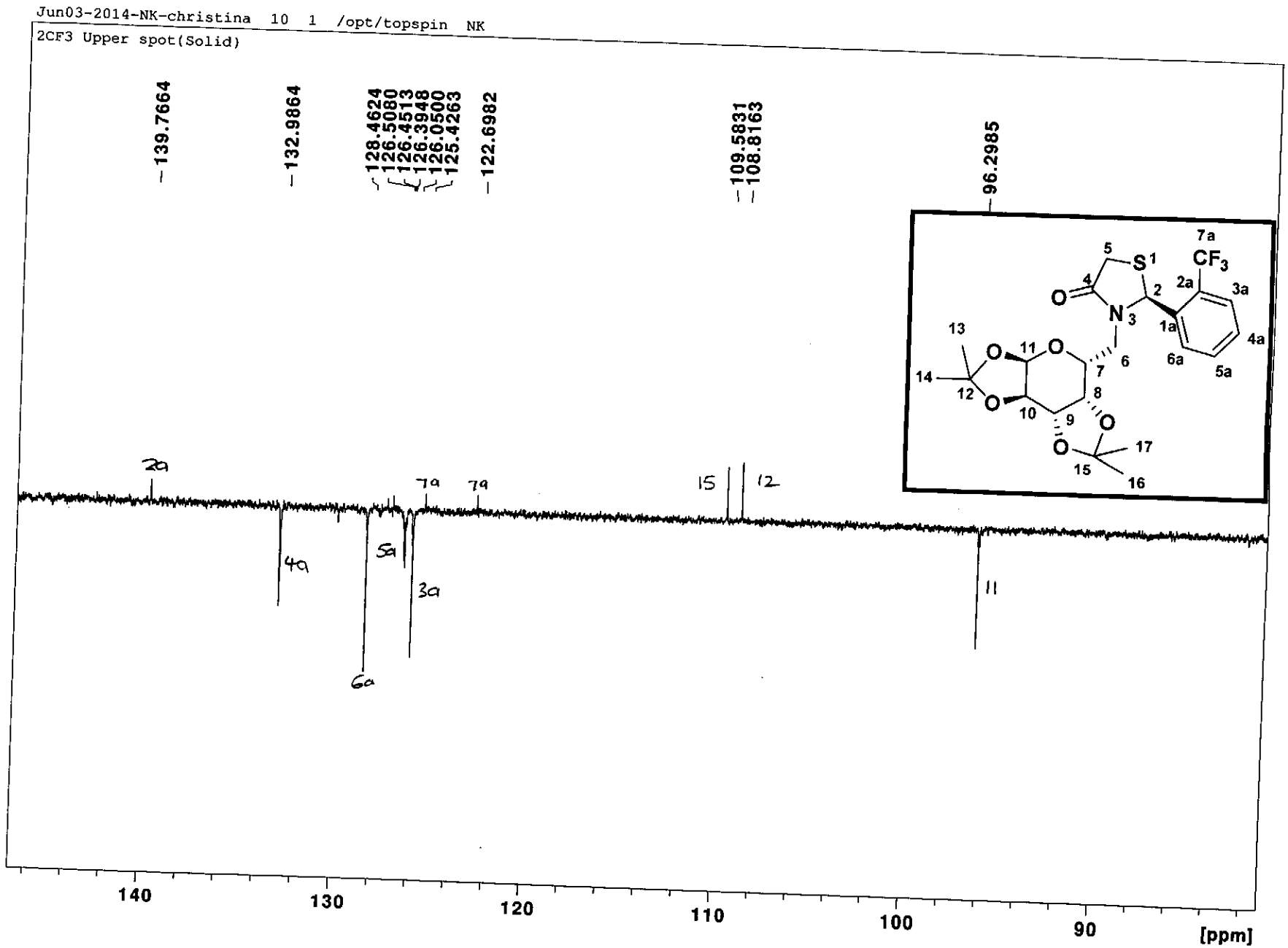
Expanded ^{1}H Spectrum of Compound 5c: 3-(2,2,7,7-Tetramethyl-tetrahydro-bis[1,3] dioxolo[4,5-b;4',5'-d]pyran-5-ylmethyl)-2-(2-trifluoromethyl-phenyl)-thiazolidin-4-one



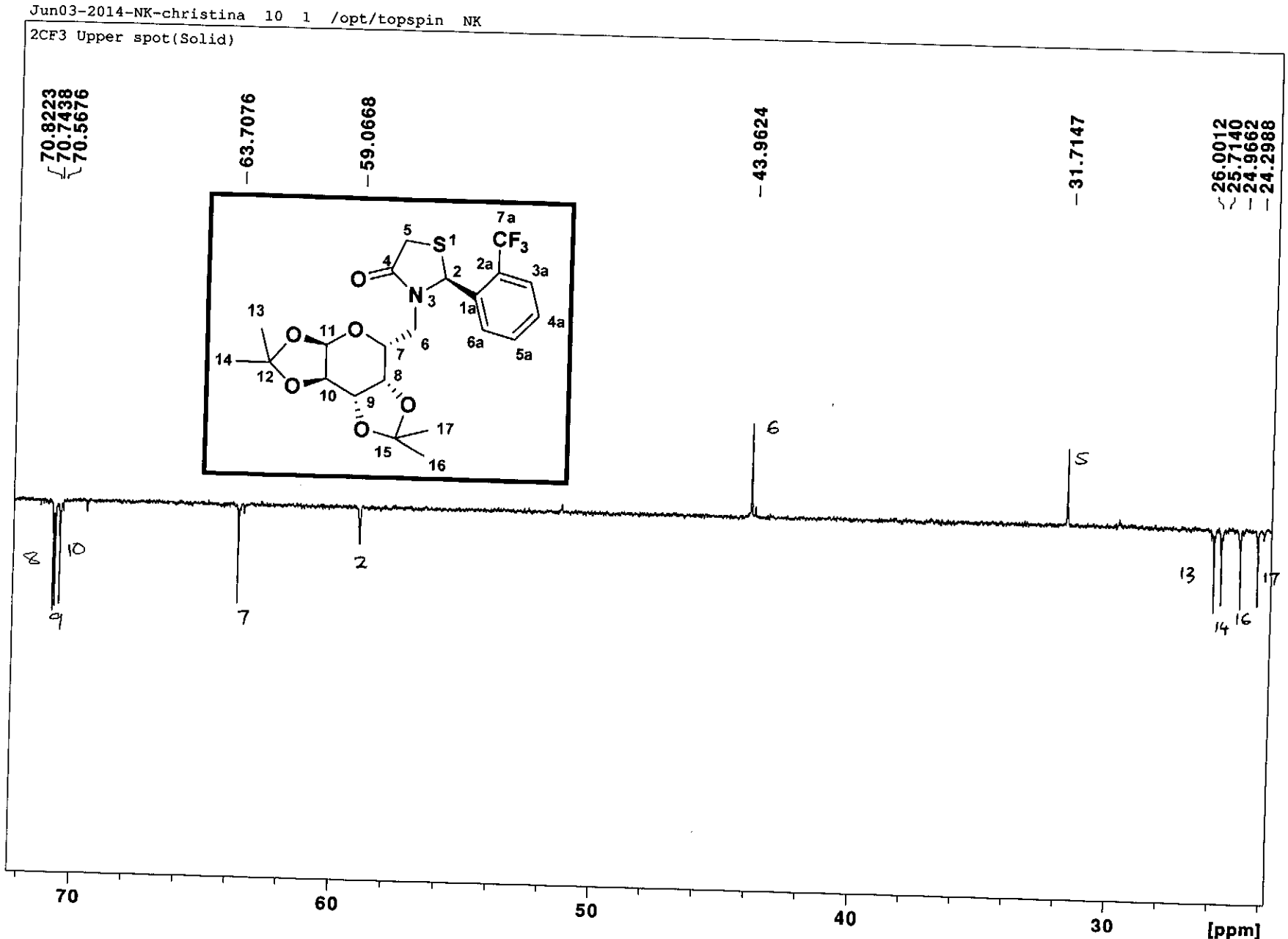
Expanded ^{1}H Spectrum of Compound 5c: 3-(2,2,7,7-Tetramethyl-tetrahydro-bis[1,3] dioxolo[4,5-b;4',5'-d]pyran-5-ylmethyl)-2-(2-trifluoromethyl-phenyl)-thiazolidin-4-one



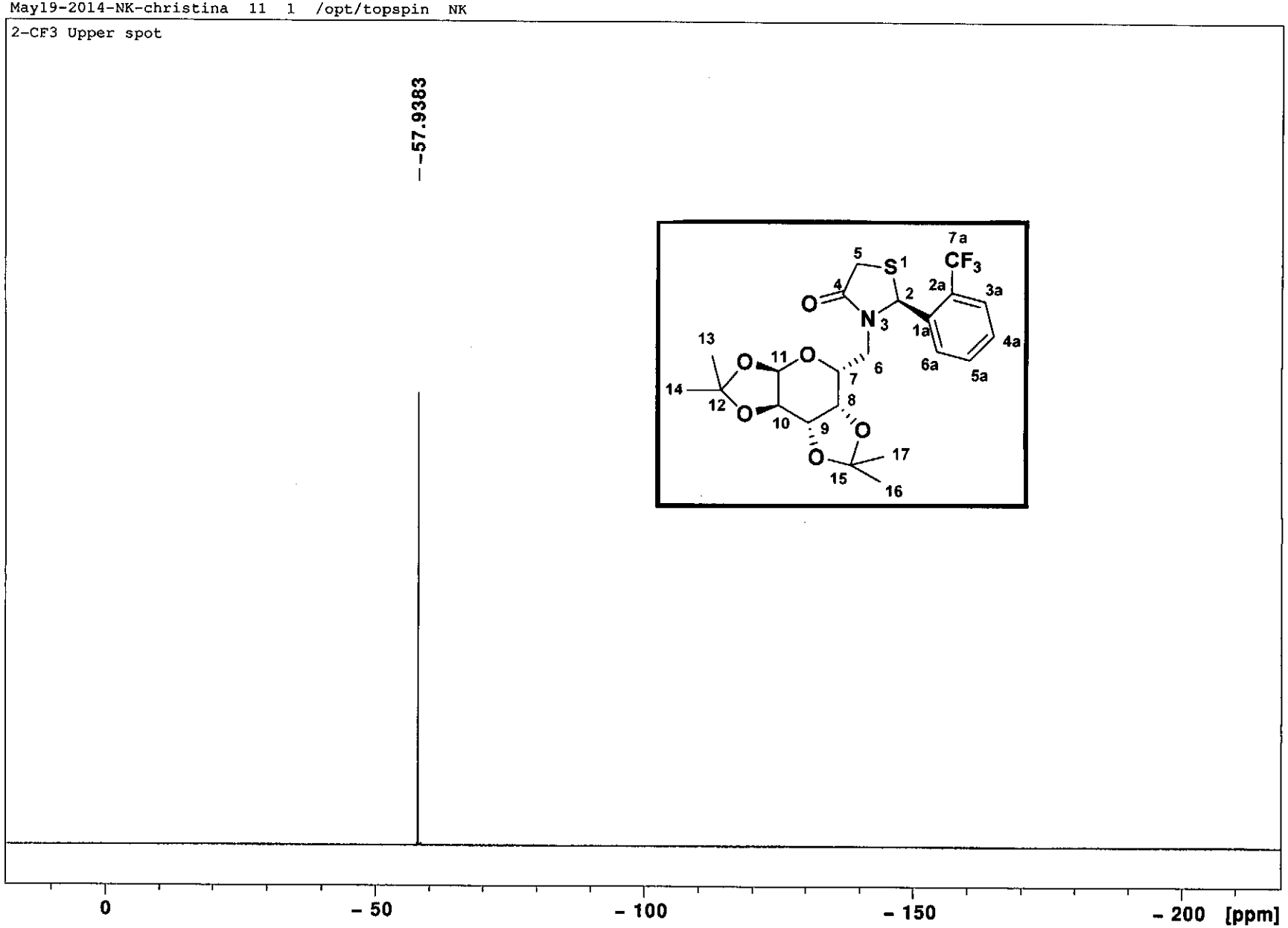
^{13}C Spectrum of Compound 5c: 3-(2,2,7,7-Tetramethyl-tetrahydro-bis[1,3] dioxolo[4,5-b; 4',5'-d]pyran-5-ylmethyl)-2-(2-trifluoromethyl-phenyl)-thiazolidin-4-one



Expanded ^{13}C Spectrum of Compound 5c: 3-(2,2,7,7-Tetramethyl-tetrahydro-bis[1,3] dioxolo[4,5-b;4',5'-d]pyran-5-ylmethyl)-2-(2-trifluoromethyl-phenyl)-thiazolidin-4-one

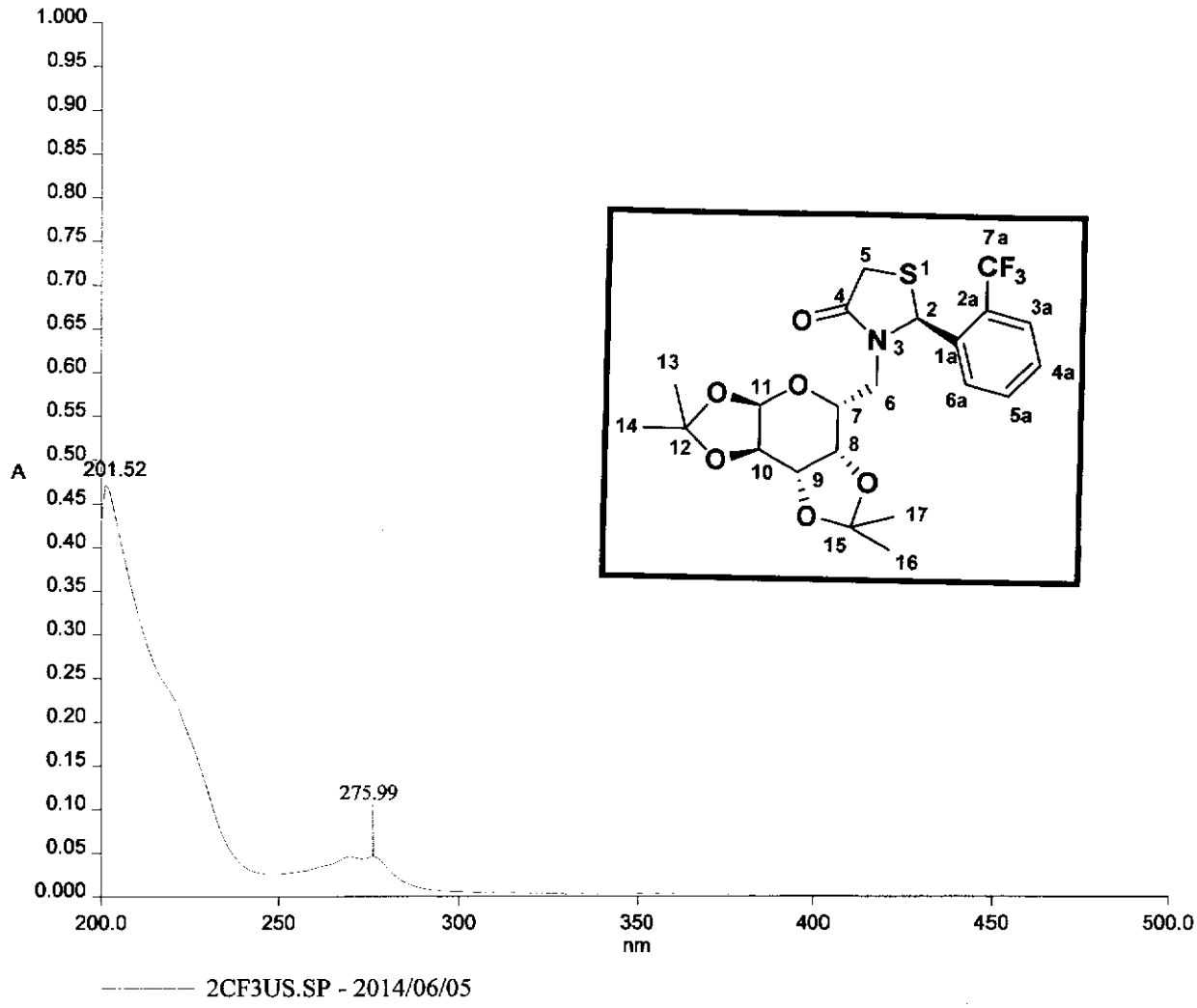


Expanded ^{13}C Spectrum of Compound 5c: 3-(2,2,7,7-Tetramethyl-tetrahydro-bis[1,3] dioxolo[4,5-b;4',5'-d]pyran-5-ylmethyl)-2-(2-trifluoromethyl-phenyl)-thiazolidin-4-one

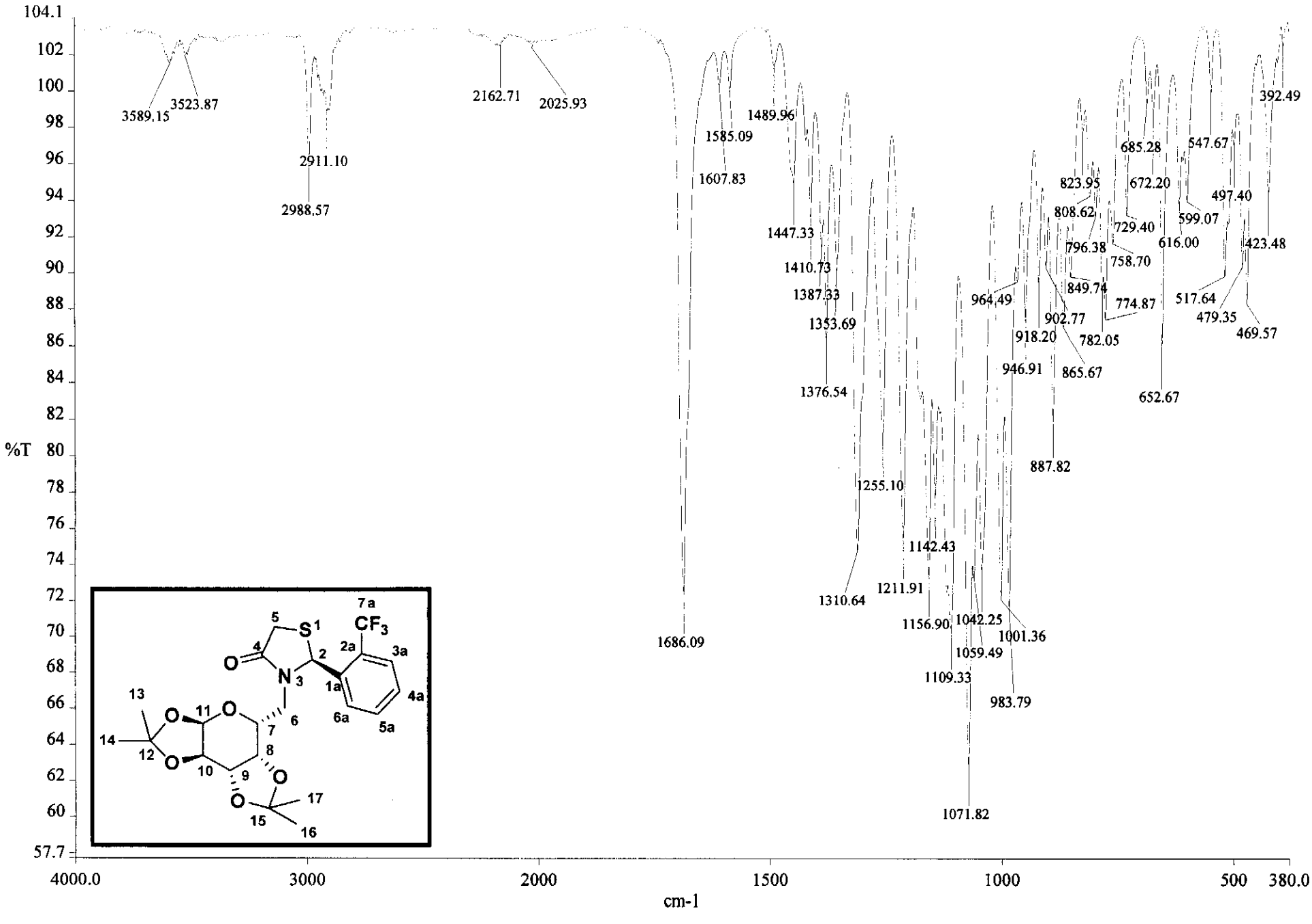


^{19}F Spectrum of Compound 5c: 3-(2,2,7,7-Tetramethyl-tetrahydro-bis[1,3]dioxolo[4,5-b;4', 5'-d]pyran-5-ylmethyl)-2-(2-trifluoromethyl-phenyl)-thiazolidin-4-one

Date: 2014/06/05 Time: 04:23:01 PM



Ultraviolet Spectrum of Compound 5c: 3-(2,2,7,7-Tetramethyl-tetrahydro-bis[1,3]dioxolo [4,5-b;4', 5'-d]pyran-5-ylmethyl)-2-(2-trifluoromethyl-phenyl)-thiazolidin-4-one



c:\pel_data\spectra\christina\2cf3 us 001

Infrared Spectrum of Compound 5c: 3-(2,2,7,7-Tetramethyl-tetrahydro-bis[1,3]dioxolo[4,5-b;4', 5'-d]pyran-5-ylmethyl)-2-(2-trifluoromethyl-phenyl)-thiazolidin-4-one

==== Shimadzu LCsolution Analysis Report ====

Acquired by	: Admin
Sample Name	: 2-trifloro up formic buffer
Sample ID	: 2-trifloro up formic buffer
Vail #	: 1
Injection Volume	: 100 uL
Data File Name	: 2-trifloro up formic buffer.lcd
Method File Name	: Pramod 09jun 2014.lcm
Batch File Name	: suger thiozolidinon.lcb
Report File Name	: Default.lcr
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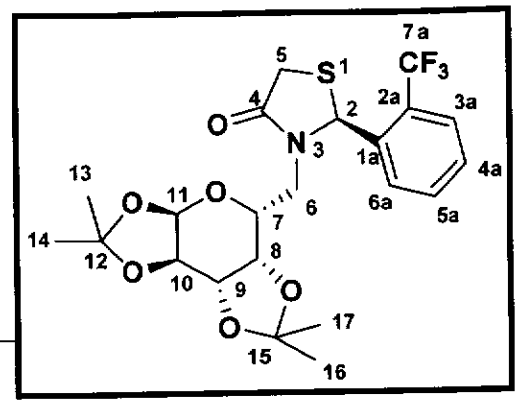
Data Processed	: 2014/06/13 03:26:21 PM



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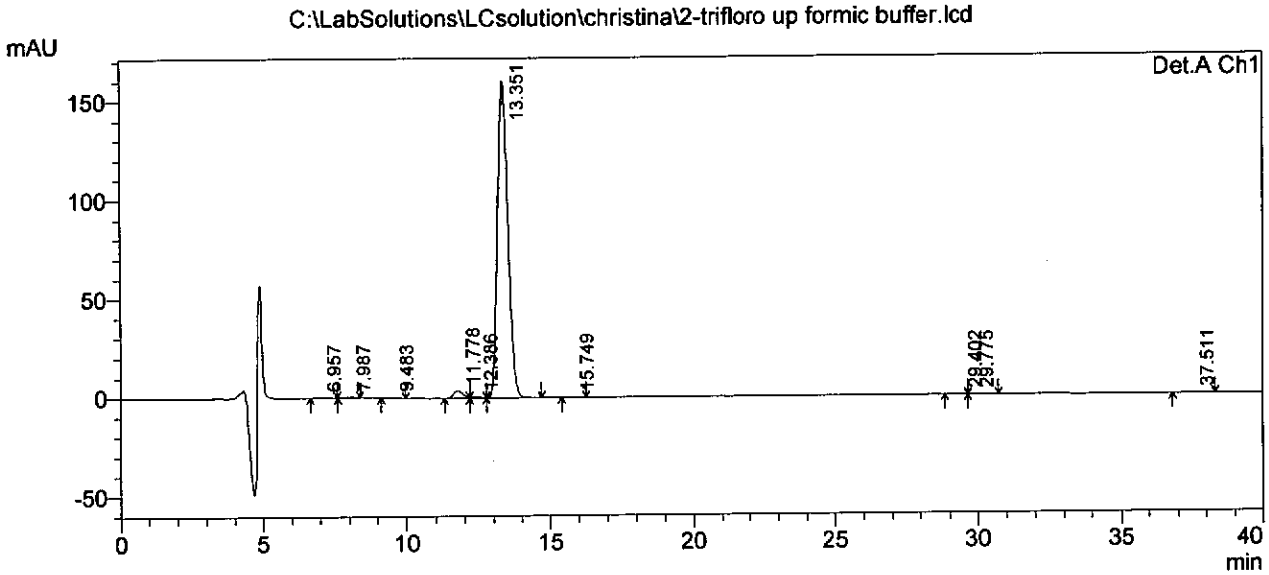


1Det.A Ch1/220nm

<Results>

PeakTable C:\LabSolutions\LCsolution\christina\2-trifloro up formic buffer.lcd

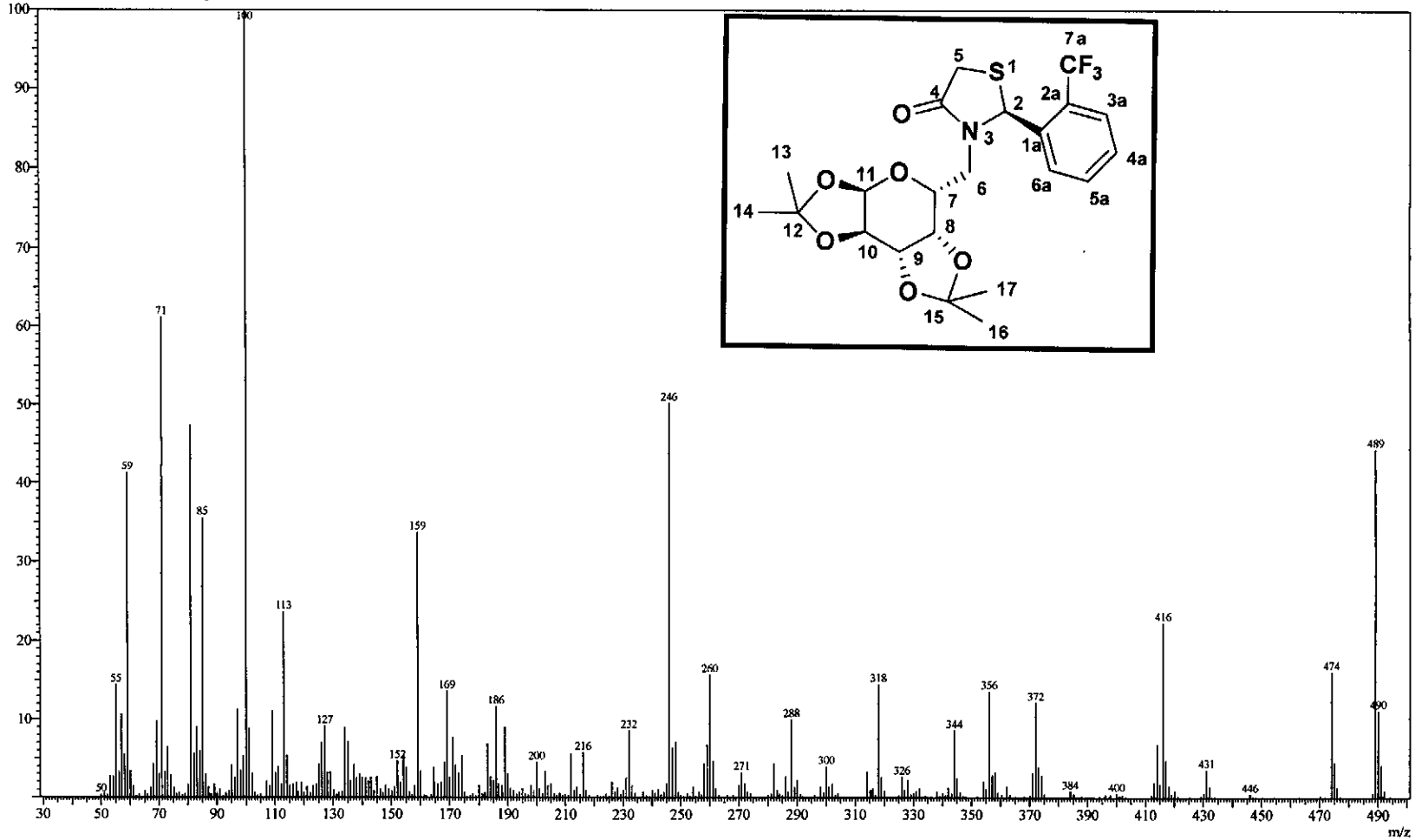
Detector A Ch1 220nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	6.957	6914	293	0.163	0.176
2	7.987	7077	292	0.167	0.175
3	9.483	10405	436	0.245	0.262
4	11.778	84920	3719	2.003	2.233
5	12.386	14080	623	0.332	0.374
6	13.351	4087356	160356	96.392	96.295
7	15.749	5316	201	0.125	0.121
8	29.402	6219	180	0.147	0.108
9	29.775	6326	186	0.149	0.112
10	37.511	11743	240	0.277	0.144
Total		4240356	166525	100.000	100.000

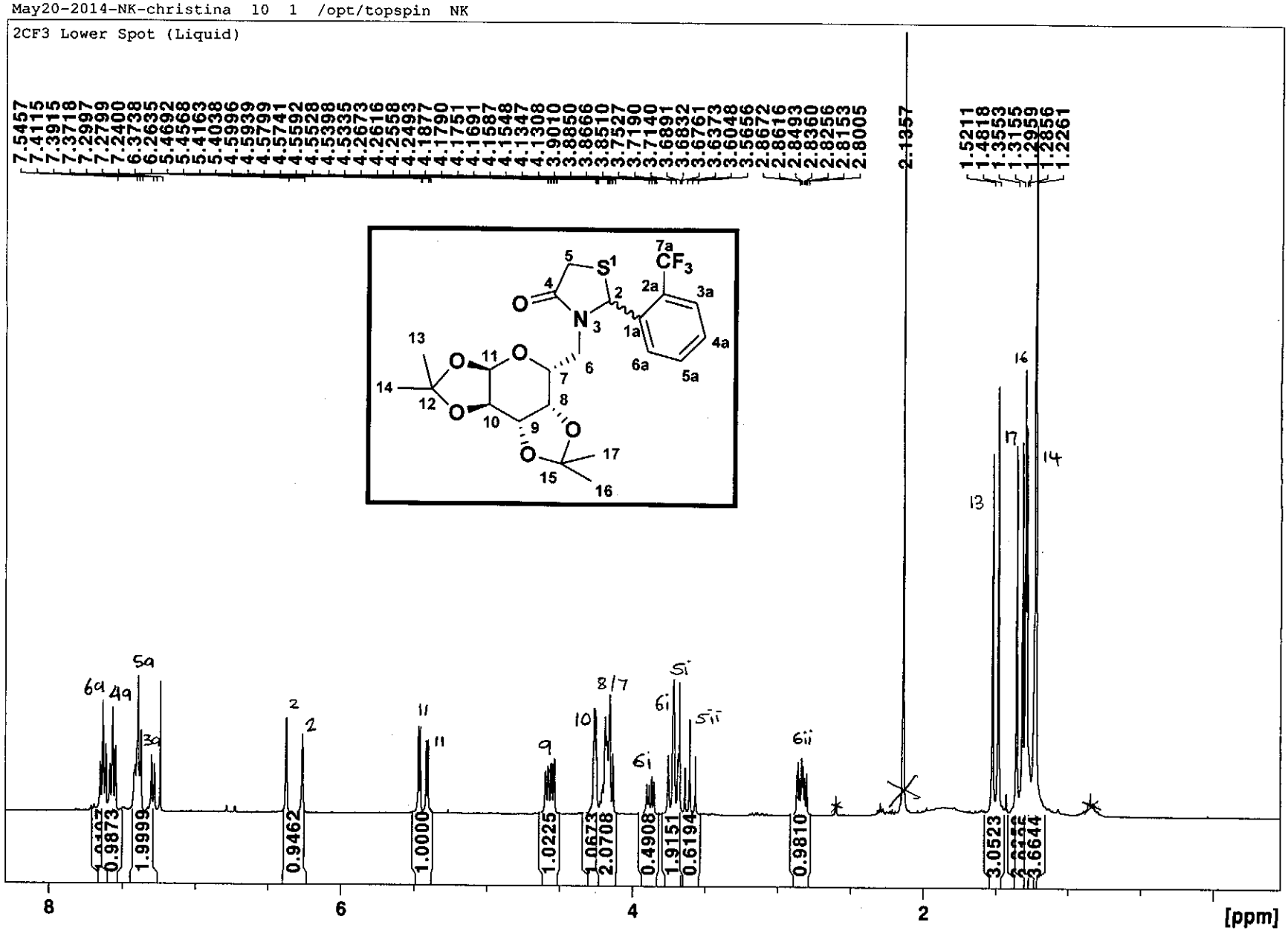
HPLC of Compound 5c: 3-(2,2,7,7-Tetramethyl-tetrahydro-bis[1,3]dioxolo[4,5-b;4', 5'-d] pyran-5-ylmethyl)-2-(2-trifluoromethyl-phenyl)-thiazolidin-4-one

Spectrum

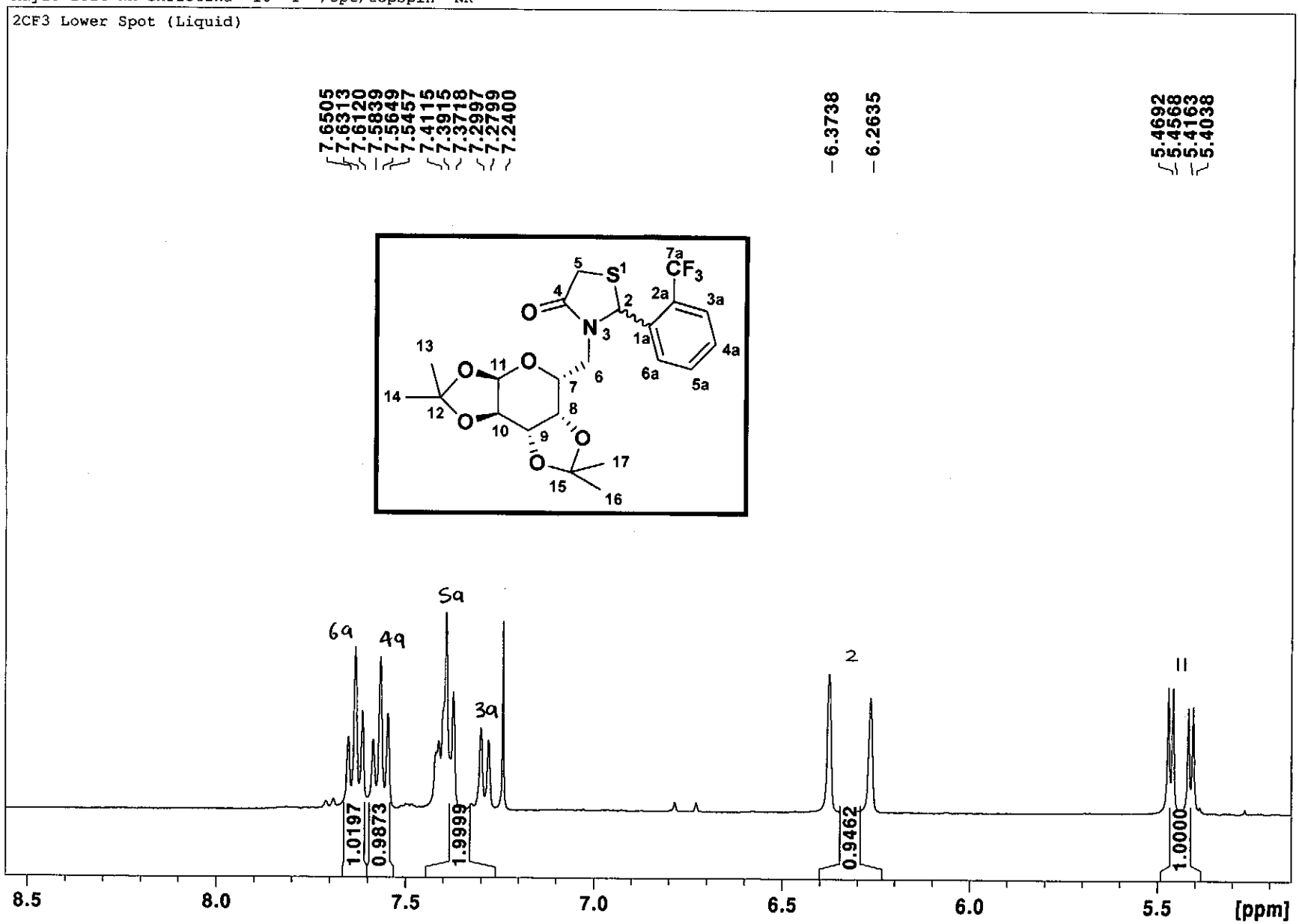
Line#:1 R.Time:15.370(Scan#:2275)
MassPeaks:583
RawMode:Averaged 15.365-15.375(2274-2276) BasePeak:100(92544)
BG Mode:Calc. from Peak Group 1 - Event 1 Scan



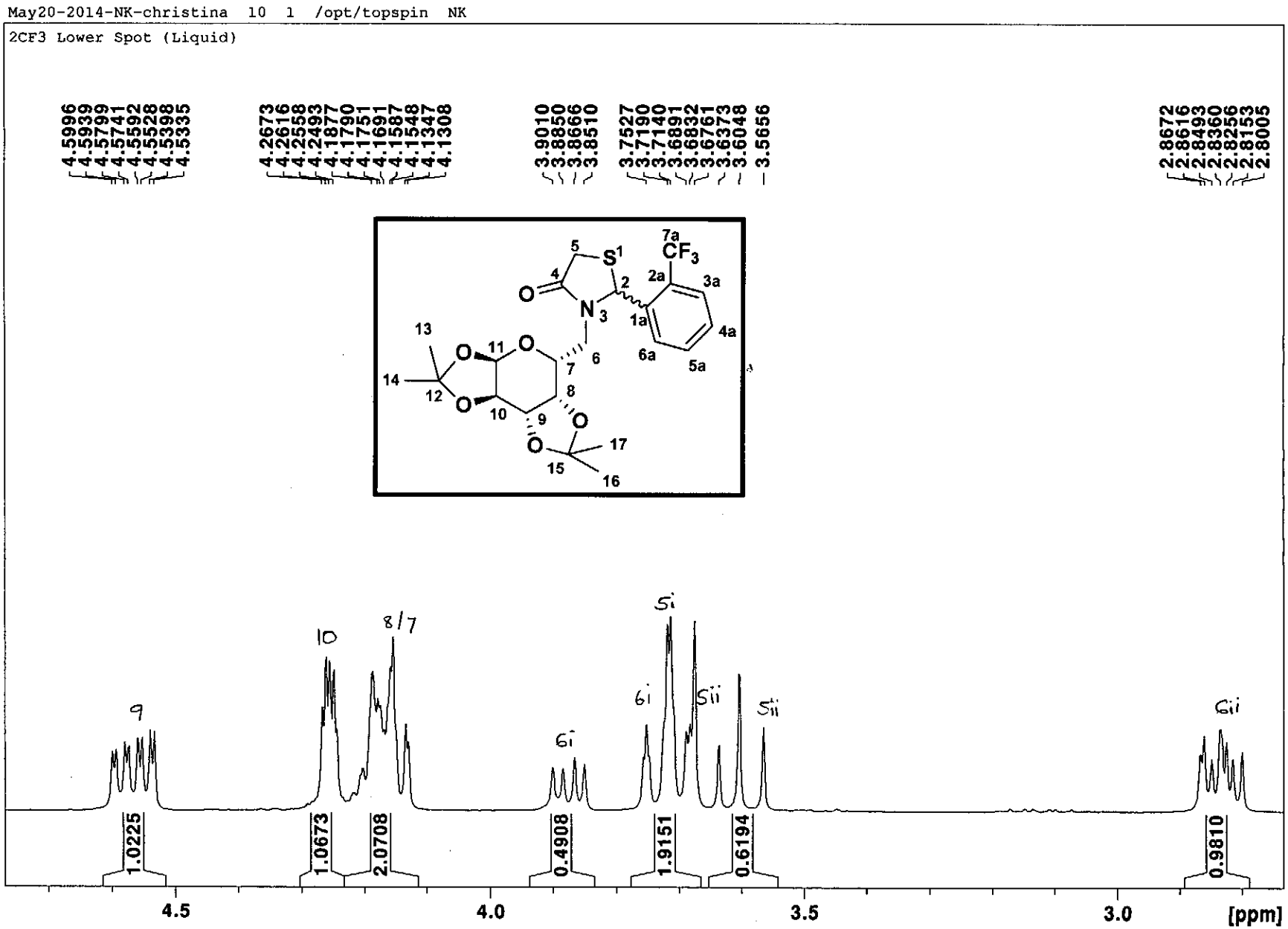
GC-MS of Compound 5c: 3-(2,2,7,7-Tetramethyl-tetrahydro-bis[1,3]dioxolo[4,5-b;4', 5'-d] pyran-5-ylmethyl)-2-(2-trifluoromethyl-phenyl)-thiazolidin-4-one



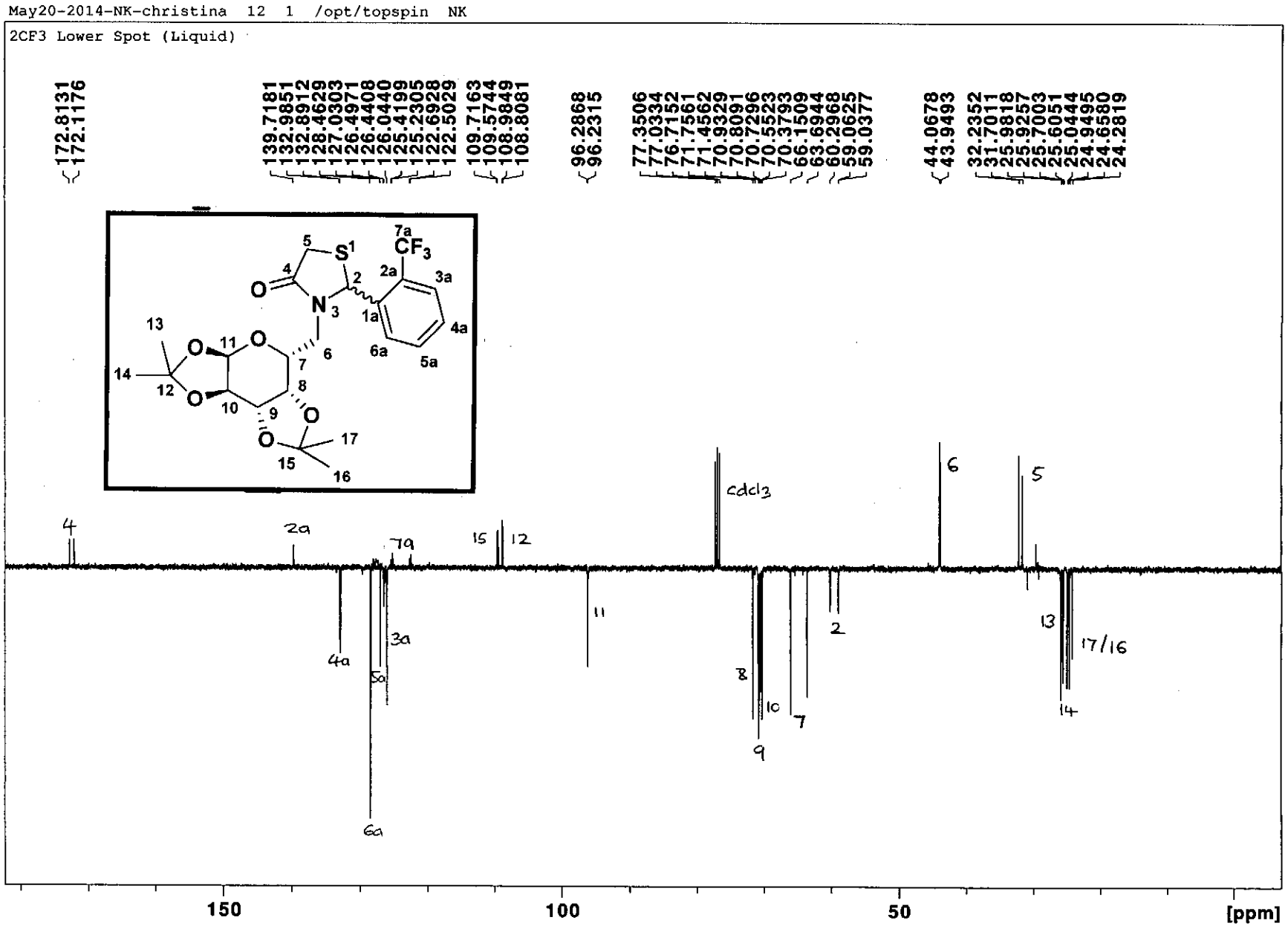
[1]H Spectrum of Compound 5c and 6c: 3-(2,2,7,7-Tetramethyltetrahydro-bis[1,3]dioxolo [4,5-b;4',5'-d]pyran-5-ylmethyl)-2-(2 trifluoromethylphenyl)thiazolidin-4-one



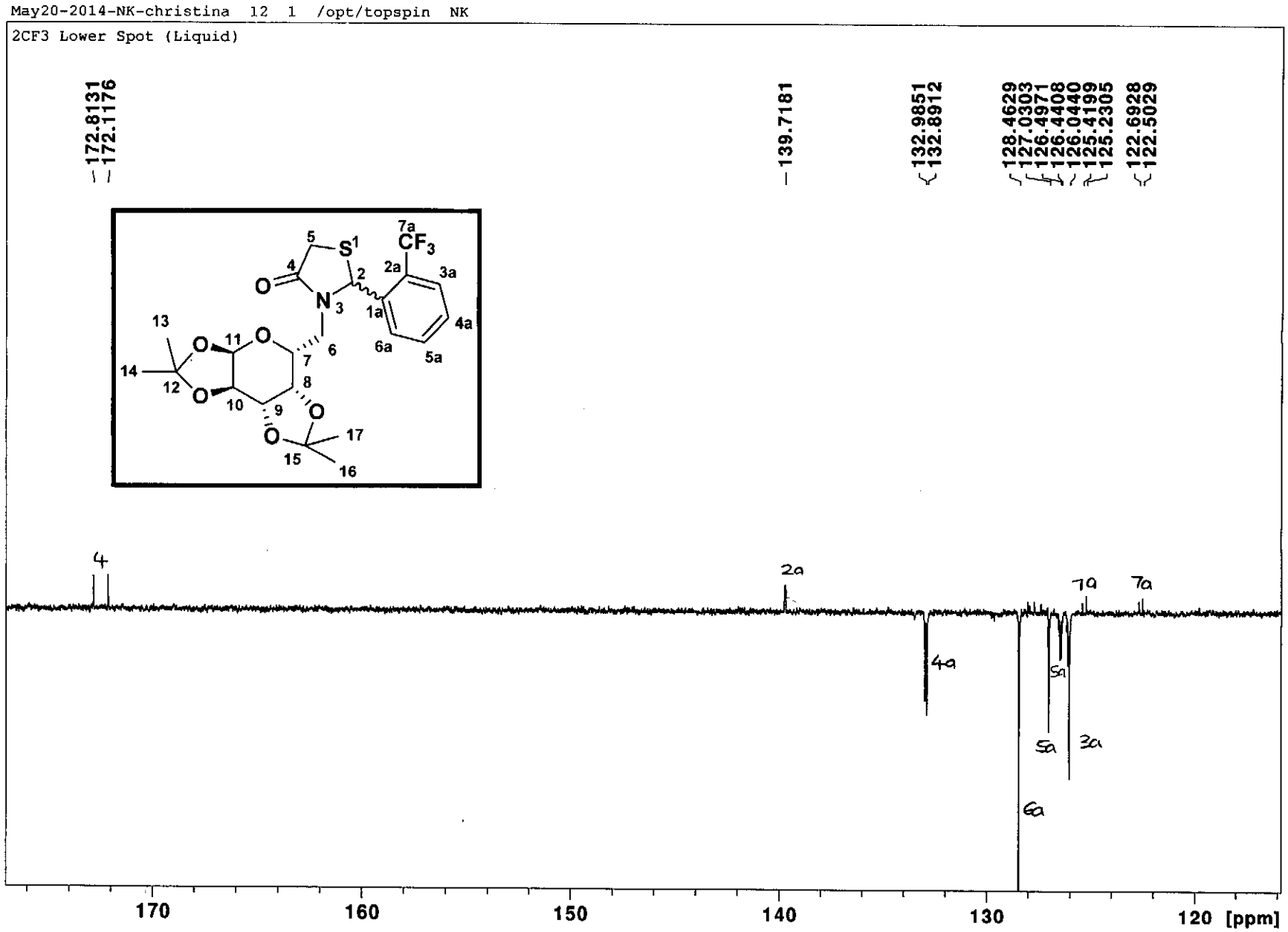
Expanded ^{1}H Spectrum of Compound 5c and 6c: 3-(2,2,7,7-Tetramethyltetrahydro-bis [1,3]dioxolo[4,5-b;4',5'-d]pyran-5-ylmethyl)-2-(2 trifluoromethylphenyl)thiazolidin-4-one



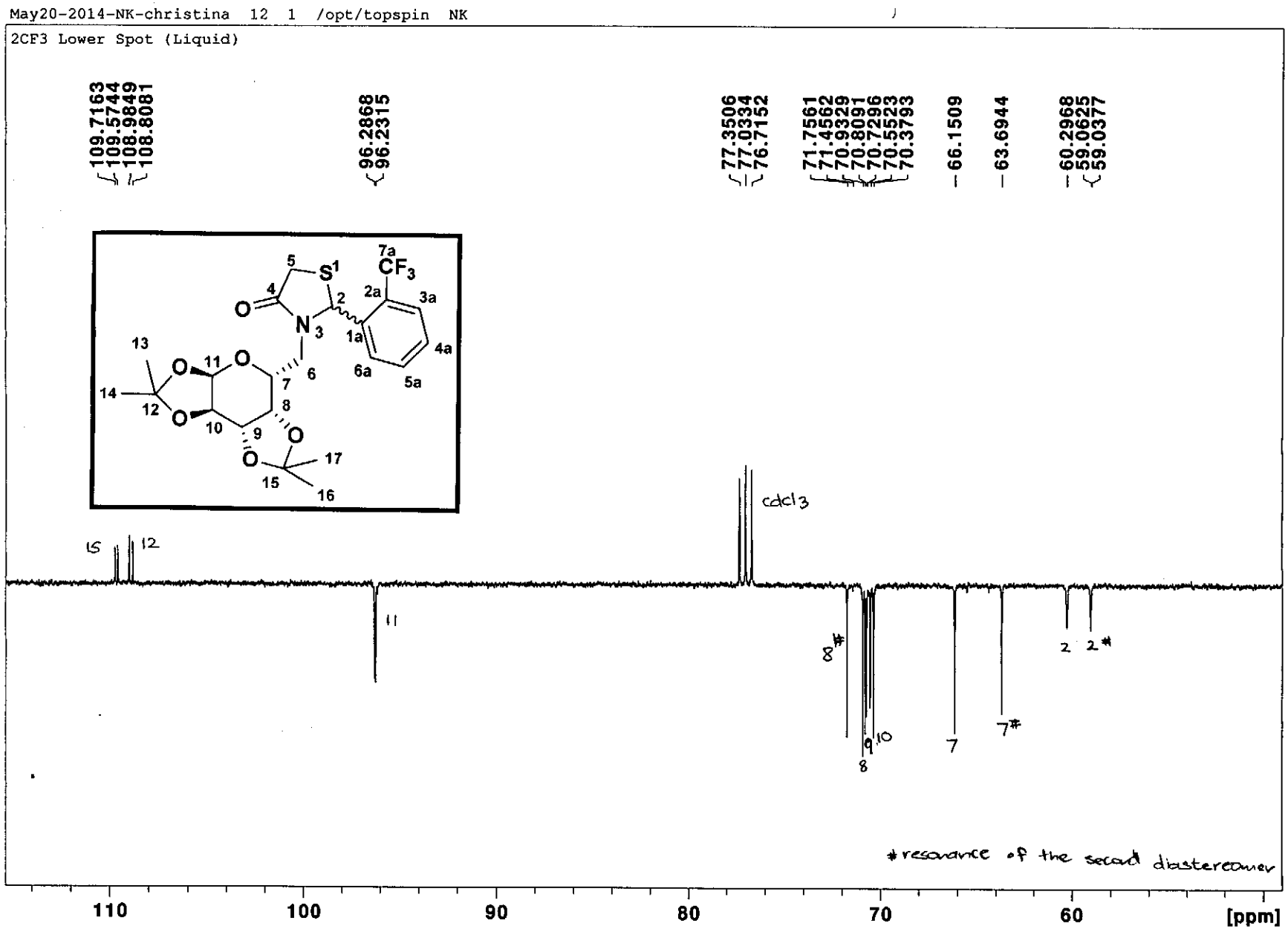
Expanded ^{1}H Spectrum of Compound 5c and 6c: 3-(2,2,7,7-Tetramethyltetrahydro-bis [1,3]dioxolo[4,5-b;4',5'-d]pyran-5-ylmethyl)-2-(2 trifluoromethylphenyl)thiazolidin-4-one



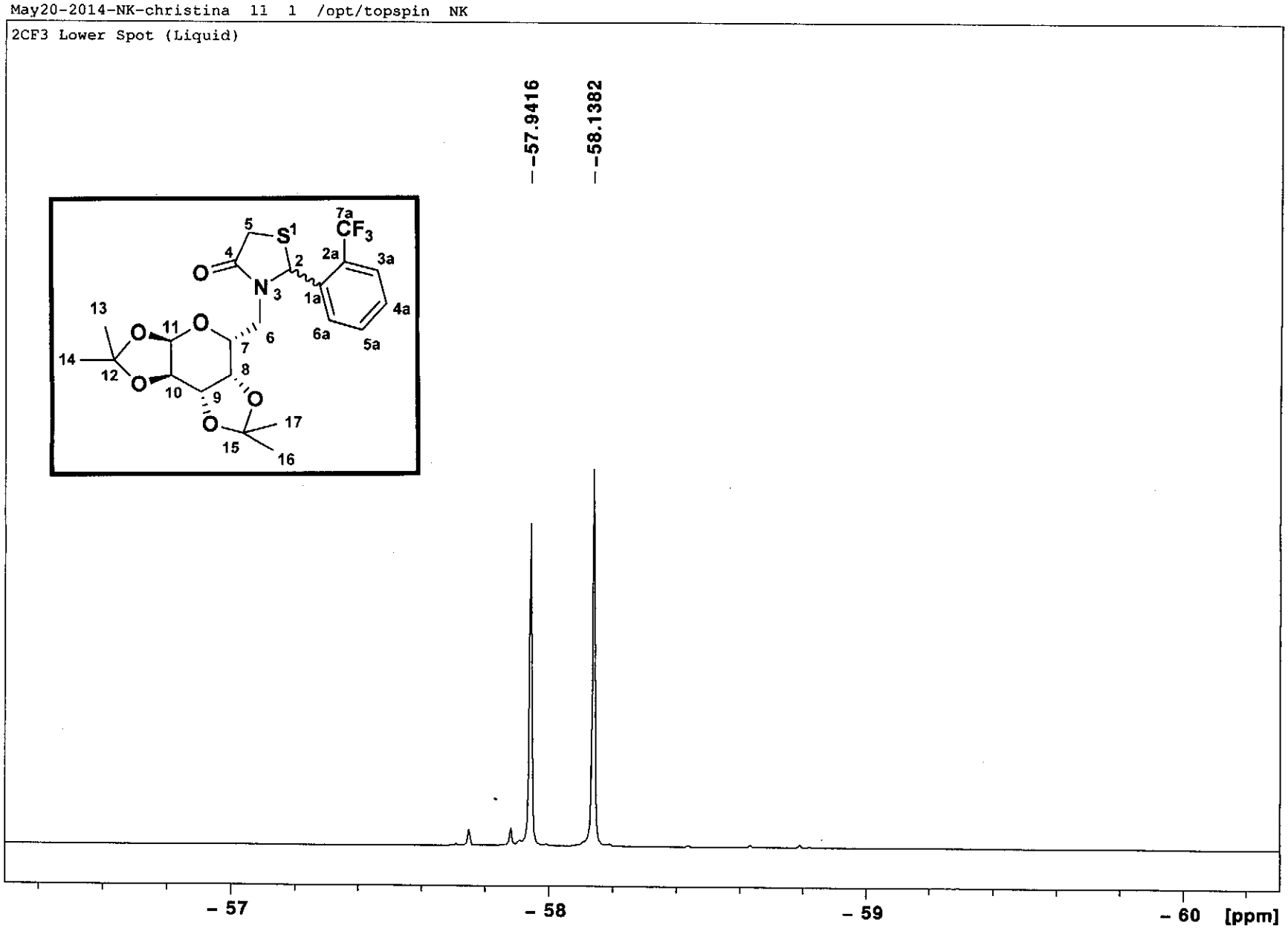
^{13}C Spectrum of Compound 5c and 6c: 3-(2,2,7,7-Tetramethyltetrahydro-bis [1,3] dioxolo [4,5-b;4',5'-d]pyran-5-ylmethyl)-2-(2 trifluoromethylphenyl)thiazolidin-4-one



Expanded ^{13}C Spectrum of Compound 5c and 6c: 3-(2,2,7,7-Tetramethyltetrahydro-bis [1,3]dioxolo[4,5-b;4',5'-d]pyran-5-ylmethyl)-2-(2 trifluoromethylphenyl)thiazolidin-4-one

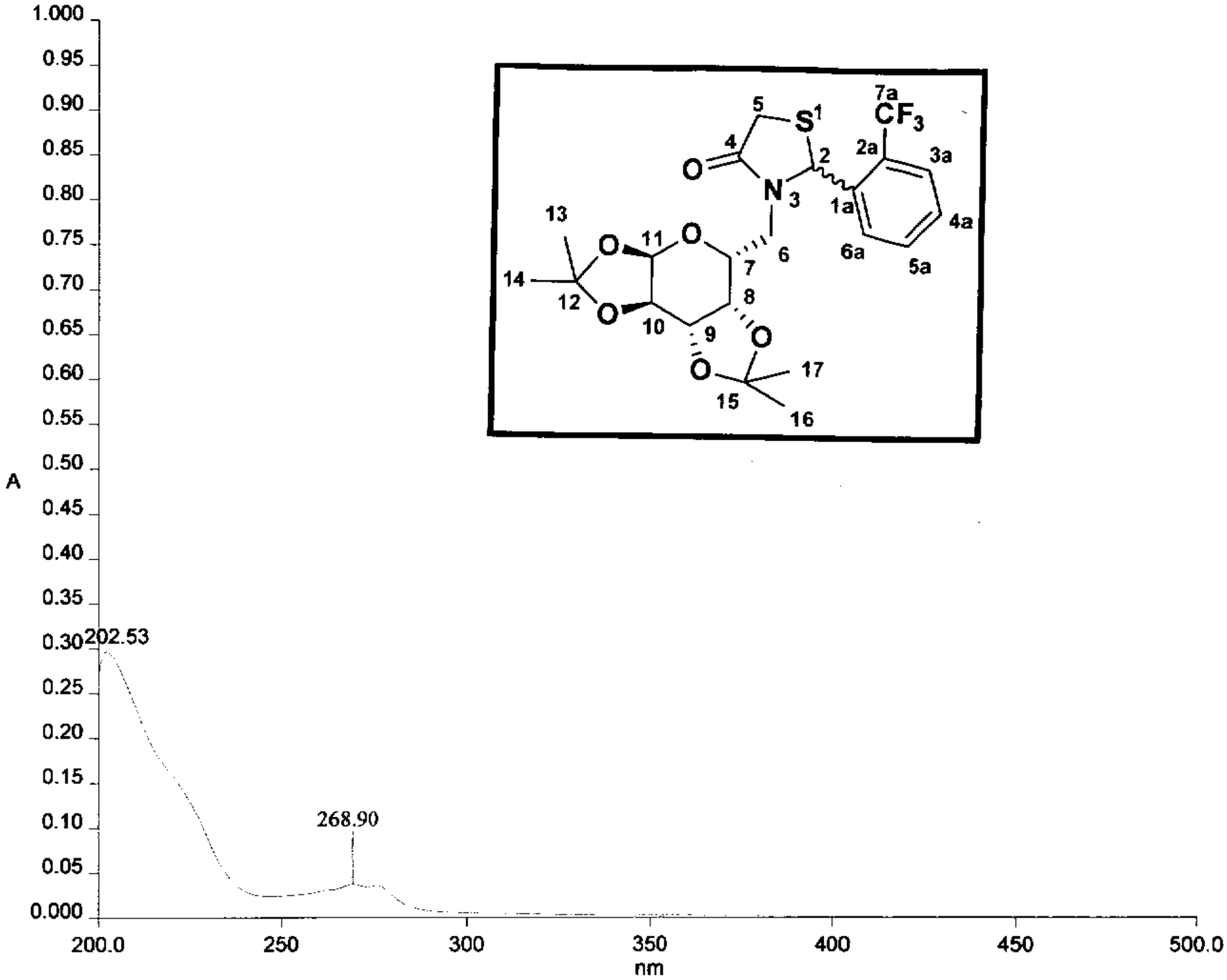


Expanded ^{13}C Spectrum of Compound 5c and 6c: 3-(2,2,7,7-Tetramethyltetrahydro-bis [1,3]dioxolo[4,5-b;4',5'-d]pyran-5-ylmethyl)-2-(2 trifluoromethylphenyl)thiazolidin-4-one



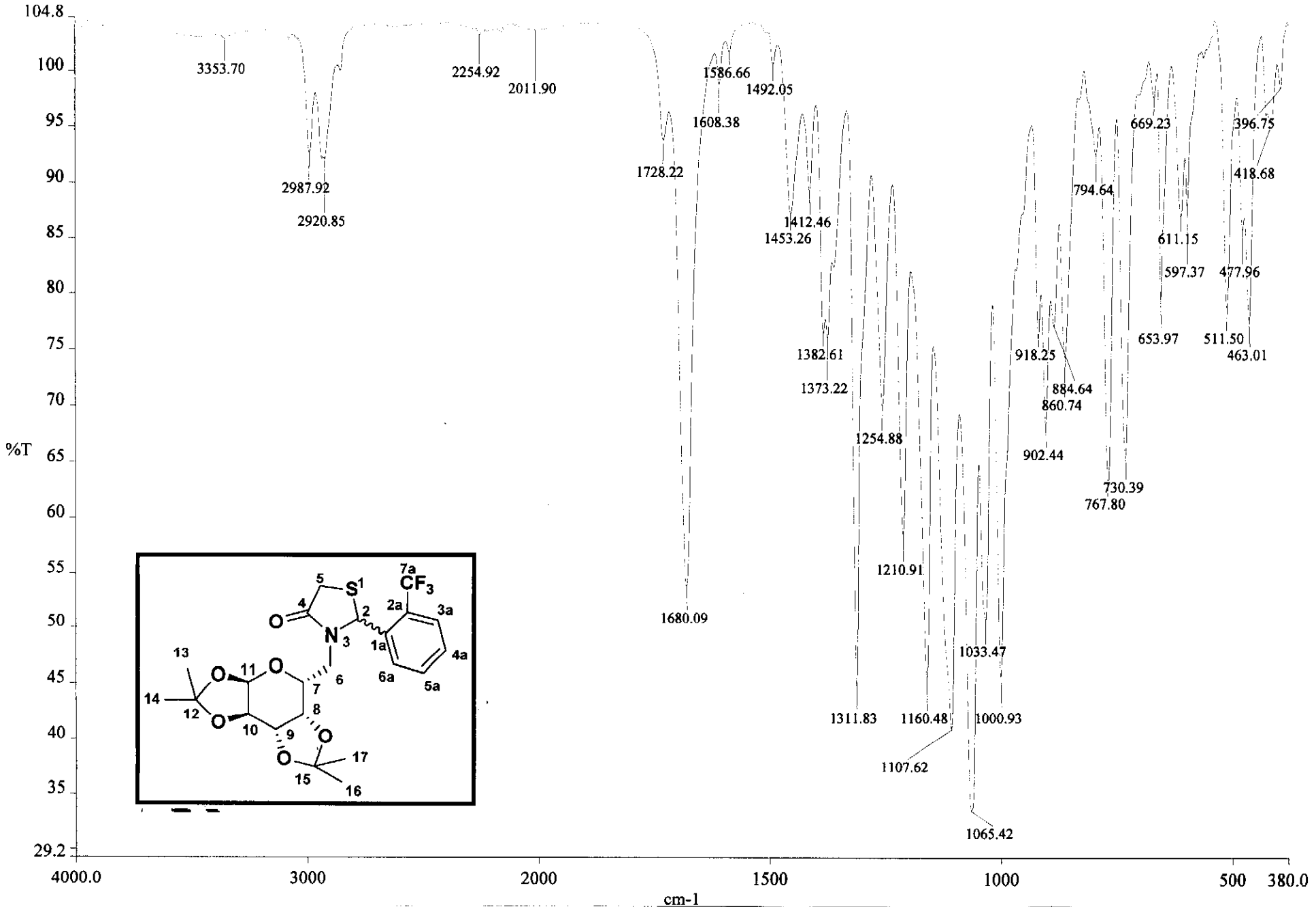
^{19}F Spectrum of Compound 5c and 6c: 3-(2,2,7,7-Tetramethyltetrahydro-bis[1,3]dioxolo [4,5-b;4',5'-d]pyran-5-ylmethyl)-2-(2 trifluoromethylphenyl)thiazolidin-4-one

Date: 2014/06/05 Time: 04:20:41 PM



2CF3LS.SP - 2014/06/05

Ultraviolet Spectrum of Compound 5c and 6c: 3-(2,2,7,7-Tetramethyltetrahydro-bis [1,3]dioxolo[4,5-b;4',5'-d]pyran-5-ylmethyl)-2-(2 trifluoromethylphenyl)thiazolidin-4-one

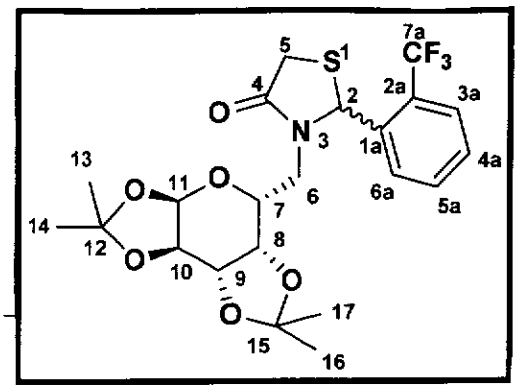


c:\pel_data\spectra\christina\2cf3 ls.001

Infrared Spectrum of Compound 5c and 6c: : 3-(2,2,7,7-Tetramethyltetrahydro-bis [1,3]dioxolo[4,5-b;4',5'-d]pyran-5-ylmethyl)-2-(2 trifluoromethylphenyl)thiazolidin-4-one

==== Shimadzu LCsolution Analysis Report ====

Acquired by	: Admin
Sample Name	: 2-trifloro Is formic buffer
Sample ID	: 2-trifloro Is formic buffer
Vail #	: 2
Injection Volume	: 100 uL
Data File Name	: 2-trifloro Is formic buffer.lcd
Method File Name	: Pramod 09jun 2014.lcm
Batch File Name	: suger thiozolidinon.lcb
Report File Name	: Default.lcr
Data Acquired	: 2014/06/17 11:48:37 AM
Data Processed	: 2014/06/17 12:28:40 PM



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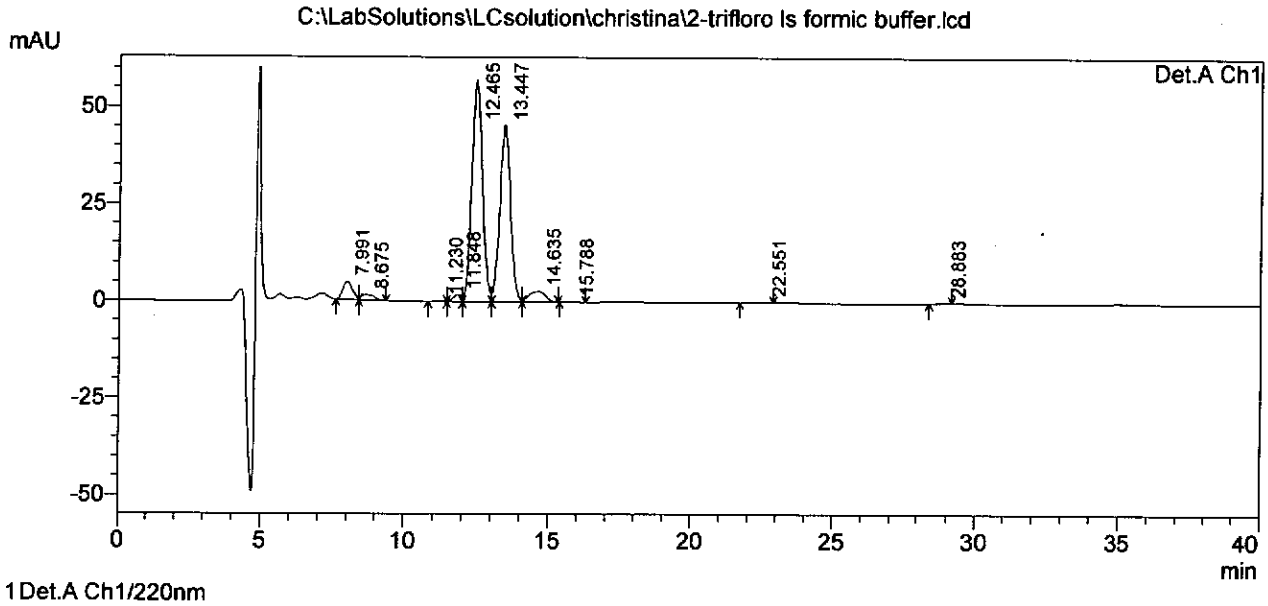


1 Det.A Ch1/220nm

<Results>

PeakTable C:\LabSolutions\LCsolution\christina\2-trifloro Is formic buffer.lcd

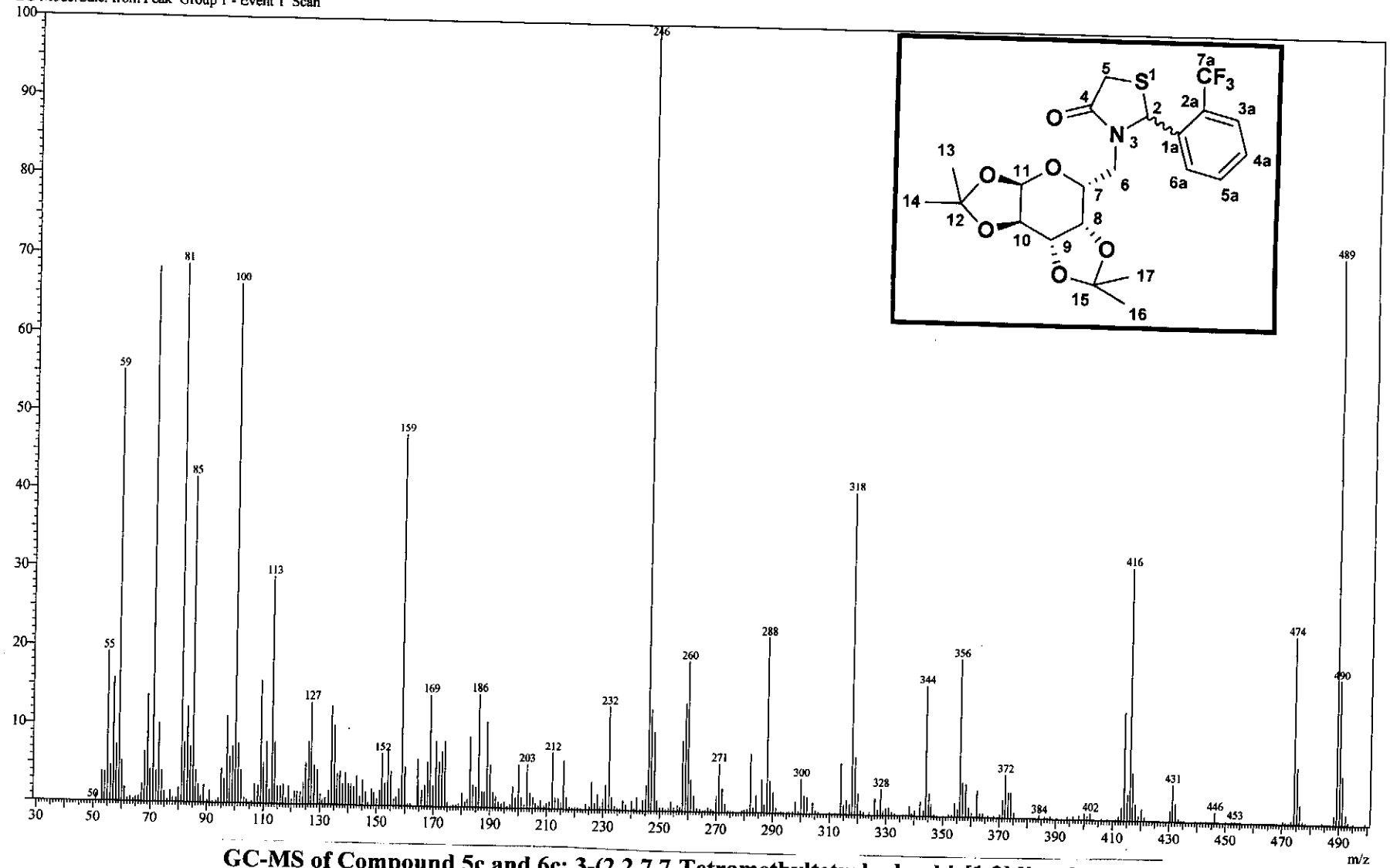
Detector A Ch1 220nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	7.991	109758	4724	3.713	4.132
2	8.675	46808	1419	1.583	1.241
3	11.230	8690	355	0.294	0.311
4	11.848	38473	1863	1.301	1.630
5	12.465	1447383	57076	48.961	49.929
6	13.447	1178784	45611	39.875	39.900
7	14.635	109195	2766	3.694	2.419
8	15.788	5833	225	0.197	0.197
9	22.551	8229	176	0.278	0.154
10	28.883	3018	98	0.102	0.086
Total		2956171	114313	100.000	100.000

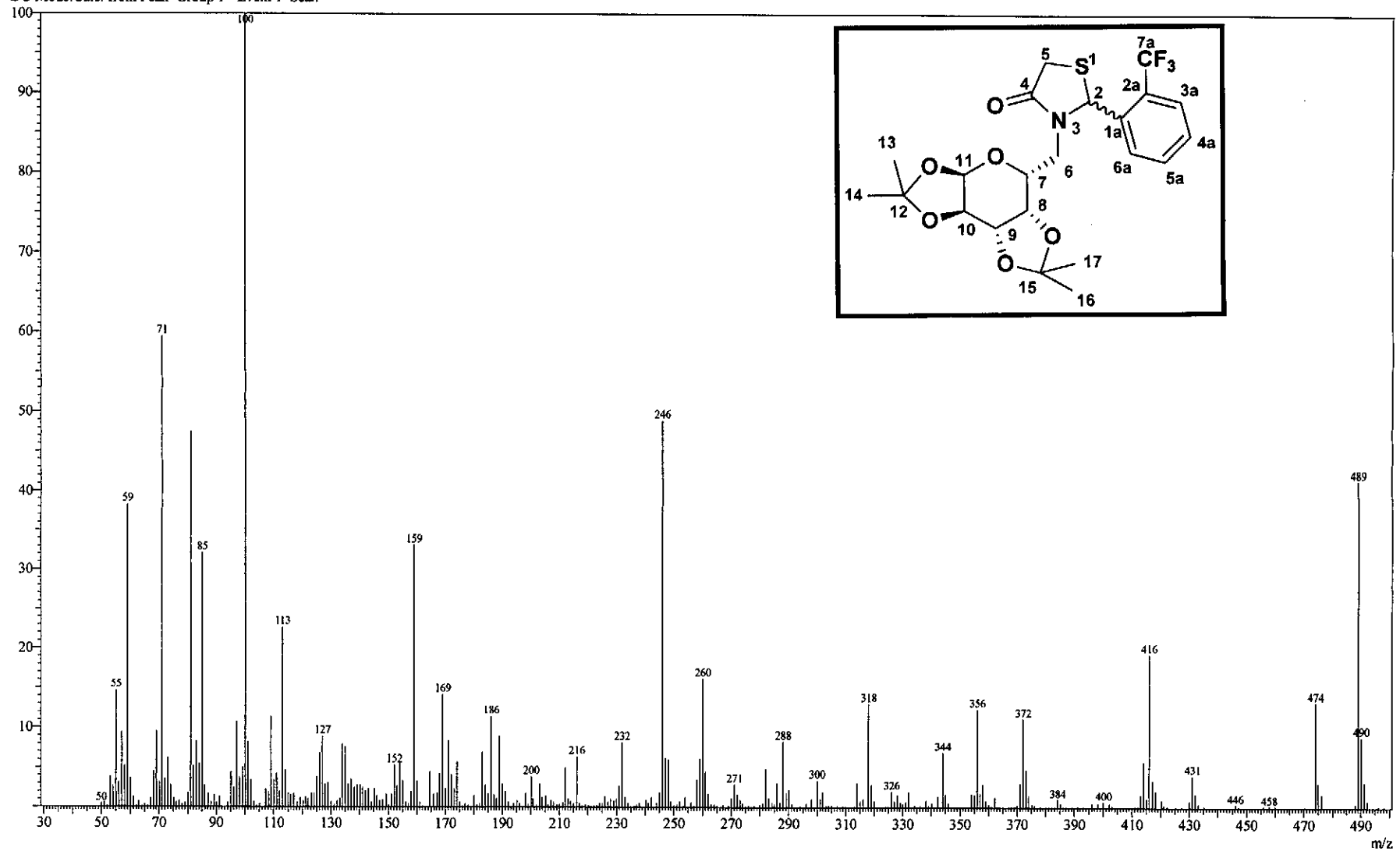
HPLC of Compound 5c and 6c: 3-(2,2,7,7-Tetramethyltetrahydro-bis[1,3]dioxolo[4,5-b;4',5'-d]pyran-5-ylmethyl)-2-(2 trifluoromethylphenyl)thiazolidin-4-one

Spectrum

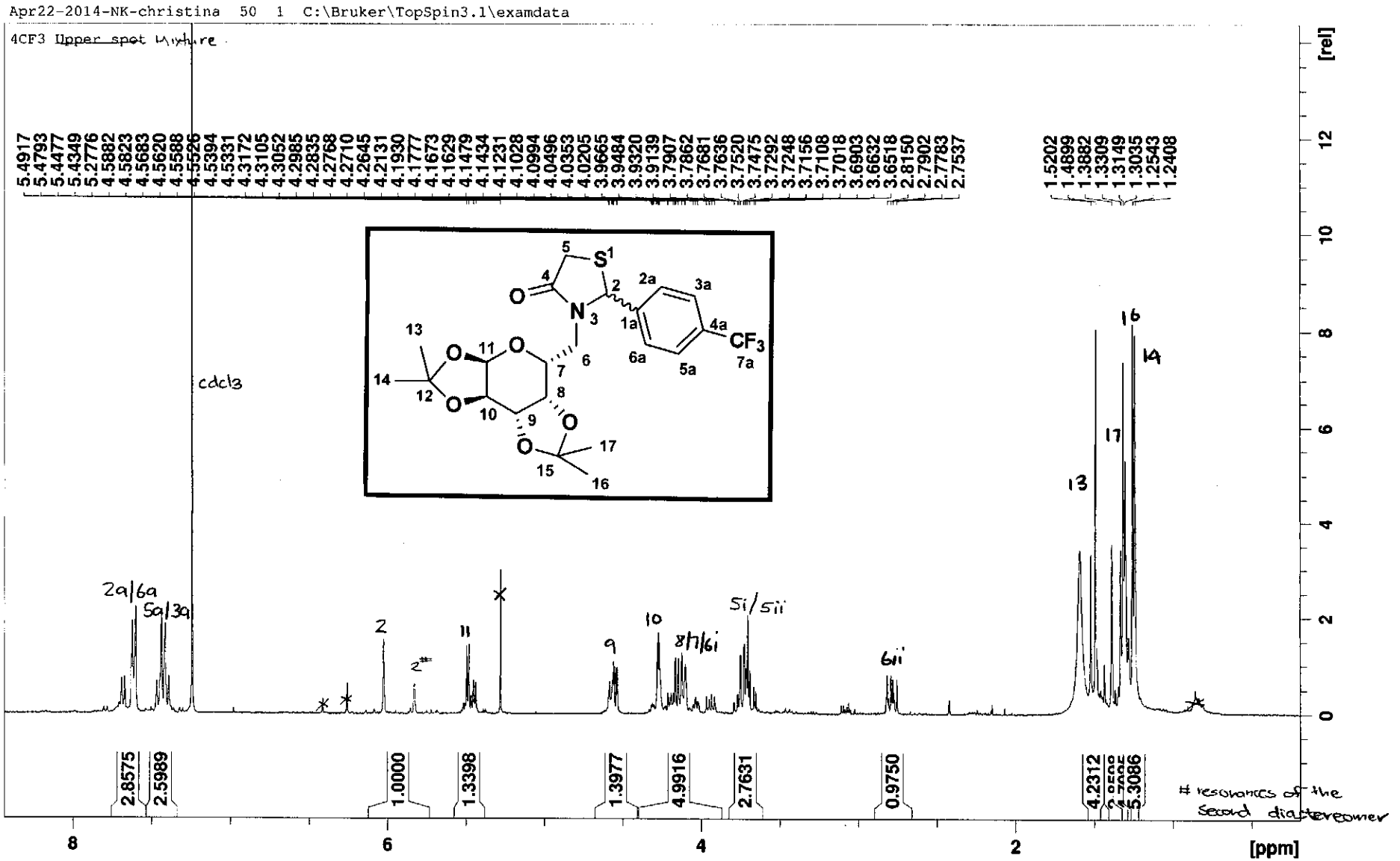
Line#:1 R.Time:15.020(Scan#:2205)
MassPeaks:579
RawMode:Averaged 15.015-15.025(2204-2206) BasePeak:246(34710)
BG Mode:Calc. from Peak Group 1 - Event 1 Scan



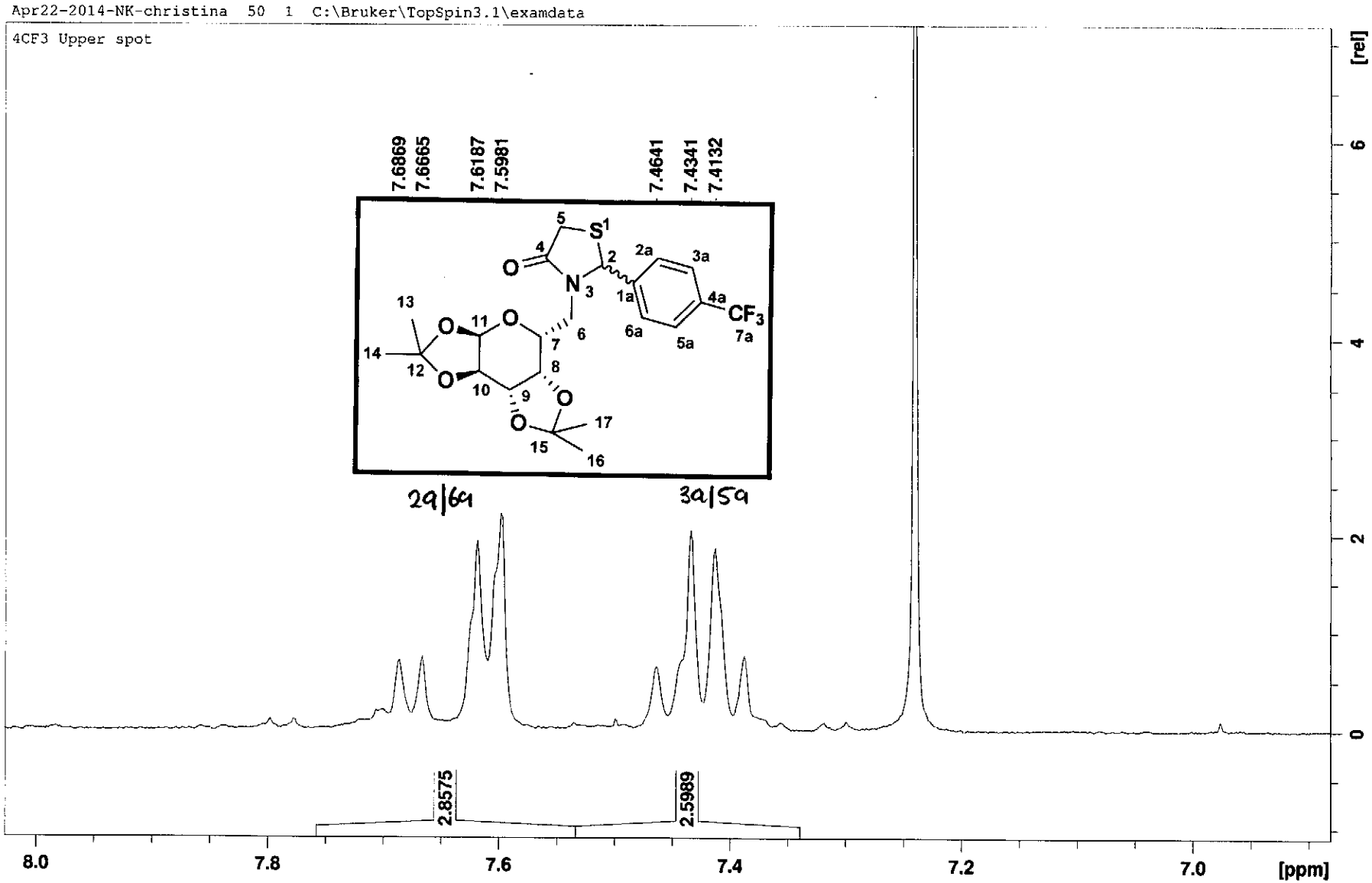
GC-MS of Compound 5c and 6c: 3-(2,2,7,7-Tetramethyltetrahydro-bis[1,3]dioxolo[4,5-b;4',5'-d]pyran-5-ylmethyl)-2-(2 trifluoromethylphenyl)thiazolidin-4-one



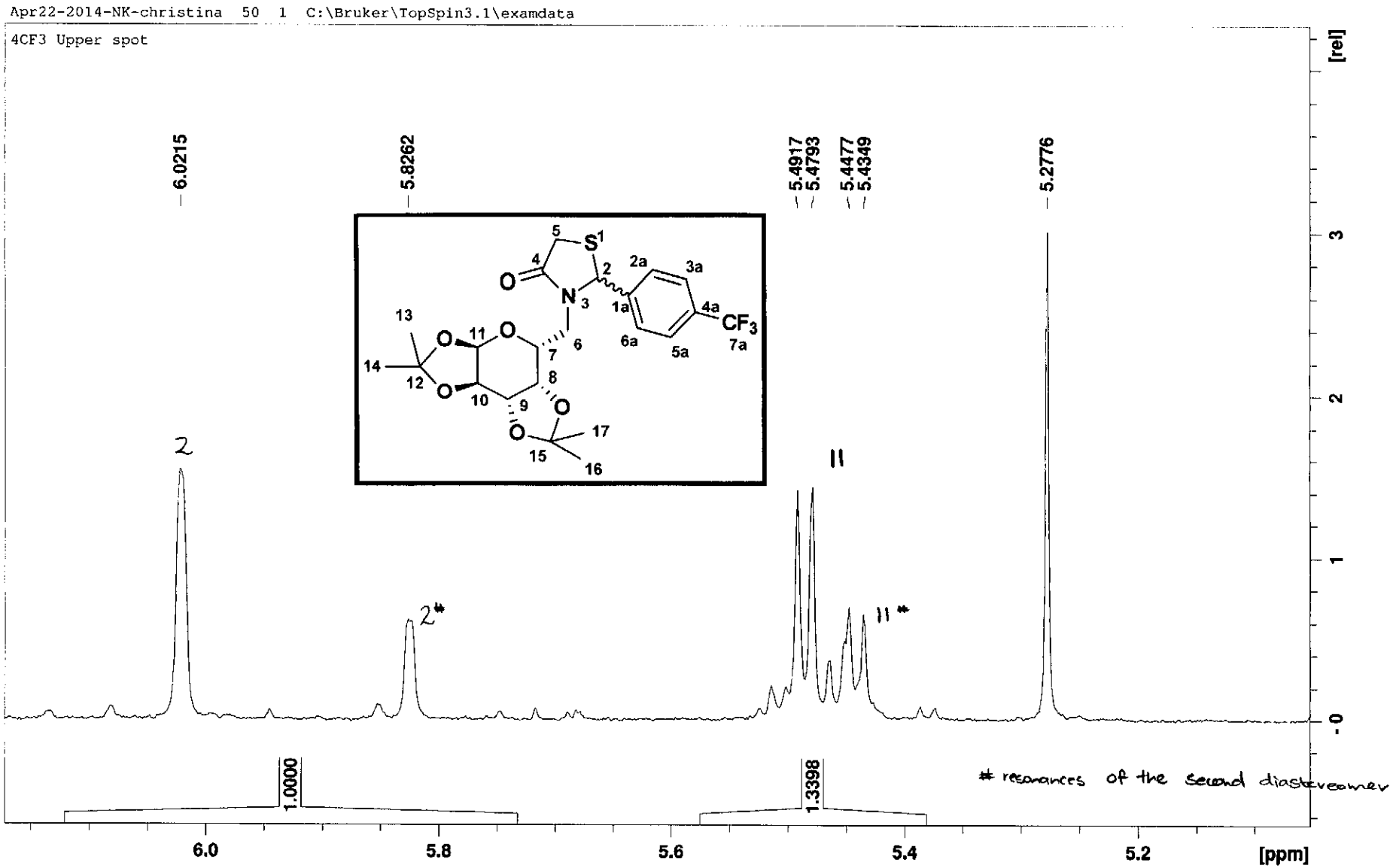
GC-MS of Compound 5c and 6c: 3-(2,2,7,7-Tetramethyltetrahydro-bis[1,3]dioxolo[4,5-b;4',5'-d]pyran-5-ylmethyl)-2-(2 trifluoromethylphenyl)thiazolidin-4-one



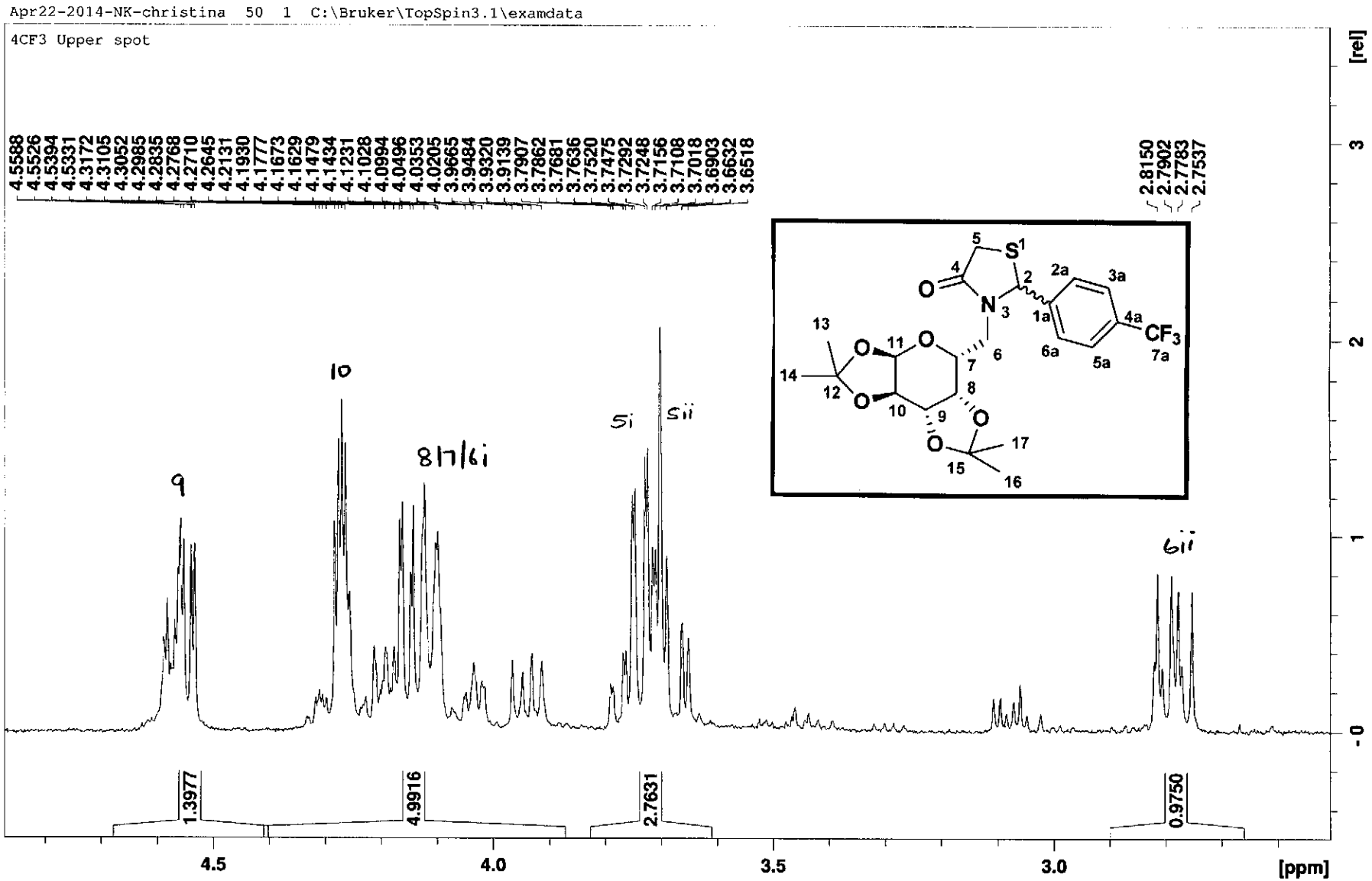
^{1}H Spectrum of Compound 5d and 6d: 3-(2,2,7,7-Tetramethyltetrahydro-bis[1,3]dioxolo [4,5-b;4',5'-d]pyran-5-ylmethyl)-2-(4-trifluoromethylphenyl)thiazolidin-4-one



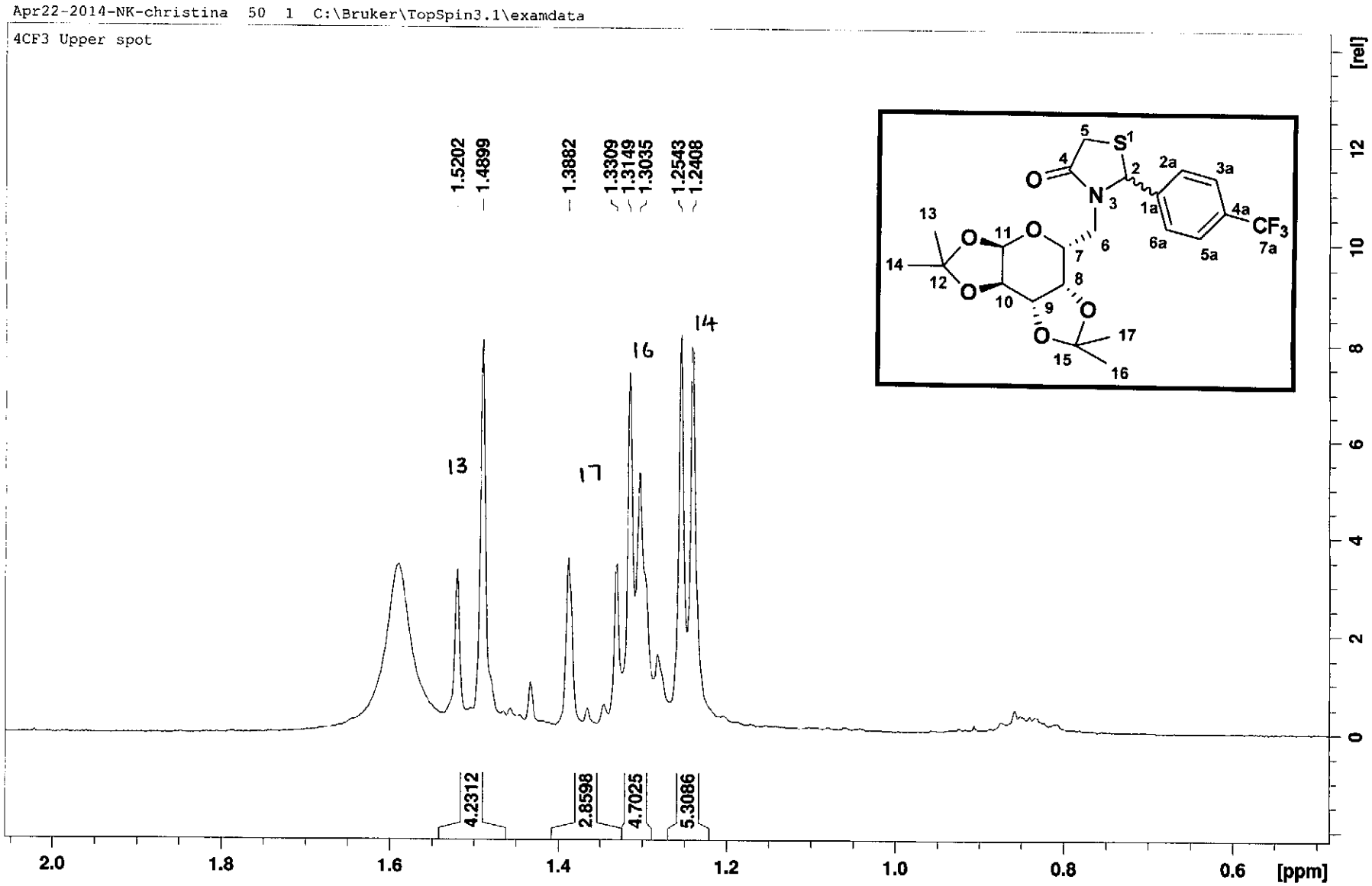
Expanded ^{1}H Spectrum of Compound 5d and 6d: 3-(2,2,7,7-Tetramethyltetrahydro-bis [1,3]dioxolo[4,5-b;4',5'-d]pyran-5-ylmethyl)-2-(4-trifluoromethylphenyl)thiazolidin-4-one



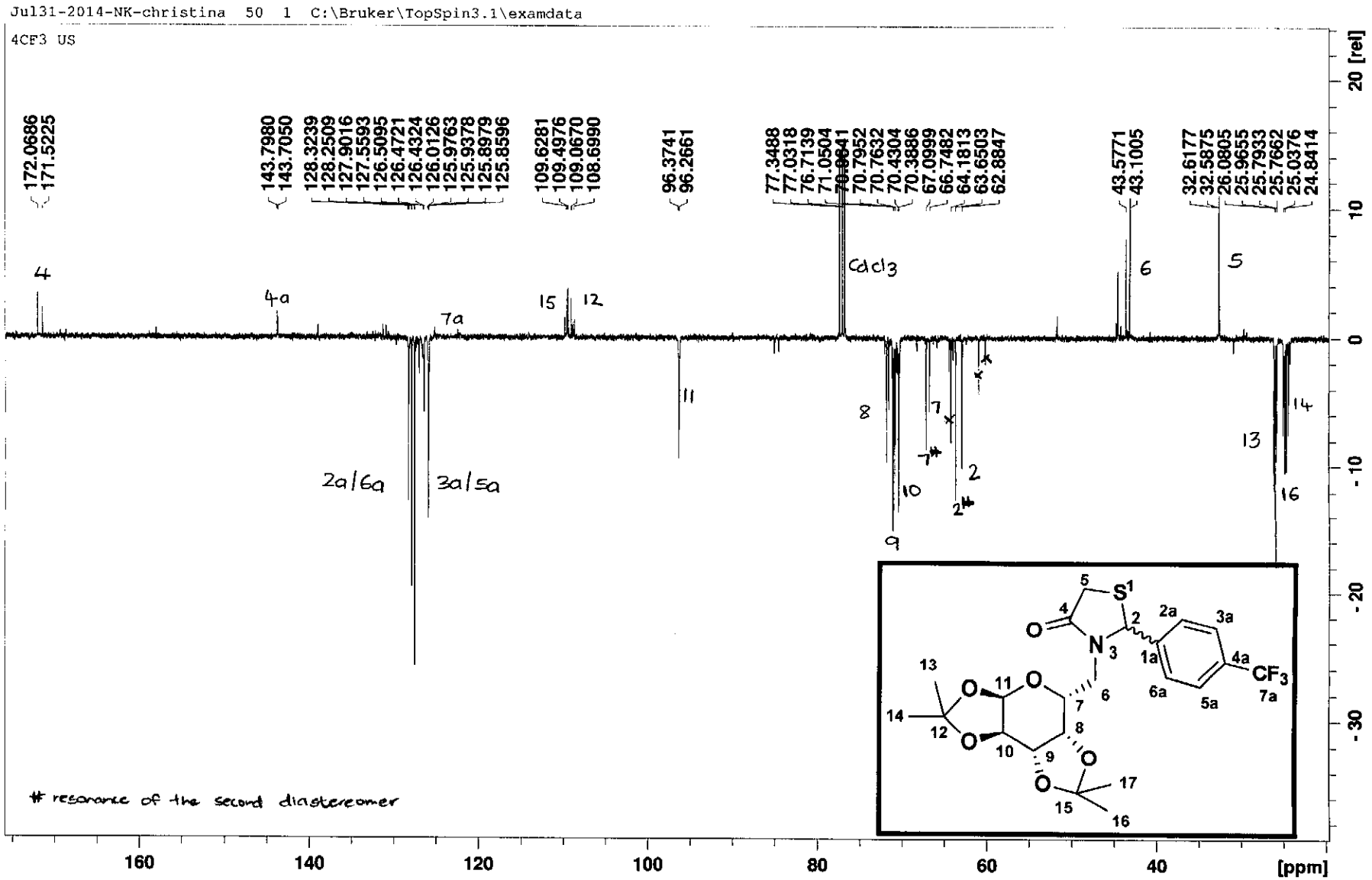
Expanded ^{1}H Spectrum of Compound 5d and 6d: 3-(2,2,7,7-Tetramethyltetrahydro-bis [1,3]dioxolo[4,5-b;4',5'-d]pyran-5-ylmethyl)-2-(4-trifluoromethylphenyl)thiazolidin-4-one



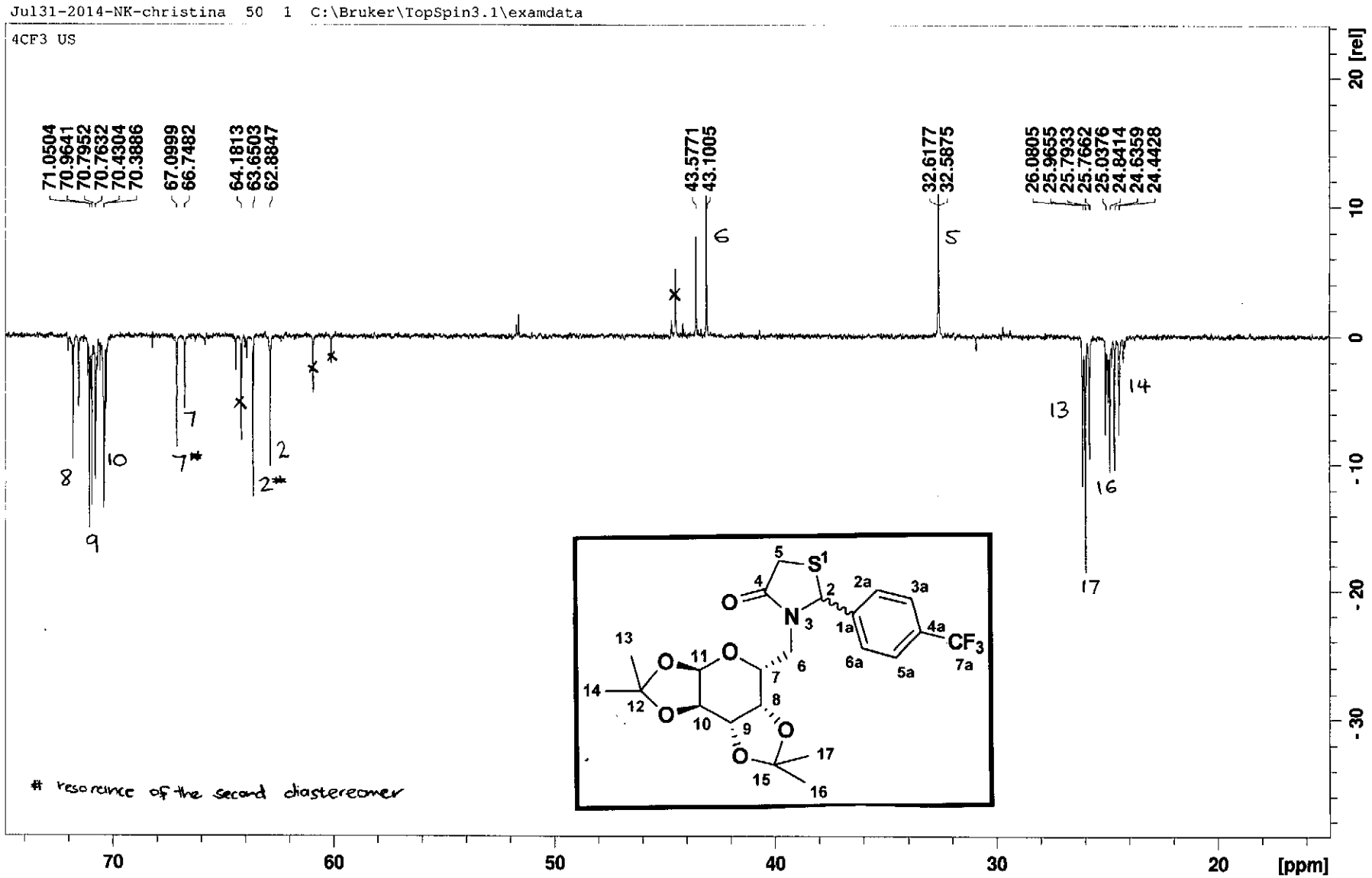
Expanded ^{1}H Spectrum of Compound 5d and 6d: 3-(2,2,7,7-Tetramethyltetrahydro-bis [1,3]dioxolo[4,5-b;4',5'-d]pyran-5-ylmethyl)-2-(4-trifluoromethylphenyl)thiazolidin-4-one



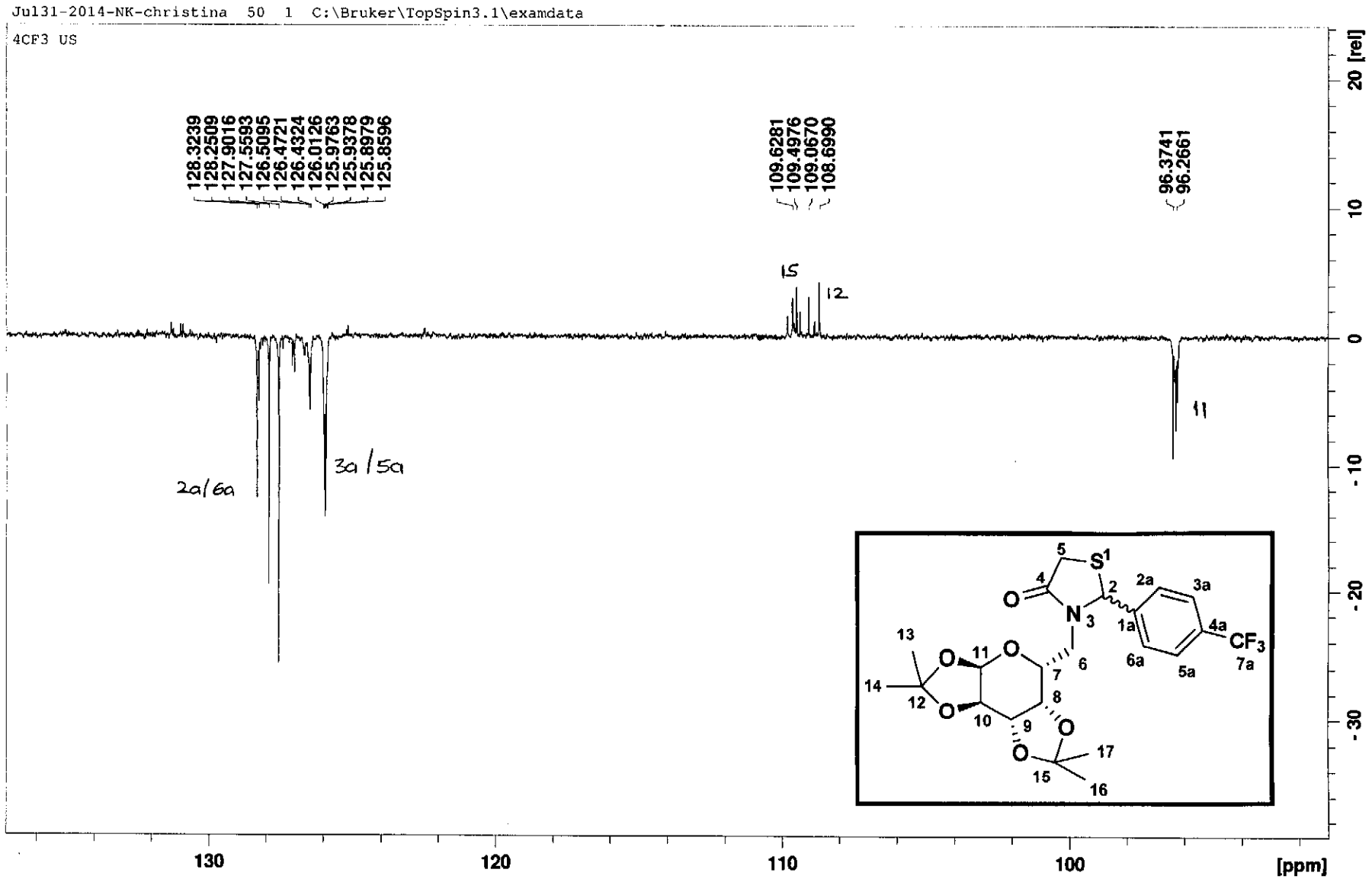
Expanded ^{1}H Spectrum of Compound 5d and 6d: 3-(2,2,7,7-Tetramethyltetrahydro-bis [1,3]dioxolo[4,5-b;4',5'-d]pyran-5-ylmethyl)-2-(4-trifluoromethylphenyl)thiazolidin-4-one



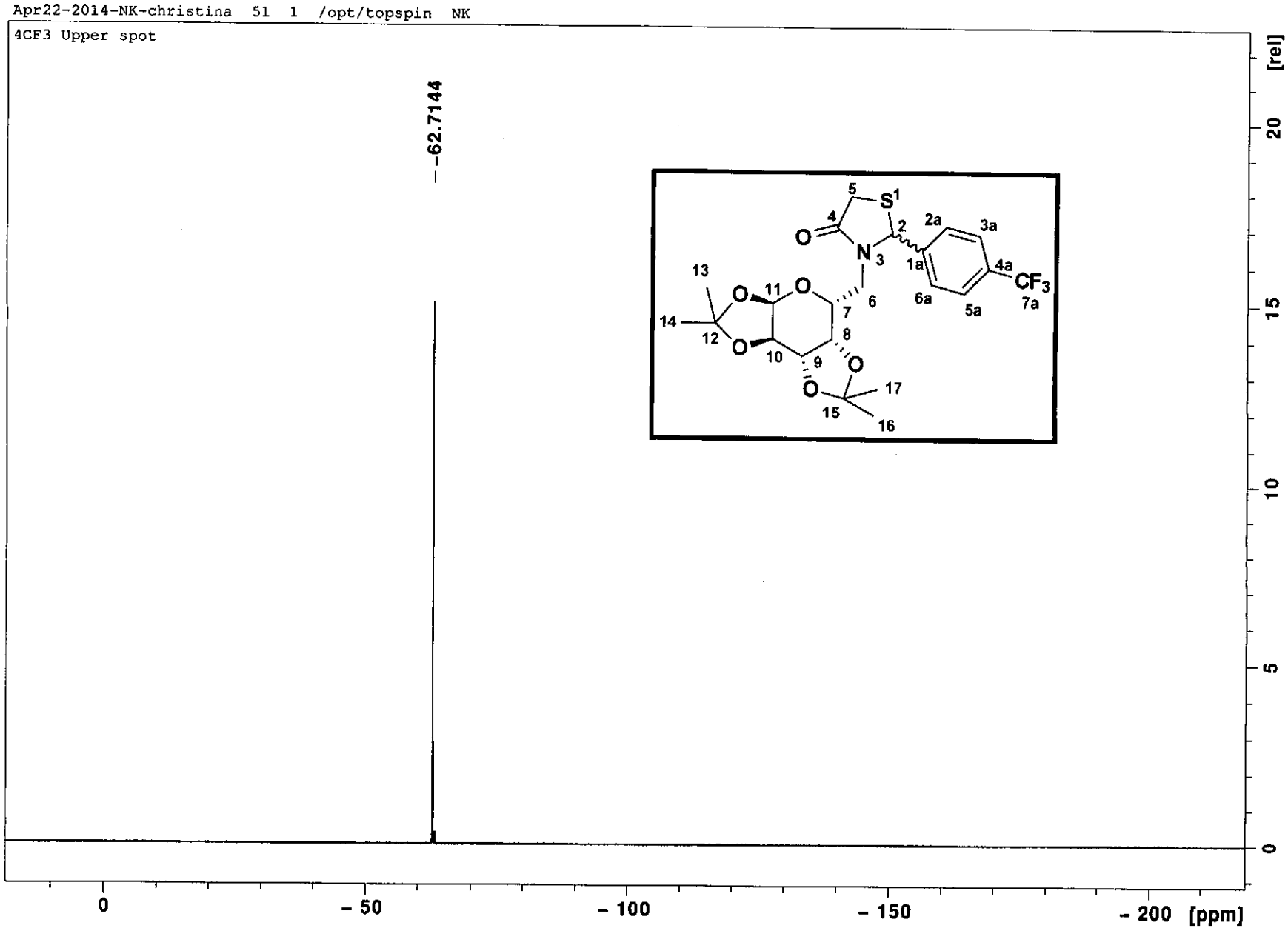
^{13}C Spectrum of Compound 5d and 6d: 3-(2,2,7,7-Tetramethyltetrahydro-bis [1,3] dioxolo[4,5-b;4',5'-d]pyran-5-ylmethyl)-2-(4-trifluoromethylphenyl)thiazolidin-4-one



Expanded ^{13}C Spectrum of Compound 5d and 6d: 3-(2,2,7,7-Tetramethyltetrahydro-bis [1,3]dioxolo[4,5-b;4',5'-d]pyran-5-ylmethyl)-2-(4-trifluoromethylphenyl)thiazolidin-4-one

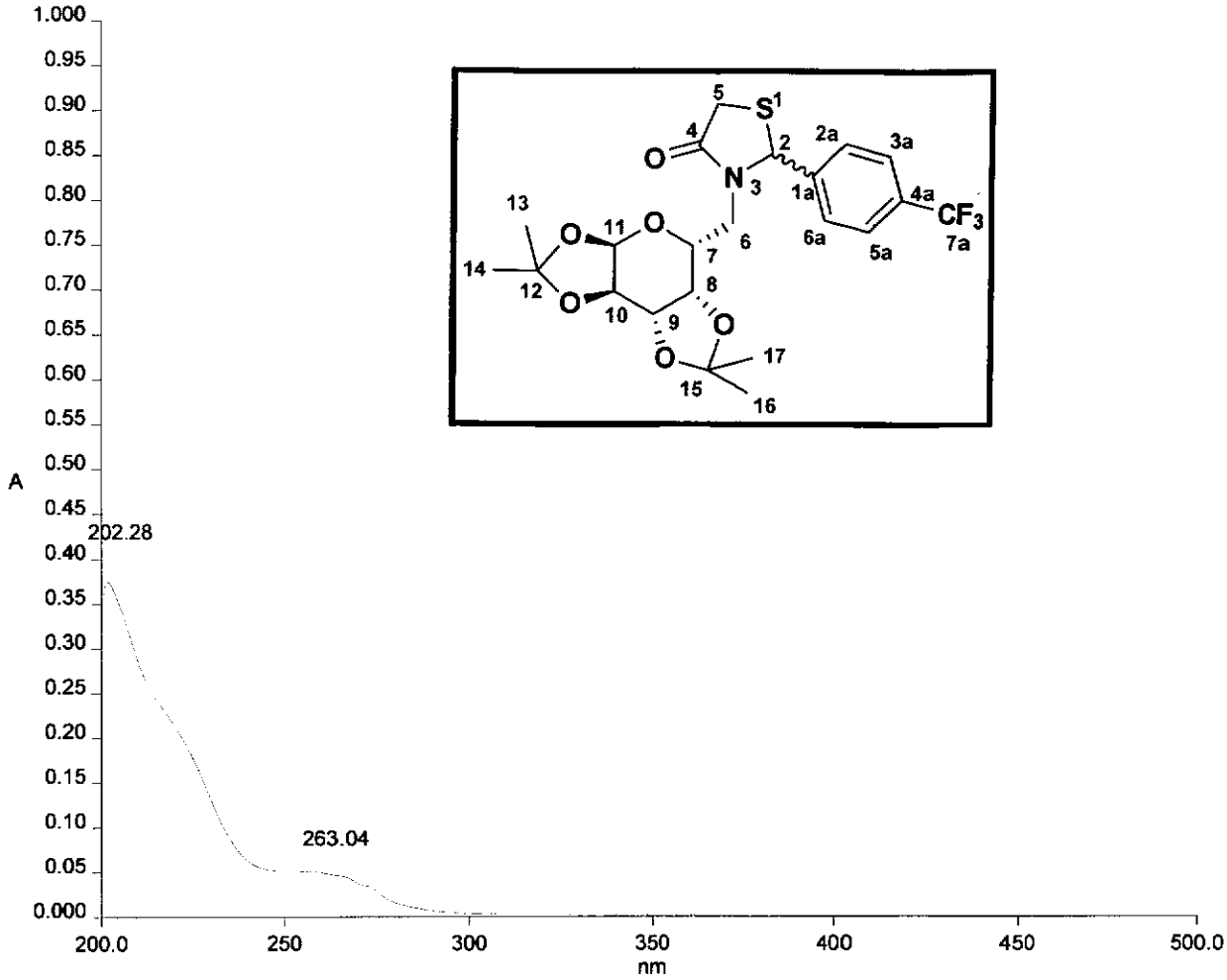


Expanded ^{13}C Spectrum of Compound 5d and 6d: 3-(2,2,7,7-Tetramethyltetrahydro-bis [1,3]dioxolo[4,5-b;4',5'-d]pyran-5-ylmethyl)-2-(4-trifluoromethylphenyl)thiazolidin-4-one

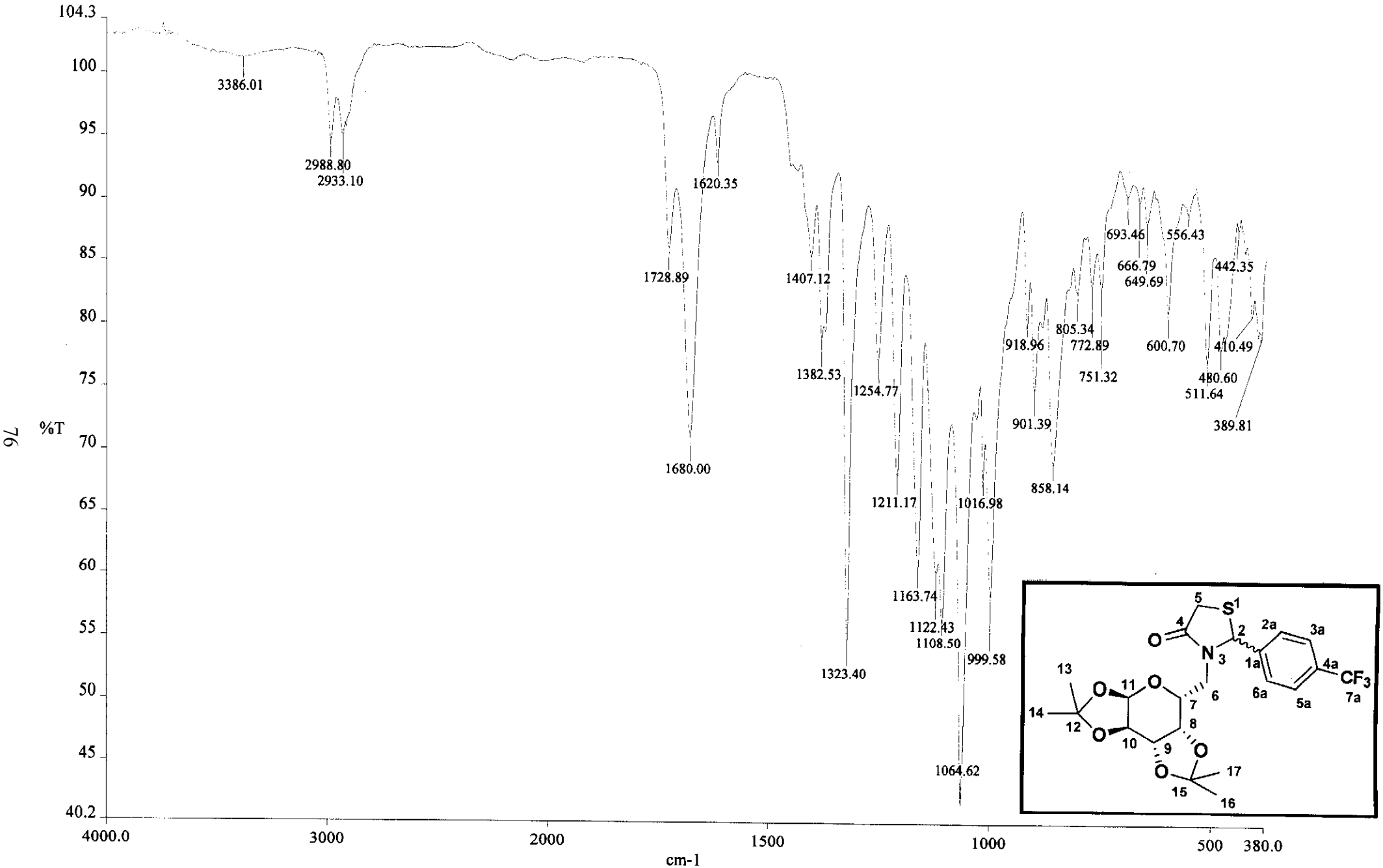


^{19}F Spectrum of Compound 5d and 6d: 3-(2,2,7,7-Tetramethyltetrahydro-bis [1,3] dioxolo[4,5-b;4',5'-d]pyran-5-ylmethyl)-2-(4-trifluoromethylphenyl)thiazolidin-4-one

Date: 2014/06/06 Time: 08:02:27 AM



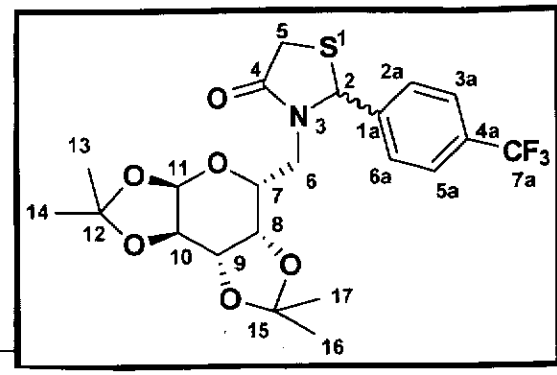
Ultraviolet Spectrum of Compound 5d and 6d: 3-(2,2,7,7-Tetramethyltetrahydro-bis [1,3]dioxolo[4,5-b;4',5'-d]pyran-5-ylmethyl)-2-(4-trifluoromethylphenyl)thiazolidin-4-one



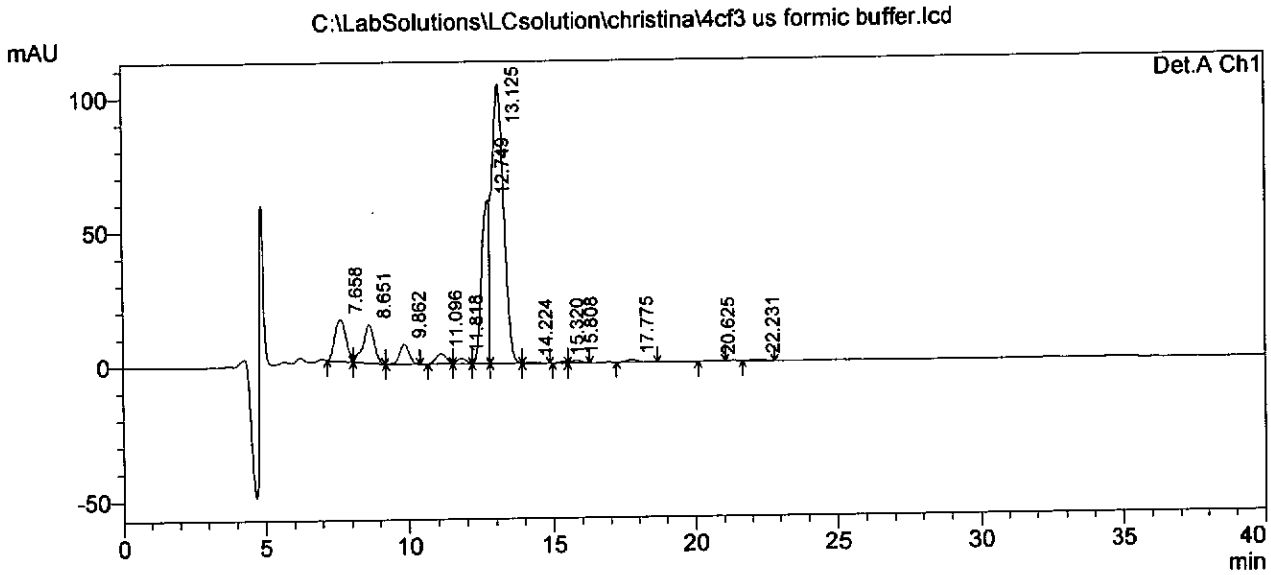
Infrared Spectrum of Compound 5d and 6d: 3-(2,2,7,7-Tetramethyltetrahydro-bis [1,3] dioxolo[4,5-b;4',5'-d]pyran-5-ylmethyl)-2-(4-trifluoromethylphenyl)thiazolidin-4-one

==== Shimadzu LCsolution Analysis Report ====

Acquired by	: Admin
Sample Name	: 4cf3 us formic buffer
Sample ID	: 4cf3 us formic buffer
Vail #	: 1
Injection Volume	: 100 uL
Data File Name	: 4cf3 us formic buffer.lcd
Method File Name	: Pramod 09jun 2014.lcm
Batch File Name	: suger thiozolidinon.lcb
Report File Name	: Default.lcr
Data Acquired	: 2014/06/17 12:32:33 PM
Data Processed	: 2014/06/17 01:12:38 PM



<Chromatogram>



1Det.A Ch1/220nm

<Results>

PeakTable C:\LabSolutions\LCsolution\christina\4cf3 us formic buffer.lcd

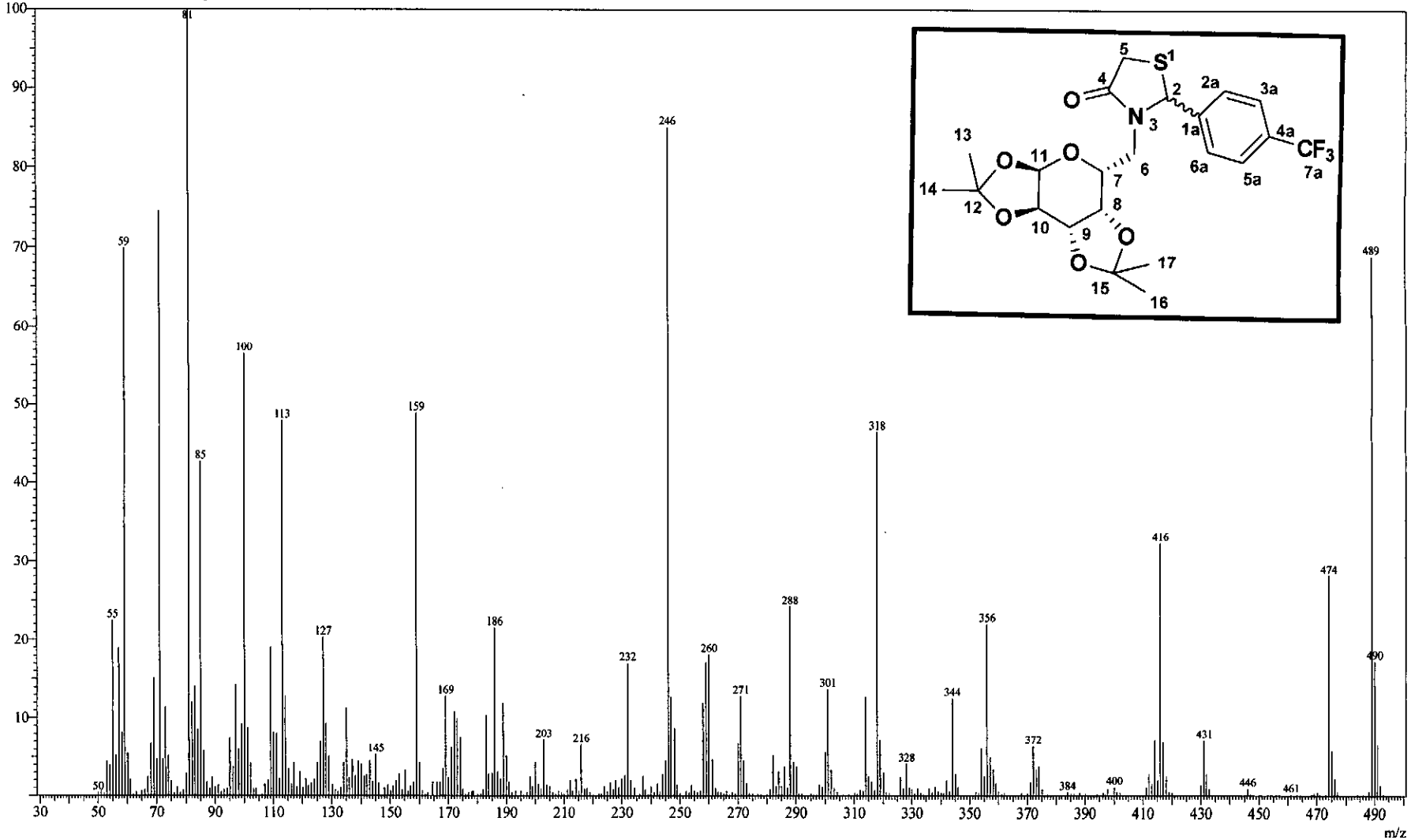
Detector A Ch1 220nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	7.658	422973	15587	8.023	7.371
2	8.651	388195	14299	7.364	6.762
3	9.862	168543	7370	3.197	3.485
4	11.096	92435	3797	1.753	1.796
5	11.818	45325	2043	0.860	0.966
6	12.749	1058088	60708	20.071	28.708
7	13.125	3001636	104155	56.938	49.254
8	14.224	9439	326	0.179	0.154
9	15.320	11605	546	0.220	0.258
10	15.808	25503	1016	0.484	0.480
11	17.775	23485	861	0.445	0.407
12	20.625	7426	257	0.141	0.122
13	22.231	17117	500	0.325	0.237
Total		5271768	211465	100.000	100.000

HPLC of Compound 5d and 6d: 3-(2,2,7,7-Tetramethyltetrahydro-bis [1,3]dioxolo[4,5-b;4',5'-d]pyran-5-ylmethyl)-2-(4-trifluoromethylphenyl)thiazolidin-4-one

Spectrum

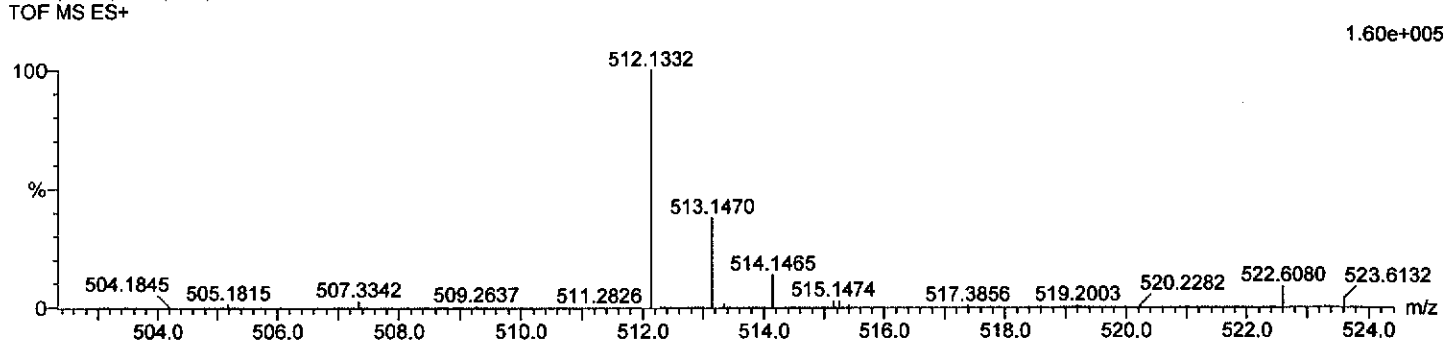
Line#:1 R.Time:14.765(Scan#:2154)
MassPeaks:571
RawMode:Averaged 14.760-14.770(2153-2155) BasePeak:81(51758)
BG Mode:Calc. from Peak Group 1 - Event 1 Scan



GC-MS of Compound 5d and 6d: 3-(2,2,7,7-Tetramethyltetrahydro-bis [1,3]dioxolo[4,5-b;4',5'-d]pyran-5-ylmethyl)-2-(4-trifluoromethylphenyl)thiazolidin-4-one

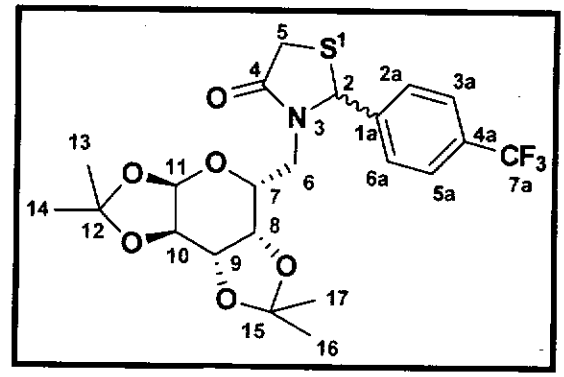
Single Mass Analysis
Tolerance = 4.0 PPM / DBE: min = -1.5, max = 100.0
Element prediction: Off
Number of isotope peaks used for i-FIT = 3

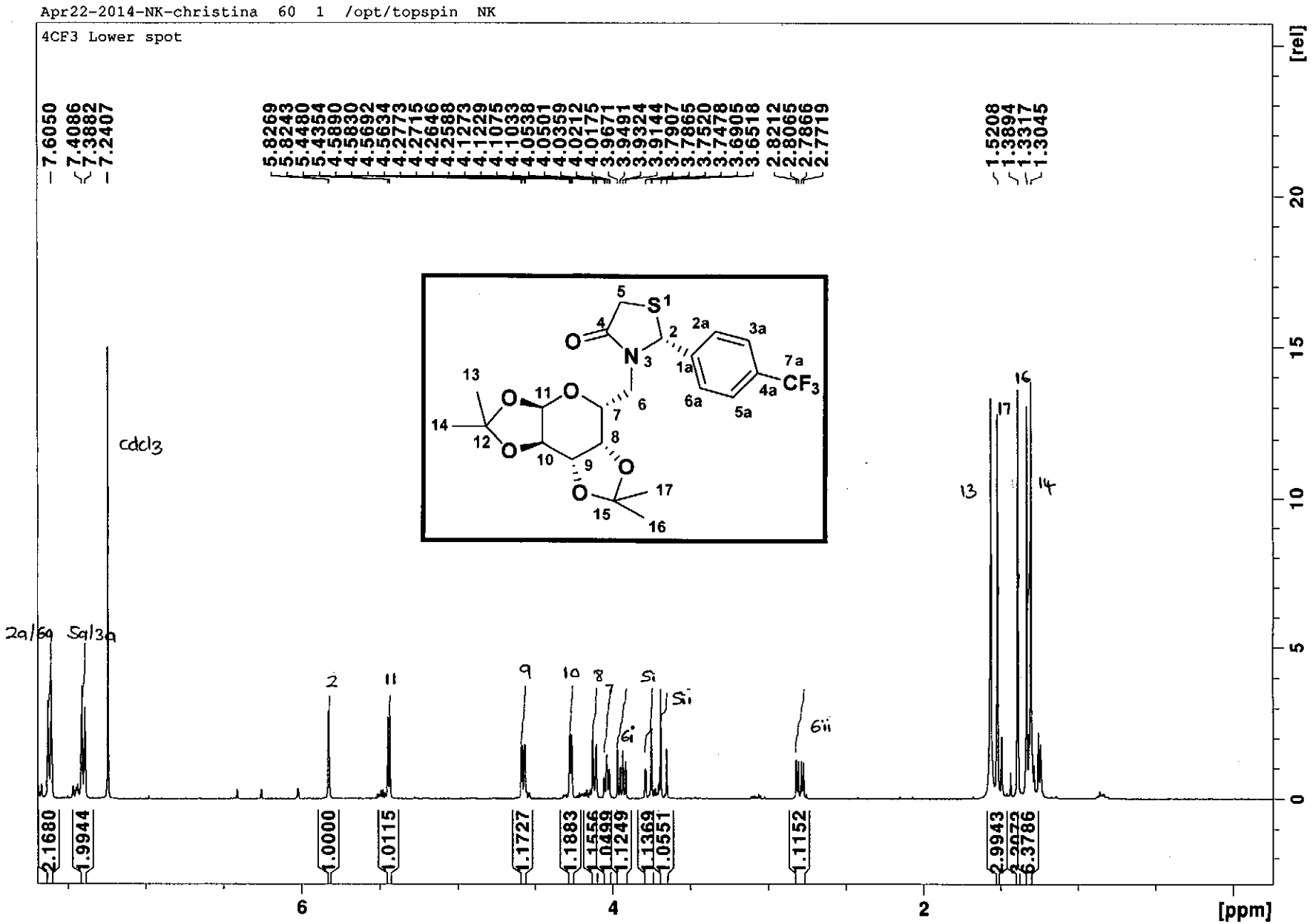
Monoisotopic Mass, Even Electron Ions
35 formula(e) evaluated with 1 results within limits (up to 20 best isotopic matches for each mass)
Elements Used:
C: 20-25 H: 25-30 N: 0-5 O: 5-10 F: 3-3 Na: 0-1 S: 1-1
4 46 (1.518) Cm (1:61)
TOF MS ES+



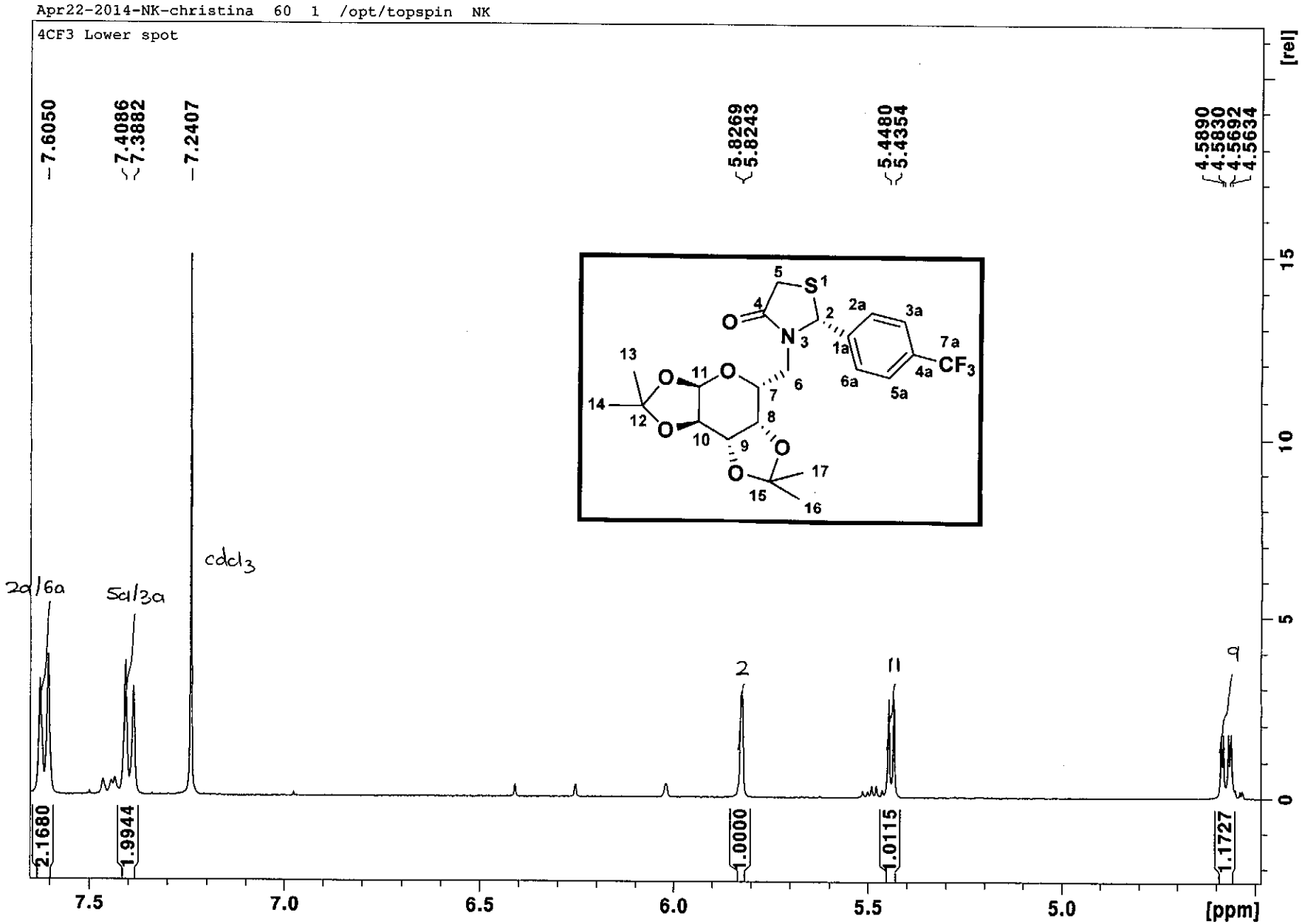
Minimum:				-1.5			
Maximum:		5.0	4.0	100.0			
Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	i-FIT (Norm)	Formula
512.1332	512.1331	0.1	0.2	8.5	523.9	0.0	C22 H26 N O6 F3 Na S

HRMS of Compound 5d and 6d: 3-(2,2,7,7-Tetramethyltetrahydro-bis [1,3]dioxolo[4,5-b;4',5'-d]pyran-5-ylmethyl)-2-(4-trifluoromethylphenyl)thiazolidin-4-one

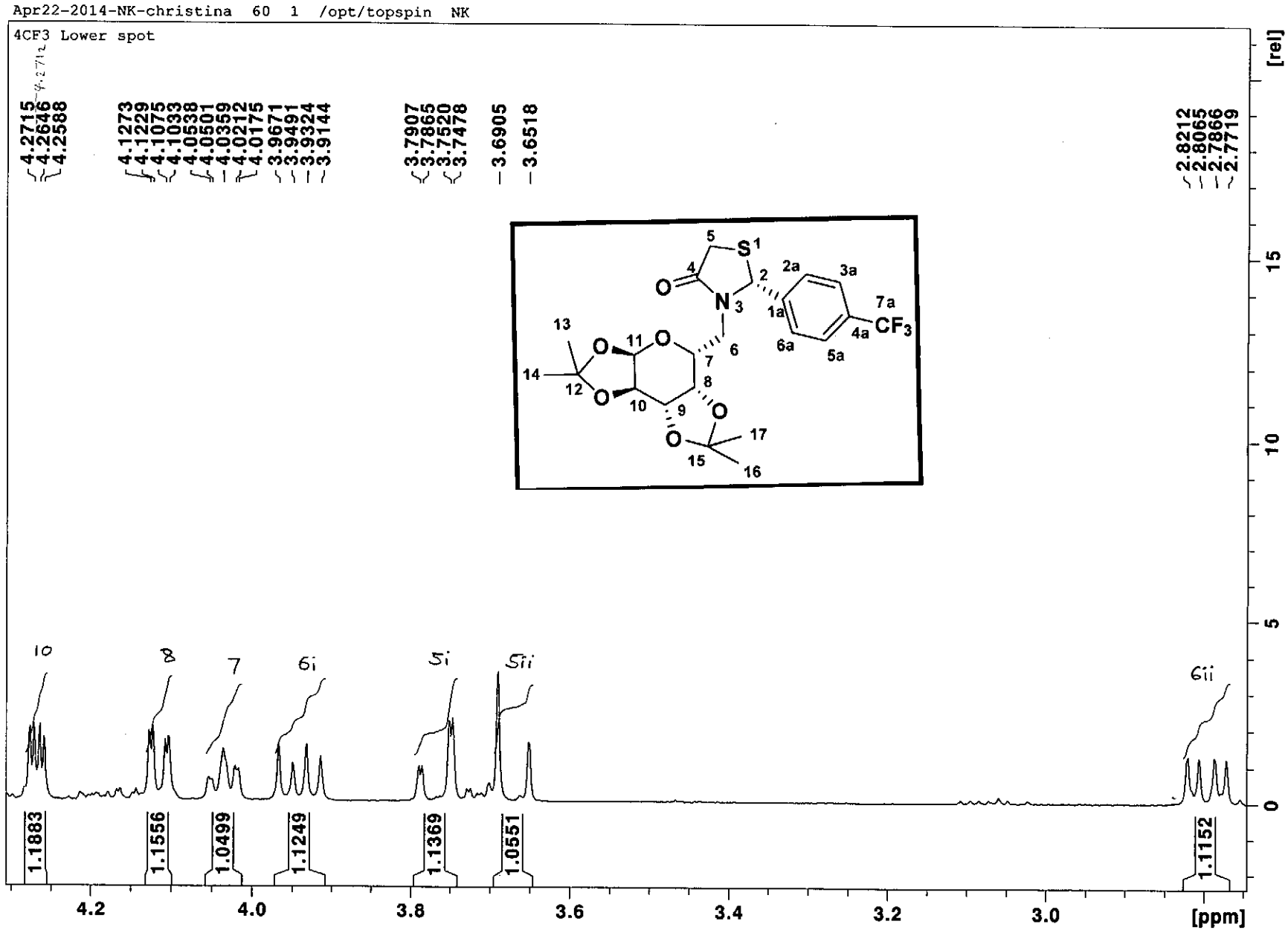




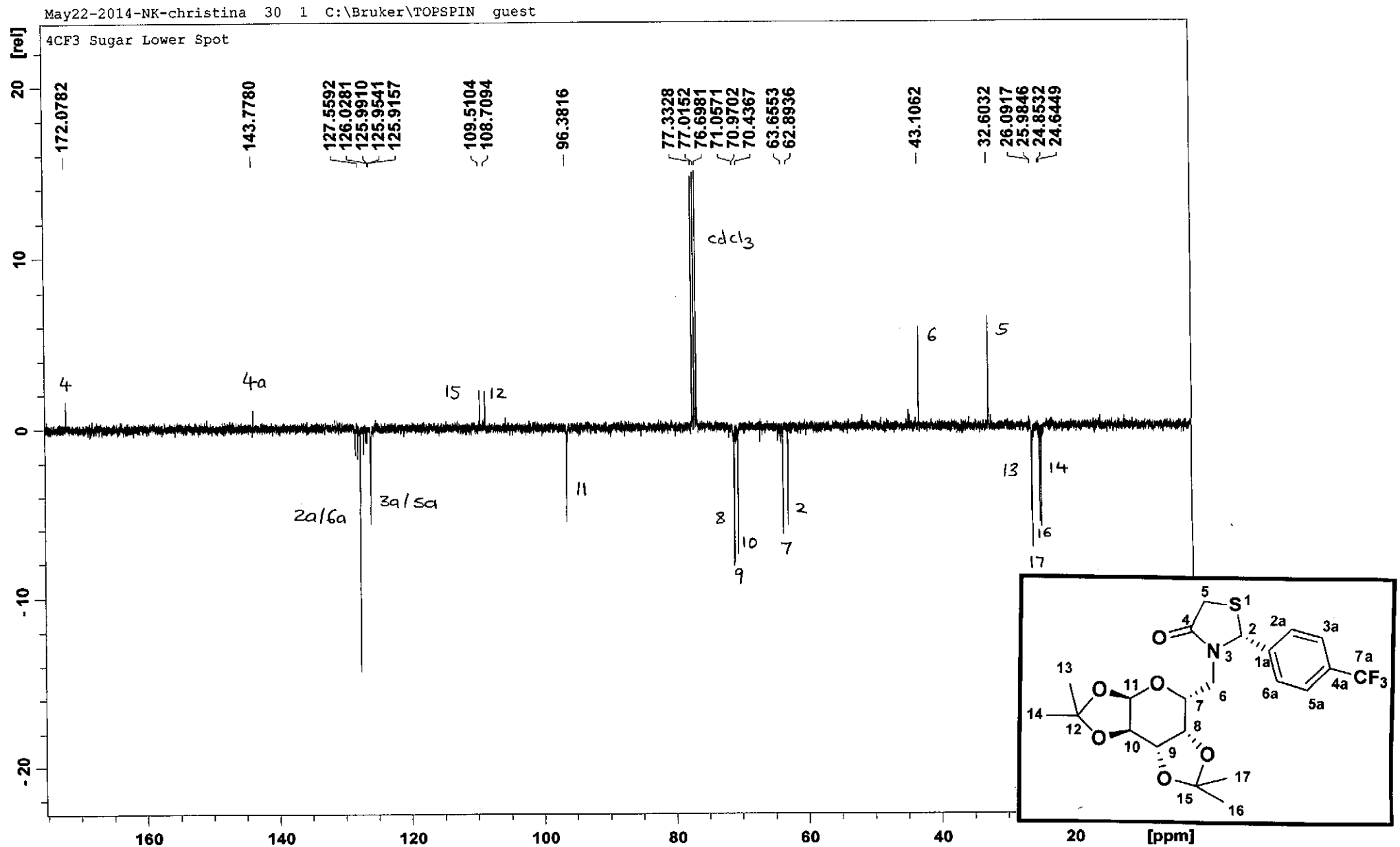
^{1}H Spectrum of Compound 6d: 3-(2,2,7,7-Tetramethyl-tetrahydro-bis[1,3] dioxolo[4,5-b; 4',5'-d]pyran-5-ylmethyl)-2-(4-trifluoromethyl-phenyl)-thiazolidin-4-one



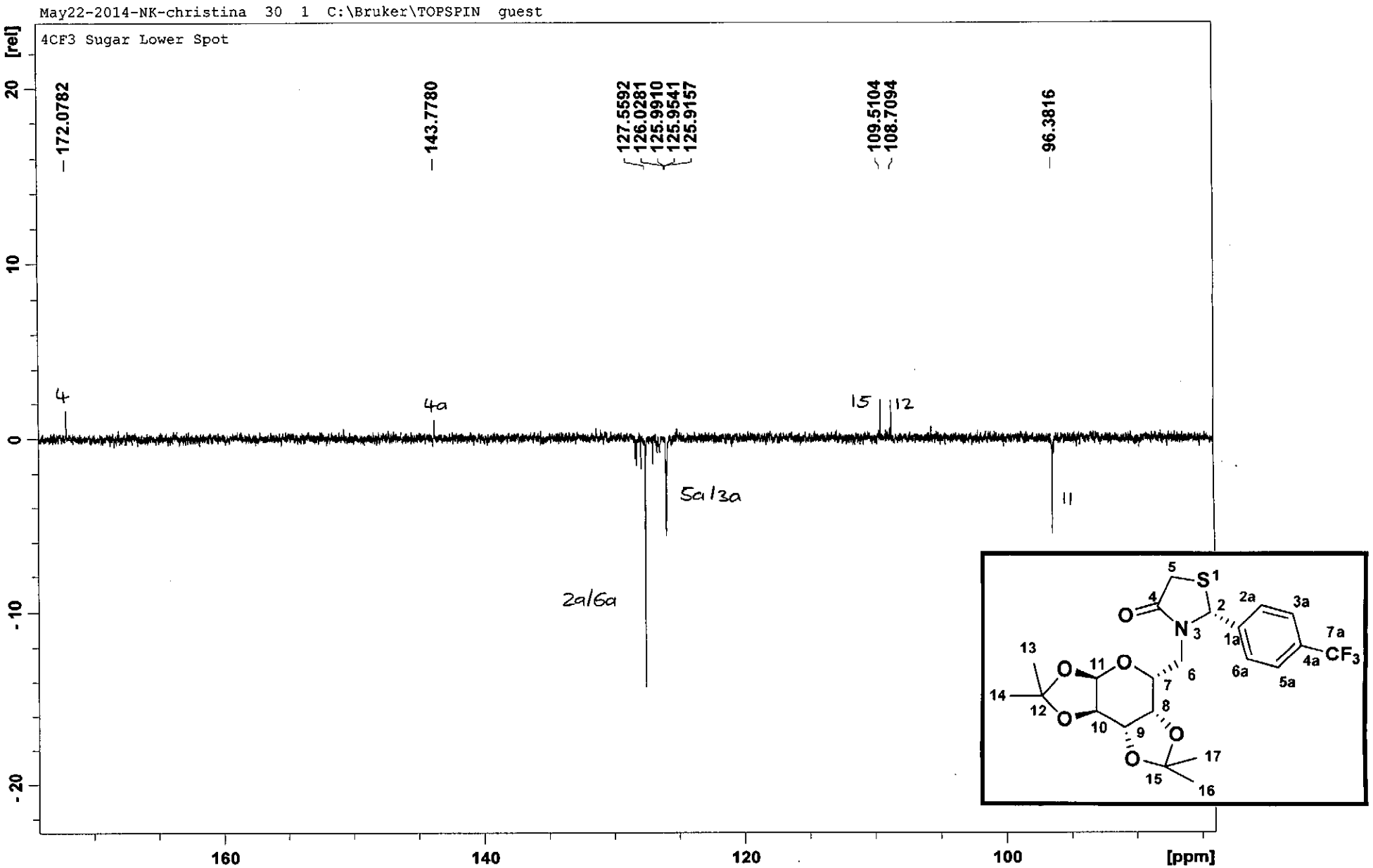
Expanded ^{1}H Spectrum of Compound 6d: 3-(2,2,7,7-Tetramethyl-tetrahydro-bis[1,3] dioxolo[4,5-b;4',5'-d]pyran-5-ylmethyl)-2-(4-trifluoromethyl-phenyl)-thiazolidin-4-one



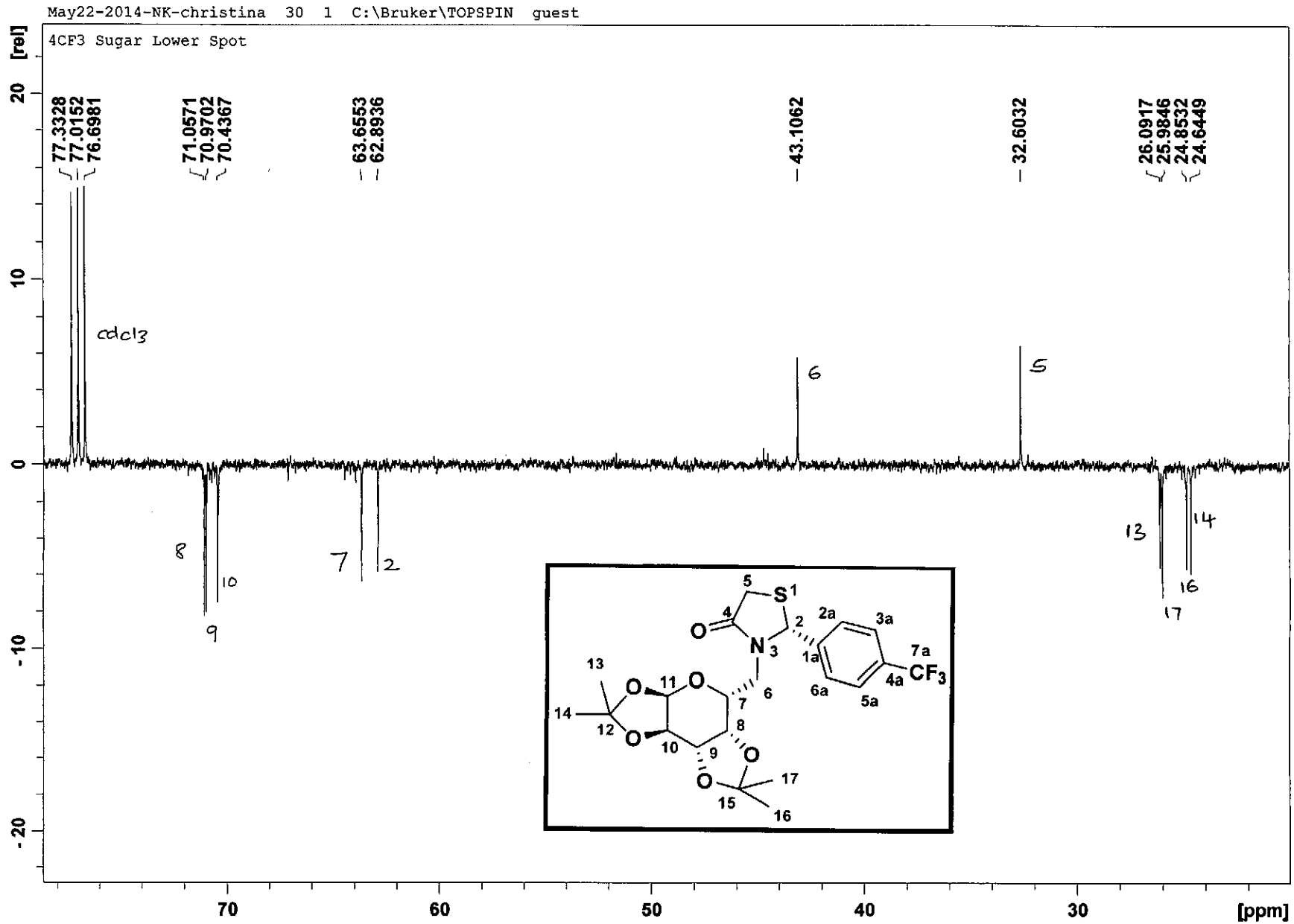
Expanded ^{1}H Spectrum of Compound 6d: 3-(2,2,7,7-Tetramethyl-tetrahydro-bis[1,3] dioxolo[4,5-b;4',5'-d]pyran-5-ylmethyl)-2-(4-trifluoromethyl-phenyl)-thiazolidin-4-one



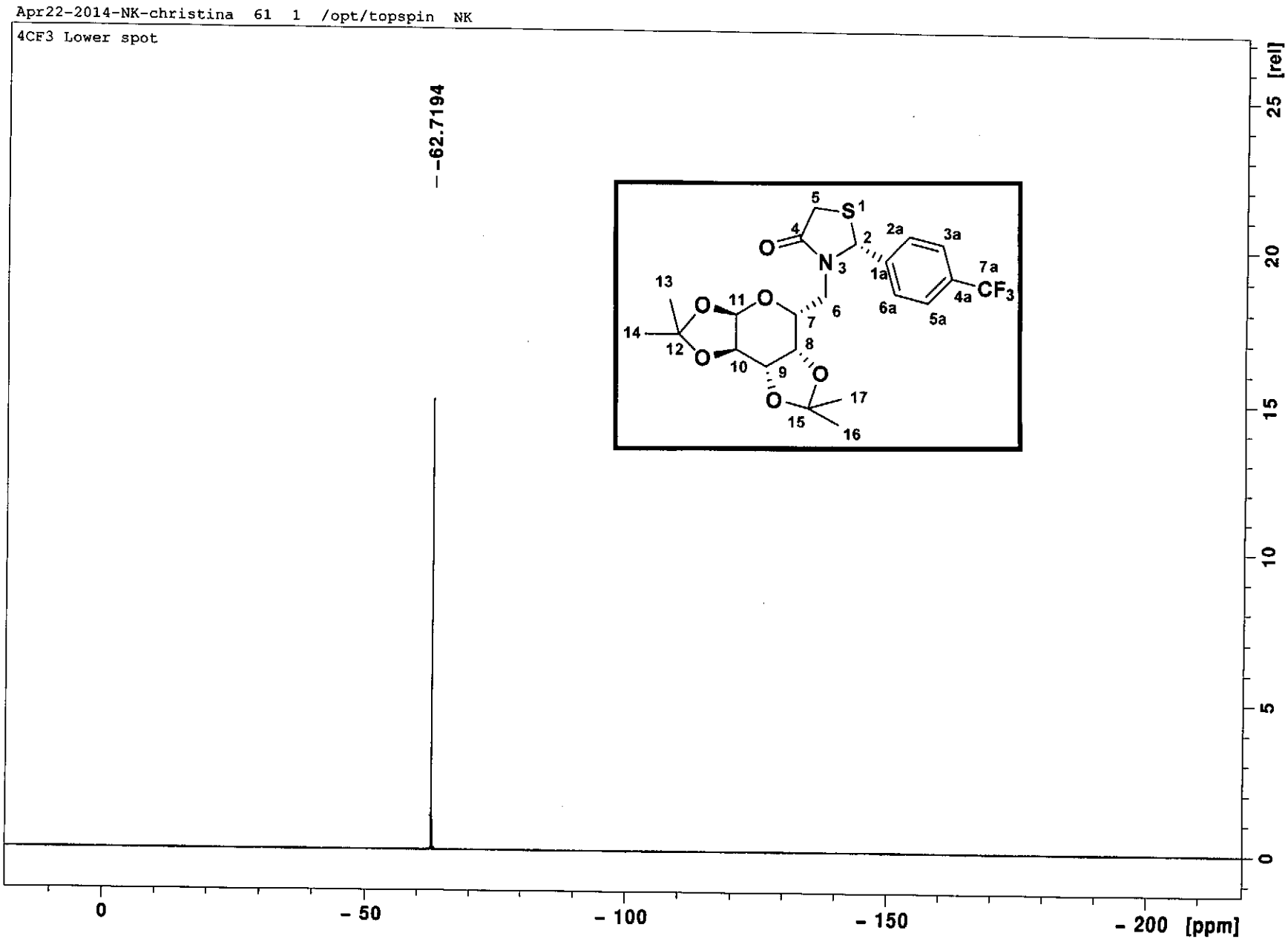
^{13}C Spectrum of Compound 6d: 3-(2,2,7,7-Tetramethyl-tetrahydro-bis[1,3] dioxolo[4,5-b;4',5'-d]pyran-5-ylmethyl)-2-(4-trifluoromethyl-phenyl)-thiazolidin-4-one



Expanded ^{13}C Spectrum of Compound 6d: 3-(2,2,7,7-Tetramethyl-tetrahydro-bis[1,3] dioxolo[4,5-b;4',5'-d]pyran-5-ylmethyl)-2-(4-trifluoromethyl-phenyl)-thiazolidin-4-one

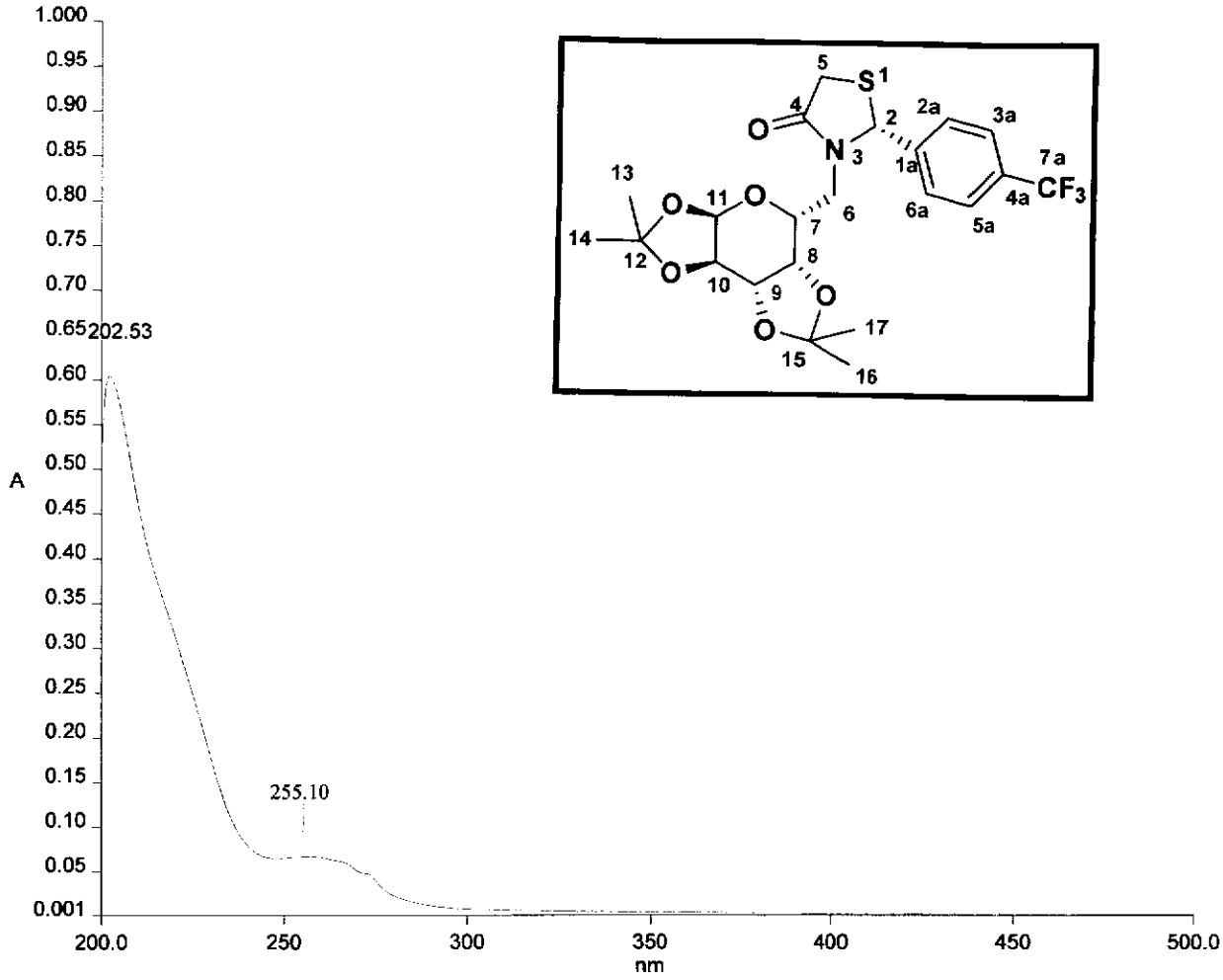


Expanded ^{13}C Spectrum of Compound 6d: 3-(2,2,7,7-Tetramethyl-tetrahydro-bis[1,3] dioxolo[4,5-b;4',5'-d]pyran-5-ylmethyl)-2-(4-trifluoromethyl-phenyl)-thiazolidin-4-one

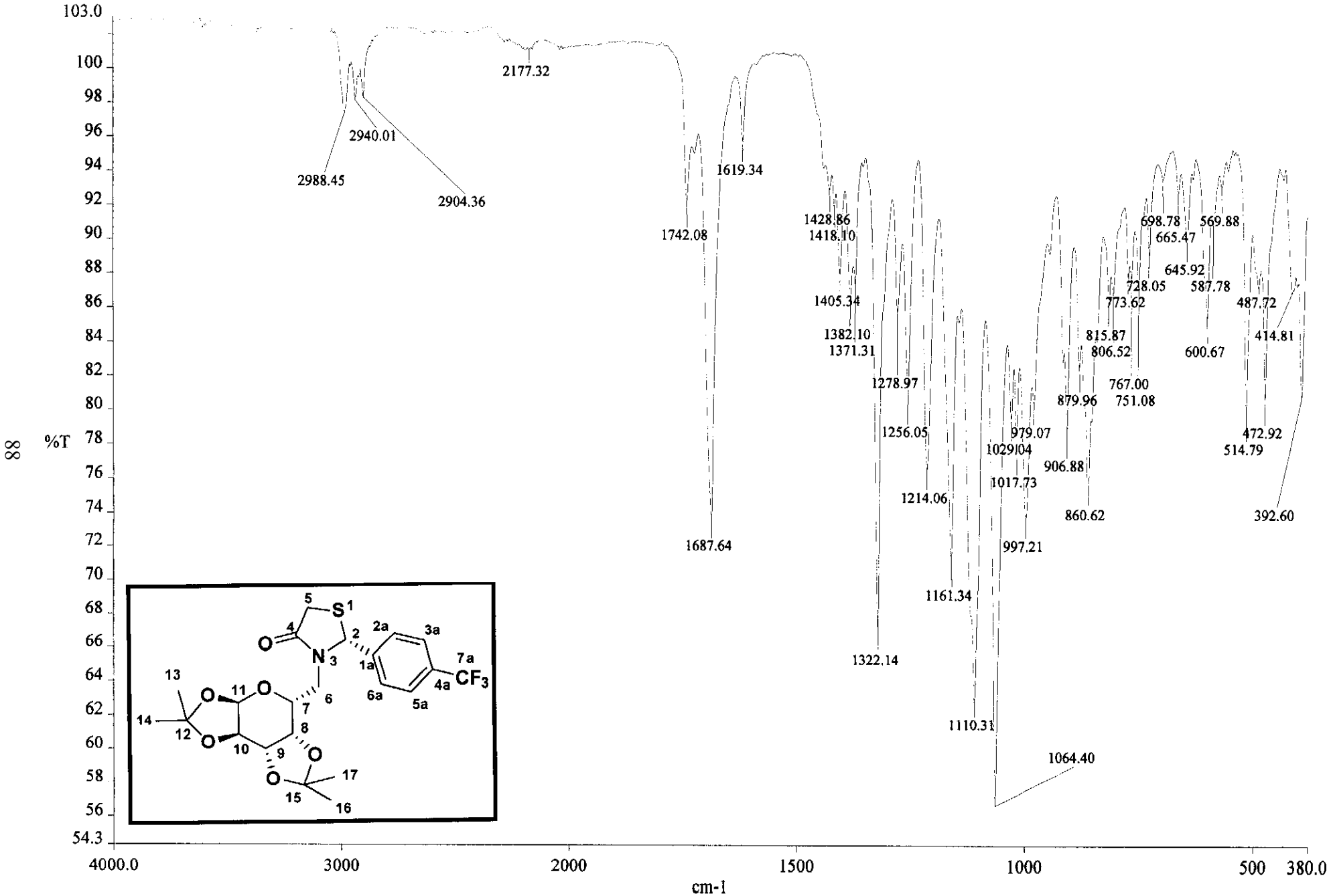


^{19}F Spectrum of Compound 6d: 3-(2,2,7,7-Tetramethyl-tetrahydro-bis[1,3] dioxolo[4,5-b; 4',5'-d]pyran-5-ylmethyl)-2-(4-trifluoromethyl-phenyl)-thiazolidin-4-one

Date: 2014/06/05 Time: 04:31:14 PM



Ultraviolet Spectrum of Compound 6d: 3-(2,2,7,7-Tetramethyl-tetrahydro-bis[1,3] dioxolo [4,5-b; 4',5'-d]pyran-5-ylmethyl)-2-(4-trifluoromethyl-phenyl)-thiazolidin-4-one

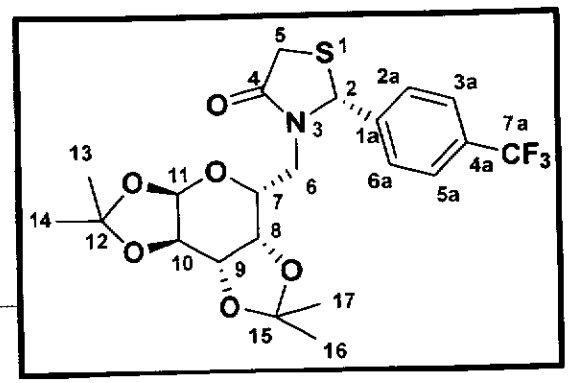


c:\pel_data\spectra\christina\4cf3 ls 001

Infrared Spectrum of Compound 6d: 3-(2,2,7,7-Tetramethyl-tetrahydro-bis[1,3] dioxolo [4,5-b; 4',5'-d]pyran-5-ylmethyl)-2-(4-trifluoromethyl-phenyl)-thiazolidin-4-one

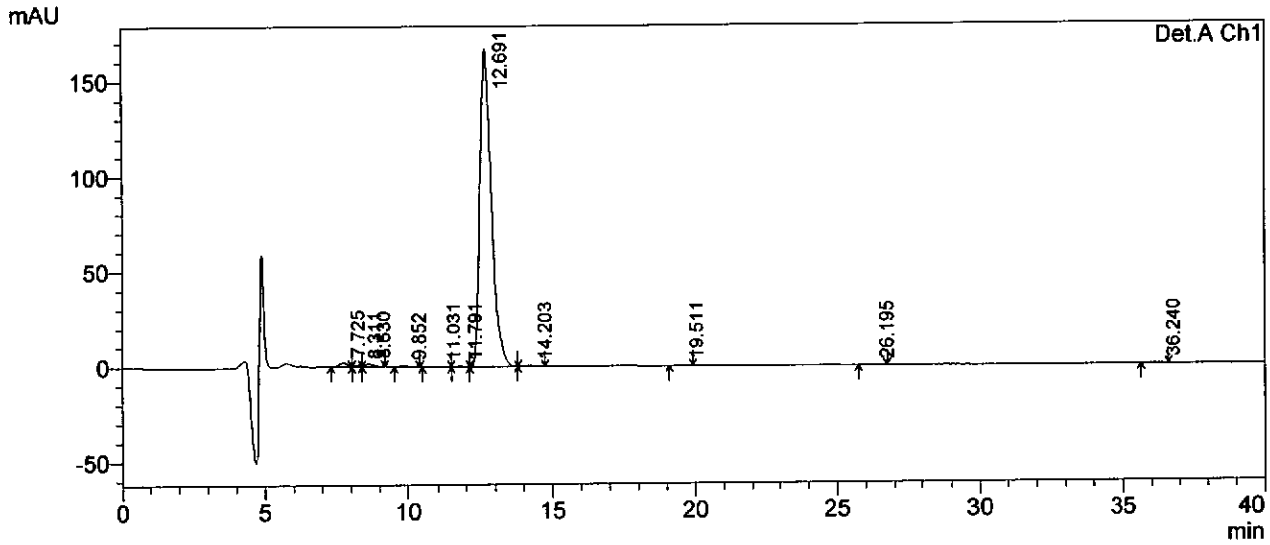
==== Shimadzu LCsolution Analysis Report ====

Acquired by	: Admin
Sample Name	: 4cf3 ls formic buffer
Sample ID	: 4cf3 ls formic buffer
Vail #	: 3
Injection Volume	: 100 uL
Data File Name	: 4cf3 ls formic buffer.lcd
Method File Name	: Pramod 09jun 2014.lcm
Batch File Name	: suger thiozolidinon.lcb
Report File Name	: Default.lcr
Data Acquired	: 2014/06/17 01:53:48 PM
Data Processed	: 2014/06/17 02:33:52 PM



<Chromatogram>

C:\LabSolutions\LCsolution\christina\4cf3 ls formic buffer.lcd



1 Det.A Ch1/220nm

<Results>

PeakTable C:\LabSolutions\LCsolution\christina\4cf3 ls formic buffer.lcd

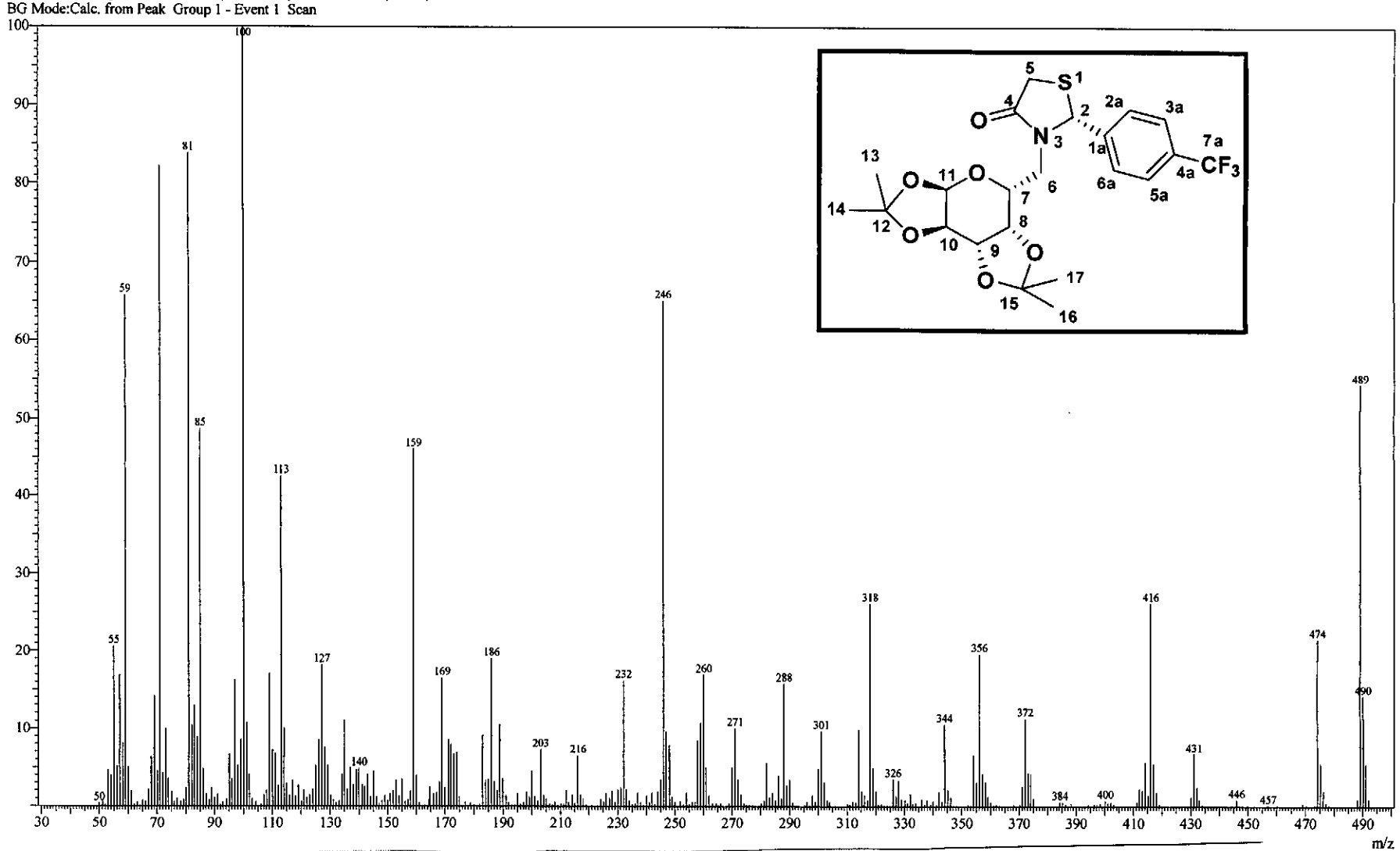
Detector A Ch1 220nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	7.725	43031	2034	0.920	1.168
2	8.311	16083	949	0.344	0.545
3	8.630	30626	1324	0.655	0.761
4	9.852	14303	693	0.306	0.398
5	11.031	12553	476	0.269	0.273
6	11.791	9744	465	0.208	0.267
7	12.691	4511034	166916	96.491	95.871
8	14.203	13004	508	0.278	0.292
9	19.511	8417	335	0.180	0.192
10	26.195	9194	220	0.197	0.126
11	36.240	7098	185	0.152	0.106
Total		4675088	174104	100.000	100.000

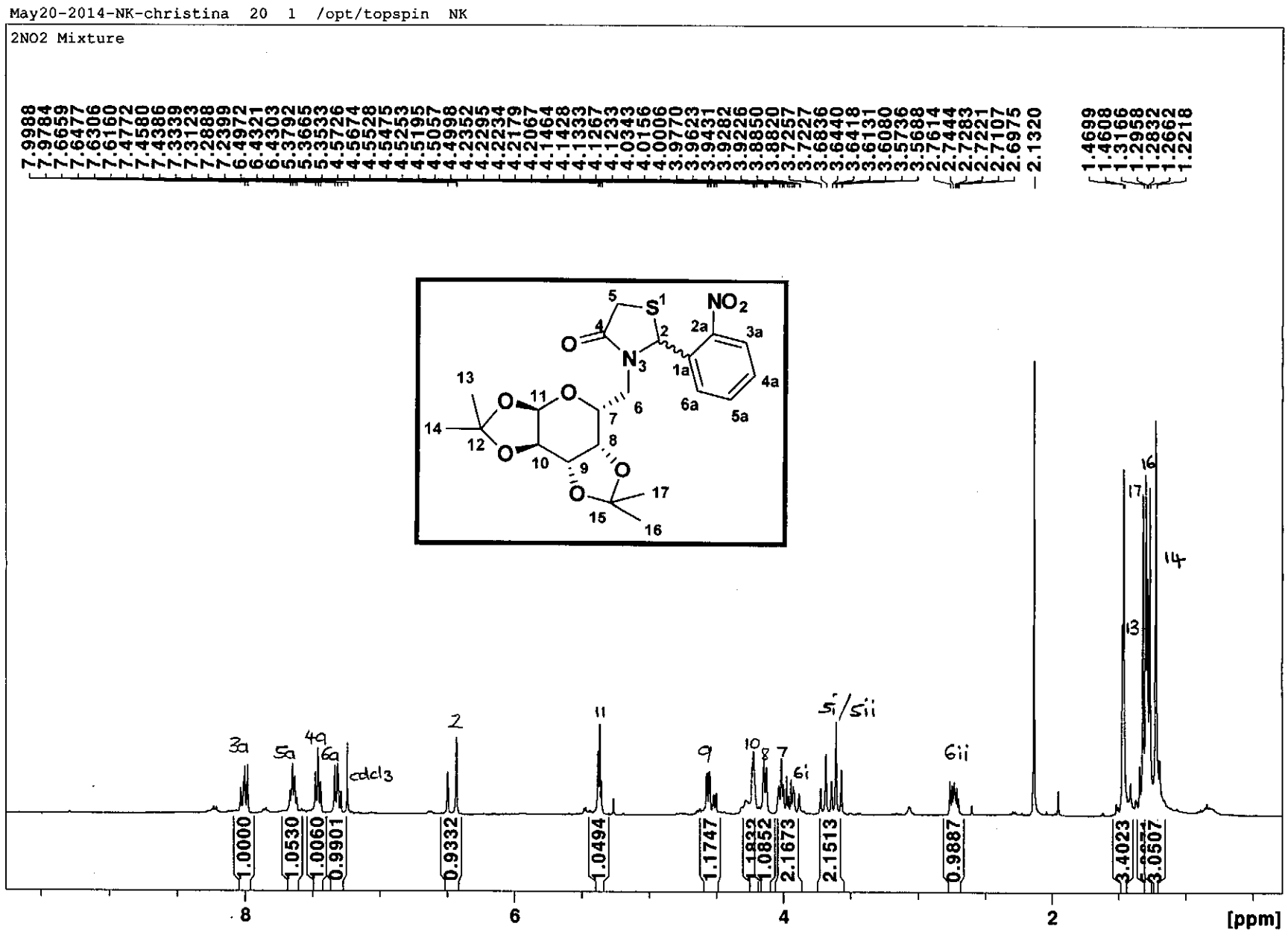
HPLC of Compound 6d: 3-(2,2,7,7-Tetramethyl-tetrahydro-bis[1,3] dioxolo[4,5-b; 4',5'-d] pyran-5-ylmethyl)-2-(4-trifluoromethyl-phenyl)-thiazolidin-4-one

Spectrum

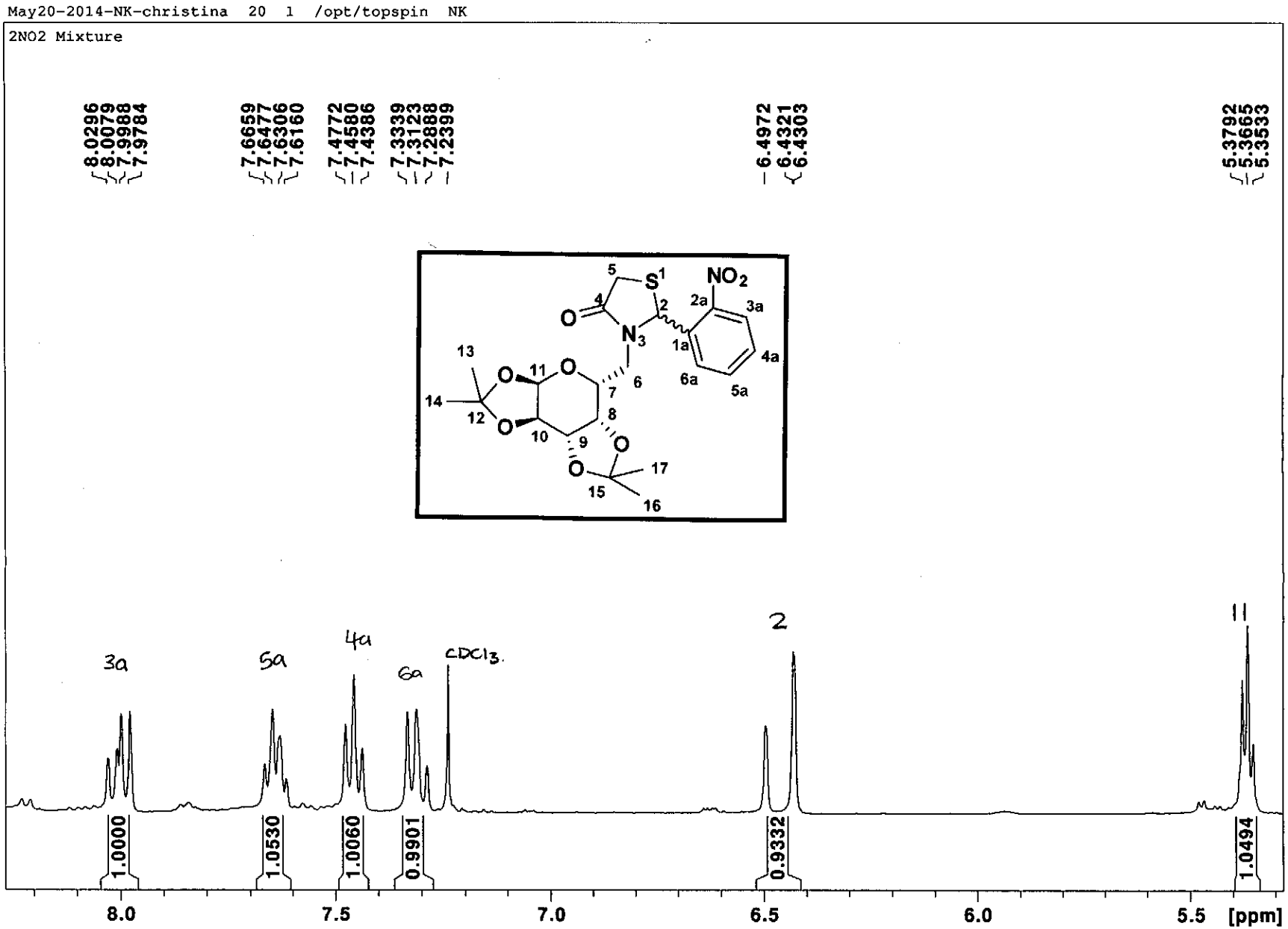
Line#:1 R.Time:15.120(Scan#:2225)
MassPeaks:552
RawMode:Averaged 15.115-15.125(2224-2226) BasePeak:100(90255)
BG Mode:Calc. from Peak Group 1 - Event 1 Scan



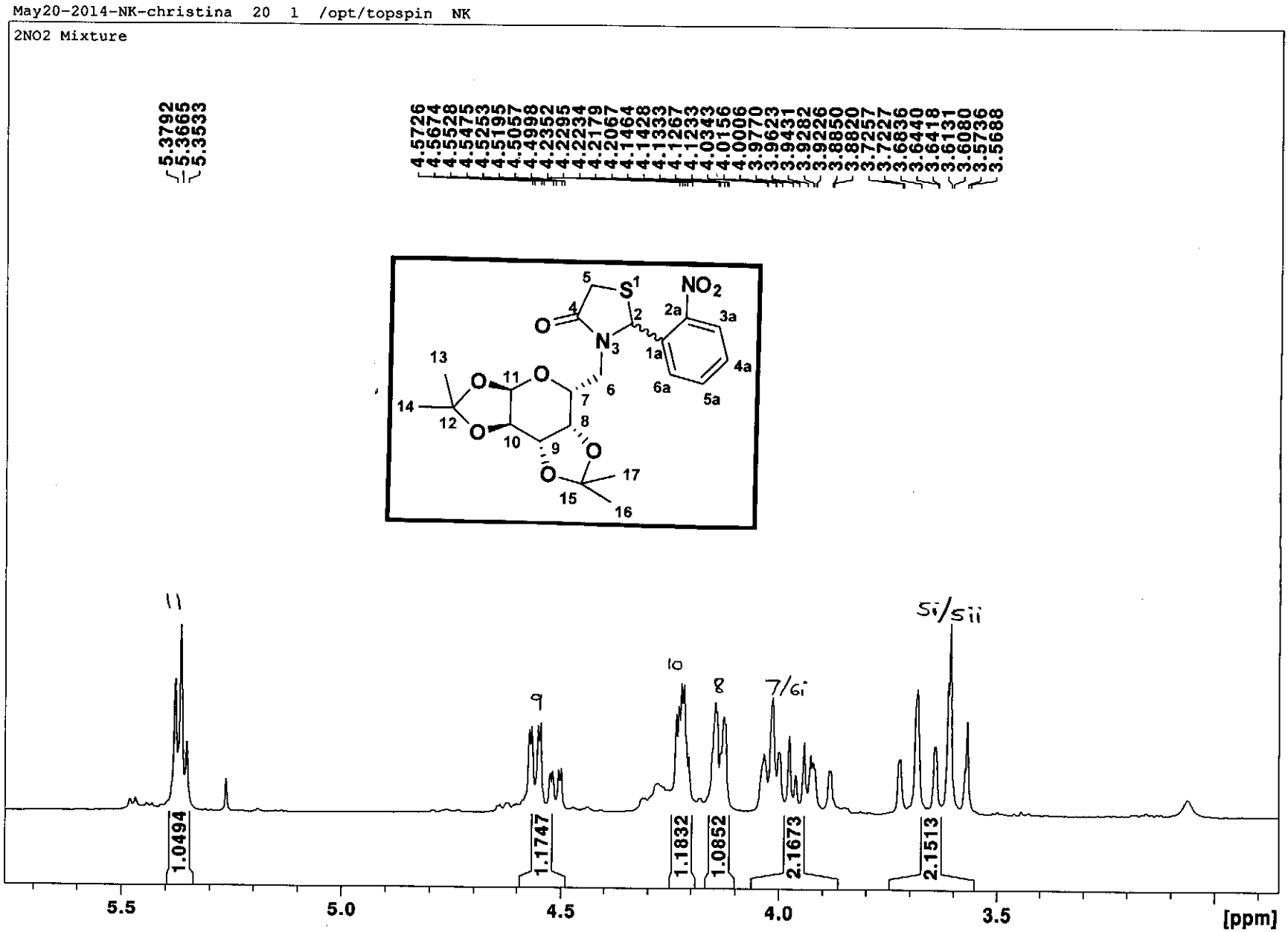
GC-MS of Compound 6d: 3-(2,2,7,7-Tetramethyl-tetrahydro-bis[1,3] dioxolo[4,5-b; 4',5'-d] pyran-5-ylmethyl)-2-(4-trifluoromethyl-phenyl)-thiazolidin-4-one



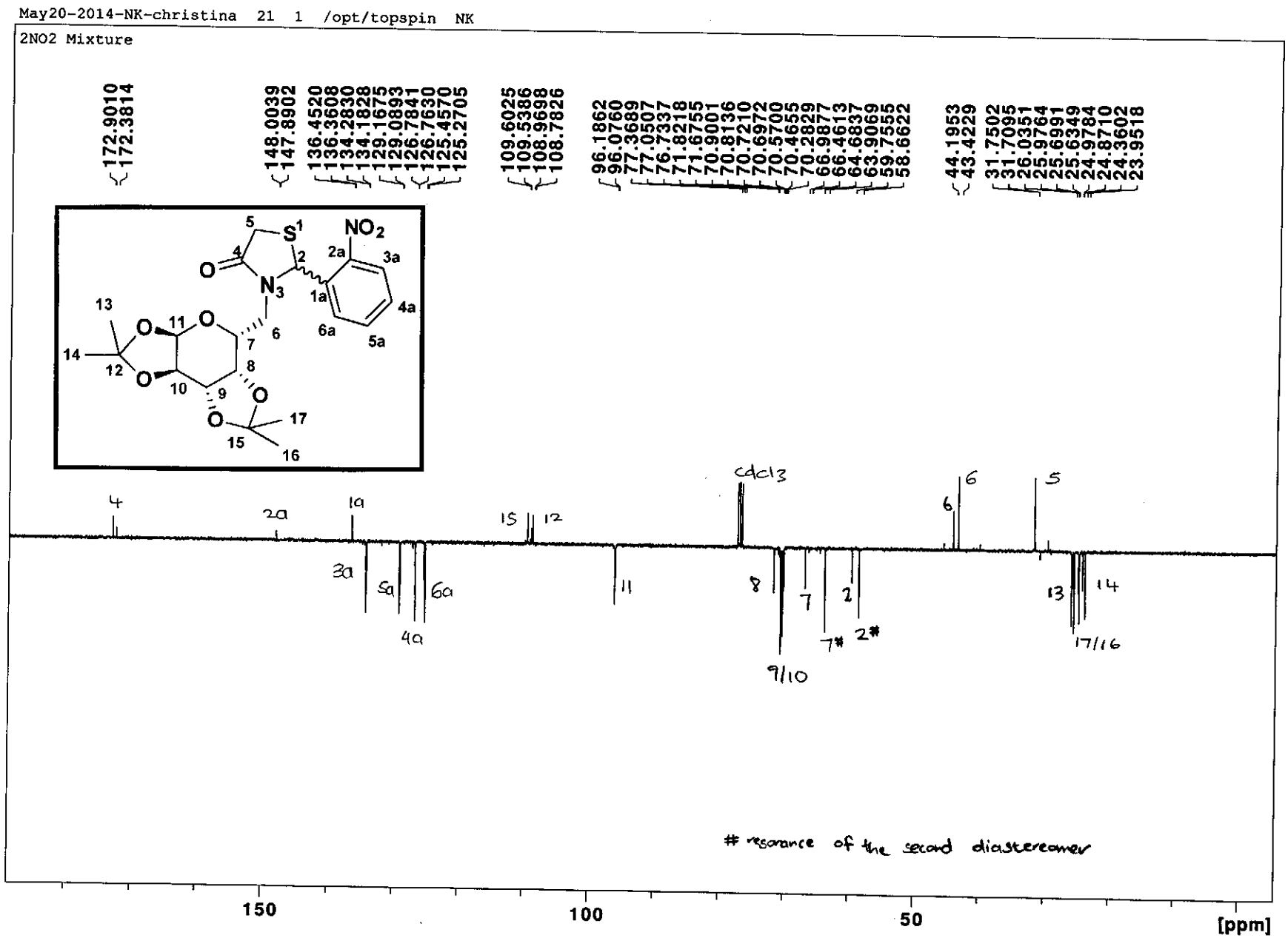
^{1}H Spectrum of Compound 5e and 6e: 2-(2-Nitrophenyl)-3-(2,2,7,7-tetramethyl-tetra hydr-bis[1,3]dioxolo[4,5-b;4',5'-d]pyran-5-ylmethyl)thiazolidin-4-one



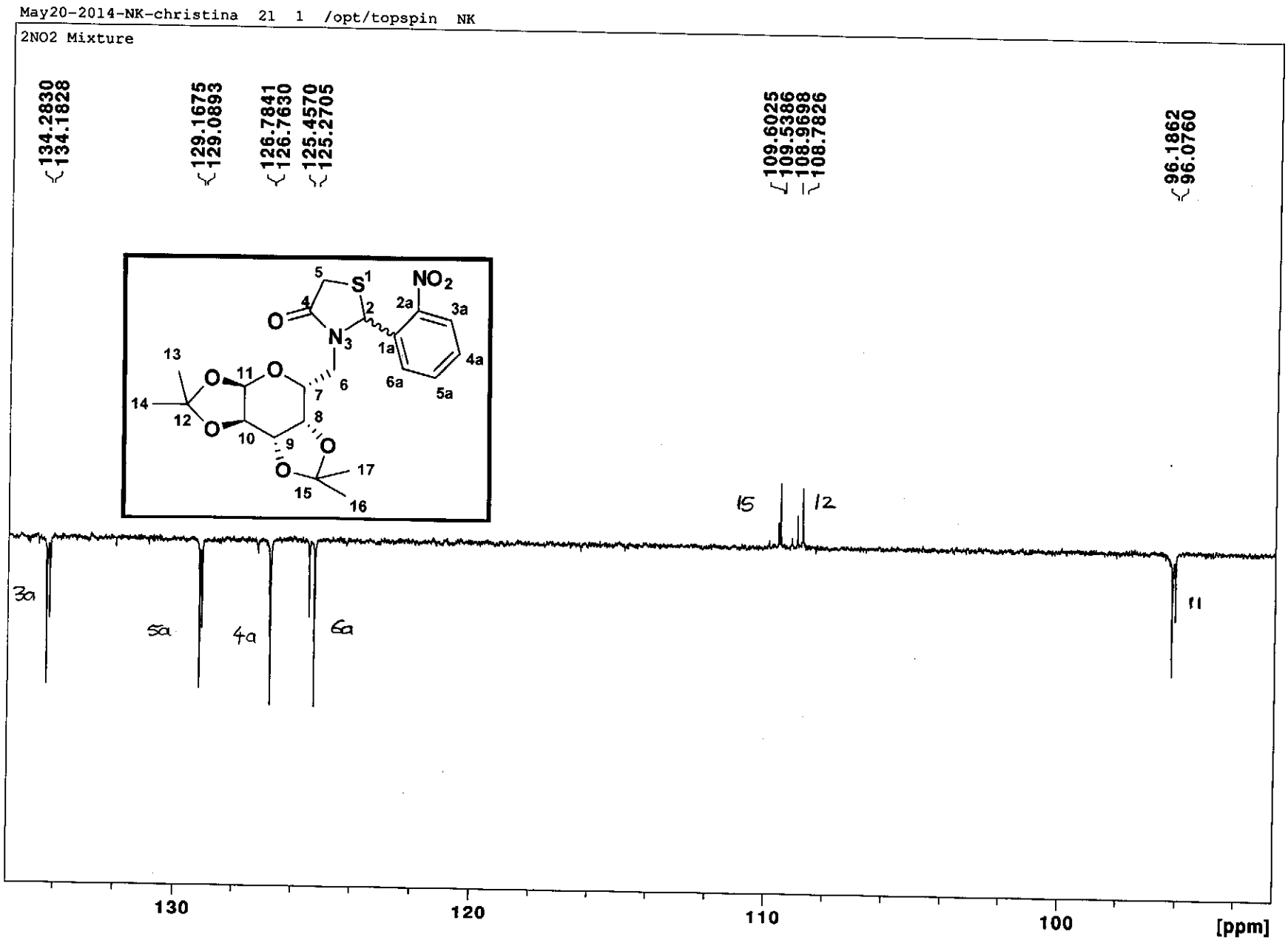
Expanded ^{1}H Spectrum of Compound 5e and 6e: 2-(2-Nitrophenyl)-3-(2,2,7,7-tetra methyl-tetrahydro-bis[1,3]dioxolo[4,5-b;4',5'-d]pyran-5-ylmethyl)thiazolidin-4-one



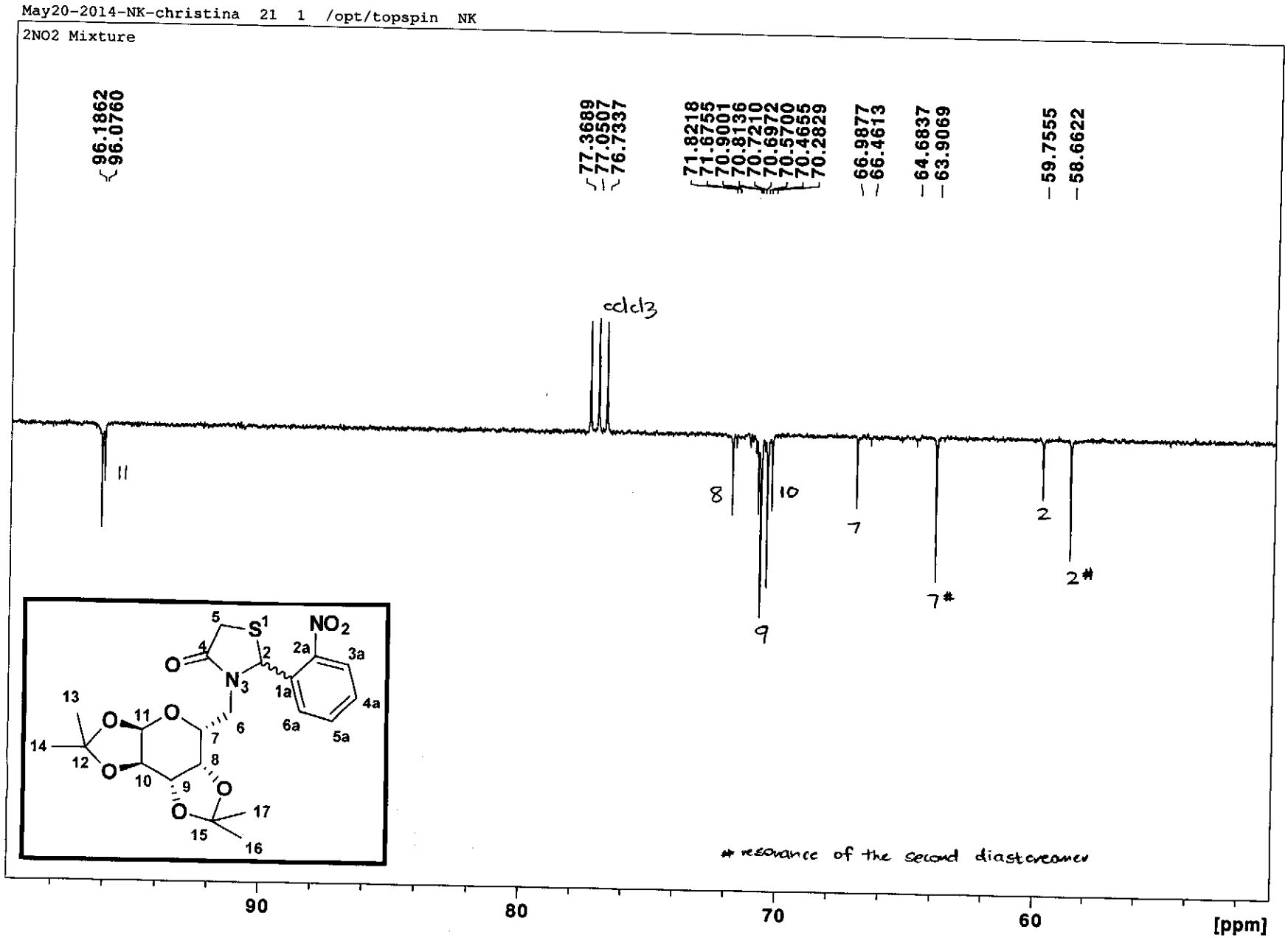
Expanded ^{1}H Spectrum of Compound 5e and 6e: 2-(2-Nitrophenyl)-3-(2,2,7,7-tetra methyl-tetrahydro-bis[1,3]dioxolo[4,5-b;4',5'-d]pyran-5-ylmethyl)thiazolidin-4-one



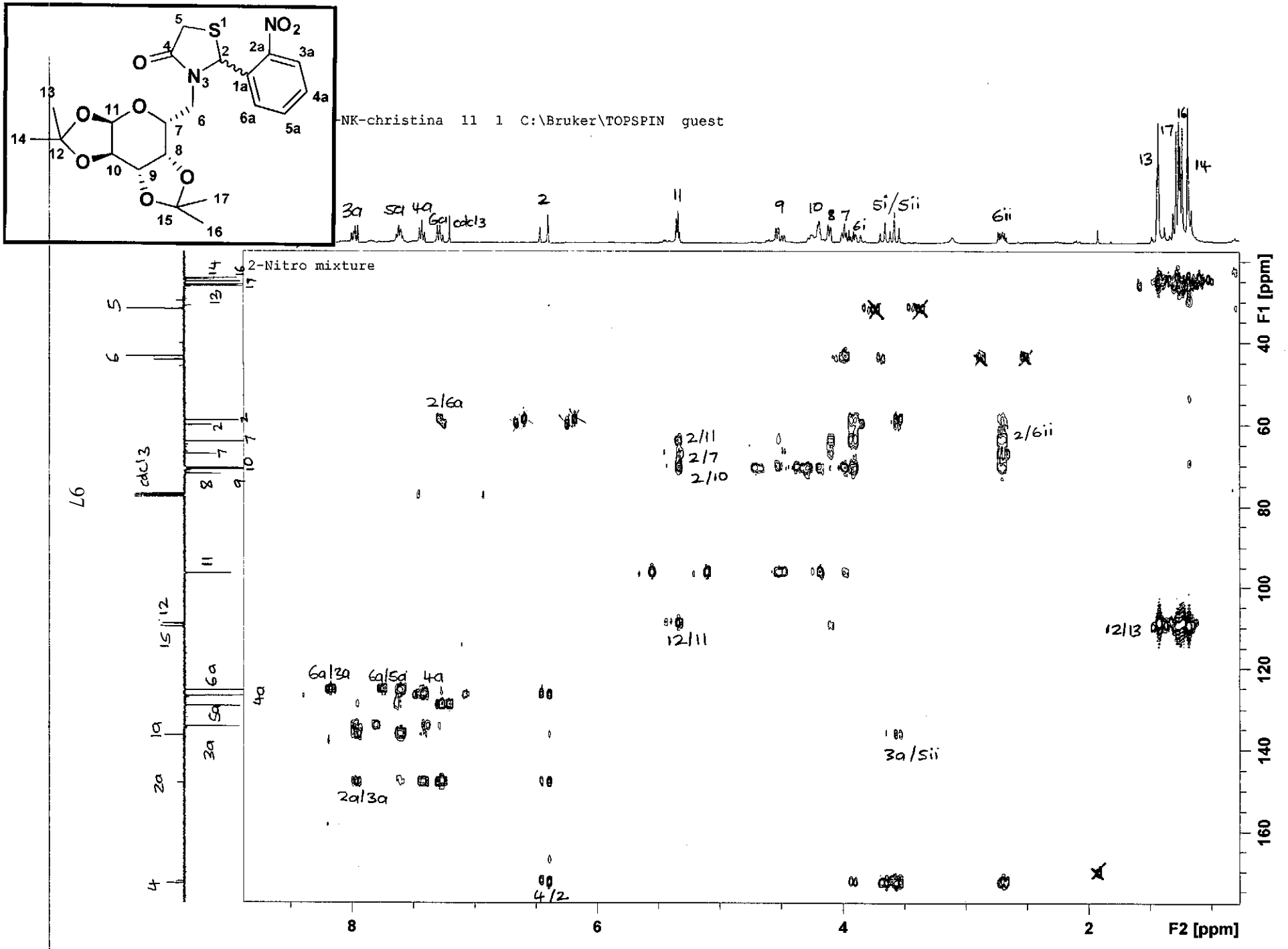
^{13}C Spectrum of Compound 5e and 6e: 2-(2-Nitrophenyl)-3-(2,2,7,7-tetramethyl-tetra hydro-bis[1,3]dioxolo[4,5-b;4',5'-d]pyran-5-ylmethyl)thiazolidin-4-one



Expanded ^{13}C Spectrum of Compound 5e and 6e: 2-(2-Nitrophenyl)-3-(2,2,7,7-tetra methyl-tetrahydro-bis[1,3]dioxolo[4,5-b;4',5'-d]pyran-5-ylmethyl)thiazolidin-4-one

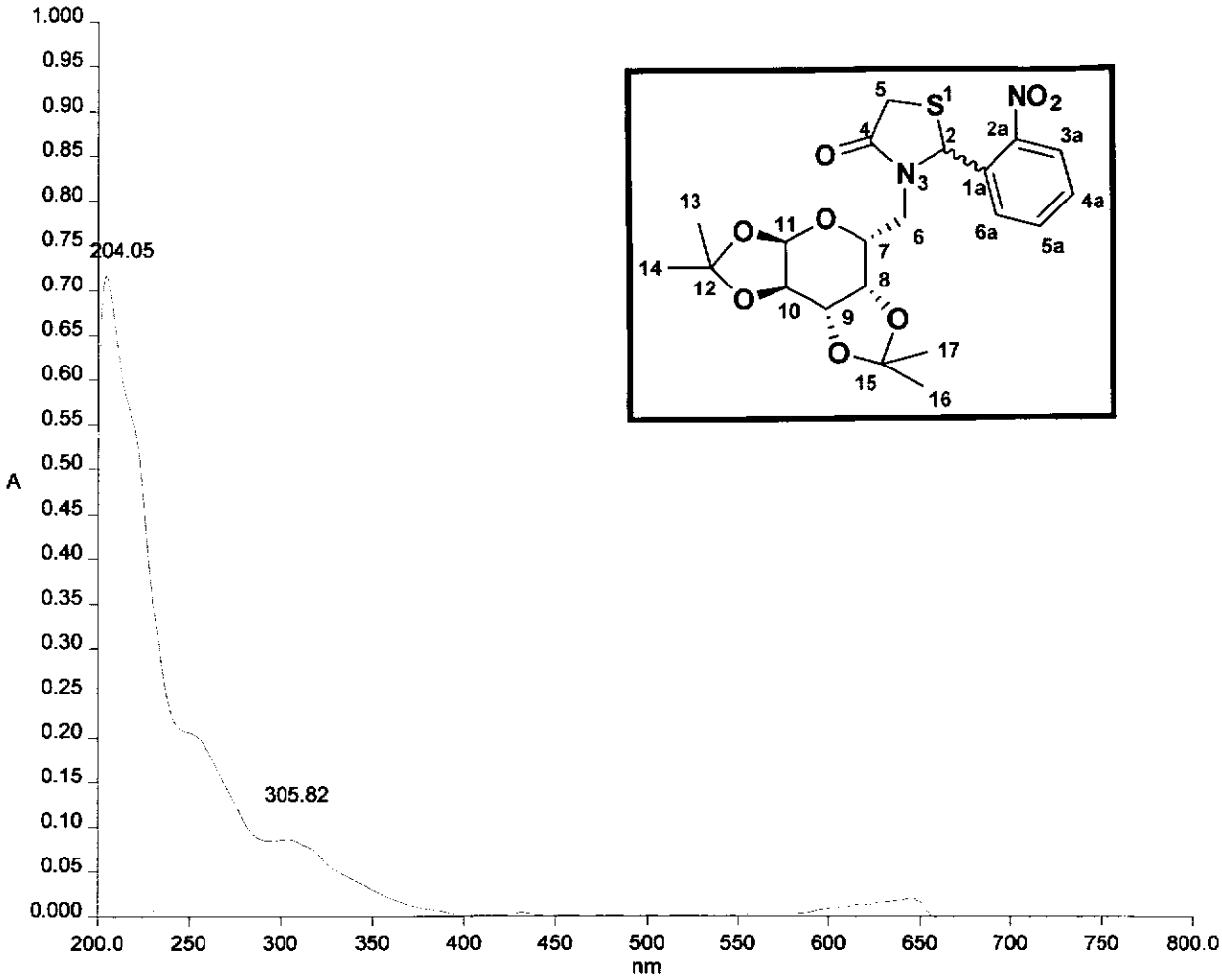


Expanded ^{13}C Spectrum of Compound 5e and 6e: 2-(2-Nitrophenyl)-3-(2,2,7,7-tetra methyl-tetrahydro-bis[1,3]dioxolo[4,5-b;4',5'-d]pyran-5-ylmethyl)thiazolidin-4-one

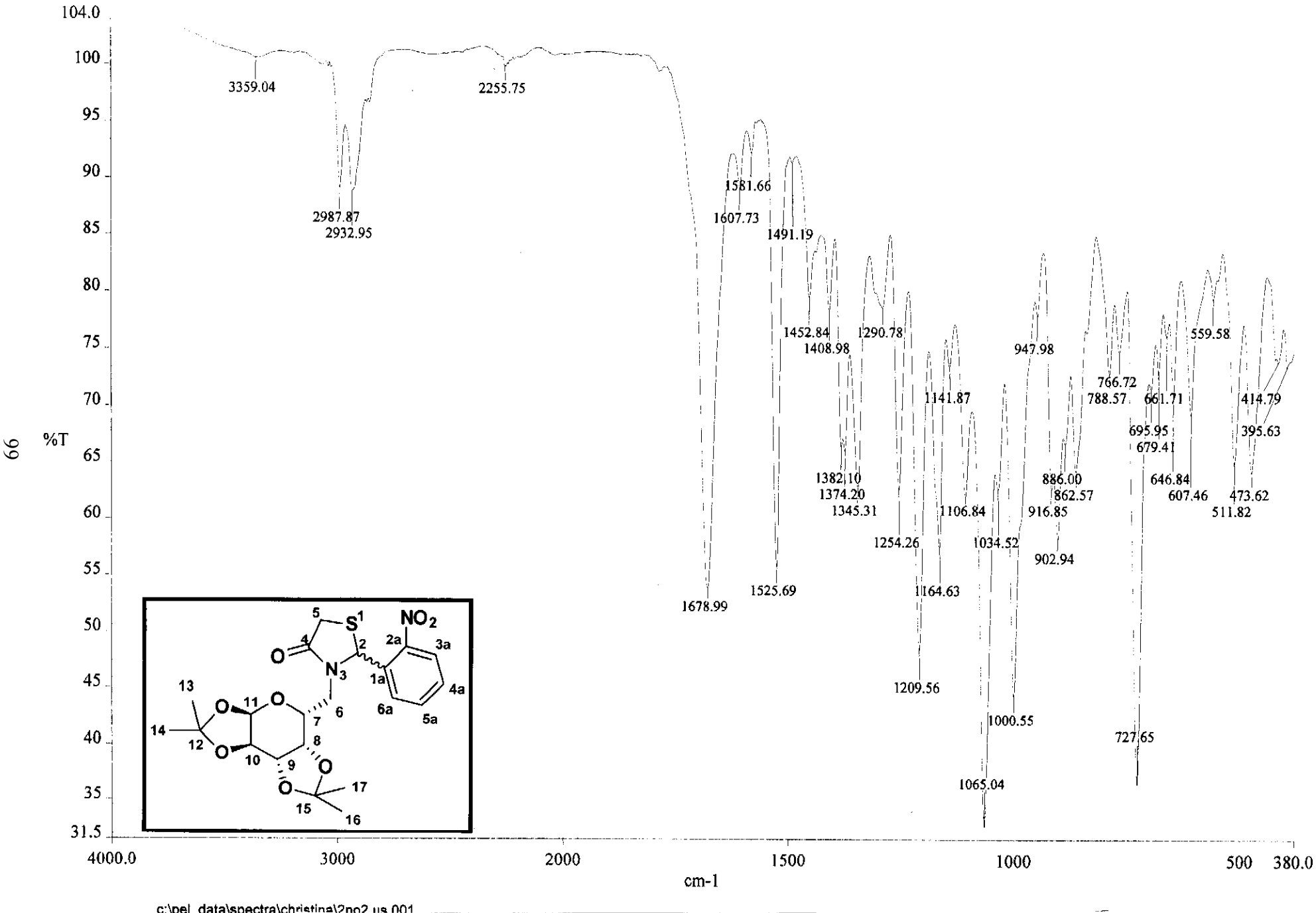


HMBC of Compound 5e and 6e: 2-(2-Nitrophenyl)-3-(2,2,7,7-tetramethyltetrahydro-*bis* [1,3]dioxolo[4,5b;4',5'd]pyran-5-ylmethyl)thiazolidin-4-one

Date: 2014/06/20 Time: 11:43:20 AM



Ultraviolet Spectrum of Compound 5e and 6e: 2-(2-Nitrophenyl)-3-(2,2,7,7-tetramethyl-tetrahydro-bis[1,3]dioxolo[4,5-b;4',5'-d]pyran-5-ylmethyl)thiazolidin-4-one

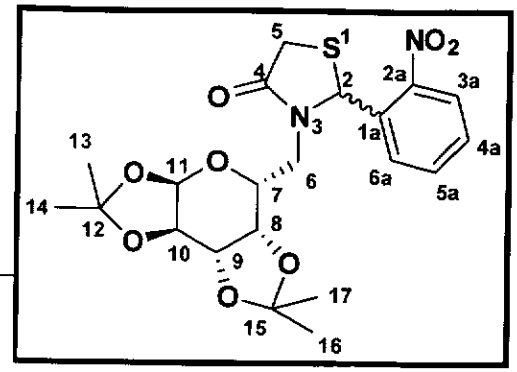


c:\pel_data\spectra\christina\2no2 us 001

Infrared Spectrum of Compound 5e and 6e: 2-(2-Nitrophenyl)-3-(2,2,7,7-tetramethyl-tetrahydro-bis[1,3]dioxolo[4,5-b;4',5'-d]pyran-5-ylmethyl)thiazolidin-4-one

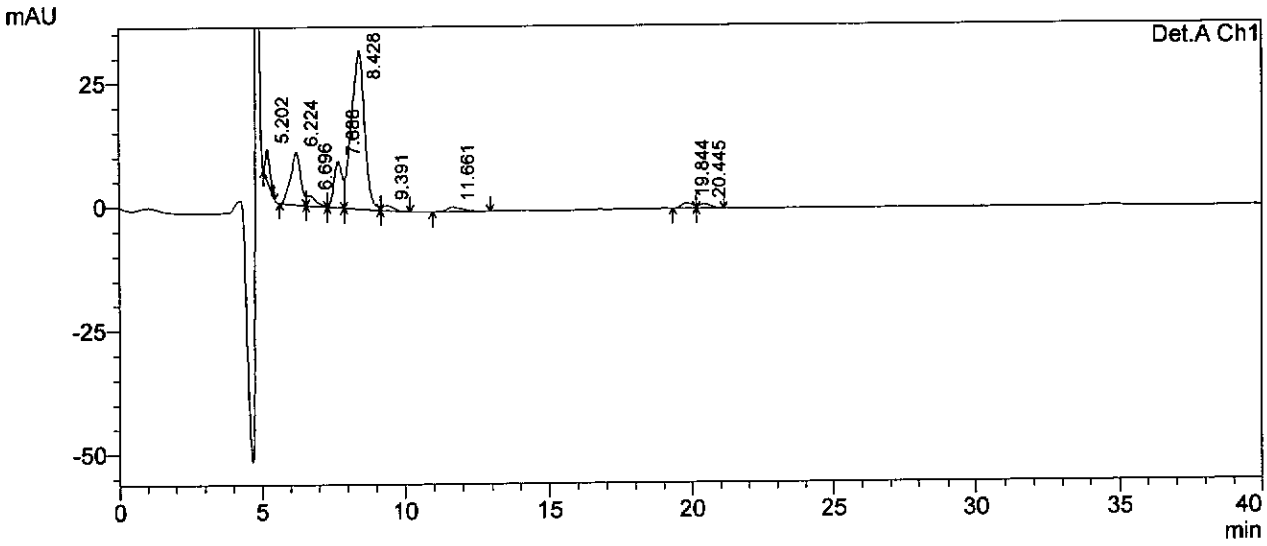
==== Shimadzu LCsolution Analysis Report ====

Acquired by	: Admin
Sample Name	: 2no2 with formic buffer
Sample ID	: 2no2 with formic buffer
Vail #	: 1
Injection Volume	: 100 uL
Data File Name	: 2no2 with formic buffer.lcd
Method File Name	: Pramod 09jun 2014.lcm
Batch File Name	: 20_03_2014.lcb
Report File Name	: Default.lcr
Data Acquired	: 2014/06/23 09:55:49 AM
Data Processed	: 2014/06/23 10:35:52 AM



<Chromatogram>

C:\LabSolutions\LCsolution\christina\2no2 with formic buffer.lcd



1Det.A Ch1/220nm

<Results>

PeakTable C:\LabSolutions\LCsolution\christina\2no2 with formic buffer.lcd

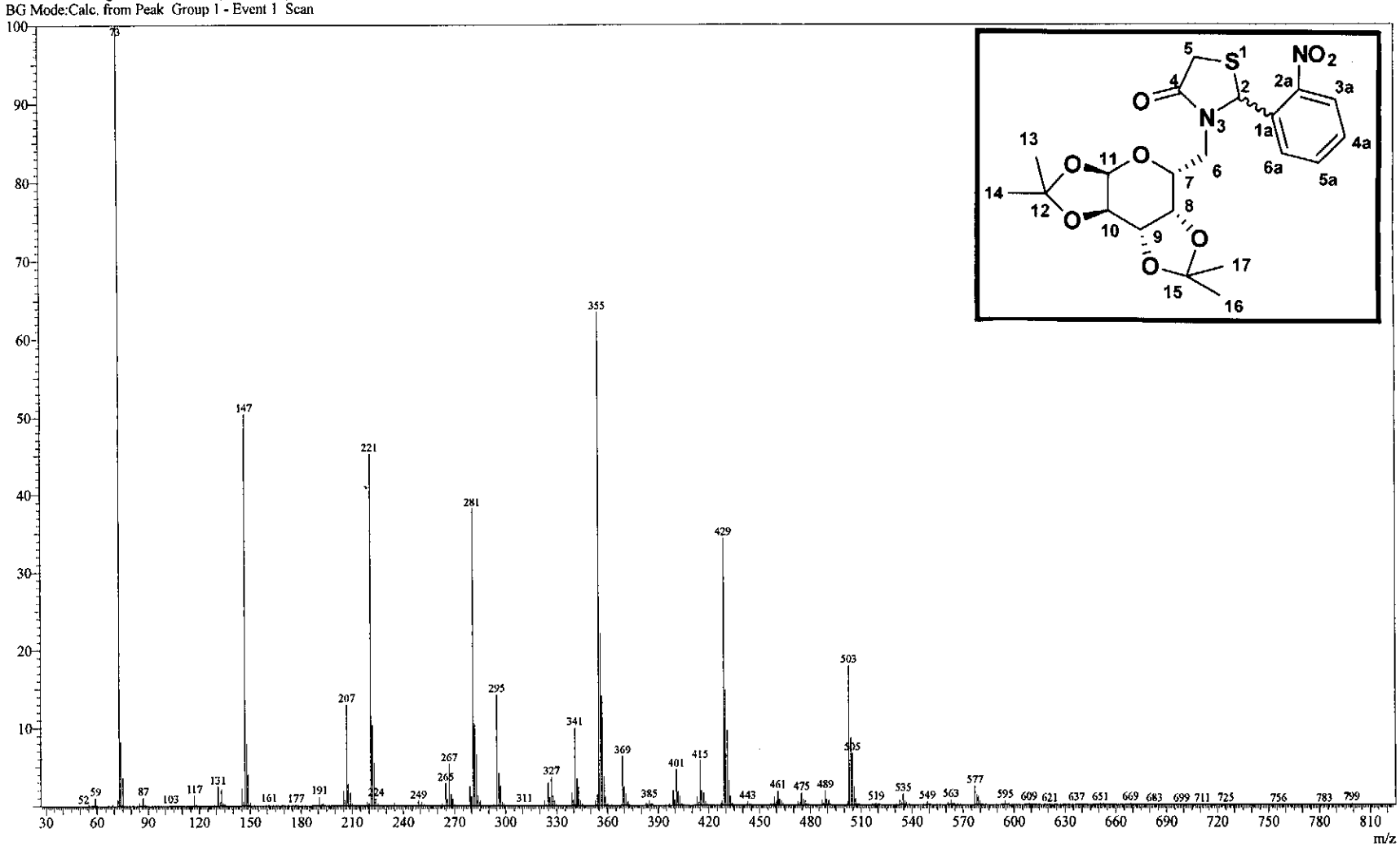
Detector A Ch1 220nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	5.202	66842	6280	3.904	9.738
2	6.224	258997	10703	15.126	16.597
3	6.696	47317	2111	2.763	3.274
4	7.688	191989	9408	11.213	14.589
5	8.428	1031440	32185	60.240	49.906
6	9.391	27661	974	1.616	1.510
7	11.661	34144	921	1.994	1.428
8	19.844	29271	1064	1.710	1.650
9	20.445	24549	843	1.434	1.308
Total		1712210	64491	100.000	100.000

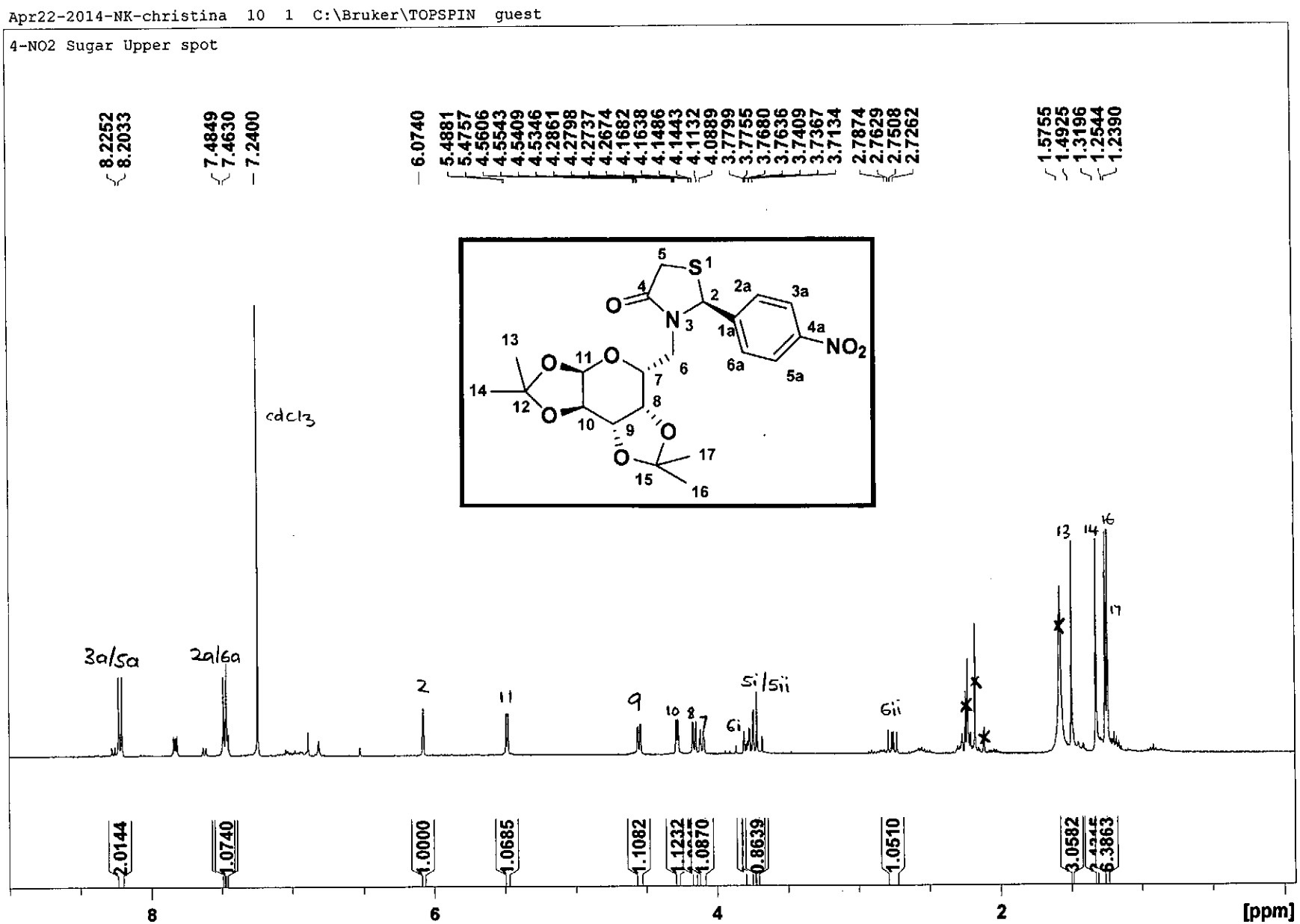
HPLC of Compound 5e and 6e: 2-(2-Nitrophenyl)-3-(2,2,7,7-tetramethyl-tetrahydro-bis [1,3]dioxolo[4,5-b;4',5'-d]pyran-5-ylmethyl)thiazolidin-4-one

Spectrum

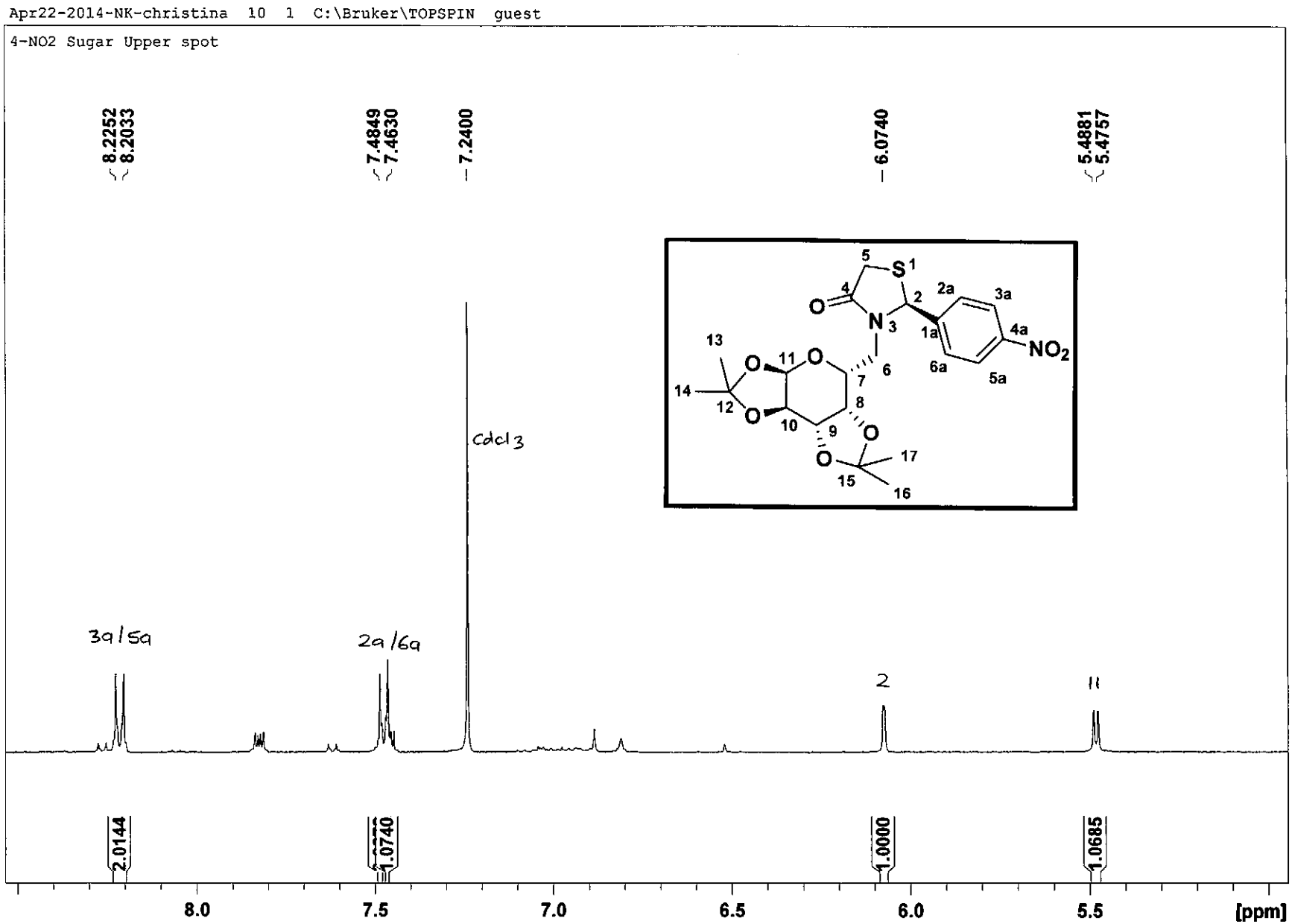
Line#:1 R.Time:13.265(Scan#:1854)
MassPeaks:579
RawMode:Averaged 13.260-13.270(1853-1855) BasePeak:73(525020)
BG Mode:Calc. from Peak Group 1 - Event 1 Scan



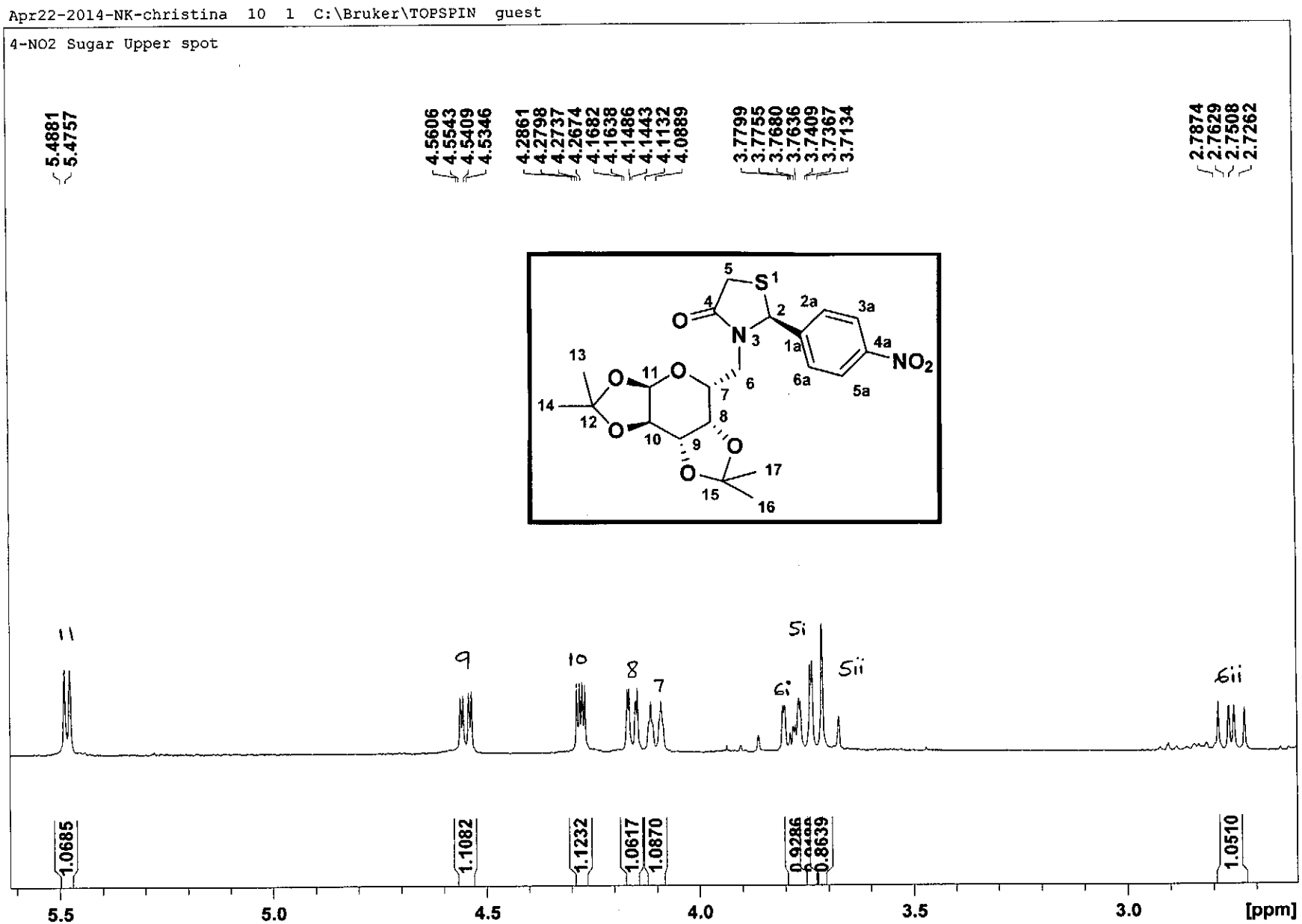
GC-MS of Compound 5e and 6e: 2-(2-Nitrophenyl)-3-(2,2,7,7-tetramethyl-tetrahydro-bis[1,3]dioxolo[4,5-b;4',5'-d]pyran-5-ylmethyl)thiazolidin-4-one



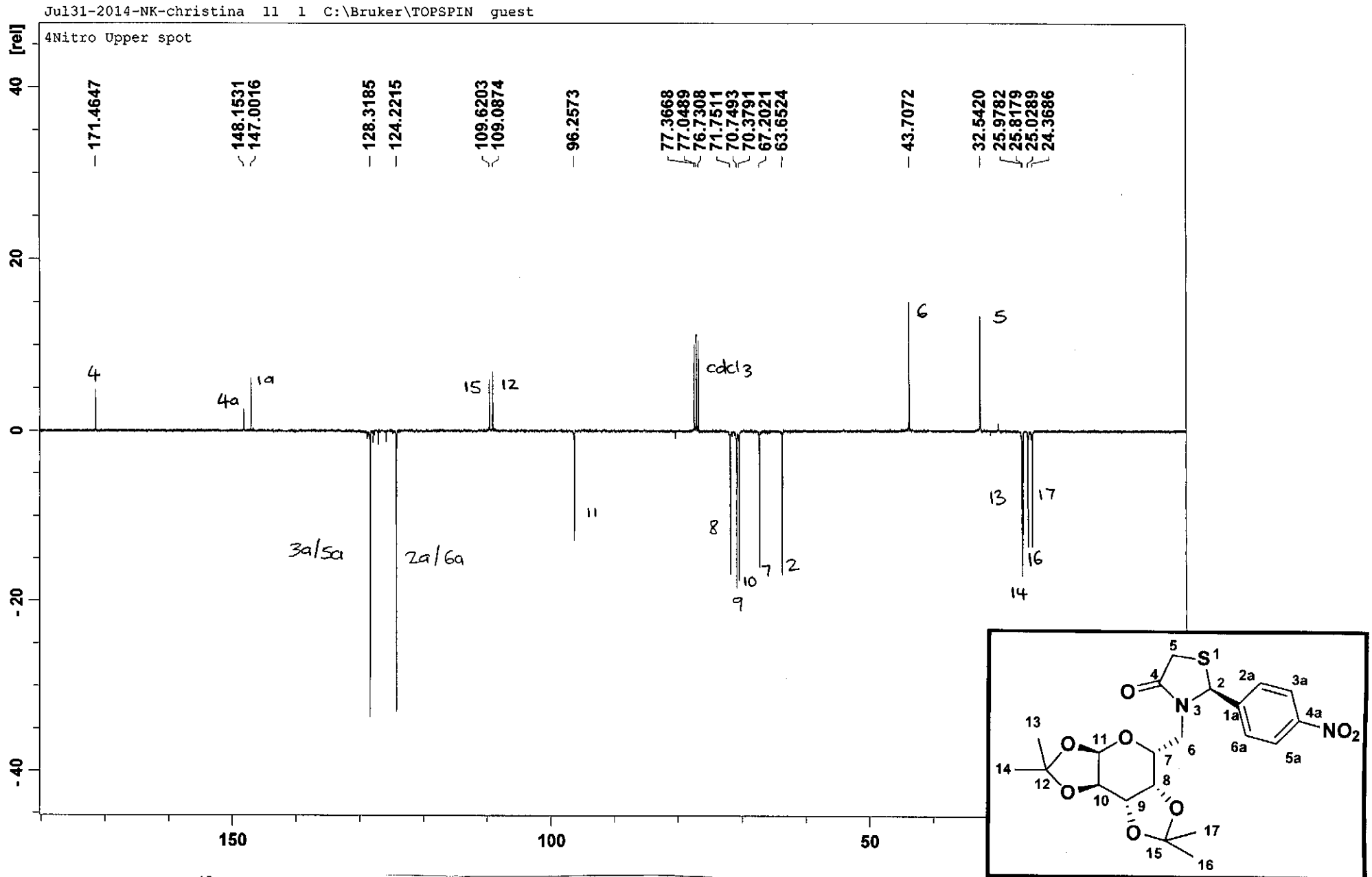
^{1}H Spectrum of Compound 5f: 2-(4-Nitro-phenyl)-3-(2,2,7,7-tetramethyl-tetrahydro-bis [1,3]dioxolo[4,5-b;4',5'-d]pyran-5-ylmethyl)-thiazolidin-4-one



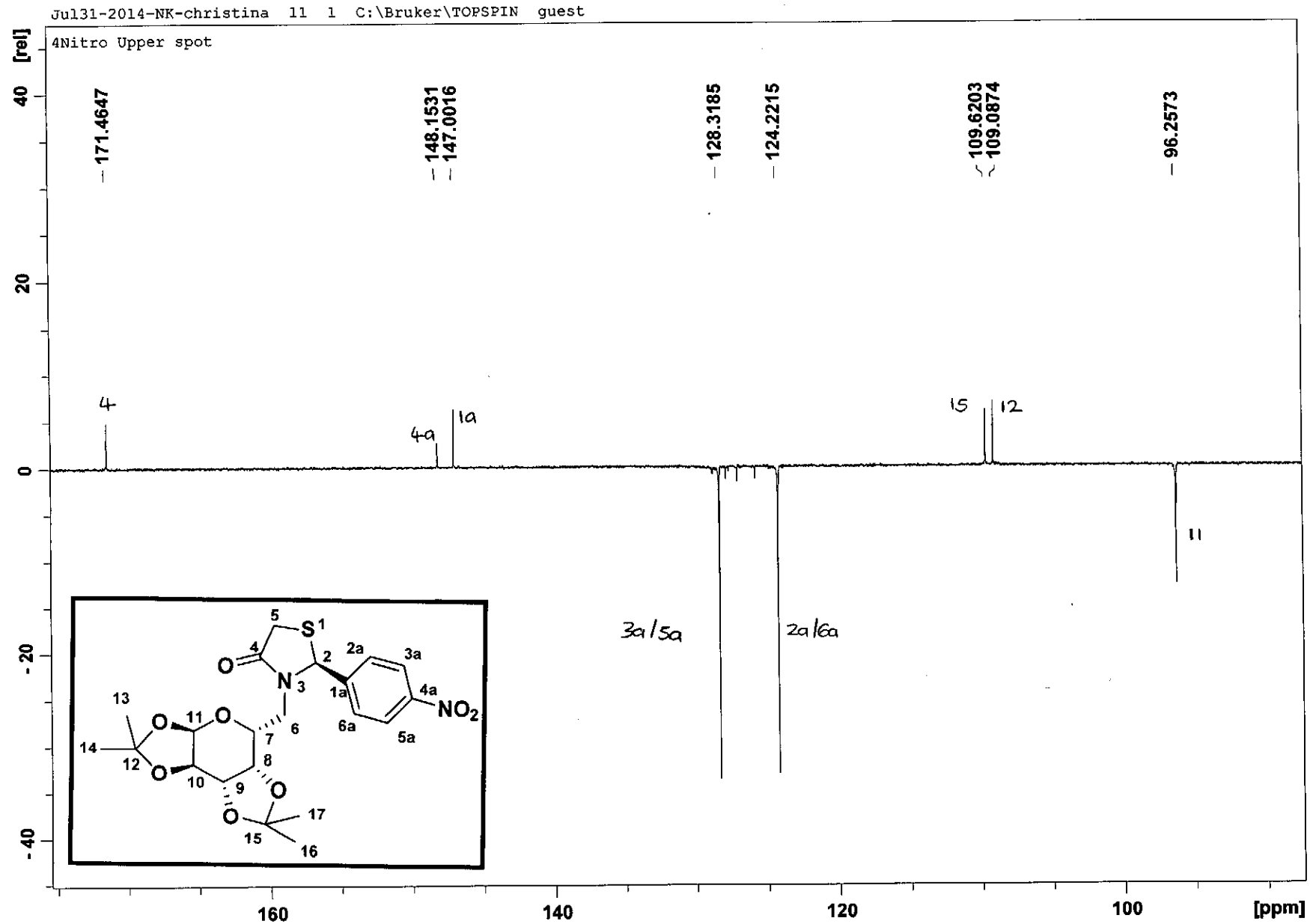
Expanded ^{1}H Spectrum of Compound 5f: 2-(4-Nitro-phenyl)-3-(2,2,7,7-tetramethyl-tetrahydro-bis[1,3]dioxolo[4,5-b;4',5'-d]pyran-5-ylmethyl)-thiazolidin-4-one



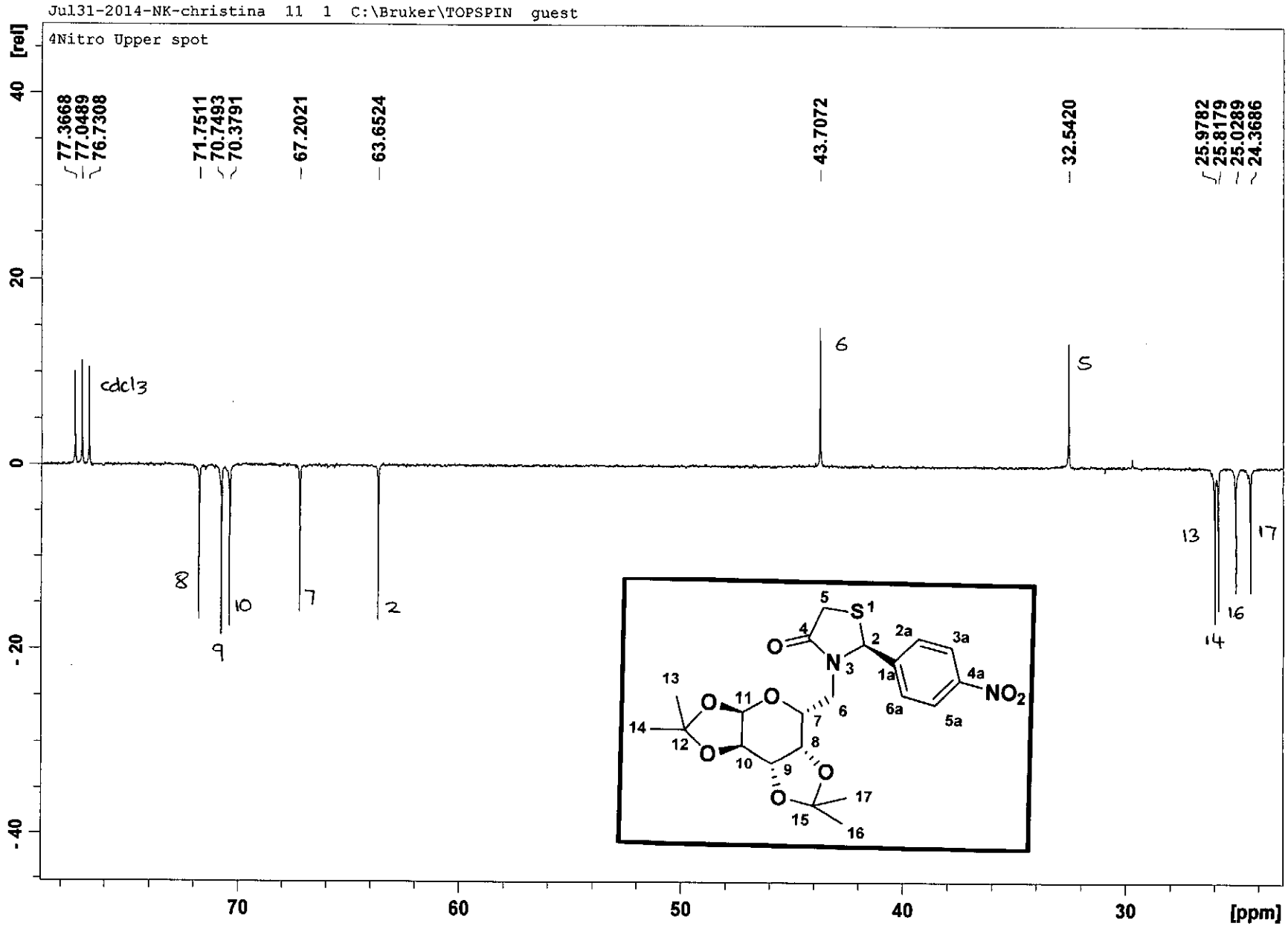
Expanded ^{1}H Spectrum of Compound 5f: 2-(4-Nitro-phenyl)-3-(2,2,7,7-tetramethyl-tetrahydro-bis[1,3]dioxolo[4,5-b;4',5'-d]pyran-5-ylmethyl)-thiazolidin-4-one



^{13}C Spectrum of Compound 5f: 2-(4-Nitro-phenyl)-3-(2,2,7,7-tetramethyl-tetrahydro-bis [1,3]dioxolo[4,5-b;4',5'-d]pyran-5-ylmethyl)-thiazolidin-4-one

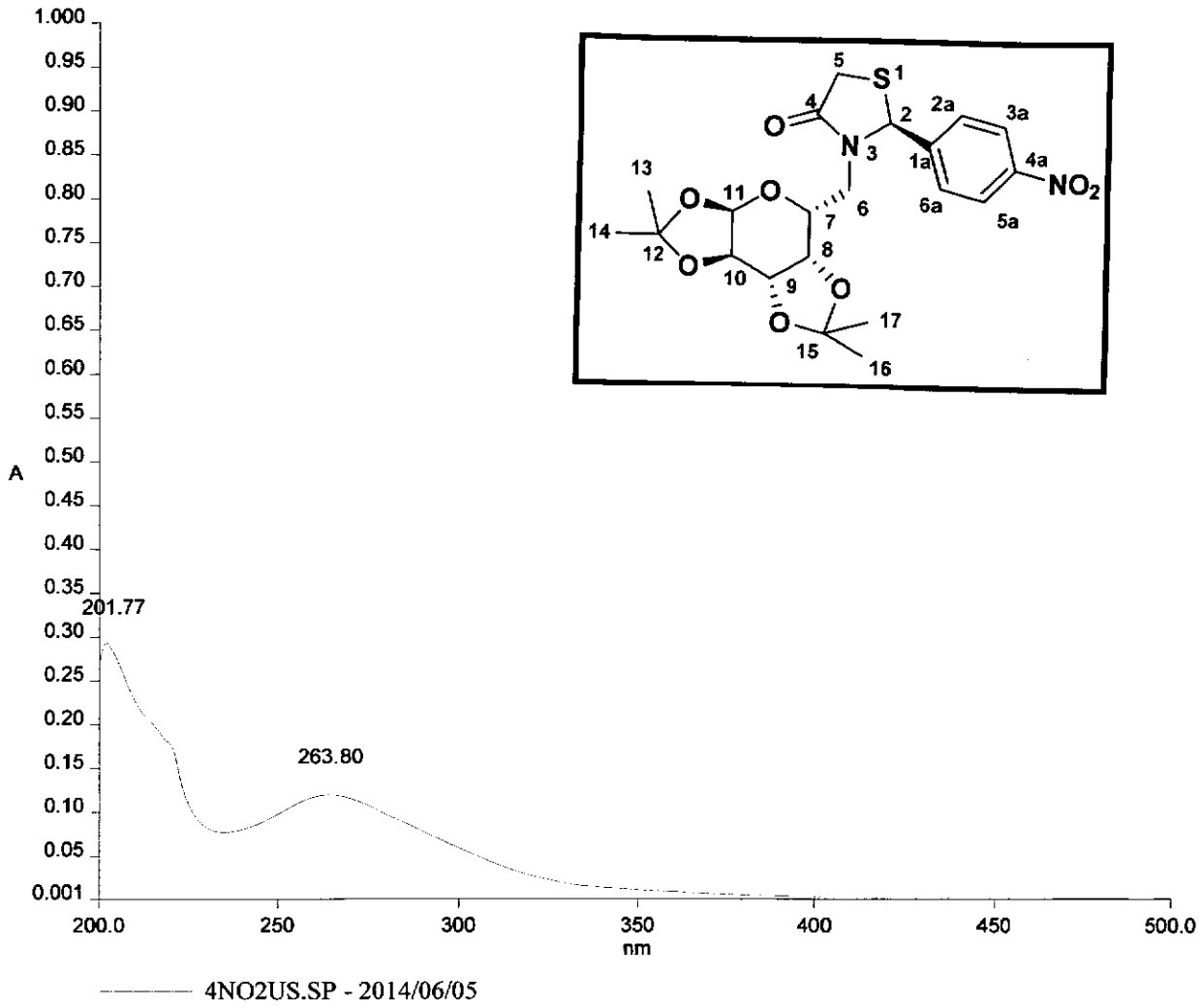


Expanded ^{13}C Spectrum of Compound 5f: 2-(4-Nitro-phenyl)-3-(2,2,7,7-tetramethyl-tetrahydro-bis[1,3]dioxolo[4,5-b;4',5'-d]pyran-5-ylmethyl)-thiazolidin-4-one

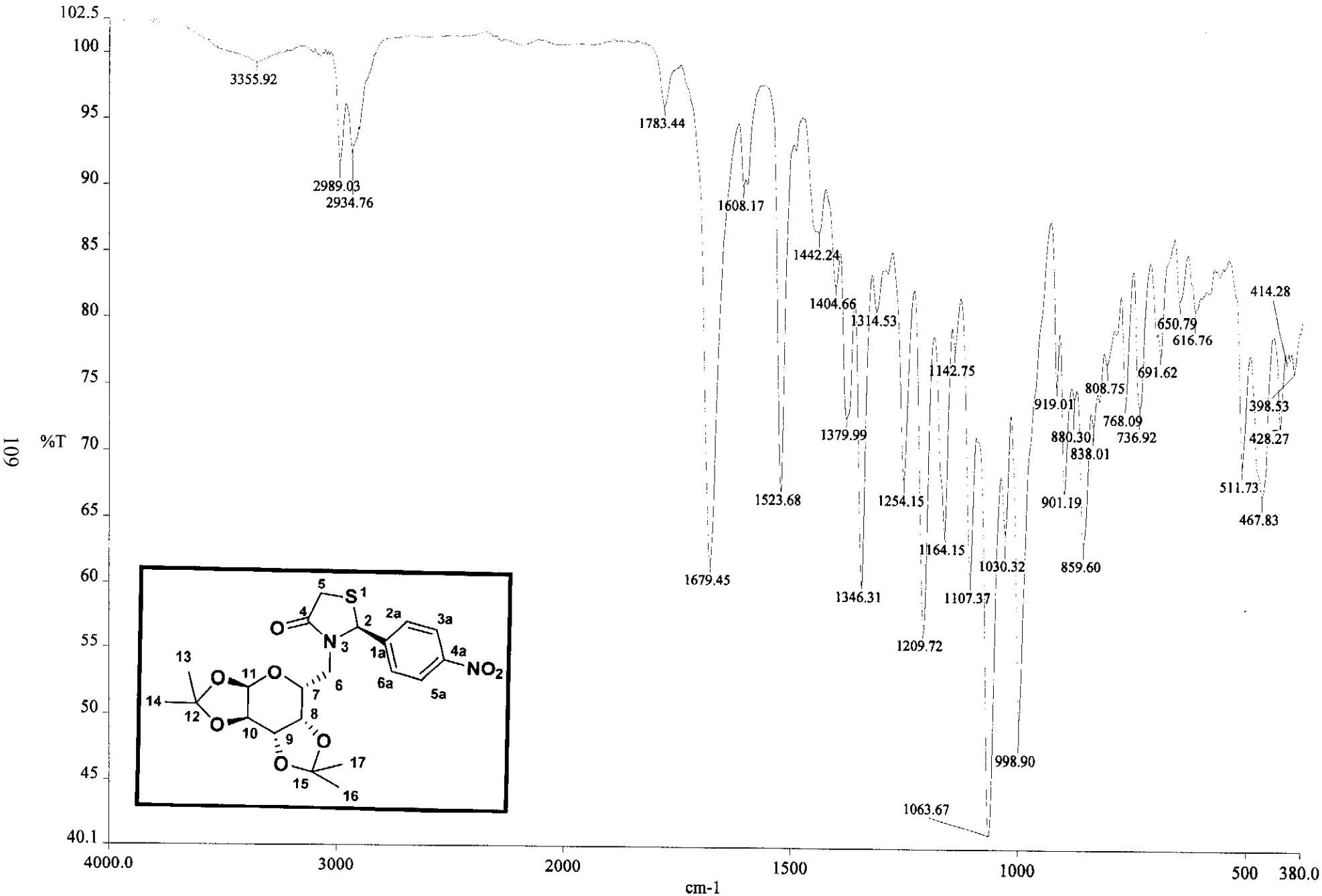


Expanded ^{13}C Spectrum of Compound 5f: 2-(4-Nitro-phenyl)-3-(2,2,7,7-tetramethyl-tetrahydro-bis[1,3]dioxolo[4,5-b;4',5'-d]pyran-5-ylmethyl)-thiazolidin-4-one

Date: 2014/06/05 Time: 04:40:15 PM



Ultraviolet Spectrum of Compound 5f: 2-(4-Nitro-phenyl)-3-(2,2,7,7-tetramethyl-tetra hydro-bis [1,3]dioxolo[4,5-b;4',5'-d]pyran-5-ylmethyl)-thiazolidin-4-one



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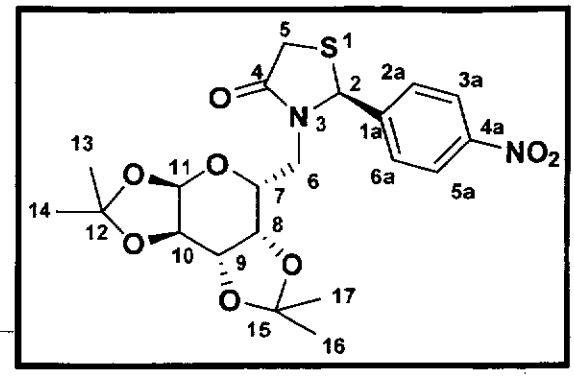
Infrared Spectrum of Compound 5f: 2-(4-Nitro-phenyl)-3-(2,2,7,7-tetramethyl-tetrahydro-bis [1,3]dioxolo[4,5-b;4',5'-d]pyran-5-ylmethyl)-thiazolidin-4-one

==== Shimadzu LCsolution Analysis Report ====

Acquired by	: Admin
Sample Name	: 4no2 us formic buffer
Sample ID	: 4no2 us formic buffer
Vail #	: 1
Injection Volume	: 100 uL
Data File Name	: 4no2 us formic buffer.lcd
Method File Name	: Pramod 09jun 2014.lcm
Batch File Name	: suger thiozolidinon.lcb
Report File Name	: Default.lcr
Data Acquired	: 2014/06/18 07:16:20 AM
Data Processed	: 2014/06/18 07:56:23 AM



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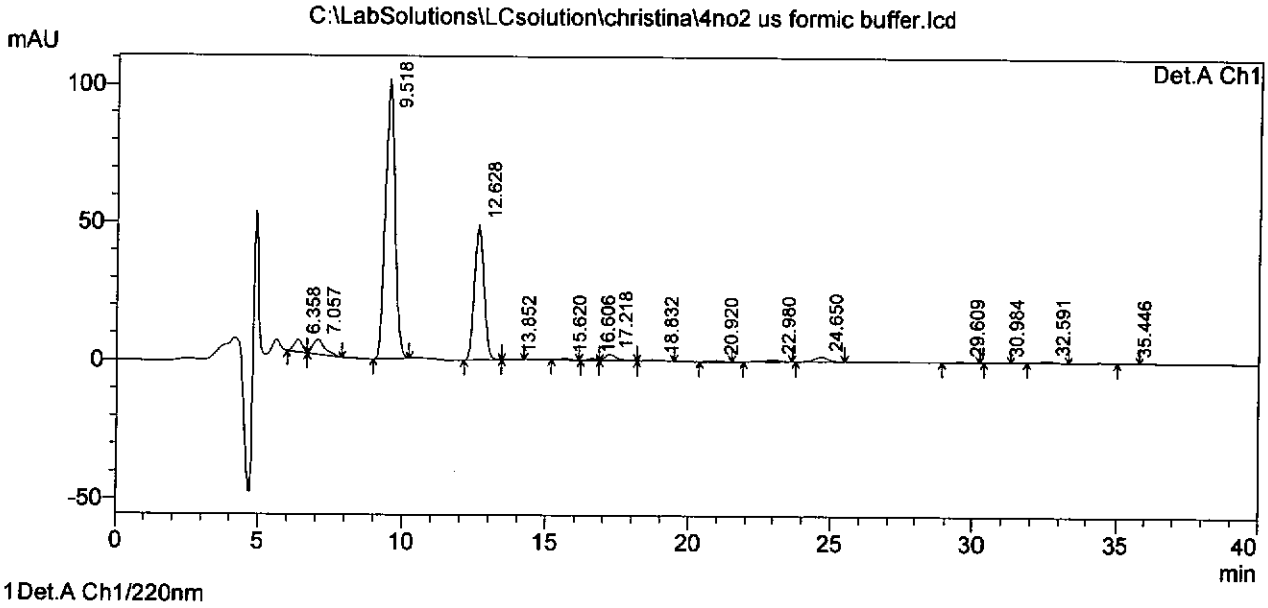


<Results>

PeakTable C:\LabSolutions\LCsolution\christina\4no2 us formic buffer.lcd

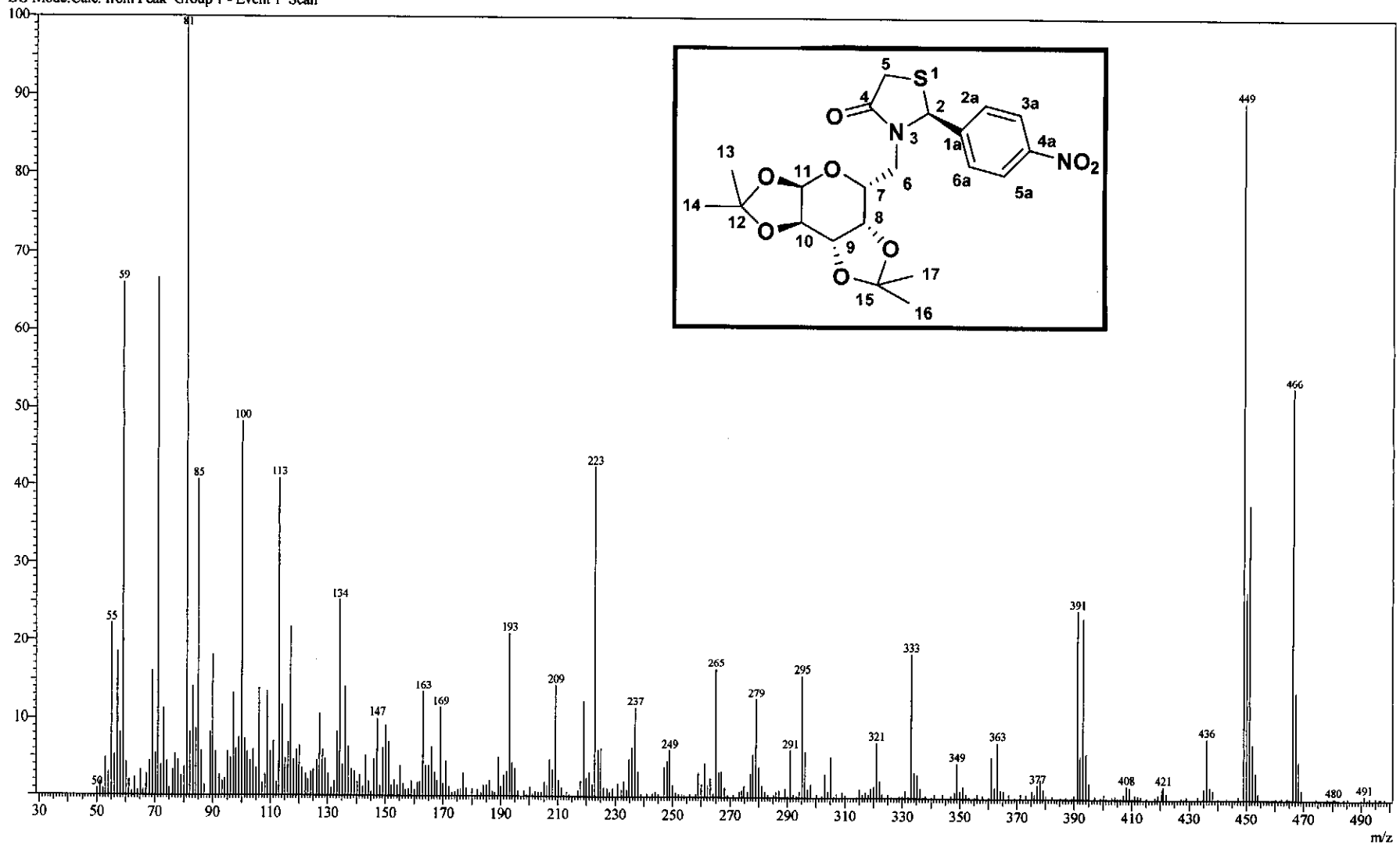
Detector A Ch1 220nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	6.358	88622	4524	2.194	2.675
2	7.057	158506	5410	3.924	3.199
3	9.518	2375920	101550	58.815	60.035
4	12.628	1137958	49150	28.170	29.057
5	13.852	6979	226	0.173	0.134
6	15.620	13126	514	0.325	0.304
7	16.606	18279	802	0.452	0.474
8	17.218	66417	2257	1.644	1.334
9	18.832	21091	546	0.522	0.323
10	20.920	11739	422	0.291	0.250
11	22.980	31487	745	0.779	0.440
12	24.650	60437	1666	1.496	0.985
13	29.609	12221	312	0.303	0.185
14	30.984	5643	159	0.140	0.094
15	32.591	25761	690	0.638	0.408
16	35.446	5496	176	0.136	0.104
Total		4039680	169150	100.000	100.000

HPLC of Compound 5f: 2-(4-Nitro-phenyl)-3-(2,2,7,7-tetramethyl-tetrahydro-bis [1,3] dioxolo[4,5-b;4',5'-d]pyran-5-ylmethyl)-thiazolidin-4-one

Spectrum

Line#:1 R.Time:24.535(Scan#:4108)
MassPeaks:528
RawMode:Averaged 24.530-24.540(4107-4109) BasePeak:81(14273)
BG Mode:Calc. from Peak Group 1 - Event 1 Scan



GC-MS of Compound 5f: 2-(4-Nitro-phenyl)-3-(2,2,7,7-tetramethyl-tetrahydro-bis [1,3] dioxolo[4,5-b;4',5'-d]pyran-5-ylmethyl)-thiazolidin-4-one

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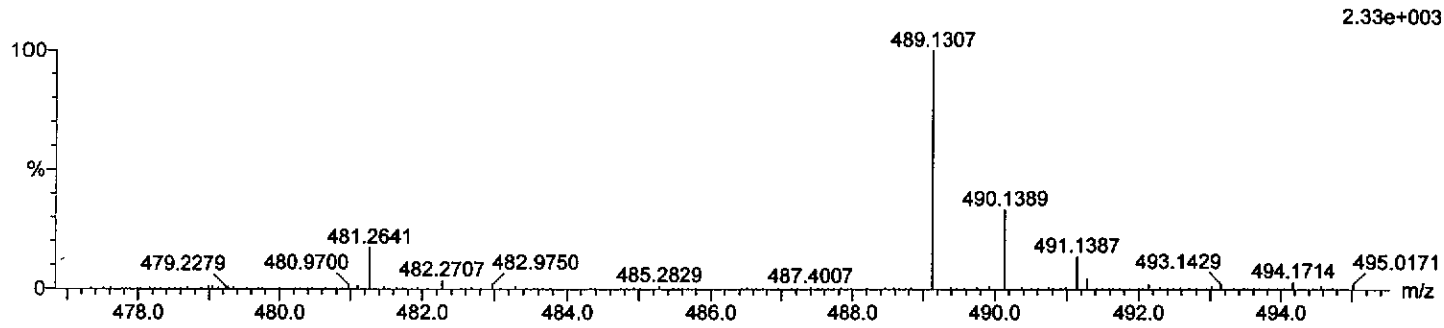
Elemental Composition Report **Page 1**

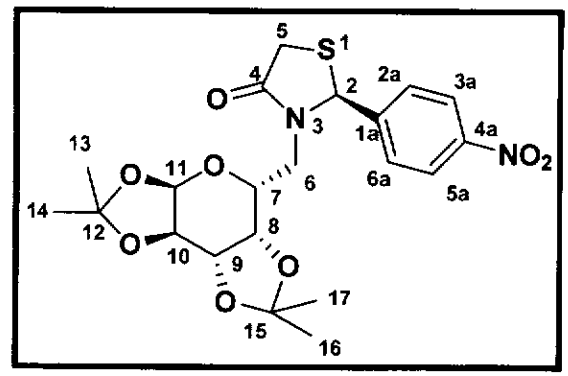
Single Mass Analysis
Tolerance = 5.0 PPM / DBE: min = -1.5, max = 100.0
Element prediction: Off
Number of isotope peaks used for i-FIT = 3

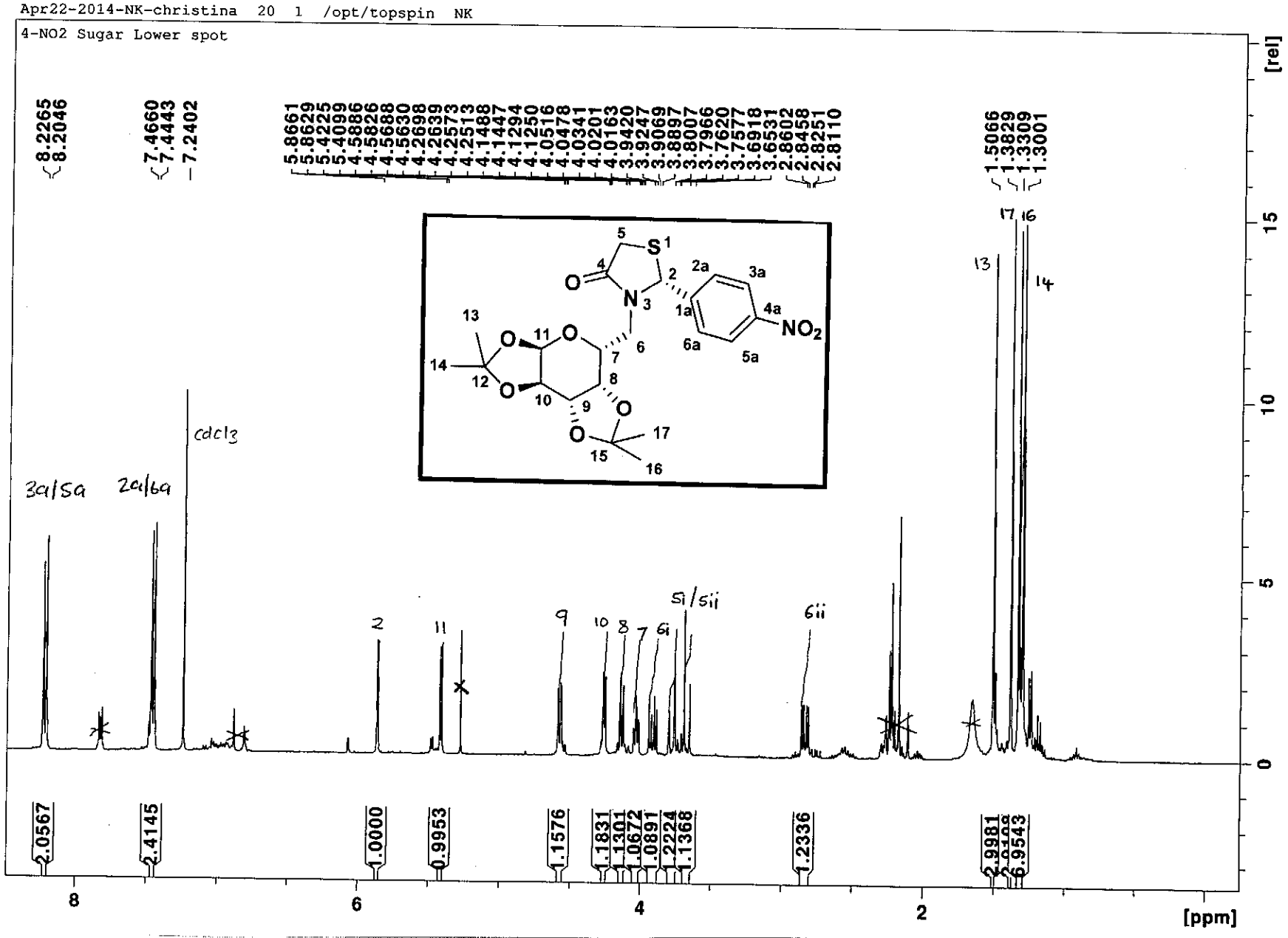
Monoisotopic Mass, Even Electron Ions
50 formula(e) evaluated with 1 results within limits (up to 20 best isotopic matches for each mass)
Elements Used:
C: 20-25 H: 25-30 N: 0-5 O: 5-10 Na: 0-1 S: 0-1
2 61 (2.023)
TOF MS ES+



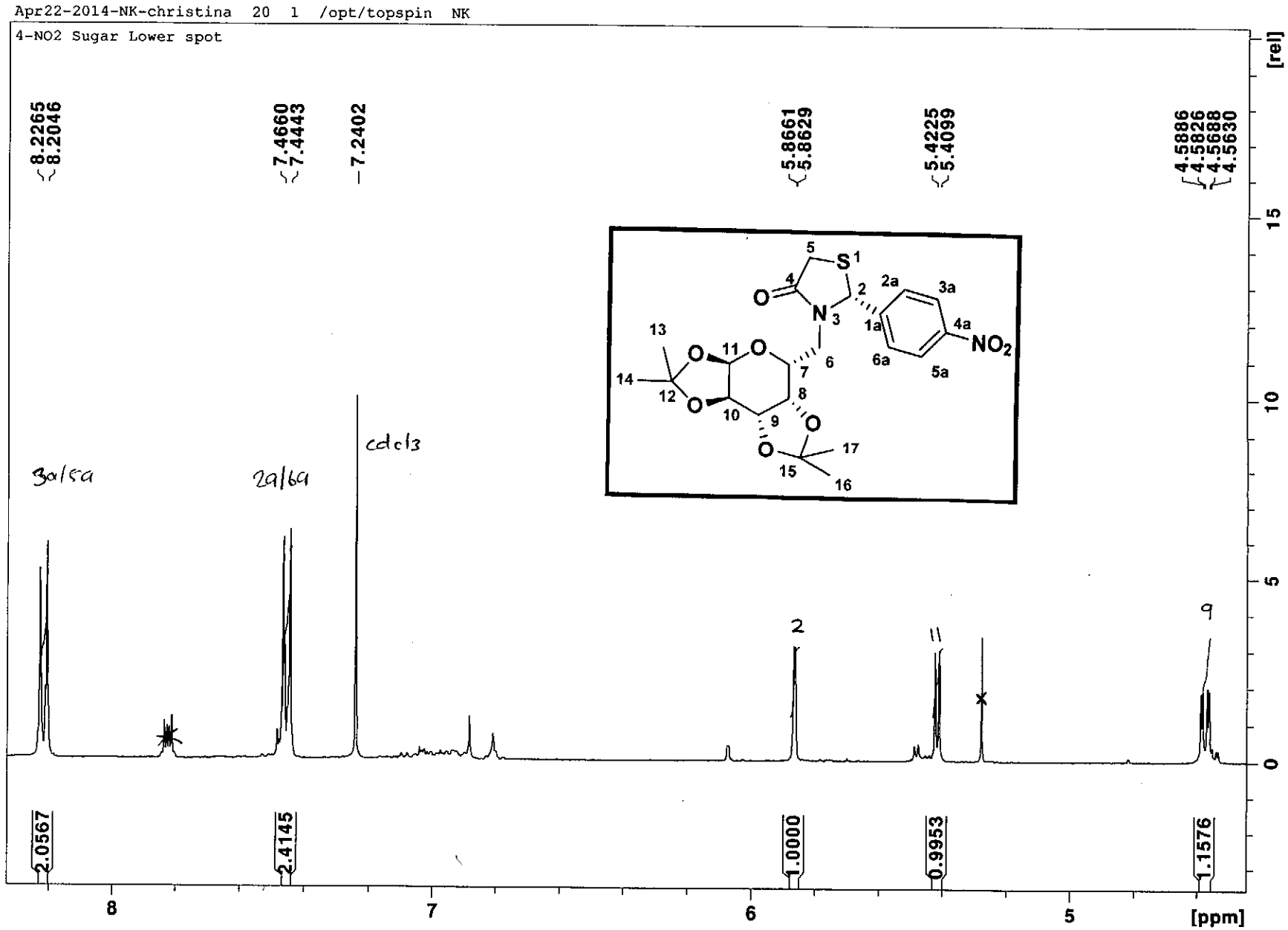
Minimum:				-1.5								
Maximum:		5.0	5.0	100.0								
Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	i-FIT (Norm)	Formula					
489.1307	489.1308	-0.1	-0.2	9.5	91.0	0.0	C21	H26	N2	O8	Na	S

HRMS of Compound 5f: 2-(4-Nitro-phenyl)-3-(2,2,7,7-tetramethyl-tetrahydro-bis [1,3] dioxolo[4,5-b;4',5'-d]pyran-5-ylmethyl)-thiazolidin-4-one

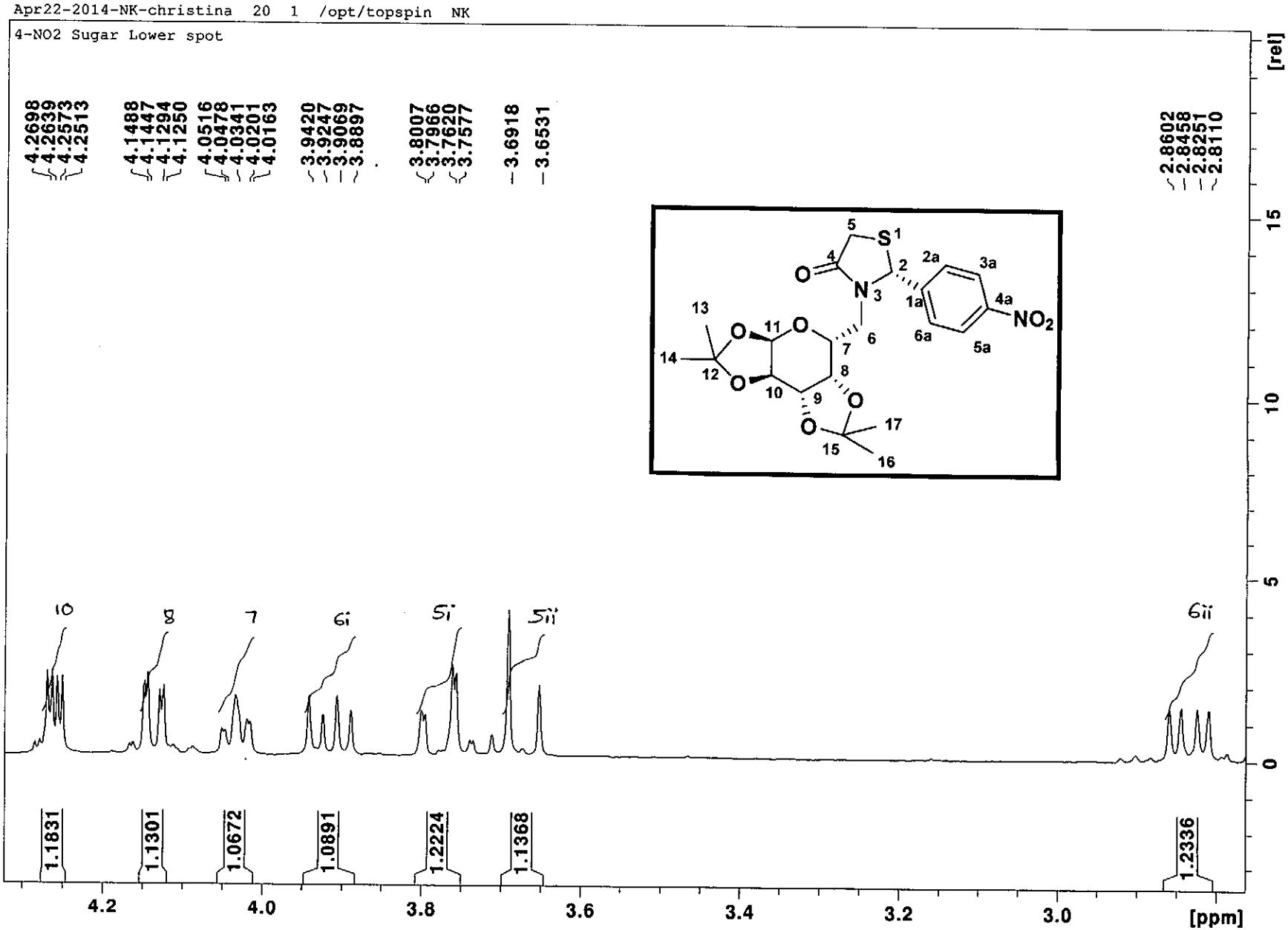




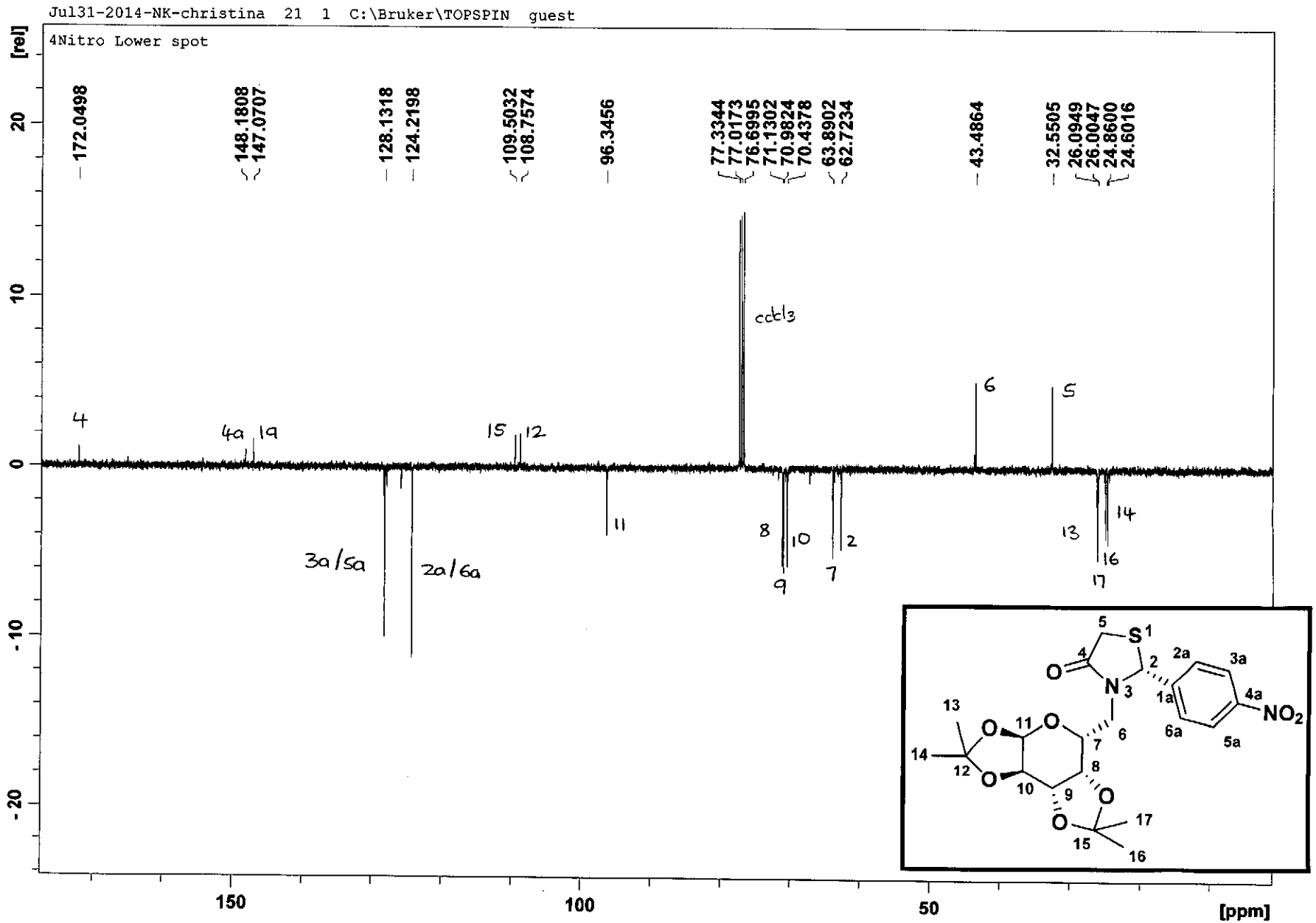
^{1}H Spectrum of Compound 6f: 2-(4-Nitro-phenyl)-3-(2,2,7,7-tetramethyl-tetrahydro-bis [1,3]dioxolo[4,5-b;4',5'-d]pyran-5-ylmethyl)-thiazolidin-4-one



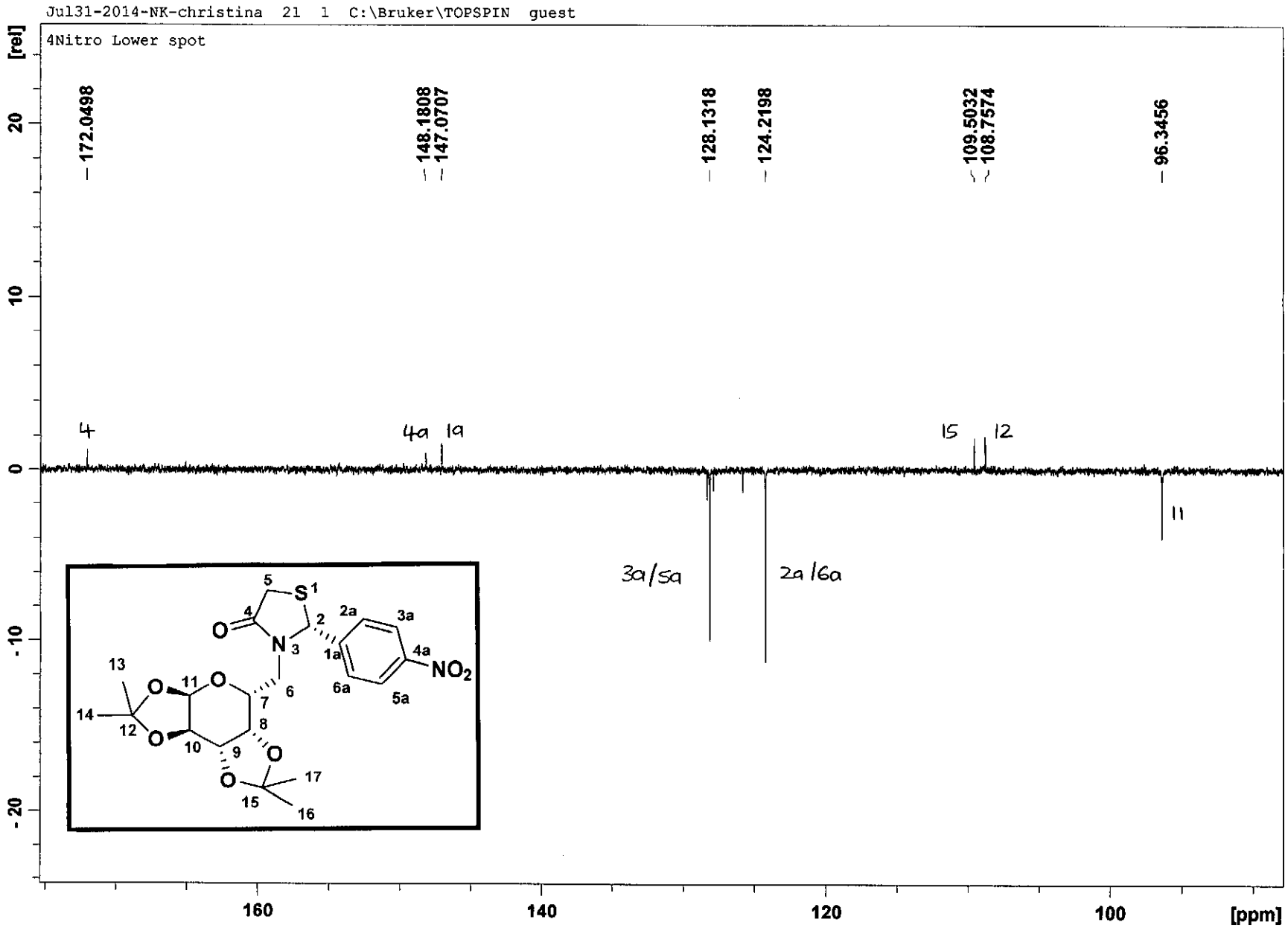
Expanded ^{1}H Spectrum of Compound 6f: 2-(4-Nitro-phenyl)-3-(2,2,7,7-tetramethyl-tetrahydro-bis[1,3]dioxolo[4,5-b;4',5'-d]pyran-5-ylmethyl)-thiazolidin-4-one



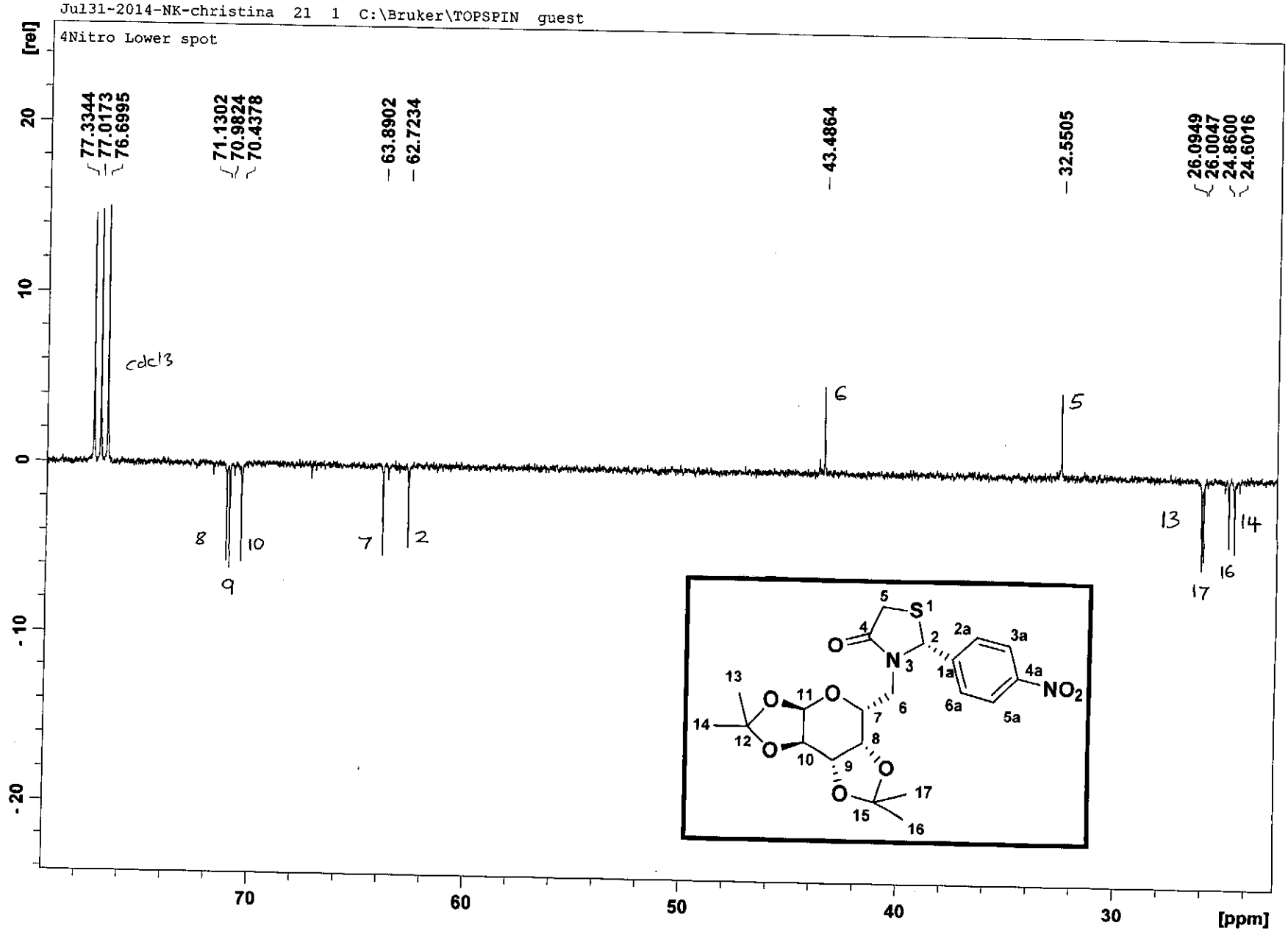
Expanded ^{1}H Spectrum of Compound 6f: 2-(4-Nitro-phenyl)-3-(2,2,7,7-tetramethyl-tetrahydro-bis[1,3]dioxolo[4,5-b;4',5'-d]pyran-5-ylmethyl)-thiazolidin-4-one



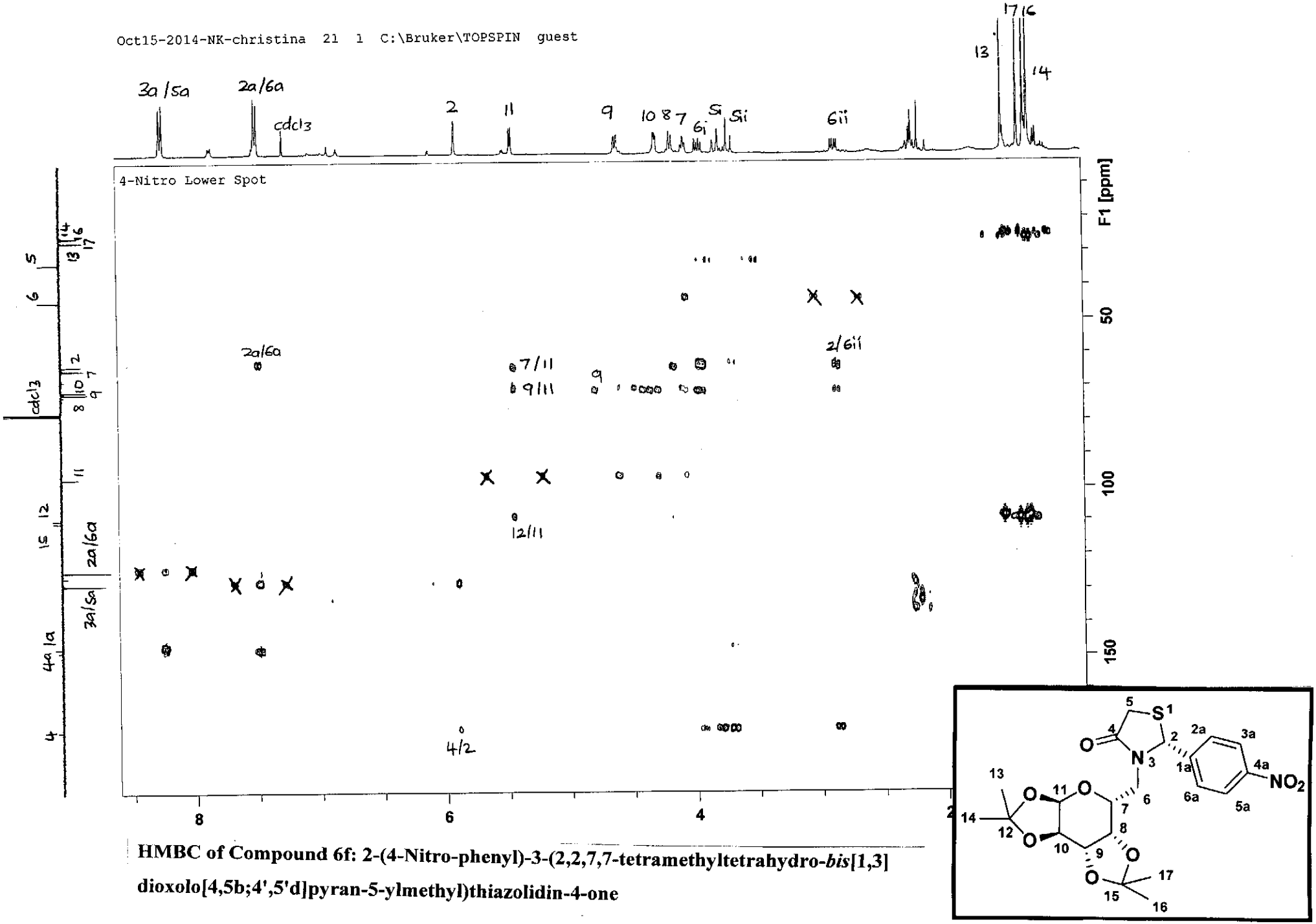
^{13}C Spectrum of Compound 6f: 2-(4-Nitro-phenyl)-3-(2,2,7,7-tetramethyl-tetrahydro-bis[1,3]dioxolo[4,5-b;4',5'-d]pyran-5-ylmethyl)-thiazolidin-4-one



Expanded ^{13}C Spectrum of Compound 6f: 2-(4-Nitro-phenyl)-3-(2,2,7,7-tetramethyl-tetrahydro-bis[1,3]dioxolo[4,5-b;4',5'-d]pyran-5-ylmethyl)-thiazolidin-4-one

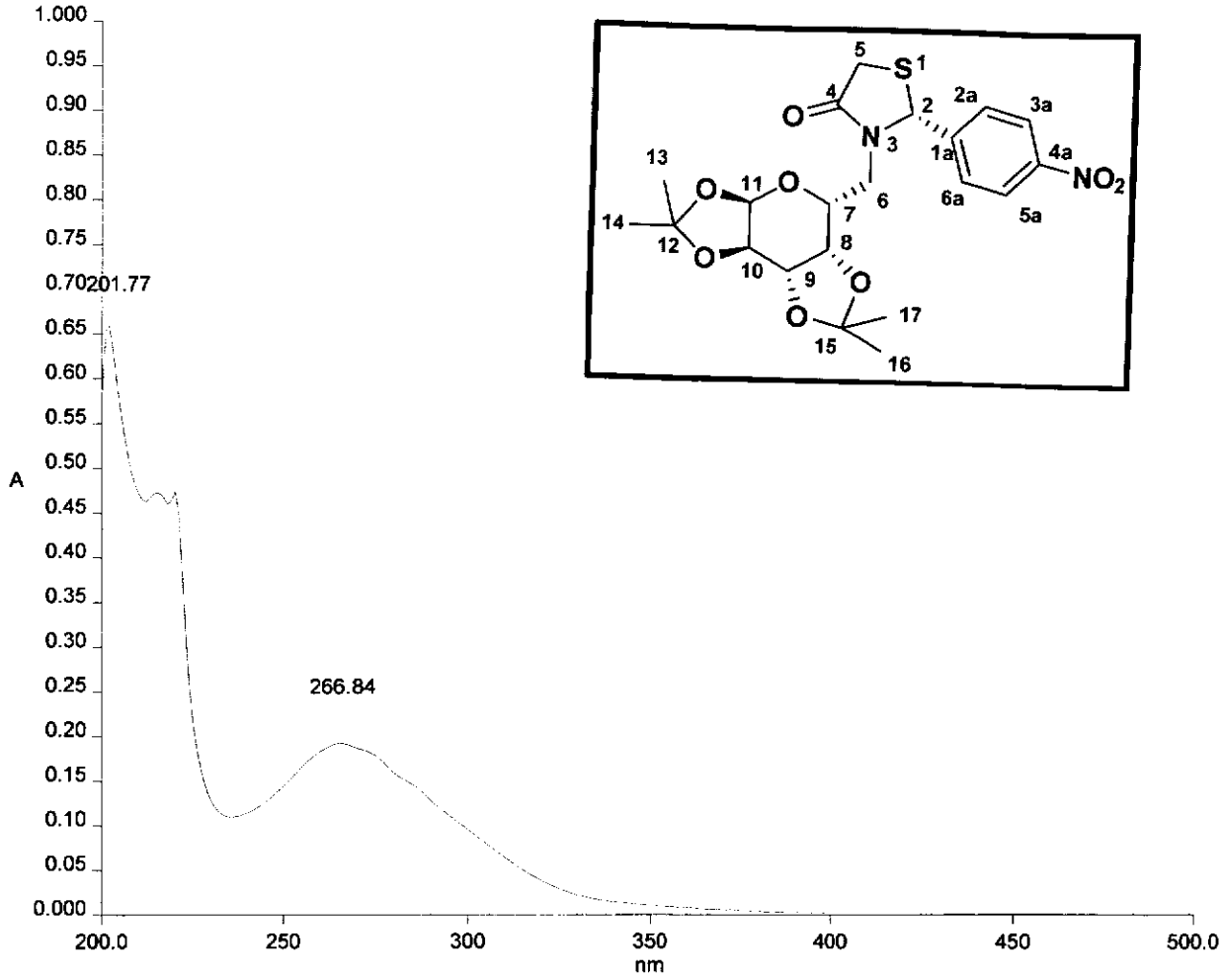


Expanded ^{13}C Spectrum of Compound 6f: 2-(4-Nitro-phenyl)-3-(2,2,7,7-tetramethyl-tetrahydro-bis[1,3]dioxolo[4,5-b;4',5'-d]pyran-5-ylmethyl)-thiazolidin-4-one

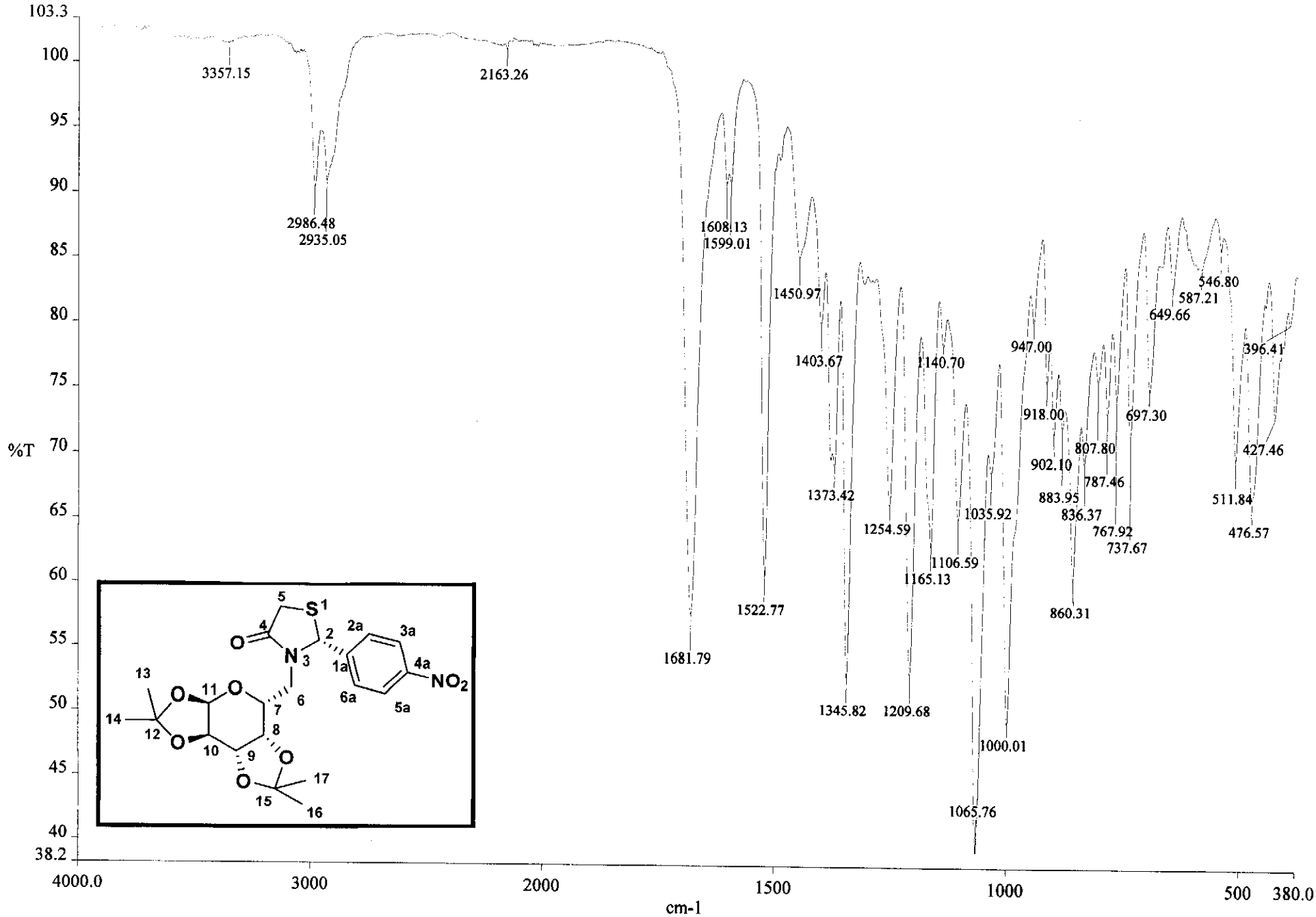


HMBC of Compound 6f: 2-(4-Nitro-phenyl)-3-(2,2,7,7-tetramethyltetrahydro-*bis*[1,3] dioxolo[4,5b;4',5'd]pyran-5-ylmethyl)thiazolidin-4-one

Date: 2014/06/05 Time: 04:39:04 PM



Ultraviolet Spectrum of Compound 6f: 2-(4-Nitro-phenyl)-3-(2,2,7,7-tetramethyl-tetra hydro-bis [1,3]dioxolo[4,5-b;4',5'-d]pyran-5-ylmethyl)-thiazolidin-4-one

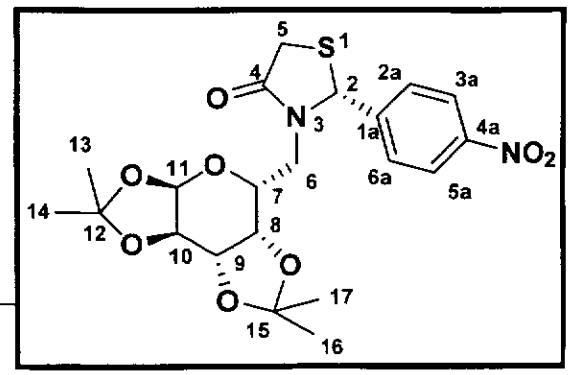


c:\pel_data\spectra\christine\4no2-h-001

Infrared Spectrum of Compound 6f: 2-(4-Nitro-phenyl)-3-(2,2,7,7-tetramethyl-tetra hydro-bis [1,3]dioxolo[4,5-b;4',5'-d]pyran-5-ylmethyl)-thiazolidin-4-one

==== Shimadzu LCsolution Analysis Report ====

Acquired by	: Admin
Sample Name	: 4no2 Is formic buffer
Sample ID	: 4no2 Is formic buffer
Vail #	: 2
Injection Volume	: 100 uL
Data File Name	: 4no2 Is formic buffer.lcd
Method File Name	: Pramod 09jun 2014.lcm
Batch File Name	: suger thiozolidinon.lcb
Report File Name	: Default.lcr
Data Acquired	: 2014/06/18 07:56:57 AM
Data Processed	: 2014/06/18 08:37:01 AM



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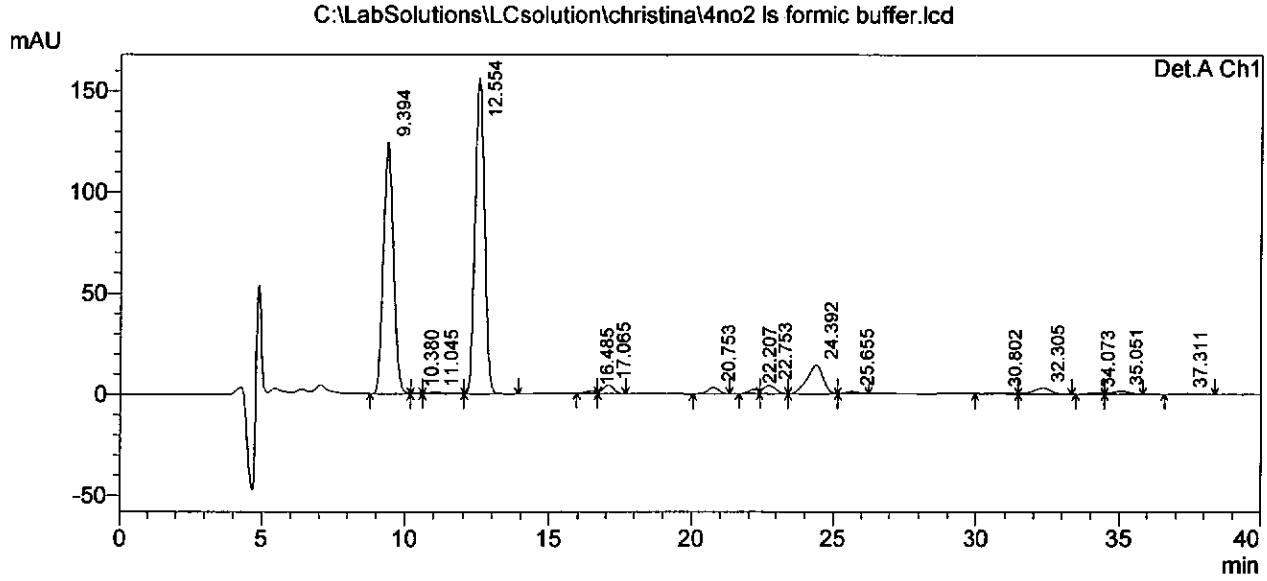


1Det.A Ch1/220nm

<Results>

PeakTable C:\LabSolutions\LCsolution\christina\4no2 Is formic buffer.lcd

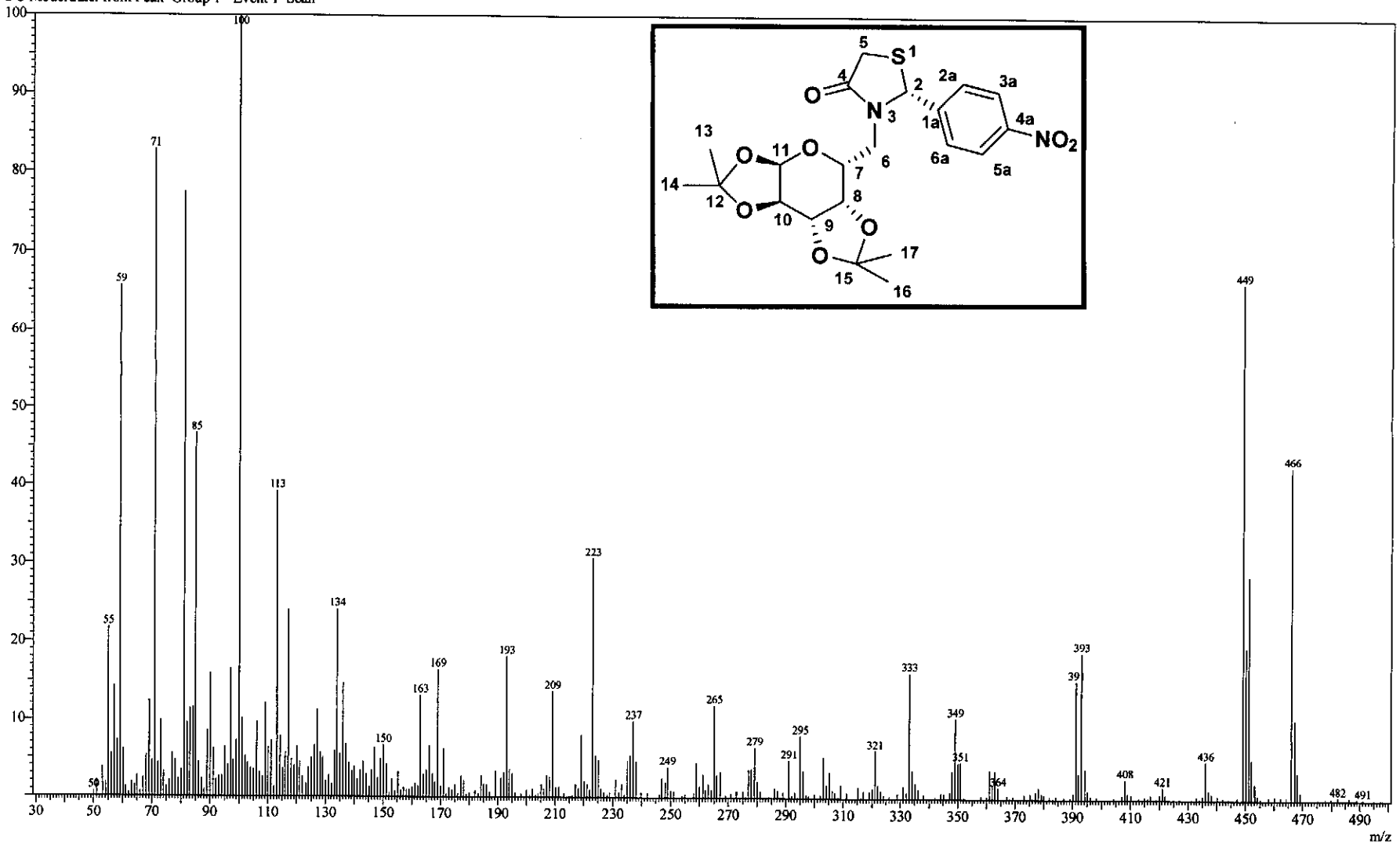
Detector A Ch1 220nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	9.394	3004520	124326	37.955	39.115
2	10.380	10602	465	0.134	0.146
3	11.045	34464	659	0.435	0.207
4	12.554	3613829	156176	45.652	49.135
5	16.485	29197	1221	0.369	0.384
6	17.065	108760	4149	1.374	1.305
7	20.753	84381	3076	1.066	0.968
8	22.207	56056	2213	0.708	0.696
9	22.753	123101	4032	1.555	1.269
10	24.392	554257	14245	7.002	4.482
11	25.655	30157	971	0.381	0.306
12	30.802	32355	652	0.409	0.205
13	32.305	134242	3133	1.696	0.986
14	34.073	22383	613	0.283	0.193
15	35.051	58178	1508	0.735	0.474
16	37.311	19575	407	0.247	0.128
Total		7916057	317848	100.000	100.000

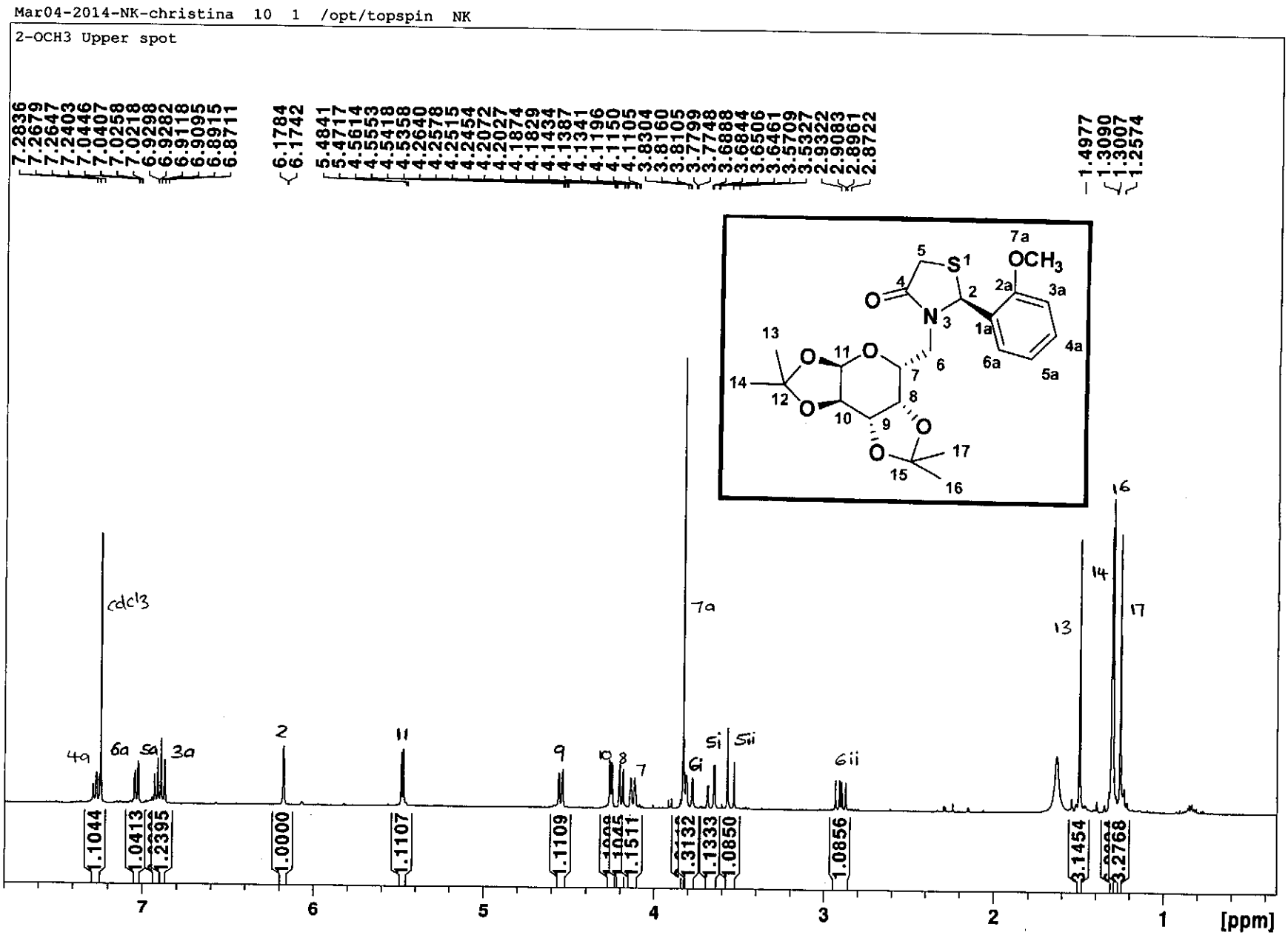
HPLC of Compound 6f: 2-(4-Nitro-phenyl)-3-(2,2,7,7-tetramethyl-tetra hydro-bis [1,3] dioxolo[4,5-b;4',5'-d]pyran-5-ylmethyl)-thiazolidin-4-one

Spectrum

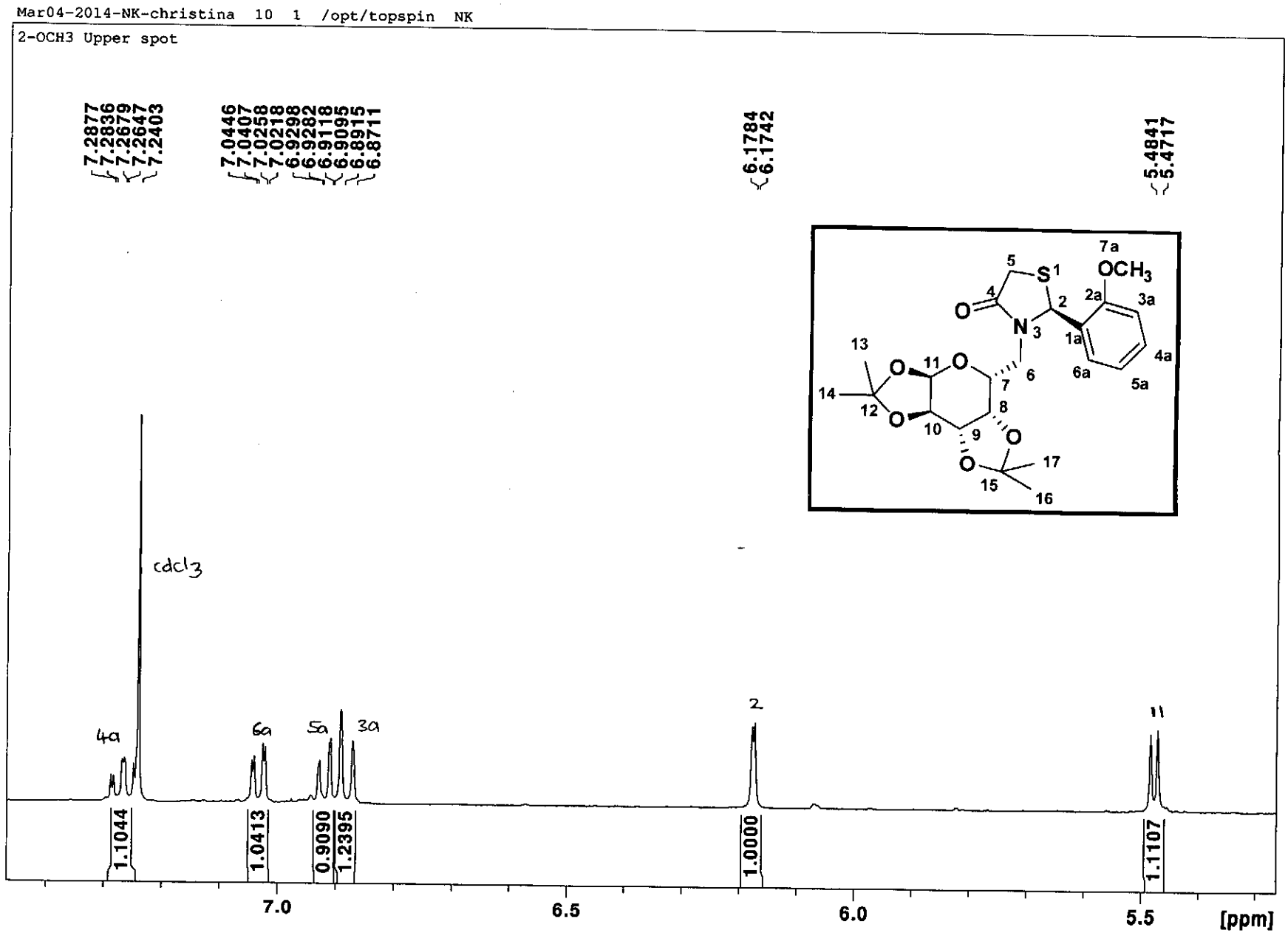
Line#:1 R.Time:25.460(Scan#:4293)
MassPeaks:510
RawMode:Averaged 25.455-25.465(4292-4294) BasePeak:100(17765)
BG Mode:Calc. from Peak Group 1 - Event 1 Scan



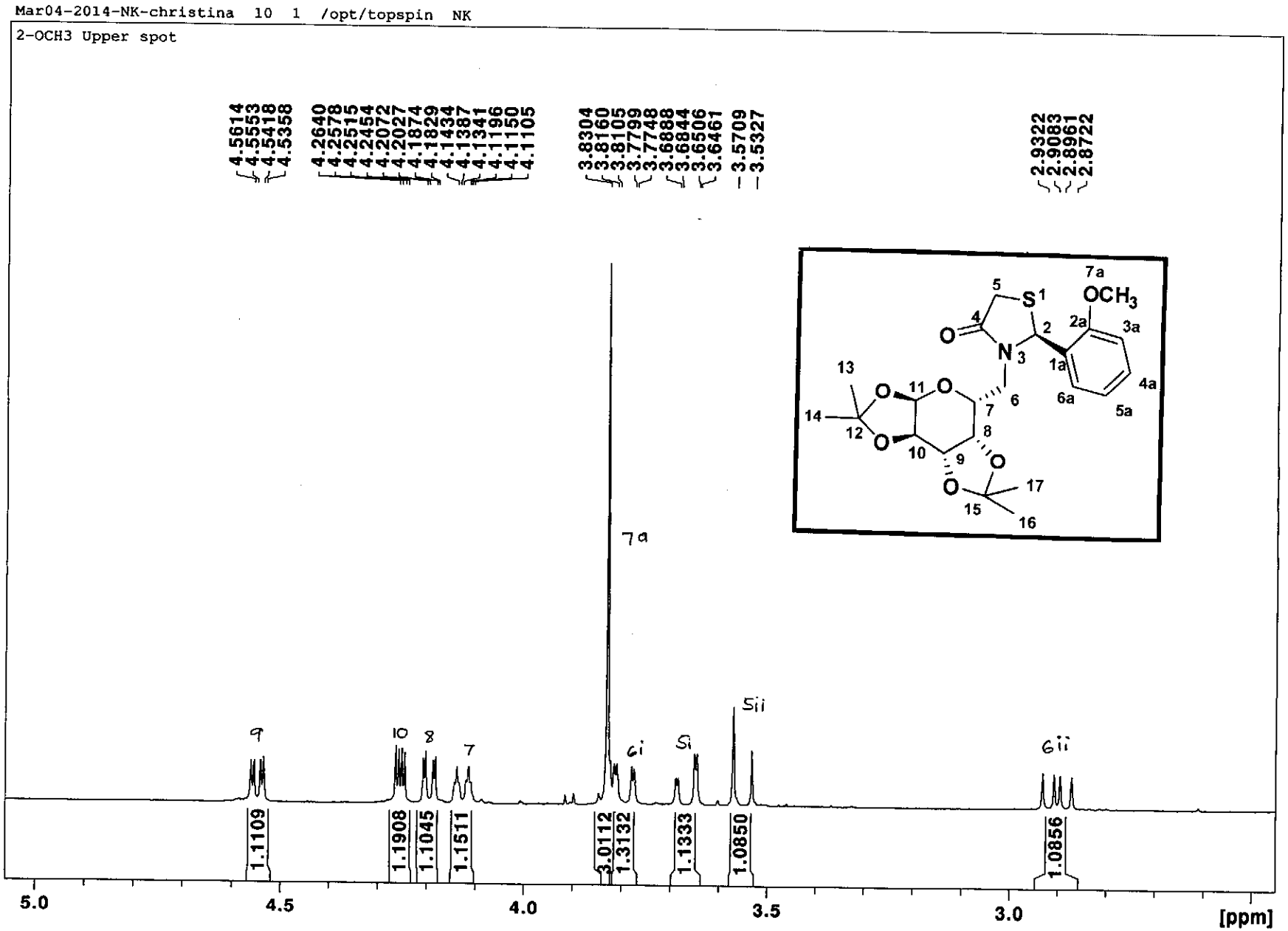
GC-MS of Compound 6f: 2-(4-Nitro-phenyl)-3-(2,2,7,7-tetramethyl-tetra hydro-bis [1,3] dioxolo[4,5-b;4',5'-d]pyran-5-ylmethyl)-thiazolidin-4-one



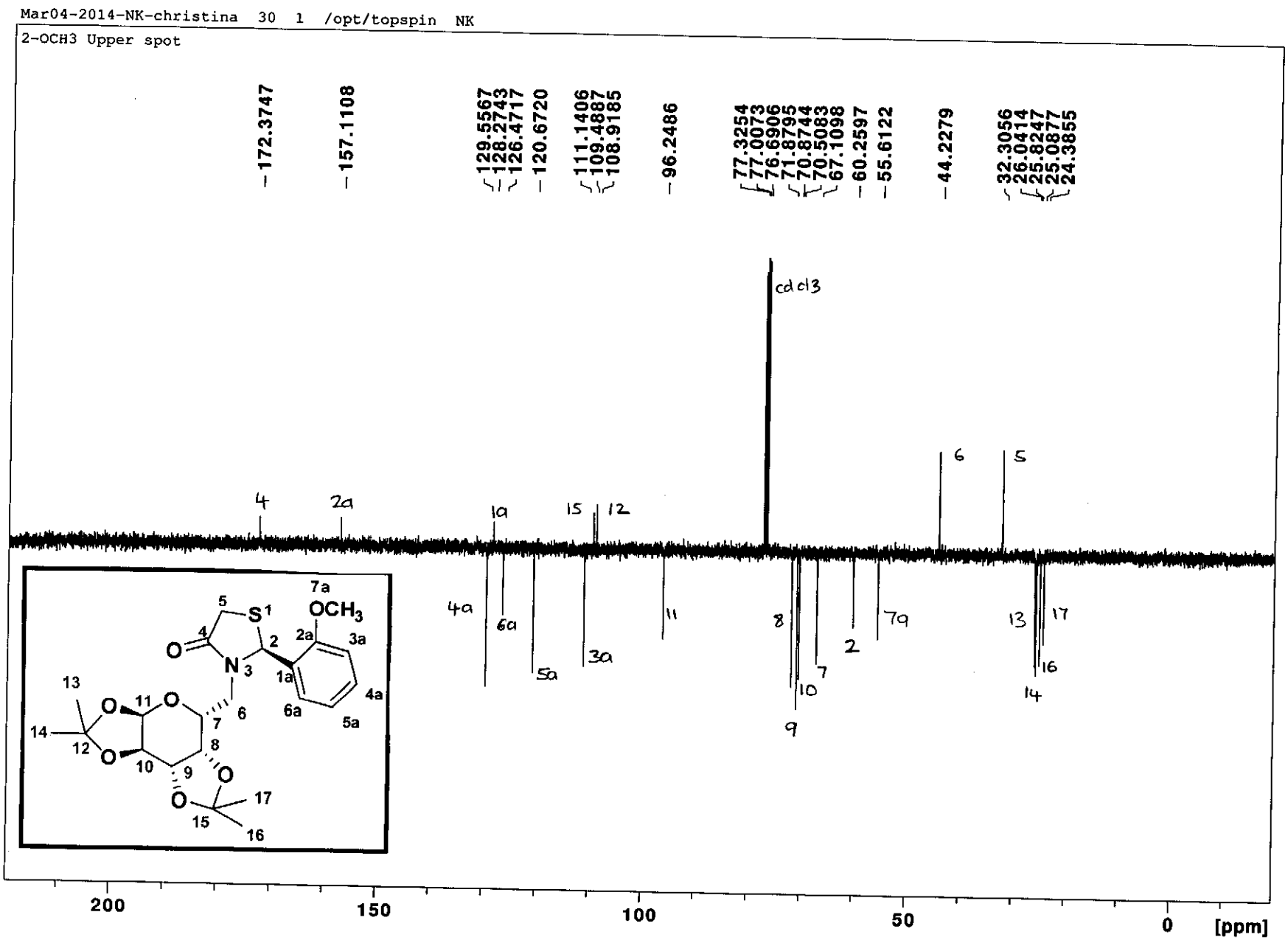
^{1}H Spectrum of Compound 5g: 2-(2-Methoxy-phenyl)-3-(2,2,7,7-tetramethyl-tetrahydro-bis[1,3]dioxolo[4,5-b;4',5'-d]pyran-5-ylmethyl)-thiazolidin-4-one



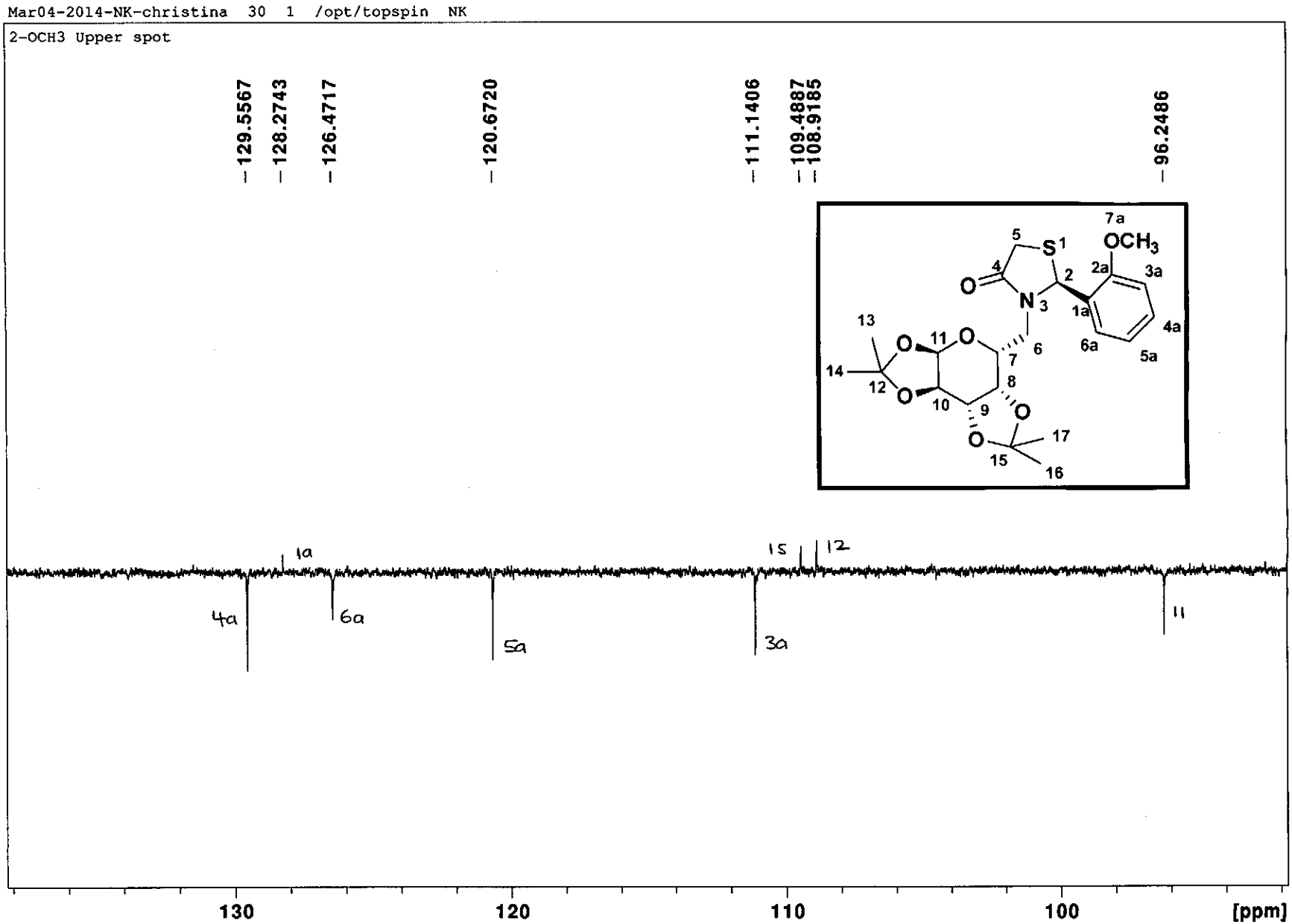
Expanded ^{1}H Spectrum of Compound 5g: 2-(2-Methoxy-phenyl)-3-(2,2,7,7-tetramethyl-tetrahydro-bis[1,3]dioxolo[4,5-b;4',5'-d]pyran-5-ylmethyl)-thiazolidin-4-one



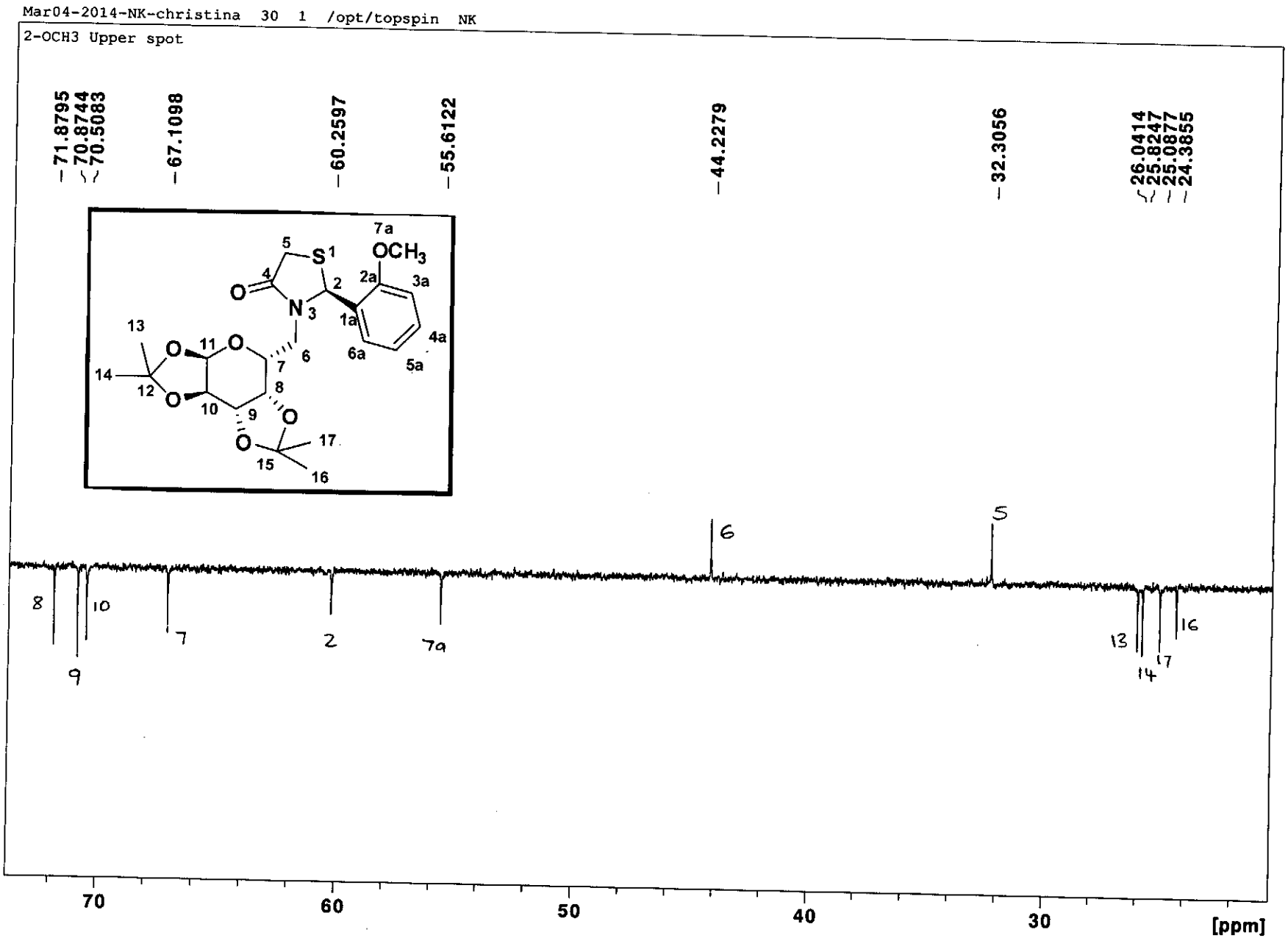
Expanded ^{1}H Spectrum of Compound 5g: 2-(2-Methoxy-phenyl)-3-(2,2,7,7-tetramethyl-tetrahydro-bis[1,3]dioxolo[4,5-b;4',5'-d]pyran-5-ylmethyl)-thiazolidin-4-one



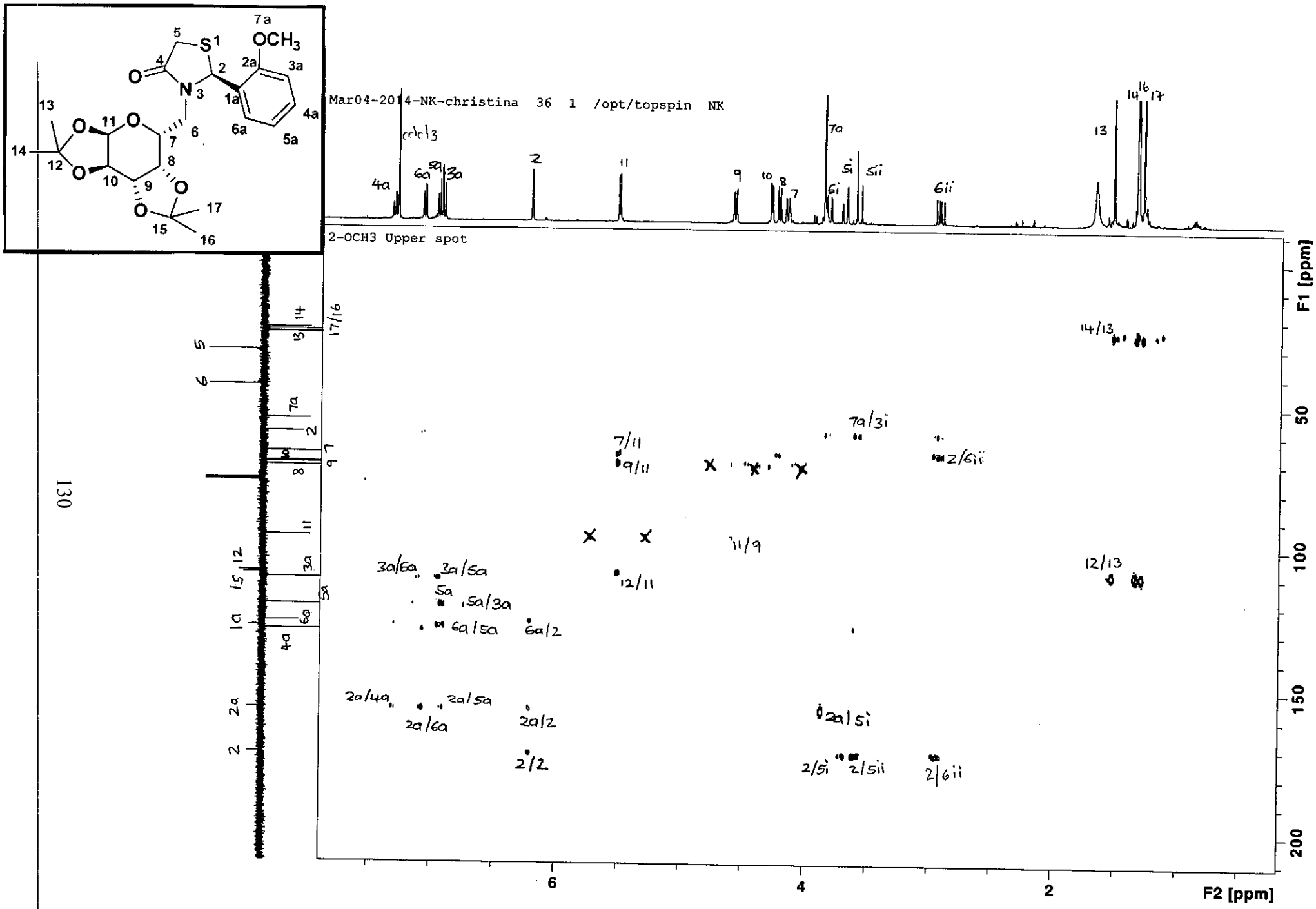
^{13}C Spectrum of Compound 5g: 2-(2-Methoxy-phenyl)-3-(2,2,7,7-tetramethyl-tetrahydro-bis[1,3]dioxolo[4,5-b;4',5'-d]pyran-5-ylmethyl)-thiazolidin-4-one



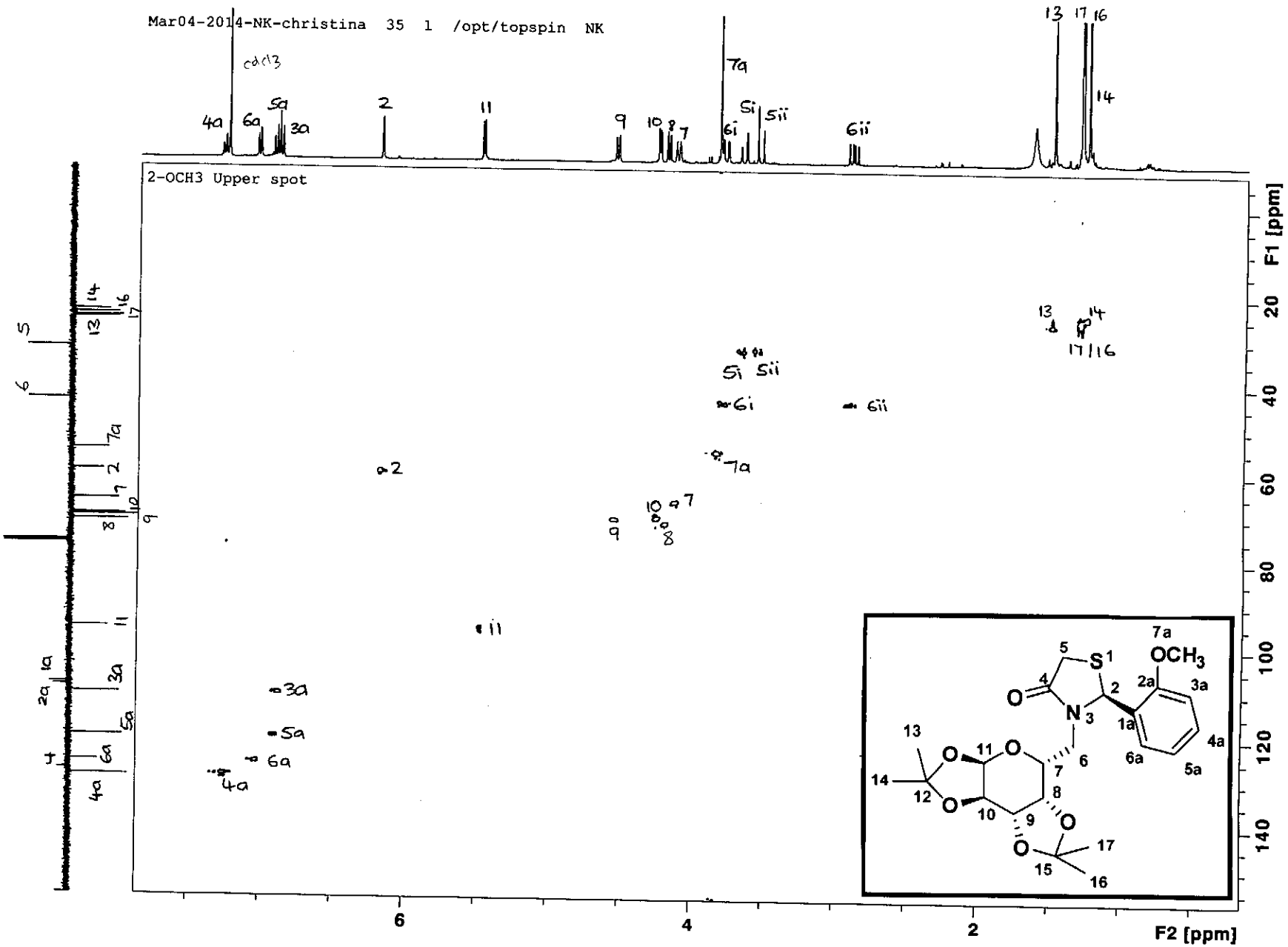
Expanded ^{13}C Spectrum of Compound 5g: 2-(2-Methoxy-phenyl)-3-(2,2,7,7-tetramethyl-tetrahydro-bis[1,3]dioxolo[4,5-b;4',5'-d]pyran-5-ylmethyl)-thiazolidin-4-one



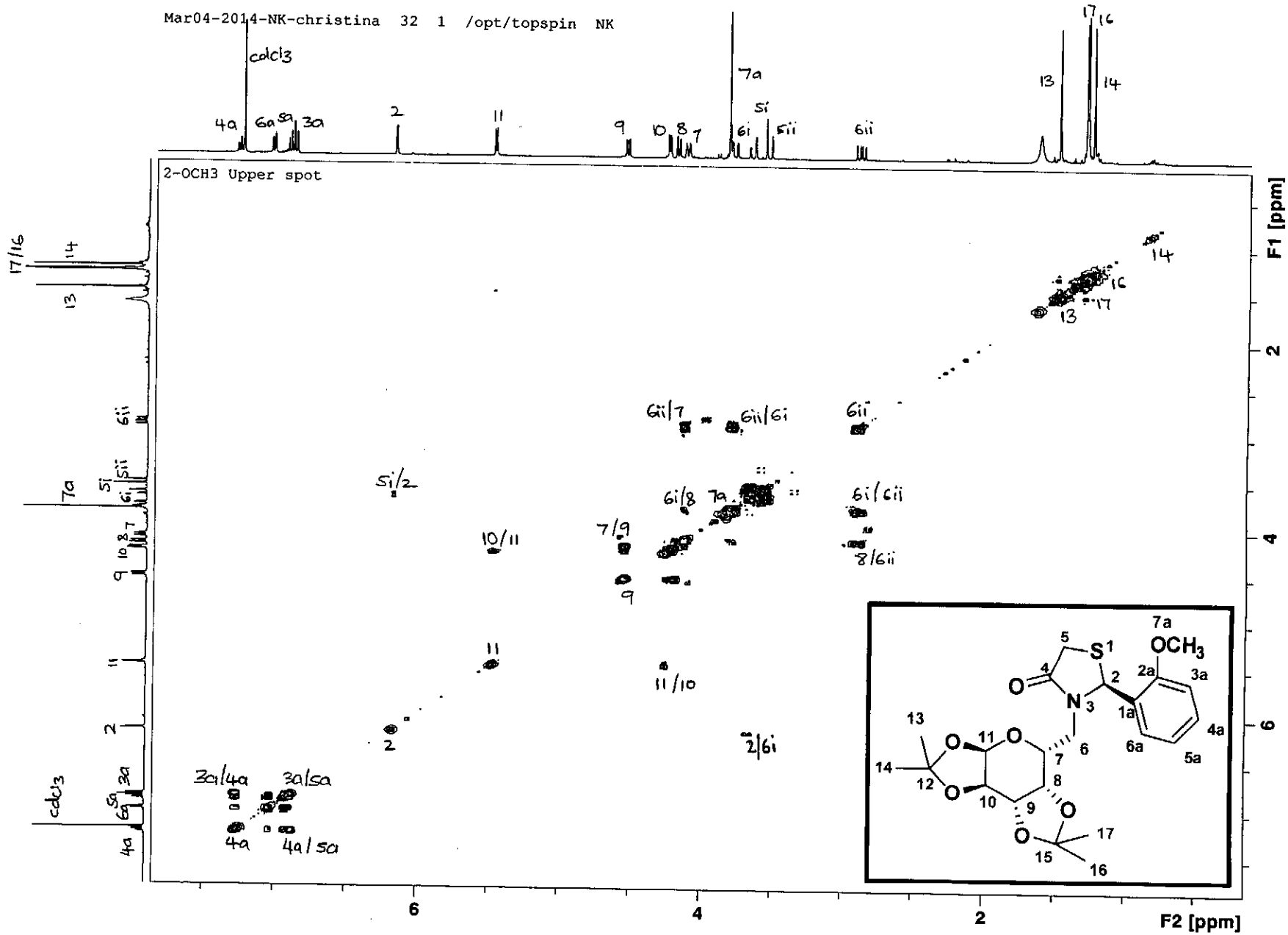
Expanded ^{13}C Spectrum of Compound 5g: 2-(2-Methoxy-phenyl)-3-(2,2,7,7-tetramethyl-tetrahydro-bis[1,3]dioxolo[4,5-b;4',5'-d]pyran-5-ylmethyl)-thiazolidin-4-one



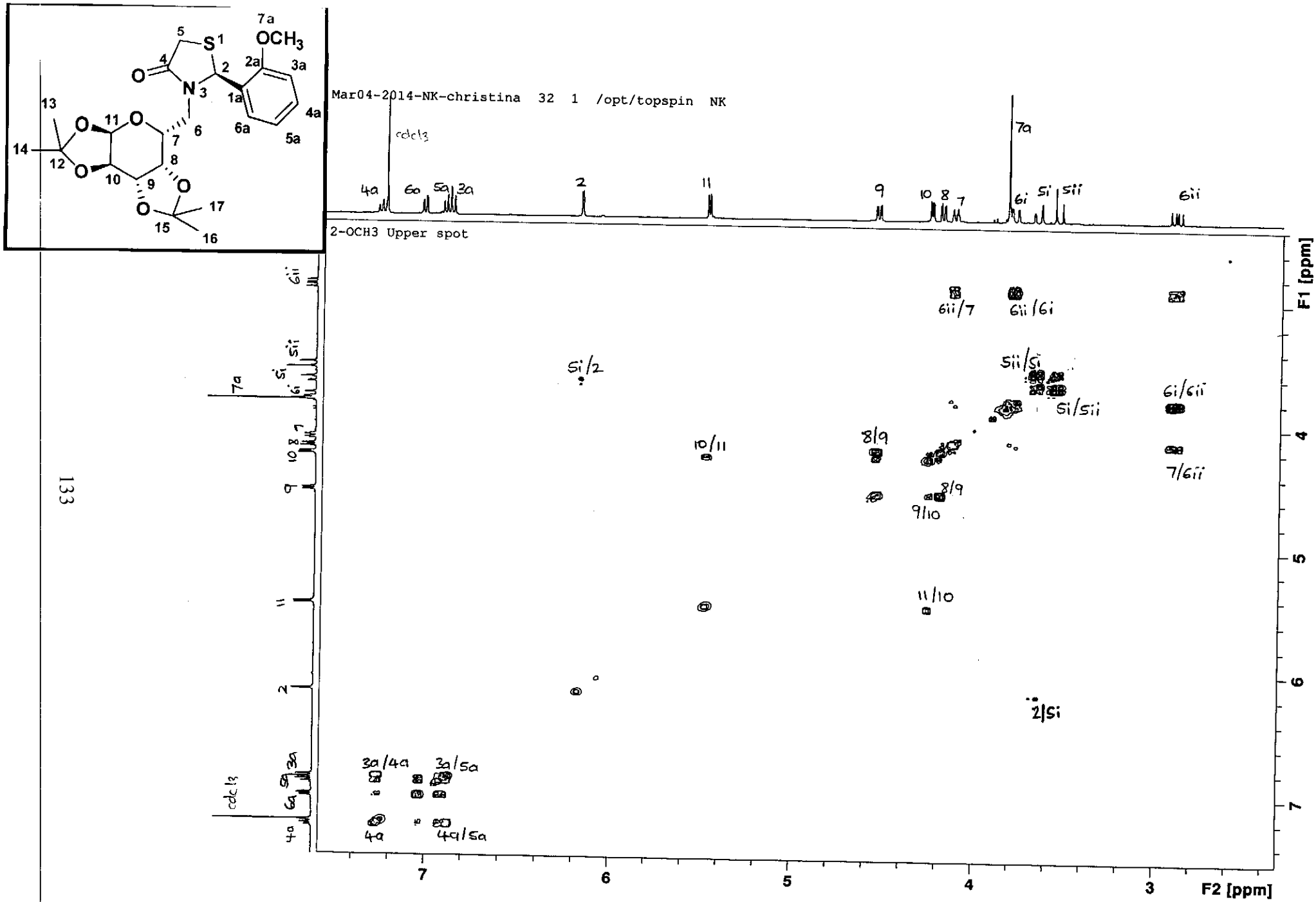
HMBC of Compound 5g: 2-(2-Methoxy-phenyl)-3-(2,2,7,7-tetramethyl-tetrahydro-bis [1,3]dioxolo[4,5-b;4',5'-d]pyran-5-ylmethyl)-thiazolidin-4-one



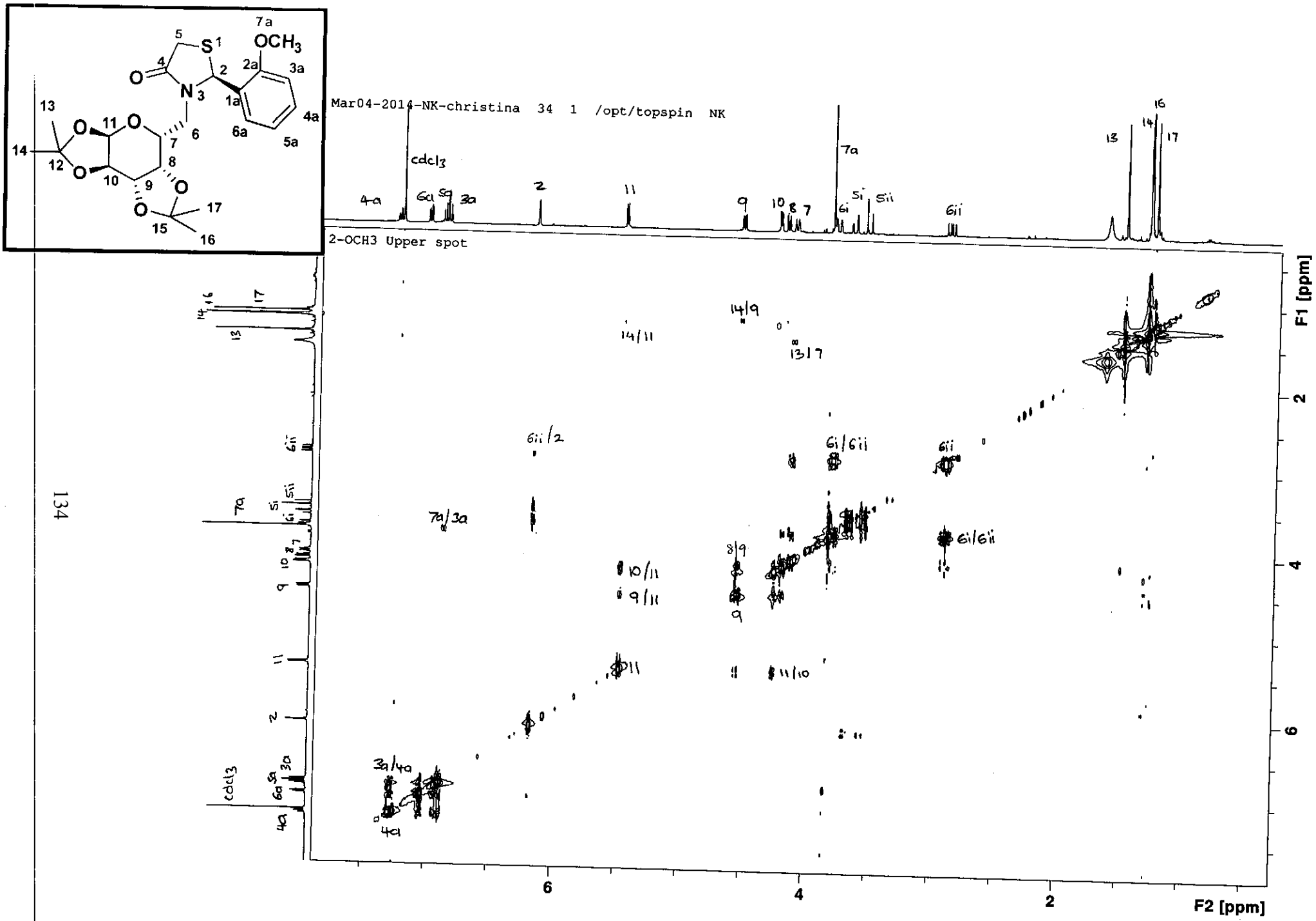
HSQC of Compound 5g: 2-(2-Methoxy-phenyl)-3-(2,2,7,7-tetramethyl-tetrahydro-bis[1,3]dioxolo[4,5-b;4',5'-d]pyran-5-ylmethyl)-thiazolidin-4-one



COSY of Compound 5g: 2-(2-Methoxy-phenyl)-3-(2,2,7,7-tetramethyl-tetrahydro-bis [1,3]dioxolo[4,5-b;4',5'-d]pyran-5-ylmethyl)-thiazolidin-4-one

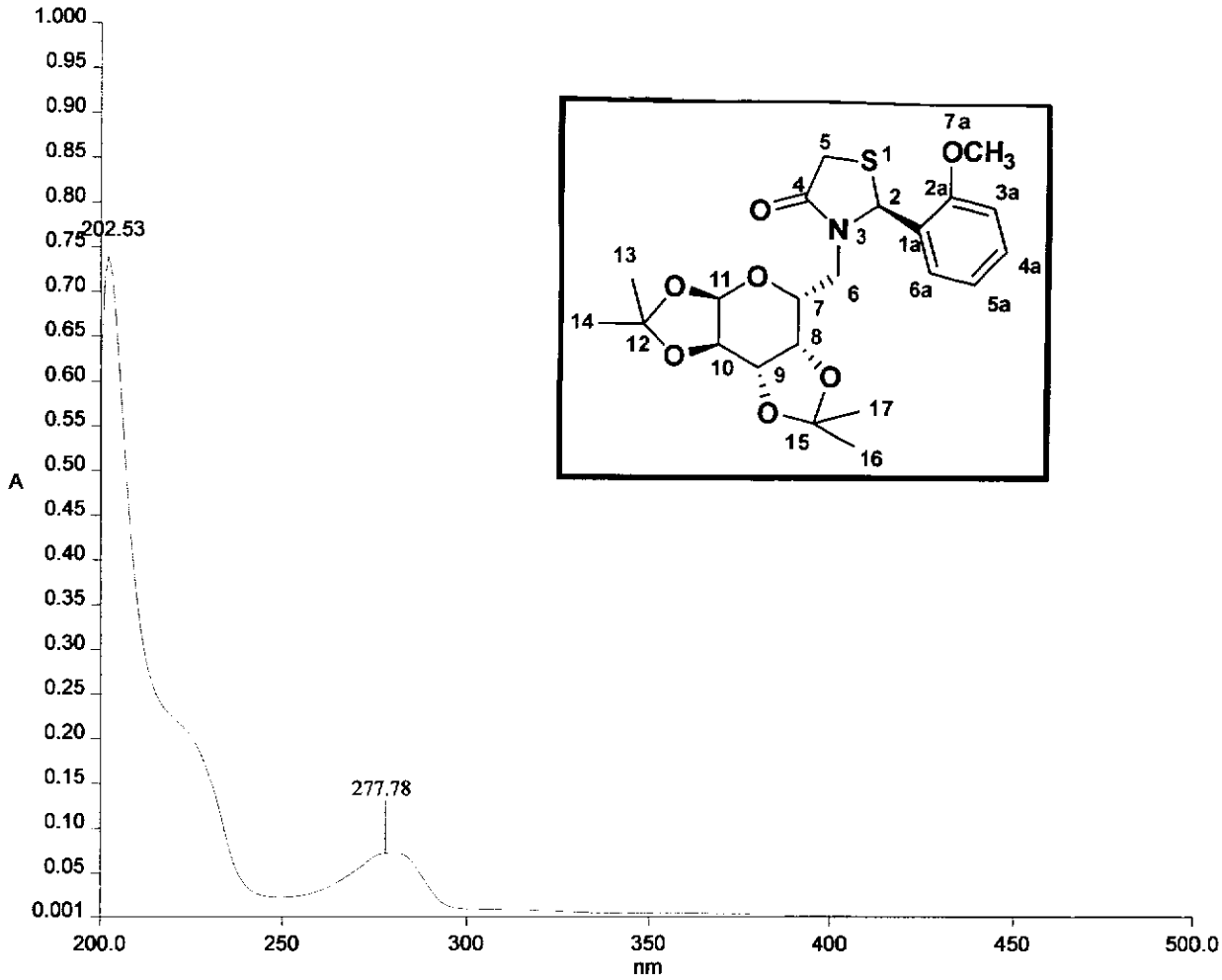


Expanded COSY of Compound 5g: 2-(2-Methoxy-phenyl)-3-(2,2,7,7-tetramethyl-tetra hydro-bis[1,3]dioxolo[4,5-b;4',5'-d]pyran-5-ylmethyl)-thiazolidin-4-one

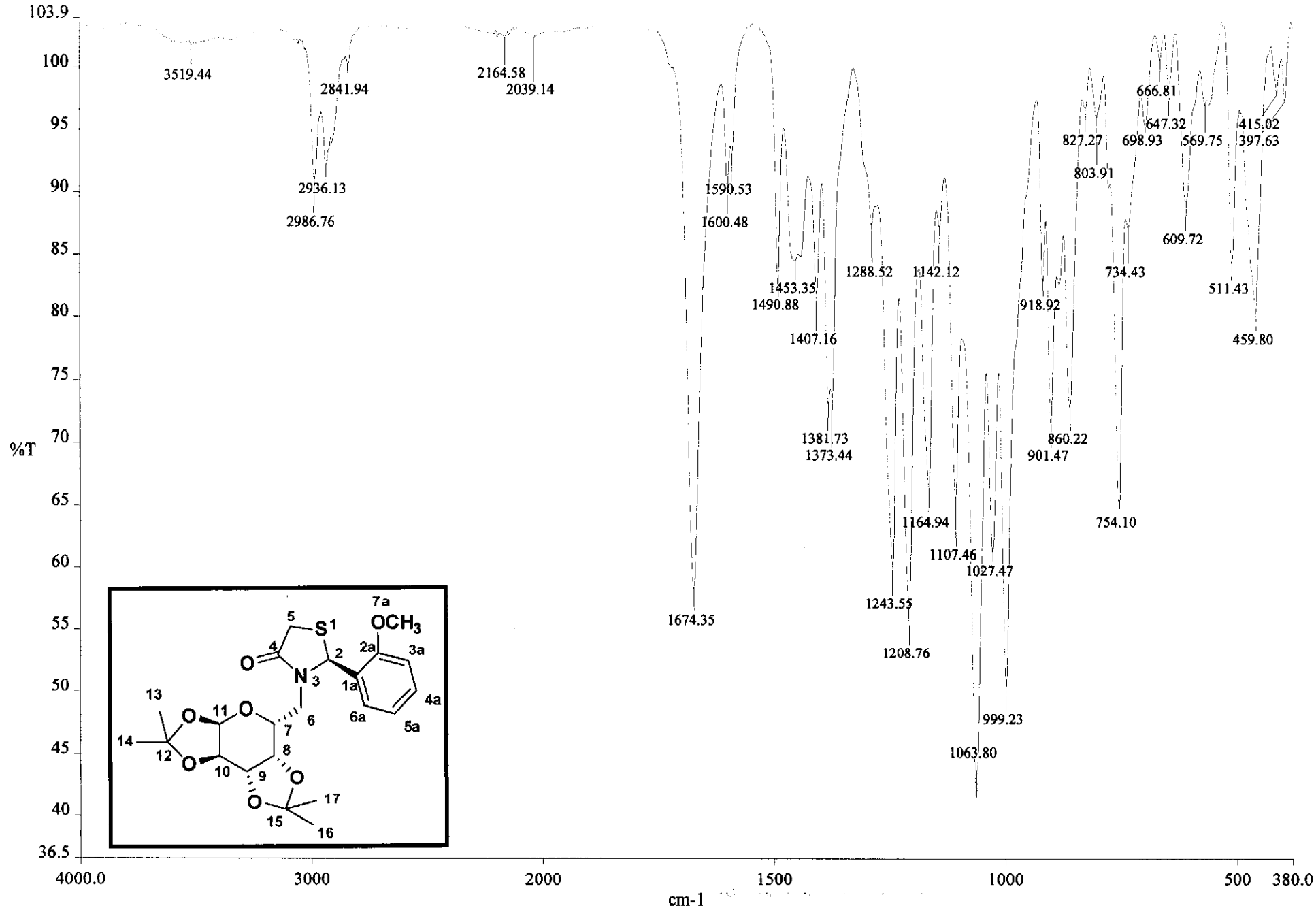


NOESY of Compound 5g: 2-(2-Methoxy-phenyl)-3-(2,2,7,7-tetramethyl-tetrahydro-bis [1,3]dioxolo[4,5-b;4',5'-d]pyran-5-ylmethyl)-thiazolidin-4-one

Date: 2014/06/05 Time: 04:29:56 PM



Ultraviolet Spectrum of Compound 5g: 2-(2-Methoxy-phenyl)-3-(2,2,7,7-tetramethyl-tetrahydro-bis[1,3]dioxolo[4,5-b;4',5'-d]pyran-5-ylmethyl)-thiazolidin-4-one

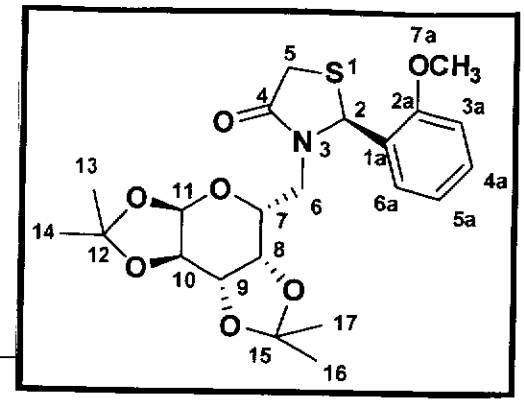


c:\pel_data\spectra\christina\2och3 us.001

Infrared Spectrum of Compound 5g: 2-(2-Methoxy-phenyl)-3-(2,2,7,7-tetramethyl-tetra hydro-bis[1,3]dioxolo[4,5-b;4',5'-d]pyran-5-ylmethyl)-thiazolidin-4-one

==== Shimadzu LCsolution Analysis Report ====

Acquired by	: Admin
Sample Name	: 2och3 us formic buffer
Sample ID	: 2och3 us formic buffer
Vail #	: 2
Injection Volume	: 100 uL
Data File Name	: 2och3 us formic buffer.lcd
Method File Name	: Pramod 09jun 2014.lcm
Batch File Name	: suger thiozolidinon.lcb
Report File Name	: Default.lcr
Data Acquired	: 2014/06/17 03:57:40 PM
Data Processed	: 2014/06/17 04:37:43 PM



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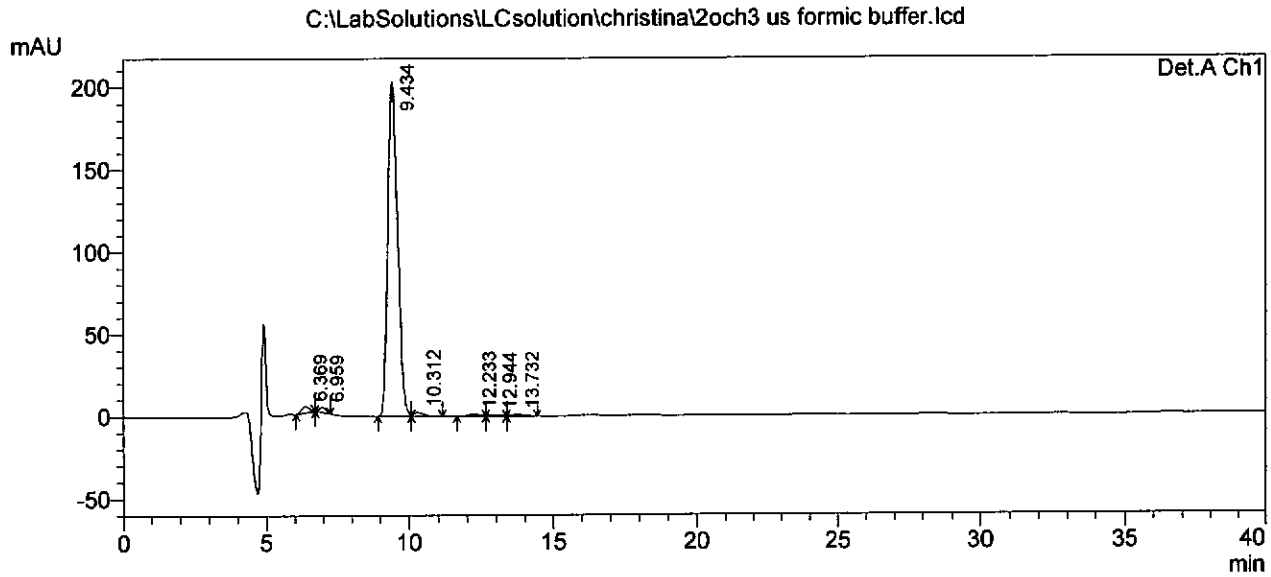


1 Det.A Ch1/220nm

<Results>

PeakTable C:\LabSolutions\LCsolution\christina\2och3 us formic buffer.lcd

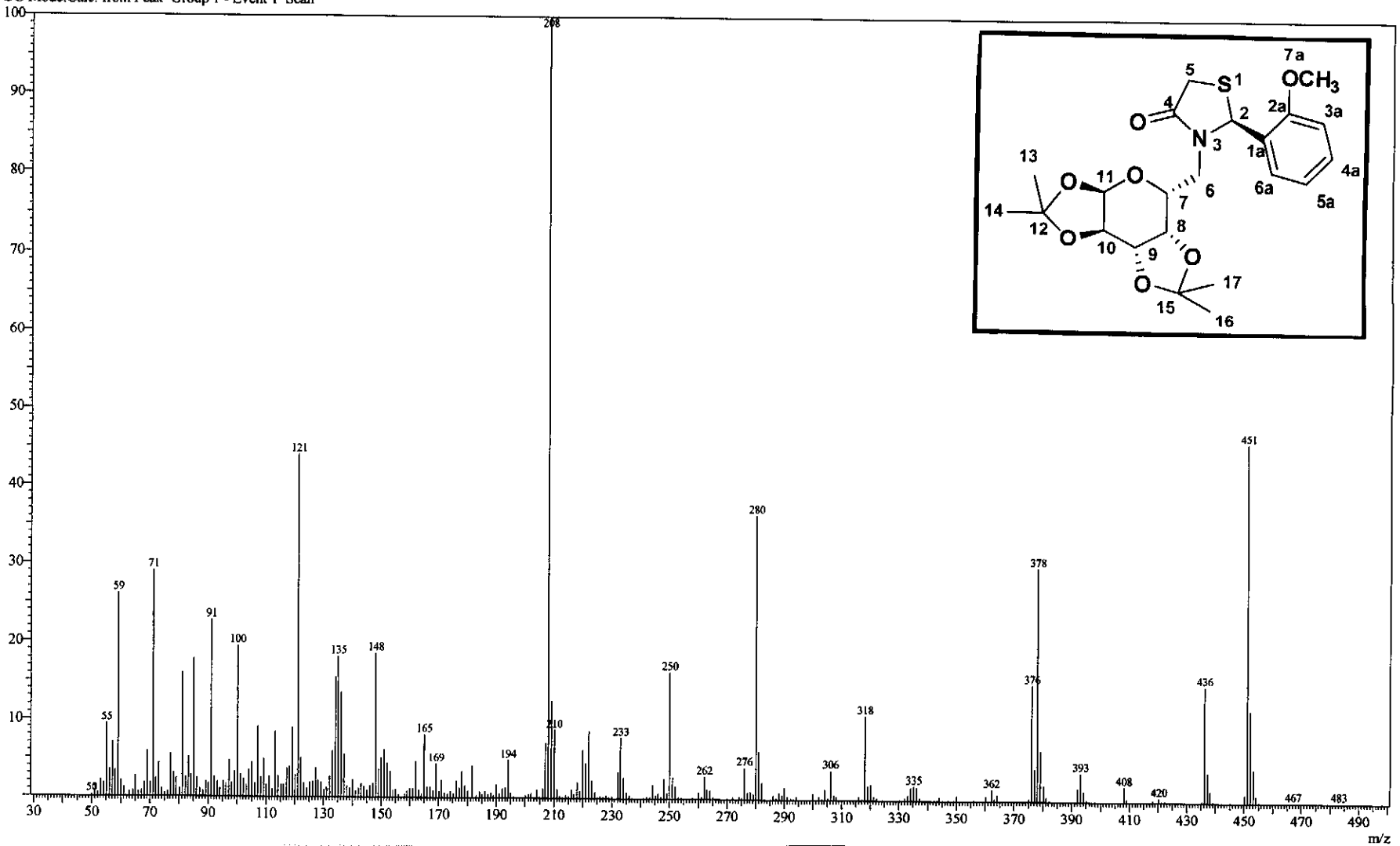
Detector A Ch1 220nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	6.369	71650	3763	1.419	1.750
2	6.959	52349	3042	1.037	1.415
3	9.434	4798294	203354	95.030	94.606
4	10.312	55931	2166	1.108	1.008
5	12.233	32371	1185	0.641	0.551
6	12.944	14335	480	0.284	0.223
7	13.732	24319	959	0.482	0.446
Total		5049249	214948	100.000	100.000

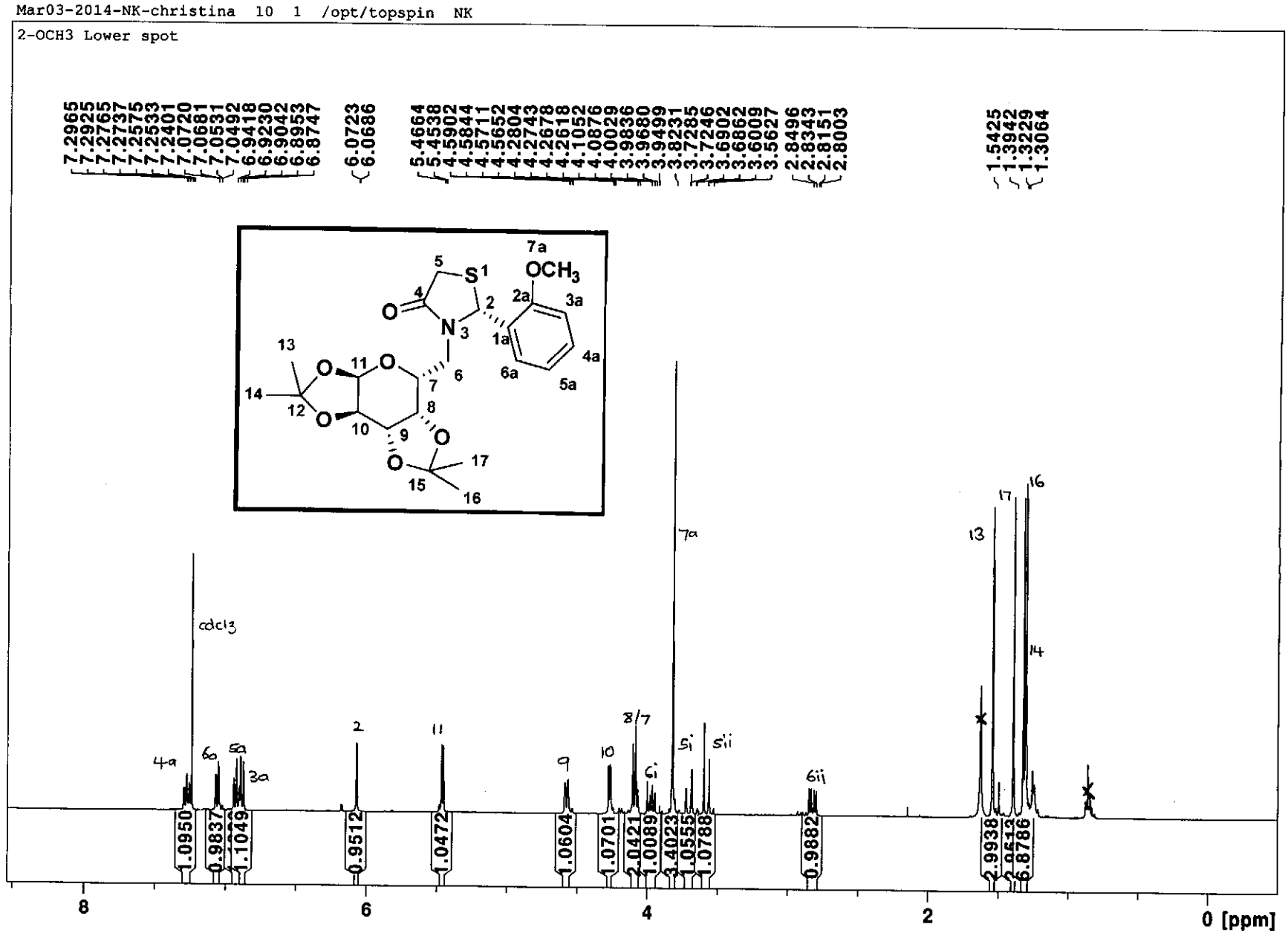
HPLC of Compound 5g: 2-(2-Methoxy-phenyl)-3-(2,2,7,7-tetramethyl-tetrahydro-bis[1,3] dioxolo[4,5-b;4',5'-d]pyran-5-ylmethyl)-thiazolidin-4-one

Spectrum

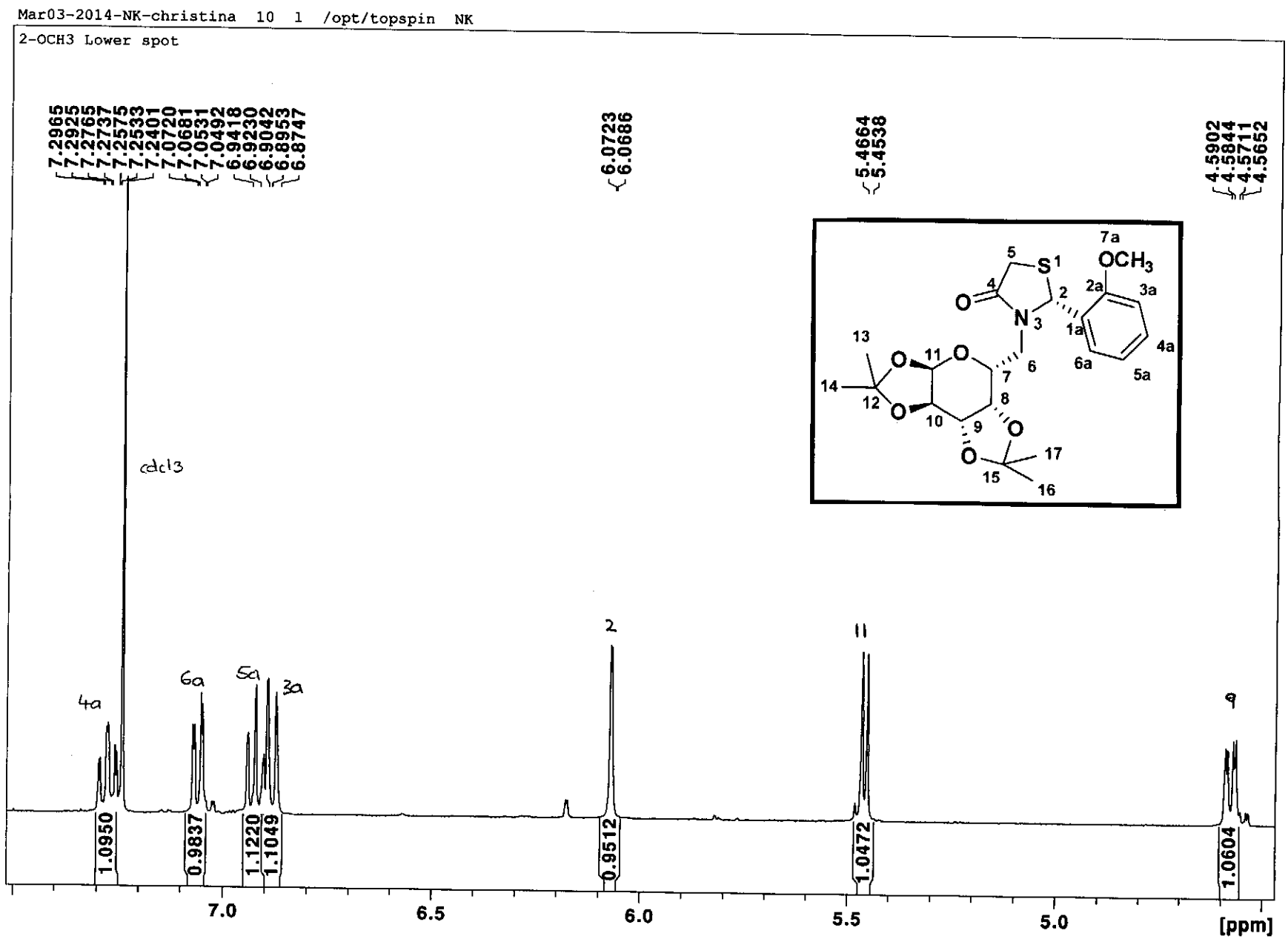
Line#:1 R.Time:18.495(Scan#:2900)
MassPeaks:559
RawMode:Averaged 18.490-18.500(2899-2901) BasePeak:208(107606)
BG Mode:Calc. from Peak Group 1 - Event 1 Scan



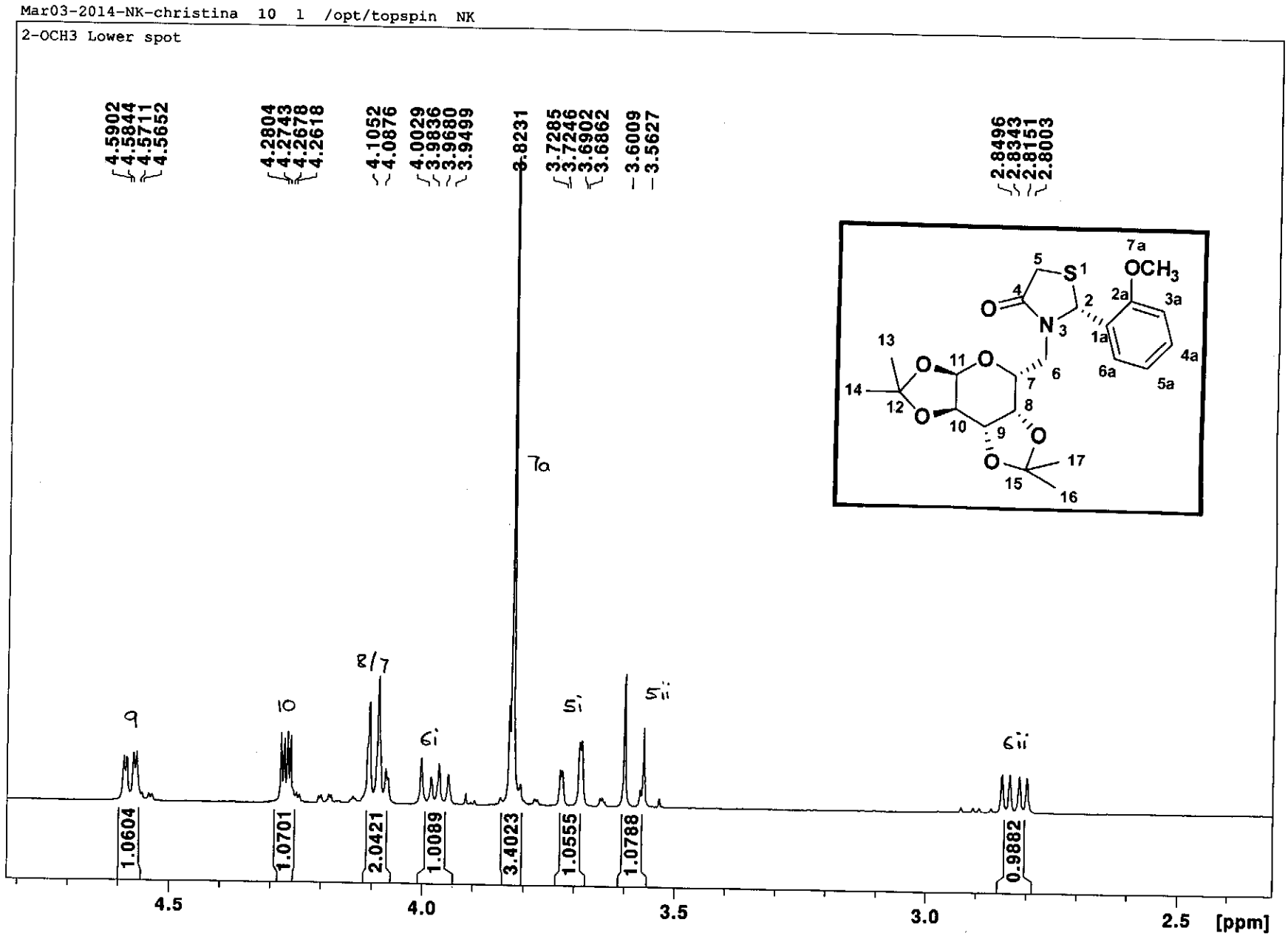
GC-MS of Compound 5g: 2-(2-Methoxy-phenyl)-3-(2,2,7,7-tetramethyl-tetrahydro-bis[1,3] dioxolo[4,5-b;4',5'-d]pyran-5-ylmethyl)-thiazolidin-4-one



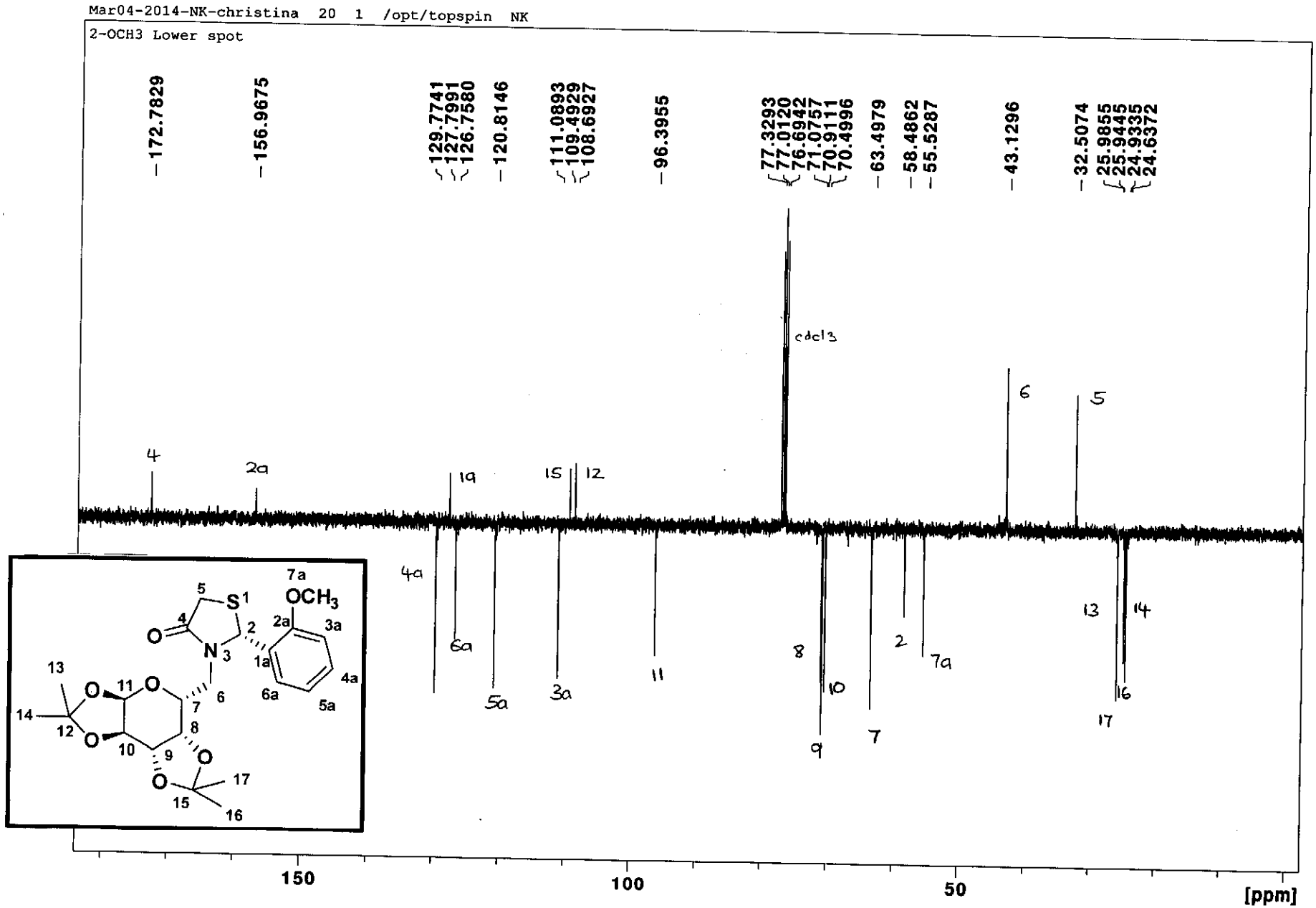
[1]H Spectrum of Compound 6g: 2-(2-Methoxy-phenyl)-3-(2,2,7,7-tetramethyl-tetrahydro-bis[1,3]dioxolo[4,5-b;4',5'-d]pyran-5-ylmethyl)-thiazolidin-4-one



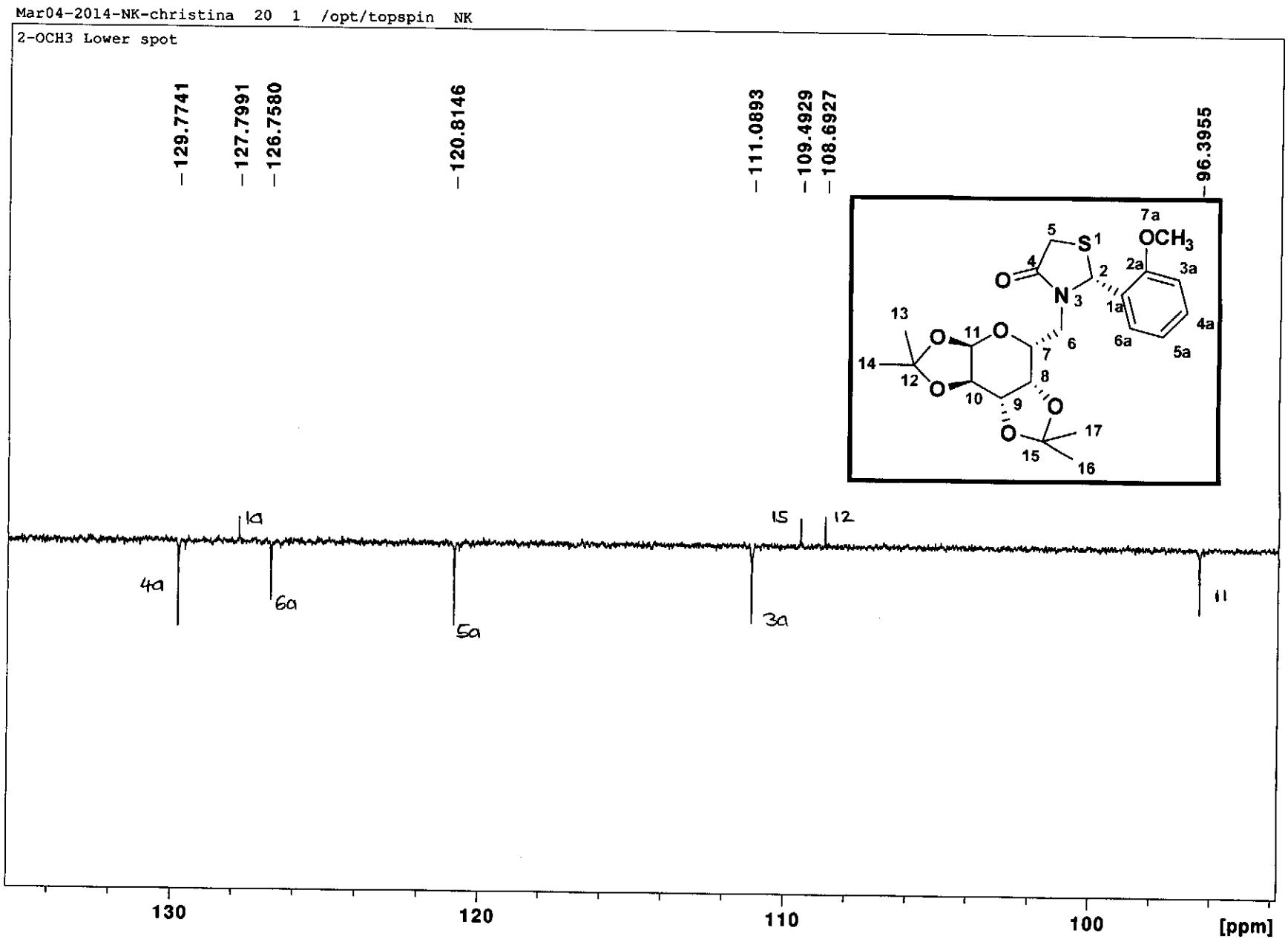
Expanded ^{1}H Spectrum of Compound 6g: 2-(2-Methoxy-phenyl)-3-(2,2,7,7-tetramethyl-tetrahydro-bis[1,3]dioxolo[4,5-b;4',5'-d]pyran-5-ylmethyl)-thiazolidin-4-one



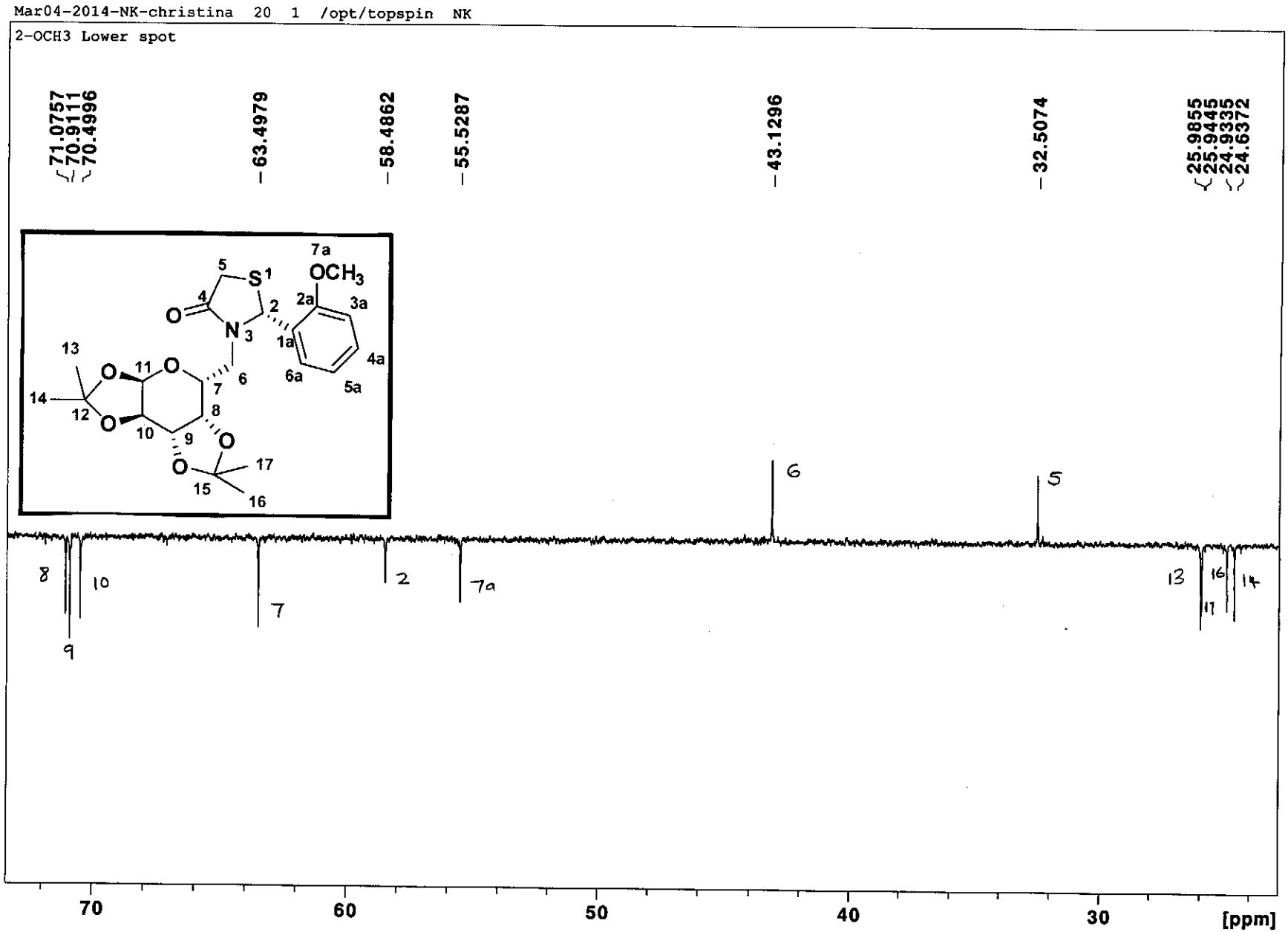
Expanded ^{1}H Spectrum of Compound 6g: 2-(2-Methoxy-phenyl)-3-(2,2,7,7-tetramethyl-tetrahydro-bis[1,3]dioxolo[4,5-b;4',5'-d]pyran-5-ylmethyl)-thiazolidin-4-one



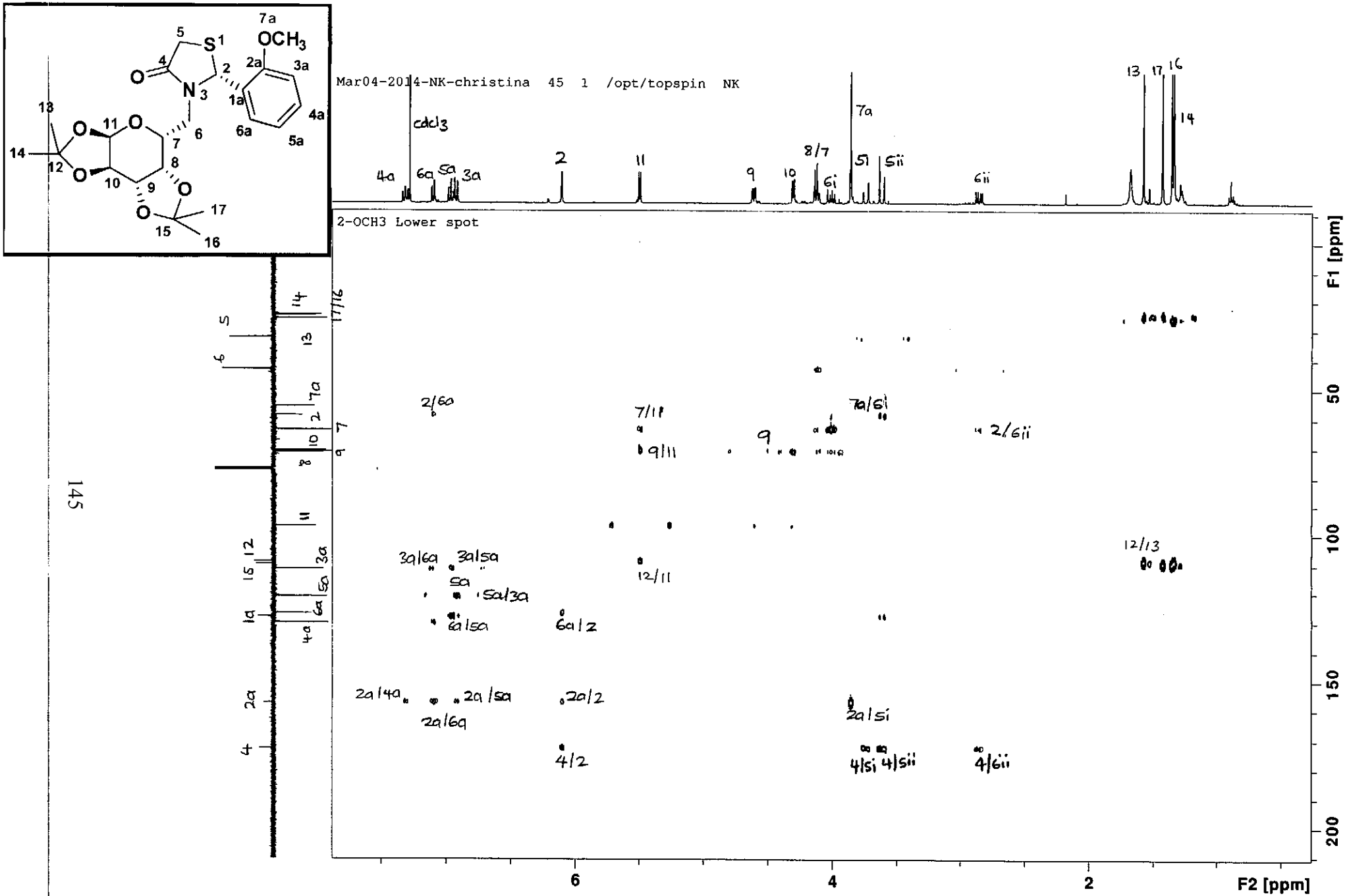
^{13}C Spectrum of Compound 6g: 2-(2-Methoxy-phenyl)-3-(2,2,7,7-tetramethyl-tetrahydro-bis[1,3]dioxolo[4,5-b;4',5'-d]pyran-5-ylmethyl)-thiazolidin-4-one



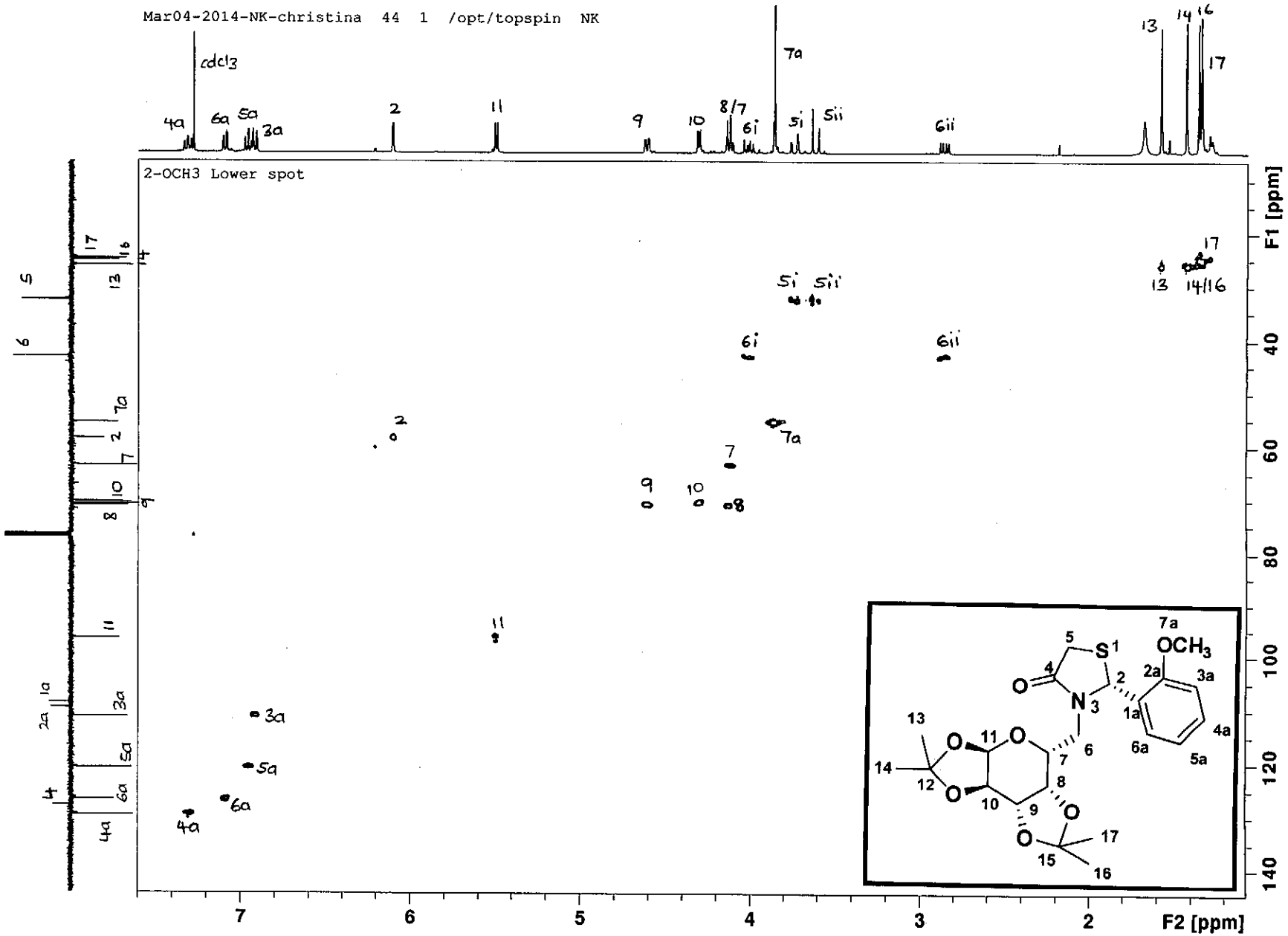
Expanded ^{13}C Spectrum of Compound 6g: 2-(2-Methoxy-phenyl)-3-(2,2,7,7-tetramethyl-tetrahydro-bis[1,3]dioxolo[4,5-b;4',5'-d]pyran-5-ylmethyl)-thiazolidin-4-one



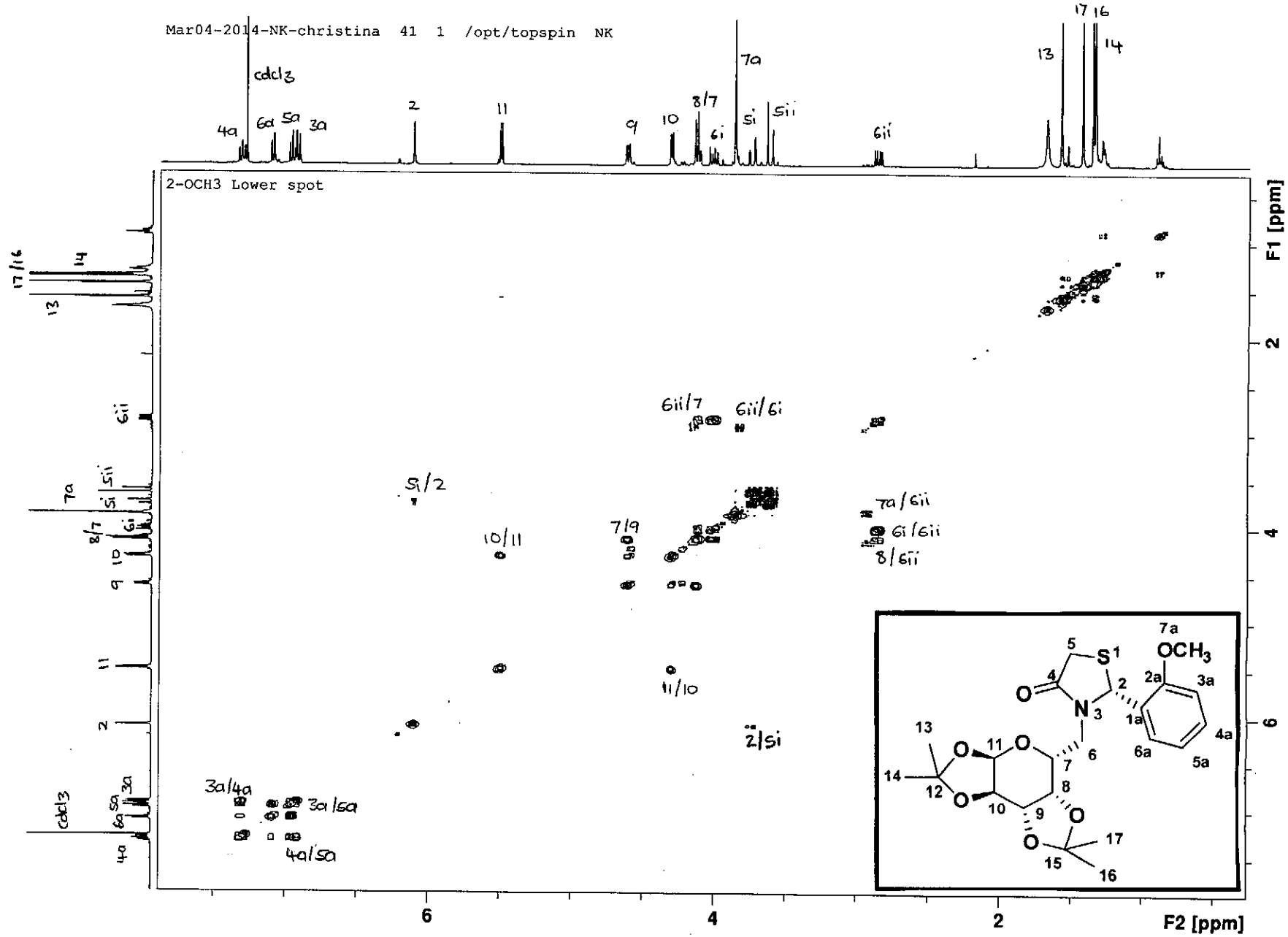
Expanded ^{13}C Spectrum of Compound 6g: 2-(2-Methoxy-phenyl)-3-(2,2,7,7-tetramethyl-tetrahydro-bis[1,3]dioxolo[4,5-b;4',5'-d]pyran-5-ylmethyl)-thiazolidin-4-one



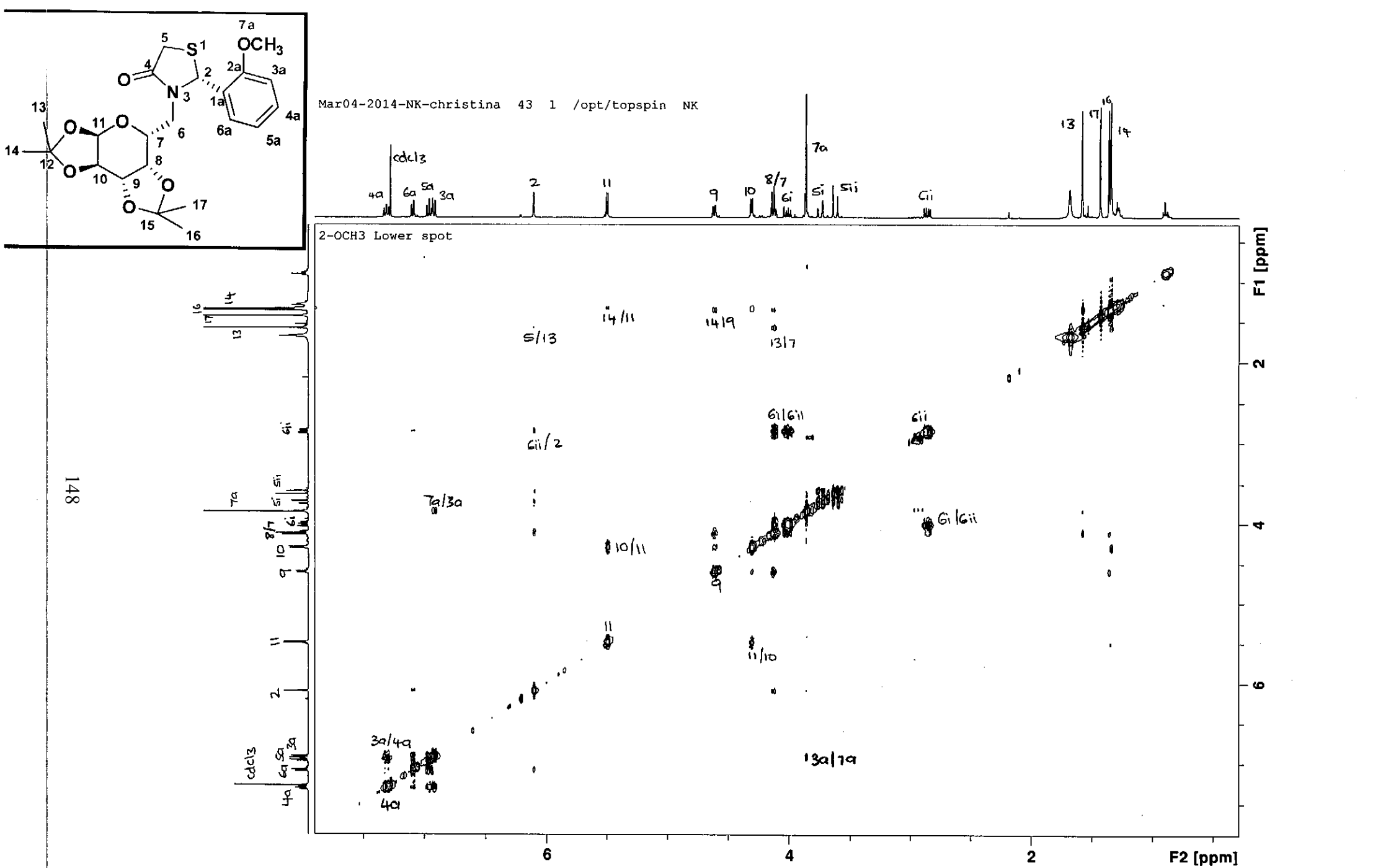
HMBC of Compound 6g: 2-(2-Methoxy-phenyl)-3-(2,2,7,7-tetramethyl-tetrahydro-bis [1,3]dioxolo[4,5-b;4',5'-d]pyran-5-ylmethyl)-thiazolidin-4-one



HSQC of Compound 6g: 2-(2-Methoxy-phenyl)-3-(2,2,7,7-tetramethyl-tetrahydro-bis [1,3]dioxolo[4,5-b;4',5'-d]pyran-5-ylmethyl)-thiazolidin-4-one

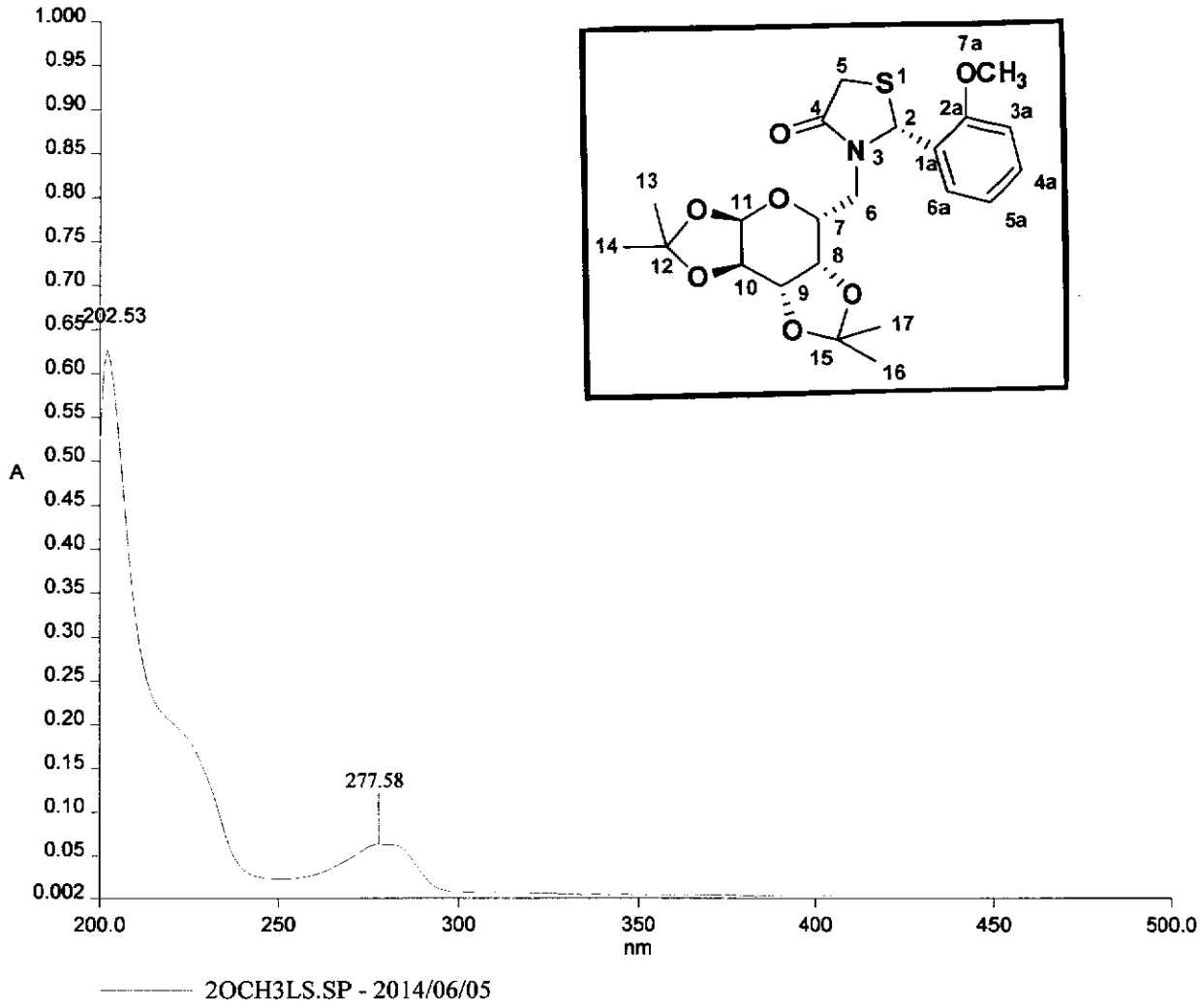


COSY of Compound 6g: 2-(2-Methoxy-phenyl)-3-(2,2,7,7-tetramethyl-tetrahydro-bis [1,3]dioxolo[4,5-b;4',5'-d]pyran-5-ylmethyl)-thiazolidin-4-one

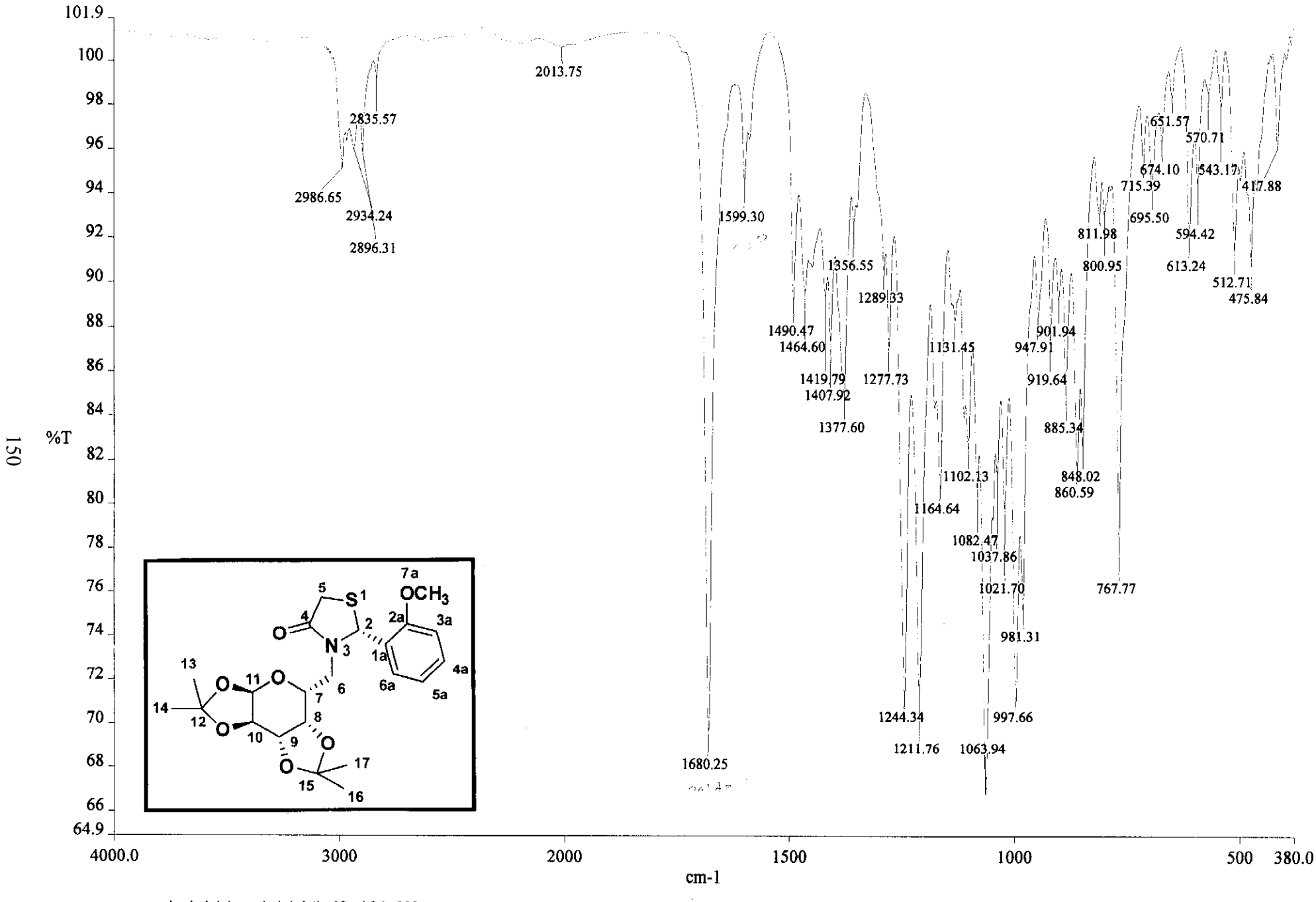


NOESY of Compound 6g: 2-(2-Methoxy-phenyl)-3-(2,2,7,7-tetramethyl-tetrahydro-bis [1,3]dioxolo[4,5-b;4',5'-d]pyran-5-ylmethyl)-thiazolidin-4-one

Date: 2014/06/05 Time: 04:28:46 PM



Ultraviolet Spectrum of Compound 6g: 2-(2-Methoxy-phenyl)-3-(2,2,7,7-tetramethyl-tetra hydro-bis[1,3]dioxolo[4,5-b;4',5'-d]pyran-5-ylmethyl)-thiazolidin-4-one

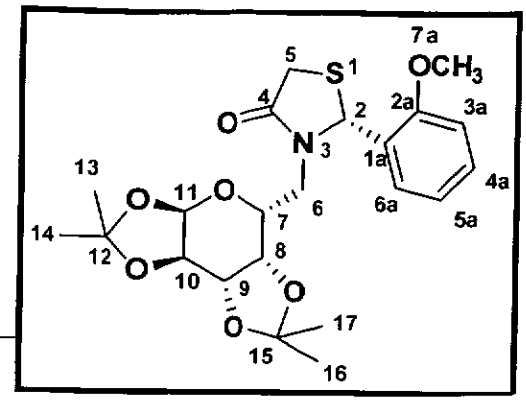


c:\pel_data\spectra\christina\2oph3-le-003

Infrared Spectrum of Compound 6g: 2-(2-Methoxy-phenyl)-3-(2,2,7,7-tetramethyl-tetra hydro-bis[1,3]dioxolo[4,5-b;4',5'-d]pyran-5-ylmethyl)-thiazolidin-4-one

==== Shimadzu LCsolution Analysis Report ====

Acquired by	: Admin
Sample Name	: 2och3 ls formic buffer
Sample ID	: 2och3 ls formic buffer
Vail #	: 3
Injection Volume	: 100 uL
Data File Name	: 4och3 ls formic buffer.lcd
Method File Name	: Pramod 09jun 2014.lcm
Batch File Name	: suger thiozolidinon.lcb
Report File Name	: Default.lcr
Data Acquired	: 2014/06/17 04:38:16 PM
Data Processed	: 2014/06/17 05:18:21 PM



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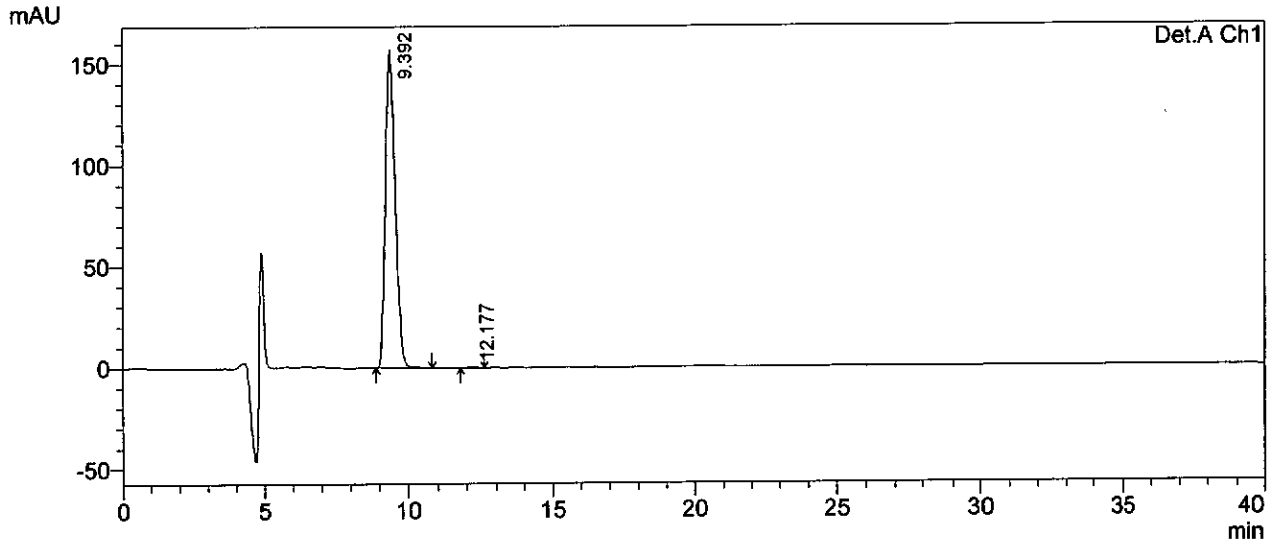

1 Det.A Ch1/220nm

<Results>

PeakTable C:\LabSolutions\LCsolution\christina\4och3 ls formic buffer.lcd

Detector A Ch1 220nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	9.392	3696714	156955	99.648	99.619
2	12.177	13051	600	0.352	0.381
Total		3709765	157556	100.000	100.000

HPLC of Compound 6g: 2-(2-Methoxy-phenyl)-3-(2,2,7,7-tetramethyl-tetrahydro-bis[1,3] dioxolo[4,5-b;4',5'-d]pyran-5-ylmethyl)-thiazolidin-4-one

Spectrum

Line#:1 R.Time:19.285(Scan#:3058)
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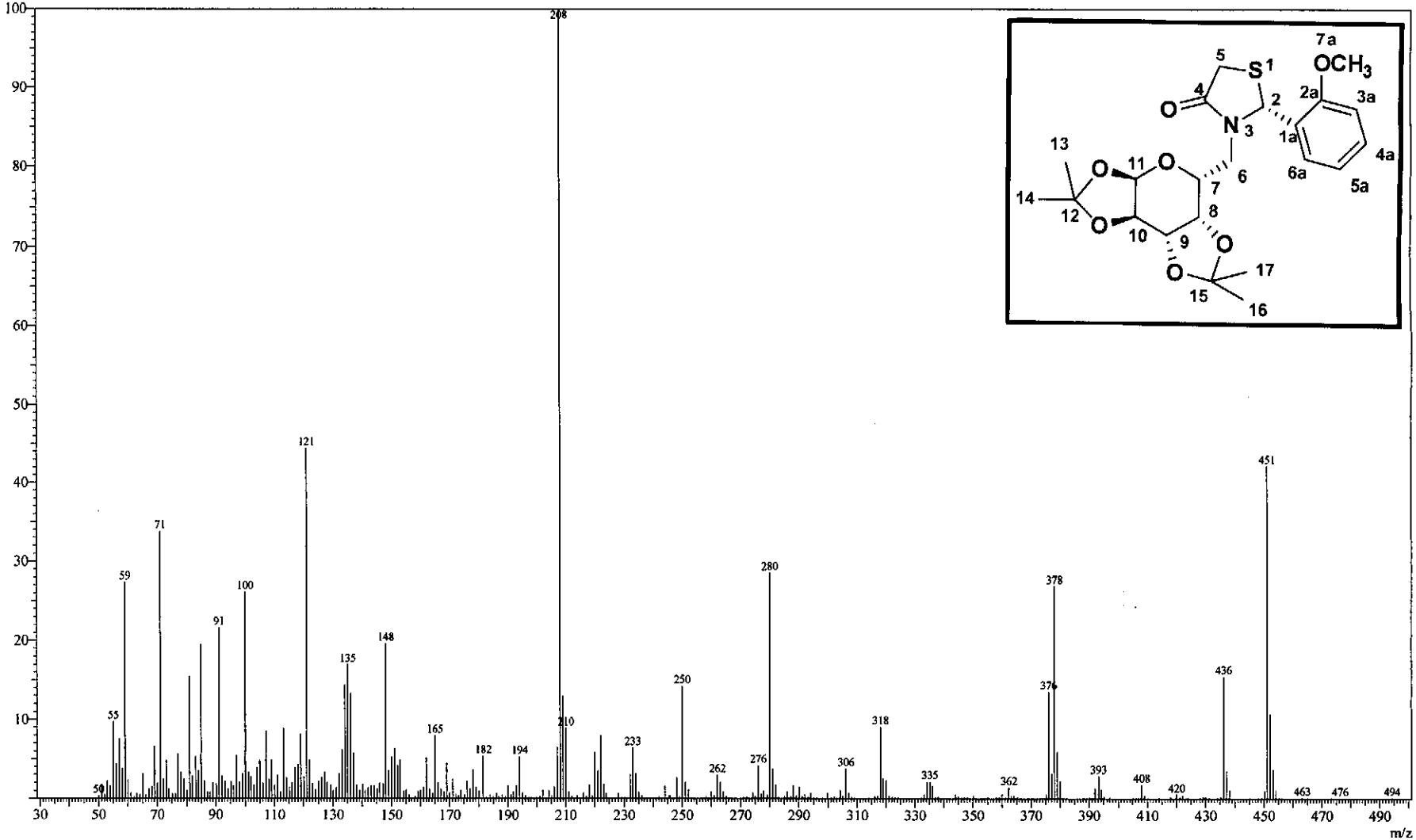
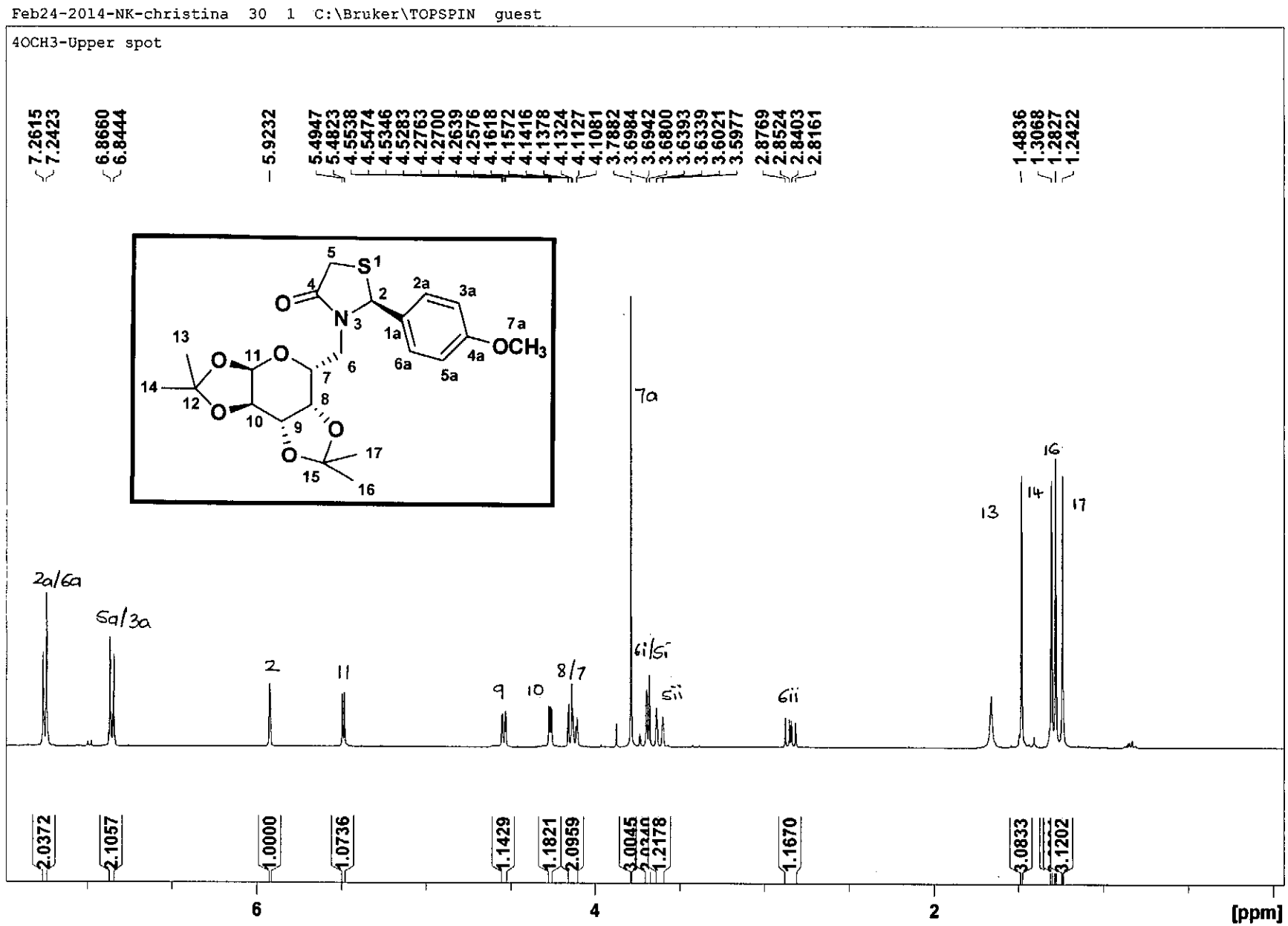
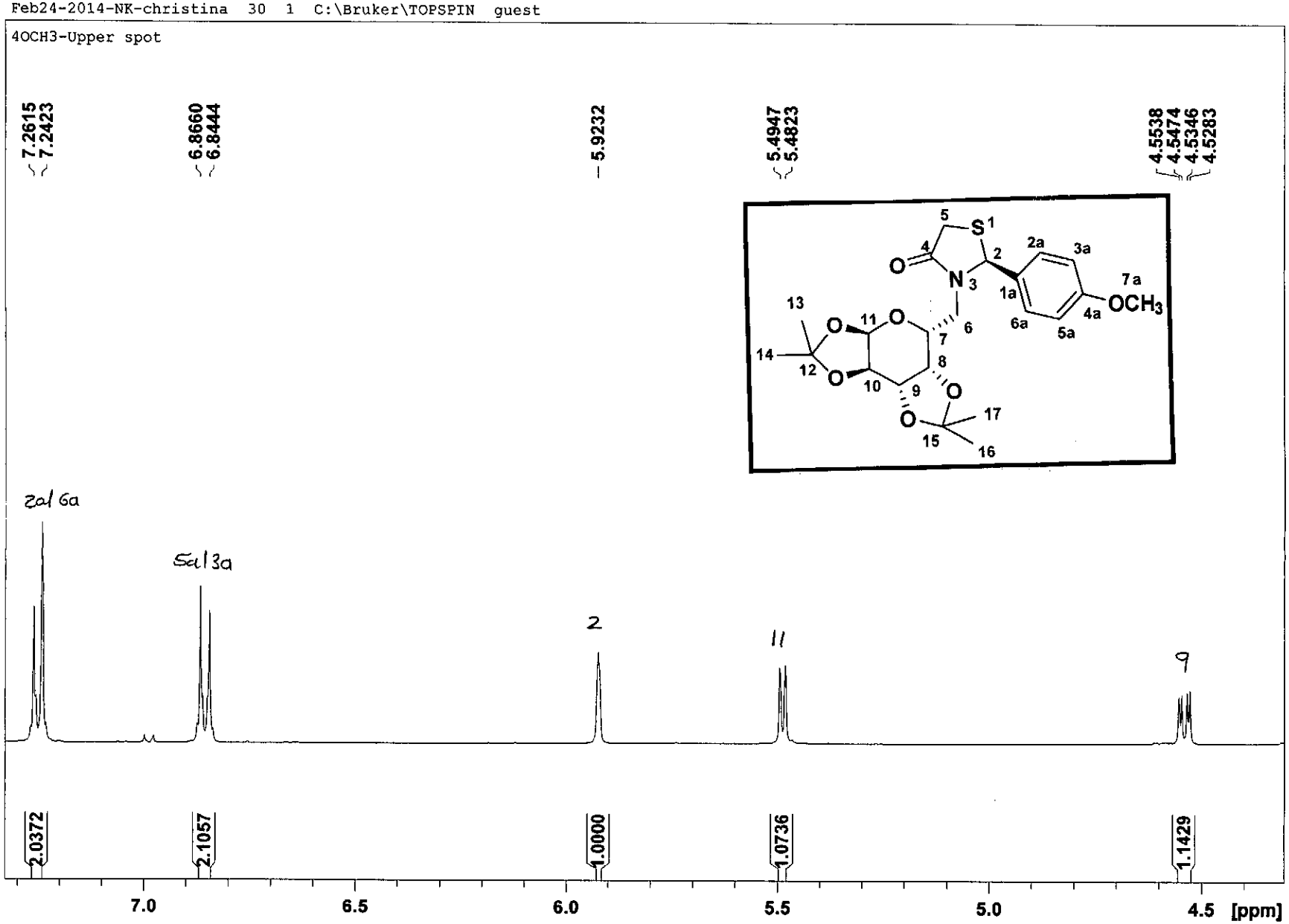
RawMode:Averaged 19.280-19.290(3057-3059) BasePeak:208(64211)
BG Mode:Calc. from Peak Group 1 - Event 1 Scan



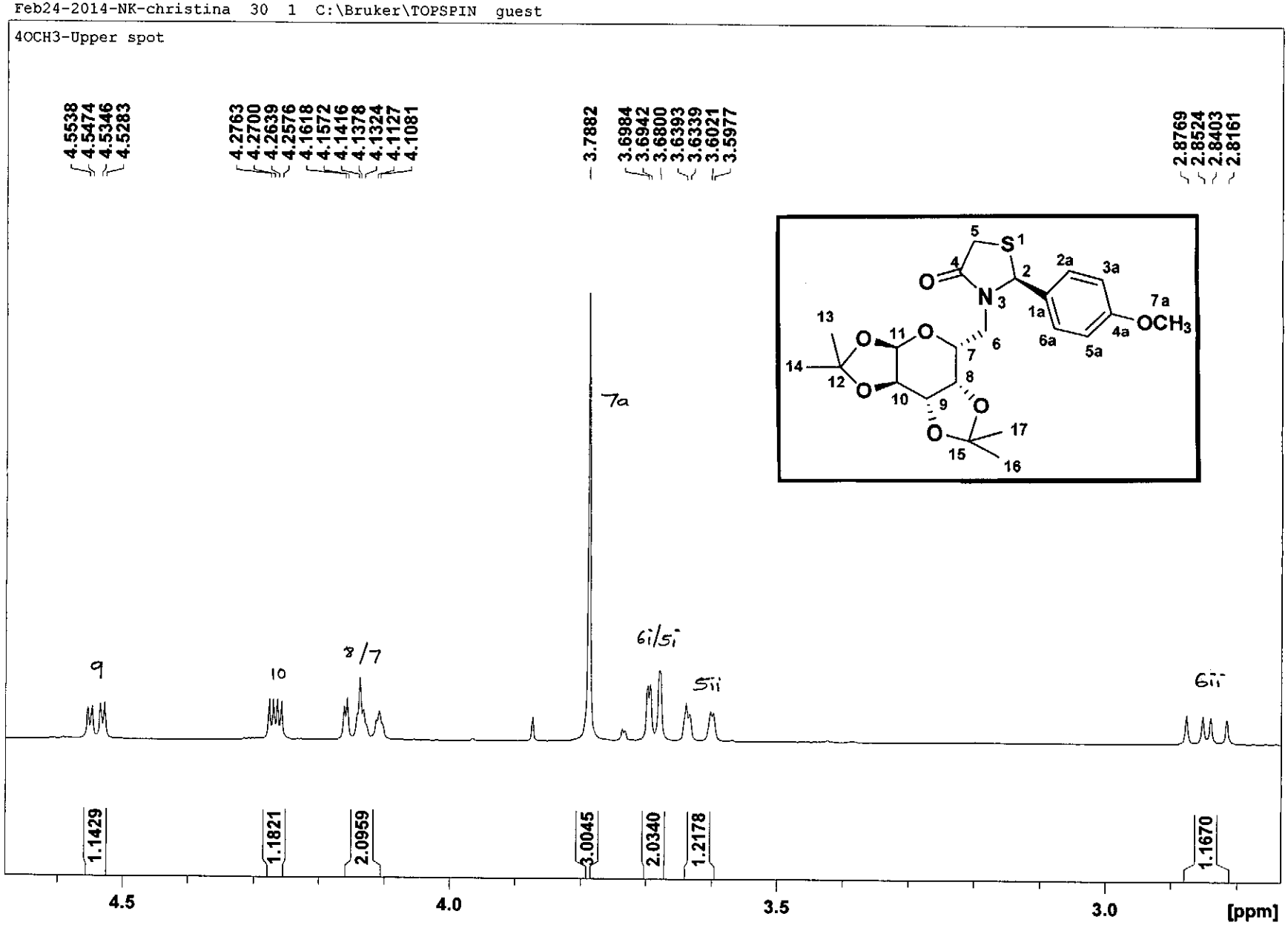
GC-MS of Compound 6g: 2-(2-Methoxy-phenyl)-3-(2,2,7,7-tetramethyl-tetrahydro-bis[1,3] dioxolo[4,5-b;4',5'-d]pyran-5-ylmethyl)-thiazolidin-4-one



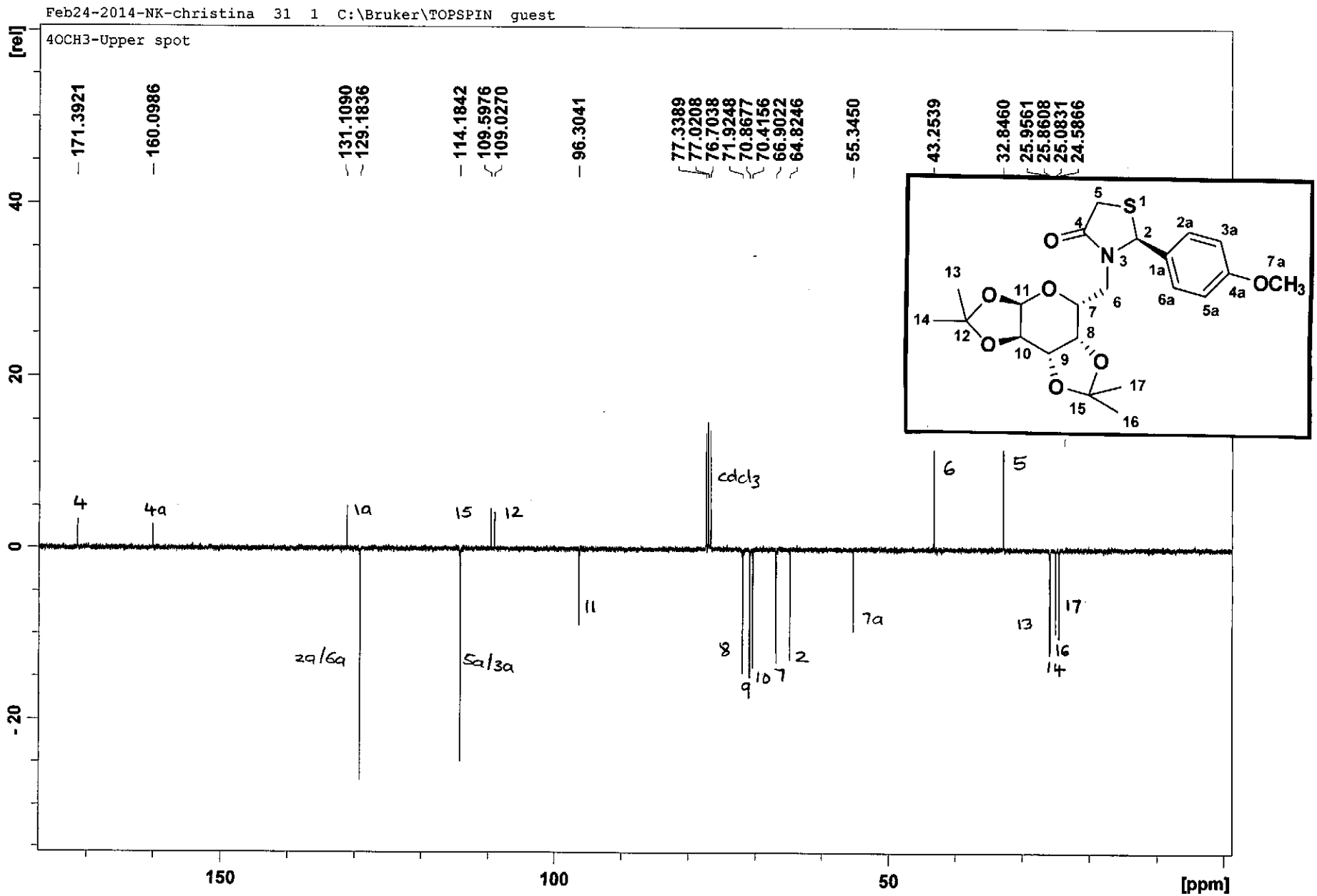
^{1}H Spectrum of Compound 5h: 2-(4-Methoxy-phenyl)-3-(2,2,7,7-tetramethyl-tetrahydro-bis[1,3]dioxolo[4,5-b;4',5'-d]pyran-5-ylmethyl)-thiazolidin-4-one



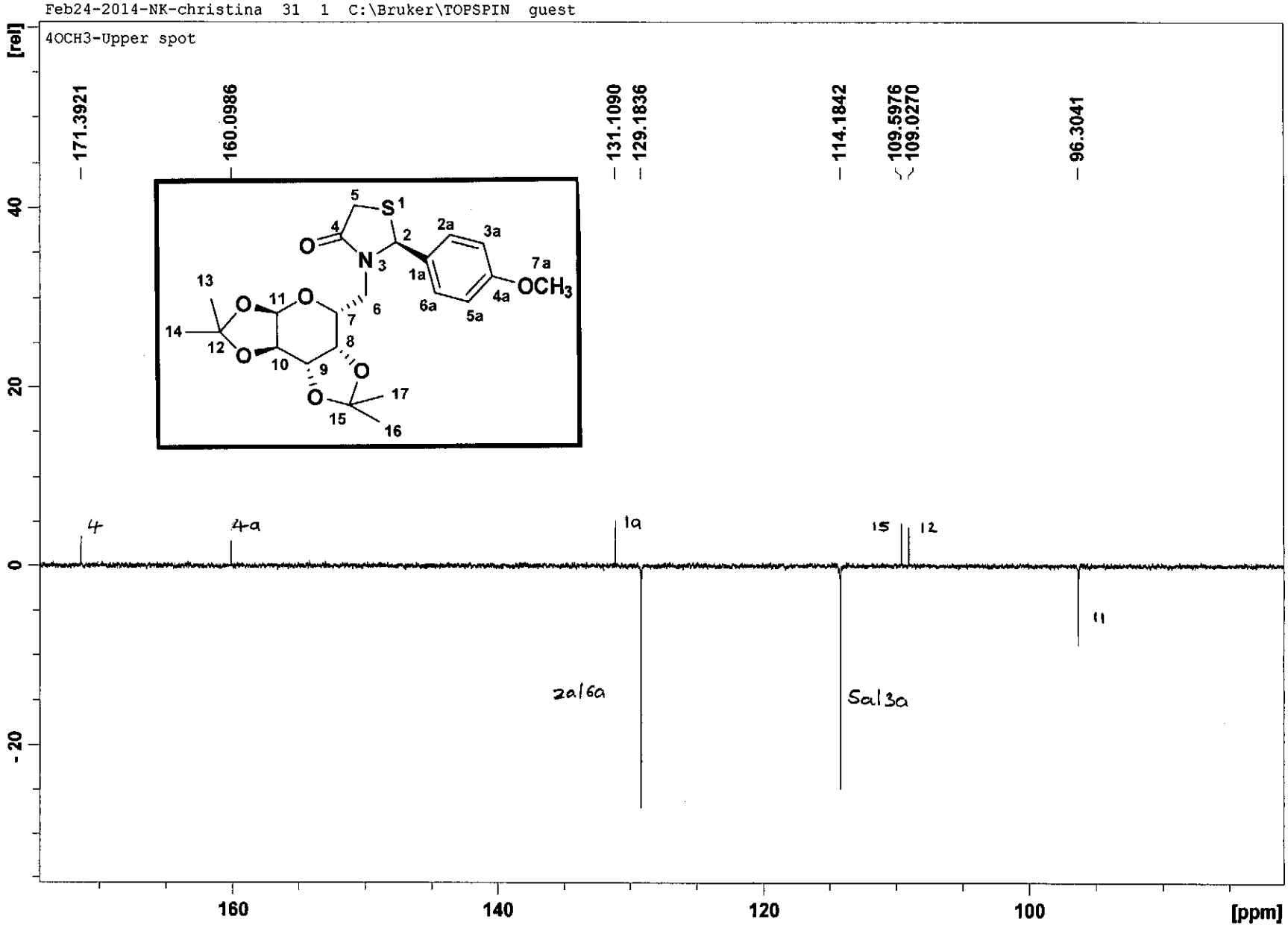
Expanded ^{1}H Spectrum of Compound 5h: 2-(4-Methoxy-phenyl)-3-(2,2,7,7-tetramethyl-tetrahydro-bis[1,3]dioxolo[4,5-b;4',5'-d]pyran-5-ylmethyl)-thiazolidin-4-one



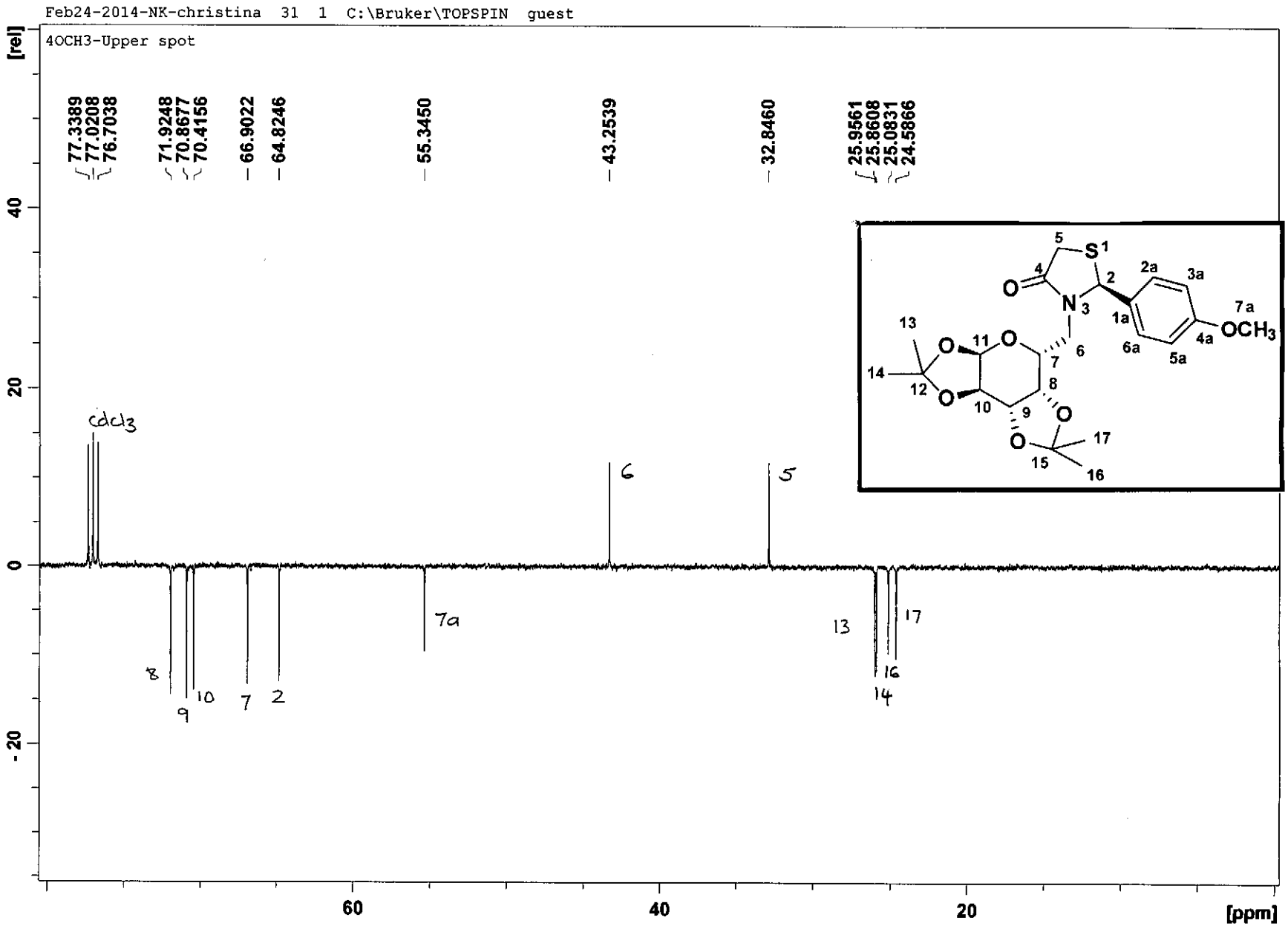
Expanded ^{1}H Spectrum of Compound 5h: 2-(4-Methoxy-phenyl)-3-(2,2,7,7-tetramethyl-tetrahydro-bis[1,3]dioxolo[4,5-b;4',5'-d]pyran-5-ylmethyl)-thiazolidin-4-one



^{13}C Spectrum of Compound 5h: 2-(4-Methoxy-phenyl)-3-(2,2,7,7-tetramethyl-tetrahydro-bis[1,3]dioxolo[4,5-b;4',5'-d]pyran-5-ylmethyl)-thiazolidin-4-one

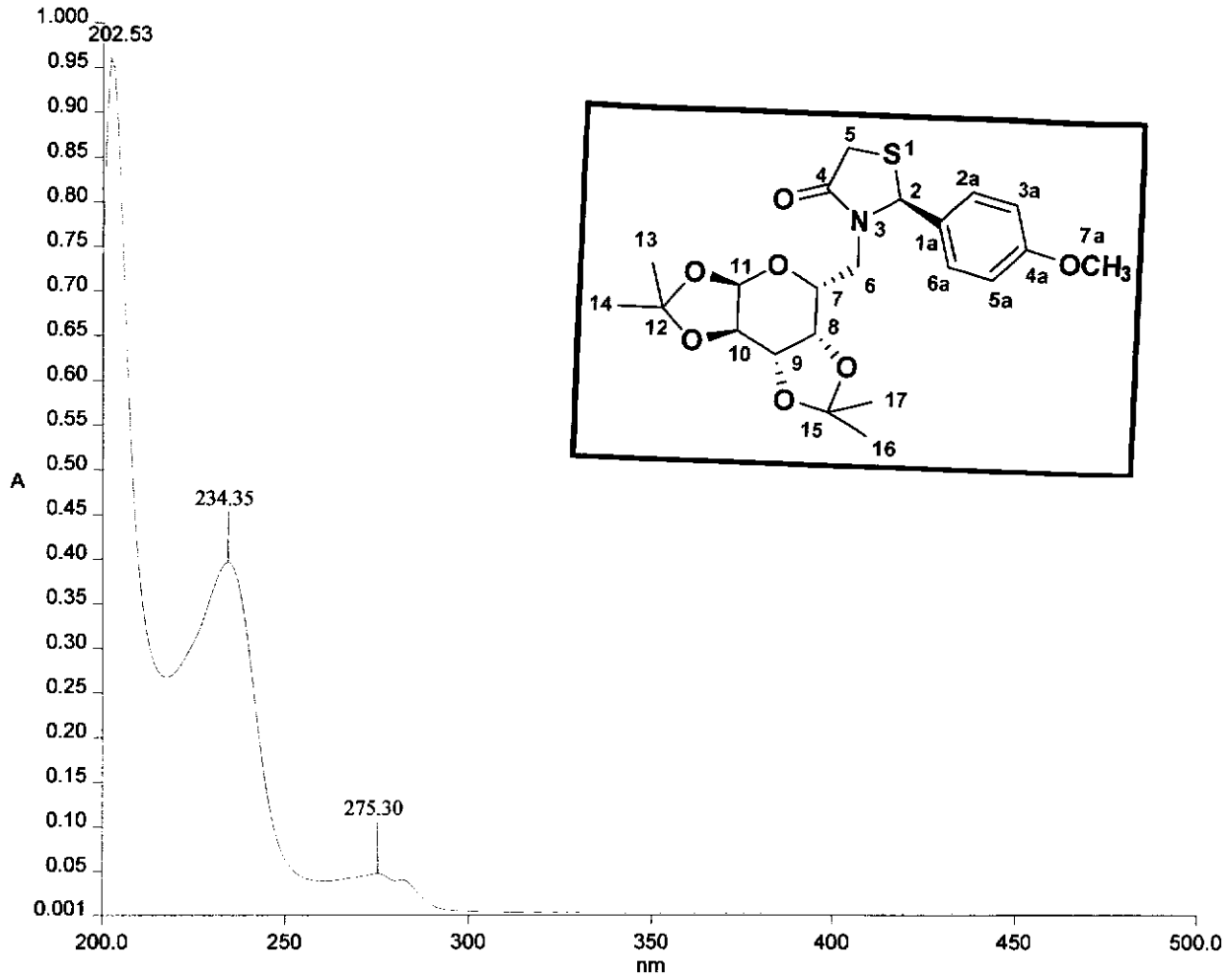


Expanded ^{13}C Spectrum of Compound 5h: 2-(4-Methoxy-phenyl)-3-(2,2,7,7-tetramethyl-tetrahydro-bis[1,3]dioxolo[4,5-b;4',5'-d]pyran-5-ylmethyl)-thiazolidin-4-one

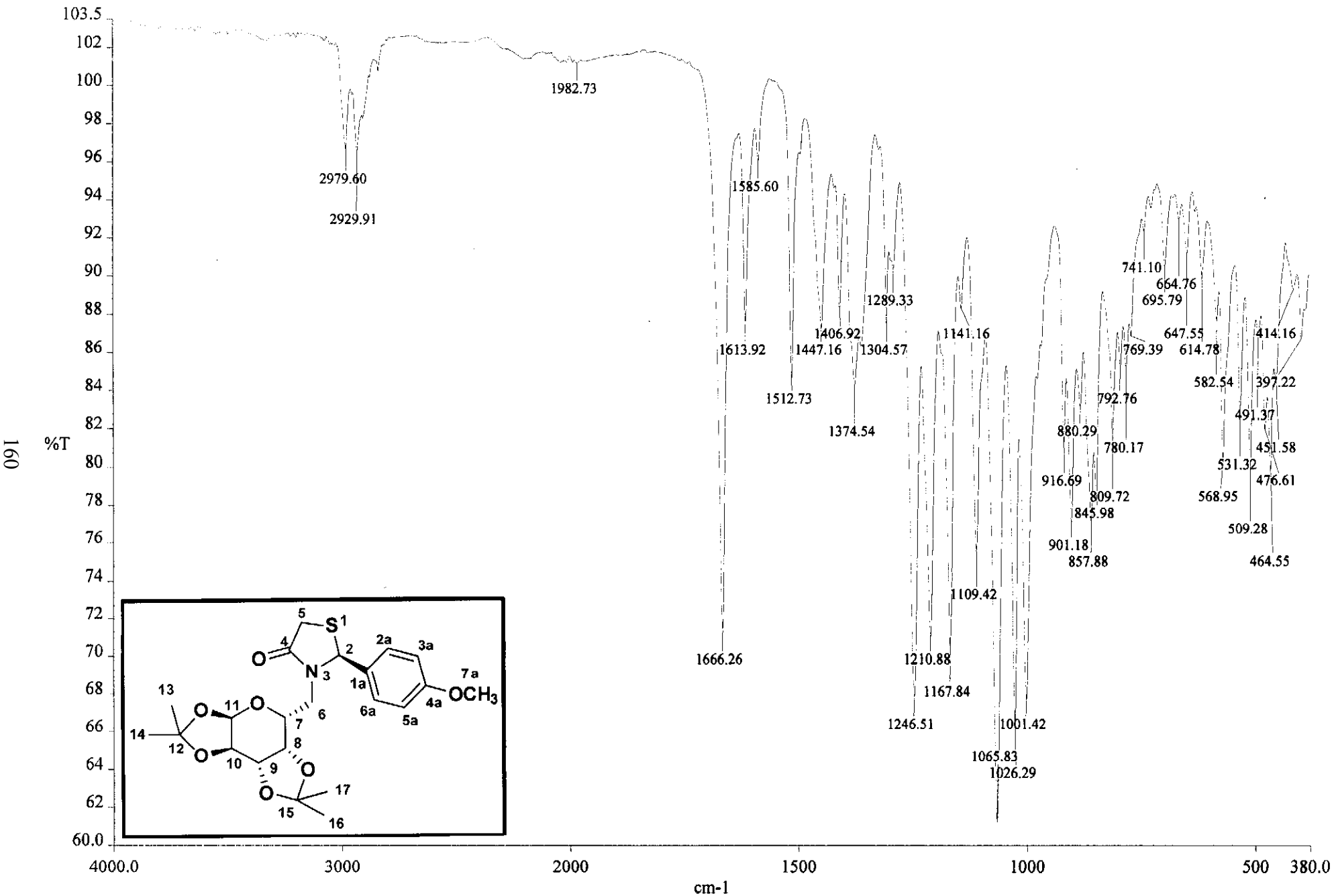


Expanded ^{13}C Spectrum of Compound 5h: 2-(4-Methoxy-phenyl)-3-(2,2,7,7-tetramethyl-tetrahydro-bis[1,3]dioxolo[4,5-b;4',5'-d]pyran-5-ylmethyl)-thiazolidin-4-one

Date: 2014/06/06 Time: 07:52:23 AM



Ultraviolet Spectrum of Compound 5h: 2-(4-Methoxy-phenyl)-3-(2,2,7,7-tetramethyl-tetra hydro-bis[1,3]dioxolo[4,5-b;4',5'-d]pyran-5-ylmethyl)-thiazolidin-4-one



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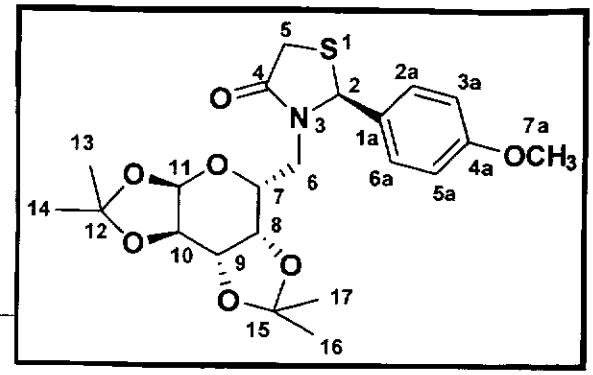
Infrared Spectrum of Compound 5h: 2-(4-Methoxy-phenyl)-3-(2,2,7,7-tetramethyl-tetra hydro-bis[1,3]dioxolo[4,5-b;4',5'-d]pyran-5-ylmethyl)-thiazolidin-4-one

==== Shimadzu LCsolution Analysis Report ====

Acquired by	: Admin
Sample Name	: 4och3 us formic buffer
Sample ID	: 4och3 us formic buffer
Vail #	: 1
Injection Volume	: 100 uL
Data File Name	: 4och3 us formic buffer.lcd
Method File Name	: Pramod 09jun 2014.lcm
Batch File Name	: suger thiozolidinon.lcb
Report File Name	: Default.lcr
Data Acquired	: 2014/06/17 03:17:04 PM
Data Processed	: 2014/06/17 03:57:06 PM



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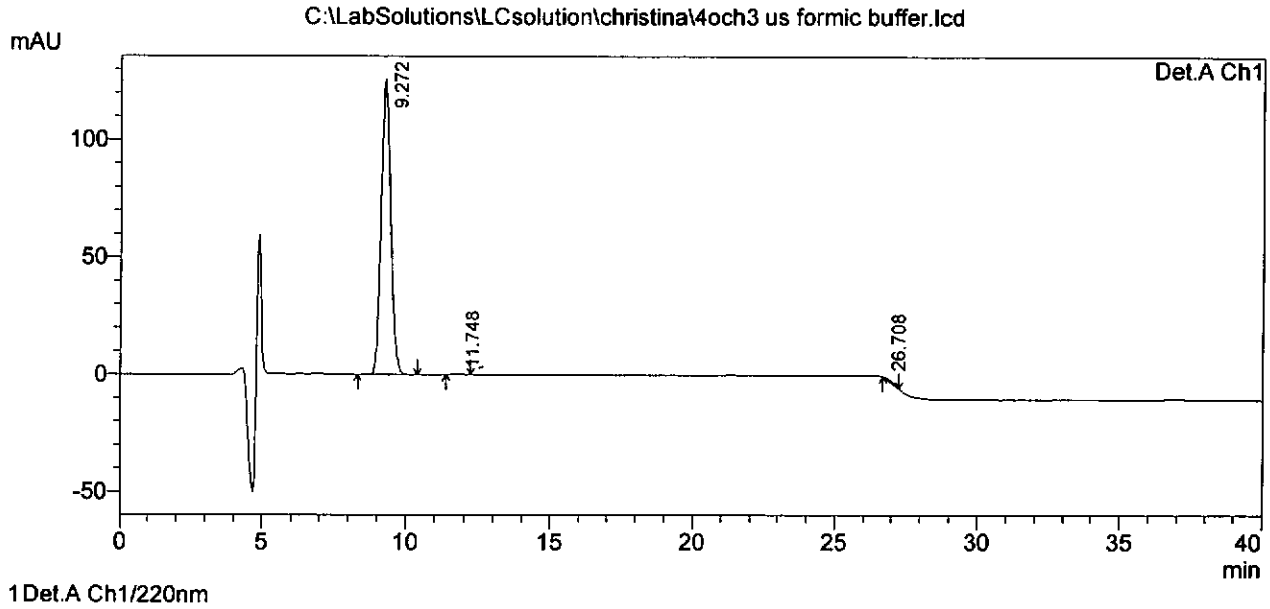


1Det.A Ch1/220nm

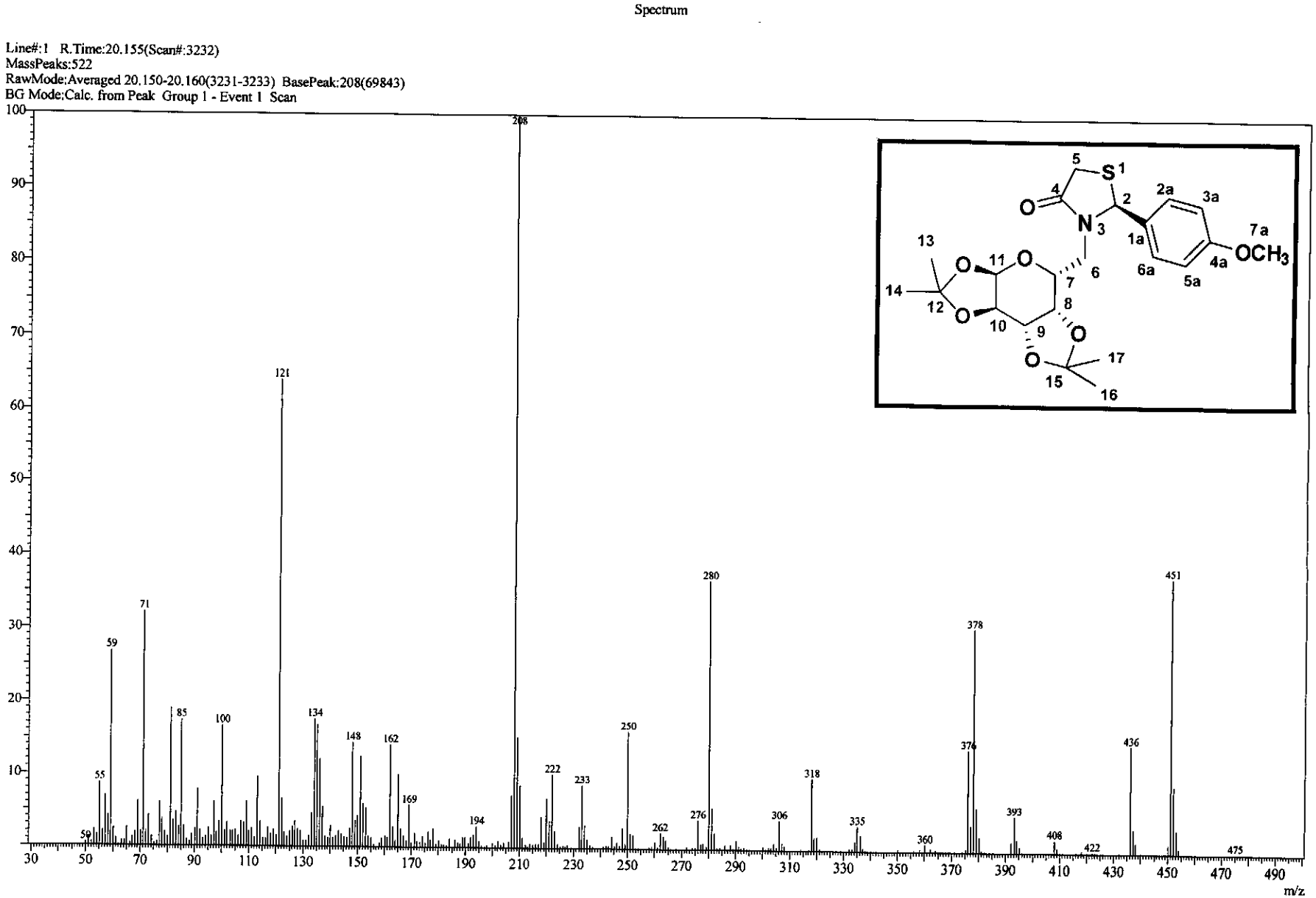
<Results>

PeakTable C:\LabSolutions\LCsolution\christina\4och3 us formic buffer.lcd

Detector A Ch1 220nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	9.272	2918219	125948	99.142	99.589
2	11.748	11530	520	0.392	0.411
3	26.708	13723	0	0.466	0.000
Total		2943472	126468	100.000	100.000

HPLC of Compound 5h: 2-(4-Methoxy-phenyl)-3-(2,2,7,7-tetramethyl-tetrahydro-bis[1,3] dioxolo[4,5-b;4',5'-d]pyran-5-ylmethyl)-thiazolidin-4-one

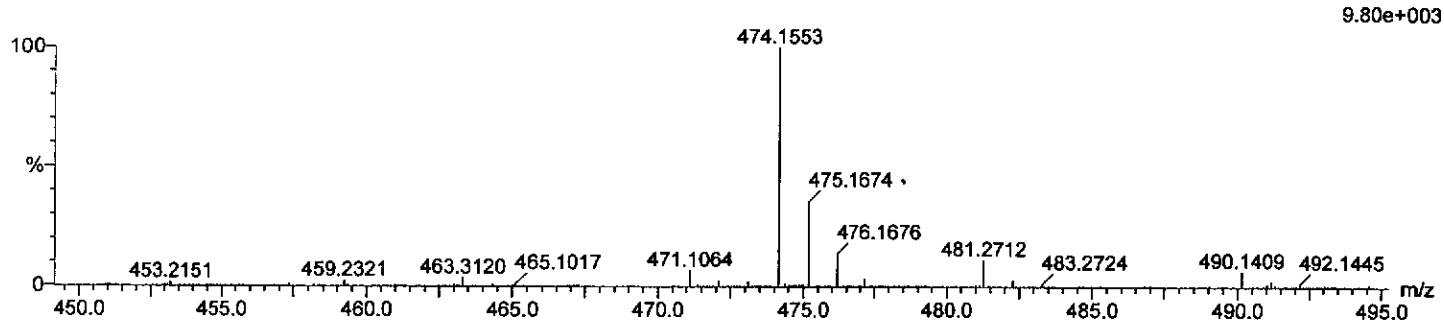


GC-MS of Compound 5h: 2-(4-Methoxy-phenyl)-3-(2,2,7,7-tetramethyl-tetrahydro-bis[1,3] dioxolo[4,5-b;4',5'-d]pyran-5-ylmethyl)-thiazolidin-4-one

Elemental Composition Report **Page 1**

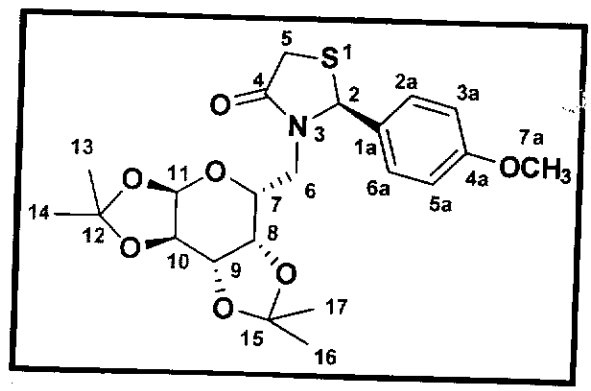
Single Mass Analysis
Tolerance = 5.0 PPM / DBE: min = -1.5, max = 100.0
Element prediction: Off
Number of isotope peaks used for i-FIT = 3

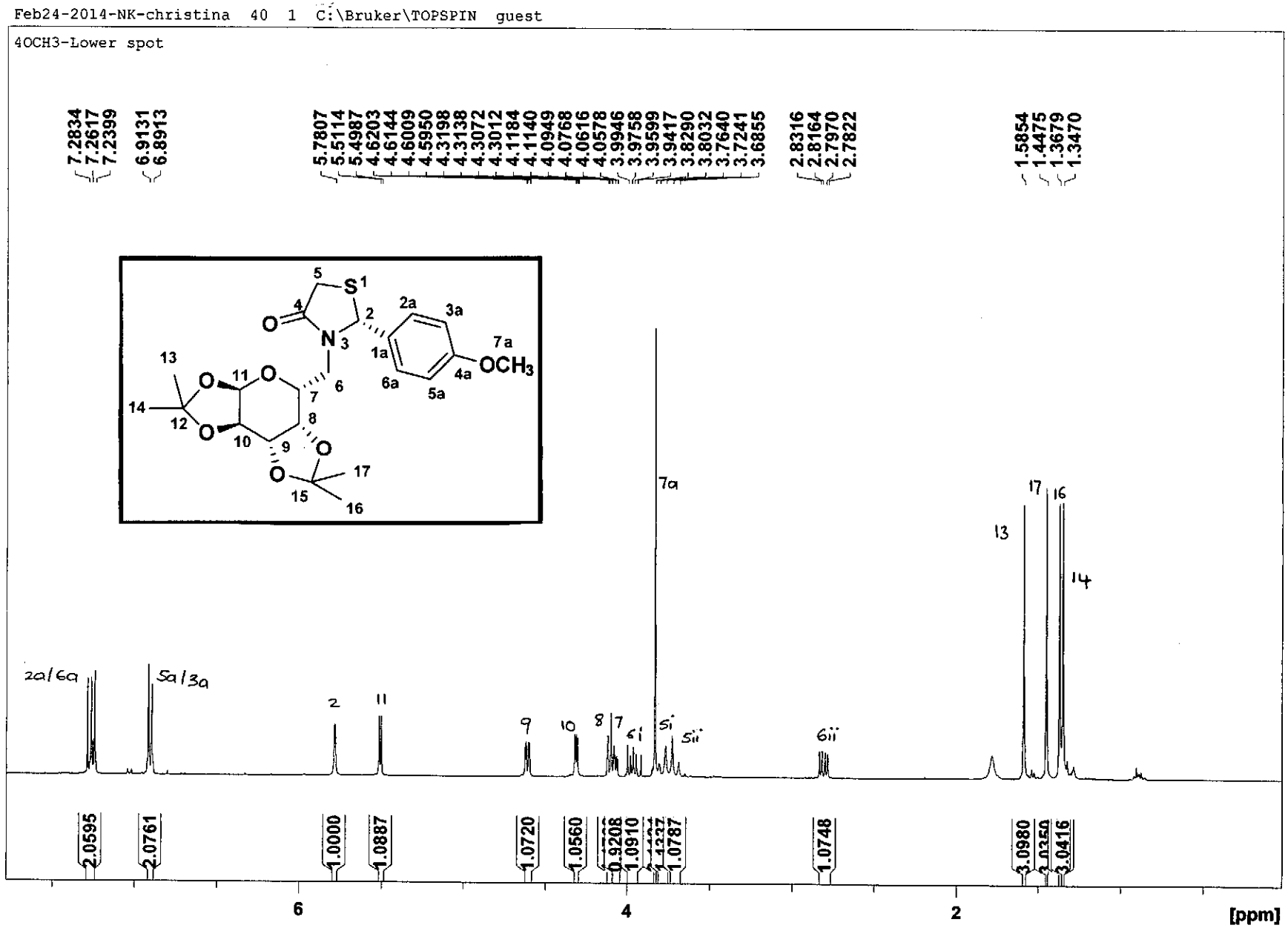
Monoisotopic Mass, Even Electron Ions
57 formula(e) evaluated with 1 results within limits (up to 20 best isotopic matches for each mass)
Elements Used:
C: 20-25 H: 25-30 N: 0-5 O: 5-10 Na: 0-1 S: 0-1
1 49 (1.620)
TOF MS ES+



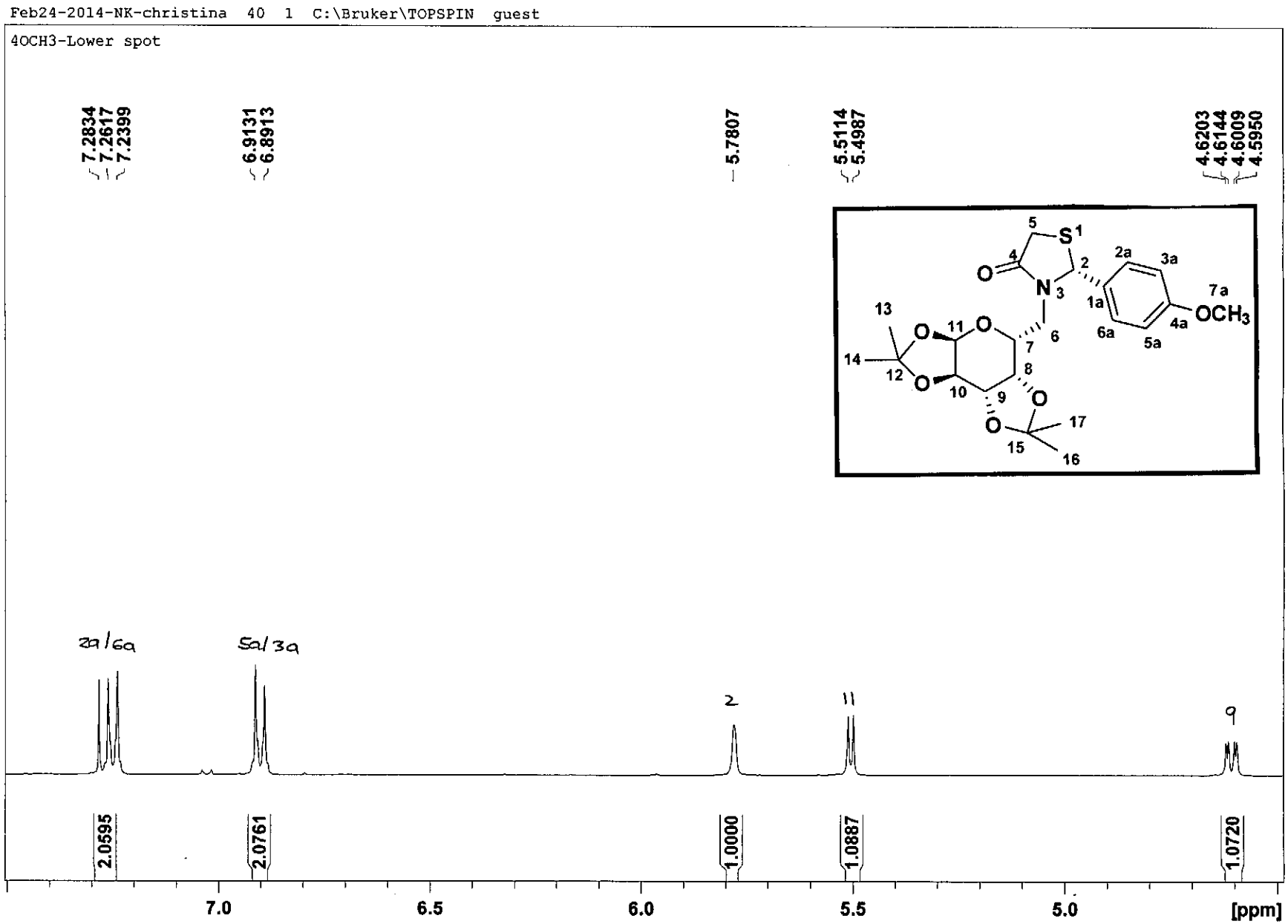
Minimum:				-1.5			
Maximum:		5.0	5.0	100.0			
Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	i-FIT (Norm)	Formula
474.1553	474.1562	-0.9	-1.9	8.5	147.1	0.0	C22 H29 N O7 Na S

HRMS of Compound 5h: 2-(4-Methoxy-phenyl)-3-(2,2,7,7-tetramethyl-tetrahydro-bis[1,3] dioxolo[4,5-b;4',5'-d]pyran-5-ylmethyl)-thiazolidin-4-one

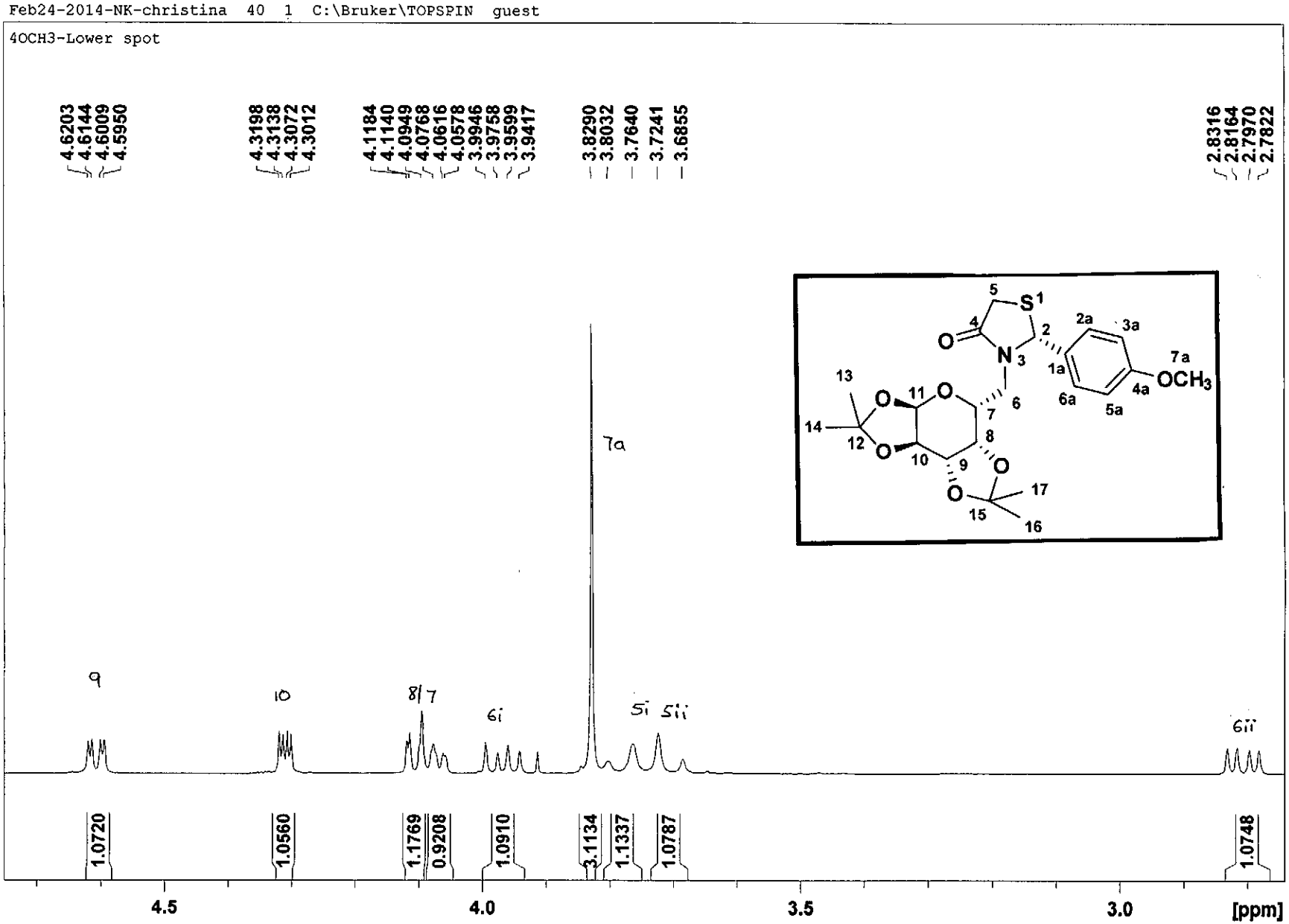




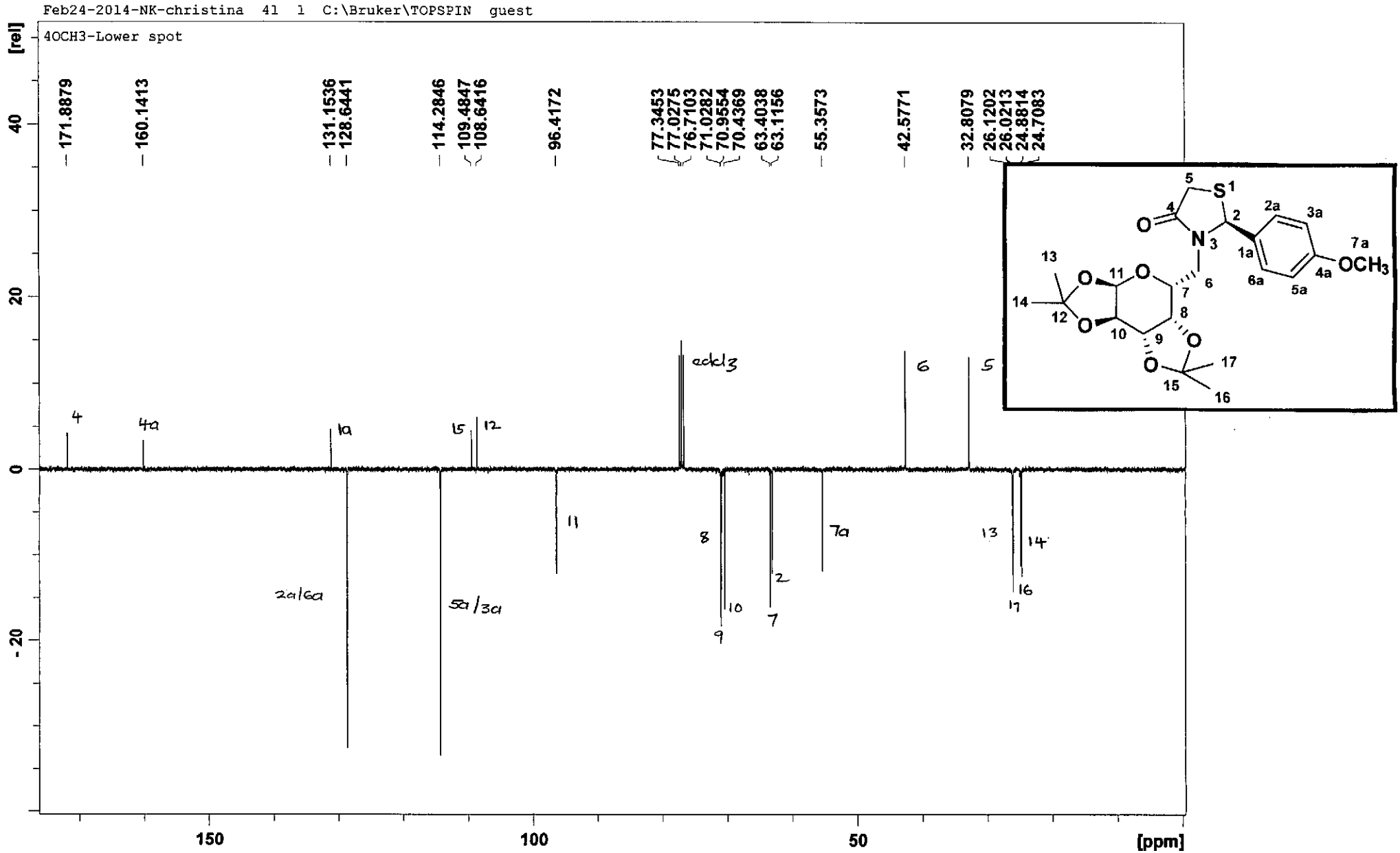
[1]H Spectrum of Compound 6h: 2-(4-Methoxy-phenyl)-3-(2,2,7,7-tetramethyl-tetrahydro-bis [1,3]dioxolo[4,5-b;4',5'-d]pyran-5-ylmethyl)-thiazolidin-4-one



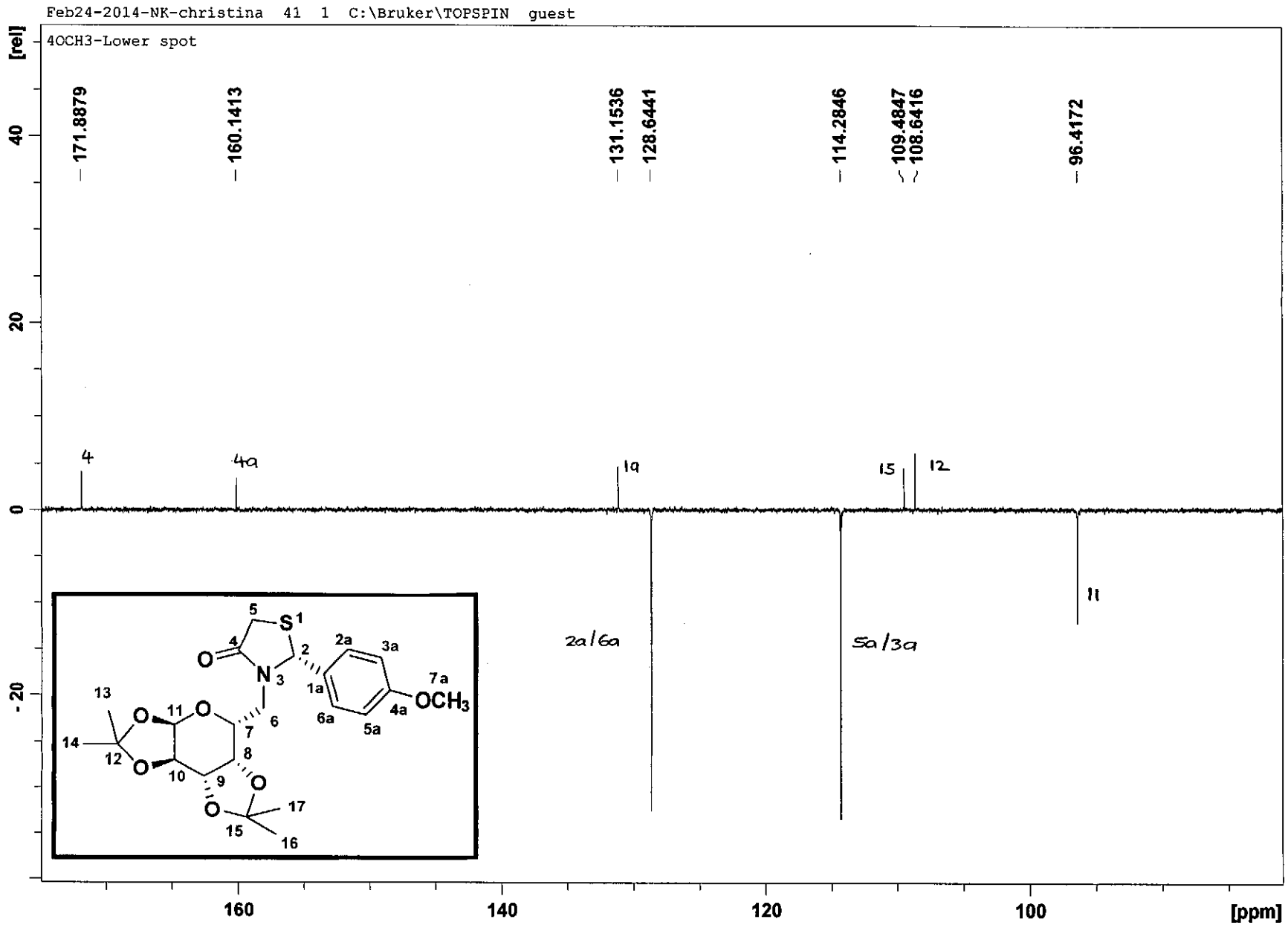
Expanded ^{1}H Spectrum of Compound 6h: 2-(4-Methoxy-phenyl)-3-(2,2,7,7-tetramethyl-tetrahydro-bis[1,3]dioxolo[4,5-b;4',5'-d]pyran-5-ylmethyl)-thiazolidin-4-one



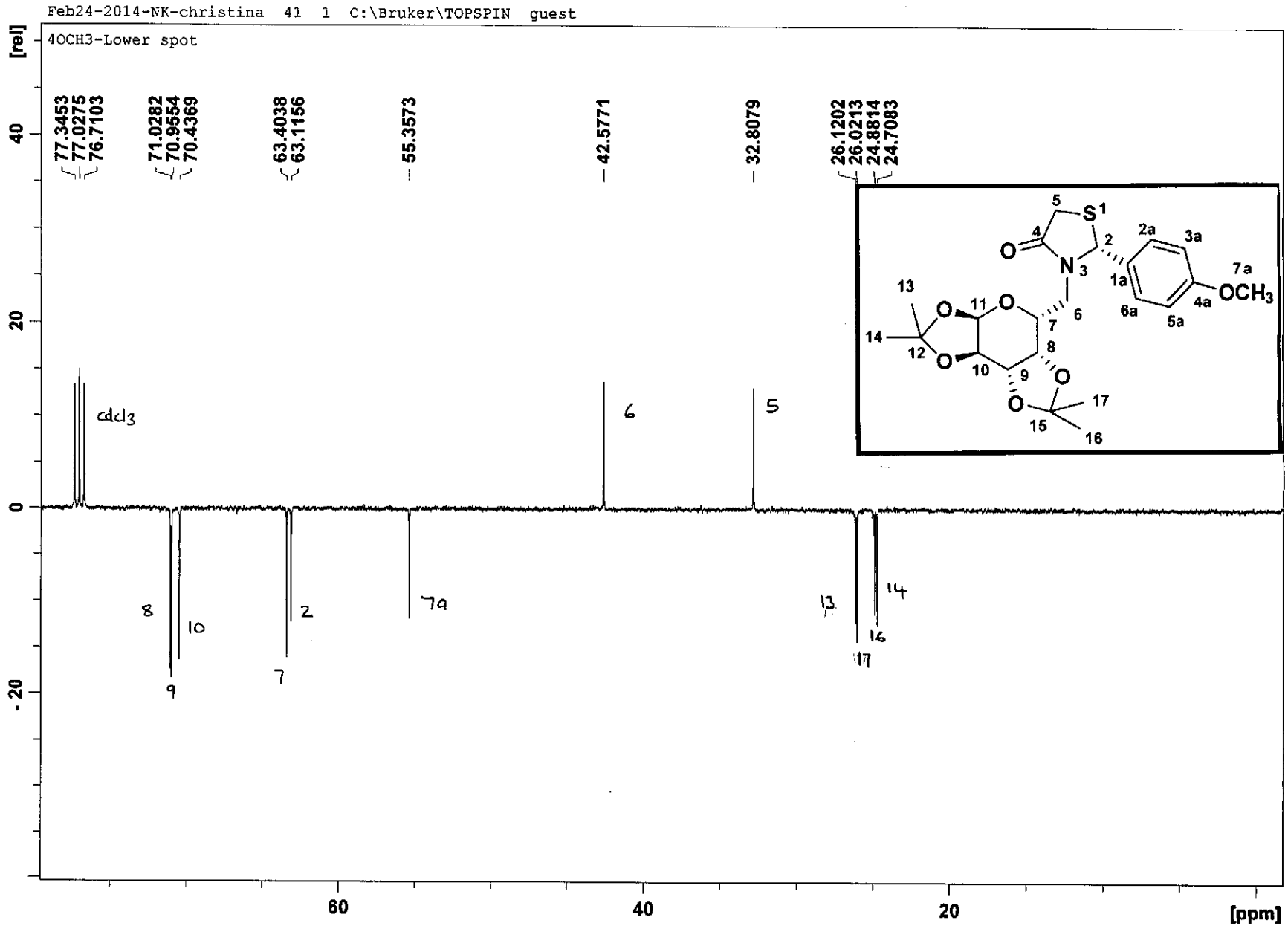
Expanded ^{1}H Spectrum of Compound 6h: 2-(4-Methoxy-phenyl)-3-(2,2,7,7-tetramethyl-tetrahydro-bis[1,3]dioxolo[4,5-b;4',5'-d]pyran-5-ylmethyl)-thiazolidin-4-one



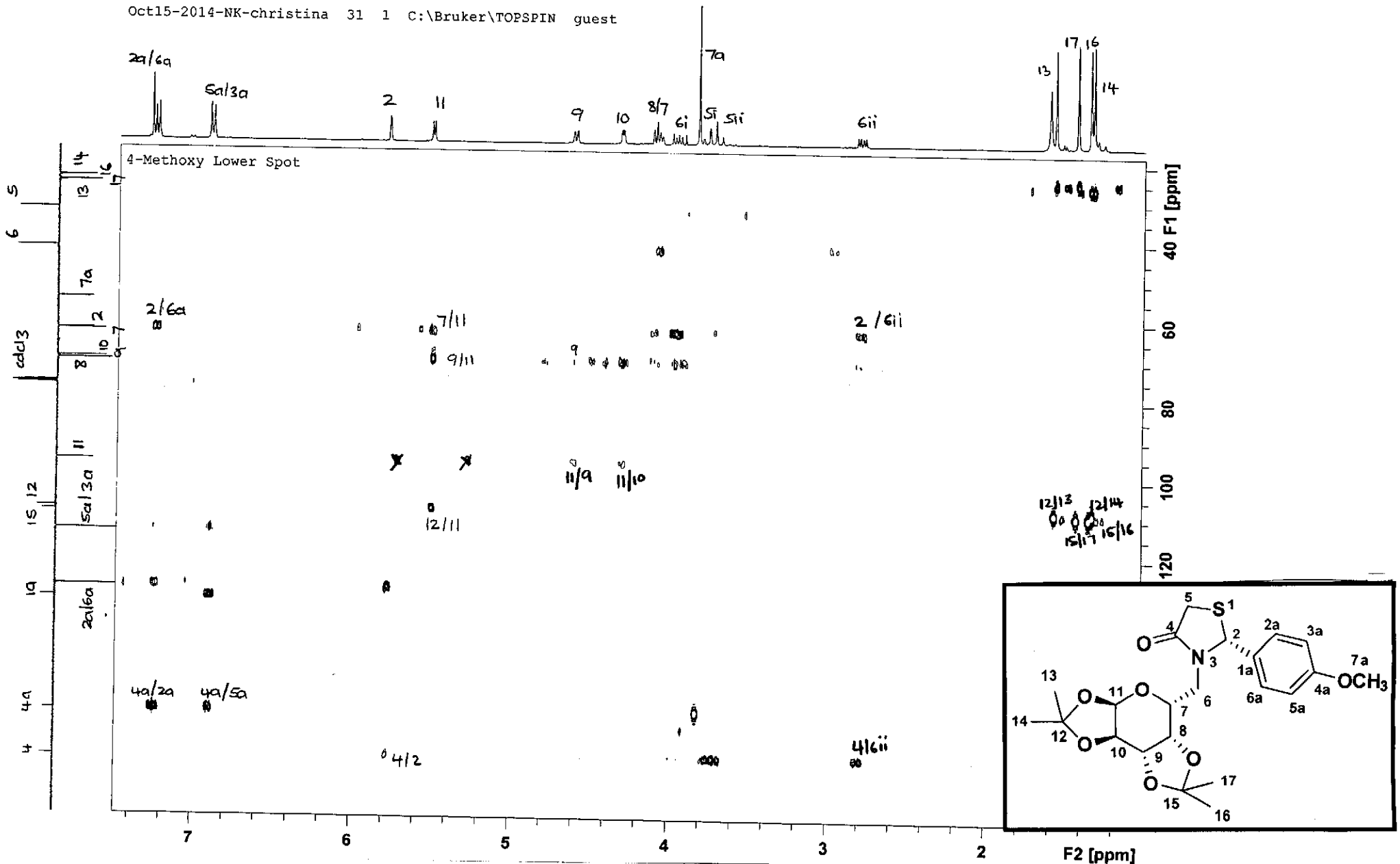
^{13}C Spectrum of Compound 6h: 2-(4-Methoxy-phenyl)-3-(2,2,7,7-tetramethyl-tetrahydro-bis[1,3]dioxolo[4,5-b;4',5'-d]pyran-5-ylmethyl)-thiazolidin-4-one



Expanded ^{13}C Spectrum of Compound 6h: 2-(4-Methoxy-phenyl)-3-(2,2,7,7-tetramethyl-tetrahydro-bis[1,3]dioxolo[4,5-b;4',5'-d]pyran-5-ylmethyl)-thiazolidin-4-one

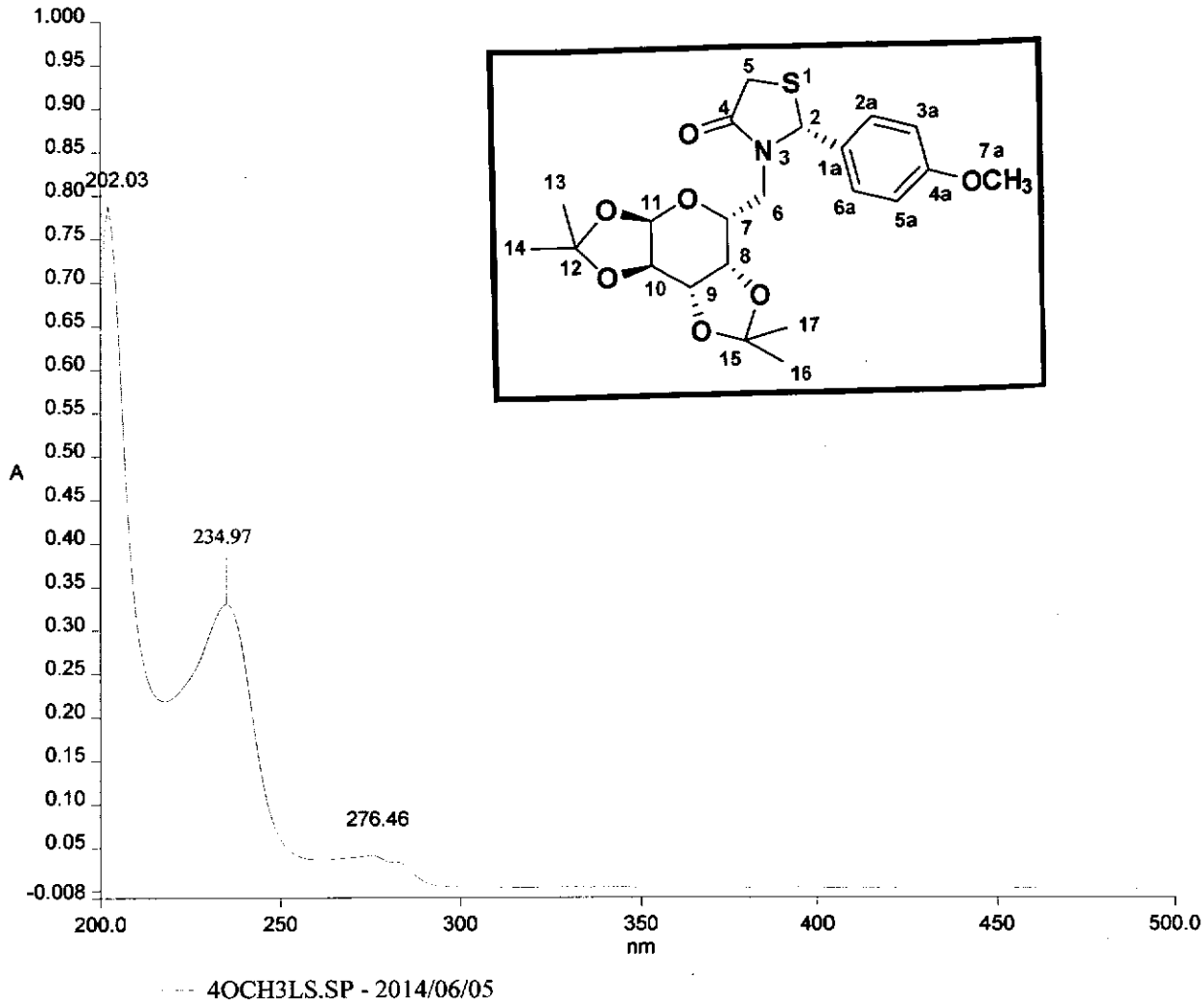


Expanded ^{13}C Spectrum of Compound 6h: 2-(4-Methoxy-phenyl)-3-(2,2,7,7-tetramethyl-tetrahydro-bis[1,3]dioxolo[4,5-b;4',5'-d]pyran-5-ylmethyl)-thiazolidin-4-one

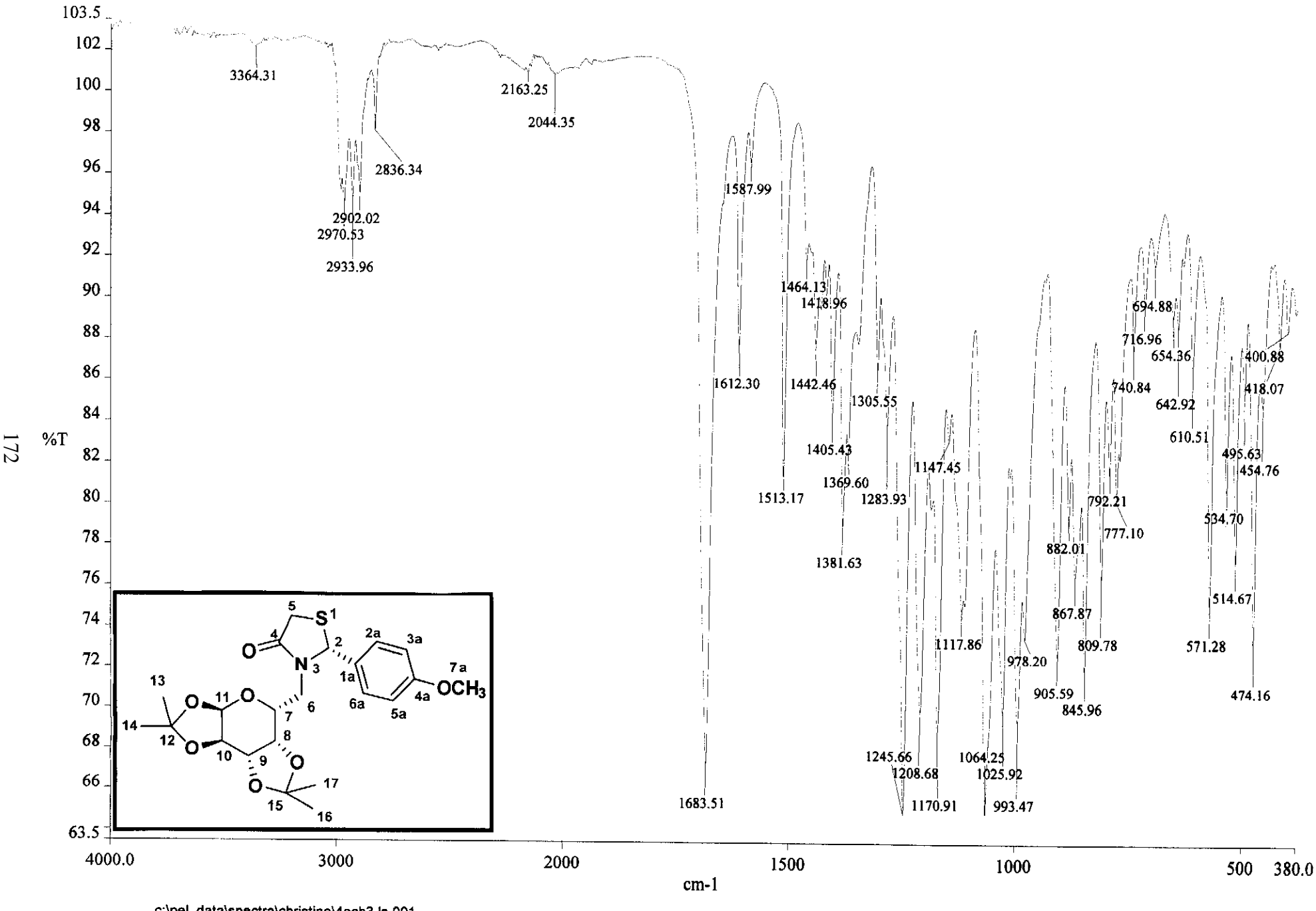


HMBC of Compound 6h: 2-(4-Methoxyphenyl)-3-(2,2,7,7-tetramethyltetrahydro-*bis* [1,3]dioxolo[4,5b;4',5'd]pyran-5-ylmethyl)thiazolidin-4-one

Date: 2014/06/06 Time: 07:55:00 AM



Ultraviolet Spectrum of Compound 6h: 2-(4-Methoxy-phenyl)-3-(2,2,7,7-tetramethyl-tetra hydro-bis [1,3]dioxolo[4,5-b;4',5'-d]pyran-5-ylmethyl)-thiazolidin-4-one

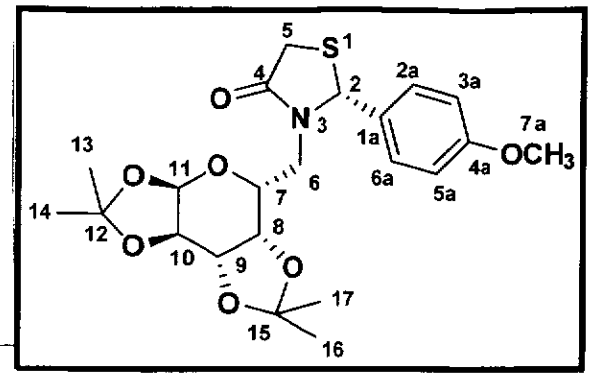


c:\pel_data\spectra\christina\4och3 is.001

Infrared Spectrum of Compound 6h: 2-(4-Methoxy-phenyl)-3-(2,2,7,7-tetramethyl-tetra hydro-bis [1,3]dioxolo[4,5-b;4',5'-d]pyran-5-ylmethyl)-thiazolidin-4-one

==== Shimadzu LCsolution Analysis Report ====

Acquired by	: Admin
Sample Name	: 4och3 LS2 formic buffer
Sample ID	: 4och3 LS2 formic buffer
Vail #	: 1
Injection Volume	: 100 uL
Data File Name	: 4och3 LS2 formic buffer.lcd
Method File Name	: Pramod 09jun 2014.lcm
Batch File Name	: suger thiozolidinon.lcb
Report File Name	: Default.lcr
Data Acquired	: 2014/06/18 10:02:23 AM
Data Processed	: 2014/06/18 10:42:27 AM



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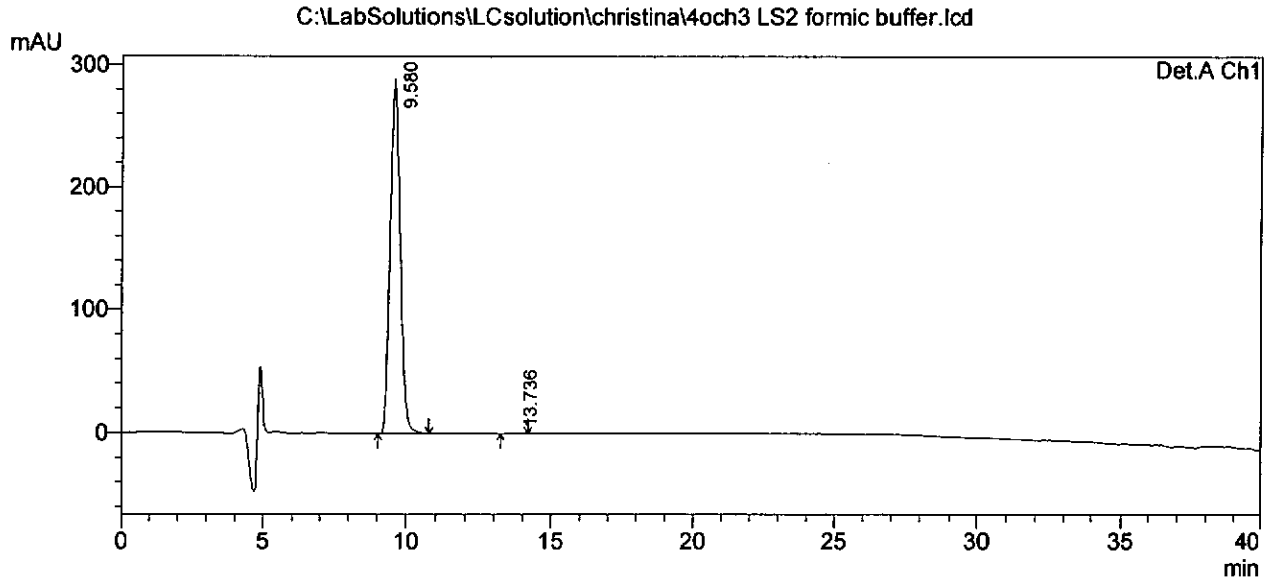


1Det.A Ch1/220nm

<Results>

PeakTable C:\LabSolutions\LCsolution\christina\4och3 LS2 formic buffer.lcd

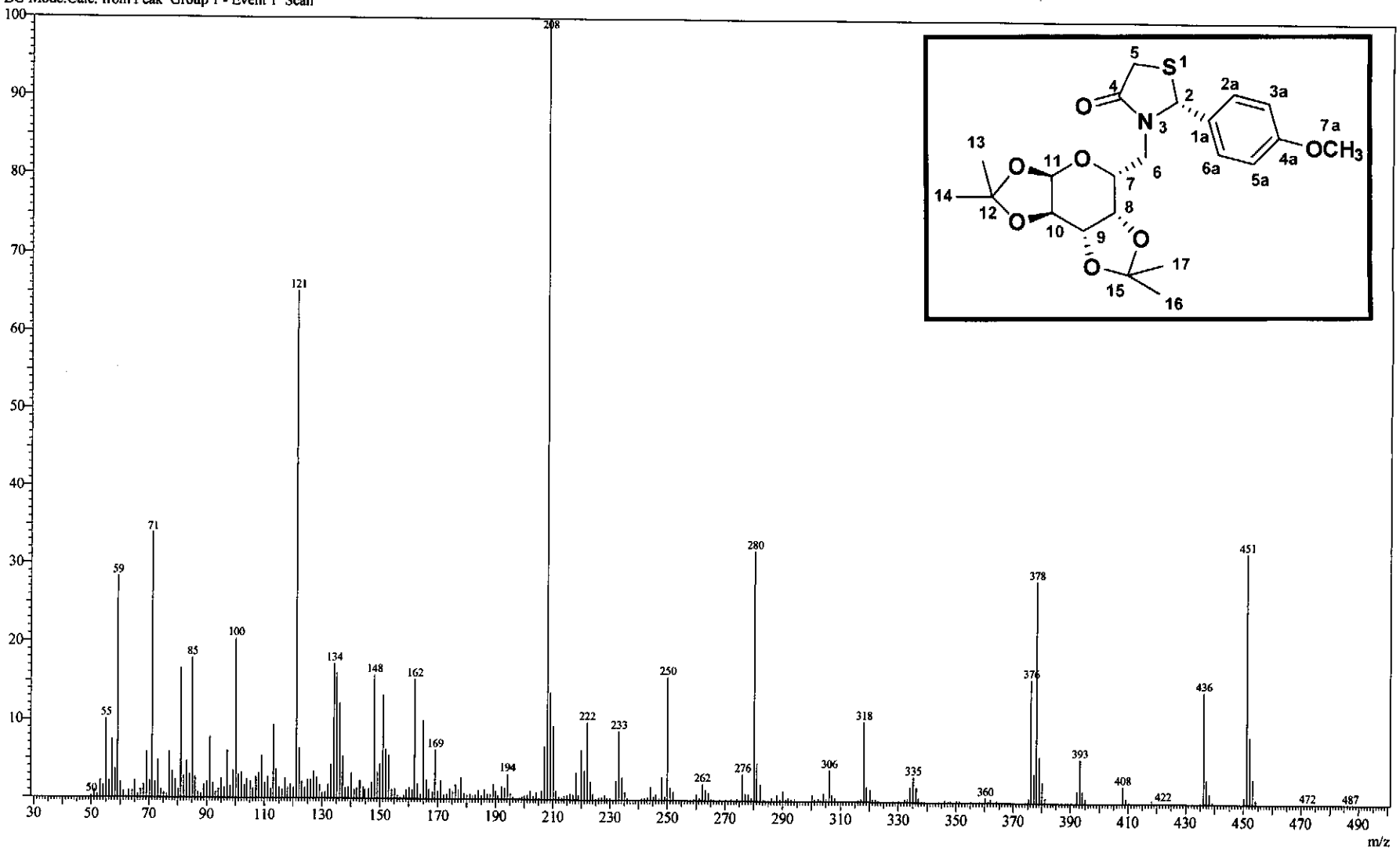
Detector A Ch1 220nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	9.580	6961885	288732	99.879	99.881
2	13.736	8412	344	0.121	0.119
Total		6970297	289076	100.000	100.000

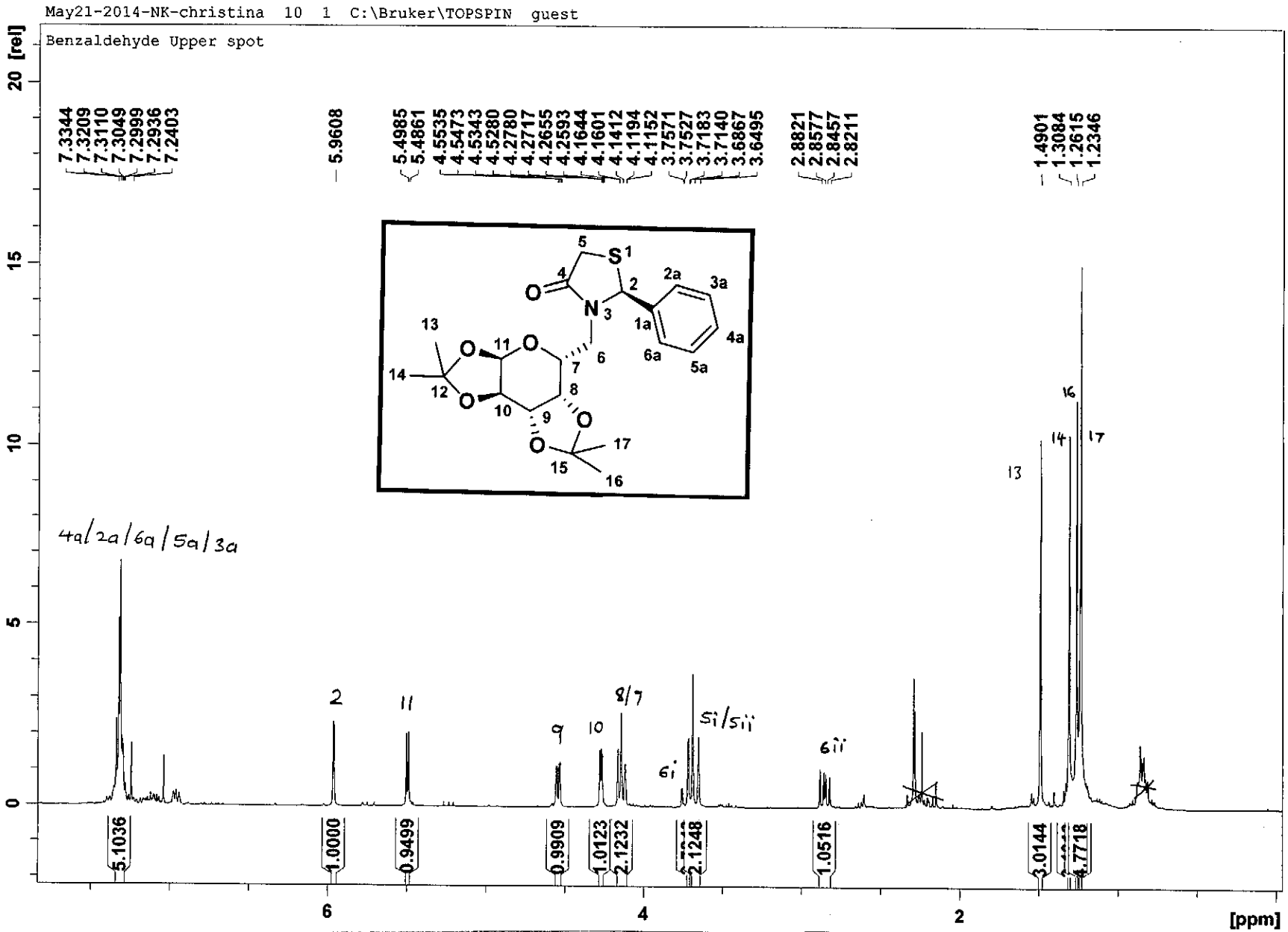
HPLC of Compound 6h: 2-(4-Methoxy-phenyl)-3-(2,2,7,7-tetramethyl-tetrahydro-bis [1,3] dioxolo[4,5-b;4',5'-d]pyran-5-ylmethyl)-thiazolidin-4-one

Spectrum

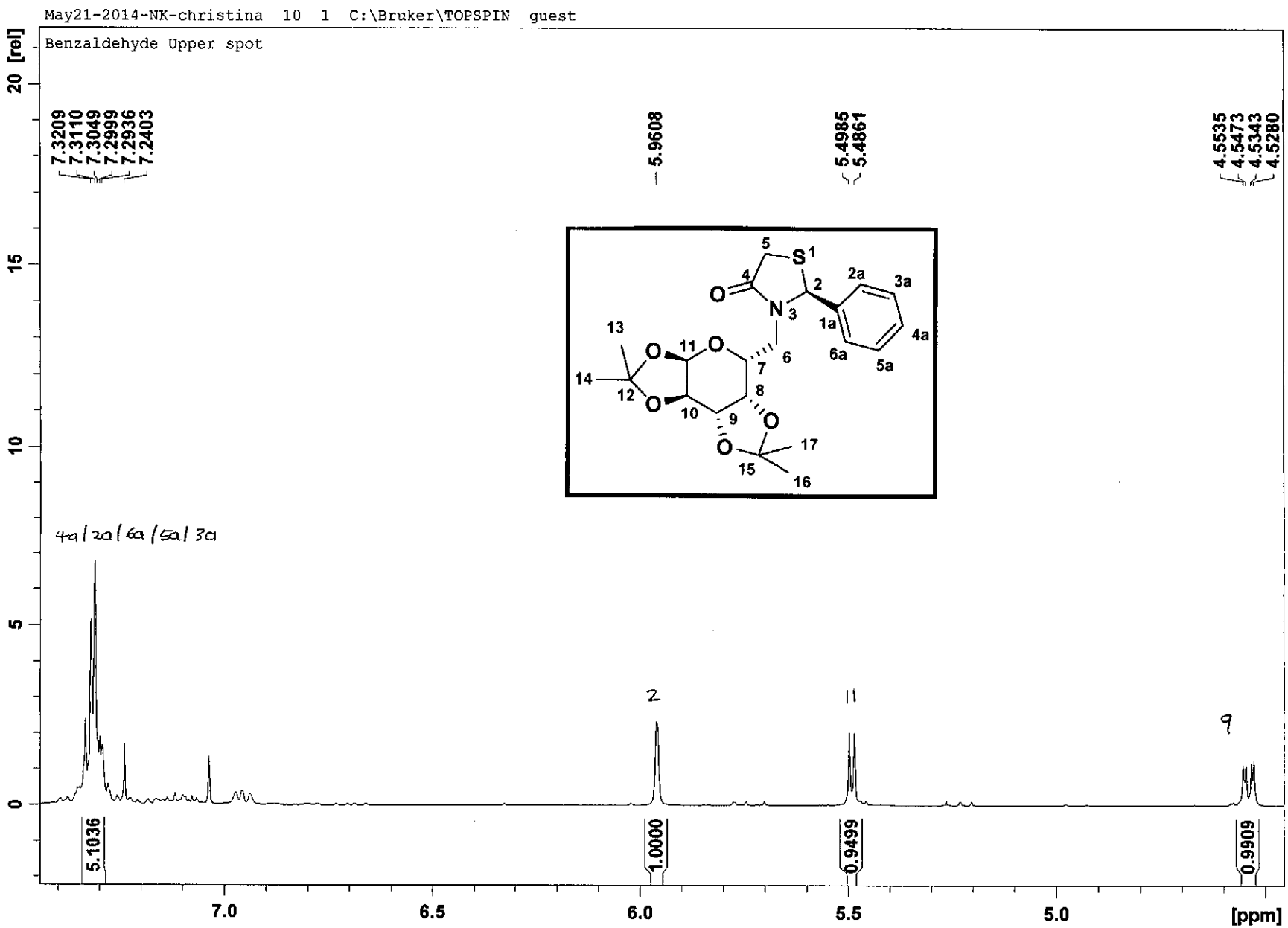
Line#:1 R.Time:20.865(Scan#:3374)
MassPeaks:554
RawMode:Averaged 20.860-20.870(3373-3375) BasePeak:208(98546)
BG Mode:Calc. from Peak Group 1 - Event 1 Scan



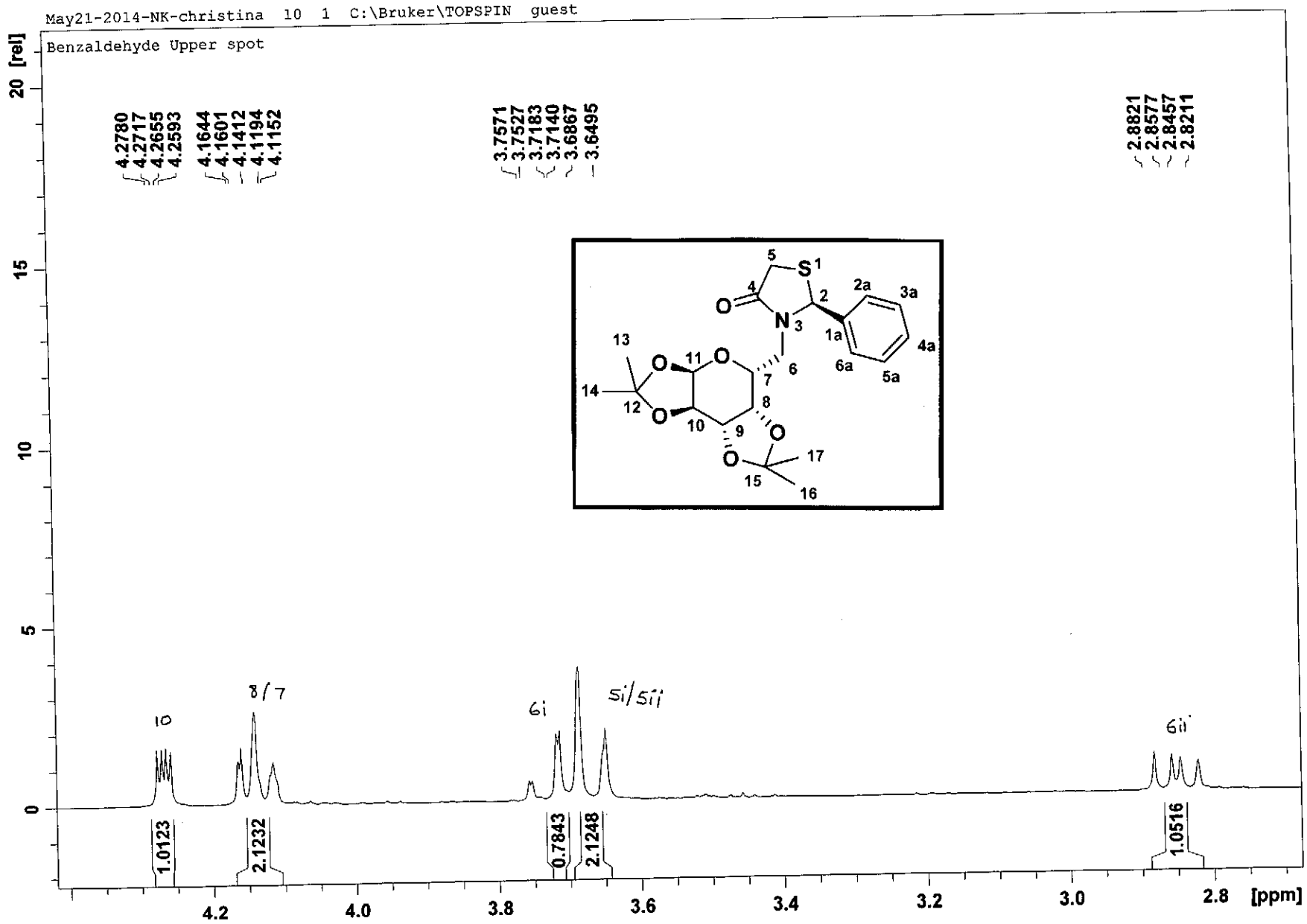
GC-MS of Compound 6h: 2-(4-Methoxy-phenyl)-3-(2,2,7,7-tetramethyl-tetrahydro-bis [1,3] dioxolo[4,5-b;4',5'-d]pyran-5-ylmethyl)-thiazolidin-4-one



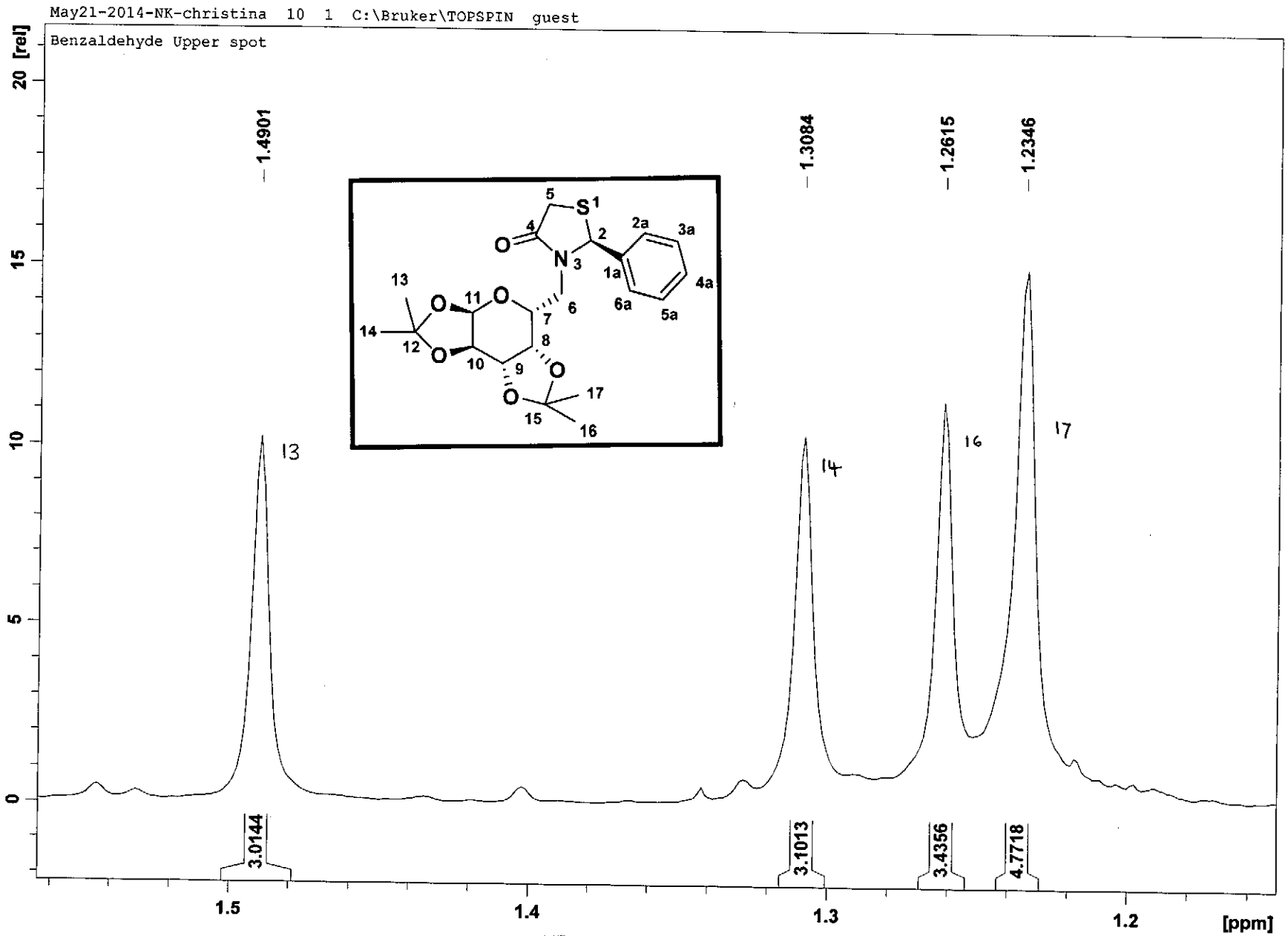
^{1}H Spectrum of compound 5i: 2-Phenyl-3-(2,2,7,7-tetramethyltetrahydro-*bis*[1,3] dioxolo[4,5b;4',5'd]pyran-5-ylmethyl)-thiazolidin-4-one



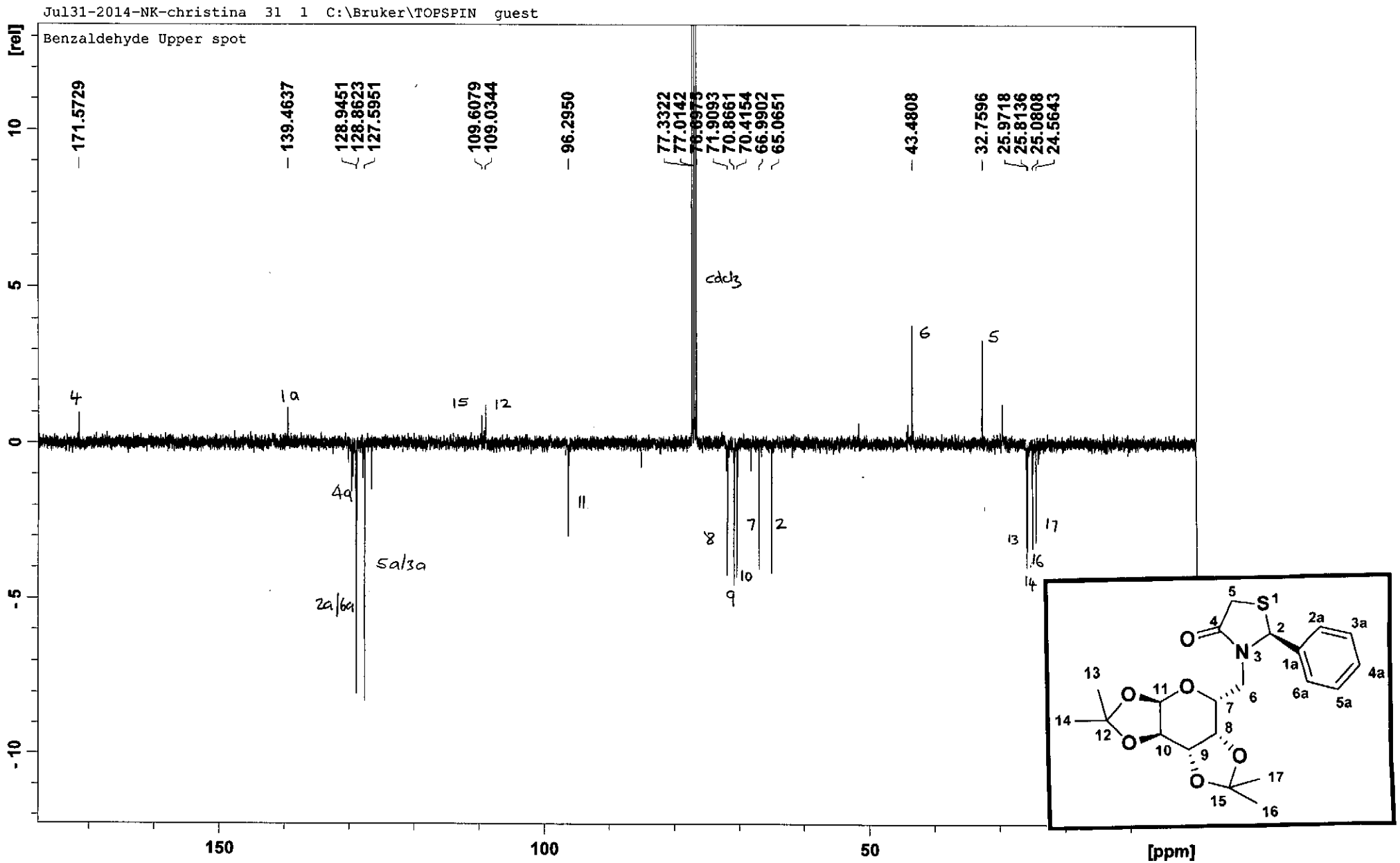
Expanded ^{1}H Spectrum of compound 5i: 2-Phenyl-3-(2,2,7,7-tetramethyltetrahydro-*bis*[1,3] dioxolo[4,5b;4',5'd]pyran-5-ylmethyl)-thiazolidin-4-one



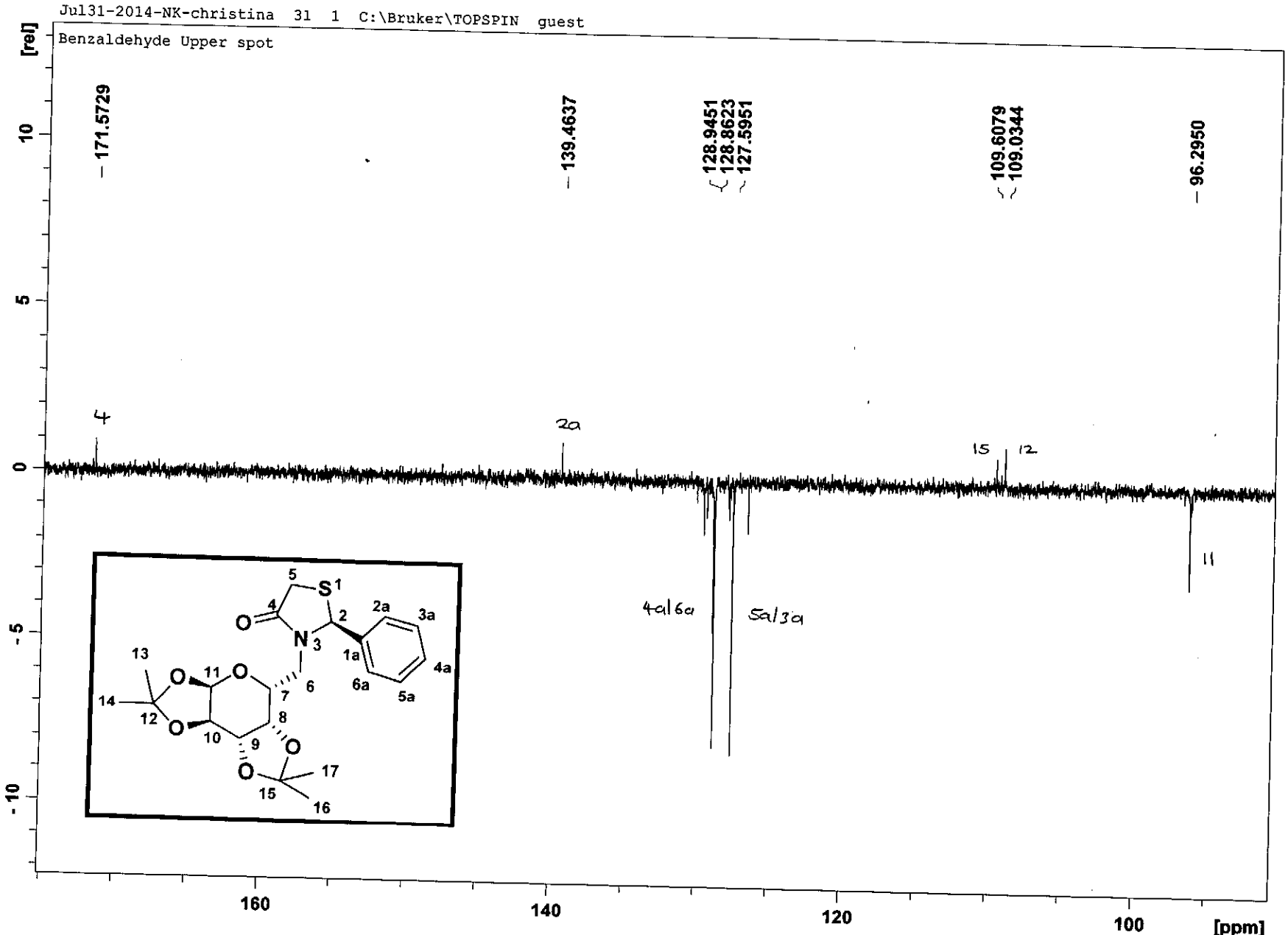
Expanded ^{1}H Spectrum of compound 5i: 2-Phenyl-3-(2,2,7,7-tetramethyltetrahydro-*bis*[1,3] dioxolo[4,5b;4',5'd]pyran-5-ylmethyl)-thiazolidin-4-one



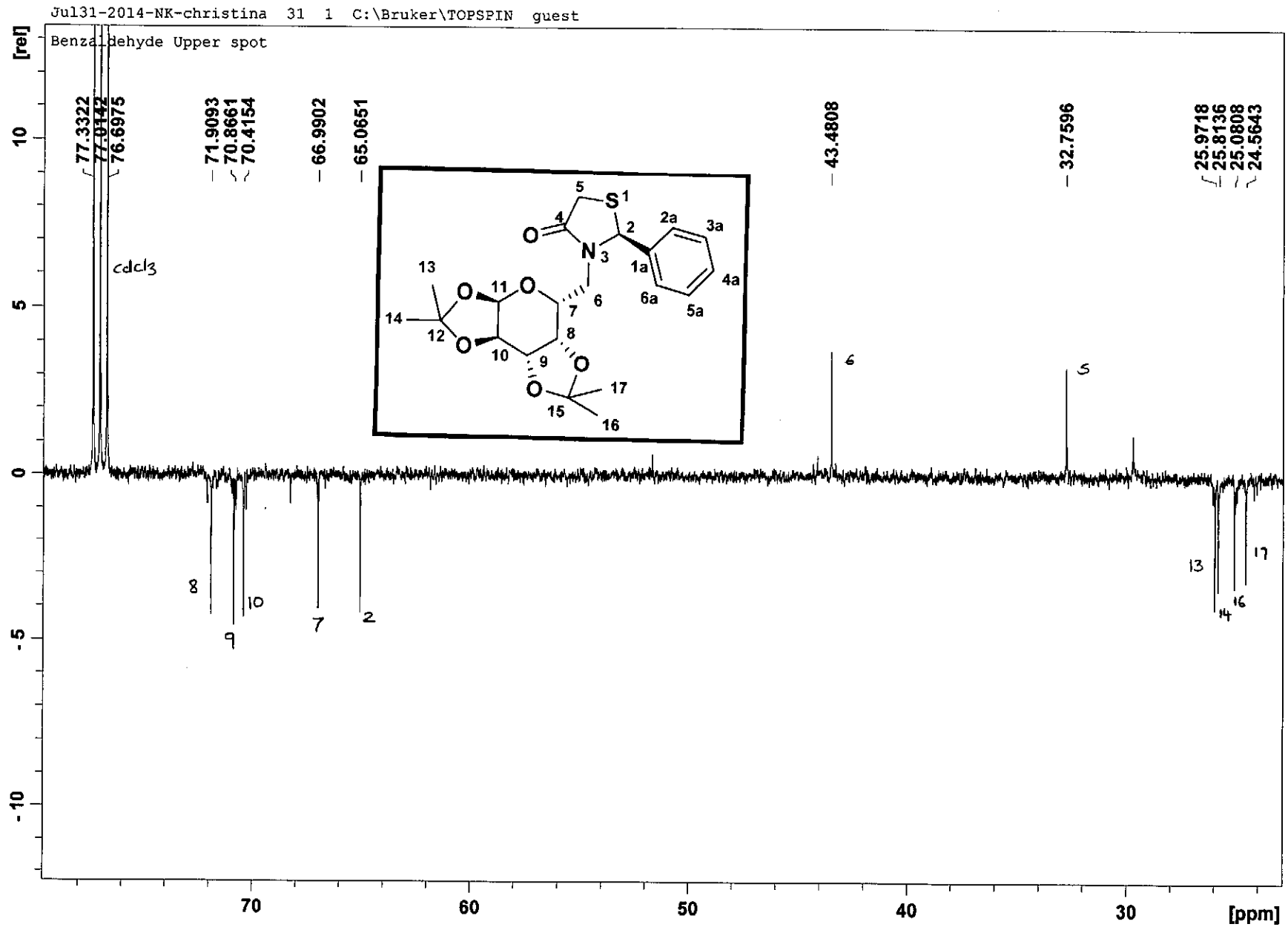
Expanded ^{1}H Spectrum of compound 5i: 2-Phenyl-3-(2,2,7,7-tetramethyltetrahydro-*bis*[1,3] dioxolo[4,5b;4',5'd]pyran-5-ylmethyl)-thiazolidin-4-one



^{13}C Spectrum of Compound 5i: 2-Phenyl-3-(2,2,7,7-tetramethyl-tetrahydro-bis[1,3]dioxolo [4,5-b;4',5'-d]pyran-5-ylmethyl)-thiazolidin-4-one

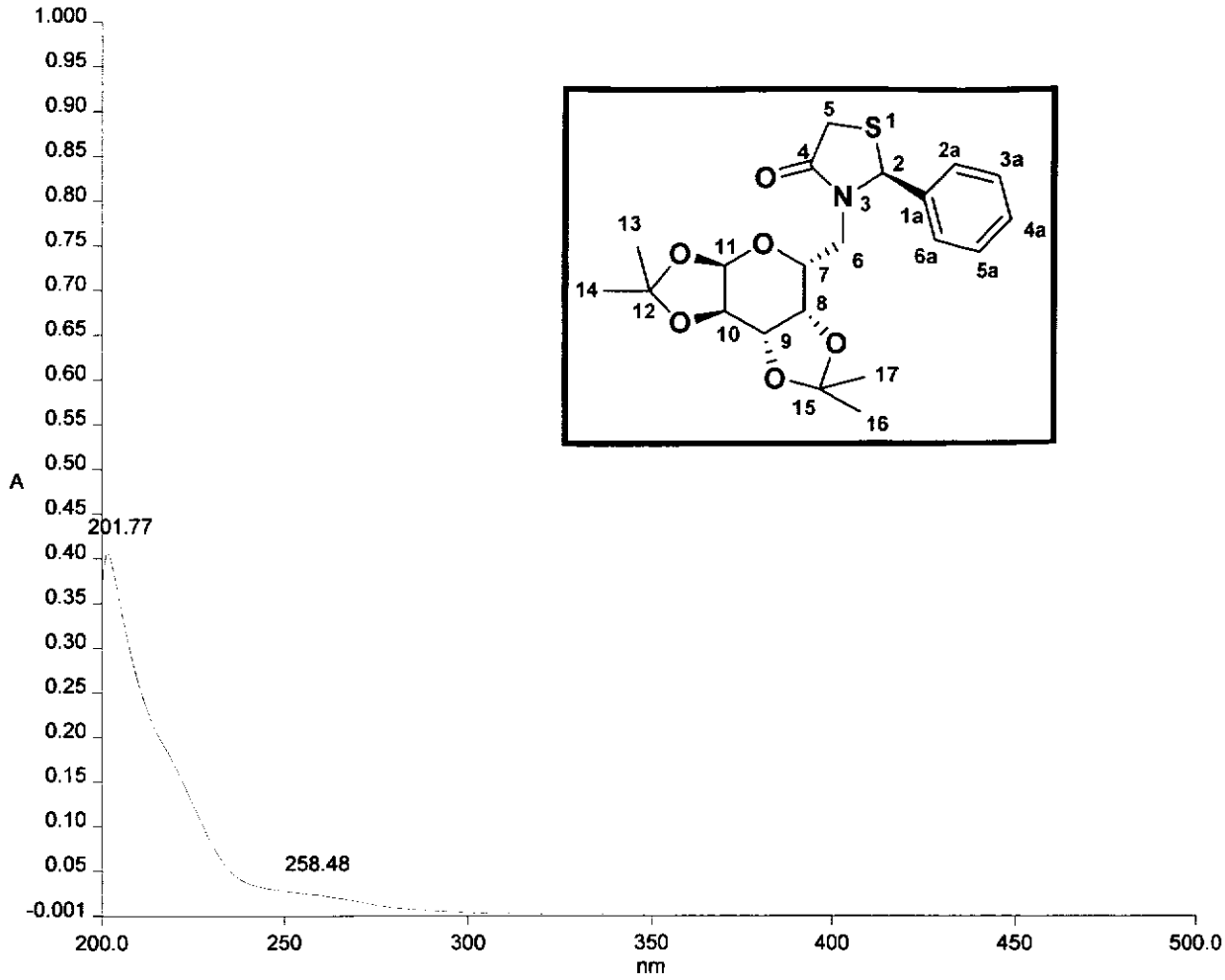


Expanded ^{13}C Spectrum of Compound 5i: 2-Phenyl-3-(2,2,7,7-tetramethyl-tetrahydro-bis[1,3]dioxolo[4,5-b;4',5'-d]pyran-5-ylmethyl)-thiazolidin-4-one

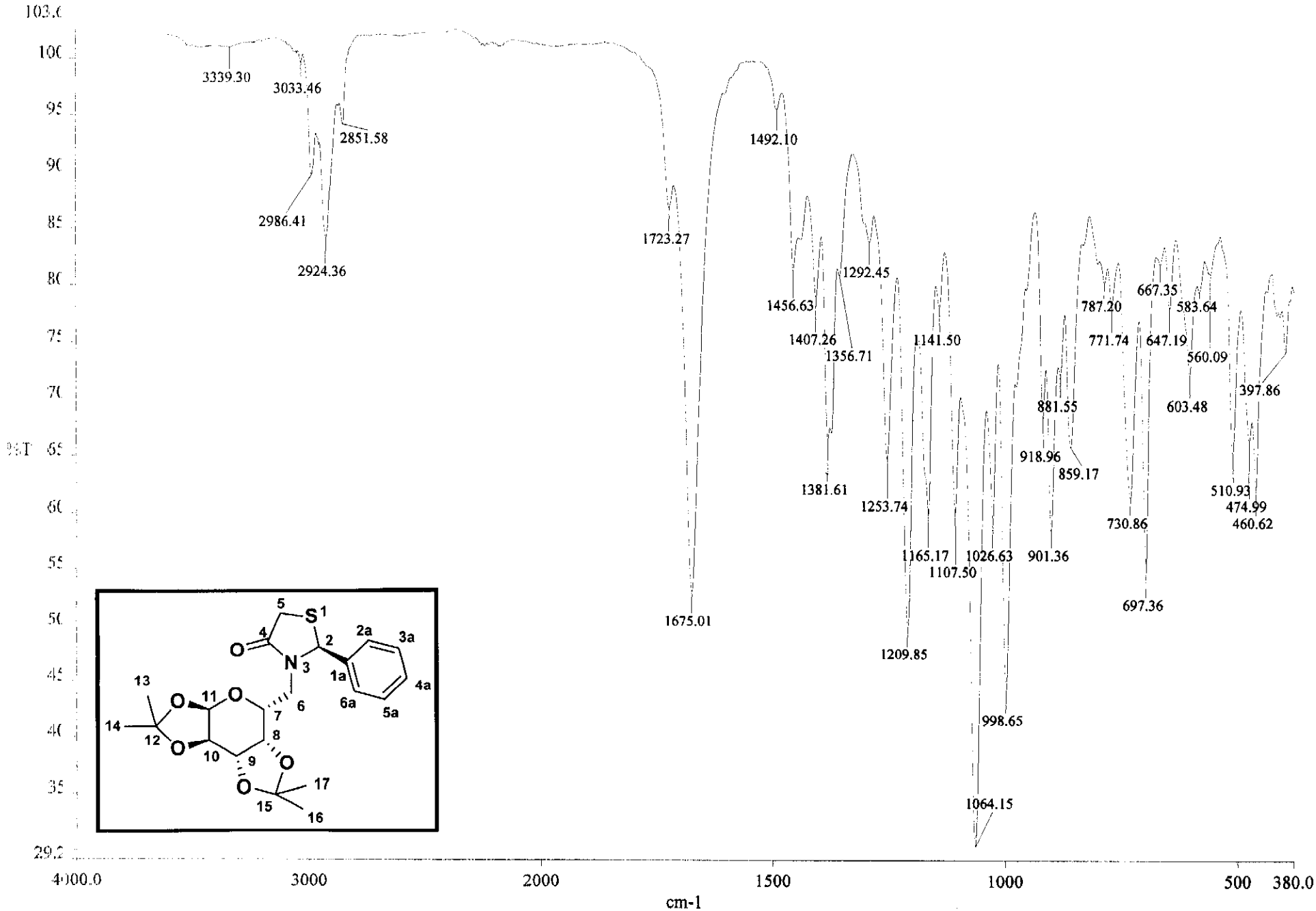


Expanded ^{13}C Spectrum of Compound 5i: 2-Phenyl-3-(2,2,7,7-tetramethyl-tetrahydro-bis[1,3]dioxolo[4,5-b;4',5'-d]pyran-5-ylmethyl)-thiazolidin-4-one

Date: 2014/06/06 Time: 07:48:42 AM



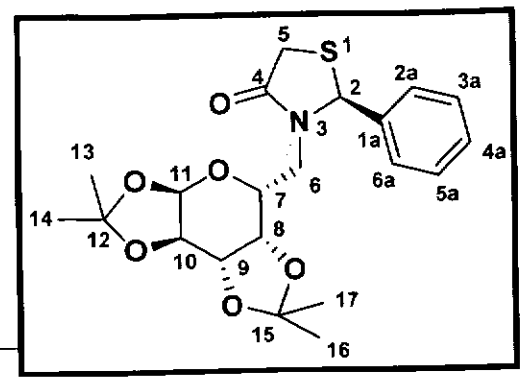
Ultraviolet Spectrum of Compound 5i: 2-Phenyl-3-(2,2,7,7-tetramethyl-tetrahydro-bis[1,3] dioxolo [4,5-b;4',5'-d]pyran-5-ylmethyl)-thiazolidin-4-one



Infrared Spectrum of Compound 5i: 2-Phenyl-3-(2,2,7,7-tetramethyl-tetrahydro-bis[1,3] dioxolo [4,5-b;4',5'-d]pyran-5-ylmethyl)-thiazolidin-4-one

==== Shimadzu LCsolution Analysis Report ====

Acquired by	: Admin
Sample Name	: benz us formic buffer
Sample ID	: benz us formic buffer
Vail #	: 4
Injection Volume	: 100 uL
Data File Name	: benz us formic buffer.lcd
Method File Name	: Pramod 09jun 2014.lcm
Batch File Name	: suger thiozolidinon.lcb
Report File Name	: Default.lcr
Data Acquired	: 2014/06/17 02:34:25 PM
Data Processed	: 2014/06/17 03:14:28 PM



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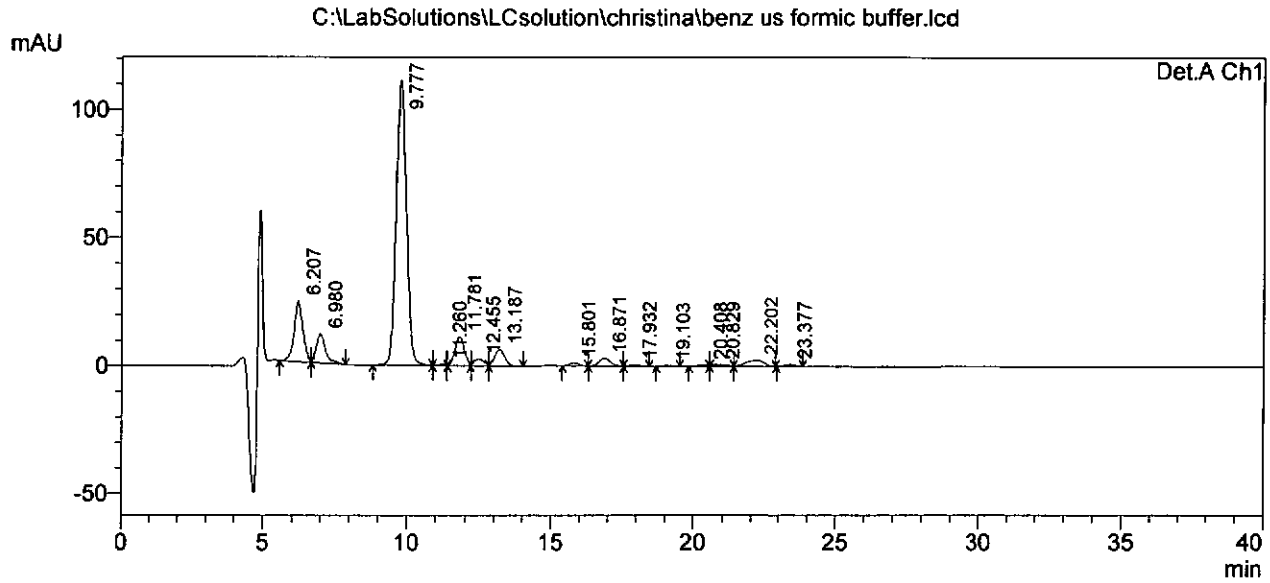


1Det.A Ch1/220nm

<Results>

PeakTable C:\LabSolutions\LCsolution\christina\benz us formic buffer.lcd

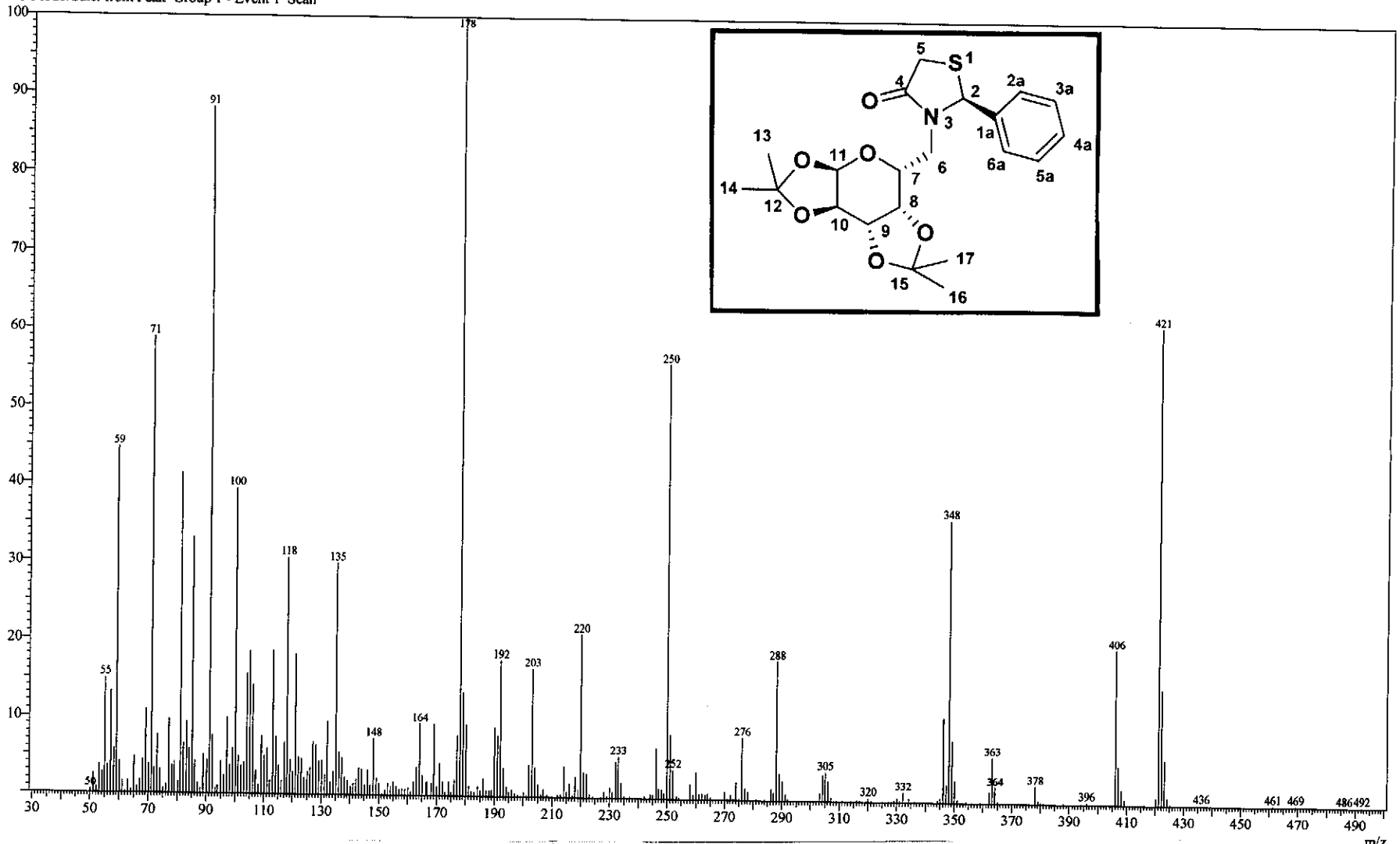
Detector A Ch1 220nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	6.207	519294	23865	12.045	13.470
2	6.980	260863	11484	6.051	6.482
3	9.777	2741954	111395	63.601	62.873
4	11.260	10682	576	0.248	0.325
5	11.781	256410	11337	5.948	6.399
6	12.455	68066	2657	1.579	1.500
7	13.187	157712	6450	3.658	3.640
8	15.801	26718	1180	0.620	0.666
9	16.871	83968	3047	1.948	1.720
10	17.932	13862	593	0.322	0.335
11	19.103	6828	272	0.158	0.154
12	20.408	13118	532	0.304	0.301
13	20.829	23004	672	0.534	0.379
14	22.202	109339	2410	2.536	1.360
15	23.377	19394	705	0.450	0.398
Total		4311212	177174	100.000	100.000

HPLC of Compound 5i: 2-Phenyl-3-(2,2,7,7-tetramethyl-tetrahydro-bis[1,3]dioxolo [4,5-b; 4',5'-d]pyran-5-ylmethyl)-thiazolidin-4-one

Spectrum

Line#:1 R.Time:16.065(Scan#:2414)
MassPeaks:489
RawMode:Averaged 16.060-16.070(2413-2415) BasePeak:178(55360)
BG Mode:Calc. from Peak Group 1 - Event 1 Scan

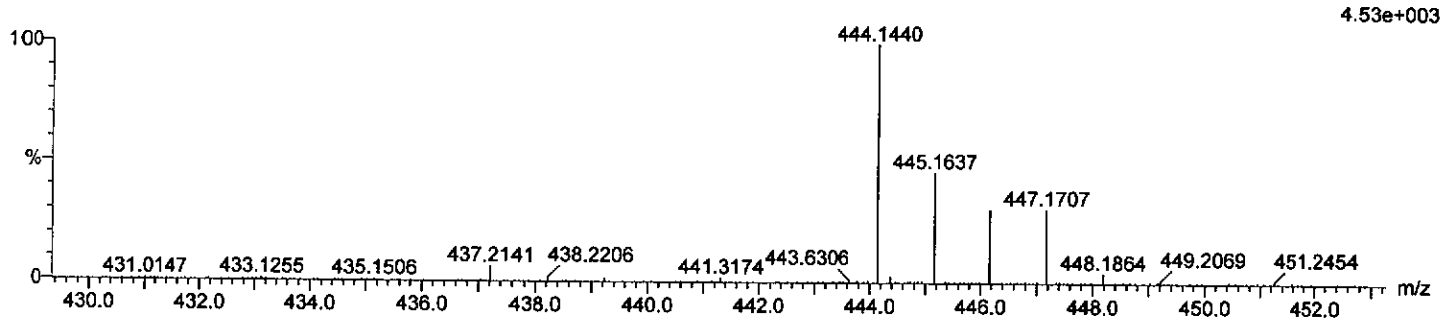


GC-MS of Compound 5i: 2-Phenyl-3-(2,2,7,7-tetramethyl-tetrahydro-bis[1,3]dioxolo [4,5-b; 4',5'-d]pyran-5-ylmethyl)-thiazolidin-4-one

Elemental Composition Report

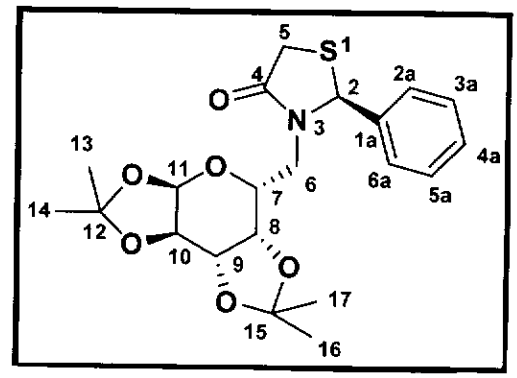
Single Mass Analysis
Tolerance = 5.0 PPM / DBE: min = -1.5, max = 100.0
Element prediction: Off
Number of isotope peaks used for i-FIT = 3

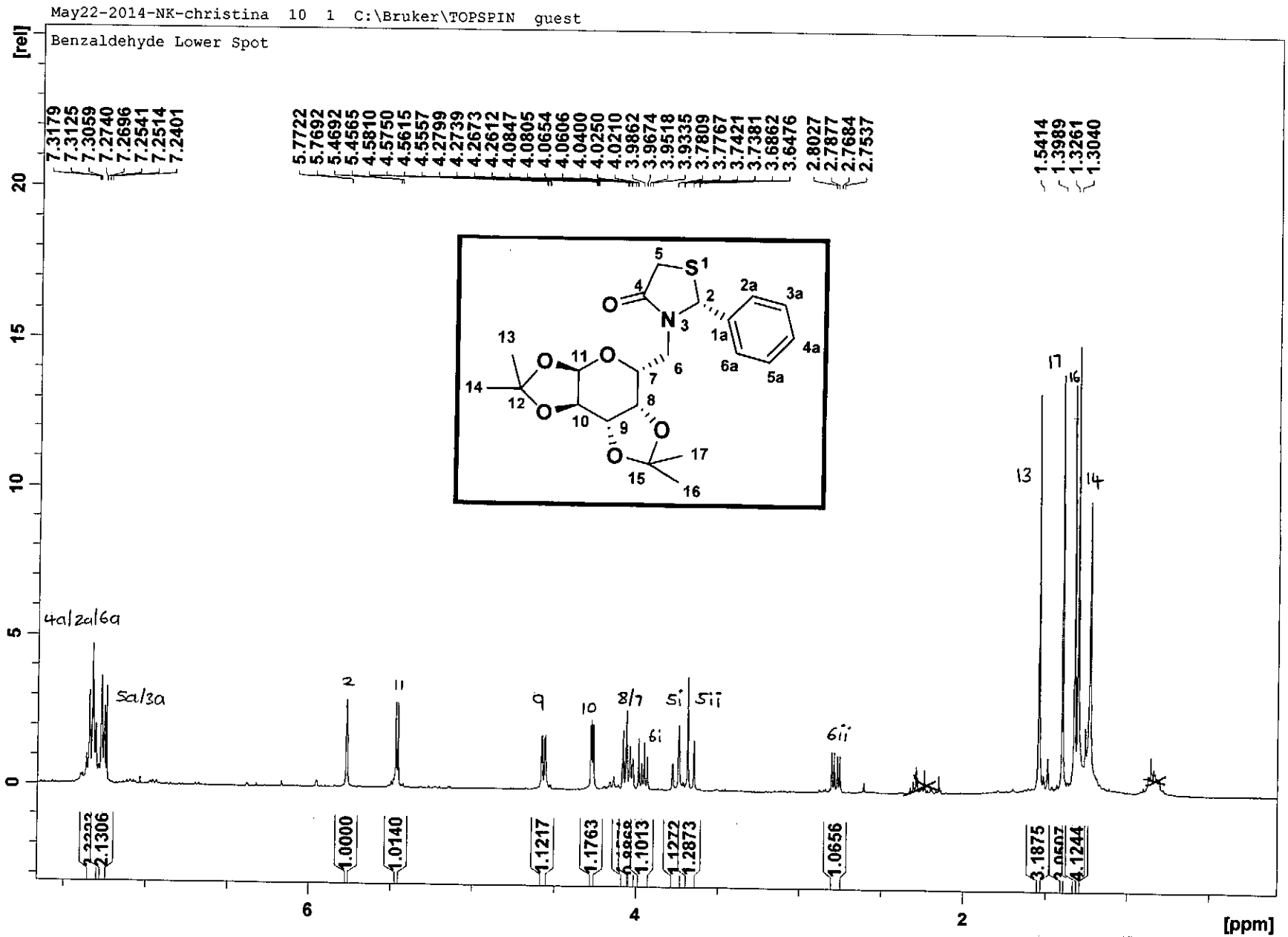
Monoisotopic Mass, Even Electron Ions
41 formula(e) evaluated with 1 results within limits (up to 20 best isotopic matches for each mass)
Elements Used:
C: 20-25 H: 25-30 N: 0-5 O: 5-10 Na: 0-1 S: 1-1
5 52 (1.720)
TOF MS ES+



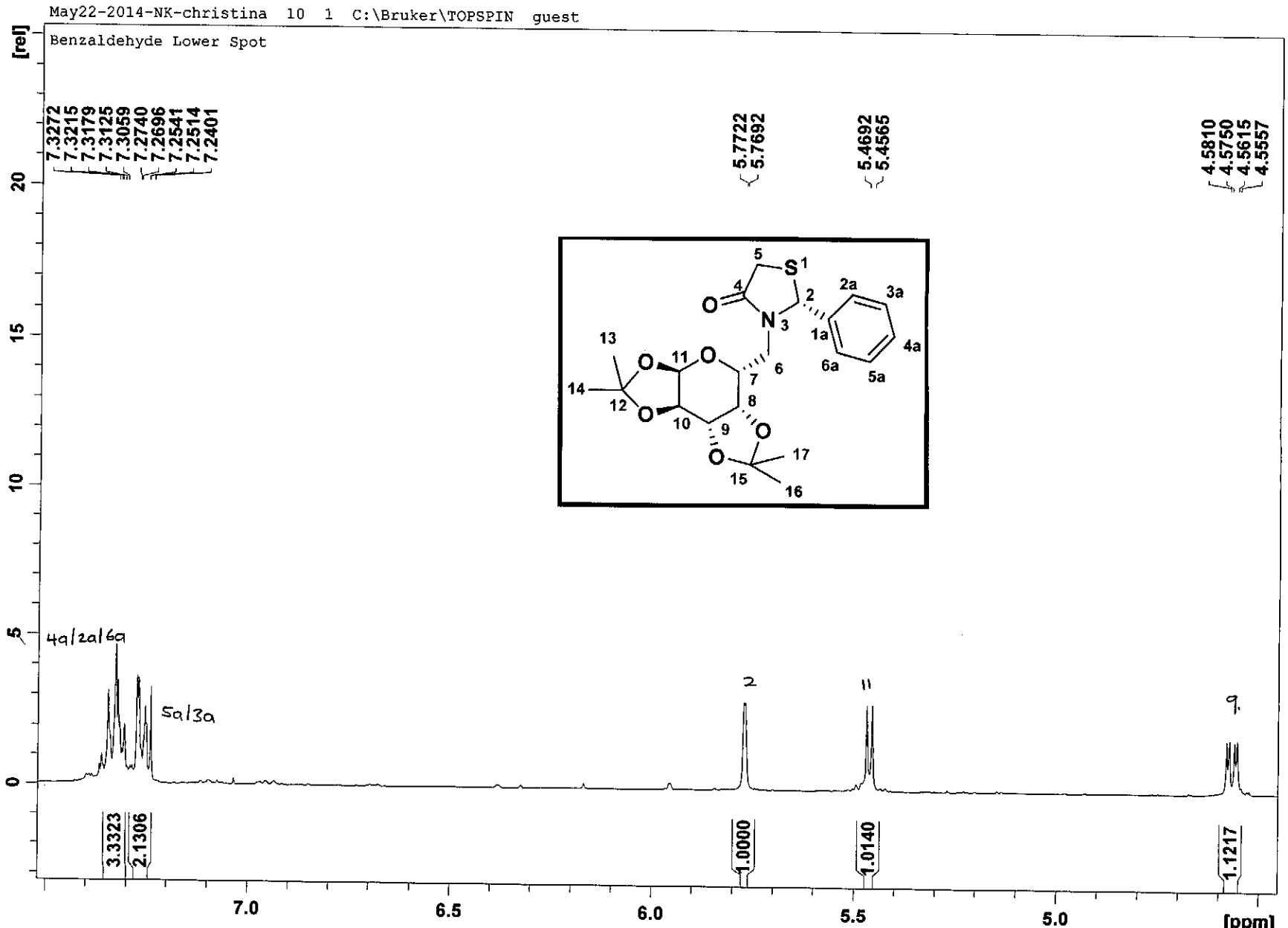
Minimum:				-1.5			
Maximum:		5.0	5.0	100.0			
Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	i-FIT (Norm)	Formula
444.1440	444.1457	-1.7	-3.8	8.5	136.5	0.0	C21 H27 N O6 Na S

HRMS of Compound 5i: 2-Phenyl-3-(2,2,7,7-tetramethyl-tetrahydro-bis[1,3]dioxolo [4,5-b; 4',5'-d]pyran-5-ylmethyl)-thiazolidin-4-one

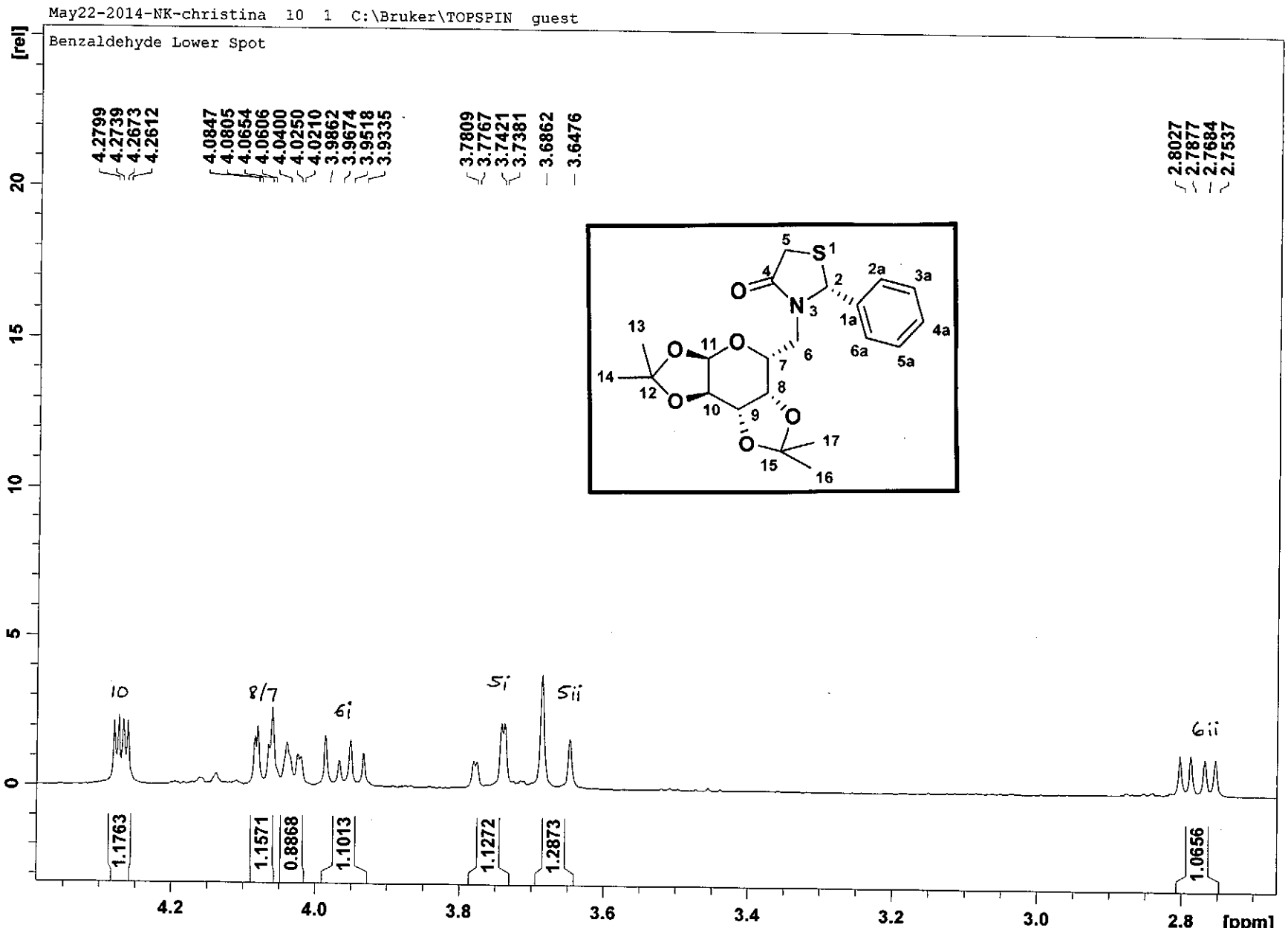




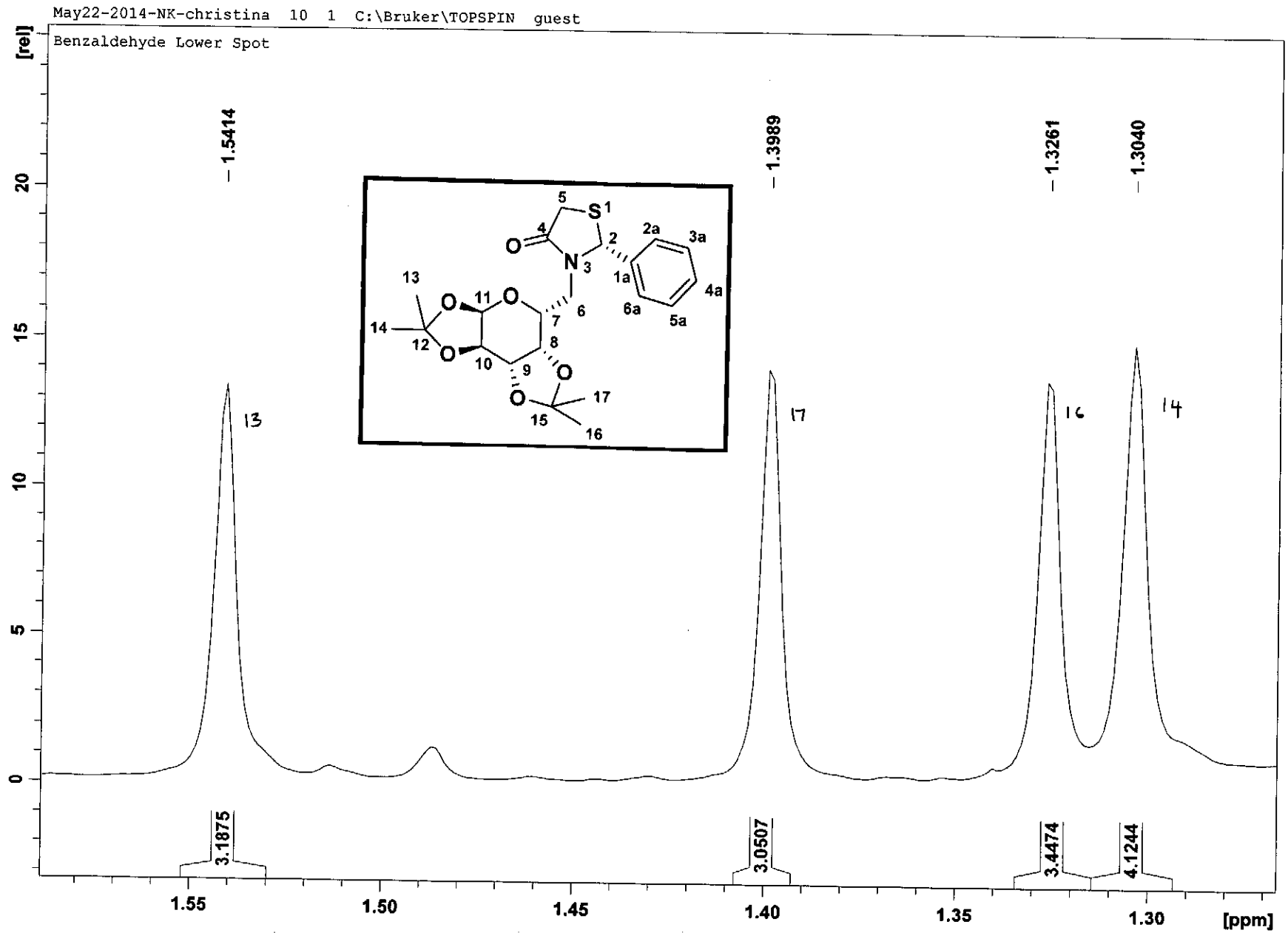
[1]H Spectrum of compound 6i: 2-Phenyl-3-(2,2,7,7-tetramethyltetrahydro-*bis*[1,3] dioxolo[4,5b;4',5'd]pyran-5-ylmethyl)-thiazolidin-4-one



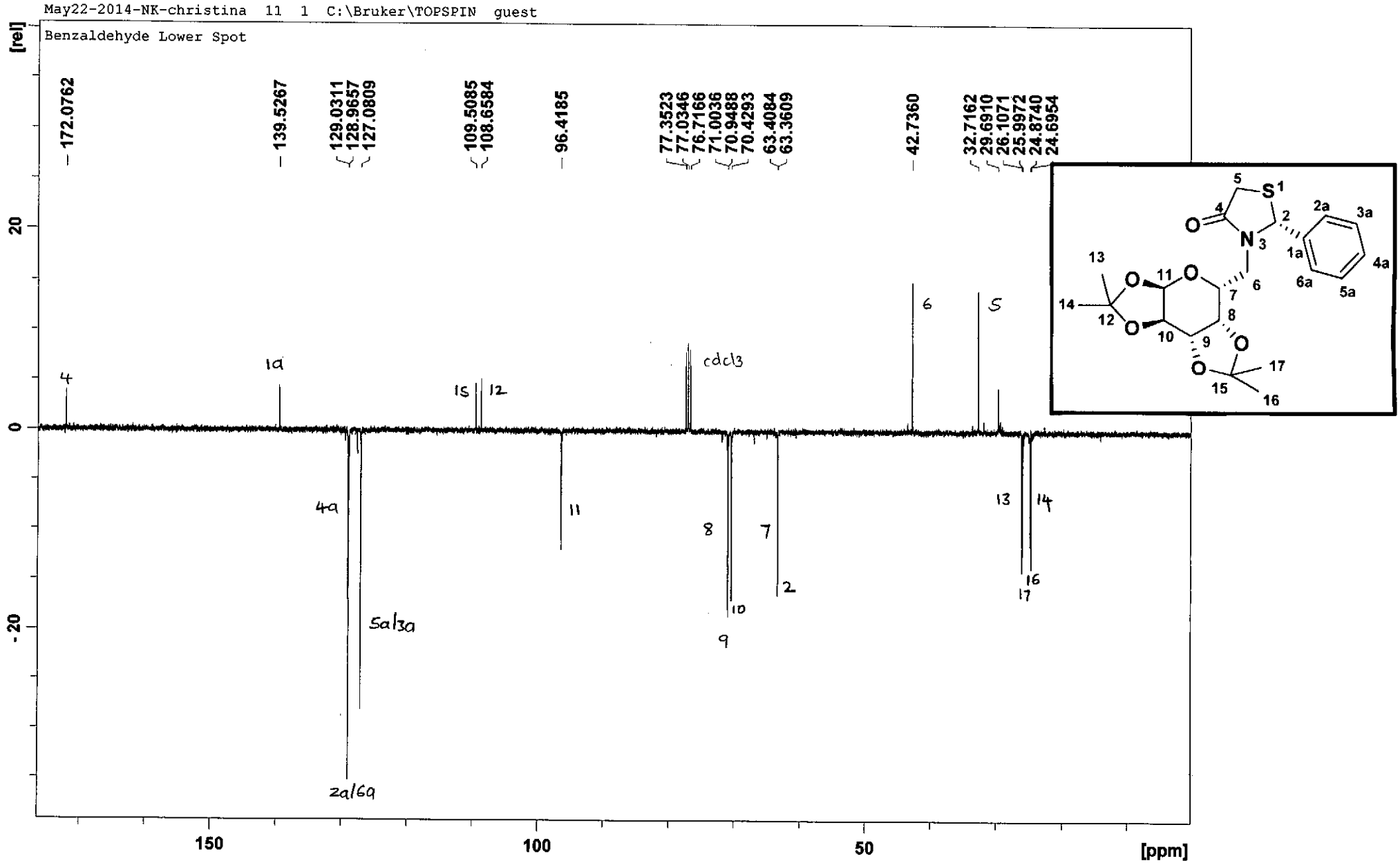
Expanded ^{1}H Spectrum of compound 6i: 2-Phenyl-3-(2,2,7,7-tetramethyltetrahydro-*bis*[1,3] dioxolo[4,5b;4',5'd]pyran-5-ylmethyl)-thiazolidin-4-one



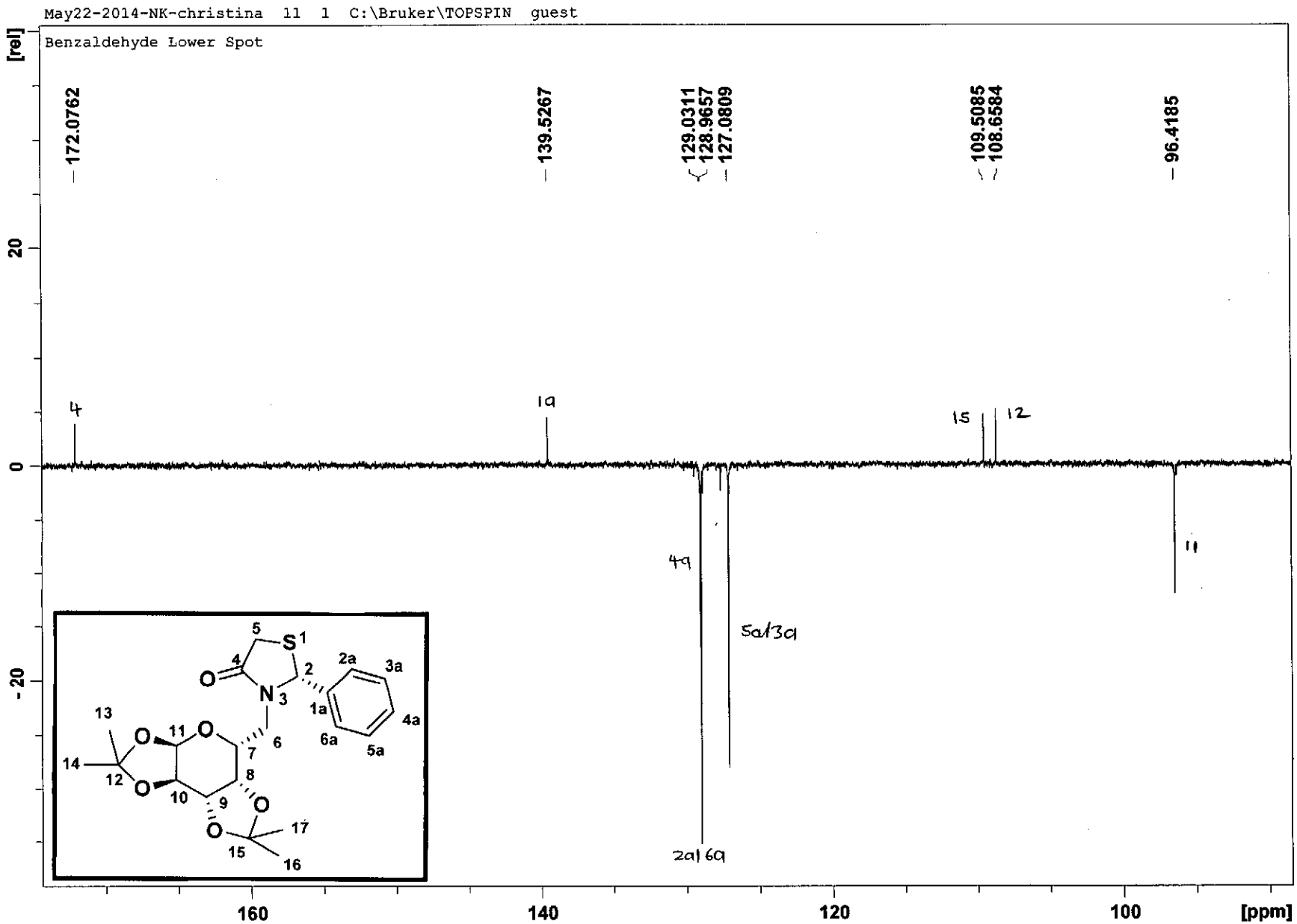
Expanded ^{1}H Spectrum of compound 6i: 2-Phenyl-3-(2,2,7,7-tetramethyltetrahydro-*bis*[1,3] dioxolo[4,5b;4',5'd]pyran-5-ylmethyl)-thiazolidin-4-one



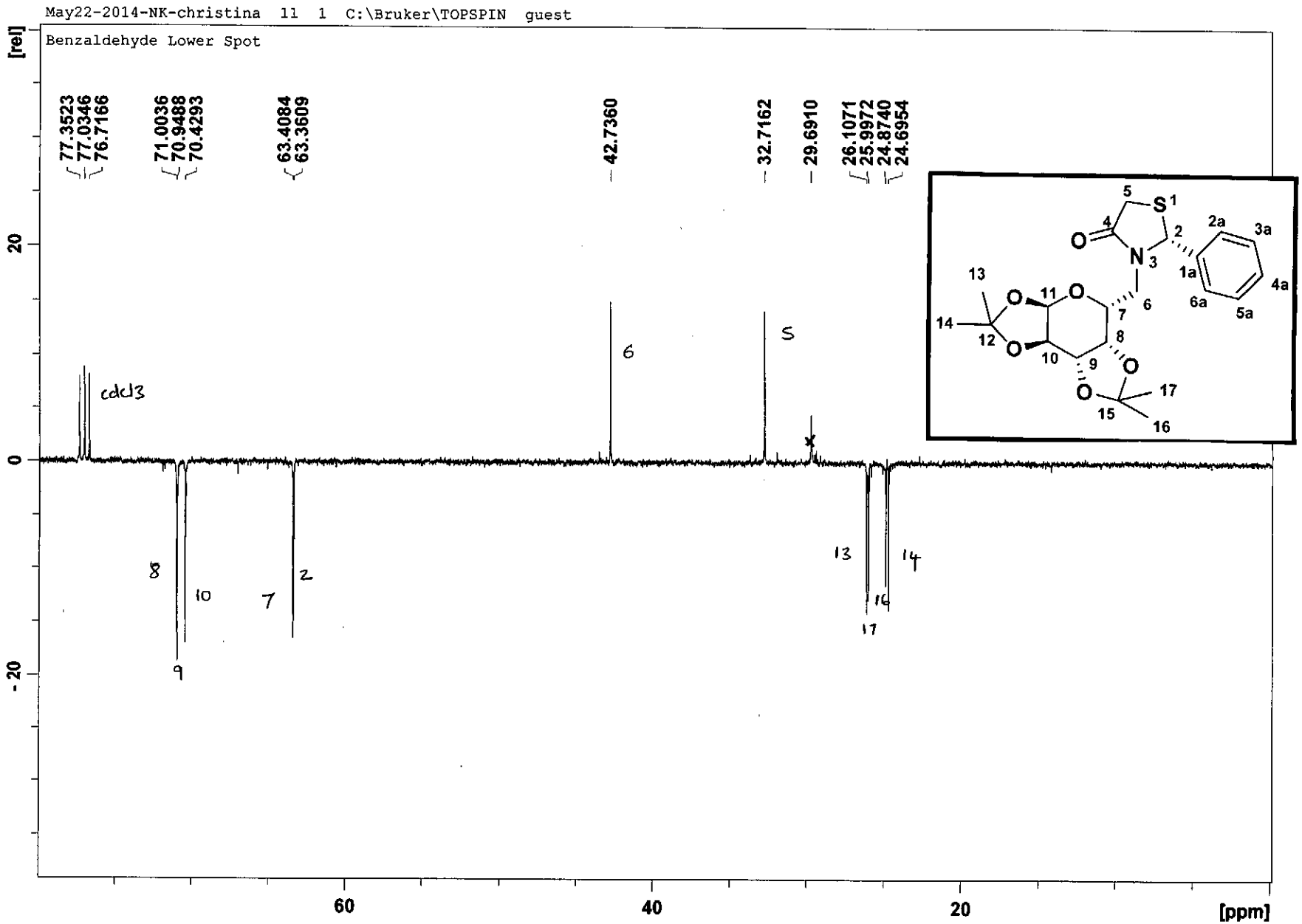
Expanded ^{1}H Spectrum of compound 6i: 2-Phenyl-3-(2,2,7,7-tetramethyltetrahydro-*bis*[1,3] dioxolo[4,5b;4',5'd]pyran-5-ylmethyl)-thiazolidin-4-one



^{13}C Spectrum of Compound 6i: 2-Phenyl-3-(2,2,7,7-tetramethyl-tetrahydro-bis [1,3]dioxolo [4,5-b;4',5'-d]pyran-5-ylmethyl)-thiazolidin-4-one

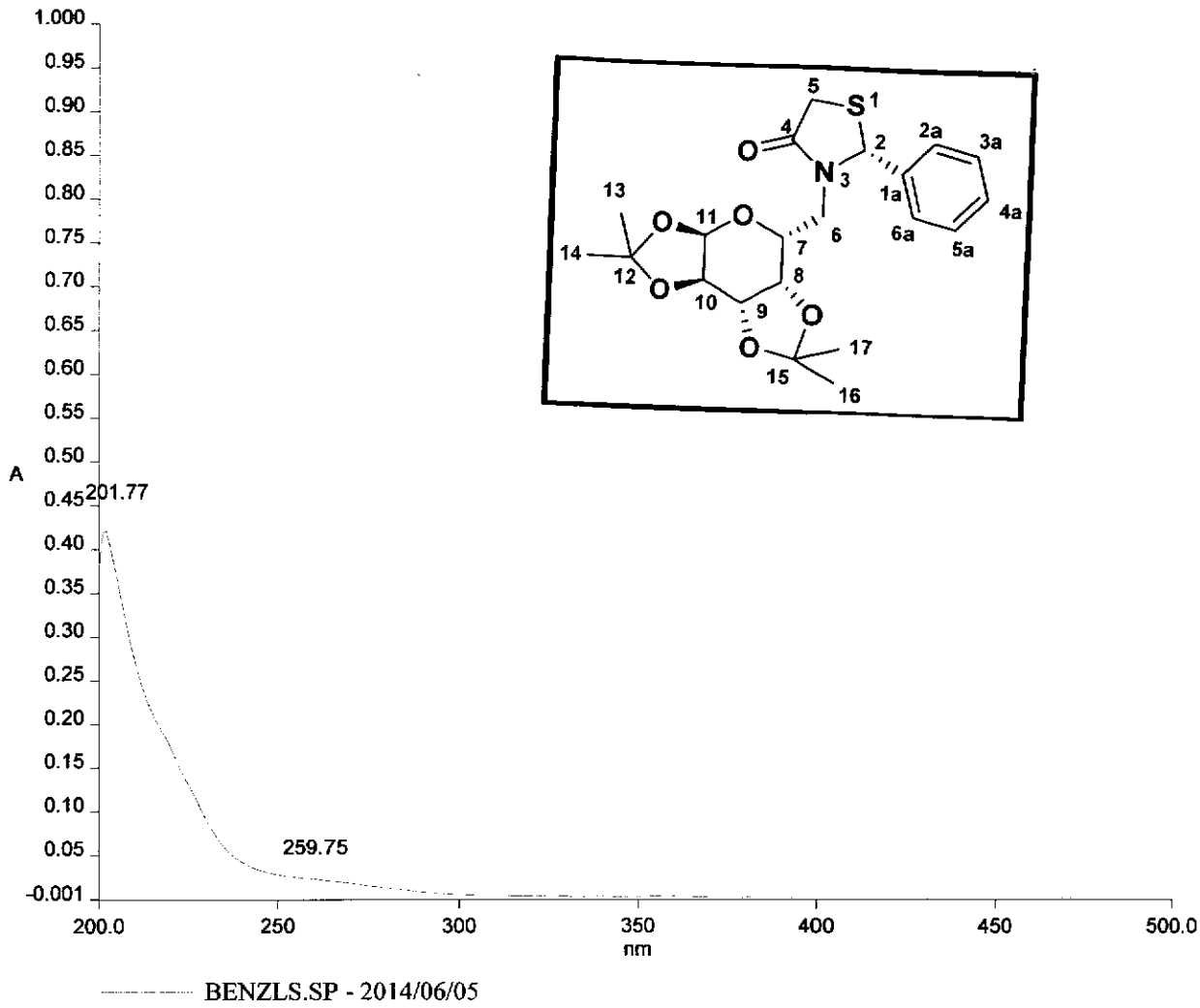


Expanded ^{13}C Spectrum of Compound 6i: 2-Phenyl-3-(2,2,7,7-tetramethyl-tetrahydro-bis [1,3]dioxolo[4,5-b;4',5'-d]pyran-5-ylmethyl)-thiazolidin-4-one

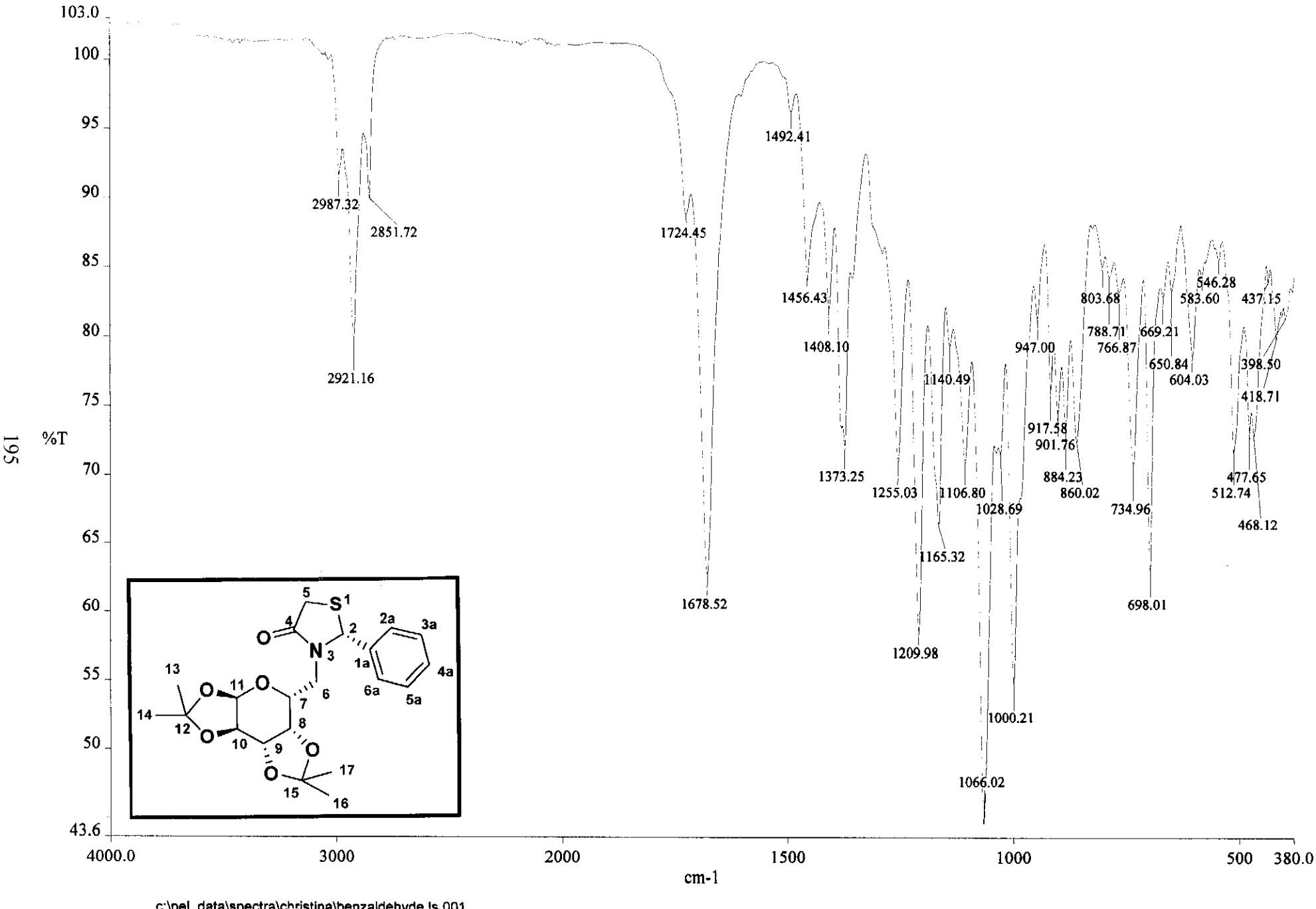


Expanded ^{13}C Spectrum of Compound 6i: 2-Phenyl-3-(2,2,7,7-tetramethyl-tetrahydro-bis [1,3]dioxolo[4,5-b;4',5'-d]pyran-5-ylmethyl)-thiazolidin-4-one

Date: 2014/06/06 Time: 07:50:18 AM



Ultraviolet Spectrum of Compound 6i: 2-Phenyl-3-(2,2,7,7-tetramethyl-tetrahydro-bis [1,3] dioxolo [4,5-b;4',5'-d]pyran-5-ylmethyl)-thiazolidin-4-one



Infrared Spectrum of Compound 6i: 2-Phenyl-3-(2,2,7,7-tetramethyl-tetrahydro-bis [1,3] dioxolo [4,5-b;4',5'-d]pyran-5-ylmethyl)-thiazolidin-4-one

==== Shimadzu LCsolution Analysis Report ====

Acquired by	: Admin
Sample Name	: benz ls with formic buffer
Sample ID	: benz ls with formic buffe
Vail #	: 3
Injection Volume	: 100 uL
Data File Name	: benz ls with formic buffe.lcd
Method File Name	: Pramod 09jun 2014.lcm
Batch File Name	: 20_03_2014.lcb
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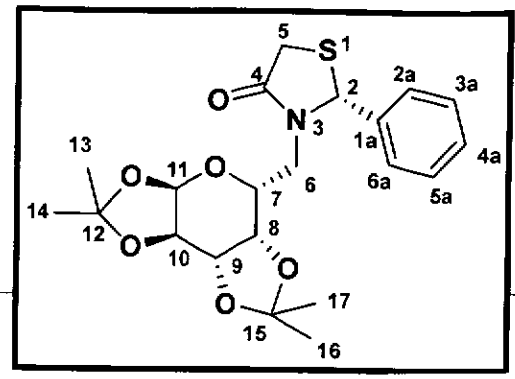

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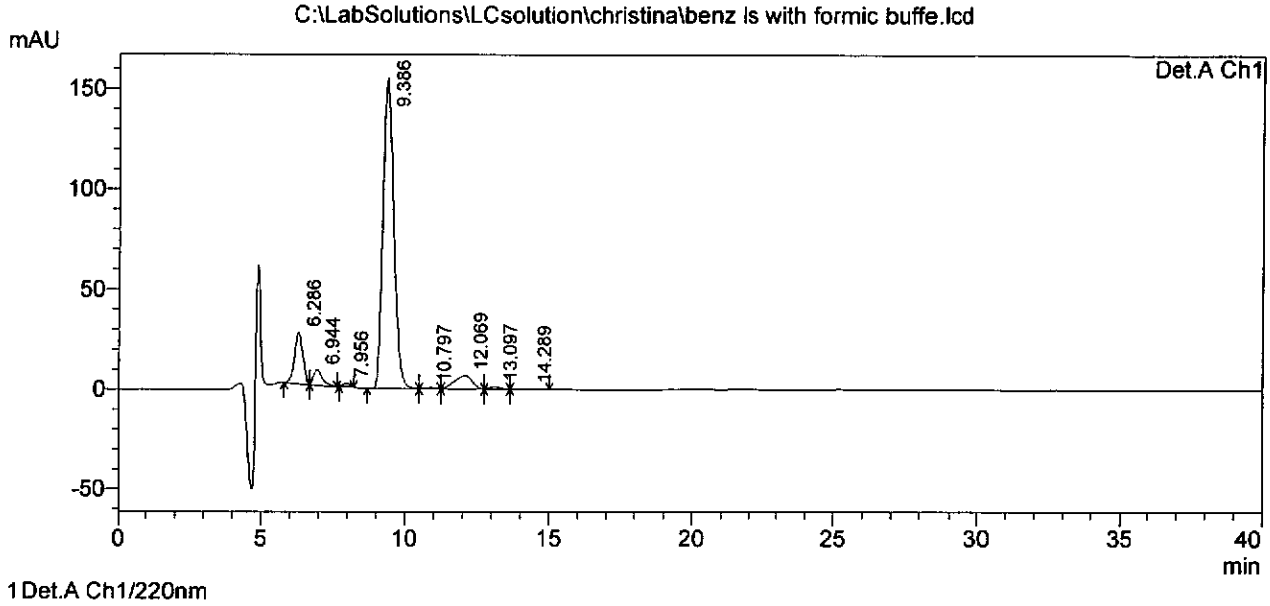


1Det.A Ch1/220nm

<Results>

PeakTable C:\LabSolutions\LCsolution\christina\benz ls with formic buffe.lcd

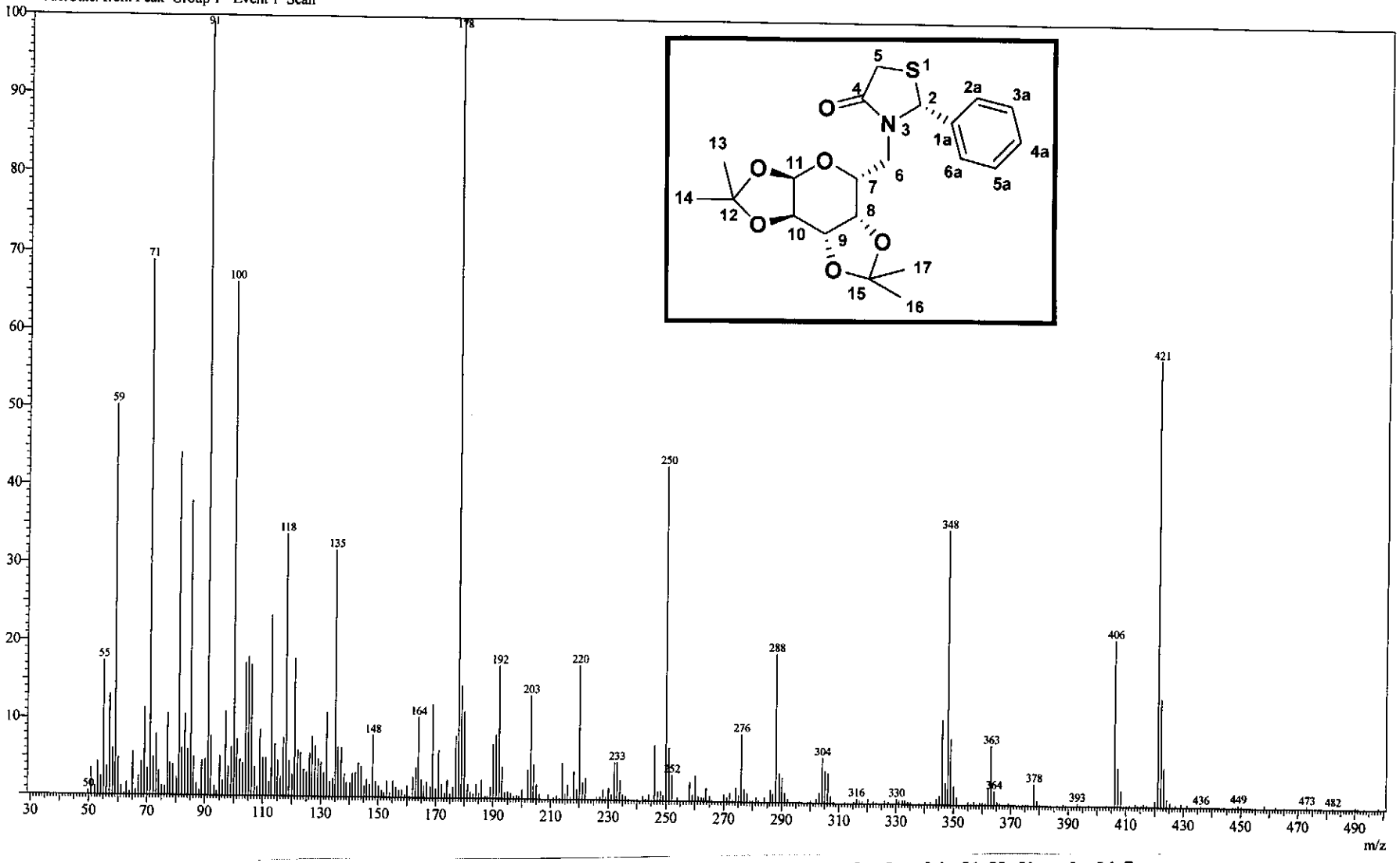
Detector A Ch1 220nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	6.286	544601	26052	10.700	13.024
2	6.944	180514	7862	3.547	3.930
3	7.956	32235	1796	0.633	0.898
4	9.386	3980404	155141	78.205	77.558
5	10.797	18053	681	0.355	0.340
6	12.069	289308	6823	5.684	3.411
7	13.097	30422	1256	0.598	0.628
8	14.289	14171	422	0.278	0.211
Total		5089708	200033	100.000	100.000

HPLC of Compound 6i: 2-Phenyl-3-(2,2,7,7-tetramethyl-tetrahydro-bis [1,3] dioxolo [4,5-b; 4',5'-d]pyran-5-ylmethyl)-thiazolidin-4-one

Spectrum

Line#:1 R.Time:16.570(Scan#:2515)
MassPeaks:537
RawMode:Averaged 16.565-16.575(2514-2516) BasePeak:178(28739)
BG Mode:Calc. from Peak Group 1 - Event 1 Scan



GC-MS of Compound 6i: 2-Phenyl-3-(2,2,7,7-tetramethyl-tetrahydro-bis [1,3] dioxolo [4,5-b;4',5'-d]pyran-5-ylmethyl)-thiazolidin-4-one

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Synthesis, Characterization & Antibacterial Evaluation of Novel Substituted Galactose Thiazolidin-4-ones

Appendix B: Crystal structure data

2014

Christina Kannigadu

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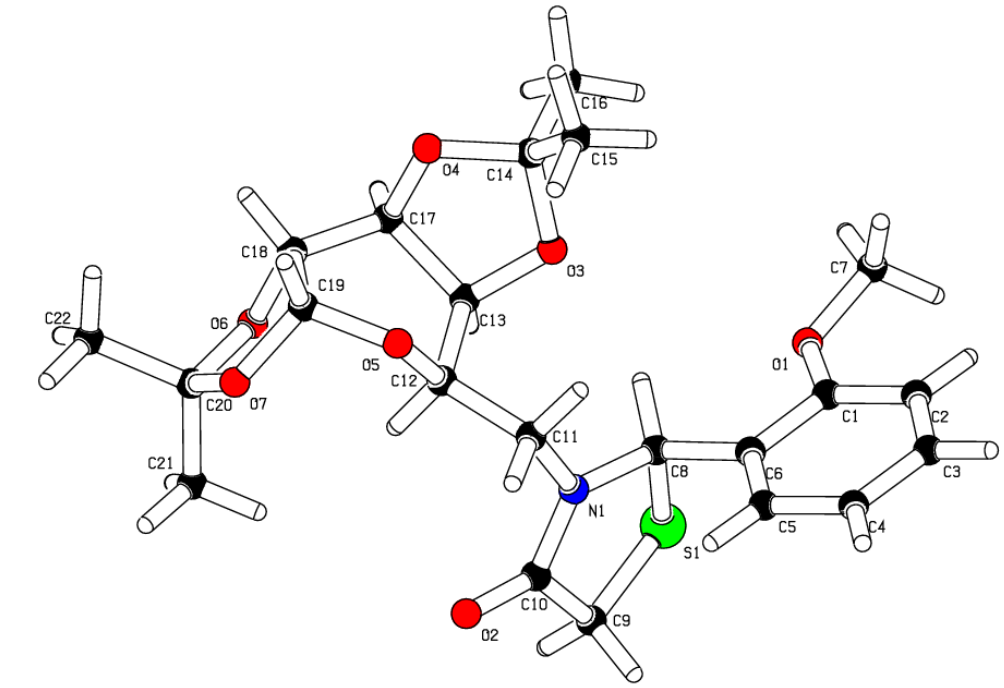

Figure 1. OLEX structure of the 2-methoxy *2R* thiazolidinone diastereomer

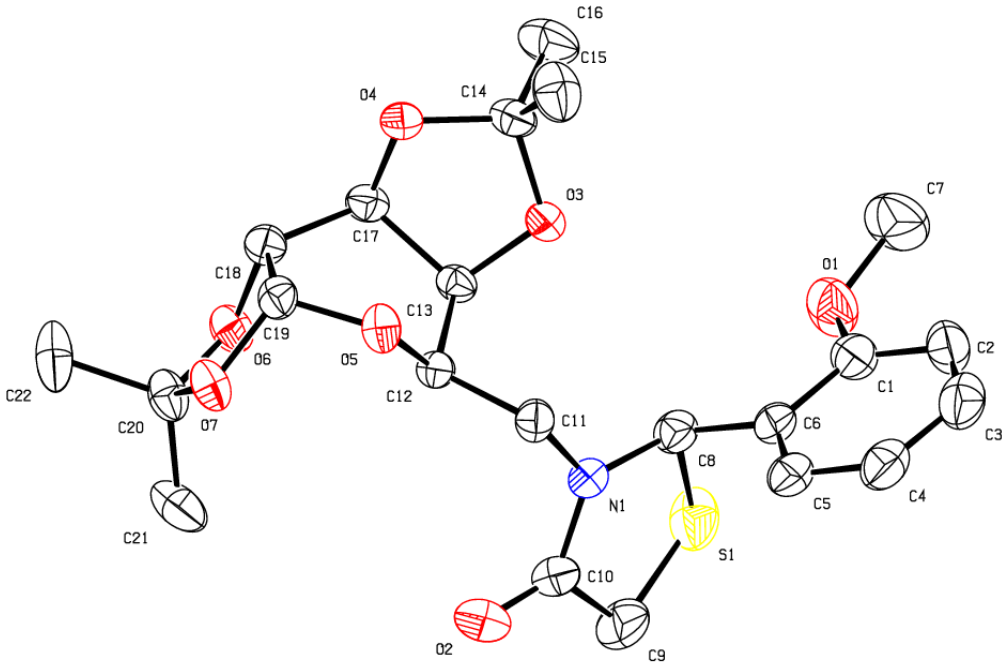

Figure 2. ORTEP structure of the 2-methoxy *2R* thiazolidinone diastereomer

Table 1. Crystal data and structure refinement for 2-methoxy *2R* thiazolidinone diastereomer

IDENTIFICATION CODE	shelx	
EMPIRICAL FORMULA	$C_{22}H_{29}NO_7S$	
FORMULA WEIGHT	451.52	
TEMPERATURE	173(2) K	
WAVELENGTH	0.71073 Å	
CRYSTAL SYSTEM	Orthorhombic	
SPACE GROUP	P 21 21 21	
UNIT CELL DIMENSIONS	a = 7.3677(6) Å	α = 90°
	b = 11.5857(9) Å	β = 90°
	c = 26.259(2) Å	γ = 90°
VOLUME	2241.4(3) $Å^3$	
Z	4	
DENSITY (CALCULATED)	1.338 $mg.m^{-3}$	
ABSORPTION COEFFICIENT	0.187 mm^{-1}	
F(000)	960	
CRYSTAL SIZE	0.505 x 0.337 x 0.252 mm^3	
THETA RANGE FOR DATA COLLECTION	1.921 to 28.373°.	
INDEX RANGES	-9<=h<=9, -15<=k<=15, -28<=l<=34	
REFLECTIONS COLLECTED	33353	
INDEPENDENT REFLECTIONS	5264 [R(int) = 0.0607]	
COMPLETENESS TO THETA = 25.242°	98.2 %	
ABSORPTION CORRECTION	Semi-empirical from equivalents	
MAX. AND MIN. TRANSMISSION	0.954 and 0.910	
REFINEMENT METHOD	Full-matrix least-squares on F^2	
DATA / RESTRAINTS / PARAMETERS	5264 / 0 / 285	
GOODNESS-OF-FIT ON F^2	1.317	
FINAL R INDICES [I>2SIGMA(I)]	R1 = 0.0597, wR2 = 0.1473	
R INDICES (ALL DATA)	R1 = 0.0775, wR2 = 0.1521	
ABSOLUTE STRUCTURE PARAMETER	0.09(7)	
EXTINCTION COEFFICIENT	n/a	
LARGEST DIFF. PEAK AND HOLE	0.350 and -0.415 $e.Å^{-3}$	

Table 2. Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters ($Å^2$x 10^3) for 2-methoxy *2R* thiazolidinone diastereomer. U(eq) is defined as one third of the trace of the orthogonalized U^{ij} tensor

	X	Y	Z	U(EQ)
C(1)	3480(7)	-1475(4)	4339(2)	40(1)
C(2)	2258(8)	-2385(5)	4305(2)	47(1)
C(3)	1838(7)	-2840(5)	3838(3)	49(1)
C(4)	2606(7)	-2415(4)	3400(2)	44(1)
C(5)	3851(7)	-1503(4)	3436(2)	39(1)
C(6)	4317(6)	-1044(4)	3900(2)	33(1)
C(7)	2936(10)	-1162(7)	5226(2)	68(2)
C(8)	5668(7)	-72(4)	3964(2)	34(1)
C(9)	8907(8)	-459(5)	3579(3)	57(2)
C(10)	7755(7)	381(4)	3280(2)	41(1)
C(11)	4783(6)	1286(4)	3251(2)	29(1)
C(12)	5153(6)	2535(4)	3388(2)	24(1)
C(13)	4852(6)	2799(4)	3948(2)	26(1)
C(14)	1897(6)	3017(4)	4260(2)	33(1)
C(15)	185(7)	2653(5)	3998(2)	48(1)
C(16)	1689(8)	3092(6)	4833(2)	50(1)
C(17)	4404(6)	4072(4)	4039(2)	29(1)
C(18)	4994(6)	4843(4)	3605(2)	30(1)
C(19)	4413(6)	4401(4)	3085(2)	29(1)
C(20)	7410(6)	5066(4)	3069(2)	35(1)
C(21)	9113(7)	4439(6)	2933(2)	51(2)
C(22)	7556(8)	6376(5)	2996(2)	52(2)
N(1)	6102(5)	527(3)	3495(2)	32(1)
O(1)	4000(6)	-962(4)	4785(2)	54(1)
O(2)	8237(6)	860(4)	2890(2)	55(1)
O(3)	3312(5)	2212(3)	4147(1)	36(1)
O(4)	2475(4)	4097(3)	4056(1)	34(1)
O(5)	3972(4)	3217(3)	3076(1)	29(1)
O(6)	6935(4)	4805(3)	3582(1)	33(1)
O(7)	5922(4)	4634(3)	2772(1)	35(1)
S(1)	7880(2)	-612(1)	4194(1)	53(1)

Table 3. Bond lengths [Å] and angles [°] for 2-methoxy *2R* thiazolidinone diastereomer

C(1)-O(1)	1.368(7)
C(1)-C(2)	1.389(8)
C(1)-C(6)	1.400(7)
C(2)-C(3)	1.371(8)
C(2)-H(2)	0.9500
C(3)-C(4)	1.374(8)
C(3)-H(3)	0.9500
C(4)-C(5)	1.402(7)
C(4)-H(4)	0.9500
C(5)-C(6)	1.373(7)
C(5)-H(5)	0.9500
C(6)-C(8)	1.513(7)
C(7)-O(1)	1.417(7)
C(7)-H(7A)	0.9800
C(7)-H(7B)	0.9800
C(7)-H(7C)	0.9800
C(8)-N(1)	1.450(6)
C(8)-S(1)	1.847(5)
C(8)-H(8)	1.0000
C(9)-C(10)	1.511(8)
C(9)-S(1)	1.792(7)
C(9)-H(9A)	0.9900
C(9)-H(9B)	0.9900
C(10)-O(2)	1.216(6)
C(10)-N(1)	1.353(6)
C(11)-N(1)	1.460(6)
C(11)-C(12)	1.515(6)
C(11)-H(11A)	0.9900
C(11)-H(11B)	0.9900
C(12)-O(5)	1.433(5)
C(12)-C(13)	1.518(6)
C(12)-H(12)	1.0000
C(13)-O(3)	1.423(5)

C(13)-C(17)	1.530(6)
C(13)-H(13)	1.0000
C(14)-O(4)	1.427(6)
C(14)-O(3)	1.430(5)
C(14)-C(15)	1.497(7)
C(14)-C(16)	1.515(7)
C(15)-H(15A)	0.9800
C(15)-H(15B)	0.9800
C(15)-H(15C)	0.9800
C(16)-H(16A)	0.9800
C(16)-H(16B)	0.9800
C(16)-H(16C)	0.9800
C(17)-O(4)	1.422(5)
C(17)-C(18)	1.510(6)
C(17)-H(17)	1.0000
C(18)-O(6)	1.433(5)
C(18)-C(19)	1.520(6)
C(18)-H(18)	1.0000
C(19)-O(7)	1.409(5)
C(19)-O(5)	1.410(5)
C(19)-H(19)	1.0000
C(20)-O(6)	1.423(6)
C(20)-O(7)	1.437(6)
C(20)-C(21)	1.493(7)
C(20)-C(22)	1.534(7)
C(21)-H(21A)	0.9800
C(21)-H(21B)	0.9800
C(21)-H(21C)	0.9800
C(22)-H(22A)	0.9800
C(22)-H(22B)	0.9800
C(22)-H(22C)	0.9800

O(1)-C(1)-C(2)	124.5(5)
O(1)-C(1)-C(6)	115.2(5)
C(2)-C(1)-C(6)	120.3(5)
C(3)-C(2)-C(1)	119.7(5)
C(3)-C(2)-H(2)	120.1
C(1)-C(2)-H(2)	120.1
C(2)-C(3)-C(4)	121.2(5)
C(2)-C(3)-H(3)	119.4
C(4)-C(3)-H(3)	119.4
C(3)-C(4)-C(5)	118.9(5)
C(3)-C(4)-H(4)	120.5
C(5)-C(4)-H(4)	120.5
C(6)-C(5)-C(4)	121.0(5)
C(6)-C(5)-H(5)	119.5
C(4)-C(5)-H(5)	119.5
C(5)-C(6)-C(1)	118.8(5)
C(5)-C(6)-C(8)	123.5(4)
C(1)-C(6)-C(8)	117.6(5)
O(1)-C(7)-H(7A)	109.5
O(1)-C(7)-H(7B)	109.5
H(7A)-C(7)-H(7B)	109.5
O(1)-C(7)-H(7C)	109.5
H(7A)-C(7)-H(7C)	109.5
H(7B)-C(7)-H(7C)	109.5
N(1)-C(8)-C(6)	114.0(4)
N(1)-C(8)-S(1)	104.2(3)
C(6)-C(8)-S(1)	111.4(3)
N(1)-C(8)-H(8)	109.0
C(6)-C(8)-H(8)	109.0
S(1)-C(8)-H(8)	109.0
C(10)-C(9)-S(1)	107.2(4)
C(10)-C(9)-H(9A)	110.3
S(1)-C(9)-H(9A)	110.3
C(10)-C(9)-H(9B)	110.3

S(1)-C(9)-H(9B)	110.3
H(9A)-C(9)-H(9B)	108.5
O(2)-C(10)-N(1)	123.9(5)
O(2)-C(10)-C(9)	124.5(5)
N(1)-C(10)-C(9)	111.6(5)
N(1)-C(11)-C(12)	110.5(4)
N(1)-C(11)-H(11A)	109.5
C(12)-C(11)-H(11A)	109.5
N(1)-C(11)-H(11B)	109.5
C(12)-C(11)-H(11B)	109.5
H(11A)-C(11)-H(11B)	108.1
O(5)-C(12)-C(11)	106.3(3)
O(5)-C(12)-C(13)	110.7(3)
C(11)-C(12)-C(13)	113.4(3)
O(5)-C(12)-H(12)	108.8
C(11)-C(12)-H(12)	108.8
C(13)-C(12)-H(12)	108.8
O(3)-C(13)-C(12)	112.1(4)
O(3)-C(13)-C(17)	103.4(3)
C(12)-C(13)-C(17)	112.1(3)
O(3)-C(13)-H(13)	109.7
C(12)-C(13)-H(13)	109.7
C(17)-C(13)-H(13)	109.7
O(4)-C(14)-O(3)	106.0(3)
O(4)-C(14)-C(15)	109.0(4)
O(3)-C(14)-C(15)	109.6(4)
O(4)-C(14)-C(16)	110.7(4)
O(3)-C(14)-C(16)	108.4(4)
C(15)-C(14)-C(16)	112.8(4)
C(14)-C(15)-H(15A)	109.5
C(14)-C(15)-H(15B)	109.5
H(15A)-C(15)-H(15B)	109.5
C(14)-C(15)-H(15C)	109.5
H(15A)-C(15)-H(15C)	109.5
H(15B)-C(15)-H(15C)	109.5

C(14)-C(16)-H(16A)	109.5
C(14)-C(16)-H(16B)	109.5
H(16A)-C(16)-H(16B)	109.5
C(14)-C(16)-H(16C)	109.5
H(16A)-C(16)-H(16C)	109.5
H(16B)-C(16)-H(16C)	109.5
O(4)-C(17)-C(18)	107.4(4)
O(4)-C(17)-C(13)	103.9(3)
C(18)-C(17)-C(13)	113.0(3)
O(4)-C(17)-H(17)	110.8
C(18)-C(17)-H(17)	110.8
C(13)-C(17)-H(17)	110.8
O(6)-C(18)-C(17)	107.5(4)
O(6)-C(18)-C(19)	103.5(4)
C(17)-C(18)-C(19)	113.4(4)
O(6)-C(18)-H(18)	110.7
C(17)-C(18)-H(18)	110.7
C(19)-C(18)-H(18)	110.7
O(7)-C(19)-O(5)	111.0(4)
O(7)-C(19)-C(18)	103.8(3)
O(5)-C(19)-C(18)	114.1(4)
O(7)-C(19)-H(19)	109.3
O(5)-C(19)-H(19)	109.3
C(18)-C(19)-H(19)	109.3
O(6)-C(20)-O(7)	104.7(3)
O(6)-C(20)-C(21)	109.3(4)
O(7)-C(20)-C(21)	109.9(4)
O(6)-C(20)-C(22)	110.2(5)
O(7)-C(20)-C(22)	109.3(4)
C(21)-C(20)-C(22)	113.1(5)
C(20)-C(21)-H(21A)	109.5
C(20)-C(21)-H(21B)	109.5
H(21A)-C(21)-H(21B)	109.5
C(20)-C(21)-H(21C)	109.5
H(21A)-C(21)-H(21C)	109.5

H(21B)-C(21)-H(21C)	109.5
C(20)-C(22)-H(22A)	109.5
C(20)-C(22)-H(22B)	109.5
H(22A)-C(22)-H(22B)	109.5
C(20)-C(22)-H(22C)	109.5
H(22A)-C(22)-H(22C)	109.5
H(22B)-C(22)-H(22C)	109.5
C(10)-N(1)-C(8)	119.6(4)
C(10)-N(1)-C(11)	119.4(4)
C(8)-N(1)-C(11)	121.0(4)
C(1)-O(1)-C(7)	118.2(5)
C(13)-O(3)-C(14)	110.3(3)
C(17)-O(4)-C(14)	107.0(3)
C(19)-O(5)-C(12)	112.8(3)
C(20)-O(6)-C(18)	106.2(3)
C(19)-O(7)-C(20)	110.5(3)
C(9)-S(1)-C(8)	92.6(3)
C(10)-N(1)-C(11)	119.4(4)
C(8)-N(1)-C(11)	121.0(4)
C(1)-O(1)-C(7)	118.2(5)
C(13)-O(3)-C(14)	110.3(3)
C(17)-O(4)-C(14)	107.0(3)
C(19)-O(5)-C(12)	112.8(3)
C(20)-O(6)-C(18)	106.2(3)
C(19)-O(7)-C(20)	110.5(3)
C(9)-S(1)-C(8)	92.6(3)
C(1)-O(1)-C(7)	118.2(5)
C(13)-O(3)-C(14)	110.3(3)
C(17)-O(4)-C(14)	107.0(3)
C(19)-O(5)-C(12)	112.8(3)
C(20)-O(6)-C(18)	106.2(3)
C(19)-O(7)-C(20)	110.5(3)
C(9)-S(1)-C(8)	92.6(3)

Table 4. Anisotropic displacement parameters ($Å^2 x\ 10^3$) for 2-methoxy *2R* thiazolidinone diastereomer. The anisotropic displacement factor exponent takes the form: $-2\pi^2[\ h^2a^{*2}U^{11} + ... + 2\ h\ k\ a^*\ b^*\ U^{12}\ ]$

	U^{11}	U^{22}	U^{33}	U^{23}	U^{13}	U^{12}
C(1)	38(3)	39(3)	44(3)	11(2)	5(2)	9(2)
C(2)	41(3)	40(3)	59(4)	15(3)	7(2)	-1(2)
C(3)	34(3)	36(3)	78(4)	9(3)	-4(3)	0(2)
C(4)	40(3)	33(2)	60(3)	-3(2)	-5(2)	5(2)
C(5)	40(3)	32(2)	44(3)	4(2)	4(2)	10(2)
C(6)	30(2)	27(2)	42(3)	4(2)	3(2)	7(2)
C(7)	79(5)	80(5)	45(3)	13(3)	16(3)	11(4)
C(8)	36(2)	30(2)	35(3)	2(2)	0(2)	6(2)
C(9)	44(3)	39(3)	88(5)	7(3)	8(3)	15(3)
C(10)	41(3)	34(2)	49(3)	-7(2)	12(2)	4(2)
C(11)	33(2)	26(2)	28(2)	1(2)	0(2)	-2(2)
C(12)	24(2)	26(2)	22(2)	2(2)	0(2)	2(2)
C(13)	24(2)	30(2)	22(2)	3(2)	2(2)	2(2)
C(14)	29(2)	41(2)	28(2)	4(2)	6(2)	5(2)
C(15)	39(3)	49(3)	54(3)	13(3)	-8(2)	-6(2)
C(16)	49(3)	68(4)	32(3)	1(3)	11(2)	6(3)
C(17)	27(2)	32(2)	26(2)	-4(2)	3(2)	0(2)
C(18)	25(2)	30(2)	35(2)	0(2)	1(2)	1(2)
C(19)	27(2)	28(2)	32(2)	8(2)	-2(2)	3(2)
C(20)	29(2)	39(2)	37(3)	13(2)	-4(2)	-5(2)
C(21)	33(2)	73(4)	49(3)	23(3)	11(2)	5(3)
C(22)	51(3)	39(3)	67(4)	22(3)	-14(3)	-18(2)
N(1)	35(2)	25(2)	37(2)	0(2)	7(2)	3(2)
O(1)	69(3)	55(2)	37(2)	7(2)	8(2)	-7(2)
O(2)	56(2)	55(2)	56(3)	-2(2)	26(2)	6(2)
O(3)	37(2)	30(2)	42(2)	7(1)	15(2)	4(1)
O(4)	28(2)	30(2)	44(2)	3(1)	9(1)	5(1)
O(5)	30(2)	30(2)	27(2)	6(1)	-8(1)	-4(1)
O(6)	26(2)	40(2)	32(2)	6(1)	-3(1)	-4(1)
O(7)	35(2)	39(2)	30(2)	9(1)	0(1)	-9(2)
S(1)	41(1)	45(1)	73(1)	18(1)	-11(1)	2(1)

Table 5. Hydrogen coordinates (x 10^4) and isotropic displacement parameters ($Å^2$x 10^3) for 2-methoxy *2R* thiazolidinone diastereomer

	X	Y	Z	U(EQ)
H(2)	1715	-2690	4605	56
H(3)	1000	-3462	3817	59
H(4)	2299	-2733	3078	53
H(5)	4380	-1198	3135	46
H(7A)	1667	-970	5153	102
H(7B)	3380	-677	5505	102
H(7C)	3027	-1976	5323	102
H(8)	5178	497	4216	41
H(9A)	10161	-161	3613	69
H(9B)	8954	-1214	3403	69
H(11A)	3544	1073	3361	35
H(11B)	4852	1190	2876	35
H(12)	6439	2722	3299	29
H(13)	5958	2582	4147	31
H(15A)	418	2558	3633	71
H(15B)	-750	3244	4048	71
H(15C)	-234	1919	4142	71
H(16A)	1480	2318	4972	74
H(16B)	656	3590	4917	74
H(16C)	2798	3416	4982	74
H(17)	4932	4344	4368	34
H(18)	4560	5652	3660	36
H(19)	3348	4859	2963	35
H(21A)	10070	4637	3177	77
H(21B)	9494	4662	2589	77
H(21C)	8891	3605	2943	77
H(22A)	6393	6738	3082	78
H(22B)	7862	6545	2641	78
H(22C)	8507	6682	3220	78

Table 6. Torsion angles [°] for 2-methoxy *2R* thiazolidinone diastereomer

O(1)-C(1)-C(2)-C(3)	-179.7(5)
C(6)-C(1)-C(2)-C(3)	-1.6(8)
C(1)-C(2)-C(3)-C(4)	0.1(8)
C(2)-C(3)-C(4)-C(5)	0.4(8)
C(3)-C(4)-C(5)-C(6)	0.6(7)
C(4)-C(5)-C(6)-C(1)	-2.1(7)
C(4)-C(5)-C(6)-C(8)	179.2(4)
O(1)-C(1)-C(6)-C(5)	-179.1(4)
C(2)-C(1)-C(6)-C(5)	2.7(7)
O(1)-C(1)-C(6)-C(8)	-0.4(6)
C(2)-C(1)-C(6)-C(8)	-178.6(4)
C(5)-C(6)-C(8)-N(1)	14.3(6)
C(1)-C(6)-C(8)-N(1)	-164.4(4)
C(5)-C(6)-C(8)-S(1)	-103.2(5)
C(1)-C(6)-C(8)-S(1)	78.1(5)
S(1)-C(9)-C(10)-O(2)	164.6(5)
S(1)-C(9)-C(10)-N(1)	-16.2(6)
N(1)-C(11)-C(12)-O(5)	171.9(3)
N(1)-C(11)-C(12)-C(13)	-66.2(5)
O(5)-C(12)-C(13)-O(3)	80.5(4)
C(11)-C(12)-C(13)-O(3)	-38.9(5)
O(5)-C(12)-C(13)-C(17)	-35.3(5)
C(11)-C(12)-C(13)-C(17)	-154.7(4)
O(3)-C(13)-C(17)-O(4)	-25.2(4)
C(12)-C(13)-C(17)-O(4)	95.8(4)
O(3)-C(13)-C(17)-C(18)	-141.3(4)
C(12)-C(13)-C(17)-C(18)	-20.3(5)
O(4)-C(17)-C(18)-O(6)	-179.1(3)
C(13)-C(17)-C(18)-O(6)	-65.1(5)
O(4)-C(17)-C(18)-C(19)	-65.4(4)
C(13)-C(17)-C(18)-C(19)	48.6(5)
O(6)-C(18)-C(19)-O(7)	-24.1(4)
C(17)-C(18)-C(19)-O(7)	-140.3(4)

O(6)-C(18)-C(19)-O(5)	96.8(4)
C(17)-C(18)-C(19)-O(5)	-19.4(5)
O(2)-C(10)-N(1)-C(8)	-179.1(5)
C(9)-C(10)-N(1)-C(8)	1.7(7)
O(2)-C(10)-N(1)-C(11)	0.8(8)
C(9)-C(10)-N(1)-C(11)	-178.4(4)
C(6)-C(8)-N(1)-C(10)	-108.5(5)
S(1)-C(8)-N(1)-C(10)	13.1(5)
C(6)-C(8)-N(1)-C(11)	71.6(5)
S(1)-C(8)-N(1)-C(11)	-166.8(3)
C(12)-C(11)-N(1)-C(10)	-81.8(5)
C(12)-C(11)-N(1)-C(8)	98.1(5)
C(2)-C(1)-O(1)-C(7)	-15.9(8)
C(6)-C(1)-O(1)-C(7)	166.0(5)
C(12)-C(13)-O(3)-C(14)	-110.8(4)
C(17)-C(13)-O(3)-C(14)	10.2(4)
O(4)-C(14)-O(3)-C(13)	8.6(5)
C(15)-C(14)-O(3)-C(13)	126.2(4)
C(16)-C(14)-O(3)-C(13)	-110.3(4)
C(18)-C(17)-O(4)-C(14)	151.3(4)
C(13)-C(17)-O(4)-C(14)	31.3(4)
O(3)-C(14)-O(4)-C(17)	-25.5(4)
C(15)-C(14)-O(4)-C(17)	-143.4(4)
C(16)-C(14)-O(4)-C(17)	91.9(4)
O(7)-C(19)-O(5)-C(12)	78.0(4)
C(18)-C(19)-O(5)-C(12)	-38.8(5)
C(11)-C(12)-O(5)-C(19)	-167.9(4)
C(13)-C(12)-O(5)-C(19)	68.5(4)
O(7)-C(20)-O(6)-C(18)	-30.7(5)
C(21)-C(20)-O(6)-C(18)	-148.4(4)
C(22)-C(20)-O(6)-C(18)	86.7(5)
C(17)-C(18)-O(6)-C(20)	154.2(4)
C(19)-C(18)-O(6)-C(20)	34.0(4)
O(5)-C(19)-O(7)-C(20)	-117.1(4)
C(18)-C(19)-O(7)-C(20)	5.8(5)

O(6)-C(20)-O(7)-C(19)	14.8(5)
C(21)-C(20)-O(7)-C(19)	132.1(4)
C(22)-C(20)-O(7)-C(19)	-103.2(5)
C(10)-C(9)-S(1)-C(8)	20.1(4)
N(1)-C(8)-S(1)-C(9)	-18.7(4)
C(6)-C(8)-S(1)-C(9)	104.6(4)