2009

Green Chemistry Using Bismuth Compounds: Bismuth(III) Triflate Catalyzed Allylation of Cyclic Acetals

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Research Honors Senior Thesis

Illinois Wesleyan University

Spring 2009

Approval Page

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By

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A PAPER SUBMITTED AS PART OF THE REQUIREMENT FOR RESEARCH HONORS IN CHEMISTRY

Approved:

April 23, 2009

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Illinois Wesleyan University, April 20, 2009

Acknowledgements

I would first like to thank my research advisor and friend, Dr. Ram Mohan, for all his support and encouragement over the past years. He has instilled a passion for chemistry in me through his teaching and for that, I am very much indebted to him. His guidance and support has been instrumental in shaping me as a scientist. I am also very grateful for the countless hours he has spent on my behalf, without which this dissertation would not have been possible.

I would also like to thank Dr. Brian Brennan, Dr. Rebecca Roesner, and Dr. Nathan Frank for serving on my thesis committee.

A special thanks is in order for the all members of the research group over the past years: Aaron Bailey and Erin Anderson for their especial patience while training me as a Sophomore; Scott Krabbe for his synthesis of dioxanes and his wonderful country music collection; Dr. Eeshwar Begari for his early work on the allylation of dioxanes; Jay Christensen, Matthew Huddle, and Josh Lacey for their work on the allylation of dioxolanes; Pash DeVore, JP Carolan, Kendall Tasche, Jason Bothwell, Dan Podgorski, Maggie Olsen, Long Le, Jamie Rogers, Herbie Yung, Justin Ernat, Ashvin Baru, Ann Palma, Veronica Angeles, Paul Sierszulski, and Phil Lazzara for making time in lab over the past years such a great time.

I also need to acknowledge Cindy Honegger for all of her help in the stockroom over the past two years. None of this work would have been possible if not for her assistance.

The Twelve Principles of Green Chemistry

1. **Prevention:** It is better to prevent waste than to treat or clean up waste after it has been created.

2. **Atom Economy:** Synthetic methods should be designed to maximize the incorporation of all materials used in the process into the final product.

3. **Less Hazardous Chemical Syntheses:** Wherever practicable, synthetic methods should be designed to use and generate substances that possess little or no toxicity to human health and the environment.

4. **Designing Safer Chemicals:** Chemical products should be designed to effect their desired function while minimizing their toxicity.

5. **Safer Solvents and Auxiliaries:** The use of auxiliary substances (e.g., solvents, separation agents, etc.) should be made unnecessary wherever possible and innocuous when used.

6. **Design for Energy Efficiency:** Energy requirements of chemical processes should be recognized for their environmental and economic impacts and should be minimized. If possible, synthetic methods should be conducted at ambient temperature and pressure.

7. **Use of Renewable Feedstocks:** A raw material or feedstock should be renewable rather than depleting whenever technically and economically practicable.

8. **Reduce Derivatives:** Unnecessary derivatization (use of blocking groups, protection/deprotection, temporary modification of physical/chemical processes) should be minimized or avoided if possible, because such steps require additional reagents and can generate waste.

9. **Catalysis:** Catalytic reagents (as selective as possible) are superior to stoichiometric reagents.

10. **Design for Degradation:** Chemical products should be designed so that at the end of their function they break down into innocuous degradation products and do not persist in the environment.

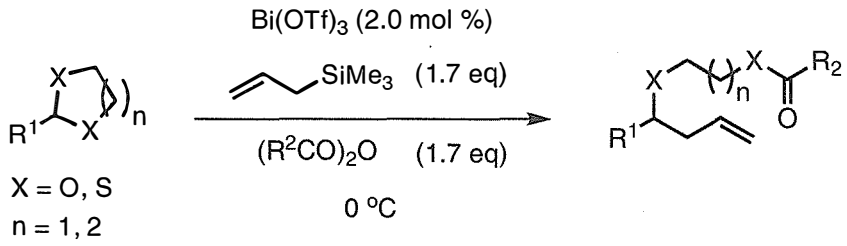
11. **Real-time analysis for Pollution Prevention:** Analytical methodologies need to be further developed to allow for real-time, in-process monitoring and control

prior to the formation of hazardous substances.

12. **Inherently Safer Chemistry for Accident Prevention:** Substances and the form of a substance used in a chemical process should be chosen to minimize the potential for chemical accidents, including releases, explosions, and fires.

Anastas, P. T.; Warner, J. C. *Green Chemistry, Theory and Practice*. Oxford University Press, New York, **1998**, 30.

Abstract



Cyclic acetals (dioxolanes, dioxanes, and dithianes) are common protecting groups in organic synthesis but they can also be converted to other useful functional groups. A bismuth(III) triflate-catalyzed multicomponent reaction involving the allylation of cyclic acetals followed by *in situ* derivatization with acid anhydrides to generate highly functionalized esters and thioesters has been developed under solvent-free conditions. Most reagents used to date for the allylation of cyclic acetals are highly corrosive or toxic and are often required in stoichiometric amounts. In contrast, the use of a relatively non-toxic and non-corrosive bismuth(III) based catalyst makes this methodology benign and attractive.

Table of Contents

I. Introduction

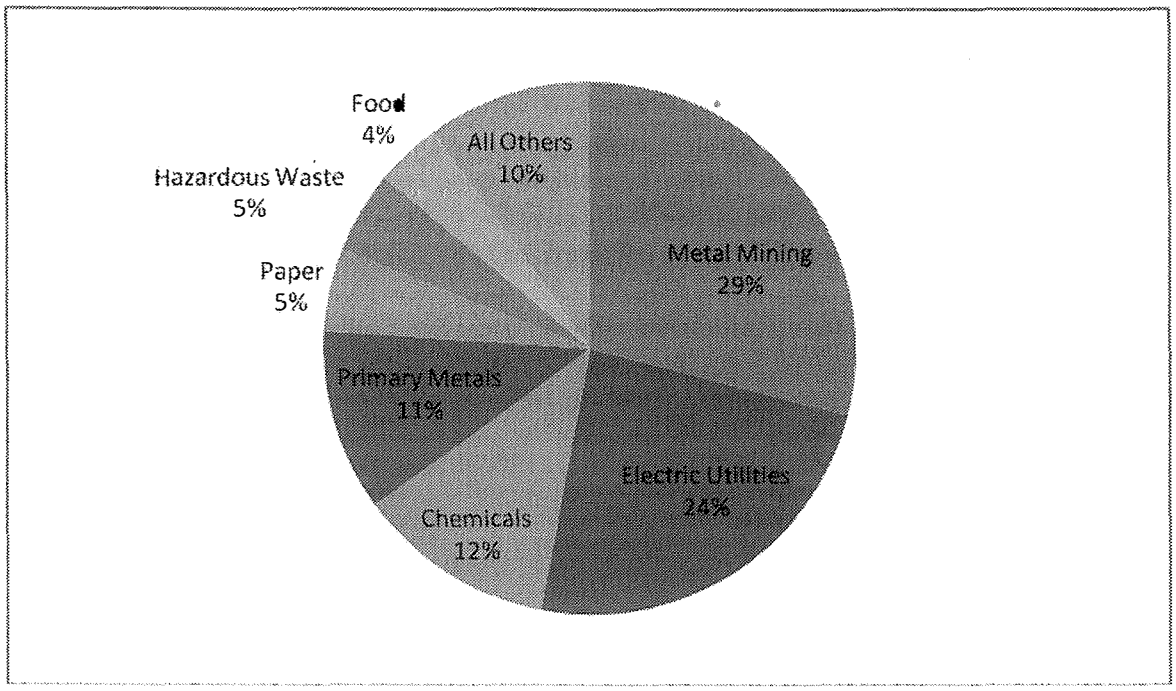
A. Green Chemistry

The contributions of the pharmaceutical industry, especially via synthetic organic chemistry, to medicine have significantly improved the quality and length of human life. The synthesis and commercial development of countless compounds now allow for the treatment of diseases that have otherwise overwhelmed mankind. Over the past century, the discovery of antibiotics and new medicines has contributed to prolonging the average human life span by nearly thirty years.[1] The development of new fertilizers and pesticides has allowed for more bountiful harvests. Despite the vast achievements of the chemical industry, the massive amounts of hazardous waste produced cannot be ignored, especially when considering current environmental issues and the hazards presented to human health. For example, in 1984 a Union Carbide pesticide plant in Bhopal, India released 42 tons of methyl isocyanate.[2] Nearly 15,000 people have lost their lives as result of this toxic gas leak and many others have suffered health problems due to exposure. Environmental drinking water contamination has also been a major issue in the aftermath of the disaster.

The United States Congress has passed many laws to help reduce the amount of chemical waste released into the environment. The most significant of these is the "Pollution Prevention Act" (PPA) passed in 1990.[3] The PPA provides guidelines and laws on pollution prevention through the proper use and disposal of chemicals. Also, source reduction and prevention have been stressed in this legislation. The government tracks the production and release of toxic chemical waste in the *Toxic Release Inventory* (TRI).[4] In 2006, the TRI indicated that the chemical industry ranks third in the amount of waste released by sector (figure 1.1). The only

industries that produce and release more waste are the relatively large metal mining and electricity sectors.

Figure 1.1: 2006 TRI Total Disposal or Release of Waste by Industry[4]



Therefore, chemists need to be more concerned with pollution in terms of hazardous waste being released into the environment. This has prompted synthetic organic chemists to consider developing environmentally friendly chemistry or *Green Chemistry*. *Green Chemistry* involves the design of chemical syntheses and processes that are more environmentally friendly, reduce waste production, and avoid use of toxic reagents.[2] The main goal of green chemistry is to minimize the use of toxic chemicals by finding safe, effective alternatives. This type of developmental strategy is an efficient way to reduce the chemical waste associated with a synthesis. Also, avoiding the use of toxic and corrosive reagents makes synthesis much safer for the chemists involved. The risk associated with the use of a chemical can be expressed as a function of both hazard and exposure (eq. 1.1).[2]

Equation 1.1

$$\text{Risk} = f[\text{hazard, exposure}]$$

Past strategies of reducing risk have involved limiting exposure to dangerous chemicals by taking safety precautions and exercising especial care when handling reagents. This strategy can be an effective way of increasing safety if exposure can truly be limited. However, due to human error and faults in protective laboratory equipment, exposure control measures often fail. Therefore, the Green Chemistry approach is to lower hazards by using inherently less toxic or non-toxic reagents. This reduces risk associated with syntheses and reduces hazardous waste overall. This concept can be accomplished through the practice of *Green Chemistry* where information about toxicity of chemicals is utilized to lower hazard and reduce waste. This has particular relevance to synthetic organic chemistry, a field in which many toxic, corrosive and difficult to dispose of chemicals continue to be used in large quantities.

One concept that can be used to reduce the amount of waste associated with a chemical synthesis is atom economy. Atom economy is a measure of the percent by mass of reactants that end up in the desired product, and hence, is a good indication of the amount of waste material associated with a process. The solvents and catalysts necessary for a synthesis are not considered. This concept was introduced by Trost in 1991.[5]

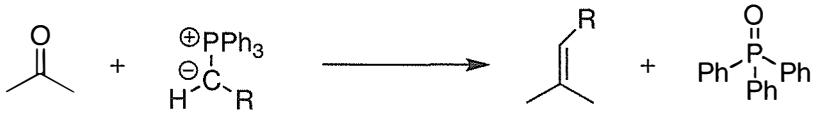
Equation 1.2

$$Atom\ Economy = \frac{Molecular\ Weight\ of\ desired\ product}{Molecular\ Weight\ of\ all\ reactants} \times 100\%$$

Many synthetic methods currently used yield byproducts that increase the amount of waste associated with a synthesis. Also, if the byproducts are toxic this makes waste disposal

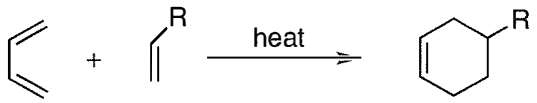
more difficult and costly. The Wittig synthesis of alkenes produces one equivalent of triphenylphosphine oxide as a byproduct for every equivalent of alkene formed (scheme 1.1).

Scheme 1.1



In contrast to the Wittig reaction, a classic example of an atom-economic reaction is the Diels-Alder cycloaddition. All of the atoms present in the diene and dienophile are present in the final cyclized product. Thus, the only chemical waste involved with this synthesis comes from any necessary solvents or catalysts (scheme 1.2).

Scheme 1.2



The design of atom-economic processes allows for reduction of the amount of raw materials needed and a decrease in waste generated. Thus, designing syntheses with this principal in mind could drastically reduce the amount of waste produced by the chemical industry while also reducing costs.

The concept of E (environmental) factor was introduced by Roger Sheldon in 1992 to evaluate the environmental impact of chemical processes.[6a] The E factor is defined in terms of the amount waste associated with a process and the amount of desired product produced (eq. 1.3).

Equation 1.3

$$E\ factor = \frac{mass\ of\ waste\ produced}{mass\ of\ product\ produced}$$

The E factor can be determined for either an individual chemical process or an entire industrial sector. Sheldon determined the E factors for a number of different chemical industries (table 1.1). He found that the E factors associated with fine chemical and pharmaceutical synthesis were relatively high when compared with more efficient industries, such as oil refining and bulk chemical synthesis. Production of waste on such a grand scale poses a major environmental concern and also hurts the cost effectiveness of numerous commercial processes.

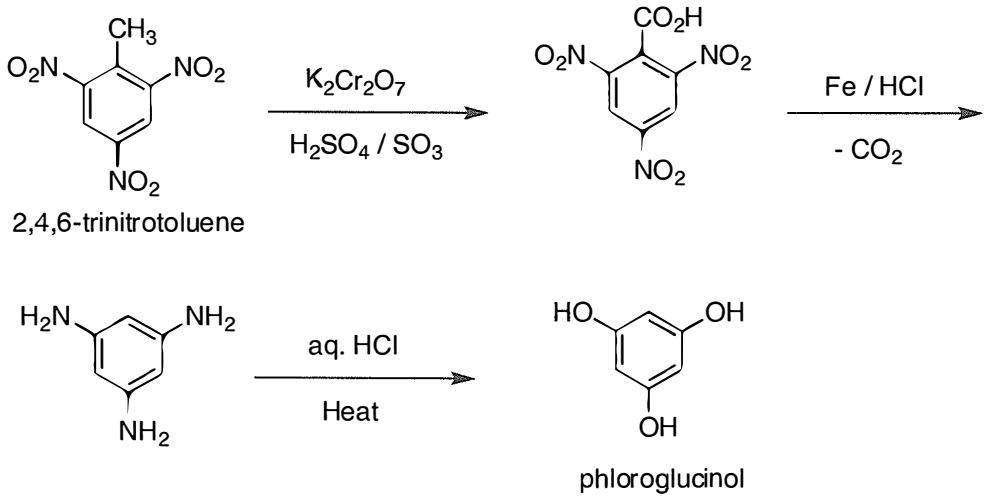
Table 1.1: E Factors of Various Chemical Industries

Industry Sector	Product produced (Tons)	E Factor (kg waste/kg product)
Oil refining	10^6-10^8	< 0.1
Bulk chemicals	10^4-10^6	< 1 - 5
Fine chemicals	10^2-10^4	5 - 50
Pharmaceuticals	10-10^3	25 - 100

The importance of considering E factors and other Green Chemistry metrics becomes readily apparent when considering synthetic processes that generate large amounts of waste. In the early 1980s, Océ Andeno closed a plant responsible for the synthesis of phloroglucinol.[6b] Phloroglucinol is used as a raw material for the synthesis of explosives and pharmaceuticals. Closure of the plant was necessary because the cost of disposing of the waste associated with the synthesis was approaching the profits associated with the sale of phloroglucinol. The synthetic strategy employed at Océ Andeno involved the oxidation of 2,4,6-trinitrotoluene (TNT) with

potassium dichromate in fuming sulfuric acid[6c] (scheme 1.3). This was followed by reduction of the nitro substituents with iron and hydrochloric acid and an *in situ* decarboxylation. Heating an acidic solution of the resulting 1,3,5-triaminobenzene yielded phloroglucinol.

Scheme 1.3



The E factor for this process was determined by Sheldon to be 40. Thus, for every kg of phloroglucinol produced, 40 kg of solid waste containing $Cr_2(SO_4)_3$, $FeCl_2$, $KHSO_4$, and NH_4Cl was generated. The cost associated with the disposal of this waste made the process impractical and resulted in the eventual closing of the Océ Andeno plant.

Though Sheldon's E factor is a good indication of the relative amount of waste produced by a given process or industry, the nature of the waste produced should also be taken into account when evaluating synthetic viability. A kilogram of sodium chloride or a similarly benign salt is not equivalent to a kilogram of a toxic compound such as a tin salt when considering the environmental implications of chemical waste disposal. All of these factors should be considered collectively when designing Green Chemistry processes.

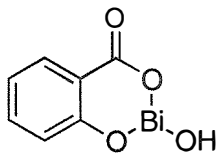
The approach to environmentally friendly chemistry in our laboratory utilizes non-toxic reagents that are highly catalytic in nature. It is in this context that bismuth compounds are very attractive as catalysts and reagents in organic synthesis.

B. Bismuth Compounds

Bismuth, the 83rd element in the periodic table, has a natural abundance of 0.008 ppm in the Earth's crust and 0.0002 ppm in sea water.[7] It is a soft, crystalline metal with a whitish-pink hue. Bismuth is the heaviest stable element and the most diamagnetic element known.

Bismuth is a remarkable element because despite its proximity on the periodic table to toxic heavy metals such as lead and antimony, it is relative non-toxic. Due to their non-toxicity, bismuth compounds have found numerous applications in cosmetics and medicine. For example, the active ingredient in the anti-diarrheal medication Pepto-Bismol™ is bismuth subsalicylate (figure 1.2). Bismuth subcitrate is the only compound known to be active against *Helicobacter pylori*, a bacterium that cause ulcers.[8] Bismuth subnitrate is used in medicine as a wound dressing and as a component in ointment for inflamed skin. Cosmetically, bismuth oxychloride is used to impart a shimmering effect to various makeup products. Bismuth is an environmentally friendly alternative to lead as the main component of shotgun cartridges used for waterfowl hunting.

Figure 1.2



Bismuth Subsalicylate

With increasing focus on developing environmentally friendly synthesis methods, bismuth compounds have also been used as catalysts in synthetic organic chemistry. Bismuth compounds have several attractive features in this respect.

There is no evidence to date to suggest that bismuth compounds are carcinogenic or mutagenic.[9] The remarkable non-toxicity of bismuth compounds has earned bismuth the distinction of a "Green" element.[10] This non-toxicity is primarily due to their insolubility in neutral aqueous solutions such as biological fluids. Bismuth compounds are poorly soluble in the blood plasma and are readily excreted via the urinary tract. The non-toxicity of bismuth's compounds is evident from a comparison of LD_{50} values for a range of common Lewis acids (table 1.2). As can be seen from table 1.2, most bismuth compounds are even less toxic than sodium chloride. Even organobismuth compounds such as triphenylbismuthine are remarkably non-toxic.

Table 1.2: LD_{50} Values of Bismuth Compounds and Comparable Salts[10]

Compound	LD_{50} (g/Kg)	Species and Route
Sodium Chloride, NaCl	3.8	Rat, Oral
Bismuth oxide, Bi_2O_3	5.0	Rat, Oral
Bismuth nitrate, $Bi(NO_3)_3 \cdot 5H_2O$	4.4	Rat, Oral
Bismuth oxychloride, BiOCl	22	Rat, Oral
Triphenylbismuthine, Ph_3Bi	180	Dog, Oral
Mercury chloride, $HgCl_2$	0.001	Rat, Oral
Cerium chloride, $CeCl_3$	2.1	Rat, Oral
Indium chloride, $InCl_3$	1.1	Rat, Oral
Samarium chloride, $SmCl_3$	2.9	Rat, Oral
Scandium chloride, $ScCl_3$	3.9	Rat, Oral
Ytterbium chloride, $YbCl_3$	4.8	Rat, Oral

Despite the fact that bismuth is not common in the Earth's crust, bismuth compounds are relatively inexpensive. This is because bismuth is a byproduct of lead, copper and tin refining. Many bismuth(III) compounds are commercially available at a low cost (table 1.3), which makes bismuth compounds even more attractive as potential catalysts.

Table 1.3: Availability of Bismuth(III) Compounds and Comparable Lewis Acids[a]

Compound	Cost/g ($)	Cost/mol ($)
Bismuth chloride, $BiCl_3$	2.25	711
Bismuth nitrate, $Bi(NO_3)_3 \cdot 5H_2O$	0.32	153
Bismuth oxide, Bi_2O_3	0.49	228
Bismuth Acetate, $Bi(C_2H_3O_2)_3$	3	1097
Bismuth trifluoromethanesulfonate, $Bi(OTf)_3$	10.60	6960
Scandium trifluoromethanesulfonate, $Sc(OTf)_3$	37	17,820
Ytterbium trifluoromethanesulfonate, $Yb(OTf)_3$	36	22,390
Trimethylsilyltriflate, TMSOTf	1.70	378
Titanium tetrachloride, $TiCl_4$	0.05	9.96

[a]Sigma-Aldrich.com

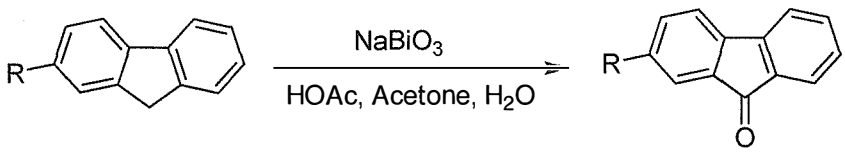
Although the hydrolysis of Bi(III) salts in water has been reported (this is discussed in more detail later, see scheme 1.36), bismuth compounds are relatively stable and tolerate small amounts of air and moisture. This contrasts sharply with moisture-sensitive Lewis acid reagents and catalysts, such as $BF_3 \cdot Et_2O$ and $TiCl_4$, that must be handled under an inert atmosphere to ensure safety and viability of the reagent.

The electron configuration of bismuth is $[Xe]4f^{14}5d^{10}6s^26p^3$. On account of weak shielding by the 4f electrons (Lanthanide contraction) bismuth(III) compounds exhibit Lewis

acidity. Thus, bismuth(III) compounds can be utilized as potential Lewis acidic catalysts for organic synthesis.

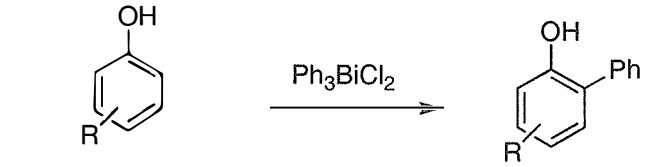
Bismuth can also exist in the +5 oxidation state. Organobismuth compounds with bismuth in the +5 oxidation state are known and have been applied in organic synthesis.[11] Bismuth(V) compounds are commonly employed as oxidizing agents. Sodium bismuthate has been used for the benzylic oxidation of aromatic compounds[12] (scheme 1.4).

Scheme 1.4



Triphenylbismuth(V) dichloride has been employed as an oxidizing agent for a variety of functionalities, including the oxidative phenylation of phenols[13] (scheme 1.5).

Scheme 1.5



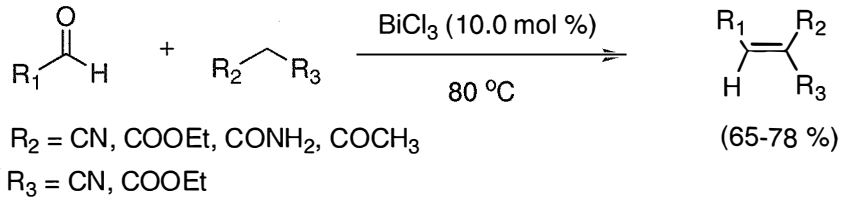
R = electron donating

Applications of Bismuth(III) Compounds as Catalysts in Organic Synthesis

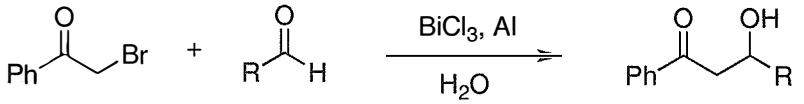
A variety of bismuth(III) compounds have been used as Lewis acid catalysts for synthetic transformations.[14] Bismuth(III) chloride is one of the most thoroughly investigated bismuth-based Lewis acids. The Knoevenagel condensation[15] (scheme 1.6), Reformatsky reaction[16] (scheme 1.7), Diels-Alder cyclization[17], Mukaiyama-aldol reaction[18] (scheme 1.8), deprotection

of acetals[19] (scheme 1.9), and the allylation of acid chlorides[20] (scheme 1.10) and aldehydes[21] (scheme 1.11) have all been reported with $BiCl_3$ as the catalyst.

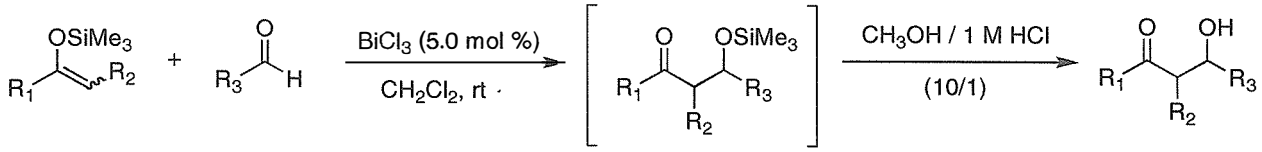
Scheme 1.6



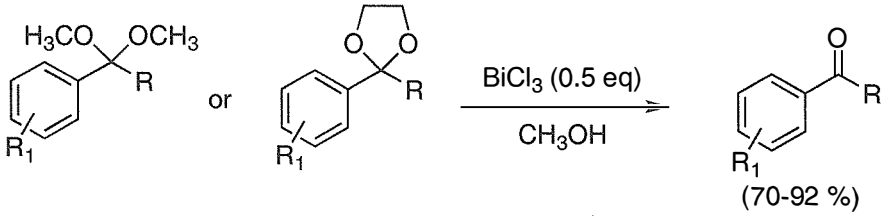
Scheme 1.7



Scheme 1.8

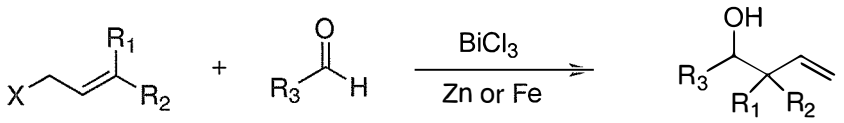


Scheme 1.9



Scheme 1.10

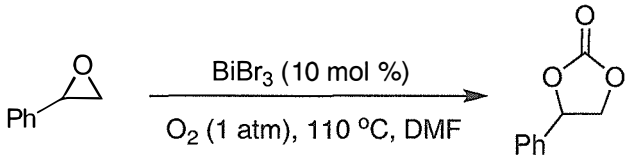
Scheme 1.11



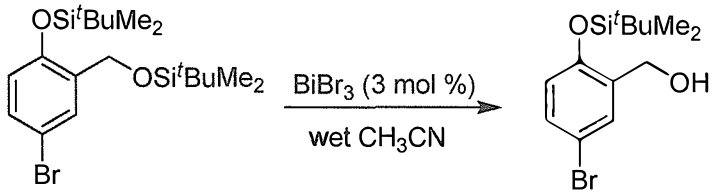
X = Cl, Br, I (45 - 99 %)

Bismuth(III) bromide has been reported as a catalyst for the oxidation of epoxides to cyclic carbonates[22] (scheme 1.12), the deprotection of alkyl TBDMS ethers[23] (scheme 1.13), the synthesis of nucleosides[24], the formation of ethers[25] (scheme 1.14), and the synthesis of tetrahydroquinoline derivatives[26] (scheme 1.15).

Scheme 1.12

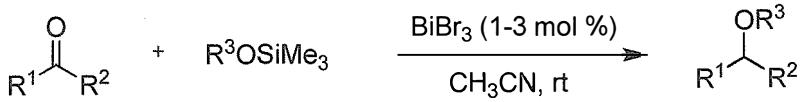


Scheme 1.13

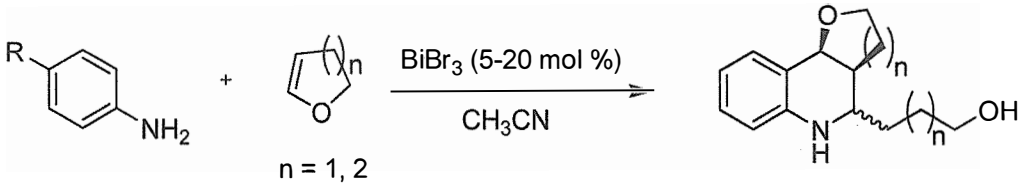


(81-85 %)

Scheme 1.14

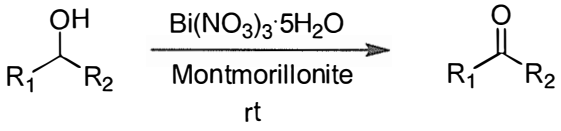


Scheme 1.15

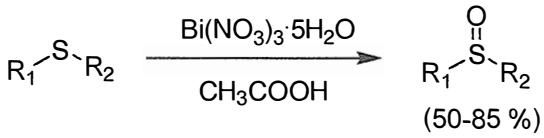


Bismuth(III) nitrate has also received significant attention in the literature. Bismuth(III) nitrate has been utilized as a catalyst for the oxidation of alcohols[27] (scheme 1.16), the oxidation of sulfides to sulfoxides[28] (scheme 1.17), the deprotection of acetals[29] (scheme 1.18) and thioacetals[30], the synthesis of acylals from aldehydes[31] (scheme 1.19), and the Biginelli reaction.[32]

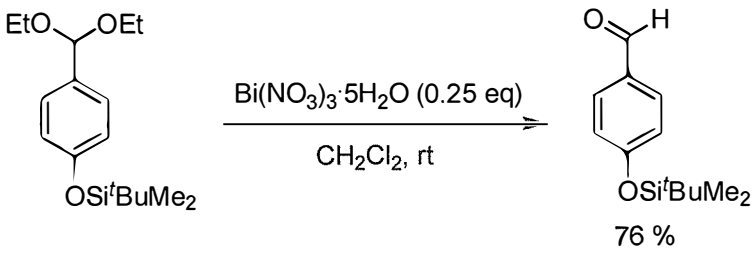
Scheme 1.16



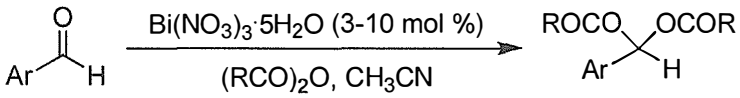
Scheme 1.17



Scheme 1.18



Scheme 1.19



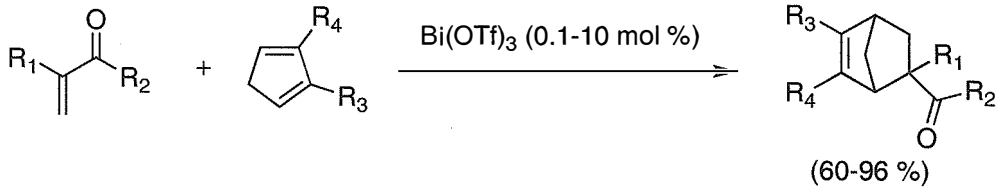
Bismuth Trifluoromethanesulfonate [Bismuth Triflate, Bi(OTf)$_3$]

Metal triflates have received significant attention in the literature as Lewis acid catalysts.[33] Likewise, bismuth triflate is the one of the most thoroughly investigated bismuth-based catalysts.[34] Bismuth triflate is a hygroscopic white solid that exists in a hydrated form at room temperature ($Bi(OTf)_3 \cdot xH_2O$ with $1 < x < 4$). Attempts to synthesize the anhydrous salt by heating $Bi(OTf)_3 \cdot 4H_2O$ result in decomposition above temperatures of 100 °C.[35] The final products of this decomposition are BiF_3 and H_2SO_4. X-ray powder diffraction[35] studies on $Bi(OTf)_3$ show that the bismuth atom is coordinated to four water molecules and four oxygen atoms from triflate groups. It was also determined that the tetrahydrate of bismuth triflate condenses into dimers.

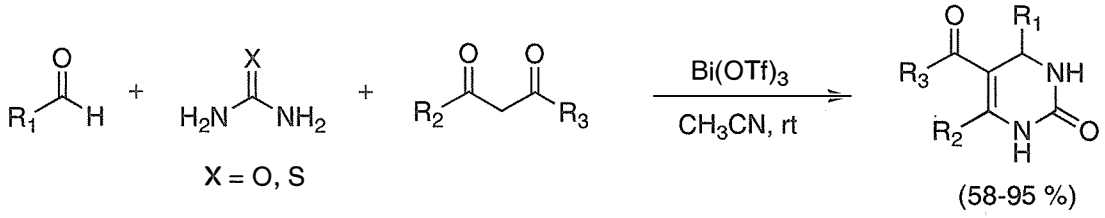
Because of the environmentally friendly nature of bismuth salts, bismuth triflate has received significant attention in the literature.[10, 34] Bismuth triflate has been used as a catalyst for Diels-Alder reactions[17, 36] (scheme 1.20), Mukaiyama aldol reactions[37] (scheme 1.34), Biginelli

reactions[38] (scheme 1.21), Friedel-Crafts acylations[39] (scheme 1.22) and alkylations[40], Beckmann rearrangements[41] (scheme 1.23), Michael-type reactions[42] (scheme 1.24), synthesis[43] and deprotection[44] of acetals, and the Sakurai allylation of a variety of functional group including aldehydes[45] (scheme 1.25), acetals[46] (scheme 1.26), epoxides[47] (scheme 1.27), aziridines[47] (scheme 1.28), and quinones[48] (scheme 1.29). This rather vast body of literature highlights the wide applicability and versatility of bismuth triflate as a catalyst in organic synthesis.

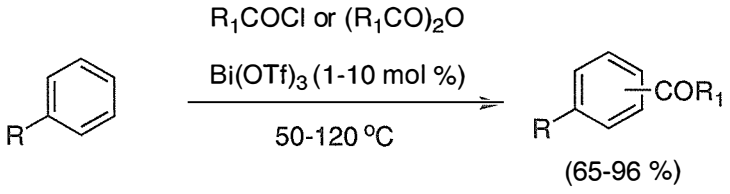
Scheme 1.20



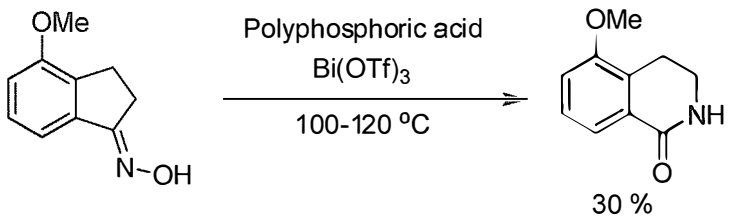
Scheme 1.21



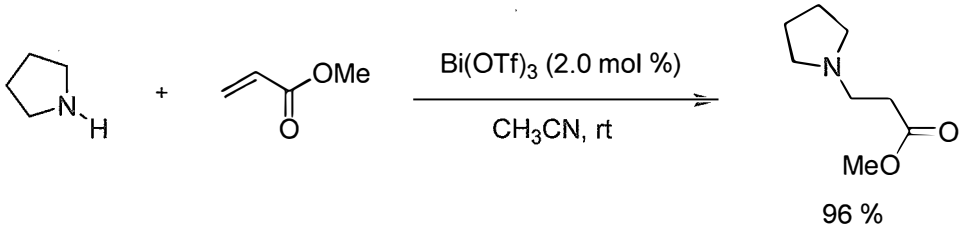
Scheme 1.22



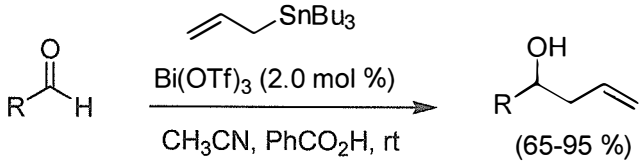
Scheme 1.23



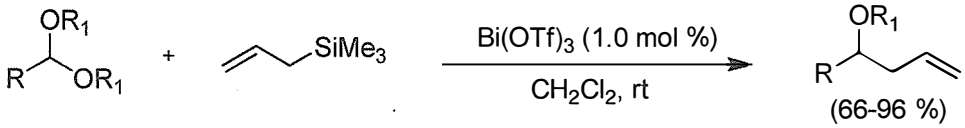
Scheme 1.24



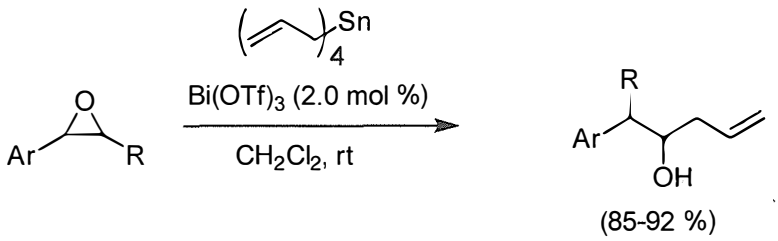
Scheme 1.25



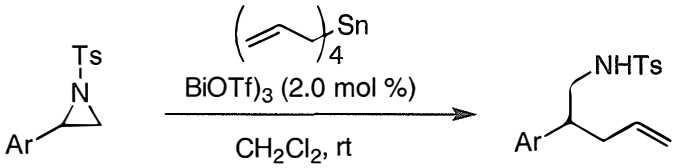
Scheme 1.26



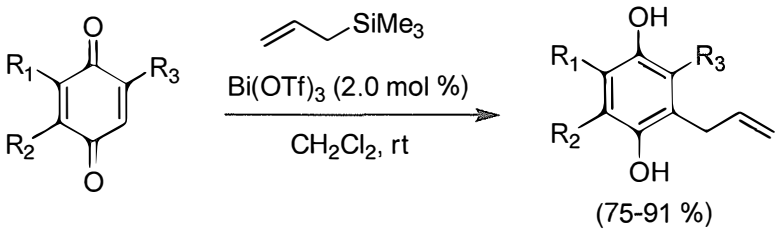
Scheme 1.27



Scheme 1.28

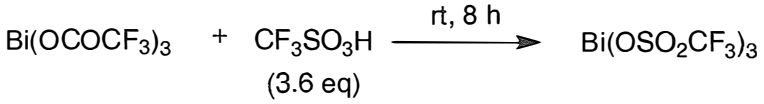


Scheme 1.29



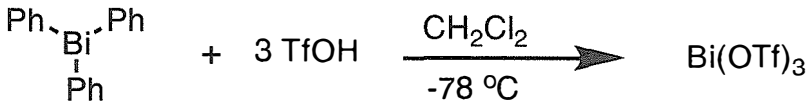
Bismuth triflate can be synthesized in the laboratory by a variety of literature methods. Verma and co-workers were the first to report a synthesis of bismuth triflate from bismuth(III) trifluoracetate and triflic acid[49] (scheme 1.30).

Scheme 1.30



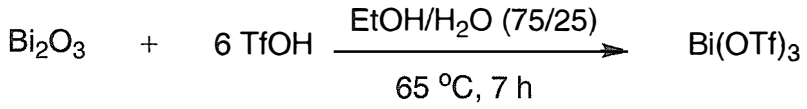
Bismuth triflate has also been synthesized by treatment of triphenylbismuth with triflic acid[50] (scheme 1.31). This method exploits the weak bismuth-carbon bonds (Bi-C bond: 143 KJ/mol[51]; C-C bond: 447 KJ/mol) in triphenylbismuth to generate bismuth triflate. This method is not, however, environmentally friendly because of the formation of three equivalents of benzene, a known carcinogen.

Scheme 1.31



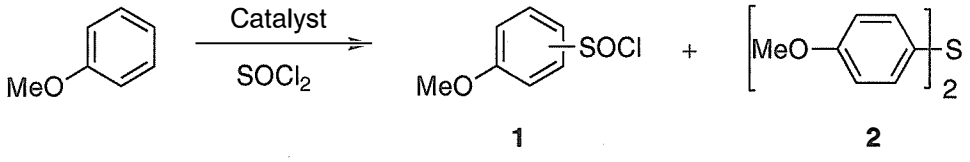
A greener method for the synthesis of bismuth triflate involves reaction of bismuth oxide and triflic acid in aqueous ethanol[52] (scheme 1.32). In this procedure, bismuth triflate is isolated by freeze-drying the solution.

Scheme 1.32



The efficiency of bismuth triflate as a Lewis acid catalyst is especially obvious when it is compared to other rare-earth triflates that have received considerably more attention in the literature. Bismuth triflate is reported to be a more effective catalyst for the chlorosulfinylation of aromatics than other triflates[53] (scheme 1.33). Bismuth triflate was sucessfully employed as a catalyst for the chlorosulfinylation of electron-rich aromatic compounds in high yields. The use of other metal triflates, such as scandium triflate and cerium triflate, resulted in significant amounts of sulfide byproduct **2**.

Scheme 1.33



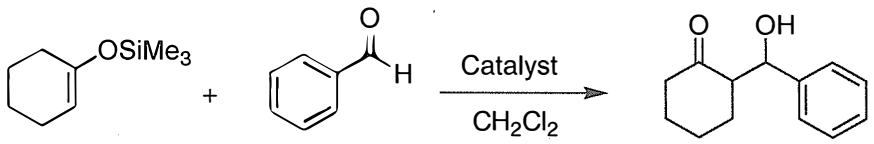
1 2

Catalyst (2.0 mol %)	Yield of **1** (%)[a]	Yield of **2** (%)[a]
$Bi(OTf)_3$	99	Trace
$Sc(OTf)_3$	14	40
$Ce(OTf)_4$	28	38
$Yb(OTf)_3$	Trace	not detected
$Sb(OTf)_3$	75	4

[a] Yield determined by ^1H NMR spectroscopy

Also, bismuth triflate is a more effective catalyst for the Mukaiyama-aldol reaction[37] than other metal triflates (scheme 1.34). 1-Trimethylsilyloxycyclohexene was successfully coupled with benzaldehyde with a low loading (1.0 mol %) of bismuth triflate. Ytterbium(III) triflate and yttrium(III) triflate were ineffective as catalysts for this reaction.

Scheme 1.34



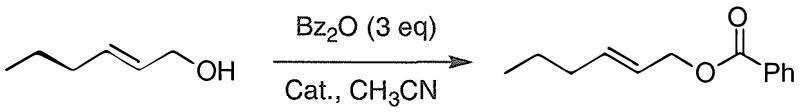
Catalyst	mol %	Temp.	T	Yield (%)
$Bi(OTf)_3$	1.0	-70 °C	0.5 h	95
$Sc(OTf)_3$	5.0	-78 °C	15 h	81
$Yb(OTf)_3$	5.0	-78 °C	15 h	trace
$Y(OTf)_3$	5.0	-78 °C	15 h	trace

Bismuth triflate is prone to hydrolysis in water yielding triflic acid (scheme 1.35). Other rare-earth metal triflates, such as scandium triflate and lanthanum triflate are not hydrolyzed in water. This unique property of bismuth triflate must be considered while dealing with acid-sensitive functional groups or proposing reaction mechanisms.

Scheme 1.35

For example, Marko and coworkers have explored the role of triflic acid in the metal triflate catalyzed acylation of alcohols[54] (scheme 1.36). It was discovered that the rate of benzoylation of alcohols catalyzed by bismuth triflate was greatly inhibited when the reaction was performed in the presence 2,6-di-*t*-butyl-4-methylpyridine (DTBMP), a very hindered organic base. Moreover, the reaction was successfully catalyzed using triflic acid. These data suggest that the acylation of alcohols is actually triflic acid catalyzed. Similar observations have been made by our group.[44]

Scheme 1.36



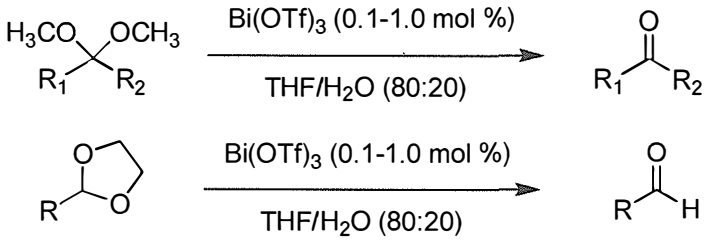
Catalyst	mol %	DTBMP (%)	t	Conversion (%)[a]
$Bi(OTf)_3$	5.0	-	7 h	17
$Bi(OTf)_3$	5.0	15.0	15 h	8
TfOH	8.0	-	5 h	30

[a] Measured by capillary GC after calibration of the response for each component

Bismuth triflate can also be used as a catalyst in aqueous solutions. For example, the synthesis of 2,3-disubstituted quinoxalines catalyzed by bismuth triflate in water been reported.[55]

The bismuth triflate catalyzed deprotection of acyclic and cyclic acetals in aqueous THF has also been reported[44] (scheme 1.37). This protocol also applicable to ketals and conjugated acetals with a low loading of bismuth triflate (0.1-1.0 mol %).

Scheme 1.37



Many reagents and catalysts are destroyed when exposed to small amounts of water. This makes the use of anhydrous solvents and reagents imperative in many cases. Catalysts and reagents must often be handled under an inert atmosphere. In contrast, most reactions catalyzed by bismuth triflate do not require dry solvents or inert atmosphere conditions.

The environmentally friendly nature of bismuth(III) triflate coupled with its ease of handling and inexpensive nature have prompted us to explore its utility as a catalyst for a variety of synthetic transformations.

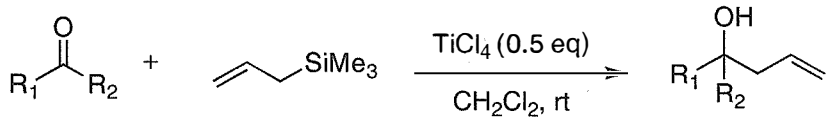
C. Literature Review: Allylation of Acetals

Hosomi-Sakurai Allylation of Acyclic Acetals

Some of most important organic transformations involve the formation of carbon-carbon bonds. These methodologies are especially important in the synthesis of pharmaceuticals and

natural products. Methods that have been developed for the formation of carbon-carbon bonds include the Suzuki Cross-Coupling[56], Friedel-Crafts acylation[57] and alkylation[58], the Michael reaction[59], Olefin Metathesis[60], and Diels-Alder cyclization.[61] The nucleophilic allylation of various carbon electrophiles is also an efficient strategy for carbon-carbon bond formation. The Hosomi-Sakurai reaction involves the Lewis or protic acid catalyzed allylation of various electrophiles using allyl silanes. This method is commonly regarded as a mild method for carbon-carbon bond formation. Hosomi and Sakurai first reported the $TiCl_4$-promoted allylation of aldehydes and ketones to yield homoallyl alcohols[62] (scheme 1.38).

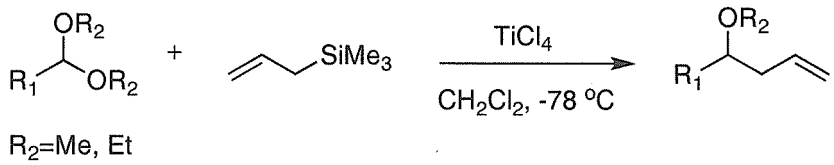
Scheme 1.38



They also successfully extended this methodology to the allylation of acyclic acetals[63] (scheme 1.39). This represents an efficient synthesis of homoallyl ethers from readily available acetal starting materials. Following their report, the allylation of acyclic acetals to yield homoallyl ethers has since been well studied with a number of different Lewis acid catalysts. These include $AlCl_3$[64], trimethylsilyl triflate[65], $BF_3{\cdot}Et_2O$[66], iodotrimethylsilane[67], trityl perchlorate[68], diphenylboryl triflate[68], bis(fluorosulfonyl)imide[69], montmorillonite[70], CuBr[71], tris(*p*-bromophenyl)aminium hexachloroantimonate[72], $Sc(OTf)_3$[73], and $BiBr_3$.[74] Many of the catalysts previously employed for this synthesis are corrosive, for example $AlCl_3$, $TiCl_4$, and TMSOTf, or toxic, for example $BF_3{\cdot}Et_2O$. Additionally, stoichiometric catalyst loadings are often necessary. Low temperatures and anhydrous conditions are also required in several of these reported

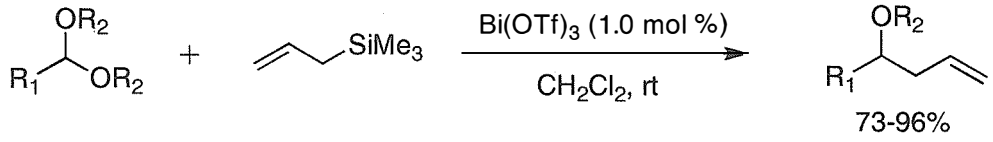
protocols. These conditions detract from the utility of these procedures in the industry because of environmental and safety concerns.

Scheme 1.39



Our group has reported the bismuth(III) triflate-catalyzed allylation of acyclic acetals and ketals to yield homoallyl ethers in good yields[75] (scheme 1.40). The allylation reactions proceeded smoothly at room temperature with a low catalyst loading (1.0 mol %).

Scheme 1.40



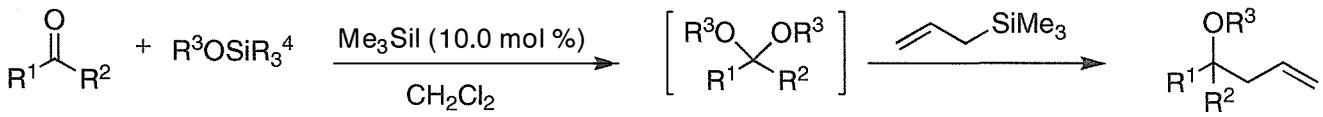
This procedure provides a highly catalytic and environmentally friendly route to homoallyl ethers compared to previously reported methodologies.

Hosomi-Sakurai Allylation of Aldehydes

In contrast to the allylation of acyclic acetals, the allylation of aldehydes and carbonyl compounds to yield homoallyl ethers has received relatively little attention in the literature. Sakurai and co-workers reported the allylation of aldehydes and ketones catalyzed by iodotrimethylsilane in the presence of alkoxysilanes to yield homoallyl ethers[76] (scheme 1.41). Trimethylsilyl triflate has also been used as a catalyst for the allylation of aldehydes in the

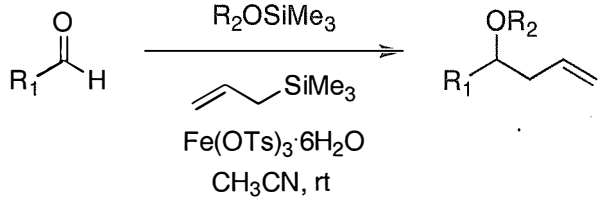
presence of alkoxysilanes to yield benzyl homoallyl ethers and *n*-hexyl homoallyl ethers.[77] Two disadvantages of this method are the utilization of a corrosive catalyst and the use of carbon tetrachloride, a carcinogenic and environmentally harmful solvent.

Scheme 1.41



We have recently reported the iron(III) *p*-toluenesulfonate catalyzed allylation of aldehydes and acetals to yield homoallyl ethers[78] (scheme 1.42). The direct conversion of aldehydes to the corresponding homoallyl ether is advantageous because few acetals are commercially available and must be typically synthesized from the corresponding aldehyde. In addition, many acetals have a poor shelf life due to their acid-sensitive nature. Moreover, most methods in the literature for the allylation of acetals only report the synthesis of homoallyl methyl or ethyl ethers. These compounds are not very amenable to further synthetic manipulation since the alkyl group appended to the homoallyl ether oxygen is an inert methyl or ethyl group. A one-pot procedure utilizing alkoxysilanes allows for the installation of functional groups that are more amenable to further synthetic manipulation. This is possible because a wide range of alkoxysilanes is commercially available including benzyloxytrimethylsilane, ethoxytrimethylsilane, and allyloxytrimethylsilane.

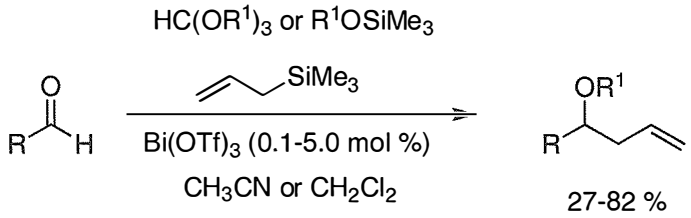
Scheme 1.42



We reported the allylation of aldehydes and ketones under mild conditions to yield homoallyl methyl ethers, homoallyl ethyl ethers, homoallyl allyl ethers, and homoallyl benzyl ethers. This protocol was applicable to both aliphatic and aryl aldehydes with low catalyst loadings (1.0-10.0 mol %). This method is especially attractive because of the utilization of iron(III) tosylate, an inexpensive and non-corrosive Lewis acid catalyst.

Our group has also reported the one-pot synthesis of homoallyl ethers from aldehydes catalyzed by bismuth(III) triflate[79] (scheme 1.43). Trialkylorthoformates or alkoxysilanes were employed to generate acetals or oxenium ions respectively, which can then undergo allylation to yield homoallyl ethers.

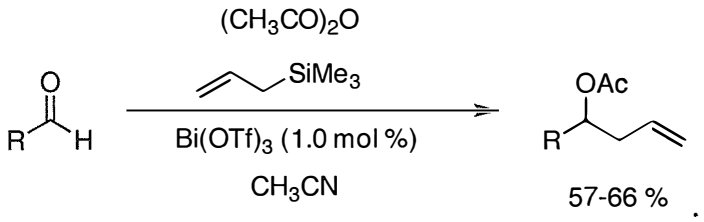
Scheme 1.43



This methodology was applicable to a variety of aryl aldehydes with a low catalyst loading. The use of alkoxytrimethylsilanes is particularly attractive because it allows for the installation of synthetically useful allyl or benzyl groups at the homoallyl ether oxygen.

The one-pot synthesis of homoallyl acetates from aldehydes catalyzed by bismuth triflate has also been reported (scheme 1.44). This procedure utilized acetic anhydride to generate the corresponding acylals, which can then undergo allylation to yield homoallyl acetates. Aldehydes with strongly electron-donating groups (*p*-methoxy) underwent diallylation under the reaction conditions. The use of a relatively non-corrosive and non-toxic catalyst coupled with the wide availability of aldehydes makes this an attractive route to homoallyl acetates

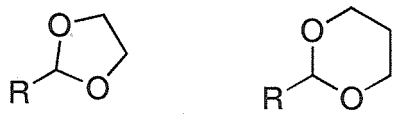
Scheme 1.44



Hosomi-Sakurai Allylation of 1,3-Dioxolanes and 1,3-Dioxanes

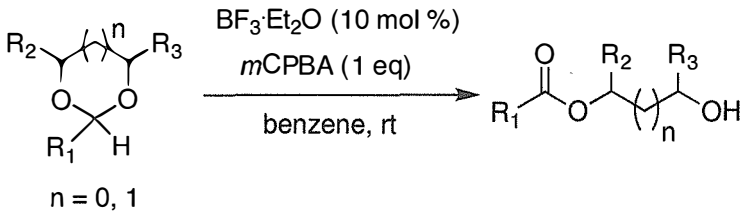
Dioxolanes and dioxanes (fig. 1.3) have been primarily utilized as acid-labile protecting groups in organic synthesis.[80]

Figure 1.3



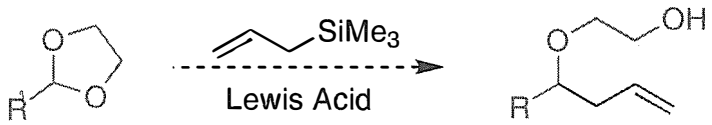
However, cyclic acetals can also be converted to other useful functional groups in the course of a synthesis. For example, the synthesis of hydroxy esters by oxidation of cyclic acetals with *m*-chloroperbenzoic acid has been reported[81] (scheme 1.45).

Scheme 1.45



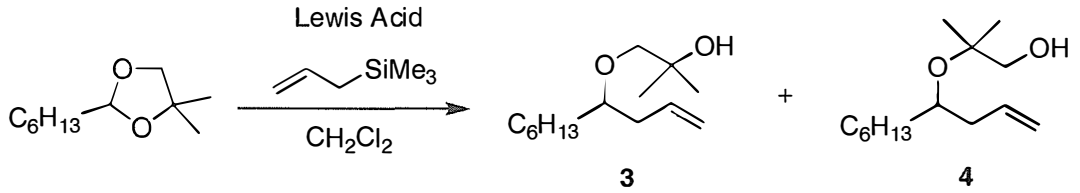
Cyclic acetals have received very little attention in the literature as substrates in the Hosomi-Sakurai reaction. Nevertheless, the ring-opening allylation of cyclic acetals ought to lead to the synthesis of highly functionalized alcohols (scheme 1.46).

Scheme 1.46



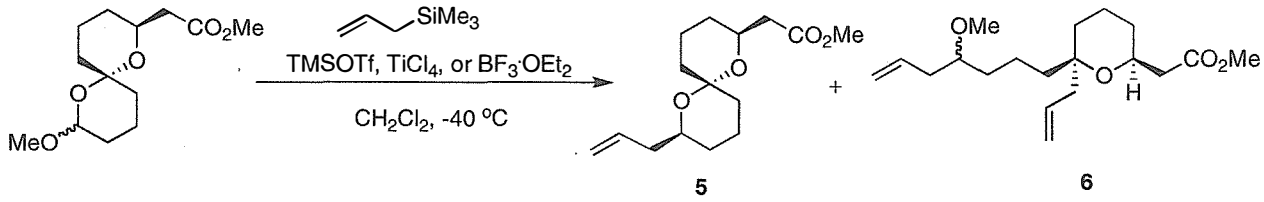
Kuwajima and co-workers reported the allylation of a substituted 1,3-dioxolane catalyzed by $TiCl_4$, $AlCl_3$, and $SnCl_4$.[82] They found that the regioselectivity of ring-opening of a 4,4-dimethyl substituted 1,3-dioxolane was dependent on the Lewis acid used and the order of addition of reagents (scheme 1.47). When $TiCl_4$ was employed as the Lewis acid, regioselectivity was dependent on the order of addition of allyltrimethylsilane and $TiCl_4$. When $AlCl_3$ and $SnCl_4$ were used, isomer **4** was the major product (1:99, **3**:**4**). They also reported that the allylation did not proceed with TMSOTf as the catalyst and allyltrimethylsilane as the allyl source. Instead, allyltributyltin, a highly toxic organotin reagent, was necessary to afford the desired allylated product under these conditions.

Scheme 1.47



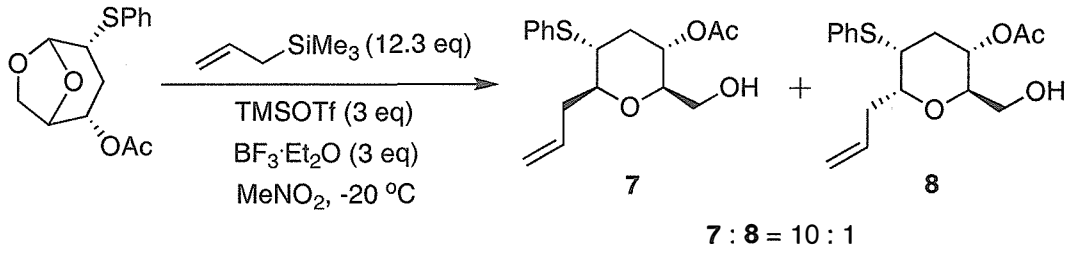
Mead and co-workers have reported the allylation of spiroketals using $BF_3{\cdot}Et_2O$, $TiCl_4$, and TMSOTf as Lewis acid catalysts[83] (scheme 1.48). Stoichiometric catalyst loadings and low temperature conditions were necessary to promote the reaction. A mixture of monoallylated (**5**) and diallylated (**6**) products was obtained in most cases. Because of these factors, this procedure is not very attractive within the context of Green Chemistry.

Scheme 1.48



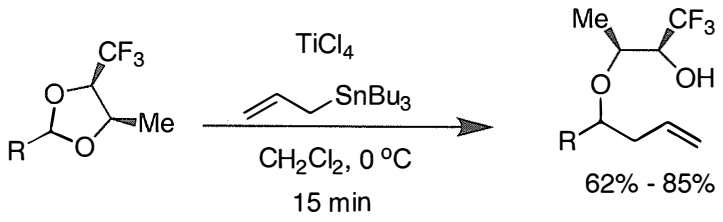
The allylation of a cyclic acetal derived from β-D-ribo-hexopyranose has been reported[84] (scheme 1.49). The allylation required stoichiometric loadings of both TMSOTf (3 eq) and $BF_3{\cdot}Et_2O$ (3 eq) with allyltrimethylsilane (12.3 eq) as the allylating agent. Moreover, the allylation yielded a mixture of isomers, only one of which, **7**, was carried on in the synthesis.

Scheme 1.49



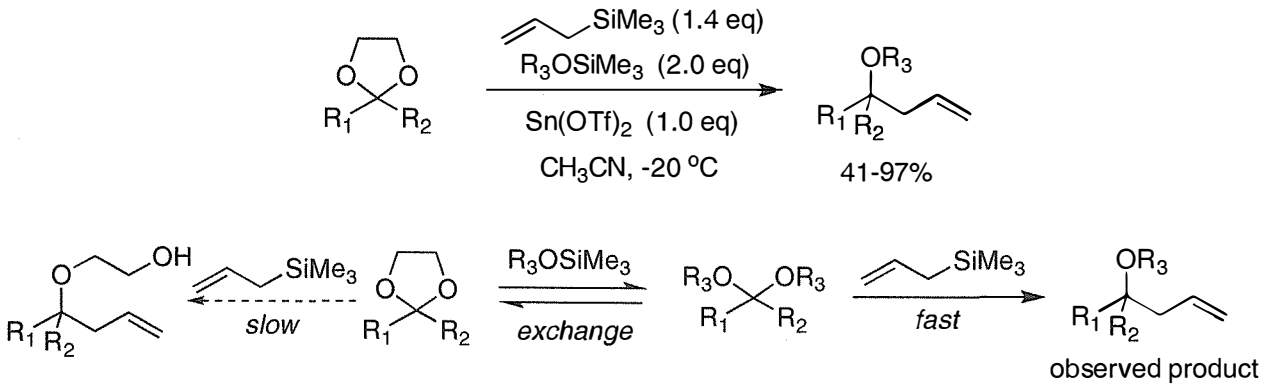
Morelli and co-workers have reported the $TiCl_4$ promoted allylation of 4-trifluoromethyl-1,3-dioxolanes[85] (scheme 1.50). This protocol was extended to only three aliphatic dioxolanes. Furthermore, highly toxic allyltributyltin was used as the source of the allyl group and a stoichiometric loading of $TiCl_4$ was necessary to afford the desired homoallyl ether product.

Scheme 1.50



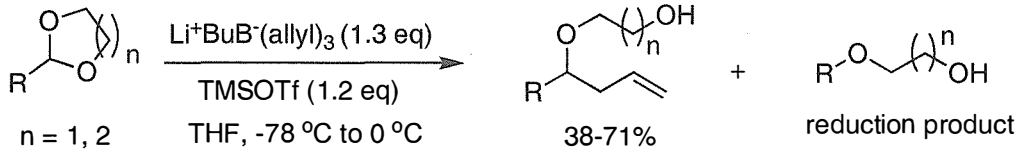
The allylation of 1,3-dioxolanes catalyzed by $Sn(OTf)_2$ in the presence of alkoxysilanes has been reported[86] (scheme 1.51). This synthesis yielded homoallyl ethers as a result of exchange between the alkoxysilane and the 1,3-dioxolane. The authors propose that the allylation of the acyclic acetal resulting from the exchange is faster than the allylation of the cyclic acetal. This reaction was applicable to a number of aliphatic and aryl dioxolanes in good yields, but a stoichiometric catalyst loading was necessary.

Scheme 1.51



The allylation of a number of 1,3-dioxolanes and 1,3-dioxanes catalyzed by TMSOTf has been reported by Hunter and co-workers[87] (scheme 1.52). This method utilized allyl borates as the source of the allyl group. The allyl borate reagents are not commercially available and must be synthesized in lab. A corrosive catalyst (TMSOTf) was employed in stoichiometric quantities and low temperature conditions were required (-78 °C). In a few cases, an alcohol byproduct arising from reduction of the cyclic acetal under the reaction conditions was also isolated in significant yield.

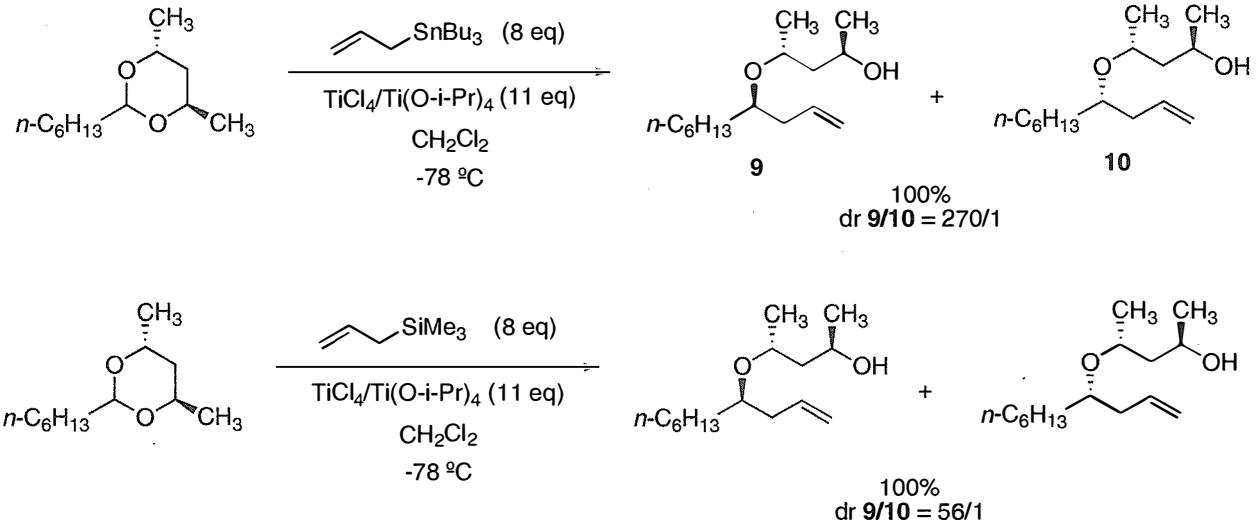
Scheme 1.52



Denmark and co-workers have reported one of the few Sakurai-Hosomi protocols utilizing 1,3-dioxanes as substrates[88] (scheme 1.53). The allylation of 4,6-dimethyl-2-hexyl-1,3-dioxane proceeded with a high degree of diastereoselectivity (270:1) with a stoichiometric loading of $TiCl_4$/Ti(O-*i*-Pr)$_4$ (11 eq) and allyltributyltin (8 eq) as the allylating agent. The

diastereoselectivity was much lower when allyltrimethylsilane was employed (56:1). The use of a corrosive Ti-based catalyst and a toxic organotin compound in superstoichiometric amounts detracts from the utility of this method.

Scheme 1.53



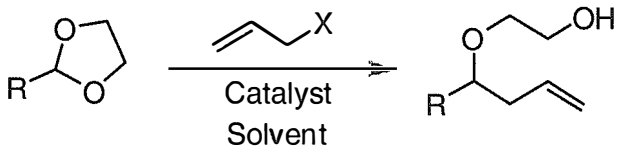
The lack of a highly catalytic, widely applicable, and environmentally-friendly method for the allylation of cyclic acetals prompted us to explore the bismuth(III) triflate-catalyzed allylation of cyclic acetals. The development of greener methods for allylation chemistry is of particular relevance because of increasing environmental concerns and the importance of carbon-carbon bond forming reactions in organic synthesis. Bismuth-based Lewis acids are particularly attractive in this respect because they are relatively non-toxic, non-corrosive, and inexpensive.

II. Results and Discussion

A. Allylation of 1,3-Dioxolanes followed by *in situ* Derivitization with Acid Anhydrides Catalyzed by Bismuth(III) Triflate

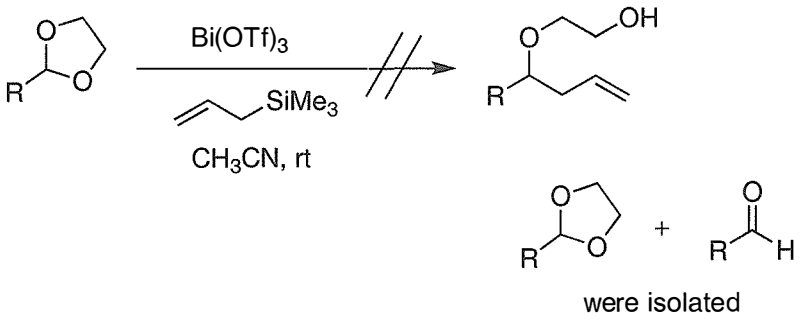
The lack of a highly catalytic and environmentally benign method for the ring-opening allylation of 1,3-dioxolanes (scheme 2.1) prompted our interest in investigating the utility of bismuth(III) triflate as a catalyst for this transformation. In contrast to the Hosomi-Sakurai allylation of aldehydes[62, 76-79] and acyclic acetals[63-75], the allylation of cyclic acetals has received very little attention.

Scheme 2.1



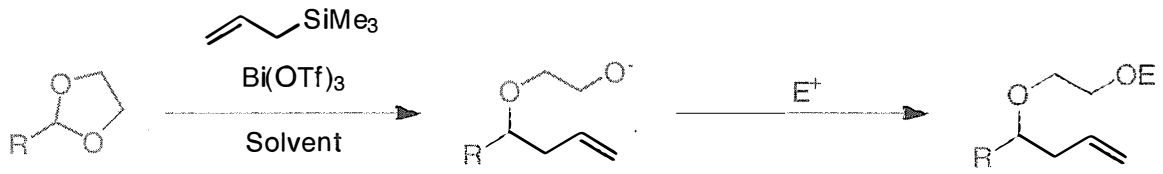
Bismuth triflate was not an effective catalyst for the allylation of 1,3-dioxolanes to yield the expected alcohol products (scheme 2.2). Instead, a mixture of starting material and the corresponding aldehyde was isolated.

Scheme 2.2



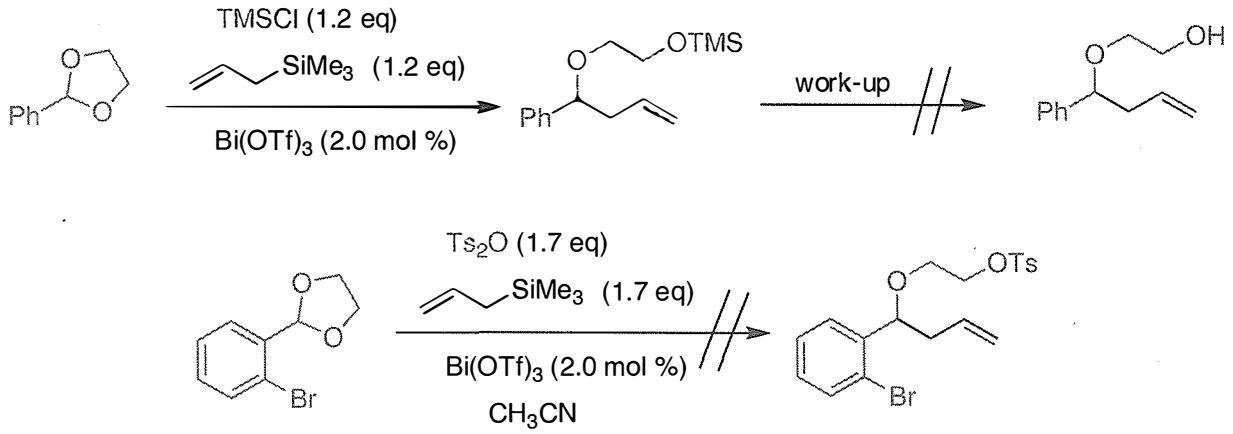
It was reasoned that one way to push the reaction might be to trap the putative alkoxide intermediate that results from addition of the allyl group with an electrophile (scheme 2.3). This method would represent a multicomponent reaction in which the alkoxide is derivatized in a one-pot process.

Scheme 2.3



Attempts to capture the alkoxide with trimethylsilylchloride or *p*-toluenesulfonic anhydride were unsuccessful (scheme 2.4). In both cases, a mixture of starting material and aldehyde was obtained.

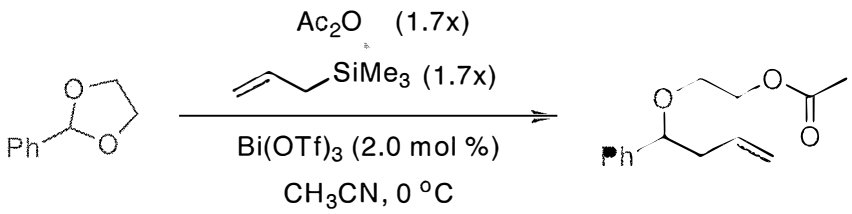
Scheme 2.4



Gratifyingly, we were able to trap the alkoxide intermediate with acetic anhydride (scheme 2.5), a protocol that allowed for the synthesis of highly functionalized esters in a one-

pot process. There are no literature reports for the allylation of cyclic acetals involving an *in situ* derivatization of the alkoxide, and thus, this new procedure is especially attractive. Such multicomponent reactions reduce the time and number of steps associated with a synthesis because isolation of intermediates is unnecessary.

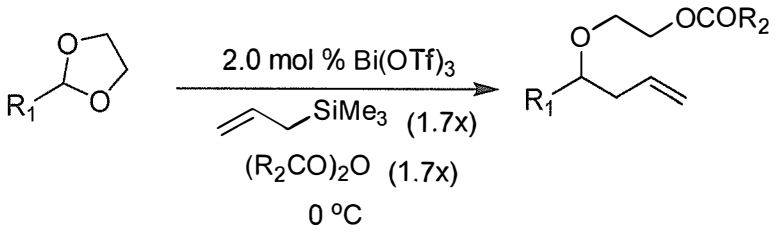
Scheme 2.5



An efficient one-pot procedure for the synthesis of highly functionalized ester products was thus developed.[89] The protocol was applied to the allylation of a number of aryl and aliphatic dioxolanes (table 2.1).

Although the initial work was performed using acetonitrile as the solvent, the reactions were also found to proceed smoothly under solvent-free conditions. This reduces the amount of waste associated with the reaction. Products were initially isolated by aqueous work-up followed by filtration through a silica column. The unacceptably low purity of crude products and the difficulty of removing anhydrides during work-up prompted us to consider a direct filtration of the reaction mixture through a silica gel column. This simple purification eliminates the need for a tedious aqueous work-up and reduces the total amount of organic waste associated with the synthesis.

Table 2.1: Bismuth(III) Triflate Catalyzed Allylation of 1,3-Dioxolanes



R_1	R_2	t	Yield (%)
p-ClC_6H_4	Me	40 min	67[a]
p-$CH_3C_6H_4$	Me	1 h	43[b]
o-BrC_6H_4	Me	1 h	62[b,c]
o-FC_6H_4	Me	1 h	61[b]
m-BrC_6H_4	Me	45 min	73[b]
$CH_3(CH_2)_8$	Me	21 h 30 min	73[b,c]
p-ClC_6H_4	^{i}Pr	35 min	36[a]
o-BrC_6H_4	^{i}Pr	4 h 30 min	47[a]
o-ClC_6H_4	^{i}Pr	1h 15 min	53[a]
$CH_3(CH_2)_8$	^{i}Pr	3 h 35 min	44[a]
o-BrC_6H_4	^{t}Bu	2 h 40 min	54[a]

[a] Reaction mixture was loaded onto silica gel and eluted with EtOAc/ heptane

[b] Product was isolated by aqueous work-up followed by flash chromatography

[c] Reaction carried out in CH_3CN at rt

This transformation was successful with a low catalyst loading (2.0 mol %) and under mild, solvent-free reaction conditions. This contrasts sharply with previous reports in which stoichiometric loadings of corrosive catalysts ($TiCl_4$, TMSOTf, $SnCl_4$) were necessary to

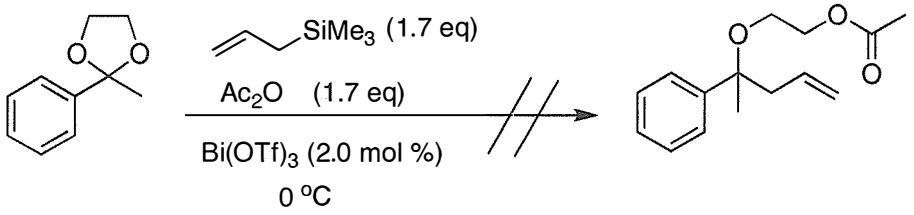
promote allylation. Reaction times were relatively short (1-4 h), with the exception of aliphatic dioxolanes which required longer reaction times. All reactions proceeded at 0 °C and under mild, solvent-free conditions. Many methods reported to date require low temperature conditions (-78 °C).

Moreover, many of the previous procedures were only applied to a few dioxolanes. Our protocol was amenable to a variety of aliphatic and substituted aryl dioxolanes. Electron-rich aryl dioxolanes underwent allylation with a low catalyst loading (2.0 mol %).

A variety of acid anhydrides such as acetic anhydride, isobutyric anhydride and trimethylacetic anhydride were successfully employed for the *in situ* derivatization of the alkoxide intermediate. However, the yield of the product dropped with use of hindered anhydrides. Thus, structural diversity can be introduced into the ester product by altering both the dioxolane and acid anhydride utilized. Furthermore, the highly functionalized product is formed via a one-pot procedure from commercially available or readily accessible dioxolane starting materials.

Attempts to apply the protocol to the allylation of 1,3-dioxolanes derived from ketones were unsuccessful. A mixture of starting material and acetophenone was isolated when the 1,3-dioxolane derived from acetophenone was subjected to the established reaction conditions (scheme 2.6).

Scheme 2.6



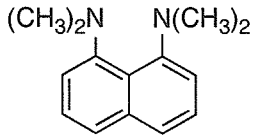
B. Mechanistic Studies on the Bismuth(III) Triflate-Catalyzed Allylation of Dioxolanes

In order to determine the mechanism by which bismuth(III) triflate is catalyzing the allylation of dioxolanes, a number of control experiments were performed (scheme 2.7). Though it was hypothesized that bismuth triflate is acting as a Lewis acid, it is also possible that the reaction is protic acid catalyzed. Triflic acid generated in solution by the hydrolysis of bismuth triflate could potentially be catalyzing the allylation of dioxolanes.

As was already established, the allylation of 2-(2-bromophenyl)-1,3-dioxolane catalyzed by bismuth triflate (2.0 mol %) proceeded to completion in an hour. The allylation does not proceed in the absence of a catalyst. When triflic acid (5.0 mol %) was used as a catalyst for the allylation, a mixture of desired product and aldehyde was detected by GC analysis of the reaction mixture.

The bismuth triflate-catalyzed allylation was also conducted in the presence of 1,8-(dimethylamino)napthalene (Proton Sponge^{TM})[90] (figure 2.1).

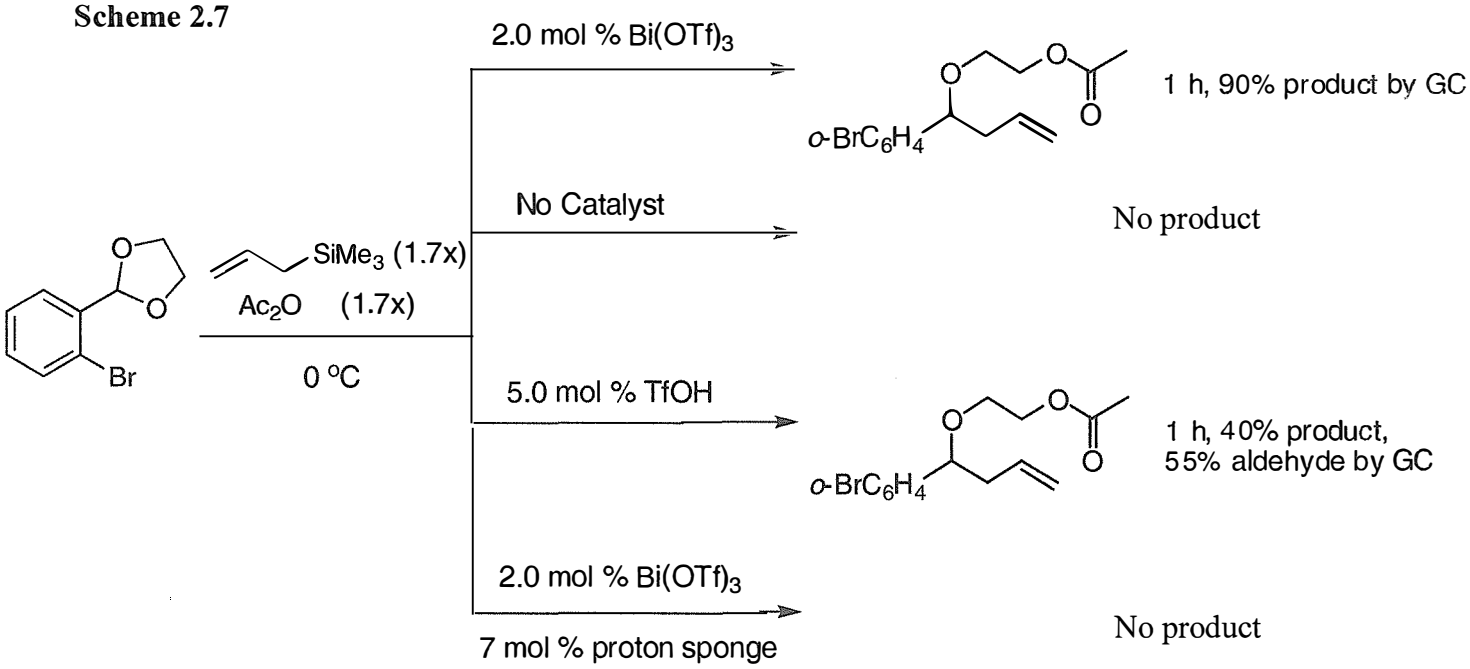
Figure 2.1



Proton Sponge™
1,8-bis(dimethylamino)napthalene

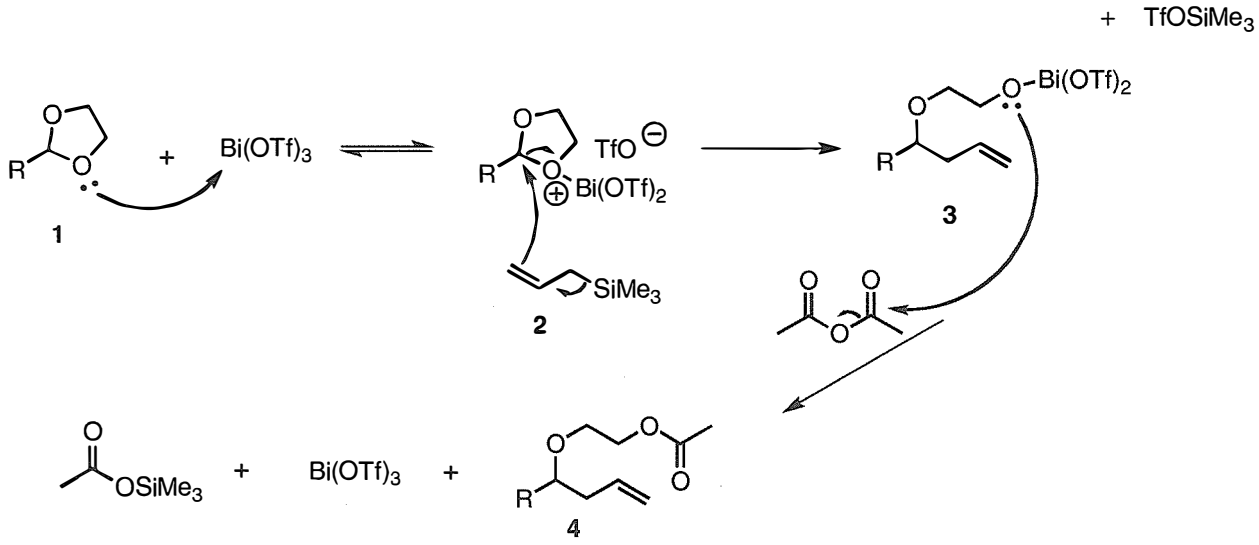
Under these conditions, no product or aldehyde was observed by GC. While this might suggest that the reaction is protic acid catalyzed, it is also possible that the amino functionalities of 1,8-(dimethylamino)napthalene are strongly coordinating to bismuth triflate, rendering it unable to catalyze the reaction. More studies are necessary to determine bismuth triflate's role in catalyzing the allylation of dioxolanes.

Scheme 2.7



A proposed mechanism for allylation involving activation of the dioxolane by bismuth triflate is shown (scheme 2.8).

Scheme 2.8

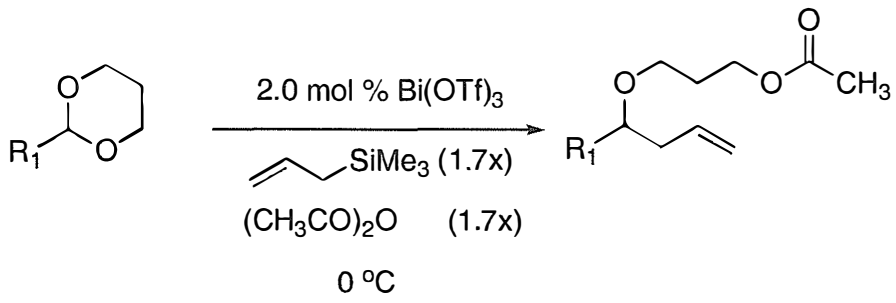


C. Allylation of 1,3-Dioxanes followed by *in situ* Derivitization with Acid Anhydrides Catalyzed by Bismuth(III) Triflate

When compared to the allylation of 1,3-dioxolanes, there is very little precedent for the allylation of 1,3-dioxanes in the literature. Furthermore, the established methods utilize stoichiometric quantities of corrosive catalysts ($TiCl_4$/Ti(O-*i*-Pr)$_4$ or TMSOTf). Hunter and coworkers utilized allyl borates as the source of the allyl group[87] (scheme 1.52). These compounds must be prepared in lab, detracting from the utility of this procedure. Denmark and coworkers utilized a large excess (8 eq) of allyltrimethylsilane or the highly toxic allyltributylstannane as the allyl source[88] (scheme 1.53). Thus, our goal was to apply the previously developed allylation methodology to the allylation of 1,3-dioxanes. This would constitute the first catalytic allylation of 1,3-dioxanes reported in the literature.

The previously developed procedure was applied to the allylation of a number of aryl and aliphatic 1,3-dioxanes (table 2.2). Though the acetal center is more electron-rich in dioxanes than dioxolanes as supported by ^{13}C NMR data, the allylations all proceeded to completion with a low catalyst loading (2.0 mol %). In all cases, acetic anhydride was used to derivatize the alkoxides *in situ*. The resulting functionalized esters were isolated in moderate to good yields.

Table 2.2: Bismuth(III) Triflate Catalyzed Allylation of 1, 3-Dioxanes

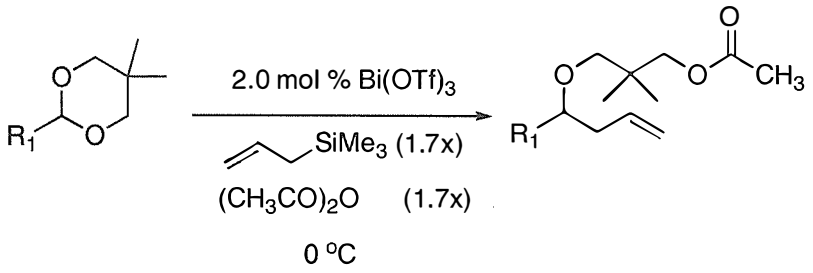


R	t	Yield[a] (%)
o-BrC_6H_4	1 h 30 min	79
p-BrC_6H_4	2 h	65
p-ClC_6H_4	2 h	70
p-$CH_3C_6H_4$	1 h 30 min	60
m-$CH_3OC_6H_4$	1 h 30 min	70
$CH_3(CH_2)_8$	4 h	75
$BrCH_2CH_2$	2 h 30 min	70

[a] Reaction mixture was loaded onto silica gel and eluted with EtOAc/ heptane

The allylation of 5,5-dimethyl substituted 1,3-dioxanes was also explored using the developed conditions. The allylation and *in situ* derivatization of aryl and aliphatic 5,5-dimethyl-1,3-dioxanes was successful under mild conditions (table 2.3). The ester products were isolated in moderate to good yields in all cases.

Table 2.3: Bismuth(III) Triflate Catalyzed Allylation of 5, 5-Dimethyl -1, 3-Dioxanes



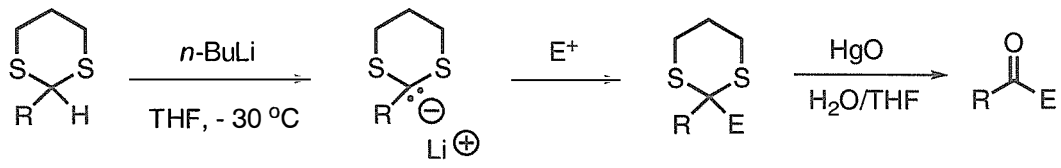
R	t	Yield (%)
p-ClC_6H_4	10 min	74[b]
p-$CH_3C_6H_4$	30 min	83[a]
$CH_3(CH_2)_8$	3 h 30 min	72[b]

[a] Reaction mixture was loaded onto silica gel and eluted with EtOAc/ heptane. [b] Product was isolated by aqueous work-up followed by flash chromatography.

D. Allylation of 1,3-Dithianes followed by *in situ* Derivitization with Acid Anhydrides Catalyzed by Bismuth(III) Triflate

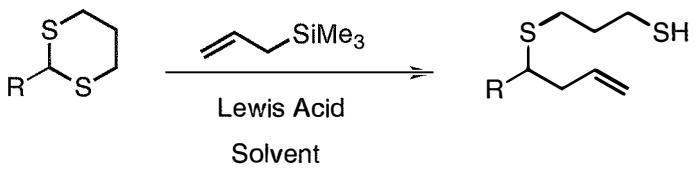
1,3-Dithianes have received significant attention in the literature as protecting groups for carbonyl compounds.[80] Also, their application in the "Umpolung" chemistry pioneered by Seebach and Corey is well precedented[91] (scheme 2.9).

Scheme 2.9



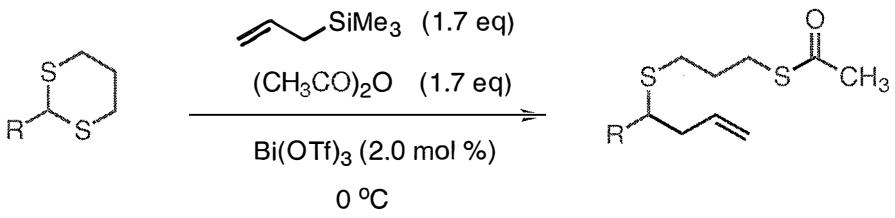
Dithianes can be also be potentially converted to other useful functional groups. To date, there has been no report of a Hosomi-Sakurai type allylation of dithianes to yield functionalized thiols (scheme 2.10).

Scheme 2.10



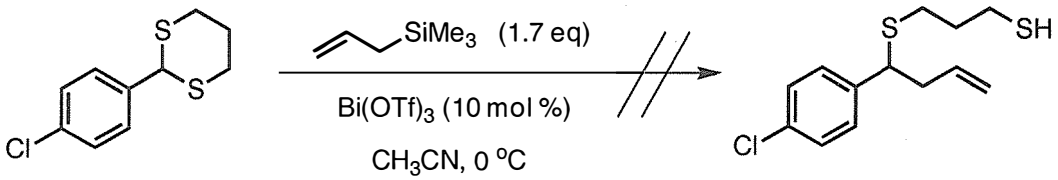
This total lack of literature precedent for the allylation of 1,3-dithianes prompted our interest in extending the established bismuth(III) triflate catalyzed allylation methodology to this functionality. A one-pot allylation and *in situ* derivatization of 1,3-dithianes with acid anhydrides would constitute an efficient synthesis of functionalized thioesters (scheme 2.11).

Scheme 2.11



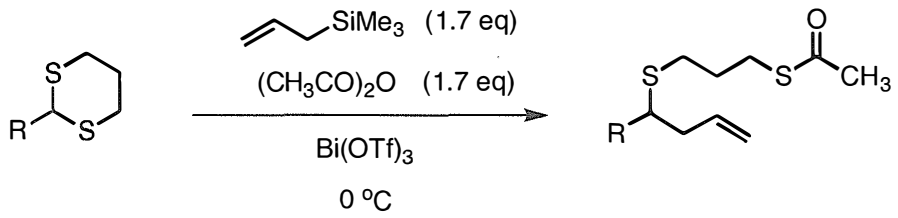
Initial attempts to allylate 2-(4-chlorophenyl)-1,3-dithiane to yield the corresponding functionalized thiol were unsuccessful (scheme 2.12). GC analysis of the reaction mixture indicated that no reaction was taking place.

Scheme 2.12



However, by using a protocol similar to the allylation of dioxolanes and dioxanes, the thiolate intermediate was successfully trapped with acetic anhydride to yield the corresponding thioester. This strategy was applied to a handful of aryl and aliphatic dithianes, yielding the corresponding thioesters in moderate to good yields (table 2.4).

Table 2.4: Bismuth(III) Triflate Catalyzed Allylation of 1,3-Dithianes



R	mol % $Bi(OTf)_3$	t	Yield[b] (%)
C_6H_5	2.0[a]	3 h 45 min	78
p-ClC_6H_4	2.0	2 h 45 min	65
m-$CH_3C_6H_4$	4.0	4 h 30 min	74
$CH_3(CH_2)_8$	10.0	3 h 30 min	63

[a] An additional 2.0 mol % $Bi(OTf)_3$ was added after 3 h. [b] Reaction mixture was loaded onto silica gel and eluted with EtOAc/ heptane.

The allylation of 1,3-dithianes proceeded smoothly under mild, solvent-free conditions with low catalyst loadings (2.0 –10.0 mol %). Although allylation of dioxolanes and dioxanes proceeded

with a 2.0 mol % loading of bismuth(III) triflate, electron-rich aryl dithianes and aliphatic dithianes required more catalyst (4.0 – 10.0 mol %) for the reactions to proceed to completion.

To the best of our knowledge, this procedure represents the first example of the application of 1,3-dithianes as substrates for the Hosomi-Sakurai reaction. Furthermore, the method utilizes a non-toxic and non-corrosive catalyst and solvent-free conditions.

Conclusions

A robust and highly catalytic method for the allylation and *in situ* derivatization of a number of cyclic acetals (dioxolanes, dioxanes, and dithianes) has been developed. There has been little precedent in the literature for the allylation of these functionalities. Most reagents used to date for the allylation of cyclic acetals are highly corrosive or toxic and are often required in stoichiometric amounts. In contrast, the use of a relatively non-toxic and non-corrosive bismuth(III) based catalyst and the lack of an aqueous waste stream make the developed methodology environmentally benign and attractive.

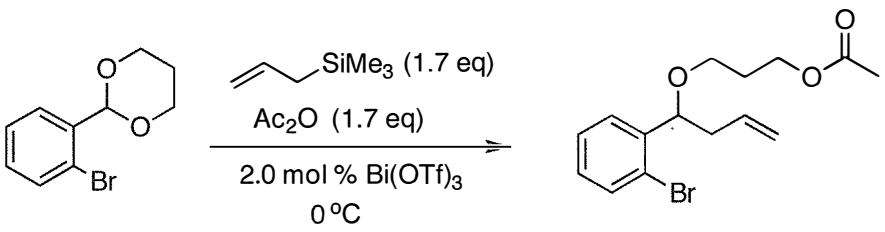
III. Experimental

A. General Experimental:

Bismuth(III) triflate was purchased from Aldrich Chemical Company and stored under vacuum. Allyltrimethylsilane was purchased from Acros Chemical Company or Aldrich Chemical Company. Acetic anhydride was purchased from Fisher Scientific. Dioxanes and dithianes were prepared in lab following procedures developed in our group or literature protocols.[80] Products were analyzed using a JEOL Eclipse NMR Spectrometer at 270 MHz for ^{1}H NMR and 67.5 MHz for ^{13}C NMR in $CDCl_3$ as the solvent. GC analysis was performed on a Varian CP-3800 Gas Chromatograph equipped with a 30 m silica-packed column with a diameter of 0.25 mm (Conditions: hold at 100 °C for 1 min; ramp at 30 °C/min until 220 °C ; hold at 220 °C; flow rate; 2.0 mL/min of He). Thin-layer Chromatography was performed on alumina backed silica gel plates. Spots were visualized under UV light (when a UV active chromophore was present) and by spraying the plate with phosphomolybdic acid followed by heating. Purifications were performed by flash chromatography on silica gel.[92] Products were characterized by ^{1}H NMR, ^{13}C NMR, and GC. Satisfactory elemental analysis or High Resolution Mass Spectrometry (HRMS) data was obtained for all new compounds.

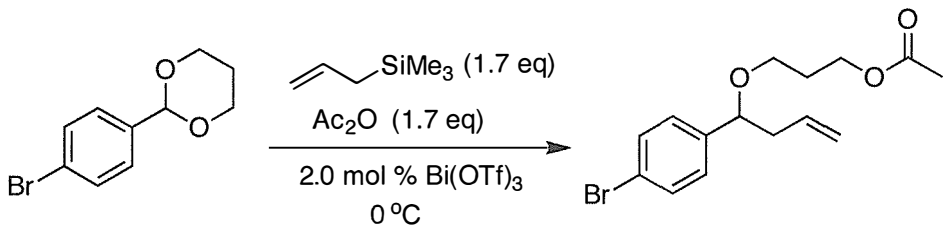
B. Bismuth(III) Triflate Catalyzed Allylation of 1,3-Dioxanes

Allylation of 2-(2-bromophenyl)-1,3-dioxane (MJS2057fr2051)



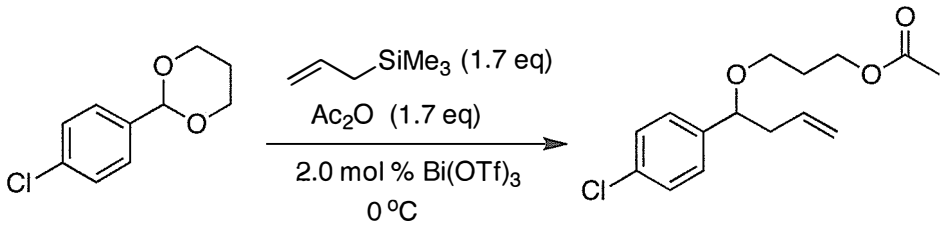
A homogeneous mixture of 2-(2-bromophenyl)-1,3-dioxane (0.2450 g, 1.008 mmol), allyltrimethylsilane (0.2723 mL, 0.1958 g, 1.713 mmol, 1.7 eq), and acetic anhydride (0.1620 mL, 0.1749 g, 1.713 mmol, 1.7 eq) was stirred at 0 °C under N_2 in a flame-dried three-neck rbf as bismuth(III) triflate (0.0132 g, 0.0202 mmol, 2.0 mol %) was added. The reaction mixture immediately acquired a light yellow color. Reaction progress was followed by gas chromatography. After 1 h 30 min, the reaction mixture was loaded onto 65 g of silica gel and eluted with EtOAc/heptane (5/95, v/v). Fifty-eight fractions (8 mL) were collected after a 100 mL prefraction. Fractions 20 to 51 were combined and concentrated to yield 0.26 g (79 %) of a clear, colorless liquid product that was determined to be 97 % pure by GC analysis and ^{1}H & ^{13}C NMR spectroscopy. ^{1}H NMR: δ 1.84-1.89 (m, 2 H), 1.99 (s, 3 H), 2.39-2.44 (m, 2 H), 3.34-3.38 (m, 2 H), 4.13-4.18 (t, 2 H, J = 6.43 Hz), 4.68-4.71 (m, 1 H), 5.00-5.07 (m, 2 H), 5.80-5.86 (m, 1 H). 7.10-7.51 (m, 4 H). ^{13}C: (15 peaks) δ 171.0, 141.2, 134.4 132.6, 128.7, 127.6, 127.6, 122.9, 117.0, 80.2, 65.4, 61.6, 41.1, 28.9, 20.9. HRMS-EI (*m/z*): M^+ calcd for $C_{15}H_{19}BrO_3Na$, 349.0415; found, 349.0423.

Allylation of 2-(4-bromophenyl)-1,3-dioxane (MJS1185fr5069)



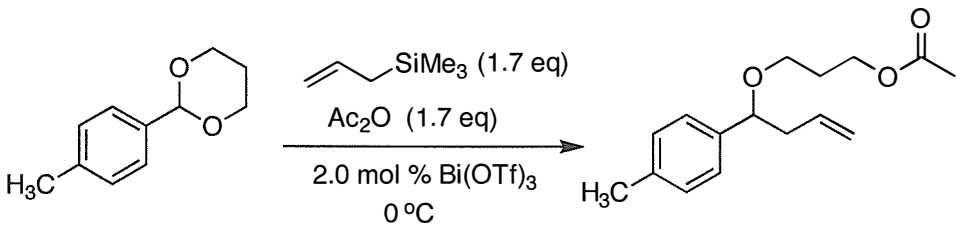
A homogenous mixture of 2-(4-bromophenyl)-1,3-dioxane (0.2501 g, 1.029 mmol), allyltrimethylsilane (0.2779 mL, 0.1998 g, 1.749 mmol, 1.7 eq), and acetic anhydride (0.1653 mL, 0.1785 g, 1.749 mmol, 1.7 eq) was stirred at 0 °C under N_2 in a flame-dried three-neck rbf as bismuth(III) triflate (0.0135 g, 0.0206 mmol, 2.0 mol %) was added. The reaction mixture immediately acquired a light yellow color. Reaction progress was followed by gas chromatography. After 2 h, the reaction mixture was loaded onto 65 g of silica gel and eluted with EtOAc/ heptane (5/95, v/v). Seventy-two fractions (8 mL) were collected after a 100 mL prefraction. Fractions 50 to 69 were combined and concentrated to yield 0.22 g (65 %) of a clear, colorless liquid product that was determined to be 98 % pure by GC analysis and ^1H & ^{13}C NMR spectroscopy. ^1H NMR: δ 1.82-1.86 (m, 2 H), 1.98 (s, 3 H), 2.32-2.50 (m, 2 H), 3.31-3.34 (m, 2 H), 4.10-4.15 (m, 3 H), 4.96-5.02 (m, 1 H), 5.65-5.76 (m, 1 H), 7.11-7.14 (d, 2 H, J = 8.15 Hz), 7.42-7.45 (d, 2 H, J = 8.15 Hz). ^{13}C: (13 peaks) δ 171.0, 141.1, 134.2, 131.4, 128.3, 121.3, 117.2, 81.5, 65.0, 61.6, 42.4, 28.9, 20.9. HRMS-EI (*m/z*): M^+ calcd for $C_{15}H_{19}BrO_3Na$, 349.0415; found, 349.0417.

Allylation of 2-(4-chlorophenyl)-1,3-dioxane (MJS1179fr8099)



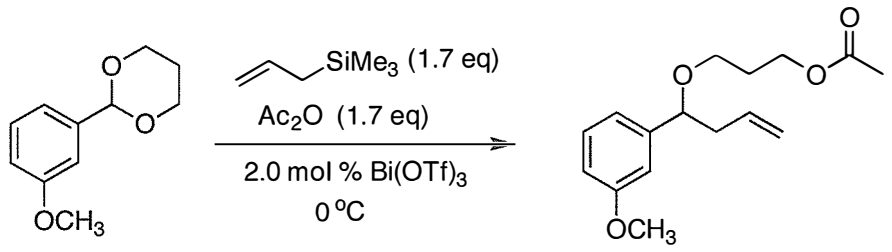
A homogenous mixture of 2-(4-chlorophenyl)-1,3-dioxane (0.2500 g, 1.259 mmol), allyltrimethylsilane (0.3399 mL, 0.2445 g, 2.140 mmol, 1.7 eq), and acetic anhydride (0.2022 mL, 0.2184 g, 2.140 mmol, 1.7 eq) was stirred at 0 °C under N_2 in a flame-dried three-neck rbf as bismuth(III) triflate (0.0165 g, 0.0252 mmol, 2.0 mol %) was added. The reaction mixture immediately acquired a light yellow color. Reaction progress was followed by gas chromatography. After 2 h, the reaction mixture was loaded onto 66 g of silica gel and eluted with EtOAc/heptane (5/95, v/v). One hundred and six fractions (4 mL) were collected. Fractions 80 to 99 were combined and concentrated to yield 0.25 g (70 %) of a clear, colorless liquid product that was determined to be 98 % pure by GC analysis and ^{1}H & ^{13}C spectroscopy. ^{1}H NMR: δ 1.82-1.89 (m, 2 H), 1.98 (s, 3 H), 2.32-2.54 (m, 2 H), 3.31-3.34 (m, 2 H), 4.11-4.20 (m, 3 H), 4.97-5.03 (m, 2 H), 5.66-5.76 (m, 1 H), 7.17-7.31 (m, 4 H). ^{13}C: (13 peaks) δ 171.0, 140.6, 134.2, 133.1, 128.4, 128.0, 117.2, 81.4, 65.0, 61.5, 42.4, 28.9, 20.9. HRMS-EI (*m/z*): M^+ calcd for $C_{15}H_{19}ClO_3Na$, 305.0920; found, 305.0913.

Allylation of 2-(4-tolyl)-1,3-dioxane (MJS2051fr3052)



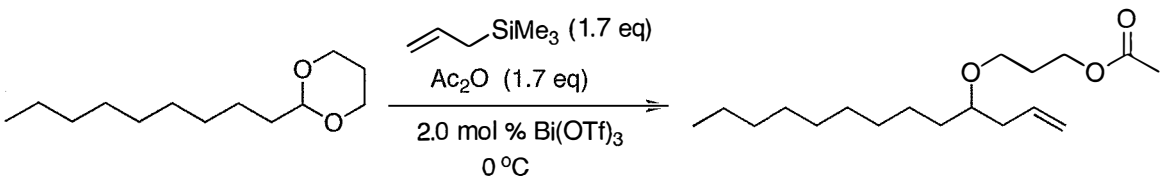
A homogenous mixture of 2-(4-tolyl)-1,3-dioxane (0.2497 g, 1.402 mmol), allyltrimethylsilane (0.3788 mL, 0.2723 g, 2.383 mmol, 1.7 eq), and acetic anhydride (0.2253 mL, 0.2433 g, 2.383 mmol, 1.7 eq) was stirred at 0 °C under N_2 in a flame-dried three-neck rbf as bismuth(III) triflate (0.0184 g, 0.0280 mmol, 2.0 mol %) was added. The reaction mixture immediately acquired a bright pink color. Reaction progress was followed by gas chromatography. After 1 h 30 min, the reaction mixture was loaded onto 60 g of silica gel and eluted with EtOAc/heptane (5/95, v/v). Sixty fractions (8 mL) were collected. Fractions 30 to 52 were combined and concentrated to yield 0.22 g (60 %) of a clear, colorless liquid product that was determined to be 99 % pure by GC analysis and ^1H & ^{13}C spectroscopy. ^1H NMR: δ 1.82-1.89 (m, 2 H), 1.98 (s, 3 H), 2.33 (s, 3 H), 2.37-2.56 (m, 2 H), 3.29-3.35 (m, 2 H), 4.11-4.16 (m, 3 H), 4.97-5.05 (m, 2 H), 5.70-5.76 (m, 1 H). 7.11-7.17 (m, 4 H). ^{13}C: (14 peaks) δ 171.1, 139.0, 137.2, 135.0, 129.0, 126.6, 116.7, 82.0, 64.8, 61.8, 42,6, 29.0, 21.1, 20.9. Anal. Calcd for $C_{16}H_{22}O_3$: C, 73.25; H, 8.45. Found: C, 73.08; H, 8.45.

Allylation of 2-(3-methoxyphenyl)-1,3-dioxane (MJS1191fr2433)



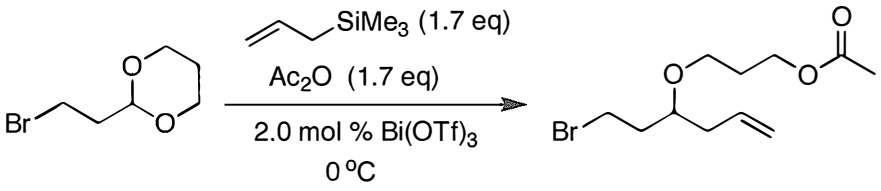
A homogenous mixture of 2-(3-methoxyphenyl)-1,3-dioxane (0.2504 g, 1.289 mmol), allyltrimethylsilane (0.3483 mL, 0.2504 g, 2.192 mmol, 1.7 eq), and acetic anhydride (0.2072 mL, 0.2237 g, 2.192 mmol, 1.7 eq) was stirred at 0 °C under N_2 in a flame-dried rbf as bismuth(III) triflate (0.0169 g, 0.0258 mmol, 2.0 mol %) was added. The reaction mixture immediately acquired a dark red color. Reaction progress was followed by gas chromatography and TLC. After 1 h 30 min, the reaction mixture was loaded onto 60 g of silica gel and eluted with EtOAc/hexanes (10/90, v/v) for fractions 1-24 and EtOAc/hexanes (20/80, v/v) for fractions 24-57. Fifty-seven fractions (8 mL) were collected after a 100 mL prefraction. Fractions 24 to 33 were combined and concentrated to yield 0.25 g (70 %) of a clear, colorless liquid that was determined to be 99 % pure by GC analysis and ^1H & ^{13}C NMR spectroscopy. ^1H NMR: δ 1.83-1.87 (m, 2 H), 1.98 (s, 3 H), 2.35-2.52 (m, 2 H), 3.30-3.38 (m, 2 H), 3.79 (s, 3 H), 4.11-4.16 (m, 3 H), 4.97-5.05 (m, 2 H), 5.70-5.80 (m, 1 H), 6.78-6.85 (m, 3 H), 7.20-7.26 (m, 1 H). ^{13}C: (16 peaks) δ 171.1, 159.7, 143.8, 134.8, 129.3, 119.0, 116.8, 112.9, 111.9, 82.0, 65.0, 61.7, 55.1, 42.5, 28.9, 20.9. Anal. Calcd for $C_{16}H_{22}O_4$: C, 69.04; H, 7.97. Found: C, 68.83; H, 7.94.

Allylation of 2-nonyl-1,3-dioxane (MJS2059fr3463)



A homogenous mixture of 2-nonyl-1,3-dioxane (0.2509 g, 1.176 mmol), allyltrimethylsilane (0.3177 mL, 0.2284 g, 1.999 mmol, 1.7 eq), and acetic anhydride (0.2041 mL, 0.1889 g, 1.999 mmol, 1.7 eq) was stirred at 0 °C under N_2 in a flame-dried rbf as bismuth(III) triflate (0.0154 g, 0.0235 mmol, 2.0 mol %) was added. The reaction mixture immediately acquired a light yellow color. Reaction progress was followed by gas chromatography and TLC. After 4 h, the reaction mixture was loaded onto 75 g of silica gel and eluted with EtOAc/hexanes (3/97, v/v). Sixty-six fractions (8 mL) were collected after a 100 mL prefraction. Fractions 34 to 63 were combined and concentrated to yield 0.25 g (75 %) of a clear, colorless liquid that was determined to be 97 % pure by GC analysis and ^{1}H & ^{13}C NMR spectroscopy. ^{1}H NMR: δ 0.85 (t, 3 H, J = 6.91 Hz), 1.24 (s, 14 H), 1.39-1.43 (m, 2 H), 1.80-1.89 (m, 2 H), 2.02 (s, 3 H), 2.22 (t, 2 H, J = 6.18 Hz), 3.20-3.29 (m, 1 H), 3.40-3.57 (m, 2 H), 4.14 (t, 2 H, J = 6.42 Hz), 5.00-5.06 (m, 2 H), 5.71-5.86 (m, 1 H). ^{13}C: (18 peaks) δ 171.1, 135.1, 116.7, 79.3, 65.2, 61.8, 38.3, 33.8, 31.9, 29.7, 29.6, 29.6, 29.4, 29.3, 25.4, 22.7, 21.0, 14.1. HRMS-EI (*m/z*): M^+ calcd for $C_{18}H_{34}O_3Na$, 321.2406; found, 321.2416.

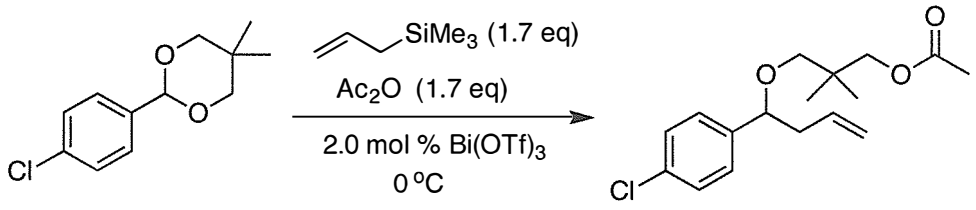
Allylation of 2-(2-bromoethyl)-1,3-dioxane (MJS2107fr4460)



A homogenous mixture of 2-(2-bromoethyl)-1,3-dioxane (0.2545 g, 1.305 mmol), allyltrimethylsilane (0.3525 mL, 0.2534 g, 2.218 mmol, 1.7 eq), and acetic anhydride (0.2097 mL, 0.2264 g, 2.218 mmol, 1.7 eq) was stirred at 0 °C under N_2 in a flame-dried rbf as bismuth(III) triflate (0.0171 g, 0.0261 mmol, 2.0 mol %) was added. The reaction mixture immediately acquired a light brown color. Reaction progress was followed by gas chromatography. After 2 h 30 min, the reaction mixture was loaded onto 60 g of silica gel and eluted with EtOAc/hexanes (5/95, v/v). Sixty fractions (8 mL) were collected. Fractions 44 to 60 were combined and concentrated to yield 0.2569 g (70 %) of a clear, colorless liquid that was determined to be 98 % pure by GC analysis and ^1H & ^{13}C NMR spectroscopy. ^1H NMR: δ 1.83-1.96 (m, 4 H), 2.03 (s, 3 H), 2.24-2.29 (m, 2 H), 3.45-3.51 (m, 4 H), 3.60-3.66 (m, 1 H), 4.11-4.16 (m, 2 H), 5.04-5.10 (m, 2 H), 5.71-5.81 (m, 1 H). ^{13}C: (11 peaks) δ 171.1, 133.9, 117.6, 76.5, 65.6, 61.6, 37.9, 37.3, 30.4, 29.2, 21.0. HRMS-EI (*m/z*): $[M + H]^+$ calcd for $C_{11}H_{20}BrO_3$, 279.0596; found, 279.0598.

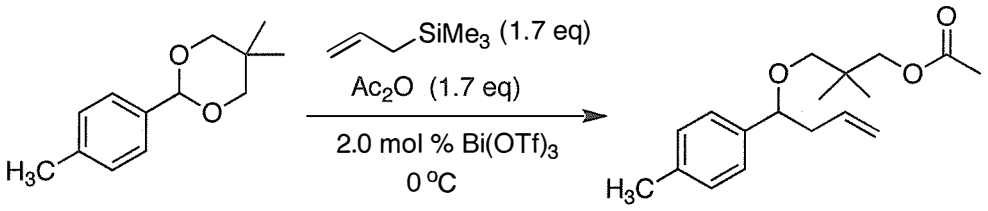
C. Bismuth(III) Triflate Catalyzed Allylation of 5,5-Dimethyl-1,3-Dioxanes

Allylation of 2-(4-chlorophenyl)-5,5-dimethyl-1,3-dioxane (EB1123fr3343)



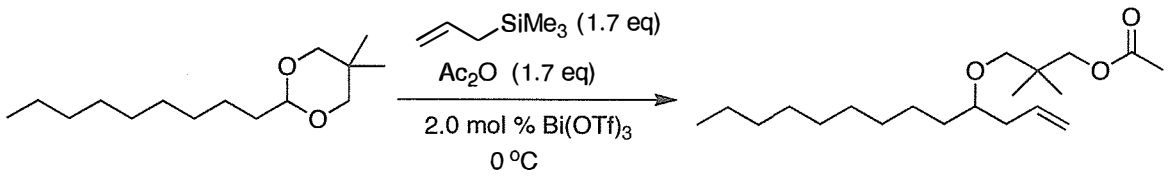
A homogenous mixture of 2-(4-chlorophenyl)-5,5-dimethyl-1,3-dioxane (0.2500 g, 1.103 mmol), allyltrimethylsilane (0.2979 mL, 0.2142 g, 1.875 mmol, 1.7 eq), and acetic anhydride (0.1786 mL, 0.1929 g, 1.875 mmol, 1.7 eq) was stirred at 0 °C under N_2 in a flame-dried three-neck rbf as bismuth(III) triflate (0.0724 g, 0.110 mmol, 10.0 mol %) was added. The reaction mixture immediately acquired a bright orange color. Reaction progress was followed by gas chromatography. After 10 min, the reaction mixture was stirred with 10% Na_2CO_3 (15 mL) for 25 minutes. The mixture was extracted with EtOAc (3 x 10 m:). The combined organic layers were washed with sat. NaCl (20 mL), dried (Na_2SO_4), and concentrated to yield 0.3360 g (98 %) of a yellow liquid that was determined to be 90 % pure by GC and ^{1}H NMR. The crude product was loaded onto 22 g of silica gel and eluted with EtOAc/ heptane (2.5/97.5, v/v). Sixty-five fractions (4 mL) were collected. Fractions 35 to 51 were combined and concentrated to yield 0.2534 g (74 %) of a clear, colorless liquid product that was determined to be 95 % pure by GC analysis and ^{1}H spectroscopy. ^{1}H NMR: δ 0.87 (s, 3H), 0.89 (s, 3 H), 1.98 (s, 3 H), 2.24-2.53 (m, 2 H), 2.95-3.05 (q, 2 H, J = 8.64 Hz), 3.87 (dd, 2 H, J = 10.63, 2.21 Hz), 4.11-4.16 (m, 1 H), 4.96-5.02 (m, 2 H), 5.66-5.81 (m, 1 H), 7.15-7.18 (m, 2 H), 7.26-7.30 (m, 2 H). ^{13}C: (14 peaks): δ 171.2, 140.9, 134.5, 133.0, 128.4, 127.9, 117.0, 81.7, 74.4, 69.7, 42.6, 35.3, 21.9, 20.9. HRMS-EI (*m/z*): M^+ calcd for $C_{17}H_{23}ClO_3Na$, 333.1233; found, 333.1247.

Allylation of 2-(4-tolyl)-5,5-dimethyl-1,3-dioxane (MJS2063fr1034)



A homogenous mixture of 2-(4-tolyl)-5,5-dimethyl-1,3-dioxane (0.2590 g, 1.256 mmol), allyltrimethylsilane (0.3392 mL, 0.2439 g, 2.135 mmol, 1.7 eq), and acetic anhydride (0.2018 mL, 0.2179 g, 2.135 mmol, 1.7 eq) was stirred at 0 °C under N_2 in a flame-dried three-neck rbf as bismuth(III) triflate (0.0165 g, 0.0251 mmol, 2.0 mol %) was added. The reaction mixture immediately acquired a light yellow color. Reaction progress was followed by gas chromatography. After 30 min, the reaction mixture was loaded onto 60 g of silica gel and eluted with EtOAc/heptane (5/95, v/v). Sixty fractions (8 mL) were collected after a 50 mL prefraction. Fractions 10 to 34 were combined and concentrated to yield 0.30 g (83 %) of a clear, colorless liquid product that was determined to be 99 % pure by GC analysis and ^{1}H & ^{13}C NMR spectroscopy. ^{1}H NMR: δ 0.88 (s, 3 H), 0.90 (s, 3 H), 1.99 (s, 3 H), 2.26-2.56 (m, 2 H), 2.33 (s, 3 H), 2.94-3.09 (dd, 2 H, J = 17.08, 8.64 Hz), 3.85-3.94 (t, 2 H, 10.58 Hz), 4.11-4.13 (m, 1 H), 4.96-5.00 (m, 2 H). 5.73-5.84 (m, 1 H), 7.13 (s, 4 H). ^{13}C: (15 peaks): δ 171.0, 139.3, 136.9, 135.1, 128.8, 126.4, 116.4, 82.1, 74.1, 69.7, 42.8, 35.3, 21.9, 21.0, 20.8. Anal. Calcd for $C_{18}H_{26}O_3$: C, 74.45; H, 9.02. Found: C, 74.15; H, 9.08.

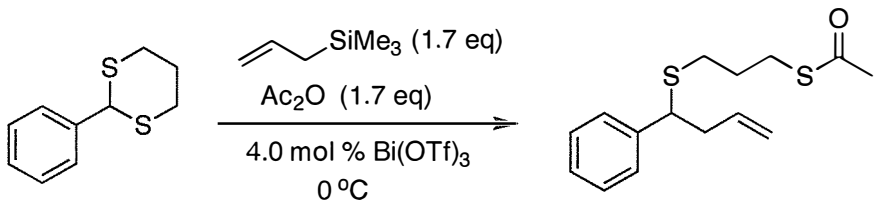
Allylation of 2-nonyl-5,5-dimethyl-1,3-dioxane (EB1125fr916)



A homogenous mixture of 2-nonyl-5,5-dimethyl-1,3-dioxane (0.2500 g, 1.031 mmol), allyltrimethylsilane (0.2786 mL, 0.2003 g, 1.754 mmol, 1.7 eq), and acetic anhydride (0.1676 mL, 0.1793 g, 1.754 mmol, 1.7 eq) was stirred at 0 °C under N_2 in a flame-dried three-neck rbf as bismuth(III) triflate (0.0135 g, 0.0206 mmol, 2.0 mol %) was added. The reaction mixture immediately acquired a pale yellow color. Reaction progress was followed by gas chromatography. After 3 h 30 min, the reaction mixture was stirred with 10% Na_2CO_3 (15 mL) for 25 minutes. The mixture was extracted with EtOAc (3 x 10 mL). The combined organic layers were washed with sat. NaCl (25 mL), dried (Na_2SO_4), and concentrated to yield 0.3152 g (98 %) of a dark brown liquid that was determined to be 83 % pure by GC and ^{1}H NMR. The crude product was loaded onto 12.5 g of silica gel and eluted with EtOAc/heptane (4/96, v/v). Twenty-five fractions (4 mL) were collected after a 100 mL prefraction. Fractions 5 to 16 were combined and concentrated to yield 0.2315 g (72 %) of a clear, colorless liquid product that was determined to be 97 % pure by GC analysis and ^{1}H & ^{13}C NMR spectroscopy. ^{1}H NMR: δ 0.85-0.89 (m, 9 H), 1.24-1.41 (m, 16 H), 2.03 (s, 3 H), 2.19 (t, 2 H, J = 6.91 Hz), 3.08-3.22 (m, 3 H), 3.86 (s, 2 H), 4.97-5.01 (m, 2 H), 5.72-5.83 (m, 1 H). ^{13}C (19 peaks): δ 171.0, 135.30, 116.48, 79.34, 74.53, 69.91, 38.29, 35.52, 33.80, 31.96, 29.81, 29.69, 29.65, 29.39, 25.36, 22.73, 22.05, 20.91, 14.15. HRMS-EI (*m/z*): M^+ calcd for $C_{20}H_{38}O_3Na$, 349.2719; found, 349.2735.

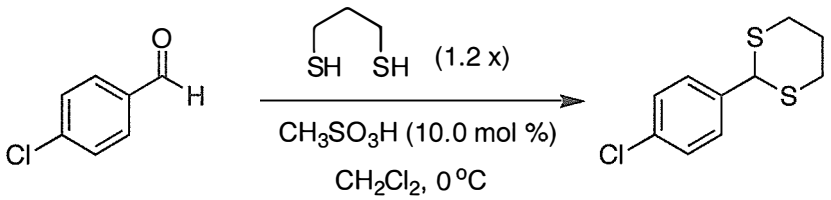
D. Bismuth(III) Triflate Catalyzed Allylation of 1,3-Dithianes

Allylation of 2-phenyl-1,3-dithiane (MJS2071fr1135)



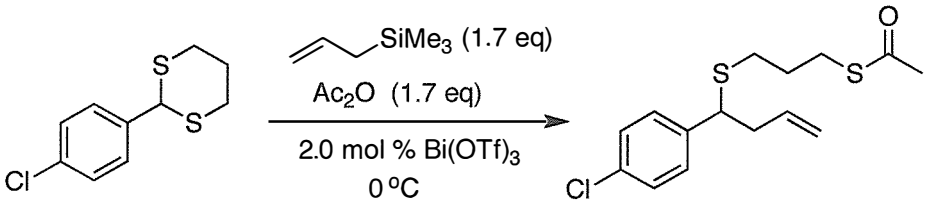
A homogenous mixture of 2-phenyl-1,3-dithiane (0.2530 g, 1.289 mmol), allyltrimethylsilane (0.3481 mL, 0.2503 g, 2.191 mmol, 1.7 eq), and acetic anhydride (0.2071 mL, 0.2236 g, 2.191 mmol, 1.7 eq) was stirred at 0 °C under N_2 in a flame-dried three-neck rbf as bismuth(III) triflate (0.0169 g, 0.0258 mmol, 2.0 mol %) was added. The reaction mixture immediately acquired a light yellow color. Reaction progress was followed by gas chromatography. After 3 h, additional bismuth(III) triflate (0.0169 g, 0.0258 mmol, 2.0 mol %) was added to the reaction mixture because starting material was detected by GC. After 3 h 45 min, the reaction mixture was loaded onto 70 g of silica gel and eluted with EtOAc/heptane (3/97, v/v) for the prefraction and EtOAC/heptane (5/95, v/v) for the fractions. Forty-eight fractions (8 mL) were collected after a 75 mL prefraction. Fractions 11 to 35 were combined and concentrated to yield 0.28 g (78 %) of a clear, colorless liquid product that was determined to be 98 % pure by GC analysis and ^{1}H spectroscopy. ^{1}H NMR: δ 1.67-1.73 (m, 2 H), 2.27-2.37 (m, 5 H), 2.56-2.61 (t, 2 H, J = 7.43 Hz), 2.80-2.88 (m, 2 H), 3.78-3.84 (t, 1 H, J = 7.43 Hz), 4.95-5.05 (m, 2 H), 5.64-5.74 (m, 1 H), 7.24-7.30 (m, 5 H). ^{13}C: (13 peaks) δ 195.5, 141.9, 135.2, 128.4, 127.8, 127.1, 116.9, 49.4, 40.8, 30.5, 29.7, 29.0, 28.0. HRMS-EI (*m/z*): M^+ calcd for $C_{15}H_{20}OS_2$, 280.0956; found, 280.0952.

Synthesis of 2-(4-chlorophenyl)-1,3-dithiane (MJS2095fr1444)



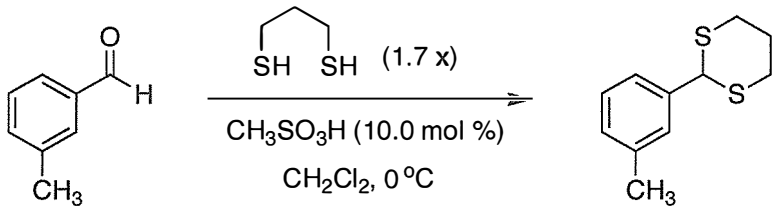
A solution of *p*-chlorobenzaldehyde (0.5428 g, 3.861 mmol) and 1,3-propanedithiol (0.4661 mL, 0.5015 g, 4.634 mmol, 1.2 eq) in CH_2Cl_2 (10 mL) was stirred at 0 °C in a three-neck rbf as methane sulfonic acid (0.0250 mL, 0.371 g, 0.386 mmol, 10.0 mol %) was added. Reaction progress was followed by gas chromatography. After 17 h 30 min, additional 1,3-propanedithiol (0.1942 mL, 0.2089 g, 1.930 mmol, 0.5 eq) and methane sulfonic acid (0.0125 mL, 0.0185 g, 0.193 mmol, 5.0 mol %) were added to the reaction mixture because SM was detected by GC. After 22 h, the reaction mixture was stirred with 2 M NaOH (20 mL) for 15 min. The mixture was extracted with CH_2Cl_2 (2 X 20 mL). The combined organic layers were washed with H_2O (2 X 40 mL) and sat. NaCl (40 mL), dried (Na_2SO_4), and concentrated to yield 0.8616 g (97 %) of a white solid that was determined to be 95 % pure by GC analysis and ^{1}H NMR. The crude product was loaded onto 50 g of silica gel and eluted with EtOAc/heptane (5/95, v/v). Sixty fractions (8 mL) were collected. Fractions 14 to 44 were combined and concentrated to yield 0.74 g (83 %) of a white solid that was determined to be >99 % pure by GC and ^{1}H NMR. ^{1}H NMR: δ 1.82-1.98 (m, 1 H), 2.13-2.21 (m, 1 H), 2.85-3.10 (m, 4 H), 5.12 (s, 1 H), 7.25-7.38 (m, 4 H).

Allylation of 2-(4-chlorophenyl)-1,3-dithiane (MJS2119fr2346)



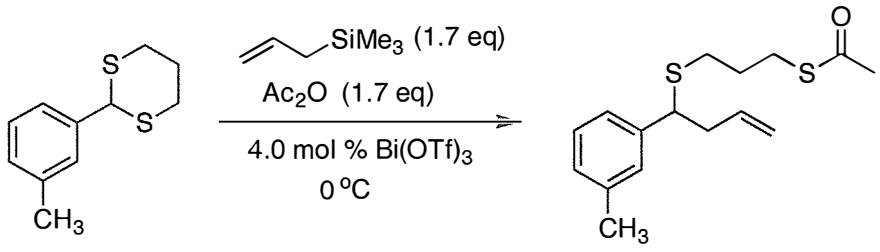
A homogenous mixture of 2-(4-chlorophenyl)-1,3-dithiane (02590 g, 1.122 mmol), allyltrimethylsilane (0.3032 mL, 0.2180 g, 1.908 mmol, 1.7 eq), and acetic anhydride (0.1803 mL, 0.1948 g, 1.908 mmol, 1.7 eq) was stirred at 0 °C under N_2 in a flame-dried three-neck rbf as bismuth(III) triflate (0.0147 g, 0.0225 mmol, 2.0 mol %) was added. The reaction mixture immediately acquired a light yellow color. Reaction progress was followed by gas chromatography. After 2 h 45 min, the reaction mixture was loaded onto 60 g of silica gel and eluted with EtOAc/heptane (3/97, v/v). Forty-eight fractions (8 mL) were collected after a 100 mL prefraction. Fractions 13 to 34 were combined and concentrated to yield 0.23 g (65 %) of a clear, colorless liquid product that was determined to be 98 % pure by GC analysis and ^{1}H spectroscopy. ^{1}H NMR: δ 1.68-1.73 (m, 2 H), 2.26-2.31 (m, 5 H), 2.51-2.58 (m 2 H), 2.75-2.91 (m, 2 H), 3.75-3.81 (t, 3 H, J = 7.40 Hz), 4.96-5.03 (m, 2 H), 5.60-5.70 (m, 1 H), 7.24-7.26 (m, 4 H). ^{13}C: (13 peaks) δ 195.6, 140.5, 134.8, 132.7, 129.2, 128.6, 117.3, 48.8, 40.8, 30.6, 29.7, 29.0, 28.0. HRMS-EI (*m/z*): M^+ calcd for $C_{15}H_{19}ClOS_2$, 314.0566; found, 314.0564.

Synthesis of 2-(3-tolyl)-1,3-dithiane (MJS2101crude)



A solution of *m*-tolualdehyde (0.5081 g, 4.229 mmol) and 1,3-propanedithiol (0.7231 mL, 0.7781 g, 7.189 mmol, 1.7 eq) in CH_2Cl_2 (10 mL) was stirred at 0 °C in a three-neck rbf as methane sulfonic acid (0.0274 mL, 0.0406 g, 0.423 mmol, 10.0 mol %) was added. The reaction mixture immediately acquired a cloudy white color. Reaction progress was followed by gas chromatography. After 18 h, the reaction mixture was stirred with 2 M NaOH (40 mL) for 15 min. The mixture was extracted with CH_2Cl_2 (3 X 20 mL). The combined organic layers were washed with H_2O (2 X 40 mL) and sat. NaCl (40 mL), dried (Na_2SO_4), and concentrated to yield 0.76 g (85 %) of a yellow liquid that was determined to be 98 % pure by GC analysis and ^1H NMR. ^1H NMR: δ 1.84-2.00 (m, 1 H), 2.12-2.19 (m, 1 H), 2.33 (s, 3 H), 2.85-3.11 (m, 4 H), 5.12 (s, 1 H), 7.08-7.28 (m, 4 H).

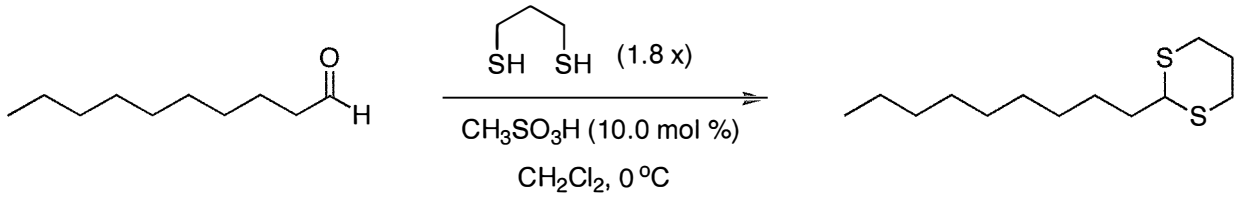
Allylation of 2-(3-tolyl)-1,3-dithiane (MJS2097fr1334)



A homogenous mixture of 2-(3-tolyl)-1,3-dithiane (0.2481 g, 1.179 mmol), allyltrimethylsilane (0.3186 mL, 0.2291 g, 2.005 mmol, 1.7 eq), and acetic anhydride (0.1895 mL, 0.2047 g, 2.005

mmol, 1.7 eq) was stirred at 0 °C under N_2 in a flame-dried three-neck rbf as bismuth(III) triflate (0.0310 g, 0.0472 mmol, 4.0 mol %) was added. Reaction progress was followed by gas chromatography. After 3 h, the reaction mixture was stirred with 10% Na_2CO_3 (20 mL) 15 minutes. The mixture was extracted with EtOAc (3 x 20 mL). The combined organic layers were washed with sat. NaCl (40 mL), dried (Na_2SO_4), and concentrated to yield 0.3263 g (94 %) of a dark brown liquid that was determined to be 83 % pure by GC and ^{1}H NMR. The crude compound was loaded onto 60 g of silica gel and eluted with EtOAc/heptane (3/97, v/v). Fifty-three fractions (8 mL) were collected. Fractions 13 to 50 were combined and concentrated to yield 0.2460 g (74 %) of a clear, colorless liquid product that was determined to be 97 % pure by GC analysis and ^{1}H spectroscopy. ^{1}H NMR: δ 1.66-1.76 (m, 2 H), 2.28 (S, 3 H), 2.33 (s, 3 H), 2.52-2.61 (t, 2 H, J = 14.34 Hz), 2.76-2.94 (m, 2 H), 3.74-3.79 (t, 1 H, J = 7.37 Hz), 4.96-5.06 (m, 2 H), 5.64-5.74 (m, 1 H). 7.01-7.25 (m, 4 H). ^{13}C: (16 peaks) δ 195.6, 141.9, 138.1, 135.4, 128.4, 128.3, 128.0, 124.9, 116.9, 49.5, 40.9, 30.6, 29.8, 29.0, 28.0, 21.5. HRMS-EI (*m/z*): M^+ calcd for $C_{16}H_{22}OS_2Na$, 317.1010; found, 317.1028.

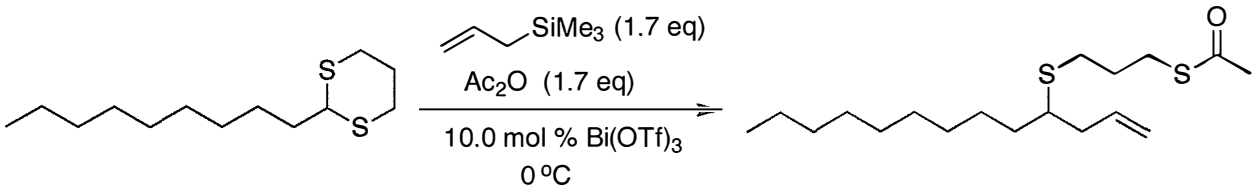
Synthesis of 2-nonyl-1,3-dithiane (MJS2113crude)



A solution of decanal (0.5662 g, 3.623 mmol) and 1,3-propanedithiol (0.6196 mL, 0.6666 g, 6.169 mmol, 1.8 eq) in CH_2Cl_2 (10 mL) was stirred at 0 °C in a three-neck rbf as methane sulfonic acid (0.024 mL, 0.035 g, 0.36 mmol, 10.0 mol %) was added. Reaction progress was followed by gas chromatography. After 18 h, the reaction mixture was stirred with 2 M NaOH

(40 mL) for 20 min. The mixture was extracted with CH_2Cl_2 (3 X 20 mL). The combined organic layers were washed with H_2O (2 X 40 mL), 2 M NaOH (3 X 20 mL), sat. NaCl (40 mL), dried (Na_2SO_4), and concentrated to yield 0.6959 g (78 %) of a clear, colorless liquid that was determined to be 97 % pure by GC analysis and ^1H NMR. ^1H NMR: δ 0.80-0.85 (t, 3 H, J = 6.91 Hz), 1.22 (s, 12 H), 1.36-1.46 (m, 2 H), 1.65-1.87 (m, 3 H) 2.03-2.10 (m, 1 H), 2.61-2.84 (m, 4 H), 3.98-4.02 (t, 1 H, J = 6.67 Hz).

Allylation of 2-nonyl-1,3-dithiane (MJS2117fr1519)



A homogenous mixture of 2-nonyl-1,3-dithiane (0.2522 g, 1.023 mmol), allyltrimethylsilane (0.2764 mL, 0.1988 g, 1.740 mmol, 1.7 eq), and acetic anhydride (0.1644 mL, 0.1776 g, 1.740 mmol, 1.7 eq) was stirred at 0 °C under N_2 in a flame-dried rbf as bismuth(III) triflate (0.0671 g, 0.102 mmol, 10.0 mol %) was added. The reaction mixture immediately acquired a light yellow color. Reaction progress was followed by gas chromatograph. After 3 h 30 min, the reaction mixture was loaded onto 60 g of silica gel and eluted with EtOAc/heptane (3/97, v/v). Eighty-eight fractions (8 mL) were collected after a 50 mL prefraction. Fractions 15 to 19 were combined and concentrated to yield 0.2127 g (63 %) of a clear, colorless liquid that was determined to be 97 % pure by GC analysis and ^1H & ^{13}C NMR spectroscopy. ^1H NMR: δ 0.83-0.88 (t, 3 H, J = 6.67 Hz), 1.24 (s, 14 H), 1.39-1.58 (m, 3 H), 1.79-1.85 (m, 2 H), 2.27-2.32 (m, 4 H), 2.51-2.64 (m, 3 H), 2.92-2.98 (t, 2 H, J = 7.15 Hz), 5.02-5.08 (m, 2 H), 5.77-5.87 (m, 1 H).

^{13}C: (15 peaks) δ 195.6, 135.7, 116.8, 45.3, 39.3, 34.2, 31.9, 30.6, 29.6, 29.3, 29.2, 28.1, 26.7, 22.7, 14.1. HRMS-EI (*m/z*): M^+ calcd for $C_{18}H_{34}OS_2Na$, 353.1949; found, 353.1963.

IV. References

(1) Breslow, R. *Chemistry Today and Tomorrow.* American Chemical Society, Washington, D.C., **1997.**

(2) Anastas, P. T.; Warner, J. C. *Green Chemistry, Theory and Practice.* Oxford University Press, New York, **1998.**

(3) Pollution Prevention Act of 1990 (1990). 42 U.S.C. 13101.

(4) Office of Pollutions Prevention and Toxins (**2006**). 2006 Toxics Release Inventory, Public Data. Release, Executive Summary, June, EPA-745-S-96-001, U.S. Environmental Agency,Washington, D.C.

(5) Trost, B. M. *Science* **1991**, 254, 1471.

(6) (a) Sheldon, R. A. *Chem. Ind. (London)* **1992**, 903. (b) Iwata, T.; Mika, H.; Fujita, Y. In *Ullmann's Encyclopedia of Industrial Chemistry* **1991**, *19*, 347. (c) Kastens, M. L.; Kaplan, J. F. *Ind. Eng. Chem.*, **1950**, *42*, 402.

(7) Emsley, J. *The Elements.* Clarendon Press, Oxford, **1989**, 31.

(8) Dorian, A. F. In *Elsevier's Encyclopaedic Dictionary of Medicine. Part D.* Elsevier: Amsterdam, **1999.**

(9) Irwing-Sax, N.; Bewis, R. J. *Dangerous Properties of Industrial Materials* Van Nostrand Reinhold: New York, **1989**.

(10) Suzuki, H.; Matano, Y. *Organobismuth Chemistry* ed. 1; Elsevier: Amsterdam, **2001.**

(11) a) Barton, D. H. R.; Finet, J. P. *Pure Appl. Chem.* **1987**, *59,* 937. b) Finet, J. P. *Chem. Rev.* **1989**, *89,* 1487.

(12) Banik, B. M.; Venkatraman, M. S.; Mukhopadhyay, C.; Becker, F. F. *Tetrahedron Lett.* **1998**, *39*, 7247.

(13) Barton, D. H. R.; Y-Bhatnager, N.; Finet, J. P.; Khamsi, J.; Motherwell, W. B.; Stanforth, S. P. *Tetrahedron* **1987**, *43*, 323.

(14) Leonard, N. M.; Wieland, L. C.; Mohan, R. S. *Tetrahedron* **2002**, *58*, 8373.

(15) Prajapati, D.; Sandhu, J. *Chem. Lett.* **1992**,1945.

(16) Shen, Z.; Zhang, J.; Zou, H.; Yang, M. *Tetrahedron Lett.* **1997**, *38,* 2733.

(17) Garrigues, B.; Gonzaga, F.; Robert, H.; Dubac, J. *J. Org. Chem.* **1997**, 62, 4880.

(18) Ohki, H.; Wada, M.; Akiba, K. *Tetrahedron Lett.* **1988**, *29,* 4719.

(19) Sabitha, G.; Babu, R.; Reddy, E.; Yadav, J. S. *Chem. Lett.* **2000**,1074.

(20) Le Roux, C.; Dubac, J. *Organometallics* **1996**, *15,*4646.

(21) Wada, M.; Ohki, H.; Akiba, K. *Tetrahedron Lett.* **1986**, 4771.

(22) Le Boisselier, V.; Postel, M.; Dunach, E. *Chem. Commun.* **1997**, 95.

(23) Bajwa, J.; Vivelo, J.; Slade, J.; Repic, O.; Blacklock, T. *Tetrahedron Lett.* **2000**, *41,* 6021.

(24) Winum, J. Y.; Kamal, M.; Barragan, V.; Leydet, A.; Montero, J. L. *Synth. Commun.* **1998**, *28,* 603.

(25) Komatsu, N.; Ishida, J.; Suzuki, H. *Tetrahedron Lett.* **1997**, *38,* 7219.

(26) Rogers, J. L.; Ernat, J. J.; Yung, H.; Mohan, R. S. *Cat. Commun.* **2009**, *10,* 625.

(27) (a) Samajdar, S.; Becker, F. F.; Banik, B. K. *Synth. Commun.* **2001**, *31,* 2691. (b) Tymonko, S. A.; Nattier, B. A.; Mohan, R. S. *Tetrahedron Lett.* **1999**, *40,* 7657.

(28) Mashraqui, S.; Mudaliar, C.; Karnik, M. *Synth. Commun.* **1998**, 939.

(29) Eash, K. J.; Pulia, M. S.; Wieland, L. C.; Mohan, R. S. *J. Org. Chem.* **2000**, *65,* 8399.

(30) Komatsu, N.; Taniguchi, A.; Uda, M.; Suzuki, H. *Chem. Commun.* **1996**, 1847.

(31) Aggen, D. H.; Arnold, J. N.; Hayes, P. D.; Smoter, N. J.; Mohan, R. S. *Tetrahedron* **2004**, *60,* 3675.

(32) Khosropour, A. R.; Khodaei, M. M.; Beygzadeh, M. *Heteroatom Chemistry* **2007**, *18,* 684.

(33) Kobayashi, S.; Sugiura, M.; Kitagawa, H.; Lam, W. W. L. *Chem. Rev.* **2002**, *102,* 2227.

(34) Gaspard-Iloughmane, H.; Le Roux, C. *Eur. J. Org. Chem.* **2004**, *12,* 2517.

(35) Louer, M.; Le Roux, C.; Dubac, J. *Chem. Mater.* **1997**, *9,* 3012.

(36) Laurent-Robert, H.; Garrigues, B.; Dubac, J. *Synlett.* **2000**, 1160.

(37) Kobayashi, S. *Eur. J. Org. Chem.* **1999**, 15.

(38) Varala, R.; Alam, M. M.; Adapa, S. R. *Synlett.* **2003**, 67.

(39) (a) Desmurs, J. R.; Labrouillere, M.; Le Roux, C.; Gaspard, H.; Laporterie, A.; Dubac, J. *Tetrahedron Lett.* **1997**, *51*, 8871. (b) Desmurs, J. R.; Labrouillere, M.; Le Roux, C.; Gaspard, H.; Laporterie, A.; Dubac, J. *Tetrahedron Lett.* **1997**, *51*, 8874.

(40) (a) Torisawa, Y.; Nishi, T.; Minamikawa, J. I. *Bioorg. Med. Chem.* **2002**, *10,* 2583. (b) Peterson, K. E.; Smith, R. C.; Mohan, R. S. *Tetrahedron Lett.* **2003**, *44,* 7723.

(41) Torisawa, Y.; Nishi, T.; Minamikawa, J. I. *Bioorg. Med. Chem.* **2002**, *12*, 387.

(42) (a) Reddy, A. V.; Ravinder, K.; Goud, T. V.; Krishnaiah, P.; Raju, T. V.; Venkateswarlu, Y. *Tetrahedron Lett.* **2003**, 44, 6257. (b) Varala, R.; Alam, M. M.; Adapa, S. R. *Synlett.* **2003**, 720.

(43) Leonard, N. M.; Oswald, M. C.; Freiberg, D. A.; Nattier, B. A.; Smith, R. C.; Mohan, R. S. *J. Org. Chem.* **2002**, *67*, 5202.

(44) Carrigan, M. D.; Sarapa, D.; Smith, R. C.; Wieland, L. C.; Mohan, R. S. *J. Org. Chem.* **2002**, *67*, 1027.

(45) Choudary, B. M.; Chidara, S.; Sekhar, C. V. R. *Synlett.* **2002**, 1694.

(46) Wieland, L. C.; Zerth, H. M.; Mohan, R. S. *Tetrahedron Lett.* **2002**, 43, 4597.

(47) Yadav, J. S.; Reddy, B. V. S.; Satheesh, G. *Tetrahedron Lett.* **2003**, *44*, 6501.

(48) Yadav, J. S.; Reddy, B. V. S.; Swamy, T. *Tetrahedron Lett.* **2003**, *44*, 4861.

(49) Singh, S.; Verma, A.; Verma, R. D. *Indian J. Chem.* **1983**, 814.

(50) Labrouillere, M.; Le Roux, C.; Gaspard, H.; Laporterie, A.; Dubac, J.; Desmurs, J. R. *Tetrahedron Lett.* **1999**, 40, 285.

(51) Skinner, H. A. *Adv. Organomet. Chem.* **1964**, *2*, 49.

(52) Peyronneau, S. M.; Arrondo, C.; Vendier, L.; Roques, N.; Le Roux, C. *J. Mol. Catal. A* **2004**, 211, 89.

(53) Peyronneau, M.; Roques, N.; Mazieres, S.; Le Roux, C. *Synlett.* **2003**, 631.

(54) Dumeunier, R.; Marko, I. E. *Tetrahedron Lett.* **2004**, *45*, 825.

(55) Yadav, J. S.; Reddy, B. V. S.; Premalatha, K.; Shankar, K. S. *Synthesis* **2008**, *23,* 3787.

(56) Herrmann, W. A. *Applied Homogeneous Catalysis with Organometallic Compounds* **2002**, *1*, 591.

(57) Sartori, G.; Raimondo, M. *Chem. Rev.* **2006**, *106*, 1077.

(58) Poulsen, T. B.; Jorgensen, K. A. *Chem. Rev.* **2008**, *108*, 2903.

(59) Little, R. D.; Masjedizadeh, M. R.; Wallquist, O.; McLoughlin, J. I. *Org. React.* **1995**, *47*, 315.

(60) Grubbs, R. H. *Tetrahedron* **2004**, *60*, 7117.

(61) (a) Engelbert, C. *Org. React.* **1984**, *32*, 1. (b) Kagan, H. B.; Olivier, R. *Chem. Rev.* **1992**, *92*, 1007.

(62) Hosomi, A; Sakurai, H. *Tetrahedron Lett.* **1976**, *16*, 1295.

(63) (a) Hosomi, A.; Endo, M.; Sakurai, H. *Chem. Lett.* **1976**, 941. (b) Hosomi, A.; Endo, M.; Sakurai, H. *Chem. Lett.* **1978**, 499.

(64) (a) Hosomi, A.; Endo, M.; Sakurai, H. *Chem. Lett.* **1978**, 499. (b) Ojima, I.; Kumagai, M. *Chem. Lett.* **1978**, 575.

(65) Tsunoda, T.; Suzuki, M.; Noyori, R. *Tetrahedron Lett.* **1980**, *21,* 71.

(66) Hosomi, A.; Endo, M.; Sakurai, H. *Chem. Lett.* **1978**, 499.

(67) Sakurai, H.; Sasaki, K.; Hosomi, A. *Tetrahedron Lett.* **1981**, *22,* 745.

(68) Mukaiyama, T.; Nagaoka, H.; Murakami, M.; Ohshima, M. *Chem. Lett.* **1985**, 977.

(69) Trehan, A.; Vij, A.; Walia, M.; Kaur, G.; Verma, R. D.; Trehan, S. *Tetrahedron Lett.* **1993**, *34,* 7335.

(70) Kawai, M.; Onaka, M.; Izumi, Y. *Chem. Lett.* **1986**, 381.

(71) Jung, M. E.; Maderna, A. *J. Org. Chem.* **2004**, *69,* 7755.

(72) Kamata, M.; Yokoyama, Y.; Karasawa, N.; Kato, M.; Hasegawa, E. *Tetrahedron Lett.* **1996**, *37,* 3483.

(73) Yadav, J. S.; Subba Reddy, B. V.; Srihari, P. *Synlett.* **2001**, 673.

(74) Komatsu, N; Uda, M.; Suzuki, H.; Takahashi, T.; Domae, T.; Wada, M. *Tetrahedron Lett.* **1997**, *38*, 7215.

(75) Wieland, L. C.; Zerth, H. M.; Mohan, R. S. *Tetrahedron Lett.* **2002**, *43,* 4597.

(76) Sakurai, H.; Sasaki, K.; Hayashi, J; Hosomi, A. *J. Org. Chem.* **1984**, *49*, 2808.

(77) Mekhalfia, A.; Marko, I. E. *Tetrahedron Lett.* **1991**, *32,* 4779.

(78) Spafford, M. J.; Anderson, E. D.; Lacey, J. R.; Palma, A. C.; Mohan, R. S. *Tetrahedron Lett.* **2007**, *48,* 8665.

(79) Anazalone, P. W.; Baru, A. R.; Danielson, E. M.; Hayes, P. D.; Nguyen, M. P.; Panico, A. F.; Smith, R. C.; Mohan, R. S. *J. Org. Chem.* **2005**, *70,* 2091.

(80) T. W. Green; P. G. M. Wuts *Protective Groups in Organic Synthesis*, Wiley-Interscience, New York, **1999**, 308-322, 724.

(81) Kim, J. Y.; Rhee, H.; Kim, M. *J. Korean Chem. Soc.* **2002**, *46*, 479.

(82) Egami, Y.; Takayanagi, M.; Tanino, K.; Kuwajima, I. *Heterocycles* **2000**, *52,* 583.

(83) Mead, K. T.; Zemribo, R. *Synlett.* **1996**, *11,* 1063.

(84) Carrel, F.; Giraud, S.; Spertini, O.; Vogel P. *Helvetica Chimica Acta* **2004**, *87,* 1048.

(85) Morelli, C. F.; Duri, L.; Saladino, A.; Speranza, G.; Manitto, P. *Synthesis* **2004**, *18,* 3005.

(86) Suzuki, T.; Oriyama, T. *Synth. Commun.* **1999**, *29,* 1263.

(87) Hunter, R.; Michael, J. P.; Tomlinson, G. D. *Tetrahedron* **1994**, *50,* 871.

(88) a) Denmark, S. E.; Almstead, N. G. *J. Am. Chem. Soc.* **1991**, *113,* 8089. c) Denmark, S. E.; Almstead, N. G. *J. Org. Chem.* **1991**, *56,* 6458. c) Denmark, S. E.; Almstead, N. G. *J. Org. Chem.* **1991**, *56,* 6485.

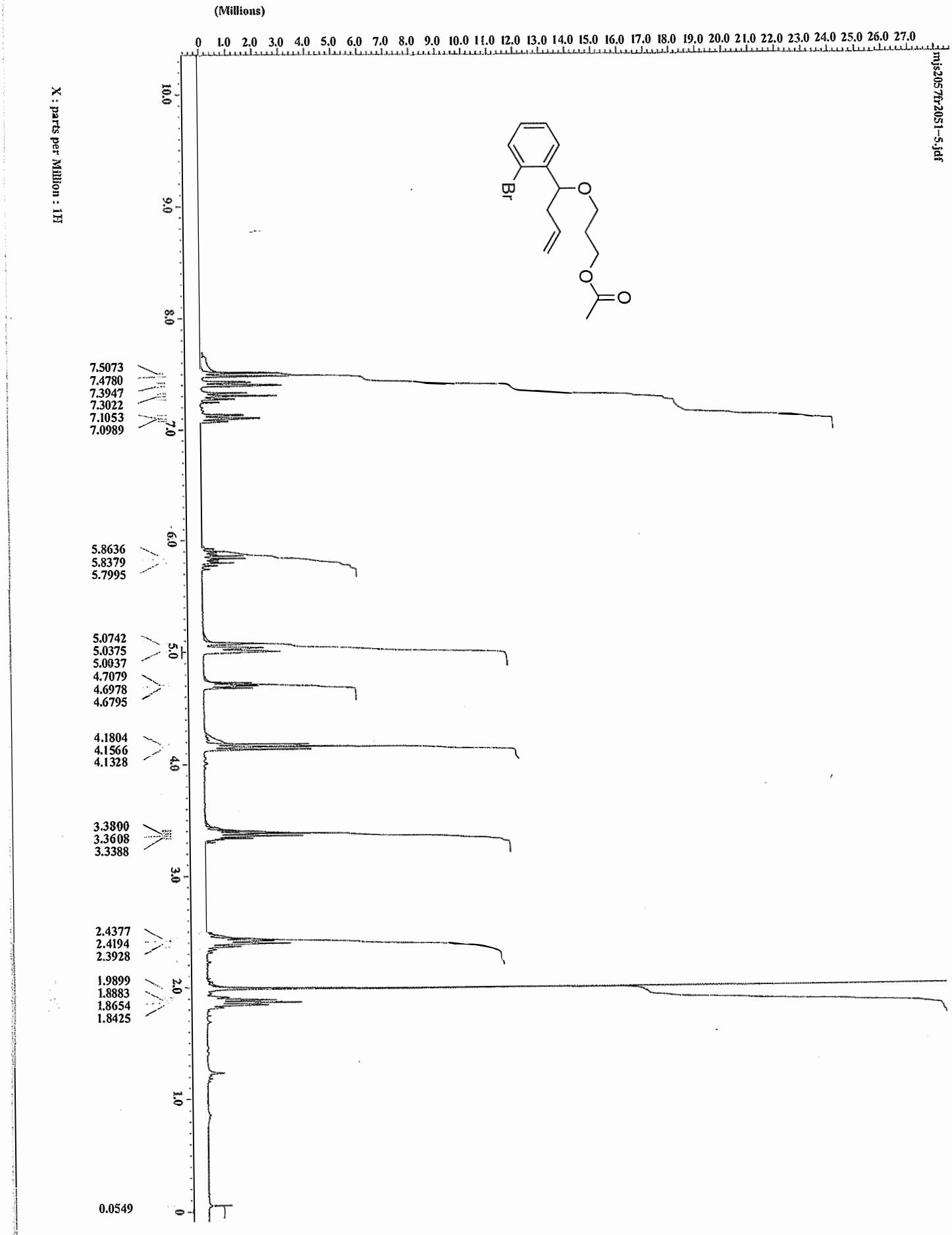
(89) Spafford, M. J.; Christensen, J. E.; Huddle, M. G; Lacey, J. R.; Mohan, R. S. *Aust. J. Chem.* **2008**, *61*, 419.

(90) Brzezinski, B; Grech, E.; Malarski, Z.; Sobczyk, L. *J. Chem. Soc. Perkin Trans. 2* **1991**, 857.

(91) Seebach, D. *Synthesis* **1977**, 357.

(92) Still, W. C.; Kahn, M.; Mitra, A. *J. Org. Chem.* **1978**, *43*, 2923.

IV. Appendix: Spectral Data



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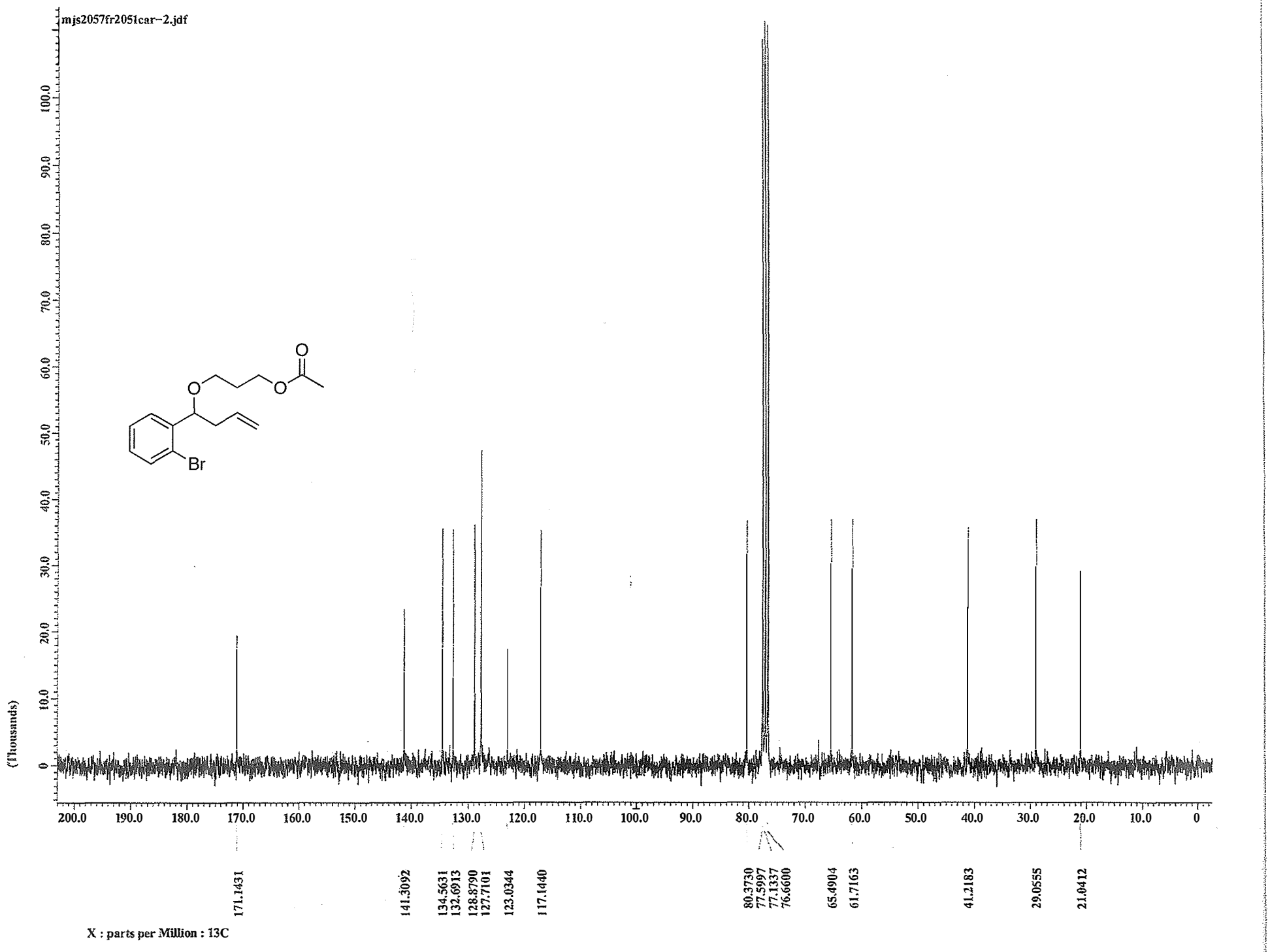
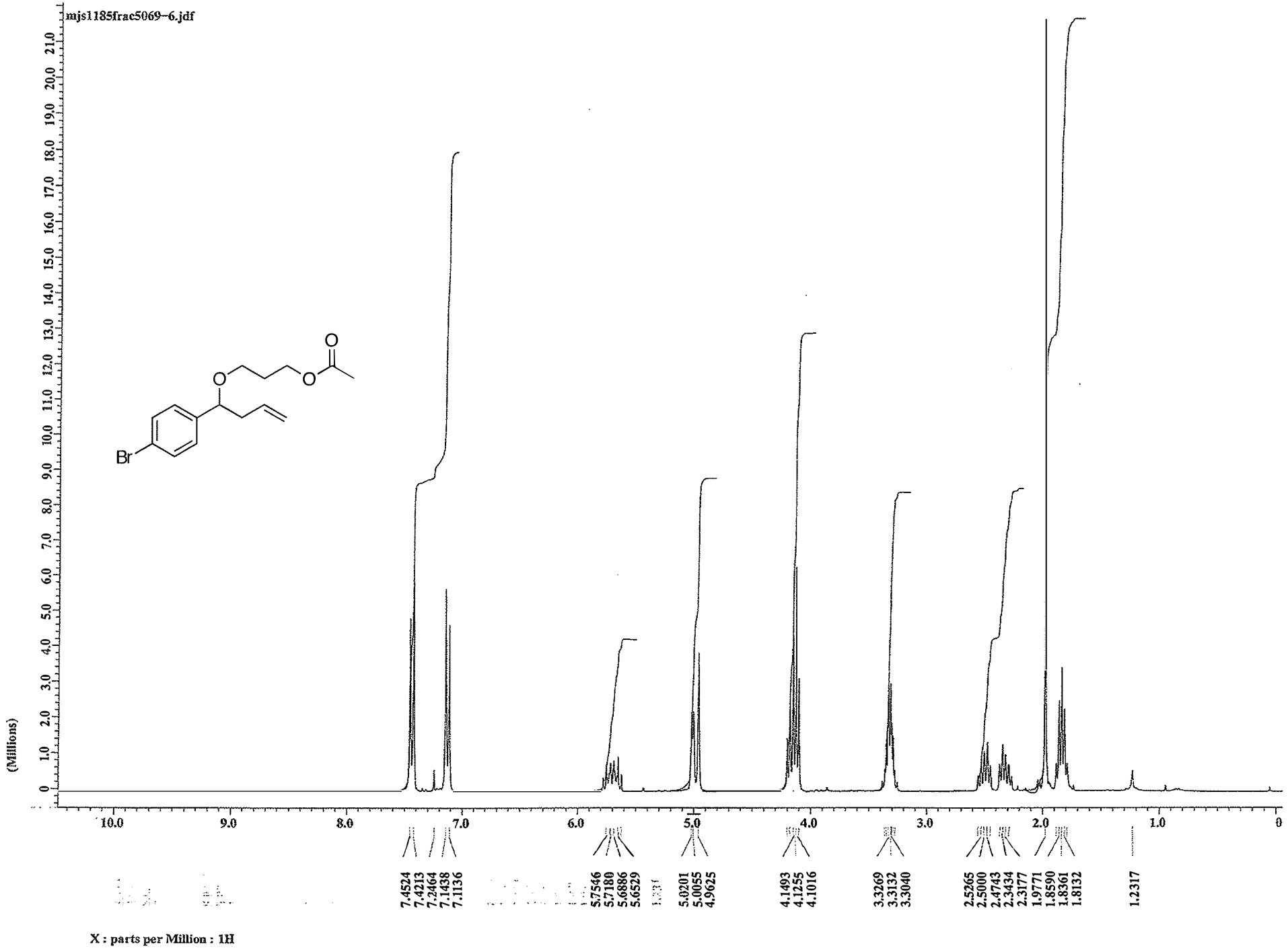
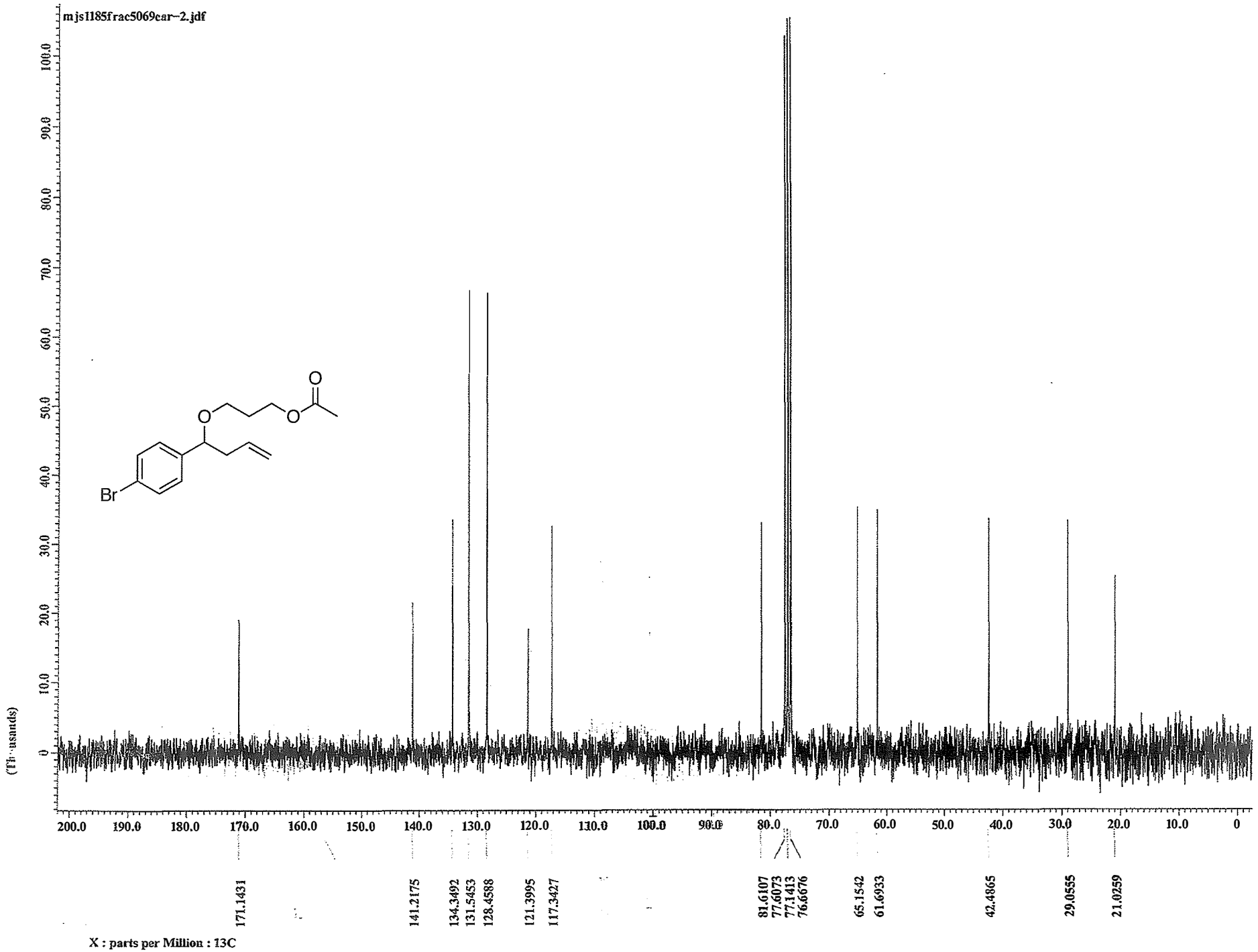


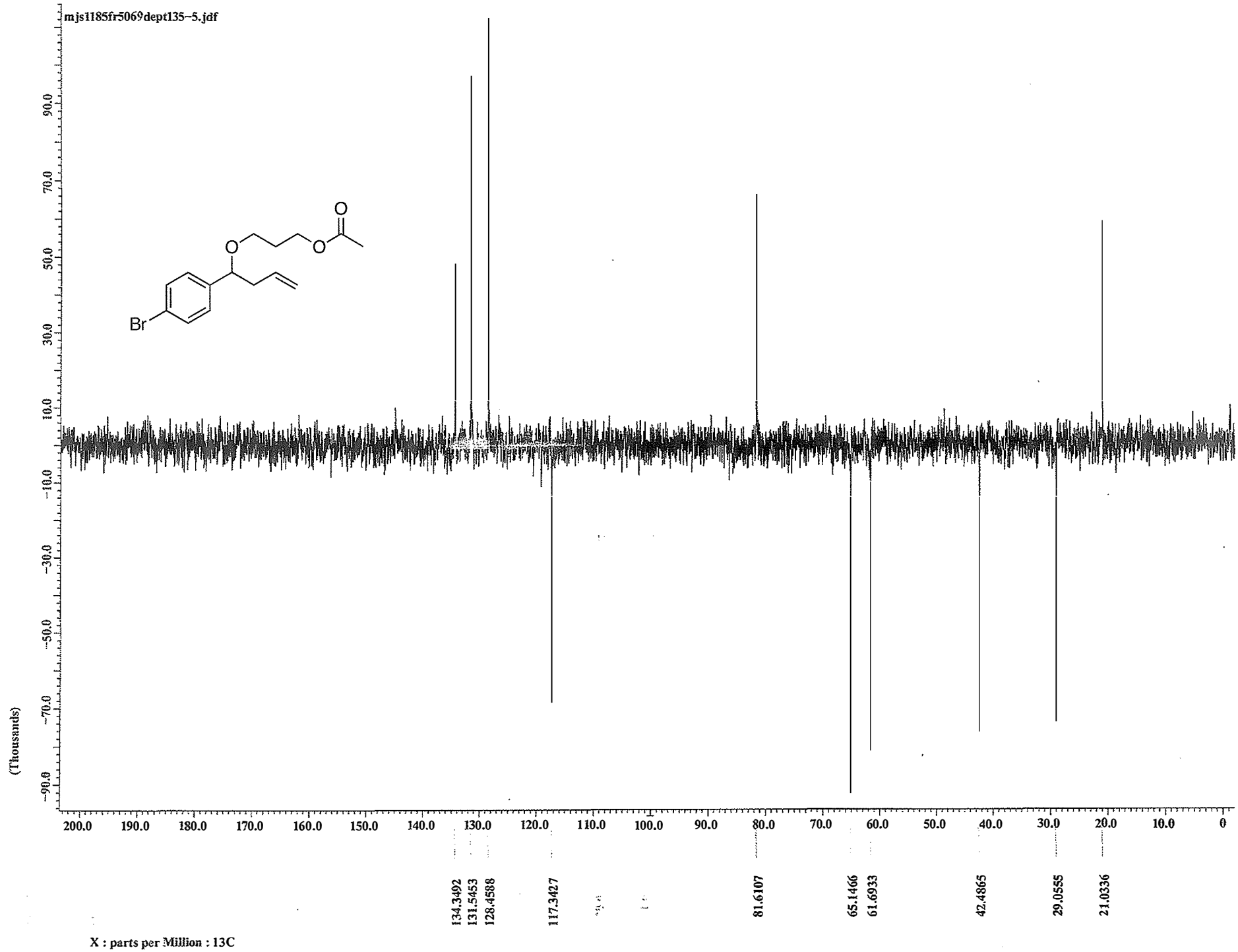
Spectrum 2 ^{13}C NMR of MJS2057fr2051



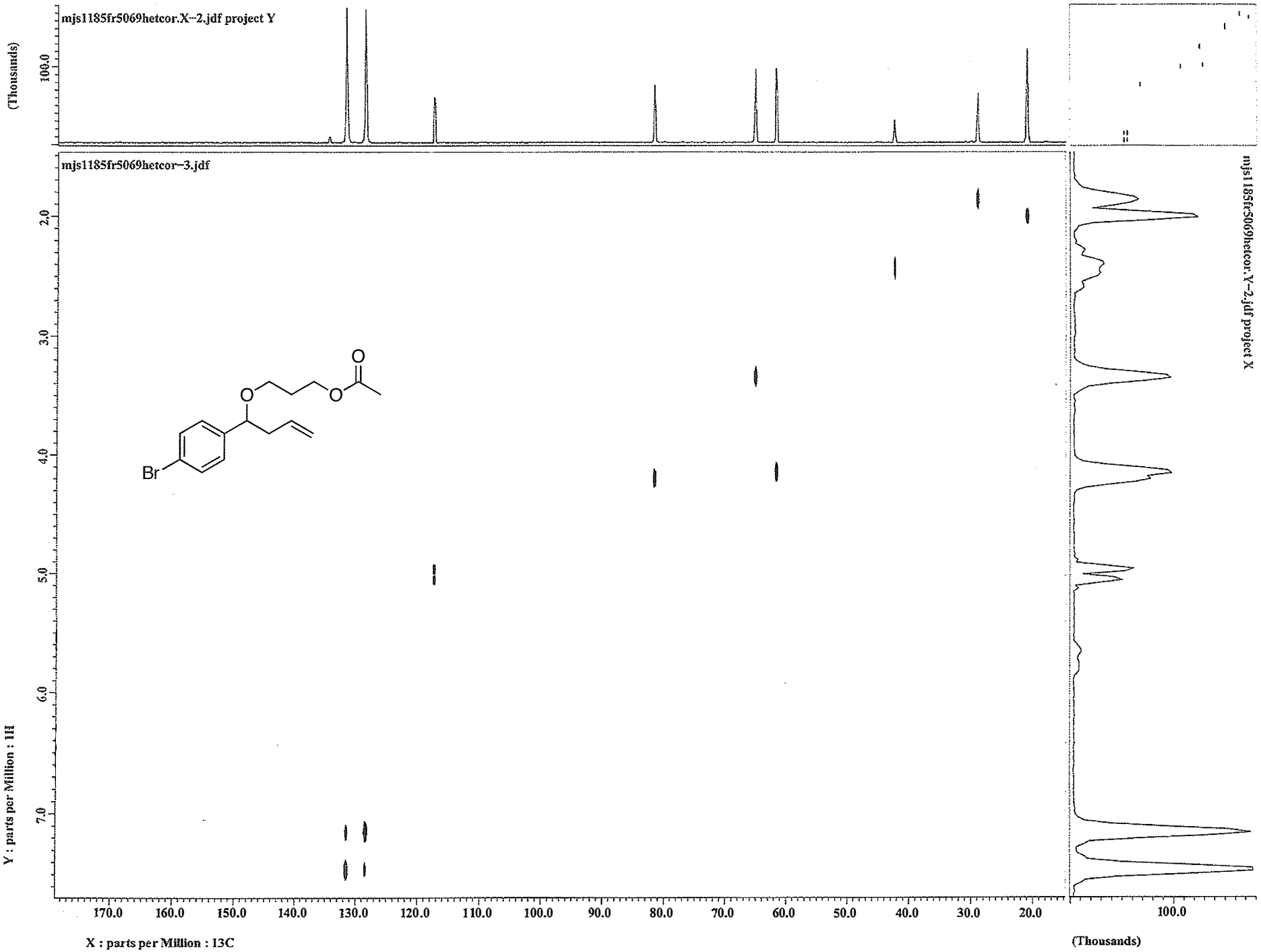
Spectrum 3 ^{1}H NMR of MJS1185fr5069



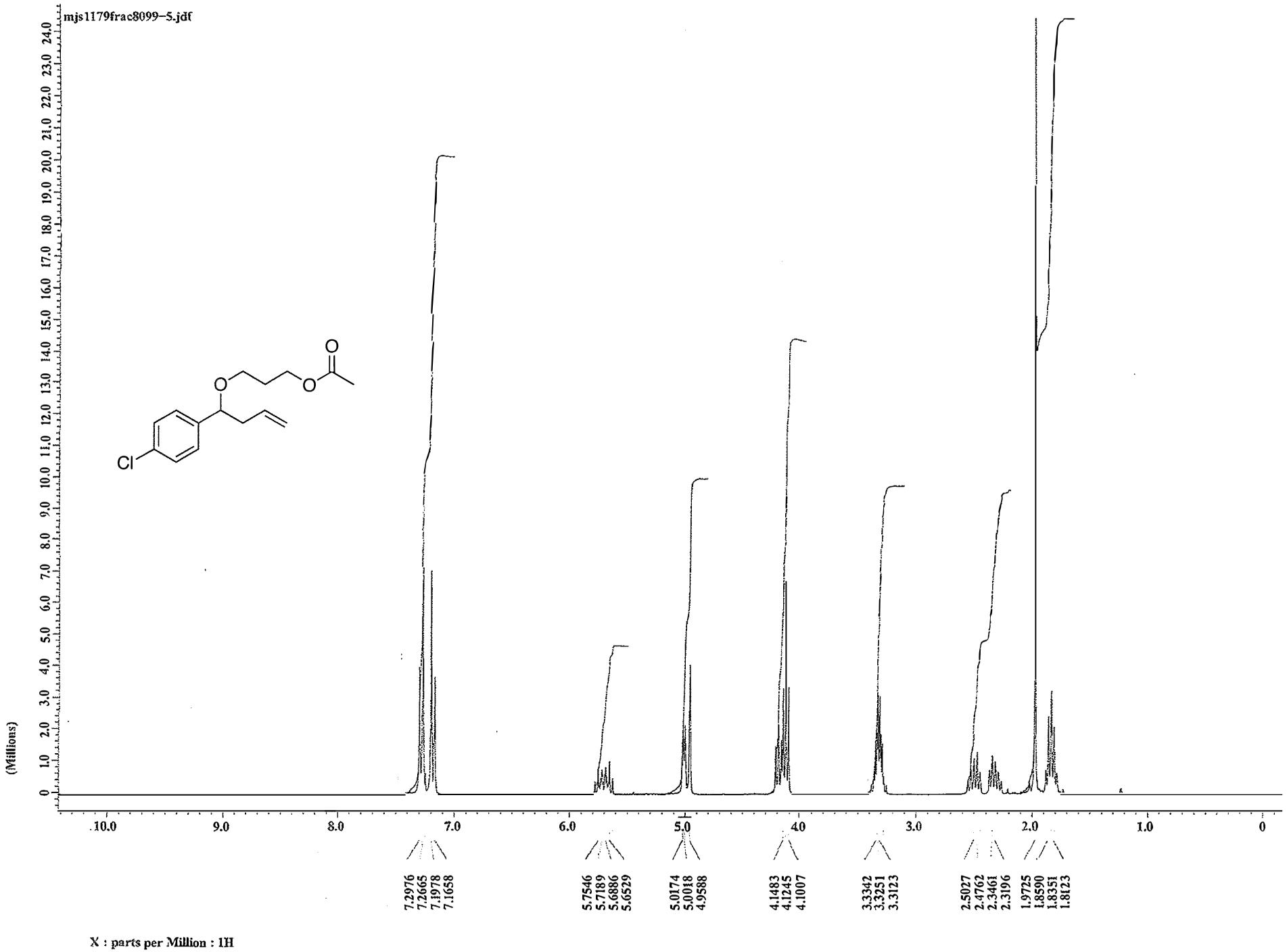
Spectrum 4 ^{13}C NMR of MJS1185fr5069



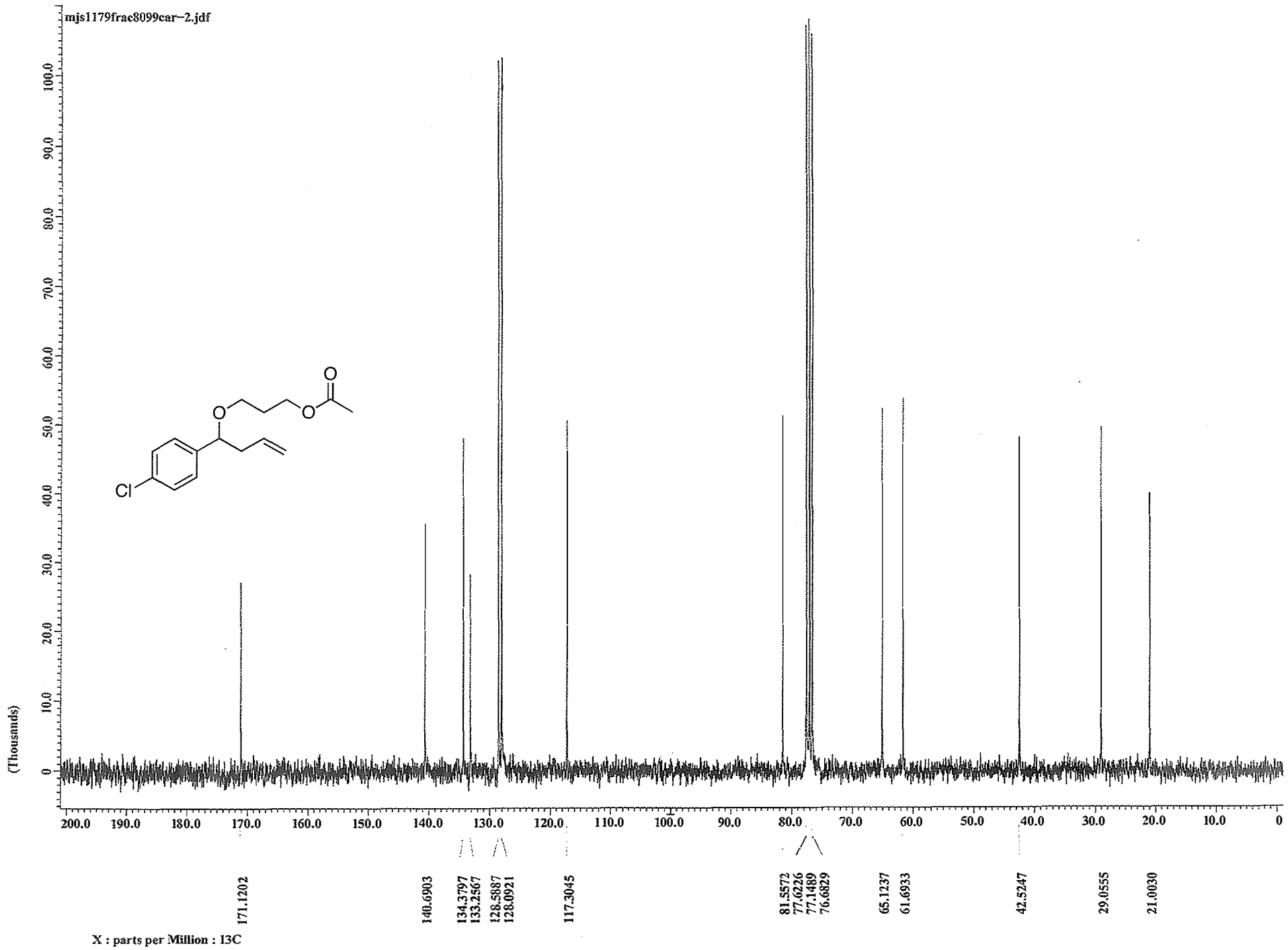
Spectrum 5 DEPT-135 of MJS1185fr5069



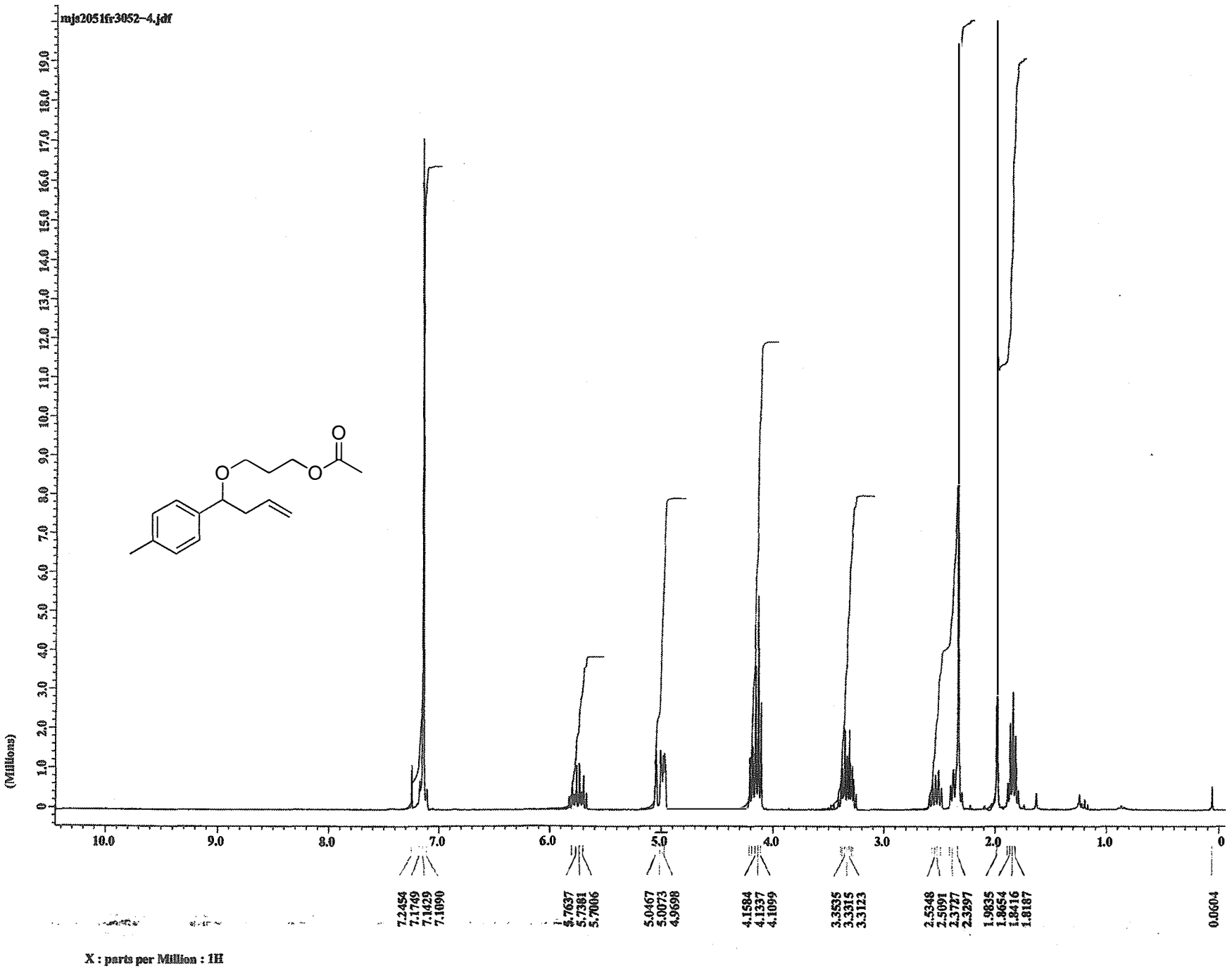
Spectrum 6 HETCOR of MJS1185fr5069



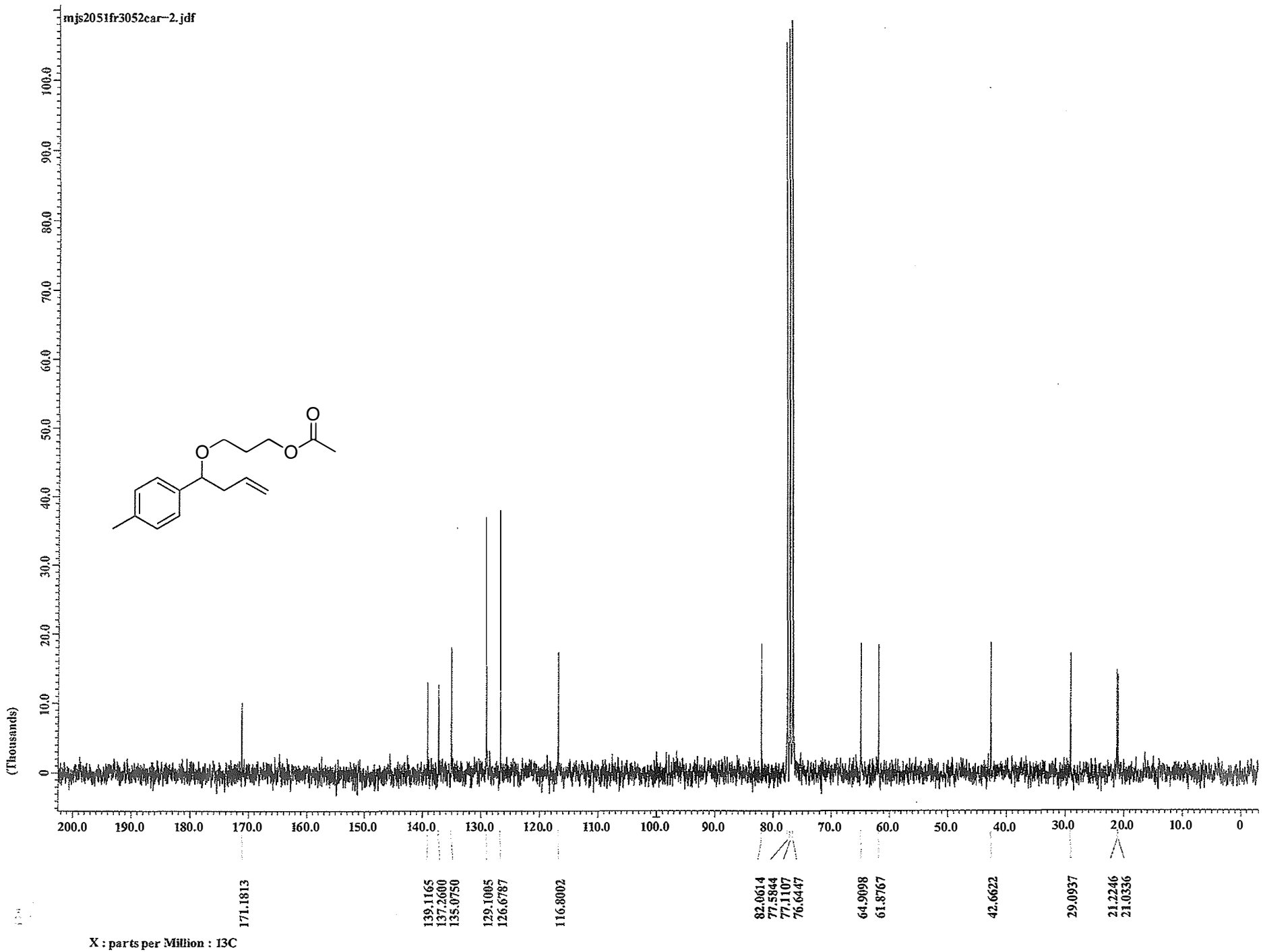
Spectrum 7 ^{1}H NMR of MJS1179fr8099



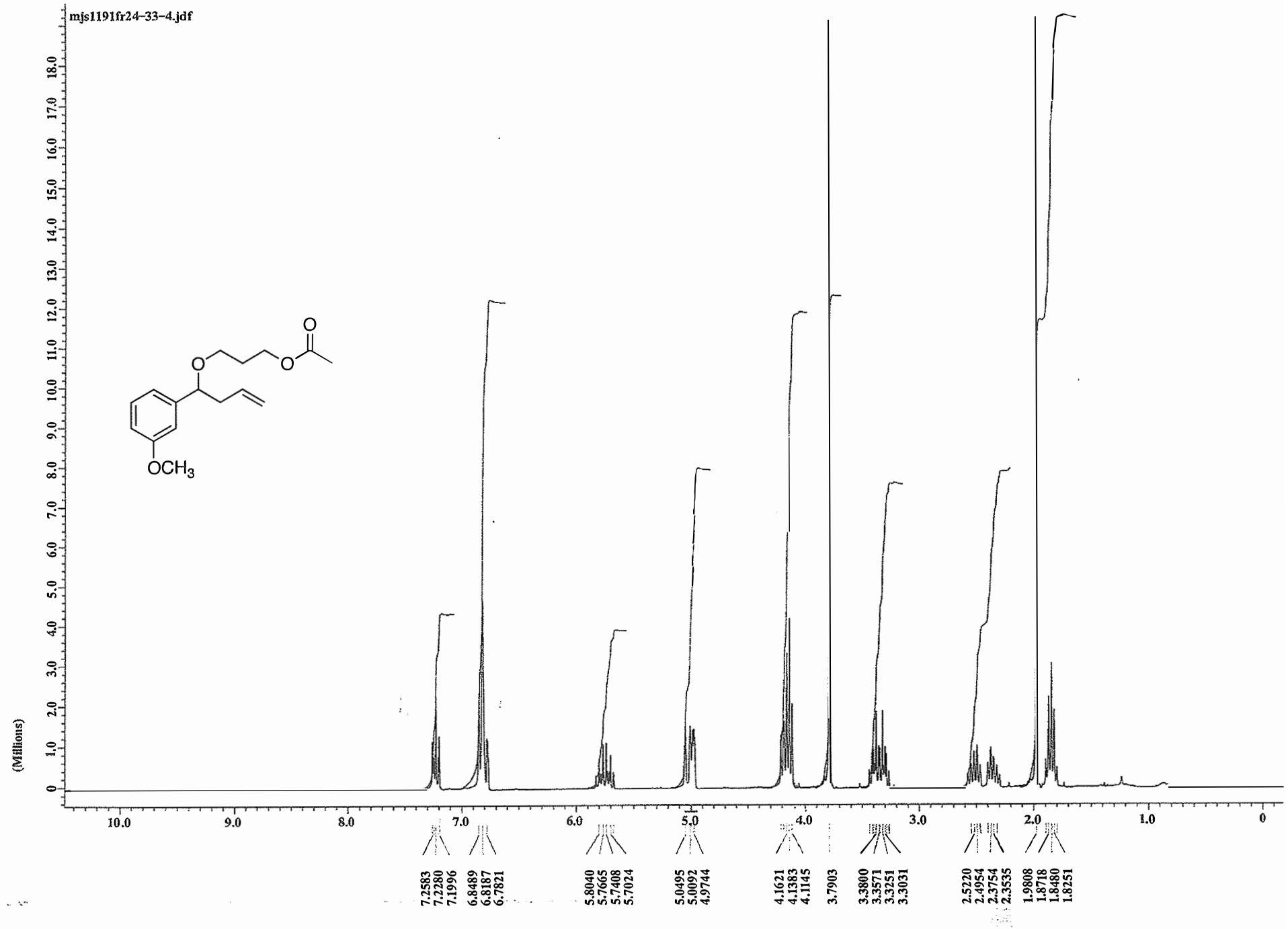
Spectrum 8 ^{13}C NMR of MJS1179fr8099



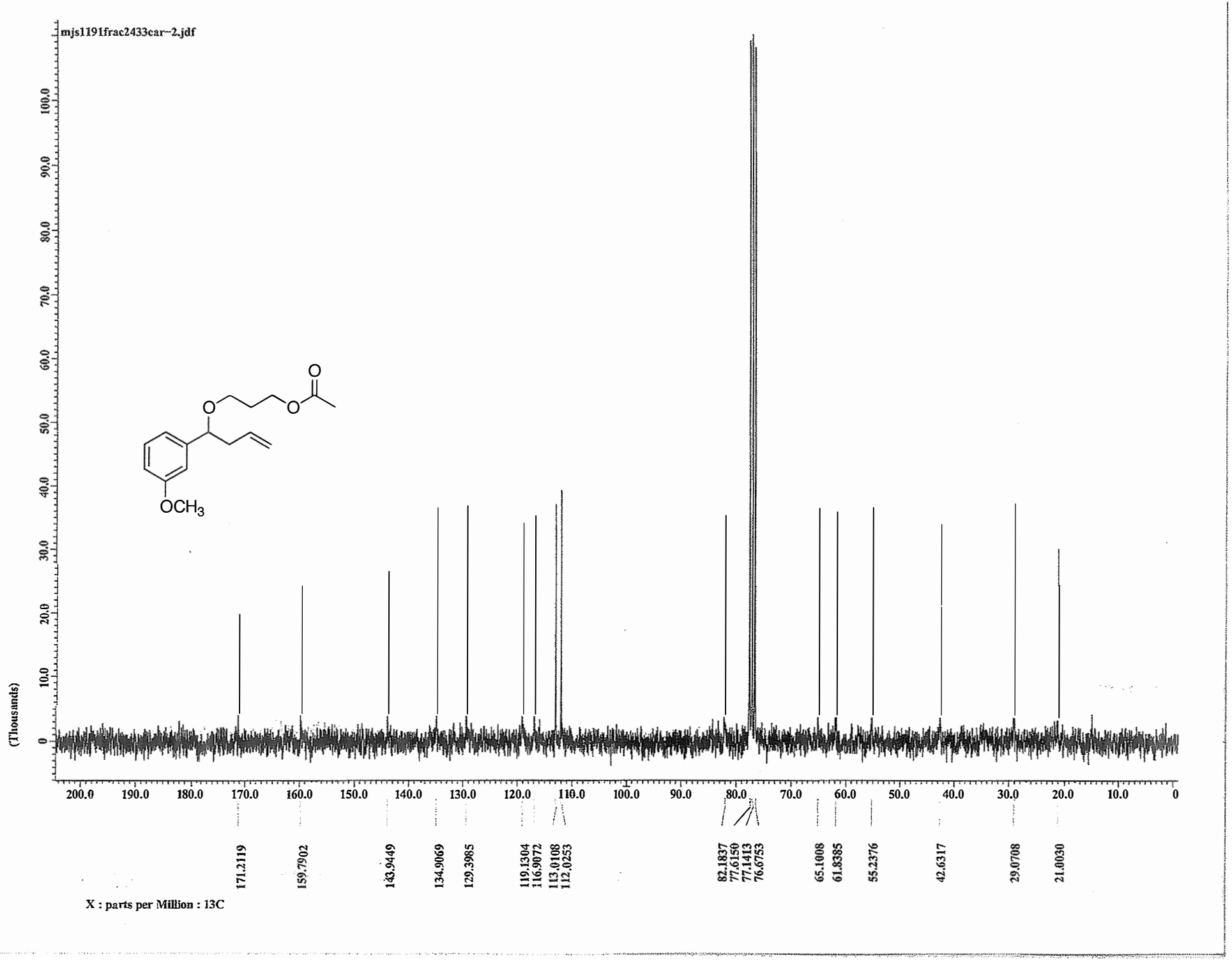
Spectrum 9 ^{1}H NMR of MJS2051fr3052



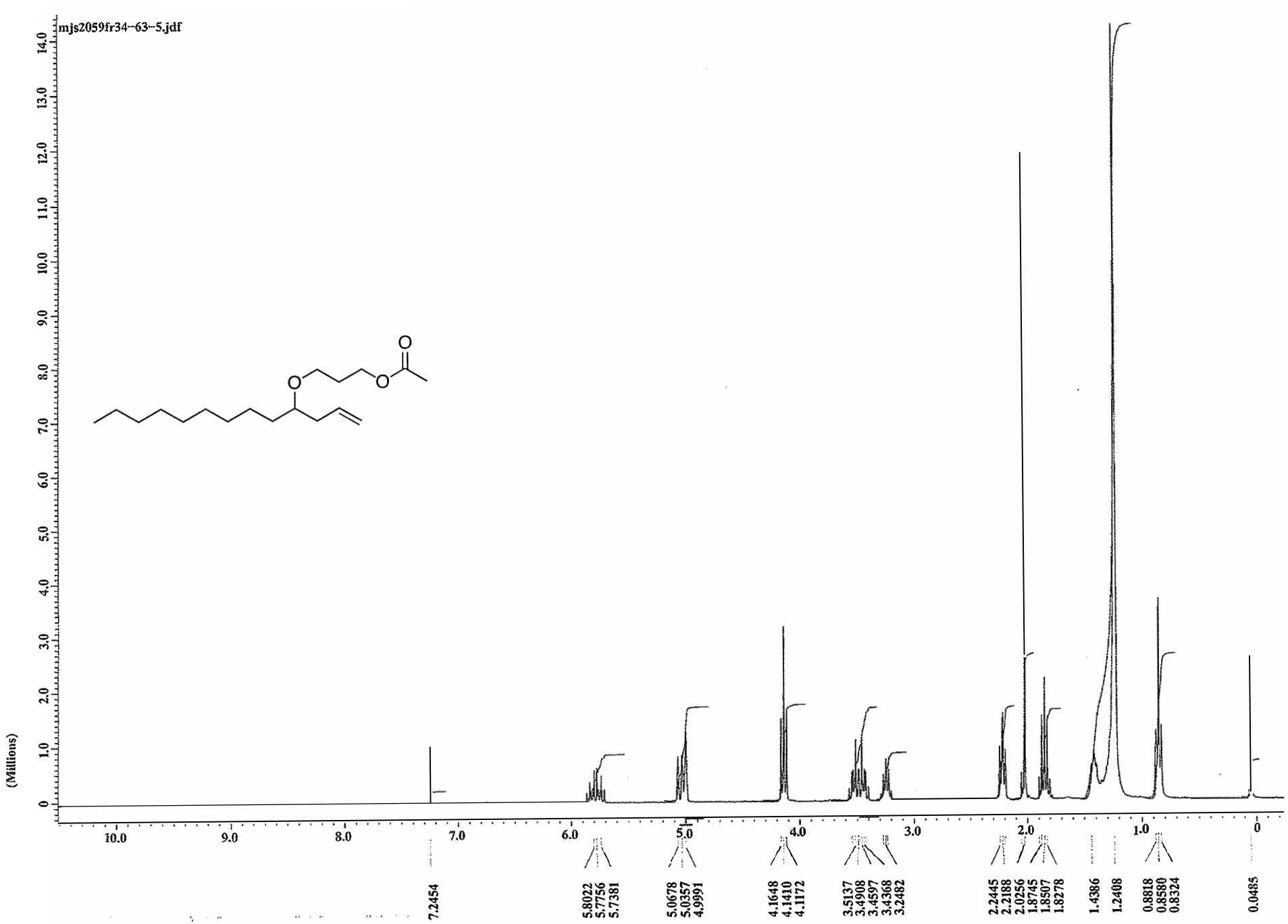
Spectrum 10 ^{13}C NMR of MJS2051fr3052



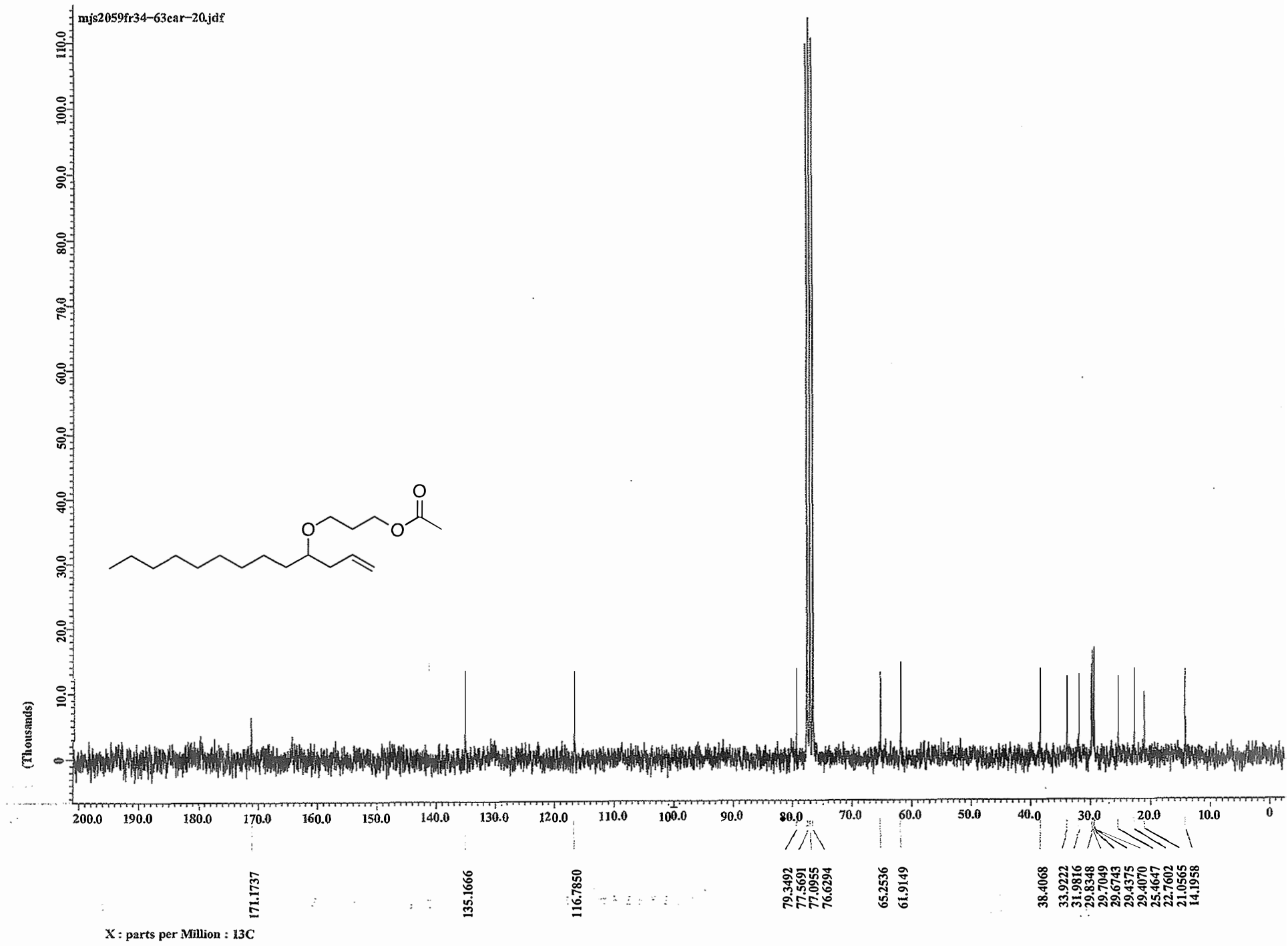
Spectrum 11 ^{1}H NMR of MJS1191fr2433



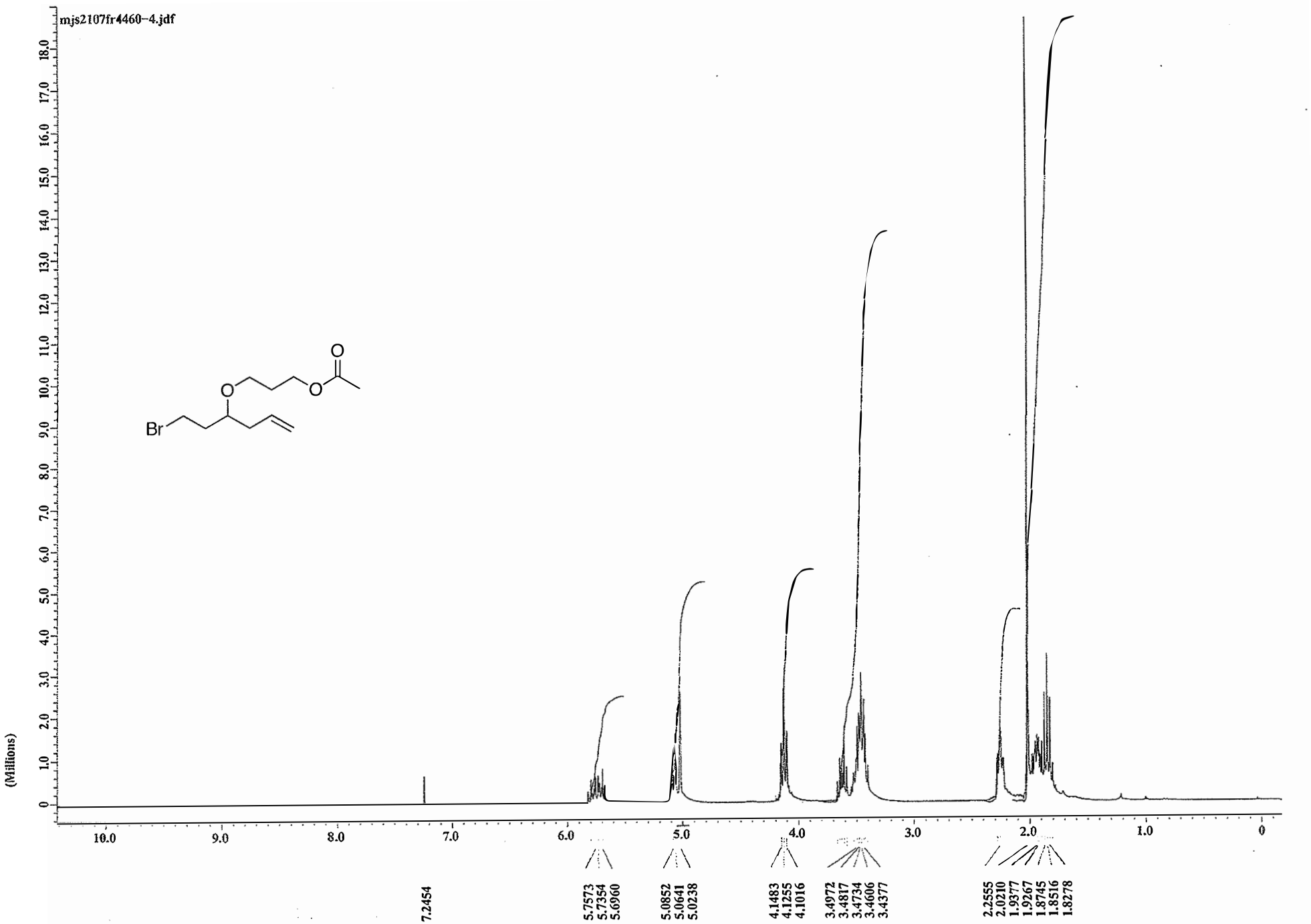
Spectrum 12 ^{13}C NMR of MJS1191fr2433



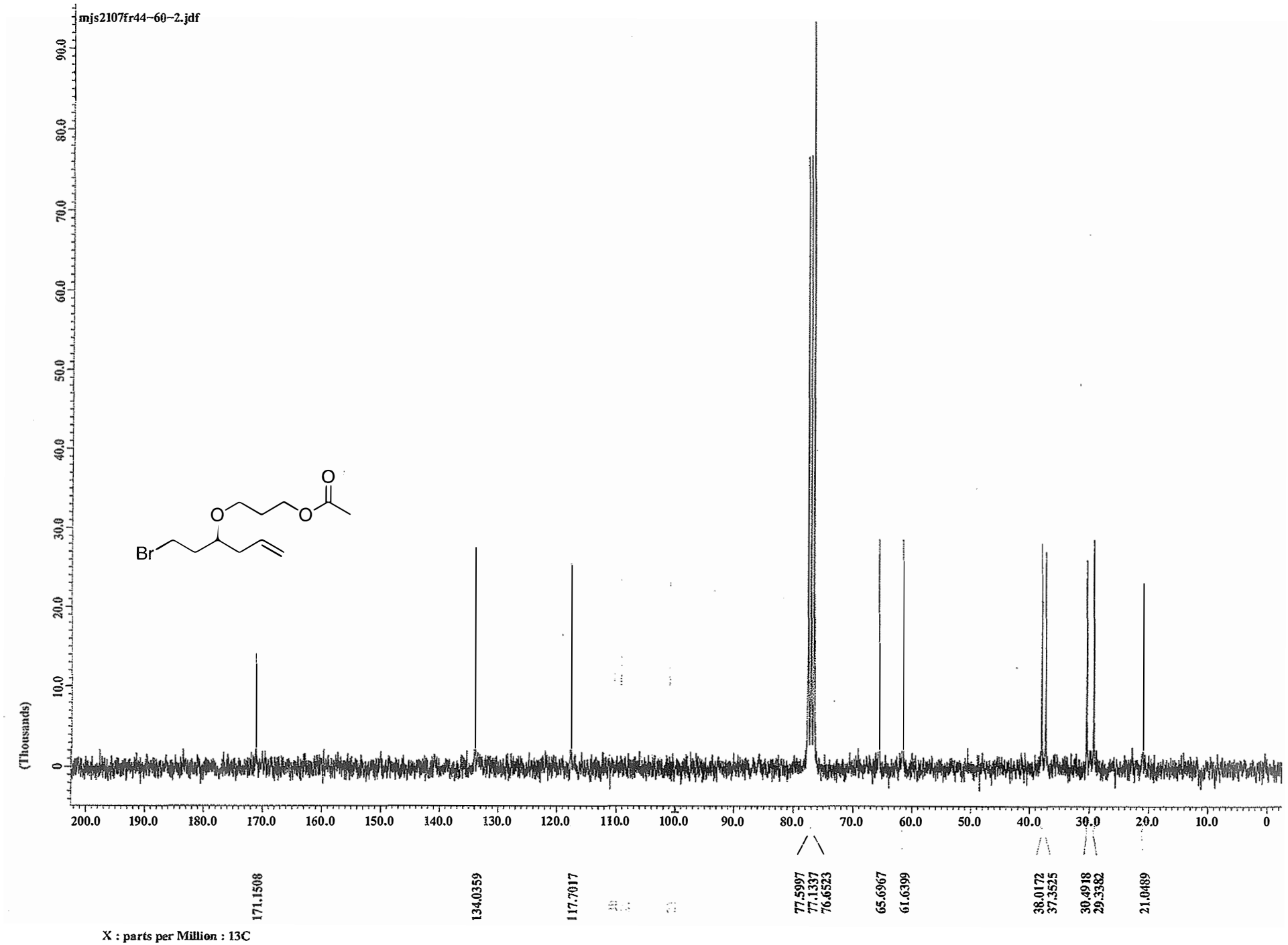
Spectrum 13 ^{1}H NMR of MJS2059fr3463



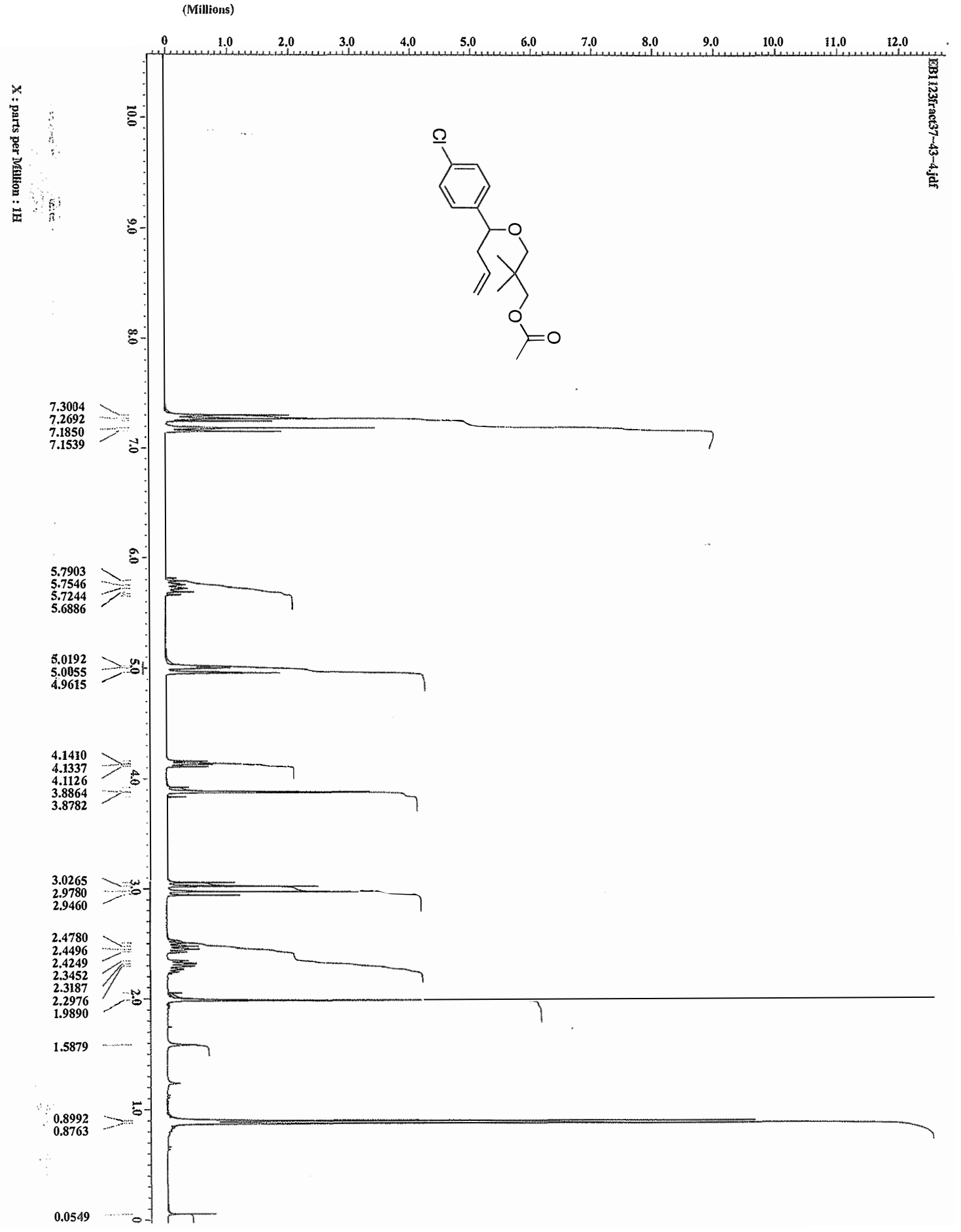
Spectrum 14 ^{13}C NMR of MJS2059fr3463



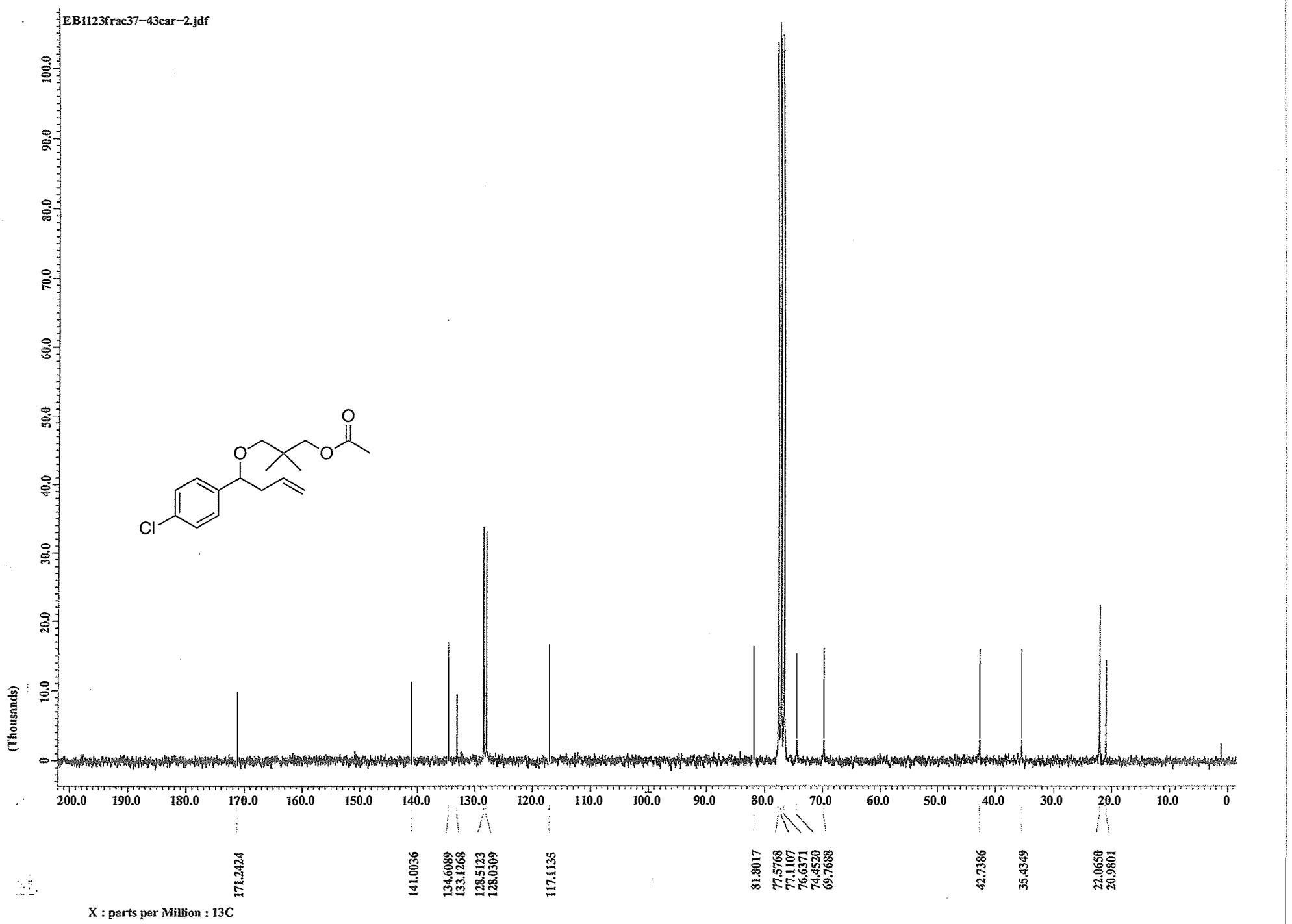
Spectrum 15 ^{1}H NMR of MJS2107fr4460



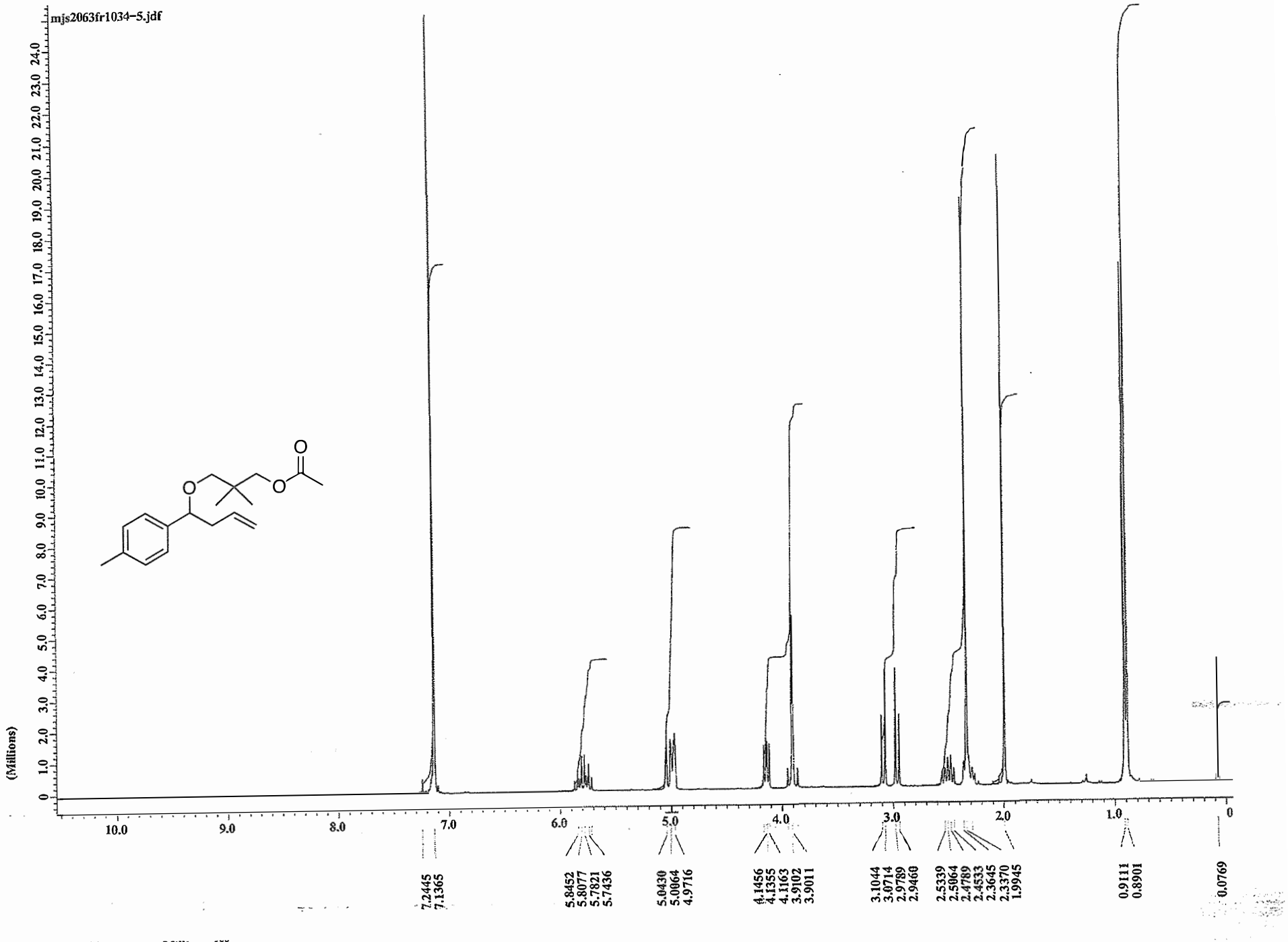
Spectrum 16 ^{13}C NMR of MJS2107fr4460



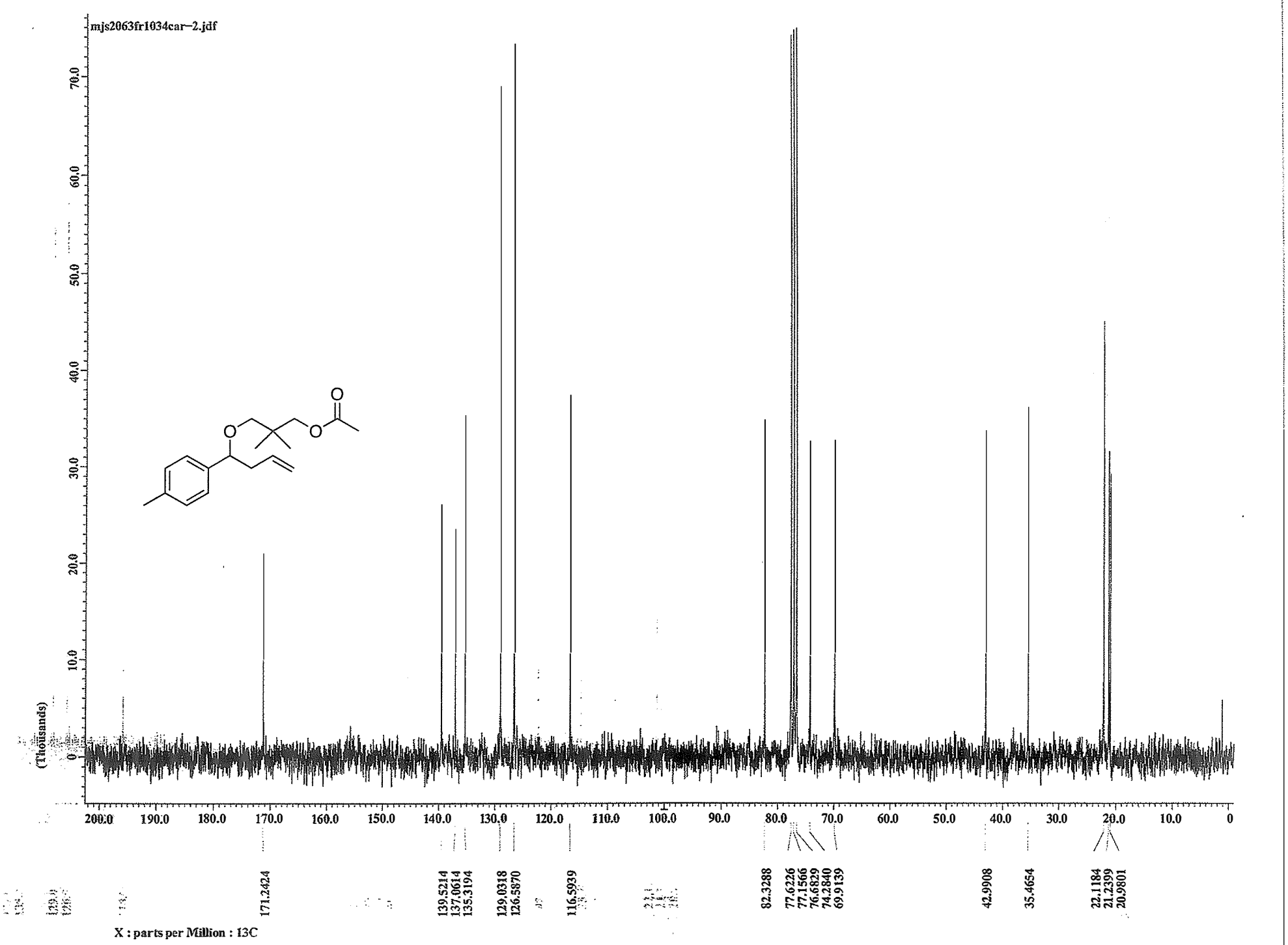
Spectrum 17 ^{1}H NMR of EB1123fr3743



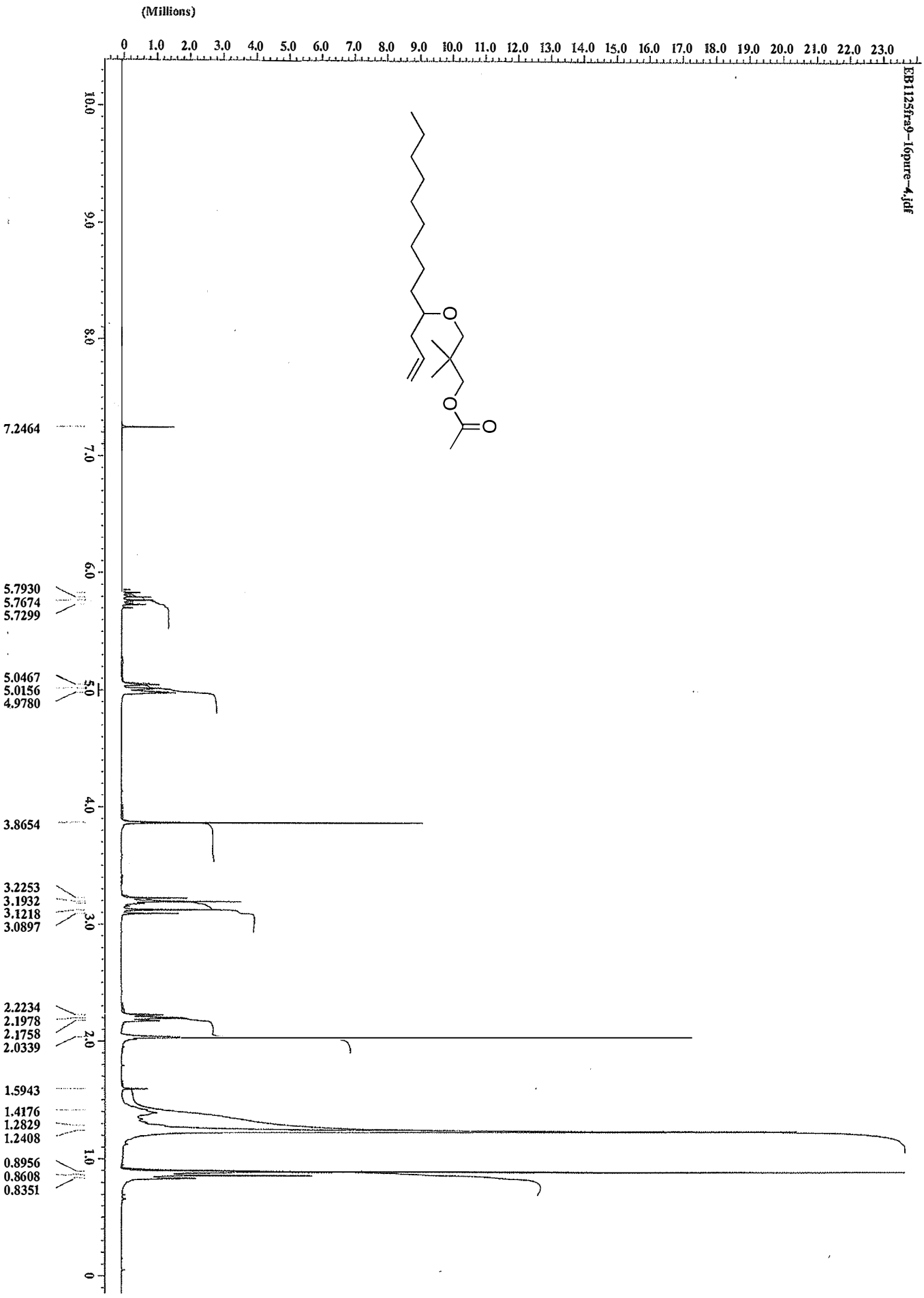
Spectrum 18 ^{13}C NMR of EB1123fr3743



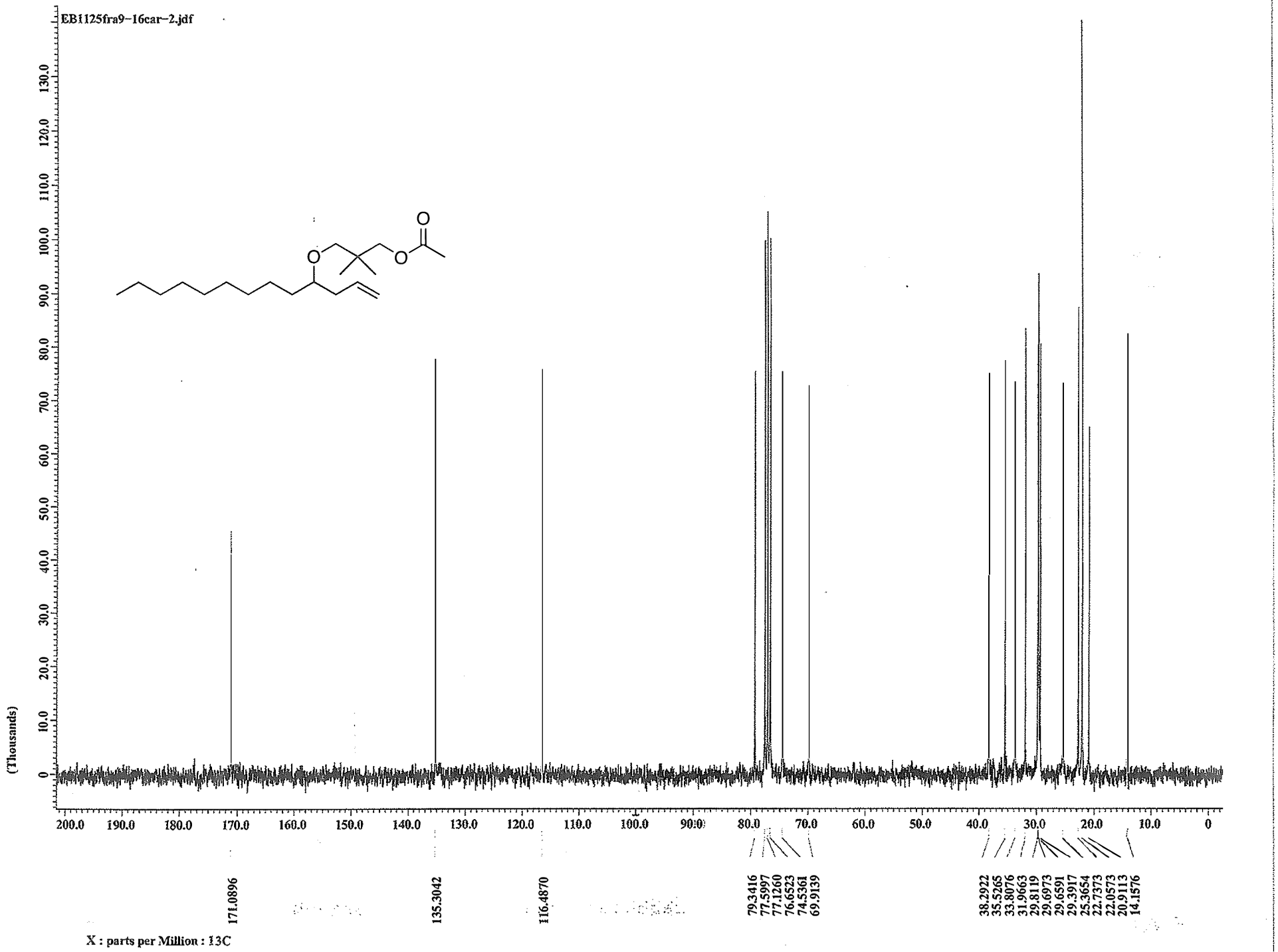
Spectrum 19 ^{1}H NMR of MJS2063fr1034



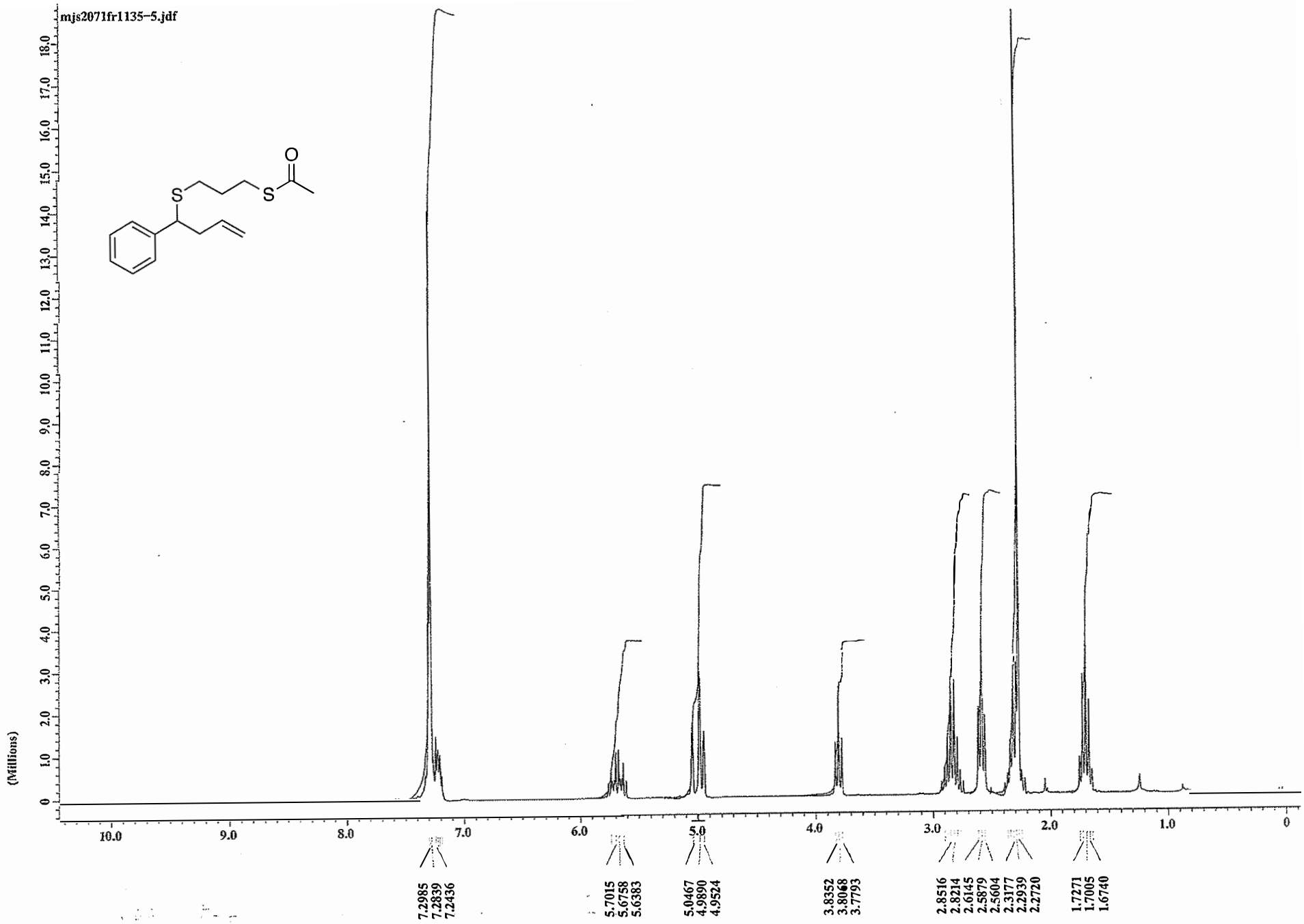
Spectrum 20 ^{13}C NMR of MJS2063fr1034



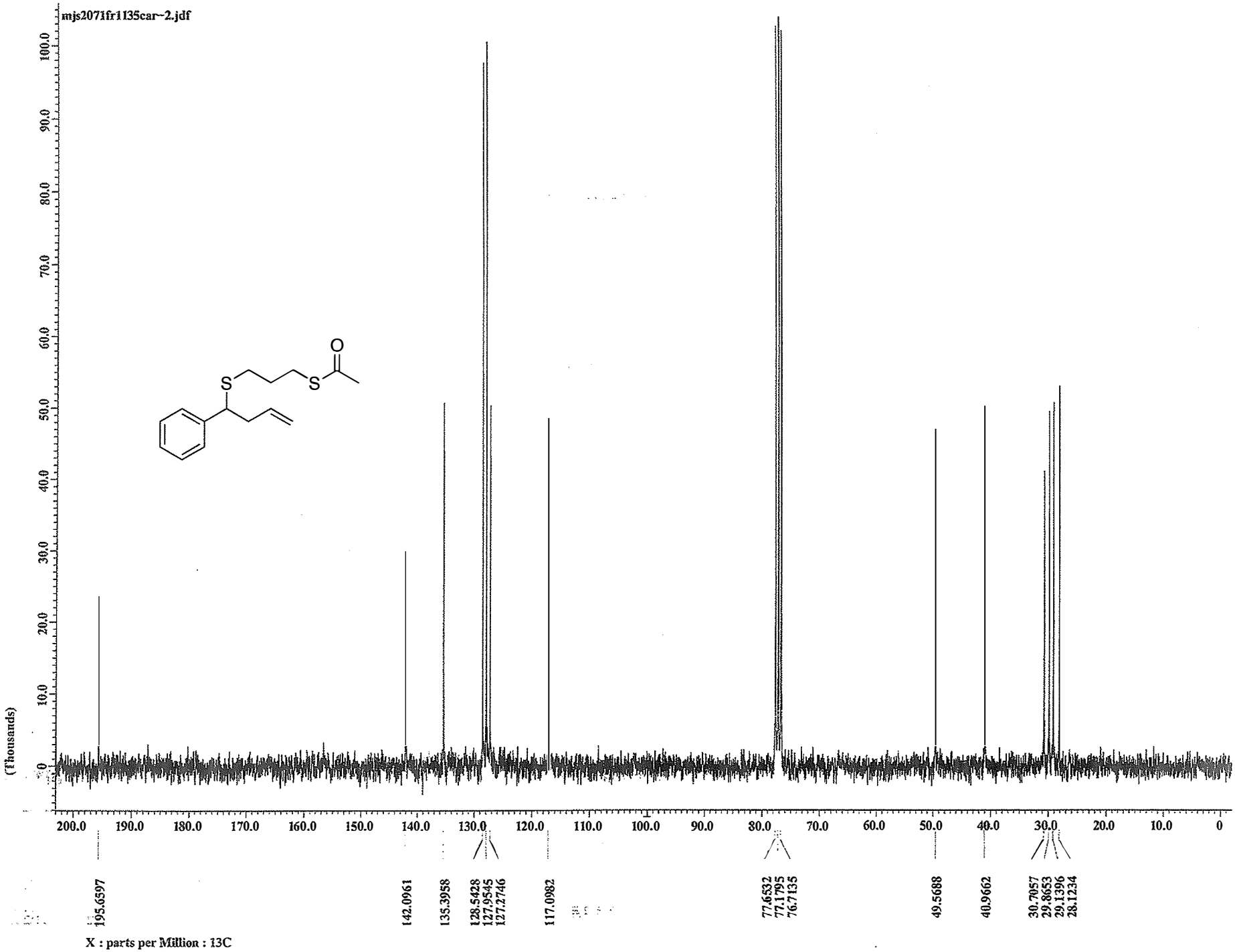
Spectrum 21 ^{1}H NMR of EB1125fr916



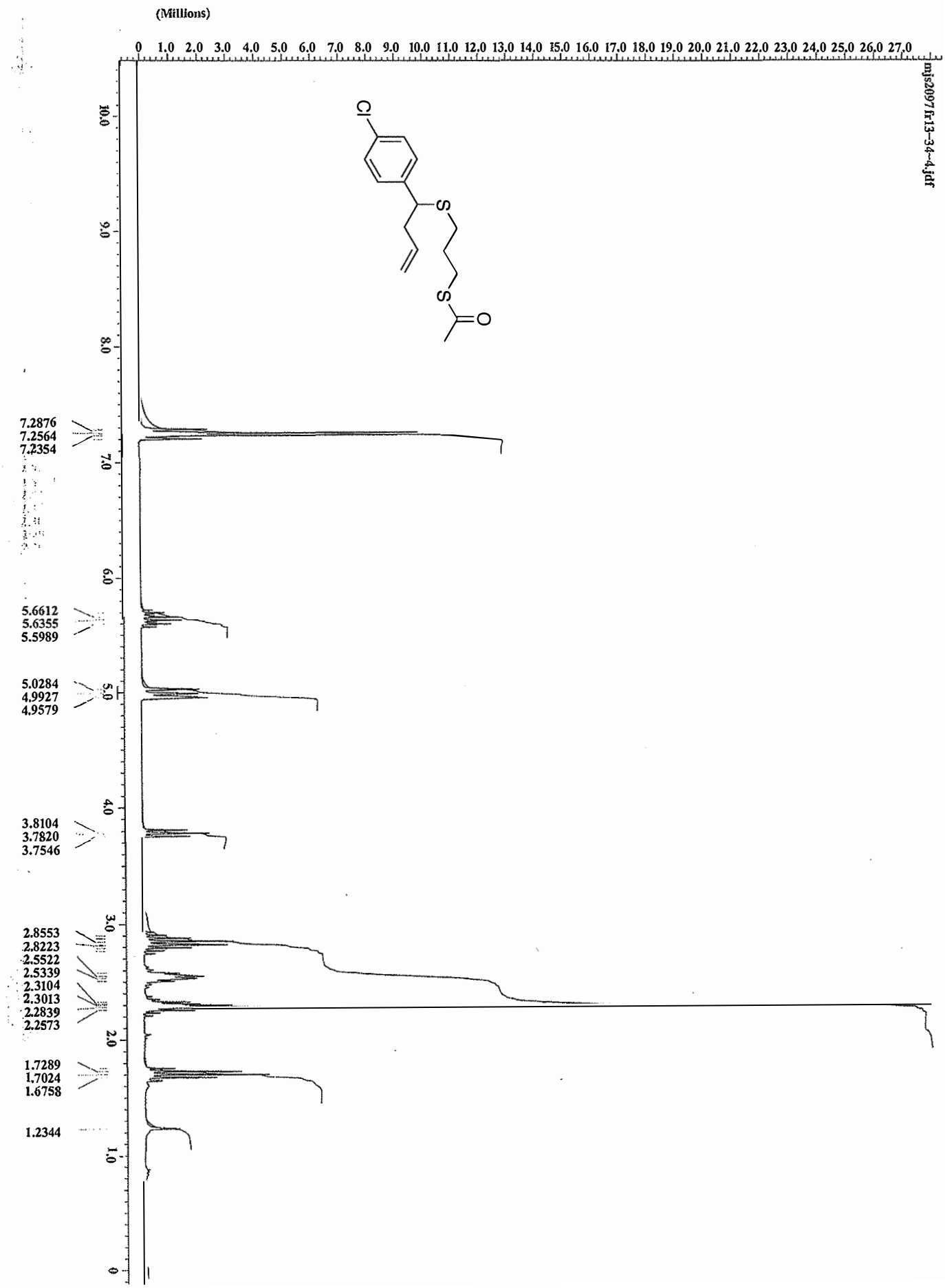
Spectrum 22 ^{13}C NMR of EB1125fr916



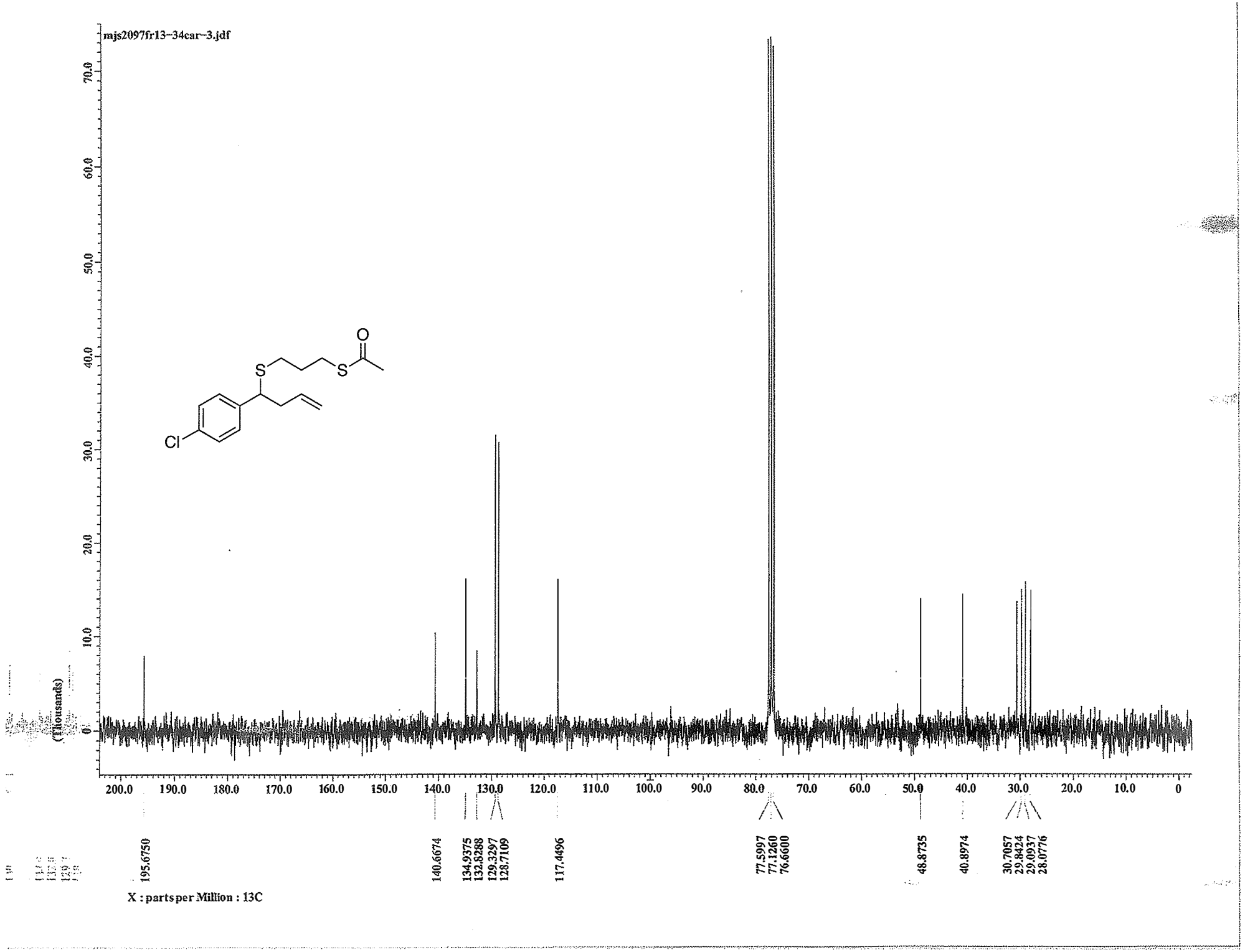
Spectrum 23 ^{1}H NMR of MJS2071fr1135



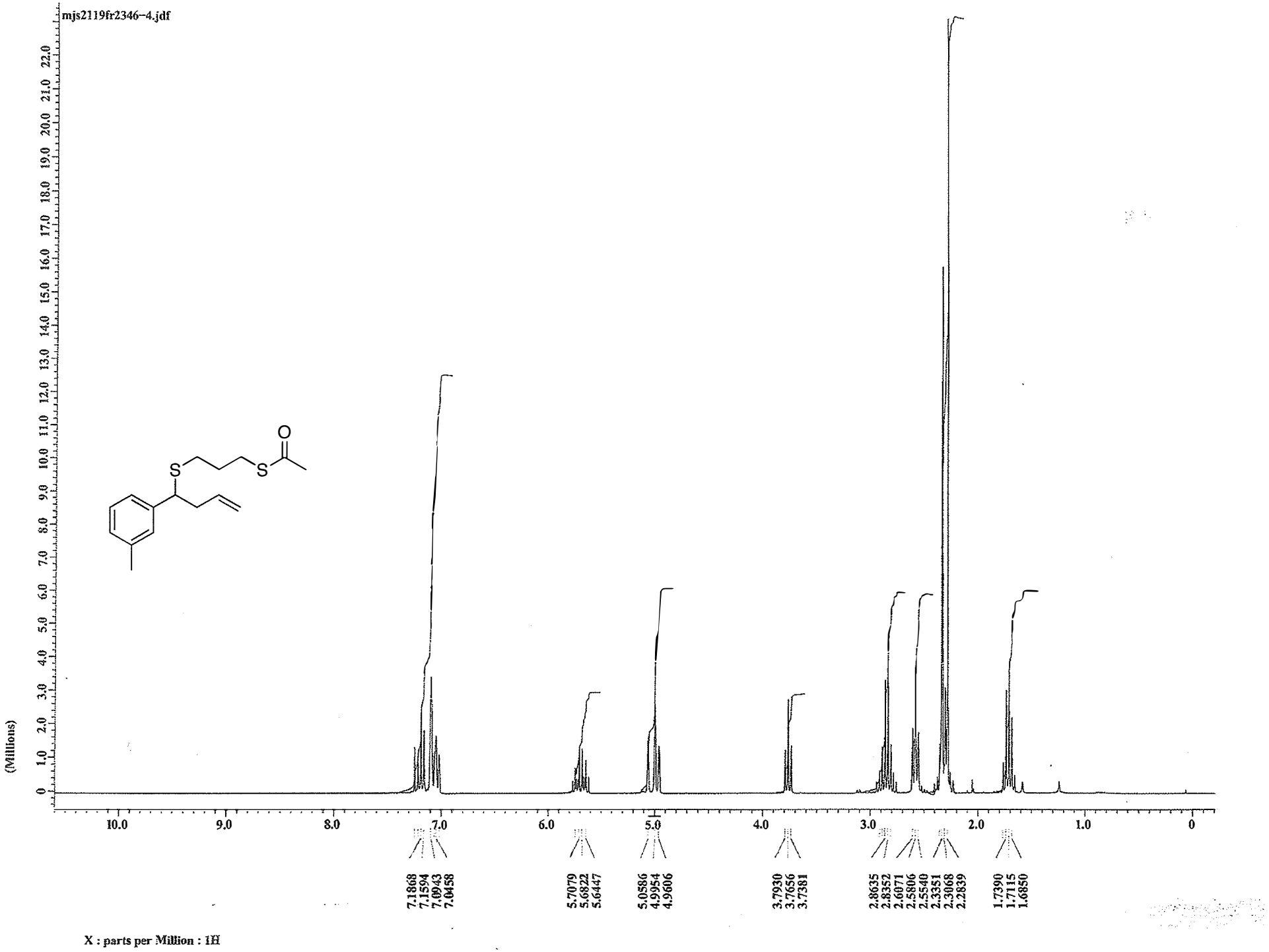
Spectrum 24 ^{13}C NMR of MJS2071fr1135



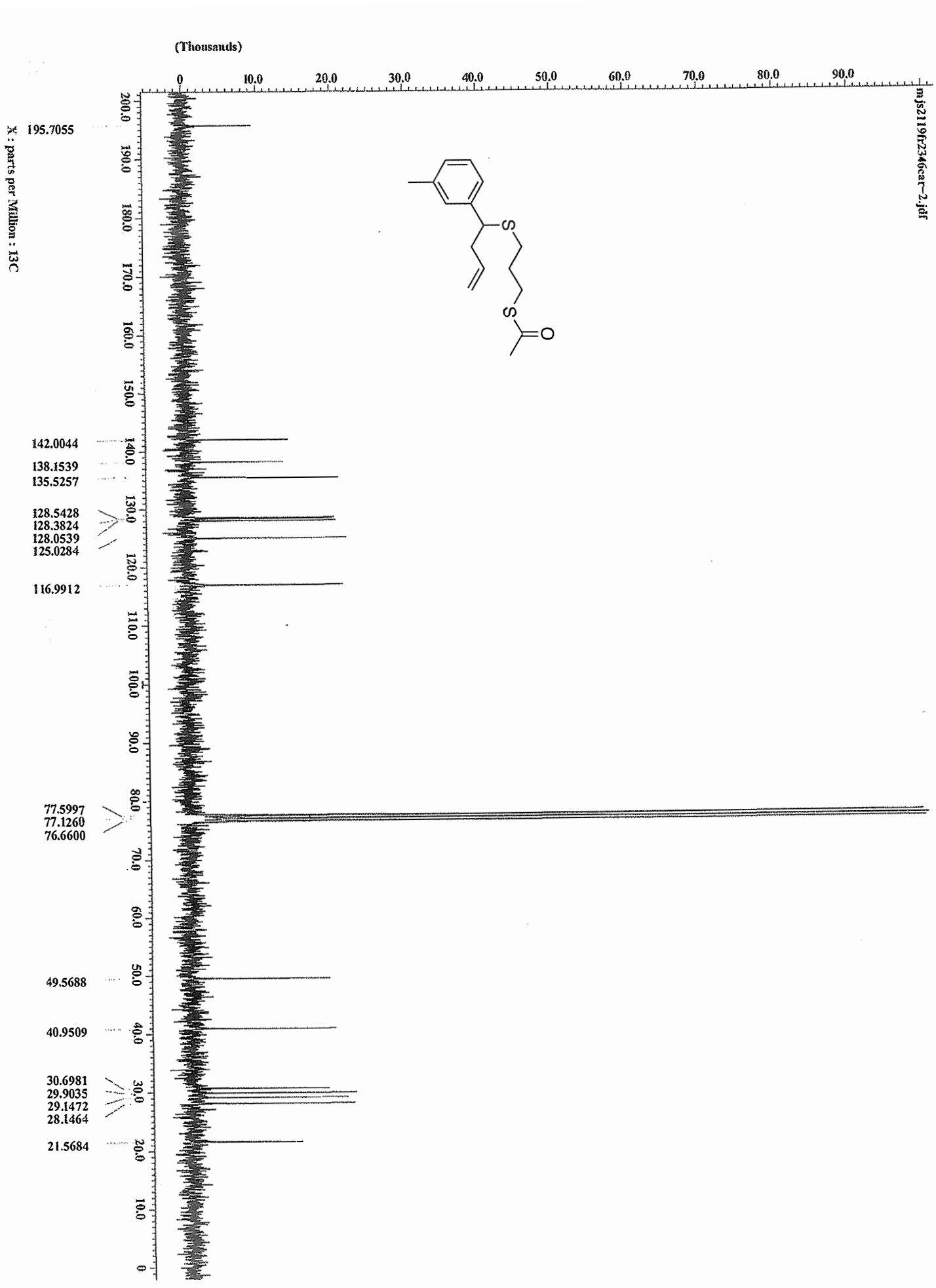
Spectrum 25 ^{1}H NMR of MJS2097fr1334



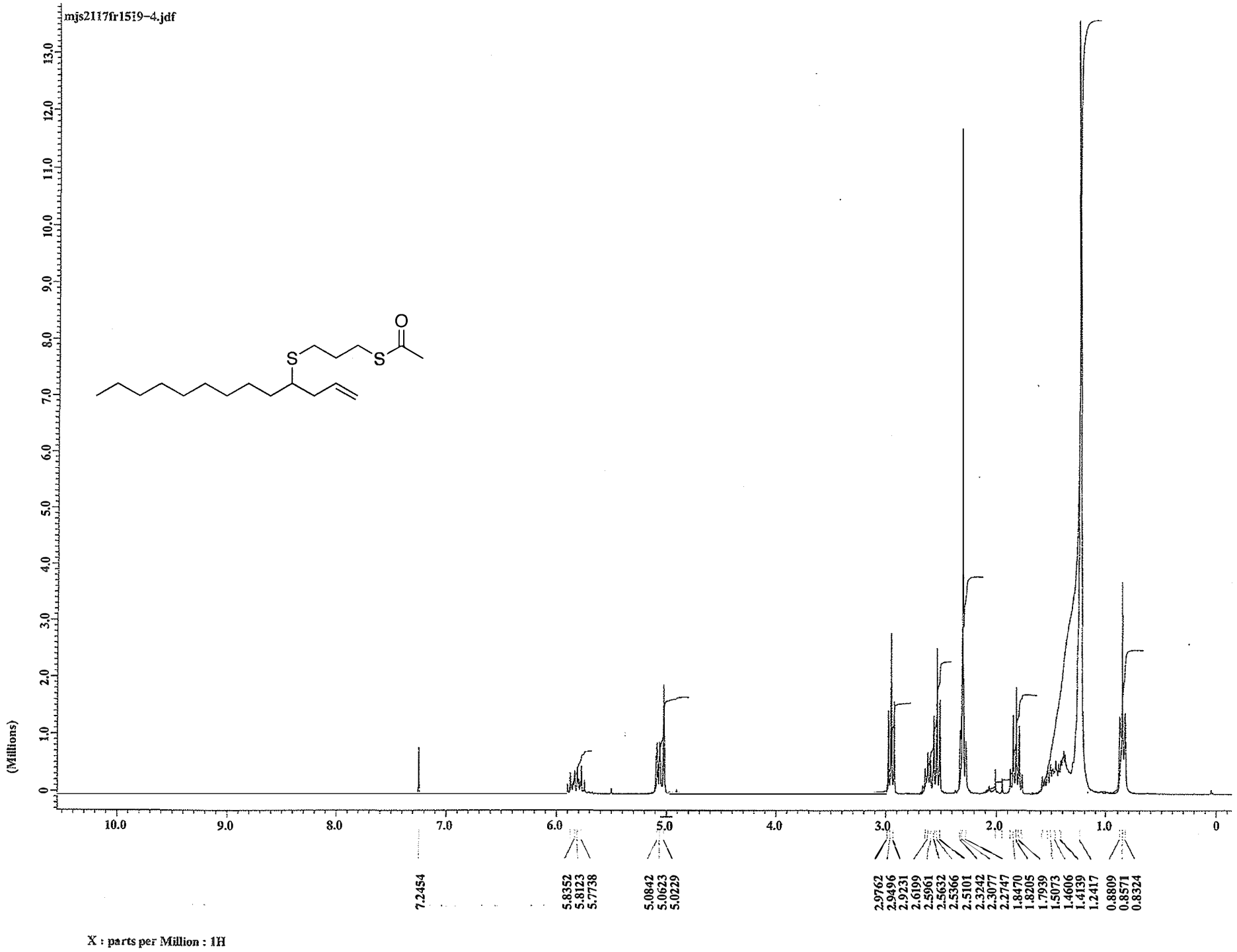
Spectrum 26 ^{13}C NMR of MJS2097fr1334



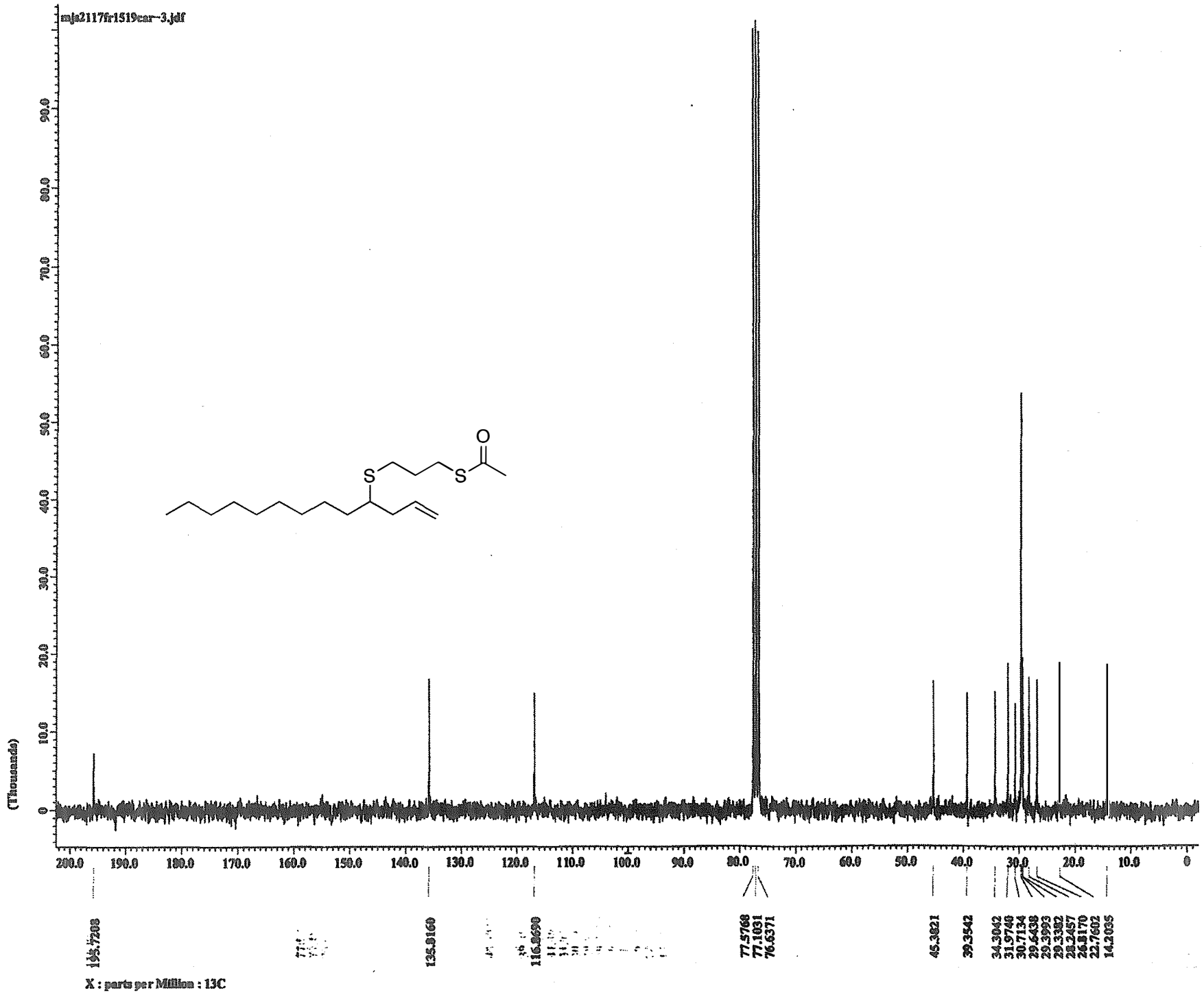
Spectrum 27 ^{1}H NMR of MJS2119fr2346



Spectrum 28 ^{13}C NMR of MJS2119fr2346



Spectrum 29 ^{1}H NMR of MJS2117fr1519



Spectrum 30 ^{13}C NMR of MJS2117fr1519