PALLADIUM CATALYZED CROSS COUPLING REACTIONS OF ALKENYL EPOXIDES AND ORGANOBORONIC ACID ESTERS

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ABSTRACT

PALLADIUM CATALYZED CROSS COUPLING REACTİONS OF ALKENYL EPOXIDES AND ORGANOBORONIC ACID ESTERS

In organic chemistry, it is a useful method to form a new allylic compounds as a result of 1-3 substitution reactions of allylic compounds which have a good leaving group. These reactions usually require a metal catalyst but one of the most challenging aspects of these applications is the process regio and stereo selectivity for a wide variety of substrate types. Other compounds such as alkenyl epoxides are also useful for 1-3 substitution reactions.

An advantage of using alkenyl oxirane compounds is that the oxirane ring is opened in the substitution step to form a hydroxyl group and resulted in the formation of allylic alcohols which are important intermediate product. Metal catalysed and regio-selective reactions of terminal alkenyl epoxides with organoborons have been reported in the literature. However, there is no successful method for internal alkenyl oxiranes. Thus, in this study, 1-3 substitution reactions of alkenyl oxiranes were successfully applied, which yielded allylic alcohols with high regio- and stereoselectivity.

ÖZET

ALKENİL EPOKSİTLERİN ORGANOBORONİK ASİT ESTERLERİYLE PALADYUM KATALİZLİ ÇAPRAZ BAĞLANMA TEPKİMELERİ

İyi bir ayrılan gruba sahip olan alilik bileşiklerin 1-3 yer değiştirme reaksiyonlarının bir sonucu olarak yeni alilik bileşiklerin oluşturulması organik kimyada yararlı bir yöntemdir. Bu reaksiyonlar genellikle bir metal katalizörü gerektirir, ancak bu uygulamaların en zorlu yönlerinden biri, çok çeşitli substrat tipleri için regio ve stereo seçimliliktir. Alkenil epoksitler gibi diğer bileşikler de 1-3 yer değiştirme reaksiyonları için yararlıdır.

Alkenil oksiran bileşiklerinin kullanımının bir avantajı, oksiran halkasının, yer değiştirme aşamasında açılarak allilik pozisyonda bir hidroksil grubu oluşturması ve bunun sonucunda önemli bir ara ürün olan allilik alkollerin oluşmasıdır. Terminal alkenil epoksitlerin organoborlarla metal katalizli ve regio-selektif reaksiyonları literatürde bildirilmiştir. Bununla birlikte, iç alkenil oksiranlar için başarılı bir yöntem yoktur. Bu nedenle, bu çalışmada, alkenil oksiranların 1-3 yer değiştirme reaksiyonları başarıyla uygulanmış, yüksek regio ve stereo-seçicilik ile allilik alkoller elde edilmiştir.

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ABBREVIATIONS

Bu	n-butyl
DCM	Dichloromethane
DIBAL-H	Diisobutylaluminium hydride
DIPA	Diissopropylamine
DMAP	4-Dimethylaminopyridine
DMP	Dess-Martin periodinane
EtOAc	Ethyl acetate
GC	Gas chromotography
h	Hour
i-Pr	Isopropyl
m-CPBA	meta-Chloroperoxybenzoic acid
mg	Miligrams
min.	Minute
mL	Mililiter
mmol	Milimoles
NEt_3	Triethylamine
NMR	Nuclear Magnetic Resonance
ON	Overnight
Ph	Phenyl
Pyr	Pyridine
RT	Room temperature
TBSCl	Tert-butyldimethylsillyl chloride
TEPA	Triethylphosphonoacetate
THF	Tetrahydrofuran
TLC	Thin Layer Chromotography

CHAPTER 1

INTRODUCTION

Transition metal catalyzed reactions with various organometallic reactants have received considerable interest in recent years. An example is the addition of an alkenyl or aryl group to an unsaturated compound which has a leaving group. In the absence of a metal catalyst, these compounds generally give the S_N2 reaction with nucleophiles. However, the presence of transition metals leads the reaction to give the product of S_N2' reaction.

In such unsaturated compounds, the selectivity shifts towards the S_N2' reaction when using hard nucleophiles such as organolithium, organozinc and grignard reagents. However, such hard nucleophiles are difficult to use because they are very air and moisture sensitive. On the other hand, organoboron compounds are easy to use in such reactions because of their high air and moisture stability. The diversity of organoboron compounds has made them usable in different coupling and substitution reactions. They havebeen used at 1-3 substitution reactions over propargylic compounds providing allenyl compounds (Moriya et al. 1994). In 2011, the palladium-catalyzed S_N2''selective reaction with organoborons was first performed on 2-ene-4-carbonate compounds (Üçüncü et al. 2011).

Vinyl epoxide compounds are one of the important intermediates which are widely used in organic synthesis. The two reactive constituents of the vinyl epoxide compounds are a strained epoxide ring and a conjugated carbon-carbon double bond to this ring.

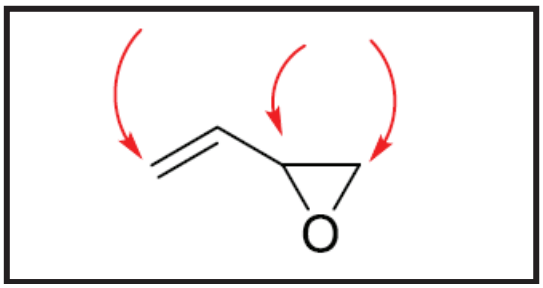


Figure 1.1. Reactive part of alkenyl oxirane

Considering these reactive elements, there are three different regioisomeric selectivities in the reaction of vinyloxiranes, particularly with nucleophilic organometallics, two of them via S_N2 reactions and the other is via S_N2'. The latter substitution type (S_N2') would form allyl alcohols which are valuable intermediates which are used commonly in variosu organic synthesis.

There are very few examples of allylic arylation reactions of alkenyl oxiranes in the literature and most of these involve highly basic organometallic reagents, such as Grignard and organozinc reagents. Thus, we have decided to improve selectivity of the method involving reactions of organoborons and internal alkenyl.

CHAPTER 2

LITERATURE WORKS

2.1.Transition- Metal-Catalyzed Allylic Arylation Reaction of Allylic Compounds

In 1994, Bäckvall reported highly regioselective reactions of allylic chlorides with aryl Grignard reagents in the presence of copper catalyst. In situ formed organocopper compounds $Ar_2CuMgBr$ and ArCu(X)MgBr were used ıt was observed that the reaction proceeded in S_N2' manner with 90% regioselectivity when ArCu(X)MgBr was used –especially when X is chloride-.(Figure 2.1.). (Bäckvall et al.,1994).

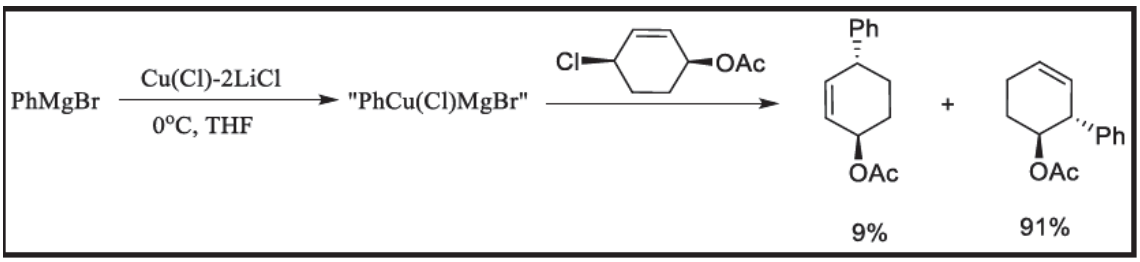


Figure 2.1. Copper(I)-catalyzed arylation reaction of an alkenyl chloride with a Grignard Reagent (Source: Bäckvall et al., 1994).

Kacprzynski et al. (2007) accomplished the synthesis of allyl silanes with 98% ee via the reactions of diaryl or dialkyl zinc reagents and silicon substitued unsaturated phosphates in the presence of a chiralN-heterocycliccarbene-ligated copper catalyst. (Figure 2.2). (Kacprzynski et al., 2007).

Asymmetric allylic substitution reaction for allyl halide compounds with aryl magnesium bromides was performed by Selim et al. 2008. Chiral copper-amidophosphane complexes were used as a catalyst, first time in the literature and provided the S_N2' product with high ee%. (Figure 2.3.). (Source: Selim et al., 2008).

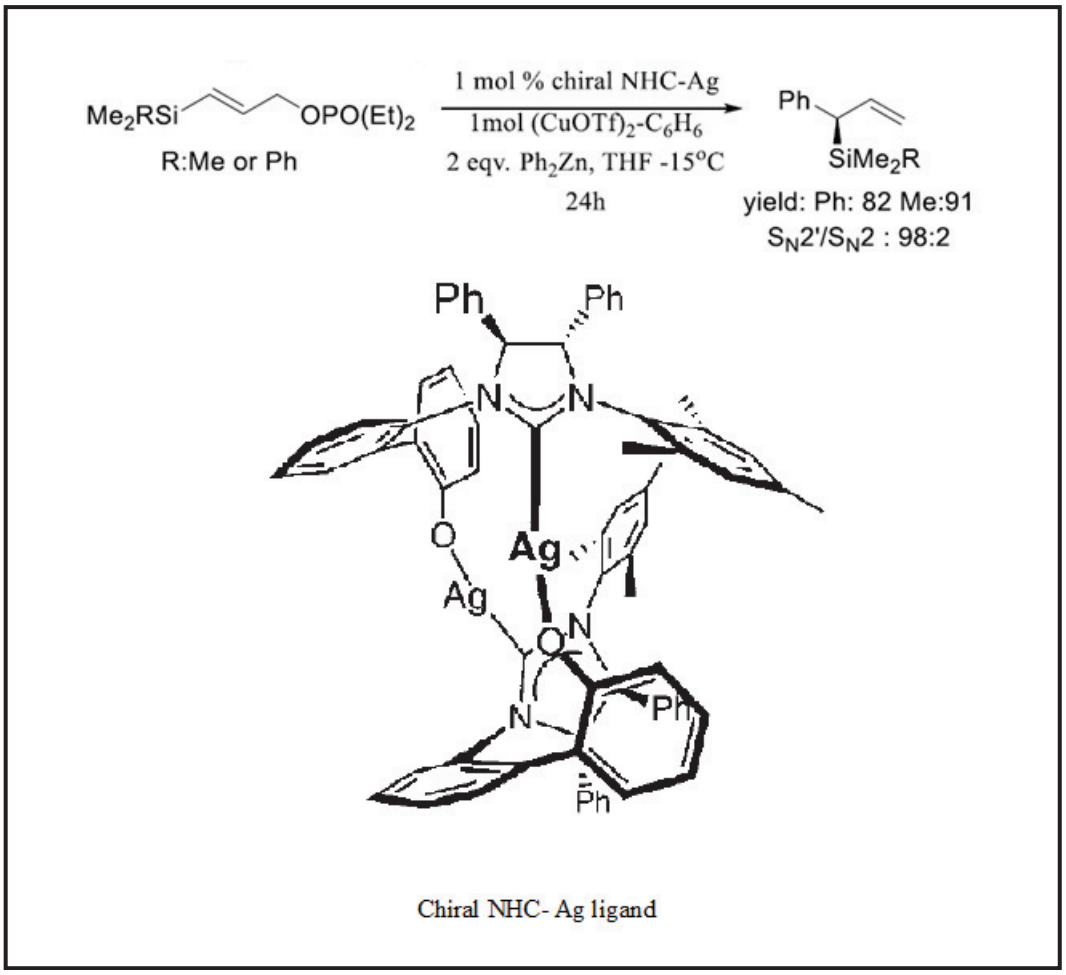


Figure 2.2. Cu-catalyzed asymmetric arylation reaction of silyl substituted alkenyl phosphono esters (Source:Kacprzynski et al., 2007).

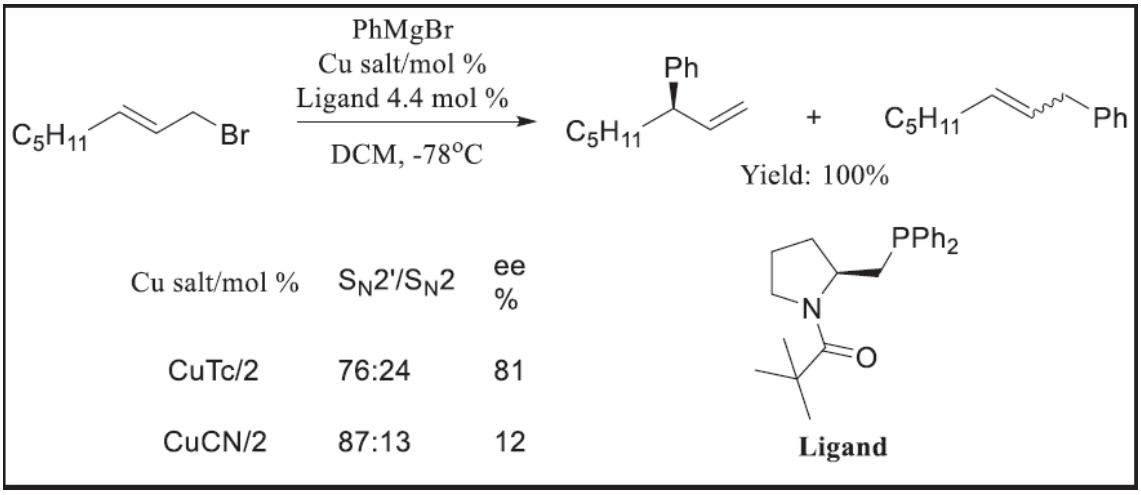


Figure 2.3. Cu catalyzed reaction of a non-cyclic allyl bromide with phenyl grignard reagent (Source: Selim et al.,2008).

They also synthesized a chiral NHC-Cu catalyst and used in allylic arylation reaction of cynnamyl bromides with Grignard reagents. The reaction produced diarylvinylmethanes with high regio and enantioselectivity.(Figure 2.4.). (Selim et al., 2009).

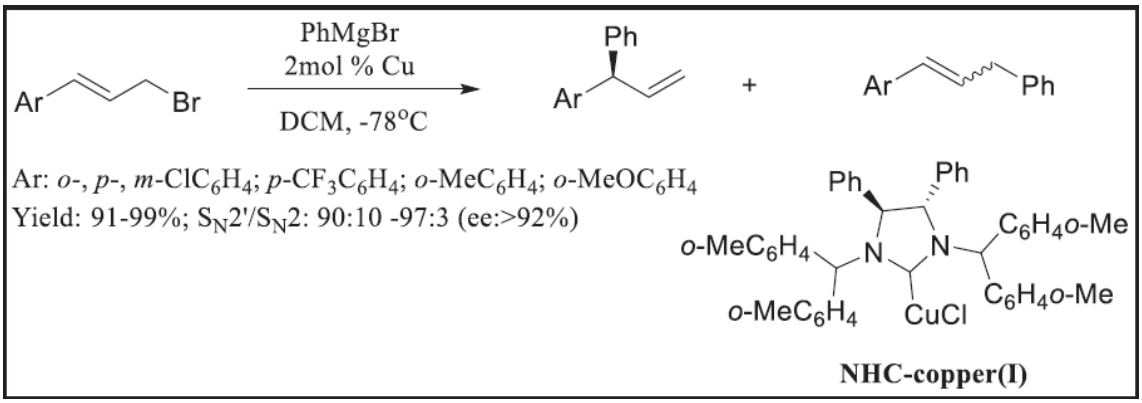


Figure 2.4. NHC-Cu(I) catalyzed reaction of phenyl substituted alkenyl compounds (Source: Selim et al., 2009).

In 2009, Polet announced a method for asymetric allylic arylation to produce diaryl alkenes. They studied first Ir-catalyzed allylic substitution reaction using arylzinc reagents. In this study, allylic compounds which have a good leaving group such as carbonate were studied. The molecules which were formed by this method had high ee (≥99%) , but poor regioselectivity (Figure 2.5.). (Source: Polet et al., 2009).

Ohmiya et al. (2008) , published a Pd-catalyzed allylic substitution reactions of allylic acetates with aryl boronic acids. The reactions gave rise to allyl-aryl couplingproducts with high γ selectivity and E/Z selectivities. (Figure 2.6.). (Source: Ohmiya et al., 2008).

Whittaker et al. (2010), reported a copper-catalyzed S_N2'-selective arylation reaction of allylic chlorides. They used Cu(I) catalyst, primary allylic electrophile and aryl boronic esters as a nucleophile. As compared to the hard nucleophiles such as grignard reagents and arylzinc compounds, aryl boronic esters provided higher regioselectivity. The method can be used on substrates with different functional groups including formyl, carbomethoxy, nitrilo, azido, chloro, bromo, and nitro groups. (Figure 2.7.).

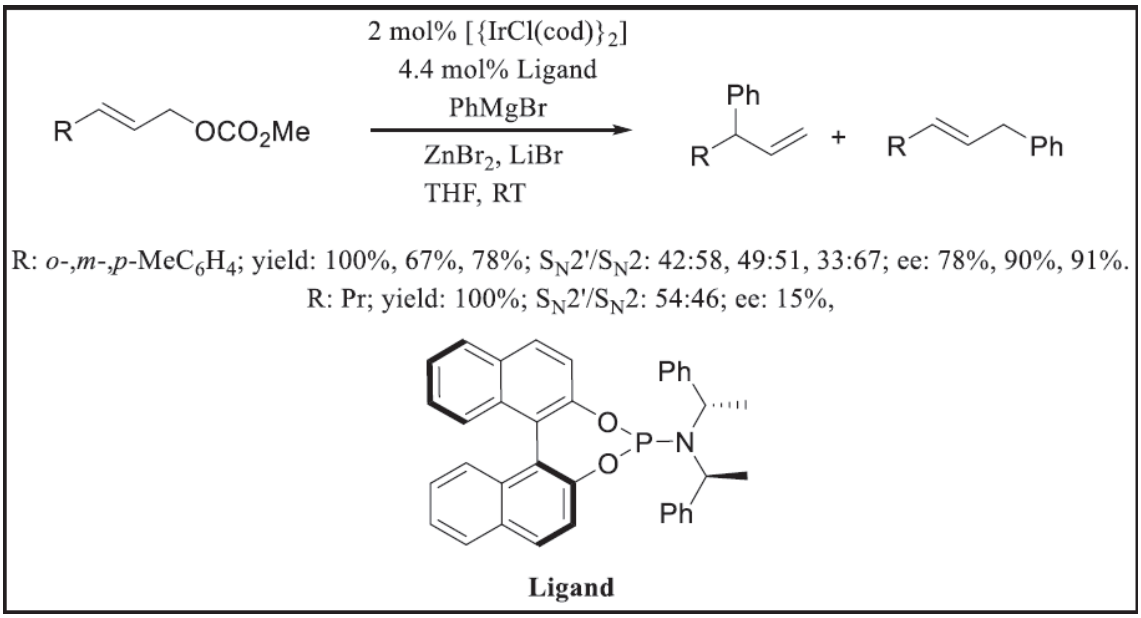


Figure 2.5. Iridium-catalyzed allylic arylation
(Source: Polet et al., 2009).

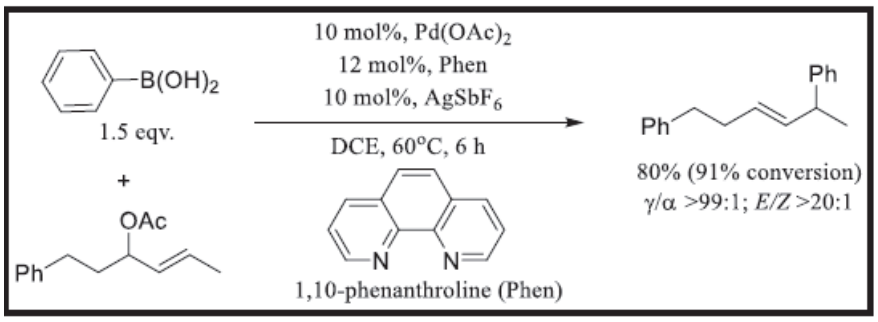


Figure 2.6. Pd-catalyzed reaction of allylic acetates with arylboronic acids
(Source: Ohmiya et al., 2008)

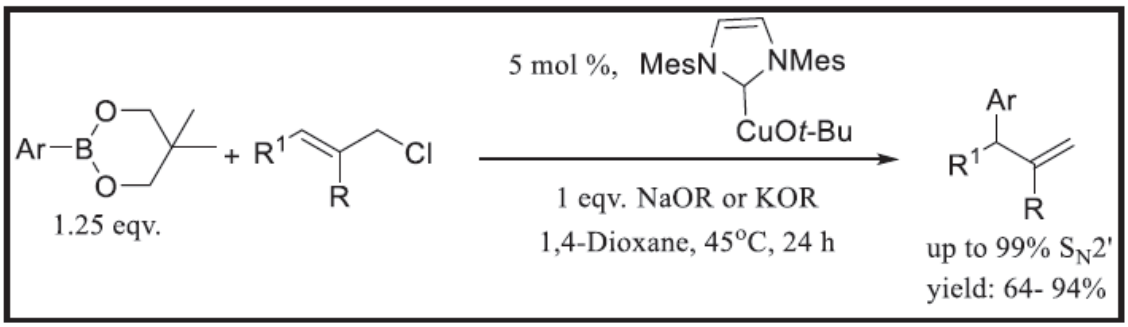


Figure 2.7. Cu catalyzed 1,3-selective substitution of allylic chlorides with aryl boronic esters (Source: Whittaker et al., 2010).

Takeda et al. (2014), reported a copper-catalyzed asymmetric allylic substitution reaction of disubstituted allyl phosphates with arylboronates to create quaternary stereocenters. They reported that when they used hydroxyl-bearing chiral N –heterocyclic carbene ligand the reactions had high region- and stereo-selectivities. (Figure 2.8.).

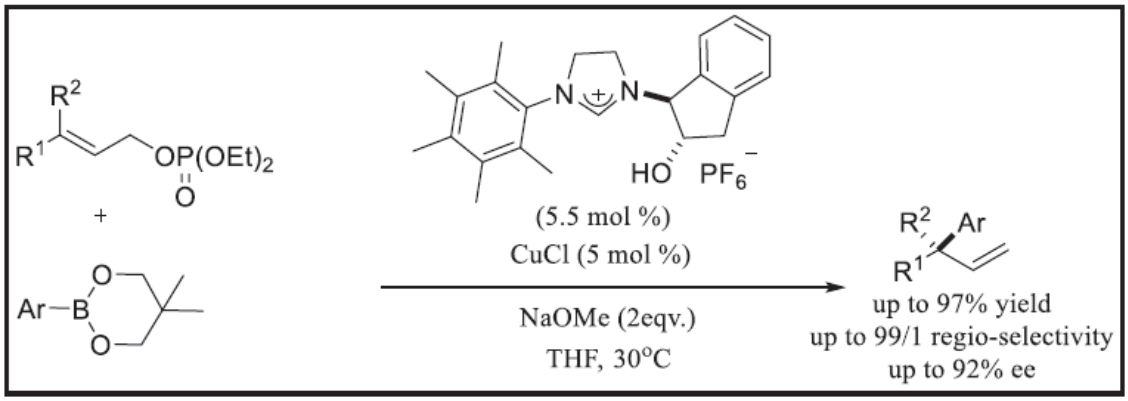


Figure 2.8. Cu-catalyzed asymmetric allylic substitution of allyl phosphates with aryl boronates (Source: Takeda et al., 2014).

2.2.Metal-Catalyzed Reactions of Vinyl Oxiranes with Grignard Reagents

Ueki et al. (2005), studied reaction of gem-difluorinated vinyloxiranes with hard nucleophiles such as RLi to provide allylic alcohols via S_N2' pathway. However, they realised that the regioselectivities of the reactions were not good. Then, they made the reaction conditions more moderate by using soft nucleophiles, such as organocuprates and obtained high regio- and stereo selectivity. (Figure 2.9.).

Millet and Alexakis (2007) published a copper catalyzed kinetic resolution reaction of 1-3 cyclohexadiene monoepoxide with grignard reagents. They noticed that the best ligand for the method was chiral ferrocenyl-based diphosphine ligand and gave high regio- and enantio-selectivities in reactions. (Figure 2.10.).

One year later, Millet and Alexakis (2008), reported another Cu-catalyzed kinetic resolution reaction of 1-3 cyclohexadiene monoepoxide with grignard reagents. In this study, they used SimplePhos ligands and reported that higher enantio- and regio-

selectivities when compared to the chiral ferrocenyl-based diphosphine ligands. Also, they showed that the method is applicable to larger Grignard reagent scale. Even with secondary Grignard reagents, it was seen that yields were moderate and enantio-selectivity was very high. (Figure 2.11.).

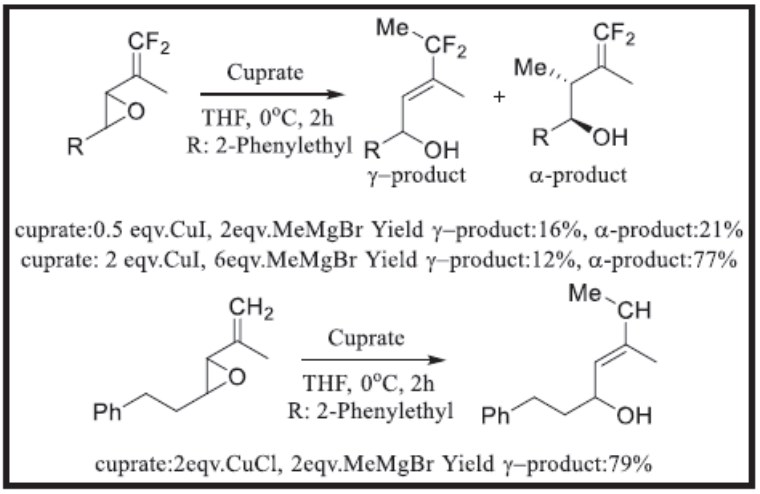


Figure 2.9.The Reaction of alkenyl oxiranes with grignard reagents (Source: Ueki et al., 2005)

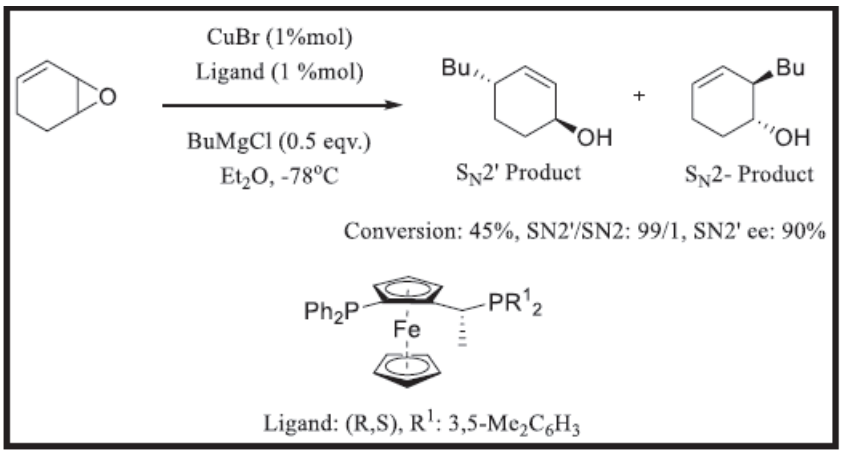
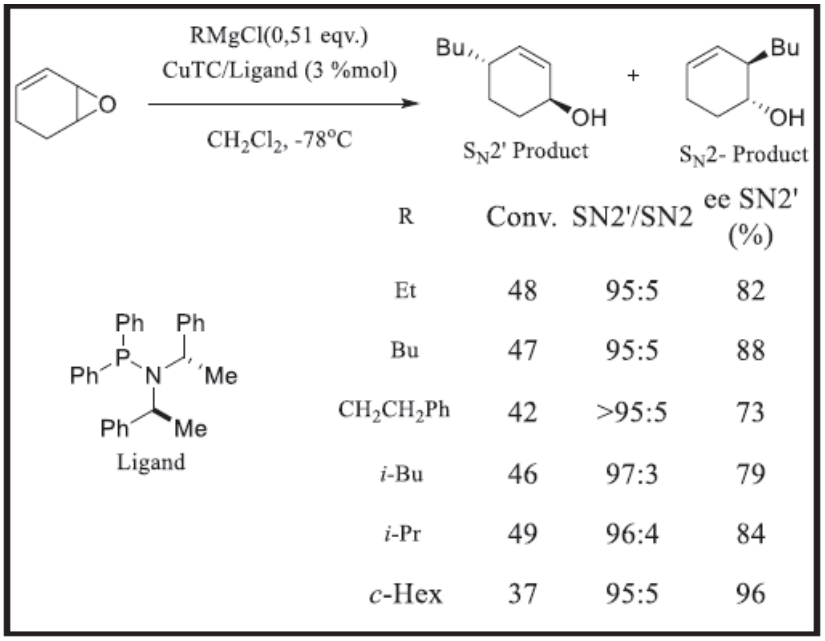


Figure 2.10. Cu catalyzed kinetic resolution of 1,3-Cyclohexadiene monoepoxide with grignard reagents (Source: Millet and Alexakis 2007).

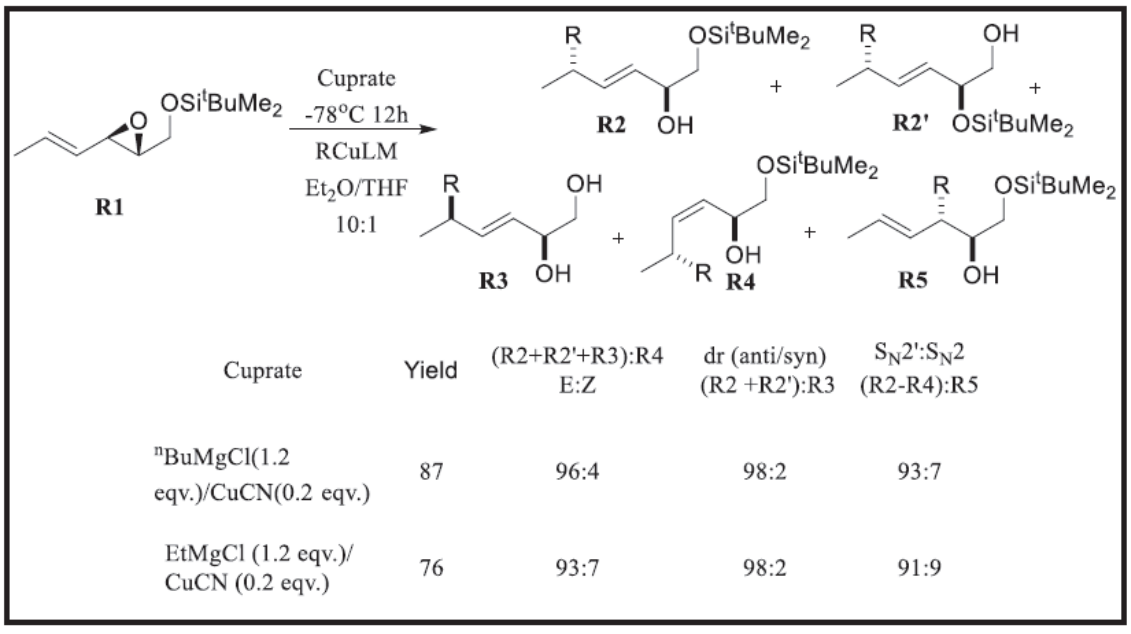
Dieter et al. (2012) reported a copper catalyzed regio- and stereo- controlled tandem bis allylic substitution reaction with different combinations of CuCN derived cuprate reagents. Starting with vinyloxirane compounds, vicinal stereogenic centers

were formed with dialkylzinc reagents. It was seen that, this method was highly enantio-selective for the S_N2' reaction. (Figure 2.12.).



R	Conv.	SN2'/SN2	ee SN2' (%)
Et	48	95:5	82
Bu	47	95:5	88
CH_2CH_2Ph	42	>95:5	73
i-Bu	46	97:3	79
i-Pr	49	96:4	84
c-Hex	37	95:5	96

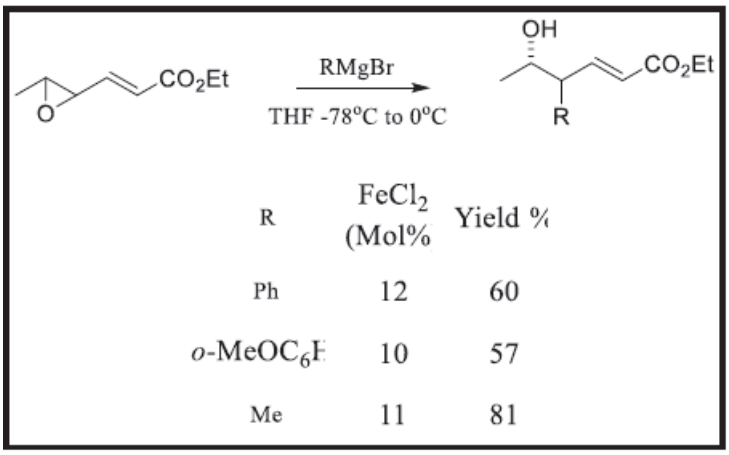
Figure 2.11. SimplePhos as efficient ligand for the copper-catalyzed kinetic resolution of cyclic vinyloxiranes with grignard reagents (Source: Millet and Alexakis, 2008).



Cuprate	Yield	(R2+R2'+R3):R4 E:Z	dr (anti/syn) (R2 +R2'):R3	$S_N2':S_N2$ (R2-R4):R5
^{n}BuMgCl(1.2 eqv.)/CuCN(0.2 eqv.)	87	96:4	98:2	93:7
EtMgCl (1.2 eqv.)/ CuCN (0.2 eqv.)	76	93:7	98:2	91:9

Figure 2.12. Copper-mediated reactions of trans-1-(tert-Butyldimethylsilyloxy)-2,3-epoxy-4-hexene (Source: Dieter et al., 2012)

Hata et al. (2010), published iron-catalyzed regio- selective reaction of γ-δ-epoxy-α-β-unsaturated ester or amides with Grignard reagents in 2010. The reaction proceeded with inversion of configuration to yield homoallyl alcohols as a single product in good yields. (Figure 2.13.).



R	$FeCl_2$ (Mol%	Yield %
Ph	12	60
o-$MeOC_6H$	10	57
Me	11	81

Figure 2.13.The iron-catalyzed reaction of vinyl oxirane
(Source: Hata et al., 2010)

2.3.Metal-Catalyzed Reactions of Vinyl Oxiranes with Organoborons

For the synthesis of allyl alcohols, region- and stereo- selective substitution reactions of vinyl oxiranes are a good strategy.

Tortosa and Mariola (2011) reported copper-catalyzed S_N2 reactions of allylic epoxides with diboronates. According to this method, enantiomerically enriched 1-4 diol compounds can be synthesized from non-racemic epoxides. (Figure 2.14.).

Crotti et al. (2009) published nickel catalyzed borylative ring openning reaction of vinyl epoxides and aziridines. The ring openning was followed by allylation of aldehydes. The products formed with high stereocontrol and had three stereogenic centers. (Figure 2.15.).

In 1982, Miyaura et al. published Pd-catalyzed reaction of vinyl oxiranes with alkenylborons. In this study, only 3,4-epoxy-1-butene was used as a vinyl epoxide compound and regio-selectivity of reactionwas not good with this substrate (Figure 2.16.).

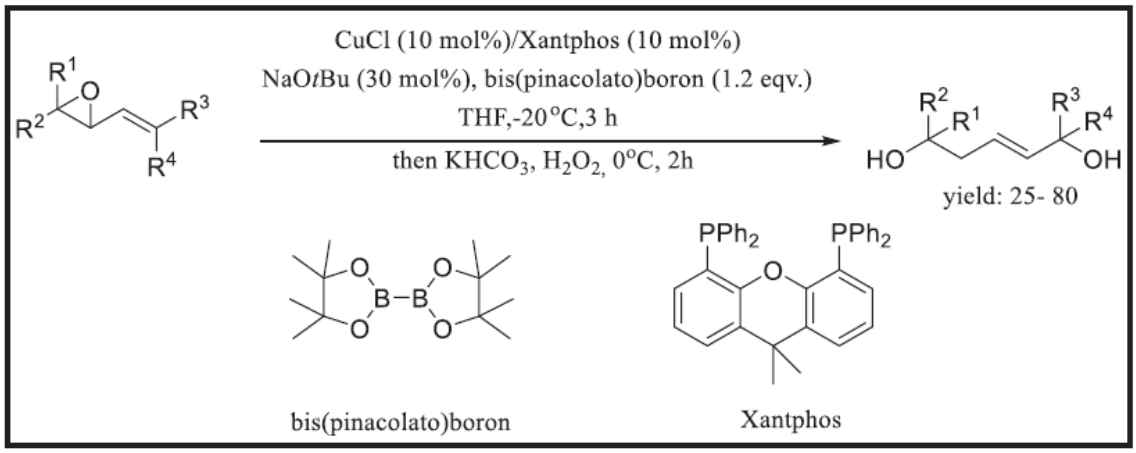


Figure 2.14. Cu-catalyzed borylation and oxidation sequence leading to 1,4-diol compounds (Source: Tortosa and Mariola, 2011).

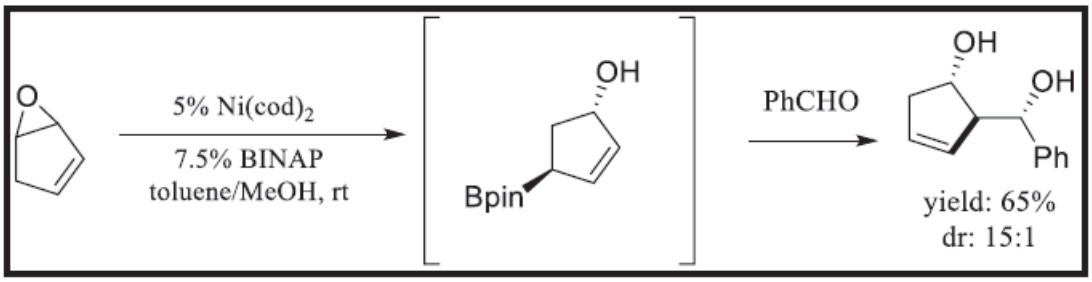
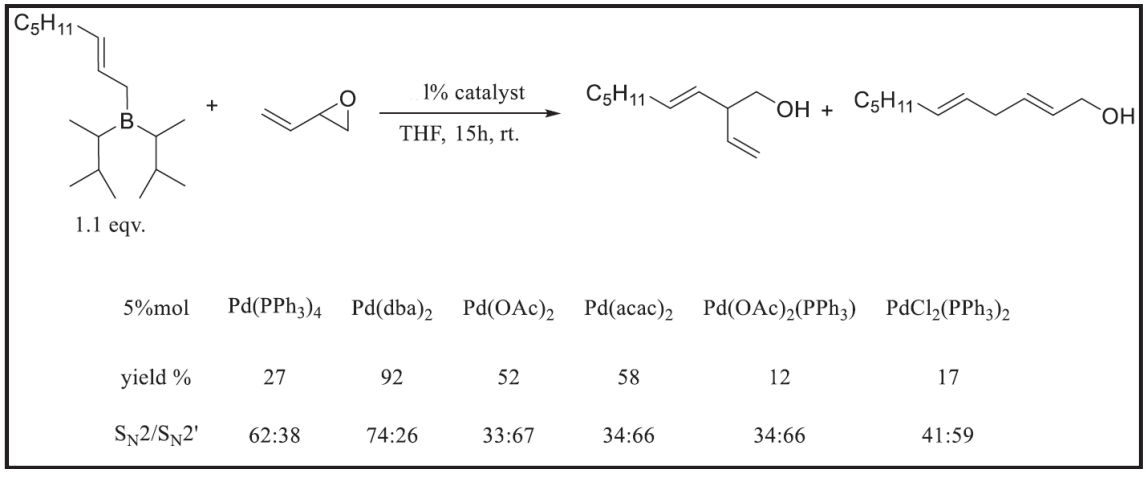


Figure 2.15.Nickel-catalyzed borylative ring opening reaction of vinyl epoxide (Source: Crotti et al., 2009)



5%mol	$Pd(PPh_3)_4$	$Pd(dba)_2$	$Pd(OAc)_2$	$Pd(acac)_2$	$Pd(OAc)_2(PPh_3)$	$PdCl_2(PPh_3)_2$
yield %	27	92	52	58	12	17
S_N2/S_N2'	62:38	74:26	33:67	34:66	34:66	41:59

Figure 2.16. Pd-catalyzed reaction of (E)-hexenylbis(1,2-dimethylpropyl) borane with 3,4-epoxy-1-butene (Miyaura et al., 1979).

Kjellgren et al. (2005) reported the Pd-Pincer complex – catalyzed reaction of terminal vinyl oxiranes with organoborons. The reaction proceeded with high regioselectivity and afforded allyl alcohols with excellent yields. (Figure 2.17.).

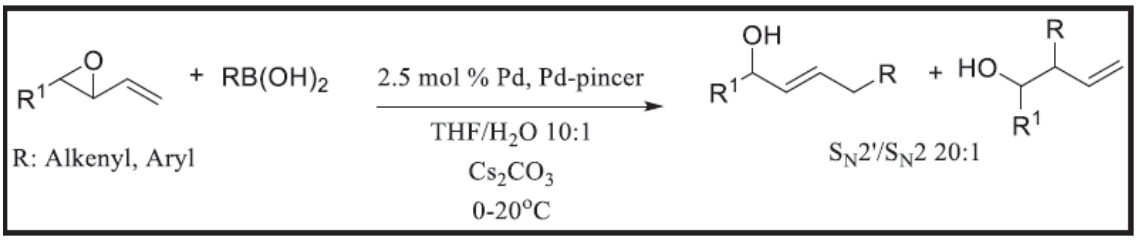


Figure 2.17. Pincer complex catalyzed cross-coupling reaction of vinyl epoxides with boronic acids (Source: Kjellgren et al., 2005).

Kıbrıs performed Pd-catalyzed, 1-3 substitution reaction of alkenyl oxiranes which contains hydroxyl groups via aryl organoborons. He started to optimization studies with the alkenyl epoxide which including a methoxy group. The results were not bad, but could be increased. (Figure 2.18.).

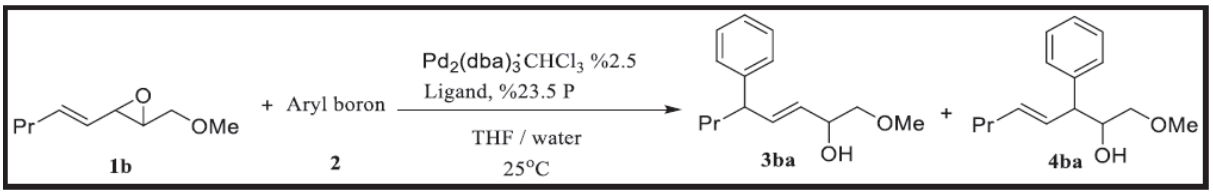


Figure 2.18. 1-3 substitution reaction of vinyl oxirane containing methoxy group.(Source: Kıbrıs,2016)

In the second step, the optimization studies were performed with the same vinyl oxirane which contains hydroxyl group. When compared with first compound, the results were beter. They observed that the addition of a ligand and an organic base have a positive effect to the reaction results. When they researched solvent scope, they found that the addition of some water affected the reaction time. Also, the catalytic effects of some of Pd complexes were examined and they observed that Pd(0) complexes were more effective than Pd(II) complexes. After studied with various organoborons, the neopentyl glycol ester boron derivative containing a phenyl group gave the best results. Thus, optimize conditions have been determined. (Figure 2.19.).

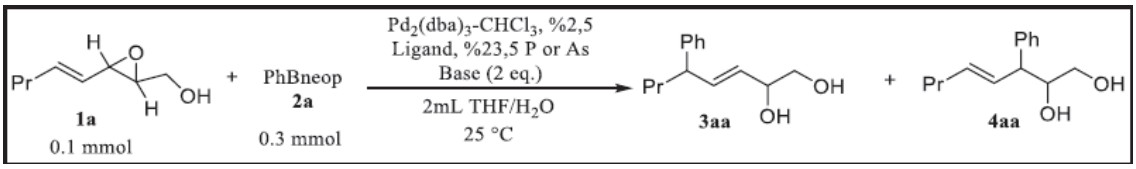


Figure 2.19. 1-3 substitution reaction of vinyl oxirane containing hydroxyl group. (Source: Kıbrıs,2016)

CHAPTER 3

EXPERIMENTAL STUDY

3.1 General

Tetrahydrofuran (THF) was purified by a solvent purification system (MBRAUN SPS-800). Dichloromethane (DCM) was dried using molecular sieve 4A. Triethylamine (NEt_3) was degased with argon before to use. $Pd_2(dba)_3.CHCI_3$ was synthesized in the laboratory (Zalesskiy and Ananikov 2012). All reactions were performed under argon atmosphere.

3.2 Synthesis of Substrates

3.2.1Synthesis of Substrate 1a and 1b

To a stirred solution of 1,4-butendiol (8.2 mL, 100 mmol) in THF (100 ml) at room temperature was added imidazole (2.24 g, 33 mmol) and TBSCl (4.53 g, 30 mmol).The reaction was stirred at room temperature for 22 h. After that extracted with Et_2O (x3) and washed with water and brine. The organic layer was dried over $MgSO_4$,filtered and concentrated under reduced pressure. The crude product was purified by column chromatography (Et_2O-hexane, 1:4) to yield mono-protected diol (4.55 g , %75 yield) as a colourless oil (**S2**) (Hwang, et al. 2013).

S2: ^{1}H NMR (400 MHz, $CDCI_3$) δ= 5.74 – 5.62 (m, 2H), 4.25 (ddd, *J* = 3.4, 1.8, 1.0 Hz, 2H), 4.19 (d, *J* = 5.5 Hz, 2H), 0.90 (s, 9H), 0.08 (s, 6H).

Dess-Martin periodinane (DMP) (7.39 g, 17.4 mmol) was dissolved in 130 mL of DCM. A solution of **S2** (3.36 g, 16.6 mmol) in 5 mL DCM was added drop by drop at room temperature. The mixture was stirred at room temperature for 1 hour. Then, aqueous $NaHCO_3$ and $Na_2S_2O_3$ solutions were added to the reaction flask and stirred

another 15 minutes. After that, the mixture was extracted with DCM and combined extracts were dried over $MgSO_4$, filtered, and concentrated under reduced pressure. Purification by column chromatography (hexane/Et_2O, 8:1) to give the aldehyde (**S3)** (2.20 g, 66%) as a colourless oil (Ding et al., 2004). According to the literature, it was expected that the formed product was Z isomer, but it was observed that E isomerized.

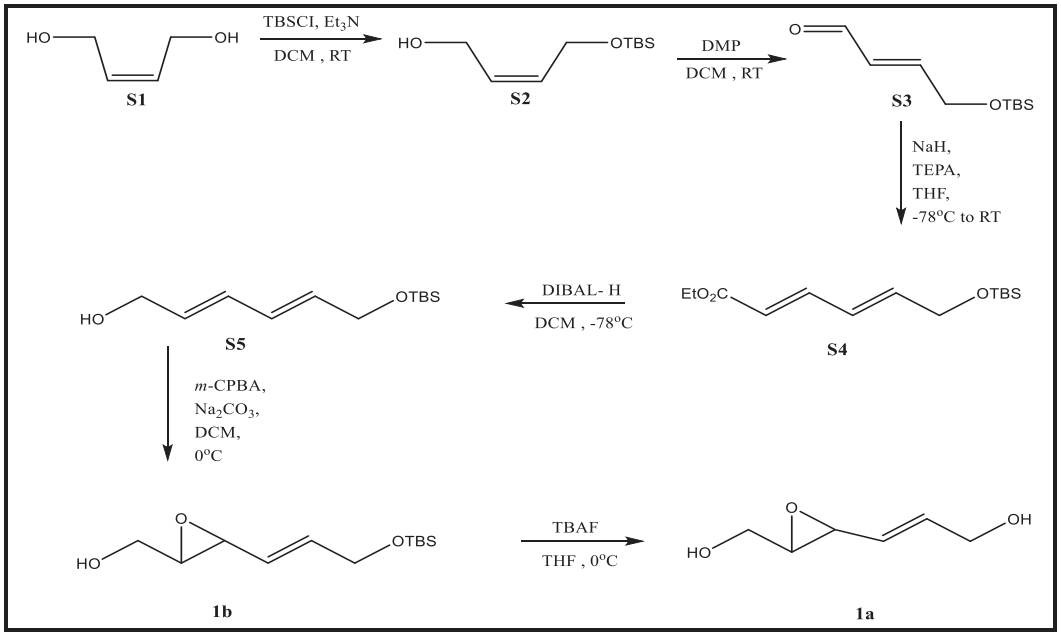


Figure 3.1. Synthesis of substrate 1a and 1b

To a suspension of NaH (289 mg, 12.1 mmol) in 20 mL of THF at -78^{0}C was added triethylphosphonoacetate (TEPA) (2.63 mL, 13.2 mmol) drop by drop. After 1 hour, a solution of **S3** (2.20 g, 11 mmol) in THF (8 mL) was added dropwise. The reaction was stirred 20 hours at RT. Extracted with Et_2O, washed with brine, dried over $MgSO_4$, filtered, and concentrated under reduced pressure. The residue was purified by column chromatography with hexane-Et_2O (8:1). It provided **(S4)** (2.58 g , 87%) as a pale yellow oil (Dias et al., 2017).

At -78 ^{0}C, the DIBAL-H solution (28.6 mmol, 1.0 M in DCM) was added dropwise to the solution of **S4** (2.58 g, 9.54 mmol, 70 mL of DCM). The reaction mixture was stirred for 80 mins at the same temperature. The mixture was allowed to rich room temperature and extraction with DCM and washed with sodium potassium tartratesolutionin order to decomposethe complex formed from DIBAL-H. The combined extracts were dried over $MgSO_4$, filtered, and concentrated under reduced

pressure. Purification was done over silica gel column using hexane-EtOAc (6:1) eluent to afford **(S5)** (2.16 g, 79%) as a colourless oil.

S5: ^{1}H NMR (400 MHz, $CDCI_3$) δ= 6.31 – 6.19 (m, 2H), 5.86 – 5.73 (m, 2H), 4.22 (d, *J* = 4.9 Hz, 2H), 4.18 (d, *J* = 5.6 Hz, 2H), 0.91 (s, 9H), 0.07 (s, 6H).

To a solution of**S5** (297 mg, 1.3 mmol) in 17 mL of DCM was added $NaHCO_3$ (179 mg, 2.13 mmol) and *m*-CPBA (70-75% , 320 mg) at 0 ^{0}C. The reaction was stirred at RT for 75 mins. The mixture was extracted with DCM, dried over $MgSO_4$, filtered and concentrated under reduced pressure. The residue was purified by Et_3N-treated silica gel column chromatography with hexane-EtOAc (4:1) to obtain **(1b)** (178 mg , 60%) as a yellow oil (Takamura , et al.,2012).

TBAF (2 mmol, 1.0 M in THF) was added dropwise to the solution of **1b** (367 mg, 1.5 mmol) in 20 mL of THF at 0 ^{0}C. The reaction was stirred for 1 hour at the same temperature. Then, the mixture was extracted with Et_2O, dried over $MgSO_4$, filtered, and concentrated under reduced pressure. The substrate was purified by Et_3N-treated silica gel column chromatography with hexane: EtOAc mixture to afford **(1a)** (143 mg, 73%).

3.2.2. Synthesis of Substrate 1c

To the mixture of methyl propiolate **S6**(40 mmol), acetic acid (13.8 mL, 240 mmol) and sodium iodide (9.6 g, 64 mmol) was stirred for 3 hour at 115 ^{0}C. After completion of the reaction, the mixture was extracted with Et_2O, washed with aqueous solutions of $NaHCO_3$, $Na_2S_2O_3$, and brine. The organic phase was dried over $MgSO_4$, filtered, and concentrated under reduced pressure. Purification by silica gel column chromotography using hexane-EtOAc mixture provided **(S7)** with 84% yields (Piers, et al.,1994)

S7: ^{1}H NMR (400 MHz, $CDCI_3$) δ =7.47 (dd, *J* = 8.9, 0.9 Hz, 1H), 6.91 (dd, *J* = 8.9, 0.8 Hz, 1H), 3.78 (s, 3H).

In the next step, the mixture of **S7** (709 mg, 3.34 mmol), $PdCI_2(PPh_3)_2$ (47 mg, 0.067 mmol), CuI (12.8 mg, 0.067 mmol) in 17 mL of Et_3N was stirred for 10 min at RT. Then, 1-hexyne (0.46 mL, 4 mmol) was added to the reaction mixture and stirredat RT for overnight. The reaction was controlled with GC. After completion of the

reaction, water was added and extracted with Et_2O. Organic layers were dried over $MgSO_4$, filtered and concentrated in vacuo.The product was purified by column chromatography with hexane-Et_2O (8:1),which afforded **(S8)** (509 mg , 91%) (Takeuchi, et al., 2000).

S8:^{1}H NMR (400 MHz, $CDCI_3$) δ= 6.15 (ddd, *J* = 4.7, 2.4, 1.2 Hz, 1H), 6.03 (dd, *J* = 11.4, 0.4 Hz, 1H), 3.75 (s, 3H), 2.45 (td, *J* = 7.1, 2.4 Hz, 2H), 1.61 – 1.53 (m, 2H), 1.50 – 1.40 (m, 2H), 0.92 (t, 3H).

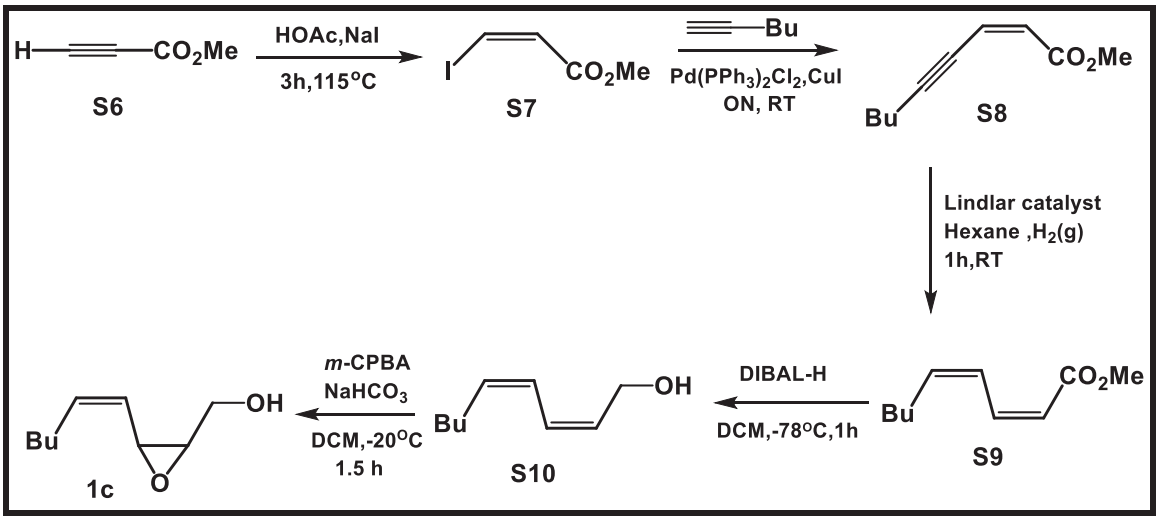


Figure 3.2. Synthesis of substrate 1c

To the reaction flask, **S8** (166 mg, 1 mmol), in 35 mL hexane was placed. Lindlar catalyst (70 mg) was added. The mixture was degased with argon for 5 minutes. After that, H_2 gas was bubbled to the reaction medium at RT for 1 hour. The reaction was controlled with GC. After the reaction was completed, the suspension was filtered through silica gel to remove the Lindlar catalyst. The solvent content was evaporated and purified with column chromatography (hexane/Et_2O, 8:1). The product (**S9)** recovered was 139 mg with 83% yield (Chen , et al., 1986).

S9: ^{1}H NMR (400 MHz, $CDCI_3$) δ= 7.29 – 7.22 (m, 1H), 6.94 (td, *J* = 11.8, 1.1 Hz, 1H), 5.95 – 5.87 (m, 1H), 5.67 (d, *J* = 11.5 Hz, 1H), 3.72 (s, 3H), 2.30 – 2.22 (m, 2H), 1.43 – 1.27 (m, 4H), 0.90 (t, 3H).

S9 (98 mg, 0,58 mmol) was dissolved in 10 mL DCM. The reaction flask was taken to -78 ^{0}C and DIBAL-H solution (1.5 mmol, 1.0 M in DCM) was added drop by drop to the solution. The reaction mixture was stirred for 1 hour at the same

temperature. After the reaction was completed, the reaction flask was warmed to RT, extracted with DCM, and washed with sodium potassium tartrate solution. The organic layer was dried over $MgSO_4$, filtered, and concentrated under reduced pressure. The product was purified with silica gel column chromatography (hexane/EtOAc, 5:1) to yield (**S10)** (52 mg, 64%) .

S10: ^{1}H NMR (400 MHz, $CDCl_3$) δ= 6.35 (ddd, *J* = 7.1, 3.7, 1.2 Hz, 1H), 6.21 (ddd, *J* = 11.7, 2.4, 1.2 Hz, 1H), 5.64 – 5.49 (m, 2H), 4.29 (dd, *J* = 6.8, 1.3 Hz, 2H), 2.21 – 2.12 (m, 2H), 1.38 – 1.27 (m, 4H), 0.89 (t, 3H).^{13}C NMR (101 MHz, $CDCl_3$) δ= 134.84, 129.18, 125.90, 122.80, 58.78, 31.77, 27.26, 22.44, 14.07.

In the next step, **S10** (52 mg, 0,37 mmol) was dissolved in 10 mL DCM and to this solution was added $NaHCO_3$ (75 mg, 0,89 mmol). The reaction flask was taken to -20 ^{0}C and *m*-CPBA (118 mg, 0.48 mmol) was added part by part. The reaction was halted after 90 mins and extracted with DCM, dried over $MgSO_4$,filtered and concentrated in vacuo. The substrate was column purified with Et_3N-treated silica gel on column chromatography (hexane/EtOAc, 4:1) to afford **(1c)** (29 mg, 51%) as a pale yellow oil.

3.2.3. Synthesis of Substrate 1d

DMAP (275 mg, 2.25 mmol) and acrolein (1.1 mL , ≈15 mmol) were added to a solution of mono-ethyl malonate (≈ 3 g, 22.5 mmol) in pyridine (8 mL). The reaction was performed in a sealed cup at 50 ^{0}C for 24 hours. After cooled to room temperature, water was added, extracted with Et_2O and washed with 15% HCl, and brine. The organic layer was dried over $MgSO_4$ and evaporated in vacuo. The crude product was purified with column chromatography by using hexane- Et_2O (10:1) to afford **(S11)** as a colourless oil, (1.74 g, 92%). (Polic , et al., 2017)

S11: ^{1}H NMR (400 MHz, $CDCl_3$) δ= 7.26 (ddd, J = 11.0, 5.8, 0.5 Hz, 1H), 6.51 – 6.41 (m, 1H), 5.91 (dd, J = 15.4, 0.6 Hz, 1H), 5.61 (dd, J = 17.0, 0.7 Hz, 1H), 5.49 (dd, J = 10.0, 0.7 Hz, 1H), 4.21 (q, 2H), 1.30 (t, 3H).

DIBAL-H (20 mmol, 1.0 M in DCM) was added drop by drop to the solution of **S11** (1.26 g, 10 mmol) in DCM (100mL), at -78^{0}C. The reaction was stirred for 1 hour at the same temperature. After the reaction was complete, the mixture was extracted

with DCM and washed with sodium potassium tartarate solution. The organic layer was dried over $MgSO_4$, filtered, and concentrated under reduced pressure. The crude product was purified by column chromatography using hexane- Et_2O (6:1) to give **(S12)** (546 mg, 65%) as a colurless oil.

S12: ^1H NMR (400 MHz, $CDCI_3$) δ= 6.41 – 6.21 (m, 2H), 5.85 (ddd, *J* = 15.0, 8.6, 3.0 Hz, 1H), 5.22 (dd, *J* = 16.6, 1.1 Hz, 1H), 5.10 (dd, *J* = 9.8, 0.7 Hz, 1H), 4.19 (d, *J* = 6.5 Hz, 2H).

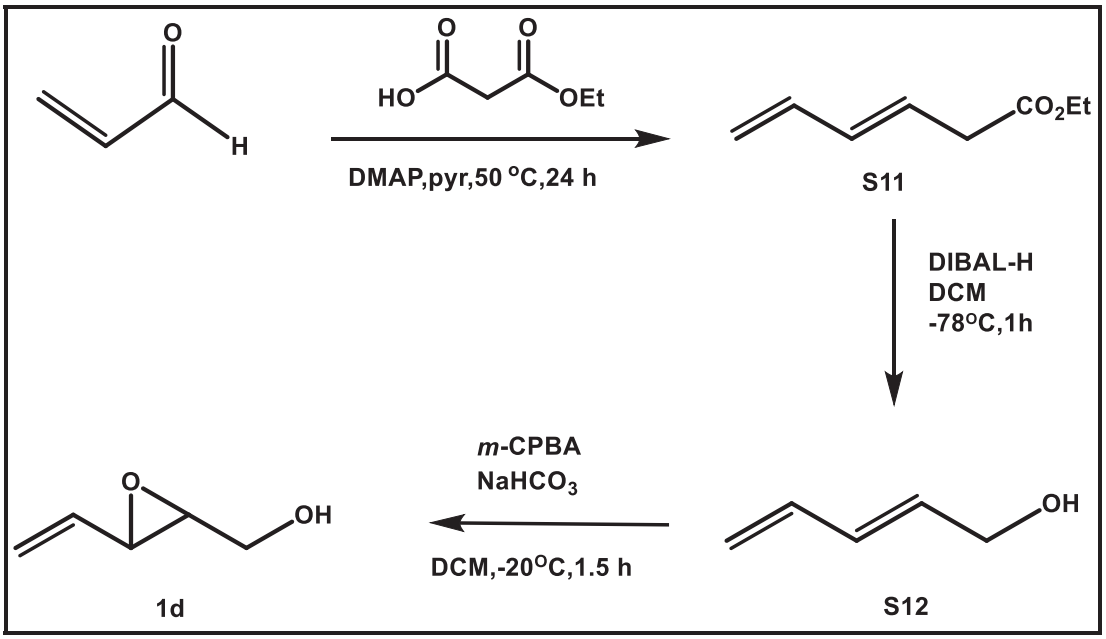


Figure 3.3. Synthesis of Substrate 1d

The **S12** (117 mg, 1.4 mmol)was dissolved in DCM (30 mL) and $NaHCO_3$ (283 mg, 3.36 mmol) was added. The reaction flask was cooled to -20 ^{0}C and *m*-CPBA (449 mg, 1.82 mmol) was added slowly while controlling the temperature. The reaction was complete after 1.5 hours and extracted with DCM. Organic layer was dried over $MgSO_4$, filtered, and evaporated. The crude product was purified immediately with column chromatography by using Et_3N treated silicagel (pentane/Et_2O, 1:1) to afford **(1d)**(73 mg, 52%) as a clear oil.

3.2.4. Synthesis of Substrate 1e

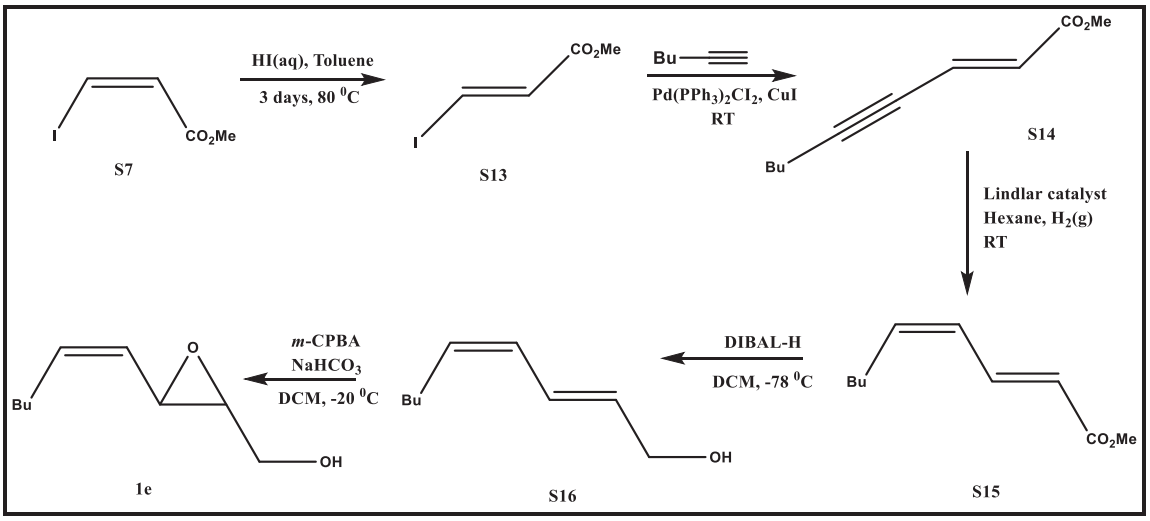


Figure 3.4. Synthesis of Substrat 1e

To the solution of **S7** (2.12 g, 10 mmol) in 3 mL toluene, 0.17 mL solution of hydroiodic acid (55% v/v) was added. The resulting mixture was heated to 80 ^{0}C for 8 h. The reaction was controlled with GC. After the reaction completed, the solution was cooled to RT and diluted with Et_2O. The organic layer was washed with saturated $NaHCO_3$ solution, $Na_2S_2O_3$ solution, and brine. The organic layer was dried over $MgSO_4$, filtered, and concentrated under reduced pressure to afford **S13** (1.4 g, 66%) as a yellow oil. (Zhang et al., 2009).

S13: ^{1}H NMR (400 MHz, $CDCI_3$) δ= 7.90 (dd, *J* = 14.8, 0.5 Hz, 1H), 6.89 (dd, *J* = 14.8, 0.4 Hz, 1H), 3.75 (s, 3H).

S13 (1.4 g, 6.6 mmol) , $PdCI_2(PPh_3)_2$ (45.38 mg, 0.0066 mmol), and CuI (12.38 mg, 0.0066 mmol) in 30 mL Et_3N was stirred 10 min at RT under argon and then 1-hexyne (575 mg, 7 mmol) was added dropwise at RT. The reaction was controlled with GC. The reaction mixture was stirred at the same temperature at 6 hours. At the end of the reaction, water was added and extracted with Et_2O. The organic layer was dried over $MgSO_4$, filtered, and concentrated under reduced pressure. The crude product was purified with silica gel coloumn chromatography by using Hexane- EtOAc mixture and provided **S14** (681.5 mg, 62%) as a yellow oil. (Takeuchi, et al., 2000).

S14: ^{1}H NMR (400 MHz,$CDCI_3$) δ= 6.69 (ddd, *J* = 15.8, 4.3, 2.2 Hz, 1H), 6.07 (d, *J* = 15.8 Hz, 1H), 3.67 (s, 3H), 2.33 – 2.28 (m, 2H), 1.51 – 1.43 (m, 2H), 1.40 – 1.31 (m, 2H), 0.85 (t, 3H).

S14 (681.5 mg, 4.1 mmol) was dissolved in 60 mL hexane and then 280 mg Lindlar catalyst and 20 drop quinoline was added at RT. The mixture was degased with argon gase for 5 minutes. After this, H_2(g) was bubbled to the reaction medium at the same temparature for 4 hours and the reaction was controlled with GC. After the reaction was completed, the suspension was filtered through silica gel to remove the Lindlar catalyst. The solvent content was evaporated and purified with column chromatography (hexane/Et_2O) to afford **S15** (563 mg, 81%) as a pale yellow oil. It should be noted that, during the experiment, over hydrogenation product is formed slightly and it is not possible to purify our main product.

S15: ^{1}H NMR (400 MHz, $CDCI_3$) δ= 7.61 (ddd, J = 15.4, 11.7, 1.1 Hz, 1H), 6.11 (dt, J= 12.2, 6.1 Hz, 1H) 5.90 – 5.82 (m, 2H), 3.75 (s, 3H), 2.34 – 2.25 (m, 2H), 1.45 – 1.34 (m, 4H), 0.91 (t, 3H).

DIBAL-H (7.7 mmol, 1.0 M in DCM) was added drop by drop to the solution of **S15** (563 mg, 3.35 mmol) in DCM (35mL), at -78^{0}C. The reaction was stirred for 1 hour at the same temperature. After the reaction was complete, the mixture was extracted with DCM and washed with sodium potassium tartrate solution. The organic layer was dried over $MgSO_4$, filtered, and concentrated under reduced pressure. The crude product was purified by column chromatography using hexane-acetone (10:1) to give **S16** (280 mg, 60%) as a colurless oil.

S16: ^{1}H NMR (400 MHz, $CDCI_3$) δ= 6.54 (dddd, J = 15.1, 11.1, 2.7, 1.4 Hz, 1H), 5.99 (t, J = 11.0 Hz, 1H), 5.81 (dt, J = 15.2, 5.9 Hz, 1H), 5.46 (dt, J = 10.9, 7.7 Hz, 1H), 4.20 (dd, J = 5.9, 0.9 Hz, 2H), 2.22 – 2.15 (m, 2H), 1.37 – 1.32 (m, 4H), 0.90 (t, 3H). ^{13}C NMR (101 MHz, $CDCI_3$) δ= 133.22, 131.48, 127.52, 126.89, 63.57, 31.75, 27.46, 22.31, 13.94.

The **S16** (218 mg, 1.54 mmol)was dissolved in DCM (30 mL) and $NaHCO_3$ (310 mg, 3.68 mmol) was added. The reaction flask was cooled to -20 ^{0}C and *m*-CPBA (70-75% , 495 mg, 2 mmol) was added slowly while controlling the temperature. The reaction was complete after 0.5 hour and extracted with DCM. Organic layer was dried over $MgSO_4$, filtered, and concentrated under reduced pressure. The crude product was purified immediately with column chromatography by using Et_3N treated silicagel (hexane/EtOAc, 4:1) to afford **(1e)** (34 mg, 14%) as a pale yellow oil. The difficulty

encountered in this step is the formation of excessive amount of the epoxide degradation product. Although we had worked at lower temperatures, we could not prevent this formation and the yield was low.

3.2.5. Synthesis of Substrate 1f

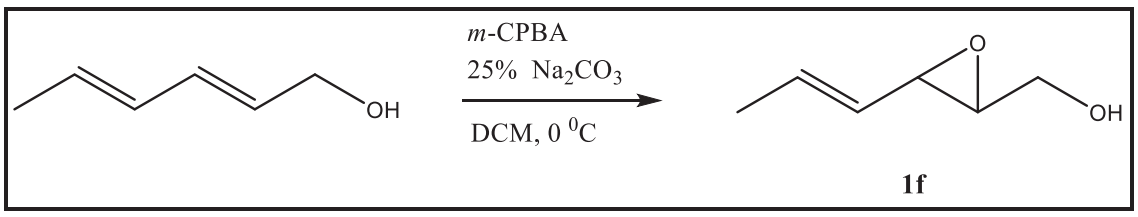


Figure 3.5. Synthesis of Substrat 1f

To the stirred solution of trans-trans-2,4-hexadien-1-ol (980 mg, 10 mmol) in DCM (160 mL) , Na_2CO_3 solution (50 mL, 25% m/v) was added. *m*-CPBA (4.2 g, 17 mmol) was added part by part to the reaction flask at 0 ^{0}C. After 1 hour, the reaction quenched with water and extracted with DCM. The organic layer was dried over $MgSO_4$, filtered and evaporated. The crude product was purified immediately with column chromatography by using Et_3N treated silicagel hexane/EtOAc (3:1) to afford **1f** (342 mg, 30%) as a yellow oil.

3.2.6. Synthesis of Substrate 1g

MeMgBr (21 mmol, 3 M in Et_2O) was added dropwise to the stirred solution of triethylphosphonoacetate (5 g, 22.5 mmol) in THF (120 mL) at RT and stirred for 15 min. After that, cyclohexanecarboxaldehyde (2.24 g, 20 mmol) in THF (120 mL) was added dropwise to the stirred solution at the same temperature and the reaction mixture heated at reflux for overnight. The reaction was quenched with saturated NH_4Cl solution and extracted with Et_2O. The combined organic layers were washed with brine, dried over $MgSO_4$, filtered and concentrated under reduced pressure. The crude product **(S17)** was used in next step without further purification. (Claridge, et al., 2008).

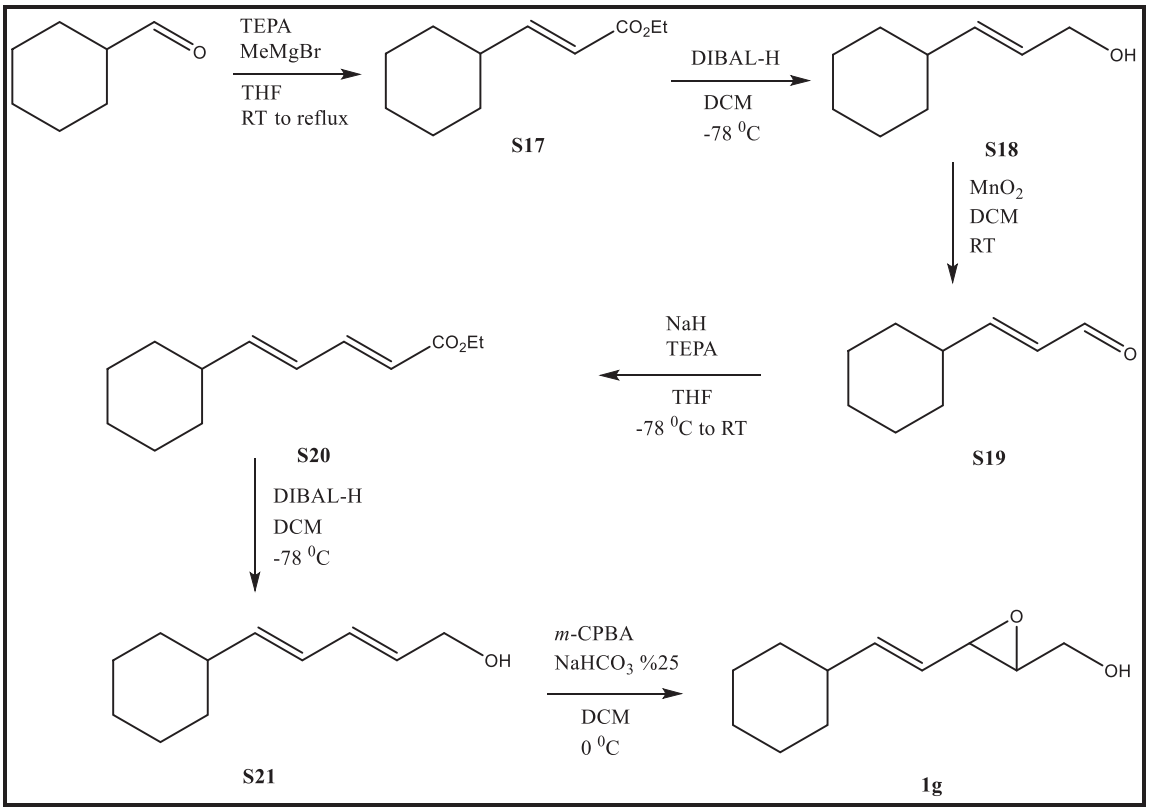


Figure 3.6. Synthesis of Substrat 1g

S17: ^{1}H NMR (400 MHz, $CDCl_3$) δ= 6.91 (ddd, J = 15.8, 6.8, 3.6 Hz, 1H), 5.75 (dd, J = 15.8, 1.5 Hz, 1H), 4.17 (q, 2H), 2.17 – 2.06 (m, 1H), 1.79 – 1.70 (m, 4H), 1.70 – 1.63 (m, 1H), 1.28 (t, 3H), 1.19 – 1.10 (m, 5H).

DIBAL-H (55 mmol, 1.0 M in DCM) was added dropwise to the stirred solution of crude **S17** in DCM (100 mL) at -78 ^{0}C and stirred for 2.5 h. The reaction quenched with saturated sodium potassium tartrate solution and extracted with DCM. The organic layer was dried over $MgSO_4$, filtered and concentrated. The crude product **(S18)** was used in next step without further purification.

S18: ^{1}H NMR (400 MHz, $CDCl_3$) δ= 5.67 – 5.53 (m, 2H), 4.07 (d, *J* = 5.3 Hz, 2H), 2.01 – 1.89 (m, 1H), 1.76 – 1.67 (m, 4H), 1.67 – 1.60 (m, 1H), 1.34 – 0.98 (m, 5H).

MnO_2 (17.4 g, 200 mmol) was added to the stirred solution of **S18** (1.4 g, 10 mmol) in DCM (100 mL) at RT. The reaction was stirred 3 hours at the same temperature. After the reaction was completed, the reaction mixture was filtered through silica gel and evaporated. The crude product **(S19)** was used in next step without further purification.

S19: ^{1}H NMR (400 MHz, $CDCl_3$) δ= 9.48 (d, *J* = 7.9 Hz, 1H), 6.76 (dd, *J* = 15.7, 6.5 Hz, 1H), 6.06 (ddd, *J* = 15.7, 7.9, 1.4 Hz, 1H), 2.32 – 2.20 (m, 1H), 1.85 – 1.73 (m, 4H), 1.73 – 1.65 (m, 1H), 1.39 – 1.10 (m, 5H).

To a suspension of NaH (250 mg, 10.4 mmol) in 17 mL of THF at -78^{0}C was added triethylphosphonoacetate (TEPA) (2.25 mL, 11.34 mmol) drop by drop. After 1 hour, a solution of **S19** (1.3 g, 9.45 mmol) in THF (7 mL) was added dropwise. The reaction was stirred 3 hours at RT. Extracted with Et_2O, washed with brine, dried over $MgSO_4$, filtered, and concentrated under reduced pressure. The crude product **(S20)** was used in next step without further purification. (Dias et al., 2017).

S20: ^{1}H NMR (400 MHz, $CDCl_3$) δ= 7.24 (dd, *J*= 15.3, 10.1 Hz, 1H), 6.08 (qd, *J* = 15.3, 8.1 Hz, 2H), 5.77 (d, *J* = 15.4 Hz, 1H), 4.22 – 4.12 (m, 2H), 2.14 – 2.00 (m, 1H), 1.77 – 1.69 (m, 4H), 1.68 – 1.61 (m, 1H), 1.27 (t,3H), 1.24 – 1.05 (m, 5H).

DIBAL-H (30 mmol, 1.0 M in DCM) was added dropwise to the stirred solution of crude **S20** in DCM (100 mL) at -78 ^{0}C and stirred for 2.5 h. The reaction quenched with saturated sodium potassium tartrate solution and extracted with DCM. The organic layer was dried over $MgSO_4$, filtered and concentrated. The crude product was purified by column chromatography using hexane-EtOAc (10:1) to give **S21** (1.17 g, 74%) as a colurless oil.

S21: ^{1}H NMR (400 MHz, $CDCl_3$) δ= 6.11 (dd, *J* = 15.2, 10.4 Hz, 1H), 5.93 (dd, *J* = 15.3, 10.4 Hz, 1H), 5.69 – 5.53 (m, 2H), 4.07 (d, *J* = 6.5 Hz, 2H), 2.02 – 1.93 (m, 1H), 1.80 – 1.68 (m,4H), 1.67 – 1.61 (m, 1H), 1.33 – 1.01 (m, 5H).

To the stirred solution of **S21** (166 mg, 1 mmol) in DCM (10 mL), Na_2CO_3 solution (4 mL, 25% m/v) was added. *m*-CPBA (320 mg, 1.3 mmol) was added part by part to the reaction flask at 0 ^{0}C. After 0.5 hour, the reaction quenched with water and extracted with DCM. The organic layer was dried over $MgSO_4$, filtered and evaporated. The crude product was purified immediately with column chromatography by using Et_3N treated silicagel hexane/EtOAc (3:1) to afford **1g** (113 mg, 68%) as a pale yellow oil.

3.3 Characterization of Alkenyl Oxiranes

The synthesized reactants were analyzed by NMR techniqueswhich were recorded on a 400 MHz spectrometer.

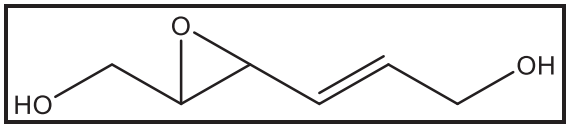


Figure 3.7. (E)-3-(3-(hydroxymethyl)oxiran-2-yl)prop-2-en-1-ol

1a: ^{1}H NMR (400MHz, $CDCI_3$) δ= 6.10 (dt, J= 15.6, 5.1 Hz, 1H), 5.50 (dd, J= 15.6, 8.0 Hz, 1H), 4.18 (s, 2H), 3.95 (d, 12.8 Hz, 1H), 3.69(d, 12.3 Hz, 1H) , 3.45 (dd , 8.0 , 2.1 Hz , 1H) , 3.12- 3.07 (m , 1H) , 1.96 (s, 1H) , 1.74 (s , 1H). ^{13}C NMR (101 MHz, $CDCI_3$) δ= 135.35, 127.59, 62.71, 61.19, 60.20, 55.20.

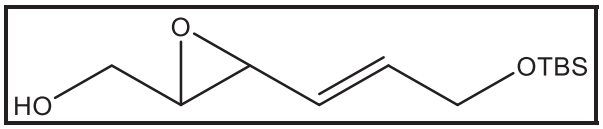


Figure 3.8.(E)-(3-(3-((tert-butyldimethylsilyl)oxy)prop-1-en-1-yl)oxiran-2-yl)methanol

1b: ^{1}H NMR (400 MHz, $CDCI_3$) δ= 6.02 (dt, *J* = 15.4, 4.4 Hz, 1H), 5.48 (ddt, *J* = 15.4, 8.0, 1.7 Hz, 1H), 4.19 (dd, *J* = 4.4, 1.8 Hz, 2H), 3.94 (dd, *J* = 12.7, 2.4 Hz, 1H), 3.67 (dd, *J* = 12.7, 4.0 Hz, 1H), 3.43 (dd, *J* = 8.1, 2.2 Hz, 1H), 3.08 (dt, *J* = 4.4, 2.3 Hz, 1H), 1.81 (bs, 1H), 0.90 (s, *J* = 1.4 Hz, 9H), 0.06 (s, 6H). ^{13}C NMR (101 MHz, $CDCI_3$) δ= 135.69, 126.11, 62.91, 61.31, 60.17, 55.41, 26.05, 18.52, -5.16.

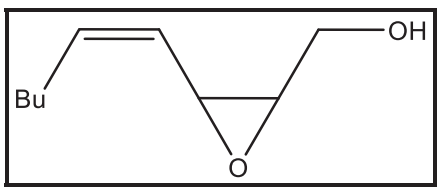


Figure 3.9.(Z)-(3-(hex-1-en-1-yl)oxiran-2-yl)methanol

1c: ^{1}H NMR (400 MHz, $CDCl_3$) δ= 5.76 (dt, *J* = 11.2, 7.6 Hz, 1H), 5.21 (ddd, *J* = 11.0, 8.3, 0.6 Hz, 1H), 3.86 – 3.64 (m, 3H), 3.34 – 3.28 (m, 1H), 2.26 – 2.13 (m, 2H), 1.42 – 1.29 (m, 4H), 0.89 (t, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ= 138.45, 122.85, 61.36, 58.35, 53.00, 31.67, 27.65, 22.36, 14.01.

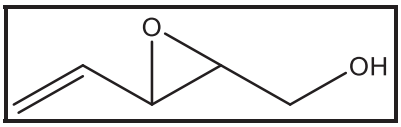


Figure 3.10.(3-vinyloxiran-2-yl)methanol

1d: ^{1}H NMR (400 MHz, $CDCl_3$) δ= 5.65 – 5.47 (m, 2H), 5.31 (dd, *J* = 9.6, 1.2 Hz, 1H), 3.95 (dd, *J* = 12.7, 2.5 Hz, 1H), 3.69 (dd, *J* = 12.7, 4.0 Hz, 1H), 3.41 (dd, *J* = 7.4, 2.2 Hz, 1H), 3.08 (ddd, *J* = 4.6, 2.7, 0.5 Hz, 1H), 1.88 (bs, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ= 134.67, 120.02, 61.11, 59.91, 55.76.

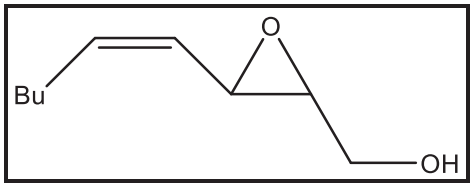


Figure 3.11.(Z)-(3-(hex-1-en-1-yl)oxiran-2-yl)methanol

1e:^{1}H NMR (400 MHz, $CDCl_3$) δ= 5.74 (ddd, *J* = 11.0, 9.6, 4.2 Hz, 1H), 5.07 (ddd, *J* = 10.6, 2.8, 1.4 Hz, 1H), 3.97 (dd, *J* = 12.6, 2.4 Hz, 1H), 3.68 (ddd, *J* = 11.0, 7.4, 2.6 Hz, 2H), 3.07 (dt, *J* = 3.9, 2.4 Hz, 1H), 2.31 – 2.11 (m, 2H), 1.84 (bs, 1H), 1.41 – 1.30 (m, 4H), 0.9 (t, 3H).^{13}C NMR (101 MHz, $CDCl_3$) δ = 137.77, 125.89, 61.25, 59.92, 51.54, 31.80, 27.62, 22.37, 14.04.

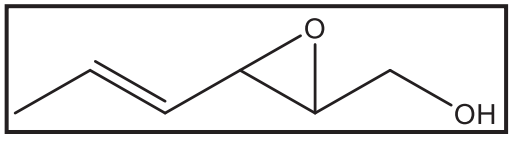


Figure 3.12.(E)-(3-(prop-1-en-1-yl)oxiran-2-yl)methanol

1f: ^{1}H NMR (400 MHz, $CDCI_3$) δ= 6.01 – 5.90 (m, 1H), 5.22 (ddq, *J* = 15.4, 8.3, 1.7 Hz, 1H), 3.93 (dd, *J* = 12.7, 2.5 Hz, 1H), 3.66 (dd, *J* = 12.7, 4.1 Hz, 1H), 3.37 (dd, *J* = 8.3, 2.3 Hz, 1H), 3.06 (dt, *J* = 4.1, 2.4 Hz, 1H), 1.74 (dd, *J* = 6.6, 1.7 Hz, 3H).^{13}C NMR (101 MHz, $CDCI_3$) δ= 132.68, 127.79, 61.43, 60.01, 55.98, 18.03.

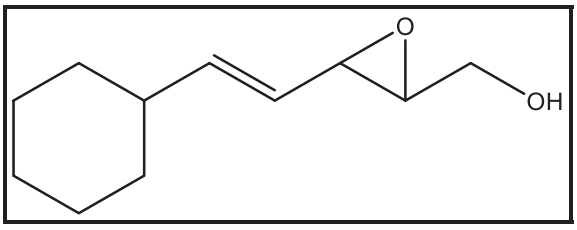


Figure 3.13.(E)-(3-(2-cyclohexylvinyl)oxiran-2-yl)methanol

1g:^{1}H NMR (400 MHz, $CDCI_3$) δ= 5.90 (dd, *J* = 15.6, 6.6 Hz, 1H), 5.13 (ddd, *J* = 15.6, 8.3, 1.3 Hz, 1H), 3.94 (dd, *J* = 12.6, 2.5 Hz, 1H), 3.66 (dd, *J*= 12.6, 4.1 Hz, 1H), 3.36 (dd, *J* = 8.3, 2.3 Hz, 1H), 3.09 – 3.03 (m, 1H), 2.03 – 1.94 (m, 1H), 1.76 – 1.61 (m, 5H), 1.33 – 1.00 (m, 5H).^{13}C NMR (101 MHz, $CDCI_3$) δ= 143.70, 123.97, 61.47, 60.16, 56.38, 40.59, 32.62, 32.57, 26.22, 26.04.

3.4. General Method for Palladium-Catalyzed Reactions of Alkenyl Oxiranes

Pd catalyst and arsine ligand was dissolved in THF (half of the volume necessary for the reaction) in the schlenk tube which was dried in oven and cooled under Ar gas. The mixture stirred at room temperature for 30 minutes. After this, respectively organoboron, base, the solution of epoxide compound in dry solvent (other half volume), and a quarter of the solvent amount of water was added. The reaction was controlled using TLC. When the reaction was completed, the mixture was filtered using short silica gel column and concentrated under reduced pressure. It must be noted based on our experience that the color of the reaction usually turned from light yellow to dark yellow when the reaction cycle is completed. The crude mixture was analyzed by ^{1}H

NMR using benzaldehyde as the internal standard and determined the NMR yield. The allyl alcohol product was purified using silica gel on column chromatography.

$Pd_2(dba)_3.CHCl_3$ (5.2 mg, 2.5%) and $AsPh_3$(14.4 mg, 22.5%) were dissolved in 2 mL of dry THF under Ar atmosphere and stirred 30 min at room temperature. Then, 2,2-dimethyl-5-phenyl-1,3,5-dioxaborinane (PhBneop) (114 mg, 0.6 mmol), diisopropylamine (40.5 mg, 0.4 mmol), vinyl oxirane (0.2 mmol) in 2 mL dry THF and 1 mL of water were successively added at RT. The reaction vessel was stirred in a preheated oil bath until the reaction is over as judged by TLC analysis. The reactions were usualy complete within 2-3 hours.

The synthesized products were analyzed by GC and GC-MS. NMR spectra in $CDCI_3$or C_6D_6 were recorded on a 400 MHz spectrometer. FTIR analyses were performed by ATR technique.

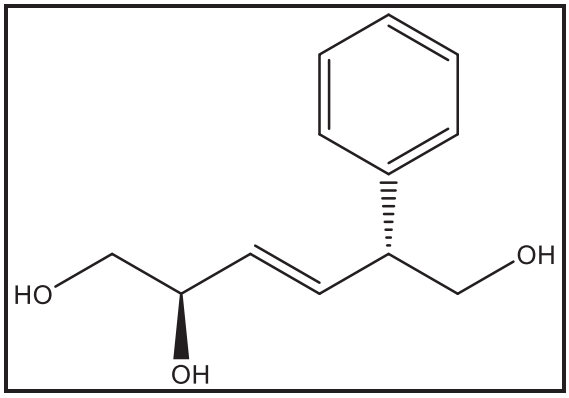


Figure 3.14.(E)-5-phenylhex-3-ene-1,2,6-triol

3aa: ^{1}H NMR (400 MHz , $CDCI_3$) δ= 7.33-7.29 (m , 2H) , 7.26-7.19 (m , 3H) , 5.98 (ddd, *J* = 15.5, 8.4, 1.1 Hz, 1H), 5.64 (ddd, *J* = 15.5, 6.1, 0.6 Hz, 1H) , 4.24 (dd, *J* = 8.8, 6.1 Hz, 1H), 3.77 (ddd, *J* = 19.2, 10.8, 7.1 Hz, 2H), 3.65 (dd, *J* = 11.4, 3.3 Hz, 1H), 3.57 – 3.46 (m, 2H). ^{13}C NMR (101 MHz, $cdcl_3$) δ = 140.73, 133.46, 131.42, 128.92, 127.87, 127.11, 72.92, 66.42, 66.34,51.59, MS (EI, m/z) 208 (M^+ , <1), 177 (5), 160 (58), 147 (7), 129 (93), 121 (16), 91 (100), 77 (17), 31 (15). FTIR (υ_{max} / cm^{-1}): 3350, 2923, 2853, 1601, 1123, 974, 875, 761, 700.

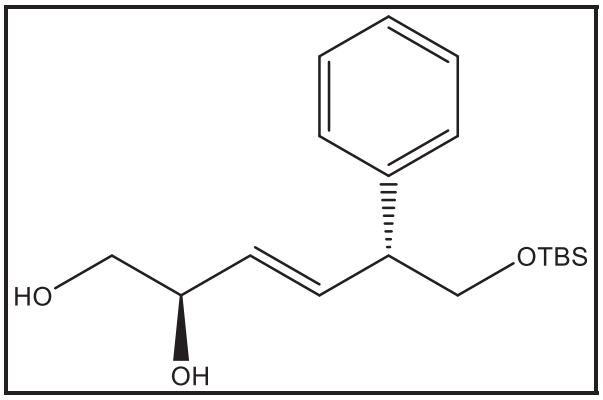


Figure 3.15.(E)-6-((tert-butyldimethylsilyl)oxy)-5-phenylhex-3-ene-1,2-diol

3ba: ^{1}H NMR (400 MHz, $CDCl_3$) δ= 7.32 – 7.27 (m, 2H), 7.24 – 7.17 (m, 3H), 6.04 (ddd, *J* = 15.6, 7.6, 1.2 Hz, 1H), 5.54 (ddd, *J* = 15.6, 6.1, 1.1 Hz, 1H), 4.25 (s, 1H), 3.81 – 3.77 (m, 2H), 3.63 (d, *J* = 13.4 Hz, 1H), 3.51 – 3.44 (m, 2H), 0.86 – 0.82 (m, 9H), -0.02 – -0.06 (m, 6H). ^{13}C NMR (101 MHz, $CDCl_3$) δ= 141.51, 134.03, 130.17, 128.53, 128.25, 126.77, 73.10, 67.25, 66.50, 51.30, 25.99, 18.42 , -5.30, MS (EI, m/z) 322 (M^+ , <1), 265 (2), 247 (6), 207 (3), 177 (4), 143 (100), 129 (33), 117 (49), 105 (36), 91 (37), 77 (9). FTIR (υ_{max} / cm^{-1}): 3351, 2927, 2856, 1493, 1471, 1255, 1102, 775, 699.

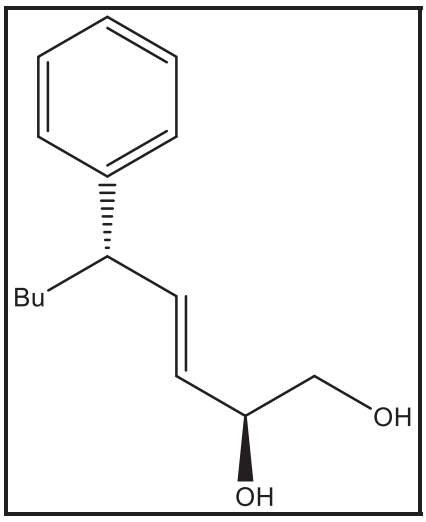


Figure 3.16. (E)-5-phenylnon-3-ene-1,2-diol

3ca: ^{1}H NMR (400 MHz, $CDCl_3$) δ= 7.23 – 7.17 (m, 2H), 7.12 – 7.05 (m, 3H), 5.81 (dd, *J* = 15.5, 7.8 Hz, 1H), 5.34 (ddd, *J* = 15.5, 6.3, 1.0 Hz, 1H), 4.12 – 4.05 (m, 1H), 3.48 (dt, *J* = 8.4, 4.2 Hz, 1H), 3.36 – 3.30 (m, 1H), 3.18 – 3.09 (m, 1H), 2.55 (bs, 1H), 1.64 - 156 (m, 2H), 1.23 – 1.02 (m, 4H), 0.76 (t, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ= 144.37, 137.54, 128.47, 127.76, 127.54, 126.19, 73.01, 66.51, 48.60, 35.44, 29.71, 22.61, 14.01. ^{1}H NMR (400 MHz, C_6D_6) δ= 7.17 – 7.10 (m, 2H), 7.09 – 7.00 (m, 3H), 5.86 (ddd, *J* = 15.5, 7.7, 1.2 Hz, 1H), 5.37 (ddd, *J* = 15.5, 5.9, 1.0 Hz, 1H), 4.08 (dd, *J* = 10.3, 5.8 Hz, 1H), 3.42 (dd, *J* = 11.2, 3.3 Hz, 1H), 3.32 (dd, *J* = 11.2, 8.0 Hz, 1H), 3.10 (q, *J* = 7.5 Hz, 1H), 1.64 – 1.57 (m, 2H), 1.23 – 1.10 (m, 4H), 0.78 (t, 3H). ^{13}C NMR (101 MHz, C_6D_6) δ= 145.02, 136.88, 128.83, 128.66, 128.03, 126.49, 73.33, 67.05, 49.11, 36.01, 30.14, 23.07, 14.28, MS (EI, m/z) 234 (M^+<1), 216 (2), 203 (74), 185 (20), 174 (3), 159 (4), 147 (21), 145 (13), 133 (24), 129 (73), 117 (29), 105 (20), 91 (100), 77 (8), 57 (19), 43(4), 39(5), 31 (7). FTIR (υ_{max} / cm^{-1}):3374, 2928, 2858, 1601, 1493, 1074, 1030, 974, 874, 760, 700.

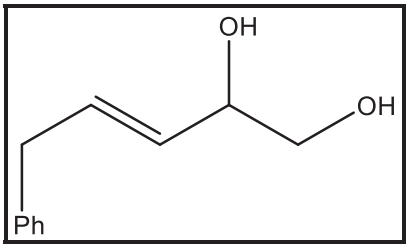


Figure 3.17. (E)-5-phenylpent-3-ene-1,2-diol

3da:^{1}H NMR (400 MHz, $CDCl_3$) δ= 7.32 – 7.27 (m, 2H), 7.24 – 7.15 (m, 3H), 5.94 (ddd, *J* = 14.8, 7.1, 6.5 Hz, 1H), 5.53 (ddt, *J* = 15.4, 6.5, 1.3 Hz, 1H), 4.27 – 4.20 (m, 1H), 3.65 (dd, *J* = 11.2, 3.5 Hz, 1H), 3.50 (dd, *J* = 11.1, 7.5 Hz, 1H), 3.39 (d, *J* = 6.8 Hz, 2H). ^{13}C NMR (101 MHz, $CDCl_3$) δ= 139.69, 132.61, 129.73, 128.51, 126.21, 72.93, 66.50, 38.70, MS (EI, m/z) 178 (M^+, 1), 160 (1), 147 (37), 143 (4), 129 (100), 117 (10), 115 (15), 105 (7), 91 (55), 87 (10), 77 (10), 75 (3), 65 (7), 51 (6), 31 (4).FTIR (υ_{max} / cm^{-1}): 3343, 2923, 2854, 1668, 1603, 1495, 1073, 1029, 971, 872, 748.

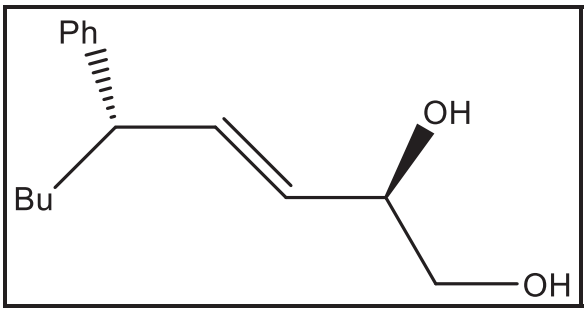


Figure 3.18. (E)-5-phenylnon-3-ene-1,2-diol

3ea: ^{1}H NMR (400 MHz, $CDCI_3$) δ= 7.32 – 7.27 (m, 2H), 7.22 – 7.15 (m, 3H), 5.89 (ddd, *J* = 15.5, 7.8, 1.1 Hz, 1H), 5.44 (ddd, *J* = 15.5, 6.6, 1.1 Hz, 1H), 4.18 (td, *J* = 6.7, 3.1 Hz, 1H), 3.59 (dd, *J* = 11.2, 3.5 Hz, 1H), 3.45 (dd, *J* = 11.2, 7.6 Hz, 1H), 3.22 (q, 1H), 2.37 (bs, 2H), 1.69 (q, 2H), 1.34 – 1.19 (m, 4H), 0.86 (t, 3H).^{13}C NMR (101 MHz, $CDCI_3$) δ= 144.46, 137.85, 128.61, 127.93, 127.67, 126.34, 73.24, 66.67, 48.76, 35.54, 29.84, 22.72, 14.12.^{1}H NMR (400 MHz, C_6D_6) δ= 7.16 – 7.11 (m, 3H), 7.08 – 7.00 (m, 2H), 5.77 (ddd, *J* = 15.5, 7.8, 1.2 Hz, 1H), 5.32 (ddd, *J* = 15.5, 6.2, 1.1 Hz, 1H), 3.97 (ddd, *J* = 6.5, 5.1, 3.1 Hz, 1H), 3.37 (dd, *J* = 11.1, 3.5 Hz, 1H), 3.25 (dd, *J* = 11.1, 7.7 Hz, 1H), 3.07 (q, 1H), 1.61 – 1.53 (m, 2H), 1.24 – 1.09 (m, 4H), 0.78 (t, 3H).^{13}C NMR (101 MHz, C_6D_6) δ= 144.98, 136.94, 128.83, 127.98, 126.52, 73.29, 66.96, 49.11, 35.97, 30.13, 23.03, 14.25, MS (EI, m/z) 234 (M^+<1), 216 (2), 203 (74), 185 (20), 174 (3), 159 (4), 147 (21), 145 (13), 133 (24), 129 (73), 117 (29), 105 (20), 91 (100), 77 (8), 57 (19), 43(4), 39(5), 31 (7).FTIR (υ_{max} / cm^{-1}): 3355, 2926, 2857, 1493, 1452, 1072, 1028, 972, 874, 758, 698.

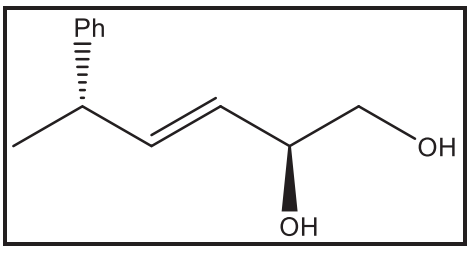


Figure 3.19. (E)-5-phenylhex-3-ene-1,2-diol

3fa: ^{1}H NMR (400 MHz, $CDCl_3$) δ= 7.32 – 7.27 (m, 2H), 7.22 – 7.17 (m, 3H), 5.95 (ddd, *J* = 15.6, 6.7, 1.0 Hz, 1H), 5.47 (ddd, *J* = 15.5, 6.5, 1.3 Hz, 1H), 4.21 (td, *J* = 7.1, 3.3 Hz, 1H), 3.61 (dd, *J* = 11.2, 3.4 Hz, 1H), 3.46 (dd, *J* = 11.5, 7.6 Hz, 2H), 2.66 (s, 2H), 1.36 (d, *J* = 7.0 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ= 145.36, 138.45, 128.60, 127.24, 127.20, 126.37, 73.16, 66.64, 42.13, 21.21. MS (EI, m/z): 192 (M+, 1>), 174 (10), 161 (22), 143 (100), 128 (32), 115 (31), 105 (27), 91 (55), 77 (40), 55 (26), 43 (23).FTIR (υ_{max} / cm^{-1}): 3365, 2924, 2854, 1492, 1452, 1377, 1120, 1076, 1028, 972, 873, 761, 699.

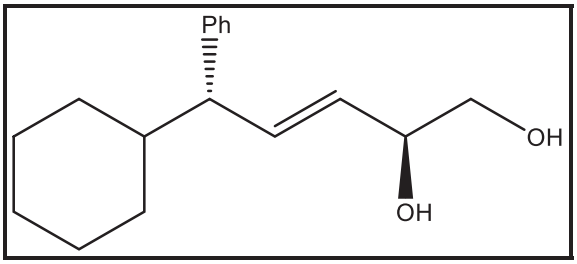


Figure 3.20. (2S,5S,E)-5-cyclohexyl-5-phenylpent-3-ene-1,2-diol

3ga: ^{1}H NMR (400 MHz, $CDCl_3$) δ= 7.30 – 7.25 (m, 2H), 7.20 – 7.15 (m, 1H), 7.14 – 7.10 (m, 2H), 5.94 (ddd, *J* = 15.4, 9.4, 1.2 Hz, 1H), 5.44 (ddd, *J* = 15.4, 6.2, 0.7 Hz, 1H), 4.19 (dddd, *J* = 7.5, 6.2, 3.5, 1.2 Hz, 1H), 3.58 (dd, J_{AB} = 11.2 Hz, J_{AX}=3.5 Hz, 1H), 3.43 (dd, J_{AB} = 11.2 Hz, J_{BX}= 7.6 Hz, 1H), 2.92 (t, 1H), 1.91 – 1.81 (m, 1H), 1.73 (dd, *J* = 10.4, 2.5 Hz, 1H), 1.65 – 1.50 (m, 3H), 1.45 – 1.35 (m, 1H), 1.28 – 1.05 (m, 3H), 0.97 – 0.70 (m, 2H).^{13}C NMR (101 MHz, $CDCl_3$) δ= 143.93, 136.27, 129.02, 128.53, 128.04, 126.20, 73.11, 66.63, 56.22, 42.44, 31.55, 31.45,26.59, 26.47, 26.45.^{1}H NMR (400 MHz, C_6D_6) δ= 7.16 – 7.10 (m, 3H), 7.04 – 6.99 (m, 2H), 5.84 (ddd, *J* = 15.3, 9.4, 1.1 Hz, 1H), 5.31 (dd, *J* = 15.4, 5.8 Hz, 1H), 3.99 – 3.93 (m, 1H), 3.31 (dd, J_{AB} = 11.1 Hz, J_{AX}= 3.5 Hz, 1H), 3.21 (dd,J_{AB} = 11.1 Hz, J_{BX}= 7.8 Hz, 1H), 2.79 (t, 1H), 1.87 (d, *J* = 13.1 Hz, 1H), 1.72 – 1.63 (m, 1H), 1.59 – 1.39 (m, 4H), 1.18 – 1.01 (m, 3H), 0.88 – 0.72 (m, 2H).^{13}C NMR (101 MHz, C_6D_6) δ= 144.47, 135.34, 129.87, 128.76, 126.35, 73.13, 66.93, 56.55, 42.67, 31.75, 31.71, 26.91, 26.77, 26.73.

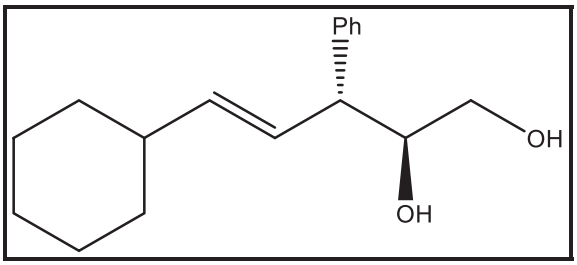


Figure 3.21. (2S,3R,E)-5-cyclohexyl-3-phenylpent-4-ene-1,2-diol

4ga: ^{1}H NMR (400 MHz, $CDCI_3$) δ= 7.34 – 7.27 (m, 2H), 7.27 – 7.17 (m, 3H), 5.71 – 5.58 (m, 2H), 3.85 – 3.77 (m, 1H), 3.54 – 3.46 (m, 1H), 3.39 – 3.26 (m, 2H), 2.03 – 1.94 (m, 1H), 1.76 – 1.61 (m,5H), 1.30 – 1.05 (m, 5H).^{13}C NMR (101 MHz, $CDCI_3$) δ= 141.34, 141.04, 128.90, 128.00, 126.90,126.86, 74.49, 64.30, 52.77, 40.86, 33.21, 33.04, 26.22, 26.12, 26.09.^{1}H NMR (400 MHz, C_6D_6) δ= 7.12 – 6.98 (m, 5H), 5.67 (dd, *J* = 15.4, 8.7 Hz, 1H), 5.42 (dd, *J* = 15.5, 6.6 Hz, 1H), 3.73 (td, *J* = 7.3, 3.1 Hz, 1H), 3.43 (dd, *J* = 11.3, 3.0 Hz, 1H), 3.35 – 3.23 (m, 2H), 1.83 – 1.71 (m, 1H), 1.58 – 1.50 (m, 4H), 1.34 – 1.26 (m, 1H), 1.12 – 0.91 (m, 5H).^{13}C NMR (101 MHz, C_6D_6) δ= 142.42, 139.95, 128.90, 128.46, 126.80, 75.06, 64.81, 52.77, 41.06, 33.38, 33.20, 26.46, 26.39, 26.35.

CHAPTER 4

RESULTS AND DISCUSSION

In this study, a number of vinyl oxiranes was synthesized and subjected to palladium-catalyzed 1,3-substitution reactions withorganoboronsunder the optimized conditions accomplished in our laboratory previously (Kıbrıs,2016). This thesis was continuation of that study and performed to widen the scope of the method. All the vinyl oxiranes synthesized in this study successfullyafforded the desired arylated allyl alcohols in good yields.

4.1. General Catalytic Reactions

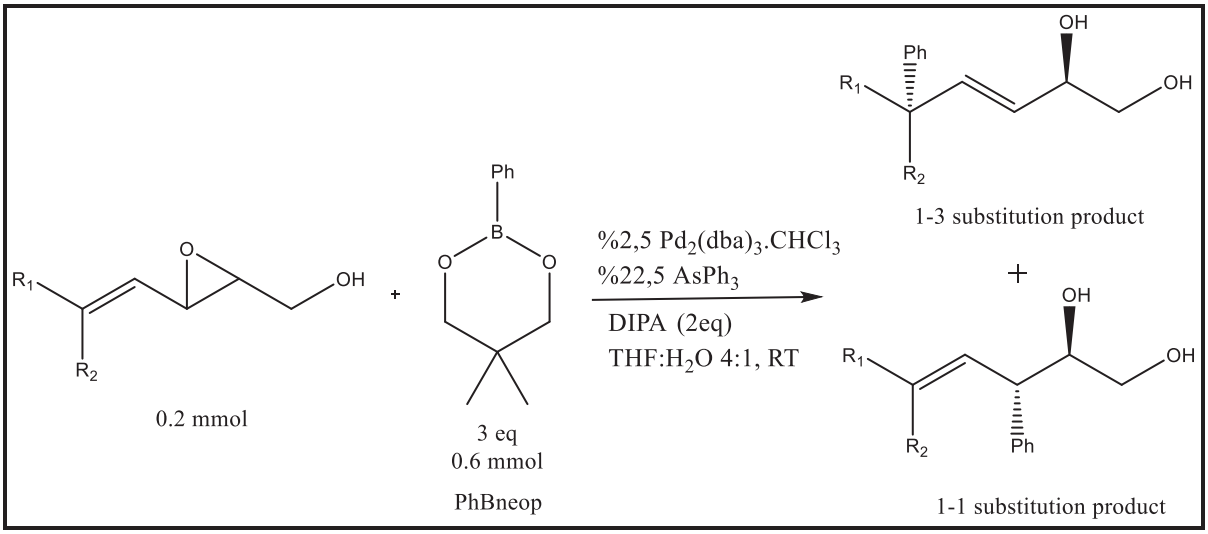


Figure 4.1.General Palladium-catalyzedreaction of vinyl oxirane with PhBneop

First of all, the reaction of avinyl oxirane with two terminal hydroxyl was investigated, purposedly to see how the yield and selectivity of the reaction would be, affected with the presence of allylic hydroxyl group **(1a)**.The reaction for this substrate with neopentyl glycol ester of Phenylboronic acid (**2a**, PhBneop) took 2.5 h for

complete conversion and the S_N2'substituted product was the main couplingproduct of the reaction, which gave rise the product **(3aa)** with 78% yield. The S_N2 substitution product **(4aa)** was also detected to form in15% yield. (Figure 4.2.).

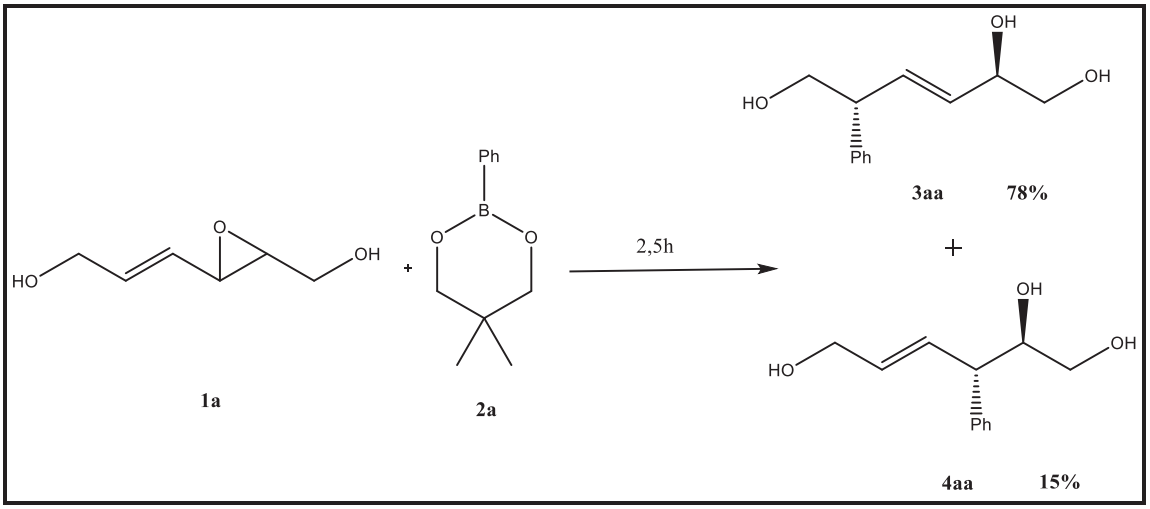


Figure 4.2. Reaction of **1a** with **2a** under optimized conditions according to figure 4.1.

Interestingly, however, when this alkenyl epoxide was used in the form where its allylic hydroxyl group was silyl protected (**1b**) no S_N2 type product (**4ba**) formation was observed to form and the desired **3ba** product was recovered in 81% yield after reaction. (Figure 4.3.).

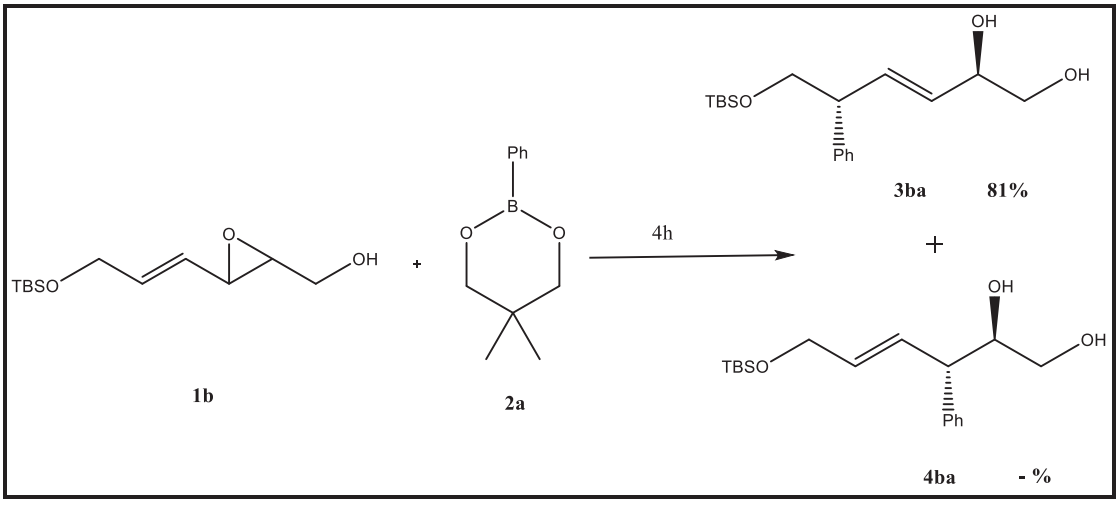


Figure 4.3. Reaction of **1b** with **2a** under optimized conditions according to figure 4.1.

It is apparent that the success of the method is not dependent on the relative configurations of alkenyl and epoxide moieties.The alkenyl epoxide **(1c with *Z,Z*-configuration)** converted completely in 2 h when reacted with **2a**, yielding both S_N2' S_N2 products in 78% (**3ca**) and 11% (**4ca**) yields, respectively. (Figure 4.4.).

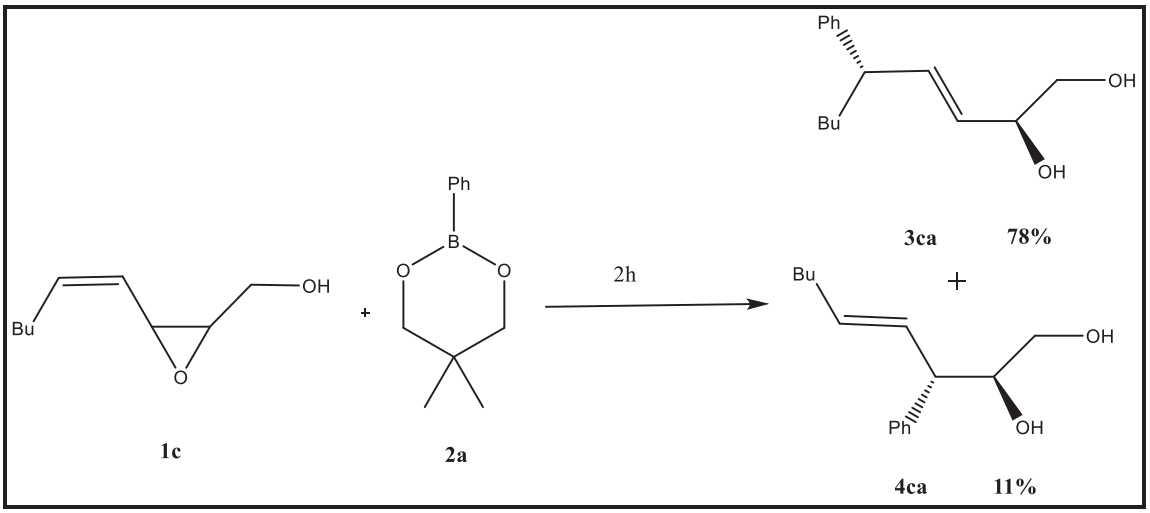


Figure 4.4. Reaction of **1c** with **2a**under optimized conditions according to figure 4.1.

Interestingly, the reaction of the alkenyl epoxide **1d** with a terminal alkenyl moiety provided the expected product **3da** in relatively low yield. (Figure 4.5.)

When the substrate used had *E*-configured epoxide moiety and *Z*-configured alkenyl moiety, the S_N2'product **3ea**, which is the diastereomeric form of **3ca**, was the only product recovered in. (Figure 4.6.).

When the reaction was performed with alkenyl oxirane which has methyl group on R^1, S_N2' product **3fa** was observed as a single product and the yield was calculated to 81%. (Figure 4.7.).

Under optimizing conditions, general catalytic reaction was performed with a reactant which has a sterically large group such as cyclohexyl in R^1. The S_N2' product **3ga** was observed with 28% yield and also S_N2 product with 28% yield. (Figure 4.8.)

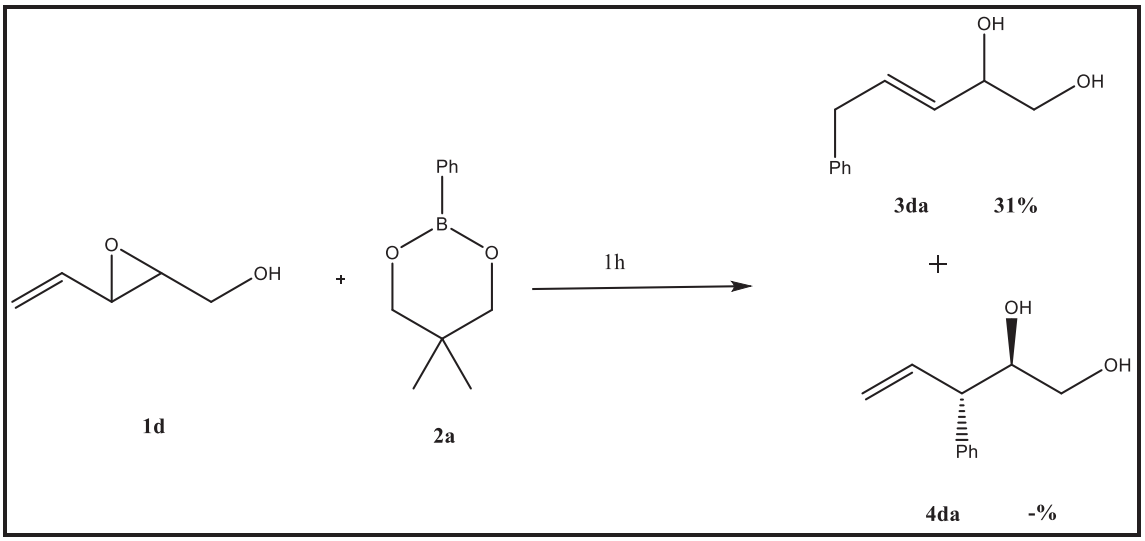


Figure 4.5. Reaction of **1d** with **2a** under optimized conditions according to figure 4.1.

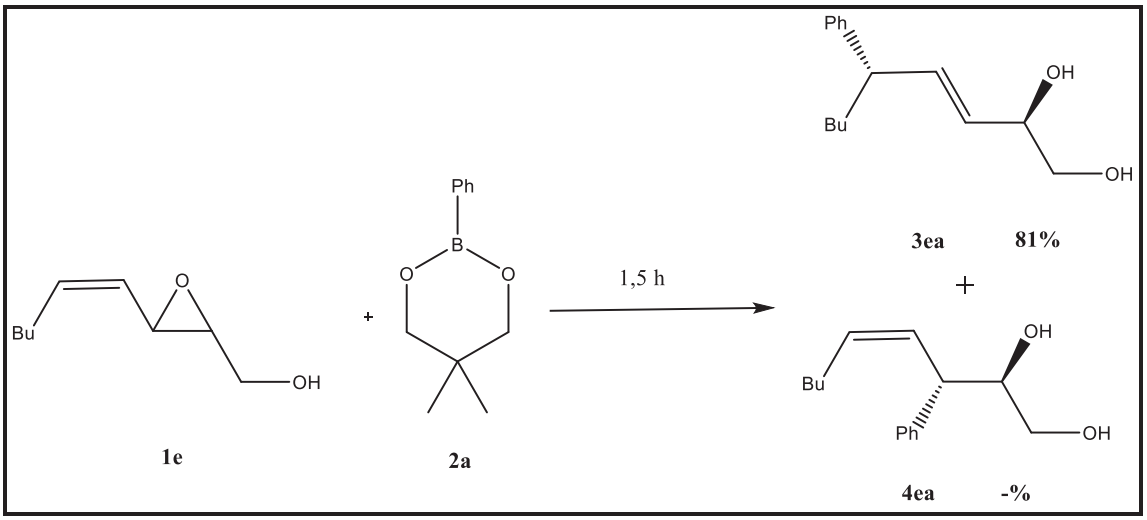


Figure 4.6. Reaction of **1e** with **2a** under optimized conditions according to figure 4.1.

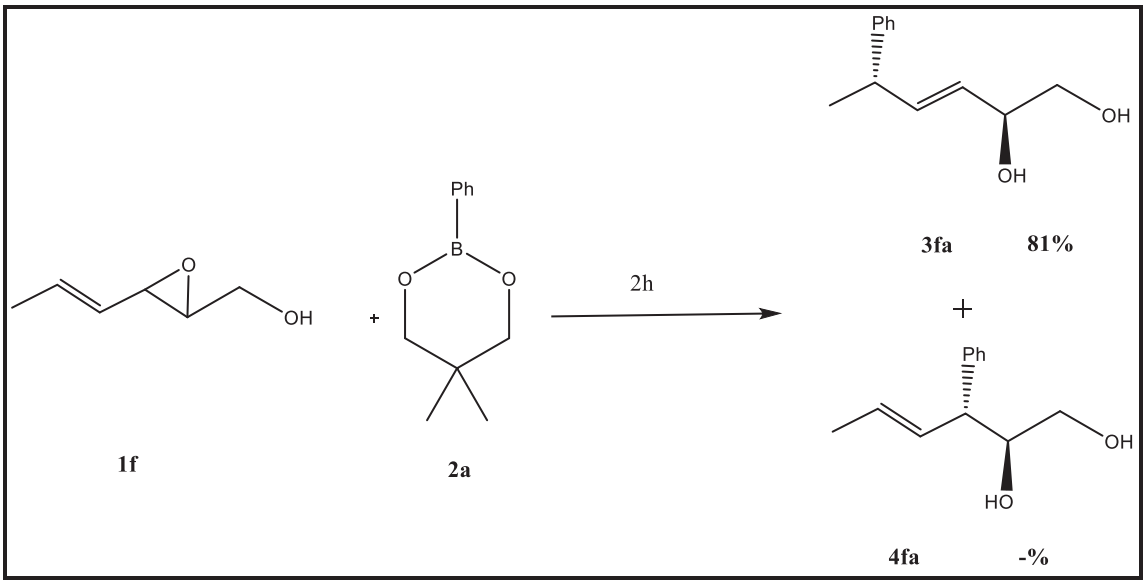


Figure 4.7. Reaction of **1f** with **2a** under optimized conditions according to figure 4.1.

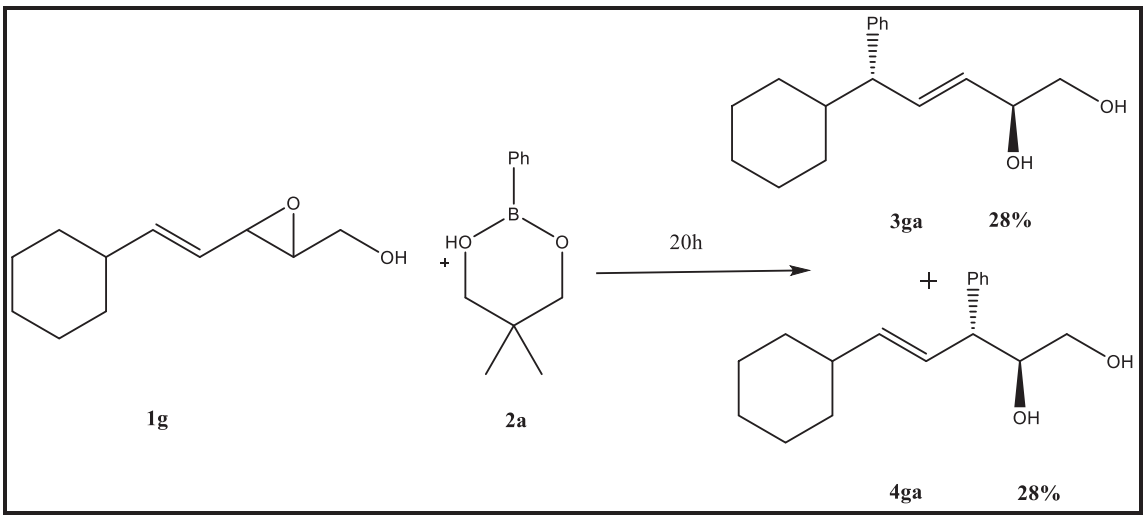


Figure 4.8. Reaction of **1g** with **2a** under optimized conditions according to figure 4.1.

4.2. General Mechanism of the Reaction

The reaction is thought to begin with the opening of the oxirane ring by the attact of the palladium to the structure from the anti-position. It is generally known that palladium participates allylic compounds inthe anti-mode. (Tsuji, 2004). The resulting

π-allylpalladium intermediate undergoes successive transmetallation and reductive elimination steps to form of S_N2'or S_N2 products.

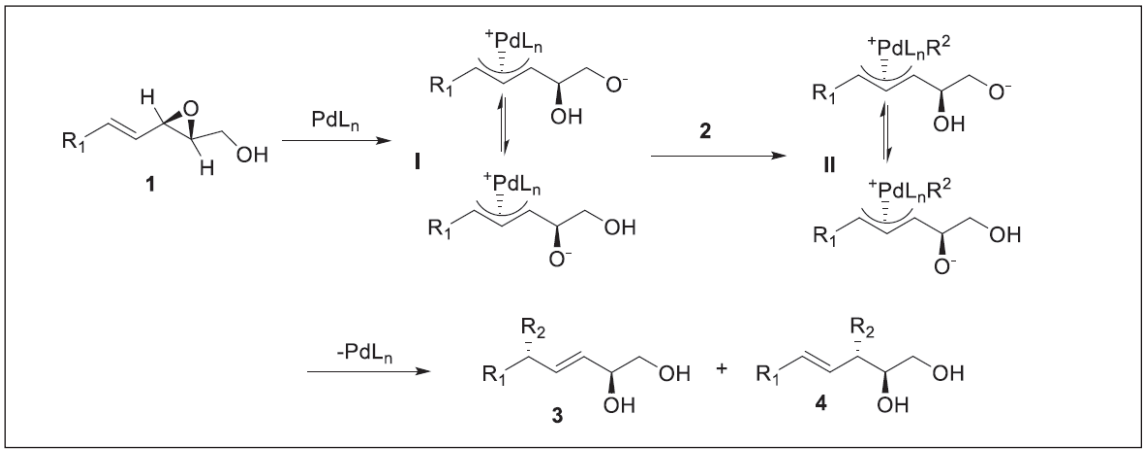


Figure 4.9. The predicted mechanism of palladium-catalyzed reaction of alkenyl epoxides with organoborons.

The bases for the positive effective of the pendant hydroxyl group to the reaction selectivity of the on the product selectivity are not yet known. However, it is possible that the hydroxyl group is potentially be coordinated with the center of the palladium and this coordination may have promoted the region- and stereo-selectivity of the process.

CHAPTER 5

CONCLUSION

The stereo- and region-selective arylation of alkenyl epoxides was the aim of the present study. In analogy to a previous study performed in this laboratory, the reactions of alkenyl epoxides having a pendant hydroxyl group with neopentyl gylicol ester of arylboronic acids in the presence of $Pd/AsPh_3$ combination proceeded in anti manner to yield S_N2' majorly.

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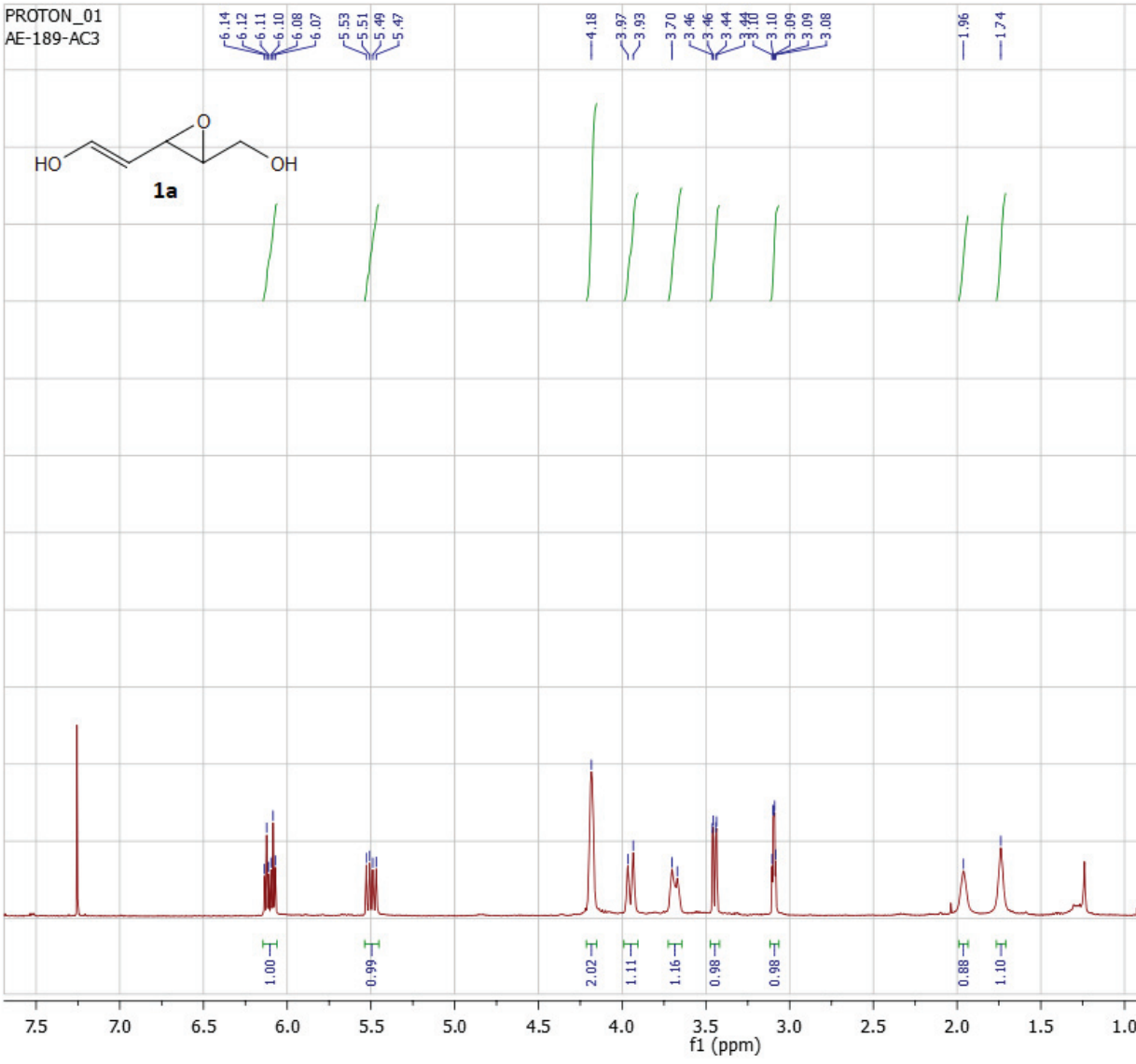
APPENDIX A

^{1}H NMR AND ^{13}C NMR SPECTRUMS OF REACTANTS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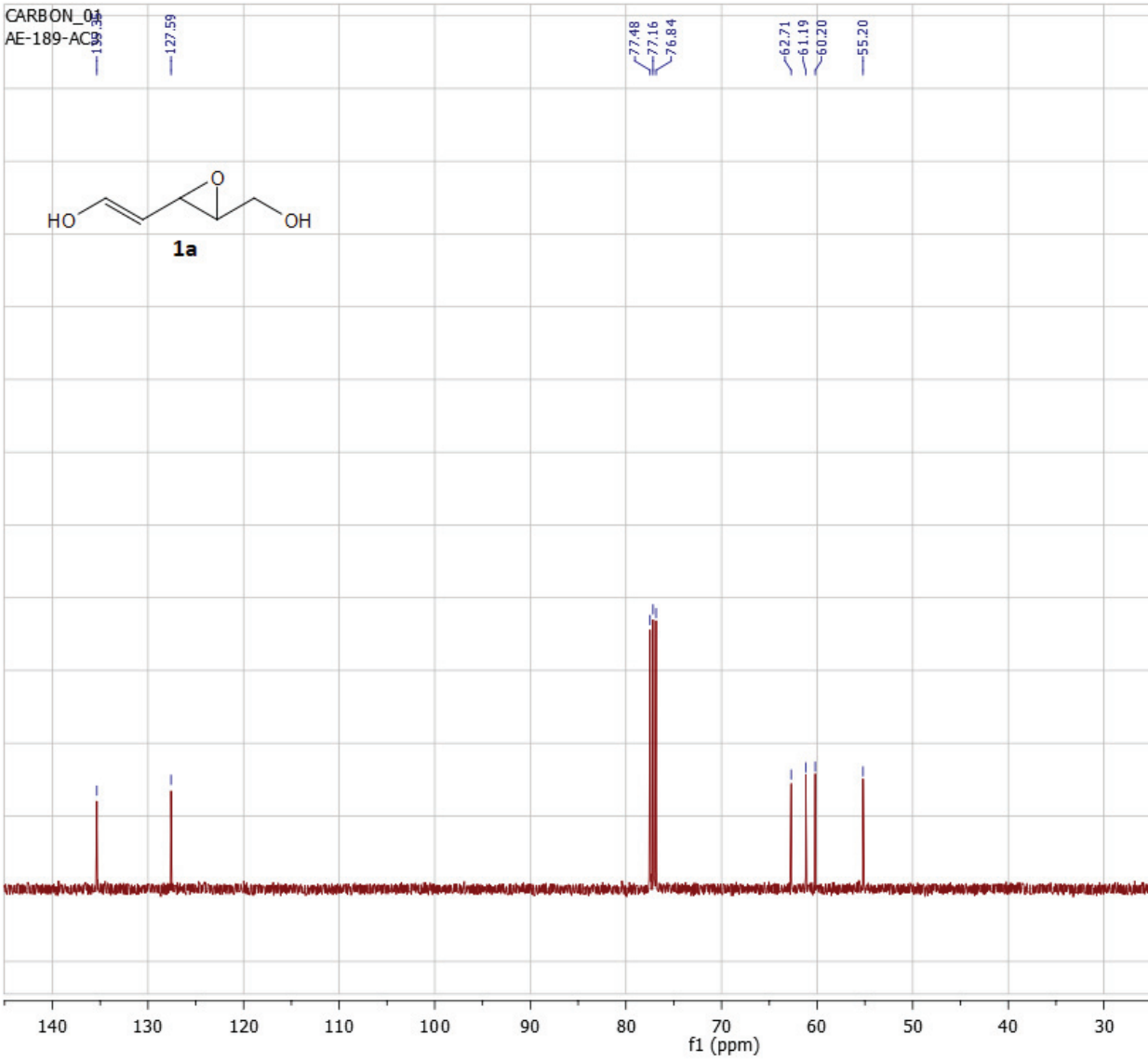
6.12
6.11
6.10
6.08
6.07
5.53
5.51
5.49
5.47
4.18
3.97
3.93
3.70
3.46
3.44
3.10
3.09
3.08
1.96
1.74
HO
O
OH
1a
1.00
0.99
2.02
1.11
1.16
0.98
0.98
0.88
1.10
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
f1 (ppm)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62.71
61.19
60.20
55.20
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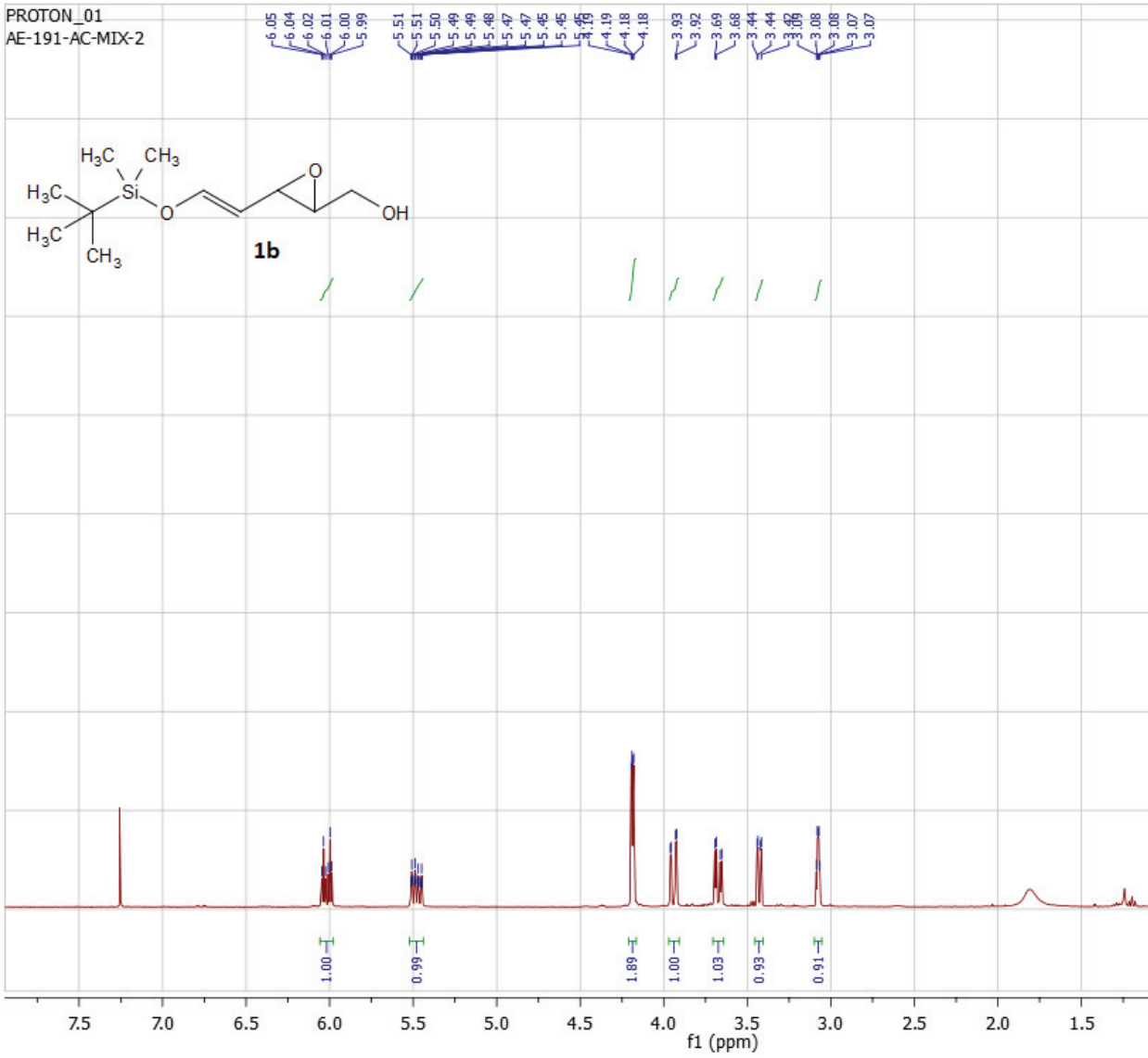
O
OH
1a
140
130
120
110
100
90
80
70
60
50
40
30
f1 (ppm)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6.02
6.01
6.00
5.99
5.51
5.51
5.50
5.49
5.49
5.48
5.47
5.47
5.45
5.45
4.19
4.18
4.18
3.93
3.92
3.69
3.68
3.44
3.44
3.08
3.08
3.07
3.07
H3C
CH3
H3C
Si
O
H3C
CH3
O
OH
1b
1.00
0.99
1.89
1.00
1.03
0.93
0.91
7.5
7.0
6.5
6.0
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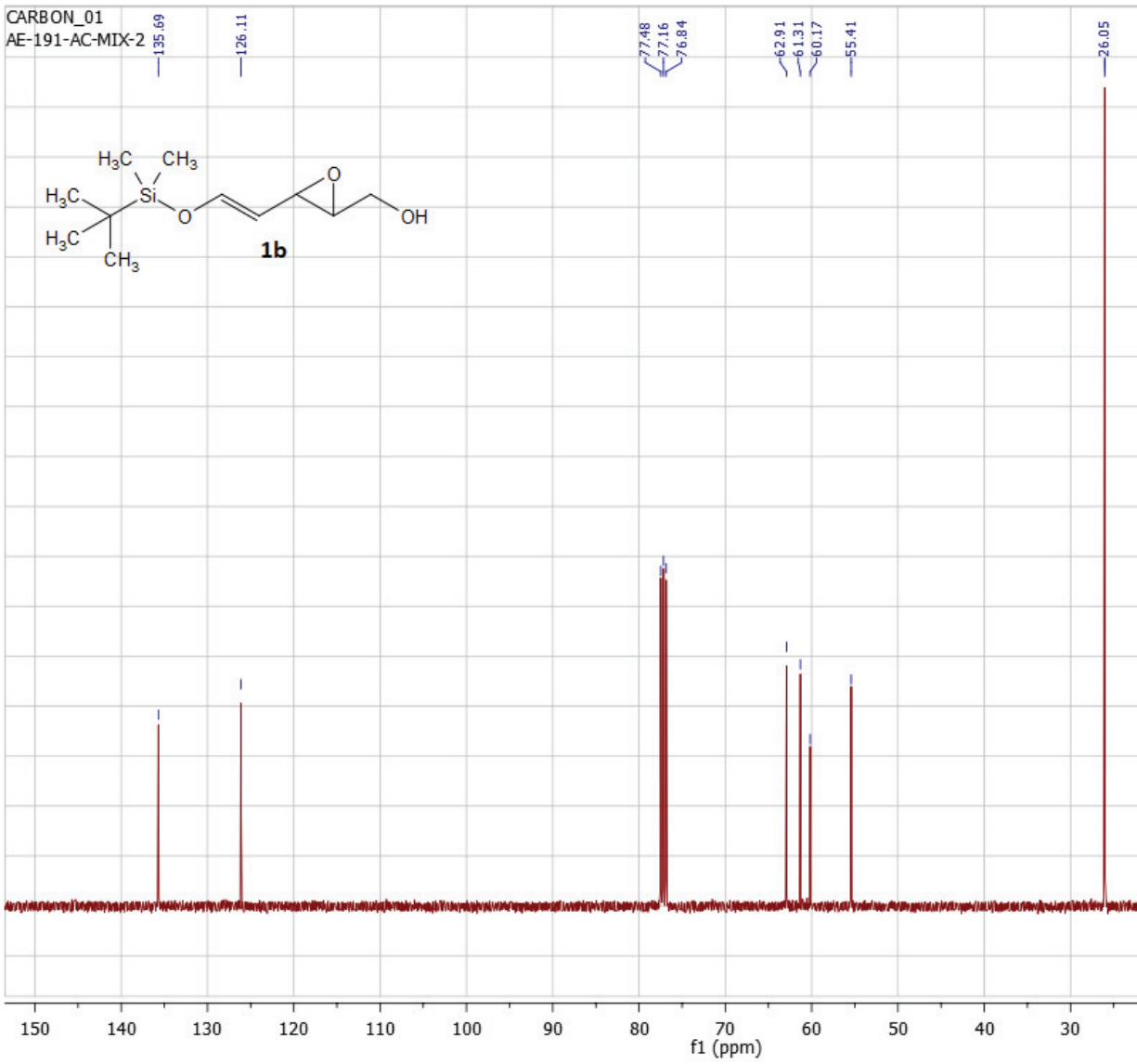
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
f1 (ppm)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55.41
26.05
H3C
CH3
Si
O
H3C
H3C
CH3
O
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130
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100
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80
70
60
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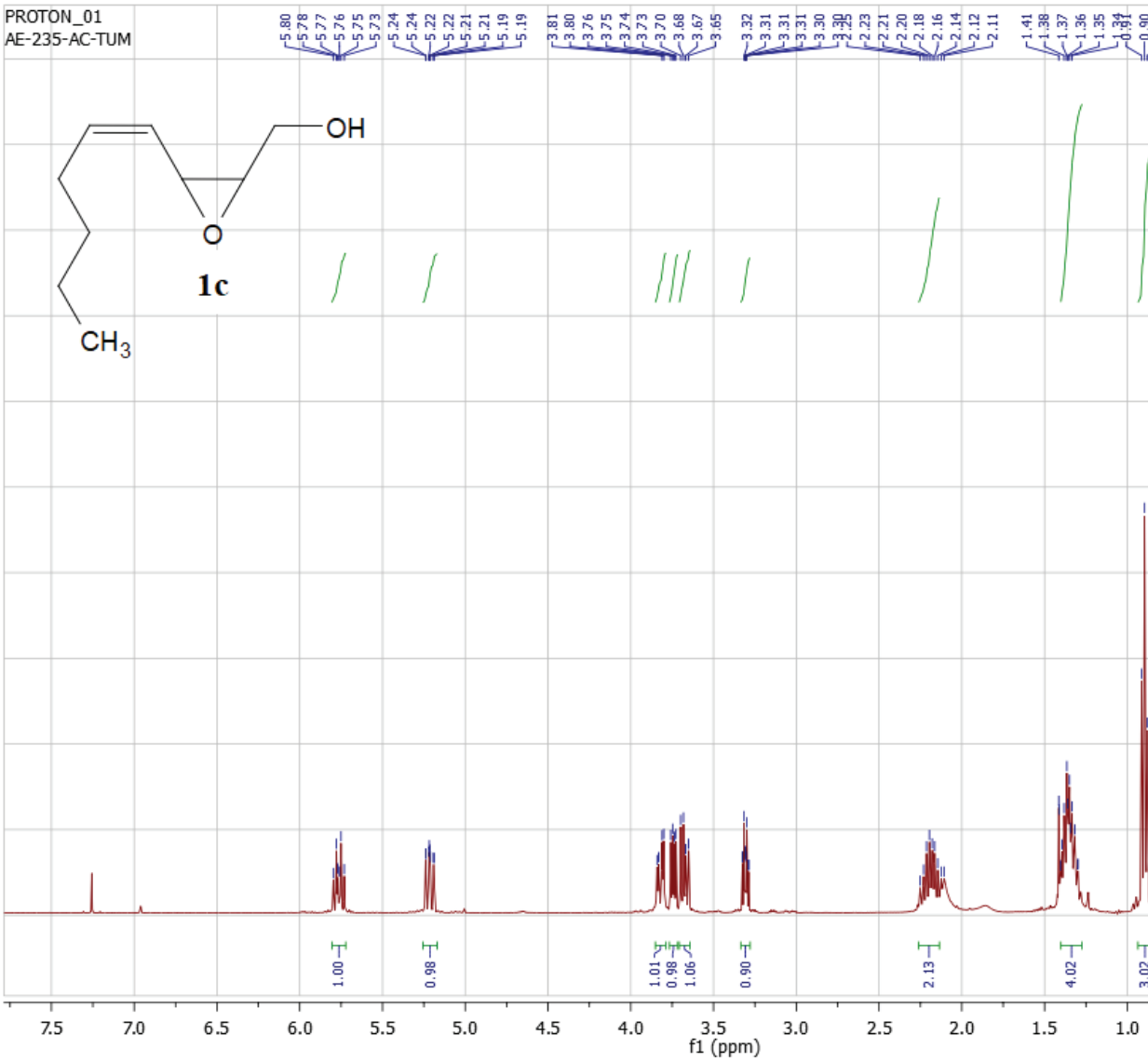
40
30
f1 (ppm)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CH3
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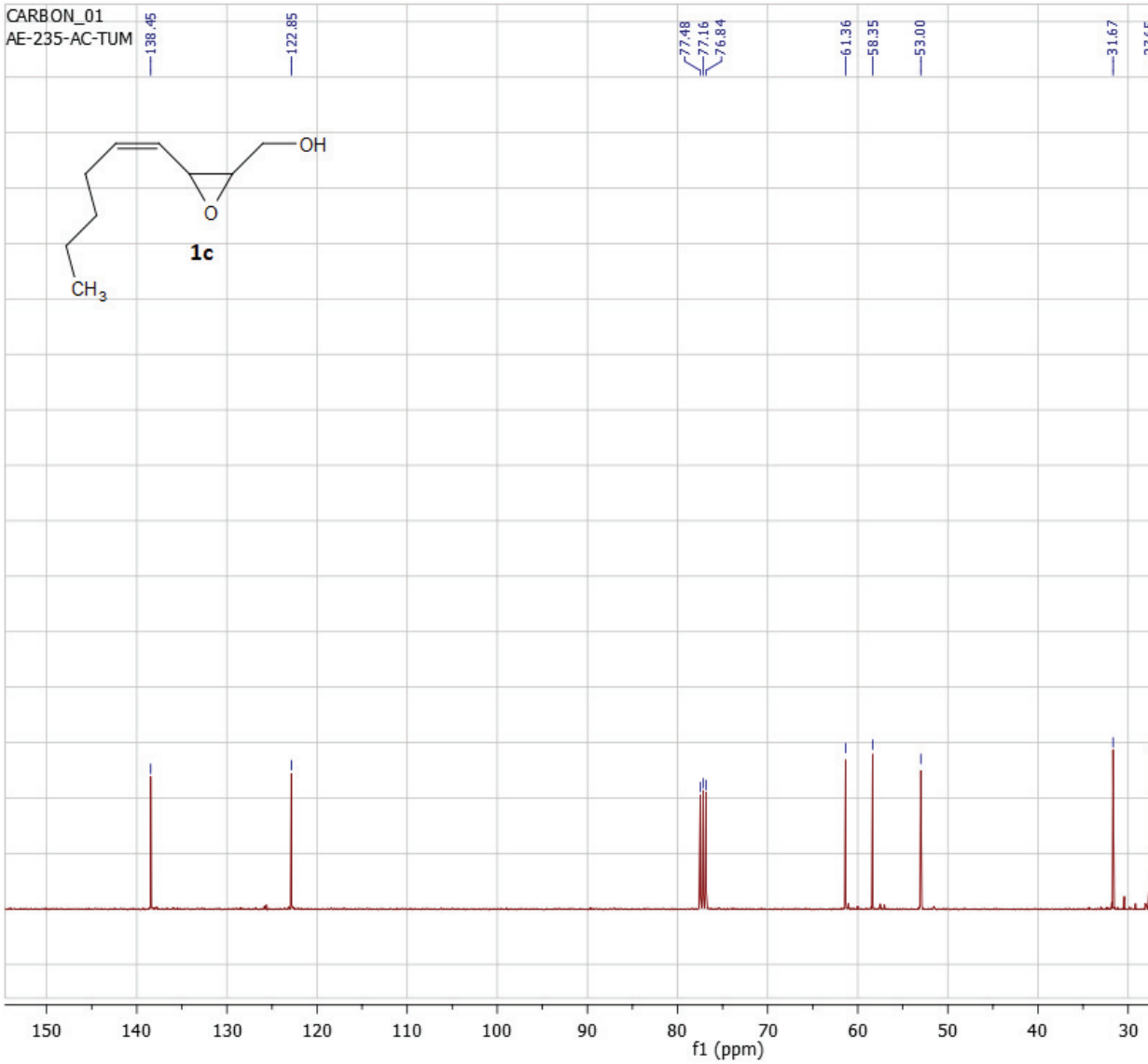
1.01
0.98
1.06
0.90
2.13
4.02
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
f1 (ppm)


CARBON_01
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77.16
76.84
61.36
58.35
53.00
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CH3
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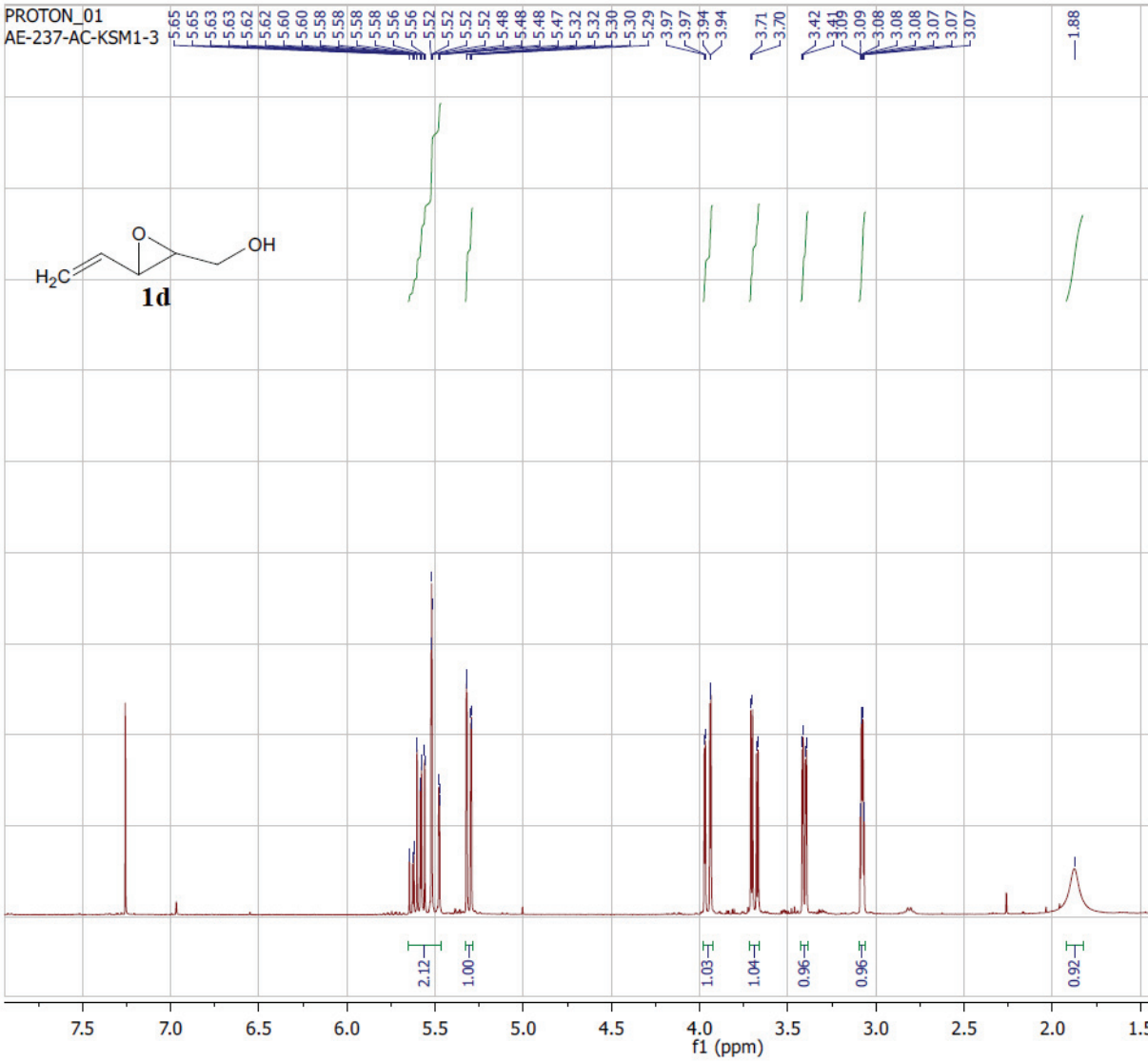
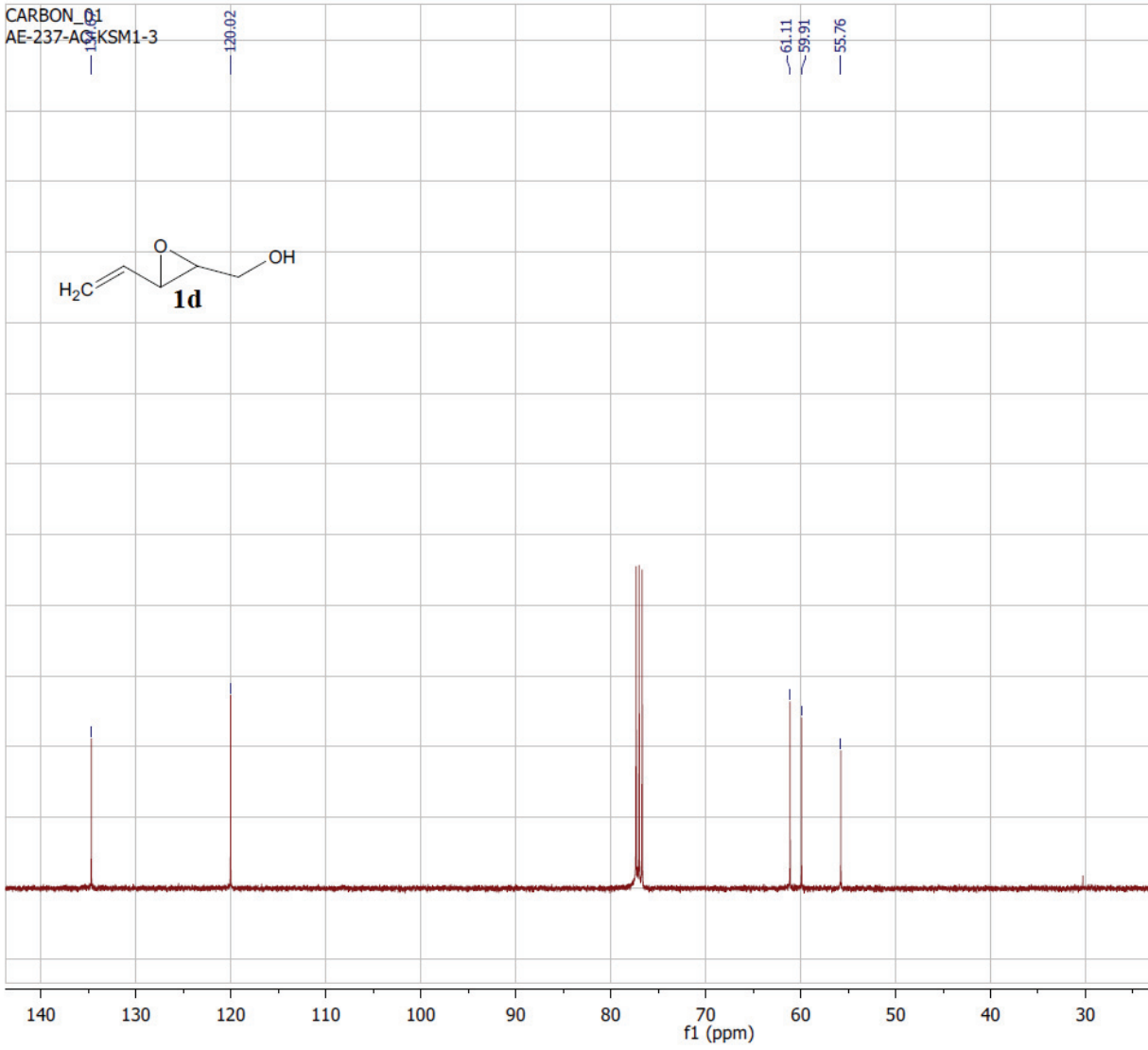
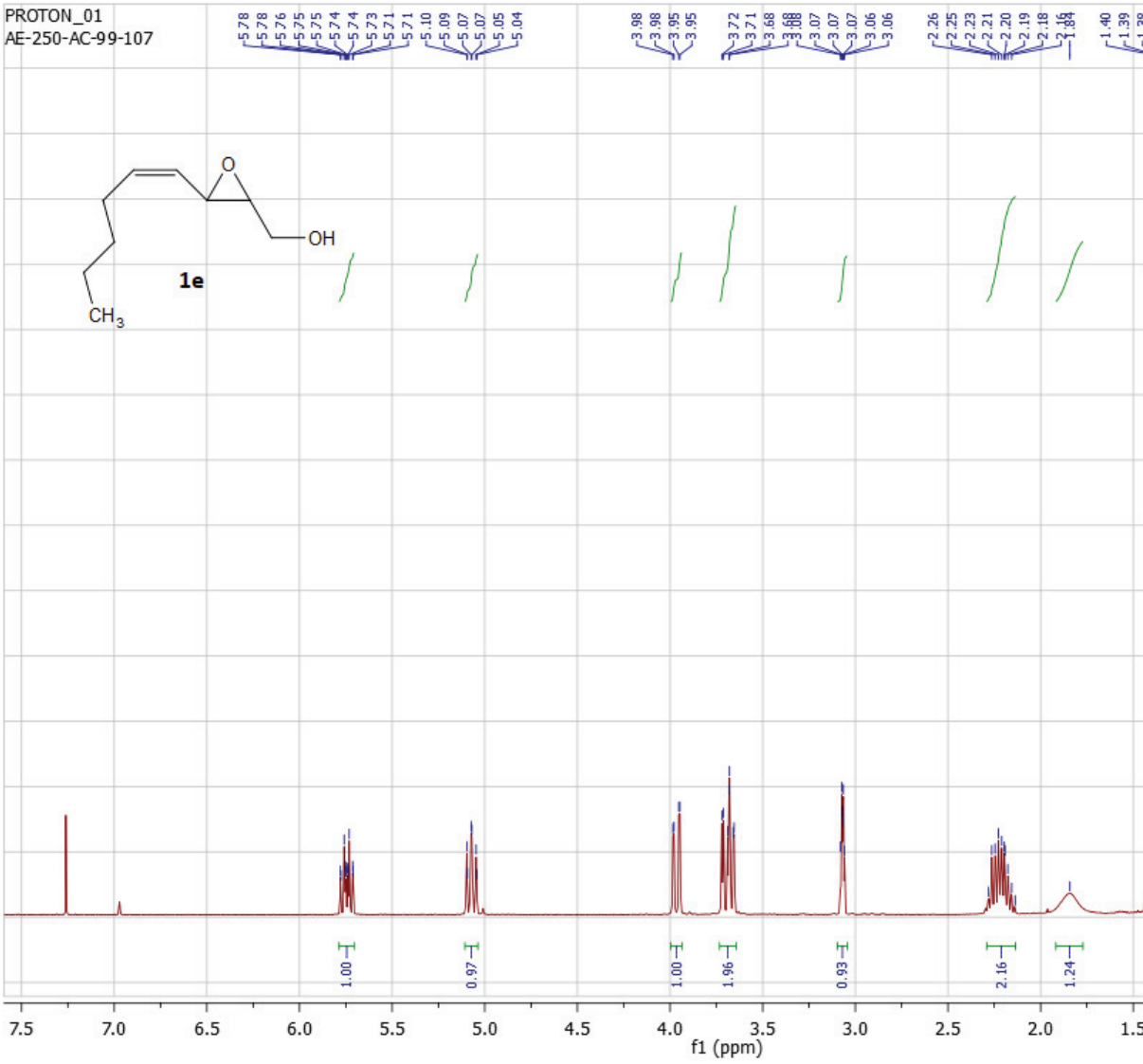
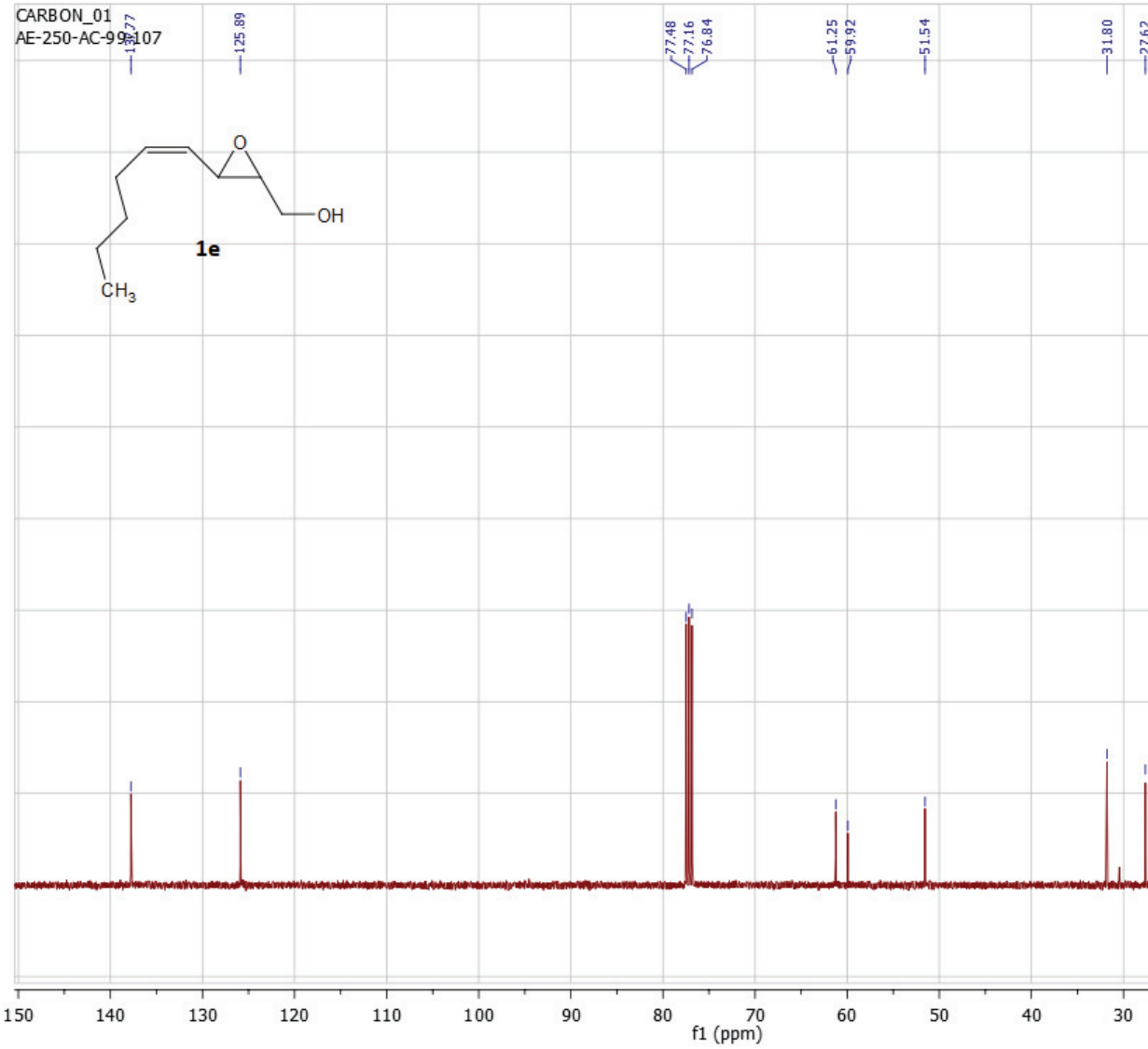
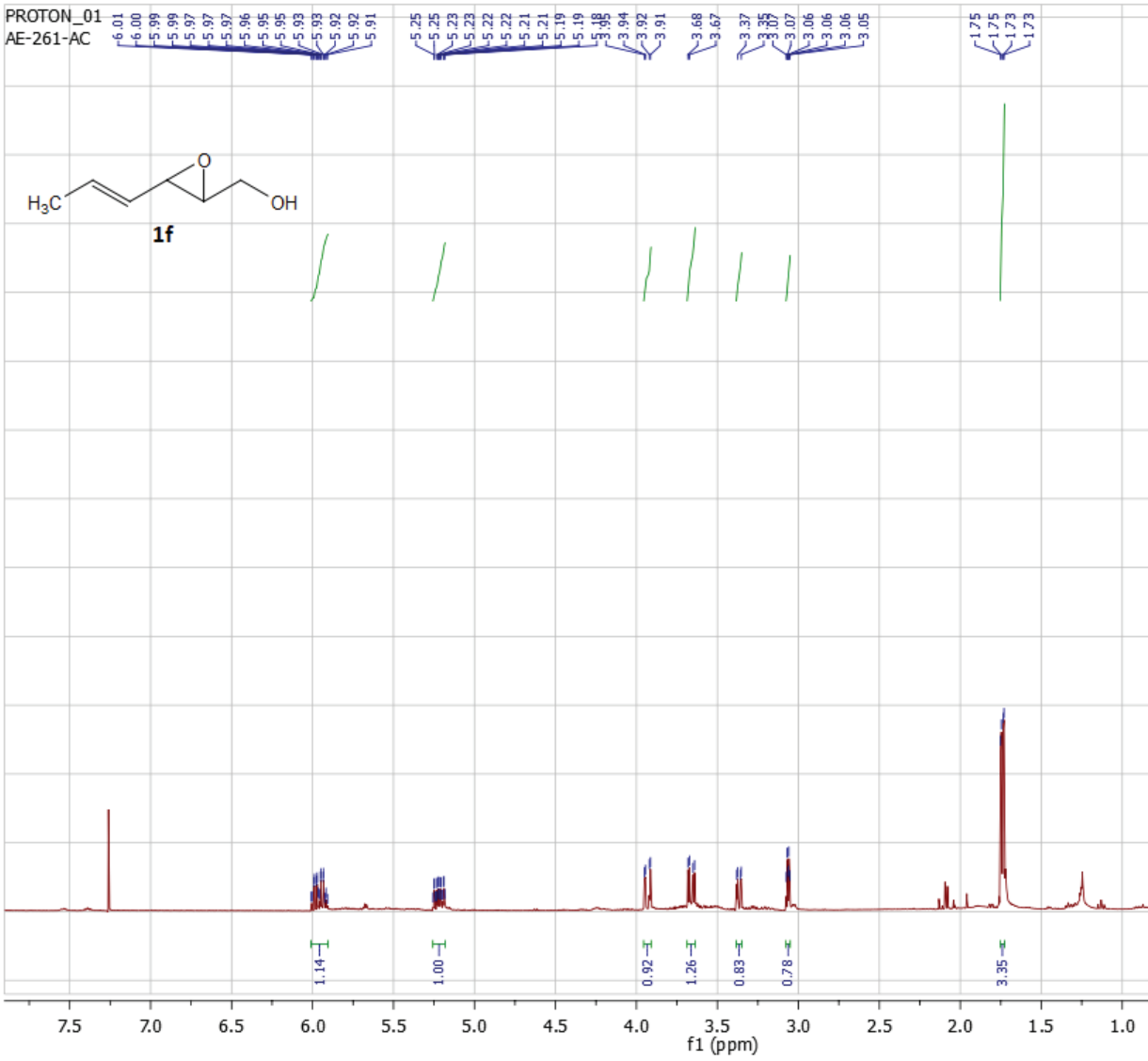
90
80
70
60
50
40
30
f1 (ppm)

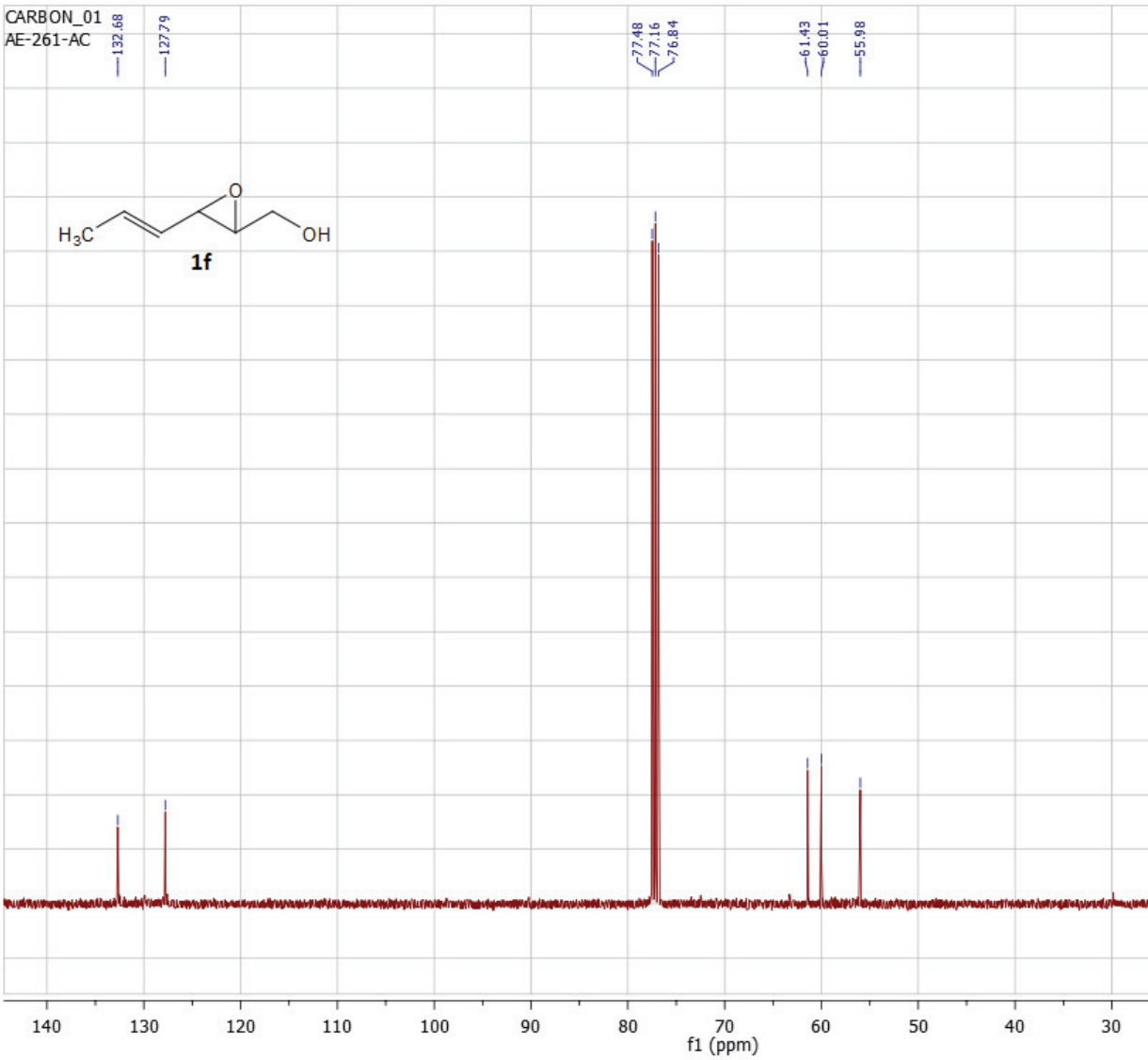

PROTON_01
AE-237-AC-KSM1-3
5.65 5.65 5.63 5.63 5.62 5.62 5.60 5.60 5.58 5.58 5.58 5.58 5.56 5.56 5.52 5.52 5.52 5.52 5.48 5.48 5.48 5.47 5.32 5.32 5.30 5.30 5.29 3.97 3.97 3.94 3.94 3.71 3.70 3.42 3.41 3.09 3.09 3.08 3.08 3.08 3.07 3.07 3.07 1.88
O
OH
H2C
1d
2.12
1.00
1.03
1.04
0.96
0.96
0.92
7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5
f1 (ppm)

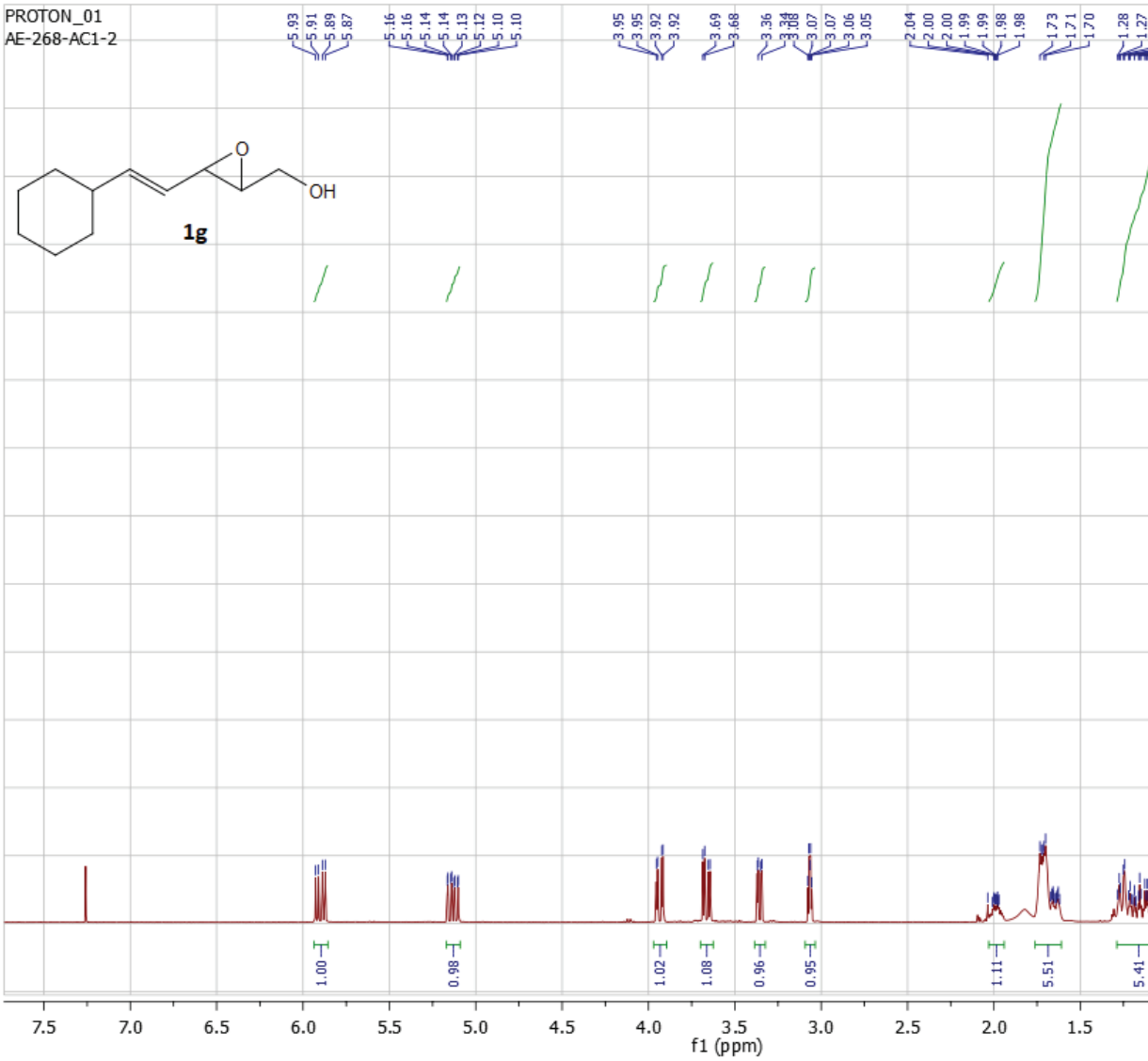

CARBON_01
AE-237-AC-KSM1-3
135.49
120.02
61.11
59.91
55.76
O
OH
H2C
1d
140
130
120
110
100
90
80
70
60
50
40
30
f1 (ppm)

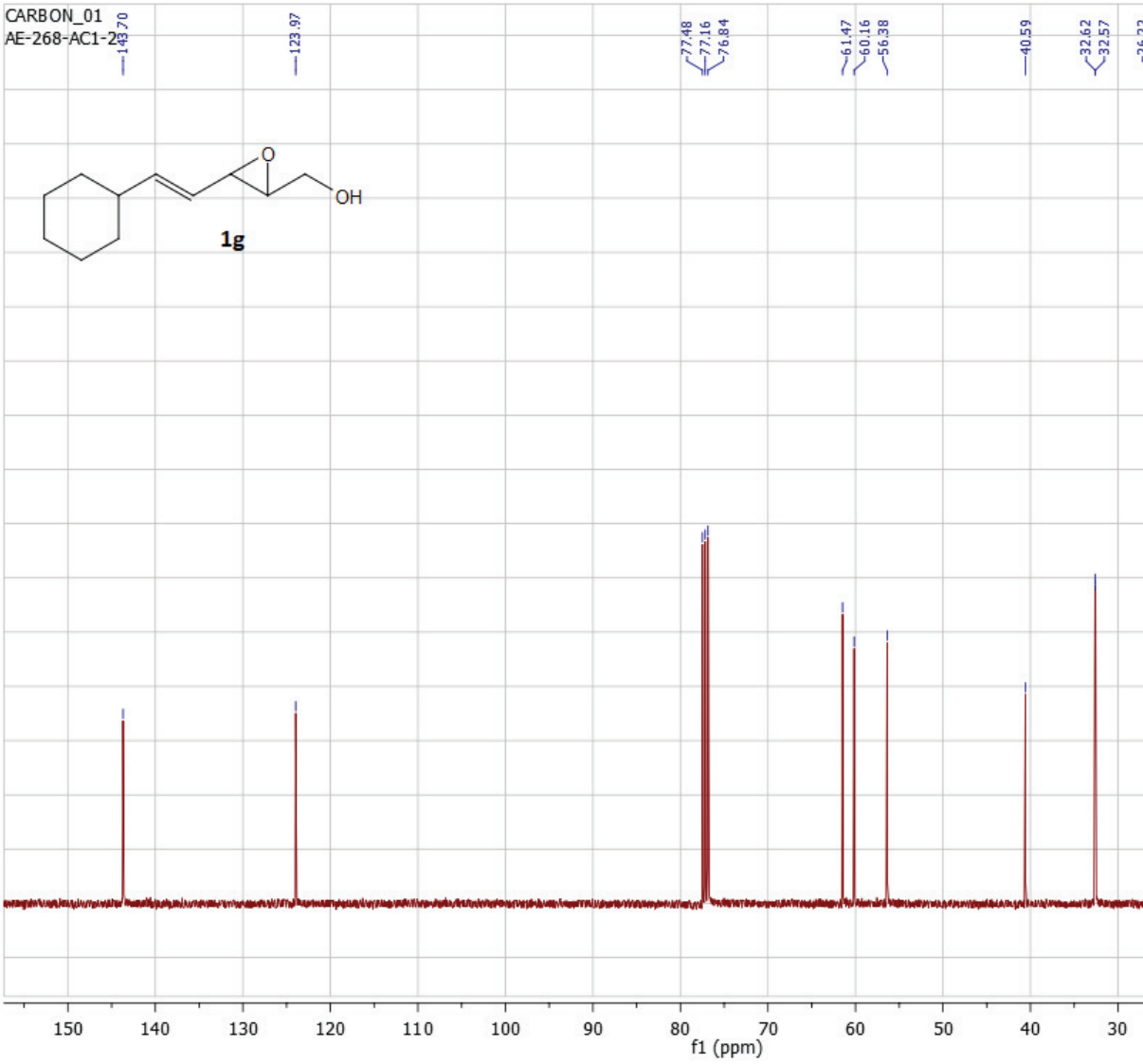

PROTON_01
AE-250-AC-99-107
O
OH
1e
CH3
1.00
0.97
1.00
1.96
0.93
2.16
1.24
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
f1 (ppm)


CARBON_01
AE-250-AC-99107
137.77
125.89
77.48
77.16
76.84
61.25
59.92
51.54
31.80
O
OH
1e
CH3
150
140
130
120
110
100
90
80
70
60
50
40
30
f1 (ppm)


PROTON_01
AE-261-AC
6.01
6.00
5.99
5.99
5.97
5.97
5.97
5.96
5.95
5.95
5.93
5.93
5.92
5.92
5.91
5.25
5.25
5.23
5.23
5.22
5.22
5.21
5.21
5.19
5.19
3.94
3.92
3.91
3.68
3.67
3.37
3.07
3.06
3.06
3.06
3.05
1.75
1.75
1.73
1.73
O
H3C
OH
1f
1.14
1.00
0.92
1.26
0.83
0.78
3.35
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
f1 (ppm)

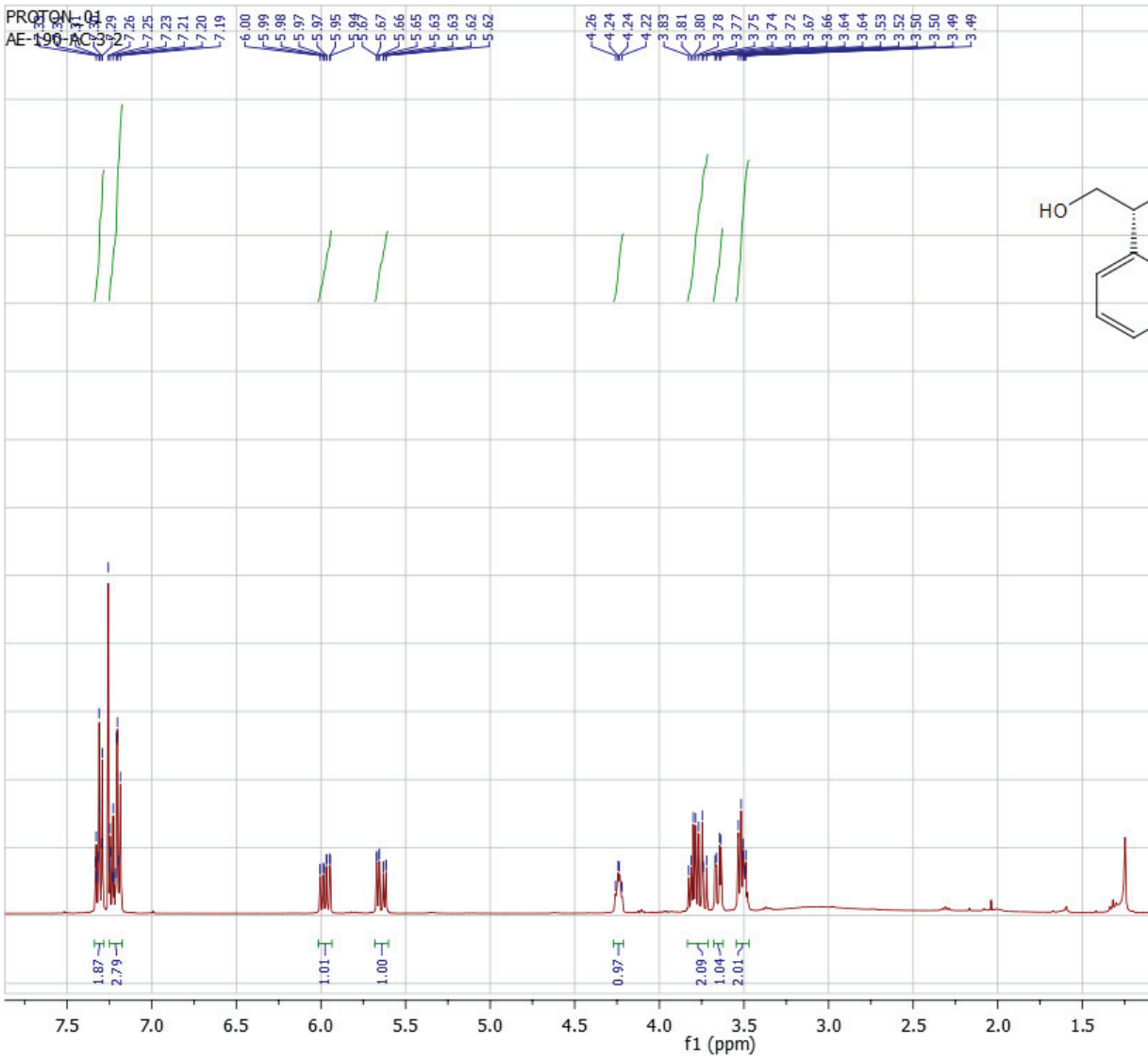

CARBON_01
AE-261-AC
132.68
127.79
77.48
77.16
76.84
61.43
60.01
55.98
O
H3C
OH
1f
140
130
120
110
100
90
80
70
60
50
40
30
f1 (ppm)

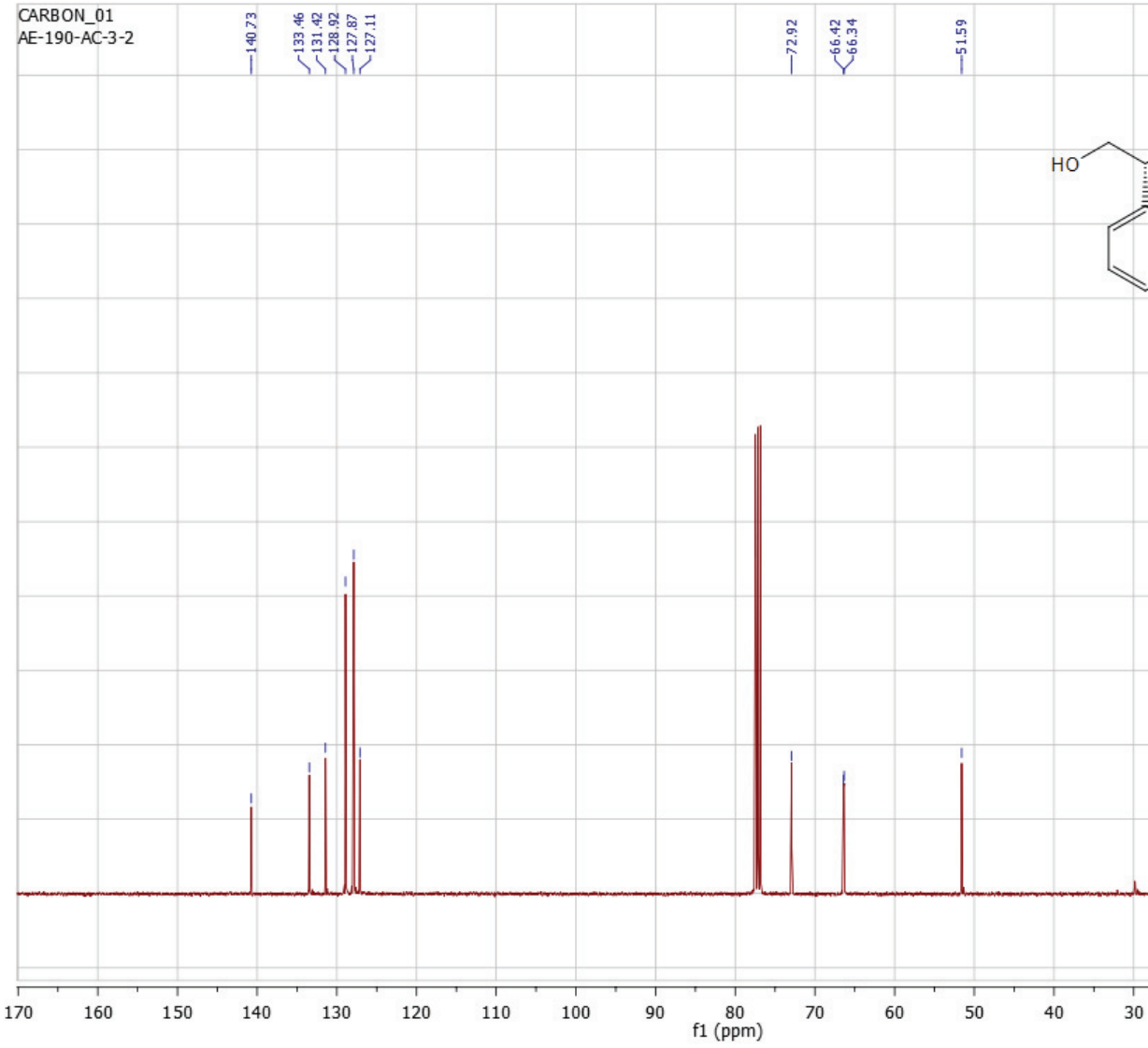

PROTON_01
AE-268-AC1-2
O
OH
1g
5.93
5.91
5.89
5.87
5.16
5.16
5.14
5.14
5.13
5.12
5.10
5.10
3.95
3.95
3.92
3.92
3.69
3.68
3.36
3.34
3.08
3.07
3.07
3.06
3.05
2.04
2.00
2.00
1.99
1.99
1.98
1.98
1.73
1.71
1.70
1.28
1.27
1.00
0.98
1.02
1.08
0.96
0.95
1.11
5.51
5.41
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
f1 (ppm)

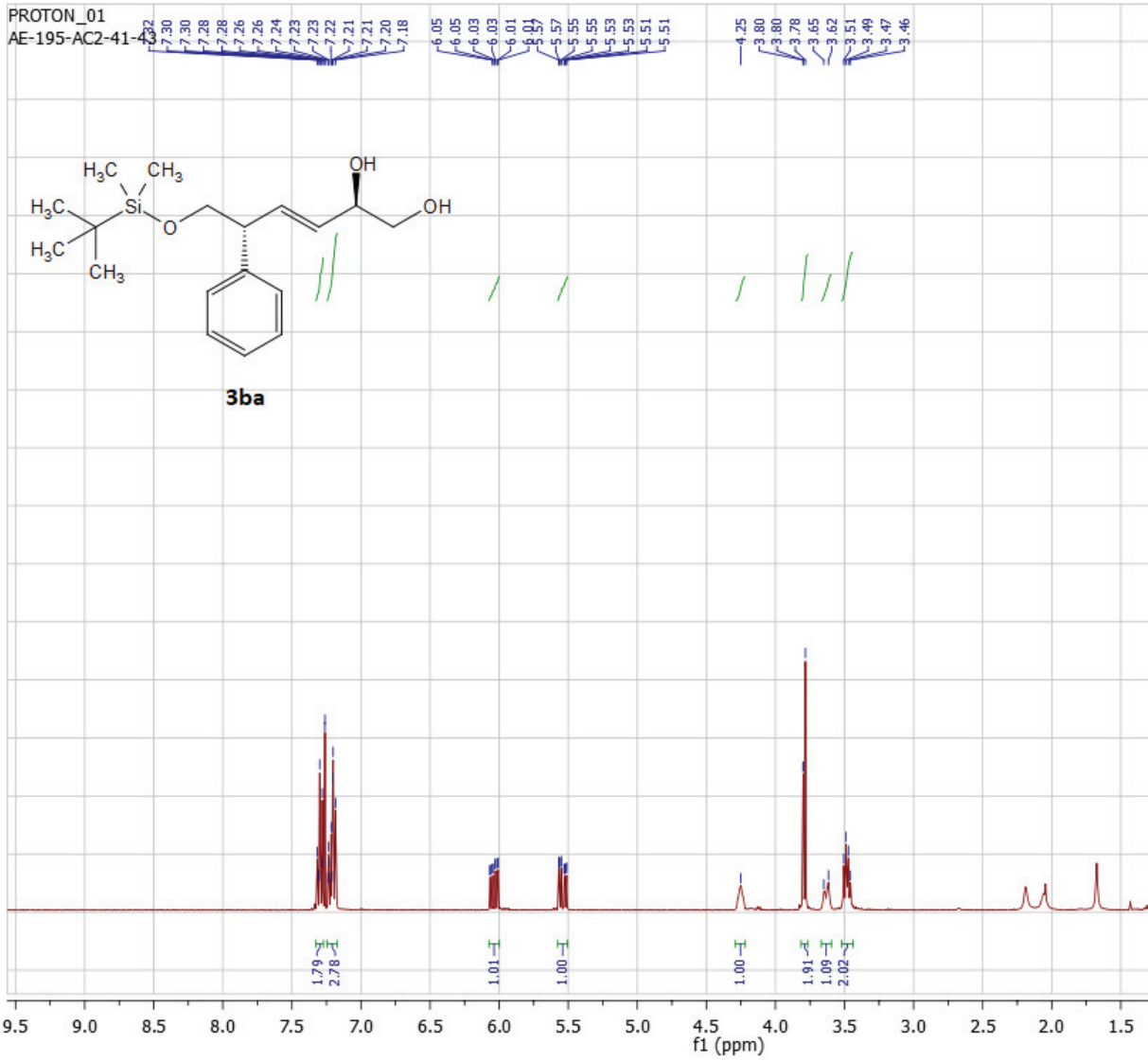

CARBON_01
AE-268-AC1-2
143.70
123.97
77.48
77.16
76.84
61.47
60.16
56.38
40.59
32.62
32.57
O
OH
1g
150
140
130
120
110
100
90
80
70
60
50
40
30
f1 (ppm)

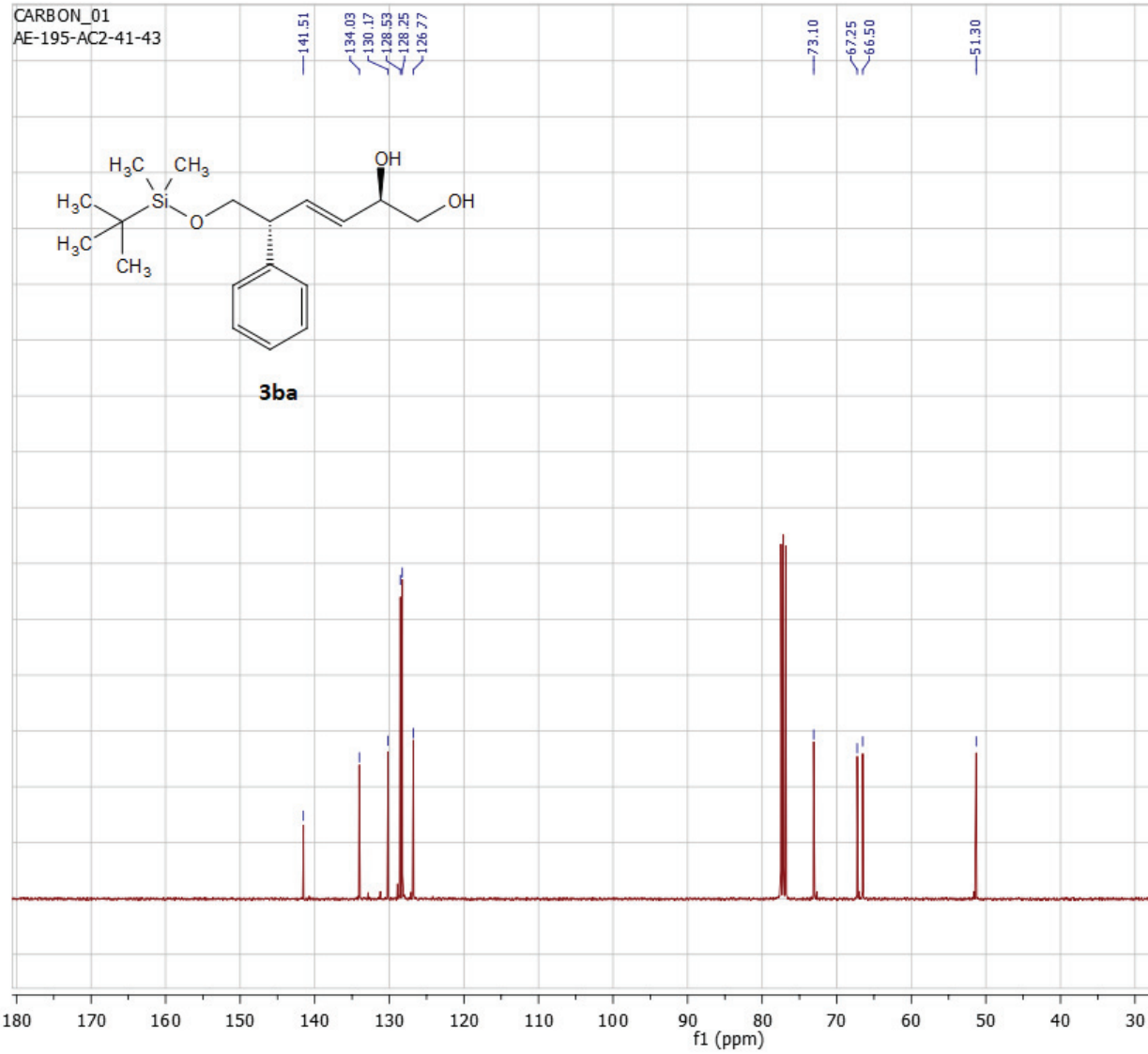
APPENDIX B

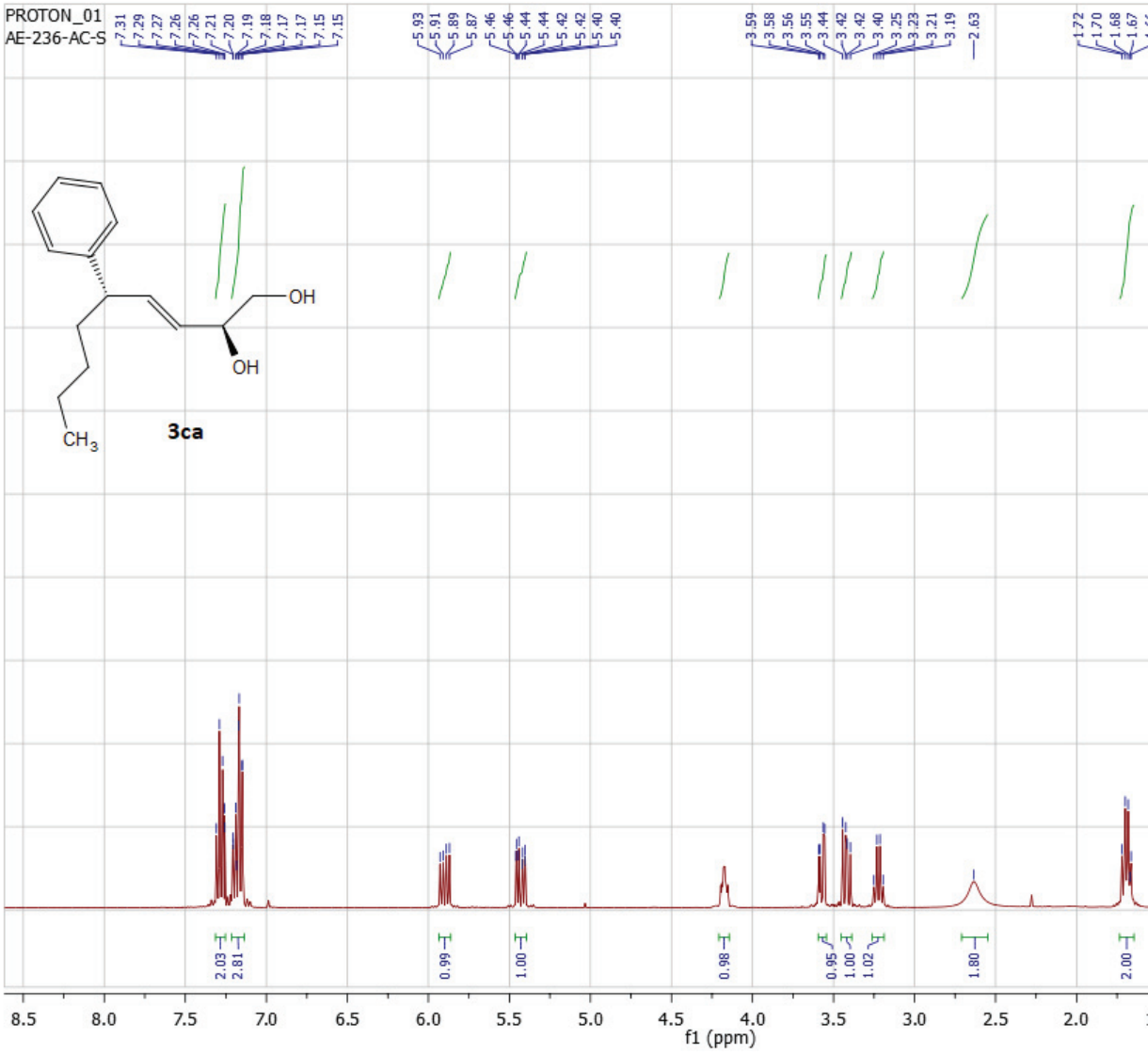
^{1}H NMR AND ^{13}CNMR SPECTRUMS OF PRODUCTS

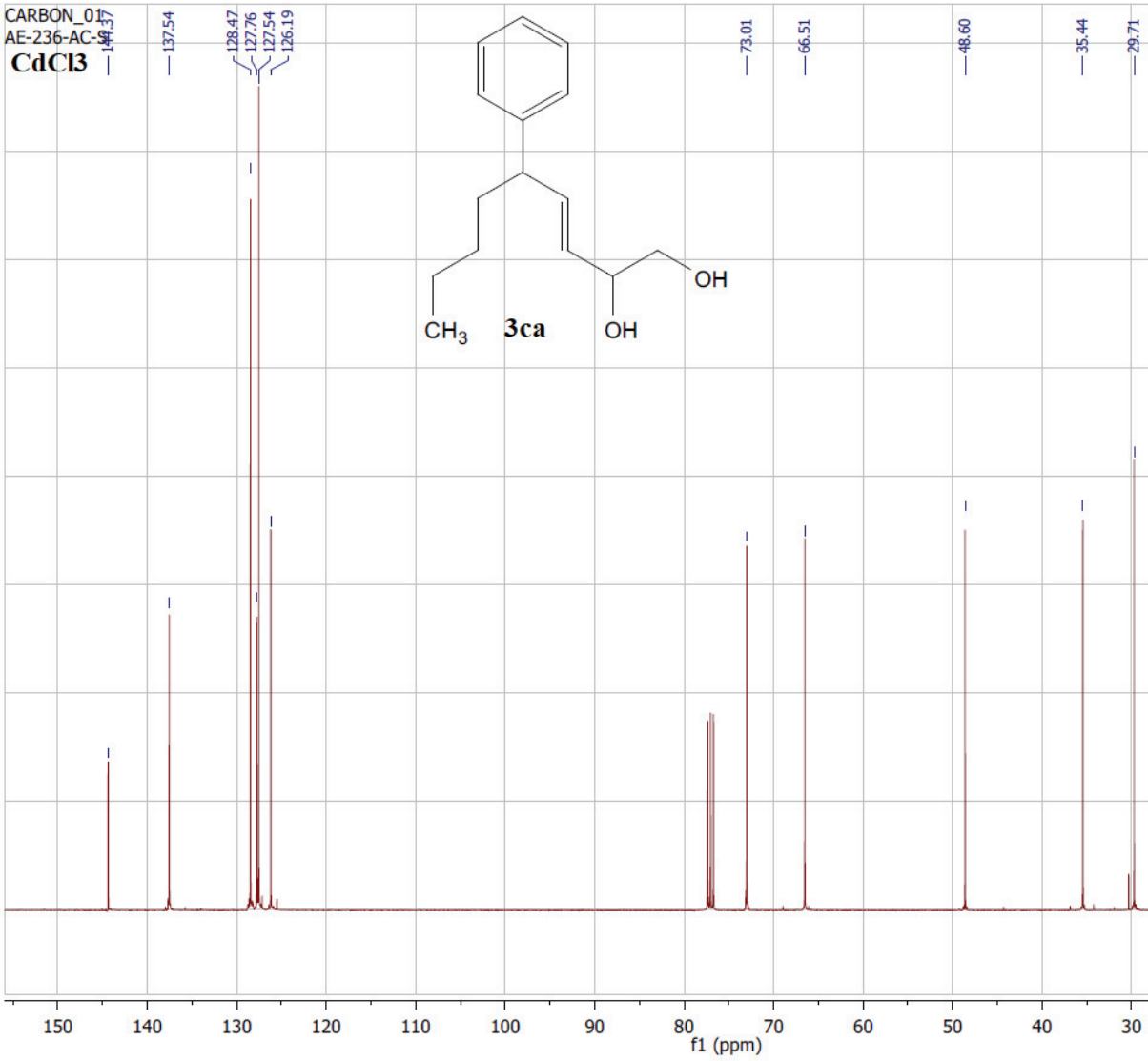

PROTON_01
AE-190-AC-3-2
HO
1.87
2.79
1.01
1.00
0.97
2.09
1.04
2.01
f1 (ppm)

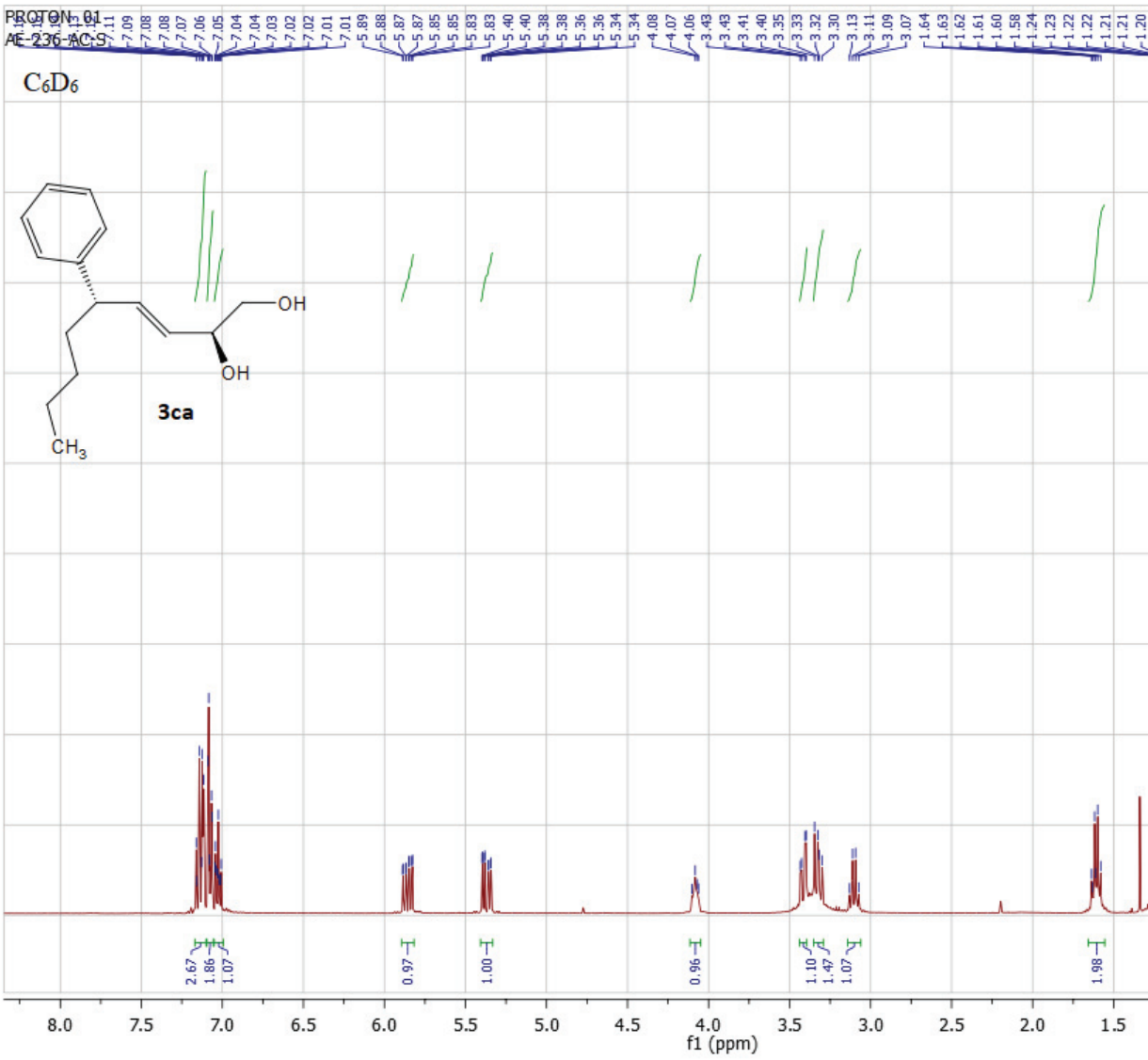

CARBON_01
AE-190-AC-3-2
140.73
133.46
131.42
128.92
127.87
127.11
72.92
66.42
66.34
51.59
HO
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
f1 (ppm)

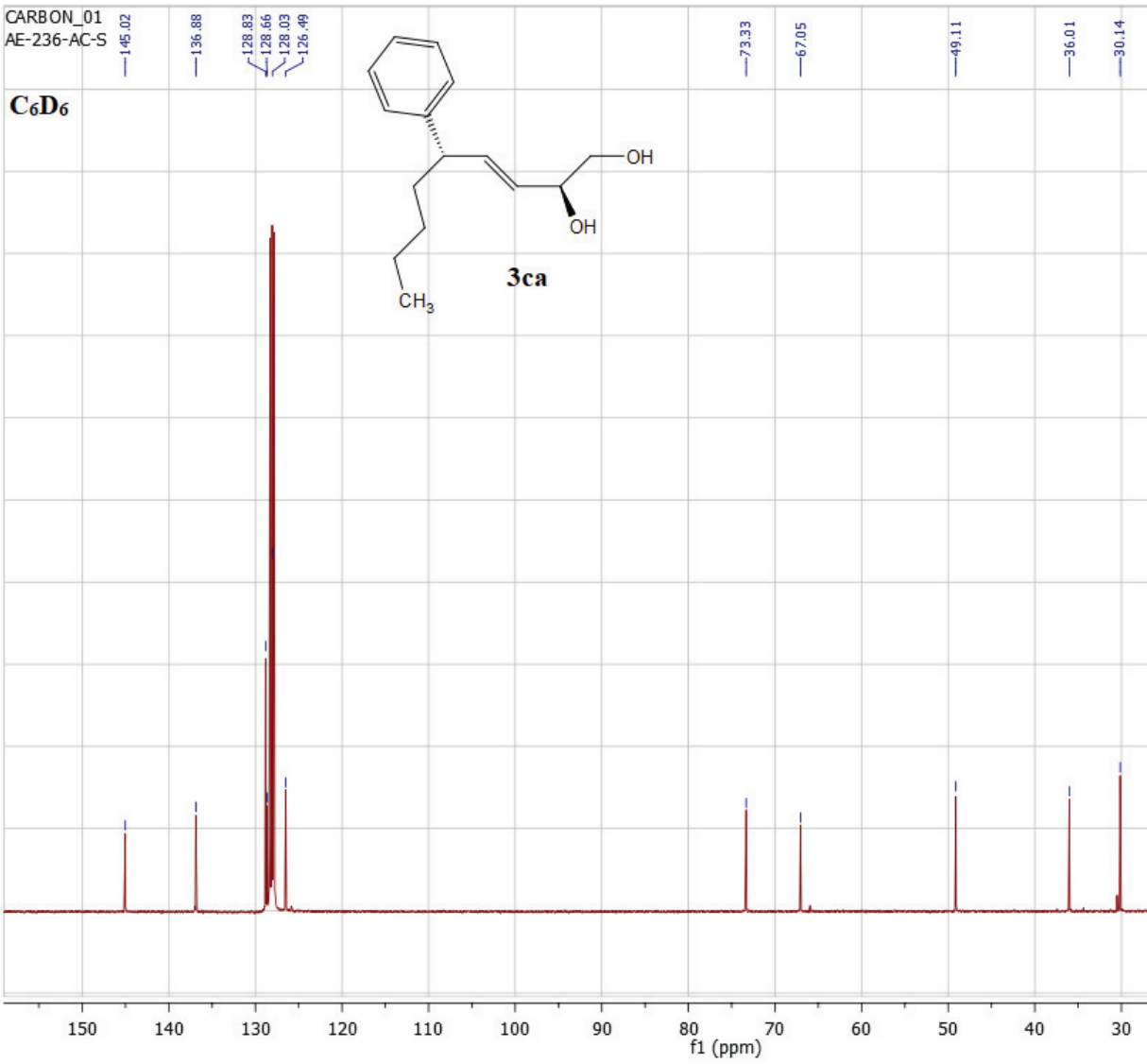

PROTON_01
AE-195-AC2-41-43
7.32 7.30 7.30 7.28 7.28 7.26 7.26 7.24 7.23 7.23 7.22 7.21 7.21 7.20 7.18
6.05 6.05 6.03 6.03 6.01 6.01 5.57 5.57 5.55 5.55 5.53 5.53 5.51 5.51
4.25 3.80 3.80 3.78 3.65 3.62 3.51 3.49 3.47 3.46
H3C CH3
H3C
Si
O
H3C
CH3
OH
OH
3ba
1.79
2.78
1.01
1.00
1.00
1.91
1.09
2.02
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5
f1 (ppm)

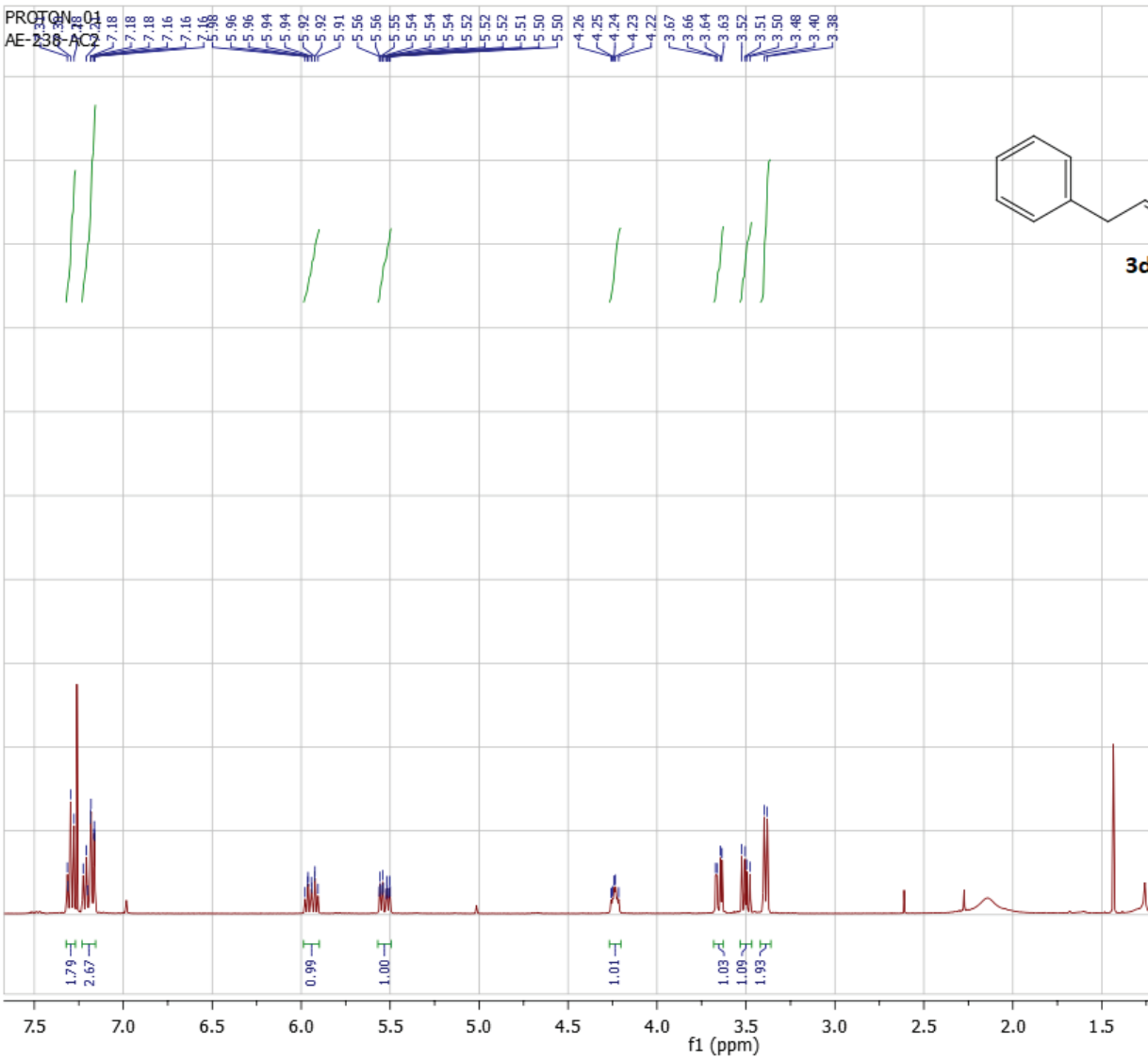

CARBON_01
AE-195-AC2-41-43
141.51
134.03
130.17
128.53
128.25
126.77
73.10
67.25
66.50
51.30
OH
OH
Si
O
3ba
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
f1 (ppm)

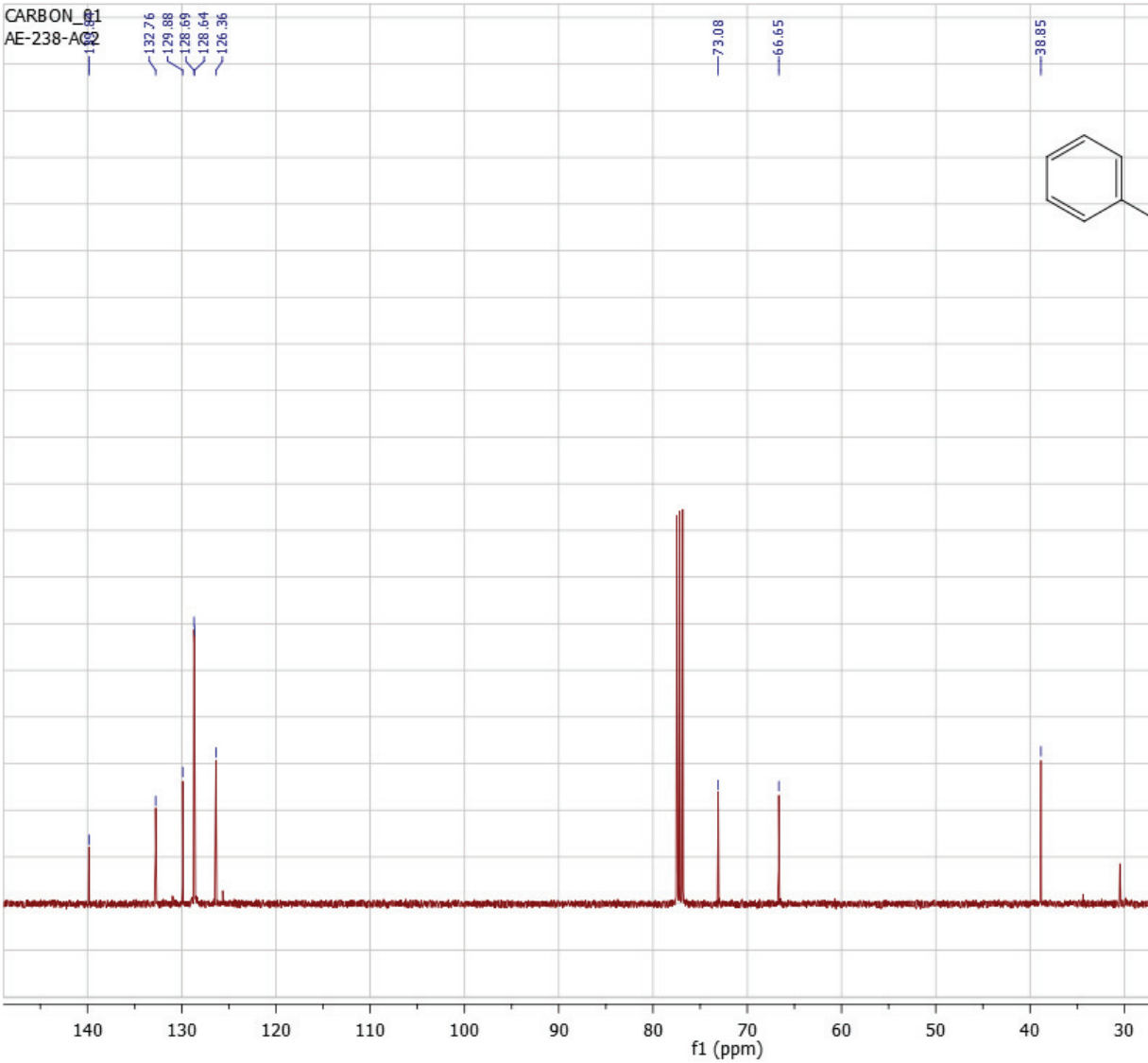

PROTON_01
AE-236-AC-S
7.31
7.29
7.27
7.26
7.26
7.21
7.20
7.19
7.18
7.17
7.17
7.15
7.15
5.93
5.91
5.89
5.87
5.46
5.46
5.44
5.44
5.42
5.42
5.40
5.40
3.59
3.58
3.56
3.55
3.44
3.42
3.42
3.40
3.25
3.23
3.21
3.19
2.63
1.72
1.70
1.68
1.67
OH
OH
CH3
3ca
2.03
2.81
0.99
1.00
0.98
0.95
1.00
1.02
1.80
2.00
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
f1 (ppm)

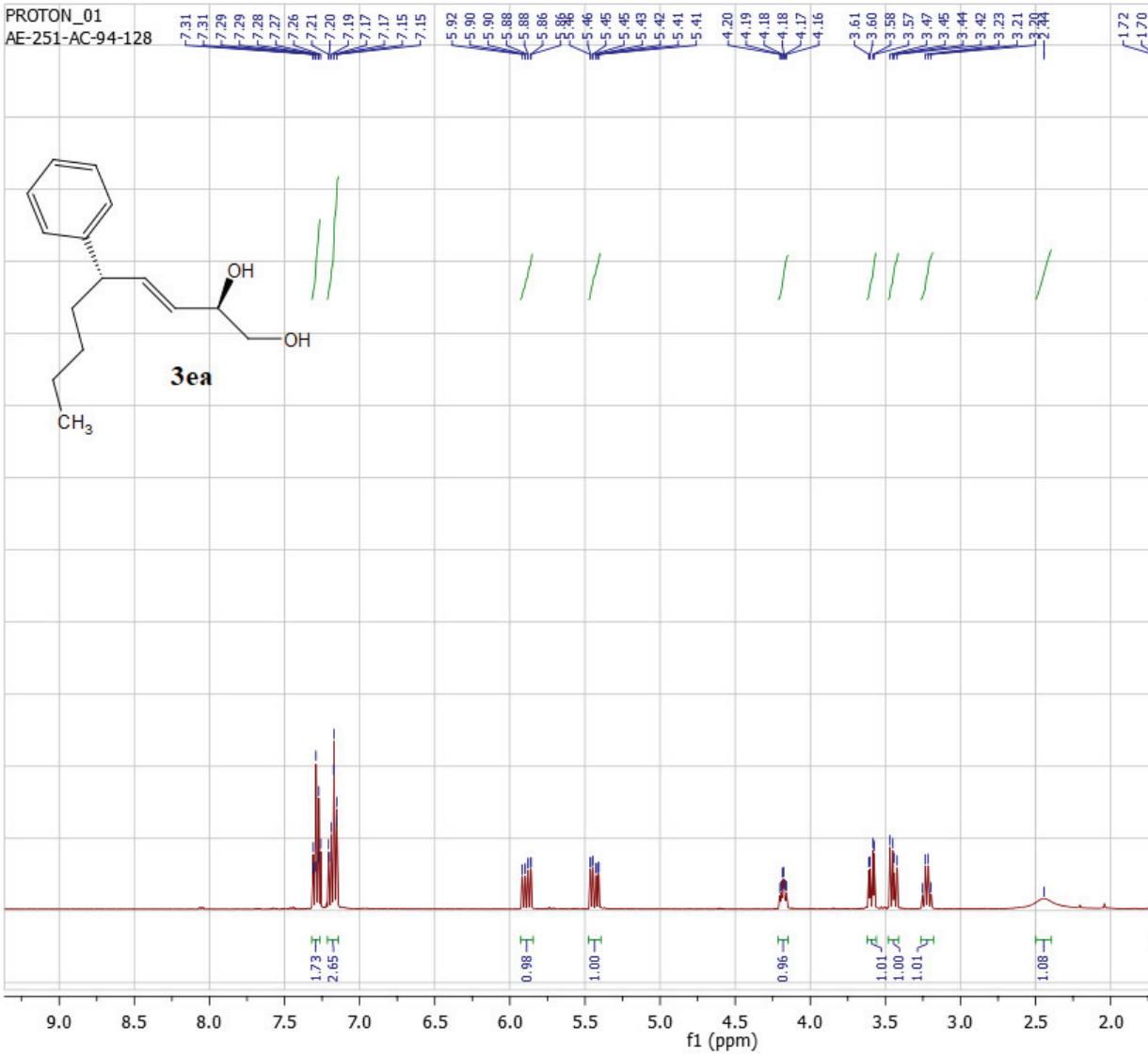

CARBON_01
AE-236-AC-S
CdCl3
144.37
137.54
128.47
127.76
127.54
126.19
73.01
66.51
48.60
35.44
29.71
OH
CH3
3ca
OH
150
140
130
120
110
100
90
80
70
60
50
40
30
f1 (ppm)

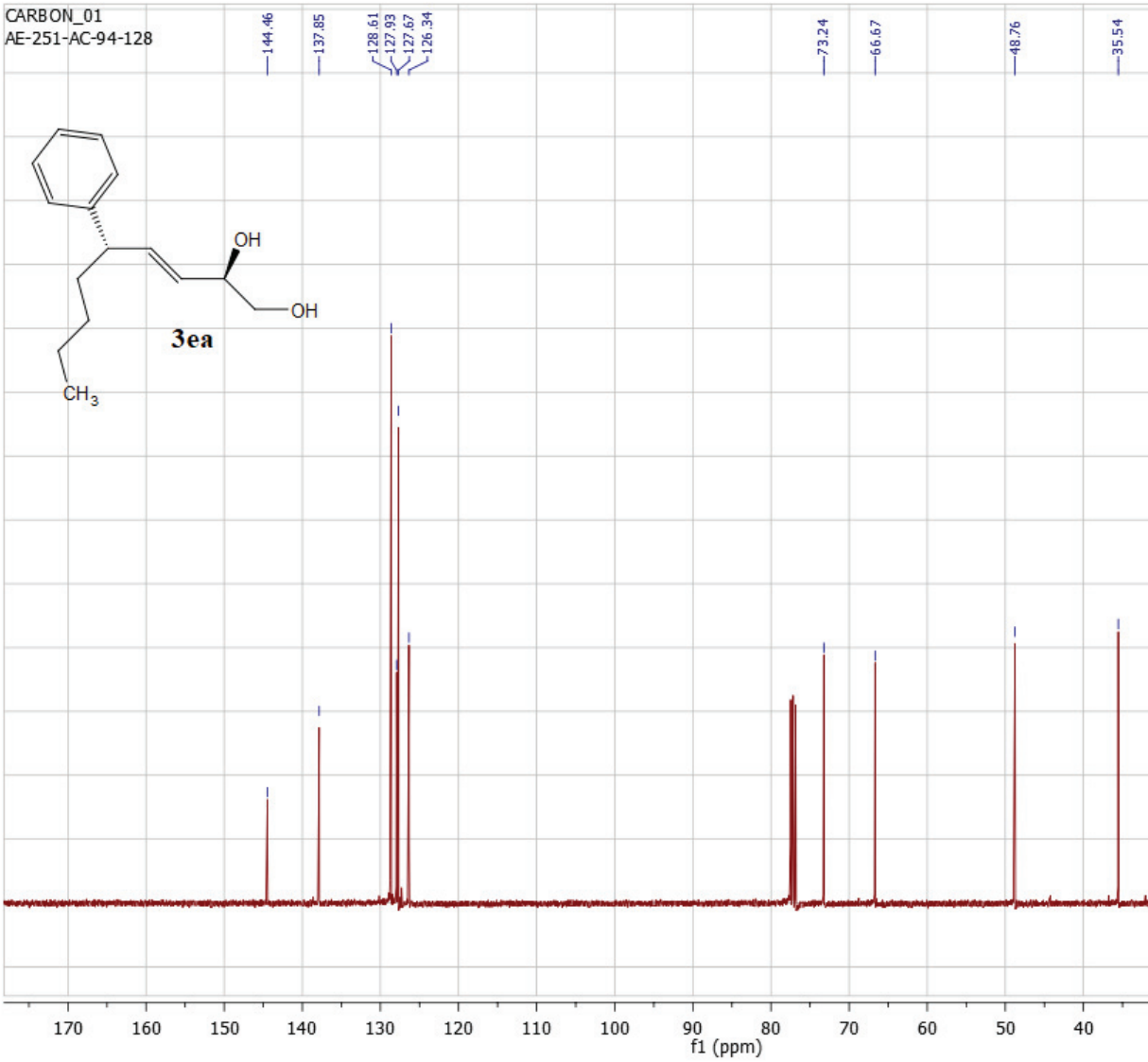

PROTON-01
AE-236-AC-S
C6D6
OH
OH
3ca
CH3
2.67
1.86
1.07
0.97
1.00
0.96
1.10
1.47
1.07
1.98
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
f1 (ppm)

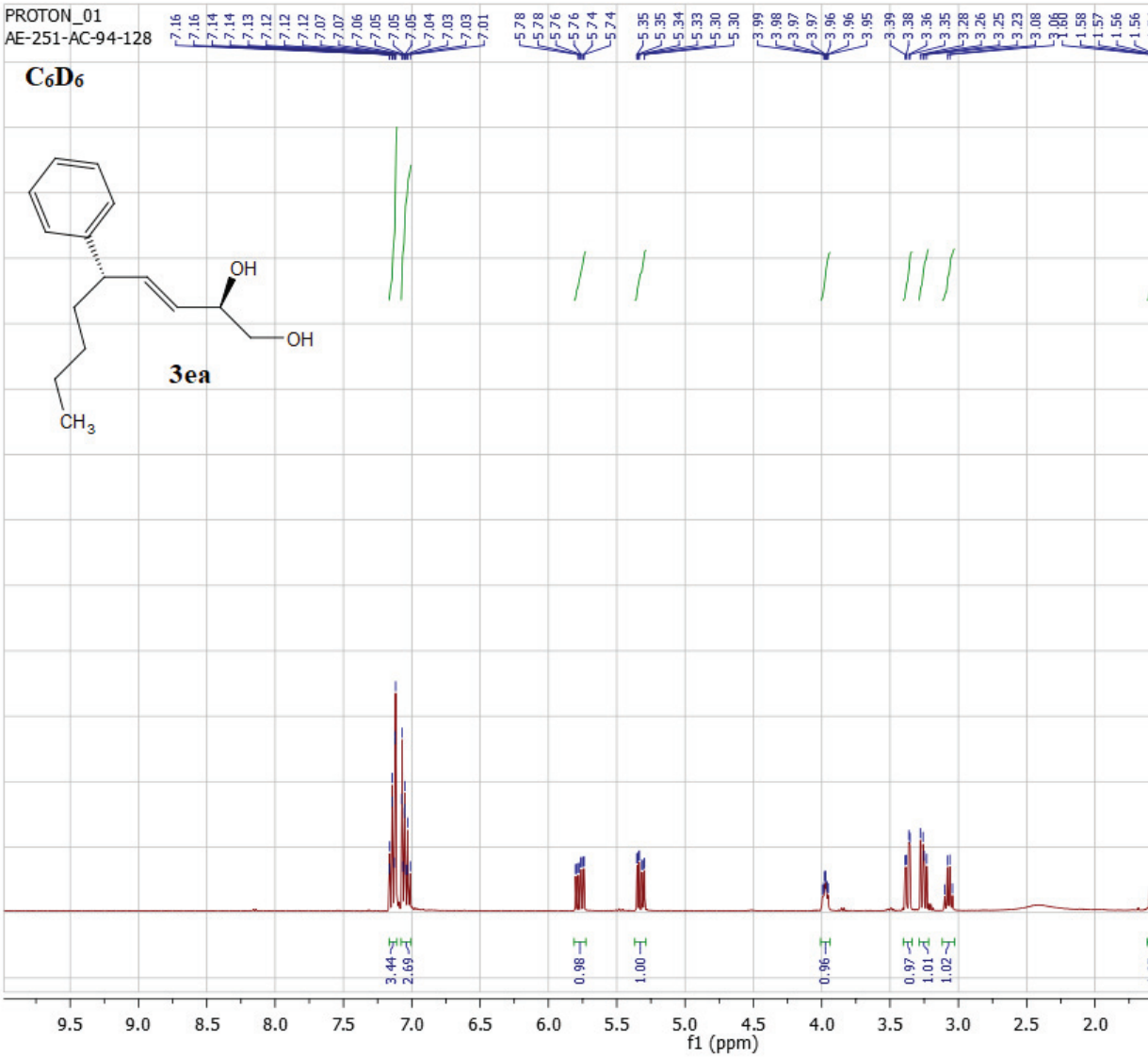

CARBON_01
AE-236-AC-S
145.02
136.88
128.83
128.66
128.03
126.49
73.33
67.05
49.11
36.01
30.14
C6D6
OH
OH
CH3
3ca
150
140
130
120
110
100
90
80
70
60
50
40
30
f1 (ppm)

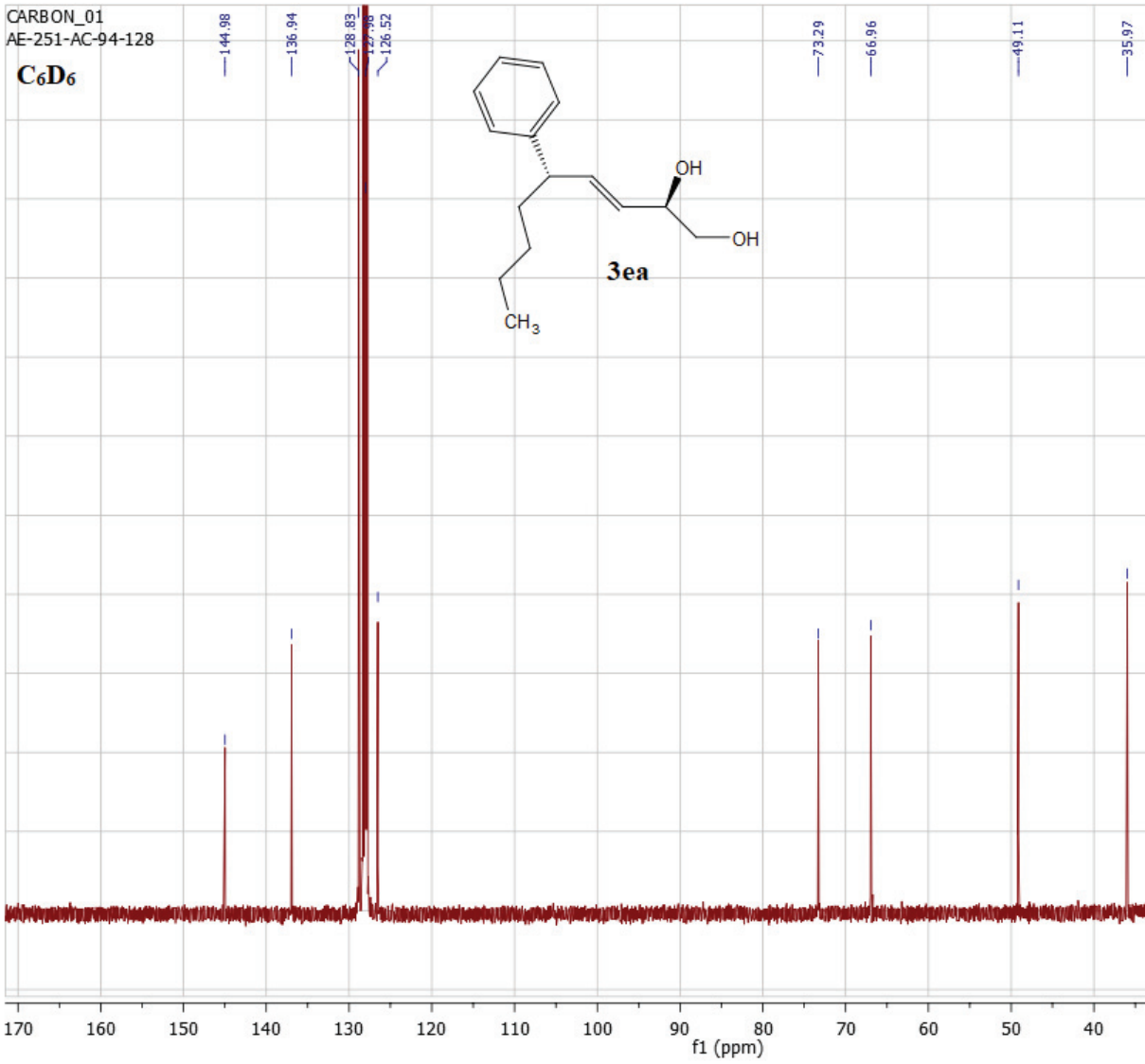

PROTON_01
AE-238-AC2
3d
1.79
2.67
0.99
1.00
1.01
1.03
1.09
1.93
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
f1 (ppm)

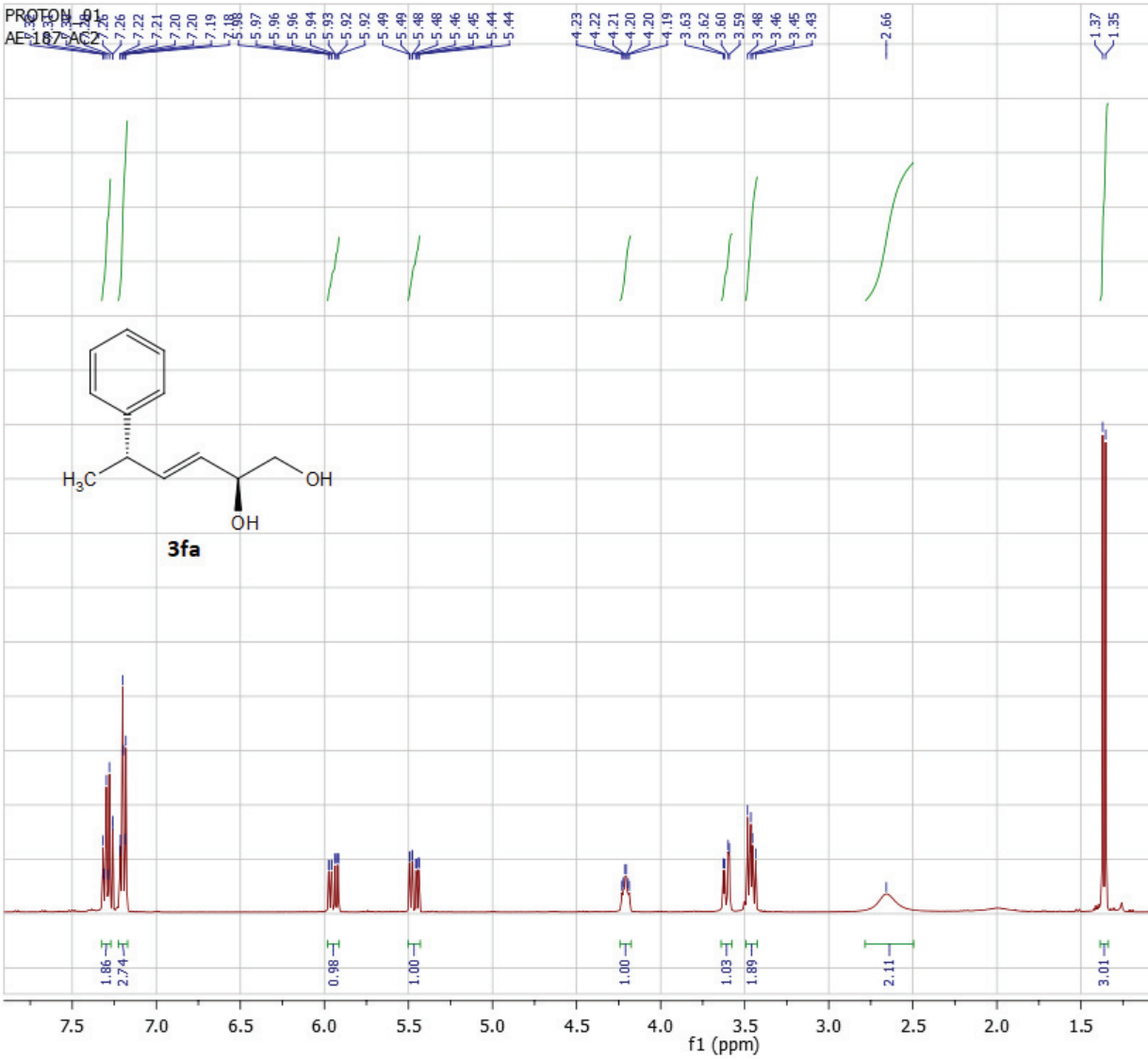

CARBON_01
AE-238-AG2
132.76
129.88
128.69
128.64
126.36
73.08
66.65
38.85
140
130
120
110
100
90
80
70
60
50
40
30
f1 (ppm)

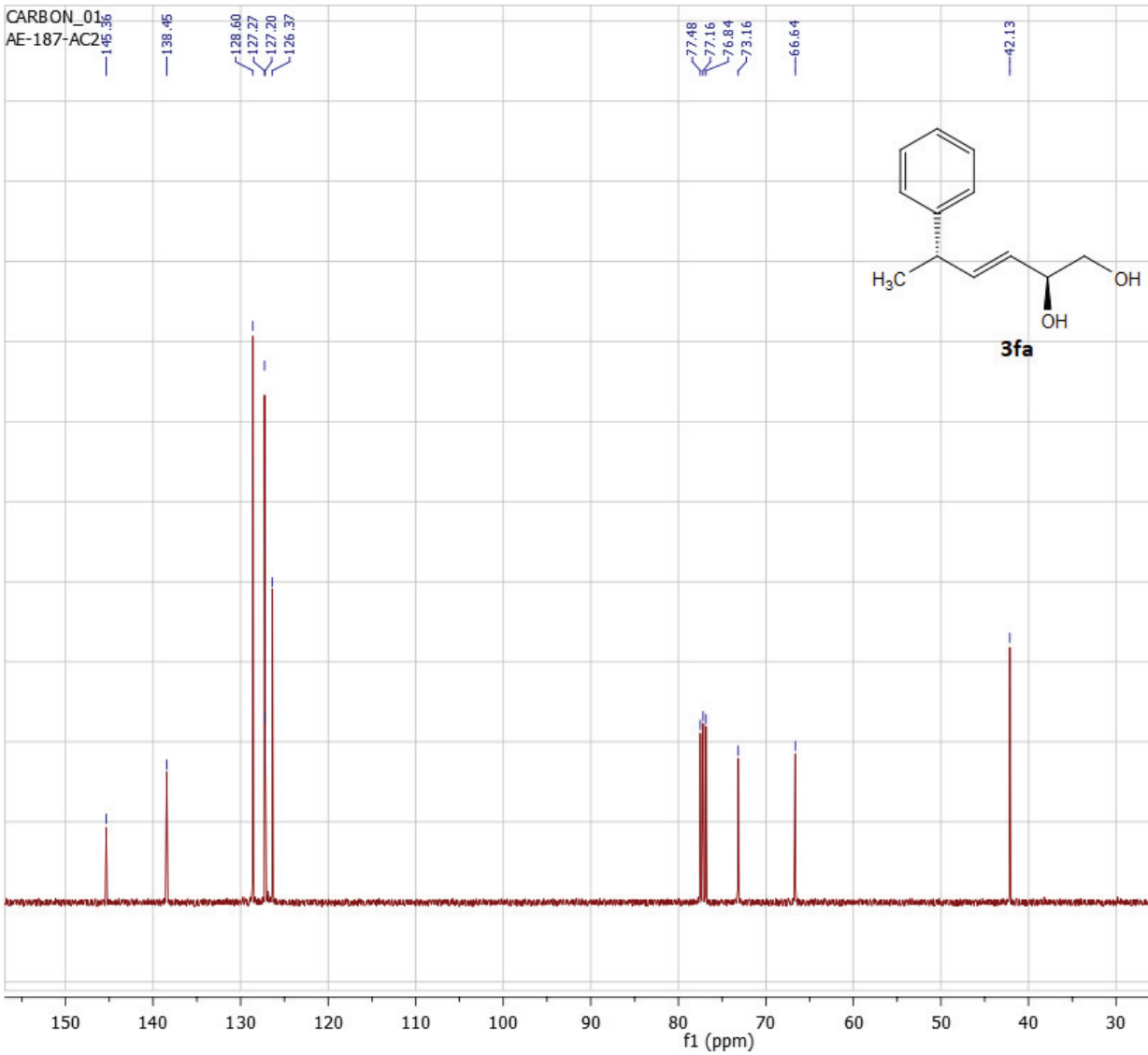

PROTON_01
AE-251-AC-94-128
OH
OH
3ea
CH3
1.73
2.65
0.98
1.00
0.96
1.01
1.00
1.01
1.08
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
f1 (ppm)

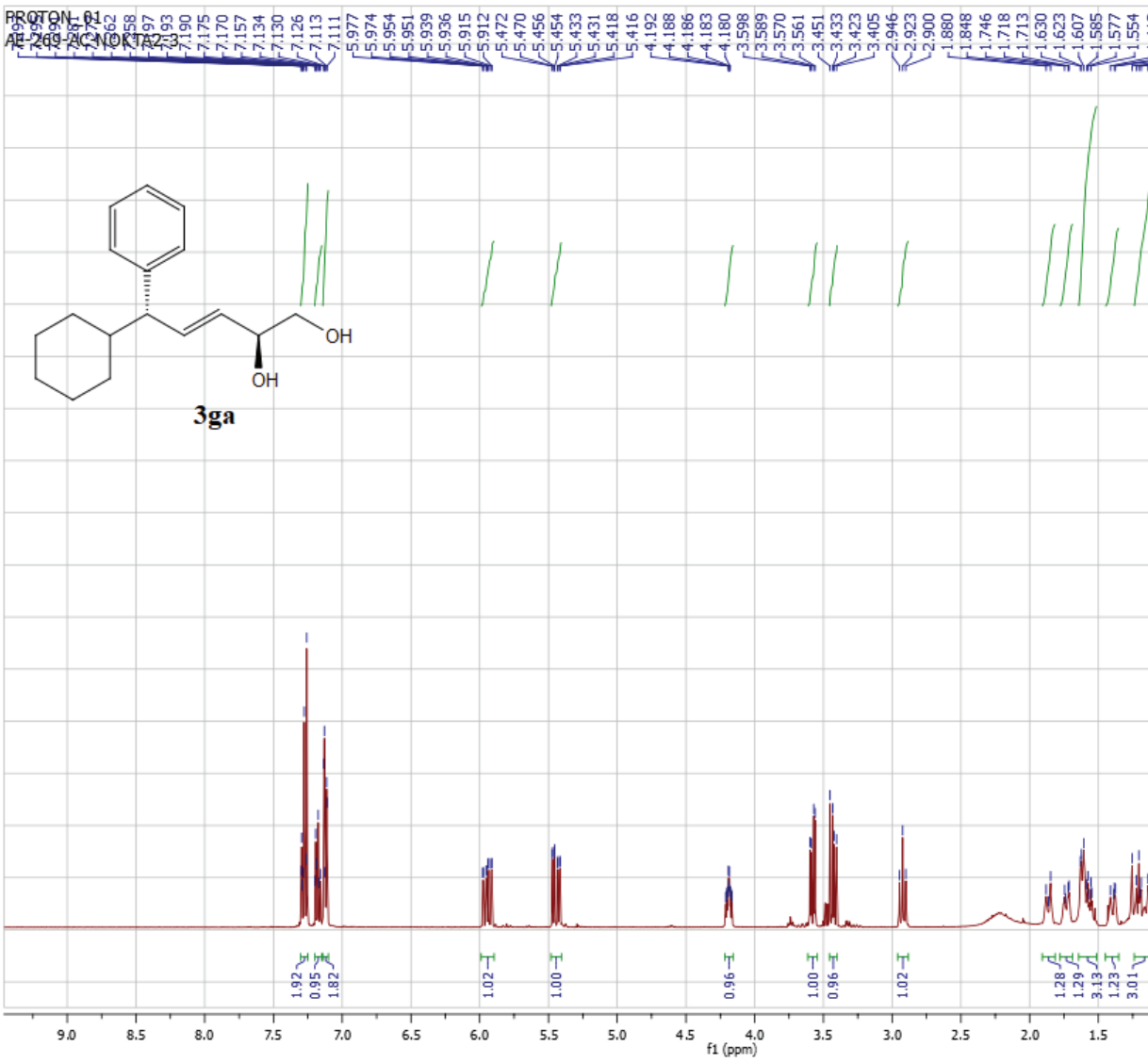

CARBON_01
AE-251-AC-94-128
144.46
137.85
128.61
127.93
127.67
126.34
73.24
66.67
48.76
35.54
OH
OH
3ea
CH3
170
160
150
140
130
120
110
100
90
80
70
60
50
40
f1 (ppm)

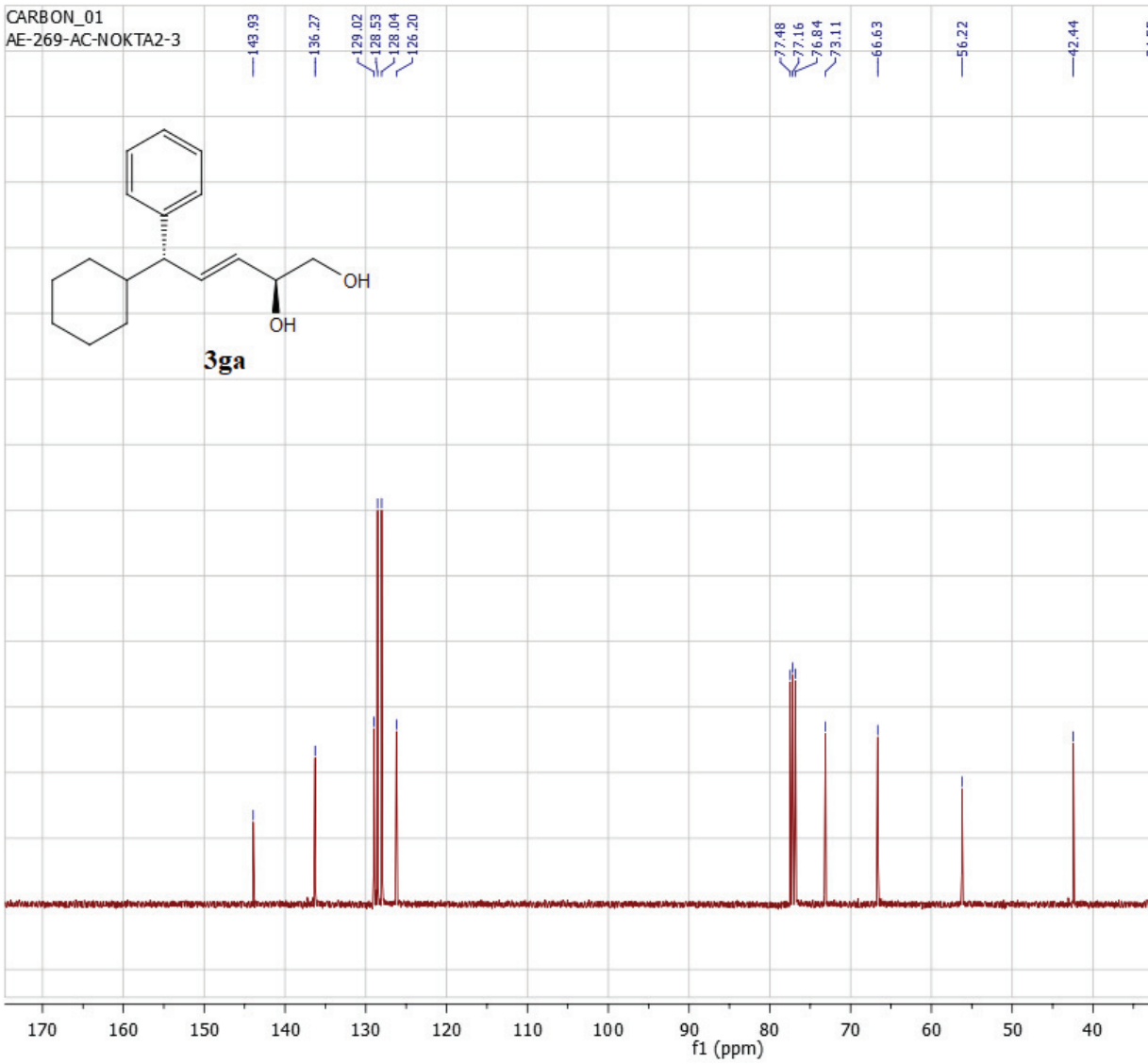

PROTON_01
AE-251-AC-94-128
C6D6
OH
OH
CH3
3ea
3.44
2.69
0.98
1.00
0.96
0.97
1.01
1.02
f1 (ppm)

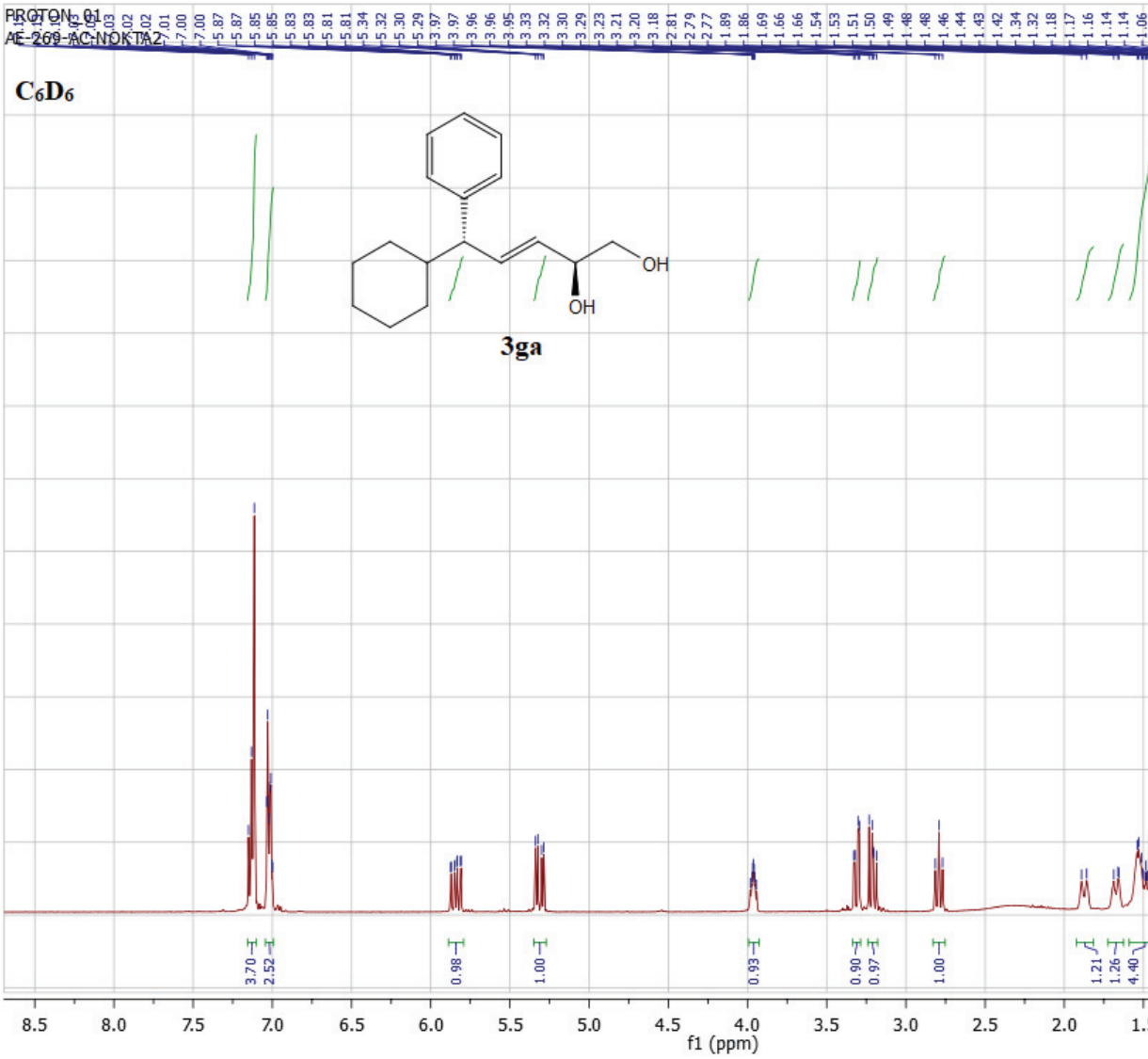

CARBON_01
AE-251-AC-94-128
C6D6
144.98
136.94
128.83
126.52
73.29
66.96
49.11
35.97
OH
OH
CH3
3ea
170
160
150
140
130
120
110
100
90
80
70
60
50
40
f1 (ppm)

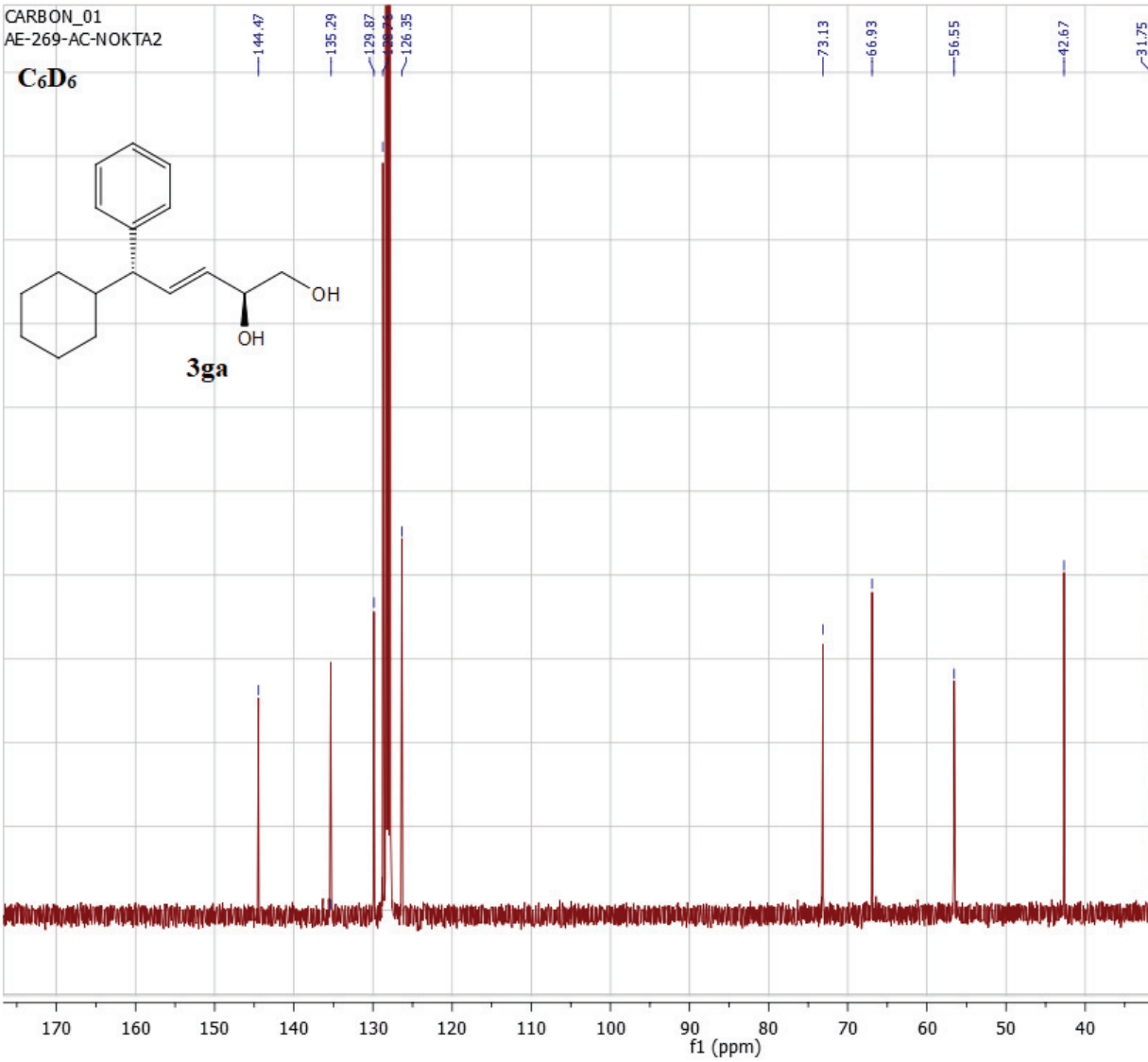

PROTON_01
AE-187-AC2
H3C
OH
OH
3fa
f1 (ppm)

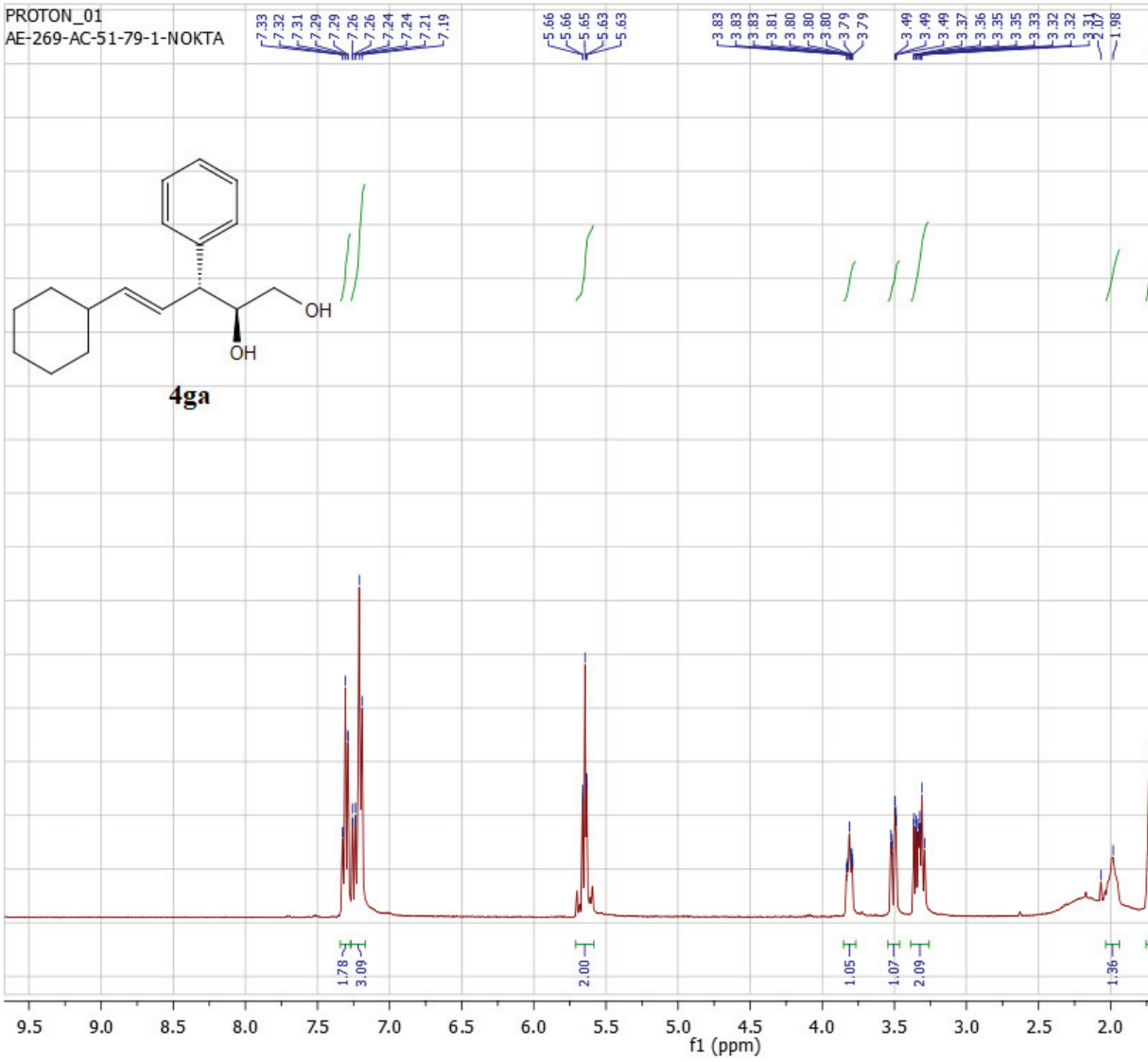

CARBON_01
AE-187-AC2
145.36
138.45
128.60
127.27
127.20
126.37
77.48
77.16
76.84
73.16
66.64
42.13
H3C
OH
OH
3fa
150
140
130
120
110
100
90
80
70
60
50
40
30
f1 (ppm)

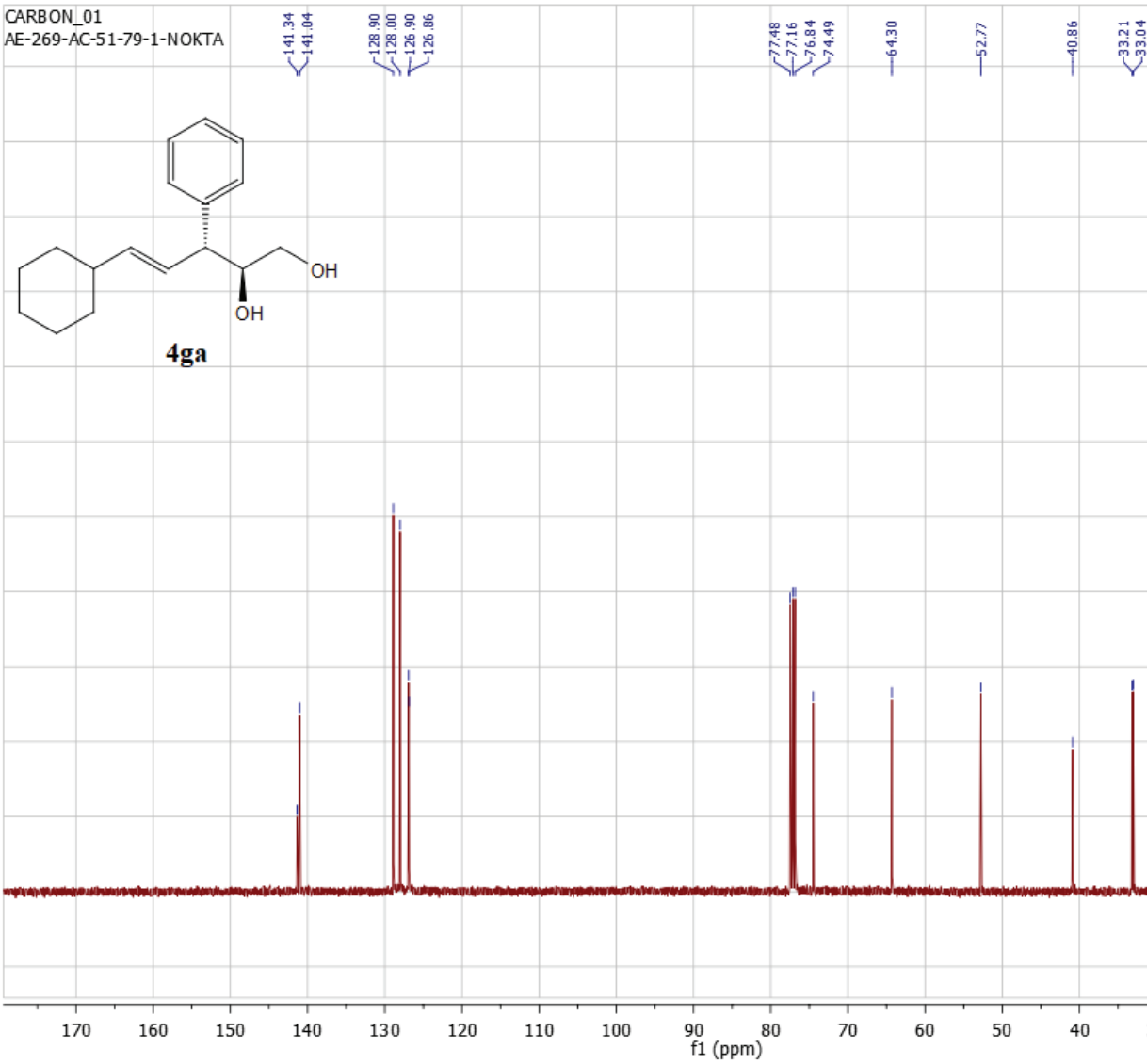

PROTON_01
AE-269-AC-NOKTA2-3
OH
OH
3ga
f1 (ppm)

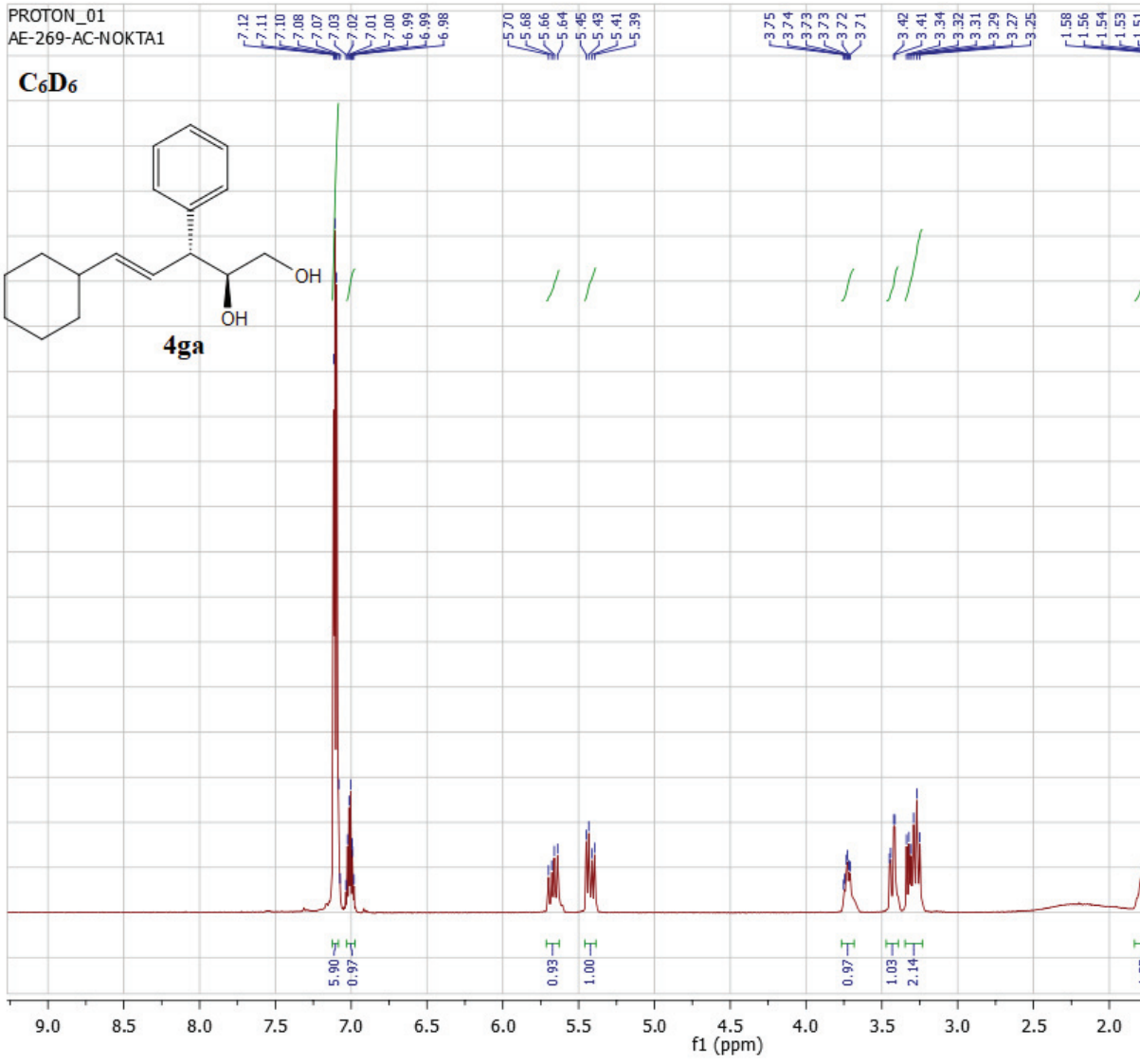

CARBON_01
AE-269-AC-NOKTA2-3
143.93
136.27
129.02
128.53
128.04
126.20
77.48
77.16
76.84
73.11
66.63
56.22
42.44
OH
OH
3ga
170
160
150
140
130
120
110
100
90
80
70
60
50
40
f1 (ppm)

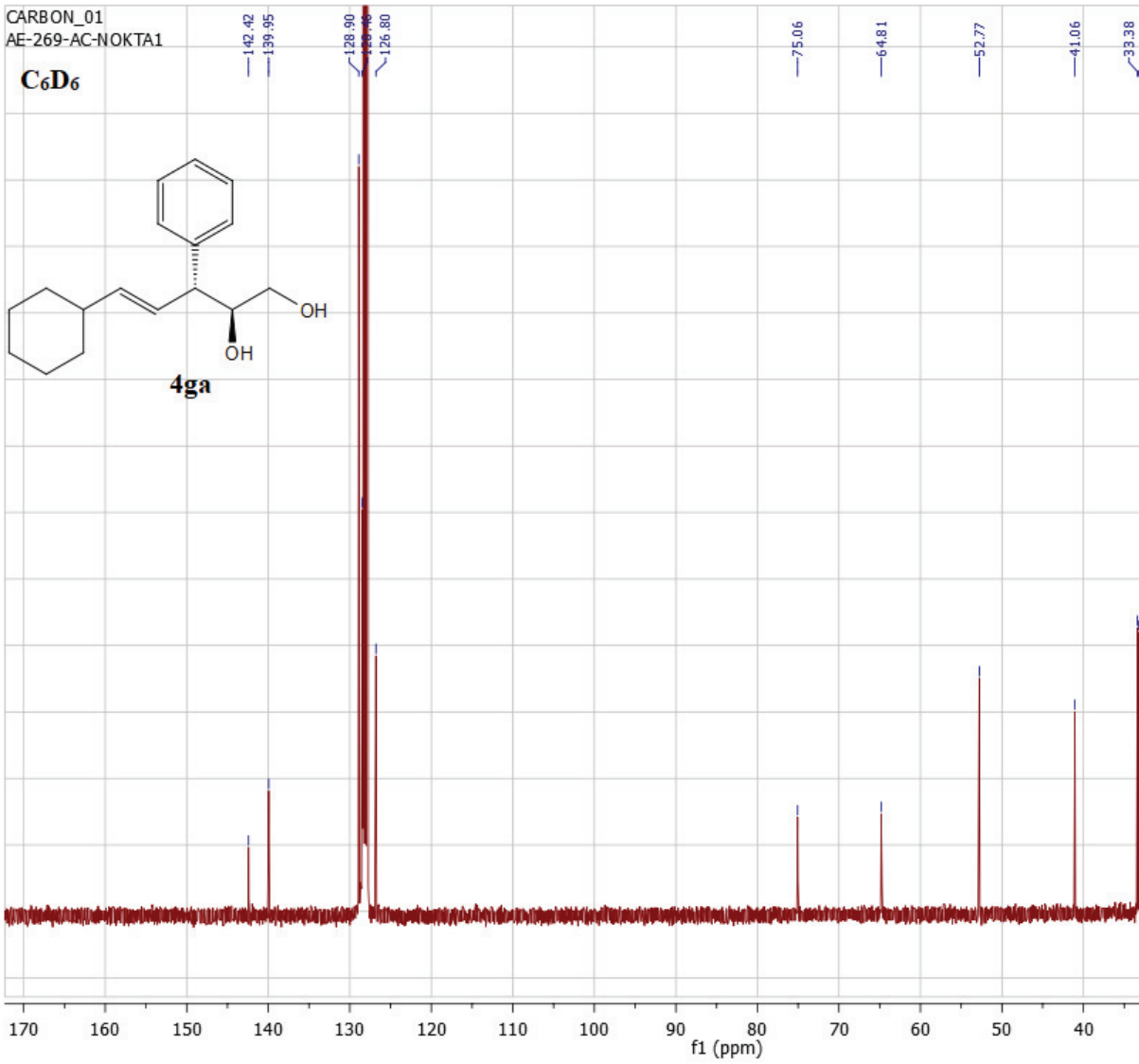

PROTON_01
AE-269-AC-NOKTAZ
C6D6
OH
OH
3ga
3.70
2.52
0.98
1.00
0.93
0.90
0.97
1.00
1.21
1.26
4.40
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
f1 (ppm)


CARBON_01
AE-269-AC-NOKTA2
C6D6
144.47
135.29
129.87
126.35
73.13
66.93
56.55
42.67
OH
OH
3ga
170
160
150
140
130
120
110
100
90
80
70
60
50
40
f1 (ppm)


PROTON_01
AE-269-AC-51-79-1-NOKTA
7.33
7.32
7.31
7.29
7.29
7.26
7.26
7.24
7.24
7.21
7.19
5.66
5.66
5.65
5.63
5.63
3.83
3.83
3.83
3.81
3.80
3.80
3.80
3.79
3.79
3.49
3.49
3.49
3.37
3.36
3.35
3.35
3.33
3.32
3.32
3.31
2.01
1.98
OH
OH
4ga
1.78
3.09
2.00
1.05
1.07
2.09
1.36
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
f1 (ppm)

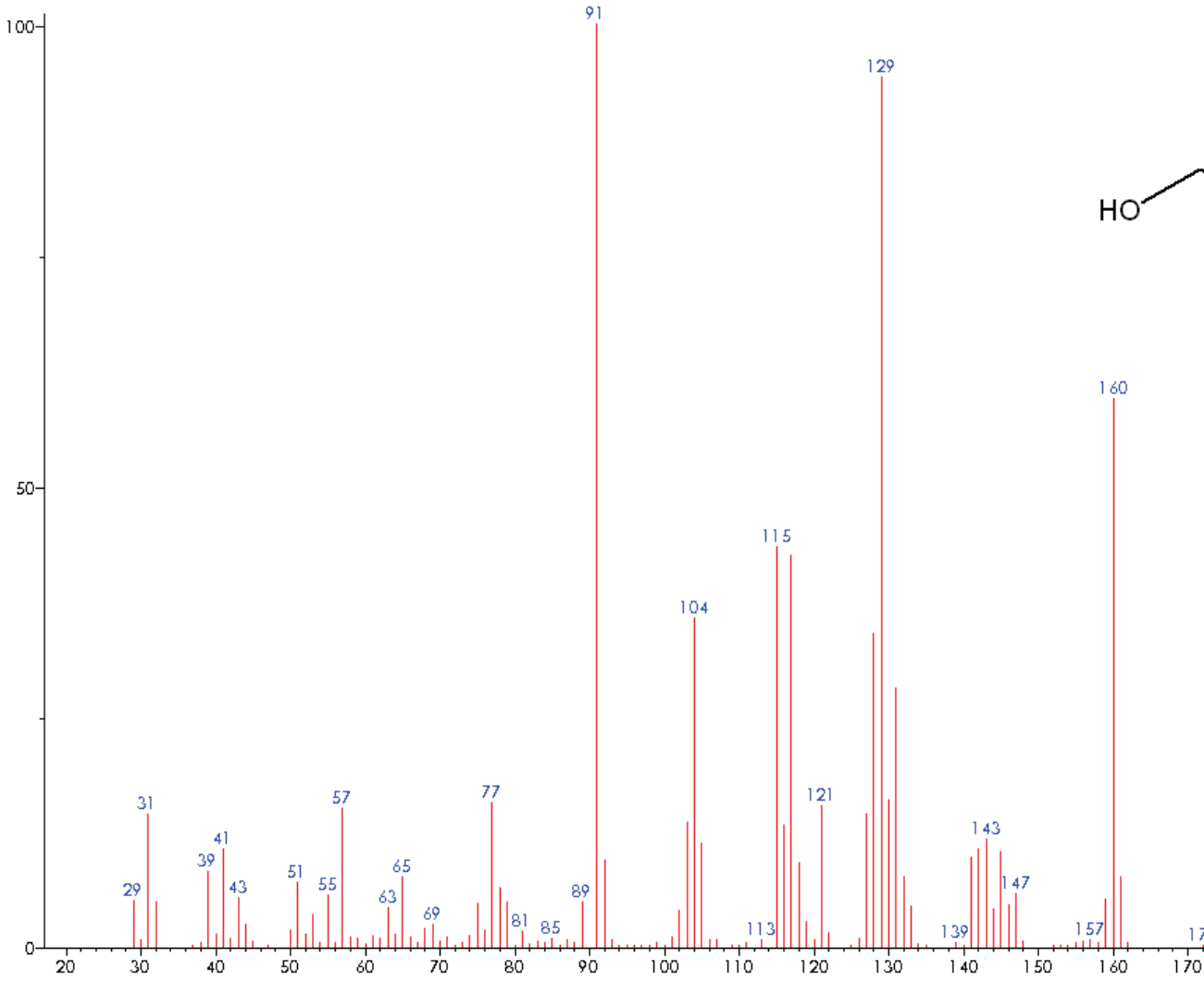

CARBON_01
AE-269-AC-51-79-1-NOKTA
141.34
141.04
128.90
128.00
126.90
126.86
77.48
77.16
76.84
74.49
64.30
52.77
40.86
33.21
33.04
OH
OH
4ga
170
160
150
140
130
120
110
100
90
80
70
60
50
40
f1 (ppm)

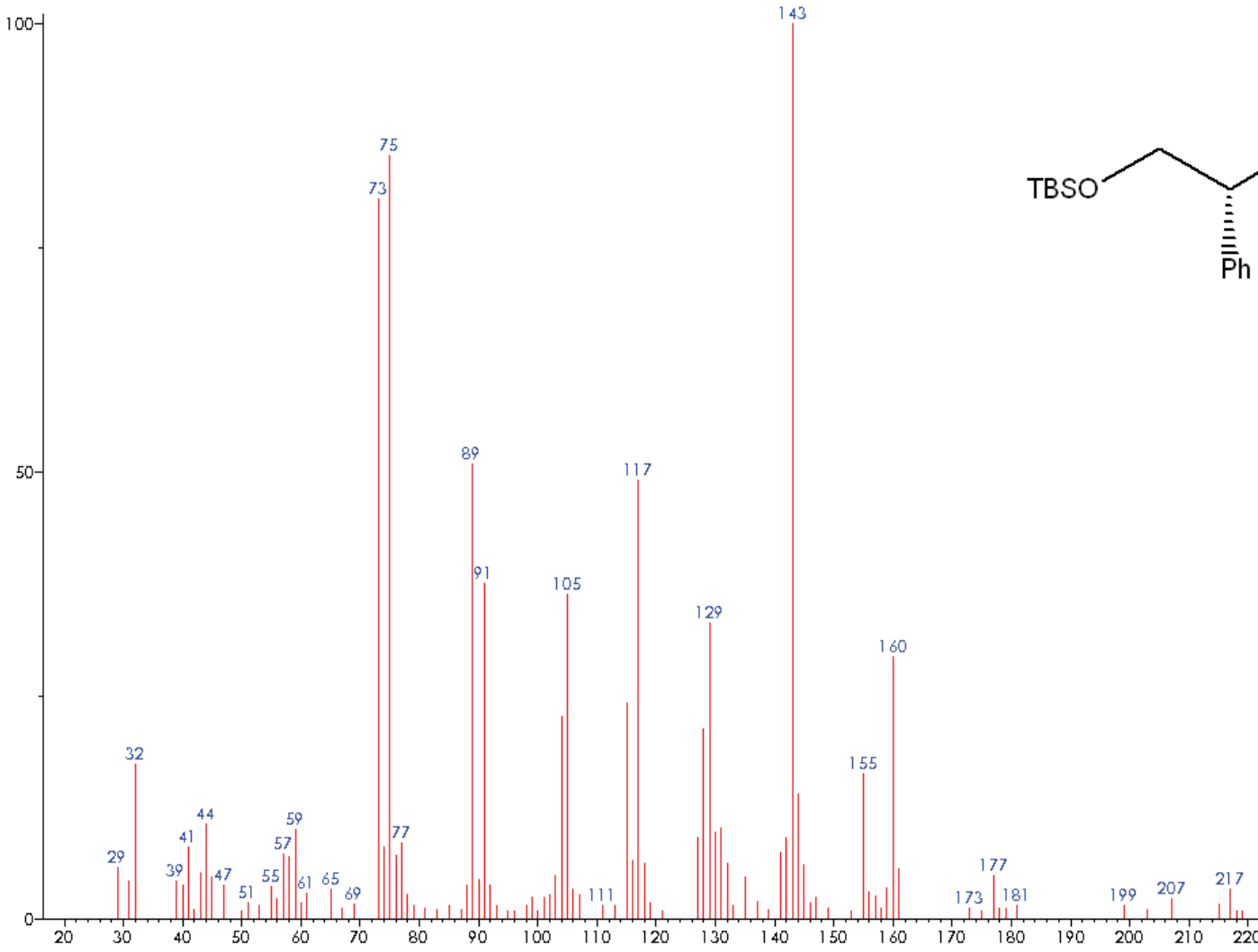

PROTON_01
AE-269-AC-NOKTA1
C6D6
OH
OH
4ga
f1 (ppm)


CARBON_01
AE-269-AC-NOKTA1
C6D6
142.42
139.95
128.90
126.80
75.06
64.81
52.77
41.06
33.38
OH
OH
4ga
170
160
150
140
130
120
110
100
90
80
70
60
50
40
f1 (ppm)

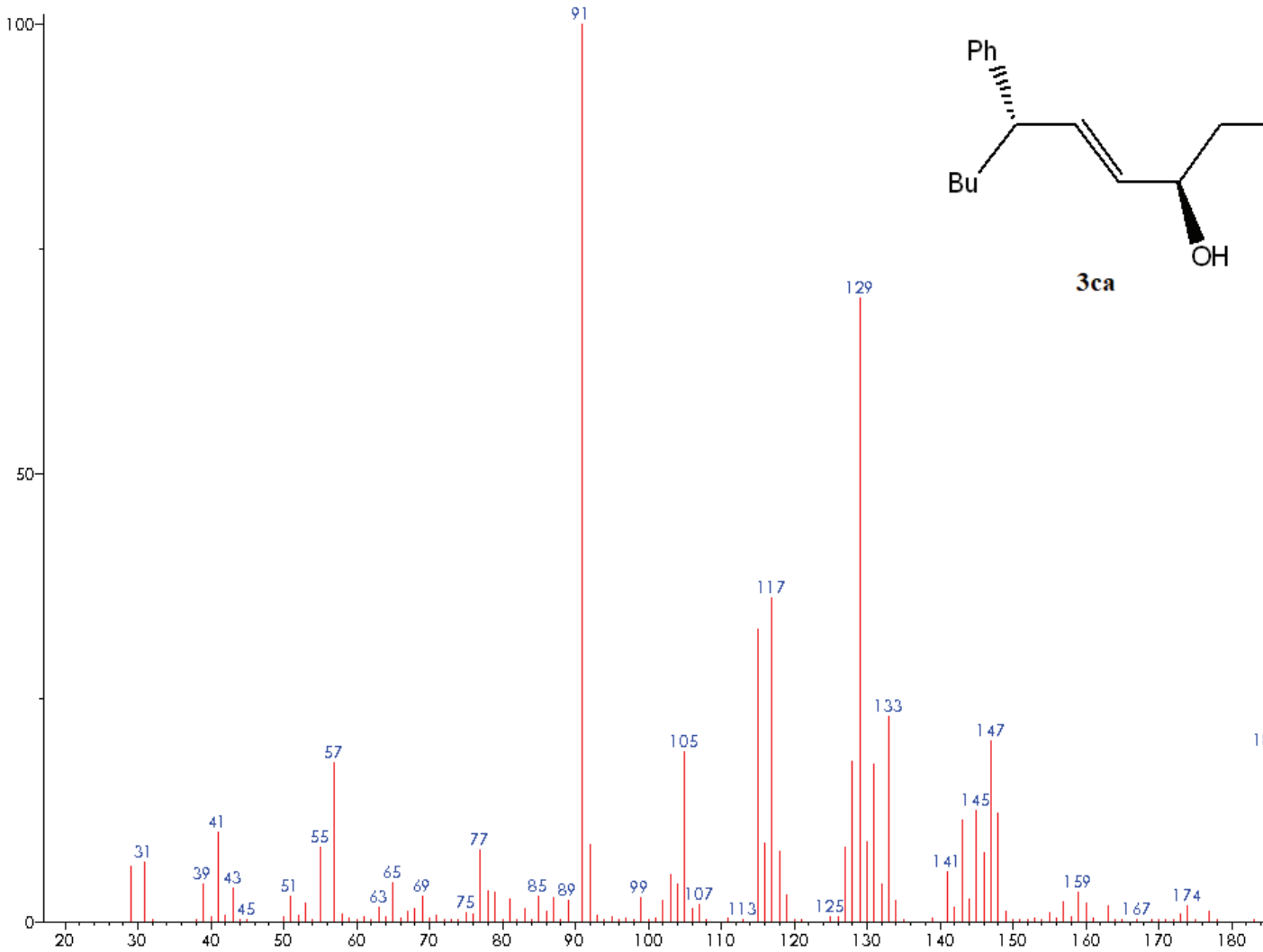
APPENDIX C

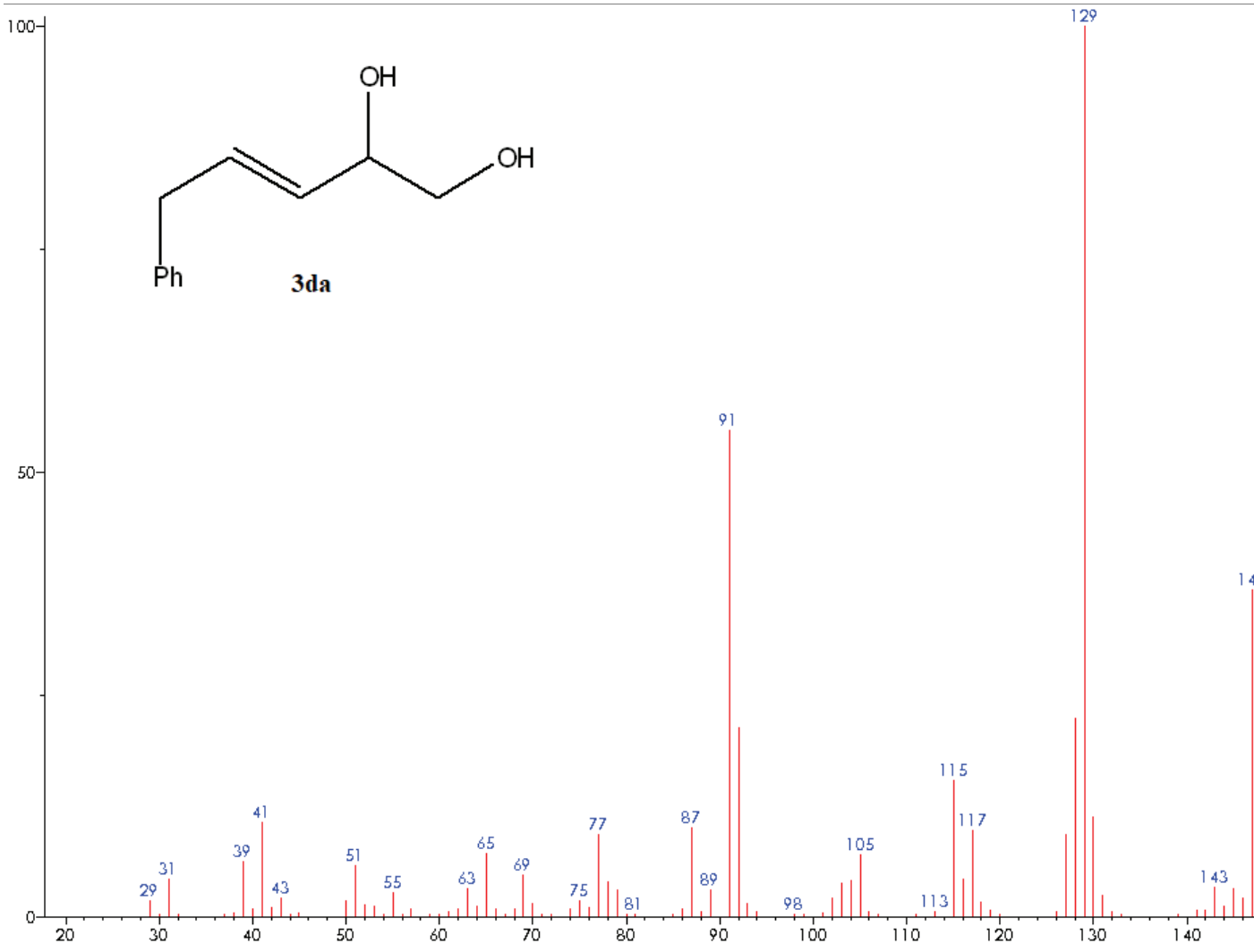
MASS SPECTRUMS OF PRODUCTS

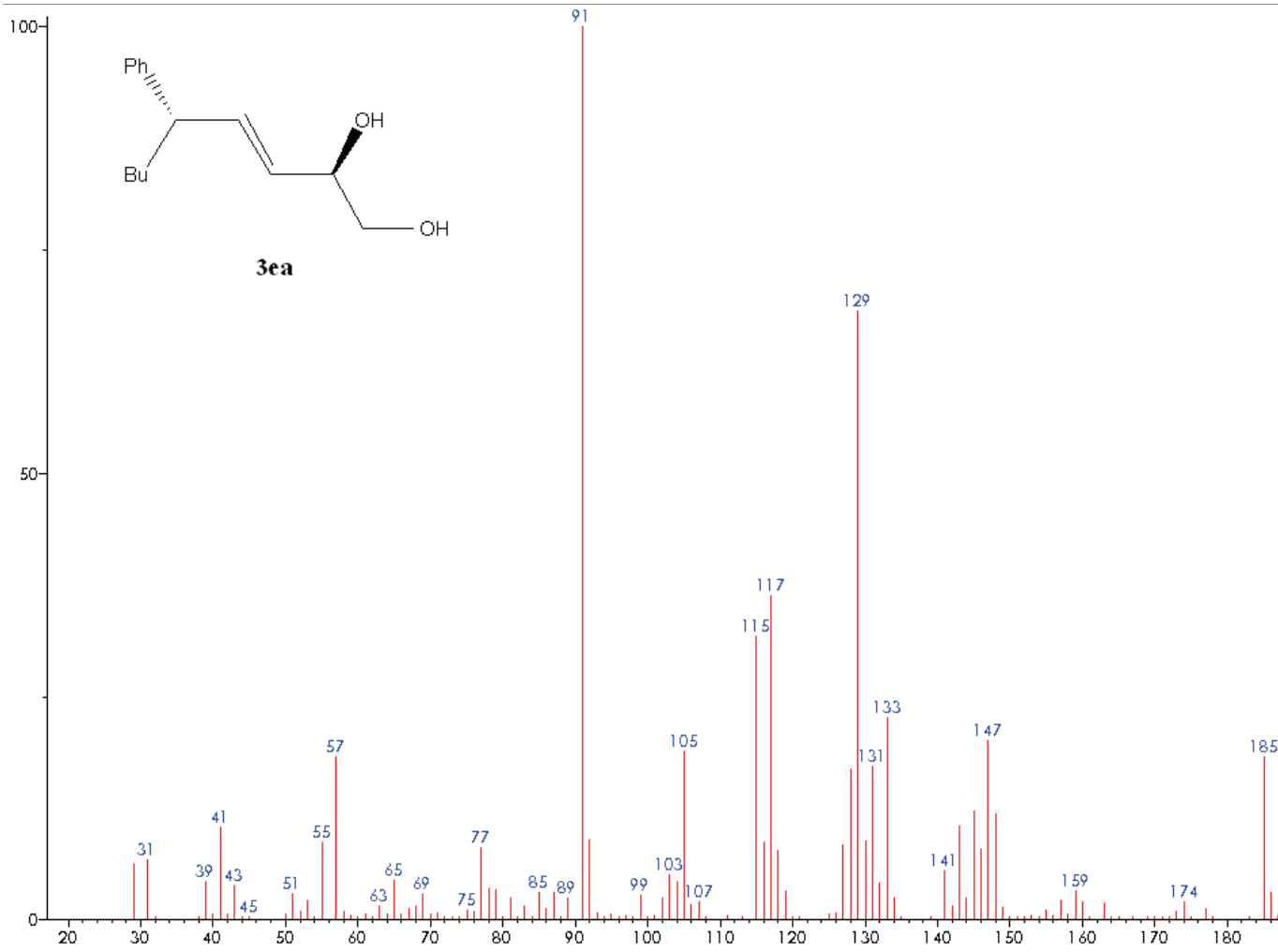

100
50
0
91
129
160
115
104
121
143
147
77
57
31
41
39
43
51
55
63
65
69
81
85
89
113
139
157
29
20
30
40
50
60
70
80
90
100
110
120
130
140
150
160
170
HO

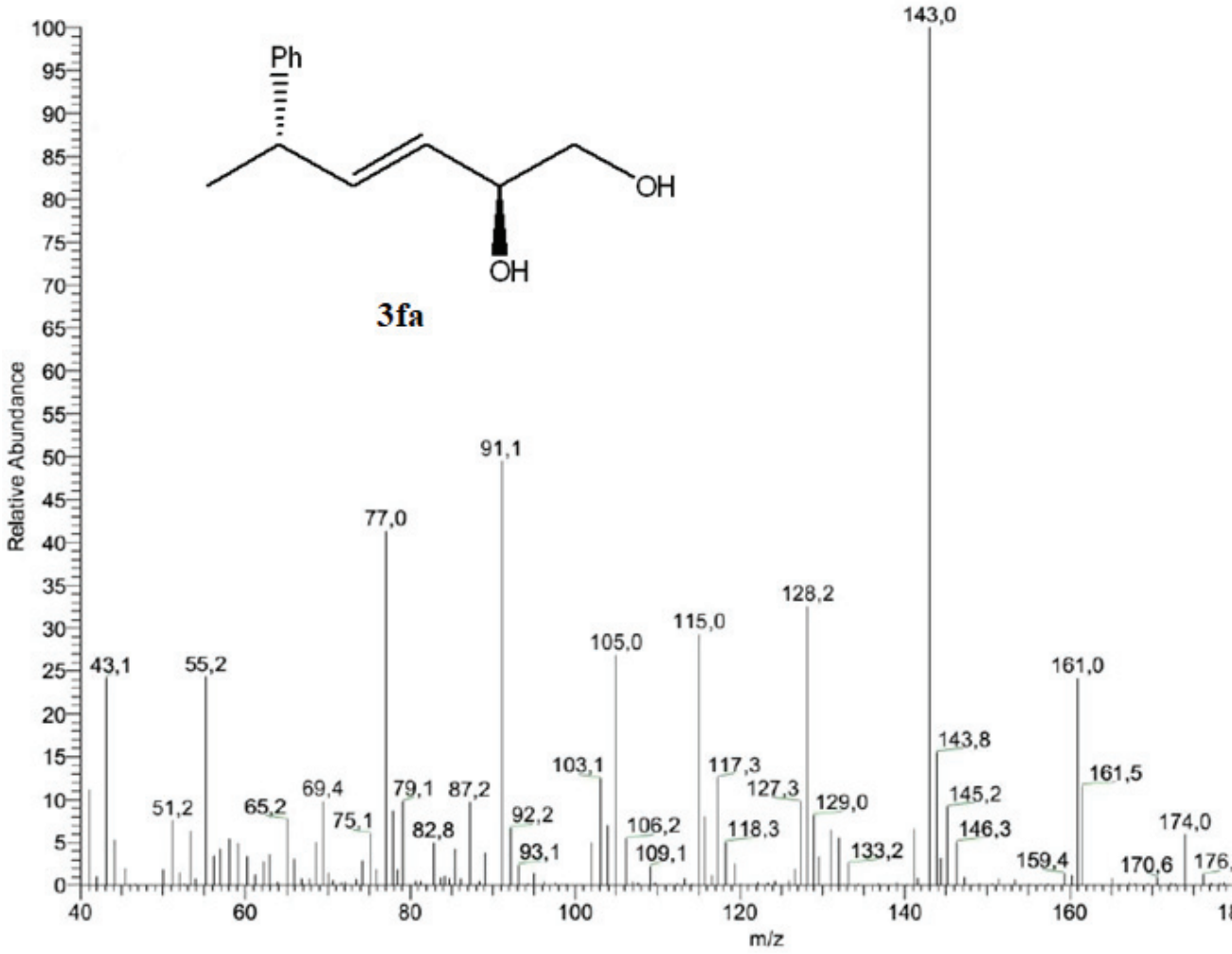

100
50
0
143
75
73
89
91
117
105
129
160
155
32
29
39
41
44
47
51
55
57
59
61
65
69
77
111
173
177
181
199
207
217
20
30
40
50
60
70
80
90
100
110
120
130
140
150
160
170
180
190
200
210
220
TBSO
Ph

88


Ph
Bu
OH
3ca
100
50
0
91
129
117
133
147
105
57
145
41
31
55
77
39
43
65
69
85
89
99
107
113
125
141
159
167
174
51
63
75
20
30
40
50
60
70
80
90
100
110
120
130
140
150
160
170
180


OH
OH
Ph
3da
100
50
0
20
30
40
50
60
70
80
90
100
110
120
130
140
29
31
39
41
43
51
55
63
65
69
75
77
81
87
89
91
98
105
113
115
117
129
143


Ph
Bu
OH
OH
3ea
100
50
0
20
30
40
50
60
70
80
90
100
110
120
130
140
150
160
170
180
91
129
117
115
133
147
105
57
131
185
41
55
77
31
39
43
65
69
51
63
75
85
89
99
103
107
141
159
174


Ph
OH
OH
3fa
Relative Abundance
m/z
143,0
91,1
77,0
128,2
115,0
105,0
43,1
55,2
161,0
143,8
103,1
117,3
161,5
127,3
145,2
69,4
79,1
87,2
129,0
51,2
65,2
75,1
92,2
106,2
146,3
174,0
82,8
118,3
93,1
109,1
133,2
159,4
170,6