TRANSITION METAL CATALYZED 1,5-SUBSTITUTION REACTIONS OF CONJUGATED ENYNE OXIRANES LEADING TO ALLYLIC HYDROXY SUBSTITUTED VINYLALLENES

A Thesis Submitted to
the Graduate School of Engineering and Sciences of
İzmir Institute of Technology
in Partial Fulfillment of the Requirements for the Degree of

DOCTOR OF PHILOSOPHY

in Chemistry

by
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August 2015
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ACKNOWLEDGEMENTS

ABSTRACT

TRANSITION METAL CATALYZED 1,5-SUBSTITUTION REACTIONS OF CONJUGATED ENYNE OXIRANES LEADING TO ALLYLIC HYDROXY SUBSTITUTED VINYLALLENES

Transition metal-catalyzed reactions are atom economical and environmentally benign processes, which make them superior to traditional stoichiometric reactions. Transition metal-catalyzed carbonylation reactions of unsaturated systems has become an important methodology for the synthesis of carbonyl containing synthetically valuable compounds.

One of these types of reactions is the alkoxycarbonylation of unsaturated systems over transition metals in the presence of alcohol and under CO atmosphere (Scrivanti, *et. al*. 1998).

Pionering works on palladium-catalyzed alkoxycarbonylation of allylic and propargylic systems with a leaving group at an apropriate positions leading to *β,γ*-unsaturated and allene esters, respectively have been established by several research groups (Tsuji, *et al.* 2004).

Recently, Artok and co-workers developed new methods for the construction of functionalized vinylallene esters via palladium-catalyzed alkoxycarbonylation of 2,4-enyne carbonates (Akpınar, *et al*. 2011). After tuning the reaction conditions precisely, the methodology could be improved to allow a high degree of center-to-axial chirality transfer (Karagöz, *et al.* 2014).

Within the context of this study, palladium-catalyzed alkoxycarbonylative 1,5-substitution of conjugated enyne oxiranes was also found to provide a diastereoselective route to (*E*)-configured 7-hydroxy-2,3,5-trienoates. The reactions proceeded in a highly stereoselective manner, possibly through sequential formation of π-allylpalladium and σ-vinylallenyl palladium complexes. The major diastereomeric form of the product was determined by the configuration of the alkenyl moiety of the substrate.

ÖZET

ALLİLİK HİDROKSİ SÜBSTİTÜE VİNİLALLENLERİN OLUŞUMUNA NEDEN OLAN GEÇİŞ METAL KATALİZLİ KONJUGE ENİNOKSİRANLARIN 1,5-SÜBSTİTÜSYON TEPKİMELERİ

Geçiş metal katalizli reaksiyon yöntemleri atom-ekonomik ve çevre dostu olmalarından dolayı klasik stokiyometrik reaksiyon yöntemlerine kıyasla gün geçtikçe daha önemli hale gelmektedirler. Doymamış sistemlerin geçiş metal katalizli karbonilasyon tepkimeleri nitelikli kimyasalların sentezinde sıklıkla kullanılan bir metot haline gelmiştir. Bu bağlamda gerçekleştirilen tepkimelerin bir alt dalı olan alkoksikarbonilasyon tepkimeleri ise karbonil grubu içeren doymamış sistemlerin sentezine, bir metal katalizörü eşliğinde, alkol ve CO gazı altında olanak sağlar (Scrivanti, *et. al*. 1998).

Propargilik ve allilik pozisyonlarında bir ayrılan grup taşıyan yapıların alkoksikarbonilasyon tepkimeleri ile sırasıyla β,γ-doymamış ve allen ester oluşturan çalışmaları git gide önem kazanmış ve çeşitli araştırma grupları tarafından başarıyla gerçekleştirilmiştir (Tsuji, *et al.* 2004).

Yakın bir süre önce çalışma grubumuz tarafından 2,4-enin karbonat yapılarının paladyum-katalizli alkoksikarbonilasyon tepkimeleri başarıyla gerçekleştirilmiş ve fonksiyonlandırılmış vinilallen ester içeren yapılar yüksek verimler ile elde edilmiştir (Akpınar, *et al*. 2011). Daha sonra titizlik ile yapılan optimizasyon çalışmaları ile metod daha da geliştirilmiş ve enantiyomerik olarak zenginleştirilmiş 2,4-enin karbonat yapılarına uygulandığında metodun merkezden eksene kiralite transferine olanak sağladığı saptanmıştır (Karagöz, *et al.* 2014).

Bu çalışma kapsamında, 2,4-enin oksiran yapılarının alkoksikarbonilasyon tepkimeleri araştırılmıştır. Geliştirilen metod yüksek verim ve diastereo seçimlilik ile (*E*)-konfigürasyonuna sahip 7-hidroksi-2,3,5-trienoat yapılarının sentezine olanak sağlamıştır.

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ABBREVIATIONS

		etc.	and other things	
Ac	Acetate	equiv.	Equivalent	
aq.	Aqueous	g	Grams	
Ar	Aryl	h.	Hour(s)	
Bu	Butyl	*i*-Pr	*Iso*-propyl	
BINAP	2,2′-bis(diphenylphosphino)-1,1′-binaphthalene	M	Molar	
		m	Meta	
BIPHEP	2,2'-bis(diphenylphosphino)-1,1'-biphenyl	*m*-CPBA acid	*meta*-Chloroperbenzoic	
		Me	Methyl	
Bn	Benzyl	mg	Milligrams	
Cy	Cyclohexyl	min.	Minutes	
dba	Dibenzylideneacetone	mL	Milliliters	
DCM	Dichloromethane	μm	Micrometer	
DIBALH hydride	Diisobutylaluminum	*o*	Ortho	
		p	Para	
DMAP	4-Dimethylaminopyridine	Ph	Phenyl	
DMF	*N,N*-Dimethylformamide	*p*-Ts	*para*-Toluenesulfonyl	
dppb	1,4-Bis(diphenylphosphino)butane	RT	Room temperature	
dppe	1,2-Bis(diphenylphosphino)ethane	t	Time	
dppf	1,1′-Bis(diphenylphosphino)ferrocene	*t*-Bu	Tertiary butyl	
		TBDMS	Tertiary butyldimethylsilyl chloride	
dpph	1,6-Bis(diphenylphosphino)hexane	THF	Tetrahydrofurane	
		Ts	Tosyl	
DPEphos	Bis[(2-diphenylphosphino)phenyl] ether	Xantphos	4,5-Bis(diphenylphosphino)-9,9-dimethylxanthene	
d.r.	Diastereomeric ratio			
Et	Ethyl			

CHAPTER 1

INTRODUCTION

Allenes are of an important class of organic compounds, which are characterized by two cumulated carbon–carbon double bonds. Biological activity, axially chiral backbone and their presence in many natural products make the allenes crucial materials for organic synthesis.

After the pioneering works in the area of carbonylation type reactions by Roelen and Reppe in 1939 and 1953, respectively, transition metal-catalyzed carbonylation reactions involving the use of carbon monoxide as a reactant have became popular method for building carbonyl containing molecules.

After the first palladium-catalyzed carbonylation reaction of propargylic compounds, bearing a leaving group, reported in 1966 (Tsuji, *et al*. 1995), the palladium-catalyzed alkoxycarbonylation reaction of propargylic derivatives under mild conditions has become an important method for the synthesis of functionalized allene derivatives.

Vinyl-substituted allenes are reactive compounds toward various cycloaddition and cyclization reactions. They exhibit particularly a higher activity and selectivity with Diels-Alder reactions, because their configurational equilibrium is more on the side of s-*cis* conformer—a prerequisite for a [4+2] cycloaddition reaction to occur effectively—than for 1, 3-dienes (Bond, *et al.* 1990). In spite of their synthetic utility in organic reactions, there are only a few methods that can generate vinylallene structures.

Propargylic carbonates, phosphates, and mesylates having a vinyl functionality can undergo palladium-catalyzed transformations in the presence of a hard or soft nucleophile as a coupling partner to afford vinylallene derivatives (Molander, *et al.* 2006, Ma*, et al.* 2003, Chen, *et al.* 2011).

Also, Artok's research group showed that the palladium-catalyzed alkoxycarbonylation reactions of 2,4-enyne carbonates lead to the formation of 2,3,5-trienoates in high yields (Akpınar, *et al.* 2011, Karagöz, *et al.* 2014).

In this study, we have developed a mild, simple and atom economical method for the diastereoselective synthesis of (*E*)-configured 7-hydroxy-2,3,5-trionates via palladium-catalyzed alkoxycarbonylative 1,5-substitution reactions of conjugated enyne

oxiranes. The reactions proceeded in a highly stereoselective manner, possibly through sequential formation of π-allylpalladium and σ-vinylallenyl palladium complexes. The major diastereomeric form of the product is determined by the configuration of the alkenyl moiety of the substrate.

CHAPTER 2

LITERATURE WORKS

2.1. Palladium(0)-Catalyzed Reactions of Propargyl Compounds

The Pd(0)-catalyzed reactions of propargylic compounds proceed through the formation of two intermediates; the σ-allenylpalladiums **1** or the propargylpalladiums **2** (Figure 2.1), (Elsevier, *et al*. 1986).
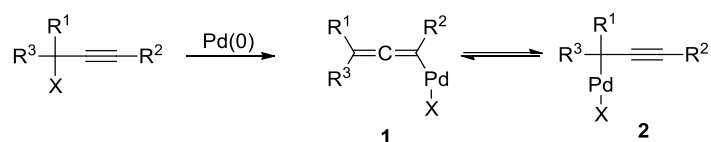

Figure 2.1. Formation of σ-allenylpalladium **1** and propargylpalladium **2**.

In consideration of the literature, depending on co-reactant types σ-allenylpalladium complexes **1** can undergo three types of transformations.
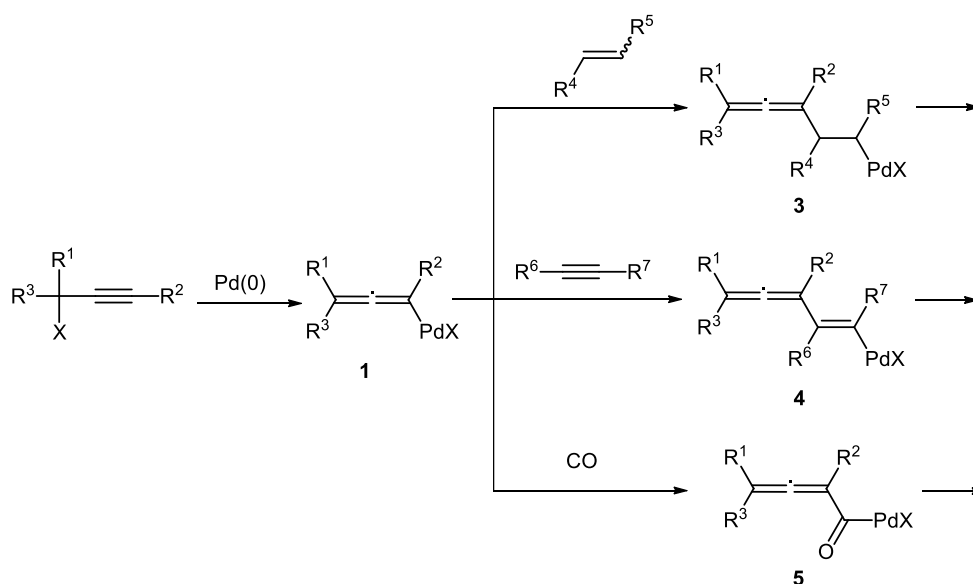

Figure 2.2. Insertion reactions of σ-allenylpalladium **1** intermediate.
(Source: Meijere, et al. 2004)

The first one is the insertion of intermediate **1** into unsaturated bonds of alkenes, alkynes, and carbon monoxide to generate the alkyl-, alkenyl- and acyl palladium intermediates **3**, **4**, and **5**, respectively. These intermediates undergo further transformations to afford synthetically valuable compounds (Figure 2.2), (Meijere, *et al*. 2004).

The second type of transformation proceed through the transmetallation of intermediate **1** with hard nucleophiles such as metal hydride, Grignard, organozinc, organosilane and organoboron reagents to afford the allene derivatives after subsequent reductive elimination (Figure 2.3), (Tsuji, *et al.* 2004).
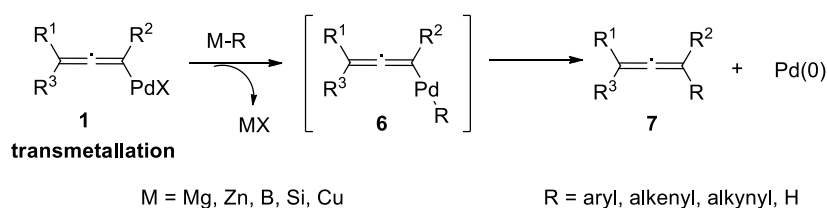
Figure 2.3. Transmetallation reaction of *σ*-allenylpalladium **1** intermediate.

And the last type of transformation is the nucleophilic attack of the nitrogen and oxygen containing nucleophiles and soft nucleophiles to the central allenic carbon atom. This nucleophilic attack results in the formation of intermediate **A**, which can be protonated to form alkene derivatives or add a second nucleophile through the formation of π-allylpalladium intermediate, resulting in the formation of alkene derivatives **B** (Figure 2.4).

Figure 2.4. Reaction of σ-allenylpalladium which involves nucleophilic attack.
(Source: Meijere, et al. 2004)

In case of propargylpalladium **2** intermediate (Figure 2.5), in the literature two common types of transformations are encountered; hydrogenolysis and β-H elimination (Tsuji, *et al.* 1995).
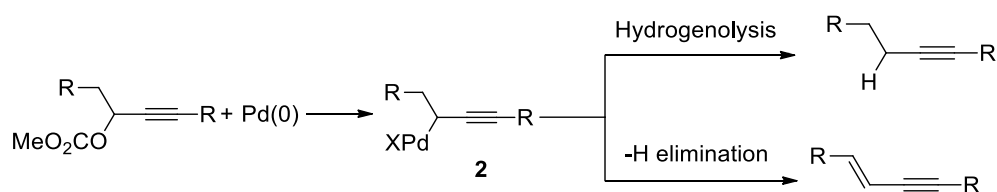
Figure 2.5. Reaction of σ-prop-2-ynylpalladium intermediate (**2**).

Pd(0)-catalyzed reactions of propargyl derivatives exhibit different reactivities depending on the substituents on the propargylic positions.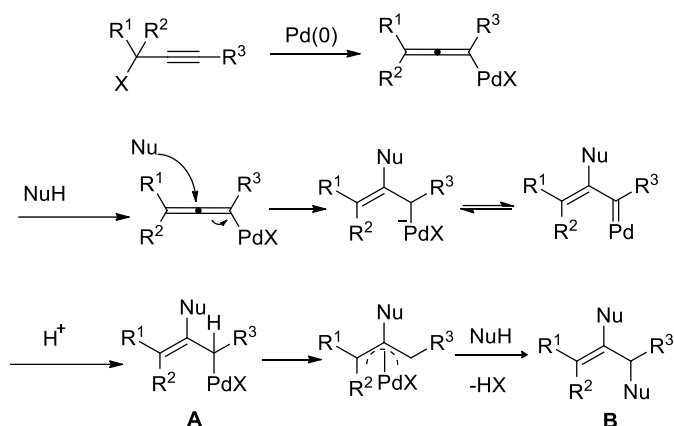 Propargyl alcohols are easily available substrates but they are the least reactive species. However, their esters such as acetates, carbonates, and phosphates are very reactive. The main factor of this reactivity difference is the leaving ability of the propargylic substituents. Acetates, carbonates, and phosphates are good leaving groups compared to alcohols.

Propargyl carbonates **8** undergo Pd(0)-catalyzed reactions under mild conditions. The key step of this transformation is the generation of σ-allenyl(methoxy)palladiums **9**. Also alkynyl oxiranes **10** behave like ester derivatives and undergo facile reactions under mild conditions by forming the complex **11** as an intermediate (Figure 2.6).

Figure 2.6. Reaction of propargyl carbonates and oxiranes.

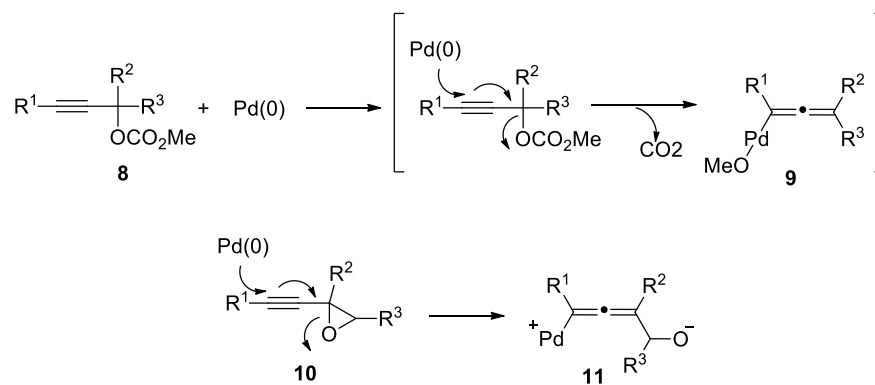## 2.2 Carbonylation Reactions of Propargylic Compounds Containing a Leaving Group

In Pd(0)-catalyzed alkoxycarbonylation reactions, alkynes substituted with a leaving group at the propargylic positions are frequently used. As discussed in the previous section, the key step of these transformation is the formation of σ-allenylpalladium **1** or **11** intermediates (Tsuji, et al. 1987). Carbon monoxide, (CO), can easily insert into this intermediate to form acyl palladium(II) species which then undergoes nucleophilic addition of alcohol to form ester derivatives. Depending on the reaction conditions mono- and dicarbonylations can take place (Figure 2.7), (Tsuji, *et al.* 1993).

X: OCOOR, OCOR, PO(OR)$_2$, Br, Ms
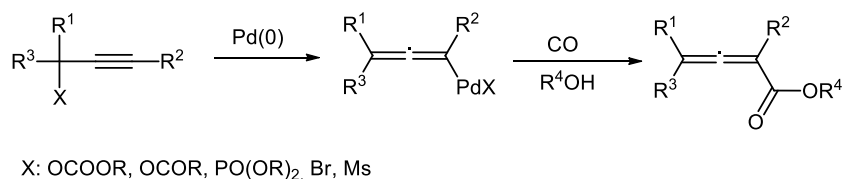
Figure 2.7. Pd(0)-catalyzed alkoxycarbonylation of propargyl compounds.

As an example from the literature, in 1986, Tsuji and co-workers reported the first alkoxycarbonylation reaction of propargyl carbonates in Pd$_2$(dba)$_3$-CHCl$_3$/PPh$_3$ catalytic system. Secondary and tertiary carbonates having internal or terminal alkyne moieties, yielded desired 2,3-dienyl carboxylate products in good yields (Figure 2.8), (Tsuji, *et al.* 1986).
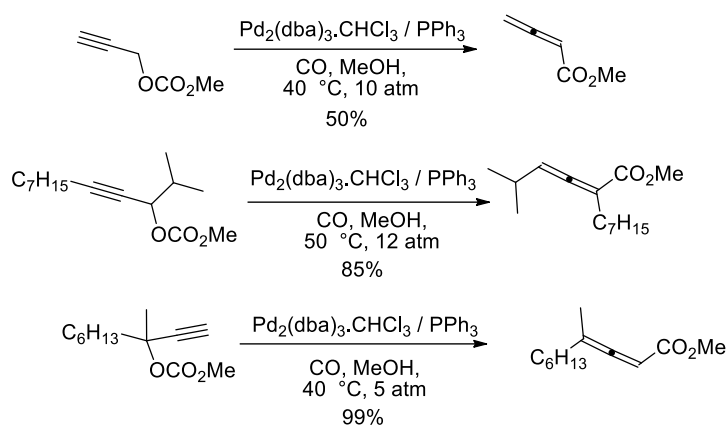
Figure 2.8. Alkoxycarbonylation of propargyl carbonates with Pd(OAc)$_2$/phosphine ligand system. (Source: Tsuji, *et al.* 1986)

Also, they reported that 2,4-dienyl carboxylate was formed instead of allenyl esters if the reaction was performed in ether, and an alcohol was used as a reactant (Figure 2.9), (Tsuji, *et al.* 1986).
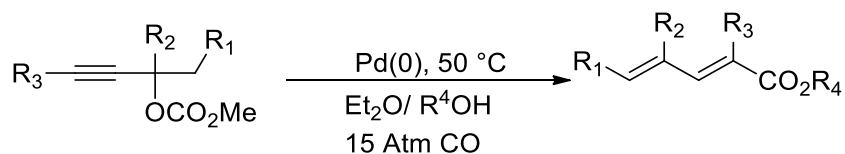
Figure 2.9. Alkoxycarbonylation of propargyl carbonates to form 2, 4-dienyl carboxylate. (Source: Tsuji, *et al.* 1986)

The carbonylation of chiral propargyl mesylates in the presence of Pd(PPh$_3$)$_4$ and under CO and in the presence of water, yielded allenic acids in good yields which were then converted stereospecifically to butenolides by treatment with AgNO$_3$. A good transfer of chirality was observed, although racemization occurred by the carbonylation of the corresponding propargyl carbonate derivative (Figure 2.10), (Marshall, *et al.* 1997).

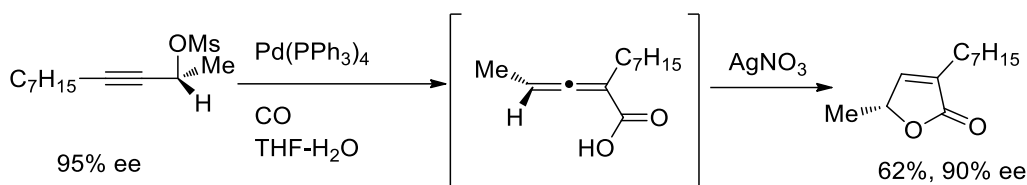Figure 2.10. Carbonylation reaction of propargylic mesylate to give optically active allenes. (Source: Marshall, *et al.* 1997)

In addition, a good transfer of chirality was observed in the carbonylation reaction of propargyl phosphates in the Pd(OAc)$_2$/1,6-bis(diphenylphosphino)hexane catalytic system and thus optically active 2,3-dienoates could be obtained with high enantiomeric excesses (Figure 2.11), (Tsuji, *et al.* 1995).
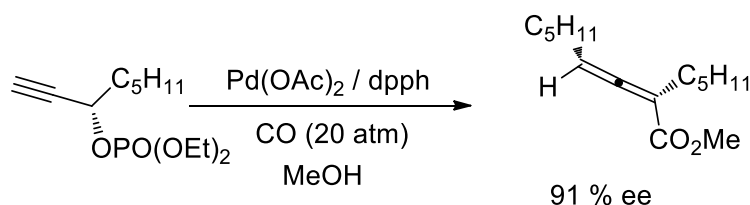
Figure 2.11. Carbonylation reaction of optically active propargylic phosphates. (Source: Tsuji, et al. 1995)

Propargyl alcohols are less reactive than their esters. Carbonylation of the tertiary propargyl alcohol at relatively harsh reaction conditions such as high CO pressures and temperatures was able to provide the formation of 2(5*H*)-furanones (Figure 2.12), (Alper, *et al.* 1997).

Figure 2.12. Alkoxycarbonylation of propargyl alcohol. (Source: Alper, *et al.* 1997)

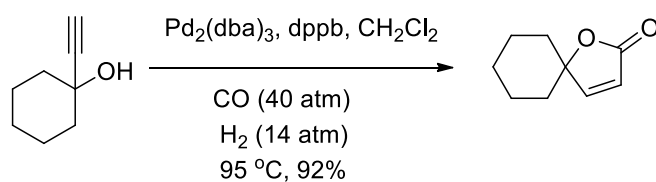The Pd(0)-catalyzed reaction of propargylic oxirane substrates with alcohols under CO atmosphere also generates hydroxy-functionalized allenic esters in good yields (Figure 2.13).
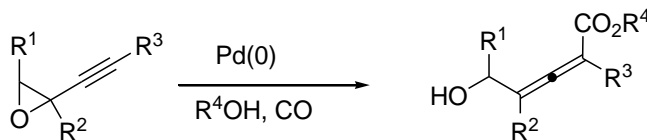

Figure 2.13. Alkoxycarbonylation of propargyl oxirane.
(Source Tsuji, *et al.* 2004)

2.3 Palladium(0)-Catalyzed Reactions of Allylic Compounds

Allylic compounds substituted with leaving groups such as acetates, carbonates, phosphates *etc.* play significantly important role in synthetic organic chemistry due to formation of π-allyl palladium complexes with palladium catalysts. Further transformation of this complex with various types of coupling partners offer many synthetically useful methods for the synthesis of valuable chemicals.

In 1965, Tsiju, *et al.* reported the first formation of π-allyl palladium complex from allylic compounds. They described the electrophilic property of π-allyl palladium complex and regeneration of the Pd(0) after coupled with pronucleophiles which offers the possibility of a catalytic process (Figure 2.14).
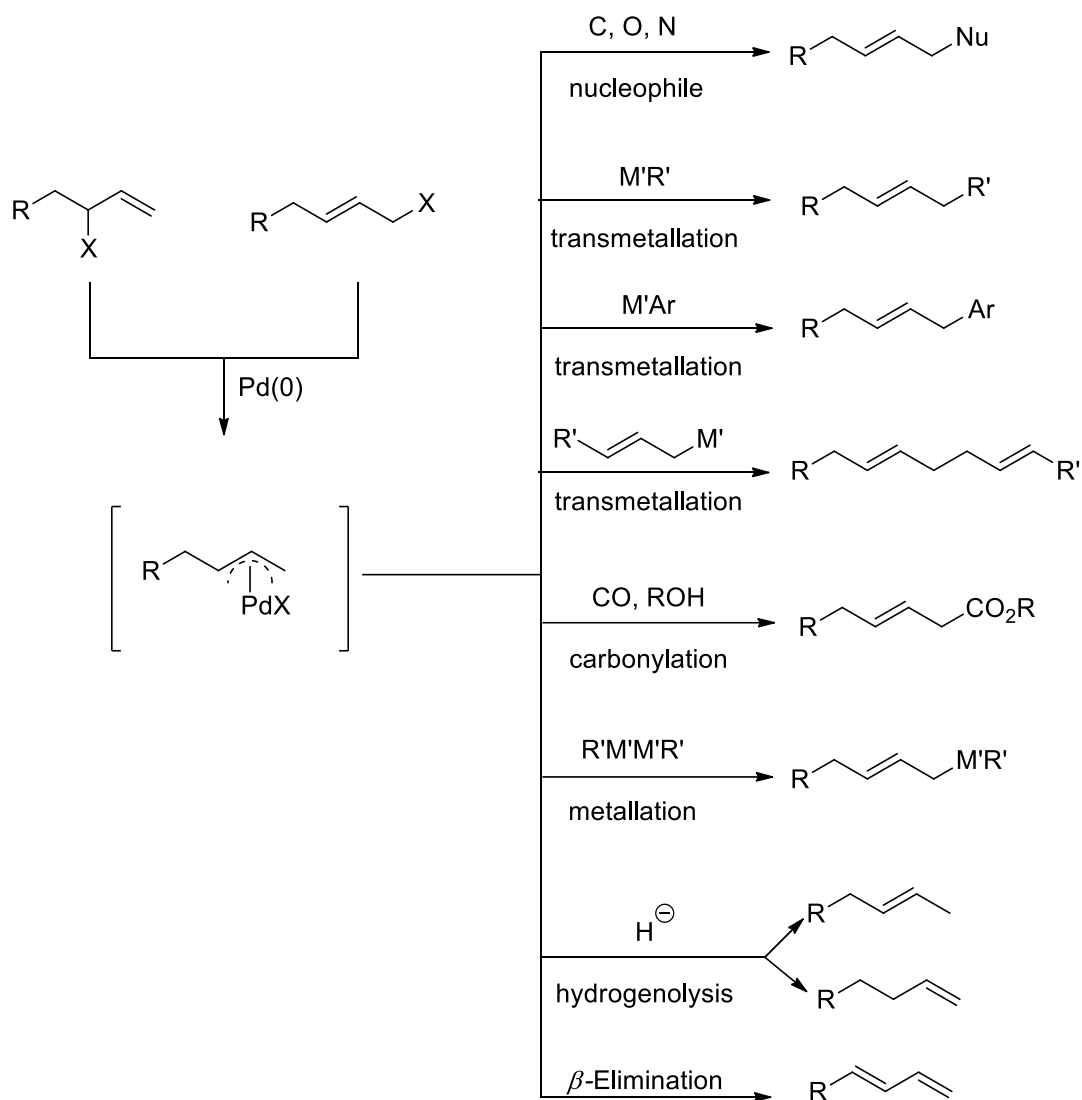
Figure 2.14. Palladium-catalyzed reactions of allylic compounds.
(Source: Tsuji, *et al.* 2004)

2.4 Carbonylation Reactions of Propargylic Compounds Containing a Leaving Group

In 1964, Tsuji, *et al.* showed that β,γ-unsaturated esters can be prepared by carbonylation of allylic compounds. According to researchers, π-allylpalladium chloride can be converted to *β,γ*-ester derivatives under CO pressures in alcohols with PdCl$_2$ as the catalyst (Figure 2.15).
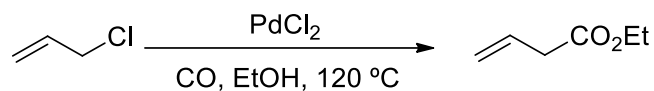
Figure 2.15. Palladium-catalyzed carbonylation reaction of 3-chloroprop-1-ene.
(Source: Tsuji, *et al.* 1964)

In 1984, Tsuji, *et al*. described the synthesis of *β,γ*-unsaturated ester derivatives by the reaction of allylic carbonates and alcohol in $Pd(OAc)_2/PPh_3$ catalytic system under mild reaction conditions (Figure 2.16).
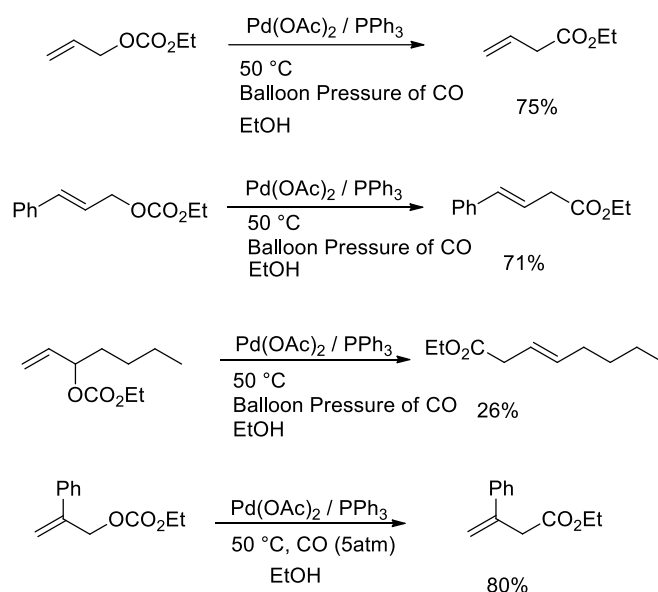

Figure 2.16. Palladium-catalyzed alkoxycarbonylation of allyl carbonates.
(Source: Tsuji, *et al.* 1984)

According to the proposed reaction mechanism, *π*-allylpalladium alkoxide intermediate can be formed from the the oxidative addition of palladium catalyst to an allyl carbonate and subsequent decarboxylation. The following carbon monoxide insertion reductive elimination steps lead to formation of *β,γ*-unsaturated ester derivatives and regeneration of the Pd(0) species (Figure 2.17).
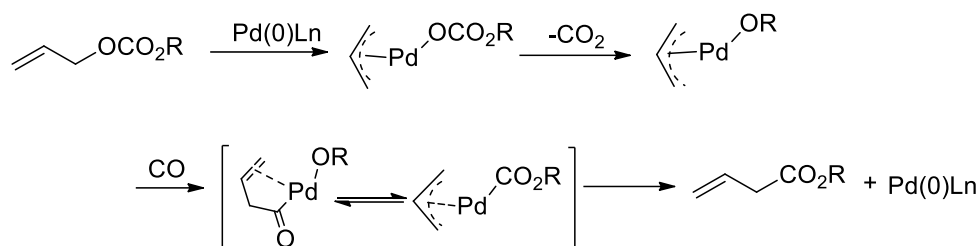
Figure 2.17. Alkoxycarbonylation mechanism of allyl carbonates.

In 1993, Murahashi, *et al.* showed that allyl phosphate derivatives are suitable reagents for Pd(0)-catalyzed carbonylation reactions, although harsh reaction conditions were required. The reaction was carried out over the $Pd_2(dba)_3$-$CHCl_3$/PPh_3 catalytic system at high CO pressures and temperatures to obtain the β,γ-unsaturated esters with high yields. It was noted that isomerization of the double bond was occurred depending on the substituents on the allyl phosphate derivatives (Figure 2.18).
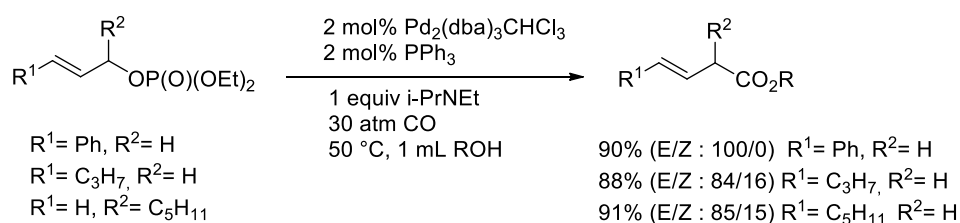

Figure 2.18. Palladium-catalyzed alkoxycarbonylation of allyl phosphates.
(Source: Murahashi, *et al.* 1993)

They also showed that β,γ-unsaturated esters could be synthesized by the reaction of allyl acetates at high CO pressures and temperatures. The reaction was carried out over the $Pd_2(dba)_3$-$CHCl_3$/PPh_3 catalytic system, and NaBr was used as a co-catalyst (Figure 2.19). NaBr accelerates the reaction because, after the generation of π-allylpalladium acetate complex ligand exchange of acetate with bromide took place, this making the CO insertion more facile (Figure 2.19), (Murahashi, *et al.* 1993).
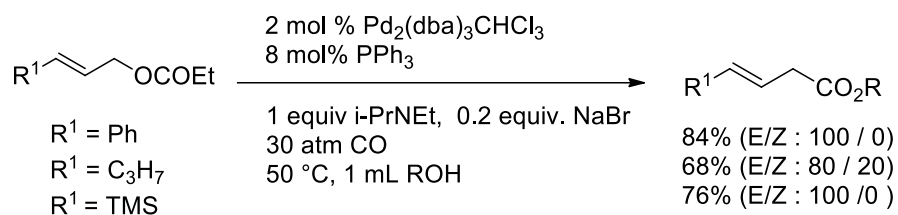
2 mol % Pd$_2$(dba)$_3$CHCl$_3$
8 mol% PPh$_3$

R^1⌒⌒OCOEt → R^1⌒⌒CO$_2$R

1 equiv i-PrNEt, 0.2 equiv. NaBr
30 atm CO
50 °C, 1 mL ROH

R^1 = Ph
R^1 = C$_3$H$_7$
R^1 = TMS

84% (E/Z : 100 / 0)
68% (E/Z : 80 / 20)
76% (E/Z : 100 /0)

Figure 2.19. Palladium-catalyzed alkoxycarbonylation of allyl acetates..
(Source: Murahashi, *et al.* 1993)

Harsh reaction conditions were needed for less reactive allylic alcohols. However, carbonylation of allylic alcohols proceeds smoothly in the presence of phenol as a nucleophile. 4-Phenyl-3-butenoate was obtained in a good yield from cinnamyl alcohol under 5 atm of CO at 100 °C with Pd$_2$(OAc)$_2$/PPh$_3$ catalytic system (Satoh, *et al.* 1997).

Ph⌒⌒OH → Ph⌒⌒CO$_2$Ph

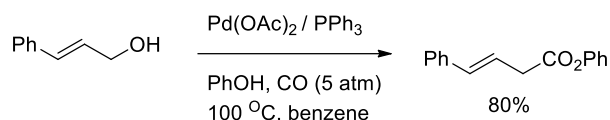Pd(OAc)$_2$ / PPh$_3$

PhOH, CO (5 atm)
100 °C, benzene

80%

Figure 2.20. Palladium-catalyzed alkoxycarbonylation of allyl alcohol.
(Source: Satoh, *et al.* 1997)

Allyl alcohol was carbonylated under a high pressure of CO$_2$ (50 atm) and CO (50 atm) mixture at 110 °C in dioxane to provide 2-butenoic acid as the major product and 3-butenoic acid as the minor product (Sakamoto, *et al.* 1996).

⌒⌒OH → ⌒⌒CO$_2$H + ⌒⌒CO$_2$H

Pd(PPh$_3$)$_4$

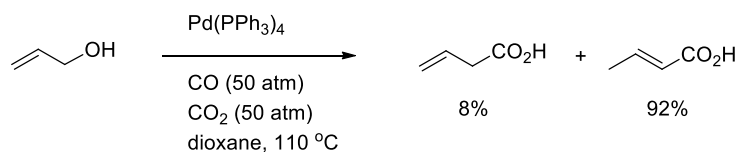CO (50 atm)
CO$_2$ (50 atm)
dioxane, 110 °C

8%   92%

Figure 2.21. Palladium-catalyzed alkoxycarbonylation of allyl alcohol.
(Source: Sakamoto, *et al.* 1996)

Pd(0)-catalyzed reactions of alkenyloxiranes afford either 1,4-adducts or 1,2-adducts. 1,4-Adducts are mainly obtained under usual conditions due to the electronic effect of the epoxide oxygen atom (Figure 2.22), (Tsuji, *et al.*1981, Trost, *et al.* 1981).
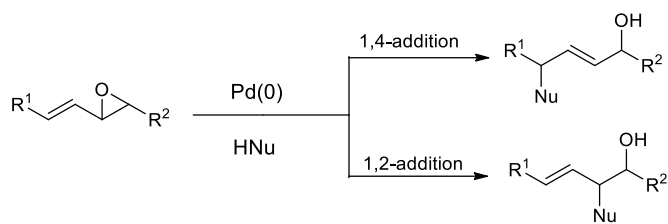
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Figure 2.22. Palladium-catalyzed nucleophilic reactions of allylic oxiranes.

β,γ-Unsaturated δ-hydroxyesters are obtained by regioselective carbonylation of isoprene oxide in EtOH using a ligand-free Pd catalyst at room temperature under high CO pressure (30 atm). (Figure 2.23), (Shimizu, *et al.* 1993).
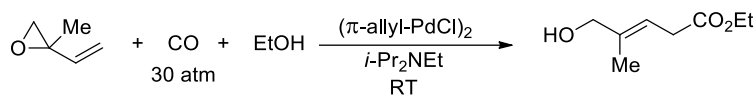

Figure 2.23. Palladium-catalyzed alkoxycarbonylation reactions of allylic oxiranes.
(Source: Shimizu, *et al.* 1993)

2.5 Synthesis of Vinylallenes

Vinylallenes are reactive compounds toward various cycloaddition and cyclization reactions. They exhibit particularly higher activity and selectivity with Diels-Alder reactions, because their configurational equilibrium is more on the side of s-*cis* conformer -a prerequisite for a [4+2] cycloaddition reaction to occur effectively-than for 1, 3-dienes (Bond, *et al.* 1990).

2.5.1 Synthesis of Vinylallenes with Grignard Reagent

In 1972, Gore, *et al*. developed a method for the synthesis of vinyl substituted allenes by the reactions of 1-chloro-2-en-4-ynes with methylmagnesium iodide and trimethylsilylmagnesium chloride in moderate to good yields (Figure 2.24). The method was just limited to methylmagnesium iodide and trimethylsilylmagnesium chloride, other Grignard reagents completely failed to yield desired vinylallene derivatives.
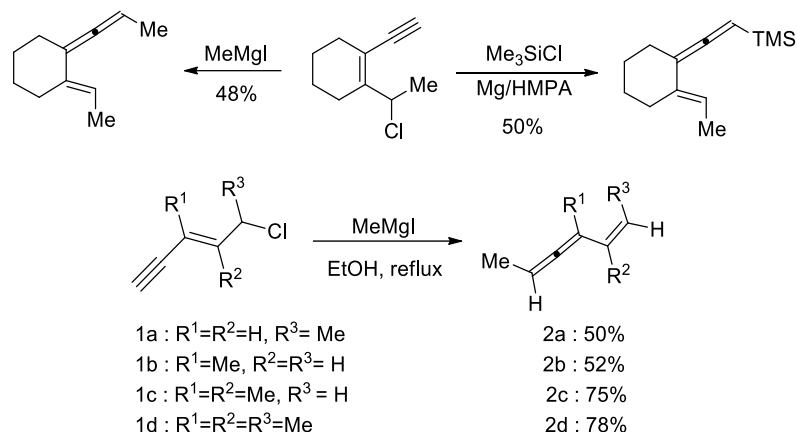
Figure 2.24. Reaction of chloro-enynes with Grignard reagents.
(Source: Gore, et al. 1972)

2.5.2 Synthesis of Vinylallenes with Organocopper Reagents

In 1999, Krause, *et al*. developed a regioselective 1,5-(S_N2'')-type reaction of (*E*)-2, 4-enyne acetates with various lithium dialkylcuprates affording the vinylallenes exclusively. However, this method afforded the desired vinylallene structures as a mixture of *E*- and *Z*- isomers. Moreover, the method was not suitable for aryl- or alkenyl lithium cuprates.

$R^1=R^2=Me$, $R^3=Bu$ 90% (E:Z = 67:33)
$R^1=R^2=Me$, $R^3=$t-Bu   93% (E:Z = 25:75)
$R^1=Me_3Si$, $R^2=$t-Bu, $R^3=Me$ 96% (E:Z = 40:60)
$R^1=Bu$, $R^2=$t-Bu, $R^3=Me$ 92% (E:Z > 99:1)
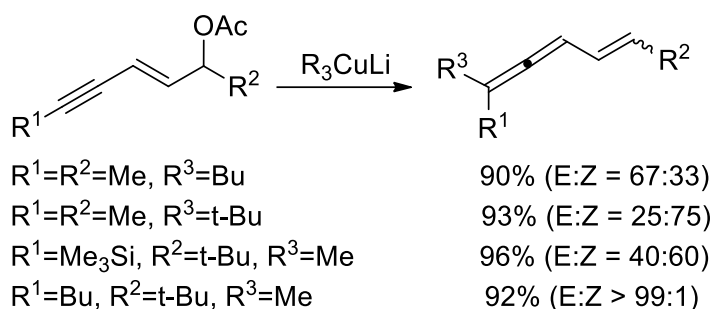
Figure 2.25. 1, 5-(S_N2'')-type Substitution reaction of enyne acetates with dialkyl cuprates. (Source: Krause, et al. 1999)

They also applied their methodology to (*E*)-2,4enyne oxirane substrates, which were treated with $Me_2CuLi \cdot LiI$ or *t*-$Bu_2CuLi \cdot LiCN$. The substrate reacted cleanly with the *tert*-butylcuprate to afford the alkylated vinylallene with a primary hydroxyl group,

whereas its reaction with the lithium dimethylcuprate reagent proceeded without coupling and led to exclusive reduction to a vinylallene.
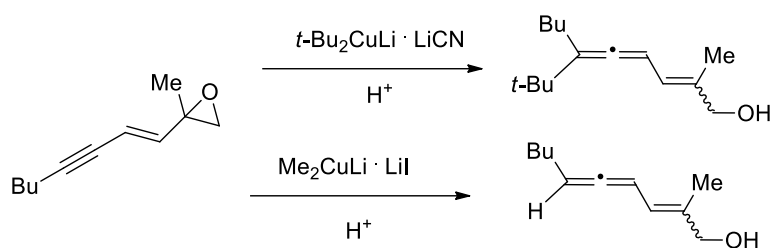

Figure 2.26. 1, 5-(S_N2'')-type Substitution reaction of enyne oxiranes with dialkyl cuprates. (Source: Krause, *et al*. 1999)

2.5.3 Palladium(0)-Catalyzed Synthesis of Vinylallene with Organozinc Reagent

In 2003, Ma, *et al*. showed that vinyl allene structures can be formed by the palladium-catalyzed coupling reaction of propargyl mesylates with alkoxycarbonylethenyl zinc complexes with excellent yields in the presence of [{PdCl(π-C$_3$H$_5$)}$_2$]/2-diphenylphosphino-2'-hydroxy-1,1'-binaphthalene (L) catalytic system under mild conditions (Figure 2.27).

R^1= TBS, R^2= n-C$_4$H$_9$(1a) 97%
R^1= TMS, R^2= n-C$_8$H$_{17}$ 95%
R^1= TMS, R^2= Bn 97%
R^1= t-Bu, R^2= n-C$_4$H$_7$ 100%
R^1= n-C$_5$H$_{11}$, R^2= H 100%
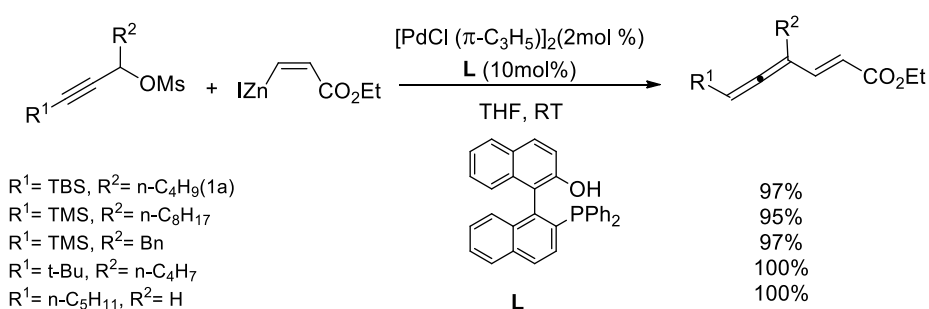
Figure 2.27. Synthesis of vinylallenes by organozinc reagents. (Source: Ma, *et al*. 2003)

2.5.4 Palladium(0)-Catalyzed Synthesis of Vinylallenes by N-Tosylhydrazone Salts

In 2011, Chen, *et al*. reported that diazo compounds generated *in-situ* from *N*-tosylhydrazone salts in the presence of a base, behave as a nucleophile and react with the propargylic carbonates to form vinylallene structures in the presence of [Pd$_2$(dba)$_3$] (Figure 2.28).

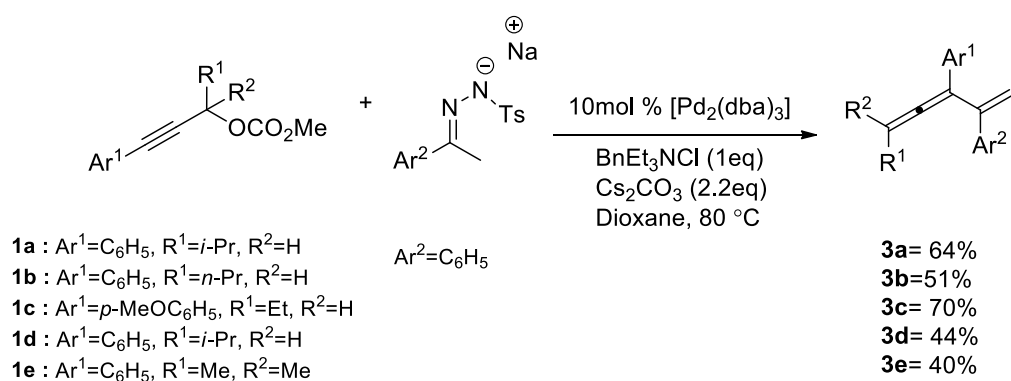**1a** : Ar^1=C$_6$H$_5$, R^1=*i*-Pr, R^2=H
1b : Ar^1=C$_6$H$_5$, R^1=*n*-Pr, R^2=H
1c : Ar^1=*p*-MeOC$_6$H$_5$, R^1=Et, R^2=H
1d : Ar^1=C$_6$H$_5$, R^1=*i*-Pr, R^2=H
1e : Ar^1=C$_6$H$_5$, R^1=Me, R^2=Me

Ar^2=C$_6$H$_5$

3a= 64%
3b=51%
3c= 70%
3d= 44%
3e= 40%

Figure 2.28. Synthesis of vinylallene by *N*-tosylhydrazone salt.
(Source: Chen, *et al.* 2011)

2.5.5 Palladium(0)-Catalyzed Synthesis of Vinylallene by Alkenyl Trifluoroborates

In 2006, Molender, *et al*. reported Pd(0)-catalyzed cross-coupling reaction of enantio-enriched propargylic carbonates and phosphates with alkenyltrifluoroborates. The method allowed center-to-axial chirality transfer and the desired vinylallene structures were synthesized in good enantiomeric excesses (Figure 2.29).
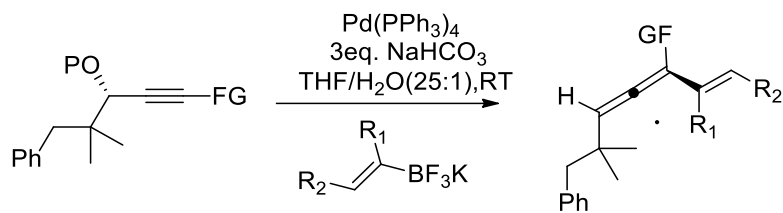
Figure 2.29. Synthesis of vinylallene by alkenyltrifluoroborates.
(Source: Molander, *et al*. 2006)

2.5.6 Rhodium(I)-Catalyzed Reaction of the (*Z*)-Enyne Acetate with Organoboronic Acids

In 2011, Üçüncü, *et al*. reported that Rh(I)-catalyzed reaction of (*Z*)-2,4-enyne acetates with organoboronic acids afforded vinylallenes. The reaction is suitable for arylboronic acids having both electron-withdrawing or -donating groups (Figure 2.30).
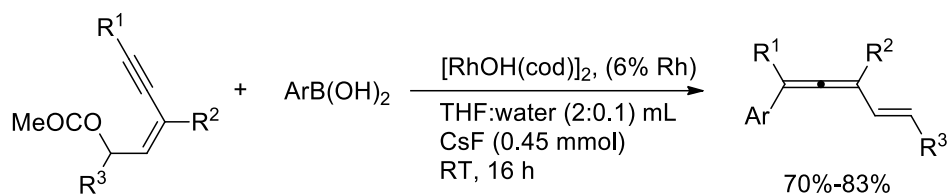

Figure 2.30. Rh(I)-catalyzed reaction of the (*Z*)-enyne acetate with organoboronic acids.
(Source: Üçüncü, *et al*. 2011)

2.5.7 Palladium(0)-Catalyzed Reaction of 2,4-Enyne Carbonates with Organoboronic Acids

Üçüncü, *et al*. also (2011), showed that arylboronic acids having different electron deficient or electron donating substituents are good coupling partner for Pd(0)-catalyzed reaction of both (*E*)- and (*Z*)-2,4-enyne carbonates, yielding exclusively the (*E*)-configured vinylallene derivatives (Figure 2.31).
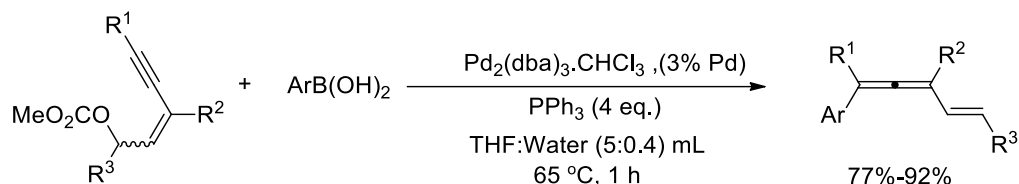
Figure 2.31. Palladium-catalyzed reaction of 2, 4-enyne carbonates with organoboronic acids. (Source: Üçüncü, *et al*. 2011)

2.5.8 Palladium(0)-Catalyzed Alkoxycarbonylation Reaction of 2,4-Enyne Carbonates

In 2011, Akpinar, *et al.* showed for the first time that conjugated (*Z*)-2,4-enyne derivatives bearing a carbonate as a leaving group at the allylic moiety underwent Pd(0)-catalyzed reaction to lead 2,3,5-trienoate products in high yields (Figure 2.32).
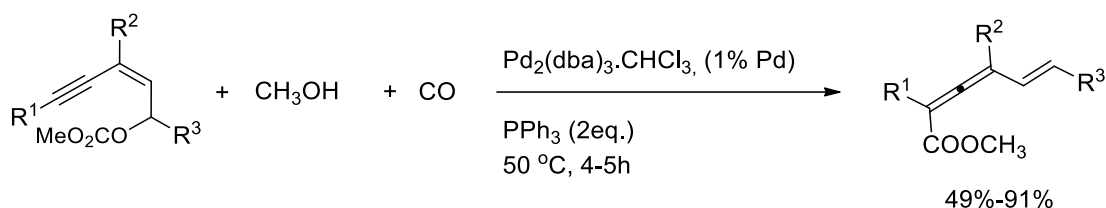
Figure 2.32. Palladium-catalyzed alkoxycarbonylation reaction of (*Z*)-2, 4-enyne carbonates. (Source: Akpınar, *et al*. 2011)

The reaction conditions were also applied to an enantio-enriched (*Z*)-2, 4-enyne carbonates. It was found that the reaction proceeded with complete racemization. But after tuning the reaction parameters, moderate to good transfer of chirality was observed depending on the olefin geometry and substituents on the alkyne moiety (Figure 2.32), (Karagöz, *et al*. 2014).
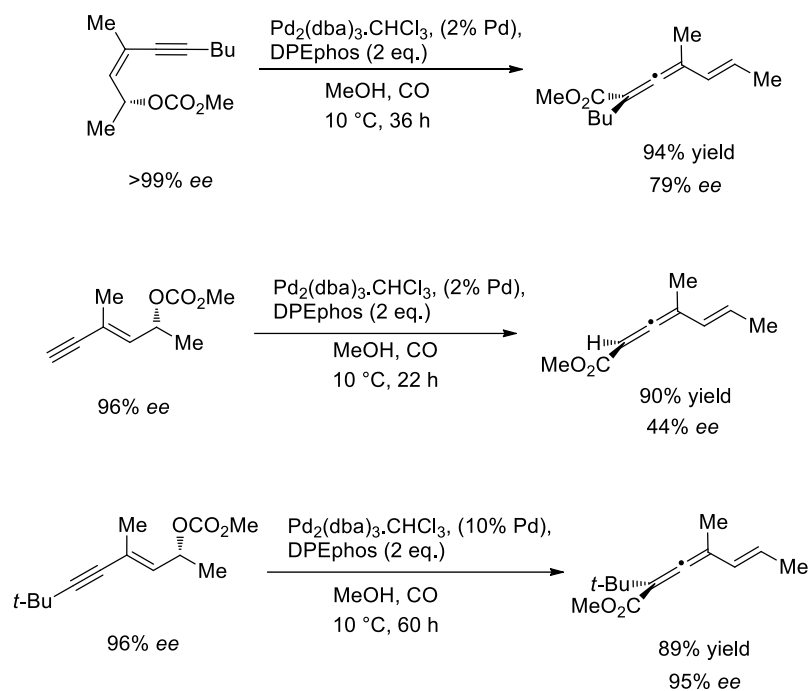
Figure 2.33. Palladium-catalyzed alkoxycarbonylation reaction of (*E* and *Z*)-2, 4-enyne carbonates leading to enantio-enriched vinylallene derivatives. (Source: Karagöz, *et al*. 2014)

2.5.9 Vinylallenes in Synthesis

Vinylallenes are valuable dienophiles in Diels-Alder reactions. As an example from the literature, Krause, *et al.* showed that vinylallenes reacted with maleic anhydride in refluxing toluene within 30 h to provide cycloadduct exclusively (Krause, *et al.* 1996).
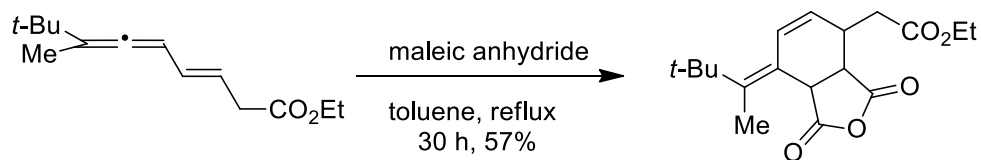
Figure 2.34. Diels-Alder reactions of vinylallenes. (Source: Krause, *et al.* 1996)

Vinylallenes are also good reactants for varios cycloisomerization reactions. In 2006, Toste, *et al.* developed a gold(I)-catalyzed cycloisomerization of vinyl allenes for the synthesis of cyclopentadienes. The mild reaction conditions of this gold(I)-catalyzed carbon–carbon bond-forming reaction provide a regiospecific method for the synthesis of highly functionalized cyclopentadienes.
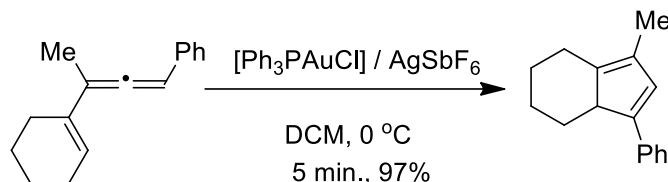
Figure 2.35. Gold-catalyzed cycloisomerization reactions of vinylallenes.
(Source: Toste, *et al*. 2006)

Also, Iwasawa, et al. developed a PtCl$_2$-catalyzed preparation of highly substituted cyclopentadiene derivatives from 1,2,4-trienes. This reaction proceeds under mild conditions to afford a variety of well-defined, highly substituted cyclopentadienes effectively.
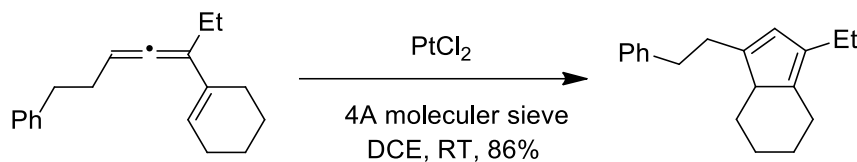
Figure 2.36. Platinium-catalyzed cycloisomerization reactions of vinylallenes.
(Source: Iwasawa, *et al*. 2006)

CHAPTER 3

EXPERIMENTAL STUDY

3.1. General Procedures for Drying the Solvents

THF, DMF, and DCM solvents were all purified by a solvent purification system. Et_2O was distilled from benzophenone-ketyl under argon prior to use. Methanol and ethanol were dried over Mg turnings in the presence of iodine and stored on molecular sieve 3Å under Ar. 1-Propanol and 2-propanol were dried first by stirring over anhydrous CaO followed by refluxing over Mg turnings in the presence of iodine. 1-Butanol was dried first by stirring over anhydrous $MgSO_4$ and then refluxed over Mg turnings in the presence of iodine. *tert*-BuOH was stirred over CaH_2 (5% w/v), distilled, and stored on molecular sieve 3Å under Ar.

3.2. Synthesis of Substrates

Syntheses of all enyne oxirane starting materials (**1**) were performed under Ar gas and purification of all synthesized molecules was performed by column chromatography on silica gel. Silica gel material used for the purification of enyne oxirane substrates had a particle size range of 60-200 mesh and treated by NEt_3 before use. It must be noted that the column chromatography of the substrate **1** on an untreated silica gel always resulted in decomposition. All other column purifications were performed on silica gel 60 (35-70 μm). All substrates appeared either colorless or pale yellow oils. The $Pd_2(dba)_3$-$CHCl_3$ complex was synthesized in the laboratory (Ukai, *et al.* 1974).

3.2.1. Synthesis of (Z)-1a
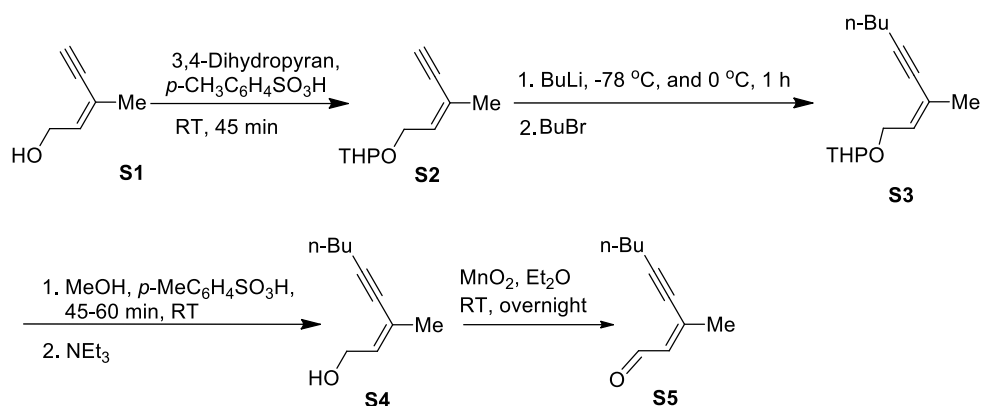
To the mixture of commercially available, (Z)-pent-2-en-4-yn-1-ol (**S1**) (1.92 g, 20 mmol) and 3,4-dihydropyran (2.2 mL, 24 mmol) was added p-toluenesulfonic acid (44 mg, 0.02 mmol) and then stirred for 45 min at room temperature (RT). Then, the mixture was diluted with 40 mL of dry THF under Ar and cooled to -78 °C. At that temperature, 24 mmol of BuLi (1.6 M in hexane, 15 mL) was added dropwise via a syringe. After stirring the reaction mixture for 1 h at 0 °C, butyl bromide (4.3 mL, 40 mmol) was added and the mixture was stirred for 5 days at reflux. The reaction was quenched by the addition of saturated $NH_4Cl(aq)$ solution and the reaction solution was extracted with Et_2O. The organic phase was washed with water, dried over $MgSO_4$, filtered, and concentrated under reduced pressure. The residue was used in the following step without any other purification (Betzer, *et al.* 1997).

To a solution of the preceding crude compound (**S3**) in methanol (60 mL) p-toluenesulfonic acid (1.2 g, 6 mmol) was added and the resulting solution was stirred at RT for 45-60 min. Then, triethylamine was added (1.8 mL), and the solution was concentrated under reduced pressure. The mixture was taken into DCM and washed with water. The combined extracts were washed with brine, dried over $MgSO_4$, filtered, and concentrated under reduced pressure. Purification by column chromatography on silica gel gave the enynol **S4** (hexane-EtOAc, yield: 2.43 g, 80%), (Ukai, *et al.* 1974).

To the solution of **S4** ($\approx$17 mmol) in 60 mL of dry diethyl ether, activated MnO_2 (30 g, 0.3 mol) was added, and the mixture was stirred overnight at RT. After filtration through Celite, the solution was concentrated under reduced pressure. The crude aldehyde (**S5**) was used in the next step (Betzer, *et al.* 1997).

23
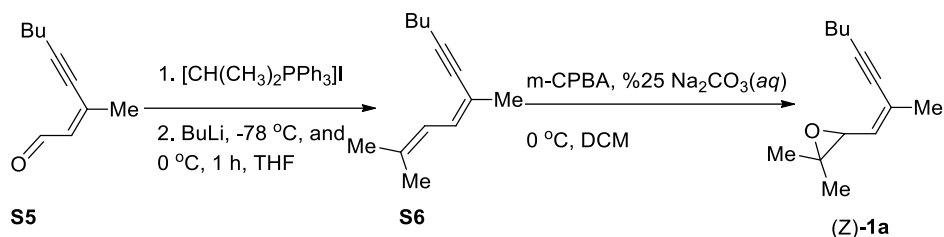
A hexane solution of BuLi (4.8 mL, 12 mmol, 2.5 M) was added dropwise to a solution of isopropyl(triphenyl)phosphonium iodide (4.32 g, 10 mmol) in THF (30 mL) at 0 °C, and stirred for further 1 h. The enyne aldehyde **S5** (1.8 g, 12 mmol), was added dropwise to the resulting mixture and stirred for 1 h at RT. The reaction was quenched by the addition of saturated NH$_4$Cl(*aq*) solution, and the organic layer was extracted with diethyl ether. The combined extracts were dried over MgSO$_4$, and chromatographed on a silica gel column to obtain pure **S3a** (hexane/EtOAc, yield: 1.65 g, 78%), (Ming-Yuan, *et al.* 2004).

To a solution of **S6** (352 mg, 2 mmol) in DCM (30 mL) was added 12 mL solution of Na$_2$CO$_3$(*aq*) (25%) followed by 3.4 mmol (587 mg) *m*-chloroperbenzoic acid dropwise at 0 ^{0}C. The mixture was stirred at same temperature and monitored with TLC until the reactant was consumed completely. At the end of the epoxidation process, the mixture was extracted with DCM, dried over anhydrous MgSO$_4$, filtered, and concentrated under reduced pressure. The crude mixture was chromatographed on NEt$_3$-pretreated short silica gel column which afforded the enyne oxirane (*Z*)-**1a** as a colorless oil (hexane-EtOAc, yield: 269 mg, 70%).

3.2.2. Synthesis of (Z)-1d
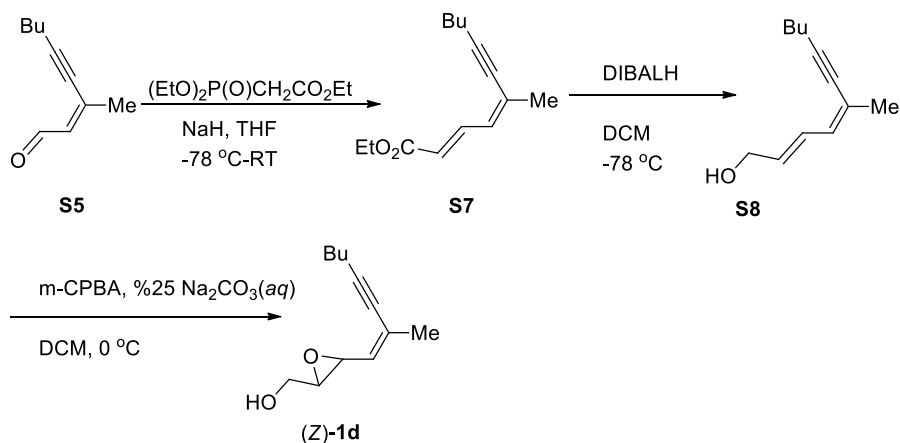
To a solution of NaH (525 g, 22 mmol) in THF (50 mL) was added triethyl phosphonoacetate (4.8 mL, 24 mmol) at 0 °C, and the mixture stirred 1 h at RT. Subsequently, to the reaction mixture was added **S5** (3 g, 20 mmol) dropwise at -78 °C and stirred for 1 h at RT. The reaction was terminated by the addition of aqueous NH$_4$Cl(*aq*) solution and extracted with Et$_2$O. The organic layer was dried over MgSO$_4$, filtered and concentrated under reduced pressure to give *E/Z* isomer 95:5 isomeric ratio. The crude mixture was purified on silica gel column to obtain **S7** in pure isomeric form (hexane-EtOAc, yield: 3.17 g, 72%), (Urabe, *et al.* 1997).

A DIBALH (44 mL, 44 mmol, 1.0 M in cyclohexane) solution was added dropwise to the solution of **S7** (3.85 g, 17.5 mmol) in DCM (120 mL) at −78 °C. After the reaction mixture was stirred for 4 h at the same temperature, 1 M HCl(*aq*) solution was added before extracting with DCM. The organic layers were combined, washed with brine, dried over MgSO$_4$, filtered, and concentrated under reduced pressure. The crude mixture was subjected to silica gel column chromatography to purify the corresponding **S8** compound (hexane-EtOAc, yield: 2.65 g, 85%), (Kajikawa, *et al.* 2009).

The epoxidation of **S8** (356 mg, 2 mmol) and isolation of the product (*Z*)-**1d** was performed as specified for (*Z*)-**1a** (hexane-EtOAc, yield: 233 mg, 60%).

3.2.3. Synthesis of (Z)-1i and (Z)-1i'
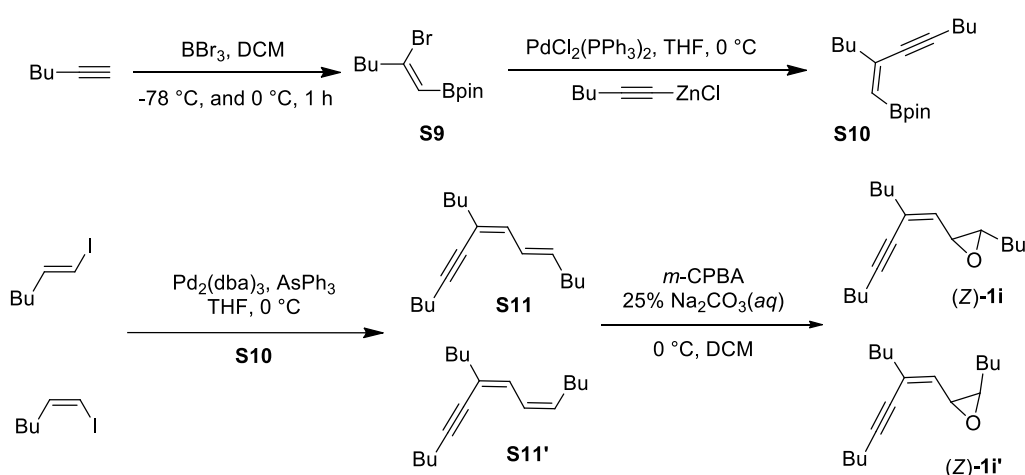
1-Hexyne (2.3 mL, 20 mmol) was added dropwise to a solution of BBr_3 (22 mL, 22 mmol, 1 M) in dry DCM at -78 °C. The mixture was allowed to warm to ambient temperature, and stirred for 1 h. The reaction mixture was re-cooled to -78 °C and a solution of 2, 3-dimethylbutan-2,3-diol (2.84g, 24 mmol) in dry DCM (20 mL) was added dropwise. Following this addition, the mixture was warmed to ambient temperature and stirred for 1 h. Then, the mixture was quenched by brine and extracted with DCM. The combined organic layers were dried over $MgSO_4$, filtered and evaporated. The residue was purified on silica gel column to afford **S9** as a colorless oil (hexane-EtOAc, yield: 3.57 g, 62%), (Wang, *et all.* 2009).

To a stirred solution of **S9** (4.64 g, 16 mmol) and $PdCl_2(PPh_3)_2$ (1 mol%, 112 mg, 0.16 mmol) in dry THF (20 mL) was added a solution of 1-hexynylzinc chloride, which was generated by treatment of 1-hexyne (1.6 g, 19.2 mmol) with BuLi (8.5 mL, 20.7 mmol, 2.5 M in hexane) in dry THF (20 mL) for 30 min at -78°C and following treatment with $ZnCl_2$ (2.72 g, 19.2 mmol) for 30 min at 0°C. The resultant reaction mixture was stirred at RT for 1 h before quenching by 0.5 M HCl(*aq*). The content of the reaction medium was extracted with ether, washed with saturated NaHCO_3(*aq*) and brine, dried over $MgSO_4$, filtered, and concentrated under reduced pressure. The residue was purified on silica gel column to afford **S10** as a colorless oil (hexane-EtOAc, yield: 3.9 g, 84%), (Wang, *et all.* 2009).

A mixture of $Pd_2(dba)_3$ (137 mg, 0.15 mmol, 3 mol % of Pd), $AsPh_3$ (184 mg, 0.6 mmol, 6 mol % of As), and 15 mL of 1 M KOH(*aq*) in 50 mL of THF was cooled to 0 °C before the addition of the compound **S10** (2.9 g, 10 mmol). Then, a THF solution (10 mL) of *trans*- (Stille, *et al.* 1987) or *cis*-1-iodo-1-hexene (Denmark, *et al.* 2005) (2.52 g, 12 mmol), which were synthesized according to the literature procedures, was added dropwise and the reaction stirred for 30 min at RT. After the completion of the reaction, water was added to the resulting mixture before extracting with ether. The combined extracts were dried over $MgSO_4$, filtered and concentrated under reduced pressure. The residue was purified on silica gel column to afford **S11** or **S11'** as yellowish oil products (hexane-EtOAc, yield of **S11**: 1.89 g, 77%; yield of **S11'**: 1.25 g, 51%), (Fang, *et al.* 2010).

To a solution of **S11** or **S11'** (492 mg, 2 mmol) in DCM (30 mL) was added 12 mL solution of Na_2CO_3(*aq*) (25%) followed by 587 mg of *m*-CPBA (3.4 mmol) at 0 °C. The mixture was stirred at the same temperature and monitored with TLC until the reactant was consumed completely. At the end of the epoxidation process, the mixture

was extracted with DCM, dried over anhydrous MgSO₄, filtered, and concentrated under reduced pressure. The crude mixture was chromatographed on NEt₃-pretreated short silica gel column which afforded the enyne oxirane (*Z*)-**1i** or (*Z*)-**1i'** in about 85% purities as pale yellow oil products (hexane-EtOAc, yield of (*Z*)-**1i**: 300 mg, 57%; yield of (*Z*)-**1i'**: 158 mg, 30%).

3.2.4. Synthesis of (*Z*)-1m
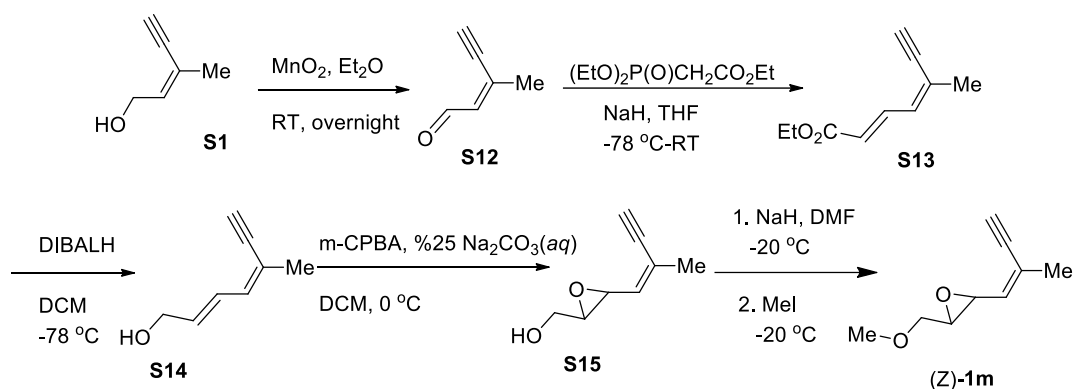
To the mixture of commercially available, (*Z*)-pent-2-en-4-yn-1-ol (**S1**) (1.92 g, 20 mmol) in 80 mL of dry diethyl ether, 37 g of activated MnO₂ (0.4 mol) was added, and the mixture was stirred overnight at RT. After filtration through Celite, the solution was concentrated under reduced pressure. The crude aldehyde was used in the next step (Betzer, *et al.* 1997).

To a solution of NaH (525 g, 22 mmol) in THF (50 mL) was added triethyl phosphonoacetate (4.8 mL, 24 mmol) at 0 °C, and the mixture stirred 1 h at RT. Subsequently, to the reaction mixture was added **S12** (1.88 g, 20 mmol) dropwise at -78 °C and stirred for 1 h at RT. The reaction was terminated by the addition of aqueous NH₄Cl(*aq*) solution and extracted with Et₂O. The organic layer was dried over MgSO₄, filtered and concentrated under reduced pressure to give *E/Z* isomer 95:5 isomeric ratio. The crude mixture was purified on silica gel column to obtain **S13** in pure isomeric form (hexane-EtOAc, yield: 2.3 g, 70%), (Urabe, *et al.* 1997).

A DIBALH (44 mL, 44 mmol, 1.0 M in cyclohexane) solution was added dropwise to the solution of **S13** (2.87 g, 17.5 mmol) in DCM (120 mL) at −78 °C. After the reaction mixture was stirred for 4 h at the same temperature, 1 M HCl(*aq*) solution was added before extracting with DCM. The organic layers were combined, washed with

brine, dried over MgSO$_4$, filtered, and concentrated under reduced pressure. The crude mixture was subjected to silica gel column chromatography to purify the corresponding **S14** compound (hexane-EtOAc, yield: 1.81g, 85%), (Kajikawa, *et al.* 2009).

The epoxidation of **S14** (244 mg, 2 mmol)**,** isolation of the product **S15,** methylation of the pendant hydroxyl group of **S15** (166 mg, 1.2 mmol), and isolation of the product (*Z*)**-1m** were performed as specified for (*Z*)**-1a** and (*Z*)**-1d**, respectively, (hexane-EtOAc**,** yield of **S15**: 166 mg, 60%; yield of (*Z*)**-1m**: 144 mg, 87%).

3.2.5. Synthesis of (*Z*)-1q and hydroxyl tethered (*Z*)-2,4-enyne oxiranes
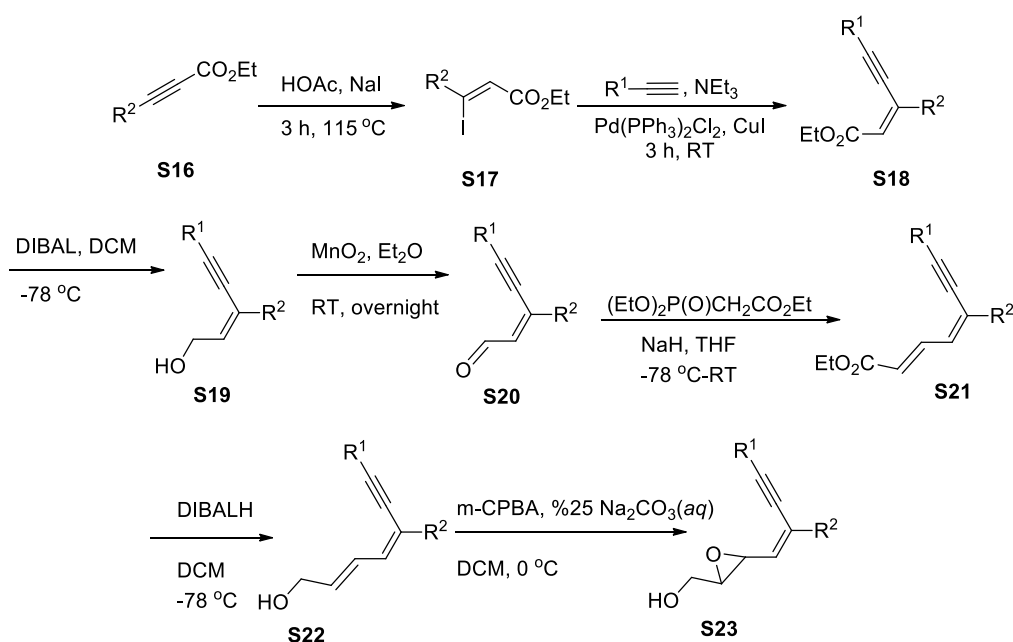
To a solution of alkynoic ester **S16** (40 mmol) and acetic acid (240 mmol, 13.8 mL or 512 mmol, 20.8 mL when **S16** is ethyl 4, 4-dimethylpent-2-ynoate and ethyl 3-cyclohexylpropiolate) was added sodium iodide (9.6 g, 64 mmol or 19.2 g, 128 mmol when **S23** is ethyl 4, 4-dimethylpent-2-ynoate and ethyl 3-cyclohexylpropiolate) and stirred for 3 h at 115 °C. After completion of the reaction, the brown mixture was transferred while hot to a separatory funnel containing water (10 mL/mmol of the ester substrate). The reaction flask was washed with a mixture of water (5 mL) and diethyl ether (30 mL/mmol of the ester substrate). The washings were combined in a separatory funnel. The phases were separated and the aqueous phase was extracted with diethyl ether.

The combined organic phases were treated sequentially with saturated aqueous NaHCO$_3$(aq), Na$_2$S$_2$O$_3$(aq) (1 M), and brine and then dried over MgSO$_4$, filtered, and concentrated under reduced pressure. The product was purified by column chromatography on silica gel (hexane-EtOAc, yields; R^2= H, 7.6 g, 84%; R^2= Me, 8.4 g, 87%; R^2= t-Bu, 9.6 g, 85%; R^2= Cy, 10.6 g, 86%), (Piers, *et al.* 1994).

A mixture of **S17** (30 mmol), PdCl$_2$(PPh$_3$)$_2$ (210.6 mg, 0.3 mmol, 1% mol of Pd), and CuI (29 mg, 0.15 mmol, 0.5% mol of Cu) in 140 mL of Et$_3$N was stirred for 10 min at RT under Ar, and then, to this mixture was added a terminal alkyne (36 mmol). The mixture was stirred at RT for 3h. At the end of the reaction, water was added to the resulting mixture and then extracted with Et$_2$O. The combined organic layers were dried over MgSO$_4$. The solvent was evaporated in vacuo and the product **S18** was purified by column chromatography on silica gel (hexane-EtOAc, yields: R^1= Bu, R^2= H, 4.97 g, 92%; R^1= Ph, R^2= Me, 5.97 g, 93%; R^1= Cy, R^2= Me, 5.94 g, 90%; R^1= *t*-Bu, R^2= Me, 4.95 g, 85%; R^1= Bu, R^2= t-Bu 6.23 g, 88%, R^1= Bu, R^2= Cy, 6.21 g, 79%).

A DIBALH (~3 eq, 1.0 M in cyclohexane) solution was added dropwise to the solution of **S18** in DCM (~6 mL/mmol **S18**) at −78 °C. After the reaction mixture was stirred for 4 h at the same temperature, 1 M HCl(aq) solution was added before extracting with DCM. The organic layers were combined, washed with brine, dried over MgSO$_4$, filtered, and concentrated under reduced pressure. The crude mixture was subjected to silica gel column chromatography to purify the corresponding **S19** compound (hexane-EtOAc; yields of **S19**: R^1= Bu, R^2= H, 3.14 g, 91%; R^1= Bu, R^2= Cy, 4.89 g, 89%;R^1= Cy, R^2= Me, 3.60 g, 81%; R^1= *t*-Bu, R^2= Me, 3.57 g, 94%; R^1= Bu, R^2= *t*-Bu, 4.2 g, 88%; R^1= Ph, R^2= Me, 3.87 g, 90%), (Kajikawa, *et al.* 2009).

To the solution of **S19** (≈20 mmol) in 70 mL of dry diethyl ether, activated MnO$_2$ (35.1 g, 0.35 mol) was added, and the mixture was stirred overnight at RT. After filtration through Celite, the solution was concentrated under reduced pressure. The crude aldehyde (**S20**) was used in the next step (Betzer, *et al.* 1997).

To a solution of NaH (1.1 eq) in THF (2.5 mL/mmol **S20**) was added triethyl phosphonoacetate (1.2 eq) at 0 °C and the mixture stirred for 1 h at RT. Subsequently, to the reaction mixture was added **S20** (6.5-10 mmol) dropwise at -78 °C, and stirred for 1 h at RT. The reaction was terminated by the addition of saturated NH$_4$Cl(aq) and extracted with Et$_2$O. The organic layer was dried over MgSO$_4$, filtered, and concentrated under reduced pressure to obtain **S21** with *E/Z* isomeric ratios varying in the range of 97:3 to 95:5 (Urabe, *et al.* 1997). The crude mixture was purified on silica gel column (hexane-

EtOAc) to obtain **S21** in pure isomeric form (yields of **S21** R^1= Bu, R^2= H, 1.48 g, 72%; R^1= Bu, R^2= Cy, 1.4 g, 68%; R^1= Cy, R^2= Me, 1.97 g, 80%; R^1= t-Bu, R^2= Me, 1.80 g, 82%; R^1= Bu, R^2= t-Bu, 2.12 g, 81%; R^1= Ph, R^2= Me, 2.04 g, 85%).

A DIBALH (~3 eq, 1.0 M in cyclohexane) solution was added dropwise to the solution of **S21** in DCM (~6 mL/mmol **S21**) at −78 °C. After the reaction mixture was stirred for 4 h at the same temperature, 1 M HCl(*aq*) solution was added before extracting with DCM. The organic layers were combined, washed with brine, dried over MgSO$_4$, filtered, and concentrated under reduced pressure. The crude mixture was subjected to silica gel column chromatography to purify the corresponding **S22** compound (hexane-EtOAc; yields of **S22**: R^1= Bu, R^2= H, 1.12 g, 95%; R^1= Bu, R^2= Cy, 1.1 g, 94%;R^1= Cy, R^2= Me, 1.55 g, 95%; R^1= t-Bu, R^2= Me, 1.39 g, 95%; R^1= Bu, R^2= t-Bu, 1.6 g, 90%; R^1= Ph, R^2= Me, 1.6 g, 92%), (Kajikawa, *et al.* 2009).

The epoxidation of **S22** (2 mmol) and isolation of the corresponding **S23** products were performed as specified for (*Z*)-**1a** (yields of **S23**: R^1= Bu, R^2= H, 0.19 g, 55%; R^1= Bu, R^2= Cy, 0.26 g, 49%; R^1= Cy, R^2= Me, 0.25 g, 57%; R^1= t-Bu, R^2= Me, (*Z*)-**1q,** 0.25 g, 65%; R^1= Bu, R^2= t-Bu, 0.24 g, 50%; R^1= Ph, R^2= Me, 0.26 g, 60%).

3.2.6. Synthesis of (*Z*)-1b, c, h, k, l, n, o, p, s
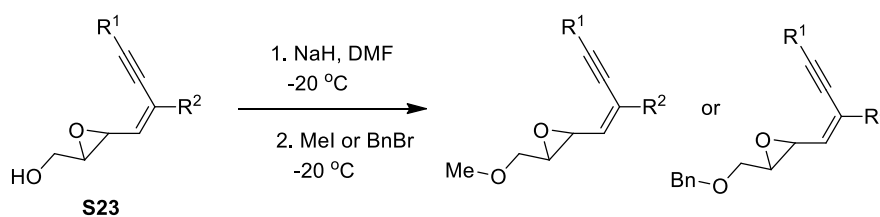
As for the alkylation of the pendant hydroxyl group of **S23**, a suspension of sodium hydride (1.1 eq) in DMF (1 mL) was added to a solution of **S23** (1 mmol) in DMF (1 mL/mmol **S23**) at -20 °C. The mixture was stirred for further 30 min before the addition of methyl iodide (1.2 eq) or benzyl bromide (1.2 eq). The mixture was stirred for 4 h at the same temperature and then the reaction was terminated by the addition of MeOH (5 mL) and brine (5 mL), and extracted with DCM. The combined extracts were dried over MgSO$_4$, filtered, and concentrated under reduced pressure. The crude mixture was subjected to column chromatography over NEt$_3$-pretreated short silica gel column to

afford the corresponding alkoxy-substituted enyne oxirane products as colorless oil (hexane-EtOAc, yields: (*Z*)-**1b**, 0.18 g, 87%; (*Z*)-**1c**, 0.22 g, 77%; (*Z*)-**1h**, 0.17 g, 90%; (*Z*)-**1k**, 0.24 g, 87%; (*Z*)-**1l**, 0.21 g, 83%; (*Z*)-**1n**, 0.19 g; 84%; (*Z*)-**1o**, 0.19 g, 90%; (*Z*)-**1p**, 0.24 g, 85%; (*Z*)-**1s**, 0.20 g, 87%), (Caldentey, *et al.* 2011).

3.2.7. Synthesis of (*Z*)-1e and (*Z*)-1r

(*Z*)-**1d**; R^1= Bu, R^2= Me
(*Z*)-**1q**; R^1= *t*-Bu, R^2= Me

S24
(*Z*)-**1e**; R^1= Bu, R^2= Me
(*Z*)-**1r**; R^1= *t*-Bu, R^2= Me
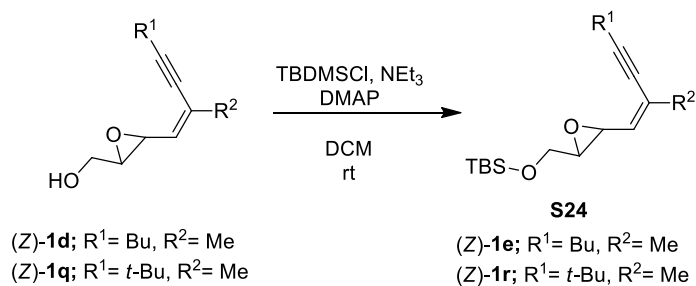
A mixture of (*Z*)-**1d** (194, mg, 1 mmol) or (*Z*)-**1q** (227 mg, 1.17 mmol), Et$_3$N (0.18 mL, 1.3 mmol), *t*-butyldimethylsilyl chloride (0.2 g, 1.3 mmol), and 4-dimethylaminopyridine (DMAP) (15 mg, 0.12 mmol) in CH$_2$Cl$_2$ (12 mL) was stirred at RT for 24 h. Then, the reaction was terminated by water and the content of the reaction flask was extracted with DCM. The organic solution was dried with MgSO$_4$, filtered, and evaporated. The residue was chromatographed over NEt$_3$-pretreated short silica gel column to afford silylated enyne oxiranes as a colorless oil (hexane-EtOAc, yields: (*Z*)-**1e**, 0.28 g, 79%; (*Z*)-**1r**, 0.25 g, 81%), (Schmidt, *et al.* 2002).

3.2.8. Synthesis of (Z)-1f and (Z)-1g
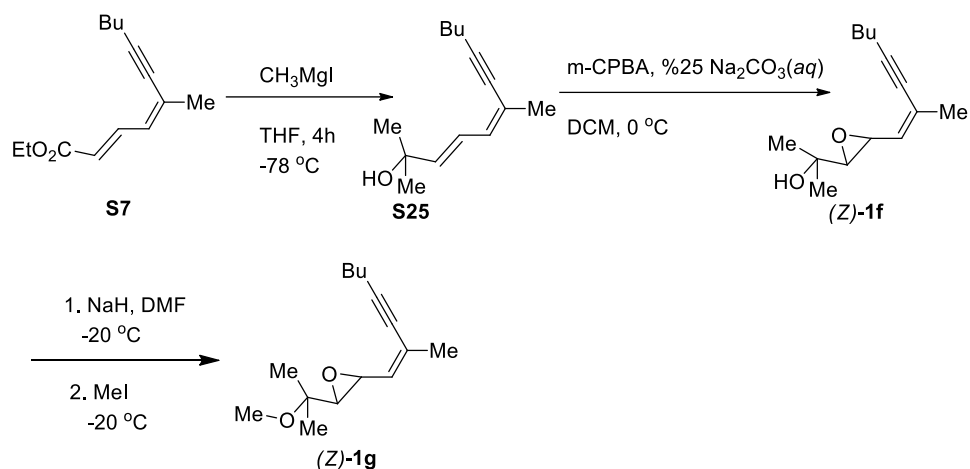
To the dry Et$_2$O (15 mL) solution of **S7** (1.1 g, 5 mmol) was added an ethereal (15 mL) solution of 2.1 eq. MeMgI (5.25 mL, 10.5 mmol, 2 M) dropwise at -50 °C, and then the mixture stirred for 6 h at the same temperature. The mixture was allowed to warm to 0 °C and quenched by the addition of 30 mL of saturated NH$_4$Cl(*aq*) solution before extracting with Et$_2$O. The combined extracts were dried over MgSO$_4$, filtered, and evaporated. The resulting residue was purified on a silica gel column to afford **S25** (hexane-EtOAc, yield: 0.49 g, 80%).

The epoxidation of **S25** (412 mg, 2 mmol), and isolation of the product (Z)-**1f** was performed as specified for (Z)-**1i** (hexane-EtOAc, yield: 0.27 g, 60%).

The hydroxyl group of (Z)-**1f** (222 mg, 1.0 mmol) was methylated as described above furnishing the enyne oxirane (Z)-**1g** in 90% yield (0.21 g).

3.2.9. Synthesis of (*E*)-1b

Synthesis of (*E*)-**1b** was performed starting from (*E*)-configured **S1** following the same method employed for the synthesis of (Z)-**1b**. Yields: (R^1= Bu, R^2= Me): (*E*)-**S7**, 1.12 g, 79%; (*E*)-**1d**, 0.83 g, 91%; (produced from 4.6 mmol of (*E*)-**S8**), 0.43 g, 47%; (*E*)-**1b** (produced from 2.2 mmol of (*E*)-**1d**), 0.40 g, 88%.

3.2.10. Synthesis of (Z)-1t
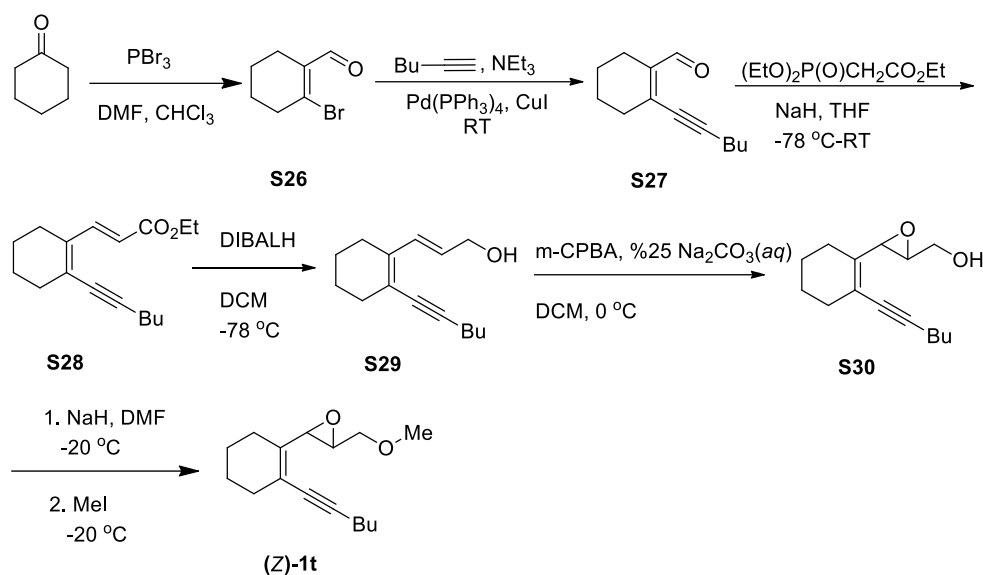
PBr₃ (1.4 mL, 13.8 mmol) was added dropwise to a mixture of DMF (1.2 mL, 15.3 mmol) and chloroform (10 mL) at 0 °C and then the resulting mixture was stirred for 1 h. Subsequently, 0.5 g of cyclohexanone (6 mmol) was added dropwise and stirred for 8 h at RT. The reaction was terminated with water, neutralized with the addition of solid NaHCO₃, and extracted with DCM. The extract was washed with brine, dried over MgSO₄, filtered, and concentrated under reduced pressure. The purification on short silica gel column provided the compound **S26** (hexane-EtOAc, 0.92 g, 81%), (Lian, *et al.* 2006).

A mixture of **S26** (945 mg, 5 mmol), Pd(PPh₃)₄ (123 mg, 0.1 mmol, 2 mol % of Pd), and CuI (21 mg, 0.1 mmol, 2 mmol % of Cu) in 10 mL of Et₃N was stirred for 10 min at RT followed by the addition of 1-hexyne (0.5 g, 6 mmol). After being stirred for 3 h at RT, water was added and extracted with Et₂O. The combined organic phases were dried over MgSO₄, filtered, and concentrated under reduced pressure. The residue was purified by column chromatography on silica gel to obtain endocyclic enyne aldehyde **S27** (hexane-EtOAc, 0.84 g, 90%), (Lian, *et al.* 2006).

The conversion of **S27** (840 mg, 4.42 mmol) to dienyne ester **S28** was performed by HWE reaction as described above (hexane-EtOAc, 0.96 g, 84%). Further successive synthetic procedures; which involved the reduction of the ester **S28** (960 mg, 3.7 mmol) to the enyne alcohol **S29** (730 mg, 91% yield), the epoxidation of **S29** (436 mg, 2 mmol)

to **S30** (260 mg, 55% yield), and finally methyl derivatization of hydroxyl group of **S30** (260 mg, 1.1 mmol) to obtain (*Z*)-**1r** (0.22 g, 90%) were all conducted as described above.

3.2.11. Synthesis of (*Z*)-1j
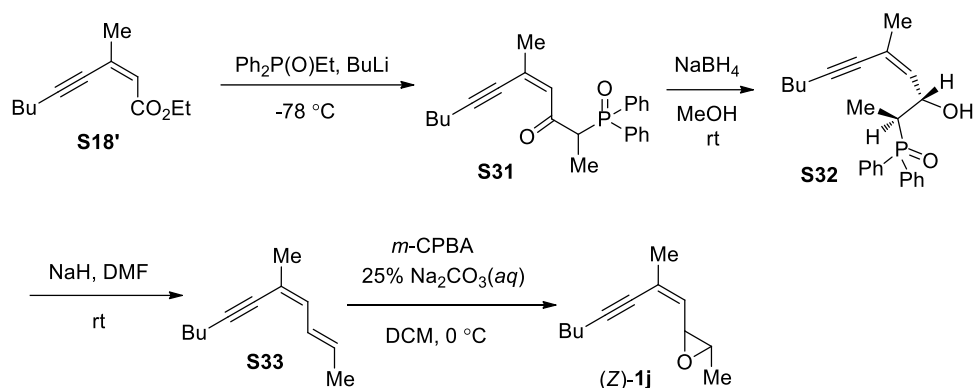
To a stirred solution of diphenylethylphosphine oxide (4.6 g, 20 mmol) in dry THF (70 mL) was added BuLi (2.5 M in hexane, 8.8 mL, 22 mmol) dropwise at 0 °C and stirred for a further 30 min. The solution was cooled to -78 °C and then the dienyne ester **S18'** (3.88 g, 20 mmol) was added dropwise. The solution was allowed to warm to ambient temperature and subsequently stirred overnight. Saturated NH$_4$Cl(*aq*) solution was added and subsequently its THF content was removed under reduced pressure. The aqueous residue was diluted with brine (20 mL) and extracted with DCM. The combined organic phases were dried over MgSO$_4$, filtered, and concentrated under reduced pressure. The product **S31** was purified by column chromatography on silica gel (hexane-EtOAc, yield: 1.9 g, 25%), (Buss, *et al.* 1985).

To a stirred solution of **S31** (1.9 g, 5 mmol) in ethanol (50 mL) was added NaBH$_4$ (189 mg, 5 mmol) in one portion and stirred for a further 8h at ambient temperature. The reaction afforded **S32** enriched in *threo* form. Saturated NH$_4$Cl(*aq*) (15 mL) was added and subsequently its ethanol content was removed under reduced pressure. The aqueous mixture was diluted with brine (20 mL), extracted with DCM. The combined organic layers were dried over MgSO$_4$, filtered, and concentrated under reduced pressure. The product **S32** was isolated in pure *threo* form by column chromatography on silica gel (hexane-EtOAc, yield: 1.31 g, 69%), (Buss, *et al.* 1985).

To a stirred solution of **S32** (1.31 g, 3.45 mmol) in DMF (50 ml) was added NaH (60% dispersion in oil; 138 mg, 3.45 mmol) in one portion at ambient temperature and

stirred for a further 3 h. The reaction was quenched by the addition 25 mL of water and 15 mL of brine and subsequently extracted with Et₂O. The combined extracts were washed with water, dried over MgSO₄, filtered, and concentrated under reduced pressure. The product **S33** was purified by column chromatography on silica gel (hexane, yield: 330 mg, 59%), (Buss, *et al.* 1985).

The epoxidation of **S33** (162 mg, 1 mmol) and isolation of the product (*Z*)-**1j** was performed as specified for (*Z*)-**1i** (Hexane-EtOAc, yield: 35.6 mg, 20%).

3.2.12. Carbamate derivatization of 2ba and crystal growth for X-ray analysis
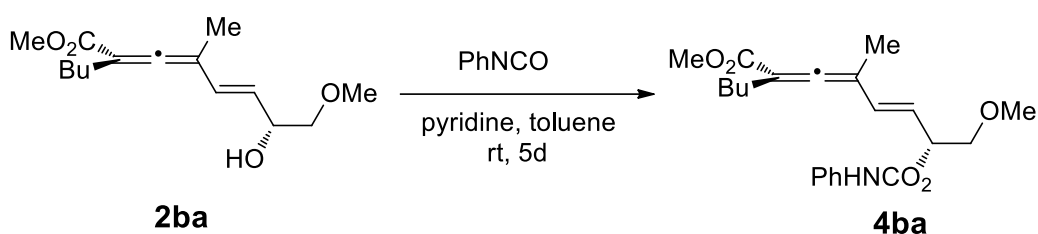
The mixture of vinylallene ester (45.2 mg, 0.2 mmol), phenyl isocyanate (31 mg, 0.26 mmol), and dry pyridine (15.8 mg, 0.2 mmol) in 2 mL of toluene was stirred at RT for 5 days. The mixture was taken into Et₂O and washed with brine, dried over MgSO₄, and filtered. The solvent was removed in vacuum, and the crude residue was purified by column chromatography on silica gel (hexane-EtOAc; 5:1, yield: 0.62 g, 80%). The pure white solid material was dissolved in a boiled hexane and gradually cooled down to 30 °C all through overnight.

3.3. Characterization of Reactants

NMR spectra were recorded on a 400 MHz spectrometer. Chemical shifts are reported in ppm downfield from Me$_4$Si.

(Z)-**1a**
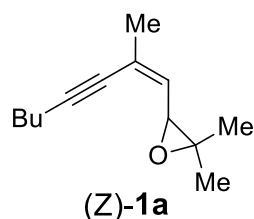
(Z)-**1a:** ^{1}H NMR (400 MHz , CDCl$_3$) δ: 5.38 (dq, J= 8.9, 1.5 Hz, 1H), 3.65 (d, J= 8.9 Hz, 1H), 2.34 (t, J= 6.8 Hz, 2H), 1.87 (s, 3H), 1.56-1.36 (m, 4H), 1.35 (s, 3H), 1.27 (s, 3H), 0.9 (t, J= 7.2 Hz, 3H); ^{13}C{1H} NMR (100 MHz, CDCl$_3$) δ: 130.7, 125.5, 95.9, 79.1, 62.6, 60.5, 30.9, 24.9, 24.2, 22.1, 19.6, 19.3, 13.7.

(Z)-**1b**
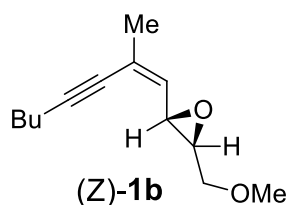
(Z)-**1b:** ^{1}H NMR (400 MHz, CDCl$_3$) δ: 5.23 (dd, J= 8.9, 1.2 Hz, 1H), 3.74 (dd, J= 8.9, 2.4 Hz, 1H), 3.71 (dd, J= 11.6, 3.2 Hz, 1H), 3.40 (dd, J= 11.6, 5.7 Hz, 1H), 3.40 (s, 3H), 3.08 (ddd, J= 5.7, 3.2, 2.4 Hz, 1H), 2.35 (t, J= 7.2 Hz, 2H), 1.87 (d, J= 1.2 Hz, 3H), 1.55-1.40 (m, 4H), 0.92 (t, J= 7.2 Hz, 3H); ^{13}C{1H} NMR (100 MHz, CDCl$_3$) δ: 131.5, 125.7, 95.9, 78.7, 72.5, 59.2, 58.3, 54.2, 30.7, 23.8, 21.9, 19.1, 13.6.

(E)-**1b**
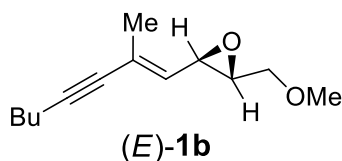
(E)-**1b:** (400 MHz, CDCl$_3$) δ: 5.35 (dd, J= 9.0, 1.0 Hz, 1H), 3.67 (dd, J= 11.3, 3.0 Hz, 1H), 3.48 (dd, J= 9.0, 2.2 Hz, 1H), 3.44 (dd, J= 11.3, 5.1 Hz, 1H), 3.38 (s, 3H), 3.06 (ddd, J= 5.1, 3.0, 2.2 Hz, 1H), 2.28 (t, J= 6.8 Hz, 2H), 1.93 (d, J= 1.0 Hz, 3H), 1.54-1.37 (m, 4H), 0.90 (t, J= 7.6 Hz, 3H); ^{13}C{1H} NMR (100 MHz, CDCl$_3$) δ: 131.3, 125.2, 90.3, 82.4, 80.0, 59.2, 58.6, 51.9, 30.7, 21.9, 18.9, 18.2, 13.6.

(Z)-**1c**
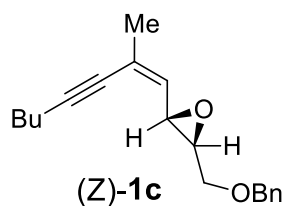
(Z)-**1c:** ^{1}H NMR (400 MHz, C$_6$D$_6$) δ: 7.24-7.22 (m, 2H), 7.14-7.10 (m, 2H), 7.05 (dt, J= 7.2, 1.6 Hz, 1H), 5.14 (dd, J= 8.9, 1.6 Hz, 1H), 4.35 (d, A of AB, J_{AB}=12.1 Hz, 1H), 4.31 (d, B of AB, J_{AB}=12.1 Hz, 1H), 4.01 (dd, J= 8.9, 2.2 Hz, 1H), 3.45 (dd, J= 11.4, 3.0 Hz, 1H), 3.25 (dd, J= 11.4, 5.5 Hz, 1H), 2.95 (ddd, J= 5.5, 3.0, 2.2 Hz, 1H), 2.06 (t, J= 6.8 Hz, 2H), 1.71 (d, J= 1.6 Hz, 3H), 1.29-1.16 (m, 4H), 0.7 (t, J= 7.2 Hz, 3H); ^{13}C{1H} NMR (100 MHz, C$_6$D$_6$) δ: 138.5, 132.8, 128.2, 127.4, 127.3, 124.8, 95.5, 79.1, 72.8, 70.0, 58.2, 53.8, 30.6, 23.5, 21.8, 18.9, 13.3.

(Z)-**1d**
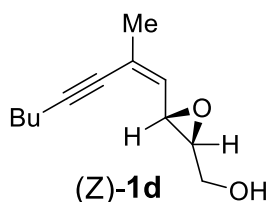
(Z)-**1d:** ^{1}H NMR (400 MHz, CDCl$_3$) δ: 5.25 (dd, J= 9.0, 1.4 Hz, 1H), 3.96 (dd, J= 12.6, 2.3 Hz, 1H), 3.87 (dd, J= 9.0, 2.3 Hz, 1H), 3.68 (dd, J= 12.6, 4.1 Hz, 1H), 3.11-3.09 (m, 1H), 2.36 (t, J= 7.0 Hz, 2H), 1.88 (d, J= 1.4 Hz, 3H), 1.56-1.39 (m, 4H), 0.92 (t, J= 7.2 Hz, 3H); ^{13}C{1H} NMR (100 MHz, C$_6$D$_6$) δ: 132.5, 124.8, 95.7, 79.1, 61.1, 59.5, 53.7, 30.6, 23.5, 21.8, 19.0, 13.3.

(Z)-**1e**
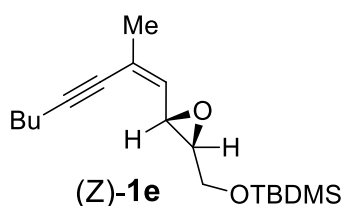
(Z)-**1e:** ^{1}H NMR (400 MHz, CDCl$_3$) δ: 5.22 (dd, J= 9.1, 1.5 Hz, 1H), 3.86 (dd, J= 12.1, 3.2 Hz, 1H), 3.76 (dd, J= 9.1, 2.4 Hz, 1H), 3.71 (dd, J= 12.1, 4.8 Hz, 1H), 3.00 (ddd, J= 4.8, 3.2, 2.4 Hz, 1H), 2.33 (t, J= 7.2 Hz, 2H), 1.86 (d, J= 1.5 Hz, 3H), 1.56-1.37 (m, 4H), 0.91 (t, J= 6.8 Hz, 3H), 0.89 (s, 9H), 0.07 (s, 3H), 0.06 (s, 3H). ^{13}C{1H} NMR (100 MHz, CDCl$_3$) δ: 131.9, 125.3, 95.7, 78.7, 63.0, 60.1, 54.3, 30.8, 25.8, 23.8, 22.0, 19.1, 18.3, 13.6, -5.3, -5.4.

(Z)-**1f** structure
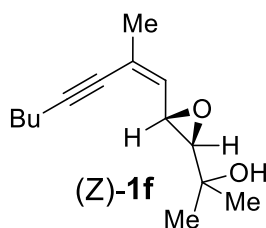
(Z)-**1f:** ¹H NMR (400 MHz, CDCl₃) δ: 5.26 (dd, *J*= 8.8, 1.6 Hz, 1H), 3.89 (dd, *J*= 8.8, 2.3 Hz, 1H), 2.88 (d, *J*= 2.3 Hz, 1H), 2.36 (t, *J*= 7.0 Hz, 2H), 1.87 (d, *J*= 1.6 Hz, 3H), 1.78 (d, *J*= 0.8 Hz, 1H), 1.57-1.40 (m, 4H), 1.31 (s, 3H), 1.25 (s, 3H), 0.92 (t, *J*= 6.8 Hz, 3H); ¹³C{1H} NMR (100 MHz, CDCl₃) δ: 132.0, 125.1, 78.8, 73.8, 64.7, 53.3, 50.7, 30.7, 23.7, 22.2, 21.9, 21.0, 19.1, 13.5.

(Z)-**1g** structure
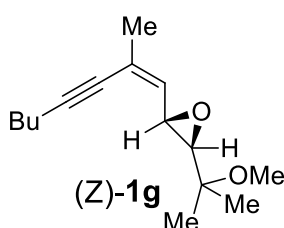
(Z)-**1g:** ¹H NMR (400 MHz, CDCl₃) δ: 5.24 (dd, *J*= 8.9, 1.5 Hz, 1H), 3.69 (dd, *J*= 8.9, 2.3 Hz, 1H), 3.29 (s, 3H), 2.87 (d, *J*= 2.3 Hz, 1H), 2.36 (t, *J*= 6.7 Hz, 2H), 1.87 (d, *J*= 1.5 Hz, 3H), 1.56-1.39 (m, 4H), 1.18 (s, 3H), 1.15 (s, 3H), 0.92 (t, *J*= 7.2 Hz, 3H); ¹³C{1H} NMR (100 MHz, CDCl₃) δ: 132.2, 125.3, 95.8, 79.0, 74.0, 64.9, 53.4, 50.9, 30.9, 23.9, 22.4, 22.0, 21.1, 19.2, 13.7.

(Z)-**1h** structure
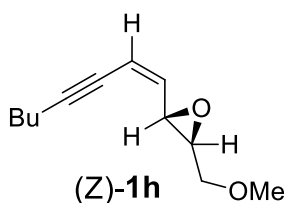
(Z)-**1h:** ¹H NMR (400 MHz, CDCl₃) δ: 5.75 (dtd, *J*= 10.8, 2.4, 0.8 Hz, 1H), 5.44 (dd, *J*= 10.8, 8.8 Hz, 1H), 3.80 (dd, *J*= 8.8, 2.2 Hz, 1H), 3.74 (dd, *J*= 11.2, 2.8 Hz, 1H), 3.44-3.38 (m, 1H), 3.41 (s, 3H), 3.11 (dt, *J*= 5.4, 2.6 Hz, 1H), 2.36 (td, *J*= 6.8, 2.3 Hz, 2H), 1.58-1.41 (m, 4H), 0.92 (t, *J*= 7.2 Hz, 3H); ¹³C{1H} NMR (100 MHz, CDCl₃) δ: 137.2, 115.4, 97.1, 72.3, 59.2, 58.2, 53.3, 50.4, 30.6, 21.9, 19.2, 13.5.

(Z)-**1i**
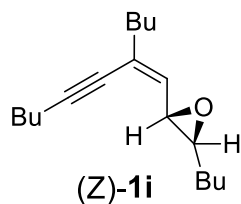
(Z)-**1i:** ^{1}H NMR (400 MHz, C$_6$D$_6$) δ: 5.32 (d, *J*= 8.7 Hz, 1H), 3.90 (dd, *J*= 8.7, 2.3 Hz, 1H), 2.71 (td, *J*= 5.5, 2.3 Hz, 1H), 2.11 (t, *J*= 6.8 Hz, 2H), 2.10 (t, *J*= 6.4 Hz, 2H), 1.54-1.15 (m, 14H), 0.84-0.70 (m, 9H); ^{13}C{1H} NMR (100 MHz, C$_6$D$_6$) δ: 137.5, 133.3, 95.7, 78.6, 59.6, 56.4, 37.4, 31.8, 30.7, 30.3, 28.0, 22.4, 22.0, 21.8, 19.0, 13.7, 13.6, 13.3.

(Z)-**1i'**
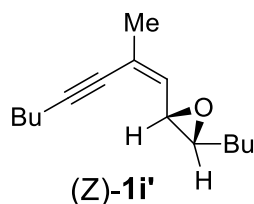
(Z)-**1i':** ^{1}H NMR (400 MHz, CDCl$_3$) δ: 5.38 (d, *J*= 9.0, 1H), 3.90 (dd, *J*= 9.0, 4.8 Hz, 1H), 3.11 (q, *J*= 4.8 Hz, 1H), 2.37 (t, *J*= 6.8 Hz, 2H), 2.15 (td, *J*= 7.6, 0.8 Hz, 2H), 1.60-1.25 (m, 14H), 0.95-0.88 (m, 9H); ^{13}C{1H} NMR (100 MHz, CDCl$_3$) δ: 130.8, 128.9, 96.4, 78.1, 59.1, 55.4, 37.5, 30.8, 30.2, 28.5, 28.2, 22.5, 21.9, 21.9, 19.2, 14.0, 13.9, 13.8.

(Z)-**1j**
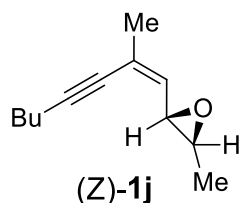
(Z)-**1j:** ^{1}H NMR (400 MHz, C$_6$D$_6$) δ: 5.16 (dd, *J*= 8.9, 1.4 Hz, 1H), 3.75 (dd, *J*= 8.9, 2.1 Hz, 1H), 2.64 (qd, *J*= 5.4, 2.1 Hz, 1H), 2.08 (t, *J*= 6.8 Hz, 2H), 1.73 (d, *J*= 1.4 Hz, 3H), 1.31-1.20 (m, 4H), 1.04 (d, *J*= 5.2 Hz, 3H), 0.72 (t, *J*= 7.2 Hz, 3H); ^{13}C{1H} NMR (100 MHz, C$_6$D$_6$) δ: 133.7, 123.9, 95.2, 79.3, 57.4, 55.2, 30.6, 23.4, 21.8, 19.0, 17.3, 13.2.

(Z)-**1k**
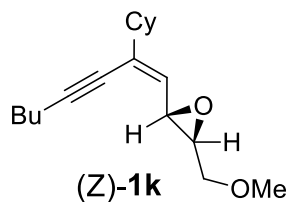
(Z)-**1k:** ^{1}H NMR (400 MHz, CDCl$_3$) δ: 5.21 (d, *J*= 8.7 Hz, 1H), 3.77 (dd, *J*= 8.7, 2.4 Hz, 1H), 3.72 (dd, *J*= 11.5, 3.1 Hz, 1H), 3.38 (dd, *J*= 11.5, 5.7 Hz, 1H), 3.40 (s, 3H),

3.07 (dt, $J= 5.7$, 2.4 Hz, 1H), 2.37 (t, $J= 7.2$ Hz, 2H), 2.02-1.97 (m, 1H), 1.76-1.20 (m, 14H), 0.92 (t, $J= 7.2$ Hz, 3H); ^{13}C{1H} NMR (100 MHz, CDCl$_3$) δ: 136.3, 129.1, 97.0, 76.7, 72.6, 59.2, 58.5, 54.3, 45.4, 31.7, 31.6, 30.8, 29.7, 26.2, 26.0, 22.0, 19.2, 13,6.

(Z)-1l
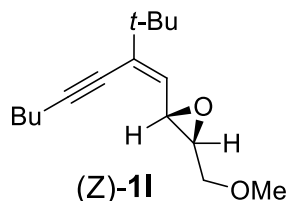
(Z)-**1l:** ^{1}H NMR (400 MHz, CDCl$_3$) δ: 5.24 (d, $J= 8.9$ Hz, 1H), 3.81 (dd, $J= 8.9$, 2.4 Hz, 1H), 3.74 (dd, $J= 11.2$, 3.1 Hz, 1H), 3.42-3.38 (m, 1H), 3.41 (s, 3H), 3.10 (ddd, $J= 5.6$, 3.1, 2.4 Hz, 1H), 2.39 (t, $J= 7.2$ Hz, 2H), 1.59-1.41 (m, 4H), 1.11 (s, 9H), 0.93 (t, $J= 7.6$ Hz, 3H); ^{13}C{1H} NMR (100 MHz, CDCl$_3$) δ: 140.2, 127.4, 97.4, 72.7, 59.2, 58.5, 54.7, 36.1, 30.8, 28.9, 21.9, 19.2, 13.6.

(Z)-**1m**
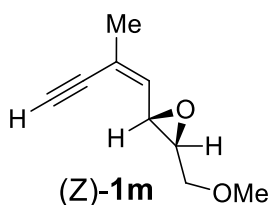
(Z)-**1m:** ^{1}H NMR (400 MHz, C$_6$D$_6$) δ: 5.10 (dq, $J= 8.9$, 1.0 Hz, 1H), 3.84 (dd, $J= 8.9$, 2.0 Hz, 1H), 3.25 (dd, $J= 11.5$, 3.0 Hz, 1H), 3.06-2.99 (m, 1H), 3.05 (s, 3H), 2.83 (ddd, $J= 5.5$, 3.0, 2.0 Hz, 1H), 2.74 (s, 1H), 1.57 (d, $J= 1.0$ Hz, 3H); ^{13}C{1H} NMR (100 MHz, C$_6$D$_6$) δ: 136.0, 122.9, 82.4, 81.5, 72.2, 58.4, 58.0, 53.2, 22.7.

(Z)-**1n**
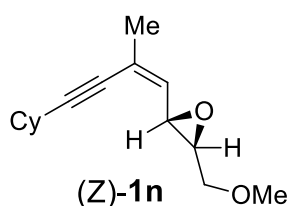
(Z)-**1n:** ^{1}H NMR (400 MHz, C$_6$D$_6$) δ: 5.14 (dq, $J= 9.0$, 1.4 Hz, 1H), 4.01 (dd, $J= 9.0$, 2.0 Hz, 1H), 3.35 (dd, $J= 11.3$, 3.2 Hz, 1H), 3.16 (dd, $J= 11.3$, 5.5 Hz, 1H), 3.09 (s, 3H), 2.91 (ddd, $J= 5.5$, 3.2, 2.0 Hz, 1H), 2.34 (m, 1H), 1.71 (d, $J= 1.4$ Hz, 3H), 1.66-1.03 (m, 10H); ^{13}C{1H} NMR (100 MHz, C$_6$D$_6$) δ: 132.7, 124.7, 99.5, 79.2, 72.4, 58.5, 58.1, 53.7, 32.5, 32.4, 29.6, 25.7, 24.6, 23.5.

(Z)-**1o**
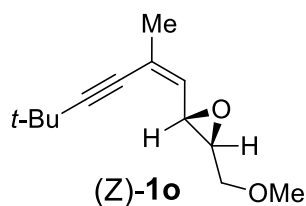
(Z)-**1o:** ^{1}H NMR (400 MHz, C$_6$D$_6$) δ: 5.12 (dd, *J*= 8.5, 1.3 Hz, 1H), 3.95 (dd, *J*= 8.5, 2.3 Hz, 1H), 3.34 (dd, *J*= 11.5, 3.1 Hz, 1H), 3.16 (dd, *J*= 11.5, 5.5 Hz, 1H), 3.09 (s, 3H), 2.90 (ddd, *J*= 5.5, 3.1, 2.3 Hz, 1H), 1.68 (d, *J*= 1.3 Hz, 3H), 1.12 (s, 9H); ^{13}C{1H} NMR (100 MHz, C$_6$D$_6$) δ: 132.8, 124.5, 103.4, 77.7, 72.4, 58.5, 58.0, 53.7, 30.6, 27.9, 23.4.

(Z)-**1p**
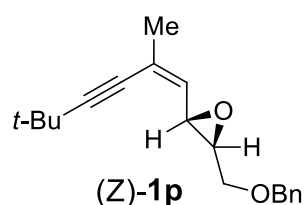
(Z)-**1p:** ^{1}H NMR (400 MHz, CDCl$_3$) δ: 7.35-7.28 (m, 5H), 5.22 (dq, *J*= 8.9, 1.4 Hz, 1H), 4.61 (d, A of AB, *J*$_{AB}$=12.0 Hz, 1H), 4.57 (d, B of AB, *J*$_{AB}$=12.0 Hz, 1H), 3.81 (dd, *J*= 11.3, 3.0 Hz, 1H), 3.76 (dd, *J*= 8.9, 2.2 Hz, 1H), 3.53 (dd, *J*= 11.3, 5.5 Hz, 1H), 3.13 (ddd, *J*= 5.5, 3.0, 2.2 Hz, 1H), 1.86 (d, *J*= 1.4 Hz, 3H), 1.24 (s, 9H); ^{13}C{1H} NMR (100 MHz, CDCl$_3$) δ: 140.0, 137.9, 131.3, 128.4, 127.7, 125.7, 104.0, 77.1, 73.3, 70.1, 58.6, 54.3, 31.0, 28.1, 23.8.

(Z)-**1q**
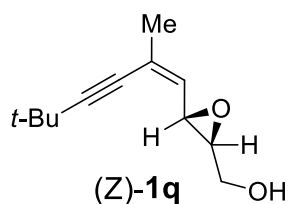
(Z)-**1q:** ^{1}H NMR (400 MHz, C$_6$D$_6$) δ: 5.17 (dd, *J*= 8.9, 1.1 Hz, 1H), 4.1 (dd, *J*= 8.9, 2.3 Hz, 1H), 3.54-3.48 (m, 1H), 3.34-3.30 (m, 1H), 2.75-2.73 (m, 1H), 1.73 (d, *J*= 1.1 Hz, 3H), 1.17 (s, 9H); ^{13}C{1H} NMR (100 MHz, C$_6$D$_6$) δ: 132.5, 124.6, 103.7, 77.6, 61.0, 59.4, 53.6, 30.6, 27.9, 23.4.

(Z)-**1r**
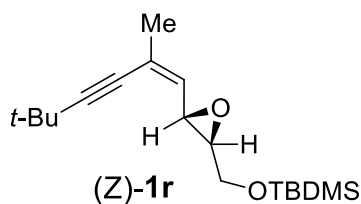
(Z)-**1r:** ^{1}H NMR (400 MHz, CDCl$_3$) δ: 5.21 (d, J= 9.0 Hz, 1H), 3.87 (dd, J= 12.0, 3.2 Hz, 1H), 3.74 (m, 2H), 3.01 (m, 1H), 1.86 (s, 3H), 1.26 (s, 9H), 0.90 (s, 9H), 0.08 (s, 6H); ^{13}C{1H} NMR: (100 MHz, CDCl$_3$) δ: 131.6, 125.3, 103.8, 77.1, 62.9, 60.2, 54.3, 31.0, 28.1, 25.9, 23.9, 18.3, -5,3.

(Z)-**1s**
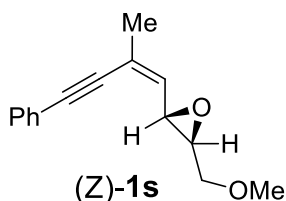
(Z)-**1s:** ^{1}H NMR (400 MHz, CDCl$_3$) δ: 7.46-7.44 (m, 2H), 7.34-7.32 (m, 3H), 5.38 (dq, J= 9.0, 1.5 Hz, 1H), 3.84 (dd, J= 9.0, 2.4 Hz, 1H), 3.74 (dd, J= 11.7, 3.2 Hz, 1H), 3.43 (dd, J= 11.7, 6.0 Hz, 1H), 3.42 (s, 3H) 3.14 (ddd, J= 6.0, 3.2, 2.4 Hz, 1H), 2.00 (d, J= 1.5 Hz, 3H); ^{13}C{1H} NMR (100 MHz, CDCl$_3$) δ: 133.1, 131.5, 128.5, 128.3, 124.9, 122.9, 94.5, 87.3, 72.5, 59.2, 58.5, 54.1, 23.4.

(Z)-**1t**
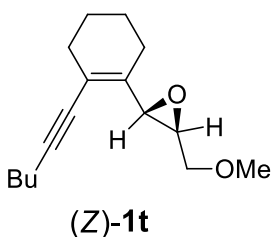
(Z)-**1t:** ^{1}H NMR (400 MHz, CDCl$_3$) δ: 4.00-3.97 (m, 1H), 3.73 (dt, J= 11.2, 2.8 Hz, 1H), 3.45-3.30 (m, 4H), 3.20 (sext, J= 2.8 Hz, 1H), 2.34 (t, J= 6.8 Hz, 2H), 2.21-2.10 (m, 2H), 2.02-1.91 (m, 2H), 1.79-1.32 (m, 6H), 0.98-0.79 (m, 5H); ^{13}C{1H} NMR (100 MHz, CDCl$_3$) δ: 137.3, 121.7, 94.2, 79.5, 73.1, 59.2, 56.2, 55.2, 30.9, 30.8, 22.4, 22.2, 21.9, 21.7, 19.2, 13.6.

S31
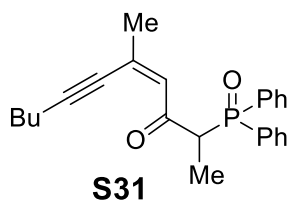
S31: [^1]H NMR (400 MHz, CDCl$_3$) δ: 7.86-7.74 (m, 4H), 7.55-7.43 (m, 6H), 6.34 (d, *J*= 1.2 Hz, 1H), 3.99 (dq, *J*= 13.5, 7.0 Hz, 1H), 2.42 (t, *J*= 7.0 Hz, 2H), 1.89 (d, *J*= 1.2 Hz, 3H), 1.60-1.51 (m, 2H), 1.47-1.38 (m, 5H), 0.92 (t, *J*= 7.0 Hz, 3H).

S32
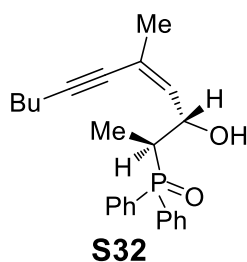
S32: [^1]H NMR (400 MHz, CDCl$_3$) δ: 7.83-7.71 (m, 4H), 7.56-7.43 (m, 6H), 5.53 (dd, *J*= 8.3, 1.2 Hz, 1H), 4.80 (dt, *J*= 13.8, 8.3 Hz, 1H), 2.82-2.71 (m, 1H), 2.15 (t, *J*= 7.2 Hz, 2H), 1.65 (d, *J*= 1.2 Hz, 3H), 1.40-1.28 (m, 4H), 1.04 (dd, *J*= 17.2, 7.4 Hz, 3H), 0.78 (t, *J*= 7.2 Hz, 3H).

S33
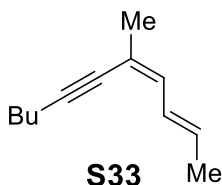
S33: [^1]H NMR (400 MHz, CDCl$_3$) δ: 6.48 (ddq, *J*= 15.4, 10.8, 1.6 Hz, 1H), 6.11 (d, *J*= 10.8 Hz, 1H), 4.80 (dq, *J*= 15.4, 7.0 Hz, 1H), 2.39 (t, *J*= 6.8 Hz, 2H), 1.86 (s, 3H), 1.79 (d, *J*= 7.0 Hz, 3H), 1.60-1.52 (m, 2H), 1.51-1.44 (m, 2H), 0.94 (t, *J*= 6.8 Hz, 3H).

3.4. General Procedure for Carbonylation Reactions

A palladium complex, phosphine ligand and 1 mL of alcohol were added successively to a Schlenck apparatus that is attached to an Ar line and stirred 1 h at 25 °C before the addition of the substrate. A CO full balloon was then fixed to the reaction vessel and 1 mL alcohol solution of the substrate was added. When the reaction was complete as judged by TLC analysis the solvent content was evaporated and the residue was purified by column chromatography on silica gel to afford **2** as a pale yellow oil.

3.5. Characterization of Products

The synthesized carbonylation products were analyzed by GC and GC-MS. NMR spectra were recorded on a 400 MHz spectrometer. Chemical shifts are reported in ppm downfield from Me_4Si. Infrared spectra were obtained by ATR method with neat samples. High-resolution mass spectral analyses of new compounds were performed using EI-High Resolution Double Focusing Magnetic Sector (ionization mode: 70 eV, emission current: 1 mA, source temperature: 160 °C, resolution: 10,000 (10% valley definition)) and ESI-LTQ Orbitrap (source voltage: +3.8 kV, capillary voltage: 41 V, capillary temperature: 275 °C, tube lens voltage: 140 V, system resolution: 60,000 (10% valley definition)). The coupling constants of olefinic protons and NOE studies confirmed (*E*)-configured structures. ^{1}H NMR analyses of vinylallene products, except that of **2ia'**, were performed in C_6D_6. With this solvent, the ^{1}H NMR signals of diastereomers were resolved adequately, allowing to determine diastereomeric ratios smoothly. In contrast, when using $CDCl_3$ solvent, diastereomeric signals were all overlapped.

2aa
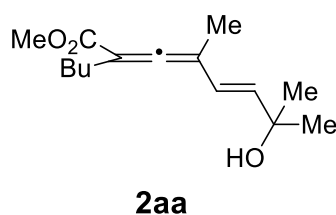
2aa: Yield: 24.9 mg (99%); ^{1}H NMR (400 MHz, $CDCl_3$) δ: 6.13 (d, *J*= 16.0 Hz, 1H), 5.76 (d, *J*= 16.0 Hz, 1H), 3.67 (s, 3H), 2.22 (t, *J*= 7.6 Hz, 2H), 1.85 (s, 3H), 1.37-1.27 (m, 10H), 0.86 (t, *J*= 7.0 Hz, 3H); ^{13}C{1H} NMR (100 MHz, $CDCl_3$) δ: 213.4, 167.7, 137.8, 122.9, 103.1, 99.7, 70.9, 52.0, 30.1, 29.8, 28.6, 22.1, 14.8, 13.8; FTIR (v_{max}/cm^{-1}): 3409, 2957, 2930, 2871, 1940, 1714, 1436, 1378, 1264, 1133, 1083, 1019, 966, 912, 723, 696; MS (EI, m/z): 252 (1, M^+), 234 (2), 205 (7), 194 (7), 179 (5), 151 (23), 135 (35), 121 (15), 107 (32), 91 (43), 77 (25), 65 (15), 59 (46), 43 (100); HRMS (ESI) $C_{15}H_{25}O_3$ $(MH)^+$, 253.1798 (calculated); 253.1799 (found).
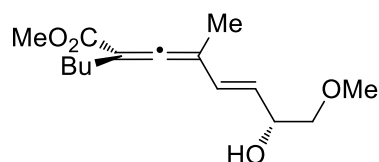
2ba

2ba: Yield: 25.2 mg (94%); ^{1}H NMR (400 MHz, C_6D_6) δ: 6.43 (dd, J= 15.7, 1.6 Hz, 1H, major), 6.41 (dd, J= 15.7, 1.6 Hz, 1H, minor), 5.51 (dd, J= 15.7, 5.5 Hz, 1H, major), 5.51 (dd, J= 15.7, 5.5 Hz, 1H, minor), 4.23-4.19 (m, 1H), 3.36 (s, 3H, major), 3.35 (s, 3H, minor), 3.03 (dd, A of ABX, J_{AB}=9.2 Hz, J_{AX}=4.0 Hz, 1H), 2.98 (dd, B of ABX, J_{AB}=9.2 Hz, J_{BX}=7.2 Hz, 1H), 2.95 (s, 3H), 2.39 (td, J= 7.5, 2.2 Hz, 2H), 2.23 (bs, 1H), 1.69 (s, 3H), 1.47-1.39 (m, 2H), 1.23 (sext, J= 7.6 Hz, 2H), 0.78 (t, J= 7.2 Hz, 3H, major), 0.78 (t, J= 7.2 Hz, 3H, minor); ^{13}C{^{1}H} NMR: (100 MHz, C_6D_6) δ: 213.5, 166.9, 129.2, 127.3, 103.1, 76.5, 70.6, 58.2, 51.3, 30.3, 28.9, 22.2, 14.5, 13.7; FTIR (v_{max}/cm^{-1}): 3419, 2955, 2928, 2870, 1943, 1715, 1456, 1436, 1379, 1266, 1241, 1193, 1129, 1016, 966; MS (EI, m/z): 268 (1, M$^+$), 236 (1), 223 (4), 205 (1), 191 (6), 151 (2), 135 (7), 121 (6), 93 (8), 91 (14), 77 (10), 59 (6), 45 (100); HRMS (ESI): $C_{15}H_{25}O_4$ (MH)$^+$, 269.1747 (calculated); 269.1747 (found).
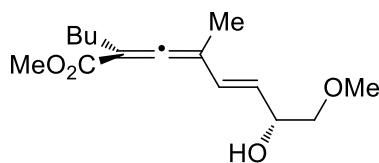
2ba'

2ba': Yield: 23.3 mg, (87%); ^{1}H NMR (400 MHz, C_6D_6) δ: 6.42 (dd, J= 15.7, 1.6 Hz, 1H, major), 6.40 (dd, J= 15.7, 1.6 Hz, 1H, minor), 5.52 (dd, J= 15.7, 5.7 Hz, 1H), 4.22-4.20 (m, 1H), 3.37 (s, 3H, major), 3.35 (s, 3H, minor), 3.03 (dd, A of ABX, J_{AB}=9.6 Hz, J_{AX}=4.0 Hz, 1H), 2.99 (dd, B of ABX, J_{AB}=9.6 Hz, J_{BX}=8.0 Hz, 1H), 2.96 (s, 3H), 2.38 (td, J= 7.6 Hz, 1.8 Hz, 2H), 2.29 (bs, 1H), 1.70 (s, 3H), 1.48-1.40 (m, 2H), 1.25 (sext, J= 7.6 Hz, 2H), 0.79 (t, J= 7.6 Hz, 3H); ^{13}C{^{1}H} NMR (100 MHz, C_6D_6) δ: 213.5, 166.9, 129.2, 103.1, 100.0, 76.5, 70.6, 58.2, 51.3, 30.3, 28.9, 22.2, 14.5, 13.7; FTIR (v_{max}/cm^{-1}): 3419, 2955, 2928, 2870, 1943, 1715, 1456, 1436, 1379, 1266, 1241, 1193, 1129, 1016, 966; MS (EI, m/z): 268 (1, M$^+$), 236 (1), 223 (4), 205 (1), 191 (6), 151 (2), 135 (7), 121 (6), 93 (8), 91 (14), 77 (10), 59 (6), 45 (100); HRMS (ESI): $C_{15}H_{25}O_4$ (MH)$^+$, 269.1747 (calculated); 269.1747 (found).
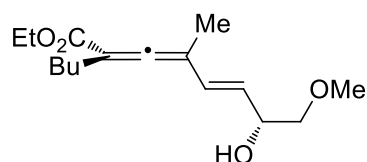
2bb

2bb: Yield: 23.7 mg (84%); ^{1}H NMR (400 MHz, C$_6$D$_6$) δ: 6.44 (dd, J= 15.4, 1.6 Hz, 1H, major), 6.43 (dd, J= 15.4, 1.6 Hz, 1H, minor), 5.54 (dd, J= 15.4, 5.6 Hz, 1H), 4.24-4.18 (m, 1H), 3.99 (q, J=7.1 Hz, 2H), 3.03 (dd, A of ABX, J_{AB}=9.6 Hz, J_{AX}=4.0 Hz, 1H), 2.98 (dd, B of ABX, J_{AB}=9.6 Hz, J_{BX}=7.6 Hz, 1H), 2.95 (s, 3H), 2.41 (td, J= 7.2, 2.4 Hz, 2H) 2.28 (bs, 1H), 1.71 (s, 3H), 1.49-1.41 (m, 2H), 1.25 (sext, J=7.2 Hz, 2H), 0.92 (t, J= 7.1 Hz, 3H, major), 0.91 (t, J= 7.1 Hz, 3H, minor) 0.79 (t, J= 7.2 Hz, 3H, major), 0.79 (t, J= 7.2 Hz, 3H, minor); ^{13}C{1H} NMR: (100 MHz, CDCl$_3$) δ: 213.5, 167.1, 128.7, 127.8, 103.1, 100.3, 76.4, 71.1, 60.8, 59.1, 30.2, 28.6, 22.2, 14.7, 14.3, 13.9; FTIR (ν$_{max}$/cm^{-1}): 3418, 2956, 2926, 2858, 1940, 1708, 1458, 1367, 1322, 1261, 1240, 1172, 1118, 1062, 1023, 965, 864, 713. MS (EI, m/z) : 282 (1, M$^+$), 238 (1), 237 (4), 209 (2), 191 (5), 135 (3), 121 (5), 107 (6), 93 (8), 91 (12), 77 (7), 65 (5), 55 (7), 45 (100); HRMS (ESI): C$_{16}$H$_{26}$O$_4$ (MH)$^+$, 283.1904 (calculated); 283.1909 (found).
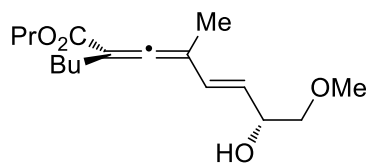

2bc

2bc: Yield: 25.8 mg (87%); ^{1}H NMR (400 MHz, C$_6$D$_6$) δ: 6.44 (dd, J= 15.8, 1.6 Hz, 1H, major), 6.43 (dd, J= 15.8, 1.6 Hz, 1H, minor), 5.53 (dd, J= 15.8, 5.6 Hz, 1H), 4.23-4.19 (m, 1H), 4.02-3.92 (m, 2H), 3.03 (dd, A of ABX, J_{AB}= 9.6 Hz, J_{AX}= 4.4 Hz, 1H), 2.98 (dd, B of ABX, J_{AB}= 9.6 Hz, J_{BX}= 7.2 Hz, 1H), 2.94 (s, 3H), 2.41 (td, J= 7.3, 1.6 Hz, 2H), 2.22 (bs, 1H), 1.72 (s, 3H), 1.49-1.33 (m, 4H), 1.25 (sext, J= 7.4 Hz, 2H), 0.79 (t, J= 7.4 Hz, 3H, major), 0.80 (t, J= 7.4 Hz, 3H, minor), 0.66 (t, J= 7.3 Hz, 3H, major), 0.65 (t, J=7.3 Hz, 3H, minor); ^{13}C{1H} NMR (100 MHz, CDCl$_3$) δ: 213.6, 167.2, 128.6, 127.9, 103.1, 100.3, 76.5, 71.1, 66.3, 59.1, 30.2, 28.5, 22.2, 22.0, 14.7, 13.9, 10.3; FTIR (ν$_{max}$/cm^{-1}): 3406, 2958, 2928, 1941, 1709, 1458, 1397, 1322, 1263, 1172, 1132, 1062, 1015, 965, 713; MS (EI, m/z): 296 (1, M$^+$), 278 (1), 251 (3), 236 (1), 209 (3), 191

(5), 135 (4), 121 (5), 91 (10), 79 (6), 65 (3), 45 (100); HRMS (ESI): $C_{17}H_{28}O_4$ (MH)$^+$, 297.2060 (calculated), 297.2065 (found).

2bd
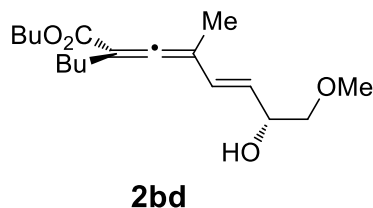
2bd: Yield: 25.7 mg (83%); ^{1}H NMR (400 MHz, C_6D_6) δ: 6.45 (dd, J= 16.0, 1.2 Hz, 1H, major), 6.43 (dd, J= 16.0, 1.2 Hz, 1H, minor), 5.53 (dd, J= 16.0, 5.6 Hz, 1H, major), 5.53 (dd, J= 16, 5.6 Hz, 1H, minor), 4.24-4.19 (m, 1H), 4.09-3.99 (m, 2H), 3.04 (dd, A of ABX, J_{AB}= 9.6 Hz, J_{AX}= 4.0 Hz, 1H), 2.99 (dd, B of ABX, J_{AB}= 9.6 Hz, J_{BX}= 7.6 Hz, 1H), 2.95 (s, 3H), 2.41 (td, J= 7.4, 2.4 Hz, 2H) 2.26 (bs, 1H), 1.75 (s, 3H, minor), 1.73 (s, 3H, major), 1.46 (quint, J= 7.2 Hz, 2H), 1.36 (quint, J= 7.4 Hz, 2H), 1.25 (sext, J= 7.2 Hz, 2H), 1.12 (sext, J= 7.4 Hz, 2H), 0.80 (t, J= 7.2 Hz, 3H, minor), 0.79 (t, J= 7.2 Hz, 3H, major), 0.68 (t, J= 7.4 Hz, 3H, major), 0.67 (t, J= 7.4 Hz, 3H, minor); ^{13}C{1H} NMR (100 MHz, CDCl$_3$) δ: 213.6, 167.2, 128.6, 127.8, 103.1, 100.3, 76.4, 71.1, 64.7, 59.1, 30.6, 30.2, 28.5, 22.2, 19.2, 14.7, 13.9, 13.7; FTIR (v_{max}/cm^{-1}): 3428, 2958, 2929, 2873, 1940, 1710, 1458, 1379, 1322, 1261, 1131, 1062, 1016, 965, 713; MS (EI, m/z): 310 (1, M$^+$), 293 (1), 265 (1), 235 (2), 207 (4), 191 (4), 161 (3), 121 (3), 105 (5), 91 (10), 79 (5), 57 (15), 45 (100); HRMS (ESI): $C_{18}H_{31}O_4$ (MH)$^+$, 311.2217 (calculated), 311.2219 (found).

2be
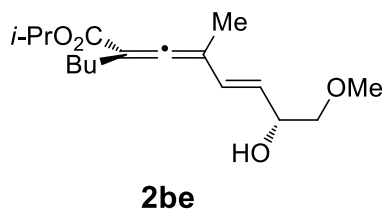
2be: Yield: 26.1 mg (88%); ^{1}H NMR (400 MHz, C_6D_6) δ: 6.43 (dd, J= 16.0, 1.6 Hz, 1H), 5.51 (dd, J= 16.0, 5.6 Hz, 1H), 5.05 (sept, J= 6.4 Hz, 1H, major), 5.05 (sept, J= 6.4 Hz, 1H, minor), 4.23-4.16 (m, 1H), 3.02 (dd, A of ABX, J_{AB}= 9.2 Hz, J_{AX}= 4.0 Hz, 1H), 2.97 (dd, B of ABX, J_{AB}= 9.2 Hz, J_{BX}= 7.6 Hz, 1H), 2.94 (s, 3H), 2.42 (td, J= 7.6, 2.0 Hz, 2H), 2.21 (bs, 1H), 1.71 (s, 3H), 1.45 (quint, J= 7.6 Hz, 2H), 1.25 (sext, J= 7.6 Hz, 2H), 1.02 (d, J= 6.4 Hz, 3H), 1.01 (d, J= 6.4 Hz, 3H), 0.79 (t, J= 7.6 Hz, 3H, major),

0.79 (t, $J= 7.6$ Hz, 3H, minor); $^{13}C\{1H\}$ NMR (100 MHz, CDCl$_3$) δ: 213.5, 166.7, 128.9, 127.6, 103.0, 100.7, 76.5, 71.1, 68.1, 59.1, 30.2, 28.6, 22.2, 21.9, 21.8, 14.7, 13.9; FTIR (ν_{max}/cm^{-1}) δ: 3442, 2957, 2927, 1942, 1706, 1457, 1373, 1322, 1264, 1107, 1062, 1014, 966,831,713; MS (EI, m/z): 296 (1, M$^+$), 282 (1), 251 (2), 209 (3), 191 (4), 180 (1), 121 (6), 107 (4), 91 (7), 77 (6), 55 (4), 45 (100); HRMS (ESI): C$_{17}$H$_{29}$O$_4$ (MH)$^+$, 297.2060 (calculated), 297.2060 (found).

2bg
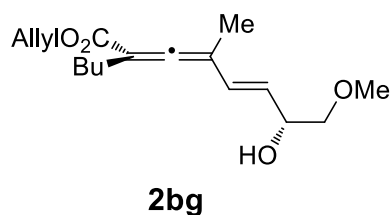
2bg: Yield: 26.8 mg (91%); ^{1}H NMR (400 MHz, C$_6$D$_6$) δ: 6.43 (dd, $J= 15.6$, 0.8 Hz, 1H), 5.72-5.62 (m, 1H), 5.52 (dd, $J= 15.6$, 5.6 Hz, 1H), 5.08 (dq, $J= 18.8$, 1.6 Hz, 1H), 4.89 (dq, $J= 6.4$, 1.6 Hz, 1H), 4.53-4.41 (m, 2H), 4.23-4.19 (m, 1H), 3.04 (dd, A of ABX, $J_{AB}= 9.6$ Hz, $J_{AX}= 4.0$ Hz, 1H), 2.99 (dd, B of ABX, $J_{AB}= 9.6$ Hz, $J_{BX}= 7.2$ Hz, 1H), 2.95 (s, 3H), 2.39 (td, $J= 7.2$, 2.0 Hz, 2H), 2.31 (bs, 1H), 1.70 (s, 3H), 1.44 (quint, $J= 7.2$ Hz, 2H), 1.24 (sext, $J= 7.2$ Hz, 2H), 0.79 (t, $J= 7.2$ Hz, 3H, minor), 0.78 (t, $J= 7.2$ Hz, 3H, major); $^{13}C\{1H\}$ NMR (100 MHz, CDCl$_3$) δ: 213.7, 166.8, 132.4, 128.5, 128.1, 117.4, 103.2, 100.0, 76.4, 71.1, 65.2, 59.1, 30.1, 28.5, 22.2, 14.7, 13.9; FTIR (ν_{max}/cm^{-1}): 3417, 2956, 2928, 2873, 1939, 1710, 1647, 1456, 1379, 1322, 1259, 1236, 1172, 1129, 1062, 1015, 965, 928, 837, 713. MS (EI, m/z): 294 (1, M$^+$), 261 (1), 249 (2), 221 (1), 191 (5), 165 (3), 121 (6), 91 (11), 77 (9), 65 (4), 55 (7), 45 (100); HRMS (ESI): C$_{17}$H$_{27}$O$_4$ (MH)$^+$, 295.1904 (calculated), 295.1910 (found).

2ca
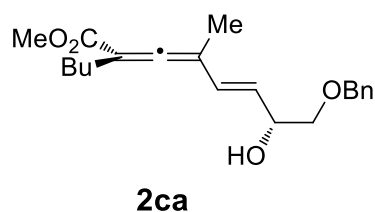
2ca: Yield: 31.0 mg (90%); ^{1}H NMR (400 MHz, C$_6$D$_6$) δ: 7.24-7.01 (m, 5H), 6.44 (dd, $J= 15.8$, 1.6 Hz, 1H, major), 6.42 (dd, $J= 15.8$, 1.6 Hz, 1H, minor), 5.49 (dd, $J= 15.8$, 5.7 Hz, 1H), 4.29-4.23 (m, 1H), 4.21 (d, A of AB, $J_{AB}=12.0$ Hz, 1H), 4.19 (d, B of AB, $J_{AB}=12.0$ Hz, 1H), 3.36 (s, 3H, major) 3.34 (s, 3H, minor), 3.18 (dd, A of ABX, $J_{AB}= 9.2$

Hz, J_{AX}= 3.6 Hz, 1H), 3.11 (dd, B of ABX, J_{AB}= 9.2 Hz, J_{BX}= 7.6 Hz, 1H), 2.38 (td, J= 7.6, 2.8 Hz, 2H), 1.69 (s, 3H), 1.42 (quint, J= 7.6 Hz, 2H), 1.23 (sext, J=7.6 Hz, 2H), 0.78 (t, J= 7.6 Hz, 3H); $^{13}C\{1H\}$ NMR (100 MHz, CDCl$_3$) δ: 213.6, 167.6, 137.7, 128.5, 128.4, 128.0, 127.9, 127.8, 103.2, 99.9, 74.0, 73.4, 71.2, 52.1, 30.1, 28.6, 22.2, 14.7, 13.9; FTIR (ν_{max}/cm^{-1}): 3416, 2954, 2928, 2869, 1943, 1714, 1454, 1435, 1379, 1322, 1266, 1134, 1016, 965, 738, 698. MS (EI, m/z): 344 (1, M$^+$), 312 (1), 279 (3), 253 (2), 191 (2), 167 (20), 149 (77), 113 (10), 104 (12), 91 (65), 70 (35), 57 (42), 57 (54), 43 (80), 41 (100); HRMS (ESI): C$_{21}$H$_{29}$O$_4$ (MH)$^+$, 345.2060 (calculated); 345.2065 (found).
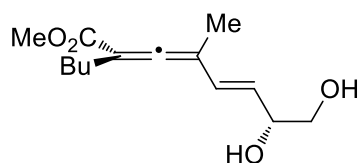
2da

2da: Yield: 21.3 mg (84%); ^{1}H NMR (400 MHz, C$_6$D$_6$): δ: 6.35 (d, J= 16.0 Hz, 1H, major), 6.34 (d, J= 16.0 Hz, 1H, minor), 5.48 (dd, J= 16.0, 5.9 Hz, 1H), 4.10-4.04 (m, 1H), 3.44-3.24 (m, 2H), 3.37 (s, 3H), 2.39 (td, J= 7.6, 3.2 Hz, 2H), 1.70 (s, 3H), 1.44 (quint, J= 7.6 Hz, 2H), 1.25 (sext, J=7.6 Hz, 2H), 0.80 (t, J= 7.6 Hz, 3H, major), 0.80 (t, J= 7.2 Hz, 3H, minor); $^{13}C\{1H\}$ NMR: (100 MHz, C$_6$D$_6$) δ: 213.6, 167.0, 129.2, 128.0, 103.2, 100.1, 72.8, 66.3, 51.4, 30.3, 28.9, 22.2, 14.5, 13.7; FTIR (ν_{max}/cm^{-1}): 3384, 2954, 2928, 2871, 1940, 1715, 1436, 1379, 1265, 1240, 1131, 1076, 1017, 965, 875; LC-MS/MS: 255 (100, MH$^+$), 237 (20), 227 (8), 225 (20), 223 (42), 207 (12), 205 (50), 195 (12), 193 (15), 177 (18), 175 (18), 163 (15), 149 (8); HRMS (ESI): C$_{14}$H$_{23}$O$_4$ (MH)$^+$, 255.1596 (calculated); 255.1591 (found).
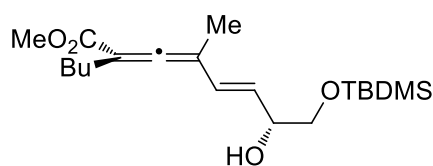
2ea

**2ea:** Yield: 30.2 mg (82%); ^{1}H NMR (400 MHz, C$_6$D$_6$) δ: 6.45 (dd, J= 15.8, 1.6 Hz, 1H, major), 6.34 (dd, J= 15.8, 1.6 Hz, 1H, minor) 5.54 (dd, J= 15.8, 5.6 Hz, 1H, major), 5.50 (dd, J= 15.8, 5.6 Hz, 1H, minor), 4.19-4.10 (m, 1H), 3.42 (dd, A of ABX, J_{AB}= 9.6 Hz, J_{AX}= 4.4 Hz, 1H), 3.37 (s, 3H), 3.31 (dd, B of ABX, J_{AB}= 9.6 Hz, J_{BX}= 7.2 Hz, 1H), 2.39 (td, J= 7.2, 1.6 Hz, 2H), 2.24 (d, J= 3.6 Hz, 1H), 1.72 (s, 3H, major), 1.69 (s, 3H, minor), 1.44 (quint, J= 7.2 Hz, 2H), 1.24 (sext, J=7.2 Hz, 2H), 0.89 (s, 9H, minor),

0.85 (s, 9H, major), 0.79 (t, J= 7.2 Hz, 3H), -0.06 (s, 6H); ^{13}C{1H} NMR (100 MHz, C$_6$D$_6$) δ: 213.5, 166.9, 129.2, 127.5, 103.1, 100.0, 72.4, 67.2, 51.3, 30.3, 28.9, 25.6, 22.2, 18.1, 14.5, 13.7, -5.6, -5.7; FTIR (v_{max}/cm^{-1}): 3465, 2954, 2928, 2858, 1940, 1716, 1463, 1435, 1361, 1258, 1118, 963, 837, 777; MS (EI, m/z): 368 (1, M$^+$), 339 (1), 311 (2), 279 (1), 249 (3), 219 (2), 191 (4), 175 (5), 159 (6), 145 (3), 121 (5), 117 (15), 105 (30), 91 (20), 77 (20), 75 (100), 73 (50), 57 (85), 41 (60); HRMS (ESI): C$_{20}$H$_{37}$O$_4$Si (MH)$^+$, 369.2456 (calculated), 369.2470 (found).
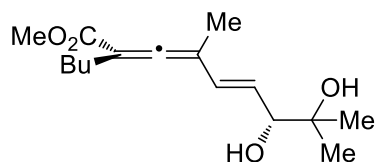
2fa

2fa: Yield: 25.4 mg (90%); ^{1}H NMR (400 MHz, C$_6$D$_6$) δ: 6.29 (dd, J= 15.7, 1.2 Hz, 1H, minor), 6.28 (dd, J= 15.7, 1.2 Hz, 1H, major), 5.63 (dd, J= 15.7, 6.6 Hz, 1H, minor), 5.62 (dd, J= 15.7, 6.6 Hz, 1H, major), 3.73 (d, J= 6.6 Hz, 1H), 3.36 (s, 3H, major), 3.34 (s, 3H, minor), 2.38 (td, J= 7.2, 1.6 Hz, 2H), 2.15 (bs, 1H), 2.00 (bs, 1H), 1.71 (s, 3H, minor), 1.71 (s, 3H, major), 1.43 (quint, J= 7.2 Hz, 2H), 1.23 (sext, J= 7.2 Hz, 2H), 1.06 (s, 3H, major), 1.05 (s, 3H, minor), 1.03 (s, 3H, minor), 1.02 (s, 3H, major), 0.78 (t, J= 7.2 Hz, 3H); ^{13}C{1H} NMR (100 MHz, C$_6$D$_6$) δ: 213.5, 166.9, 129.3, 128.4, 103.2, 100.0, 79.2, 72.3, 51.3, 30.3, 28.8, 26.1, 23.8, 22.1, 14.5, 13.6; FTIR (v_{max}/cm^{-1}): 3407, 2956, 2929, 2860, 1940, 1714, 1436, 1377, 1265, 1242, 1133, 1015, 965, 898; MS (EI, m/z): 282 (2, M$^+$), 250 (2), 222 (1), 191 (3), 164 (4), 134 (4), 121 (20), 91 (7), 77 (16), 65 (5), 59 (100), 43 (37); HRMS (ESI): C$_{16}$H$_{27}$O$_4$ (MH)$^+$: 283.1904 (calculated), 283.1908 (found).
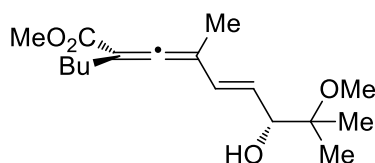
2ga

2ga: Yield: 26.3 mg (89%); ^{1}H NMR (400 MHz, C$_6$D$_6$) δ: 6.45 (dd, J= 15.8, 1.6 Hz, 1H), 5.68 (dd, J= 15.8, 6.2 Hz, 1H), 3.96 (d, J= 6.2 Hz, 1H), 3.36 (s, 3H, major), 3.33 (s, 3H, minor), 2.86 (s, 3H), 2.44 (bs, 1H), 2.38 (td, J= 7.6, 1.6 Hz, 2H), 1.72 (s, 3H), 1.43 (quint, J= 7.6 Hz, 2H), 1.23 (sext, J= 7.6 Hz, 2H), 0.93 (s, 3H), 0.88 (s, 3H), 0.78 (t, J= 7.6 Hz, 3H); ^{13}C{1H} NMR (100 MHz, C$_6$D$_6$) δ: 213.4, 166.9, 129.1, 103.2, 99.9, 77.6,

77.1, 51.3, 48.6, 30.3, 28.9, 22.1, 20.2, 19.2, 14.6, 13.7; FTIR (v_{max}/cm^{-1}): 3446, 2953, 2928, 2859, 1939, 1712, 1459, 1435, 1380, 1321, 1264, 1241, 1118, 1062, 1015, 965, 861, 833, 740, 713; MS (EI, m/z): 296 (1, M$^+$), 265 (1), 233 (1), 221 (1), 191 (1), 121 (3), 91 (5), 74 (4), 73 (100), 59 (5), 43 (20); HRMS (ESI): $C_{17}H_{29}O_4$ (MH)$^+$: 297.2060 (calculated), 297.2063 (found).
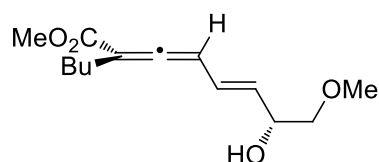
2ha

2ha: Yield: 22.1 mg (87%): ^{1}H NMR (400 MHz, C_6D_6) δ: 6.24 (ddd, J= 15.2, 10.6, 1.6 Hz, 1H), 5.98 (dt, J= 10.6, 2.7 Hz, 1H), 5.46 (ddd, J= 15.2, 4.8, 0.8 Hz, 1H), 4.16-4.08 (m, 1H), 3.36 (s, 3H, major), 3.35 (s, 3H, minor), 2.99 (dd, A of ABX, J_{AB}= 9.6 Hz, J_{AX}= 4.0 Hz, 1H), 2.93 (dd, B of ABX, J_{AB}= 9.6 Hz, J_{BX}= 7.6 Hz, 1H), 2.93 (s, 3H), 2.41-2.29 (m, 2H), 2.20 (bs, 1H), 1.42 (quint, J= 7.2 Hz, 2H), 1.23 (sext, J= 7.2 Hz, 2H), 0.79 (t, J= 7.2 Hz, 3H, minor), 0.78 (t, J= 7.2 Hz, 3H, major); ^{13}C{1H} NMR (100 MHz, C_6D_6) δ: 213.8, 166.6, 132.7, 124.1, 101.9, 97.0, 76.3, 70.3, 58.2, 51.3, 30.2, 28.6, 22.1, 13.6. FTIR (v_{max}/cm^{-1}): 3423, 2955, 2930, 2872, 1941, 1716, 1436, 1322, 1268, 1133, 1062, 967, 853, 713; MS (EI, m/z): 254 (1, M$^+$), 223 (1), 209 (2), 177 (4), 149 (3), 135 (4), 125 (6), 107 (8), 91 (7), 77 (10), 65 (5), 59 (10), 45 (100); HRMS (ESI): $C_{14}H_{23}O_4$ (M)$^+$: 255.1591 (calculated), 255.1593 (found).
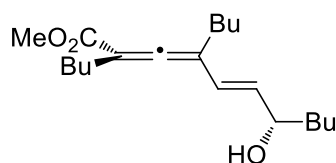
2ia

2ia: Yield: 26.4 mg (82%); ^{1}H NMR (400 MHz, CDCl$_3$) δ: 6.08 (d, J= 15.8 Hz, 1H), 5.72 (dd, J= 15.8, 6.8 Hz, 1H), 4.16 (q, J= 6.8 Hz, 1H), 3.70 (s, 3H), 2.31-2.15 (m, 4H), 1.62-1.28 (m, 16H), 0.93 (m, 9H); ^{13}C{1H} NMR: (100 MHz, CDCl$_3$) δ: 213.1, 167.8, 132.8, 126.2, 108.2, 101.4, 73.1, 52.0, 37.0, 30.3, 29.6, 28.7, 28.3, 27.6, 22.6, 22.4, 22.3, 14.0, 13.9, 13.8; FTIR (v_{max}/cm^{-1}): 3418, 2956, 2929, 2860, 1937, 1716, 1465, 1435, 1378, 1265, 1133, 1072, 964; MS (EI, m/z): 322 (1, M$^+$), 236 (3), 194 (5), 163 (5), 119 (5), 105 (6), 91 (17), 85 (12), 69 (30), 57 (50), 41 (100); HRMS (ESI): $C_{20}H_{35}O_3$ (MH)$^+$: 323.2581 (calculated), 323.2584 (found).

2ia'
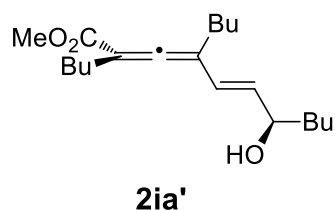
2ia': Yield: 25.5 mg (80%); ^{1}H NMR (400 MHz, CDCl$_3$) δ: 6.08 (d, J= 15.7 Hz, 1H), 5.72 (dd, J= 15.7, 6.7 Hz, 1H), 4.17 (q, J= 6.7 Hz, 1H), 3.71 (s, 3H), 2.30-2.14 (m, 4H), 1.71-1.18 (m, 15H), 0.97-0.82 (m, 9H); ^{13}C{1H} NMR (100 MHz, CDCl$_3$) δ: 213.1, 167.8, 132.8, 126.1, 108.2, 101.4, 73.0, 52.0, 37.1, 30.4, 29.6, 28.7, 28.4, 27.6, 22.6, 22.4, 22.3, 14.0, 13.9; FTIR (v_{max}/cm^{-1}): 3422, 2956, 2928, 2859, 1937, 1716, 1465, 1435, 1379, 1264, 1132, 1074, 963; MS (EI, m/z): 322 (1, M$^+$), 236 (20), 231 (21), 205 (20), 195 (36), 194 (90), 179 (35), 177 (42), 165 (39), 163 (50), 152 (38), 135 (55), 121 (61),107 (68), 105 (60), 93(72), 91 (74), 85 (69), 79 (62), 57 (100), 55 (41); HRMS (ESI) C$_{20}$H$_{35}$O$_3$ (MH)$^+$: 323.2581 (calculated), 323.2584 (found).

2ja
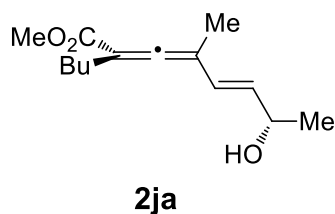
2ja: Yield: 20.7 mg (87%); ^{1}H NMR (400 MHz, C$_6$D$_6$) δ: 6.16 (dd, J= 15.6, 1.2 Hz, 1H), 5.50 (dd, J= 15.6, 6.2 Hz, 1H, minor), 5.49 (dd, J= 15.6, 6.2 Hz, 1H, major), 4.03 (quint, J= 6.2 Hz, 1H), 3.38 (s, 3H, major), 3.37 (s, 3H, minor), 2.39 (td, J= 7.4, 1.2 Hz, 2H), 1.70 (s, 3H), 1.49-1.41 (m, 2H), 1.25 (sext, J= 7.4 Hz, 2H), 1.04 (d, J= 6.2 Hz, 3H), 0.80 (t, J= 7.4 Hz, 3H, minor), 0.80 (t, J= 7.4 Hz, 3H, major); ^{13}C{1H} NMR (100 MHz, C$_6$D$_6$) δ: 213.3, 166.9, 134.7, 125.2, 103.1, 99.9, 68.0, 51.2, 30.3, 28.9, 23.1, 22.1, 14.5, 13.6; FTIR (v_{max}/cm^{-1}): 3410, 2956, 2928, 1941, 1715, 1436, 1322, 1266, 1135, 1062, 1016, 965, 714; MS (EI, m/z): 238 (3, M$^+$), 205 (5), 194,(15), 181 (15), 164 (13), 151 (55), 135 (45), 121 (100), 107 (30), 93 (90), 77 (45), 65 (10), 55 (14), 43 (92); HRMS (ESI): C$_{14}$H$_{23}$O$_3$ (MH)$^+$: 239.1648 (calculated), 239.1652 (found).

MeO$_2$C$_{\prime\prime\prime}$ / Bu — • — Cy / OMe / HO
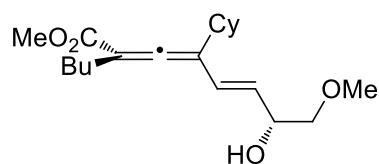
2ka

2ka: Yield: 29.9 mg (89%): ^{1}H NMR (400 MHz, C$_6$D$_6$) δ: 6.27 (dd, J= 15.8, 1.4 Hz, 1H, major), 6.26 (dd, J= 15.8, 1.4 Hz, 1H, minor), 5.78 (dd, J= 15.8, 5.5 Hz, 1H), 4.27-4.23 (m, 1H), 3.38 (s, 3H, major), 3.37 (s, 3H, minor), 3.05 (dd, A of ABX, J_{AB}= 9.6 Hz, J_{AX}= 4.0 Hz, 1H), 3.02 (dd, B of ABX, J_{AB}= 9.6 Hz, J_{BX}= 7.2 Hz, 1H), 2.94 (s, 3H), 2.46-2.41 (m, 2H), 2.34 (bs, 1H), 2.16-2.09 (m, 1H), 2.03-1.99 (m, 1H), 1.92-1.87 (m, 1H), 1.66-1.60 (m, 2H), 1.54-1.45 (m, 3H), 1.33-1.01 (m, 7H), 0.81 (t, J= 7.2 Hz, 3H, major), 0.81 (t, J= 7.2 Hz, 3H, minor); ^{13}C NMR (100 MHz, C$_6$D$_6$) δ: 212.3, 167.1, 129.0, 125.9, 113.8, 102.7, 76.5, 70.8, 58.2, 51.3, 38.0, 32.8, 32.4, 30.6, 29.0, 26.4, 26.4, 26.2, 22.4, 13.7; FTIR (v_{max}/cm^{-1}): 3426, 2925, 2853, 1924, 1713, 1435, 1322, 1263, 1240, 1195, 1173, 1119, 1062, 1016, 964, 890, 841, 713; MS (EI, m/z): 336 (2, M$^+$), 291 (60), 273 (8), 259 (100), 241 (20), 231 (30), 213 (27), 203 (30), 189 (19), 175 (21), 161 (22), 145 (21), 133 (21), 119 (19), 105 (25), 91(47), 79 (33), 67 (21), 55 (45), 45 (65); HRMS (ESI): C$_{20}$H$_{33}$O$_4$ (MH)$^+$: 337.2380 (calculated), 337.2384 (found)**.**

MeO$_2$C$_{\prime\prime\prime}$ / Bu — • — t-Bu / OMe / HO
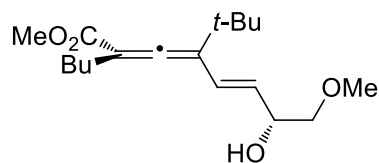
2la

2la: Yield: 21.1 mg (68%); ^{1}H NMR (400 MHz, C$_6$D$_6$) δ: 6.22 (dd, J= 15.6, 1.6 Hz, 1H, major), 6.21 (dd, J= 15.6, 1.6 Hz, 1H, minor), 5.92 (dd, J= 15.6, 5.2 Hz, 1H), 4.23-4.15 (m, 1H), 3.38 (s, 3H), 3.01 (dd, A of ABX, J_{AB}= 9.2 Hz, J_{AX}= 3.6 Hz, 1H), 2.95 (dd, B of ABX, J_{AB}= 9.2 Hz, J_{BX}= 7.6 Hz, 1H), 2.92 (s, 3H), 2.44-2.37 (m, 2H), 2.29 (bs, 1H), 1.51-1.46 (m, 2H), 1.26 (sext, J=7.2 Hz, 2H), 1.07 (s, 9H), 0.81 (t, J= 7.2 Hz, 3H); ^{13}C{1H} NMR (100 MHz, C$_6$D$_6$) δ: 208.6, 167.4, 132.0, 123.6, 117.1, 102.7, 76.4, 70.6, 58.2, 51.3, 33.8, 30.5, 30.1, 28.9, 22.4, 13.7; FTIR (v_{max}/cm^{-1}): 3455, 2957, 2929, 2871, 1940, 1713, 1459, 1435, 1395, 1363, 1322, 1264, 1239, 1195, 1172, 1132, 1062, 1017, 963, 713; LC-MS/MS: 311 (67, MH$^+$), 292 (19), 279 (80), 261 (27), 255 (10), 251 (5), 247 (10), 237 (9), 229 (60), 223 (100), 219 (8), 205 (8), 201 (9), 191 (8), 179 (26), 177 (8), 169 (10); HRMS (ESI): C$_{18}$H$_{31}$O$_4$ (MH)$^+$: 311.2223 (calculated), 311.2220 (found).
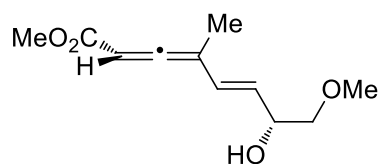
2ma

2ma: Yield: 17.2 mg (81%); ^{1}H NMR (400 MHz, C$_6$D$_6$) δ: 6.29 (d, $J=$ 16.0 Hz, 1H, major), 6.26 (d, $J=$ 15.9 Hz, 1H, minor), 5.69-5.66 (m, 1H), 5.47 (ddd, $J=$ 15.9, 5.2, 1.2 Hz, 1H), 4.17-4.12 (m, 1H), 3.32 (s, 3H, major), 3.31 (s, 3H, minor), 3.00 (dd, A of ABX, $J_{AB}=$ 9.6 Hz, $J_{AX}=$ 4.0 Hz, 1H), 2.95 (dd, B of ABX, $J_{AB}=$ 9.6 Hz, $J_{BX}=$ 7.2 Hz, 1H), 2.95 (s, 3H), 2.08 (bs, 1H), 1.55 (d, $J=$ 2.7 Hz, 3H); ^{13}C{1H} NMR (100 MHz, C$_6$D$_6$) δ: 216.1, 165.0, 130.2, 126.0, 103.5, 87.5, 76.3, 70.5, 58.2, 51.1, 14.0; FTIR (v_{max}/cm^{-1}): 3429, 2925, 1944, 1721, 1438, 1395, 1260, 1196, 1153, 1126, 1028, 966, 840; MS (EI, m/z): 212 (2, M$^+$), 193 (1), 167 (3), 135 (6), 110 (6), 107 (11), 81 (5), 77 (20), 67 (6), 59 (11), 45 (100); HRMS (ESI): C$_{11}$H$_{17}$O$_4$ (MH$^+$): 213.1121 (calculated), 213.1120 (found).
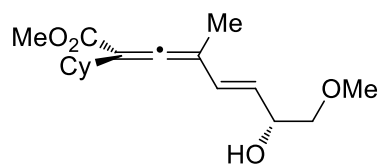
2na

2na: Yield: 27.0 mg (92%); ^{1}H NMR (400 MHz, C$_6$D$_6$) δ: 6.46 (dd, $J=$ 15.7, 1.6 Hz, 1H), 5.53 (dd, $J=$ 15.7, 5.5 Hz, 1H), 4.27-4.20 (m, 1H), 3.36 (s, 3H, major), 3.35 (s, 3H, minor), 3.05 (dd, A of ABX, $J_{AB}=$ 9.6 Hz, $J_{AX}=$ 4.0 Hz, 1H), 3.00 (dd, B of ABX, $J_{AB}=$ 9.6 Hz, $J_{BX}=$ 7.2 Hz, 1H), 2.96 (s, 3H), 2.64 (tt, $J=$ 11.4, 3.4 Hz, 1H), 2.33 (bs, 1H), 1.95 (d, $J=$ 11.4 Hz, 2H), 1.71 (s, 3H), 1.64-1.55 (m, 2H), 1.53-1.45 (m, 1H), 1.30-0.94 (m, 5H); ^{13}C NMR (100 MHz, C$_6$D$_6$) δ: 213.2, 166.6, 129.1, 105.9, 104.3, 76.5, 70.6, 58.2, 51.2, 37.6, 32.8, 26.4, 26.3, 26.0, 14.6; FTIR (v_{max}/cm^{-1}): 3420, 2924, 2851, 1936, 1712, 1435, 1369, 1322, 1254, 1228, 1192, 1128, 1093, 1071, 1026, 997, 965, 891, 872, 780; MS (EI, m/z): 294 (2, M$^+$), 262 (1), 249 (2), 217 (3), 189 (1), 171 (4), 135 (2), 119 (3), 105 (5), 91 (6), 77 (6), 67 (4), 55 (8), 45 (100); HRMS (ESI): C$_{17}$H$_{27}$O$_4$ (MH)$^+$: 295.1904 (calculated), 295.1908 (found).
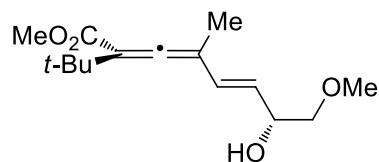
2oa

2oa: Yield: 23.9 mg (89%); ^{1}H NMR (400 MHz, C$_6$D$_6$) δ: 6.43 (dd, J= 15.8, 1.6 Hz, 1H), 5.51 (dd, J= 15.8, 5.6 Hz, 1H), 4.25-4.20 (m, 1H), 3.32 (s, 3H, major), 3.30 (s, 3H, minor), 3.04 (dd, A of ABX, J_{AB}= 9.6 Hz, J_{AX}= 4.4 Hz, 1H), 2.99 (dd, B of ABX, J_{AB}= 9.6 Hz, J_{BX}= 7.2 Hz, 1H), 2.96 (s, 3H), 2.34 (bs, 1H), 1.68 (s, 3H), 1.29 (s, 9H); ^{13}C{1H} NMR (100 MHz, C$_6$D$_6$) δ: 212.4, 165.9, 128.9, 108.8, 103.2, 76.5, 70.7, 58.2, 50.9, 34.2, 29.3, 14.6; FTIR (ν_{max}/cm^{-1}): 3419, 2955, 2870, 1934, 1717, 1435, 1362, 1322, 1258, 1226, 1132, 1062, 965; MS (EI, m/z): 268 (1, M$^+$), 236 (1), 223 (2), 191 (3), 163 (5), 145 (5), 135 (15), 119 (5), 105 (6), 91 (12), 79 (15), 65 (5), 59 (7), 57 (25), 45 (100); HRMS (ESI): C$_{15}$H$_{25}$O$_4$ (MH)$^+$: 269.1747 (calculated), 269.1748 (found).
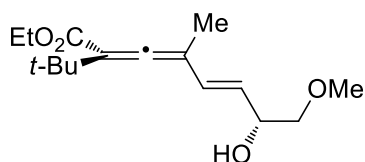
2ob

2ob: Yield: 25.7 mg (91%): ^{1}H NMR (400 MHz, C$_6$D$_6$) δ: 6.44 (dd, J= 15.5, 1.6 Hz, 1H, major), 6.42 (dd, J= 15.5, 1.6 Hz, 1H, minor), 5.52 (dd, J= 15.5, 6.0 Hz, 1H), 4.23-4.19 (m, 1H), 3.95 (qd, J= 7.2 Hz, 1.2 Hz, 2H), 3.03 (dd, A of ABX, J_{AB}= 9.6 Hz, J_{AX}= 4.0 Hz, 1H), 2.99 (dd, B of ABX, J_{AB}= 9.6 Hz, J_{BX}= 7.2 Hz, 1H), 2.95 (s, 3H), 2.32 (bs, 1H), 1.70 (s, 3H), 1.31 (s, 9H), 0.89 (t, J= 7.2 Hz, 3H); ^{13}C{1H} NMR (100 MHz, CDCl$_3$) δ: 212.1, 166.2, 129.0, 127.4, 109.2, 103.1, 76.5, 71.1, 60.3, 59.1, 34.2, 29.5, 14.8, 14.2; FTIR (ν_{max}/cm^{-1}): 3420, 2959, 1939, 1713, 1459, 1366, 1322, 1255, 1223, 1112, 1060, 965; MS (EI, m/z): 282 (2, M$^+$), 249 (1), 237 (3), 208 (2), 191 (4), 163 (6), 135 (15), 105 (7), 91 (11), 77 (16), 65 (4), 57 (18), 45 (100); HRMS (ESI): C$_{16}$H$_{27}$O$_4$ (MH)$^+$; 283.1904 (calculated), 283.1908 (found).
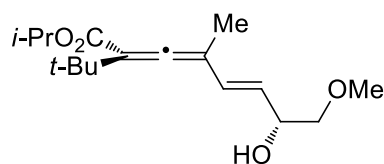
2oe

2oe: Yield: 26.0 mg (88%) ^{1}H NMR (400 MHz, C$_6$D$_6$) δ: 6.43 (dd, J= 15.6, 1.6 Hz, 1H), 5.53 (dd, J= 15.6, 5.6 Hz, 1H), 5.01 (sept, J= 6.4 Hz, 1H), 4.22-4.19 (m, 1H), 3.03 (dd, A of ABX, J_{AB}= 9.6 Hz, J_{AX}= 4.4 Hz, 1H), 2.99 (dd, B of ABX, J_{AB}= 9.6 Hz, J_{BX}= 7.6 Hz, 1H), 2.95 (s, 3H, major), 2.94 (s, 3H, minor), 2.26 (bs, 1H), 1.71 (s, 3H), 1.31 (s, 9H), 1.00 (d, J= 6.4 Hz, 3H), 0.99 (d, J= 6.4 Hz, 3H); ^{13}C{^{1}H} NMR (100 MHz, CDCl$_3$) δ: 211.8, 165.9, 129.1, 127.3, 109.7, 103.1, 76.5, 71.1, 67.8, 59.0, 34.1, 29.5, 21.8, 21.8, 14.7; FTIR (ν_{max}/cm^{-1}): 3410, 2960, 2926, 2896, 2825, 1935, 1708, 1458, 1373, 1322, 1255, 1226, 1049, 1021, 964, 833, 783, 713; MS (EI, m/z): 296 (1, M$^+$), 278 (1), 251 (2), 236 (2), 191 (6), 163 (7), 135 (15), 105 (14), 91 (17), 77 (16), 65 (5), 57 (40), 45 (100); HRMS (ESI): C$_{17}$H$_{29}$O$_4$ (MH)$^+$: 297.2060 (calculated); 297.2064 (found).
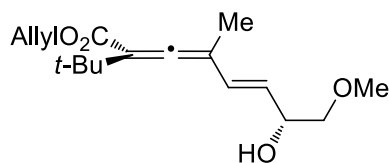
2og

2og: Yield: 25.9 mg (88%); ^{1}H NMR (400 MHz, C$_6$D$_6$) δ: 6.42 (dd, J= 15.6, 1.6 Hz, 1H, major), 6.40 (dd, J= 15.6, 1.6 Hz, 1H, minor), 5.64 (ddt, J= 17.2, 10.8, 4.8 Hz, 1H,), 5.53 (dd, J= 15.6, 5.6 Hz, 1H), 5.08 (dq, J= 17.2, 1.6 Hz, 1H), 4.87 (dq, J= 10.8, 1.6 Hz, 1H), 4.48-4.37 (m, 2H), 4.24-4.19 (m, 1H), 3.03 (dd, A of ABX, J_{AB}= 9.6 Hz, J_{AX}= 4.0 Hz, 1H), 2.99 (dd, B of ABX, J_{AB}= 9.6 Hz, J_{BX}= 7.2 Hz, 1H), 2.95 (s, 3H, major), 2.94 (s, 3H, minor), 2.28 (bs, 1H), 1.69 (s, 3H), 1.30 (s, 9H); ^{13}C{^{1}H} NMR (100 MHz, CDCl$_3$) δ: 212.4, 165.7, 132.5, 128.7, 127.7, 117.1, 108.9, 103.2, 76.5, 71.1, 64.7, 59.1, 34.2, 29.4, 14.8; FTIR (ν_{max}/cm^{-1}): 3410, 2957, 2927, 1935, 1713, 1647, 1457, 1398, 1362, 1321, 1252, 1217, 1172, 1131, 1061, 1027, 1016, 964, 928, 836, 781, 713; MS (EI, m/z): 294 (1, M$^+$), 249 (3), 236 (2), 191 (4), 163 (5), 135 (6), 105 (5), 91 (10), 77 (9), 65 (3), 57 (16), 45 (100); HRMS (EI): C$_{17}$H$_{27}$O$_4$ (MH)$^+$: 295.1904 (calculated), 295.1907 (found).
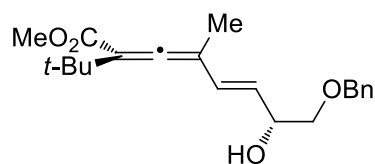
2pa

2pa: Yield: 29.6 mg (86%); ^{1}H NMR (400 MHz, C$_6$D$_6$) δ: 7.17-7.05 (m, 5H), 6.43 (dd, J= 15.8, 1.6 Hz, 1H), 5.49 (dd, J= 15.8, 5.6 Hz, 1H), 4.28-4.24 (m, 1H), 4.20 (s, 2H, major), 4.17 (s, 2H, minor), 3.31 (s, 3H), 3.19 (dd, A of ABX, J_{AB}= 9.2 Hz, J_{AX}= 3.6 Hz, 1H), 3.12 (dd, B of ABX, J_{AB}= 9.2 Hz, J_{BX}= 7.2 Hz, 1H), 2.32 (bs, 1H), 1.67 (s, 3H), 1.34 (s, 9H, minor), 1.29 (s, 9H, major); ^{13}C{1H} NMR: (100 MHz, CDCl$_3$) δ: 212.4, 166.5, 137.8, 128.8, 128.5, 127.9, 127.8, 127.7, 108.8, 103.1, 74.0, 73.4, 71.2, 51.6, 34.2, 29.4, 14.8; FTIR (v_{max}/cm^{-1}): 3422, 2954, 2865, 1934, 1715, 1496, 1479, 1454, 1434, 1391, 1362, 1257, 1225, 1104, 1060, 1029, 965, 781, 737, 698; MS (EI, m/z): 344 (2, M$^+$), 311 (2), 296 (2), 223 (2), 191 (3), 168 (4), 135 (11), 107 (7), 91 (100), 57 (50), 41 (25); HRMS (ESI): C$_{21}$H$_{29}$O$_4$ (MH)$^+$: 345.2060 (calculated), 345.2068 (found).
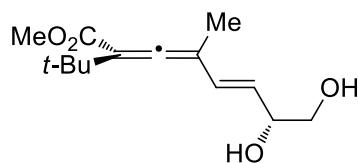
2qa

2qa: Yield: 22.1 mg (87%); ^{1}H NMR (400 MHz, C$_6$D$_6$) δ: 6.32 (dd, J= 15.8, 1.6 Hz, 1H, major), 6.09 (dd, J= 15.8, 6.0 Hz, 1H, minor), 5.74 (dd, J= 15.8, 1.6 Hz, 1H, minor), 5.43 (dd, J= 15.8, 6.0 Hz, 1H, major), 4.03-3.99 (m, 1H), 3.35 (dd, A of ABX, J_{AB}= 11.2 Hz, J_{AX}= 3.6 Hz, 1H), 3.32 (s, 3H), 3.23 (dd, B of ABX, J_{AB}= 11.2 Hz, J_{BX}= 7.2 Hz, 1H), 2.44 (bs, 1H), 2.22 (bs, 1H), 1.67 (s, 3H, major), 1.57 (s, 3H, minor), 1.34 (s, 9H, minor), 1.29 (s, 9H, major); ^{13}C NMR (100 MHz, C$_6$D$_6$) δ: 212.4, 165.9, 128.9, 108.9, 103.2, 72.8, 66.3, 50.9, 34.1, 29.3, 14.6; NMR (100 MHz, CDCl$_3$) δ: 212.4, 166.5, 129.2, 127.9, 108.9, 103.1, 73.0, 66.4, 51.7, 34.2, 29.4, 14.8; FTIR (v_{max}/cm^{-1}): 3368, 2955, 2926, 2865, 1934, 1717, 1641, 1458, 1434, 1363, 1257, 1225, 1060, 1029, 965, 925, 862, 781; MS (EI, m/z): 254 (3, M$^+$): 207 (7), 194 (11), 179 (10), 148 (13), 119 (15), 105 (20), 91 (35), 73 (20), 59 (20), 57 (100), 41 (50); HRMS (EI): C$_{14}$H$_{23}$O$_4$ (MH)$^+$: 255.1591 (calculated), 255.1590 (found).
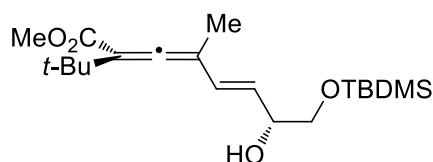
2ra

2ra: Yield: 30.9 mg, (84%): ^{1}H NMR (400 MHz, C$_6$D$_6$) δ: 6.43 (dd, J= 15.6, 1.6 Hz, 1H, major), 6.41 (dd, J= 15.6, 1.6 Hz, 1H, minor), 5.53 (dd, J= 15.6, 5.6 Hz, 1H), 4.17-4.12 (m, 1H), 3.42 (dd, A of ABX, J_{AB}= 10.0 Hz, J_{AX}= 4.0 Hz, 1H), 3.32 (dd, B of ABX, J_{AB}= 10.0 Hz, J_{BX}= 7.6 Hz, 1H), 3.32 (s, 3H), 2.23 (bs, 1H), 1.71 (s, 3H), 1.29 (s, 9H), 0.85 (s, 9H), -0.06 (s, 6H); ^{13}C{1H} NMR (100 MHz, C$_6$D$_6$) δ: 212.4, 165.9, 129.1, 108.8, 103.2, 72.5, 67.2, 50.9, 34.1, 29.3, 25.6, 18.1, 14.6, -5.6, -5.7; FTIR (v_{max}/cm^{-1}): 3467, 2954, 2927, 2857, 1935, 1718, 1462, 1434, 1362, 1256, 1225, 1111, 1062, 1005, 963, 837, 777; MS (EI, m/z): 368 (1, M$^+$), 351 (1), 311 (3), 279 (2), 237 (10), 223 (8), 191 (10), 177 (15), 163 (20), 159 (43), 145 (20), 135 (25), 105 (30), 89 (45), 75 (85), 73 (100), 57 (55), 41 (38); HRMS (ESI): C$_{20}$H$_{37}$O$_4$Si (MH)$^+$: 369.2456 (calculated), 369.2463 (found).
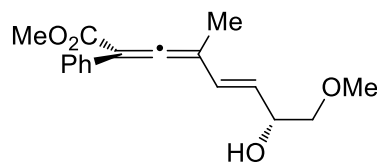
2sa

2sa: Yield: 25.1 mg (87%); ^{1}H NMR (400 MHz, C$_6$D$_6$) δ: 7.71-7.67 (m, 2H), 7.14-7.11 (m, 2H), 7.03-6.99 (m, 1H), 6.41 (dd, J= 15.8, 1.2 Hz, 1H, major), 6.38 (dd, J= 15.8, 1.2 Hz, 1H, minor), 5.56 (dd, J= 15.8, 5.6 Hz, 1H), 4.21-4.16 (m, 1H), 3.38 (s, 3H, major), 3.36 (s, 3H, minor), 3.03-2.96 (m, 2H), 2.96 (s, 3H), 2.30 (bs, 1H), 1.68 (s, 3H); ^{13}C{1H} NMR (100 MHz, C$_6$D$_6$) δ: 215.9, 165.8, 133.2, 130.5, 128.7, 128.2, 127.5, 126.2, 104.4, 102.7, 76.4, 70.6, 58.2, 51.5, 14.2; FTIR (v_{max}/cm^{-1}): 3419, 2922, 2851, 1926, 1716, 1492, 1434, 1369, 1321, 1273, 1195, 1171, 1123, 1062, 1039, 964, 918, 898, 781, 694; MS (EI, m/z): 288 (2, M$^+$), 256 (3), 211 (5), 183(5), 155 (17), 115 (8), 89 (4), 77 (9), 51 (5), 45 (100); HRMS (ESI): C$_{17}$H$_{21}$O$_4$ (MH)$^+$: 289.1434 (calculated), 289.1439 (found).
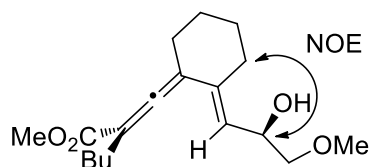
2ta

2ta: Yield: 25.4 mg (82%); ^{1}H NMR (400 MHz, C$_6$D$_6$) δ: 5.80 (d, J= 8.2, 1.6 Hz, 1H, minor), 5.75 (dt, J= 8.2, 1.6 Hz, 1H, major), 4.55-4.50 (m, 1H), 3.36 (s, 3H), 3.08-3.03 (m, 2H), 2.96 (s, 3H), 2.40 (td, J= 7.6, 2.8 Hz, 2H), 2.25-2.11 (m, 4H), 1.60-1.20 (m, 4H), 0.86-0.78 (m, 5H); ^{13}C{1H} NMR (100 MHz, C$_6$D$_6$) δ: 207.1, 167.4, 137.2, 125.6, 109.3, 99.6, 76.3, 66.9, 58.3, 51.4, 30.7, 30.5, 28.9, 28.5, 25.6, 25.5, 22.2, 13.9; FTIR (ν_{max}/cm^{-1}): 3456, 2928, 2857, 2859, 1946, 1713, 1436, 1436, 1266, 1241, 1128, 1063, 957; MS (EI, m/z): 308 (1, M$^+$), 276 (25), 231 (65), 201 (35), 175 (40), 161 (50), 117 (55), 91 (95), 77 (40), 55 (30), 45 (100); HRMS (ESI): C$_{18}$H$_{29}$O$_4$ (MH)$^+$: 310.2067 (calculated), 310.2067 (found).
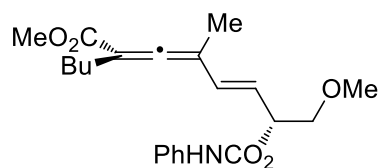
4ba

4ba: M.P.: 67-69 °C; ^{1}H NMR (400 MHz, CDCl$_3$) δ: 7.38 (d, J=7.6 Hz, 2H), 7.32-7.28 (m, 2H), 7.06 (tt, J=7.6, 1.2 Hz, 1H), 6.72 (bs, 1H), 6.33 (dd, J=15.8, 1.2 Hz, 1H), 5.70 (dd, J= 15.8 Hz, 6.4 Hz, 1H), 5.53 (qd, J= 5.6, 1.2 Hz, 1H), 3.70 (s, 3H), 3.60 (d, J=2.4 Hz, 1H), 3.59 (d, J=0.8 Hz, 1H), 3.42 (s, 3H), 2.25 (t, J= 7.6 Hz, 2H), 1.89 (s, 3H), 1.40-1.28 (m, 4H), 0.88 (t, J= 7.6 Hz, 3H); ^{13}C{1H} NMR (100 MHz, CDCl$_3$) δ: 213.8, 167.5, 152.6, 137.7, 130.0, 129.1, 124.8, 123.5, 118.6, 103.0, 100.0, 74.1, 73.5, 59.3, 52.1, 30.1, 28.6, 22.1, 14.7, 13.9.

CHAPTER 4

RESULTS AND DISCUSSION

We initiated our study using the enyne oxirane (*Z*)-**1a** whose oxirane terminus is dimethyl substituted. We were pleased to observe that, with just our first attempt, the substrate (*Z*)-**1a** was converted to the desired 2,3,5-trienoate product **2aa**, which is exclusively in (*E*)-configuration, and carries a hydroxyl group on the allylic position, almost quantitatively under very mild reaction conditions; the conversion was complete within just 1 h, when the reaction was performed in the presence of a $Pd_2(dba)_3$-$CHCl_3$ (0.5 mol % Pd) and PPh_3 (2 mol %) combination in MeOH, and under balloon pressure of CO at 25 °C (Table 4.1, entry 1). The catalyst loading could even be reduced by half (0.25% Pd, 1% PPh_3) without compromising the product yield (entry 2). The optimum PPh_3/Pd ratio appears to be 4:1, because any deviation from this ratio resulted in a decrease in the reaction rate (entries 1-4). Finally, the controlled experiments proved that no conversion for the substrate would be possible in the absence of a phosphine ligand or a palladium source (entries 5 and 6).

Table 4.1. Methoxycarbonylation of Enyne Oxirane (*Z*)-**1a**.[a]
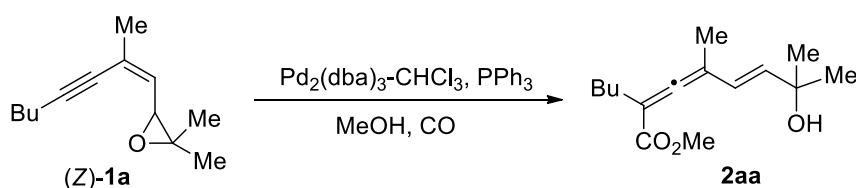
entry	Pd %	PPh₃%	*t* (h)	yield%[b]
1	0.5	2	1	>99[c]
2	0.25	1	2	>99
3	0.5	3	3	>99
4	0.25	0.5	5	>99
5	1	0	16	0
6	0	4	16	0

[a]Reaction conditions: 0.3 mmol of (*Z*)-**1a**, 2 mL of MeOH, under CO filled balloon, 25 °C. [b]Determined by ^{1}H NMR analysis using benzaldehyde as the internal standard. [c]Isolated yield.

Having determined that the enyne oxirane (*Z*)-**1a** is a perfectly amenable reagent toward palladium catalysis as a means to synthesize vinylallene structures, we next probed the diastereoselectivity—directly associated with the level of center-to-axial chirality transfer—of the method over the substrate (*Z*)-**1b**, using a variety of mono- and bidentate ligands. The corresponding vinylallene product **2ba** was in 96% yield with a good diastereomeric ratio (92:8) when PPh$_3$ was used as the ligand (Table 4.2, entry 1). The relative configuration of its major diastereomer was determined by X-ray crystallography of its phenylcarbamate derivative (Figure 4.1), (Kuş, *et al*. 2015).
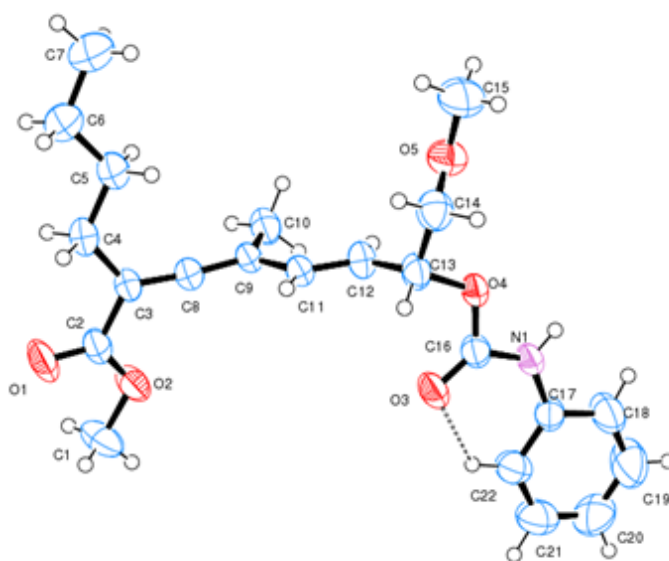
Figure 4.1. X-ray crystallographic structure of the phenylcarbamate derivative of **2ba**.

Typically, comparable yields are obtained with a variety of monodentate phosphine ligands tested herein, with varying reaction times required for a full conversion. However, it has been found that the level of the chirality transfer is strongly dependent on the ligand type that is used. The reactions in the presence of a prepared catalyst Pd(PPh$_3$)$_4$ or P(2-MeC$_6$H$_4$)$_3$ ligand proceeded with similar selectivities when compared with PPh$_3$ (entries 2 and 3), whereas electron rich phosphines and a heteroaryl substituted phosphine all showed inferior stereoselectivities (entries 4-7). The best diastereoselectivity was obtained with the use of an electron poor phosphine ligand, P(4-CF$_3$C$_6$H$_4$)$_3$, which afforded **2ba** with 94% yield and 94:6 diastereoselective ratio (dr) within just 30 min (entry 8). Finally, the use of bidentate ligands brought about dismal selectivities or low activities in some cases (entries 9-14).

Table 4.2. The Effect of Ligand on Methoxycarbonylation of (Z)-**1ba**.
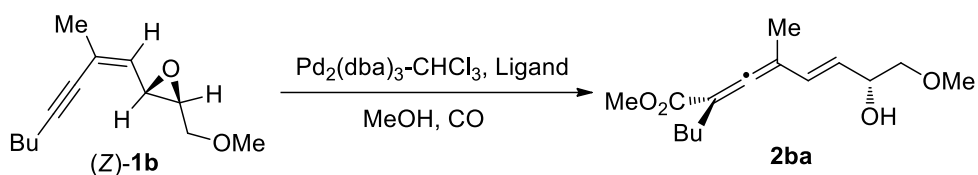
entry	ligand	t (h)	yield%[b]	dr[c]
1	PPh₃	1	96	92:8
2	PPh₃[d]	4	89	92:8
3	P(2-MeC₆H₄)₃	0.5	92	92:8
4	P(2-OMeC₆H₄)₃	0.5	97	87:13
5	P(4-OMeC₆H₄)₃	1	95	86:14
6	PPh₂Me	2.5	81	80:20
7	Tris(2-furyl)phosphine	1	94	83:17
8	P(4-CF₃C₆H₄)₃	0.5	94[e]	94:6
9	dppf	1	72	90:10
10	dppe	3	96	86:14
11	dppb	1.5	89	86:14
12	Xantphos	1.5	92	86:14
13	(±)-BINAP	9.5	44[f]	85:15
14	BIPHEP	10	0	-

[a]Reaction conditions: 0.1 mmol of (Z)-**1b**, 2 mL of MeOH, 1 mol % of Pd, P/Pd ratio is 4:1, under CO filled balloon, 25 °C. dppf: 1,1′-bis(diphenylphosphino)ferrocene; dppe: 1,2-bis(diphenylphosphino)ethane; dppb: 1,4-bis(diphenylphosphino)butane; Xanthphos: 4,5-bis(diphenylphosphino)-9,9-dimethylxanthene; BINAP: 2,2′-bis(diphenylphosphino)-1,1′-binaphthalene; BIPHEP: 2,2′-bis(diphenylphosphino)-1,1′-biphenyl. [b]Determined by ¹H NMR analysis using benzaldehyde as the internal standard. [c]Diastereomeric ratio (dr) was determined by ¹H NMR. [d]Pd(PPh₃)₄ was the catalyst of this reaction. [e]Isolated yield. [f]The conversion of (Z)-1b was 49%.111

Having determined P(4-CF₃C₆H₄)₃ as the optimal ligand, next we explored the suitability of a number of alcohol reagents for their reactions with (Z)-**1b**. Except those with *t*-BuOH (Table 4.3, entry 5), the vinylallene products could be obtained at yields within the range of 83-91% with all alcohol reagents tested herein. Surprisingly, however, the reactions performed with alkyl alcohols, including EtOH, PrOH, BuOH, and *i*-PrOH; all proceeded with relatively lower stereoselectivities (entries 1-5). Nevertheless, gratifyingly an additional functionality could be introduced to a 7-hydroxy-2,3,5-trienoate structure with the use of allyl alcohol, which yielded the corresponding product **2bg** in 91% yield and with 93:7 dr, albeit with higher Pd loading to complete the reaction (entries 6-7).

Table 4.3. Alkoxycarbonylation of Enyne Oxirane (Z)-**1a**.[a]
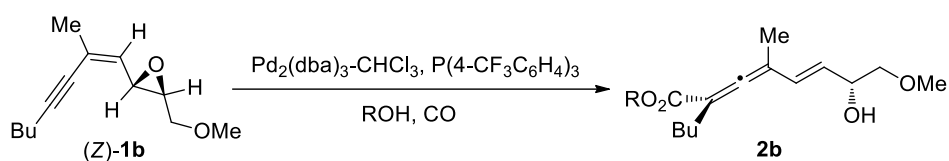
entry	ROH	product	t (h)	yield %	dr[b]
1	EtOH	**2bb**	1	84	80:20
2	PrOH	**2bc**	3	87	88:12
3	BuOH	**2bd**	4	83	86:14
4	*i*-PrOH	**2be**	2	88	86:14
5	*t*-BuOH	**2bf**	10	0	-
6[c]	Allyl	**2bg**	6	25	93:7
7[d]	alcohol		1	91	93:7

[a]Performed under the conditions of Table 4.2. [b]Determined by ^{1}H NMR. [c]Conversion of (Z)-**1b** was 75%. [d]Reaction was performed with 3 mol % of Pd and 12 mol % of ligand.

It seems that the method is also suitable for enyne oxiranes containing an (E)-configured alkenyl moiety; a carbonylation reaction of (E)-**1b** in MeOH under the standard conditions (conditions denoted in Table 4.2) required remarkably longer reaction period for complete conversion, and resulted in a diastereomer of **2ba** (**2ba'**) with a high yield, but slightly decreased selectivity of 92:8 dr (Figure 4.2). This result also proves that the configuration of alkenyl moiety of substrate regulates the stereomeric outcome of the product. Nonetheless, because of some difficulties encountered during the synthesis of enyne oxiranes with (E)-alkenyl group, such as partial isomerization of the alkenyl group, further studies were continued using only (Z)-configured reagents.
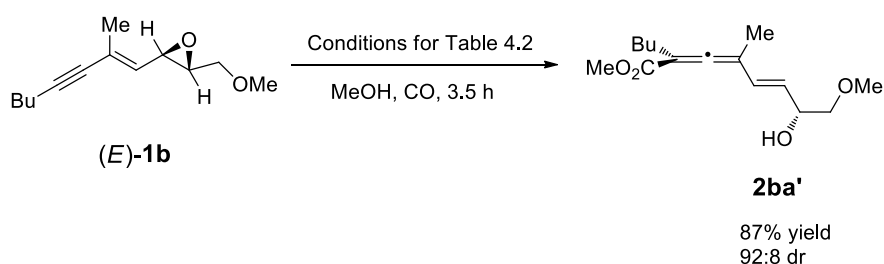
Figure 4.2. Methoxycarbonylation of (E)-**1b**

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Next we explored the scope of the protocol over a variety of substrates containing (*Z*)-alkenyl and (*E*)-oxirane moieties. Except in one case, alkoxycarbonylation reactions proceeded rather smoothly and provided the expected products at yields within the range of 81-92%.

It was interesting to observe that the form of pendant oxygen functionality within R^3 group is an important factor for the stereoselectivity of the process. Substituting the methoxymethyl group in R^3 position with a benzyloxymethyl group ((*Z*)-**1c**) had no detectable effect on both the reactivity and stereoselectivity (Table 4.4, entry 1). However, when R^3 was a carbinol group ((*Z*)-**1d**) or its hydroxyl group was silyl protected ((*Z*)-**1e**), the corresponding methoxycarbonylated products **2da** and **2ea** were obtained with 90:10 and 89:11 dr, respectively (entries 2 and 3).

The same trend was also obvious for the reactions of (*Z*)-**1f** and (*Z*)-**1g**, where R^3 is dimethylcarbinol and dimethylmethoxy methyl, respectively. Though comparably good yields could be achieved with both reagents, the products **2fa** and **2ga** were obtained with significantly different level of stereoselectivities, 85:15 and 95:5 dr, respectively (entries 4 and 5).

It seems that for an effective stereoselectivity, the alkenyl carbon that is proximal to the alkynyl moiety is required to be fully substituted, because the carbonylative reaction of the enyne oxirane containing a disubstituted alkenyl moiety ((*Z*)-**1h**) with MeOH proceeded with an inferior stereoselectivity (entry 6). As a model for substrates with all alkyl substituents, the enyne oxirane (*Z*)-**1i**, where all R^1, R^2, and R^3 positions were occupied by butyl groups, also gave rise to the expected product **2ia** with a high selectivity of 93:7 dr (entry 7). However, (*Z*)-**1j** possessing a methyl group in the R^3 interestingly afforded the lowest dr (82:18) as compared to other enyne oxiranes tested herein (entry 8). While the method tolerated a larger cyclohexyl group in the R^2 (entry 9) under the reaction conditions, the presence of the *tert*-butyl group at this position ((*Z*)-**1l**) brought about the formation of an allylic esterified byproduct (**3la**) along with the desired product **2la** with a high dr (entry 10).

It was also intriguing to find that there appears to be a direct relation between the diastereoselectivity and the size of R^1 (entries 11-13). For instance, when (*Z*)-**1m**, which contains a terminal alkynyl moiety, was subjected to the methoxycarbonylation, the product **2ma** was obtained with only 88:12 dr Nevertheless, the substrate (*Z*)-**1o** ($R^1 = t$-Bu) afforded the expected product **2oa** in an excellent level of selectivity (97:3 dr).

The remarkable improvement on the stereoselectivity of the process that was gained with the presence of the *tert*-butyl group on the alkynyl moiety appears enduring; in contrast to the results obtained with (Z)-**1b**, when R^1= *tert*-butyl, the replacement of the methoxy group with benzyloxy ((Z)-**1p**), hydroxyl ((Z)-**1q**), or silyl protected ((Z)-**1r**) groups within R^3 only slightly impacted the dr of the corresponding products (entries 14-16).

Table 4.4. Alkoxycarbonylation of Enyne Oxiranes.[a]
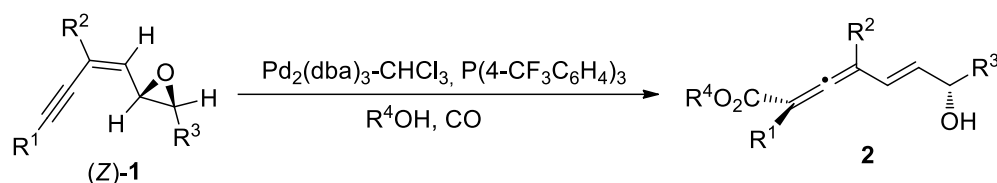
Entry	Reactant	Time (min)	Product	Yield (%)	dr[b]
1	(Z)-**1c**	30	**2ca**	90	94/6
2	(Z)-**1d**	100	**2da**	84	90/10
3	(Z)-**1e**	50	**2ea**	82	89/11
4	(Z)-**1f**	60	**2fa**	90	85/15
5	(Z)-**1g**	45	**2ga**	89	95/5
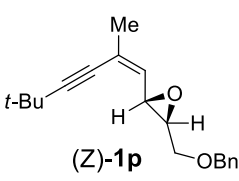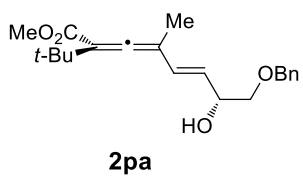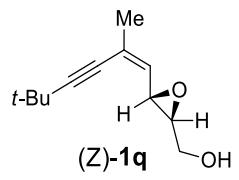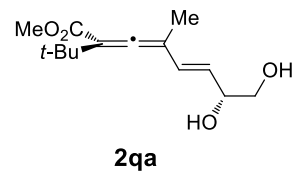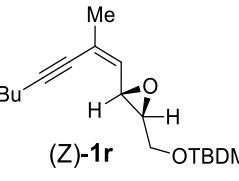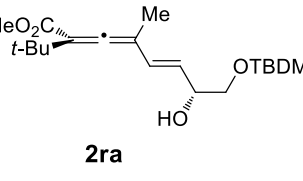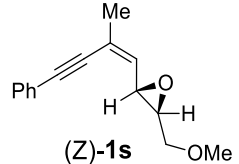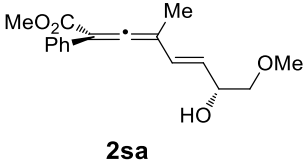
(cont. on next page)

Table 4.4. (cont.)

6	(Z)-**1h**	45	**2ha**	87	85/15
7	(Z)-**1i**	90	**2ia**	82	93/7
8	(Z)-**1j**	70	**2ja**	87	82/18
9	(Z)-**1k**	50	**2ka**	89	94/6
10	(Z)-**1l**	110	**2la**	68	95/5
			+ **3la**	14	ND[c]
11	(Z)-**1m**	300	**2ma**	81	88/12
12	(Z)-**1n**	90	**2na**	92	94/6
13	(Z)-**1o**	90	**2oa**	89	97/3

(cont. on next page)

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Table 4.4. (cont.)

14	(Z)-**1p**	45	**2pa**	86	96/4
15	(Z)-**1q**	30	**2qa**	87	94/6
16	(Z)-**1r**	45	**2ra**	84	96/4
17	(Z)-**1s**	45	**2sa**	87	88/12

[a]Performed under the conditions of Table 4.2. [b]Determined by ^{1}H NMR. [c]Not determined.

The enyne oxirane (Z)-**1s** with a phenyl substituent at alkynyl terminus yielded the product **2sa** with 88:12 dr (entry 20), and the substrate **1t** having an endocyclic double bond also successfully underwent methoxycarbonylation to generate an exocyclic conjugated vinylallene structure **2ta** with a relatively lower but synthetically still useful dr (Figure 4.3).
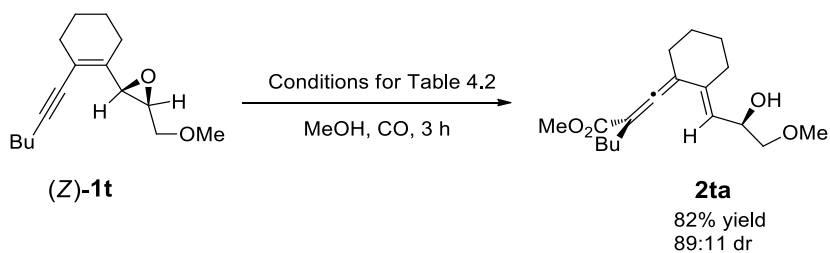
Figure 4.3. Methoxycarbonylation of (Z)-**1t**

Moreover, the carbonylative reaction of (*Z*)-**1o** with other alcohols also provided the corresponding vinylallenes with high dr values (Table 4.5).

Table 4.5. Alkoxycarbonylation of Enyne Oxirane (*Z*)-**1o**.[a]
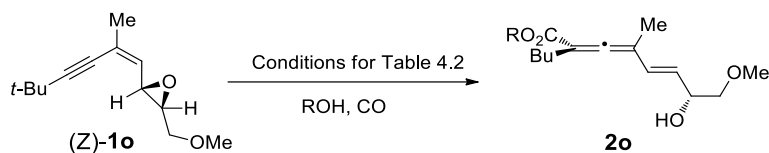
entry	ROH	product	t (h)	yield %	dr[b]
1	EtOH	**2ob**	2	91	95:5
2	*i*-PrOH	**2oe**	3	88	94:6
3[c]	Ally alcohol	**2og**	1	88	95:5

[a]Performed under the conditions of Table 4.2. [b]Determined by ^{1}H NMR. [c]Reaction was performed with 3 mol % of Pd and 12 mol % of ligand.

The mechanisms illustrated in Figure 4 are proposed to account for the stereoselective formation of **2** and **2'**. The reaction cycle should begin with ring-opening by the attack of a palladium complex to both (*Z*)-**1** and (*E*)-**1** in *anti*-mode, leading to the formation of π-allylpalladium complexes **A** and **A'**, respectively, given the formation of vinylallenes exclusively in (*E*)-configuration for both intermediates (**A** and **A'**), the alkanolate group (CHR^{3}O$^-$) on the planar allyl ligand should be oriented *syn* with respect to the middle allylic C-H. These intermediates additionally undergo a palladium shift to the far alkynyl carbon proceeding mainly with retention to form vinylallenyl palladium complexes **B** and **B'**, respectively. The relative position of the R^2 group and alkynyl moiety on **A** and **A'** may also be inverted via the π-σ-π interconversion into **C** and **C'**, respectively, before undergoing such a Pd shift. The favored configuration of this side of the complex should be regulated by the inherent structure of R^2. For instance when R$_2$ is hydrogen the thermodynamically more stable π-allyl complexes should bear alkynyl and CHR^{3}O$^-$ moieties in *syn*, *syn* positions (**A'** and **C**).
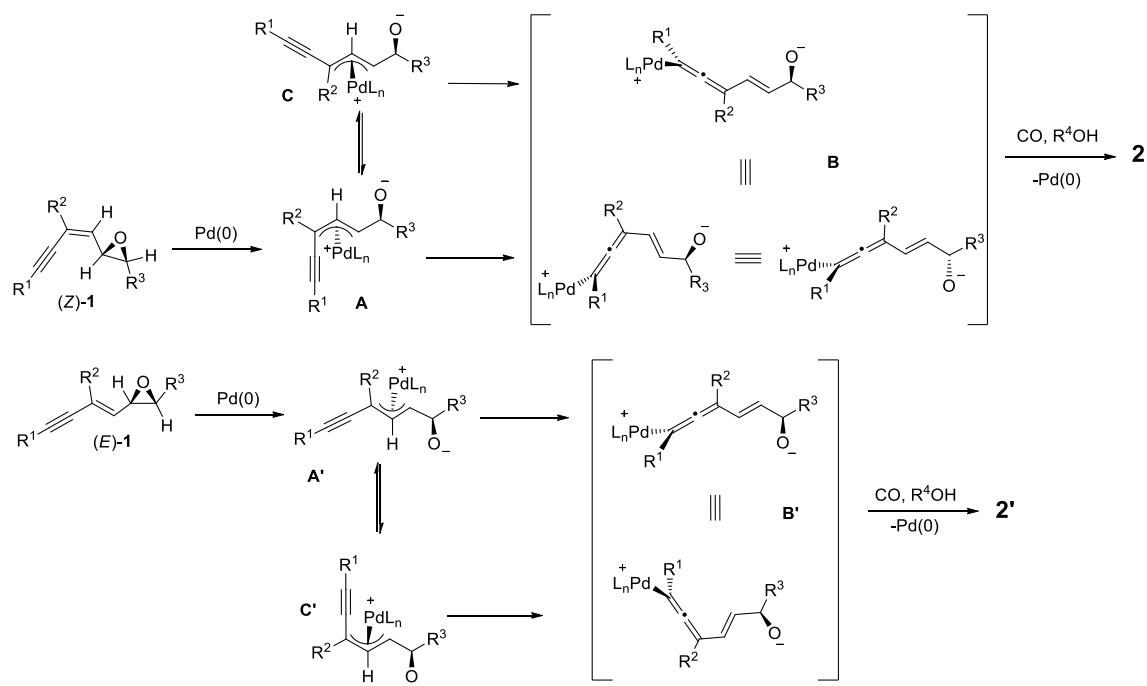
Figure 4.4. The Mechanism of Alkoxycarbonylation of Conjugated Enyne Oxiranes.

However, such configurational transitions cannot alter the outcome of the reaction, because both isomeric intermediates **C** and **C'** would also lead to **B** and **B'**, respectively. These σ-allenylpalladium complexes undergo successive CO insertion and reductive elimination, as verified previously, to yield **2** and **2'** stereoselectively.

The loss of stereochemical integrity of the resulting products should take place during the course of the reaction cycle because subjecting the purified **2ba** again to the standard conditions for 4 h had no influence on its original diastereomeric ratio. Though we cannot completely disregard the occurrence of the π-allylpalladium isomerization or its formation through *syn*-attack of the palladium, the back side migration of the palladium over the alkynyl side (by inversion of configuration) could be the primary basis for the formation of the minor diastereomeric form in each case, and particularly increased sizes of R^1 and R^2 might have limited the occurrence of such transitions in an inverted manner. However, the presence of a highly encumbered group, such as *tert*-butyl, at R^2 also retards the effective migration of the π-allyl coordinated palladium, and as a result (*Z*)-**1l** partly underwent allylic alkoxycarbonylation to form the byproduct **3la**.

Finally, the enyne oxirane (*Z*)-**1i'** containing a (*Z*)-configured oxirane moiety was also the subjected to the standard reaction conditions. The reaction proceeded smoothly in accordance to the proposed mechanism, and thus yielded the vinylallene product **2ia'**, which is the diastereomer of **2ia** (see entry 7 of Table 4.4), with a high level of dr (Figure 4.5).
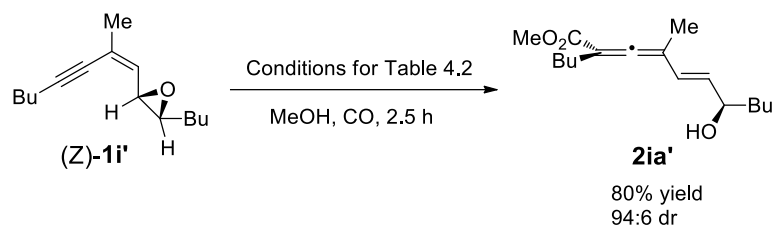
Figure 4.5. Methoxycarbonylation of (*Z*)-**1i**.

CHAPTER 5

CONCLUSION

In summary, we have developed a mild, simple and atom economical method for the synthesize of *anti*-substituted (*E*)-configured vinylallenes bearing a hydroxyl group on the allylic position via palladium-catalyzed alkoxycarbonylative 1,5-substitution reactions of conjugated enyne oxiranes.

The optimization studies showed that the reactions can be performed in the presence of $Pd_2(dba)_3$-$CHCl_3$ catalyst, an electron poor phosphine ligand, $P(4-CF_3C_6H_4)_3$, and balloon pressure of carbon monoxide, which afforded the desired vinyallene structures with good yields and diastereoselectivities.

The reactions proceeded in a highly stereoselective manner, possibly through sequential formation of π-allylpalladium and σ-vinylallenyl palladium complexes and the major diastereomeric form of the product is determined by the configuration of the alkenyl moiety of the substrate.

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APPENDIX A

1H NMR and 13C NMR SPECTRUMS OF REACTANTS AND PRODUCTS

Agilent Technologies

(Z)-**1a**

Me

Bu

Me

O

Me

3.682
3.660

2.383
2.366
2.348
1.897
1.893
1.556
1.553
1.539
1.536
1.531
1.519
1.466
1.448
1.429
1.370
1.293
0.942
0.923
0.906

-0.003

7   6   5   4   3   2   1   ppm

4.61   4.54   9.62   14.39   22.93   14.69   14.40   14.81

Sample Name:
  MK-1a
Data Collected on:
  vnmrs400-vnmrs400
Archive directory:
  /home/user1/vnmrsys/data
Sample directory:
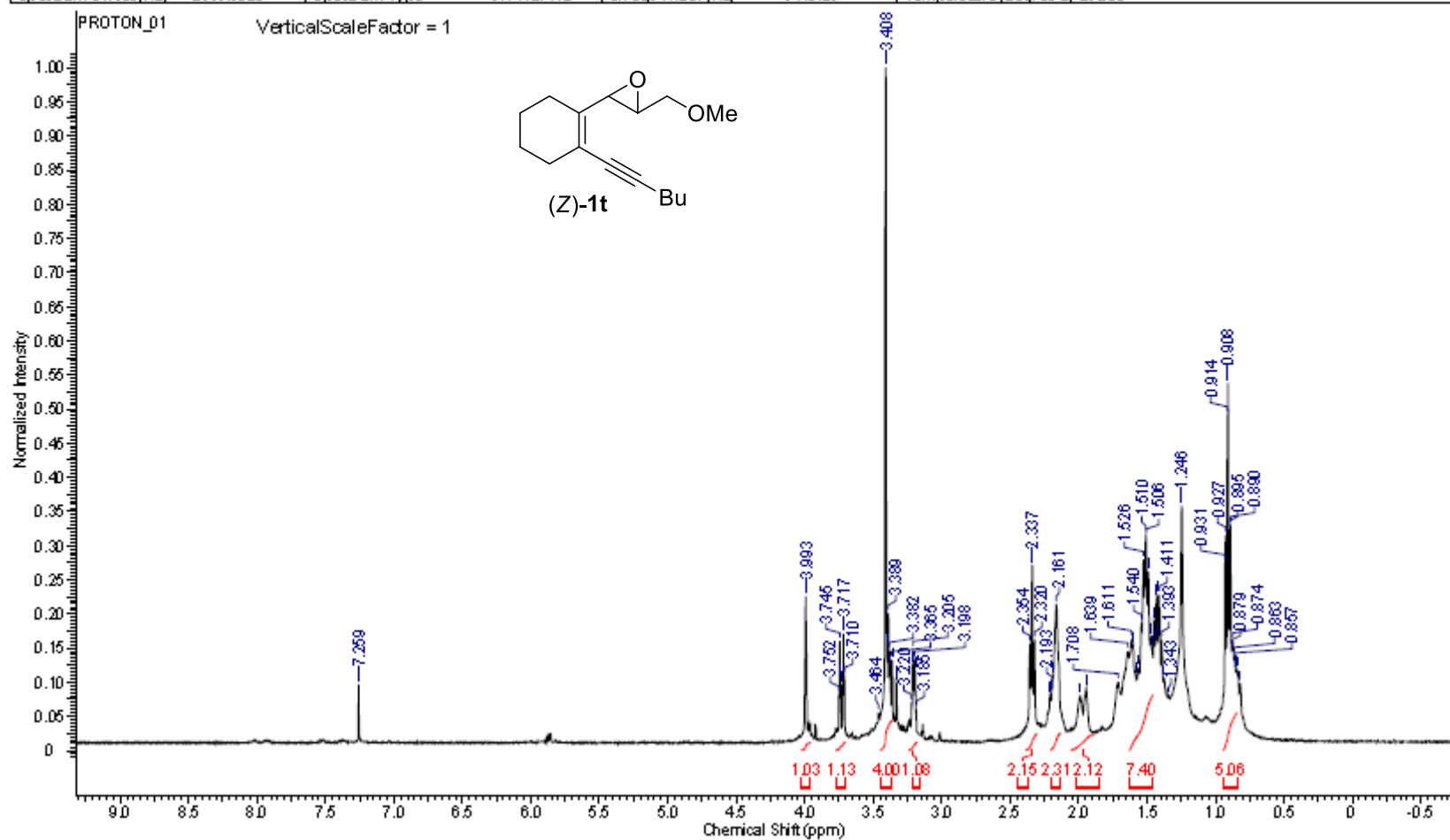 MK-1a_20141021_01
FidFile: CARBON

Pulse Sequence: CARBON (s2pul)
Solvent: cdcl3
Data collected on: Oct 21 2014

Temp. 25.0 C / 298.1 K
Operator: user1

Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 1.311 sec
Width 25000.0 Hz
256 repetitions
OBSERVE C13, 100.5589851 MHz
DECOUPLE H1, 399.9181065 MHz
Power 46 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
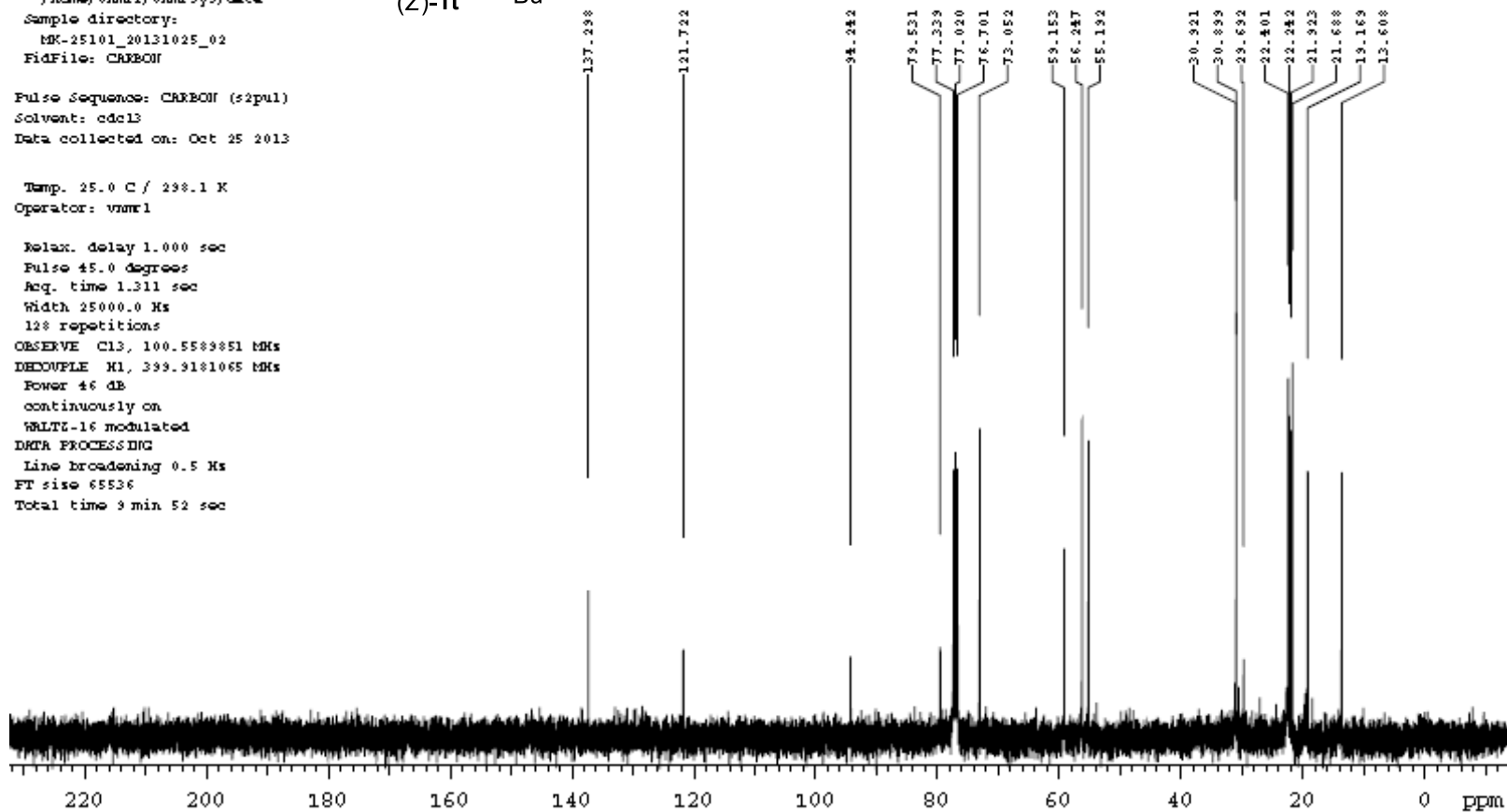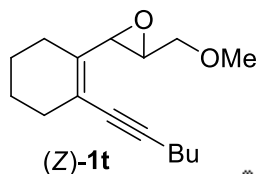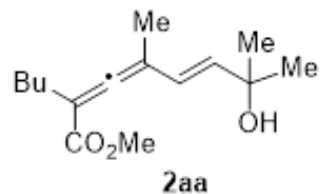Line broadening 0.5 Hz
FT size 65536
Total time 38 min

Agilent Technologies

(Z)-**1a**

Peaks: 130.592, 125.394, 95.805, 78.977, 77.331, 77.012, 76.694, 62.476, 60.359, 30.754, 24.799, 24.040, 21.923, 19.473, 19.154, 13.578

150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm

Me

Bu

H

OMe

H

(Z)-1b

Agilent Technologies

5.244
5.241
5.221
5.218
3.749
3.743
3.730
3.726
3.722
3.720
3.702
3.694
3.420
3.410
3.404
3.391
3.377
3.093
3.088
3.086
3.080
3.073
3.071
3.065
2.372
2.355
2.337
1.870
1.868
1.595
1.583
1.551
1.547
1.533
1.530
1.524
1.512
1.507
1.495
1.456
1.444
1.439
1.437
1.425
1.418
1.400
0.939
0.921
0.903

8   7   6   5   4   3   2   1   ppm

4.45

9.33   19.24   4.49

9.76

14.90

22.91

14.93

FZ-FX048-13C

Sample Name:
 FZ-FX048-13C
Data Collected on:
 vnmrs400-vnmrs400
Archive directory:
 /home/vnmr1/vnmrsys/data
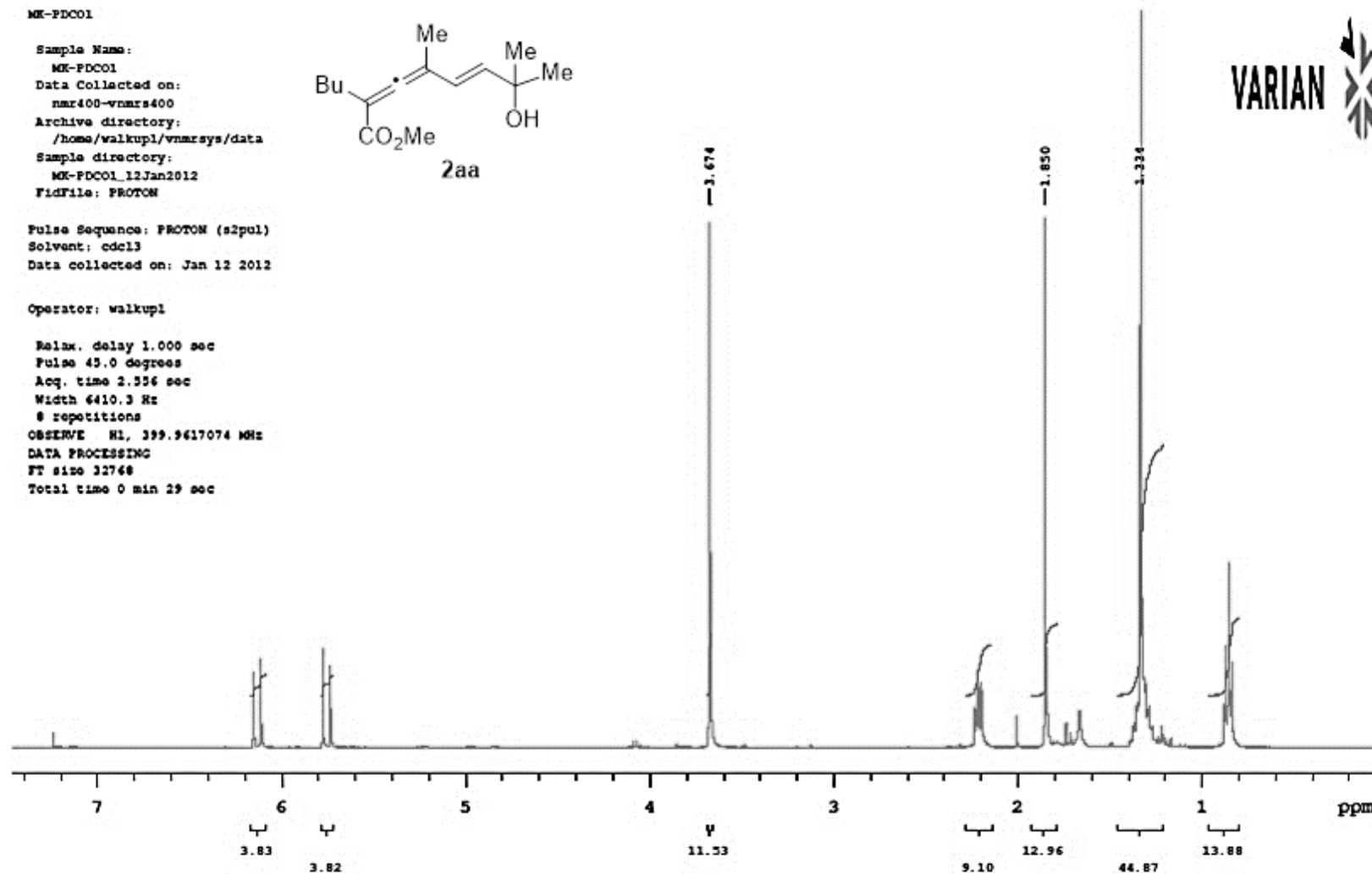Sample directory:
 FZ-FX048-13C_20130912_01
FidFile: CARBON

Pulse Sequence: CARBON (s2pul)
Solvent: cdcl3
Data collected on: Sep 12 2013

Temp. 25.0 C / 298.1 K
Operator: vnmr1

Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 1.311 sec
Width 25000.0 Hz
512 repetitions
OBSERVE C13, 100.5589851 MHz
DECOUPLE H1, 399.9181065 MHz
 Power 46 dB
 continuously on
 WALTZ-16 modulated
DATA PROCESSING
 Line broadening 0.5 Hz
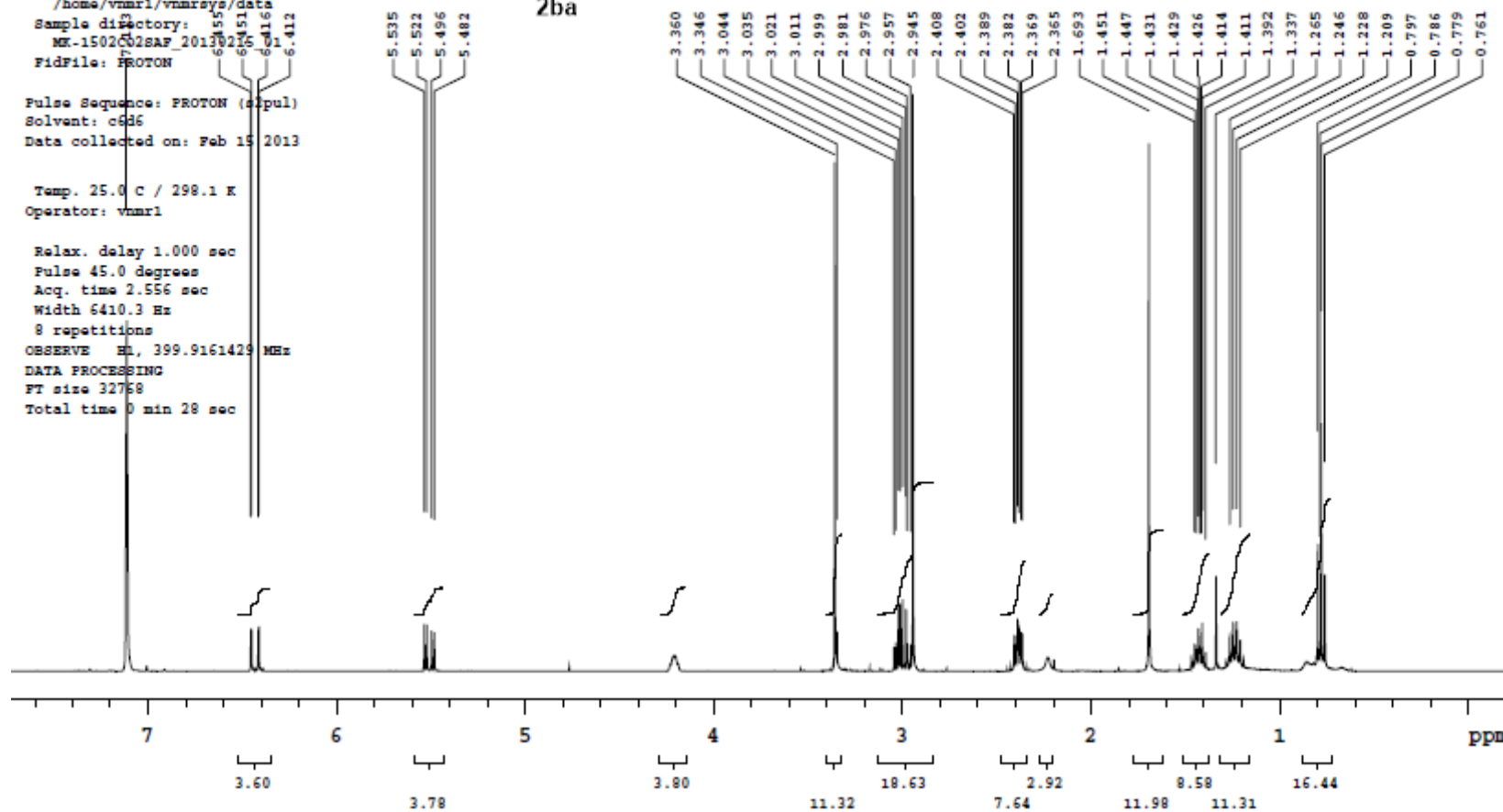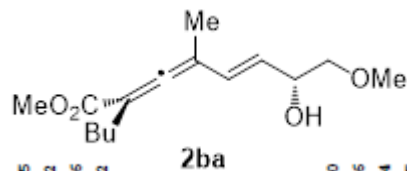FT size 65536
Total time 19 min

Agilent Technologies

(Z)-**1b**
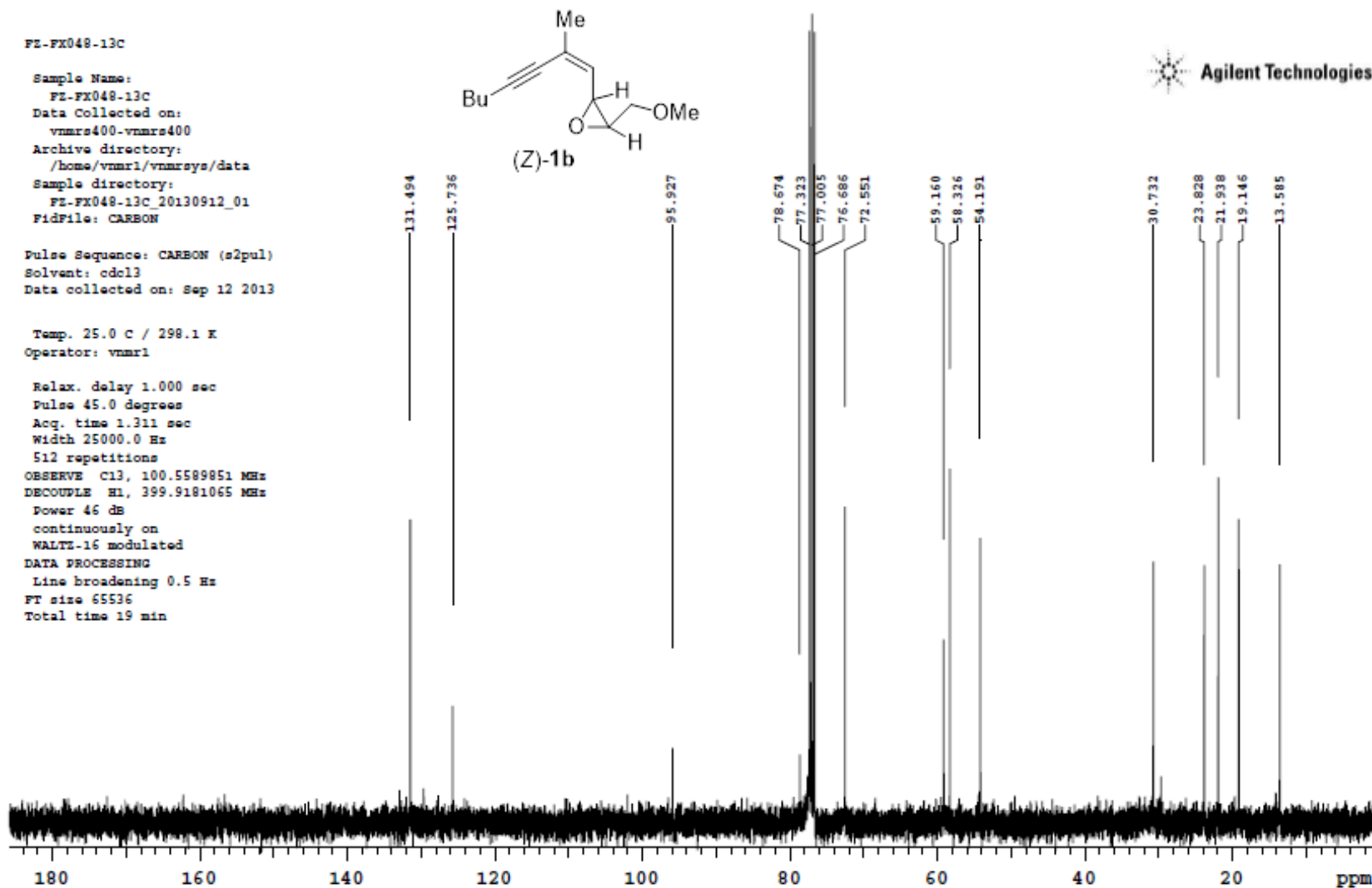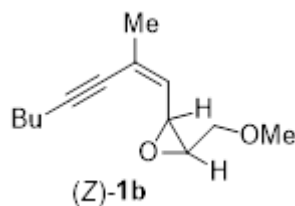
Acquisition Time (sec)	2.5559	Comment	Gradient Shimming			Date	Dec 19 2013
Date Stamp	Dec 19 2013	File Name	C:\USERS\FIRAT\DESKTOP\MELIH\MELIH\MK-1812 OME 20131219 01\PROTON 01.FID\FID				
Frequency (MHz)	399.92	Nucleus	1H	Number of Transients	8	Original Points Count	16384
Points Count	16384	Pulse Sequence	s2pul	Receiver Gain	48.00	Solvent	CHLOROFORM-d
Spectrum Offset (Hz)	2399.5020	Spectrum Type	STANDARD	Sweep Width (Hz)	6410.26	Temperature (degree C)	25.000

PROTON_01   VerticalScaleFactor = 1

(E)-1b

(E)-1b

Agilent Technologies

FZ-FX077

Sample Name:
  FZ-FX077
Data Collected on:
  vnmrs400-vnmrs400
Archive directory:
  /home/vnmr1/vnmrsys/data
Sample directory:
  FZ-FX077_20140521_01
FidFile: PROTON

Pulse Sequence: PROTON (s2pul)
Solvent: cdcl3
Data collected on: May 21 2014

Temp. 25.0 C / 298.1 K
Operator: vnmr1

Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 2.556 sec
Width 6410.3 Hz
8 repetitions
OBSERVE   H1, 399.9161069 MHz
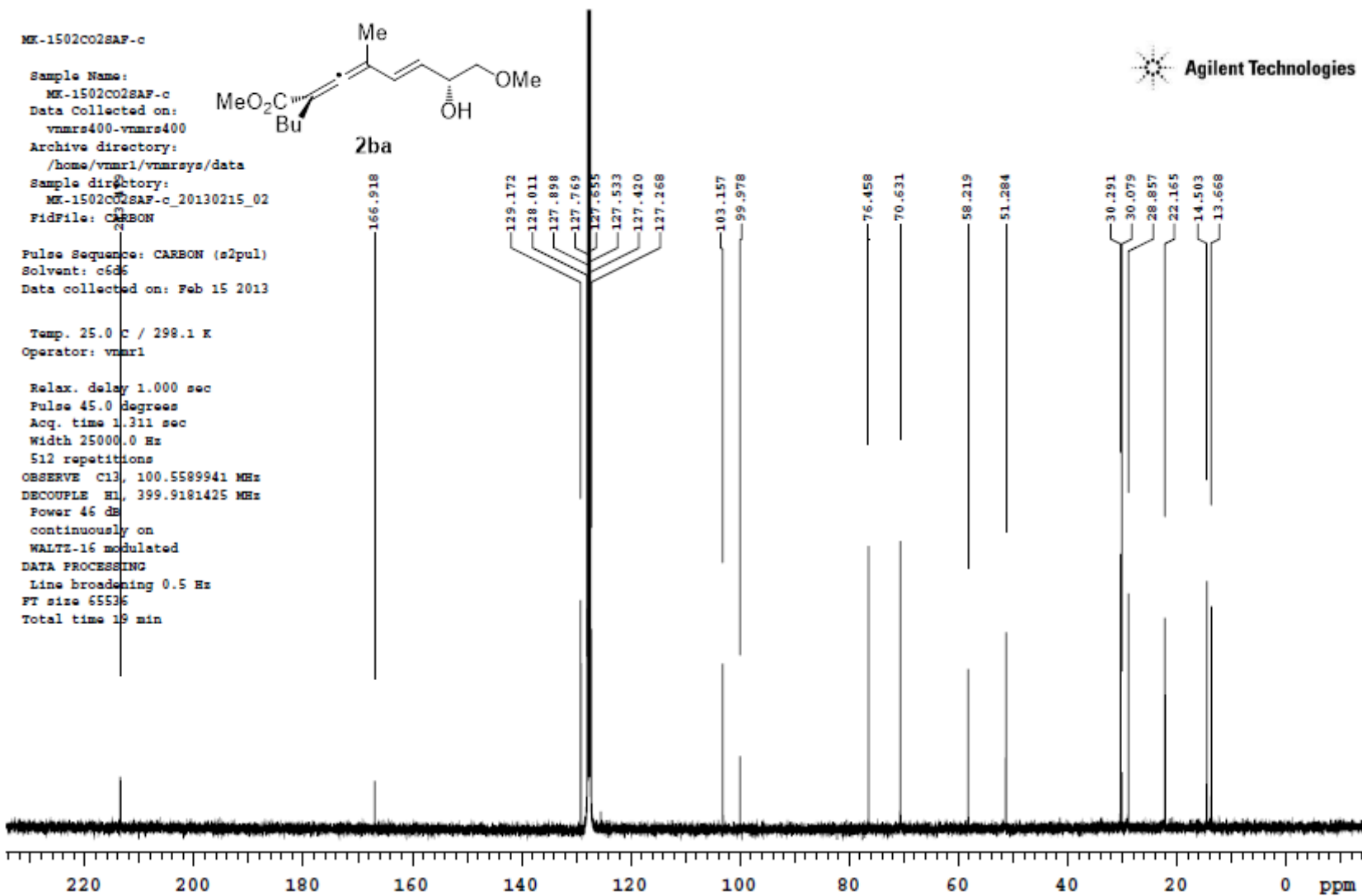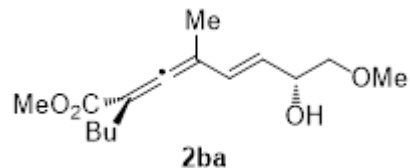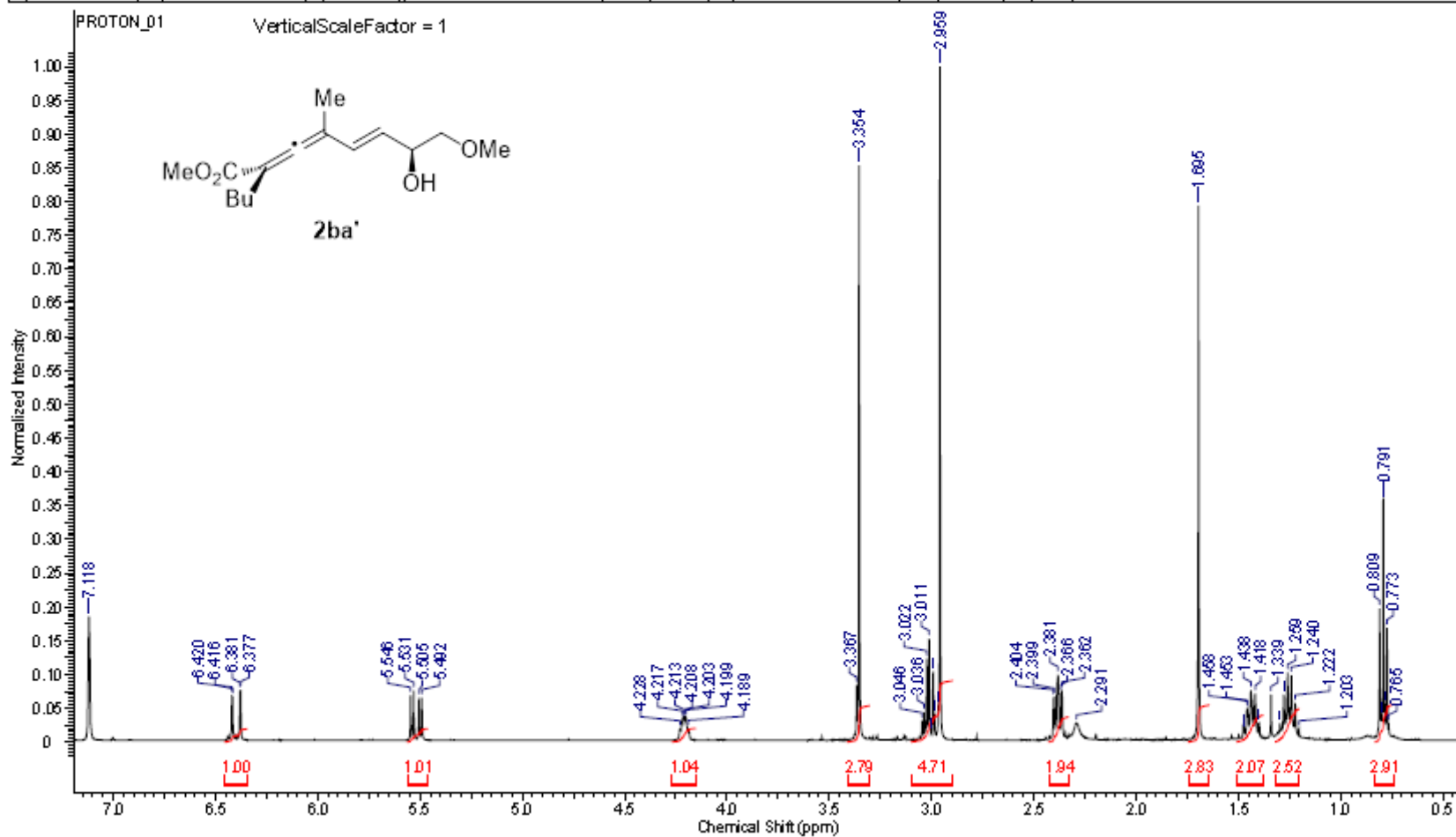DATA PROCESSING
FT size 32768
Total time 0 min 28 sec

(Z)-1d

84
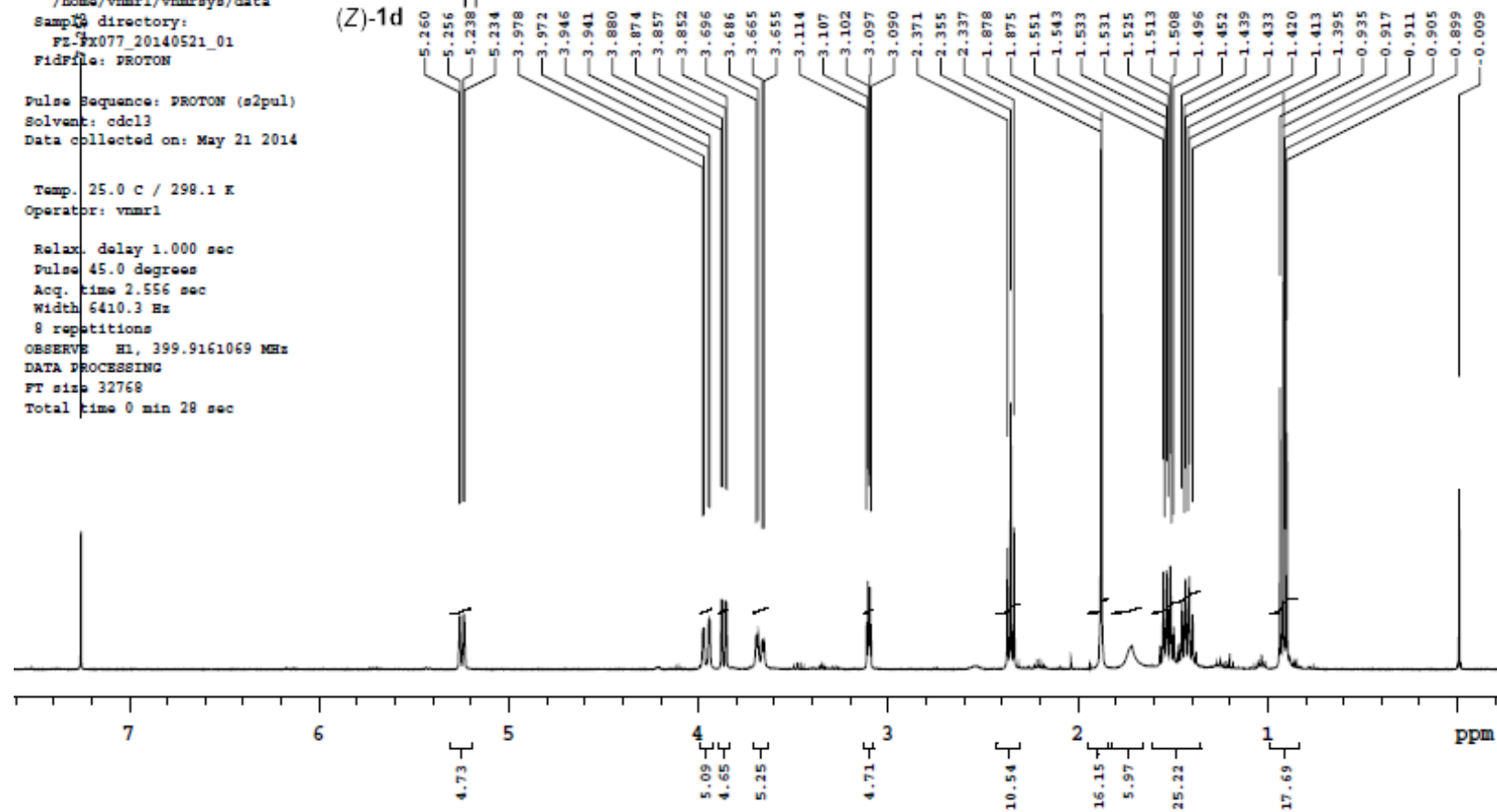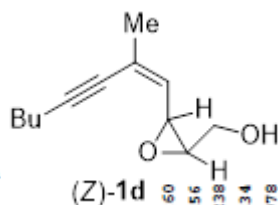
exp41 CARBON

         SAMPLE   PRESATURATION
date   Nov 5 2012   satmode   n
solvent   c6d6   wet   n
file /home/vnmr1/v~   SPECIAL
nmrsys/data/LEVENT~ temp   not used
 ARTOK/MELIH/MELIH~ gain   30
/MK-05-11-12-SAF-T~ spin   20
_20121105_02/CARBO~ hst   0.008
        N_01.fid   pw90   11.700
     ACQUISITION   alfa   10.000
sw   25000.0   FLAGS
at   1.311   il   n
np   65536   in   n
fb   17000   dp   y
bs   64   hs   nn
d1   1.000   PROCESSING
nt   1000   lb   0.50
ct   1000   fn   not used
     TRANSMITTER   DISPLAY
tn   C13   sp   -1437.7
sfrq   100.570   wp   24999.2
tof   1531.2   rfl   1438.5
tpwr   54   rfp   0
pw   5.850   rp   -176.5
      DECOUPLER   lp   0
dn   H1   PLOT
dof   0   wc   268
dm   yyy   sc   0
decwave   w   vs   165204
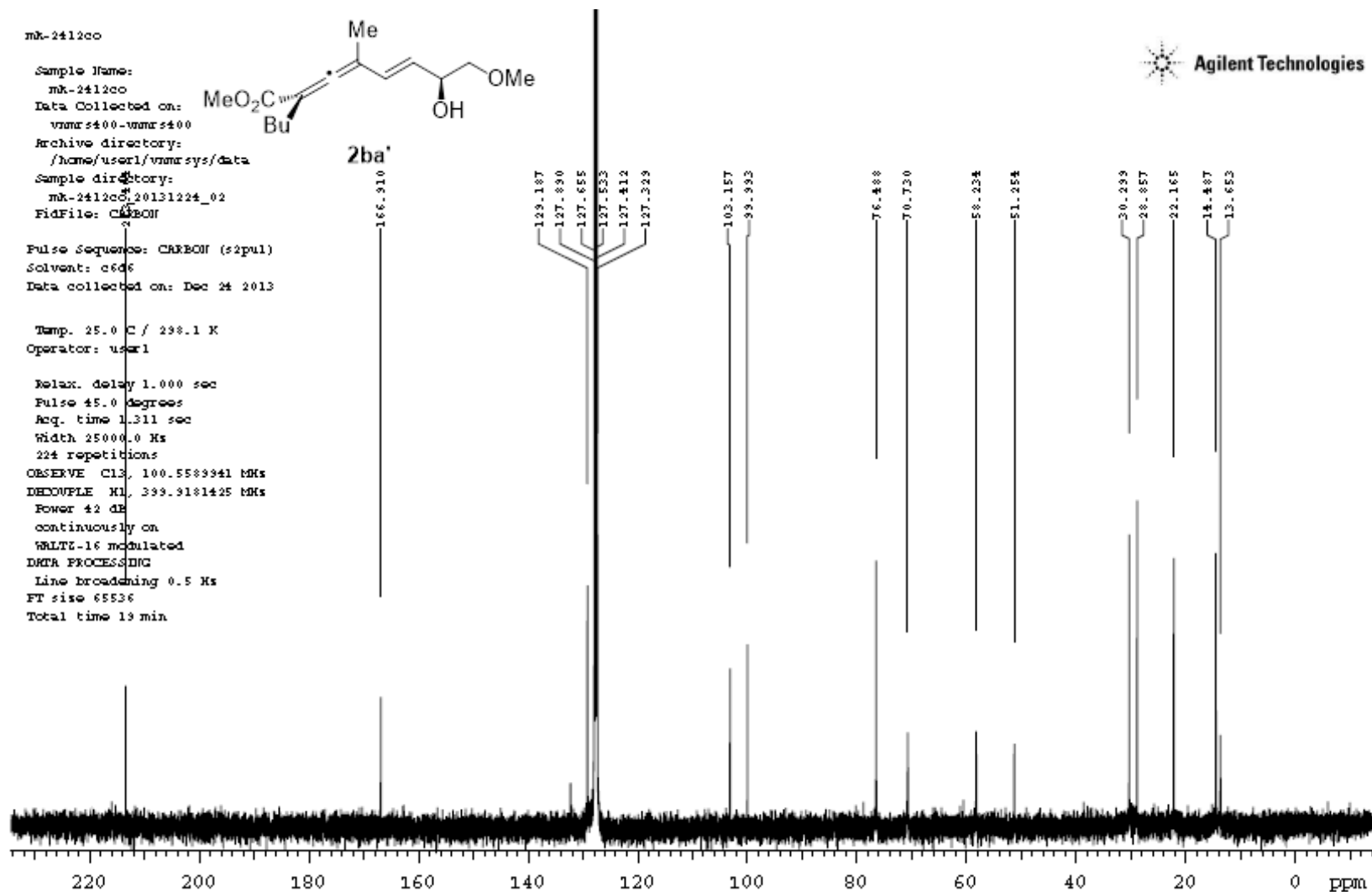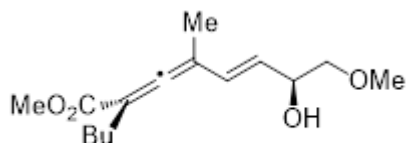dpwr   46   th   10
dmf   10101   ai   cdc   ph
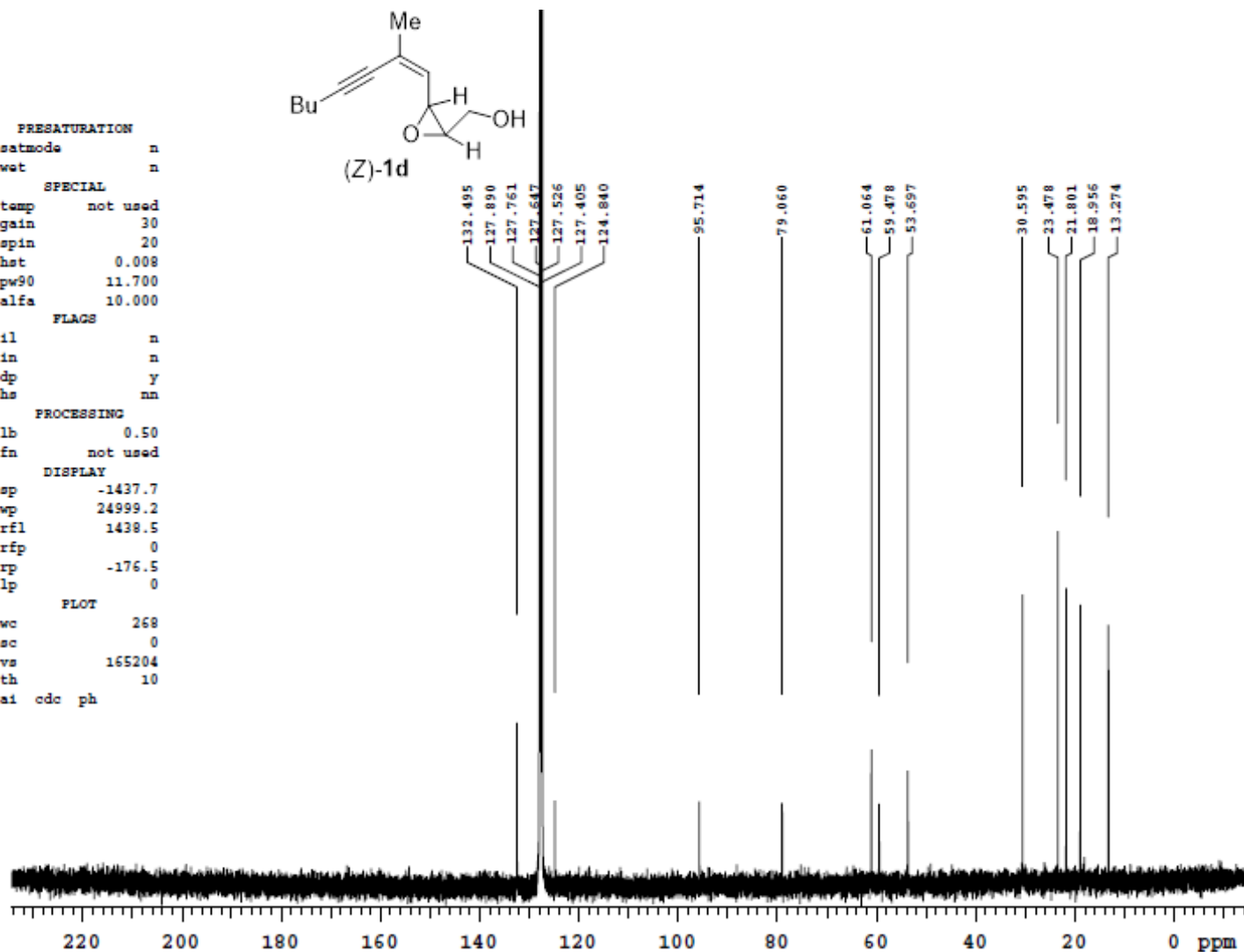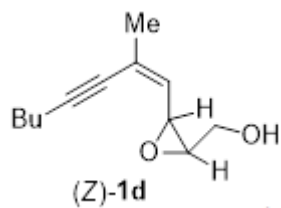
MK-OTBS-REACT

Sample Name:
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Data Collected on:
  vnmrs400-vnmrs400
Archive directory:
  /home/user1/vnmrsys/data
Sample directory:
  MK-OTBS-REACT_20140930_01
FidFile: PROTON_01

Pulse Sequence: PROTON (s2pul)
Solvent: cdcl3
Data collected on: Sep 30 2014

Temp. 25.0 C / 298.1 K
Operator: user1

Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 2.556 sec
Width 6410.3 Hz
8 repetitions
OBSERVE   H1, 399.9161069 MHz
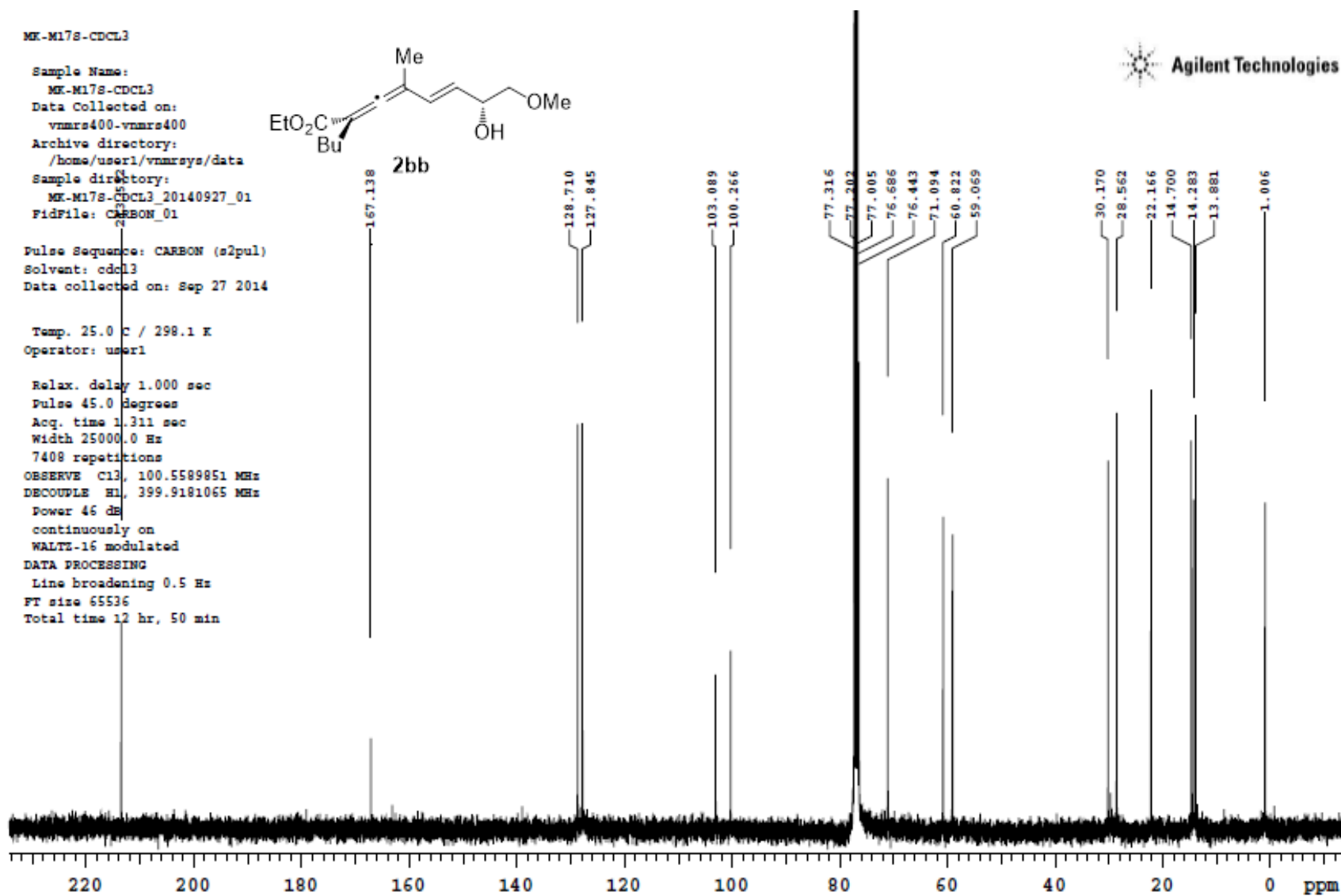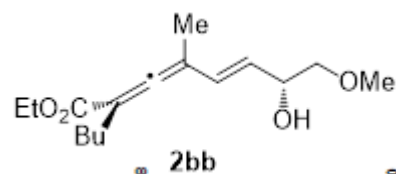DATA PROCESSING
FT size 32768
Total time 0 min 28 sec

(Z)-1e

Sample Name:
  MK-OTBS-REACT
Data Collected on:
  vnmrs400-vnmrs400
Archive directory:
  /home/user1/vnmrsys/data
Sample directory:
  MK-OTBS-REACT_20140930_01
FidFile: CARBON_01

Pulse Sequence: CARBON (s2pul)
Solvent: cdcl3
Data collected on: Sep 30 2014

Temp. 25.0 C / 298.1 K
Operator: user1

Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 1.311 sec
Width 25000.0 Hz
368 repetitions
OBSERVE C13, 100.5589851 MHz
DECOUPLE H1, 399.9181065 MHz
Power 46 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
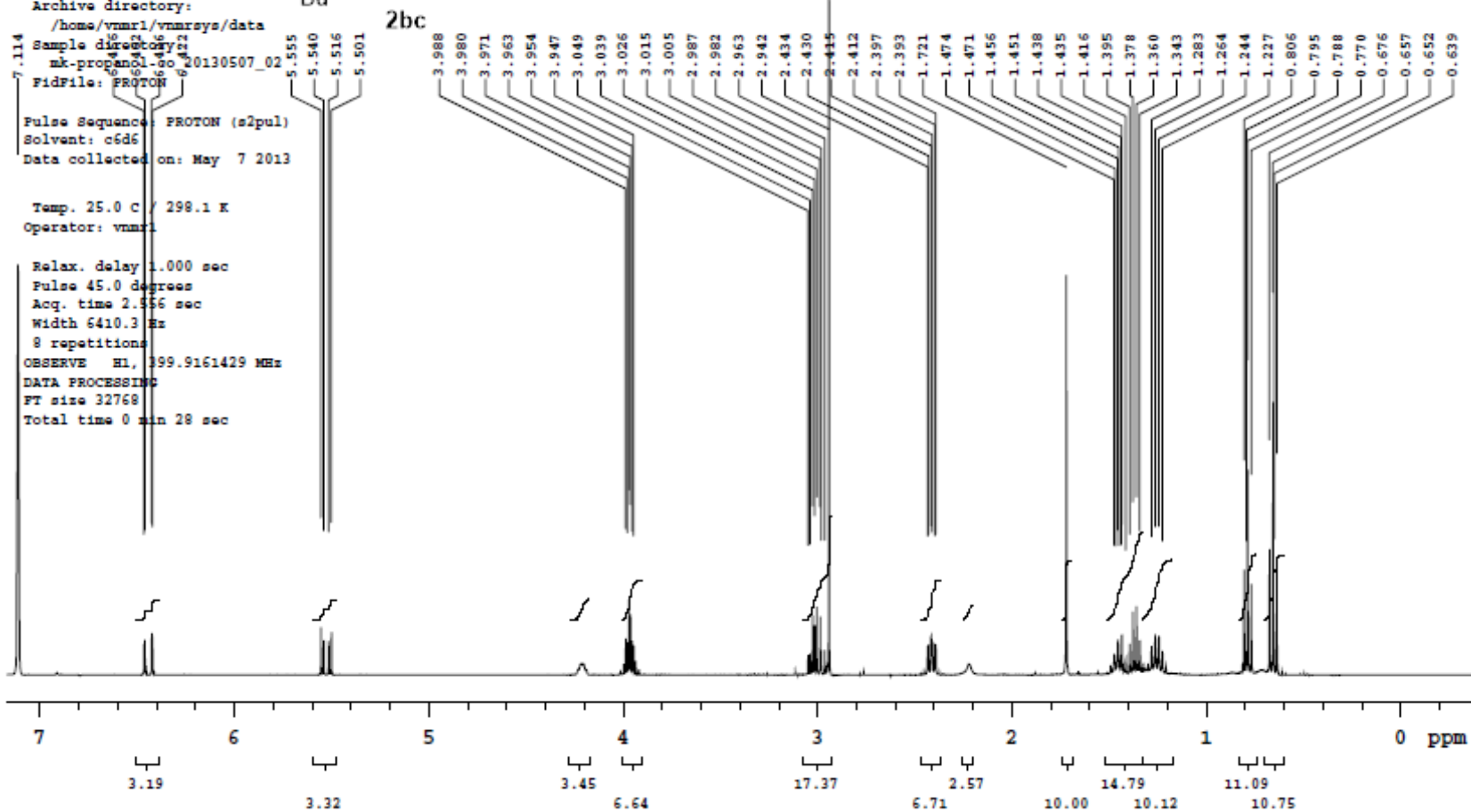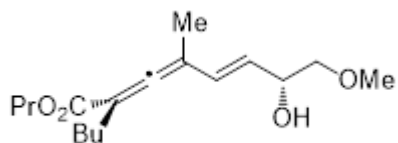Line broadening 0.5 Hz
FT size 65536
Total time 38 min

Me

Bu

H
OTBDMS
O
H

(Z)-1e

131.866
125.281
95.669
78.697
77.346
77.027
76.709
63.022
60.108
54.320
30.792
25.838
23.797
21.984
19.139
18.304
13.562
-5.337
-5.352
-5.367

160   140   120   100   80   60   40   20   0   ppm

(Z)-1f

88

(Z)-**1f**

Agilent Technologies

131.449
125.508
95.109
78.643
77.308
76.997
76.678
67.809
66.064
54.046
30.724
27.735
24.859
23.835
21.931
19.146
13.562

68

MK-1g

Sample Name:
MK-1g
Data Collected on:
vnmrs400-vnmrs400
Archive directory:
/home/user1/vnmrsys/data
Sample directory:
MK-1g_20141020_01
FidFile: PROTON

Pulse Sequence: PROTON (s2pul)
Solvent: cdcl3
Data collected on: Oct 20 2014

Temp. 25.0 C / 298.1 K
Operator: user1

Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 2.556 sec
Width 6410.3 Hz
8 repetitions
OBSERVE   H1, 399.9161069 MHz
DATA PROCESSING
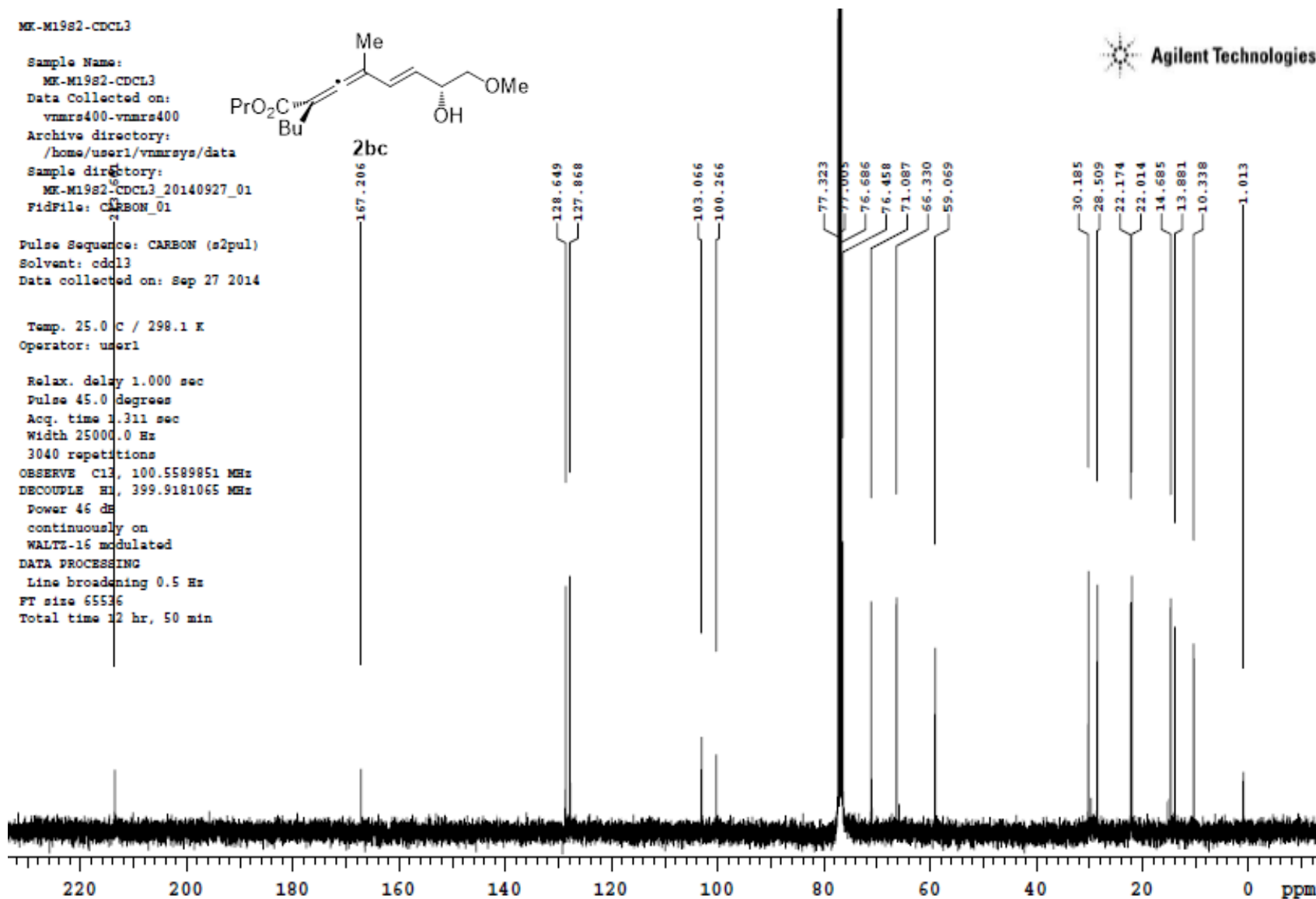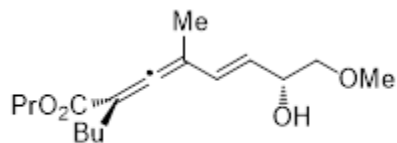FT size 32768
Total time 0 min 28 sec

(Z)-1g

Agilent Technologies

MK-1g

Sample Name:
  MK-1g
Data Collected on:
  vnmrs400-vnmrs400
Archive directory:
  /home/user1/vnmrsys/data
Sample directory:
  MK-1g_20141020_01
FidFile: CARBON

Pulse Sequence: CARBON (s2pul)
Solvent: cdcl3
Data collected on: Oct 20 2014

Temp. 25.0 C / 298.1 K
Operator: user1

Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 1.311 sec
Width 25000.0 Hz
432 repetitions
OBSERVE C13, 100.5589851 MHz
DECOUPLE H1, 399.9181065 MHz
Power 46 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
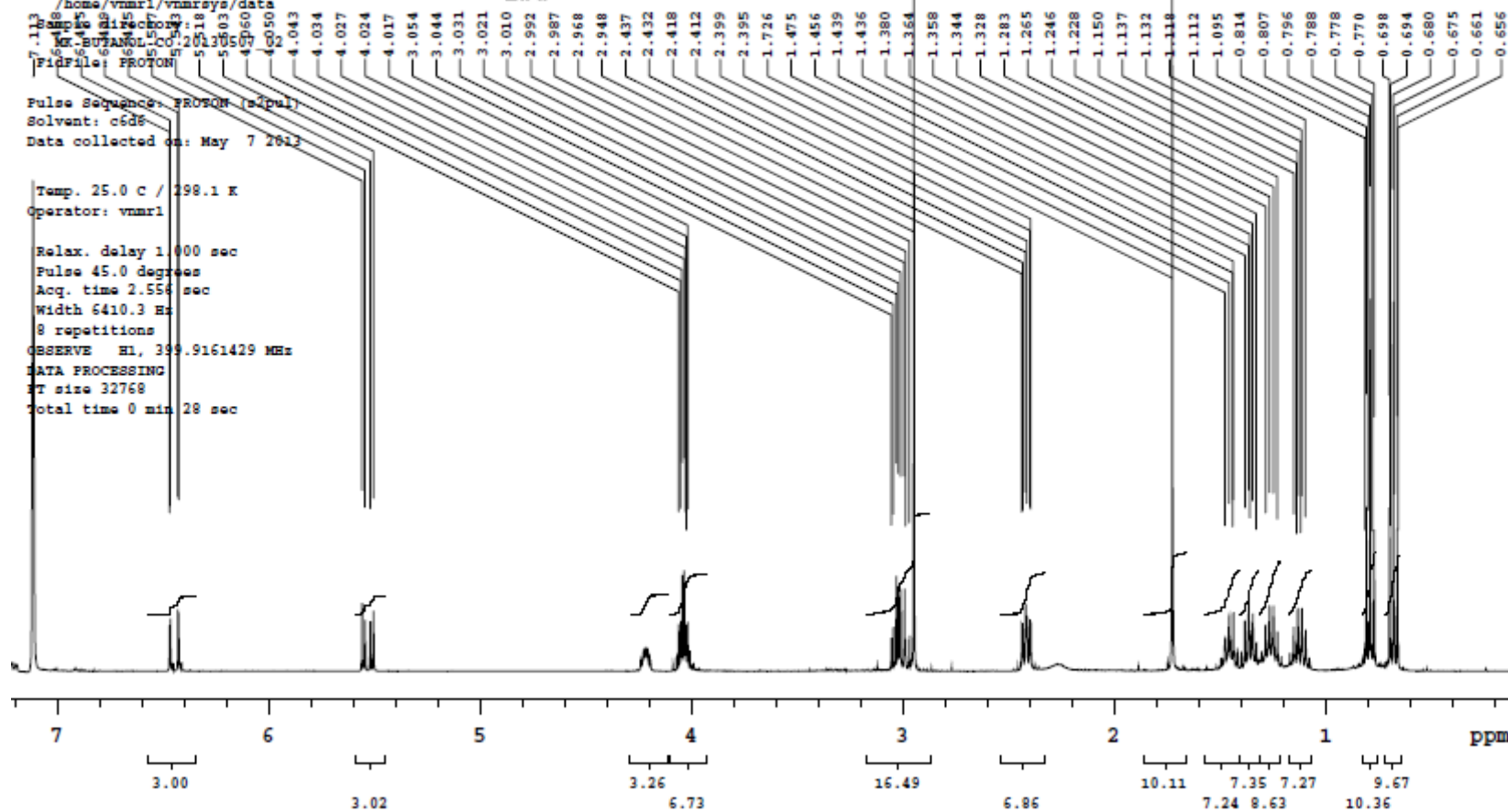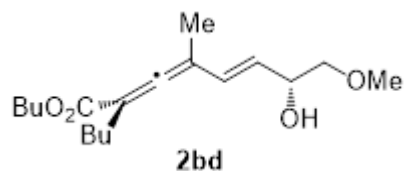Line broadening 0.5 Hz
FT size 65536
Total time 6 hr, 25 min

(Z)-**1g**

91

Acquisition Time (sec)	2.5559	Comment	Gradient Shimming	Date	Jul 31 2013	Date Stamp	Jul 31 2013
File Name	C:\USERS\FiRAT\DESKTOP\EPOXIDE\210T092-FINAL RAPORU\NMR FIDS\MELIH\MK-3107OME_20130731_01\PROTON_01.FID\FID						
Frequency (MHz)	399.92	Nucleus	1H	Number of Transients	8	Original Points Count	16384
Points Count	16384	Pulse Sequence	s2pul	Receiver Gain	56.00	Solvent	CHLOROFORM-d
Spectrum Offset (Hz)	2399.5020	Spectrum Type	STANDARD	Sweep Width (Hz)	6410.26	Temperature (degree C)	25.000

PROTON_01

VerticalScaleFactor = 1

(Z)-1h

MK-3107OME
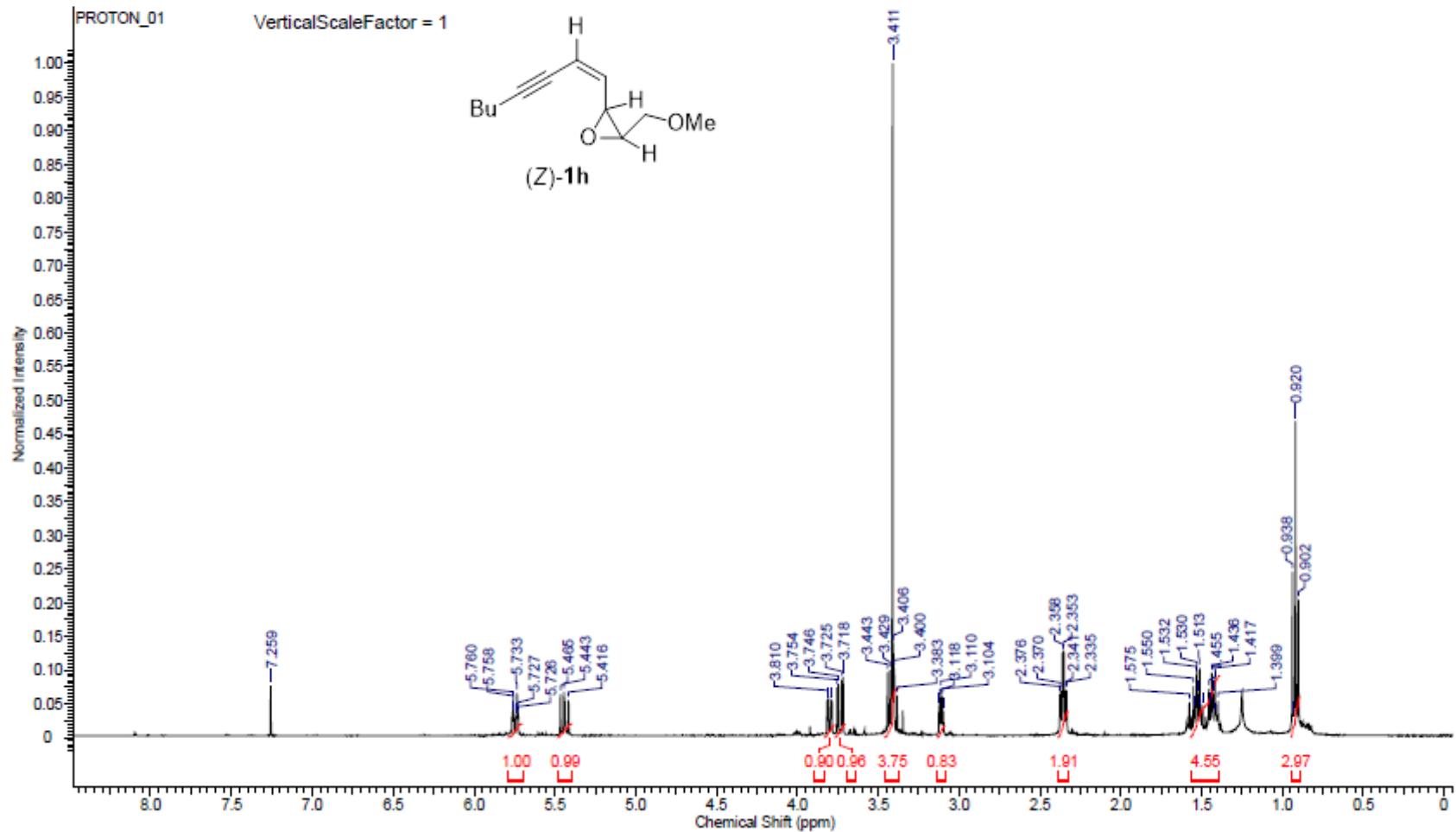
Sample Name:
 MK-3107OME
Data Collected on:
 vnmrs400-vnmrs400
Archive directory:
 /home/vnmr1/vnmrsys/data
Sample directory:
 MK-3107OME_20130731_02
FidFile: CARBON

Pulse Sequence: CARBON (s2pul)
Solvent: cdcl3
Data collected on: Jul 31 2013

Temp. 25.0 C / 298.1 K
Operator: vnmr1

Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 1.311 sec
Width 25000.0 Hz
80 repetitions
OBSERVE C13, 100.5589851 MHz
DECOUPLE H1, 399.9181065 MHz
 Power 46 dB
 continuously on
 WALTZ-16 modulated
DATA PROCESSING
 Line broadening 0.5 Hz
FT size 65536
Total time 19 min

(Z)-**1h**
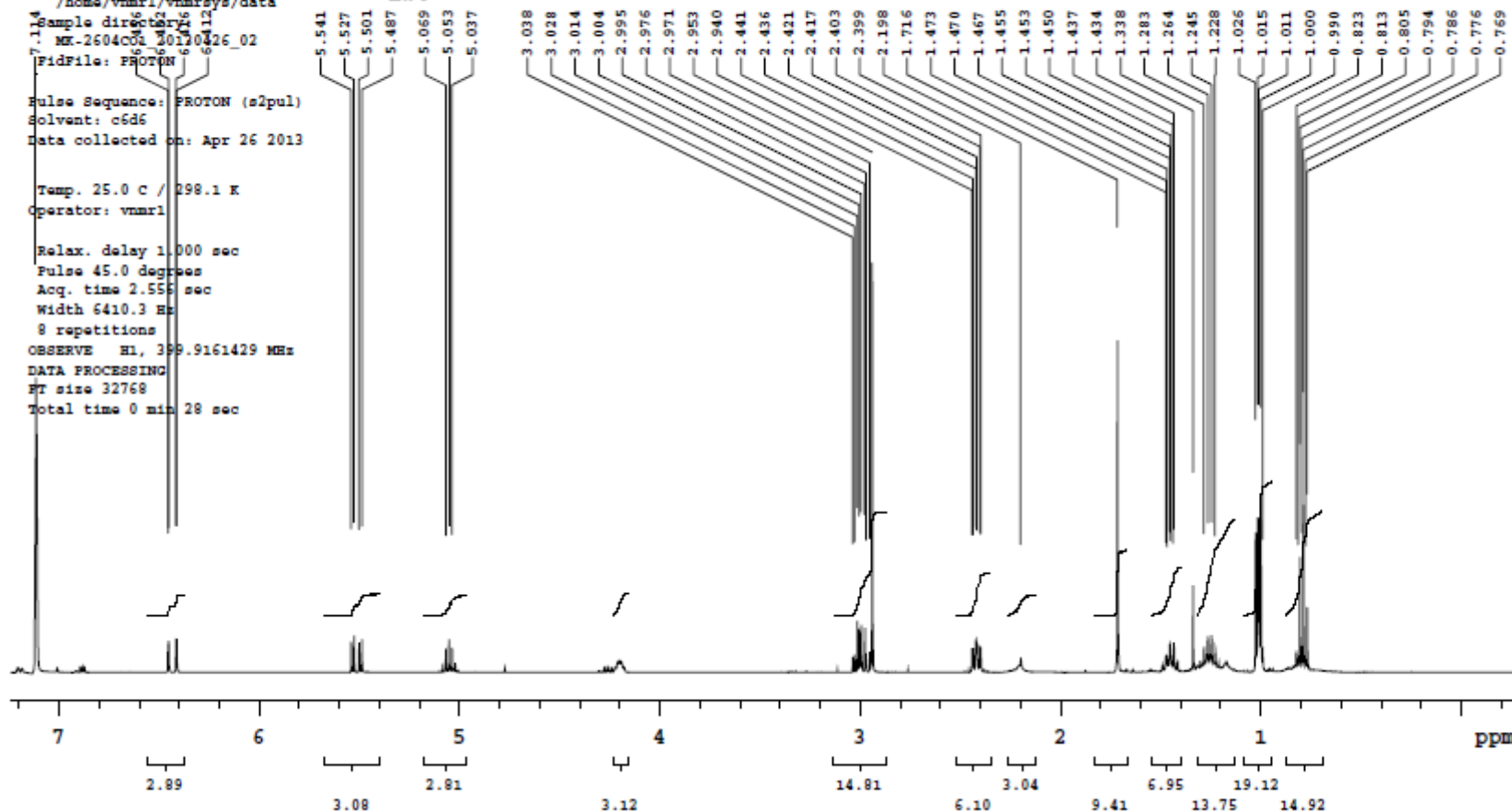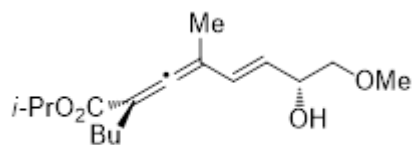
137.162
124.165
115.380
97.103
77.316
76.997
76.678
76.094
72.324
59.175
58.250
53.280
50.420
30.641
21.938
19.222
13.555

180   160   140   120   100   80   60   40   20   ppm
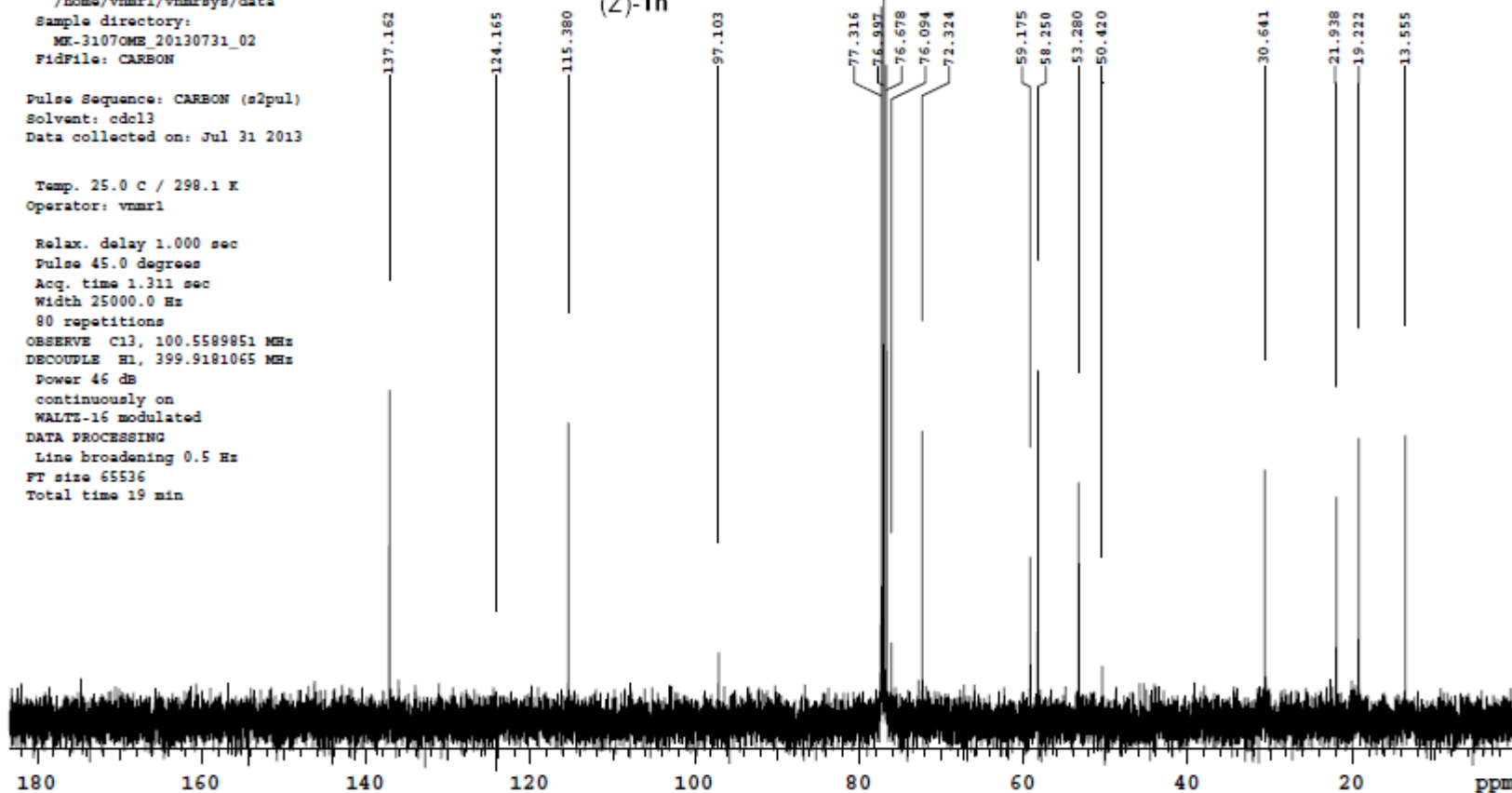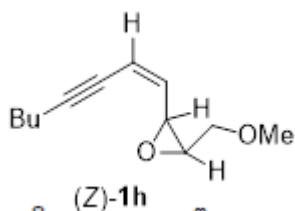
Acquisition Time (sec)	2.5559	Comment	mk-bu-y	Date	Jun 29 2013	Date Stamp	Jun 29 2013
File Name	C:\USERS\FiRAT\DESKTOP\EPOXIDE\210T092-FINAL RAPORU\NMR FIDS\MELIH\MK-BU-Y_20130629_02\PROTON_01.FID\FID						
Frequency (MHz)	399.92	Nucleus	1H	Number of Transients	8	Original Points Count	16384
Points Count	16384	Pulse Sequence	s2pul	Receiver Gain	46.00	Solvent	BENZENE-d6
Spectrum Offset (Hz)	2399.5100	Spectrum Type	STANDARD	Sweep Width (Hz)	6410.26	Temperature (degree C)	25.000

mk-monometilreac

(Z)-**1j**

7 6 5 4 3 2 1 ppm

4.18

3.76

3.98

10.66

16.53

27.85

16.54

16.48

96

(Z)-1j

133.686
127.867
127.387
123.93
95.183
79.314
57.359
55.201
30.646
23.432
21.770
18.963
17.286
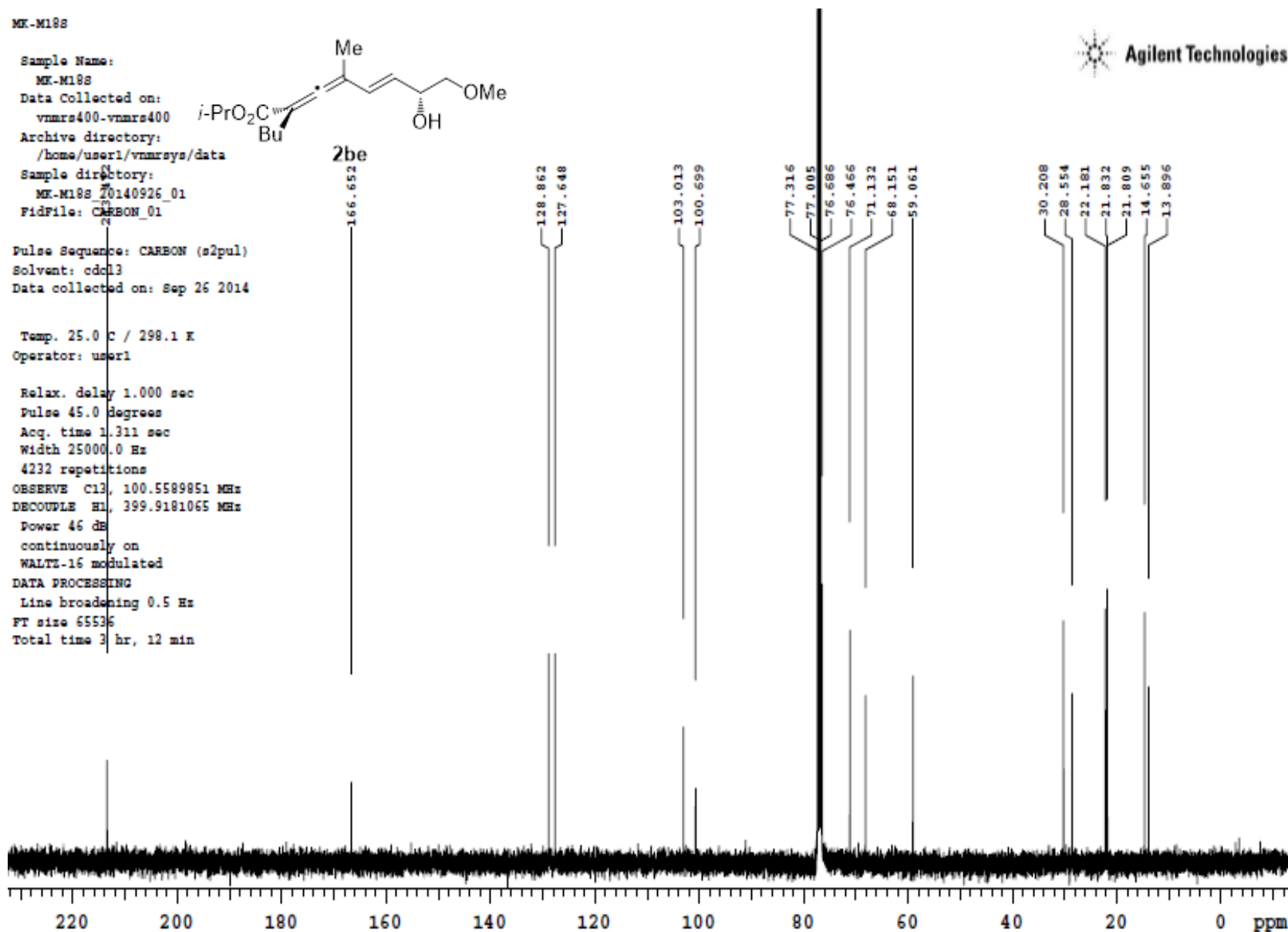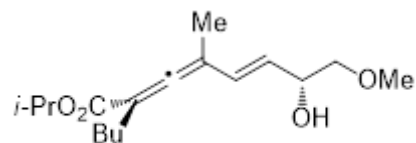13.221

160   140   120   100   80   60   40   20   ppm

Sample Name:
  MK-CHOME
Data Collected on:
  vnmrs400-vnmrs400
Archive directory:
  /home/user1/vnmrsys/data
Sample directory:
  MK-CHOME_20141230_01
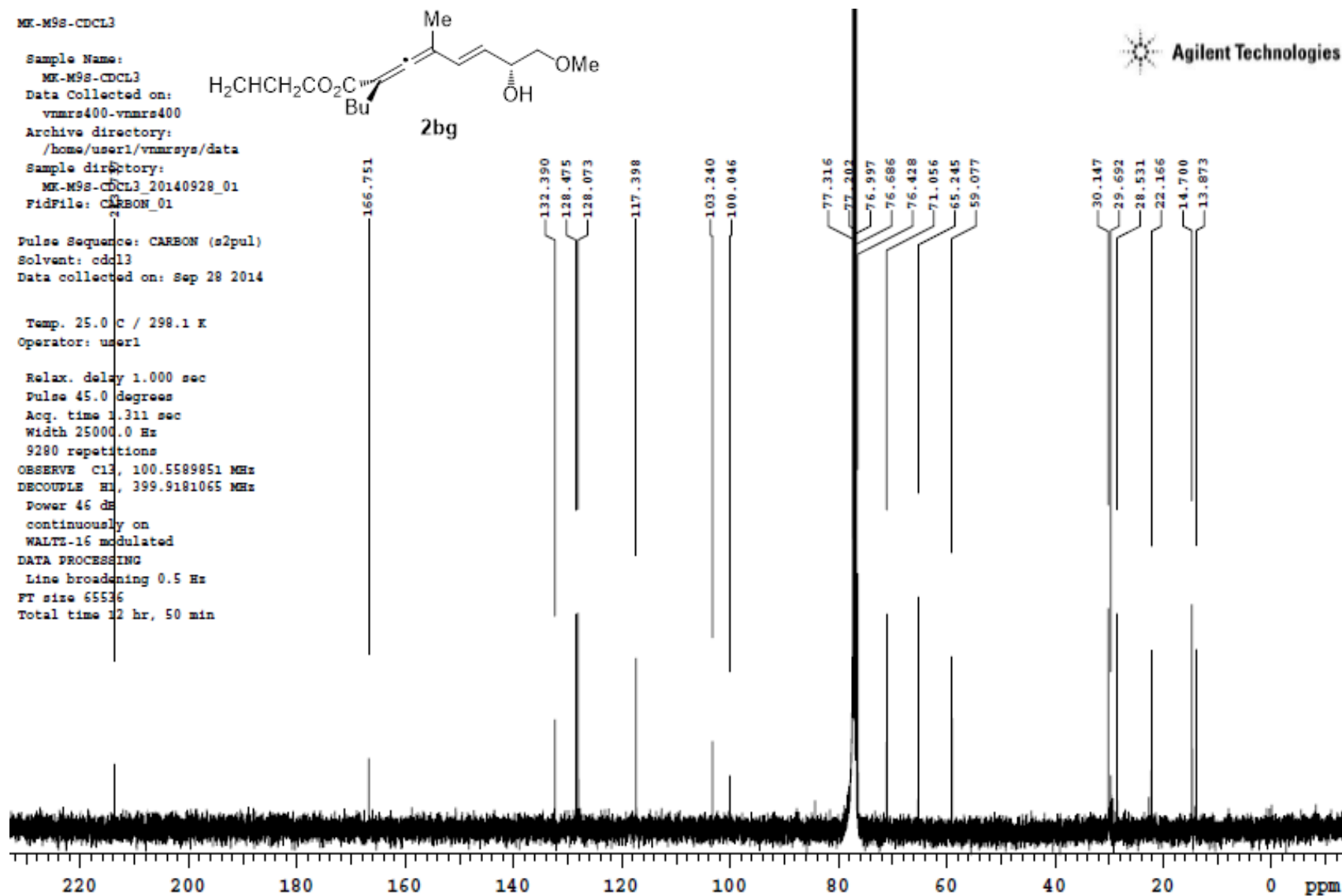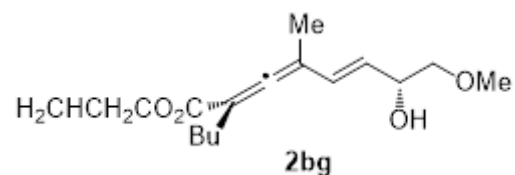FidFile: PROTON

Pulse Sequence: PROTON (s2pul)
Solvent: cdcl3
Data collected on: Dec 30 2014

Temp. 25.0 C / 298.1 K
Operator: user1

Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 2.556 sec
Width 6410.3 Hz
8 repetitions
OBSERVE   H1, 399.9161069 MHz
DATA PROCESSING
FT size 32768
Total time 0 min 28 sec

(Z)-**1k**

Agilent Technologies

Agilent Technologies

Cy

H

Bu

H

OMe

(Z)-1k

O

136.297
129.082
96.958
77.346
77.210
77.027
76.709
72.627
59.150
58.470
54.251
45.420
31.748
31.604
30.823
29.692
26.179
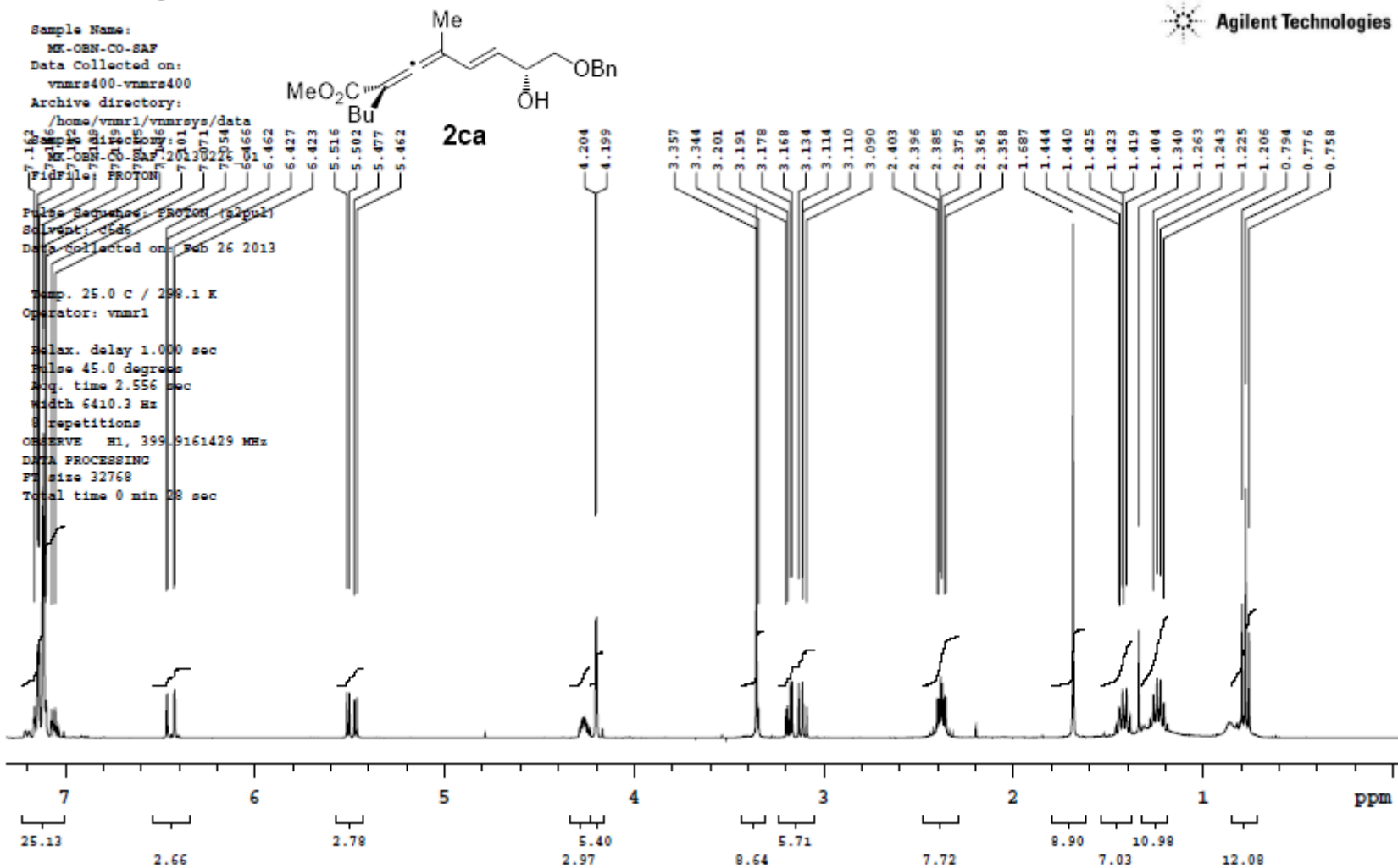25.959
21.961
19.192
13.585

160   140   120   100   80   60   40   20   ppm

66

Sample Name:
MK-1211-EPO
Data Collected on:
vnmrs400-vnmrs400
Archive directory:
/home/vnmr1/vnmrsys/data
Sample directory:
MK-1211-EPO_20131112_01
FidFile: PROTON

Pulse Sequence: PROTON (s2pul)
Solvent: cdcl3
Data collected on: Nov 12 2013

Temp. 25.0 C / 298.1 K
Operator: vnmr1

Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 2.556 sec
Width 6410.3 Hz
8 repetitions
OBSERVE   H1, 399.9161069 MHz
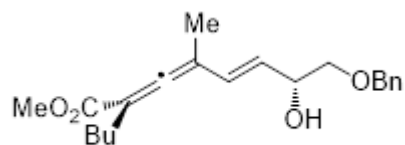DATA PROCESSING
FT size 32768
Total time 0 min 28 sec

(Z)-1l

Agilent Technologies

5.254
5.231

3.821
3.816
3.800
3.794
3.753
3.745
3.723
3.717
3.424
3.412
3.408
3.395
3.380
3.103
2.407
2.389
2.371
1.576
1.570
1.553
1.551
1.533
1.461
1.459
1.439
1.252
1.168
1.120
1.110
1.106
1.101
1.016
1.011
0.947
0.928
0.911

3.43
3.32
3.78
13.26
3.42
7.46
18.90
32.84
13.60

Sample Name:
  MK-1211-EPO
Data Collected on:
  vnmrs400-vnmrs400
Archive directory:
  /home/vnmr1/vnmrsys/data
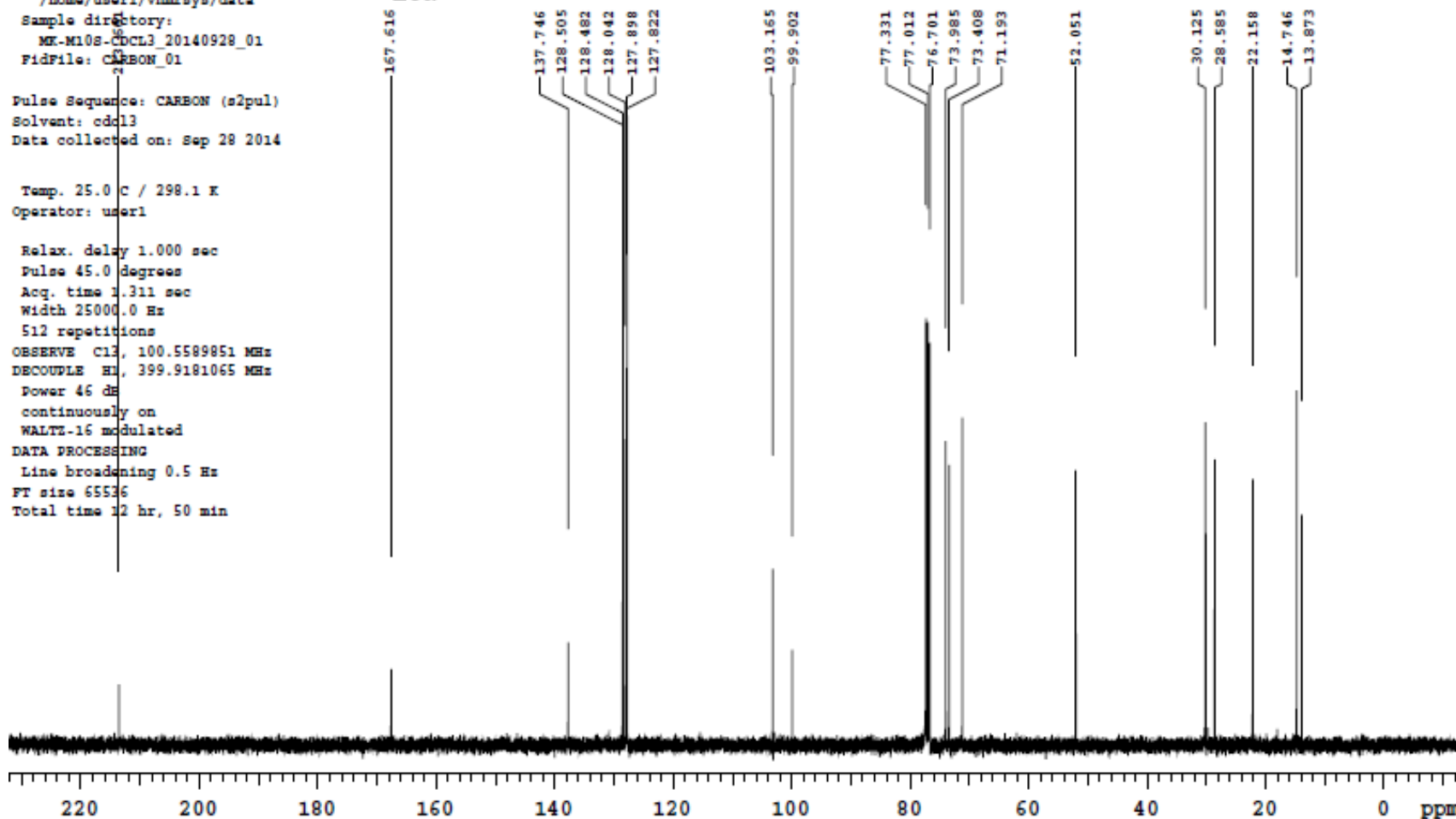Sample directory:
  MK-1211-EPO_20131112_02
FidFile: CARBON

Pulse Sequence: CARBON (s2pul)
Solvent: cdcl3
Data collected on: Nov 12 2013

Temp. 25.0 C / 298.1 K
Operator: vnmr1

Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 1.311 sec
Width 25000.0 Hz
264 repetitions
OBSERVE C13, 100.5589851 MHz
DECOUPLE H1, 399.9181065 MHz
 Power 46 dB
 continuously on
 WALTZ-16 modulated
DATA PROCESSING
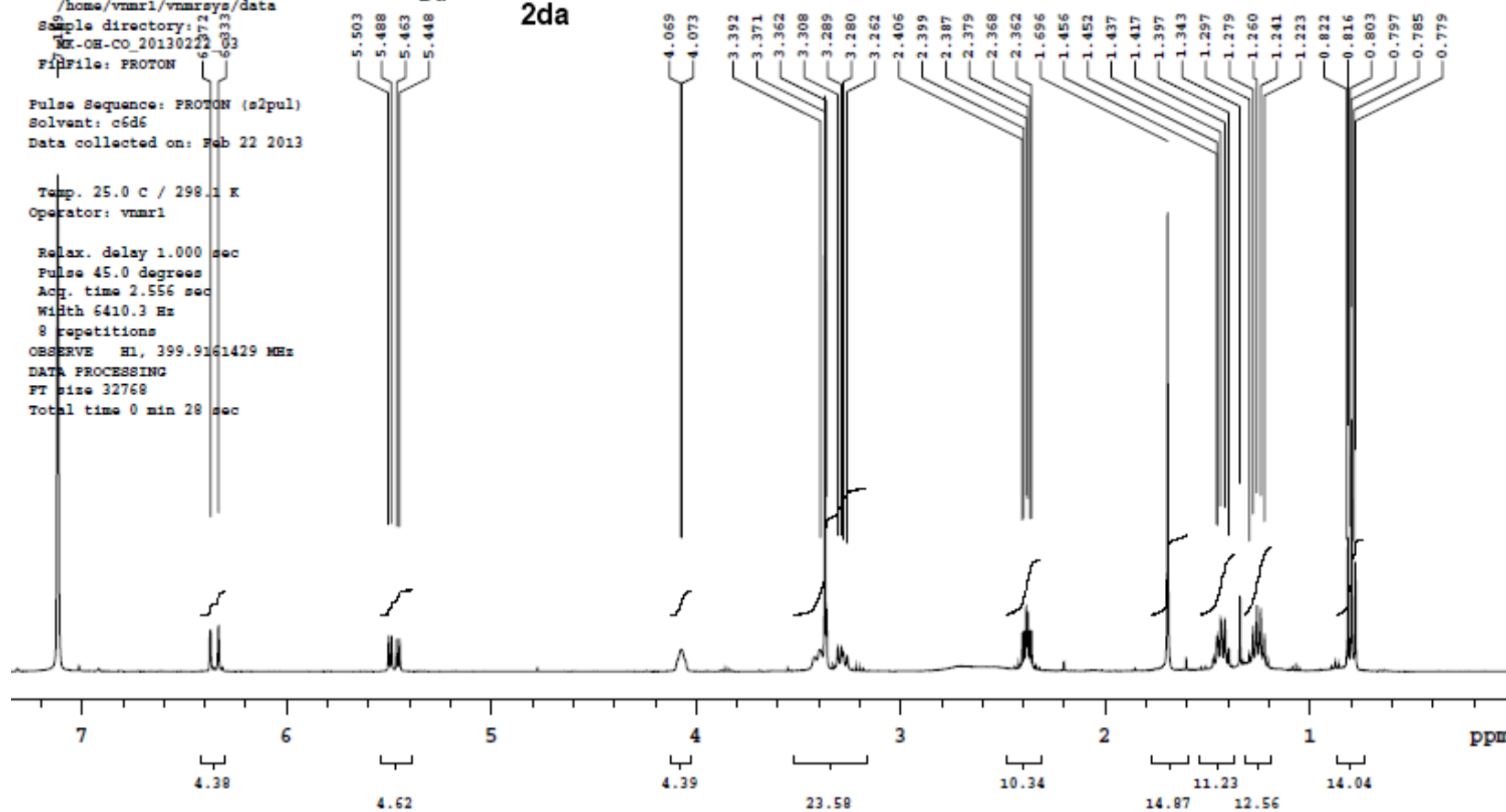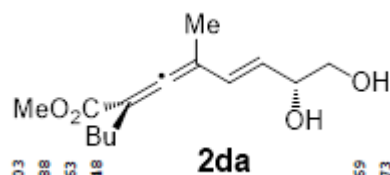 Line broadening 0.5 Hz
FT size 65536
Total time 38 min

t-Bu

H

Bu

H

O

OMe

(*Z*)-**1l**

Agilent Technologies

140.235
127.367
97.429
77.323
76.686
72.665
59.168
58.515
54.722
36.172
30.838
29.692
29.358
28.941
28.888
25.686
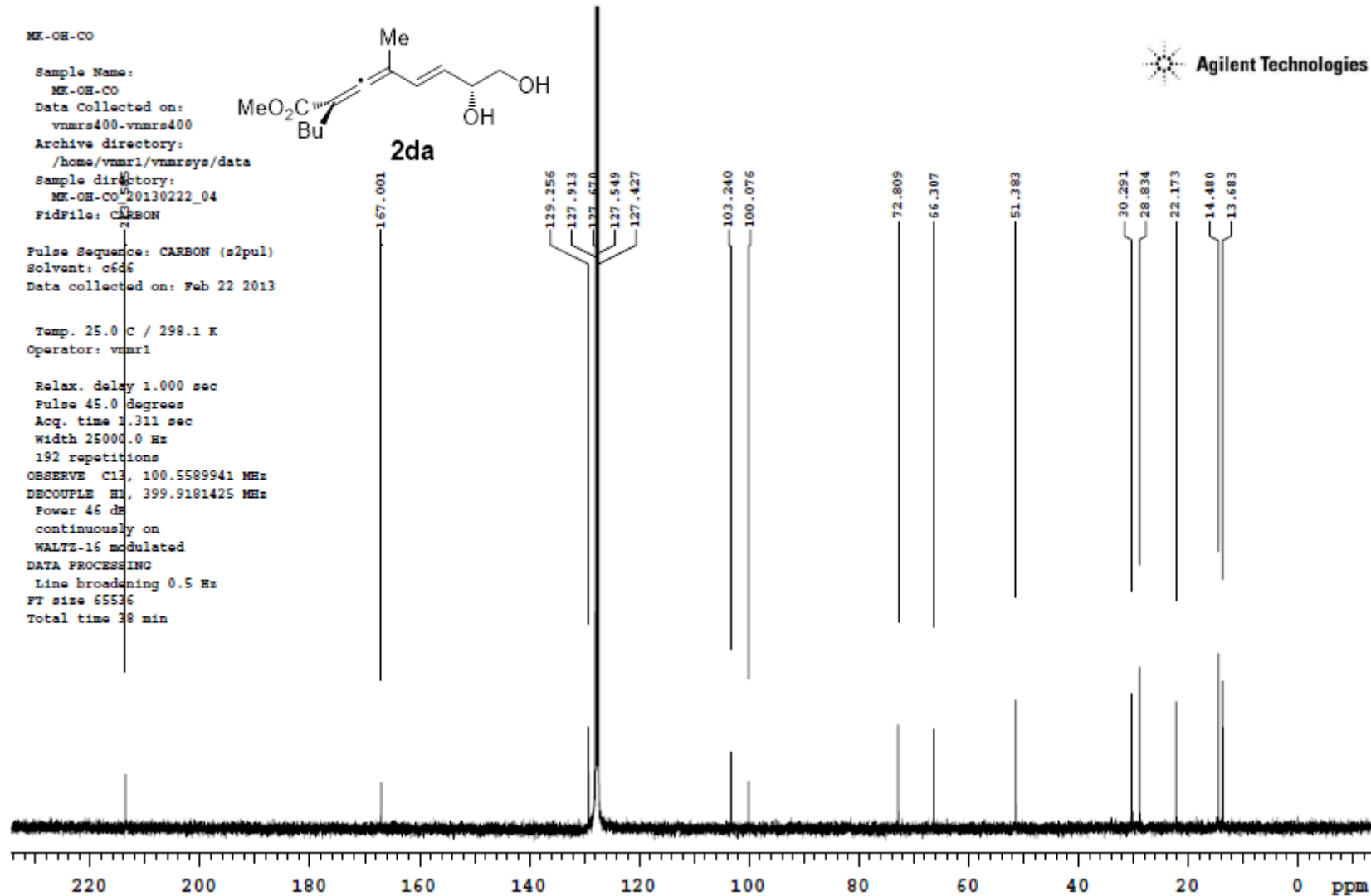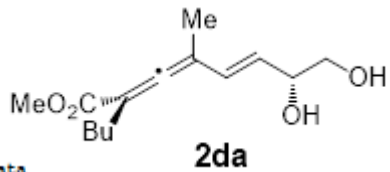21.984
19.169
13.585

180 160 140 120 100 80 60 40 20 ppm

Sample Name:
 MK-1206E
Data Collected on:
 vnmrs400-vnmrs400
Archive directory:
 /home/vnmr1/vnmrsys/data
Sample directory:
 MK-1206E_20130612_03
FidFile: CARBON

Pulse Sequence: CARBON (s2pul)
Solvent: c6d6
Data collected on: Jun 12 2013

Temp. 25.0 C / 298.1 K
Operator: vnmr1

 Relax. delay 1.000 sec
 Pulse 45.0 degrees
 Acq. time 1.311 sec
 Width 25000.0 Hz
 128 repetitions
OBSERVE C13, 100.5589941 MHz
DECOUPLE H1, 399.9181425 MHz
 Power 46 dB
 continuously on
 WALTZ-16 modulated
DATA PROCESSING
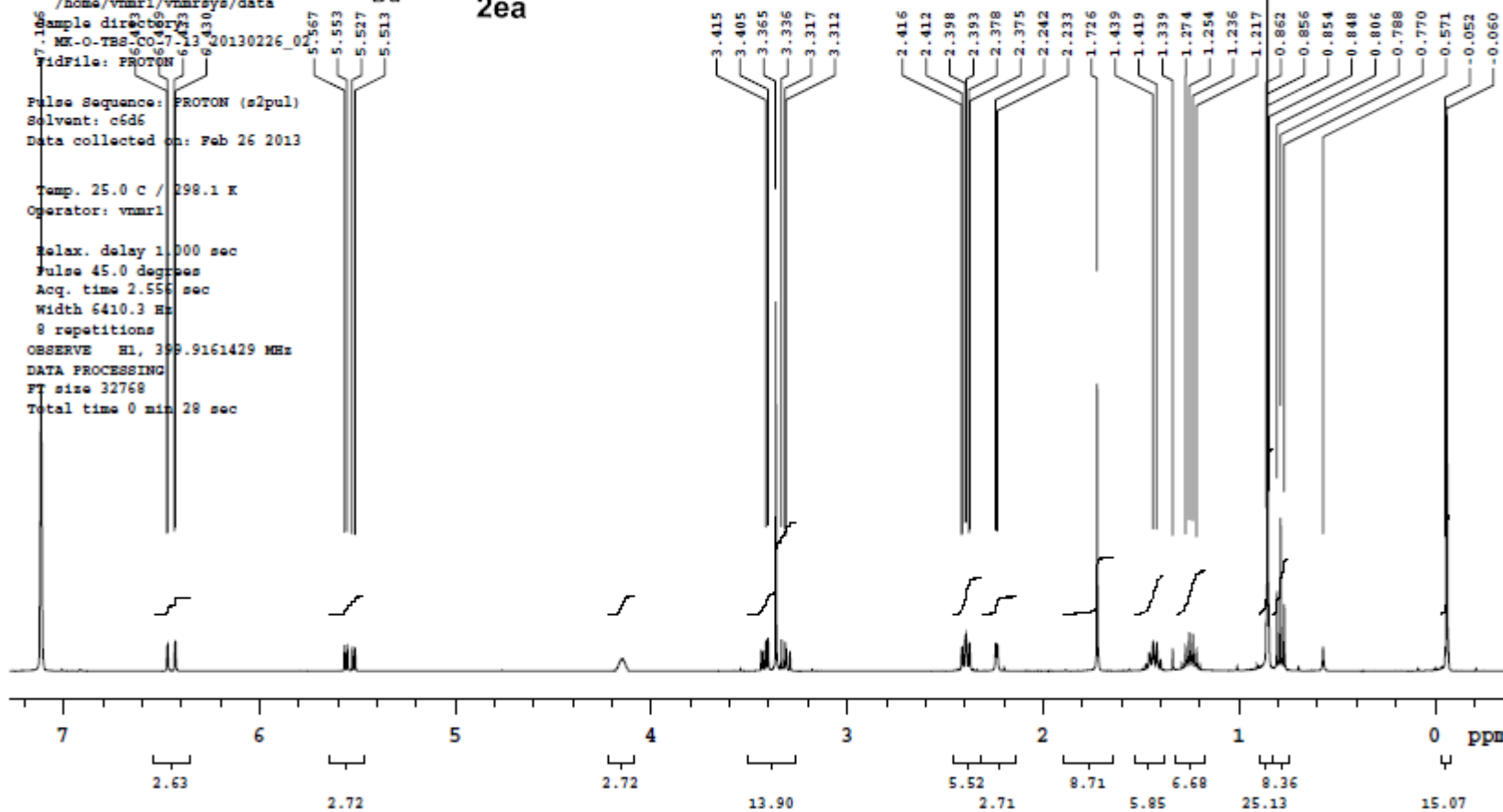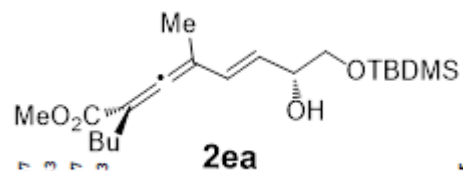 Line broadening 0.5 Hz
FT size 65536
Total time 9 min 52 sec

Me

H

H

OMe

O

(Z)-**1m**

Agilent Technologies

135.993
127.898
127.662
127.533
127.420
122.898
82.391
81.541
72.224
58.431
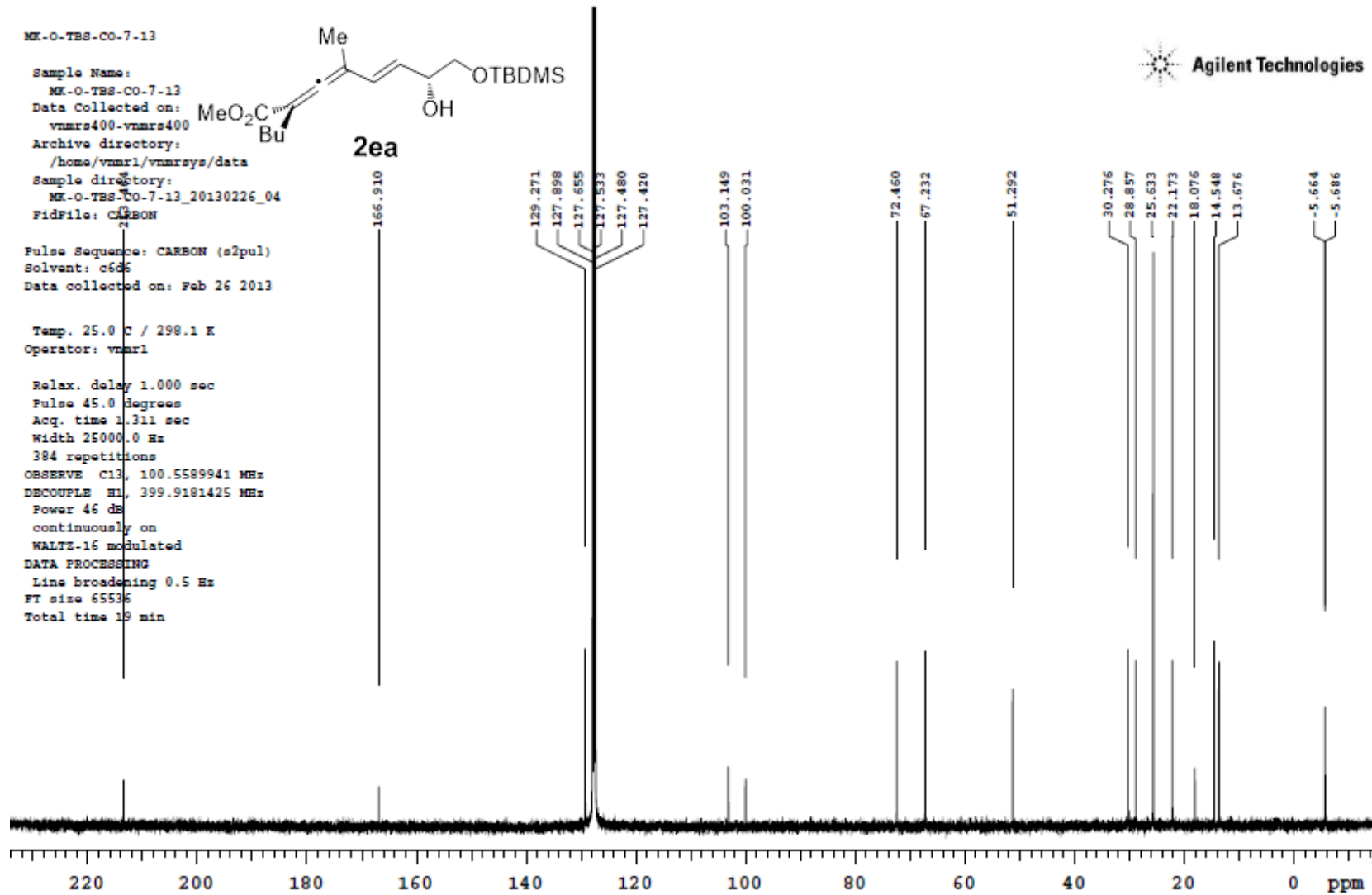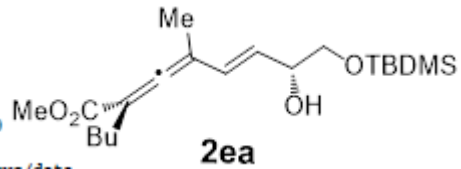57.968
53.227
22.674

180　160　140　120　100　80　60　40　20　ppm

mk-2506eome

Sample Name:
   mk-2506eome
Data Collected on:
   vnmrs400-vnmrs400
Archive directory:
   /home/vnmr1/vnmrsys/data
Sample directory:
   mk-2506eome_20130625_03
FidFile: CARBON

Pulse Sequence: CARBON (s2pul)
Solvent: c6d6
Data collected on: Jun 25 2013

Temp. 25.0 C / 298.1 K
Operator: vnmr1

Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 1.311 sec
Width 25000.0 Hz
5000 repetitions
OBSERVE C13, 100.5589941 MHz
DECOUPLE H1, 399.9181425 MHz
Power 46 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.5 Hz
FT size 65536
Total time 3 hr, 12 min

(Z)-**1n**

132.746
128.110
128.011
127.905
127.776
127.662
127.533
127.420
124.704
99.500
79.182
72.414
58.469
58.059
53.758
32.507
32.484
29.639
25.724
24.563
23.516

180   160   140   120   100   80   60   40   20   ppm

105

Agilent Technologies

132.769
127.905
127.662
127.420
124.468
103.452
77.702
72.391
58.462
58.006
53.667
30.617
27.863
23.410

Me

H

t-Bu

H

O

OMe

(Z)-1o

160   140   120   100   80   60   40   20   ppm

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(Z)-1p

137.936
131.350
128.391
127.701
125.675
103.992
77.316
77.096
76.997
76.686
73.264
70.055
58.568
54.289
30.952
28.069
23.843

180   160   140   120   100   80   60   40   20   ppm

109

MK-1410E

Agilent Technologies

Me

H

t-Bu

H

O

OH

(Z)-**1q**

132.518
127.898
127.662
127.553
127.420
124.658
103.665
77.641
60.996
59.433
53.621
30.617
30.595
27.878
23.410

180   160   140   120   100   80   60   40   20   ppm

111

Acquisition Time (sec)	2.5559	Comment	MK-1807E1	Date	Jul 18 2013	Date Stamp	Jul 18 2013
File Name	C:\USERS\FIRAT\DESKTOP\EPOXIDE\210T092-FINAL RAPORU\NMR FIDS\MELIH\MK-1807E1_20130718_02\PROTON_01.FID\FID						
Frequency (MHz)	399.92	Nucleus	1H	Number of Transients	8	Original Points Count	16384
Points Count	16384	Pulse Sequence	s2pul	Receiver Gain	60.00	Solvent	CHLOROFORM-d
Spectrum Offset (Hz)	2399.5020	Spectrum Type	STANDARD	Sweep Width (Hz)	6410.26	Temperature (degree C)	25.000

PROTON_01   VerticalScaleFactor = 1

(Z)-1r

Me

H

t-Bu

H

OTBDMS

O

(Z)-1r

Agilent Technologies

131.639
125.296
103.825
77.308
77.141
76.990
76.671
62.908
60.169
54.335
30.982
28.061
25.884
23.941
18.342
−5.299

180   160   140   120   100   80   60   40   20   0   ppm

Acquisition Time (sec)	2.5559	Comment	Gradient Shimming	Date	Jul 30 2013	Date Stamp	Jul 30 2013
File Name	C:\USERS\FİRAT\DESKTOP\EPOXIDE\210T092-FINAL RAPORU\NMR FIDS\MELIH\MK-2907OME_20130730_01\PROTON_01.FID\FID						
Frequency (MHz)	399.92	Nucleus	1H	Number of Transients	8	Original Points Count	16384
Points Count	16384	Pulse Sequence	s2pul	Receiver Gain	60.00	Solvent	CHLOROFORM-d
Spectrum Offset (Hz)	2399.5020	Spectrum Type	STANDARD	Sweep Width (Hz)	6410.26	Temperature (degree C)	25.000

PROTON_01   VerticalScaleFactor = 1

114

Me

H

Ph

H

OMe

O

(Z)-**1s**

Agilent Technologies

133.141
131.525
128.475
128.353
124.954
122.921
94.470
87.277
77.323
77.005
76.686
72.483
59.206
58.455
54.130
23.448

160   140   120   100   80   60   40   20   ppm

Acquisition Time (sec)	2.5559	Comment	Gradient Shimming			Date	Oct 25 2013
Date Stamp	Oct 25 2013	File Name	C:\USERS\FiRAT\DESKTOP\MELIH\MK-25101_20131025_01\PROTON_01.FID\FID				
Frequency (MHz)	399.92	Nucleus	1H	Number of Transients	8	Original Points Count	16384
Points Count	16384	Pulse Sequence	s2pul	Receiver Gain	50.00	Solvent	CHLOROFORM-d
Spectrum Offset (Hz)	2399.5020	Spectrum Type	STANDARD	Sweep Width (Hz)	6410.26	Temperature (degree C)	25.000

PROTON_01   VerticalScaleFactor = 1

(Z)-1t

Agilent Technologies

137.298
121.722
94.242
79.531
77.339
77.020
76.701
73.052
59.153
56.247
55.192
30.321
30.899
29.692
22.401
22.242
21.923
21.688
19.169
13.608

(Z)-1t

220   200   180   160   140   120   100   80   60   40   20   0   ppm

MK-PDCO1

2aa

VARIAN

3.674

1.850

1.334

7   6   5   4   3   2   1   ppm

3.83   3.82   11.53   9.10   12.96   44.87   13.88

2aa

167.723
137.837
122.905
103.157
99.653
77.334
77.016
76.699
70.994
52.044
33.098
29.781
28.612
22.125
14.818
13.866

Agilent Technologies

Me

MeO2C

Bu

OMe

OH

2ba

5.535
5.522
5.495
5.482

3.360
3.346
3.044
3.035
3.021
3.011
2.999
2.981
2.976
2.957
2.945
2.408
2.402
2.389
2.382
2.369
2.365
1.693
1.451
1.447
1.431
1.429
1.426
1.414
1.411
1.392
1.337
1.265
1.246
1.228
1.209
0.797
0.786
0.779
0.761

7   6   5   4   3   2   1   ppm

3.60

3.78

3.80

11.32

18.63

7.64

2.92

11.98   11.31

8.59

16.44

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2ba

166.918
129.172
128.011
127.898
127.769
127.655
127.533
127.420
127.268
103.157
99.978
76.458
70.531
58.219
51.284
30.291
30.079
28.857
22.165
14.503
13.668

220   200   180   160   140   120   100   80   60   40   20   0   ppm
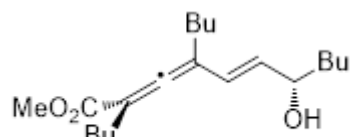
121

PROTON_01   VerticalScaleFactor = 1

2ba'

mk-2412co

Sample Name:
  mk-2412co
Data Collected on:
  vnmrs400-vnmrs400
Archive directory:
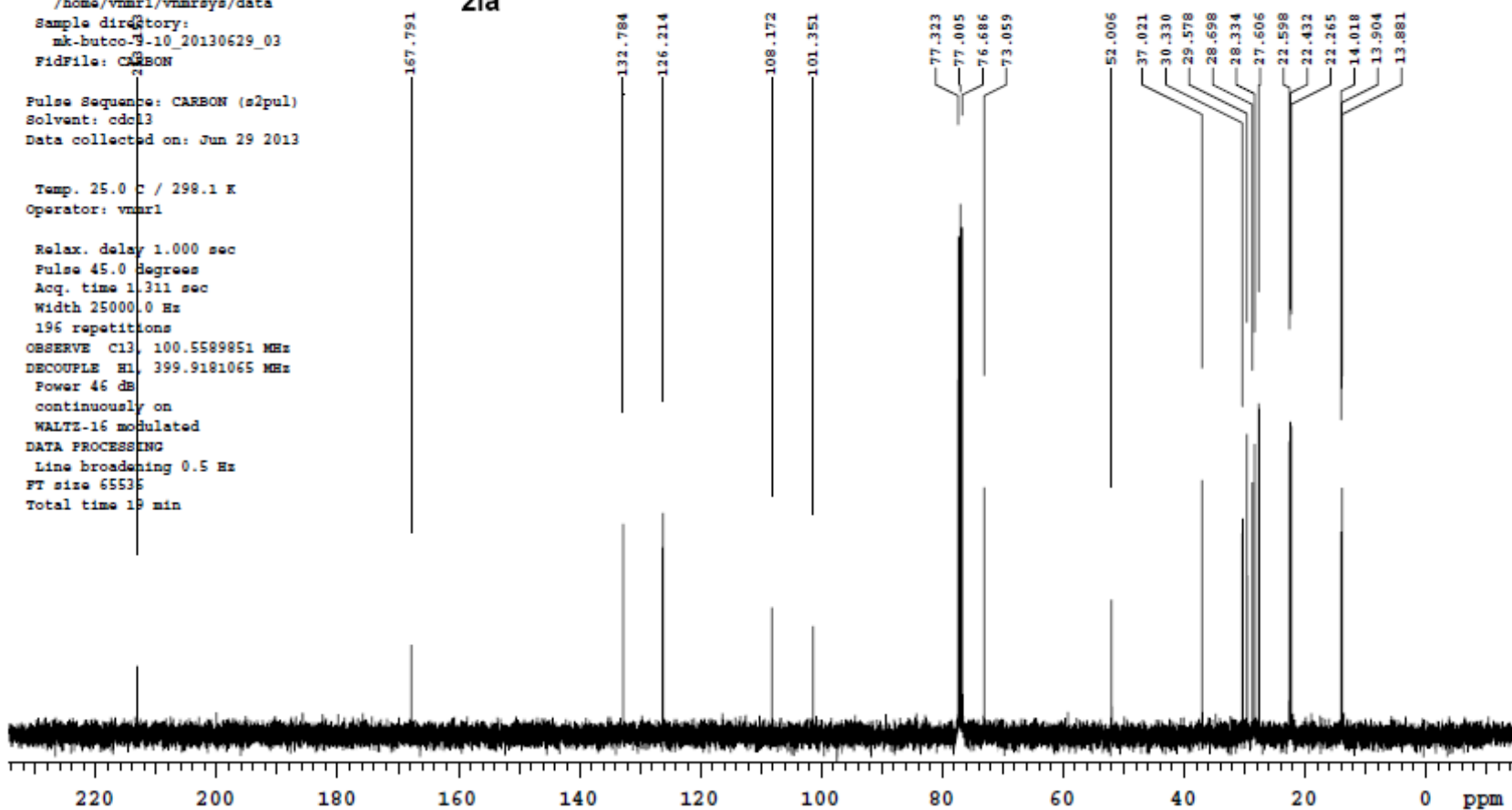 /home/user1/vnmrsys/data
Sample directory:
  mk-2412co_20131224_02
FidFile: CARBON

Pulse Sequence: CARBON (s2pul)
Solvent: c6d6
Data collected on: Dec 24 2013

Temp. 25.0 C / 298.1 K
Operator: user1

Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 1.311 sec
Width 25000.0 Hz
224 repetitions
OBSERVE C13, 100.5589941 MHz
DECOUPLE H1, 399.9181425 MHz
Power 42 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.5 Hz
FT size 65536
Total time 19 min

Me

MeO$_2$C

Bu

OMe

OH

2ba'

166.910

129.187
127.890
127.655
127.533
127.412
127.329

103.157
99.993

76.488
70.730

58.234

51.254

30.299
28.857

22.165

14.487
13.653

Agilent Technologies

220 200 180 160 140 120 100 80 60 40 20 0 ppm

123

Gradient Shimming

Sample Name:
  MX-2504CO
Data Collected on:
  vnmrs400-vnmrs400
Archive directory:
  /home/vnmr1/vnmrsys/data
Sample directory:
  MX-2504CO_20130426_01
FidFile: PROTON

Pulse Sequence: PROTON (s2pul)
Solvent: c6d6
Data collected on: Apr 26 2013

Temp. 25.0 C / 298.1 K
Operator: vnmr1

Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 2.556 sec
Width 6410.3 Hz
8 repetitions
OBSERVE   H1, 399.9161429 MHz
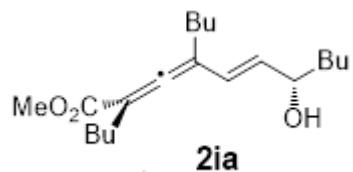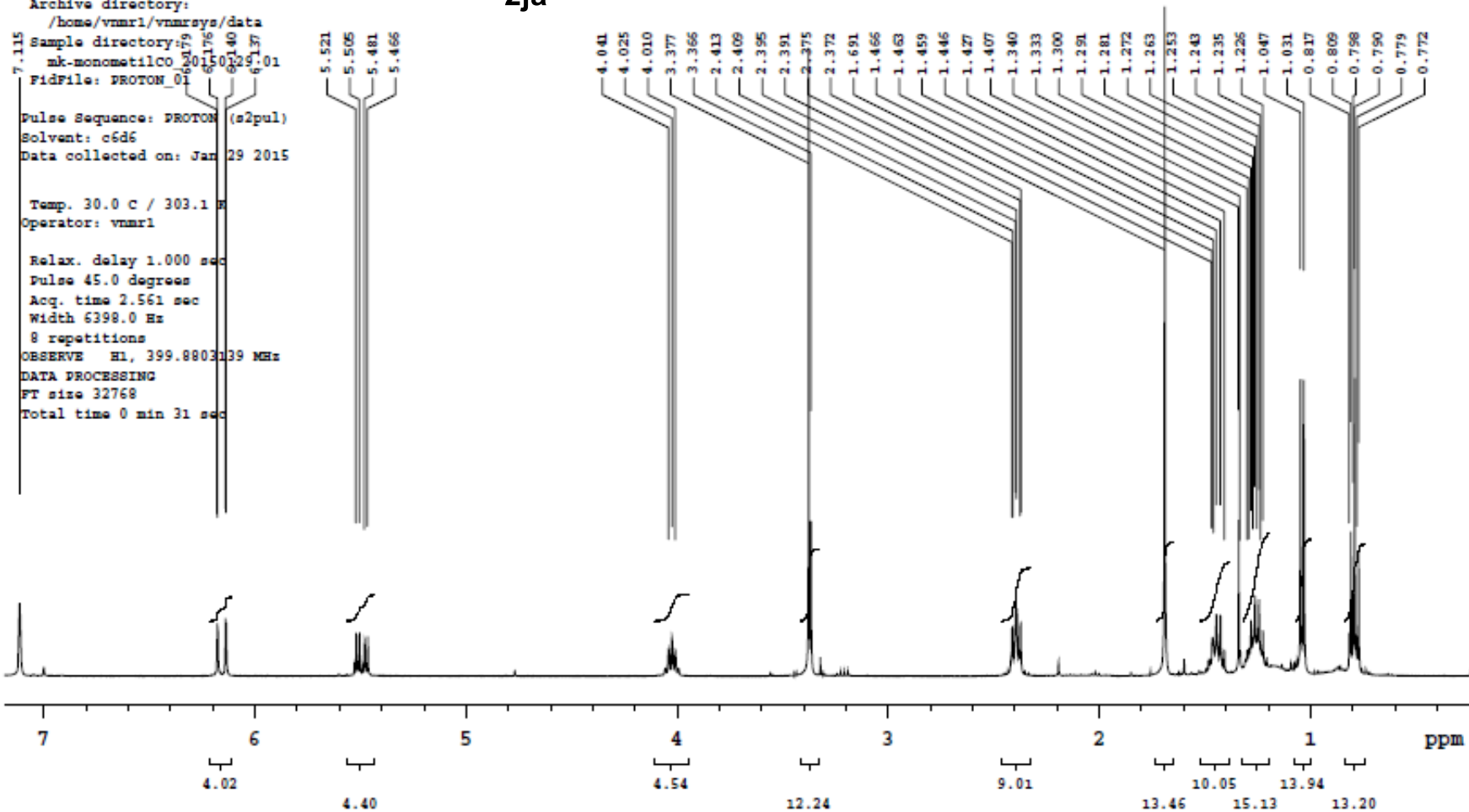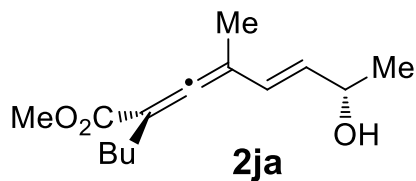DATA PROCESSING
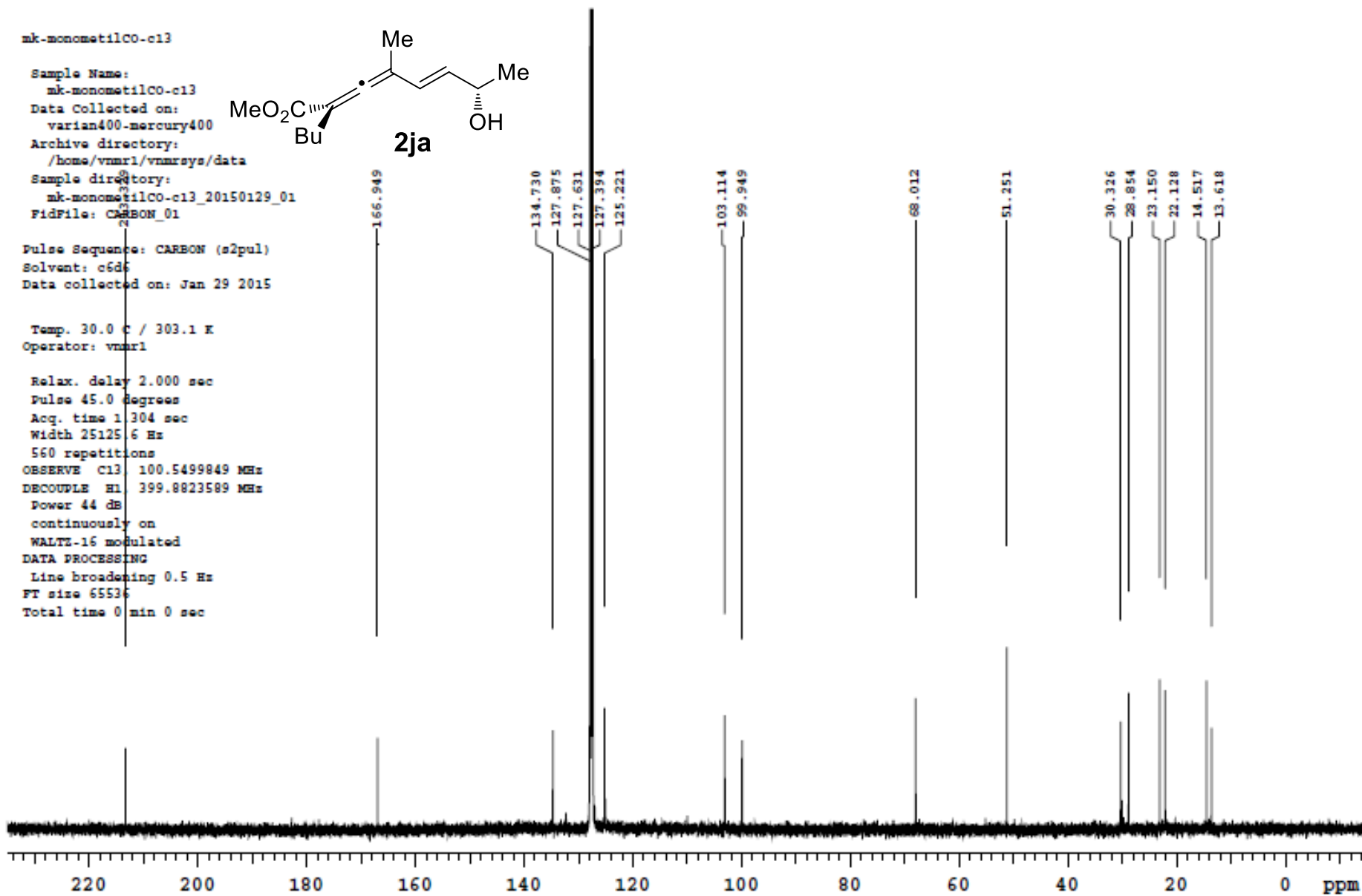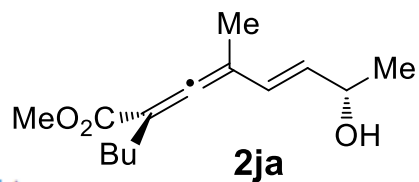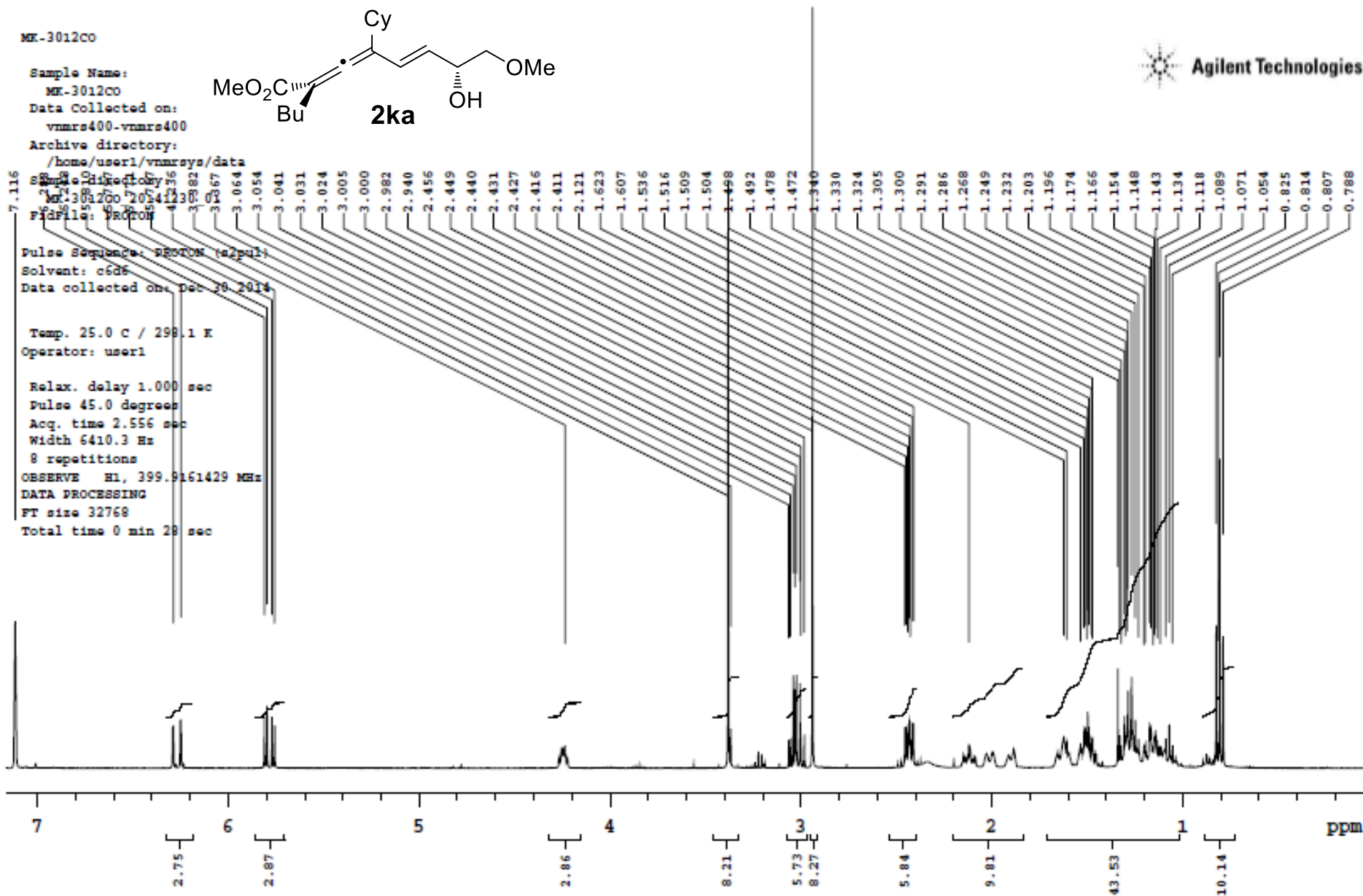FT size 32768
Total time 0 min 28 sec

2bb
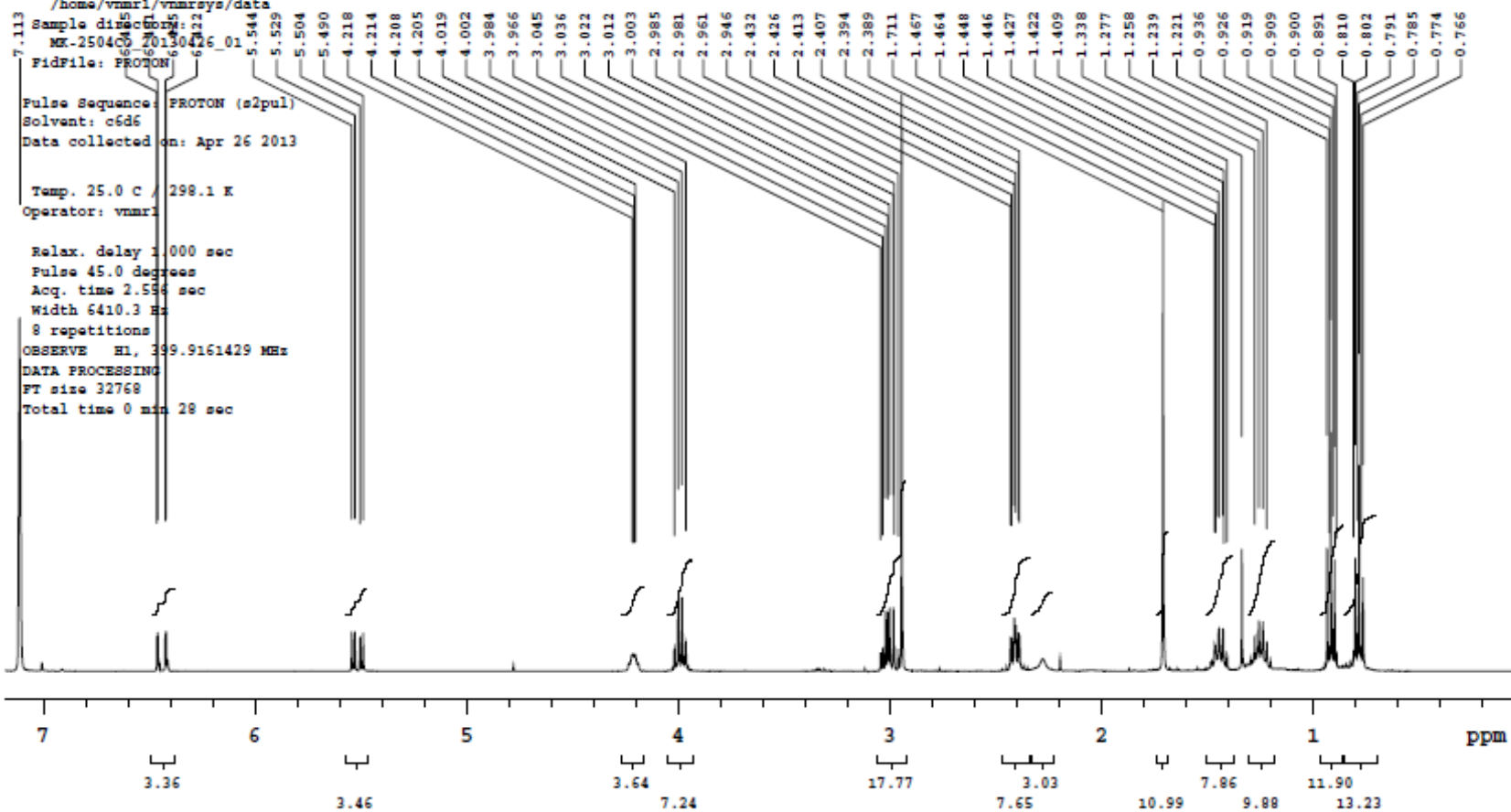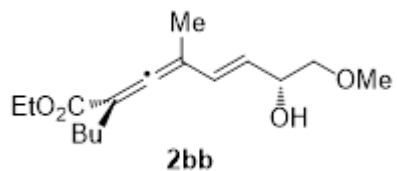
MK-M178-CDCL3

Sample Name:
  MK-M178-CDCL3
Data Collected on:
  vnmrs400-vnmrs400
Archive directory:
  /home/user1/vnmrsys/data
Sample directory:
  MK-M178-CDCL3_20140927_01
FidFile: CARBON_01

Pulse Sequence: CARBON (s2pul)
Solvent: cdcl3
Data collected on: Sep 27 2014

Temp. 25.0 C / 298.1 K
Operator: user1

Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 1.311 sec
Width 25000.0 Hz
7408 repetitions
OBSERVE C13, 100.5589851 MHz
DECOUPLE H1, 399.9181065 MHz
 Power 46 dB
 continuously on
 WALTZ-16 modulated
DATA PROCESSING
 Line broadening 0.5 Hz
FT size 65536
Total time 12 hr, 50 min

2bb

167.138
128.710
127.845
103.089
100.266
77.316
77.202
77.005
76.586
76.443
71.094
60.822
59.069
30.170
28.562
22.166
14.700
14.283
13.881
1.006

125

2bc

Agilent Technologies

Gradient Shimming

Sample Name:
  MX-BUTANOL-CO
Data Collected on:
  vnmrs400-vnmrs400
Archive directory:
  /home/vnmr1/vnmrsys/data
Sample directory:
  MX-BUTANOL-CO_20130507_02
FidFile: PROTON

Pulse Sequence: PROTON (s2pul)
Solvent: c6d6
Data collected on: May 7 2013

Temp. 25.0 C / 298.1 K
Operator: vnmr1

Relax. delay 1.000 sec
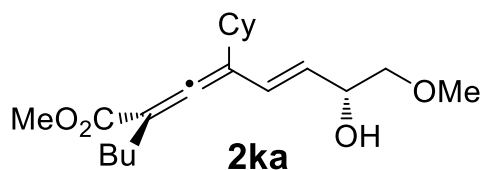Pulse 45.0 degrees
Acq. time 2.556 sec
Width 6410.3 Hz
8 repetitions
OBSERVE H1, 399.9161429 MHz
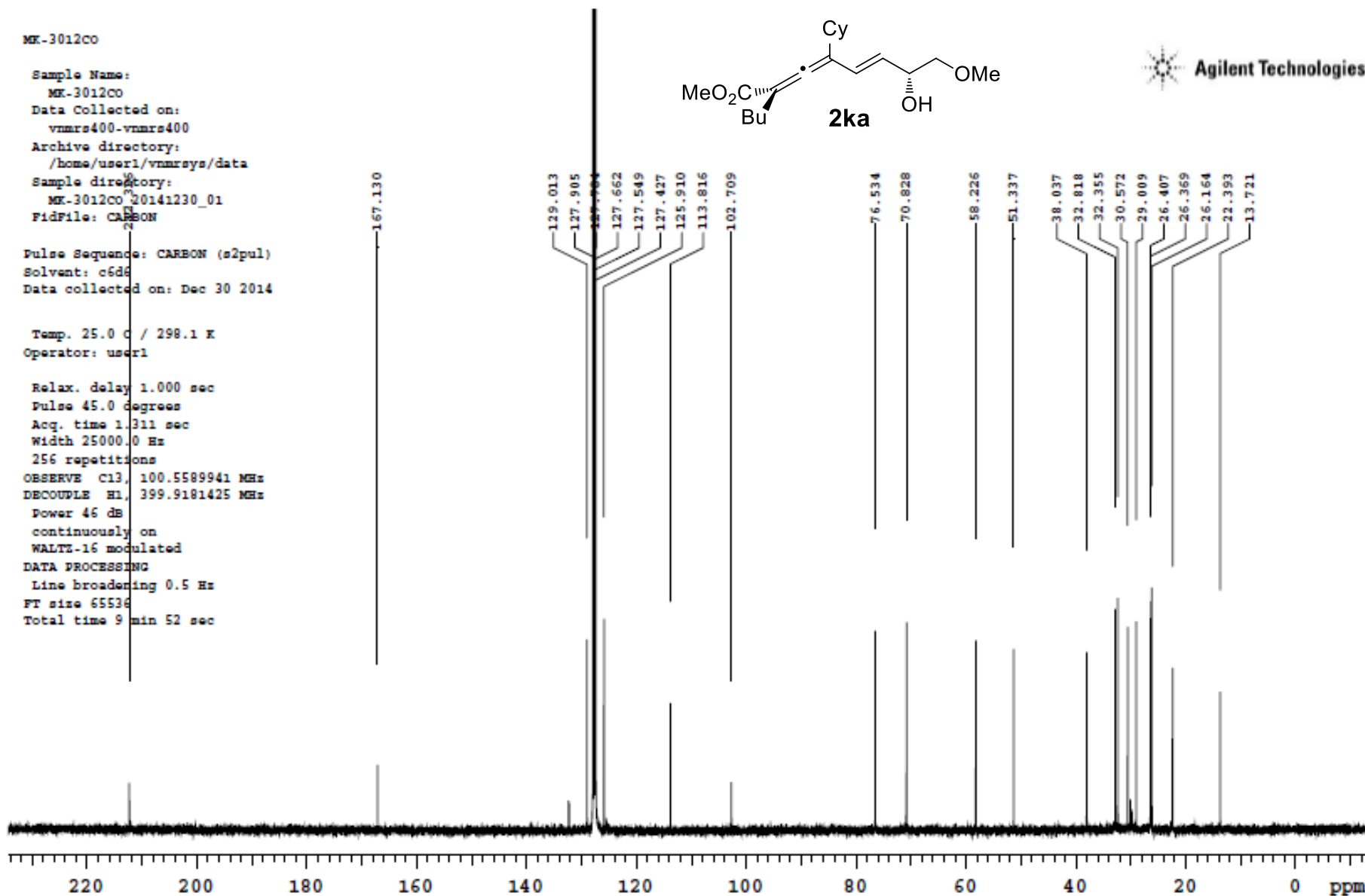DATA PROCESSING
FT size 32768
Total time 0 min 28 sec

2bd

Me

BuO₂C

Bu

OMe

OH

2bd

Agilent Technologies

167.206

128.649
127.845

103.074
100.289

77.316
77.202
76.997
76.678
76.458
71.079
64.721
59.069

30.641
30.185
28.509
22.174
19.154
14.593
13.881
13.722

220 200 180 160 140 120 100 80 60 40 20 0 ppm
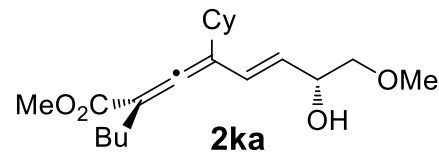
129

MX-2604CO1

Sample Name:
  MX-2604CO1
Data Collected on:
  vnmrs400-vnmrs400
Archive directory:
  /home/vnmr1/vnmrsys/data
Sample directory:
  MX-2604CO1_20130426_02
FidFile: PROTON

Pulse Sequence: PROTON (s2pul)
Solvent: c6d6
Data collected on: Apr 26 2013

Temp. 25.0 C / 298.1 K
Operator: vnmr1

Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 2.556 sec
Width 6410.3 Hz
8 repetitions
OBSERVE   H1, 399.9161429 MHz
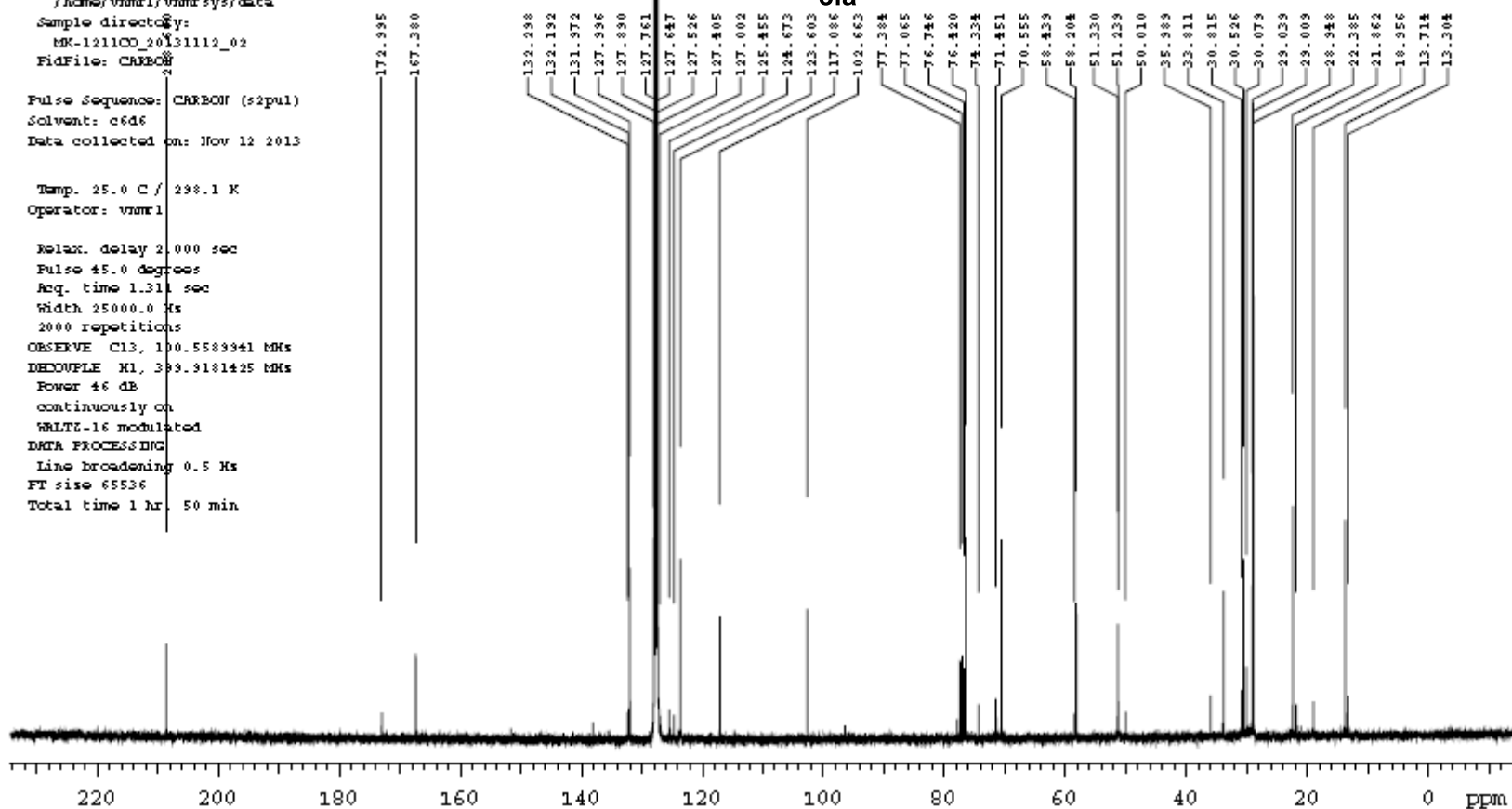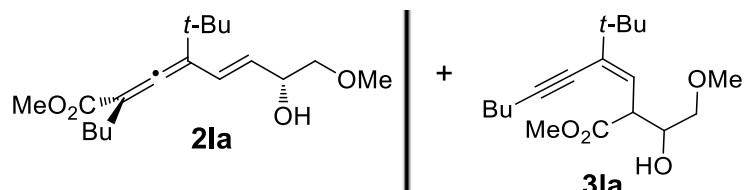DATA PROCESSING
FT size 32768
Total time 0 min 28 sec

2be

i-PrO₂C — Me — OMe — OH — Bu

2.89   3.08   2.81   3.12   14.81   6.10   3.04   9.41   6.95   13.75   19.12   14.92

7   6   5   4   3   2   1   ppm

130

MK-M18S

2be

Agilent Technologies

Peaks: 166.652, 128.862, 127.648, 103.013, 100.699, 77.316, 77.005, 76.686, 76.466, 71.132, 68.151, 59.061, 30.208, 28.554, 22.181, 21.832, 21.809, 14.655, 13.896

220 200 180 160 140 120 100 80 60 40 20 0 ppm

Gradient Shimming

Me

H₂CHCH₂CO₂C

Bu

OMe

OH

2bg

7   6   5   4   3   2   1   ppm

2bg

Agilent Technologies

166.751

132.390
128.475
128.073

117.398

103.240
100.046

77.316
77.202
76.997
76.686
76.428
71.056
65.245
59.077

30.147
29.692
28.531
22.166
14.700
13.873

220 200 180 160 140 120 100 80 60 40 20 0 ppm

133

Agilent Technologies

2ca

Agilent Technologies

2ca

Agilent Technologies

2da

5.503 5.488 5.463 5.448
4.069 4.073
3.392 3.371 3.362 3.308 3.289 3.280 3.262
2.406 2.399 2.387 2.379 2.368 2.362
1.696 1.456 1.452 1.437 1.417 1.397 1.343 1.297 1.279 1.260 1.241 1.223
0.822 0.816 0.803 0.797 0.785 0.779

7   6   5   4   3   2   1   ppm

4.38   4.62   4.39   23.58   10.34   14.87 11.23 14.04
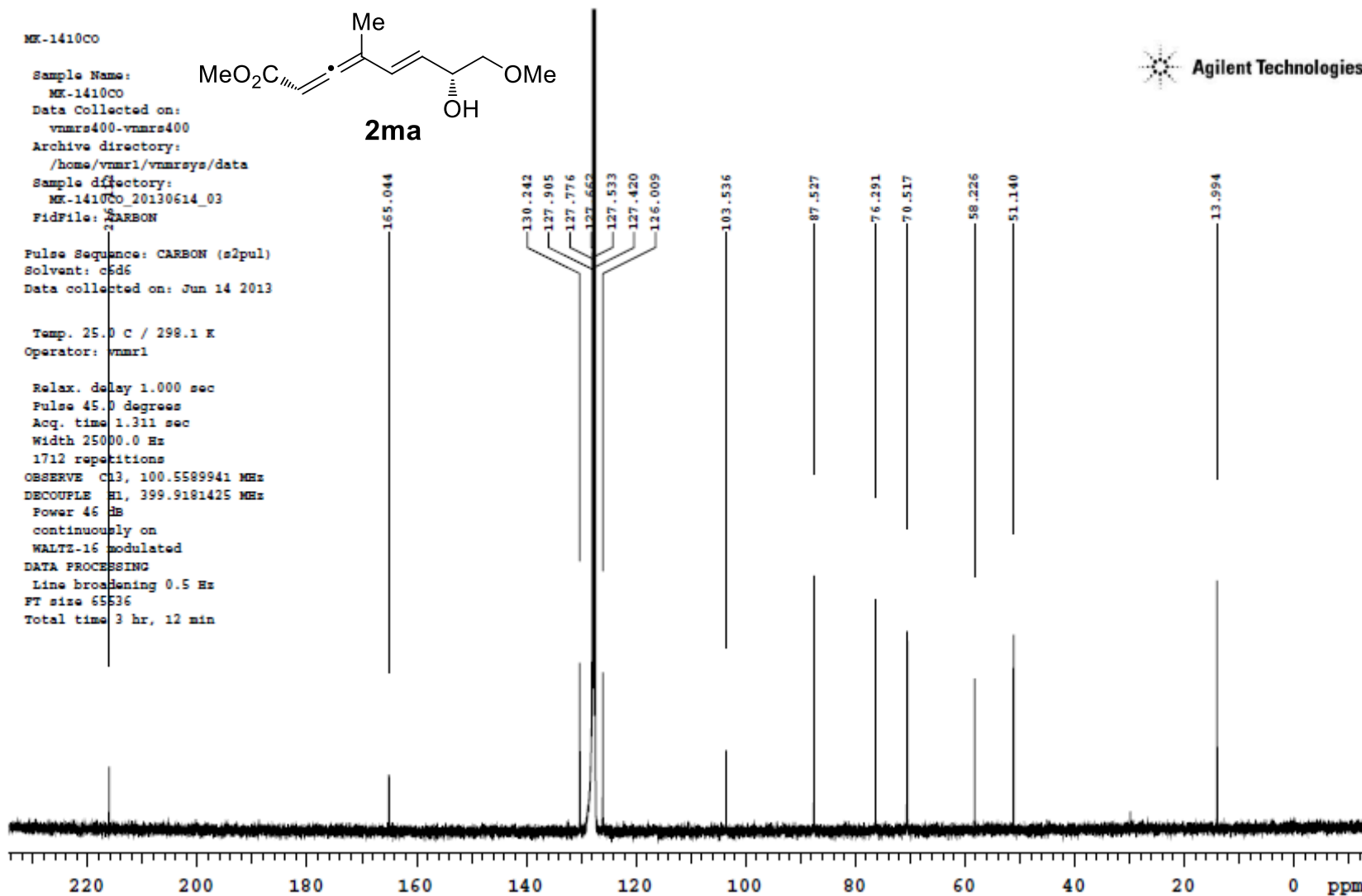   12.56

Sample Name:
  MK-OH-CO
Data Collected on:
  vnmrs400-vnmrs400
Archive directory:
  /home/vnmr1/vnmrsys/data
Sample directory:
  MK-OH-CO_20130222_04
FidFile: CARBON

Pulse Sequence: CARBON (s2pul)
Solvent: c6d6
Data collected on: Feb 22 2013

Temp. 25.0 C / 298.1 K
Operator: vnmr1

Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 1.311 sec
Width 25000.0 Hz
192 repetitions
OBSERVE C13, 100.5589941 MHz
DECOUPLE H1, 399.9181425 MHz
Power 46 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.5 Hz
FT size 65536
Total time 38 min

2da

Agilent Technologies

167.001
129.256
127.913
127.670
127.549
127.427
103.240
100.076
72.809
66.307
51.383
30.291
28.834
22.173
14.480
13.683

220 200 180 160 140 120 100 80 60 40 20 0 ppm

MK-O-TBS-CO-7-13

Sample Name:
  MK-O-TBS-CO-7-13
Data Collected on:
  vnmrs400-vnmrs400
Archive directory:
  /home/vnmr1/vnmrsys/data
Sample directory:
  MK-O-TBS-CO-7-13_20130226_02
FidFile: PROTON

Pulse Sequence: PROTON (s2pul)
Solvent: c6d6
Data collected on: Feb 26 2013

Temp. 25.0 C / 298.1 K
Operator: vnmr1

Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 2.556 sec
Width 6410.3 Hz
8 repetitions
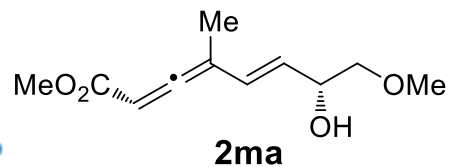OBSERVE   H1, 399.9161429 MHz
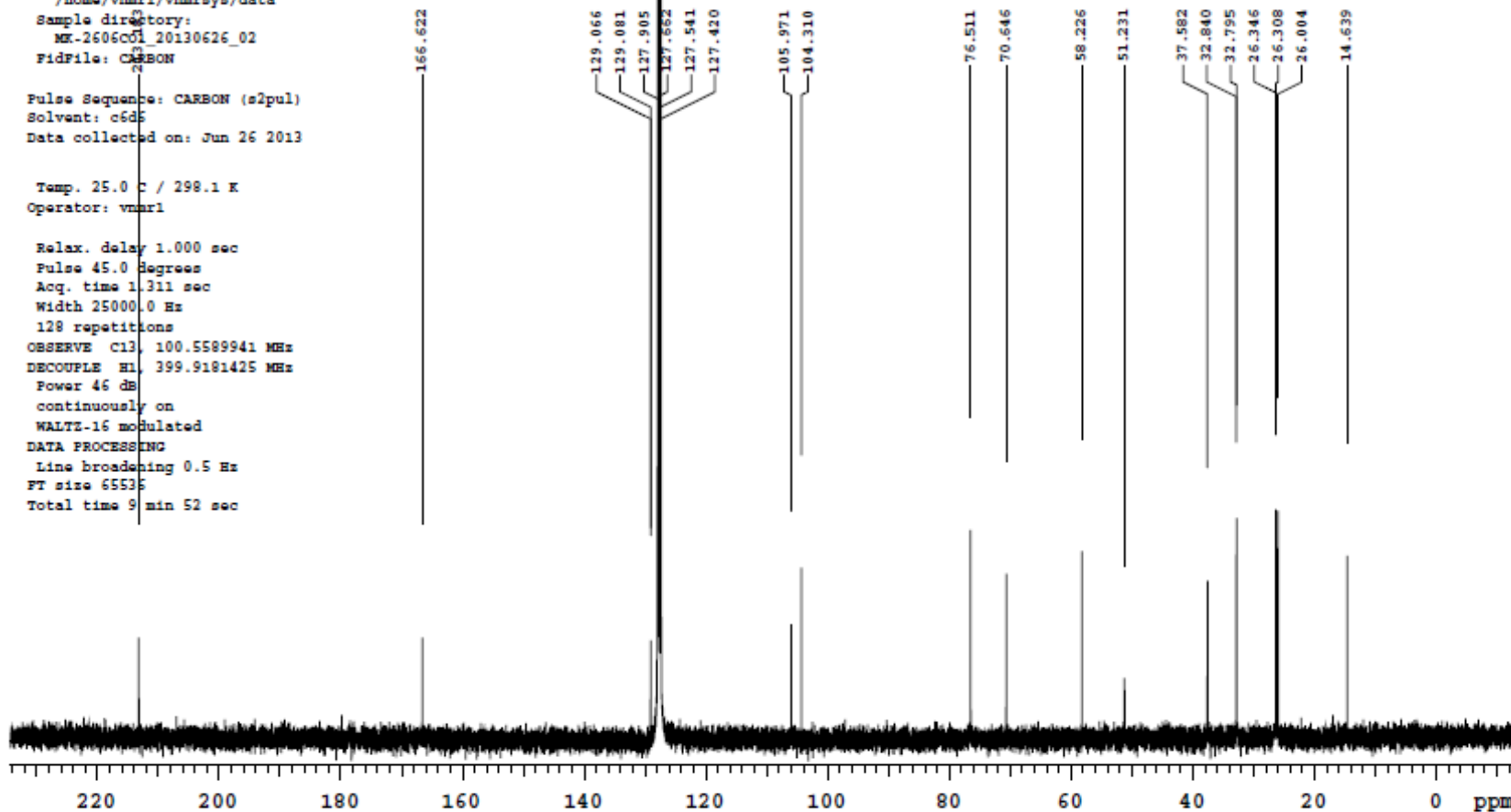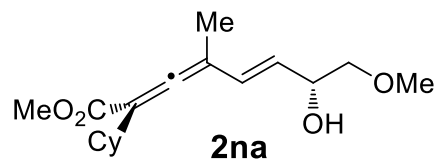DATA PROCESSING
FT size 32768
Total time 0 min 28 sec

2ea

Agilent Technologies

MX-O-TBS-CO-7-13

Sample Name:
MX-O-TBS-CO-7-13
Data Collected on:
vnmrs400-vnmrs400
Archive directory:
/home/vnmr1/vnmrsys/data
Sample directory:
MX-O-TBS-CO-7-13_20130226_04
FidFile: CARBON

Pulse Sequence: CARBON (s2pul)
Solvent: c6d6
Data collected on: Feb 26 2013

Temp. 25.0 C / 298.1 K
Operator: vnmr1

Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 1.311 sec
Width 25000.0 Hz
384 repetitions
OBSERVE C13, 100.5589941 MHz
DECOUPLE H1, 399.9181425 MHz
Power 46 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
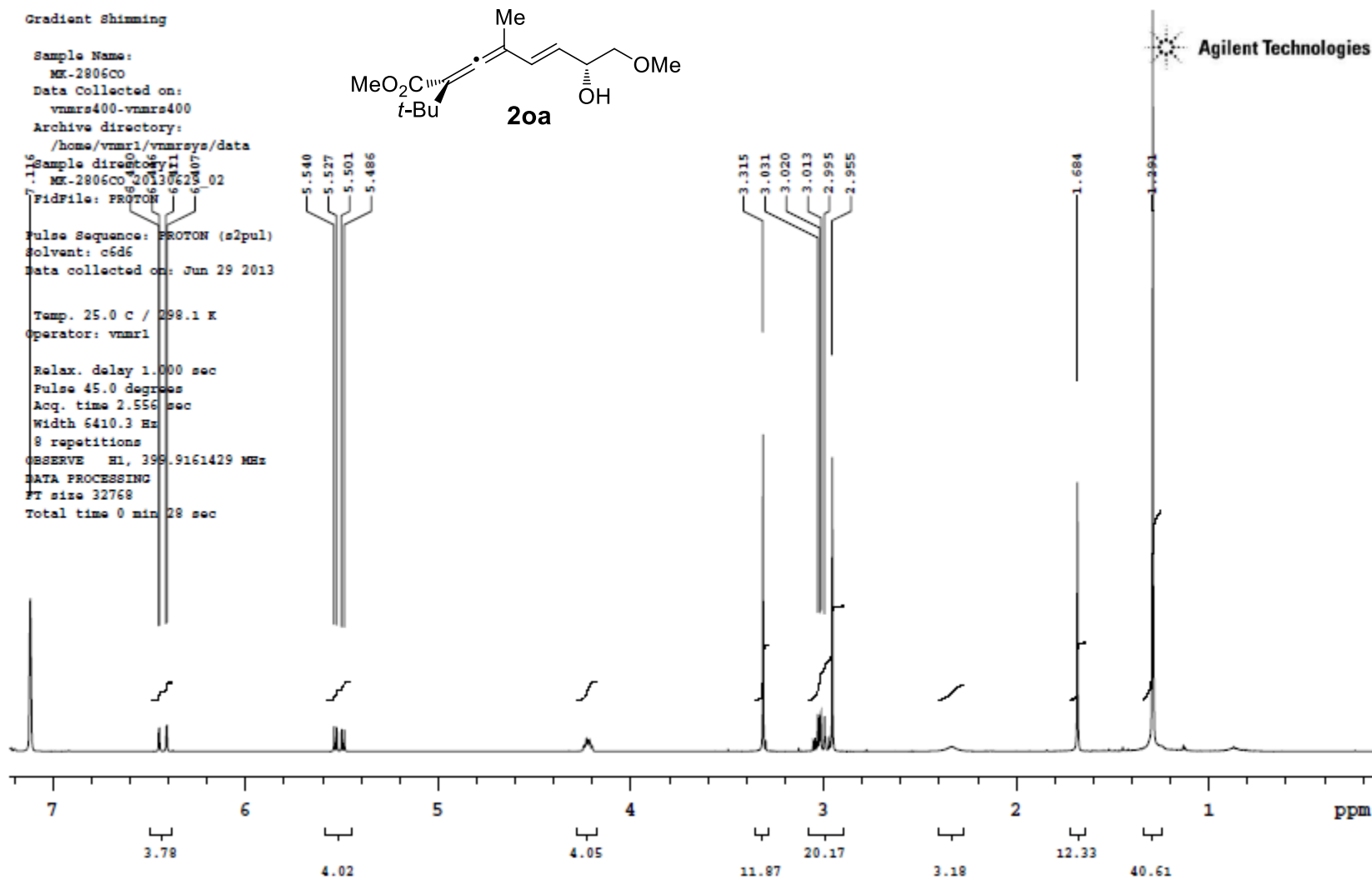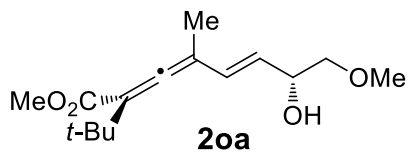Line broadening 0.5 Hz
FT size 65536
Total time 19 min

166.910

129.271
127.898
127.655
127.533
127.480
127.420

103.149
100.031

72.460
67.232

51.292

30.276
28.857
25.633
22.173
18.076
14.548
13.676

-5.664
-5.686

Me

MeO₂C **Bu** **OTBDMS** **ŌH** **2ea**

220 200 180 160 140 120 100 80 60 40 20 0 ppm

2fa

3.363

1.707

1.061
1.018

0.784

7   6   5   4   3   2   1   ppm

0.39
1.46
0.34
1.66

3.92

4.16

9.10
1.57

7.21

3.47
2.91

11.18

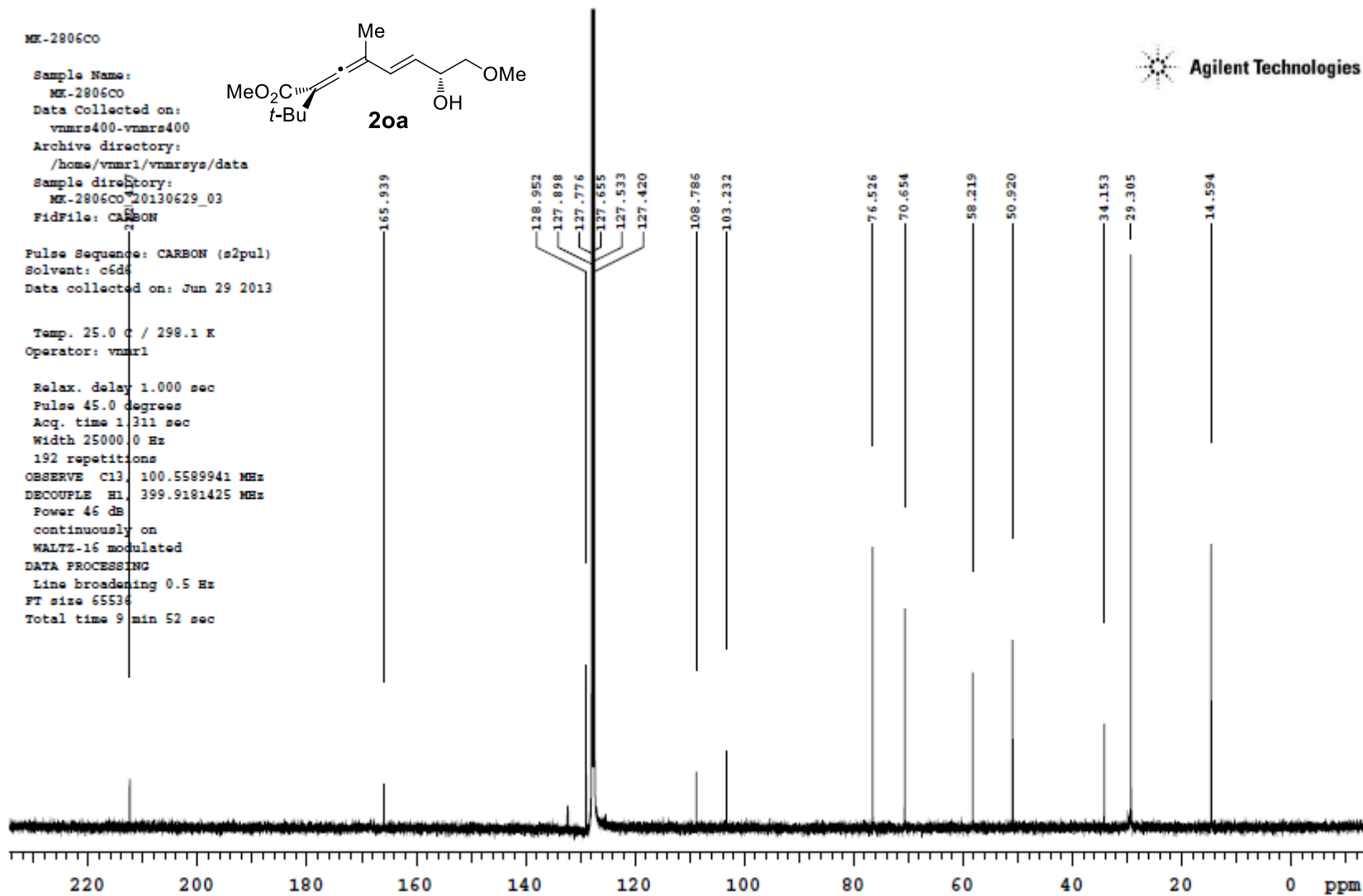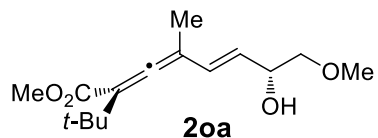9.16

9.39

9.51
2.37
11.36

10.84

MK-1207CO2

Sample Name:
  MK-1207CO2
Data Collected on:
  vnmrs400-vnmrs400
Archive directory:
  /home/vnmr1/vnmrsys/data
Sample directory:
  MK-1207CO2_20130712_03
FidFile: CARBON

Pulse Sequence: CARBON (s2pul)
Solvent: c6d6
Data collected on: Jul 12 2013

Temp. 25.0 C / 298.1 K
Operator: vnmr1

Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 1.311 sec
Width 25000.0 Hz
512 repetitions
OBSERVE C13, 100.5589941 MHz
DECOUPLE H1, 399.9181425 MHz
 Power 46 dB
 continuously on
 WALTZ-16 modulated
DATA PROCESSING
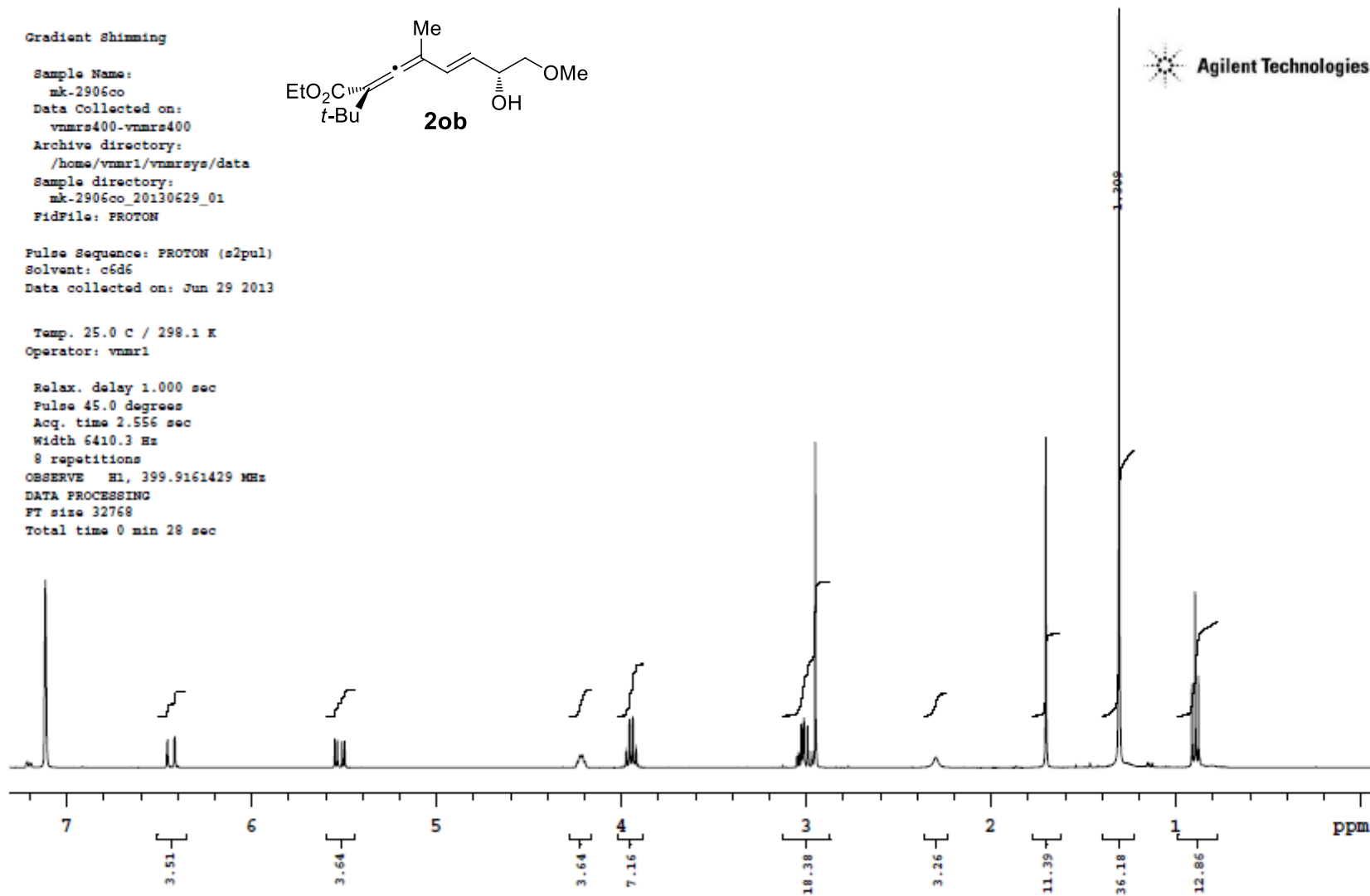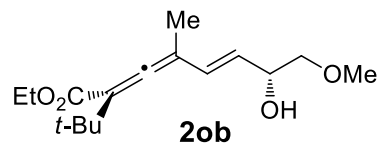 Line broadening 0.5 Hz
FT size 65536
Total time 19 min

2fa

Agilent Technologies

165.948
129.324
128.497
127.890
127.655
127.526
127.412
103.210
100.046
79.204
72.255
51.337
30.306
28.827
26.058
23.827
22.150
22.105
14.495
13.645

220 200 180 160 140 120 100 80 60 40 20 0 ppm

Agilent Technologies

2ga

7.114

3.356

2.853

1.723

0.933
0.877

3.45

3.47

3.48

9.19

9.06

3.15
7.06

10.24

7.79

8.56

11.21
11.28
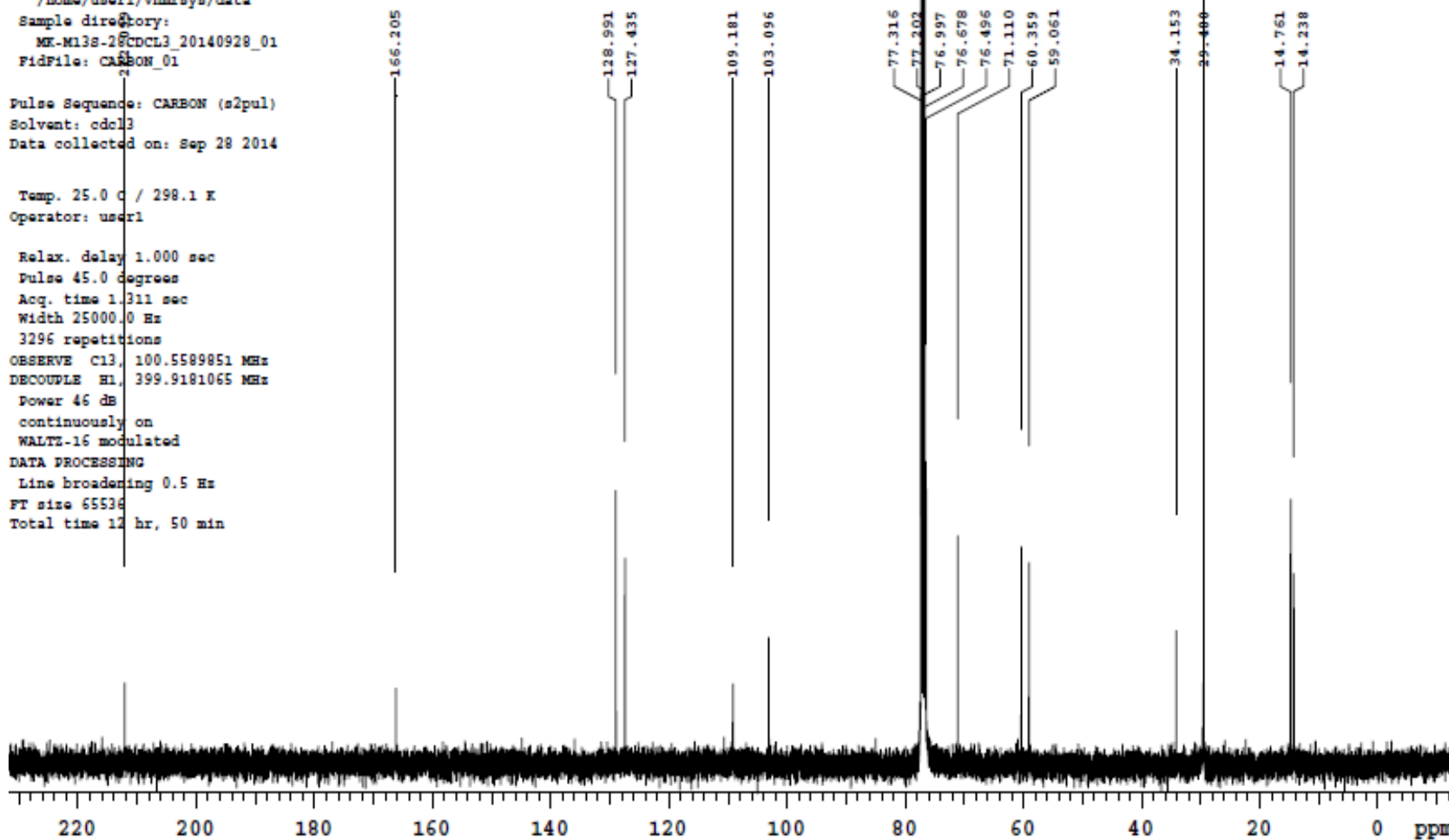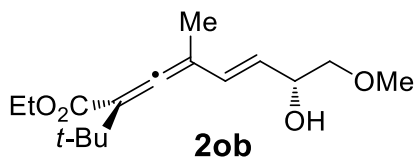11.21

7   6   5   4   3   2   1   ppm
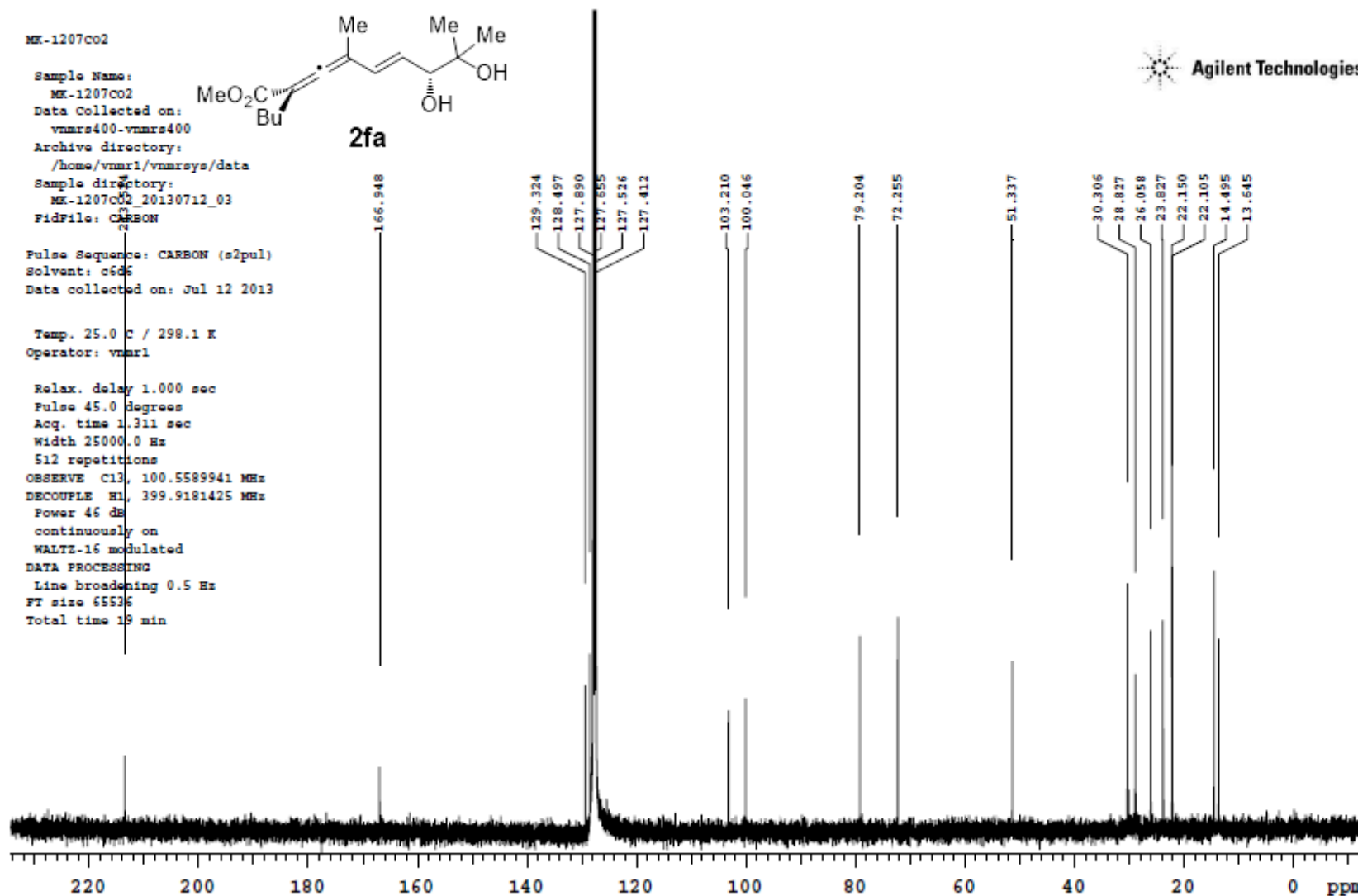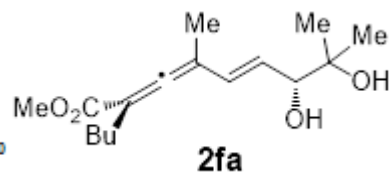
MK-1307CO

Sample Name:
  MK-1307CO
 Data Collected on:
  vnmrs400-vnmrs400
 Archive directory:
  /home/vnmr1/vnmrsys/data
 Sample directory:
  MK-1307CO.20130713_03
 FidFile: CARBON

Pulse Sequence: CARBON (s2pul)
Solvent: c6d6
Data collected on: Jul 13 2013

 Temp. 25.0 C / 298.1 K
Operator: vnmr1

 Relax. delay 1.000 sec
 Pulse 45.0 degrees
 Acq. time 1.311 sec
 Width 25000.0 Hz
 124 repetitions
OBSERVE C13, 100.5589941 MHz
DECOUPLE H1, 399.9181425 MHz
 Power 46 dB
 continuously on
 WALTZ-16 modulated
DATA PROCESSING
 Line broadening 0.5 Hz
FT size 65536
Total time 19 min

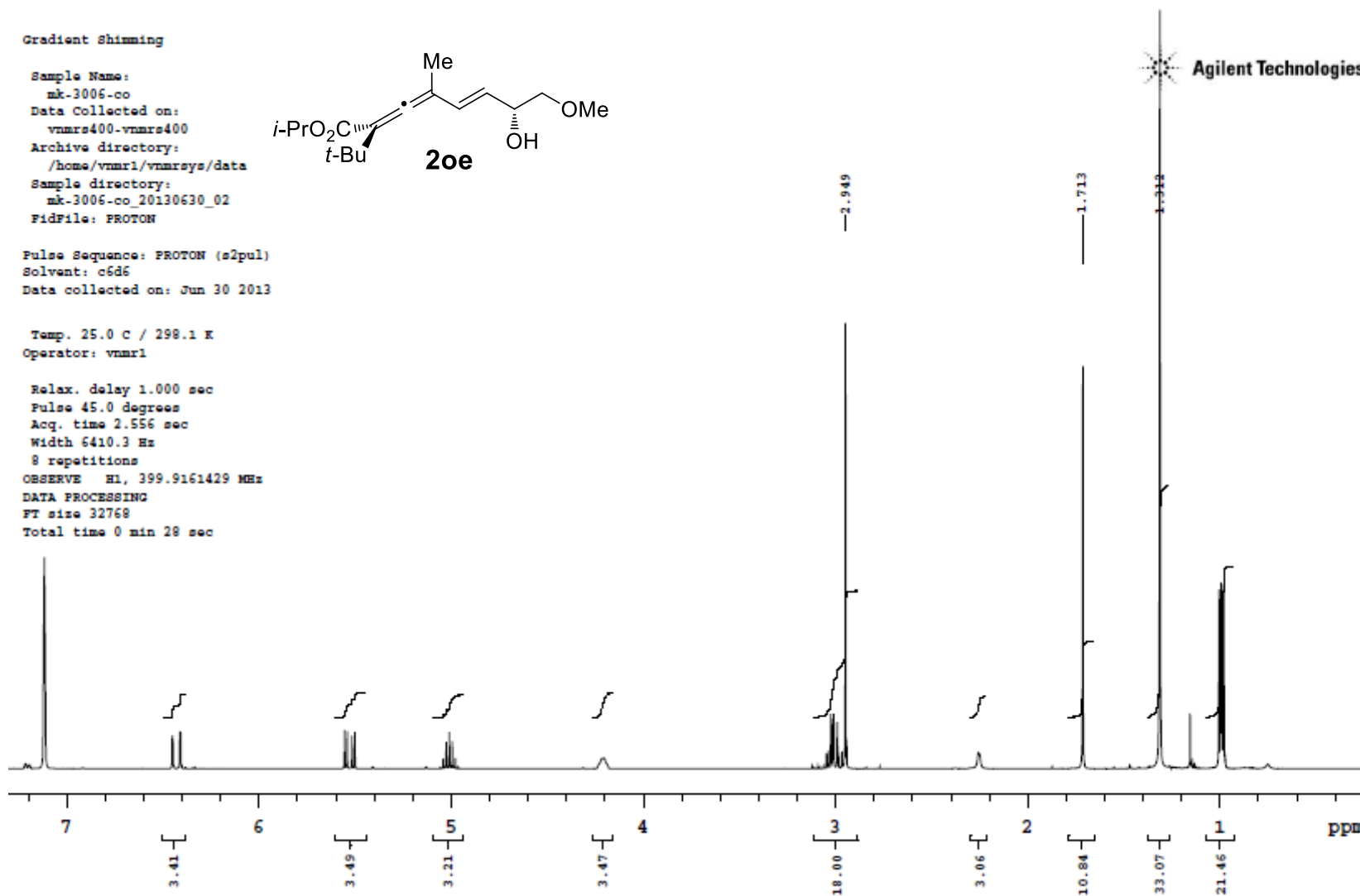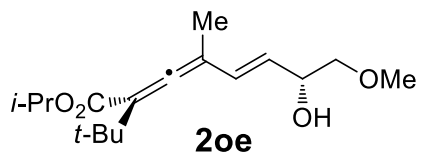**2ga**

166.933
129.081
127.943
127.890
127.547
127.526
127.405
103.248
99.932
77.604
77.118
51.262
48.636
30.314
28.872
22.112
20.223
19.153
14.563
13.653

220 200 180 160 140 120 100 80 60 40 20 0 ppm

143

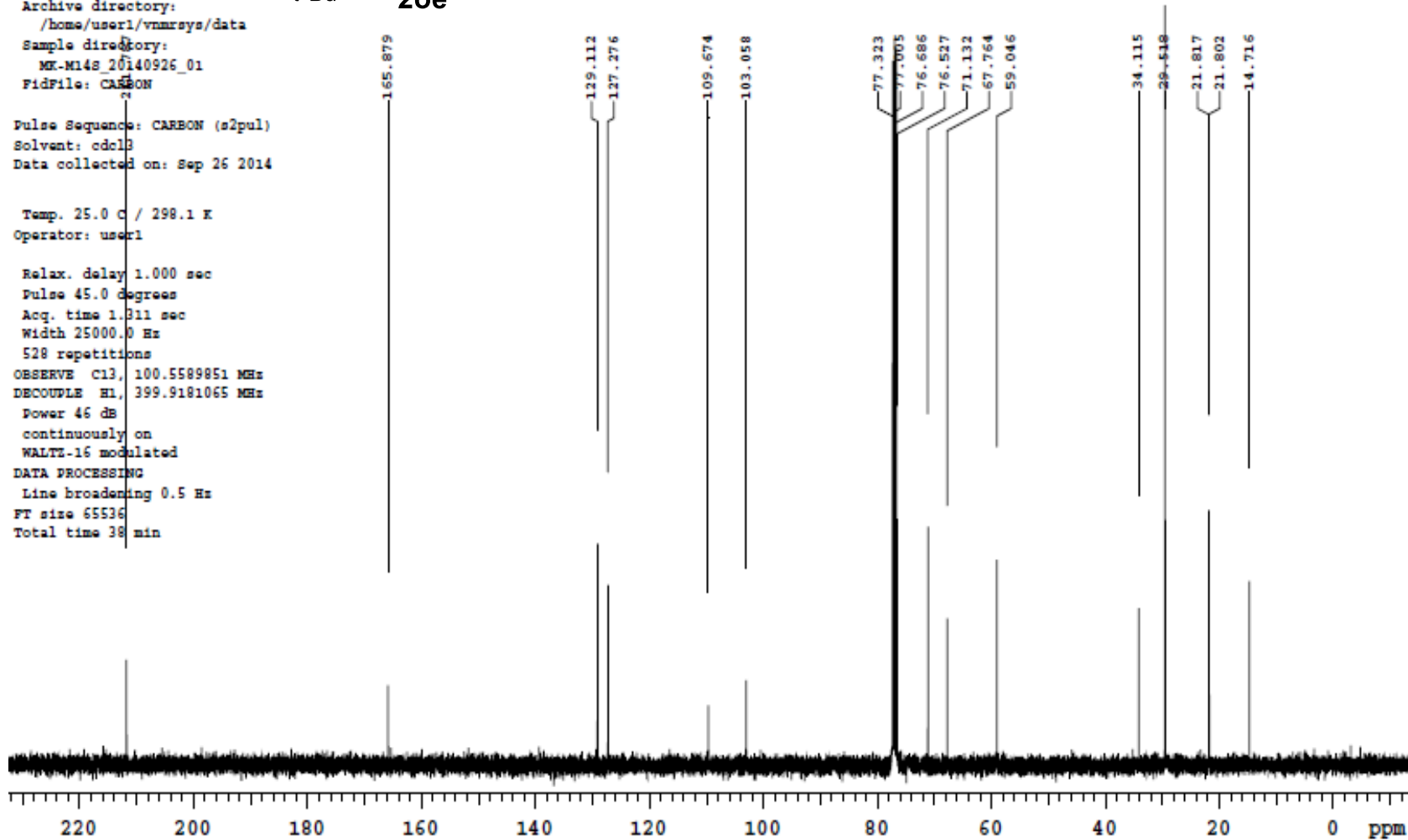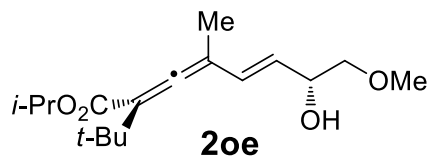Agilent Technologies

2ha

MeO$_2$C

Bu

OMe

OH
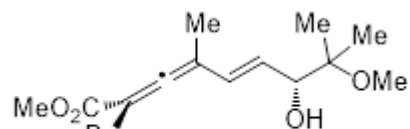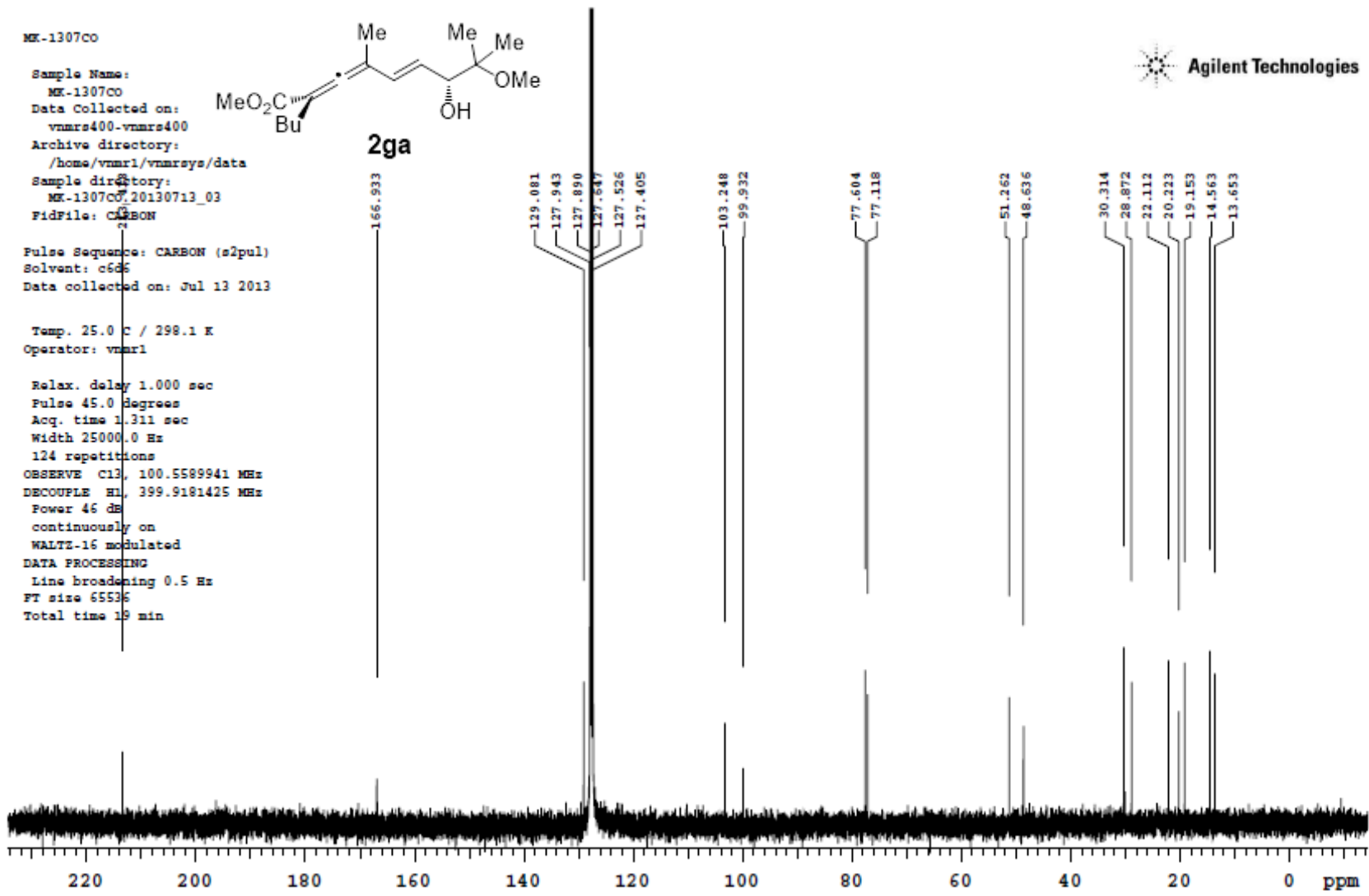
mk-3107co

Sample Name:
  mk-3107co
Data Collected on:
  vnmrs400-vnmrs400
Archive directory:
  /home/vnmr1/vnmrsys/data
Sample directory:
  mk-3107co_20130731_02
FidFile: CARBON

Pulse Sequence: CARBON (s2pul)
Solvent: c6d6
Data collected on: Jul 31 2013

Temp. 25.0 C / 298.1 K
Operator: vnmr1

Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 1.311 sec
Width 25000.0 Hz
120 repetitions
OBSERVE C13, 100.5589941 MHz
DECOUPLE H1, 399.9181425 MHz
Power 46 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.5 Hz
FT size 65536
Total time 23 min

2ha

Agilent Technologies

166.584
132.708
127.890
127.655
127.412
124.127
101.943
97.025
76.268
70.358
70.282
58.188
51.330
30.177
28.645
22.143
13.623

2ia

146

2ia

147

2ja

7.115
6.779
6.775
6.740
6.737
5.521
5.505
5.481
5.465
4.041
4.025
4.010
3.377
3.365
2.413
2.409
2.395
2.391
2.375
2.372
1.691
1.466
1.463
1.459
1.446
1.427
1.407
1.340
1.333
1.300
1.291
1.281
1.272
1.263
1.253
1.243
1.235
1.226
1.047
1.031
0.817
0.809
0.798
0.790
0.779
0.772

7 6 5 4 3 2 1 ppm

4.02
4.40
4.54
12.24
9.01
13.46
10.05
15.13
13.94
13.20

148

mk-monometilCO-c13

Sample Name:
  mk-monometilCO-c13
Data Collected on:
  varian400-mercury400
Archive directory:
  /home/vnmr1/vnmrsys/data
Sample directory:
  mk-monometilCO-c13_20150129_01
FidFile: CARBON_01

Pulse Sequence: CARBON (s2pul)
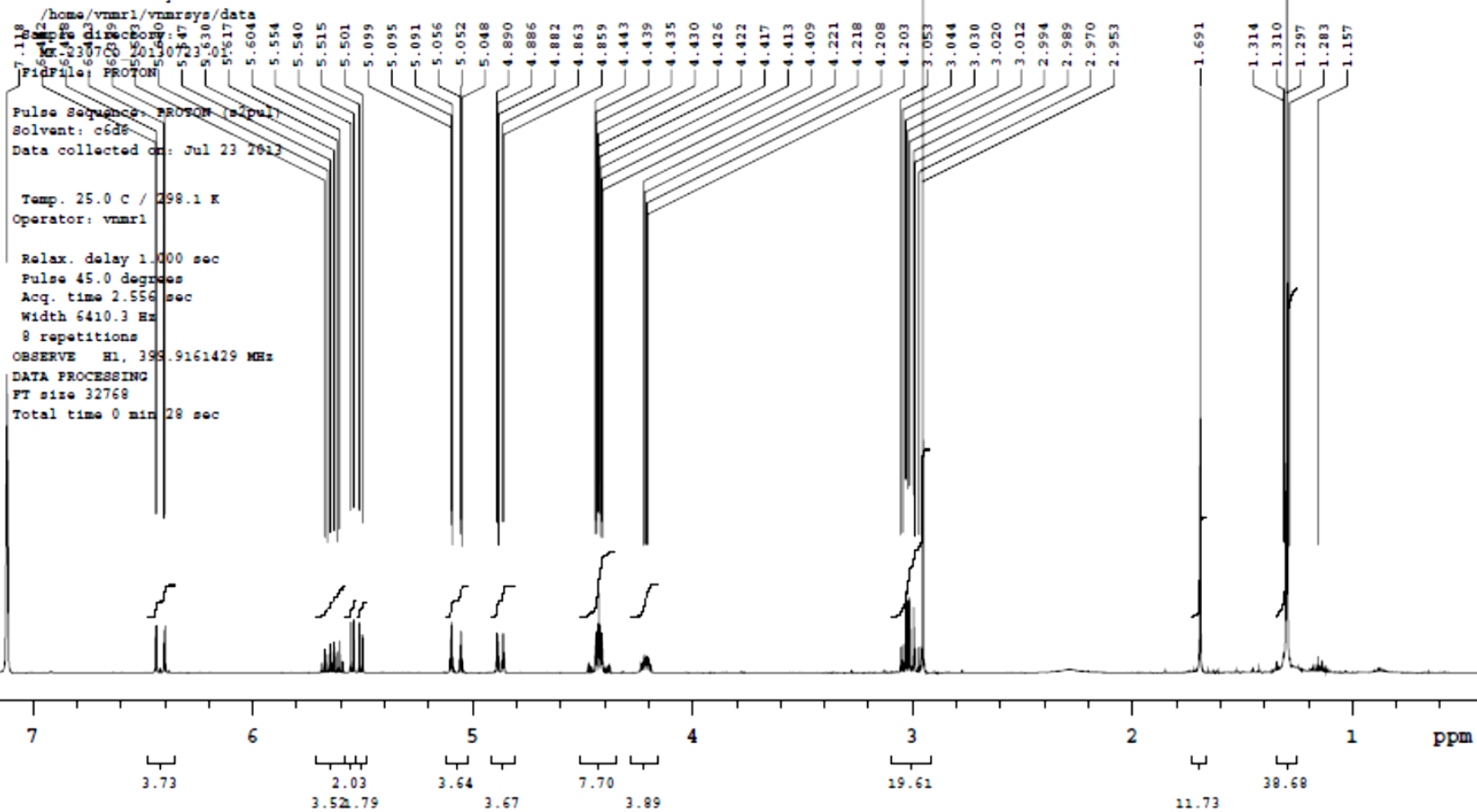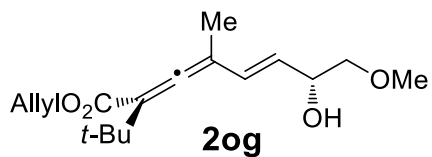Solvent: c6d6
Data collected on: Jan 29 2015

Temp. 30.0 c / 303.1 K
Operator: vnmr1

Relax. delay 2.000 sec
Pulse 45.0 degrees
Acq. time 1.304 sec
Width 25125.6 Hz
560 repetitions
OBSERVE C13, 100.5499849 MHz
DECOUPLE H1, 399.8823589 MHz
Power 44 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.5 Hz
FT size 65536
Total time 0 min 0 sec

166.949
134.730
127.875
127.631
127.394
125.221
103.114
99.949
68.012
51.251
30.326
28.854
23.150
22.128
14.517
13.618

2ja

MK-3012CO
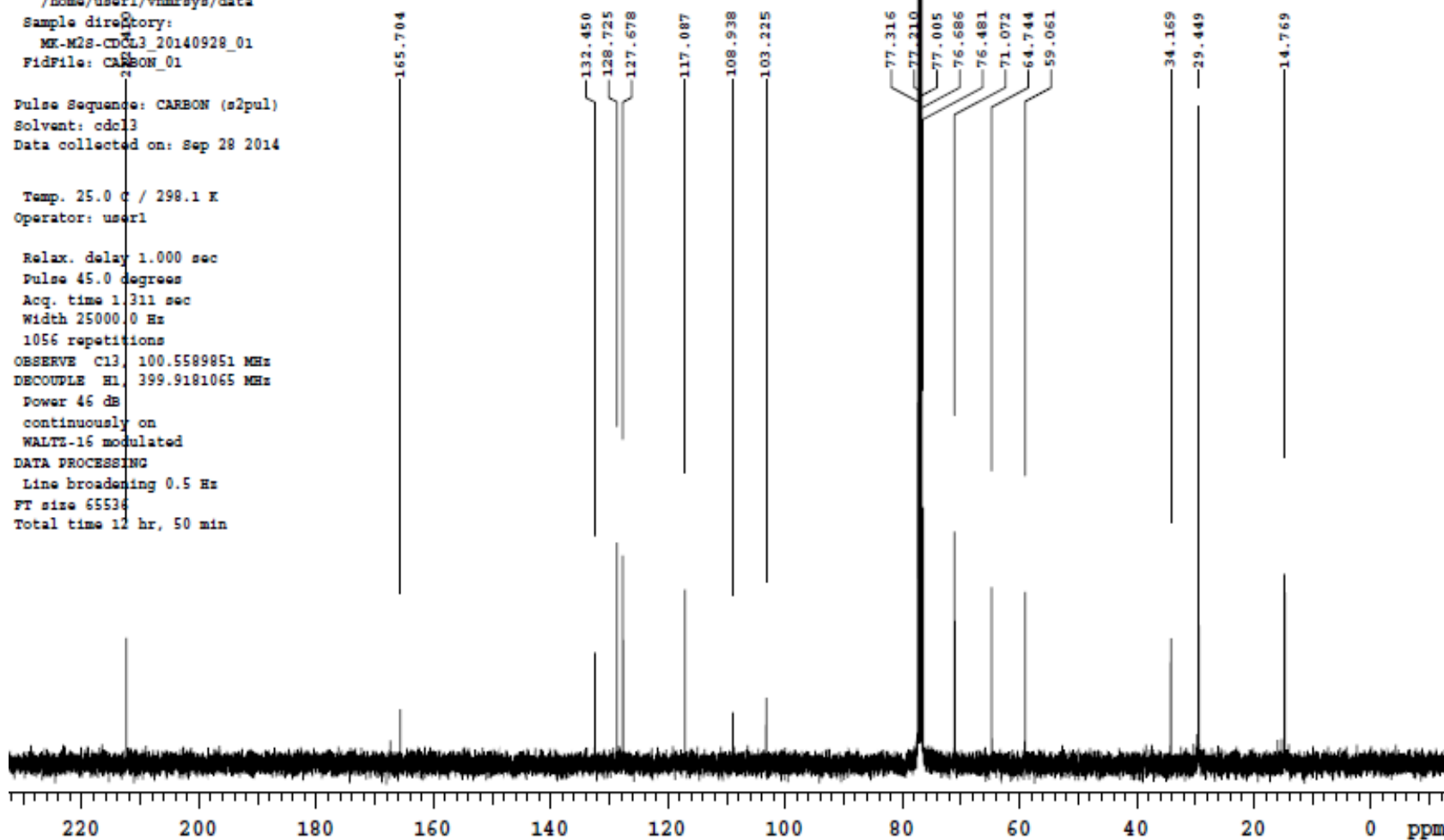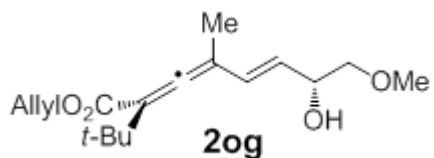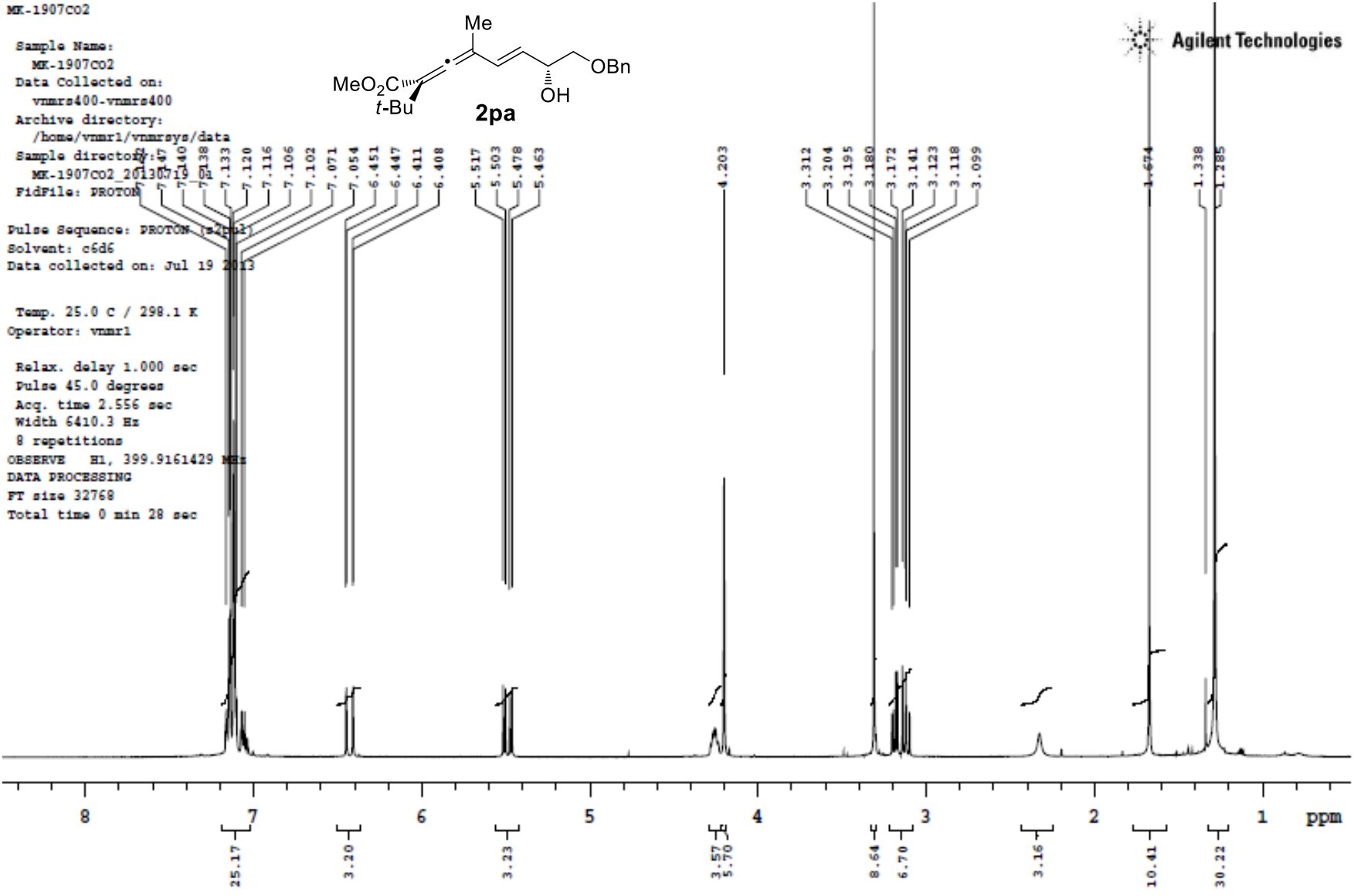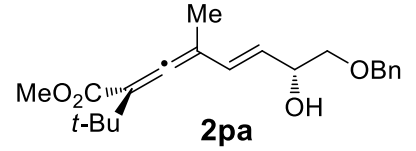
Sample Name:
  MK-3012CO
Data Collected on:
  vnmrs400-vnmrs400
Archive directory:
  /home/user1/vnmrsys/data
Sample directory:
  MK-3012CO_20241230_01
FidFile: PROTON

Pulse Sequence: PROTON (s2pul)
Solvent: c6d6
Data collected on: Dec 30 2014

Temp. 25.0 C / 298.1 K
Operator: user1

Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 2.556 sec
Width 6410.3 Hz
8 repetitions
OBSERVE H1, 399.9161429 MHz
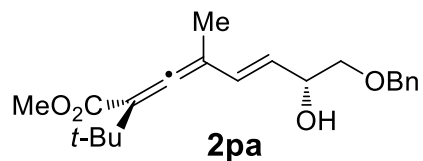DATA PROCESSING
FT size 32768
Total time 0 min 28 sec

2ka

150

Agilent Technologies

167.130
129.013
127.905
127.762
127.662
127.549
127.427
125.910
113.816
102.709
76.534
70.828
58.226
51.337
38.037
32.818
32.355
30.572
29.009
26.407
26.369
26.164
22.393
13.721

MeO2C — Cy — OMe
2ka
Bu — OH

151

Gradient Shimming

Sample Name:
MK-1211CO
Data Collected on:
vnmrs400-vnmrs400
Archive directory:
/home/vnmr1/vnmrsys/data
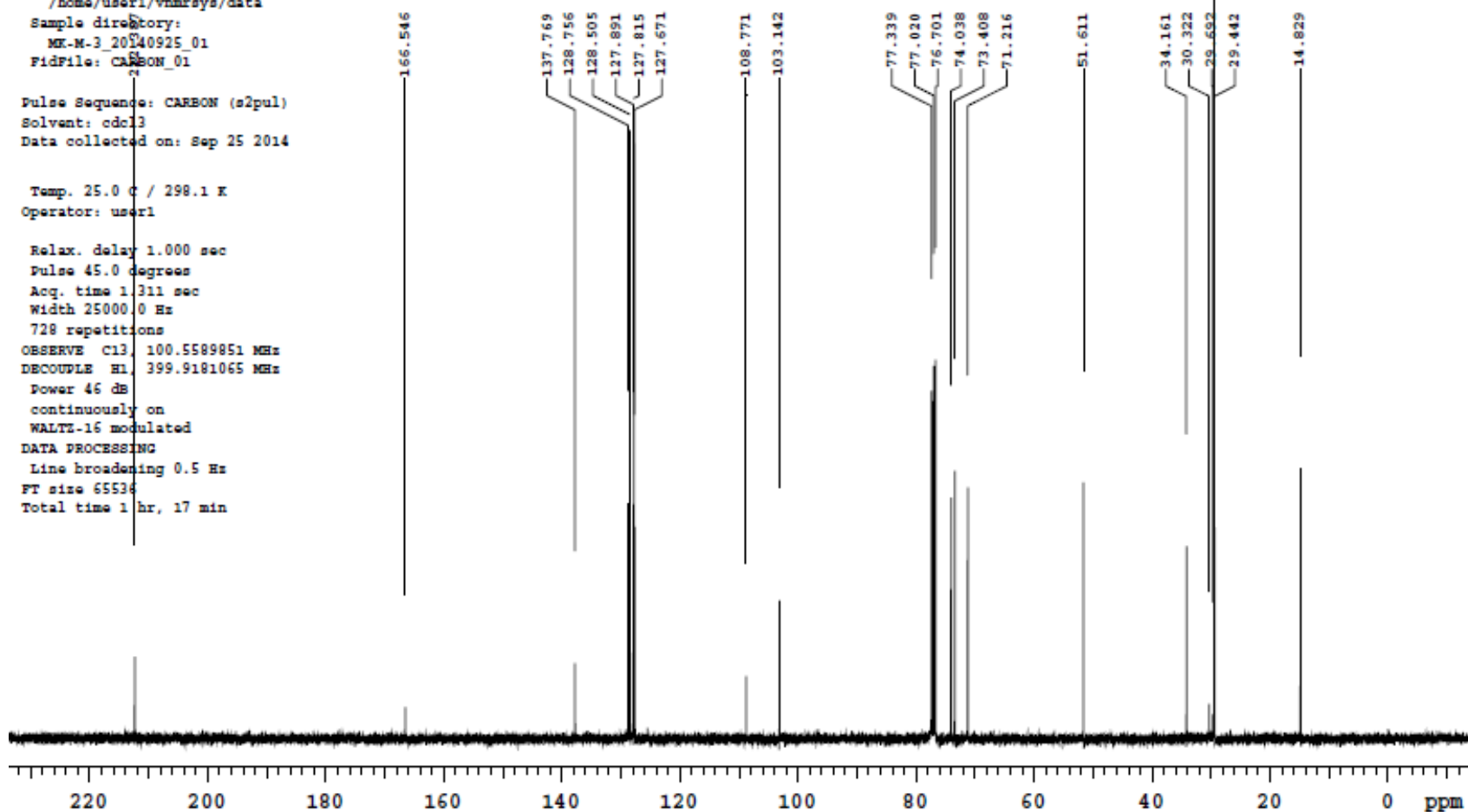Sample directory:
MK-1211CO_20131112_01
FidFile: PROTON

Pulse Sequence: PROTON (s2pul)
Solvent: c6d6
Data collected on: Nov 12 2013

Temp. 25.0 C / 298.1 K
Operator: vnmr1

Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 2.556 sec
Width 6410.3 Hz
8 repetitions
OBSERVE   H1, 399.9161429 MHz
DATA PROCESSING
FT size 32768
Total time 0 min 28 sec

2Ia

3Ia

172.995
167.380
132.298
132.192
131.972
127.996
127.880
127.761
127.647
127.526
127.405
127.002
126.455
125.673
123.603
117.086
102.663
77.384
77.065
76.746
76.420
74.334
71.451
70.555
58.439
58.204
51.330
51.239
50.010
35.989
33.811
30.815
30.526
30.079
23.039
23.009
20.948
20.385
20.862
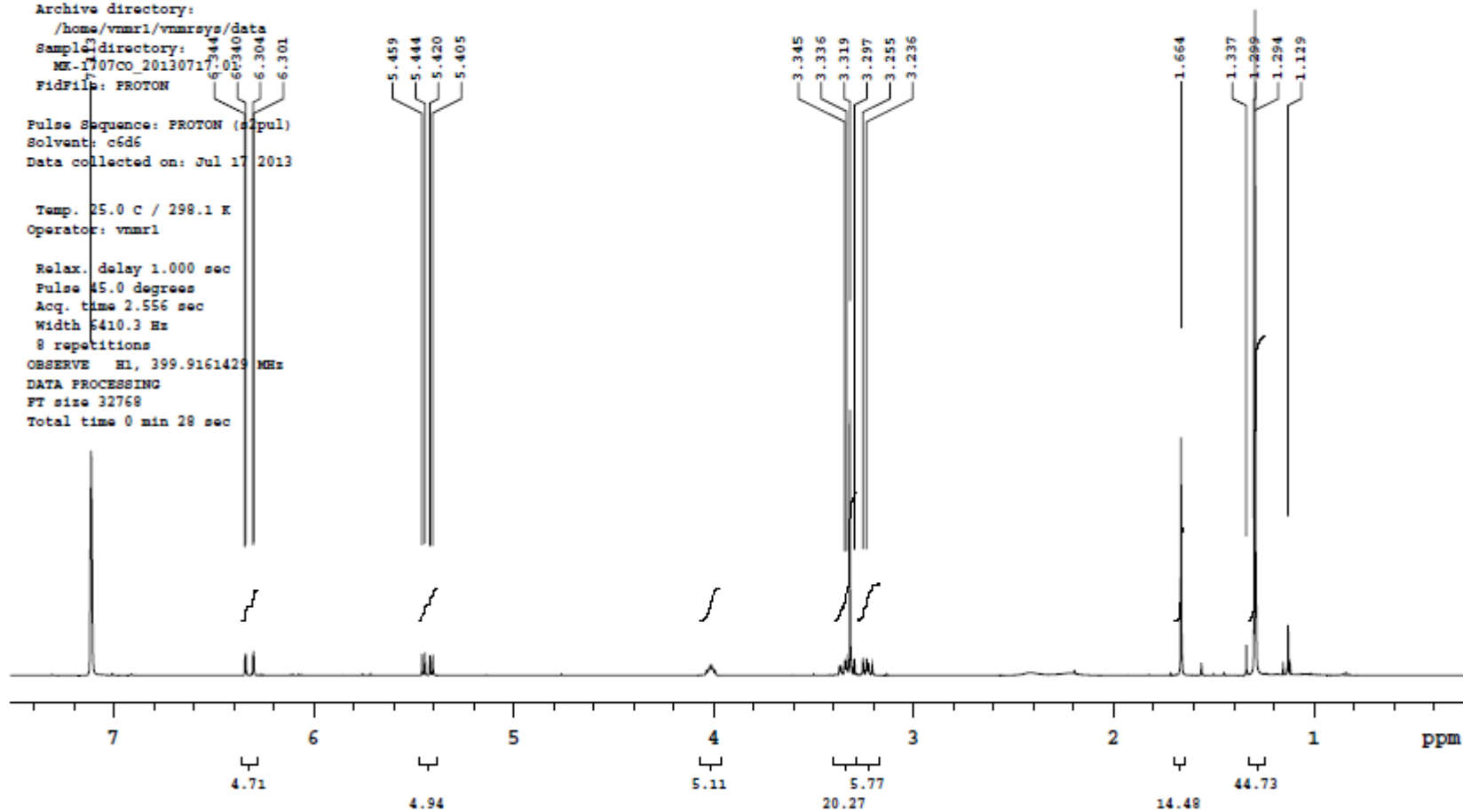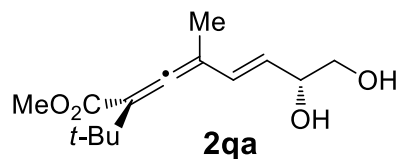21.862
18.956
13.714
13.304

Gradient Shimming

Sample Name:
  MM-1410CO
Data Collected on:
  vnmrs400-vnmrs400
Archive directory:
  /home/vnmr1/vnmrsys/data
Sample directory:
  MM-1410CO_20130614_02
FidFile: PROTON

Pulse Sequence: PROTON (s2pul)
Solvent: c6d6
Data collected on: Jun 14 2013

Temp. 25.0 C / 298.1 K
Operator: vnmr1

Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 2.556 sec
Width 6410.3 Hz
64 repetitions
OBSERVE   H1, 399.9161429 MHz
DATA PROCESSING
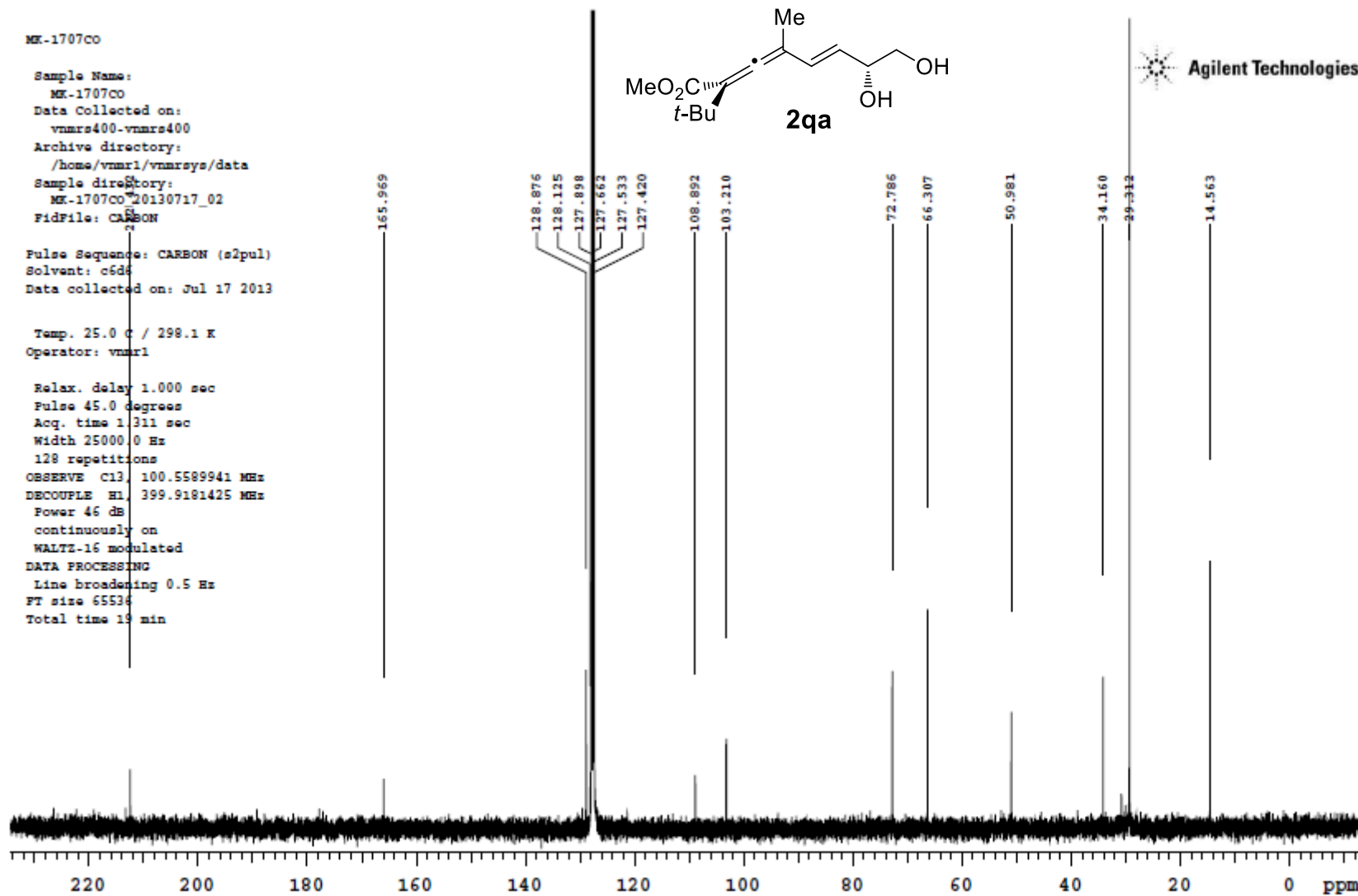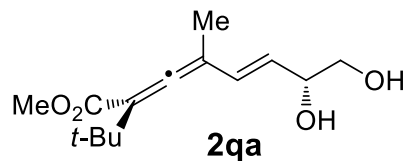FT size 32768
Total time 3 min 48 sec

2ma

3.318
2.946
1.559
1.553

6.15
5.58
6.73
6.55
15.89
2.37
33.70
23.04

7   6   5   4   3   2   1   ppm

MK-1410CO

Agilent Technologies

2ma

165.044
130.242
127.905
127.776
127.662
127.533
127.420
126.009
103.536
87.527
76.291
70.517
58.226
51.140
13.994

220   200   180   160   140   120   100   80   60   40   20   0   ppm
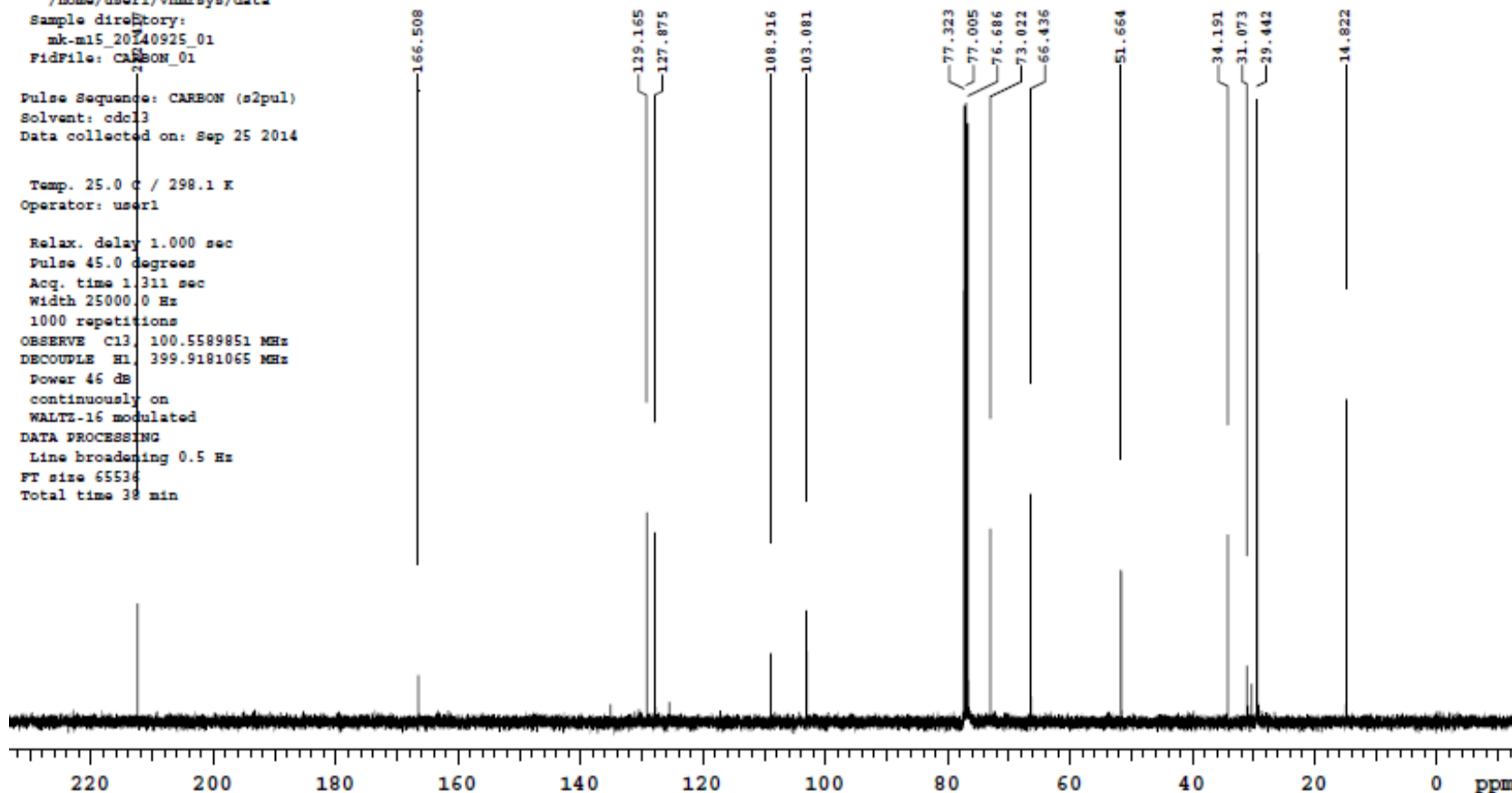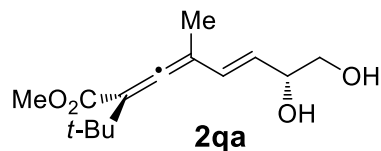
Gradient Shimming

Sample Name:
  MK-2606CO1
Data Collected on:
  vnmrs400-vnmrs400
Archive directory:
  /home/vnmr1/vnmrsys/data
Sample directory:
  MK-2606CO1_20130626_01
FidFile: PROTON

Pulse Sequence: PROTON (s2pul)
Solvent: c6d6
Data collected on: Jun 26 2013

Temp. 25.0 C / 298.1 K
Operator: vnmr1

Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 2.556 sec
Width 6410.3 Hz
8 repetitions
OBSERVE H1, 399.9161429 MHz
DATA PROCESSING
FT size 32768
Total time 0 min 28 sec

2na

156

MK-2606CO1
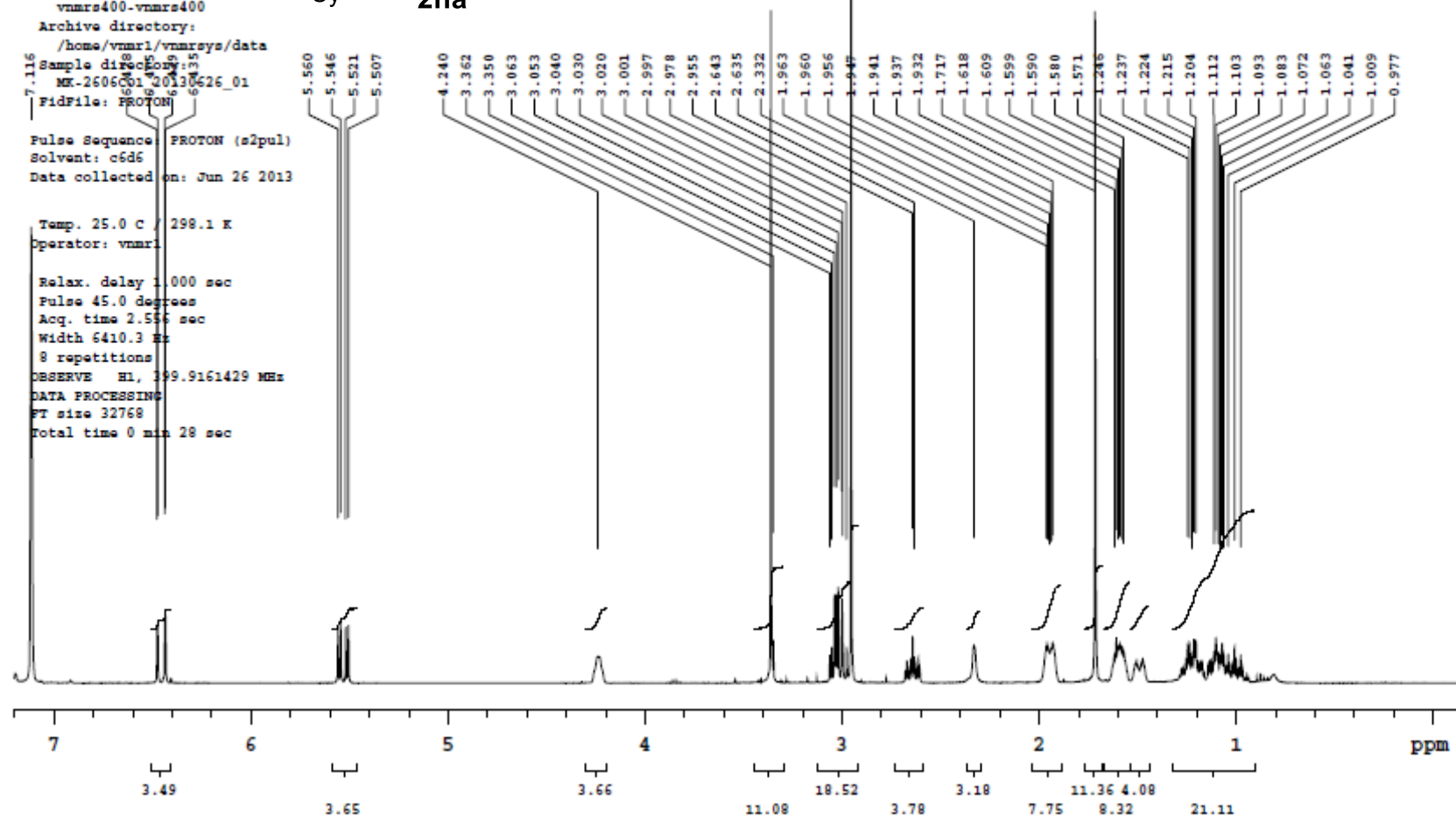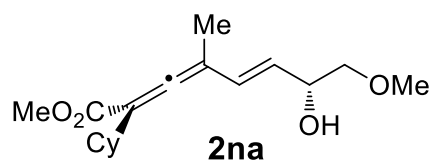
Sample Name:
  MK-2606CO1
Data Collected on:
  vnmrs400-vnmrs400
Archive directory:
  /home/vnmr1/vnmrsys/data
Sample directory:
  MK-2606CO1_20130626_02
FidFile: CARBON

Pulse Sequence: CARBON (s2pul)
Solvent: c6d6
Data collected on: Jun 26 2013

Temp. 25.0 C / 298.1 K
Operator: vnmr1

Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 1.311 sec
Width 25000.0 Hz
128 repetitions
OBSERVE C13, 100.5589941 MHz
DECOUPLE H1, 399.9181425 MHz
 Power 46 dB
 continuously on
 WALTZ-16 modulated
DATA PROCESSING
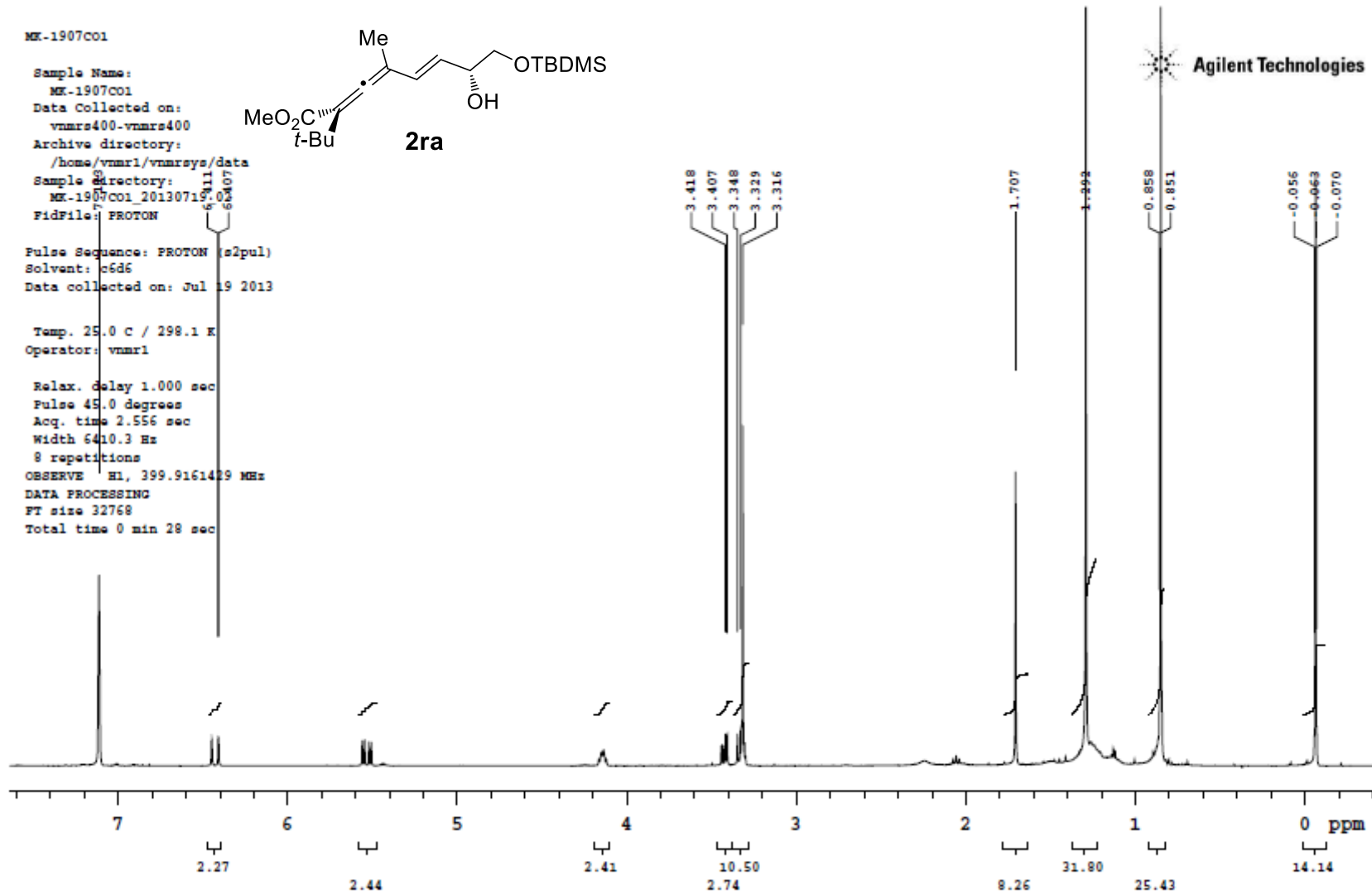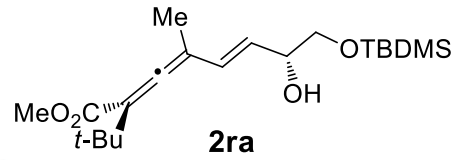 Line broadening 0.5 Hz
FT size 65536
Total time 9 min 52 sec

Agilent Technologies

2oa

MK-2806CO

Agilent Technologies

2oa

Peaks: 165.939, 128.952, 127.898, 127.776, 127.655, 127.533, 127.420, 108.786, 103.232, 76.526, 70.654, 58.219, 50.920, 34.153, 29.305, 14.594

159

Gradient Shimming
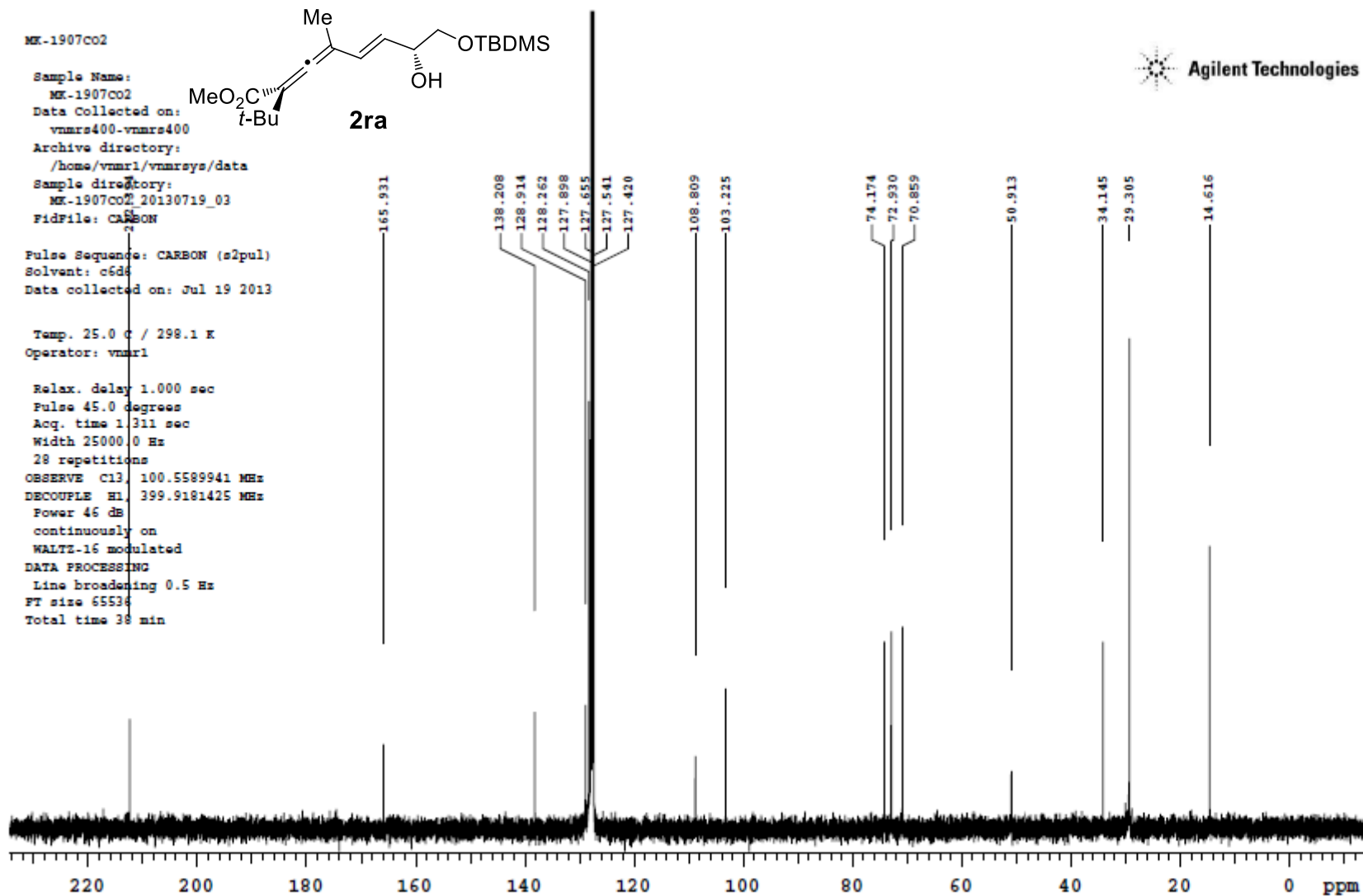
 Sample Name:
  mk-2906co
 Data Collected on:
  vnmrs400-vnmrs400
 Archive directory:
  /home/vnmr1/vnmrsys/data
 Sample directory:
  mk-2906co_20130629_01
 FidFile: PROTON

Pulse Sequence: PROTON (s2pul)
Solvent: c6d6
Data collected on: Jun 29 2013

 Temp. 25.0 C / 298.1 K
Operator: vnmr1

 Relax. delay 1.000 sec
 Pulse 45.0 degrees
 Acq. time 2.556 sec
 Width 6410.3 Hz
 8 repetitions
OBSERVE   H1, 399.9161429 MHz
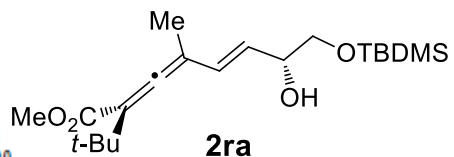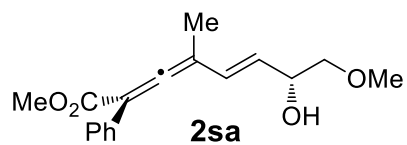DATA PROCESSING
FT size 32768
Total time 0 min 28 sec

2ob

3.51 3.64 3.64 7.16 18.38 3.26 11.39 36.18 12.85

Agilent Technologies

2ob

2oe

Agilent Technologies

2.949
1.713
1.313

7   6   5   4   3   2   1   ppm

3.41   3.49   3.21   3.47   18.00   3.06   10.84   33.07   21.46

Sample Name:
  MK-M148
Data Collected on:
  vnmrs400-vnmrs400
Archive directory:
  /home/user1/vnmrsys/data
Sample directory:
  MK-M148_20140926_01
FidFile: CARBON

Pulse Sequence: CARBON (s2pul)
Solvent: cdcl3
Data collected on: Sep 26 2014

Temp. 25.0 C / 298.1 K
Operator: user1

Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 1.311 sec
Width 25000.0 Hz
528 repetitions
OBSERVE C13, 100.5589851 MHz
DECOUPLE H1, 399.9181065 MHz
Power 46 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.5 Hz
FT size 65536
Total time 38 min

Me

i-PrO2C

t-Bu

OMe

OH

2oe

165.879
129.112
127.276
109.674
103.058
77.323
77.005
76.686
76.527
71.132
67.764
59.046
34.115
29.518
21.817
21.802
14.716

220   200   180   160   140   120   100   80   60   40   20   0   ppm

Gradient Shimming

Sample Name:
MX-2307CO
Data Collected on:
vnmrs400-vnmrs400
Archive directory:
/home/vnmr1/vnmrsys/data
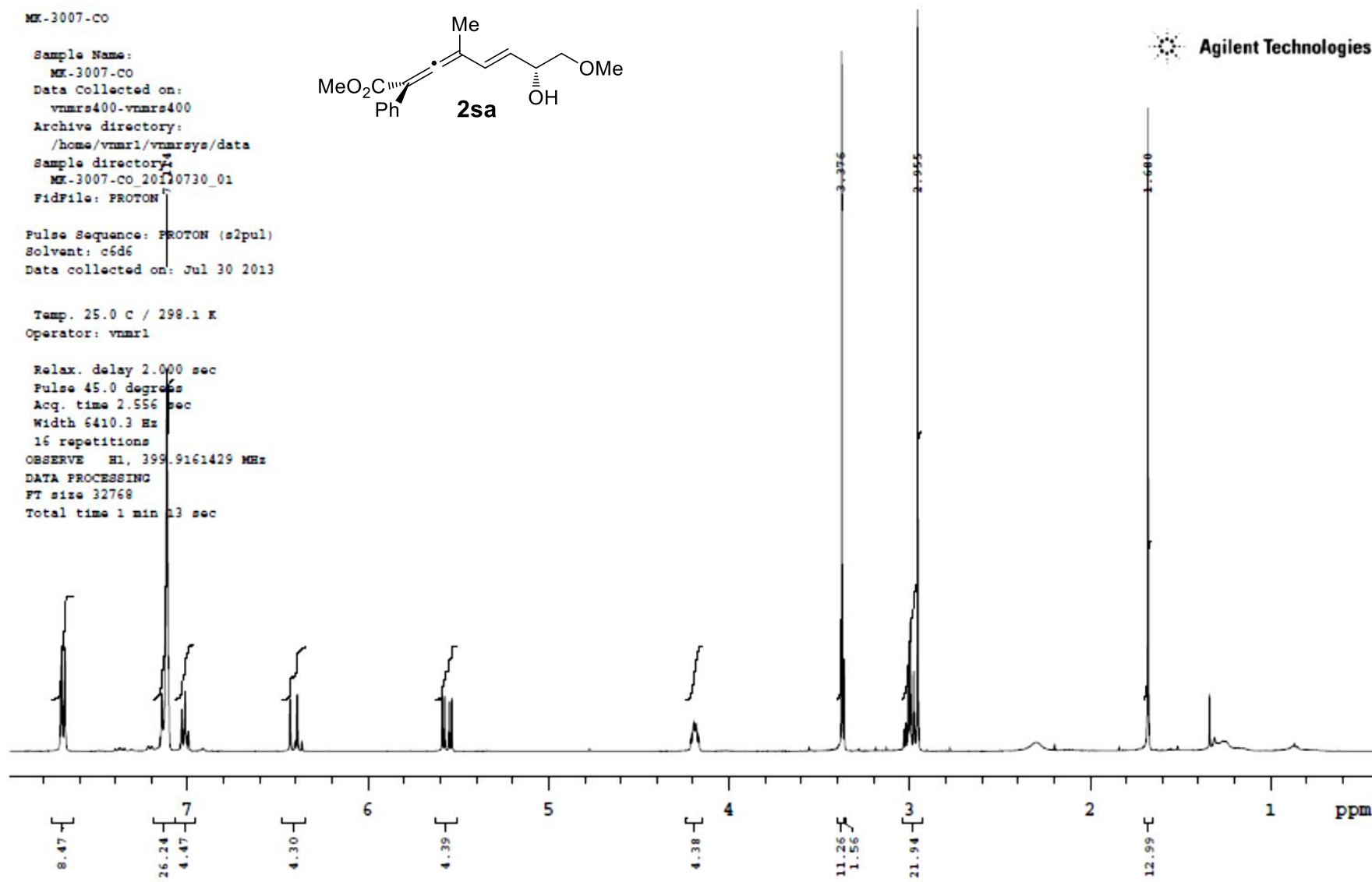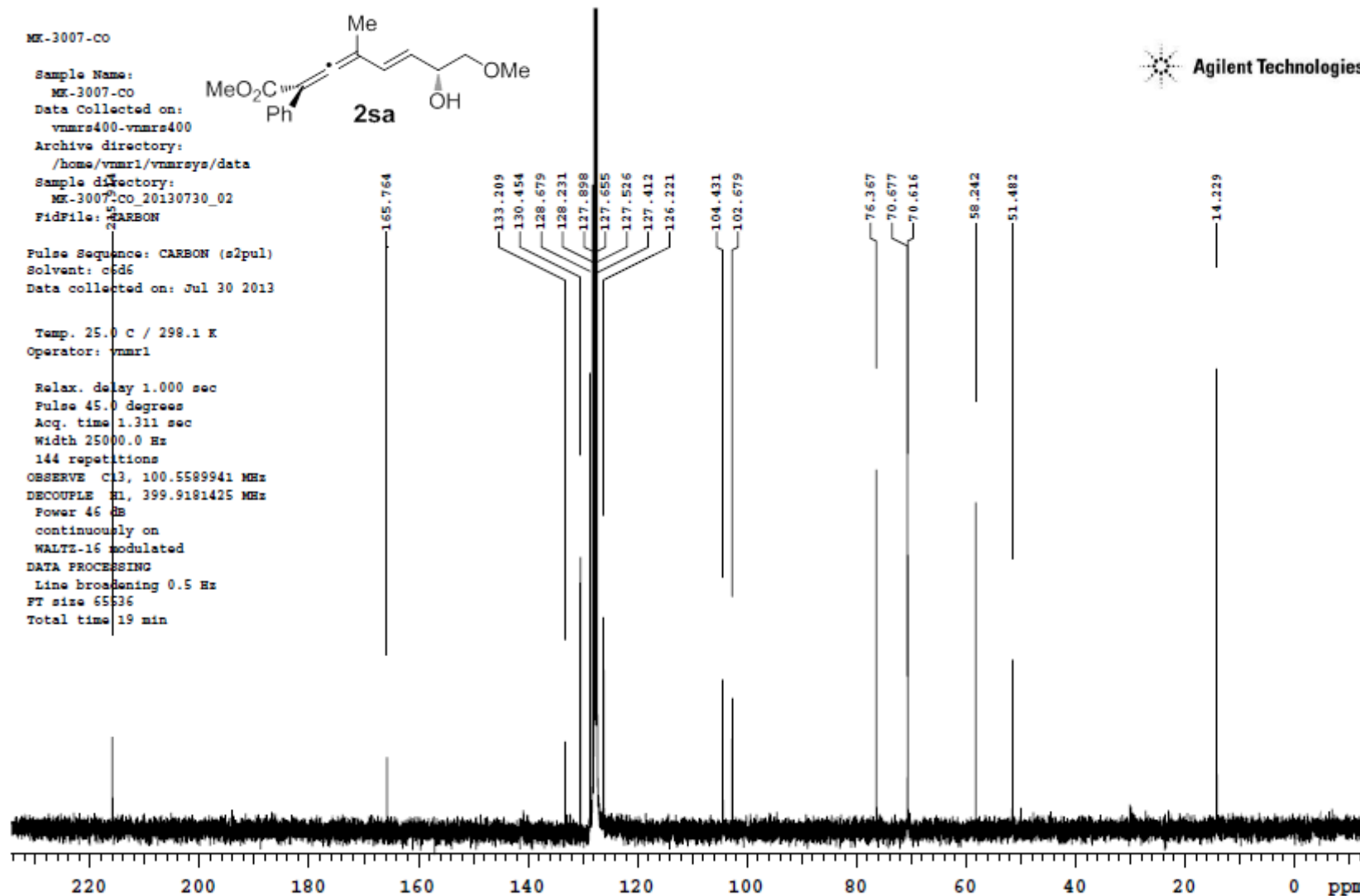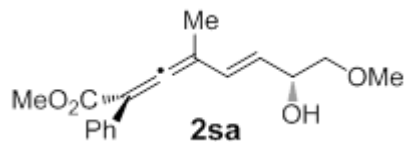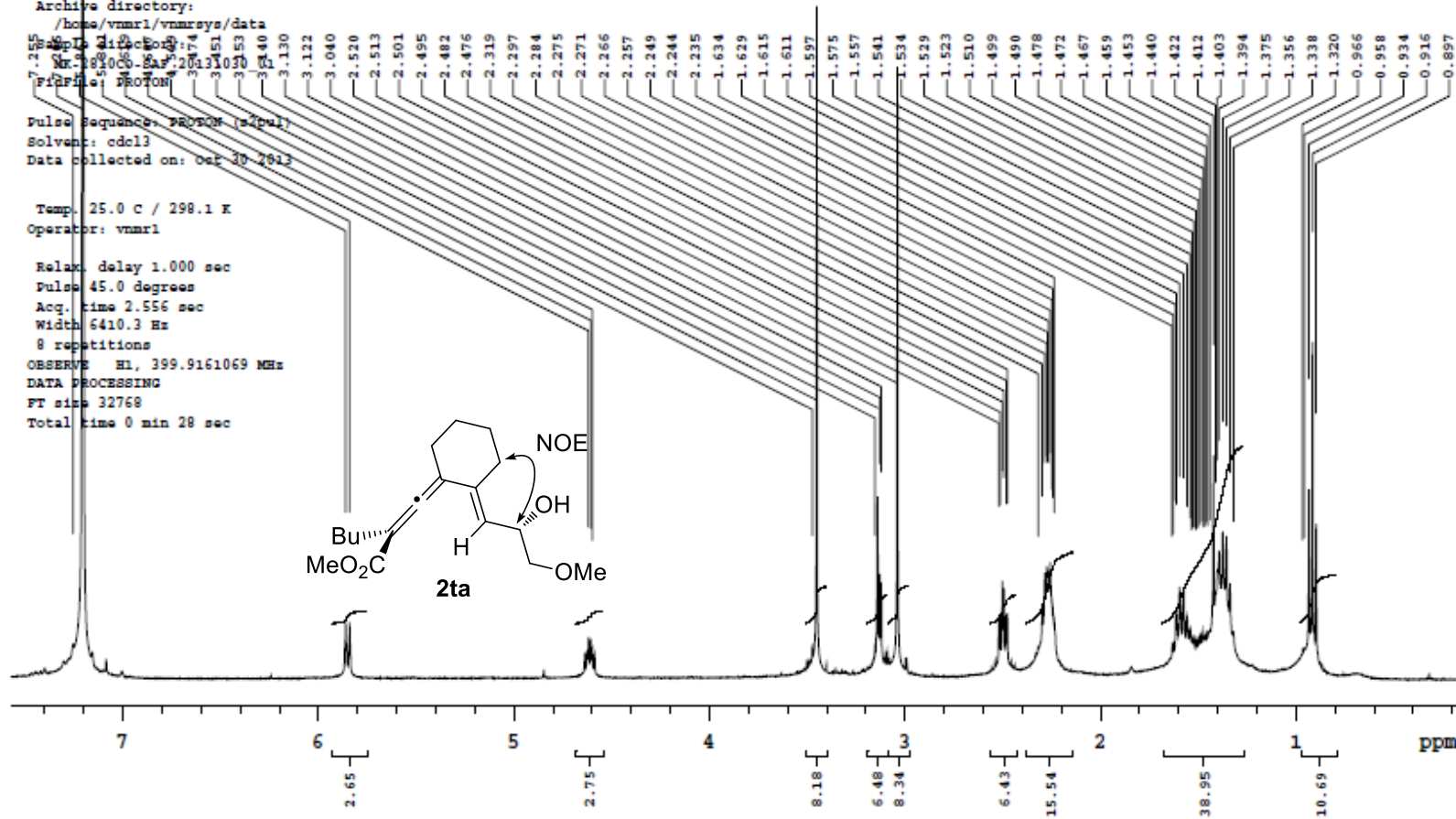Sample directory:
MX-2307CO_20130723-01
FidFile: PROTON

Pulse Sequence: PROTON (s2pul)
Solvent: c6d6
Data collected on: Jul 23 2013

Temp. 25.0 C / 298.1 K
Operator: vnmr1

Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 2.556 sec
Width 6410.3 Hz
8 repetitions
OBSERVE   H1, 399.9161429 MHz
DATA PROCESSING
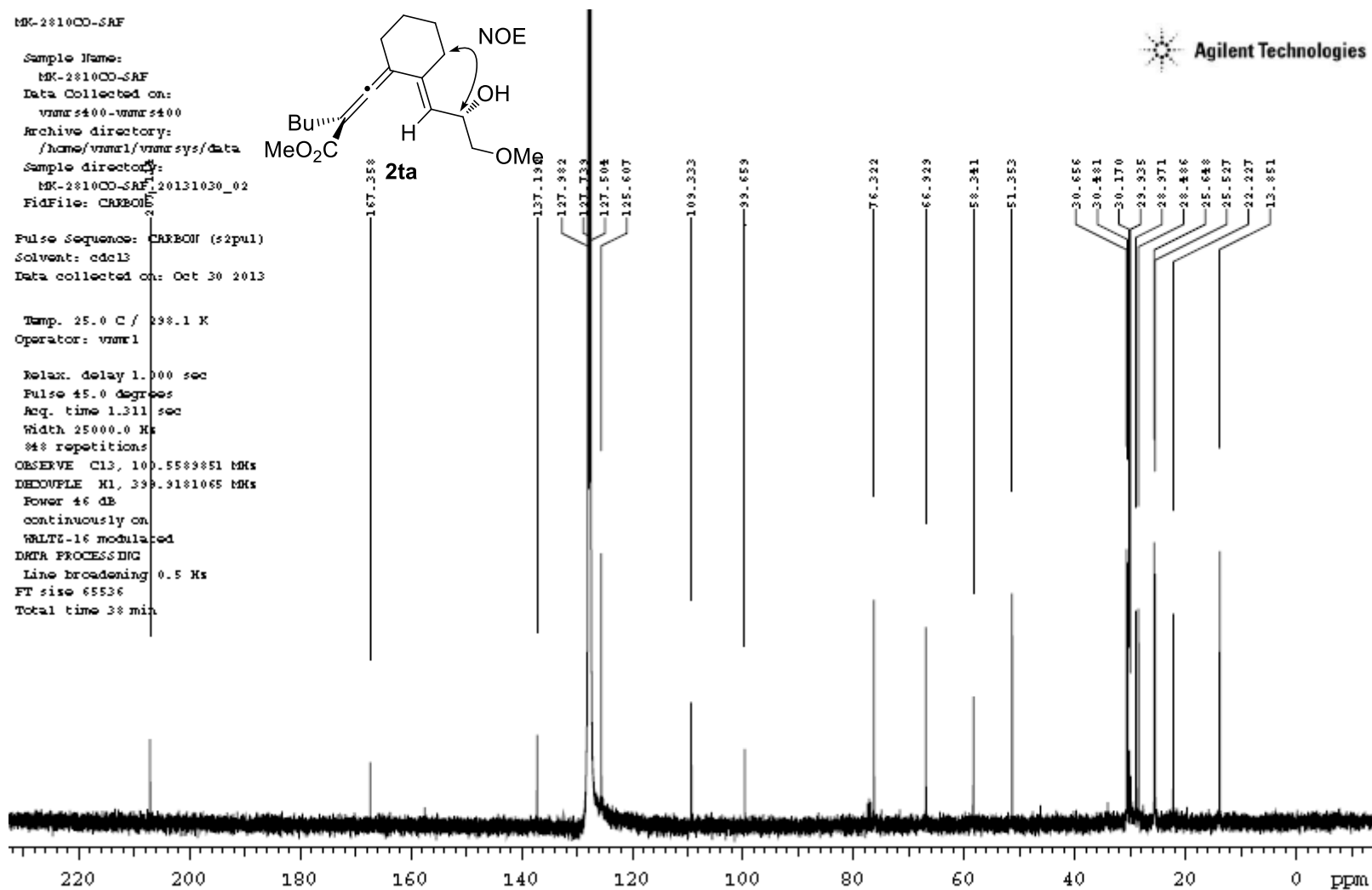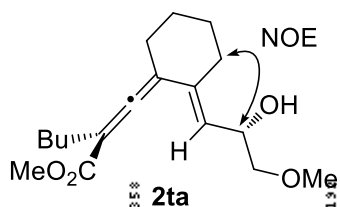FT size 32768
Total time 0 min 28 sec

Agilent Technologies

2og

Me
AllylO$_2$C
t-Bu
OH
OMe

3.73   2.03   3.64   7.70   19.61   38.68
3.52 1.79   3.67   3.89   11.73

7   6   5   4   3   2   1   ppm

MK-M2S-CDCL3

Sample Name:
  MK-M2S-CDCL3
Data Collected on:
  vnmrs400-vnmrs400
Archive directory:
  /home/user1/vnmrsys/data
Sample directory:
  MK-M2S-CDCL3_20140928_01
FidFile: CARBON_01

Pulse Sequence: CARBON (s2pul)
Solvent: cdcl3
Data collected on: Sep 28 2014

Temp. 25.0 C / 298.1 K
Operator: user1

Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 1.311 sec
Width 25000.0 Hz
1056 repetitions
OBSERVE C13, 100.5589851 MHz
DECOUPLE H1, 399.9181065 MHz
Power 46 dB
continuously on
WALTZ-16 modulated
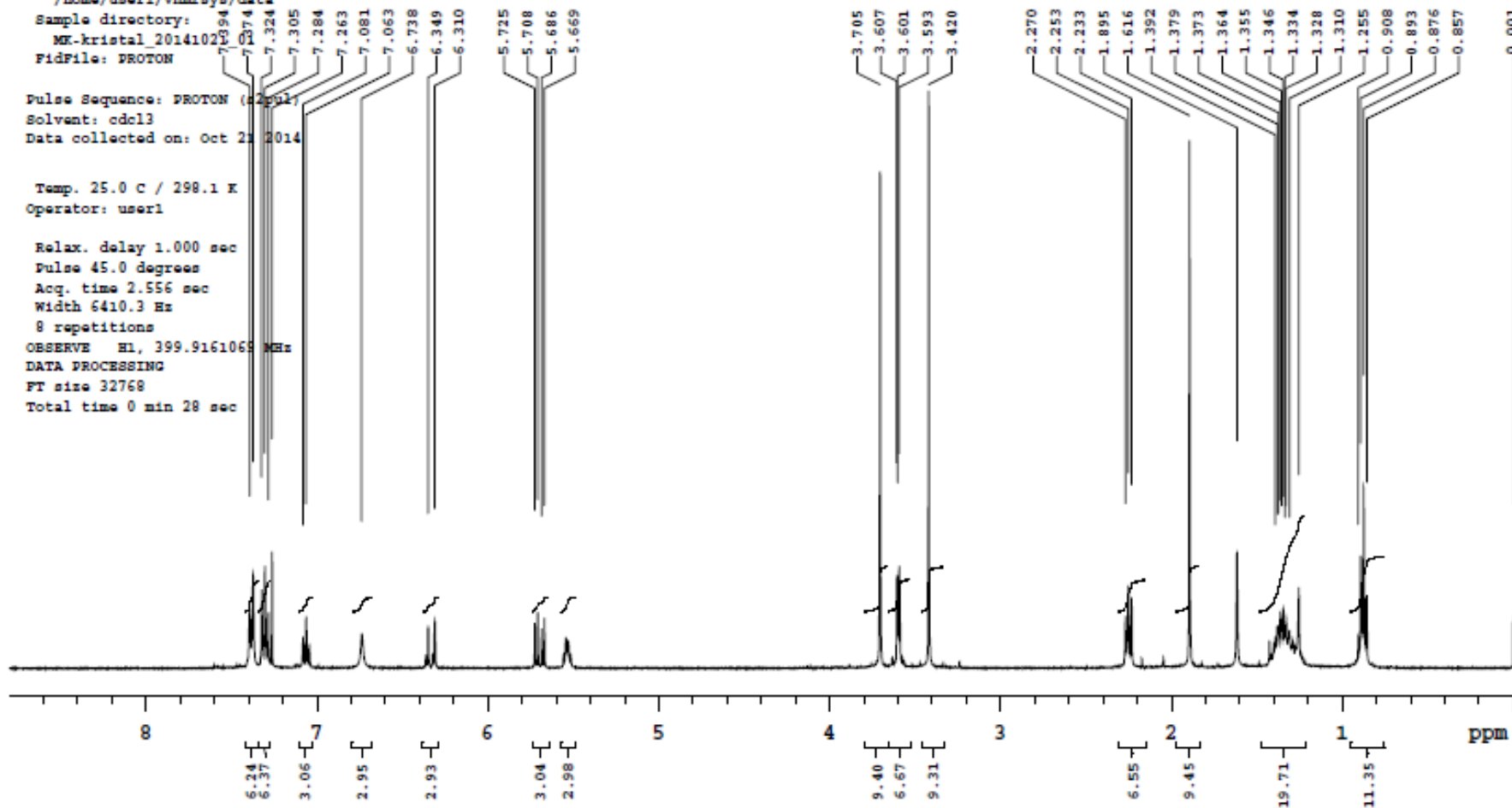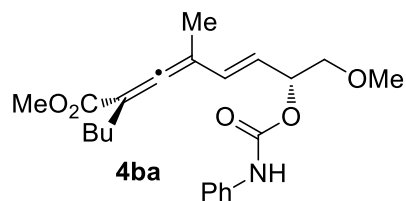DATA PROCESSING
Line broadening 0.5 Hz
FT size 65536
Total time 12 hr, 50 min

Me

AllylO₂C

t-Bu

OMe

OH

2og

165.704
132.450
128.725
127.678
117.087
108.938
103.225
77.316
77.210
77.005
76.686
76.481
71.072
64.744
59.061
34.169
29.449
14.769

220 200 180 160 140 120 100 80 60 40 20 0 ppm

Sample Name:
  MK-1907C02
Data Collected on:
  vnmrs400-vnmrs400
Archive directory:
  /home/vnmr1/vnmrsys/data
Sample directory:
  MK-1907C02_20130719_01
FidFile: PROTON

Pulse Sequence: PROTON [s2pul]
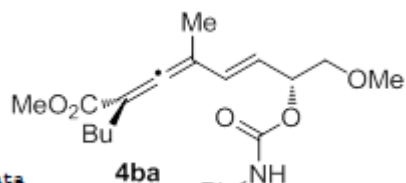Solvent: c6d6
Data collected on: Jul 19 2013

Temp. 25.0 C / 298.1 K
Operator: vnmr1

Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 2.556 sec
Width 6410.3 Hz
8 repetitions
OBSERVE   H1, 399.9161429 MHz
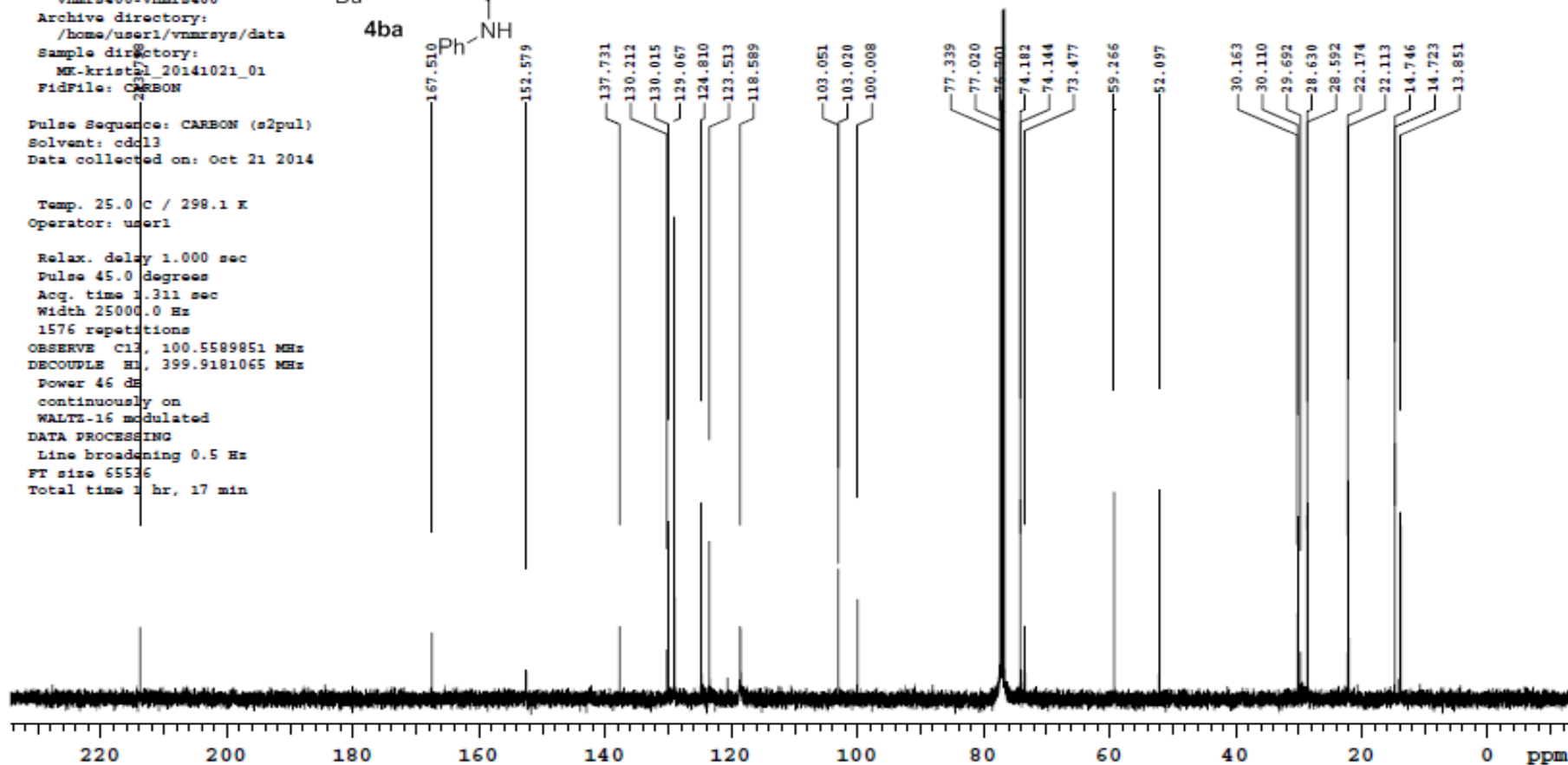DATA PROCESSING
FT size 32768
Total time 0 min 28 sec

Agilent Technologies

Sample Name:
  MK-M-3
Data Collected on:
  vnmrs400-vnmrs400
Archive directory:
  /home/user1/vnmrsys/data
Sample directory:
  MK-M-3_20140925_01
FidFile: CARBON_01

Pulse Sequence: CARBON (s2pul)
Solvent: cdcl3
Data collected on: Sep 25 2014

Temp. 25.0 C / 298.1 K
Operator: user1

 Relax. delay 1.000 sec
 Pulse 45.0 degrees
 Acq. time 1.311 sec
 Width 25000.0 Hz
 728 repetitions
OBSERVE C13, 100.5589851 MHz
DECOUPLE H1, 399.9181065 MHz
 Power 46 dB
 continuously on
 WALTZ-16 modulated
DATA PROCESSING
 Line broadening 0.5 Hz
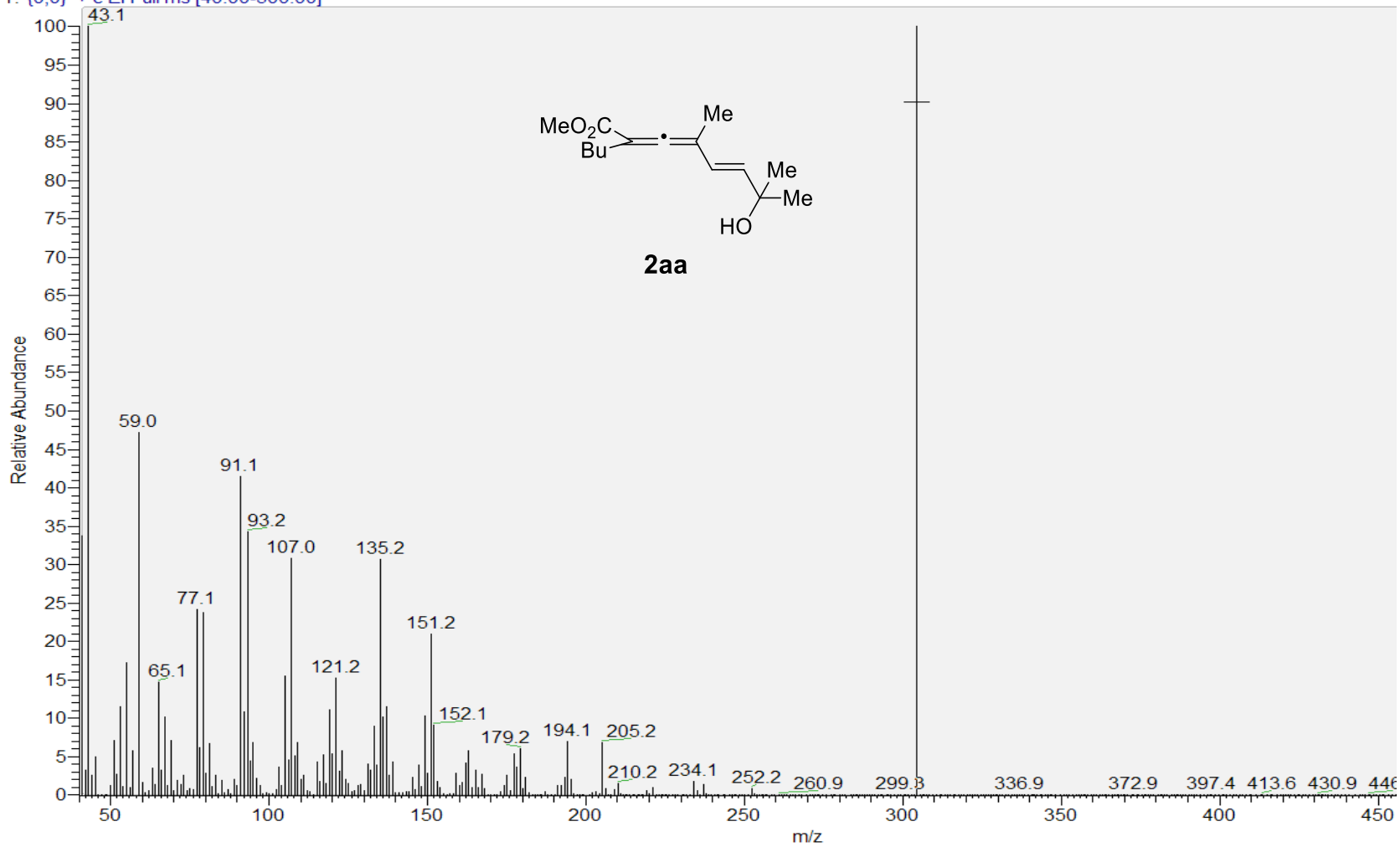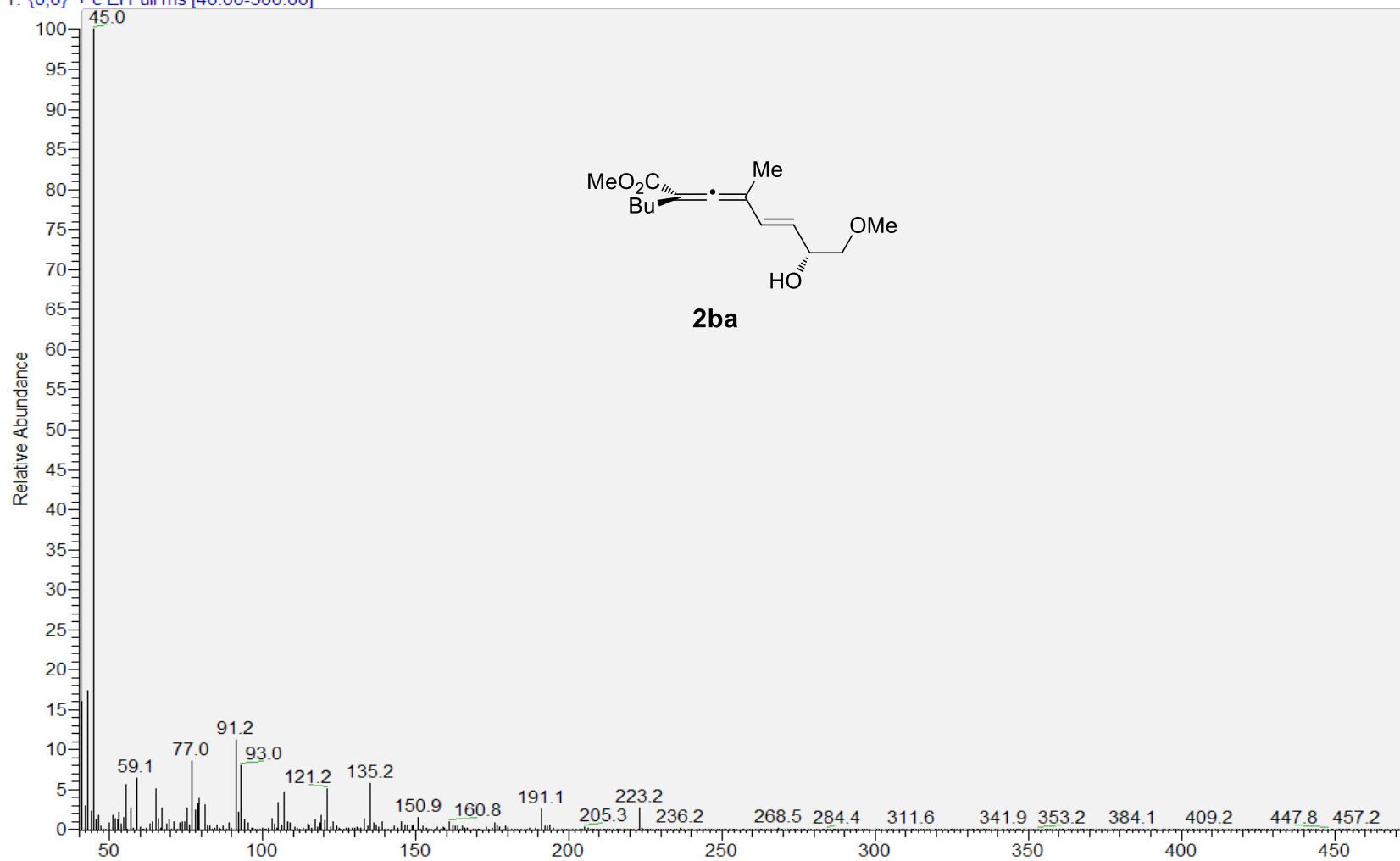FT size 65536
Total time 1 hr, 17 min

2pa

Agilent Technologies

166.546
137.769
128.756
128.505
127.891
127.815
127.671
108.771
103.142
77.339
77.020
76.701
74.038
73.408
71.216
51.611
34.161
30.322
29.692
29.442
14.829

220 200 180 160 140 120 100 80 60 40 20 0 ppm

Agilent Technologies

2qa

4.71   4.94   5.11   5.77   20.27   14.48   44.73

2qa

165.969
128.876
128.125
127.898
127.662
127.533
127.420
108.892
103.210
72.786
66.307
50.981
34.160
29.312
14.563

220 200 180 160 140 120 100 80 60 40 20 0 ppm

Sample Name:
  mk-m15
Data Collected on:
  vnmrs400-vnmrs400
Archive directory:
  /home/user1/vnmrsys/data
Sample directory:
  mk-m15_20140925_01
FidFile: CARBON_01

Pulse Sequence: CARBON (s2pul)
Solvent: cdcl3
Data collected on: Sep 25 2014

Temp. 25.0 C / 298.1 K
Operator: user1

Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 1.311 sec
Width 25000.0 Hz
1000 repetitions
OBSERVE C13, 100.5589851 MHz
DECOUPLE H1, 399.9181065 MHz
Power 46 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.5 Hz
FT size 65536
Total time 38 min

2qa

Peaks: 166.508, 129.165, 127.875, 108.916, 103.081, 77.323, 77.005, 76.686, 73.022, 66.436, 51.664, 34.191, 31.073, 29.442, 14.822

Agilent Technologies

2ra

7   6   5   4   3   2   1   0 ppm

2.27   2.44   2.41   10.50   2.74   8.26   31.80   25.43   14.14

MK-1907CO2

Sample Name:
  MK-1907CO2
Data Collected on:
  vnmrs400-vnmrs400
Archive directory:
  /home/vnmr1/vnmrsys/data
Sample directory:
  MK-1907CO2_20130719_03
FidFile: CARBON

Pulse Sequence: CARBON (s2pul)
Solvent: c6d6
Data collected on: Jul 19 2013

Temp. 25.0 C / 298.1 K
Operator: vnmr1

Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 1.311 sec
Width 25000.0 Hz
28 repetitions
OBSERVE C13, 100.5589941 MHz
DECOUPLE H1, 399.9181425 MHz
Power 46 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.5 Hz
FT size 65536
Total time 38 min

Me
MeO₂C
t-Bu
OTBDMS
OH
2ra

Agilent Technologies

165.931
138.208
128.914
128.262
127.898
127.655
127.541
127.420
108.809
103.225
74.174
72.930
70.859
50.913
34.145
29.305
14.616

220 200 180 160 140 120 100 80 60 40 20 0 ppm

Agilent Technologies

2sa

3.376
3.055
1.680

8.47
26.24
4.47
4.30
4.39
4.38
11.26
1.56
21.94
12.99

7   6   5   4   3   2   1   ppm

MK-3007-CO

Sample Name:
  MK-3007-CO
Data Collected on:
  vnmrs400-vnmrs400
Archive directory:
  /home/vnmr1/vnmrsys/data
Sample directory:
  MK-3007-CO_20130730_02
FidFile: CARBON

Pulse Sequence: CARBON (s2pul)
Solvent: c6d6
Data collected on: Jul 30 2013

Temp. 25.0 C / 298.1 K
Operator: vnmr1

Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 1.311 sec
Width 25000.0 Hz
144 repetitions
OBSERVE C13, 100.5589941 MHz
DECOUPLE H1, 399.9181425 MHz
Power 46 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.5 Hz
FT size 65536
Total time 19 min

2sa

4ba

Agilent Technologies

7.394 7.374 7.324 7.305 7.284 7.263 7.081 7.053 6.738 6.349 6.310 5.725 5.708 5.686 5.669 3.705 3.607 3.601 3.593 3.420 2.270 2.253 2.233 1.895 1.616 1.392 1.379 1.373 1.364 1.355 1.346 1.334 1.328 1.310 1.255 0.908 0.893 0.876 0.857 0.001

6.24 6.37 3.06 2.95 2.93 3.04 2.98 9.40 6.67 9.31 6.55 9.45 19.71 11.35

8 7 6 5 4 3 2 1 ppm

Agilent Technologies

4ba

Peak labels: 167.510, 152.579, 137.731, 130.212, 130.015, 129.067, 124.810, 123.513, 118.589, 103.051, 103.020, 100.008, 77.339, 77.020, 76.701, 74.182, 74.144, 73.477, 59.266, 52.097, 30.163, 30.110, 29.692, 28.630, 28.592, 22.174, 22.113, 14.746, 14.723, 13.851

APPENDIX B

MASS SPECTRUMS OF PRODUCTS

2aa

2ba

2bb

2bc
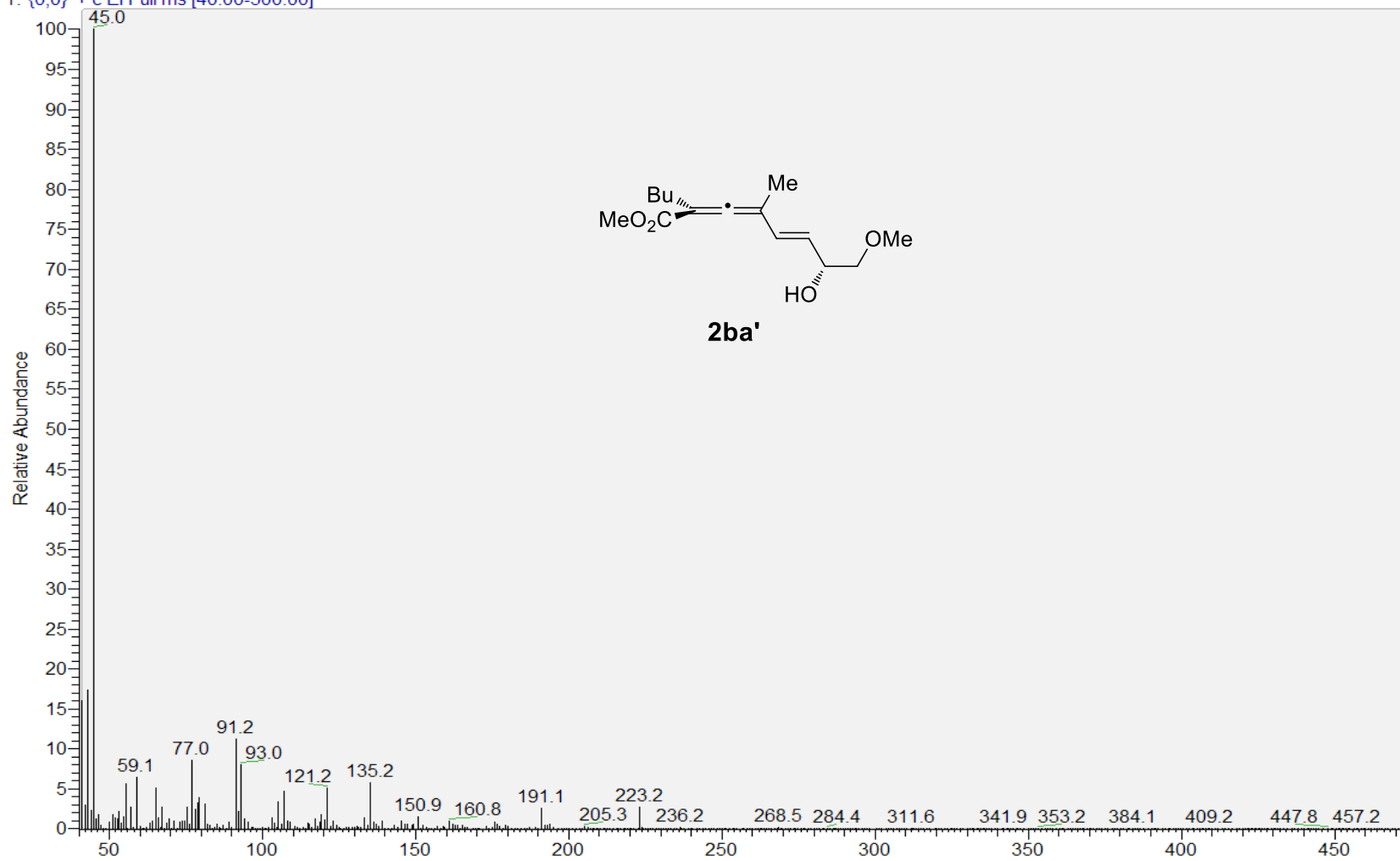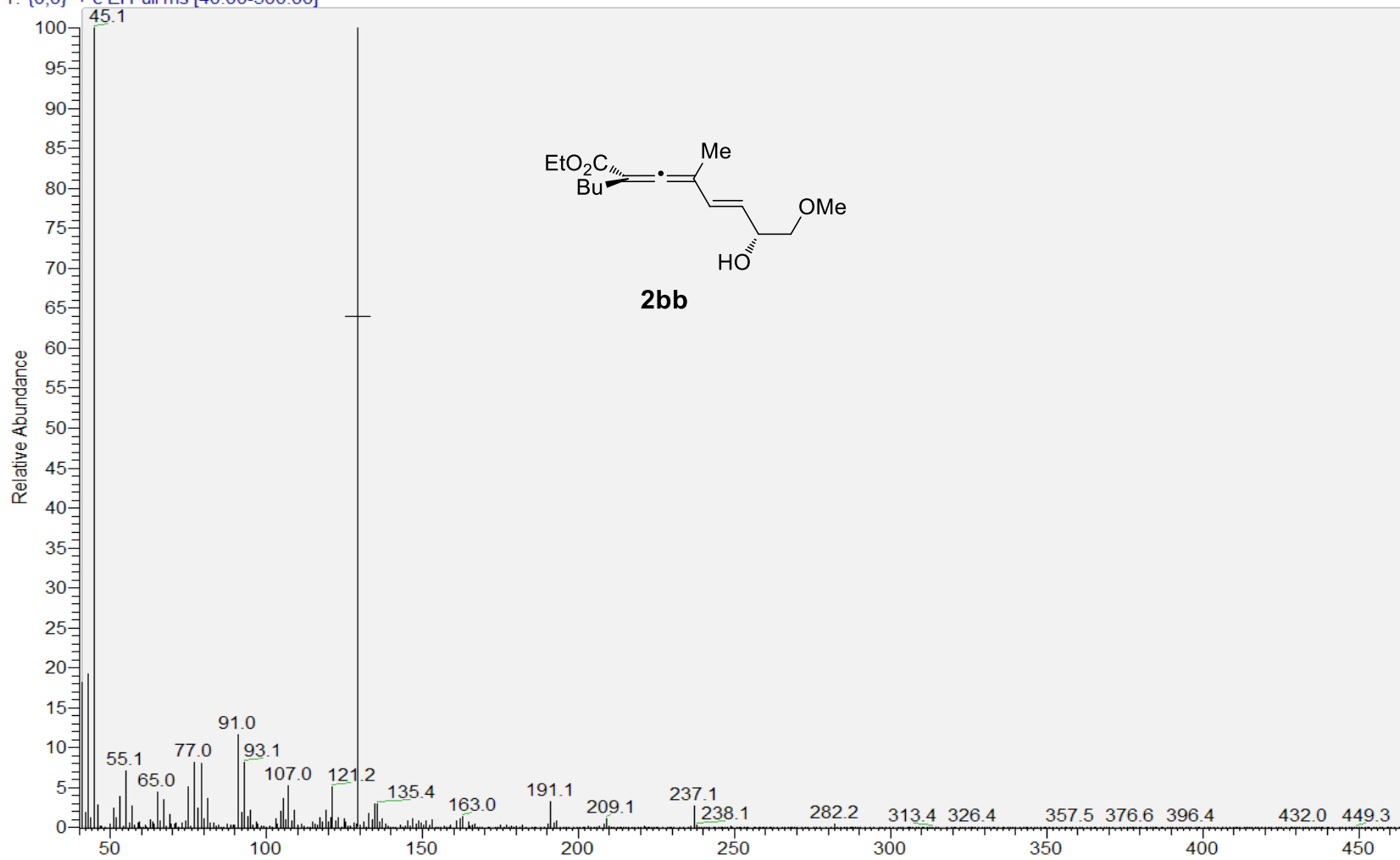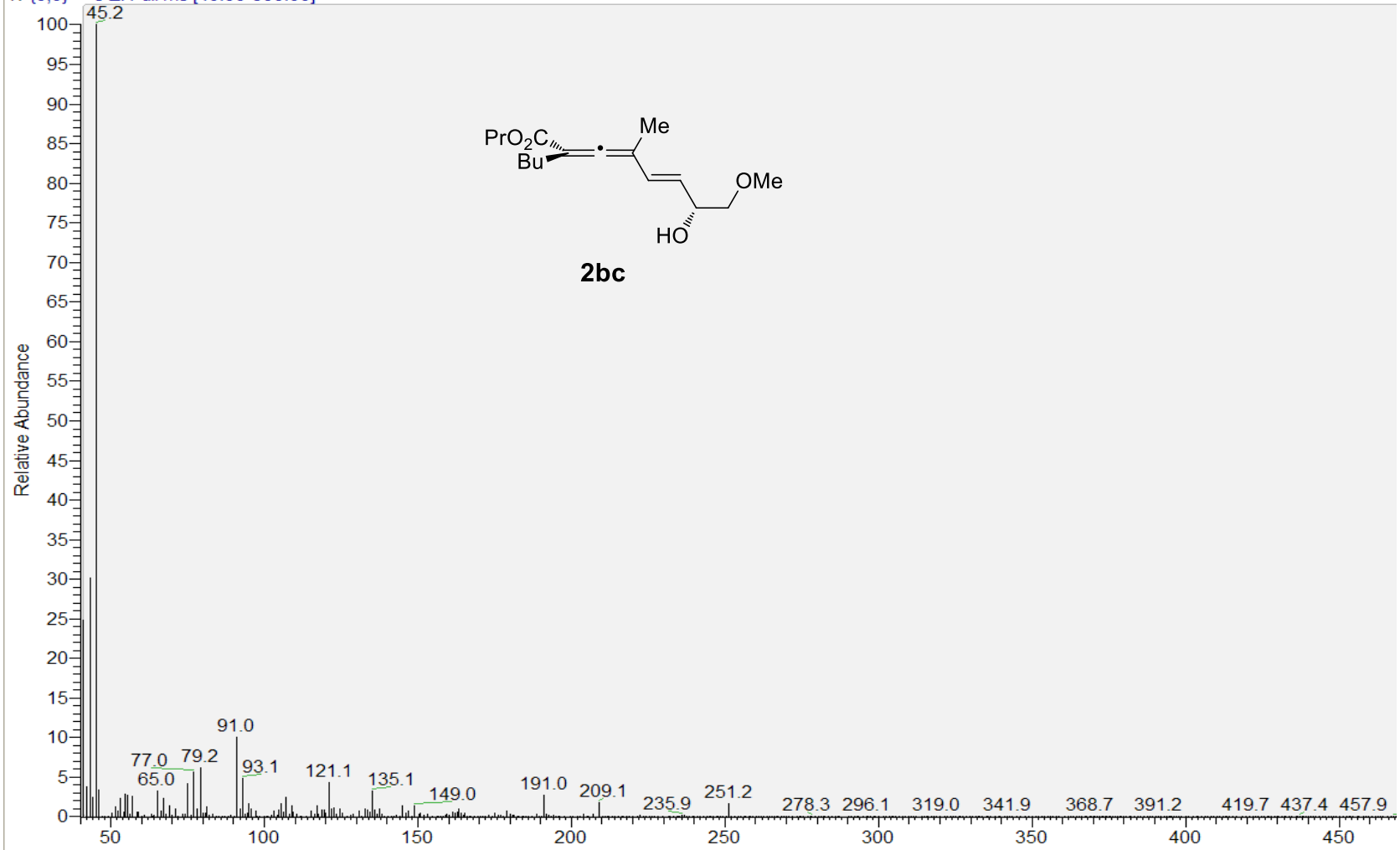
MK-M20 #4009 RT: 19.63 AV: 1 NL: 1.12E6
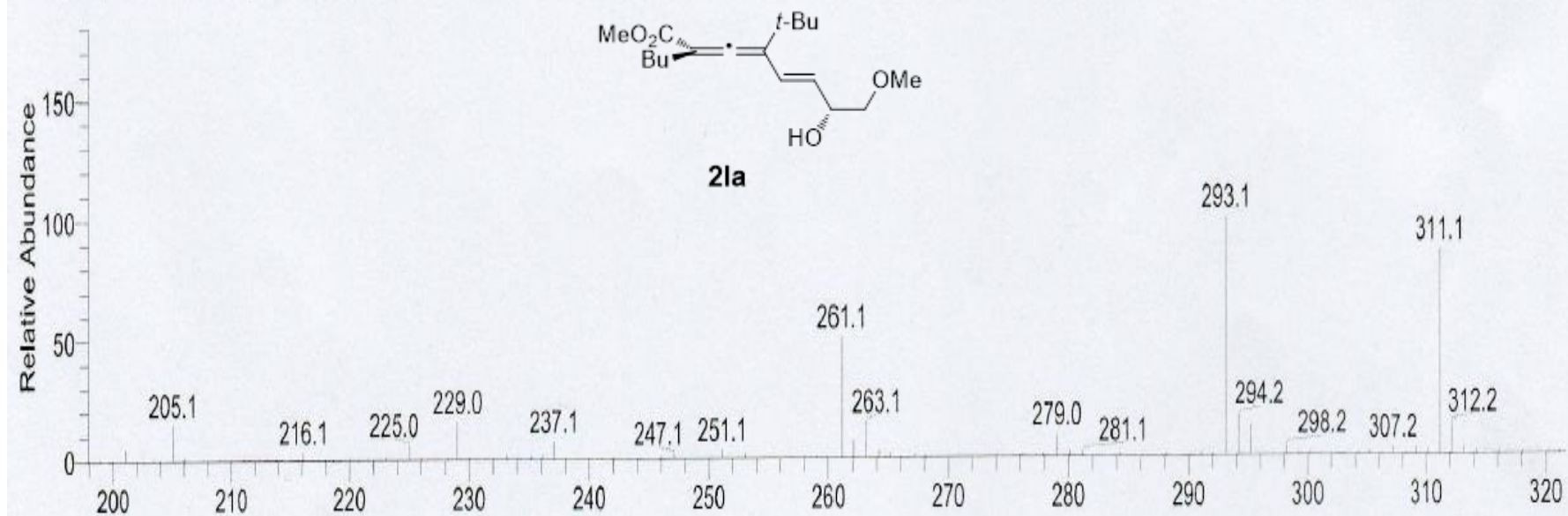T: {0,0} + c EI Full ms [40.00-500.00]

2be

2ea

2ga

2ha
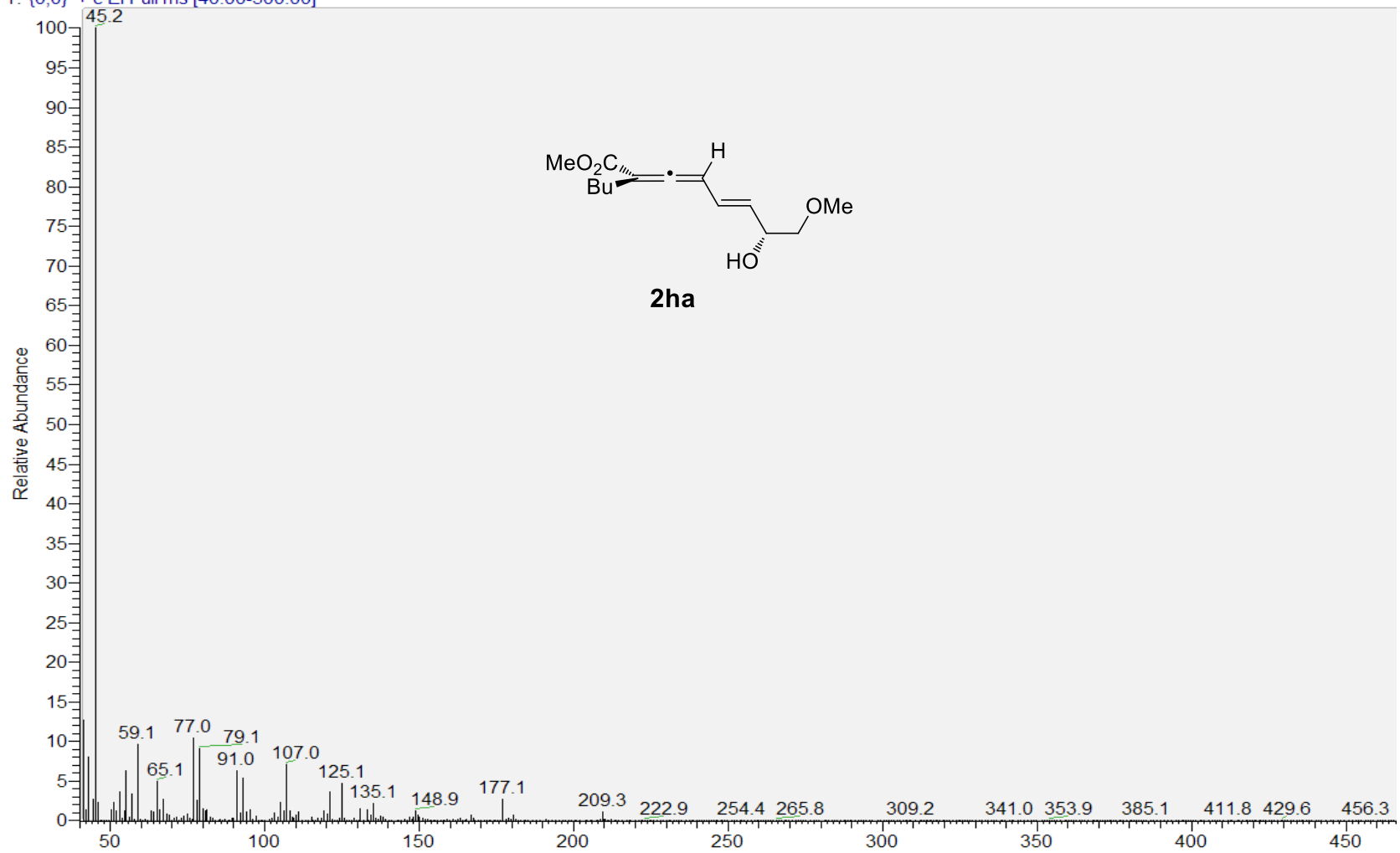
MK-M21 #4127   RT: 20.03   AV: 1   NL: 1.09E7
T: {0,0} + c EI Full ms [40.00-500.00]

2ia

2ja

2ka
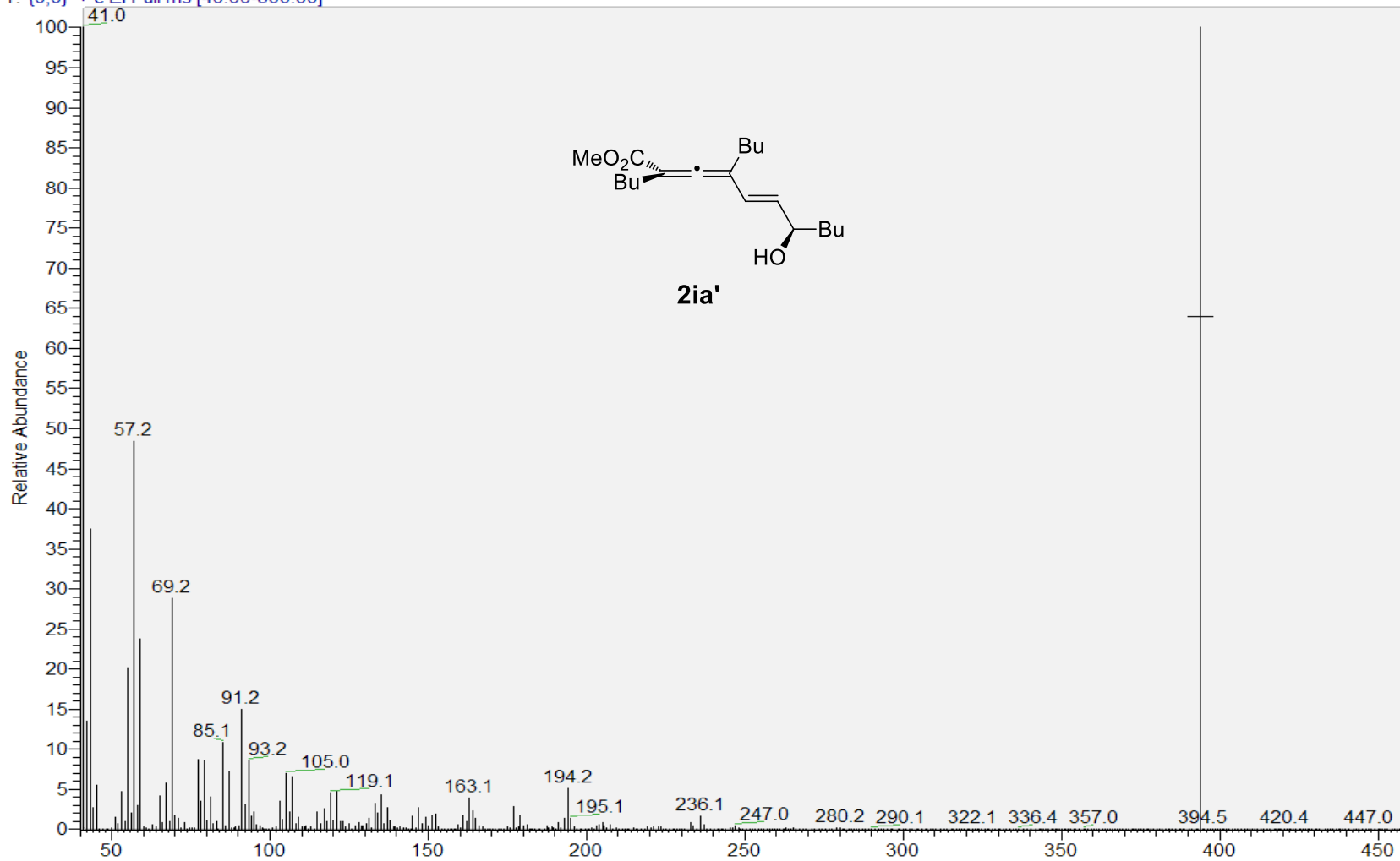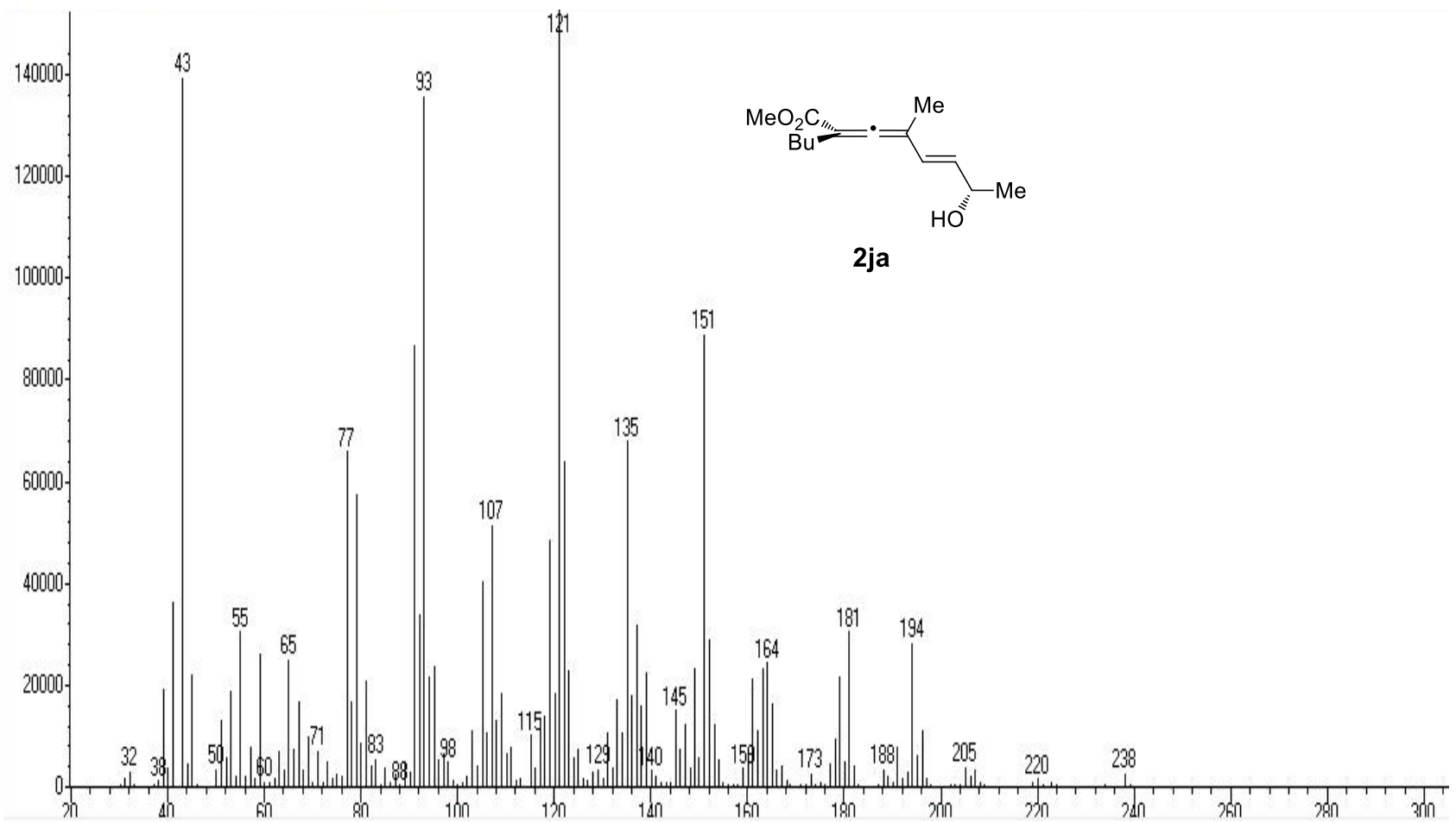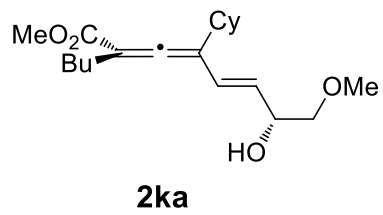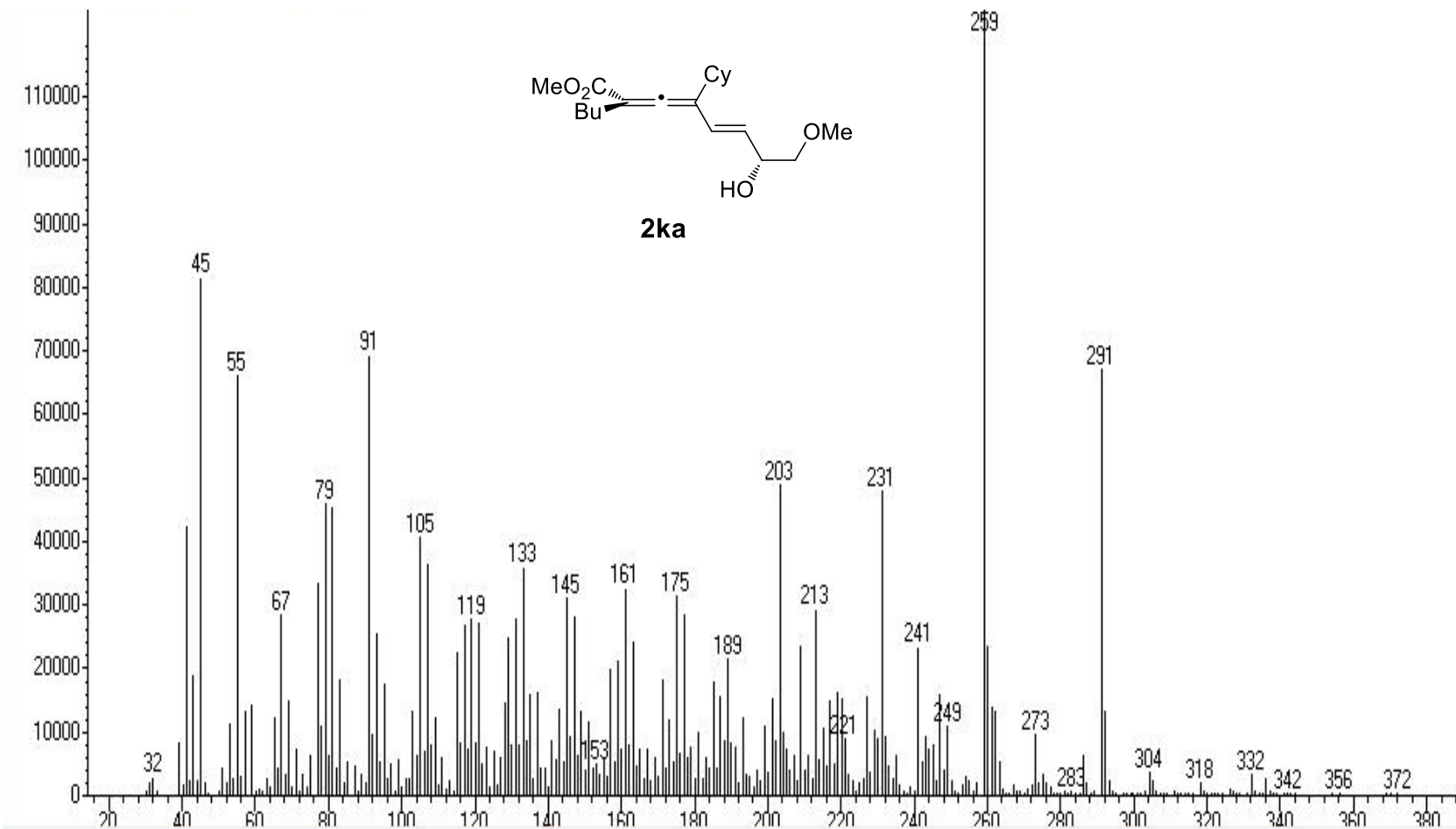
ea-m26#165-211 RT: 2.14-2.74 AV: 47 SB: 40 1.16-1.67 NL: 1.22E4
T: + c ESI [50.00-1000.00]

2ma

2na

2oa

2ob

2ra
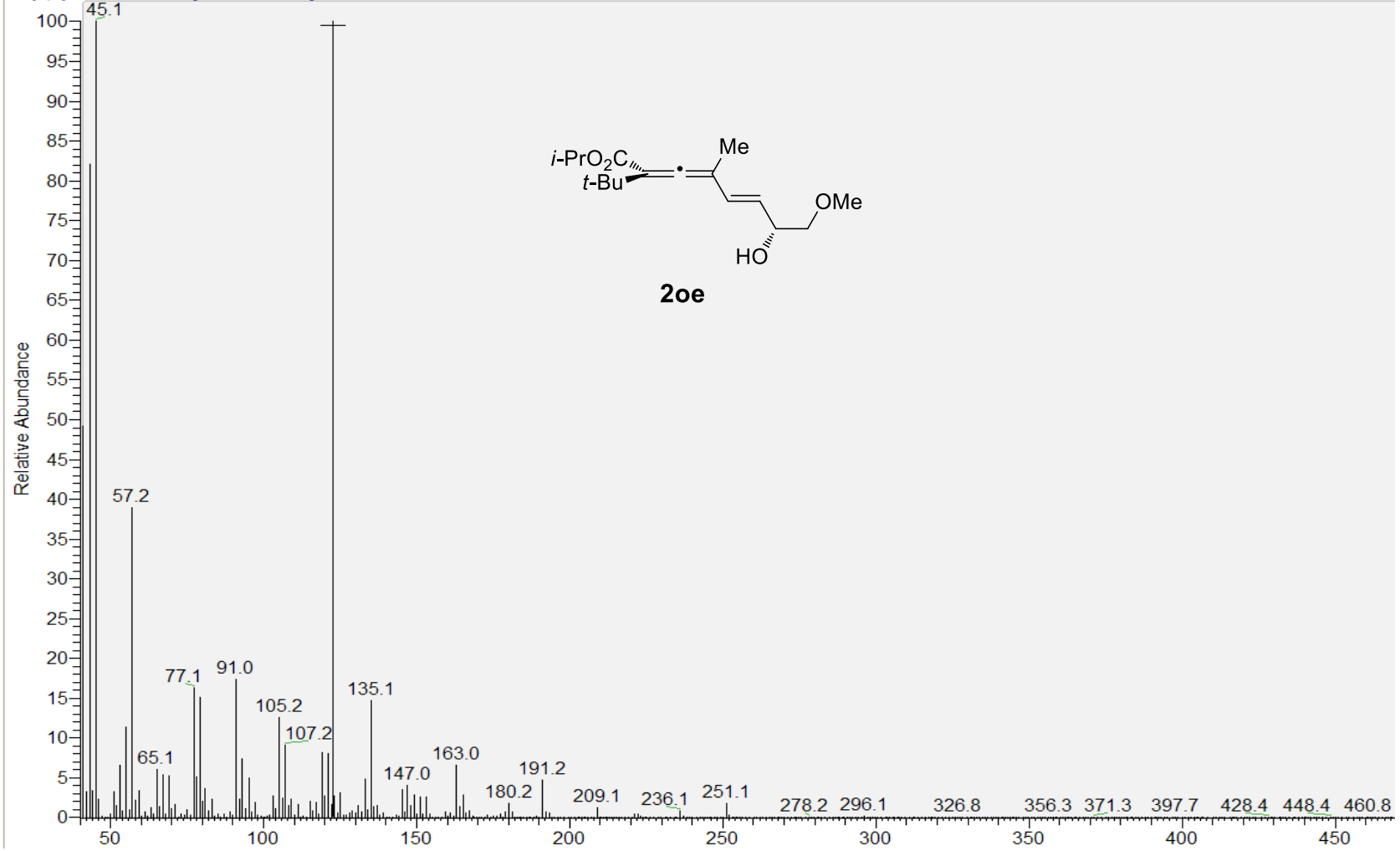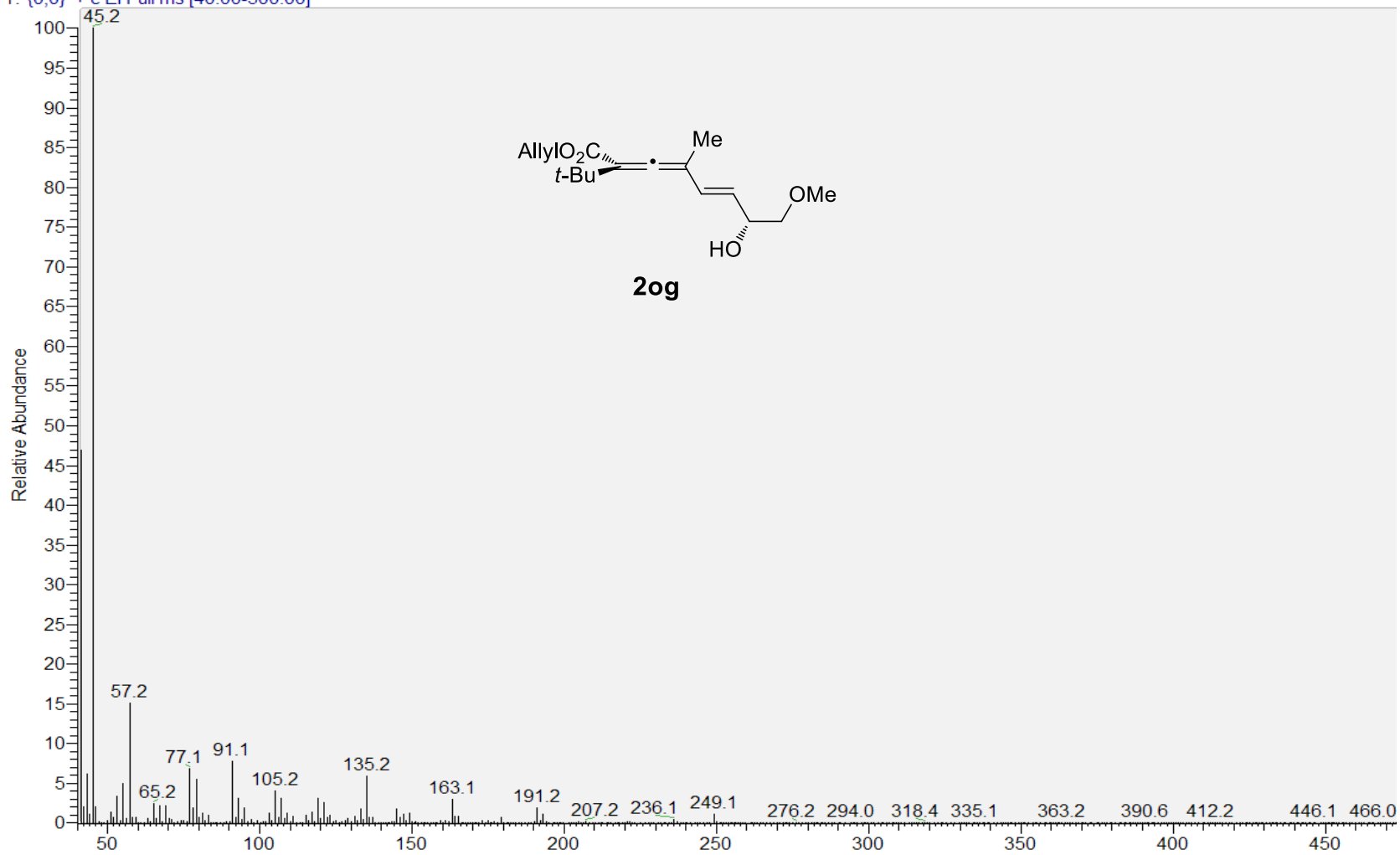
MELİH KUŞ

Place of Birth / Date: Izmir / 1984

RESEARCH

Transition metal catalyzed C-C bond forming reactions, new reaction strategies

EDUCATION

2009-2015   Doctor of Philosophy: The Graduate School of Engineering and Sciences Izmir Institute of Technology

2007-2009   Master of Science: The Graduate School of Engineering and Sciences Izmir Institute of Technology

2002-2007   Bachelor of Science: Department of Chemistry-Izmir Institute of Technology

PUBLICATIONS

- Kus, M.; Artok, L.; Aygün, M. Palladium-Catalyzed Alkoxycarbonylation of Conjugated Enyne Oxiranes: A Diastereoselective Method in Synthesis of 7-Hydroxy-2,3,5-Trionates *J. Org. Chem.*, 80, 5494-5506, 2015.

- Karagöz, E.S.; Kus, M.; Akpinar, G.E.; Artok, L. Regio- and Stereoselective Synthesis of 2,3,5-Trionates by Palladium Catalyzed Alkoxycarbonylation of Conjugated Enyne Carbonates *J. Org. Chem.*, 79, 9222-9230, 2014.

- Üçüncü, M.; Karakus, E.; Kus, M.; Akpınar, G. E.; Aksın-Artok, Ö.; Krause, N.; Karaca, S.; Elmacı, N.; Artok, L. Rhodium- and Palladium-Catalyzed 1,5-Substitution Reactions of 2-En-4-yne Acetates and Carbonates with Organoboronic Acids *J. Org. Chem.*, 76, 5959-5971, 2011.

- Ziyanak, F.; Kus, M.; Artok, L. Rhodium-Catalysed Alkoxycarbonylative Cyclisation Reactions of 1,6-Enynes *Adv. Synth. Catal.* 353, 6, 897, 2011.

- Akpınar, G. E.; Kuş, M.; Üçüncü, M.; Karakuş, E.; Artok, L. Palladium-Catalyzed Alkoxycarbonylation of (Z)-2-En-4-yn Carbonates Leading to 2,3,5-Trienoates *Org. Lett.* 13, 748, 2011.

- Artok, L.; Kus, M.; Ürer, B. N.; Türkmen, G.; Aksın-Artok, Ö. Rhodium Catalysed Chemo-and Stereoselective Arylative and Alkenylative Cyclisation Reactions of Unsymmetric Diynes Containing a Terminal Alkyne Moiety with Organoboronic Acids *Org.Biomol. Chem.* 8, 2060, 2010.

- Artok, L.; Kus, M.; Aksın-Artok, Ö.; Dege, F. N.; Özkılınç, F. Y. Rhodium Catalyzed Reaction of Internal Alkynes with Organoborons Under CO Atmosphere: A Product Tunable Reaction *Tetrahedron*, 65, 9125, 2009.

- Kus, M.; Artok-Aksin, Ö.; Ziyanak, F.; Artok, L. Synthesis of Alpha-Beta-Unsaturated Ketones by Rhodium-Catalyzed Carbonylative Arylation of Internal Alkynes with Arylboronic Acids *Synlett,* 17, 2587, 2008

CONFERENCES

- 8th Asian-European Symposium on Metal-Mediated Efficient Organic Synthesis (AES-MMEOS 2014), Izmir Institute of Technology, İzmir, Turkey, 7 -10 September 2014. (Organizing Committee)

- Chemical Physics IX Congress, Izmir Institute of Technology, İzmir, Turkey, 14 -16 October 2010. (Organizing Committee)

- EU-COST D40 (Innovative Catalysis: New Processes and Selectivities), Gazi University, Ankara, Turkey, 25-27 May 2010 .(Poster)

-Organometallic Chemistry and Cataylst, İnonü Universty, Malatya, Turkey, 16-17 May 2010 (Poster)

-XXII. National Chemistry Congress, Eastern Mediterranean Universty, Cyprus, 6-10 October 2008 (Oral Presentation)

-X. National Spectroscopy Congrees, Izmir Institute of Technology, İzmir, Turkey, 04-07 July 2007 (Organizing Commitee)