RHODIUM-CATALYSED ALKOXYCARBONYLATIVE CYCLISATION REACTIONS OF 1,6-ENYNES

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ABSTRACT

RHODIUM-CATALYSED ALKOXYCARBONYLATIVE CYCLISATION REACTIONS OF 1,6-ENYNES

Transition metal-catalyzed carbonylation reactions of unsaturated systems that contain alkynyl moiety became usually used methodology for the synthesis of biologically active α,β unsaturated carbonyl compounds (Mise et. al., 1983, Yoneda et. al., 1999, Artok et. al., 2009). One type of these reactions is the alkoxycarbonylation reaction of unsaturated systems for the C-C bond formation with transition metals in the presence of alcohol and CO (Scrivanti et. al., 1998). In literature beside alkynes enyne molecules that contain more than one unsaturated moiety could also undergo transition metal-catalyzed carbonylation reactions (Rivero et. al., 2003, Shibata, 2006). Pauson-Khand reactions are well known and used reactions in literature for enyne molecules These type of reactions are transition metal-catalyzed carbonylative cyclization reactions of enyne molecules. However in literature there is no such an example for the alkoxycarbonylative reactions of 1,6-enynes.

In this study rhodium-catalyzed alkoxycarbonylative cyclization reactions of 1,6 enyne molecules in the presence of alcohol and CO was performed.

ÖZET

1,6-ENİNLERİN RODYUM KATALİZLİ ALKOKSİKARBONİLATİF HALKALAŞMA TEPKİMELERİ

Alkinil gruplu doymamış bileşiklerin geçiş metal katalizli karbonilasyon tepkimeleri biyolojik açıdan önemli α,β doymamış karbonil bileşiklerinin sentezinde sıklıkla kulanılan bir metot haline gelmiştir (Mise et. al., 1983, Yoneda et. al., 1999, Artok et. al., 2009). Bu bağlamda gerçekleştirilen tepkimelerin bir koluda doymamış sistemlerin geçiş metal katalizli alkol ve CO varlığında C-C bağ oluşumu ile α,β doymamış ester eldesiyle sonuçlanan alkoksikarbonilasyon tepkimeleridir (Scrivanti et. al., 1998). Literatürde alkinlerin yanısıra çoklu doymamış gruplar içeren enin yapılarınında geçiş metal katalizli karbonilasyon tepkimeleri mevcuttur (Rivero et. al., 2003, Shibata, 2006) Birden çok doymamış grup içeren sistemler için Pauson-Khand tipi reaksiyonlar literatürde çok karşılan tip reaksiyonlardır. Bu tip reaksiyonlar geçiş metal katalizörü varlığında karbonilatif halkalaşma reaksiyonlarıdır. Fakat literatürden elde ettiğimiz bilgilere göre 1,6-enin bileşiklerinin alkoksikarbonilatif tipi reaksiyonlarına rastlanmamıştır.

Bu çalışmada 1,6-enin molekülleri CO ve alkol ile rodyum katalizörü varlığında halkalaştırmalı alkoksikarbonilasyon ürünlerine dönüştürülmektedir. Alkoksikarbonilasyon tepkimesinin enin türevlerinde ilk defa uygulanması açısından bu çalışma önem taşımaktadır.

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CHAPTER 1

INTRODUCTION

In last decades transition metal-catalyzed carbonylation reactions, involving the use of carbon monoxide as reactant, became popular for building carbonyl content molecules. The first reaction was performed by Roelen in 1939 as cobalt-catalyzed alkene hydroformylation. which is also considered as the milestone of homogenous catalysis.

Transition metal-catalyzed carbonylation reactions of alkynes are important for the formation of α,β unsaturated carbonyl compounds that are highly biological active molecules (Mise et. al., 1983, Yoneda et. al., 1999, Artok et. al.,2009). Alkoxycarbonylation reactions of alkynes are commonly used branch of these type of reactions that concluded with formation of α,β unsaturated esters (Scrivanti et. al., 1998)

Beside alkynes unsaturated systems that contain both alkynyl and olefinic moiety can undergo transition metal-catalyzed carbonylation reactions. Pauson-Khand type reactions are commonly used reactions for the synthesis of cyclopentanone derivatives by the way of both inter- and intramolecular carbonylative cyclization reaction (Shibata et. al., 2006).

Unsaturated systems (enynes, diynes, etc.) molecules can undergo not onyl Pauson-Khand type reactions but also noncarbonylative cyclization reactions. In the presence of transition metals and a nucleophile, enynes could be cyclized mostly in one pot (Shintani et. al., 2005)

CHAPTER 2

LITERATURE WORKS

2.1.Transition Metal-Catalyzed Carbonylation Reactions of Alkynes

Carbonylation of alkynes in the presence of homogeneous metal catalysts has synthetic and industrial importance due to possibility of obtaining α,β-unsaturated carboxylic acid derivatives in one step. Type of carboxylic acid derivative changes in accordance with nucleophilic partner of carbon monoxide (Figure 2.1).

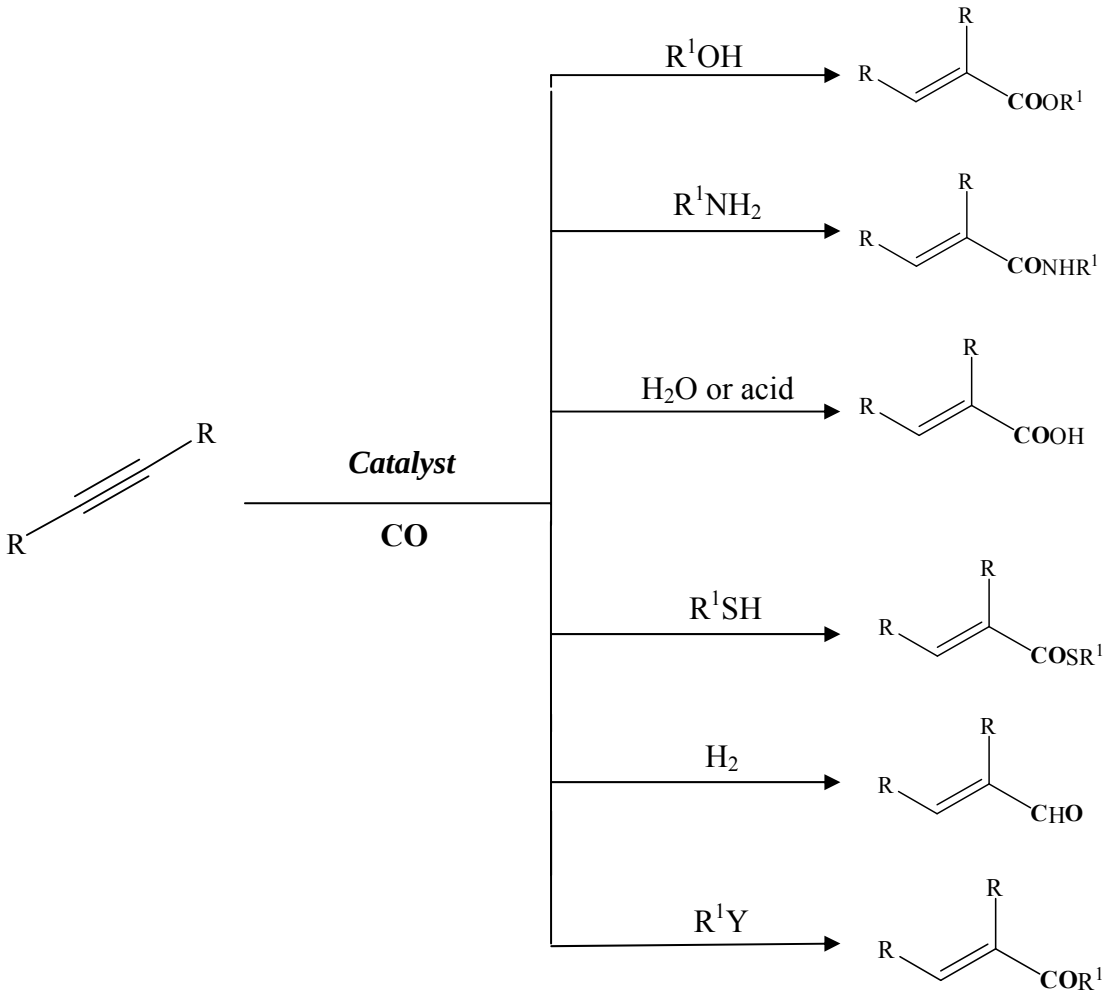


Figure 2.1.Carbonylation products of alkynes depending on the nucleophilic partner

2.1.1.Aminocarbonylation of Alkynes

Chung and co-workers have reported that Cobalt-Rhodium heterobimetallic nanoparticle-catalyzed synthesis of α,β-unsaturated amides from internal alkynes (Figure 2.2).They found that Co_2Rh_2 was quite effective for the aminocarbonylation reaction of internal alkynes.

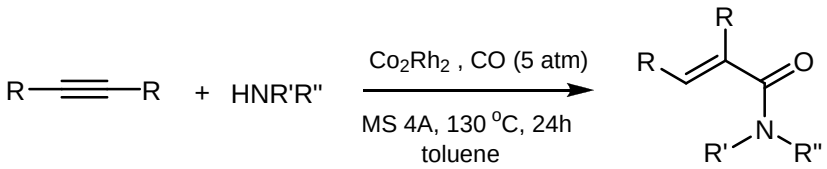


Figure 2.2. Cobalt-Rhodium heterobimetallic nanoparticle-catalyzed synthesis of α,β-unsaturated amides

Maleimide derivatives could also be synthesized by the aminocarbonylation process. Chatani and co workers showed that in the presence of $Rh_4(CO)_{12}$ / $P(OEt)_3$ reaction of alkynes with CO and pyridine-2-ylmethylamine resulted in formation of maleimide derivatives (Figure 2.3).

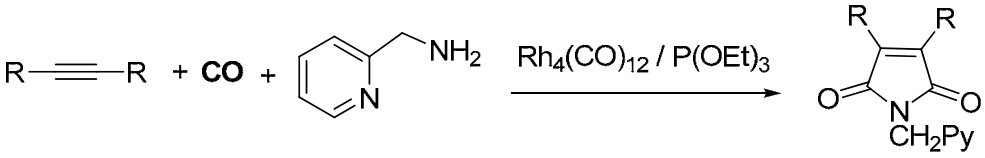


Figure 2.3.Synthesis of maleimides by the Rh-catalyzed carbonylation of alkynes with pyridin-2-ylmethylamine

When benzylamine was used instead of pyridin-2-ylmethylamine, they observed α,β-unsaturated amide and succinamide in moderate yields.This result showed that coordination of pyridine nitrogen in pyridin-2-ylmethylamine to rhodium is required to proceed the reaction (Figure 2.4)

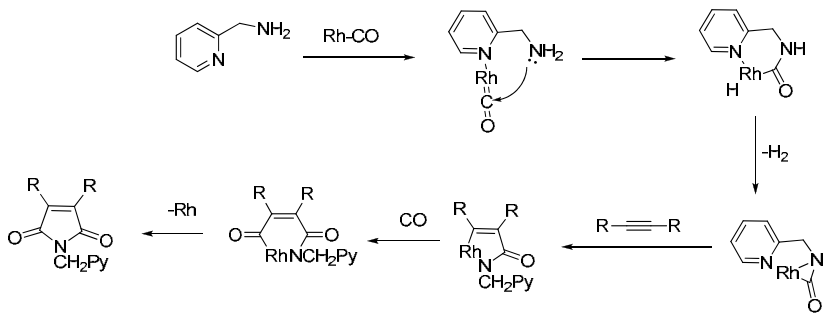


Figure 2.4.Proposed reaction mechanism of synthesis of maleimide

2.1.2.Hydroxycarbonylation of Alkynes

Acrylic acids could be easily combined with monomers to form homo- and copolymers that are used in the manufacture of various plastics, adhesives, coatings etc. For this reason, the synthesis of acrylic acid derivatives is important. Hydrocarboxylation of alkynes with CO and an acid promoter is a valuable option to synthesize acrylic acids. In 1993 Zargarian and Alper reported that palladium(0) catalyzed hydrocarboxylation of alkynes with formic acid in high yields and proceeded with excellent regioselectivity with terminal alkynes and moderate level of regioselectivity with internal alkynes (Figure 2.5)

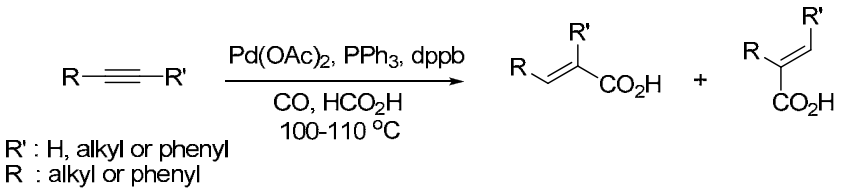


Figure 2.5.Palladium-catalyzed hydroxycarbonylation of alkynes

On the basis of literature precedents and deuterium labeled studies a reaction mechanism has been proposed for the $Pd(OAc)_2$-catalyzed hydroxycarbonylation of alkynes with formic acids (Figure 2.6). The first step is the reduction of Pd(II) to Pd(0) in CO atmosphere with phosphine ligand (Step A) and then coordination to the alkyne (Step B). Pd(0) species are electron rich and are known to form Pd-H bond in the presence of strong acids (Step C). 1,2-Addition of Pd-H to triple bond (Step D) following insertion of CO to the Pd-C bond (Step E) and nucleophilic substitution of palladium leads to formation of products (Step F).

2.1.3.Thiocarbonylation of Alkynes

In 1997 Ogawa and co-workers performed highly regioselective hydrothiocarboxylation of terminal alkynes over $Pt(PPh_3)_4$ catalyst precursor (Figure 2.7). As previous studies the $RhH(CO)(PPh_3)_3$ catalyzed thioformylation of terminal alkynes with PhSH and CO shows excellent level of regioselectivity according to the position of PhSH and CO group.(Ogawa et.al., 1995). When Pt was used instead of Rh as transition metal catalyst changes chemo- and regioselectivity (Figure 2.7). The

proposed reaction pathway starts with formation of *trans*-PtH(SPh)$(PPh_3)_2$ and then insertion of CO to Pt-S bond followed by regioselective acylplatination of acetylene and reductive elimination of the product.

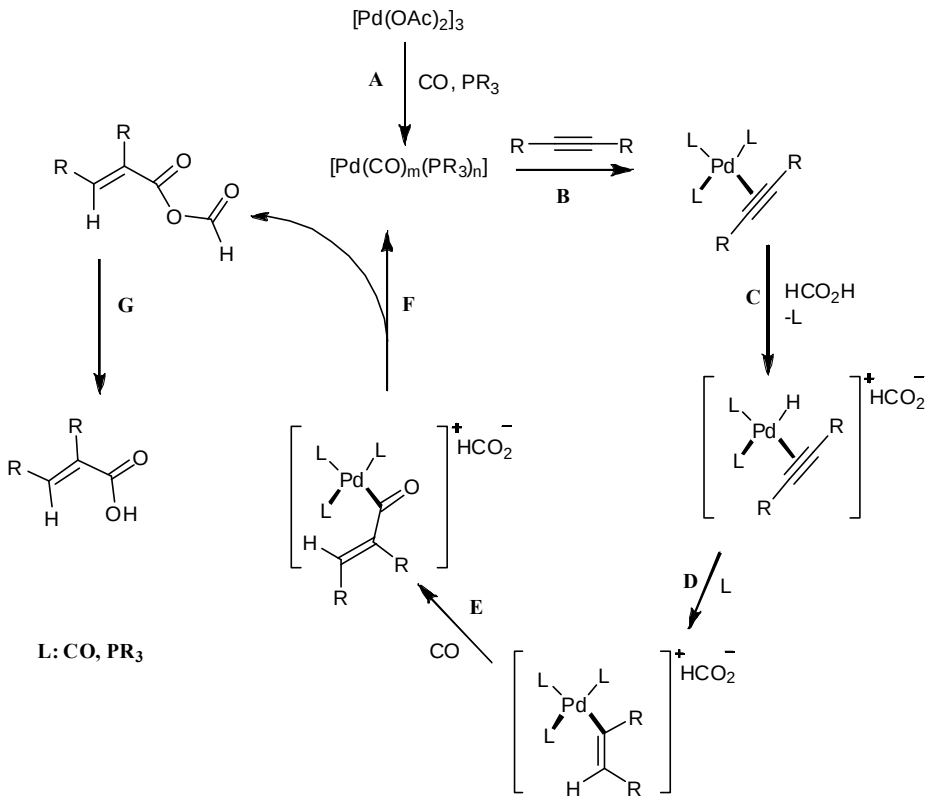


Figure 2.6.Mechanism of $Pd(OAc)_2$-catalyzed hydroxycarbonylation of alkynes

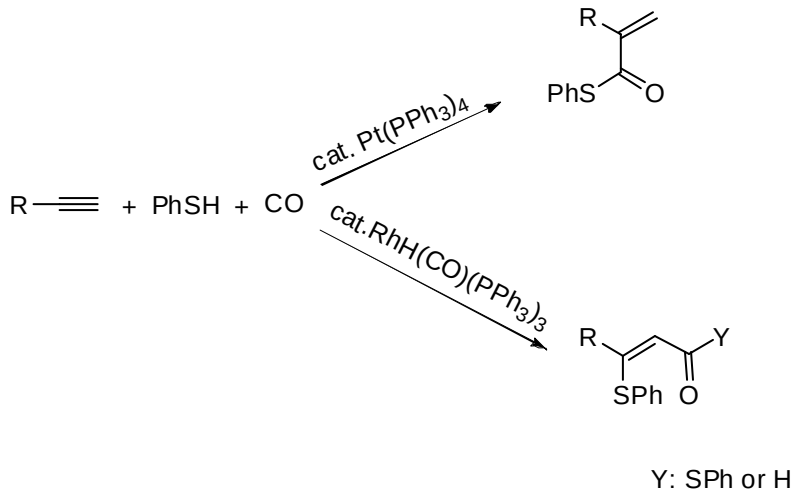


Figure 2.7.Difference between Pt and Rh catalyzed thiocarboxylation of acetylenes

2.1.4.Hydroformylation of Alkynes

Buchwald and co-workers performed hydroformylation of internal alkynes by rhodium-catalyzed to α,β-unsaturated aldehydes (Figure 2.8). Their studies revealed that not only desired product but also the hydrogenation product of alkyne and a saturated aldehyde were obtained, because of H_2.

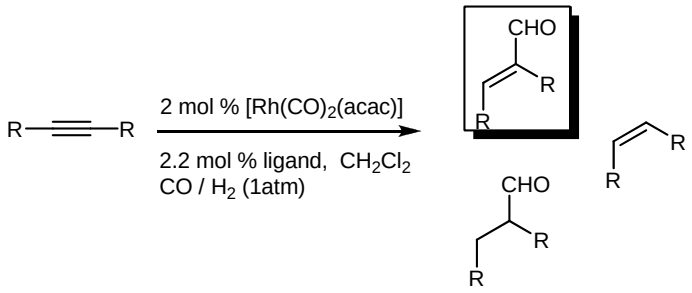


Figure 2.8.Rhodium-catalyzed hydroformylation of alkynes

However using a phosphine ligand (Figure 2.9) and reducing the pressure of gas combination (CO/H_2) to 1 atm provides selectivity for the formation of α,β-unsaturated aldehyde with high yields.

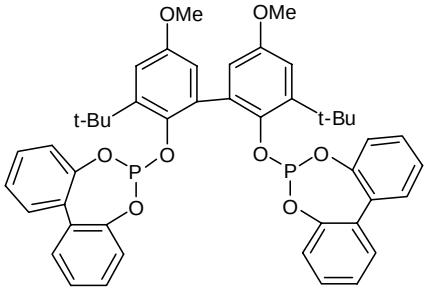


Figure 2.9.Phosphine ligand

2.1.5.Organoborons in Carbonylation of Alkynes

Beside the protic nucleophiles and H_2 organoboron reagents can also act as nucleophilic partner of CO in carbonylation reaction of alkynes to obtain α,β-unsaturated ketones and double carbonylated cyclic products (furanone derivatives). Artok and co-workers performed a product tunable raction that rhodium-catalyzed

carbonylative arylation of internl alkynes to synthesize mainly α,β-unsaturated ketones, 5-aryl-2(5H)-furanones and inda(e)nones (Figure 2.10).

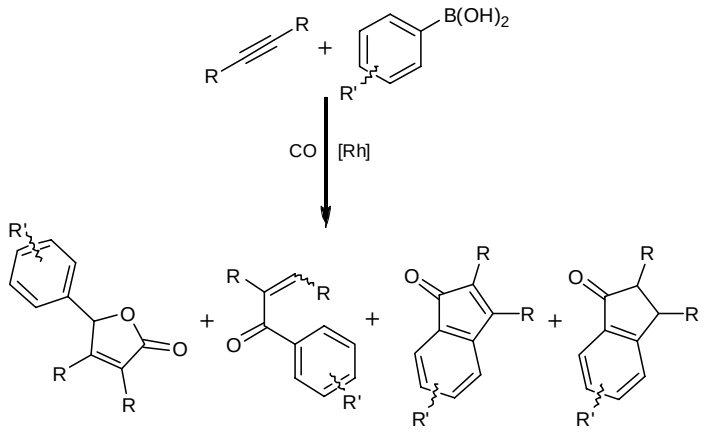


Figure 2.10.Rhodium catalyzed reaction of internal alkynes with organoborons under CO atmosphere

It is worthy to mention about product tunibility. The product selectivity can be tuned by modifying the reaction conditions. The key step of reaction is transmetallation between aryboronic acid and rhodium complex to form arylrhodium intermediate and then aroylrhodium specie forms by the insertion of CO to C-Rh bond (Figure 2.11).

Figure 2.11.Formation of aroylrhodium species from arylboronic reagents

2.1.6.Hydroesterification of Alkynes

The hydroesterification of simple alkynes that forms α,β-unsaturated esters is a compherensive studied process, which is usually operated over a Pd based catalyst in the presence of an alcohol reagent. In 1998 Scrivanti and co-workers reported the mechanistic aspect of alkoxycarbonylation of alkynes in the presence of the $Pd(OAc)_2/PPh_2Py/CH_3SO_3H$ catalytic system (Figure 2.12).

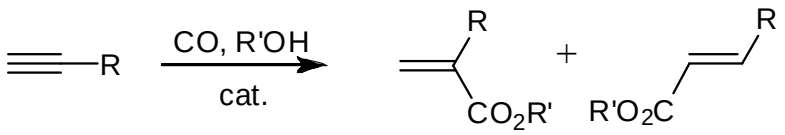


Figure 2.12 Alkoxycarbonylation of alkynes with Pd catalyst

They reported two possible reaction pathway according to deuterium labeled and literature studies (Norton et. al., 1979). One of these involves formation of an (alkoxycarbonyl)palladium complex generated by the insertion of CO into Pd-OR bond then migration of the carboalkoxy moiety on one of carbon atoms of triple bond in alkyne π coordinated to metal center and finally protonolysis of vinyl intermediate (Figure 2.13).

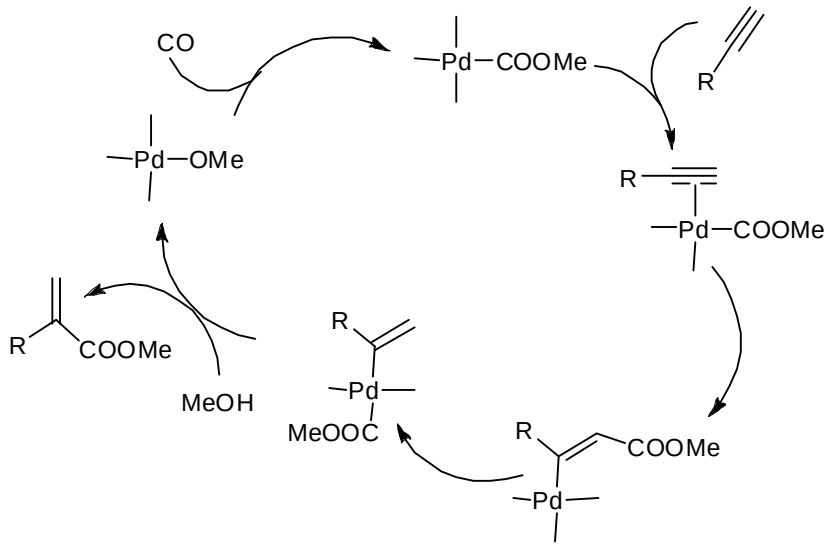


Figure 2.13.(Alkoxycarbonyl)palladium intermediate mechanism for alkoxycarbonylation of alkynes

The other possible pathway starts with formation of Pd-H species, then insertion of alkyne to Pd-H bond to give a (σ-vinyl)palladium complex and CO insertion to Pd-C bond and keeping up alcoholysis to produce the ester and regenerating the hydride (Figure 2.14).

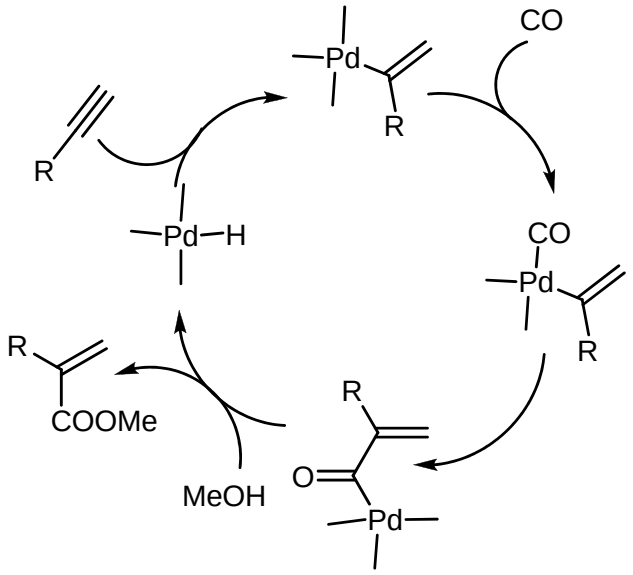
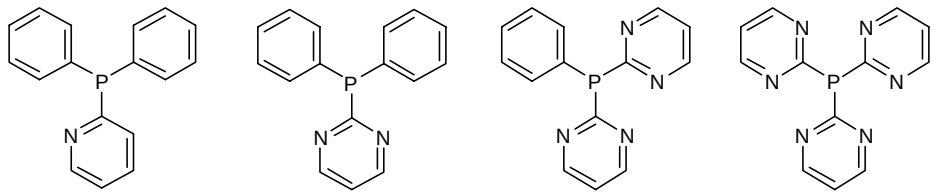


Figure 2.14.Hydropalladation intermediate mechanism for alkoxycarbonylation of alkynes

In 1998 Reetz and co-workers developed a new ligand class (Figure 2.15) for transition metal catalysis and used in hydroesterification of both terminal and symmetrical internal alkynes.



1 **2** **3** **4**

Figure 2.15.N/P ligands for transition metal catalysis

When they combine these ligands with $Pd(OAc)_2$ complex in carbonylation of alkynes, they obtained best result with ligand **2** (Figure 2.16).

R: n-C_4H_9	> 97%	R: C_6H_5	97%
R: t-C_4H_9	83%	R: C_2H_5	48%
R: C_6H_5	> 97%		
R: $Si(CH_3)_3$	25%		

Figure 2.16.Alkoxycarbonylation of alkynes with $Pd(OAc)_2$ / phosphine ligand system

Beside the straight chain alcohols, aryl alcohols (Itoh et. al., 1992) and cyclic and bicyclic alcohols (Monteiro et. al., 1997) can be used for Pd catalyzed synthesis of α,β-unsaturated esters from alkynes with high regioslectivity and yield.

There are also a few reported cases in which alkynes were carbonylated in alcohol reagents in the presence of rhodium complexes. However, the latter rhodium catalysed method often resulted in double incorporation of the carbonyl moiety. In 1983 Mise and co-workers reported that the Rh-catalyzed carbonylation of internal alkynes in ethanol gave a 5-ethoxy-5*H*-furan-2-one derivative as the main product (Figure 2.17).

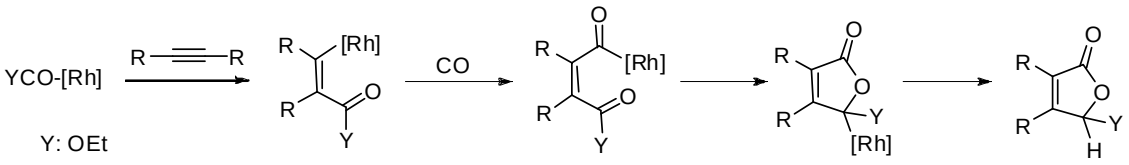


Figure 2.17.Rh-catalyzed carbonylation of internal alkynes in ethanol

In their optimized conditions $Rh_4(CO)_{12}$ cluster is used as the rhodium precursor and Na_2CO_3 as a base.

The carbonylation of phenyl substituted acetylenes in the presence of alcohols was found to form 3-alkoxycarbonylindanones (Yoneda et. al., 1999). The reaction was performed in dioxane and methanol was used as equivalent with aspect to the substrate (Figure 2.18). The reaction was also successful with different type of alcohols likewise C_2 and C_8 alcohols and benzyl alcohol derivatives.

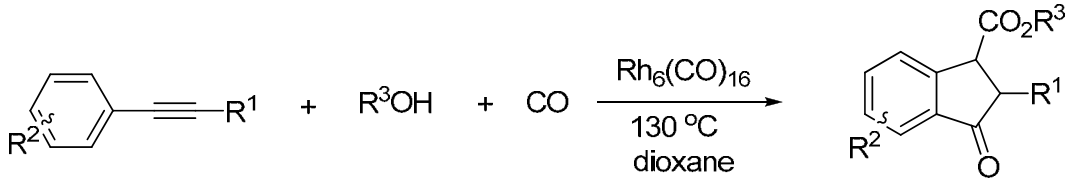


Figure 2.18.Synthesis of 3-alkoxycarbonylindanones by Rh-catalyzed carbonylation of alkynes

Two reaction pathways could be possible; one involves the formation of non-alkoxycarbonylated indenone derivative and hydroesterification of double bond, the other one is formation of alkoxycarbonylated indenone derivative and hydrogenation of that intermediate to produce the product. But when non-alkoxycarbonylated indenone was performed in alkoxycarbonylation condition, it seems that no product formation.So

the other pathway is acceptable for the formation of final indanone product (Figure 2.19). Formation of alkoxycarbonylated indenone is not possible because α,β-unsaturated compounds undergo hydrogenation by the catalysis of $Rh_6(CO)_{16}$ under water-gas shift reaction conditions (Joh et. al., 1993).

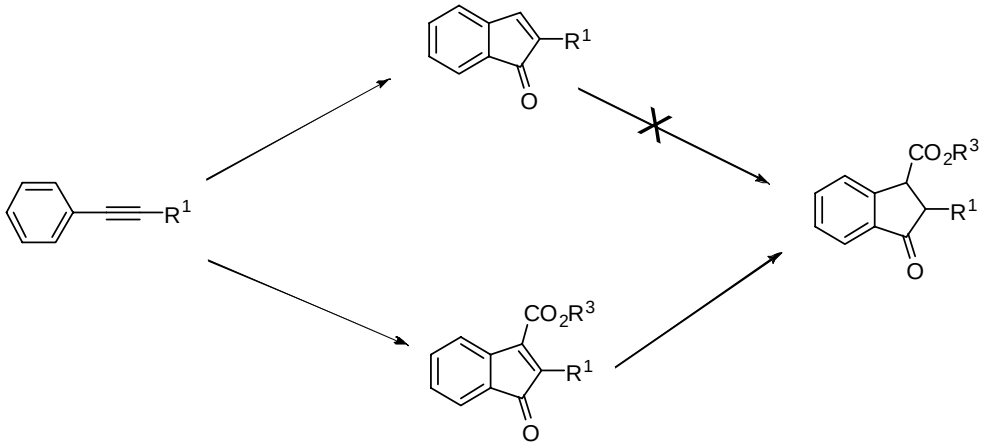


Figure 2.19.Reaction patways for the formation of indanone

Chatani and co-workers reported that the rhodium catalyzed carbonylation of internal alkynes with pyridin-2-ylmethanol proceeded through a chelate-assisted transformation and a double-hydroesterification, resulting in 1,4-dicarboxylate esters.

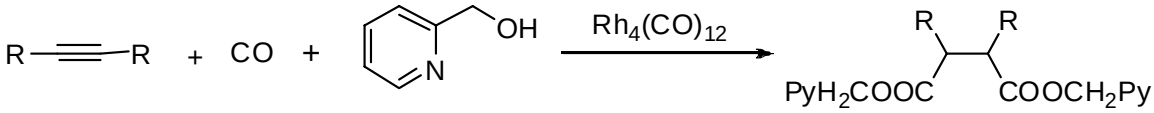


Figure 2.20.Rhodium catalyzed carbonylation of internal alkynes with pyridin-2-ylmethanol

When the reaction was performed with benzyl alcohol instead of pyridin-2-ylmethanol, corresponding 1,4-dicarboxylate does not form. This result explains the necessity of pyridin-2-ylmethanol because of coordination of nitrogen in pyridine to rhodium for the synthesis of saturated diester. The proposed rection mechanism does not include two consecutive hydroesterification of alkynes but the formation of ketene intermediate (Figure 2.21).

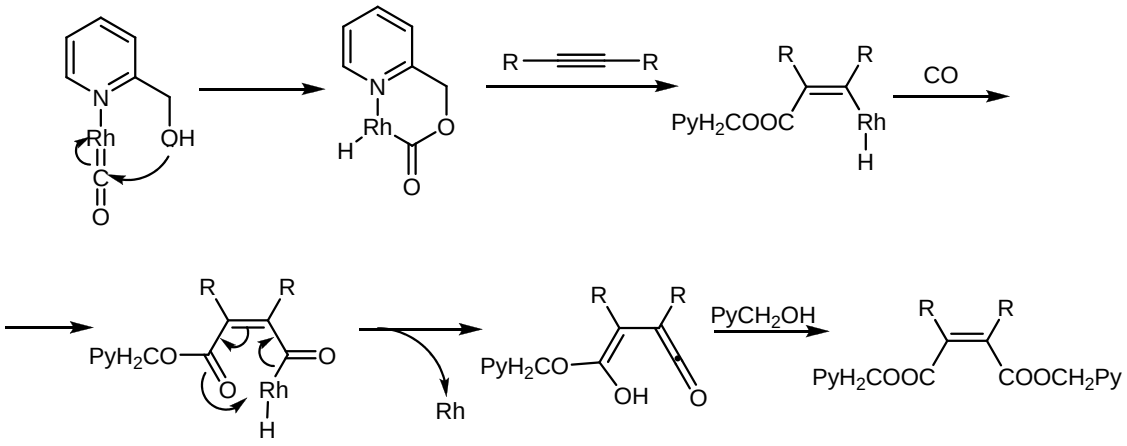


Figure 2.21.Proposed mechanism of Rh-catalyzed carbonylation of internal alkynes with pyridin-2-ylmethanol

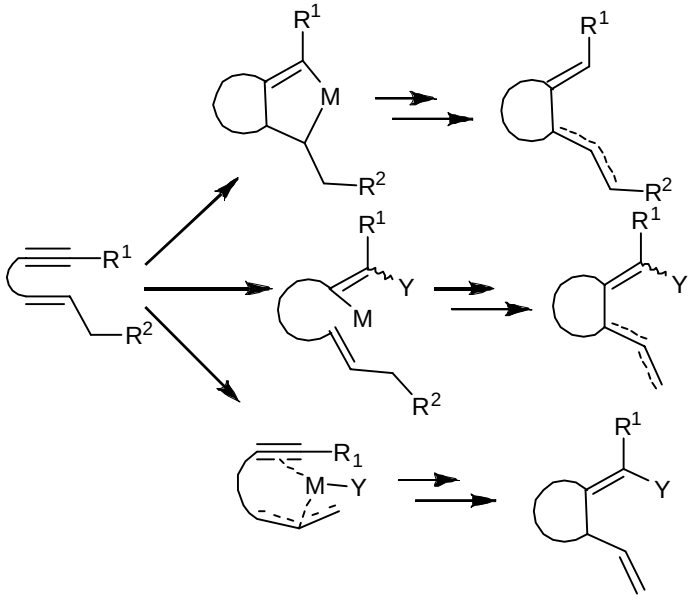
When Rh catalyzed reactions are compared with Pd catalyzed reactions, there are some differences mostly in mechanically. The main difference is the character of carbon atom that bonded to Pd and Rh. While Pd bonded carbon atom has electrophilic character, Rh bonded one has nucleophilic property. For this reason Rh catalyzed carbonylation reactions of alkynes mainly results in double carbonylated products. This property also makes Rh gaining usage in consecutive C-C bond formation reactions.

2.2.Rhodium-Catalyzed Cyclization Reactions of Unsaturated Systems

Transition metal catalyzed carbocyclization reactions of dienes, diynes, enynes, ynals, enediynes, diynals and triynes are important methods for the synthesis of cyclic compounds in one step. Rhodium is commonly used metal for cyclization reactions because it provides high level of regio- and stereoselectivity. And also thanks to carborhodation, cascade type cyclization reactions are very powerful, valuable and atom-economy method, especially in existence of a nucluophilic partner like organoborons.

2.2.1.Rhodium-Catalyzed Cyclization Reactions of 1,6-Enyne Derivatives

1,6-Enynes are suitable starting materials for the construction of five or six membered rings and tolerates different type of functionality. In recent years, rhodium-catalyzed cyclization reactions of 1,6 enynes are widely used for C-C bond forming reactions.



M: transition metal ; R^2: H or leaving group ; Y: H or nucleophile

Figure 2.22.Possible Mechanisms of the Cyclization of 1,6-Enynes

Zhang and co-workers reported formation of functionalized cyclopentanes by rhodium-catalyzed from 1,6 enynes (Figure 2.23).

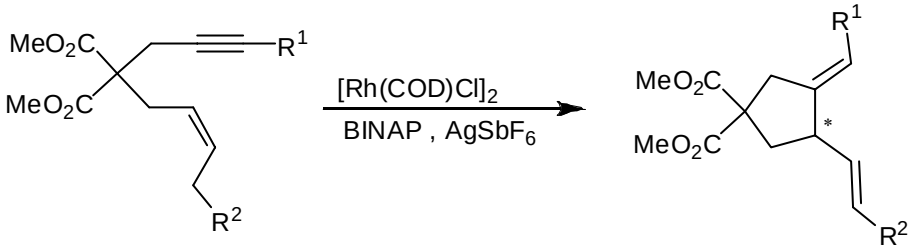


Figure 2.23.Rhodium-catalyzed cyclization of 1,6 enynes

They achieved highly efficient Rh(I)-catalyzed intramolecular Alder-ene type cycloisomerization in good yields and also only 1,4 dienes were observed with high level of regio- and stereoselectivity.According to the starting material cyclopentanone derivatives were also synthesized. The key step for the reaction is the formation of highly coordinatively unsaturated metallic moiety to bind the enyne (Figure 2.24).

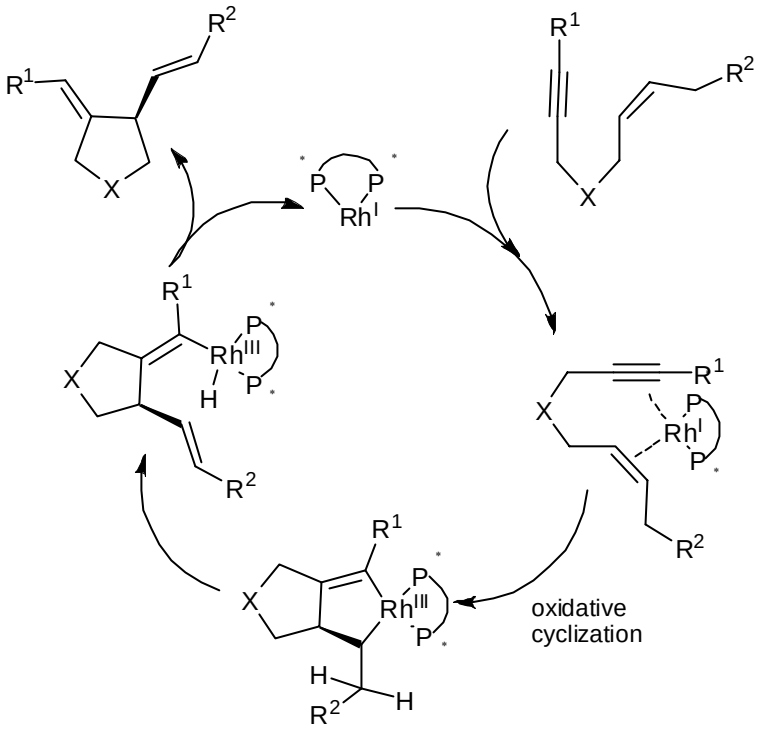


Figure 2.24 Proposed mechanism for the cyclization of enynes

Again Zhang et.al. reported rhodium-catalyzed cycloisomerization of 1,6 enynes with an intramolecular halogen shift. This one is also efficient method for the synthesis of cyclopentanone derivatives (Figure 2.25)

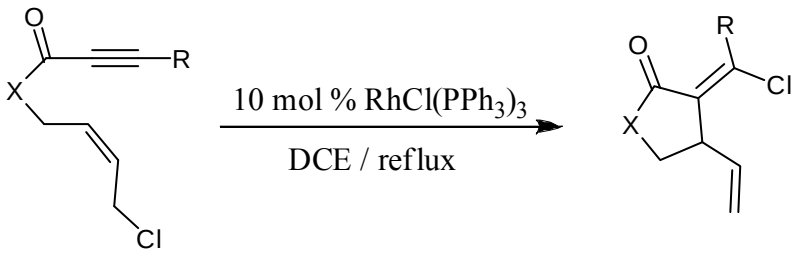


Figure 2.25.Cycloisomerization of 1,6 enynes with an intramolecular halogen shift.

On the basis of the typical Rh-catalyzed enyne isomerization a reaction mechanism was proposed by through a oxidative cylometalation intermediate and then β-halide and reductive elimination generates the product (Figure 2.26).

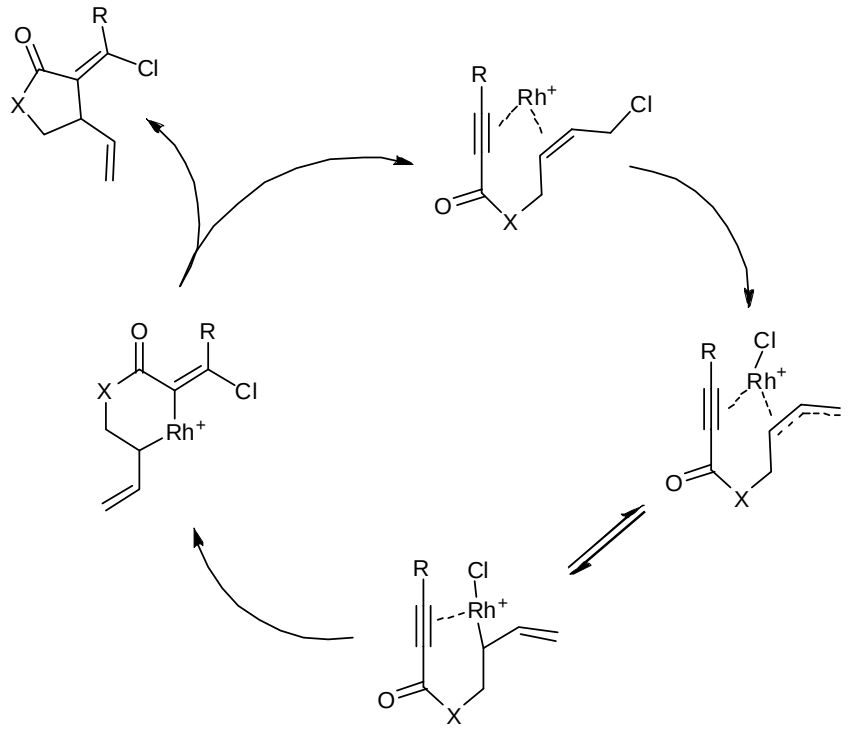


Figure 2.26.Proposed mechanism for the Cycloisomerization of 1,6 enynes with an intramolecular halogen shift.

Aryboronic acids are good nucleophiles for the addition of aryl groups to alkynes and rhodium could be commonly used for this purpose, because arylrhodium species that forms by transmetalation between Rh and arylboronic acid, can easily undergo 1,2 adition to a triple bond regioselectively. This addition presents an opportunity for cascade type reaction to construct more than one C-C bond in one pot. In 2005 Murakami et. al. reported that Rh-catalyzed cyclization of 1,6 enynes that have a leaving group in allylic position which is triggered by regioselective addition of arylboronic acids. The reaction is initiated by the regioselective 1,2-addition of arylrhodium to triple bond and followed by intramolecular carborhodation onto double bond of alkene. Finally, β-elemination of the oxygen bearing leaving group gives the cyclic product (Figure 2.27). It is noteworthy to say β-oxygen elimination is prefered to β-hydrogen elimination in the final step.

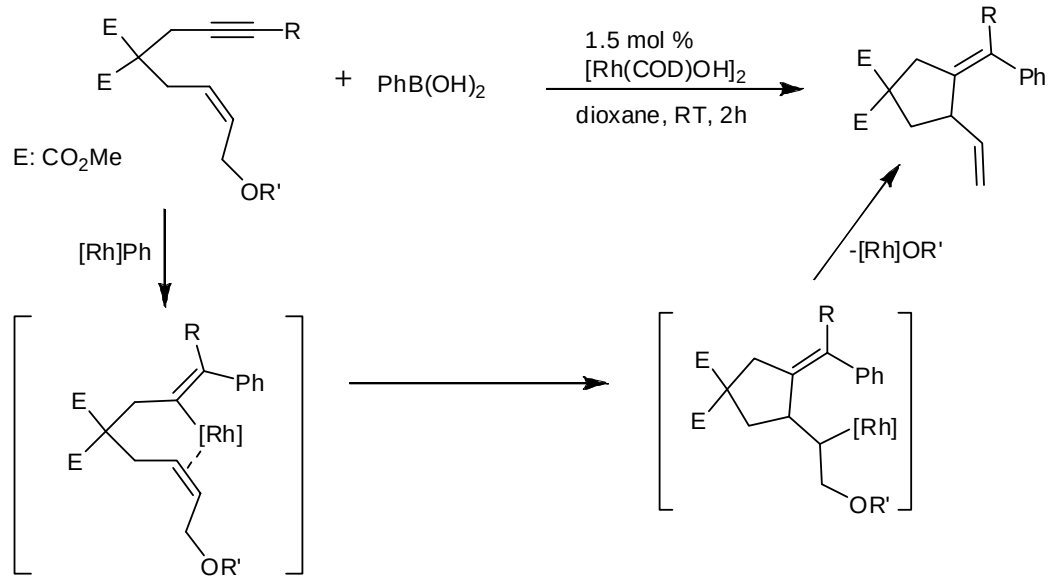


Figure 2.27.Rhodium-catalyzed cyclization of 1,6-enynes triggered by addition of arylboronic acids

Hayashi and co-workers reported that rhodium-catalyzed arylative cyclization of alkyne tethered an electron deficient olefin proceeded chemoselectively. Also enantioselectivity is ensured by chiral diene ligands (Figure 2.28). When (S)-binap is used as a ligand, a mixture of three different phenylated products are obtained nonselectively. In contrast when (S,S)-Bn-bod*(Figure 2.29) is used both product selectivity and enantioselectivity dramatically increased.

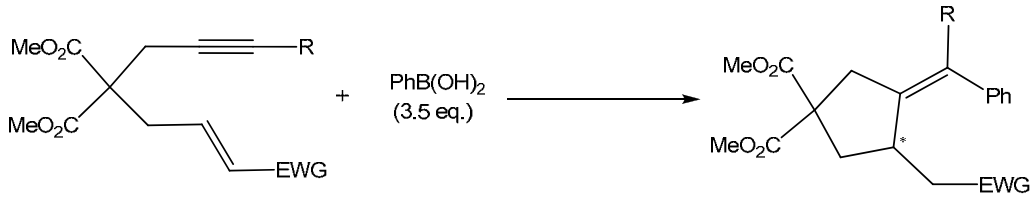


Figure 2.28.Rhodium-catalyzed arylative cyclization

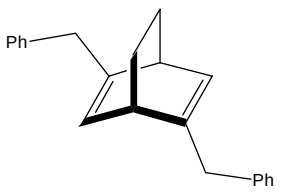


Figure 2.29.(S,S)-Bn-bod*

Reaction starts with the formation of arylrhodium intermediate and 1,2 addition to triple bond, followed by carborhodation and demetalation process leading to a chiral cyclic product (Figure 2.30).

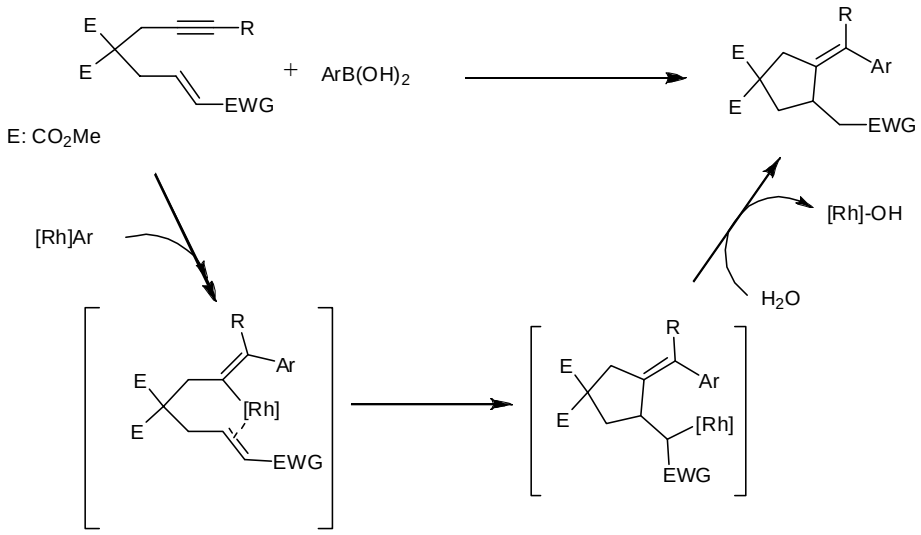


Figure 2.30.Proposed mechanism of arylative cyclization by rhodium catalyzed

2.2.2. Rhodium-Catalyzed Carbonylative Cyclization of 1,6 Enynes (Pauson Khand Reaction)

Hence the five-membered carbonyl containing rings are motifs in biologically active and natural products, synthesis of them has been studied in large scale. One of the most effective method is the three component transition metal mediated [2+2+1] cyclization of an alkyne, an alkene and carbon monoxide This type of reactions are referred to as Pauson-Khand Reactions (PKR). In 1973 the first [2+2+1] cyclization reactions were performed with stochiometric dicobalt octacarbonyl [$Co_2(CO)_8$] by Pauson and Khand. PKR could be performed as both inter- and intramolecular types. In recent years the catalytic PKR became an important process for which rhodium is one of the commonly used transition metal catalyst.

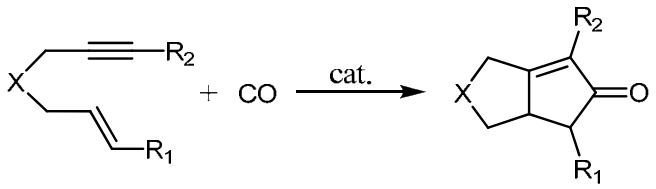


Figure 2.31.A ypical example of intramolecular PKR

In 2001 Narasaka and co-workers reported that inter- and intramolecular PKR of 1,6 and 1,7 enynes catalyzed by $[RhCl(CO)_2]_2$ under CO atmosphere to synthesize cyclopentenone derivatives (Figure 2.32).

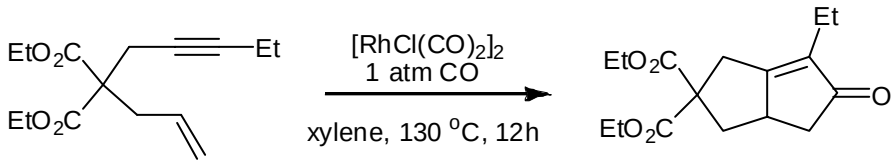


Figure 2.32.Rh-catalyzed PKR

The PKR of enynes with an electron deficient olefinic side led to two different types of carbocyclic products (Figure 2.33).

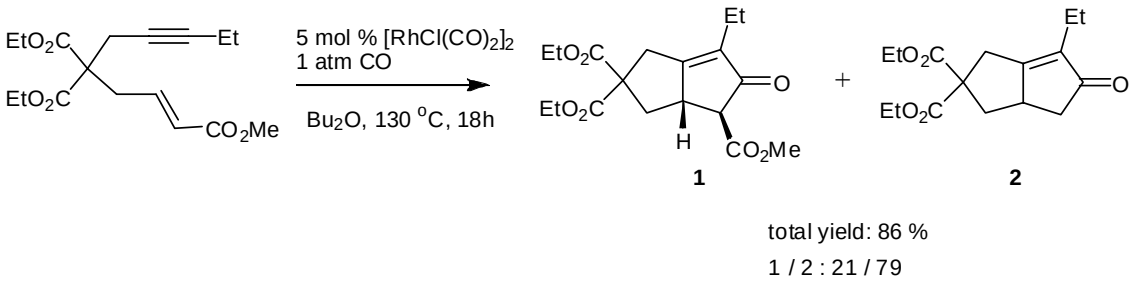


Figure 2.33.Rh-catalyzed PKR of an electron deficient olefin containing 1,6 enyne

Demethoxycarbonylated product (product **2** in Figure 2.33) was the major product. In early stage of the reaction product **1** was the major one. and heating of product **1** without any catalyst gave demethoxycarbonylated product in two hours.

CHAPTER 3

EXPERIMENTAL STUDY

3.1.General Procedures for Drying the Solvents

THF was distilled from benzophenone-ketyl under argon until the soluliton became purple color, prior to use. DMF was dried over CaH_2 and distilled at 80 °C under vacuum (20 mmHg). Methanol and ethanol were dried over Mg turnings in the presence of iodine and stored on molecular sieve 3A under Ar. 1-Propanol and 2-propanol were dried first by stirring over an anhydrous CaO (dried at 800 ^oC for 6 hours) and then refluxing over Mg turnings in the presence of iodine. 1-Butanol was dried first by stirring over an anhydrous $MgSO_4$ (dried 250 ^oC under vacuum for 3 hours) and then refluxing over Mg turnings in the presence of iodine. Acetonitrile was dried with CaH_2.

3.2.General Procedures for the Synthesis of Enyne Molecules

Synthesis of (E)-4,4-diethyl 1-methyl oct-1-en-6-yne-1,4,4-tricarboxylate (1a):

To a suspension of NaH (168 mg, 7 mmol) in dry THF (50 mL) was added diethyl malonate (2.88 g, 18 mmol) at 0 °C, and then the mixture was stirred at room temperature for 1 h. To this was added 1-bromo-2-butyne (0.92 g, 7 mmol) in dry THF(10 mL) at 0 °C and the resulting mixture was stirred for 8 h at room temperature. The reaction was quenched with water, and then extracted with Et_2O. The organic layer was dried over $MgSO_4$, filtered, and concentrated under vacuum. The residue was chromatographed on silica gel with Et_2O/hexane=1/10 to afford diethyl 2-(but-2-ynyl)malonate as pale yellow oil (0.91 g, 61% yield) (Shintani, et al. 2005) (Figure 3.1).

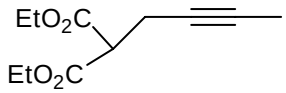


Figure 3.1.Diethyl 2-(but-2-ynyl)malonate

A solution of diethyl 2-(but-2-ynyl)malonate (0.91 g, 4.30 mmol) in dry THF (15 mL) was added to a suspension of NaH (124 mg, 5.16 mmol) in dry THF (10 mL) at 0 °C, and the mixture was stirred for 1 h. Methyl 4-bromocrotonate (924 mg, 5.16 mmol) was then added to it at 0 °C, and the resulting mixture was stirred for 8 h at room temperature. The reaction was quenched with water, and then extracted with Et_2O. The organic layer was dried over $MgSO_4$, filtered, and concentrated under vacuum. The residue was chromatographed on silica gel with EtOAc / hexane =1/10 to afford compound (*E*)-4,4-diethyl 1-methyl oct-1-en-6-yne-1,4,4-tricarboxylate as a pale yellow oil (1.06 g, 80% yield) (Shintani et al., 2005) (Figure 3.2).

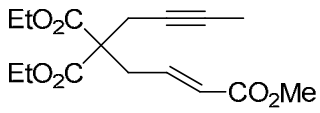


Figure 3.2.(*E*)-4,4-diethyl 1-methyl oct-1-en-6-yne-1,4,4-tricarboxylate

Synthesis of (E)-4,4-diethyl 1-methyl non-1-en-6-yne-1,4,4-tricarboxylate (1b):

To a suspension of NaH (240 mg, 10 mmol) in dry THF (50 mL) was added diethyl malonate (4.0 g, 25 mmol) at 0 °C, and then the mixture was stirred at room temperature for 1 h. To this was added 1-bromo-2-pentyne (1.47 g, 10 mmol) in dry THF (10 mL) at 0 °C and the resulting mixture was stirred for 10 h at room temperature. The reaction was quenched with water, and then extracted with Et_2O. The organic layer was dried over $MgSO_4$, filtered, and concentrated under vacuum. The residue was chromatographed on silica gel with Et_2O/hexane=1/10 to afford diethyl 2-(pent-2-ynyl)malonate as pale yellow oil (1.63 g, 72 % yield) (Shintani, et al. 2005) (Figure 3.3).

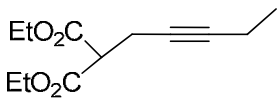


Figure 3.3.Diethyl 2-(pent-2-ynyl)malonate

A solution of diethyl 2-(pent-2-ynyl)malonate (1.63 g, 7.20 mmol) in dry THF (15 mL) was added to a suspension of NaH (208 mg, 8.65 mmol) in dry THF (10 mL) at 0 °C, and the mixture was stirred for 1 h. Methyl 4-bromocrotonate (1.55 g, 8.65 mmol) was then added to it at 0 °C, and the resulting mixture was stirred for 8 h at room

temperature. The reaction was quenched with water, and then extracted with Et_2O. The organic layer was dried over $MgSO_4$, filtered, and concentrated under vacuum. The residue was chromatographed on silica gel with EtOAc / hexane =8/100 to afford compound (*E*)-4,4-diethyl 1-methyl non-1-en-6-yne-1,4,4-tricarboxylate as a pale yellow oil (2.0 g, 86% yield) (Shintani, et al. 2005) (Figure 3.4).

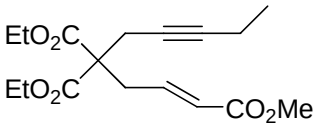


Figure 3.4.(*E*)-4,4-diethyl 1-methyl non-1-en-6-yne-1,4,4-tricarboxylate

Synthesis of (E)-4,4-diethyl 1-methyl 8-methoxyoct-1-en-6-yne-1,4,4-tricarboxylate (1c):

To a suspension of NaH (240 mg, 10 mmol) in THF (10 mL) was added diethyl malonate (4.0 g, 25 mmol) at 0 °C, and then the mixture was stirred at room temperature for 1 h. The resulting mixture was cooled to 0 °C, then 4-methoxybut-2-ynyl methanesulfonate (Jeon et. al. 2003) (1.78 g, 10 mmol) was added. After the mixture had been stirred at room temperature for 3 h, saturated aqueous solution of NH_4Cl was added at 0 °C and the aqueous layer was extracted with EtOAc. The combined organic layers were washed with water and brine, dried over $MgSO_4$, and concentrated in vacuo. The residue was purified by silica gel column chromatography by EtOAc / hexane =1/6 to afford diethyl 2-(4-methoxybut-2-ynyl)malonate (1.72 g, 71% yield) (Takimoto et.al. 2006) (Figure 3.5).

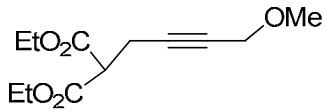


Figure 3.5.Diethyl 2-(4-methoxybut-2-ynyl)malonate

To a suspension of NaH (187 mg, 7.8 mmol) in DMF (30 mL) was added diethyl 2-(4-methoxybut-2-ynyl)malonate (1.72 g, 7.1 mmol) at 0 °C, and then, the mixture has been stirred at room temperature for 1 h. The resulting mixture was cooled to 0 °C and methyl 4-bromocrotonate (1.92 g, 10.7 mmol) and NaI (107 mg, 0.71 mmol) were added. After the mixture had been stirred at room temperature for 2 h, saturated aqueous solution of NH_4Cl was added at 0 °C. The aqueous layer was extracted with EtOAc. The

combined organic layers were washed with water and brine, dried over $MgSO_4$, and concentrated in vacuo. The residue was purified by silica gel column chromatography by EtOAc / hexane =1/5 to afford (*E*)-4,4-diethyl 1-methyl 8-methoxyoct-1-en-6-yne-1,4,4-tricarboxylate as a colorless oil (2.13 g, 88% yield) (Takimoto et.al. 2006) (Figure 3.6).

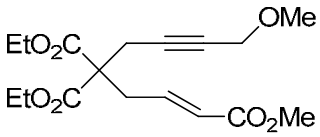


Figure 3.6.(*E*)-4,4-diethyl 1-methyl 8-methoxyoct-1-en-6-yne-1,4,4-tricarboxylate

Synthesis of (E)-dimethyl 2-(but-2-ynyl)-2-(4-oxo-4-phenylbut-2-enyl)malonate (1d):

Dimethyl malonate (2.45 mL, 21.3 mmol) was added to a solution of NaOMe (1.27 g, 23.4 mmol) in MeOH (16 mL), and the mixture was stirred for 15 min at 50 °C. Bromoacetaldehyde dimethyl acetal (2.67 mL, 22.5 mmol) was then added to this mixture, and the resulting solution was stirred for 72 h at 80 °C. After cooling to room temperature, the mixture was poured into aqueous NaCl (saturated) solution and extracted with Et_2O. The organic layer was dried over $MgSO_4$, filtered, and concentrated under vacuum. The residue was chromatographed on silica gel with EtOAc/hexane=1/2 to afford dimethyl 2,2-dimethoxyethylmalonate as a pale yellow oil (2.67 g, 12.1 mmol; 57% yield) (Shintani et. al. 2005) (Figure 3.7).

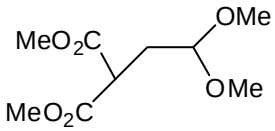


Figure 3.7.Dimethyl 2-(2,2-dimethoxyethyl)malonate

Dimethyl 2,2-dimethoxyethylmalonate (2.67g, 12.1 mmol) was added dropwisely to a suspension of NaH (348 mg, 14.5 mmol) in THF (50 mL) at 0 °C, and the mixture was stirred for 1 h. 1-Bromo-2-butyne (1.32 mL, 15.1 mmol) was then added to it at 0 °C, and the resulting mixture was stirred for 4 h at room temperature. The reaction was quenched with water, and then extracted with Et_2O. The organic layer was dried over $MgSO_4$, filtered, and concentrated under vacuum. The residue was chromatographed on silica gel with EtOAc/hexane=1/2 to afford dimethyl 2-(but-2-

ynyl)-2-(2,2-dimethoxyethyl)malonate as a pale yellow oil (2.6 g, 9.6 mmol; 80% yield) (Shintani et. al. 2005) (Figure 3.8).

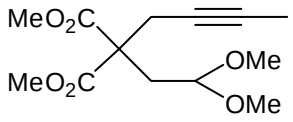


Figure 3.8.Dimethyl 2-(but-2-ynyl)-2-(2,2-dimethoxyethyl)malonate

To a solution of the acetal prepared above (2.6 g, 9.6 mmol) in CH_2Cl_2 (150 mL) was added aqueous formic acid solution (88%, 90 mL), then the mixture was stirred at room temperature for 30 min. The mixture was diluted with CH_2Cl_2 and organic layer was separated, washed with water, dried over $MgSO_4$, filtered, and concentrated under vacuum. The residue was chromatographed on silica gel with Et_2O/hexane=1/2 to afford dimethyl 2-(but-2-ynyl)-2-(2-oxoethyl)malonate as a pale yellow oil (1.95 g, 8.64 mmol; 90 % yield) (Takimoto et. al. 2006) (Figure 3.9).

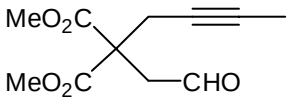


Figure 3.9.Dimethyl 2-(but-2-ynyl)-2-(2-oxoethyl)malonate

To a solution of aldehyde (975 mg, 4.32 mmol), which was prepared according to the procedures described above, in CH_2Cl_2 (70 mL) was added phenylcarbonylmethylene triphenylphosphorane (Kuroda et. al. 2004) (2.28 g, 6.0 mmol) and the mixture was stirred at room temperature for 24 h. After the solvent had been evaporated, the residue was purified by silica gel column chromatography (hexane/EtOAc = 5/1) to afford (*E*)-dimethyl 2-(but-2-ynyl)-2-(4-oxo-4-phenylbut-2-enyl)malonate as a pale yellow oil (688 mg, 2.1 mmol; 48% yield) (Takimoto et. al. 2006) (Figure 3.10).

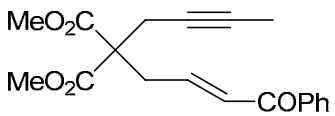


Figure 3.10.(*E*)-dimethyl 2-(but-2-ynyl)-2-(4-oxo-4-phenylbut-2-enyl)malonate

Synthesis of (E)-dimethyl 2-(but-2-ynyl)-2-(4-oxopent-2-enyl)malonate (1e):

(*E*)-dimethyl 2-(but-2-ynyl)-2-(4-oxopent-2-enyl)malonate was synthesized with the reaction of dimethyl 2-(but-2-ynyl)-2-(2-oxoethyl)malonate (975 mg, 4.32 mmol) (Figure 3.9) and 1-(triphenylphosphonilidene)-2-propanone (1.9 g, 6.0 mmol) (Ramirez and Dershowitz, 1957) with stirring the mixture for 18 h at room temperature. After the solvent had been evaporated, the residue was purified by silica gel column chromatography (hexane/EtOAc = 6/1) to afford (*E*)-dimethyl 2-(but-2-ynyl)-2-(4-oxopent-2-enyl)malonate as a colorless oil (692 mg, 2.6 mmol; 60% yield) (Takimoto et. al. 2006) (Figure 3.11).

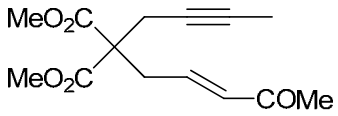


Figure 3.11.(*E*)-dimethyl 2-(but-2-ynyl)-2-(4-oxopent-2-enyl)malonate

Synthesis of (E)-ethyl non-2-en-7-ynoate(1f):

To a solution of 5-hexyn-1-ol (490 mg, 5 mmol) in Et_2O (10 mL) and 3,4-dihydro-2*H*-pyran (504 mg, 6 mmol) was added *p*-toluenesulfonic acid (11 mg, 0.05 mmol). After one night at 20 °C, the mixture was diluted with Et_2O and washed with water, saturated aqueous NH_4Cl, water, and brine. The organic layer was dried over $MgSO_4$, filtered, and concentrated in vacuum. The product was used without purification for the next step (Betzer et. al. 1997) (Figure 3.12).

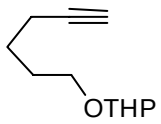


Figure 3.12.2-(hex-5-ynyloxy)tetrahydro-2*H*-pyran

To a solution of 2-(hex-5-ynyloxy)tetrahydro-2*H*-pyran in THF (5 mL) at -78 °C was added *n*-BuLi (1.6 M solution in hexane, 6 mmol). The cold bath was removed, and the mixture was stirred at 0 °C for 1 h and cooled to -78 °C before addition of iodomethane (2.13 g, 15 mmol). The solution was stirred overnight at 20 °C and quenched at 0 °C with saturated aqueous NH_4Cl. The mixture was allowed to warm to 20 °C and then extracted with Et_2O and dried over $MgSO_4$. The product was used without purification for the next step (Betzer et. al. 1997) (Figure 3.13).

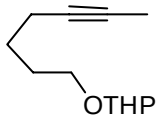


Figure 3.13.2-(hept-5-ynyloxy)tetrahydro-2*H*-pyran

A solution of the preceding compound in methanol (20 mL) was treated with *p*-toluenesulfonic acid (330 mg, 1.5 mmol) and stirred at 20 °C for 20 min. Then Et_3N was added (0.5 mL), and the solution was concentrated in vacuo. The mixture was taken in dichloromethane 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 by Et_2O / hexane : 1/2 gave title product as a colorless oil (448 mg, 4.0 mmol) (Betzer et. al. 1997) (Figure 3.14).

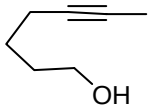


Figure 3.14.Hept-5-yn-1-ol

To a suspension of Dess-Martin periodinane (1.89 g, 4.4 mmol) in CH_2Cl_2 (30 mL) was added a solution of hept-5-yn-1-ol (448mg, 4 mmol) in CH_2Cl_2 (10 mL) at 0 °C, and the mixture was stirred at room temperature for 5 h. To this were added saturated $NaHCO_3$ aq. and saturated Na_2S_2O3 aq. After the mixture had been stirred for several minutes, it was extracted with EtOAc. The combined organic layers were washed with brine, dried over $MgSO_4$. The product was used without purification for the next step (Takimoto et. al. 2006) (Figure 3.15).

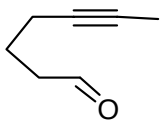


Figure 3.15.Hept-5-ynal

To a suspension of NaH (72 mg, 3 mmol) in THF (10 mL) was added triethyl phosphonoacetate (805 mg, 3.6 mmol) at 0 ^{o}C. After the solution was stirred at room temperature for 45 min., hept-5-ynal (297 mg, 2.7 mmol) was added at –78 ^{o}C. Then the mixture was stirred at room temperature for 30 min. The reaction was terminated by

addition of aq. NH_4Cl solution and Et_2O. The organic layer was separated, washed with 1 M HCl and aq $NaHCO_3$ solution and dried over $MgSO_4$. The residue was purified by silica gel column chromatography by EtOAc / hexane =1/10 to afford (E)-ethyl non-2-en-7-ynoate (243 mg, 51% yield) (Urabe et. al. 1997) (Figure 3.16).

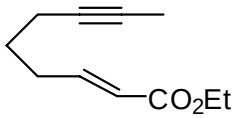


Figure 3.16.(E)-ethyl non-2-en-7-ynoate

Synthesis of (E)-ethyl 4-(but-2-ynyloxy)but-2-enoate(1g):

At -10 ^{O}C, 3,4-dihydro-2*H*-pyran(8.4 g, 100 mmol) was added over a period of 45 min to a mixture of 50 mg of p-toluenesulfonic acid in 55 mL (1.0 mol) of ethylene glycol. The reaction mixture was stirred for 1 h at -10 ^{o}C and then for 2 h at room temperature. The mixture was poured into 200 mL of 1 M NaOH and extracted with CH_2Cl_2 (5 x 200 mL). The combined organic layers were dried on $MgSO_4$ and concentrated in vacuo (de Vries et. al. 1993) (Figure 3.17).

Figure 3.17.2-(tetrahydro-2*H*-pyran-2-yloxy)ethanol

To a suspension of NaH (576 mg, 24 mmol) in THF (40 mL) was added 2-(tetrahydro-2*H*-pyran-2-yloxy)ethanol (2.92 g, 20 mmol) at 0 °C, and then, the mixture was stirred at room temperature for 1.5 h. The resulting mixture was cooled to 0 °C and 1-bromo-2-butyne (3.57 g, 30 mmol) was added. The mixture was stirred at room temperature overnight. The reaction was quenched with water and extracted with Et_2O and dried over $MgSO_4$. The residue was purified by silica gel column chromatography using Et_2O/hexane =1/5 to afford 2-(2-(but-2-ynyloxy)ethoxy) tetrahydro-2*H*-pyran (2.57 g, 65% yield) (Figure 3.18).

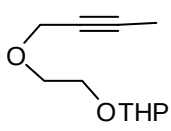


Figure 3.18.2-(2-(but-2-ynyloxy)ethoxy) tetrahydro-2*H*-pyran

A solution of the preceding compound (2.57 g, 13 mmol) in methanol (40 mL) was treated with *p*-toluenesulfonic acid (688 mg, 4 mmol) and stirred at 20 °C for 20 min. Then Et_3N was added (1.1 mL), and the solution was concentrated *in vacuo*. The mixture was taken into dichloromethane 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 with EtOAc / hexane = 1/2 gave the title product as a colorless oil (918 mg, 62% yield) (Betzer et. al. 1997) (Figure 3.19).

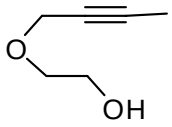


Figure 3.19.2-(but-2-ynyloxy)ethanol

To a suspension of Dess-Martin periodinane (3.77 g, 8.8 mmol) in CH_2Cl_2 (60 mL) was added a solution of 2-(but-2-ynyloxy)ethanol (912 mg, 8.0 mmol) in CH_2Cl_2 (20 mL) at 0 °C, and the mixture was stirred at room temperature for 5 h. To this were added saturated $NaHCO_3$ aq. and saturated Na_2S_2O3 aq. After the mixture had been stirred for several minutes, it was extracted with EtOAc. The combined organic layers were washed with brine and dried over $MgSO_4$. The product was used without purification for the next step (Takimoto et. al. 2006) (Figure 3.20).

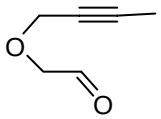


Figure 3.20.2-(but-2-ynyloxy)acetaldehyde

To a suspension of NaH (132 mg, 5.5 mmol) in THF (20 mL) was added triethyl phosphonoacetate (1.34 g, 6 mmol) at 0 ^oC. After the solution was stirred at room temperature for 45 min., 2-(but-2-ynyloxy)acetaldehyde (560 mg, 5 mmol) was added at – 78 ^oC. Then the mixture was stirred at room temperature for 30 min. The reaction was terminated by addition of aq. NH_4Cl solution and Et_2O. The organic layer was separated, washed with 1 M HCl and aq $NaHCO_3$ solution and dried over $MgSO_4$. The residue was purified by silica gel column chromatography with EtOAc/hexane =1/10 to

afford (*E*)-ethyl 4-(but-2-ynyloxy)but-2-enoate as a colorless oil (455 mg, 50% yield) (Urabe et. al. 1997) (Figure 3.21).

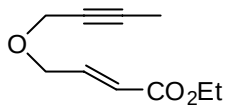


Figure 3.21.(*E*)-ethyl 4-(but-2-ynyloxy)but-2-enoate

Synthesis of (E)-methyl 4-(N-(but-2-ynyl)-4-methylphenylsulfonamido)but-2-enoate(1h):

To suspension of K_2CO_3(1.38 g, 10 mmol, anhydrous) in dry CH_3CN, p-toluensulfonamide (6.85 g, 40 mmol) and 1-bromo-2-butyne (1.32 g, 10 mmol) was added. The mixture was refluxed for 2 h. The reaction was quenched with water and extracted with Et_2O. The organic layer was washed with brine and dried over $MgSO_4$. The residue was purified by silica gel column chromatography using EtOAc / hexane =1/3 to afford N-(but-2-ynyl)-4-methylbenzenesulfonamide (1.36 g, 61% yield) (Tanaka et. al. 2006) (Figure 3.22).

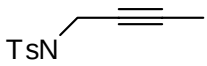


Figure 3.22.N-(but-2-ynyl)-4-methylbenzenesulfonamide

To suspension of K_2CO_3(830 mg, 6 mmol, anhydrous) in dry CH_3CN, N-(but-2-ynyl)-4-methylbenzenesulfonamide (670 mg, 3 mmol) and methyl 4-bromocrotonate (1.07 g, 6 mmol) was added. The mixture refluxed for 3 h. The reaction was quenched with water and extracted with Et_2O. The organic layer was washed with brine and dried over $MgSO_4$. The residue was purified by silica gel column chromatography using EtOAc/hexane =1/5 to afford (*E*)-methyl 4-(N-(but-2-ynyl)-4-methylphenylsulfonamido)but-2-enoate (795 mg, 82% yield) (Tanaka et. al. 2006) (Figure 3.23).

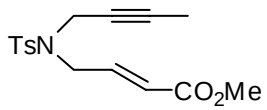


Figure 3.23.(*E*)-methyl 4-(N-(but-2-ynyl)-4-methylphenylsulfonamido)but-2-enoate

Synthesis of diethyl 2-(but-2-ynyl)-2-(3-cyanoallyl)malonate(1i):

To a stirred solution of methanesulfonyl chloride (3.43 g, 30 mmol) in pyridine (50 ml) 2-(tetrahydro-2*H*-pyran-2-yloxy)ethanol (2.94 g, 20 mmol) (Figure 3.17) was added. After the mixture was stirred at room temperature for 1 h, Et_2O and 1 N NaOH mixture were added to the reaction medium and aqueous layer was extracted with Et_2O twice. The organic layer was washed with 0.5 N NaOH solution three times and dried with $MgSO_4$.(4.03 g, 90% yield, crude) (Hewson et. al. 1985) (Figure 3.24).

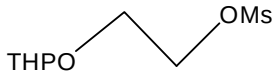


Figure 3.24.2-(tetrahydro-2H-pyran-2-yloxy)ethyl methanesulfonate

To a suspension of NaH (432 mg, 18 mmol) in DMF (40 mL) was added diethyl malonate (5.76 g, 36 mmol) at 0 °C, and then the mixture was stirred at room temperature for 1 h. To this was added 2-(tetrahydro-2*H*-pyran-2-yloxy)ethyl methanesulfonate (4.03 g, 18 mmol) in DMF (20 mL) at 0 °C. After the mixture had been stirred at 80 °C for 50 h, the saturated aqueous solution of NH_4Cl was added at 0 °C. The aqueous layer was extracted with EtOAc and the combined organic layers were washed with water and brine, dried over $MgSO_4$, and concentrated in vacuo. The residue was purified by silica gel column chromatography EtOAc/hexane=1/5 to afford diethyl 2-(2-(tetrahydro-2*H*-pyran-2-yloxy)ethyl)malonate (4.15 g, 80% yield) (Takimoto et. al. 2006) (Figure 3.25).

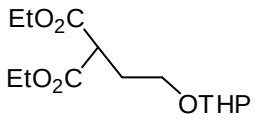


Figure 3.25.Diethyl 2-(2-(tetrahydro-2*H*-pyran-2-yloxy)ethyl)malonate

To a suspension of NaH (415 mg, 17.3 mmol) in dry THF (20 mL) was added diethyl 2-(2-(tetrahydro-2H-pyran-2-yloxy)ethyl)malonate (4.15 g, 14.4 mmol) at 0 °C, and then the mixture was stirred at room temperature for 1 h. To this was added 1-bromo-2-butyne (2.87 g, 21.6 mmol) in dry THF(10 mL) at 0 °C and the resulting mixture was stirred overnight at room temperature. The reaction was quenched with water, and then extracted with Et_2O. The organic layer was dried over $MgSO_4$, filtered, and concentrated under vacuum. The residue was chromatographed on silica gel with

EtOAc/hexane=1/10 to afford diethyl 2-(but-2-ynyl)-2-(2-(tetrahydro-2*H*-pyran-2-yloxy)ethyl)malonate (2.45 g, 50% yield) (Shintani et. al. 2005) (Figure 3.26).

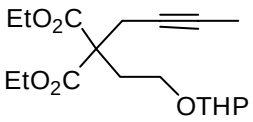


Figure 3.26.Diethyl 2-(but-2-ynyl)-2-(2-(tetrahydro-2*H*-pyran-2-yloxy)ethyl)malonate

A solution of the preceding compound (2.45 g, 7.2 mmol) in methanol (20 mL) was treated with *p*-toluenesulfonic acid (408 mg, 2.1 mmol) and stirred at 20 °C for 20 min. Then Et_3N was added (0.5 mL), and the solution was concentrated *in vacuo*. The mixture was taken into dichloromethane 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 with EtOAc / hexane = 1/2 gave the title product as a colorless oil (1.29 g, 70% yield) (Betzer et. al. 1997) (Figure 3.27).

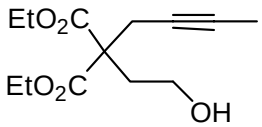


Figure 3.27.diethyl 2-(but-2-ynyl)-2-(2-hydroxyethyl)malonate

To a suspension of Dess-Martin periodinane (2.37 g, 5.5 mmol) in CH_2Cl_2 (40 mL) was added a solution of diethyl 2-(but-2-ynyl)-2-(2-hydroxyethyl)malonate (1.29, 5.0 mmol) in CH_2Cl_2 (15 mL) at 0 °C, and the mixture was stirred at room temperature for 5 h. To this were added saturated $NaHCO_3$ aq. and saturated $Na_2S_2O_3$ aq. After the mixture had been stirred for several minutes, it was extracted with EtOAc. The combined organic layers were washed with brine and dried over $MgSO_4$. The product was used without purification for the next step (Takimoto et. al. 2006) (Figure 3.28).

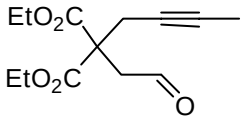


Figure 3.28.Diethyl 2-(but-2-ynyl)-2-(2-oxoethyl)malonate

To a solution of diethyl 2-(but-2-ynyl)-2-(2-oxoethyl)malonate (~3.5 mmol) in benzene (50 mL) was added (triphenylphosphonilidene)acetonitrile (1.49 g, 4.55 mmol), and the mixture was stirred at room temperature for 14 h. After the solvent had been evaporated, the residue was purified by silica gel column chromatography EtOAc/hexane= 1/10 to afford diethyl 2-(but-2-ynyl)-2-(3-cyanoallyl)malonate (872 mg, 90% yield, E / Z = 3 / 1) (Takimoto et. al. 2006) (Figure 3.29).

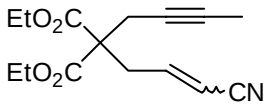


Figure 3.29.Diethyl 2-(but-2-ynyl)-2-(3-cyanoallyl)malonate

Synthesis of dimethyl 2-(but-2-ynyl)-2-(3-cyanoallyl)malonate(1j):

To the solution of dimethyl 2-(2,2-dimethoxyethyl)malonate(Figure 3.7) prepared above (1.67 g, 9.6 mmol) in CH_2Cl_2 (150 mL) was added aqueous formic acid solution (88%, 90 mL), then the mixture was stirred at room temperature for 30 min. The mixture was diluted with CH_2Cl_2 and organic layer was separated, washed with water, dried over MgSO4, filtered, and concentrated under vacuum. The residue was chromatographed on silica gel with Et_2O/hexane=1/2 to afford dimethyl 2-(2-oxoethyl)malonate as a pale yellow oil (1.39 g, 8.0 mmol; 83 % yield) (Takimoto et. al. 2006).

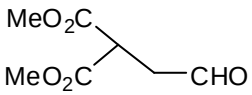


Figure 3.30 Dimethyl 2-(2- oxoethyl)malonate

To a solution of dimethyl 2-(2- oxoethyl)malonate (8.0 mmol) in benzene (100 mL) was added (triphenylphosphonilidene)acetonitrile (3.43 g, 10.5 mmol), and the mixture was stirred at room temperature for 14 h. After the solvent had been evaporated, the residue was purified by silica gel column chromatography EtOAc/hexane= 1/5 to afford dimethyl 2-(3-cyanoallyl)malonate (1.34 g, 85% yield, E / Z = 3 / 1) (Takimoto et. al. 2006). After extensive column chromatography studies with hexane-ethyl acetate system, 2.3 mmol(453 mg) pure E izomer was obtained.

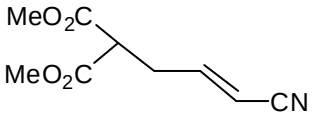


Figure 3.31 Dimethyl 2-(3-cyanoallyl)malonate

To a suspension of NaH (68 mg, 2.8 mmol) in dry THF (15 mL) was added dimethyl 2-(3-cyanoallyl)malonate (453 mg, 2.3 mmol) at 0 °C, and then the mixture was stirred at room temperature for 1 h. To this was added but-2-ynyl methanesulfonate (Jeon et. al., 2003) (0.52 g, 3.5 mmol) in dry THF (15 mL) at 0 °C and the resulting mixture was stirred for 9 h at room temperature. The reaction was quenched with water, and then extracted with Et_2O. The organic layer was dried over $MgSO_4$, filtered, and concentrated under vacuum. The product was obtained E/Z izomer as 9/1 ratio. The residue was chromatographed on silica gel with EtOAc/hexane=1/5 to afford dimethyl 2-(but-2-ynyl)-2-(3-cyanoallyl)malonate colorless oil as (348 mg, 50% yield) (Takimoto et.al. 2006).

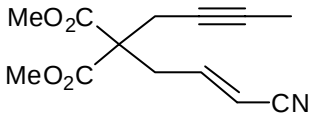


Figure 3.32 Dimethyl 2-(but-2-ynyl)-2-(3-cyanoallyl)malonate

Synthesis of diethyl 2-allyl-2-(but-2-ynyl)malonate(1k):

Diethyl allylmalonate (800 mg, 5 mmol) and 1-bromo-2-butyne (731.5 mg, 5.5 mmol) were added sequentially to a stirred suspension of NaH (132 mg, 5.5 mmol) in THF (50 mL) at 0 °C. The reaction mixture was stirred for 18 h at room temperature, quenched with water and extracted with EtOAc. The EtOAc extracts were washed with brine, dried with $MgSO_4$ and concentrated under vacuum. The resulting residue was chromatographed EtOAc / hexane = 1/5to yield diethyl 2-allyl-2-(but-2-ynyl)malonate (983 mg, 78% yield) (Kinder et. al. 2006) (Figure 3.30).

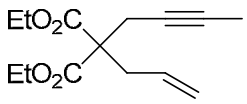


Figure 3.33 Diethyl 2-allyl-2-(but-2-ynyl)malonate

3.3.General Procedure for the Synthesis of Rh Complexes

$[Rh(cod)Cl]_2$ was synthesized in our laboratory. 7.3 mmol $RhCl_3.3H2O$, 6 mL 1,5-cyclooctadiene, (cod), 3 mL H_2O, and 35 mL EtOH were added into a 100-mL round-bottomed flask containing with a magnetic stirrer bar. Reaction mixture was refluxed overnight under nitrogen atmosphere (82% yield). In literature Na_2CO_3 was used as a base but we did not because the colour of the crystals should be yellow but when we used base the colour turned to olive green. (Giordano and Crabtree 1979).

$[Rh(cod)OH]_2$ was also synthesized in our laboratory (Uson, et al. 1985). $[Rh(cod)Cl]_2$ (0.65 mmol) in acetone (35 mL) was added to a round-bottom flask which contained a solution of potassium hydroxide (1.337 mmol) in water (4 mL). The mixture was stirred for two hours at room temperature, then yellow suspension was concentrated to ~10 mL with evaporation Then, 15 mL of water was added. Solid part was taken by filtration over a fine sintered-glass filter and it was washed with water (ten times in 5 mL portions) and vacuum-dried over phosphorus(V) oxide.

Also $[RhCl(CO)_2]_2$ was synthesized in our laboratory (Roberto et. al. 1993). $RhCl_3.3H_2O$ and SiO_2 (70-230 mesh, 60 Å as pour size) was mixed as the ratio of 1.5 % by weight according to Rh/SiO_2 and stirred in degassed water for overnight under Ar atmosphere. Then the slurry was dried under vacuo and was stayed 24 h in CO atmosphere (baloon pressure). This powder was extracted with acetone under Ar atmosphere and solvent was evaporated. Final black-brown solid was dissolved with dichloromethane and crystallized with pentane and dried under vacuo.

3.4.General Procedure for Rh Catalyzed Alkoxycarbonylative Cyclization of 1,6 Enynes

A mixture of enyne (0.3 mmol), $[Rh(COD)Cl]_2$ (5 mol% Rh) and hexadecane (0.15 mmol, as an internal standard) in solvent (5:0.05-MeOH:H_2O, pre-dried and degassed before used) was added into glass insert which was then placed into a stainless-steel reactor. Reactor was evacuated and purged with 10 atm CO twice. Then reactor was pressurized to 10 atm with CO and the mixture was stirred magnetically in a pre-heated oil bath for 16 h. After cooling reactor, the reaction mixture was recovered

with ethyl acetate. After that, a sample was taken from reaction mixture and diluted with ethyl acetate, then analyzed by GC and GC-MS and
isolated by column chromatography.

3.5.Characterization of Products

3.5.1.GC method

The samples were analyzed by GC/MS (HP GC/MS 6890/5973N on a HP-5MS, 30m, 0.25 mm capillary column, 5% phenylmethoxysiloxane with 0.25μm film thickness) and GC (19091J-413 HP-6890N on a 30m, 0.25 mm capillary column (5% dimetylsiloxane, 95% phenyldimethylsiloxane with a 0.25 μm film thickness and FID detector).

The GC program applied throughout the analysis is as follows: the column temperature was 40 °C at the beginning of the program and it was heated with a rate of 10 °C/min up to 300 °C, then it was kept at this temperature for 15 min. Throughout the analysis the injector and detector temperatures were kept constant at 280 °C and 320 °C, respectively. The analysis was performed on a split mode with a split ratio of 1/50.

For the calculation of amount of products and reactants, response factor of each product and reactant was determined on GC. For this purpose hexadecane was used as internal standard. The response factor of each compound was determined according to the amounts and areas under the peaks of internal standard and standard compound of interest. For the determination of response factor of a compound, a known amount of standard compound together with a known amount of internal standard dissolved and diluted with ethyl acetate, and then was injected to GC. After the analysis according to equation (3.1) response factor of compound was determined.

$$\text{R.F.} = \frac{\text{Area of internal standard}}{\text{Area of compound}} \times \frac{\text{Amount of compound}}{\text{Amount of internal standard}} \qquad (3.1)$$

In order to calculate the amount of both reactant and product at the end of reaction was determined by equation (3.2), according to peak area on GC analysis.

$$\text{Amount of compound} = \frac{\text{Amount of internal standard}}{\text{Area of internal standard}} \times \text{R.F.} \times \text{Area of compound} \quad (3.2)$$

3.5.2.Other Methods

NMR spectra were recorded on a Varian VnmrJ 400 spectrometer, a Varian Mercury AS 400 at, or a Bruker DRX 400 spectrometer. Infrared spectra were obtained using Perkin–Elmer Spectrum 100 by ATR method with neat samples. Mass analysis was performed with GC-MS (HP 6890/5973N) and HRMS analysis was recorded with HPLC-ESI-HRMS and GC-EI-HRMS (Thermo Electron). Melting Points were determined using an Electrothermal Melting Point Apparatus 9200.

Enyne 1a: ^{1}H-NMR (400 MHz, $CDCl_3$) δ: 6.79 (dt, *J*=16.4, 7.6 Hz, 1H), 5.92 (dt, *J*=14.8, 1.2 Hz, 1H), 4.19 (q, *J*=7.6 Hz, 4H), 3.71 (s, 3H), 2.90 (dd, *J*=7.6, 0.6 Hz, 2H), 2.73 (q, *J*= 2.4 Hz, 2H), 1.73 (t, *J*=2.1 Hz, 3H), 1.23 (t, *J*=7.6 Hz, 6H); ^{13}C-NMR (101 MHz, $CDCl_3$) δ: 169.6, 166.4, 142.8, 125.0, 79.5, 73.0, 61.9, 56.8, 51.6, 35.1, 23.5, 14.1, 3.6; FTIR (ν_{max}/cm^{-1}): 2952, 1729, 1658, 1443, 1275, 1188, 1172; MS (EI, m/z): 310 (5, M^+), 281 (50), 237 (90), 211 (48), 177 (41), 165 (100), 18 (44), 105 (40).

Enyne 1b: ^{1}H-NMR (400 MHz, $CDCl_3$) δ: 6.70 (dt, *J*=15.2, 7.6 Hz, 1H), 5.83 (dd, *J*=7.8, 1.0 Hz, 1H), 4.11 (q, *J*=7.6 Hz, 4H), 3.62 (s, 3H), 2.81 (dd, *J*=6.8, 0.6 Hz, 2H), 2.64 (t, *J*=2.4 Hz, 2H), 2.03 (tq, *J*=8.0, 2.4 Hz, 2H), 1.16 (t, *J*=7.6 Hz, 6H), 0.99 (t, *J*=8.0 Hz, 3H); ^{13}C-NMR (101 MHz, $CDCl_3$) δ: 169.4, 166.2, 142.6, 124.8, 85.4, 73.1, 61.7, 56.7, 51.4, 34.9, 23.3, 19.1, 14.0, 12.2; FTIR (ν_{max}/cm^{-1}): 2954, 1727, 1659, 1443, 1274, 1189, 1172; MS (EI, m/z): 324 (5, M^+) 295 (65), 251 (85), 179 (100), 151 (42), 117 (42), 91 (45).

Enyne 1c: ^{1}H-NMR (400 MHz, $CDCl_3$) δ: 6.68 (dt, *J*=8.0, 15.6 Hz, 1H), 5.81 (dt, *J*=15.6, 1.2 Hz, 1H), 4.10 (q, *J*=7.2 Hz, 4H), 3.94 (t, *J*=2.4 Hz, 2H), 3.60 (s, 3H), 3.21 (s, 3H), 2.81 (dd, *J*=7.6, 0.6 Hz, 2H), 2.73 (t, *J*=2.4 Hz, 2H), 1.14 (t, *J*=7.2 Hz,

6H); ^{13}C-NMR (101 MHz, $CDCl_3$) δ: 169.0, 166.0, 142.1, 125.0, 80.6, 79.5, 61.8, 59.7, 57.1, 56.4, 51.3, 34.9, 23.3, 13.9; FTIR (ν_{max}/cm^{-1}): 2936, 1727, 1274, 1184; MS (EI, m/z): 295 (100), 145 (30), 73 (50).

Enyne 1d: ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.90(d, *J*= 7.2 Hz, 2H), 7.56(t, *J*= 7.2 Hz, 1H), 7.46(t, *J*=7.6 Hz, 2H), 6.96(d, *J*= 15.2 Hz, 1H), 6.87-6.79(m, 1H), 3.75(s, 3H), 3.04(dd, *J*= 7.6, 0.8 Hz, 2H), 2.79(q, *J*= 2.8 Hz, 2H), 1.78(t, *J*= 2.4 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 190.5, 170.1, 142.4, 137.7, 133.0, 130.0, 128.7, 79.8, 73.0, 57.2, 53.1, 35.9, 23.8, 3.7, FT-IR (ν_{max}/cm^{-1}): 2953, 1733, 1436, 1202, 694; GC-MS (EI m/z) 328 (50, M^+), 313 (55), 269 (80), 209 (75), 184 (100), 165 (25), 105 (30)

Enyne 1e: ^{1}H NMR (400 MHz, $CDCl_3$) δ: 6.57 (dt, *J*=15.7, 7.7 Hz, 1H), 6.05 (d, *J*=15.8 Hz,1H), 3.67 (s, 6H), 2.85 (dd, *J*=7.7, 1.1 Hz, 2H), 2.67 (q, *J*=2.5 Hz, 2H), 2.16 (s, 3H), 1.68 (t, *J*=2.5 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 198.0, 169.9, 141.3, 134.7, 79.7, 72.7, 57.0, 52.9, 35.5, 26.9, 23.7, 3.4; FT-IR (ν_{max}/cm^{-1}): 2957, 1740, 1681, 1197; GC-MS (EI m/z) 266 (<1, M^+), 251 (25), 207 (85), 147 (100), 122 (80), 105 (30)

Enyne 1f: ^{1}H NMR (400 MHz, $CDCl_3$) δ: 6.95 (dt, *J*=16, 6.4 Hz, 1H), 5.84 (dt, *J*=15.6, 1.6 Hz, 1H), 4.18 (qd, *J*=6.8, 1.2 Hz, 2H), 2.30 (q, *J*=7.2 Hz, 2H), 2.18-2.14 (m, 2H), 1.77 (t, *J*=2.8 Hz, 3H), 1.63 (quint, *J*=7.2 Hz, 2H), 1.28 (td, *J*=5.6, 1.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 166.6, 148.3, 121.9, 78.2, 76.3, 60.2, 31.2, 27.3, 18.2, 14.3, 3.4, FT-IR (ν_{max}/cm^{-1}): 2930, 1718, 1262 cm^{-1}; GC-MS (EI m/z): 127 (100), 99 (50), 53 (45).

Enyne 1g: ^{1}H NMR (400 MHz, $CDCl_3$) δ: 6.95 (dt, *J*=16.4, 4.8 Hz,1H), 6.08 (dt, *J*=15.6, 2.0 Hz, 1H), 4.22-4.14 (m, 6H), 1.85 (t, *J*=1.2 Hz, 3H), 1.28 (td, *J*=6.8, 1.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 166.2, 143.7, 121.6, 83.1, 74.6, 68.0, 60.4, 58.5, 14.2, 3.6; FT-IR (ν_{max}/cm^{-1}): 2956, 1724, 1302, 1265 1027; GC-MS (EI m/z): 152 (15), 123 (65), 85 (45), 109 (40), 58 (100).

Enyne 1h: ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.71 (d, *J*=4.2 Hz, 2H), 7.30 (d, *J*=3.8 Hz, 2H), 6.81 (dt, *J*=8.0, 5.6 Hz, 1H), 6.02 (dt, *J*=7.8, 1.6 Hz, 1H), 3.99 (q, *J*=1.2 Hz, 2H), 3.94 (dd, *J*=0.8, 2.8 Hz, 2H), 3.71 (s, 3H), 2.4 (s, 3H), 1.52 (t, *J*=4.8 Hz, 3H), ^{13}C NMR (100 MHz, $CDCl_3$) δ: 165.9, 143.7, 142.0, 135.6, 129.4, 127.7, 127.4, 123.7, 82.3, 71.2, 51.6, 47.2, 37.3, 21.4, 3.1; FT-IR (ν_{max}/cm^{-1}): 3045, 1719, 1277, 1157; GC-MS (EI m/z): 223 (65), 195 (80),163 (80), 149 (85), 91 (100).

Enyne 1i: *E*-isomer: ^{1}H-NMR (400 MHz, $CDCl_3$) δ: 6.64 (dt, *J*=16.0, 8.0 Hz, 1H), 5.44 (dt, *J*=16.0, 1.6 Hz, 1H), 4.18-4.25 (m, 4H), 2.90 (dd, *J*=7.6, 1.6 Hz, 2H), 2.73 (q, *J*=2.4 Hz, 2H), 1.75 (t, *J*=2.8 Hz, 3H), 1.25 (t, *J*=7.2 Hz, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ: 169.3, 150.1, 116.9, 103.5, 80.0, 72.6, 62.1, 56.6, 36.5, 23.9, 14.1, 3.5; MS (EI, m/z) 277 (<1, M^+), 232 (12), 203 (30), 178 (15), 165 (100), 130 (46), 103 (15), 77 (14); *Z*-isomer: ^{1}H-NMR (400 MHz, $CDCl_3$) δ: 6.47 (dt, *J*=11.2, 7.6 Hz, 1H), 5.44 (dt, *J*=10.8, 1.6 Hz, 1H), 4.18-4.25 (m, 4H), 3.15 (dd, *J*=8.0, 1.2 Hz, 2H), 2.75 (q, *J*=2.4 Hz, 2H), 1.76 (t, *J*=2.8 Hz, 3H), 1.26 (t, *J*=7.2 Hz, 6H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ: 169.4, 148.8, 115.4, 102.8, 80.3, 72.5, 62.1, 56.6, 34.8, 23.9, 14.1, 3.5.

Product 3aa: Colorless oil; ^{1}H-NMR (400 MHz, $CDCl_3$) δ: 4.19 (q, *J*=7.6 Hz, 2H), 4.14 (q, *J*=7.6 Hz, 2H), 3.75-3.85 (m, 1H), 3.69 (s, 3H), 3.64 (s, 3H), 3.16 (d, J_{AB}=18.0 Hz, 1H), 2.98 (d, J_{AB}=18.0 Hz, 1H), 2.69 (dd, *J*=16.0, 3.6 Hz, 1H), 2.61 (dd, *J*=18.0, 8.4 Hz, 1H), 2.27 (dd, *J*=14.0, 4.0 Hz, 1H), 2.21 (dd, *J*=16.4, 11.2 Hz, 1H), 1.85 (d, *J*=1.2 Hz, 3H), 1.24 (t, *J*= 7.2 Hz, 3H), 1.20 (t, *J*=7.2 Hz, 3H); ^{13}C-NMR (101 MHz, $CDCl_3$) δ: 172.5, 171.8, 171.4, 167.5, 156.9, 121.1, 61.9, 61.7, 58.1 ,51.6, 51.5, 40.5, 39.4, 39.1, 38.5, 16.5, 13.94, 13.91; FTIR (ν_{max}/cm^{-1})**:** 2984, 2964, 1727, 1439, 1368, 1251, 1160, 1096, 1016, 859, 774; MS (EI, m/z): 370 (<1, M^+), 338 (85), 278 (39), 265 (60), 237 (100), 191 (60), 177 (48), 163 (41), 105 (50), 91 (33); HRMS (EI, m/z, [M^+])**:** 370.1628 (calculated), 370.1619 (found).

Product 3ab: Colorless oil; ^{1}H-NMR (400 MHz, $CDCl_3$) δ: 4.13-4.25 (m, 6H), 3.88-3.77 (m, 1H), 3.66 (s, 3H), 3.17 (d, J_{AB}=18.0 Hz, 1H), 2.99 (d, J_{AB}=18.0 Hz, 1H), 2.73 (dd, *J*=16.0, 3.6 Hz, 1H), 2.63 (dd, *J*=14.0, 8.4 Hz, 1H), 2.29 (dd, *J*=14.0, 4.0 Hz, 1H), 2.24 (dd, *J*=16.0, 10.8 Hz, 1H), 1.87 (d, *J*=1.2 Hz, 3H), 1.27 (t, *J*= 6.8 Hz, 3H), 1.26 (t, *J*=7.2 Hz, 3H), 1.23 (t, *J*=7.2 Hz, 3H); ^{13}C-NMR (101 MHz, $CDCl_3$) δ: 172.8, 172.1, 171.6, 167.4, 156.4, 121.7, 62.1, 62.0, 60.6, 58.4, 51.7, 40.7, 39.6, 39.3, 38.8, 16.8, 14.4, 14.19, 14.15; FTIR (ν_{max}/cm^{-1})**:** 2977, 2929, 2860, 1731, 1702, 1642, 1445, 1366, 1241, 1185, 1107, 1046, 862, 773; MS (EI, m/z): 384 (5, M^+), 311 (30), 278 (65), 251 (65), 237 (100), 205 (70), 177 (70), 105 (60); HRMS (EI, m/z, [M^+])**:** 384.1784 (calculated), 384.1770 (found).

Product 3ac: Colorless oil; ^{1}H-NMR (400 MHz, $CDCl_3$) δ: 4.01-4.23 (m, 6H), 3.77-3.88 (m, 1H), 3.65 (s, 3H), 3.14 (d, J_{AB}=18.0 Hz, 1H), 2.99 (d, J_{AB}=18.4 Hz, 1H), 2.72 (dd, *J*=16.0, 3.2 Hz, 1H), 2.62 (dd, *J*=14.0, 8.4 Hz, 1H), 2.29 (dd, *J*=14.0, 3.6 Hz, 1H), 2.23 (dd, *J*=16.0, 10.4 Hz, 1H), 1.87 (d, *J*=1.2 Hz, 3H), 1.66 (sext, *J*=7.6 Hz, 2H),

1.25 (t, *J*= 7.2 Hz, 3H), 1.21 (t, *J*=7.2 Hz, 3H), 0.93 (t, *J*=7.6 Hz, 3H); FTIR (ν_{max}/cm^{-1})**:** 2967, 2929, 1729, 1705, 1642, 1437, 1241, 1186, 1107, 1063, 732; ^{13}C-NMR (101 MHz, $CDCl_3$) δ: 172.7, 172.1, 171.6, 167.4, 156.5, 121.7, 66.3, 62.1, 61.9, 58.4, 51.7, 40.7, 39.6, 39.3, 38.7, 22.1, 16.8, 14.2, 14.1, 10.7; MS (EI, m/z): 352 (90), 279 (65), 251 (65), 205 (100); HRMS (EI, m/z, [M$^+$])**:** 398.1941 (calculated), 398.1934 (found).

Product 3ad: Colorless oil; ^{1}H-NMR (400 MHz, $CDCl_3$) δ: 4.05-4.23 (m, 6H), 3.75-3.85 (m, 1H), 3.64 (s, 3H), 3.16 (d, J_{AB}=18.0 Hz, 1H), 2.97 (d, J_{AB}=18.0 Hz, 1H), 2.71 (dd, *J*=16.0, 3.6 Hz, 1H), 2.61 (dd, *J*=14.0, 8.0 Hz, 1H), 2.28 (dd, *J*=14.0, 4.0 Hz, 1H), 2.21 (dd, *J*=16.0, 11.6 Hz, 1H), 1.85 (d, *J*=1.2 Hz, 3H), 1.60 (quint, *J*=6.8 Hz, 2H), 1.36 (sext, *J*=7.2 Hz, 2H), 1.24 (t, *J*=7.2 Hz, 3H), 1.20 (t, *J*=7.2 Hz, 3H), 0.91 (t, *J*=7.6 Hz, 3H); ^{13}C-NMR (101 MHz, $CDCl_3$) δ: 172.5, 171.9, 171.4, 167.2, 156.3, 121.5, 64.3, 61.9, 61.7, 58.1, 51.5, 40.5, 39.3, 39.1, 38.5, 30.6, 19.2, 16.6, 14.0, 13.9, 13.7; FTIR (ν_{max}/cm^{-1})**:** 2961, 2943, 2917, 1726, 1445, 1367, 1248, 1175, 1108, 1017, 860, 733; MS (EI, m/z): 398 (< 1), 366 (10), 338 (100), 278 (60), 265 (58), 251 (49), 237 (75), 223 (23), 205 (31), 191 (38), 177 (52), 163 (31), 149 (26), 105 (41), 91 (25); HRMS (EI, m/z, [M$^+$])**:** 412.2097 (calculated), 412.2089 (found).

Product 3ae: Colorless oil; ^{1}H-NMR (400 MHz, $CDCl_3$) δ: 5.05 (hept, *J*=6.4 Hz, 1H), 4.14-4.25 (m, 4H), 3.76-3.88 (m, 1H), 3.67 (s, 3H), 3.18 (d, J_{AB}=17.2 Hz, 1H), 2.98 (d, J_{AB}=18.0 Hz, 1H), 2.74 (dd, *J*=16.0, 3.6 Hz, 1H), 2.61 (dd, *J*=14.0, 8.4 Hz, 1H), 2.30 (dd, *J*=14.0, 4.0 Hz, 1H), 2.24 (dd, *J*=16.0, 11.2 Hz, 1H), 1.29-1.20 (m, 12H), ^{13}C-NMR (101 MHz, $CDCl_3$) δ: 127.8, 172.2, 171.7, 167.0, 155.7, 122.1, 68.0, 62.1, 61.9, 58.4, 51.7, 40.7, 39.6, 39.3, 38.8, 22.1, 21.9, 16.9, 14.2, 13.4; FTIR (ν_{max}/cm^{-1})**:** 2981, 2923, 1729, 1701, 1639, 1437, 1367, 1240, 1183, 1100, 1015, 861, 774; MS (EI, m/z): 324 (40), 251 (70), 223 (100), 91 (50); HRMS (EI, m/z, [M$^+$])**:** 398.1941 (calculated), 398.1939 (found).

Product 3af: Colorless oil; ^{1}H-NMR (400 MHz, $CDCl_3$) δ: 5.90-6.00 (m, 1H), 5.24 (dd, *J*=17.6, 1.2 Hz, 1H), 5.22 (dd, *J*=10.4, 1.2 Hz, 1H), 4.62 (d, *J*=5.6 Hz, 2H), 4.22 (q, *J*=7.2 Hz, 2H), 4.18 (q, *J*=7.6 Hz, 2H), 3.79 (s, 1H), 3.67 (s, 3H), 3.19 (d, *J*=18.0 Hz, 1H), 3.02 (d, J_{AB}=18.0 Hz, 1H), 2.73 (dd, J_{AB}=16.0, 4.0 Hz, 1H), 2.64 (dd, *J*=14.0, 8.4 Hz, 1H), 2.30 (dd, *J*=14.4, 4.0 Hz, 1H), 2.24 (dd, *J*=16.0, 11.2 Hz, 1H), 1.91 (s, 3H), 1.27 (t, *J*=7.2 Hz, 3H), 1.23 (t, *J*=7.2 Hz, 3H); ^{13}C-NMR (101 MHz, $CDCl_3$) δ: 172.7, 172.0, 171.5, 166.8, 157.3, 132.4, 121.3, 118.3, 65.3, 62.1, 61.9, 58.3, 51.7, 40.8, 39.5, 39.3, 38.6, 16.7, 14.2, 14.1; FTIR (ν_{max}/cm^{-1})**:** 2954, 2928, 1730, 1645,

1437, 1367, 1241, 1186, 1108, 1047; MS (EI, m/z): 396 (<1, M^+), 364 (15), 323 (13), 310 (20), 291 (20), 338 (90), 278 (60), 265 (65), 237 (100), 205 (50), 191 (60), 177 (70), 105 (65); HRMS (ESI, m/z, [$(M+H)^+$])**:** 397.1857 (calculated), 397.1846 (found).

Product 3ba: Colorless oil; ^{1}H-NMR (400 MHz, $CDCl_3$) δ: 4.12-4.24 (m, 4H), 3.73-3.82 (m, 1H), 3.71 (s, 3H), 3.66 (s, 3H), 3.15 (d, J_{AB}=17.6 Hz, 1H), 3.06 (d, J_{AB}=17.6 Hz, 1H), 2.63-2.72 (m, 2H), 2.19-2.32 (m, 2H), 1.26 (t, *J*= 7.2 Hz, 3H), 1.23 (t, *J*=7.2 Hz, 3H), 1.00 (d, *J*=7.2 Hz, 3H); ^{13}C-NMR (101 MHz, $CDCl_3$) δ: 172.7, 171.8, 171.5, 167.7, 155.9, 127.9, 62.0, 61.9, 58.4, 51.7, 51.5, 39.8, 39.2, 39.1, 24.2, 14.15, 14.11, 13.2; FTIR (ν_{max}/cm^{-1})**:** 2955, 2924, 2982, 1729, 1710, 1637, 1435, 1236, 1187, 1111, 1019, 860, 790, 733; MS (EI, m/z): 384 (<1, M^+), 352 (21), 338 (98), 311 (26), 278 (59), 265 (60), 251 (58), 237 (100), 205 (65), 191 (55), 177 (71), 163 (41), 149 (32), 133 (24), 105 (56), 91 (36), 77 (19); HRMS (EI, m/z, [M^+])**:** 384.1784 (calculated), 384.1770 (found).

Product 3ca: Colorless oil; ^{1}H-NMR (400 MHz, $CDCl_3$) δ: 4.20 (q, *J*=7.2 Hz, 2H), 4.15-4.19 (m, 2H), 4.15 (q, *J*=7.2 Hz, 2H), 3.85-3.78 (m, 1H), 3.73 (s, 3H), 3.66 (s, 3H), 3.30 (s, 3H), 3.22 (d, *J*=6.4 Hz, 2H), 2.72 (dd, *J*=16.4, 4.0 Hz, 1H), 2.67 (dd, *J*=17.6, 8.4 Hz, 1H), 2.31 (dd, *J*=10.0, 4.0 Hz, 1H), 2.22 (dd, *J*=14.4, 5.2 Hz, 1H), 1.25 (t, *J*=6.8 Hz, 3H), 1.21 (t, *J*=7.2 Hz, 3H); ^{13}C-NMR (101 MHz, $CDCl_3$) δ: 172.4, 171.6, 171.2, 166.9, 162.9, 123.3, 69.6, 62.0, 61.9, 58.4, 58.1, 51.8, 51.7, 40.1, 39.5, 38.8, 14.1; FTIR (ν_{max}/cm^{-1})**:** 2963, 2952, 1728, 1435, 1366, 1229, 1187, 1090, 1018, 860; MS (EI, m/z): 399 (<1), 369 (3), 343 (8), 313 (10), 269 (90), 195 (100); HRMS (ESI, m/z, [$(M+Na)^+$])**:** 423.1623 (calculated), 423.1626 (found).

Product 3da: Light yellow oil; ^{1}H-NMR (400 MHz, $CDCl_3$) δ: 7.92-7.98 (m, 2H), 7.50-7.57 (m, 1H), 7.41-7.47 (m, 2H), 3.92-4.03 (m, 1H), 3.71 (s, 3H), 3.66 (s, 6H), 3.36 (dd, *J*=17.2, 3.2 Hz, 1H), 3.29 (d, J_{AB}=18.4 Hz, 1H), 3.06 (d, J_{AB}=18.4 Hz, 1H), 2.94 (dd, *J*=17.2, 10.4 Hz, 1H), 2.70 (dd, *J*=14.0, 8.4 Hz, 1H), 2.27 (dd, *J*=14.0, 3.6 Hz, 1H), 1.91 (s, 3H); ^{13}C-NMR (101 MHz, $CDCl_3$) δ: 198.7, 172.7, 172.0, 167.7, 158.0, 137.2, 133.1, 128.7, 128.2, 121.0, 58.3, 53.0, 51.6, 43.5, 41.0, 39.6, 39.0, 16.7; FTIR (ν_{max}/cm^{-1})**:** 3068, 2951, 2801, 1732, 1705, 1685, 1448, 1434, 1260, 1242, 1200, 1101, 1077, 752, 690; MS (EI, m/z): 388 (<5, M^+), 356 (10), 328 (20), 191 (40), 105 (100), 77 (20); HRMS (EI, m/z, [M^+])**:** 388.1517 (calculated), 388.1510 (found).

Product 3ea: Colorless oil; ^{1}H-NMR (400 MHz, $CDCl_3$) δ: 3.82-3.86 (m, 1H), 3.75 (s, 3H), 3.71 (s, 3H), 3.68 (s, 3H), 3.16 (d, J_{AB}=18.0 Hz, 1H), 3.03 (d, J_{AB}=18.0 Hz,

1H), 2.79 (dd, *J*=16.8, 3.2 Hz, 1H), 2.60 (dd, *J*=14.0, 8.0 Hz, 1H), 2.35 (dd, *J*=16.8, 10.8 Hz, 1H), 2.20 (dd, *J*=14.0, 3.6 Hz, 1H), 2.11 (s, 3H), 1.86 (s, 3H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ: 207.3, 172.6, 172.0, 167.6, 158.0, 120.7, 58.2, 53.1, 51.6, 48.4, 40.8, 39.5, 38.7, 30.0, 16.6; FTIR (ν_{max}/cm^{-1})**:** 2955, 2924, 2850, 1734, 1676, 1629, 1436, 1361, 1329, 1254, 1203, 982; MS (EI, m/z): 294 (40), 266 (15), 251 (35), 234 (20), 207 (30), 191 (100), 165 (50); HRMS (EI, m/z, [M^+])**:** 326.1360 (calculated), 326.1363 (found).

Product 3fa: Colorless oil, ^{1}H-NMR (400 MHz , $CDCl_3$): δ 4.17-4.10 (m, 2H), 3.73 (s, 3H), 2.58 (dd, *J*=3.6, 7.6 Hz, 1H), 2.35-2.27 (m, 2H), 2.23-2.16 (m, 1H), 1.84 (s, 2H), 1.79 (d, *J*=7.2 Hz, 2H), 1.76-1.71 (m, 3H), 1.67-1.60 (m, 1H), 1.30 -1.23 (m, 3H) ^{13}C-NMR (100 MHz, $CDCl_3$): δ 172.7, 168.1, 161.7, 119.7, 60.2, 40.7, 37.9, 33.1, 28.9, 24.8, 22.1, 16.4, 14.2 FTIR (ν_{max}/cm^{-1})**:** 2927, 1713, 1650, 1436, 1368, 1271, 1159, 1096, 1039, 979, 861, 749 MS (EI, m/z): 240 (10, M+), 228(100), 155(30), 91(50) HRMS (ESI, m/z, [M^{+}])**:** 240.1362 (calculated), 240.1367 (found)

Product 3ga: Colorless oil; ^{1}H-NMR (400 MHz , $CDCl_3$) δ: 4.49 (d, J_{AB}=16.0 Hz, 1H), 4.25 (d, J_{AB}=16.4 Hz, 1H), 4.13 (q, *J*=7.6 Hz, 2H), 3.98 (d, *J*=8.8 Hz, 1H), 3.75-3.79 (m, 1H), 3.73 (s, 3H), 2.56-2.62 (m, 1H), 2.40-2.48 (m, 1H), 1.87-1.97 (m, 1H), 1.77 (s, 3H), 1.24 (t, *J*=7.6 Hz, 3H); ^{13}C-NMR (101 MHz, $CDCl_3$) δ: 172.3, 167.1, 156.4, 118.8, 73.9, 71.3, 60.5, 51.6, 40.8, 36.8, 15.7, 14.2; FTIR (ν_{max}/cm^{-1})**:** 2955, 2927, 1718, 1436, 1373, 1277, 1200, 1176, 1116, 1020, 989, 771; MS (EI, m/z): 242 (≤ 5, M^+), 210 (100), 196 (12), 182 30), 169 (50), 153 (42), 136 (30), 109 (45), 95 (40), 79 (30); HRMS (ESI, m/z, [$(M+H)^+$])**:** 243.1237 (calculated), 243.1226 (found).

Product 3ha: White solid; M.P: 116-118 ^{o}C; ^{1}H-NMR (400 MHz, $CDCl_3$) δ: 7.71 (d, *J*=8.0 Hz, 2H), 7.51 (d, *J*=4.0 Hz, 2H), 4.13 (dt, *J*=16.4, 1.6 Hz, 1H), 3.77-3.84 (m, 1H), 3.70 (s, 6H), 3.57 (d, *J*=9.6 Hz, 1H), 3.49 (dd, *J*=12.4, 1.2 Hz, 1H), 2.94 (ddd, *J*=10.0, 6.0, 1.2 Hz, 1H), 2.59 (ddd, J_{AB}=12.4, 3.2, 1.2 Hz, 1H), 2.51 (dd, J_{AB}=16.4, 10.0 Hz, 1H), 2.44 (s, 3H), 1.76-1.78 (m, 3H); ^{13}C-NMR (101 MHz, $CDCl_3$) δ: 172.3, 166.7, 152.0, 144.1, 131.6, 129.8, 128.0, 121.5, 53.4, 52.0, 51.8, 51.7, 39.5, 37.1, 21.5, 15.9; FTIR (ν_{max}/cm^{-1})**:** 2954, 2924, 2852, 1713, 1436, 1347, 1269, 1160, 815, 735, 664, 599, 648; MS (EI, m/z): 381 (15, M^+), 369 (10), 327 (15), 295 (35), 269 (100), 195 (65); HRMS (ESI, m/z, [$(M+H)^+$])**:** 382.1319 (calculated), 382.1322 (found).

Product 3ia: Colorless oil; ^{1}H-NMR (400 MHz, $CDCl_3$) δ: 4.24 (q, *J*=7.2 Hz, 2H), 4.18 (q, *J*=7.2 Hz, 2H), 3.73 (s, 3H), 3.16 (d, J_{AB}=18.4 Hz, 1H), 3.06 (d, J_{AB}=18.0

Hz, 1H), 2.76 (dd, *J*=16.4, 4.0 Hz, 1H), 2.69 (dd, *J*=14.0, 8.8 Hz, 1H), 1.89 (d, *J*=1.2 Hz, 3H), 1.29 (t, *J*=7.2 Hz, 3H), 1.23 (t, *J*=7.2 Hz, 3H); ^{13}C-NMR (101 MHz, $CDCl_3$) δ: 171.5, 170.9, 167.2, 154.7, 123.0, 118.6, 62.0, 61.9, 57.9, 51.7, 40.5, 39.3, 38.6, 21.9, 16.6, 14.0; FTIR (ν_{max}/cm^{-1})**:** 2982, 2224, 1727, 1644, 1436, 1367, 1254, 1188, 1129, 1109, 860, 772, 745; MS (EI, m/z): 337 (<1, M^+), 305 (40), 263 (15), 232 (100), 204 (35), 158 (15); HRMS (ESI, m/z, [$(M+H)^+$])**:** 338.1605 (calculated), 338.1599 (found).

Product 3ja: Colorless oil, ^{1}H-NMR (400 MHz , $CDCl_3$): δ 3.79(s, 3H), 3.73(s, 6H), 3.18(dt, *J*=18.0, 1.6 Hz, 1H), 3.08(d, *J*= 18.4 Hz, 1H), 2.79-2.64(m, 2H), 2.53-2.44(m, 2H), 1.90(d, *J*= 1.6 Hz, 3H), ^{13}C-NMR (100 MHz, $CDCl_3$): δ171.8, 171.4, 167.2, 154.4, 123.2, 118.6, 57.8, 53.2, 53.2, 51.8, 40.6, 39.2, 38.7, 21.9, 16.6, FTIR (ν_{max}/cm^{-1})**:** 2857, 1711, 1644, 1496, 1453, 1268, 1197, 1095, 1028, 907, 772, 735, 697 MS (EI, m/z): 309 (≤ 1,M+), 207(80), 179(25), 131(30), 103(45), 77(100), 51(40).

Product 6aa: ^{1}H-NMR (400 MHz , $CDCl_3$): δ 6.66 (td, *J*=7.6, 1.2 Hz, 1H), 4.19 (q, *J*= 7.2 Hz, 4H), 3.72 (s, 3H), 2.75 (d, J=8.0 Hz, 2H), 1.86 (s, 3H), 1.25(t, *J*=7.6 Hz, 6H), ^{13}C-NMR (100 MHz, $CDCl_3$): δ 171.7, 168.3, 135.9, 130.8, 61.7, 53.4, 51.9, 34.8, 20.1, 14.2, 12.8, FTIR (ν_{max}/cm^{-1})**:** 2876, 2851, 1732, 1462, 1377, 1296, 1239, 1193, 1106, 1020, 860, 802, 740, MS (EI, m/z): 286 (5, M+), 241 (40), 181 (100), 174 (90), 167 (40), 153 (50), 125 (40), 79 (30)

Product 6aa': ^{1}H-NMR (400 MHz , $CDCl_3$): δ 6.98 (q, *J*= 7.2 Hz, 1H), 4.23-4.19 (q, *J*= 7.2 Hz, 4H), 3.68 (s, 3H), 3.04 (s, 2H), 1.80 (d, J= 7.6 Hz, 3H), 1.30 (s, 3H), 1.24 (t, 6H, J= 7.2 Hz), ^{13}C-NMR (100 MHz, $CDCl_3$): δ 172.2, 141.4, 128.8, 61.5, 53.7, 51.9, 31.0, 19.7, 15.2, 14.1, FTIR (ν_{max}/cm^{-1})**:** 2876, 2851, 1732, 1462, 1377, 1296, 1239, 1193, 1106, 1020, 860, 802, 740, MS (EI, m/z): 286 (<5, M+), 254 (10), 153 (100), 139 (65), 153 (50), 125 (30)

Product 6ba: ^{1}H-NMR (400 MHz , $CDCl_3$): δ 7.86 (s, 1H), 7.38-7.35 (m, 3H), 7.25-7.14 (m, 5H), 7.04 (d, *J*=1.6 Hz, 2H), 3.80 (s, 3H), ^{13}C-NMR (100 MHz, $CDCl_3$): δ 168.5, 140.7, 136.1, 134.8, 132.7, 130.8, 129.9, 129.2, 128.8, 128.4, 128.1, 52.6, FTIR (ν_{max}/cm^{-1}): 2926, 1701, 1623, 1492, 1435, 1276, 1247, 1204, 1166, 1076, 1036, 1018, 933, 792, 774, 756, 707, 561, MS (EI, m/z): 238(<1, M+), 205 (10), 178 (100), 152 (10), 121 (85), HRMS (EI, m/z, [M^+]): 238.0994 (calculated), 238.0991 (found).

Product 6ca: ^{1}H-NMR (400 MHz , $CDCl_3$): δ 6.74 (t, *J*=7.6 Hz, 1H), 3.71 (s, 3H), 2.28-2.24 (m, 2H), 2.15-2.12 (m, 2H), 1.45-1.37 (m, 4H), 0.95-0.87 (m, 6H), ^{13}C-NMR (100 MHz, $CDCl_3$): δ 168.7, 142.9, 132.3, 51.6, 30.7, 28.8, 22.6, 22.2, 14.1, 14.0,

FTIR (ν_{max}/cm^{-1}): 2960, 2872, 1712, 1644, 1463, 1435, 1281, 1215, 1145, 1108, 1066, 917, 822, 754, MS (EI, m/z):170 (90, M+), 141(100), 127(60), 109(85), 81(90), 69(75).

Product 6da: ^{1}H-NMR (400 MHz , $CDCl_3$): δ 7.69 (d, *J*= 1.6 Hz, 1H), 7.39 (d, *J*= 4.4 Hz, 4H), 7.34-7.31 (m, 1H), 3.82 (s, 3H), 2.13 (s, 3H), ^{13}C-NMR (100 MHz, $CDCl_3$): δ 169.3, 139.1, 136.0, 129.8, 128.5, 128.5, 52.2, 14.2, FTIR (ν_{max}/cm^{-1}): 2947, 1966, 1706, 1633, 1449, 1435, 1245, 1214, 117, 950, 933, 766, 708, 693, 591, MS (EI, m/z):176 (75, M+), 144 (60), 115 (100), 91 (25).

Product 6da': ^{1}H-NMR (400 MHz , $CDCl_3$): δ 7.40-7.36 (m, 2H), 7.34-7.30 (m, 1H), 7.19-7.16 (m, 3H), 3.73(s, 3H), 1.74 (d, *J*= 7.2 Hz, 3H), ^{13}C-NMR (100 MHz, $CDCl_3$): δ 167.8, 140.4, 135.2, 134.8, 129.9, 128.2, 127.5, 52.2, 15.6, FTIR (ν_{max}/cm^{-1}): 3417, 3057, 2949, 2851, 1713, 1639, 1495, 1434, 1247, 1194, 1109, 1041, 1028,894, 770, 698, 680, MS (EI, m/z):176 (80, M+), 145 (40), 115 (100), 91 (35).

CHAPTER 4

RESULTS AND DISCUSSION

In this study rhodium catalyzed carbonylation of 1,6 enynes possessing an electron-deficient alkenyl moiety in an alcohol reagent in the presence of a rhodium complex proceeded stereo- and chemoselectivly to afford exocyclic α,β enoates. The configuration of the olefinic group was assigned by an NOE study (Figure 4.1).

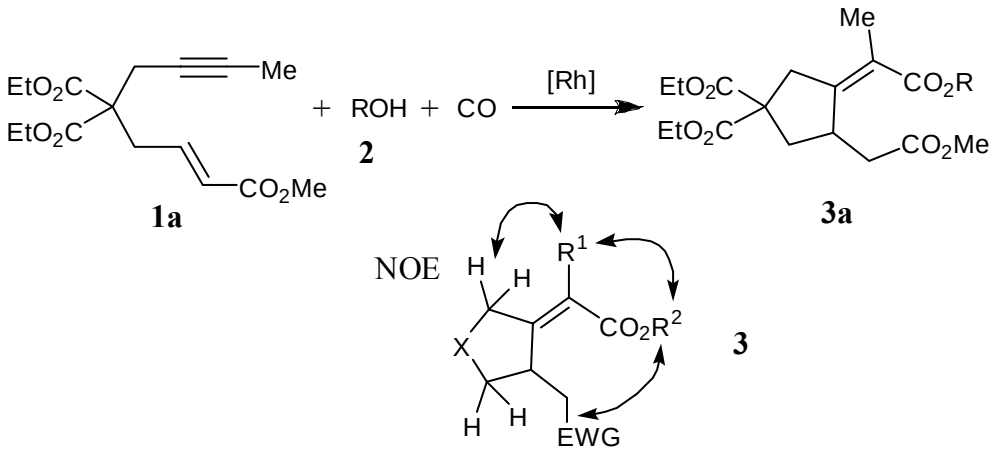


Figure 4.1.Alkoxycarbonylative cyclization of enyne **1a**

1,6 Enyne having an ester functionality on the olefinic site (**1a**) and methanol as alcohol reagent was used during optimization process. During optimization of reaction conditions reaction temperature, CO pressure, water amount and rhodium complex derivatives were investigated.

We initially attempted to determine the optimum reaction temperature. Best result was obtained at 100 ^{o}C reaction temperature. Increasing the reaction temperature to 120 ºC reduced the selective formation of the desired product, owing to the increased formation of intricate by-products, the conversion of the enyne **1a** was not complete at the lower reaction temperatures of 50 ºC and 80 ºC (Table 4.1, entries 4-5).

The CO pressure was set at 10 atm as optimum condition(Table 4.1, entry 1). Beside 10 atm, 5 and 15 atm of CO was investigated (Table 4.1, entries7-8). Both CO pressures caused decreasing in the formation of product **3aa**.

The presence of a small amount of water within the reaction mixture seems beneficial for the formation of **3aa** (Table 4.1). The presence of 50 mg of water in the reaction medium caused an increase in the formation of **3aa** (entry 2), but a larger content of water (250 mg) was detrimental to the selectivity of the process (entry 3).

Table 4.1.Effect of reaction parameters on the rhodium-catalyzed methoxycarbonylative cyclisation of **1a**.[a)]

Entry	*T* [ºC]	P_{CO} [atm]	Water [mg]	Conv. [%][a)]	Yield **3aa** [%][b)]
1	100	10	0	100	75
2	100	10	50	100	82
3	100	10	250	100	53
4	50	10	50	47	24
5	80	10	50	88	67
6	120	10	50	100	42
7	100	5	50	100	68
8	100	15	50	100	71

[a)] Reactions were run with 0.3 mmol of **1a** and $[RhCl(cod)]_2$ (5% Rh) in 5 mL of methanol for 16 h. [b)]Determined by GC

The activity of various rhodium complexes was also surveyed at the 5% of rhodium loading level (Table 4.2). The complexes, $Rh(cod)_2BF_4$, $[RhCl(CO)]_2$, $[RhCl(nbd)]_2$, and $[RhCl(cod)]_2$ displayed similarly higher activities compared to the other complexes tested (entries 1-9), the yields being within the range of 77-82% with these complexes (entries 1-4). A somewhat lower but reasonable yield can be obtained even with the non-ligated $RhCl_3 \bullet 3\ H_2O$ compound (entry 5).

Table 4.2.Effect of the nature of the catalyst precursor on the rhodium-catalyzed methoxycarbonylative cyclisation of **1a**.[a)]

Entry	Catalyst	Conv. [%] [b)]	Yield **3aa** [%] [b)]
1	$Rh(cod)_2BF_4$	100	78
2	$[RhCl(CO)]_2$	100	79
3	$[RhCl(nbd)]_2$	100	77
4	$[RhCl(cod)]_2$	100	82
5	$RhCl_3 \bullet 3\ H_2O$	100	68
6	$[RhCl(C_2H_4)_2]_2$	100	61
7	$[Rhacac(C_2H_4)_2]_2$	100	45
8	$[RhOH(cod)]_2$	100	52
9	$[Rh(PPh_3)_3(CO)H]$	100	72
10	$[RhCl(cod)]_2$ + 20% PPh_3	45	23
11	$[RhCl(cod)]_2$ + 20% $P(OPh)_3$	71	50
12	$[RhCl(cod)]_2$ + 10% dppe	14	10
13	$[RhCl(cod)]_2$ + 10% dppp	65	31
14	$[RhCl(cod)]_2$ + 5.5% R,S-BINAP	48	25
15[c)]	$[RhCl(cod)]_2$	100	81
16[d)]	$[RhCl(cod)]_2$	100	70

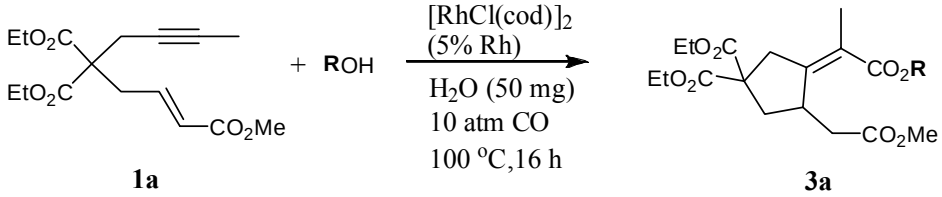
[a)] Reactions were run with 0.3 mmol of **1a**, 50 mg of water, and 5% of Rh at 100 ºC under 10 atm of CO pressure in 5 mL of methanol for 16 h. [b)] Determined by GC. [c)] Performed with 10% of Rh. [d)]Performed with 3% of Rh.

In contrast with the activity of the phosphine- ligated rhodium complex, $[Rh(PPh_3)_3(CO)H]$, which led to relatively good result (entry 9), the presence of PPh_3, $P(OPh)_3$, or bidentate phosphorous ligands greatly reduced the activity of the rhodium catalyst coming from the $[RhCl(cod)]_2$ complex (entries 10-14). It was needless to use higher concentration of rhodium, since a comparable result was also obtained at the 10% Rh loading level (entry 15). Yet the yield decreased when using a lower levels of catalyst loading (3% Rh) (entry 16).

After the optimization studies we determined the optimum reaction conditions as 100 ^{o}C temperature, 10 atm of CO, 50 mg of water and choosed $[RhCl(cod)]_2$ (5 % Rh) as catalyst precursor.

Then we investigated the scope of the method for various alcohols and enyne reagents under the optimum reaction conditions. The carbonylative reaction of **1a** with MeOH, EtOH, or primary saturated C_3 and C_4 alcohols all gave rise to the corresponding cyclic products in good isolated yields (Table 4.3, entries 1-4). Moderate yields of **3a** products could also be obtained with a bulky alcohol, *i*-propyl alcohol, or a functionalized alcohol, allyl alcohol (entries 5 and 6).

Table 4.3. Rhodium-catalyzed alkoxycarbonylative reaction of **1a** with various alcohols.[a)]



1a **3a**

Entry	**R**OH	Isolated Yield [%]
1	MeOH	79 (**3aa**)
2	EtOH	66 (**3ab**)
3	PrOH	64 (**3ac**)
4	BuOH	64 (**3ad**)
5	*i*-PrOH	43 (**3ae**)
6	Allyl alcohol	54 (**3af**)

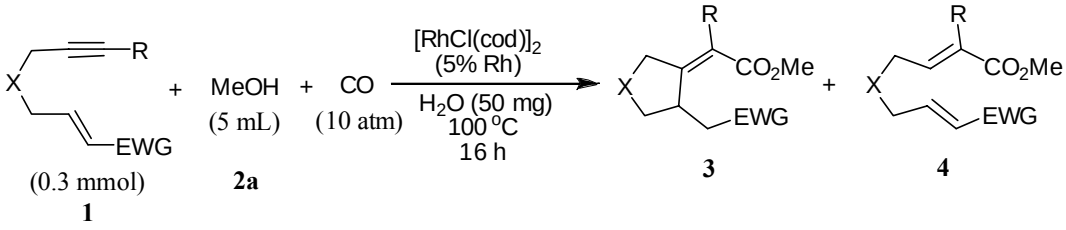
[a)]Reactions were run with 0.3 mmol of **1a**, 50 mg of water, and $[RhCl(cod)]_2$ (5% Rh) at 100 ºC under 10 atm of CO pressure in 5 mL of alcohol for 16 h.

The scope of enyne substrates were also surveyed with different tether types, substituent groups on both alkynyl and olefinic part (Table 4.4). The method is suitable for enynes having a malonate based tether bearing an ethyl (**1b**) or CH_2OMe (**1c**) substituent on the alkynyl group for providing the corresponding methyl 2-(cyclopentenylidene)acetate in good isolated yields (entries 1-2).Beside ester functionality on alkenyl part, phenyl ketone (**1d**) and methyl ketone (**1e**) were also applicable groups (entries 3-4). Enyne **1f**, having a trimethylene tether, gave a complex

mixture and consequently, the desired product **3fa** was obtained in low yield as determined by ^{1}H-NMR analysis (entry 5). Also with oxygen-bridged enyne **1g**, good yield was obtained (entry 6).

Interestingly, the presence of a nitrogen functionality within the structure of enyne as a linker (**1h**) or a substituent on the olefinic site (**1i**), gave rise to hydroesterification products **4ha** and **4ia** in addition to the formation of the desired products **3ha** and **3ia**, respectively (entries 7 and 8). When reaction was performed with enyne **1k,** reactant was consumed and undefined complex mixture formd but no product formation. So this result indicates that the olefinic moiety must be sufficiently electrophilic to be amenable to undergoing intramolecular carborhodation (entry 9).

Table 4.4.Rhodium-catalyzed methoxycarbonylative reaction of 1,6-enynes.



Entry	X	R	EWG	Isolated Yield [%] **3:4**
1	$C(CO_2Et)_2$	Et	CO_2Me	61:0 (**3ba**)
2	$C(CO_2Et)_2$	CH_2OMe	CO_2Me	62:0 (**3ca**)
3[a]	$C(CO_2Me)_2$	Me	COPh	64:0 (**3da**)
4	$C(CO_2Me)_2$	Me	COMe	71:0 (**3ea**)
5	CH_2	Me	CO_2Et	31:0 (**3fa**)
6	O	Me	CO_2Et	68:0 (**3ga**)
7	NTs	Me	CO_2Me	41:14 (**3ha**)
8[b]	$C(CO_2Et)_2$	Me	CN	44:22 (**3ia**)
9	$C(CO_2Et)_2$	Me	H	0 (**3ka**)
10[c]	$C(CO_2Me)_2$	Me	CN	52:9 (**3ja**)

[a)]Performed with 8% of Rh. [b)] The substrate **1i** was an isomeric mixture of *E* and *Z* (3/1) [c)] The substrate **1j** was isomeric mixture of E and Z (9/1).

We performed reaction with alkyne **5a** which lacks an alkenyl moity A regio-isomeric hydroesterified mixture was formed from **5a** indicating that coordination of the alkenyl moiety to the rhodium has no significant influence on the reactivity of **1**

toward alkoxycarbonylation, but rather governed the resulting regioselectivity with enynes (Figure 4.2).

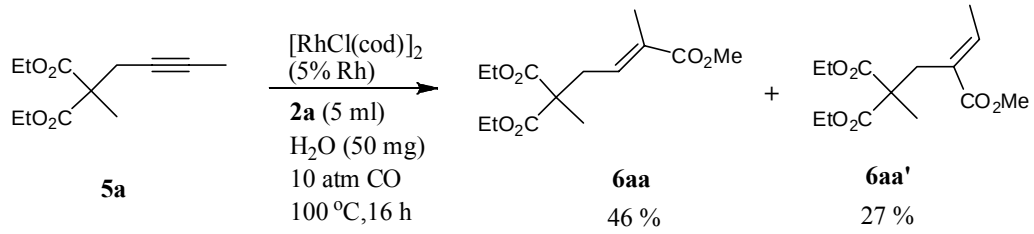
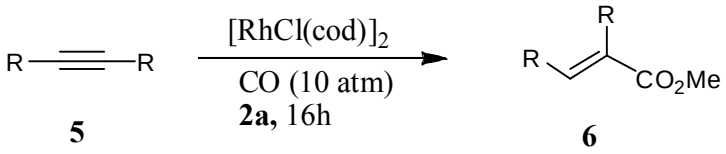


Figure 4.2.Rhodium-catalyzed methoxycarbonylation of diethyl 2-(but-2-ynyl)-2-methylmalonate (**5a**).

The method was also applied on several simple alkynes (Table 4.5). (*E*)-Methyl 2,3-diphenylacrylate (**6ba**) product was recovered in 65% yield from the reaction of diphenyl acetylene in MeOH under the established conditions for enynes **1** (entry 1). Modification of experimental conditions which involved a lower reaction temperature of 80 °C and catalyst loading (3% Rh) with respect to the substrate improved the yield to 75% (entry 2). The method was also suitable for a dialkylacetylene, 4-octyne (entry 3), yet not regioselective for hydroesterification of an unsymmetric alkyne, 1-phenylpropyne (entry 4).

Table 4.5.Rhodium-catalyzed hydroesterification of alkynes.



Entry	R	Isolated Yield [%]
1[a)]	Ph	65 (**6ba**)
2[b)]	Ph	75 (**6ba**)
3[b)]	Pr	73 (**6ca**)
4[b)]	Ph, Me	80 (1:1)[c)] (**6da**)

[a)] Performed under the conditions of Table 4.4. [b)] Performed with 1mmol of **5** and 3% Rh in 10 ml of **2a** at 80 °C.[c)] Isomeric ratio

In view of the results obtained with enynes and alkynes, the rhodium-catalyzed alkoxycarbonylative cyclization of 1,6-enynes should proceed through a carboalkoxyrhodium intermediate **A** (Mise et. al. 1983) followed by intramolecular *cis* addition to the triple bond in a regioselective manner to give the alkenylrhodium(I) **B** (Figure 4.3). Intra-carborhodation onto the tethered double bond (**C**) and subsequent protodemetalation steps generate the desired cyclized product **3**.

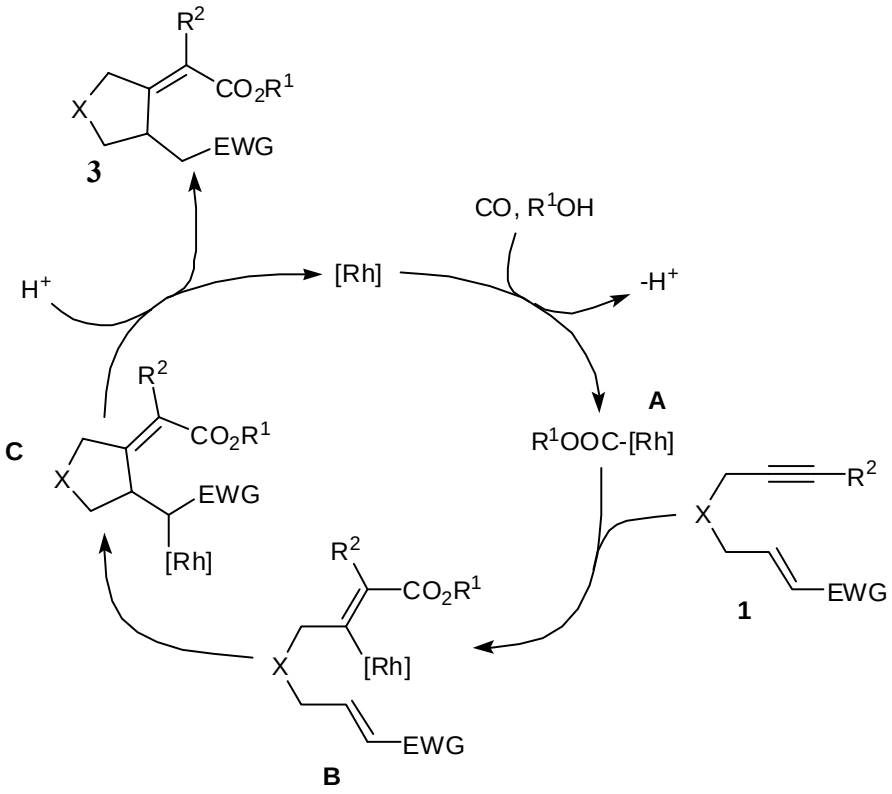


Figure 4.3.Reaction mechanism of alkoxycarbonylation of 1,6-enynes.

Relatively stronger intramolecular coordination of the rhodium with the nitrogen functionality within the intermediate **B** could account for the formation of hydroesterification products when reacted with either the enyne **1h** or **1i** (Figure 4.4). Existence of such coordinative interactions may obviate the next carborhodation step (formation of the intermediate **C**), leading to the protodemetalated hydroesterification products **4ha** and **4ia**, respectively. It should be noted that the substrate **1i** was a mixture of *E*- and *Z*- isomers in the ratio of 3 to 1, and such a coordinative interaction should be more achievable with the *Z*-configured isomer since its spatial arrangement would allow the rhodium and the nitrile group to adopt a closer distance. When reaction was

performed with substrate **1j** that the isomeric ratio (E and Z) was 9/1, formation of hydroesterification product(**4ja**) decreased (Table 4.4). So, this result supports that the Z isomer caused the formation of hydroesterification product.

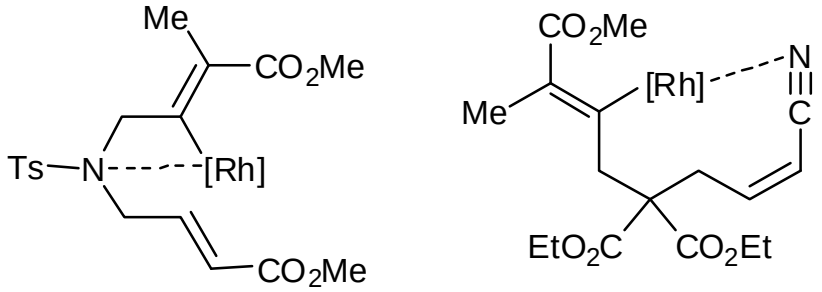


Figure 4.4.Alkenylrhodium(I) intermediates (**C**) which may arise from the enynes **1h** and ***Z*-1i**.

CHAPTER 5

CONCLUSION

In this study we succeeded that rhodium catalyzed carbonylation of 1,6 enyne derivatives with an alkenyl moiety substituted by an electron withdrawing group in an alcohol constructs five-membered rings with an exocyclic alkenyl ester group.

This study is really important owing to lots of natural products and biologically active molecules contain cyclopentane and five-membered heterocyclic units and functionalized five-membered rings are valuable building blocks for the production of complex molecules.

In summary we developed a new methodology for the synthesis of biologically active functionalized five-membered rings in atom economical and mild way.

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APPENDIX A

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

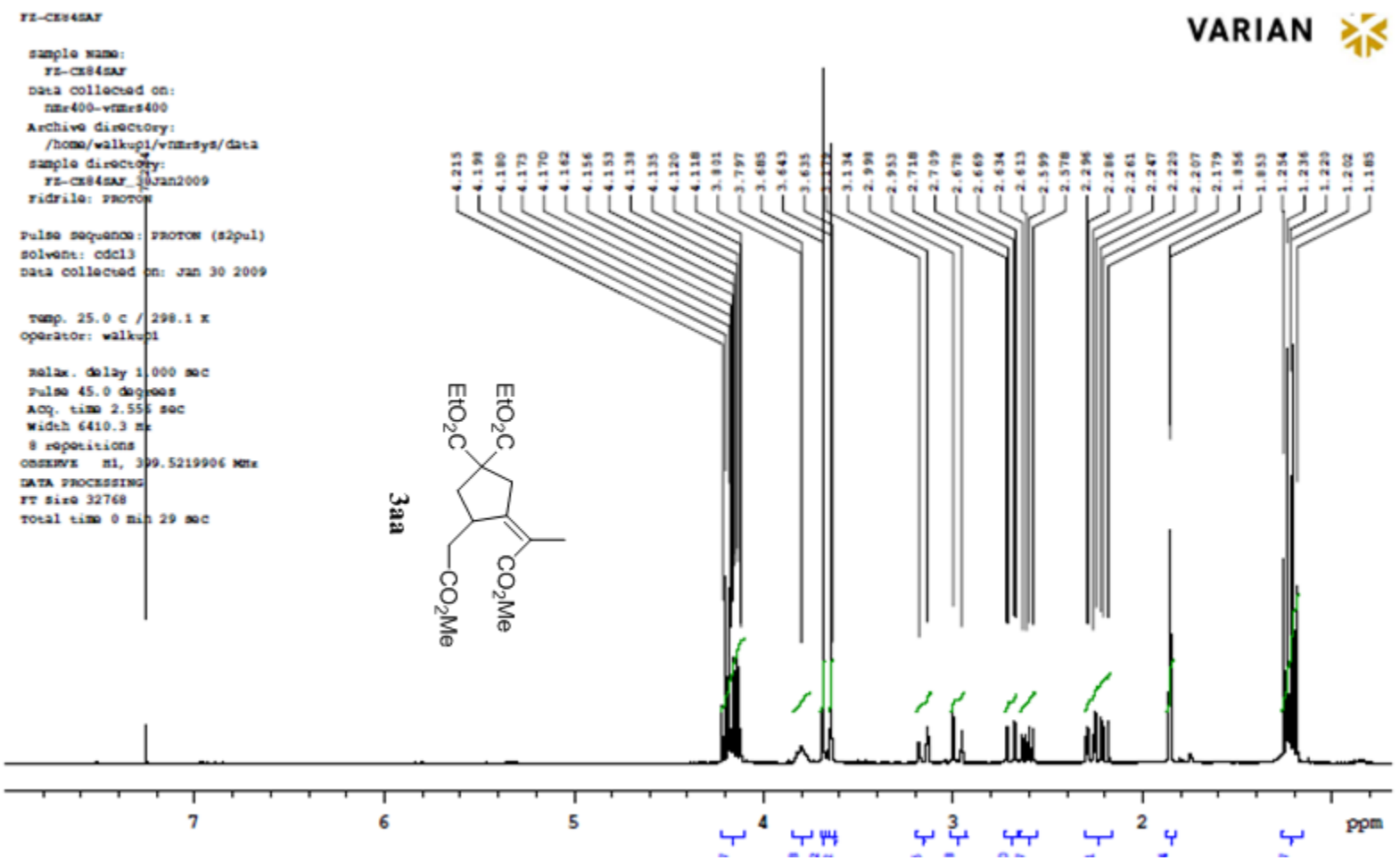

Figure A.1. [1] H NMR of (Z)-diethyl 3-(1-methoxy-1-oxopropan-2-ylidene)-4-(2-methoxy-2-oxoethyl)cyclopentane-1,1-dicarboxylate

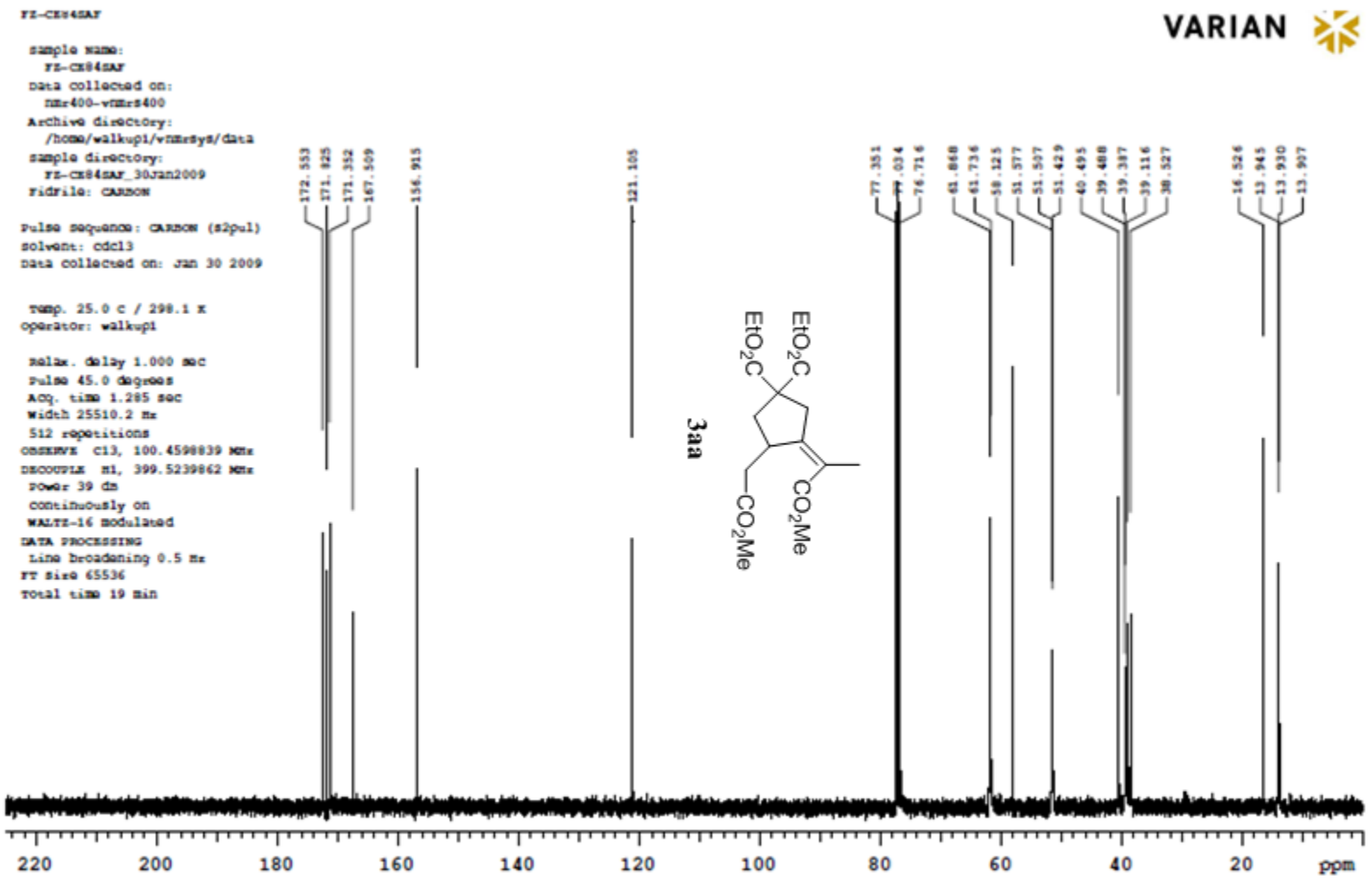

Figure A.2. ^{13}C NMR of (Z)-diethyl 3-(1-methoxy-1-oxopropan-2-ylidene)-4-(2-methoxy-2-oxoethyl)cyclopentane-1,1-dicarboxylate

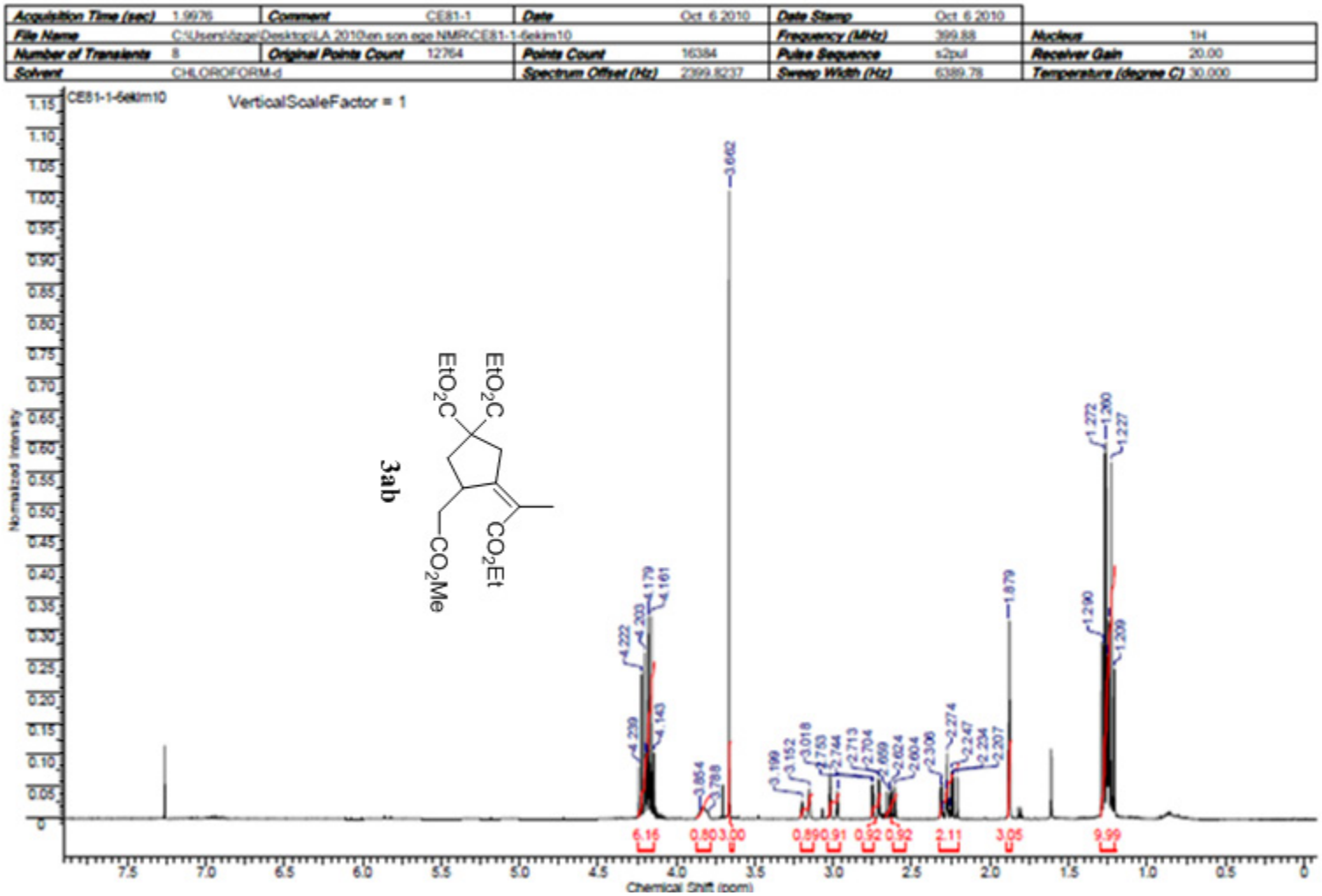

Figure A.3. [1] H NMR of (Z)-diethyl 3-(1-ethoxy-1-oxopropan-2-ylidene)-4-(2-methoxy-2-oxoethyl)cyclopentane-1,1-dicarboxylate

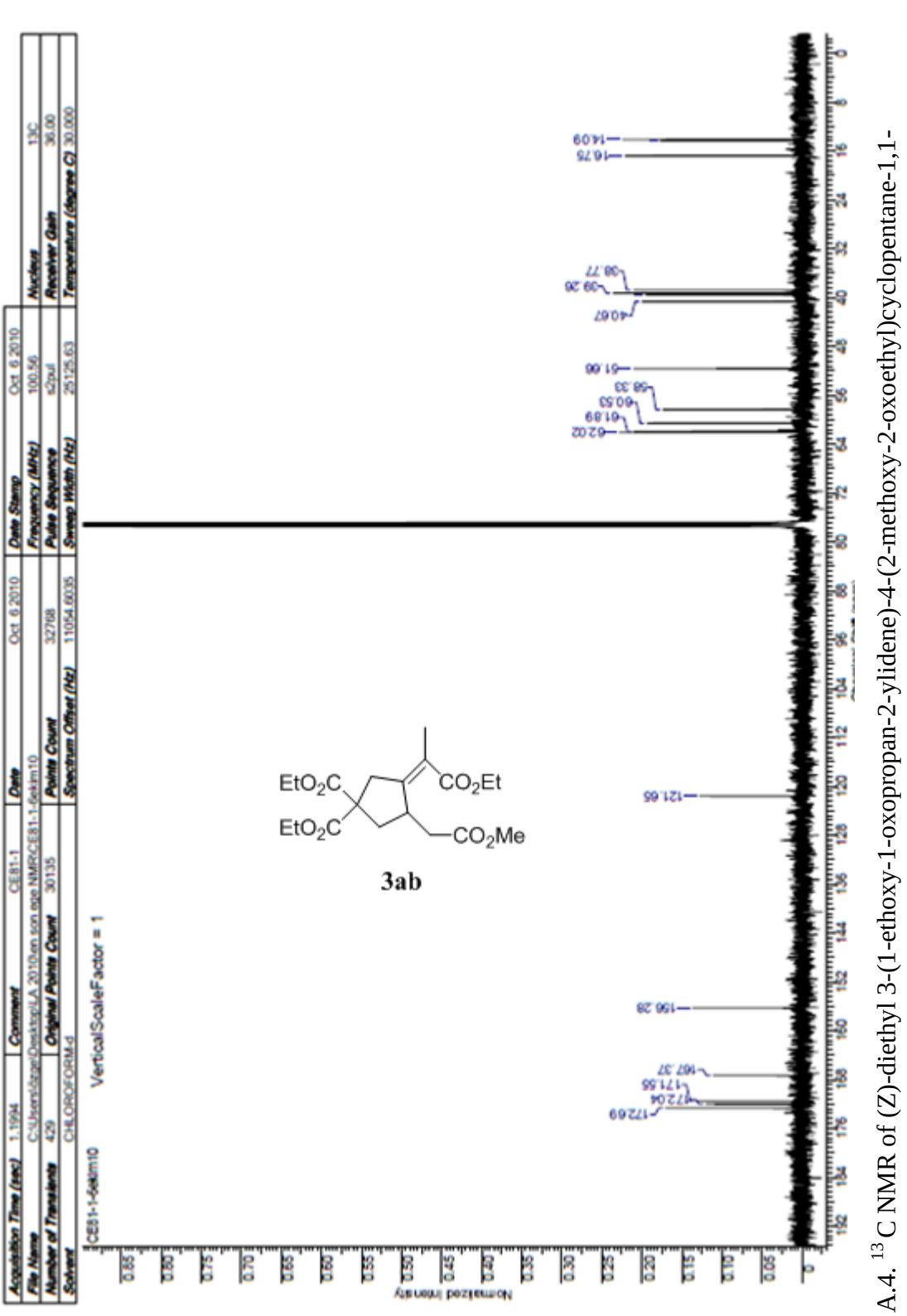

Figure A.4. ^{13}C NMR of (Z)-diethyl 3-(1-ethoxy-1-oxopropan-2-ylidene)-4-(2-methoxy-2-oxoethyl)cyclopentane-1,1-dicarboxylate

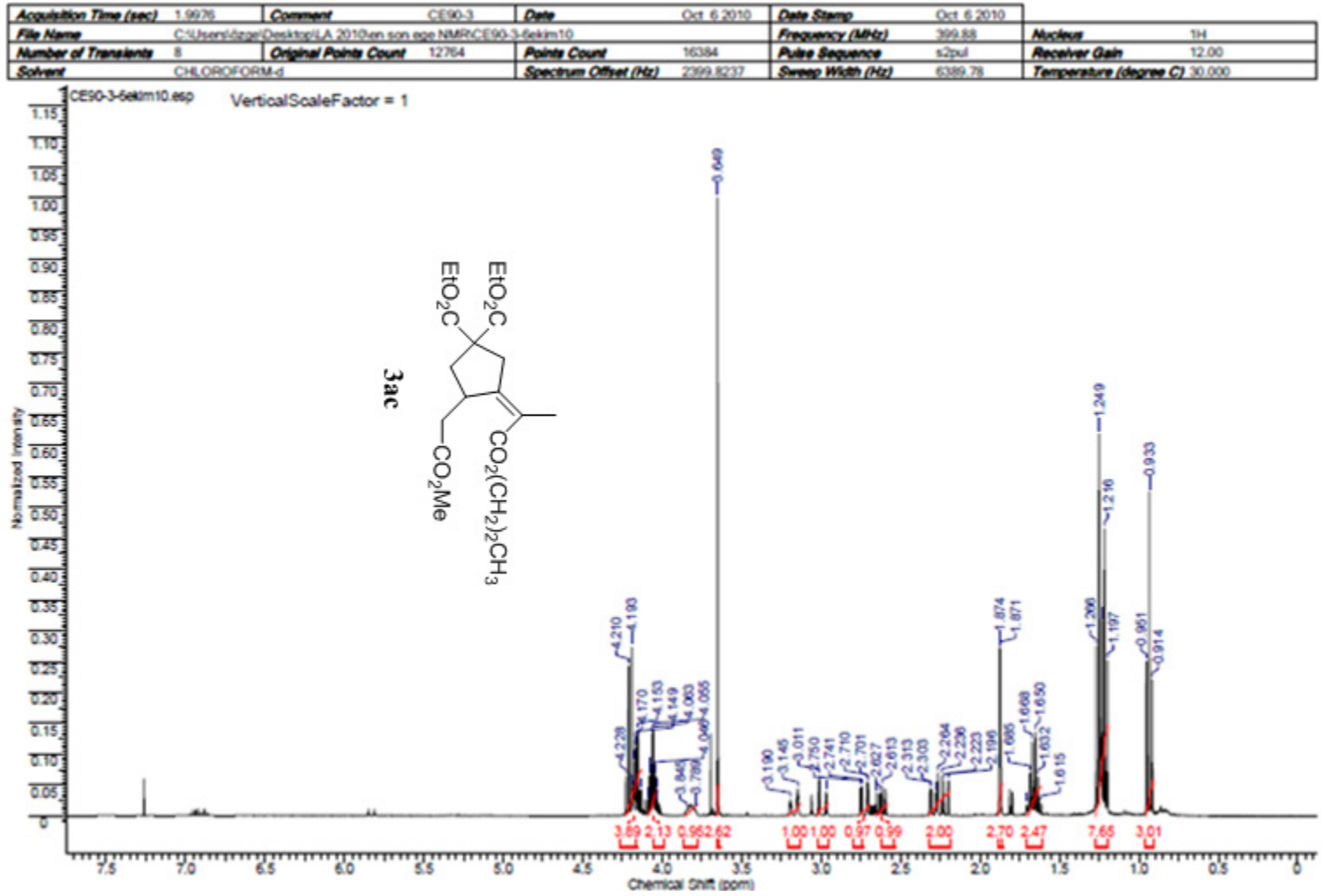

Figure A.5. [1] H NMR of (Z)-diethyl 3-(2-methoxy-2-oxoethyl)-4-(1-oxo-1-propoxypropan-2-ylidene)cyclopentane-1,1-dicarboxylate

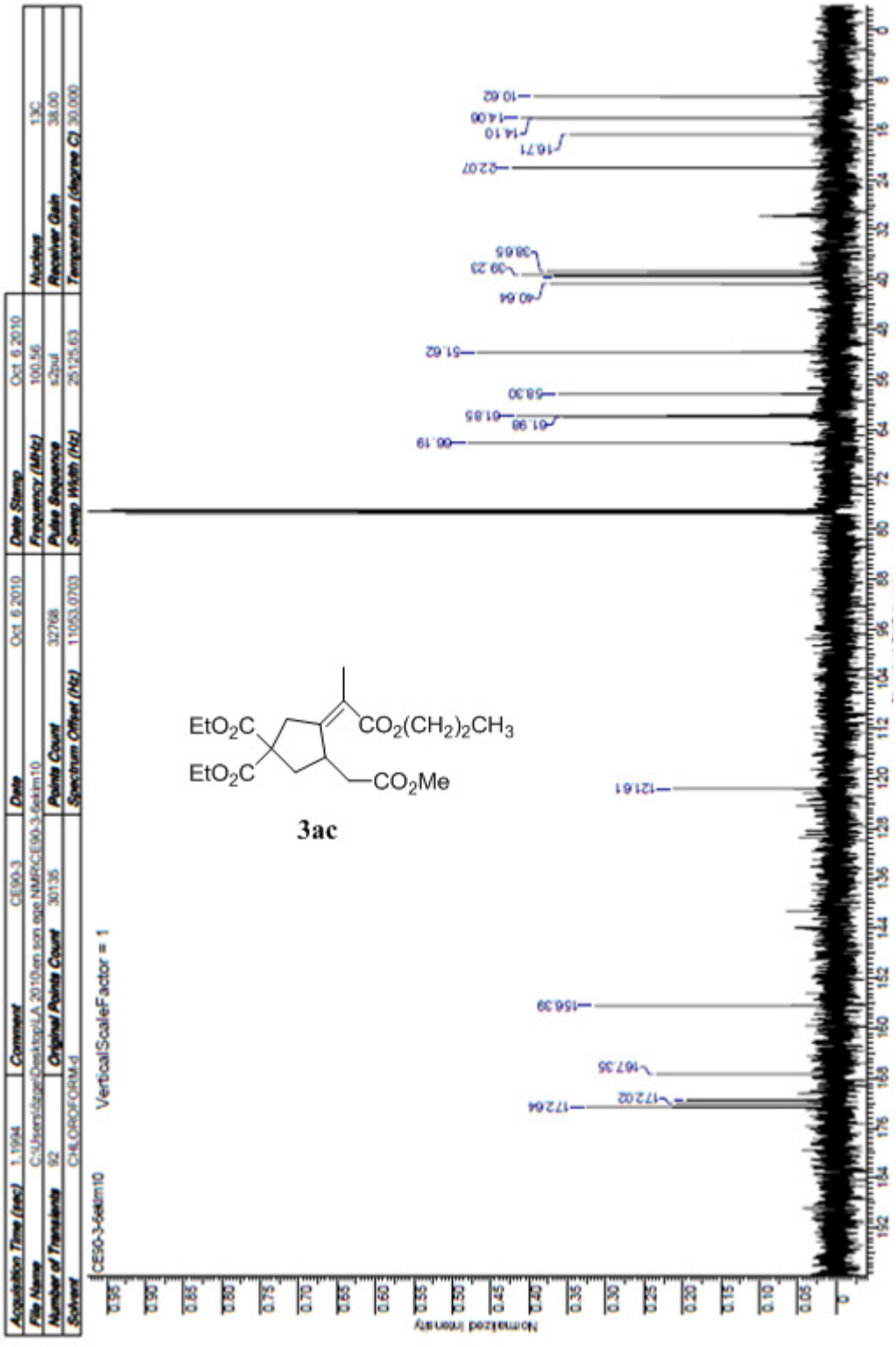

Figure A.6. ^{13}C NMR of Z)-diethyl 3-(2-methoxy-2-oxoethyl)-4-(1-oxo-1-propoxypropan-2-ylidene)cyclopentane-1,1-dicarboxylate

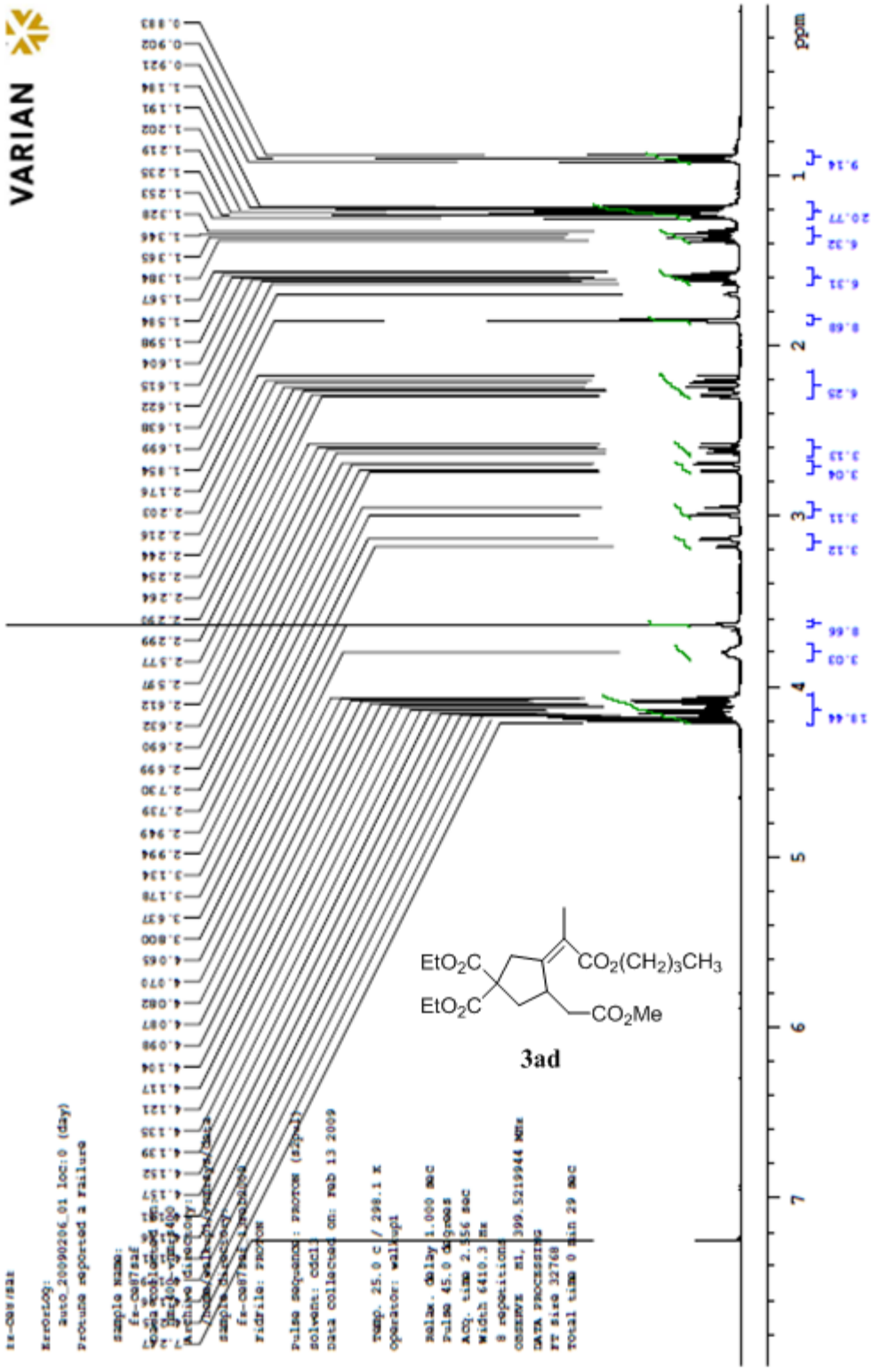

Figure A.7. ^{1}H NMR of (Z)-diethyl 3-(1-butoxy-1-oxopropan-2-ylidene)-4-(2-methoxy-2-oxoethyl)cyclopentane-1,1-dicarboxylate

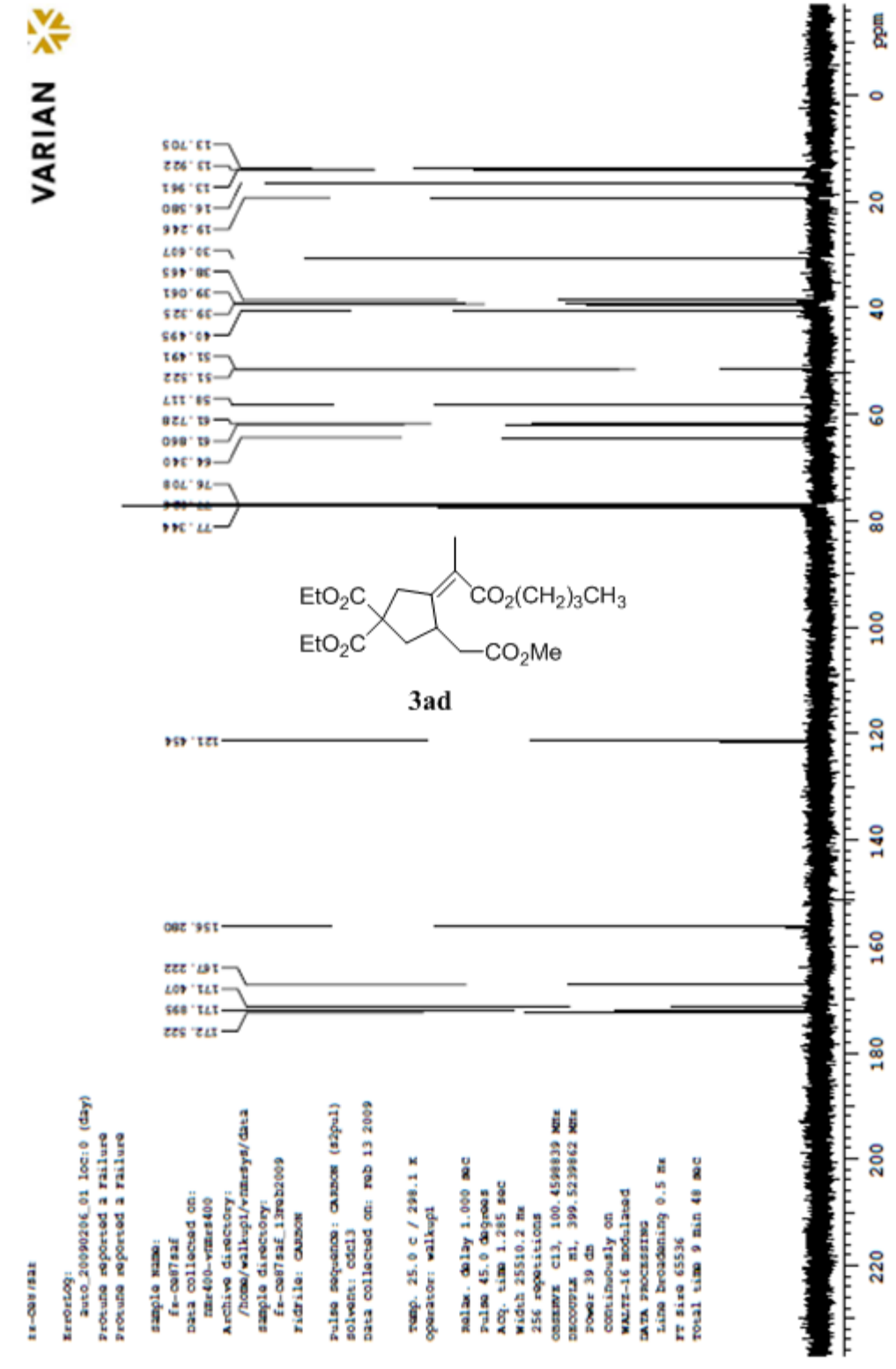

Figure A.8. ^{13}C NMR of (Z)-diethyl 3-(1-butoxy-1-oxopropan-2-ylidene)-4-(2-methoxy-2-oxoethyl)cyclopentane-1,1-dicarboxylate

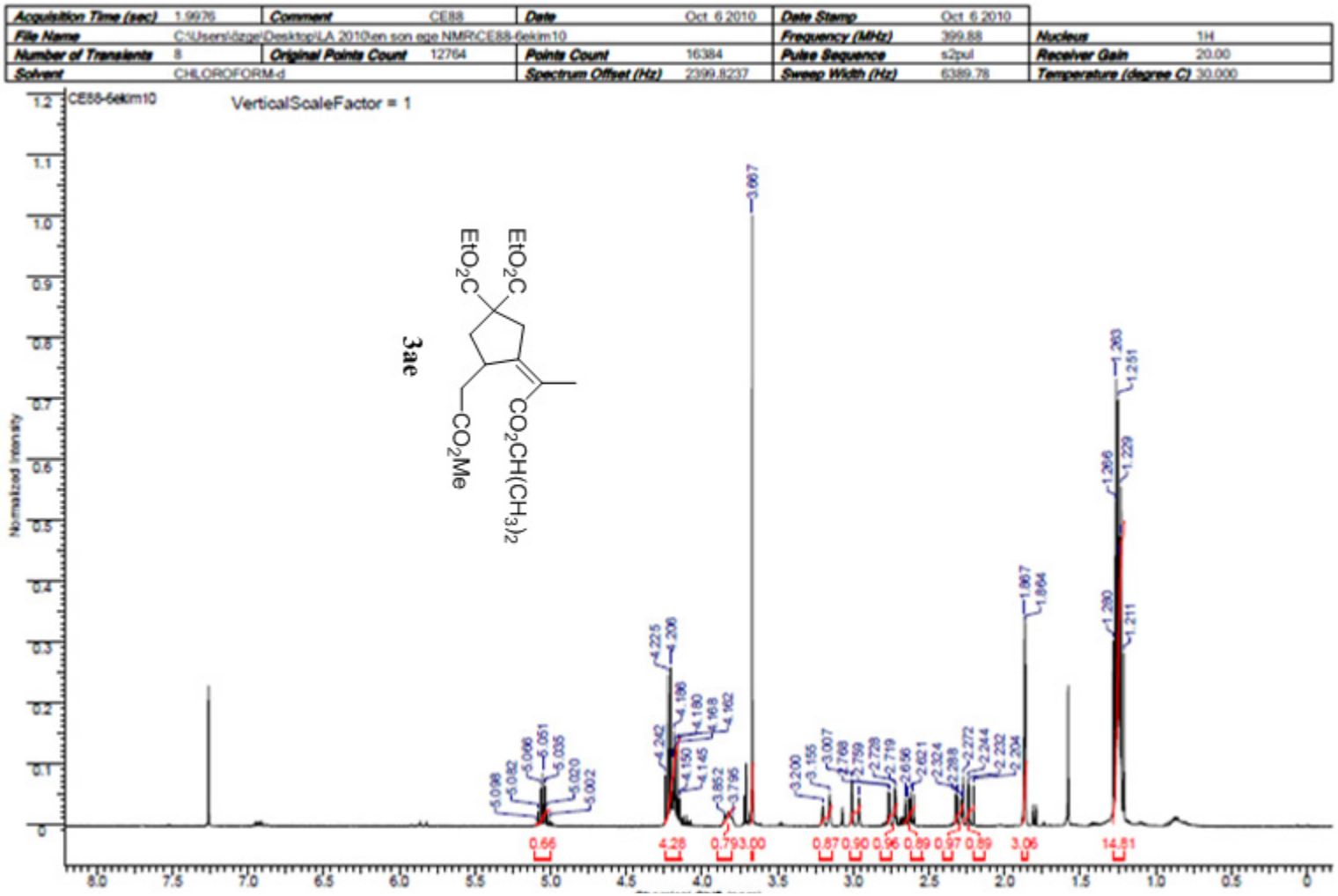

Figure A.9. [1] H NMR of (Z)-diethyl 3-(1-isopropoxy-1-oxopropan-2-ylidene)-4-(2-methoxy-2-oxoethyl)cyclopentane-1,1-dicarboxylate

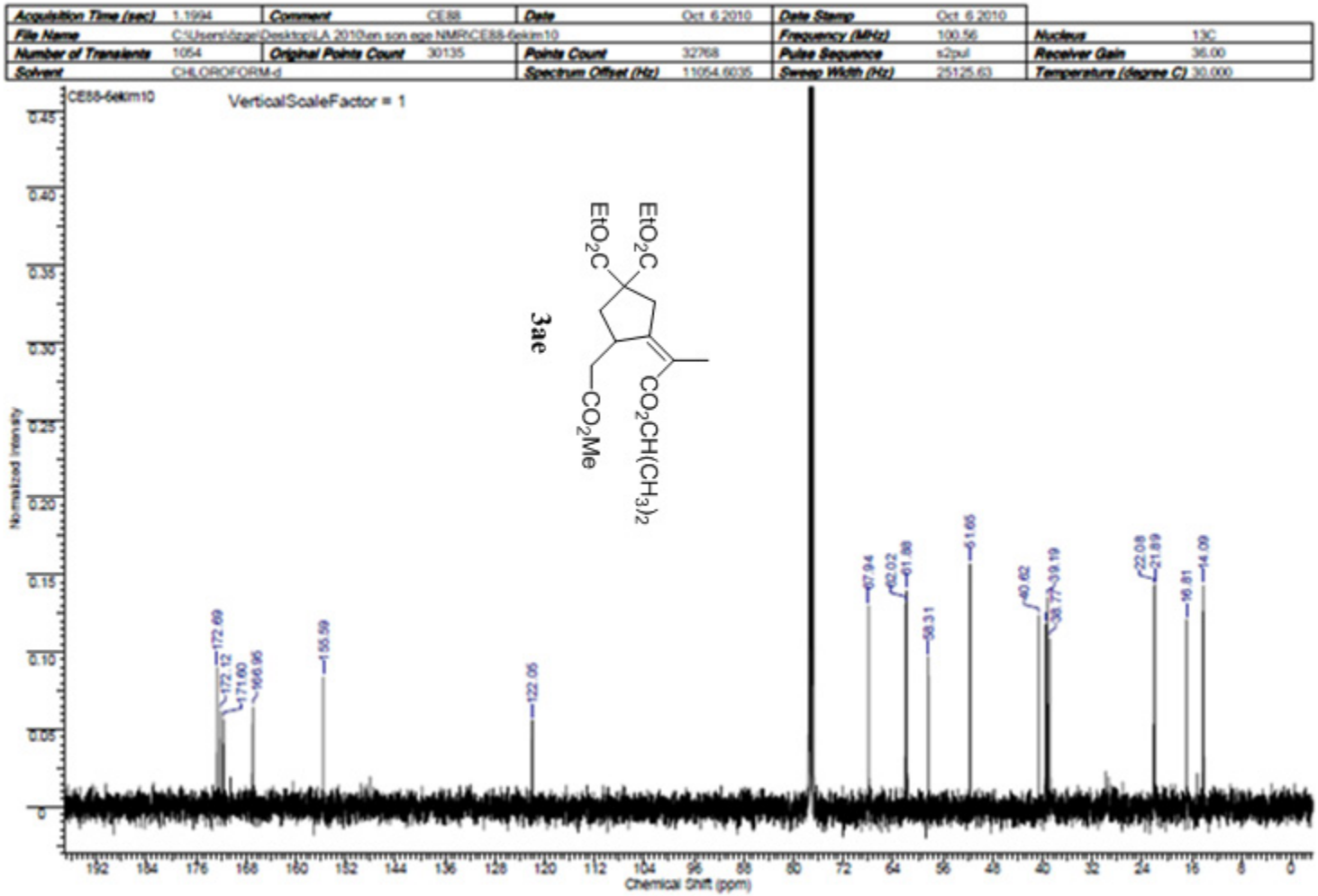

Figure A.10. ^{13}C NMR of (Z)-diethyl 3-(1-isopropoxy-1-oxopropan-2-ylidene)-4-(2-methoxy-2-oxoethyl)cyclopentane-1,1-dicarboxylate

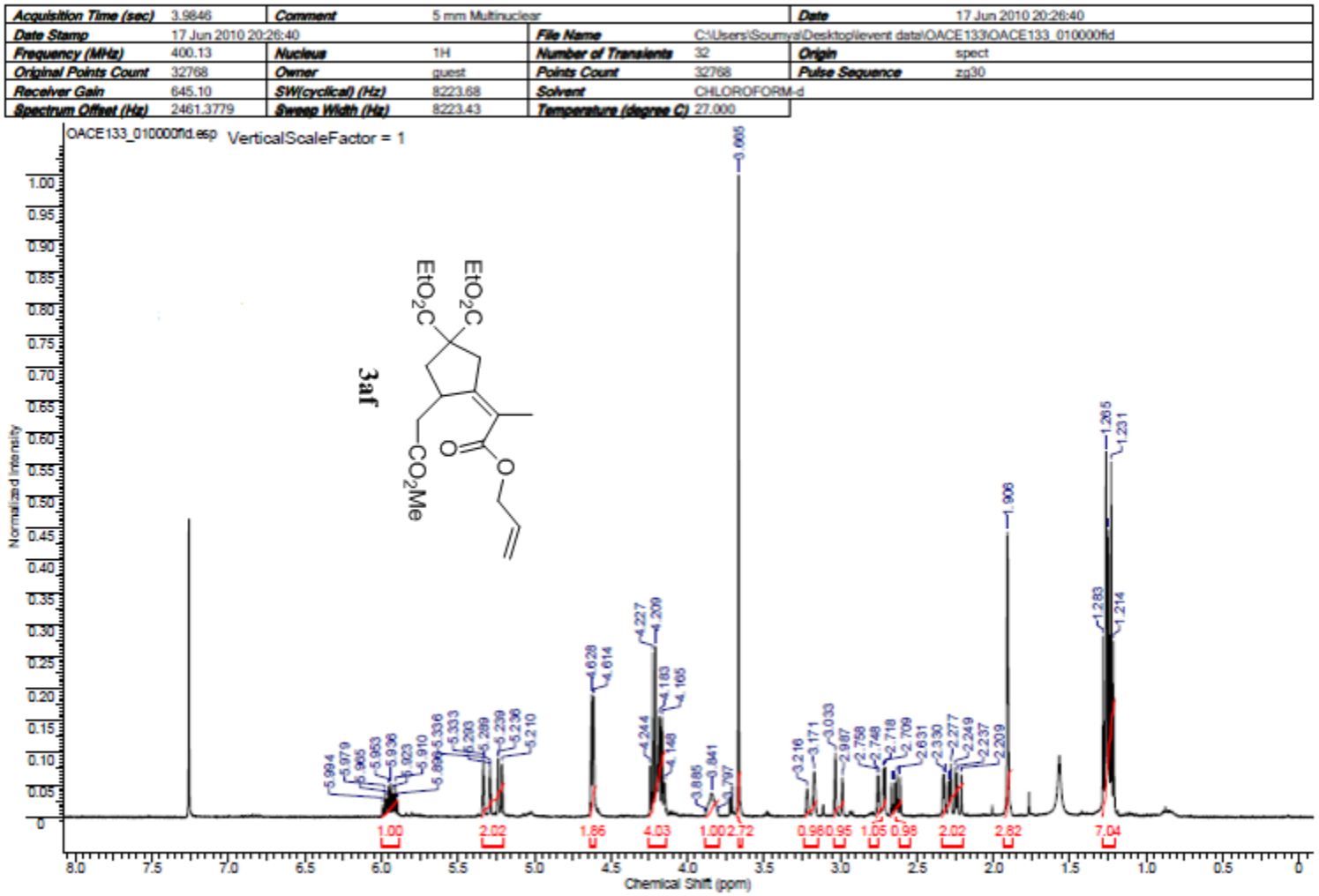

Figure A.11. [1] H NMR of (Z)-diethyl 3-(1-(allyloxy)-1-oxopropan-2-ylidene)-4-(2-methoxy-2-oxoethyl)cyclopentane-1,1-dicarboxylate

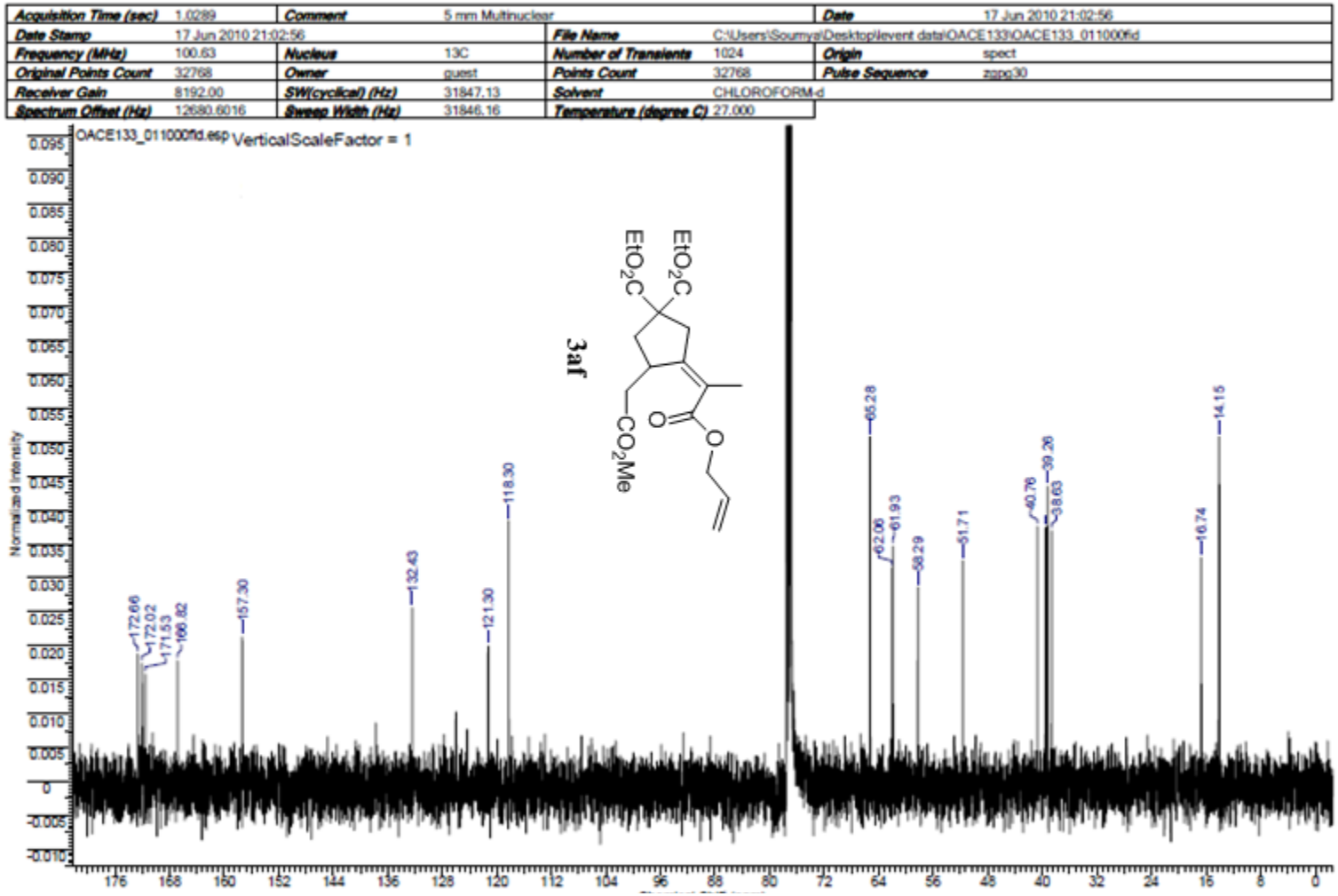

Figure A.12. ^{13}C NMR of (Z)-diethyl 3-(1-(allyloxy)-1-oxopropan-2-ylidene)-4-(2-methoxy-2-oxoethyl)cyclopentane-1,1-dicarboxylate

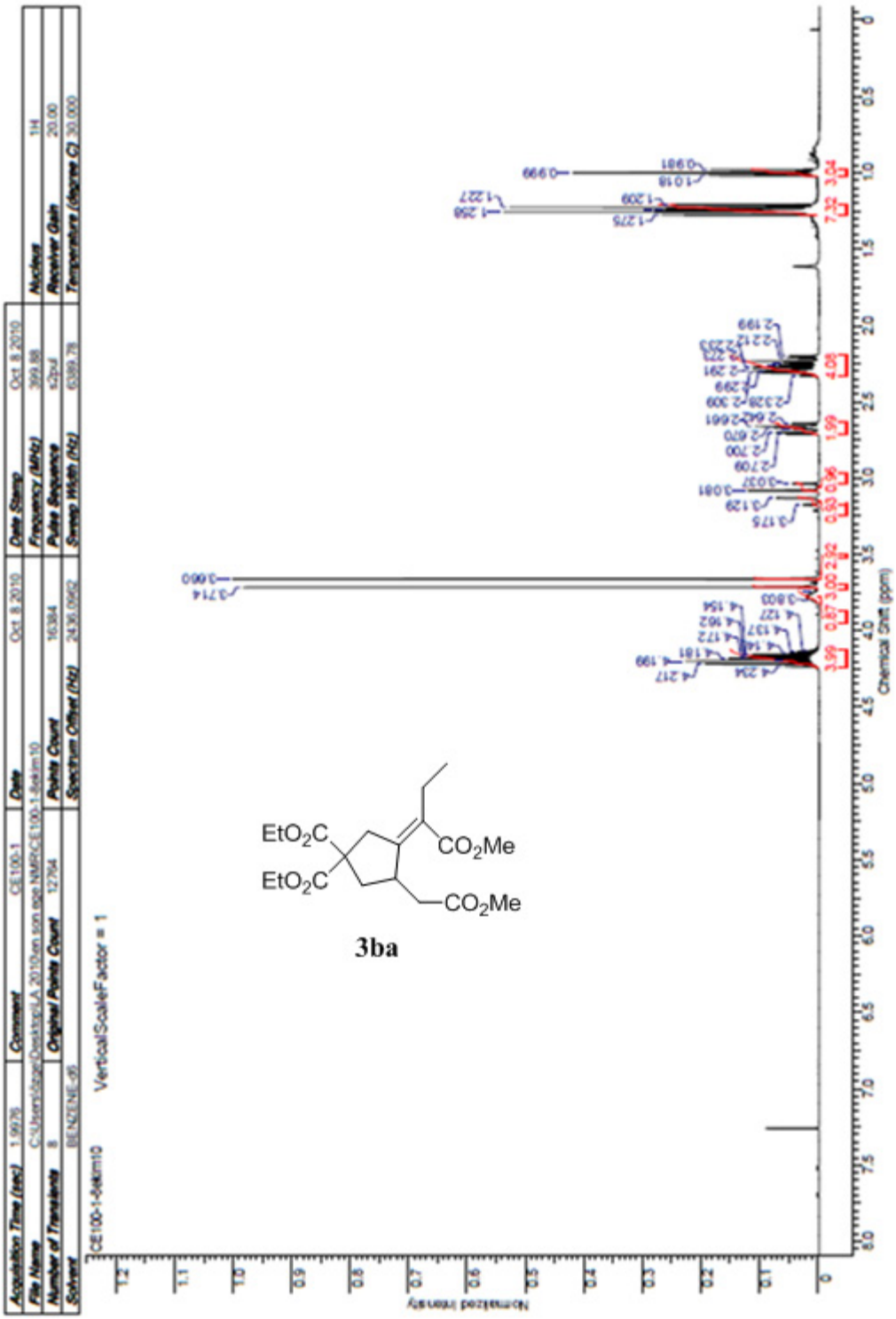

Figure A.13. ^{1} H NMR of (Z)-diethyl 3-(1-methoxy-1-oxobutan-2-ylidene)-4-(2-methoxy-2-oxoethyl)cyclopentane-1,1-dicarboxylate

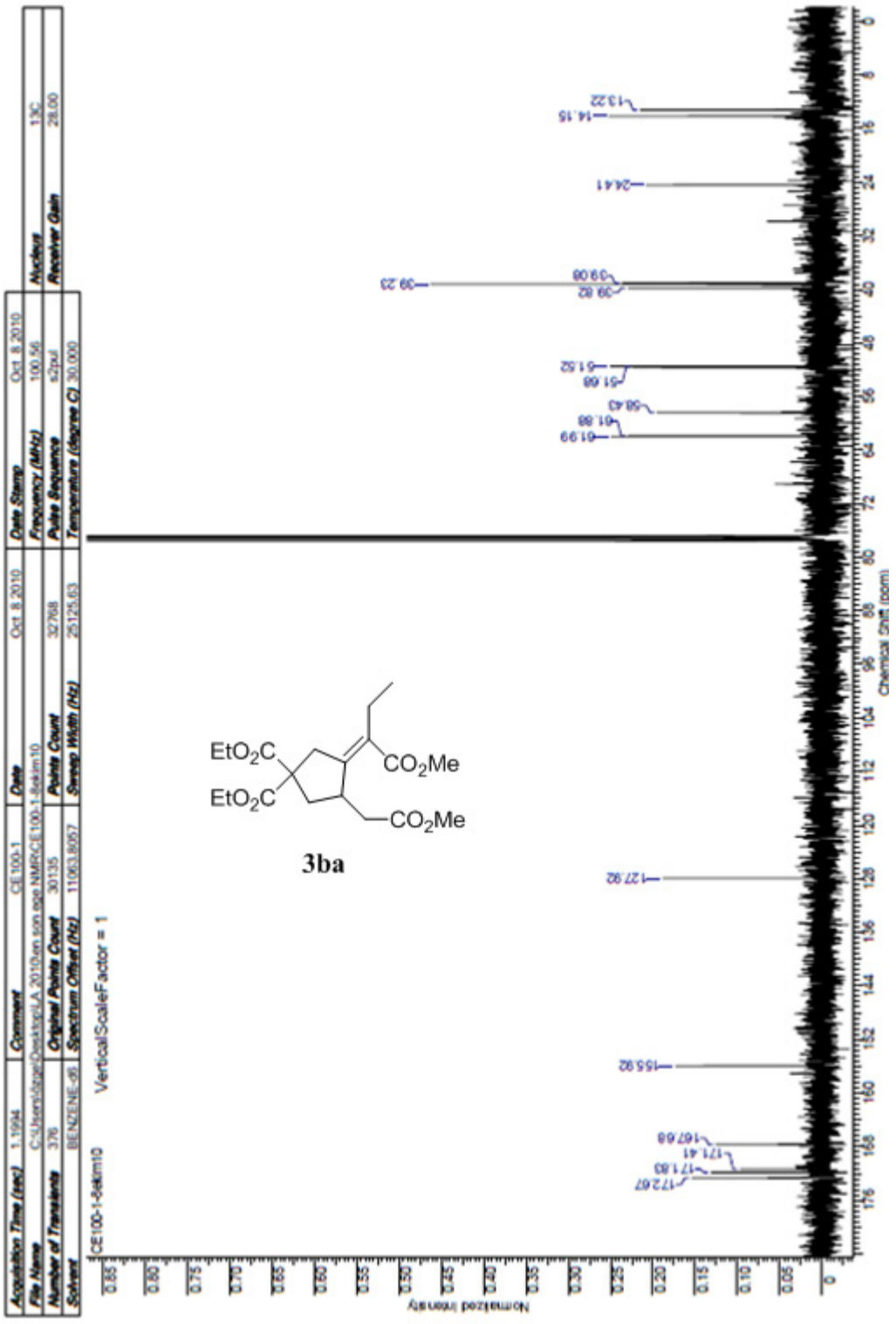

Figure A.14. ^{13}C NMR of (Z)-diethyl 3-(1-methoxy-1-oxobutan-2-ylidene)-4-(2-methoxy-2-oxoethyl)cyclopentane-1,1-dicarboxylate

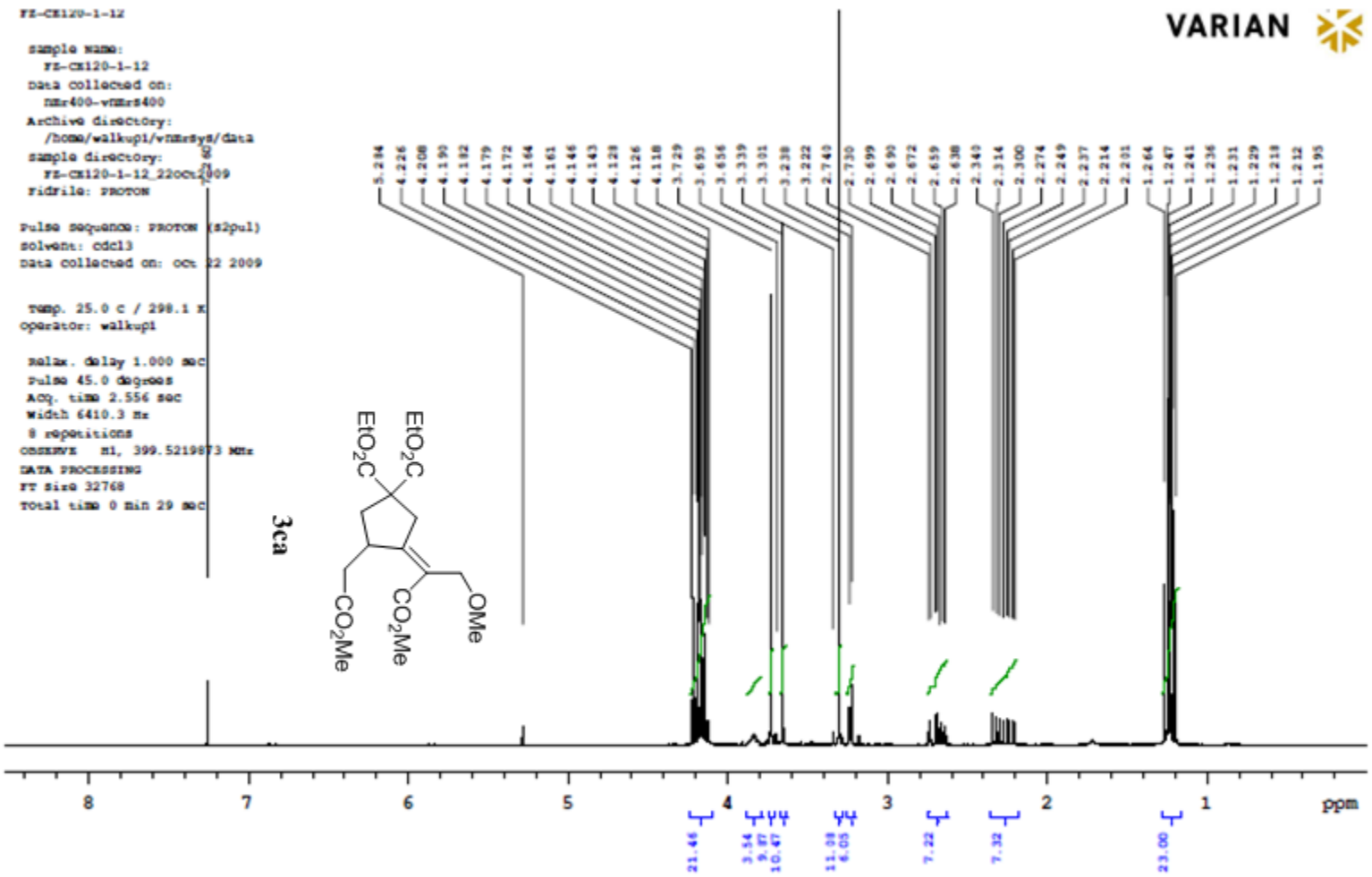

Figure A.15. [1] H NMR of (Z)-diethyl 3-(1,3-dimethoxy-1-oxopropan-2-ylidene)-4-(2-methoxy-2-oxoethyl)cyclopentane-1,1-dicarboxylate

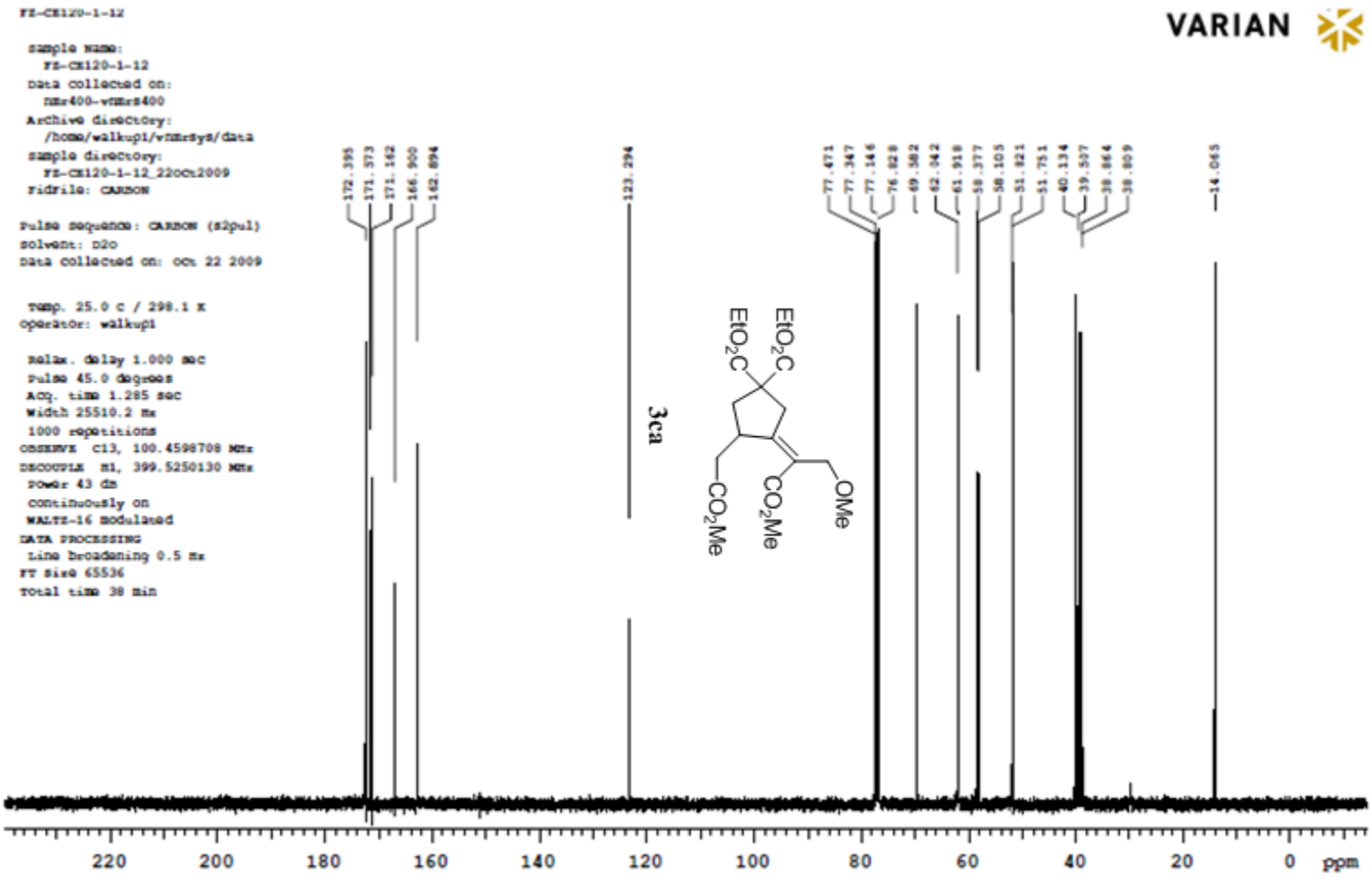

Figure A.16. ^{13}C NMR of (Z)-diethyl 3-(1,3-dimethoxy-1-oxopropan-2-ylidene)-4-(2-methoxy-2-oxoethyl)cyclopentane-1,1-dicarboxylate

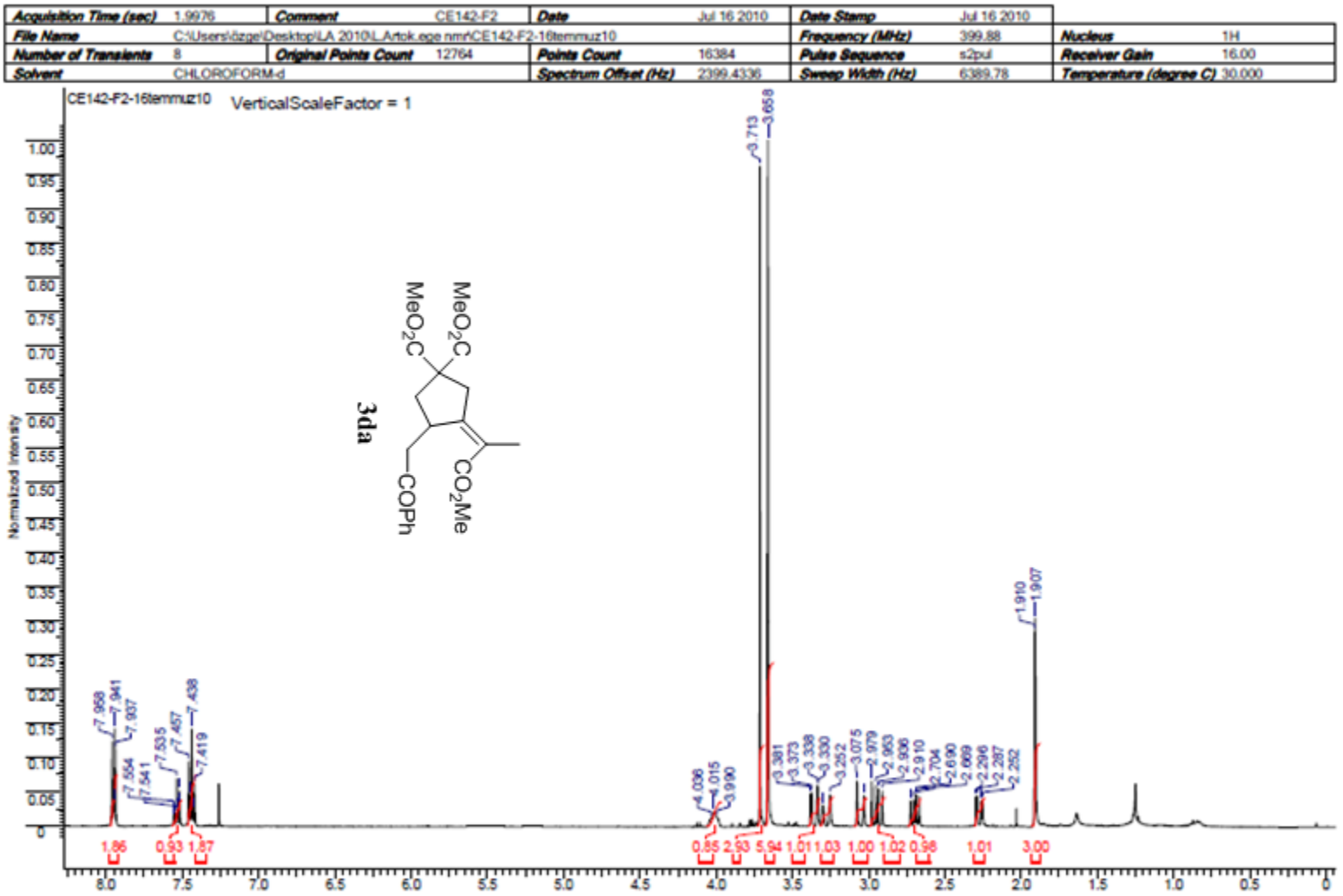

Figure A.17. [1] H NMR of (Z)-dimethyl 3-(1-methoxy-1-oxopropan-2-ylidene)-4-(2-oxo-2-phenylethyl)cyclopentane-1,1-dicarboxylate

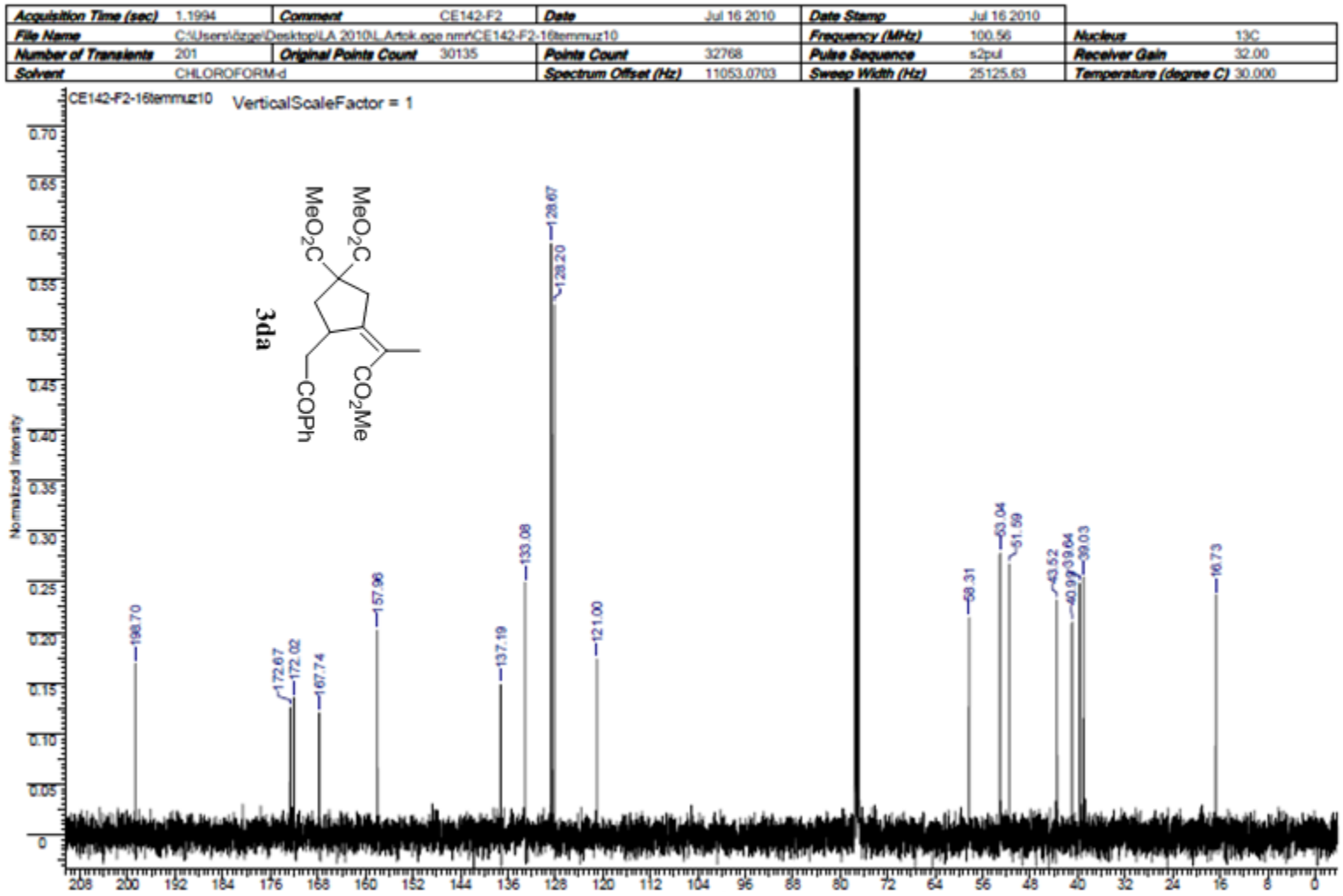

Figure A.18. ^{13}C NMR of (Z)-dimethyl 3-(1-methoxy-1-oxopropan-2-ylidene)-4-(2-oxo-2-phenylethyl)cyclopentane-1,1-dicarboxylate

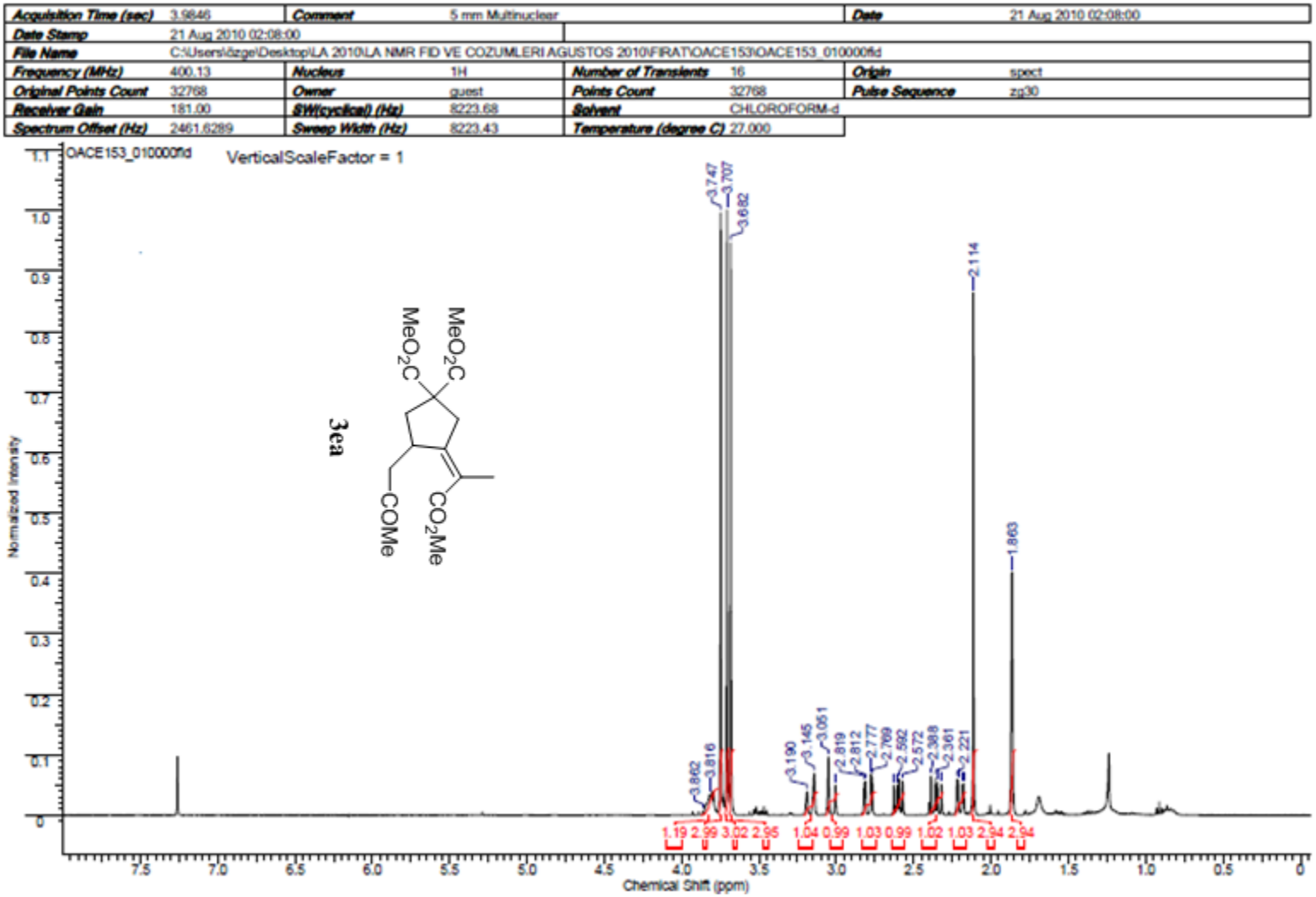

Figure A.19. [1] H NMR of (Z)-dimethyl 3-(1-methoxy-1-oxopropan-2-ylidene)-4-(2-oxopropyl)cyclopentane-1,1-dicarboxylate

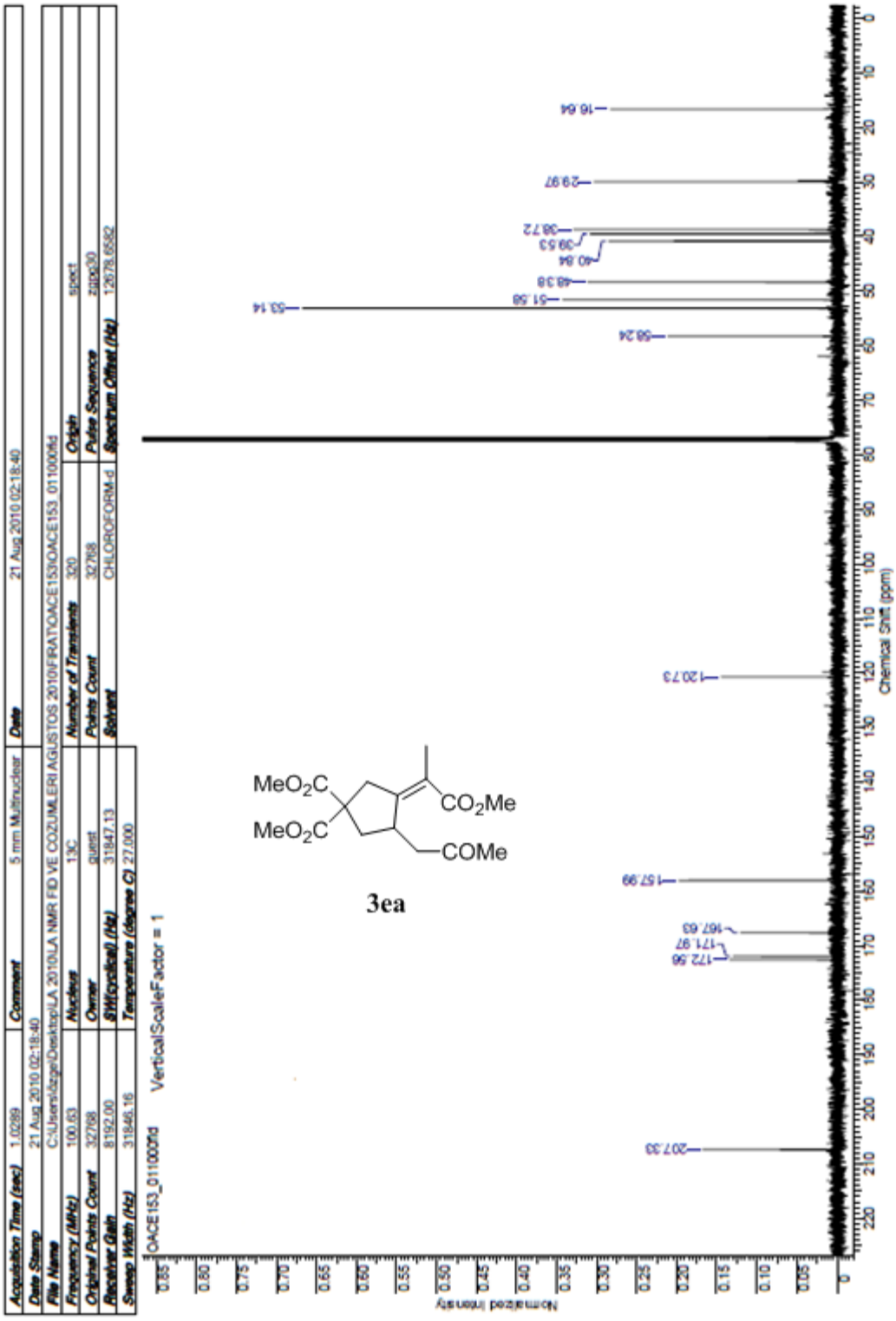

Figure A.20. ^{13}C NMR of (Z)-dimethyl 3-(1-methoxy-1-oxopropan-2-ylidene)-4-(2-oxopropyl)cyclopentane-1,1-dicarboxylate

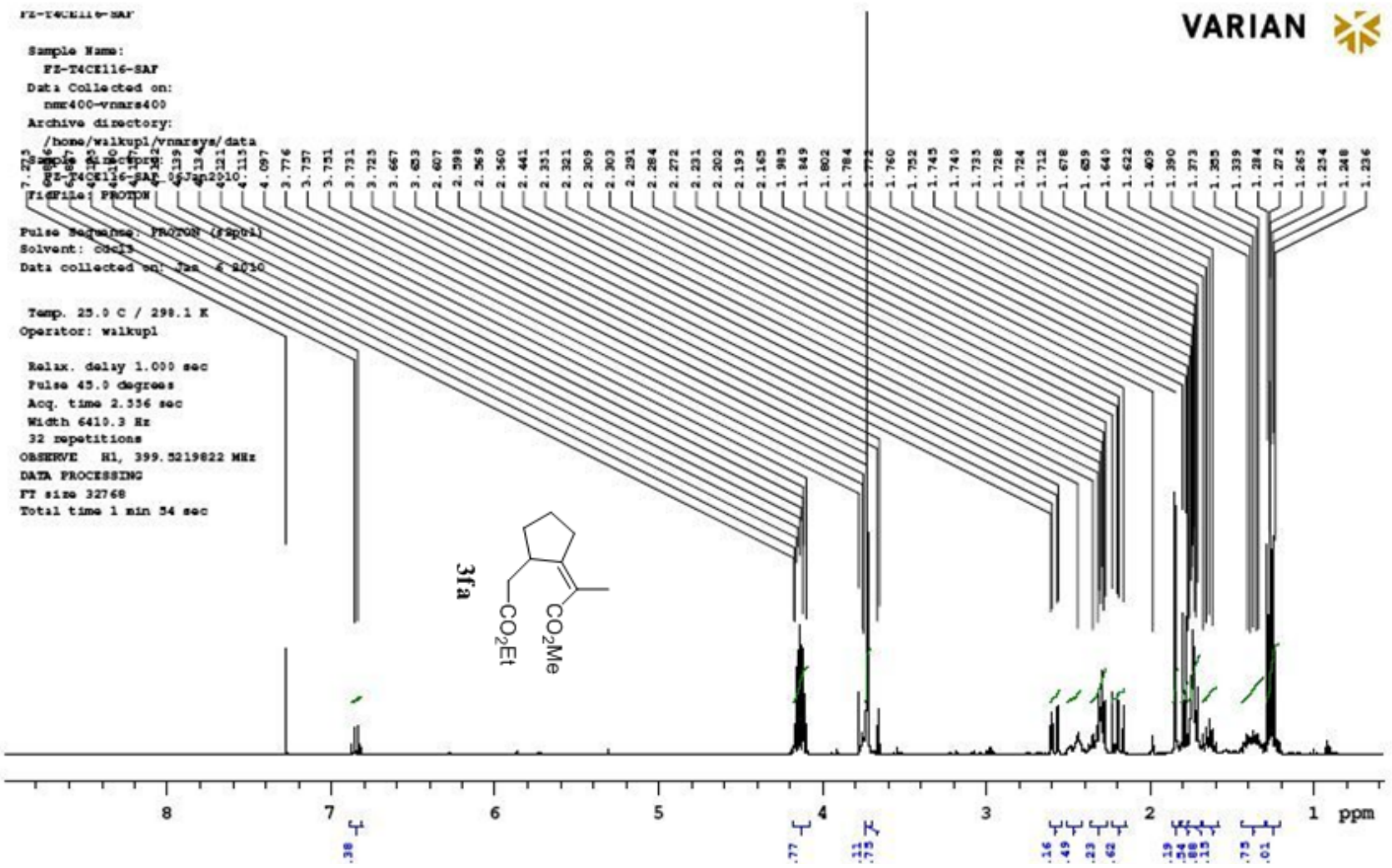

Figure A.21. [1] H NMR of (Z)-methyl 2-(2-(2-ethoxy-2-oxoethyl)cyclopentylidene)propanoate

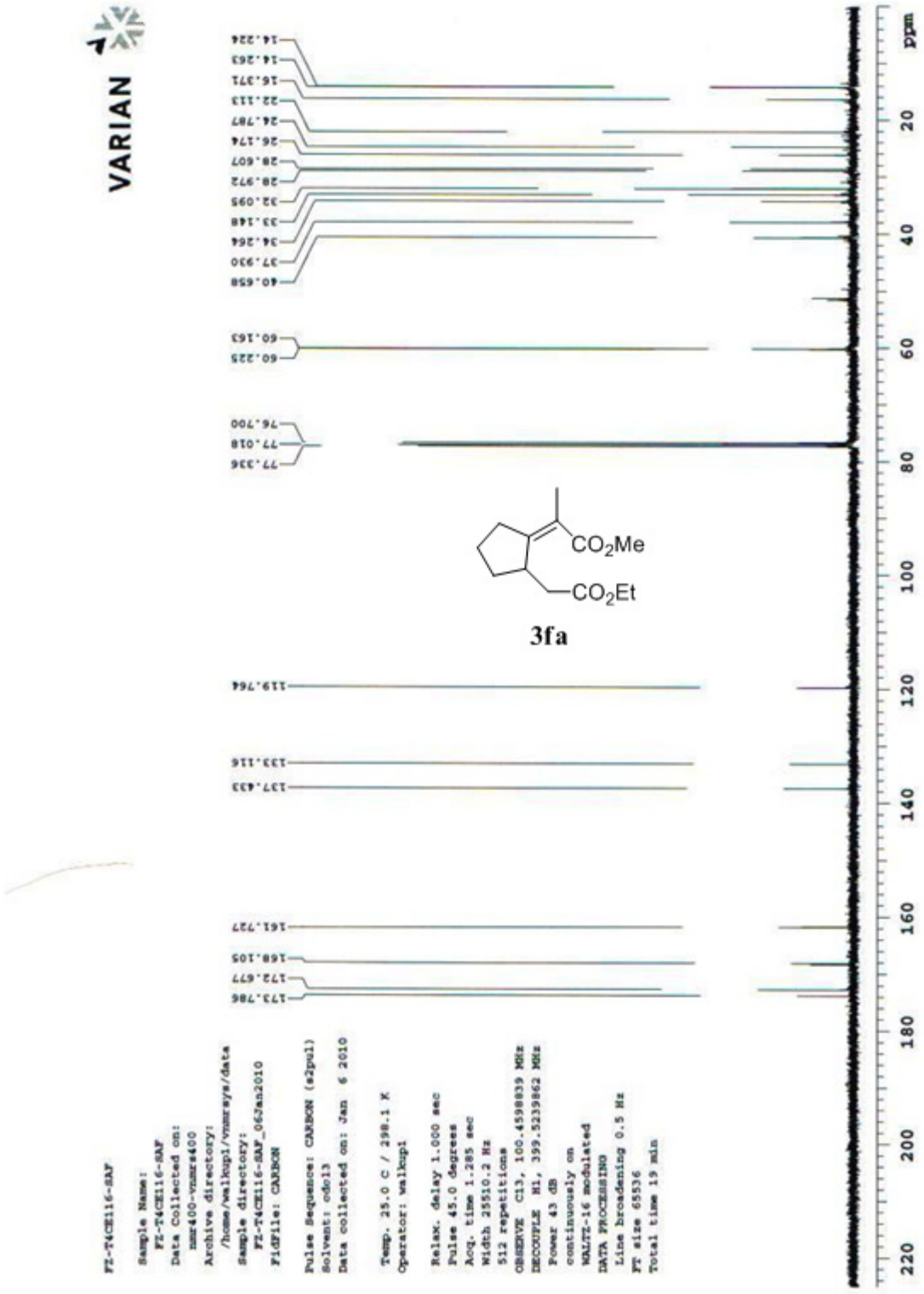

Figure A.22. ^{13}C NMR of (Z)-methyl 2-(2-(2-ethoxy-2-oxoethyl)cyclopentylidene)propanoate

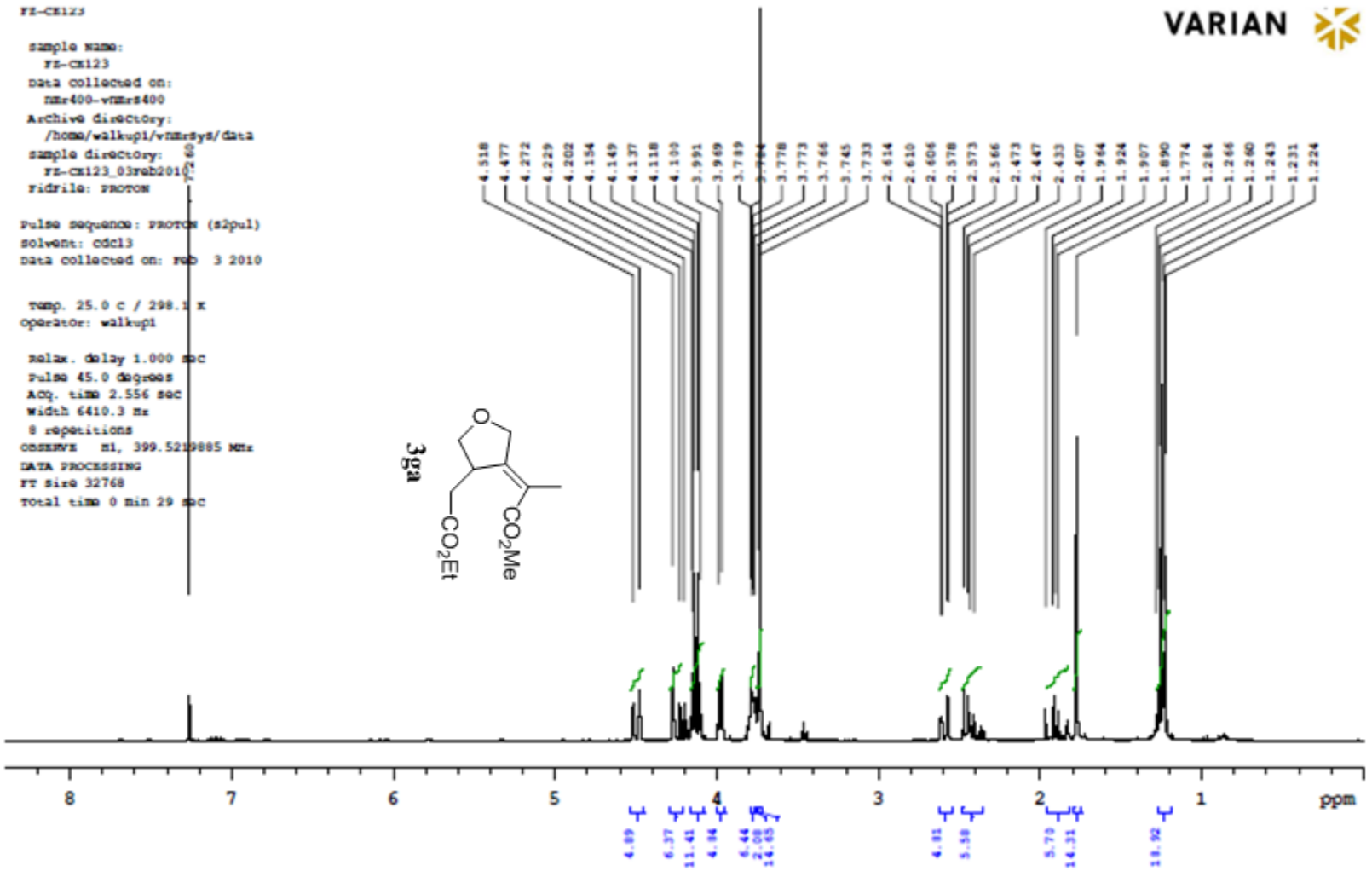

Figure A.23 [1] H NMR of (E)-methyl 2-(4-(2-ethoxy-2-oxoethyl)dihydrofuran-3(2*H*)-ylidene)propanoate

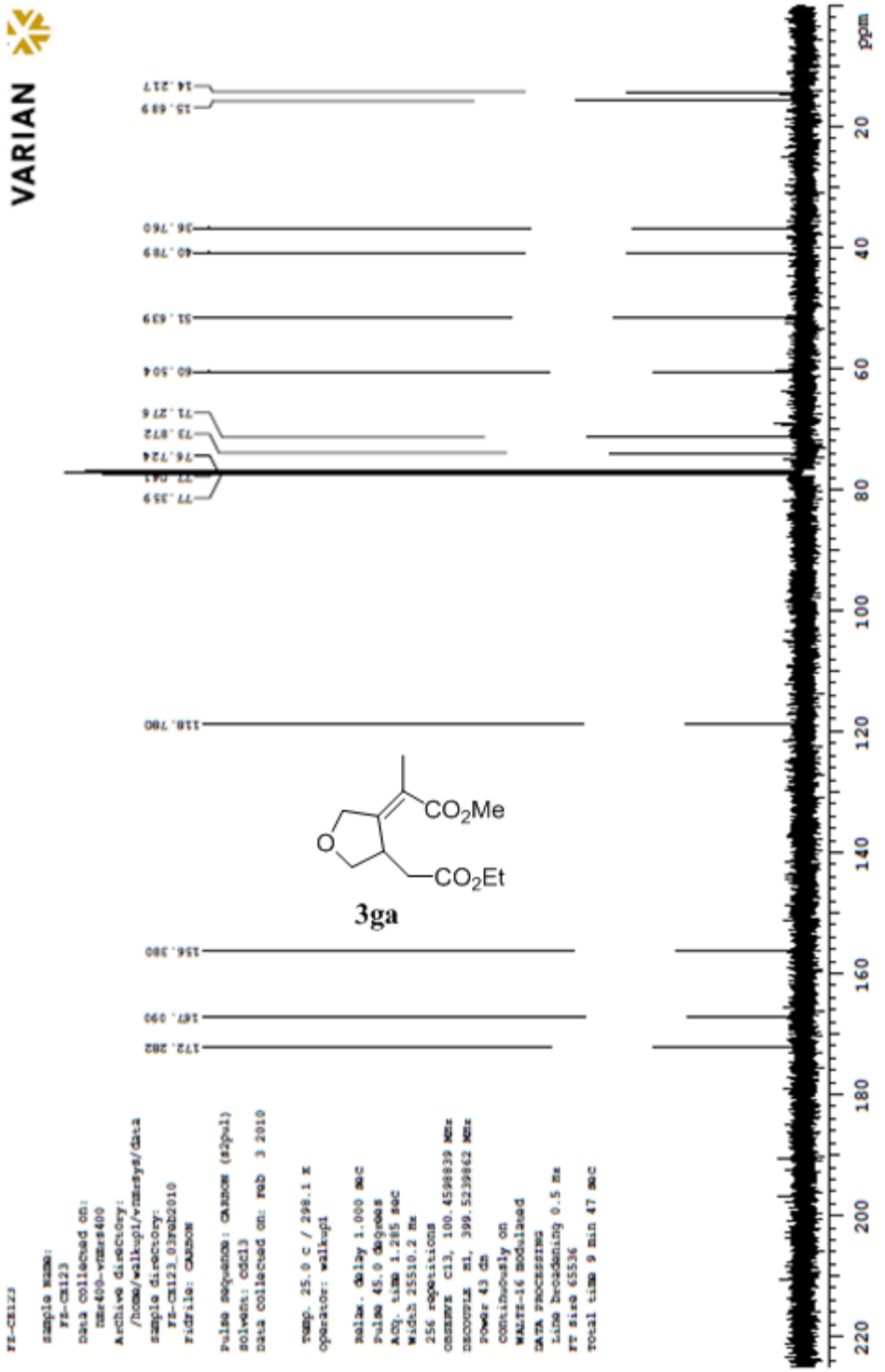

Figure A.24 ^{13}C NMR of (E)-methyl 2-(4-(2-ethoxy-2-oxoethyl)dihydrofuran-3(2*H*)-ylidene)propanoate

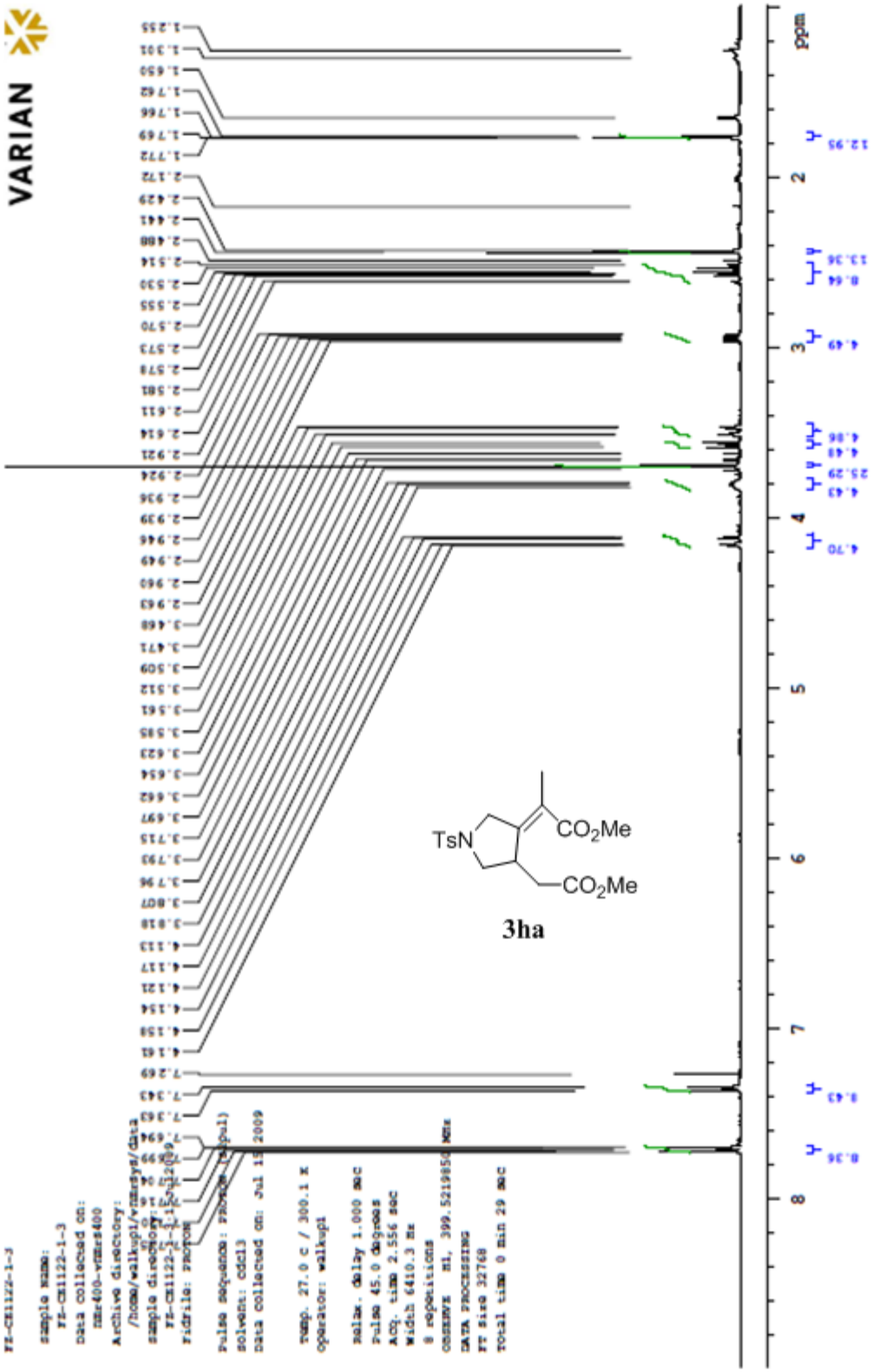

Figure A.25 ^{1}H NMR of (E)-methyl 2-(4-(2-methoxy-2-oxoethyl)-1-tosylpyrrolidin-3-ylidene)propanoate

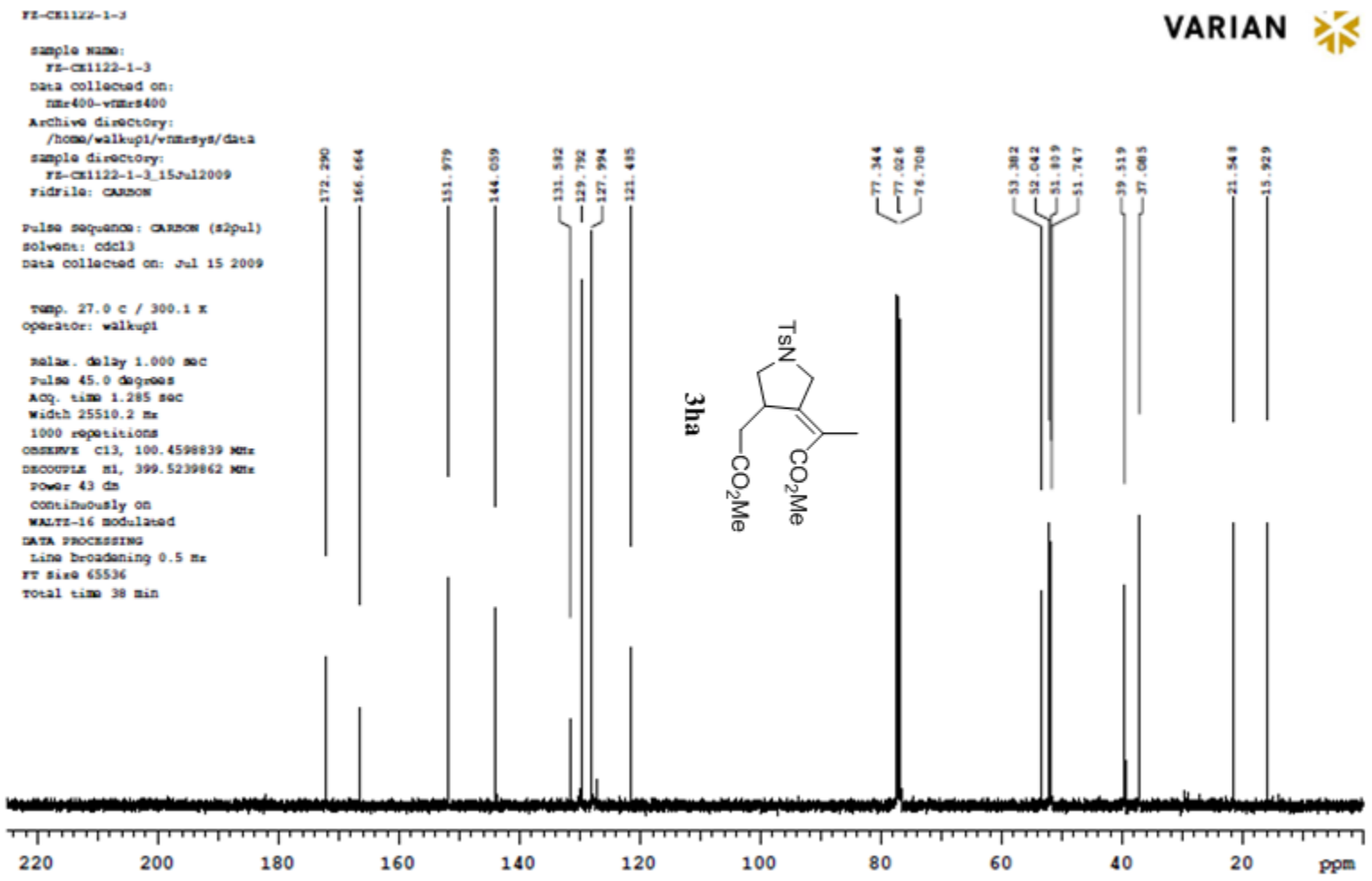

Figure A.26 ^{13} C NMR of (E)-methyl 2-(4-(2-methoxy-2-oxoethyl)-1-tosylpyrrolidin-3-ylidene)propanoate

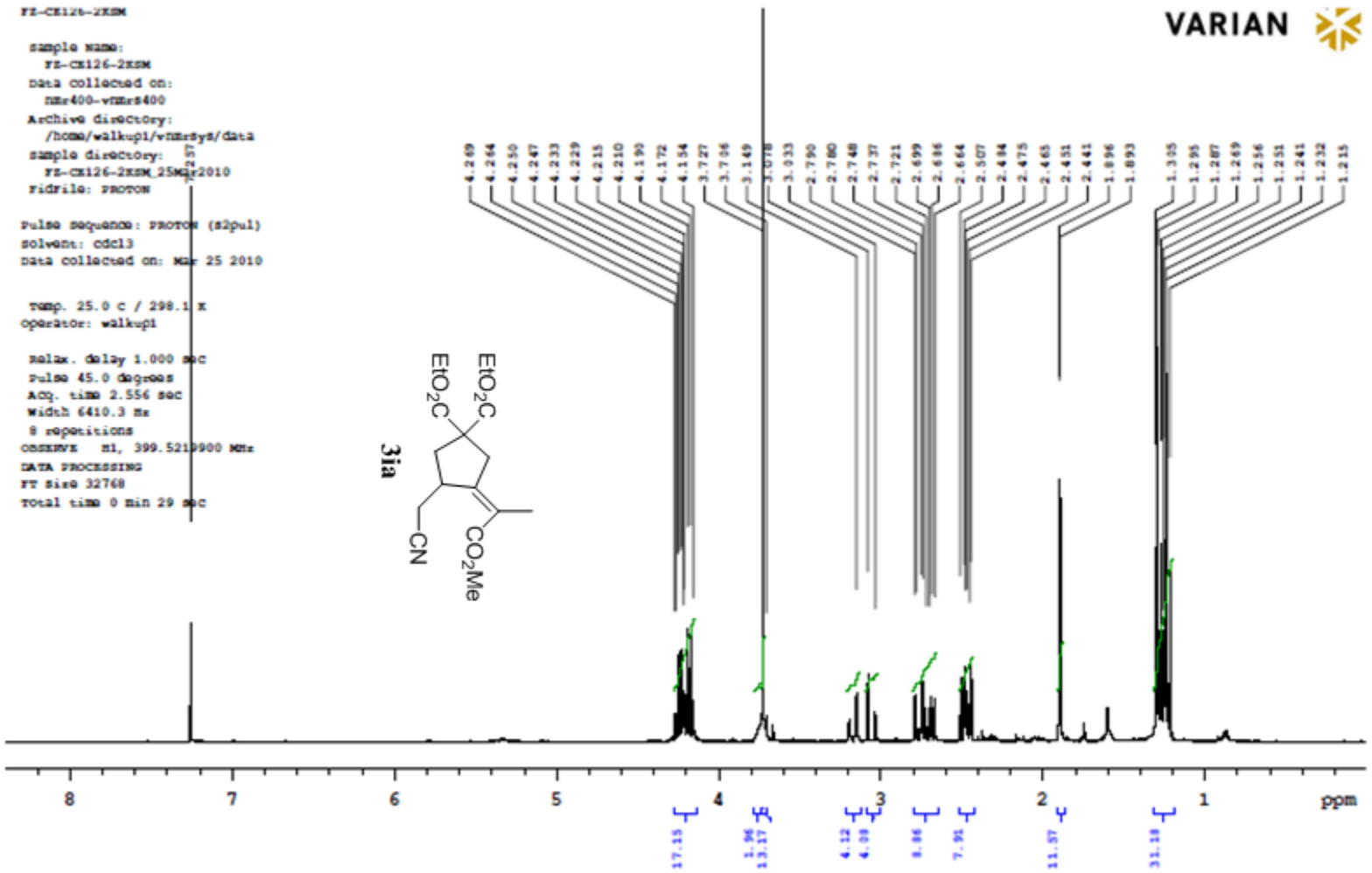

Figure A.27 ^{1} H NMR of (Z)-diethyl 3-(cyanomethyl)-4-(1-methoxy-1-oxopropan-2-ylidene)cyclopentane-1,1-dicarboxylate

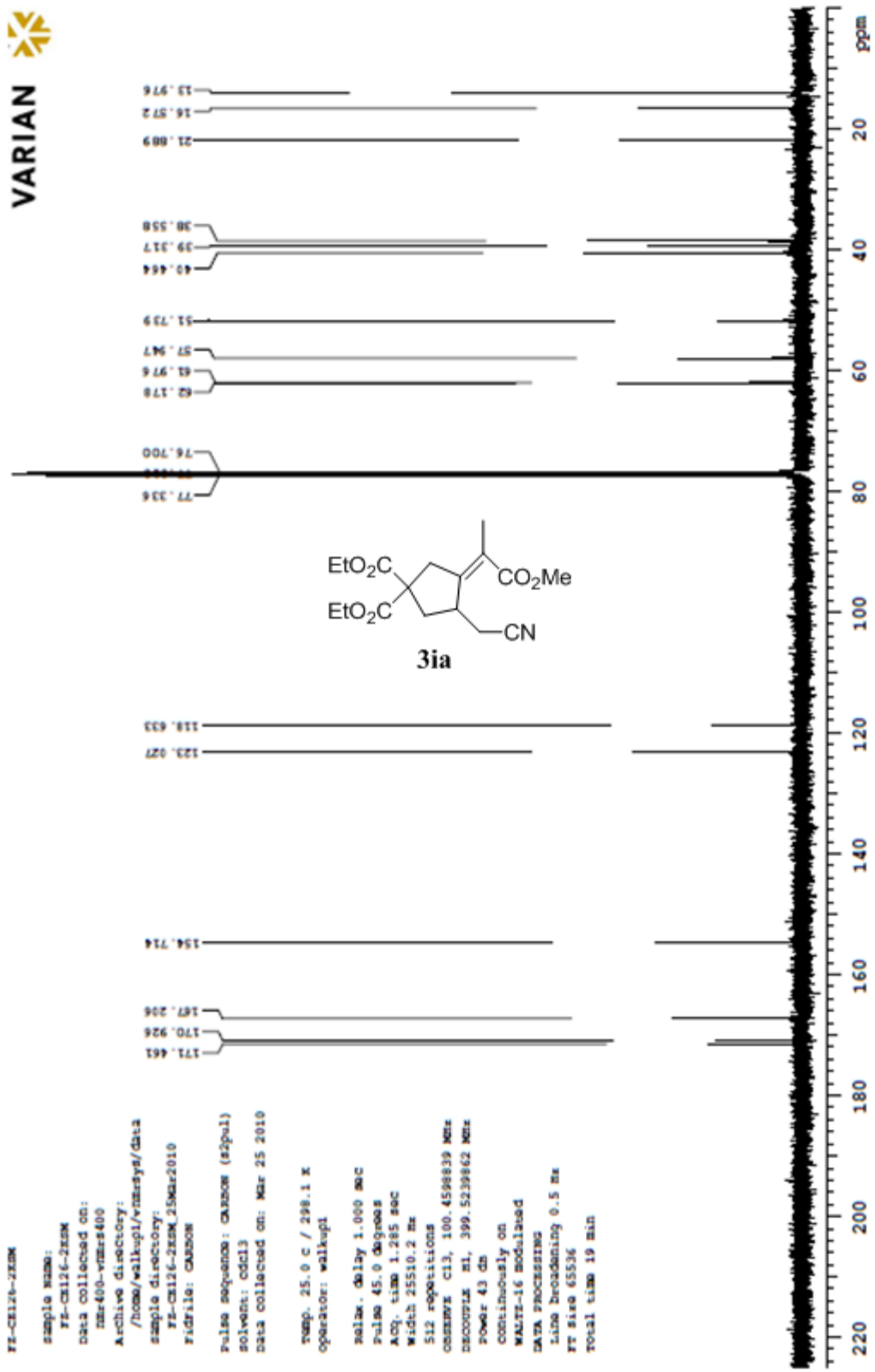

Figure A.28 ^{13}C NMR of (Z)-diethyl 3-(cyanomethyl)-4-(1-methoxy-1-oxopropan-2-ylidene)cyclopentane-1,1-dicarboxylate

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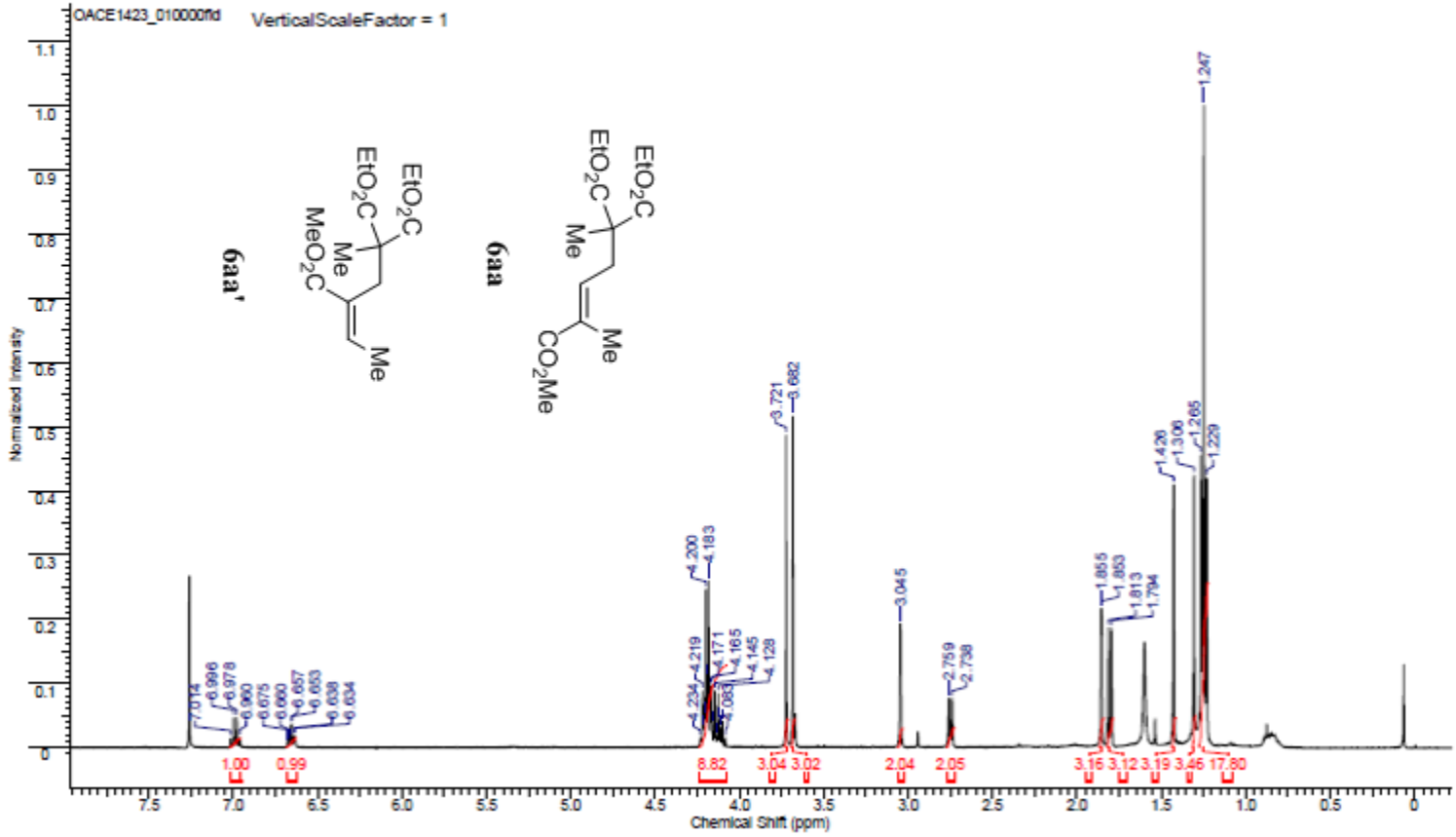

Figure A.29 [1] H NMR of (E)-2,2-diethyl 5-methyl hex-4-ene-2,2,5-tricarboxylate and (E)-2,2-diethyl 4-methyl hex-4-ene-2,2,4-tricarboxylate

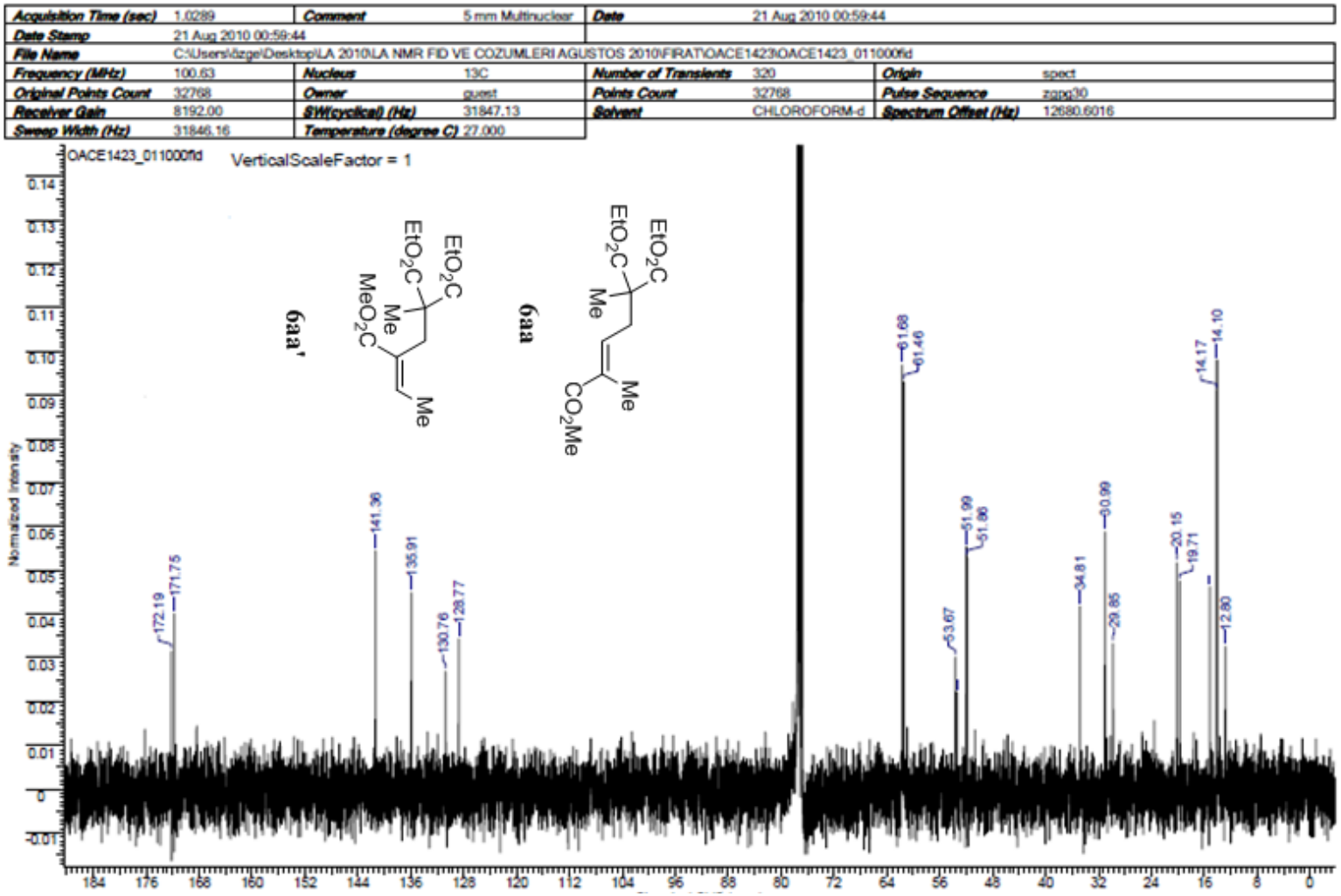

Figure A.30 ^{13} C NMR of (E)-2,2-diethyl 5-methyl hex-4-ene-2,2,5-tricarboxylate and (E)-2,2-diethyl 4-methyl hex-4-ene-2,2,4-tricarboxylate

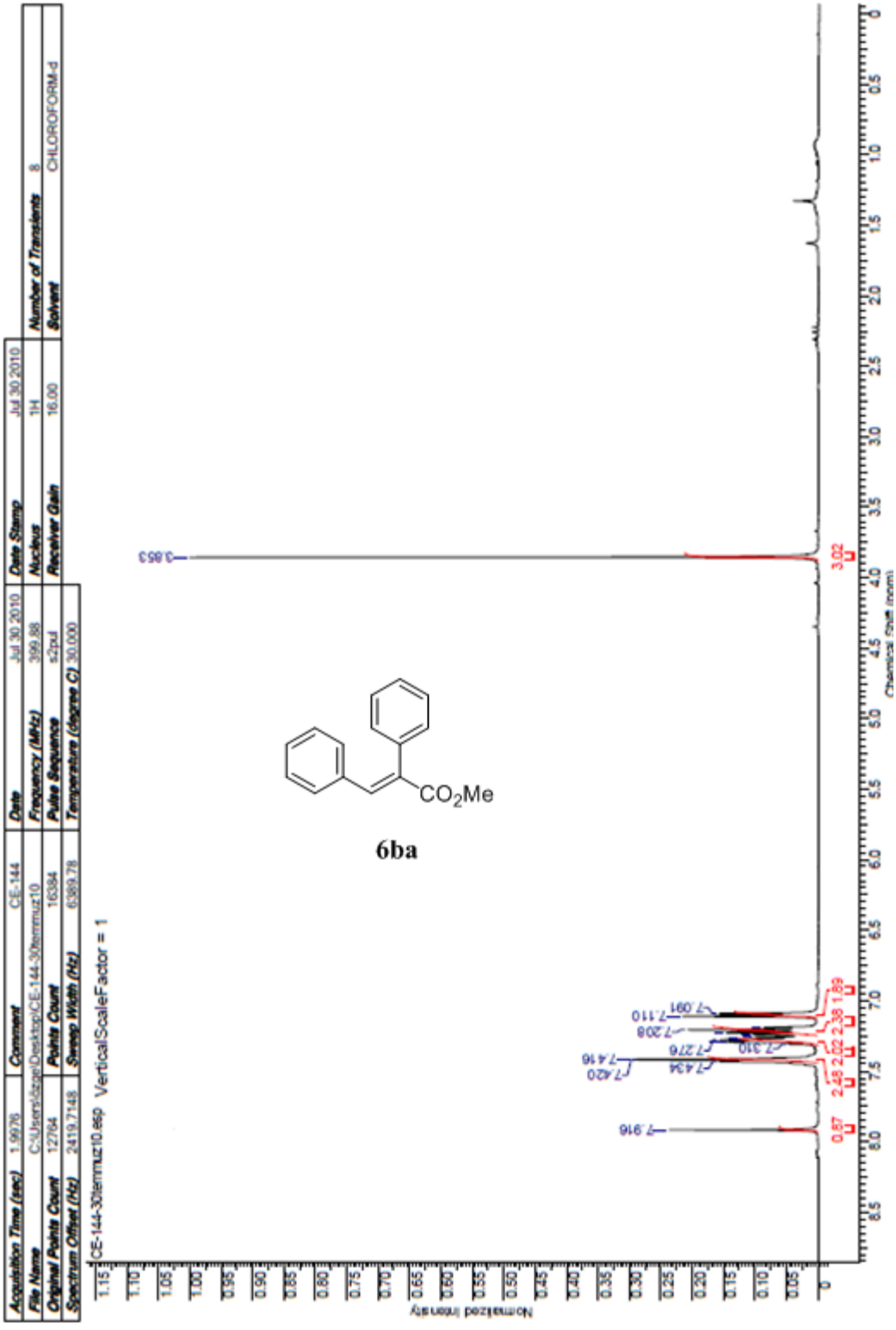

Figure A.31 ^{1}H NMR of (E)-methyl 2,3-diphenylacrylate

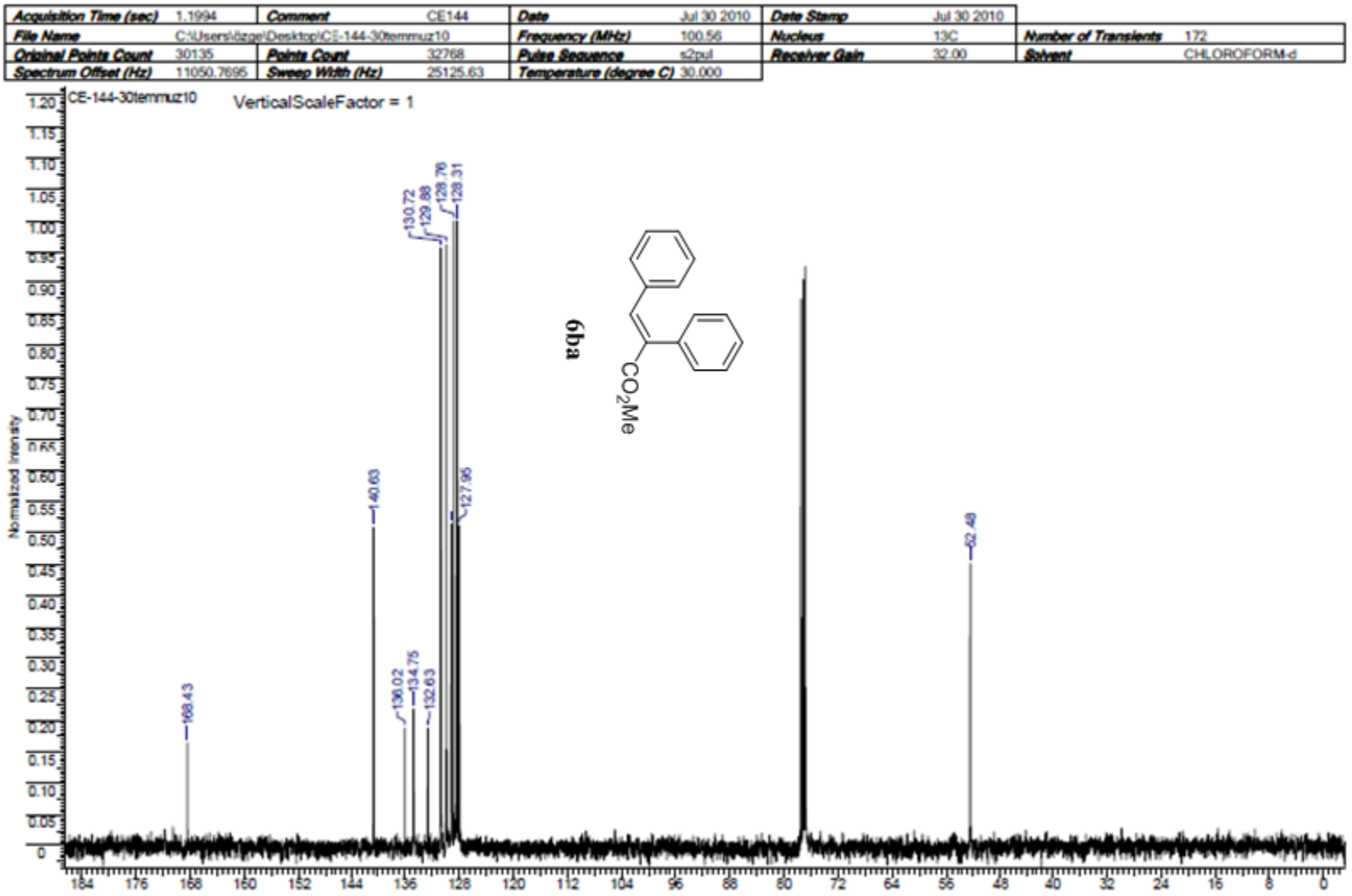

Figure A.32 ^{13}C NMR of (E)-methyl 2,3-diphenylacrylate

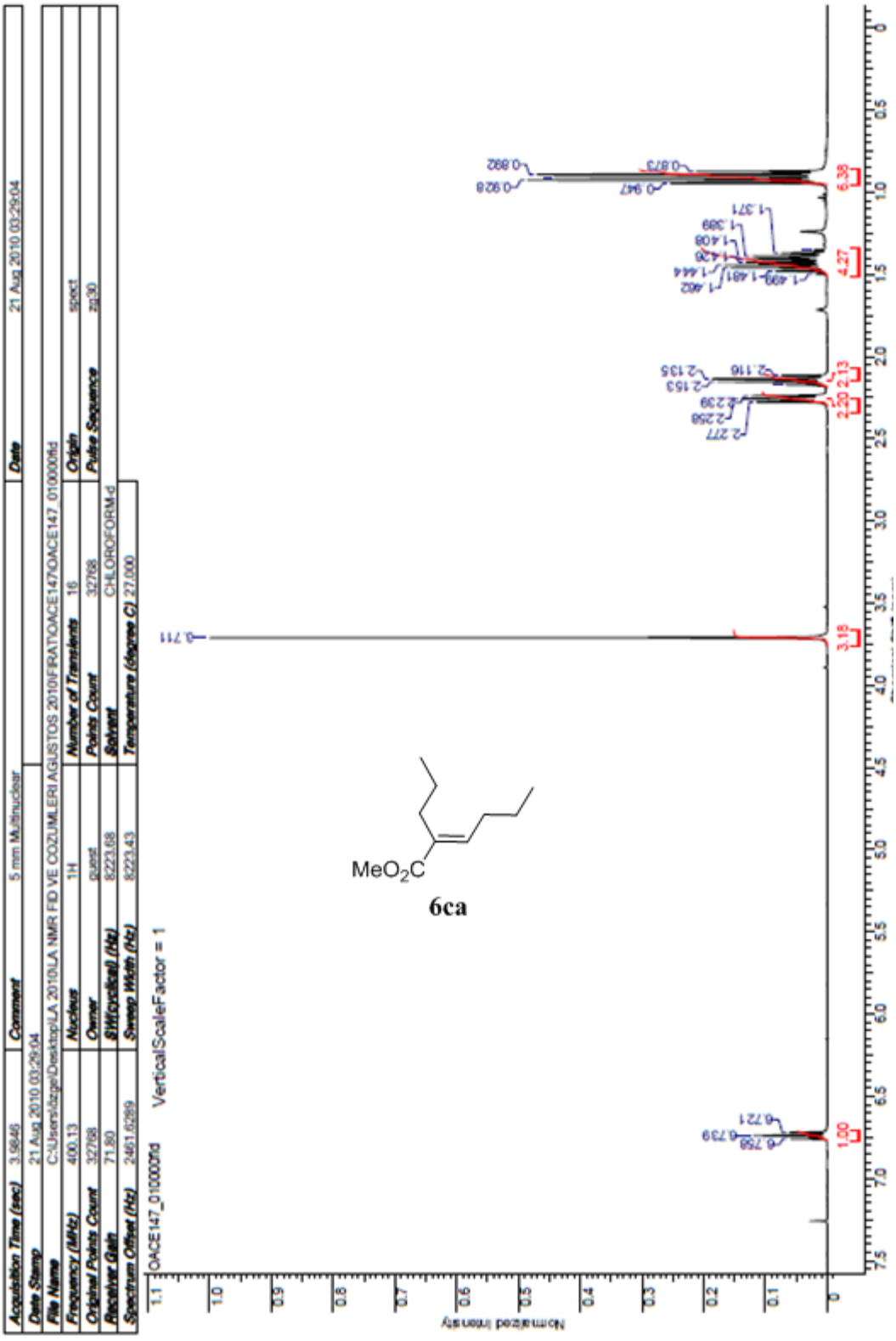

Figure A.33 ^{1}H NMR of (E)-methyl 2-propylhex-2-enoate

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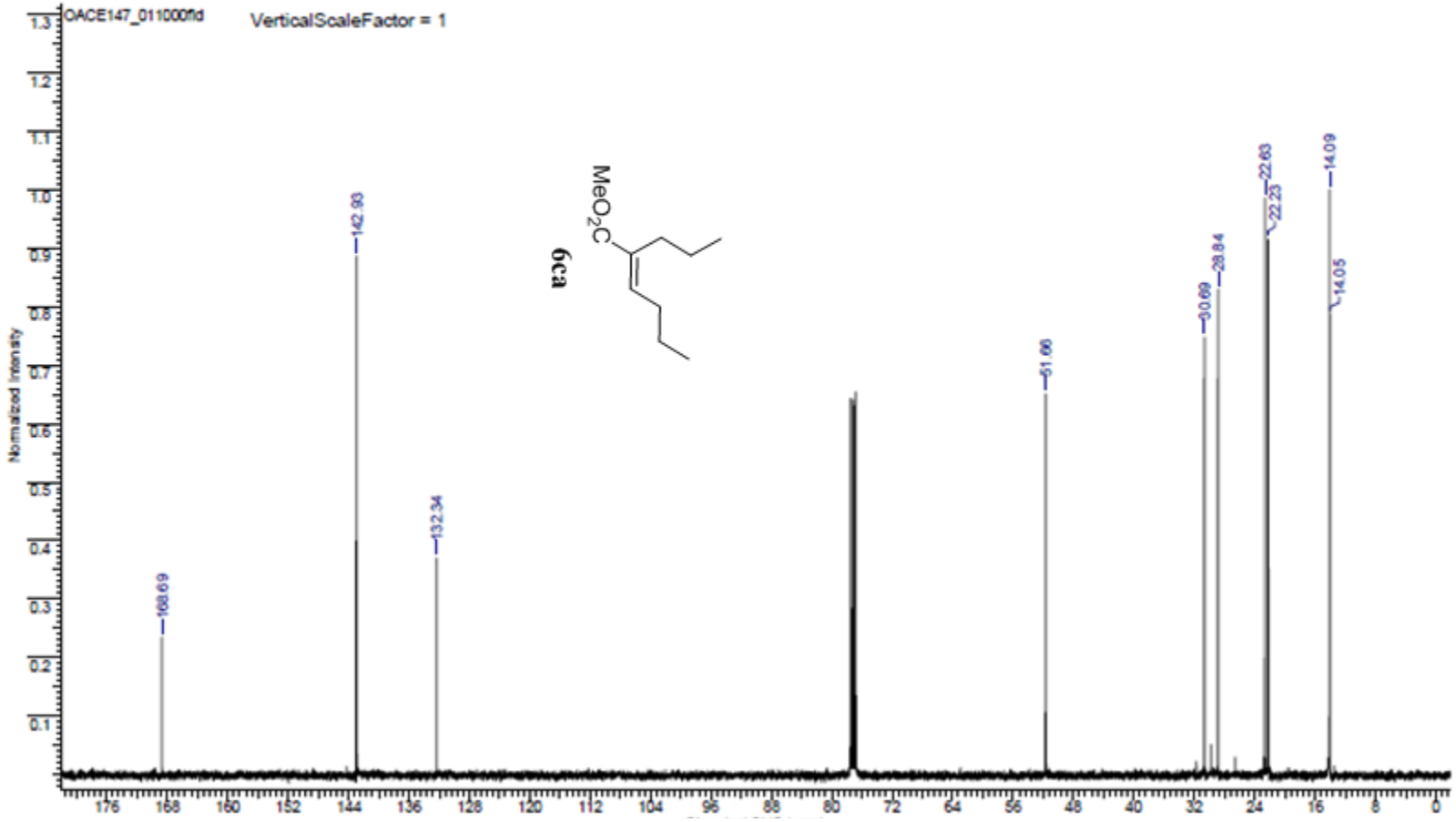

Figure A.34 ^{13} C NMR of (E)-methyl 2-propylhex-2-enoate

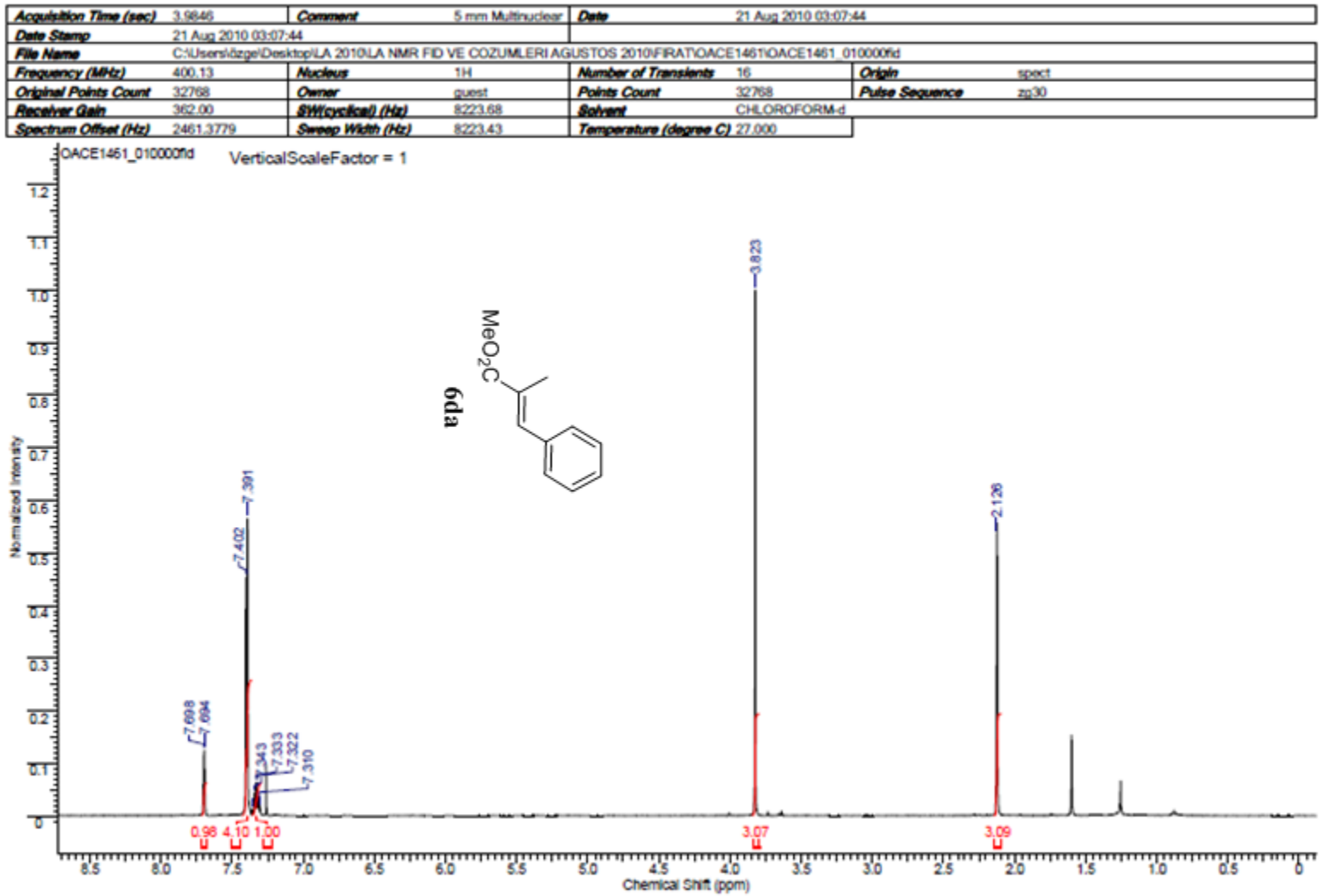

Figure A.35 [1] H NMR of (E)-methyl 2-methyl-3-phenylacrylate

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Receiver Gain	8192.00	SW(cyclical) (Hz)	31847.13	Solvent	CHLOROFORM-d	Spectrum Offset (Hz)	12679.6299
Sweep Width (Hz)	31846.16	Temperature (degree C)	27.000				

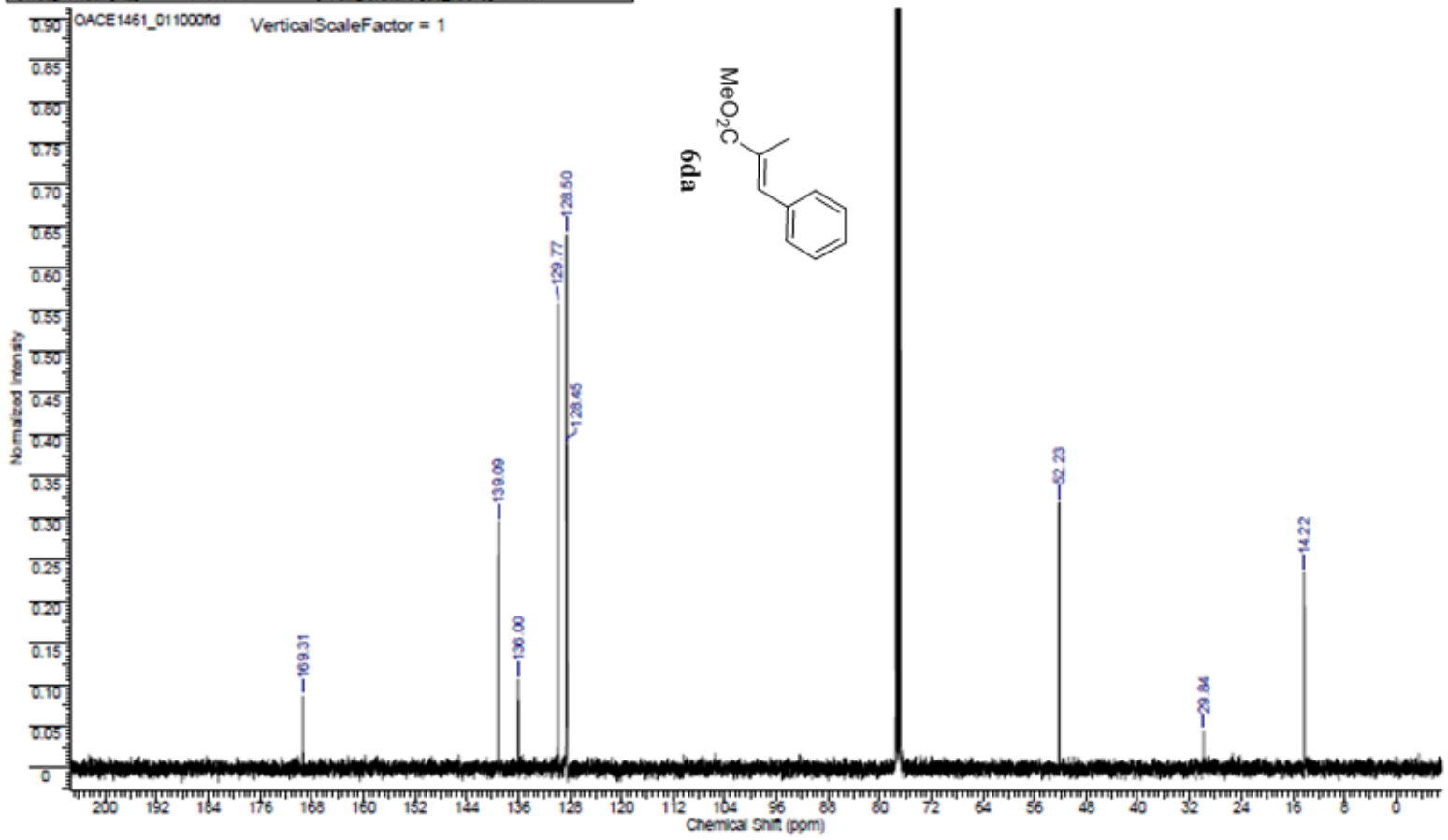

Figure A.36 ^{13} C NMR of (E)-methyl 2-methyl-3-phenylacrylate

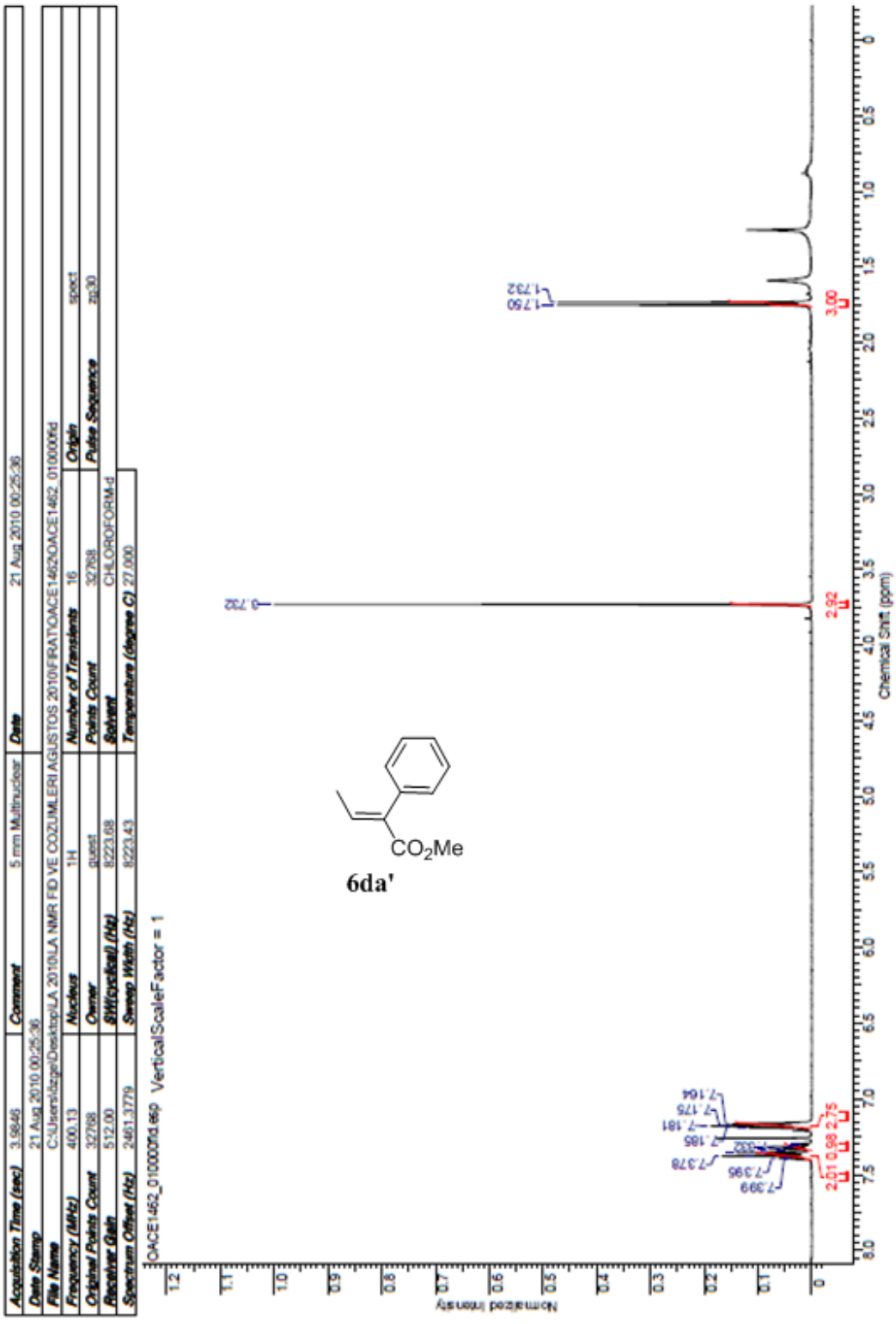

Figure A.37 ^{1}H NMR of (E)-methyl 2-phenylbut-2-enoate

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Sweep Width (Hz)	31846.16	Temperature (degree C)	27.000				

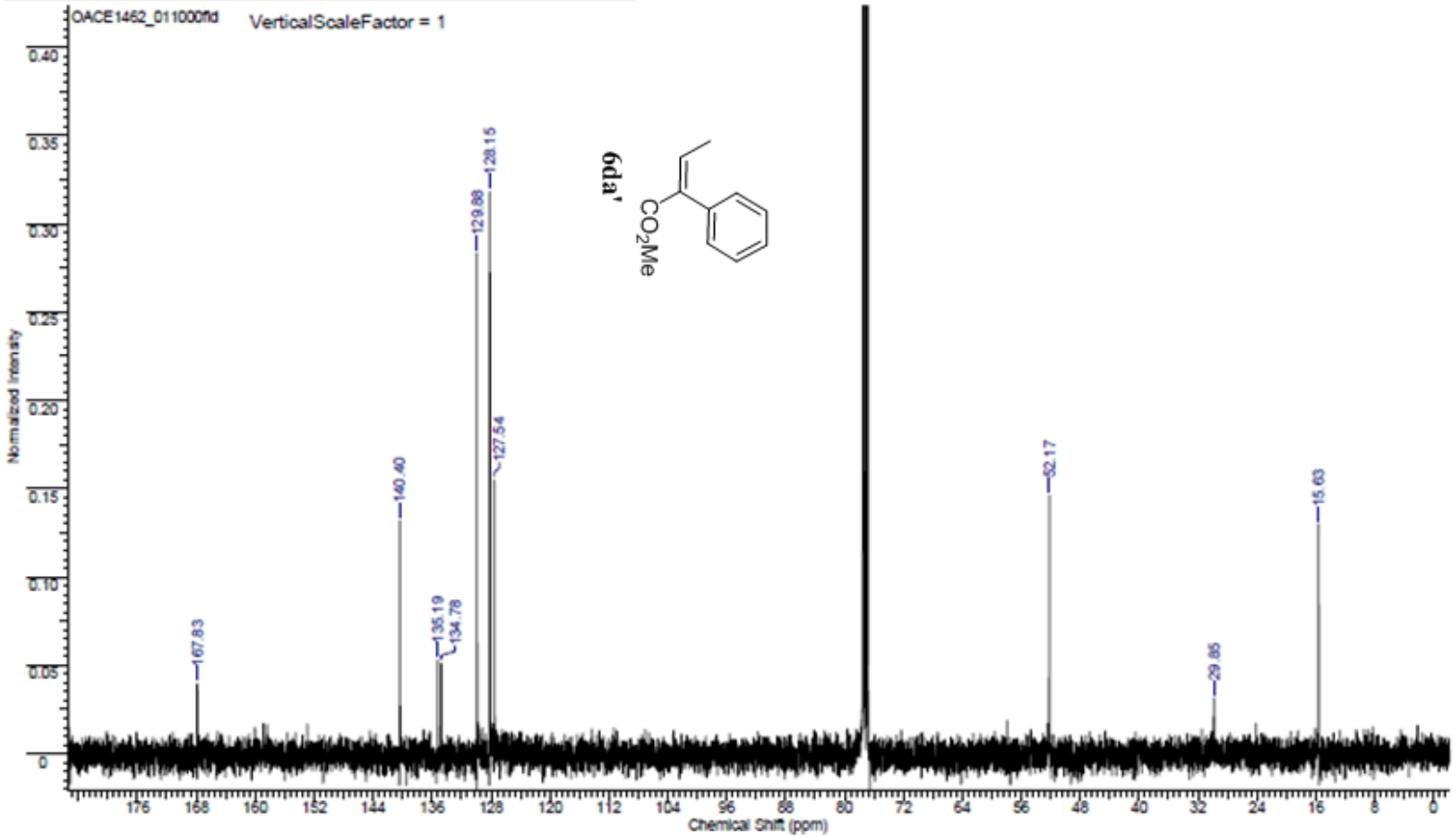

Figure A.38 ^{13} C NMR of (E)-methyl 2-phenylbut-2-enoate

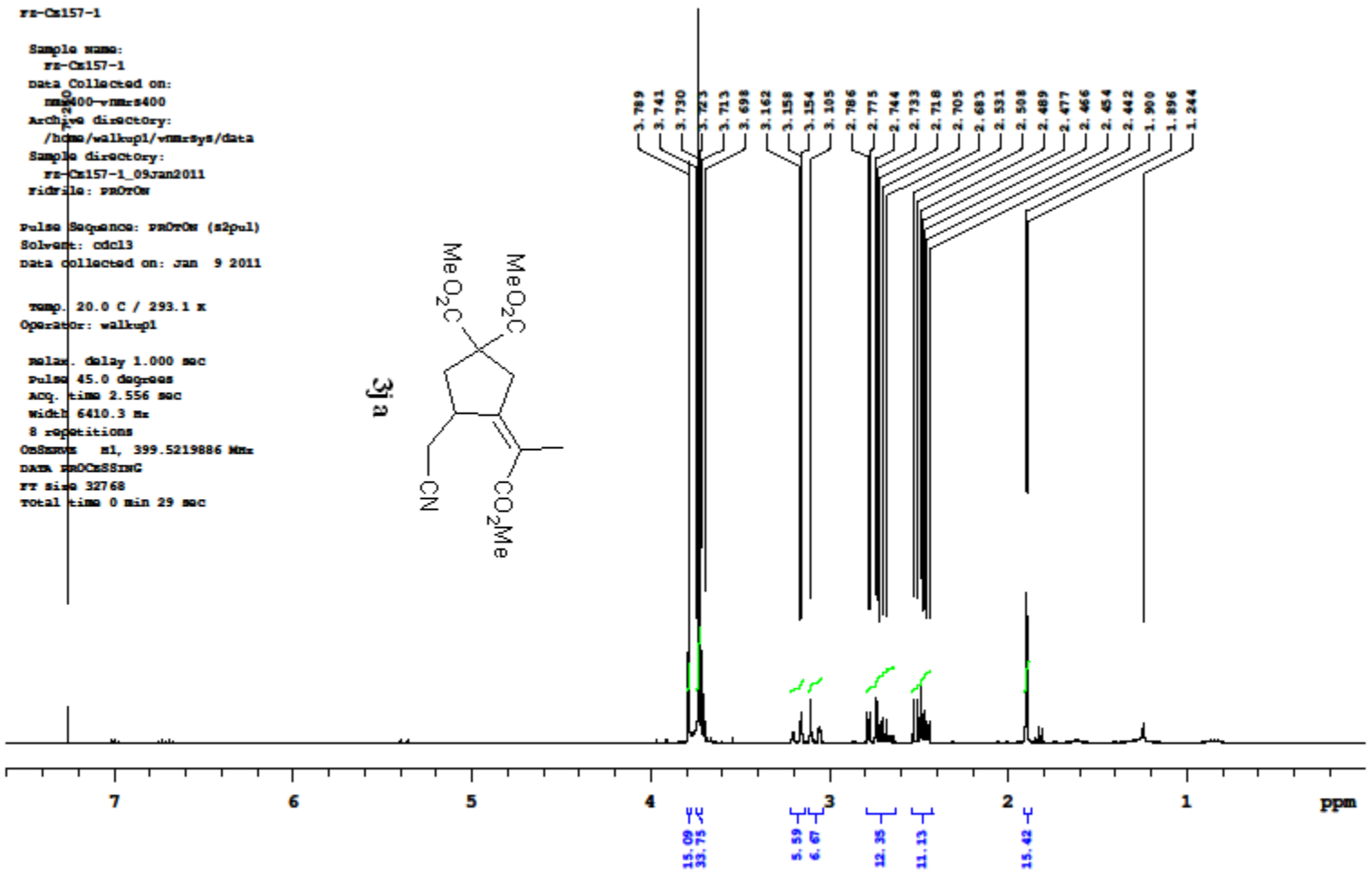

Figure A.39 ^{1}H NMR of (Z)-dimethyl 3-(cyanomethyl)-4-(1-methoxy-1-oxopropan-2-ylidene)cyclopentane-1,1-dicarboxylate

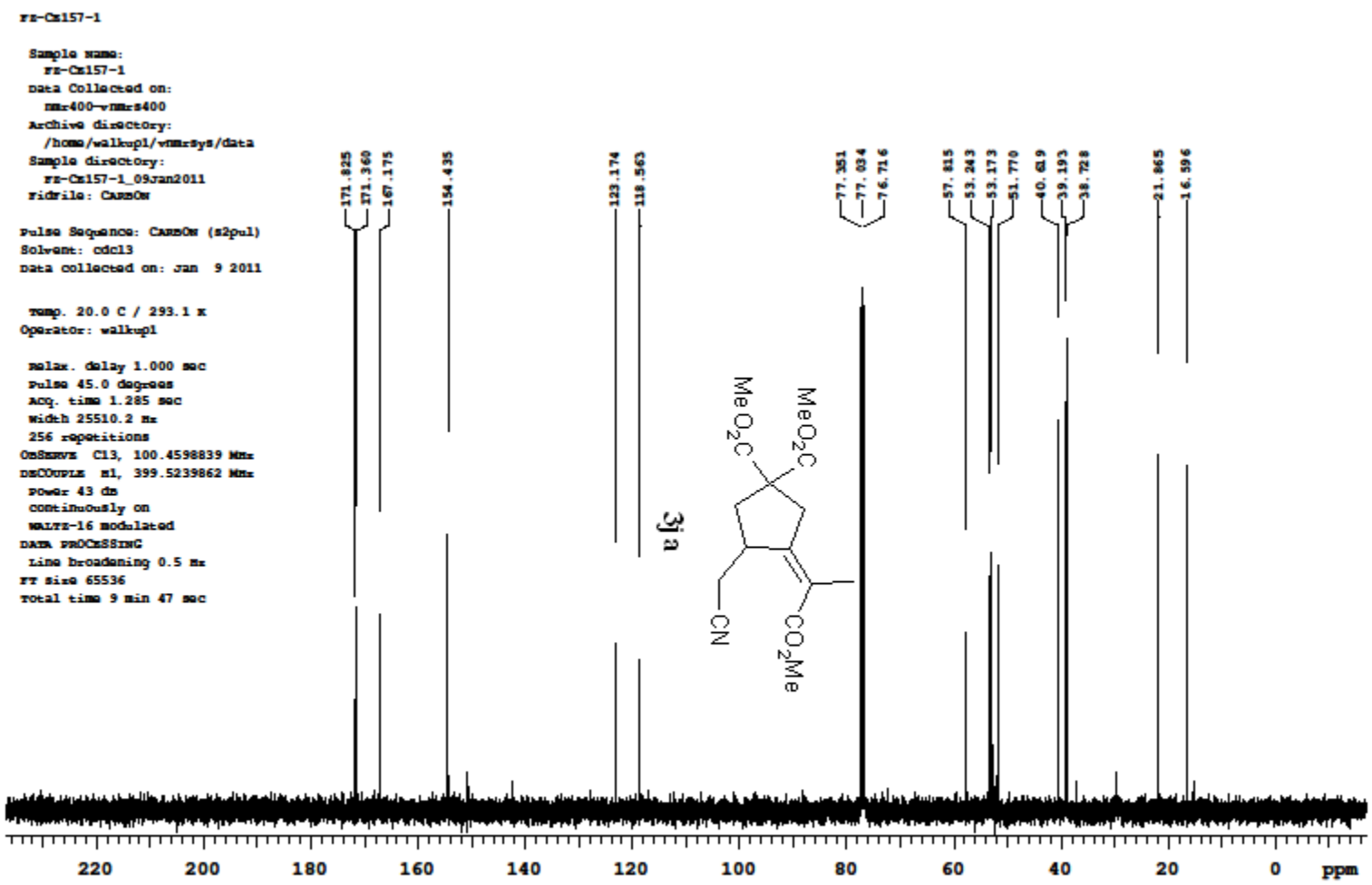

Figure A.40 ^{13}C NMR of (Z)-dimethyl 3-(cyanomethyl)-4-(1-methoxy-1-oxopropan-2-ylidene)cyclopentane-1,1- dicarboxylate

APPENDIX B

MASS SPECTRUMS OF PRODUCTS

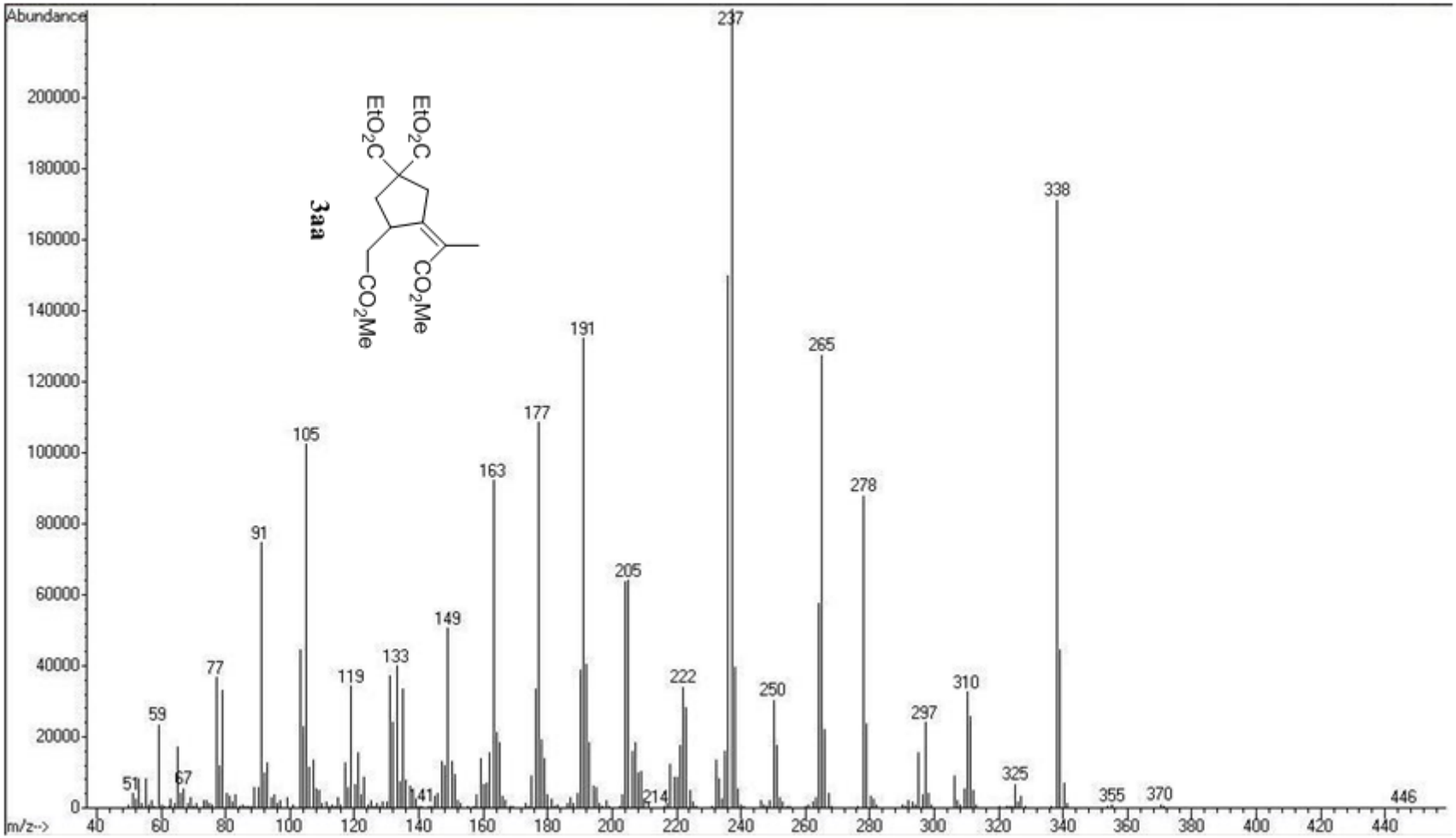

Figure B.1. Mass spectrum of (Z)-diethyl 3-(1-methoxy-1-oxopropan-2-ylidene)-4-(2-methoxy-2-oxoethyl)cyclopentane-1,1-dicarboxylate

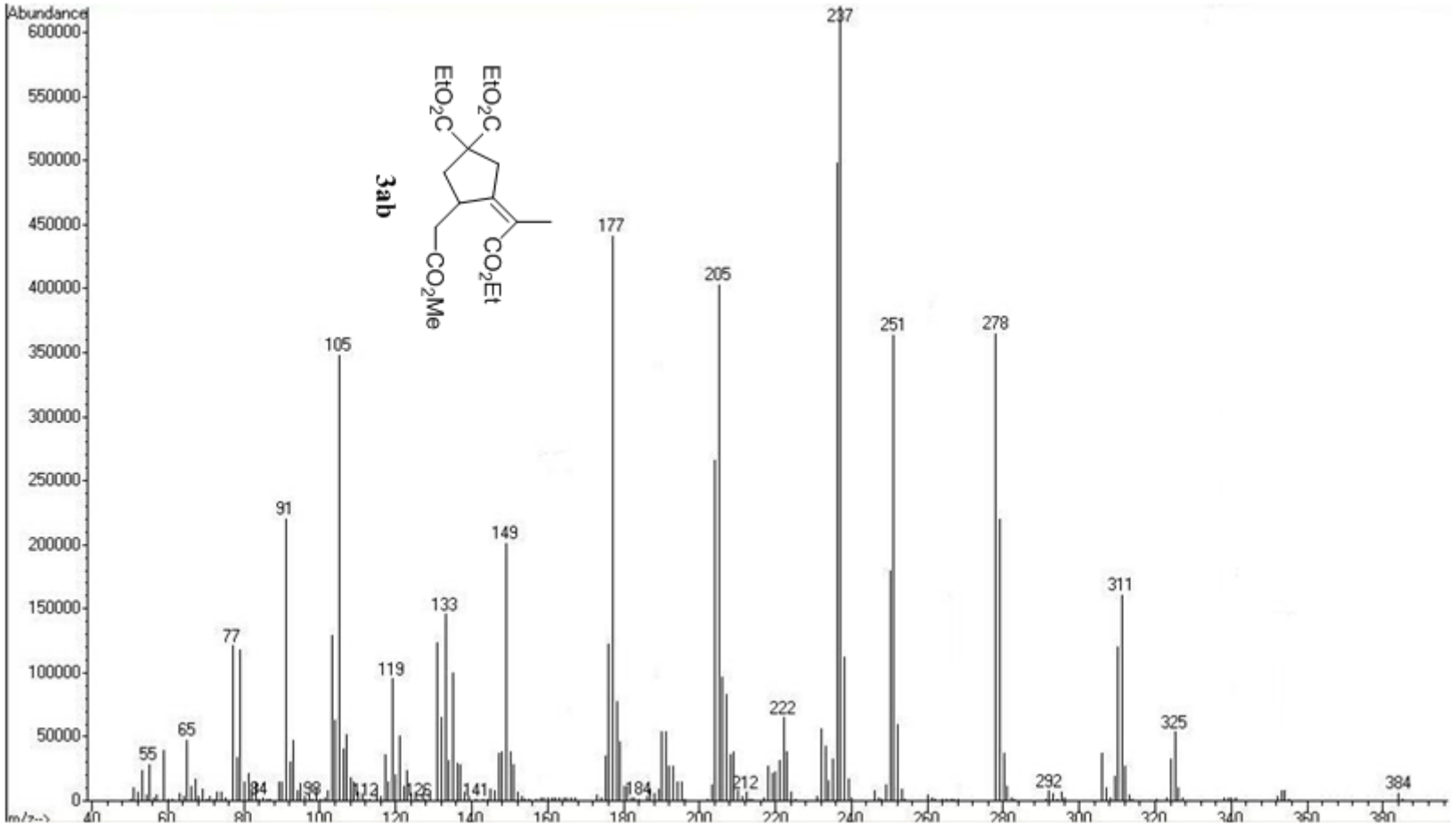

Figure B.2. Mass spectrum of (Z)-diethyl 3-(1-ethoxy-1-oxopropan-2-ylidene)-4-(2-methoxy-2-oxoethyl)cyclopentane-1,1-dicarboxylate

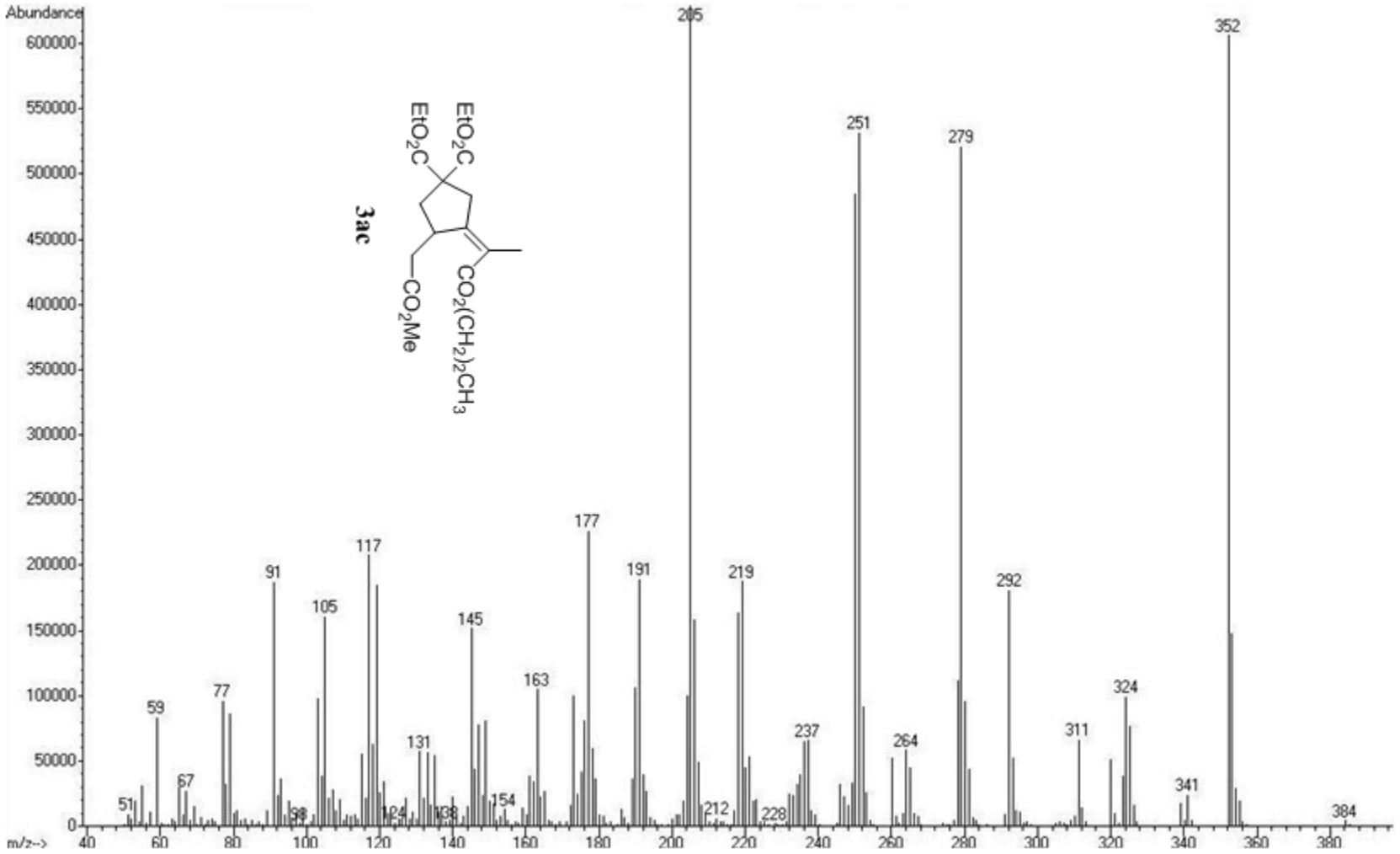

Figure B.3. Mass spectrum of (Z)-diethyl 3-(2-methoxy-2-oxoethyl)-4-(1-oxo-1-propoxypropan-2-ylidene)cyclopentane-1,1-dicarboxylate

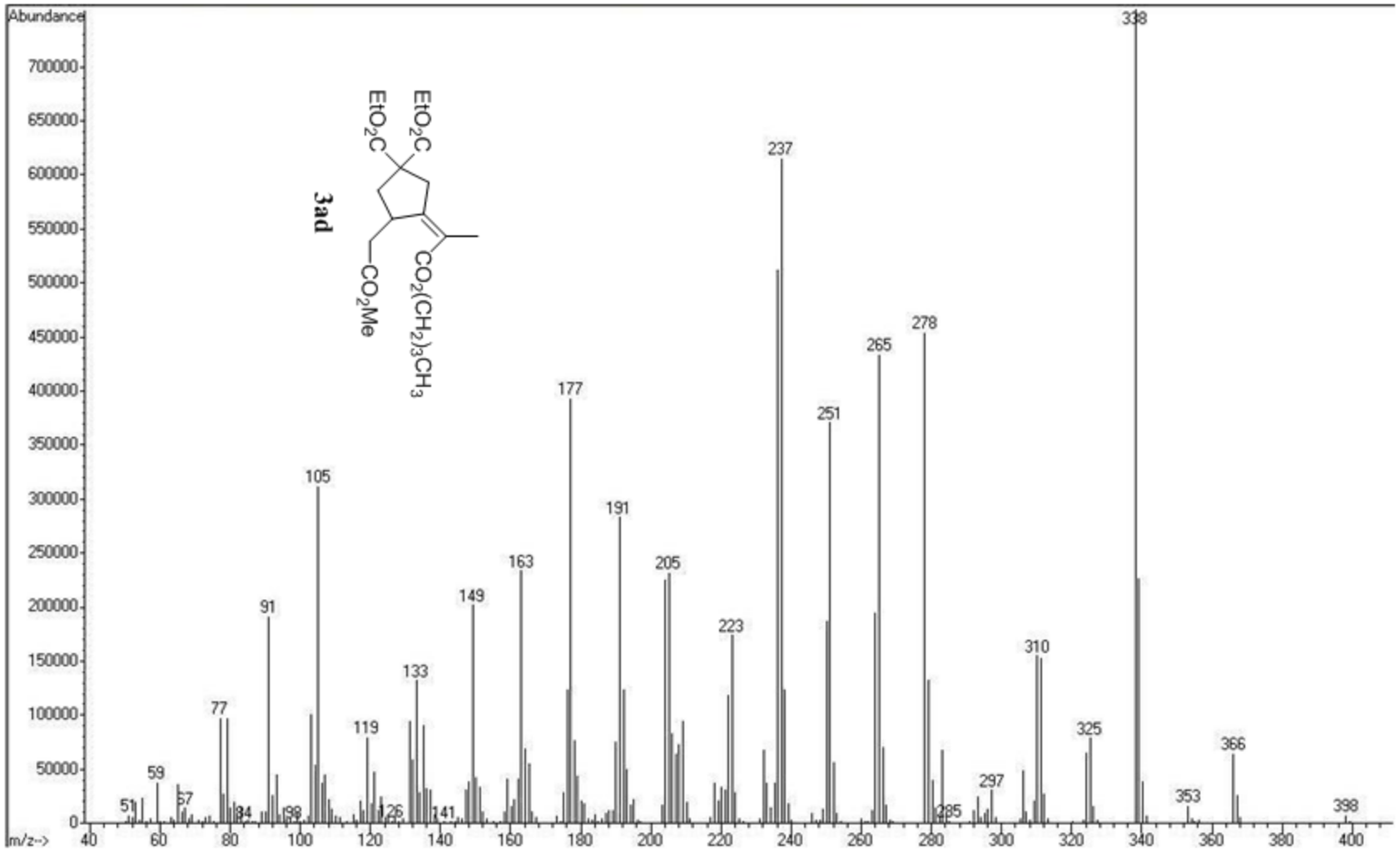

Figure B.4. Mass spectrum of (Z)-diethyl 3-(1-butoxy-1-oxopropan-2-ylidene)-4-(2-methoxy-2-oxoethyl)cyclopentane-1,1-dicarboxylate

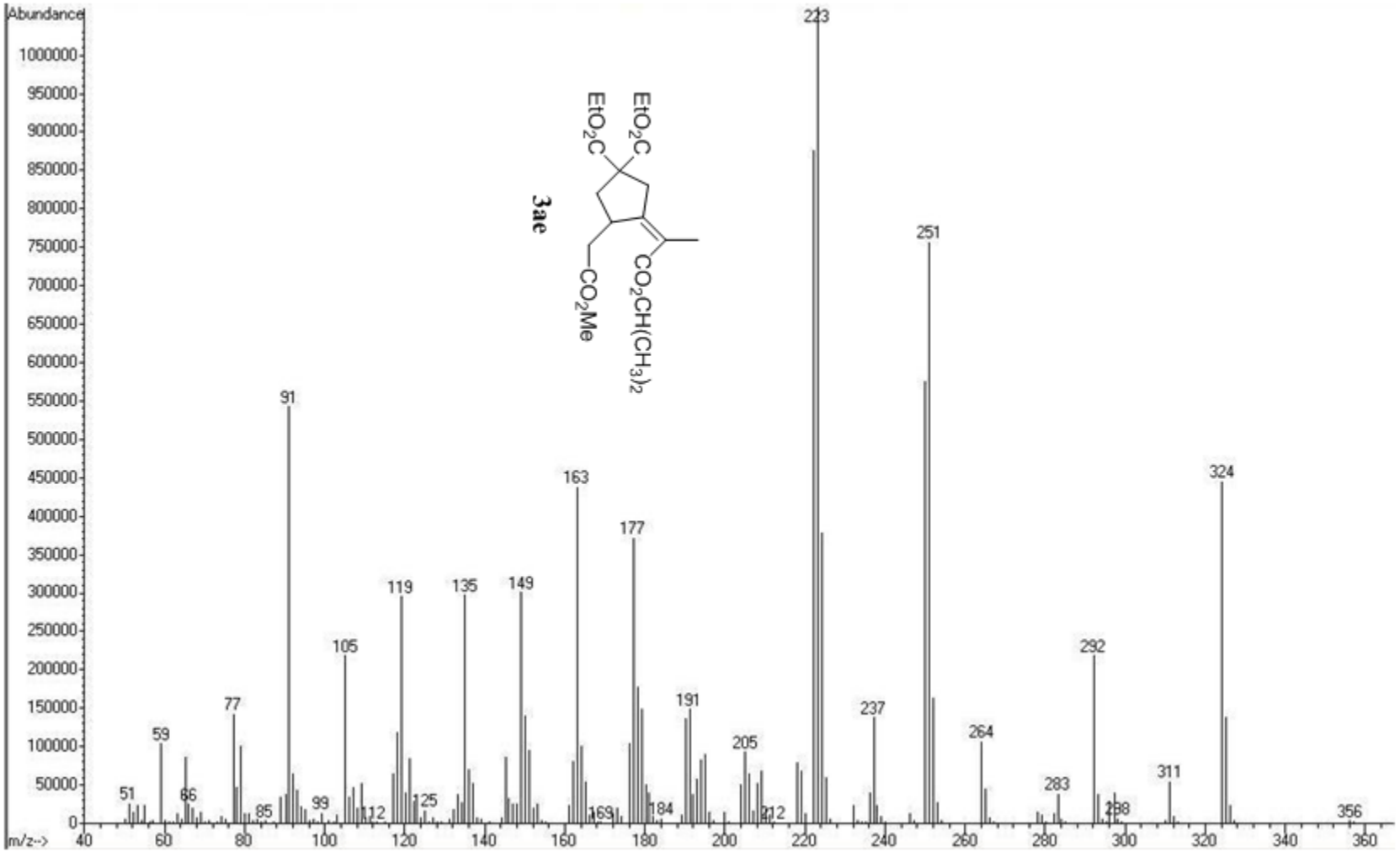

Figure B.5. Mass spectrum of (Z)-diethyl 3-(1-isopropoxy-1-oxopropan-2-ylidene)-4-(2-methoxy-2-oxoethyl)cyclopentane-1,1-dicarboxylate

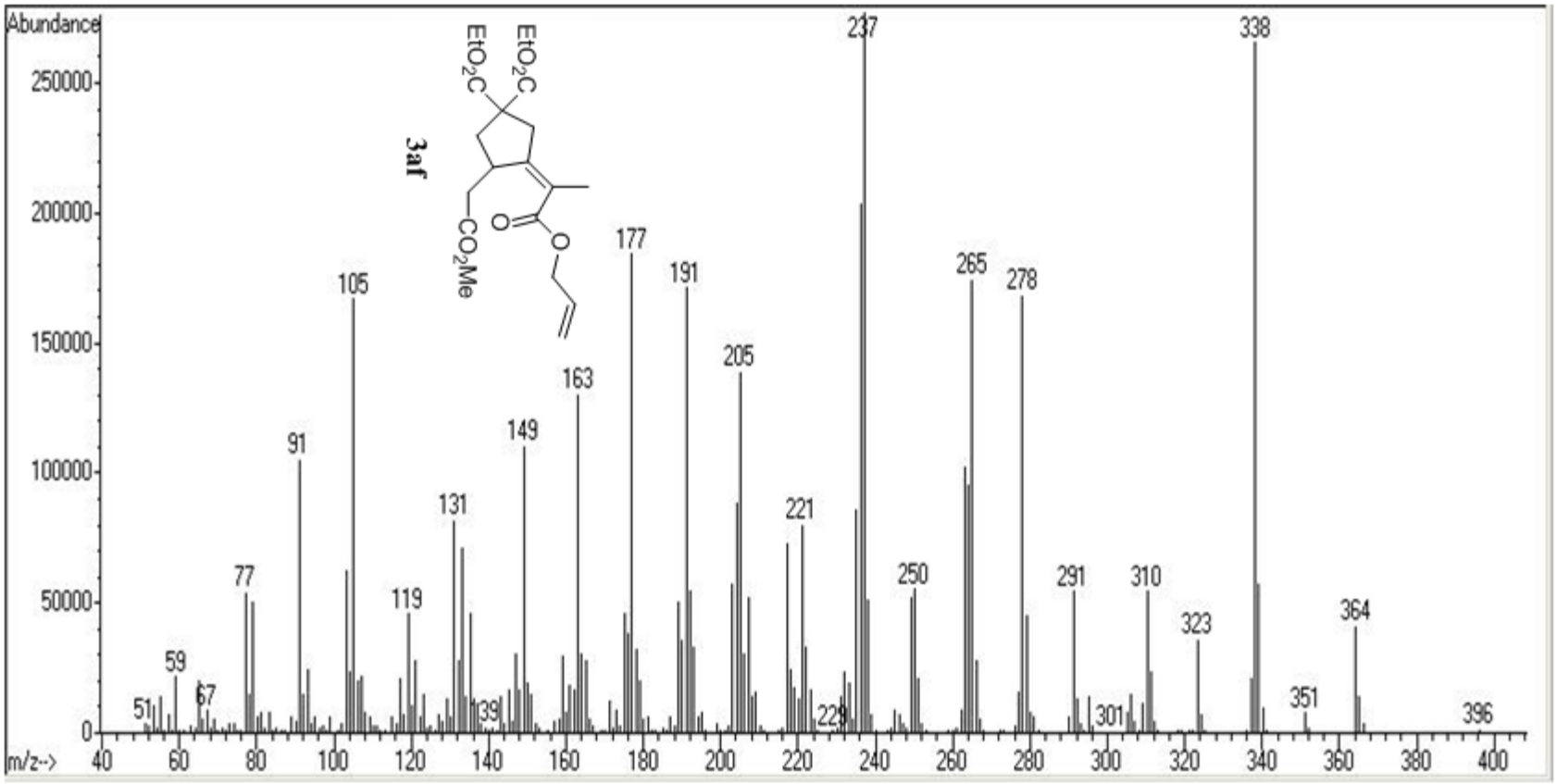

Figure B.6. Mass spectrum of (Z)-diethyl 3-(1-(allyloxy)-1-oxopropan-2-ylidene)-4-(2-methoxy-2-oxoethyl)cyclopentane-1,1-dicarboxylate

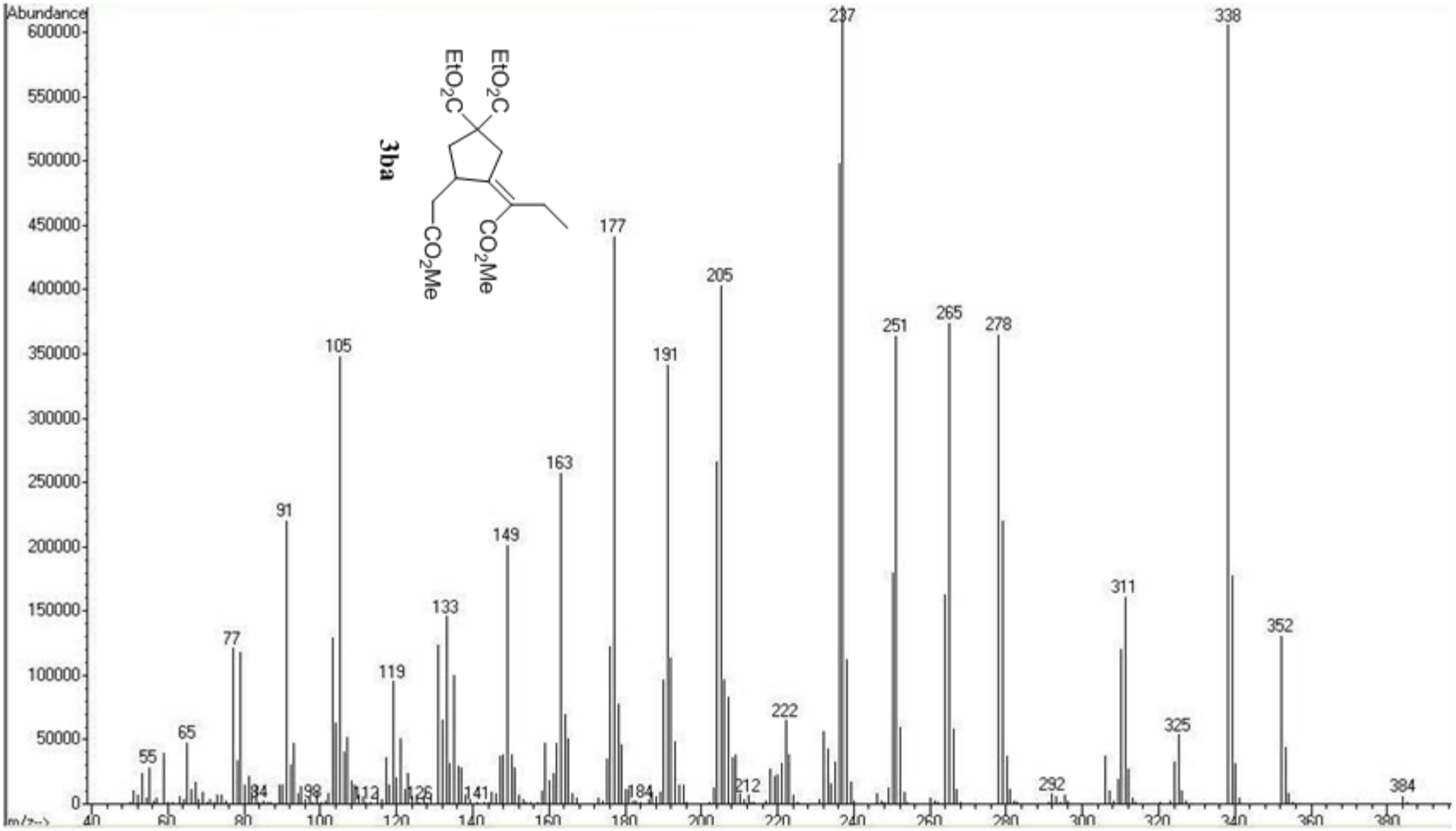

Figure B.7. Mass spectrum of (Z)-diethyl 3-(1-methoxy-1-oxobutan-2-ylidene)-4-(2-methoxy-2-oxoethyl)cyclopentane-1,1-dicarboxylate

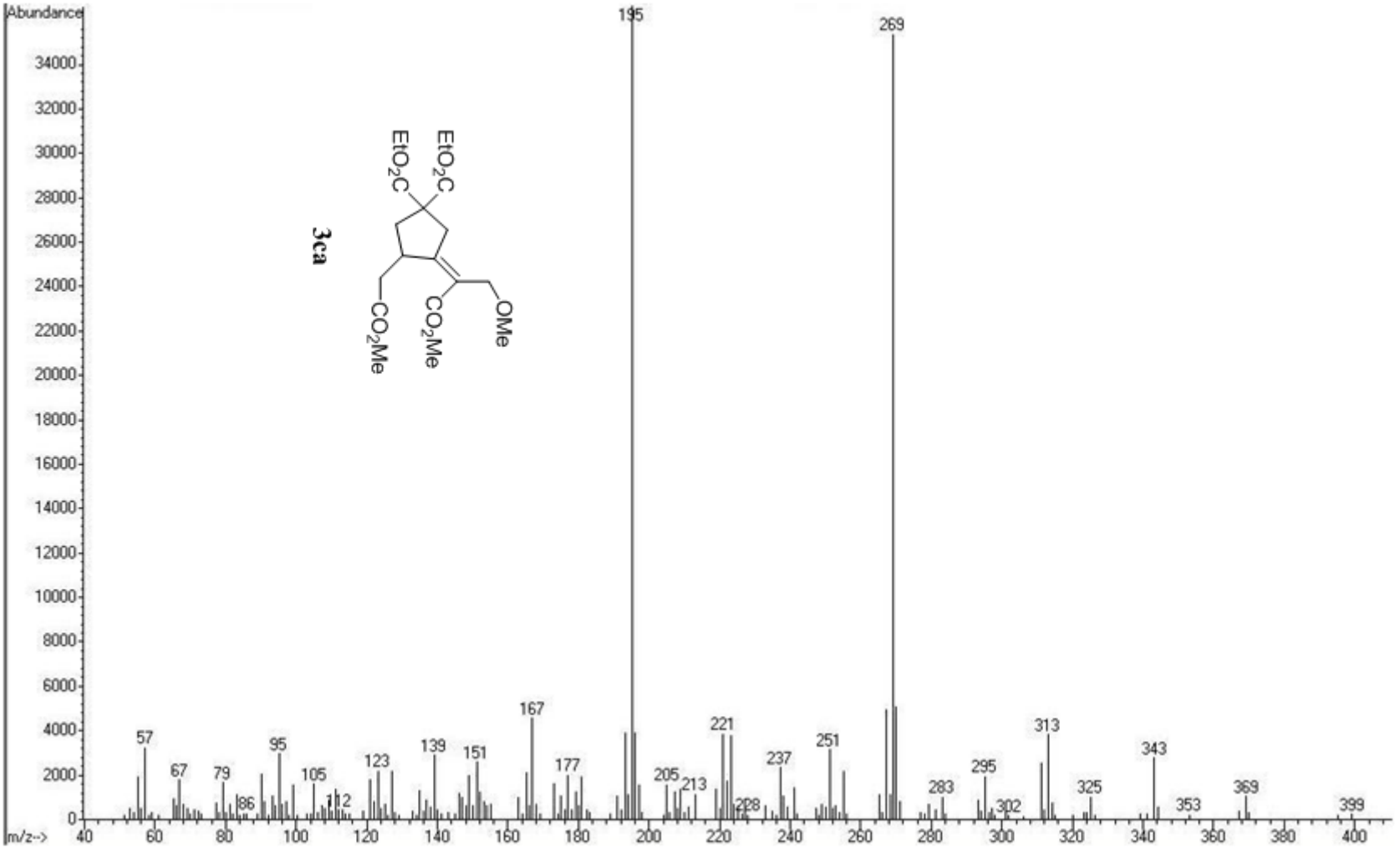

Figure B.8. Mass spectrum of (Z)-diethyl 3-(1,3-dimethoxy-1-oxopropan-2-ylidene)-4-(2-methoxy-2-oxoethyl)cyclopentane-1,1-dicarboxylate

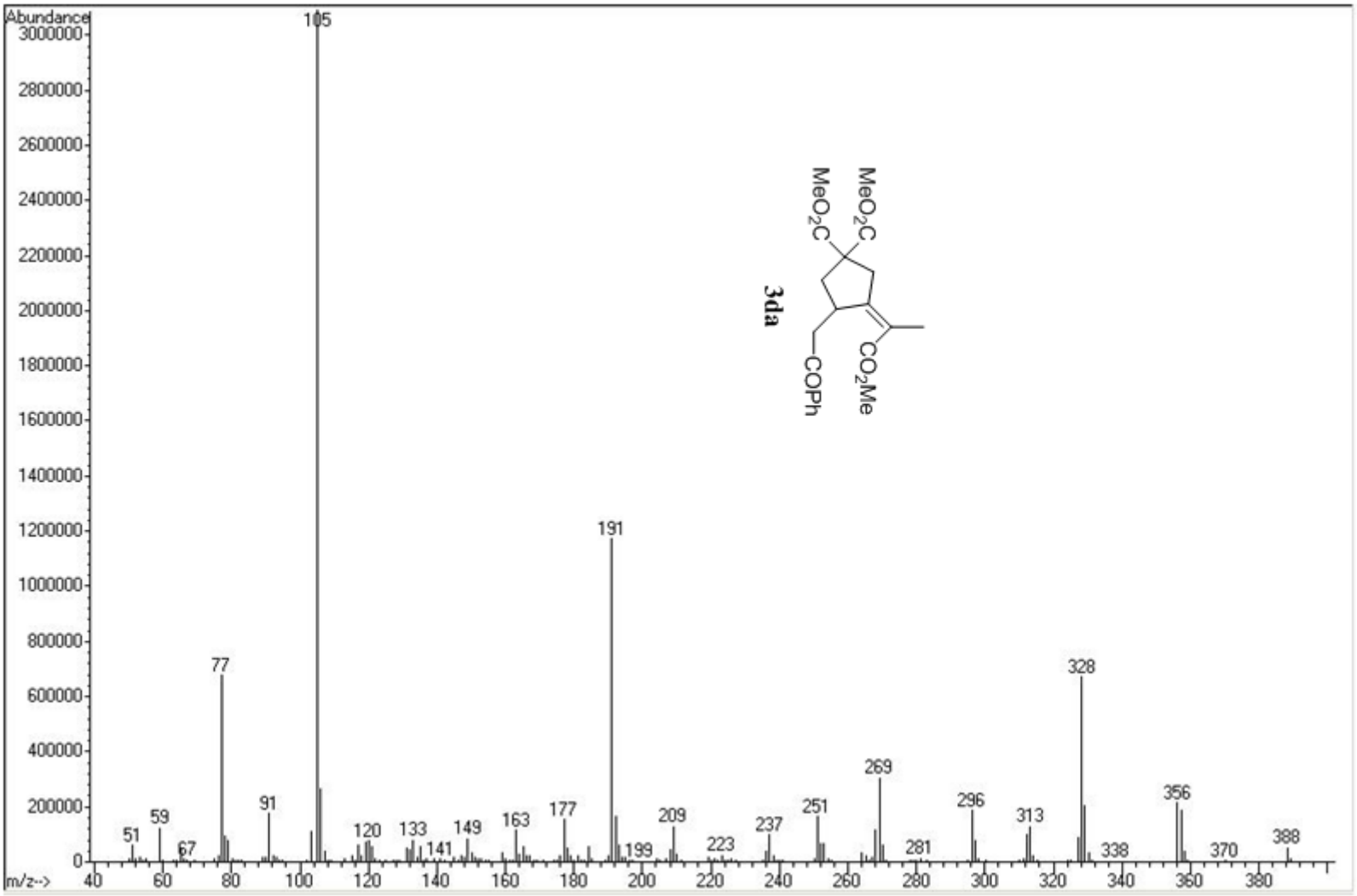

Figure B.9. Mass spectrum of (Z)-dimethyl 3-(1-methoxy-1-oxopropan-2-ylidene)-4-(2-oxo-2-phenylethyl)cyclopentane-1,1-dicarboxylate

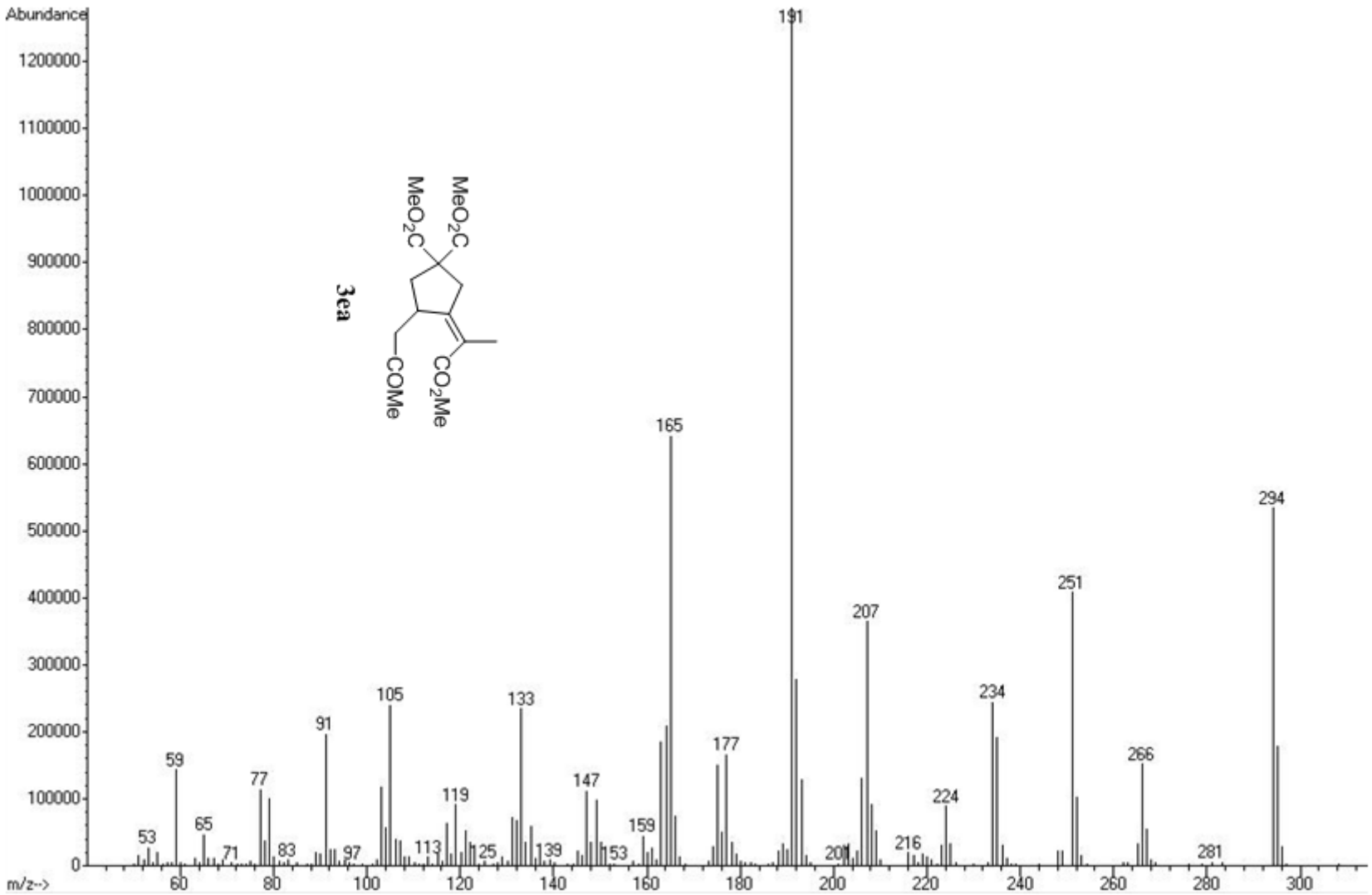

Figure B.10. Mass spectrum of (Z)-dimethyl 3-(1-methoxy-1-oxopropan-2-ylidene)-4-(2-oxopropyl)cyclopentane-1,1-dicarboxylate

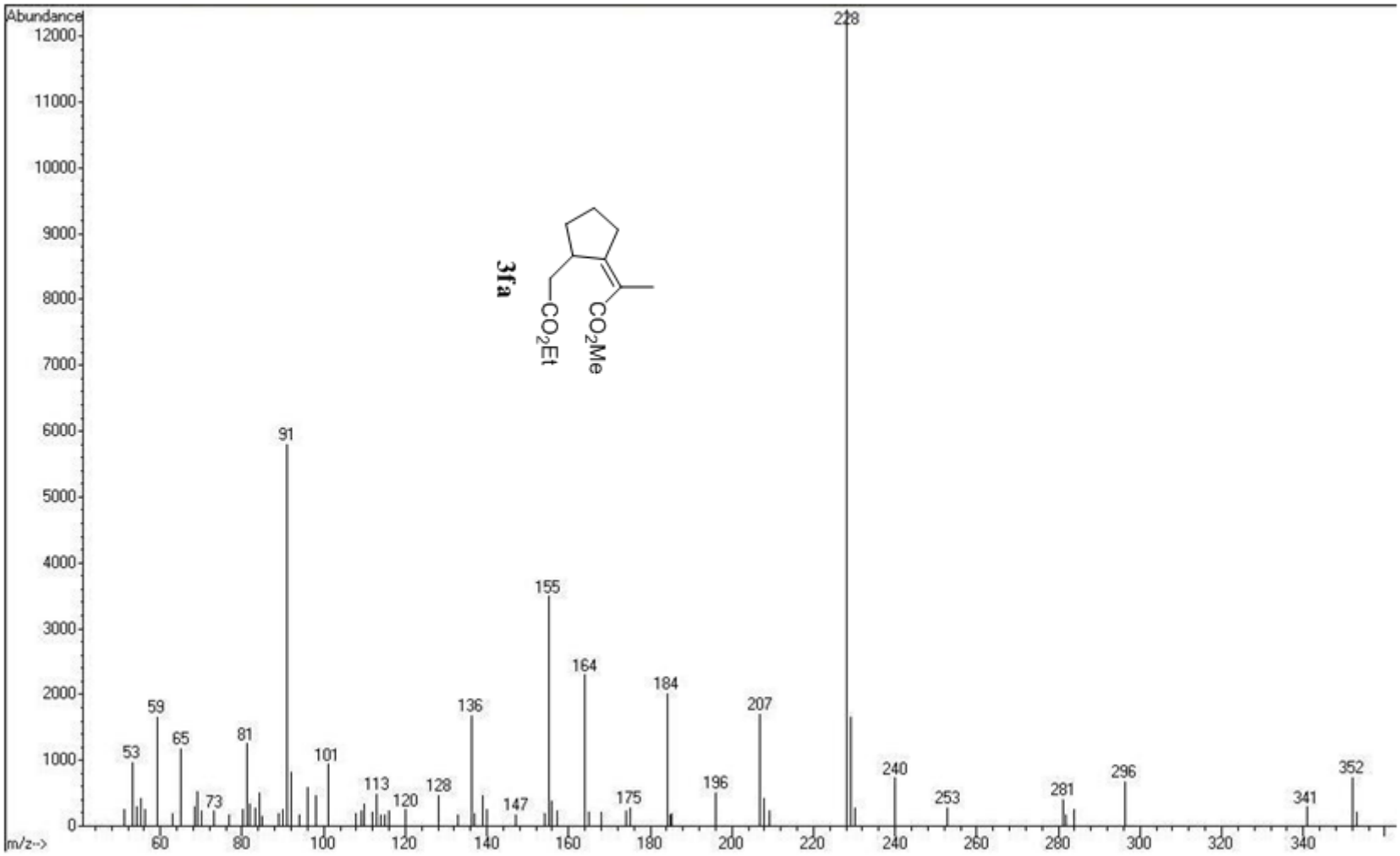

Figure B.11. Mass spectrum of (Z)-methyl 2-(2-(2-ethoxy-2-oxoethyl)cyclopentylidene)propanoate

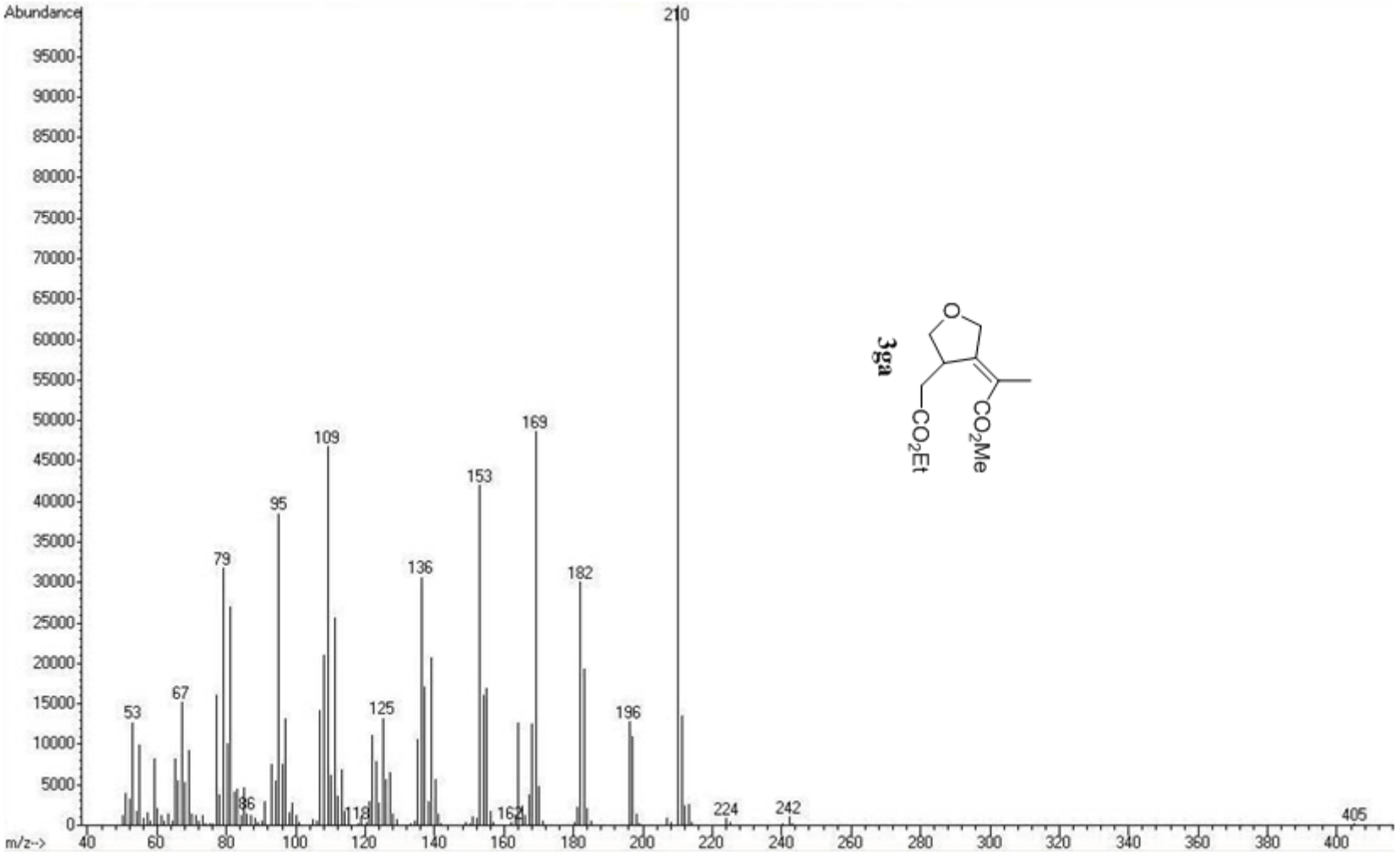

Figure B.12. Mass spectrum of (E)-methyl 2-(4-(2-ethoxy-2-oxoethyl)dihydrofuran-3(2*H*)-ylidene)propanoate

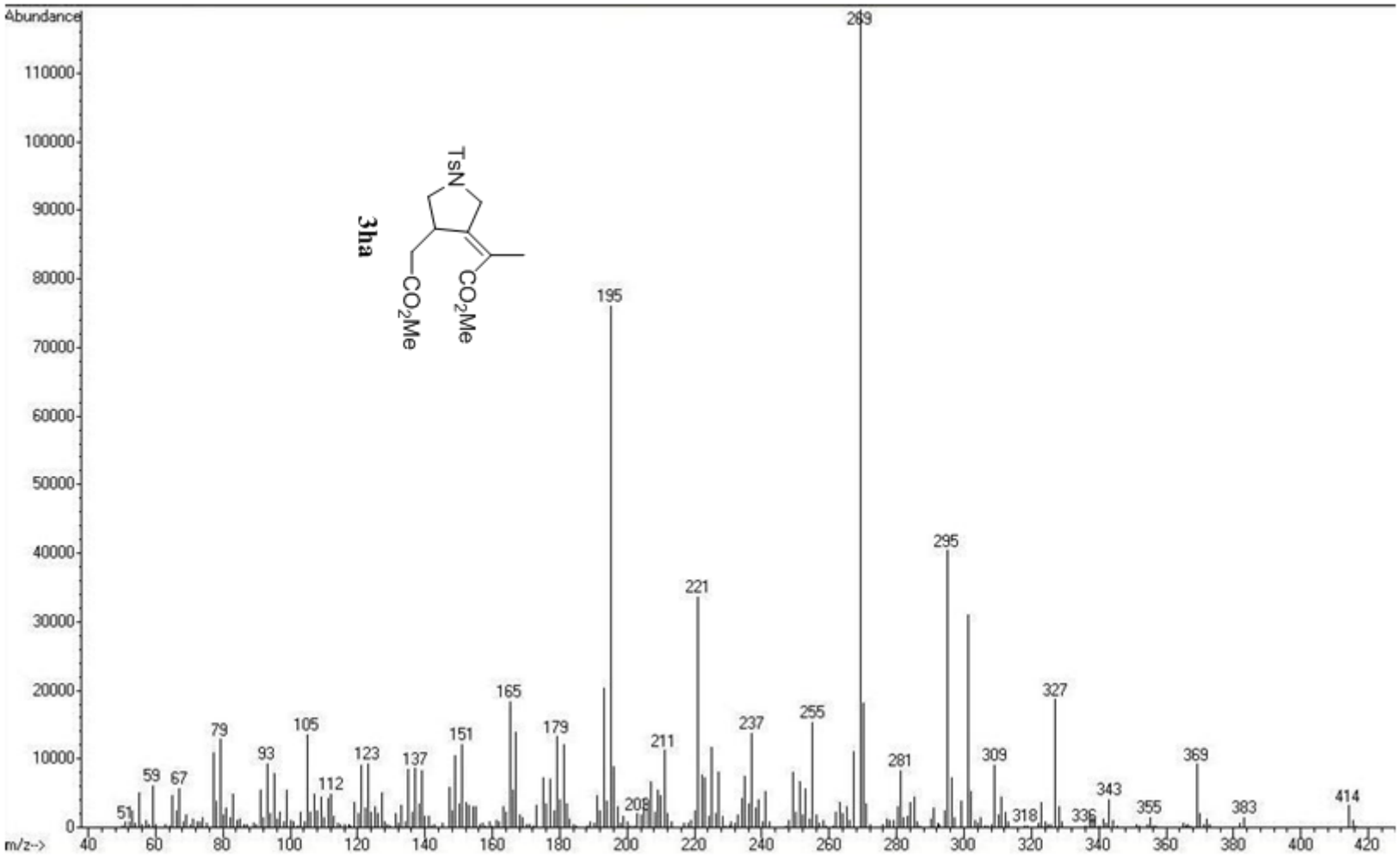

Figure B.13. Mass spectrum of (E)-methyl 2-(4-(2-methoxy-2-oxoethyl)-1-tosylpyrrolidin-3-ylidene)propanoate

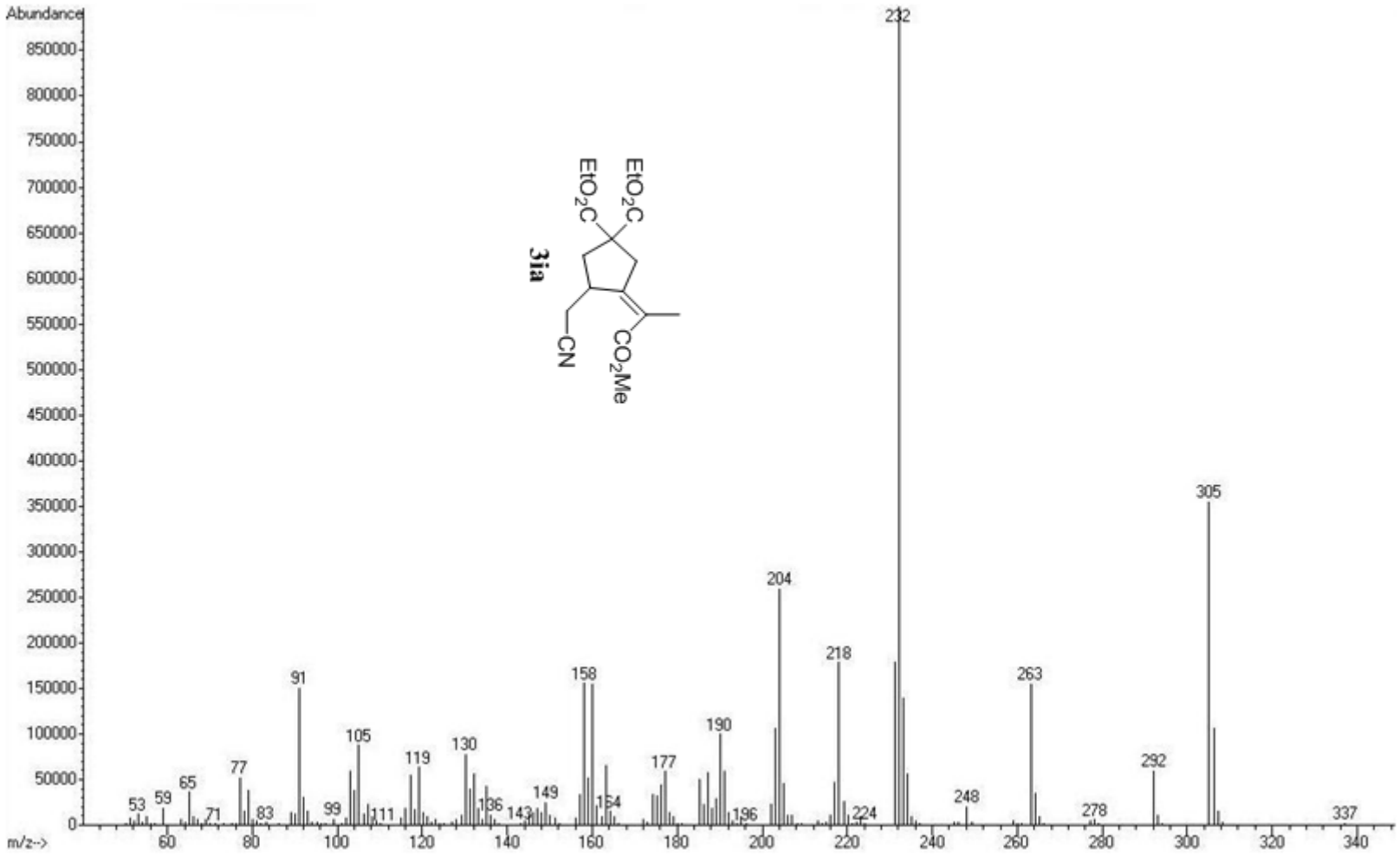

Figure B.14. Mass spectrum of (Z)-diethyl 3-(cyanomethyl)-4-(1-methoxy-1-oxopropan-2-ylidene)cyclopentane-1,1-dicarboxylate

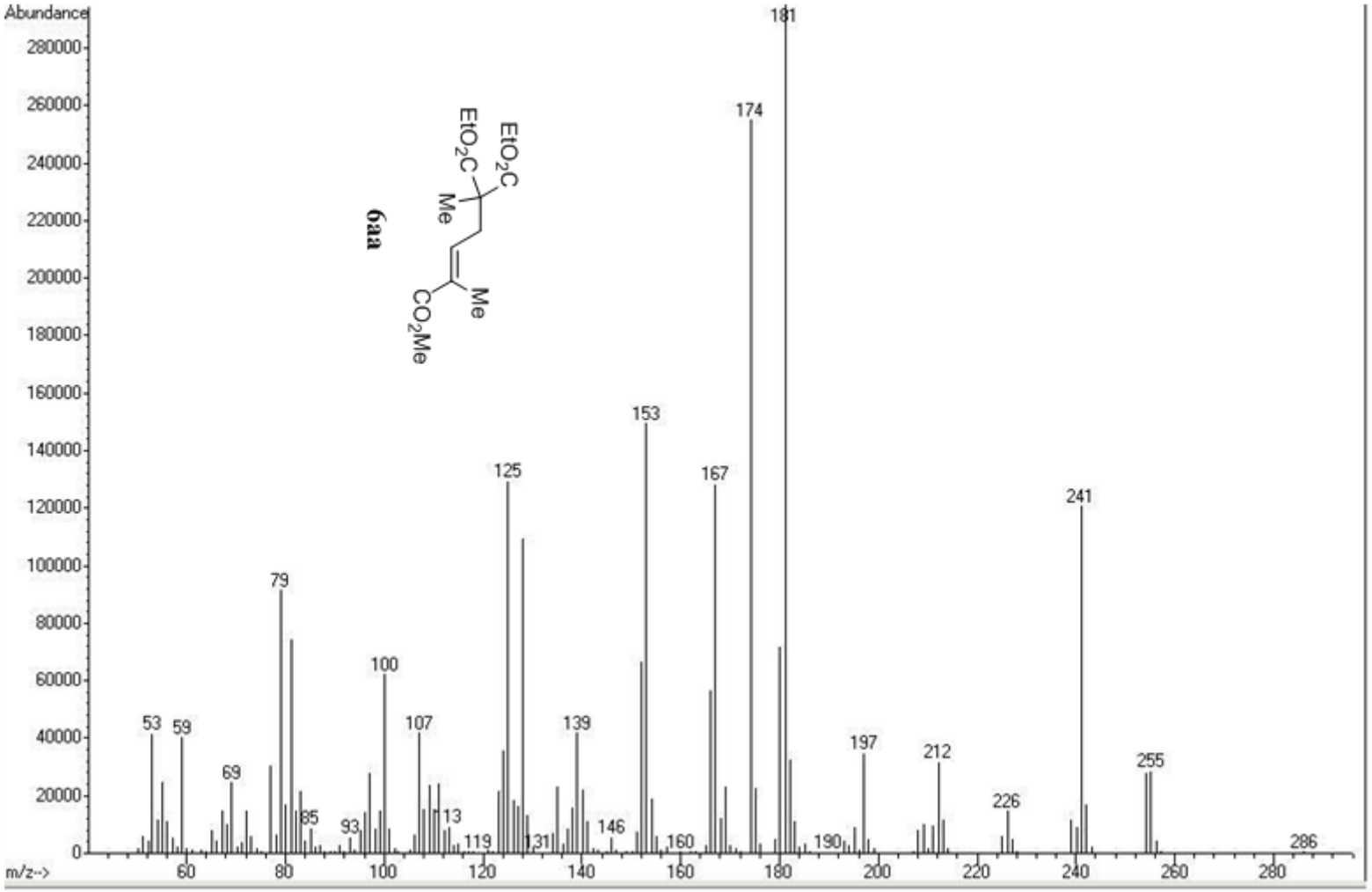

Figure B.15. Mass spectrum of (E)-2,2-diethyl 5-methyl hex-4-ene-2,2,5-tricarboxylate

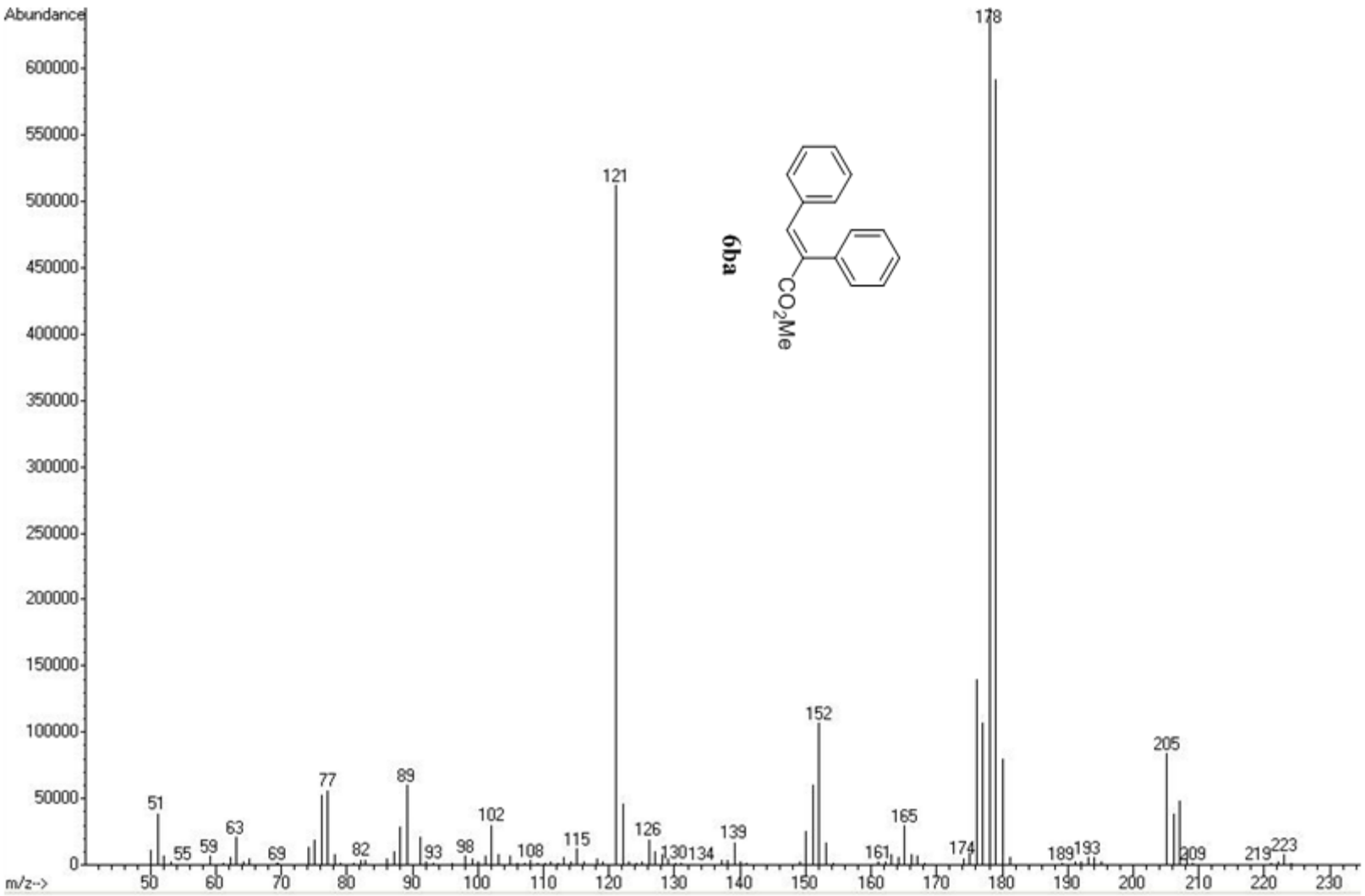

Figure B.16. Mass spectrum of (E)-methyl 2,3-diphenylacrylate

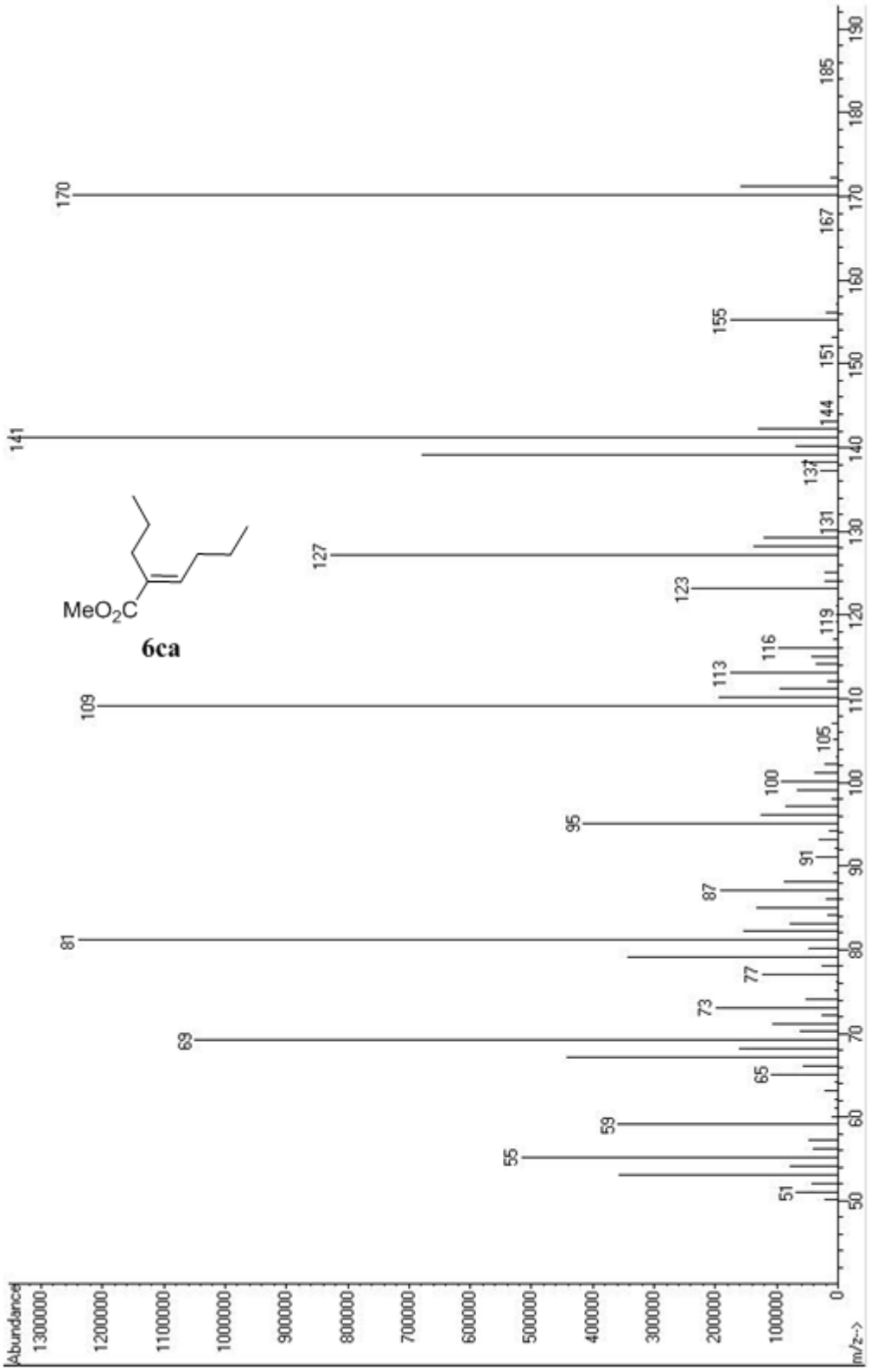

Figure B.17. Mass spectrum of (E)-methyl 2-propylhex-2-enoate

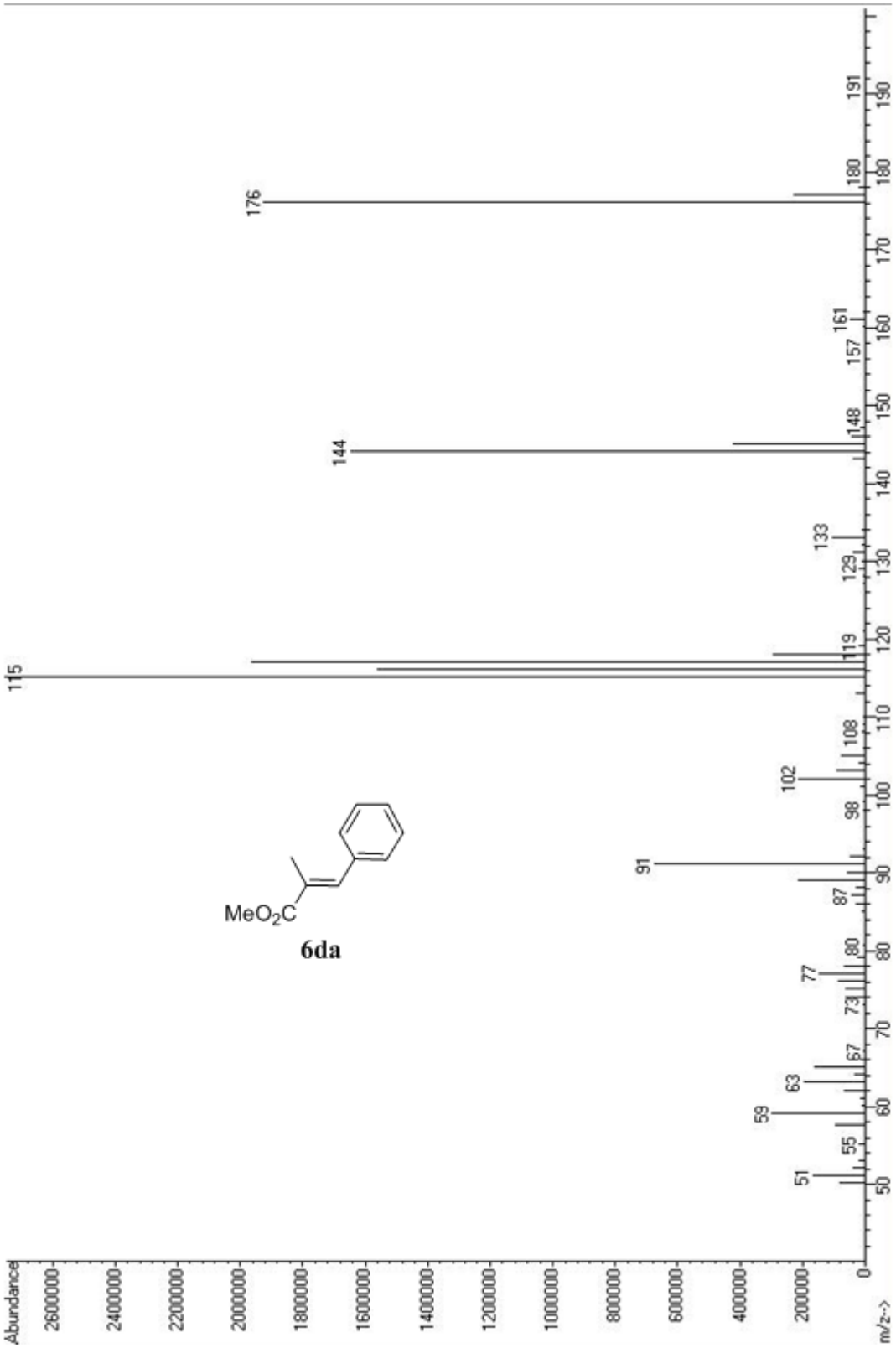

Figure B.18. Mass spectrum of (E)-methyl 2-methyl-3-phenylacrylate

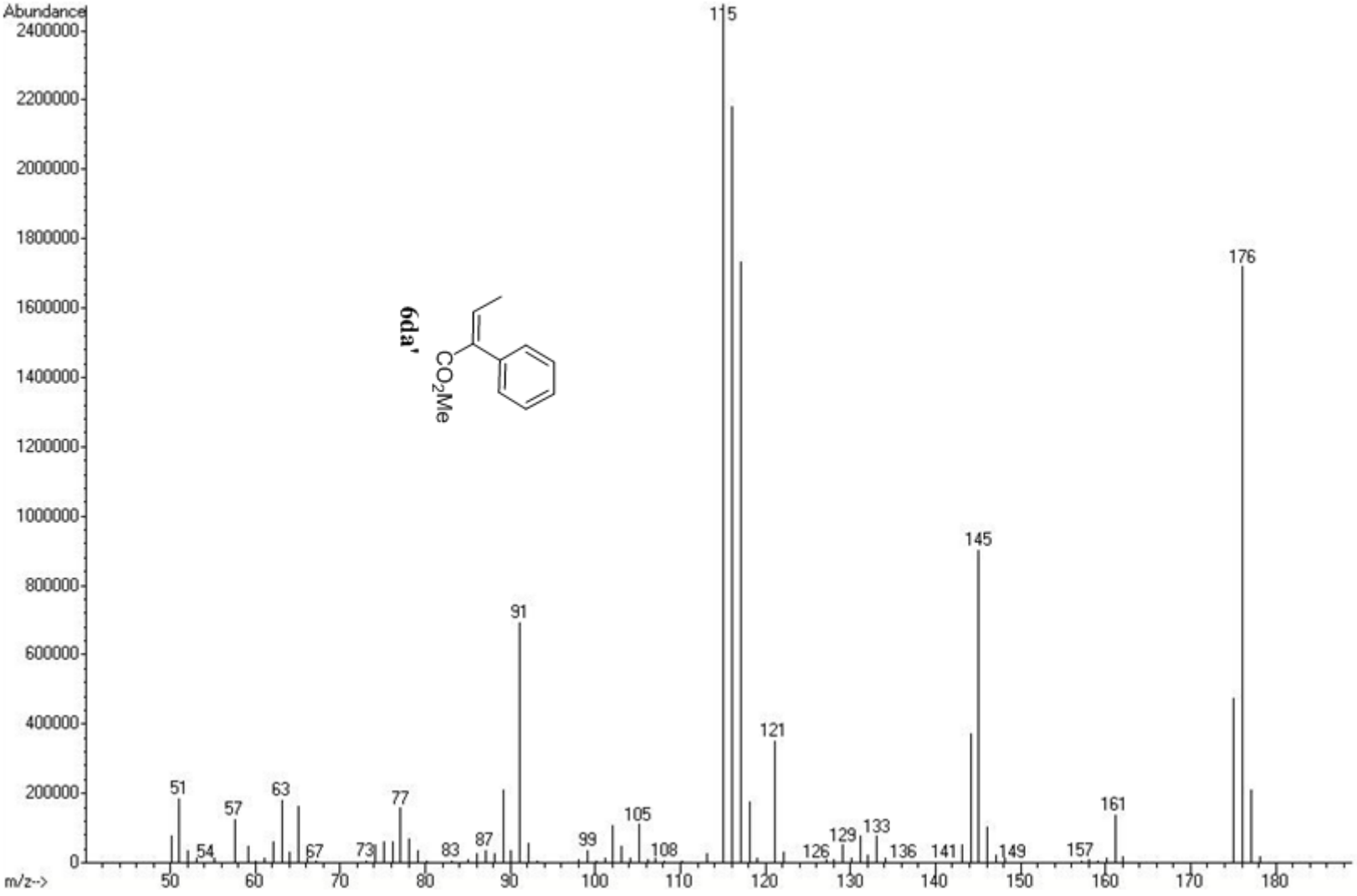

Figure B.19. Mass spectrum of (E)-methyl 2-phenylbut-2-enoate

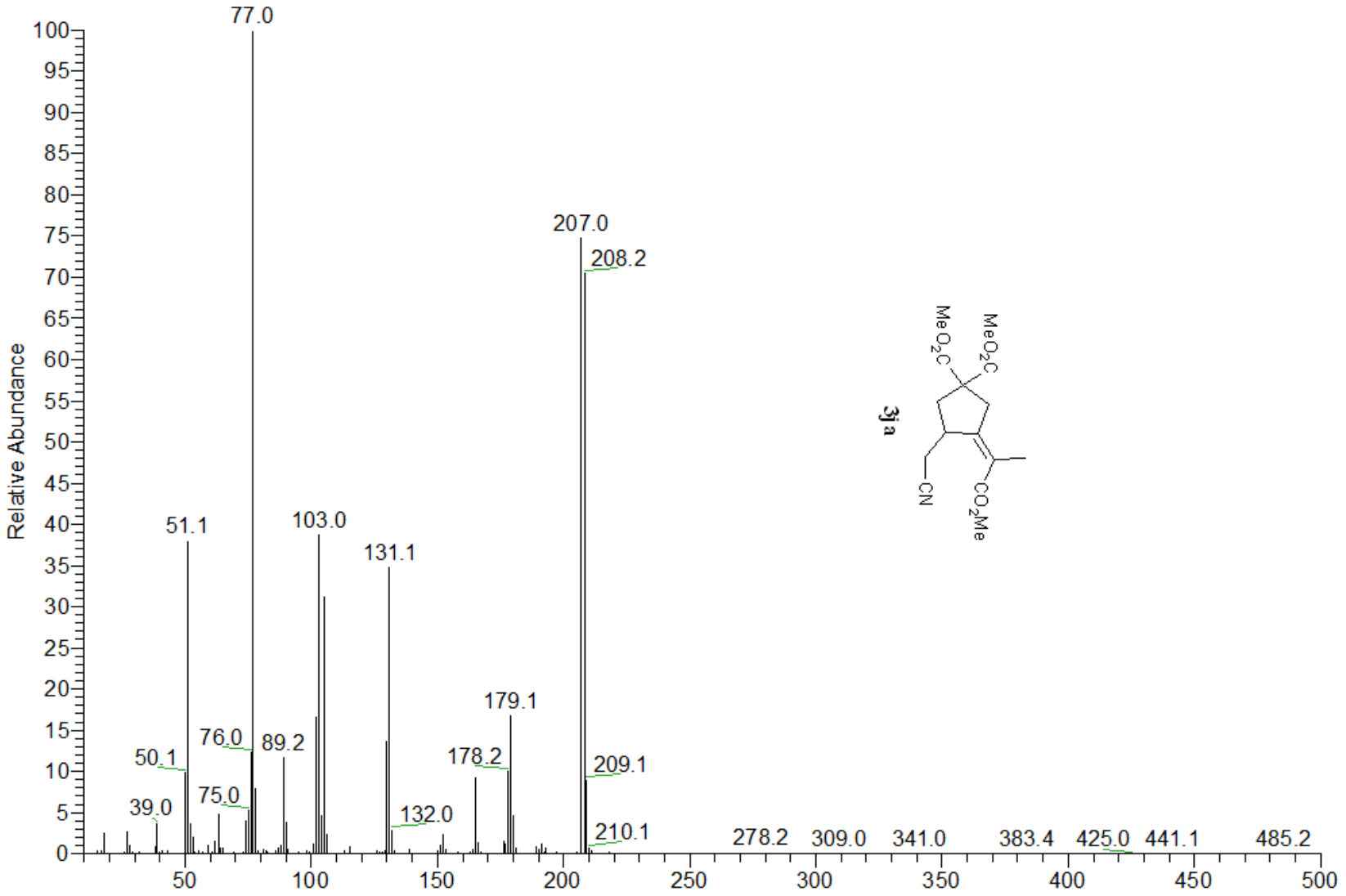

Figure B.20. Mass spectrum of (Z)-dimethyl 3-(cyanomethyl)-4-(1-methoxy-1-oxopropan-2-ylidene)cyclopentane-1,1-dicarboxylate

APPENDIX C

FTIR SPECTRUMS OF PRODUCTS

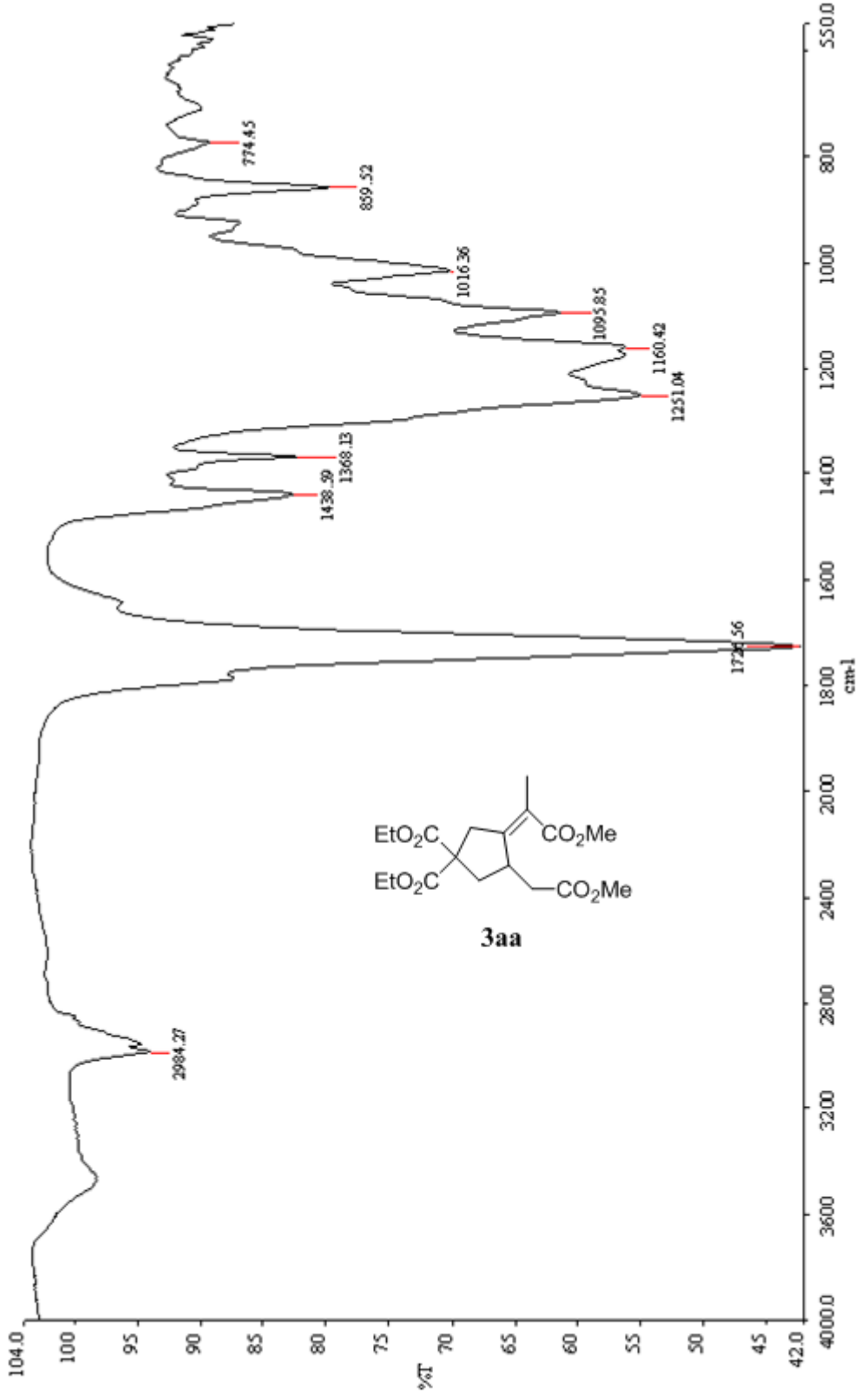

Figure C.1. FT-IR spectrum of (Z)-diethyl 3-(1-methoxy-1-oxopropan-2-ylidene)-4-(2-methoxy-2-oxoethyl)cyclopentane-1,1-dicarboxylate

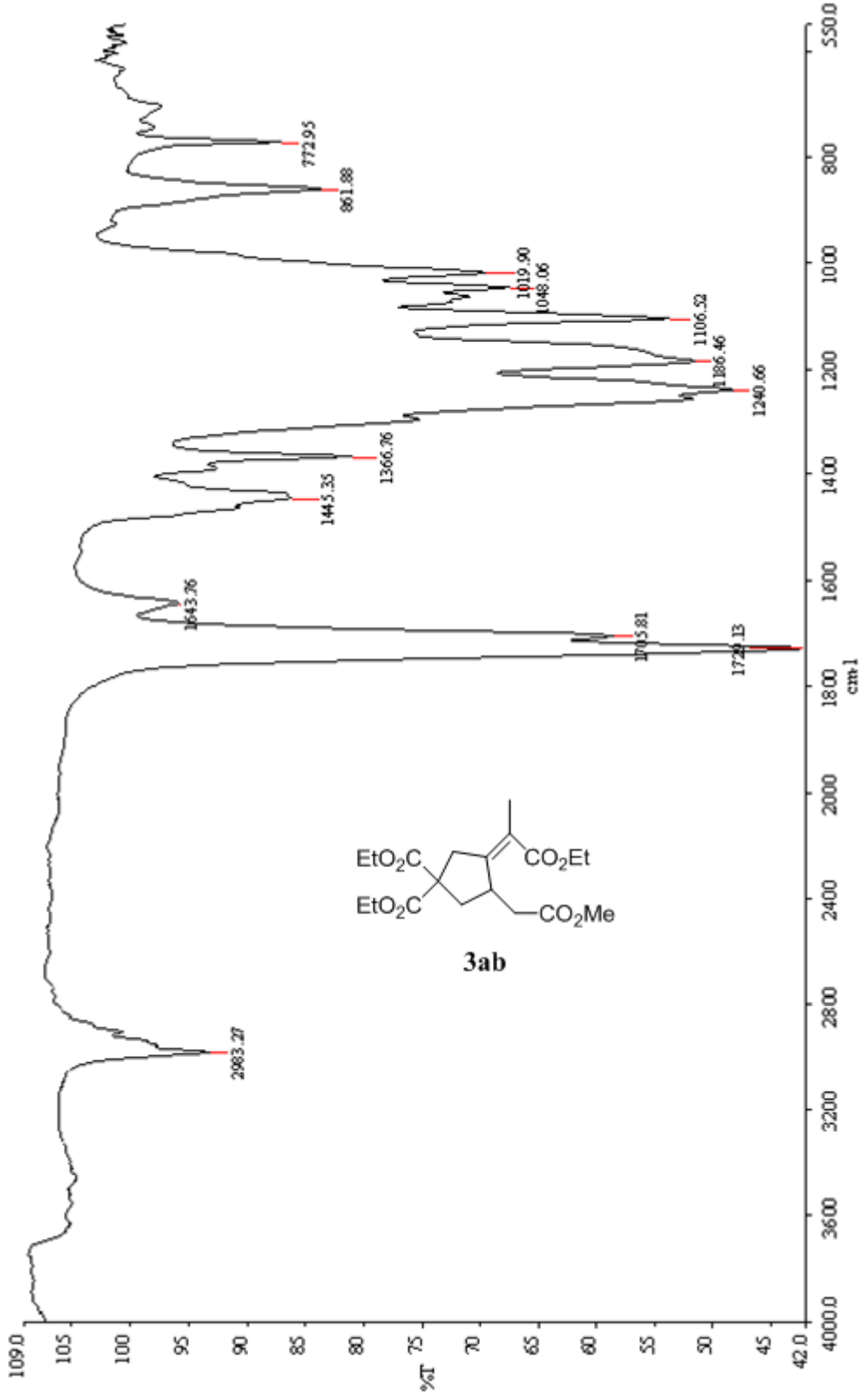

Figure C.2. FT-IR spectrum of (Z)-diethyl 3-(1-ethoxy-1-oxopropan-2-ylidene)-4-(2-methoxy-2-oxoethyl)cyclopentane-1,1-dicarboxylate

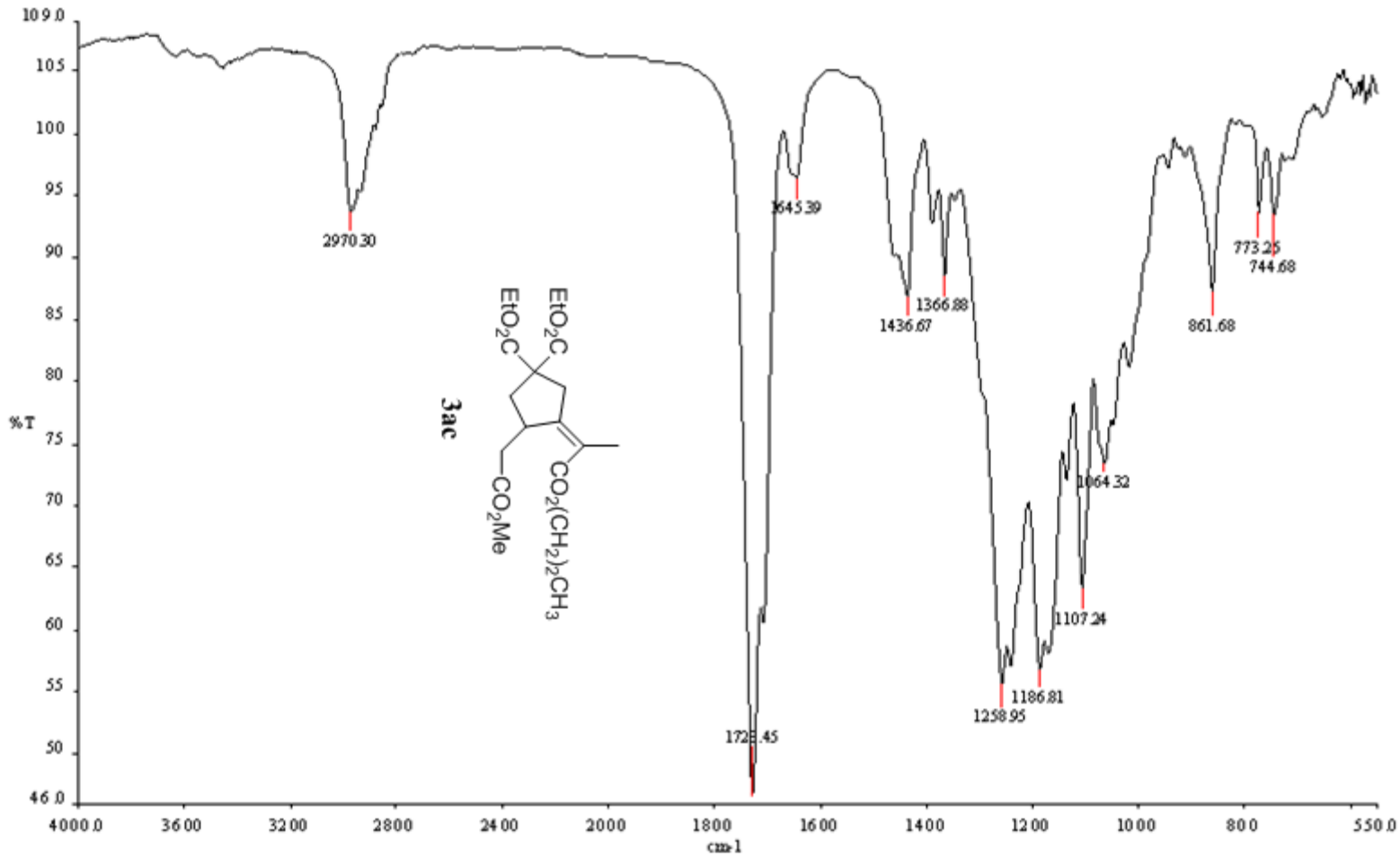

Figure C.3. FT-IR spectrum of (Z)-diethyl 3-(2-methoxy-2-oxoethyl)-4-(1-oxo-1-propoxypropan-2-ylidene)cyclopentane-1,1-dicarboxylate

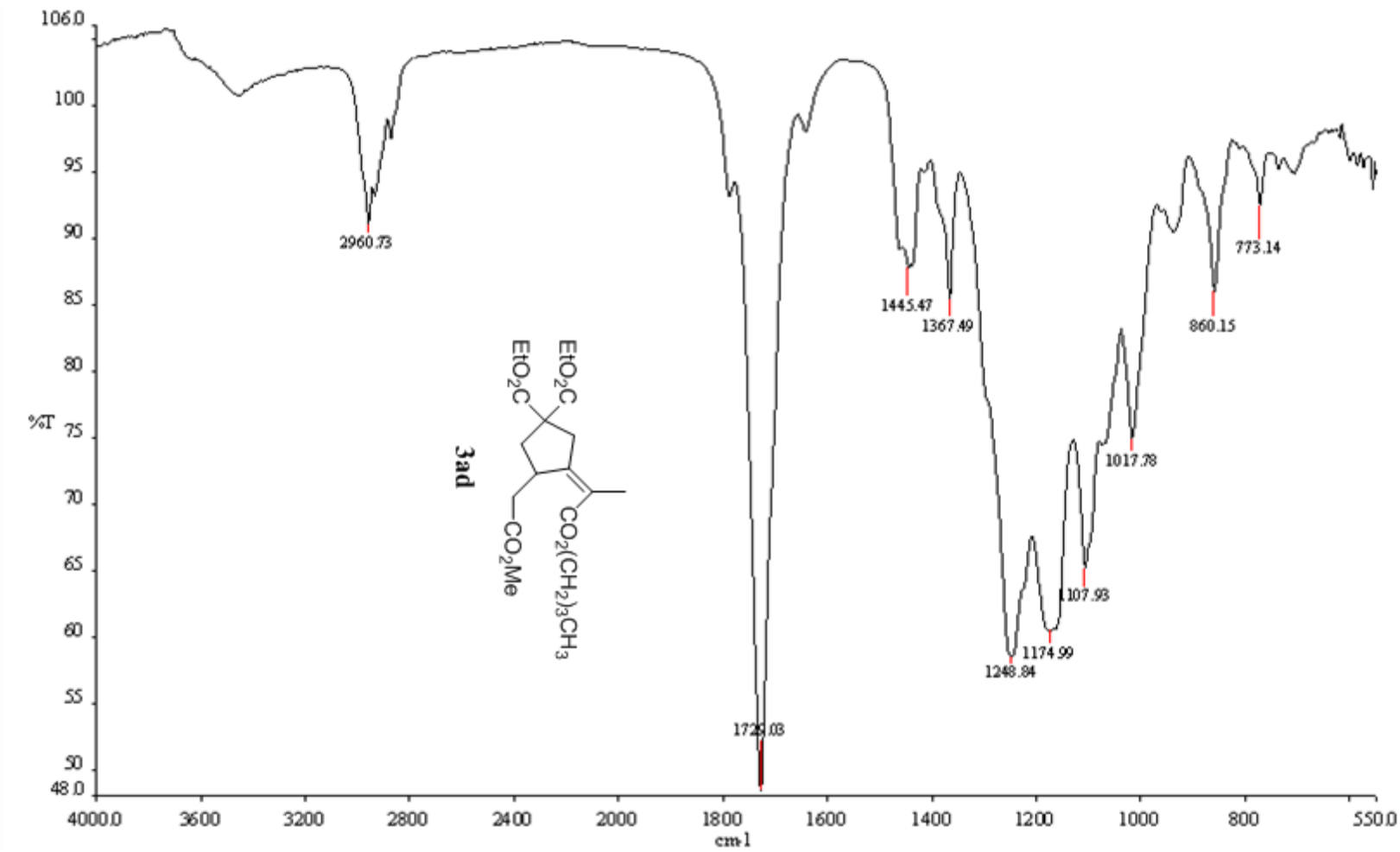

Figure C.4. FT-IR spectrum of (Z)-diethyl 3-(1-butoxy-1-oxopropan-2-ylidene)-4-(2-methoxy-2-oxoethyl)cyclopentane-1,1-dicarboxylate

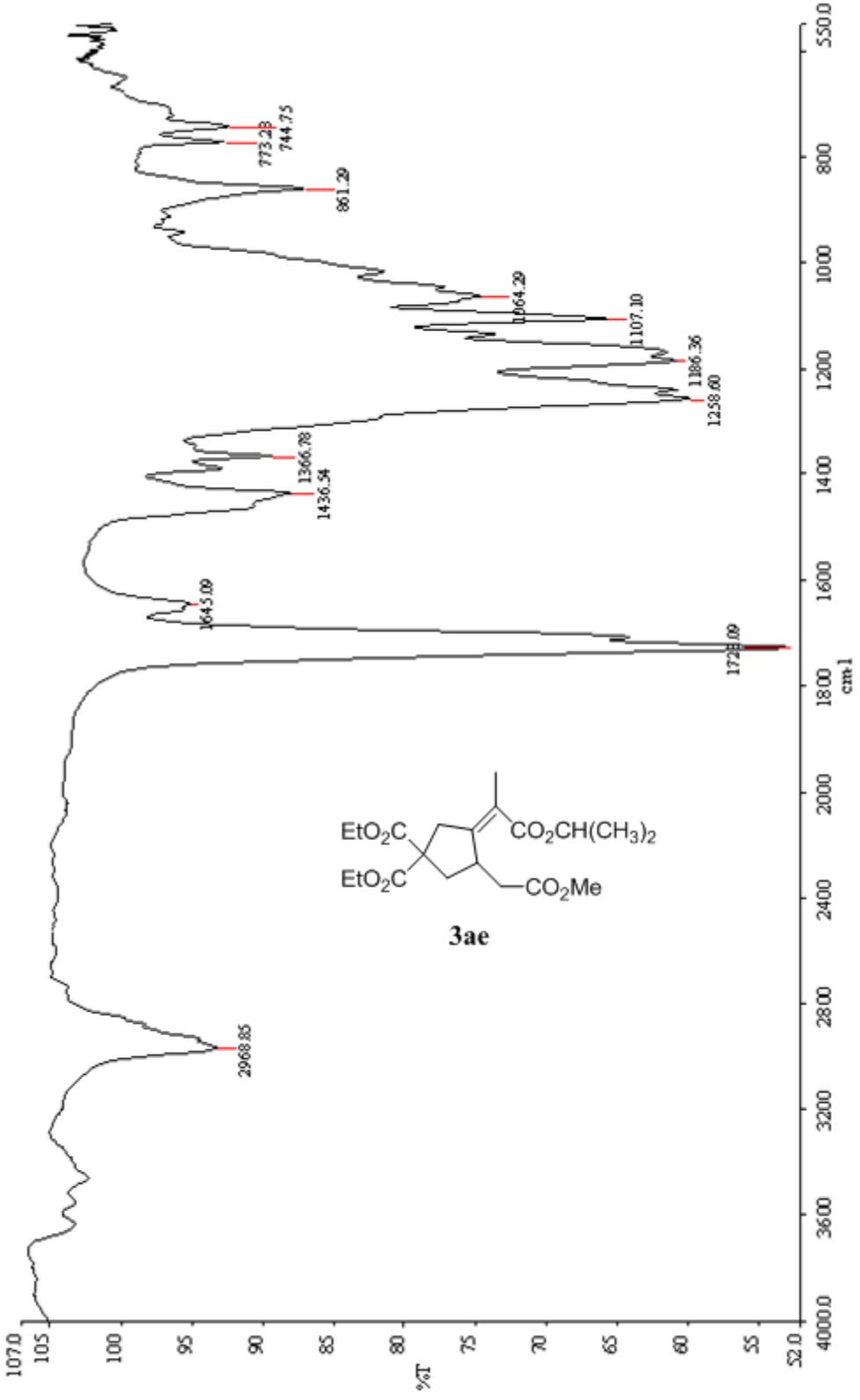

Figure C.5. FT-IR spectrum of (Z)-diethyl 3-(1-isopropoxy-1-oxopropan-2-ylidene)-4-(2-methoxy-2-oxoethyl)cyclopentane-1,1-dicarboxylate

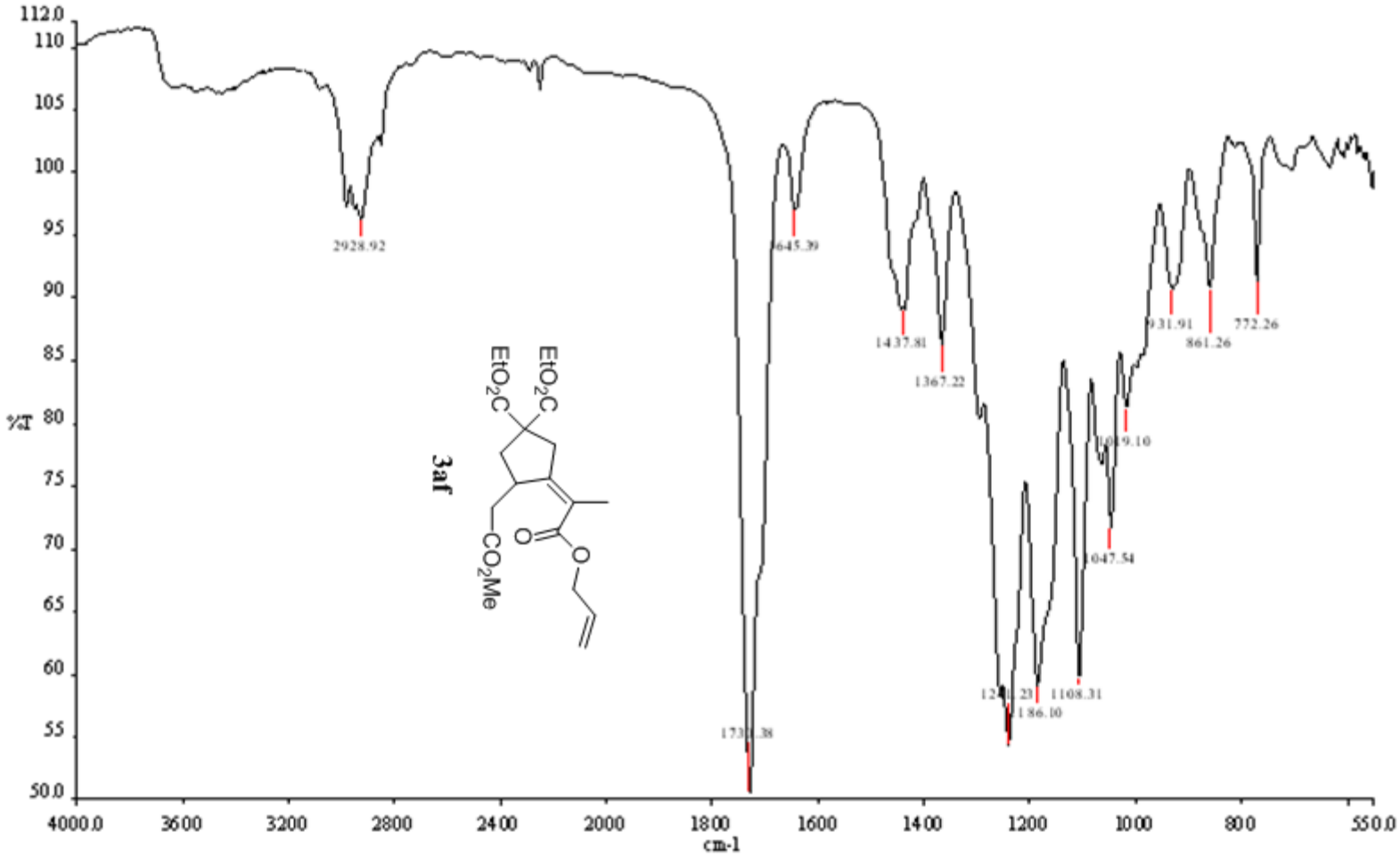

Figure C.6. FT-IR spectrum of (Z)-diethyl 3-(1-(allyloxy)-1-oxopropan-2-ylidene)-4-(2-methoxy-2-oxoethyl)cyclopentane-1,1-dicarboxylate

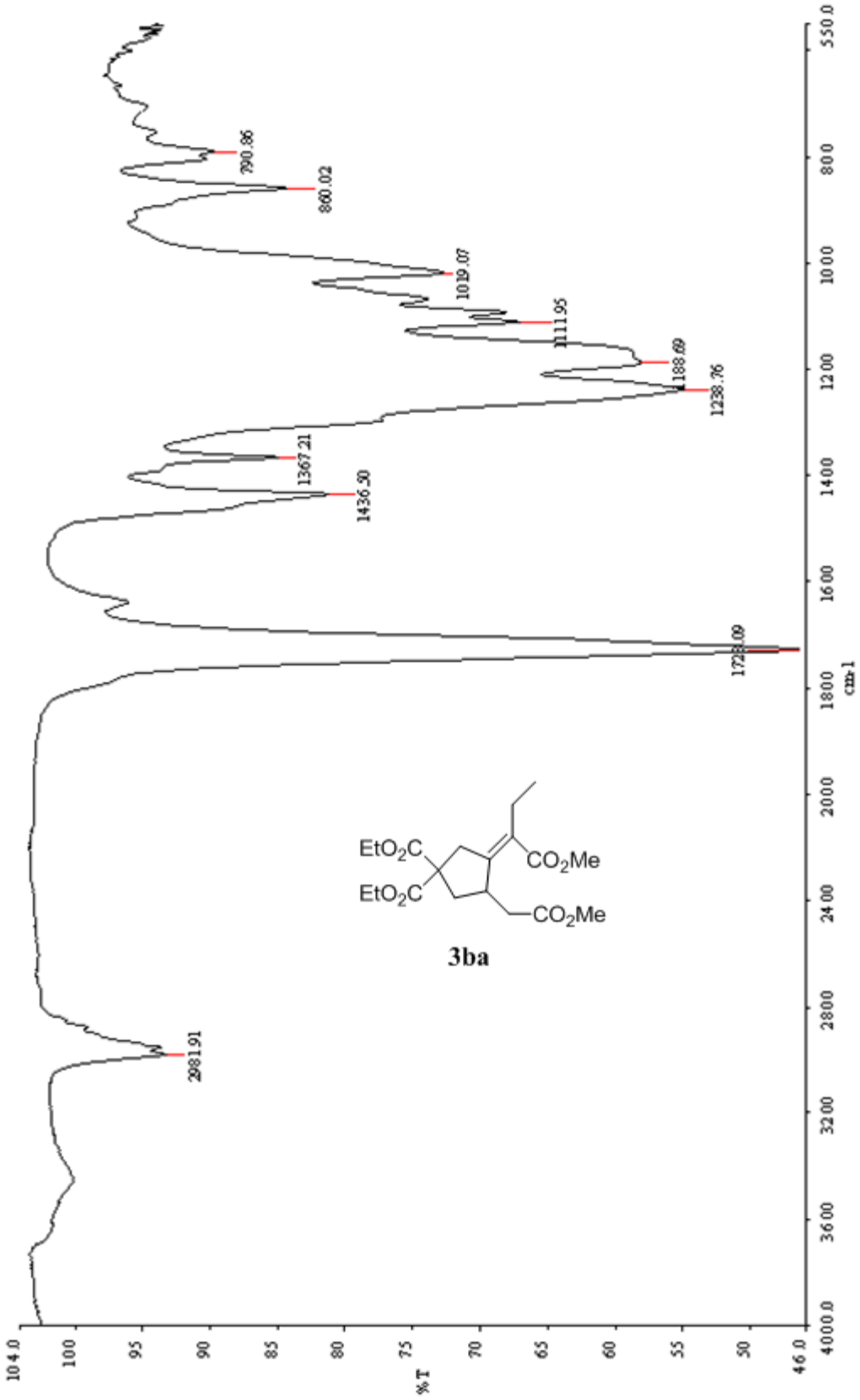

Figure C.7. FT-IR spectrum of (Z)-diethyl 3-(1-methoxy-1-oxobutan-2-ylidene)-4-(2-methoxy-2-oxoethyl)cyclopentane-1,1-dicarboxylate

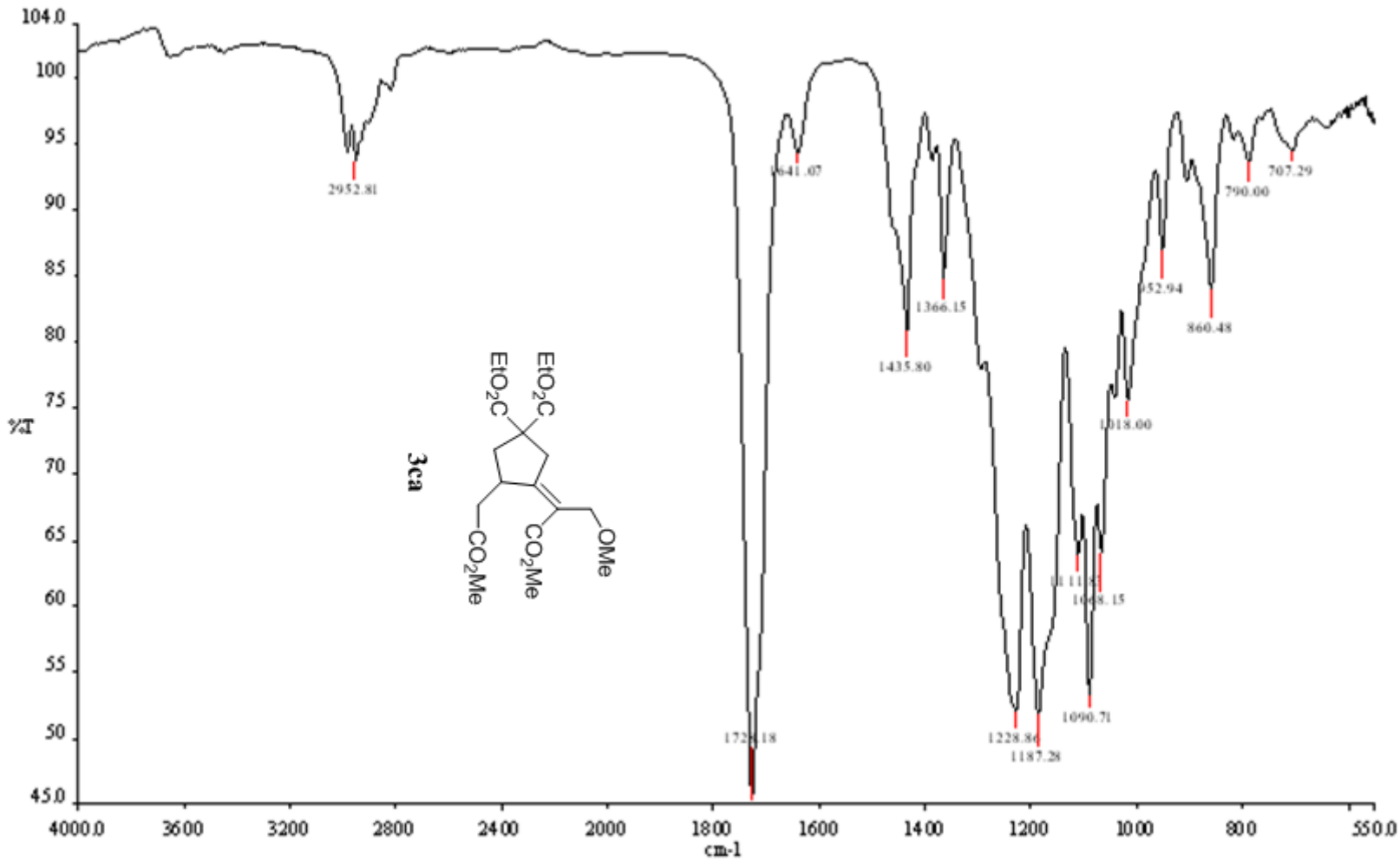

Figure C.8. FT-IR spectrum of (Z)-diethyl 3-(1,3-dimethoxy-1-oxopropan-2-ylidene)-4-(2-methoxy-2-oxoethyl)cyclopentane-1,1-dicarboxylate

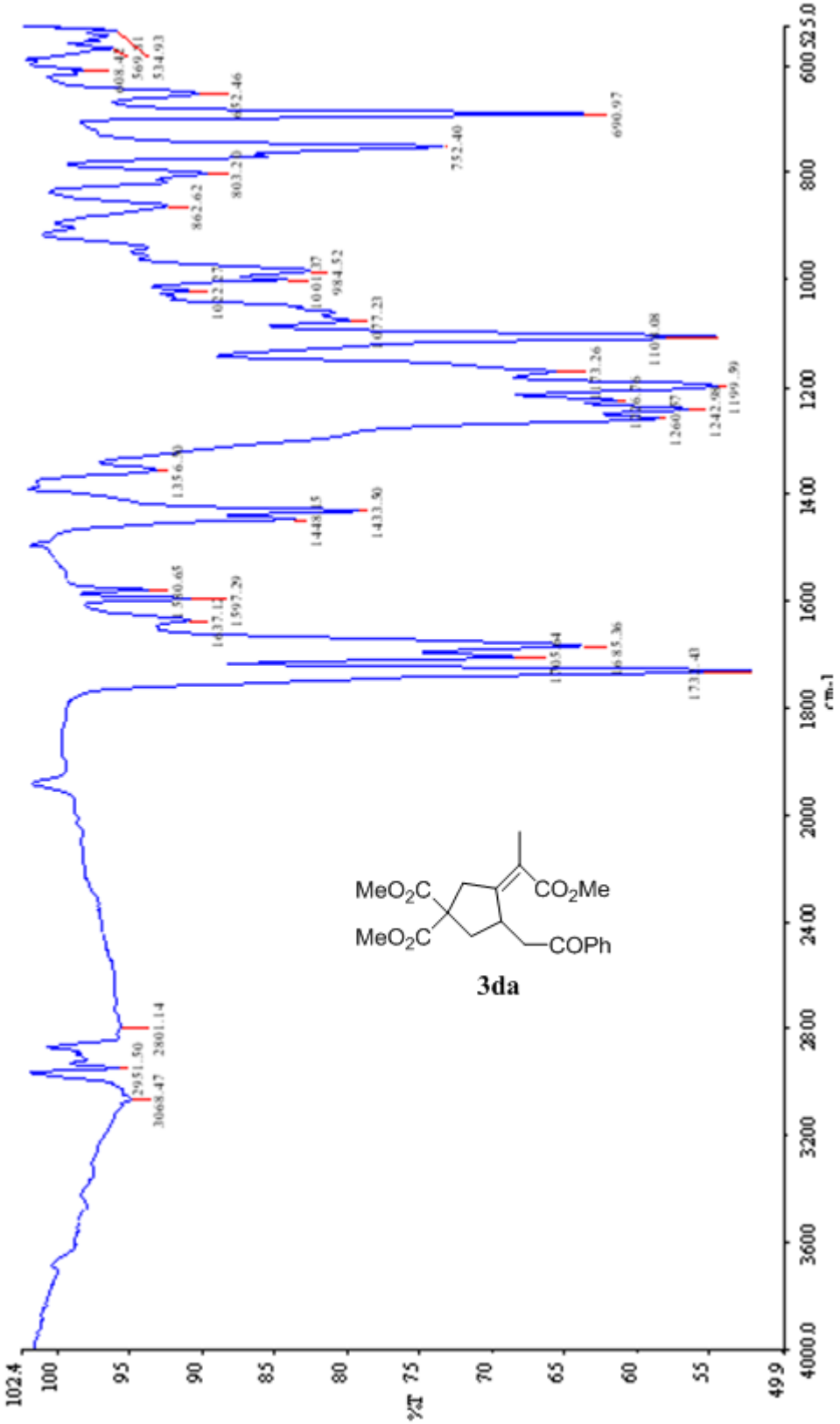

Figure C.9. FT-IR spectrum of (Z)-dimethyl 3-(1-methoxy-1-oxopropan-2-ylidene)-4-(2-oxo-2-phenylethyl)cyclopentane-1,1-dicarboxylate

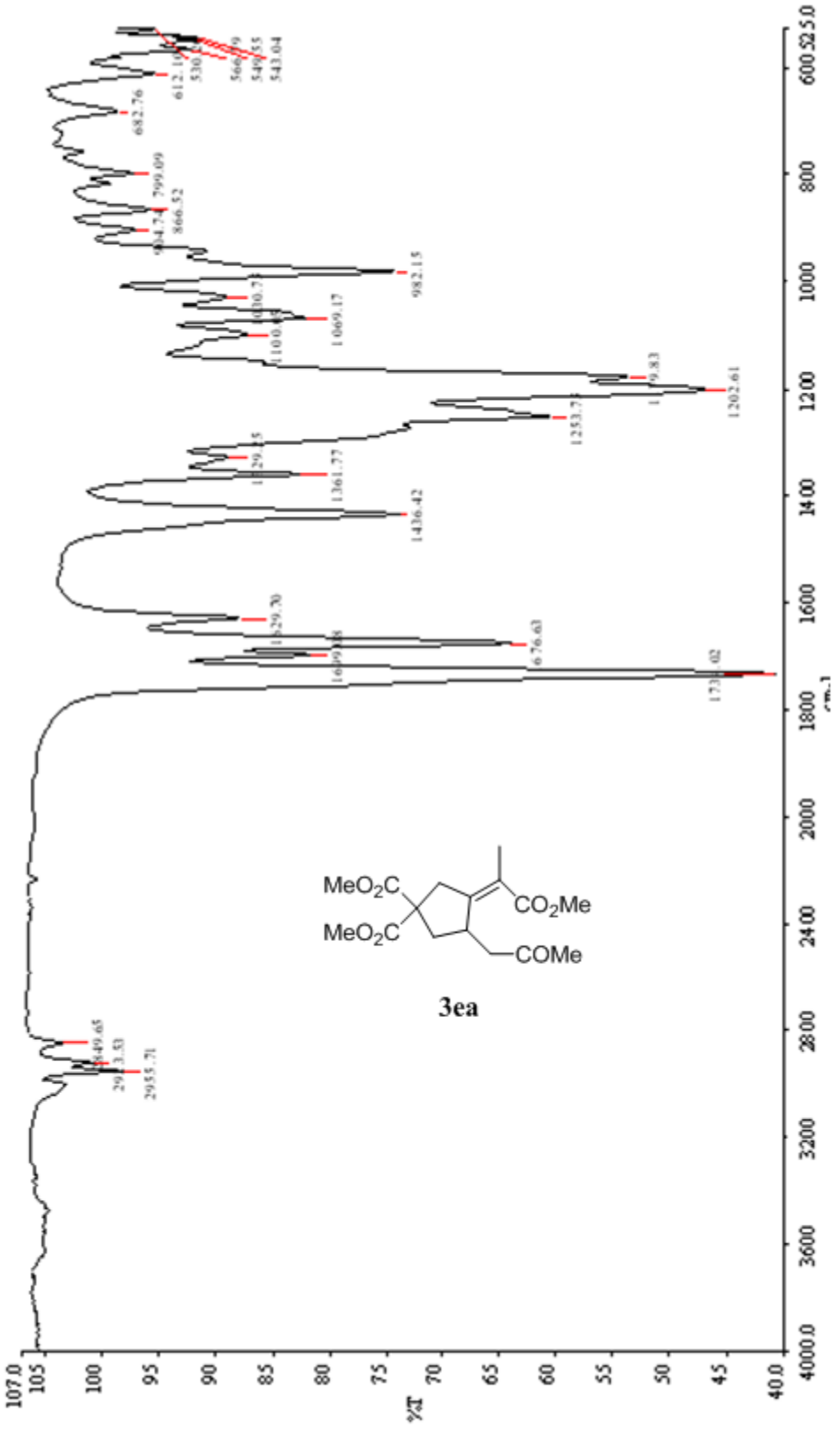

Figure C.10. FT-IR spectrum of (Z)-dimethyl 3-(1-methoxy-1-oxopropan-2-ylidene)-4-(2-oxopropyl)cyclopentane-1,1-dicarboxylate

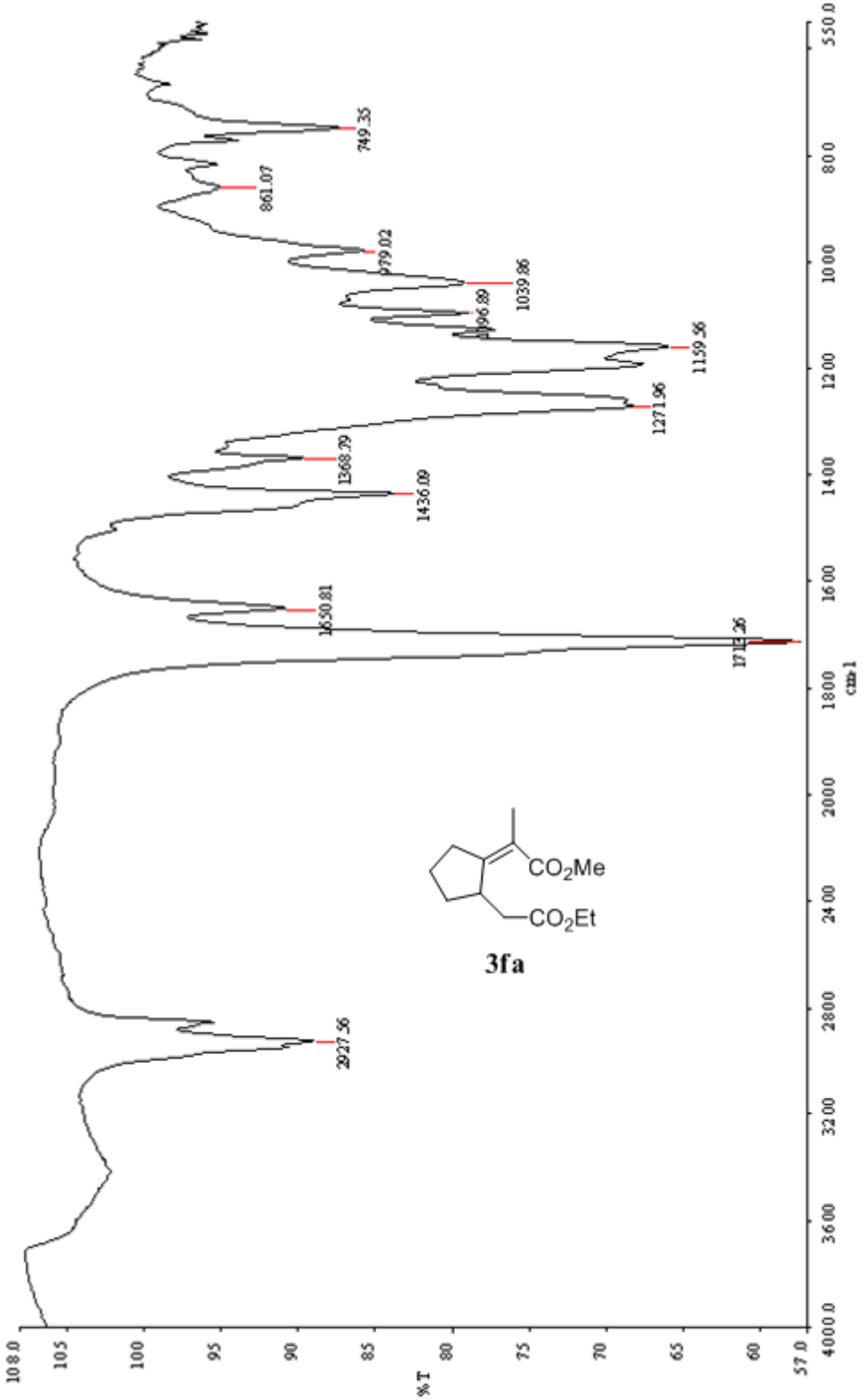

Figure C.11. FT-IR spectrum of (Z)-methyl 2-(2-(2-ethoxy-2-oxoethyl)cyclopentylidene)propanoate

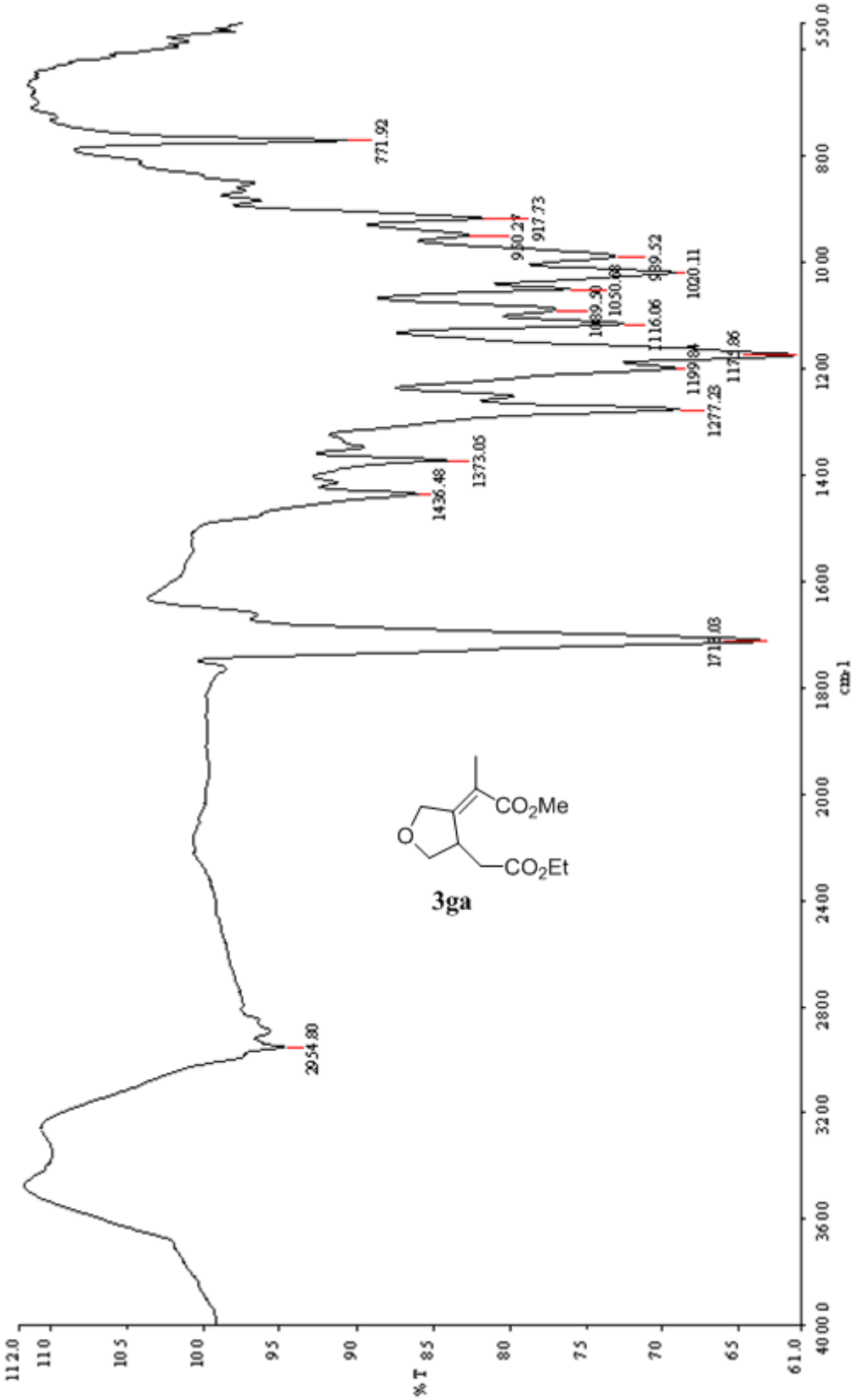

Figure C.12. FT-IR spectrum of (E)-methyl 2-(4-(2-ethoxy-2-oxoethyl)dihydrofuran-3(2*H*)-ylidene)propanoate

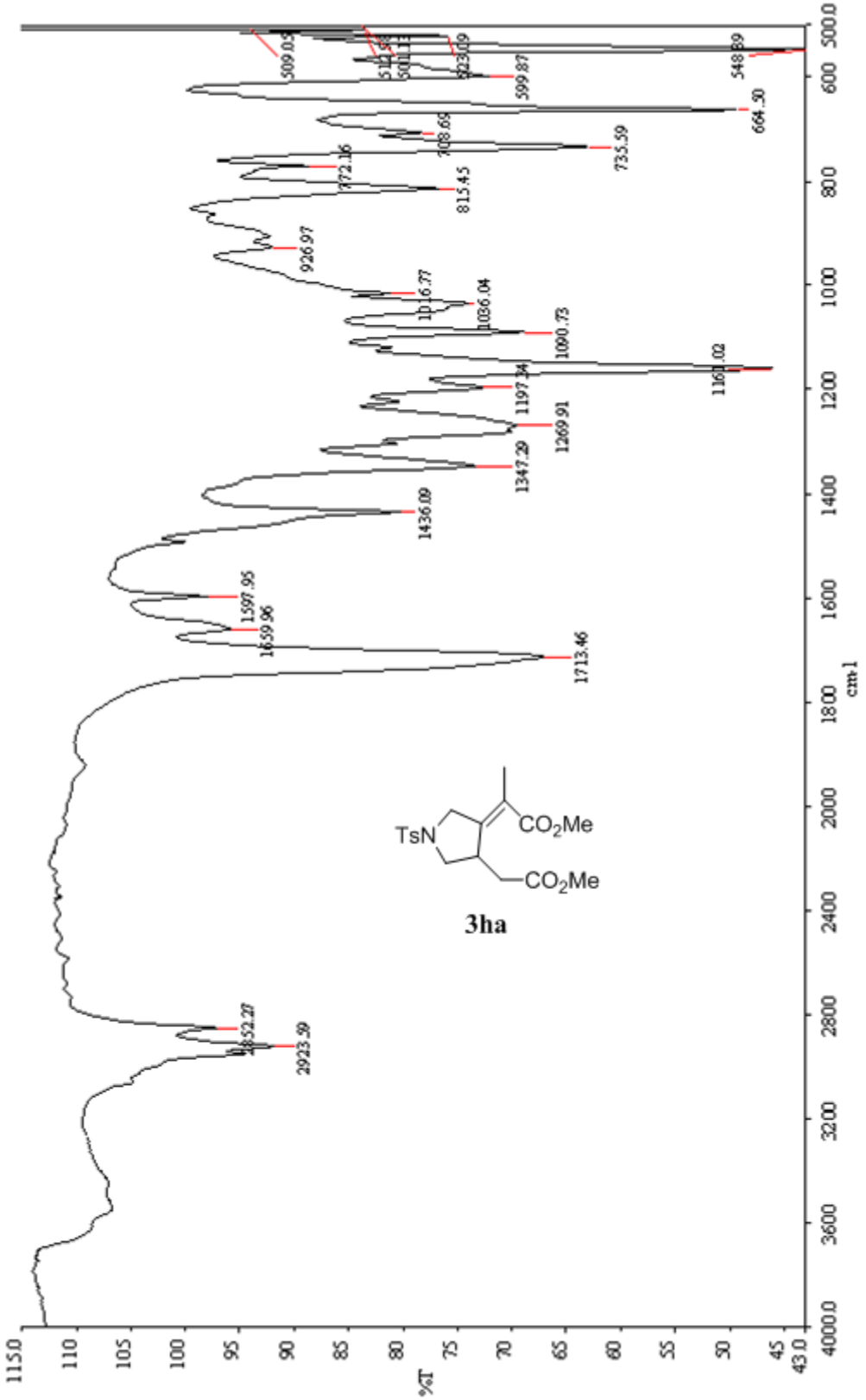

Figure C.13. FT-IR spectrum of (E)-methyl 2-(4-(2-methoxy-2-oxoethyl)-1-tosylpyrrolidin-3-ylidene)propanoate

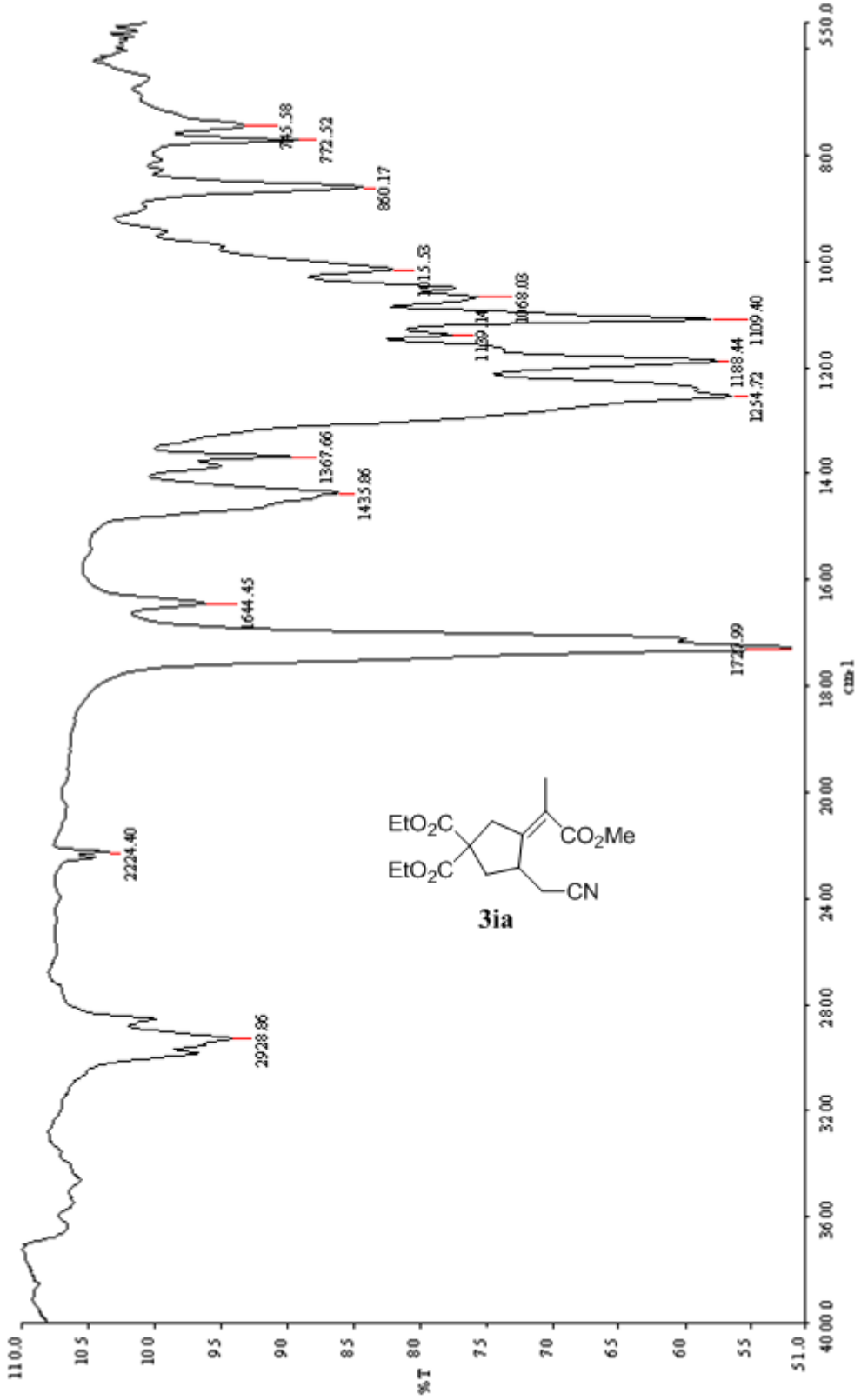

Figure C.14. FT-IR spectrum of (Z)-diethyl 3-(cyanomethyl)-4-(1-methoxy-1-oxopropan-2-ylidene)cyclopentane-1,1-dicarboxylate

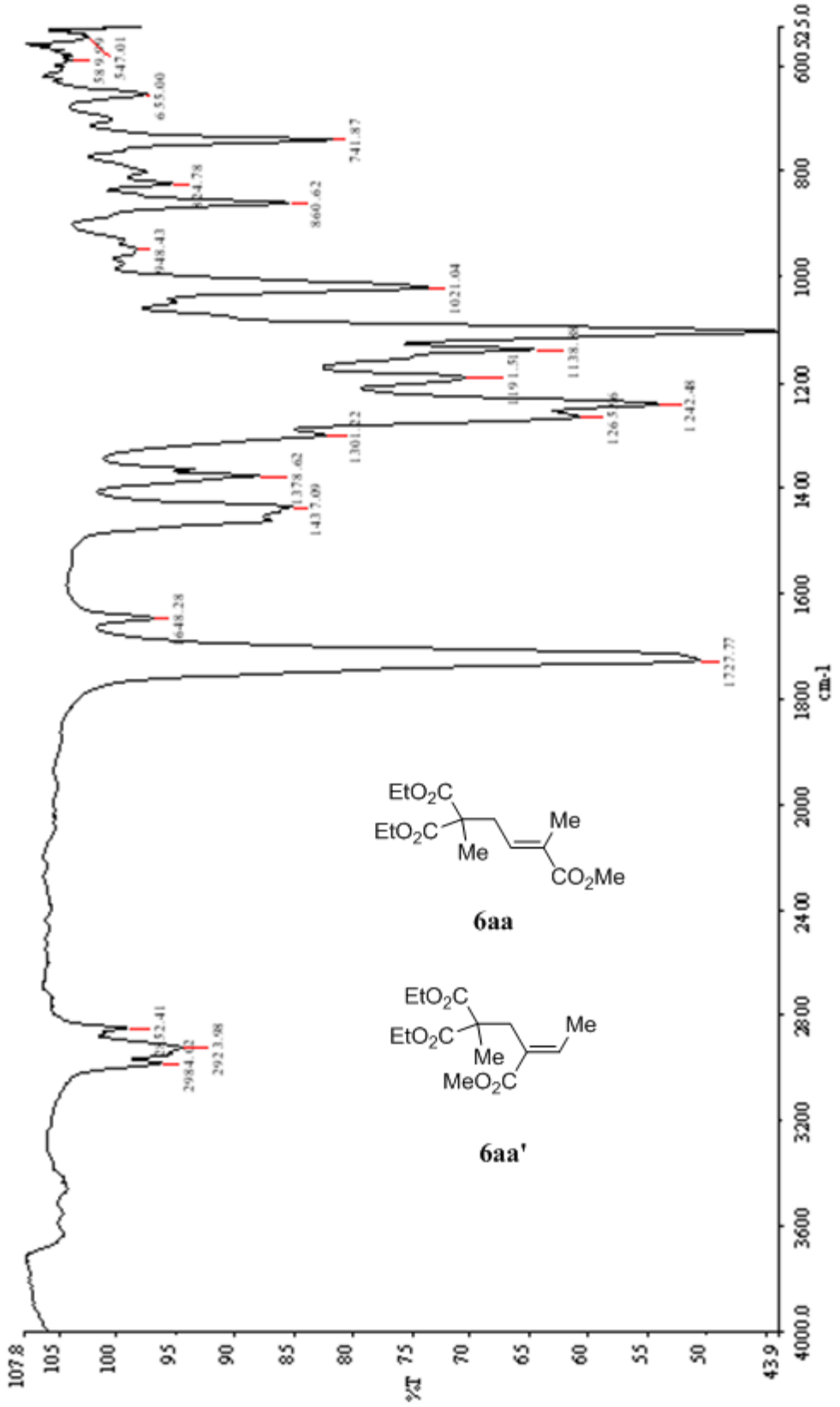

Figure C.15. FT-IR spectrum of (E)-2,2-diethyl 5-methyl hex-4-ene-2,2,5-tricarboxylate and (E)-2,2-diethyl 4-methyl hex-4-ene-2,2,4-tricarboxylate

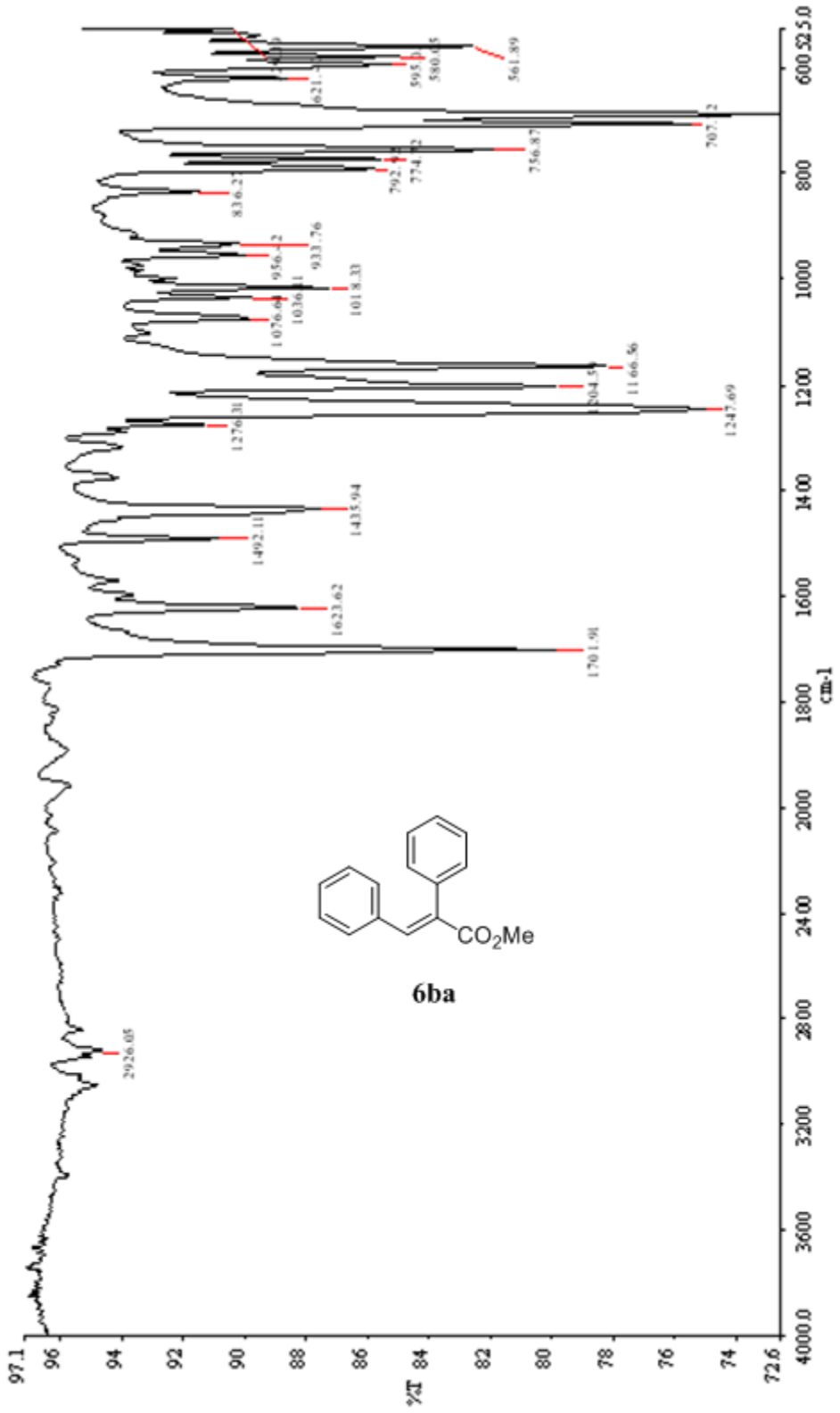

Figure C.16. FT-IR spectrum of (E)-methyl 2,3-diphenylacrylate

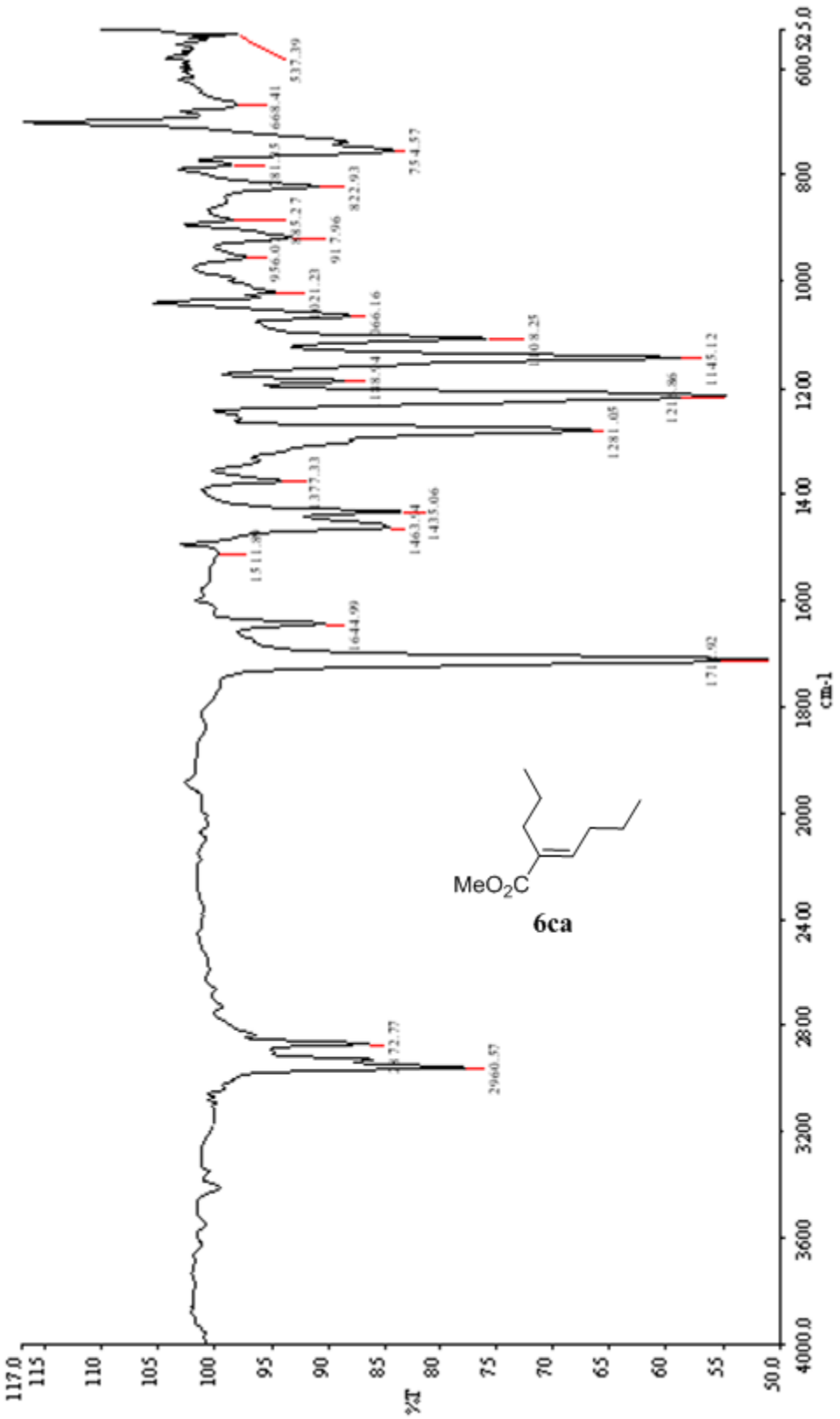

Figure C.17. FT-IR spectrum of (E)-methyl 2-propylhex-2-enoate

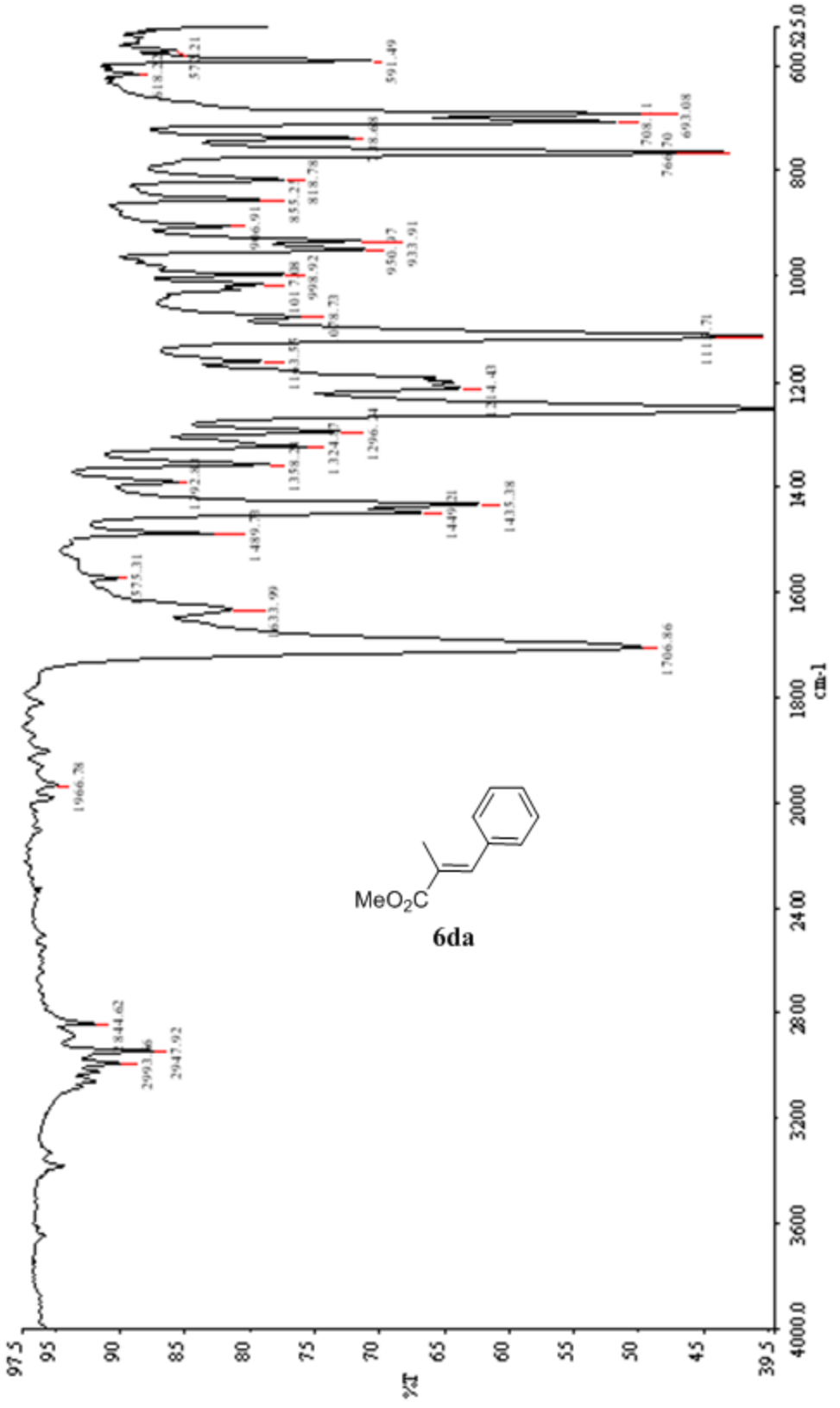

Figure C.18. FT-IR spectrum of (E)-methyl 2-methyl-3-phenylacrylate

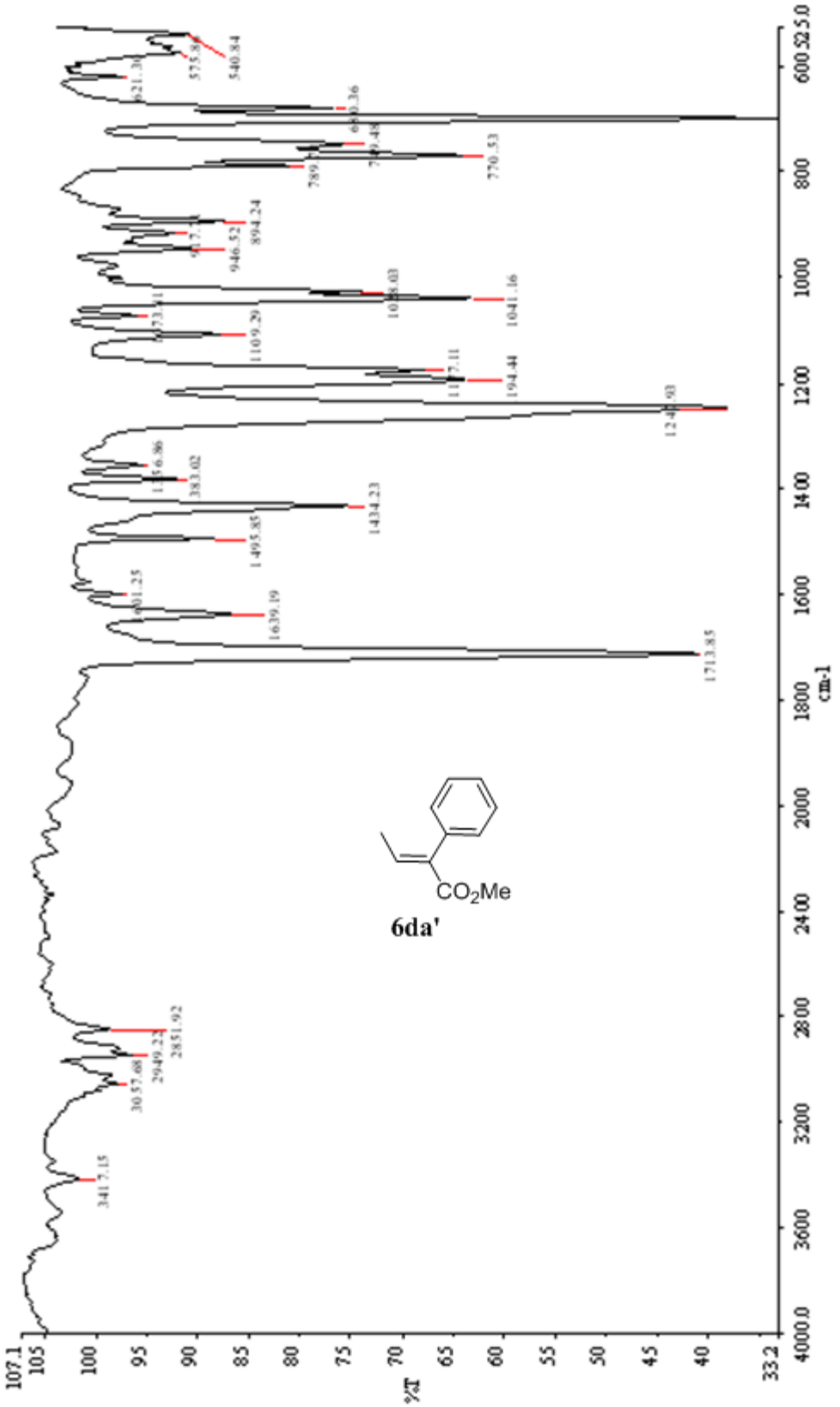

Figure C.19. FT-IR spectrum of (E)-methyl 2-phenylbut-2-enoate

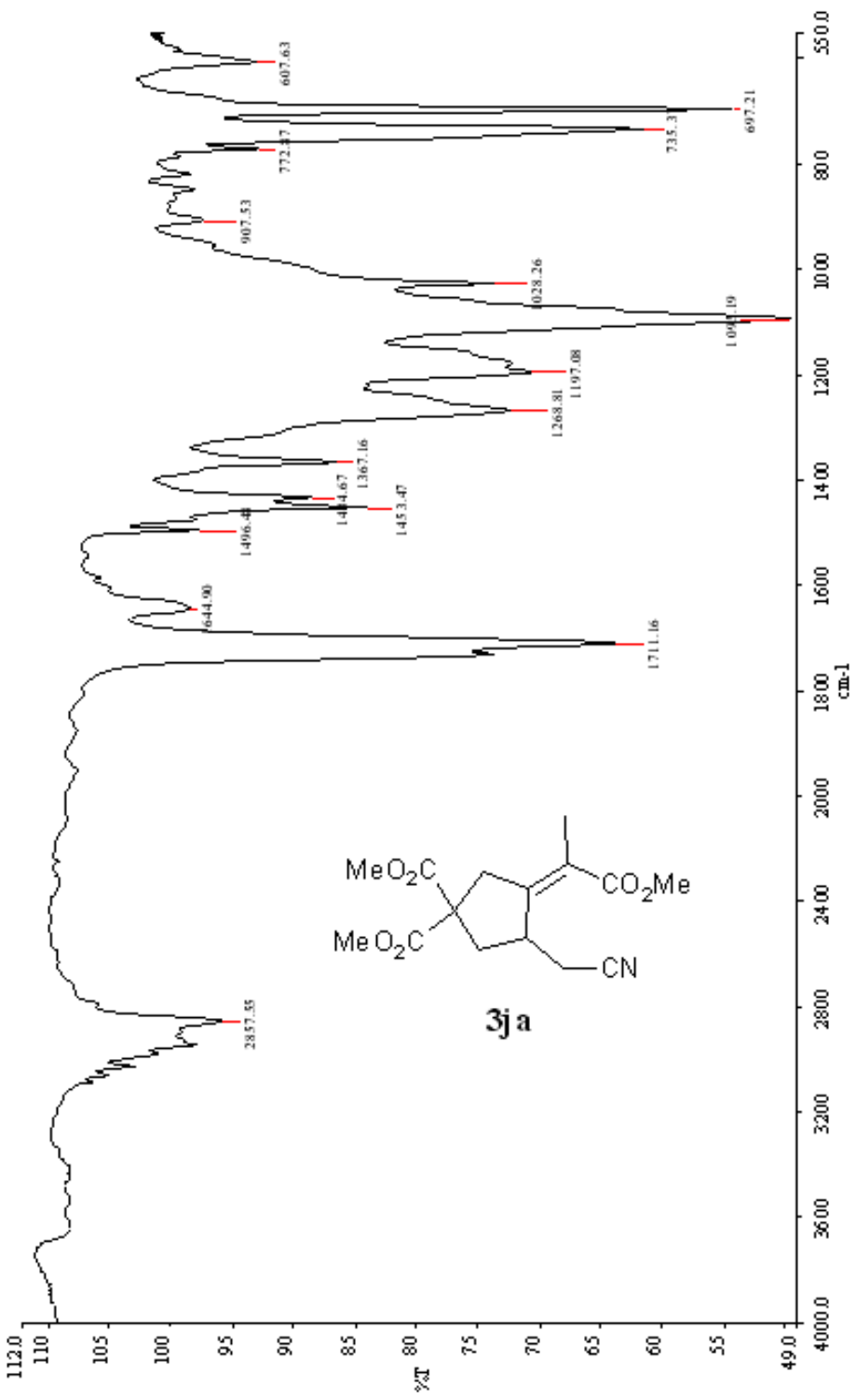

Figure C.20. FT-IR spectrum of (Z)-dimethyl 3-(cyanomethyl)-4-(1-methoxy-1-oxopropan-2-ylidene)cyclopentane-1,1-dicarboxylate