RHODIUM CATALYZED ARYLATIVE CYCLIZATION OF DIYNES WITH ARYLBORONIC ACIDS

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by
Bağdagül ÜRER

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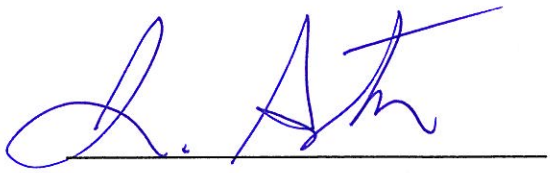

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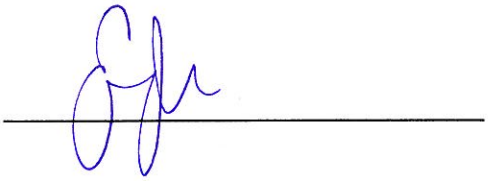

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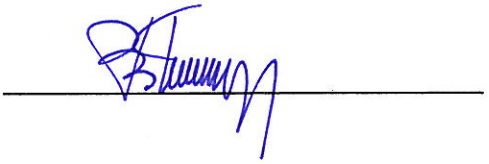

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ABSTRACT

RHODIUM CATALYZED ARYLATIVE CYCLIZATION OF DIYNES WITH ARYLBORONIC ACIDS

This study reveals that *exo*-conjugated cyclic dienes can be synthesized by rhodium(I) catalyzed arylative cyclization of unsymmetric diyne molecules with arylboronic acids. Cyclic dienes are important reagents in organic chemistry because they easily undergo [4+2] cycloaddition reactions with dienophiles and also, they are useful intermediates in the synthesis of complex polycyclic compounds.

To form carbon–carbon bonds, transition metal catalyzed arylative cyclization reactions of unsaturated reagents with arylboronic acids is a useful and efficient way in organic synthesis. For this purpose, rhodium catalyzed arylative cyclization of enyne type unsaturated reagents have been found significantly in literature.

In this study, unsymmetric diyne type molecules were reacted with arylboronic acids in the presence of a rhodium complex under argon atmosphere. The reactions proceeded effectively in methanol as a solvent under very mild reaction conditions.

ÖZET

DİİNLERİN ARİLBORONİK ASİTLER İLE RODYUM KATALİZLİ ARİLATİF HALKALAŞMA TEPKİMELERİ

Bu çalışma *ekzo*-konjuge siklik dienlerin, simetrik olmayan diinlerin arilboronik asitler ile rodyum katalizli arilatif halkalaşma tepkimeleri ile sentezlenebileceklerini göstermektedir.

Doymamış bileşiklerin geçiş metal katalizli arilatif halkalaşma tepkimeleri ile karbon-karbon bağı oluşturmaları organik sentezlerde kullanışlı ve etkili bir yöntemdir. Bu amaçla enin tipi doymamış bileşikler ile gerçekleştirilen rodyum katalizli arilatif halkaşma tepkimeleri literatürde çok sayıda yer almaktadır.

Bu çalışmada, simetrik olmayan diin tipi moleküllerin bir rodyum kompleksi ortamında arilboronik asitler ile argon atmosferi altında reaksiyonları gerçekleştirilmiştir. Çözücü olarak metanol kullanılması ile reaksiyonlar etkin bir biçimde yürütülmüştür.

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ABBREVIATIONS

Acac = acetylacetate

BINAP = 2,2-bisdiphenylphosphino-1,1-binaphthyl

COD = 1,5-cyclooctadiene

Dppb = 1,4-bis(diphenylphosphino)butane

DME = dimethoxyethane

DMF = dimethylformamide

Nbd = norbornadiene

SDS = sodium dodecyl sulfate

S, S bn-bod = (S, S)-2,5-dibenzylbicyclo [2.2.2]octa-2,5-diene

TPPDS = triphenylphosphinodisulfate

THF = tetrahydrufuran

THT = tetrahydrothiophene

CHAPTER 1

INTRODUCTION

Sakai et al. reported in 1997 that arylboronic acids can undergo conjugate addition to α,β-unsaturated ketones in the presence of a rhodium catalyst (Sakai, et al. 1997). Since then, as its utility for the carbon-carbon bond formation, this method has become increasingly clear and, -interest in the rhodium(I) catalyzed addition of organoboron species to unsaturated functionalities has grown dramatically in organic chemistry (Hayashi, et al. 2001, Fagnou and Lautens 2003).

Due to the high functional-group compatibility, ready availability, and stability of organoboronic acids, a rhodium-catalyzed addition of organoboronic acids to unsaturated carbon-carbon, or carbon-heteroatom bonds is a useful strategy for the construction of carbon-carbon bonds (Hayashi and Yamasaki 2003, Fagnou and Lautens 2003, Bolm, et al. 2001). To form arylrhodium(I) species that are capable of inducing the nucleophilic arylation of various electrophilic sites, organoboron reagents undergo transmetallation with rhodium species (Sakai, et al. 1997, Fagnou and Lautens 2003).

Recently, several examples of rhodium-catalyzed tandem cyclization reactions with organoboron reagents have been described (Cauble, et al. 2003, Bocknack, et al. 2004, Lautens and Yoshida 2002, Lautens and Mancuso 2004, Miura, et al. 2007). A series of dienes, enynes, and diynes has been widely utilized for the transition metal catalyzed cyclization reactions, since the cyclization of these compounds is a geometrically favored process (Nakamura and Yamamoto 2004).

In the literature, there are various reports for rhodium catalyzed cyclization reactions of organoboronic acids with enyne type unsaturated reagents (Shintani, et al. 2005(a), Miura, et al. 2005(a)). In 2002, Liu and Widenhoefer reported a study about cationic rhodium catalyzed cyclization/hydrosilylation of 1,6-diynes but that was not an arylative cyclization reaction. In 2007, Miura et al. reported that diynes having malonate based tethers react with arylboronic acids in the presence of $[Rh(cod)(OH)]_2$ in dioxane:H_2O at room temperature to give 1,2-dialkylidienenecycloalkanes.

Diyne molecules are very versatile intermediate reagents for the synthesis of various fine chemicals. Furthermore, functionalized 1,2-dialkyldienecyclopentanes can

easily undergo [4+2] cycloaddition reactions with dienophiles and be useful reagents in synthesis of complex polycyclic compounds.

In this thesis, we have developed rhodium catalyzed arylative cyclization reactions of unsymmetric diynes with a terminal alkyne functionality with electronically and sterically different arylboronic acids efficiently under mild conditions to yield conjugated exo-cyclic dienes.

CHAPTER 2

TRANSITION METAL CATALYZED REACTIONS OF ORGANOBORONS

2.1. Organoborons

Organoborons are chemical compounds having aryl or alkyl functional groups on the boron atom. The term *organoboron* refers to a compound which has at least one C-B bond. Organoboron compounds generally exist either as tricoordinate or as tetracoordinate species. The trisubstituted derivatives of boron are called *boranes*, which may exist either as essentially trigonal planar monomeric species or as aggregates in which the boron atoms occupy the central position of an essentially tetrahedral configuration. Infact, essentially all monoorganoboranes (RBH_2) and diorganoboranes (R_2BH) as well as the parent borane (BH_3) exist as dimers, whereas triorganoboranes (R_3B) are usually monomeric.

Boronic acids and their derivatives are among the most useful classes of organoboron molecules. Unlike many organometallic derivatives and most organoboranes, boronic acids are usually stable to air and moisture, and are of relatively low toxicity and environmental impact. The reactions of organoborons can be carried out in aqueous containing solvents and are widely functional-group tolerant.

Boronic acids are used extensively in organic chemistry as chemical building blocks and intermediates predominantly in Suzuki coupling reactions. A key concept in its chemistry is transmetallation of its organic residue to a transition metal.

2.2. Transition Metal Catalyzed Reactions of Organoborons

Transition metals have many properties that make their chemistry very different from, main group elements, and those properties can make them uniquely suited toward certain tasks. Most of them have to do with far greater variability and therefore tunability of transition metal complexes. This is mostly due to the fact that transition metal compounds tend to have partially populated d-orbitals and are relatively closely spaced together. A transition metal can do lots of different things, change in many different

ways, and do so with relatively small energy barriers, which makes for very fast reactions. Moreover, transition metal compounds can exhibit variable oxidation states, with finely controlled and tunable redox potentials, because the d-orbital energies and spacings can be selectively altered with different ligands.

As a result of those properties, many of the highly critical reactions in organic chemistry employ transition metal compounds as catalysts.

2.2.1. Rhodium Catalyzed Carbon-Carbon Bond Forming Reactions of Organometallic Compounds

In recent years, rhodium catalysts have been used with organometallic reagents in the formation of new C-C bonds. In the past twenty years there has been dramatic growth in the use of transition metal catalysts for synthetically important organic transformations. Nowadays, there is an increased attention to rhodium catalysts for carbon-carbon bond forming reactions. High activity allows the use of metal concentrations as low as 10^{-3} M. Moreover, in carbon-carbon bond forming reactions, palladium involves a redox process, Pd(II)/Pd(0), but rhodium remains 1+ through the reaction, that means formal oxidation step does not change.

The rhodium catalyzed addition/cyclization reactions of organoborons occurs by transmetallation of rhodium/boron generating an intermediate organorhodium(I) species and this arylrhodium(I) species reacts with unsaturated functionalities (Figure 2.1).

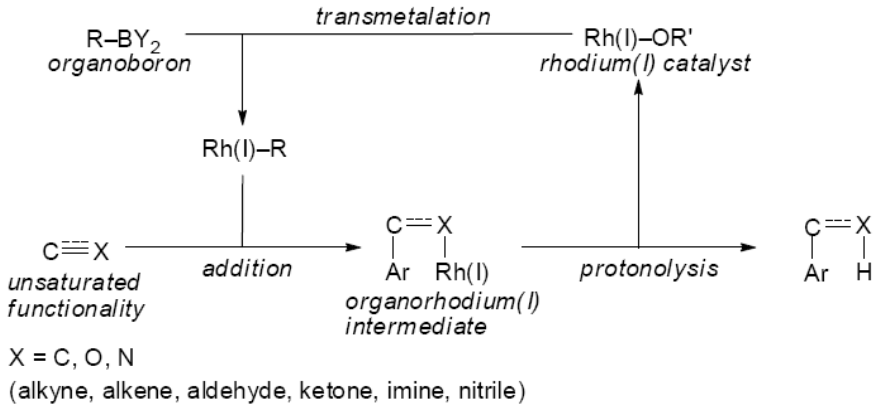


Figure 2.1. General reaction pathway of Rh(I)-catalyzed addition of organoborons

When rhodium's possible catalytic cycle was compared with other transition metals, palladium, nickel and platinum, rhodium represents a different and interesting catalytic cycle (Figure 2.2.,Figure 2.3.). In catalytic reactions, oxidation state of rhodium lies between the (I) and (III) oxidation states and as a consequence transmetallation process occurs at two points. Transmetallation can occur with rhodium(I) to generate an organorhodium(I) capable of reacting in new ways. However, catalytic cycles for palladium, nickel and platinum, transmetallation occurs with the metal(II) species because catalytic cycles shuttles between the (0) and (II) oxidation states and to design viable reactions, a suitable electrophilic component must be incorporated that will oxidatively add to the metal(0) complex to produce the organometal(II) species.

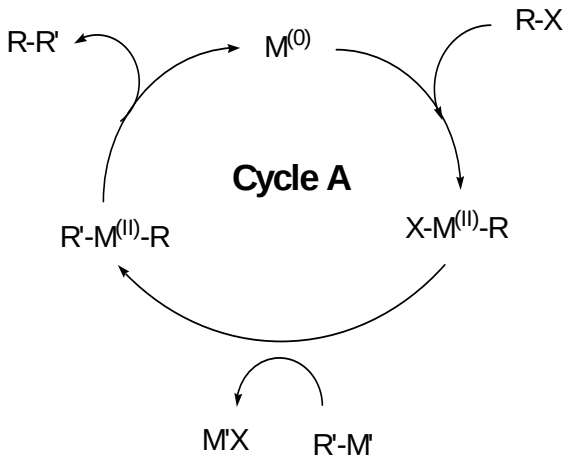


Figure 2.2. Generalized catalytic cycle for Ni, Pd and Pt
(Source: Fagnou and Lautens 2003)

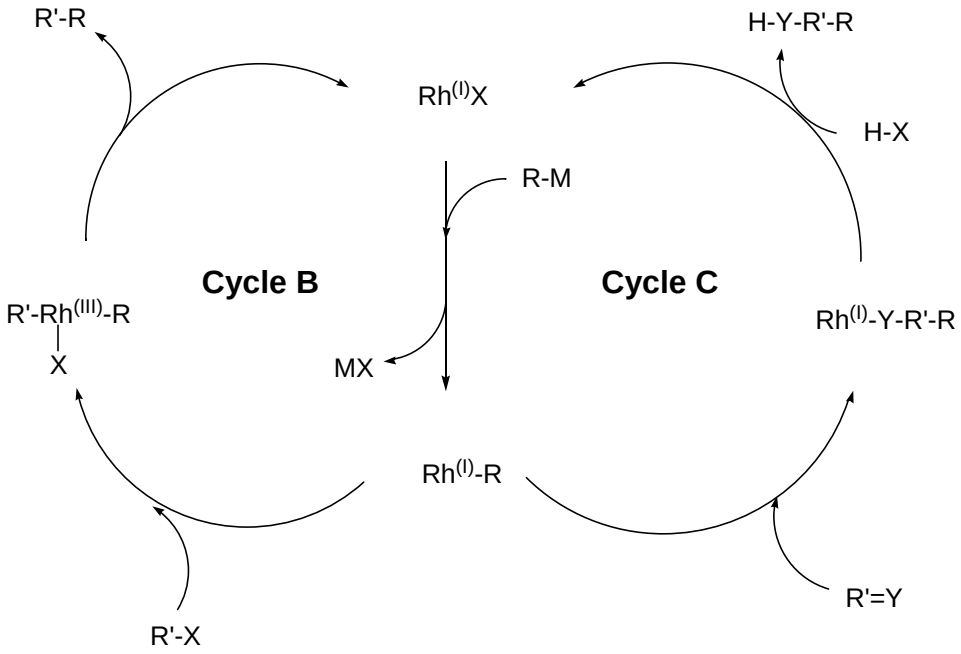


Figure 2.3. Possible catalytic cycles with Rh-catalysts
(Source: Fagnou and Lautens 2003)

Since oxidative addition is still a viabla pathway, addition of a suitable electrophile will produce a catalytic cycle illustrated as cycle B. Alternatively, the organorhodium complex can be coupled with units of unsaturation in organic compounds as illustrated in cycle C. The outcome of cycle C is a net R,H-addition across the unsaturated unit (Fagnou and Lautens 2003).

A wide variety of organometallic compounds reacts with rhodium(I) halides to generate rhodium-aryl complexes.

2.2.1.1. Reactions of Organometallic Compounds with Rhodium Complexes

In 1968, Keim reported that treatment of $[RhCl(PPh_3)_3]$ complex with phenylmagnesium bromide gives rhodium-aryl complex in a high yield (Keim 1968) (Figure 2.4). Carbonyl-rhodim aryl complexes were synthesized by treatment of $[Rh(CO)Cl(PPh_3)_2]$ with diarylzinc nucleophiles in THF by Krug and Hartwig 2002 (Figure 2.5).

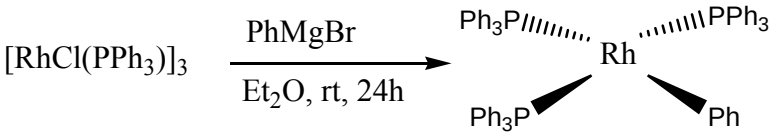


Figure 2.4. Formation of rhodium-aryl complex
(Source: Keim 1968)

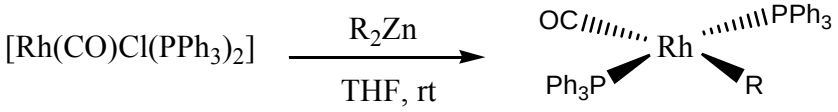


Figure 2.5. Formation of carbonyl rhodium-aryl complex
(Source: Krug and Hartwig 2002)

Rhodium-aryl complexes have been prepared by transmetallation with rhodium(I) precursors, rhodium(II) complexes have also been employed and Figure 2.6. shows treatment of $[Rh_2(CO_2Me)_4]$ with diphenylmagnesium and trimethylphosphine (Figure 2.6.) (Jones and Wilkonson 1979).

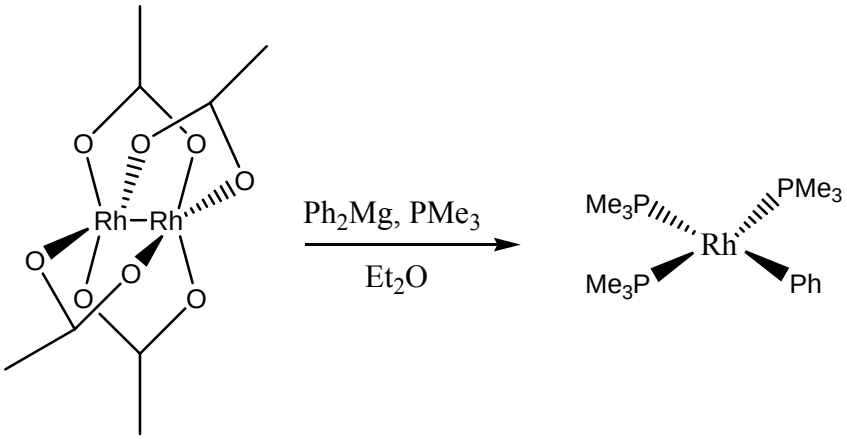


Figure 2.6. Formation of rhodium(I)-aryl complex
(Source: Wilkinson and Jones 1979)

Rhodium(III) aryl complexes have also been prepared and rhodium(III) chloride undergoes exchange of ligand with a variety of organometallic reagents. In 1991, Wilkinson et al. reported a reaction of $[RhCl_3(tht)_3]$ with aryl Grignard reagents to generate trisaryl complexes showing in Figure 2.7.(tht = tetrahydrothiophene)

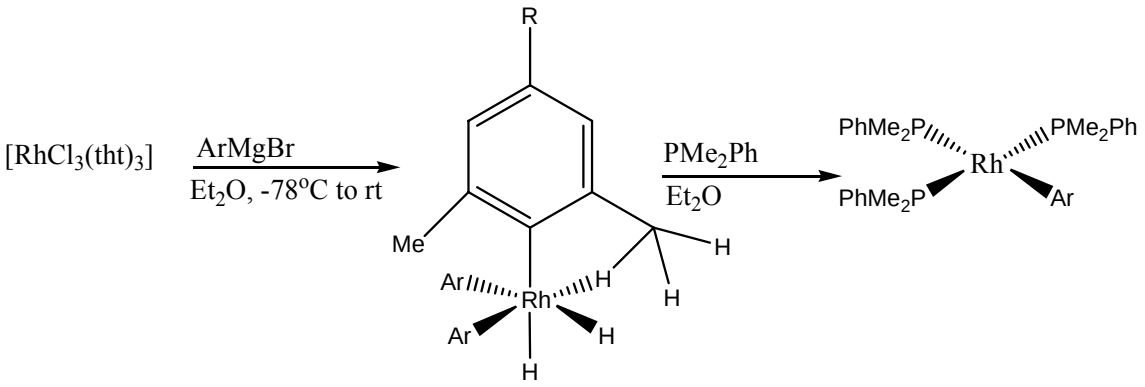


Figure 2.7. Formation of rhodium(I)-aryl complex
(Source: Wilkinson, et al. 1991)

2.2.1.2. Reactions of Aryl Rhodium(I) Complexes

In 1997, Sakai et al. reported a study about rhodium(I) catalyzed conjugate 1,4-addition of aryl and alkenylboronic acids to enones (Figure 2.8). The catalytic cycle involved arylrhodium(I) species which was generated from transmetallation of rhodium(I)enolate with arylboronic acid and resulted in the insertion of the enone into the Ar-Rh bond and the B-Rh transmetallation was the key step as shown in Figure 2.8. and Figure 2.9.

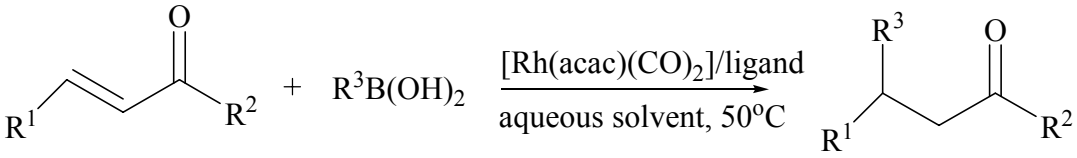


Figure 2.8. Rh-catalyzed conjugate addition of arylboronic acids to enones
(Source: Sakai, et al. 1997)

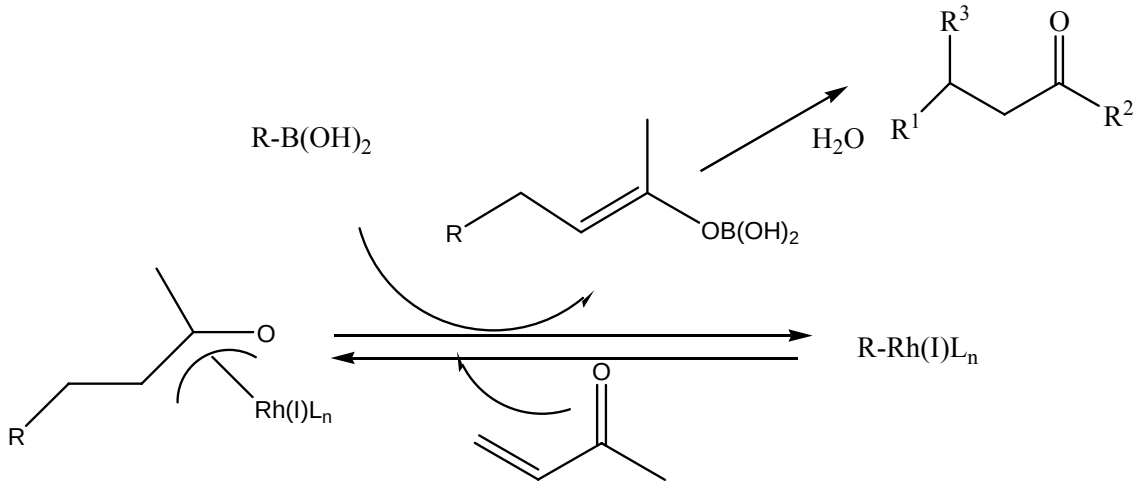


Figure 2.9. Rh-catalyzed addition of arylboronic acids to enones
(Source: Sakai, et al. 1997)

The first enantioselective variant of this type of reactions was reported by Takava et al. in 1998. They reported asymmetric 1,4-addition of arylboronic acids which proceeds with high enantioselectivity in the presence of chiral phosphine-rhodium catalyst and asymmetric alkenylboronic acids were also successful (Figure 2.10.).

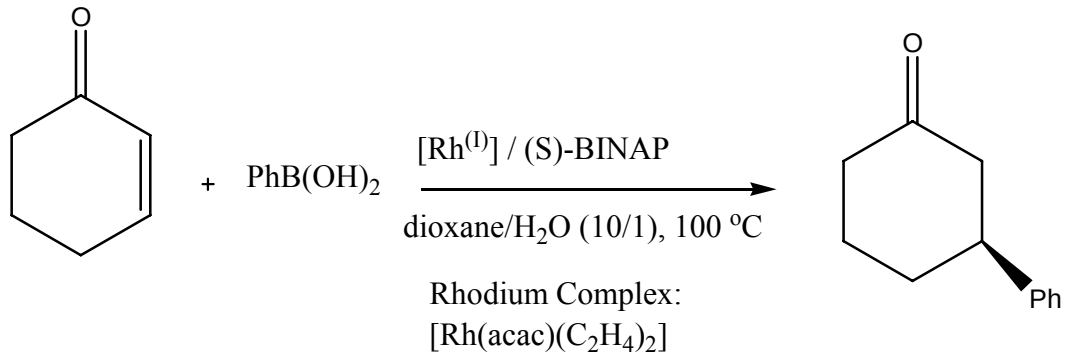


Figure 2.10. Rh-catalyzed asymmetric 1,4-additions of arylboronic acids to enones
(Source: Takaya, et al. 1998)

In 2001, Sakuma and Miyaura reported conjugate addition of arylboronic acids to α,β-unsaturated amides in the presence of a rhodium(I)-binap (Figure 2.11.) and compared to enones, α,β-unsaturated amides showed low reactivity. To overcome this reactivity problem, addition of catalytic amount of bases such as K_2CO_3 or KOH, was found to be very effective to complete the reaction.

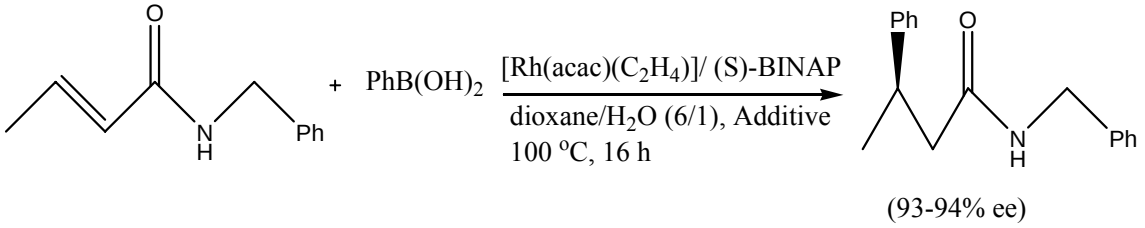


Figure 2.11. Rhodium(I)-catalyzed addition of arylboronic acids to α,β-unsaturated amides (Source: Sakuma and Miyaura 2001)

The first examples of rhodium catalyzed addition of arylboronic acids to alkenylphosphonates was reported by Hayashi and co-workers (Hayashi, et al. 1999). Using a rhodium complex generated from $[Rh(acac)(C_2H_4)_2]$ and (S)-BINAP, the products were resulted in high yields and good enantioselectivities (Figure 2.12.).

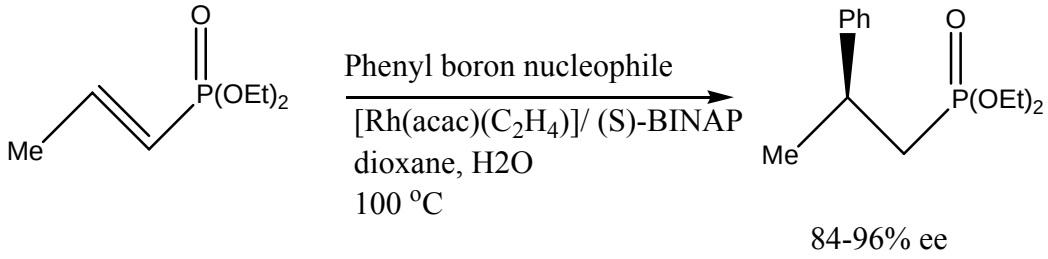


Figure 2.12. Rh-catalyzed addition of arylboronic acids to 1-alkenylphosphonates (Source: Hayashi, et al. 1999)

In 2000, Hayashi et al showed that α-substituted nitroalkanes were good reagents in the rhodium catalyzed asymmetric addition of arylboronic acids. Treatment of 1-nitrocyclohexene with phenylboronic acid in the presence of $[Rh(acac)(C_2H_4)_2]$ and (S)-BINAP in dioxane/water mixture at 100 °C for 3h yielded a diastereomer product mixture with high enantioselectivity (Figure 2.13.).

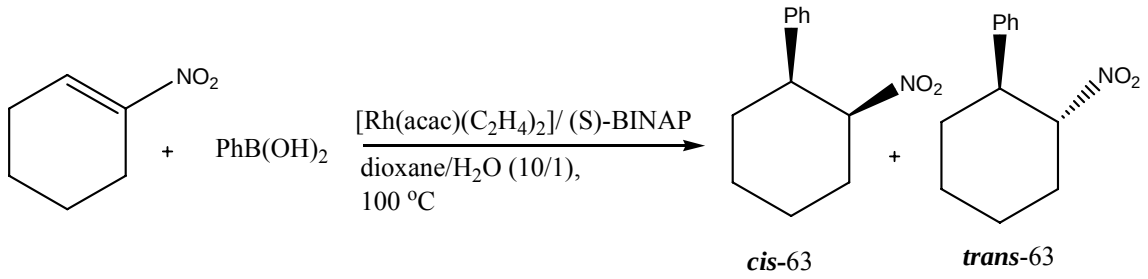


Figure 2.13. Rh-catalyzed addition of arylboronic acids to nitroalkenes
(Source: Hayashi, et al. 2000)

In 1998, Sakai et al. reported that rhodium catalyzed addition reactions of aryl and alkenylboronic acids to aldehydes yielded secondary alcohols (Figure 2.14.). They proposed a mechanism which involves a nucleophilic attack of the aryl group on the arylrhodium(I) species and reactions were facilitated by the presence of an electron withdrawing group on the aldehyde and an electron donating group on the arylboronic acid.

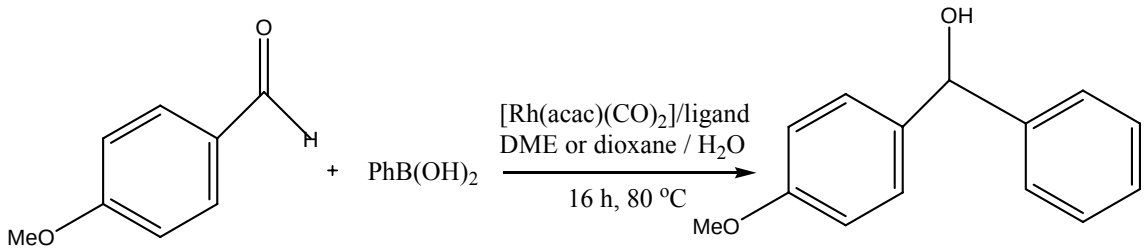


Figure 2.14. Rh-catalyzed 1,2-addition of arylboronic acids to carbonyls
(Source: Sakai, et al. 1998)

Rhodium has also recently found application in addition of carbon functionalities to unactivated alkenes and alkynes.

In 2001, Lautens et al. reported an addition reaction of styrene with arylboronic acid in the presence of catalytic $[Rh(cod)Cl]_2$ and TPPDS media with addition of SDS and sodium carbonate in neat water giving arylation product stilbene (Figure 2.15.).

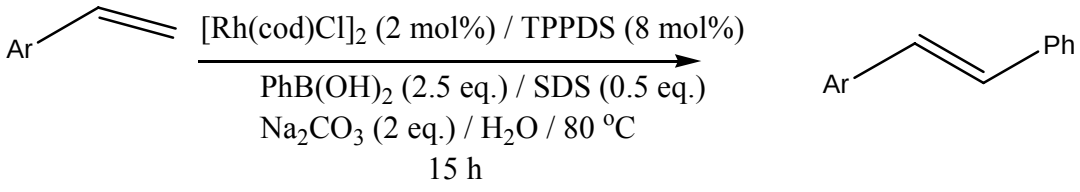


Figure 2.15. Rh-catalyzed coupling reactions of alkenes with arylboronic acids (Source: Lautens, et al. 2001)

In 2001, Hayashi et al. reported another example of the rhodium catalyzed reactions of internal alkynes with organoboronic acids whose catalytic cycle involves 1,4-shift of rhodium from an alkenyl carbon to an ortho position of aryl carbon surprisingly. The reaction of 4-octyne was performed under that conditions which shown in Figure 2.16.

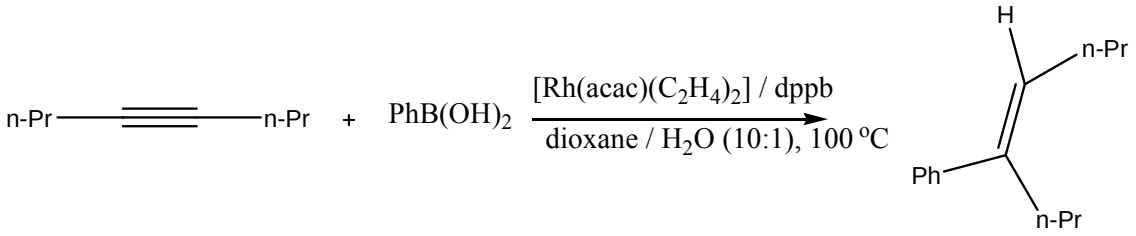


Figure 2.16. Rhodium catalyzed hydroarylation of alkynes with arylboronic acids (Source: Hayashi, et al. 2001)

Lautens and Yoshida (2002) studied rhodium catalyzed addition reactions of pyridine substitutes alkynes with arylboronic acids. They obtained the trisubstituted alkenes as a single regio and stereoisomer in good yields (Figure 2.17). The presence of the pyridyl nitrogen on *ortho* position had a dramatic effect in obtaining a single regioisomer. They observed that having the alkynyl group at the *meta* and *para* positions on the pyridine ring caused the failed of the addition reaction.

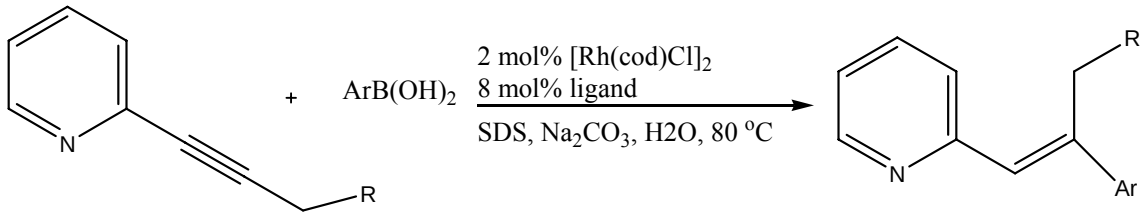


Figure 2.17. Rh-catalyzed addition of arylboronic acids to pyridine substituted alkynes (Source: Lautens and Yoshida 2002)

2.2.1.3. Rhodium-Catalyzed Cyclization Reactions of Organoborons to Unsaturated Systems

Transition metal catalyzed arylative cyclization of unsaturated reagents comprising more than one multiple double bonds is becoming a popular method in simultaneous formation of both intra and intermolecular carbon-carbon bond formation (Fagnau and Lautens 2003).

In the literature there are many studies about the rhodium-catalyzed cyclization reactions of organoborons to enyne type unsaturated compounds.

In 2005(b), Miura et al. studied rhodium-catalyzed intramolecular cyclization reaction of 1,6-enynes having an allylic ether moiety with arylboronic acids (Figure 2.18.). Rhodium catalyzed reaction of arylboronic acids with 1,6-enyne resulted in an arylative product. This reaction contained multiple carbon-carbon bond forming steps to afford the product. In the catalytic cycle, transmetallation of rhodium(I) with phenylboronic acid generates arylrhodium(I) intermediate and added onto the alkyne (A), the intramolecular carborhodation to allylic double bond occurred, leading to intermediate B. Finally, β-elimination of methoxy group afforded the cyclization product and a catalytically active methoxorhodium(I) species (Figure 2.18.).

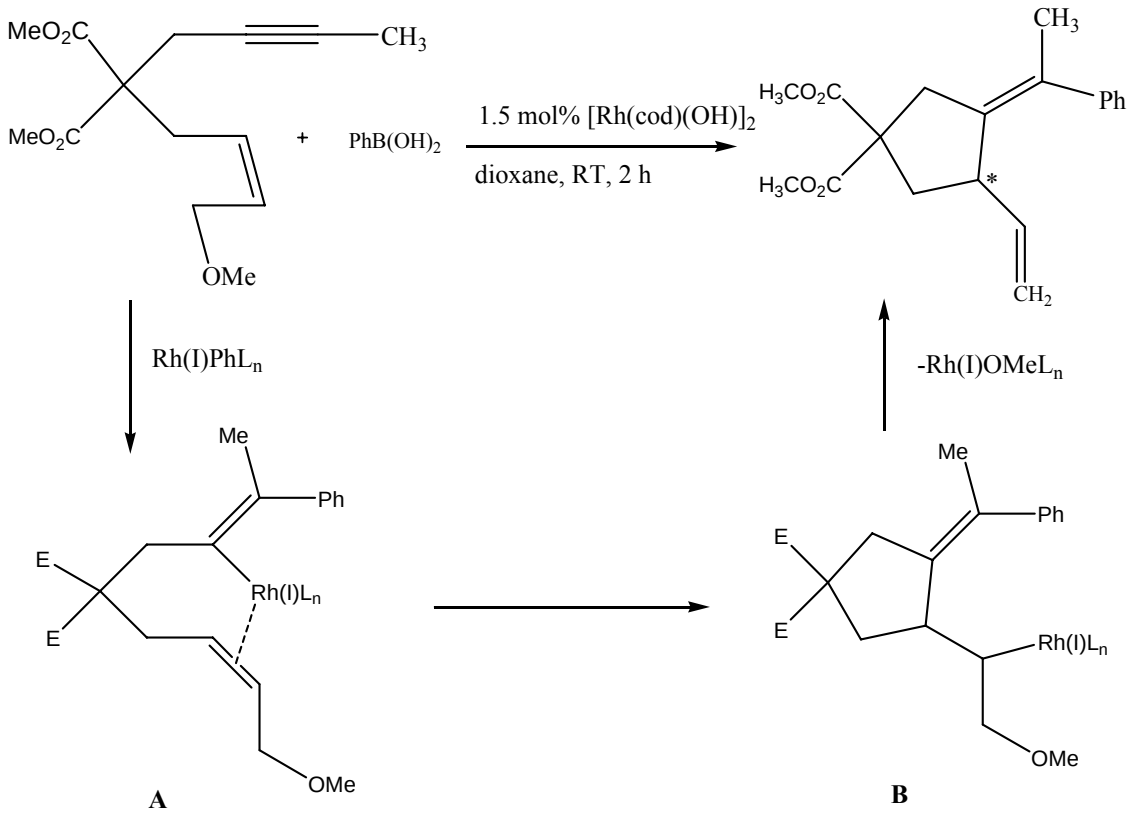


Figure 2.18. Rh-catalyzed cyclization reaction of 1,6-enynes with arylboronic acids (Source: Miura, et al. 2005(b))

In 2005(a), Shintani et al. reported highly chemo and enantioselective arylative cyclization reactions of alkyne tethered electron deficient olefins (Figure 2.19). Using a rhodium-chiral diene ligand instead of using biphosphine ligands, they obtained higher reactivity and enantioselectivity. They also examined electron-withdrawing groups on the olefinic part to obtain five-membered carbocycles with high chemoselectivity and enantioselectivity (90-99 % ee).

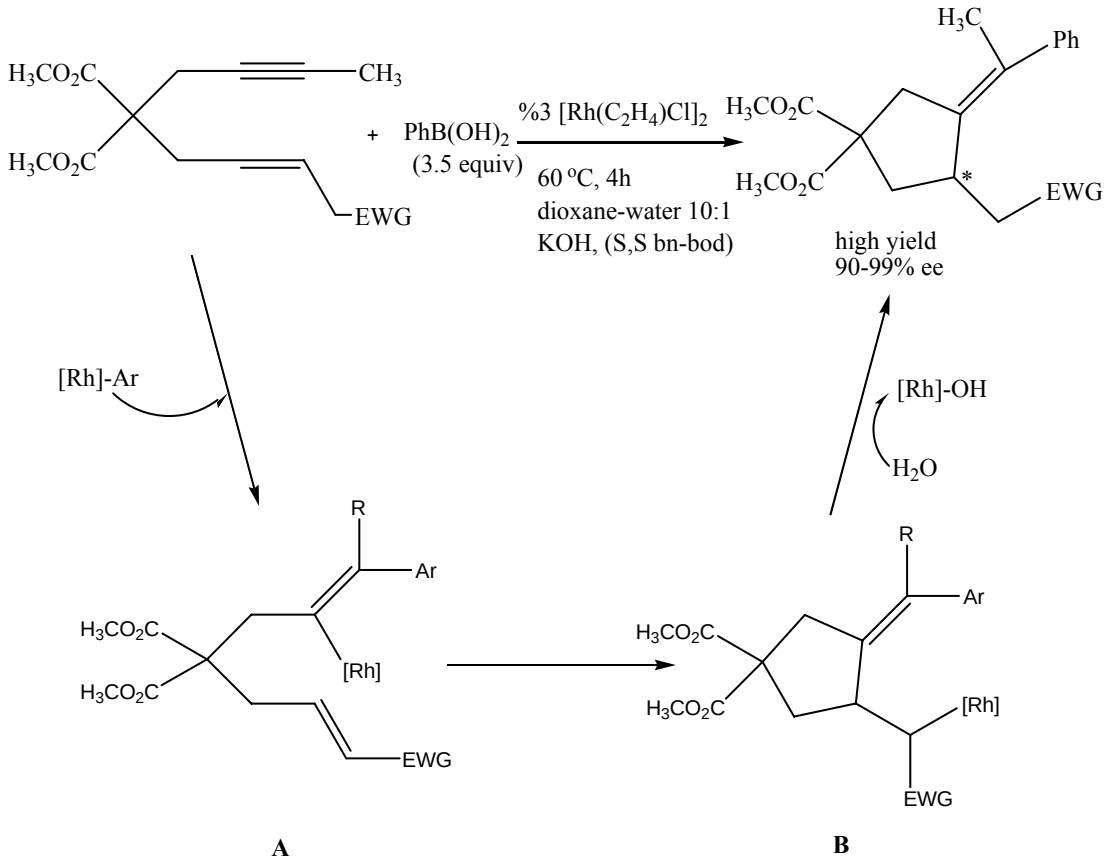


Figure 2.19. Rh-catalyzed arylative cyclization of alkyne-tethered electron deficient olefins (Source: Shintani, et al. 2005(a))

In 2006, Chen and Lee reported another example of arylative cyclization of 1,5-enynes. Their study described a new addition-cyclization reaction that occurs through a novel mechanism involving a metal vinylidene-mediated geminal carbometalation of alkynes (Figure 2.20.). Cyclization reaction of 1,5-enynes based on 1,1-carbofunctionalization process (Figure 2.21.).

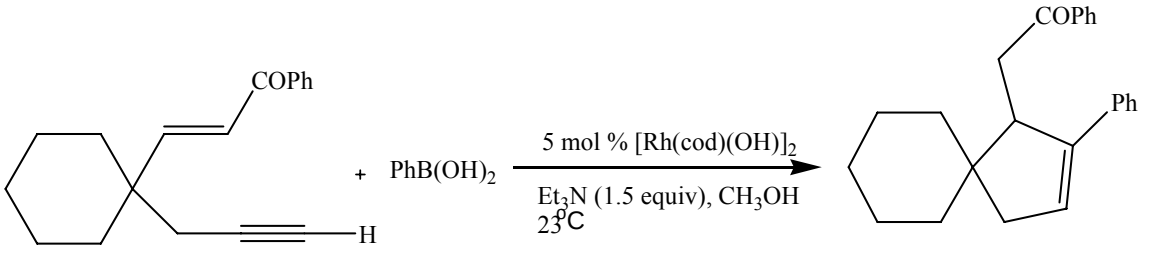


Figure 2.20. Rh-catalyzed phenylative cyclization of 1,5-enyne (Source: Chen and Lee 2006)

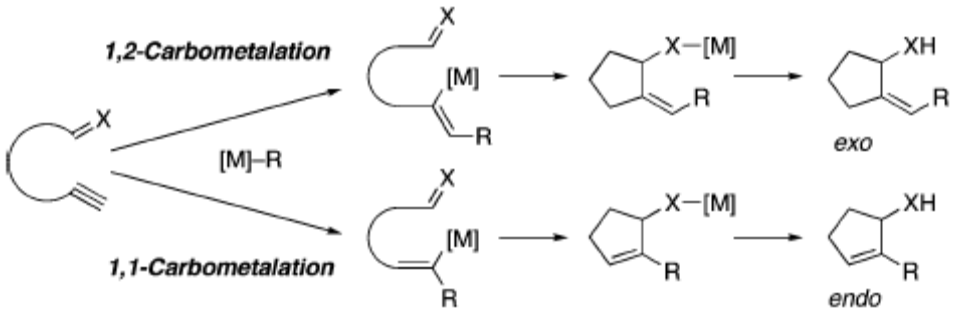
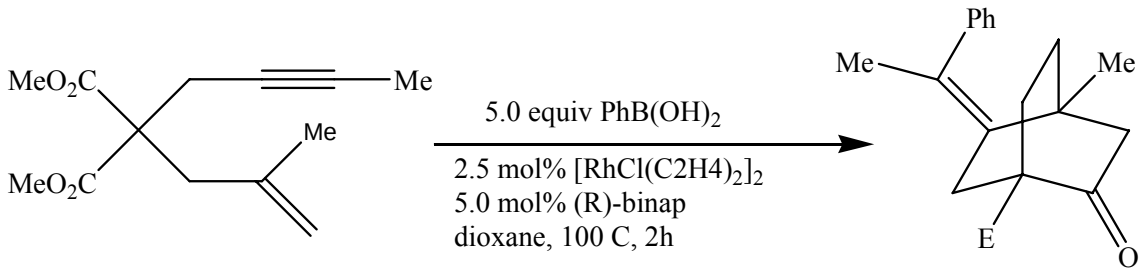


Figure 2.21. Addition-Cyclization via Carbometallation of Alkynes
(Source: Chen and Lee 2006)

As a consequence of intermolecular coupling 1,2-carbometalation occurs, it converts an alkyne to an *exo*-alkene upon ring closure. A 1,1-carbometalation pathway would offer an alternative reaction motif that gives rise to an *endo*-product but has remained unexplored (Chen and Lee 2006). The phenylative cyclization reaction was examined using both acyclic and cyclic enones and substituents at the allylic and propargylic positions and resulted in good yields.

Another study about cyclization reactions was reported by Miura et al. (2005(c)). They synthesized enantioselective bicyclo[2.2.1]heptan-2-one cyclic ketone derivatives by the reaction of organorhodium(I) species with unsymmetrical acetylenic ester groups (Figure 2.21.). The importance of this study is its being the first report which prompts intramolecular acylations with an ester group to form cyclic ketones. In literature, there are many examples that show organorhodium species to undergo nucleophilic addition to aldehydes, ketones, imines, and acid anhydrides (Sakai, et al. 1998, Takezawa, et al. 2002, Ueda, et al. 2000, Frost et al. 2001). However, there are no examples of such addition reaction with ester reagents.



1,6-enyne

60%, 89% ee

Figure 2.22. Rh-catalyzed cyclization of acetylenic ester by addition of arylboronic acids (Source: Miura, et al. 2005(c))

In 2006, Miura et al. reported another rhodium catalyzed arylative cyclization of 1,6-enynes which yielded vinylcyclopropane type compounds (Figure 2.23.). Vinylcyclopropanes have an important role in organic chemistry because they are biologically active compounds and therefore they developed a new approach to the vinylcyclopropane structure and this approach consists of multiple carborhodation steps different from other reaction pathways (Figure 2.24).

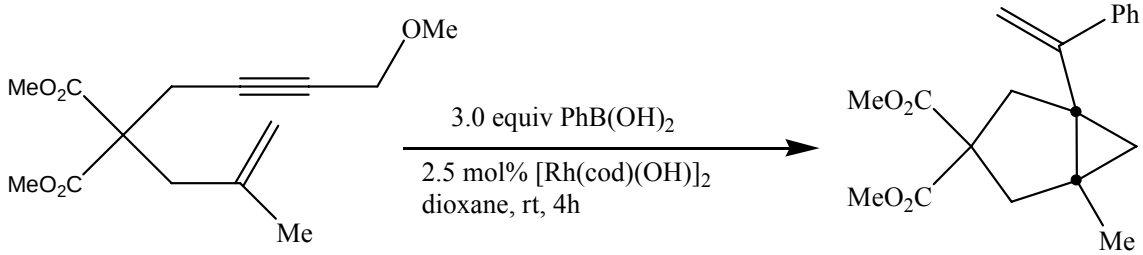


Figure 2.23. Rhodium catalyzed arylative cyclization of 1,6-enyne (Source: Miura, et al. 2006)

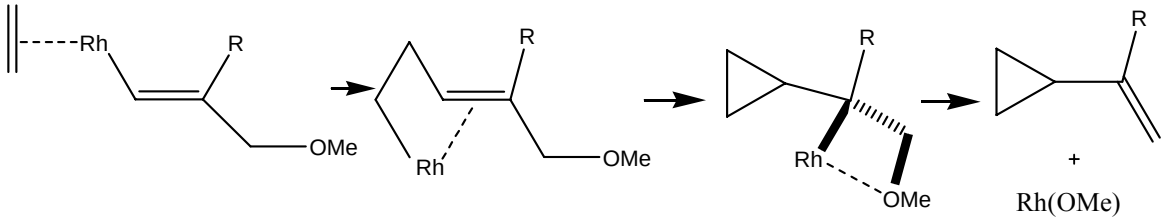


Figure 2.24. Intramolecular 3-*exo*-trig-cyclization and termination step with *β*-oxygen elimination (Source: Miura, et al. 2006)

They showed that vinylcyclopropane, three membered ring, is obtained by coordination of the methoxy group. Also, they performed a control experiment and used a 1,6-enyne lacking a methoxy moity and no cyclopropane formation was observed (Figure 2.25).

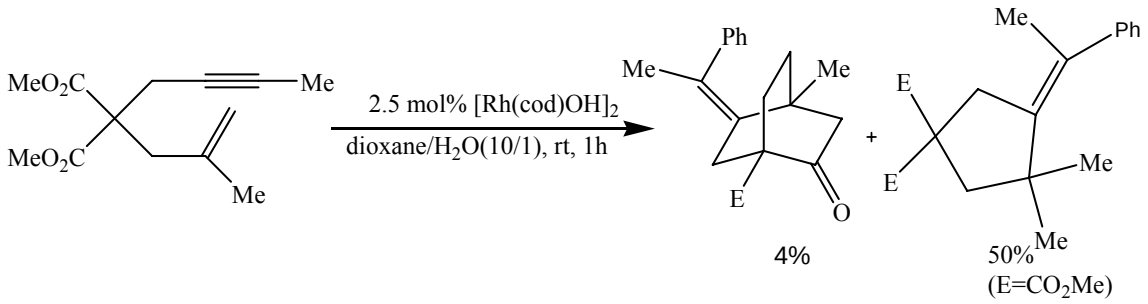


Figure 2.25. Rhodium catalyzed arylative cyclization of 1,6-enyne
(Source: Miura, et al. 2006)

In 2005(b), Shintani et al. reported that the addition/cyclization of arylboronic acids to alkynals leads to cyclic allylic alcohols by the use of a rhodium/diene catalyst (Figure 2.26.). The reaction took place successfully by the use of a chiral diene ligand, (S,S)-Bn-bod, while phosphorus based ligands failed.

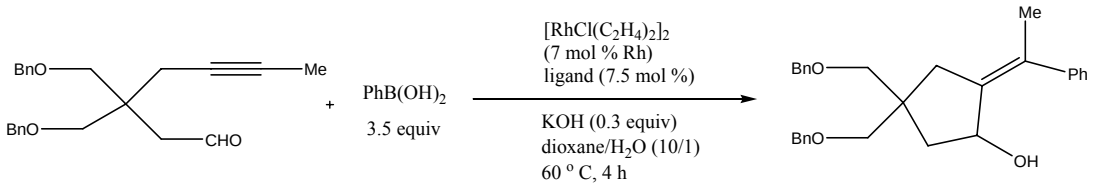


Figure 2.26. Rh-catalyzed arylative cyclization of alkynal with phenylboronic acid
(Source: Shintani, et al. 2005(b))

For the first time the reactivity of a cyano group for nucleophilic addition of an organorhodium species was demonstrated in a study by Miura et al. in 2005(b). When an alkynyl nitrile was treated with phenylboronic acid in the presence of $[Rh(cod)OH]_2$ in dioxane at 60 ^oC under a nitrogen atmosphere cyclization products were obtained as a mixture of E and Z isomers together with an addition product (5% yield) (Figure 2.27.). In proposed mechanism, the catalytic cycle was initiated with transmetallation of

rhodium(I) with phenylboronic acid and a cis-1,2-addition took place onto the alkyne. Finally, the *N*-rhodium imine was hydrolyzed to give α,β-unsaturated ketone.

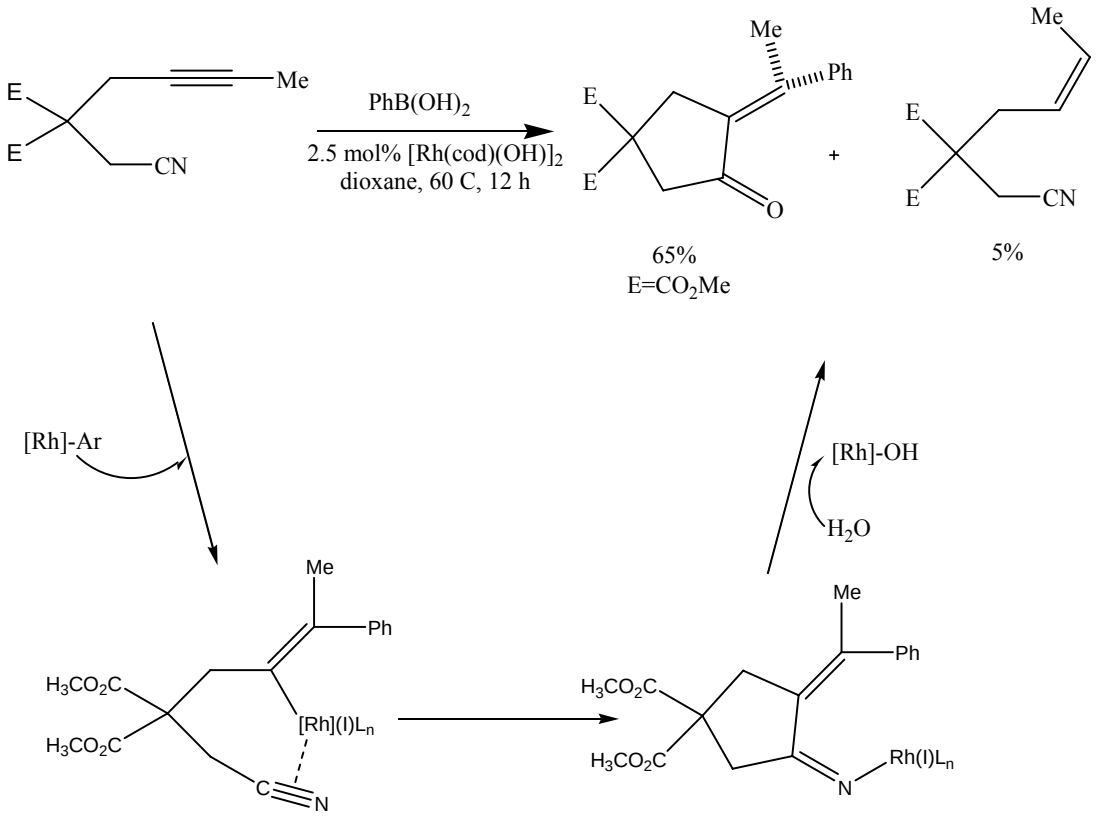


Figure 2.27. Rhodium catalyzed arylative cyclization of alkynyl nitriles with arylboronic acids (Source: Miura, et al. 2005(b))

Alkynones were also shown to undergo rhodium catalyzed arylative cyclization reactions (Miura, et al. 2007). The catalytic cycle again started with transmetallation process and followed by the ketonic carbonyl group directed carborhodation to the triple bond. The intramolecular nucleophilic addition to the carbonyl group proceeded by an exo mode and the product was released by protodemetalation (Figure 2.28.).

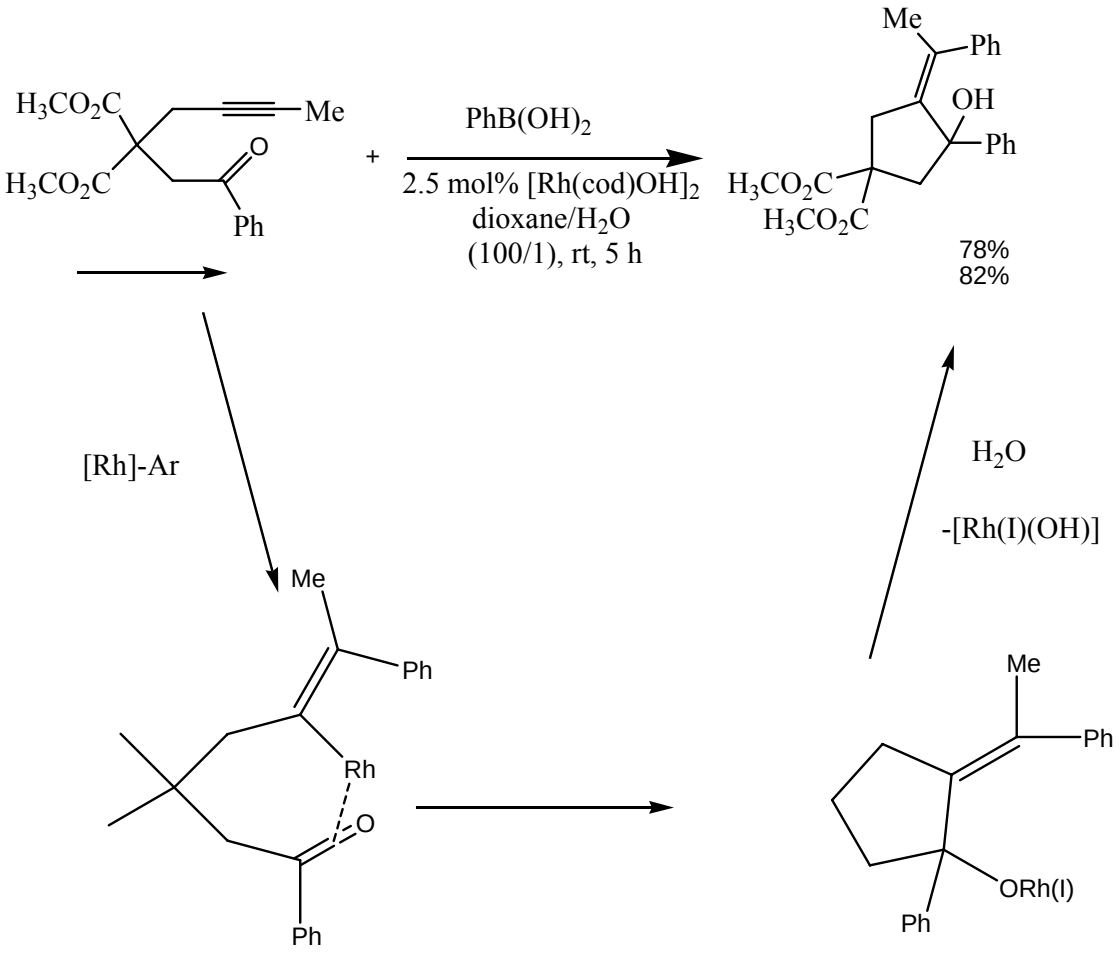


Figure 2.28. Rh-catalyzed arylative cyclization of alkynones induced by the addition of boronic acids (Source: Miura, et al. 2007)

In 2007, Miura et al. reported symmetric arylative cyclization reactions of 1,6-diynes. They used malonate-based tethers diyne molecules in the presence of rhodium(I) catalyst with arylboronic acids leading to the stereoselective formation of 1,2-dialkylidenecycloalkanes in good yields (Figure 2.29.) and obtained that catalytic process worked well with sterically and electronically different boronic acids. However, they showed no successful application with nonsymmetric diynes.

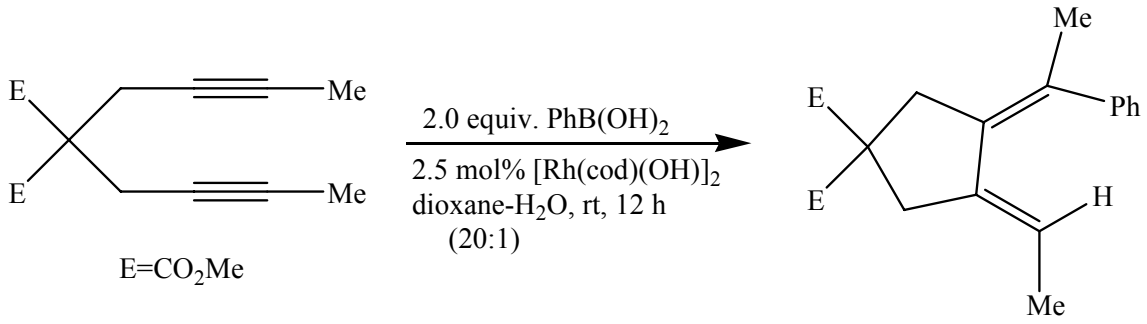


Figure 2.29. Rh-catalyzed arylative cyclization of diynes by the addition of arylboronic acids (Source: Miura, et al. 2007)

CHAPTER 3

EXPERIMENTAL STUDY

3.1. Procedures for Synthesis of Diyne Molecules

Diyne compounds were synthesized based on the literature in our laboratory.

The synthesis of diethyl 2-(prop-2-ynyl)malonate (1):

Diethyl malonate (0.9 g, 6.16 mmol) was added slowly with a dropping funnel into a suspension of NaH (0.162g, 6.15 mmol) in THF (40 ml) at 0 ^{0}C in a schlenk tube. The mixture was stirred for 2 hours at room temperature and gas evolution was controlled with a bubbler. Then, the mixture was cooled to 0 ^{0}C and propargyl bromide (6.15 mmol) was added. The reaction mixture was stirred at room temperature overnight, quenched with water and extracted with diethyl ether. The organic layer was washed with brine, dried over magnesium sulfate and concentrated under high vacuum. The residue was purified by silica gel chromatography using hexane:ether mixture (100:4 gradient elution) and the product (Figure 3.1) was obtained as a colorless oil (Yield: 45%) (Shintani, et al. 2005).

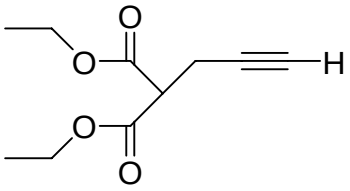


Figure 3.1. Diethyl 2-(prop-2-ynyl)malonate

The synthesis of diethyl 2-(but-2-ynyl)-2-(prop-2-ynyl)malonate (1a):

The compound **1** (2.73 mmol) was added to a suspension of NaH (0.08 g, 3.28 mmol) in THF (20 ml) at 0 ^{0}C. After the mixture was stirred for 2 hours at room temperature, 1-bromo-2-butyne (3.28 mmol) was added slowly with dropping funnel at 0 ^{o}C and stirred overnight at room temperature. The mixture was quenched with water and extracted with diethyl ether, the organic layer washed with brine, and dried over

magnesium sulfate and concentrated under high vacuum. The residue was purified by silica gel chromatography by hexane:ether mixture (100:4 gradient elution) and obtained the product as a colorless oil (Yield: 78%) (Tekavec, et al. 2004).

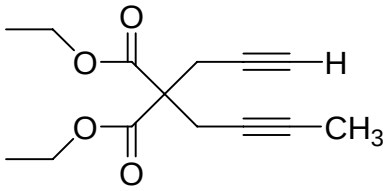


Figure 3.2. Diethyl 2-(but-2-ynyl)-2-(prop-2-ynyl)malonate

The synthesis of diethyl 2-(pent-2-ynyl)-2-(prop-2-ynyl)malonate (1b):

Diethyl 2-(pent-2-ynyl)-2-(prop-2-ynyl)malonate (1b) (Figure 3.3) was synthesized with the reaction of **1** and 1-bromo-2-pentyne (3.28 mmol) employing the method for the synthesis of **1a**. The crude product was purified by silica gel column chromatography hexane:ether (100:4 gradient elution) (Yield: 80%) (Tekavec, et al. 2004).

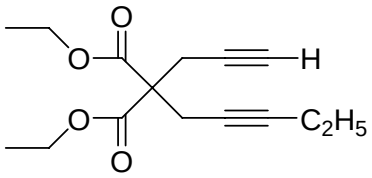


Figure 3.3. Diethyl 2-(pent-2-ynyl)-2-(prop-2-ynyl)malonate

The synthesis of diethyl 2-methyl-2-(prop-2-ynyl)malonate (5):

In a schlenk tube which included a suspension of NaH (3 mmol) in THF, compound **1** (3 mmol) was added with a dropping funnel at 0 ^{0}C, gas evolution being observed during this addition. After the reaction mixture was stirred at room temperature for 2 hours, the reaction mixture was cooled to 0 ^{0}C and CH_3I (4.2 mmol) was added slowly. The mixture was stirred for 5 hours and quenched with saturated ammonium chloride solution (40 ml). The aqueous layer was seperated and extracted with diethyl ether. After that, the combined organic layers was washed with saturated sodium chloride, dried over magnesium sulfate and concentrated in vacuo. The residue was

purified by silica gel column chromatography with hexane:ether (100:5 gradient elution)(Yield:60%) (Figure 3.4).

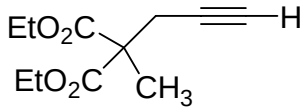


Figure 3.4. Diethyl 2-methyl-2-(prop-2-ynyl)malonate

The synthesis of diethyl 2-(but-2-ynyl)malonate (7a):

Diethyl malonate (0.9 g, 6.16 mmol) was added slowly with a dropping funnel into a suspension of NaH (0.162g, 6.15 mmol) in THF (40 ml) at 0 ^{0}C in a schlenk tube. The mixture was stirred for 2 hours at room temperature and gas evolution was controlled with a bubbler. Then, the mixture was cooled to 0 ^{0}C and 1-bromo-2-butyne (6.15 mmol) was added. The reaction mixture was stirred at room temperature overnight, quenched with water and extracted with diethyl ether. The organic layer was washed with brine, dried over magnesium sulfate and concentrated under high vacuum. The residue was purified by silica gel chromatography using hexane:ether mixture (100:5 gradient elution) and the product (Figure 3.5) was obtained as a colorless oil (Yield: 50%) (Shintani, et al. 2005).

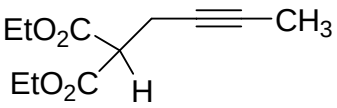


Figure 3.5. Diethyl 2-(but-2-ynyl)malonate

The synthesis of diethyl 2-(but-2-ynyl)-2-methylmalonate (7):

Diethyl 2-(but-2-ynyl)-2-methylmalonate (7) was synthesized with the reaction of **7a** and CH_3I employing the method for the synthesis of **5** (Figure 3.6). The crude product was purified by silica gel column chromatography hexane:ether (100:6 gradient elution) (Yield: 80%).

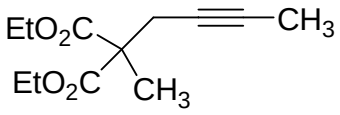


Figure 3.6. Diethyl 2-(but-2-ynyl)-2-methylmalonate

The synthesis of 1-(prop-2-ynyloxy)pent-2-yne (1f):

In a schlenk tube which included a suspension of NaH (0.5 g, 21 mmol) in THF (40 ml), 2-propyn-1-ol (1.12 g, 20 mmol) in THF was added with a dropping funnel at 0 ^{0}C, gas evolution being observed during this addition. After the reaction mixture was stirred at room temperature for 2 hours, the reaction mixture was cooled to 0 ^{0}C and 1-bromo-2-pentyne (3.8 g, 26 mmol) was added slowly. The mixture was stirred for 5 hours and quenched with saturated ammonium chloride solution (50 ml). The aqueous layer was seperated and extracted with diethyl ether. After that, the combined organic layers was washed with saturated sodium chloride, dried over magnesium sulfate and concentrated- in vacuo. The residue was purified by silica gel column chromatography with pentane and pale yellow oily product was obtained (Yield:50%) **(**Xiong, et al. 1995).

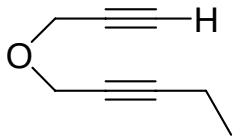


Figure 3.7. 1-(prop-2-ynyloxy)pent-2-yne

The synthesis of 2,2-di(prop-2-ynyl)malonate (1i) :

2,2-di(prop-2-ynyl)malonate (1i), (Figure 3.8.) was prepared according to the following procedure. To a suspension of NaH (0.66 g, 27.2 mmol) in THF at 0 ^{0}C, 2 molar equivalent of diethylmalonate (1.62 g, 13.6 mmol) was added slowly under argon atmosphere and the reaction mixture was stirred for an hour. Then, propargyl bromide (27.2 mmol) was added with a dropping funnel at 0 ^{o}C and stirred overnight at room temperature, then quenched with water and extracted with diethyl ether. Organic layer was washed with brine, dried over magnesium sulphate, and concentrated under vacuum. The residue was purified with by silica gel column chromatography with hexane:ether

mixture (100:4 gradient elution), pale yellow oily product was obtained (yield:88%) (Liu and Widenhoefer 2002).

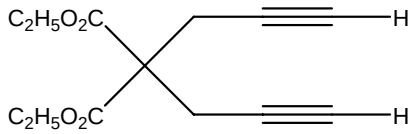


Figure 3.8. Diethyl 2,2-di(prop-2-ynyl)malonate

The synthesis of diethyl 2-(3-(1-hydroxycyclohexyl)prop-2-ynyl)-2-(prop-2-ynyl)malonate (1e) :

To prepare diethyl 2-(3-(1-hydroxycyclohexyl)prop-2-ynyl)-2-(prop-2-ynyl) malonate (1e) (Figure 3.9), n-BuLi (1.6 M in hexane 10 mmol, 6.25 ml) was added to a stirred solution of 2,2-di(prop-2-ynyl)malonate (2.36g, 10 mmol) in THF at -78 ^{o}C, and the resulting mixture was stirred at -78 ^{o}C until no gas evolution was observed with a bubbler. Then, cyclohexanone was added slowly by the help of a syringe. The mixture was stirred for 1 hour and then cooled gradually to room temperature and stirred for overnight. The reaction mixture was quenched with water and extracted with diethyl ether. The organic layer was washed with water, dried over anhydrous magnesium sulfate, and concentrated under vacuum. The product was purified by silica gel column chromatography method with a hexane:ethyl acetate (100:8 gradient elution) elute to obtain 58% yield of 2-(3-(1-hydroxycyclohexyl)prop-2-ynyl)-2-(prop-2-ynyl)malonate (1e), as yellow oil (Trost and Rudd 2005).

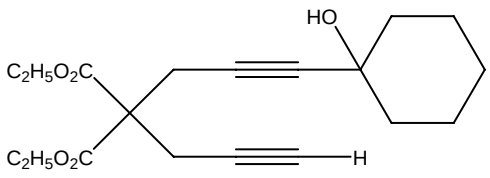


Figure 3.9. Diethyl 2-(3-(1-hydroxycyclohexyl)prop-2-ynyl)malonate

The synthesis of diethyl 2-(but-2-ynyl)-2-(but-3-ynyl)malonate (1h):

To synthesize diethyl 2-(but-2-ynyl)-2-(but-3-ynyl)malonate (1h), (Figure 3.10), we followed two steps. For the first step, sodium ethoxide (0.357 g, 5.25 mmol) and ethanol (5 ml) was stirred and heated at 50 ^{o}C using an oil bath under an argon atmosphere. Then, diethylmalonate (0.68 g, 5.15 mmol) was added to the mixture through the dropping funnel and the mixture was refluxed and checked with a bubbler to control gas evolution. When no more gas evolution observed, 4-Bromo-1-butyne (5 mmol, 0.48 ml) was added to the mixture and refluxed until neutral to moist litmus. The reaction mixture was quenched with water and extracted with diethylether. The organic layer was washed with water, dried over magnesium sulfate, and concentrated under vacuum. For the second step, the product of the first step was alkylated by using 1-bromo-2-butyne. In a mixture of NaH (0.062g, 2.56 mmol) in 15 ml THF, the product of the first step (0.45 g, 2.13 mmol) was added slowly with a dropping funnel at 0 ^{o}C and stirred at room temperature for 1 hour. 1-Bromo-2-butyne (2.56 mmol, 0.22 ml) was added gradually at 0 ^{o}C and stirred overnight at room temperature. The reaction mixture was quenched with water and extracted with diethylether. The organic layer was washed with water and dried over magnesium sulfate, and concentrated under vacuum. The mixture was purified by silica gel column chromatography using hexane:ethyl acetate solvent mixture 100:6 gradient elution; colorless oil; yield: 74% (Adams and Kamm 1941).

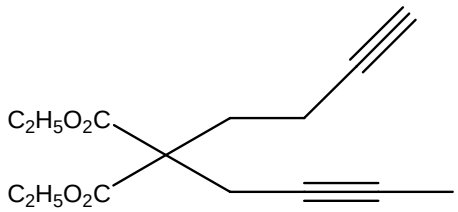


Figure 3.10. Diethyl 2-(but-2-ynyl)-2-(but-3-ynyl)malonate

The synthesis of N-(prop-2-ynyl)-N-tosylbut-2-yn-1-amine (1g):

The substrate having sulfonamide group was also synthesized in two steps. For the first step, to a stirred suspension of K_2CO_3 (1.74 g, 12.6 mmol) in acetonitrile (15 ml) was added p-toluenesulfonamide (0.60 g, 2.52 mmol) and propargyl bromide (0.55 ml, 6.28 mmol), and the resulting mixture refluxed for 2 hours. Then, the mixture was

extracted with diethyl ether and the organic layer was washed with brine, dried over magnesium sulfate, and concentrated under vacuum. The crude product was purified by silica gel column chromatography with hexane:ethyl acetate mixture (100:6 gradient elution), and obtained as pale yellow (Figure 3.11) (Tanaka, et al. 2006).

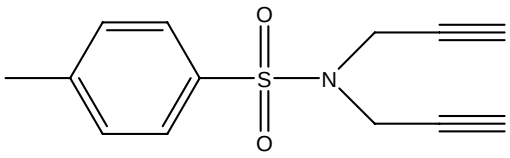


Figure 3.11. N-(prop-2-ynyl)-N-tosylprop-2-yn-1-amine

N-(prop-2-ynyl)-N-tosylprop-2-yn-1-amine (0.32 g, 1.21mmol) was taken in THF (25 ml) and n-BuLi (1.6 M in hexane, 2.38 ml) was added in stirring mixture slowly with a dropping funnel at -78 ^{o}C and then CH_3I (0.31 ml, 5 mmol) was added into the mixture and stirred overnight at room temperature. The reaction mixture was extracted with diethyl ether and the organic layer was dried over magnesium sulfate and concentrated under vacuum. The crude product was purified by silica gel column chromatography using hexane:acetone mixture (100:4 gradient elution), and obtained as a colorless oil (Figure 3.12) (Tanaka, et al. 2006).

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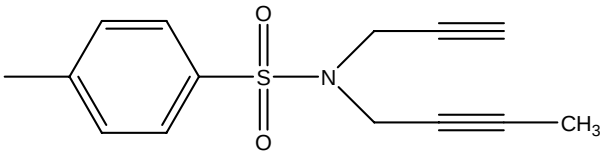


Figure 3.12. N-(prop-2-ynyl)-N-tosylbut-2-yn-1-amine

The synthesis of diethyl 2-(3-phenylprop-2-ynyl)-2-(prop-2-ynyl)malonate (1j):

Synthesis of diethyl 2-(3-phenylprop-2-ynyl)-2-(prop-2-ynyl)malonate (1j) involves 3 steps. At first step diethyl malonate (0.9g, 6.15 mmol) was added suspension of NaH (0.162 g, 6.15 mmol) in THF (40 mL) at 0 ^{0}C. The mixture was stirred 2 hours at room temperature. Propargyl bromide (6.15 mmol) was added to the mixture at 0 ^{0}C.

The mixture was stirred overnight at room temperature, quenched with H_2O, and extracted with Et_2O. The organic leayer was washed with brine, dried over magnesium sulfate, and concentrated under vacuum. The mixture was purified by silica gel column chromatography using hexane:ether mixture (100:4 gradient elution) and obtained as colorless oil (Yield: 45%) (Takimoto, et al. 2006).

The second step: To a solution of aryl iodide (1.6 mmol) and the alkyne (2 mmol, obtained from the first step) in 10 mL Et_3N was added 2 mol % $Pd(PPh_3)Cl_2$ with respect to the aryl halide. The mixture was stirred at room temperature for five minutes, after that 1 mol of % CuI was added to the mixture. Then reaction flask was placed in a preheated oil bath at 50 ^oC and vigorously stirred under an argon atmosphere. Small amounts of samples were periodically taken by the help of a syringe during the reaction, diluted in ethyl acetate and analyzed by GC to check whether all alkyne was consumed in the reaction. Then the residue was purified by column chromatography on silica gel using hexane:ethylacetate mixture (100:4 gradient elution) to give the pure product as a yellow oil (Figure 3.13) (Yield: 75%) (Roesch and Larock 2001).

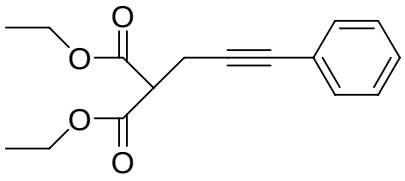


Figure 3.13. Sonagashira-Coupling Product

The third step: The alkyne obtained from the second step (1.5 mmol) was added to suspension of NaH (0.04 g, 1.8 mmol) in THF (20 mL) at 0 ^0C. The mixture was stirred at room temperature for 2 hours. Propargyl bromide (2 mmol) was added to the mixture at 0 ^0C. The mixture was stirred overnight at room temperature, quenched with water, and extracted with diethyl ether. The organic layer washed with brine, dried over magnesium sulfate, and concentrated under vacuum. Silica gel column chromatography of the residue hexane:ether (100:4 gradient elution) gave the product as a yellow oil (Yield: 83%) (Shintani, et al. 2005).

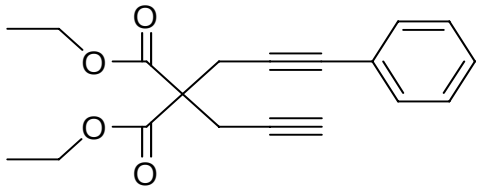


Figure 3.14. Diethyl 2-(3-phenylprop-2-ynyl)-2-(prop-2-ynyl)malonate

The synthesis of diethyl 2-(3-(trimethylsilyl)prop-2-ynyl)-2-(prop-2-ynyl)malonate (1c):

In order to synthesize trimehylsilyl substituted diyne (1c), diethyl malonate (4g, 25 mmol) was added into the suspension of NaH (240 mg, 10 mmol) in THF (15 ml) at 0 ^{0}C. The mixture was stirred at room temperature for 2 hours. 3-Bromo-1-(trimethylsilyl)-1-propyne (1.91g, 10 mmol) was added to the mixture at 0 ^{0}C. The mixture was stirred overnight at room temperature, quenched with water, and extracted with diethyl ether. The organic layer washed with brine, dried over magnesium sulfate, and concentrated under vacuum. Silica gel column chromatography of the residue hexane:ether mixture (100:7 gradient elution) gave the product as colorless oil (66% yield) (Takimoto, et al. 2006).

Second Step: The product that obtained from the first step (0.91g, 3.36 mmol) was added to a suspension of NaH (121 mg, 5.04 mmol) in THF (10 mL) at 0 ^{0}C. The mixture was stirred 2 h at room temperature. Propargyl bromide (595 mg, 5.04 mmol) was added to the mixture at 0 ^{0}C. The mixture was stirred overnight at room temperature, quenched with water, and extracted with diethyl ether. The organic layer was washed with brine, dried over magnesium sulfate, and concentrated under vacuum. The silica gel column chromatography of the residue hexane:ether (100:10 gradient elution) gave the product as a pale yellow oil (67% yield).

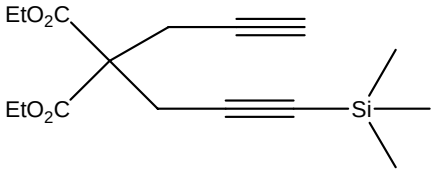


Figure 3.15. Diethyl 2-(3-(trimethylsilyl)prop-2-ynyl)-2-(prop-2-ynyl)malonate

The synthesis of (E)-4,4-diethyl 1-methyl hept-1-en-6-yne-1,4,4-tricarboxylate (6):

In order to synthesize 1,6-enyne, (E)-4,4-diethyl 1-methyl hept-1-en-6-yne-1,4,4-tricarboxylate (6), the following procedure was performed.

As a first step, diethyl malonate (4.8g, 30 mmol) was added to the suspension of NaH (360 mg, 15 mmol) in THF (20 mL) at 0 ^{0}C. The mixture was stirred at room temperature for 2 h. Propargyl bromide (1.79g, 15 mmol) was added to the mixture at 0 ^{0}C. The mixture was stirred overnight at room temperature, quenched with water, and extracted with diethyl ether. The organic layer was washed with brine, dried over magnesium sulfate, and concentrated under vacuum. Silica gel column chromatography of the residue with hexane:ether (100:4 gradient elution) gave the product as a colorless oil (60% yield) (Shintani, et al. 2005).

As a second step product that obtained from the first step (1.5g, 7.55 mmol) was added to the suspension of NaH (181 mg, 7.55 mmol) in THF (10 mL) at 0 ^{0}C. The mixture was stirred at room temperature 2 h. Methyl 4-bromocrotonate (1.35g, 7.55 mmol) was added to the mixture at 0 ^{0}C. The mixture was stirred for overnight at room temperature, quenched with water, and extracted with diethyl ether. The organic layer was washed with brine, dried over magnesium sulfate, and concentrated under vacuum. Silica gel column chromatography of the residue with hexane:ethyl acetate (100:13 gradient elution) gave the product as a pale yellow oil (71% yield) (Shintani, et al. 2005).

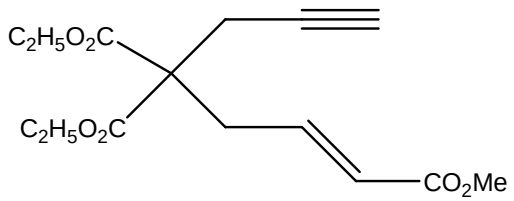


Figure 3.16. (E)-4,4-diethyl-1-methyl hept-1-en-6-yne-1,4,4-tricarboxylate

The synthesis of diethyl 2-(4-hydroxybut-2-ynyl)-2-(prop-2-ynyl)malonate (1d):

In order to synthesize a primary alcohol substituted diyne, diethyl 2-(4-hydroxybut-2-ynyl)-2-(prop-2-ynyl)malonate (1d), first 4-chloro-2-butyne-1-ol was synthesized; to a solution of 860 mg. (10 mmol) of 2-butyne-l,4-diol in 7 ml of dry benzene and 869 mg. (11 mmol) of dry pyridine was added, 1309 mg. (11 mmol) of

thionyl chloride dropwise over a period of 6 h, while the temperature was maintained in the temperature range of 10 and 20 ^{o}C. The reaction mixture was stirred for an additional hour and allowed to stand overnight at room temperature. The mixture was then poured into 50 ml of icewater and the benzene layer was separated. The aqueous layer was extracted with 250 ml portions of ether four times and the ether extracts were combined with the original benzene layer. The combined organic extracts were washed with a saturated sodium bicarbonate solution, then with cold water and dried over Drierite. The crude product was used for the next step.

To a solution of diethyl propargyl malonate (1.15g, 5.8 mmol) in DMF (60 mL) was slowly added NaH (0.28 g, 7.05 mmol) at 0 ºC. To this was added 2-(4-chloro-but-2-ynyloxy)-tetrahydro-pyran (1.09 g, 5.8 mmol) and sodium iodide (88 mg, 0.58 mmol). The reaction mixture was slowly warmed to r.t. and stirred for 36 h. The reaction was then cooled to 0 ºC and quenched with 1 M HCl (100 mL). The mixture was then stirred further for 4 h to completely remove the THP group. The DMF/aqueous layer was then extracted with ether. The combined organic layers were washed with water and brine to remove DMF, dried over magnesium sulfate, and the solvent was removed in vacuo to give the crude product which was purified on silica with hexane:ether mixture (100:7) to yield 0.75 g (55%) of the corrosponding product as a pale yellow oil (Trost and Rudd 2005).

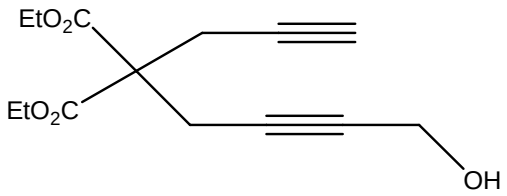


Figure 3.17. Diethyl 2-(4-hydroxybut-2-ynyl)-2-(prop-2-ynyl)malonate

The synthesis of diethyl 2,2-di(but-2-ynyl)malonate (1l):

To synthesize 2,2-di(but-2-ynyl)malonate, (1l), substrate, to a suspension of NaH (0.65 g, 27.2 mmol) in THF at 0 ^{0}C, 1-bromo-2-butyne (4 g, 27.2 mmol) and diethylmalonate (1.62 g, 12.3 mmol) were added slowly under argon atmosphere. The reaction mixture was stirred for overnight and then quenched with water and extraction process was performed with diethyl ether. Then, organic layer was washed with anhydrous magnesium sulfate, and concentrated under vacuum. After that, the residue

was purified by column chromatography (hexane:ether) on silica gel to give the pure product and product was obtained as a colorless oil (Liu and Widenhoefer 2002).

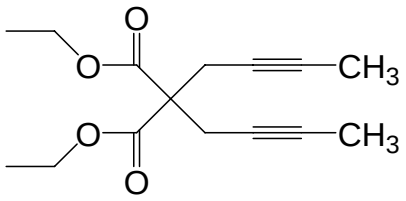


Figure 3.18. Diethyi 2,2-di(but-2-ynyl)malonate

The synthesis of triethyl hepta-1,6-diyne-1,4,4-tricarboxylate (1m):

To an oven dried flask containing 2,2-di-prop-2-ynyl malonate (1i) (4.8 mmol) and dry THF(40 ml) was added Li-HMDS (5.3 ml, 0.9 M in THF, 4.8 mmol)at -78 ^{o}C under argon. The solution was stirred for 30 min, and then ethylchloroformate (0.41 mL, 5.3 mmol) was added dropwise. After 2 h, the reaction was quenched with saturated aqueous NH_4Cl, warmed to room temperature, extracted with diethyl ether, and the organic layer was dried over magnesium sulfate. The solvent was then removed in vacuo to give the crude product, which was further purified by silica gel chromatography (hexane:ether) to give the product (50 % yield) (Figure 3.19) (Trost and Rudd 2005).

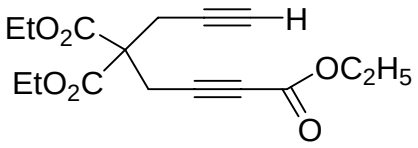


Figure 3.19. Triethyl hepta-1,6-diyne-1,4,4-tricarboxylate

3.2. General Procedure for Drying the Solvents

THF (tetrahydrofuran) was dried by using Na wire and benzophenone. Na wire was added into a flask with THF and benzophenone and refluxed under a nitrogen atmosphere until the blue color of the benzophenone ketyl radical persists. Dry THF was collected and used immediately.

For drying of methanol (200 mL), Mg turnings (1.00 mg), iodine (100 mg), and 10 mL methanol was added into a 250 mL round-bottom flask. This mixture was heated

under inert atmosphere until iodine disappears. More iodine was added if stream of bubbles is not observed. Then the remainder methanol was added to the mixture when no magnesium turnings was observed and refluxed for 3 hours and collected onto a 3A molecular sieve beads (10% w/v) and waited at least 1 day before use (Leonard, et al. 1998).

Acetone was dried over anhydrous calcium sulfate. Acetone and anhydrous calcium sulfate was added into a flask and it was refluxed for 3 hours under nitrogen atmosphere and used immediately (Ward 1961).

3.3. General Procedure for the Synthesis of Rh Complexes

$[Rh(cod)OMe]_2$ was synthesized according to literature methods. A round-bottomed flask containing a magnetic stirrer bar was charged with a solution of $[Rh(cod)Cl]_2$ (175 mg, 0.355 mmol) in dichloromethane (15 mL). The addition of a solution of KOH (40 mg, 0.173 mmol) in methanol (5 mL) gave rise to the immediate precipitation of a yellow solid. After being stirred for 30 minutes at room temperature, the solvent was completely removed in a rotary evaporater. Then, 10 mL of methanol and subsequently 15 mL of water were added to the residue, after which the solid was collected by filtration using a fine sintered-glass filter, washed with water (5- ml, ten portions) and vacuum dried over phosphorus (V) oxide (Uson, et al. 1985).

$[Rh(cod)Cl]_2$ was synthesized in our laboratory. 7.3 mmol $RhCl_3.3H_2O$, 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 didn't because the clour 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.

3.4. General Procedure for Rh-Catalyzed Arylative Cyclization Reactions of Diynes with Arylboronic Acids

Acetylphenylboronic acid, 4-hydroxyphenylboronic acid 4-methylphenylboronic acid, 4-methoxyphenylboronic acid, 2-methoxyphenylboronic acid, 2-methylphenyl boronic acid, thiophene-3-boronic acid, 1-bromo-2-butyne and diethylmalonate were supplied from Alfa Aesar. 4-(Trifloromethyl) phenyl boronic acid, *trans*-2-phenylvinyl boronic acid, propargyl bromide, 4-bromo-1-butyne and 1-bromo-2-pentyne were supplied from Aldrich. 3,4-diflorophenylboronic acid and 3-tolylboronic acid were supplied from Acros Organics. Phenylboronic acid was supplied from Merck or Fluka. Rhodium(III) chloride hydrate was supplied from Precious Metal.

A mixture of arylboronic acid (0.24 mmol for unsymetrical diins), diyne (0.2 mmol), $[Rh(cod)OMe]_2$ (3 mol % Rh), methanol (2 ml, pre-dried and degassed before used), water (50 microliter, degassed before used) was added into a schlenk tube containing a magnetic stirring bar and charged with argon atmosphere. Small amounts of sample were taken periodically by the help of a syringe and analyzed with GC and product isolation was done by flash chromatography, using hexane:triehtylamine (100:1)-ethylacetate solvent system. All of the isolated products were colorless or pale yellow oil.

3.5. Characterization of Products

The samples were analyzed by GC/MS (HP GC/MS 6890/5973N or Varian Star 3400CX/Satrun 2000 on a HP- 5MS, 30m, 0.25 mm capillary column, 5% phenylmethoxysiloxane with 0.25μm film thickness) and GC (19091J-413 HP-5 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 300 °C, respectively. The analysis was performed on a split mode with a split ratio of 1/50.

The synthesized reactants and isolated products were characterized by NMR (Varian VnmrJ 400) and HRMS (High Resolution Mass Spectroscopy; HPLC-ESI-HRMS, GC-EI-HRMS and DI-EI-HRMS; -direct inlet ionization; (Thermo Electron).

Product 2la: ^{1}H NMR (400 MHz, $CDCl_3$) δ: 1.19 (t, *J*=7.2 Hz, 6H), 1.34, (d, *J*=6.8 Hz, 3H), 1.93 (s, 3H), 2.9 (s, 2H), 3.0 (s, 2H), 4.15 (q, *J*=7.2 Hz, 4H), 4.67-4.72 (m, 1H), 7.04-7.25 (m, 5H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 14.3, 15.4, 24.2, 38.2, 40.0, 57.3, 61.8, 121.3, 126.5, 128.2, 128.8, 130.3, 132.6, 136.5, 144.8, 172.0; MS(EI, *m/z*): 342 (19 M^+), 268 (100), 239 (69), 195 (96), 167 (44); HRMS (*m/z*, M^+): 342.1826 (calculated), 342.1822 (found).

Product 2aa: ^{1}H NMR (400 MHz, $CDCl_3$) δ: 1.26 (t, *J* = 7.0 Hz, 6H), 1.55 (d, *J* = 7.2 Hz, 3H), 3.01 (s, 2H), 3.08 (d, *J* = 2.0, 2H), 4.22 (q, *J* = 7.2 Hz, 4H), 5.73-5.78 (m, 1H), 6.33 (s, 1H), 7.14-7.34 (m, 5H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 14.1, 15.1, 38.1, 43.4, 57.0, 61.6, 122.0, 122.2, 126.4, 128.2, 128.5, 135.2, 138.0, 138.2, 171.5; MS(EI, *m/z*): 328 (12 M^+), 254 (92), 181 (100); HRMS (*m/z*, M^+): 328.1669 (calculated), 328.1671 (found).

Product 2ab: ^{1}H NMR (400 MHz, $CDCl_3$) δ: 1.26 (t, *J* = 7.0 Hz, 6H), 1.56 (d, *J* = 7.2 Hz, 3H), 2.32 (s, 3H), 3.00 (d, *J* = 1.6 Hz, 2H), 3.07 (d, *J* = 1.6 Hz, 2H), 4.22 (q, *J* = 7.6 Hz, 4H), 5.79-5.84 (m, 1H), 6.29 (s, 1H), 7.07 (d, *J* = 8.0 Hz, 2H), 7.22 (d, *J* = 8.0 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 14.0, 15.1, 21.2, 38.1, 43.4, 57.0, 61.5, 121.9, 122.0, 128.4, 128.9, 134.9, 135.3, 136.0, 137.6, 171.5; MS(EI, *m/z*): 342 (15 M^+), 268 (100), 195 (99); HRMS (*m/z*, M^+): 342.1826 (calculated), 342.1818 (found).

Product 2ac: ^{1}H NMR (400 MHz, $CDCl_3$) δ: 1.26 (t, *J* = 7.2 Hz, 6H), 1.57 (d, *J* = 7.6 Hz, 3H), 3.00 (s, 2H), 3.06 (d, *J* = 2.0 Hz, 2H), 3.80 (s, 3H), 4.21 (q, *J* = 7.2 Hz, 4H), 5.80-5.83 (m, 1H), 6.27 (s, 1H), 6.81 (d, *J* = 8.8 Hz, 2H), 7.26 (d, *J* = 8.4 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 14.1, 15.1, 38.1, 43.4, 55.1, 55.2, 57.0, 61.5, 113.6, 121.6, 121.7, 129.7, 130.3, 135.4, 137.2, 158.1, 171.5; MS(EI, *m/z*): 358 (53 M^+), 284 (38), 211 (72); HRMS (*m/z*, M^+): 358.1775 (calculated), 358.1776 (found).

Product 2ad: ^{1}H NMR (400 MHz, $CDCl_3$) δ: 1.22 (t, *J* = 7.2 Hz, 6H), 1.77 (d, *J* = 6.8 Hz, 3H), 3.00 (s, 2H), 3.29 (d, *J* = 1.6 Hz, 2H), 4.219 (q, *J* = 7.2 Hz, 2H), 4.221 (q, *J*=7.2 Hz, 2H), 5.95-6.01 (m, 1H), 6.67 (s, 1H), 6.80 (d, *J* = 8.4 Hz, 2H), 7.19 (d, *J* = 8.8 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 14.0, 15.0, 36.8, 39.5, 58.4, 61.7, 114.8, 115.3,

118.5, 130.1, 130.3, 136.2, 139.1, 154.6, 171.7; MS(EI, *m/z*): 344 (58 M^+), 270 (88), 197 (100); HRMS (*m/z*, M^+): 344.1618 (calculated), 344.1619 (found).

Product 2ae: ^{1}H NMR (400 MHz, $CDCl_3$) δ: 1.27 (t, *J* = 7.0 Hz, 6H), 1.57 (d, *J* = 7.2 Hz, 3H), 2.58 (s, 3H), 3.02 (s, 2H), 3.09 (d, *J* = 1.6, 2H), 4.23 (q, *J* = 7.2 Hz, 4H), 5.76-5.81 (m, 1H), 6.32 (s, 1H), 7.44 (d, *J* = 8.4 Hz, 2H), 7.86 (d, *J* = 8.8 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 14.0, 15.1, 26.5, 37.9, 43.3, 56.9, 61.6, 120.8, 123.3, 128.4, 128.7, 135.1, 135.2, 140.4, 143.3, 171.3, 197.7; MS(EI, *m/z*): 370 (33 M^+), 296 (93), 254 (100), 223 (54), 181 (49); HRMS (*m/z*, M^+): 370.1775 (calculated), 370.1771 (found).

Product 2af: ^{1}H NMR (400 MHz, $CDCl_3$) δ: 1.27 (t, *J* = 7.2 Hz, 6H), 1.57 (d, *J* = 7.2 Hz, 3H), 3.02 (s, 2H), 3.09 (d, *J* = 1.6, 2H), 4.23 (q, *J* = 7.2 Hz, 4H), 5.71-5.74 (m, 1H), 6.30 (s, 1H), 7.45 (d, *J* = 8.4 Hz, 2H), 7.51 (d, *J* = 8.4 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 14.1, 15.1, 37.9, 43.3, 56.9, 61.6, 120.4, 123.2, 125.2 (q, *J*=15.6 Hz), 128.8, 135.1, 140.2, 141.8, 171.3; MS(EI, *m/z*): 396 (17 M^+), 322 (100), 249 (15); HRMS (*m/z*, M^+): 396.1543 (calculated), 396.1540 (found).

Product 2ag: ^{1}H NMR (400 MHz, $CDCl_3$) δ: 1.26 (t, *J* = 7.0 Hz, 6H), 1.55 (d, *J* = 7.2 Hz, 3H), 2.30 (s, 3H), 3.00 (s, 2H), 3.08 (d, *J* = 1.6, 2H), 4.22 (q, *J* = 7.2 Hz, 4H), 5.75-5.80 (m, 1H), 6.31 (s, 1H), 6.99 (d, *J* = 6.0 Hz, 1H), 7.12-7.14 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 14.1, 15.1, 21.3, 38.1, 43.4, 57.0, 61.6, 122.1, 125.5, 127.2, 128.1, 129.1, 135.2, 137.8, 137.9, 171.5; MS(EI, *m/z*): 342 (21 M^+), 269 (100), 196 (79); HRMS (*m/z*, M^+): 342.1826 (calculated), 342.1825 (found).

Product 2ah: ^{1}H NMR (400 MHz, $CDCl_3$) δ: 1.27 (t, *J* = 7.0 Hz, 6H), 1.50 (d, *J* = 6.8 Hz, 3H), 2.20 (s, 3H), 3.0 (s, 2H), 3.12 (d, *J* = 1.6 Hz, 2H), 4.219 (q, *J* = 7.2 Hz, 2H), 4.22 (q, *J* = 7.0 Hz, 2H), 5.27-5.33 (m, 1H), 6.33 (s, 1H), 7.08-7.18 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 13.1, 14.2, 18.7, 37.3, 42.3, 56.3, 60.5, 120.2, 121.0, 124.6, 125.7, 127.7, 128.8, 134.7, 134.9, 136.5, 137.0, 170.5; MS(EI, *m/z*): 342 (21 M^+), 269 (100), 196 (88); HRMS (*m/z*, M^+): 342.1826 (calculated), 342.1834 (found).

Product 2ai: ^{1}H NMR (400 MHz, $CDCl_3$) δ: 1.26 (t, *J* = 7.2 Hz, 6H), 1.58 (d, *J* = 6.8 Hz, 3H), 3.00 (s, 2H), 3.06 (d, *J* = 2.0 Hz, 2H), 4.22 (q, *J* = 7.2 Hz, 4H), 5.70-5.73 (m, 1H), 6.21 (s, 1H), 6.99-7.17 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 14.1, 15.1, 37.9, 43.2, 56.9, 61.6, 116.9, 117.1, 117.2, 117.3, 119.7, 123.0, 124.67, 124.71, 124.73, 124.76, 135.9, 139.5, 147.6, 147.8, 148.8, 149.0, 150.2, 151.3, 150.1, 151.4, 171.3; MS(EI, *m/z*): 364 (25 M^+), 290 (100), 217 (27); HRMS (*m/z*, M^+): 364.1481 (calculated), 364.1488 (found).

Product 2aj: ^{1}H NMR (400 MHz, $CDCl_3$) δ: 1.25 (t, *J* = 7 Hz, 6H), 1.62 (d, *J* = 6.8 Hz, 3H), 3.02 (s, 2H), 3.06 (d, *J* = 1.6 Hz, 2H), 4.22 (q, *J* = 7.2 Hz, 4H), 5.89-5.95 (m, 1H), 6.23 (s, 1H), 7.10-7.22 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 14.1, 15.1, 38.0, 43.2, 57.0, 61.6, 116.1, 122.3, 122.5, 124.7, 128.0, 135.7, 138.4, 138.5, 171.5; MS(EI, *m/z*): 334 (7 M^+), 260 (24), 173 (100); HRMS (*m/z*, M^+): 334.1233 (calculated), 334.1227 (found).

Product 2ak: ^{1}H NMR (400 MHz, $CDCl_3$) δ: 1.25 (t, *J* = 7.2 Hz, 6H), 1.82 (d, *J* = 8.8 Hz, 3H), 3.04 (s, 2H), 3.07 (s, 2H), 4.20 (q, *J* = 7.2 Hz, 4H), 6.01-6.06 (m, 1H), 6.16 (d, *J* = 10.8, 1H), 6.53 (d, *J* = 15.6 Hz, 1H), 7.2 (q, *J* = 8 Hz, 1H), 7.25-7.45 (m, 5H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 14.0, 15.6, 38.2, 43.1, 57.2, 61.6, 123.3, 123.4, 125.7, 126.4, 127.3, 128.6, 132.6, 137.5, 137.7, 138.9, 171.4; MS(EI, *m/z*): 354 (7 M^+), 279 (100), 206 (11); HRMS (*m/z*, M^+): 354.1826 (calculated), 354.1835 (found).

Product 2ba: ^{1}H NMR (400 MHz, $CDCl_3$) δ: 0.83 (t, *J* = 7.6 Hz, 3H), 1.26 (t, *J* = 7.2 Hz, 6H), 1.95 (q, *J* = 7.2, 2H), 3.00 (s, 2H), 3.08 (d, *J* = 2 Hz, 2H), 4.22 (q, *J* = 7.2 Hz, 4H), 5.70 (tt, J=2.4, 7.6, 1H), 6.33 (s, 1H), 7.10-7.40 (m, 5H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 13.2, 14.1, 23.0, 37.9, 43.2, 57.1, 61.5, 122.2, 126.4, 128.1, 128.5, 129.5, 133.6, 138.0, 138.3, 171.5; MS(EI, *m/z*): 342 (18 M^+), 268 (100), 239 (79), 195 (93), 165 (63); HRMS (*m/z*, M^+): 342.1826 (calculated), 342.1821 (found).

Product 2ca: ^{1}H NMR (400 MHz, $CDCl_3$) δ: 0.2 (s, 9H), 1.45 (t, *J* = 7.0 Hz, 6H), 3.25 (d, *J* = 2.0 Hz, 2H), 3.28 (*J* = 2.0 Hz, 2H), 4.396 (q, *J* = 7.2 Hz, 2H), 4.402 (q, *J* = 7.2 Hz, 2H), 6.07 (t, *J* = 2.0 Hz, 1H), 6.62 (s, 1H), 7.35 (t, *J* = 7.2 Hz, 1H), 7.41-7.45 (m, 2H), 7.53 (d, *J* = 7.2 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: -0.5, 14.2, 41.9, 42.4, 57.5, 61.7, 124.9, 126.5, 126.9, 128.2, 128.7, 137.5, 139.1, 149.8, 171.5; MS(EI, *m/z*): 386 (7, M^+), 313 (89), 195 (100), 165 (27), 73 (30); HRMS (*m/z*, M^+): 386.1908 (calculated), 386.1911 (found).

Product 2da: ^{1}H NMR (400 MHz, $CDCl_3$) δ: 1.26 (t, *J* = 7.2 Hz, 6H), 1.68 (s (OH), 1H), 3.03 (s, 2H), 3.12 (d, *J* = 1.6 Hz, 2H), 4.07 (d, *J* = 7.2 Hz, 2H), 4.21 (q, *J* = 7.2 Hz, 4H), 5.80-5.85 (m, 1H), 6.46 (s, 1H), 7.16-7.33 (m, 5H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 14.2, 38.2, 42.8, 57.2, 60.6, 61.9, 124.6, 125.3, 127.0, 128.53, 128.55, 137.3, 137.53, 137.58, 171.4; (MS(EI, *m/z*): 344 (<1 M^+), 326 (27), 253 (69), 207 (51), 179 (100), 165 (39); HRMS (*m/z*, M^+): 344.1618 (calculated), 344.1608 (found).

Product 2ea: ^{1}H NMR (400 MHz, $CDCl_3$) δ: 1.10-1.60 (m, 10H), 1.26 (t, *J* = 7.2 Hz, 6H), 3.08 (d, *J* = 2 Hz, 2H), 3.29 (d, *J* = 2 Hz, 2H), 4.21 (q, *J* = 7.2 Hz, 4H), 5.79

(t, *J* = 2 Hz, 1H), 6.41 (s, 1H), 7.10-7.38 (m, 5H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 14.1, 22.3, 25.2, 38.6, 38.8, 57.6, 61.6, 72.1, 123.2, 126.6, 128.3, 128.6, 133.3, 135.3, 137.9, 139.4, 171.5, MS(EI, *m/z*): 394(39), 320 (62), 247 (62), 173 (100); HRMS (*m/z*, M^+): 412.2244 (calculated), 412.2251 (found).

Product 2fa: ^{1}H NMR (400 MHz, $CDCl_3$) δ: 0.87 (t, *J* = 7.4 Hz, 3H), 1.89 (q, *J* = 8.4 Hz, 2H), 4.52 (m, 4H), 5.8 (tt, J = 2.4, 7.4 Hz, 1H), 6.36 (s, 1H), 7.20-7.40 (m, 5H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 13.3, 23.3, 71.6, 74.7, 119.5, 126.8, 126.9, 128.3, 128.4, 133.8, 137.1; MS(EI, *m/z*): 200 (14 M^+), 185 (16), 170 (92), 155 (16), 141 (100), 128 (51), 115 (47), 105 (56), 91 (60), 77 (31); HRMS (*m/z*, M^+): 200.1187 (calculated), 200.1196 (found).

Product 2ga: ^{1}H NMR (400 MHz, $CDCl_3$) δ:1.49 (d, *J* = 7.2 Hz, 3H), 2.44 (s, 3H), 3.97 (s, 2H), 4.02 (d, *J* = 2.0 Hz, 2H), 5.67-5.76 (m, 1H), 6.31 (s, 1H), 7.19-7.30 (m, 5H), 7.34 (d, *J* = 8.0 Hz, 2H), 7.75 (d, *J* = 8.0 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 15.3, 21.7, 51.8, 55.2, 122.3, 122.5, 127.2, 128.1, 128.3, 128.6, 129.9, 132.5, 132.8, 134.0, 136.9, 143.9; MS(EI, *m/z*): 339 (26 M^+), 281 (12), 207 (91), 183 (100), 168 (69), 155 (54), 141 (45), 129 (61), 115 (31), 91 (66); HRMS (*m/z*, $(M+H)^+$): 340.13658 (calculated), 340.13667 (found). (400 MHz, $CDCl_3$)

Product 2ha: ^{1}H NMR (400 MHz, $CDCl_3$) δ: 1.26 (t, *J* = 7.2 Hz, 6H), 1.57 (d, *J* = 7.0 Hz, 3H), 2.26 (t, *J* = 6.4 Hz, 2H), 2.40 (t, *J* = 6.4 Hz, 2H), 2.94 (s, 2H), 4.20 (q, *J* = 7.2 Hz, 4H), 5.32 (q, *J* = 3.2 Hz, 1H), 6.14 (s, 1H), 7.05-7.32 (m, 5H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 13.2, 14.1, 32.8, 33.6, 34.7, 56.3, 61.4, 122.9, 124.5, 125.9, 127.8, 128.7, 132.2, 137.8, 142.6, 171.1; MS(EI, *m/z*): 342 (9, M^+), 268 (100), 196 (39); HRMS (*m/z*, M^+): 342.1826 (calculated), 342.1822 (found).

Product 2ia: ^{1}H NMR (400 MHz, $CDCl_3$) δ: 1.26 (t, *J* = 7.0 Hz, 6H), 3.06 (t, *J* = 2.0 Hz, 2H), 3.15 (d, *J* = 1.6 Hz, 2H), 4.21 (q, *J* = 7.0 Hz, 4H), 4.91 (s, 1H), 5.12 (d, *J* = 2.0 Hz, 1H), 6.49 (s, 1H), 7.17-7.36 (m, 5H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 14.0, 42.8, 43.0, 57.1, 61.6, 111.0, 124.9, 126.8, 128.3, 128.4, 137.1, 137.6, 142.5, 171.3; MS(EI, *m/z*): 314 (16 M^+), 240 (94), 167 (100); HRMS (*m/z*, M^+): 314.1513 (calculated), 314.1517 (found).

Product 6a: ^{1}H NMR (400 MHz, $CDCl_3$) δ: 1.26 (t, *J* = 7.3 Hz, 6H), 2.09 (dd, *J* = 14.0, 6.2 Hz, 1H), 2.17 (dd, *J* = 15.6, 11.0 Hz, 1H), 2.60 (dd, *J* = 16.4, 3.4 Hz, 1H), 2.80 (dd, *J* = 13.6, 8.2 Hz, 1H), 3.02 (d, *J* = 16.4 Hz, 1H), 3.23 (d, *J* = 16.4 Hz, 1H), 3.63 (s, 3H), 3.62-2.70 (m. 1H), 4.20 (q, *J* = 7.2 Hz, 2H), 4.21 (q, *J* = 7.2 Hz, 2H), 6.41 (s,

1H), 7.16-7.33 (m, 5H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 14.00, 14.04, 36.3, 37.4, 40.1, 43.1, 51.6, 58.3, 61.6, 61.7, 123.6, 126.6, 128.1, 128.4, 136.9, 143.7, 171.3, 171.7, 172.7; MS(EI, *m/z*): 374 (21 M^+), 300 (100), 254 (44), 240 (25), 227 (43), 194 (23), 167 (75), 153 (57), 91 (41); HRMS (*m/z*, M^+): 374.1724 (calculated), 374.1722 (found).

CHAPTER 4

RESULTS AND DISCUSSION

In this thesis study, rhodium catalyzed arylative cyclization reactions of unsymmetric diynes with aryl- and alkenylboronic acids carried out efficiently in a highly regio- and stereoselective manner, yielding conjugated exo-cyclic dienes under mild conditions.

4.1. Rh-Catalyzed Arylative Cyclization of Diynes with Arylboronic Acids

Unsymmetric diynes with a terminal alkyne moiety were the substrates mainly employed in this study to verify relative preference of the carborhodation process between internal and terminal alkyne sites.

We initially attempted a reaction with an unsymmetric 1,6-diyne **1a** and phenylboronic acid mixture (1:1.2) in the presence of $[Rh(cod)OH]_2$ (3% Rh) in dioxane-water (40:1) at room tempature, which is a slightly modified method employed for the arylative cyclization of internal 1,6-diynes by Murakami et al. (2007). Suprisingly, this experimental condition failed to produce any product and the starting material was recovered (Table 4.1, entry 1). Diyne **1a** was also completely unreactive under the conditions that generated [Rh]-OH species in-situ from $[Rh(cod)Cl]_2$ complex in tetrahydrofuran (THF), 1,2-dimethoxyethane (DME), and dioxane solvents, respectively (Table 4.1, entries 2-4).

Nonetheless, **1a** and phenylboronic acid could effectively be coupled with complete conversion within just 1 h, in the presence of $[Rh(cod)OCH_3]_2$ complex (3% Rh), and in methanol-water (40:1) solvent system in a regio- and stereoselective manner to provide an arylative exocylic conjugated diene product **2aa** in a good isolated yield (Table 4.1, entry 5). The aryl group was incorporated exclusively into the terminal alkyne site and the configurations of the exocyclic double bonds were assigned by an NOE study (Figure 4.1).

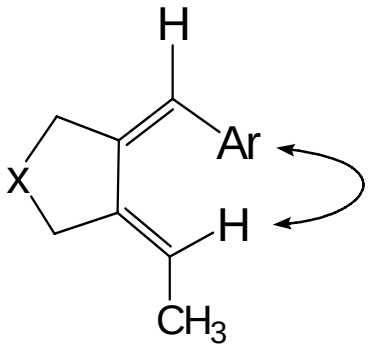
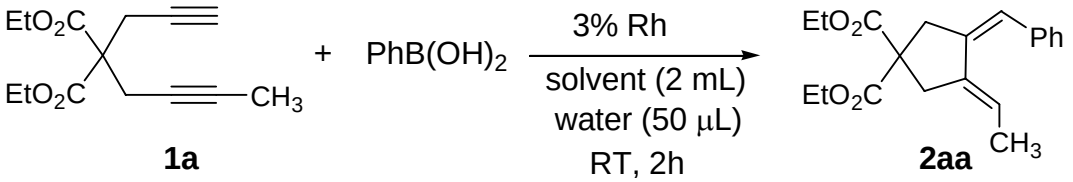


Figure 4.1. Stereochemistry of arylation product determined by NOE-NMR study

A similar result was also obtained under an in-situ [Rh]-OCH_3 generating condition which involved the use of $[Rh(cod)Cl]_2$/KOH combination in CH_3OH solvent, (Table 4.1, entry 6). Interestingly, analogous $[Rh(nbd)Cl]_2$ complex proved less effective (Table 4.1, entry 7), indicating that cod is a better ligand partner than nbd for the catalytic activity of the rhodium species in this reaction. $[Rh(cod)Cl]_2$ and $[Rh(cod)OH]_2$ complexes showed little and moderate activities, respectively, in the absence of a base additive in CH_3OH (Table 4.1, entries 8-9), suggesting that the effective exchange of anionic ligands with alkoxo ligand is needed to render higher activity to the rhodium complex.

Table 4.1 Rh-catalyzed reaction of diethyl 2-(but-2-ynyl)-2-(prop-2-ynyl)malonate (1a) with phenylboronic acid, optimization study



1a **2aa**

0.2 mmol 0.24 mmol

Entry	Complex	Solvent	Additive (0.1 mmol)	Conversion [%][a]	Yield [%][a]
1	$[Rh(cod)OH]_2$	Dioxane	-	0	0
2	$[Rh(cod)Cl]_2$	THF	KOH	0	0
3	$[Rh(cod)Cl]_2$	DME	KOH	0	0
4	$[Rh(cod)Cl]_2$	Dioxane	KOH	0	0
5[b]	$[Rh(cod)OCH_3]_2$	CH_3OH	-	100	77 (73)
6	$[Rh(cod)Cl]_2$	CH_3OH	KOH	100	73
7	$[Rh(nbd)Cl]_2$	CH_3OH	KOH	77	37
8	$[Rh(cod)Cl]_2$	CH_3OH	-	47	16
9	$[Rh(cod)OH]_2$	CH_3OH	-	100	51

a Calculated by 1H NMR relative to an internal standard (1,3,5-trimethoxybenzene). Isolated yields are given in paranthesis.
b Reaction time is 1 h.

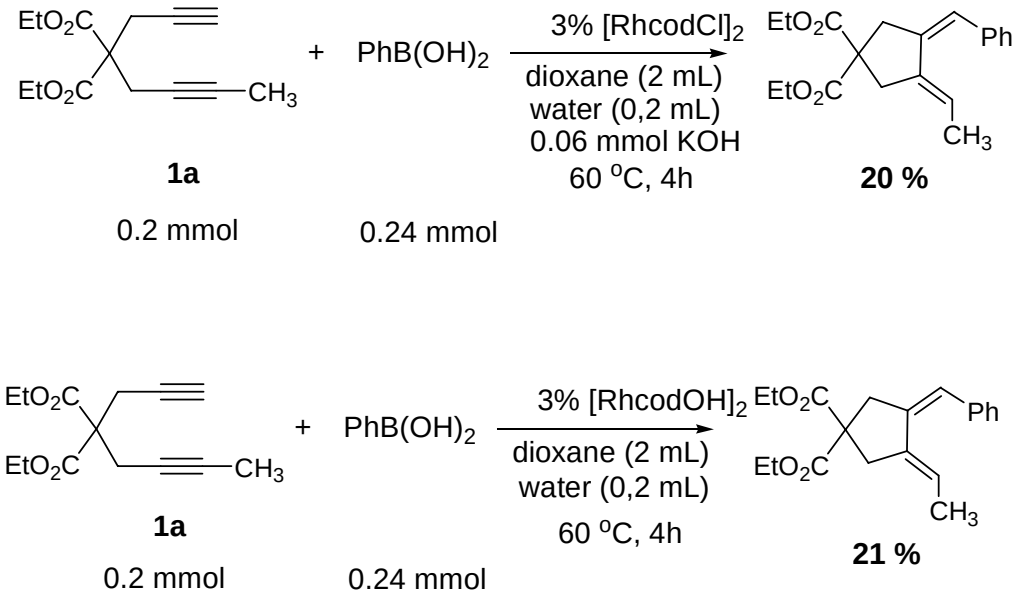


Figure 4.2. Rh-catalyzed reaction of diethyl 2-(but-2-ynyl)-2-(prop-2-ynyl)malonate (1a) with phenylboronic acid

Figure 4.2 showed that $[Rh(cod)Cl]_2$ and $[Rh(cod)OH]_2$ complexes showed little activities in dioxane solvent with diyne **1a** even after 4 h of the reaction at 60 ^{0}C. The catalytic process worked well with enyne reagent which involved the use of $[Rh(cod)Cl]_2$/KOH combination in dioxane solvent but the conversion of enyne was incomplete with the use of $Rh(cod)OH]_2$/dioxane combination even after 5 hours of the reaction at room temperature (Figure 4.3).

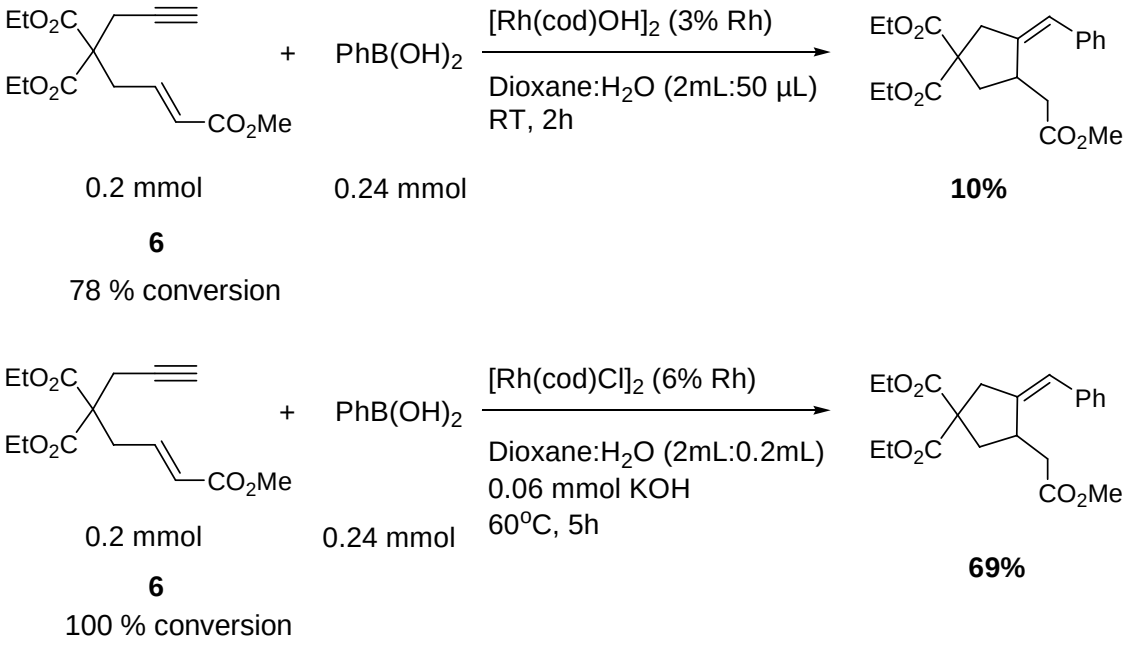
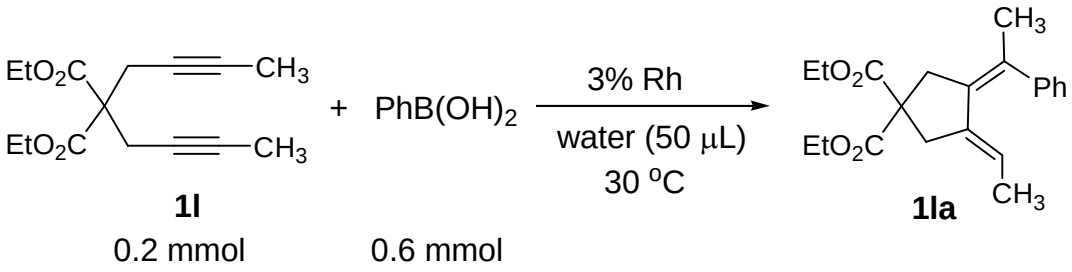


Figure 4.3. Rh-catalyzed reaction of diethyl (E)-4,4-diethyl 1-methyl hept-1-en-6-yne-1,4,4-tricarboxylate (1k) with phenylboronic acid in dioxane medium

The $[Rh(cod)OCH_3]_2/CH_3OH$ system also proved to be superior compared to the $[Rh(cod)OH]_2$/dioxane combination for the arylative cyclization of a methyl substituted internal symmetric diyne **1l**. The conversion of the substrate **1l** was incomplete with the use of $Rh(cod)OH]_2$/dioxane combination even after 5 h of the reaction (Table 4.2, entry 1), whereas the reaction proceeded to completion in just 30 minutes to afford a high yield of the corresponding product **1l** (Table 4.2, entry 2).

The reason for the higher activity of [Rh]-OCH_3 species as compared to [Rh]-OH species is not clear presently, however, it can not be attributed to solely differences in their tranmetalation activities, because there are satisfactory number of evidences that [Rh]-OH complexes can efficiently catalyze reactions of organoborons with various electrophilic reagents at room temperature, which are invariably initiated by transmetalation of Rh(I) with organoboron (Miura, et al. 2009, Miura, et al. 2005, Miura, et al. 2006, and Hayashi, et al. 2002). The methoxo-ligated rhodium might also be facilitating later carborhodation steps more effectively.

Table 4.2. Rh-catalyzed reaction of diethyl 2,2-di(but-2-ynyl)malonate (1l) with phenylboronic acid



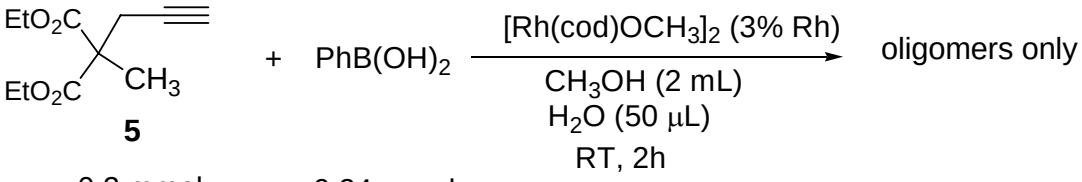
1l 0.2 mmol

0.6 mmol

1la

Entry	Rh complex	Solvent	Time (h)	Conversion [%][a]	Yield [%][a]
1	$[Rh(cod)OH]_2$	Dioxane	5	82	74
2	$[Rh(cod)OCH_3]_2$	CH_3OH	0.5	100	96 (75)

[a] Calculated by GC. Isolated yields are given in paranthesis.



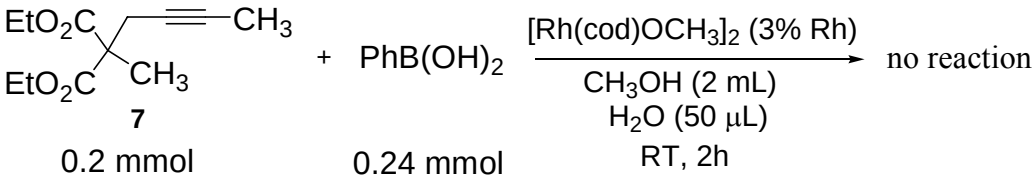
5

0.2 mmol

0.24 mmol

100% conversion

Figure 4.4. Rh-catalyzed reaction of diethyl 2-(prop-2-ynyl)malonate with phenylboronic acid



7

0.2 mmol

0.24 mmol

Figure 4.5. Rh-catalyzed reaction of diethyl 2-methyl-2-(prop-2-ynyl)malonate with phenylboronic acid

Figure 4.4 showed that the substrate **5** which have a terminal alkyne moiety failed give any arylation product, the substrate totally consumed via oligomerization.

This result indicates that 1,2-addition into the terminal alkyne has to be facilitated through the interaction of another intramolecular functional group to the metal center under the established condition and the substrate **7** showed no reaction under same reaction conditions (Figure 4.5).

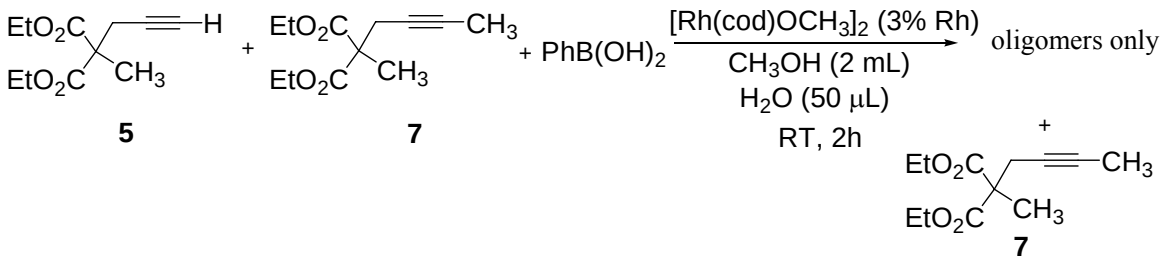
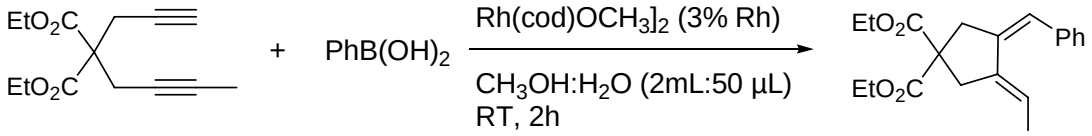


Figure 4.6. Rh-catalyzed reaction of diethyl 2-(prop-2-ynyl)malonate and diethyl 2-methyl-2-(prop-2-ynyl)malonate with phenylboronic acid

A mixture of diethyl 2-(prop-2-ynyl)malonate, (**5**) and diethyl 2-methyl-2-(prop-2-ynyl)malonate, (**7**) failed in arylative cyclization reaction, only substrate **5** consumed via oligomerization and substrate **7** was completely unreactive (Figure 4.6).

After having determined the effective conditions, unsymmetrical terminal diyne **1a** underwent cyclization reactions with electron rich and poor arylboronic acids substituted with electron-donating groups at *meta*- or *para*- positions (**2b-g**) and reactions resulted in good yields (Table 4.3, Entries 1-6). When the reaction was performed with *o*-tolylboronic acid, which was more sterically hindered, a good yield of product **2ah** was obtained (Table 4.3, Entry 7). Also, a disubstituted phenylboronic acid, a heteroarylboronic acid, and an alkenylboronic acid was found as suitable boronic acids for the cyclization reaction, yielding related cyclized products **2ai-k** in the range of 68-74% (Table 4.3, Entries 8-10).



0.2 mmol 0.6 mmol 80 %

1a

Figure 4.7. Rh-catalyzed reaction of diethyl 2-(but-2-ynyl)-2-(prop-2-ynyl)malonate with phenylboronic acid

We performed a reaction with 1,6-diyne **1a** and phenylboronic acid mixture as a mixture of 1:3 in the presence of $[Rh(cod)OMe]_2$ (3 % Rh) in $MeOH:H_2O$ at room temperature and cyclization product was obtained in a good yield (Figure 4.7).

Table 4.3. Rh-catalyzed arylative cyclization reaction of diethyl 2-(but-2-ynyl)-2-(prop-2-ynyl)malonate (1a) with various organoboronic acids

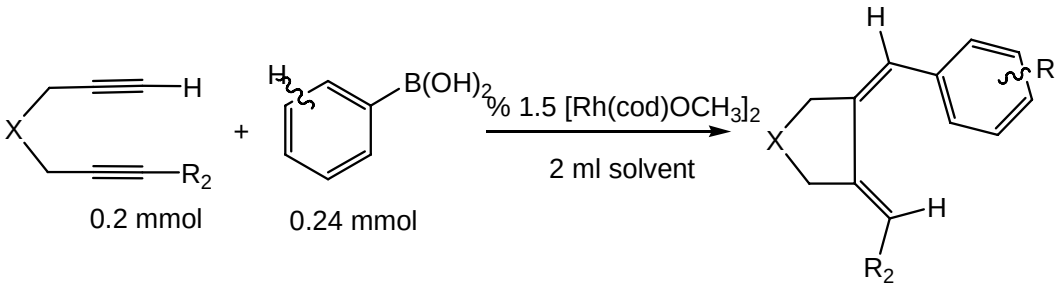
Entry	R	Time, h	Isolated Yield , %
1	p-CH_3	1	68 **(2ab)**
2	p-OCH_3	1	72 **(2ac)**
3	p-OH	2	61 **(2ad)**
4	p-$COCH_3$	2	72 **(2ae)**
5	p-CF_3	2	70 **(2af)**
6	m-CH_3	2	66 **(2ag)**
7	o-CH_3	4	74 **(2ah)**
8	3,4-difluoro	1	74 **(2ai)**
9	Thiophene-3	2	68 **(2aj)**
10	Trans-2-phenylvinyl	2	80 **(2ak)**

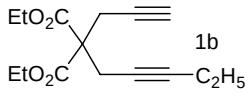
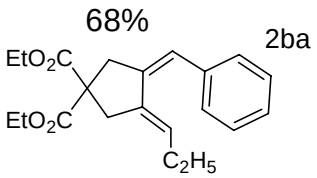
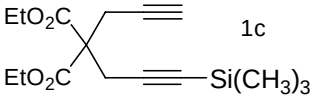
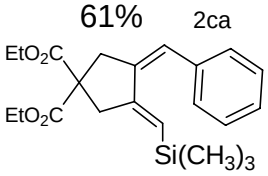
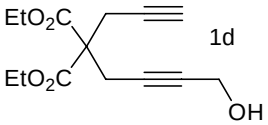
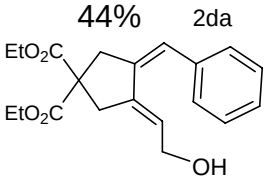
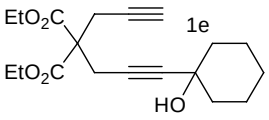
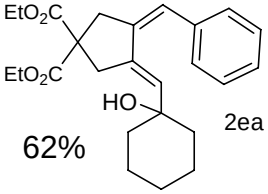
The scope of unsymmetric diyne substrates were also surveyed with different tether types, and substituent groups on one of the alkyne terminus. The unsymmetric 1,6-diynes having a malonate-based tether with $–C_2H_5$ **1b** and $–Si(CH_3)_3$ **1c**, substituents at one of the propargylic position and primary and tertiary 1,6-diynols were all applicable substrates which converted in regio- and stereoselective manners to the corresponding 1,2- dialkylidenecyclopentane products in good yields (Table 4.4, Entries 1-4).

Bearing sulfonamide group diyne reagent **1g** and allylic propargylic diyne ether **1f** was used as effective reagents in cyclization reaction (Table 4.4, Entries 5-6).

We also have succeded arylative cyclization reaction with 1,7-diyne **1h** and yielded the six membered ring exocyclic diene in a moderate amounts together with small amount of its stereoisomer with unassigned structure in the ratio of 15/1 (Table 4.4, Entry 7).

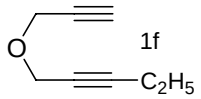
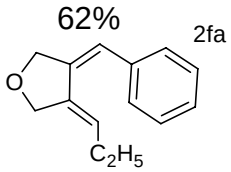
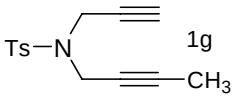
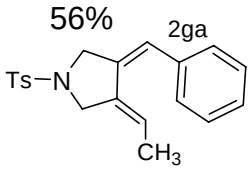
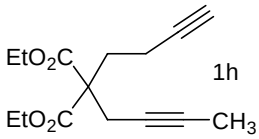
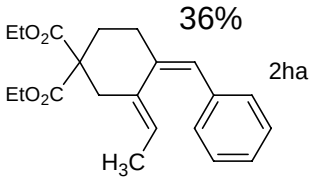
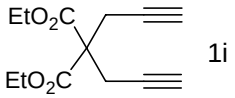
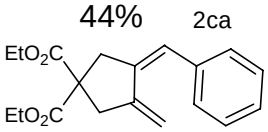
Table 4.4. Rh-catalyzed arylative cyclization reactions of diynes having a terminal alkyne terminus with phenylboronic acid



Entry	Diyne	Time, h	Isolated Yield , %
1		4	
2		2	
3		2	
4		2	

(cont. on next page)

Table 4.4. (cont) Rh-catalyzed arylative cyclization reactions of diynes having a terminal alkyne terminus with phenylboronic acid

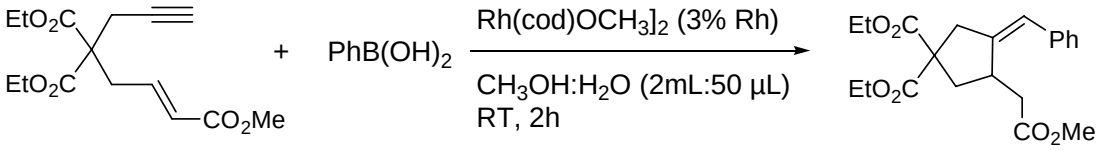
5		2	
6		2	
7		2	
8		2	

[a] $[Rh(cod)OCH_3]_2$ (3%Rh), 2 mL solvent (CH_3OH:H_2O; 100:2.5), RT: Room Temperature

A symmetric diyne (**1i**) which bears two terminal alkyne moities underwent arylative cyclization reaction under optimized conditions with a relatively lower yield (Table 4.4, Entry 8).

The reaction pathway worked well with an enyne reagent (**6**) which bearing an unsubstituted alkyne functionality and cyclization product was obtained in 80% of isolated yield (Table 4.5).

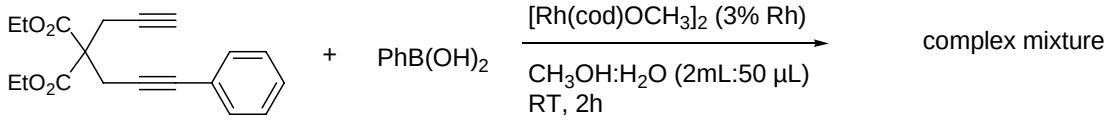
Table 4.5. Rhodium catalyzed reaction of diethyl (*E*)-4,4-diethyl 1-methyl hept-1-en-6-yne-1,4,4-tricarboxylate (1k) with phenylboronic acid



0.2 mmol 0.24 mmol

6 **6a**

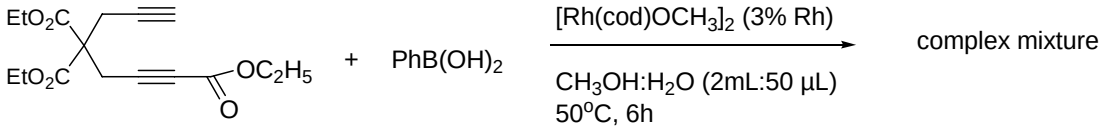
Time (hour)	T(^{0}C)	Solvent (100:2.5)	Isolated Yield (%)
2	RT	MeOH:H_2O	80



0.2 mmol 0.24 mmol

1j

100% conversion



0.2 mmol 0.24 mmol

1m

100% conversion

Figure 4.8. Rh-catalyzed reaction of diethyl 2-(3-phenylprop-2-ynyl)-2-(prop-2-ynyl)malonate and triethyl hepta-1,6-diyne-1,4,4-tricarboxylate with phenylboronic acid

The reactions with ester functionalized electron deficient diyne molecule and also phenyl substituted diyne molecule were performed under given conditions in Figure 4.8. According to the characterization process we obtained complex mixture instead of having arylative cyclization product.

4.2. Proposed Mechanism of Rh-Catalyzed Arylative Cyclization Reactions of Diynes with Arylboronic Acids

In Figure 4.9, proposed mechanism for formation of exocyclic dienes is shown.

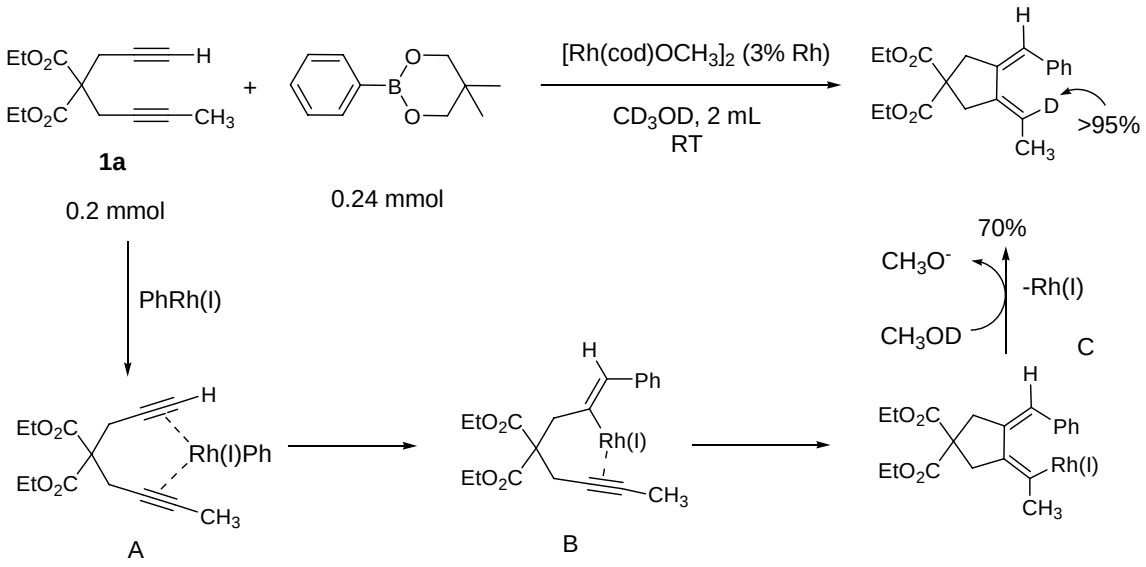


Figure 4.9. The reaction mechanisn for the Rh-catalyzed arylative cyclization of diynes with arylboronic acids

Vinylidene formation which is a common intermadiete in rhodium catalysis of terminal alkynes, is unlikely in our case considering the product profile (Chen and Lee 2006). Likewise, that the reaction of diyne **1a** with a phenylboronate ester in CD_3OD produced **1aa**-d_1 with a deuterium introduction only at the vinylic position, proposes the following mechanism: coordination of organorhodium to the unsaturated carbon-carbon bonds triggers vicinal addition across the unhindered terminal alkyne (A), which follows by intra-carborhodation onto the next unsaturated carbon-carbon bond (B). Hydrometalation at the last step produces the product and regenerates the catalytically active Rh(I) complex (C).

CHAPTER 5

CONCLUSION

In this thesis study, we have succeded rhodium-catalyzed arylative cyclization reactions of unsymmetrical diynes with arylboronic acids both regio- and stereoselectively to yield conjugated exocyclic dienes. The arylation took place selectively at the terminal alkyne site under mild conditions.

$[Rh(cod)OCH_3]_2$ was found as the most effective complex in catalyzing the reactions in methanol at room temperature.

This study is really important for being the first in the literature because of using terminal unsymmetrical diynes for rhodium catalyzed arylative cyclization reactions.

The yield of cyclization products was higher with para- and meta- substituted phenylboronic acids than sterically hindered ortho- substituted phenylboronic acid, 2-methylbenzeneboronic acid.

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APPENDIX A

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

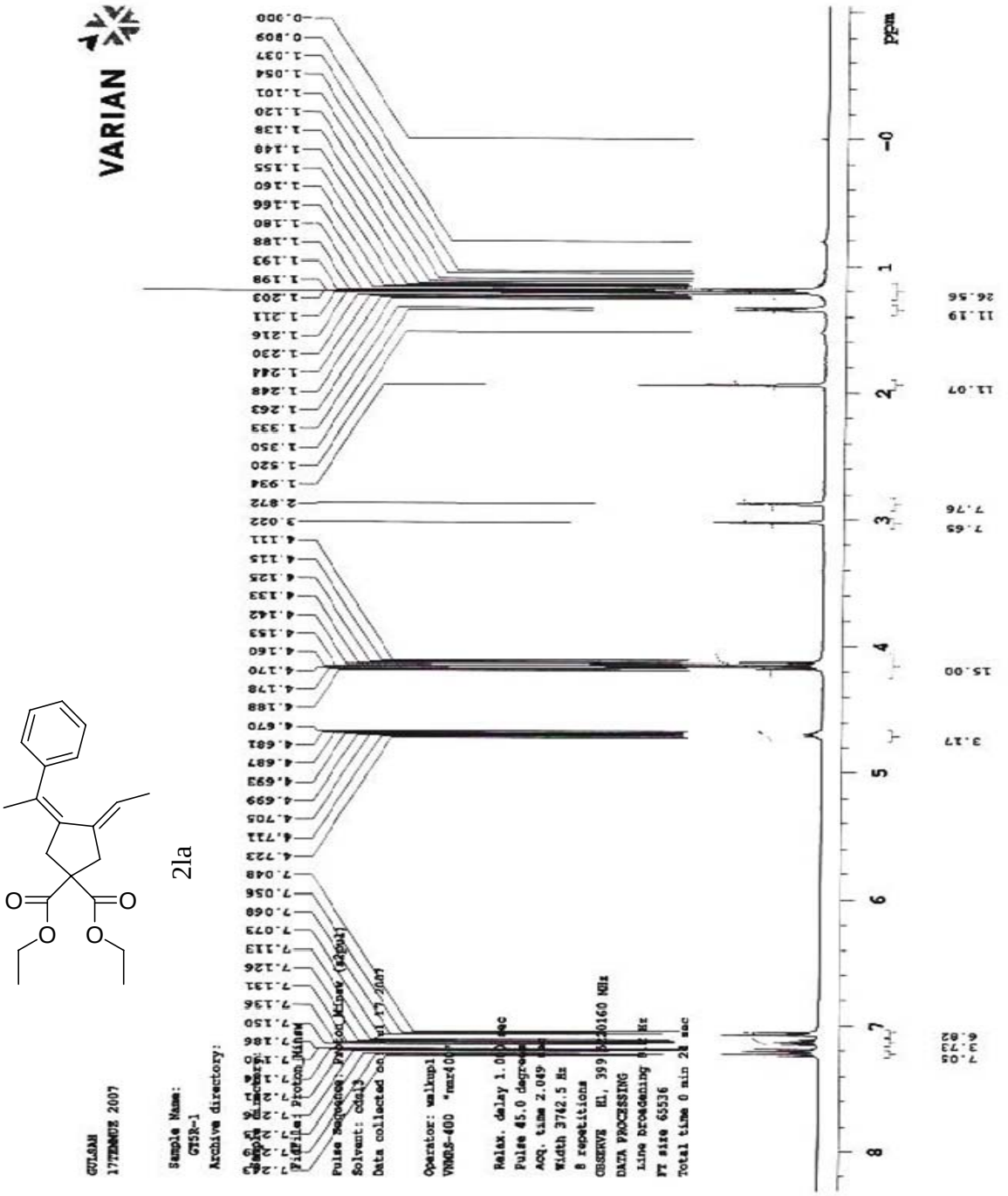

Figure A.1. ^{1}H NMR of (3E,4Z)-diethyl 3-ethylidene-4-(1-phenylethylidene)cyclopentane-1,1-dicarboxylate

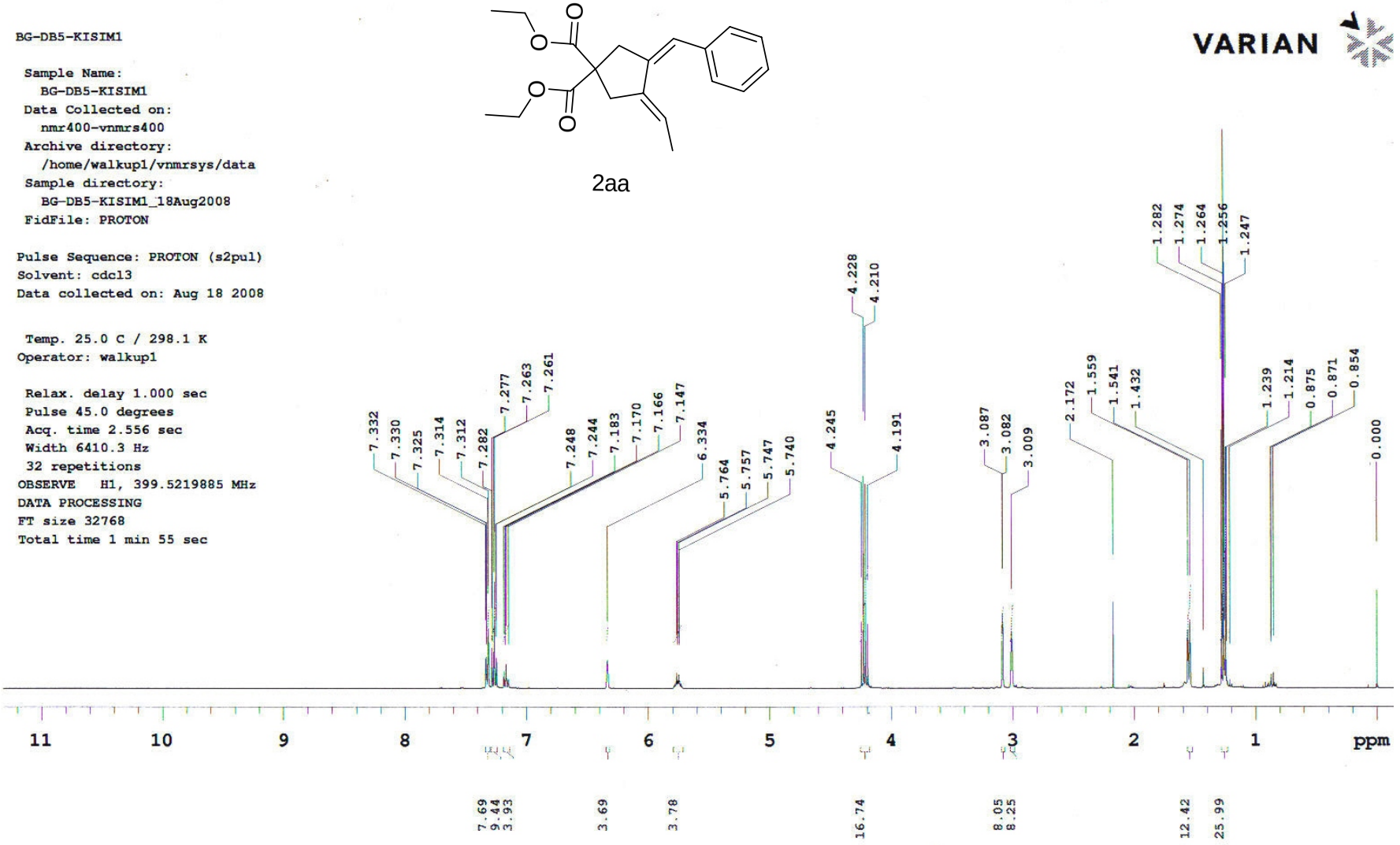

Figure A.2. ^{1}H NMR (3Z,4E)-diethyl 3-benzylidene-4-ethylidenecyclopentane-1,1-dicarboxylate

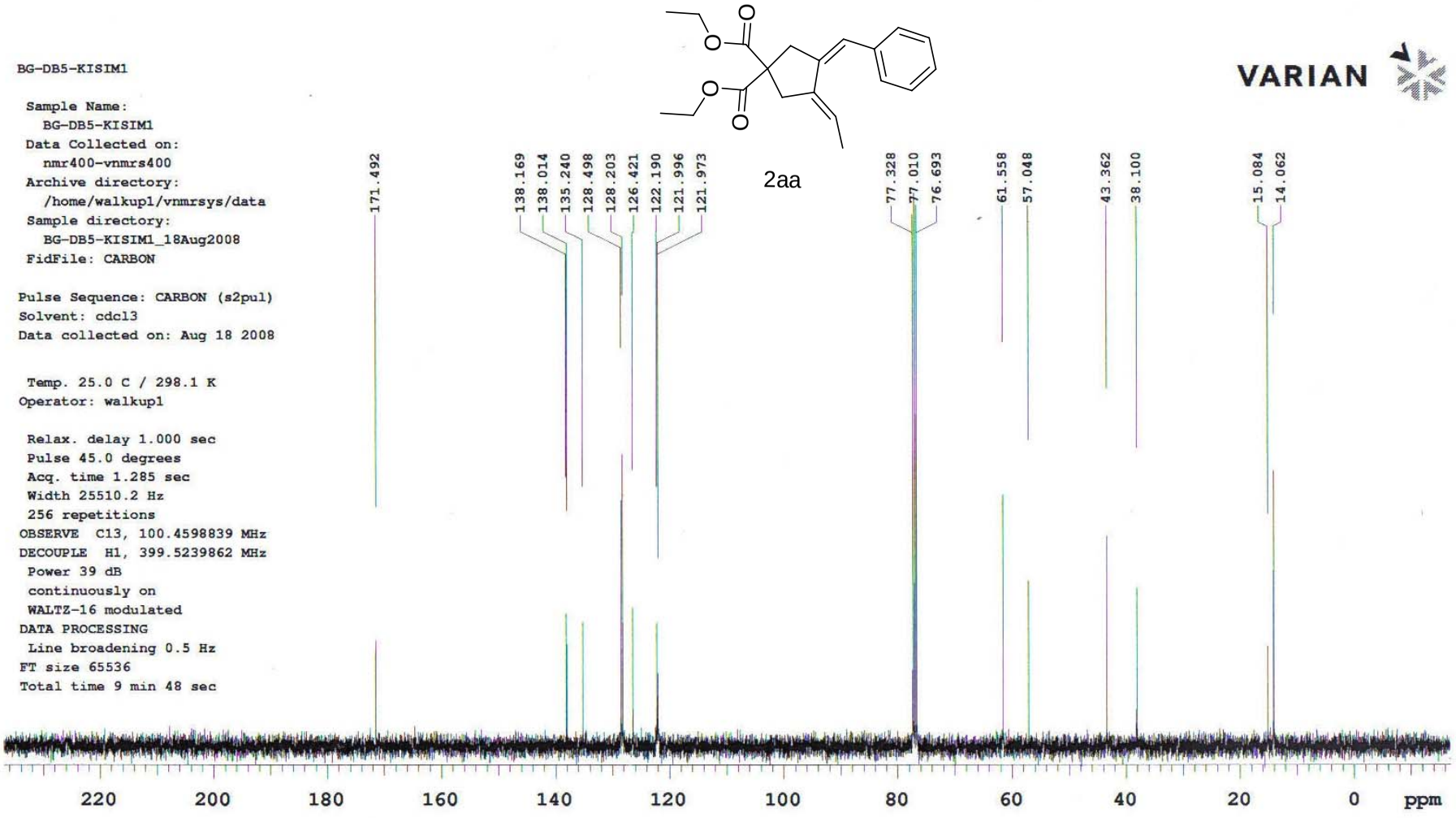

Figure A.3. ^{13}C NMR (3Z,4E)-diethyl 3-benzylidene-4-ethylidenecyclopentane-1,1-dicarboxylate

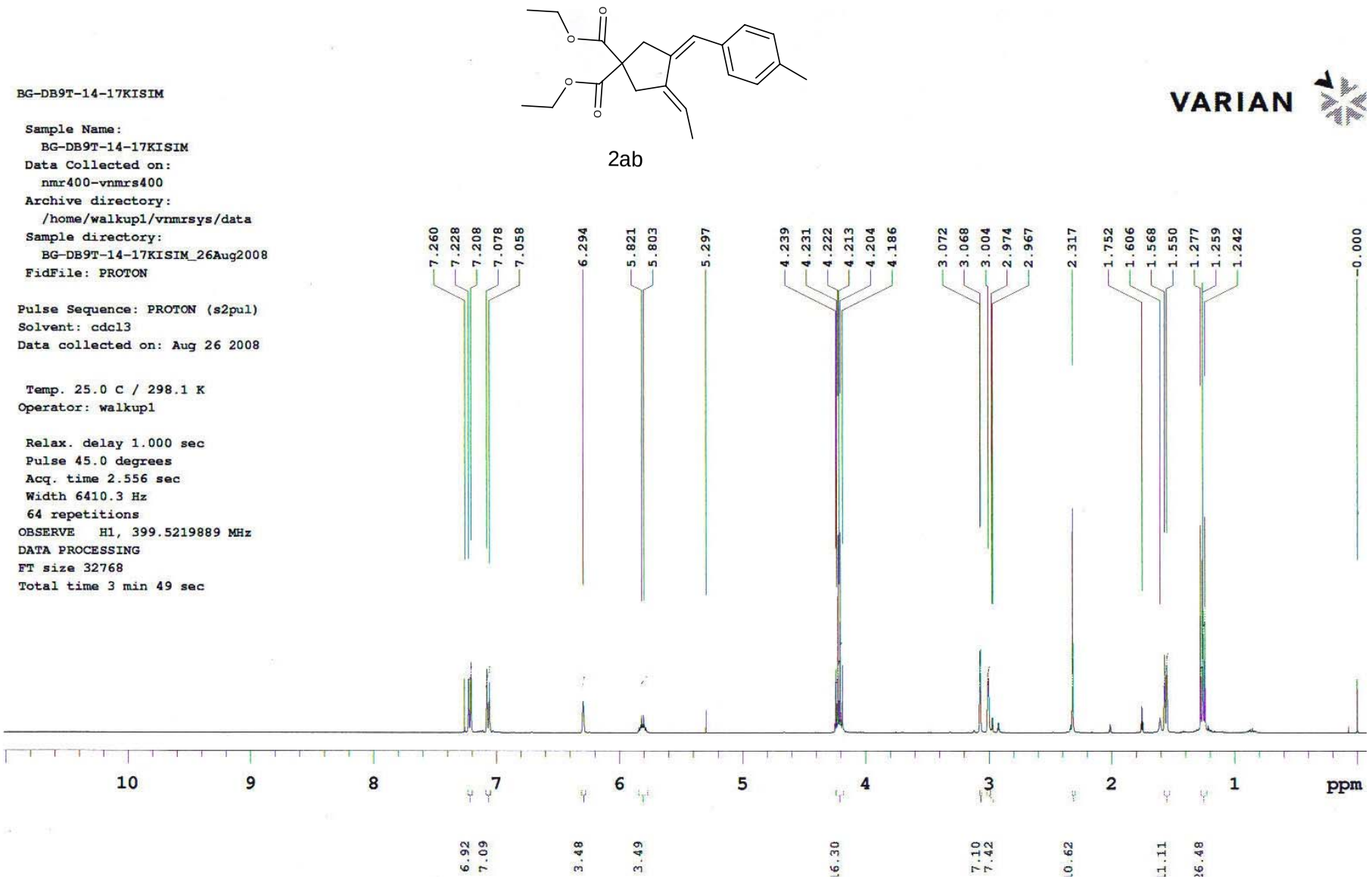

Figure A.4. ^{1}H NMR of (3Z,4E)-diethyl 3-(4-methylbenzylidene)-4-ethylidenecyclopentane-1,1-dicarboxylate

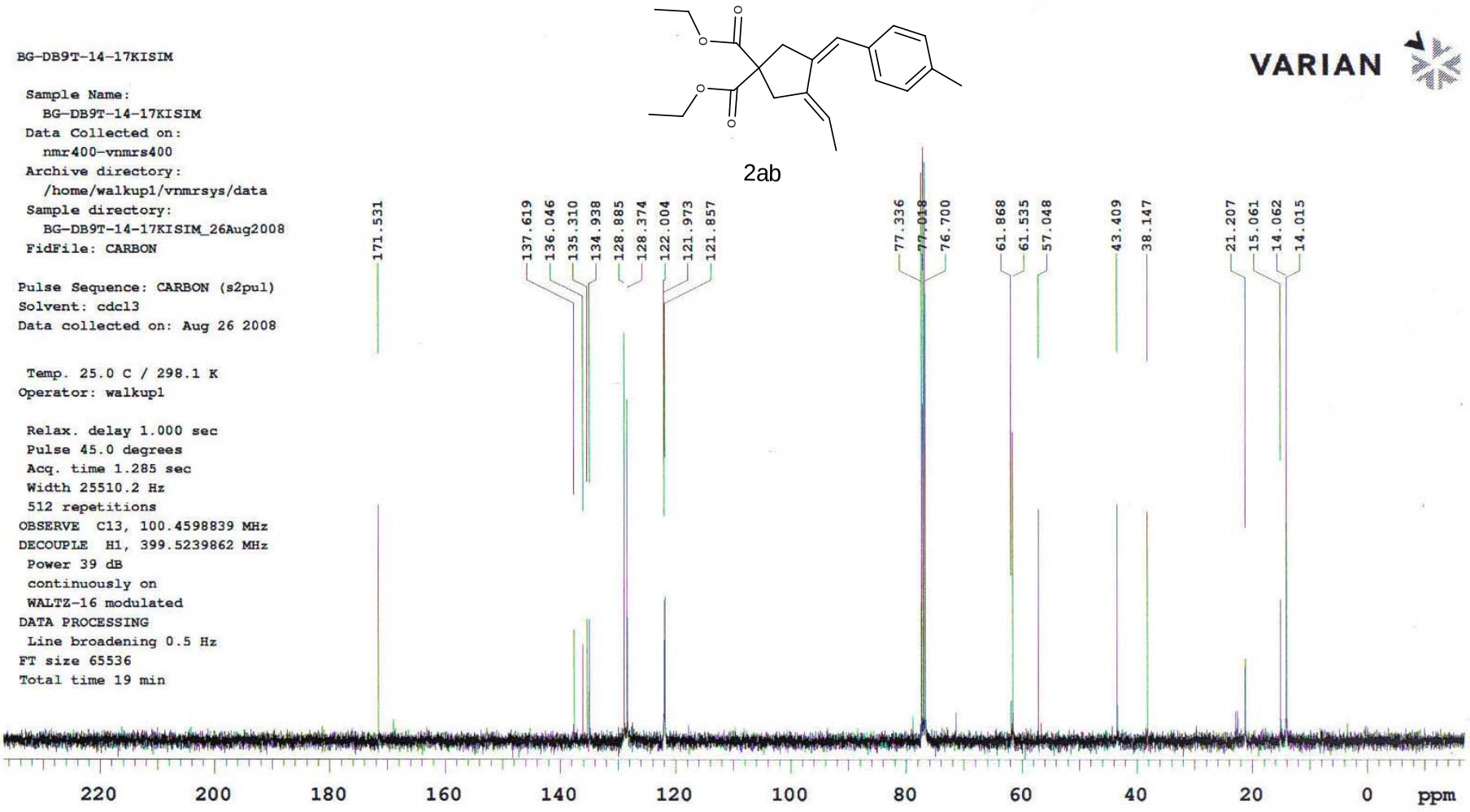

Figure A.5. ^{13}C NMR of (3Z,4E)-diethyl 3-(4-methylbenzylidene)-4-ethylidenecyclopentane-1,1-dicarboxylate

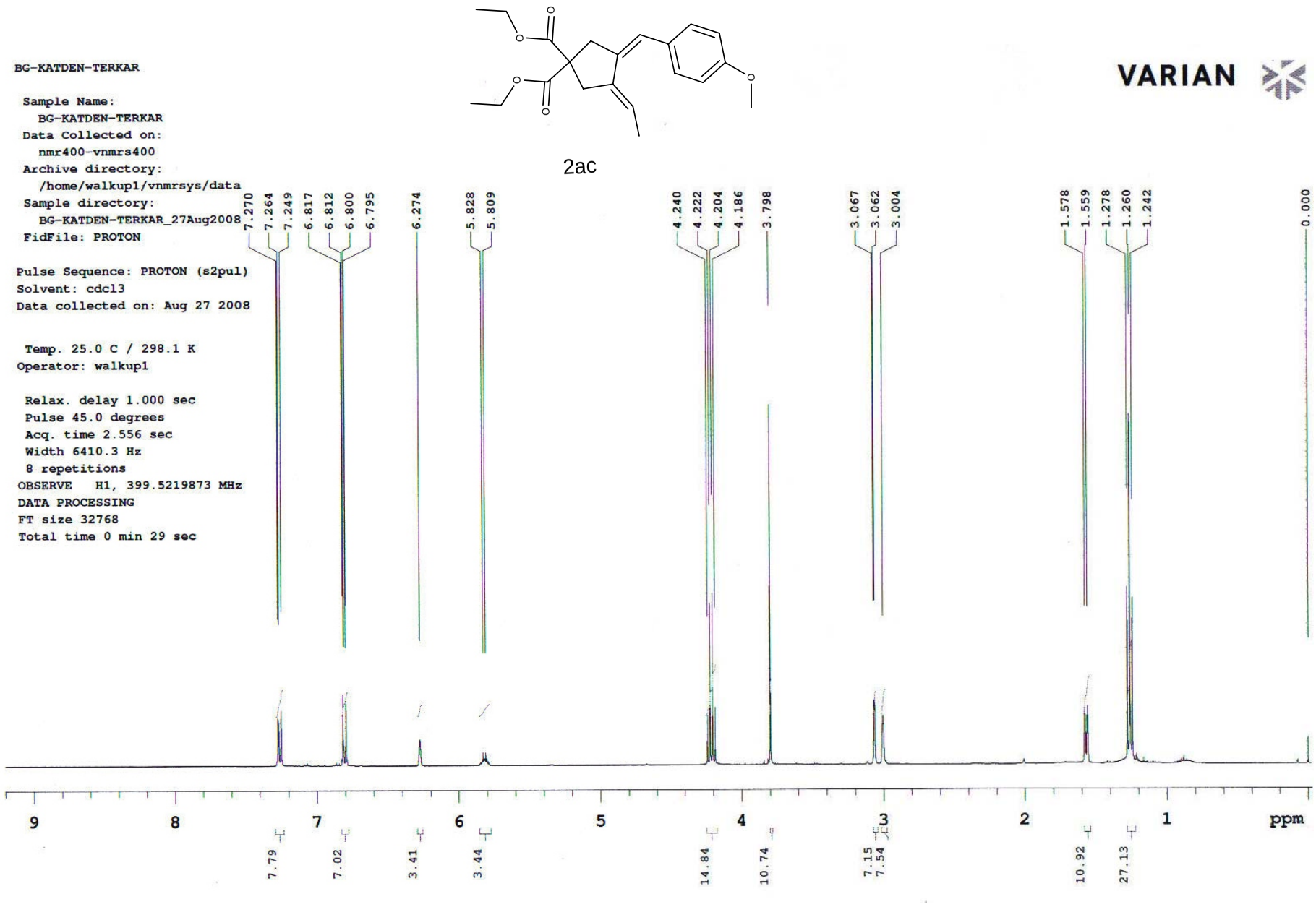

Figure A.6. ^{1}H NMR of (3Z,4E)-diethyl 3-(4-methoxybenzylidene)-4-ethylidenecyclopentane-1,1-dicarboxylate

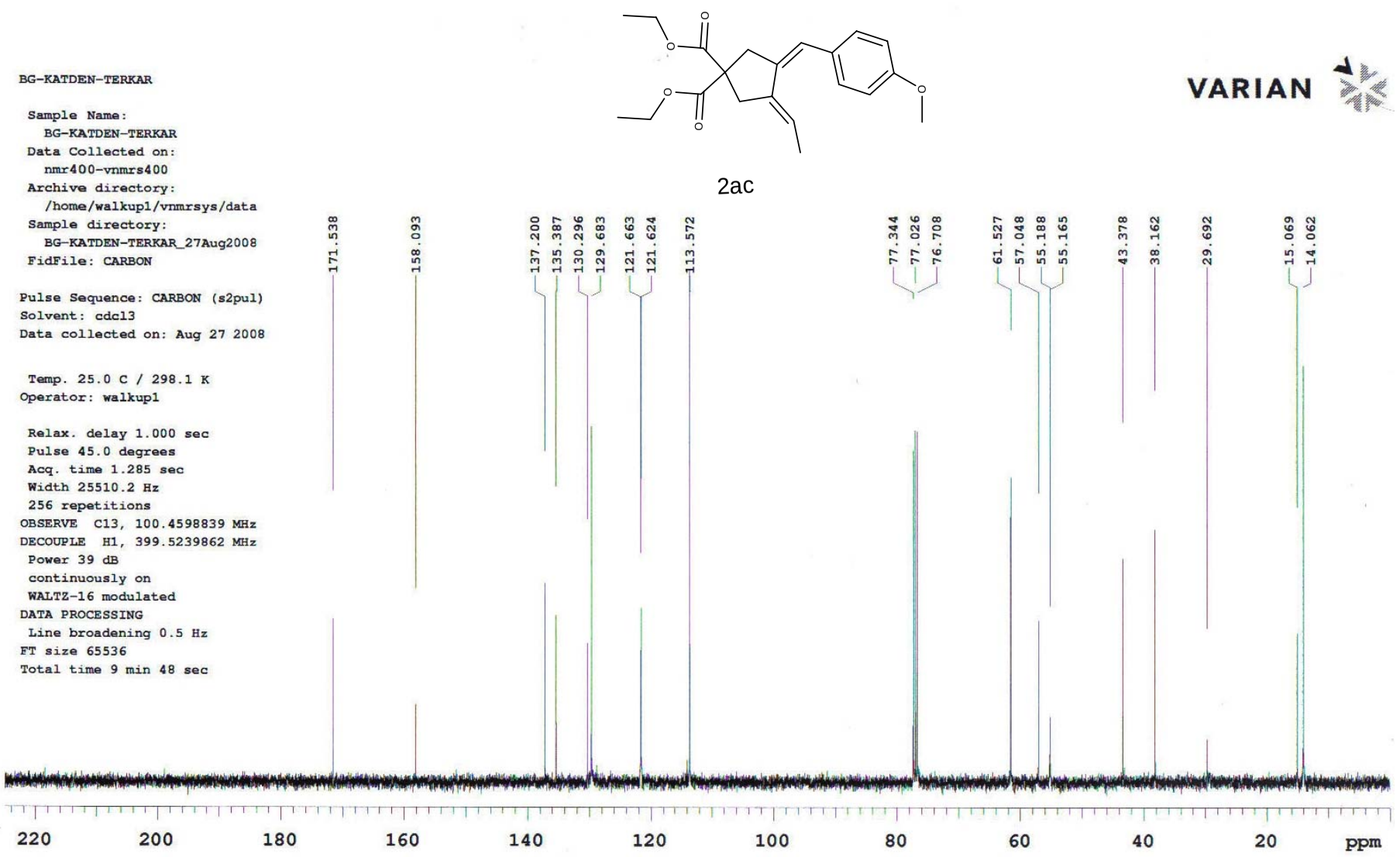

Figure A.7. ^{13}C NMR of (3Z,4E)-diethyl 3-(4-methoxybenzylidene)-4-ethylidenecyclopentane-1,1-dicarboxylate

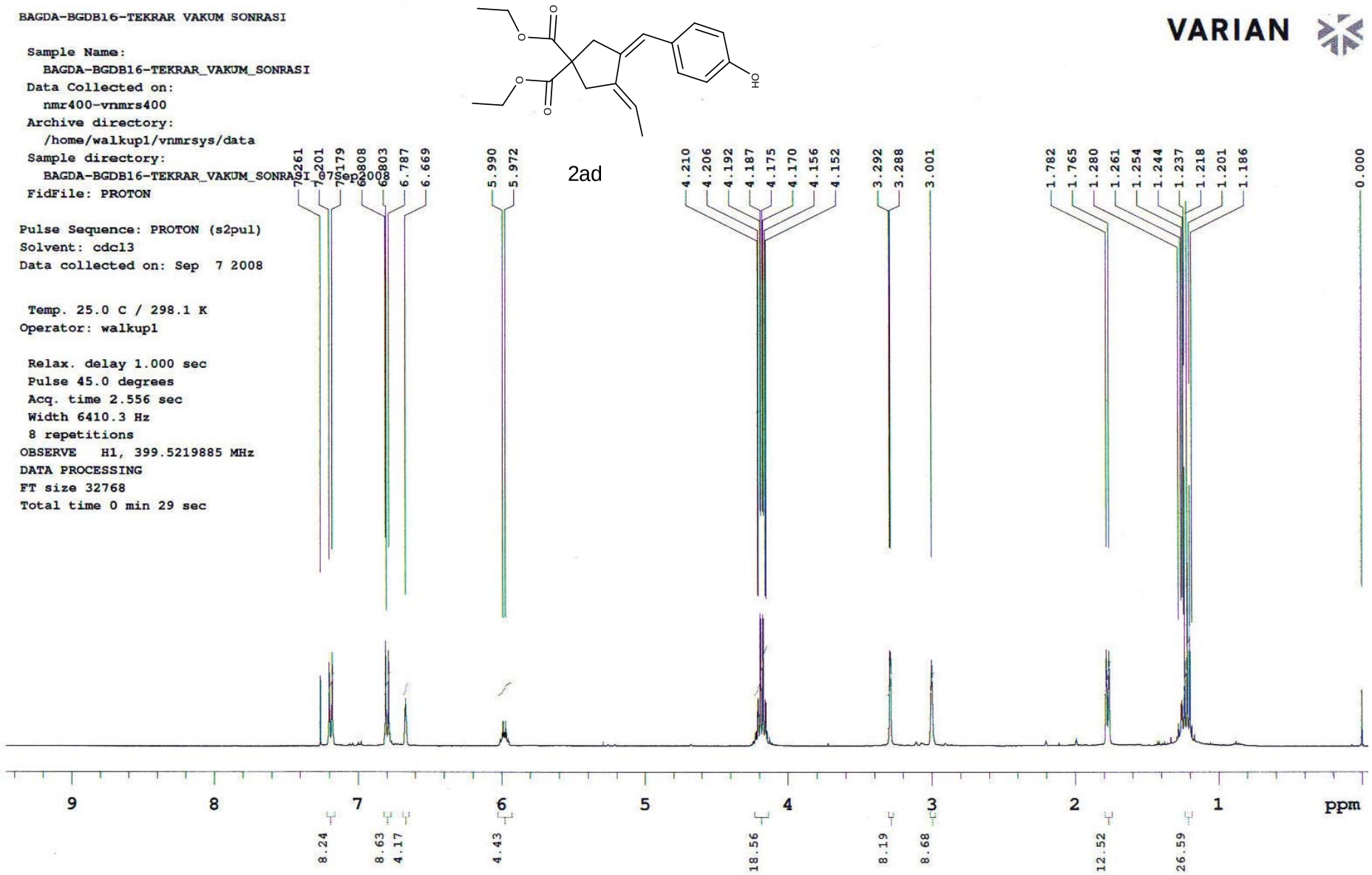

Figure A.8. ^{1}H NMR of (3Z,4E)-diethyl 3-(4-hydroxybenzylidene)-4-ethylidenecyclopentane-1,1-dicarboxylate

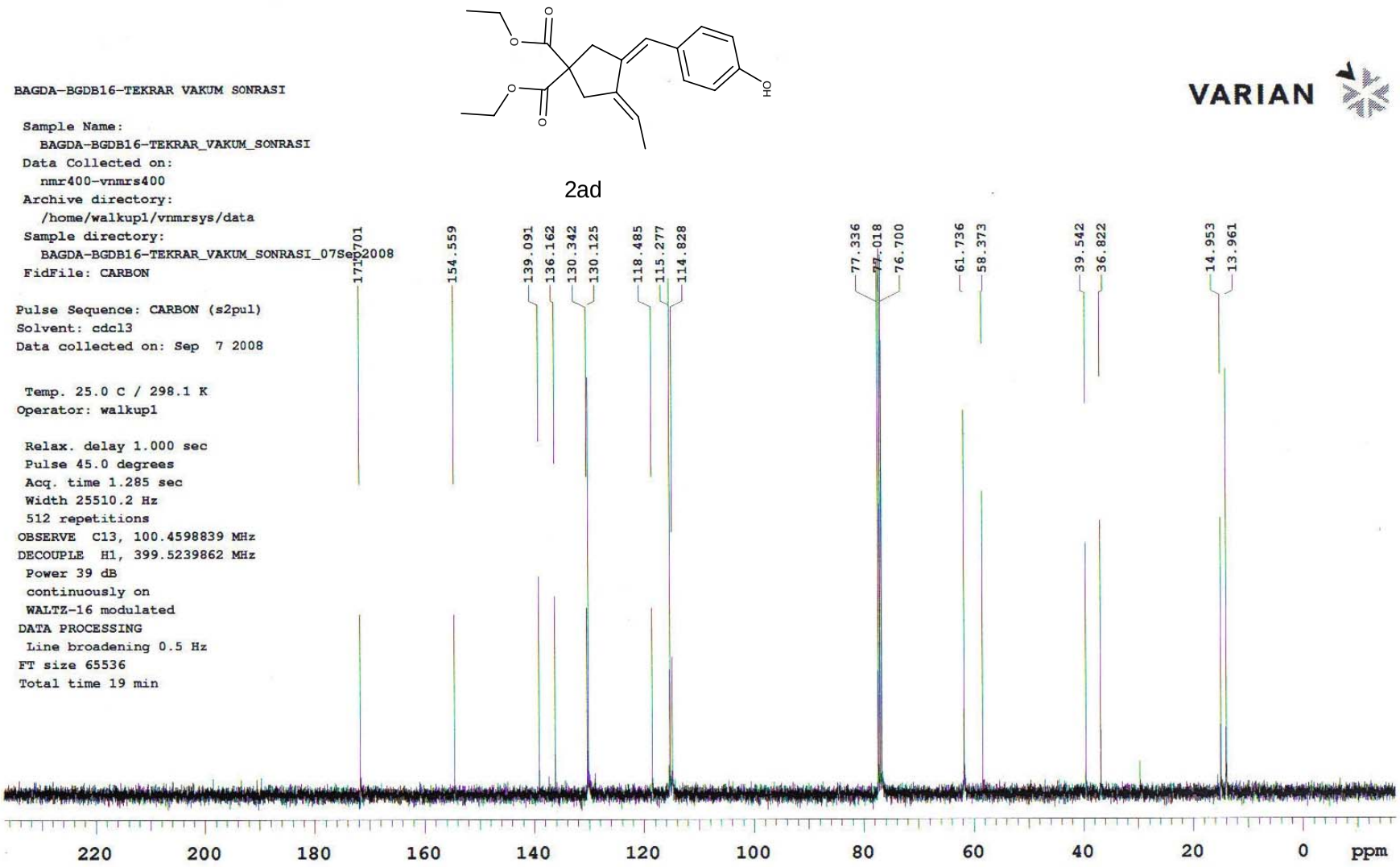

Figure A.9. ^{13}C NMR of (3Z,4E)-diethyl 3-(4-hydroxybenzylidene)-4-ethylidenecyclopentane-1,1-dicarboxylate

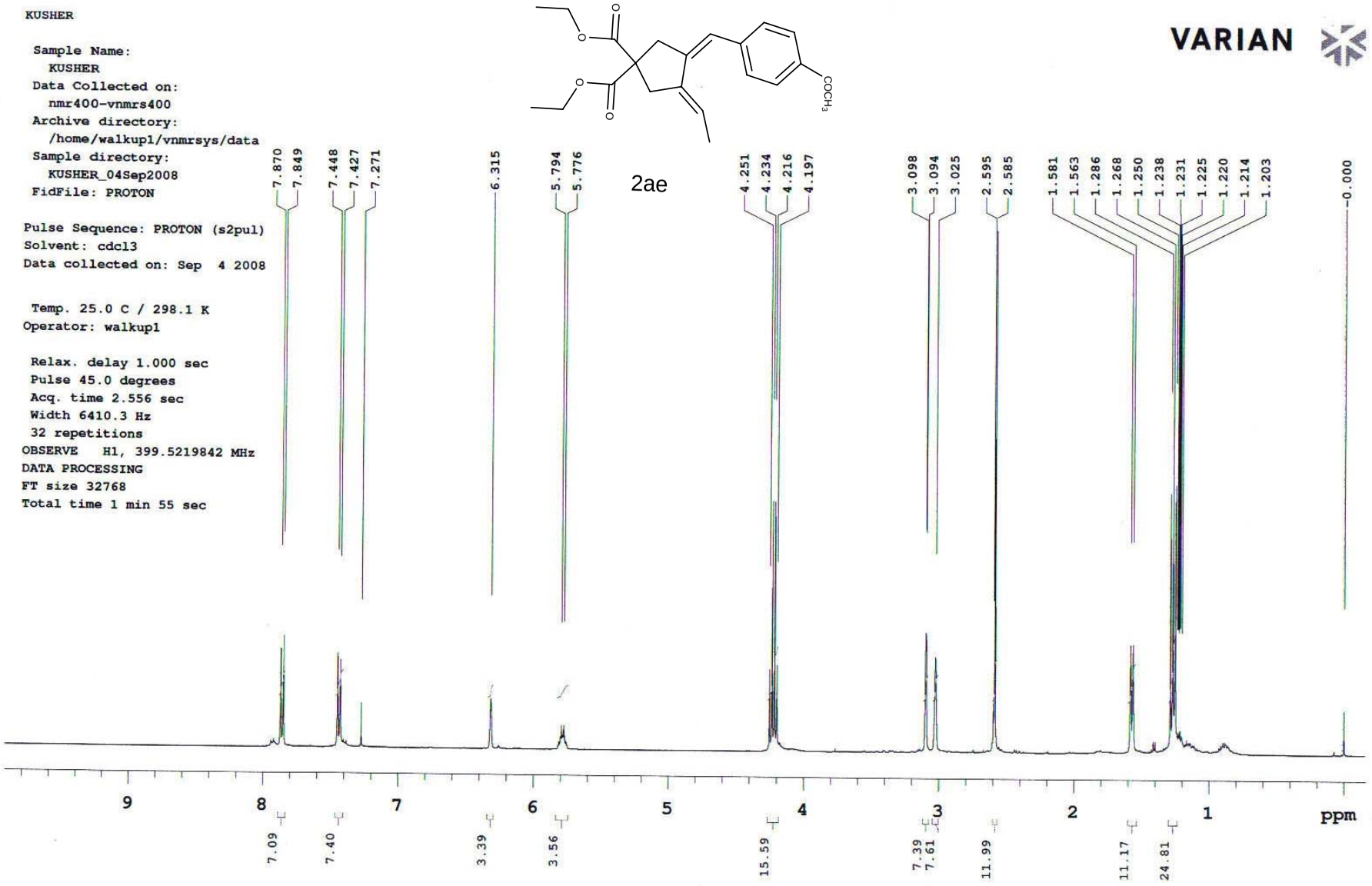

Figure A.10. ^{1}H NMR of (3Z,4E)-diethyl 3-(4-acetylbenzylidene)-4-ethylidenecyclopentane-1,1-dicarboxylate

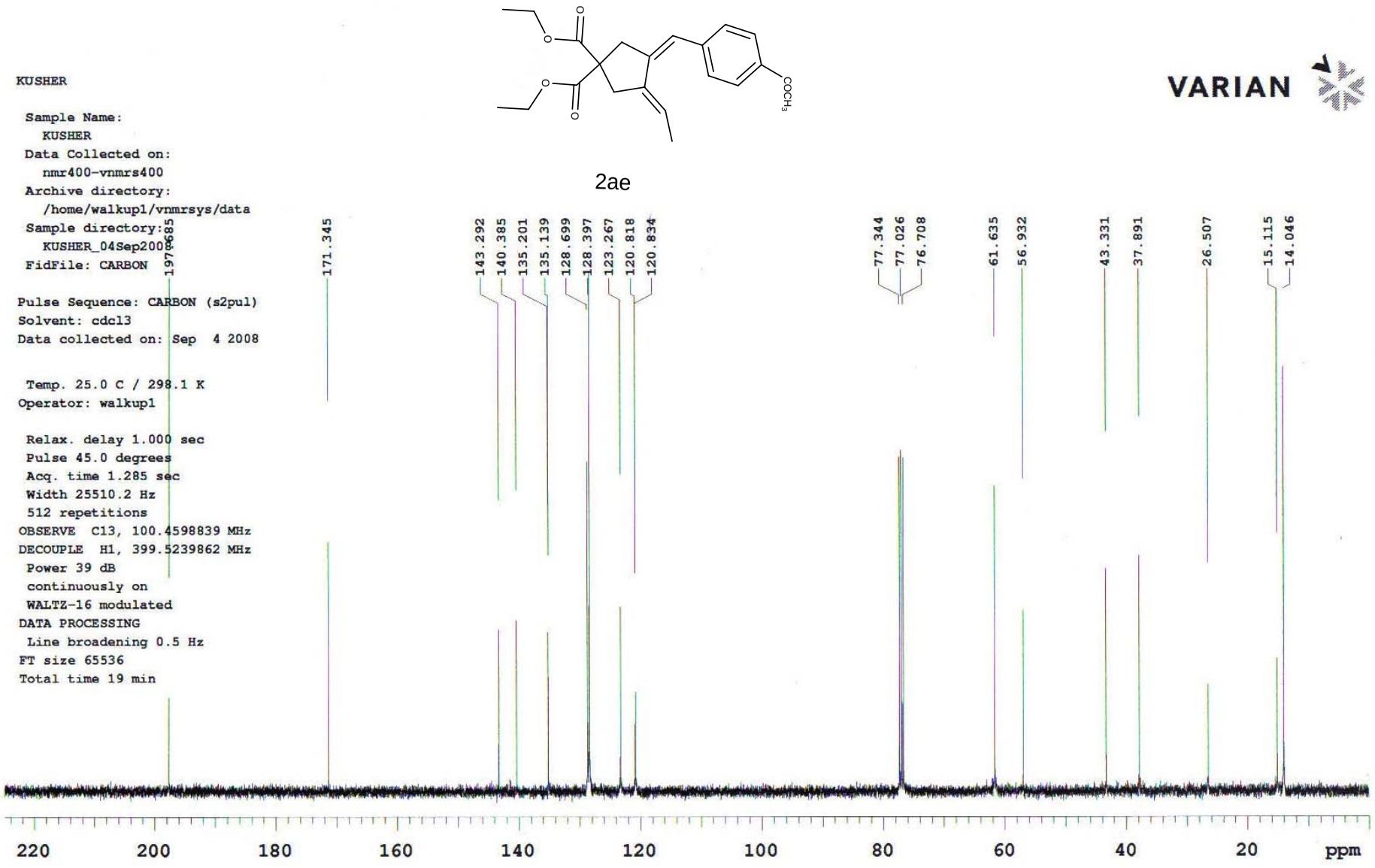

Figure A.11. ^{13}C NMR of (3Z,4E)-diethyl 3-(4-acetylbenzylidene)-4-ethylidenecyclopentane-1,1-dicarboxylate

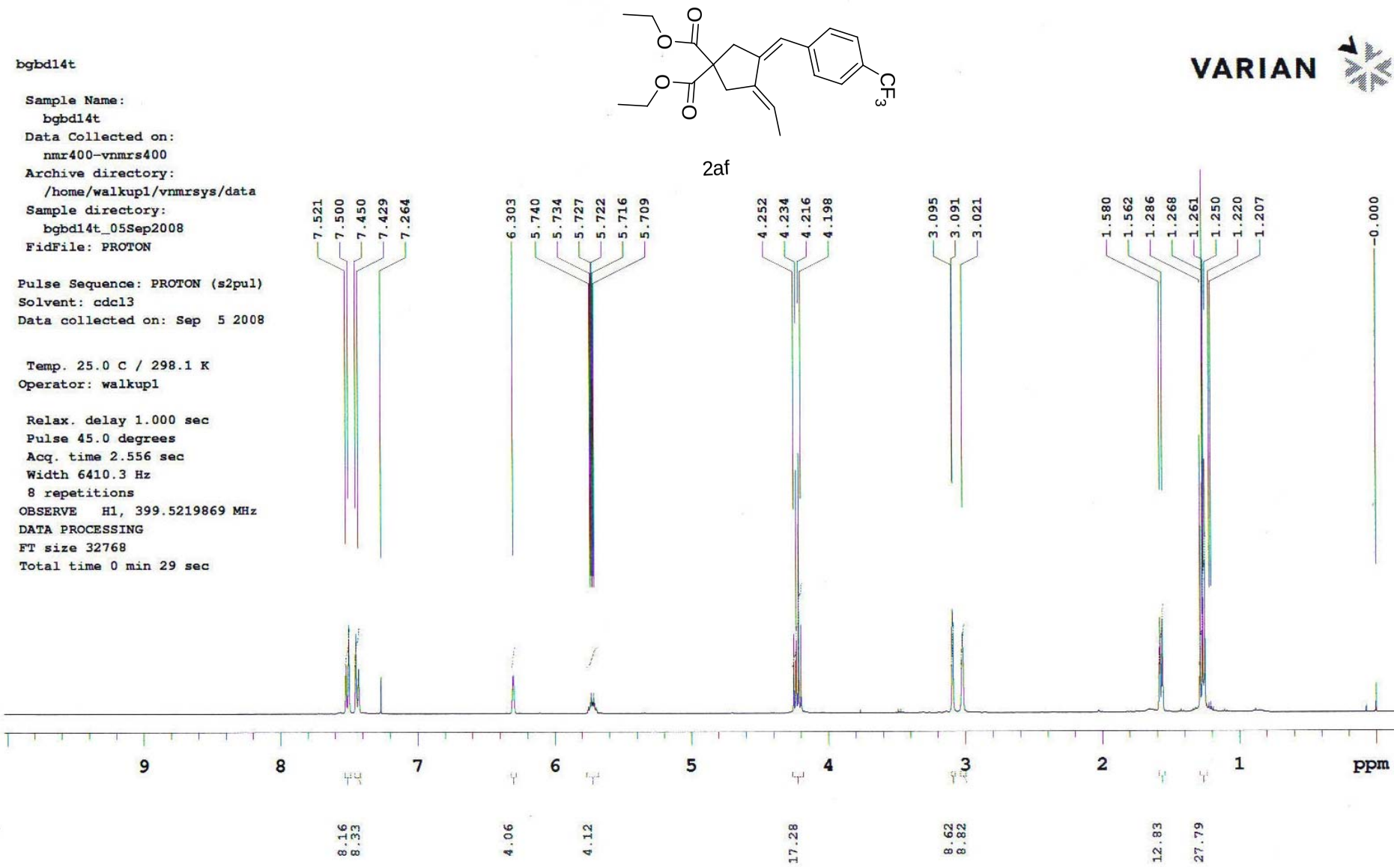

Figure A.12. ^{1}H NMR of (3Z,4E)-diethyl 3-(4-trifluoromethyl)benzylidene)-4-ethylidenecyclopentane-1,1-dicarboxylate

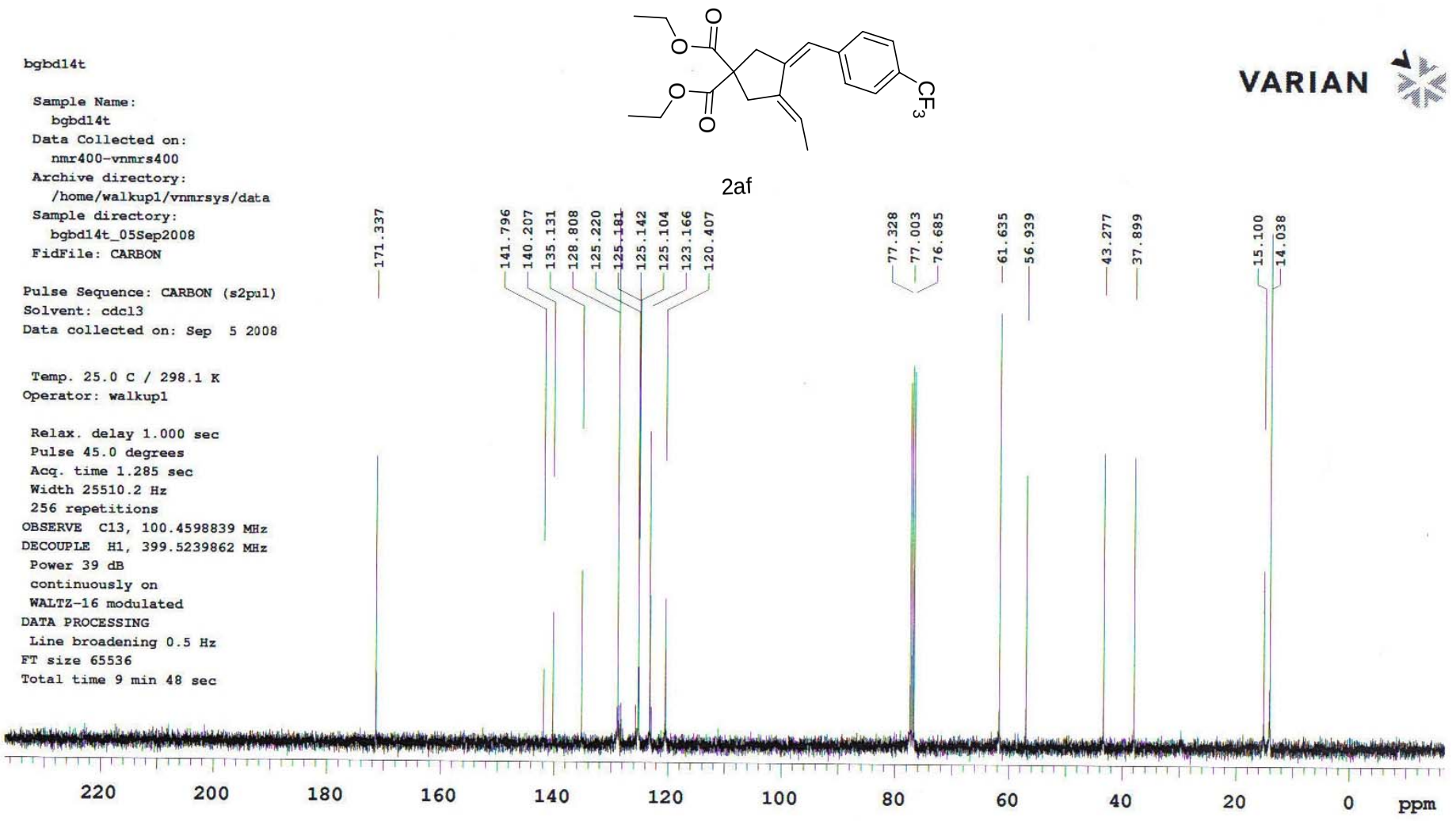

Figure A.13. ^{13}C NMR of (3Z,4E)-diethyl 3-(4-trifluoromethyl)benzylidene)-4-ethylidenecyclopentane-1,1-dicarboxylate

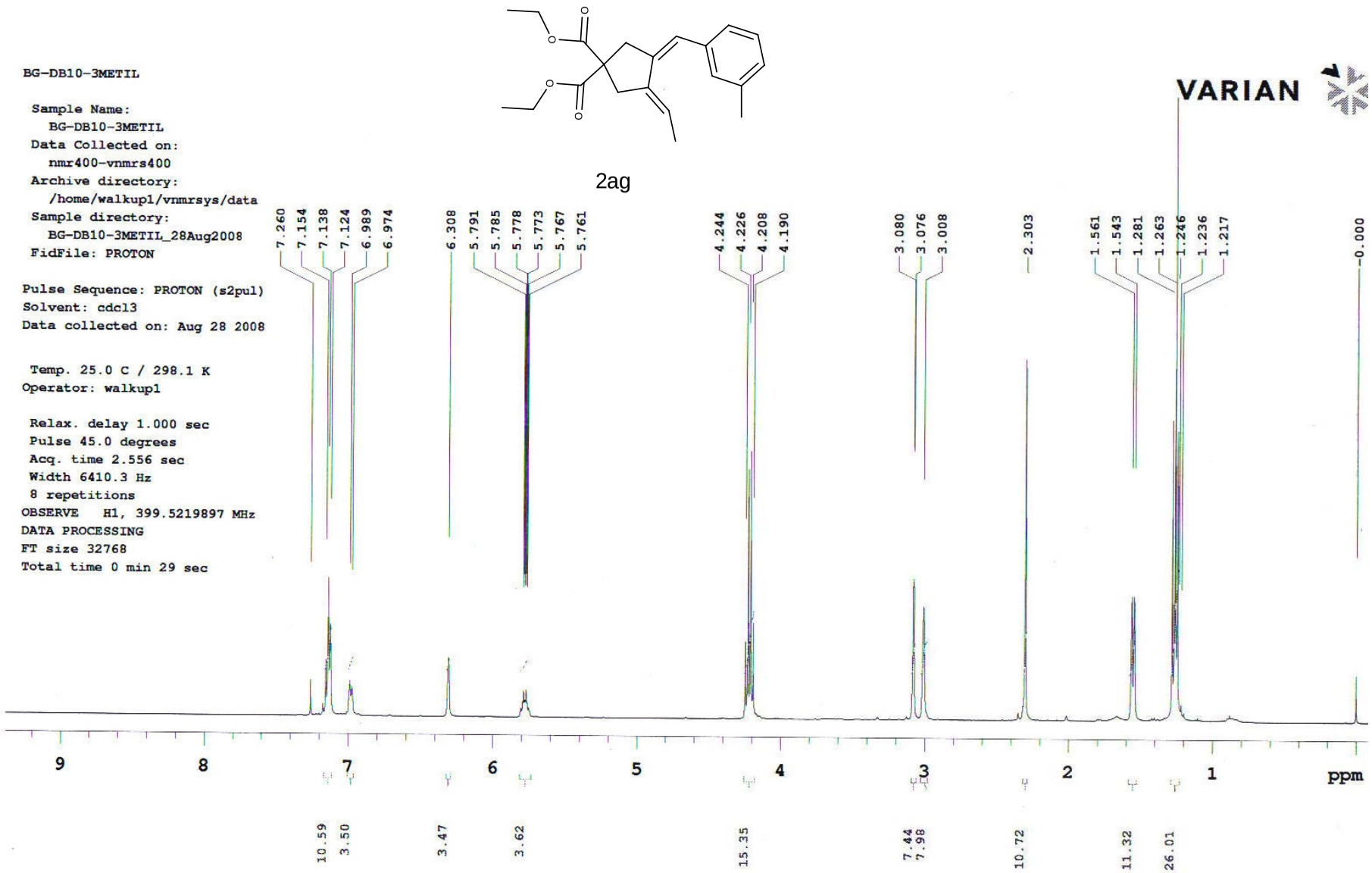

Figure A.14. ^{1}H NMR of (3Z,4E)-diethyl 3-(3-methylbenzylidene)-4-ethylidenecyclopentane-1,1-dicarboxylate

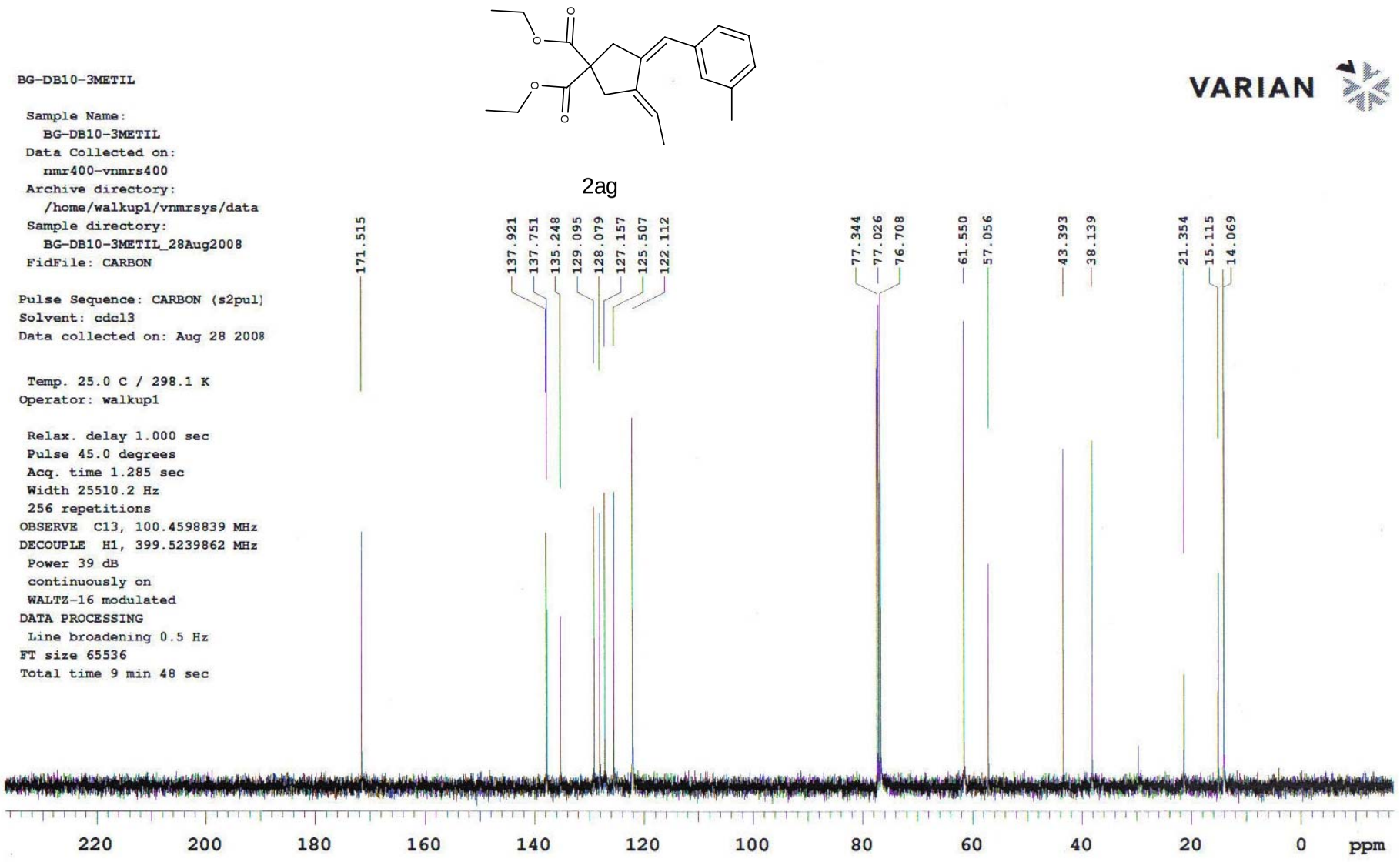

Figure A.15. ^{13}C NMR of (3Z,4E)-diethyl 3-(3-methylbenzylidene)-4-ethylidenecyclopentane-1,1-dicarboxylate

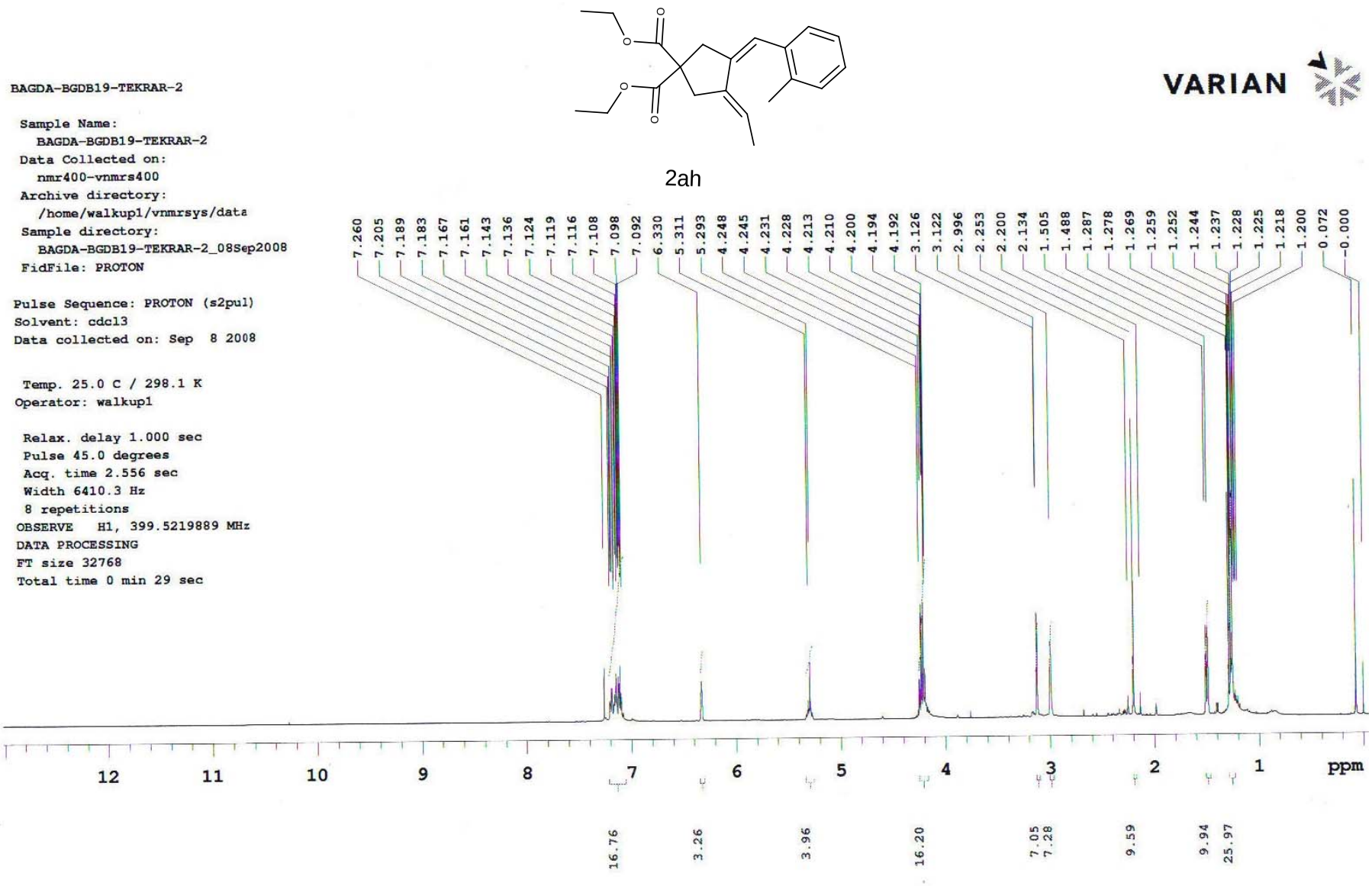

Figure A.16. ^{1}H NMR of (3Z,4E)-diethyl 3-(2-methylbenzylidene)-4-ethylidenecyclopentane-1,1-dicarboxylate

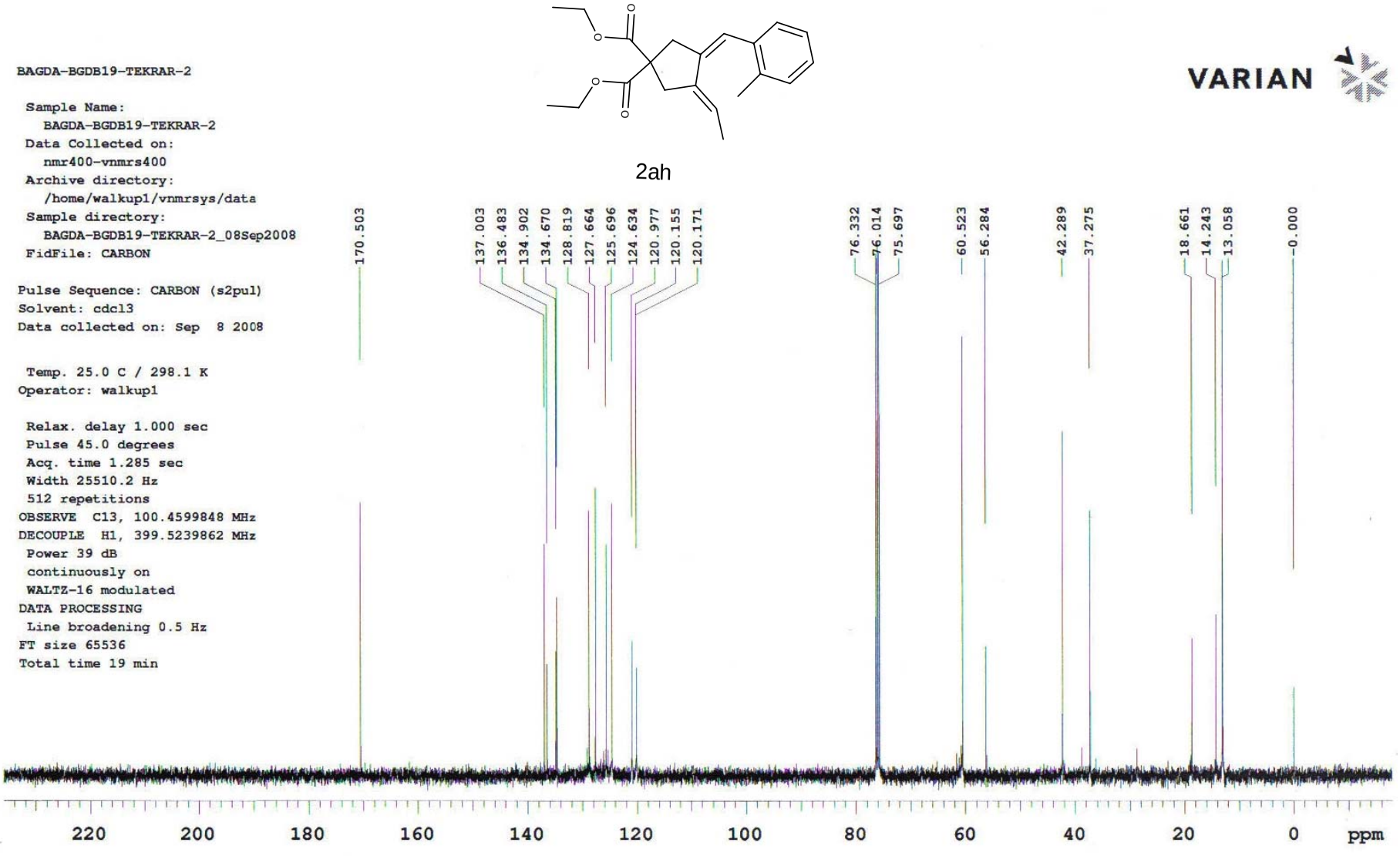

Figure A.17. ^{13}C NMR of (3Z,4E)-diethyl 3-(2-methylbenzylidene)-4-ethylidenecyclopentane-1,1-dicarboxylate

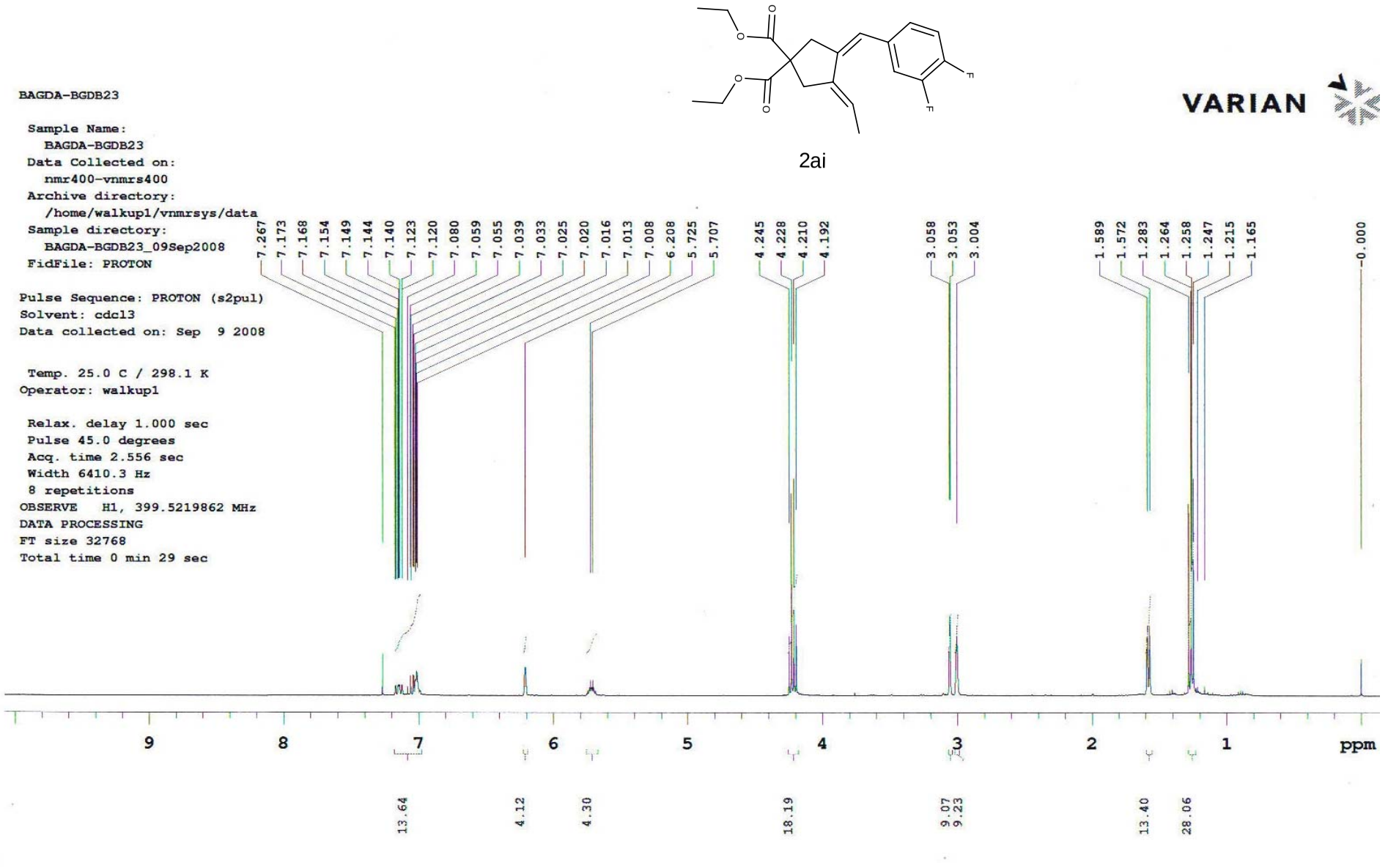

Figure A.18. ^{1}H NMR of (3Z,4E)-diethyl 3-(3,4-difluorobenzylidene)-4-ethylidenecyclopentane-1,1-dicarboxylate

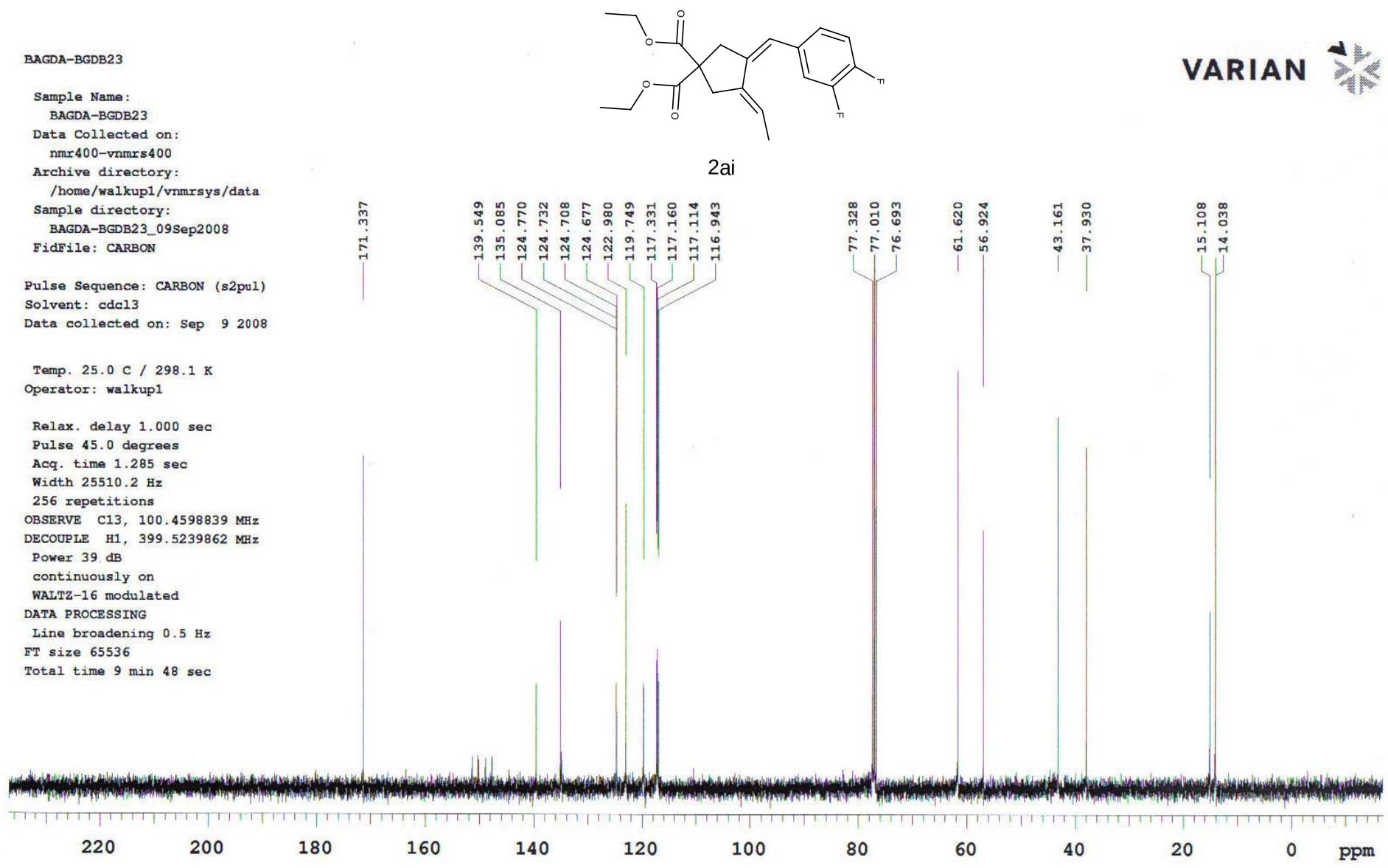

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Figure A.19. ^{13}C NMR of (3Z,4E)-diethyl 3-(3,4-difluorobenzylidene)-4-ethylidenecyclopentane-1,1-dicarboxylate

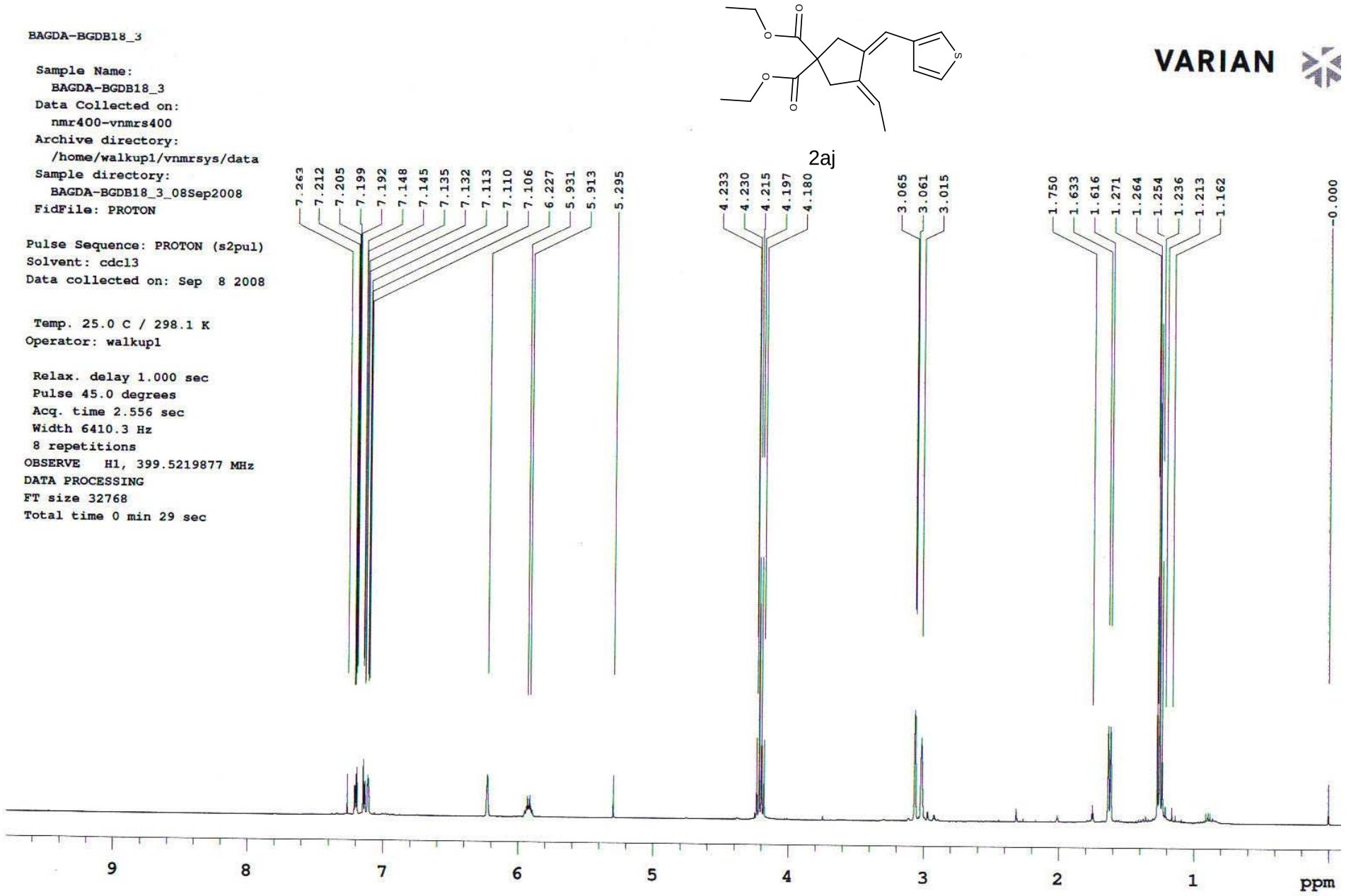

Figure A.20. ^{1}H NMR of (3E,4Z)-diethyl 3-ethylidene-4-((thiophen-3-yl)methylene)cyclopentane-1,1-dicarboxylate

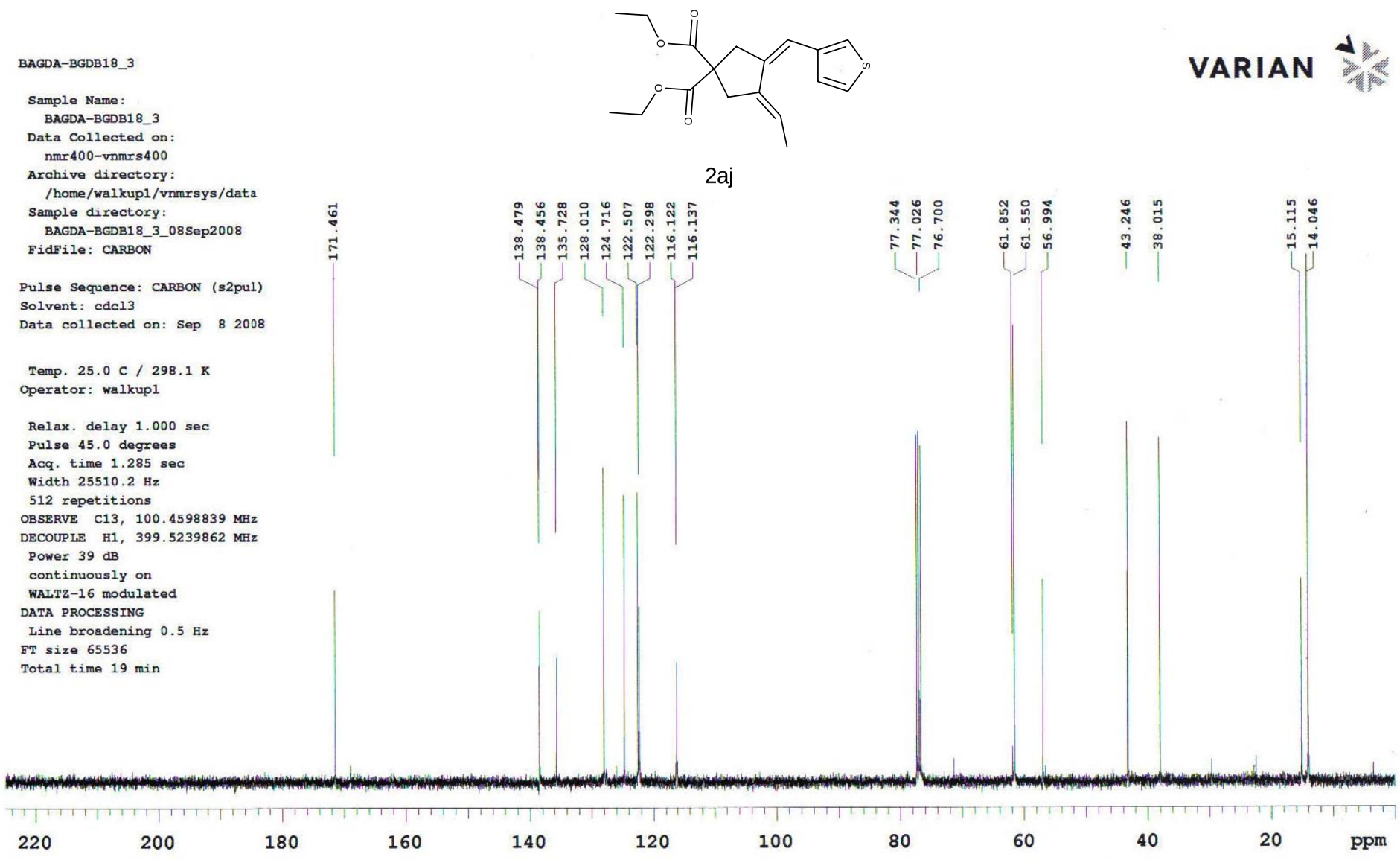

Figure A.21. ^{13}C NMR of (3E,4Z)-diethyl 3-ethylidene-4-((thiophen-3-yl)methylene)cyclopentane-1,1-dicarboxylate

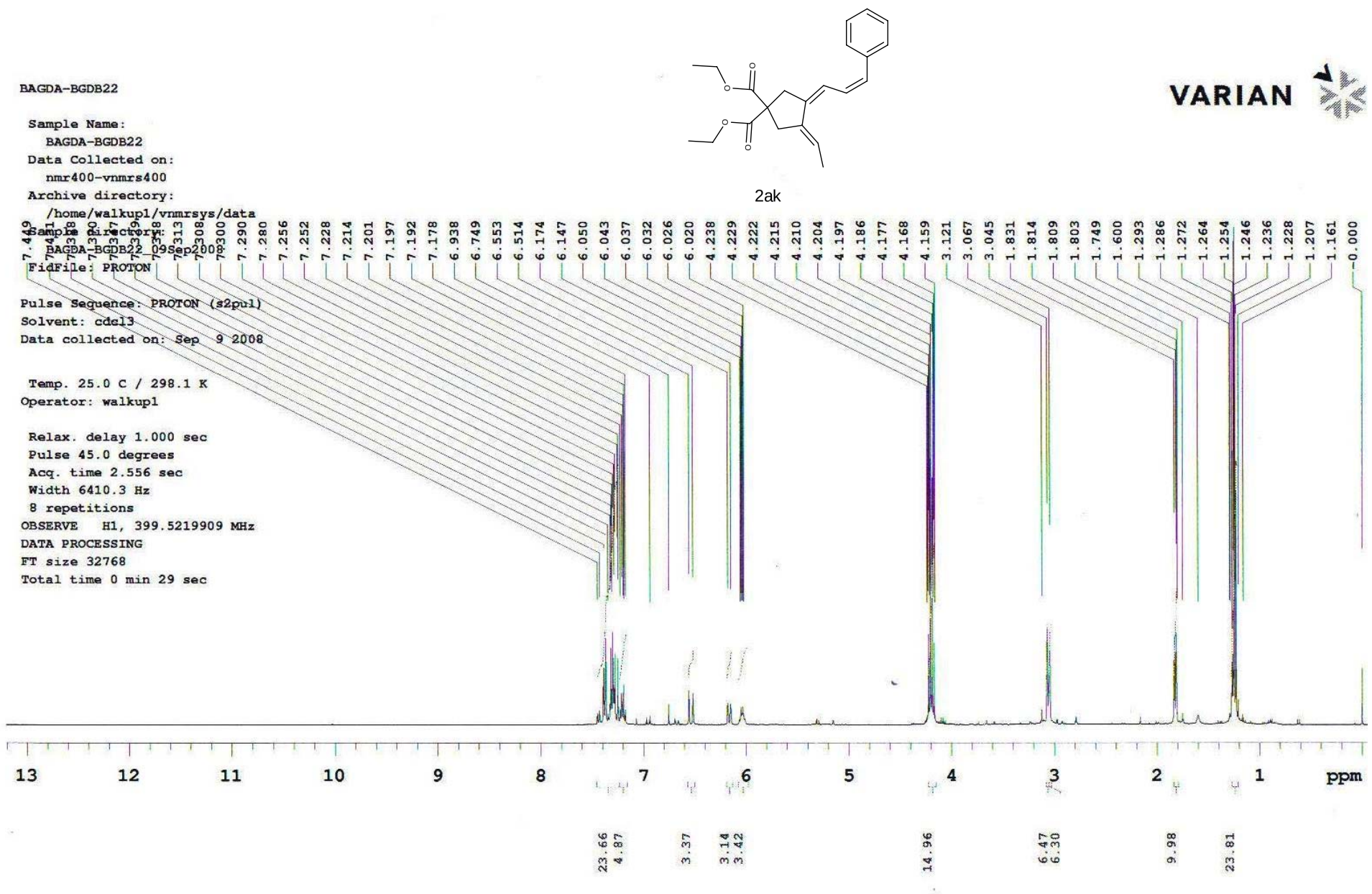

Figure A.22. ^{1}H NMR of (3E,4Z)-diethyl 3-ethylidene-4-((Z)-3-phenylallylidene)cyclopentane-1,1-dicarboxylate

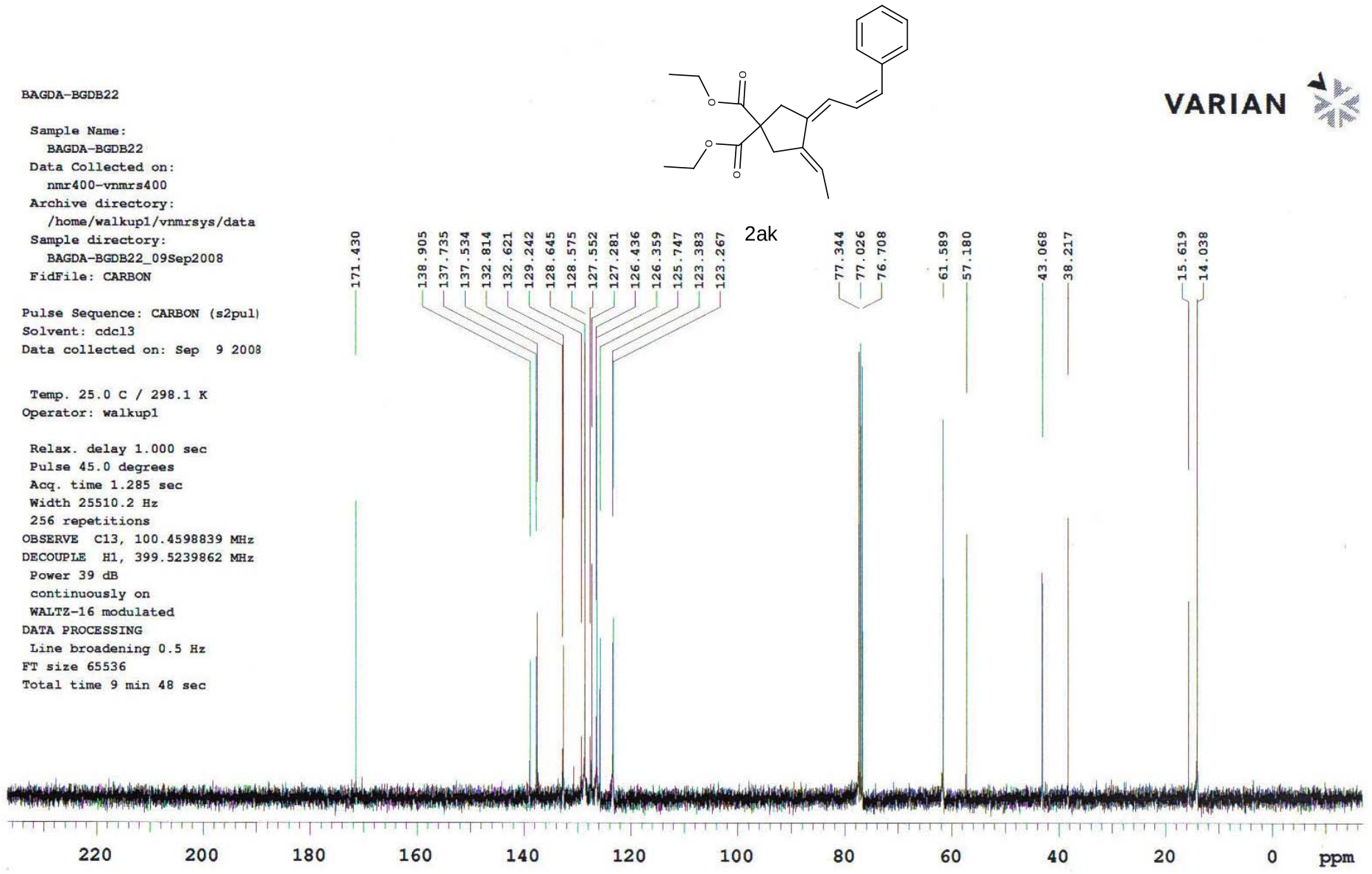

Figure A.23. ^{13}C NMR of (3E,4Z)-diethyl 3-ethylidene-4-((Z)-3-phenylallylidene)cyclopentane-1,1-dicarboxylate

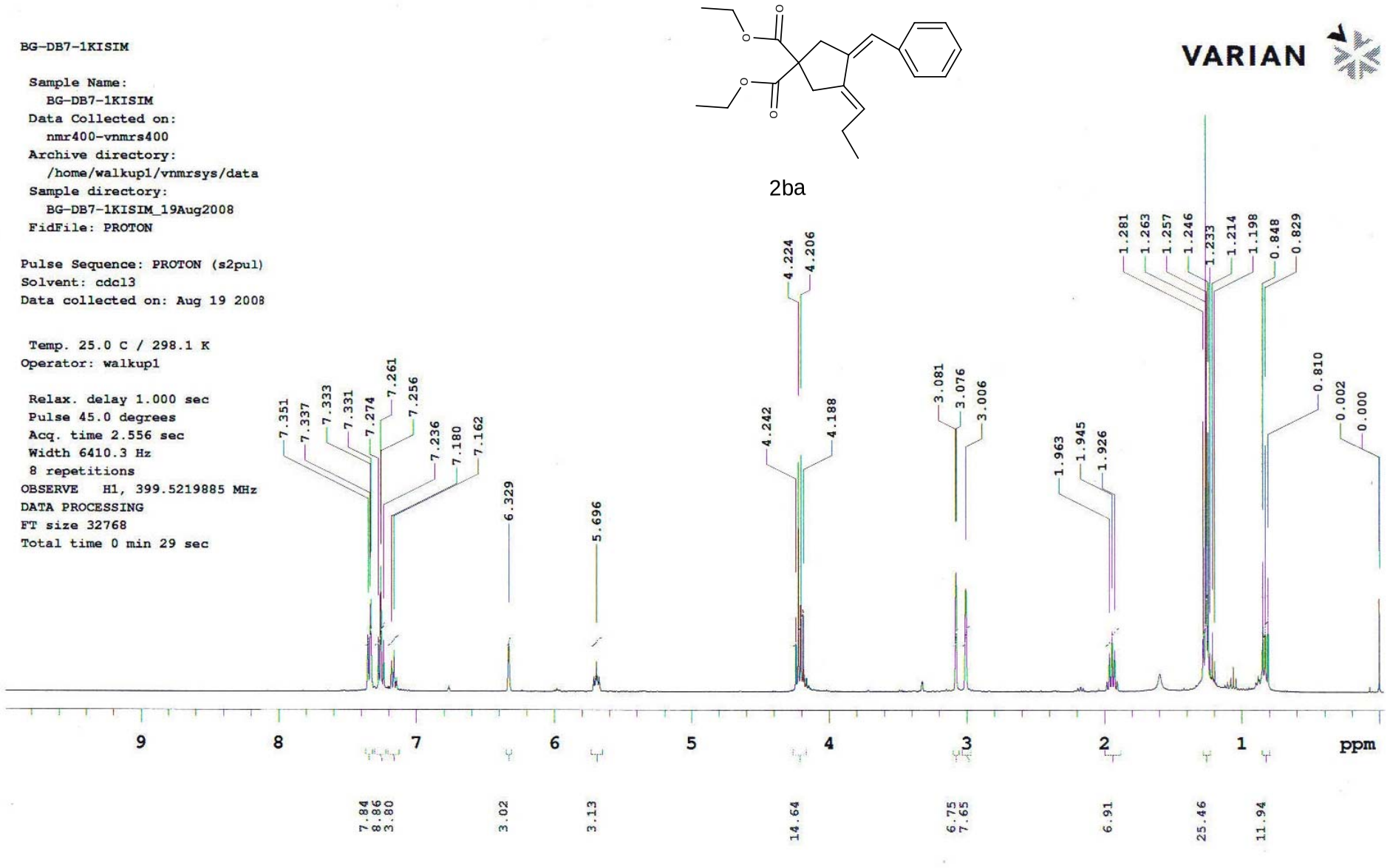

Figure A.24. ^{1}H NMR of (3Z,4E)-diethyl 3-benzylidene-4-propylidenecyclopentane-1,1-dicarboxylate

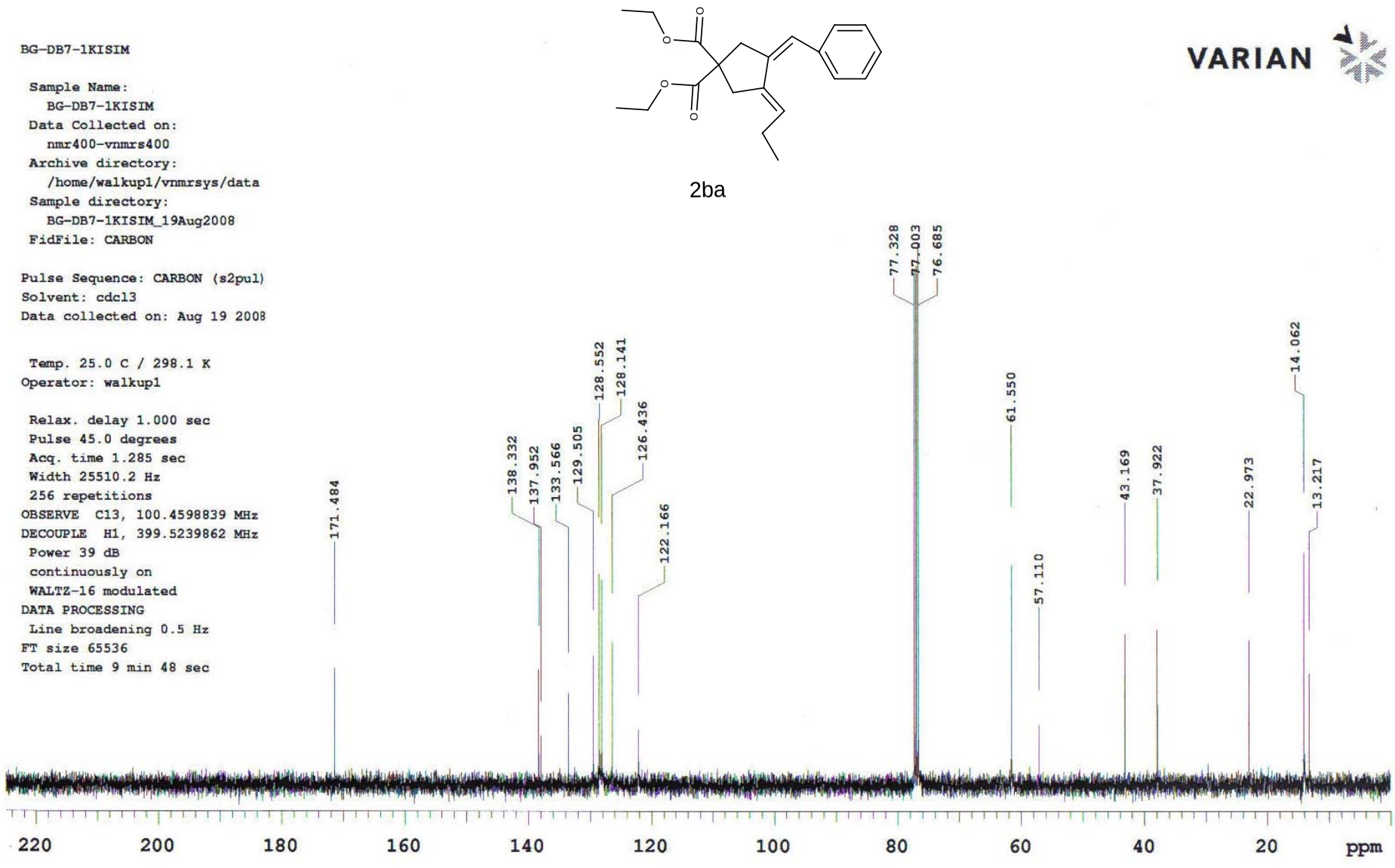

Figure A.25. ^{13}C NMR of (3Z,4E)-diethyl 3-benzylidene-4-propylidenecyclopentane-1,1-dicarboxylate

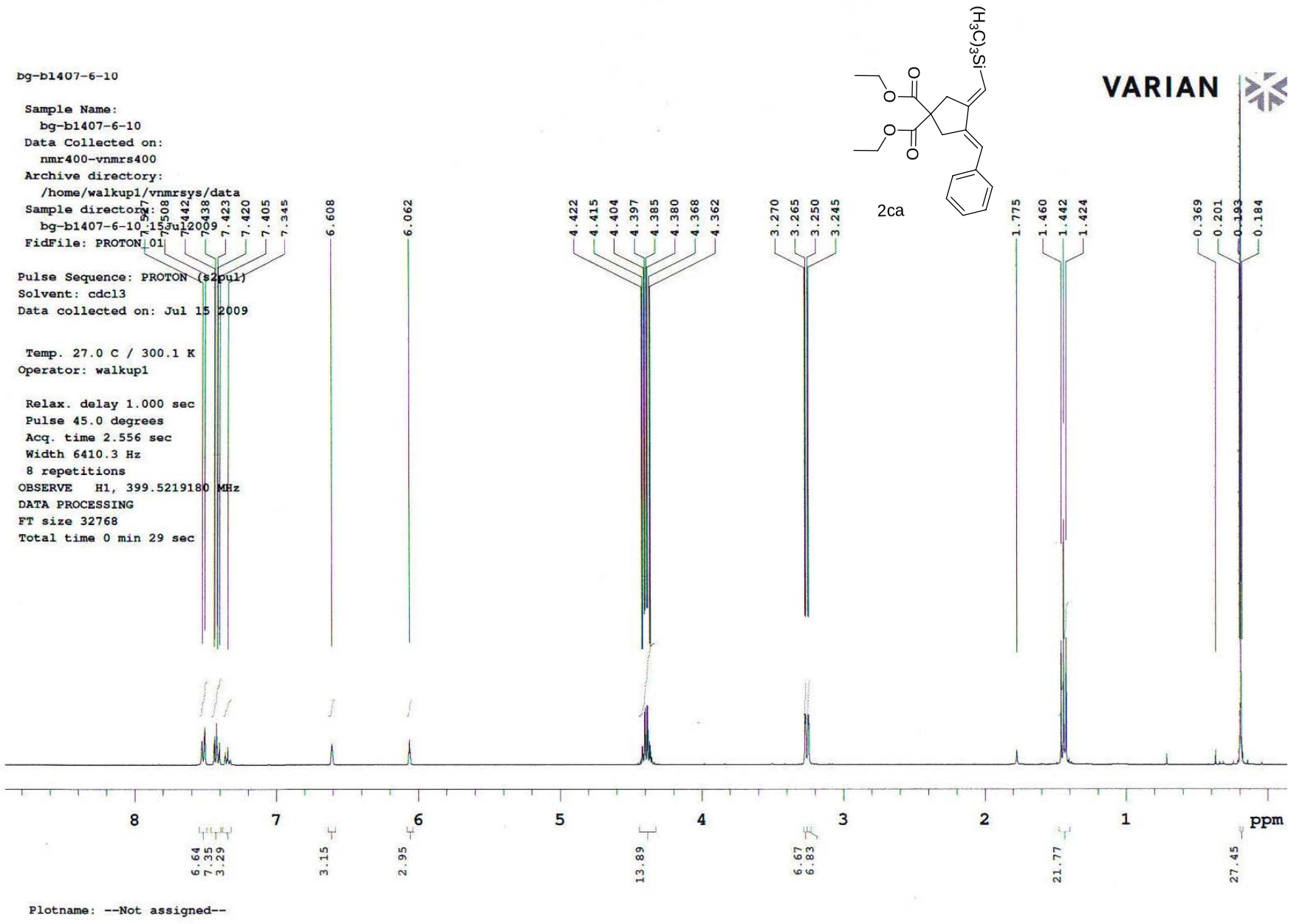

Figure A.26. ^{1}H NMR of (3E,4E)-diethyl 3-benzylidene-4-((trimethylsilyl)methylene)cyclopentane-1,1-dicarboxylate

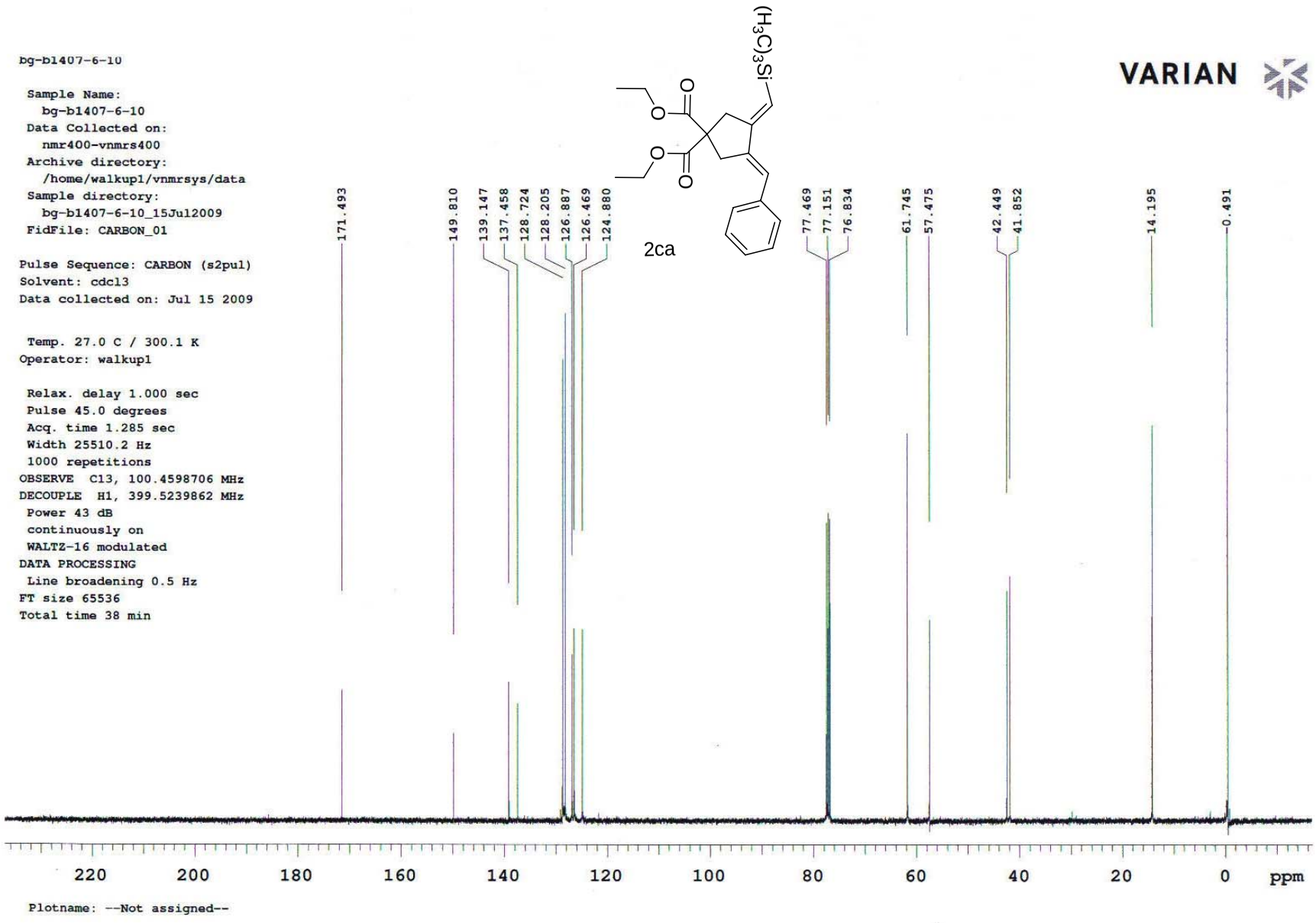

Figure A.27. ^{13}C NMR of (3E,4E)-diethyl 3-benzylidene-4-((trimethylsilyl)methylene)cyclopentane-1,1-dicarboxylate

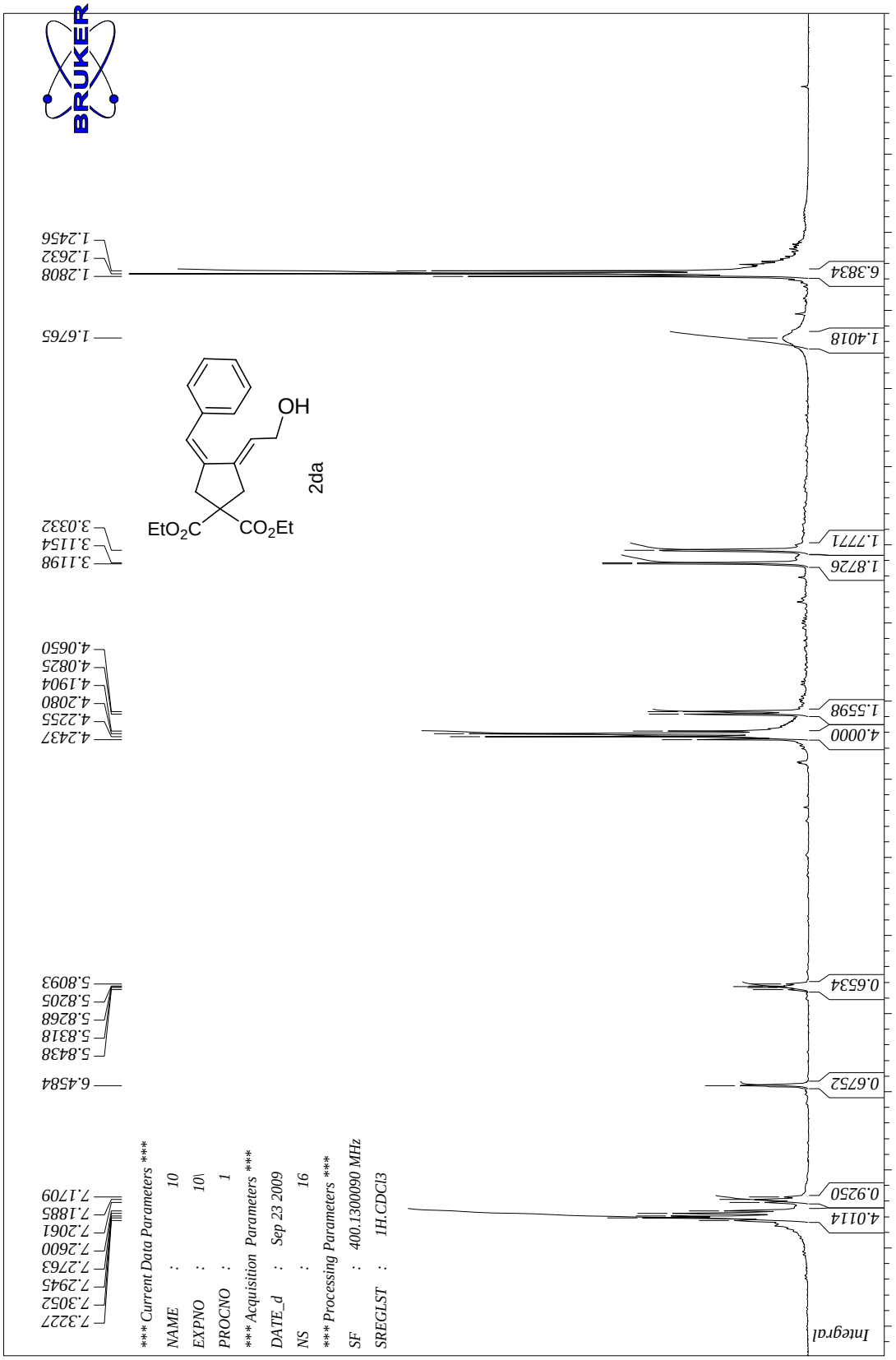

Figure A.28. ^{1}H NMR of (3Z,4E)-diethyl 3-benzylidene-4-(2-hydroxyethylidene)cyclopentane-1,1-dicarboxylate

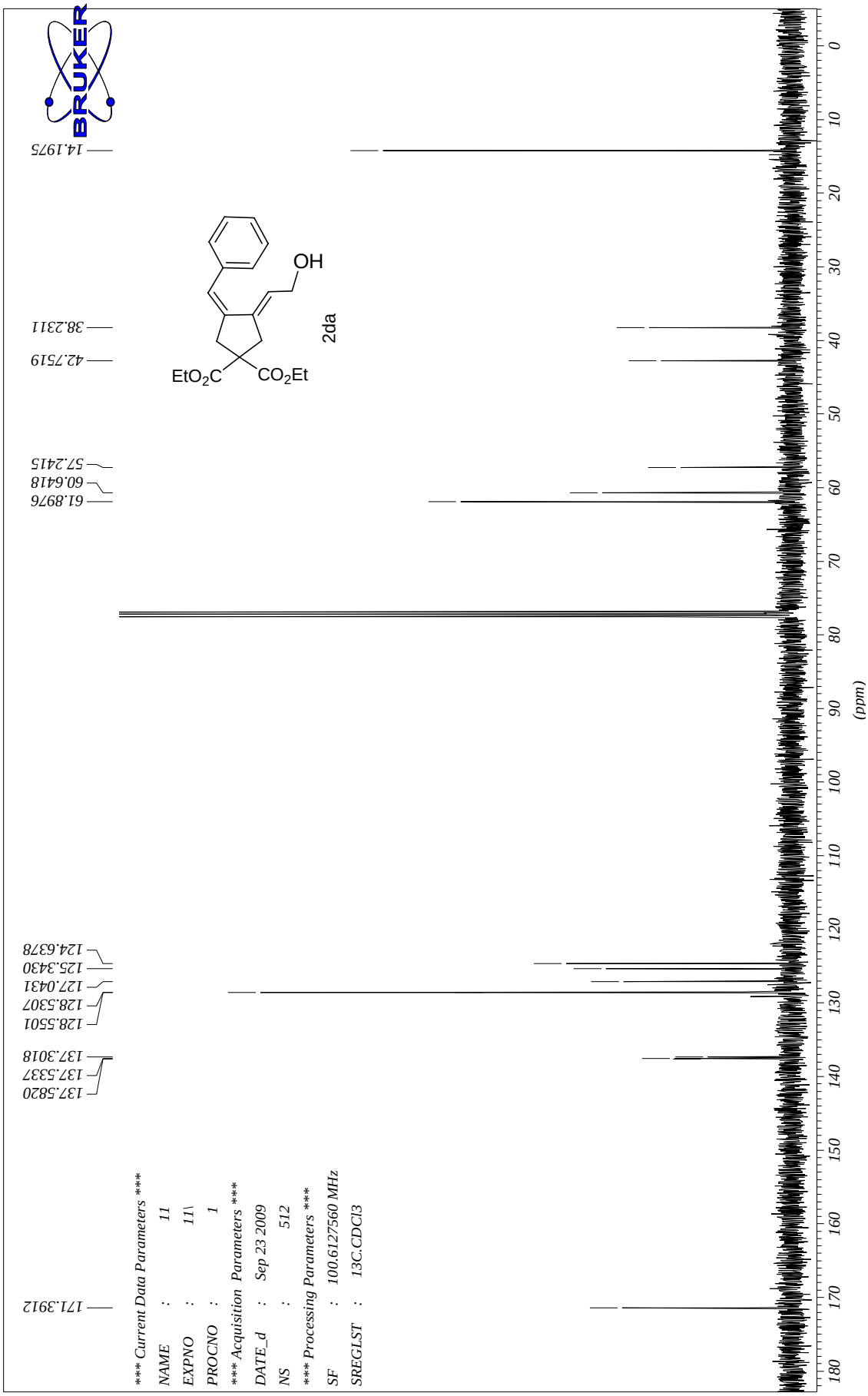

Figure A.29. ^{13}C NMR of (3Z,4E)-diethyl 3-benzylidene-4-(2-hydroxyethylidene)cyclopentane-1,1-dicarboxylate

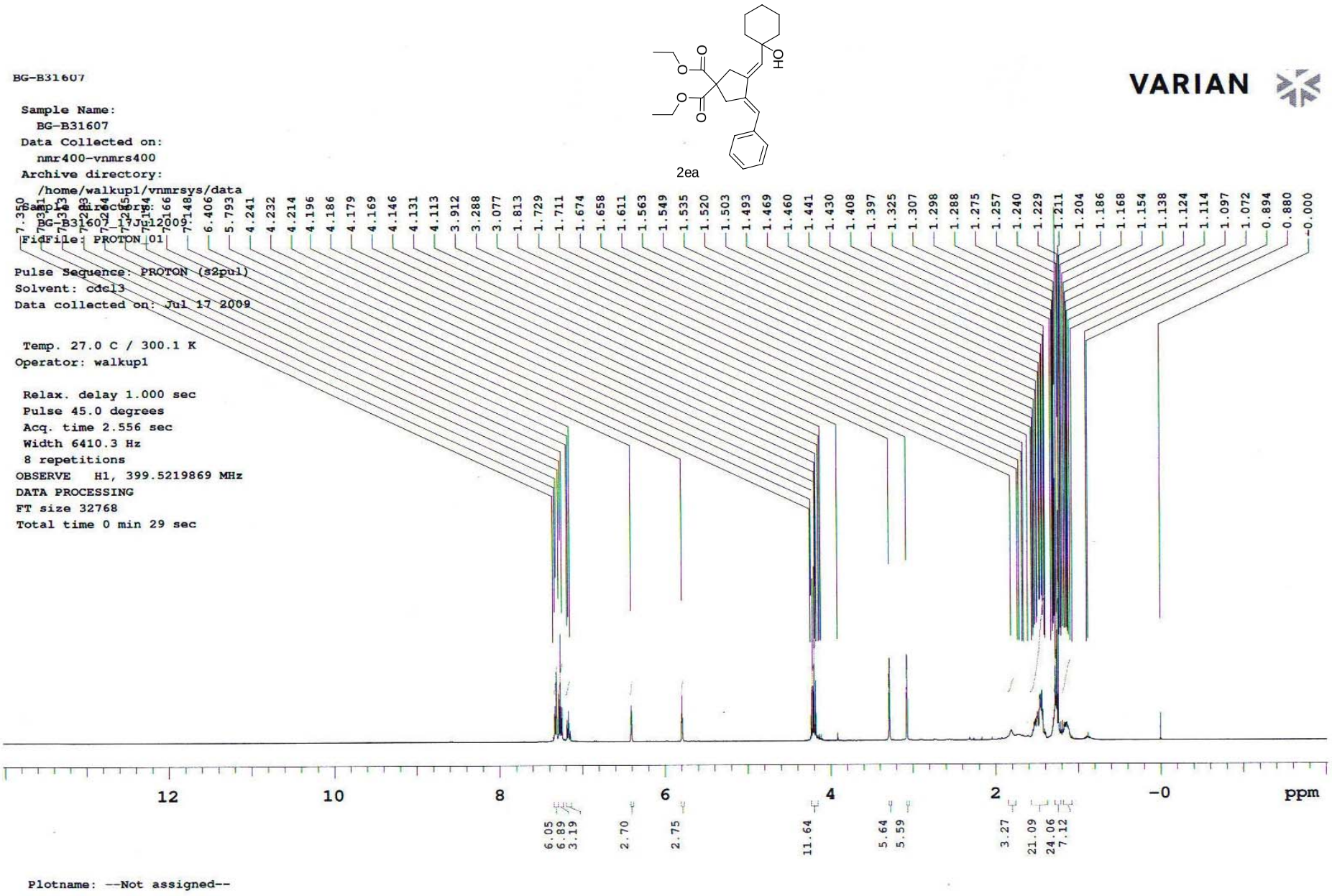

Figure A.30. ^{1}H NMR of (3E,4E)-diethyl 3-benzylidene-4-((1-hydroxycyclohexyl)methylene)cyclopentane-1,1-dicarboxylate

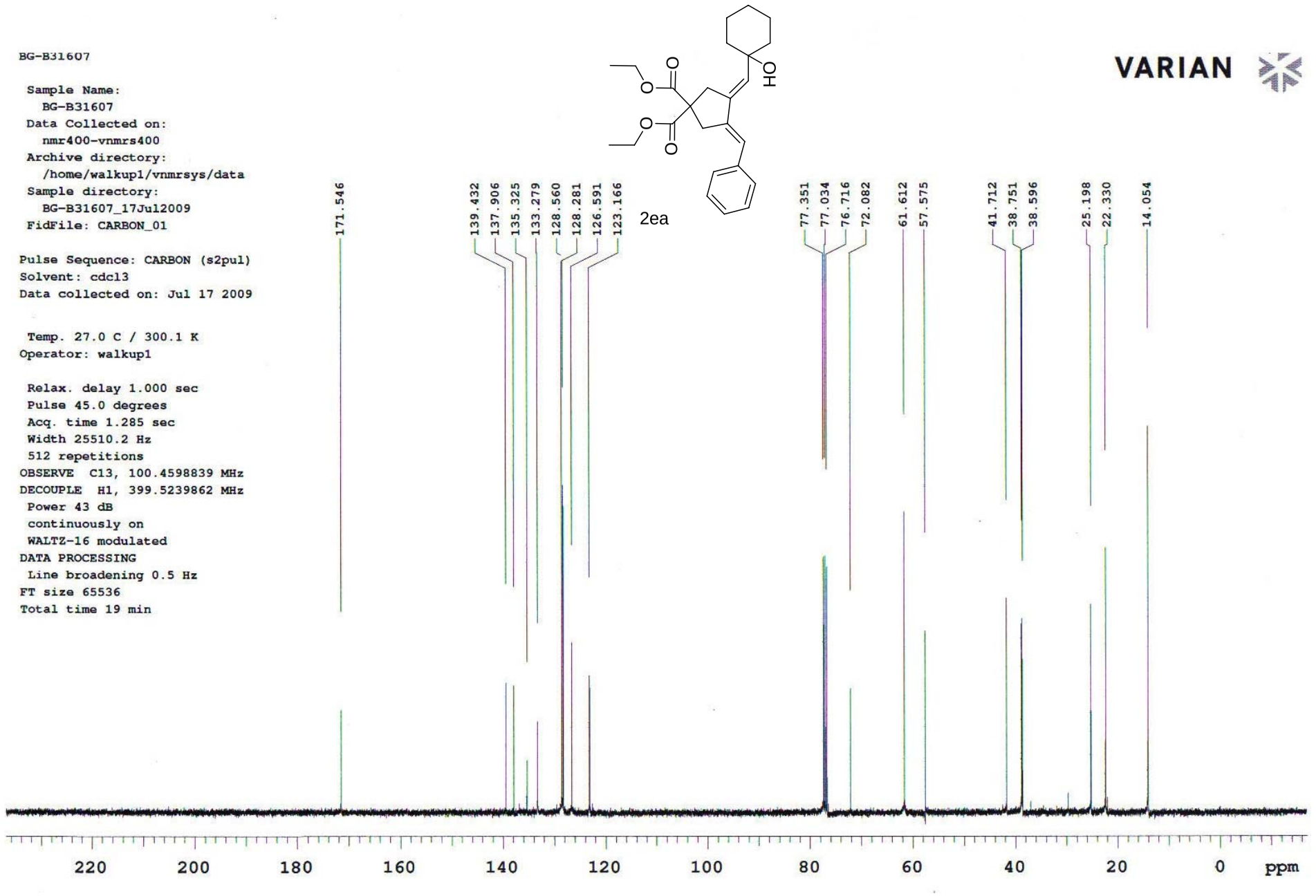

Figure A.31. ^{13}C NMR of (3E,4E)-diethyl 3-benzylidene-4-((1-hydroxycyclohexyl)methylene)cyclopentane-1,1-dicarboxylate

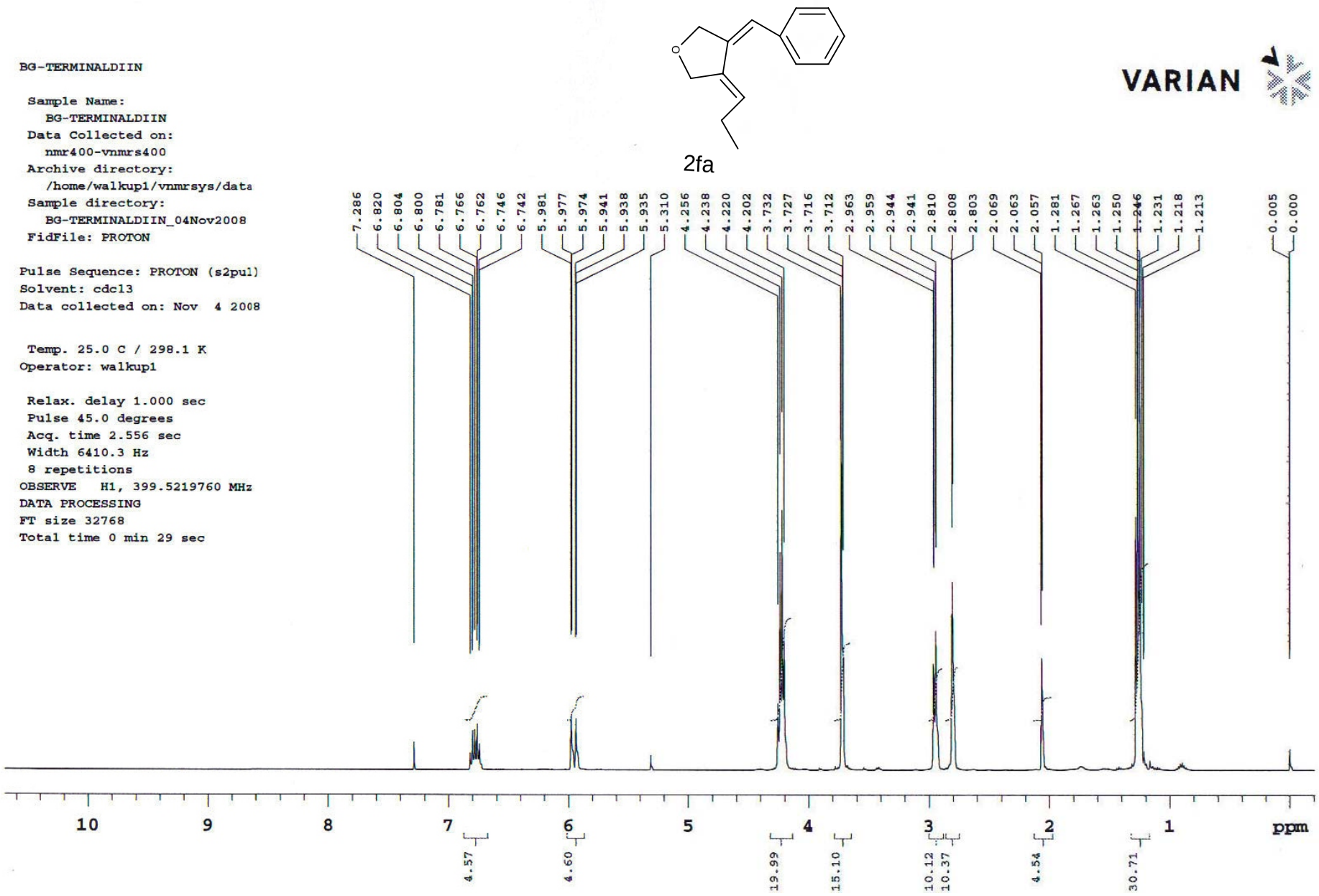

Figure A.32. ^{13}C NMR of (3E,4Z)-3-benzylidene-tetrahydro-4-propylidenefuran

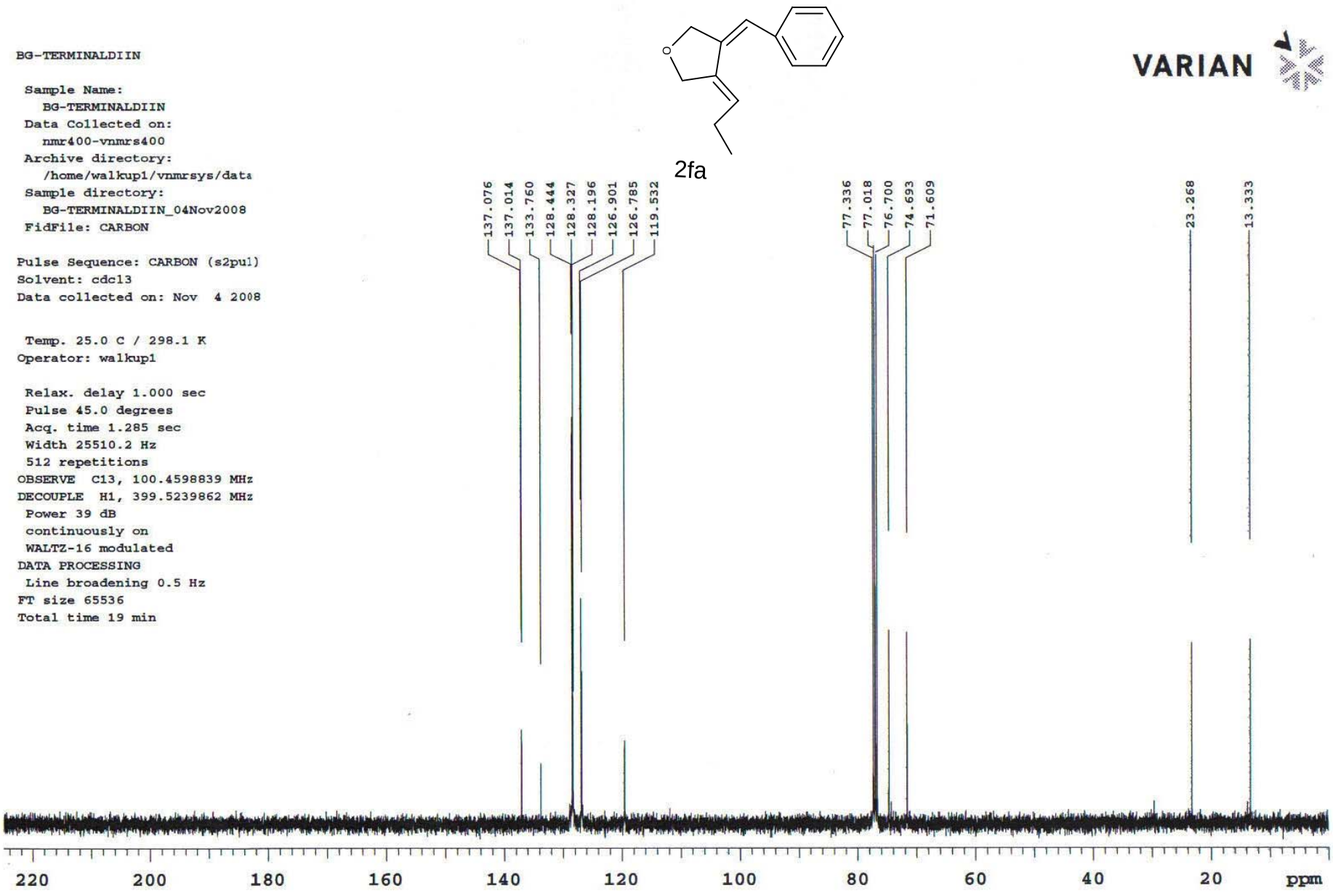

Figure A.33. ^{13}C NMR of (3E,4Z)-3-benzylidene-tetrahydro-4-propylidenefuran

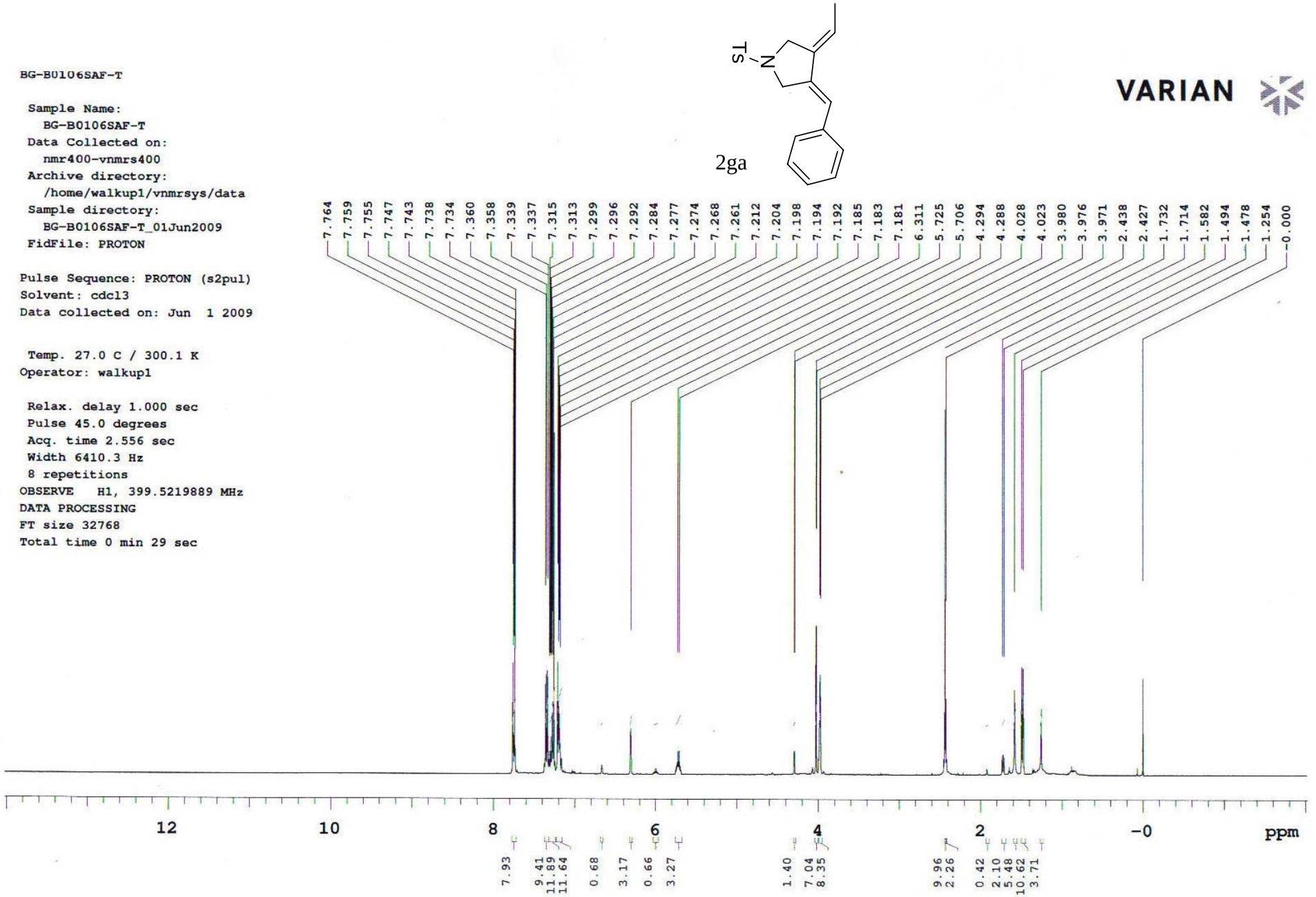

Figure A.34. ^{1}H NMR of (3Z,4Z)- 3-benzylidene-4-ethylidene-1-tosylpyrrolidine

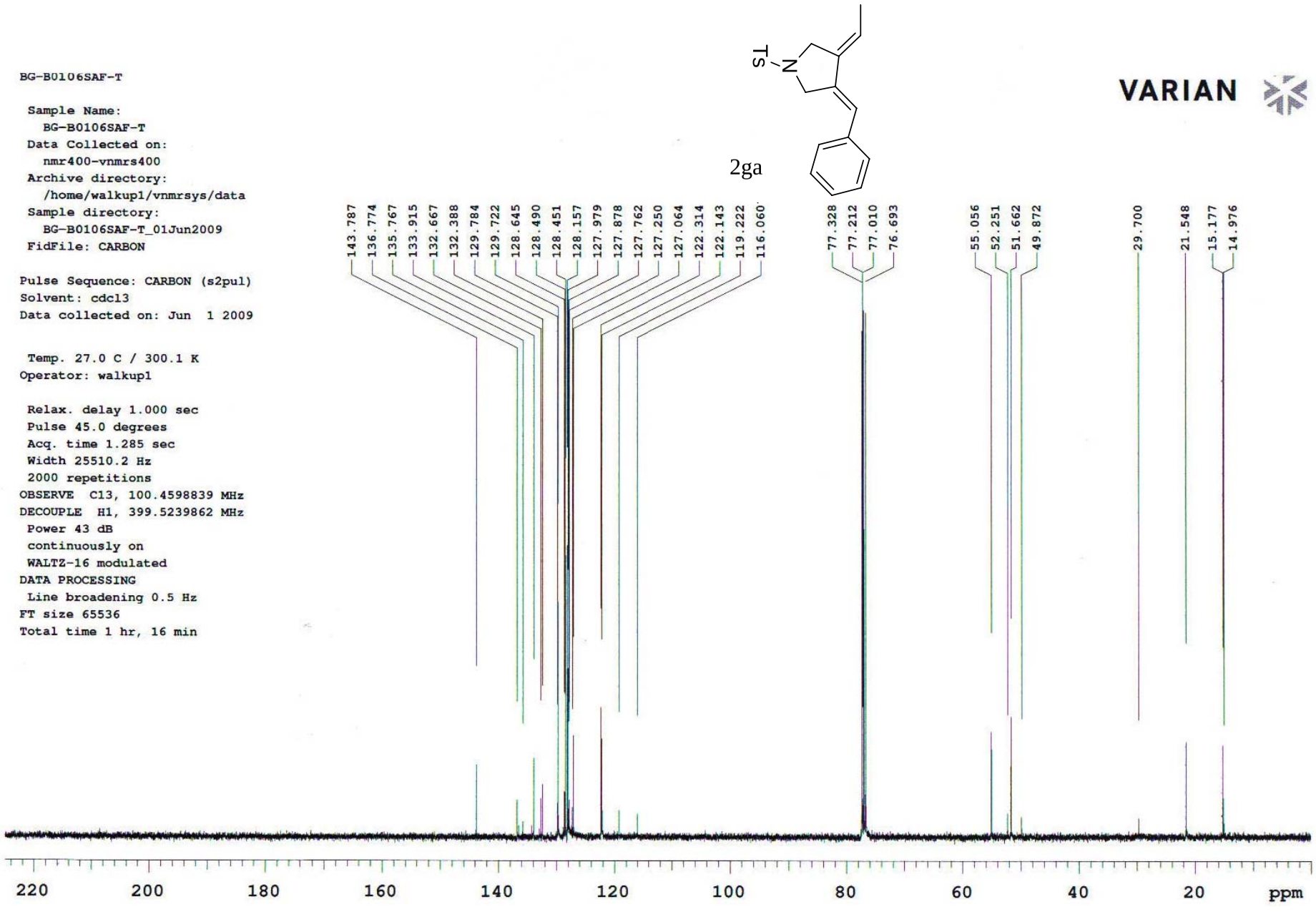

Figure A.35. ^{13}C NMR of (3Z,4Z)- 3-benzylidene-4-ethylidene-1-tosylpyrrolidine

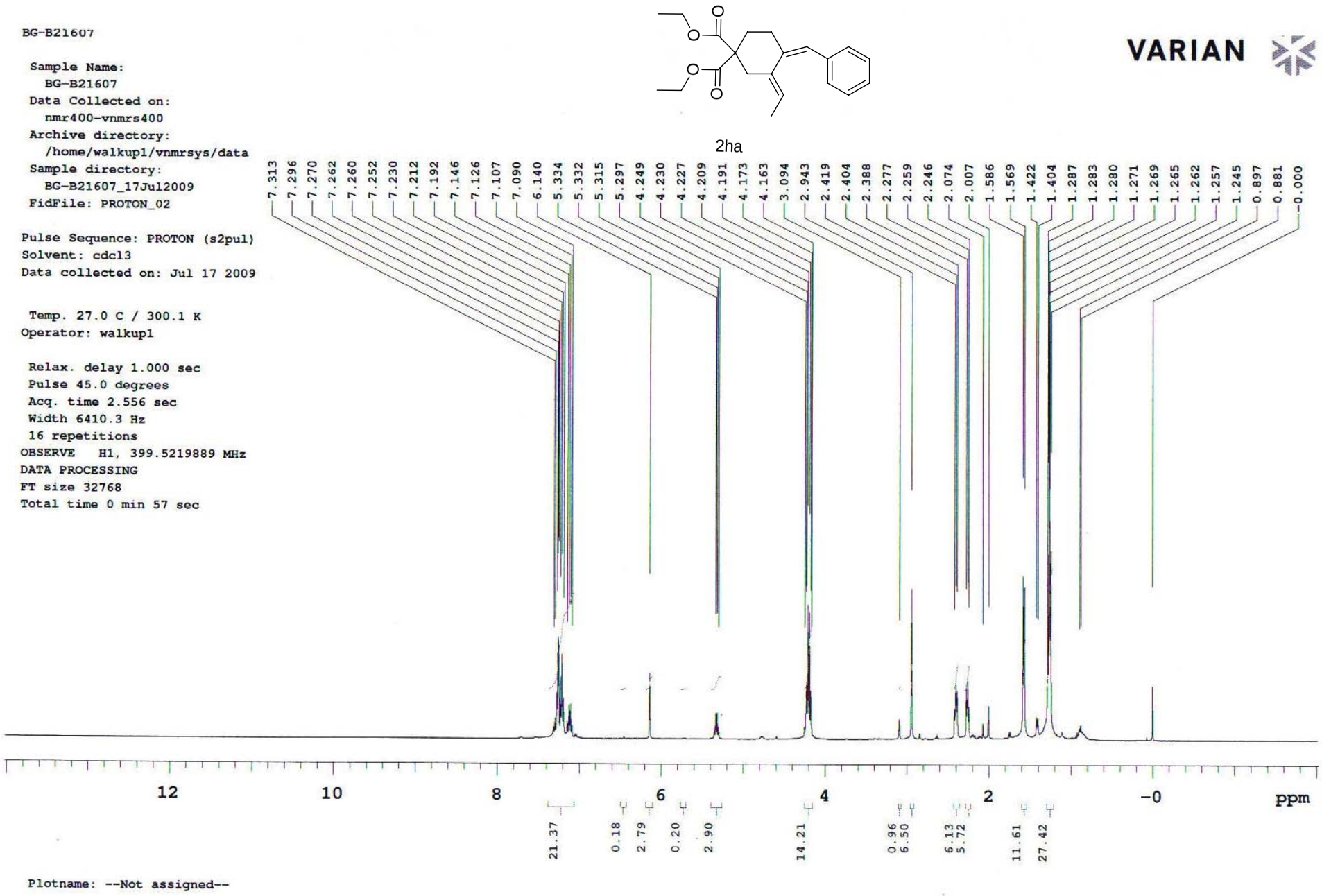

Figure A.36. ^{1}H NMR of (3E,4Z)- diethyl-4-benzylidene-3-ethylidenecyclohexane-1,1-dicarboxylate

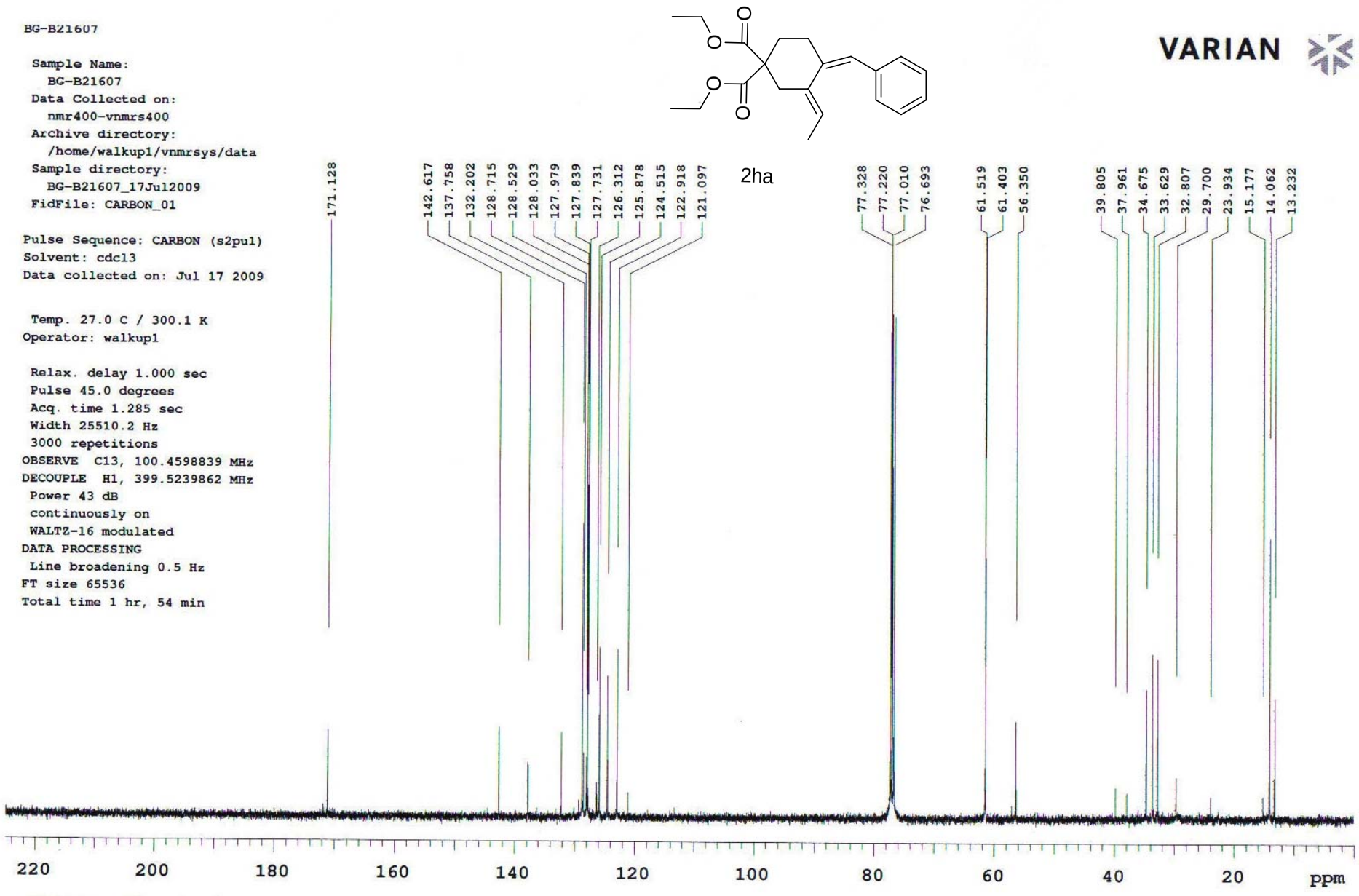

Figure A.37. ^{13}C NMR of (3E,4Z)- diethyl-4-benzylidene-3-ethylidenecyclohexane-1,1-dicarboxylate

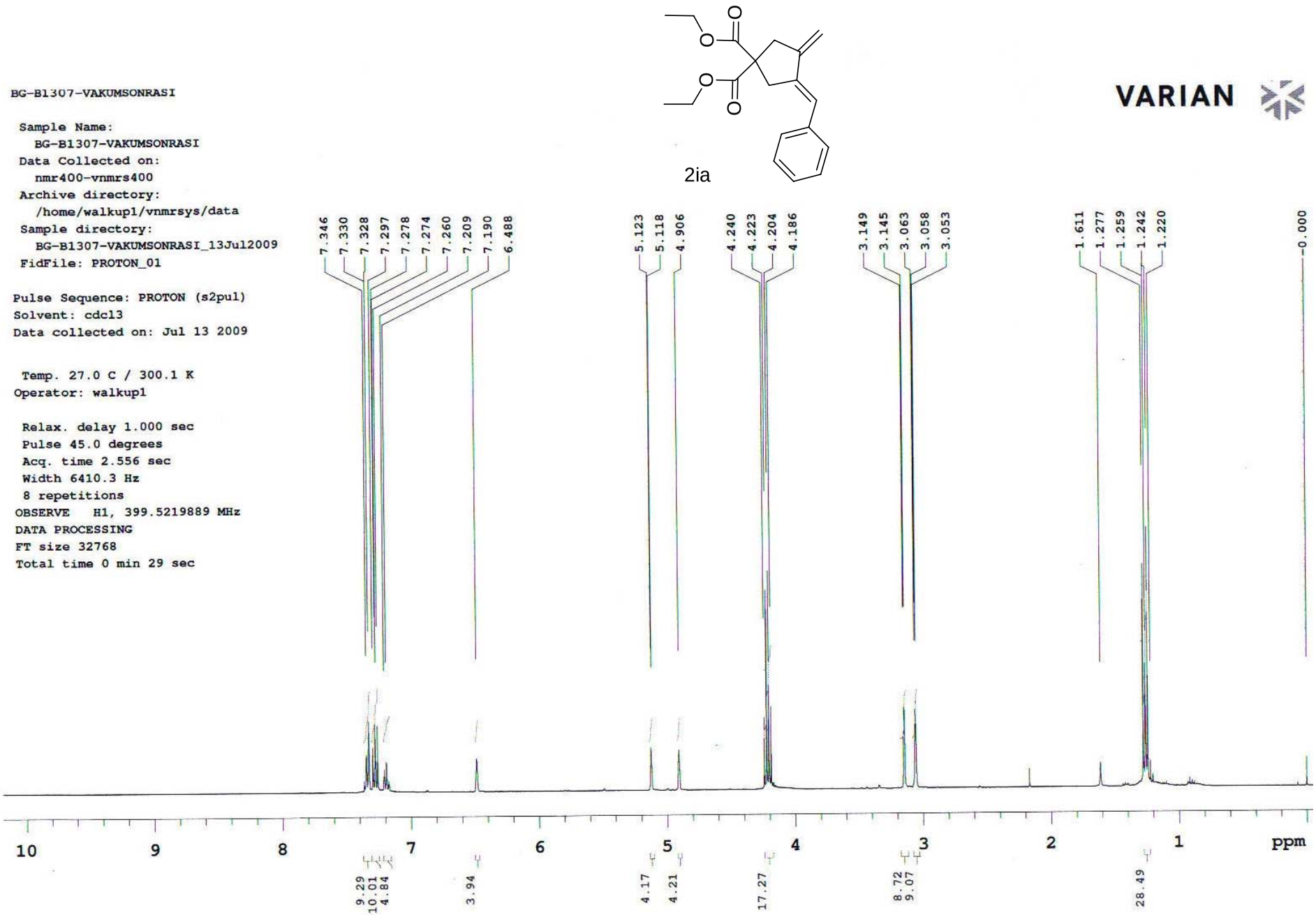

Figure A.38. ^{1}H NMR of (3E)- diethyl-3-benzylidene-4-methylenecyclopentane-1,1-dicarboxylate

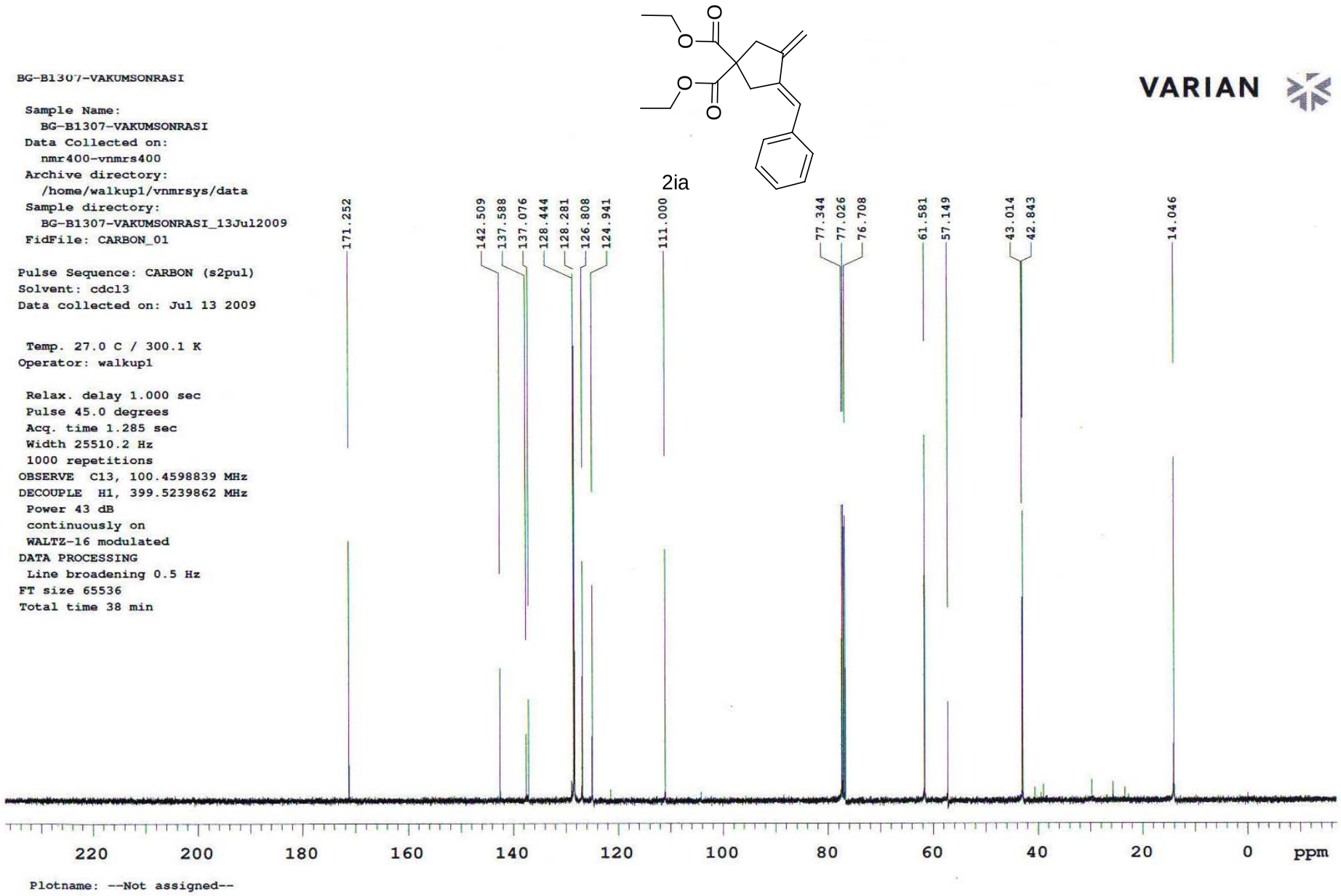

Figure A.39. ^{13}C NMR of (3E)- diethyl-3-benzylidene-4-methylenecyclopentane-1,1-dicarboxylate

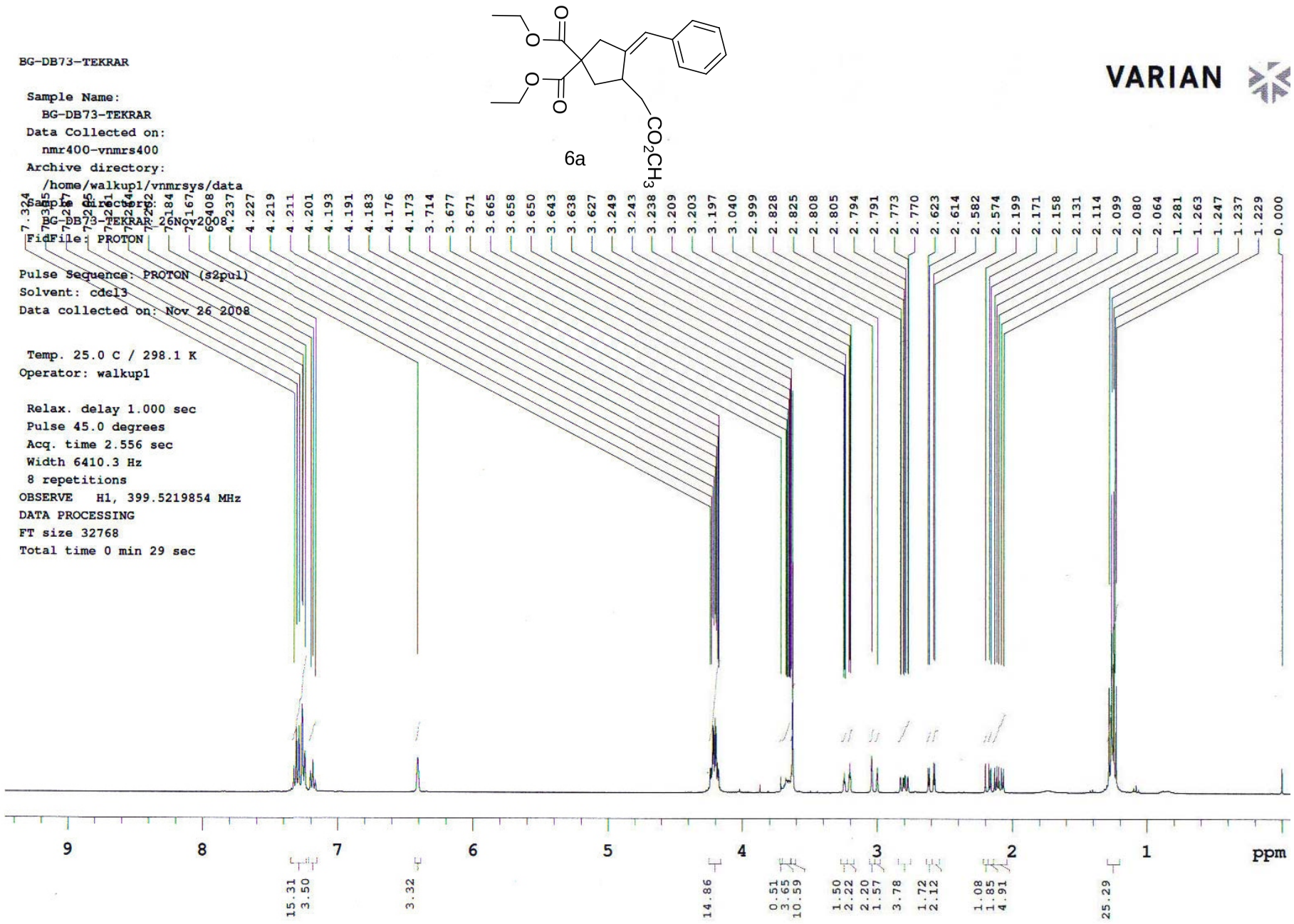

Figure A.40. ^{1}H NMR of (Z)- diethyl 3-((methoxycarbonyl)methyl)-4-benzylidenecyclopentane-1,1-dicarboxylate

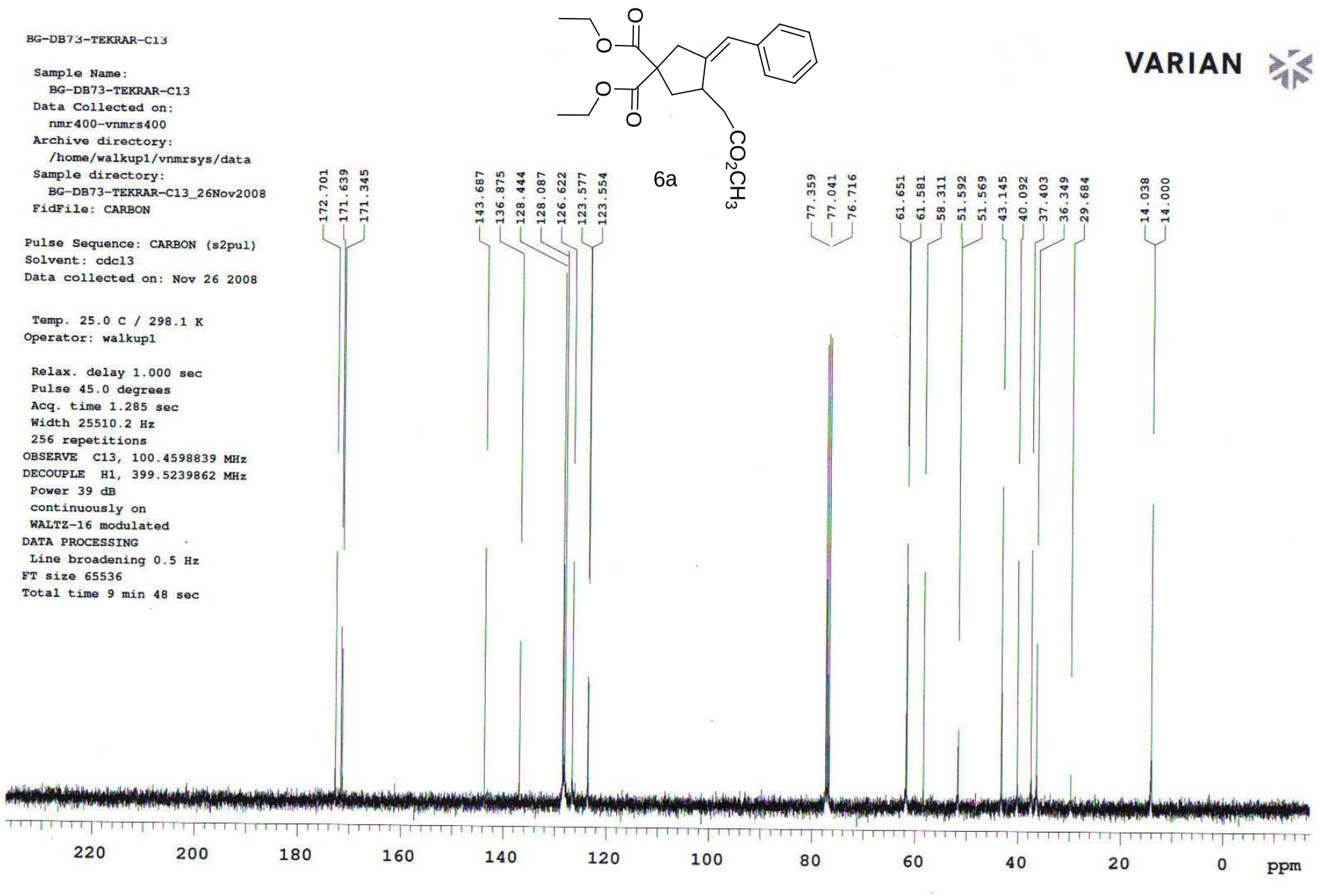

Figure A.41. ^{13}C NMR of (Z)- diethyl 3-((methoxycarbonyl)methyl)-4-benzylidenecyclopentane-1,1-dicarboxylate

APPENDIX B

MASS SPECTRUMS OF CYCLIZATION PRODUCTS

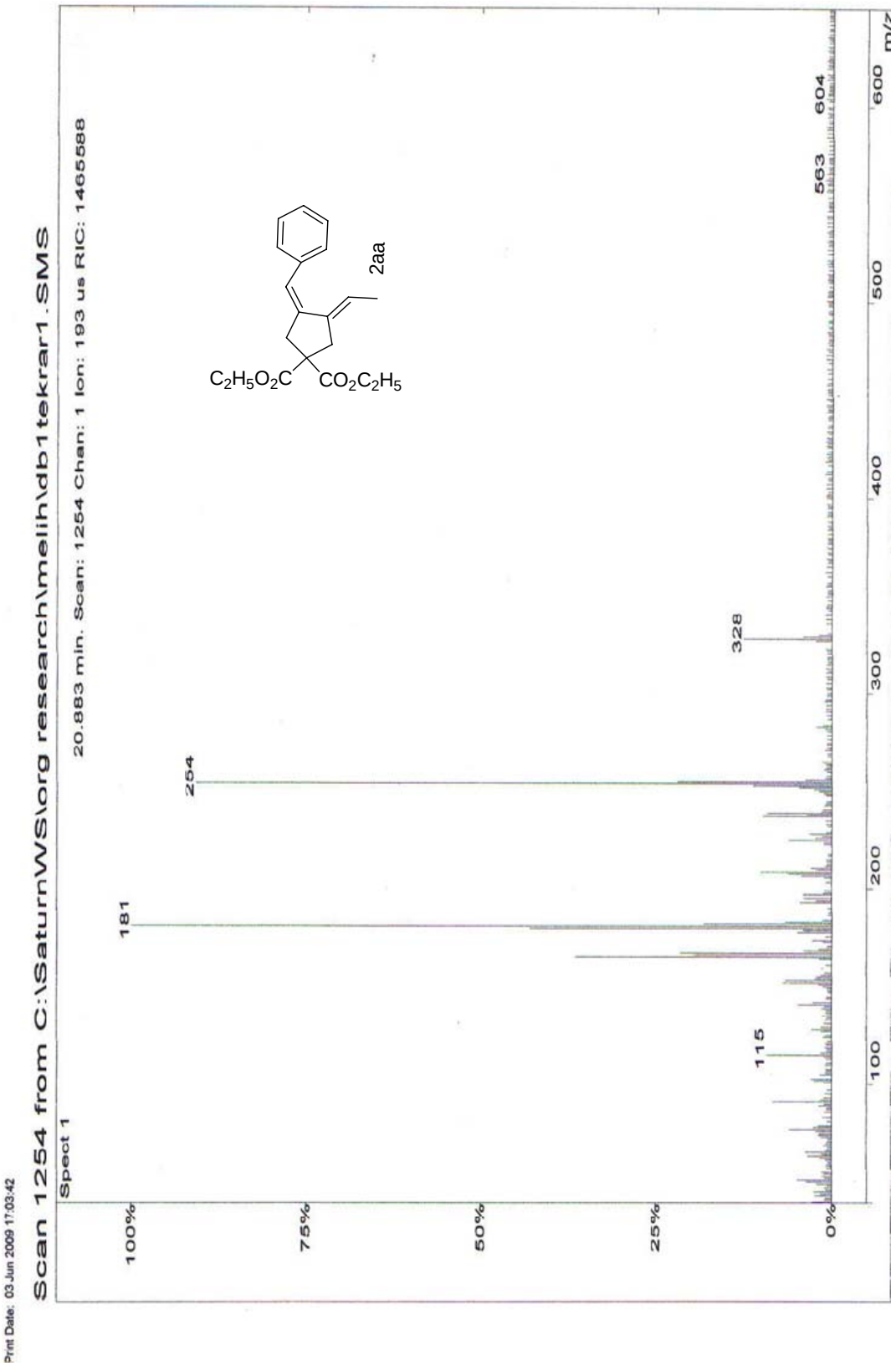

Figure B.1. GC-MS spectrum of (3Z,4E)-diethyl 3-benzylidene-4-ethylidenecyclopentane-1,1-dicarboxylate

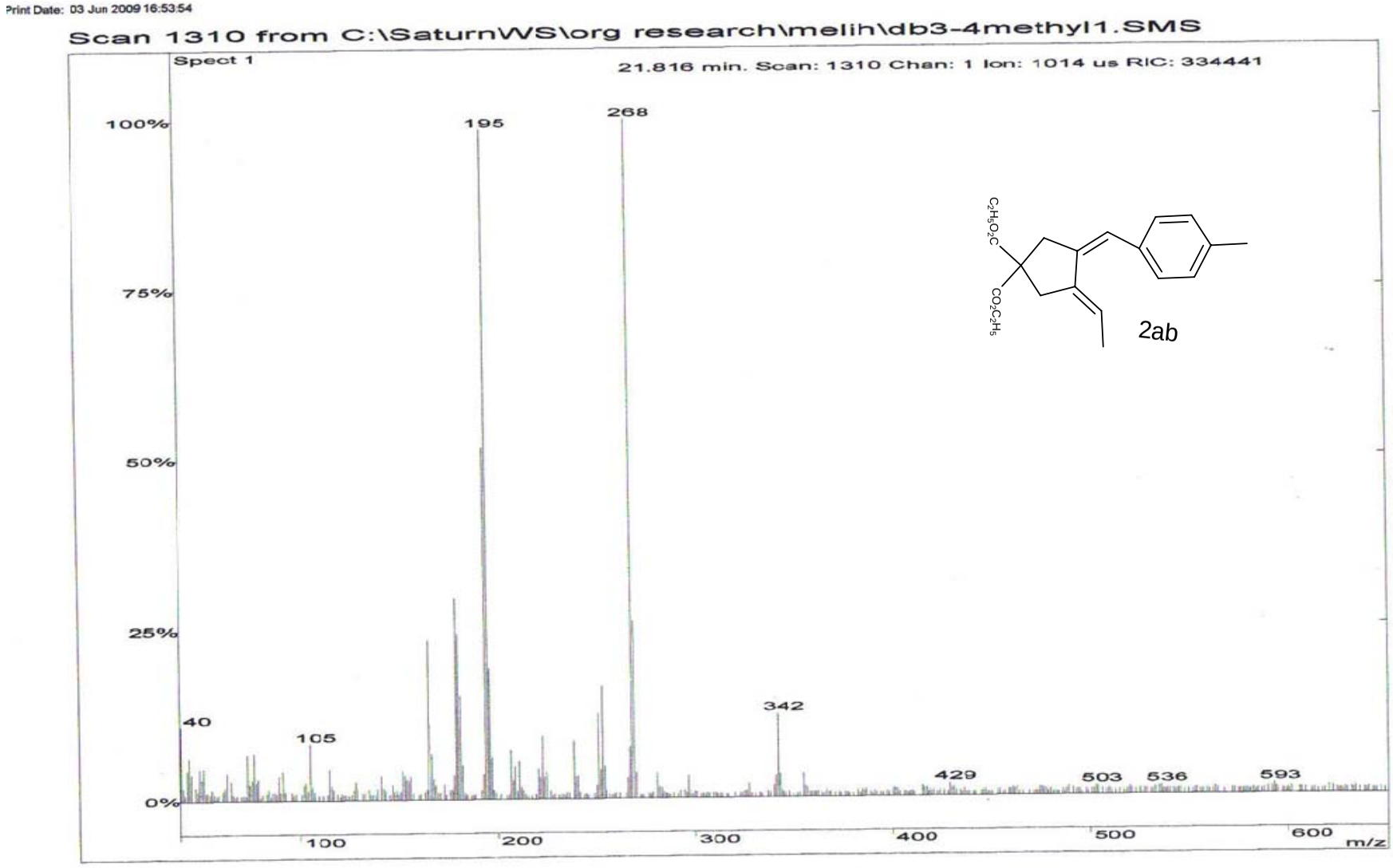

Figure B.2. GC-MS spectrum of (3Z,4E)-diethyl 3-benzylidene-4-ethylidenecyclopentane-1,1-dicarboxylate

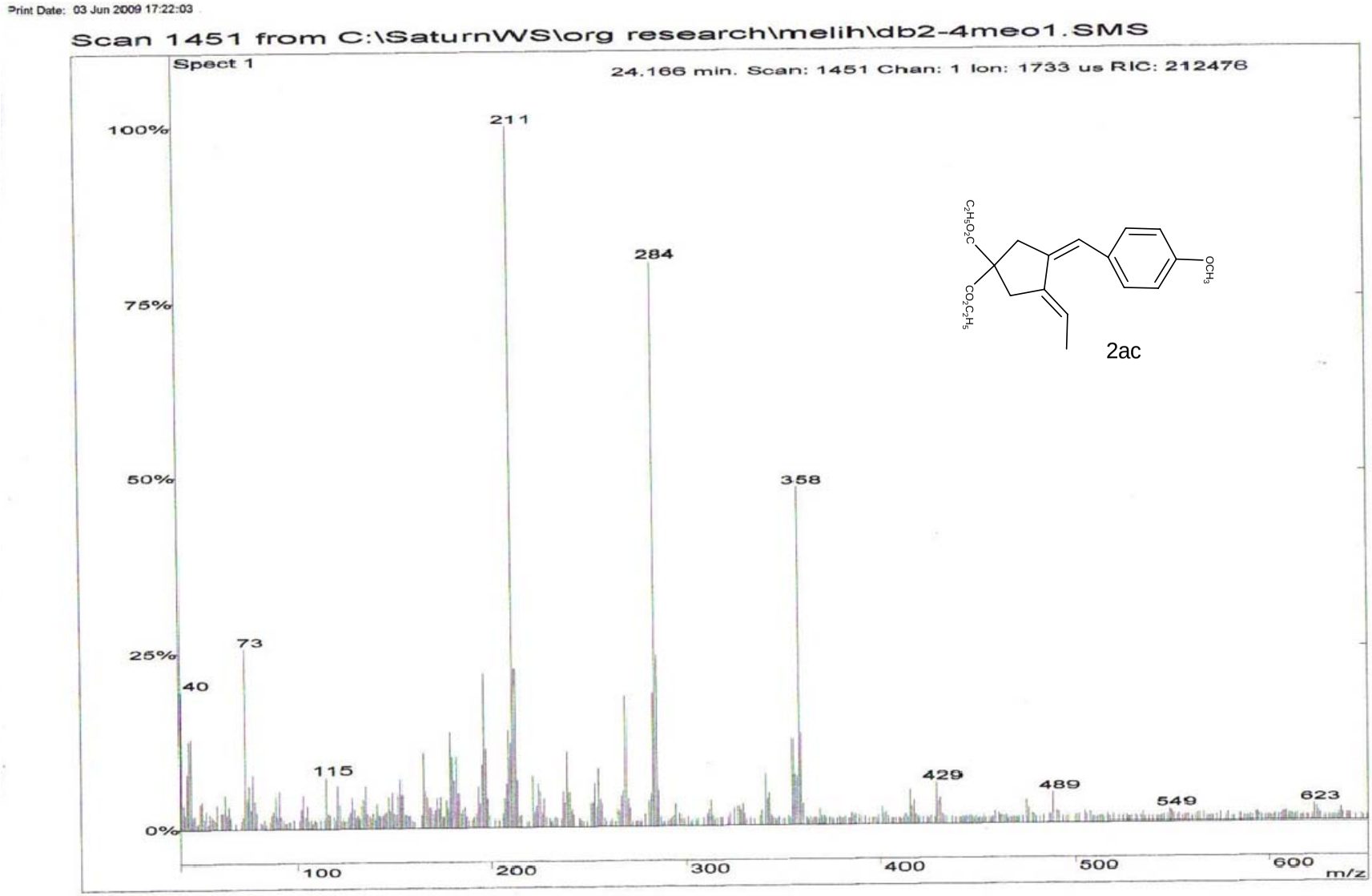

Figure B.3. GC-MS spectrum of (3Z,4E)-diethyl 3-(4-methoxybenzylidene)-4-ethylidenecyclopentane-1,1-dicarboxylate

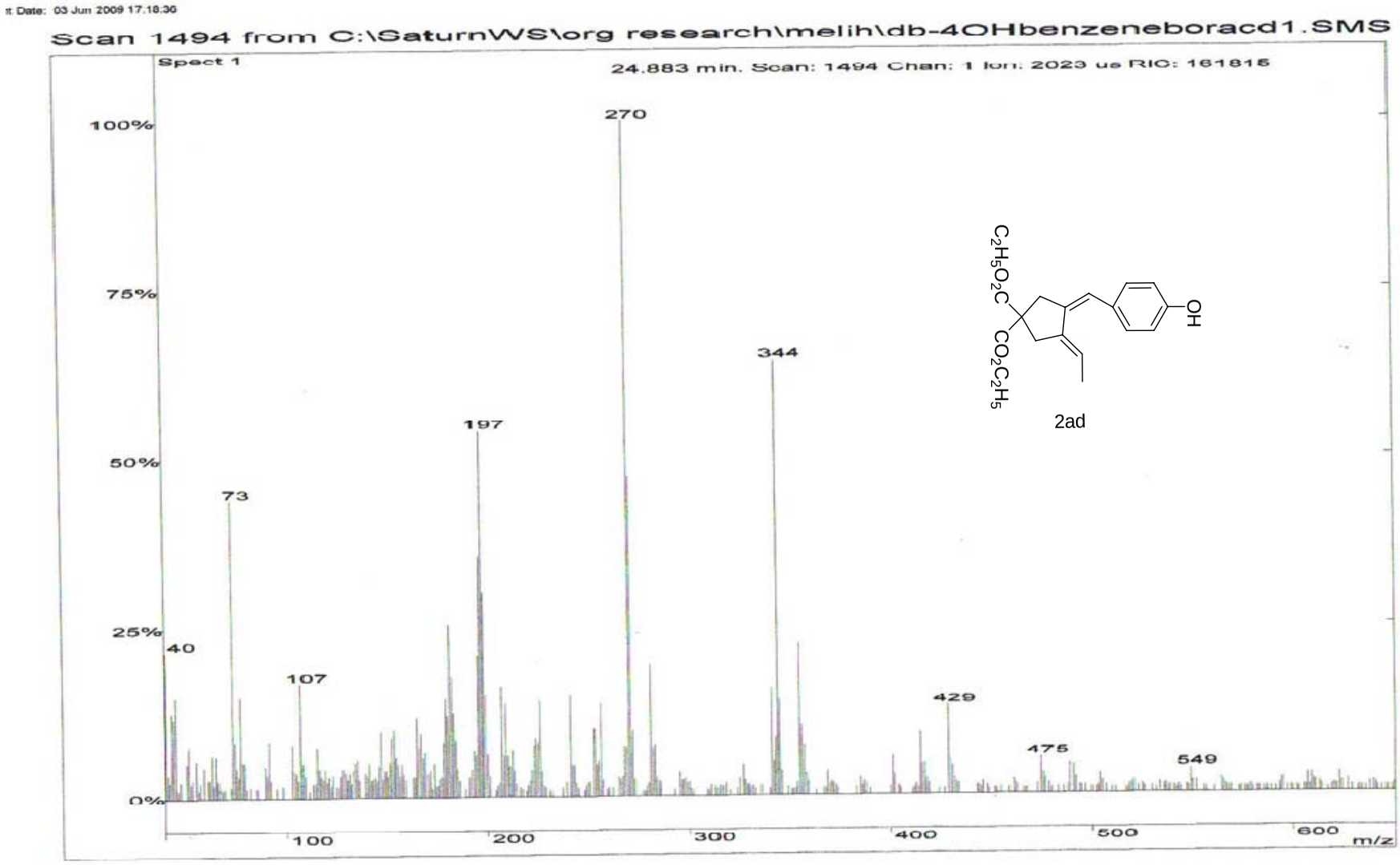

Figure B.4. GC-MS spectrum of (3Z,4E)-diethyl 3-(4-hydroxybenzylidene)-4-ethylidenecyclopentane-1,1-dicarboxylate

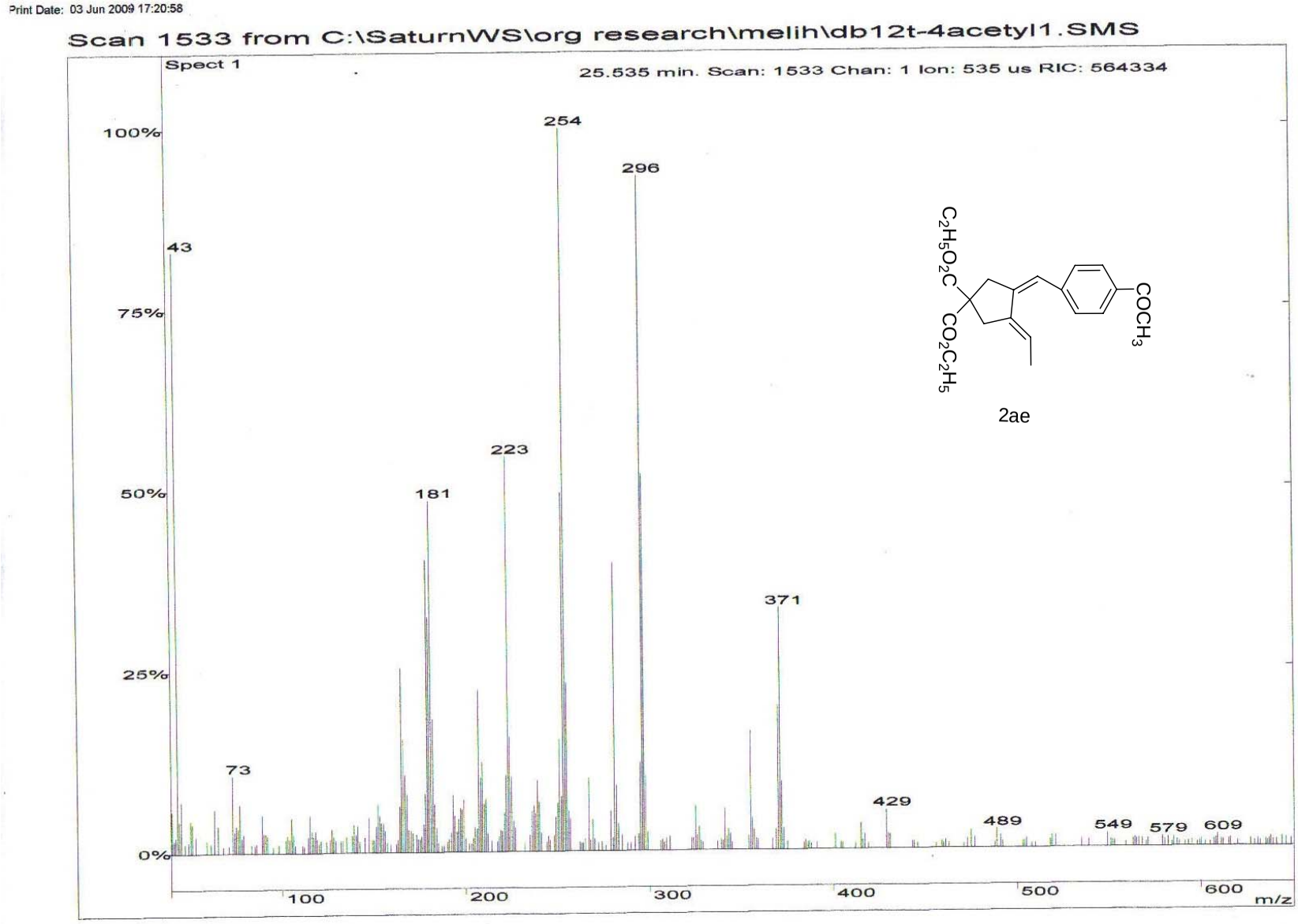

Figure B.5. GC-MS spectrum of (3Z,4E)-diethyl 3-(4-acetylbenzylidene)-4-ethylidenecyclopentane-1,1-dicarboxylate

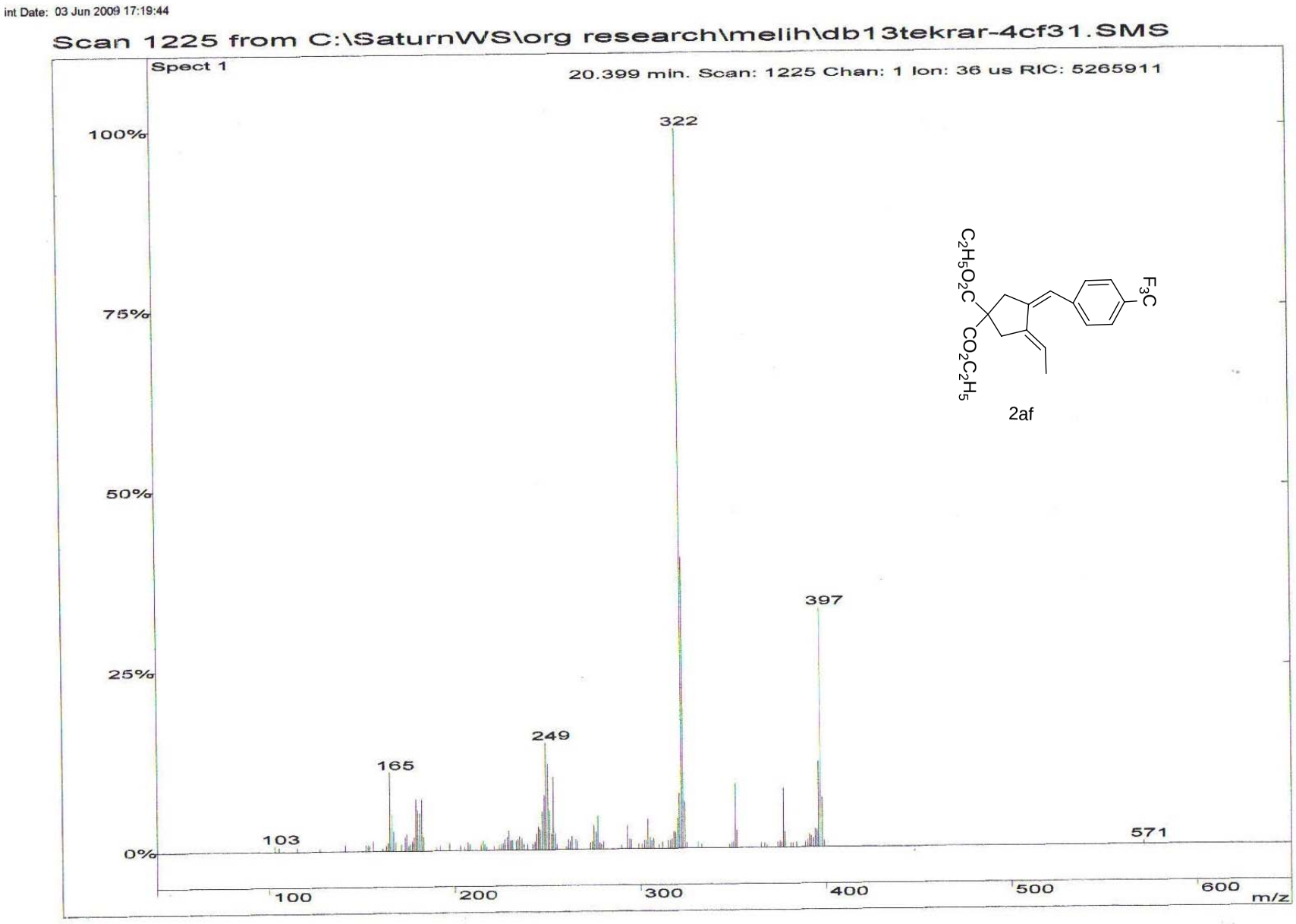

Figure B.6. GC-MS spectrum (3Z,4E)-diethyl 3-(4-(trifluoromethyl)benzylidene)-4-ethylidenecyclopentane-1,1-dicarboxylate

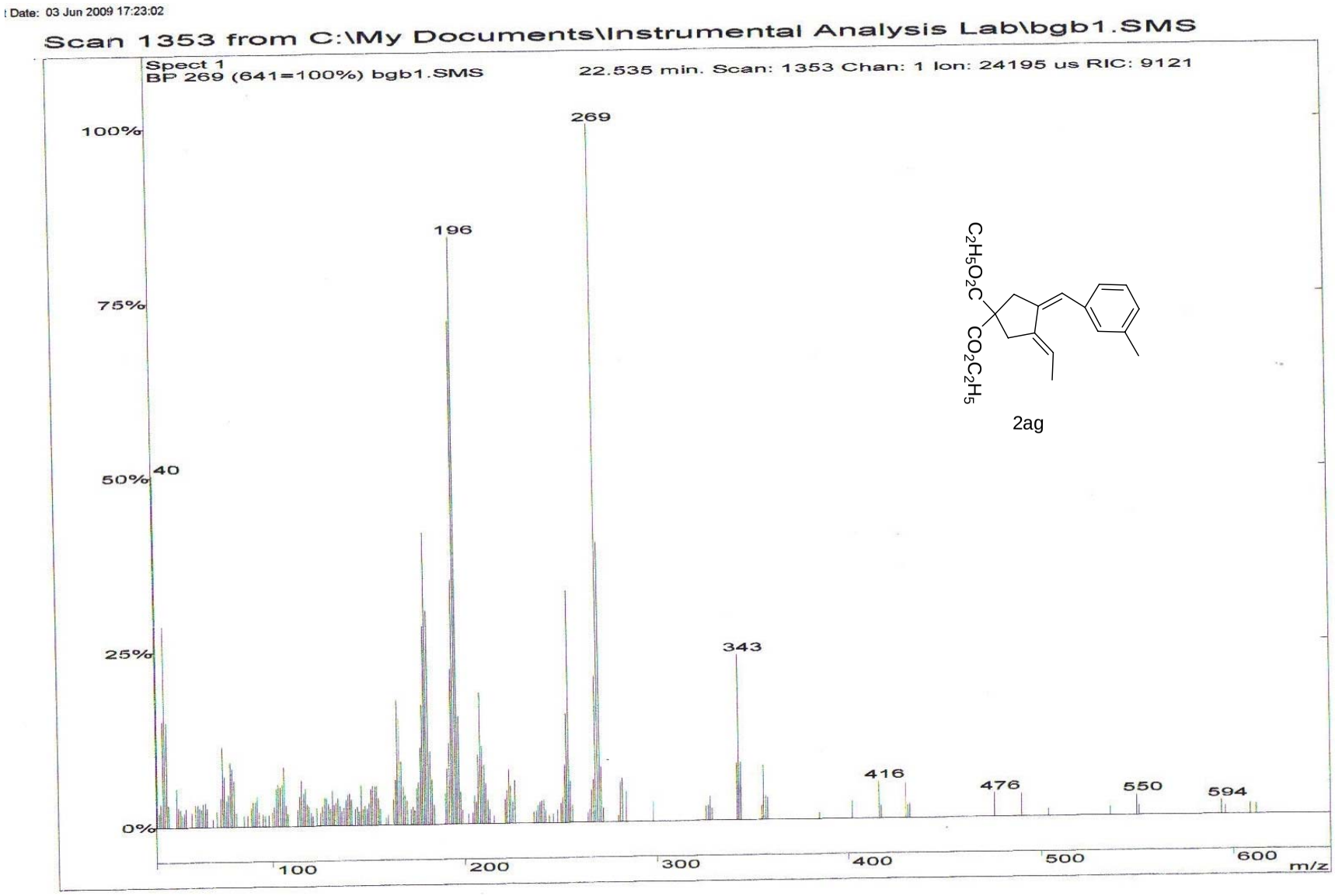

Figure B.7. GC-MS spectrum of (3Z,4E)-diethyl 3-(3-methylbenzylidene)-4-ethylidenecyclopentane-1,1-dicarboxylate

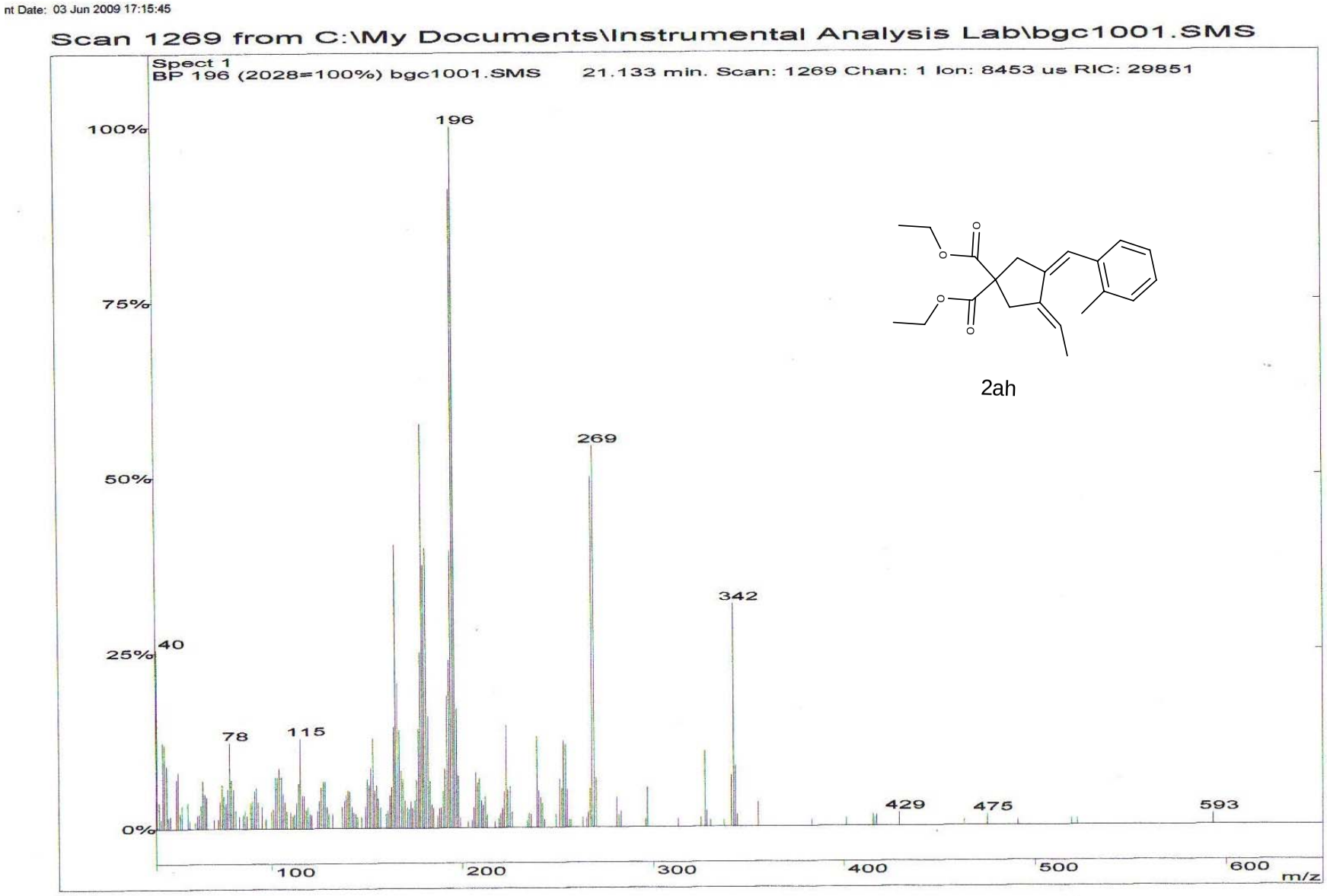

Figure B.8. GC-MS spectrum of (3Z,4E)-diethyl 3-(1-m-tolylbenzylidene)-4-ethylidenecyclopentane-1,1-dicarboxylate

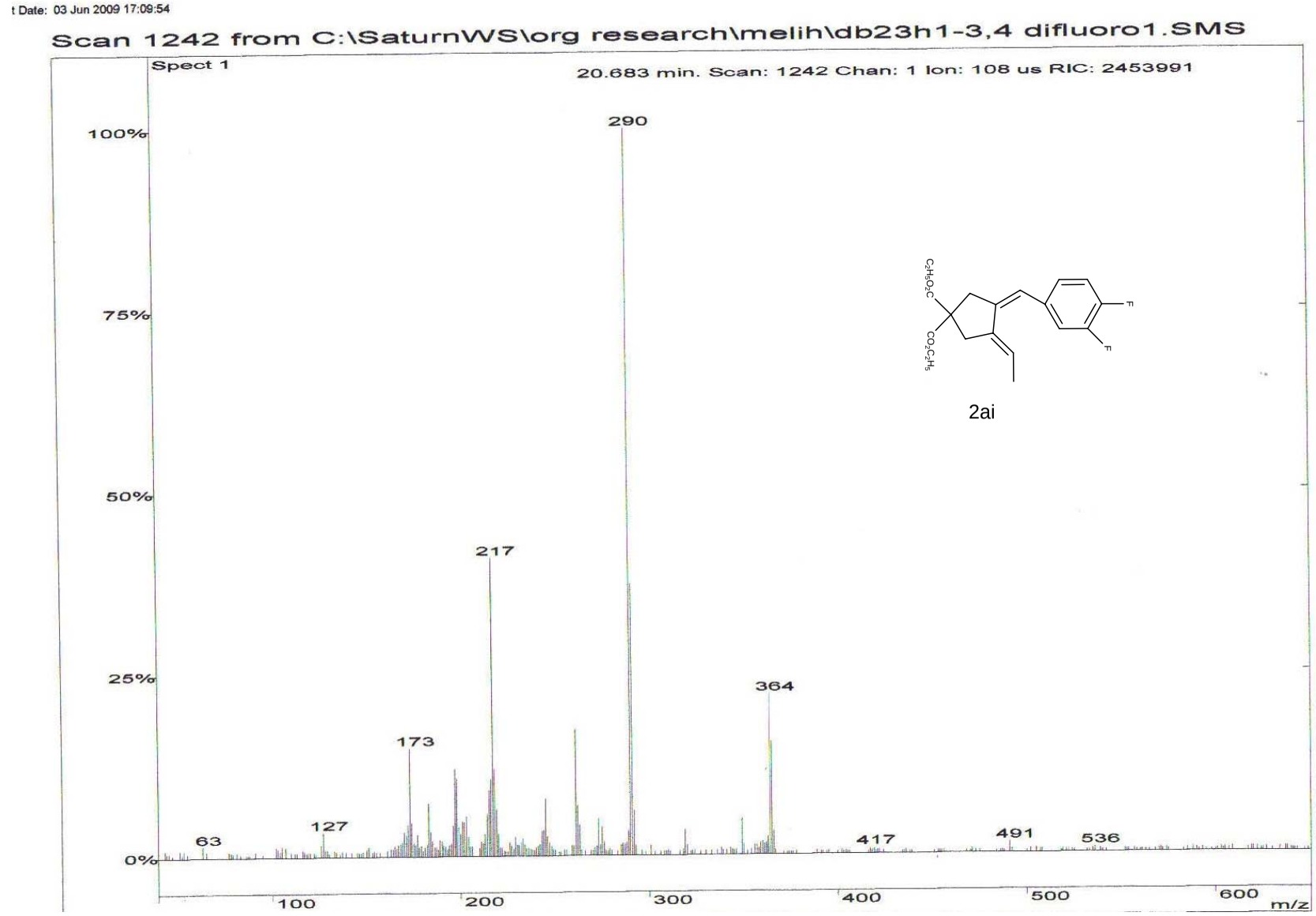

Figure B.9. GC-MS spectrum of (3Z,4E)-diethyl 3-(3,4-difluorobenzylidene)-4-ethylidenecyclopentane-1,1-dicarboxylate

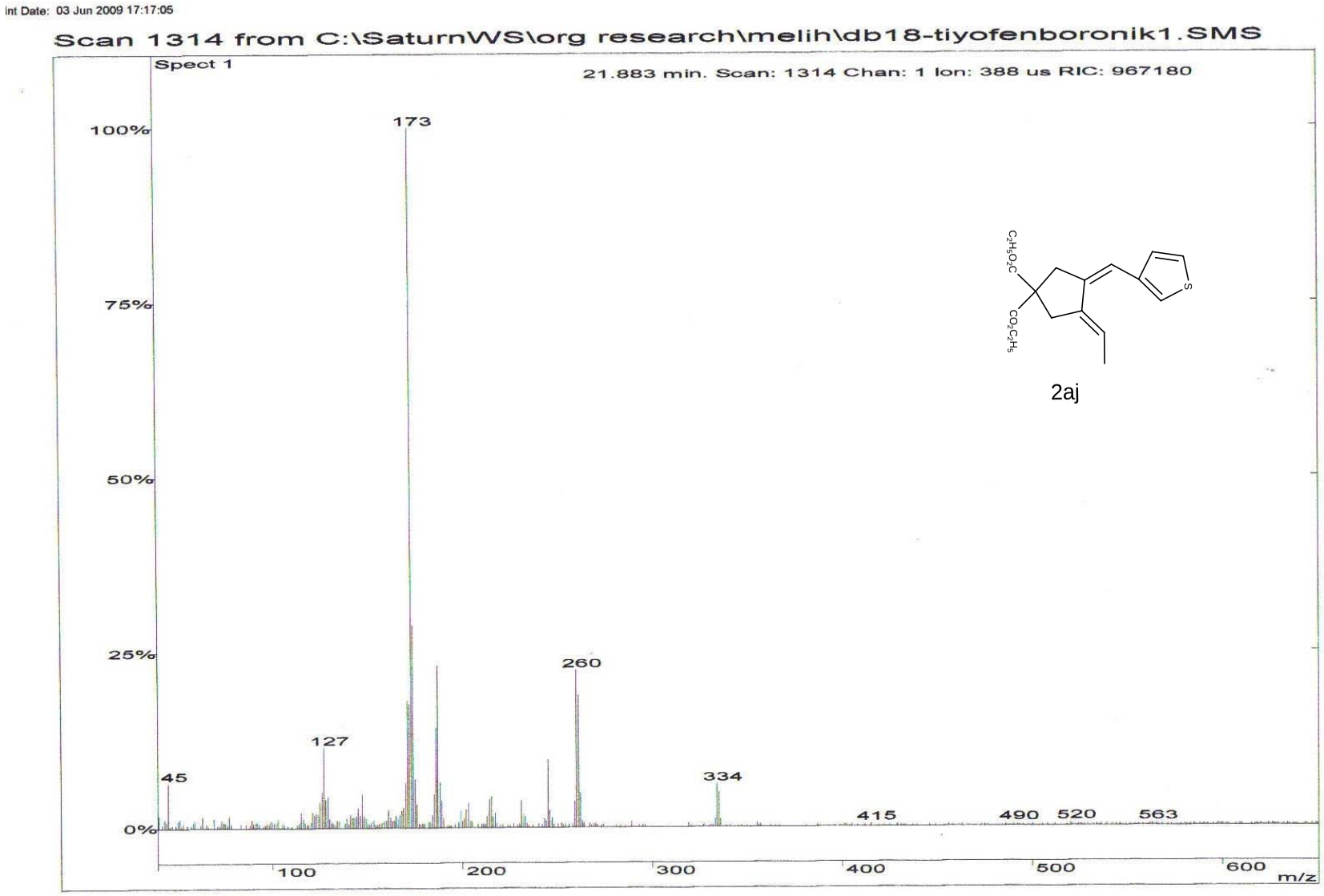

Figure B.10. GC-MS spectrum of (3E,4Z)-diethyl 3-ethylidene-4-((thiophen-3-yl)methylene)cyclopentane-1,1-dicarboxylate

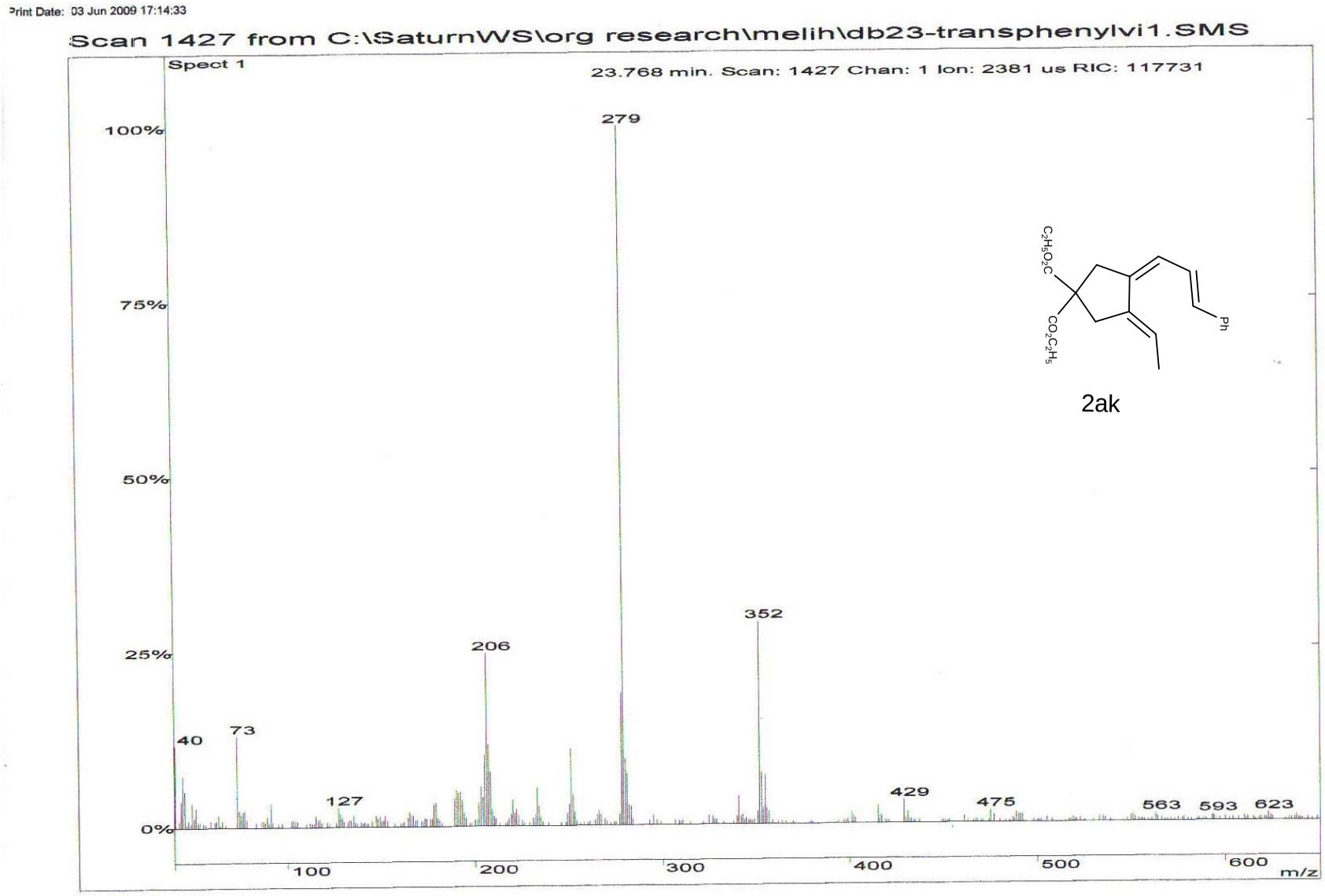

Figure B.11. GC-MS spectrum of (3E,4Z)-diethyl 3-ethylidene-4-((E)-3-phenylallylidene)cyclopentane-1,1-dicarboxylate

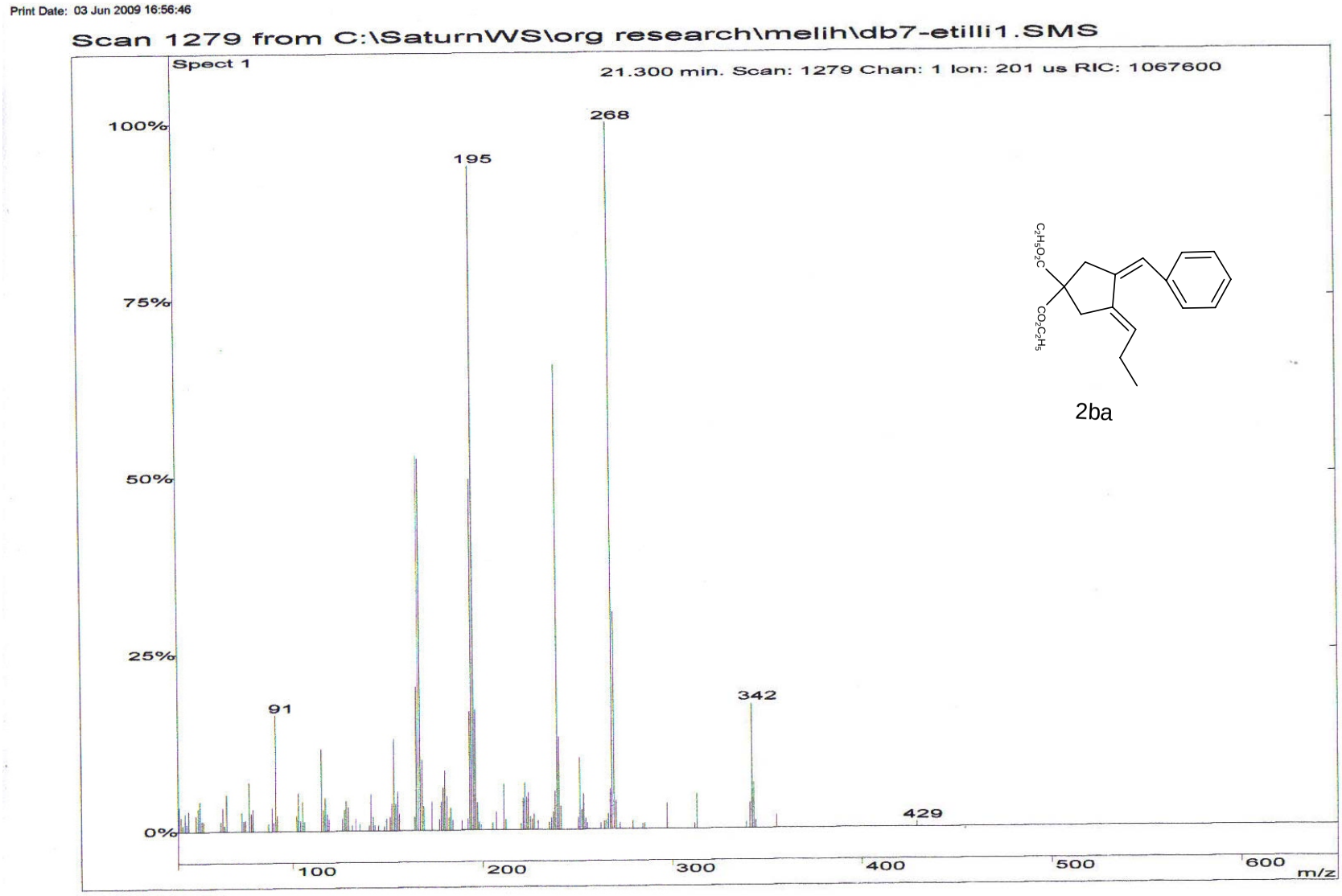

Figure B.12. GC-MS spectrum of (3Z,4E)-diethyl 3-benzylidene-4-propylidenecyclopentane-1,1-dicarboxylate

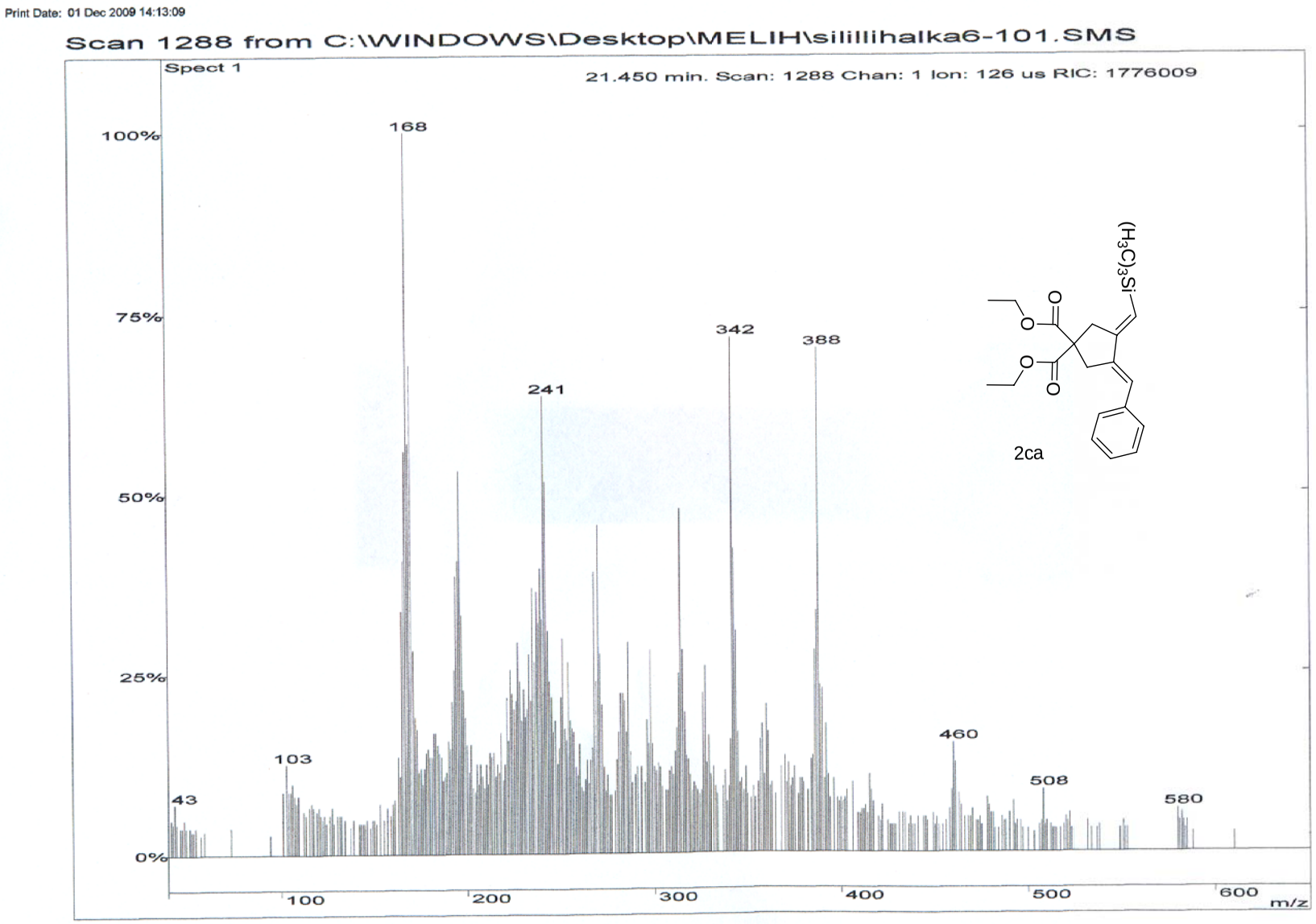

Figure B.13.GC-MS Spectrum of (3E,4E)-diethyl 3-benzylidene-4-((trimethylsilyl)methylene)cyclopentane-1,1-dicarboxylate

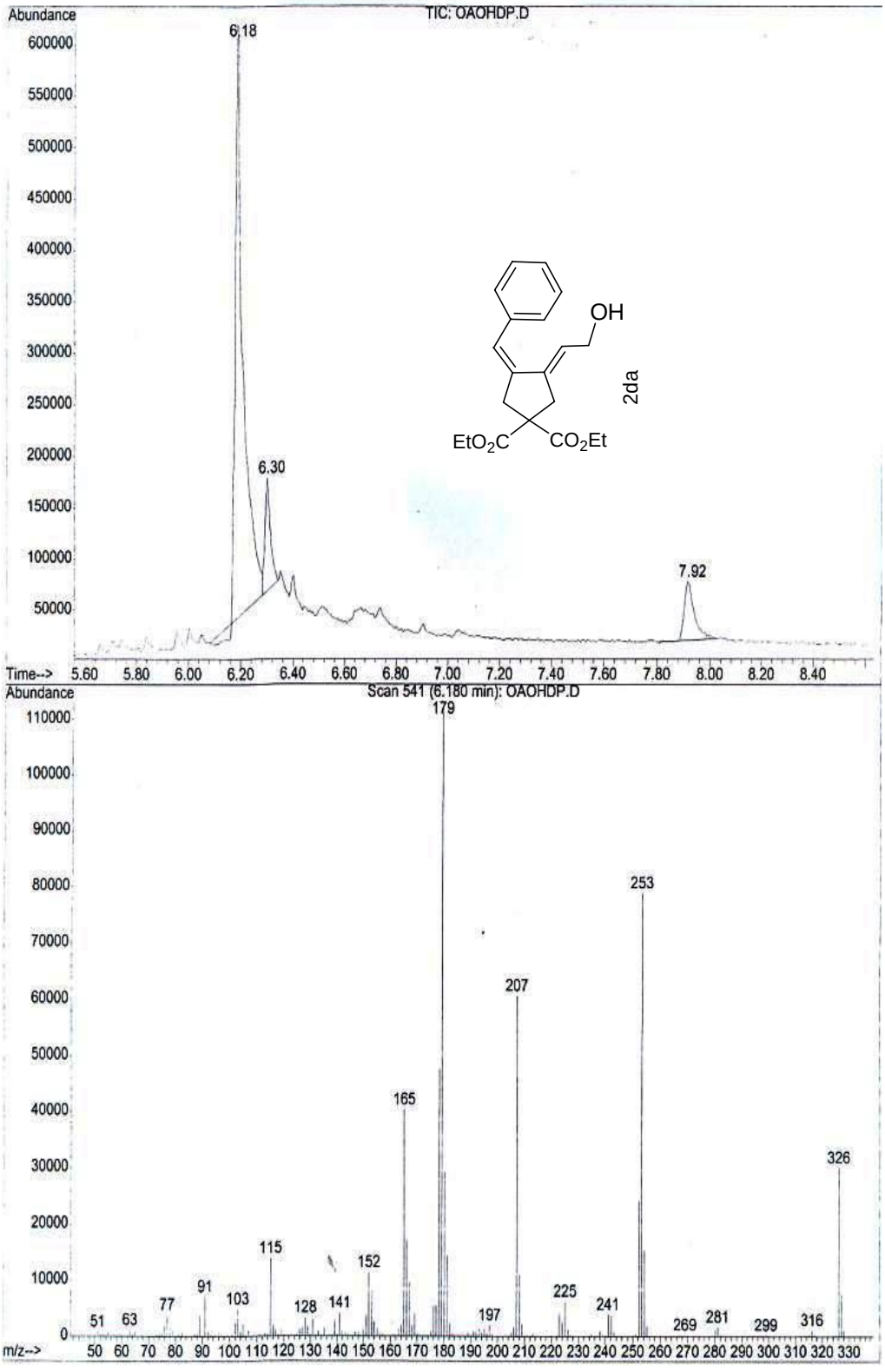

Figure B.14 GC-MS spectrum of (3Z,4E)-diethyl 3-benzylidene-4-(2-hydroxyethylidene)cyclopentane-1,1-dicarboxylate

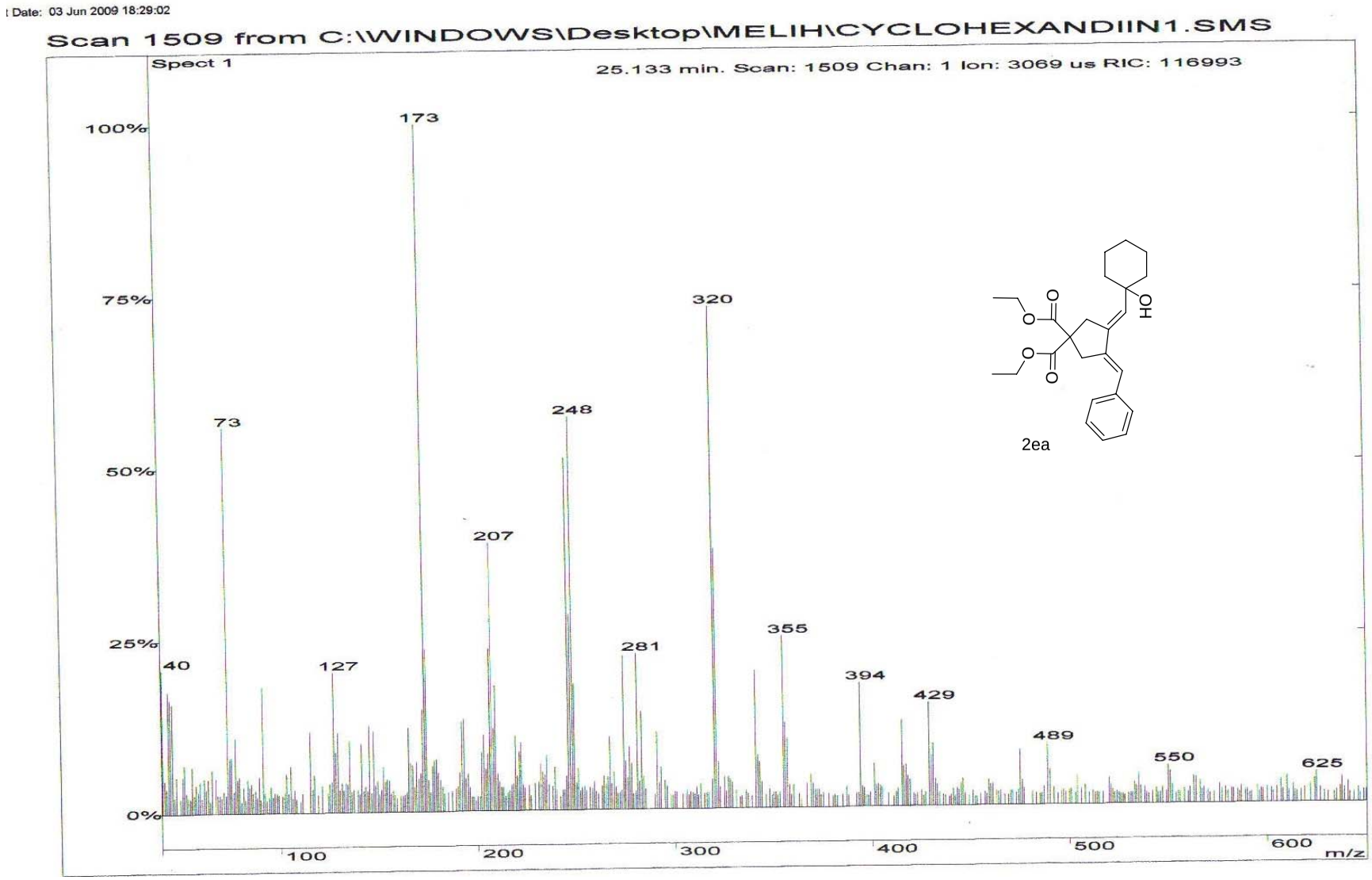

Figure B.15.GC-MS Spectrum of (3E,4E)-diethyl 3-benzylidene-4-((1-hydroxycyclohexyl)methylene)cyclopentane-1,1-dicarboxylate

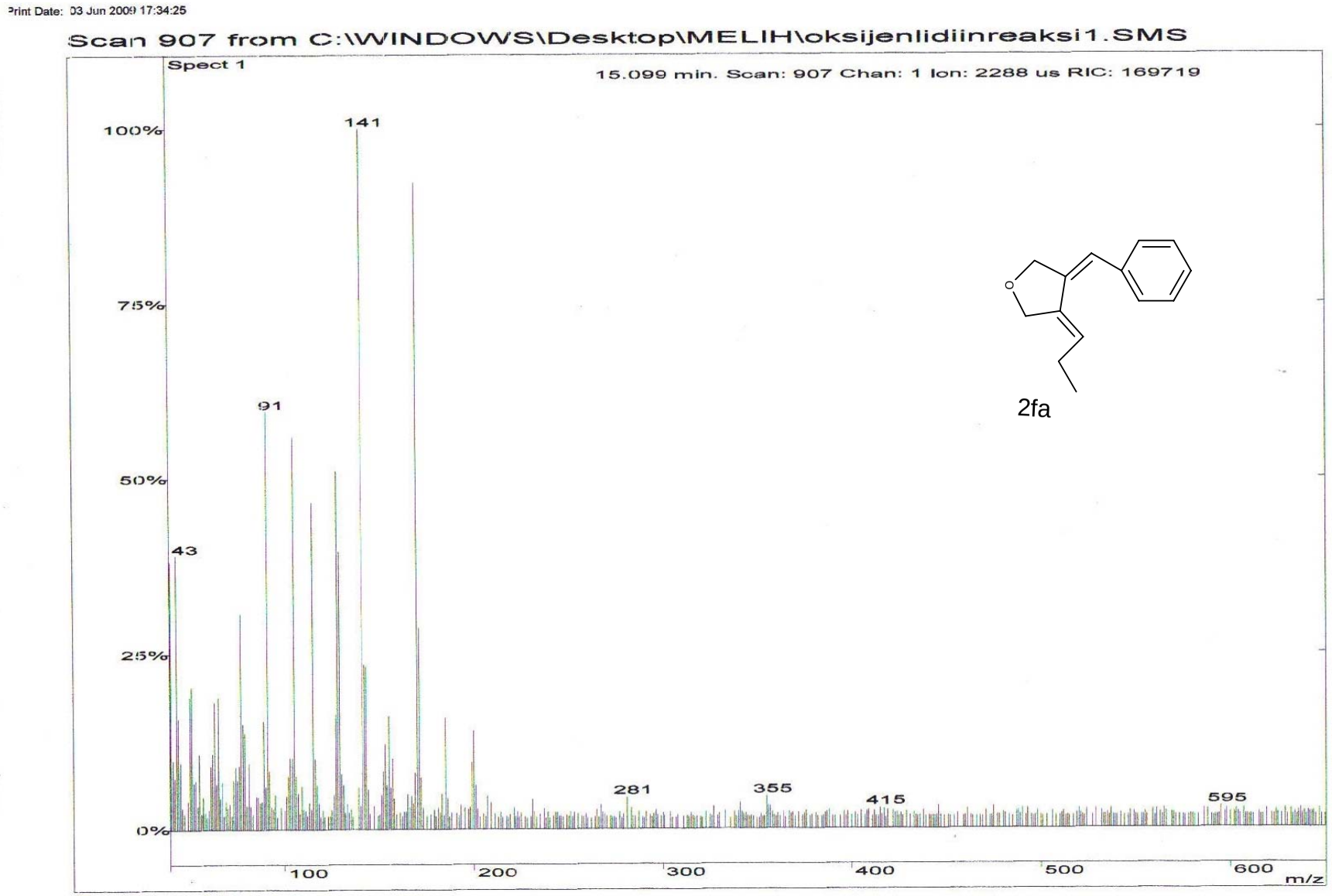

Figure B.16. GC-MS Spectrum of (3E,4Z)-3-benzylidene-tetrahydro-4-propylidenefuran

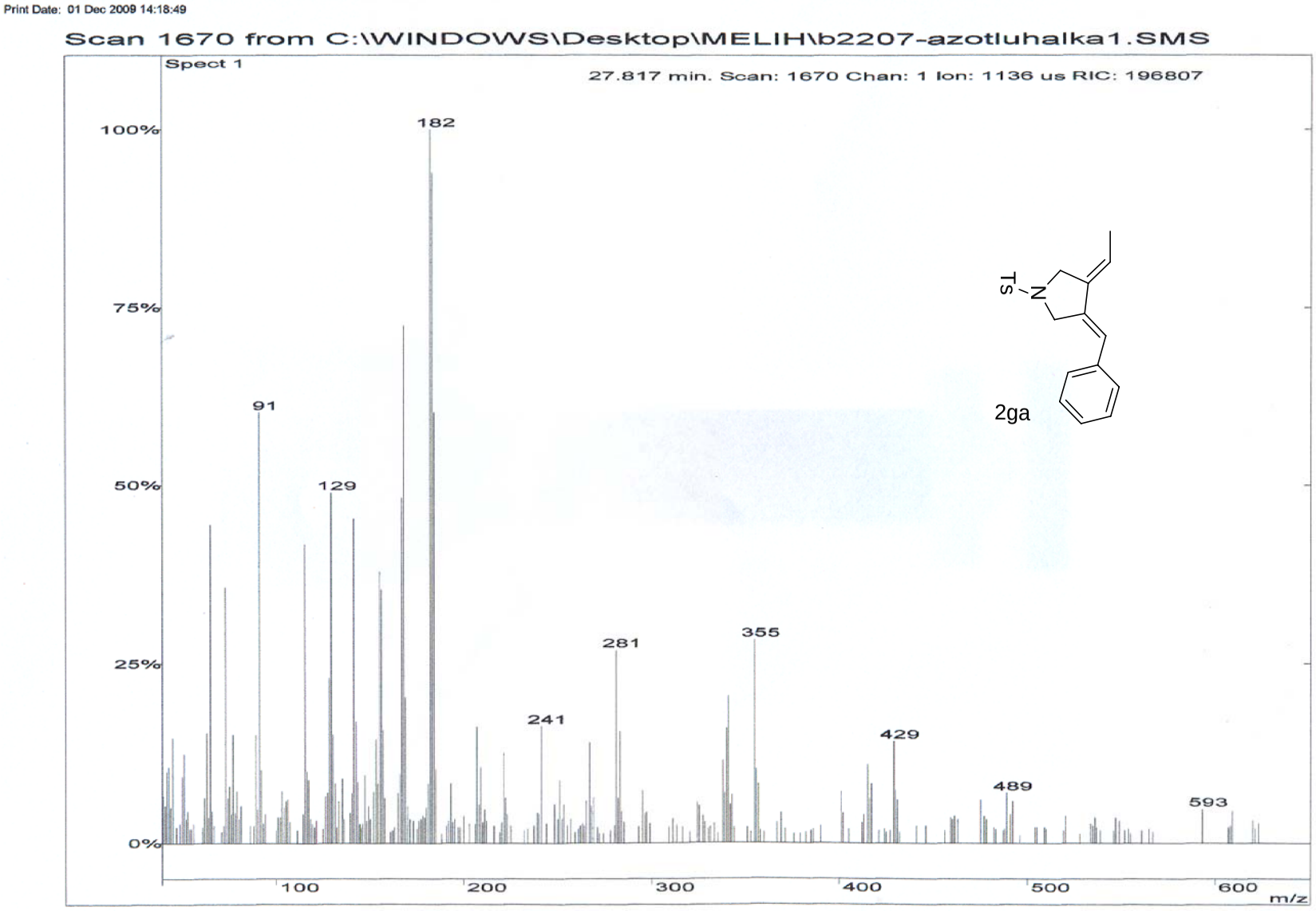

Figure B.17. GC-MS Spectrum of (3Z,4Z)- 3-benzylidene-4-ethylidene-1-tosylpyrrolidine

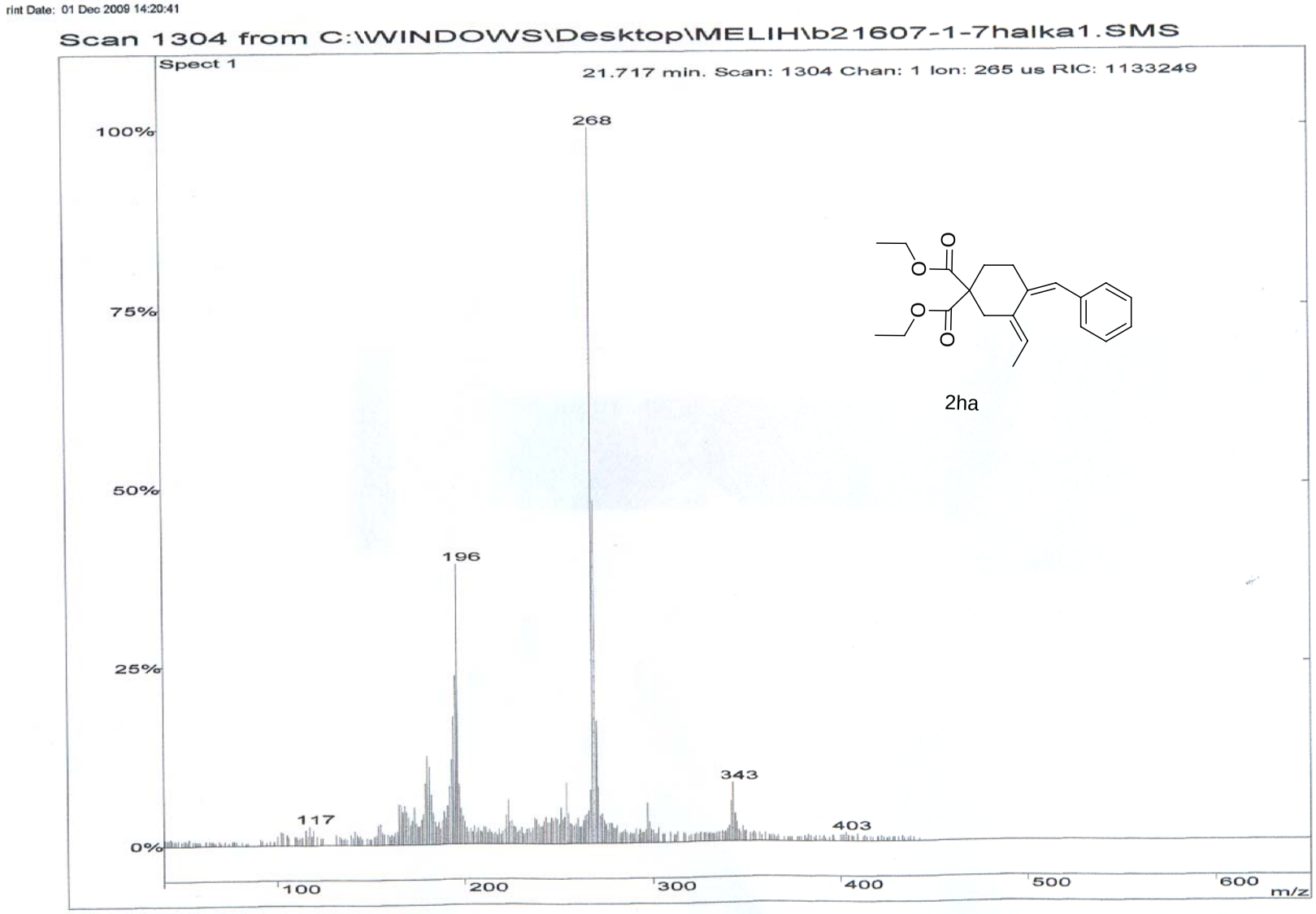

Figure B.18.GC-MS Spectrum of (3E,4Z)- diethyl-4-benzylidene-3-ethylidenecyclohexane-1,1-dicarboxylate

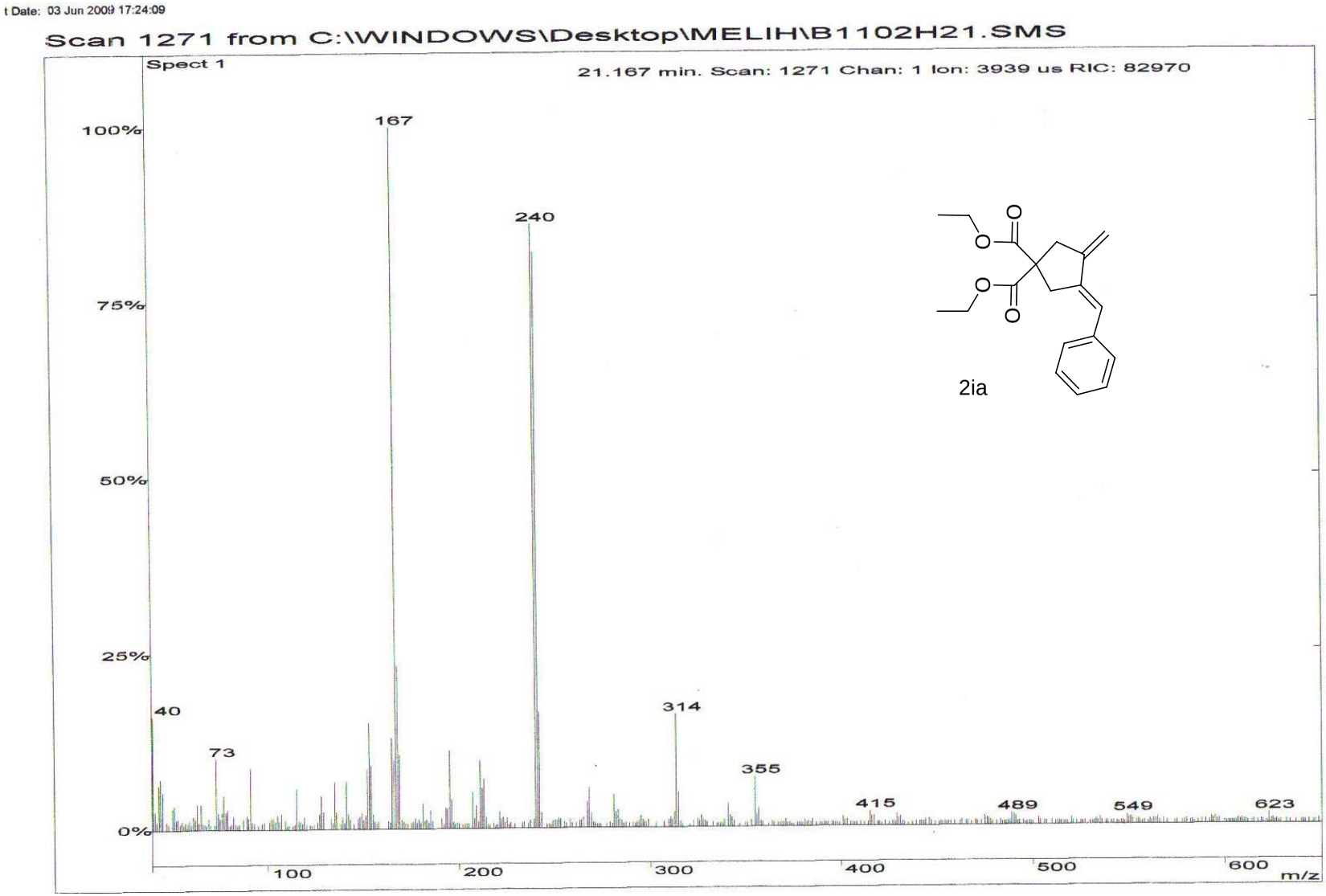

Figure B.19. GC-MS Spectrum of (3E)- diethyl-3-benzylidene-4-methylenecyclopentane-1,1-dicarboxylate

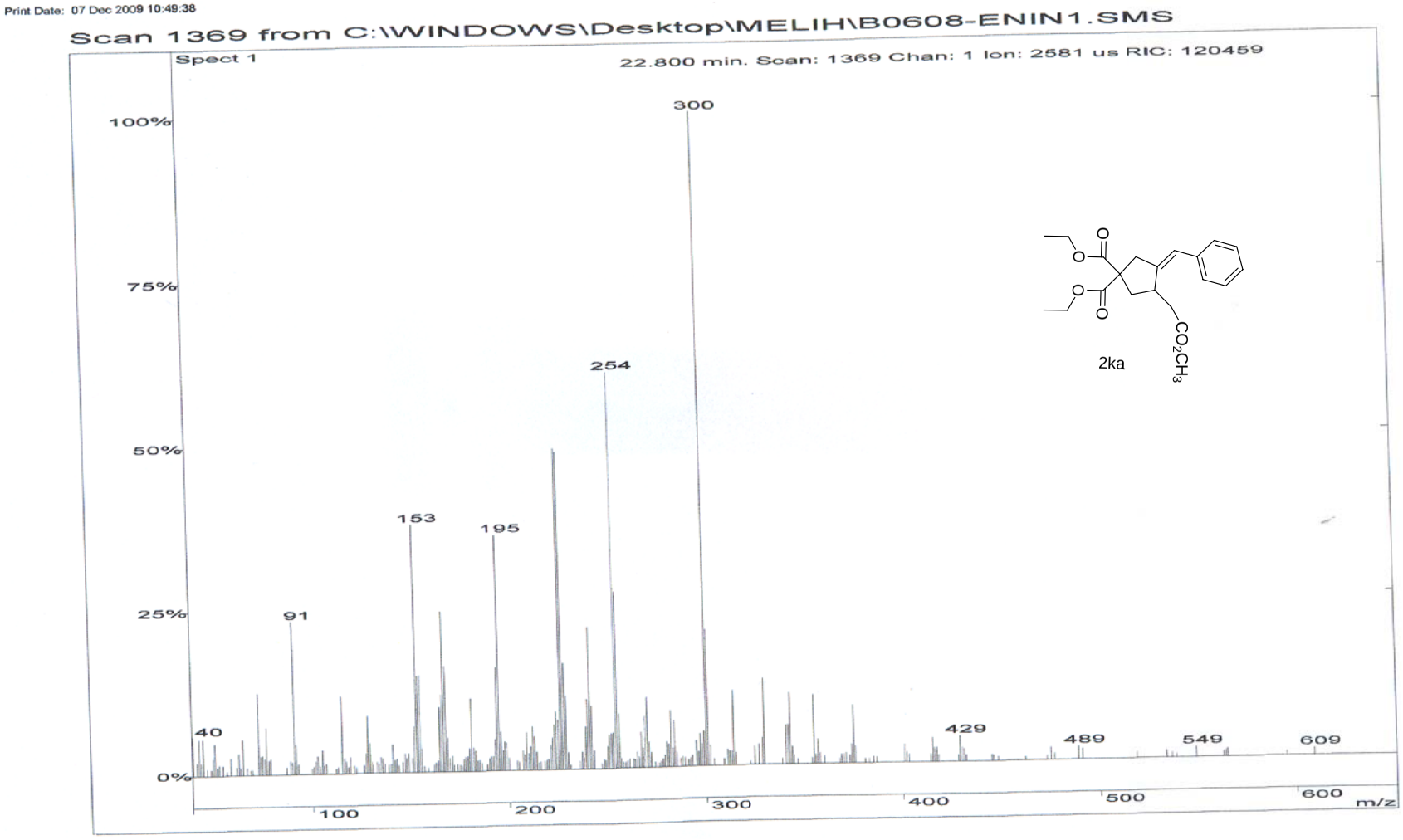

Figure B.20.GC-MS spectrum of (Z)- diethyl 3-((methoxycarbonyl)methyl)-4-benzylidenecyclopentane-1,1-dicarboxylate