SYNTHESIS OF α,β-UNSATURATED KETONES BY RHODIUM-CATALYZED CARBONYLATIVE ARYLATION OF INTERNAL ALKYNES WITH ARYLBORONIC ACIDS

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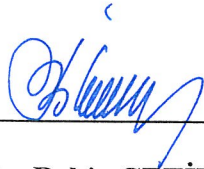
MASTER OF SCIENCE

in Chemistry

by
Melih KUŞ

July 2009
İZMİR

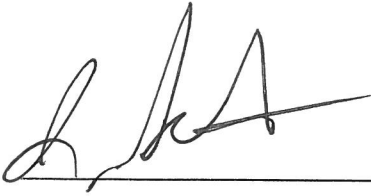We approve the thesis of **Melih KUŞ**

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ABSTRACT

SYNTHESIS OF α,β-UNSATURATED KETONES BY RHODIUM-CATALYZED CARBONYLATIVE ARYLATION OF INTERNAL ALKYNES WITH ARYLBORONIC ACIDS

α,β-Unsaturated ketones are important key reagents in organic synthesis. They are commonly synthesised through an aldol condensation reaction.

Since Hayashi et al. reported the first Rh-catalyzed addition of aryl- and alkenylboronic acids to α,β-unsaturated ketones, the Rh-catalyzed addition of organoboron reagents to various unsaturated systems has become increasingly popular as a method of constructing C–C bonds. Organoboron reagents readily undergo transmetalation with Rh to form arylrhodium(I) species that are capable of inducing the nucleophilic arylation of various electrophilic sites (Sakai, et al. 1997, Hayashi and Yamasaki 2003).

In this work, we have succesfully performed another example of the Rh-catalyzed reaction of arylboronic acids: a reaction of arylboronic acids with alkynes under a CO atmosphere to yield α,β-unsaturated ketones (Kuş, et al. 2008).
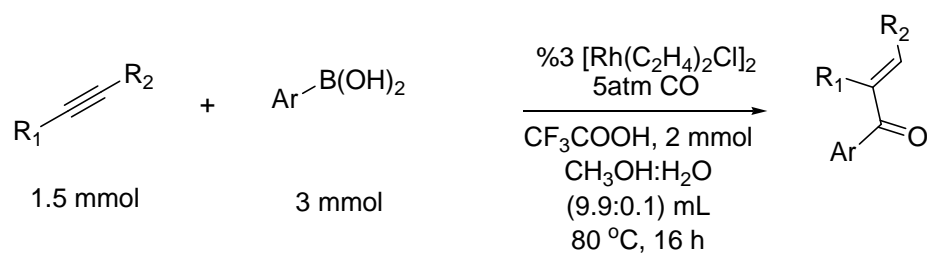
As a consequence, the methodology established in this study proposes a relatively mild and simple way for the synthesis of α,β-unsaturated ketones .

ÖZET

ALKİNLERİN ARİLBORONİK ASİTLER İLE RODYUM KATALİZLİ KARBONİLATİF ARİLASYONU İLE α,β-DOYMAMIŞ KETONLARIN SENTEZİ

α,β-doymamış ketonlar bir çok organik reaksiyonda çıkış maddesi olarak kullanılabilirler. α,β-doymamış ketonlar genellikle aldol kondensasyon reaksiyonları sonucu elde edilebilirler.

α,β-doymamış ketonlara alkenil ve arilboronik asitlerin rodyum katalizli katılma tepkimeleri ilk olarak Hayashi ve grubu tarafından gerçekleştirilmesinden itibaren organoboron reaktiflerinin çeşitli doymamış sistemlere rodyum katalizli katılma tepkimeleri karbon-karbon bağı oluşturan bir metod olarak her geçen gün daha önem kazanmaktadır. Organoboron reaktifleri rodyum ile hızla transmetalasyona uğrayarak arilrodyum(I) yapılarını oluştururlar ve yapılar çeşitli elektrofilik kısımlarından nükleofilik arilasyonu sağlarlar (Sakai, et al. 1997, Hayashi and Yamasaki 2003).

Biz bu çalışmada arilboronik asitlerin rodyum katalizli diğer bir tip tepkimesini başarıyla gerçekleştirdik. Bu tepkimede alkinlerin arilboronik asitler ile rodyum katalizli karbonilatif arilasyonu ile α,β-doymamış ketonlar sentezlendi (Kuş, et al. 2008).
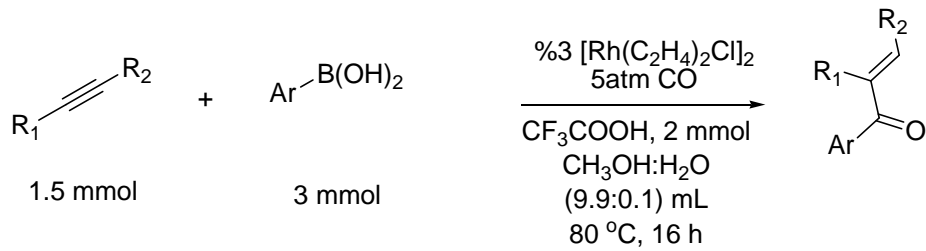
Sonuç olarak geliştirdiğimiz method α,β-doymamış ketonların sentezi için bizlere kolay ve ılımlı bir yol sağlamıştır.

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CHAPTER 1

INTRODUCTION

Addition of organometallic reagents to electrophilic systems is one of the most useful processes in organic synthesis. Often used organometallic reagents for these reactions are organolithiums, organomagnesiums, and organozincs in the presence of copper or nickel catalysts, usually give the desired conjugate addition products in high yields. The major problems are incompatibility with some functional groups, sensitivity of the organometallic substrates to air and noncatalyzed 1,2-addition as a competitive reaction. The use of an active catalyst in combination with a less reactive organometallic reagent like organoborons would solve these problems. Since the last decade, considerable efforts have been consumed on catalytic asymmetric conjugate addition (Sibi and Manyem 2000, Krause and Hoffmann-Röder 2001). The most successful example is given by Hayashi and co-workers, they achieved to add organoborons to unsaturated systems with high yield and enantioselectivity (Hayashi and Yamasaki 2003). The reaction has the advantage of permitting the introduction of sp^2 carbons to a wide range of electrophilic systems under mild reaction conditions.

In this thesis we have developed a mild and simple method for the rhodium-catalyzed carbonylative synthesis of α,β-unsaturated ketones by using various alkynes and arylboronic acids. This method offered both atom economy and environmentally benign process for the synthesis of α,β-unsaturated ketones.

CHAPTER 2

TRANSITION METAL CATALYZED REACTIONS OF ORGANOBORONS

2.1. Cataytic Cycle of Rhodium and Group 10 Metals

Generalized Catalytic Cycle for Ni, Pd and Pt Catalysts

$R\text{-}R'$ $M^{(0)}$ $R\text{-}X$

Cycle A

$R\text{-}M^{(II)}\text{-}R$ $X\text{-}M^{(II)}\text{-}R$

$M'X$ $R'\text{-}M'$
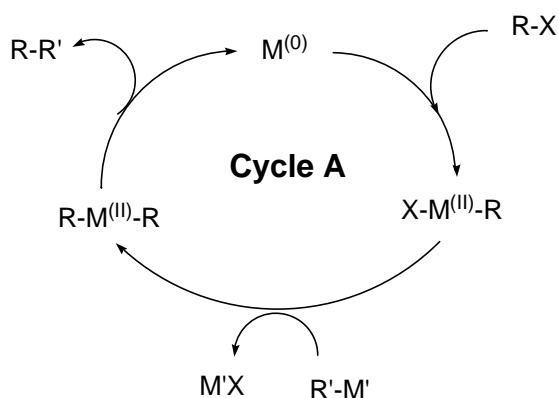
Possible Catalytic Cycles with Rh Catalysts

$R'\text{-}R$ $H\text{-}Y\text{-}R'\text{-}R$

$Rh^{(I)}X$ $H\text{-}X$

$R\text{-}M$

Cycle B   **Cycle C**

$R'\text{-}Rh^{(III)}\text{-}R$
X $Rh^{(I)}\text{-}Y\text{-}R'\text{-}R$

MX

$Rh^{(I)}\text{-}R$

$R'\text{-}X$ $R'=Y$

Figure 2.1. Generalized catalytic cycle for Rh and group 10 metals

When generalized catalytic cycles of nickel, palladium, platinum and rhodium catalysts are compared it is clear that rhodium presents new and interesting catalytic possibilities. In general nickel, platinum, and palladium typically operate within catalytic cycles shuttling between the (0) and (II) oxidation states. As a result, transmetalation can only occur with the metal(II) species. To design viable reactions, organometal(II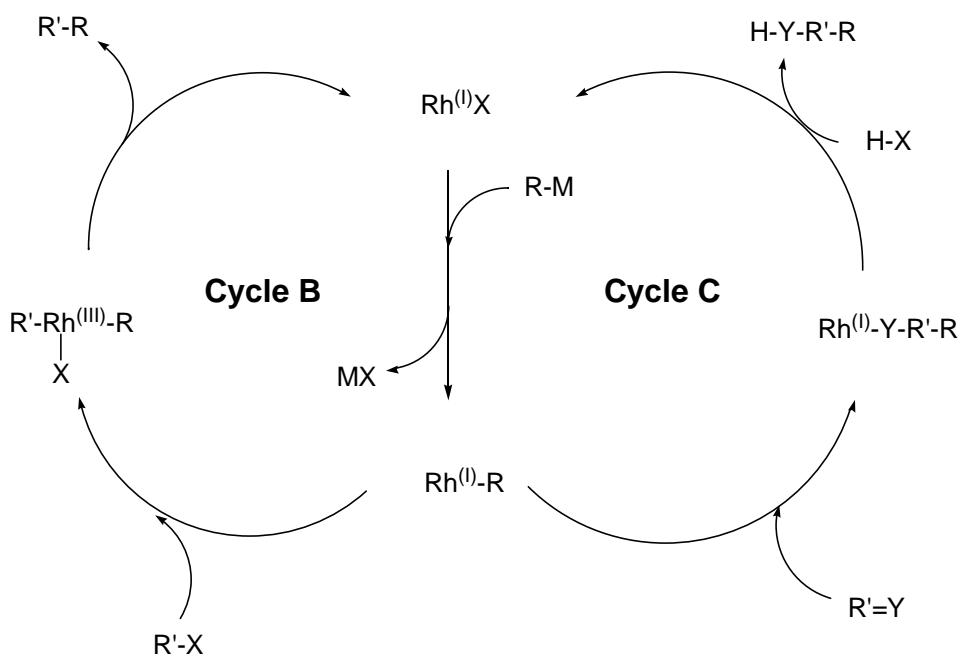) species should be produced so it is clear that a suitable electrophilic component must be incorporated that will oxidatively add to the metal(0) complex in order to produce organometal(II) species. After this step in order to undergo transmetalation with the metal(II) complex an organometallic component must be selected to subsequently reductively couple with the electrophile. The result is a catalytic cycle illustrated in Figure 2.1 as cycle A.

In contrast to nickel, platinum, and palladium, rhodium typically shuttles between the (I) and (III) oxidation states in catalytic reactions with organometallics. So theoretically transmetalation can occur at two points in the catalytic cycle. Transmetalation can occur with rhodium(I) to generate an organorhodium-(I) complex capable of reacting in new ways instead of an electrophile that will oxidize the metal in the early stages of the catalytic cycle.

Because oxidative addition is still a viable pathway, addition of a suitable electrophile will produce a catalytic cycle illustrated as Figure 2.1 cycle B. As illustrated in Figure 2.1 cycle C, the organorhodium complex could be coupled with units of unsaturation in organic compounds. This possibility takes advantage of the protic lability of rhodium-heteroatom and rhodium-carbon bonds. The outcome of cycle C is a net R,H-addition across the unsaturated unit.

The catalytic processes described in Figure 2.1 is the ability of several organometallics to undergo transmetalation with rhodium(I) and rhodium(III) complexes. Such processes are useful to understanding how rhodium can behave catalytically. In Figure 2.1, the newly generated organorhodium complex, Rh-R, is proposed to react both by oxidative insertion of suitable electrophiles and by the insertion of unsaturated species into the rhodium-carbon bond.

2.2. Boronic Acids

Boronic acids and their derivatives are the most useful classes of organoboron molecules. Unlike many organometallic derivatives, boronic acids are usually stable to air and moisture and they have relatively low toxicity and environmental impact. According to whether the boron-oxygen or the carbon-boron bonds are involved, the reactions of boronic acids can be divided into two categories.

2.2.1. Reactions involving the B-O bonds

Boroxine formation : Most boronic acids readily undergo dehydration to form cyclictrimeric anhydrides (boroxines). This tends to occur spontaneously at room temperature.
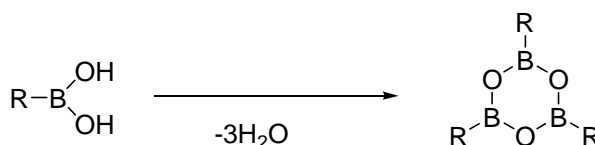

Figure 2.2. Boroxine formation

Boronate formation : The ease with which boronic acids react with diols, to give cyclic boronic esters (boronates) has led to their application in a number of areas, especially in organic transformations (Figure 2.3).
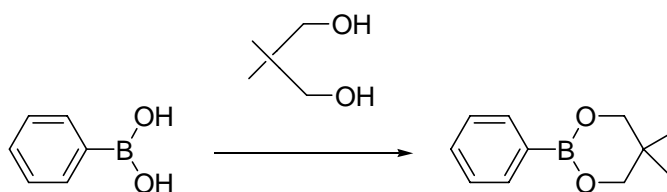

Figure 2.3. Boronate formation

2.2.2. Most known reaction involving the C-B bond: Suzuki-Miyaura Reaction

In these reactions, displacement of boron by an electrophilic species takes place with formation of a new carbon-carbon or carbon-heteroatom bond.

The discovery by Suzuki and Miyaura that arylboronic acids undergo palladium-catalyzed cross-coupling with aryl halides in the presence of a base (Figure 2.4) has stimulated enormous interest in the application of this type of coupling reactions.

$$R_1-BY_2 \ + \ R_2-X \ \xrightarrow[\text{Base}]{\overset{\text{Pd}}{\text{catalyst}}} \ R_1-R_2$$
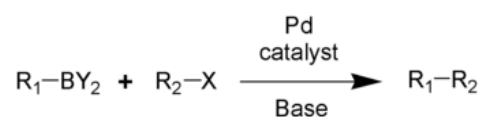
Figure 2.4. Suzuki and Miyaura reaction

Previously many of the methods employed for such syntheses involve the direct coupling of highly-reactive organometallic reagents (Grignard, organolithium, etc.) with aryl halides in the presence of various catalysts. Such reactions are of limited utility, since the presence of many functional groups interferes. On the other hand, boronic acids which are air-stable materials of relatively low toxicity, will undergo the Suzuki reaction in the presence of a wide variety of functional groups. The successful coupling of the more readily available, but normally unreactive aryl chlorides has been achieved under modified conditions, using either palladium (Shen 1997, Littke and Fu 1998) or nickel catalysts (Indolese 1997, Saito, et al. 1997).

A catalytic cycle for the Suzuki reaction is outlined in Figure 2.5.
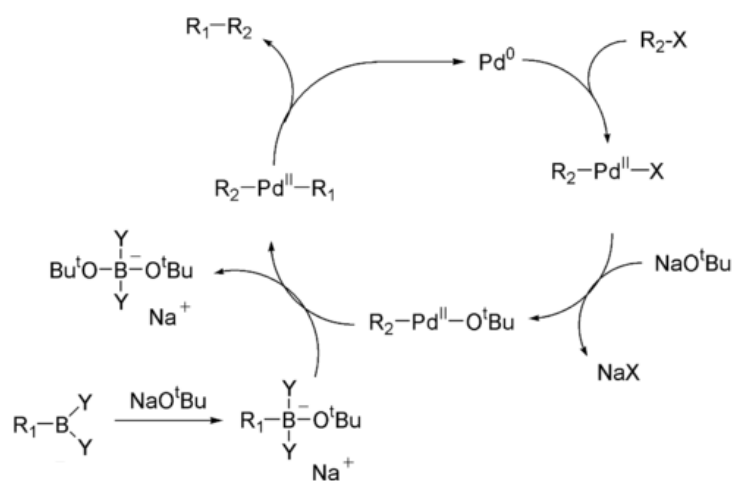
Figure 2.5. Suzuki and Miyaura reaction mechanism

The addition of organometallic reagents to unsaturated systems is an important method for the construction of new carbon-carbon bonds. Reactions of transition metals in combination with organoborons have become increasingly popular method for this type of construction. It is known that organoboron reagents readily undergo transmetalation with Rh to form arylrhodium(I) species that are capable of inducing the nucleophilic arylation of various electrophilic species. Although organocopper complexes have been widely used as an arylating species other related reactions induced by transition metals with organoboron reagents provided additional applications and extension of this type of reactions.

2.3. Structural Properties of Aryl-Rhodium Complexes

Several crystal structures of aryl-rhodium complexes have been examined with various kinds of ligands. To minimize the steric interactions between the aryl group and the adjacent ligands the orientation of the aryl ring should be orthogonal to the square plane of the complex. (Figure 2.6)
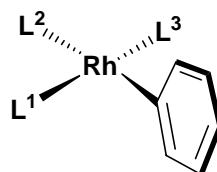
Figure 2.6. Rhodium-aryl complexes characterized crystallographically

Also in Figure 2.7 it can be easily observed that *ortho*-substituents on the arene situated above or below the square plane block the vacant coordination sites. When bulky *ortho* substituents are present the rate of associative ligand processes with these complexes may retard. Bidentate binding of the arene becomes possible when an *ortho*-substituent bearing lone pair electrons exists. For example in Figure 2.7, as a result of the *ortho*-methoxy group binding to the rhodium metal this complex is proposed to possess a trigonal bipyramidal structure. Higher air and thermal stability is achieved with compared to the phenyl analogue as a result of this binding mode (Jones and Wilkinson 1979).
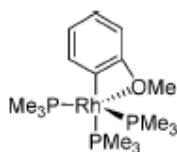

Figure 2.7. Effect of o-substituent
(Source: Jones and Wilkinson 1979)

2.4. Reactions of Aryl-Rhodium Complexes

Almost all of the rhodium catalyzed carbon-carbon bond forming reactions, a common side reaction is the catalytic demetalation of the organometallic component due to the use of protic media. These demetalations are catalyzed by the rhodium metal and occur because the aryl-rhodium bond can be more sensitive to protonolysis than the original organometallic compound from which it is derived

2.4.1. Carbon-Carbon Bond Forming Processes where Rhodium Undergoes a Change in Oxidation

Hegedus and co-workers reported a rhodium-mediated alkylation/arylation reaction of carboxylic acid chlorides. Treatment of aryl-rhodium complex with acetyl chloride in THF at -78 °C generates benzophenone in good yield with regeneration of the rhodium-chloride complex. The mechanism was proposed as octahedral rhodium(III) complex was formed via oxidative addition of the acid chloride followed by reductive elimination of the acyl and aryl ligands. Compared to the corresponding rhodium-chloride, the high reactivity of the aryl-rhodium complex toward oxidative addition is illustrated by the fact that the rhodium-chloride complex is inert toward the acid chlorides under these conditions (Hegadus, et al. 1973).
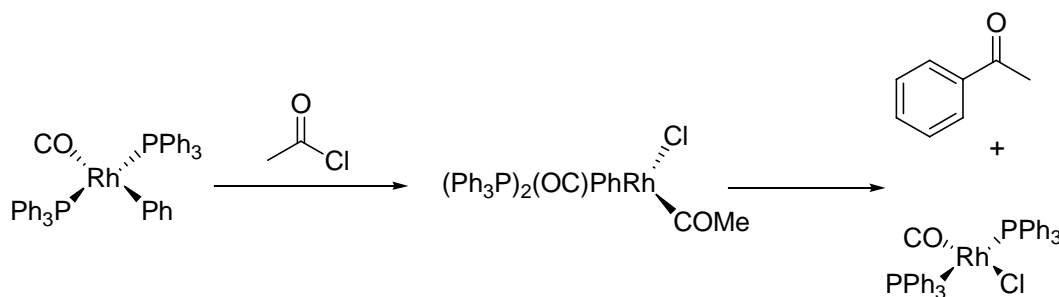
Figure 2.8. Rhodium-mediated alkylation/arylation reaction of carboxylic acid chlorides
(Source: Hegadus, et al. 1973)

A similar type of reaction using alkyl halides as the electrophilic component reported by Schwartz, et al. in 1972. For the generation of rhodium (III) complex, vinyl-rhodium complex could be reacted with iodomethane. Reductive elimination of the vinyl and methyl ligands by heating generates a new carbon-carbon bond with retention of alkene stereochemistry (Schwartz, et al. 1972).
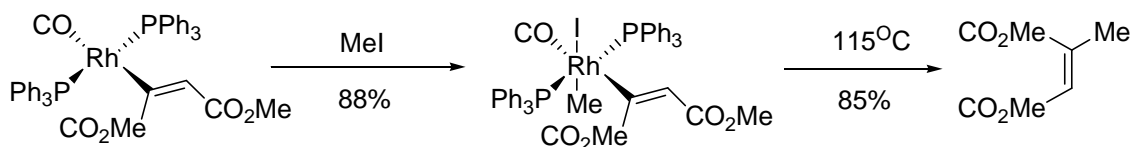
Figure 2.9. Rh-catalyzed alkylation using alkyl halides as an electrophilic component
(Source: Schwartz, et al. 1972)

2.4.2. Carbon-Carbon Bond Forming Reactions Through the Formation of an Aryl-Rhodium Intermediate

In organic chemistry addition of organometallics to unsaturated system is an important process. In this regard the use of metal catalysts in combination with an organometallic reagent has been particularly effective. Although the most commonly used metal is copper, (Alexakis 1998, Krause 2001) works with other metals have appeared in recent years. Frequently as the organometallic component like grignard reagents, organolithiums, or diorganozincs are employed while they provide high yields in many cases like chemoselectivity and limits in their use.

Of particular importance, copper catalysts and Grignard or diorganozinc reagents have significant advances in arylative addition reactions, but for the success with these reagents the use of low temperatures and strictly anhydrous reaction conditions are required. Rhodium catalyzed reactions represent an attractive alternative to these other type addition reactions because these reactions are insensitive to the presence of water, occur under mild conditions, and can be carried out with a wide range of substrates.

In 1997, the important progress was achieved by Miyaura and co-workers. They reported that rhodium(I) complexes catalyze the 1,4-addition of aryl and alkenyl boronic acids to enones in excellent yield. They examined a variety of ligands by using [Rh(acac)(CO)$_2$] as the rhodium(I) source. Bis(phosphine) ligands possessing large bite angles were shown to give the best results. Providing good reactivity the presence of water was required. Associated with these reactions enals could undergo selectively 1,4-additions under a mild reaction conditions with high chemoselectivity (Sakai, et al. 1997).
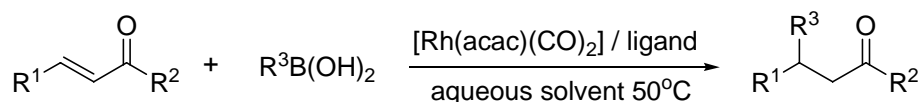
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Figure 2.10. Rh-catalyzed addition reaction of boronic acids to enones
(Source: Sakai, et al. 1997)

In 1998, the important progress was kept on. Hayashi and co-workers reported the first enantioselective variant of this transformation. To achieve high yields and enantioselectivity, the solvent was changed to a 10/1 mixture of dioxane and water, the temperature was increased to 100 °C, and the rhodium source was changed from [Rh(acac)(CO)$_2$] to [Rh(acac)(C$_2$H$_4$)$_2$] (Takaya, et al. 1997).
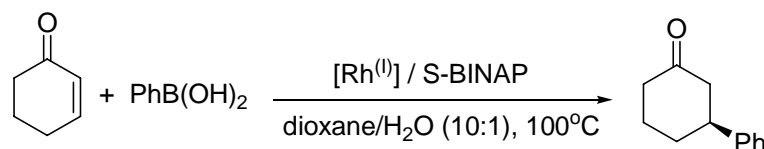

Figure 2.11. Enantioselective Rh-catalyzed addition reaction of boronic acids to enones
(Source: Takaya, et al. 1997)

It is known that reactions with acrylates were much less reactive than the corresponding enones. The reactivity was affected by the nature of the ester substituent. For example, treatment of the given acrylate (R: Me, Et) with 5 equiv of PhB(OH)$_2$ and catalytic [Rh(acac)(C$_2$H$_4$)$_2$]/(S)- BINAP in dioxane/water (10/1) at 100 °C leads to complete consumption of starting materials. However when R is isopropyl or *tert*-butyl, the product is obtained in only 42 and 21% yields, respectively. Consumption of the nucleophile prior to complete reaction of reactant is the reason of the poor results with large ester substituents. This is the result of competitive deboronation of the phenylboronic acid. Changing the nucleophile to a lithium phenylborate species generated in situ from phenyllithium, trimethylborate, and water gives better results (Takaya, et al. 1999).

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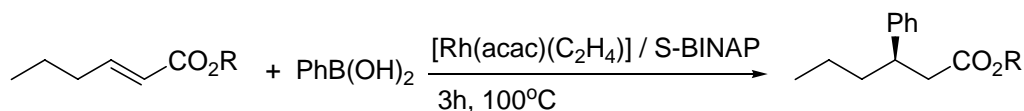
Figure 2.12. Rh-catalyzed addition reaction of boronic acids to acrylates
(Source: Takaya, et al. 1999)

Compared to enones, like acrylates α,β-unsaturated amides also suffered from poor reactivity. A study on the effects of additives revealed that complete conversion can occur by the use of an aqueous base. According to the authors the addition bases will influence the transformation of the Rh(acac) precatalyst into the Rh(OH) catalyst (Sakuma and Miyaura 2001).
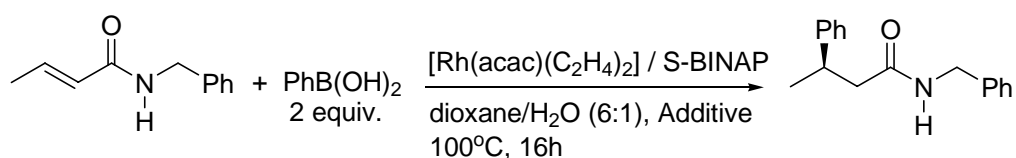

Figure 2.13. Rh-catalyzed addition reaction of boronic acids to α,β-unsaturated amides
(Source: Sakuma and Miyaura 2001)

Slightly modified conditions were required in these reactions for α,β-unsaturated lactams to be employed as substrates. For the synthesis of (-)-paroxetine which is a biologically active species, Hayashi and co-workers envisioned that 1,4-addition of a 4-fluorobenzene nucleophile to lactam giving the product enantioselectively. The reaction of lactam with $4\text{-}FC_6H_4\text{-}B(OH)_2$ gave 17% yield. The low yield was caused from the instability of the 4-fluorophenyl rhodium(I) intermediate toward protonolysis which is resulted in consumption of the arylboronic acid prior to complete reaction of lactam. To overcome this problem, Hayashi found that performing the reaction at 40 °C instead of 100 °C and also by using 4-fluorophenylboroxine in combination with only 1 equiv of water relative to boron, the product could be obtained in 63% yield and 97% ee (Senda, et al. 2001).
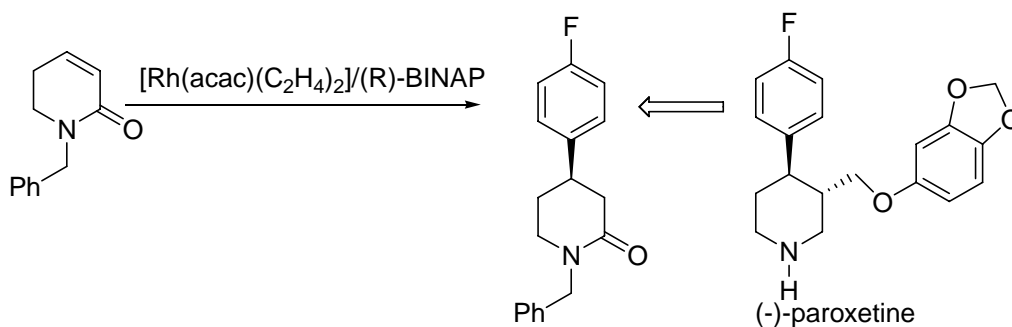
Figure 2.14. Rh-catalyzed addition reaction of boronic acids to α,β-unsaturated lactams
(Source: Senda, et al. 2001)

Also Hayashi noted that theorically using arylboroxines in combination with 1 equiv. of water should give the same result with the corresponding arylboronic acid with no water added. Against all odds, the yields were regularly higher when the boroxine/ water mixture was employed.
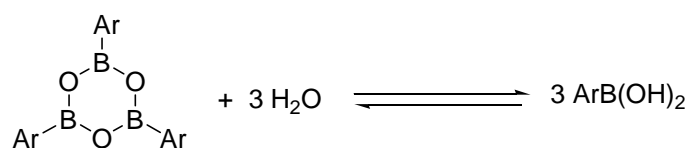
Figure 2.15. Formation of arylboronic acids from aryl boroxines

In asymmetric catalysis alkenylphosphonates have not received the same level of attention compared to other Michael acceptors. The first examples of asymmetric additions to alkenylphosphonates were reported by Hayashi, in 1999. High yields and excellent enantioselectivities could be obtained by using a catalyst generated from [Rh(acac)(C$_2$H$_4$)$_2$] and (S)-BINAP. The solvent system of dioxane and water (10:1) that typically employed was found to deactivate the catalyst and provide the product in only 44% isolated yield and 84% ee. The large excess of water present in the medium was responsed in this catalyst inactivation. Using phenylboroxine, (PhBO)$_3$, as the nucleophile instead of pheylboronic acid and using only 1 equiv of water relative to boron, the product was obtained in 94% yield and 96% ee. No reaction occurred under anhydrous conditions showed us that the small amount of water is essential for good conversion (Hayashi, et al. 1999).
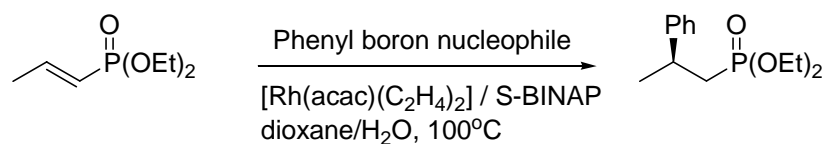
Figure 2.16. Rh-catalyzed addition reaction of boronic acids to alkenylphosphonates
(Source: Hayashi, et al. 1999)

Because of their low reactivity, activated alkenes bearing R-substituents were typically not employed in these types of reactions. Recently, the rhodium-catalyzed asymmetric 1,4-addition of arylboronic acids to R-substituted nitroalkenes was performed by Hayashi and co-workers. Treatment of 1-nitrocyclohexene with 5 equiv of phenylboronic acid and catalytic [Rh(acac)(C$_2$H$_4$)$_2$]/(S)-BINAP in a dioxane/water mixture (10/1) at 100 °C for 3 h gives the corresponding product in 79% yield as an 87/13 mixture of cis/trans isomers and >98% ee (Hayashi, et al. 2000).
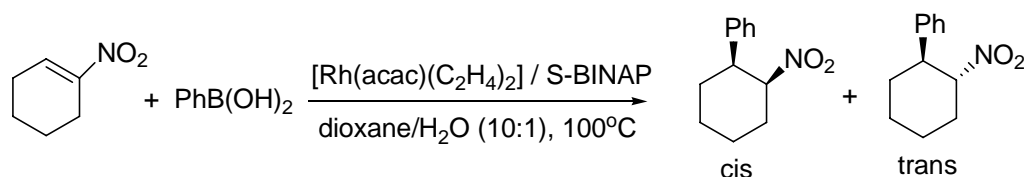
Figure 2.17. Rh-catalyzed addition reaction of boronic acids to 1-nitroalkenes
(Source: Hayashi, et al. 2000)

Unsaturated systems are considered as electrophilic systems. And Hayashi has described a rhodium-catalyzed hydroarylation reaction of internal alkynes that gives trisubstituted alkenes in high yield and *E*-selectivity (Hayashi, et al. 2001).
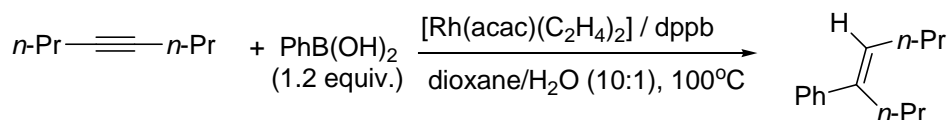
Figure 2.18. Rh-catalyzed addition reaction of boronic acids to alkynes
(Source: Hayashi, et al. 2001)

All of these results show that an aryl group attached to a rhodium acts as a nucleophile and induces the nucleophilic arylation with various electrophiles. From this point of view transmetalation of arylboron species with the catalyst (Rh) and followed

by insertion into CO which is an electrophilic species forms an aroylrhodium intermediate as in shown Figure 2.19.
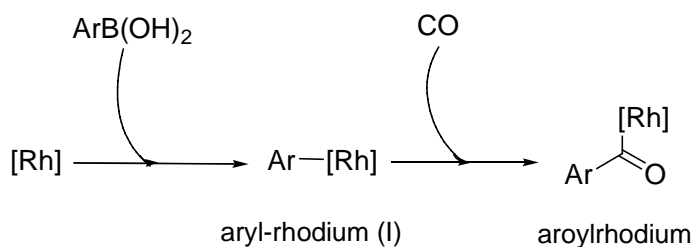
Figure 2.19. Formation of aroyl-rhodium species

Aroylrhodium species now act as nucleophile and attack various electrophiles especially unsaturated systems. This type of mechanism leads to a reaction type which is named as "Carbonylative Arylation."

Transition metal catalyzed carbonylation type reactions are important methods for the synthesis of carbonyl compounds. The most common used transition metals are rhodium and palladium. The most common reactions are Pd(0) catalyzed carbonylation and Rh(I) catalyzed nucleophilic addition type reactions. In the formation of active arylation complex, behaviour of palladium is different than rhodium.

In Pd(0) catalyzed reactions, active arylation complex is formed via oxidative addition of Pd(0) to arylhalides.
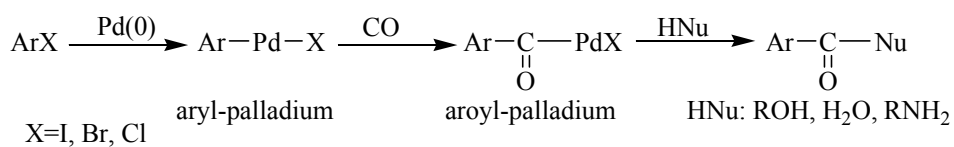
Figure 2.20. Formation of arylative complex with Pd

After oxidative addition of Pd(0) to aryl halide, aryl palladium is formed, addition of this species to carbon monoxide resulted in the formation of aroyl-palladium intermediate. Aroyl-palladium behaves as an electrophile and depending on the nucleophile the carbonyl containing compounds are formed. But behaviour of Pd(II) is different than Pd(0) and similar to Rh(I). The Pd(II) is coordinated to π-electrons of the

unsaturated systems. This coordination activating unsaturated hydrocarbons toward nucleophilic attacks.

Carbonylation of aryl chlorides requires harsher conditions than other C–C coupling reactions because of the presence of a good π-acceptor ligand like CO, which not only reduces the tendency towards oxidative addition at the metal centre but may also promote the formation of palladium clusters. The introduction of basic ligands also overcomes the problem of palladium agglomeration and palladium clustering (Rodriguez, et al. 2005).
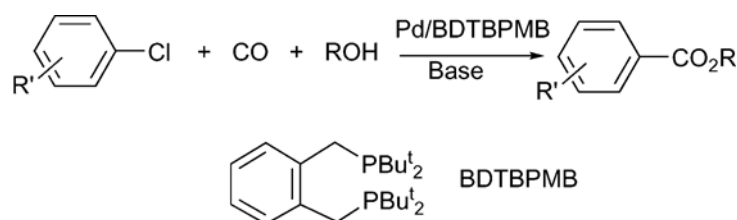
Figure 2.21. Pd-catalyzed carbonylative synthesis of esters
(Source: Rodriguez, et al. 2005)

Acrylamides are valuable monomers which are used to produce several important polymeric materials. An alternative method for the direct and clean synthesis of substituted acrylamides could be the carbonylation of alkynes in the presence of amines. Matteoli et al. reported that the carbonylation of phenylacetylene has been studied in the presence of the catalytic system formed by palladium acetate in combination with (2- pyridyl) diphenylphosphine and methanesulfonic acid. The catalytic activity is strongly influenced by the nature of the amine, good reaction rates are achieved using amines of low basicity such as aniline (Matteoli, et al. 2004).
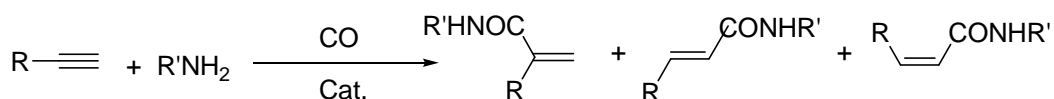
Figure 2.22. Pd-catalyzed carbonylative synthesis of acrylamides
(Source: Matteoli, et al. 2004)

Alkenes can be converted into carboxylic acids with carbon monoxide and water or in acidic medium using palladium catalysts. Effects of different palladium precursor systems as well as the influence of the phosphorus ligand on the hydroxycarbonylation

of styrene have been studied. Mono- and diphosphines behave differently when they are used as ligands in this reaction and it has been proposed that there may be two catalytic systems. Regioselectivity in linear or branched acids can be controlled by using diphosphines or monophosphines, respectively (Claver, et al. 2000).
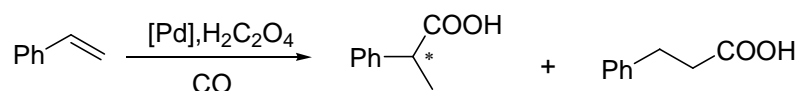
Figure 2.23. Pd-catalyzed carbonylative synthesis of carboxylic acids
(Source: Claver, et al. 2000)

The carbonylative esterification reaction of 1-alkynes, CO, and methanol catalyzed by palladium–phosphine complexes has been studied in acetonitrile media. Branched α,β-unsaturated ester was mainly produced in the presence of a catalytic amount of a palladium complex containing PPh_3 (Akao, et al. 2000).
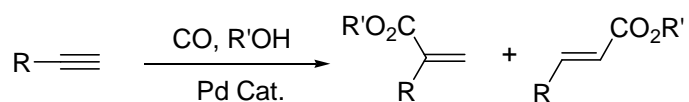
Figure 2.24. Pd-catalyzed carbonylative synthesis of α,β-unsaturated esters
(Source: Akao, et al. 2000)

Negishi and co-workers showed that Pd-catalyzed carbonylation of alkynes in the presence of aryl halides and a base resulted in the formation of γ-lactams (Negishi, et al. 1995).
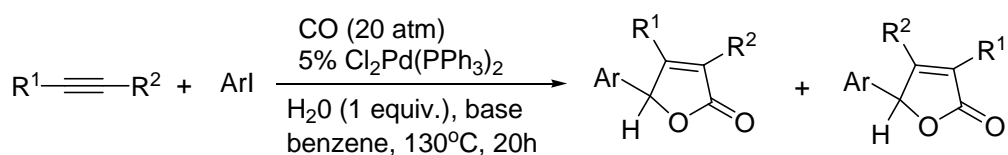
Figure 2.25. Pd-catalyzed carbonylative synthesis of γ-lactams
(Source: Negishi, et al. 1995)

Another work was reported by Miura and co-workers that aryl iodides undergo cross-carbonylation with five-membered cyclic olefins, in the presence of palladium catalysts to give the corresponding aryl ketones (Satoh, et al. 1995).
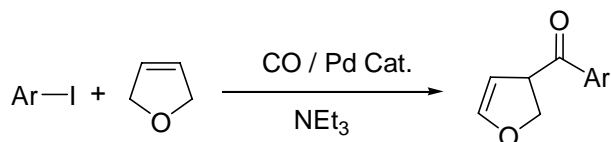
Figure 2.26. Pd-catalyzed carbonylative synthesis of aryl ketones
(Source: Satoh, et al. 1995)

Although the major limitation to the carbonylative approach of the Suzuki reactions often lies in the formation of significant amounts of biaryl products, which results from direct coupling without carbon monoxide insertion, Castanet and co-workers have shown that the carbonylative Suzuki cross-coupling of pyridyl iodides and bromides with arylboronic acids yielded pyridyl aryl ketones in good yields (Bonnaire, et al. 2003).
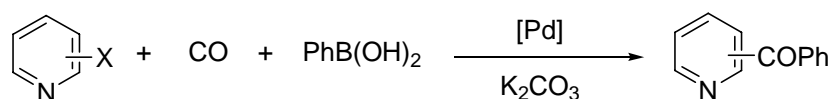
Figure 2.27. Pd-catalyzed carbonylative Suzuki cross-coupling of pyridyl iodides and bromides with arylboronic acids (Source: Bonnaire, et al. 2003)

And also Miyaura and co-workers showed that, carbonylative cross-coupling reaction of arylboronic acids with aryl electrophiles (ArI, ArBr,and ArOTf) to yield unsymmetrical biaryl ketones in the presence of a palladium catalyst and a base (Ishiyama, et al. 1998).
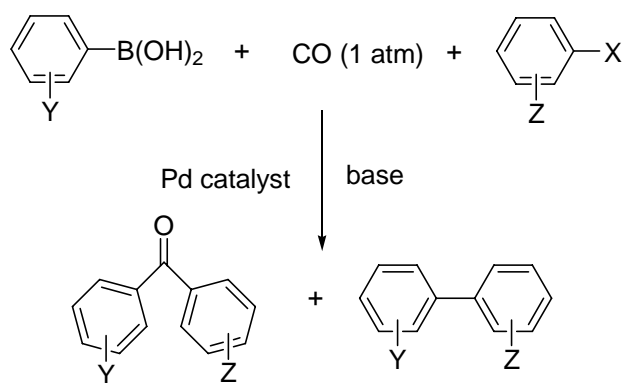
Figure 2.28. Pd-catalyzed carbonylative cross-coupling reaction of arylboronic acids with aryl electrophiles (Source: Ishiyama, et al. 1998)

In case, in the presence of rhodium complex, active arylation complex, aryl-rhodium is formed via the transmetalation between rhodium and organoboron species. Aryl-rhodium species can be carbonylated to led to an aroyl rhodium intermediate which shows nucleophilic character.
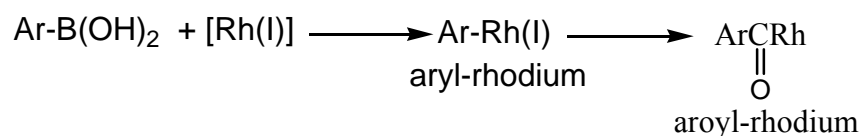
Figure 2.29. Formation of aroyl-rhodium species from arylboronic acids

These in-situ formed aroyl-rhodium species have been shown to react with methyl vinyl ketones to yield 1,4-diketones (Sauthier, et al. 2004), and with terminal alkynes to yield α,β-unsaturated ketones (Dheur, et al. 2007). The reactions of internal alkynes with arylboronic acids under 20 atm CO was shown to proceed through consecutive aroylation and carbonylative cyclization to form butenolides (Aksin, et al. 2006).
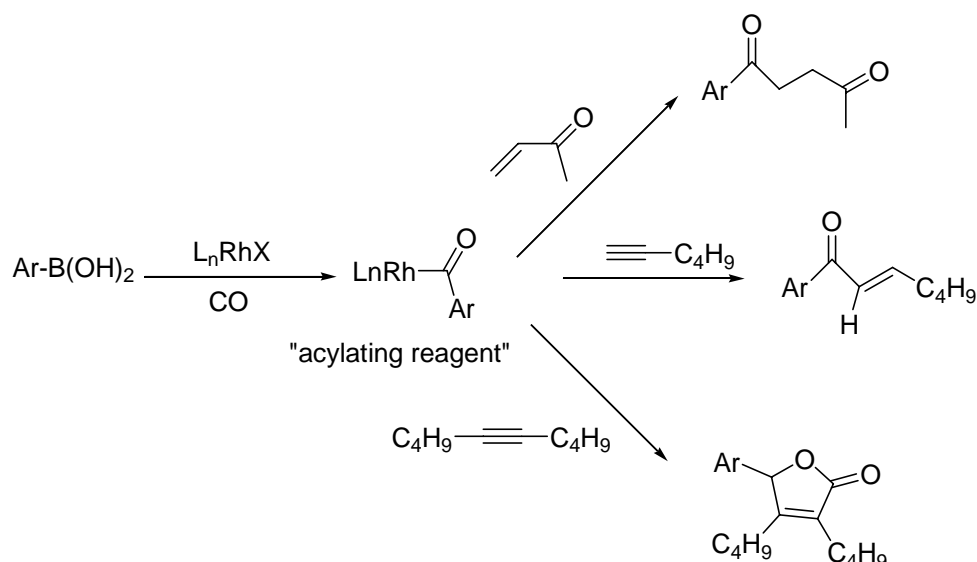
Figure 2.30. Rh-catalyzed carbonylative arylation of unsaturated systems
(Source: Dheur, et al. 2007)

An important report was shown by Chatani and co-workers in the development of a new carbonylation reaction of alkynes with 2-bromophenylboronic acid leading to the formation of indenones. The reaction involves a consecutive Rh-catalyzed regioselective addition of an arylrhodium(I) species to alkynes and the oxidative addition of C-Br bonds in the adjacent phenyl ring to the resulting vinylrhodium(I) species as key steps (Harada, et al. 2007).
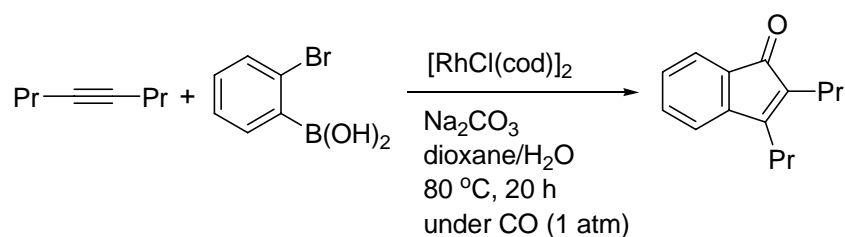
Figure 2.31. Rh-catalyzed carbonylative arylation of alkynes with 2-bromophenylboronic acids (Source: Harada, et al. 2007)

Job and co-workers have reported the catalytic preparation of 3,4-disubstituted 2(5H)-furanones by the rhodium-catalyzed reductive carbonylation of alkynes under water-gas shift reaction conditions. When a mixture of alkyne and a catalytic amount of $Rh_6(CO)_{16}$, in the presence of Et_3N in THF was heated under a pressure of CO, 3,4-diphenyl-2(5H)-furanone was obtained in a good yield (Job, et al. 1994).
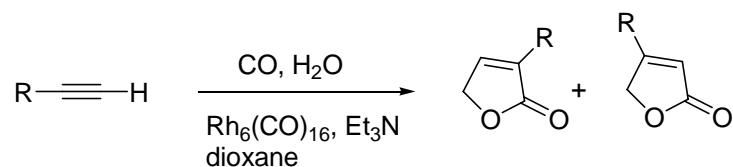
Figure 2.32. Rh-catalyzed reductive carbonylation of internal alkynes
(Source: Job, et al. 1994)

Hayashi and co-workers describe that a rhodium catalyzed regioselective coupling of ortho-carbonylated arylboronic acids and alkynes under mild conditions, to gives indenols in relatively high enantioselectivity (Shintani, et al. 2005).
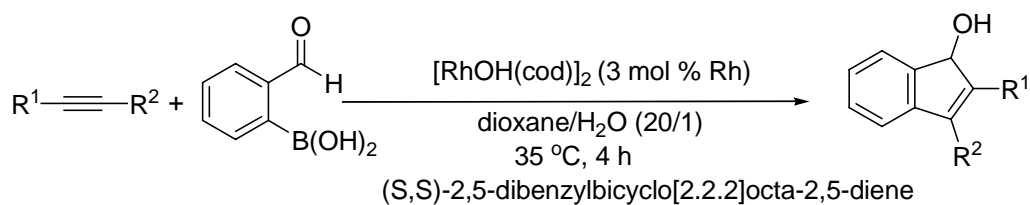
Figure 2.33. Rh-catalyzed coupling of *ortho*-carbonylated arylboronic acids and alkynes
(Source: Shintani, et al. 2005)

CHAPTER 3

EXPERIMENTAL STUDY

3.1. General Procedures for Synthesis of Alkynes by Sonogashira C-C Coupling Reactions

Given procedure is representative procedure for the synthesis of alkynes **1h**, **1i**, **1j** and **1k** by Sonogashira reaction. (See appendices D) Aryl halide (bromo or iodo, 10 mmol) and alkyne (12 mmol) in 40 mL Et$_3$N was added 2 mol % Pd(PPh$_3$)$_2$Cl$_2$ with respect to the aryl halide. The mixture was stirred at room temperature for five minutes, after that 1 mol % CuI was added to the mixture. Then reaction flask was placed in a preheated oil bath at 50 ^{o}C and vigorously stirred under an argon atmosphere. The reaction was periodically followed by GC until the reaction was stopped when no further increase in the formation of coupling product was observed or all alkyne was consumed. The solution was cooled to the room temperature, and filtration was done in order to get rid of the ammonium salts and the solution was concentrated in vacuo under reduced pressure. Then the residue was purified by column chromatography on silica gel to give the pure product (Roesch and Larock 2001).

3.2. General Procedure for Drying of Solvents

For 200 ml MeOH, 1 g Mg-turnings, 100 mg iodine and 10 mL methanol was put into a 250 mL round-bottom flask. The mixture was heated under inert atmosphere until the iodine colour and the Mg-turnings disappear. Added more iodine (100 mg) if Mg-turnings did not disappear. Then the remainder MeOH (190ml) was added. The

solution was refluxed for 3 hours and it was distilled onto 3A sieve beads (10% w/v). and stored at least 1 day before using it (Leonard, Lygo and Procter 1998).

3.3. General Procedure for Rh Catalyzed Carbonylative Addition Reactions of Arylboronic Acids to Alkynes

4-Chlorobenzeneboronic acid, 4-Methoxyphenylboronic acid, 4-Methylphenylboronic acid, 4-(triflouro)methyl phenylboronic acid 1-phenyl-1-propyne, methyl-2-butynoate, methyl-2-heptynoate, ethyl phenylpropiolate, 4,4-dimethyl-2-pentyne were supplied from Alfa Aesar. Diphenylacetylene, bis(ethylene)rhodium(I) chloride dimer (53% Rh) and tetradecane were supplied from Merck. 3-Tolylboronic acid was supplied from Acros, 4-Octyne was suppiled from ABCR and 1-phenyl-1-pentyne was supplied from Avocado. Phenylboronic acid was supplied from Fluka. 4-Methoxyphenylboronic acid (Percec et al. 2001; Li et al. 2002) and $[Rh(C_2H_4)_2Cl]_2$ (Cramer et al. 1974) were also synthesized in our laboratory according to literature.

A mixture of arylboronic acid (3 mmol), alkyne (1.5 mmol), $[Rh(C_2H_4)_2Cl]_2$ (3 mol% Rh), CF_3COOH (2 mmol), and tetradecane (0.5 mmol, as an internal standard) in 10mL solvent (9.9:0.1-MeOH:H_2O, pre-dried and degassed before used) was added into glass insert which was then placed into a stainless-steel reactor. Reactor was evacuated and purged with 5 atm CO twice. Then reactor was pressurized to 5 atm with CO and the mixture was stirred magnetically in a pre-heated oil bath. After cooling reactor, the reaction mixture was recovered with ethyl acetate. After that, a sample was taken from reaction mixture and diluted with ethyl acetate, then analyzed by GC and GC-MS and isolated by flash chromatography.

3.4. Characterization of Products

3.4.1. GC Method

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

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

3.4.1.1. Calculation of Reactant and Product Amount on GC

For the calculation of amount of reactants and products, response factor of each reactant and product for the set temperature program of GC was determined. As internal standard, tetradecane was used. The amount of internal standard does not change throughout the reaction, so the response factor of each compound was determined according to the amounts and areas under the peaks of internal standard and standard compound of interest. For the determination of response factor of a compound, a known amount of standard compound together with a known amount of internal standard dissolved and diluted with ethyl acetate, and then was injected to GC. After the analysis was complete according to the set temperature program, the equation (3.1) was used for the determination of response factor of that compound.

$$R.F. \quad = \quad \frac{\text{internal standart area}}{\text{compound area}} \quad x \quad \left(\frac{\text{compound amount}}{\text{internal standart amount}} \right) \qquad (3.1)$$

In order to calculate the amount of both reactant and products at the end of reaction, aliquots of reaction sample taken from the glass-reactor and diluted samples were injected to GC. At the end of GC analysis, taking the amount of tetradecane and the area under the tetradecane peak into account, equation (3.2) was used in order to calculate the amount of reactant and products at the end of reaction:

$$\text{amount of compound} \quad = \quad \left(\frac{\text{internal standart amount}}{\text{internal standart area}} \right) \quad x \ R.F. \ x \ \text{compound area} \qquad (3.2)$$

3.4.1.2. Calculation of Reactant Conversion, Product Yield and Recovery

Reactant conversion at any time is calculated using equation 3.3:

$$(\text{Reactant Conversion})_t \% \quad = \quad \frac{\left((\text{Reactant})_i - (\text{Reactant})_t \right)}{(\text{Reactant})_i} \quad x \ 100 \qquad (3.3)$$

where $(\text{reactant})_i$ is the weight of reactant at the beginning of the reaction and $(\text{reactant})_t$ is the weight of reactant at time t.

Product yield of a molecule was calculated according to the following equation 3.4:

$$\text{Product Yield} \quad = \quad \frac{\text{mole of product}_t}{\text{initial mole of alkyne}} \qquad (3.4)$$

3.5. Other Methods

All products were determined by NMR (Varian VnmrJ 400), FT-IR (Perkin-Elmer Spectrum 100), GC-MS (GC-Varian star 3400CX, MS-VarianSaturn 2000 Gc-Ms-Ms), HPLC-ESI-HRMS, GC-EI-HRMS and DI-EI-HRMS (direct inlet ionization), (Thermo Electron). Melting Points were determined using an Electrothermal Melting Point Apparatus 9200.

(E,Z)-1,2,3-triphenylprop-2-en-1-one (3aa): Hexane/ethyl acetate; **(E-3aa):** white solid; M.P. (°C): 98.7-99.2 (lit.: 99-101,[7a] 103-103.5,[7b] 96.5-97.5[7c]); ^{1}H NMR (400 MHz, CDCl$_3$) δ: 7.07-7.56 (m, 14H), 7.86 (d, J = 7.2 Hz, 2H); ^{13}C NMR (100 MHz, CDCl$_3$) δ: 126.4, 128.0, 128.2, 128.4, 128.7, 128.8, 128.9, 129.7, 130.1, 133.6, 135.4, 136.3, 138.0, 140.8, 199.4; MS (EI, m/z): 284 (93, M$^+$), 256 (5), 206 (9), 178 (31), 105 (100), 77 (20); FTIR (ATR) ν (cm^{-1}) CO 1649 (lit.: 1661,[7a] 1640[7c]); HRMS (m/z, M$^+$): 284.1196 (calculated), 284.1189 (found); **(Z-3aa):** yellow solid; M.P. (°C): 78.0-84.1 (lit.: 85-87,[7a] 88-89,[7b] 82.5-83.5[7c]); ^{1}H NMR (400 MHz, CDCl$_3$) δ: 7.10-7.50 (m, 14H), 7.99 (d, J = 6.8 Hz, 2H); ^{13}C NMR (100 MHz, CDCl$_3$) δ: 127.9, 128.2, 128.3, 128.8, 128.9, 129.7, 129.8, 130.3, 132.2, 134.8, 136.5, 138.2, 140.1, 140.8, 197.6; MS (EI, m/z): 284 (87, M$^+$), 256 (7), 206 (20), 178 (47), 105 (100), 77 (83); FTIR (ATR) ν (cm^{-1}) CO: 1660 (lit.: 1671,[7a] 1661[7c]); HRMS (m/z, M$^+$): 284.1196 (calculated), 284.1197 (found).

(E,Z)-1-(4-methoxyphenyl)-2,3-diphenylprop-2-en-1-one (3ab): Hexane/benzene; hexane/dichloromethane; **(E-3ab):** white solid; M.P. (°C): 81.1-84.3 (lit.: 84-84.3[7c]); ^{1}H NMR (400 MHz, CDCl$_3$) δ: 3.85 (s, 3H), 6.92 (d, J = 8.8 Hz, 2H), 7.09-7.36 (m, 11H), 7.90 (d, J = 8.8 Hz, 2H); ^{13}C NMR (100 MHz, CDCl$_3$) δ: 55.5, 113.6, 127.9, 128.2, 128.6, 128.8, 129.6, 130.2, 130.4, 132.3, 135.0, 136.8, 137.8, 141.0, 163.1, 196.3; MS (EI, m/z): 314 (47, M$^+$), 197 (14), 178 (14), 135 (100), 107 (9), 92 (10), 77 (19); FTIR

(ATR) ν (cm^{-1}) CO: 1633 (lit.: 1640[7c]); HRMS (*m/z*, M$^+$): 314.1301 (calculated), 314.1294 (found); **(Z-3ab):** pale yellow solid; M:P. (°C): 88.7-89.2 (lit.: 78-79[7c]); ^{1}H NMR (400 MHz, CDCl$_3$) δ: 3.79 (s, 3H), 6.83 (d, *J* = 8.8 Hz, 2H), 7.12-7.48 (m, 11H), 7.97 (d, *J* = 8.8 Hz, 2H); ^{13}C NMR (100 MHz, CDCl$_3$) δ: 55.4, 114.0, 126.3, 127.9, 128.1, 128.4, 128.8, 129.4, 129.5, 132.1, 135.5, 138.2, 140.9, 164.0, 197.9; MS (EI, *m/z*): 314 (58, M$^+$), 197 (18), 178 (19), 135 (100), 107 (12), 92 (13), 77 (23); FTIR (ATR) ν (cm^{-1}) CO: 1657 (lit.: 1655[7c]). HRMS (*m/z*, M$^+$): 314.1301 (calculated), 314.1301 (found).

(E,Z)-2,3-diphenyl-1-*p*-tolylprop-2-en-1-one (3ac): Hexane/benzene; **(E-3ac):** white solid; M.P. (°C): 90.8-91.8; ^{1}H NMR (400 MHz, CDCl$_3$) δ: 2.41 (s, 3H), 7.08-7.39 (m, 13H), 7.79 (d, *J* = 8.0 Hz, 2H); ^{13}C NMR (100 MHz, CDCl$_3$) δ: 21.6, 126.3, 127.9, 128.2, 128.8, 128.8, 129.0, 129.6, 130.1, 130.3, 134.9, 135.3, 136.7, 139.1, 140.9, 143.0, 197.5; MS (EI, *m/z*): 298 (75, M$^+$), 283 (15), 205 (6), 181 (23), 178 (25), 119 (100), 91 (48); FTIR (ATR) ν (cm^{-1}) CO: 1643; HRMS (*m/z*, M$^+$): 298.1352 (calculated), 298.1346 (found); **(Z-3ac):** pale yellow solid; M.P. (°C): 59.8-61.8; ^{1}H NMR (400 MHz, CDCl$_3$) δ: 2.32 (s, 3H), 7.10-7.47 (m, 13H), 7.89 (d, *J* = 8.4 Hz, 2H); ^{13}C NMR (100 MHz, CDCl$_3$) δ: 21.7, 126.3, 128.0, 128.1, 128.5, 128.8, 129.5, 129.7, 129.9, 134.0, 135.5, 138.1, 141.0, 144.7, 199.0; MS (EI, *m/z*): 298 (100, M$^+$), 283 (12), 182 (20), 119 (55), 91 (11); FTIR (ATR) ν (cm^{-1}) CO: 1654; HRMS (*m/z*, M$^+$): 298.1352 (calculated), 298.1341 (found).

(E,Z)-2,3-diphenyl-1-*m*-tolylprop-2-en-1-one (3ad): Hexane/benzene; **(E-3ad):** further column chromatographed with hexane/ethyl acetate; white solid; M.P. (°C): 66.3-68.7; ^{1}H NMR (400 MHz, CDCl$_3$) δ: 2.40 (s, 3H), 7.06-7.38 (m, 13H); 7.64 (d, *J* = 7.6 Hz, 1H), 7.68 (s, 1H); ^{13}C NMR (100 MHz, CDCl$_3$) δ: 21.4, 127.06, 127.9, 128.08, 128.2, 128.8, 128.9, 129.7, 130.2, 130.3, 132.9 134.9, 136.6, 138.2, 138.2, 140.0, 140.9, 197.9; MS (EI, *m/z*): 298 (75, M$^+$); 283 (10), 181 (23), 178 (25), 119 (100), 91 (48); FTIR (ATR) ν (cm^{-1}) CO: 1635; HRMS (*m/z*, M$^+$): 298.1352 (calculated), 298.1351 (found); **Z-3ad:** yellow oil; ^{1}H NMR (400 MHz, CDCl$_3$) δ: 2.32 (s, 3H), 7.10-7.48 (m, 13H), 7.65 (d, *J* = 8 Hz, 1H), 7.83 (s, 1H); ^{13}C NMR (100 MHz, CDCl$_3$) δ: 21.3, 126.3, 127.3, 128.0, 128.1, 128.4, 128.6, 128.8, 129.9, 129.9, 134.5, 135.5, 136.3, 138.1,

138.5, 141.0, 199.5; MS (EI, *m/z*): 298 (92, M$^+$), 283 (11), 181 (25), 178 (30), 119 (100), 91 (33); FTIR (ATR) ν (cm^{-1}) CO: 1660; HRMS (*m/z*, M$^+$): 298.1352 (calculated), 298.1359 (found).

(E,Z)-1-(4-chlorophenyl)-2,3-diphenylprop-2-en-1-one (3ae): Hexane/ethyl acetate; **(E-3ae):** yellow paste; ^{1}H NMR (400 MHz, CDCl$_3$) δ: 7.05-7.45 (m, 13H), 7.78 (d, *J* = 8.4, 2H); MS (EI, *m/z*): 318 (100, M$^+$), 283 (27), 178 (55), 139 (52), 111 (25), 75 (13), 50 (10); FTIR (ATR) ν (cm^{-1}) CO: 1645; HRMS(*m/z*, M$^+$) 318.0806 (calculated); 318.0804 (found); **(Z-3ae):** yellow paste; ^{1}H NMR (400 MHz, CDCl$_3$) δ: 7.14-7.45 (m, 13H), 7.91 (d, *J* = 10.4, 2H); ^{13}C NMR (100 MHz, CDCl$_3$) δ:126.3, 128.2, 128.3, 128.5, 128.8, 128.9, 129.1, 129.2, 129.8, 130.4, 130.5, 131.0, 131.1, 134.7, 135.2, 137.7, 140.1, 140.3, 198.1; MS (EI, *m/z*): 318 (100, M$^+$), 283 (48), 178 (75), 139 (82), 111 (51), 75 (35), 50 (25); FTIR (ATR) ν (cm^{-1}) CO: 1665; HRMS(*m/z*, M$^+$) 318.0806 (calculated); 318.0805 (found).

(E)-1-phenyl-2-propylhex-2-en-1-one (3ba): Hexane/ethyl acetate; pale yellow oil; ^{1}H NMR (400 MHz, CDCl$_3$) δ: 0.94 (t, *J* = 7.4 Hz, 3H), 0.96 (t, *J* = 7.4 Hz, 3H), 1.41-1.52 (m, 4H), 2.27 (q, *J* = 7.2 Hz, 2H), 2.47 (t, *J* = 7.2 Hz, 2H), 6.20 (t, *J* = 7,6 Hz, 1H); 7.38-7.43 (m, 2H), 7.47-7.52 (m, 1H), 7.63-7.67 (m, 2H); ^{13}C NMR (100 MHz, CDCl$_3$) δ: 14.0, 14.1, 22.2, 28.7, 30.9, 128.0, 129.3, 131.4, 139.1, 141.2, 145.7, 199.0; MS (EI, *m/z*): 216 (100, M$^+$), 173 (7), 145 (9), 105 (27), 77 (5); FTIR (ATR) ν (cm^{-1}) CO: 1647; HRMS (*m/z*, M$^+$): 216.1509 (calculated), 216.1507 (found).

(E)-1-(4-methoxyphenyl)-2-propylhex-2-en-1-one (3bb): Hexane/ethyl acetate; pale yellow oil; ^{1}H NMR (400 MHz, CDCl$_3$) δ: 0.91-0.98 (m, 6H), 1.41-1.51 (m, 4H), 2.26 (q, *J* = 7.2 Hz, 2H), 2.46 (t, *J* = 7.6 Hz, 2H), 3.86 (s, 3H), 6.11 (t, *J* = 7.6 Hz, 1H), 6.91 (d, *J* = 8.8 Hz, 2H), 7.71 (d, *J* = 8.8 Hz, 2H); ^{13}C NMR (100 MHz, CDCl$_3$) δ: 14.0, 14.1, 22.2, 22.3, 29.2, 30.7, 55.4, 113.3, 131.4, 131.8, 141.1, 143.1, 162.6, 198.0; MS (EI, *m/z*): 246 (14, M$^+$), 203 (22), 175 (18), 135 (100), 107 (10), 92 (14), 77 (21); FTIR (ATR) ν (cm^{-1}) CO: 1641; HRMS: 246.1614 (calculated), 246.1603 (found).

(*E*)-2-propyl-1-p-tolylhex-2-en-1-one (3bc): Hexane/ethyl acetate; pale yellow oil; ^{1}H NMR (400 MHz, CDCl$_3$) δ: 0.94 (t, *J* = 7.6 Hz, 6H), 1.46 (sext, *J* = 7.6 Hz, 4H), 2.26 (q, *J* = 7.6 Hz, 2H), 2.40 (s, 3H), 2.46 (t, *J* = 8.0 Hz, 2H), 6.16 (t, *J* = 7.4 Hz, 1H), 7.21 (d, *J* = 8.0 Hz, 2H), 7.59 (d, *J* = 8.0 Hz, 1H); ^{13}C NMR (100 MHz, CDCl$_3$) δ: 14.0, 14.1, 21.5, 22.2, 22.3, 28.9, 30.8, 128.7, 129.6, 136.2, 141.2, 142.1, 144.6, 198.8; MS (EI, *m/z*): 230 (36, M$^+$), 215 (92), 201 (20), 187 (38), 173 (29), 159 (39), 145 (22), 119 (100), 91 (71); FTIR (ATR) ν (cm^{-1}) CO: 1645; HRMS (*m/z*, M$^+$): 230.1665 (calculated), 230.1662 (found).

(E)-methyl 3-(4-methoxyphenyl)hept-2-enoate (3cb): Hexane/ethyl acetate; pale yellow oil; NMR (400 MHz, CDCl$_3$) δ: 0.89 (t, *J* = 7.2 Hz, 3H), 1.40-1.50 (m, 4H), 2.98 (t, *J* = 7.6 Hz, 2H), 3.76 (s, 3H), 3.88 (s, 3H), 5.99 (s, 1H), 6.95 (d, *J* = 9.2 Hz, 2H), 7.84 (d, *J* = 9.2 Hz, 2H); ^{13}C NMR (100 MHz, CDCl$_3$) δ: 13.8, 22.9, 29.2, 30.5, 51.5, 55.5, 113.8, 122.0, 128.8, 132.2, 157.9, 163.9, 166.1, 196.5; MS (EI, *m/z*): 276 (28, M$^+$), 245 (20), 217 (22), 135 (100); FTIR (ATR) ν (cm^{-1}) CO: 1654, 1722 (-COOCH$_3$); HRMS: 276.1356 (calculated); 276.1355 (found)

(E)-methyl 4-(4-*p*-tolyl)-3-butyl-4-oxobut-2-enoate (3cc): Hexane/ethyl acetate, yellow oil; ^{1}H NMR (400 MHz, CDCl$_3$) δ: 0.9 (t, *J* = 7.4 Hz, 3H), 1.36-1.51 (m, 4H), 2.40 (s, 3H), 2.98 (t, *J* = 7.8 Hz, 2H), 3.76 (s, 3H), 6.0 (s, 1H), 7.27 (d, *J* = 8.0 Hz, 2H), 7.73 (d, *J* = 8.0 Hz, 2H); ^{13}C NMR (100 MHz, CDCl$_3$) δ: 13.8, 21.7, 22.9, 28.9, 30.5, 51.5, 122.9, 129.3, 130.0, 133.5, 144.3, 157.5, 166.1, 197.6; MS (EI, *m/z*): 260 (25, M$^+$), 245 (29), 229 (65), 214 (46), 119 (100); FTIR (ATR): ν (cm^{-1}): 1659 (CO), 1724 (COOCH$_3$); HRMS(*m/z*, M$^+$) 260.1407 (calculated); 260.1406 (found).

(*E*)-methyl 4-(4-methoxyphenyl)-3-methyl-4-oxobut-2-enoate (3db): Hexane/ethyl acetate; pale yellow oil; ^{1}H NMR (400 MHz, CDCl$_3$) δ: 2.42 (d, *J* = 1.6 Hz, 3H), 3.77 (s, 3H), 3.88 (s, 3H), 6.09 (q, *J* = 1.6, 1H), 6.95 (d, *J* = 9.2 Hz, 2H), 7.83 (d, *J* = 8.8 Hz, 2H); ^{13}C NMR (100 MHz, CDCl$_3$) δ: 16.0, 51.6, 55.5, 113.9, 123.0, 128.1, 132.2, 153.1, 163.9, 166.3, 196.5; MS (EI, *m/z*): 234 (16, M$^+$), 203 (20), 135 (100), 107 (10), 92 (10), 77 (10), 62 (9); FTIR (ATR) ν (cm^{-1}) CO: 1651, 1720 (-COOCH$_3$); HRMS: 234.0887 (calculated), 234.0884 (found).

(*E*)-2-methyl-1,3-diphenylprop-2-en-1-one (3ea): Hexane/ethyl acetate; yellow oil; ^{1}H NMR (400 MHz, CDCl$_3$) δ: 2.27 (d, *J* = 1.6, 3H), 7.18 (d, *J* = 1.6, 1H), 7.30-7.56 (m, 8H), 7.71-7.77 (m, 2H); ^{13}C NMR (100 MHz, CDCl$_3$) δ: 14.4, 128.2, 128.5, 128.6, 129.5, 129.7, 131.7, 135.8, 136.9, 138.5, 142.2, 199.5; MS (EI, *m/z*): 222 (100, M$^+$), 207 (33), 115 (32), 77 (48); FTIR (ATR) ν (cm^{-1}) CO: 1642; HRMS (*m/z*, M$^+$): 222.1039 (calculated), 222.1032 (found).

(*E*)-1-(4-methoxyphenyl)-2-methyl-3-phenylprop-2-en-1-one (3eb): Hexane/ethyl acetate; yellow oil; ^{1}H NMR (400 MHz, CDCl$_3$) δ: 2.25 (d, *J* = 1.6 Hz, 3H), 3.87 (s, 3H), 6.95 (d, *J* = 9.2 Hz, 2H), 7.10 (d, *J* = 1.6, 1H), 7.30-7.43 (m, 5H), 7.81 (d, *J* = 9.2 Hz, 2H); ^{13}C NMR (100 MHz, CDCl$_3$) δ: 14.9, 55.5, 113.5, 128.3, 128.4, 129.6, 130.7, 132.0, 137.0, 140.0, 162.8, 198.3; MS (EI, *m/z*): 252 (38, M$^+$), 135 (100), 145 (15), 115 (26); FTIR (ATR) ν (cm^{-1}) CO: 1638; HRMS: 252.1145 (calculated), 252.1138 (found).

(E)-2-methyl-3-phenyl-1-*p*-tolylprop-2-en-1-one (3ec): Hexane/ethyl acetate; yellow oil ^{1}H NMR (400 MHz, CDCl$_3$) δ: 2.26 (d, *J* = 1.6 Hz, 3H), 2.42 (s, 3H), 7.15 (d, *J* = 1.6 Hz, 1H), 7.27 (d, *J* = 8.0 Hz, 2H), 7.30-7.42 (m, 5H), 7.68 (d, *J* = 8.0 Hz, 2H); ^{13}C NMR (100 MHz, CDCl$_3$) δ: 14.6, 21.6, 128.5, 128.9, 129.7, 129.8, 135.6, 135.9, 137.0, 141.3, 142.4, 199.2; MS (EI, *m/z*): 236 (100, M$^+$), 219 (12), 119 (25); FTIR (ATR): ν (cm^{-1}) CO: 1642; HRMS(*m/z*, M$^+$) 236.1196 (calculated); 236.1194 (found).

3fb and 3fb': Hexane/ethyl acetate; **(*E*)-2-benzylidene-1-(4-methoxyphenyl)pentan-1-one (3fb):** pale yellow oil; ^{1}H NMR (400 MHz, CDCl$_3$) δ: 0.98 (t, *J* = 7.2 Hz, 3H), 1.57 (sext, *J* = 7.6 Hz, 2H), 2.71 (t, *J* = 7.8 Hz, 2H), 3.89 (s, 3H), 6.95 (d, *J* = 9.2 Hz, 2H), 6.98 (s, 1H), 7.30-7.42 (m, 5H), 7.85 (d, *J* = 9.2 Hz, 2H); ^{13}C NMR (100 MHz, CDCl$_3$) δ: 14.3, 22.0, 30.2, 55.5, 113.5, 128.1, 128.4, 129.1, 130.9, 132.1, 135.9, 138.5, 142.4, 163.0, 198.2; MS (EI, *m/z*): 280 (56, M$^+$), 251 (15), 173 (16), 135 (100); FTIR (ATR) ν (cm^{-1}) CO: 1636; HRMS: 280.1458 (calculated); 280.1460 (found). **(*E*)-1-(4-methoxyphenyl)-2-phenylhex-2-en-1-one (3fb'):** pale yellow oil; ^{1}H NMR (400 MHz, CDCl$_3$) δ: 0.92 (t, *J* = 7,2 Hz, 3H), 1.49 (sext, *J* = 7,6 Hz, 2H), 2.24 (q, *J* = 7.2 Hz, 2H), 3.85 (s, 3H), 6.35 (t, *J* = 7.4 Hz, 1H), 6.89 (d, *J* = 9.2 Hz, 2H), 7.23-7.38 (m, 5H), 7.81 (d, *J* = 9.2 Hz, 2H); ^{13}C NMR (100 MHz, CDCl$_3$) δ: 13.9, 22.5, 31.4, 55.4, 113.4, 127.3, 128.2, 129.4, 130.8, 132.2, 136.5, 141.6, 142.2, 162.9, 196.1; MS (EI, *m/z*): 280 (12,

M$^+$), 251 (39), 135 (100); FTIR (ATR) ν (cm^{-1}) CO: 1638; HRMS (*m/z*, M$^+$): 280.1458 (calculated), 280.1460 (found)

(E)-2-(4-methoxybenzylidene)-1-p-tolylhexan-1-one (3hc): Hexane/ethyl acetate; yellow paste; ^{1}H NMR (400 MHz, CDCl$_3$) δ: 0.93 (t, *J* = 7.2 Hz, 3H), 1.42 (sext, *J* = 7.2, 2H), 1.55 (pent, *J* = 7.6 Hz, 2H), 2.41 (s, 3H), 2.75 (t, *J* = 7.8 Hz, 2H), 3.82 (s, 1H), 6.92 (d, *J* = 8.8 Hz, 2H), 7.0 (s, 1H), 7.24 (d, *J* = 8.0 Hz, 2H), 7.33 (d, *J* = 9.2 Hz, 2H), 7.68 (d, *J* = 8.0 Hz, 2H); ^{13}C NMR (100 MHz, CDCl$_3$) δ: 13.9, 21.6, 23.0, 27.6, 30.9, 55.3, 113.9, 128.3, 128.8, 129.8, 130.3, 130.9, 136.2, 140.2, 140.2, 140.6, 142.3, 159.8, 199.2: MS(EI, *m/z*): MS (EI, *m/z*): 308 (100, M$^+$), 293 (14), 265 (10), 119 (32); FTIR (ATR): ν (cm^{-1}) CO: 1641; HRMS(*m/z*, M$^+$) 308.1771 (calculated); 308.1769 (found).

(E)-2-(2-methoxybenzylidene)-1-*p*-tolylhexan-1-one (3ic): Hexane/ethyl acetate; yellow oil: ^{1}H NMR (400 MHz, CDCl$_3$) δ: 0.87 (t, *J* = 7.2 Hz, 3H), 1.35 (sext, *J* = 7.6 Hz, 2H), 1.49 (pent, *J* = 7.6 Hz, 2 H), 2.40 (s, 3H), 2.65 (t, *J* = 7.2 Hz, 2H), 3.76 (s, 3H), 6.87 (d, *J* = 8.0 Hz, 1H), 6.98 (t, *J* = 7.6 Hz, 1H), 7.18 (s, 1H), 7.24 (d, *J* = 8.0 Hz, 2H), 7.30 (t, *J* = 7.6 Hz, 1H), 7.36 (d, *J* = 7.6 Hz, 1H), 7.78 (d, *J* = 8.0 Hz, 2H); ^{13}C NMR (100 MHz, CDCl$_3$) δ: 13.9, 21.6, 22.9, 27.8, 30.9, 55.4, 110.5, 120.2, 125.1, 128.8, 129.5, 129.6, 130.1, 135.9, 136.0, 141.9, 142.6, 157.3, 199.0; MS (EI, *m/z*): 308 (57, M$^+$), 277 (100), 119 (75); FTIR (ATR): ν (cm^{-1}) CO: 1656; HRMS(*m/z*, M$^+$) 308.1771 (calculated); 308.1775 (found).

(E)-1-(4-methoxyphenyl)-2-((thiophen-2-yl)methylene)hexan-1-one (3jb): Hexane/ethyl acetate; yellow oil; ^{1}H NMR (400 MHz, CDCl$_3$) δ: 0.96 (t, *J* = 7.2 Hz, 3H), 1.48 (pent, *J* = 6.8 Hz, 2H), 1.53-1.61 (m, 2H), 2.86 (t, *J* = 7.2 Hz, 2H), 3.88 (s, 3H), 6.95 (d, *J* = 9.2 Hz, 2H), 7.08 (dd, *J* = 3.6, 5.2, Hz 1H), 7.15 (d, *J* = 3.6 Hz, 1H), 7.19 (s, 1H), 7.47 (d, *J* = 5.2 Hz, 1H), 7.75 (d, *J* = 9.2 Hz, 2H); ^{13}C NMR (100 MHz, CDCl$_3$) δ: 14.0, 23.2, 28.6, 30.4, 55.4, 113.6, 127.3, 128.9, 131.6, 131.8, 138.6, 139.2, 162.7, 197.8; MS(EI, *m/z*): 300 (62, M$^+$), 269 (19), 135 (100), 203 (16); FTIR (ATR): ν (cm^{-1}): 1636; HRMS(*m/z*, M$^+$): 300.1179 (calculated), 300.1178 (found).

3-tert-butyl-5-(4-methoxyphenyl)-4-methylfuran-2(5H)-one (3mb): ^{1}H NMR (400 MHz, CDCl$_3$) δ: 1.39 (s, 9H), 1.91 (s, 3H), 3.81 (s, 3H), 5.37 (s, 1H), 6,89 (d, *J* = 9.2, 2H), 7.11 (d, *J* = 9.2, 2H); ^{13}C NMR (100 MHz, CDCl$_3$) δ: 14.1, 29.3, 33.3, 55.3, 84.2,

114.3, 127.1, 128.5, 156.2, 160.3, 173.3; MS(EI, *m/z*): 260 (72, M$^+$), 245 (30), 135 (100), 108 (71); FTIR (ATR) ν (cm^{-1}) CO: 1740; HRMS(*m/z*, M$^+$) 260.1407 (calculated); 260.1412 (found).

3-tert-butyl-5-hydroxy-5-(4-methoxyphenyl)-4-methylfuran-2(5H)-one (3mb'): ^{1}H NMR (400 MHz, CDCl$_3$) δ: 1.34 (s, 3H), 1.95 (s, 3H), 3.81 (s, 3H), 6.89 (d, *J* = 8.8, 2H), 7.34 (d, *J* = 8.8, 2H); ^{13}C NMR (100 MHz, CDCl$_3$) δ: 12.3, 29.3, 33.2, 55.3, 104.3, 113.9, 127.1, 129.2, 133.1, 156.8, 160.2, 171.4; MS(EI, *m/z*): 276 (76, M$^+$), 258 (9), 243 (17), 231 (100), 220 (26); FTIR (ATR) ν (cm^{-1}) CO: 1763; HRMS(*m/z*, M$^+$) 276.1365 (calculated); 276.1351 (found).

CHAPTER 4

RESULT AND DISCUSSION

Carbonylative coupling of arylboronic acids with unsaturated substrates is believed to proceed through an acylrhodation step by an in-situ generated acylrhodium complex.
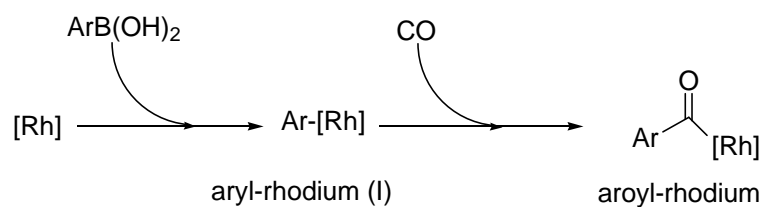
Figure 4.1. Formation of acyl-rhodium species

Our research group has recently shown that carbonylation of an arylboronic acid and internal alkyne mixture in the presence of a rhodium complex can yield the α,β-unsaturated ketone **(3)**, 5-aryl-2(5H)-furanone **(4)**, indenone **(5)**, and indanone **(6)** products (Aksin et al. 2006). (Figure 4.2)
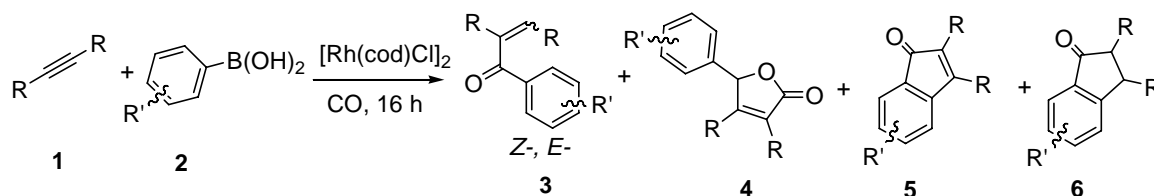
Figure 4.2. Products of carbonylative arylation reaction of alkynes with arylboronic acids

During optimization of reaction conditions for selective construction of **3**, we have determined that prompt protodemetalation of the alkenylrhodium intermediate **(C)**, before insertion of CO, which leads to the product **4**, would result in an α,β-unsaturated ketone **(3)**; hence, we have considered that the presence of an acidic additive would promote the protodemetalation step, provided that the catalyst retains its activity.
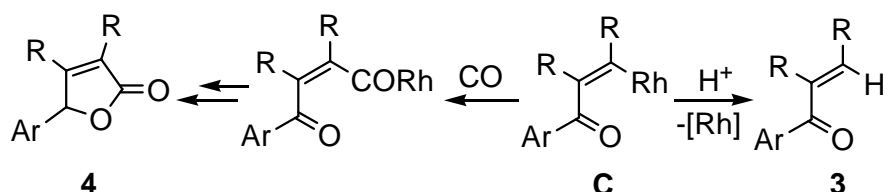
Using diphenyl acetylene and phenylboronic acid as a probe molecule effect of many variables, such as Rh complex, solvent, acid additives, CO pressure and temperature on the reaction efficiency were studied. (Table 4.1)

Table 4.1 Optimization for the selective constraction of enone

| | | | | | | **%Product**[a] | | | | | | |
No	Catalyst	P, atm	T, °C	Solvent	Additive, mmol	% Conv.	E-3aa	Z-3aa	4aa	5aa	6aa	7aa
1	[Rh(cod)Cl]₂	20	80	CH₃OH	HCOOH, 1	100	6	5	30	1	2	26
2	[Rh(cod)Cl]₂	20	80	CH₃OH	CH₃COOH, 1	100	6	5	60	1	2	17
3	[Rh(cod)Cl]₂	20	80	CH₃OH	NH₄Cl, 1	61	6	2	5	1	1	9
4	[Rh(cod)Cl]₂	20	80	CH₃OH	CF₃COOH, 1	100	21	17	21	3	2	5
5	[Rh(cod)Cl]₂	20	80	CH₃OH	CF₃COOH, 5	100	21	21	11	3	1	5
6	[Rh(cod)Cl]₂	20	70	CH₃OH	CF₃COOH, 5	63	15	5	5	1	1	5

Table 4.2 (cont.) Optimization for the selective constraction of enone

7	[Rh(cod)Cl]$_2$	20	120	CH$_3$OH	CF$_3$COOH, 5	98	16	21	12	7	2	8
8	[Rh(cod)Cl]$_2$	10	80	CH$_3$OH	CF$_3$COOH, 6	100	33	29	9	3	5	7
9	[Rh(cod)Cl]$_2$	5	80	CH$_3$OH	CF$_3$COOH, 6	100	30	35	7	11	4	4
10	[Rh(cod)Cl]$_2$	1	80	CH$_3$OH	CF$_3$COOH, 6	100	22	30	3	20	9	2
11	[Rh(cod)Cl]$_2$	5	80	CH$_3$OH	CF$_3$COOH, 10	100	31	35	6	11	4	3
12	[Rh(cod)Cl]$_2$	5	80	CH$_3$OH	-	100	19	28	11	6	8	5
13	RhCl$_3$.3H$_2$O	5	80	CH$_3$OH	CF$_3$COOH, 10	24	2	3	11	11	12	-
14	[Rh(CO)$_2$Cl]$_2$	5	80	CH$_3$OH	CF$_3$COOH, 10	100	32	38	8	12	5	4
15	Rh(C$_2$H$_4$)$_2$acac	5	80	CH$_3$OH	CF$_3$COOH, 10	100	25	37	9	5	4	5
16	[Rh(cod)OH]$_2$	5	80	CH$_3$OH	CF$_3$COOH, 10	100	27	40	6	8	7	3
17	[Rh(C$_2$H$_4$)$_2$Cl]$_2$	5	80	CH$_3$OH	CF$_3$COOH, 10	100	31	42	7	18	6	2
18	[Rh(C$_2$H$_4$)$_2$Cl]$_2$	5	80	C$_2$H$_5$OH	CF$_3$COOH, 10	88	26	25	41	13	4	-
19	[Rh(C$_2$H$_4$)$_2$Cl]$_2$	5	80	Dioxane	CF$_3$COOH, 10	100	15	24	18	4	1	≤1
20	[Rh(C$_2$H$_4$)$_2$Cl]$_2$	5	80	CH$_3$OH	CF$_3$COOH, 2	100	29	45	10	15	7	2
21	[Rh(C$_2$H$_4$)$_2$Cl]$_2$[b]	5	80	CH$_3$OH	CF$_3$COOH, 2	100	27	40	10	9	4	3
22	[Rh(C$_2$H$_4$)$_2$Cl]$_2$[c]	5	80	CH$_3$OH	CF$_3$COOH, 2	100	29	39	6	17	8	2
23	[Rh(C$_2$H$_4$)$_2$Cl]$_2$	5	80	CH$_3$OH	p-CH$_3$-C$_6$H$_4$SO$_3$H, 2	71	20	19	1	4	5	1
24	[Rh(C$_2$H$_4$)$_2$Cl]$_2$/dppb[d]	5	80	CH$_3$OH	CF$_3$COOH, 2	52	4	1	34	1	1	-
25[e]	[Rh(C$_2$H$_4$)$_2$Cl]$_2$[e]	5	80	CH$_3$OH	CF$_3$COOH, 2	100	29	40	11	3	11	4

[a] GC yield, 1mmol 1a, 3 mmol 2a, Rh 3%, 9.9 mL solvent, 0.1 mL H$_2$O, cod: cyclooctadien, acac: acetyl acetonate, dppb: 1,4-bis(diphenylphosphino)butane, [b] 5% Rh. [c] 1% Rh. [d] 3% dppb, [e] 1.5 mmol 1a, 3 mmol 2a.

A mixture of diphenyl acetylene and phenylboronic acid (1 mmol and 3 mmol, respectively) was first reacted in a CH$_3$OH:H$_2$O (9.9:0.1) solvent mixture in the presence of [Rh(cod)Cl]$_2$ (Rh 3%) and 1 mmol of HCOOH at 80°C, under 20 atm of CO

pressure for 16 h (Table 1, entry 1). The major yields of the reaction were **4aa** and a methoxycarbonylated product of diphenyl acetylene, methyl 2,3-diphenylacrylate (**7aa**). A related enone product, **3aa**, formed as a mixture of *E*- and *Z*-isomers in low yield. The use of CH_3COOH as a proton source caused a further increase in the production of **4aa** (entry 2). Overall product recovery was very low in the presence of the NH_4Cl additive (entry 3). The formation of the *E*- and *Z*-isomers of **3aa**, however, increased to a 38% GC yield when CF_3COOH was used as an acid additive (entry 4). A 5-fold increase in the concentration of CF_3COOH had little influence on the yield of **3aa** (entry 5). Decreasing the reaction temperature to 70°C led to a significant decrease in reactivity (entry 6) and a somewhat lower yields of enones were obtained at the elevated temperature, 120°C (entry 7).

The effect of CO pressure was also examined (entries 8-10). Decreasing the CO pressure to 5 atm increased the yield of **3aa** to 65%, and this pressure was set as an optimum parameter. Further decreases of the CO pressure to 1 atmosphere led to increased yields of the byproducts **5aa** and **6aa**.

Generally, variation of CF_3COOH concentration had little effect on the reaction efficiency (compare entries 4, 5,9, 17 and 20). Nevertheless, lower yields of the *E*- and *Z*-**3aa** were obtained in its absence (entry 12). Activities of several of rhodium catalyst precursors were also examined at a reaction temperature of 80 °C, under 5 atm of CO pressure and in the presence of 10 mmol of CF_3COOH (entries 13-17). $RhCl_3.3H_2O$ was highly inactive, affording only 24% of conversion from **1a**. The reaction appeared to show little response upon variation of the other precursors; however, slightly higher *E*- and *Z*-**3aa** products were obtained with $[Rh(CO)_2Cl]_2$ or $[Rh(C_2H_4)_2Cl]_2$ complexes.

Ethanol and dioxane can not substitute methyl alcohol as the lower yields of **3aa** products were obtained by the use of these solvents (entries 18 and 19). No further improvement was gained in the reaction efficiency when the Rh loading was increased to 5%, while the reaction proceeded efficiently even at 1% Rh level without significant loss of activity (entries 21 and 22). Employment of *p*-tolylsulfonic acid as an additive and dppb as a ligand reduced the activity of the catalyst (entries 23 and 24, respectively). It seems that the method does not require large excesses of arylboronic acids, since the reaction was also remarkably effective when a phenylboronic acid:diphenyl acetylene ratio of 3:1.5 was employed.

So all of these experimental results were considered and optimum reaction conditions were determined as 80 °C, 5 atm CO, $[Rh(C_2H_4)_2Cl]_2$ as a pre-catalyst (Rh 3%), and CF_3COOH as a proton source (2 mmol).

Rh-catalyzed carbonylative reactions of various *p-, m-* and *o-* substituted phenylboronic acids with diphenyl acetylene was investigated under the optimal conditions.

The reaction of diphenyl acetylene (**1a**) with several *p-, m-* and *o-* substituted phenylboronic acids yielded mixtures of both *Z-* and *E*-isomers of the corresponding enones (**3a**). The products were isolated separately by flash chromatography on silica gel (Table 2) along with byproducts furanones (**4a**), indenones (**5a**), indanones (**6a**) and a direct methoxycarbonylated product of diphenyl acetylene, methyl 2,3-diphenylacrylate (**7a**).

Table 4.3 Reaction of diphenyl acetylene (1a) with several *p-, m-* and *o-* substituted phenylboronic acids

2a: R = H
2b: R = *p*-OCH₃
2c: R = *p*-CH₃
2d: R = *m*-CH₃
2e: R =Cl
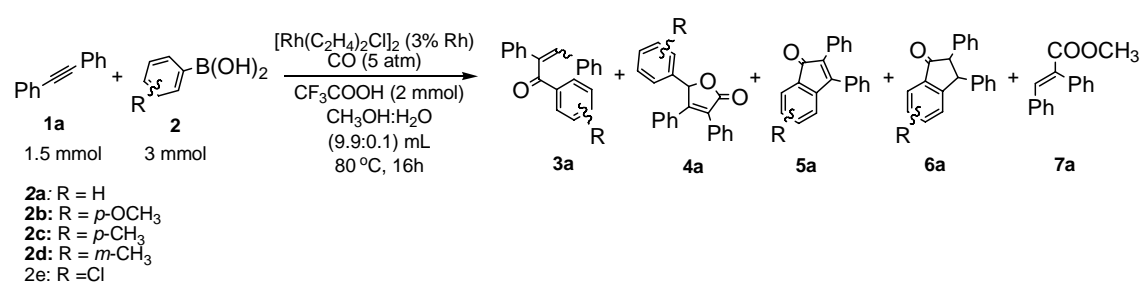
Entry	2	Yield (%)				
		3a[a]	4a[b]	5a[b]	6a[b]	7a[b]
1	2a	3aa (33 Z, 25 E)	4aa (11)	5aa (3)	6aa (12)	(4)
2	2b	3ab (45 Z, 31 E)	4ab (5)	5ab (2)	6ab (1)	(3)
3	2c	3ac (55 Z, 16 E)	4ac (8)	5ac (<1)	6ac (5)	(2)
4	2d	3ad (29 Z, 32 E)	4ad (7)	5ad (3)	6ad (9)	(5)
5	2e	3ae (20 Z, 17 E)	4ad (3)	5ad (5)	6ad (4)	(20)

[a]: Isolated product. [b]: Determined by GC

The reaction of arylboronic acid **2a** with alkyne **1a** afforded the isolated products *E*- and *Z*-**3aa** in overall yield of 58% and produced byproducts at 30% yield (entry 1). Arylboronic acids, **2b** and **2c**, which have methoxy and methyl groups, respectively, at the *para*-position of the phenyl ring gave the corresponding hydroacylation products in yields of 76% for both *E*- and *Z*-**3ab** and 70% yields for both *E*- and *Z*-**3ac**. Lower amounts of byproducts (11 and 16%, respectively, entries 2 and 3) were generated when using these arylboronic acids. The reaction with *m*-tolylboronic acid, **2d**, proceeded to give the corresponding enones (*E*- and *Z*-**3ad**) in an overall yield of 61%, along with 24% formation of the byproducts (entry 4).

The reactions involving *o*-tolylboronic or *p*-(trifluoromethyl)phenylboronic acids with alkyne **1a** resulted in correspondingly low enone yields, remarkably increased amount of side-products, and even yielded significant amounts of corresponding hydroarylation products, triarylacetylene structures. The lowest yield of enone was obtained due to reaction of **1a** with **2e**. These results indicate that enone formation is responsive to the sterical and electronic nature of arylboronic acids.

The isomers of the onene molecules **3a** were identified or estimated according to comparing their IR carbonyl frequencies and melting points based on the literature. It has been reported that existence of steric inhibition of the enone resonance in *Z*-enones results in the appearance of their carbonyl absorption bands at relatively higher wavenumbers than those of the *E*-isomers. (Duke et al. 1972, Black et al.1953, Mittal et al. 1985).

Hydroaroylation proceeded exclusively with *syn*-selectivity for other alkynes, which have only one aryl substituent or none, yielding only the *E*-isomer of the corresponding enones as determined by NOE studies.
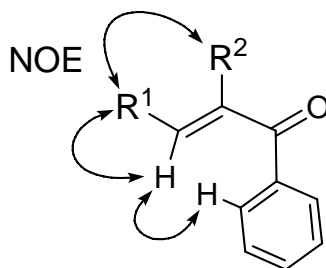
The carbonylative reaction of 4-octyne (**1b**) with **2a** yielded relatively low isolated yield of *E*-**3ba** (30%) (entry 1). Better yields of *E*-**3bb** and *E*-**3bc** were obtained via the reaction of **1b** and arylboronic acids, **2b** and **2c**, at yields of 57% and 53%, respectively (entries 2 and 3). Reactions were also regioselective for those alkynes that had been activated with an ester functionality. The aroyl group was introduced selectively at the β-position with respect to the electron-withdrawing group (entries 4-6). High regioselectivity was also observed with 1-phenylpropyne (**1e**), the aroyl group primarily introduced at the methyl substituted acetylenic carbon, giving **3ea**, **3eb** and **3ec** predominantly upon reaction with the arylboronic acids **2a**, **2b** and **2c** respectively, which are separable from their regioisomers (entries 7-9). Nevertheless, the presence of a larger alkyl group on the alkynyl carbon somewhat reduced its regioselectivity, probably due to increased steric hindrance (entry 10). The presence of an electron-donating methoxy group on the *o*- or *p*- positions of 1-phenylpentyne had modest effect on regioselectivity. (entry 12-14) A complex mixture of products was obtained for the reaction of 1-pyridylpentyne, **1k**. The corresponding enone products were isolated as a 1:1 ratio of regio-isomers, whereas a higher yield and better regioselectivity could be attained when using 1-thienylpentyne, **1j**. (entry 15 and 16) When we used an alkyne that had been activated with an ester functionality, **1l**, 9% dimer keton product was formed along with the formation of 17% enone product. This dimerization was responsible for this low enone formation. Suprisingly, 2(5*H*)-furanone product and an its hydrated compound were isolated from the carbonylative reaction of 4,4-dimethylpent-2-yne (**3mb**) with **2b** under the general conditions applied for enone synthesis. The latter product was formed by conversion of an isomer during silica gel column chromatography and determined by GC-MS.
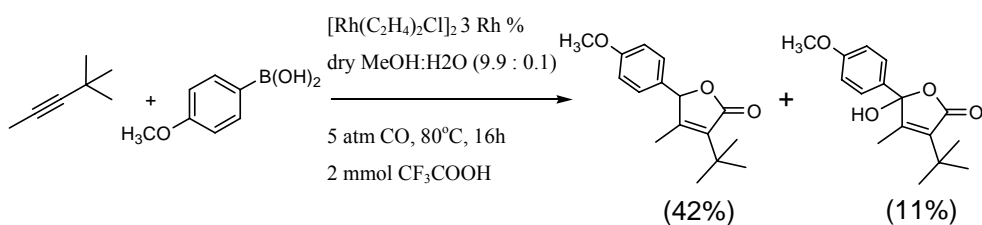
Table 4.4 Reactions of alkynes with arylboronic acids

R^1—≡—R^2 (**1**, 1.5 mmol) + R^3-C$_6$H$_4$-B(OH)$_2$ (**2**, 3 mmol) →
[Rh(C$_2$H$_4$)$_2$Cl]$_2$ (3% Rh), CO (5 atm), CF$_3$COOH (2 mmol), CH$_3$OH:H$_2$O (9.9:0.1) mL, 80 °C, 16 h → **3** + **3'**
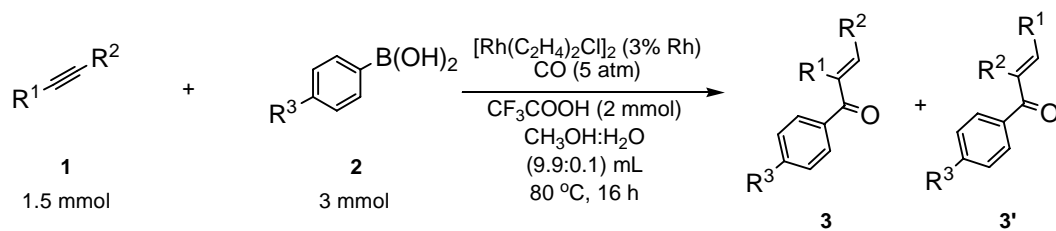
1b: R^1 = R^2 = n-C$_3$H$_7$
1c: R^1 = n-C$_4$H$_9$, R^2 = CO$_2$CH$_3$
1d: R^1 = CH$_3$, R^2 = CO$_2$CH$_3$
1e: R^1 = CH$_3$, R^2 = C$_6$H$_5$
1f: R^1 = n-C$_3$H$_7$, R^2 = C$_6$H$_5$
1g: R^1 = CH$_3$, R^2 = C(CH$_3$)$_3$
1h: R^1 = n-C$_4$H$_9$, R^2 = p-CH$_3$OC$_6$H$_5$
1i: R^1 = n-C$_4$H$_9$, R^2 = o-CH$_3$OC$_6$H$_5$
1j: R^1 = n-C$_4$H$_9$, R^2 = thienyl
1k: R^1 = n-C$_4$H$_9$, R^2 = C$_5$H$_5$N
1l: R^1 = n-CO$_2$C$_2$H$_5$, R^2 = C$_6$H$_5$
1m: R^1 = CH$_3$, R^2 = C(CH$_3$)$_3$

2a: R^3 = H
2b: R^3 = OCH$_3$
2c: R^3 = CH$_3$

Entry	1	2	Yield (%) 3	3'
1	1b	2a	3ba (30)	-
2	1b	2b	3bb (57)	-
3	1b	2c	3bc (53)	-
4	1c	2b	3cb (64)	(<1)[b]
5	1c	2c	3cc (52)	-
6	1d	2b	3db (54)	(2)[b]
7	1e	2a	3ea (42)	(3)[b]
8	1e	2b	3eb (74)	(6)[b]
9	1e	2c	3ec (76)	-
10	1f	2b	3fb (41)	(13)[a]
11	1m	2b	3mb (42)	(11)[a]
12	1h	2c	3hc (37)	(6)[b]
13	1i	2c	3ic (33)	(6)[b]
14	1i[c]	2c	3ic (39)	(7)[b]
15	1j	2b	3jb (52)	(5)[b]
16	1k	2b	3kb (31)	(14)[b]
17	1l	2b	3lb (17)	

[a]: isolated yield, [b]: GC yield, [c]: Rh 5%

As for the reaction mechanism, transmetalation of arylboronic acid with the Rh catalyst is probably followed by insertion of CO into the arylrhodium bond (Figure 4.3). The resultant aroylrhodium (**B**) undergoes 1,2-addition to the alkyne in a *syn* fashion to give a vinylrhodium species (**C**), which then should undergo protodemetalation to afford the *E*-enone. Nevertheless, one may consider that exchange of Rh on alkenyl carbon and aryl hydrogen at the *ortho*-position with respect to the carbonyl functionality (**D**) and subsequent protodemetalation of aryl-attached Rh could be an alternative route to the end product in analogy to the Rh-catalyzed hydroarylation of alkynes with arylboronic acids (1,4-shift) as shown by Hayashi et al. We eliminated this route by considering the result of the similar reaction of **1b** with D_5-PhB(OH)$_2$ under a CO atmosphere, where indeed no contribution of the proton on the carbonyl tethered phenyl ring or deuterium on the β-unsaturated carbon of the related enone product was detected.
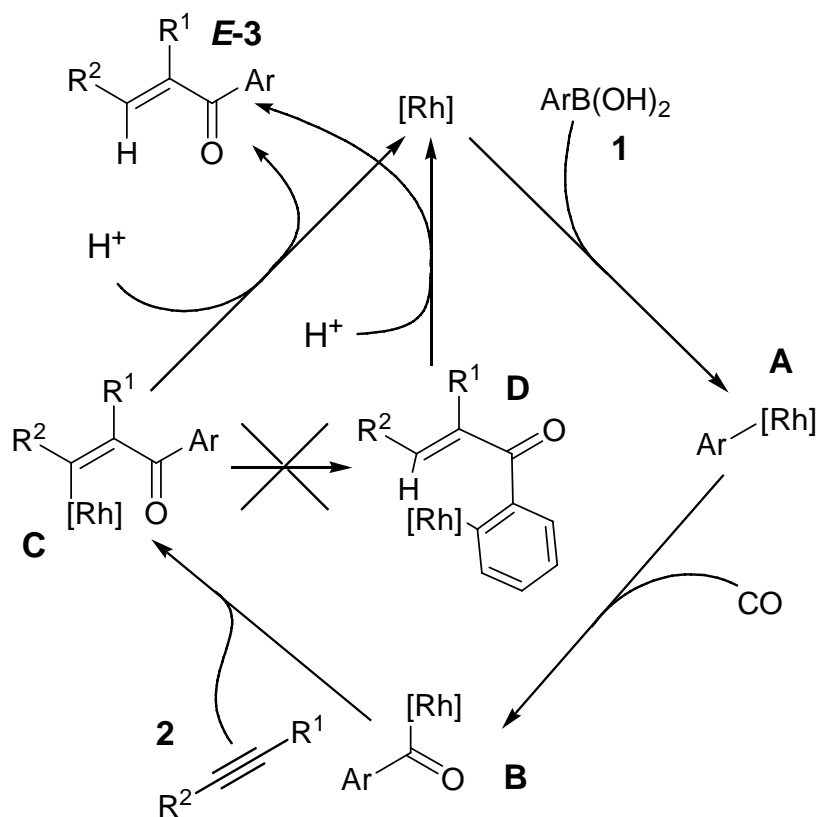
Figure 4.3. General reaction mechanism for the enone synthesis

A question yet remained as to how the mixture of *E*- and *Z*-isomers are formed with diphenyl acetylene. An experiment using the pure *E*-isomer of **3ab** under the general reaction protocol, but in the absence of arylboronic acid brought about an isomerization to the *Z*-configuration in about 25% yield. Although this result shows that *E*-enones formed from diphenyl acetylene can isomerize partly during the course of the carbonylative arylation reactions, it can not account for the *Z:E* ratios given in Table 1. Probably the intermediate **C** can also undergo isomerization which is facilitated by the extended conjugation when the alkenyl carbons are substituted with two aryl groups.
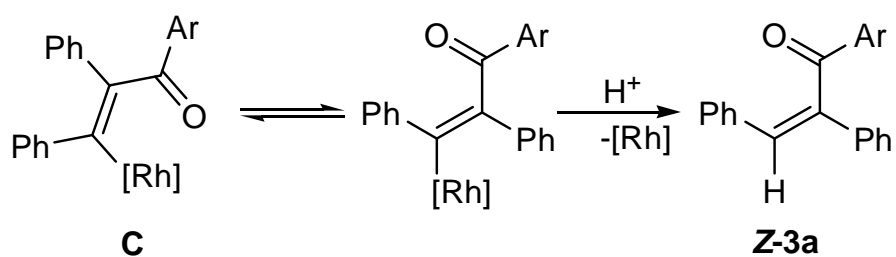
CHAPTER 5

CONCLUSION

In this thesis study, rhodium-catalyzed carbonylative additions of phenylboronic acids to various alkynes were investigated.

Electronic nature of the arylboronic acids is responsible for the enone formation. Electron rich arylboronic acids resulted in good yields.

Reactions were regioselective for alkynes that had been activated with an ester functionality. The aroyl group was introduced selectively at the β-position with respect to the electron-withdrawing group. And also an internal alkyne which have only one aryl substituent or none, gave the corresponding enone stereospesifically, only the *E*-isomer of the enone is formed.

In summary, the methodology established in this study demonstrates, an atom economical, relatively mild, and simple way to synthesize α,β-unsaturated ketones selectively.

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APPENDIX A
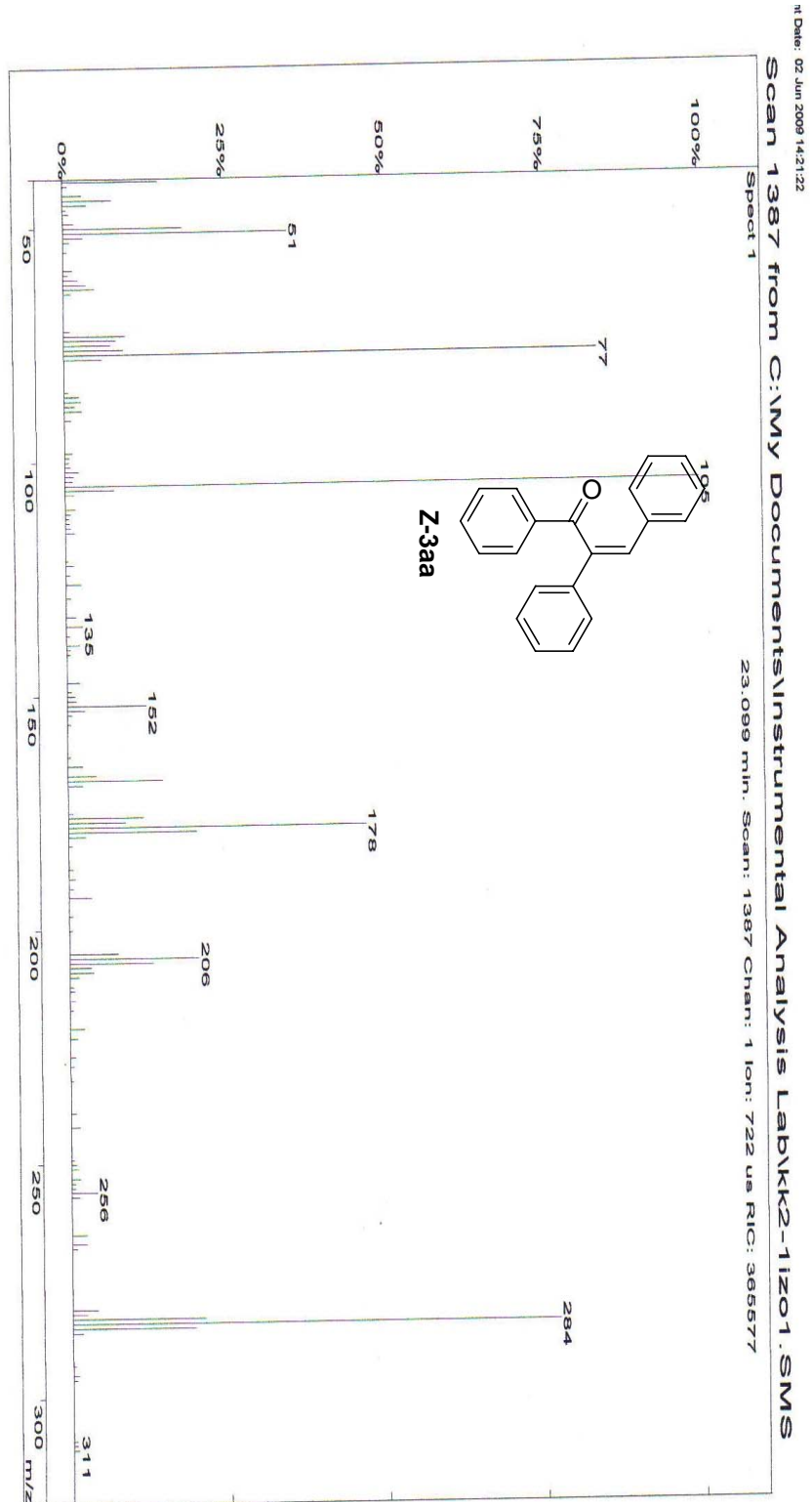
Figure A.1. Mass spectrum of (Z)-1,2,3-triphenylprop-2-en-1-one
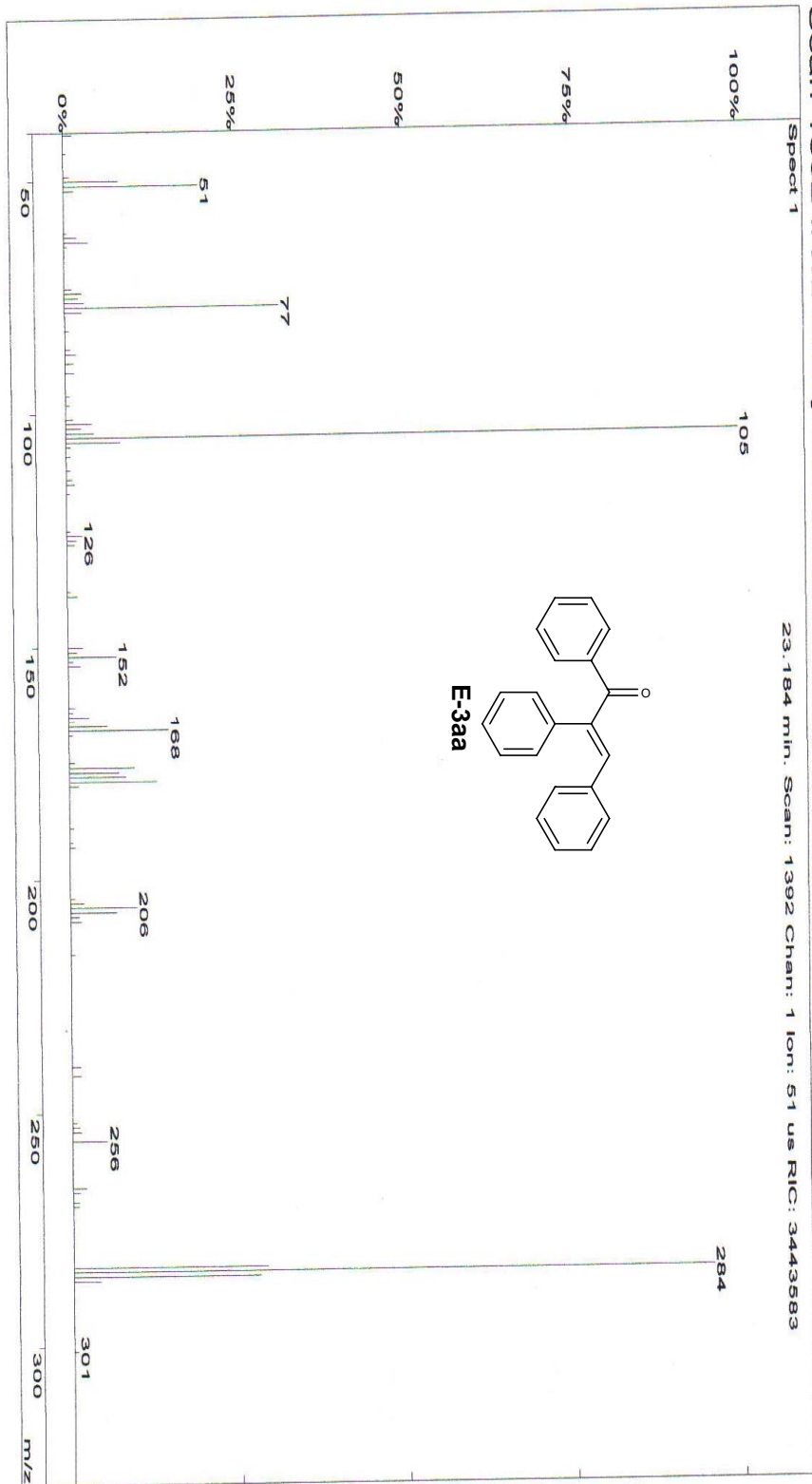
Figure A.2. Mass spectrum of (*E*)-1,2,3-triphenylprop-2-en-1-one
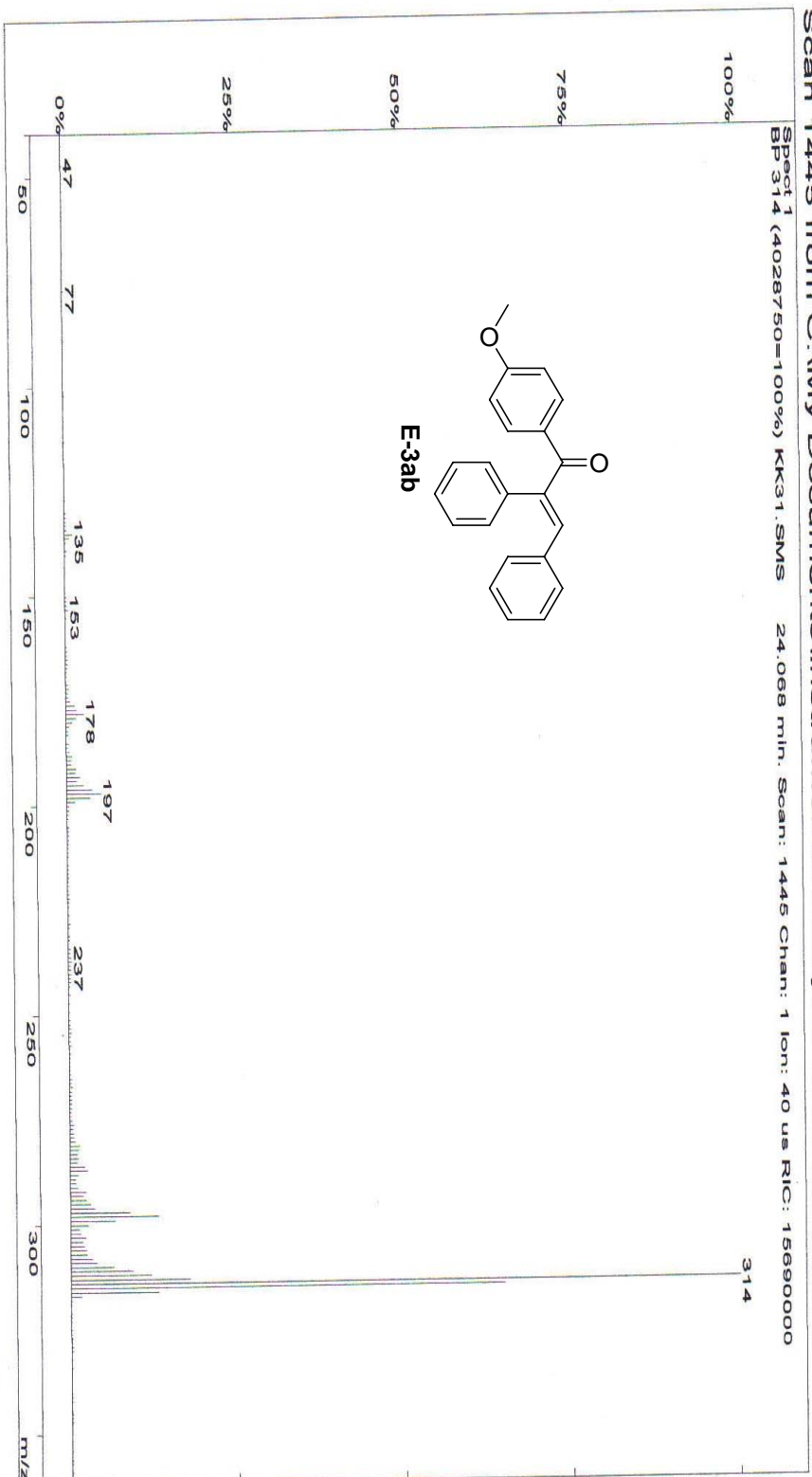
Figure A.3. Mass spectrum of (*E*)-1-(4-methoxyphenyl)-2,3-diphenylprop-2-en-1-one
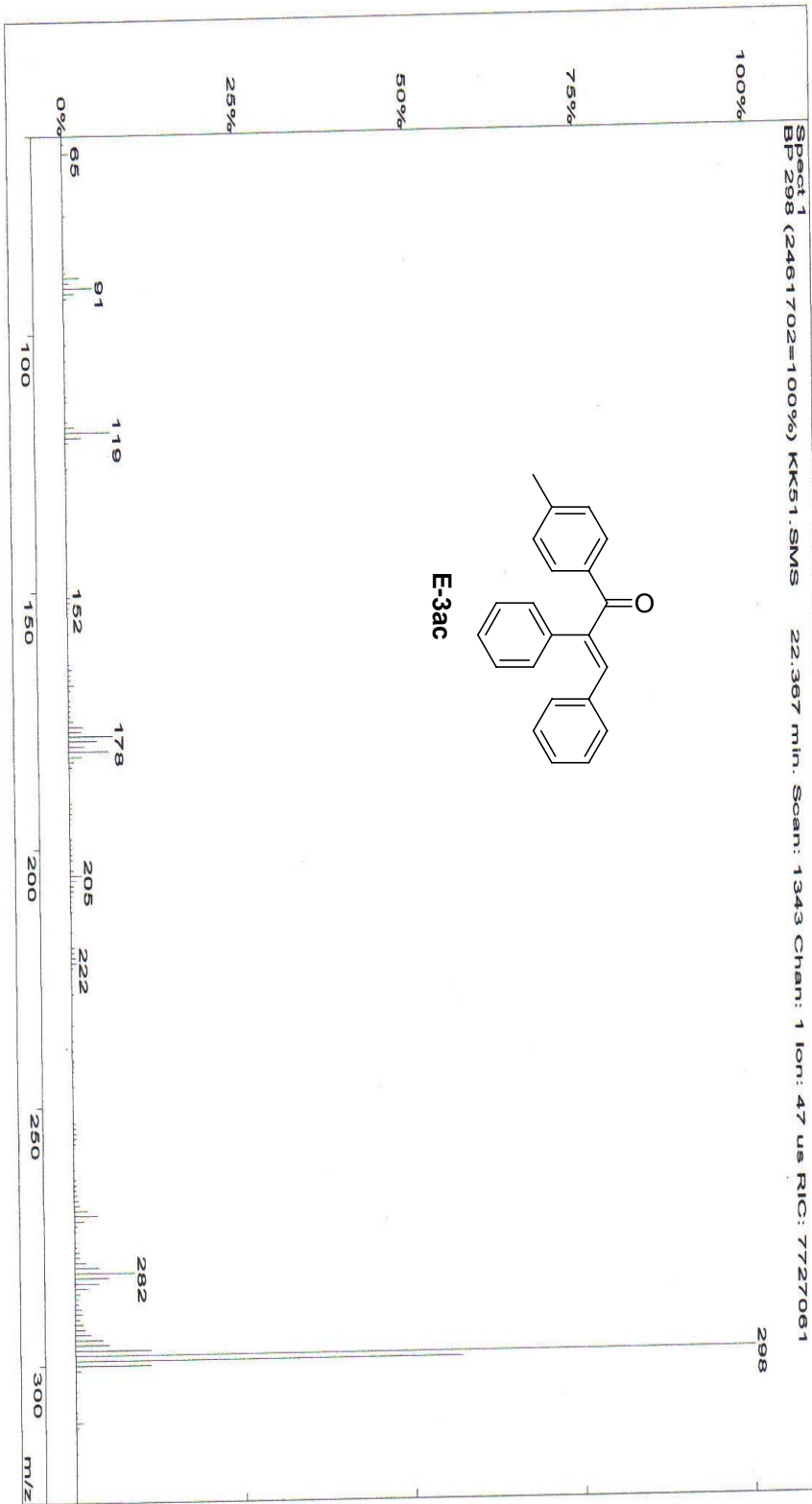
Figure A.4. Mass spectrum of (*E*)-2,3-diphenyl-1-*p*-tolylprop-2-en-1-one

Figure A.5. Mass spectrum of (Z)-2,3-diphenyl-1-*m*-tolylprop-2-en-1-one

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Spect 1

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E-3ad
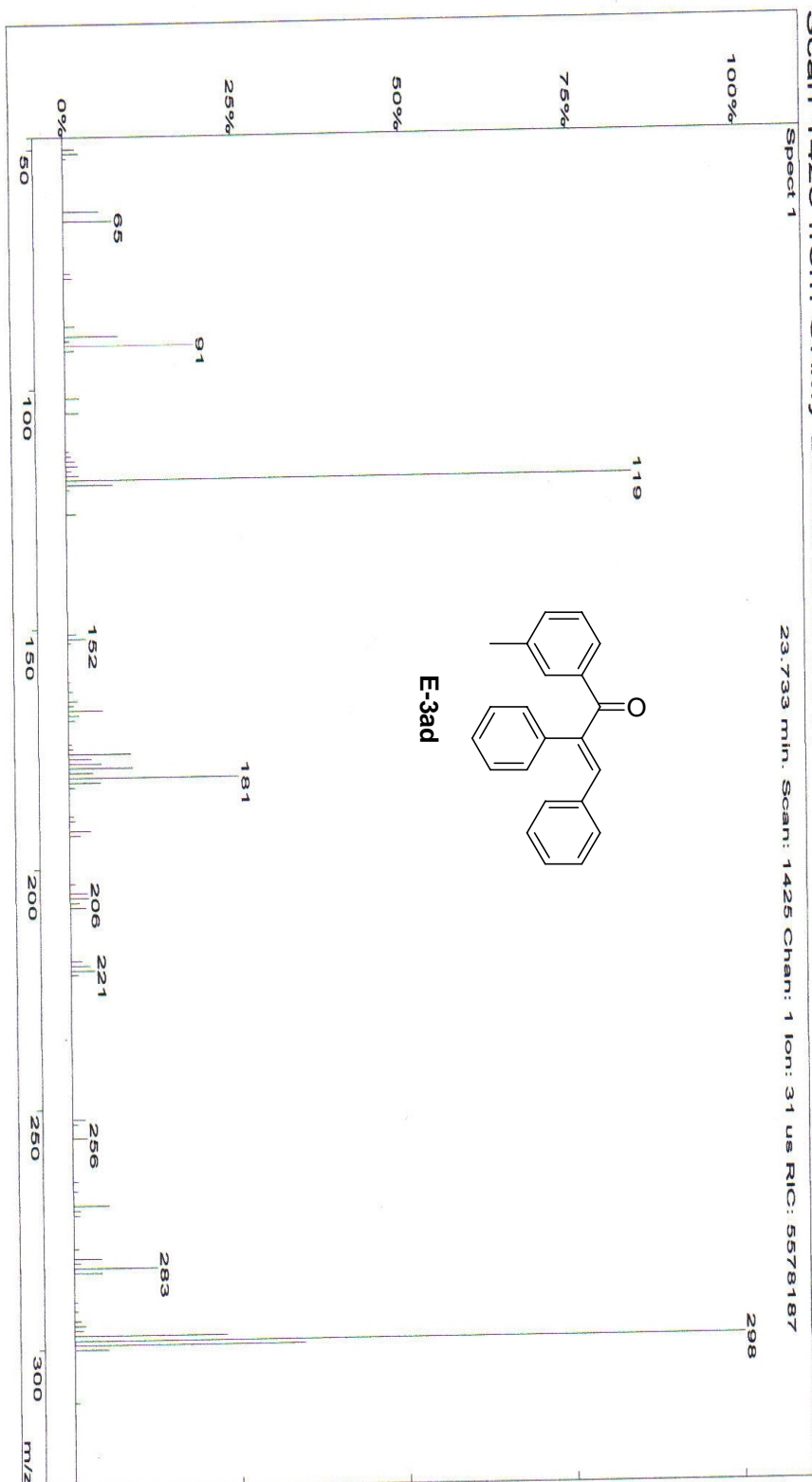
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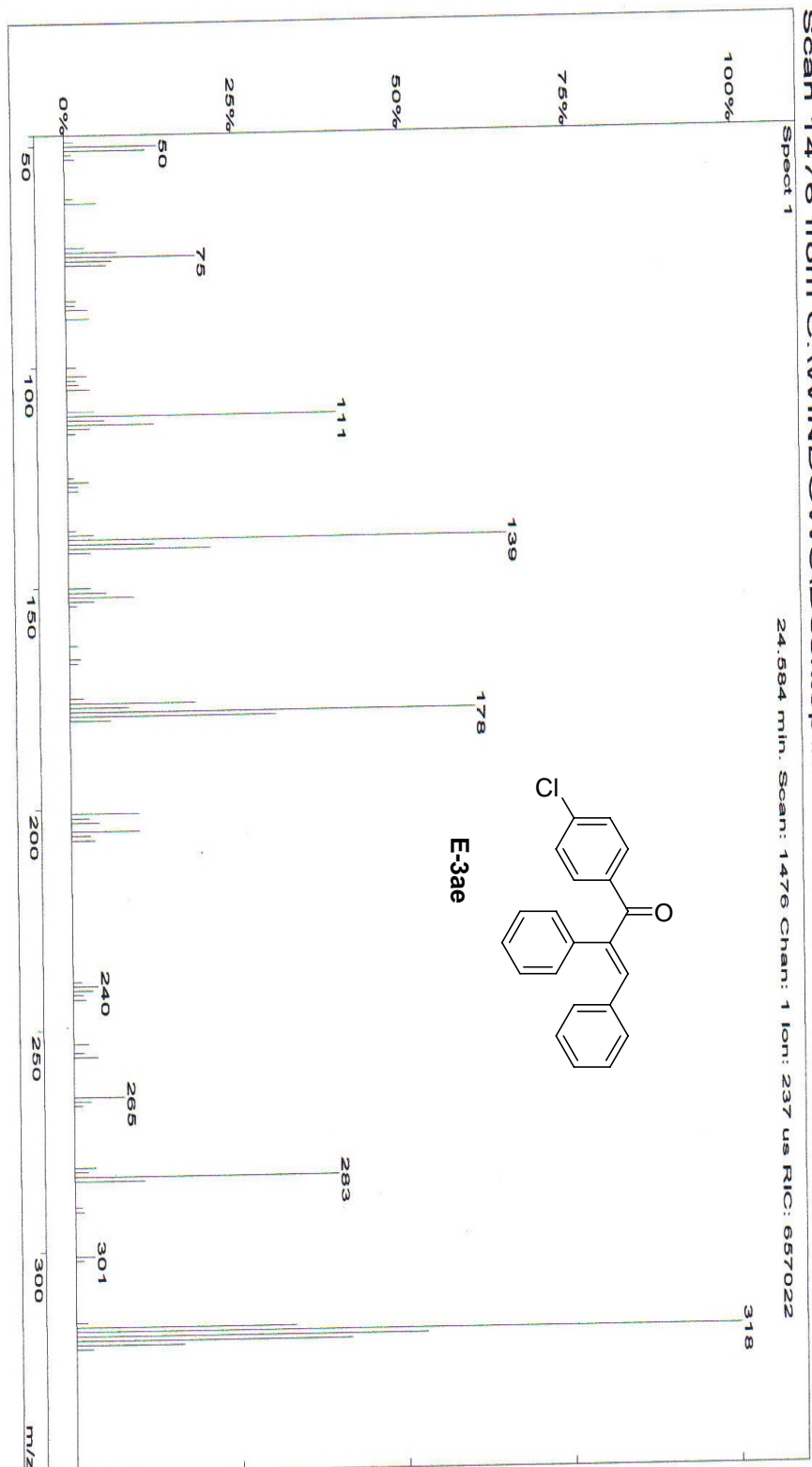
Figure A.7. Mass spectrum of (*E*)-1-(4-chlorophenyl)-2,3-diphenylprop-2-en-1-one
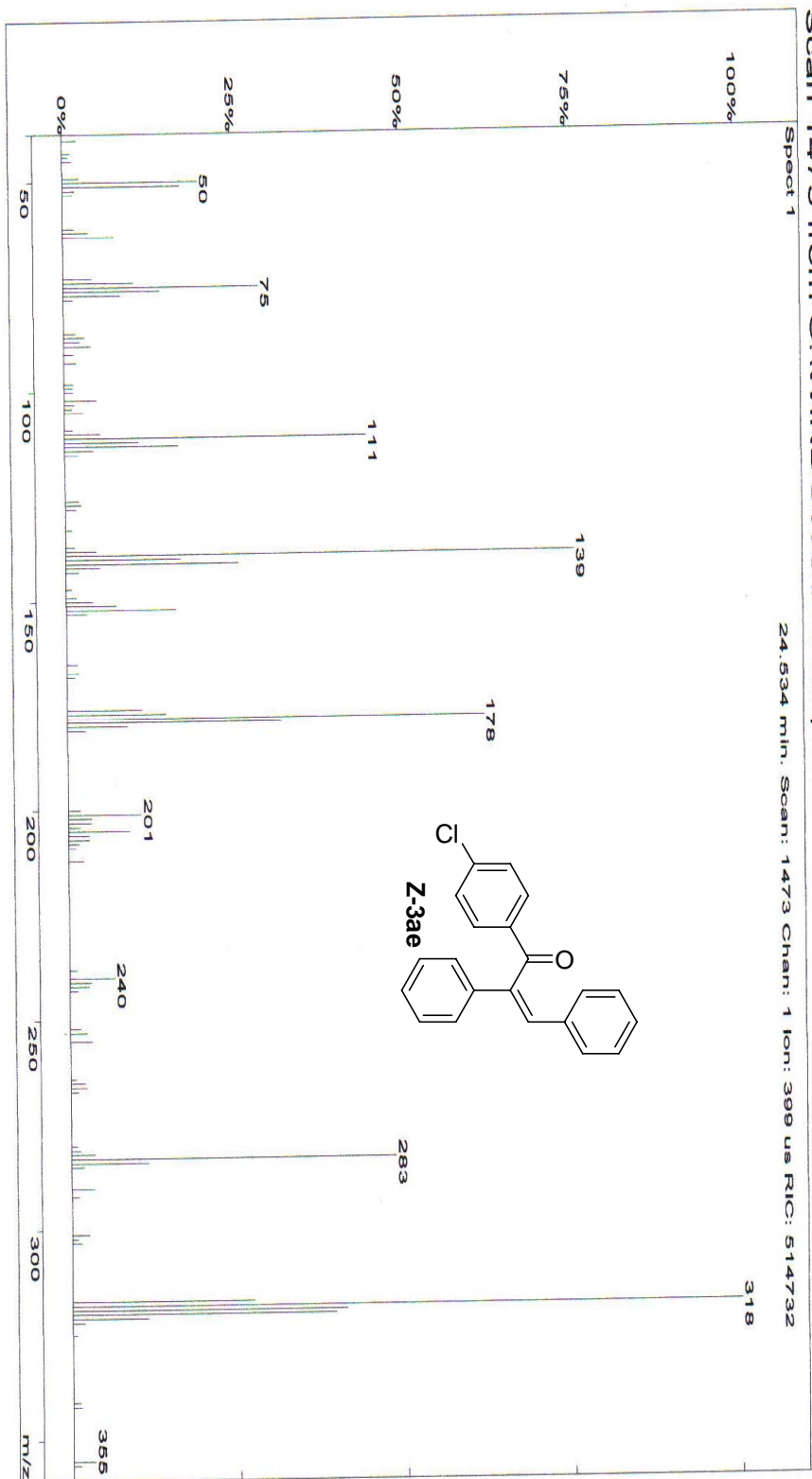
Figure A.8. Mass spectrum of (Z)-1-(4-chlorophenyl)-2,3-diphenylprop-2-en-1-one

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Spect 1

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E-3ba
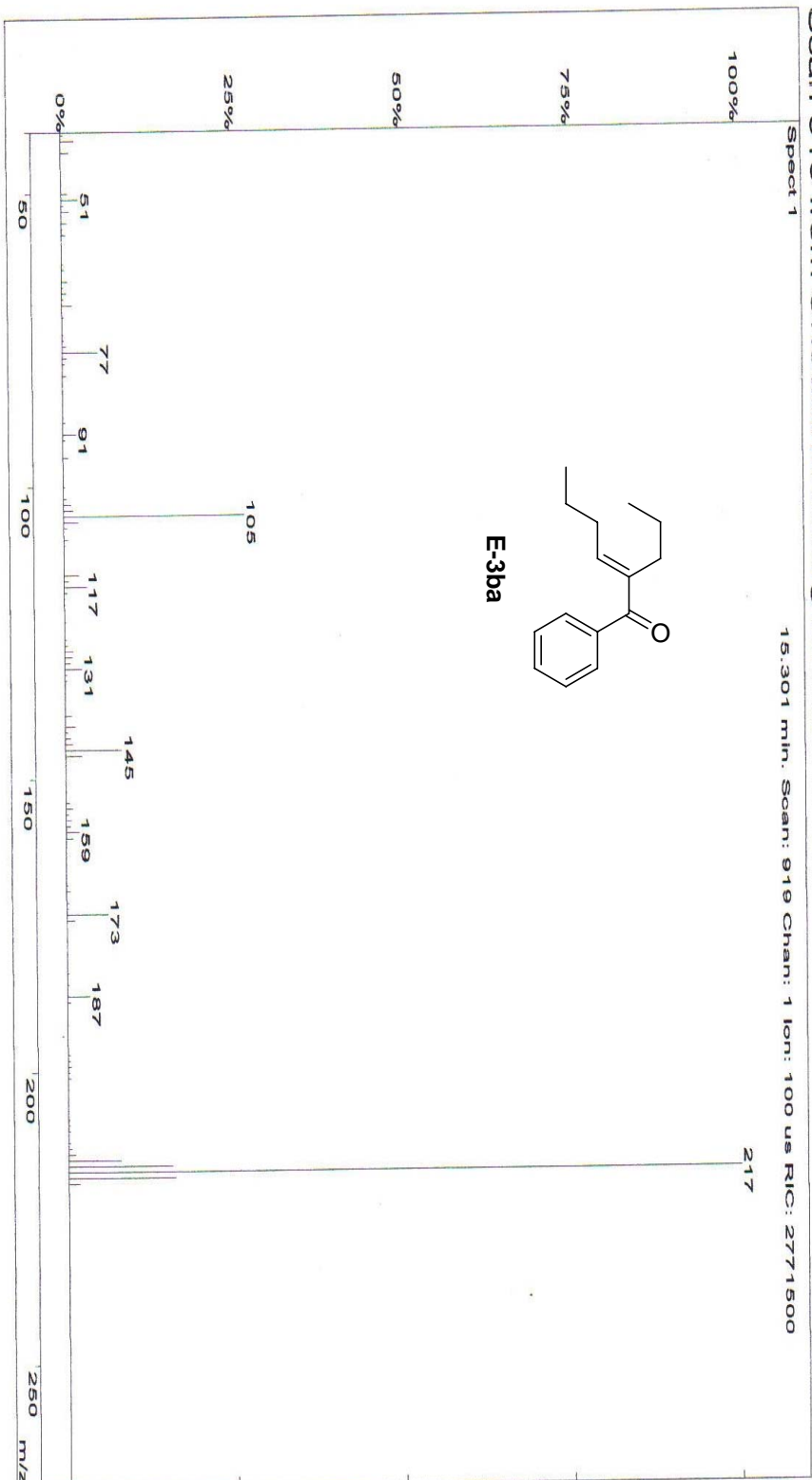
Figure A.9. Mass spectrum of (*E*)-1-phenyl-2-propylhex-2-en-1-one

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Spect 1

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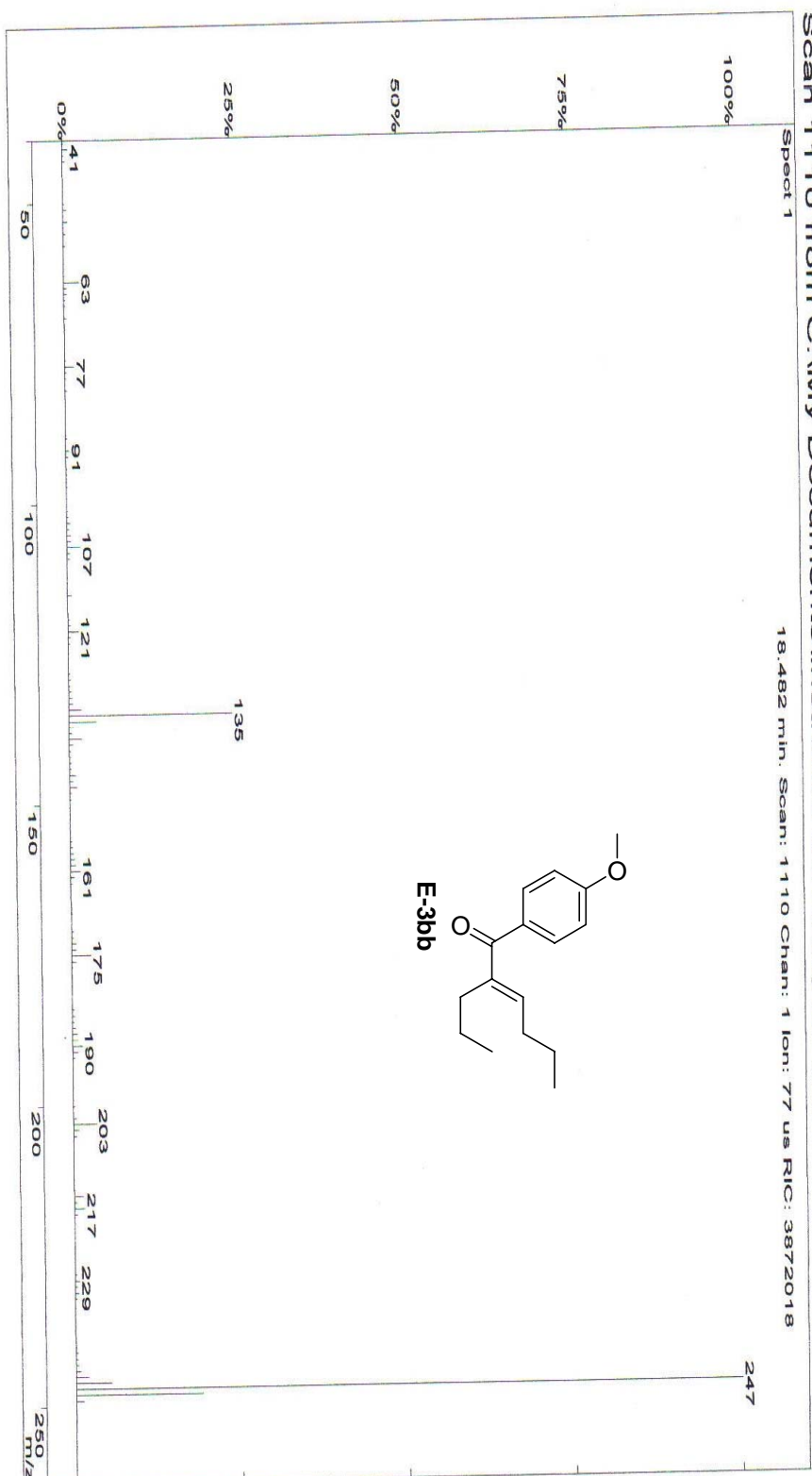
Figure A.10. Mass spectrum of (*E*)-1-(4-methoxyphenyl)-2-propylhex-2-en-1-one
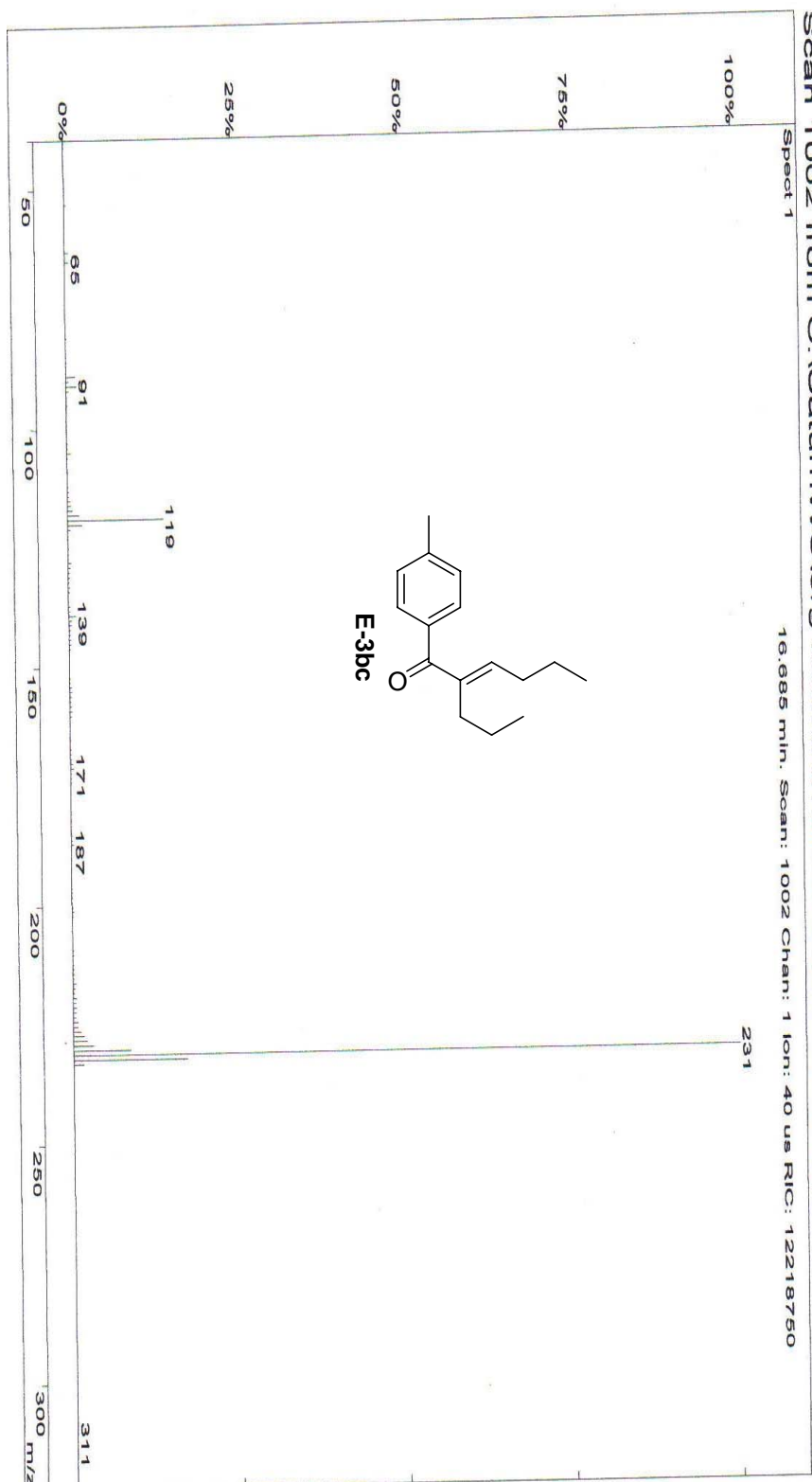
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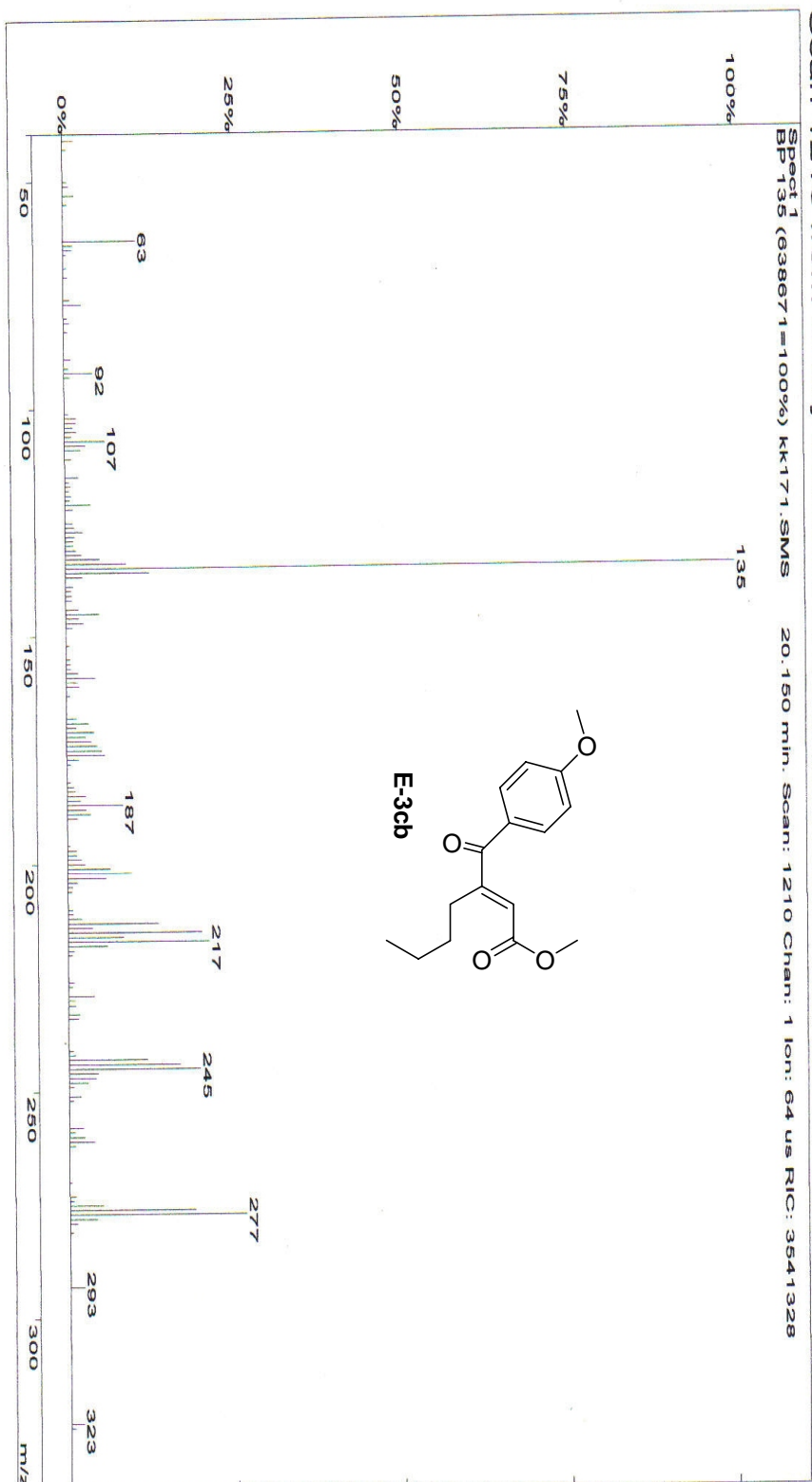
Figure A.12. Mass spectrum of (*E*)-methyl 3-(4-methoxyphenyl)hept-2-enoate
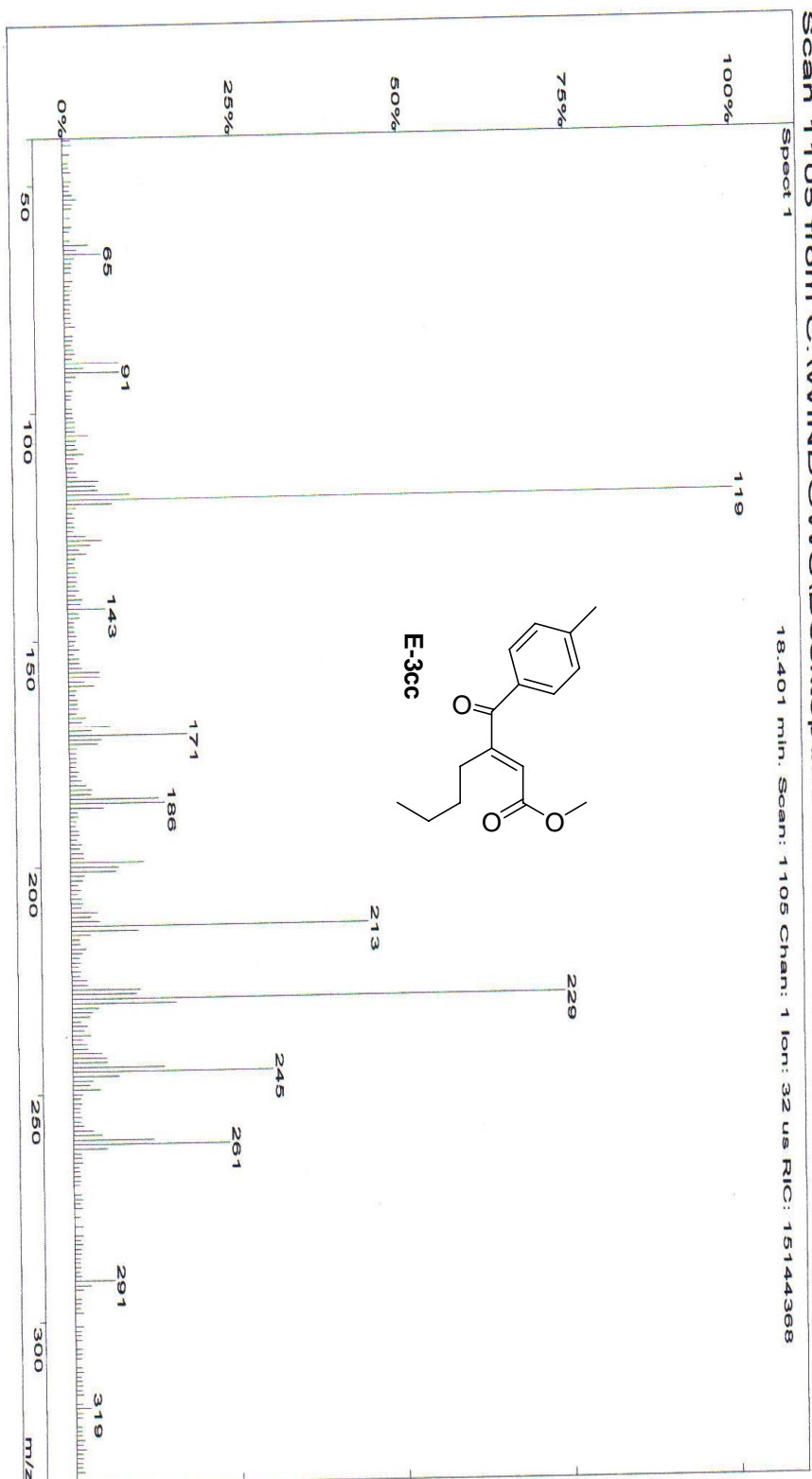
Figure A.13. Mass spectrum of (*E*)-methyl 3-(4-methylphenyl)hept-2-enoate
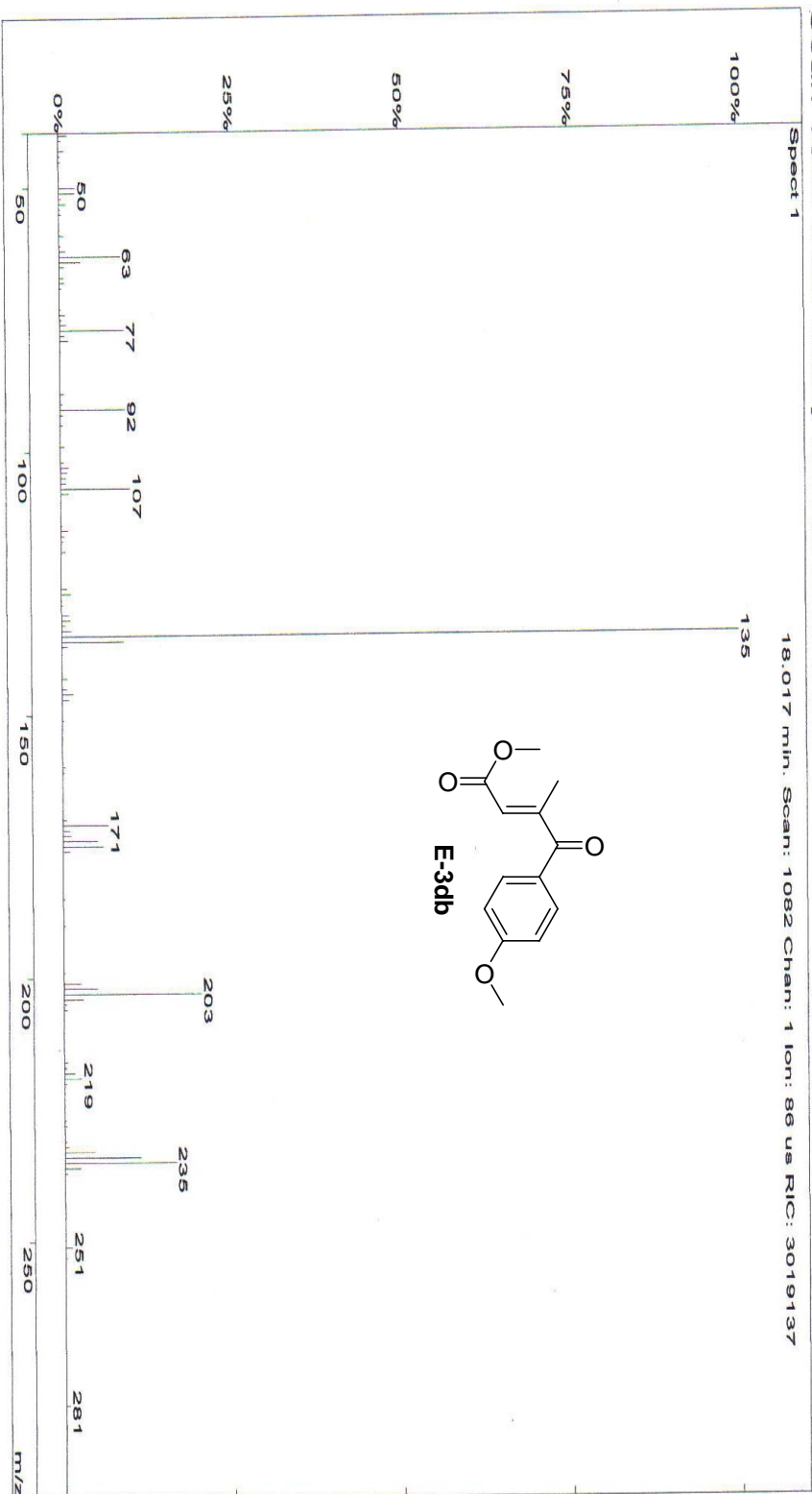
Figure A.14. Mass spectrum of (*E*)-methyl 4-(4-methoxyphenyl)-3-methyl-4-oxobut-2-enoate

Scan 1119 from c:\windows\desktop\melih\MKK54811.SMS

Spect 1

18.634 min. Scan: 1119 Chan: 1 Ion: 840 us RIC: 385715

E-3ea
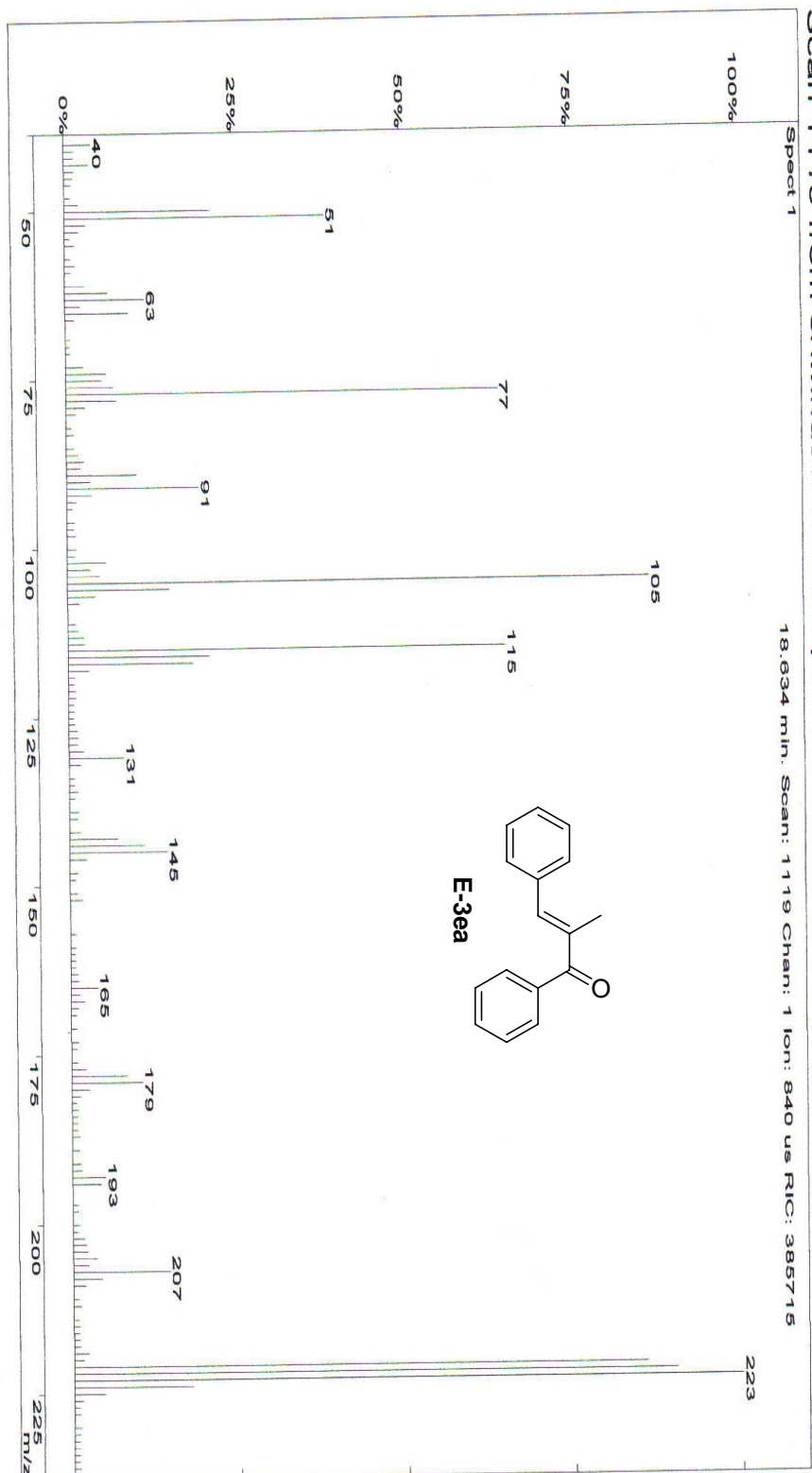
Figure A.15. Mass spectrum of (*E*)-2-methyl-1,3-diphenylprop-2-en-1-one
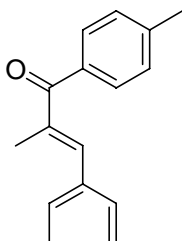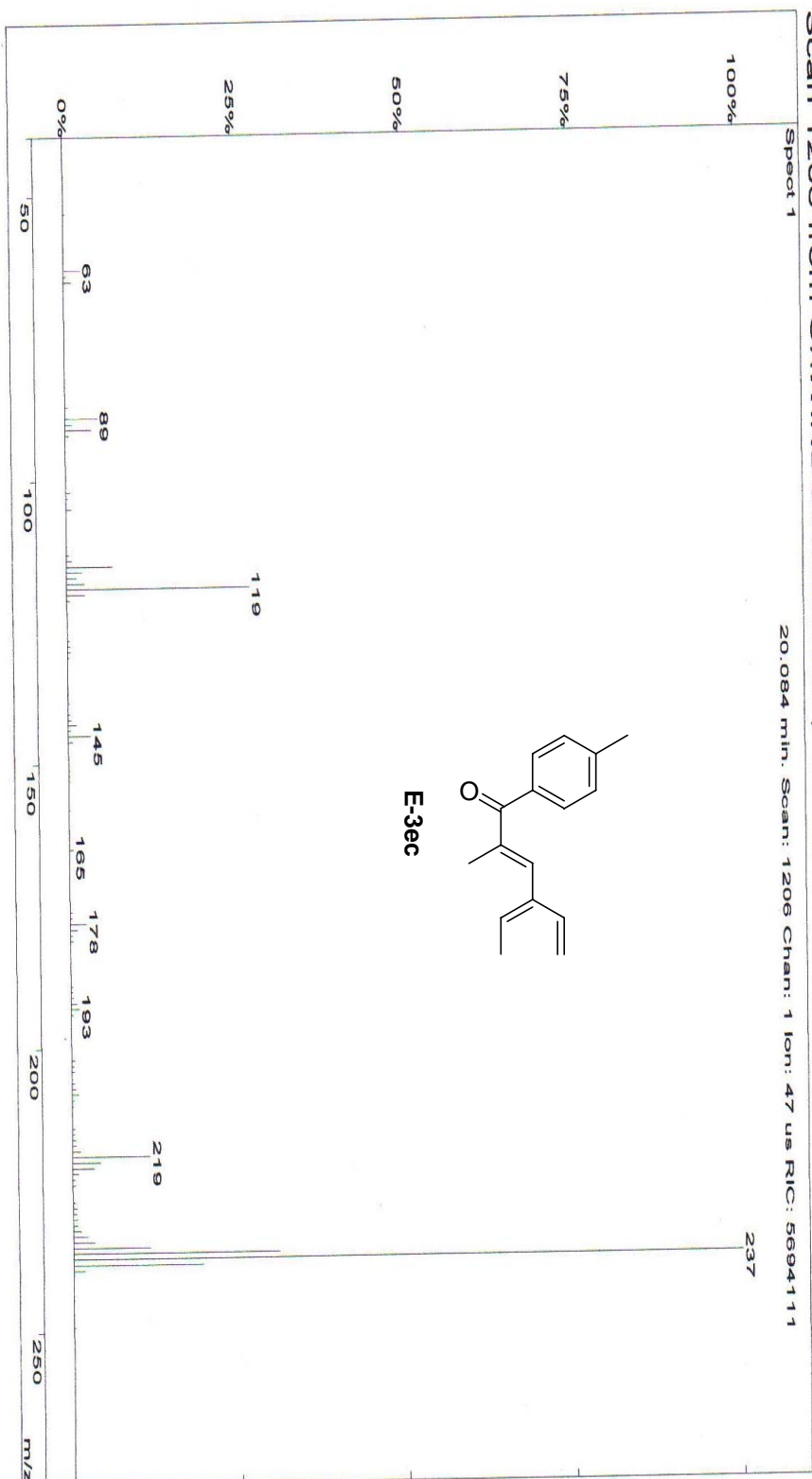
Figure A.16. Mass spectrum of (*E*)-2-methyl-3-phenyl-1-p-tolylprop-2-en-1-one

Scan 1350 from c:\windows\desktop\melih\KK161.SMS

Spect 1
BP 135 (175526=100%) KK161.SMS   22.484 min. Scan: 1350 Chan: 1 Ion: 190 us RIC: 1456889

E-3fb
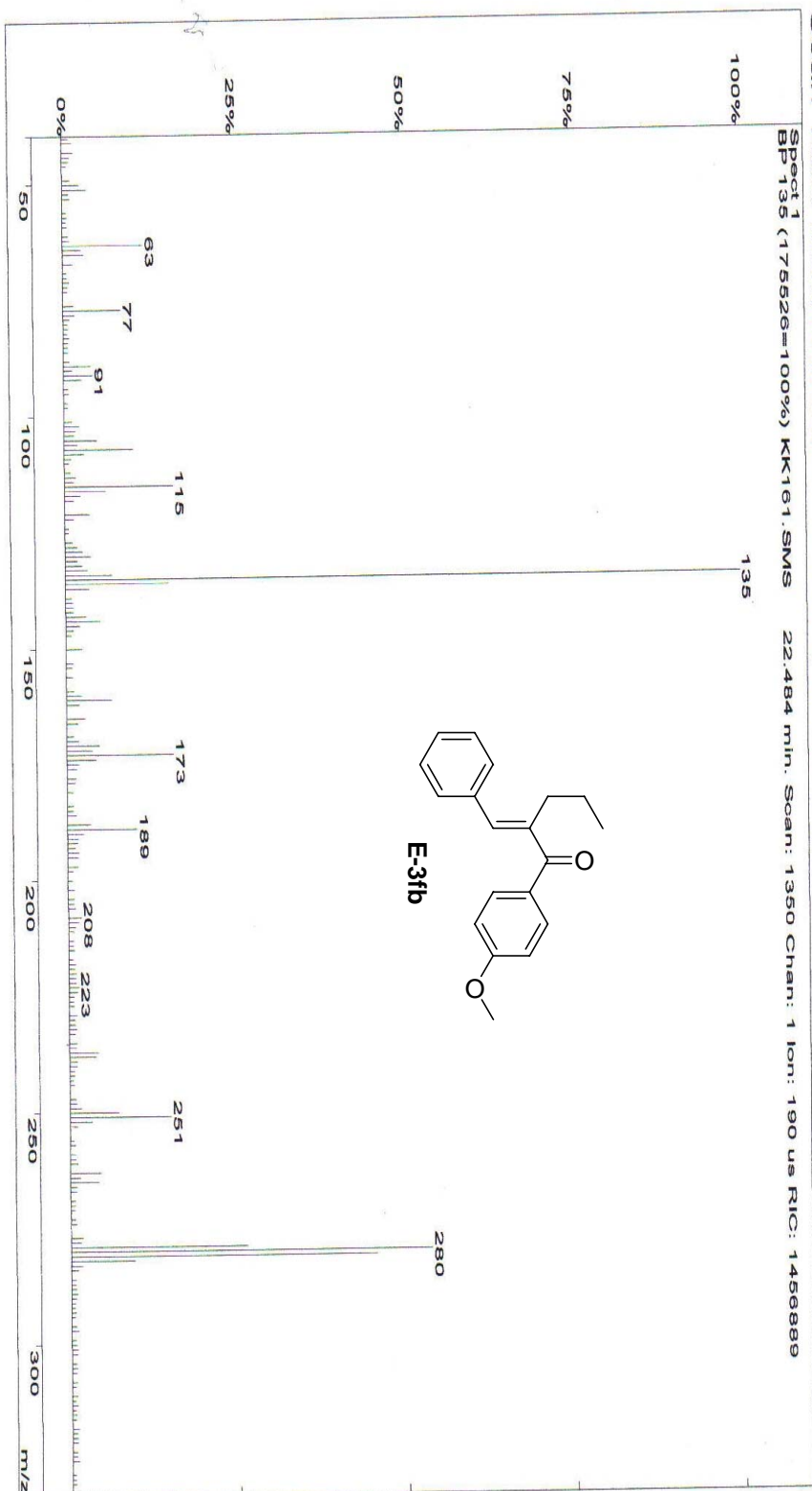
Figure A.17. Mass spectrum of (*E*)-2-benzylidene-1-(4-methoxyphenyl)pentan-1-one

Scan 1280 from c:\windows\desktop\melih\KK161.SMS

Spect 1
BP 135 (20301=100%) KK161.SMS   21.317 min. Scan: 1280 Chan: 1 Ion: 1511 us RIC: 213502

E-3fb'
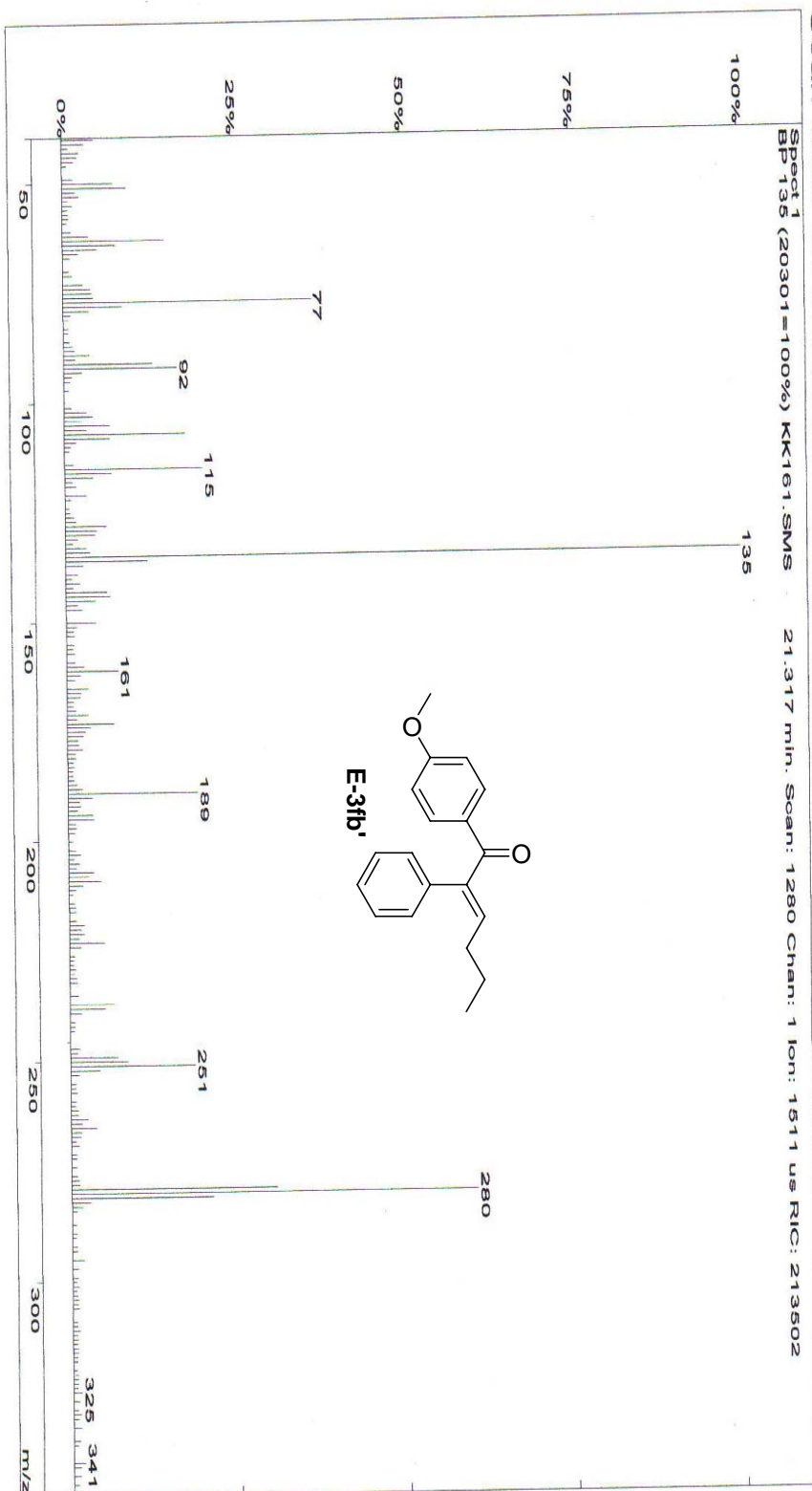
Figure A.18. Mass spectrum of (*E*)-1-(4-methoxyphenyl)-2-phenylhex-2-en-1-one

Scan 1448 from C:\WINDOWS\Desktop\MELIH\10021.SMS

Spect 1
BP 309 (890416=100%) 10021.SMS   24.118 min, Scan: 1448 Chan: 1 Ion: 60 us RIC: 6710660

E-3hc
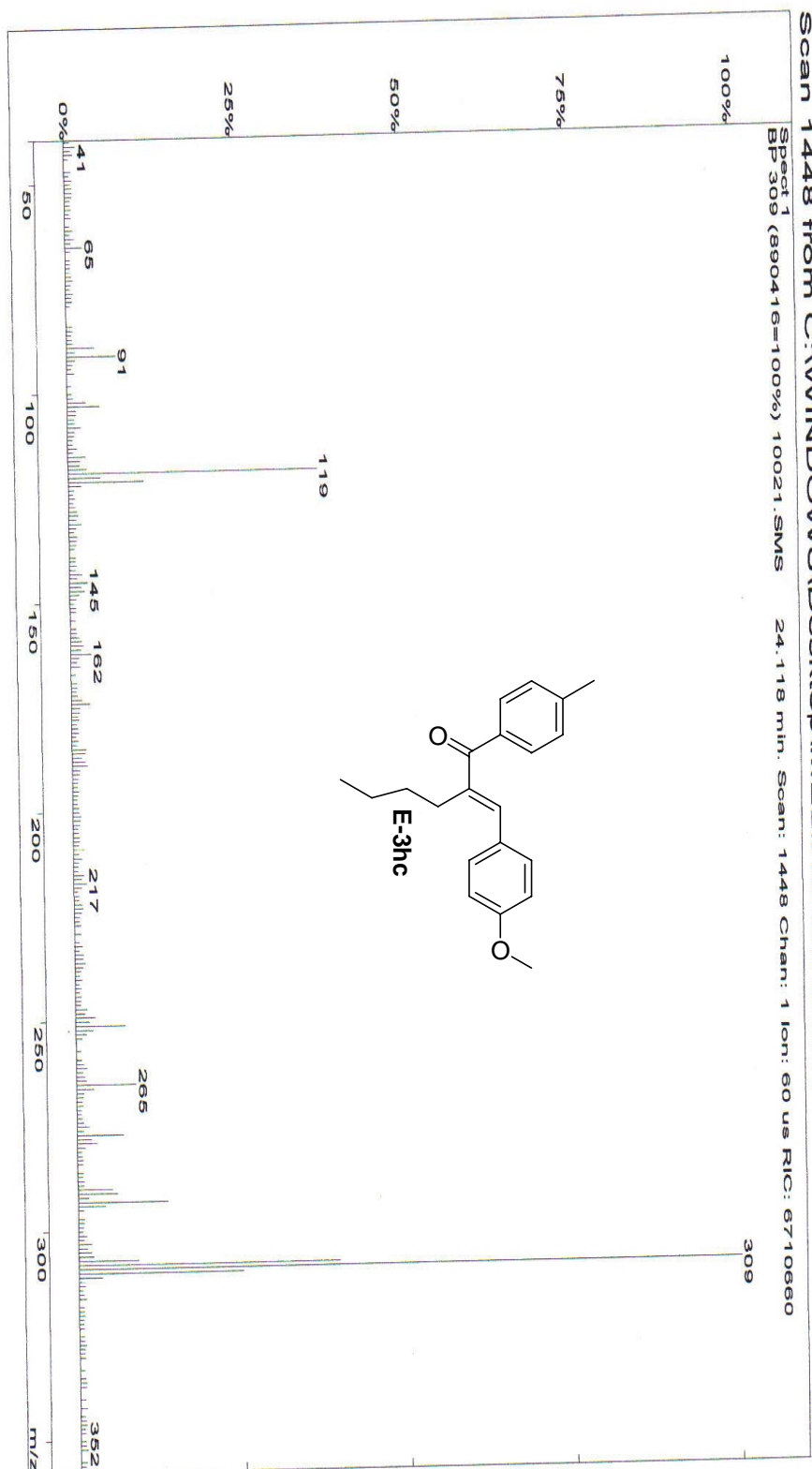
Figure A.19. Mass spectrum of (*E*)-2-(4-methoxybenzylidene)-1-p-tolylhexan-1-one
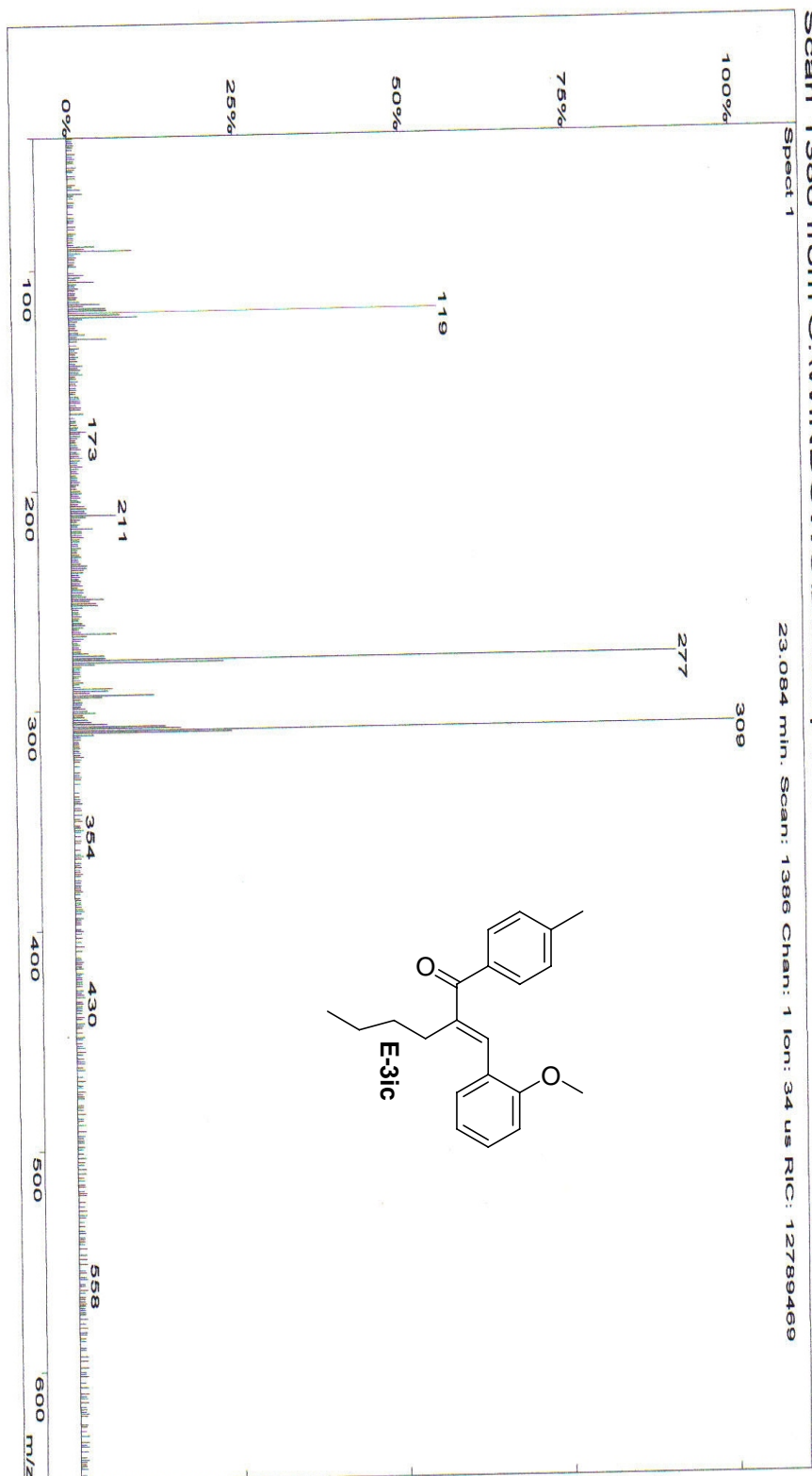
Figure A.20. Mass spectrum of (*E*)-2-(2-methoxybenzylidene)-1-p-tolylhexan-1-one
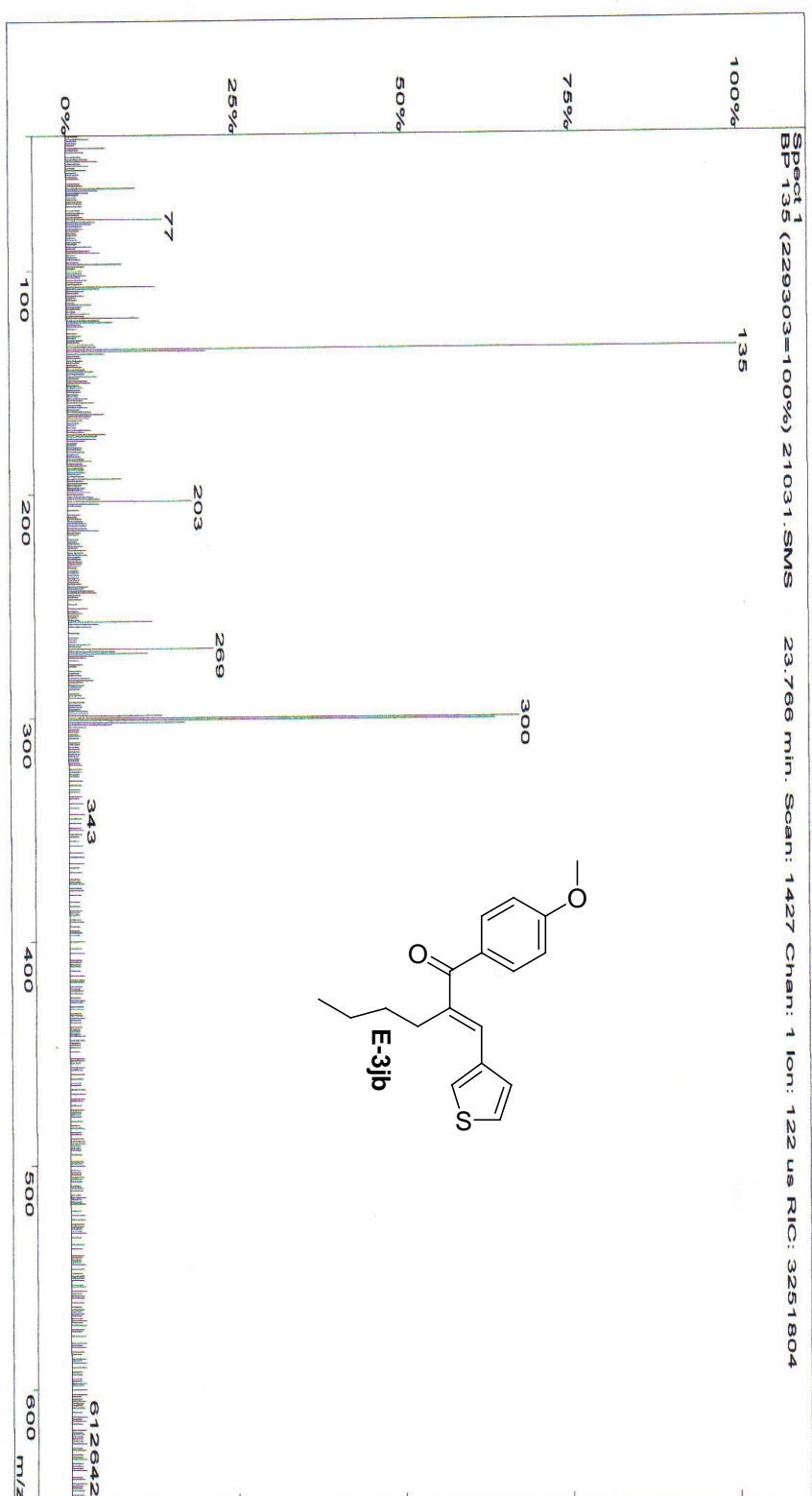
Figure A.21. Mass spectrum of (*E*)-1-(4-methoxyphenyl)-2-((thiophen-3-yl)methylene)hexan-1-one
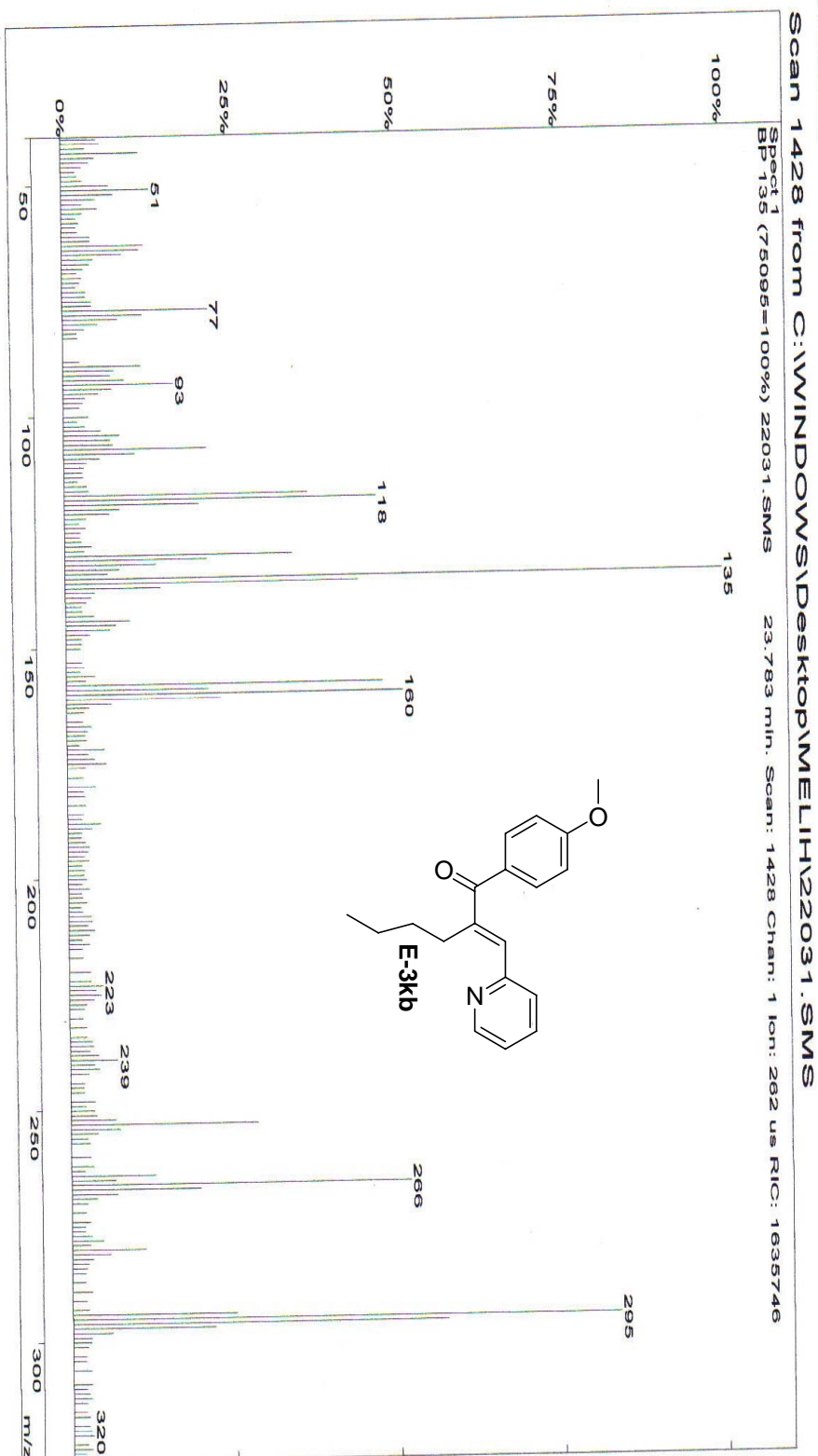
Figure A.22. Mass spectrum of (*E*)-1-(4-methoxyphenyl)-2-((pyridin-2-yl)methylene)hexan-1-one
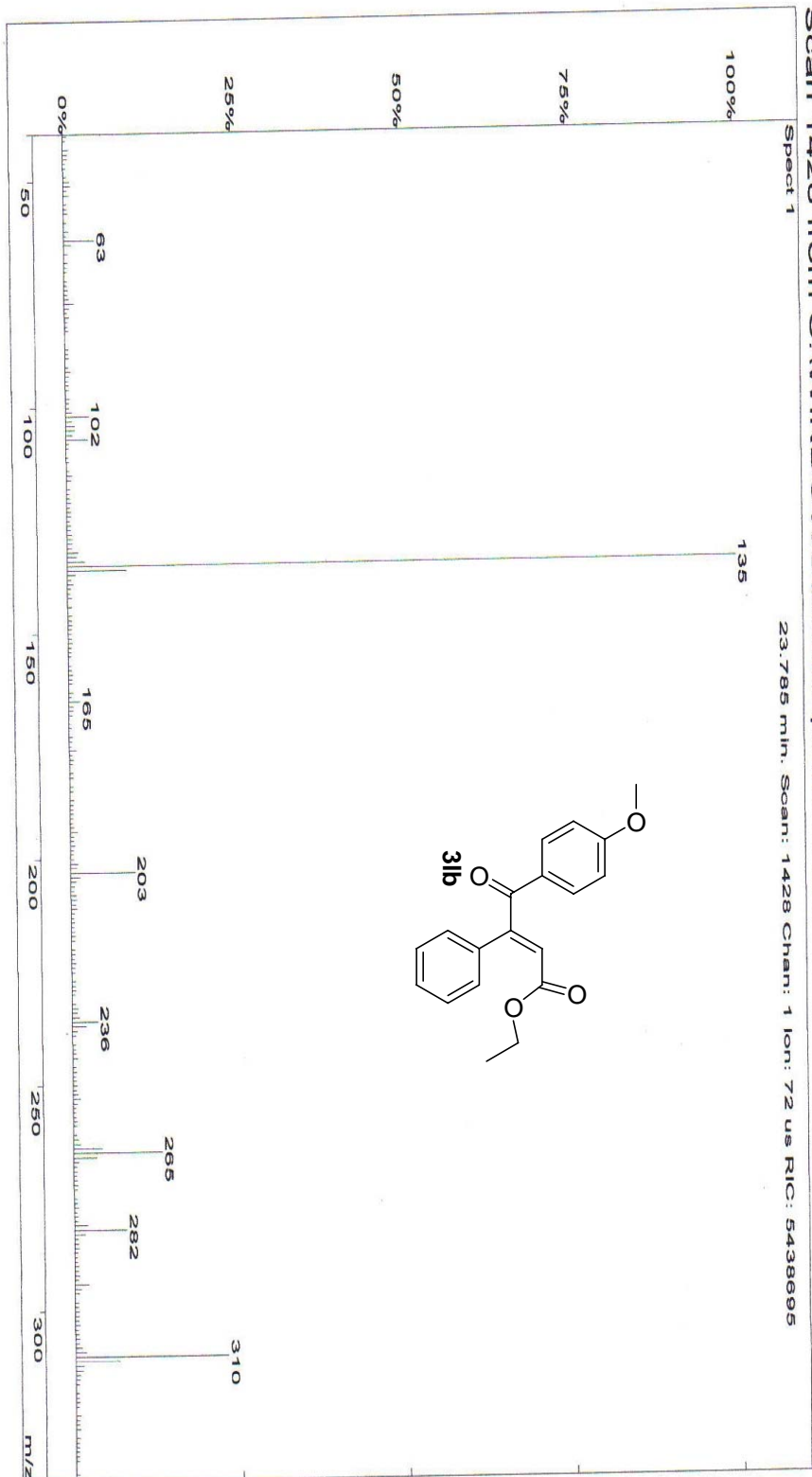
Figure A.23. Mass spectrum of (*E*)-ethyl 4-(4-methoxyphenyl)-4-oxo-3-phenylbut-2-enoate

Scan 1210 from C:\SaturnWS\org research\melih\t3kk281.SMS

Spect 1

20.149 min. Scan: 1210 Chan: 1 Ion: 83 us RIC: 2337249
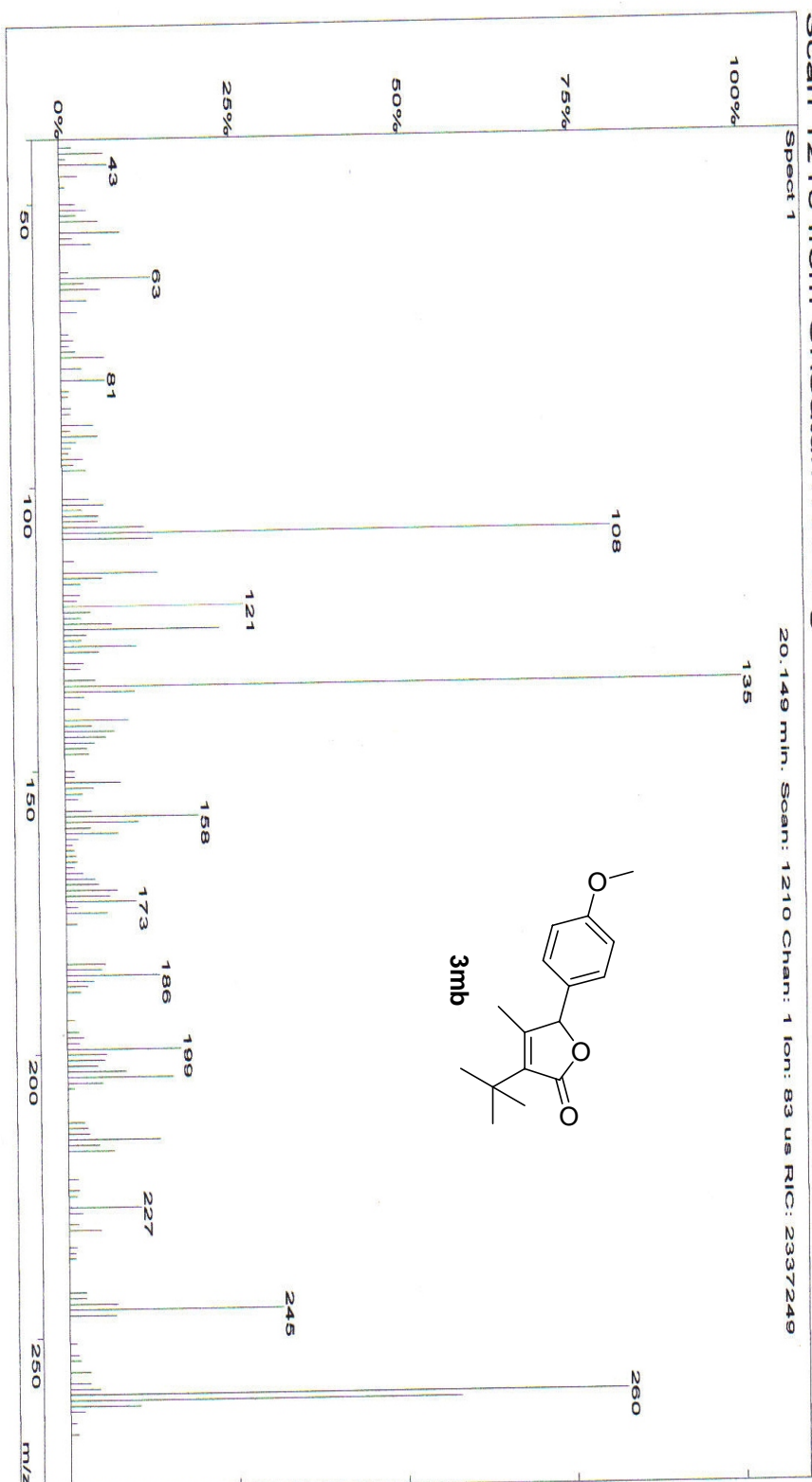
Figure A.24. Mass spectrum of 3-tert-butyl-5-(4-methoxyphenyl)-4-methylfuran-2(5H)-one
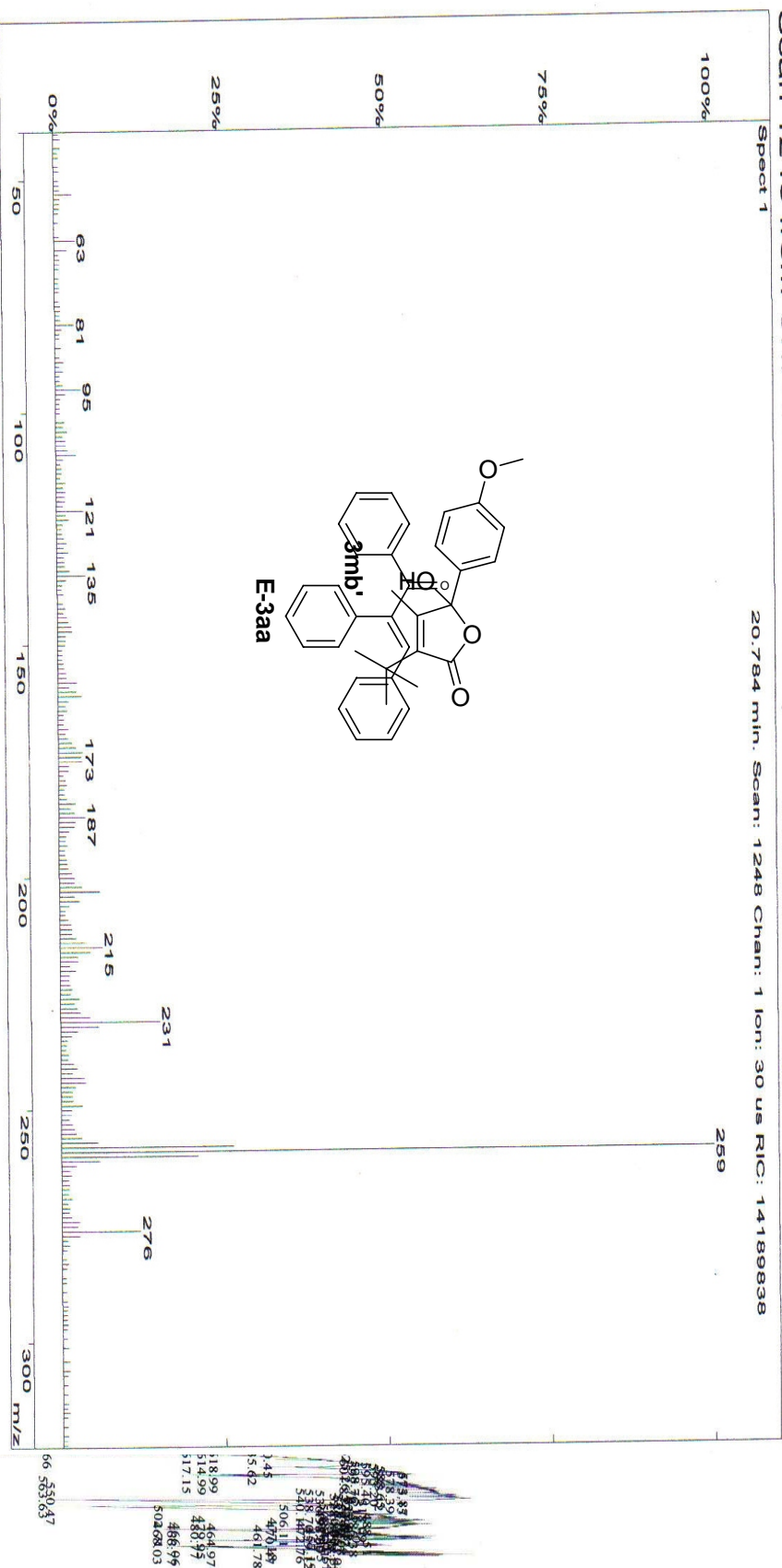
Figure B.1. FTIR spectrum of (*E*)-1,2,3-triphenylprop-2-en-1-one
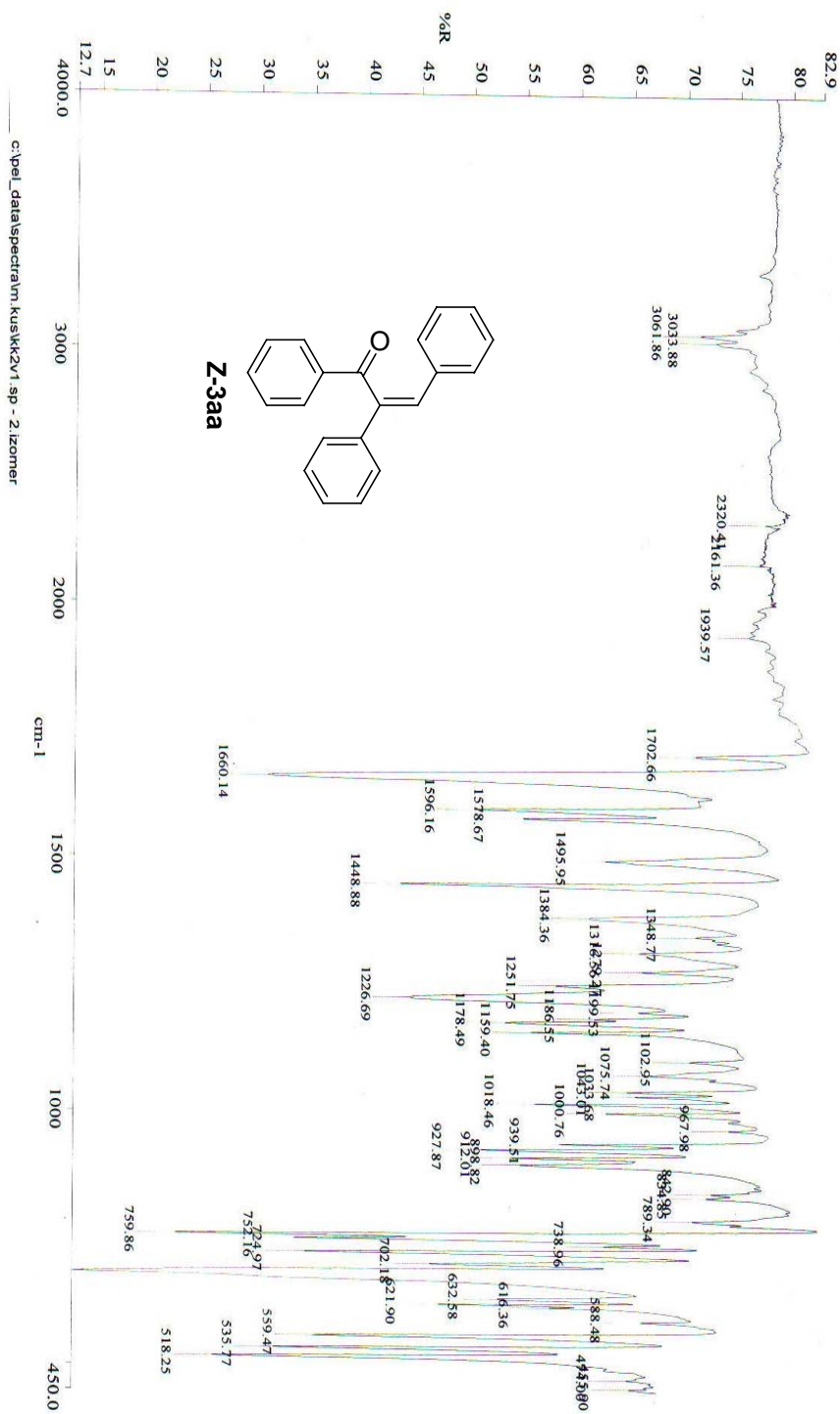
Figure B.2. FTIR spectrum of (Z)-1,2,3-triphenylprop-2-en-1-one
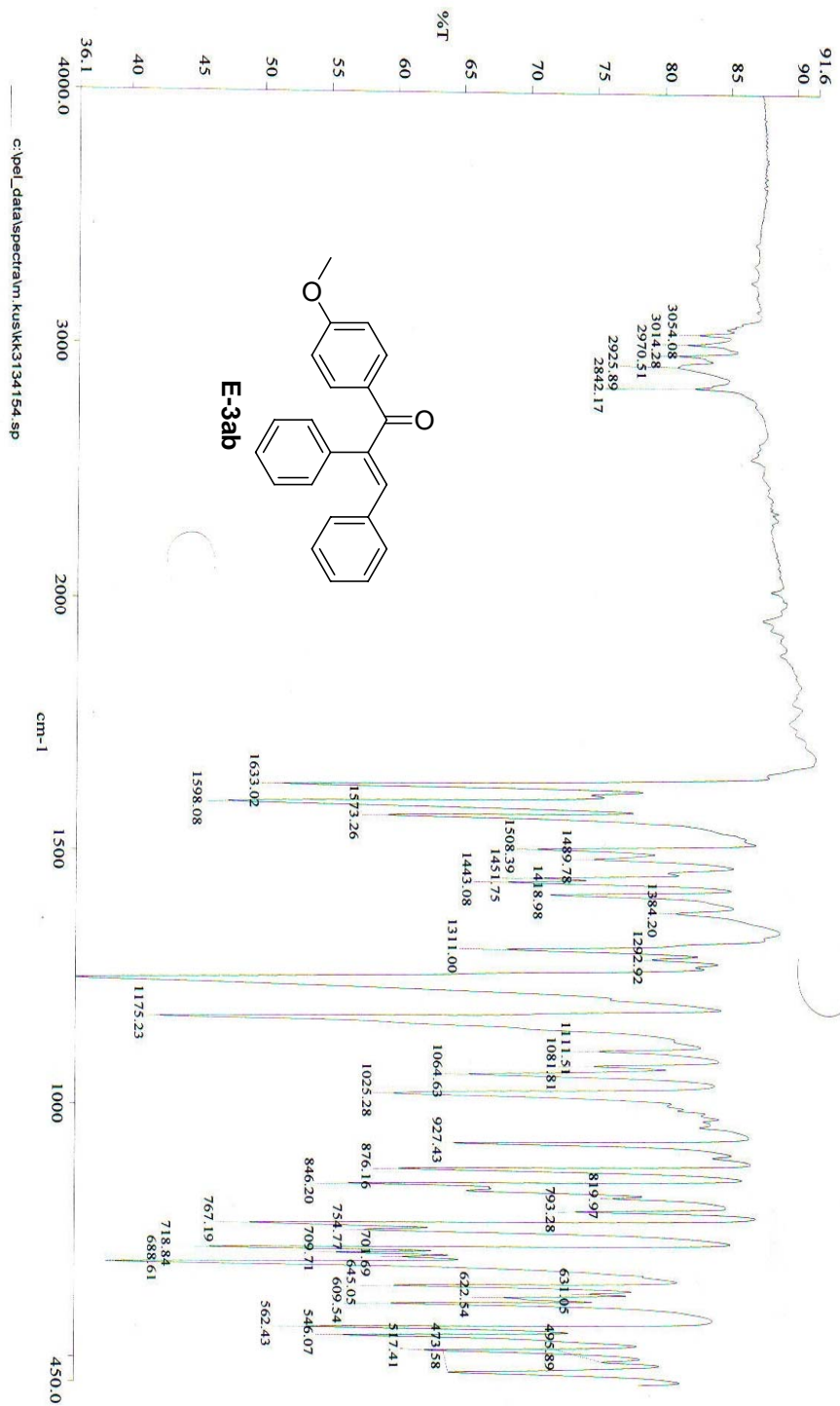
Figure B.3. FTIR spectrum of (*E*)-1-(4-methoxyphenyl)-2,3-diphenylprop-2-en-1-one
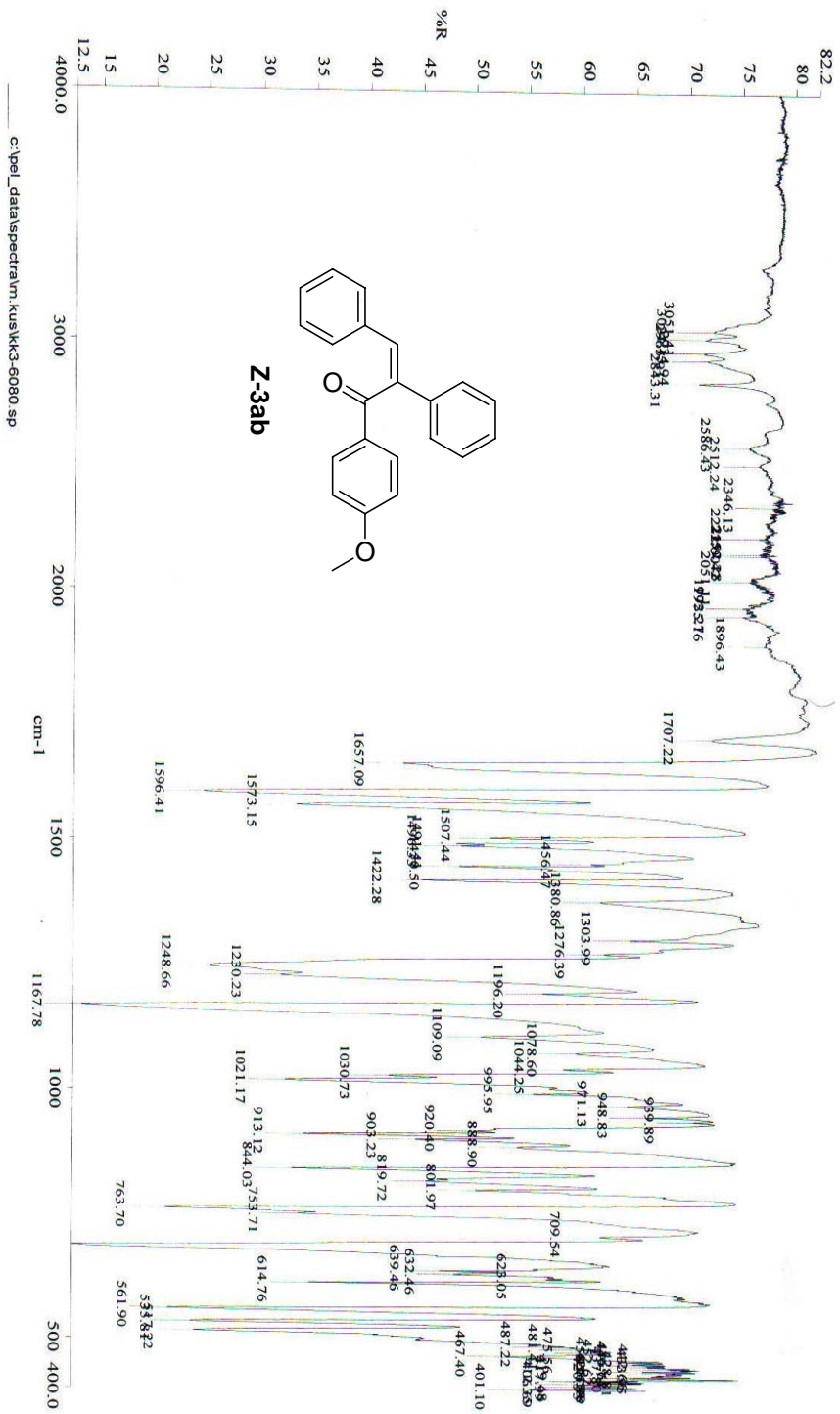
Figure B.4. FTIR spectrum of (Z)-1-(4-methoxyphenyl)-2,3-diphenylprop-2-en-1-one
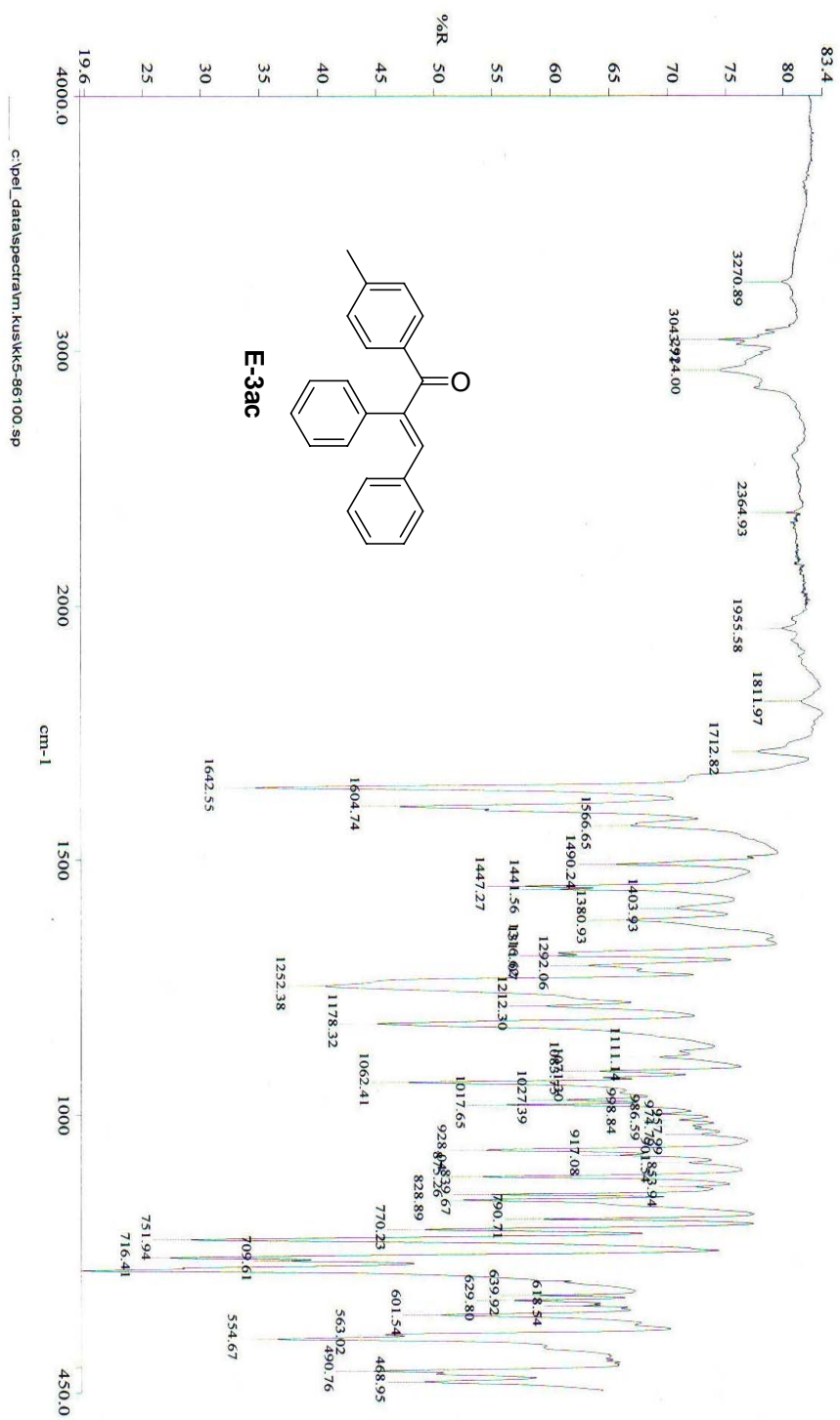
Figure B.5. FTIR spectrum of (*E*)-2,3-diphenyl-1-*p*-tolylprop-2-en-1-one
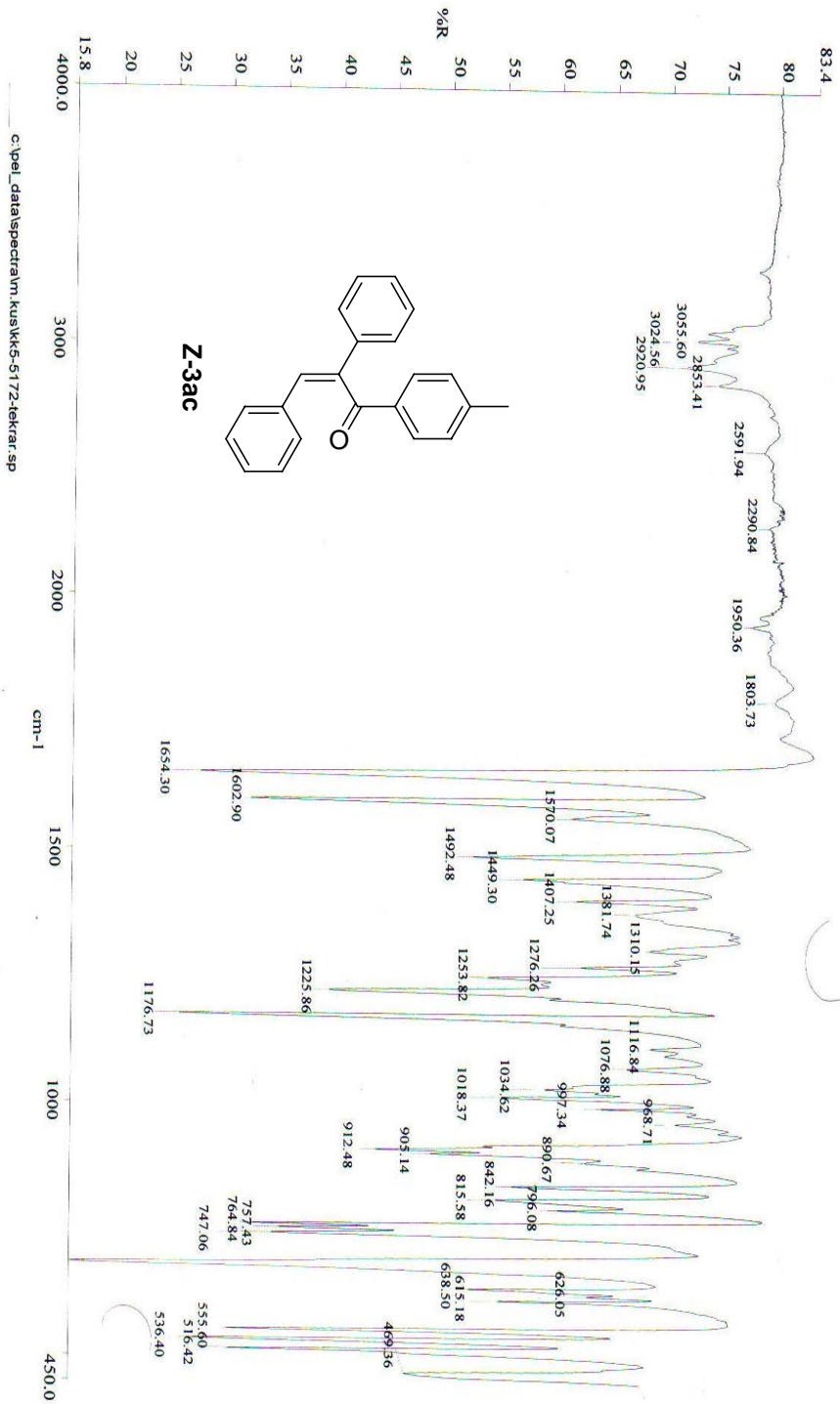
Figure B.6. Mass spectrum of (Z)-2,3-diphenyl1-1-*p*-tolylprop-2-en-1-one
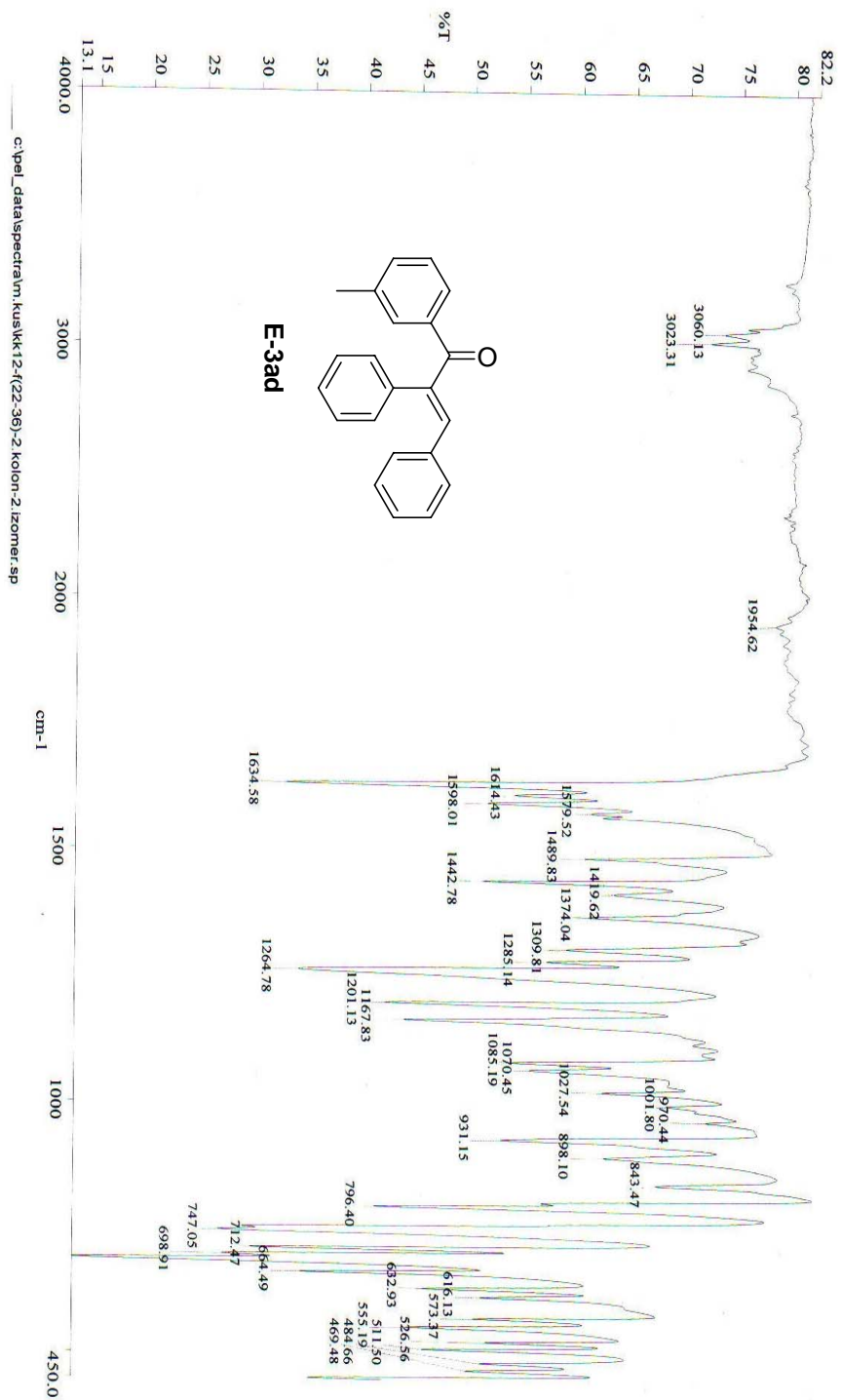
Figure B.7. FTIR spectrum of (*E*)-2,3-diphenyl1-1-*m*-tolylprop-2-en-1-one
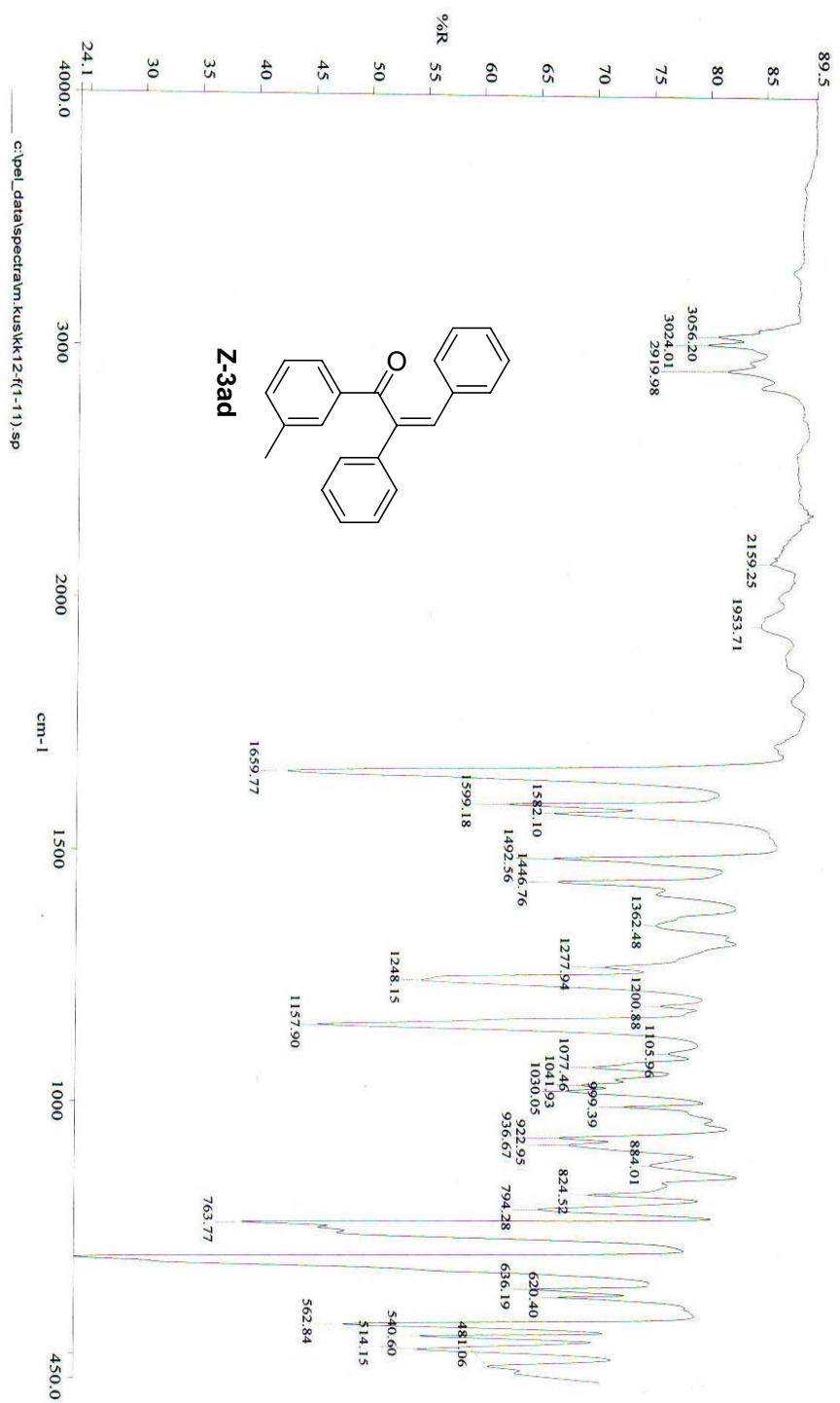
Figure B.8. FTIR spectrum of (*Z*)-2,3-diphenyl-1-1-*m*-tolylprop-2-en-1-one

78
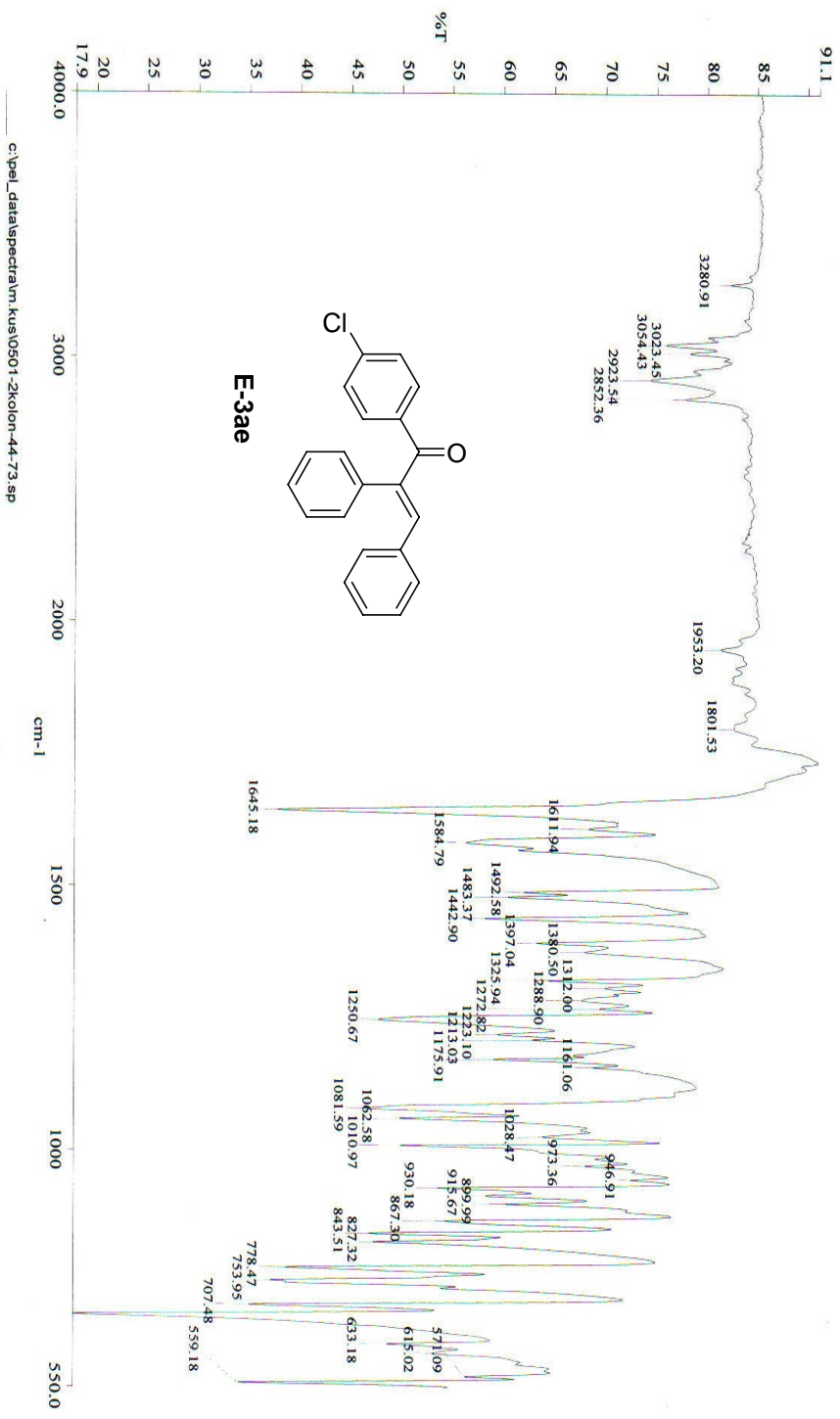
Figure B.9. FTIR spectrum of (*E*)-1-(4-chlorophenyl)-2,3-diphenylprop-2-en-1-one
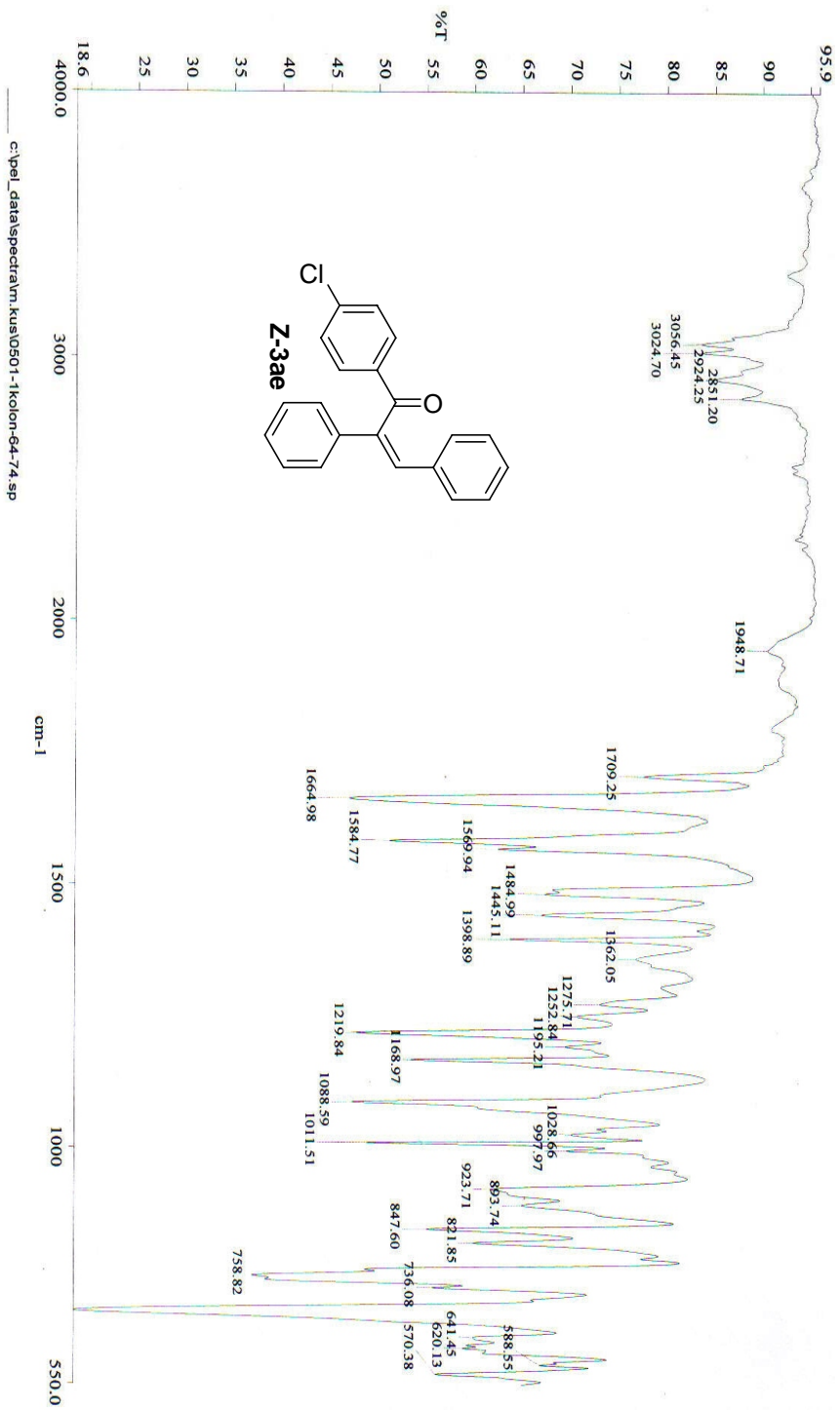
Figure B.10. FTIR spectrum of (Z)-1-(4-chlorophenyl)-2,3-diphenylprop-2-en-1-one
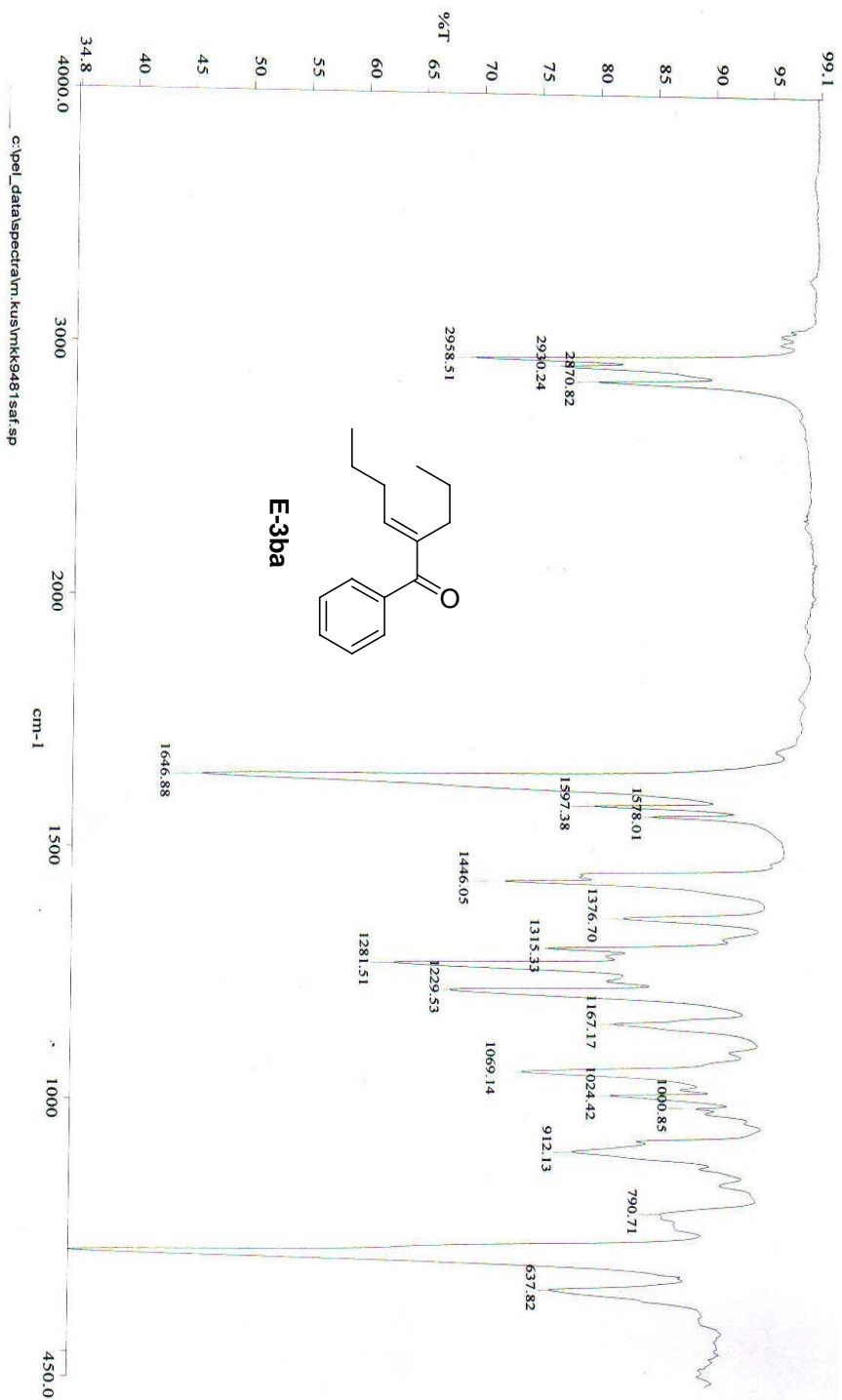
Figure B.11. FTIR spectrum of (*E*)-1-phenyl-2-propylhex-2-en-1-one

81
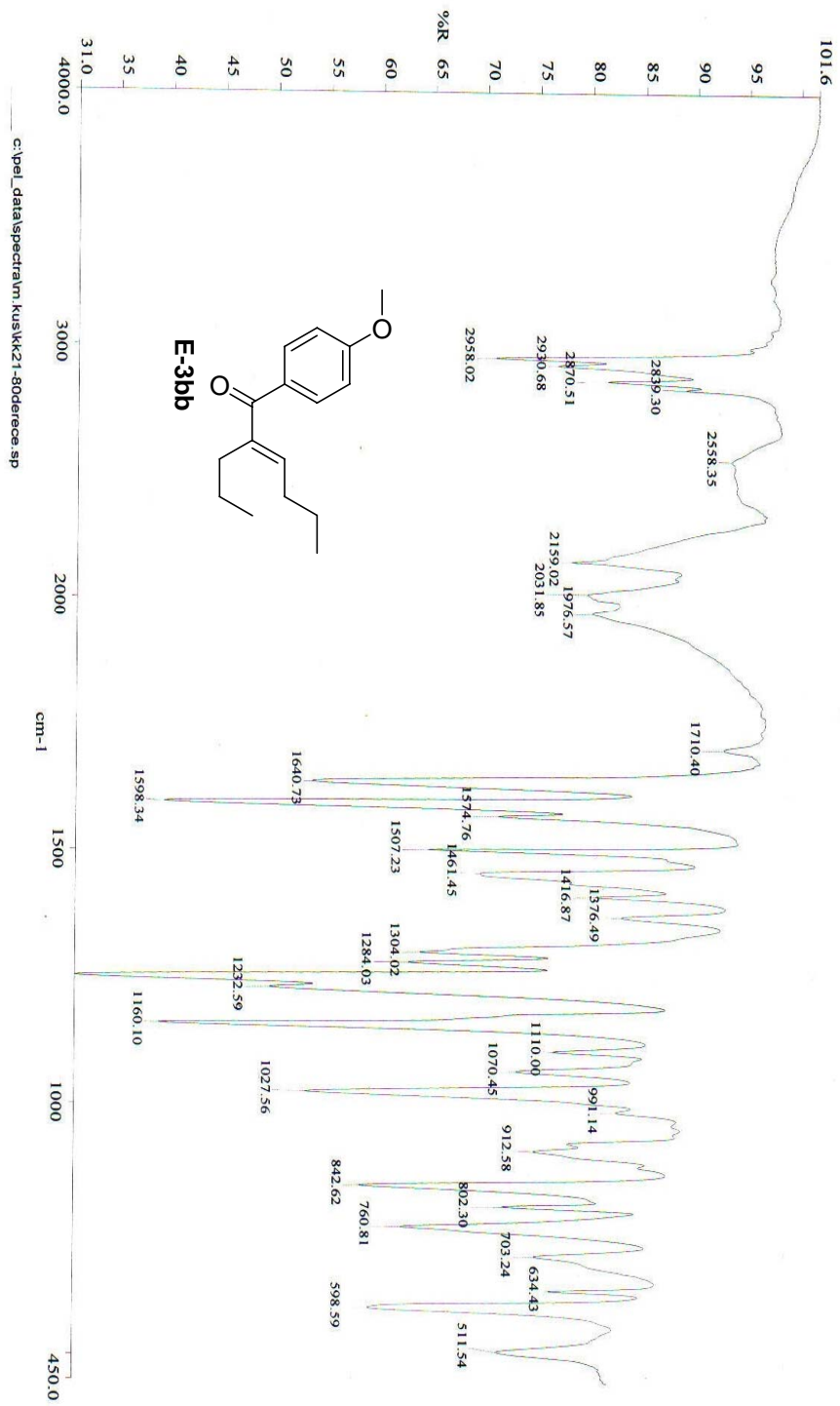
Figure B.12. FTIR spectrum of (*E*)-1-(4-methoxyphenyl)-2-propylhex-2-en-1-one
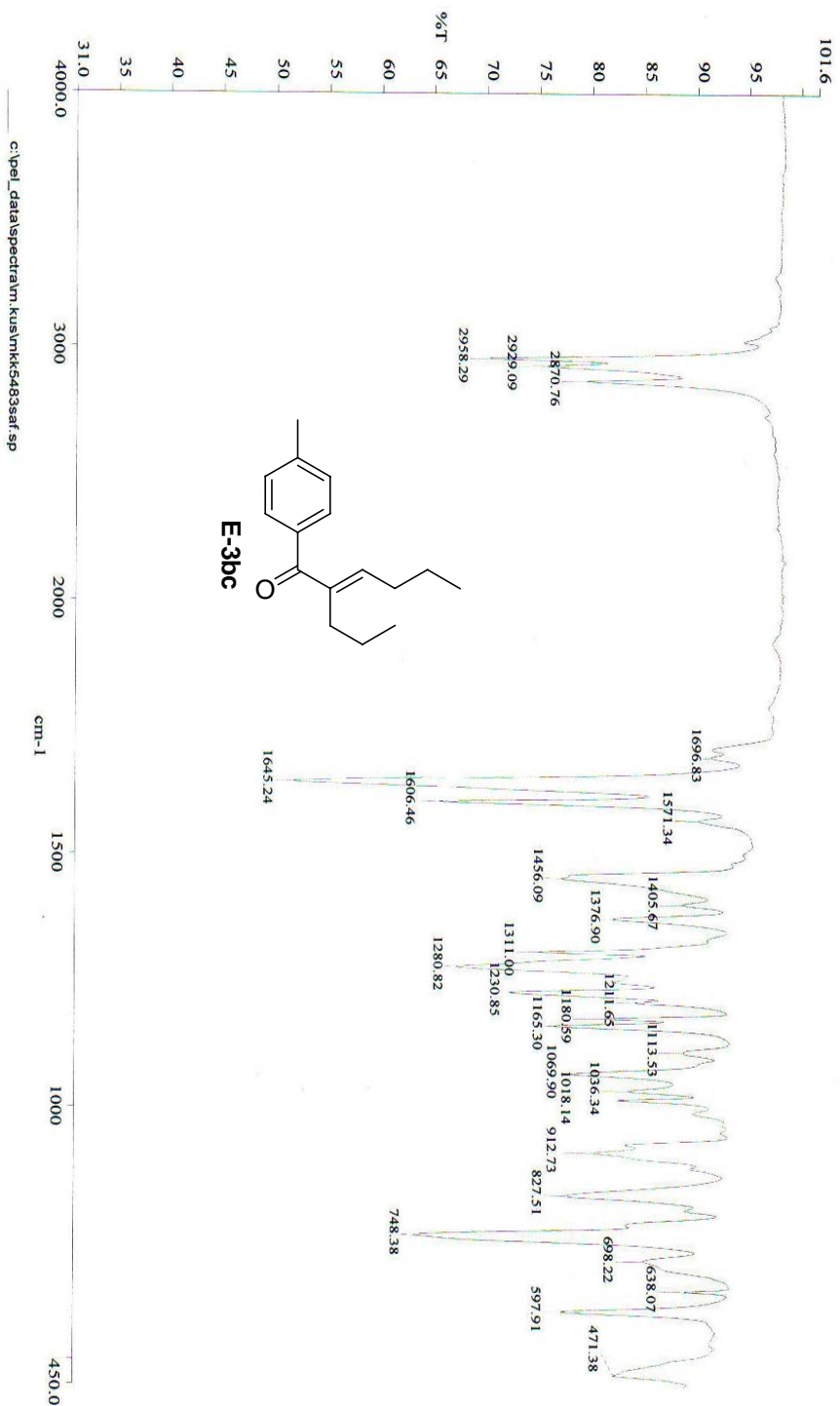
Figure B.13. FTIR spectrum of (*E*)-2-propyl-1-p-tolylhex-2-en-1-one

83
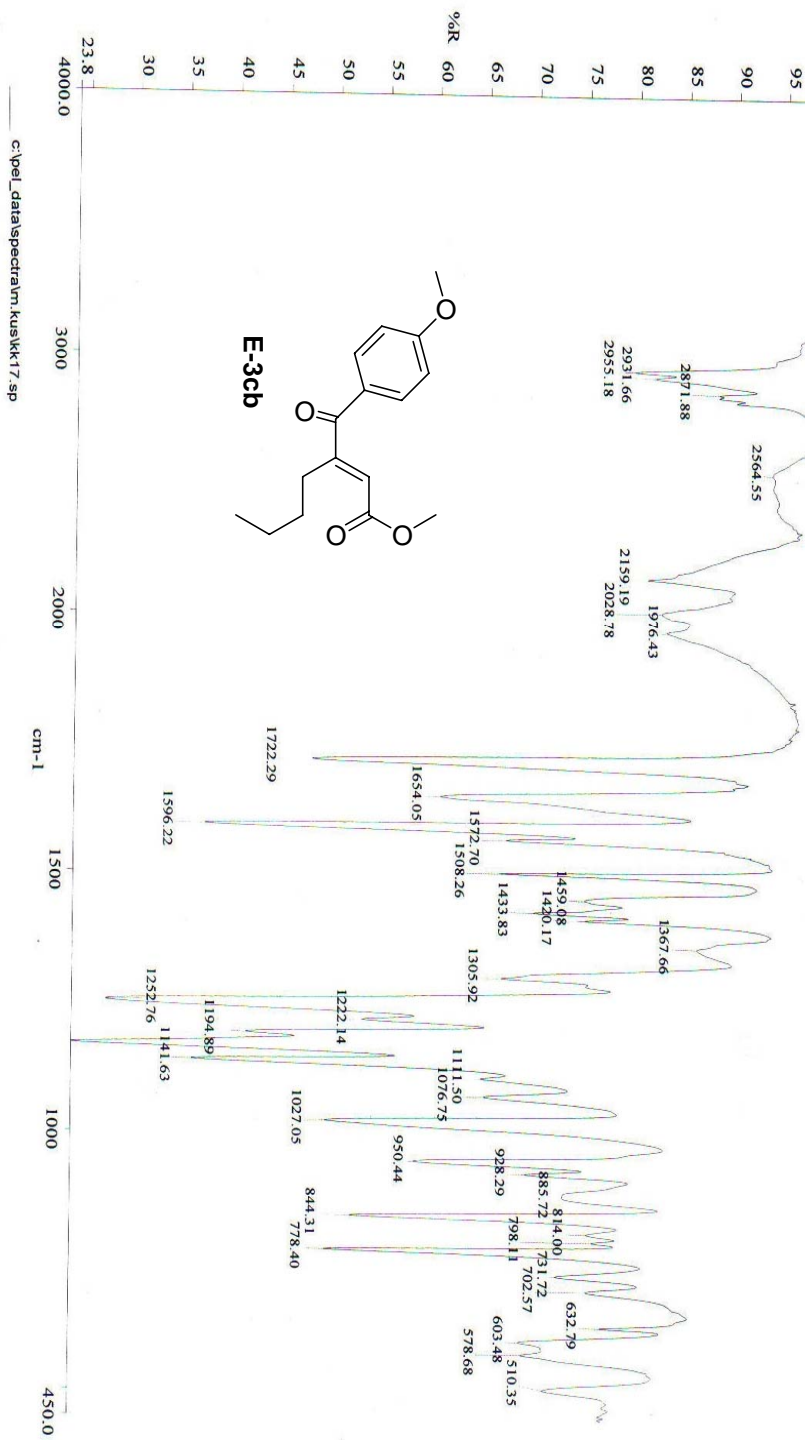
Figure B.14. FTIR spectrum of (*E*)-methyl 3-(4-methoxyphenyl)hept-2-enoate
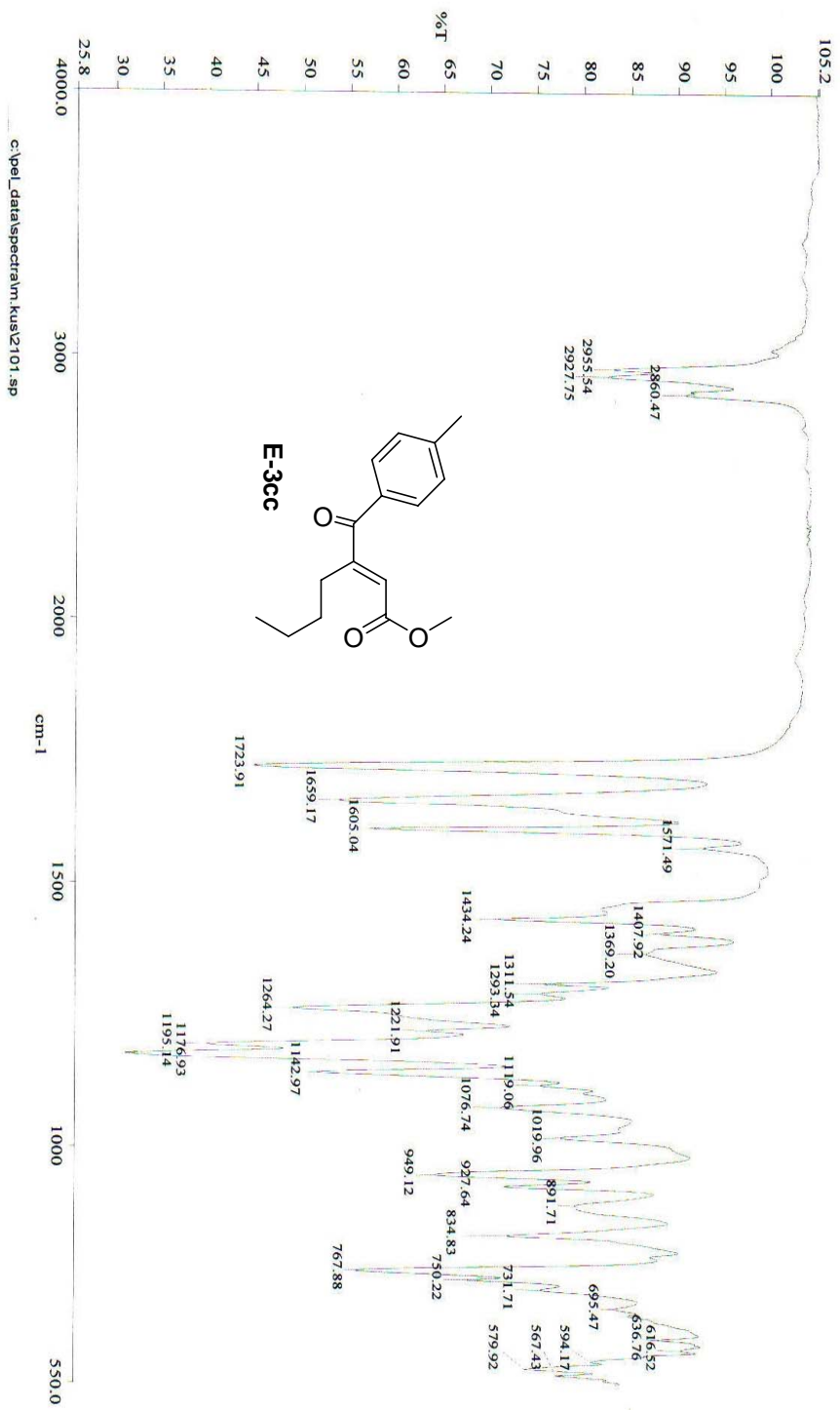
Figure B.15. FTIR spectrum of (*E*)-methyl 3-(4-methylphenyl)hept-2-enoate
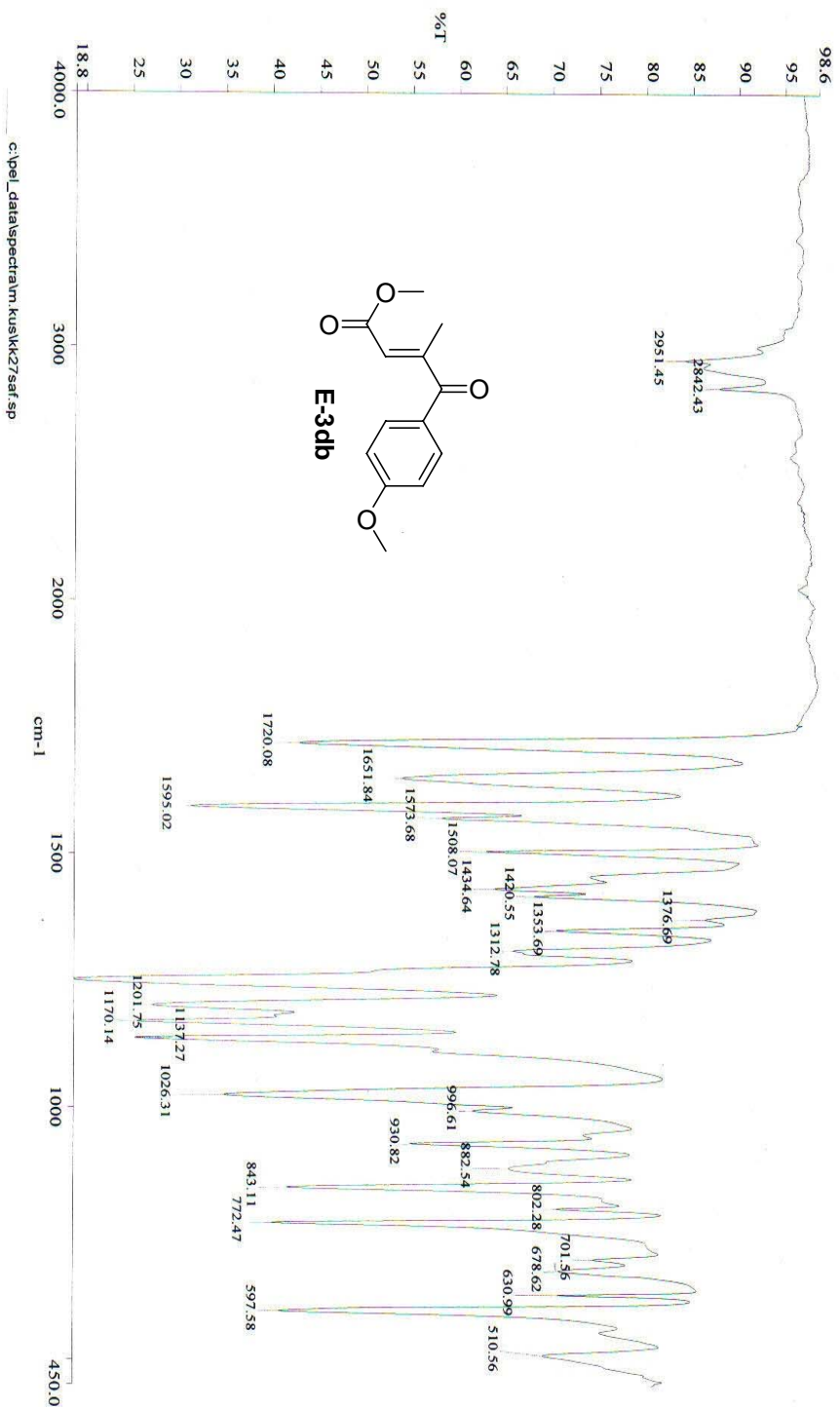
Figure B.16. FTIR spectrum of (*E*)-methyl 4-(4-methoxyphenyl)-3-methyl-4-oxobut-2-enoate
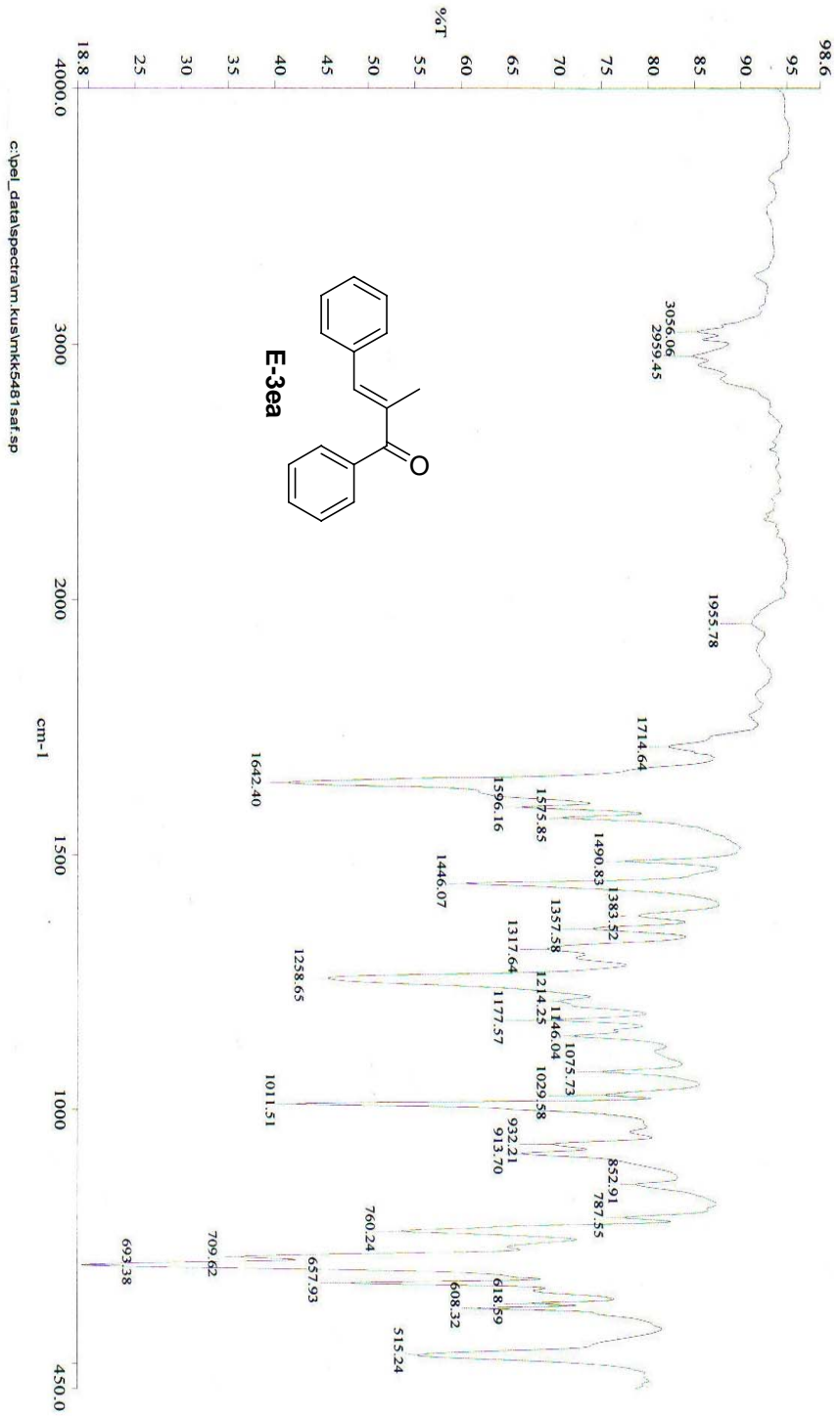
Figure B.17. FTIR spectrum of (*E*)-2-methyl-1,3-diphenylprop-2-en-1-one
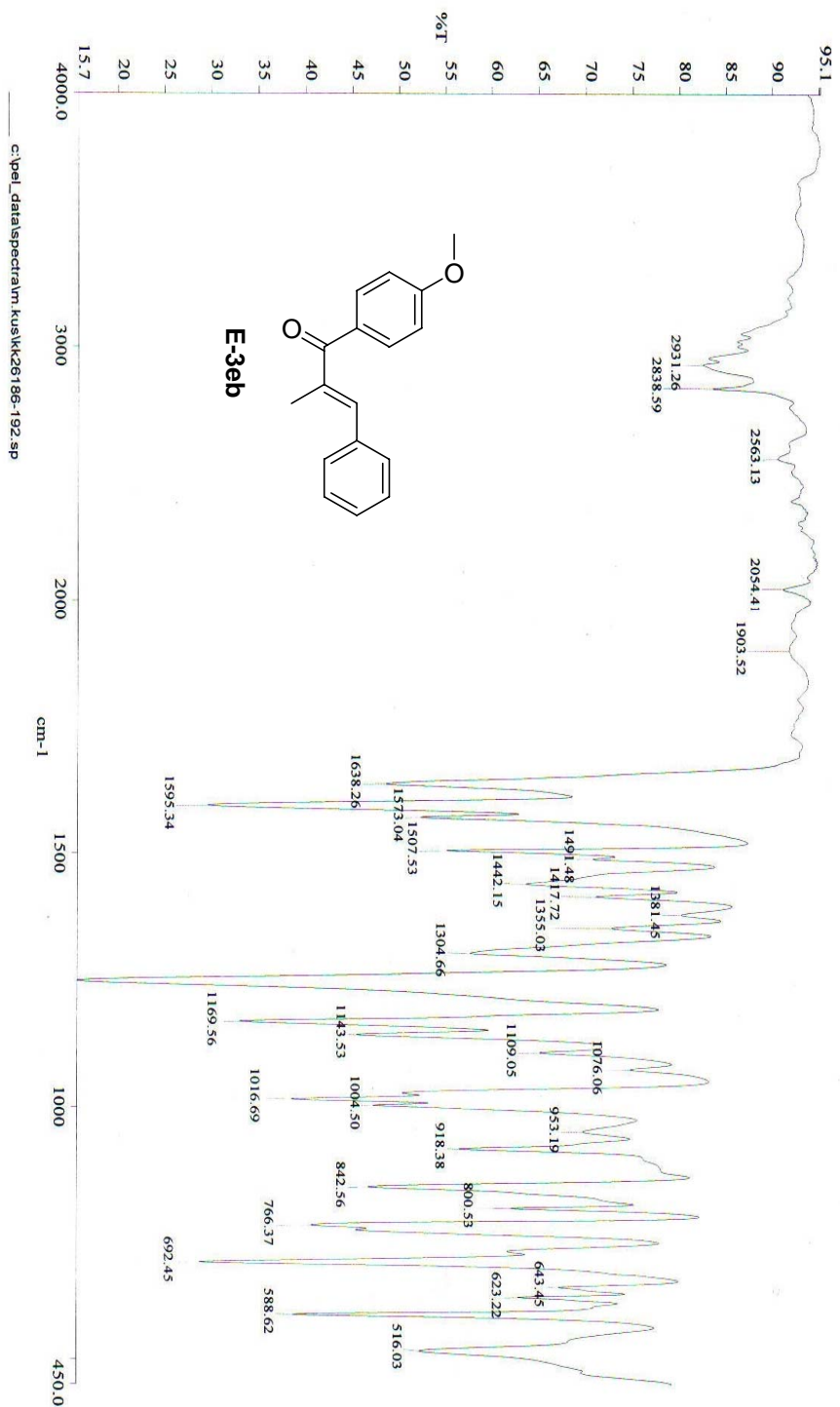
Figure B.18. FTIR spectrum of (*E*)-1-(4-methoxyphenyl)-2-methyl-3-phenylprop-2-en-1-one
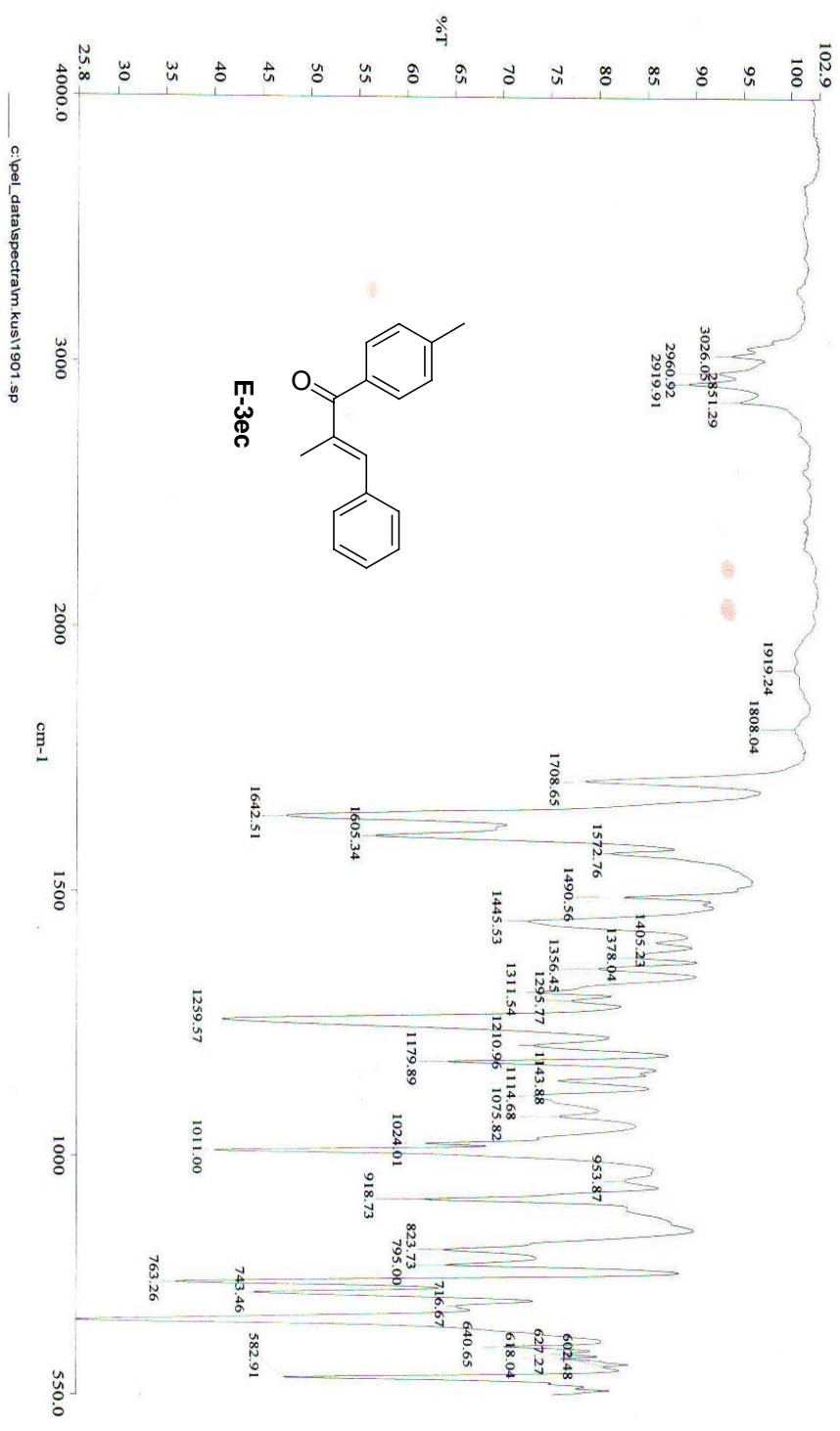
Figure B.19. FTIR spectrum of (*E*)-2-methyl-3-phenyl-1-1-p-tolylprop-2-en-1-one
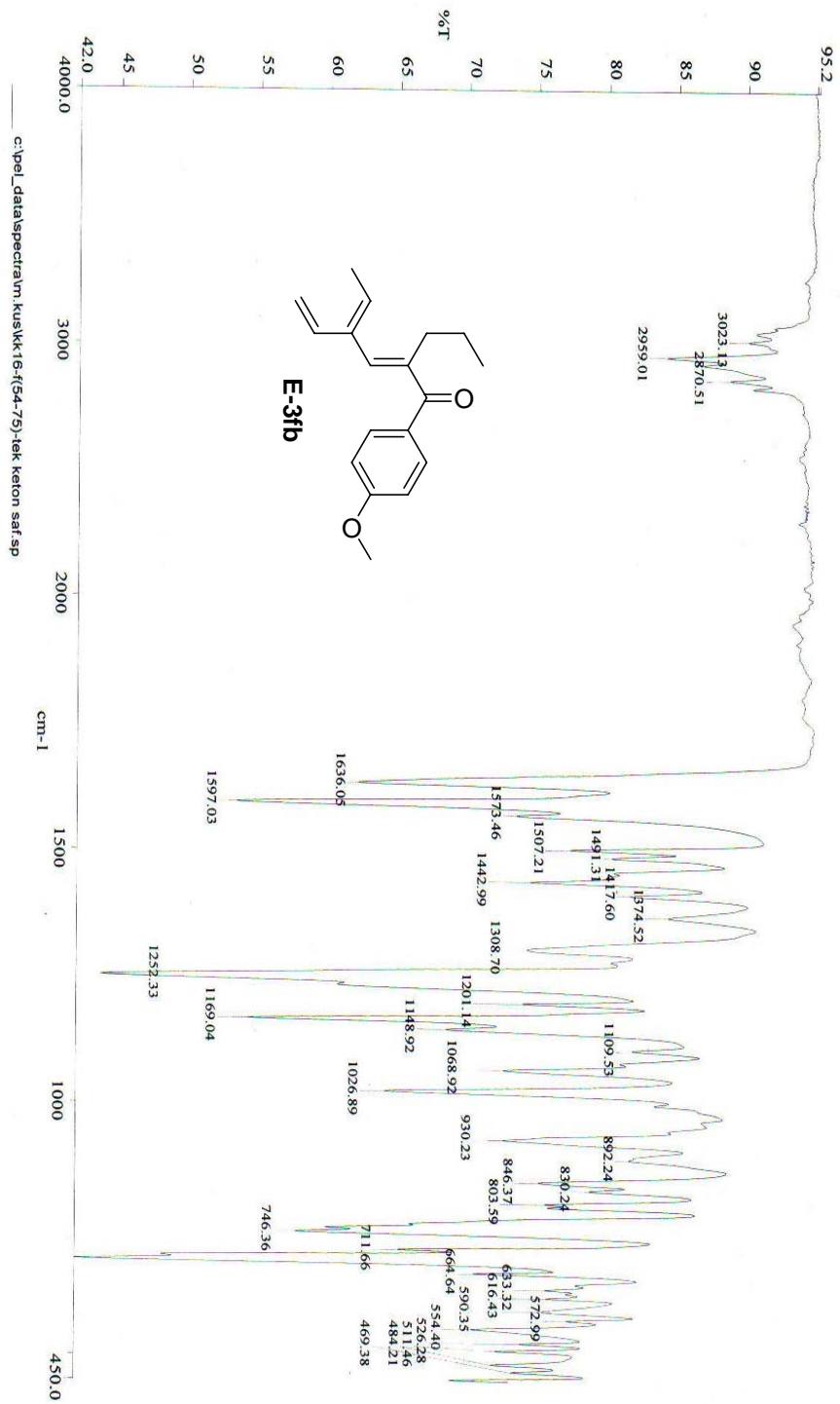
Figure B.20. FTIR spectrum of (*E*)-2-benzylidene-1-(4-methoxyphenyl)pentan-1-one

90
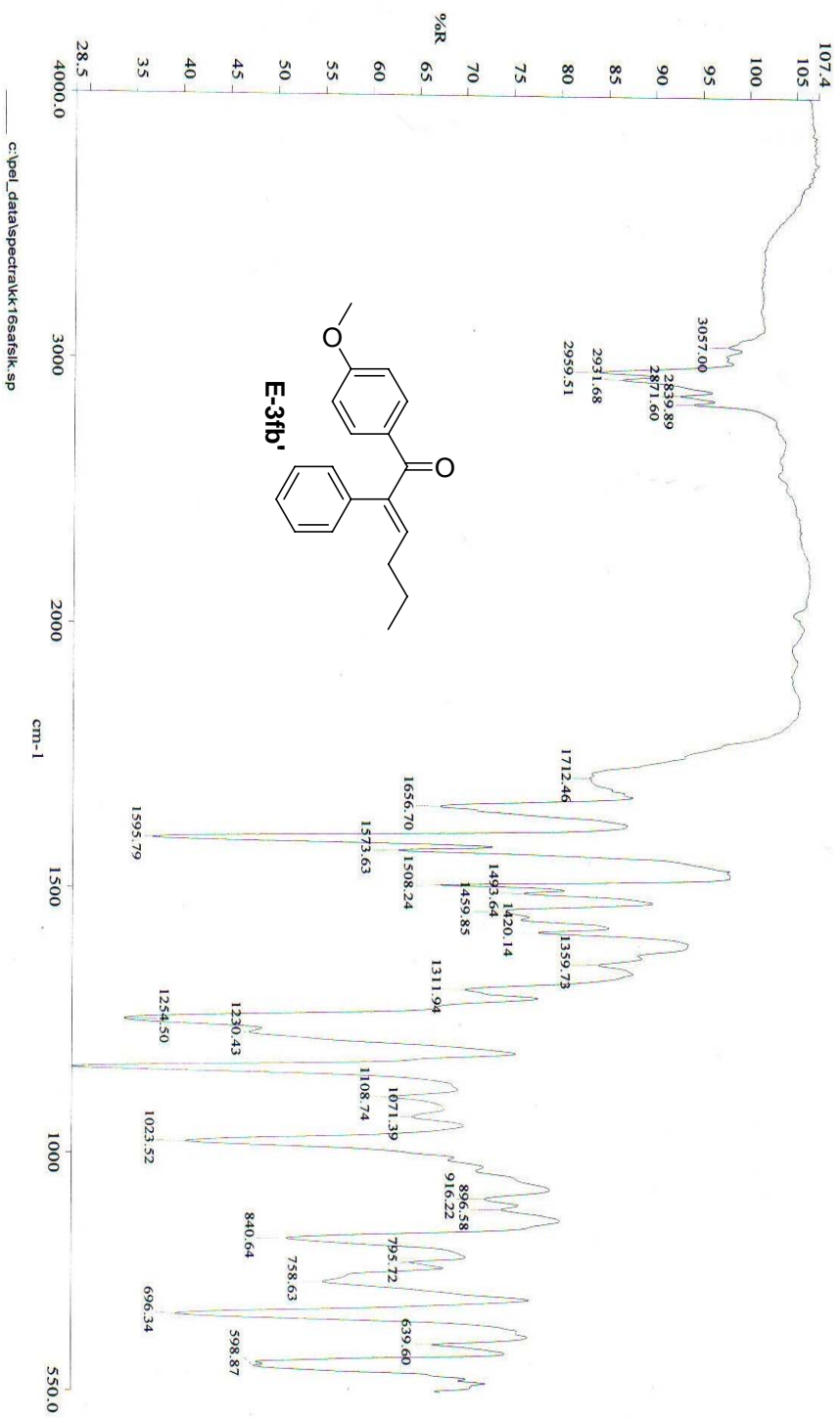
Figure B.21. FTIR spectrum of 3-(4-methoxyphenyl)-4,5-diphenylfuran-2(*5H*)-one
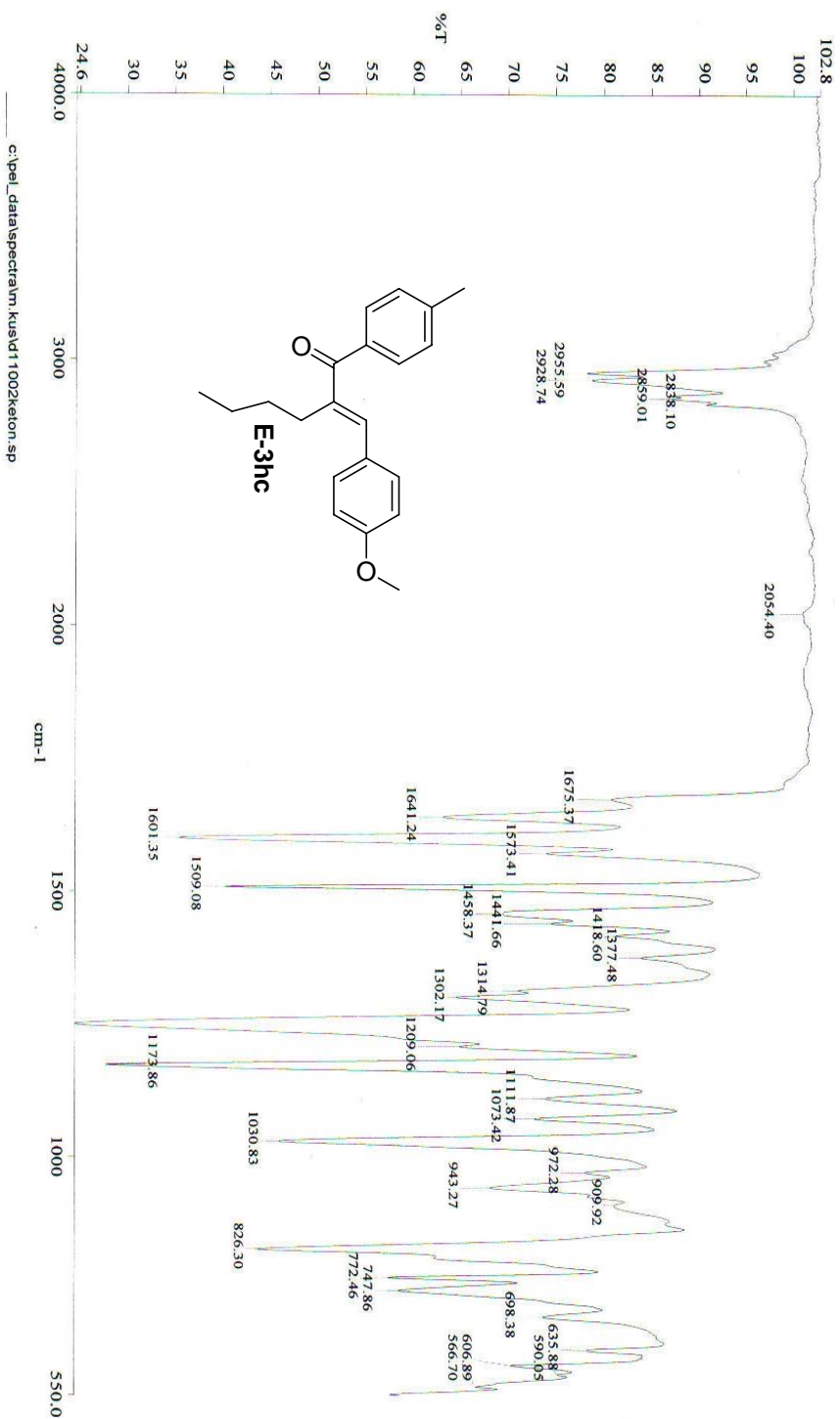
Figure B.22. FTIR spectrum of (*E*)-2-(4-methoxybenzylidene)-1-p-tolylhexan-1-one
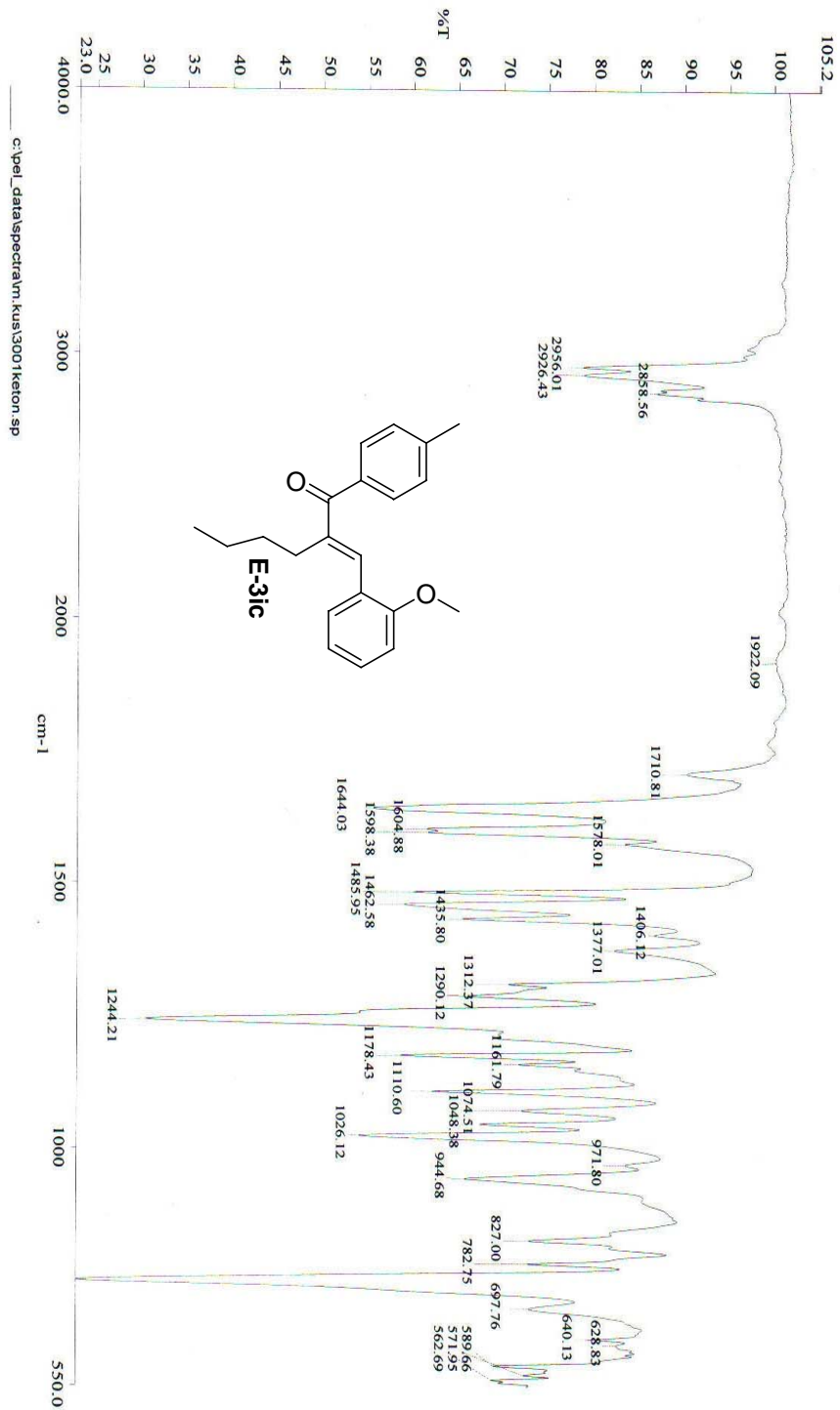
Figure B.23. FTIR spectrum of (*E*)-2-(2-methoxybenzylidene)-1-p-tolylhexan-1-one
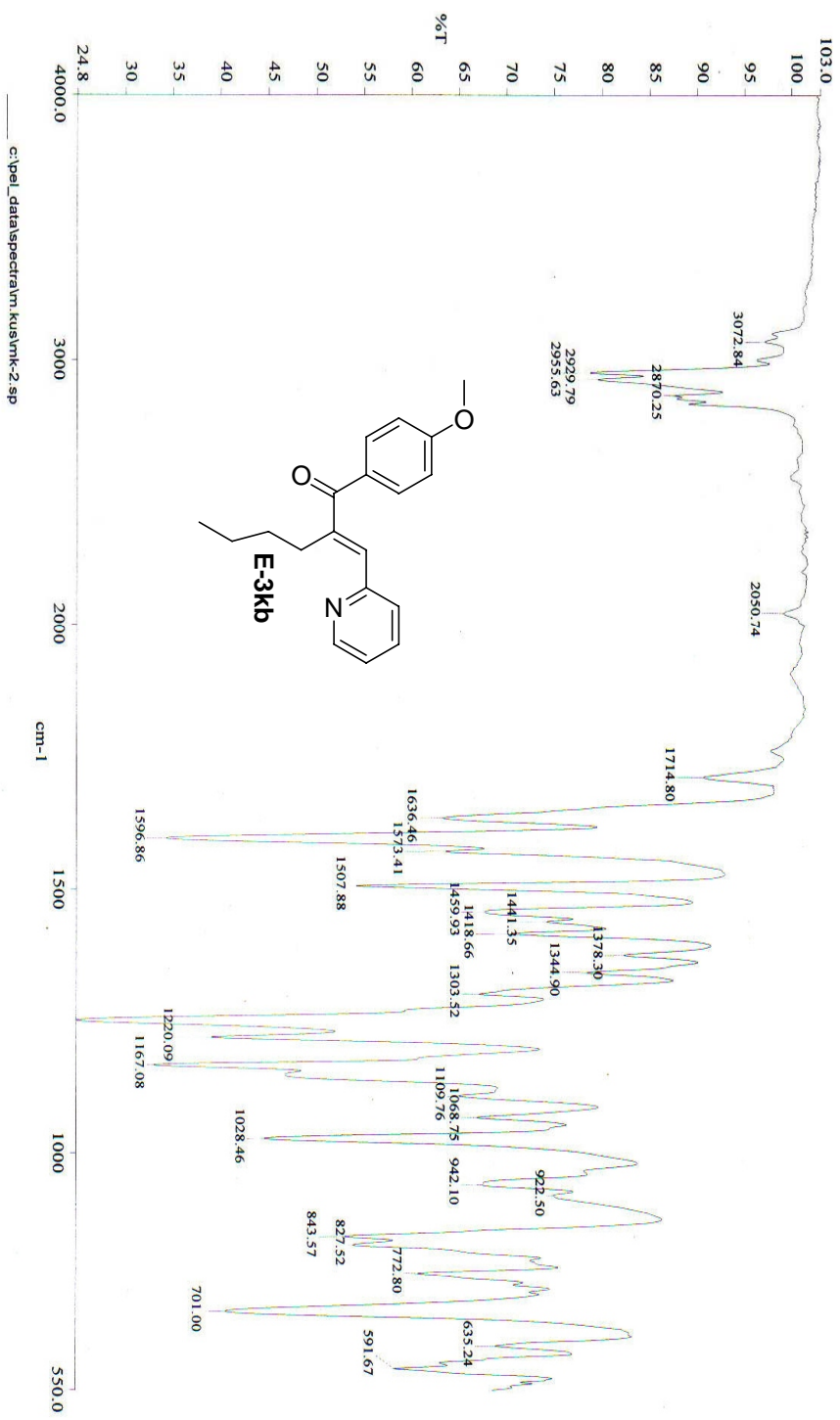
Figure B.24. FTIR spectrum of (*E*)-1-(4-methoxyphenyl)-2-((pyridin-2-yl)methylene)hexan-1-one

94
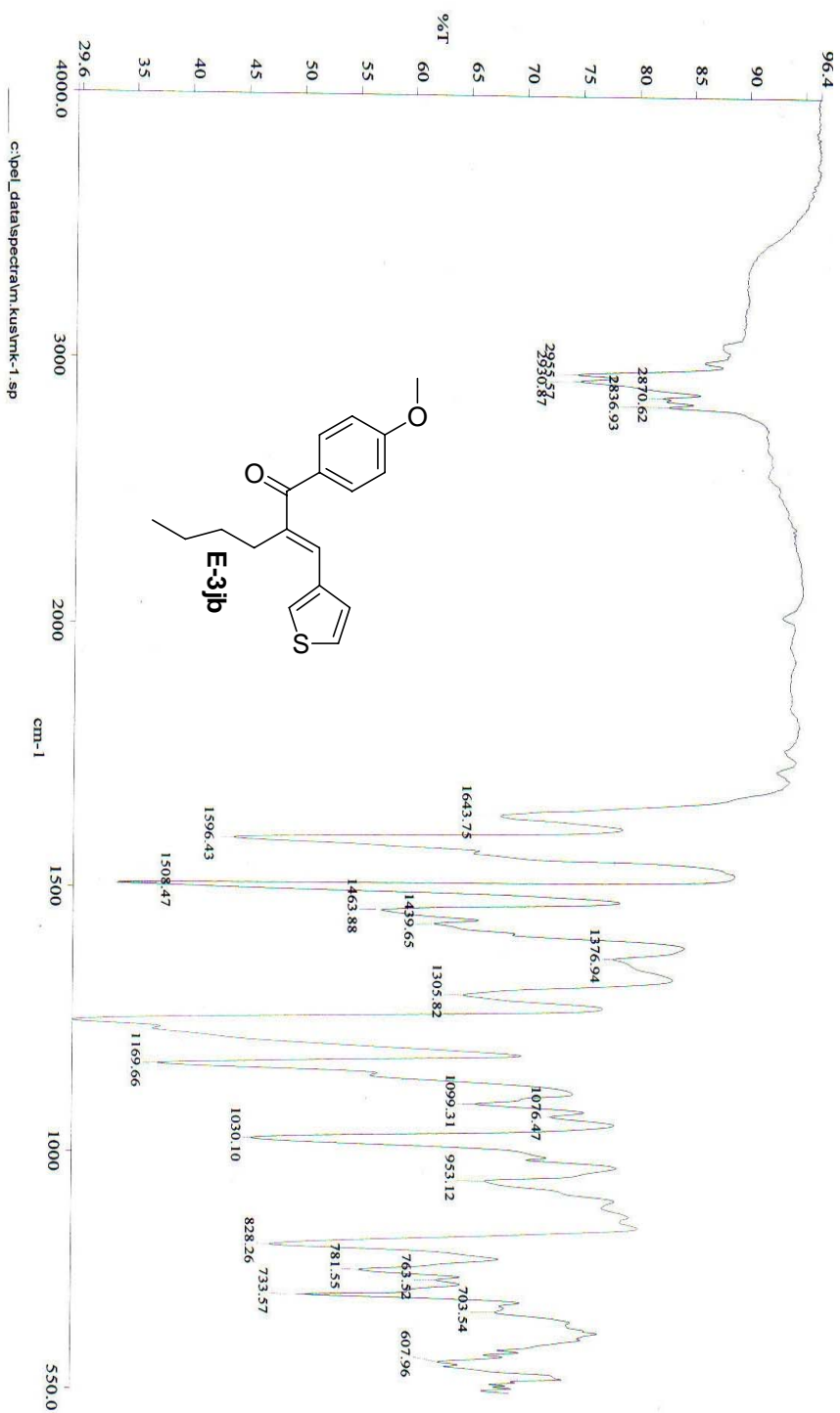
Figure B.25. FTIR spectrum of (*E*)-1-(4-methoxyphenyl)-2-((thiophen-3-yl)methylene)hexan-1-one
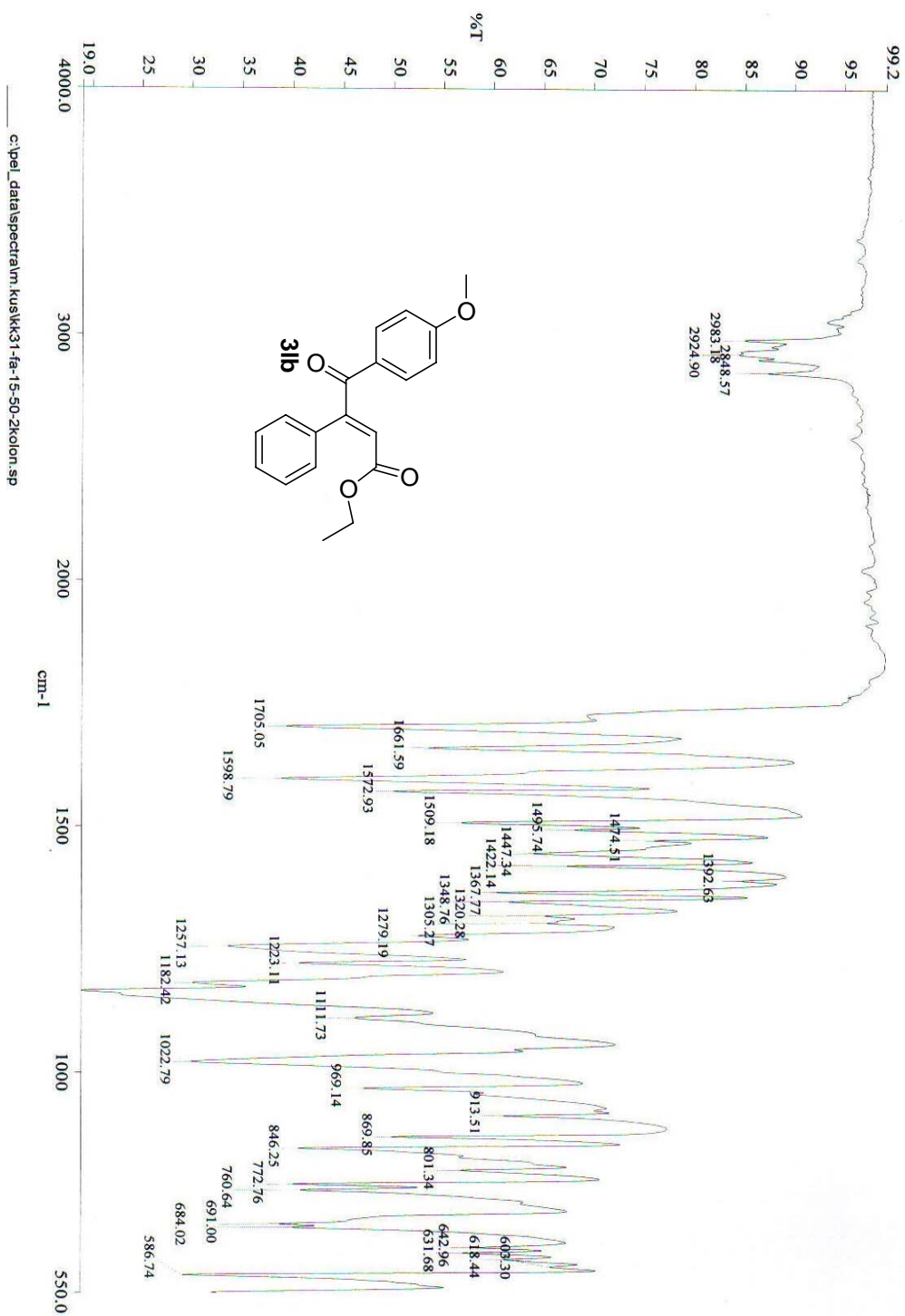
Figure B.26. FTIR spectrum of (*E*)-ethyl 4-(4-methoxyphenyl)-4-oxo-3-phenylbut-2-enoate

96
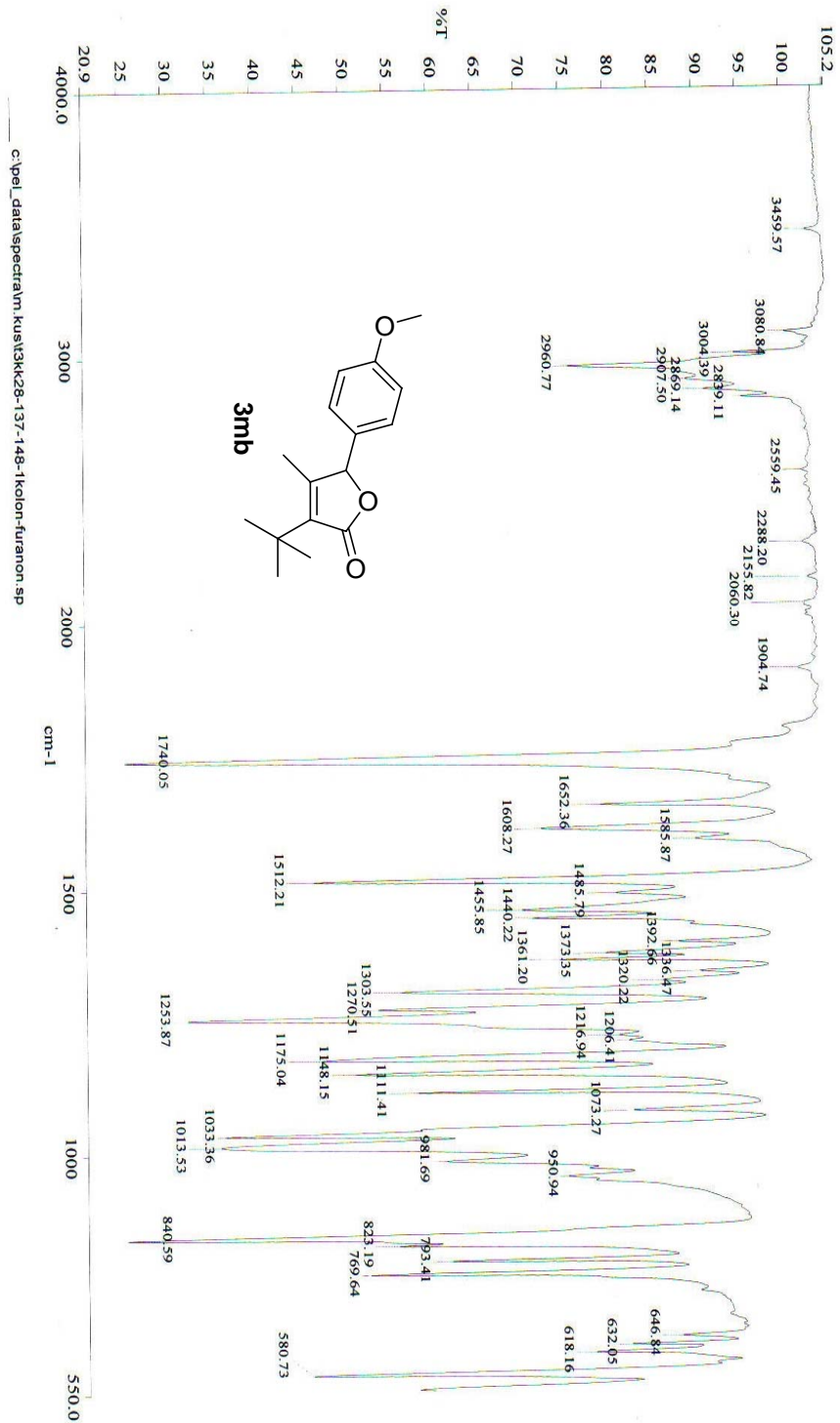
Figure B.27. FTIR spectrum of 3-tert-butyl-5-(4-methoxyphenyl)-4-methylfuran-2(5H)-one
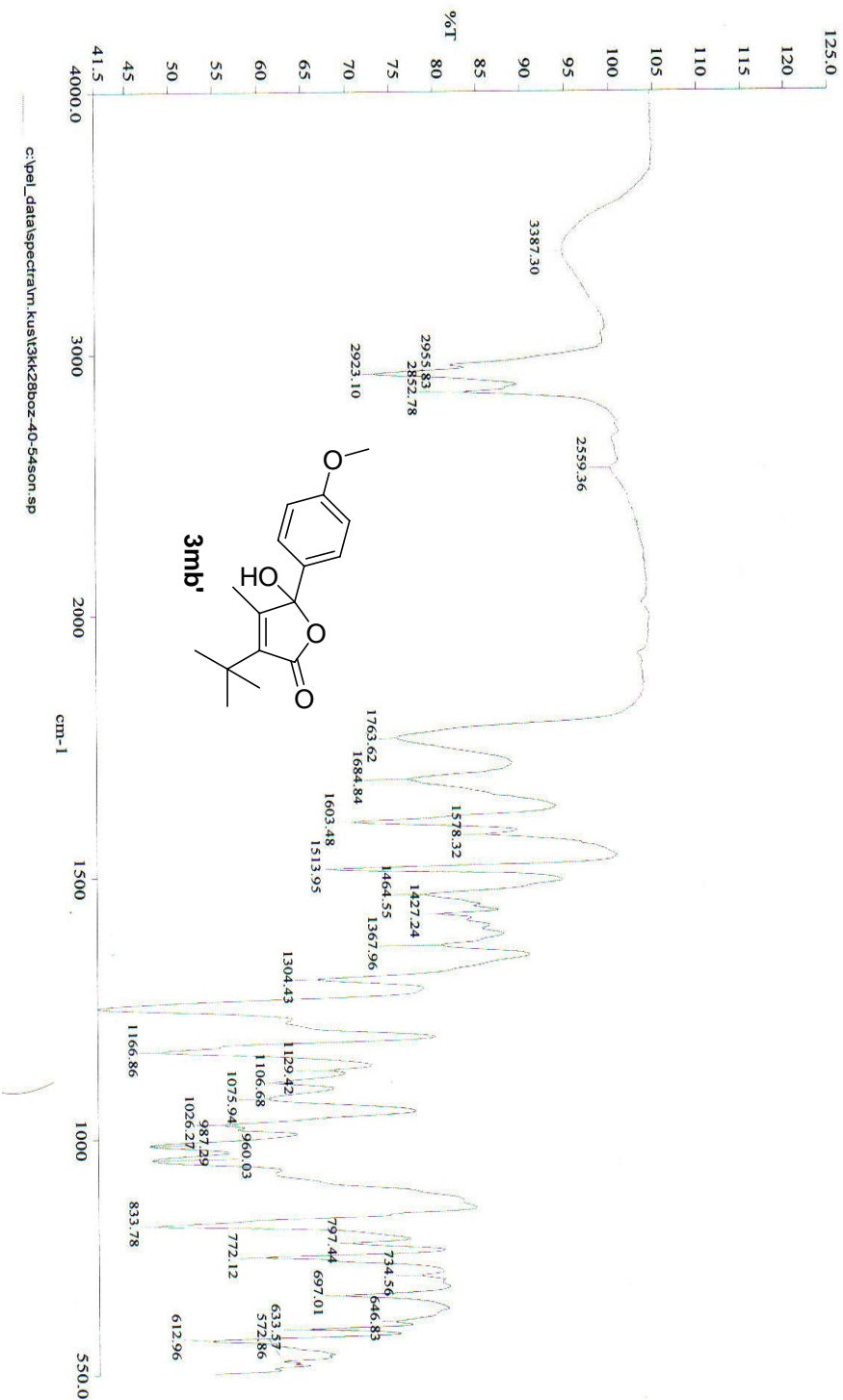
Figure B.28. FTIR spectrum of 3-tert-butyl-5-hydroxy-5-(4-methoxyphenyl)-4-methylfuran-2(5H)-one

APPENDIX C

Figure C.1. ^{1}H NMR of (*E*)-1,2,3-triphenylprop-2-en-1-one

VARIAN

E-3aa

MELIH-KK2-1IZO-C

Sample Name:
  MELIH-KK2-1IZO-C
Data Collected on:
  nmr400-vnmrs400
Archive directory:
  /home/walkup1/vnmrsys/data
Sample directory:
  MELIH-KK2-1IZO-C_10Mar2008
FidFile: CARBON

Pulse Sequence: CARBON (s2pul)
Solvent: cdcl3
Data collected on: Mar 10 2008

Temp. 25.0 C / 298.1 K
Operator: walkup1

Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 1.285 sec
Width 25510.2 Hz
512 repetitions
OBSERVE C13, 100.4598839 MHz
DECOUPLE H1, 399.5339868 MHz
Power 39 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.5 Hz
FT size 65536
Total time 19 min

76.693
77.010
77.328

126.359
127.924
128.017
128.250
128.281
128.444
128.730
128.777
128.831
128.854
128.932
129.660
129.707
129.784
130.133
130.334
132.156
134.790
136.503
138.185
140.145
140.788
197.62
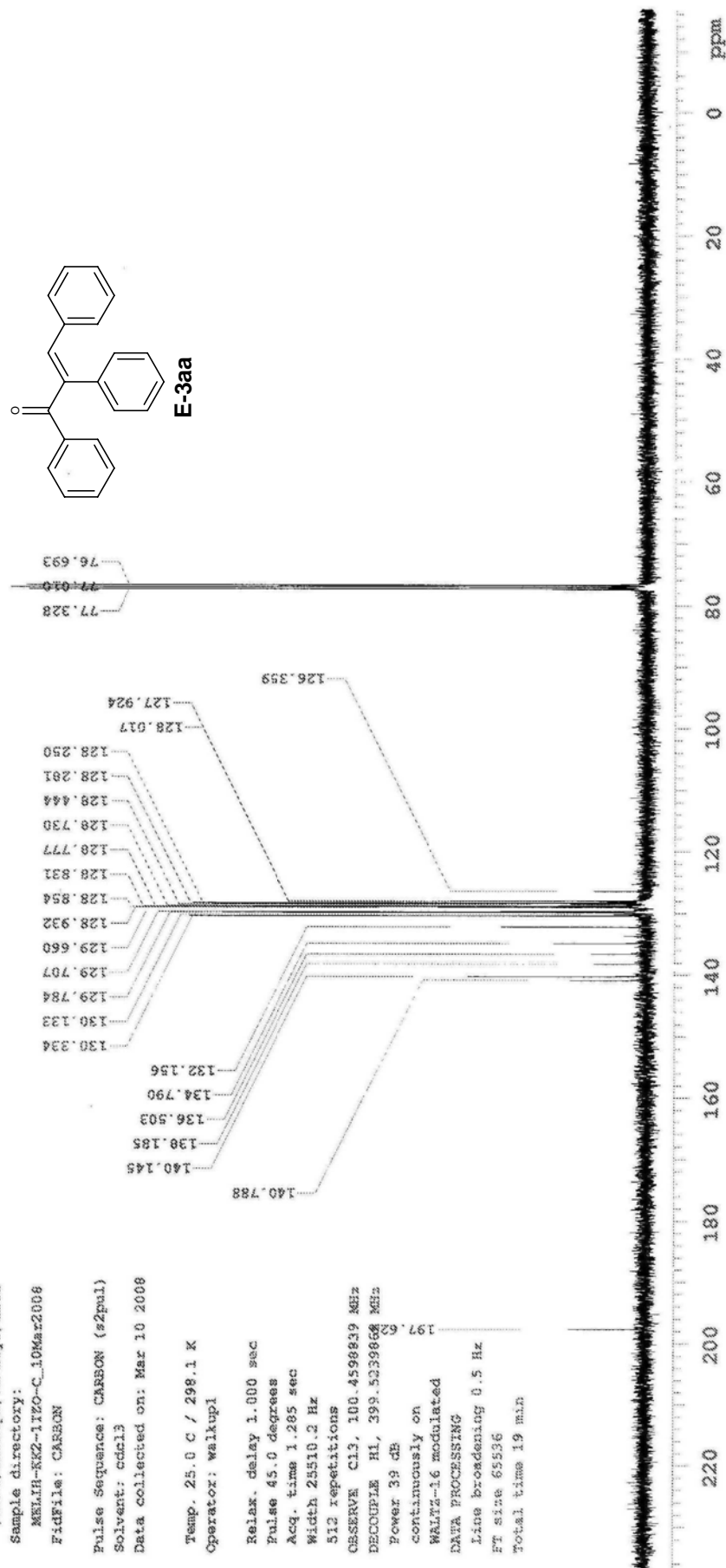
Figure C.2. ¹³C NMR of (*E*)-1,2,3-triphenylprop-2-en-1-one

100

MELIH
12 KASIM 2007

Sample Name:
KK2K3 12 11 2007
Archive directory:

Sample directory:

FidFile: Proton

Pulse Sequence: Proton (s2pul)
Solvent: cdcl3
Data collected on: Nov 12 2007

Temp. 23.0 C / 296.1 K
Operator: walkup1
VNMRS-400 "nmr400"

Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 2.049 sec
Width 6410.3 Hz
8 repetitions
OBSERVE H1, 399.5220000 MHz
DATA PROCESSING
Line broadening 0.2 Hz
FT size 65536
Total time 0 min 24 sec

7.126
7.139
7.143
7.150
7.154
7.166
7.169
7.187
7.192
7.230
7.279
7.285
7.294
7.297
7.314
7.318
7.323
7.329
7.333
7.338
7.345
7.350
7.354
7.357
7.435
7.439
7.442
7.449
7.451
7.456
7.463
7.469
7.473
7.974
7.978
7.982
7.995
7.998

Z-3aa

11.13   44.79
10.18   85.93

ppm
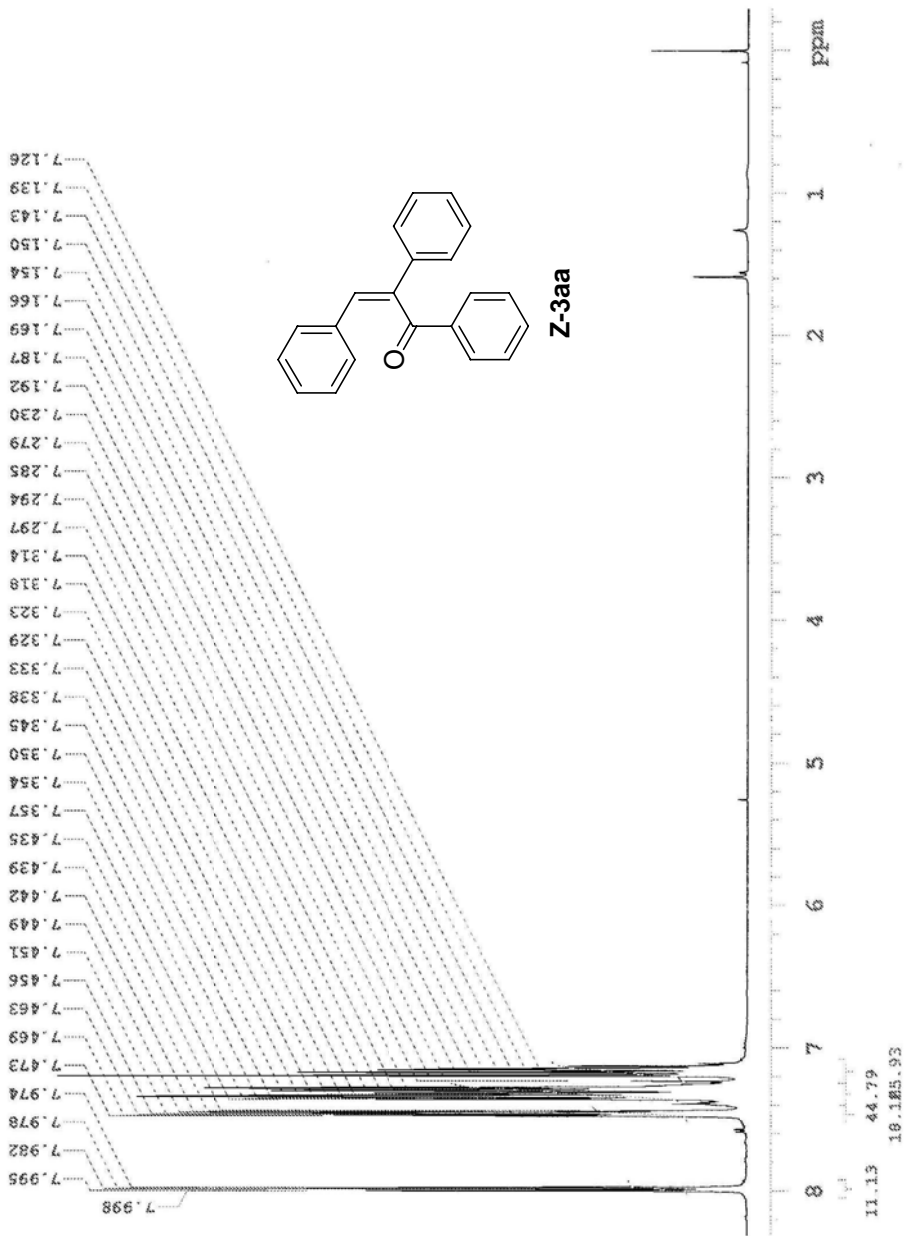
Figure C.3. ¹H NMR of (Z)-1,2,3-triphenylprop-2-en-1-one

101

Figure C.4. ^{13}C NMR of (*Z*)-1,2,3-triphenylprop-2-en-1-one
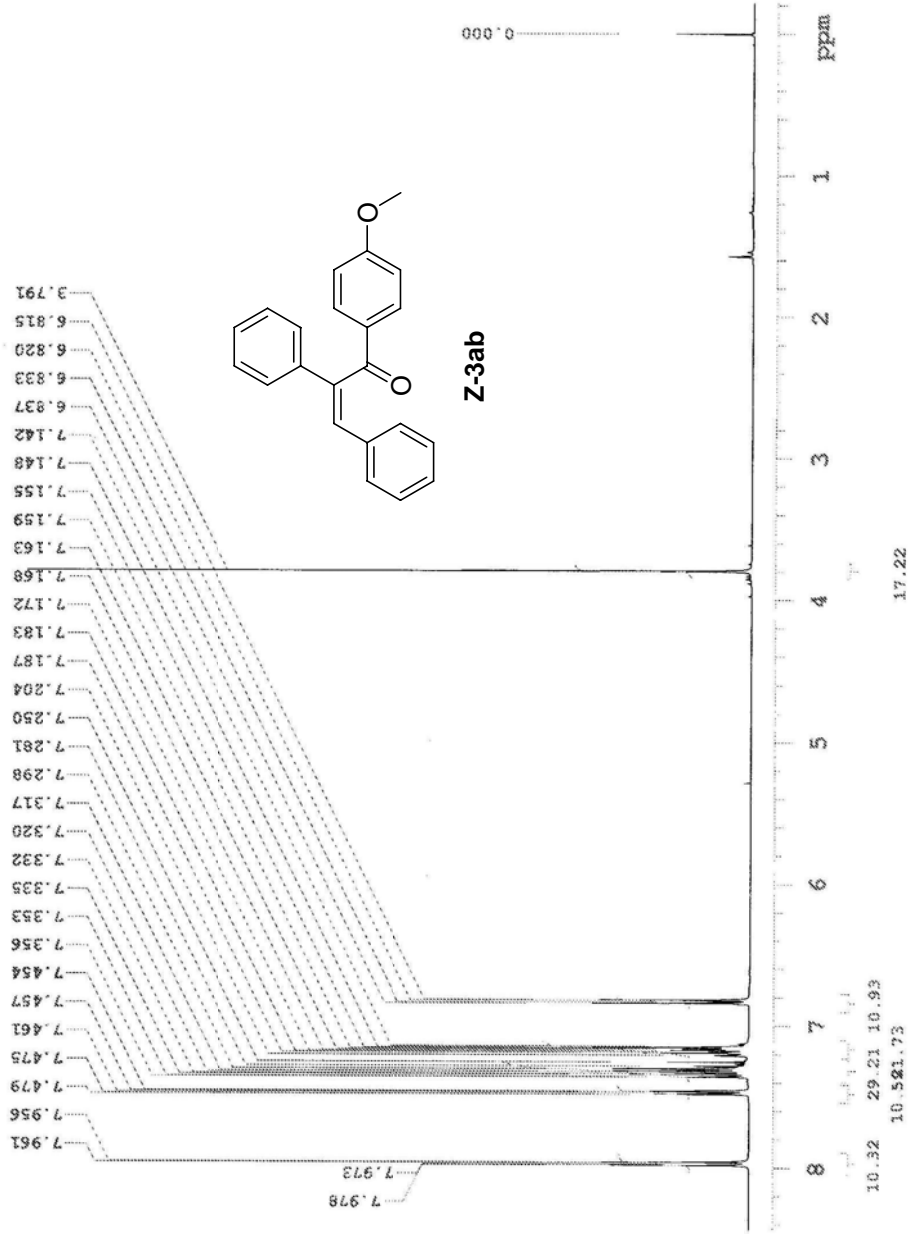
Figure C.5. ^{1}H NMR of (Z)-1-(4-methoxyphenyl)-2,3-diphenylprop-2-en-1-one

Figure C.6. ^{13}C NMR of (Z)-1-(4-methoxyphenyl)-2,3-diphenylprop-2-en-1-one

Figure C.7. ¹H NMR of (*E*)-1-(4-methoxyphenyl)-2,3-diphenylprop-2-en-1-one
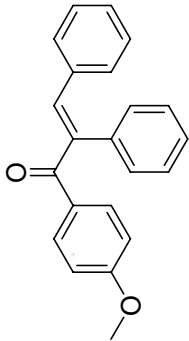
Figure C.8. ^{13}C NMR of (*E*)-1-(4-methoxyphenyl)-2,3-diphenylprop-2-en-1-one

Figure C.9. ¹H NMR of (*Z*)-2,3-diphenyl-1-*p*-tolylprop-2-en-1-one

Figure C.10. ^{13}C NMR of (*Z*)-2,3-diphenyl-1-*p*-tolylprop-2-en-1-one
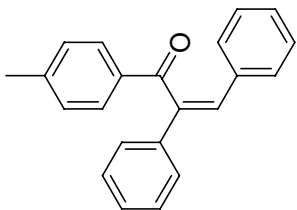
MK-KK55172
MK-KK55172
1. IZOMER
21 OCAK 2008

Sample Name:
  MK-KK55172-21OCAK2008
Archive directory:

Sample directory:

FidFile: Carbon

Pulse Sequence: Carbon (s2pul)
Solvent: cdcl3
Data collected on: Jan 21 2008

Temp. 25.0 C / 298.1 K
Operator: walkup1
VNMRS-400 "nmr400"

Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 1.300 sec
Width 24509.8 Hz
512 repetitions
OBSERVE C13, 100.4598839 MHz
DECOUPLE H1, 399.5239865 MHz
Power 39 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.5 Hz
FT size 65536
Total time 0 min 24 sec

Z-3ac

198.984

144.654
140.984
138.110
135.489
133.955

129.875
129.718
129.525
128.840
128.453
128.147
127.954
126.331

77.369
77.049
76.728

21.728

Figure C.11. ^{1}H NMR of (*E*)-2,3-diphenyl-1-*p*-tolylprop-2-en-1-one

Figure C.12. ^{13}C NMR of (*E*)-2,3-diphenyl-1-*p*-tolylprop-2-en-1-one

Z-3ad

Figure C.13. ^{1}H NMR of (*Z*)-2,3-diphenyl-1-*m*-tolylprop-2-en-1-one

Figure C.14. ^{13}C NMR of (Z)-2,3-diphenyl-1-*m*-tolylprop-2-en-1-one

E-3ad

10.2411.73

Figure C.15. ^{1}H NMR of (*E*)-2,3-diphenyl-1-*m*-tolylprop-2-en-1-one

Figure C.16. ^{13}C NMR of (*E*)-2,3-diphenyl-1-*m*-tolylprop-2-en-1-one

E-3ad

Peaks (ppm): 197.855, 140.928, 139.990, 138.223, 138.154, 136.573, 134.852, 132.938, 130.319, 130.195, 129.652, 128.878, 128.754, 128.234, 128.079, 127.886, 127.064, 77.328, 77.010, 76.693, 21.377

MELIH-KK12-21AO
exp1 CARBON

SAMPLE   PRESATURATION
date   Mar 11 2008   satmode   n
solvent   cdcl3   wet   n
file /home/walkup1~
/vnmrsys/data/ARTO~   SPECIAL
K GROUP/MELIH/MELI~   temp   25.0
H-KK12-21AO_11Mar2~   gain   not used
008/CARBON_01.fid   spin   20
ACQUISITION   hst   0.008
sw   25510.2   pw90   9.400
at   1.285   alfa   10.000
np   65536   FLAGS
fb   17000   il   n
bs   64   in   n
d1   1.000   dp   y
nt   512   hs   nn
ct   512   PROCESSING
TRANSMITTER   lb   0.50
tn   C13   fn   not used
sfrq   100.471   DISPLAY
tof   1529.7   sp   -1704.5
tpwr   54   wp   25510.2
pw   4.700   rfl   1704.5
DECOUPLER   rfp   0
dn   H1   rp   -173.0
dof   0   lp   0
dm   yyy   PLOT
dmm   w   wc   265
dmf   39   sc   0
dpwr   9400   vs   2824
                      th   10
                      ai cdc ph

114

Figure C.17. ^{1}H NMR of (*E*)-1-(4-chlorophenyl)-2,3-diphenylprop-2-en-1-one

E-3ae

115

Figure C.18. ^{13}C NMR of (*E*)-1-(4-chlorophenyl)-2,3-diphenylprop-2-en-1-one

Figure C.19. ^{1}H NMR of (Z)-1-(4-chlorophenyl)-2,3-diphenylprop-2-en-1-one

Figure C.20. ^{13}C NMR of (*Z*)-1-(4-chlorophenyl)-2,3-diphenylprop-2-en-1-one

Z-3ae

76.708
77.026
77.344

126.343
128.227
128.343
128.552
128.831
128.963
129.095
129.172
129.792
130.404
130.482
131.016
131.047
134.736
135.248
137.712
140.137
140.331

198.

118

Figure C.21. ^{1}H NMR of (*E*)-1-phenyl-2-propylhex-2-en-1-one

E-3ba

Peak labels (ppm):
0.924, 0.928, 0.938, 0.943, 0.957, 0.962, 0.975, 1.430, 1.448, 1.466, 1.485, 1.502, 2.241, 2.258, 2.277, 2.295, 2.450, 2.470, 2.488, 6.178, 6.197, 6.216, 7.262, 7.385, 7.388, 7.402, 7.405, 7.408, 7.421, 7.424, 7.426, 7.471, 7.474, 7.478, 7.488, 7.493, 7.511, 7.638, 7.641, 7.646, 7.655, 7.659, 7.662

Integrations: 30.76, 20.58, 9.98, 10.39, 4.50, 8.31, 1.62, 5.27

MELIH-MKK9481

exp1 PROTON

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/vnmrsys/data/ARTO~
K GROUP/MELIH/MELI~
H-MKK9481_16Apr200~
8-duzeltilmis/PROT~
ON_01.fid

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np   32768
fb   4000
bs   32
d1   1.000
nt   8
ct   8

TRANSMITTER
tn   H1
sfrq   399.524
tof   399.5
tpwr   61
pw   4.550

DECOUPLER
dn   C13
dof   0
dm   nnn
dmm   W40_HCN5mm
dpwr   34
dmf   29412

PRESATURATION
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wet   n

SPECIAL
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gain   not used
spin   20
hst   0.008
pw90   9.100
alfa   10.000

FLAGS
il   n
in   n
dp   y
hs   nn

PROCESSING
fn   not used

DISPLAY
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wp   6410.3
rfl   806.4
rfp   0
rp   122.7
lp   0

PLOT
wc   265
sc   0
vs   175
th   8
ai   cdc ph

13.953
14.139
22.206
28.677
30.855
76.716
77.034
77.351
127.994
129.342
131.388
139.091
141.230
145.702

E-3ba

Figure C.22. ^{13}C NMR of (E)-1-phenyl-2-propylhex-2-en-1-one

120
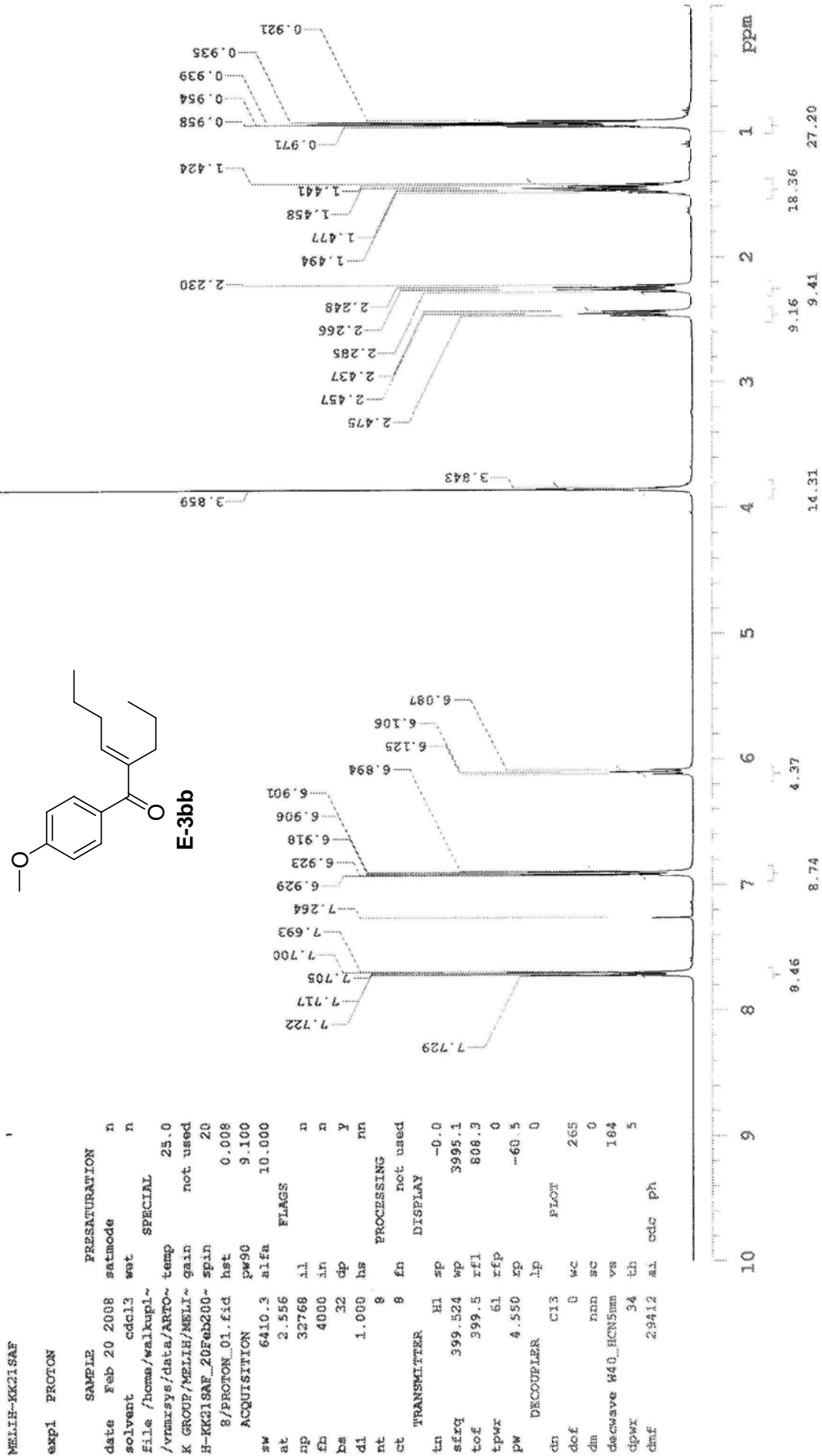
Figure C.23. ^{1}H NMR of (E)-1-(4-methoxyphenyl)-2-propylhex-2-en-1-one

Figure C.24. ^{13}C NMR of (*E*)-1-(4-methoxyphenyl)-2-propylhex-2-en-1-one

Figure C.25. ^{1}H NMR of (*E*)-2-propyl-1-p-tolylhex-2-en-1-one

E-3bc

Figure C.26. ^{13}C NMR of (*E*)-2-propyl-1-p-tolylhex-2-en-1-one

E-3bc

198.840

144.578
142.052
141.215
136.232
129.606
128.684

77.351
77.034
76.716

30.769
29.684
28.063
22.253
22.175
21.493
14.139
13.953

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

MELIH-MKK5483

expl CARBON

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tof   1529.7   wp   25510.2
tpwr   54   rfl   1704.5
pw   4.700   rfp   0
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dn   H1   lp   0
dof   0   PLOT
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dmm   w   sc   0
dacwave   vs   607
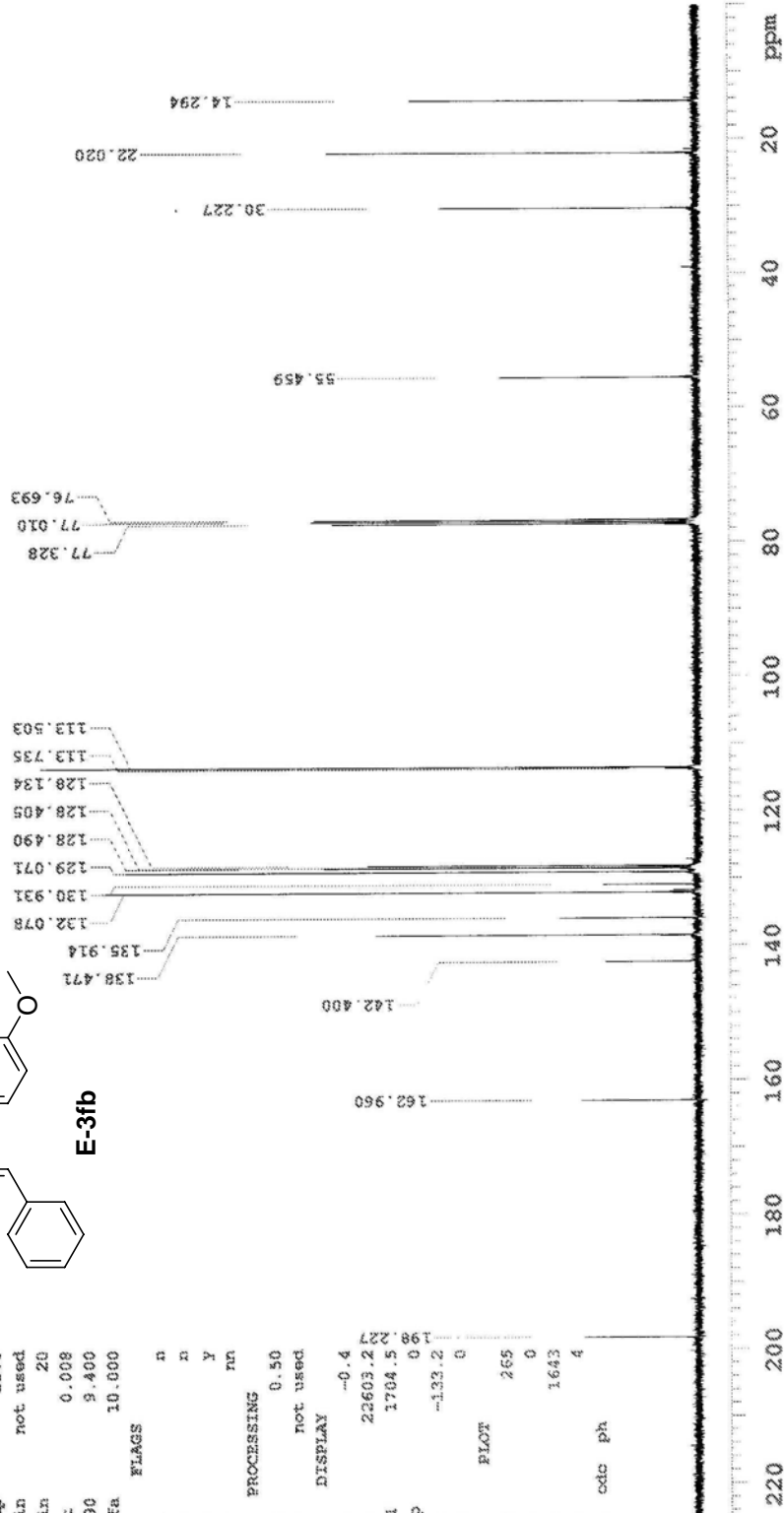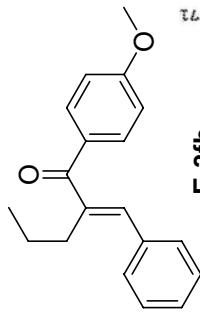dpwr   39   th   6
dmf   9400   ai cdc ph

124
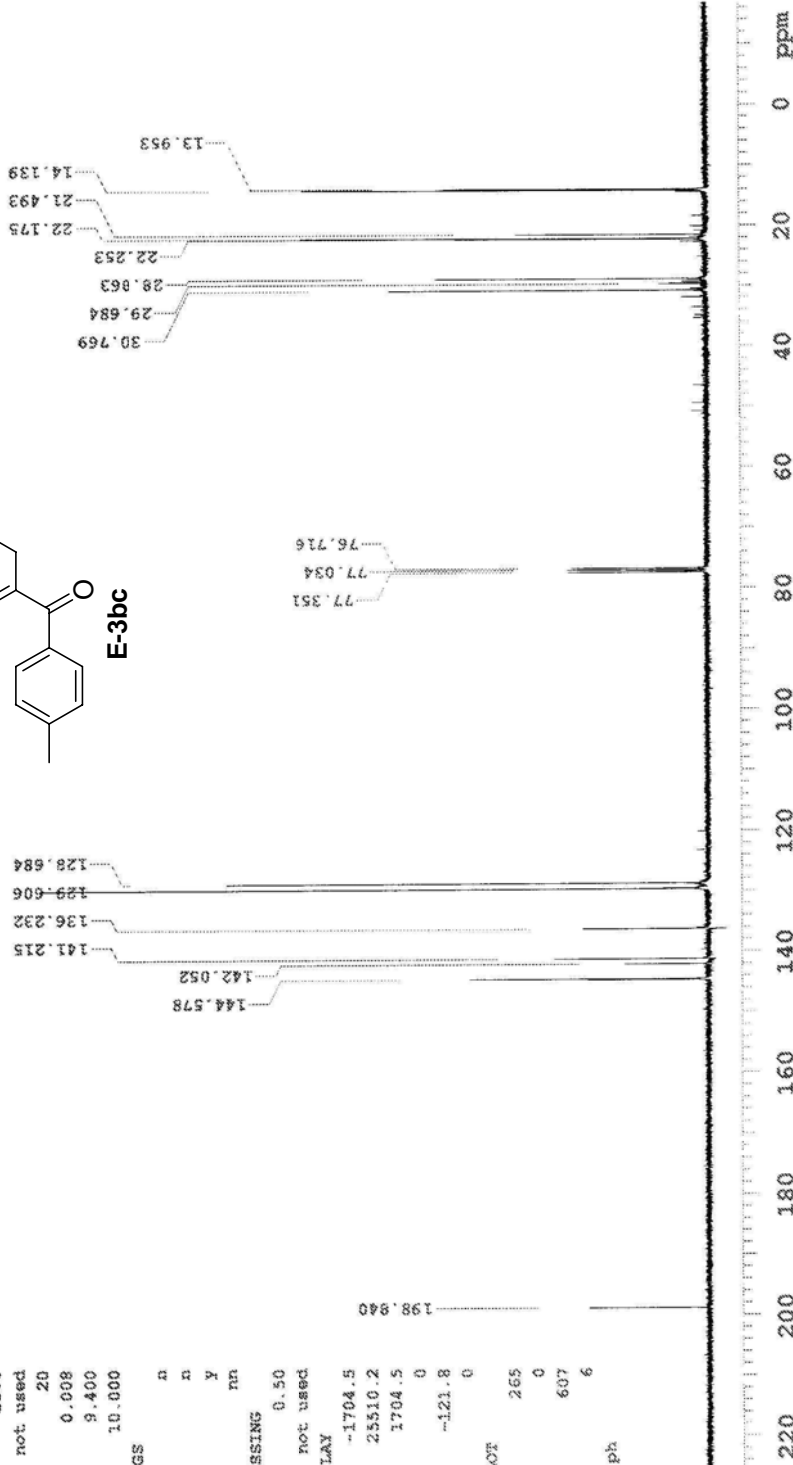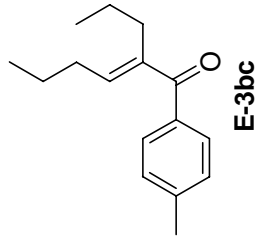
Figure C.27. ^{1}H NMR of (*E*)-methyl 3-(4-methoxyphenyl)hept-2-enoate

13.775
22.880
29.219
30.483
51.538
55.529
76.693
77.010
77.328
113.836
121.957
128.769
132.241
157.876
163.905
166.121
196.515

E-3cb

ppm

Figure C.28. ^{13}C NMR of (*E*)-methyl 3-(4-methoxyphenyl)hept-2-enoate

126

ppm

0.877
0.896
0.908
0.914
1.257
1.355
1.375
1.393
1.410
1.430
1.443
1.449
1.455
1.468
1.481
1.489
2.424
2.436
2.961
2.981
3.000
3.761
3.777

6.023

7.258
7.260
7.271
7.279
7.723
7.743

17.04
20.71
15.57
9.07
13.80
4.05
10.29
9.47

E-3cc

mk-0501-38-62

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Data Collected on:
    nmr400-vnmrs400
Archive directory:
    /home/walkup1/vnmrsys/data
Sample directory:
    mk-0501-38-62_23Jan2009
FidFile: PROTON

Pulse Sequence: PROTON (s2pul)
Solvent: cdcl3
Data collected on: Jan 23 2009

Temp. 25.0 C / 298.1 K
Operator: walkup1

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Pulse 45.0 degrees
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8 repetitions
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DATA PROCESSING
FT size 32768
Total time 0 min 29 sec

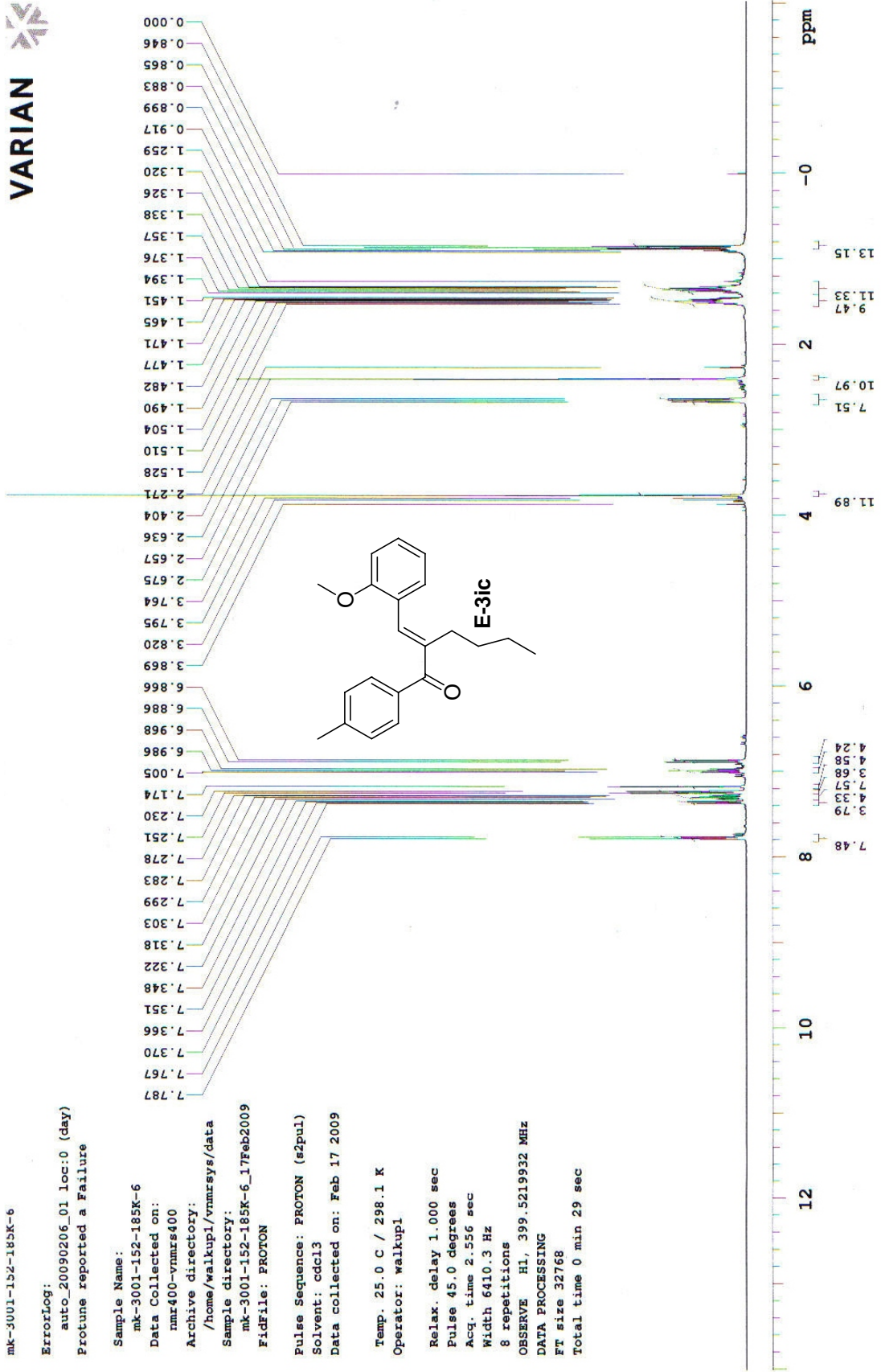Figure C.29. ^{1}H NMR of (*E*)-methyl 3-(4-methylphenyl)hept-2-enoate

Figure C.30. ^{13}C NMR of (*E*)-methyl 3-(4-methylphenyl)hept-2-enoate

128

Figure C.31. ^{1}H NMR of (*E*)-methyl 4-(4-methoxyphenyl)-3-methyl-4-oxobut-2-enoate

129

Figure C.32. ^{13}C NMR of (*E*)-methyl 4-(4-methoxyphenyl)-3-methyl-4-oxobut-2-enoate

MELIH-MK-KK27

exp1 CARBON

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PRESATURATION
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H-MK-KK27_19Mar200~ spin   20
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at   1.285   FLAGS
np   65536   il   n
fb   17000   in   n
bs   64   dp   y
d1   1.000   hs   nn
nt   512   PROCESSING
ct   512   lb   0.50
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tpwr 54   rfl   1704.5
pw   4.700   rfp   0
DECOUPLER   rp   -167.1
dn   H1   lp   0
dof   0   PLOT
dm   yyy   wc   265
dmm   w   sc   0
dmf   9400   vs   1435
                    th   5
                    ai cdc ph

E-3db

196.476
166.323
163.890
153.079
132.233
128.165
123.027
113.859
77.328
77.010
76.693
55.537
51.569
15.983

130

2.265
2.268
2.310
7.175
7.179
7.243
7.311
7.317
7.325
7.330
7.334
7.340
7.347
7.372
7.375
7.379
7.387
7.393
7.395
7.401
7.407
7.415
7.422
7.425
7.428
7.432
7.442
7.447
7.450
7.461
7.465
7.470
7.510
7.513
7.517
7.527
7.532
7.550
7.733
7.736
7.741
7.750
7.754
7.757

E-3ea

19.84

12.0027701
7.09920

Figure C.33. ¹H NMR of (E)-2-methyl-1,3-diphenylprop-2-en-1-one

131

E-3ea

14.434
76.747
77.065
77.382
128.211
128.289
128.327
128.482
128.599
129.404
129.497
129.699
131.660
135.798
136.867
138.518
142.214

ppm

Figure C.34. ^{13}C NMR of (E)-2-methyl-1,3-diphenylprop-2-en-1-one

132

Figure C.35. ^{1}H NMR of (*E*)-1-(4-methoxyphenyl)-2-methyl-3-phenylprop-2-en-1-one

E-3eb

E-3eb

14.906

55.451

76.716
77.034
77.351

113.487

128.320
128.444
129.583
130.660
131.977
135.961
136.983
140.029

162.781

198.313

ppm
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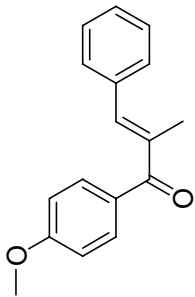
MELIH-MK-KK26

exp1 CARBON

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H-MK-KK26_19Mar200~ spin   20
8/CARBON_01.fid   hst   0.008
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at   1.285   FLAGS
np   65536   il   n
fb   17000   in   n
bs   64   dp   y
d1   1.000   hs   nn
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tof   1529.7   wp   22603.2
tpwr   54   rfl   1704.5
pw   4.700   rfp   0.0
DECOUPLER   rp   -161.0
dn   H1   lp   0
dof   0   PLOT
dm   yyy   wc   265
dmm   w   sc   0
dmf   9400   vs   1375
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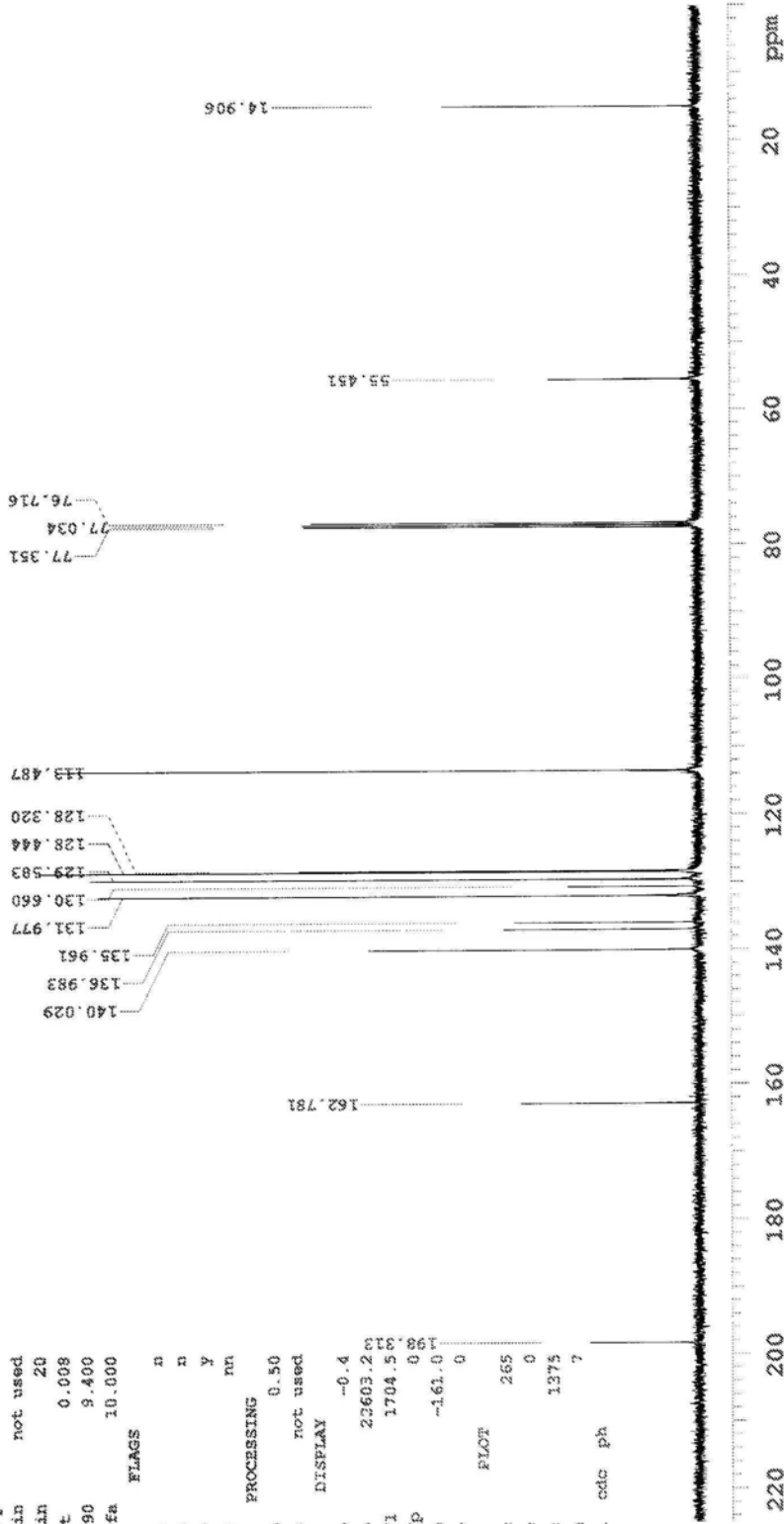
Figure C.36. ^{13}C NMR of (E)-1-(4-methoxyphenyl)-2-methyl-3-phenylprop-2-en-1-one

134

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mk-1901-151-160-t

Data Collected on:
nmr400-vnmrs400

Archive directory:
/home/walkup1/vnmrsys/data

Sample directory:
mk-1901-151-160-t_22Jan2009

FidFile: PROTON

Pulse Sequence: PROTON (s2pul)
Solvent: cdcl3
Data collected on: Jan 22 2009

Temp. 25.0 C / 298.1 K
Operator: walkup1

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Pulse 45.0 degrees
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Width 6410.3 Hz
8 repetitions
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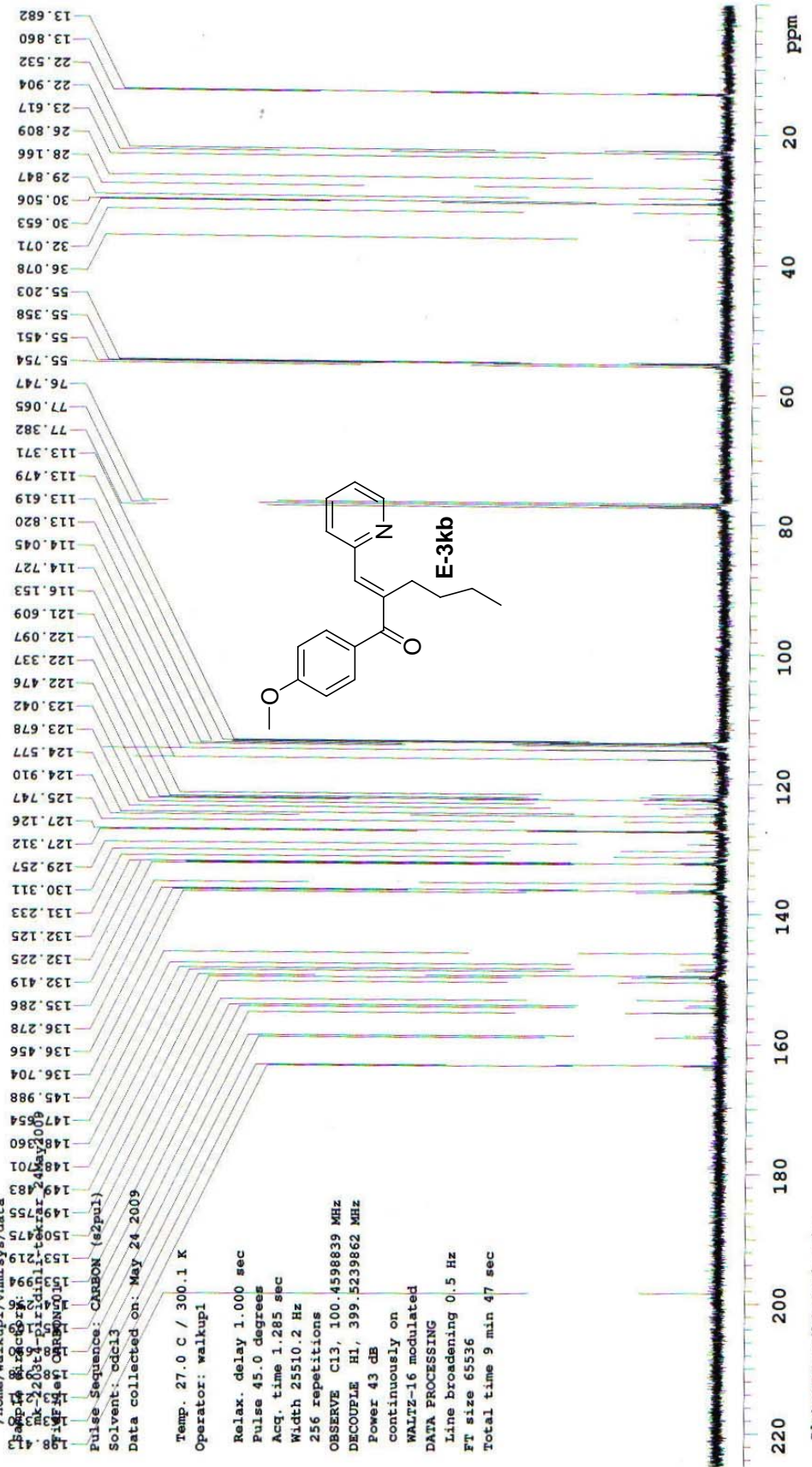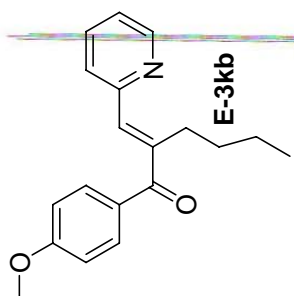DATA PROCESSING
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Total time 0 min 29 sec

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1.740
2.118
2.122
2.255
2.259
2.289
2.352
2.418
2.426

3.722
3.813

7.151
7.155
7.240
7.242
7.261
7.305
7.310
7.319
7.324
7.328
7.335
7.341
7.370
7.373
7.380
7.385
7.391
7.400
7.406
7.413
7.421
7.668
7.673
7.688

0.002

16.48
17.40

5.98
12.42
9.15
26.80
11.77
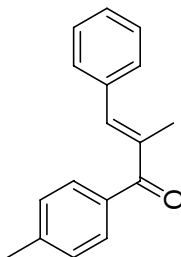
E-3ec
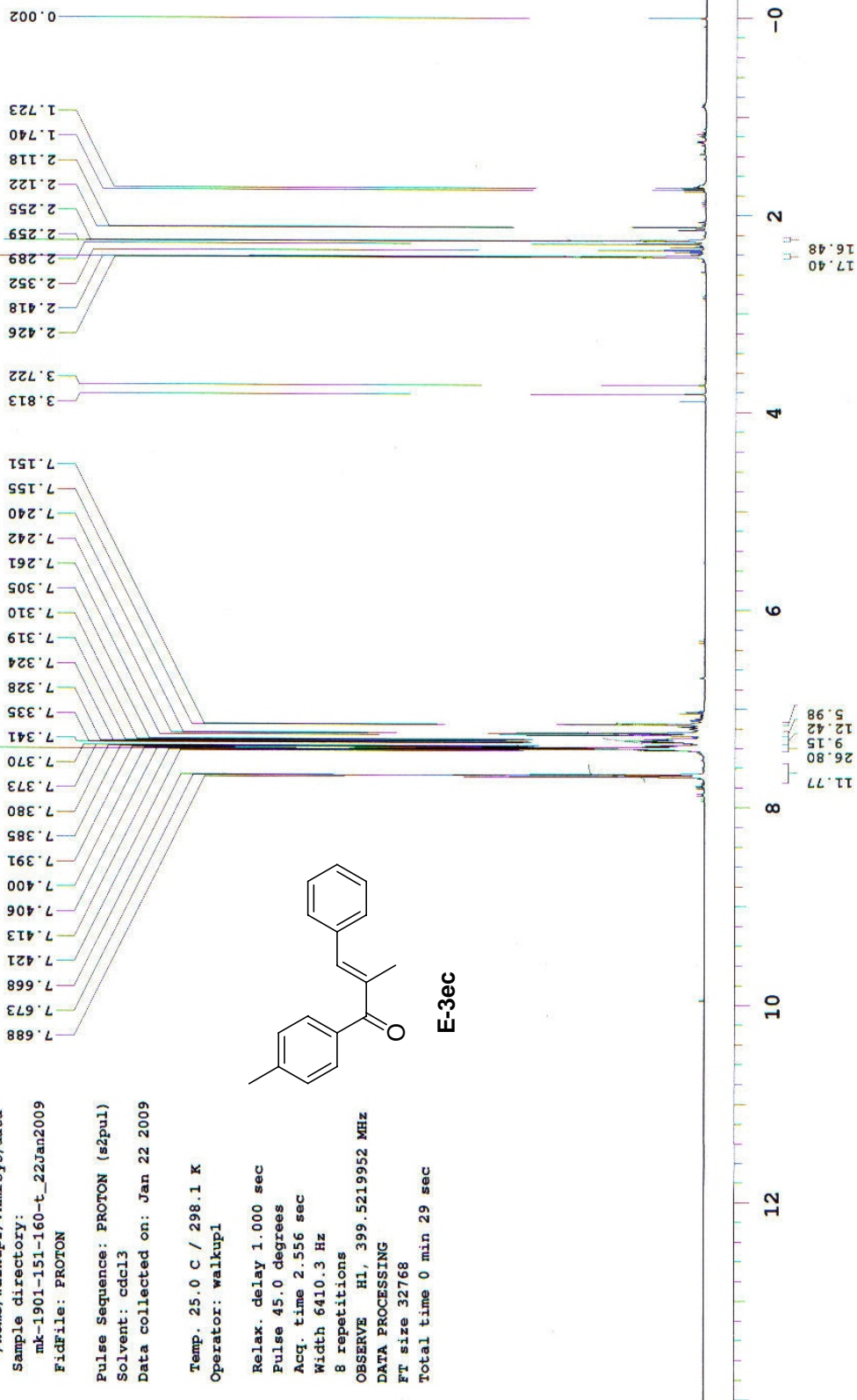
Figure C.37. ^{1}H NMR of (*E*)-2-methyl-3-phenyl-1-p-tolylprop-2-en-1-one

135

Figure C.38. ^{13}C NMR of (*E*)-2-methyl-3-phenyl-1-p-tolylprop-2-en-1-one

136

Figure C.39. ^{1}H NMR of (*E*)-2-benzylidene-1-(4-methoxyphenyl)pentan-1-one

Figure C.40. ^{13}C NMR of (*E*)-2-benzylidene-1-(4-methoxyphenyl)pentan-1-one

138

expl PROTON

SAMPLE   PRESATURATION
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K16-63-105_16Feb20~ spin   20
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at   2.556   FLAGS
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fb   4000   in   n
bs   32   dp   y
d1   1.000   hs   nn
nt   8   PROCESSING
ct   8   fn   not used
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tof   399.5   rfl   808.3
tpwr   61   rfp   0
pw   4.550   rp   15.1
  DECOUPLER   lp   0
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dof   0   wc   265
dm   nnn   sc   0
dmwave W40_HCN5mm   vs   456
dpwr   34   th   8
dmf   29412   ai   cdc ph

E-3fb'

Figure C.41. ¹H NMR of (E)-1-(4-methoxyphenyl)-2-phenylhex-2-en-1-one
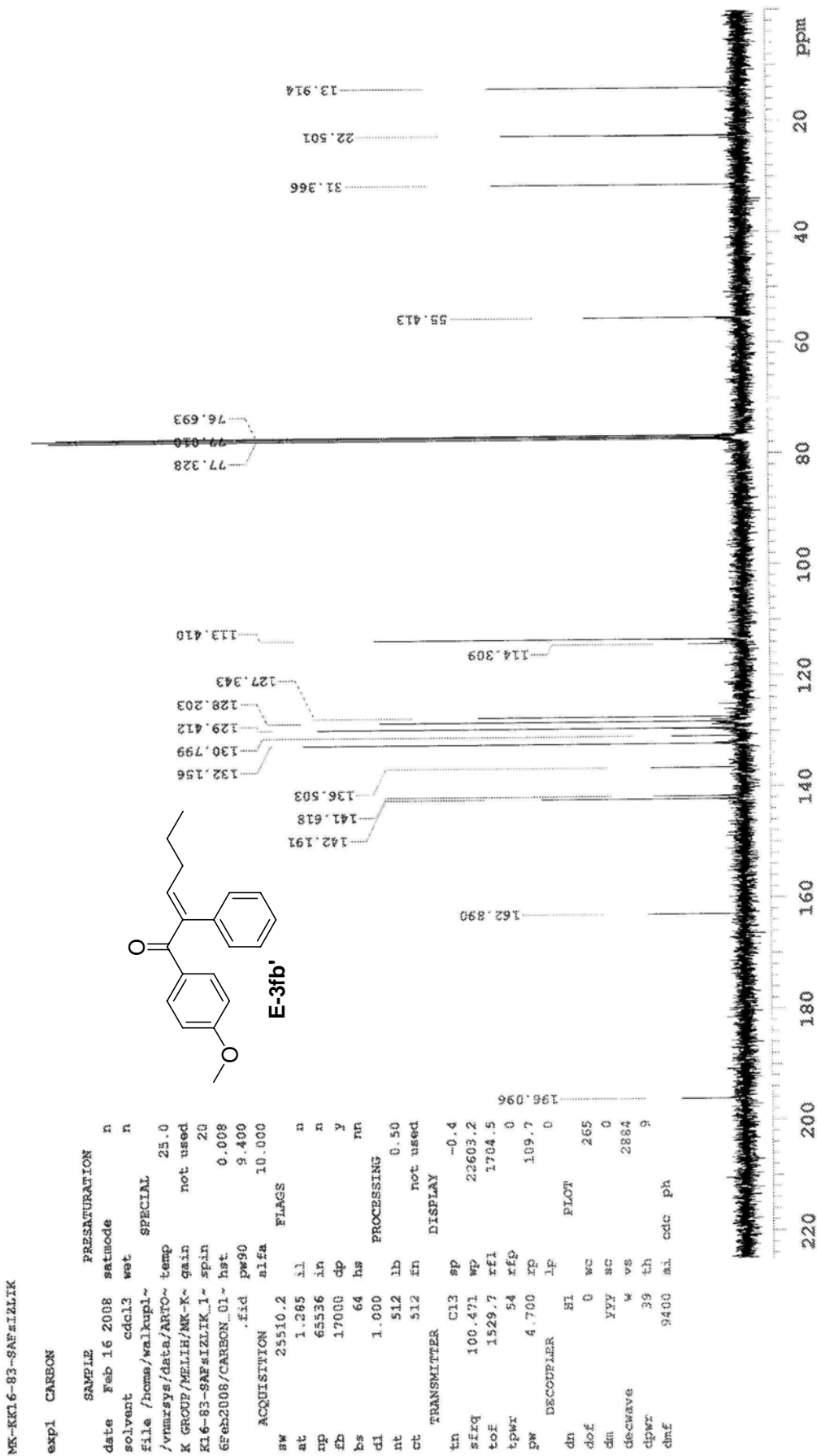
Figure C.42. ^{13}C NMR of (*E*)-1-(4-methoxyphenyl)-2-phenylhex-2-en-1-one

140

Figure C.43. ^{1}H NMR of (*E*)-2-(4-methoxybenzylidene)-1-p-tolylhexan-1-one

VARIAN

E-3hc

13.860
13.961
13.976
21.548
22.462
22.563
23.028
24.330
27.577
30.888
31.614
38.248
55.289
55.405
76.778
77.096
77.413
113.588
113.658
113.999
128.289
128.847
129.273
129.552
129.792
129.823
130.203
130.296
130.923
136.216
140.246
140.595
142.315
159.782
163.308

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

mk-d11002-keton-tekrar-C

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Data Collected on:
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Archive directory:
  /home/walkup1/vnmrsys/data
Sample directory:
  mk-d11002-keton-tekrar-C_24May2009
FidFile: CARBON01

Pulse Sequence: CARBON (s2pul)
Solvent: cdcl3
Data collected on: May 24 2009

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Operator: walkup1

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Pulse 45.0 degrees
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Width 25510.2 Hz
256 repetitions
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DECOUPLE H1, 399.5239862 MHz
  Power 43 dB
  continuously on
  WALTZ-16 modulated
DATA PROCESSING
  Line broadening 0.5 Hz
FT size 65536
Total time 9 min 47 sec

199.119
199.196
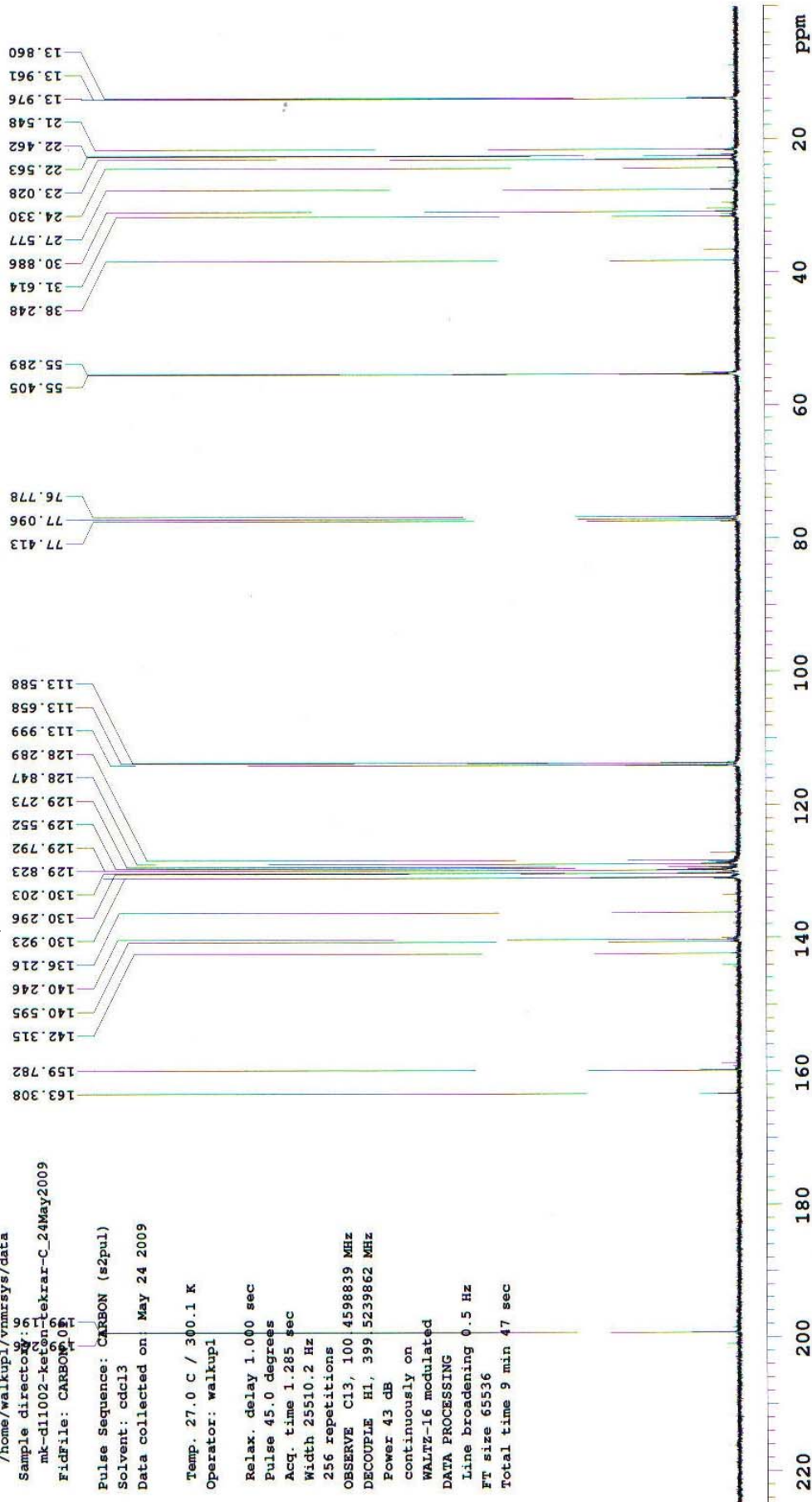
Plotname: --Not assigned--

Figure C.44. ^{13}C NMR of (E)-2-(4-methoxybenzylidene)-1-p-tolylhexan-1-one

142

VARIAN

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Integration values: 13.15, 11.33, 9.47, 10.97, 7.51, 11.89, 4.24, 4.58, 3.68, 7.57, 4.33, 3.79, 7.48

E-3ic

Figure C.45. ¹H NMR of (E)-2-(2-methoxybenzylidene)-1-p-tolylhexan-1-one

E-3ic

13.876

21.586
22.896
27.832
30.886

55.413

76.724
77.041
77.359

110.496
120.198
125.057
128.738
128.800
128.916
129.373
129.544
129.645
130.063
130.117
135.883
135.999
141.850
142.586

157.334

ppm

20

40

60

80

100

120

140

160

180

200

220

E-3jb

Figure C.46. ^{13}C NMR of *(E)*-2-(2-methoxybenzylidene)-1-p-tolylhexan-1-one

144

Plotname: --Not assigned--

Figure C.47. ^{1}H NMR of (*E*)-1-(4-methoxyphenyl)-2-((thiophen-3-yl)methylene)hexan-1-one

Figure C.48. ^{13}C NMR of (E)-1-(4-methoxyphenyl)-2-((thiophen-3-yl)methylene)hexan-1-one

146
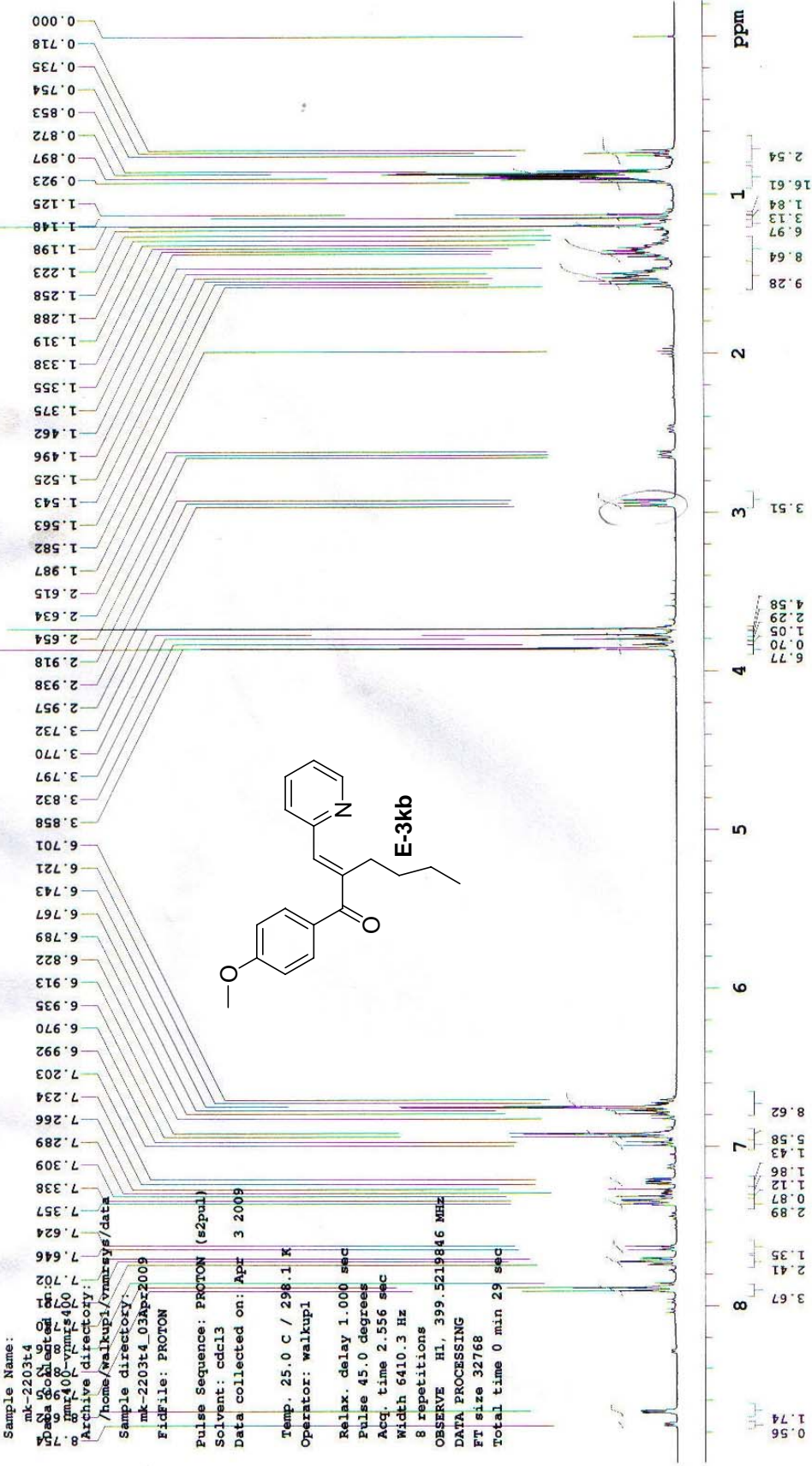
Figure C.49. ^{1}H NMR of (*E*)-1-(4-methoxyphenyl)-2-((pyridin-2-yl)methylene)hexan-1-one

147

Figure C.50. ^{13}C NMR of (*E*)-1-(4-methoxyphenyl)-2-((pyridin-2-yl)methylene)hexan-1-one

VARIAN

E-3kb

Peak labels (ppm):
13.682, 13.860, 22.532, 22.904, 23.617, 26.809, 28.166, 29.847, 30.506, 30.653, 32.071, 36.078, 55.203, 55.358, 55.451, 55.754, 76.747, 77.065, 77.382, 113.371, 113.479, 113.619, 113.820, 114.045, 114.727, 116.153, 121.609, 122.097, 122.331, 122.476, 123.042, 123.678, 124.577, 124.910, 125.747, 127.126, 127.312, 129.257, 130.311, 131.233, 132.125, 132.225, 132.419, 135.286, 136.278, 136.456, 136.704, 145.988, 147.654, 148.360, 148.701, 149.483, 149.755, 150.475, 153.219, 153.994, 158.41

148

Figure C.51. ¹H NMR of (*E*)-ethyl 4-(4-methoxyphenyl)-4-oxo-3-phenylbut-2-enoate

Figure C.52. ^{13}C NMR of (*E*)-ethyl 4-(4-methoxyphenyl)-4-oxo-3-phenylbut-2-enoate

Figure C.53. ^{1}H NMR of 3-tert-butyl-5-(4-methoxyphenyl)-4-methylfuran-2(5H)-one

Figure C.54. ^{13}C NMR of 3-tert-butyl-5-(4-methoxyphenyl)-4-methylfuran-2(5H)-one

152

Figure C.55. ¹H NMR of 3-tert-butyl-5-hydroxy-5-(4-methoxyphenyl)-4-methylfuran-2(5H)-one

153

Figure C.56. ^{13}C NMR of 3-tert-butyl-5-hydroxy-5-(4-methoxyphenyl)-4-methylfuran-2(5H)-one

154

Figure D.1. ^{1}H NMR of 2-(hex-1-ynyl)thiophene

Figure D.2. ^{13}C NMR of 2-(hex-1-ynyl)thiophene

Figure D.3. ^{1}H NMR of 2-(hex-1-ynyl)pyridine

Figure D.4. ^{13}C NMR of 2-(hex-1-ynyl)pyridine

Figure D.5. ¹H NMR of 1-(hex-1-ynyl)-2-methoxybenzene

Figure D.6. ^{13}C NMR of 1-(hex-1-ynyl)-2-methoxybenzene

Figure D.7. ^{1}H NMR of 1-(hex-1-ynyl)-4-methoxybenzene

161

Figure D.8. ^{13}C NMR of 1-(hex-1-ynyl)-4-methoxybenzene

APPENDIX D

Scan 881 from C:\WINDOWS\Desktop\MELIH\2801sg411.SMS

Spect 1
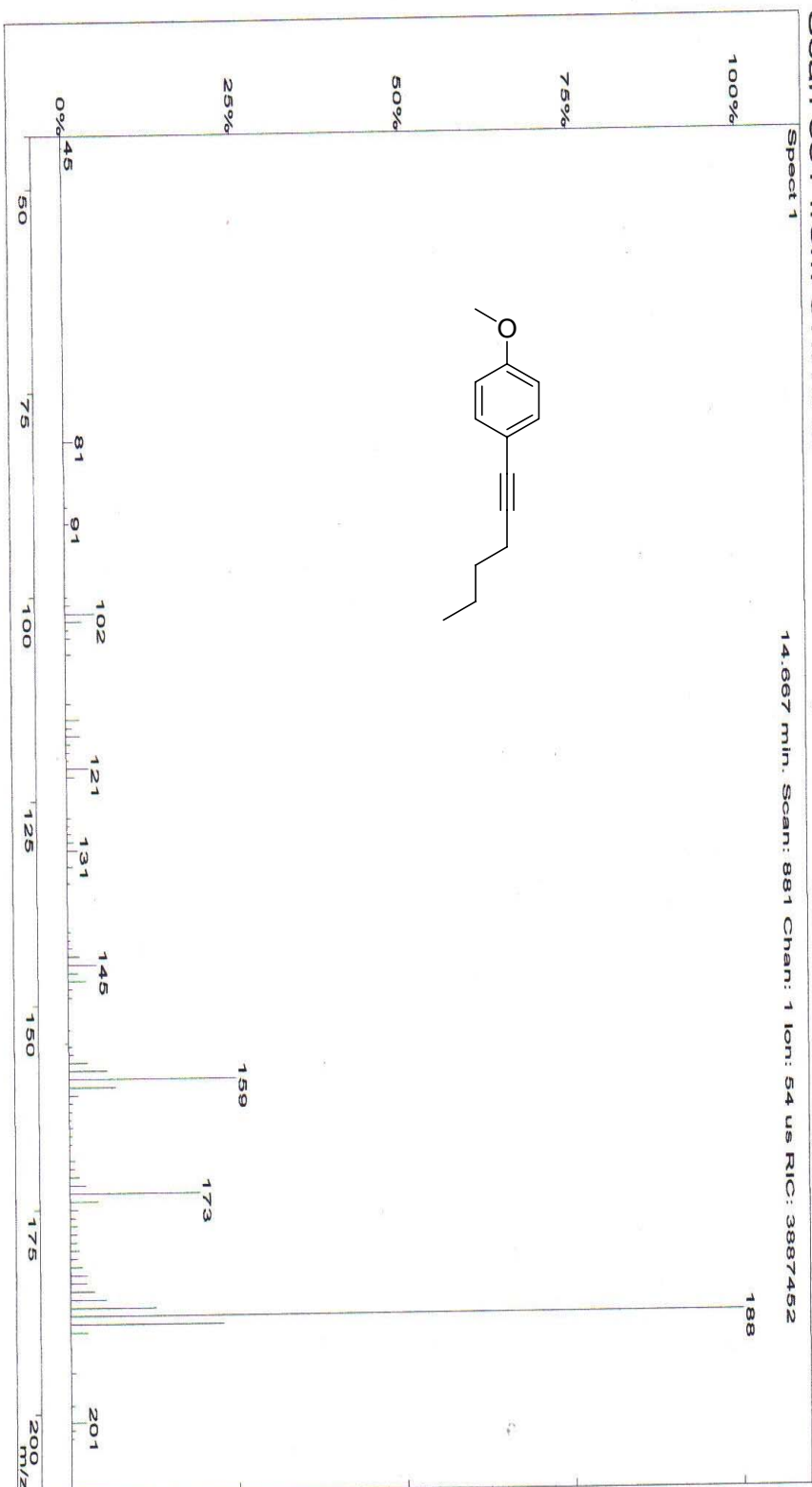
14.667 min. Scan: 881 Chan: 1 Ion: 54 us RIC: 3887452

Figure D.9. Mass spectrum of 1-(hex-1-ynyl)-4-methoxybenzene

Scan 751 from C:\WINDOWS\Desktop\MEL\H\SG120031.SMS

Spect 1

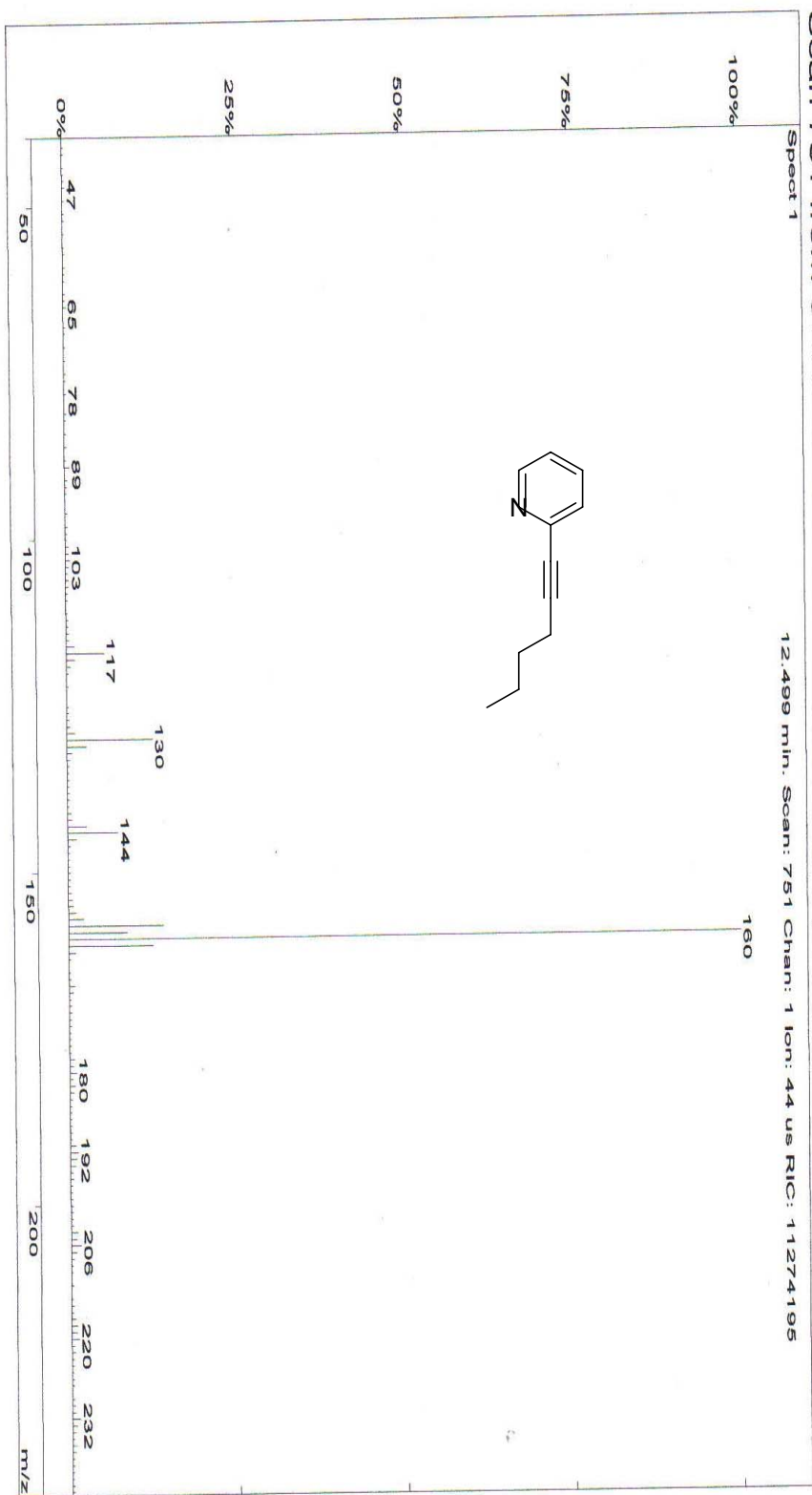12.499 min. Scan: 751 Chan: 1 Ion: 44 us RIC: 11274195

Figure D.10. Mass spectrum of 2-(hex-1-ynyl)pyridine

Scan 678 from C:\WINDOWS\Desktop\MELIH\SG22003\1.SMS
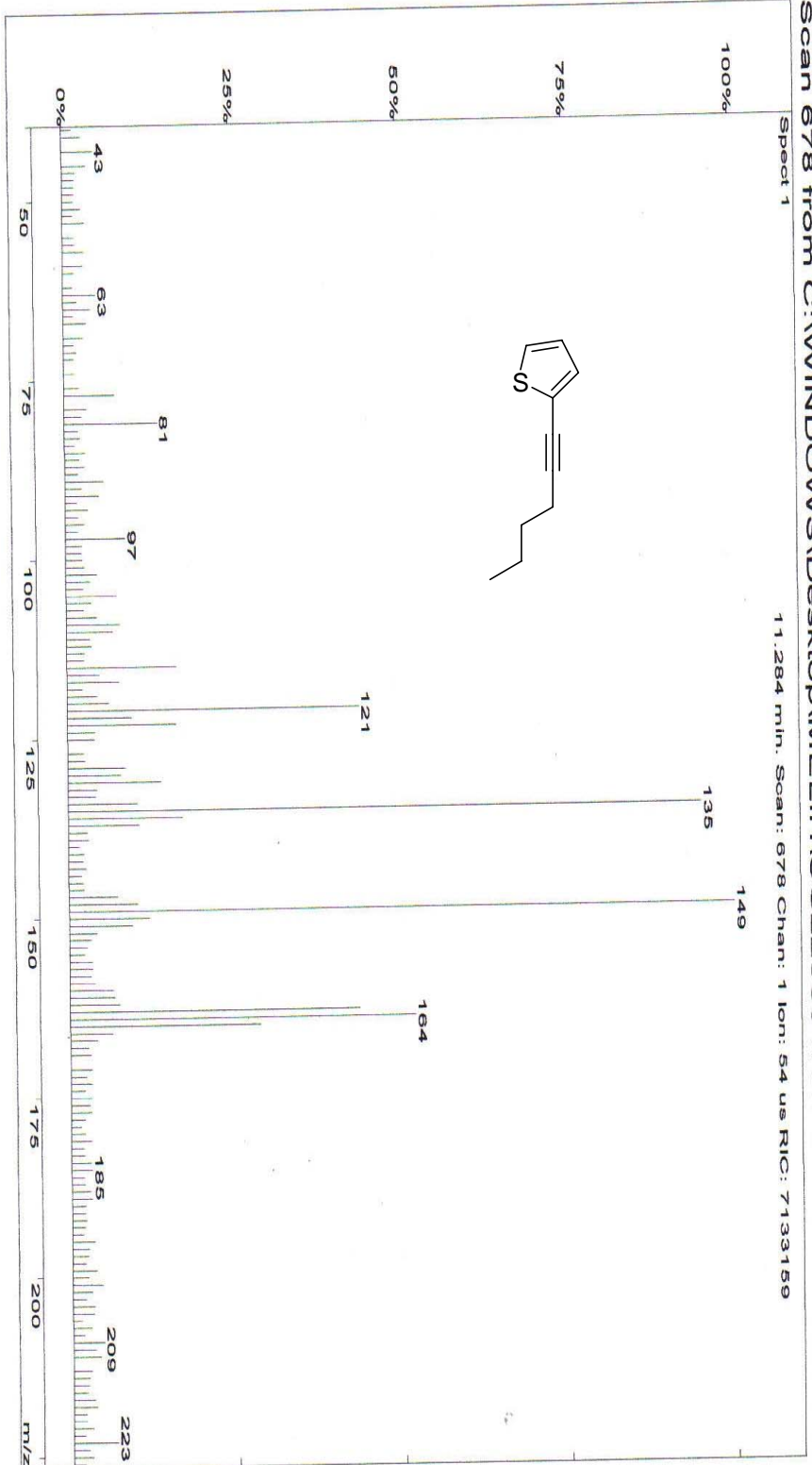
Spect 1

11.284 min. Scan: 678 Chan: 1 Ion: 54 us RIC: 7133159

Figure D.11. Mass spectrum of 2-(hex-1-ynyl)thiophene