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Utilization of phosphorus ylides towards the synthesis of extended cinnamaldehydes and stellettins

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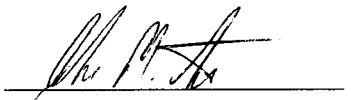

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Utilization of Phosphorous Ylides towards the Synthesis of Extended Cinnamaldehydes and Stellettins

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BY

John M. Saathoff

THESIS

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FOR THE DEGREE OF

Master of Science in Chemistry

IN THE GRADUATE SCHOOL, EASTERN ILLINOIS UNIVERSITY
CHARLESTON, ILLINOIS

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Utilization of Phosphorous Ylides towards the Synthesis of Extended Cinnamaldehydes and Stellettins

John M. Saathoff

Research Advisor: Dr. E. Treadwell

Eastern Illinois University

Chemistry Department

July 19, 2012

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Abstract:

Phosphorus ylides have been utilized in three synthetic approaches; two involving the synthesis of photochromic cinnamaldehyde semicarbazones and a final scheme towards the synthesis of the isomalabaricane natural products. The targeted cinnamaldehyde semicarbazones varied both in the length of the conjugated system as well as the position and type of phenyl ring substituents, because these variations could impact their degree of photochromicity. The three step synthesis of the extended cinnamaldehyde semicarbazones involved a Wittig condensation, hydrolysis of acetal protecting group, and formation of imine and was completed in respectable cumulative yields; 42.4% yield for semicarbazones with n = 1 double bonds, 61.9% yield for a semicarbazone with n = 2, and 33.5% yield for a semicarbazone with n = 3. A faster, more economical purification method involving filtrations for removing $Ph_3P{=}O$ was employed, compared to the alternative SiO_2 gel column chromatography.

After at least 1-1.5 weeks, "light" and "dark" forms of the semicarbazones were examined and the photochromicity quantified. In total 24 semicarbazones were made and of those 20 exhibited photochromicity to some degree. Our data contradicted the work of Heilbron *et al.*, in that 4-methoxycinnamaldehyde semicarbazone was more photochromic than 2-methoxycinnamaldehyde semicarbazone. Visual comparisons, the Behr color system, UV-Vis absorption data in CH_3CN, and Spartan calculations were used to investigate the photochromic color change between the "light" and "dark" versions of semicarbazones from n = 1 to n = 3. It was found that extending the conjugated system, and adding OMe groups to the phenyl ring, all produced quantifiable shifts in photochromicity between the "light" and "dark" versions of the semicarbazones,

yet the position of OMe groups on the ring was more important than the number. We were unable to observe the "switch" from dark to light form by either UV-Vis or ^{13}C NMR, and while Spartan calculations were useful in showing the most likely conformational changes, the calculated $\Delta\lambda_{max's}$ didn't match the experimental $\Delta\lambda_{max's}$.

A crystal structure of 2,4,6-trimethoxycinnamaldehyde semicarbazone (JMS 18-9) showed planarity from the ring to the imine group, only straying from planarity by a slight 6° bend between the carbonyl and the primary amine of the semicarbazone subunit, that is hydrogen bound to a second 2,4,6-trimethocycinnamaldehyde semicarbazone unit.

A second synthesis for extended cinnamaldehyde semicarbazones required the preparation of a 4C phosphorus ylide instead of a 2C ylide starting material. Following literature precedence *cis*-1,4-butanediol was monosilylated, converted to an allylic chloride, and then to a 4-(diethylphosphono)-2-butenol in a 39% overall yield. Chlorination instead of the bromination as done by Sun *et al.* was more cost effective, yet was more troublesome in obtaining pure halide. The use of impure alcohol didn't allow for oxidation to the butenal.

The third project involved studies toward the synthesis of stellettins. This involved the synthesis of 1,3-bisphosphonoacetone (BPA), in 70.7% overall yield from 1,3-dichloroacetone using Corbel's route. Monocondensations of BPA attempted using Masamune-Roush conditions did not yield products, but model studies using triethyl phosphonoacetate gave evidence of product formation with 2-chloro-cyclohexanone, cyclohexanone, 2-nitrobenzaldehyde, *p*-nitroacetophenone, 2-methylbutyraldehyde, and crotonaldehyde. Optimized experimental conditions included using DMSO instead of CH_3CN, and premixing and heating to reflux LiCl, the phosphonoacetone, DBU and

DMSO for 15-45 minutes before adding the various ketones/aldehydes. Unfortunately when the BPA was employed under the optimized Masamune-Roush conditions no reaction occurred and only the starting material, elimination product, or dicondensate were recovered. The same is true when other condensations conditions, including Buchi, Wittig, and strong base, were attempted.

Acknowledgements:

I would like to thank full heartedly my research advisor, Dr. Edward M. Treadwell. His guidance, patience, and knowledge have been unprecedented during my academic career at Eastern Illinois University, as well as in this work. Along with serving these many roles, he has also been a great friend throughout these past years.

Next, I would like to thank my friends and family. My friends have kept my stress level at a minimum, by giving me courage and confidence to tackle many barriers throughout my academic career. More importantly special thanks are given to my family, specifically my sister, father, mother, step-father and grandmother, whom no matter what were always guiding, caring, trustful, and supportive over the years.

During the troubling times at EIU, the chemistry department at Indiana State University and specifically Dr. Richard W. Fitch opened their door and allowed us access to their NMR. Without this generous gift the analysis of many of our compounds would not have been reported herein, thus for this I am extremely grateful. Also, I would like to thank Dr. Kraig Wheeler for his assistance in obtaining and solving the crystal structures.

I would like to think the community of Eastern Illinois University, especially the Graduate School, and the College of Sciences, for helping to funding these projects, as well as the Chemistry Department for the continued support of extraordinary higher education. Finally, I would like to thank my thesis committee; Dr. Kraig Wheeler, Dr. Sean Peebles, and Dr. Mary Konkle, for their assistance, patience, support, and guidance throughout this work.

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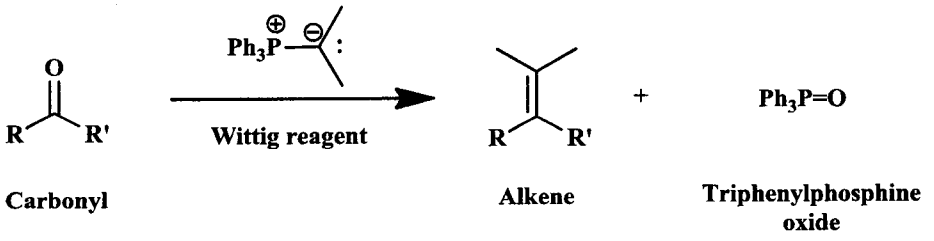
INTRODUCTION

Phosphorus ylides have many different applications in synthesis including preparing materials chemistry and natural products. In the early 1950s, Wittig and co-workers published the synthesis of alkenes using a phosphorus-based carbon nucleophile (a Wittig reagent).[1] Georg Wittig was awarded the Nobel Prize in Chemistry in 1979 for this discovery.[2]

A Wittig reagent is an organophosphorus reagent where the phosphorus atom bears a positive charge, along with three latent carbon groups (Scheme 1.1), and a fourth adjacent carbon carries a negative charge. Thus a Wittig reagent is a sub-class of an ylide, which is a species containing adjacent oppositely charged atoms.

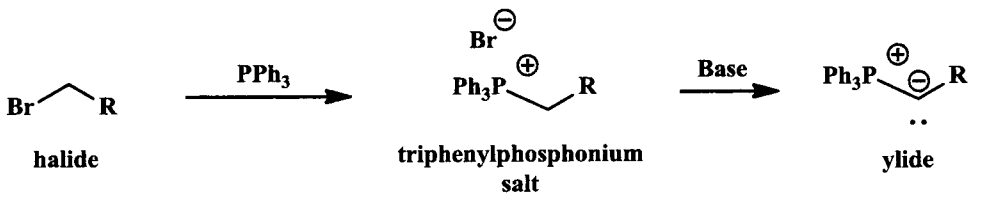
The Wittig reaction involves the treatment of a carbonyl compound with a Wittig reagent, where a nucleophilic attack occurs at the carbonyl group and a new carbon-carbon bond is formed. Additionally, a phosphorus by-product, triphenylphosphine oxide ($Ph_3P=O$) is formed (Scheme 0.1).



Scheme 0.1: General Wittig reaction.

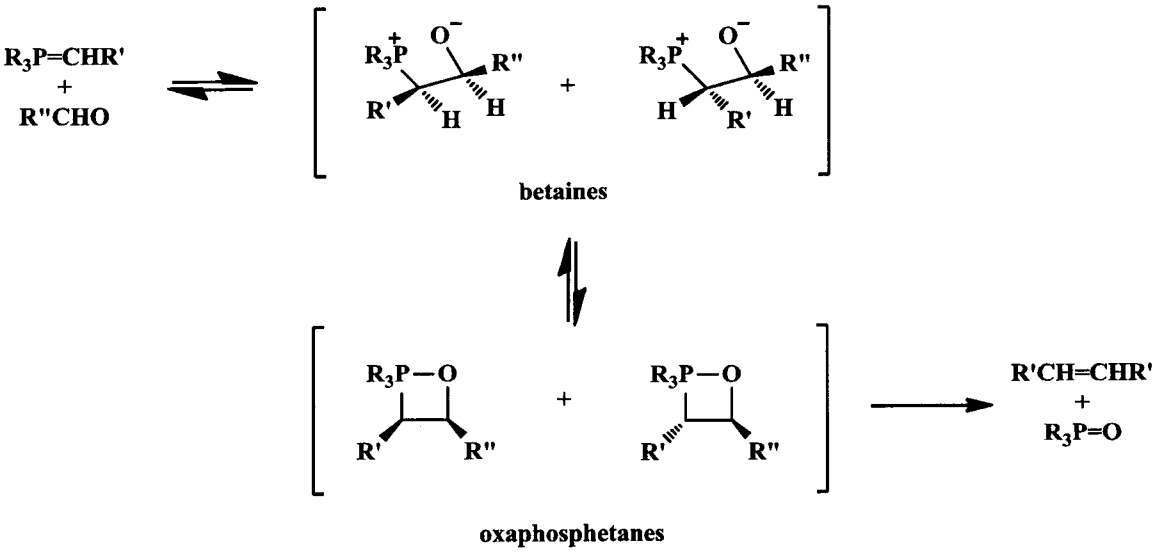
The Wittig reagent can be made in a straightforward manner, as seen in Scheme 0.2. A phosphine, such as triphenylphosphine, is reacted with an alkyl halide in an S_N2

reaction to form an alkyltriphenylphosphonium salt, which then upon treatment with base generates a resonance stabilized carbanion (the ylide).



Scheme 0.2: Typical ylide formation.

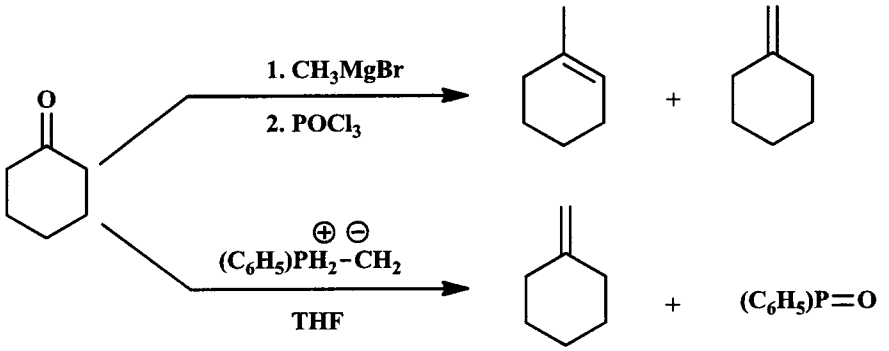
The initial mechanistic step of the Wittig reaction involves the creation of a four-membered cyclic phosphorane (1,2-oxaphosphetane) as the only intermediate, but in the mid 1960s Wittig and co-workers discovered that the mechanism also formed a zwitterionic phosphorus betaine intermediate (Scheme 0.3).[1] To date it is known that both the betaine and the 1,2-oxaphosphetane are involved, but there is debate as to which is formed first.



Scheme 0.3: Wittig reaction mechanism.

Evidence for the betaine intermediate came from several experimental results: 1) the formation *in situ* of stable adducts between betaines and lithium halide salts, 2) the trapping of betaines as β-hydroxy phosphonium salts by addition of acid at low temperatures, and 3) the pronounced effect of lithium salts on alkene stereochemistry.[1]

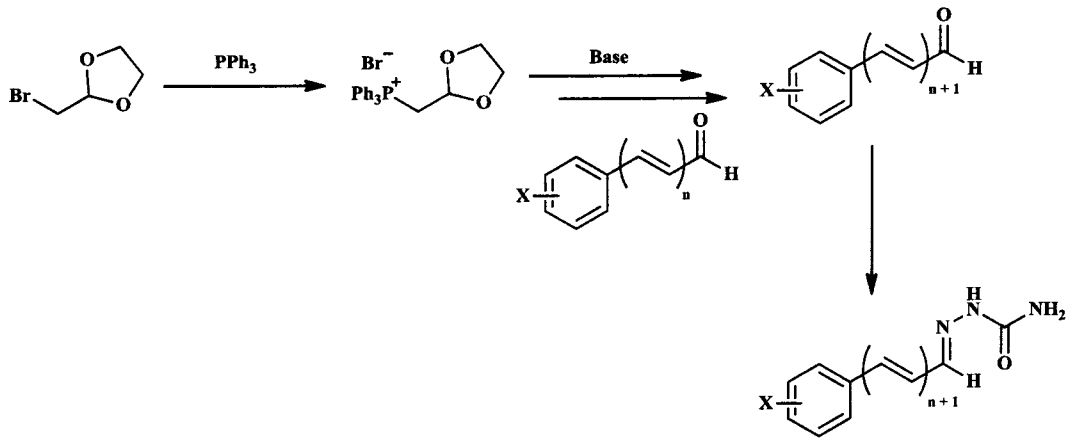
The true value of the Wittig reaction is that it yields an alkene directly. The C=C bond in the product is usually formed where the C=O bond was in the reactant, with no other alkene regioisomers formed as can be the case in other alkene forming reactions. For example, the Wittig reaction of cyclohexanone with methylenetriphenylphosphorane yields only a single alkene product, methylenecyclohexane. But in contrast, addition of methylmagnesium bromide to cyclohexanone followed by dehydration with $POCl_3$ yields a mixture of two alkenes (Scheme 0.4).[2]



Scheme 0.4: Stereoselectivity of the Grignard reaction vs the Wittig reaction.

The first project focusing on material chemistry involves the use of a Wittig reagent to create extended cinnamaldehydes from benzaldehydes/cinnamaldehydes, which will be used to create extended cinnamaldehyde semicarbazones (Scheme 0.5). The poor *cis/trans* selectivity of the Wittig reaction makes it undesirable for projects that require stereospecific reaction outcomes. However this is not of major concern in the materials

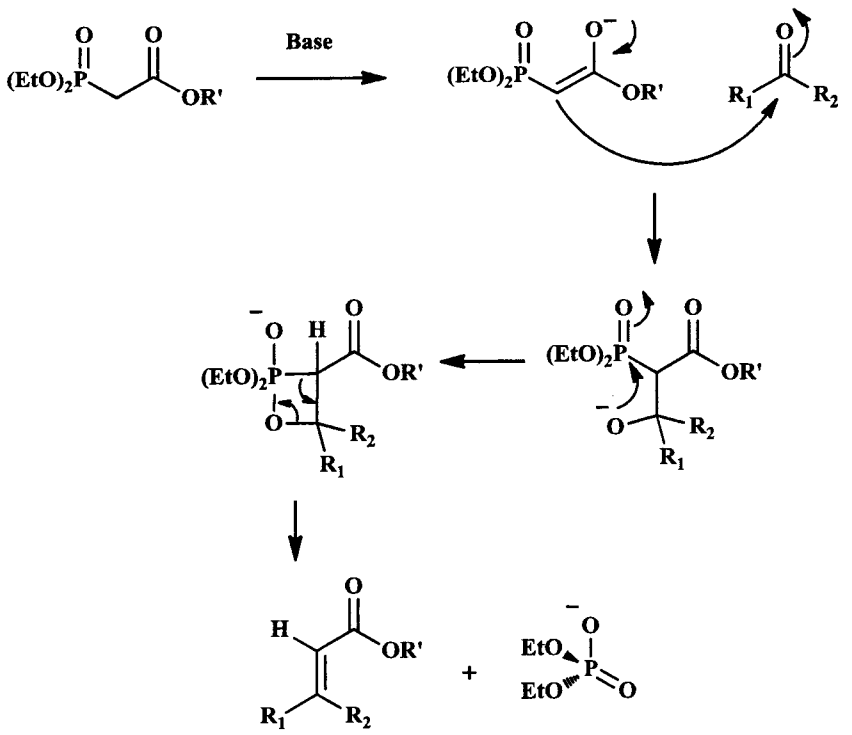
chemistry project, because the extended cinnamaldehyde semicarbazones are far more energetically stable in the *E* isomer form as well as the almost complete isomerization in the third step of our synthesis.



Scheme 0.5: Synthesis of extended cinnamaldehydes from Wittig product.

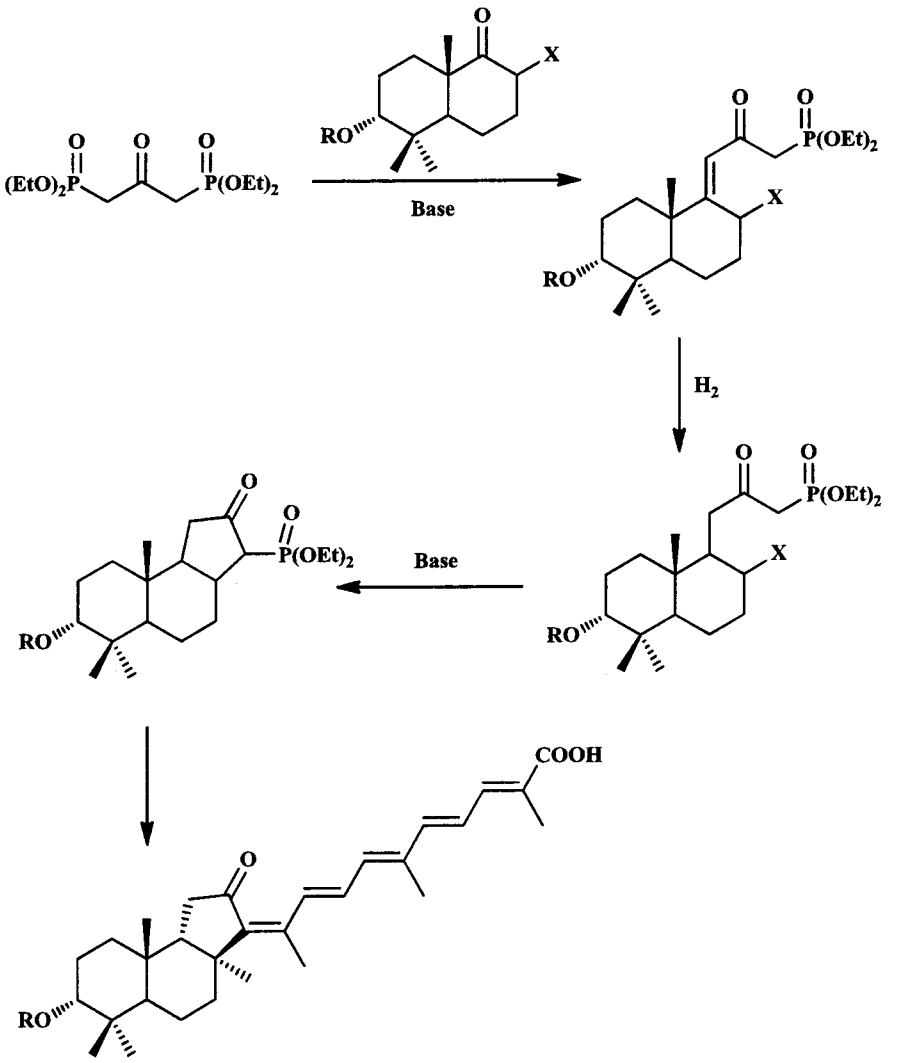
In contrast the second project involves a Horner-Wadsworth-Emmons (HWE) reaction, instead of a Wittig reaction. The HWE condensation is a Wittig like reaction, with three distinct differences; 1) the stereoselectivity, 2) easier by-product removal, 3) and the use of different phosphorus ylide.[1,3]

First, the Wittig reaction conditions are not easily tailored to give stereoselectivity, but the HWE reaction conditions can be easily modified to give either the *cis* or *trans* isomer.[3] Second, the Wittig reaction produces $Ph_3P{=}O$ as a by-product which is time consuming to remove due to its limited solubility. In contrast, the phosphonate by-product produced via the HWE (Scheme 0.6) is water soluble and can easily be separated from the desired product. Finally, the HWE reaction uses a phosphonyl enolate as the phosphorus ylide species. The phosphonyl enolate attacks a carbonyl species to form a new C-C bond, and a phosphonic acid is eliminated to form the alkene (Scheme 0.6).



Scheme 0.6: Mechanism of a HWE reaction.

The second project involves the synthesis of stellettins using an uncommon HWE condensation reaction. The canonical HWE reaction involve a compound with only one phosphonyl group; however this project employs a α,α'-bisphosphonate. This methodology envisions stepwise HWE condensations; first the installation a phosphonyl component onto the decalin core, followed by ring closure *via* a substitution reaction, and finally installing an alkenyl side chain by a second HWE reaction (Scheme 0.7).



Scheme 0.7: Synthesis of stellettins from 1,3-bisphosphonoacetone.

CHAPTER 1

SYNTHESIS OF EXTENDED CINNAMALDEHYDE SEMICARBAZONES FROM WITTIG REAGENT

Introduction:

Materials chemistry involves the creation of materials that have useful bulk properties to perform a function or meet a challenge. An early example is polyvinyl chloride (PVC), it's the third most produced plastic and is widely used in construction because it is durable, cheap, and easily worked.[4] A more recent example is the azobenzenes, with their *cis-trans* isomerization, that have been used in molecular switches.[5] This isomerization is brought about by absorption of electromagnetic radiation called photochromism. Photochromism is the capacity of a compound to change color when light is applied and then change back again when the light is removed (*i.e.* placed in a dark environment).[6] This phenomenon is mainly exhibited in compounds when they are in solution, *i.e.* spiro-oxazines, diarylethenes, and fulgides (Figure 1.1).[5,7]

However, in special cases photochromicity can be observed in compounds that are in the solid state. As an example, solid state compounds are used in photochromic sunglasses, which darken upon exposure to sunlight (UV radiation). The solid state compounds in glass lenses are usually inorganic, metal-containing compounds (*i.e.* silver chloride)[8] while the plastic lenses contain organic compounds (*i.e.* indolino spironaphthoxazine).[9] Photochromic materials are also used in the field of supramolecular chemistry as molecular switches,[5] data storage,[10a,10b] cosmetics,[6] and clothing.[11]

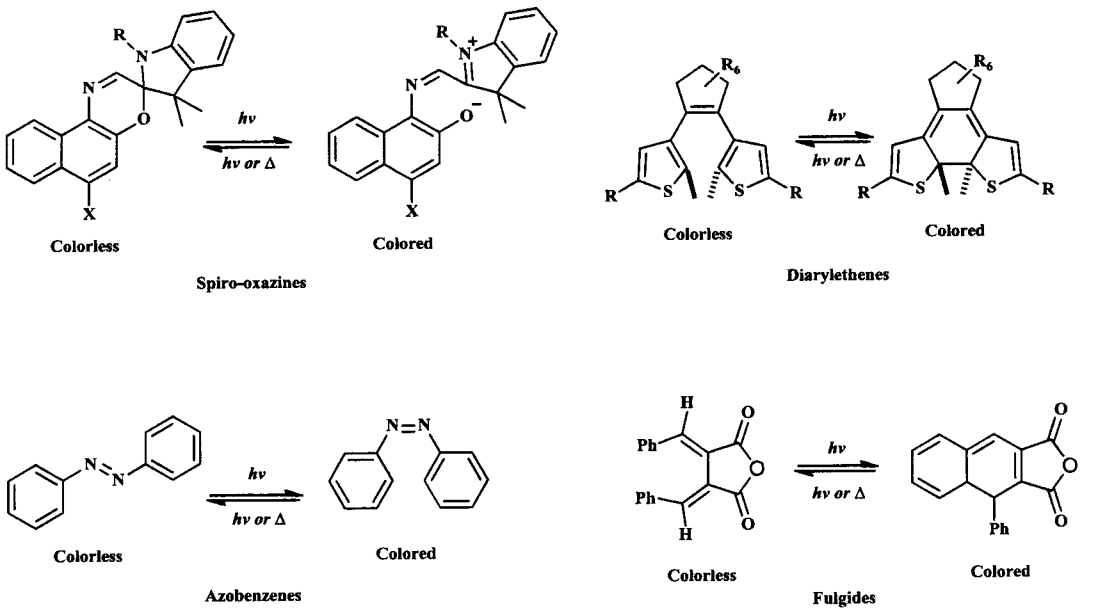


Figure 1.1: Examples of known photochromic compounds.[5,7]

Reports by I.M. Heilbron *et al.* described the solid-state photochromicity of cinnamaldehyde semicarbazone **(4a)** and its methoxy derivatives.[12] Heilbron and colleagues found that cinnamaldehyde **(4a)**, along with its *ortho*-methoxy **(4c)** and *para*-methoxy **(4b)** derivatives exhibited reverse photochromism. Further, they noted that the *ortho*-methoxy **(4c)** derivative showed a more intense photochromic change while *para*-methoxy **(4b)** derivative showed only a slight photochromic change compared to cinnamaldehyde **(4a)**. They also reported that the *meta*-methoxy **(4d)** and the *ortho*-nitro **(4e)** derivatives did not show photochromicity (Figure 1.2). This data suggests that an electron-donating group (*i.e.* methoxy) *ortho* or *para* on the phenyl ring will display photochromicity, while a methoxy *meta* to the ring will not. Also, having an electron-withdrawing group (*i.e.* nitro) *ortho* on the ring doesn't convey photochromicity onto the compound.

Heilbron and Wilson only looked at a select few compounds, that didn't cover the full span of compounds available. Thus, this study seeks to determine the ability and degree of substituents to affect cinnamaldehyde photochromicity, where two factors will be systematically explored; 1) the length of the conjugated system between the ring and the imine (C=N), and 2) the number, location, and type of substituents off the phenyl ring (Scheme 1.1).

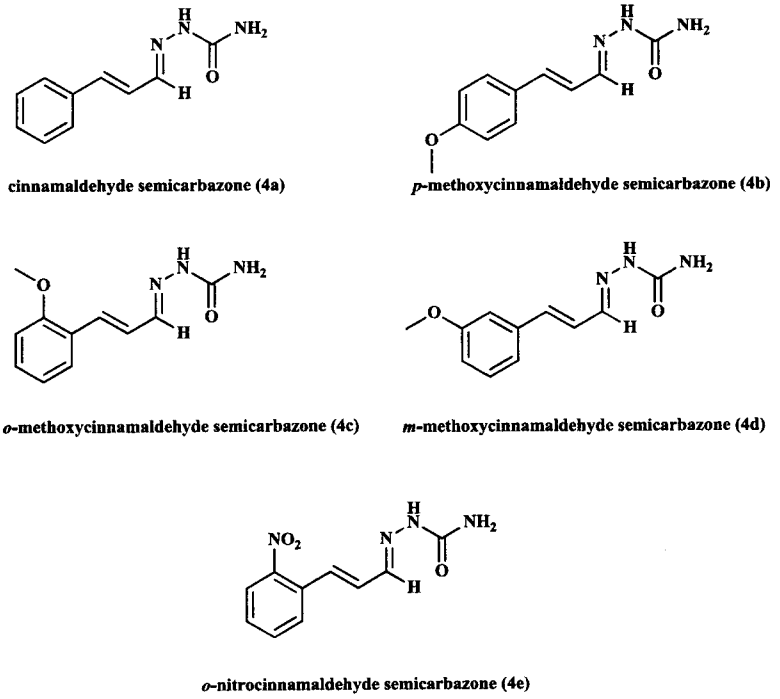


Figure 1.2: Cinnamaldehyde semicarbazones reported by Heilbron *et al.*[12]

It is well known that the color an organic compound appears is related to the length of its conjugated system, which is directly proportional to the amount/wavelength of light it absorbs. The change in energy (ΔE) can be related to the energy state (n), Planck's constant (h, 6.626×10^{-34} Js), the mass of electron (m, 9.110×10^{-31} kg), and the length of the conjugated system (L) (Equation 1.1) using particle in a box theory.[13]

$$\Delta E = E_{n+1} - E_n = (2n + 1) * h^2/8mL^2 \qquad (1.1)$$

From ΔE, the wavelength (λ) can be found using Equation 1.2, where c is the speed of light ($3.00x10^8$ m/s).

$$\lambda = hc/\Delta E \qquad (1.2)$$

An example of how the length of the conjugated system affects the color can be seen in lycopene and phytofluene (Figure 1.3). Lycopene contains a long acyclic conjugated chain that results in a strong red color (λ_{max} = 470 nm). Alternatively, the shorter conjugated system of phytofluene is orange in color (λ_{max} = 348 nm).[14]

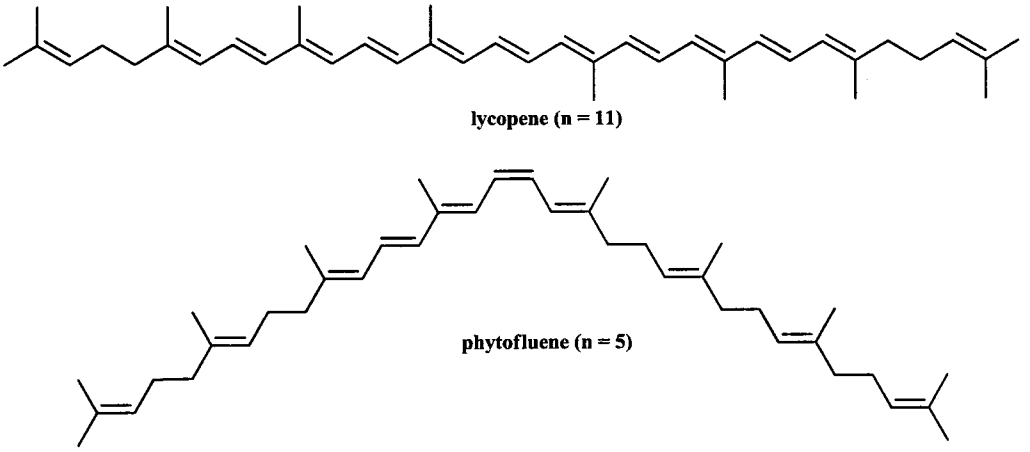


Figure 1.3: Structures of lycopene and phytofluene.[14]

Likewise, molecular orbital calculations show that the energy differences between the highest occupied molecular orbital (HOMO) and the lowest unoccupied molecular orbital (LUMO) decreases as the extent of the conjugation increases.[13] So with every double bond added, the system absorbs photons of lower energy, thus moving the wavelength of absorption into the UV/Visible region of the electromagnetic spectrum. It can then be hypothesized that a more conjugated system would have a higher degree of photochromicity than a less conjugated system. It's also key too note that conjugated

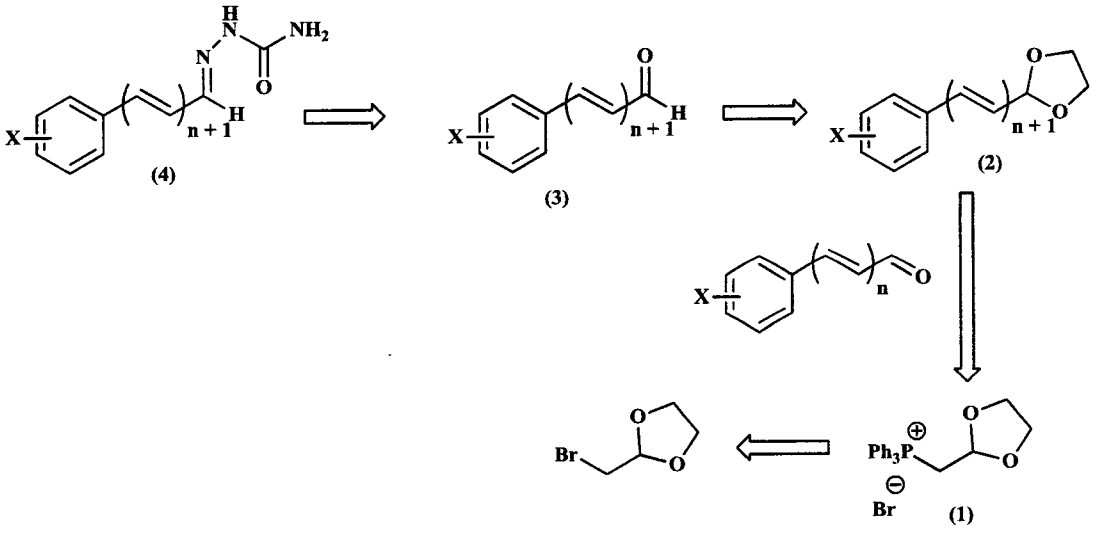
systems conjugate best when the molecule is planar, since it allows for the best overlap of the p-orbitals. These absorbance wavelengths can be calculated using a graphical interface (*i.e.* Spartan v'10) to input the chemical structure, and then subjected to lengthy quantum mechanical functions.

Secondly, altering the substituents off the phenyl ring impacts the wavelength of absorption. This may alter the photochromicity of a compound due to electronic and/or steric effects. Electron-donating groups (EDG), like methoxy ($-OCH_3$) groups, produce an increase in the UV-Vis absorption wavelength. Conversely, electron-withdrawing groups (EWG) like nitro ($-NO_2$) groups, produce a decrease in the wavelength. This is because the energies of the HOMO and the LUMO are also affected by EWGs.

Robert Burns Woodward, while looking at the ultraviolet spectra of various enones, developed a set of empirical rules that enabled the prediction of the wavelength at which the π to π^* transition occurs. The effect of the addition of substituents at various positions can be calculated using these rules; *i.e.* extending the conjugation by a double bond will increase the λ_{max} by 30 nm, while a methoxy group (depending on its location) will add between 17 – 35 nm.[15] However substituents positioned off the ring can also affect the absorbance of the conjugated system in other ways. Steric hindrance can be caused by these substituents which could also play a major role in the absorbance of conjugated systems and thus the photochromicity of the compound. The sterics of placing substituents off the phenyl ring of the cinnamaldehyde semicarbazone is predicted to cause the molecule to bend out of plane disrupting the p orbital overlap and decreasing the λ_{max} of the system.

The systems reported herein, to determine if it's synthetically possible to tune the degree of photochromicity, 1) contain up to 3 olefinic bonds and 2) are either mono, di, or tri substituted with OMe and/or OH groups. These systems are more expansive and complex than those of Heilbron and Wilson, and since the aldehydes are not commercially available a synthetic route is needed to create these semicarbazone precursors.

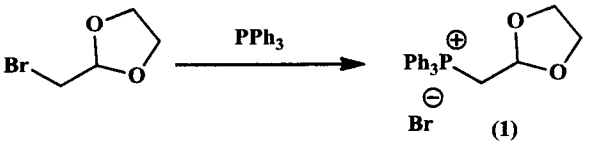
The (Scheme 1.1) retrosynthetic approach involves forming the cinnamaldehyde semicarbazone **(4)** from a cinnamaldehyde **(3)**, which can be readily formed by acidic hydrolysis of an acetal **(2)**. The formation of the acetal **(2)** is possible *via* a Wittig condensation of an aldehyde with a two-carbon phosphonium ylide **(1)** which can be produced as reported by T. M. Cresp *et al.*[16] This synthetic scheme is very versatile, so that the conditions do not need to be changed when using the different cinnamaldehyde derivatives.



Scheme 1.1: Retrosynthesis of semicarbazones **(4)** from Wittig reagent **(1)** and various substituted benzaldehydes.

Results & Discussion:

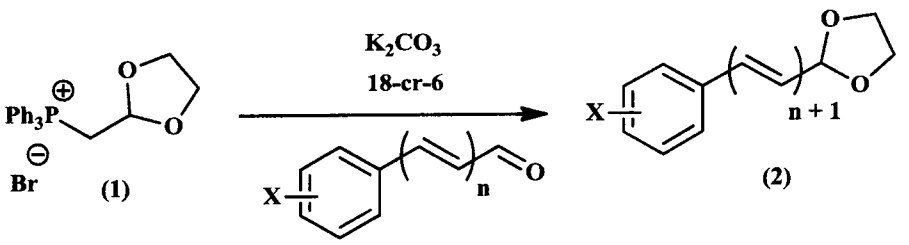
The Wittig reagent **(1)** has been prepared repeatedly (JMS 1) in favorable yields (51%), as reported by T. M. Cresp *et al.*[16]



Scheme 1.2: Synthesis of Wittig reagent.[16]

The first attempt, JMS 1-1, was heated excessively (at 70% rheostat setting) for ~ 28 hrs, and turned the mixture into a black sludge producing an extremely low yield due to decomposition. Heating at a lower temperature (at 30% rheostat setting) produced a orange powder which after recrystallization from a 1 : 1 mixture of CH_2Cl_2 : ether afforded the product in higher yields. The ^1H NMR spectrum showed a distinctive doublet of doublets (J = 4.43 Hz, J_{HP} = 8.53 Hz) for two hydrogen's (2H) at 4.4409 ppm corresponding to the CH_2 adjacent to the phosphorus and peaks for 15H total, at 7.6243, 7.7048, 7.7766 ppm, corresponding to the three aromatic phenyl groups. The ^{31}P NMR spectrum showed a single peak at 21.65 ppm corresponding to the phosphonium ylide as opposed to a peak a -5.00 ppm which would correspond to the free phosphine.[17]

The compounds chosen for the Wittig condensation reactions (Scheme 1.3) followed three considerations: 1) previous photochromic work by Heilbron *et al.*, 2) electronic and steric effects of the substituents, and 3) the effects of extending the conjugated system.



Scheme 1.3: Preparation of extended acetals **(2)** from Wittig reagent **(1)**.

The work of Heilbron *et al.*,[12] using cinnamaldehyde, its *o*, *m*, and *p*-methoxy derivatives, and *o*-nitrocinnamaldehyde was repeated to give support to their results and used as a photochromic control for our research. The effect of extending the conjugated system of these compounds was tested by preparing compounds with polyene systems (n > 1). Focus was placed on methoxy compounds since the *ortho*-methoxy was reported to show an increase in photochromicity. To test the effect of electronics and sterics three different series were used; 1) dimethoxy derivatives, 2) trimethoxy derivatives, and 3) hydroxyl containing (including vanillin and isovanillin) series.

Wittig condensations are usually carried out by a strong base under inert atmospheric conditions, but this requires strictly anhydrous solvents and pyrophoric bases which are difficult to work with. Previous studies showed that the Wittig condensation with substituted benzaldehydes could be performed using a weak base and crown ether. The crown ether facilitates chelation of the metal and is thus interchangeable depending on the weak base used. Thus, the previously stated benzaldehydes and cinnamaldehydes were reacted with the Wittig reagent under these conditions (Table 1.1).[18a,18b]

In the 1st condensation attempt, 1 equiv. of 3,4,5-trimethoxybenzaldehyde, 3.3 equiv. of Na_2CO_3 and 0.92 equiv. of 15-C-5 were used to afford 3.25 g of crude material. SiO_2 flash chromatography to purify the mixture gave two fractions (0.35 g and 0.19 g) but

upon NMR analysis it was confirmed that these fractions contained no peaks corresponding to the product (JMS 7-1a).

The base was changed from Na_2CO_3 to the stronger K_2CO_3, which also required the use of 18-Cr-6 instead of 15-Cr-5 in order to chelate the larger potassium (K). JMS 7-1b used again 3,4,5-trimethoxybenzaldehyde (1 equiv.) to give 11.13 g of crude material. After SiO_2 purification to remove the triphenylphosphine oxide (PPh_3=O) byproduct, the yield was 78.1% (1.061 g). ^{1}H NMR analysis showed peaks at 6.09 (1H, dd, J = 6.03 Hz, J = 15.8 Hz, H_e) and 6.70 (1H, d, J = 15.8 Hz, H_d) corresponding to the *trans*-alkene and

Table 1.1: Yields and *Cis* : *Trans* ratios for the Wittig condensation reactions **(2)** under 18-Cr-6/K_2CO_3 conditions.

Acetal	Yield	X	n	*Cis* : *Trans* Ratio
JMS 7-18	89.0%	H	2	
JMS 7-19	68.3%	"	3	
JMS 7-4	67.3%	2-OMe	2	
JMS 7-7	14.6%	"	3	
JMS 7-9c	84.6%	4-OMe	2	
JMS 7-15	58.5%	"	3	
JMS 7-17	98.3%	3-OMe	1	
JMS 7-10	83.2%	2,5-diOMe	1	
JMS 7-12	24.9%	3,5-diOMe	1	
JMS 7-13	79.9%	2,4-diOMe	1	59.3 : 40.7
JMS 7-2b	25.5%	2,4,6-triOMe	1	36.4 : 63.6
JMS 7-3b	21.6%	2,4,5-triOMe	1	61.0 : 39.0
JMS 7-5	53.1%	2,3,4-triOMe	1	
JMS 7-1b	78.1%	3,4,5-triOMe	1	58.0 : 42.0
JMS 7-11	43.7%	"	2	
JMS 7-16	20.7%	4-OH	1	
JMS 7-6b	63.1%	4-OH, 3-OMe	1	
JMS 7-8	21.0%	3-OH, 4-OMe	1	
JMS 7-14	96.0%	"	2	

peaks at 5.70 (1H, dd, J = 7.28 Hz, J = 11.6 Hz, H_e) and 6.67 (1H, d, J = 7.78 Hz, H_d) corresponding to the *cis*-alkene. The coupling constants (J) were used to determine which of the peaks corresponded to which isomer, since in the *trans*-isomers (J = 14-18 Hz) the J is usually higher than that of *cis*-isomers (J = 8-12 Hz). So it was determined that the doublet of doublets at 6.09 ppm (J = 15.8 Hz) was from the *trans*-isomer and the signal at 5.70 ppm (J = 11.6 Hz) was for the *cis*-isomer. Using the integrals from the ^{1}H NMR spectrum the *cis* : *trans* ratio was determined to be 58.0 : 42.0, this is in correlation with the typical stereochemistry obtained from the Wittig reaction. Finally, the ^{1}H NMR spectra showed peaks for the presence of the acetal group at 5.41 ppm (1H, d, J = 6.03 Hz, H_f) for the *trans*-isomer, and 5.52 ppm (1H, d, J = 7.28 Hz, H_f) for the *cis*-isomer.

These condensation reactions produce gram amounts of $Ph_3P{=}O$ (MW = 278.28 g/mol) as a white solid that is easily detectable using NMR analysis, but is quite difficult to remove. The NMR spectra (Figure 1.4) before SiO_2 purification (top) shows the distinct series of peaks, for $Ph_3P{=}O$, around ~7.40 – 7.70 ppm, which after purification (bottom) disappear.

There are a few important things to note when using SiO_2 purification. First, due to the acidic nature of SiO_2, extensive isomerization of the *cis* isomer to the *trans* isomer is seen in the extended acetal **(2)**. The spectra before purification shows a 1.39 : 1.00 mixture of *cis* : *trans* isomer, but after purification the ratio changes to 0.36 : 1.00 (H3, Figure 1.11). However, as previously stated, the stereochemistry of the Wittig product is not of major concern because the extended acetals will be cleaved in an acidic environment which isomerizes them to the more stable *trans* isomer.

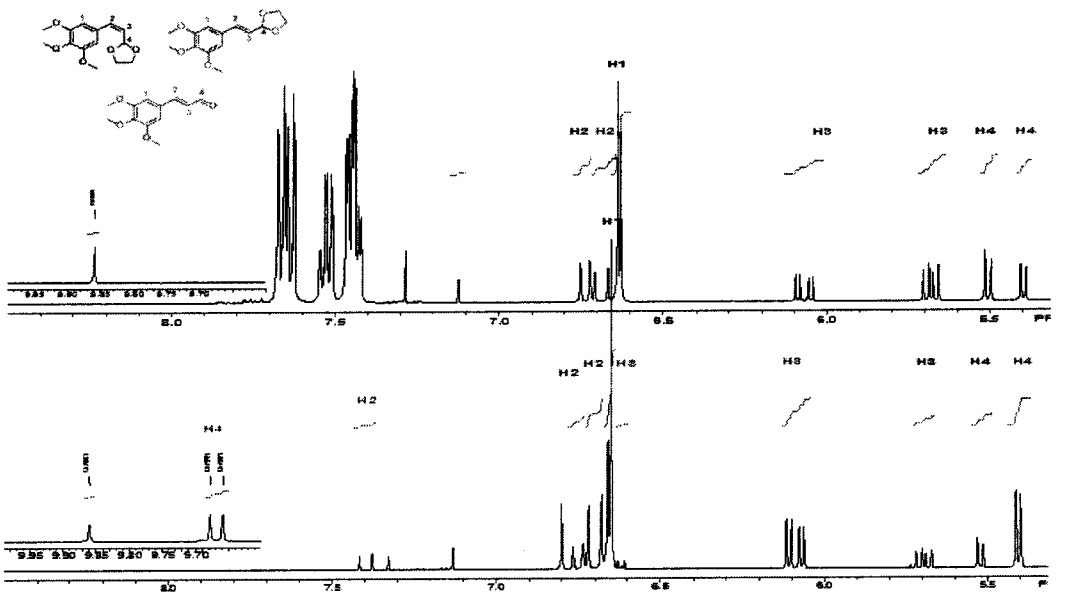


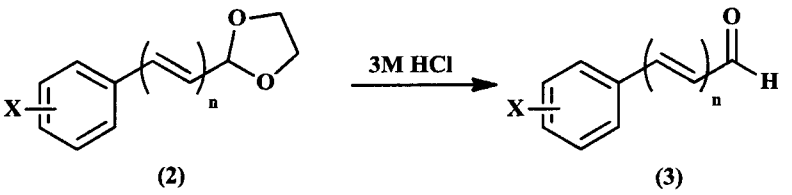
Figure 1.4: ^{1}H NMR spectra of Wittig JMS 7-1b before (top) and after (bottom) SiO_2 purification.

Second, also because of the acidity of SiO_2, the acetal **(2)** may be hydrolyzed to the aldehyde **(3)**. This is visible by a more downfield doublet past ~9.50 ppm in the ^{1}H NMR spectrum corresponding to the extended aldehyde, which can be distinguished from the starting material aldehyde by its splitting. Lastly, minor traces of starting material aldehyde may still be present after purification since the starting material has a similar R_f to the product (0.42 vs 0.37), but this is not of major concern because the recrystallization used to purify the semicarbazones **(4)** should remove these trace amounts. SiO_2 gel purification to remove $Ph_3P{=}O$ has some drawbacks; it's time-consuming and uses large amounts of organic solvents, making it environmentally and economically inadequate. Thus a new purification method should be found that avoids these limitations.[19] Filtering the crude Wittig condensation products over sand and Celite during work-up removed some (~10%) of the $Ph_3P{=}O$, but not all of it. A less time-consuming and more effective

method was developed. The crude mixture was filtered through sand and Celite and then the filtrate was suspended (after removal of the solvent) in reagent acetone (10 mL acetone/10 g material). Ether (10 mL ether/10 g material) was added to the solution and finally 3 volumes of hexane in 10 min intervals (400 mL hexane/10 g material) was added. This solution was then filtered over a large plug of SiO_2 gel and Celite to afford a clear solution of pure acetals **(2)**. It is key to note that if the reaction didn't go to completion, this purification method will not remove the starting aldehyde impurity, only the $Ph_3P=O$. This purification method, although fast and economical, does not give material that is equal in purity as material obtained from a SiO_2 gel column.

The overall yields (Table 1.1) of the Wittig condensation reaction vary drastically, which was caused by three things; 1) the different reactivities of the various aldehydes, *i.e.* 2-nitro is more reactive than 2-methoxy, 2) the ability to find a suitable solvent system for the Si gel chromatography, and 3) the purity of the Wittig reagent. The reactivity of the aldehydes is inherent, but the solvent system is not. The solvent system must allow for the separation of the acetal **(2)** while maintaining an R_f of ~0.35. Finally, if a reaction used impure Wittig, then the reactivity is low and thus the probability of having more leftover starting material is higher. Also if the reaction is done on a small scale with <200 mg of aldehyde it is probable that the percent yield of the reaction will be low due to the small amounts involved.

Upon purification the condensation products **(2)** were reacted under acidic conditions (Scheme 1.4) to remove the acetal protecting group and give the extended aldehyde **(3)** (Table 1.2). Due to the simplicity of the reaction and work-up, product yields were in the



Scheme 1.4: Deprotection of acetal **(2)** to form extended aldehyde **(3)**.

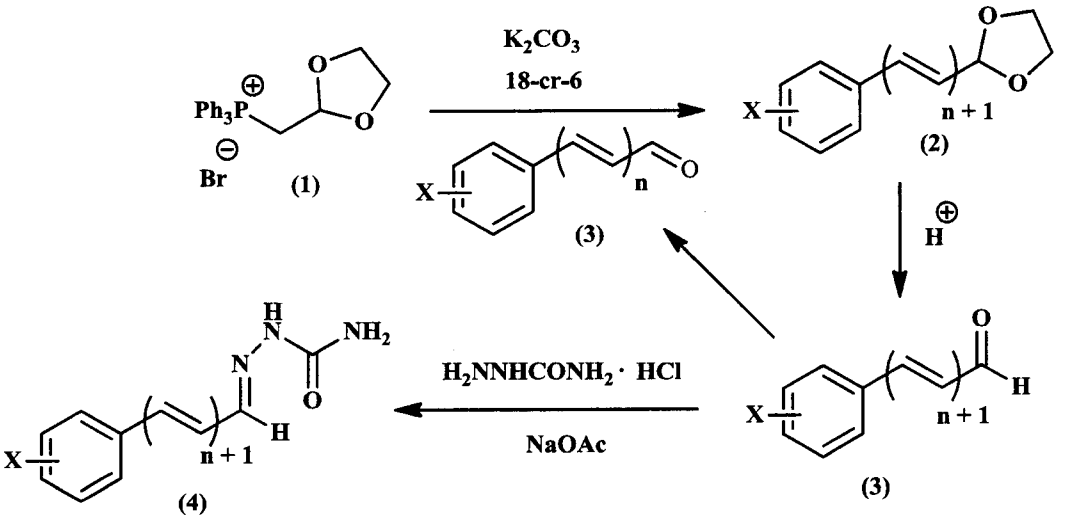
higher 80% range with minimal amounts of remaining starting material. Also the acidity of the reaction leads to a complete isomerization from *cis* to *trans* which is seen in all but one of the reactions (JMS 16-3). JMS 16-3 showed only a slight isomerization from *cis* to *trans*, but there is no indication as to why the product didn't undergo complete

Table 1.2: Yields and *Cis* : *Trans* ratio for the deprotection of acetal **(2)**.

Aldehyde	Yield	X	n	*Cis* : *Trans*
JMS 16-17	96.0%	H	2	
JMS 16-18	87.8%	"	3	
JMS 16-2	100%	2-OMe	2	0:100
JMS 16-6b	99.8%	4-OMe	2	88.6:11.4
JMS 16-14	94.6%	"	3	
JMS 16-16	89.5%	3-OMe	1	
JMS 16-9	83.7%	2,5-diOMe	1	
JMS 16-11	92.9%	3,5-diOMe	1	
JMS 16-12	77.6%	2,4-diOMe	1	
JMS 16-4	72.2%	2,4,6-triOMe	1	0:100
JMS 16-5	76.0%	2,4,5-triOMe	1	0:100
JMS 16-3	77.5%	2,3,4-triOMe	1	0:100
JMS 16-1	90.4%	3,4,5-triOMe	1	0:100
JMS 16-10	82.9%	"	2	
JMS 16-15	98.2%	4-OH	1	
JMS 16-7	70.1%	4-OH, 3-OMe	1	
JMS 16-8	91.9%	3-OH, 4-OMe	1	
JMS 16-13	87.9%	"	2	

isomerization. ^{1}H NMR analysis of the aldehyde **(3)** showed that the doublet at ~6.50 ppm pertaining to the acetal was no longer present, while a doublet at ~9.80 ppm was seen corresponding to the newly formed aldehyde **(3)**.

At this point the extended aldehydes **(3)** could be used to make extended semicarbazones **(4)**, or some of the mass could be cycled through again to make even more extended aldehydes. This decision depended directly on the amount of aldehyde. Using the overall cumulative yield for the 3 step process, it was determined that at least ~250 mg of aldehyde **(3)** is needed to make it through the complete synthesis (Scheme 1.5) and anything less will lead to a shortage of material after the purification of the acetal **(2)**.



Scheme 1.5: Cycling extended aldehyde **(3)** to Wittig or semicarbazone reaction.

For example aldehyde JMS 16-6 (1.3669 g), produced from acetal JMS 7-9, was split; 1.0869 g underwent a second Wittig condensation to give acetal JMS 7-15 with 3 double bonds (n = 3), while 0.2800 g went on to create semicarbazone JMS 18-8 with 2 double bond (n = 2).

The semicarbazone reaction (the final reaction) is straight-forward and extremely fast (~1.5 days including purification); the extended aldehydes **(3)** are reacted with semicarbazide HCl, filtered/dried overnight and recrystallized in various solvents to give the extended semicarbazones **(4)** (Table 1.3). Table 1.3 displays more semicarbazones than there are aldehydes in Table 1.2, because five of the semicarbazones (JMS 18-1 – JMS 18-5) were made from commercially available cinnamaldehydes, which could simply undergo the final semicarbazone reaction.

Table 1.3: Yields for preparation of semicarbazones **(4)**.

Semicarbazone	Yield	X	n	Recryst. Solvent	m.p. (°C)
JMS 18-1	77.5%	H	1	95% EtOH	221 - 224
JMS 18-23	64.5%	"	2	95% EtOH	201 - 205
JMS 18-24	37.7%	"	3	95% EtOH	214 - 217
JMS 18-3	84.3%	2-OMe	1	95% EtOH	199 - 202
JMS 18-7	23.3%	"	2	95% EtOH	196 - 199
JMS 18-2	83.5%	4-OMe	1	95% EtOH	203 - 205
JMS 18-8	65.3%	"	2	1-BuOH	228 - 231
JMS 18-20	41.7%	"	3	100% EtOH	225 - 227
JMS 18-22	64.5%	3-OMe	1	95% EtOH	175 - 180
JMS 18-15	49.2%	2,5-diOMe	1	95% EtOH	208 - 211
JMS 18-17	47.6%	3,5-diOMe	1	95% EtOH	178 -182
JMS 18-18	68.9%	2,4-diOMe	1	1-BuOH	179 - 182
JMS 18-9	77.5%	2,4,6-triOMe	1	100% EtOH	195 - 199
JMS 18-10	25.9%	2,4,5-triOMe	1	95% EtOH	215 - 218
JMS 18-12	37.6%	2,3,4-triOMe	1	95% EtOH	173 - 176
JMS 18-6	78.9%	3,4,5-triOMe	1	95% EtOH	206 - 208
JMS 18-16	22.1%	"	2	1:1 H_2O:EtOH	191 - 194
JMS 18-21	46.0%	4-OH	1	DMSO	215 - 217
JMS 18-13	69.7%	4-OH, 3-OMe	1	Pyridine	207 - 210
JMS 18-14	26.6%	3-OH, 4-OMe	1	Pyridine	204 - 208
JMS 18-19	35.9%	"	2	Pyridine	201 - 205
JMS 18-4	86.2%	2-NO_2	1	95% EtOH	219 - 221
JMS 18-5	73.8%	β-phenyl	1	95% EtOH	220 - 224

^{1}H NMR analysis of the newly formed semicarbazones **(4)** showed two broad peaks at ~6.22 ppm and ~9.94 ppm pertaining to the primary and secondary amines, respectively. Also, the doublet at ~9.80 ppm for the aldehyde **(3)** has been shifted upfield in the ^{1}H NMR spectra to ~7.06 ppm corresponding to the imine of the semicarbazone group. The same can be seen in the ^{13}C NMR spectrum as the aldehyde at ~196.12 ppm has shifted to ~144.85 ppm corresponding again to the imine. The NMR spectra for the semicarbazones **(4)** only showed the presence of the most stable *trans* isomer.

The solubility of these semicarbazones in the alcoholic recrystallization solvents seems to decrease as the conjugation increases, as it should because increasing the conjugation makes the molecule more non-polar, but using too large an amount of solvent leads to lower yields. The low yields on extended semicarbazones (n = 2, 3), are also due to small amounts of starting aldehyde impurity and possibly from the difficulty of transferring small amounts of material.

The melting points for the light semicarbazones **(4)** were determined, but they were not for the dark semicarbazones **(4)** due to the quick conversion of dark species to light species (~minutes).

The semicarbazones **(4)** were divided into two equal portions and placed in vials to be analyzed for photochromicity. The "light" semicarbazone was placed on the lab bench where overhead light was readily available, while the "dark" semicarbazone was wrapped in aluminum foil and placed in a desk drawer out of light.

Our classification of the "light" and "dark" forms of the compounds involved the use of a standard color system, in this case the Behr® (paint) color system[20] (Table 1.4). This was done by comparing the "light" and "dark" version to color sample cards; for the

"dark" versions the color was determined in a dimly lit room and the compound was only exposed to the small amount of light for no more than a minute. The difference in the Behr number system can be used to determine the degree of change between the two forms. A number change in the first part, *i.e.* 380B-7 to 330B-7, indicates the colors are on different cards, and only slightly differ in color. Also the colors become paler with decreasing numbers. So for instance 380B-7 is a brighter color, while 330B-7 is paler. A change in the hyphenated number, *i.e.* 310A-1 to 310A-3, indicates the colors are on the same card, and greatly differ in color. The colors become more intense with increasing number. So for instance, 310A-1 is a pale ivory while 310A-3 is a deeper manila. Each card has 3 or 4 color sample on it, and the letters A, B, and C indicate three different tone series. Thus it is difficult to tell without looking at the card the color difference if they switch series (*i.e.* with 4-OH, 3-OMe which goes from Clam Chowder (330C-3) to Cornmeal (310B-4).

Our data can be compared to that of Heilbron's *et al.*,[12] which stated that cinnamaldehyde semicarbazone (n = 1) **(4a)** and 2-methoxycinnamaldehyde semicarbazone (n = 1) **(4c)** showed very drastic color changes, while 4-methoxycinnamaldehyde semicarbazone (n = 1) **(4b)** showed only a subtle change. Looking at Table 1.4, we see that cinnamaldehyde semicarbazone (n = 1) displays a slight shift in color, but our results contradict Heilbron's for 2-methoxy **(4c)** and 4-methoxy **(4b)**. 2-methoxy-cinnamaldehyde semicarbazone (n = 1) shows a subtle, unquantifiable change, while 4-methoxycinnamaldehyde semicarbazone (n = 1) shows a more intense photochromic shift of 1. Also, Heilbron described the semicarbazones as quickly reversible and the semicarbazones here (Table 1.4) are only quickly reversible in one

direction. It takes ~1-1.5 weeks for the compound to adopt the "dark" color, but only a matter of minutes to revert back to the "light" form. Also 2-nitrocinnamaldehyde and 3-methoxycinnamaldehyde semicarbazones showed no color change and were determined not to be photochromic, which is exactly as described by Heilbron *et al.* Thus our results back up those of Heilbron in all but one aspect, in that the 4-methoxy derivative displays a more prominent change than that of the 2-methoxy.

Table 1.4: Behr color name/number of "light" and "dark" semicarbazones **(4)**.

X	n	Light Behr Color (Behr Number)	Dark Behr Color (Behr Number)
H	1	Ruffled Clam (350A-1)	Morning Sunlight (360A-2)
	2	Banana Split (360A-3)	Lemon Soufflé (350-4)
	3	Saffron Thread (310B-7)	Darker Saffron Thread (310B-7)
2-OMe	1	Moonlit Yellow (380A-2)	Moonlit Yellow (380A-2)
	2	Bicycle Yellow (370A-3)	Lemon Sorbet (330B-6)
4-OMe	1	Moon Mist (370A-1)	Pale Daffodil (370A-2)
	2	Banana Split (360A-3)	Summer Harvest (380A-3)
	3	Saffron Thread (310B-7)	Darker Saffron Thread (310B-7)
3-OMe	1	Powder Sand (340C-1)	Powder Sand (340C-1)
2,5-diOMe	1	Lemon Tart (380B-6)	Marigold (380B-7)
3,5-diOMe	1	Ripe Wheat (310E-3)	Ripe Wheat (310E-3)
2,4-diOMe	1	Custard Cream (370C-2)	Lightweight Beige (330C-2)
2,4,6-triOMe	1	Pale Daffodil (370A-2)	Banana Split (360A-3)
2,4,5-triOMe	1	Lemon Drops (340B-4)	Cheerful Hue (330B-4)
2,3,4-triOMe	1	Pineapple Soda (340B-6)	Flame Yellow (360B-6)
3,4,5-triOMe	1	Summer Harvest (380A-3)	Darker Summer Harvest (380A-3)
	2	Vibrant (370B-6)	Yellow Flash (370B-7)
4-OH	1	Citrus (360B-5)	Flame Yellow (360B-6)
4-OH, 3-OMe	1	Clam Chowder (330C-3)	Cornmeal (310B-4)
3-OH, 4-OMe	1	Twenty Carat (310B-6)	Spiced Butternut (310B-5)
	2	Clair de Lune (300E-3)	Clair de Lune (300E-3)
2-NO_2	1	Saffron Thread (310B-7)	Saffron Thread (310B-7)
β-phenyl	1	White	Darker White

Normally in photochromic compounds the "light" version is paler (less intensely colored) than the brighter (more intensely colored) "dark" version. This can be seen in *p*-methoxycinnamaldehyde (Table 1.4) whose "light" version (370A-1) was paler than the "dark" version (370A-2). However it is possible for this to be reversed, *i.e.* the "light" version is brighter/more intensely colored than the paler "dark" version. Looking at Table 1.4, we see that both 2,3,4-triOMe (n = 1) and 3-OH, 4-OMe display reversed photochromicity. For instance, 3-OH, 4-OMe (n = 1) was Twenty Carat (310B-6) in color and the "dark" version was Spiced Butternut (310B-5) in color.

The photochromic color change between the "light" and "dark" versions of the new semicarbazones can be viewed with respect to; 1) the extension of conjugation, 2) the addition of methoxy groups, and 3) hydroxyl containing (including vanillin and isovanillin) series. First we will focus on the photochromic changes with respect to the extent of conjugation. All of the extended semicarbazones from Table 1.4 displayed a more dramatic photochromic shift, from n = 1 to n = 2. Looking at 4-methoxycinnamaldehyde (n = 1) we see a slight shift of only 1, and that extending the conjugation to n = 2 leads to a change of 20. However, for both cinnamaldehyde and its 4-methoxy derivative, extending the conjugation even further, from n = 2 to n = 3, led to a darker overall color, but only a subtle photochromic shift. These compounds should be recrystallized again to verify the results, and more n = 3 semicarbazones **(4)** need to be made before a conclusion is drawn about the n = 3 series. It's clear that our hypothesis that extended the conjugation should lead to enhanced photochromicity was in fact valid going from when n = 1 to n = 2. Next, we can move on to discuss the trends associated with the addition of methoxy groups on the photochromicity.

The photochromicity of the addition of a single OMe has already been discussed when comparing results with those of the Heilbron study. Since having one OMe at either the *para* or *ortho* position gave greater degrees of photochromicity, it can be hypothesized that placing two OMe groups *ortho* and *para* to the ring should lead to a more pronounced photochromic shift. This is exactly what is seen as 2,4-diOMe shows the highest shift between "light" and "dark" form of 40. Our data, along with Heilbron's, shows that *meta*-OMe alone is not photochromic, however maybe it would be possible to make *meta*-OMe photochromic by the addition of a second OMe group. The addition of a second *meta*-OMe group (as with 3,5-diOMe) unsurprisingly still gave a nonphotochromic compound, while the addition of an *ortho*-OMe (as with 2,5-diOMe) gave a feebly photochromic compound. However conclusions on diOMe species with one *meta* OMe group, cannot be made until 3,4-diOMe is examined.

Finally we can look at the trends associated with adding three methoxy groups (triOMe) to the phenyl ring. All of the triOMe semicarbazones show photochromicity with 2,4,6-trimethoxycinnamaldhyde semicarbazone displaying the most drastic shift of 1. The semicarbazone in its "light" form is Pale Daffodil (370A-2) in color but changes to Banana Split (360B-3) in its "dark" form.

The final trend we can examine is the full or partial replacement of methoxy groups with hydroxyl groups (including vanillin and isovanillin). We have seen that the addition of OMe groups *ortho* and *para* to the phenyl ring will lead to enhanced photochromic shifts. However, is it only OMe groups that give this change or can other groups such as hydroxy (OH) groups give the same result? To answer this question a compound with the OH group *para* to the phenyl ring was made and a significant change of 1 was seen in the

photochromicity (the same amount as seen with the *para*-OMe group). So the replacement of OMe groups with OH groups will lead to photochromic compounds. But what happens when there is more than one group on the ring? Both vanillin (4-OH, 3-OMe) and isovanillin (3-OMe, 4-OH) gave shifts of 1, though vanillin also shifted by 20 and from the C to the B series. This suggest that OH groups are more powerful, since greater photochromicity was seen when this group was at the *ortho* and/or *para* position.

Based on these findings, we can draw some conclusions; 1) the addition of OMe groups can increase the intensity of photochromicity of semicarbazones if they are placed at the *ortho* or *para* positions, 2) OMe groups promote greater photochromicity than OMe by themselves and/or when paired together.

Having looked at the color change between the "light" and "dark" forms of one compound, we can look at the effect of extending the conjugation on the color between the "light" form of different compounds. We expect to see a difference in color, from pale to darker colors because the extension of conjugation leads to deep darker colors. This is exactly what we see in all cases of extension in Table 1.4, each of the extended conjugated systems shows a color difference of at least 10 from a paler color to a brighter color; *i.e.* 4-methoxycinnamaldehyde semicarbazone changes from Moon Mist (370A-1) for n = 1 to Banana Split (360A-3) for n = 2 to Saffron Thread (310B-7) for n = 3. Next we can look at trends in the difference of color associated with the addition of OMe groups between the "light" forms of various cinnamaldehyde semicarbazones.

The addition of methoxy groups to cinnamaldehyde semicarbazone (n = 1) should promote a difference in color between the various "light" semicarbazones, due to their electron-donating effects. All of the monomethoxy semicarbazones (n = 1) show a

difference of 10 or greater color in their from cinnamaldehyde semicarbazone (n = 1). It can be hypothesized that placing two OMe groups *ortho* and *para* to the ring should lead to an even more pronounced color difference than the monomethoxy semicarbazones (n = 1). However this is not seen, the dimethoxy semicarbazones (n = 1) show the difference in color from cinnamaldehyde semicarbazone as do the monomethoxy semicarbazones (n = 1), *i.e.* 2,4-diOMe is Custard Cream (370C-2) in color while 4-OMe is Moon Mist (370A-1) in color. The exception is the 3,5-diOMe (n = 1) derivative, which is much darker (brownish) when compared to cinnamaldehyde semicarbazone (n = 1) (cream colored). Adding three OMe groups should produce even more drastic color differences to produce deep dark colors. Looking at the data from Table 1.4 this is exactly what is seen, all of the semicarbazones show color differences from the cream color (Ruffled Clam (350A-1) for cinnamaldehyde semicarbazone) to drastically more intense yellows. Thus it can be concluded that the addition of one OMe groups to the phenyl ring leads to significant differences in color when compared to cinnamaldehyde semicarbazone. The addition of a second OMe group doesn't lead to much more of a difference, but the addition of three OMe groups gives much more intensely colored compounds. However, is it only OMe groups that give this change or can other compounds such as hydroxy (OH) groups give the same result? To answer this question we can examine the addition of a single OH group placed *para* to the ring, and compare this to the 4-OMe derivative, which produced such a drastic difference in color from cinnamaldehyde semicarbazone. Looking at Table 1.4 we see that 4-OH (n = 1) does produce a difference in color to the darker yellowish Citrus (360B-5), which is much more drastic than the color difference of 4-OMe (n = 1), compared to the cream colored cinnamaldehyde semicarbazone. A second

question can then be asked, does the OH produce a more pronounced color change than the OMe when they are paired together? Unfortunately this cannot be answered, as the compound for direct comparison -3,4-dimethoxycinnamaldehyde semicarbazone- was not prepared.

Leaving evaluation based on the Behr system behind, it can be said that displaying photochromicity requires the semicarbazones **(4)** to absorb light in order to undergo the change, which is most likely exciting an electron from the ground state to an excited state. This absorbance can be measured using UV-Vis absorbance spectroscopy. The semicarbazones were only soluble in dimethyl sulfoxide (DMSO) and acetonitrile (CH_3CN), however the UV-Vis cutoff range, the solvent itself begins to absorb for DMSO at 268 nm, which might obscure some important peaks. Thus, the spectra were obtained in CH_3CN; this gave a spectral cutoff of 190 nm, allowing for more of the semicarbazone **(4)** UV-Vis spectra to be obtained.

The first noticeable trait of the UV-Vis data (Table 1.5, Appendix 1.2) is that many different bands are present, which come from the absorbance of the aromatic ring, the conjugated chain, and/or the semicarbazone group (C=O/C=N). In order to determine where the semicarbazone group absorbs, the spectrum of acetone semicarbazone was obtained because it contains neither a ring system nor a conjugated chain. It was determined that the semicarbazone subunit absorbed around ~200 nm, using acetone semicarbazone (λ_{max} = 223.0 nm, ε = 4.61E+04 M^{-1} cm^{-1}). Substituted aromatic rings display three absorption bands at 180 nm, 200 nm, and 254 nm.[15] Using Woodward rules it can be predicted that the addition of methoxy groups will raise the λ_{max} by 6 nm per group and the addition of a double bond will add 30 nm.[15] Thus a semicarbazone with

one OMe group and a conjugated system of n = 1 should display three distinct absorption bands for the phenyl ring ~216 nm (phenyl ring), ~256 nm and ~290 nm. This is in fair agreement to the experimental spectrum for 2-methoxycinnamaldehdye, which shows λ_{max} is at 213.5 and 280.5 nm. A comparison of the cinnamaldehyde **(3)** and semicarbazone **(4)** spectra, using Tables 1.5, Table 1.6, and Appendix 1.1, show that it is possible to distinguish semicarbazones **(4)** from the cinnamaldehydes and that all the $\lambda_{max's}$ change, not just for the C=O/C=N absorption.

Table 1.5: Absorption wavelengths (λ) and molar absorptivity (ε) of cinnamaldehydes **(3)** and semicarbazones **(4)** in CH_3CN.*

X		n	λ	ε (E+04)	λ	ε (E+04)	λ	ε (E+04)
H	Cinn	1	283.5	9.81	224.5	42.5	206	3.81
	Semi		308.5	25.2	232.0	5.59	200.5	7.73
4-OMe	Cinn	1	315.5	14	231.0	5.32		
	Semi		321.5	13.3	235.0	2.52	227.5	2.17
β-phenyl	Cinn	1	295	14.8				
	Semi		315	21.5	234.5	11.5		

* λ values are in nm and ε values are in M^{-1} cm^{-1}.

Looking at the Table 1.5 and Appendix 1.2, we see that all the semicarbazones **(4)** absorb light between 232.0 nm and 257.0 nm, which is higher than the 223.0 nm observed for acetone semicarbazone. This red-shift is due to 1) the conjugated system as well as 2) the substituents off the phenyl ring. Some semicarbazones **(4)** in Table 1.10 don't show $\lambda_{max's}$ in this region as this peak is buried under other peaks. The lowest energy phenyl ring absorption had a λ_{max} around ~280 – 320 nm depending on the number, type, and position of the substituents.

Table 1.6: Absorption wavelengths (λ) and molar absorptivity (ε) of the semicarbazone group of the "light" form of semicarbazones **(4)**.*

X	n	λ	ε (E+04)
H	1	232.0	5.59
2-OMe	1	234.0	2.02
	2	245.5	28.5
4-OMe	1	235.0	2.52
	2		
3,4,5-triOMe	1	240.5	10.9
	2	257.0	0.180
2,4,6-triOMe	1	247.0	5.76
2,4,5–triOMe	1	244.0	9.72
2,3,4-triOMe	1	249.0	7.06
2,5-diOMe	1		
3-OH, 4-OMe	1		
3-OMe, 4-OH	1		
2-NO_2	1		
X	1	234.5	11.5
Acetone	1	223.0	4.61

* λ values are in nm and ε values are in M^{-1} cm^{-1}.

Using the information gained from the UV-Vis, trends can be drawn based on two main aspects of the semicarbazones **(4)**; 1) effects from the number, type, and position of substituents, and 2) the effect of extending the conjugation (Tables 1.5, 1.6, A.1 and A.2).

The first trend that can be drawn from the UV-Vis absorbance data deals with the effects of the substituents. As previously stated, the position of the substituent can play a key role in the overall physical characteristics of the phenyl system. Focusing on the effect of placing a single OMe on the phenyl ring, relative to cinnamaldehyde semicarbazone itself, gives a significant red-shift (308.5 nm to 321.5 nm) when it is at the *para* positions but a significant blue shift (308.5 nm to 297.5 nm) when it is at the *ortho* position. This is most likely due to better overlap of p-orbitals due to a more planar

molecule, since the *ortho* OMe may sterically cause the ring to bend relative to the chain. Extending the conjugated system in this series of compounds give the same effect; 2-OMe (212.5 nm) is red-shifted, but not as much as the less extended 4-OMe (n = 1).

The addition of more methoxy groups onto the phenyl ring should increase the $\lambda_{max's}$. From Table A.2, this is in fact what's occurring as more OMe groups give an additive increase in wavelength. For example, 2-OMe absorbs at 297.5 nm but upon addition of another OMe at the 5-position the wavelength is increased slightly to 299.0 nm (2,5-diOMe). When yet another OMe group is added the wavelength increased from 299.0 nm (2,5-diOMe) to 302.0 nm (2,4,5-triOMe).

So what effect would another EDG, *i.e.* an OH group, have when it is free and/or paired with an OMe group? Looking at the UV-Vis data for 4-OMe, 3-OH/4-OMe, and 3-OMe/4-OH we see a couple of things. First when comparing 4-OMe and 3-OH,4-OMe, we see that upon the addition of a *meta* OH group a blue-shift is seen (321.5 nm to 319.0). However, if the OMe is *meta* and an OH is place *para* to it a red-shift occurs (321.5 nm to 325.0 nm).

As previously stated, extending the conjugation of any system will lead to red-shift of the λ_{max}. Thus upon extension of the semicarbazone **(4)** conjugated system, an increase in wavelength should be seen. Each of the extended systems in our data set show this property; for 2-OMe, 234.0 nm (n = 1) to 245.5 nm (n = 2), and for 3,4,5-triOMe, 240.5 nm (n = 1) to 252.0 nm (n = 2) for the semicarbazone unit.

Based on our findings it's safe to conclude that the type, number, and position of the substituents each play a significant role, but neither is more critical than the next, in the absorbance of the semicarbazone **(4)**. So just having a single EDG does signify a red-

shift, however the position *ortho* or *para* is more critical, yet having a single EDG in the *ortho* or *para* position still doesn't guarantee an increase in absorbance. The same goes for multiple groups, it's possible for a single OMe group to exhibit more red-shift than a diOMe; *i.e.* 4-OMe (321.5 nm) compared to 2,5-diOMe (299.0 nm). Unfortunately no trends regarding the λ_{max} or energy compared to the presence or intensity of photochromicity could be seen.

Our first detection method of photochromicity in semicarbazones has been the Behr® color system.[20] Since UV-Vis measures the wavelength at which different compounds absorb light, it's our hypothesis that UV-Vis could be used to view differences between the "light" and "dark" versions. Thus a second UV-Vis experiment (Table 1.7) was done to determine the absorbance spectra of the "dark" semicarbazones **(4)**.

Table 1.7: Comparison of absorption wavelengths (λ) and molar absorptivity (ε) for the "light" and "dark" semicarbazones **(4)**.*

Cpd	X	n	λ	ε	λ	ε
Dark	H	1	309.0	1.94E+04	231.5	6.72E+03
Light			308.5	2.88E+05	225.5	1.25E+05
Dark	4-OMe	1	311.5	1.01E+04	234.0	4.51E+03
Light			321.5	1.57E+05	223.5	1.10E+05
Dark	β-phenyl	1	314.0	4.62E+04	228.5	2.40E+04
Light			314.5	4.25E+05	235.5	1.95E+05

* λ values are in nm and ε values are in M^{-1} cm^{-1}.

The UV-Vis spectra of the "light" and "dark" semicarbazones **(4)** were obtained and compared. The semicarbazone band (~220 nm) shows more of a change in λ_{max} than does the phenyl ring band (~300 nm) as expected. Looking at the absorbance of the cinnamaldehyde semicarbazone and 4-methoxycinnamaldehyde semicarbazone it is clear that there is a red-shift occurring between the 'light' and "dark" versions. However β-

phenylcinnamaldehyde semicarbazone gives a blue-shift that correlates well with the fact that this compound displays reversed photochromicity. It is interesting that the molar absorptivity (ε) of each of the semicarbazones band (~220 nm) shows a decrease from "light" to "dark" with cinnamaldehyde semicarbazone and 4-methoxycinnamaldehyde semicarbazone being more drastic and β-phenylcinnamaldehyde semicarbazone being more subtle. It is important to note that this data suggests that these compounds, in addition to being photochromic in the solid-state, are indeed also photochromic in solution.

We have previously seen that UV-Vis can be used to distinguish between the "light" and "dark" version. Next we wondered if it would be possible to observe a "switch" of a "dark" semicarbazone to a "light" versions using UV-Vis, since they "switch" back to the "light" version fairly quickly in the solid state. This experiment was done on the same semicarbazones used in the UV-Vis "light"/"dark" studies (Table 1.7).A "dark" sample was placed in the UV-Vis spectrometer, scanned, and then set out on the bench with the room lights fully on. After 10 minutes, it was placed back in the spectrometer. After two hours scans were taken every 45 min until the total time elapsed was 10 hours. Unfortunately a difference in the spectra was not seen, which was most likely because the "switch" from "dark" to "light" is extremely fast and we missed it, or that during the experimental set-up the "dark" semicarbazone was exposed to light and "switched".

We hypothesized that physical change accompanying the color "switch" was due to a rotation about the imine (C=N) bond of the semicarbazone group (Figure 1.5) and is the reason for the exhibited photochromicity of these semicarbazones **(4)**. This is based off the Hantzsch-Werner hypothesis,[21] which states that physically isomeric imines exist, and

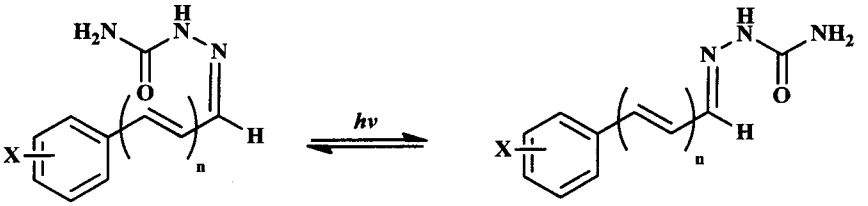


Figure 1.5: Hypothetical structure of the "light" and "dark" semicarbazones.

since the semicarbazone group of our compounds **(4)** contain an imine they should exist as stereoisomeric semicarbazones **(4)**.

Given this structural change, using ^{13}C NMR we might be able to distinguish between the "light" and "dark" species, and be able to assign which isomer (*cis* or *trans*) the "light" and "dark" species. Unfortunately none of the obtained NMR's for the "dark" versions were significantly different from the "light" versions. As with the UV-Vis study, it is possible that the "dark" species "switched" too quickly in solution, during the process of obtaining the spectra. nOe/NOESY experiments might be better to distinguish the "light" and "dark" forms, as it determines which groups are spatially "close" in the molecule.

The photochromicity of these semicarbazones **(4)** have been reported, herein, as well as their absorbance spectra, using UV-Vis. It was of interest to compare our experimental absorbance data to calculated values. We previously discussed the use of ΔE to find the absorption wavelength of a compound using Equation 1.2.

$$\lambda = hc/\Delta E \qquad (1.2)$$

Spartan v'10 can be used to perform molecular orbital (MO) calculations to theoretically determine the change in energy (ΔE) between the LUMO and HOMO, which can then be plugged into Equation 1.2 to obtain a theoretical wavelength of

absorbance. If the values agree, theoretical (MO data) values, could be used to evaluate the effects of altering the conjugation length, as well as substituent position, type, and number prior to making the compound. Density-Functional Theorem (DFT) energy calculations are a type of fast and rough MO empirical calculation that provides reasonable data.

First though, a conformer distribution was performed on the semicarbazone to determine the lowest energy conformers. Then DFT energy calculations using a 6-31G* basis set were performed on the lowest energy semicarbazone conformer, to determine the energy of the HOMO-LUMO gap when various substituents were added and the conjugated system was extended.

Looking at the data (Table 1.8), the one trend that stands out is that the increase of conjugation correlates with a decrease in the HOMO-LUMO gap (2-OMe with n = 1 equals 393.60 kJ/mol while 2-OMe with n = 2 equals 364.80 kJ/mol). But looking at trends for the substituents, no trends pertaining to the position can be determined; *i.e.* all 3 isomers of the monomethoxy compound show the same values ($\Delta E_{LUMO-HOMO}$ = 393.60 kJ/mol). This tells us that the $\Delta E_{LUMO-HOMO}$ Spartan calculations at this level can't be used to predict differences in location of substituents.

Looking at the number of substituents we see that with an increase in substituents comes a decrease in the molecules ground state energy, but no trend can be seen in the HOMO-LUMO gap. For instance, the gap decreases when going from 2-OMe (393.60 kJ/mol) to 2,4-diOMe (374.40 kJ/mol), but the increases in going to 2,4,6-triOMe (432.00 kJ/mol).

Table 1.8: Change in HOMO-LUMO energy ($\Delta E_{LUMO-HOMO}$) of semicarbazones **(4)**.

	$\Delta E_{LUMO-HOMO}$ (kJ/mol)		
X	**n =1**	**n = 2**	**n = 3**
H	412.8	364.8	326.4
4-OMe	393.6	393.6	326.4
2-OMe	393.6	364.8	
3-OMe	393.6		
2,5-diOMe	393.6		
3,5-diOMe	403.2		
2,4-diOMe	374.4		
2,4,6-triOMe	432.0		
2,4,5-triOMe	374.4		
2,3,4-triOMe	403.2		
3,4,5-triOMe	403.2	355.2	
4-OH	393.6		
4-OH, 3-OMe	384.0		
3-OH, 4-OMe	384	355.2	
2-NO_2	384.0		
β-phenyl	412.8		

One can speculate that a slight difference would be seen between semicarbazones **(4)** containing OH and OMe groups due to their electron-donating nature. However, *p*-OMe and *p*-OH display the same HOMO-LUMO gap (393.60 kJ/mol), showing that Spartan doesn't differentiate overall between the two groups. This is also true if both are present on the phenyl ring, as 3-OMe/4-OH and 3-OH/4-OMe have the same energy gap.

From the HOMO-LUMO gap, it is possible to calculate a theoretical wavelength of absorbance. It can be seen in Table 1.9 that the calculated values are all different than the experimental, for example with cinnamaldehyde semicarbazone (λ_{calc} = 289.739 nm and λ_{exp} = 308.500 nm) and its monomethoxy derivatives; 4-OMe (λ_{calc} = 303.929 nm and λ_{exp} = 321.500 nm), 2-OMe (λ_{calc} = 303.929 nm and λ_{exp} = 297.500 nm). The difference between the experimental and calculated values differ from 6.4 to 18.8 nm, so no

significant trend can be found, but recall that also Spartan gave the same calculated values for all three of the methoxy isomers, showing it doesn't differentiate between EDG substituents at this level. Another possible reason for the large discrepancy is that the calculated values were determined in vacuum with no environmental factors affecting the molecules. The experimental values however were not done in vacuum and thus can have solvent and intermolecular effects associated with them.

Table 1.9: Calculated (λ_{calc}) and measured (λ_{exp}) absorption wavelengths for the "light" versions of semicarbazones **(4)** using Spartan v'10.

	λ_{calc} (nm)			λ_{exp} (nm)		
X	**n = 1**	**n = 2**	**n = 3**	**n = 1**	**n = 2**	**n = 3**
H	289.793	327.924	366.503	308.500		
4-OMe	303.929	303.929	366.503	321.500	341.500	
2-OMe	303.929	327.924		297.500	345.500	
3-OMe	303.929					
2,5-diOMe	303.929			299.000		
3,5-diOMe	296.693					
2,4-diOMe	319.515					
2,4,6-triOMe	276.913			330.500		
2,4,5-triOMe	319.515			302.000		
2,3,4-triOMe	296.693			321.000		
3,4,5-triOMe	296.693	336.786		320.500	344.000	
4-OH	303.929					
4-OH, 3-OMe	311.527			325.000		
3-OH, 4-OMe	311.527	336.786		319.000		
2-NO_2	311.527			292.500		
β-phenyl	289.793			315.000		

It was previously mentioned that the p-orbitals in conjugated semicarbazone systems overlap best when the molecule is planar in configuration, thus the photochromicity could also be affected if the molecule becomes significantly nonplanar, due to the substitutions

on the phenyl ring. Measuring torsional angles of the lowest energy conformers from our Spartan calculations could give us a clue as to which molecules deviate significantly from planarity, and thus show any correlation between torsional angles and photochromicity (Table 1.10).

The most drastic changes in angles stem from the syn- and anti- clinal configurations along the chain in the molecule. These drastic differences may possibly mean that, even in the stable anti-clinal configuration, the conjugated units of the semicarbazones are still slightly nonplanar. From Table 1.10 we see that the ABCD angle measuring the planarity between the phenyl ring and the first double bond ranges from 127.00° to 150.00° with some slight variation (*i.e.* 2,4-diOMe = 174.23°); this confirms that the semicarbazones stray significantly from planarity (180°). Amongst the OMe derivatives we would expect the *ortho*-methoxy derivatives to be the least planar because of steric hindrance between the group and the chain of the molecule, forcing it out of planarity. This is exactly what is shown as the 2,4,6-trimethoxy derivatives show a range of 113° to 143° for the ABCD angle.

Looking at the EFGH angle measuring the planarity between the C=N (imine) and the NH-C (amide) bonds, this value ranges from 166° to 179° and is fairly planar. Finally, the FGHI angle measuring the planarity between the N-N and the C-NH_2 (amide) bonds, is around 4.00° with only a few variations (*i.e.* 2,4-diOMe = 44.93°) suggesting that in general the compounds are syn-clinal around the FGHI bond and close to planarity.

For the n = 1 semicarbazones which have more than one significant lowest energy conformation, the first conformer has anti-clinal geometry around the alkene and imine units (CDEF 179.00° - 179.82°), while in the second conformer these units are syn-clinal

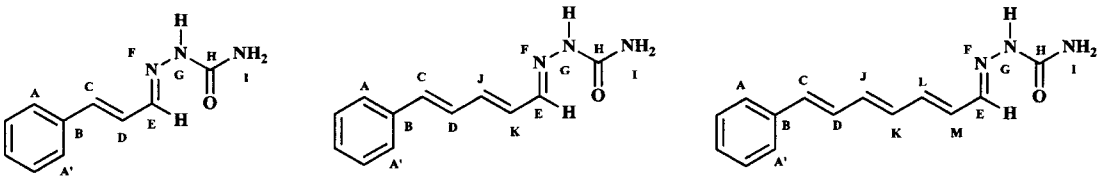


Table 1.10: Calculated Spartan torsional angles of semicarbazones **(4)**.

X	n	Conf	ABCD	CDEF* JKEF+ LMEF#	CDJK**	JKLM	EFGH	FGHI
H	1	1	144.7	179.66			179.54	4.35
		2	142.75	9.31			179.43	4.28
	2	1	141.68	179.75	179.56		179.70	4.41
		2	142.54	179.68	45.35		179.57	4.37
		3	141.11	17.26	179.07		179.08	4.02
	3	1	141.76	179.77	179.48	179.99	179.68	4.39
		2	141.85	179.99	179.76	45.65	179.76	4.49
		3	178.99	177.55	1.19	178.35	171.17	44.87
		4	142.96	179.78	46.49	179.78	179.69	4.4
4-OMe	1	1	145.49	179.83			179.79	4.46
		3	141.75	14.58			179.84	4.81
	2	1	141.82	179.79	179.48		179.65	4.39
		3	142.49	179.92	45.22		179.74	4.45
	3	1	141.93	179.86	179.45	179.94	179.67	4.35
		3	142.02	179.96	179.76	45.63	179.77	4.48
		5	143.21	179.80	46.53	179.7	179.70	4.4
2-OMe	1	1	141.78	179.82			179.45	4.45
		3	144.18	14.61			179.65	4.75
	2	1	141.29	179.65	179.42		179.61	4.38
		3	140.62	179.62	44.46		179.56	4.41
2-NO_2	1	1	130.16	179.71			168.79	44.03
		4	113.82	14.97			179.16	4.09
β-phenyl	1	1	128.97	176.79			179.36	4.27
		4	124.95	37.06			172.00	4.42
3,4,5-triOMe	1	1	143.32	179.37			179.64	4.43
	2	1	136.29	179.88	179.45		179.70	4.3
		8	140.9	179.86	45.2		179.78	4.39

2,4,6-triOMe	1	1	113.12	178.42		166.00	21.6
		5	127.12	13.02		179.05	4.77
2,4,5-triOMe	1	1	142.16	179.69		179.49	4.57
2,3,4-triOMe	1	1	142.92	179.58		179.73	4.38
2,5-diOMe	1	1	142.48	179.63		179.53	4.47
3,5-diOMe	1	1	144.16	179.46		179.81	4.42
		5	144.19	16.98		179.22	4
2,4-diOMe	1	1	174.23	176.62		169.39	44.93
		4	142.52	179.16		179.63	4.41
		5	137.14	24.85		179.34	4.49
3-OMe, 4-OH	1	1	142.64	179.57		179.93	4.41
3-OH, 4-OMe	1	1	145.49	179.48		179.71	4.53
	2	1	143.35	179.71	179.51	179.67	4.39
		2	143.13	45.18	179.73	179.62	4.45
		7	144.37	179.55	14.64	179.08	3.96
4-OH	1	1	144.32	179.82		179.81	4.48
		3	143.61	16.81		179.03	3.92

Conf. = conformer, where lower number is lower energy conformer.
* for n = 1
** for n > 1
+ for n = 2
# for n = 3

(9.31° – 16.98°). However the chain remains close to planar in either conformation; except for β-phenyl semicarbazone, which is much planar in the syn-clinal (37.06°) due to the sterics of the second β-phenyl group.

Likewise, a similar trend can be seen for all of the n = 2 semicarbazones; though they show syn- and anti-clinal conformations between the two alkene groups. The angle for CDJK (measuring the planarity between the first double bond and the second double bond) ranges from 179.45° - 179.56° for the first conformer and between 45.20° – 45.35° for the second conformer. Looking at the n = 2 semicarbazones which have 3

conformations, the highest energy conformers (the 3rd conformer) is anti-clinal with respect to the C-C double bond but syn-clinal between the second double bond and the imine (17.26°).

The data (Table 1.10), suggests then that the substituents do not affect much the planarity of the semicarbazones, and should not affect the absorption or photochromicity due to geometrical (steric) considerations. While Spartan tells us that these semicarbazones exist in more than one conformer, in most cases this is not a major concern, as planarity is maintained in all of the conformers. To date, no correlations from the prediction of Spartan data allow for whether a semicarbazone will be photochromic or not. Spartan predicts the conformation of the compound in the gas phase, and crystal structures would be needed to compare or contrast the Spartan data.

Up to this point we have been focusing mostly on the manipulating the photochromic system so that the compound absorbs more in the visible region, which could increase the photochromicity. However it is important to note that photochromicity is not solely related to the absorbance of the compound, other properties may play an essential role, *i.e.* the crystal packing of the compound is very important.

The crystal structure of the semicarbazone **(4),** identified as the compound with the most dramatic photochromic change (JMS 18-9, 2,4,6-trimethoxycinnamaldehyde semicarbazone), was solved and refined (Figure 1.6) using SHELXS-97 and SHELXL-97 (Sheldrick, 1997)[22,23] to give a model with R2 = 0.0547 (Table A.3).

Crystal of semicarbazone **(4)** (Figure 1.6) were grown via slow evaporation of a 95% EtOH solution. Because the crystal structure revealed residual solvent molecules included in the crystal lattice, a second batch of crystals were grown using CH_3CN. Crystals from

this growth experiments, and subsequent data collection at -173 °C, also indicated 2,4,6-trimethoxycinnamalde-

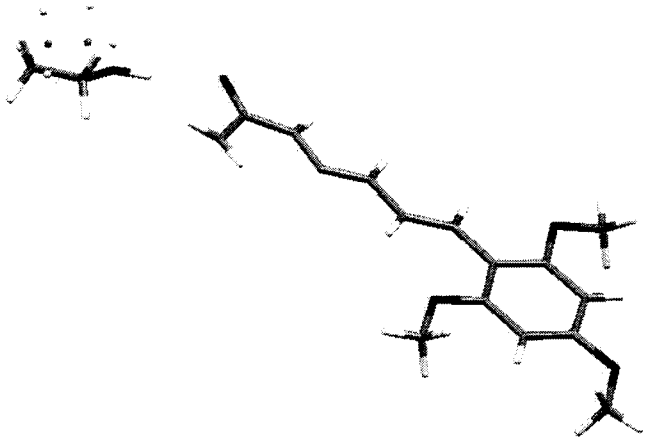


Figure 1.6: Crystal structure of 2,4,6-trimethoxycinnamaldehyde (JMS 18-9), grown from 95% EtOH

hyde semicarbazone (Figure 1.7). The crystal structure was solved using the SHELXS-97 and SHELXL-97 (Sheldrick, 1997)[22,23] producing a R2 value of 0.0318 (Table A.4).

By comparing the two structures, we see that they are both anti-clinal in configuration along the chain but syn-clinal at the terminus, and are equivalent in terms of planarity. The first structure was somewhat planar, showing a 13° bend between the carbonyl (C=O) and the primary amine (NH_2) of the semicarbazone, while the second crystal structure shows complete planarity from the ring to the imine group, only straying from planarity by a slight 6° bend from the carbonyl and the primary amine. This slight bend out of planarity is due to the hydrogen bonding of one molecule with another molecule of 2,4,6-trimethoxycinnamaldehyde semicarbazone unit.

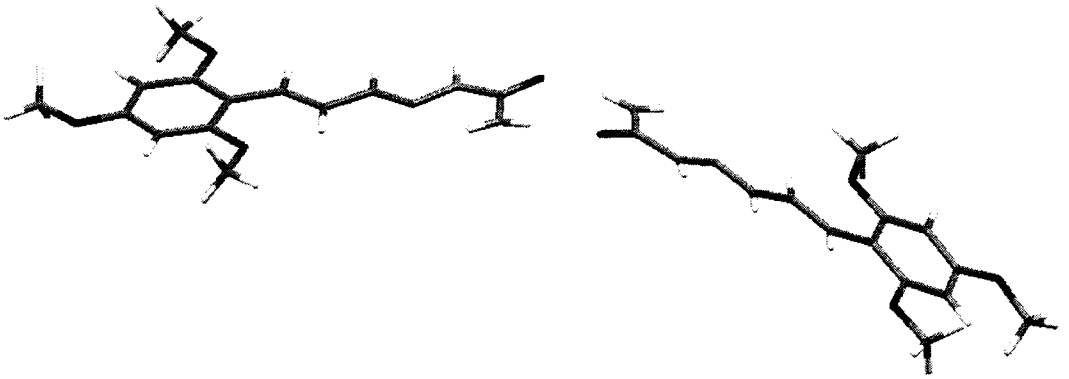


Figure 1.7: Crystal structure of 2,4,6-trimethoxycinnamaldehyde (JMS 18-9), grown from CH_3CN.

This shows that in the solid state the semicarbazones **(4)** prefer to be in the anti-clinal configuration and the substituents in 2,4,6-trimethoxy-cinnamaldehyde semicarbazone don't cause steric hindrance that would distort the molecule out of planarity. In fact, even though the crystal structure is tightly packed, there possibly is enough room to allow for rotation of the imine bond, allowing our hypothesis that the rotation of the imine is the reason for the exhibited photochromicity of these semicarbazones **(4)**.

Conclusions:

The synthesis (Scheme 1.1) of 24 semicarbazones **(4)** has been completed in respectable cumulative yields via a 3 step synthesis; a 42.4% yield for to n = 1 semicarbazones, a 61.9% yield for n = 2, and a 33.5% yield for n = 3 semicarbazones. The lower yields for the n = 1 and n = 3 stem from the purity of the Wittig reagent and difficulties in purifying the extended semicarbazones. The preparation of the Wittig itself never gave a yield higher than 51.0%, even though the report literature is 67.0%.[16]

A process that is faster and more economical than SiO_2 gel purification for removing $Ph_3P=O$ from the acetals was implemented, although it won't remove any unreacted starting material aldehyde.[19]

All semicarbazones **(4)** displayed photochromicity with the exceptions of 2-nitrocinnamaldehyde and 3-methoxycinnamaldehyde semicarbazones. We believe that the rotation of the C=N bond is the reason for the exhibited photochromicity of these semicarbazones **(4)**, but efforts to observe this or even differences between light and dark versions by ^{13}C NMR were unsuccessful. Classification of the extent of photochromicity was done via a standard color system [the Behr (paint) color system (Table 1.4)]. Our data was similar to what Heilbron's *et al.*[12] reported for their semicarbazones except it was the 2-methoxycinnamaldehyde semicarbazone (n = 1) that showed a subtle, unquantifiable change, while 4-methoxycinnamaldehyde semicarbazone (n = 1) showed a photochromic shift of 1.

The extent or degree of photochromic color change between the "light" and "dark" versions of a given semicarbazone 1) increased with increasing extension of the conjugated system; 2) increased with the addition of OMe groups, though the number of EDGs doesn't play as significant role as their position and; 3) OH groups promote photochromicity better than OMe groups separately and/or when paired together.

Looking between the colors of the different semicarbazone, extending the conjugation produced a difference in color from pale to more intense (brighter) colors. Also the addition of one or three OMe group gives more dramatically different colored semicarbazones, while the addition of a second OMe group does not give much of a difference, compared to the others. Finally, OMe and OH groups at the *para* position

produce the greatest difference in hue though the *para*-OH produces a far greater difference in colors between different compounds.

The UV-Vis absorbance spectrum of the semicarbazones was obtained, and it was found that the semicarbazone units absorb light between 232.0 nm and 257.0 nm, with the red-shift due to the substituents of the phenyl ring and extending the conjugated system. However some of the semicarbazones **(4)** had their absorbance in this region observed by other peaks. The phenyl ring absorption around ~280 nm also depended on the number, type, and position of the substituents, and the extent of the conjugated system.

While the type, number, and position of the substituents each play a significant role in the location of the λ_{max} but neither variable is more critical than the next. However an extension of the semicarbazone **(4)** gave a significant increase in the λ_{max}.

The UV-Vis spectra showed significant differences between the "light" and "dark" versions, suggesting that these compounds, along with being photochromic in the solid-state, are also photochromic in solution. However we were unable to observe the "dark" to the "light" "switch" with 4-methoxycinnamaldehyde semicarbazone (JMS 18-2) using UV-Vis absorbance spectroscopy.

Spartan v'10 was used to theoretically determine the $\Delta E_{LUMO-HOMO}$, and this was compared to the experimental (UV-Vis data). An increase of conjugation correlated to a decrease in the HOMO-LUMO gap, which is as expected because conjugation increases the wavelength due to a decrease in HOMO-LUMO gap. While no trends in the ΔE pertaining to the position was determined. An increase in the number of substituents, consistently gave a decrease in the compound total energy, but no trend can be seen in the

HOMO-LUMO gap. No trend can be found for the type of substituents. Additionally Spartan didn't differentiate between the two different EDGs (OMe and OH). The calculated values were all significantly higher than the experimental values, except when n = 1. The Spartan calculations at this level were not that illuminating, and could not be used to help determine photochromicity.

The Spartan calculations were also used to evaluate if the molecules were planar in configuration as this allows for best overlap of the p-orbitals. All of the semicarbazones were bent slightly out of planarity ~179.00° throughout the conjugated system, ~4.00° for the semicarbazone group, and ~141.00° for the phenyl ring to the first double bond of the conjugated system, but again no correlations between the planarity/geometry and actual photochromicity can be observed.

A crystal structure was obtained of 2,4,6-trimethoxycinnamaldehyde semicarbazone showed that it was almost completely planar, yet showed the inclusion of EtOH solvent molecules. A second crystal structure shows complete planarity from the ring to the conjugated system and only strayed from planarity by a slight bend at the semicarbazone subunit, due to hydrogen bonding to a second semicarbazone unit.

This tells us that in the solid state the semicarbazones **(4)** do prefer to be in the anti-clinal configuration and the substituents don't push the molecule out of planarity due to sterics. In fact, even though the crystal structure is tightly packed it seems that there is enough room to allow for rotation of the imine bond.

From all this information, we can conclude that these semicarbazones **(4)** are photochromic, expect for 2-nitrocinnamaldehyde and 3-methoxycinnamaldehyde semicarbazones. Also, it is clear from the crystal structure that there is enough room to

allow for rotation of the imine bond, yet more information must be obtained to prove our rotation hypothesis. This can be done by the production of more crystal structure of the "light" and if possible "dark" species. Also, if a crystal structure of either 2-nitrocinnamaldehyde or 3-methoxycinnamaldehyde semicarbazones could be obtained and it showed enough or not enough room to allow or not allow for rotation, this could prove or disprove the rotation hypothesis.

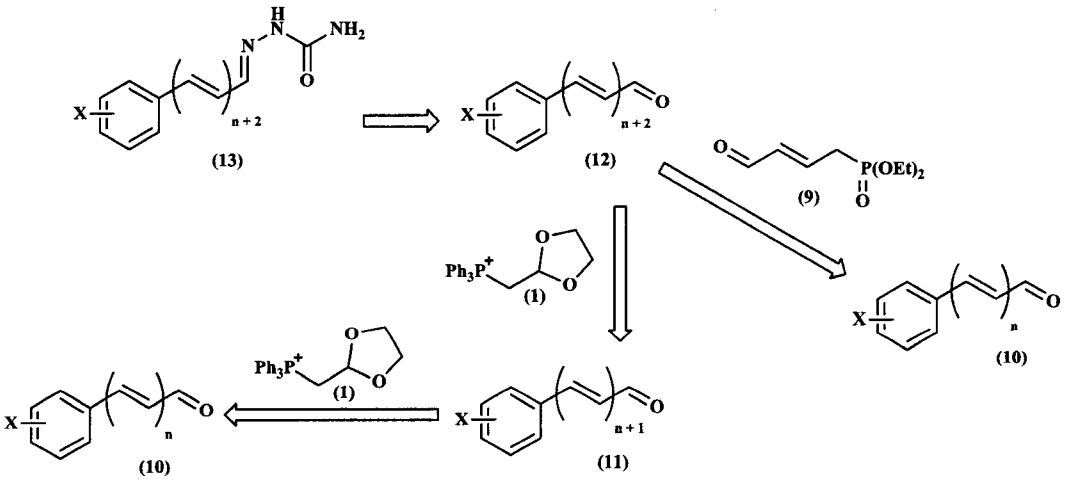
More time needs to be placed into analyzing the UV-Vis and Spartan data, as there is probably still more key information that can be gathered from here. More "light" vs "dark" UV-Vis and NMR analysis should be done, along with using UV-Vis to determine when the semicarbazones "switch". Once this is determined, time needs to be spent on trying to isolate the "light" and "dark" versions. Finally more conjugated systems (n = 3 and higher) need to be created to continue on in the determination of whether extension increases photochromicity.

CHAPTER 2

SYNTHESIS OF EXTENDED CINNAMALDEHYDE SEMICARBAZONES FROM BUT-2-ENE-1, 4-DIOL

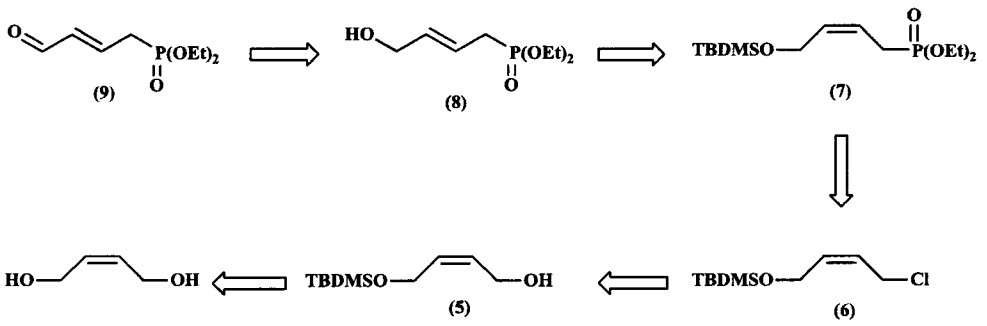
Introduction:

Our first synthetic approach, as seen in Chapter 1, allows for the production of extended cinnamaldehyde semicarbazones in three facile steps, but it still has limitations. One of the major limitations is the addition of only one double bond to the aldehyde at a time, thus requiring a sequential, longer protocol when n > 1 (Path A, Scheme 2.1). Our second approach (Path B, Scheme 2.1), however, allows for the addition of two double bonds at a time. This approach envisions the creation of extended cinnamaldehyde semicarbazones (**13**, n = 2 and n = 3) directly from a benzaldehyde (n = 1) or cinnamaldehyde (n = 2) respectively, using a phosphoryl butenal **(9),** in only two steps.



Scheme 2.1: Retrosynthetic scheme for the production of extended cinnamaldehyde **(12)** from phosphoryl butenal **(9)** vs phosphonium bromide **(9)**.

The synthesis (Scheme 2.2) of the phosphoryl butenal **(9)** has already been reported by M. Sun *et al.*,[24] and used as a building block for synthesis of phospholipids.



Scheme 2.2: Retrosynthetic scheme for the production of phosphoryl butenal **(9)** from but-2-ene-1, 4-diol.

The phosphoryl butenal **(9)** can be obtained from the oxidation of alcohol **(8)**, which can be created after hydrolytic removal of the silane protecting group in the phosphonate **(7)**. The phosphoryl TBDMS ether **(7)** can be formed from the Arbuzov reaction of chloride **(6)**, which is simply a chlorinated version of the monosilyl ether **(5)**. The monosilyl ether **(5)** can be formed after a mono protection of but-2-ene-1,4-diol using *tert*-butyldimethylsilyl chloride (TBDMSCl).

Results and Discussion:

The first step (Scheme 2.3) in the preparation of the phosphoryl butenal **(9)** involves the monoprotection of *cis*-but-2-ene-1,4-diol with TBDMSCl to give the monosilyl ether **(5)**. This reaction has produced average yields of 74.8% using DMAP and imidazole. The ^{1}H NMR spectrum of silane **(5)** shows peaks at 0.0739 ppm (6H, s), and 0.894 ppm (9H, s) corresponding to the addition of the silyl group. It was clear that only the monosilyl

Scheme 2.3: Formation of monosilyl ether **(5)**.

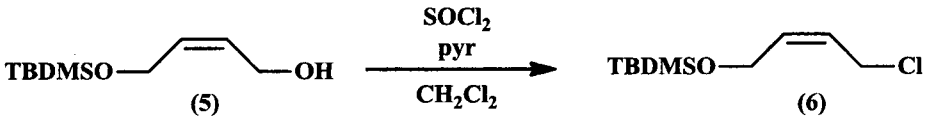
product was formed and not the disilyated, by the integration compared to the doublet at 4.19 (2H, d, J = 5.77 Hz). During the work-up, the diol is washed away due to its high water solubility meaning the monosilyl ether **(5)** product didn't need purification. The ^{13}C NMR spectrum confirmed there was no remaining starting material in the sample.

Sun *et al.* brominated the alcohol **(8)** using *bis*(1,2-diphenylphosphino)ethane (DIPHOS) and tetrabromomethane, while our approach used a chlorination instead. This is because the chlorination uses thionyl chloride ($SOCl_2$), which is less expensive and more practical than the bromination used in Sun's synthesis.

Chlorination of the monosilyl ether produced varying yields (Table 2.1). This is most likely due to the chlorinated monosilyl ether **(6)** having a low boiling point and upon removal of the solvent under reduced pressure some of the product **(6)** was also removed. The chlorinated ether **(6)** has a lower boiling point than the solvent (pyridine), thus it should come off first or at the same time as pyridine. If the reaction was done using a solvent with a lower boiling point, *i.e.* CH_2Cl_2, the yield could be increased because the CH_2Cl_2 could be removed with less heat and so no loss of silane. However, to avoid this problem the solvent was removed under reduced pressure with no heat, which drastically increased the yield.

Vacuum distillation was first used to purify the chlorinated monosilyl ether **(6)** because we were under the hypothesis that due to its liquid nature this would be the easiest way to remove the leftover pyridine. Unfortunately the vacuum distillation did not

Table 2.1: Percent yields for chlorinated monosilyl ether **(6)** upon removal of solvent with and without heat.



Chlorinated Monosilyl ether	Percent yield	Conditions
Trial 1, JMS 3-1	19.0%	w/ heat
Trial 2, JMS 3-2	32.7%	w/o heat
Trial 3, JMS 3-3	53.0%	w/o heat
Trial 4, JMS 3-4	12.9%	w/o heat
Trial 5, JMS 3-5	61.2%	w/o heat
Trial 6, JMS 3-6	47.6%	w/o heat
Trial 7, JMS 3-7	39.2%	w/o heat
Trial 8, JMS 3-8	43.6%	w/o heat
Trial 9, JMS 3-9	32.4%	w/o heat

afford product, and instead the crude product only decomposed. Silca gel chromatography was the second purification method chosen, and did successfully remove the pyridine to afford the pure chlorinated monosilyl ether **(6)**. It can be questioned as to why the pyridine is needed in the reaction and the reaction couldn't be done without pyridine. The pyridine acts as a base and thus without the removal of the hydrogen from the hydroxyl group this reaction could not fully occur.

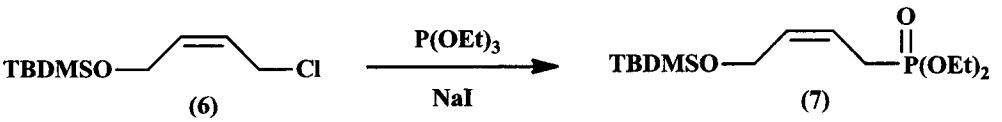
After purification using SiO_2 gel chromatography the ^1H NMR spectrum was obtained for the monosilyl ether **(6)**. The ^1H NMR for pure **(6)** shows an downfield shift

of the vinylic signal from 4.17 ppm (2H, d, H_a) to 4.24 ppm (2H, d, H_f) corresponding to the substitution of the chlorine atom for the alcohol group.

The phosphonate TBDMS ether **(7)** was created *via* an Arbuzov reaction as reported by Helquist *et al.*,[25] using chlorinated monosilyl ether JMS 3 **(6)** with triethyl phosphite ($P(OEt_3)$) and sodium iodide (NaI) in toluene (Table 2.2). The NaI promotes the Finkelstein reaction, which involves the *in situ* conversion of an alkyl chloride or an alkyl bromide to an alkyl iodide. Sun's synthesis didn't require the addition of NaI because their synthesis used an alkyl bromide, which is more reactive than the alkyl chloride used here.[24]

The ^1H NMR spectra of phosphonate TBDMS ether JMS 4 **(7)** showed that the doublet at 4.27 ppm (2H, d, J = 5.77, H_f), was now a doublet of doublets at 2.64 ppm (2H, dd, J = 8.03 Hz, J_{HP} = 22.3 Hz, H_f) , as well as the appearance of peaks for the ethoxy groups at 1.34 ppm (CH_3) and 4.13 ppm (CH_2).

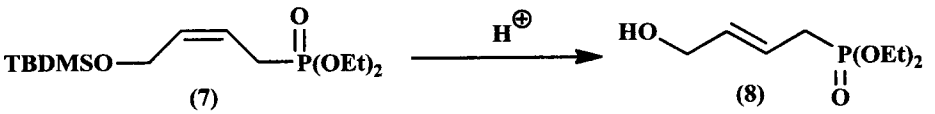
Table 2.2: Percent yields for the production of phosphonate TBDMS ether **(7)**.



phosphonate TBDMS ether	Percent yield
Trial 1, JMS 4-1	69.6%
Trial 2, JMS 4-2	73.0%
Trail 3, JMS 4-3	68.2%

Hydrolytic removal of the TBDMS group from ether **(7)** was performed to afford the alcohol **(8)** (Table 2.3). The ^{1}H NMR spectrum showed a loss of the singlets at 0.08 ppm and 0.91 ppm corresponding to the TBDMS protecting groups, along with an upfield shift of the CH_2 group from 4.25 ppm to 4.03 ppm, corresponding to liberating the ether **(7)** to give the alcohol **(8)**. The hydrolysis of ether **(7)** also caused isomerization of the olefin which is evident by the formation of a second doublet of doublets at ~1.66 ppm (2H, dd, J = 7.53 Hz, J = 18.1 Hz, H_c) giving a *cis* : *trans* ratio of 17 : 83.

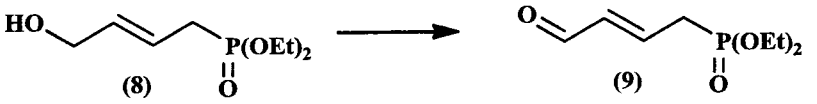
Table 2.3: Percent yields for the production of alcohol **(8)**.



alcohol	Percent yield
Trail 1, JMS 13-1	s. mat
Trail 2, JMS 13-2	87.3%
Trial 3, JMS 13-3	s. mat

The crude alcohol **(8)** was subjected to oxidization using pyridinium dichromate (PDC) (Scheme 2.4) but, unfortunately, no product was obtained; only starting material was recovered. The ^{1}H NMR should have shown a loss of the singlet at 4.03 ppm corresponding to the alcohol **(8)** and the addition of a doublet at ~9.68 ppm corresponding to the aldehyde **(9)**.

Unpurified alcohol **(8)** was used during the oxidation process, and it is hypothesized that the impurities led to undesired side reactions, so the starting material alcohol **(8)**,



Scheme 2.4: Oxidation of alcohol (8) to phosphoryl aldehyde **(9)**.

must be pure. Another possible problem is the amount of alcohol **(8)** this reaction was attempted on, as only 0.222 g was used in the reaction.

Conclusion:

The monoprotection of *cis*-but-2-ene-1,4-diol with *tert*-butyldimethylsilyl chloride (TBDMSCl) gave the monosilyl ether **(5)** in exceptional yields (59.9%, 74.9%, and 89.7%) and without any difficulties. The chlorination step was more troublesome, as the monosilyl chloride **(6)** has a low boiling point and some was lost along with the solvent being removed under reduced pressure; using no heat when roto-vapping diminished this problem (Table 2.2). Phosphonate TBDMS ether **(7)** was afforded in decent yields (Table 2.3) after an Arbuzov reaction on monosilyl ether JMS 3 **(6)** in toluene, and the TBDMS group was removed to afford the alcohol **(8)** (Table 2.4). The synthesis to the aldehyde **(9)** is far more troublesome than it should be due to both the low boiling point of chlorinated monosilyl ether **(6)** and undesired side reactions in the oxidation step stemming from impure starting materials. The overall yield (39%) for this synthesis, using the chlorination of the monosilyl ether **(5)**, is comparable to the yield (49.6%) to that reported by Sun *et al.*[24] Thus if pure alcohol **(8)** was used in the oxidation step to form aldehyde **(9)** then it may be worth using chlorine over bromine.

CHAPTER 3

SYNTHESIS OF ISOMALABARICANES FROM 1,3-BISPHOSPHONO-ACETONE

Introduction:

The second aspect of this research involves the synthesis of a class of natural products called isomalabaricanes. Isomalabaricanes are a rare group of ~ 33 triterpenoids that contain a tricyclic [6.6.5] ring system and are found in various genera of marine sponges.[26] Natural tricyclic isomalabaricanes differ in the substituents located off both the "A"-ring and the side chain as well as the length of the side chain; *i.e.* the globostellatic acids contain a NaO_2C group off the "A"-ring and a hydroxy end group while the jaspiferals contain an aldehyde group both off the "A"-ring and as an end group (Figure 3.1).[27a,27b] Isomalabaricanes were first reported by B. N. Ravi *et al.*[28] in 1981, when stellettin B, and the methyl esters of stellettins F, H, and I were isolated from the genus *Jaspis stellifera*. In 1982, B. N. Ravi *et al.* again isolated four new isomalabaricanes from *Jaspis stellifera,* although this time the compounds contained only long conjugated side chains at the C-13 position.[29] J. Clardy *et al.* in 1982 isolated and elucidated, using single x-ray crystallography, the crystal structure of stellettin A.[30] Stellettins C, D, E, and F were reported in 1994 by J. Y. Su *et al.*[31] and again in 1996 by T. C. McKee *et al.*[32] respectively.

The stellettins A/B, C/D, and E/F occur as pairs of inseparable geometrical isomers at the C-13 olefin. These were tested as isomeric pairs due to the rapid isomerization upon exposure of the pure compounds to light. It was initially reported that isomalabaricanes significantly inhibit the growth of L1210 and KB cancer cells.[33] McKee

et al.[34] reported that stellettins A/B, C/D, and E/F were active in the National Cancer Institute's (NCI) 60-cell line anticancer screens. Stellettin C/D produced a mean 50% growth inhibition (GI_{50}) of 0.09 μM, while stellettins A/B and E/F gave GC_{50} values of 0.28 μM and 0.98 μM, respectively. Stellettin C/D showed great sensitivity and selectivity against leukemia and tumors of the brain, *i.e.* central nervous system.[33] These medicinally relevant properties make the stellettins possible drug candidates, but to fully explore their potential large quantities must be used.

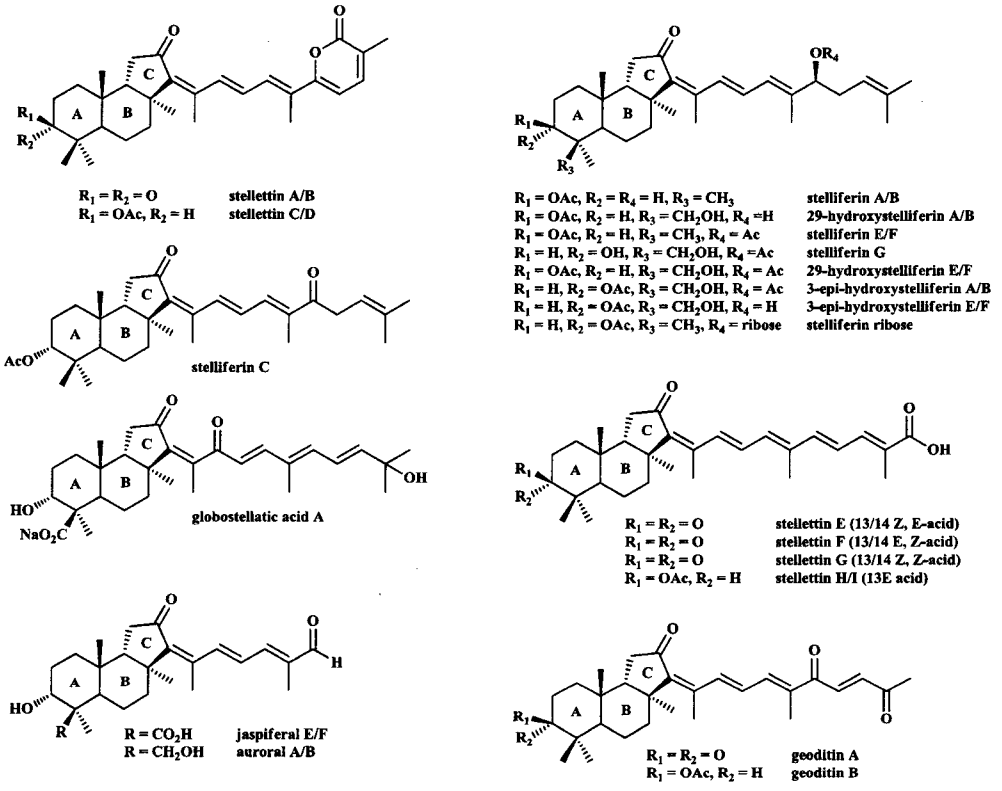
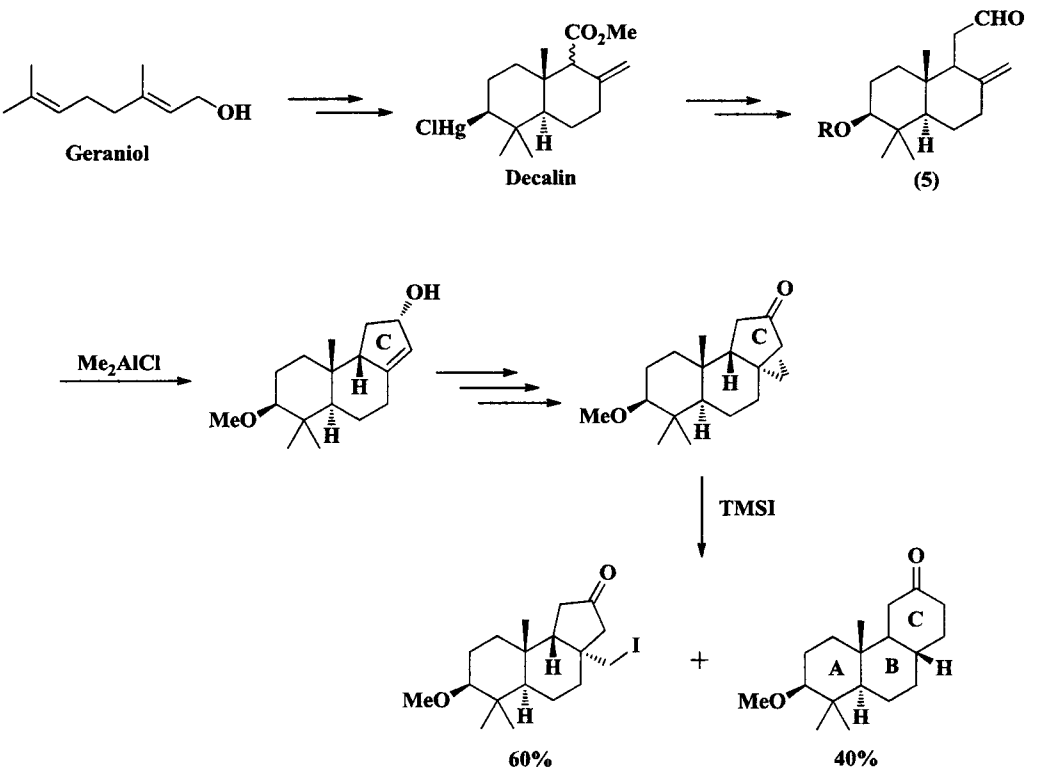


Figure 3.1: Structures of various isomalabaricanes.

Isolation from the natural source only affords miniscule quantities of stellettins, *i.e.* McKee used a lengthy isolation to obtain only 24.2 mg of stellettins C/D from 1 kg of sponges (0.00242% yield).[32] In order to obtain enough material for biological testing,

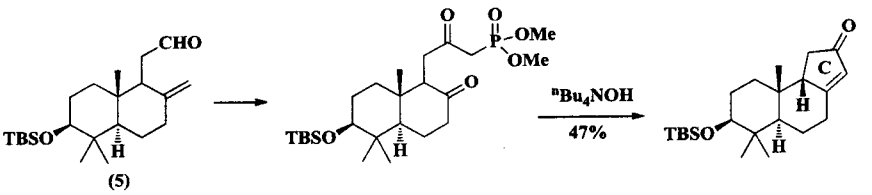
many organisms would have to be harvested which is neither cost nor time effective; and this could lead to the organism's extinction. A synthetic approach will lead to reproducible and superior amounts of stellettins, while also allowing for modifications to the structure leading to other possible drug candidates. To date, there are two groups which have used different routes to synthesize the tricyclic ring system of the isomalabaricanes.

The first synthesis of the tricyclic ring system was reported by D. Heissler *et al.*[35] involving the creation of an enantiomerically pure decalin which comprises both the "A" and "B"-rings of the tricyclic from commercially available geraniol by Weiler's method.[36] The key cyclization to form the "C"-ring was catalyzed by a chlorodimethylaluminium cyclization of the aldehyde in a 66% yield forming the tricyclic (Scheme 3.1). Using Furukawa's modification of the Simmons-Smith cyclopropanation it is possible to add functionality at the C-13 position. Thus the C-ring underwent a cyclopropanation, and oxidization of the alcohol using a ruthenium species to give the ketone. Opening the cyclopropyl ring with TMSI gave a 6 : 4 mixture of the desired cyclopentyl C-ring compound and the undesired cyclohexyl C-ring compound due to poor regioselectivity. Upon formation of the C-ring the next step involves the regioselective addition of a side chain at the C-13 position, but Heissler was unable to proceed any further due to the unanticipated difficulty in opening the cyclopropane. This is the main limitation associated with Heissler's synthesis, the tricyclic must contain C-13 functionality or at least allow for easy addition of this functionality.



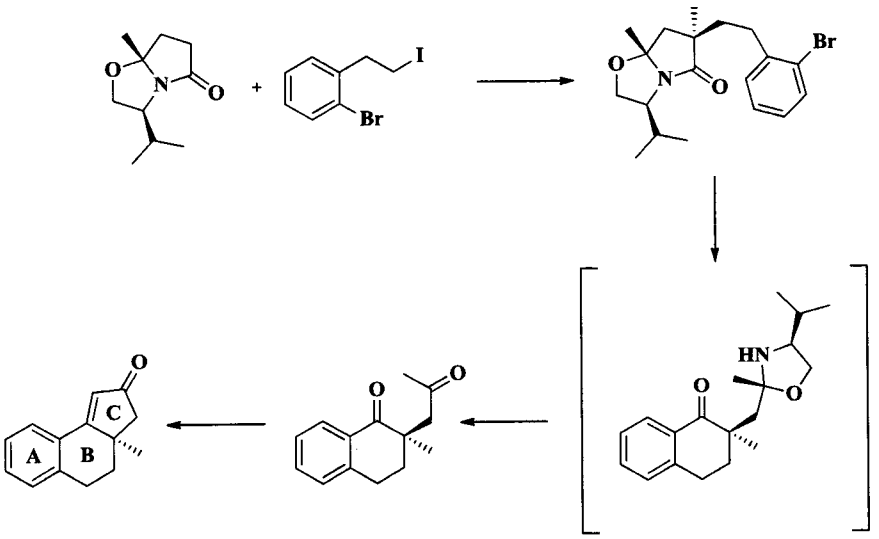
Scheme 3.1: D. Heissler *et al.*[35] synthetic attempt towards the tricyclic ring system of the stellettins.

Heissler reported (Scheme 3.2) the HWE precursor of the α,β-unsaturated ketone target, which is of significant purpose to our research because we employ a HWE reaction. The pre-cyclization intermediate **(5)** was oxidized and underwent esterification, followed by treatment with dimethyl methylphosphonate and ozonolysis to create the HWE precursor. The α,β-unsaturated ketone was formed with tetrabutylammonium hydroxide in 1:1 benzene : water and/or under Masamune-Roush conditions (DBU, LiCl, MeCN).



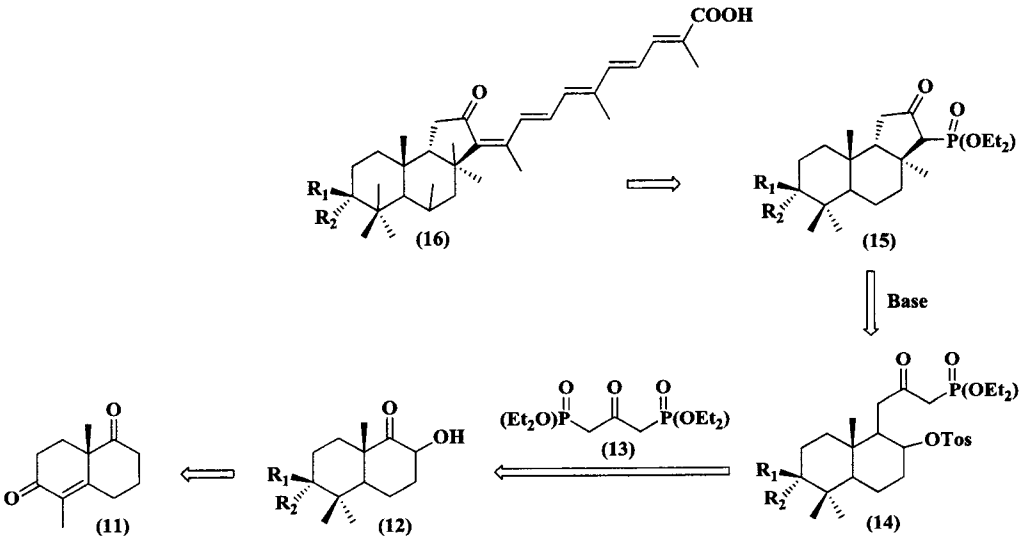
Scheme 3.2: D. Heissler *et al.*[35] synthetic attempt towards the tricyclic ring system of the stellettins using HWE.

A. I. Meyers *et al.* reported another synthetic approach to the tricyclic ring system of isomalabaricanes, as an illustration of their new methodology. Reaction of a chiral bicyclic lactam with 1-(2-bromophenyl)-2-iodoethane followed by direct methylation (Scheme 3.3) formed an enantiomerically pure decalin intermediate, which comprised both the "A" and "B"-rings of the tricyclic, under basic conditions.[37] The decalin was further cyclized into the desired tricyclic ring system using an Aldol condensation. Meyers's route has two limitations; 1) functionality at the C-13, and 2) the A-ring is aromatic and thus extremely hard to reduce and substitute.



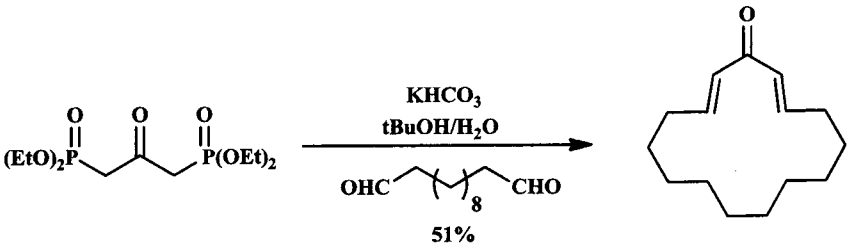
Scheme 3.3: A. I. Meyers *et al.*[37] synthetic attempt towards the tricyclic ring system of the stellettins.

The previous two syntheses have focused on constructing the [6.6.5] core but have had limitations of low yields and the lack of functionality at the C-13 position. Thus it would be more appropriate to focus on a starting material that would solve both of these problems and create the desired tricyclic. Our approach (Scheme 3.4) envisions the use of the phosphono group of hydrindanone **(15)** to create the isomalabaricanes **(16)**. This hydrindanone is hypothesized to be straight-forward and simple to create, while also providing functionality at the C-13 position in the form of a phosphonate group originally from 1,3-bisphosphonoacetone (BPA) **(13)**. The hydrindanone **(15)** can be created from the mono condensation of a α-substituted decalone **(12)** and one of the phosphonate groups of BPA **(13)**, followed by base-catalyzed cyclization. The protected decalin can be created from a hydroxylated decalin, which can be created from a decalin **(11)** starting material.



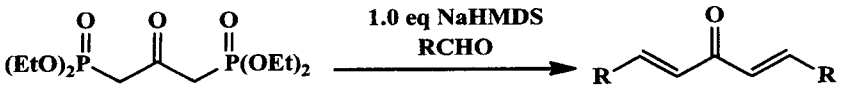
Scheme 3.4: Retrosynthetic scheme for the preparation of stellettins.

The synthesis of a tricyclic system using α-substituted decalone **(12)** and BPA **(13)** to create a hydrindanone **(15)** has never been reported; the original studies of BPA by G. Buchi *et al.*[38] reacted BPA in the presence of potassium bicarbonate ($KHCO_3$) with linear dialdehydes to form macrocyclic α,α'-dienones that led to perfumes (Scheme 3.5).



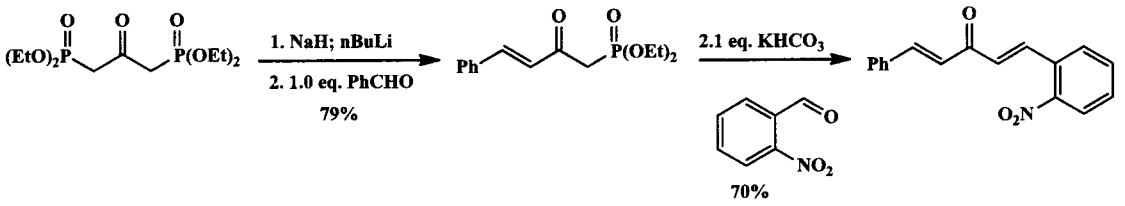
Scheme 3.5: Buchi's synthesis of macrocyclic dienones from BPA.[38]

Buchi observed monocondensation products when the reaction was performed at room temperature (42%), but when they were heated at reflux the dienones were formed (51%). Buchi's reaction used both ends of BPA in a single reaction, to give *E,E*- (47%) and *E,Z*-α,α'-dienones (4%). Buchi's reactions used only linear dialdehydes and thus were not relevant to our research, which envisions sequential condensations as previously stated and thus conditions for this had to be first developed. The initial attempts at condensation via the monoanion formed using NaHMDS with pentanal (R - $(CH_2)_3CH_3$) and benzaldehyde (R - C_6H_5) afforded only the dicondensate in 5.7% and 15.2% yield, respectively (Scheme 3.6).[39] These reactions failed possibly because upon making a molecule of the monocondensate it is deprotonated by the anion of BPA, due to the monocondensate being more acidic, and this monocondensate anion then undergoes a second HWE reaction.



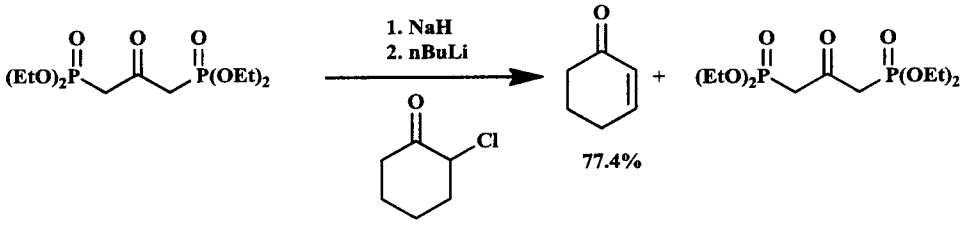
Scheme 3.6: Failed monocondensation reaction of BPA.

Successful sequential condensations were realized in our group by employing the dianion, prepared by treatment of BPA with sodium hydride (NaH) followed by subsequent metalation with *n*-butyl lithium (*n*-BuLi).[40] This allowed for the reaction of a single end of BPA and then reaction of the other end with a weak base like $KHCO_3$ to give the desired unsymmetric product (Scheme 3.7).[41]



Scheme 3.7: Established sequential condensation of BPA employing the dianion.

However, these conditions could fail for hydrindanone precursors due to two reasons. First, it's possible that a competing E2 reaction occurred because of the strongly basic conditions along with the presence of a leaving group (*i.e.* Cl), so that an elimination product is formed. Secondly if a solution of ketone is treated with a base, it is possible that Claisen-Schmidt condensation(s) could occur. However, we only see evidence of the E2 product (Scheme 3.8).[42] Thus in order to obtain a sequential monocondensation reaction with BPA, new synthetic methodology must be found.

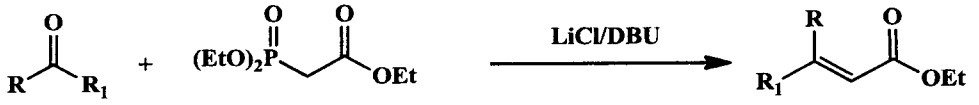


Scheme 3.8: Failed monocondensation of 2-chlorocyclohexanone under strongly basic conditions.

Since BPA had to be synthesized and because it could take many attempts to find the optimal methodology, model studies were also done using commercially available triethyl phosphonoacetate. Using a new approach that employed Masamune-Roush[43] conditions, this phosphonate was reacted with various substituted ketones and aldehydes (Scheme 3.9).

Masamune-Roush conditions use LiCl and an amine in a type of modified Horner-Wadsworth-Emmons (HWE) reaction. The Li^+ ion forms a coordination complex with the β-keto phosphonate, which increases the acidity of the α-H making deprotonation by a weaker amine, (*i.e.* DBU) possible. This allows for the creation of reactive species under simpler, milder conditions than when using stronger, air-sensitive bases. Masamune-Roush conditions could thus be used to synthesize the hydrindanone (**17**, Scheme 3.13).

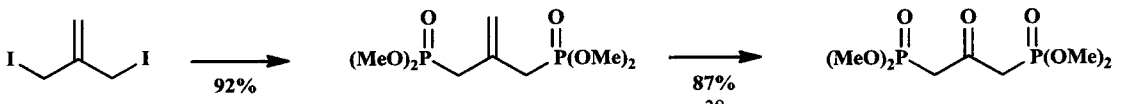
Our research envisions a HWE reaction using one of the phosphono group of BPA **(13)** to generate the tricyclic core, followed by a second HWE reaction with the second phosphono group of BPA **(13)** to append a side chain at the C-13 position to complete the isomalabaricanes **(16)**.



Scheme 3.9: Milder Masamune-Roush condensation conditions.

Results and Discussion:

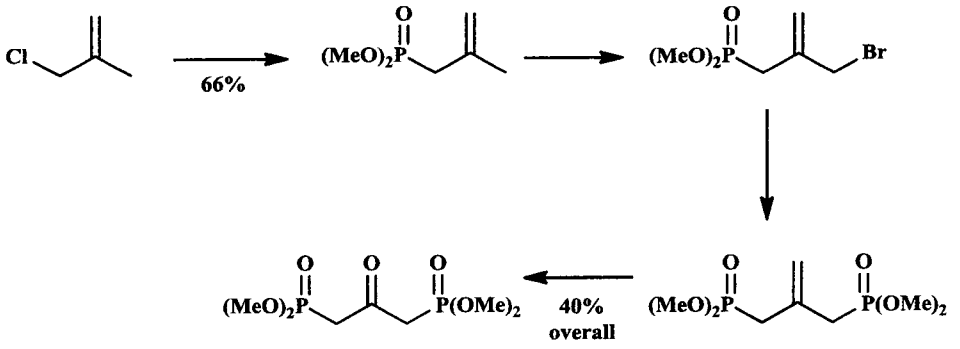
Our synthesis employs 1,3-bisphosphonoacetone (BPA), which must first be synthesized. G. Buchi *et al.*[38] used two different synthetic routes to prepare BPA. The first route (Scheme 3.10) starts with an Arbuzov reaction of 3-iodo-2-(iodomethyl)prop-1-ene and trimethyl phosphite to give the phosphonate. After oxidative cleavage in methanol at -20 °C, and avoiding aqueous work-up, vacuum distillation afforded the water-soluble BPA.



Scheme 3.10: 1st synthetic approach of G. Buchi *et al.*[38] for the preparation of BPA.

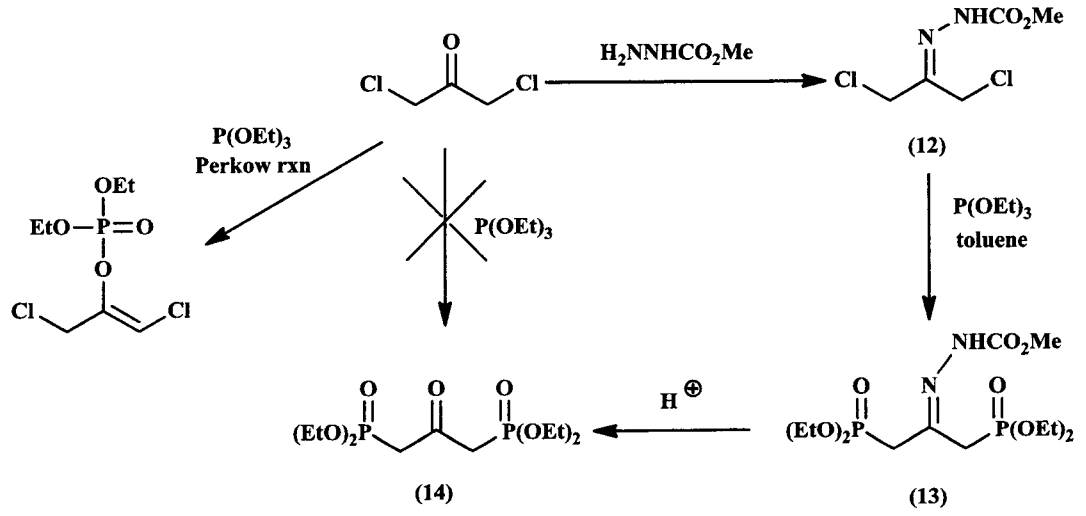
The second route (Scheme 3.11) condenses methallyl chloride with trimethyl phosphite in the presence of nickel bromide to afford the phosphonate. Bromination with *N*-bromosuccinimide followed by substitution with trimethyl phosphite produced the bisphosphonate. After rapid distillation under reduced pressure, ozonization afforded BPA.

The approaches used by Buchi include difficult conditions (*i.e.* methanol at -20 °C and ozonization) and multiple purification techniques. The synthetic scheme doesn't require harsh conditions, and only requires a single SiO_2 gel chromatography during the last step to afford pure BPA, starting from 1,3-dichloroacetone.



Scheme 3.11: 2nd synthetic approach of G. Buchi *et al.*[38] for the preparation of BPA.

It is important to note that direct preparation of BPA **(14)** from 1,3-dichloroacetone via an Arbuzov reaction cannot be achieved due to a competing Perkow reaction (Scheme 3.13),[44] thus the synthesis of B. Corbel *et al.* was used, where 1,3-dichloroacetone was first protected as the hydrazone (**12**, Scheme 3.12).[45]



Scheme 3.12: Synthetic approach to BPA **(14)** from 1,3-dichloroacetone.

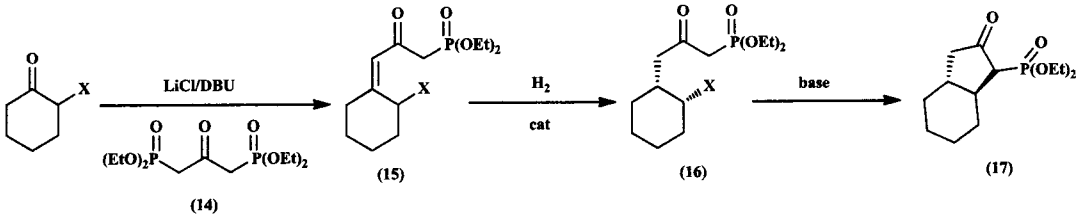
Protection of 1,3-dichloroacetone with methyl hydrazinocarboxylate gave crystalline hydrazone **(12)** in very high yields (98.6% and 71.3%). The melting point (128-131 °C,

129-133 °C) of this hydrazone was within agreement with the literature values (128-130 °C).[45] The ^{1}H NMR spectrum showed that the product was the hydrazone **(12)** as a new peak at 3.8809 ppm (3H, s) was observed.

The hydrazone **(12)** underwent an Arbuzov reaction to produce the protected bisphosphonate **(13)** with an average 59.1% yield. The ^{31}P NMR spectrum obtained for **(13)** had an important peak at 22.93 ppm corresponding to the phosphonate (10 – 30 ppm), while the phosphite starting material appears between 93 – 140 ppm. In the ^{1}H NMR spectrum the methylene signals changed from singlets at 4.19 and 4.33 ppm to doublets (J = 23.8 Hz and J = 24.6 Hz) at 2.93 and 3.10 ppm respectively, due to coupling from the phosphorus.

Bisphosphonoacetone **(14)** was produced from an acidic cleavage reaction of the imine **(13)** with high average yield of 87.7%. After purification using SiO_2 flash chromatography, the ^{1}H NMR spectrum no longer showed peaks at 3.71 (3H, s, H_e) corresponding to the methyl of the carboxyl group **(13)**, while the ^{31}P NMR gave a single peak at 22.113 ppm (2P). In summary BPA can be synthesized in 3 steps, with a single purification, and on a multi-gram scale in good yield (81.9%).

Upon successful preparation, condensation reactions were explored using BPA **(14)** and various substrates to produce a monocondensate (**15**, Scheme 3.13) which could be taken on to hydrindanone **(17)**.



Scheme 3.13: Synthetic approach for the production of hydrindanone **(16)**.

The substrates used were 2-chlorocyclohexanone, chloroacetone, and 2-nitrobenzaldehyde. 2-chlorocyclohexanone was chosen because after condensation removal of the acidic α-hydrogen could give the desired [6.5] ring system (Scheme 3.13). However, it is possible that the steric hindrance of the ring will inhibit the reaction. Using chloroacetone will shed light on this because it is a linear molecule yet still has 2 reactive centers including the electron-withdrawing group (Cl) that allows for ring formation. Aldehydes are more reactive than ketones, and compounds that contain electron-withdrawing groups are also very reactive, thus 2-nitrobenzaldehyde was chosen because it is an aldehyde and contains a strong electron-withdrawing group, *i.e.* NO_2.

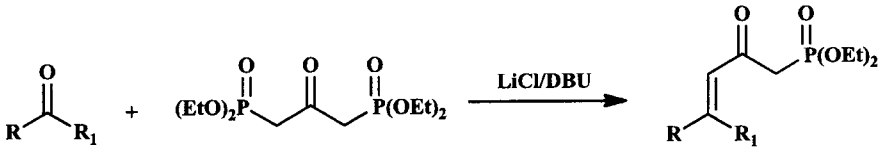
Unfortunately, these condensation reactions didn't yield the desired products (Table 3.1). The ^{1}H and ^{13}C NMR spectra of the worked-up reactions showed only peaks corresponding to BPA and the various substrates. The synthesis of BPA makes it a precious resource and it would be unwise to use it in numerous reactions that didn't work. Thus, model reactions were run with a commercially available compound of similar nature to BPA.

Model studies for the monocondensation using mild bases.

Using triethyl phosphonoacetate, the first set of model studies were conducted on various substituted ketones employing LiCl and DBU. Each experiment gave a drastically different outcome (Table 3.2), but from this information three things were inferred. First comparing model reactions JMS M-1g and JMS M-1i (Table 3.2) we see only DMSO gives product, compared to using CH_3CN as the solvent. However, it's important to note that the elimination product was only seen when using DMSO as a solvent (JMS M-1c

and JMS M-1e). Second, when comparing JMS M-1a and JMS M-1d we see that simply premixing the triethyl phosphonoacetate, LiCl, and DBU for 15-45 minutes prior to adding the carbonyl doesn't lead to better yields than simply mixing all components at the same time. Finally, comparing JMS M-1a and JMS M-1g we conclude that premixing and heating the triethyl phosphonoacetate, LiCl, and DBU to reflux for 15-45 minutes, before adding the substituted ketone, greatly improved the success of the reaction.

Table 3.1: Percent yields for the reaction of BPA with various substrates.



Substituted Substrate	Experiment number	Solvent	Outcome
chloroacetone	11-1	DMSO	---
2-chlorocyclohexanone	10-1	DMSO	---
	10-3	CH_3CN	---
2-nitrobenzaldehyde	9-1	DMSO	---

DMSO produces better results than CH_3CN, but as both are polar aprotic solvents and able to stabilize Li^+ ion, the difference in the results is inferred to be from the dielectric constant, which is the relative measure of its polarity. Also, the two solvents have drastically different boiling points (CH_3CN = 82°C and DMSO = 189°C), thus requiring the use of more heat to reflux the reaction which in turn could lead to the formation of the elimination product. Premixing and heating allow for coordination of the Li^+ between the phosphonate and the carbonyl oxygens without the presence of competing chelating carbonyl oxygen in the ketone. It is this coordination that increases the acidity of the α-H,

making deprotonation by a weaker amine, *i.e.* DBU, significantly easier. Each reaction was followed via TLC, and ^{1}H and ^{13}C NMR spectra for the crude reaction products were done.

Of the conducted reactions (Table 3.2), only three showed (JMS M-1g, JMS M-1i, and JMS M-9a) creation of the product, amongst 57.6%, 35.9%, and 48.4% of the recovered mass, respectively. Upon ^{1}H NMR analysis it was determined, in each of the reactions, that the desired product was the minor component; in both JMS M-1g and JMS M-1i the major component was starting material, but the elimination product was the major product of JMS M-9a. However, the ^{1}H NMR spectrum showed a doublet at 5.54 ppm (1H, d J = 2.01 Hz) corresponding to the vinylic hydrogen and a triplet at 6.21 ppm (1H, t, J = 2.76 Hz) corresponding to the hydrogen off the alpha-carbon for each of the model studies. Further analysis of JMS M-1i using ^{13}C NMR and DEPT analysis, showed that the condensation product was a mixture of *E*/*Z* stereoisomers which is apparent by four peaks at 112.02 (1C, CH), 115.34 (1C, CH), 126.67 (1C, CH), and 126.87 (1C, CH) corresponding to the vinylic carbon.

^{1}H NMR analysis of the other seven reactions showed that mainly only the starting material triethyl phosphonoacetate was present. Even the slightest amount of H_2O could hinder the condensation reaction, thus the use of "wet" LiCl and solvents would be troublesome in the reaction. However, "dry" LiCl and solvents were both used in these reactions and still no desired product was formed.

The competing reaction that was previously reported (Scheme 3.7), in which the 2-chlorocyclohexanone undergoes an elimination reaction, was observed in some cases, to form the cyclohex-2-enone. With such a low reaction success rate a new substrate that

could not undergo a competing elimination reaction was studied, to avoid this side reaction. To do this a substituted ketone was chosen that didn't contain a leaving group, but still had the same sterics in JMS M-7a *i.e.* 2-methylcyclohexanone. Unfortunately, after premixing and heating, no product was formed from the reaction. At this point the goal was to prove that this reaction was reproducible and/or high yielding and in fact was possible, so it was a logical choice to move to using a very reactive substrate.

Table 3.2: Model monocondensation reactions with various substituted ketones and aldehydes.

Substrate	Experiment number	Premixing & heating	Solvent	Outcome
2-chlorocyclohexanone	M-1a	Neither	DMSO	s. mat.
	M-1b	Neither	DMSO	s. mat.
	M-1c	Premixing	DMSO	33% elimn
	M-1d	Premixing	DMSO	s. mat.
	M-1e	Both	DMSO	33% elimn
	M-1f	Heating	CH_3CN	unknown cpd.
	M-1g	Both	DMSO	26% product
	M-1h	Neither	DMSO	s. mat.
	M-1i	Both	CH_3CN	product (minor)
	M-9a	Neither	CH_3CN	elimn
cyclohexanone	M-4a	Neither	DMSO	product (76.5%)
2-methylcyclohexanone	M-5a	Both	DMSO	s. mat.
2-pentanone	M-3a	Premixing	DMSO	s. mat.
2-nitrobenzaldehyde	M-2a	Neither	DMSO	product (45%)
	M-2b	Premixing	DMSO	product (36.4%)
p-nitroacetophenone	M-6a	Both	CH_3CN	product (35%)
2-methylbutyraldehyde	M-7a	Neither	CH_3CN	product (27%)
crotonaldehyde	M-8a	Neither	CH_3CN	product (47%)

Aldehydes are more reactive than ketones because they are less sterically hindered, and do not have inductive effects from carbons on both sides, and moreover compounds with EWG are very reactive, thus 2-nitrobenzaldehyde was used. The reactions were performed under different conditions; 1) with neither premixing nor heating, and 2) with just premixing.

Using NMR analysis it was possible to confirm that both reactions produced the desired product in 40.9% (JMS M-2a) and 36.4% (JMS M-2b) yields, respectively. ^{1}H NMR showed the disappearance of the aldehyde signal at 10.36 ppm (1H, s) and the presence of vinylic signals at 7.95 ppm (1H, ddd, J = 0.76 Hz, J = 1.51 Hz, J = 8.03 Hz) and 6.29 ppm (1H, d, J = 15.8 Hz) as well as 8.07 ppm (1H, dd, J = 1.25 Hz, J = 8.28 Hz) and 6.02 ppm (1H, d, J = 11.8 Hz) for the trans and *cis* isomer, respectively.

With confirmation that these conditions do in fact work, two new hypotheses were tested to determine the scope of the reaction. These hypotheses revolve around the type of substrate used in the condensation reaction. Masamune and Roush used typical saturated aliphatic aldehydes (*i.e.* isobutyraldehyde), unsaturated aldehydes (*i.e.* crotonaldehyde), and aromatic aldehydes (*i.e.* benzaldehyde) in their condensation studies, thus in our hands these substrates should produce decent yields.

The first hypothesis to be tested involved the comparing of the reactivity between cyclic and linear substrates, as the cyclic system could be sterically affecting the reactivity of the condensation reaction. Thus various linear aldehydes and ketones substrates were chosen; *i.e.* 2-pentanone (JMS M-3a), 2-methylbutyraldehyde (JMS M-7a), and crotonaldehyde (JMS M-8a) (Table 3.2) and reacted under specific conditions. ^{1}H NMR analysis of the 2-pentanone (JMS M-3a) condensation reaction showed that

only 2-pentanone and triethyl phosphonoacetone were recovered after work-up. The ^{1}H NMR spectrum of JMS M-7a showed a peak at 5.72 ppm (1H, dd, J = 1.25, J = 15.8 Hz) corresponding to the creation of a double bond. ^{1}H NMR analysis of JMS M-8a showed a couple of things; it displayed peaks for the newly formed double bond at 5.72 ppm (1H, d, J = 15.3 Hz) and 7.20 ppm (1H, dd, J = 9.54 Hz, J = 15.6 Hz). It also showed that the product was contaminated with both triethyl phosphonoacetone and crotonic acid. The presence of crotonic acid tells us that the crotonaldehyde starting material was impure, because the oxidation couldn't have occurred during the reaction as there are no oxidizers in the reaction vessels and it was closed to the environment, thus the low yield was in part due to impure starting material.

The second hypothesis was that the reaction required unsubstituted substrates to be used in the condensation reaction. This was tested using cyclohexanone (JMS M-4a), under neither premixing nor heating conditions with DMSO as a solvent to afford the crude product in 69.5% (contaminated with unreacted BPA), ^{1}H NMR analysis showed a peak a 5.53 ppm (1H, s, H_c) corresponding to the vinylic hydrogen. The ^{13}C NMR spectrum also showed the creation of the double bond represented by peaks at 112.90 ppm and 163.41 ppm.

With successful model condensation studies, BPA was incorporated into the reaction under the same reaction conditions as stated above with the more reactive crotonaldehyde and 2-methylbutyraldehyde. Unfortunately when using CH_3CN, premixing, and heating none of the substrates gave the desired product, giving instead unreacted BPA; this shows that under Masamune-Roush conditions (LiCl/DBU) BPA cannot form the substituted alkene (15, Table 3.3). Drying the solvents and LiCl, as well as placing the BPA under

vacuum to remove any impurities, still didn't allow the reaction to work. It is plausible that the coordination complex made by the Li^+ didn't form, which didn't increase the acidity of the α-H, making deprotonation by DBU difficult.

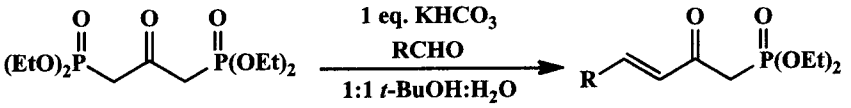
With Masamune-Roush conditions not giving the desired product, the condensation was attempted under; 1) Buchi conditions,[36] and 2) previously used Wittig conditions. Buchi was able to produce a monocondensation reaction with BPA and $KHCO_3$ in aqueous *t*-BuOH and linear dialdehydes at room temperature (42%). These model reactions were done with BPA and chloroacetone, crotonaldehyde, and 2-nitrobenzaldehyde.

Table 3.3: Monocondensation reactions of BPA with various substituted ketones and aldehydes under Masamune-Roush conditions.

Substituted Substrate	Experiment number	Premixing & heating	Solvent	Amount S. Mat. Recovered
crotonaldehyde	19-1a	Both	CH_3CN	41%
	19-1b	Both	CH_3CN	26%
2-methylbutyraldehyde	20-1a	Neither	CH_3CN	21%
	20-1b	Neither	CH_3CN	27%

For the last two substrates, upon ^1H and ^{13}C NMR analysis the desired monocondensation product was not present and once again only unreacted BPA was recovered (Table 3.4). Analysis of ^1H and ^{13}C NMR spectra of the chloroacetone reaction (JMS 22-2a) showed peaks corresponding to only the dicondensate product.

Table 3.4: Monocondensation reactions of BPA under Buchi conditions.

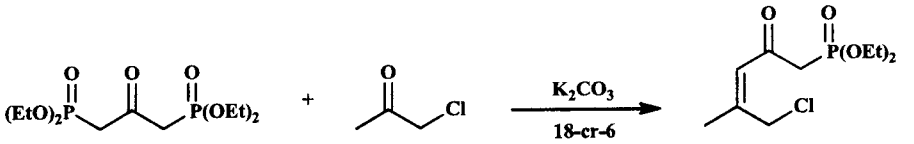


Substituted Substrate	Experiment number	Outcome
crotonaldehyde	22-1a	100% BPA
chloroacetone	22-2a	61% BPA
	22-2b	65% BPA
2-nitrobenzaldehyde	22-3a	100% dicondensate
	22-3b	100% dicondensate

These reactions were stirred at room temperature (25 °C) for 6 hrs, which according to the reports of Buchi should produce the monocondensate product. It is possible that heat would have caused a reaction.

Another alternative reaction is the Wittig condensation similar to the reaction used in Chapter 1 (Scheme 1.1). This reaction should be possible because BPA is a phosphorus ylide, thus BPA was reacted with chloroacetone in the presence of a weak base (K_2CO_3) and 18-crown-6, the reaction failed to yield the desired product (Table 3.5). Attempts at condensation via the monoanion,[39] using NaH and various substrates, were then visited (table 3.6). These reactions used triethyl phosphonoacetate and BPA, which had been placed under vacuum for 1 hr to remove traces of H_2O/solvent.

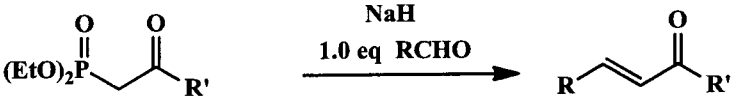
Table 3.5: Percent yields for the model BPA condensation reaction using K_2CO_3 and 18-C-6



Substituted Substrate	Experiment number	Percent yield
chloroacetone	21-1a	---

However, only the reaction employing 2-nitrobenzaldehyde (JMS M-11) produced the desired product, visible via ^{1}H NMR analysis by the presence of as a doublet at 6.32 ppm (1H, d, J = 15.8 Hz).

Table 3.6: Monocondensation reactions using NaH.



R'	Substituted Substrate	Experiment number	Outcome
OEt	chloroacetone	M-10a	56% s. mat.
		M-12	trace s. mat.
OEt	2-nitrobenzaldehyde	M-11	11% product
$CH_2P(O)(OEt)_2$	2-chlorocyclohexanone	14-1	s. mat.
$CH_2P(O)(OEt)_2$	chloroacetone	15-1a	44% s. mat.
		15-1b	67% s. mat.
		15-1c	trace s. mat.

Conclusions:

Synthesis of BPA has been achieved in 70.7% overall yield; unfortunately when employed under the Masamune-Roush conditions no reaction occurred and only the starting material, elimination product, or dicondensate were recovered. The same is true when, Buchi (Table 3.4), Wittig (Table 3.5), and strong base (Table 3.6) conditions were attempted.

The Masamune-Roush model studies using triethyl phosphonoacetate have afforded the desired product as the minor component (Table 3.2) and various substrates *i.e.* 2-chlorocyclohexanone (JMS M-1g & JMS M-1i), cyclohexanone (JMS M-4a), 2-nitrobenzaldehyde (JMS M-2a), *p*-nitroacetophenone (JMS M-6a), 2-methylbutyraldehyde (JMS M-7a), and crotonaldehyde (JMS M-8a). Yet these condensation reactions only afford the desired product as the minor component. However, it has been concluded that DMSO is a better solvent than CH_3CN; it was also found that the order in which the reactants are added to the system must be specific. LiCl, the phosphonoacetone, DBU and DMSO must all be added first and the system heated to reflux for 15-45 minutes. Only after the allotted time has elapsed and the system is cooled to room temperature, can the various ketones/aldehydes be added and stirred overnight.

New model study conditions need to be employed and the conditions reported herein need to be revisited to conclude that they do not give the desired products.

Experimental:

General Experimental:

Reactions were stirred under N_2 atmosphere in oven/flame dried round-bottom flasks unless otherwise stated. Toluene and CH_2Cl_2 were stored over 4-Å molecular sieves. Pyridine was distilled from KOH and stored over 4-Å molecular sieves. LiCl was dried using a drying pistol with xylenes as the solvent. THF was distilled from sodium/benzophenone and stored over 4-Å molecular sieves. Chloroacetone was distilled and dried over $CaSO_4$, placed over 4-Å molecular sieves, and stored in the freezer. DMSO and CH_3CN were distilled from CaH_2 and stored over 4-Å molecular sieves. TLC analyses were performed on EMD Chemicals aluminum-backed F_{254} SiO_2 gel plates, using UV light, iodine, and/or vanillin to visualize. Flash chromatography was performed as described by Still *et al.*[46] (Fisher SiO_2 gel, 60-200 mesh). NMR spectra were obtained on a 400 MHz Bruker Avance FT-NMR spectrometer, using Sigma-Aldrich chloroform-d 99.8% D, containing 0.03% (v/v) TMS for ^1H and ^{13}C spectra, and an external 85% aqueous H_3PO_4 sample was for ^{31}P spectra. ^1H and ^{13}C NMR spectra for semicarbazones were obtained using Sigma-Aldrich DMSO-d_6. NMR spectra were processed using Bruker's TopSpin and/or ACD-NMR Processor. Melting points are uncorrected. UV-Vis spectra were obtained on a UV-3100 Shimadzu UV-Vis-NIR Recording Spectrophotometer, and the spectra were processed using Shimadzu's UVProbe software. Crystal structures were obtained using a Bruker P4 diffractometer and processed using SHELXL-97 (Sheldrick, 1997).

Molecular Modeling:

Molecular modeling calculations were done using Spartan v'10.[47] A conformer distribution search was performed for each semicarbazone **(4)** using the PM3 semi-empirical methods to converge. Energy calculations for the major and minor conformers (based on the Boltzmann values) using density functional theory methods with 6-31G* basis set, displaying both orbital's & energy, and UV-Vis. The HOMO, LUMO, potential HOMO, potential LUMO, and electrostatic potential map surfaces were calculated as well for the semicarbazones **(4)**.

(1, 3-dioxolan-2-ylmethyl)-triphenylphosphonium bromide (JMS 1-1)

Triphenylphosphine, 31.26 g (0.1192 mol, 1 equiv.) and 12.29 mL (0.1198 mol, 1 equiv.) of 2-bromomethyl-1,3-dioxolane were stirred in a 100 mL r.b. flask at reflux for 28 hours. The solution went through three color changes: white to clear (~11 min), clear to yellow (~24 – 44 min) and yellow to orange (~54 min). After 28 hours the black solution was cooled and diluted with CH_2Cl_2 (300 mL). The black solution was filtered and the solid washed with 300 mL of anhydrous ether to afford a black powder. The black powder was recrystallized from CH_2Cl_2/Et_2O to form crystals of the Wittig compound (0.83 g, 0.0019 mol, 1.6%), m.p. 152 ° – 156 °C, (lit. 172 ° – 174 °C).[16]

(JMS 1-2)

As above, triphenylphosphine 23.43 g (0.08933 mol, 1 equiv.) and 9.20 mL (0.0898 mol, 1 equiv.) of bromomethyl-1,3-dioxolane were stirred in a 100 mL r.b. flask and heated at reflux for 24 hours, forming an orange liquid. TLC showed the reaction had gone to completion (10:1 Hex : EtOAc, starting materials (R_f = 0.46) and JMS 1-2 (R_f = 0.77)). The cooled solution was filtered and washed with ~150 mL of ether, to form an

orange colored powder. This powder was recrystallized in CH_2Cl_2/Et_2O to form white crystals of the Wittig compound (6.36 g, 0.0148 mol, 16.6%), m.p. 179 ° – 184 °C. A second crop gave 0.99 g (0.00231 mol, 2.59%), m.p. 177 ° – 183 °C, of the Wittig compound.[16]

(JMS 1-3)

JMS 1-2 was repeated as above, to give white crystals of the Wittig compound (19.34 g, 0.04505 mol, 51.0%), m.p. 189 ° – 193 °C.[16]

^{1}H NMR: δ 3.61 (2H, d, J = 7.28 Hz, H_b), 3.69 (2H, d, J = 7.02 Hz, H_a), 4.42 (2H, dd, J = 4.02 Hz, J_{HP} = 12.8 Hz, H_d), 5.45 (1H, td, J = 6.28 Hz, J = 13.1 Hz, H_c), 7.66 (6H, m), 7.76 (3H, m), 7.83 (6H, m).

^{31}P NMR: δ 21.6423 (1P)

(JMS 1-4)

The experiment above was repeated using triphenylphosphine, 23.00 g (0.08769 mol, 1 equiv.) and 9.00 mL (0.08770 mol, 1 equiv.) of bromomethyl-1,3-dioxolane to give white crystals of the Wittig compound (7.90 g, 0.0184 mol, 21.0%), m.p. 182 ° – 188 °C. A second crop gave 0.780 g (0.00182 mol, 2.08%), m.p. 183 ° – 186 °C, of the Wittig compound.[16]

(JMS 1-5)

The experiment above was repeated using triphenylphosphine, 10.06 g (0.03835 mol, 1 equiv.) and 3.80 mL (0.037997 mol, 0.99 equiv.) of bromomethyl-1,3-dioxolane to give white crystals of the Wittig compound (4.89 g, 0.0114 mol, 30.0%).[16]

(JMS 1-6)

The experiment above was repeated using triphenylphosphine, 12.19 g (0.04648 mol, 1 equiv.) and 4.80 mL (0.04648 mol, 1 equiv.) of bromomethyl-1,3-dioxolane to give white crystals of the Wittig compound (6.2289 g, 0.01451 mol, 31.2%), m.p. 190 ° - 193 °C.[16]

(JMS 1-7)

The experiment above was repeated using triphenylphosphine, 10.1715 g (0.038796 mol, 1 equiv.) and 3.400 mL (0.038796 mol, 1 equiv.) of bromomethyl-1,3-dioxolane to give white crystals of the Wittig compound (3.7855 g, 0.008818 mol, 22.7%), m.p. 186 ° – 189 °C. A second crop gave 0.6758 g (0.001574 mol, 4.06%), m.p. 183 ° – 186 °C, of the Wittig compound.[16]

(*Z/E*)-2-(3,4,5-trimethoxystyryl)-1,3-dioxolane (JMS 7-1a)

In a 100 mL r.b. flask 3,4,5-trimethoxybenzaldehyde (0.50 g, 0.0025 mol, 1 equiv.), and Wittig JMS 1-2 (1.40 g, 0.00275 mol, 1.1 equiv.), was dissolved in 20 mL of "dry" CH_2Cl_2. 15-Crown-5 ether (0.59 g, 0.0027 mol, 1.08 equiv.) was dissolved in a small amount of CH_2Cl_2 and added to the round bottom. Anhydrous Na_2CO_3 (1.16 g, 0.0109 mol, 4.36 equiv.) was also added to the solution, which was then heated at reflux overnight (≈ 24 hrs). TLC (10:1 Hexanes : EtOAc) showed the reaction had gone to completion: starting materials (R_f = 0.13) and JMS 7-1a (R_f = 0.74) . The solution was filtered through sand and Celite and the CH_2Cl_2 was removed under reduced pressure to afford 3.25 g of crude JMS 7-1a. JMS 7-1a was purified by SiO_2 gel column chromatography using 1:1 Hex : EtOAc to give 2 fractions of 0.35 g and 0.19 g.

Fractions A and B: ^1H NMR showed no peaks pertaining to pure JMS 7-1a.

General Experimental for Wittig Condensation:

In a 100 mL r.b. flask the aldehyde (1 equiv.), Wittig (1.1 equiv.), and 20 mL of "dry" CH_2Cl_2 were combined. 18-Crown-6 ether (0.35 equiv.) was dissolved in a small amount of CH_2Cl_2 and added to the round bottom. Anhydrous K_2CO_3 (3.3 equiv.) was also added to the solution, which was heated at reflux overnight (~ 24 hrs). The solution was then filtered through sand and Celite and the CH_2Cl_2 was removed under reduced pressure to afford crude acetal **(2)**, contam. with $Ph_3P=O$. Purification by SiO_2 gel column chromatography was done on the crude acetal **(2)**.

(JMS 7-1b)

According to the general procedure, 3,4,5-trimethoxybenzaldehyde (1.00 g, 0.00510 mol, 1 equiv.), Wittig JMS 1-2 (2.41 g, 0.00561 mol, 1.1 equiv.), 20 mL of "dry" CH_2Cl_2, 18-Crown-6 ether (0.48 g, 0.0018 mol, 0.35 equiv.), and anhydrous K_2CO_3 (2.35 g, 0.0170 mol, 3.3 equiv.) were used. TLC (1:1 Hex : EtOAc) produced spots for 3,4,5-trimethoxy-benzaldehyde (R_f = 0.42) and JMS 7-1b (R_f = 0.37). This afforded 11.18 g crude JMS 7-1b (contam. with $Ph_3P=O$). JMS 7-1b was purified by SiO_2 gel column chromatography using 1:1 Hex : EtOAc to give 3 fractions of 0.013 g, 1.027 g, and 0.034 g. Fraction 1 was contaminated with $Ph_3P=O$, while fraction 2 and 3 gave pure JMS 7-1b (1.061 g, 0.003984 mol, 78.1%, 58 : 42 *cis* : *trans* isomers ratio)

^1H NMR (*trans*-isomer): δ 3.85 (3H, s, H_a), 3.86 (6H, s, H_b), 3.95 (2H, m), 4.07 (2H, m), 5.41 (1H, d, J = 6.03 Hz, H_f), 6.09 (1H, dd, J = 6.03 Hz, J = 15.8 Hz, H_e), 6.65 (2H, s, H_c), 6.70 (1H, d, J = 15.8 Hz, H_d).

^{1}H NMR (*cis*-isomer): δ 3.85 (3H, s, H_a), 3.86 (6H, s, H_b), 3.95 (2H, m,), 4.07 (2H, m), 5.52 (1H, d, J = 7.28 Hz, H_f), 5.70 (1H, dd, J = 7.28 Hz, J = 11.6 Hz, H_e), 6.65 (2H, s, H_c), 6.67 (1H, d, J = 7.78 Hz, H_d).

(*Z/E*)-2-(2,4,6-trimethoxystyryl)-1,3-dioxolane (JMS 7-2b)

JMS 7-1b was repeated using; 2,4,6-trimethoxybenzaldehyde (1.00 g, 0.00510 mol, 1 equiv.), Wittig JMS 1-2 (2.41 g, 0.00561 mol, 1.1 equiv.), 20 mL of "dry" CH_2Cl_2, 18-Crown-6 ether (0.48 g, 0.0018 mol, 0.35 equiv.) and anhydrous K_2CO_3 (2.35 g, 0.0168 mol, 3.3 equiv.) to afford crude Wittig JMS 7-2b (contam. with Ph_3P=O). TLC (1:1 Hex : EtOAc) gave an R_f = 0.35 for JMS 7-2b. JMS 7-2b was purified by SiO_2 gel column chromatography using 1:1 Hex : EtOAc to give 0.35 g of pure JMS 7-2b (0.0013 mol, 25.5%) and 0.21 g of pure JMS 16-4 (0.00094 mol, 18.4%) with a 36.4 : 63.6 *cis* : *trans* ratio.

^{1}H NMR (*trans*-isomer): δ 3.78 (3H, s, H_a), 3.797 (3H, s, H_b), 3.802 (3H, s, H_c), 3.92 (2H, m), 4.04 (2H, m), 5.33 (1H, d, J = 7.03 Hz, H_g), 6.10 (2H, s, H_d), 6.49 (1H, dd, J = 6.52 Hz, J = 16.3 Hz, H_f), 7.05 (1H, d, J = 16.3 Hz, H_e).

^{1}H NMR (*cis*-isomer): δ 3.82 (3H, s, H_a), 3.84 (3H, s, H_b), 3.85 (3H, s, H_c), 3.98 (2H, m), 4.11 (2H, q, J = 7.28 Hz, H_i), 5.29 (1H, d, J = 7.66 Hz, H_g), 5.66 (1H, dd, J = 7.91 Hz, J =11.4 Hz, H_f), 6.12 (2H, s, H_d), 6.46 (1H, d, J = 11.5 Hz, H_e).

(JMS 7-3b)

The experiment above was repeated with exactly the same amounts to afford crude JMS 7-3b (contam. with Ph_3P=O). TLC (1:1.5 Hex : EtOAc) gave an R_f = 0.42 for JMS 7-3b. JMS 7-3b was purified by SiO_2 gel column chromatography using 2:1 Hex : EtOAc to give 0.28 g of pure JMS 7-3b (0.0011 mol, 21.6%) with a 61.0 : 39.0 *cis* : *trans* ratio.

^{1}H NMR (*trans*-isomer): δ 3.82 (3H, s, H_a), 3.85 (3H, s, H_c), 3.90 (3H, s, H_d), 3.96 (2H, m), 4.07 (2H, m), 5.42 (1H, dd, J = 0.76 Hz, J = 6.53 Hz, H_h), 6.06 (1H, dd, J = 6.53 Hz, J = 16.1 Hz, H_g), 6.49 (1H, s, H_b), 7.00 (1H, s, H_e), 7.08 (1H, dt, J = 0.75 Hz, J = 16.6 Hz, H_f).

^{1}H NMR (*cis*-isomer): δ 3.82 (3H, s, H_a), 3.85 (3H, s, H_c), 3.91 (3H, s, H_d), 3.96 (2H, m), 4.07 (2H, m), 5.48 (1H, dd, J = 1.00 Hz, J = 7.53 Hz, H_h), 5.91 (1H, dd, J = 7.53 Hz, J =11.5 Hz, H_g), 6.51 (1H, s, H_b), 6.93 (1H, dt, J = 0.50 Hz, J = 11.5 Hz, H_f), 7.12 (1H, s, H_e)

2-((1*Z/E*,3*Z/E*)-4-(2-methoxyphenyl)buta-1,3-dien-1-yl)-1,3-dioxolane (JMS 7-4)

JMS 7-1b was repeated using 2-methoxycinnamaldehyde (0.827 g, 0.00510 mol, 1 equiv.), Wittig JMS 1-3 (2.41 g, 0.00561 mol, 1.1 equiv.), 20 mL of "dry" CH_2Cl_2, 18-Crown-6 ether (0.48 g, 0.0018 mol, 0.35 equiv.), and anhydrous K_2CO_3 (2.35 g, 0.0168 mol, 3.3 equiv.) to afford crude JMS 7-4 (contam. with Ph_3P=O). TLC (8:1 Tol : MeOH) produced spots for 2-methoxycinnamaldehyde (R_f = 0.53) and JMS 7-4 (R_f = 0.63). JMS 7-4 was purified by SiO_2 gel column chromatography using 1.5:1 Hex : EtOAc to give 0.796 g of pure JMS 7-4 (0.00343 mol, 67.3%).

(*Z/E*)-2-(2,3,4-trimethoxystyryl)-1,3-dioxolane (JMS 7-5)

JMS 7-1b was repeated using 2,3,4-trimethoxybenzaldehyde (1.00 g, 0.00510 mol, 1 equiv.), Wittig JMS 1-3 (2.41 g, 0.00561 mol, 1.1 equiv.), 20 mL of "dry" CH_2Cl_2, 18-Crown-6 ether (0.48 g, 0.0018 mol, 0.35 equiv.), and anhydrous K_2CO_3 (2.35 g, 0.0168 mol, 3.3 equiv.) to afford crude JMS 7-5 (contam. with Ph_3P=O). TLC (1:1.5 Hex : EtOAc) gave an R_f = 0.47 for JMS 7-5. JMS 7-5 was purified by SiO_2 gel column

chromatography using 1:1 Hex : EtOAc to give 0.722 g of pure JMS 7-5 (0.00271 mol, 53.1%).

(*Z/E*)-4-(2-(1,3-dioxolan-2-yl)vinyl)-2-methoxyphenol (JMS 7-6b)

JMS 7-1b was repeated using 4-hydroxy-3-methoxybenzaldehyde (0.791 g, 0.00520 mol, 1 equiv.), Wittig JMS 1-4 (2.46 g, 0.00572 mol, 1.1 equiv.), 20 mL of "dry" CH_2Cl_2, 18-Crown-6 ether (0.481 g, 0.00182 mol, 0.35 equiv.) and anhydrous K_2CO_3 (2.38 g, 0.0172 mol, 3.3 equiv.) to afford crude JMS 7-6b (contam. with Ph_3P=O). TLC (1:2 Hex : EtOAc) produced spots for 4-hydroxy-3-methoxybenzaldehyde (R_f = 0.36) and JMS 7-6b (R_f = 0.40). JMS 7-6b was purified by SiO_2 gel column chromatography using 1:1.5 Hex : EtOAc to give 0.73 g of JMS 7-6b (0.0033 mol, 63.5%, contam. with 4-hydroxy-3-methoxybenzaldehyde).

2-((1*Z/E*,3*Z/E*,5*Z/E*)-6-(2-methoxyphenyl)hexa-1,3,5-trien-1-yl)-1,3-dioxolane (JMS 7-7)

JMS 7-1b was repeated using aldehyde JMS 16-2 (0.10 g, 0.00053 mol, 1 equiv.), Wittig JMS 1-3 (0.20 g, 0.00047 mol, 1.1 equiv.), 10 mL of "dry" CH_2Cl_2, 18-Crown-6 ether (0.049 g, 0.00019 mol, 0.35 equiv.) and anhydrous K_2CO_3 (0.242 g, 0.0018 mol, 3.3 equiv.) to afford crude JMS 7-7 (contam. with Ph_3P=O). TLC (1:1 Hex : EtOAc) produced an R_f = 0.40 for JMS 7-7. JMS 7-7 was purified by SiO_2 gel column chromatography using 6:4 Tol : EtOAc to give 0.02 g of pure JMS 7-7 (7.74E-5 mol, 14.6%).

(*Z/E*)-5-(2-(1,3-dioxolan-2-yl)vinyl)-2-methoxyphenol (JMS 7-8)

JMS 7-1b was repeated using 3-hydroxy-4-methoxybenzaldehyde (0.791 g, 0.00520 mol, 1 equiv.), Wittig JMS 1-4 (2.46 g, 0.00572 mol, 1.1 equiv.), 20 mL of "dry" CH_2Cl_2,

18-Crown-6 ether (0.481 g, 0.00182 mol, 0.35 equiv.) and anhydrous K_2CO_3 (2.38 g, 0.0172 mol, 3.3 equiv.) to afford crude JMS 7-8 (contam. with $Ph_3P{=}O$). TLC (1:2.5 Hex : EtOAc) produced an $R_f = 0.34$ for JMS 7-8. JMS 7-8 was purified by SiO_2 gel column chromatography using 1:2 Tol : EtOAc to give 0.2426 g of pure JMS 7-8 (0.001092 mol, 21.0%).

2-((1*Z/E*,3*Z/E*)-4-(4-methoxyphenyl)buta-1,3-dien-1-yl)-1,3-dioxolane (JMS 7-9a)

JMS 7-1b was repeated using *p*-methoxycinnamaldehyde (0.69 g, 0.0043 mol, 1 equiv.), Wittig JMS 1-4 (2.40 g, 0.00560 mol, 1.3 equiv.), 20 mL of "dry" CH_2Cl_2, 18-Crown-6 ether (0.48 g, 0.0018 mol, 0.42 equiv.) and anhydrous K_2CO_3 (2.32 g, 0.0168 mol, 3.3 equiv.) to afford crude JMS 7-9a (contam. with $Ph_3P{=}O$). TLC (1:1.5 Hex : EtOAc) produced an $R_f = 0.52$ for JMS 7-9a. JMS 7-9a was purified by SiO_2 gel column chromatography using 1:1 Hex : EtOAc to give 0.43 g of pure JMS 7-9a (0.0019 mol, 44.2%) with a 78.2 : 21.8 *cis'trans* : *trans'cis* ratio.

^{1}H NMR (*cis'trans*-isomer): δ 3.72 (3H, s, H_a), 3.86 (2H, m), 3.97 (2H, m), 5.45 (1H, dd, J = 6.78 Hz, J = 11.1 Hz, H_g), 5.77 (1H, d, J = 6.77 Hz, H_h), 6.36 (1H, t, J = 11.1 Hz, H_e), 6.52 (1H, d, J = 15.3, H_d), 6.81 (2H, d, J = 8.78 Hz, H_c), 7.01 (1H, dd, J = 11.3 Hz, J = 15.3 Hz, H_g), 7.32 (2H, d, J = 8.79 Hz, H_b).

^{1}H NMR (*trans'cis*-isomer): 5.28 (1H, d, J = 6.27 Hz, H_h), 5.69 (1H, dd, J = 6.02 Hz, J = 15.3 Hz, H_g), 6.85 (1H, d, J = 8.79 Hz, H_d), 7.28 (2H, d, J = 8.53 Hz, H_c), 7.42 (1H, d, J = 8.78 Hz, H_b).

(JMS 7-9b)

JMS 7-9a was repeated using *p*-methoxycinnamaldehyde (0.8244 g, 0.005083 mol, 1 equiv.), Wittig JMS 1-7 (2.40 g, 0.005591 mol, 1.1 equiv.), 15 mL of "dry" CH_2Cl_2, 18-

Crown-6 ether (0.4702 g, 0.001779 mol, 0.35 equiv.) and anhydrous K_2CO_3 (2.3178 g, 0.01677 mol, 3.3 equiv.) to afford crude JMS 7-9b (contam. with $Ph_3P=O$). TLC (1:1 Hex : EtOAc) produced an R_f = 0.48 for JMS 7-9b. JMS 7-9b was filtered through sand/Celite and the CH_2Cl_2 was removed. Acetone (10 mL) was added to the crude mixture and stirred vigorously, ether (10 mL) was added, followed by three additions of hexanes (40 mL). The mixture was finally filtered through sand/Celite with a SiO_2 gel plug to give 0.6661 g of pure JMS 7-9b (0.002868 mol, 56.4%).

(JMS 7-9c)

JMS 7-9a was repeated using *p*-methoxycinnamaldehyde (0.5724 g, 0.003329 mol, 1 equiv.), Wittig JMS 1-7 (1.5151 g, 0.003529 mol, 1 equiv.), 15 mL of "dry" CH_2Cl_2, 18-Crown-6 ether (0.3264 g, 0.001235 mol, 0.35 equiv.) and anhydrous K_2CO_3 (1.6101 g, 0.01165 mol, 3.3 equiv.) to afford crude JMS 7-9c (contam. with $Ph_3P=O$). TLC (1:1 Hex : EtOAc) produced an R_f = 0.52 for JMS 7-9b. JMS 7-9c was purified as stated in JMS 7-9b to give 0.6932 g of pure JMS 7-9c (0.002984 mol, 84.6%).

(*Z/E*)-2-(2,5-dimethoxystyryl)-1,3-dioxolane (JMS 7-10)

JMS 7-1b was repeated using 2,5-dimethoxybenzaldehyde (0.85 g, 0.0051 mol, 1 equiv.), Wittig JMS 1-4 (2.40 g, 0.00560 mol, 1.1 equiv.), 20 mL of "dry" CH_2Cl_2, 18-Crown-6 ether (0.48 g, 0.0018 mol, 0.35 equiv.) and anhydrous K_2CO_3 (2.32 g, 0.0168 mol, 3.3 equiv.) to afford crude JMS 7-10 (contam. with $Ph_3P=O$). TLC (1:1 Hex : EtOAc) produced spots for both the *cis* and *trans* isomers of JMS 7-10 (R_f = 0.39 and 0.43, respectively). JMS 7-10 was purified as stated in JMS 7-9b to give 1.003 g of crude JMS 7-10 (contam. with 2,5-dimethoxybenzaldehyde and $Ph_3P=O$).

2-((1*Z/E*,3*Z/E*)-4-(3,4,5-trimethoxyphenyl)buta-1,3-dien-1-yl)-1,3-dioxolane (JMS 7-11)

JMS 7-1b was repeated using aldehyde JMS 16-1 (0.20 g, 0.00090 mol, 1 equiv.), Wittig JMS 1-6 (0.42 g, 0.00099 mol, 1.1 equiv.), 15 mL of "dry" CH_2Cl_2, 18-Crown-6 ether (0.085 g, 0.00032 mol, 0.35 equiv.) and anhydrous K_2CO_3 (0.41 g, 0.0030 mol, 3.3 equiv.) to afford crude JMS 7-10 (contam. with $Ph_3P=O$). TLC (1:1 Hex : EtOAc) produced an $R_f = 0.48$ for JMS 7-11. JMS 7-11 was purified as stated in JMS 7-9b to give 0.1150 g of pure JMS 7-11 (0.0003934 mol, 43.7%).

(*Z/E*)-2-(3,5-dimethoxystyryl)-1,3-dioxolane (JMS 7-12)

JMS 7-1b was repeated using 3,5-dimethoxybenzaldehyde (1.00 g, 0.00602 mol, 1 equiv.), Wittig JMS 1-6 (2.58 g, 0.00602 mol, 1 equiv.), 20 mL of "dry" CH_2Cl_2, 18-Crown-6 ether (0.558 g, 0.00211 mol, 0.35 equiv.) and anhydrous K_2CO_3 (2.749 g, 0.001987 mol, 3.3 equiv.) to afford crude JMS 7-12 (contam. with $Ph_3P=O$). JMS 7-12 was purified as stated in JMS 7-9b to give 0.3543 g of pure JMS 7-11 (0.001500 mol, 24.9%).

(*Z/E*)-2-(2,4-dimethoxystyryl)-1,3-dioxolane (JMS 7-13)

JMS 7-1b was repeated using 2,4-dimethoxybenzaldehyde (0.864 g, 0.00520 mol, 1 equiv.), Wittig JMS 1-6 (2.456 g, 0.00572 mol, 1.1 equiv.), 20 mL of "dry" CH_2Cl_2, 18-Crown-6 ether (0.480 g, 0.00182 mol, 0.35 equiv.) and anhydrous K_2CO_3 (2.377 g, 0.0172 mol, 3.3 equiv.) to afford crude JMS 7-13 (contam. with $Ph_3P=O$). TLC (1:1 Hex : EtOAc) produced an $R_f = 0.45$ for JMS 7-13. JMS 7-13 was purified as stated in JMS 7-9b to give 0.982 g of pure JMS 7-13 (0.004156 mol, 79.9%) with a 59.3 : 40.7 *cis* : *trans* ratio.

^{1}H NMR (*trans*-isomer): δ 3.78 (6H, s, H_a), 3.92 (2H, m), 4.05 (2H, m), 5.41 (1H, d, J = 6.06 Hz, H_h), 6.14 (1H, dd, J = 5.81 Hz, J = 15.9 Hz, H_g), 6.56 (1H, d, J = 2.15 Hz, J = 5.69 Hz, H_e), 6.69 (1H, s, H_d), 6.74 (1H, d, J = 15.9 Hz, H_e), 7.01 (1H, s, H_f).

^{1}H NMR (*cis*-isomer): δ 3.79 (6H, s, H_a), 3.96 (2H, m), 4.07 (2H, m), 5.53 (1H, d, J = 7.57 Hz, H_h), 5.71 (1H, dd, J = 7.33 Hz, J = 11.6 Hz, H_g), 6.40 (1H, m), 6.41 (1H, s, H_f), 6.56 (1H, d, J = 2.15 Hz, J = 5.69 Hz, H_e), 6.75 (1H, d, J = 11.2 Hz, H_e).

5-((1*Z/E*,3*Z/E*)-4-(1,3-dioxolan-2-yl)buta-1,3-dien-1-yl)-2-methoxyphenol (JMS 7-14)

JMS 7-1b was repeated using aldehyde JMS 16-8 (0.2192 g, 0.001230 mol, 1 equiv.), Wittig JMS 1-7 (0.5280 g, 0.001230 mol, 1 equiv.), 20 mL of "dry" CH_2Cl_2, 18-Crown-6 ether (0.1138 g, 0.0004305 mol, 0.35 equiv.) and anhydrous K_2CO_3 (0.5609 g, 0.004059 mol, 3.3 equiv.) to afford crude JMS 7-14 (contam. with Ph_3P=O). TLC (1:1 Hex : EtOAc) produced an R_f = 0.13 for JMS 7-14. JMS 7-14 was purified as stated in JMS 7-9b to give 0.2931 g of pure JMS 7-14 (0.001181 mol, 96.0%).

2-((1*Z/E*,3*Z/E*,5*Z/E*)-6-(4-methoxyphenyl)-hexa-1,3,5-trien-1-yl)-1,3-dioxolane (JMS 7-15)

JMS 7-1b was repeated using aldehyde JMS 16-6b (1.0869 g, 0.005775 mol, 1 equiv.), Wittig (2.4791 g, 0.005775 mol, 1 equiv.), 25 mL of "dry" CH_2Cl_2, 18-Crown-6 ether (0.5342 g, 0.002021 mol, 0.35 equiv.) and anhydrous K_2CO_3 (2.6343 g, 0.01906 mol, 3.3 equiv.) to afford crude JMS 7-15 (contam. with Ph_3P=O). JMS 7-15 was purified as stated in JMS 7-9b to give 0.8729 g of pure JMS 7-14 (0.003379 mol, 58.5%).

(*Z/E*)-4-(2-(1,3-dioxolan-2-yl)vinyl)phenol (JMS 7-16)

JMS 7-1b was repeated using *p*-hydroxybenzaldehyde (1.0535 g, 0.008627 mol, 1 equiv.), Wittig (3.7035 g, 0.008627 mol, 1 equiv.), 20 mL of "dry" CH_2Cl_2, 18-Crown-6

ether (0.7980 g, 0.003019 mol, 0.35 equiv.) and anhydrous K_2CO_3 (3.9323 g, 0.02847 mol, 3.3 equiv.) to afford crude JMS 7-16 (contam. with $Ph_3P=O$). TLC (1:1 Hex : EtOAc) produced an $R_f = 0.51$ for JMS 7-16. JMS 7-16 was purified as stated in JMS 7-9b to give 0.3425 g of pure JMS 7-16 (0.001782 mol, 20.7%).

(*Z/E*)-2-(3-methoxystyryl)-1,3-dioxolane (JMS 7-17)

JMS 7-1b was repeated using *m*-anisaldehyde (0.4553 mL, 0.003735 mol, 1 equiv.), Wittig (1.7603 g, 0.004100 mol, 1.09 equiv.), 20 mL of "dry" CH_2Cl_2, 18-Crown-6 ether (0.3447 g, 0.001304 mol, 0.35 equiv.) and anhydrous K_2CO_3 (1.6989 g, 0.01230 mol, 3.3 equiv.) to afford crude JMS 7-17 (contam. with $Ph_3P=O$). TLC (1:1 Hex : EtOAc) produced spots for both *m*-anisaldehyde and JMS 7-17 ($R_f = 0.46$ and 0.41, respectively). JMS 7-17 was purified as stated in JMS 7-9b to give 0.7539 g of pure JMS 7-17 (0.003659 mol, 98.0%).

2-((1*Z/E*,3*Z/E*)-4-phenylbuta-1,3-dien-1-yl)-1,3-dioxolane (JMS 7-18)

JMS 7-1b was repeated using *trans*-cinnamaldehyde (0.7715 mL, 0.006130 mol, 1 equiv.), Wittig (2.8948 g, 0.006743 mol, 1.1 equiv.), 20 mL of "dry" CH_2Cl_2, 18-Crown-6 ether (0.5672 g, 0.002146 mol, 0.35 equiv.) and anhydrous K_2CO_3 (2.7942 g, 0.02023 mol, 3.3 equiv.) to afford crude JMS 7-18 (contam. with $Ph_3P=O$). TLC (1:1 Hex : EtOAc) produced an $R_f = 0.46$ for JMS 7-18. JMS 7-18 was purified as stated in JMS 7-9b to give 1.1035 g of pure JMS 7-18 (0.005456 mol, 89.0%).

2-((1*E*,3*E*,5*E*)-6-phenylhexa-1,3,5-trien-1-yl)-1,3-dioxolane (JMS 7-19)

JMS 7-1b was repeated using aldehyde JMS 16-17 (0.6436 g, 0.004068 mol, 1 equiv.), Wittig (1.9211 g, 0.004475 mol, 1.1 equiv.), 20 mL of "dry" CH_2Cl_2, 18-Crown-6 ether (0.3754 g, 0.001424 mol, 0.35 equiv.) and anhydrous K_2CO_3 (1.8536 g, 0.01342

mol, 3.3 equiv.) to afford crude JMS 7-19 (contam. with $Ph_3P=O$). TLC (1:1 Hex : EtOAc) produced an $R_f = 0.72$ for JMS 7-19. JMS 7-19 was purified as stated in JMS 7-9b to give 0.6342 g of pure JMS 7-19 (0.002778 mol, 68.3%).

General experimental for acetal (2) deprotection:

To a 25 mL r.b. flask, pure acetal (1 equiv.), reagent acetone, and 3M HCl (1 equiv.) were added and the solution was stirred for ~ 3 hrs. TLC (1:1.5 Hex : EtOAc) was done and visualized using UV light. The reaction was extracted with CH_2Cl_2 (3 x10 mL) and then dried with $MgSO_4$, before removal under reduced pressure to afford aldehyde **(3)**.

(*E*)-3-(3,4,5-trimethoxyphenyl)acrylaldehyde (JMS 16-1)

Pure JMS 7-1b (1.192 g, 0.00448 mol, 1 equiv.), 5 mL reagent acetone and 3M HCl (1.5 mL, 0.00448 mol, 1 equiv.) afforded 0.901 g of JMS 16-1 (0.00405 mol, 90.4%) as a white solid. TLC (1:1.5 Hex : EtOAc) produced spots for JMS 7-1b ($R_f = 0.44$) and JMS 16-1 ($R_f = 0.22$).

^{1}H NMR: δ 3.91 (9H, br, H_a), 6.65 (1H, dd, J = 7.78 Hz, J = 15.8 Hz, H_d), 6.80 (2H, s, H_b), 7.41 (1H, d, J = 15.8 Hz, H_c), 9.69 (1H, d, J = 7.77 Hz, H_e).

^{13}C NMR: δ 56.19 (2C, C_1), 60.01 (C_2), 105.65 (2C, C_5), 127.94 (C_6), 129.42 (C_8), 140.91 (C_4), 152.73 (C_7), 153.53 (2C, C_3), 193.44 (C_9).

(2*E*,4*E*)-5-(2-methoxyphenyl)penta-2,4-dienal (JMS 16-2)

The above experiment was repeated using pure JMS 7-4 (0.796 g, 0.00343 mol, 1 equiv.), acetone (5 mL) and 1.14 mL of 3M HCl (0.00343 mol, 1 equiv.) to afford 0.646 g JMS 16-2 (0.00343 mol, 100%, contam. with 2-methoxycinnamaldehyde 1 : 0.23

product : starting material ratio) as a yellow gel. TLC (1:1 Hex : EtOAc) gave an R_f = 0.41 for JMS 16-2.

^{1}H NMR: δ 3.89 (3H, s, H_a), 6.25 (1H, dd, J = 8.03 Hz, J = 15.3 Hz, H_i), 6.94 (1H, dd, J = 8.29 Hz, J = 13.6 Hz, H_e), 6.97 (1H, td, J = 7.53 Hz, J = 4.52 Hz, H_d), 7.06 (1H, dd, J = 10.8 Hz, J = 15.6 Hz, H_h), 7.30 (1H, d, J = 4.02 Hz, H_g), 7.33 (1H, td, J = 7.71 Hz, J = 1.75 Hz, H_c), 7.38 (1H, d, J = 15.6 Hz, H_f), 7.54 (1H, dd, J = 1.50 Hz, J = 7.53 Hz, H_b), 9.60 (1H, d, J = 8.03 Hz, H_j).

^{13}C NMR: δ 55.49 (C_1), 111.10 (C_3), 120.80 (C_5), 122.92 (C_8), 124.52 (C_9), 126.66 (C_7), 127.68 (C_4), 130.88 (C_{11}), 137.75 (C_6), 153.34 (C_{10}), 193.73 (C_{12}).

(*E*)-3-(2,3,4-trimethoxyphenyl)acrylaldehyde (JMS 16-3)

The above experiment was repeated using pure JMS 7-5 (0.722 g, 0.00271 mol, 1 equiv.), acetone (5 mL) and 0.903 mL of 3M HCl (0.00271 mol, 1 equiv.) to afford 0.597 g JMS 16-3 (0.00269 mol, 99.3%, contam. with 2,3,4-trimethoxybenzaldehyde in a 1 : 0.28 product : starting material ratio) as a yellow-green liquid. TLC (1:1.5 Hex : EtOAc) gave an R_f = 0.49 for JMS 16-3.

^{1}H NMR: δ 3.66 (3H, s, H_a), 3.70 (3H, s, H_b), 3.75 (3H, s, H_c), 6.47 (1H, dd, J = 7.78 Hz, J = 16.1 Hz, H_d), 6.54 (1H, d, J = 8.78 Hz, H_e), 7.12 (1H, d, J = 7.79 Hz, H_f), 7.51 (1H, d, J = 16.1 Hz, H_g), 9.44 (1H, d, J = 7.78 Hz, H_h).

^{13}C NMR: δ 55.44 (C_1), 60.14 (C_2), 60.81 (C_3), 107.23 (C_4) 120.30 (C_8), 122.95 (C_6), 126.93 (C_9), 141.65 (C_7), 147.26 (C_{10}), 152.69 (C_5), 155.93 (C_{11}), 193.44 (C_{12}).

(*E*)-3-(2,4,6-trimethoxyphenyl)acrylaldehyde (JMS 16-4)

The above experiment was repeated using pure JMS 7-2b (0.48 g, 0.0018 mol, 1 equiv.), acetone (5 mL) and 0.60 mL of 3M HCl (0.0018 mol, 1 equiv.) to afford 0.29 g

JMS 16-4 (0.0013 mol, 72.2%) as a brownish-orange solid. TLC (1:1 Hex : EtOAc) gave an $R_f = 0.32$ for JMS 16-4.

^{1}H NMR: δ 3.77 (3H, s, H_b), 3.78 (6H, s, H_a), 6.02 (2H, s, H_c), 6.95 (1H, dd, J = 8.29 Hz & J = 16.1 Hz, H_e), 7.76 (1H, d, J = 16.1 Hz, H_d), 9.49 (1H, d, J = 8.03 Hz, H_f).

^{13}C NMR: δ 55.14 (C_1), 55.42 (2C, C_6), 90.11 (C_3), 105.36 (C_5) 128.42 (C_8), 144.70 (C_7), 161.07 (C_4), 163.80 (C_2), 196.12 (C_9).

(*E*)-3-(2,4,5-trimethoxyphenyl)acrylaldehyde (JMS 16-5)

The above experiment was repeated using pure JMS 7-3b (0.28 g, 0.0011 mol, 1 equiv.), acetone (5 mL) and 0.37 mL of 3M HCl (0.0011 mol, 1 equiv.) to afford 0.17 g JMS 16-5 (0.00076 mol, 76.0%) as a solid. TLC (1:1.5 Hex : EtOAc) gave an $R_f = 0.38$ for JMS 16-5. M.p. 134 ° – 138 °C.

^{1}H NMR: δ 3.80 (3H, s, H_a), 3.84 (3H, s, H_b), 3.89 (3H, s, H_c), 6.45 (1H, br, H_f), 6.57 (1H, dd, J = 7.91 Hz, J = 15.9 Hz, H_g), 6.96 (1H, br, H_d), 7.74 (1H, d, J = 16.1 Hz, H_e), 9.57 (1H, d, J = 7.78 Hz, H_h)

^{13}C NMR: δ 55.86 (C_1), 56.03 (C_2), 56.17 (C_3), 96.29 (C_9), 110.28 (C_7), 114.22 (C_6) 126.14 (C_{11}), 143.12 (C_8), 147.58 (C_5), 153.09 (C_{10}), 153.97 (C_4), 194.02 (C_{12}).

(2*E*,4*E*)-5-(4-methoxyphenyl)penta-2,4-dienal (JMS 16-6a)

The above experiment was repeated using pure JMS 7-9a (0.43 g, 0.0019 mol, 1 equiv.), acetone (5 mL) and 0.70 mL of 3M HCl (0.0021 mol, 1.1 equiv.) to afford 0.34 g JMS 16-6a (0.0018 mol, 94.7%) as a yellowish-orange solid with an 88.6 : 11.4 *trans'trans* : *trans'cis* ratio. TLC (1:1.5 Hex : EtOAc) gave an $R_f = 0.51$ for JMS 16-6a. M.p. 58 ° – 60 °C.

^{1}H NMR (*trans*'*trans*-isomer): δ 3.90 (3H, s, H_a), 6.28 (1H, dd, J = 8.03 Hz, J = 15.1 Hz, H_g), 6.93 (1H, ddd, J = 0.59 Hz, J = 10.5 Hz, J = 15.3 Hz, H_f), 6.97 (2H, d, J = 8.78 Hz, H_c), 7.03 (1H, d, J = 15.6 Hz, H_d) 7.32 (1H, dd, J = 10.5 Hz, J = 15.1 Hz, H_e), 7.51 (2H, d, J = 9.04 Hz, H_b), 9.65 (1H, d, J = 7.78 Hz, H_h).

^{1}H NMR (*trans*'*cis*): 6.67 (1H, dd, J = 7.78 Hz, J = 15.8 Hz, H_g), 7.58 (2H, d, J = 8.53 Hz, H_b), 9.71 (1H, d, J = 7.78 Hz, H_h).

^{13}C NMR: δ 54.79 (C_1), 113.93 (2C, C_3), 123.51 (C_7), 127.86 (C_5), 128.73 (2C, C_4), 129.93 (C_9), 141.84 (C_6), 152.30 (C_8), 160.43 (C_2), 192.96 (C_{10}).

(JMS 16-6b)

The above experiment was repeated using pure JMS 7-9ba and JMS 7-9c (1.3694 g, 0.005895 mol, 1 equiv.), acetone (20.0 mL) and 1.965 mL of 3M HCl (0.005895 mol, 1 equiv.) to afford 1.1070 g JMS 16-6b (0.005881 mol, 99.8%) as a yellow solid. TLC (1:1 Hex : EtOAc) gave an R_f = 0.48 for JMS 16-6b. M.p. 59 ° – 63 °C.

(*E*)-3-(4-hydroxy-3-methoxyphenyl)acrylaldehyde (JMS 16-7)

The above experiment was repeated using pure acetal JMS 7-6b (0.73 g, 0.00328 mol, 1 equiv.), acetone (5 mL) and 1.09 mL of 3M HCl (0.00328 mol, 1.1 equiv.) to afford 0.41 g JMS 16-7 (0.00230 mol, 70.1%, contam. with 4-hydroxy-3-methoxybenzaldehyde in a 1 : 0.35 product : starting material ratio) as a yellow solid. TLC (1:1.5 Hex : EtOAc) gave an R_f = 0.41 for JMS 16-7.

^{1}H NMR: δ 3.90 (3H, s, H_a), 5.87 (1H, s, H_b), 6.63 (1H, dd, J = 7.78 Hz, J = 15.8 Hz, H_g), 7.12 (1H, d, J = 1.76 Hz, H_e), 7.15 (1H, d, J = 1.50 Hz, J = 9.78 Hz H_d), 7.31 (1H d, J = 8.03 Hz, H_c) 7.42 (1H, d, J = 16.1 Hz, H_f), 9.67 (1H, d, J = 7.53 Hz, H_h).

^{13}C NMR: δ 55.82 (C_1), 110.79 (C_7), 117.04 (C_4), 122.66 (C_5), 127.43 (C_8), 129.33 (C_6), 148.41 (C_9), 150.11 (C_3), 152.17 (C_2), 193.33 (C_{10}).

(*E*)-3-(3-hydroxy-4-methoxyphenyl)acrylaldehyde (JMS 16-8)

The above experiment was repeated using pure acetal JMS 7-8 (0.2034 g, 0.0009152 mol, 1 equiv.), acetone (5 mL) and 0.3051 mL of 3M HCl (0.0009152 mol, 1 equiv.) to afford 0.1498 g JMS 16-8 (0.0008407 mol, 91.9%) as a yellow solid. M.p. 79 ° – 82 °C.

(*E*)-3-(2,5-dimethoxyphenyl)acrylaldehyde (JMS 16-9)

The above experiment was repeated using pure acetal JMS 7-10 (1.003 g, 0.004245 mol, 1 equiv.), acetone (10 mL) and 1.415 mL of 3M HCl (0.004245 mol, 1 equiv.) to afford 0.6835 g JMS 16-9 (0.003556 mol, 83.8%, contam. with 2,5-dimethoxybenzaldehyde and Ph_3P=O) as a yellow solid. TLC (1:1.5 Hex : EtOAc) gave an R_f = 0.44 for JMS 16-9. M.p. 61 ° – 65 °C.

^{1}H NMR: δ 3.80 (3H, s, H_a), 3.87 (3H, s, H_d), 6.75 (1H, dd, J = 7.91 Hz, J = 15.9 Hz, H_g), 6.89 (1H, d, J = 9.03, H_b), 6.98 (1H, dd, J = 3.01 Hz, J = 9.03 Hz, H_c), 7.08 (1H, d, J = 3.01 Hz, H_e), 7.83 (1H, d, J = 16.1 Hz, H_f), 9.69 (1H, d, J = 7.78 Hz, H_h).

^{13}C NMR: δ 55.76 (C_6), 56.05 (C_1), 112.89 (C_7), 118.47 (C_4), 123.39 (C_3), 129.08 (C_8), 132.11 (C_{10}), 147.79 (C_9), 152.76 (C_2), 153.51 (C_5), 194.37 (C_{11}).

(2*E*,4*E*)-5-(3,4,5-trimethoxyphenyl)penta-2,4-dienal (JMS 16-10)

The above experiment was repeated using pure acetal JMS 7-11 (0.1150 g, 0.0003934 mol, 1 equiv.), acetone (5 mL) and 0.1311 mL of 3M HCl (0.0003934 mol, 1 equiv.) to afford 0.08100 g JMS 16-10 (0.0003263 mol, 82.9%) as a yellow solid. TLC (1:1 Hex : EtOAc) gave an R_f = 0.31 for JMS 16-10. M.p. 84 ° – 89 °C.

(*E*)-3-(3,5-dimethoxyphenyl)acrylaldehyde (JMS 16-11)

The above experiment was repeated using pure acetal JMS 7-12 (0.3543 g, 0.001500 mol, 1 equiv.), acetone (5 mL) and 0.5000 mL of 3M HCl (0.001500 mol, 1 equiv.) to afford 0.2677 g JMS 16-11 (0.001393 mol, 92.9%, contam. with 3,5-dimethoxybenzaldehyde) as a oil.

^{13}C NMR: δ 55.56 (2C, C_1), 98.38 (C_3), 105.63 (2C, C_4), 130.49 (C_7), 148.37 (C_5), 159.92 (C_6), 166.16 (2C, C_2), 194.63 (C_8).

(*E*)-3-(2,4-dimethoxyphenyl)acrylaldehyde (JMS 16-12)

The above experiment was repeated using pure acetal JMS 7-13 (0.9270 g, 0.003924 mol, 1 equiv.), acetone (10 mL) and 1.308 mL of 3M HCl (0.003924 mol, 1 equiv.) to afford 0.5853 g JMS 16-12 (0.003045 mol, 77.6%) as a green solid. TLC (1:1 Hex : EtOAc) gave an R_f = 0.37 for JMS 16-12. M.p. 57 ° – 61 °C.

(2*E*,4*E*)-5-(3-hydroxy-4-methoxyphenyl)penta-2,4-dienal (JMS 16-13)

The above experiment was repeated using pure acetal JMS 7-14 (0.2931 g, 0.001181 mol, 1 equiv.), acetone (5 mL) and 0.3937 mL of 3M HCl (0.001181 mol, 1 equiv.) to afford 0.2120 g JMS 16-13 (0.001038 mol, 87.9%, contam. with Ph_3P=O) as an orangeish-yellow solid. TLC (1:1 Hex : EtOAc) gave an R_f = 0.28 for JMS 16-13. M.p. 92 ° – 95 °C.

^{1}H NMR: δ 3.85 (3H, s, H_a), 5.89 (1H, s, H_e), 6.19 (1H, ddt, J = 2.28 Hz, J = 7.84 Hz, J = 14.9 Hz, H_i), 6.56 (1H, ddd, J = 1.01 Hz, J = 7.58 Hz, J = 15.7 Hz, H_g), 6.88 (3H, m, H_e, & H_d), 7.23 (2H, m), 9.55 (1H, d, J = 8.08 Hz, H_j).

^{13}C NMR: δ 56.06 (C_1), 112.05 (C_3), 115.96 (C_6), 124.16 (C_4), 124.70 (C_9), 125.53 (C_5), 130.84 (C_{11}), 142.00 (C_8), 146.16 (C_7), 146.33 (C_2), 152.39 (C_{11}), 193.54 (C_{12}).

(2*E*,4*E*,6*E*)-7-(4-methoxyphenyl)hepta-2,4,6-trienal (JMS 16-14)

The above experiment was repeated using pure acetal JMS 7-15 (0.8729 g, 0.003379 mol, 1 equiv.), acetone (20 mL) and 1.126 mL of 3M HCl (0.003379 mol, 1 equiv.) to afford 0.6853 g JMS 16-14 (0.003198 mol, 94.6%) as a dark orange solid. TLC (1:1 Hex : EtOAc) gave an $R_f = 0.43$ for JMS 16-14.

^{1}H NMR: δ 3.78 (3H, s, H_a), 6.15 (1H, dddd, J = 1.27 Hz, J = 7.84 Hz, J = 15.2 Hz, J = 24.3 Hz, H_g), 6.44 (1H, tm), 6.72 (2H, m), 6.80 (2H, m), 6.89 (2H, m), 7.15 (1H, dddd, J = 2.28 Hz, J = 10.4 Hz, J = 14.9 Hz, J = 25.5 Hz, H_f), 7.39 (1H, ddd, J = 1.76 Hz, J = 8.58 Hz, J = 19.9 Hz, H_e), 9.54 (1H, d, J = 6.57, H_j).

^{13}C NMR: δ 54.87 (C_1), 114.21 (2C, C_4), 123.93 (C_6), 125.30 (C_5), 128.30 (2C, C_3) 128.97 (C_9), 138.09 (C_8), 141.92 (C_{10}), 143.44 (C_2), 151.62 (C_7), 160.27 (C_{11}) 193.12 (C_{12}).

***E*-3-(4-hydroxyphenyl)acrylaldehyde (JMS 16-15)**

The above experiment was repeated using pure acetal JMS 7-16 (0.1949 g, 0.001014 mol, 1 equiv.), acetone (10 mL) and 0.3380 mL of 3M HCl (0.001014 mol, 1 equiv.) to afford 0.1476 g JMS 16-15 (0.0009962 mol, 98.2%, contam. with 4-hydroxybenzaldehyde in a 1 : 1 ratio) as a yellow gel. TLC (1:1 Hex : EtOAc) gave an R_f = 0.36 for JMS 16-15.

^{1}H NMR: δ 5.86 (1H, t, J = 13.8 Hz, H_a), 6.60 (1H, dd, J = 7.78 Hz, J = 15.7 Hz, H_e), 7.16 (2H, d, J = 8.59 Hz, H_c), 7.43 (1H, d, J = 15.9 Hz, H_d), 7.54 (1H, d, J = 8.59 Hz, H_b), 9.65 (1H, d, J = 7.83 Hz, H_f).

^{13}C NMR: δ 116.50 (C_1) 127.03 (C_2), 130.10 (C_3), 131.69 (C_4), 151.96 (C_5), 158.76 (C_6), 193.40 (C_7).

_E_-3-(3-methoxyphenyl)acrylaldehyde (JMS 16-16)

The above experiment was repeated using pure acetal JMS 7-17 (0.7030 g, 0.004334 mol, 1.27 equiv.), acetone (10 mL) and 1.1363 mL of 3M HCl (0.003409 mol, 1 equiv.) to afford 0.4948 g JMS 16-16 (0.003051 mol, 89.5%, contam. with 3-methoxybenzaldehyde in a 1 : 0.38 product : starting material ratio) as a dark orange oil. TLC (1:1 Hex : EtOAc) gave an $R_f = 0.48$ for JMS 16-16.

^{1}H NMR: δ 3.87 (3H, s, H_a), 6.73 (1H, dd, J = 7.58 Hz, J = 15.9 Hz, H_g), 7.02 (1H, d, J = 2.52 Hz, J = 8.33 Hz, H_c), 7.10 (1H, s, H_e), 7.18 (1H, d, J = 7.58 Hz, H_d), 7.37 (1H, t, J = 7.84 Hz, H_c), 7.49 (1H, d, J = 15.9 Hz, H_f), 9.73 (1H, d, J = 7.57 Hz, H_h).

^{13}C NMR: δ 55.33 (C_1), 113.26 (C_7), 117.06 (C_3), 121.17 (C_5), 123.51 (C_8) 128.82 (C_9), 130.08 (C_4), 135.31 (C_6), 152.62 (C_2), 193.60 (C_{10}).

(2*E*,4*E*)-5-phenylpenta-2,4-dienal (JMS 16-17)

The above experiment was repeated using pure acetal JMS 7-18 (1.1035 g, 0.005456 mol, 1 equiv.), acetone (20 mL) and 1.8187 mL of 3M HCl (0.005456 mol, 1 equiv.) to afford 0.8287 g JMS 16-17 (0.005238 mol, 96.0%, contam. with cinnamaldehyde in a 1 : 0.50 product : starting material ratio) as a dark orange oil. TLC (1:1 Hex : EtOAc) gave an $R_f = 0.50$ for JMS 16-17.

^{1}H NMR: δ 6.26 (1H, dd, J = 8.08 Hz, J = 14.9 Hz, H_j), 6.72 (1H, dd, J = 7.83 Hz, J = 16.2 Hz, H_g), 7.01 (2H, m), 7.27 (1H, ddd, J = 2.28 Hz, J = 7.58 Hz, J = 15.2 Hz, H_a), 7.35 (2H, m), 7.45 (1H, m), 7.49 (1H, m), 9.60 (1H, dd, J = 0.76 Hz, J = 8.08 Hz, H_i).

^{13}C NMR: δ 126.20 (C_1), 127.56 (C_2), 128.96 (C_3), 129.71 (C_5), 131.63 (C_7), 135.61 (C_8), 142.46 (C_6), 152.05 (C_4), 193.57 (C_9).

(2*E*,4*E*,6*E*)-7-phenylhepta-2,4,6-trienal (JMS 16-18)

The above experiment was repeated using pure acetal JMS 7-19 (0.6342 g, 0.002778 mol, 1 equiv.), acetone (10 mL) and 0.9260 mL of 3M HCl (0.002778 mol, 1 equiv.) to afford 0.4494 g JMS 16-18 (0.002439 mol, 87.8%) as a dark orangeish-red oil. TLC (1:1 Hex : EtOAc) gave an R_f = 0.83 for JMS 16-18. The ^{1}H NMR was difficult to analyze due to a high degree of overlap and a 1 : 1 ratio stereoisomers.

^{1}H NMR: δ 6.21 (1H, dd, J = 8.34 Hz, J = 15.4 Hz, H_j), 6.29 (1H, dd, J = 7.83 Hz, J = 14.9 Hz, H_h), 6.21 (1H, dd, J = 11.4 Hz, J = 13.9 Hz, H_g), 9.60 (1H, m).

^{13}C NMR: δ 126.20 (C_1), 127.02, 127.55 (C_2), 127.72 (C_3), 128.46 (C_4), 128.53 (C_5), 128.58 (C_6), 128.63 (C_7), 128.73 (C_8), 128.85 (C_9), 128.95 (C_{10}), 129.71 (C_{11}), 131.20 (C_{12}), 131.63 (C_{13}), 131.98 (C_{14}), 132.16 (C_{15}), 138.37 (C_{16}), 142.46 (C_{17}), 142.74 (C_{18}), 151.75 (C_{19}), 152.04 (C_{20}), 193.50 (C_{21}), 193.57 (C_{22}), 193.57 (C_{23}).

General experimental for semicarbazone (4) production:

To a 50 mL Erlenmeyer flask was added semicarbazide HCl, sodium acetate (NaOAc) trihydrate, and solvent. Once fully dissolved, the aldehyde (JMS 16) was added and stirred for ~45 mins to form a solid. The solid was collected by filtration and air dried overnight. The solid was recrystallized in a solvent to form crystals of the semicarbazone, which were classified using the Behr system and m.p. were obtained.

***E*-Cinnamaldehyde Semicarbazone (JMS 18-1)**

Semicarbazide HCl (0.887 g, 0.00795 mol, 1.05 equiv.), NaOAc trihydrate (1.236 g, 0.009082 mol, 1.20 equiv.), 10 mL of a 1:1 mixture of D.I. H_2O and 95% EtOH, and *trans*-cinnamaldehyde (0.952 mL, 0.00757 mol, 1 equiv.) gave a powder.

Recrystallization in 95% EtOH (50 mL) afforded shiny needles (1.11 g, 0.00587 mol, 77.5%) Ruffled Clam (350A-1) in color, m.p. 221 ° – 224 °C. Lit. m.p. 217 °C.[12]

^{1}H NMR: δ 6.36 (2H, broad, H_h), 6.87 (1H, d, J = 2.51 Hz, H_d), 6.88 (1H, d, J = 3.51, H_f), 7.29 (1H, tt, J = 1.26 Hz, J = 7.27 Hz, H_a), 7.36 (2H, t, J = 7.28 Hz, H_b), 7.52 (2H, dd, J = 1.51, J = 8.54 Hz, H_c), 7.71 (1H, dd, J = 2.13 Hz, J = 5.90 Hz, H_e), 10.25 (1H, broad, H_g).

^{13}C NMR: δ 125.78 (C_6), 126.82 (2C, C_3), 128.57 (C_1), 128.97 (2C, C_2), 136.24 (C_5), 136.44 (C_4), 142.26 (C_7), 156.82 (C_8).

_E_-4-methoxycinnamaldehyde Semicarbazone (JMS 18-2)

Semicarbazide HCl (0.72 g, 0.00648 mol, 1.05 equiv.), NaOAc trihydrate (1.01 g, 0.00740 mol, 1.20 equiv.), 100% EtOH (10 mL), and *trans*-4-methoxycinnamaldehyde (1.00 g, 0.00617 mol, 1 equiv.) gave a powder. Recrystallization in 95% EtOH (55 mL) afforded the semicarbazone (1.13 g, 0.00515 mol, 83.5%), which was Moon Mist (370A-1) in color, m.p. 203 ° – 205 °C. Lit. m.p. 202 °C.[12]

^{1}H NMR: δ 3.75 (3H, s, H_a), 6.32 (2H, broad, H_h), 6.73 (1H, dd, J = 8.79 Hz, J = 16.1 Hz, H_e), 6.92 (2H, d, J = 9.04 Hz, H_b), 7.46 (2H, d, J = 8.79 Hz, H_c), 7.68 (1H, d, J = 8.79 Hz, H_c), 10.15 (1H, broad, H_g).

^{13}C NMR: δ 55.31 (C_1), 114.43 (2C, C_3), 123.51 (C_7), 128.32 (2C, C_4), 128.94 (C_5), 136.33 (C_6), 142.70 (C_8), 156.87 (C_9), 159.69 (C_2)

_E_-2-methoxycinnamaldehyde Semicarbazone (JMS 18-3)

Semicarbazide HCl (0.72 g, 0.00648 mol, 1.05 equiv.), NaOAc trihydrate (1.01 g, 0.00740 mol, 1.20 equiv.), 10 mL of a 1:1 mixture of D.I. H_2O and 95% EtOH, and *trans*-2-methoxycinnamaldehyde (1.00 g, 0.00617 mol, 1 equiv.) gave a powder.

Recrystallization in 95% EtOH (40 mL) afforded the semicarbazone (1.14 g, 0.00520 mol, 84.3%), which was Moonlit Yellow (380A-2) in color, m.p. 199 ° – 202 °C. Lit. m.p. 200 °C.[12]

^{1}H NMR: δ 3.82 (3H, s, H_a), 6.33 (2H, broad, H_j), 6.90 (1H, dd, J = 9.03 Hz, J = 16.3 Hz, H_g), 6.92 (1H, td, J = 0.76 Hz, J = 7.53 Hz, H_d), 7.01 (1H, d, J = 16.3 Hz, H_f), 7.02 (1H, dd, J = 0.88 Hz, J = 8.53 Hz, H_b), 7.27 (1H, ddd, J = 1.51 Hz, J = 7.28 Hz, J = 8.78 Hz, H_c), 7.53 (1H, dd, J = 1.76 Hz, J = 7.78 Hz, H_e), 7.69 (1H, d, J = 9.03 Hz, H_h), 10.18 (1H, broad, H_g).

^{13}C NMR: δ 55.51 (C_1), 111.52 (C_3), 120.73 (C_5), 124.48 (C_7), 126.33 (C_9), 127.10 (C_4), 129.78 (C_6), 131.23 (C_{10}), 142.76 (C_8), 156.64 (C_{11}), 156.68 (C_2).

_E_-2-nitrocinnamaldehyde Semicarbazone (JMS 18-4)

Semicarbazide HCl (0.33 g, 0.0029 mol, 1.05 equiv.), NaOAc trihydrate (0.46 g, 0.0034 mol, 1.20 equiv.), D.I. H_2O (10 mL), and 2-nitrocinnamaldehyde (0.50 g, 0.0028 mol, 1 equiv.) gave a powder. Recrystallization in 95% EtOH (81 mL) afforded the semicarbazone (0.57 g, 0.0024 mol, 86.2%), which was saffron thread (310B-7) in color, m.p. 219 ° – 221 °C.

^{1}H NMR: δ 6.36 (2H, broad, H_i), 6.93 (1H, dd, J = 9.10 Hz, J = 15.7 Hz, H_f), 7.13 (1H, d, J = 15.7 Hz, H_e), 7.55 (1H, t, J = 7.58 Hz, H_c), 7.72 (1H, t, J = 7.33 Hz, H_b), 7.72 (1H, d, J = 9.35 Hz, H_g), 7.88 (1H, d, J = 7.83 Hz, H_d), 7.98 (1H, d, J = 8.09 Hz, H_a), 10.35 (1H, broad, H_h).

^{13}C NMR: δ 124.58 (C_2), 127.91 (C_8), 129.17 (C_5), 129.81 (C_6), 130.42 (C_3), 130.69 (C_4), 133.54 (C_9), 141.07 (C_7), 147.71 (C_1), 156.35 (C_{10}).

2-phenylcinnamaldehyde Semicarbazone (JMS 18-5)

Semicarbazide HCl (0.28 g, 0.0025 mol, 1.05 equiv.), NaOAc trihydrate (0.392 g, 0.00288 mol, 1.20 equiv.), 100% EtOH (10 mL), and 2-phenylcinnamaldehyde (0.50 g, 0.0028 mol, 1 equiv.). Recrystallization in 95% EtOH (30 mL) afforded the semicarbazone as shiny white flakes (0.47 g, 0.0018 mol, 73.8%), m.p. 220 ° – 224 °C.

^{1}H NMR: δ 6.32 (2H, broad, H_n), 6.78 (1H, d, J = 9.79 Hz, H_l), 7.20 (2H, m), 7.24 (2H, m), 7.34 (3H, m), 7.45 (3H, m), 7.52 (1H, d, J = 10.0 Hz, H_k), 10.08 (1H, broad, H_m).

^{13}C NMR: δ 124.64 (C_{10}), 127.22 (2C, C_2), 128.15 (C_1), 128.35 (C_9), 128.67 (2C, C_8), 128.70 (2C, C_3), 130.05 (2C, C_7), 138.29 (C_{11}), 140.17 (C_4), 140.88 (C_6), 145.88 (C_5), 156.51 (C_{12}). Anal. Calcd for $C_{16}H_{15}N_3O$: C, 72.43; H, 5.70; N, 15.84. Found: C, 72.32; H, 5.64; N, 15.76.

***E*-3,4,5-trimethoxycinnamaldehyde Semicarbazone (JMS 18-6)**

Semicarbazide HCl (0.11 g, 0.00095 mol, 1.05 equiv.), NaOAc trihydrate (0.15 g, 0.0011 mol, 1.20 equiv.), 20 mL of a 1:1 mixture of D.I. H_2O and 95% EtOH, and aldehyde JMS 16-1 (0.20 g, 0.00090 mol, 1 equiv.) gave a powder. Recrystallization in D.I. H_2O (75 mL) and 95% EtOH (14 mL) afforded the semicarbazone (0.19 g, 0.00071 mol, 78.9%), which was Summer Harvest (380A-3) in color, m.p. 206 ° – 208 °C.

JMS 18-6 (Light):

^{1}H NMR: δ 3.65 (3H, s, H_b), 3.79 (6H, s, H_a), 6.27 (2H, broad, H_h), 6.79 (1H, d, J = 16.1 Hz, H_d), 6.84 (2H, s, H_c), 6.87 (1H, dd, J = 8.78 Hz, J = 16.1 Hz, H_e), 7.67 (1H, d, J = 8.79 Hz, H_f), 10.15 (1H, broad, H_g).

^{13}C NMR: δ 55.99 (2C, C_1), 60.21 (C_2), 104.18 (2C, C_5), 125.31 (C_8), 131.98 (C_6), 136.57 (C_7), 137.96 (C_9), 142.21 (C_3), 153.17 (2C, C_4), 156.66 (C_{10}). Anal. Calcd for $C_{13}H_{17}N_3O_4$: C, 55.91; H, 6.13; N, 15.05. Found: C, 56.24; H, 6.11; N, 14.96.

***E,E*-5-(2-methoxyphenyl)penta-2,4-dienal Semicarbazone (JMS 18-7)**

Semicarbazide HCl (0.21 g, 0.0019 mol, 1.05 equiv.), NaOAc trihydrate (0.30 g, 0.0022 mol, 1.20 equiv.), 10 mL of a 1:1 mixture of D.I. H_2O and 95% EtOH, and aldehyde JMS 16-2 (0.33 g, 0.0018 mol, 1 equiv.) gave a powder. Recrystallization 95% EtOH (16 mL) afforded the semicarbazone (0.11 g, 0.00042 mol, 23.3%), which was Bicycle Yellow (370A-3) in color, m.p. 196 ° – 199 °C.

^{1}H NMR: δ 3.86 (3H, s, H_a), 6.33 (2H, broad, H_l), 6.43 (1H, dd, J = 9.54 Hz, J = 15.3 Hz, H_g), 6.77 (1H, dd, J = 10.0 Hz, J = 15.1 Hz, H_h), 6.97 (1H, t, J = 7.91 Hz, H_c), 7.02 (1H, d, J = 15.8 Hz, H_f), 7.04 (1H, t, J = 8.54 Hz, H_d), 7.09 (1H, dd, J = 9.79 Hz, J = 15.6 Hz, H_i), 7.30 (1H, ddd, J = 1.51 Hz, J = 7.28 Hz, J = 8.28 Hz, H_e), 7.62 (1H, td, J = 1.75 Hz, J = 8.03 Hz, H_b), 7.65 (1H, d, J = 9.54 Hz, H_j), 10.16 (1H, broad, H_k).

^{13}C NMR: δ 55.59 (C_1), 111.58 (C_3), 120.78 (C_8), 125.18 (C_9), 126.48 (C_7), 129.03 (C_5), 129.04 (C_{11}), 129.22 (C_4), 129.48 (C_6), 137.79 (C_{12}), 142.13 (C_{10}), 156.63 (C_{13}), 156.64 (C_2). Anal. Calcd for $C_{13}H_{15}N_3O_2$: C, 63.66; H, 6.16; N, 17.13. Found: C, 63.75; H, 6.21; N, 17.13

***E,E*-5-(4-methoxyphenyl)penta-2,4-dienal Semicarbazone (JMS 18-8)**

Semicarbazide HCl (0.20 g, 0.0018 mol, 1.05 equiv.), NaOAc trihydrate (0.27 g, 0.0020 mol, 1.20 equiv.), 10 mL of a D.I. H_2O and 95% EtOH, and aldehyde JMS 16-6 (0.28 g, 0.0015 mol, 1 equiv.) gave a powder. Recrystallization in 1-butanol (35 mL)

afforded the semicarbazone (0.24 g, 0.00098 mol, 65.3%), which was Banana Split (360A-3) in color, m.p. 228 ° – 231 °C.

^{1}H NMR: δ 3.76 (3H, s, H_a), 6.28 (2H, broad, H_j), 6.36 (1H, dd, J = 9.54 Hz, J = 15.6 Hz, H_g), 6.65 (1H, dd, J = 10.9 Hz, J = 15.2 Hz, H_h), 6.69 (1H, d, J = 15.7 Hz, H_f), 6.92 (1H, d, J = 9.04 Hz, H_b), 6.92 (1H, dd, J = 10.7 Hz, J = 15.4 Hz, H_e), 7.46 (1H, d, J = 8.79 Hz, H_c), 7.60 (1H, d, J = 9.54 Hz, H_d), 10.09 (1H, broad, H_i). Anal. Calcd for $C_{13}H_{15}N_3O_2$: C, 63.66; H, 6.16; N, 17.13. Found: C, 63.09; H, 6.13; N, 17.07.

_E_-2,4,6–trimethoxycinnamaldehyde Semicarbazone (JMS 18-9)

Semicarbazide HCl (0.14 g, 0.0013 mol, 1.05 equiv.), NaOAc trihydrate (0.19 g, 0.0014 mol, 1.20 equiv.), 10 mL of a 1:1 mixture of D.I. H_2O and 95% EtOH, and aldehyde JMS 16-4 (0.26 g, 0.0012 mol, 1 equiv.) gave a powder. Recrystallization in 100% EtOH (35 mL) afforded the semicarbazone (0.26 g, 0.00093 mol, 77.5%), which was Pale Daffodil (370A-2) in color, m.p. 195 ° – 199 °C.

^{1}H NMR: δ 3.81 (3H, s, H_a), 3.83 (6H, s, H_c), 6.22 (2H, broad, H_h), 6.26 (2H, s, H_b), 6.92 (1H, d, J = 16.1 Hz, H_d), 6.87 (1H, dd, J = 9.28 Hz, J = 16.3 Hz, H_e), 7.57 (1H, d, J = 9.30 Hz, J = , H_f), 9.94 (1H, broad, H_g).

^{13}C NMR: δ 55.40 (C_1), 55.88 (2C, C_2), 90.99 (2C, C_4), 106.07 (C_6), 126.00 (C_7), 127.84 (C_8), 144.85 (C_9), 156.66 (C_{10}), 159.32 (2C, C_5), 161.12 (C_3). Anal. Calcd for $C_{13}H_{17}N_3O_4$: C, 55.91; H, 6.13; N, 15.05. Found: C, 55.66; H, 6.13; N, 14.59.

Slow evaporation from 95% EtOH afforded transparent plate shaped monoclinic crystals (emt06): $\omega/2\theta$ scans, absorption correction: numerical (SHELXS-97; Sheldrick, 1997),[22] 9833 measured reflections, 3136 independent reflections, 1610 reflections with $I > 2\sigma$

(I), unit cell lengths: 14.084(2), 8.7858(13), 15.135(2), unit cell angles: 90.00, 113.634(2), 90.00, wavelength: Mo_k, room temperature (23 °C), R2 = 0.0505

Slow evaporation from CH_3CN afforded plate transparent shaped triclinic crystals (emt06): $\omega/2\theta$ scans, absorption correction: numerical (SHELXS-97; Sheldrick, 1997),[22] 9994 measured reflections, 4787 independent reflections, 4397 reflections with $I > 2\sigma$ (I), unit cell lengths: 8.2031(2), 12.7085(3), 14.0626(3), unit cell angles: 93.127(1), 101.646(1), 105.448(1) wavelength: Cu_k, low temperature (-173 °C), R2 = 0.0318

_E_-2,4,5-trimethoxycinnamaldehyde Semicarbazone (JMS 18-10)

Semicarbazide HCl (0.064 g, 0.00057 mol, 1.05 equiv.), NaOAc trihydrate (0.088 g, 0.00065 mol, 1.20 equiv.), 10 mL of a 1:1 mixture of D.I. H_2O and 95% EtOH, and aldehyde JMS 16-5 (0.12 g, 0.00054 mol, 1 equiv.) gave a powder. Recrystallization in 95% EtOH (10 mL) afforded the semicarbazone (0.05 g, 0.00014 mol, 25.9%), which was Lemon Drops (340B-4) in color, m.p. 215 ° – 218 °C.

Acetone Semicarbazone (JMS 18-11)

Semicarbazide HCl (1.01 g, 0.00904 mol, 1.05 equiv.), NaOAc trihydrate (1.40 g, 0.0103 mol, 1.20 equiv.), a mixture of D.I. H_2O (10 mL) and 95% EtOH (4 mL), and reagent acetone (0.632 mL, 0.0109 mol, 1 equiv.) gave a powder. Recrystallization in CH_2Cl_2 (10 mL) afforded the semicarbazone as a white powder (0.38 g, 0.0033 mol, 30.3%), m.p. 189 ° - 190 °C. Lit. m.p.187 °C.[48]

_E_-2,3,4-trimethoxycinnamaldehyde Semicarbazone (JMS 18-12)

Semicarbazide HCl (0.212 g, 0.00190 mol, 1.05 equiv.), NaOAc trihydrate (0.295 g, 0.00217 mol, 1.20 equiv.), D.I. H_2O (5 mL), and aldehyde JMS 16-3 (0.403 g, 0.00181 mol, 1 equiv.) gave a powder. Recrystallization in D.I H_2O (13 mL) and 95% EtOH (8

mL) afforded the semicarbazone (0.19 g, 0.00068 mol, 37.6%), which was Pineapple Soda (340B-6) in color, m.p. 173 ° - 176 °C.

^{1}H NMR: δ 3.75 (3H, s, H_a), 3.79 (3H, s, H_b), 3.81 (3H, s, H_c) 6.28 (2H, broad, H_j), 6.80 (1H, dd, J = 9.04 Hz, J = 16.3 Hz, H_g), 6.84 (1H, d, J = 8.79 Hz H_d), 6.90 (1H, d, J = 16.32 Hz, H_f), 7.33 (1H, d, J =8.78 Hz, H_e), 7.67 (1H, d, J = 9.03 Hz, J = , H_h), 10.13 (1H, broad, H_i).

^{13}C NMR: δ 55.94 (C_3), 60.45 (C_2), 61.17 (C_1), 108.54 (C_7), 121.42 (C_8), 122.62 (C_{11}), 124.87 (C_9), 130.67 (C_{12}), 141.92 (C_{10}), 142.70 (C_5), 151.28 (C_4), 153.76 (C_6), 156.57 (C_{13}). Anal. Calcd for $C_{13}H_{17}N_3O_4$: C, 55.91; H, 6.13; N, 15.05. Found: C, 55.86; H, 6.29; N, 14.56.

_E_-4-hydroxy-3-methoxycinnamaldehyde Semicarbazone (JMS 18-13)

Semicarbazide HCl (0.188 g, 0.00169 mol, 1.05 equiv.), NaOAc trihydrate (0.263 g, 0.00193 mol, 1.20 equiv.), 95% EtOH (5 mL), and aldehyde JMS 16-7 (0.287 g, 0.00161 mol, 1 equiv.) gave a powder. Recrystallization in pyridine (25 mL) afforded the semicarbazone (0.2629 g, 0.0001122 mol, 69.7%) with a : *cis* : *trans* ratio, which was Clam Chowder (330C-3) in color, m.p. 207 ° - 210 °C.

^{1}H NMR: δ 3.80 (3H, s, H_a), 5.78 (1H, s, H_b), 6.27 (2H, broad, H_j), 6.83 (1H, m), 7.07 (1H, m), 7.14 (1H, m), 7.22 (1H, m), 7.67 (1H, m), 10.16 (1H, broad, H_i).

^{1}H NMR: δ 3.80 (3H, s, H_a), 5.78 (1H, s, H_b), 6.27 (2H, broad, H_j), 6.83 (1H, m), 7.07 (1H, m), 7.14 (1H, m), 7.22 (1H, m), 7.67 (1H, m), 10.16 (1H, broad, H_i).

^{13}C NMR: δ 55.63 (C_1), 110.09 (C_3), 116.83 (C_6), 120.00 (C_4), 124.63 (C_9), 131.44 (C_5), 136.07 (C_8), 142.13 (C_{10}), 145.78 (C_7), 149.82 (C_2), 156.53 (C_{11}).

_E_-3-hydroxy-4-methoxycinnamaldehyde Semicarbazone (JMS 18-14)

Semicarbazide HCl (0.1623 g, 0.001455 mol, 1.05 equiv.), NaOAc trihydrate (0.2263 g, 0.001663 mol, 1.20 equiv.), 95% EtOH (5 mL), and aldehyde JMS 16-8 (0.2468 g, 0.001386 mol, 1 equiv.) gave a powder. Recrystallization in pyridine (16 mL) afforded the semicarbazone (0.0866 g, 0.0003681 mol, 26.6%) with a 1.56 : 1.00 *cis* : *trans* ratio, which was Twenty Carat (310B-6) in color, m.p. 204 ° - 208 °C.

^{1}H NMR (*trans*-isomer) : δ 3.77 (3H, s, H_a), 5.85 (1H, s, H_b), 6.26 (2H, broad, H_j), 6.74 (1H, dd, J = 3.01 Hz, J = 8.78 Hz, H_d), 6.78 (1H, s, H_e), 7.01 (1H, m), 7.43 (1H, m), 7.56 (2H, m), 7.62 (2H, m), 10.13 (1H, broad, H_i).

^{1}H NMR (*cis*-isomer): δ 3.75 (3H, s, H_a), 5.83 (1H, s, H_b), 6.46 (2H, broad, H_j), 6.70 (1H, dd, J = 3.01 Hz, J = 8.78 Hz, H_d), 6.82 (1H, s, H_e), 7.16 (1H, m), 7.27 (1H, m), 7.56 (2H, m), 7.62 (2H, m), 10.16 (1H, broad, H_i).

_E_-2,5-dimethoxycinnamaldehyde Semicarbazone (JMS 18-15)

Semicarbazide HCl (0.3022 g, 0.002710 mol, 0.85 equiv.), NaOAc trihydrate (0.4215 g, 0.003097 mol, 0.98 equiv.), 10 mL of a mixture of D.I. H_2O and 95% EtOH, and aldehyde JMS 16-9 (0.6098 g, 0.003173 mol, 1 equiv.) gave a powder. Recrystallization in 95% EtOH (15 mL) afforded the semicarbazone (0.3892 g, 0.001561 mol, 49.2%), which was Lemon Tart (380B-6) in color, m.p. 208 ° - 211 °C.

^{1}H NMR: δ 3.73 (3H, s, H_a), 3.77 (3H, s, H_d), 6.29 (2H, broad, H_j), 6.86 (1H, dd, J = 3.01 Hz, J = 9.03 Hz, H_c), 6.92 (1H, dd, J = 8.28 Hz, J = 16.3 Hz, H_g), 6.95 (1H, d, J = 9.28 Hz, H_h), 6.99 (1H, d, J = 16.5 Hz, H_f), 7.10 (1H, d, J = 3.36 Hz, H_b), 7.67 (1H, d, J = 8.28 Hz, H_e), 10.17 (1H, broad, H_i).

^{13}C NMR: δ 55.44 (C_6), 56.04 (C_1), 111.56 (C_7), 112.84 (C_4), 115.25 (C_3), 125.15 (C_8), 126.66 (C_{10}), 130.96 (C_{11}), 142.59 (C_9), 151.06 (C_2), 153.28 (C_5), 156.54 (C_{12}). Anal. Calcd for $C_{12}H_{15}N_3O_3$: C, 57.82; H, 6.07; N, 16.86. Found: C, 58.26; H, 6.1; N, 16.72.

(2*E*,4*E*)-5-(3,4,5-trimethoxyphenyl)penta-2,4-dienal Semicarbazone (JMS 18-16)

Semicarbazide HCl (0.0368 g, 0.0003303 mol, 1.05 equiv.), NaOAc trihydrate (0.0514 g, 0.0003775 mol, 1.20 equiv.), 95% EtOH (5 mL), and aldehyde JMS 16-10 (0.0781 g, 0.0003146 mol, 1 equiv.) gave a powder. Recrystallization from a 10 mL 1:1 mixture of D.I. H_2O and 95% EtOH afforded the semicarbazone (0.0212 g, 0.00006943 mol, 22.1%), which was Vibrant (370B-6) in color, m.p. 191 ° - 194 °C.

^1H NMR: δ 3.66 (3H, s, H_a), 3.80 (6H, s, H_b & H_c), 6.27 (2H, broad, H_l), 6.38 (1H, dd, J = 9.48 Hz, J = 15.5 Hz, H_i), 6.66 (1H, dd, J = 10.5 Hz, J = 15.0 Hz, H_h), 6.67 (1H, d, J = 15.4 Hz H_f), 6.82 (2H, s, H_d & H_e), 7.05 (1H, dd, J = 11.1 Hz, J = 15.4 Hz, H_g), 7.59 (1H, d, J = 9.60 Hz, H_j), 10.12 (1H, broad, H_k).

***E*-3,5-dimethoxycinnamaldehyde Semicarbazone (JMS 18-17)**

Semicarbazide HCl (0.1508 g, 0.001352 mol, 1.05 equiv.), NaOAc trihydrate (0.2104 g, 0.001546 mol, 1.20 equiv.), 95% EtOH (5 mL), and aldehyde JMS 16-11 (0.2476 g, 0.001288 mol, 1 equiv.) gave a powder. Recrystallization in 95% EtOH (14 mL) afforded the semicarbazone (0.1529 g, 0.0006134 mol, 47.6%), which was Ripe Wheat (310E-3) in color, m.p. 178 ° -182 °C.

^1H NMR: δ 3.79 (3H, s, H_a), 3.83 (3H, s, H_c), 6.22 (2H, broad, H_j), 6.55 (3H, m), 6.77 (1H, dd, J = 8.84 Hz, J = 15.4 Hz, H_g), 6.67 (1H, d, J = 16.2 Hz H_f), 7.46 (1H, d, J = 8.59 Hz, H_e), 7.54 (1H, d, J = 8.84 Hz, H_d), 10.03 (1H, broad, H_i).*

_E_-2,4-dimethoxycinnamaldehyde Semicarbazone (JMS 18-18)

Semicarbazide HCl (0.2238 g, 0.002007 mol, 1.05 equiv.), NaOAc trihydrate (0.3121 g, 0.002293 mol, 1.20 equiv.), 95% EtOH (5 mL), and aldehyde JMS 16-12 (0.3674 g, 0.001911 mol, 1 equiv.) gave a powder. Recrystallization in 1-butanol (20 mL) afforded the semicarbazone (0.3281 g, 0.001316 mol, 68.9%), which was Custard Cream (370C-2) in color, m.p. 179 ° - 182 °C.

^{1}H NMR: δ 3.33 (3H, s, H_a), 3.75 (3H, s, H_2), 6.27 (2H, broad, H_j), 6.43 (1H, m), 6.69 (2H, m), 6.79 (1H, d, J = 16.2 Hz, H_f), 6.89 (1H, dd, J = 8.84 Hz, J = 15.9 Hz, H_g), 7.66 (1H, d, J = 8.08 Hz, J = , H_h), 10.20 (1H, broad, H_i).*

^{13}C NMR: δ 55.22 (2C, C_1), 100.73 (C_3), 104.54 (2C, C_4), 126.26 (C_5), 136.17 (C_7), 138.15 (C_8), 141.67 (C_6), 156.42 (C_9), 160.65 (2C, C_2).

(2*E*,4*E*)-5-(3-hydroxy-4-methoxyphenyl)penta-2,4-dienal Semicarbazone (JMS 18-19)

Semicarbazide HCl (0.1216 g, 0.001090 mol, 1.05 equiv.), NaOAc trihydrate (0.1696 g, 0.001246 mol, 1.20 equiv.), 95% EtOH (5 mL), and aldehyde JMS 16-13 (0.2120 g, 0.001038 mol, 1 equiv.) gave a powder. Recrystallization in pyridine (50 mL) afforded the semicarbazone (0.0974 g, 0.0003728 mol, 35.9%), which was Clair de Lune (300E-3) in color, m.p. 201 ° - 205 °C.

(2*E*,4*E*,6*E*)-7-(4-methoxyphenyl)hepta-2,4,6-trienal Semicarbazone (JMS 18-20)

Semicarbazide HCl (0.1294 g, 0.001160 mol, 1.05 equiv.), NaOAc trihydrate (0.1805 g, 0.001326 mol, 1.20 equiv.), 95% EtOH (5 mL), and aldehyde JMS 16-14 (0.2368 g, 0.001105 mol, 1 equiv.) gave a powder. Recrystallization in a mixture of 100% EtOH

(600 mL) and DMSO (6 mL) afforded the semicarbazone (0.1249 g, 0.0004604 mol, 41.7%), which was Saffron Thread (310B-7) in color, m.p. 225 ° - 227 °C.

_E_-4-hydroxycinnamaldehyde Semicarbazone (JMS 18-21)

Semicarbazide HCl (0.0627 g, 0.0005620 mol, 1.05 equiv.), NaOAc trihydrate (0.0874 g, 0.0006422 mol, 1.20 equiv.), 95% EtOH (5 mL), and aldehyde JMS 16-15 (0.0793 g, 0.0005352 mol, 1 equiv.) gave a powder. Recrystallization in DMSO (7 mL) afforded the semicarbazone (0.0505 g, 0.0002461 mol, 46.0%), which was Citrus (360B-5) in color, m.p. 215 ° - 217 °C.

^{1}H NMR: δ 5.90 (1H, s, H_a), 6.26 (2H, broad, H_h), 6.76 (1H, dd, J = 8.71 Hz, J = 16.0 Hz, H_e), 6.84 (1H, d, J = 16.4 Hz, H_d), 7.10 (2H, d, J = 8.08 Hz, H_b), 7.51 (2H, d, J = 8.08 Hz, H_c), 7.66 (1H, d, J = 8.84 Hz, H_f), 10.14 (1H, broad, H_g).

_E_-3-methoxycinnamaldehyde Semicarbazone (JMS 18-22)

Semicarbazide HCl (0.3246 g, 0.002910 mol, 1.05 equiv.), NaOAc trihydrate (0.4525 g, 0.003325 mol, 1.20 equiv.), 95% EtOH (5 mL), and aldehyde JMS 16-16 (0.4495 g, 0.002771 mol, 1 equiv.) gave a powder. Recrystallization in 95% EtOH (16 mL) afforded the semicarbazone (0.3917 g, 0.001787 mol, 64.5%), which was Powder Sand (340C-1) in color, m.p. 175 ° - 180 °C. Lit. m.p. 197 °C.[12]

^{1}H NMR: δ 3.77 (3H, s, H_a), 6.28 (2H, broad, H_j), 6.87 (1H, dd, J = 7.58 Hz, J = 16.4 Hz, H_g), 6.86 (1H, s, H_e), 6.90 (1H, d, J = 16.4 Hz, H_f), 7.09 (1H, d, J = 7.57 Hz, H_b & H_d), 7.27 (1H, t, J = 7.32 Hz, H_c), 7.68 (1H, d, J = 7.32 Hz, H_h), 10.20 (1H, broad, H_i).

^{13}C NMR: δ 55.06 (C_1), 111.46 (C_3), 114.37 (C_7), 119.25 (C_5), 125.98 (C_9), 129.79 (C_4), 136.08 (C_8), 137.59 (C_6), 141.73 (C_{10}), 156.43 (C_{11}), 159.56 (C_2).

(2*E*,4*E*)-5-phenylpenta-2,4-dienal Semicarbazone (JMS 18-23)

Semicarbazide HCl (0.3230 g, 0.002896 mol, 1.05 equiv.), NaOAc trihydrate (0.4505 g, 0.003310 mol, 1.20 equiv.), 95% EtOH (5 mL), and aldehyde JMS 16-17 (0.4363 g, 0.002758 mol, 1 equiv.) gave a powder. Recrystallization in 95% EtOH (90 mL) afforded the semicarbazone (0.3591 g, 0.001668 mol, 60.5%), which was Banana Split (360A-3) in color, m.p. 201 ° - 205 °C.

^{1}H NMR: δ 6.26 (2H, broad, H_j), 6.42 (1H, dd, J = 9.60 Hz, J = 15.4 Hz, H_g), 6.69 (1H, dd, J = 10.9 Hz, J = 15.4 Hz, H_e), 6.74 (1H, d, J = 15.7 Hz, H_d), 7.08 (1H, dd, J = 10.9 Hz, J = 15.7 Hz, H_f), 7.27 (1H, t, J = 7.33 Hz, H_a), 7.35 (2H, t, J = 7.46 Hz, H_b), 7.50 (2H, d, J = 7.83 Hz, H_c), 7.60 (1H, d, J = 9.60 Hz, H_h), 10.14 (1H, broad, H_i). Anal. Calcd for $C_{12}H_{13}N_3O$: C, 66.96; H, 6.09; N, 19.52. Found: C, 66.31; H, 6.11; N, 19.62.

(2*E*,4*E*,6*E*)-7-phenylhepta-2,4,6-trienal Semicarbazone (JMS 18-24)

Semicarbazide HCl (0.3253 g, 0.002917 mol, 1.20 equiv.), NaOAc trihydrate (0.4537 g, 0.003334 mol, 1.37 equiv.), 95% EtOH (5 mL), and aldehyde JMS 16-18 (0.4494 g, 0.002439 mol, 1 equiv.) gave a powder. Recrystallization in 95% EtOH (160 mL) afforded the semicarbazone (0.2217 g, 0.0009188 mol, 37.7%), which was Saffron Thread (310B-7) in color, m.p. 214 ° - 217 °C.

(*Z*/*E*)-4-{[tert-butyl-(dimethyl)silyl]oxy}but-2-en-1-ol (JMS 2-1)[24]

To a 500 mL r.b. flask was added *cis*-but-2-ene-1, 4-diol (12.00 g, 0.1362 mol, 2.0 equiv.), 4-dimethylaminopyridine (DMAP), (0.84 g, 0.0068 mol, 0.10 equiv.), imidazole (11.53 g, 0.1694 mol, 2.5 equiv.) and 360 mL of CH_2Cl_2. A solution of TBDMSCl (10.08 g, 0.06688 mol, 1 equiv.) in 24 mL of CH_2Cl_2 was added via addition funnel over ≈ 4 hrs and the solution was allowed to stir overnight. TLC showed the reaction had gone

to completion (3:1 Hex : EtOAc, starting materials (R_f = 0.58) and JMS 2-3 (R_f = 0.15)). The mixture was washed sequentially with deionized water (300 mL), conc. NH_4Cl (100 mL) and brine (200 mL). The organic layers were dried with $MgSO_4$. The solvent was removed under reduced pressure to afford 12.15 g of crude JMS 2-1 (0.06004 mol, 89.7%) as a pale yellow oil.

^{1}H NMR: δ 0.08 (6H, s, H_b), 0.90 (12H, s, H_a), 4.19 (2H, d, J = 5.77 Hz, H_f), 4.25 (2H, d, J = 5.27 Hz, H_c), 5.68 (2H, dt, J = 5.77 Hz, J = 17.06 Hz H_d & H_e).

$^{13}C^3$ NMR: δ -5.30 (2C, C_3), 18.27 (C_1), 25.84 (3C, C_2), 58.68 (C_7), 59.52 (C_4), 130.04 (C_6), 131.16 (C_5)

(JMS 2-2)

The procedure above was repeated exactly, to give 8.11 g of crude JMS 2-2 (0.0401 mol, 59.9%).

(JMS 2-3)

The procedure above was repeated exactly, to give 10.13 g of crude JMS 2-3 (0.0501 mol, 74.9%).

***tert*-butyl{[4-chlorobut-2-en-1-yl]oxy}dimethylsilane (JMS 3-1)**

Alcohol JMS 2-1 (12.15 g, 0.06004 mol, 1equiv.) was added to a 100 mL r.b. flask and placed in an ice bath. Pyridine (5.32 mL, 0.0660 mol, 1.1 equiv.) was added, and then thionyl chloride ($SOCl_2$), 5.46 mL (0.0752 mol, 1.25 equiv.) was added dropwise over ≈ 180 min. After ≈ 3 hrs of stirring the mixture turned a yellowish brown color. TLC (6:1 Hex : EtOAc) showed that the reaction had gone to completion (JMS 2-1 (R_f = 0.61), JMS 3-1 (R_f = 0.43). D.I. H_2O (20 mL) was added to the mixture and it was extracted with ether (3 x 15 mL) and washed with D.I. H_2O (4 x 25 mL). The organic ether layer

was removed under reduced pressure to give 2.52 g of crude JMS 3-1. Purification by vacuum distillation gave 4 fractions, none of which were product.

(JMS 3-2)

The experiment above was repeated 4 times using alcohol JMS 2-2 (1.00 g, 0.00494 mol, 1equiv.), CH_2Cl_2 (0.366 mL), pyridine (0.435 mL, 0.00539 mol, 1.1 equiv.), and $SOCl_2$ (0.442 mL, 0.00609 mol, 1.23 equiv.), to give 0.35 g, 0.57 g, 0.14 g, 0.65 g of crude JMS 3-2.

(JMS 3-3)

Experiment 3-2 was repeated on the same scale, but the solvent was removed under reduced pressure at room temperature, to afford 0.57 g of crude JMS 3-3.

(JMS 3-4)

Experiment 3-3 was repeated on the same scale to give 0.14 g of crude JMS 3-4.

(JMS 3-5)

Experiment 3-3 was repeated on the same scale to give 0.65 g of crude JMS 3-5.

Purification of JMS 3-2, 3-3, 3-4, 3-5

JMS 3-2, 3-3, 3-4, and 3-5 were combined and purified using silica (60 - 200 mesh) gel column chromatography using a solvent system of Hex : EtOAc with 97:3 ratio. Pure JMS 3 was obtained (0.44 g) with a 0.46 R_f.

JMS Pur 3 (2)

^{1}H NMR: δ 0.08 (6H, s, H_b), 0.90 (9H, s, H_a), 4.27 (2H, d, J = 5.77, H_f), 4.60 (2H, d, J = 6.69 Hz, H_c), 5.59 (1H, td, J = 1.76 Hz, J = 6.74 Hz, J = 13.5 Hz, H_d), 5.77 (1H, td, J = 1.50 Hz, J = 5.77 Hz, J = 11.3 Hz, H_e).

^{13}C NMR: δ -5.29 (2C, C_3), 25.84 (3C, C_1), 31.56 (C_2), 57.97 (C_7), 59.49 (C_4), 123.76 (C_6), 134.73 (C_5)

(JMS 3-6)

Experiment 3-3 was repeated using JMS 2-2 (1.02 g, 0.00504 mol, 1equiv.), CH_2Cl_2 (0.3758 mL), pyridine (0.4463 mL, 0.005540 mol, 1.1 equiv.), and $SOCl_2$ (0.4584 mL, 0.00628 mol, 1.25 equiv.) to give 0.53 g of crude JMS 3-6.

(JMS 3-7)

Experiment 3-3 was repeated using JMS 2-2 (3.031 g (0.01498 mol, 1equiv.), CH_2Cl_2 (1.1193 mL), pyridine (1.329 mL, 0.01649 mol, 1.1 equiv.), and $SOCl_2$ (1.369 mL, 0.01877 mol, 1.25 equiv.) to give 1.30 g of crude JMS 3-7.

(JMS 3-8)

Experiment 3-3 was repeated using JMS 2-2 (2.164 g, 0.0107 mol, 1 equiv.), CH_2Cl_2 (0.8005 mL), pyridine (0.9506 mL, 0.01180 mol, 1.1 equiv.), and $SOCl_2$ (0.9705 mL, 0.01331 mol, 1.25 equiv.) to give 1.029 g of crude JMS 3-8.

(JMS 3-9)

Experiment 3-3 was repeated using JMS 2-2 (1.300 g, 0.00642 mol, 1 equiv.), CH_2Cl_2 (0.479 mL), pyridine (0.569 mL, 0.00706 mol, 1.1 equiv.), and $SOCl_2$ (0.584 mL, 0.00801 mol, 1.25 equiv.). TLC (6:1 Hex : EtOAc) to produce spots for JMS 2-2 (R_f = 0.65 & 0.09) and JMS 3-9 (R_f = 0.44). The reaction was worked-up as previously stated to yield 0.46 g of crude JMS 3-9.

(JMS 3-10)

Experiment 3-3 was repeated using JMS 2-2 (1.00 g, 0.00494 mol, 1 equiv.), CH_2Cl_2 (0.458 mL), pyridine (0.446 mL, 0.00554 mol, 1.1 equiv.), and $SOCl_2$ (0.376 mL,

0.00518 mol, 1.25 equiv.). TLC (6:1 Hex : EtOAc) to produce a spots for JMS 3-10 (R_f = 0.44). The reaction was worked-up as previously stated to yield minuscule amounts of JMS 3-10.

(JMS 3-11)

Experiment 3-10 was repeated on the same scale to give minuscule amounts of crude JMS 3-11.

Diethyl [4-{[*tert*-butyl(dimethyl)silyl]oxy}but-2-en-1-yl]phosphonate (JMS 4-1)[25]

In a 10 mL r.b. flask, JMS 3-1 (0.5146 g, 0.002330 mol, 1 equiv.), triethyl phosphite (0.4995 mL, 0.003102 mol, 1.33 equiv.), and sodium iodide (0.6706 g, 0.004474 mol, 1.92 equiv.) were heated to reflux and stirred for ≈ 21 hrs in 6 mL of toluene. TLC (6:1 Hex : EtOAc) showed that the reaction had gone to completion: (JMS 3 (R_f = 0.56), JMS 4-1 (R_f = 0.31)). CH_2Cl_2 (10 mL) was added to the mixture and it was washed with 10% aq. $Na_2S_2O_3$ (10 mL) and extracted with CH_2Cl_2 (10 mL). The organic layer was dried with $MgSO_4$ and removed under reduced pressure to give 0.52 g of crude JMS 4-1 (0.0016 mol, 69.6%) as a clear oil.

^{1}H NMR: δ 0.08 (6H, s, H_b), 0.91 (9H, s, H_a), 1.34 (6H, m), 2.64 (2H, dd, J = 8.03 Hz, J_{HP} = 22.3 Hz, H_f), 4.13 (4H, m), 4.25 (2H, m), 7.17 (1H, dd, J = 2.76 Hz, J = 7.53 Hz, H_d), 7.26 (1H, dd, J = 4.27 Hz, J = 11.6 Hz, H_e).

(JMS 4-2)

The above experiment was repeated using pure JMS 3 (0.5146 g, 0.002330 mol, 1 equiv.), triethyl phosphite (0.4995 mL, 0.003102 mol, 1.33 equiv.), sodium iodide (0.1799 g, 0.001200 mol, 0.52 equiv.) and toluene (6 mL) to give 0.562 g of crude JMS 4-2 (0.0017 mol, 73.0%).

(JMS 4-3)

The above experiment was repeated using pure JMS 3 (0.234 g, 0.00106 mol, 1 equiv.), triethyl phosphite (0.2281 mL, 0.001417 mol, 1.33 equiv.), sodium iodide (0.0826 g, 0.000551 mol, 0.52 equiv.) and toluene (6 mL). TLC (6:1 Hex : EtOAc) showed that the reaction had gone to completion: (JMS 3 (R_f = 0.46), JMS 4-3 (R_f = 0.47)). The reaction was extracted with CH_2Cl_2 (3x10 mL) and dried with $MgSO_4$ and removed under reduced pressure to give 0.233 g of crude JMS 4-3 (0.000723 mol, 68.2%).

(*Z/E*)-diethyl (4-hydroxybut-2-en-1-yl)phosphonate (JMS 13-1)[24]

To a 10 mL r.b. JMS 4-2 (0.145 g, 0.000450 mol, 1 equiv.), 2 mL acetone, and 1 M H_2SO_4 (0.5 mL, 0.0005 mol, 1.1 equiv.) were added and stirred for 3 hrs. TLC (1:2 Hex : EtOAc) produced spots for JMS 4-2 (R_f = 0.31) and JMS 13-1 (R_f = 0.16). The reaction was extracted with CH_2Cl_2 (3x5 mL) and then dried with $MgSO_4$, before removal under reduced pressure to afford 0.076 g of crude JMS 13-1 (0.000365 mol, 81.1%) as a clear oil.

^1H & ^{13}C NMR showed no peaks pertaining to JMS 13-1.

(JMS 13-2)

The above reaction was repeated using JMS 4-3 (0.222 g, 0.000688 mol, 1 equiv.), 2 mL acetone, and 1 M H_2SO_4 (0.5 mL, 0.0005 mol, 1.1 equiv.) to afford 0.125 g of JMS 13-2 (0.0006 mol, 87.3%).

^1H NMR (*cis*-isomer): δ 1.25 (6H, m), 1.66 (2H, dd, J = 7.53 Hz, J_{HP} = 18.1 Hz, H_c), 3.40 (2H, s, H_f), 4.03 (4H, m), 5.06 (1H, broad, H_g), 5.45 (1H, m), 5.84 (4H, m).

^{1}H NMR (*trans*-isomer): δ 1.25 (6H, m), 2.61 (2H, dd, J = 8.28 Hz, J_{HP} = 22.6 Hz, H_c), 3.40 (2H, s, H_f), 4.03 (6H, m), 5.06 (1H, broad, H_g), 5.45 (2H, m).

^{13}C NMR: δ 16.21 (2C, C_1), 25.57 (C_3), 57.71 (C_6), 61.76 (2C, C_2), 130.86 (C_5), 134.11 (C_4).

(JMS 13-3)

The above reaction was repeated using JMS 4-2 (0.048 g, 0.000149 mol, 1 equiv.), 2 mL acetone, and 1 M H_2SO_4 (0.5 mL, 0.0005 mol, 1.1 equiv.). TLC (1:2.5 Hex : EtOAc) produced spots for JMS 4-2 (R_f = 0.31) and JMS 13-3 (R_f = 0.19). The reaction was worked-up as previously stated to afford 0.044 g of crude JMS 13-3.

(*Z/E*)-diethyl (4-oxobut-2-en-1-yl)phosphonate (JMS 17-1)

To a 25 mL r.b. 3Å molecular sieve powder (0.268 g), PDC (0.268 g, 0.000713 mol, 2.09 equiv.) and 15 mL dry CH_2Cl_2 were added. JMS 13-1 (0.071 g, 0.000341 mol, 1 equiv.) was then added drop wise, ~3 hrs, using a cannula and stirred overnight. TLC (1:6 Hex : EtOAc) produced spots for PDC (R_f = 0.13) and JMS 17-1 (R_f = 0.27). The reaction was filtered through Si gel, washed with EtOAc (3x10 mL), dried with $MgSO_4$, before removal under reduced pressure to afford 0.035 g of crude JMS 17-1 as a clear oil. ^{1}H & ^{13}C NMR showed no peaks pertaining to JMS 17-1, only peaks for JMS 13-1.

(JMS 17-2)

The above reaction was repeated using 3Å molecular sieve powder (0.147 g), PDC (0.147 g, 0.000391 mol, 2.09 equiv.), 15 mL dry CH_2Cl_2, and JMS 13-2 (0.039 g, 0.000187 mol, 1 equiv.) to afford 0.013 g of crude JMS 17-2 as clear oil.

^{1}H & ^{13}C NMR showed no peaks pertaining to JMS 17-1, only peaks for JMS 13-1.

Methyl 2-(1, 3-dichloropropan-2-ylidene)hydrazinecarboxylate (JMS 5-1)[45]

To a 250 mL r.b. flask, 1,3-dichloroacetone (10.01 g, 0.07884 mol, 1.01 equiv.), methyl hydrazinocarboxylate (7.03 g, 0.0780 mol, 1 equiv.), and 95% EtOH (75 mL) were added. The mixture was open to normal atmospheric conditions and stirred for ≈ 2 hrs, during which time a white solid formed. The white solid (13.06 g, 0.0656 mol, 84.1%) was obtained by filtration, washed 2x with 95% EtOH and allowed to dry overnight in the desiccator. The melting point of JMS 5-1 was 128° - 131 °C (lit. 136 ° – 138 °C).[45]

^{1}H NMR: δ 3.89 (3H, s, H_a), 4.19 (2H, s, H_b), 4.33 (2H, s, H_c), 8.33 (1H, s, H_d).

(JMS 5-2)

The experiment above was repeated with exactly the same amounts to afford 9.44 g of JMS 5-2 (0.0474 mol, 60.8%), m.p. 129 ° - 133 °C.

Methyl 2-(1, 3-bis (diethoxyphosphoryl) propan-2-ylidene)hydrazinecarboxylate (JMS 6-1)

Toluene (115.5 mL), JMS 5-1 (5.00 g, 0.0251 mol, 1 equiv.) and triethyl phosphite (9.08 mL, 0.0528 mol, 2.11 equiv.) were added to a 250 mL r.b. The mixture was heated to reflux for ≈ 5 hrs. The toluene was removed under reduced pressure, following which CH_2Cl_2 (50 mL) and D.I. H_2O (50 mL) were added to the mixture. After washing the aqueous layer with CH_2Cl_2 (3 x ≈ 33.1 mL), the organic layers were dried with $MgSO_4$ and CH_2Cl_2 was removed under reduced pressure. Crude JMS 6-1 (6.39 g, 0.0159 mol, 63.6%) was afforded as a yellowish colored oil.

(JMS 6-2)

The experiment above was repeated with exactly the same amounts to afford 2.90 g of crude JMS 6-2 (0.007 mol, 28.8%). TLC (3:1 Hex : EtOAc), showed that the reaction had gone to completion: starting materials ($R_f = 0.43$) and JMS 6-1 ($R_f = 0.11$).

(JMS 6-3)

Experiment 6-2 was repeated using toluene (120 mL), JMS 5-1 (3.66 g, 0.0184 mol, 1 equiv.) and $P(OEt)_3$ (6.65 mL, 0.0388 mol, 2.11 equiv.) to give 6.28 g of crude JMS 6-3 (JMS 6-3: 78.4%, $O{=}P(OEt)_3$: 6.4%) . TLC (1:1 Hex : EtOAc), gave an $R_f = 0.67$ for JMS 6-3.

^1H NMR: δ 1.26 (12H, m), 2.93 (2H, d, J_{HP} = 23.8 Hz, H_c), 3.10 (2H, d, J_{HP} = 24.6 Hz, H_d), 3.71 (3H, s, H_e), 4.07 (8H, m), 9.46 (1H, s, H_d).

P^{31} NMR: δ 22.93

(JMS 6-4)

Experiment 6-2 was repeated using toluene (120 mL), JMS 5-1 and JMS 5-2 (4.683 g, 0.02353 mol, 1 equiv.) and $P(OEt)_3$ (7.994 mL, 0.04965 mol, 2.11 equiv.) to give 8.399 g of JMS 6-4 (0.02088 mol, 88.7%).

1, 3-bis(diethylphosphono)acetone (JMS 8-1)

Acetone (12.84 mL), and JMS 6-1 (6.39 g, 0.0159 mol, 1 equiv.) were placed in a 100 mL r.b. flask. Upon addition of 19.12 mL of 3M HCl (0.05736 mol, 3.61 equiv.) the solution was stirred for ≈ 5 hrs. TLC (90:10 CH_2Cl_2 : MeOH) showed the reaction had going to completion: JMS 6-1 ($R_f = 0.81$) and JMS 8-1 ($R_f = 0.67$). D.I. H_2O (50 mL) was added and the organic layer was removed under reduced pressure. The aqueous layer was extracted with CH_2Cl_2 (3 x 50 mL), dried with $MgSO_4$, and the CH_2Cl_2 was removed

under reduced pressure to afford 4.70 g of crude JMS 8-1. JMS 8-1 was purified by SiO_2 column chromatography using a 95:5 CH_2Cl_2 : MeOH to give 3 fractions: 1.17 g, 2.03 g, 0.98 g. Fractions 1 and 3 contained product (2.15 g, 0.00651 mol, 40.9%), while fraction 2 contained only unreacted starting material.

JMS 8-1 (1) and JMS 8-1 (3)

^1H NMR: δ 1.25 (12H, t, J = 5.92 Hz, H_a), 3.17 (4H, d, J_{HP} = 22.64 Hz, H_c), 4.06 (8H, m).

^{31}P NMR: δ 22.50

(JMS 8-2)

The above experiment was repeated using acetone (28.73 mL), JMS 6-2 (11.35 g, 0.02821 mol, 1 equiv.), 3M HCl (28.74 mL, 0.08622 mol, 3.06 equiv.). TLC (10:1 CH_2Cl_2 : MeOH) showed the reaction had going to completion: JMS 6-2 (R_f = 0.53) and JMS 8-2 (R_f = 0.11). The same work-up was employed to give 7.54 crude JMS 8-2. JMS 8-2 was purified by SiO_2 column chromatography using 95:5 CH_2Cl_2 : MeOH to afford 5 fractions: 0.96 g, 0.21 g, 5.23 g, 1.49 g, and 0.96 g. Fraction 1 (No spots) contained unreacted starting material. Fractions 2 and 3 contained semi-pure JMS 8-2 (#1 T1-3 and #1 T4-6), which were recollected. Fractions 4 and 5 contained 2.45 g of pure JMS 8-2, with some toluene (0.00742 mol, 26.3%) TLC (98:2 CH_2Cl_2 : MeOH) produced R_f = 0.46.

(JMS 8-3)

The above experiment was repeated using acetone (14.98 mL), JMS 6-3 (5.92 g, 0.0147 mol, 1 equiv.) and 2.271 mL of 3M HCl (0.00681 mol, 0.46 equiv.) to afford 4.74 g JMS 8-3 (0.0144 mol, 98.0%).

(JMS 8-4)

The above experiment was repeated using acetone (13.36 mL), JMS 6-4 (8.399 g, 0.02088 mol, 1 equiv.) and 0.696 mL of 3M HCl (0.02088 mol, 5.0 equiv.) to afford 5.7081 g JMS 8-3 (0.01728 mol, 82.8%).

Diethyl (4-(2-nitrophenyl)-2-oxobut-3-en-1-yl)phosphonate (JMS 9-1)

To a 10 mL r.b. 0.0305 g LiCl (0.000719 mol, 1.09 equiv.), 3 mL dry DMSO and a stir bar were added. 2-nitrobenzaldehyde, 0.0997 g (0.000660 mol, 1 equiv.) was added to the mixture with a syringe, followed by 1,3-bisphosphonoacetone (0.1982 g, 0.0006006 mol, 0.91 equiv.) and DBU (0.0982 mL, 0.000660 mol, 1 equiv.). The solution was heated at reflux for 4 hrs, and then stirred overnight at room temperature. TLC (3:1 Hex : EtOAc) produced no product spots on the plate. The reaction was quenched with 10 mL conc. NH_4Cl and extracted with 20 mL CH_2Cl_2. The organic layer was washed with D.I. H_2O (4x20 mL) and then dried with $MgSO_4$, before removal under reduced pressure to afford 0.148 g of material.

^1H NMR showed no peaks pertaining to JMS 9-1.

(*Z/E*)-diethyl ((4*E*,6*E*)-2-oxoocta-4,6-dien-1-yl)phosphonate (JMS 19-1a)

JMS 9-1 was repeated using 0.171 g LiCl (0.00403 mol, 12.8 equiv.), 3 mL dry CH_3CN, 1,3-bisphosphonoacetone (0.16 g, 0.000484 mol, 1.54 equiv.), DBU (0.0796 mL, 0.000532 mol, 1.69 equiv.), and crotonaldehyde (0.0260 mL, 0.00314 mol, 1 equiv.). The reaction was worked up as previously described to yield 0.066 g of 1,3-bisphosphonoacetone.

^1H NMR showed no peaks pertaining to pure JMS 19-1a.

(JMS 19-1b)

The above experiment was repeated using 0.101 g LiCl (0.00238 mol, 7.58 equiv.), 3 mL dry CH_3CN, 1,3-bisphosphonoacetone (0.16 g, 0.000484 mol, 1.54 equiv.), DMAP (0.0650 g, 0.000532 mol, 1.69 equiv.), and crotonaldehyde (0.0260 mL, 0.000314 mol, 1 equiv.). The reaction was worked up as previously described to yield 0.042 g of 1,3-bisphosphonoacetone.

Diethyl (3-(2-chlorocyclohexylidene)-2-oxopropyl)phosphonate (JMS 10-1)

JMS 9-1 was repeated using 0.0305 g LiCl (0.000719 mol, 1.2 equiv.), 3 mL dry DMSO, 2-chlorocyclohexanone (0.0754 mL, 0.000660, 1.1 equiv.), 1,3-bisphosphonoacetone (0.1982 g, 0.0006006, 1 equiv.), and 0.0982 mL DBU (0.000660, 1.1 equiv.). TLC (3:1 Hex : EtOAc) produced an $R_f = 0.22$. The reaction was worked-up as stated above to afford 0.058 g of crude JMS 10-1. JMS 10-1 was purified using SiO_2 column chromatography with 1:1.5 Hex : EtOAc to give 3 fractions. The fractions contained 0.025 g of unreacted starting material ($R_f = 0.58$ and 0.22).

(JMS 10-2)

The above experiment was repeated using 0.0246 g LiCl (0.000580 mol, 1.2 equiv.), 3 mL dry CH_3CN, 1,3-bisphosphonoacetone (0.16 g, 0.000484, 1 equiv.), DBU (0.0796 mL, 0.000532, 1.1 equiv.), and 2-chlorocyclohexanone (0.0608 mL, 0.000617, 1.27 equiv.). TLC (3:1 Hex : EtOAc) produced no product spots on the plate. The reaction was worked-up as stated above to afford 0.18 g of starting material.

^1H & ^{13}C NMR showed no peaks pertaining to the JMS 10-2, only peaks for 2-chlorocyclohexanone.

(JMS 10-3)

The above experiment was repeated using 0.166 g LiCl (0.00392 mol, 7.37 equiv.), 3 mL dry CH_3CN, 1,3-bisphosphonoacetone (0.16 g, 0.000484, 0.91 equiv.), DBU (0.0796 mL, 0.000532, 1 equiv.), and 2-chlorocyclohexanone (0.0608 mL, 0.000532, 1 equiv.). TLC (2:1 Hex : EtOAc) produced no product spots on the plate. The reaction was worked-up as stated above to afford 0.046 g of crude JMS 10-3 (contam. with 2-chlorocyclohexanone and BPA).

^{1}H NMR showed no peaks pertaining to the JMS 10-3, only peaks for 2-chlorocyclohexanone and BPA.

Diethyl (5-chloro-4-methyl-2-oxopent-3-en-1-yl)phosphonate (JMS 11-1)

JMS 9-1 was repeated using 0.0305 g LiCl (0.000719 mol, 1.09 equiv.), 3 mL dry DMSO, chloroacetone (0.0526 mL, 0.000660 mol, 1 equiv.), 1,3-bisphosphonoacetone (0.1982 g (0.0006006, 0.91 equiv.) and DBU (0.0982 mL, 0.000660 mol, 1 equiv.). TLC (3:1 Hex : EtOAc) produced no product spots. The reaction was worked-up as stated above to afford 0.027 g of crude material.

^{1}H NMR showed no peaks pertaining to pure JMS 11-1.

Diethyl (3-(2-chlorocyclohexylidene)-2-oxopropyl)phosphonate (JMS 14-1)

In a 10 mL r.b. 1,3-bisphosphonoacetone (0.075 g, 0.00023 mol, 1.01 equiv.) was placed under vacuum for 1 hr. After 1 hr, 5 mL of dry THF was added and the reaction was placed in an ice bath. NaH (60% disp in oil, 0.0139 g, 0.000348 mol, 1.55 equiv.) was added and stirred for 30 min. After 30 min 2-chlorocyclohexanone (0.0257 mL, 0.000225 mol, 1 equiv.) was added, the flask was removed from the ice bath, and stirred overnight. TLC (1:1.5 Hex : EtOAc) produced spots for 2-chlorocyclohexanone (R_f =

0.35) and JMS 14-1 (R_f = 0.57). The reaction was quenched with 10 mL conc. NH_4Cl and extracted with EtOAc (2x10 mL). The organic layer was washed with brine (2x10 mL) and then dried with $MgSO_4$, before removal under reduced pressure to afford 0.067 g of crude JMS 14-1.

^1H NMR showed no peaks pertaining to pure JMS 14-1.

(*Z/E*)-diethyl (5-chloro-4-methyl-2-oxopent-3-en-1-yl)phosphonate (JMS 15-1a)

The above reaction was repeated using 1,3-bisphosphonoacetone (0.096 g, 0.00029 mol, 1.01 equiv.), 5 mL dry THF, NaH (60% disp. in oil, 0.0178 g, 0.000445 mol, 1.55 equiv.), and chloroacetone (0.0232 mL, 0.000288 mol, 1 equiv.). TLC (1:1.5 Hex : EtOAc) produced spots for chloroacetone (R_f = 0.39) and JMS 15-1a (R_f = 0.52). The reaction was worked-up as previously stated to yield 0.042 g of crude JMS 15-1a.

^1H NMR showed no peaks pertaining to pure JMS 15-1a, only peaks for 1,3-bisphosphonoacetone.

(JMS 15-1b)

The above reaction was repeated using 1,3-bisphosphonoacetone (0.066 g, 0.00020 mol, 1.01 equiv.), 5 mL dry THF, NaH (60% disp. in oil, 0.0081 g, 0.000203 mol, 1.03 equiv.), and chloroacetone (0.0159 mL, 0.000198 mol, 1 equiv.) to yield 0.044 g of crude JMS 15-1b.

^1H NMR showed no peaks pertaining to pure JMS 15-1b, only peaks for 1,3-bisphosphonoacetone.

(JMS 15-1c)

The above reaction was repeated using 1,3-bisphosphonoacetone (0.974 g, 0.00295 mol, 1.01 equiv.), 5 mL dry THF, NaH (60% disp. in oil, 0.175 g, 0.00438 mol, 1.5

equiv.), and chloroacetone (0.235 mL, 0.00292 mol, 1 equiv.) to yield miniscule amounts of JMS 15-1c.

^{1}H, ^{13}C, & ^{31}P NMR showed no peaks pertaining to pure JMS 15-1c, only peaks for 1,3-bisphosphonoacetone.

(*Z/E*)-diethyl (5-methyl-2-oxohept-3-en-1-yl)phosphonate (JMS 20-1a)

To a 100 mL r.b. 0.0321 g dry LiCl (0.000757 mol, 1.18 equiv.) and 20 mL dry CH_3CN were added. 1,3-bisphosphonoacetone (0.25 g, 0.000757 mol, 1.18 equiv.), DBU (0.0960 mL, 0.000642 mol, 1 equiv.), and 2-methylbutyraldehyde (0.0687 mL, 0.000642 mol, 1 equiv.) were added respectively. The reaction was worked up as previously described to yield 0.053 g of 1,3-bisphosphonoacetone.

(JMS 20-1b)

The above reaction was repeated using 0.0848 g dry LiCl (0.00199 mol, 3.11 equiv.), 20 mL dry CH_3CN, 1,3-bisphosphonoacetone (0.25 g, 0.000757 mol, 1.18 equiv.), DBU (0.0960 mL, 0.000642 mol, 1 equiv.), and 2-methylbutyraldehyde (0.0687 mL, 0.000642 mol, 1 equiv.). TLC (2:1 Hex : EtOAc) produced spots for 2-methylbutyraldehyde (R_f = 0.07) and JMS 20-1b (R_f = 0.69). The reaction was worked up as previously stated to yield 0.068 g of 1,3-bisphosphonoacetone.

(JMS 21-1a)

JMS 7-1b was repeated using chloroacetone (0.217 mL, 0.00270 mol, 1 equiv.), 1,3-bisphosphonoacetone (0.981 g, 0.00297 mol, 1.1 equiv.), 25 mL of "dry" CH_2Cl_2, 18-Crown-6 ether (0.249 g, 0.000945 mol, 0.35 equiv.) and anhydrous K_2CO_3 (1.231 g, 0.00891 mol, 3.3 equiv.). TLC (9:1 CH_2Cl_2 : MeOH) produced spots for chloroacetone

(R_f = 0.66) and JMS 21-1a (R_f = 0.72). The reaction was worked up as previously stated to yield 1.0939 g of crude material.

(JMS 22-1a)

To a 100 mL r.b. 0.0485 g $KHCO_3$ (0.000484 mol, 1 equiv.) in 25 mL D.I. H_2O was added. 1,3-bisphosphonoacetone (0.16 g, 0.000484 mol, 1 equiv.) in 25 mL *t*-BuOH was then added. Crotonaldehyde (0.0196 mL, 0.000237 mol, 0.49 equiv.) was added and the mixture was stirred for 6 hrs at 25 °C. The reaction was worked up as previously described to yield 0.164 g of 1,3-bisphosphonoacetone.

(JMS 22-2a)

To a 100 mL r.b. 1,3-bisphosphonoacetone (0.4709 g, 0.001426 mol, 1 equiv.) and distilled chloroacetone (0.0954 mL, 0.001186 mol, 0.83 equiv.) in 20 mL *t*-BuOH was added. $KHCO_3$ (0.1428 g, 0.001426 mol, 1 equiv.) in 20 mL D.I. H_2O was then added and the mixture was heated at reflux for 5 hrs. The product was extracted with ether (3 x 20 mL) and washed with brine (3 x 20 mL) to afford 0.2872 g of 1,3-bisphonoacetone.

(JMS 22-2b)

The above reaction was repeated using; 1,3-bisphosphonoacetone (0.5703 g, 0.001727 mol, 1 equiv.) and distilled chloroacetone (0.0115 mL, 0.001433 mol, 0.83 equiv.) in 20 mL *t*-BuOH, and $KHCO_3$ (0.1729 g, 0.001727 mol, 1 equiv.) in 20 mL D.I. H_2O except the mixture was heated at reflux overnight. The reaction was worked up as previously described to yield 0.3685 g of 1,3-bisphosphonoacetone.

(JMS 22-3a)

The above reaction was repeated using; 1,3-bisphosphonoacetone (0.5239 g, 0.001586 mol, 1 equiv.) and 2-nitrobenzaldehyde (0.1989 g, 0.001316 mol, 0.83 equiv.)

in 20 mL *t*-BuOH, and $KHCO_3$ (0.1588 g, 0.001586 mol, 1 equiv.) in 20 mL D.I. H_2O. The reaction was worked up as previously described to yield 0.4632 g of the dicondensate.

2-oxocyclohexyl 4-methylbenzenesulfonate (JMS 12-1)

To a 10 mL r.b. were added, cyclohexanone (0.075 mL, 0.00072 mol, 1 equiv.), Koser reagent (0.31 g, 0.00079, 1.1 equiv.) and CH_3CN (5 mL) and the mixture was heated at reflux for 5 hrs and stirred overnight at room temperature. TLC (7:3 Hex : EtOAc) gave an R_f = 0.65. The CH_3CN was removed under reduced pressure and the crude oil was dissolved in 20 mL of CH_2Cl_2. The organic layer was washed with D.I. H_2O (2 x 30 mL), dried with $MgSO_4$ and removed under reduced pressure to afford a white solid, which was then washed with hexanes (2 x 2 mL).

Ethyl 2-(2-chlorocyclohexylidene)acetate (JMS M-1a)

To a 10 mL r.b. 0.0153 g LiCl (0.000360 mol, 1.2 equiv.), 3 mL dry DMSO, 2-chlorocyclohexanone (0.0377 mL, 0.000330 mol, 1.1 equiv.), triethyl phosphonoacetate (0.0596 mL, 0.000300 mol, 1 equiv.) and DBU (0.0494 mL, 0.000330 mol, 1.1 equiv.) were added and the mixture was allowed to stir overnight. TLC (3:1 Hex : EtOAc) produced spots for 2-chlorocyclohexanone (R_f = 0.46) and JMS M-1a (R_f = 0.39). The reaction was quenched with 10 mL conc. NH_4Cl and extracted with CH_2Cl_2 (20 mL). The organic layer was washed with D.I. H_2O (4 x 20 mL), dried with $MgSO_4$ and removed under reduced pressure to afford minuscule amount of JMS M-1a.

^1H & ^{13}C NMR showed no peaks pertaining to the JMS M-1a, only peaks for 2-chlorocyclohexanone and triethyl phosphonoacetate.

(JMS M-1b)

The above experiment was repeated with exactly the same amounts to afford 0.07 g of crude JMS M-1b.

^{1}H NMR showed no peaks pertaining to the JMS M-1b.

(JMS M-1c)

To a 10 mL r.b. LiCl (0.0306 g, 0.000722 mol, 1.20 equiv.), 3 mL dry DMSO, triethyl phosphonoacetate (0.1192 mL, 0.0006028 mol, 1 equiv.) and DBU, 0.0988 mL (0.000662 mol, 1.09 equiv.) were added and stirred. After 10 min, 2-chlorocyclohexanone (0.0754 mL, 0.000662 mol, 1 equiv.) was added to the mixture and stirred overnight. The reaction was quenched with 10 mL conc. NH_4Cl and CH_2Cl_2 (20 mL) was added to the mixture. The organic layer was washed with D.I. H_2O (4 x 20 mL), dried with $MgSO_4$ and removed under reduced pressure to afford 0.036 g of 2-chlorocyclohexenone and a significant amount of the elimination product (cyclohex-2-enone, 1.4 : 1 cyclohex-2-enone : 2-chlorocyclohexenone).

(JMS M-1d)

The above reaction was repeated using 0.1742 g LiCl (0.004109 mol, 1.20 equiv.), 3 mL dry DMSO, triethyl phosphonoacetate (0.6805 mL, 0.003430 mol, 1 equiv.), DBU (1.0154 mL, 0.006786 mol, 1.98 equiv.), and 2-chlorocyclohexanone (0.4309 mL, 0.003770 mol, 1.10 equiv.) to afford 0.236 g of triethyl phosphonoacetate.

(JMS M-1e)

JMS M-1c was repeated exactly except it was heated to reflux for 45 min prior to the addition of 2-chlorocyclohexanone (0.4309 mL, 0.003770 mol, 0.63 equiv.). TLC (3:1 Hex : EtOAc) produced spots for 2-chlorocyclohexanone (R_f = 0.26) and JMS M-1e (R_f =

0.72). The work-up was identical as before to yield 0.12 g (33%) of the elimination product (cyclohex-2-enone).

(JMS M-1f)

JMS M-1e was repeated exactly except CH_3CN was used instead of DMSO. The mixture was heated to reflux and stirred overnight. TLC (2:1 Hex : EtOAc) produced an R_f = 0.58 for JMS M-8a. The reaction was quenched with 5 mL NH_4Cl and 20 mL CH_2Cl_2 was added to the mixture. The mixture was washed with D.I. H_2O (4x20 mL) and then dried with $MgSO_4$. CH_2Cl_2 was removed under reduced pressure to afford 0.31 g of crude material that was neither starting material nor desired product by ^1H NMR.

(JMS M-1g)

JMS M-1e was repeated using 0.153 g LiCl (0.00361 mol, 11.9 equiv.), 3 mL dry DMSO, triethyl phosphonoacetate (0.0596 mL, 0.000301 mol, 1 equiv.), DBU (0.0494 mL, 0.000331 mol, 1.10 equiv.), and 2-chlorocyclohexanone (0.0377 mL, 0.000331 mol, 1.10 equiv.). TLC (3:1 Hex : EtOAc) produced an R_f = 0.62 for JMS M-1g. The reaction was worked up as above to yield crude JMS M-1g (0.04 g, 0.000190 mol, 57.6%, contam. with triethyl phosphonoacetate).

(JMS M-1h)

Experiment JMS M-1a was repeated only differing in that 0.0352 g LiCl (0.000830 mol, 2.76 equiv.) was used. TLC (3:1 Hex : EtOAc) produced an R_f = 0.62 for JMS M-1h for JMS M-4. The work-up was identical as before to yield 0.07 g of crude material that was starting material.

(JMS M-1i)

JMS M-1e was repeated exactly except with CH_3CN instead of DMSO. TLC (2:1 Hex : EtOAc) produced an $R_f = 0.72$ for JMS M-1i. The work-up was identical as before to yield 0.25 g of crude JMS M-1i (0.00123 mol, 35.9%) as minor component.

^{1}H NMR: δ 1.17 (3H, m), 1.28 (4H, m), 1.59 (2H, m), 2.01 (2H, m), 4.06 (2H, m), 5.54 (1H, d J = 2.01 Hz, H_c), 6.21 (1H, t, J = 2.76 Hz, H_d)

^{13}C NMR (*cis*/*trans*-isomers) w/DEPT: δ 14.10 (1C, C_1, CH_3), 22.24 (C1, C_8, CH_2), 23.73 (C1, C_7, CH_2), 33.60 (1C, C_6, CH_2), 39.29 (1C, C_9, CH_2), 54.39 (1C, C_{10}, CH), 60.51 (1C, C_2, CH_2), 112.02 (1C, C_4, CH), 115.34 (1C, C_4, CH), 126.67 (1C, C_4, CH), 126.87 (1C, C_4, CH), 158.07 (1C, C_5), 170.59 (1C, C_3).

(*Z*/*E*)-ethyl-3-(2-nitrophenyl)but-2-enoate (JMS M-2a)

JMS M-1a was repeated using 0.0306 g LiCl (0.000720 mol, 1.2 equiv.), 6 mL dry DMSO, 2-nitrobenzaldehyde (0.0906 g, 0.000661 mol, 1.1 equiv.), triethyl phosphonoacetate (0.1192 mL, 0.0006008 mol, 1 equiv.) and DBU (0.0988 mL, 0.000661 mol, 1.1 equiv.) to afford crude JMS M-2a (0.06 g, 0.00027 mol, 44.9%) with a 18.8 : 86.2 *cis* : *trans* ratio.

^{1}H NMR (*trans*-isomer): δ 1.26 (3H, t, J = 7.16 Hz, H_a), 4.20 (2H, q, J = 7.19 Hz, H_b), 6.29 (1H, d, J = 15.8 Hz, H_c), 7.59 (2H, m), 7.95 (1H, ddd, J = 0.76 Hz, J = 1.51 Hz, J = 8.03 Hz, H_f), 8.01 (1H, d, J = 15.8 Hz, H_d).

^{1}H NMR (*cis*-isomer): δ 1.02 (3H, t, J = 7.12 Hz, H_a), 3.93 (2H, q, J = 7.11 Hz, H_b), 6.02 (1H, d, J = 11.8 Hz, H_c), 7.48 (1H, m), 7.59 (2H, m), 8.01 (1H, d, J = 15.8 Hz, H_h), 8.07 (1H, dd, J = 1.25 Hz, J = 8.28 Hz, H_e).

(JMS M-2b)

JMS M-1c was repeated exactly to afford crude JMS M-2b (0.053 g, 0.00024 mol, 36.4%, contam. with starting material) with a 14.5 : 85.5 *cis* : *trans* ratio.

(*Z/E*)-ethyl 3-methylhex-2-enoate (JMS M-3a)

JMS M-1c was repeated exactly, except 2-pentanone (0.0699 mL, 0.000661, 1 equiv.), was used in place of 2-nitrobenzaldehyde to afford 0.028 g of 2-pentanone and triethyl phosphonoacetate.

Ethyl 2-cyclohexylideneacetate (JMS M-4a)

JMS M-1c was repeated using 0.2353 g LiCl (0.00555 mol, 1.20 equiv.), 3 mL dry DMSO, triethyl phosphonoacetate (0.919 mL, 0.00463 mol, 1 equiv.), DBU (1.37 mL, 0.00916 mol, 1.98 equiv.) and cyclohexanone (0.5275 mL, 0.00509 mol, 1.10 equiv.) to afford crude JMS M-4a (0.596 g, 0.00354 mol, 76.5%).

^{1}H NMR: δ 1.26 (3H, t, J = 7.14 Hz, H_a), 1.64 (4H, m), 1.70 (1H, m), 1.84 (2H, m), 2.31 (2H, t, J = 6.7 Hz, H_g), 4.11 (2H, q, J = 7.13 Hz, H_b), 5.53 (1H, s, H_c).

^{13}C NMR: δ 14.13 (C_1), 22.62 (C_8), 28.27 (2C, C_7), 29.71 (C_9), 37.88 (C_6), 60.30 (C_2), 112.90 (C_4), 163.41 (C_5), 166.73 (C_3).

(*Z/E*)-ethyl 2-(2-chlorocyclohexylidene)acetate (JMS M-5a)

As before in JMS M-1e; 0.174 g LiCl (0.000411 mol, 1.20 equiv.), 3 mL DMSO, triethyl phosphonoacetate (0.681 mL, 0.000343 mol, 1 equiv.) and DBU (1.015 mL, 0.000679 mol, 1.98 equiv.) were heated at reflux 45 min before addition of 2-methylcyclohexanone (0.292 mL, 0.000377 mol, 1.10 equiv.). The work-up was identical as before to yield 0.11 g of 2-methylcyclohexanone.

***E*-ethyl 3-(4-nitrophenyl)but-2-enoate (JMS M-6a)**

JMS M-1e was repeated using 0.103 g LiCl (0.00243 mol, 0.88 equiv.), 3 mL dry CH_3CN, triethyl phosphonoacetate (0.5476 mL, 0.00276 mol, 1 equiv.), DBU (0.0453 mL, 0.00303 mol, 1.10 equiv.), and *p*-nitroacetophenone (0.4999 g, 0.00303 mol, 1.10 equiv.). TLC (2:1 Hex : EtOAc) produced spots for *p*-nitroacetophenone ($R_f = 0.32$) and JMS M-6a ($R_f = 0.46$). The reaction was worked up as previously described to yield 0.33 g of crude JMS M-6a (0.23 g, 0.00098 mol, 35.0%) with a 70.7 : 29.6 product : s. mat. ratio.

^{1}H NMR: δ 1.33 (3H, t, J = 7.28 Hz, H_a), 2.60 (3H, d, J = 1.5 Hz, H_d), 4.25 (2H, q, J = 7.28 Hz, H_b), 6.19 (1H, q, J = 1.26 Hz, H_c), 7.62 (2H, d, J = 8.78 Hz, H_e), 8.24 (2H, d, J = 9.03 Hz, H_f).

^{13}C NMR: δ 14.27 (C_1), 17.91 (C_5), 60.29 (C_2), 120.14 (C_4), 123.79 (2C, C_9), 127.22 (2C, C_8), 141.35 (C_{10}), 148.58 (C_7), 152.67 (C_6), 166.10 (C_3)

***E*-ethyl 4-methylhex-2-enoate (JMS M-7a)**

To a 100 mL r.b. 0.0848 g dry LiCl (0.00201 mol, 1 equiv.) and 20 mL dry CH_3CN were added. Triethyl phosphonoacetone (0.398 mL, 0.00201 mol, 1 equiv.), DBU (0.254 mL, 0.00169 mol, 0.84 equiv.), and 2-methylbutyraldehyde (0.182 mL, 0.0169 mol, 0.84 equiv.) were added respectively. The reaction was worked up as previously described to yield 0.176 g crude JMS M-7a (0.000548 mol, 27%) with a 44.9 : 55.1 ratio to triethyl phosphonoacetone.

^{1}H NMR: δ 0.83 (3H, t, J = 7.53 Hz, H_i), 0.99 (3H, d, J = 6.77 Hz, H_g), 1.23 (6H, t, J = 7.78 Hz, H_a), 1.35 (2H, m), 2.16 (1H, m), 2.91 (2H, d, J_{HP} = 21.6 Hz, H_c), 4.14 (4H, q, J

= 7.02 Hz, H_b), 5.72 (1H, dd, J = 1.25, J = 15.8 Hz, H_d), 6.80 (1H, dd, J = 7.78 Hz, J = 15.6 Hz, H_e).

(2*Z/E*,4*Z/E*)-ethyl hexa-2,4-dienoate (JMS M-8a)

The above reaction was repeated using exactly the same amount except crotonaldehyde (0.0830 mL, 0.001002 mol, 0.50 equiv.) was used in place of 2-methylbutyraldehyde. TLC (2:1 Hex : EtOAc) produced an R_f = 0.49 for JMS M-8a. The reaction was worked up as previously stated to yield 0.091 g (47%) of crude material that was a 72 : 28 ratio of product to s. mat.

^{1}H NMR: δ 1.27 (3H, m), 1.81 (3H, d, J = 5.77 Hz, H_g), 4.14 (2H, m), 5.72 (1H, d, J = 15.3 Hz, H_c), 5.83 (1H, J = 15.8 Hz, H_e), 6.12 (1H, dq, J = 10.3 Hz, J = 16.1 Hz, H_f), 7.20 (1H, dd, J = 9.54 Hz, J = 15.6 Hz, H_d).

***E*-ethyl 2-(2-chlorocyclohexylidene)acetate (JMS M-9a)**

The above reaction was repeated using 0.151 g dry LiCl (0.00352 mol, 1 equiv.), 20 mL dry CH_3CN, triethyl phosphonoacetone (0.714 mL, 0.00352 mol, 1 equiv.), DBU (0.464 mL, 0.00310 mol, 0.88 equiv.), and 2-chlorocyclohexanone (0.354 mL, 0.00310 mol, 0.88 equiv.). TLC (2:1 Hex : EtOAc) produced spots from 2-chlorocyclohexanone (R_f = 0.37) and JMS M-9a (R_f = 0.49). The reaction was worked up as previously stated to yield 0.299 g of crude material.

^{1}H NMR showed minor peaks pertaining to the JMS M-9a, but also showed major peaks for 2-chlorocyclohexenone, triethyl phosphonoacetone and the elimination product (cyclohex-2-enone).

(*Z/E*)-ethyl 4-chloro-3-methylbut-2-enoate (JMS M-10a)

In a 10 mL r.b. triethyl phosphonoacetone (0.085 g, 0.00038 mol, 1 equiv.) was placed under vacuum for 1 hr. After 1 hr, 5 mL of dry THF was added and the reaction was placed in an ice bath. NaH (0.0153 g, 0.000383 mol, 1.01 equiv.) was added and stirred for 30 min. After 30 min chloroacetone (0.0302 mL, 0.000375 mol, 0.99 equiv.) was added, the flask was removed from the ice bath, and stirred overnight. The reaction was quenched with 10 mL sat. NH_4Cl and extracted with EtOAc (2x10 mL). The organic layer was washed with brine (2x10 mL) and then dried with $MgSO_4$, before removal under reduced pressure to afford 0.048 g of crude material.

^1H NMR showed no peaks pertaining to the JMS M-10a only peaks for triethyl phosphonoacetone.

(*Z/E*)-ethyl 3-(2-nitrophenyl)acrylate (JMS M-11)

The above reaction was repeated using triethyl phosphonoacetone (1.00 g, 0.00446 mol, 1 equiv.), 5 mL of dry THF, NaH (0.0180 g, 0.00451 mol, 1.01 equiv.), and 2-nitrobenzaldehyde (0.668 g, 0.00442 mol, 0.99 equiv.). The reaction was worked-up as previously stated to afford 0.516 g of crude material, containing JMS M-11 as the minor component and 2-nitrobenzaldehyde and triethyl phosphonoacetone as the major components, in a 1.00 : 2.77 : 1.17 ratio.

(*Z/E*)-ethyl 4-chloro-3-methylbut-2-enoate (JMS M-12)

The above reaction was repeated using triethyl phosphonoacetone (1.01 g, 0.00449 mol, 1 equiv.), 5 mL of dry THF, NaH (0.267 g, 0.00668 mol, 1.49 equiv.), and chloroacetone (0.358 mL, 0.00445 mol, 0.99 equiv.). The reaction was worked-up as previously stated to afford miniscule amounts of JMS M-12.

^{1}H NMR showed no peaks pertaining to the JMS M-12 only peaks for chloroacetone and triethyl phosphonoacetone.

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Table A.1: Absorption wavelengths (λ) and molar absorptivity (ε) of cinnamaldehydes (3).*

X	n	λ	ε (E+04)	λ	ε (E+04)	λ	ε (E+04)	λ	ε (E+04)
H	1			283.5	9.81	224.5	42.5	206.0	3.81
2-OMe	1	330.5	0.0745	280.5	0.127	229.5	0.0723	213.5	0.0757
	2	338.5	0.394	310.5	0.351			196.0	55.3
4-OMe	1			315.5	14.0	231.0	5.32		
	2	343.0	15.0			241.0	5.57		
3,4,5-triOMe	1			314.0	17.0	235.5	17.0		
2,4,6-triOMe	1	330.5	12.4			246.0	4.34	201.0	10.1
2,4,5–triOMe	1	363.5	8.32	297.0	6.62	244.0	4.85	223.5	3.92
2,5-diOMe	1								
2-NO_2	1					248.5	10.5		
β-phenyl	1			295.0	14.8				

* λ values are in nm and ε values are in M^{-1} cm^{-1}.

Table A.2: Absorption wavelengths (λ) and molar absorptivity (ε) of the "light" versions of semicarbazones (4).*

X	n	λ	ε (E+04)	λ	ε (E+04)	λ	ε (E+04)	λ	ε (E+04)
H	1			308.5	25.2	232.0	5.59	200.5	7.73
2-OMe	1	330.0	6.14	297.5	6.02	234.0	2.02	208.0	2.01
	2	345.5	189			245.5	28.5	212.5	36.6
4-OMe	1			321.5	13.3	235.0	2.52	227.5	2.17
	2	341.5	4280						
3,4,5-triOMe	1			320.5	21.5	240.5	10.9		
	2	344.0	1.14			257.0	0.180	200.0	0.473
2,4,6-triOMe	1	330.5	19.6			247.0	5.76	202.0	7.51
2,4,5–triOMe	1	353.0	26.4	302.0	21.1	244.0	9.72	204.0	11.3
2,3,4-triOMe	1			321.0	21.6	249.0	7.06	206.0	26.2
2,5-diOMe	1	346.0	0.547	299.0	0.890			205.0	2.15
3-OH, 4-OMe	1			319.0	0.00699				
3-OMe, 4-OH	1			325.0	0.237				
2-NO_2	1			292.5	16.8				
β-phenyl	1			315.0	21.5	234.5	11.5		
Acetone	1					223.0	4.61		

* λ values are in nm and ε values are in M^{-1} cm^{-1}.

Table A.3: Crystal data, data collection, and refinement parameters for the crystal structure (Figure 1.6) of 2,4,6-trimethoxycinnamaldehyde semicarbazone (JMS 18-9) grown from 95% EtOH.

Crystal data

$C_{13}H_{17}N_3O_4$	F(000) = 592
M_r = 279.30	-
Monoclinic, $P\,2_1/n$	D_x = 1.081 Mg m^{-3}
Hall symbol: -*P* 2x*n*	Melting point: - K
a = 14.084 (2) Å	Mo *K*α radiation, λ = 0.71073 Å
b = 8.7858 (13) Å	Cell parameters from ? reflections
c = 15.135 (2) Å	θ = -°
α = 90.00°	μ = 0.08 mm^{-1}
β = 113.634 (2)°	*T* = 296 K
γ = 90.00°	-
V = 1715.7 (4) $Å^3$	× × mm
Z = 4	

Data collection

-	3136 independent reflections
Radiation source: fine-focus sealed tube	1610 reflections with $I > 2\sigma(I)$
graphite	R_{int} = 0.055
Detector resolution: -	θ_{max} = 25.4°, θ_{min} = 1.7°
Scans: -	$h = -16 \rightarrow 16$
Absorption correction: -	$k = -10 \rightarrow 10$
T_{min} = -, T_{max} = -	$l = -17 \rightarrow 18$
9833 measured reflections	

Refinement

Refinement on F^2	Secondary atom site location: difference Fourier map
Least-squares matrix: full	Hydrogen site location: inferred from neighbouring sites
$R[F^2 > 2\sigma(F^2)] = 0.051$	H atoms treated by a mixture of independent and constrained refinement
$wR(F^2) = 0.13$	$w = 1/[\sigma^2(F_o^2) + (0.0637P)^2 + 0.4144^P]$ where $P = (F_o^2 + 2F_c^2)/3$
S = 0.97	$(\Delta/\sigma)_{max} = 0.073$
3136 reflections	$\Delta\rho_{max} = 0.24$ e Å^{-3}
235 parameters	$\Delta\rho_{min} = -0.17$ e Å^{-3}
3 restraints	Extinction correction: none
0 constraints	
Primary atom site location: structure-invariant direct methods	Flack parameter: -
	Roger parameter: -

Table A.4: Crystal data, data collection, and refinement parameters for the crystal structure (Figure 1.7) of 2,4,6-trimethoxycinnamaldehyde semicarbazone (JMS 18-9) grown from CH_3CN.

Crystal data

$C_{13}H_{17}N_3O_4$	F(000) = 592
M_r = 279.30	-
Triclinic, $P\bar{1}$	D_x = 1.349 Mg m^{-3}
Hall symbol: -P 1	Melting point: - K
a = 8.2031 (2) Å	Cu $K\alpha$ radiation, λ = 1.54178 Å
b = 12.7085 (3) Å	Cell parameters from 9994 reflections
c = 14.0626 (3) Å	θ = 3.2–71.4°
α = 93.127 (1)°	μ = 0.85 mm^{-1}
β = 101.646 (1)°	T = 100 K
γ = 105.448 (1)°	Transparent plate, light yellow
V = 1374.82 (6) Å^3	0.47 × 0.35 × 0.32 mm
Z = 4	

Data collection

Bruker APEXII CCD diffractometer	4787 independent reflections
Radiation source: fine-focus sealed tube	4397 reflections with $I > 2\sigma(I)$
graphite	R_{int} = 0.022
Detector resolution: 8.33 pixels mm^{-1}	θ_{max} = 68.2°, θ_{min} = 3.2°
phi and ω scans	$h = -9 \rightarrow 9$
Absorption correction: multi-scan SADABS (Bruker, 2010)	$k = -15 \rightarrow 15$
T_{min} = 0.694, T_{max} = 0.772	$l = -16 \rightarrow 16$
17697 measured reflections	

Refinement

Refinement on F^2	Secondary atom site location: difference Fourier map
Least-squares matrix: full	Hydrogen site location: inferred from neighbouring sites
$R[F^2 > 2\sigma(F^2)] = 0.032$	H atoms treated by a mixture of independent and constrained refinement
$wR(F^2) = 0.085$	$w = 1/[\sigma^2(F_o^2) + (0.0471P)^2 + 0.4144^P]$ where $P = (F_o^2 + 2F_c^2)/3$
S = 1.05	$(\Delta/\sigma)_{max} = 0.001$
4908 reflections	$\Delta\rho_{max} = 0.18$ e Å^{-3}
385 parameters	$\Delta\rho_{min} = -0.22$ e Å^{-3}
0 restraints	Extinction correction: none
0 constraints	
Primary atom site location: structure-invariant direct methods	

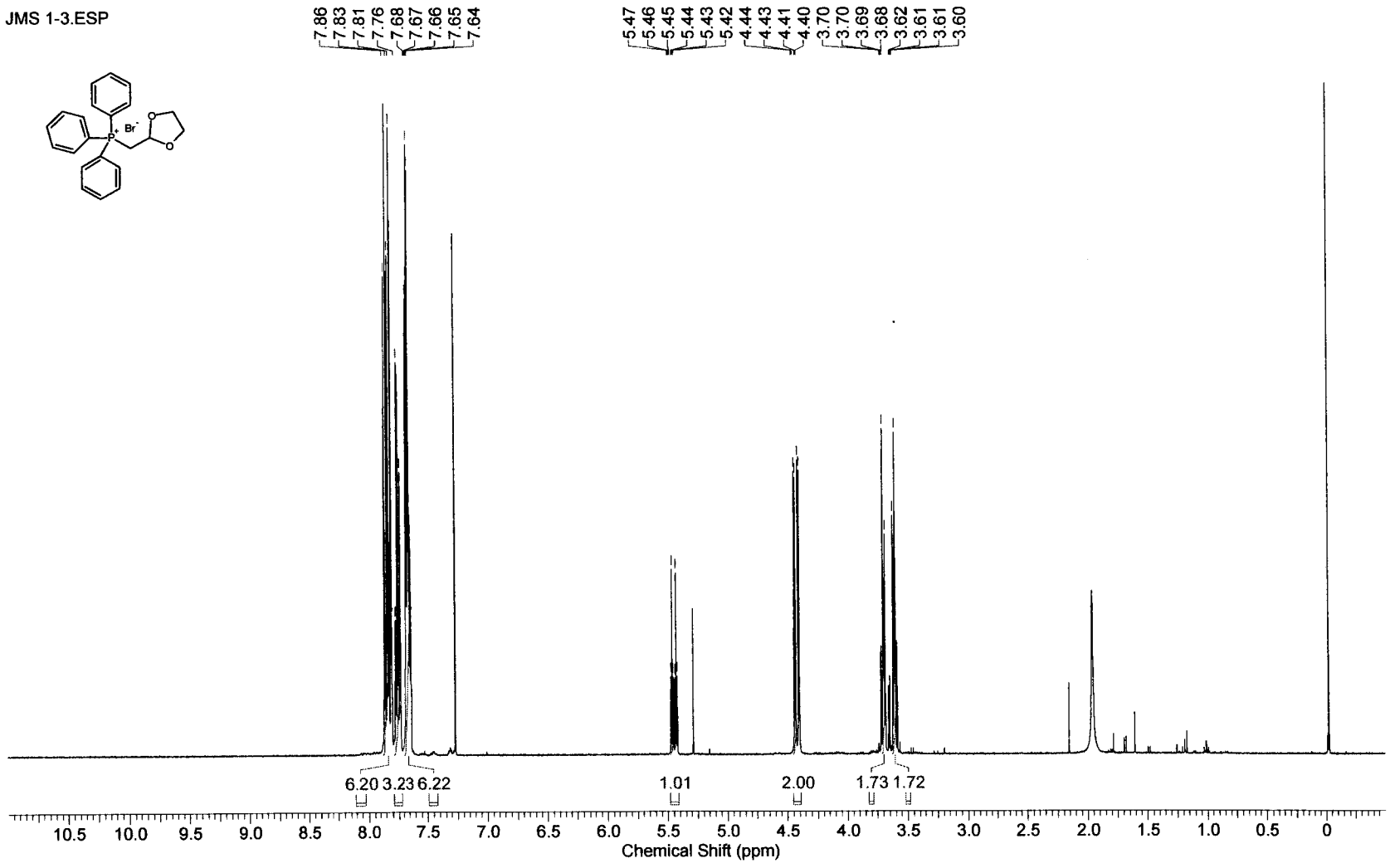

Figure A.1: ^{1}H NMR Spectrum of (1,3-dioxolan-2-ylmethyl)-triphenylphosphonium bromide (JMS 1-3)

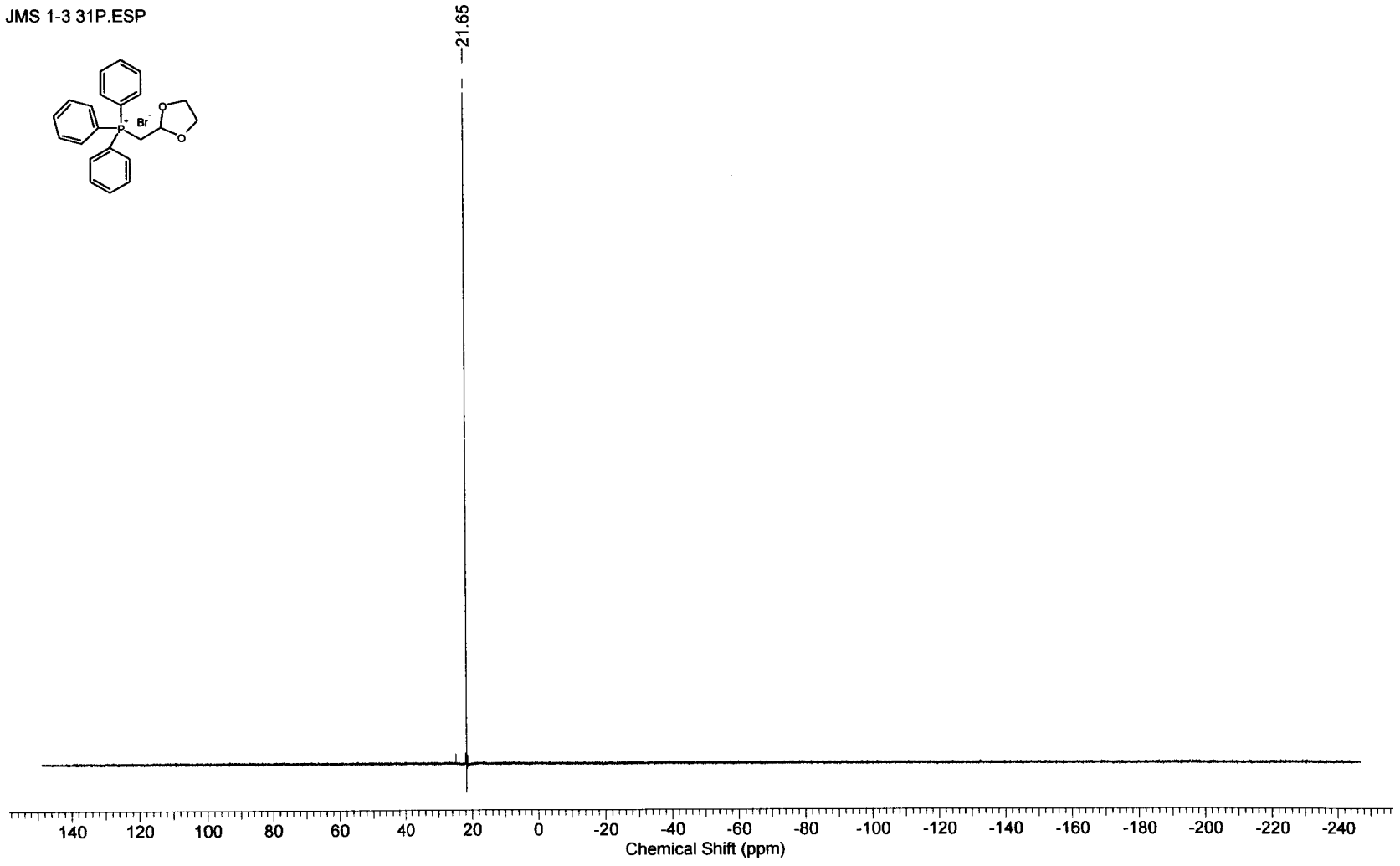

Figure A.2: ^{31}P NMR Spectrum of (1,3-dioxolan-2-ylmethyl)-triphenylphosphonium bromide (JMS 1-3)

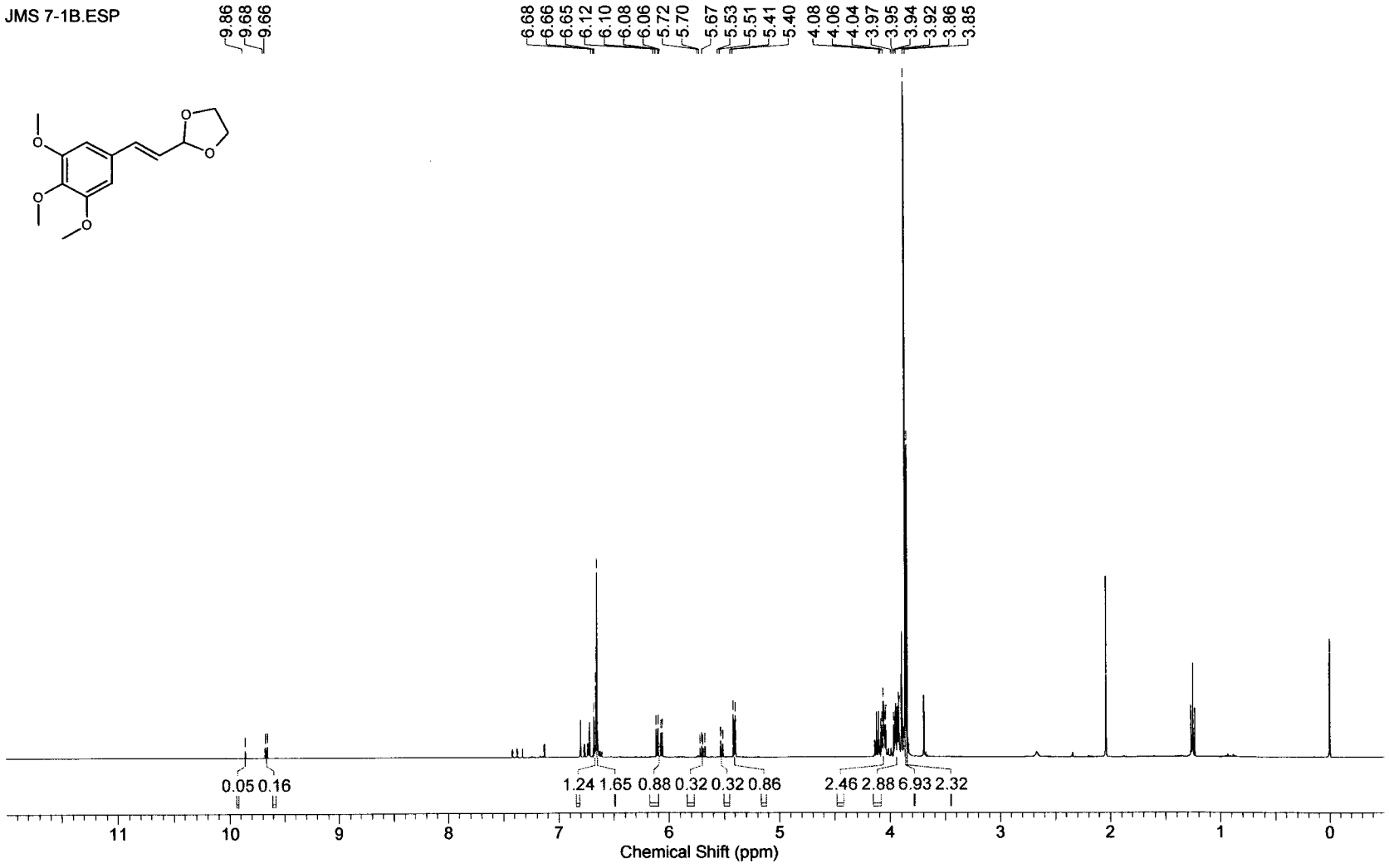

Figure A.3: ^{1}H NMR Spectrum of (*Z*/*E*)-2-(3,4,5-trimethoxystyryl)-1,3-dioxolane (JMS 7-1b)

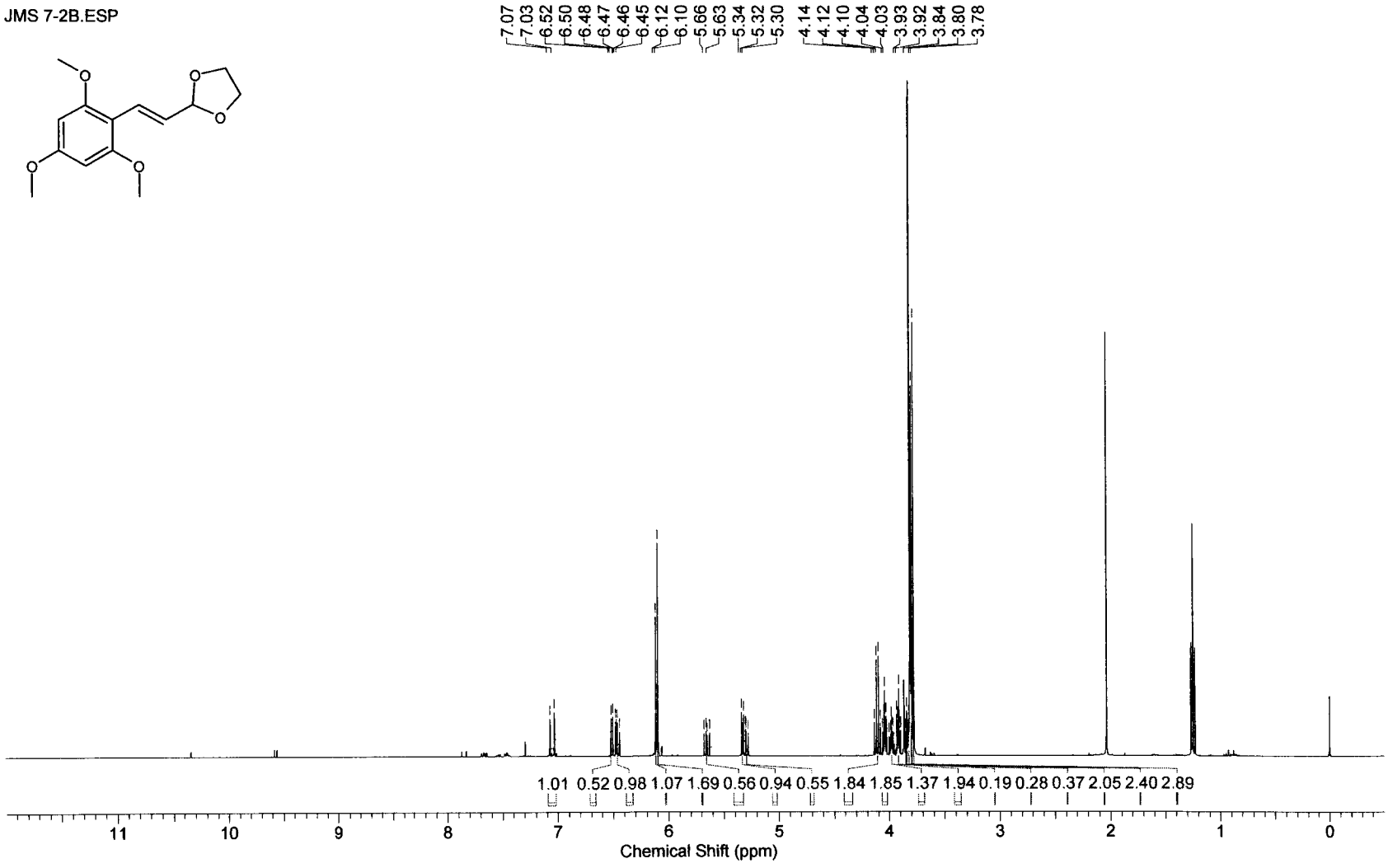

Figure A.4: ^{1}H NMR Spectrum of (*Z*/*E*)-2-(2,4,6-trimethoxystyryl)-1,3-dioxolane (JMS 7-2b)

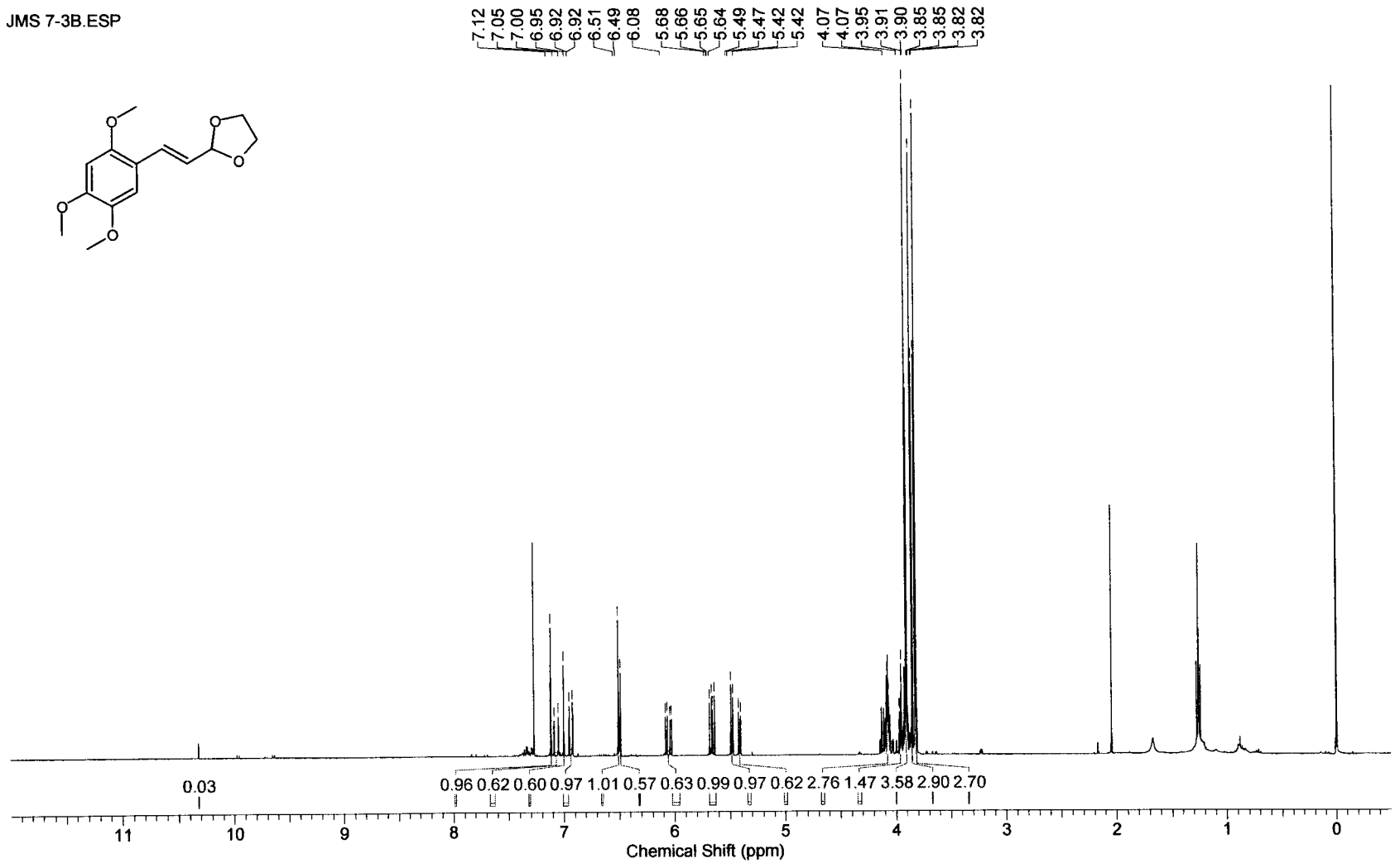

Figure A.5: ^{1}H NMR Spectrum of (*Z*/*E*)-2-(2,4,5-trimethoxystyryl)-1,3-dioxolane (JMS 7-3b)

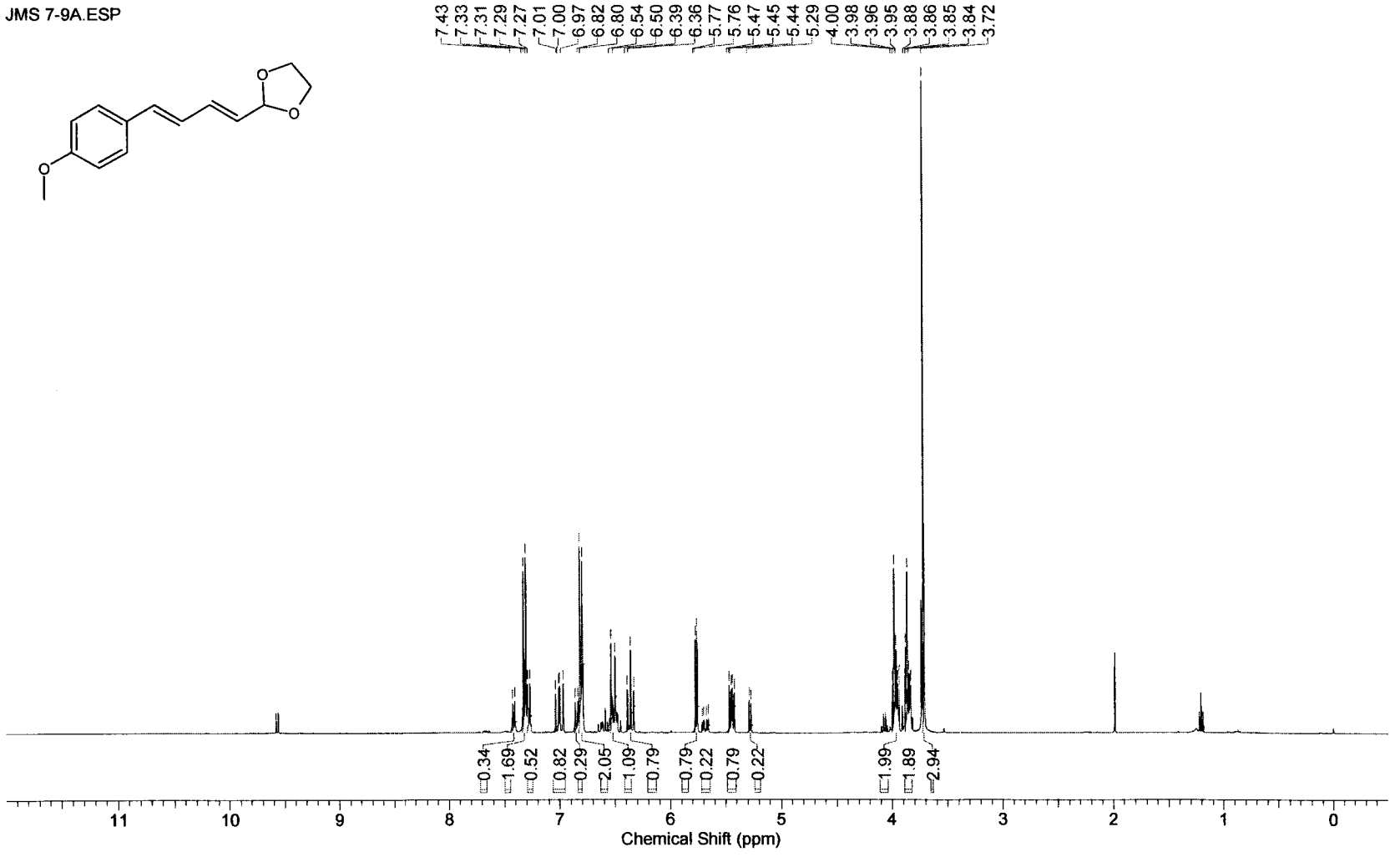

Figure A.6: ^{1}H NMR Spectrum of 2-((1*Z*/*E*,3*Z*/*E*)-4-(4-methoxyphenyl)buta-1,3-dien-1-yl)-1,3-dioxolane (JMS 7-9a)

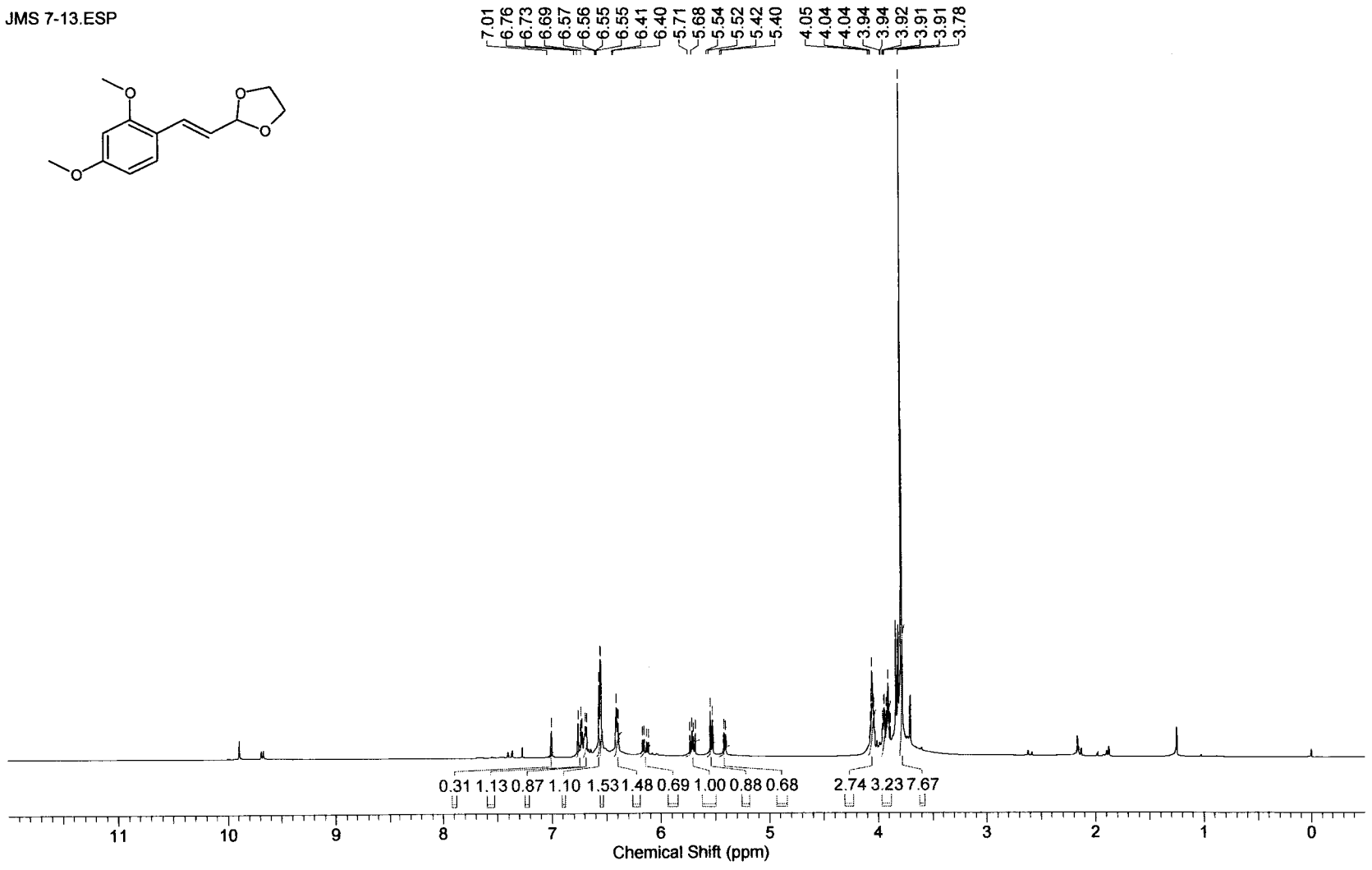

Figure A.7: ^{1}H NMR Spectrum of (*Z*/*E*)-2-(2,4-dimethoxystyryl)-1,3-dioxolane (JMS 7-13)

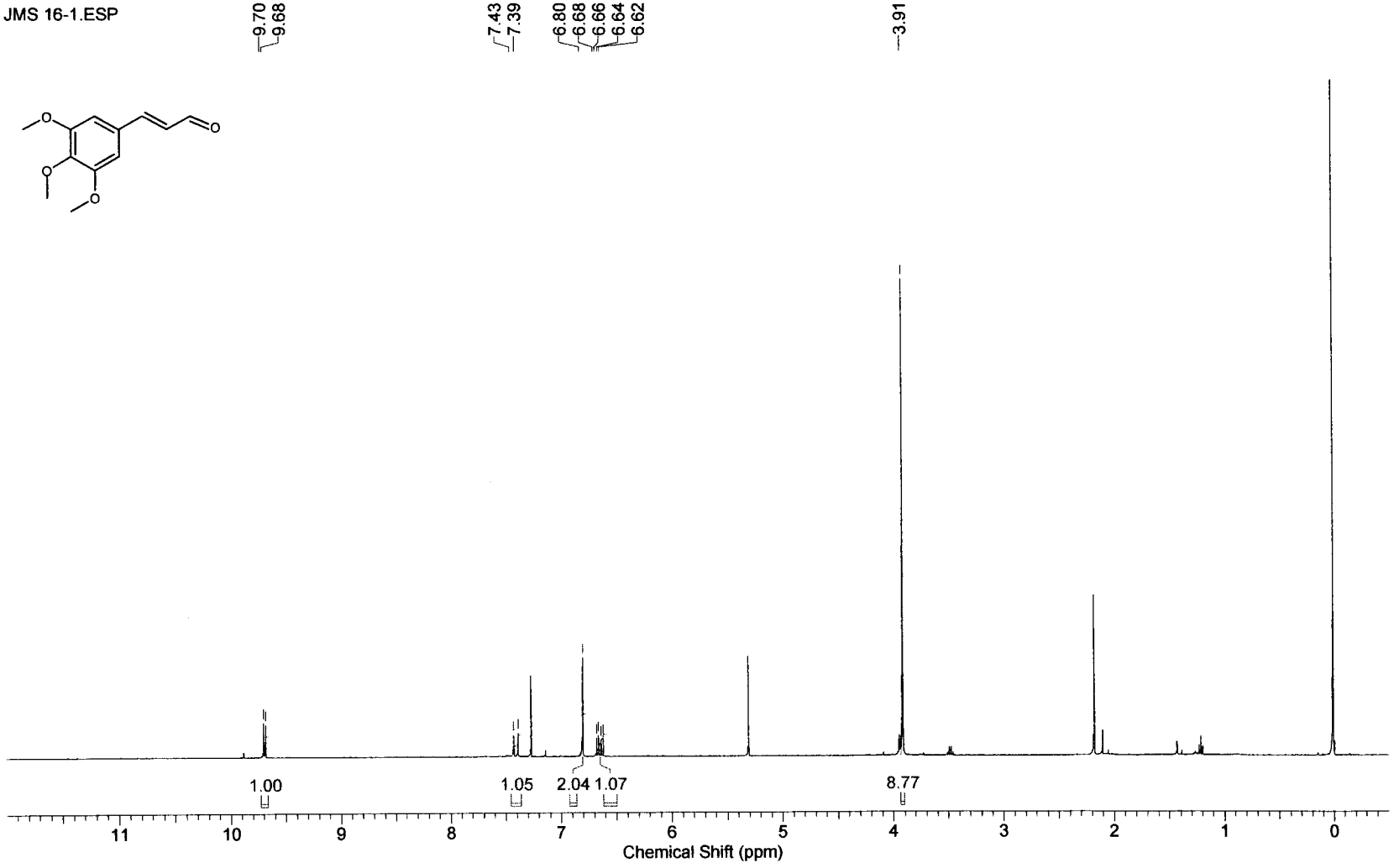

Figure A.8: ^{1}H NMR Spectrum of (*E*)-3-(3,4,5-trimethoxyphenyl)acrylaldehyde (JMS 16-1)

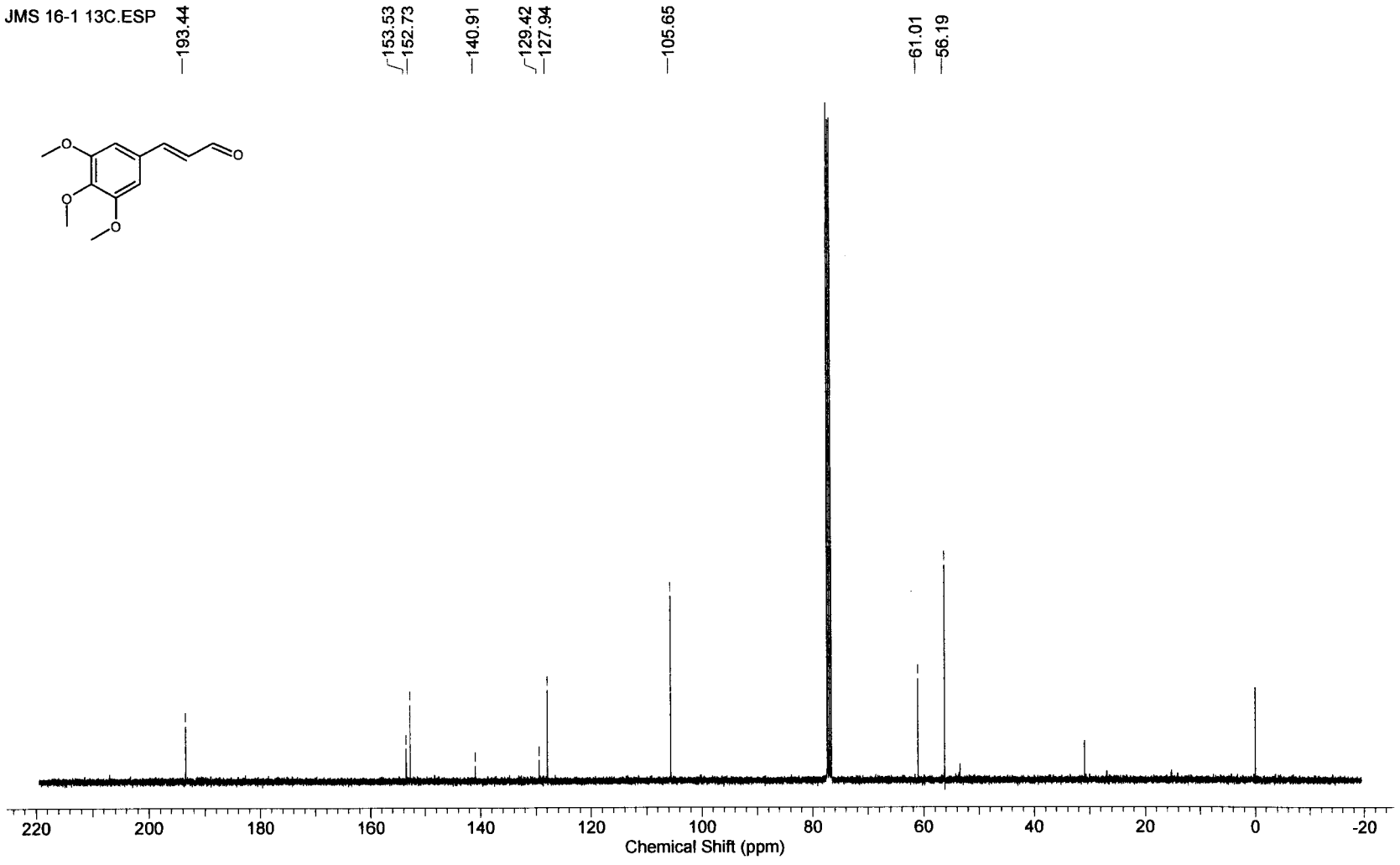

Figure A.9: ^{13}C NMR Spectrum of (*E*)-3-(3,4,5-trimethoxyphenyl)acrylaldehyde (JMS 16-1)

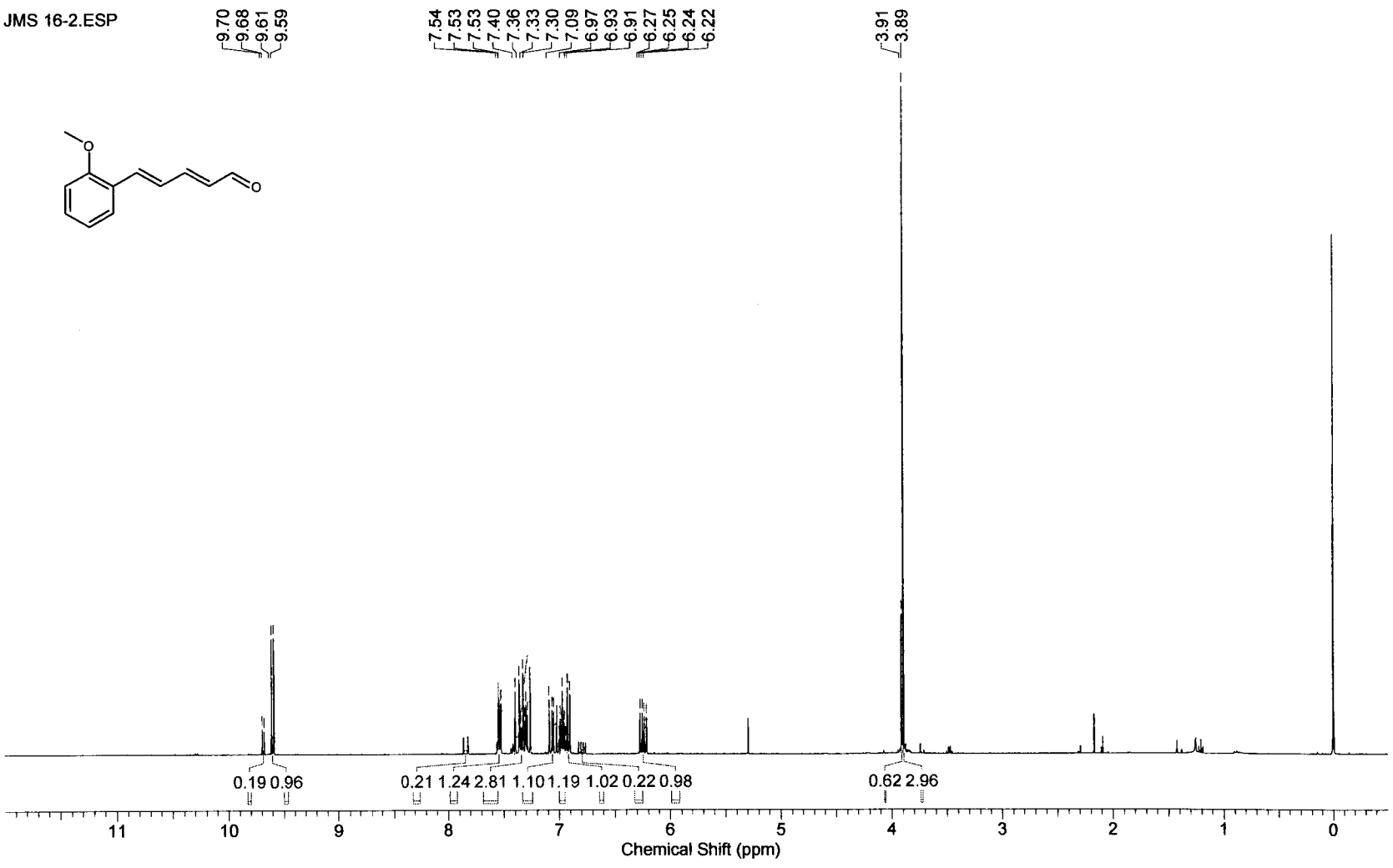

Figure A.10: ^{1}H NMR Spectrum of (2*E*,4*E*)-5-(2-methoxyphenyl)penta-2,4-dienal (JMS 16-2)

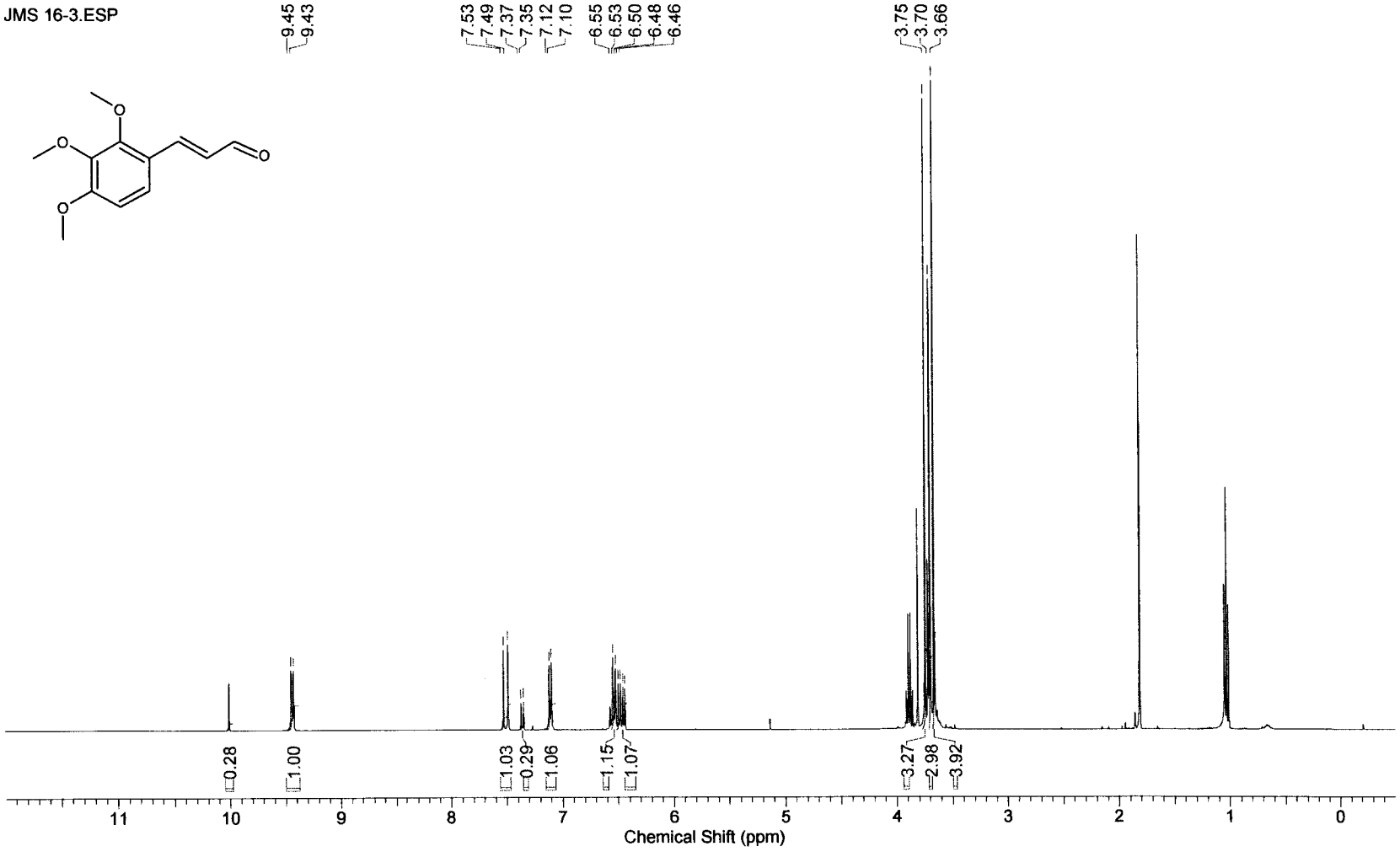

Figure A.11: ^{1}H NMR Spectrum of (*E*)-3-(2,3,4-trimethoxyphenyl)acrylaldehyde (JMS 16-3)

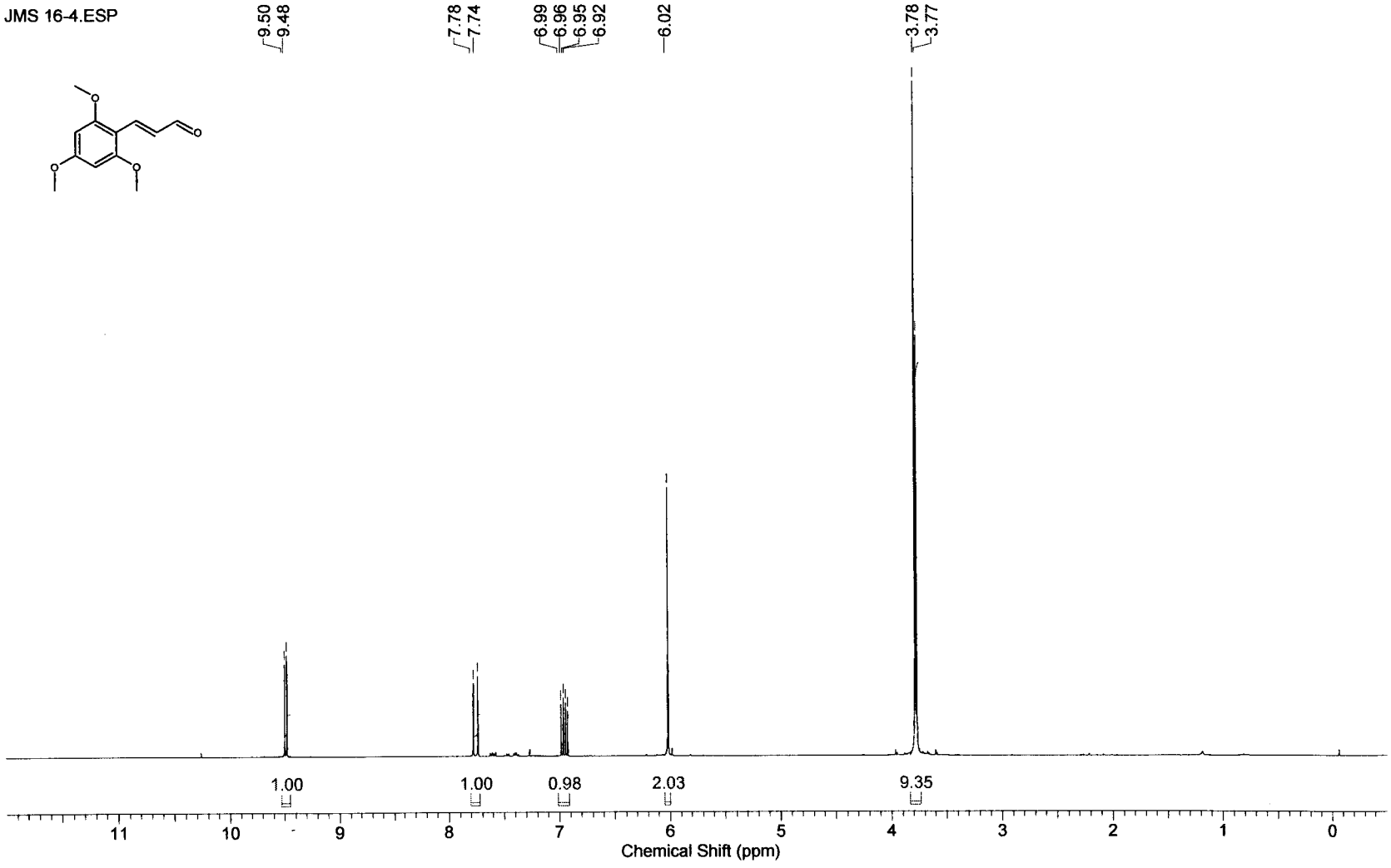

Figure A.12: ^{1}H NMR Spectrum of (*E*)-3-(2,4,6-trimethoxyphenyl)acrylaldehyde (JMS 16-4)

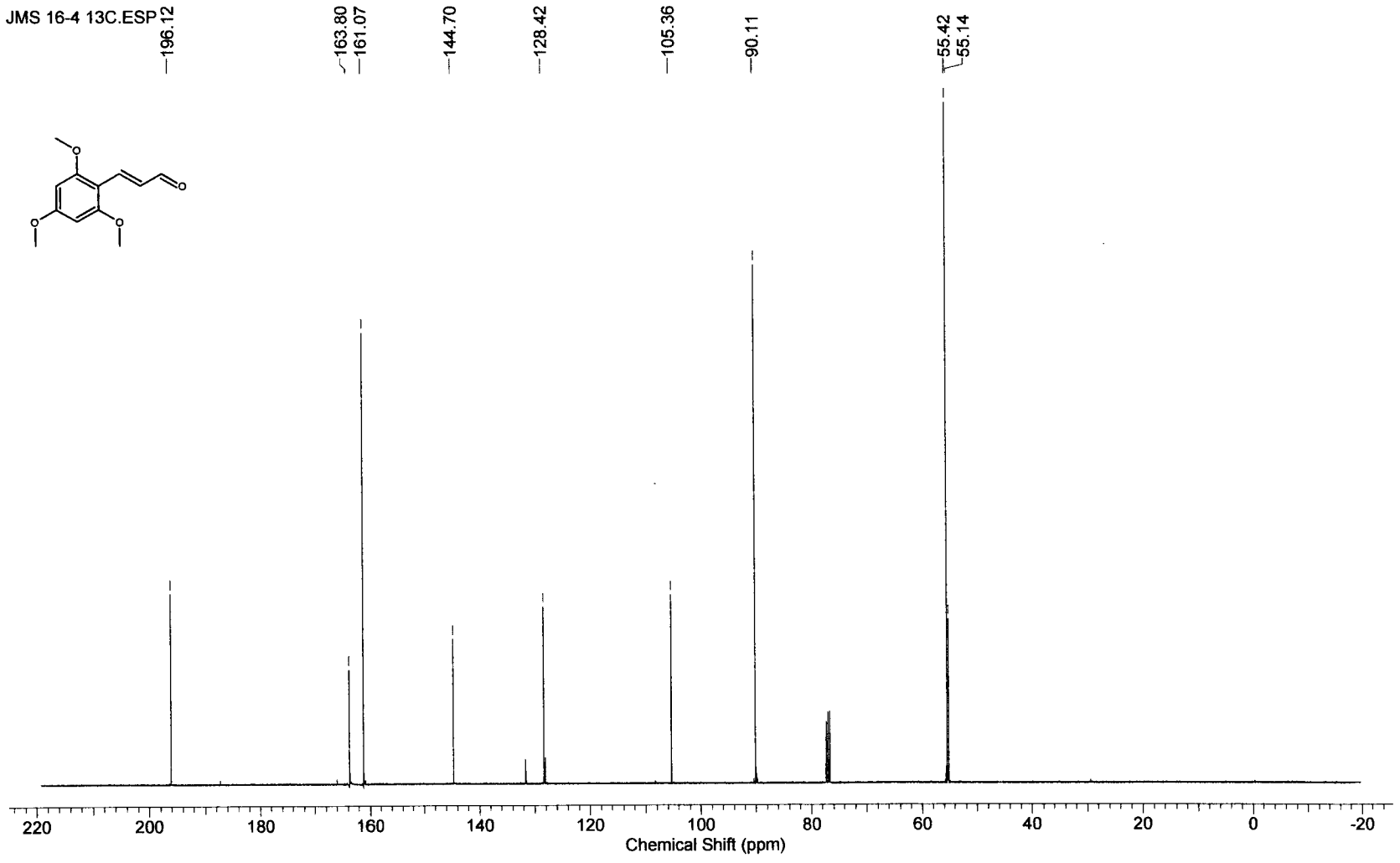

Figure A.13: ^{13}C NMR Spectrum of (*E*)-3-(2,4,6-trimethoxyphenyl)acrylaldehyde (JMS 16-4)

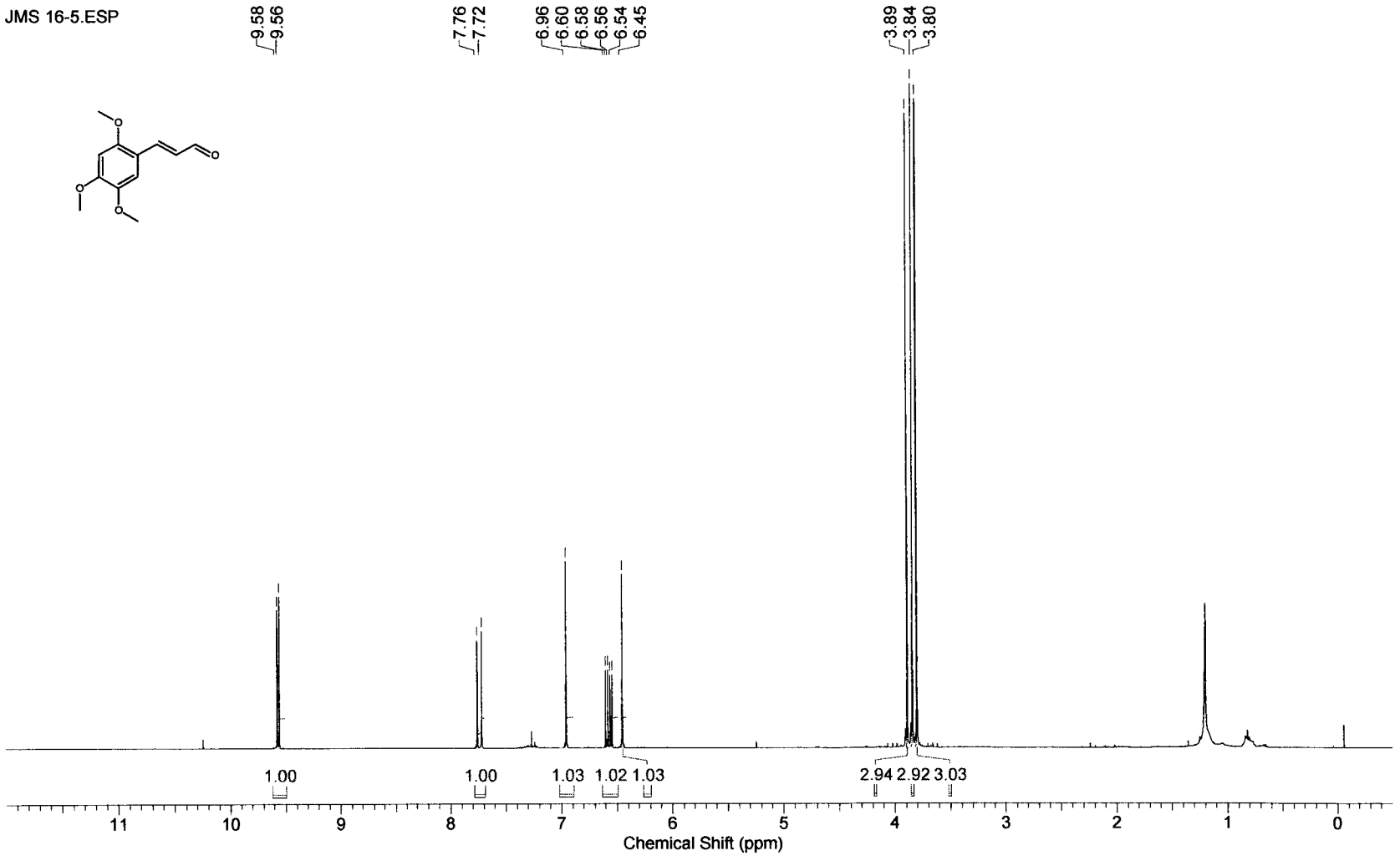

Figure A.14: ^{1}H NMR Spectrum of (*E*)-3-(2,4,5-trimethoxyphenyl)acrylaldehyde (JMS 16-5)

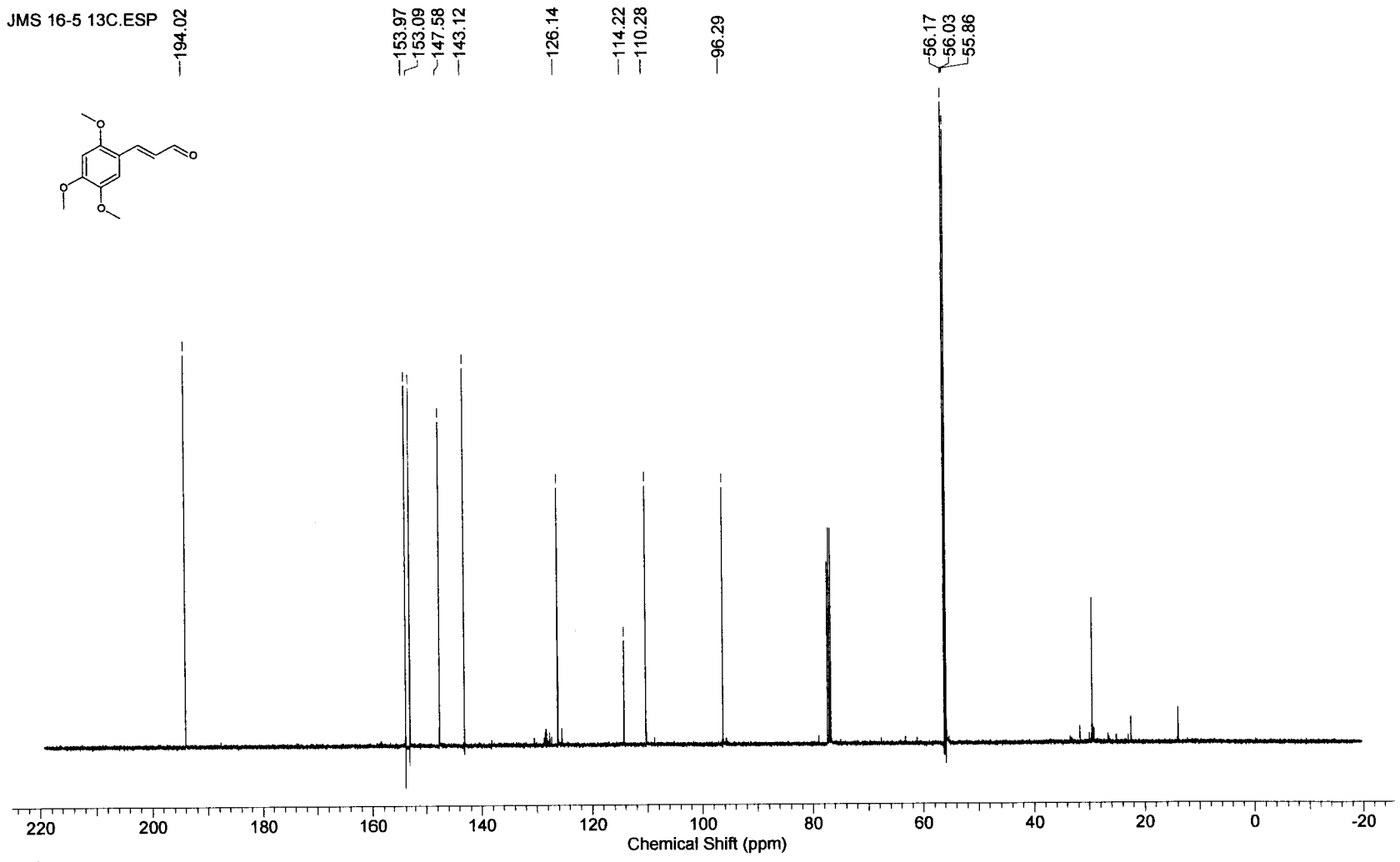

Figure A.15: ^{13}C NMR Spectrum of (*E*)-3-(2,4,5-trimethoxyphenyl)acrylaldehyde (JMS 16-5)

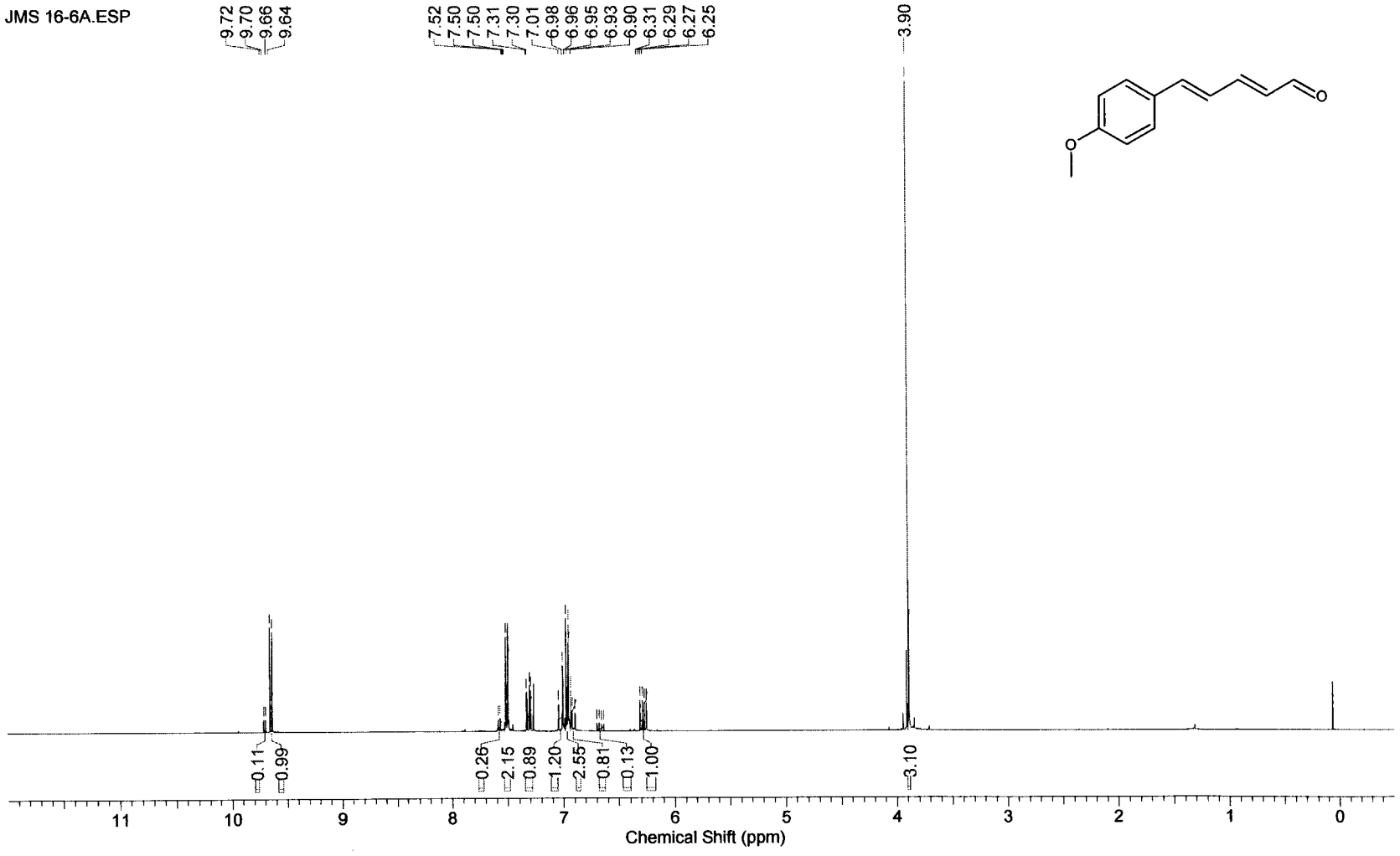

Figure A.16: ^{1}H NMR Spectrum of (2*E*,4*E*)-5-(4-methoxyphenyl)penta-2,4-dienal (JMS 16-6a)

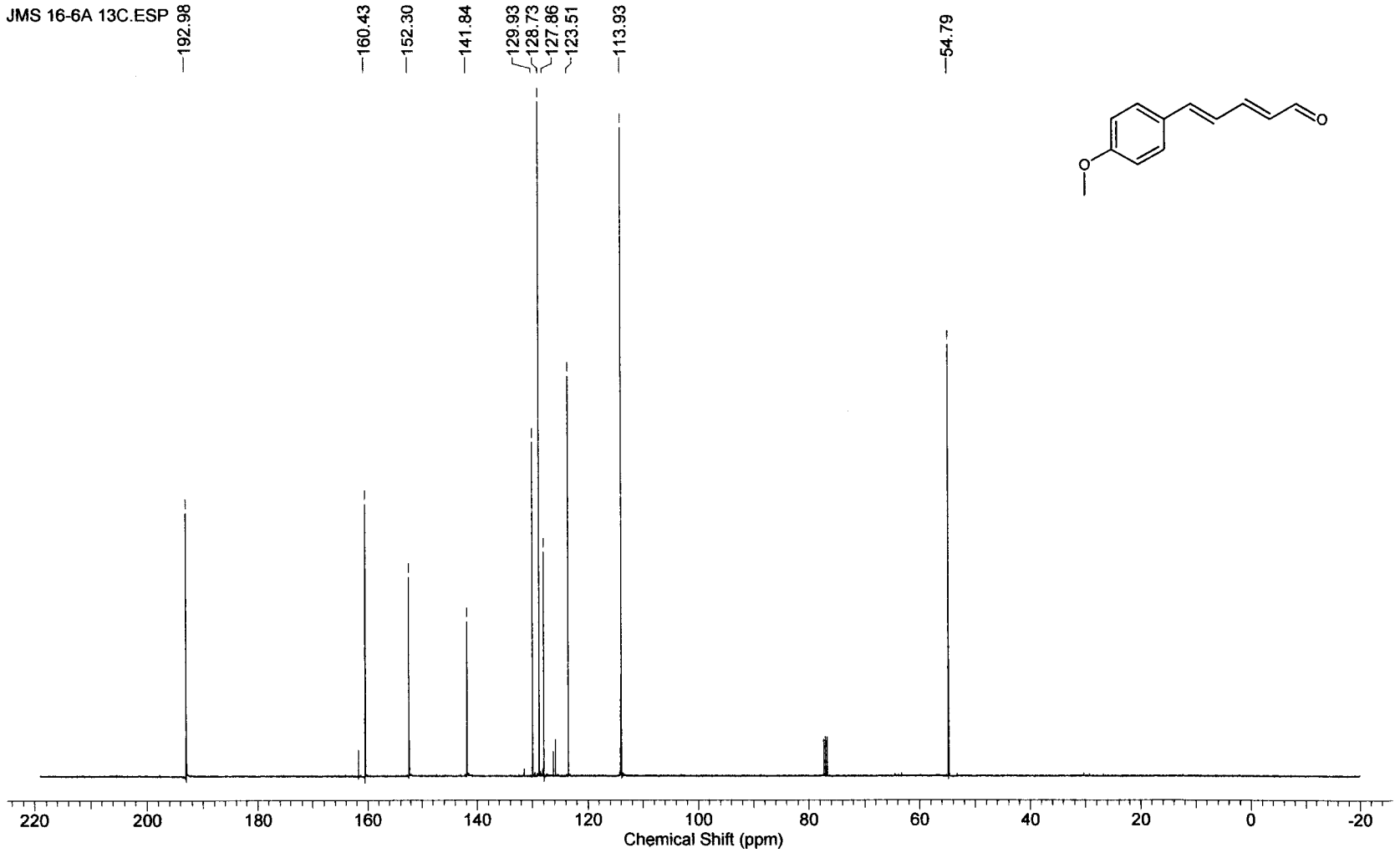

Figure A.17: ^{13}C NMR Spectrum of (2*E*,4*E*)-5-(4-methoxyphenyl)penta-2,4-dienal (JMS 16-6a)

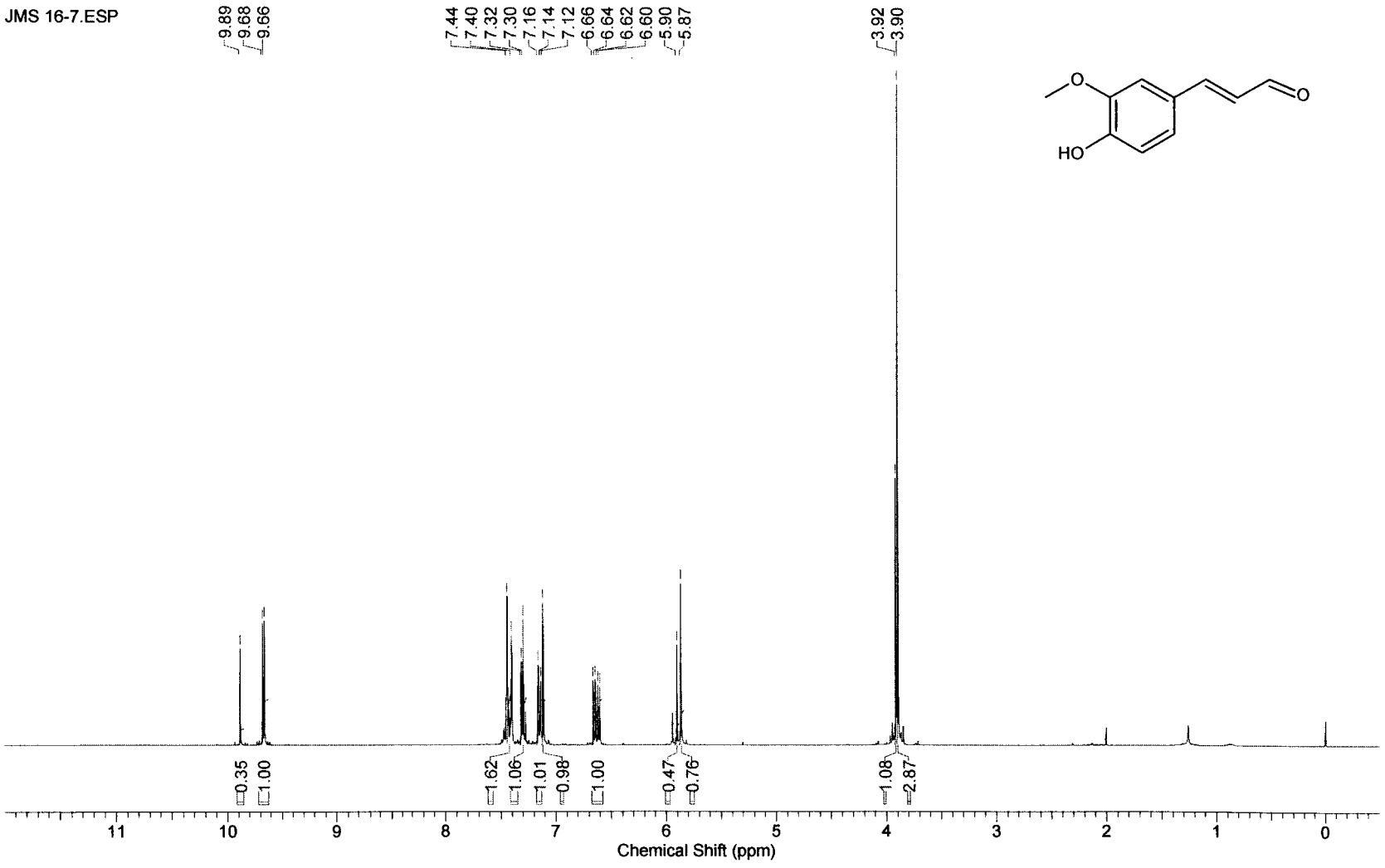

Figure A.18: ^{1}H NMR Spectrum of (*E*)-3-(4-hydroxy-3-methoxyphenyl)acrylaldehyde (JMS 16-7)

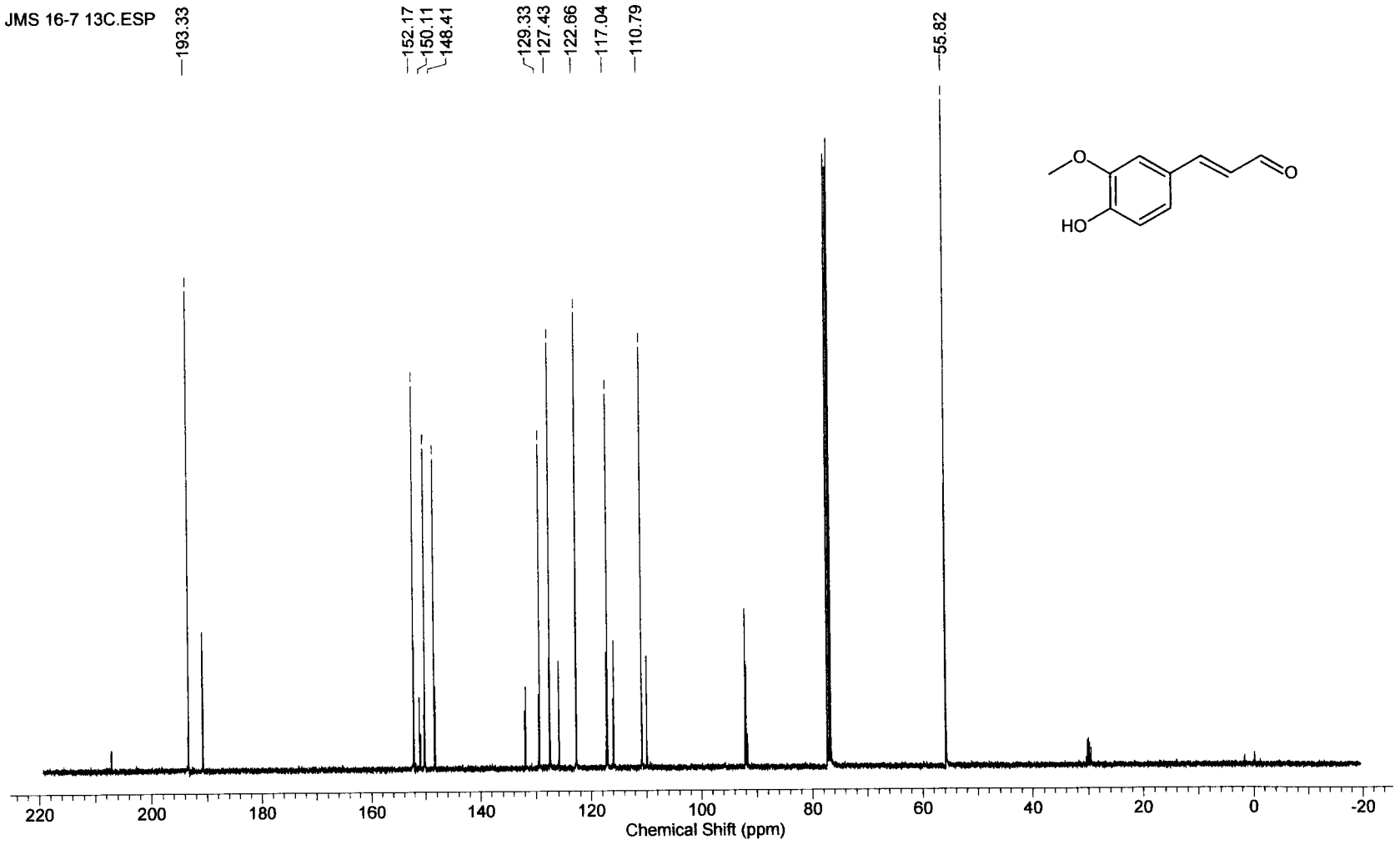

Figure A.19: ^{13}C NMR Spectrum of (*E*)-3-(4-hydroxy-3-methoxyphenyl)acrylaldehyde (JMS 16-7)

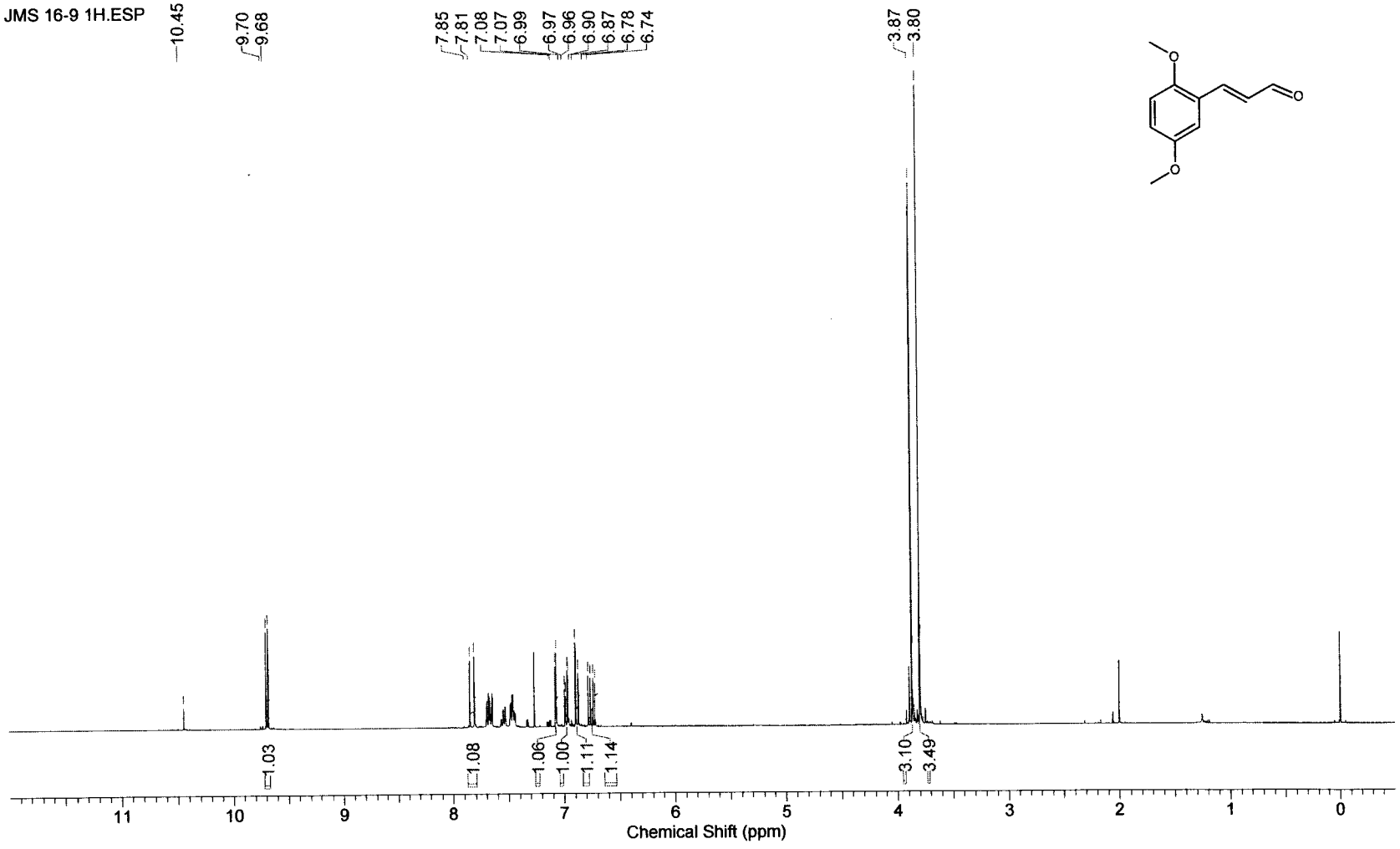

Figure A.20: ^{1}H NMR Spectrum of (*E*)-3-(2,5-dimethoxyphenyl)acrylaldehyde (JMS 16-9)

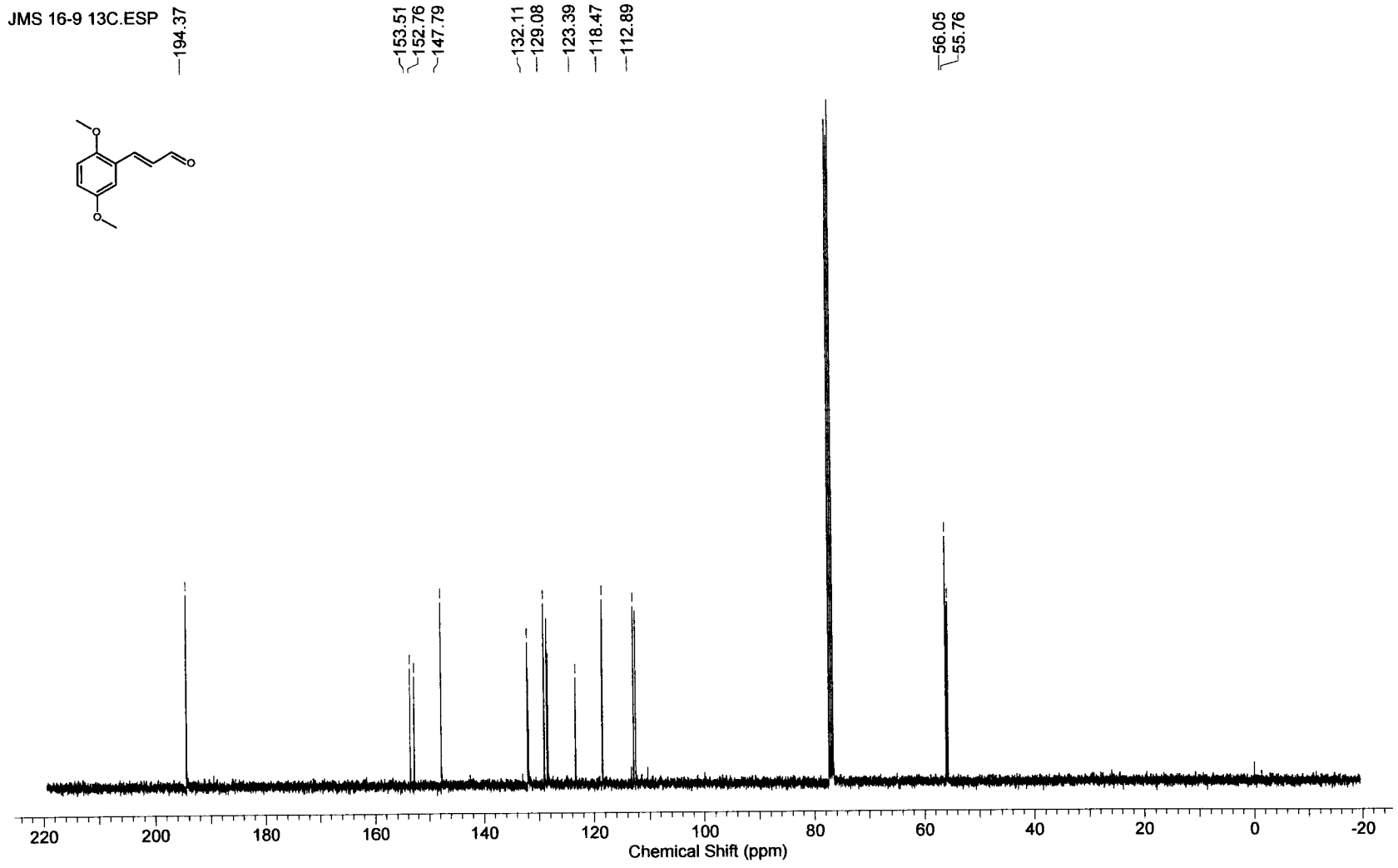

Figure A.21: ^{13}C NMR Spectrum of (*E*)-3-(2,5-dimethoxyphenyl)acrylaldehyde (JMS 16-9)

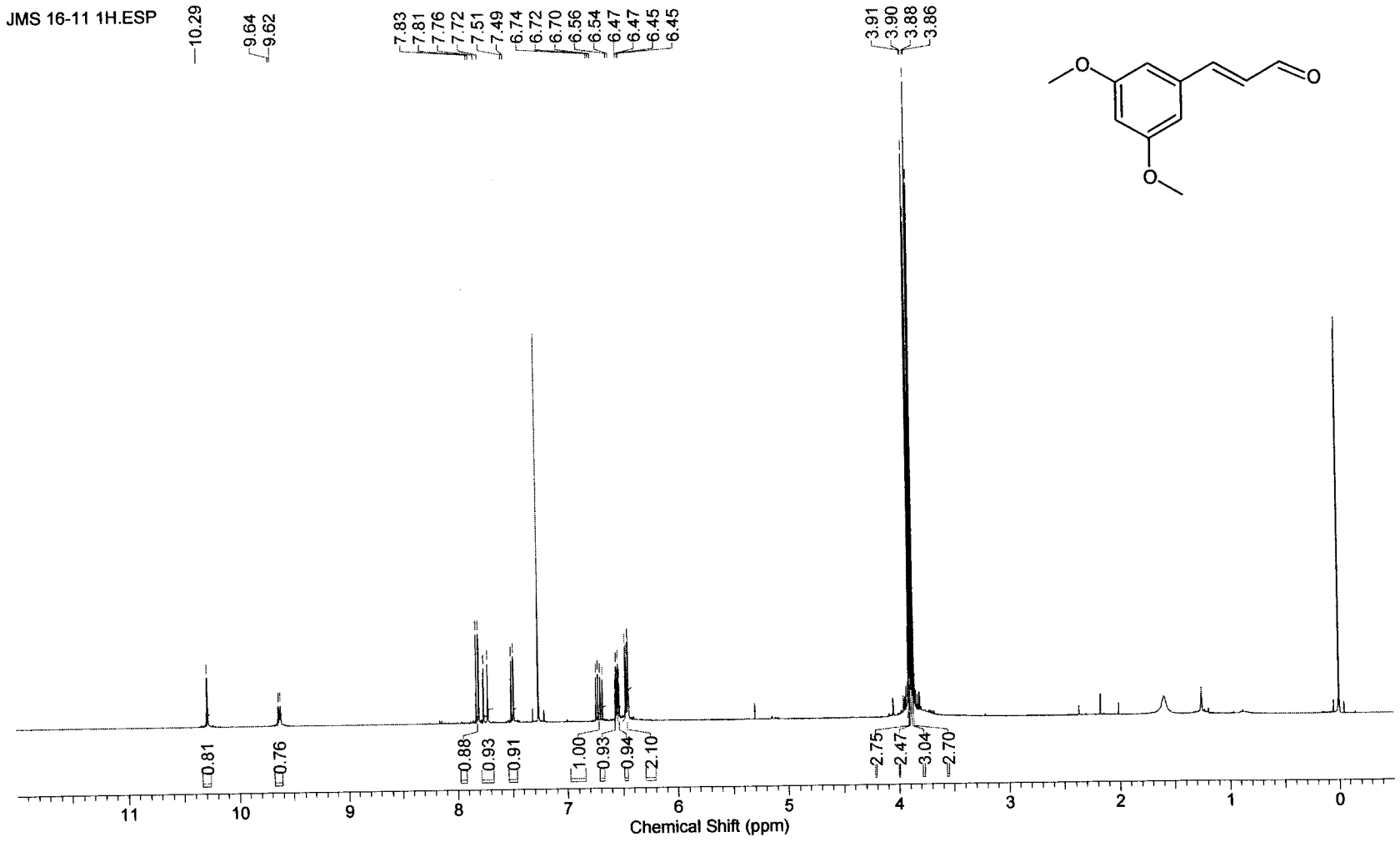

Figure A.22: ^{1}H NMR Spectrum of (*E*)-3-(3,5-dimethoxyphenyl)acrylaldehyde (JMS 16-11)

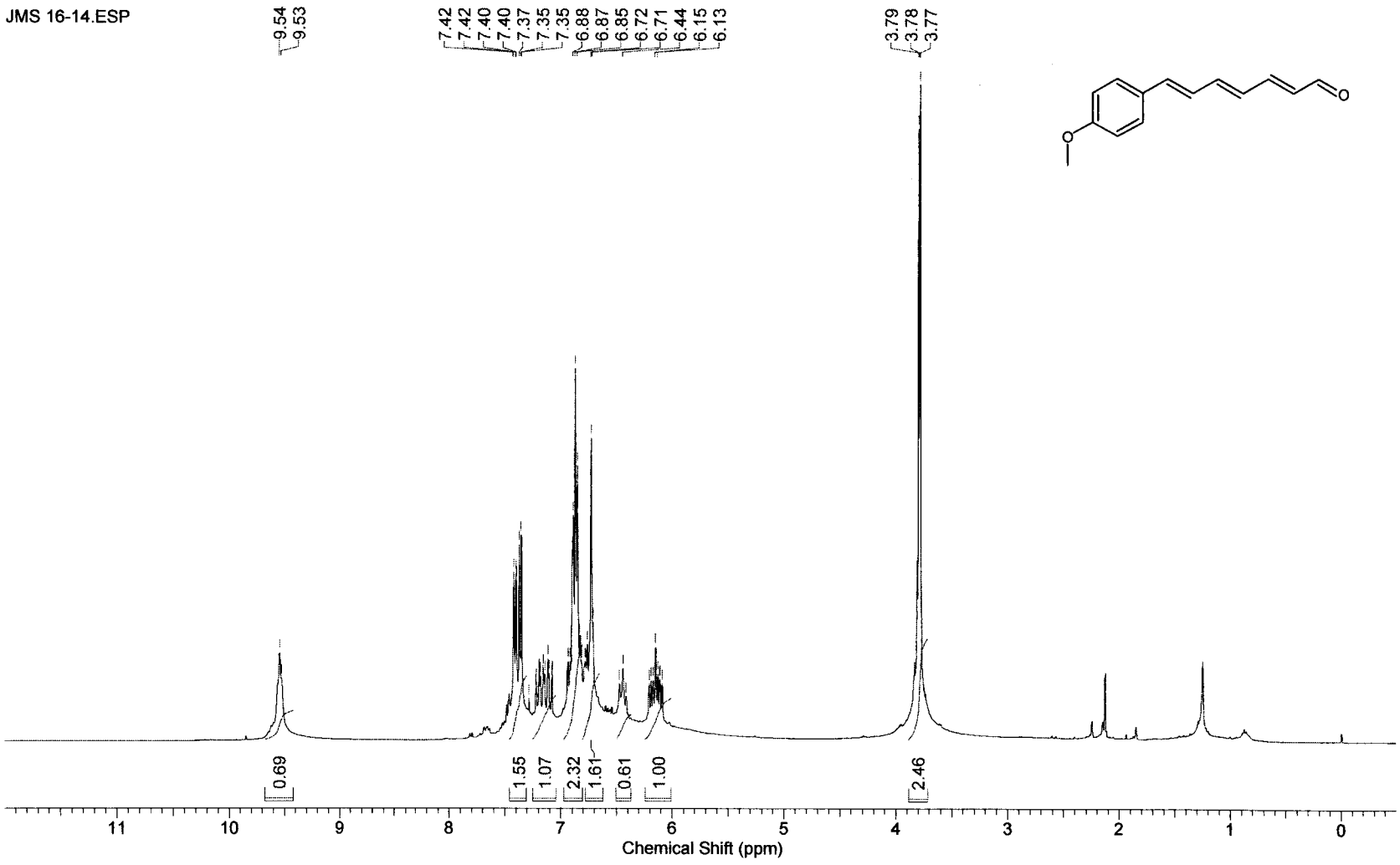

Figure A.23: ^{1}H NMR Spectrum of (2*E*,4*E*,6*E*)-7-(4-methoxyphenyl)hepta-2,4,6-trienal (JMS 16-14)

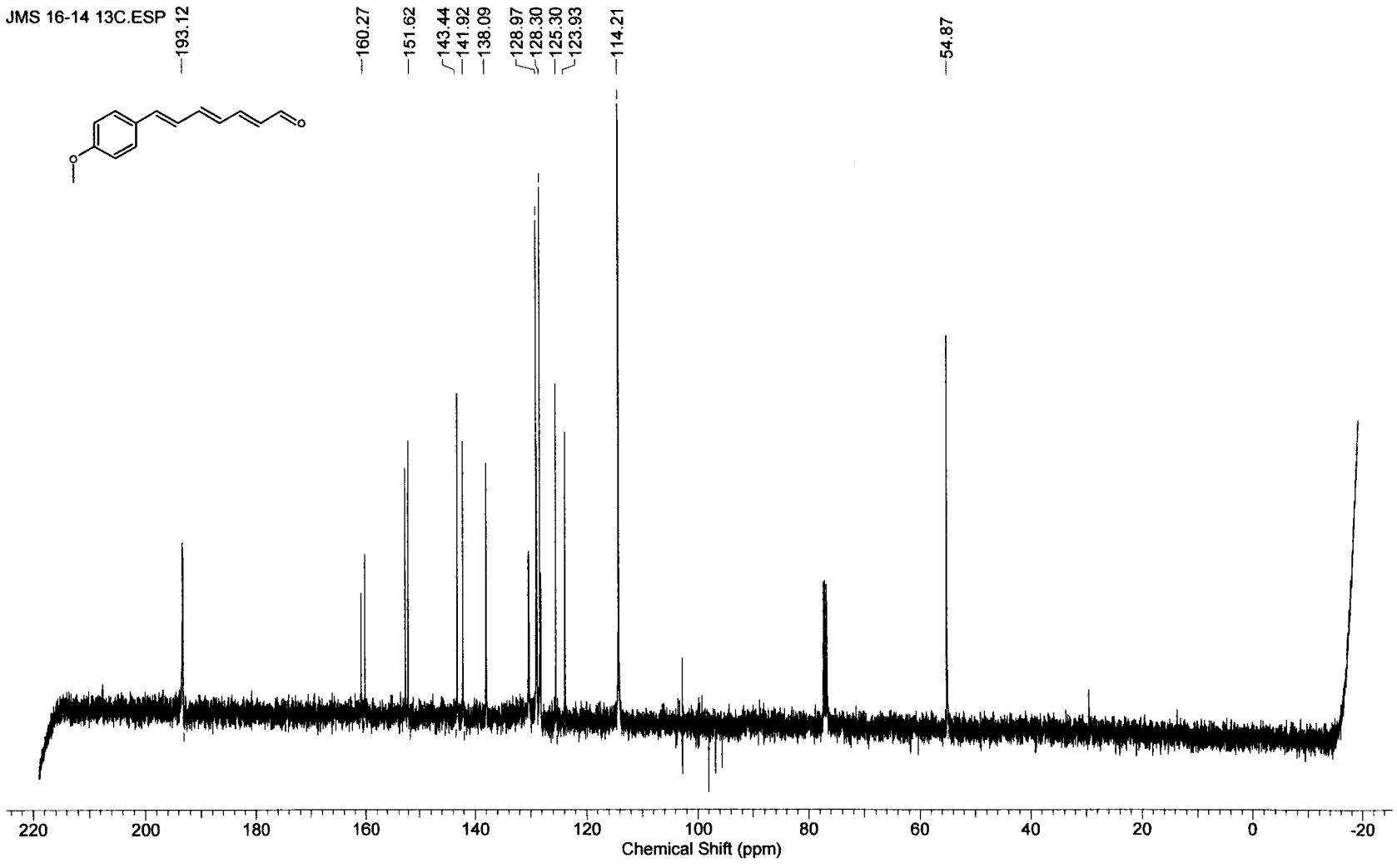

Figure A.24: ^{13}C NMR Spectrum of (2*E*,4*E*,6*E*)-7-(4-methoxyphenyl)hepta-2,4,6-trienal (JMS 16-14)

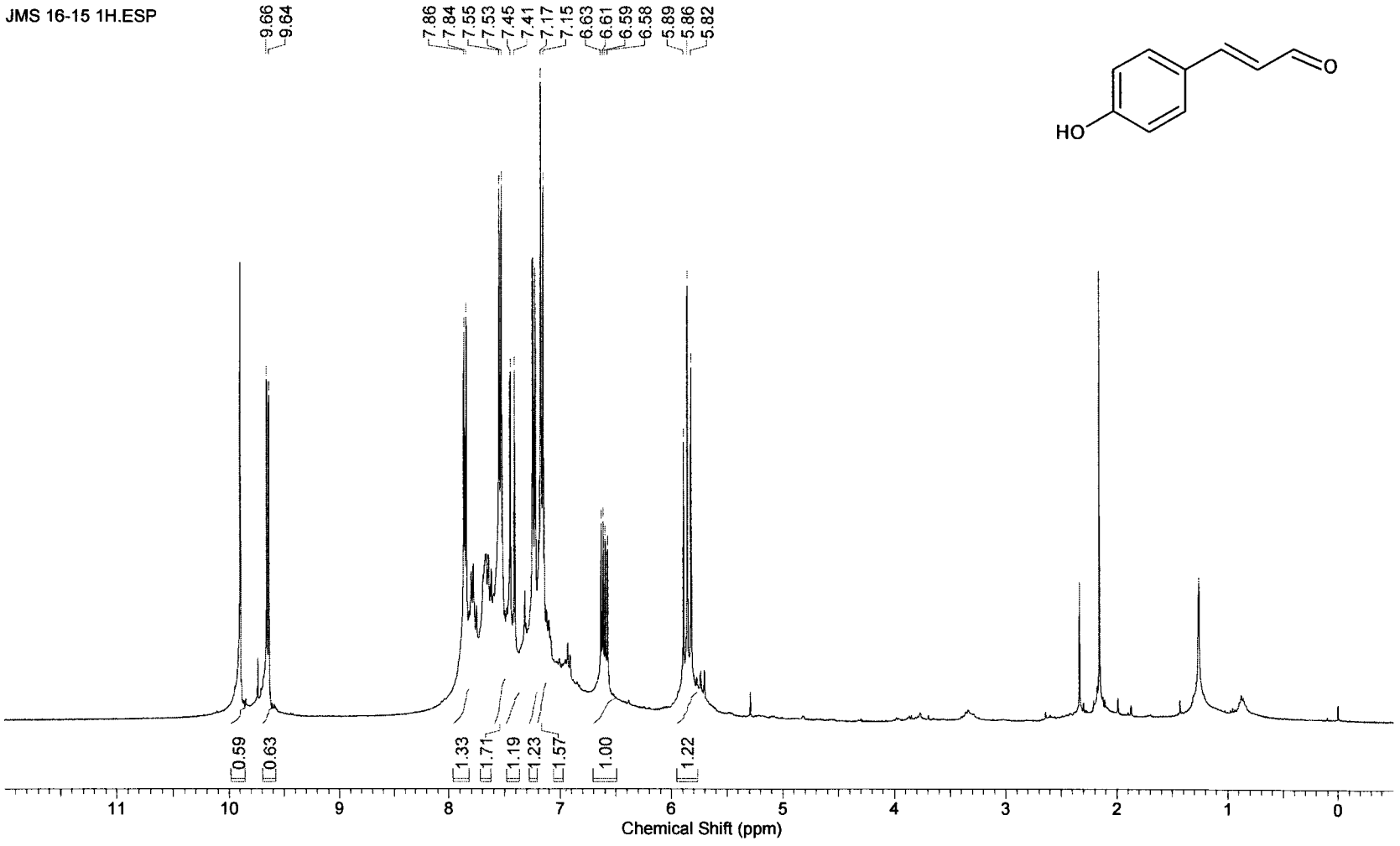

Figure A.25: ^{1}H NMR Spectrum of *E*-3-(4-hydroxyphenyl)acrylaldehyde (JMS 16-15)

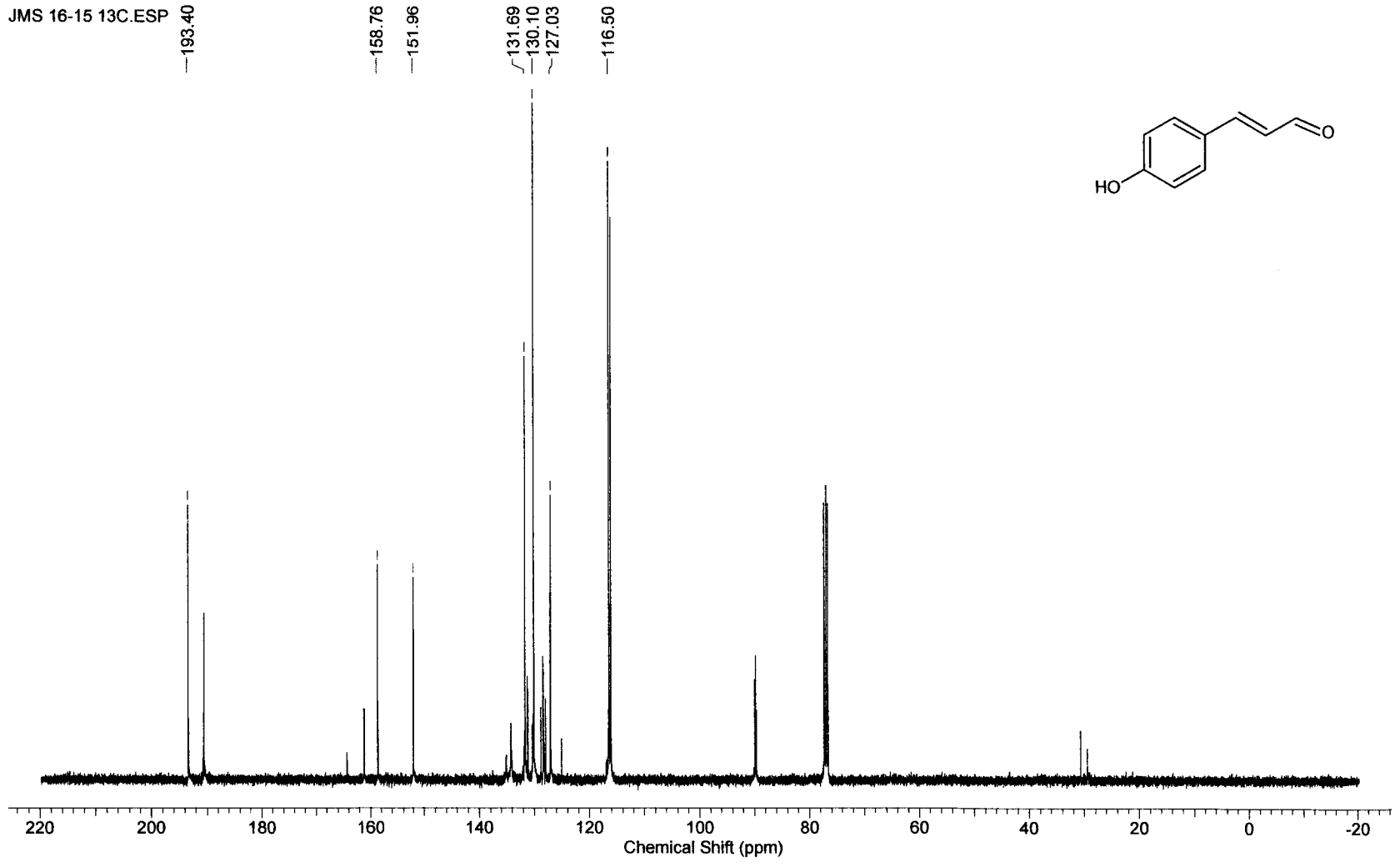

Figure A.26: ^{13}C NMR Spectrum of *E*-3-(4-hydroxyphenyl)acrylaldehyde (JMS 16-15)

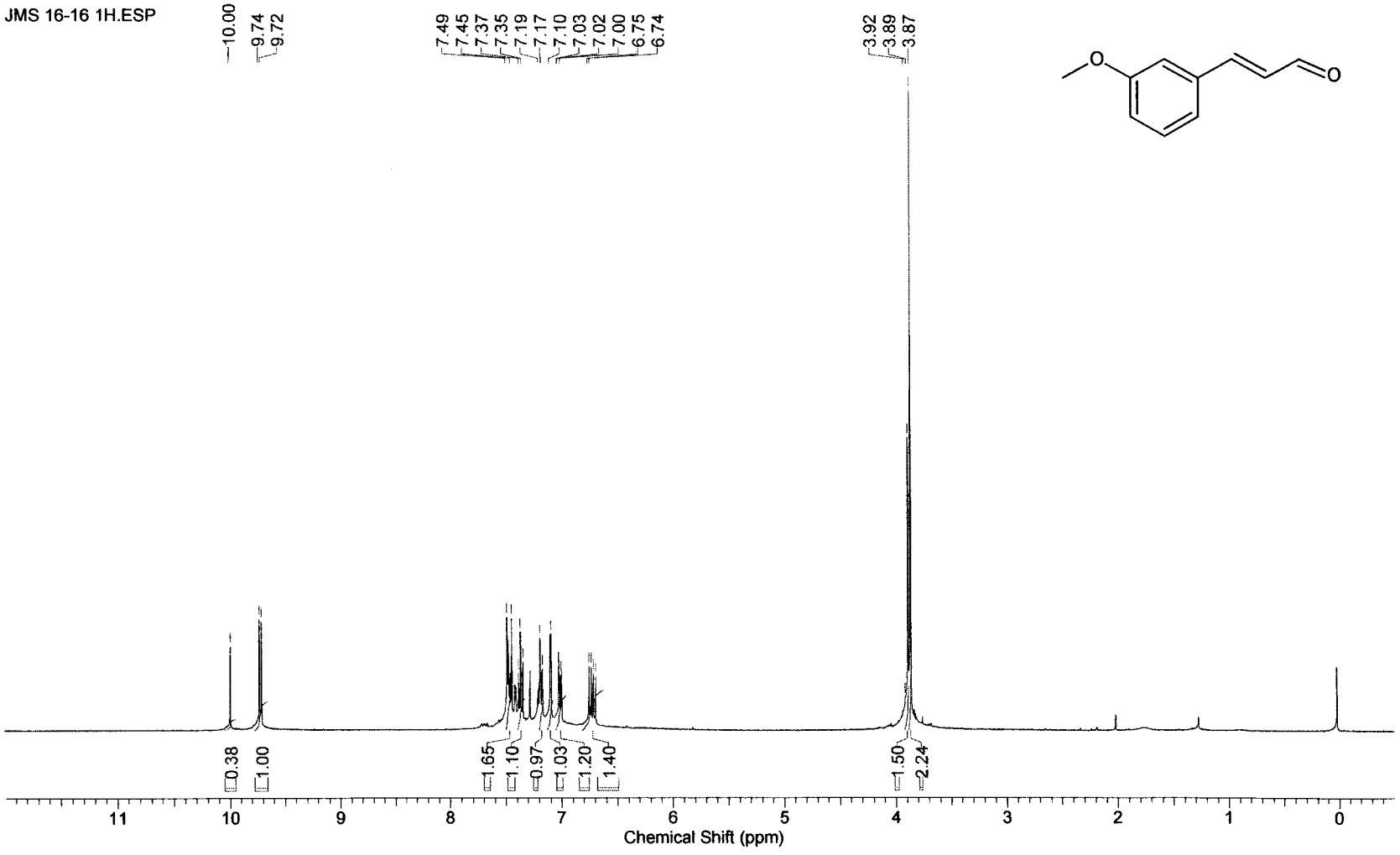

Figure A.27: ^{1}H NMR Spectrum of *E*-3-(3-methoxyphenyl)acrylaldehyde (JMS 16-16)

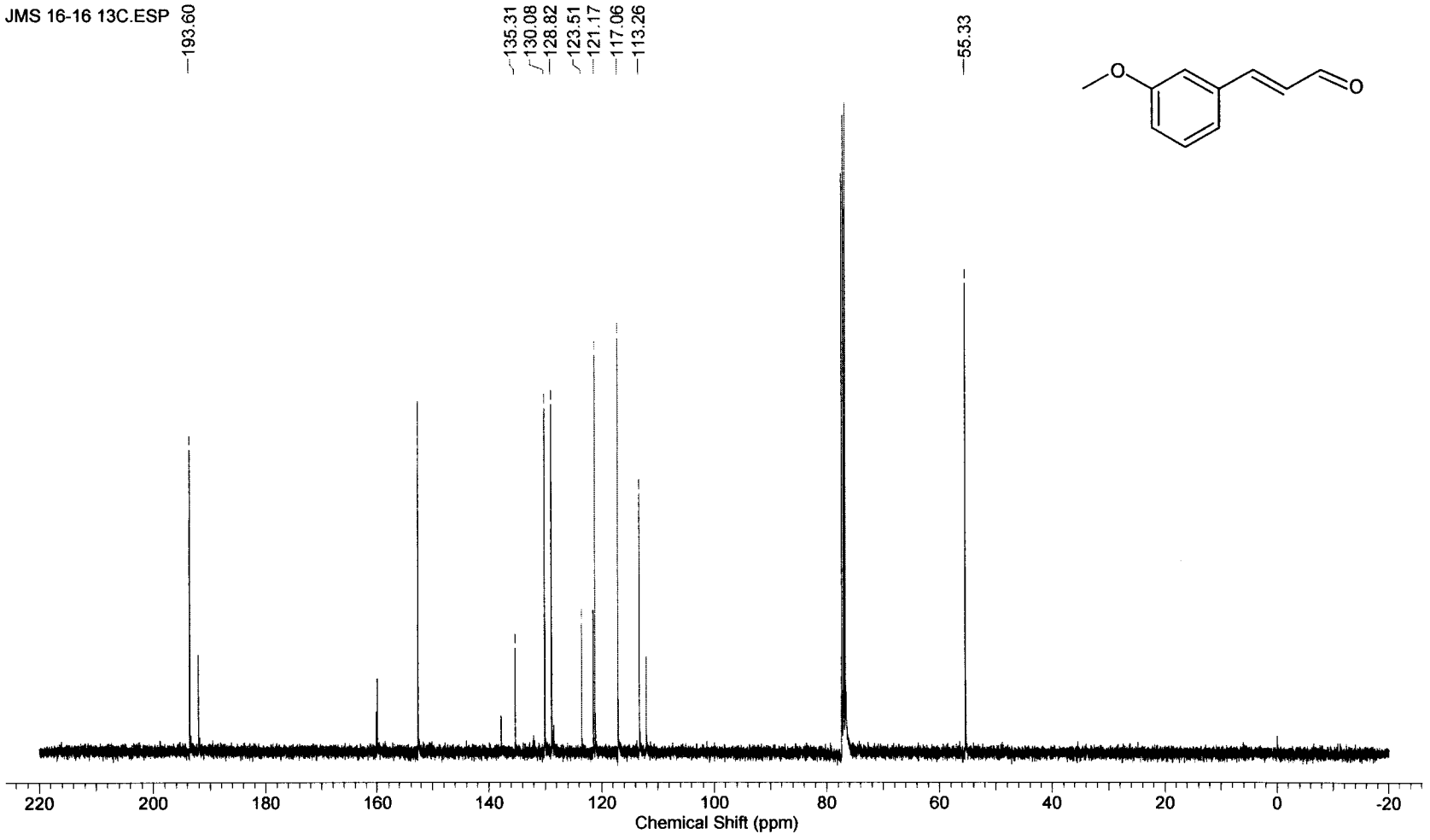

Figure A.28: ^{13}C NMR Spectrum of *E*-3-(3-methoxyphenyl)acrylaldehyde (JMS 16-16)

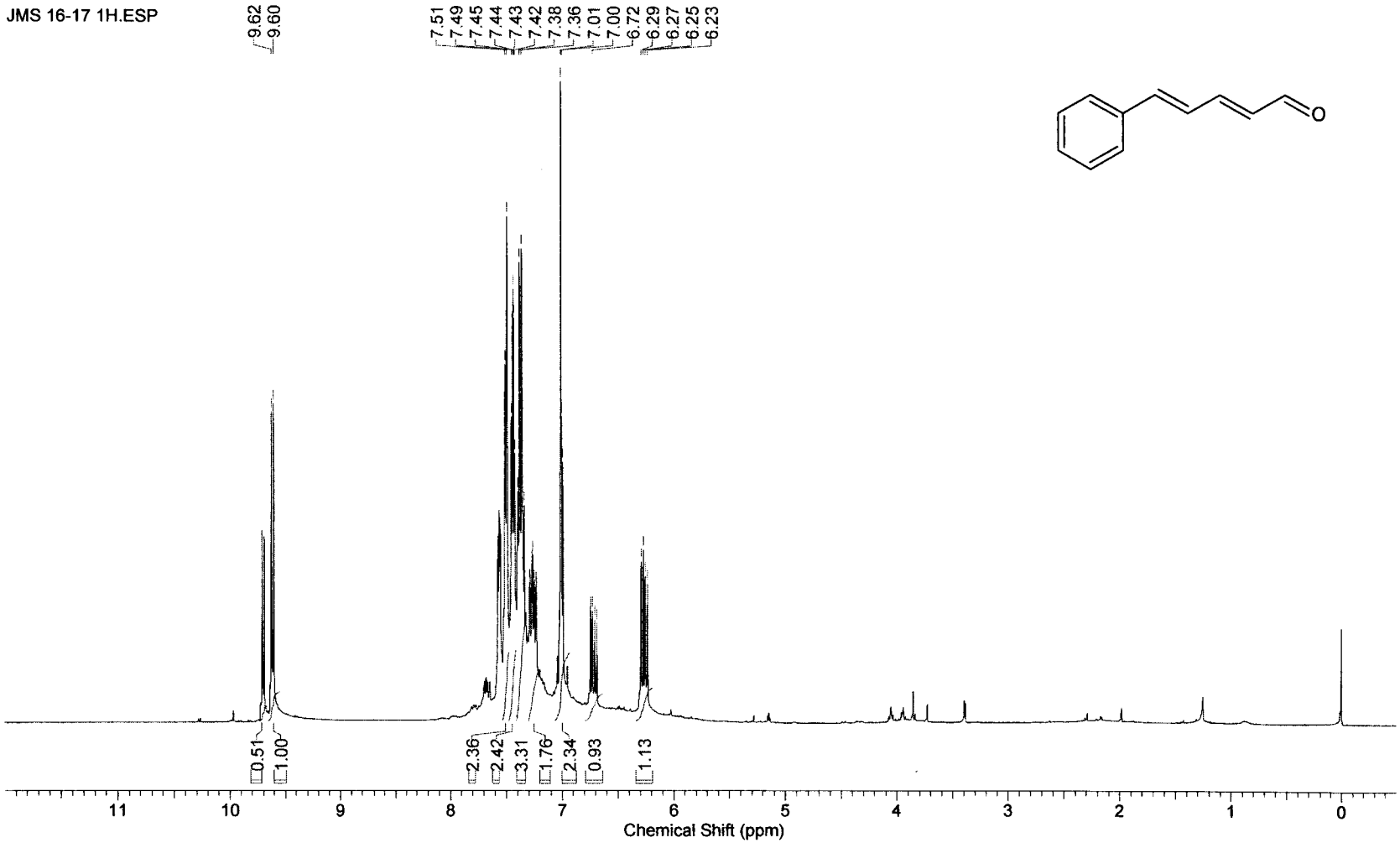

Figure A.29: ^{1}H NMR Spectrum of (2*E*,4*E*)-5-phenylpenta-2,4-dienal (JMS 16-17)

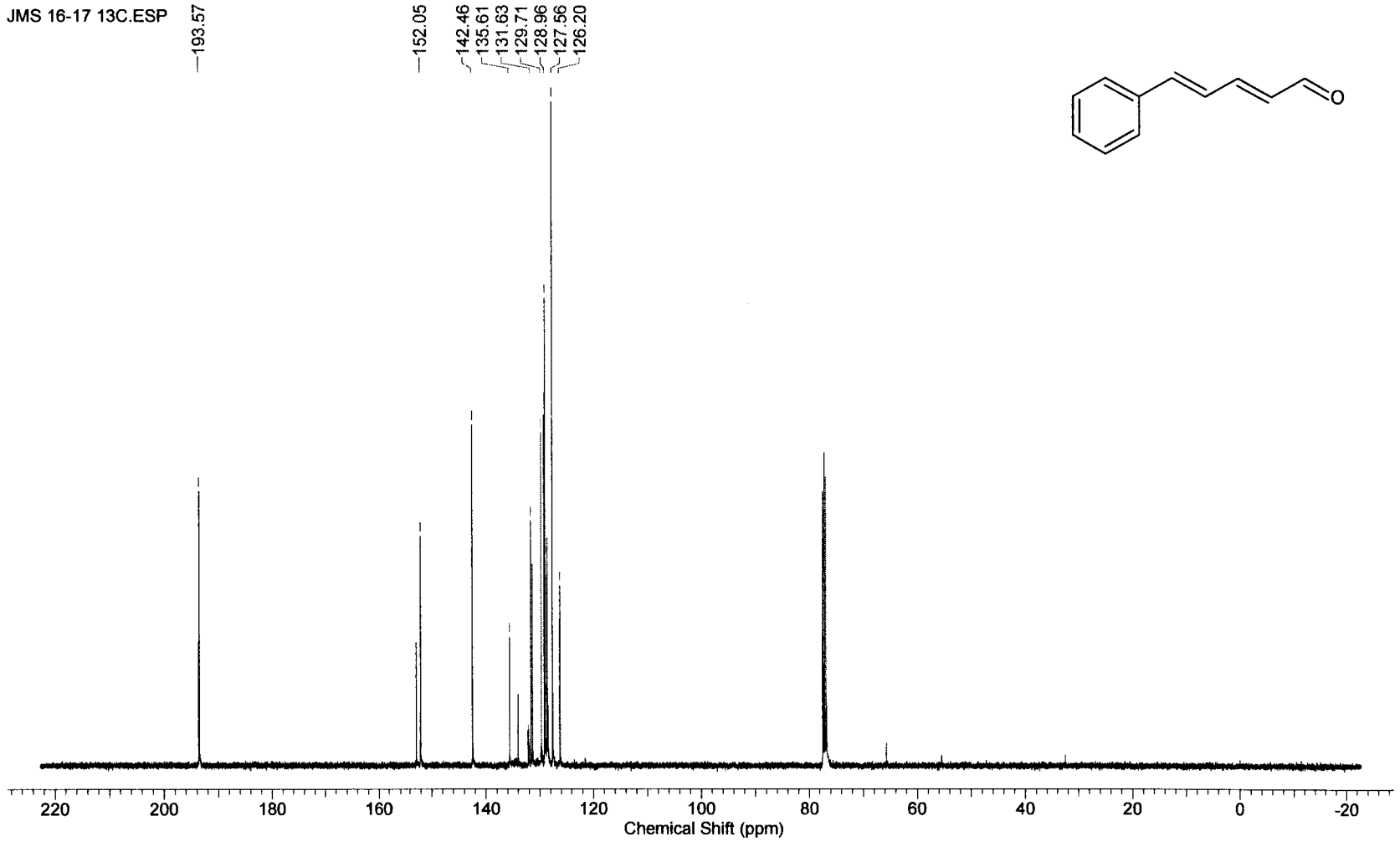

Figure A.30: ^{13}C NMR Spectrum of (2*E*,4*E*)-5-phenylpenta-2,4-dienal (JMS 16-17)

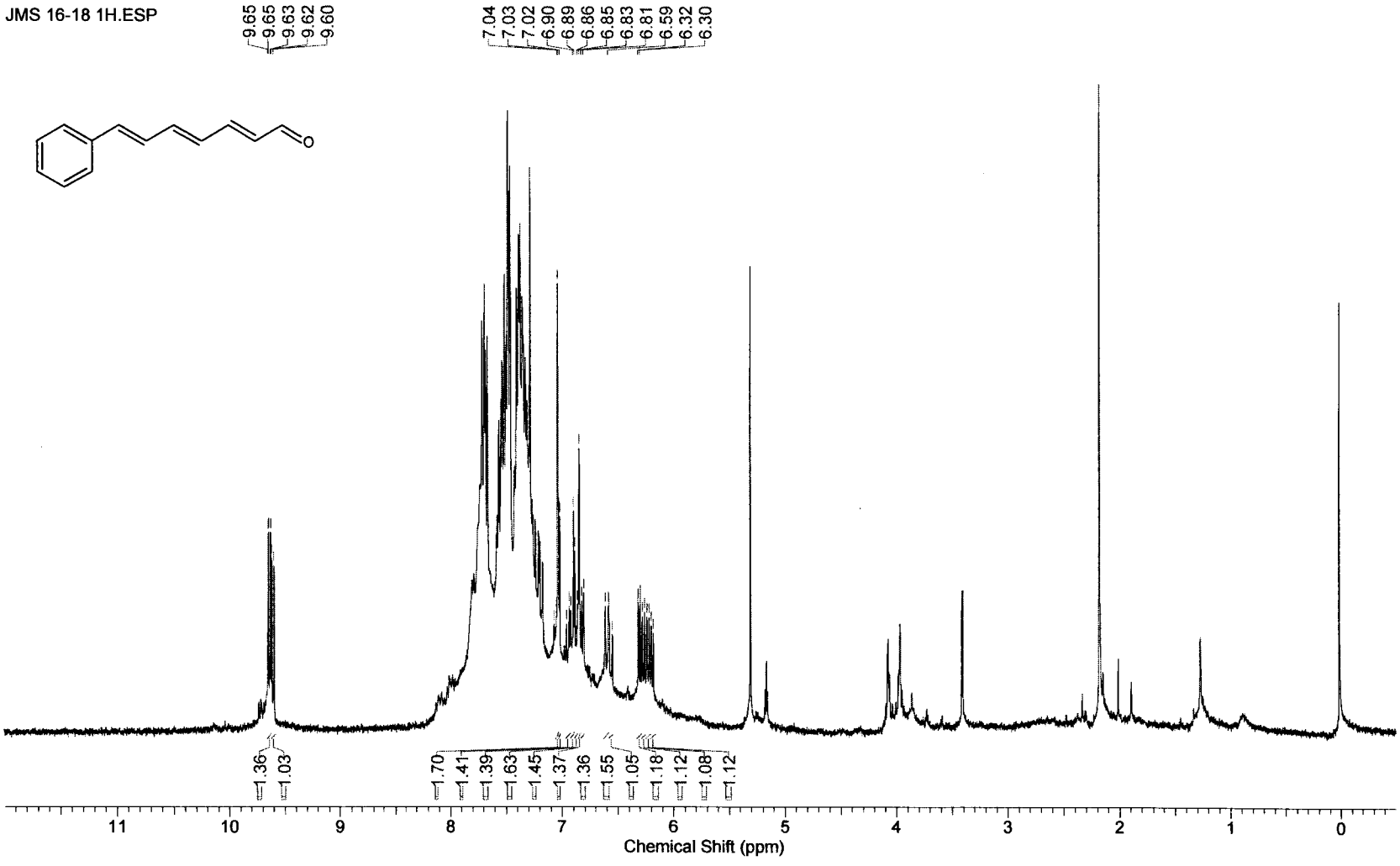

Figure A.31: ^{1}H NMR Spectrum of (2*E*,4*E*,6*E*)-7-phenylhepta-2,4,6-trienal (JMS 16-18)

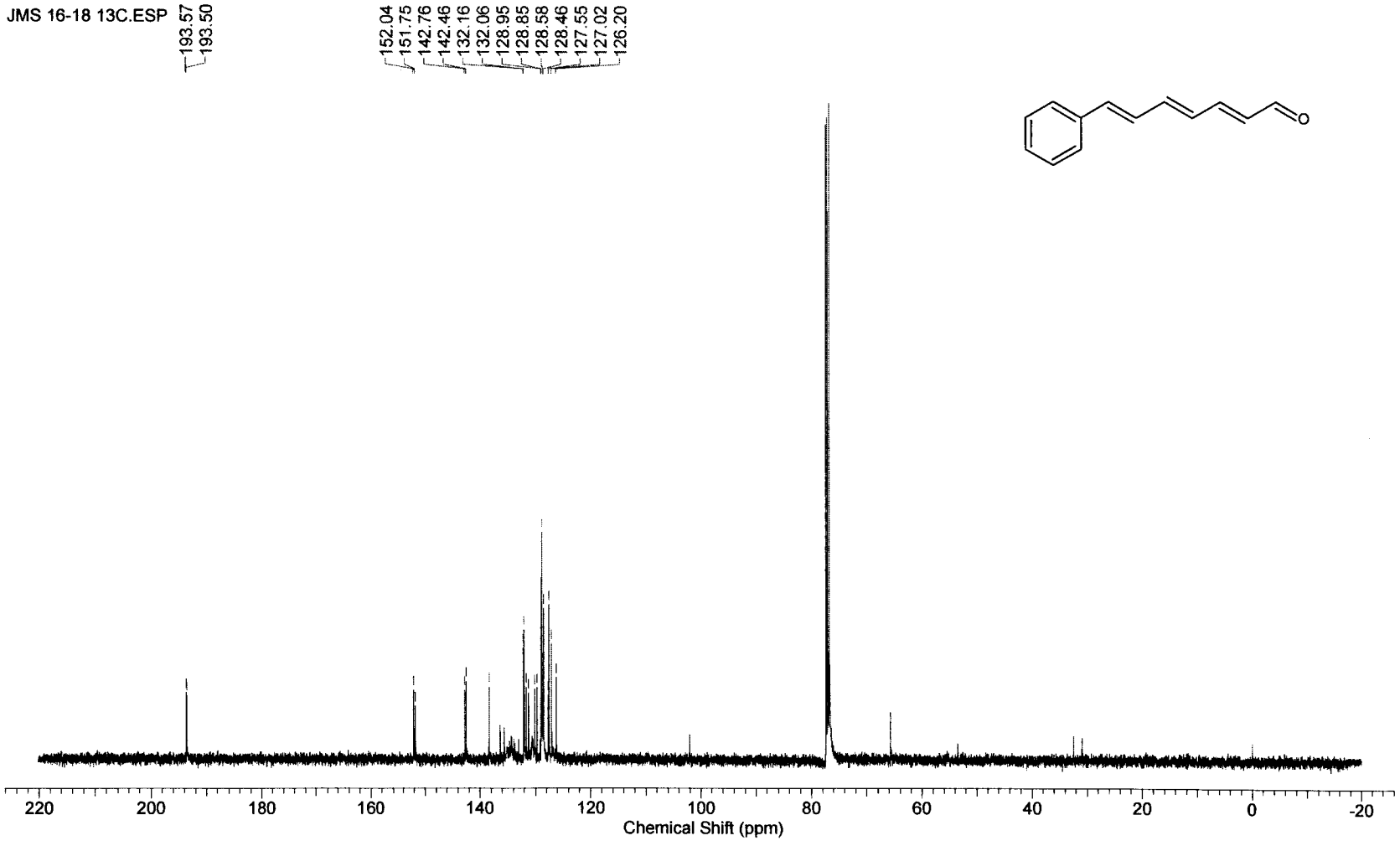

Figure A.32: ^{13}C NMR Spectrum of (2*E*,4*E*,6*E*)-7-phenylhepta-2,4,6-trienal (JMS 16-18)

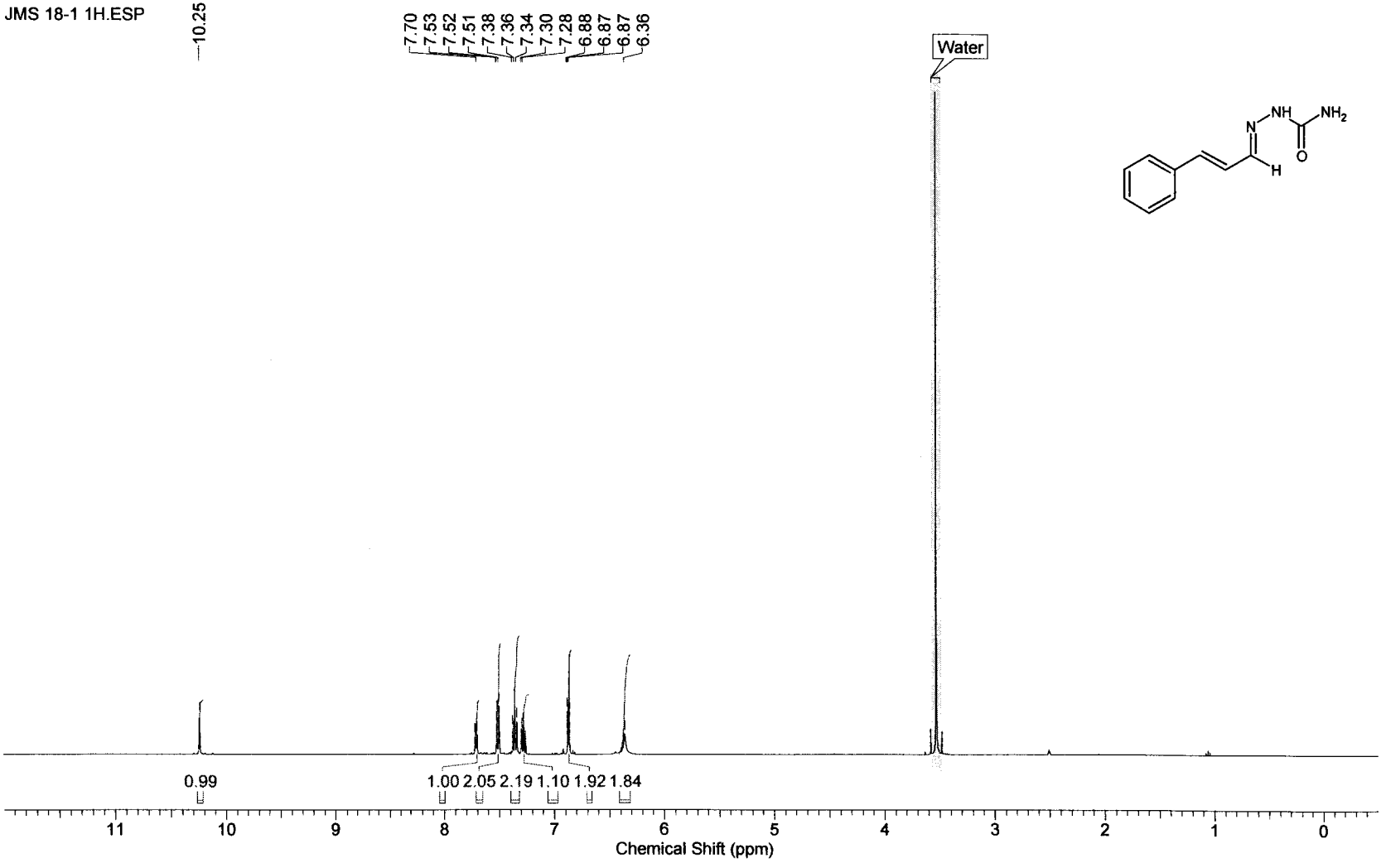

Figure A.33: ^{1}H NMR Spectrum of *E*-Cinnamaldehyde Semicarbazone (JMS 18-1)

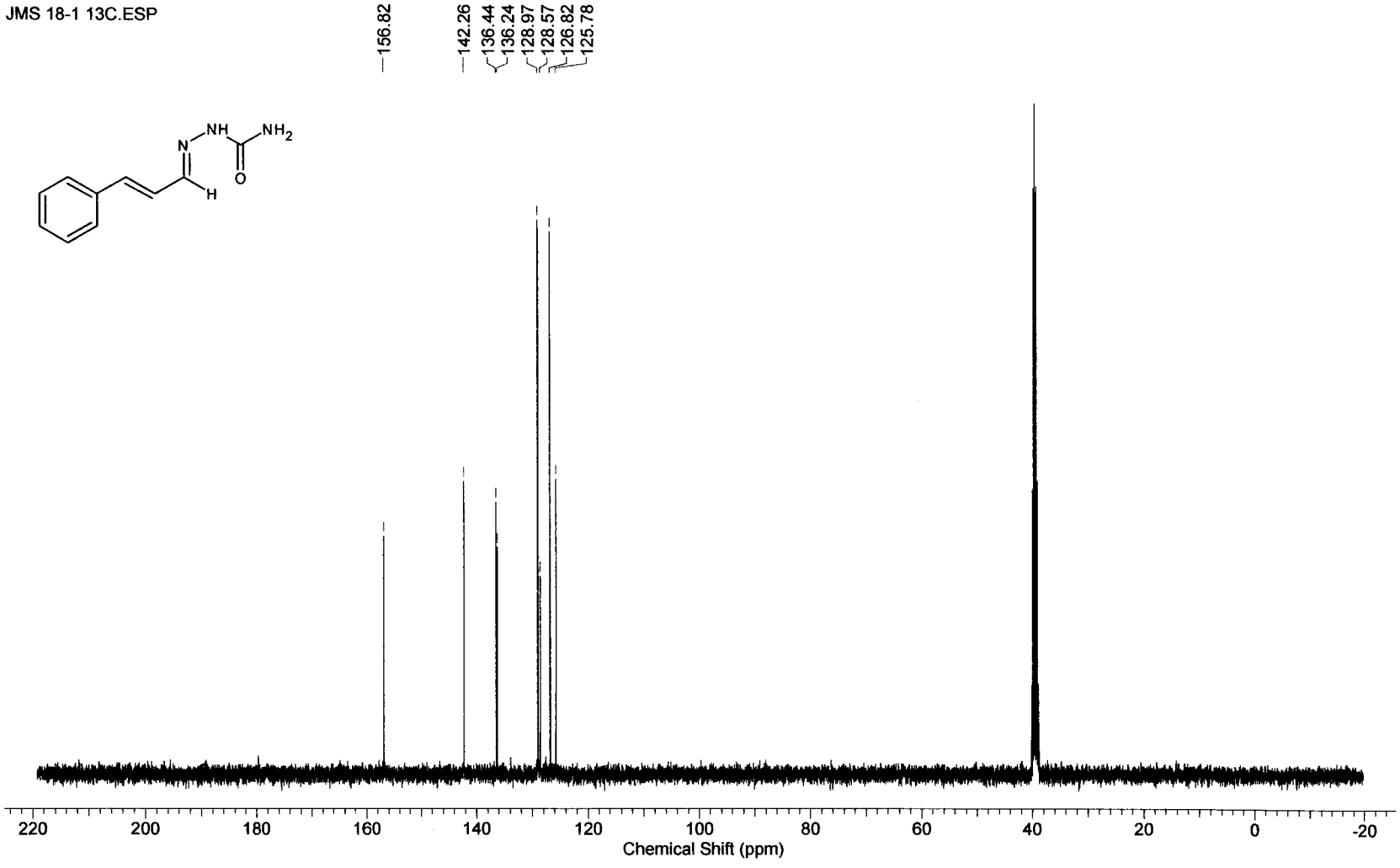

Figure A.34: ^{13}C NMR Spectra of Cinnamaldehyde Semicarbazone (JMS 18-1)

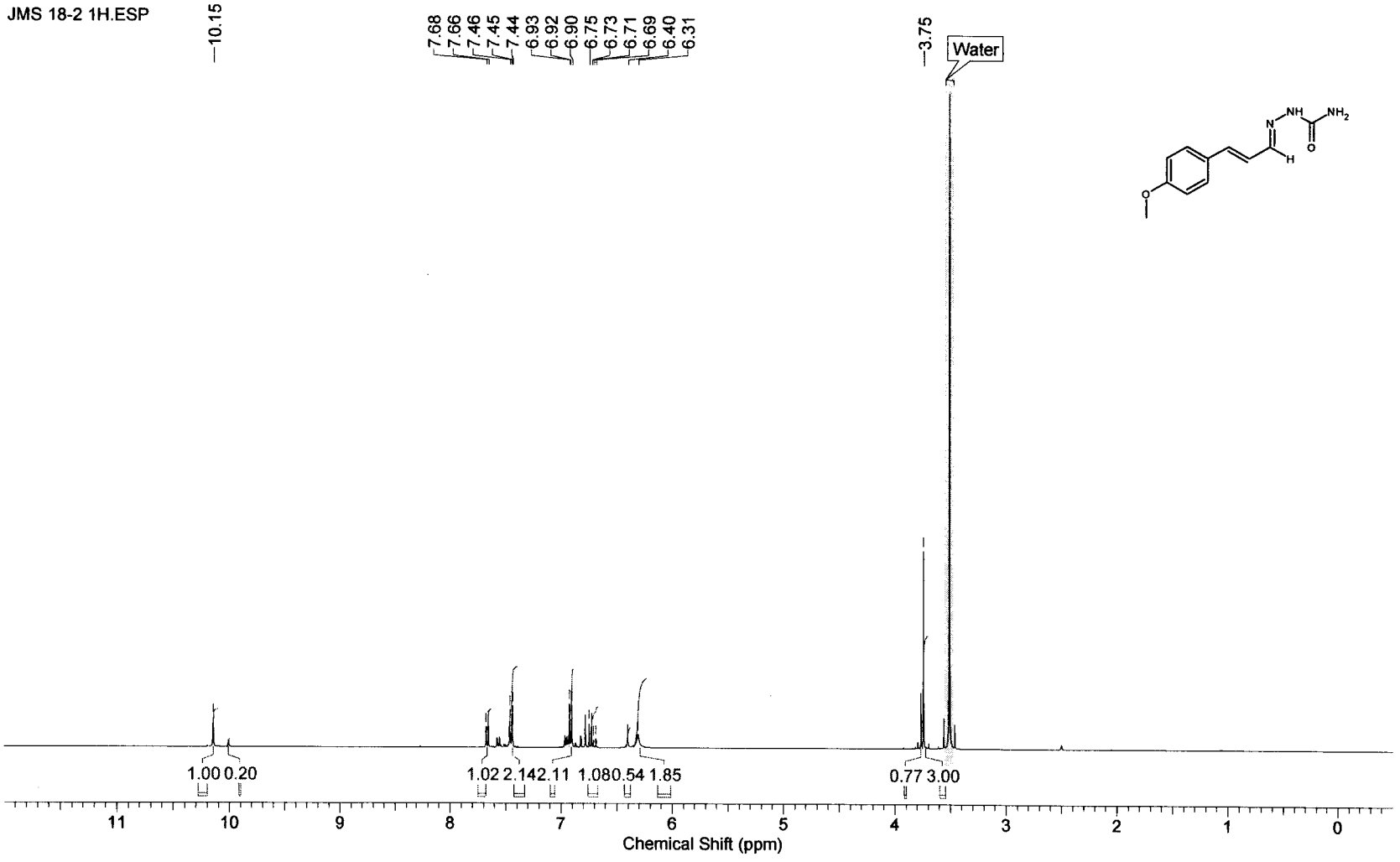

Figure A.35: ^{1}H NMR Spectrum of *E*-4-methoxycinnamaldehyde Semicarbazone (JMS 18-2)

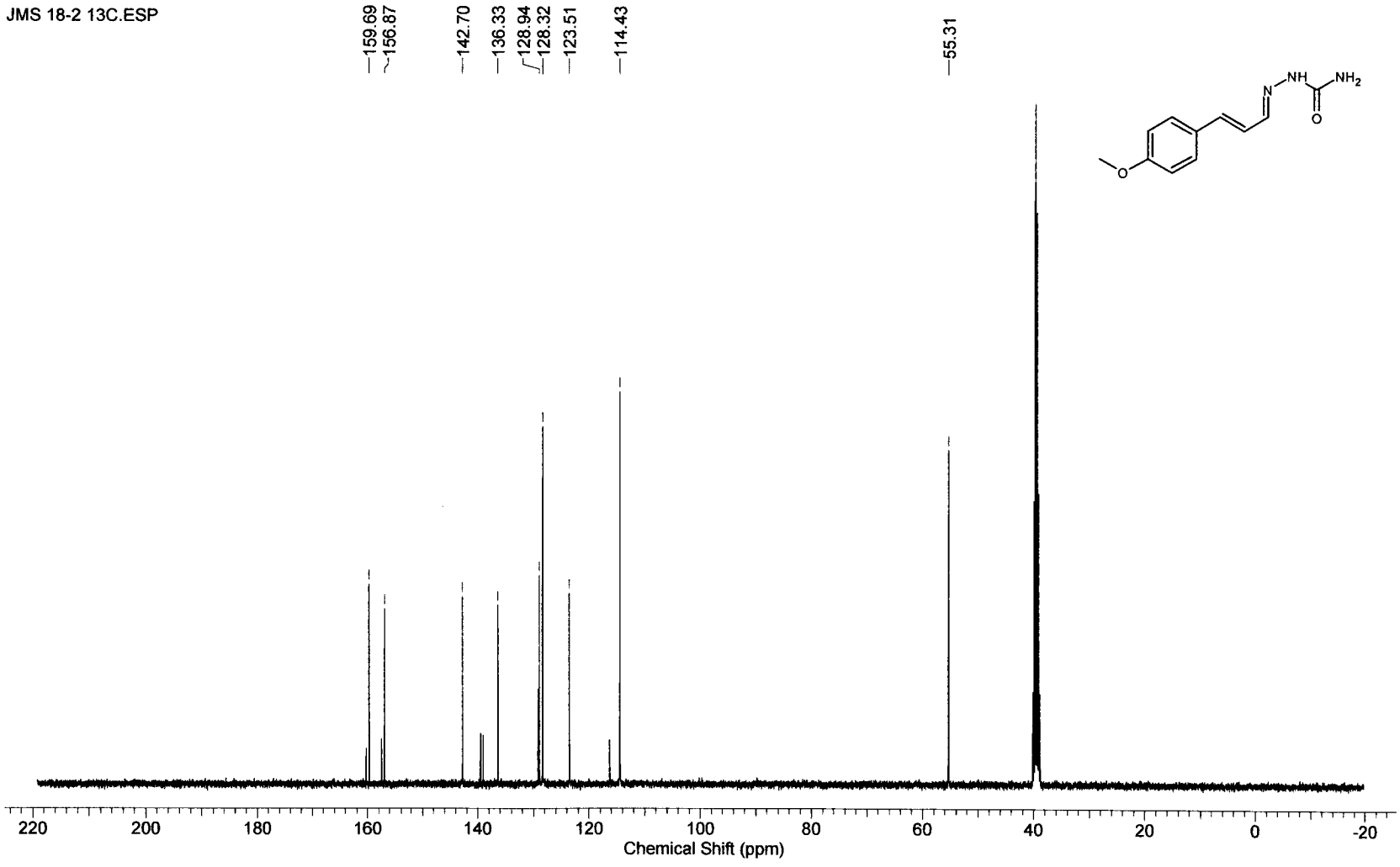

Figure A.36: ^{13}C NMR Spectrum of *E*-4-methoxycinnamaldehyde Semicarbazone (JMS 18-2)

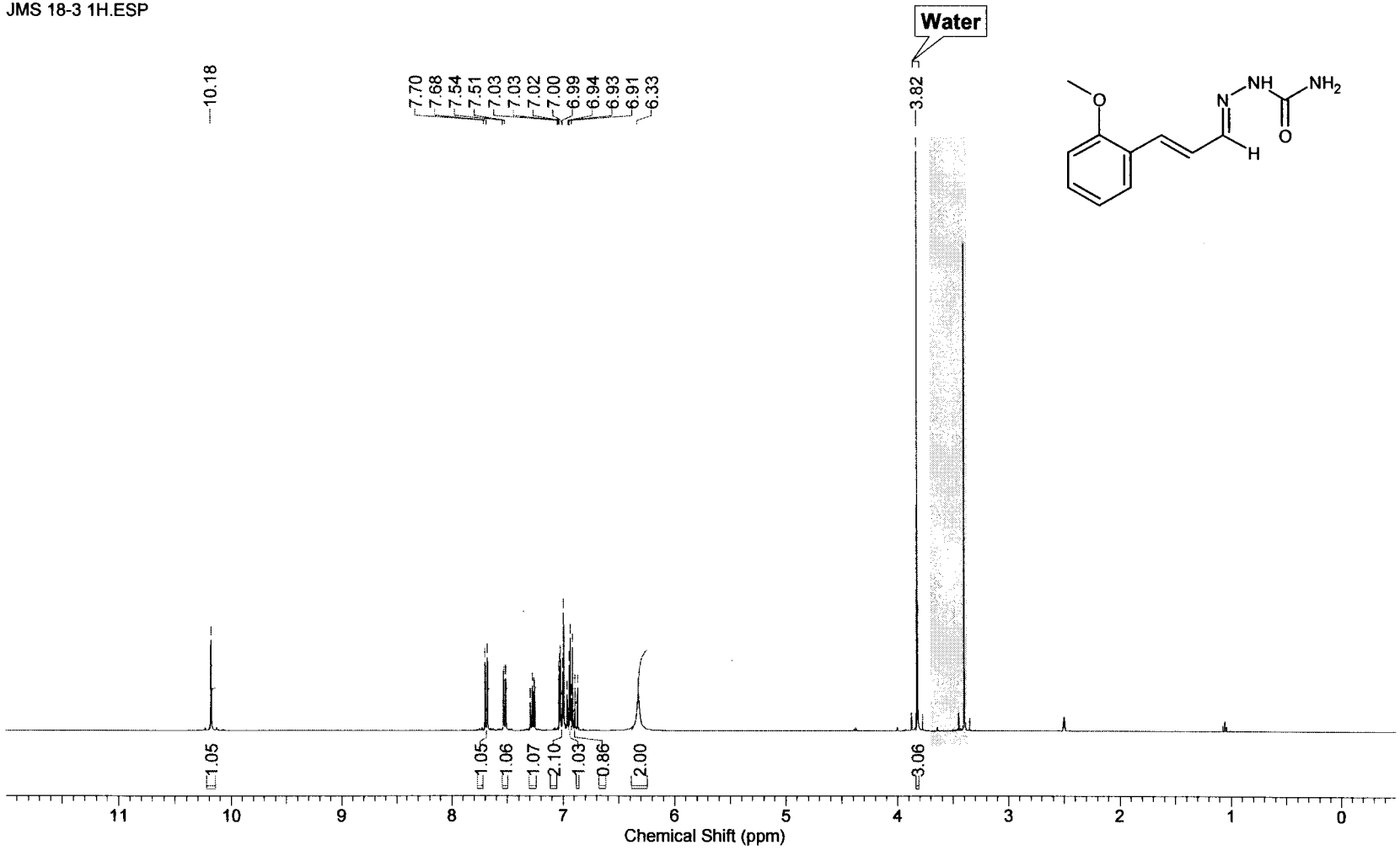

Figure A.37: ^{1}H NMR Spectrum of *E*-2-methoxycinnamaldehyde Semicarbazone (JMS 18-3)

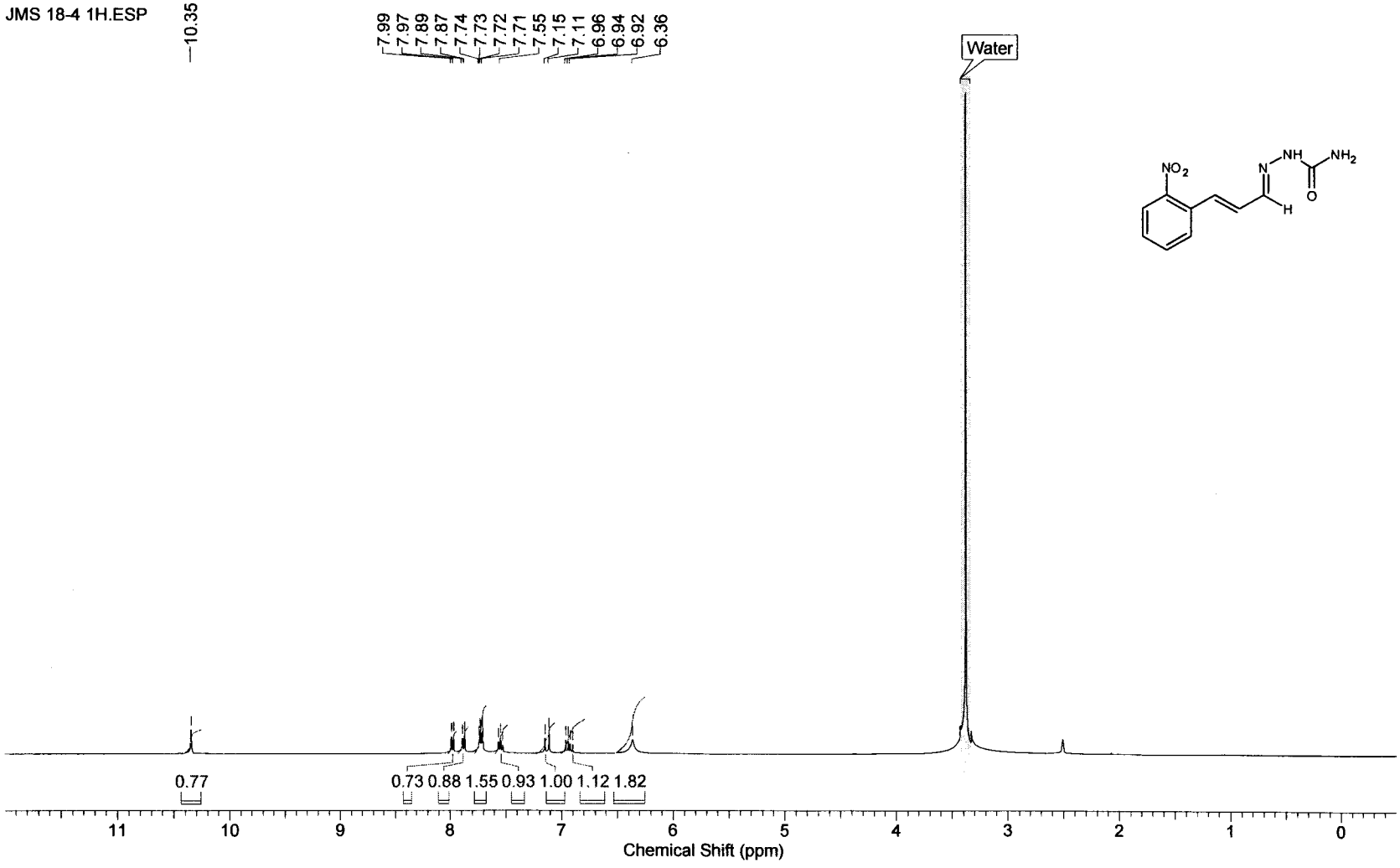

Figure A.38: ^{1}H NMR Spectrum of *E*-2-nitrocinnamaldehyde Semicarbazone (JMS 18-4)

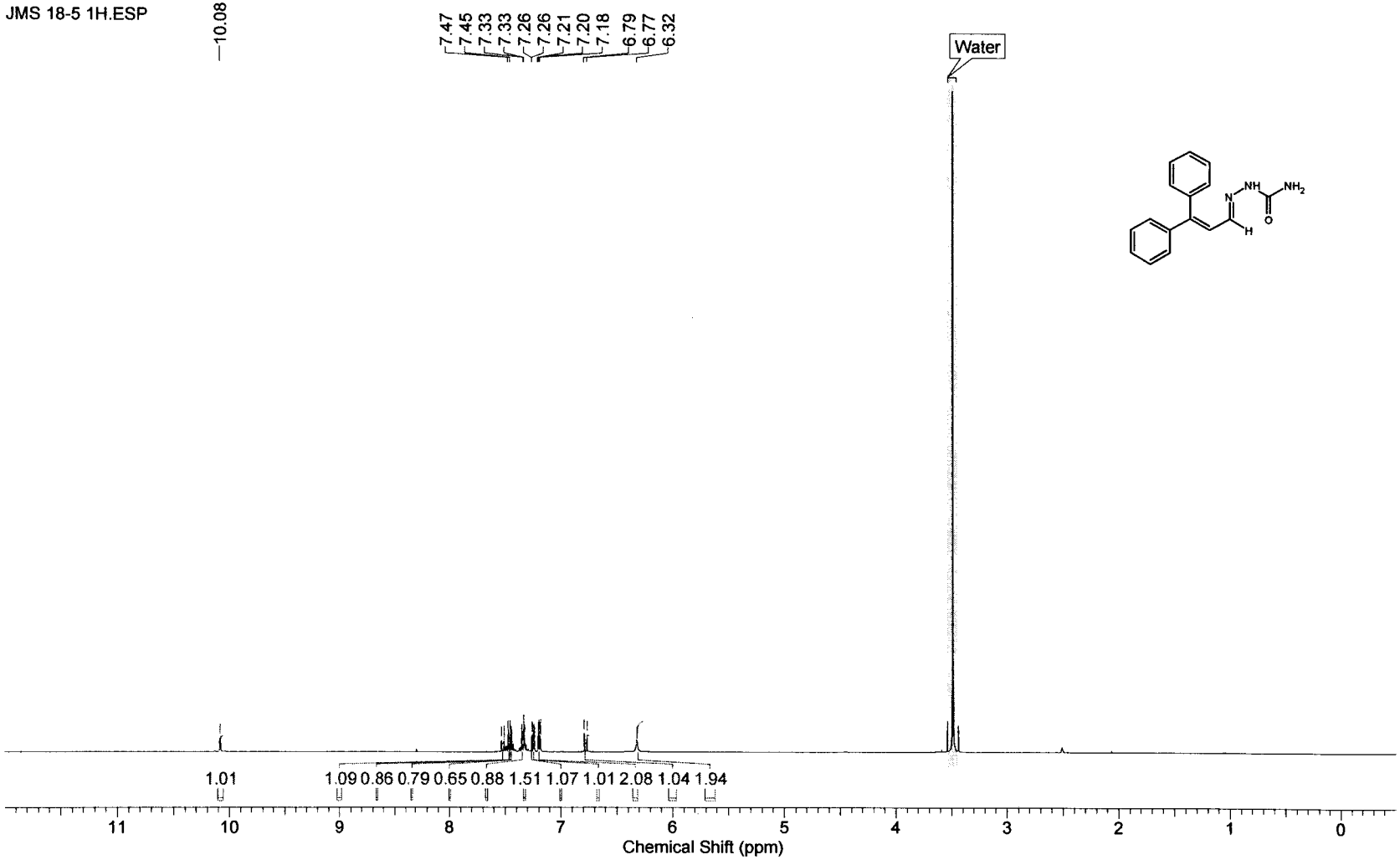

Figure A.39: ^{1}H NMR Spectrum of 2-phenylcinnamaldehyde Semicarbazone (JMS 18-5)

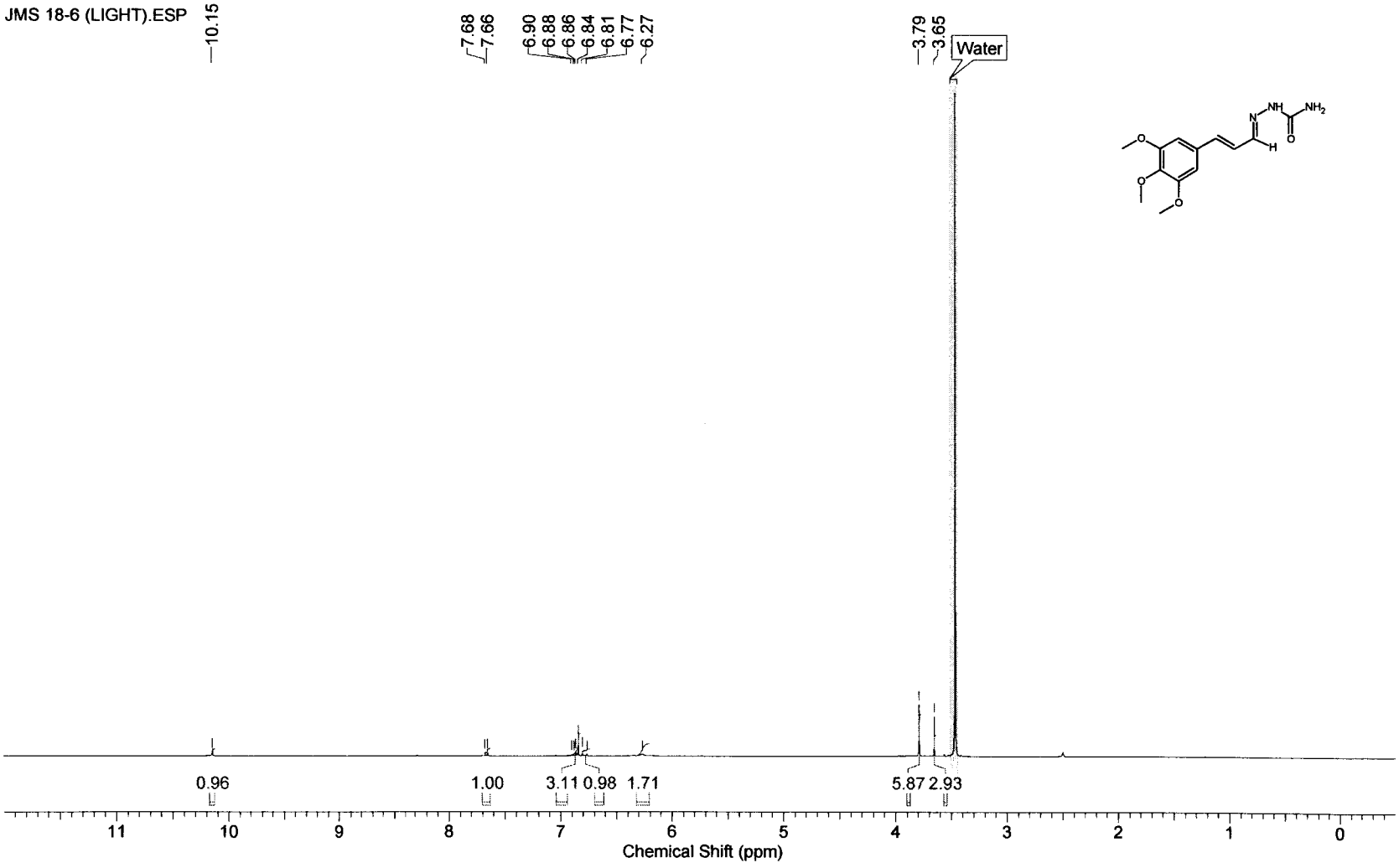

Figure A.40: ^{1}H NMR Spectrum of *E*-3,4,5-trimethoxycinnamaldehyde Semicarbazone (JMS 18-6)

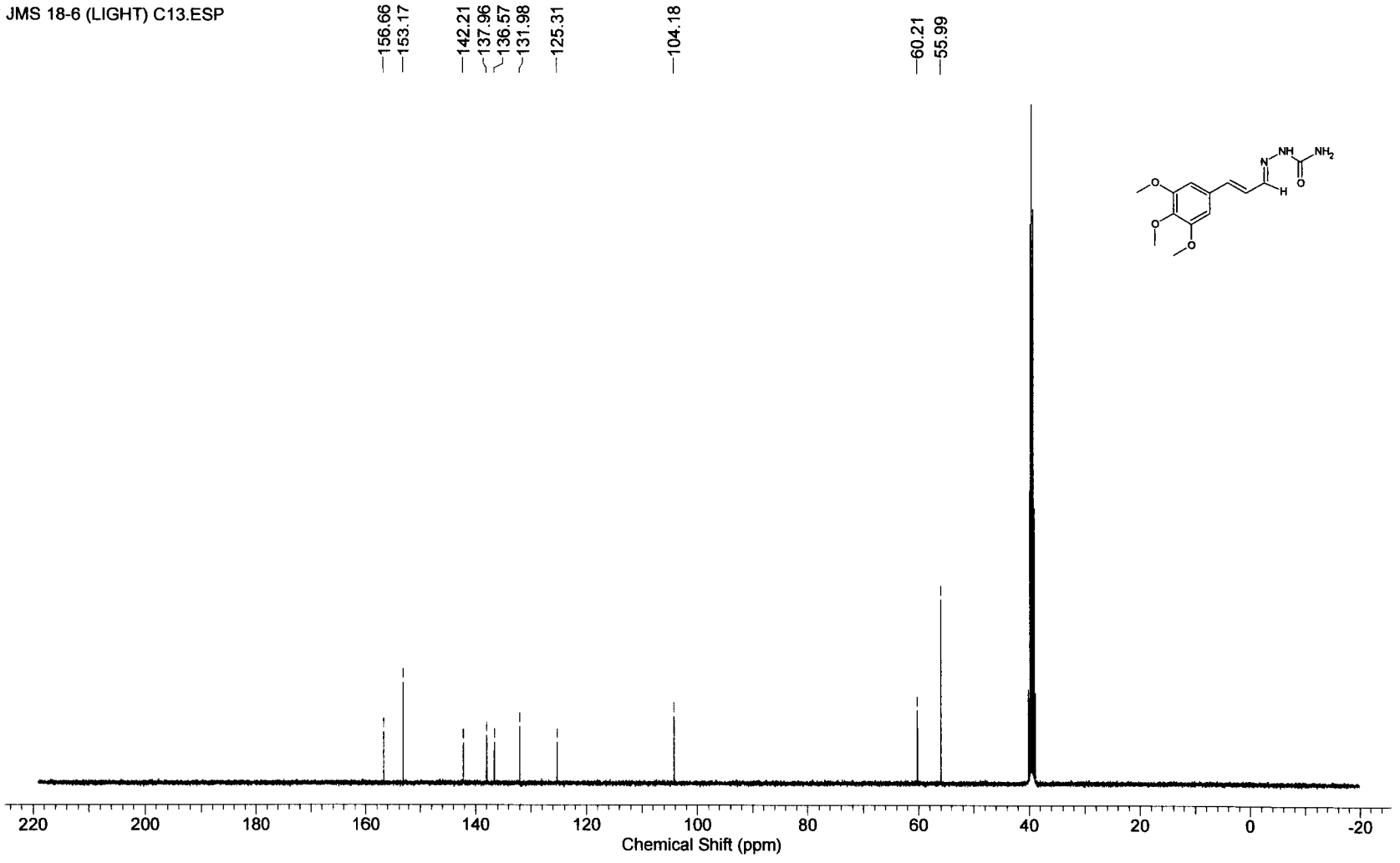

Figure A.41: ^{13}C NMR Spectrum of *E*-3,4,5-trimethoxycinnamaldehyde Semicarbazone (JMS 18-6)

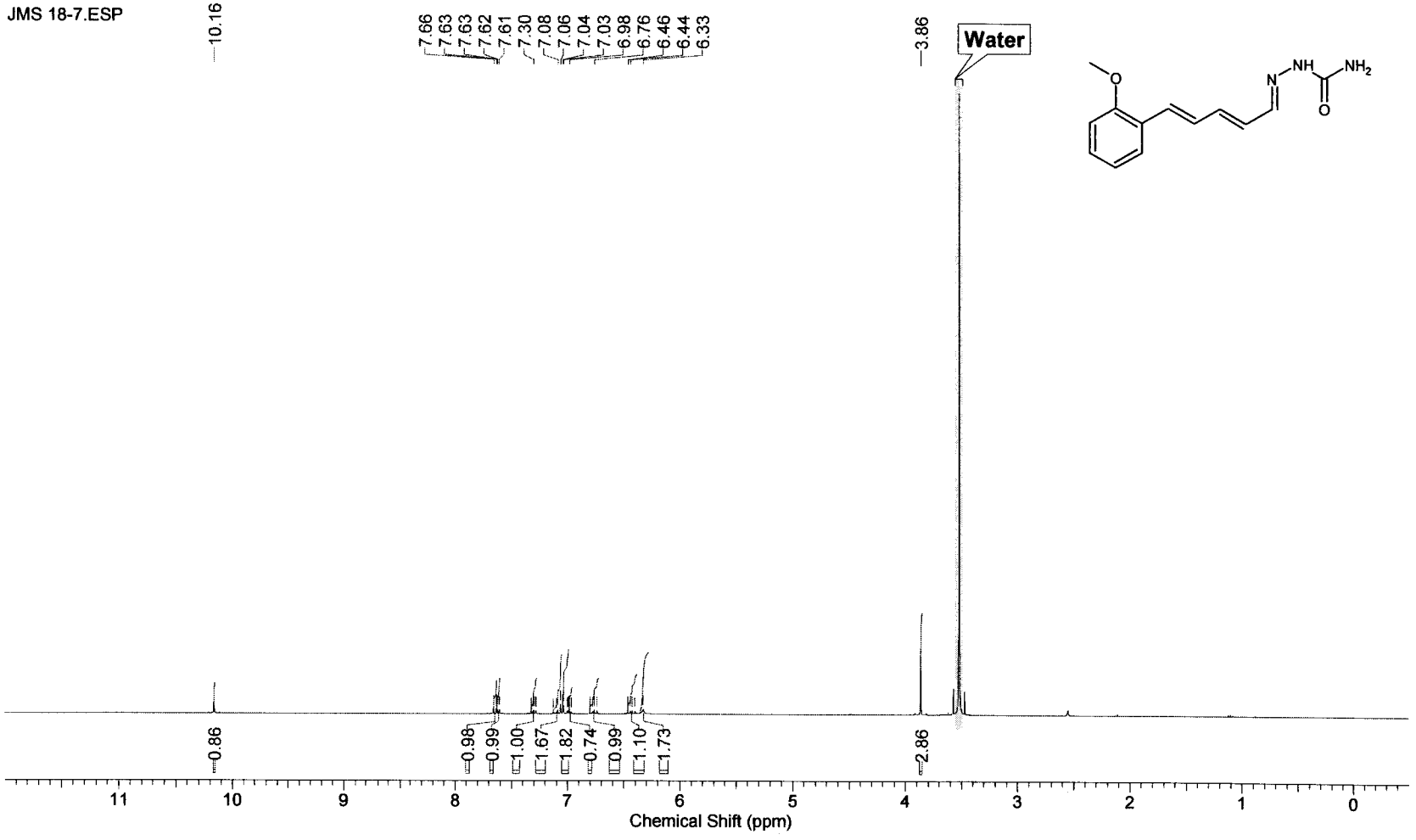

Figure A.42: ^{1}H NMR Spectrum of *E,E*-5-(2-methoxyphenyl)penta-2,4-dienal Semicarbazone (JMS 18-7)

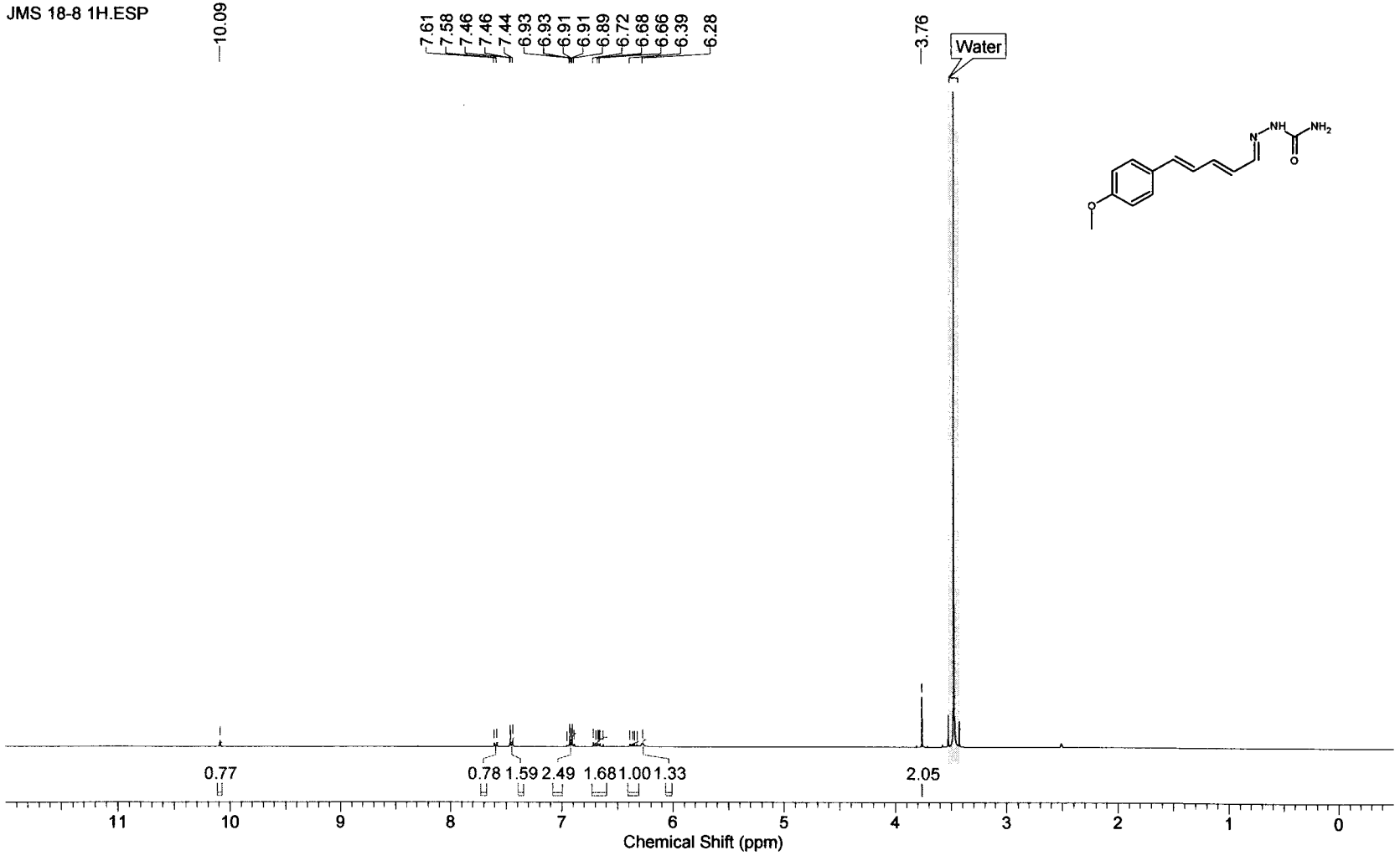

Figure A.43: ^{1}H NMR Spectrum of *E,E*-5-(4-methoxyphenyl)penta-2,4-dienal Semicarbazone (JMS 18-8)

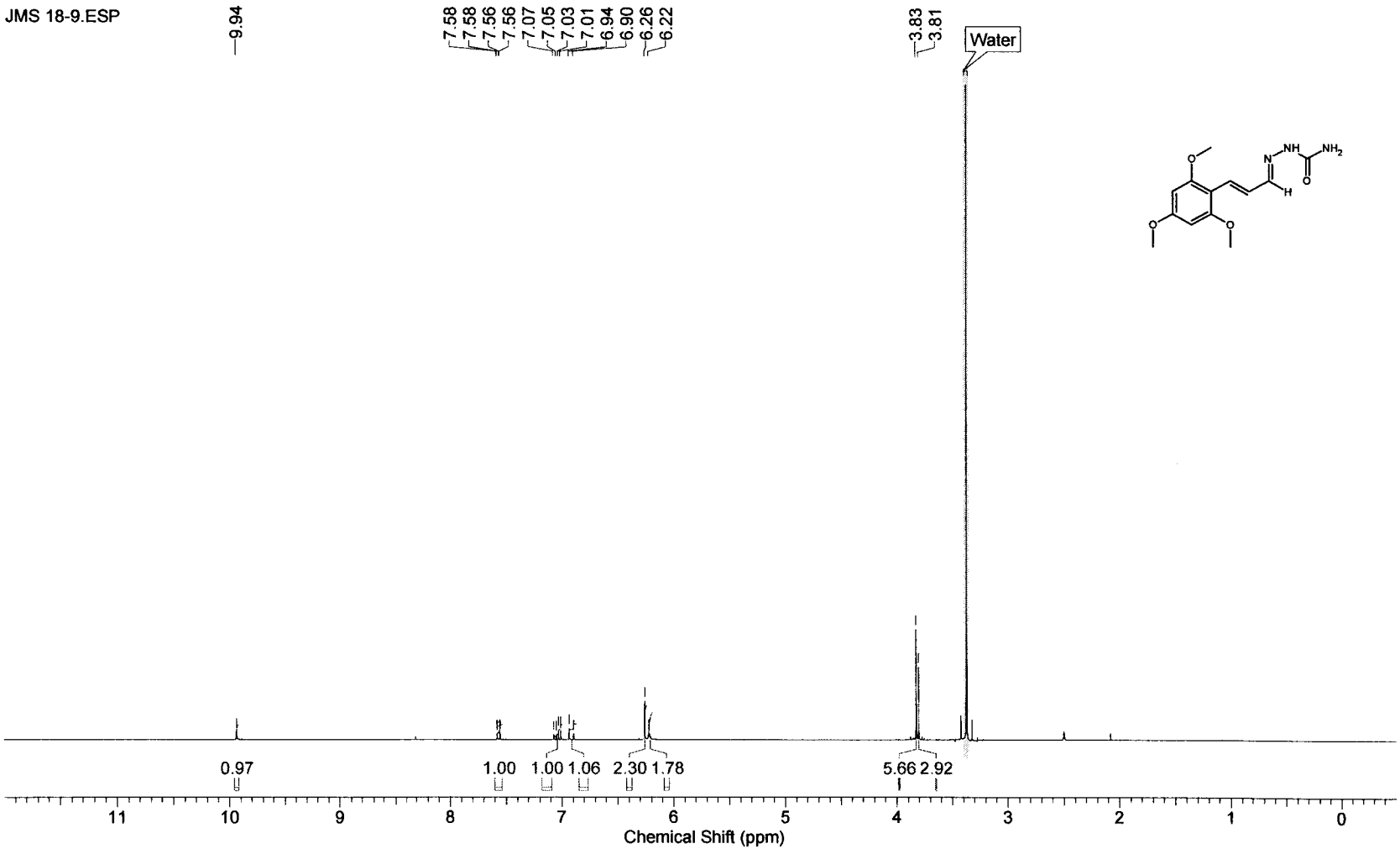

Figure A.44: ^{1}H NMR Spectrum of **E**-2,4,6-trimethoxycinnamaldehyde Semicarbazone (JMS 18-9)

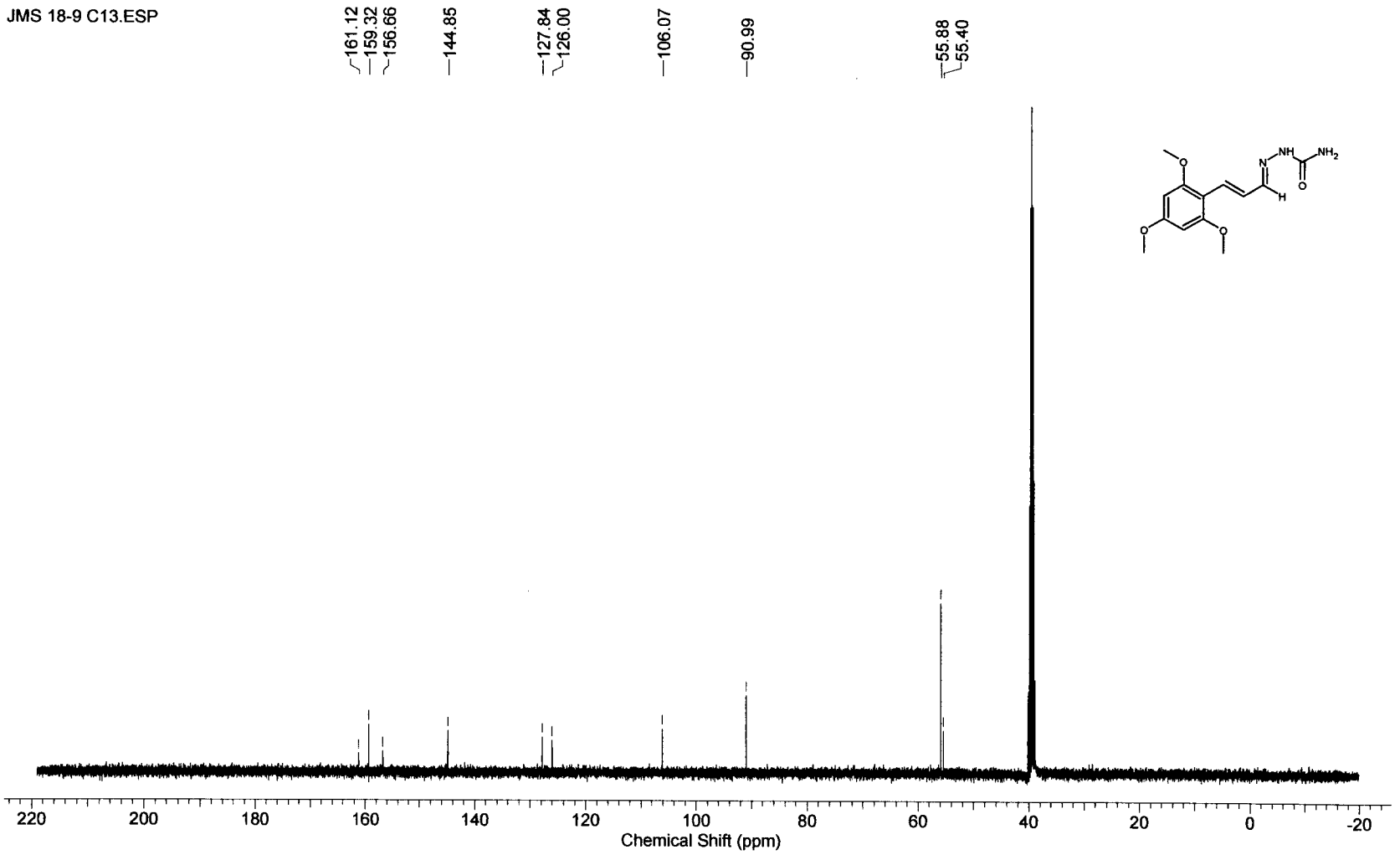

Figure A.45: ^{13}C NMR Spectrum of *E*-2,4,6-trimethoxycinnamaldehyde Semicarbazone (JMS 18-9)

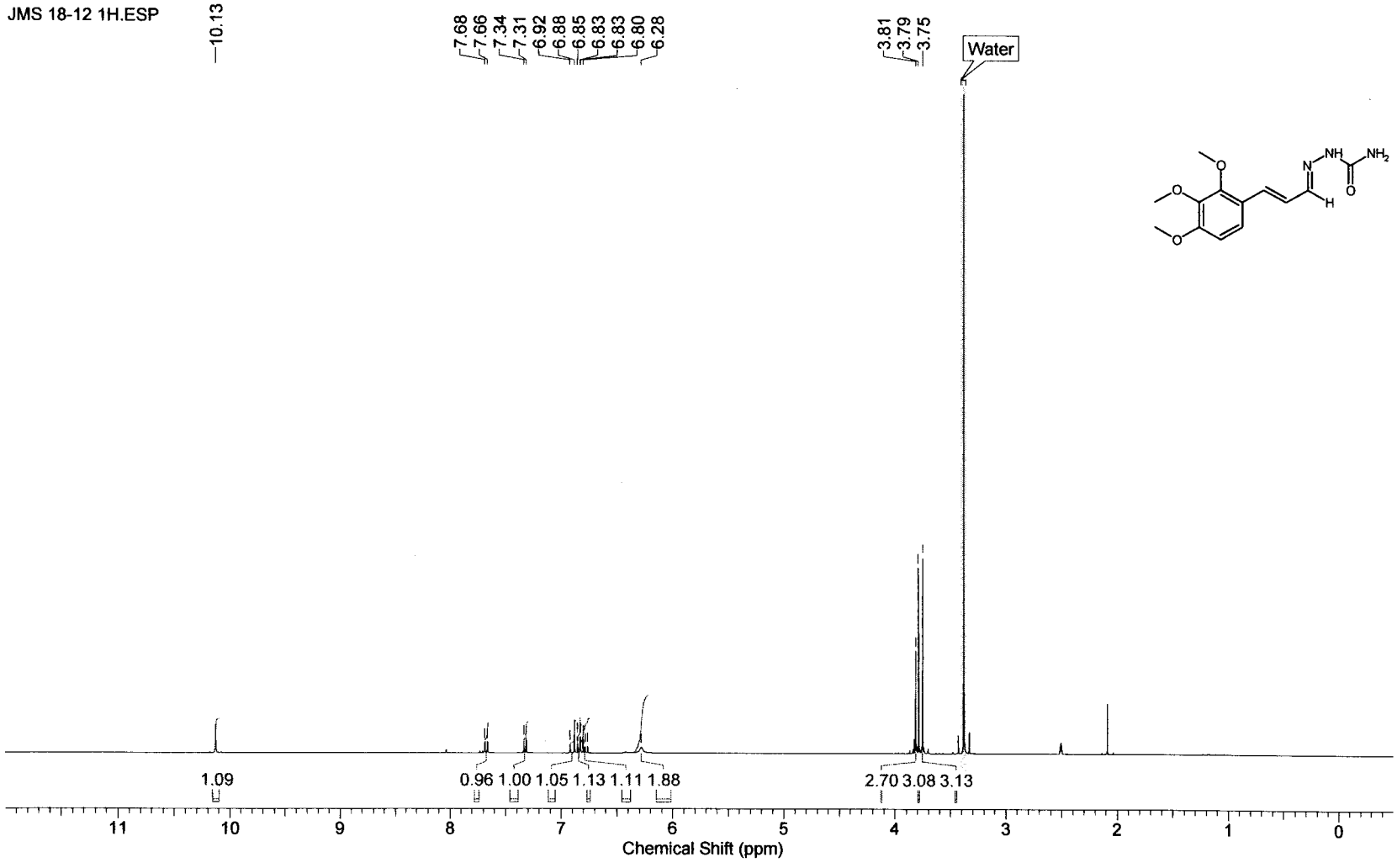

Figure A.46: ^{1}H NMR Spectrum of *E*-2,3,4-trimethoxycinnamaldehyde Semicarbazone (JMS 18-12)

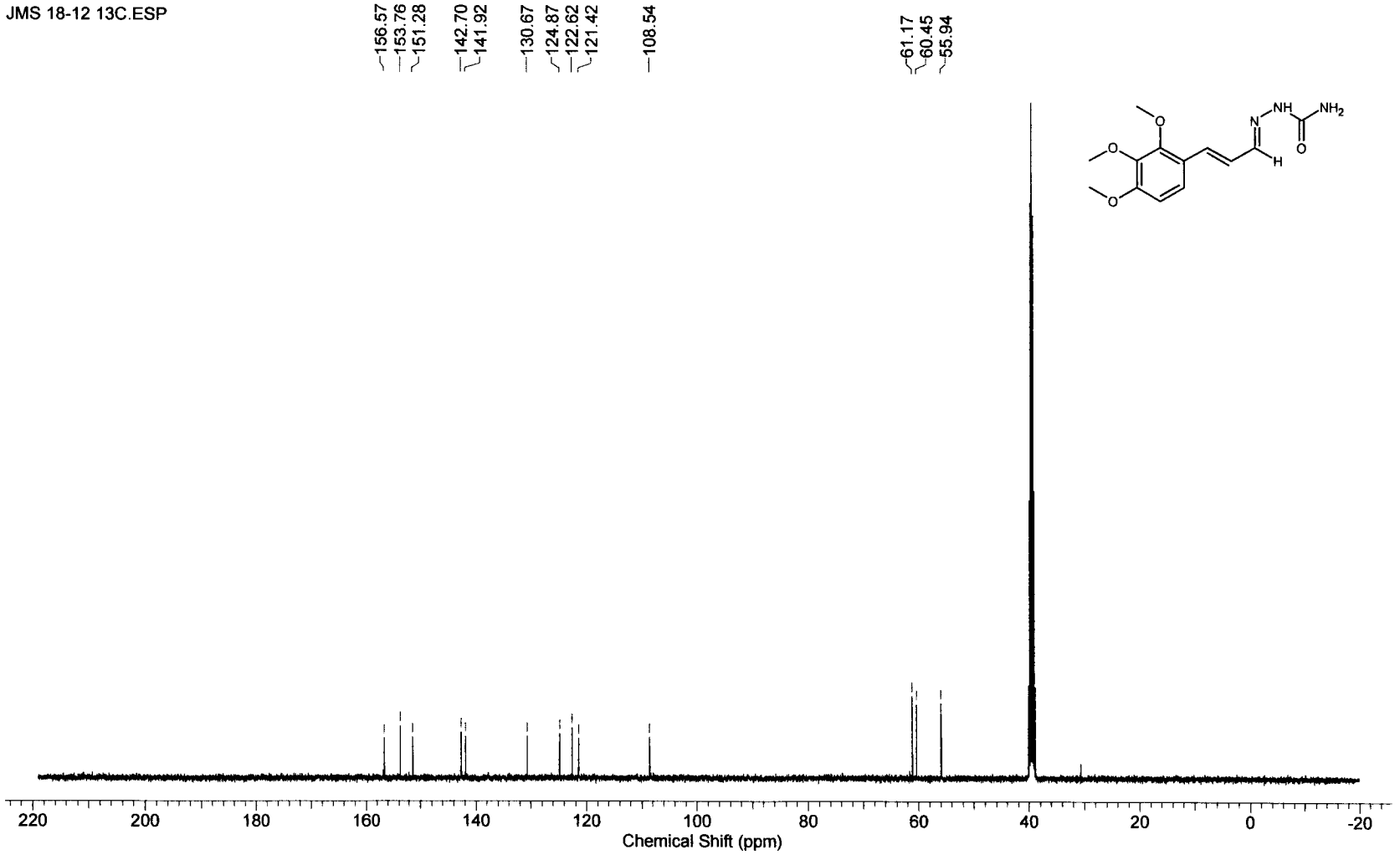

Figure A.47: ^{13}C NMR Spectrum of *E*-2,3,4-trimethoxycinnamaldehyde Semicarbazone (JMS 18-12)

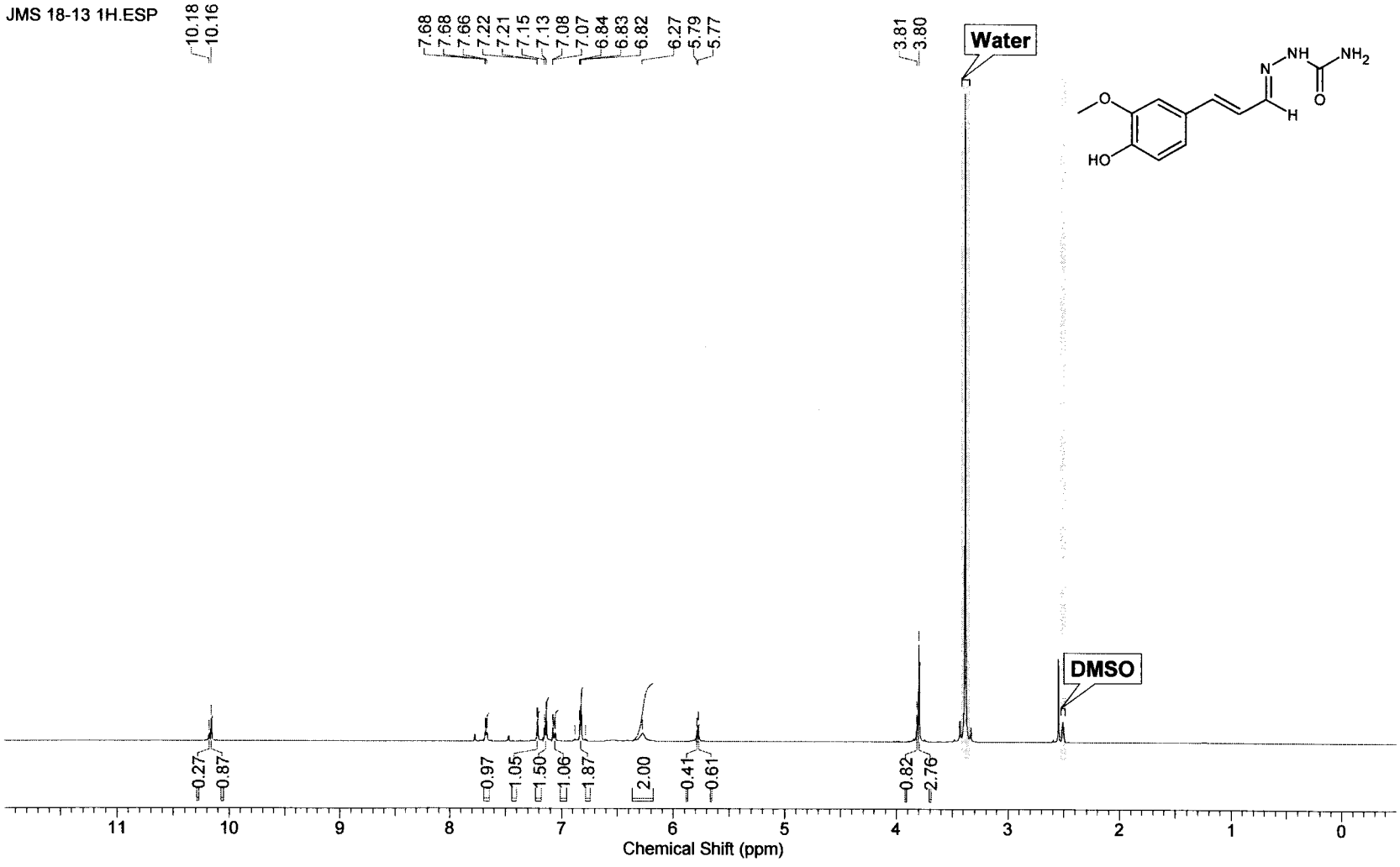

Figure A.48: ^{1}H NMR Spectrum of *E*-4-hydroxy-3-methoxycinnamaldehyde Semicarbazone (JMS 18-13)

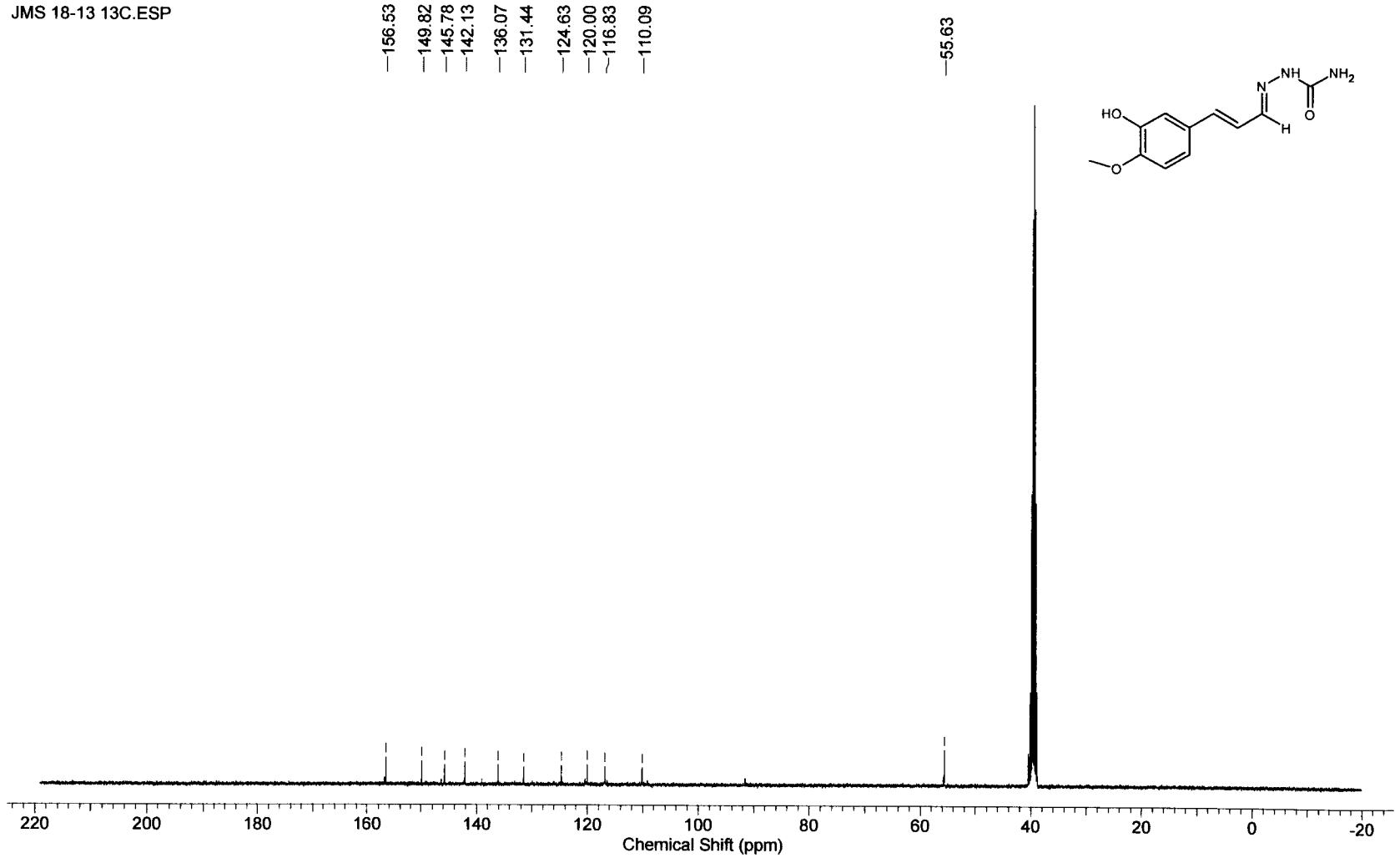

Figure A.49: ^{13}C NMR Spectrum of *E*-4-hydroxy-3-methoxycinnamaldehyde Semicarbazone (JMS 18-13)

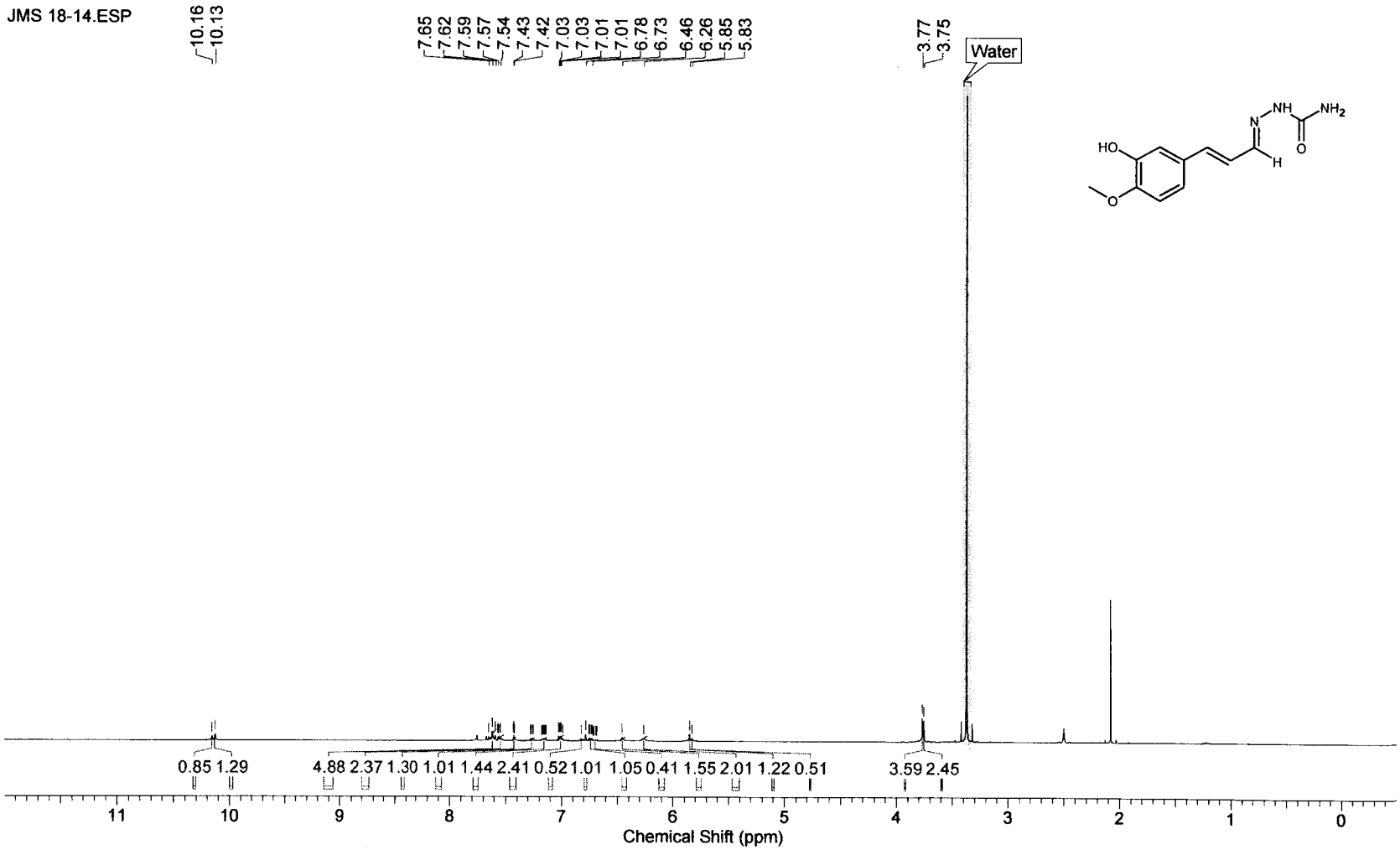

Figure A.50: ^{1}H NMR Spectrum of *E*-3-hydroxy-4-methoxycinnamaldehyde Semicarbazone (JMS 18-14)

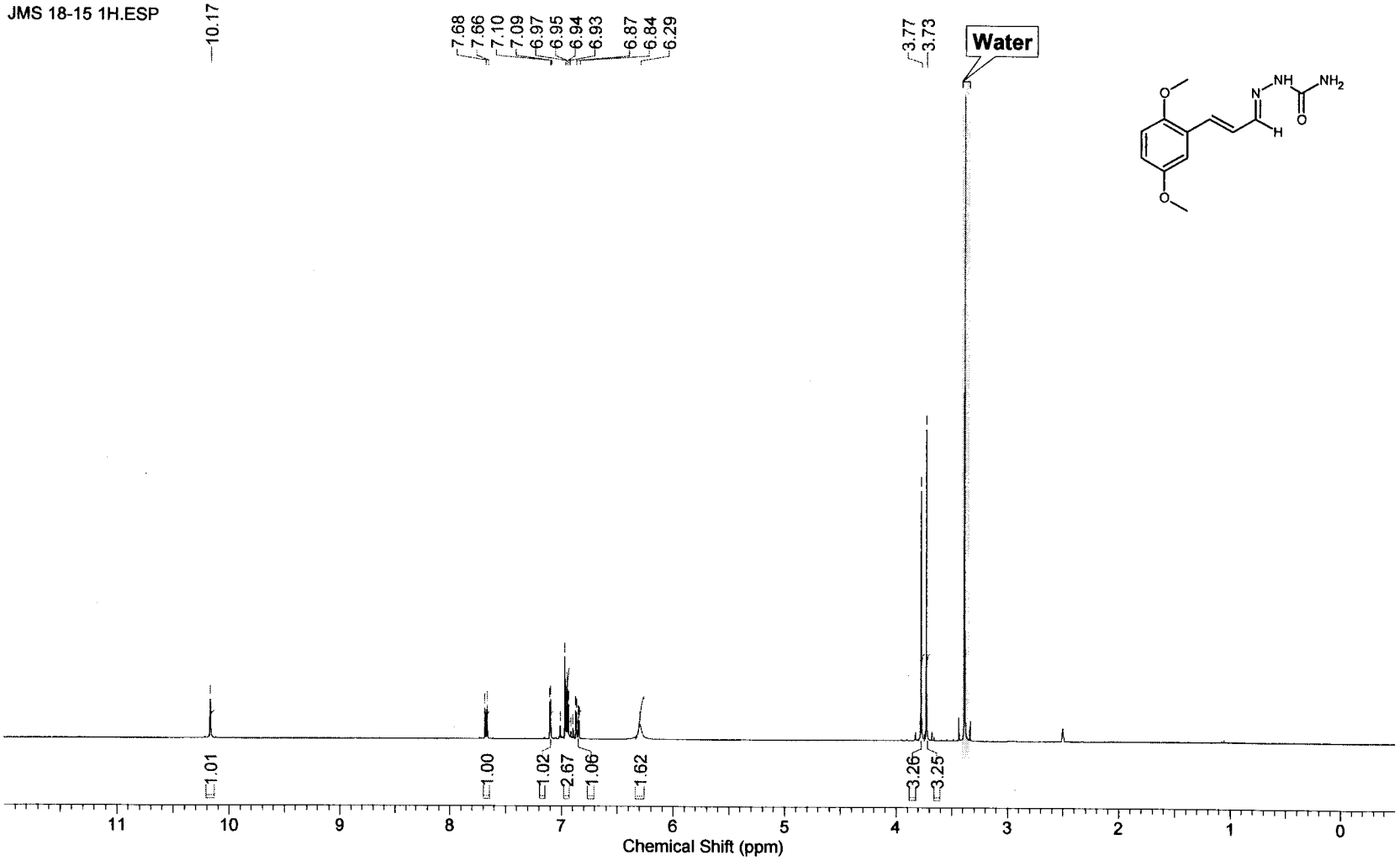

Figure A.51: ^{1}H NMR Spectrum of *E*-2,5-dimethoxycinnamaldehyde Semicarbazone (JMS 18-15)

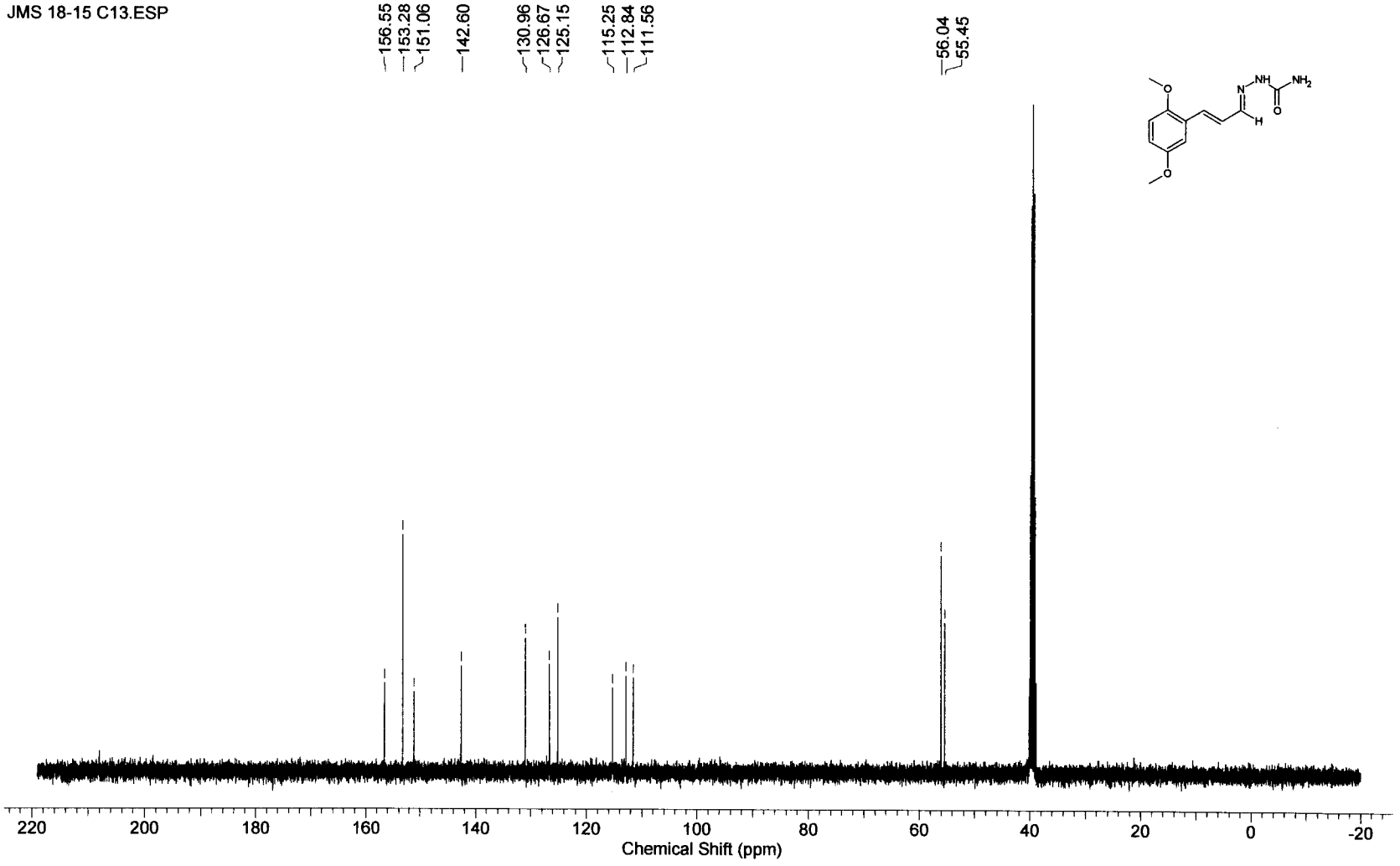

Figure A.52: ^{13}C NMR Spectrum of *E*-2,5-dimethoxycinnamaldehyde Semicarbazone (JMS 18-15)

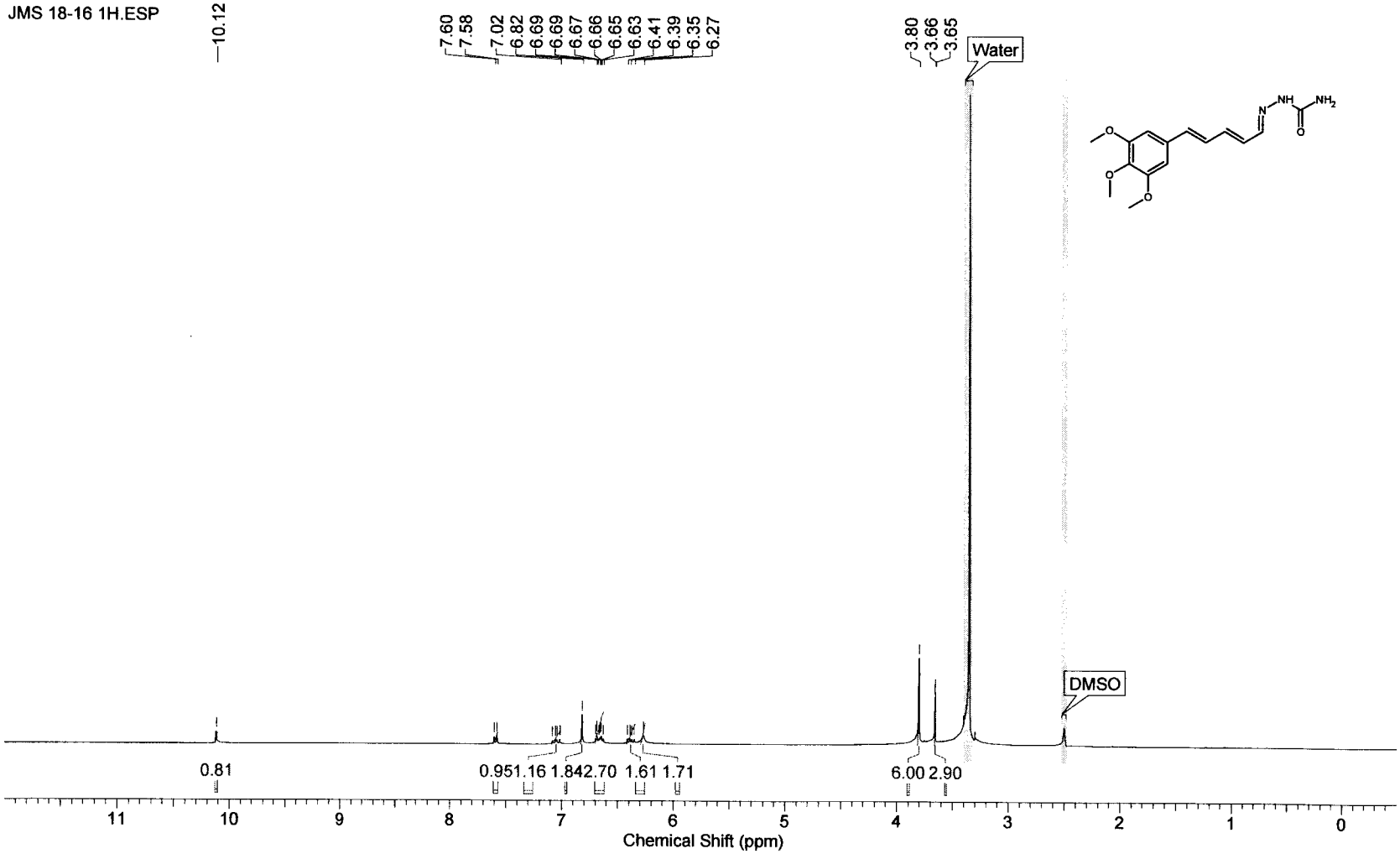

Figure A.53: ^{1}H NMR Spectrum of (2*E*,4*E*)-5-(3,4,5-trimethoxyphenyl)penta-2,4-dienal Semicarbazone (JMS 18-16)

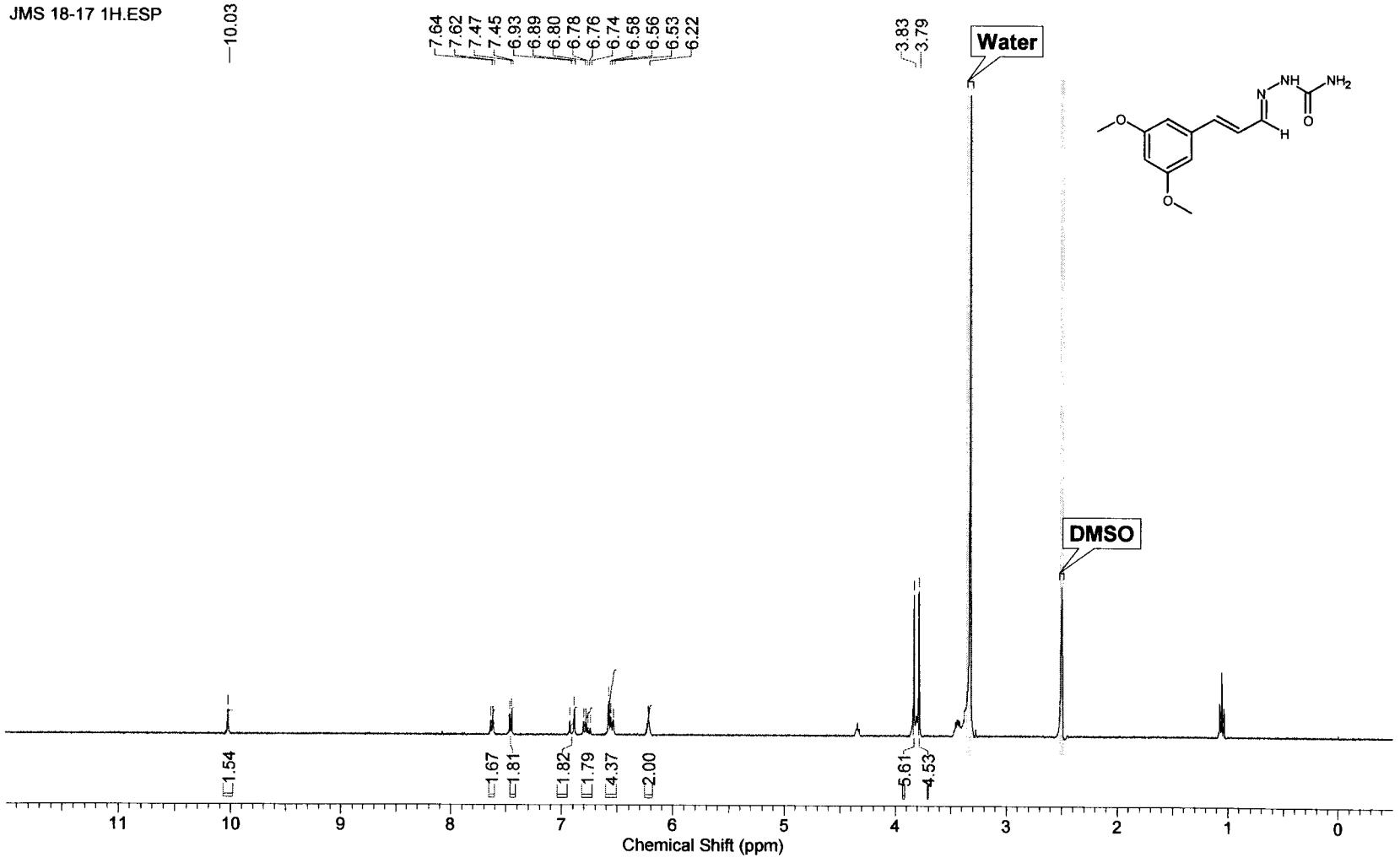

Figure A.54: ^{1}H NMR Spectrum of *E*-3,5-dimethoxycinnamaldehyde Semicarbazone (JMS 18-17)

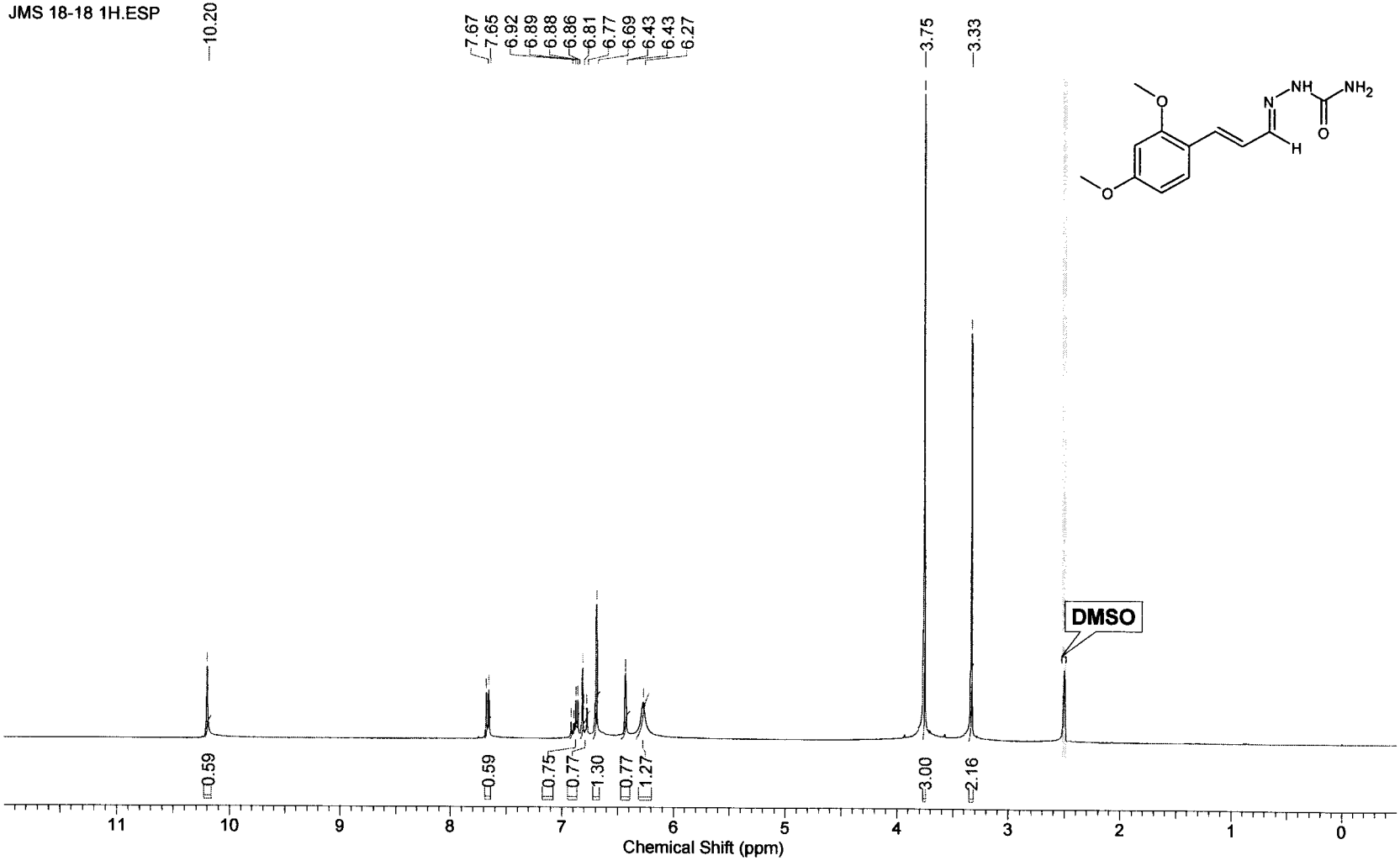

Figure A.55: ^{1}H NMR Spectrum of *E*-2,4-dimethoxycinnamaldehyde Semicarbazone (JMS 18-18)

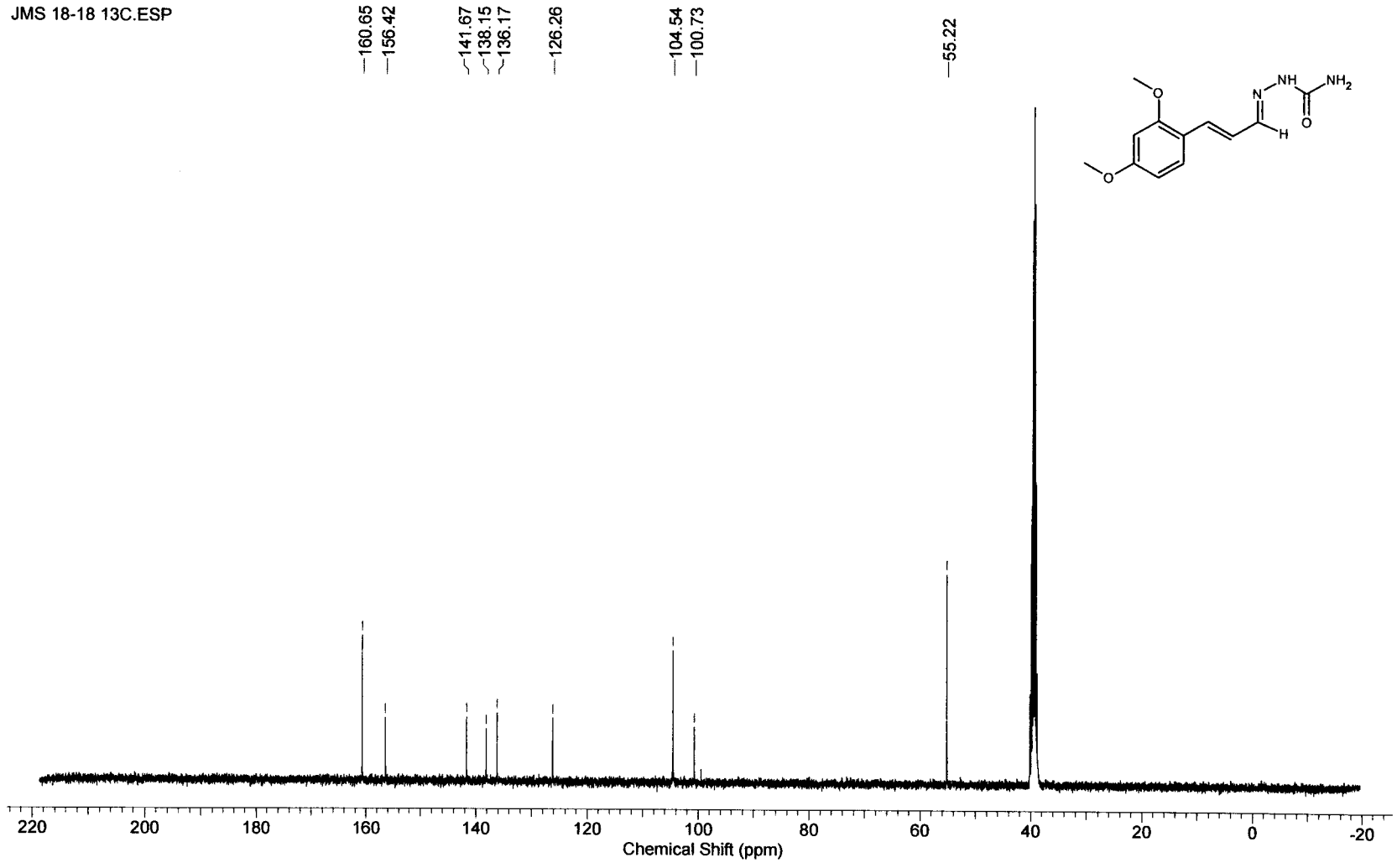

Figure A.56: ^{13}C NMR Spectrum of *E*-2,4-dimethoxycinnamaldehyde Semicarbazone (JMS 18-18)

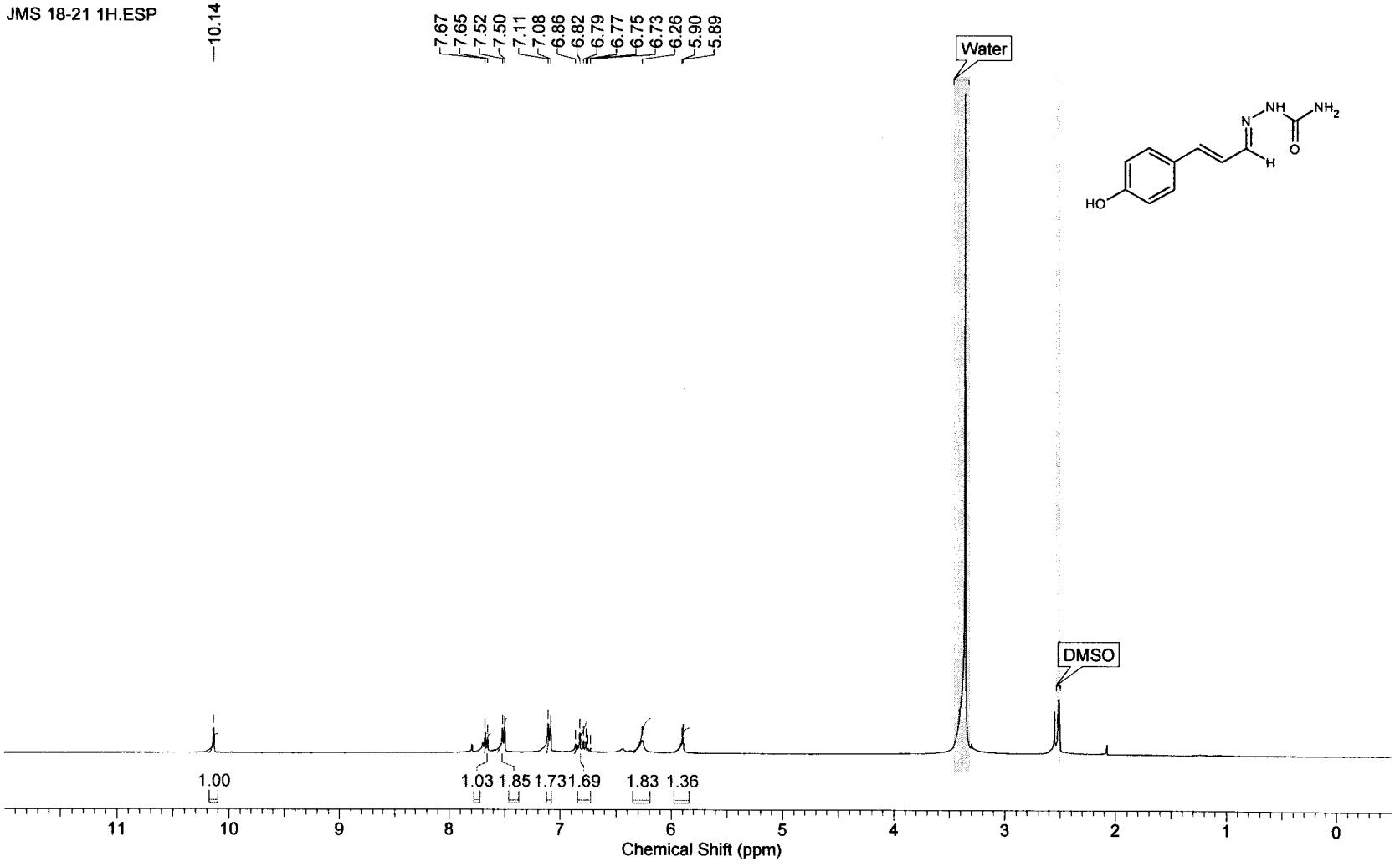

Figure A.57: ^{1}H NMR Spectrum of *E*-4-hydroxycinnamaldehyde Semicarbazone (JMS 18-21)

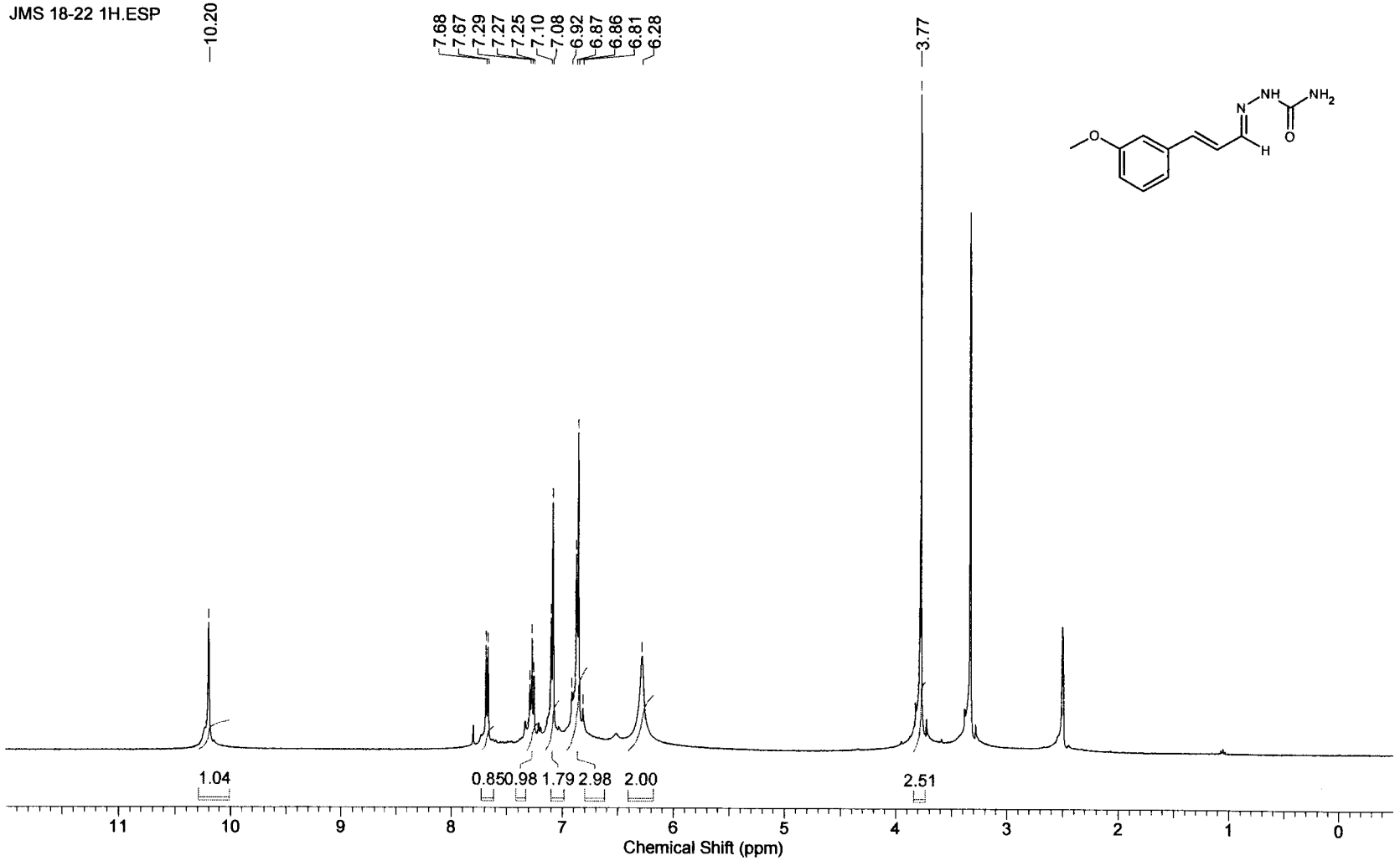

Figure A.58: ^{1}H NMR Spectrum of *E*-3-methoxycinnamaldehyde Semicarbazone (JMS 18-22)

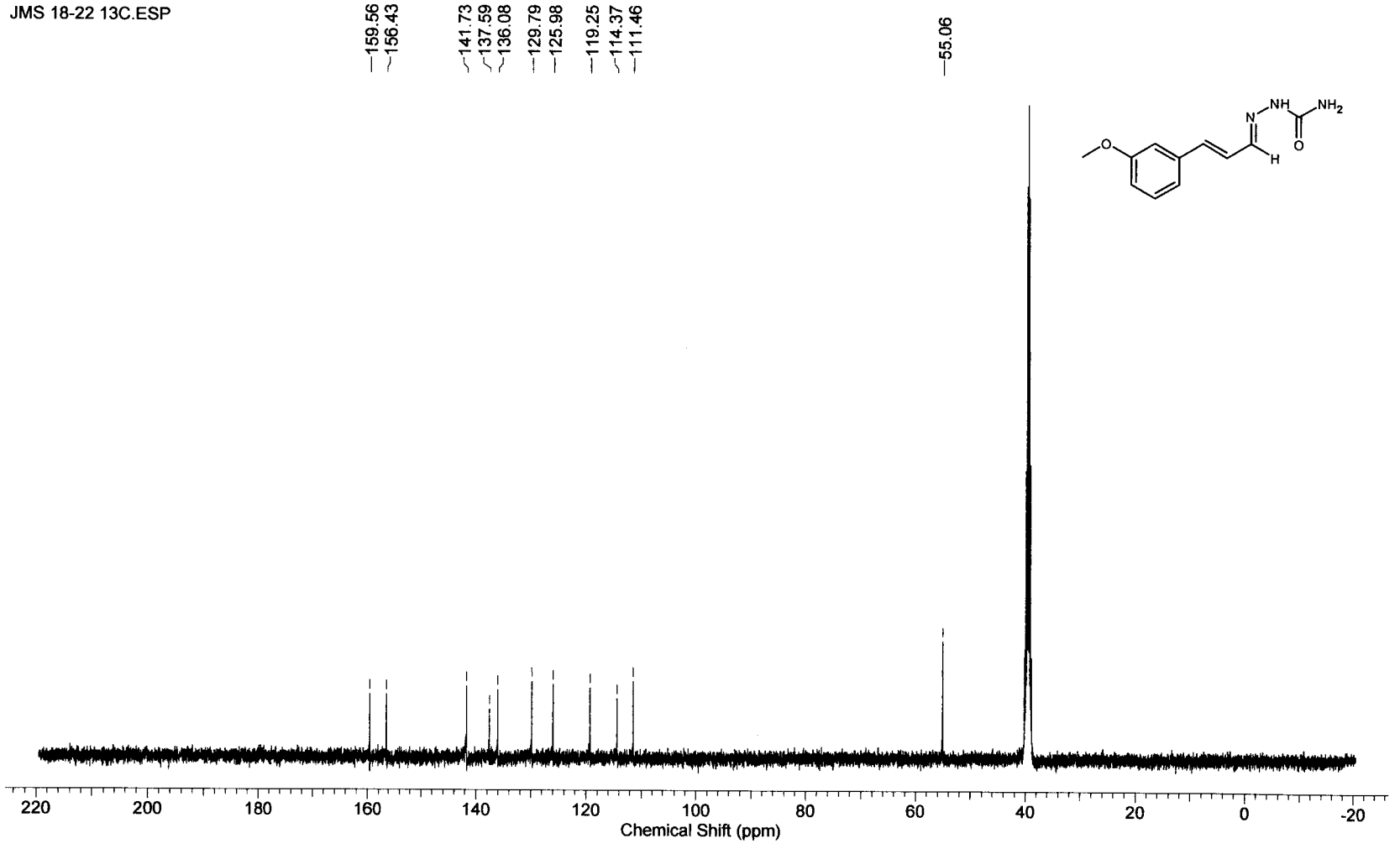

Figure A.59: ^{13}C NMR Spectrum of *E*-3-methoxycinnamaldehyde Semicarbazone (JMS 18-22)

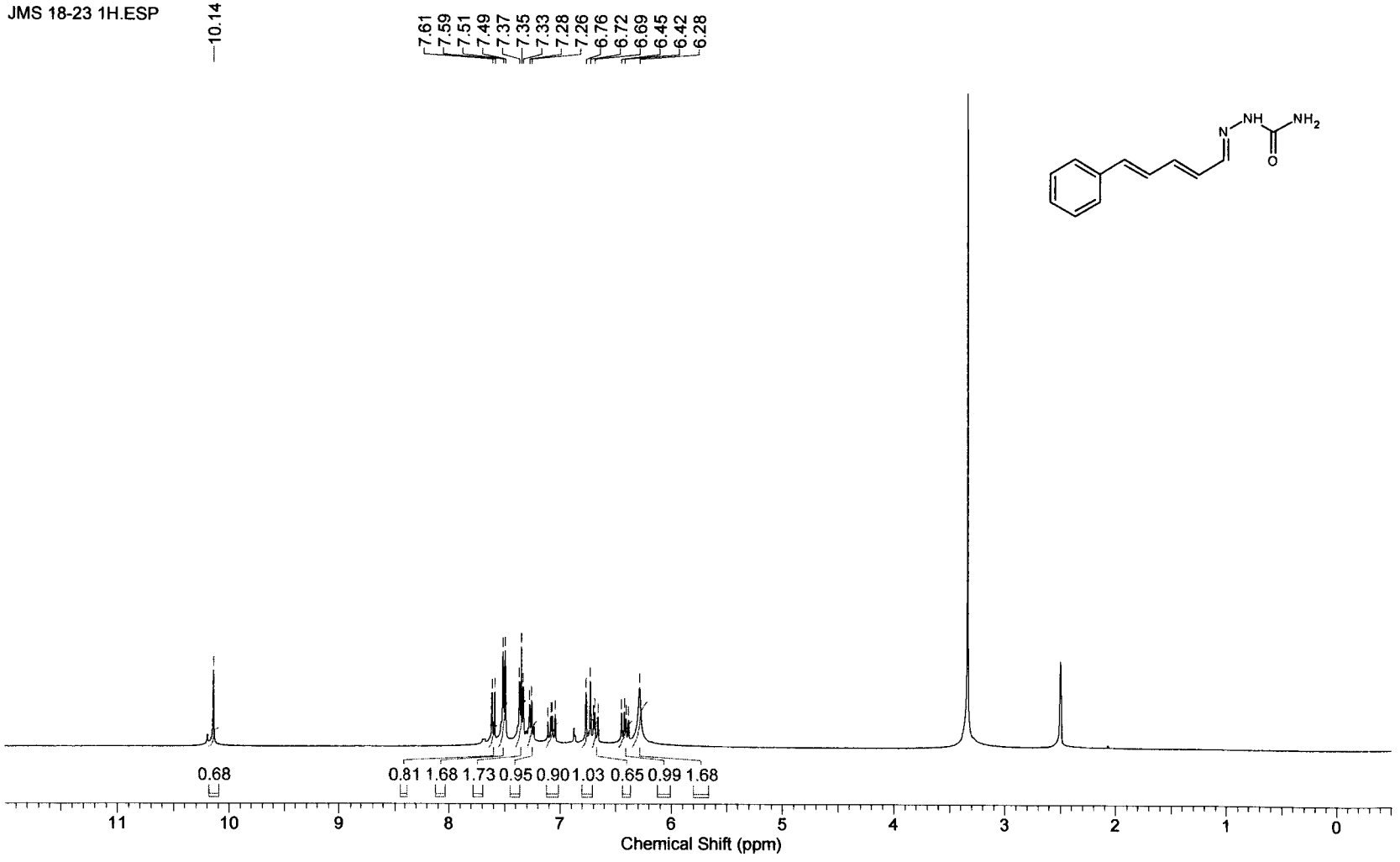

Figure A.60: ^{1}H NMR Spectrum of (2*E*,4*E*)-5-phenylpenta-2,4-dienal Semicarbazone (JMS 18-23)

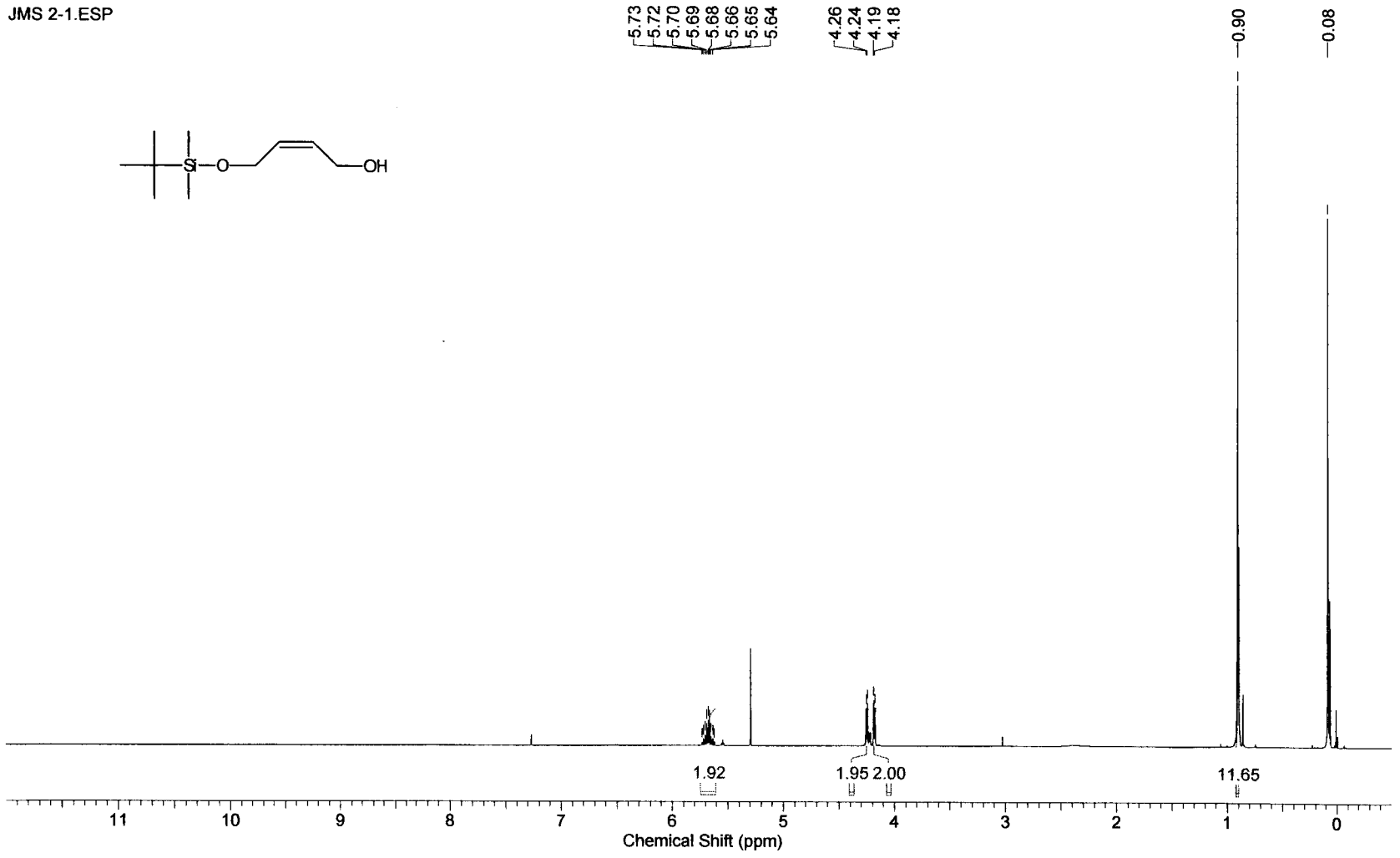

Figure A.61: ^{1}H NMR Spectrum of (*Z*/*E*)-4-{[tert-butyl-(dimethyl)silyl]oxy}but-2-en-1-ol (JMS 2-1)

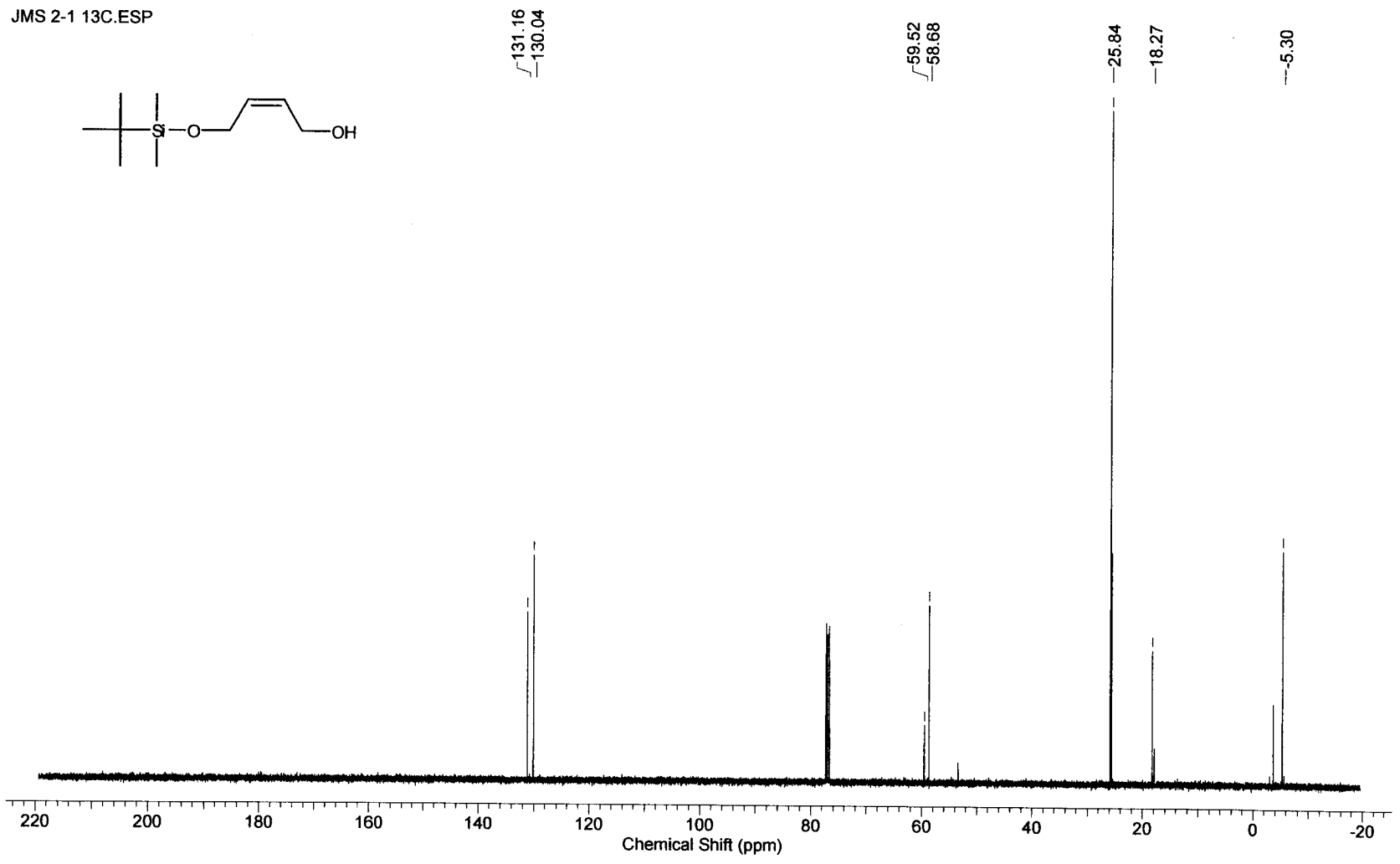

Figure A.62: ^{13}C NMR Spectrum of (*Z*/*E*)-4-{[tert-butyl-(dimethyl)silyl]oxy}but-2-en-1-ol (JMS 2-1)

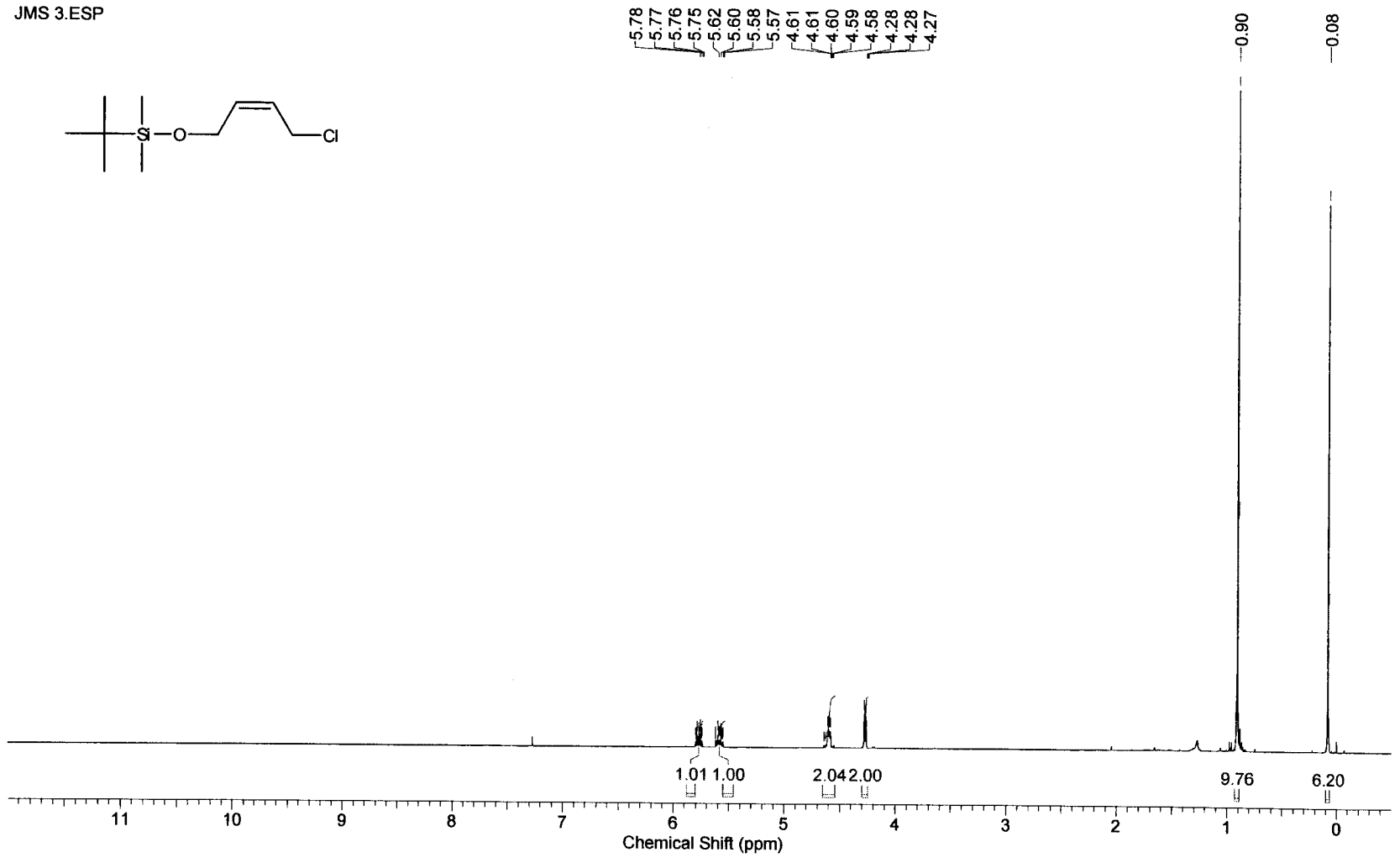

Figure A.63: ^{1}H NMR Spectrum of *tert*-butyl{[4-chlorobut-2-en-1-yl]oxy}dimethylsilane (JMS 3)

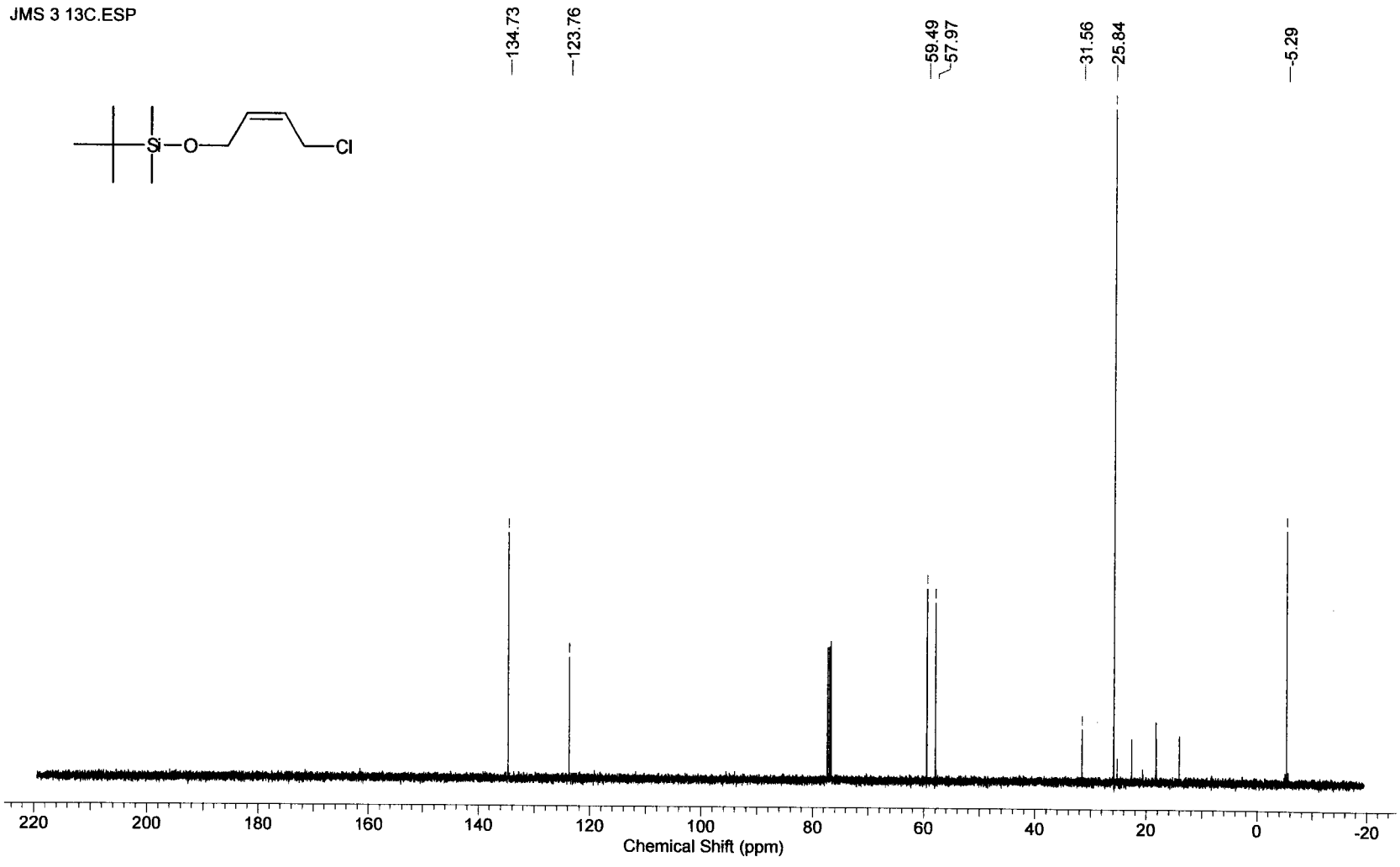

Figure A.64: ^{13}C NMR Spectrum of *tert*-butyl{[4-chlorobut-2-en-1-yl]oxy}dimethylsilane (JMS 3)

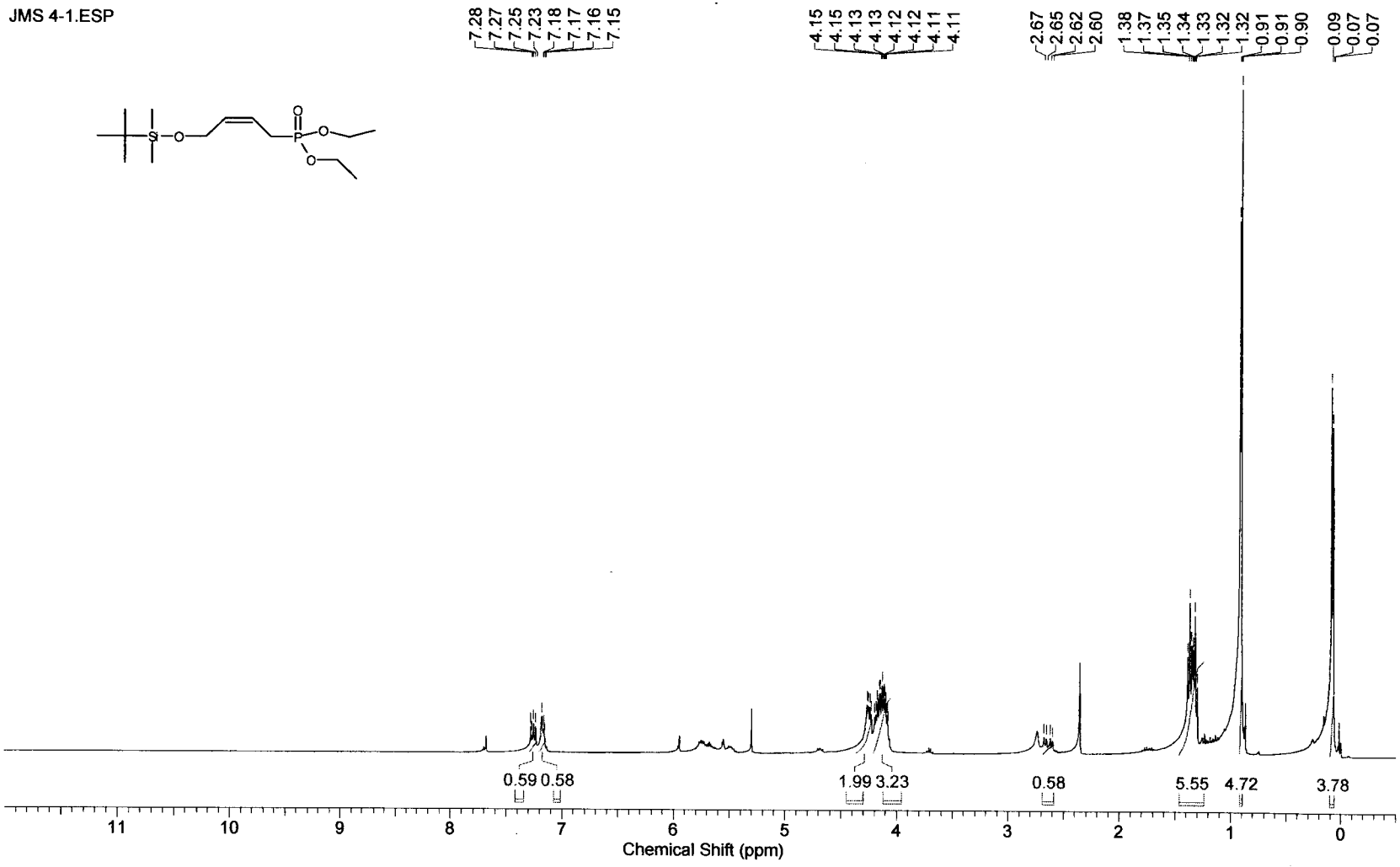

Figure A.65: ^{1}H NMR Spectrum of Diethyl [4-{[*tert*-butyl(dimethyl)silyl]oxy}but-2-en-1-yl]phosphonate (JMS 4-1)

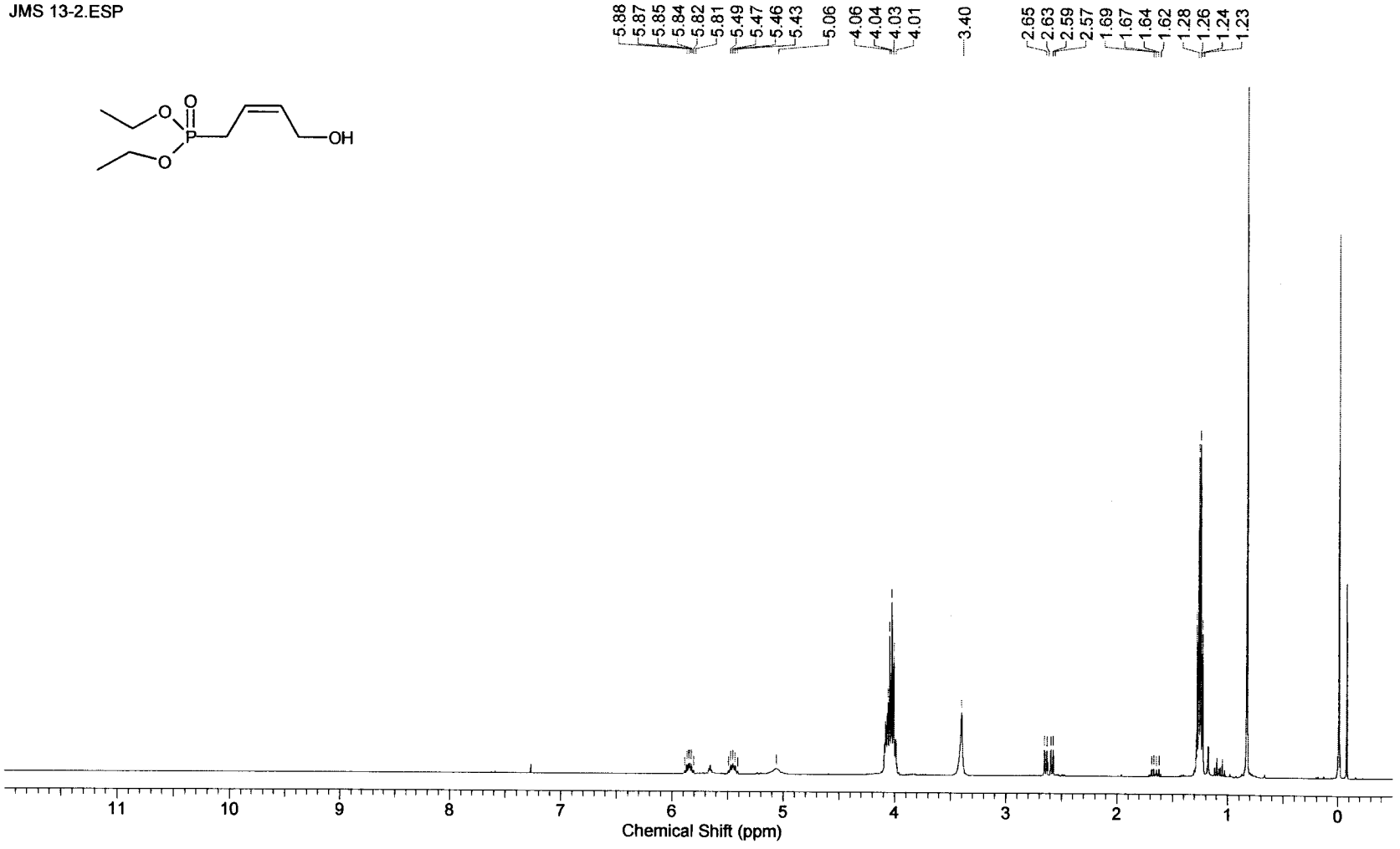

Figure A.66: ^{1}H NMR Spectrum of (*Z*/*E*)-diethyl (4-hydroxybut-2-en-1-yl)phosphonate (JMS 13-2)

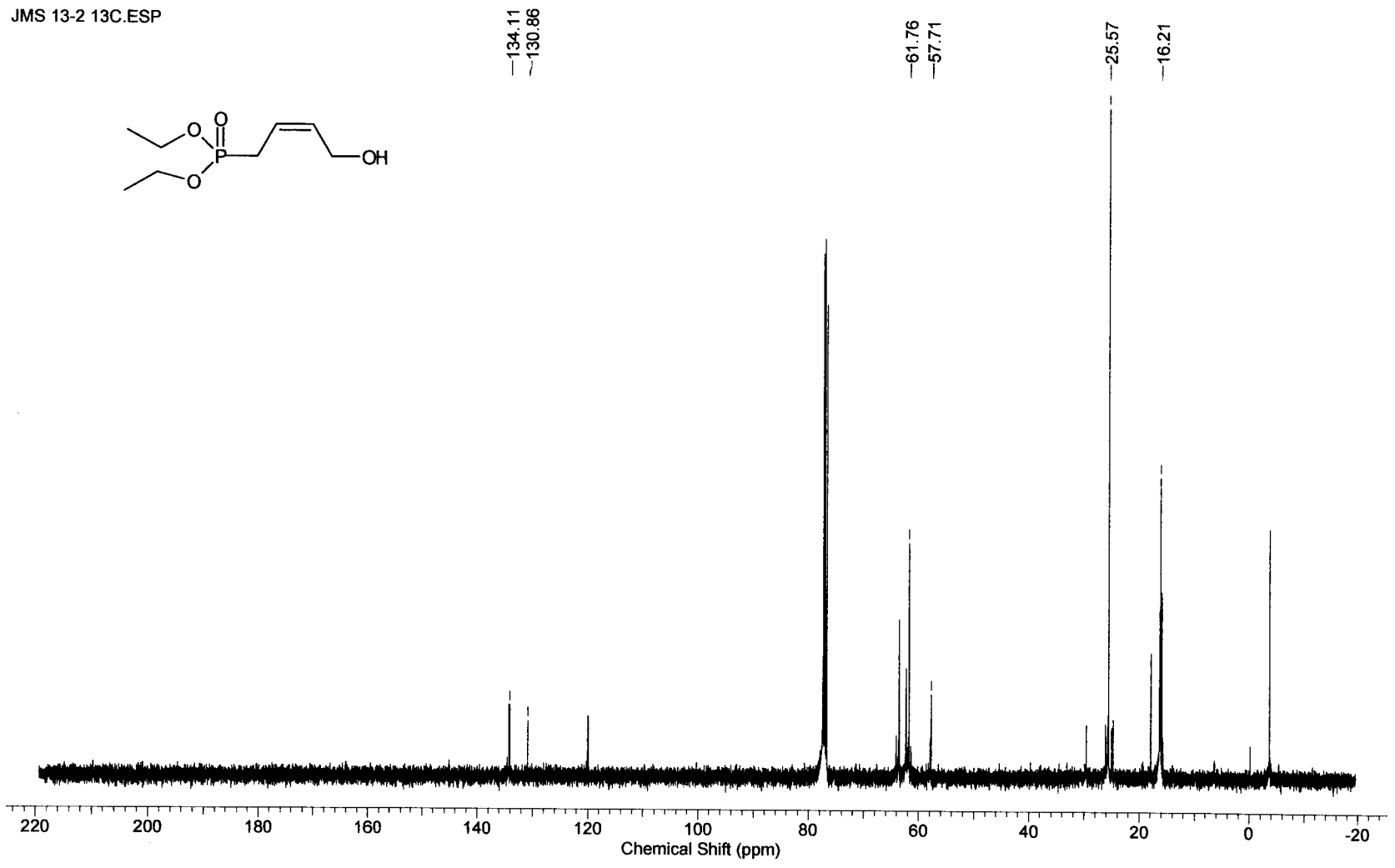

Figure A.67: ^{13}C NMR Spectrum of (*Z*/*E*)-diethyl (4-hydroxybut-2-en-1-yl)phosphonate (JMS 13-2)

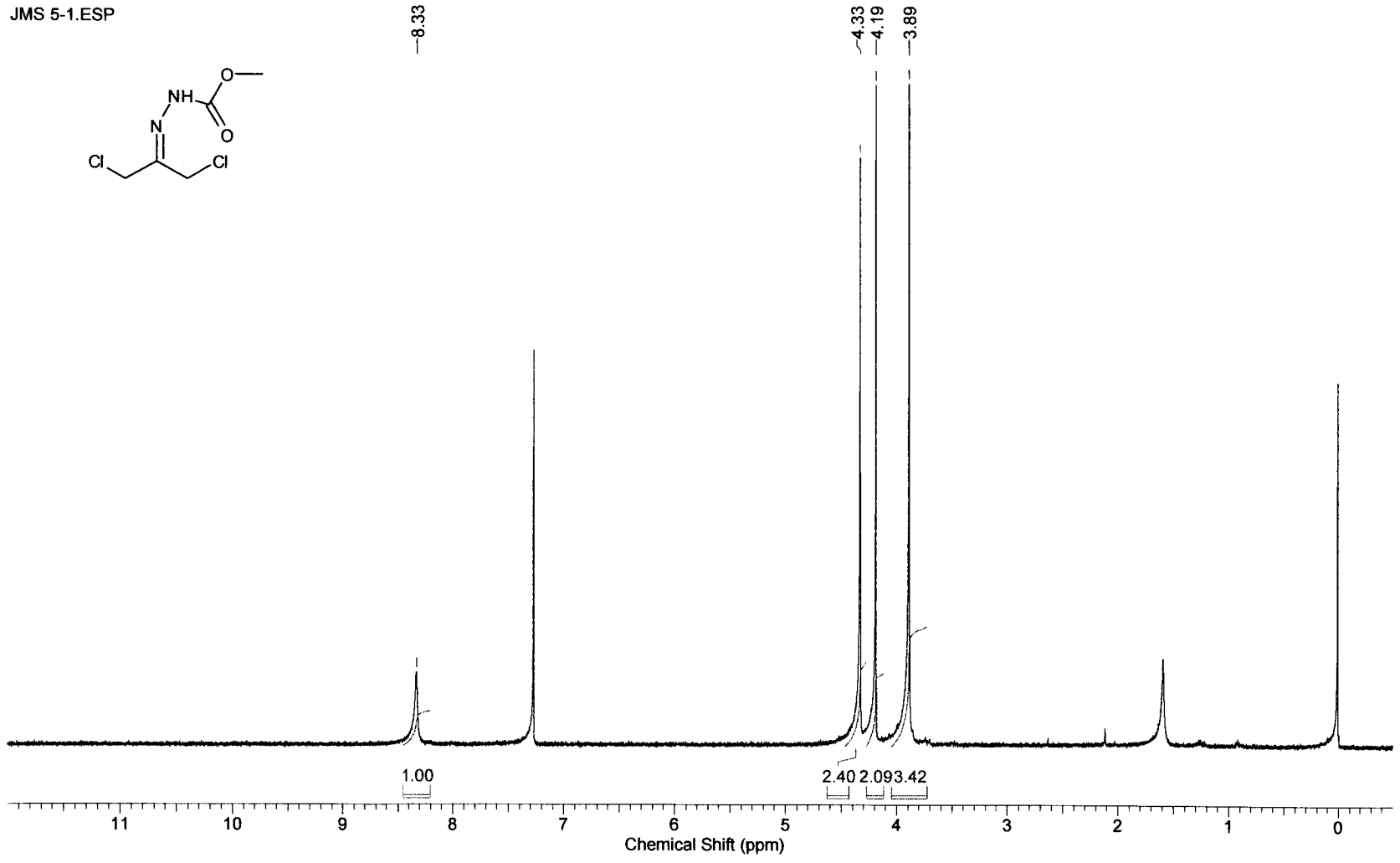

Figure A.68: ^{1}H NMR Spectrum of Methyl 2-(1,3-dichloropropan-2-ylidene)hydrazinecarboxylate (JMS 5-1)

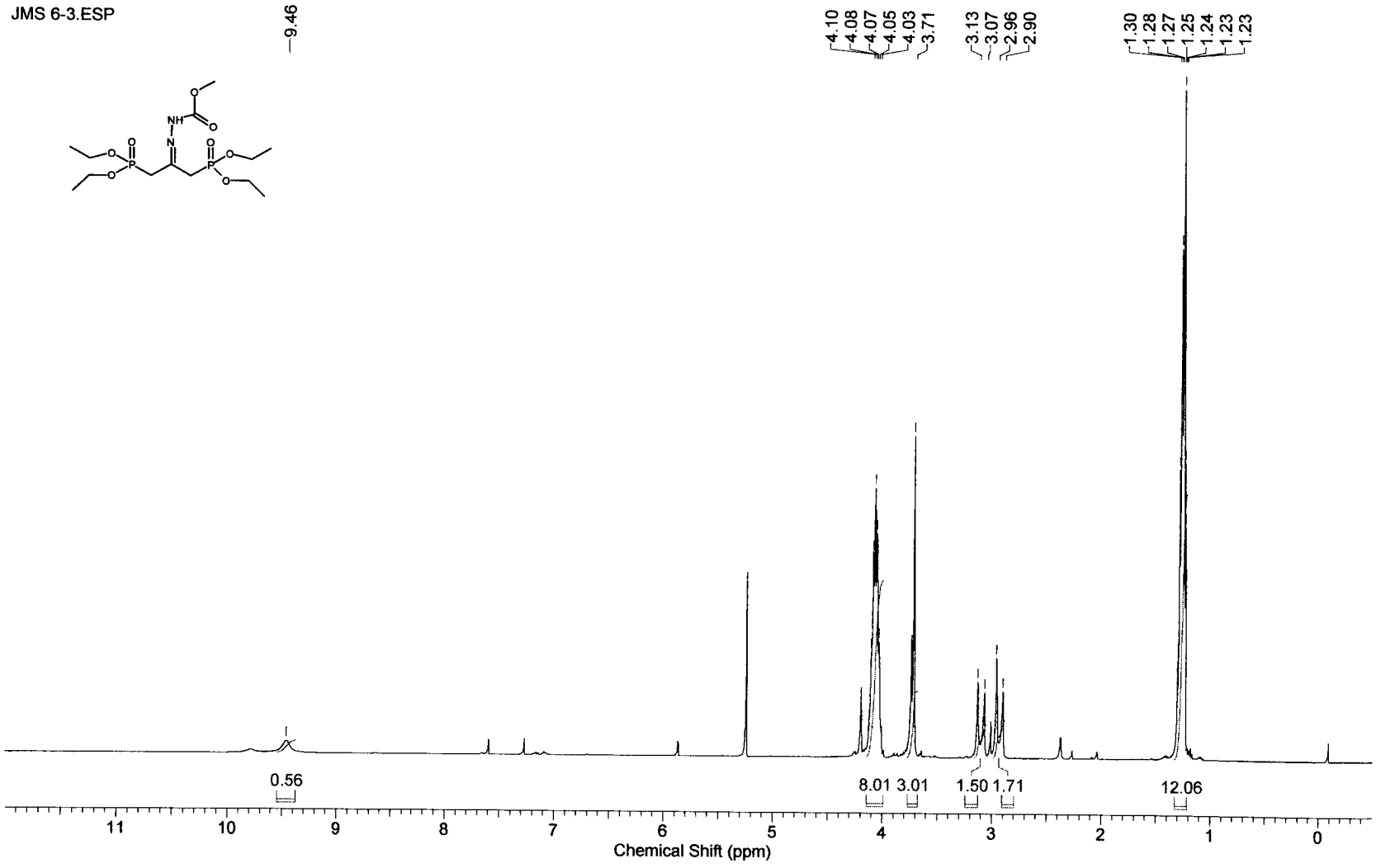

Figure A.69: ^{1}H NMR Spectrum of Methyl 2-(1,3-bis (diethoxyphosphoryl) propan-2-ylidene)hydrazinecarboxylate (JMS 6-3)

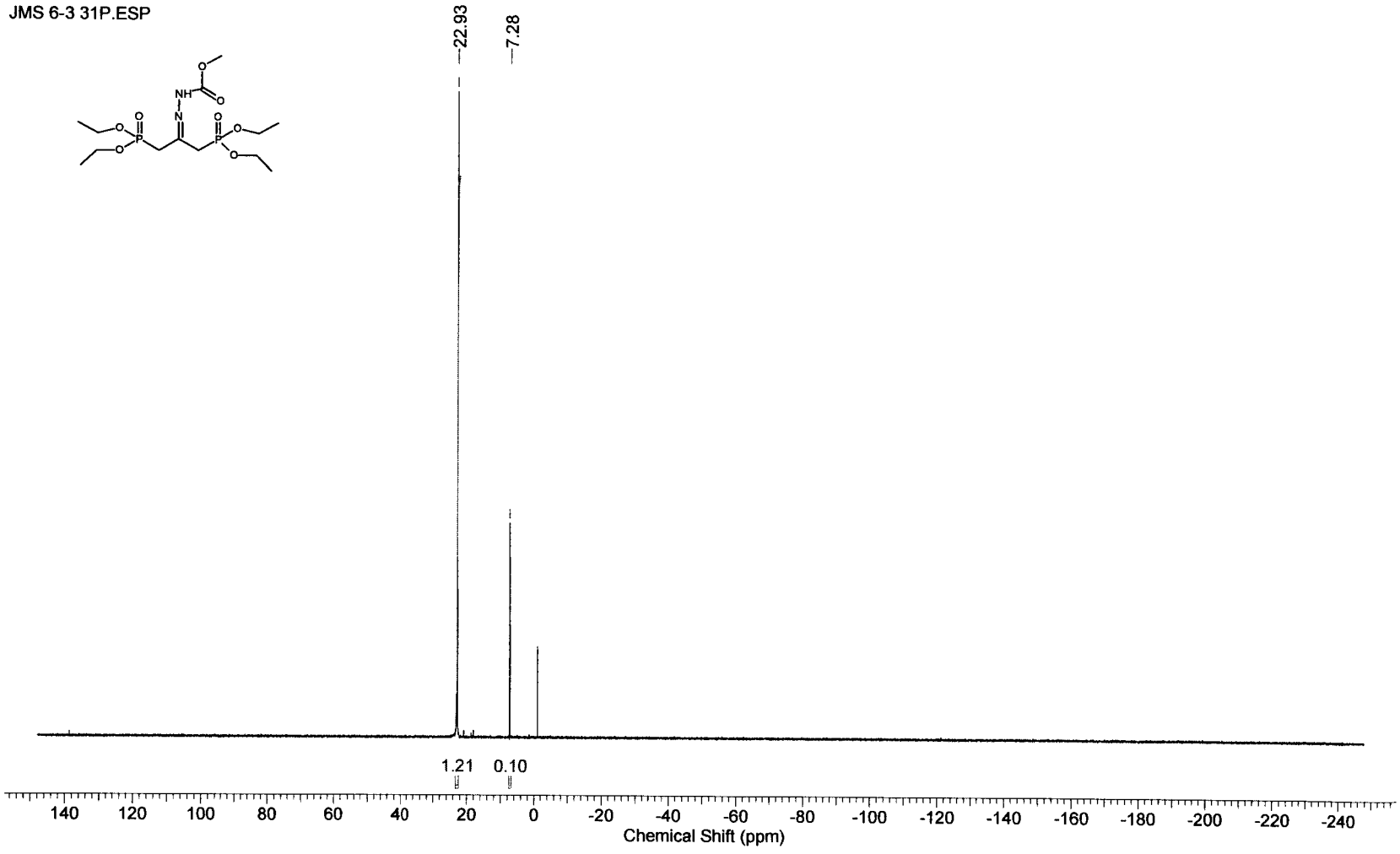

Figure A.70: ^{31}P NMR Spectrum of Methyl 2-(1,3-bis (diethoxyphosphoryl) propan-2-ylidene)hydrazinecarboxylate (JMS 6-3)

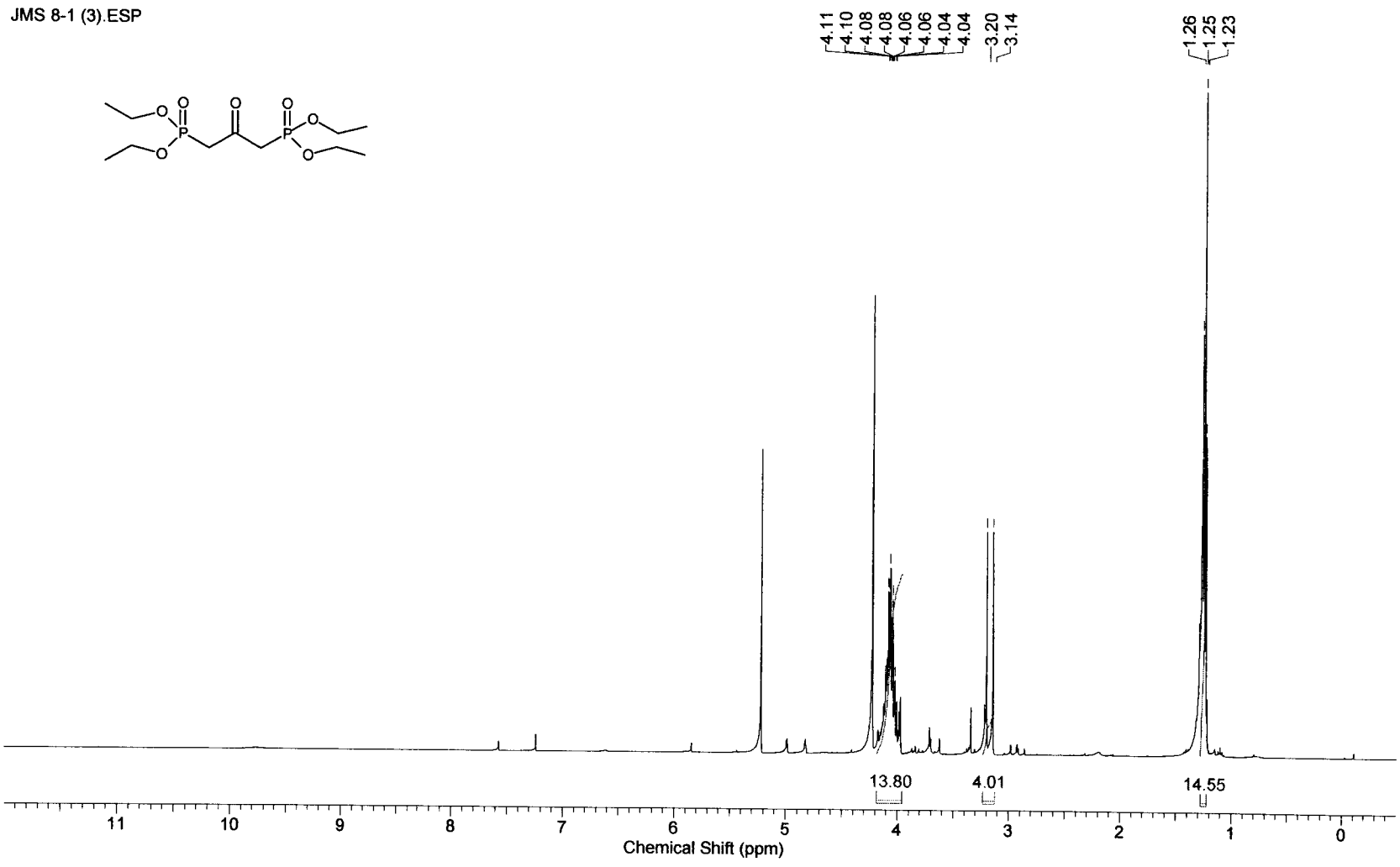

Figure A.71: ^{1}H NMR Spectrum of 1,3-bis(diethylphosphono)acetone (JMS 8-1)

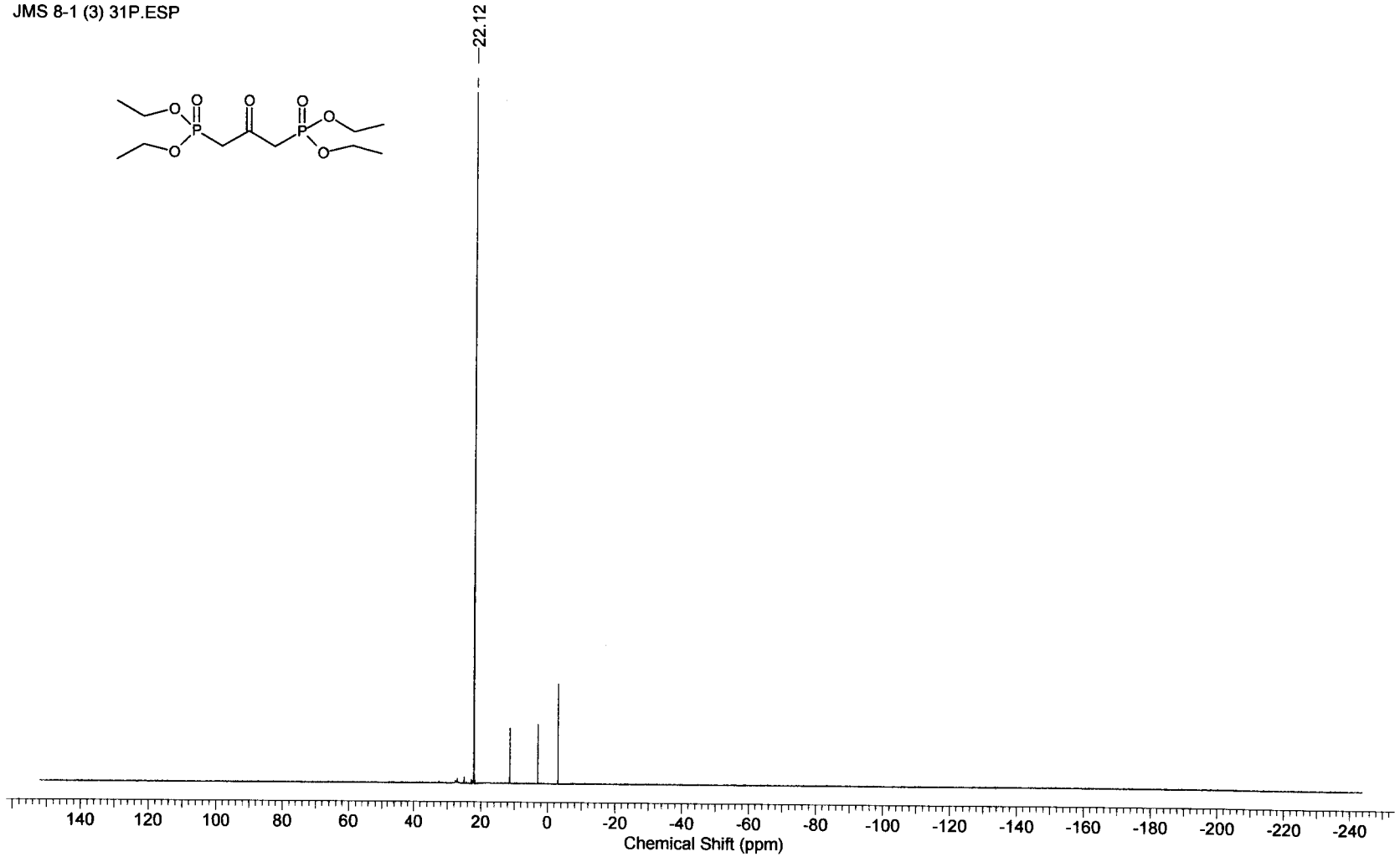

Figure A.72: ^{31}P NMR Spectrum of 1,3-bis(diethylphosphono)acetone (JMS 8-1)

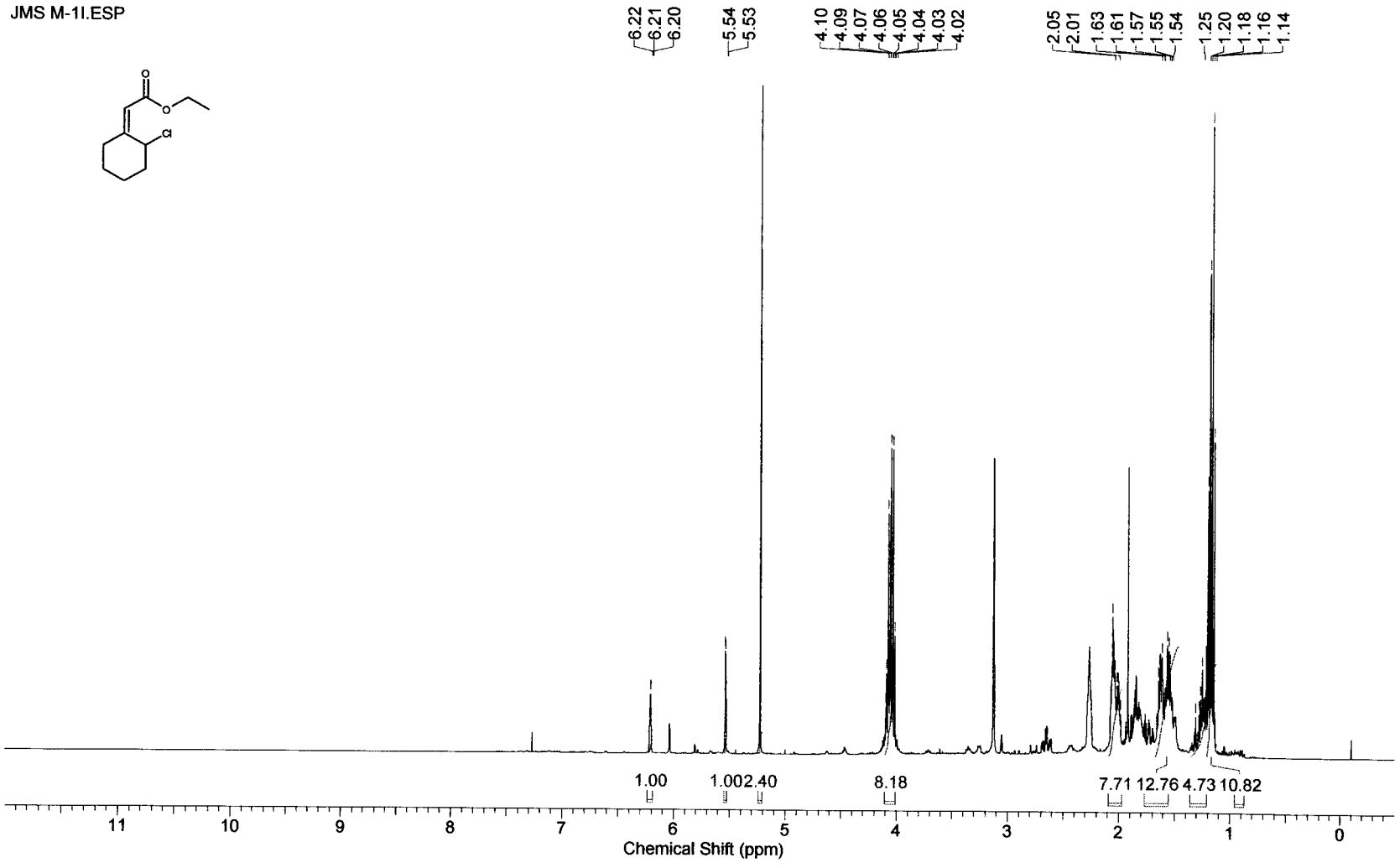

Figure A.73: ^{1}H NMR Spectrum of Ethyl 2-(2-chlorocyclohexylidene)acetate (JMS M-1i)

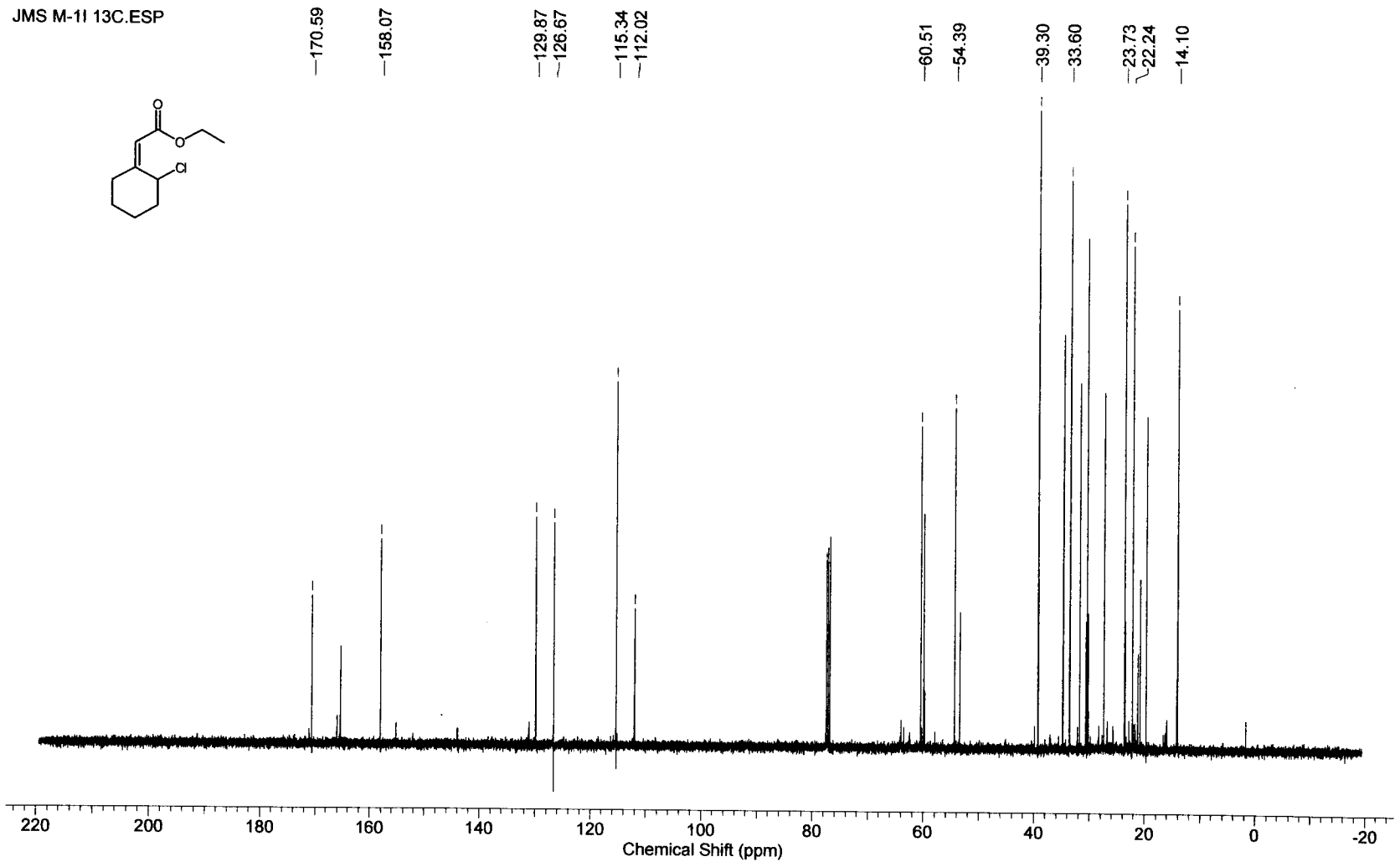

Figure A.74: ^{13}C NMR Spectrum of Ethyl 2-(2-chlorocyclohexylidene)acetate (JMS M-1i)

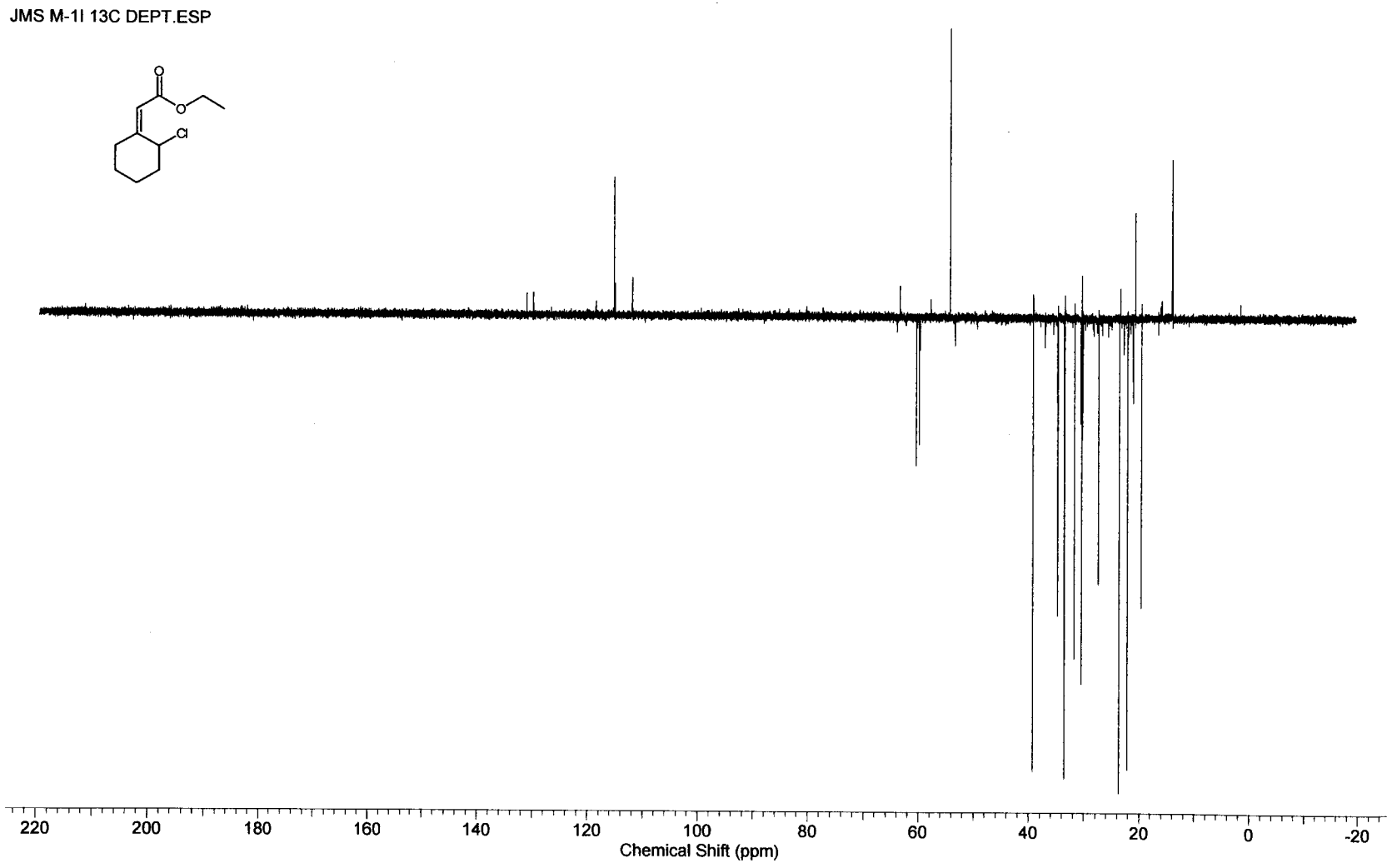

Figure A.75: ^{13}C DEPT NMR Spectrum of Ethyl 2-(2-chlorocyclohexylidene)acetate (JMS M-1i)

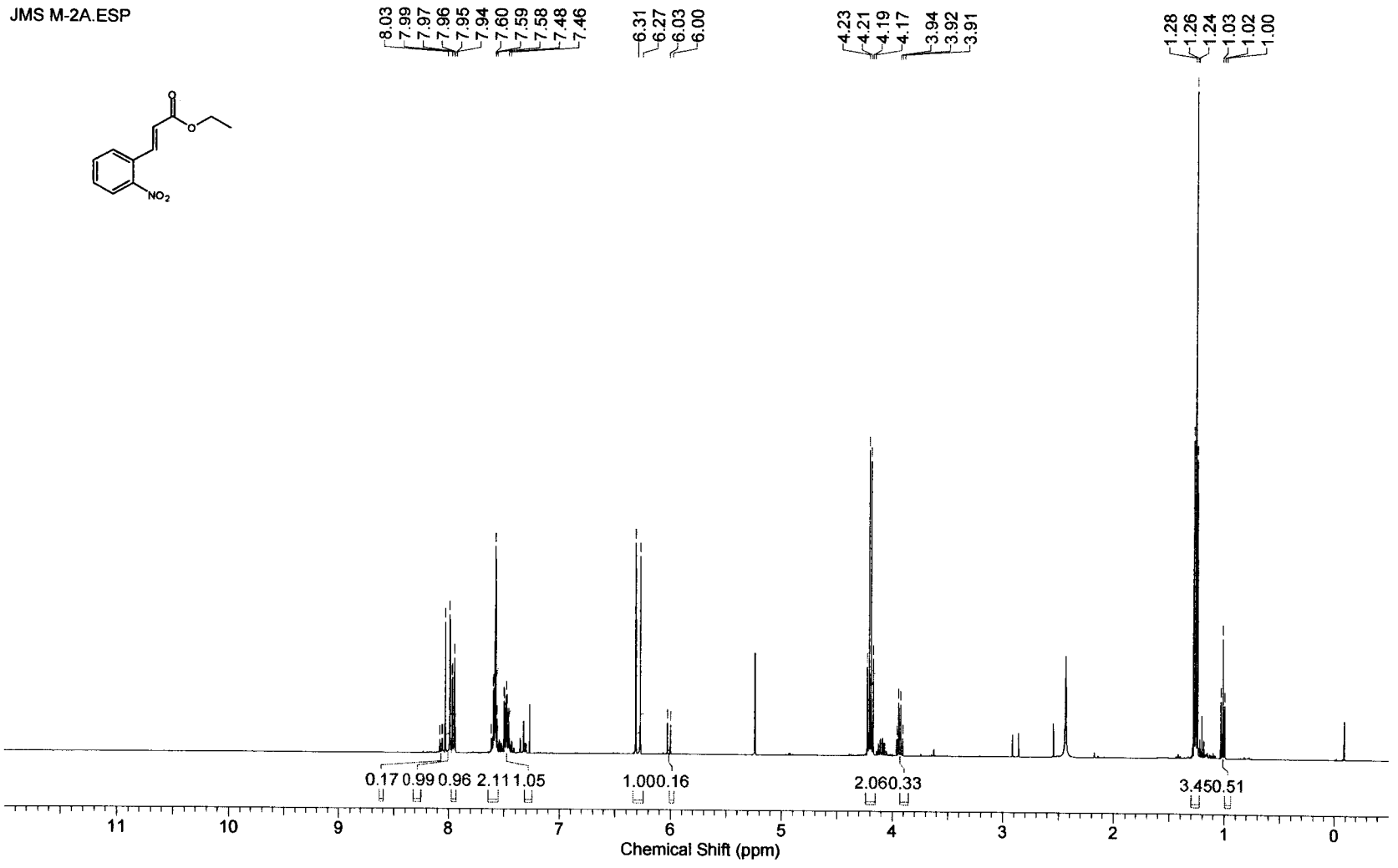

Figure A.76: ^{1}H NMR Spectrum of (*Z*/*E*)-ethyl 3-(2-nitrophenyl)but-2-enoate (JMS M-2a)

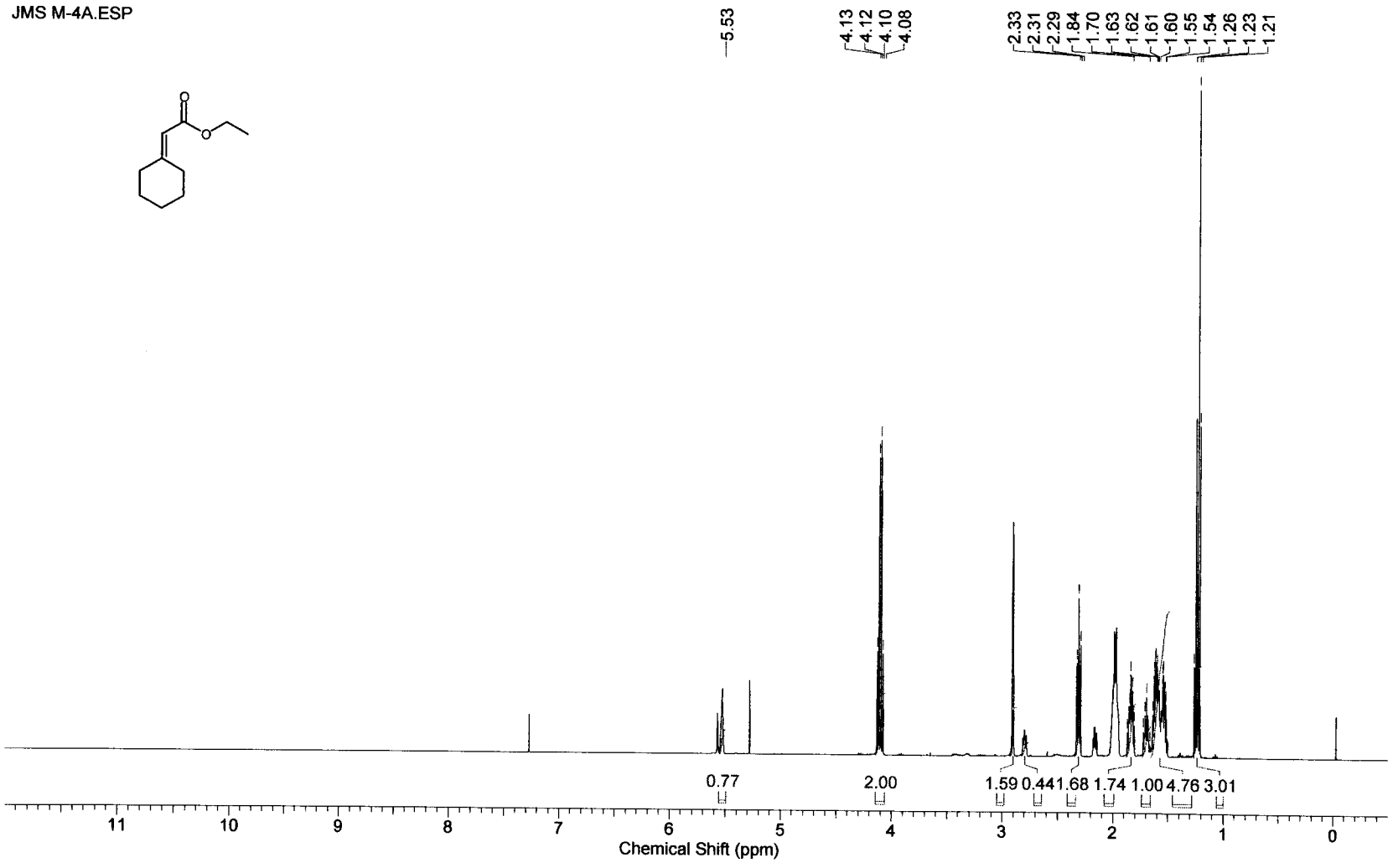

Figure A.77: ^{1}H NMR Spectrum of Ethyl 2-cyclohexylideneacetate (JMS M-4a)

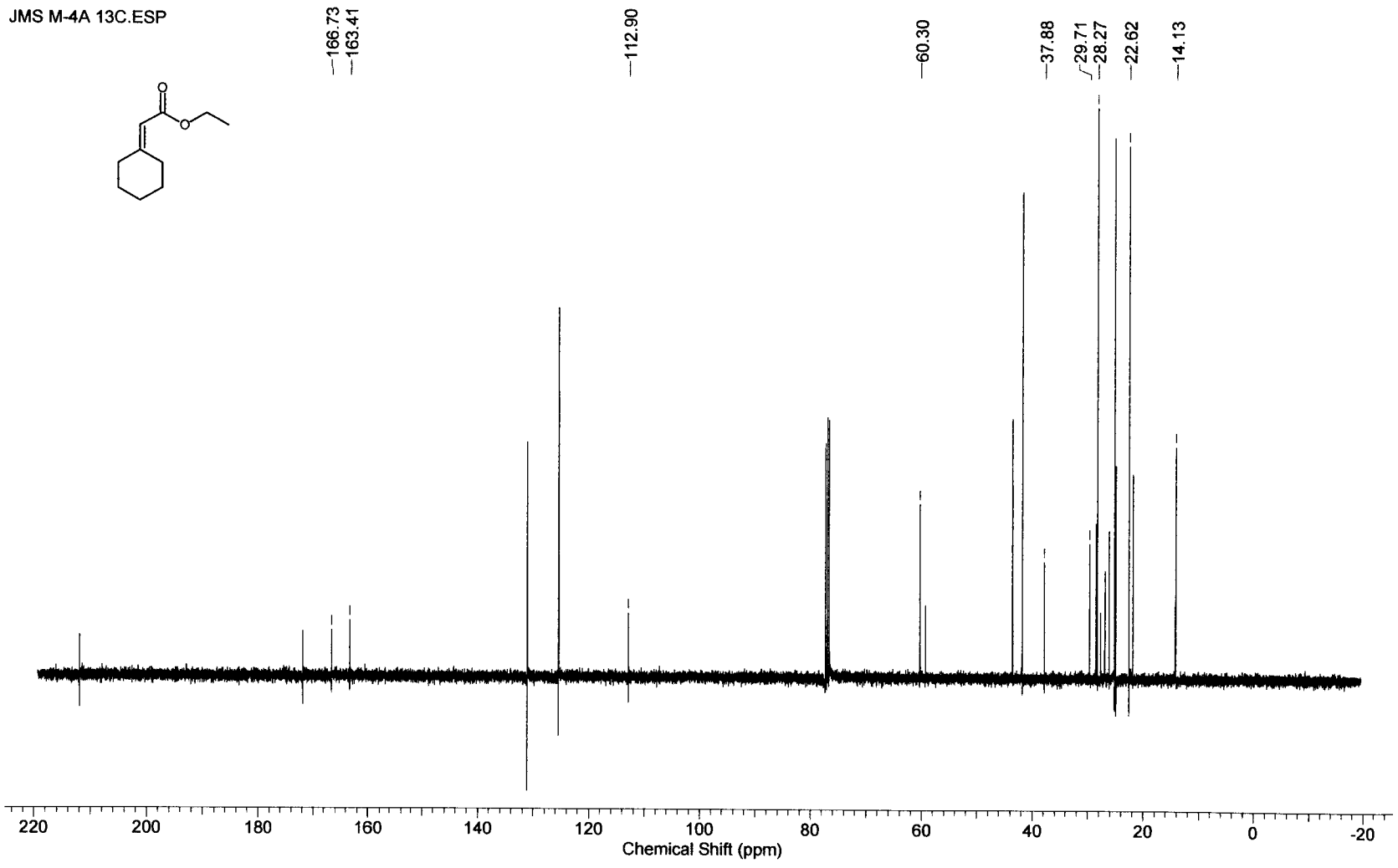

Figure A.78: 13H NMR Spectrum of Ethyl 2-cyclohexylideneacetate (JMS M-4a)

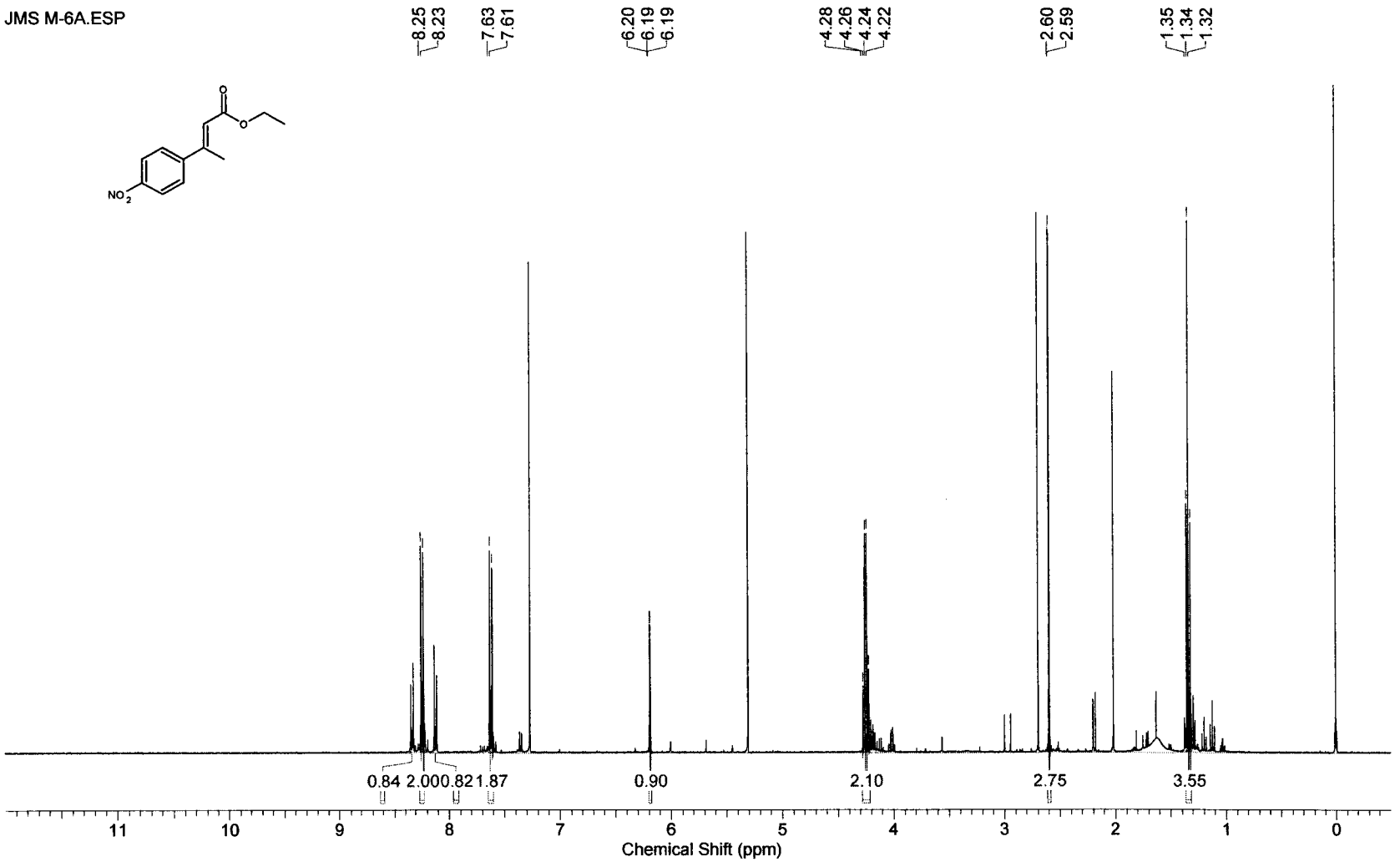

Figure A.79: ^{1}H NMR Spectrum of *E*-ethyl 3-(4-nitrophenyl)but-2-enoate (JMS M-6a)

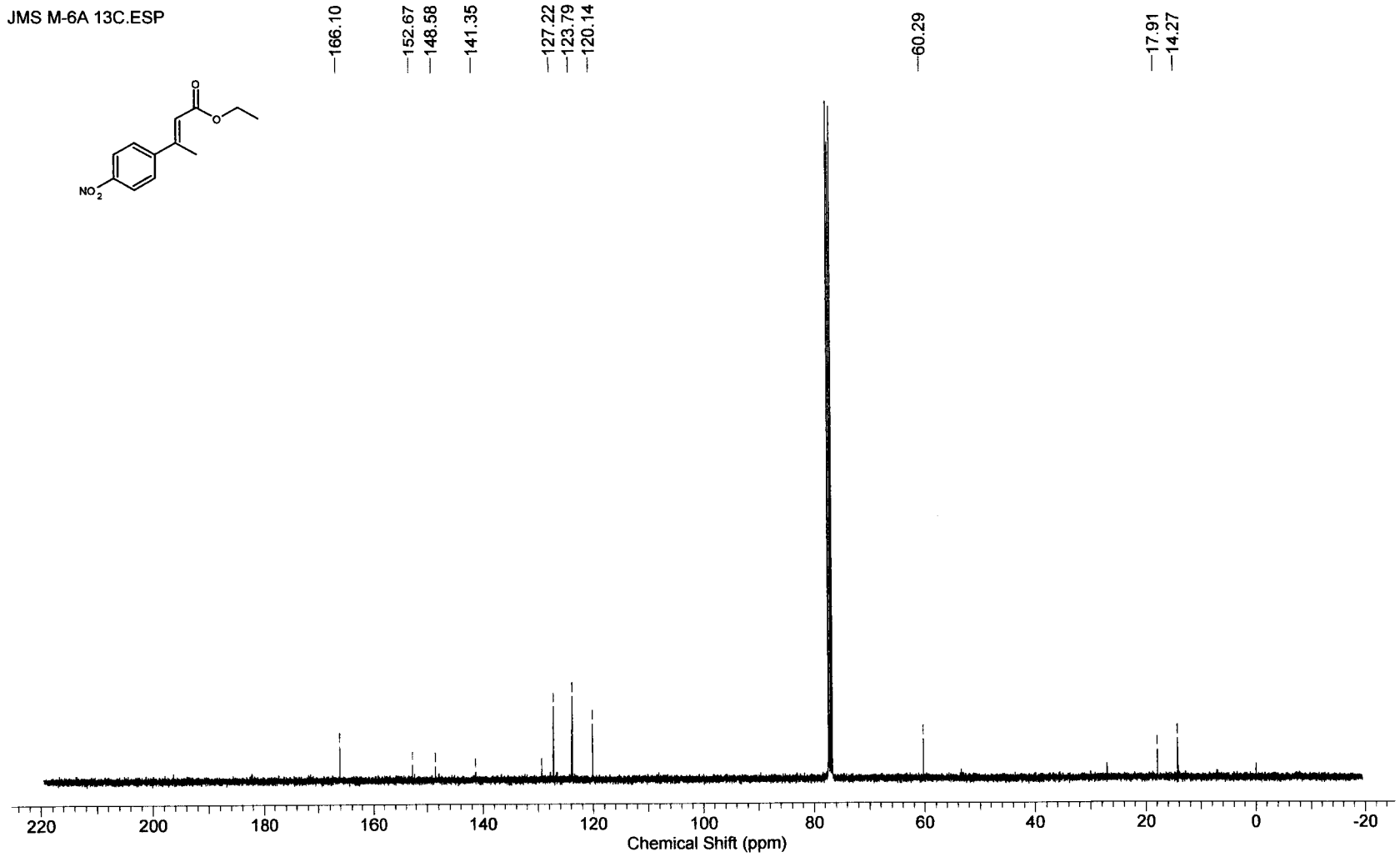

Figure A.80: ^{13}C NMR Spectrum of *E*-ethyl 3-(4-nitrophenyl)but-2-enoate (JMS M-6a)

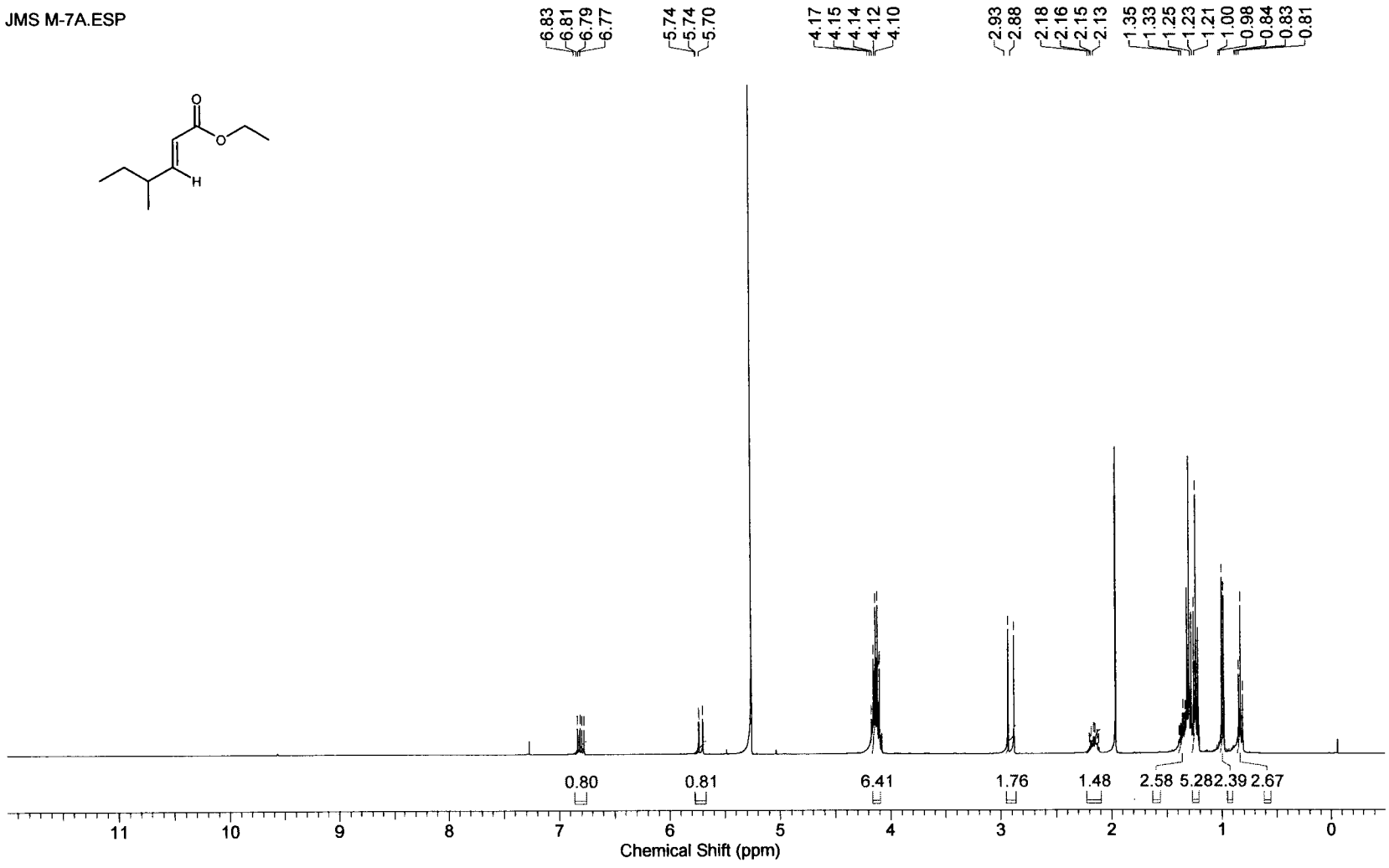

Figure A.81: ^{1}H NMR Spectrum of *E*-ethyl 4-methylhex-2-enoate (JMS M-7a)

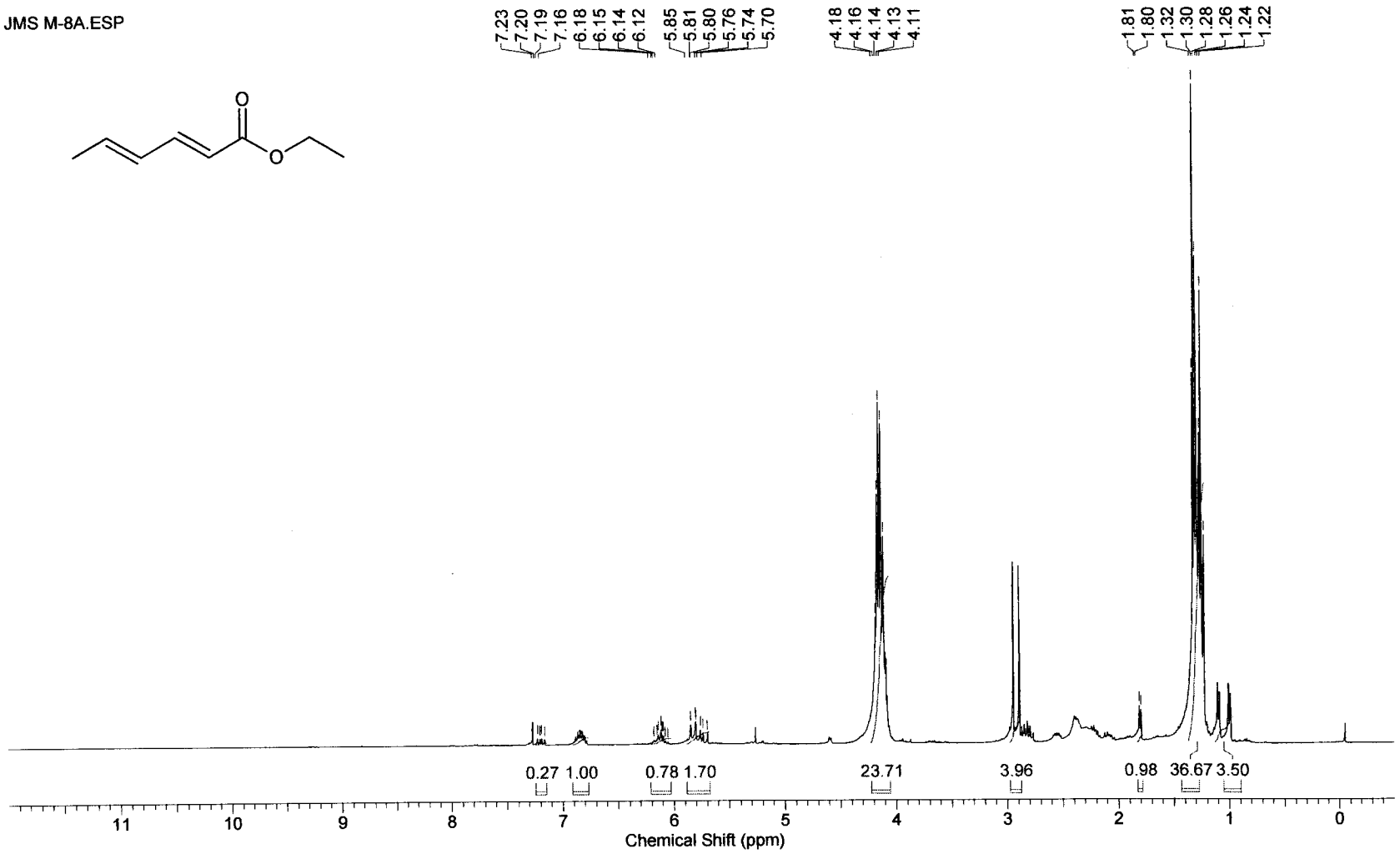

Figure A.82: ^{1}H NMR Spectrum of (2*Z*/*E*,4*Z*/*E*)-ethyl hexa-2,4-dienoate (JMS M-8a)