Development of the Interrupted Nazarov Cyclization of Allenyl Vinyl Ketones, with Application to the Total Synthesis of the Cyclooctane Natural Product Roseadione

by

Vanessa M. Marx

Submitted in partial fulfilment of the requirements
for the degree of Doctor of Philosophy

at

Dalhousie University
Halifax, Nova Scotia
May 2011

DALHOUSIE UNIVERSITY

DEPARTMENT OF CHEMISTRY

The undersigned hereby certify that they have read and recommend to the Faculty of Graduate Studies for acceptance a thesis entitled "Development of the Interrupted Nazarov Cyclization of Allenyl Vinyl Ketones, with Application to the Total Synthesis of the Cyclooctane Natural Product Roseadione" by Vanessa M. Marx in partial fulfilment of the requirements for the degree of Doctor of Philosophy.

Dated: May 19, 2011

Supervisor: _____

Readers: _____

_____

_____

Departmental Representative: _____

DALHOUSIE UNIVERSITY

DATE: May 19, 2011

AUTHOR: Vanessa M. Marx

TITLE: Development of the Interrupted Nazarov Cyclization of Allenyl Vinyl Ketones, with Application to the Total Synthesis of the Cyclooctane Natural Product Roseadione

DEPARTMENT OR SCHOOL: Department of Chemistry

DEGREE: PhD CONVOCATION: October YEAR: 2011

_____

Signature of Author

There is no such thing as failure - only success and learning experiences.

Table of Contents

LIST OF FIGURES

LIST OF SCHEMES

LIST OF TABLES

ABSTRACT

The development of the interrupted Nazarov cyclization of allenyl vinyl ketones is presented. The intermediate oxyallyl cation, derived from an allenyl vinyl ketone, may be trapped efficiently by a divergent array of nucleophilic species generating functionalized cyclopent-2-enone products. Allenyl vinyl ketones are also a versatile source of cyclic molecules via a tandem reaction sequence terminated via reaction with acyclic dienes, cyclic dienes, aza-heterocycles, electron-rich alkenes, or styrenes by the formation of an additional ring by a [4 + 3] and/or [3 + 2] cyclization or by the formation of one additional carbon-carbon bond. The bicyclic compounds generated by these processes are densely substituted, and would be difficult to access as succinctly in other ways. The products of these interrupted Nazarov reactions generally reflect excellent regio- and stereoselectivity in the trapping reaction. In some instances, equilibrating conditions were shown to enhance the proportion of one product at the expense of another or to provide a different carbon skeleton. This process appears fairly general, and can be conducted with unsubstituted or alkyl, aromatic, or heteroaromatic allenyl vinyl ketones. The exceptional affinity of allenyl vinyl ketones to undergo interrupted Nazarov reactions is likely a result of the increased longevity of the intermediate oxyallyl cation, due in part to the increased resonance stabilization provided by the allene unit. The high regioselectivity noted in the trapping process was computationally and experimentally confirmed to be a result of a localization of the positive charge in the intermediate oxyallyl cation.

The application of this recently developed methodology towards the synthesis of the natural product (+)-roseadione is also described. The tandem Nazarov/[4 + 3] cascade of allenyl vinyl ketones provides a unique manner in which to access the tricyclic core of this cyclooctanoid natural product, a molecule which, to date, has never been synthesized.

LIST OF ABBREVIATIONS AND SYMBOLS USED

α	alpha
Å	angstrom
β	beta
δ	chemical shift *or* partial charge
Δ	heat
Ac	acetate
aq	aqueous
AVK	allenyl vinyl ketone
Bn	benzyl
br	broad
BOC	*tert*-butoxycarbonyl
n-Bu	*normal*-butyl
t-Bu	*tertiary*-butyl
cod	1,5-cyclooctadiene
COSY	correlation spectroscopy
Cp	cyclopentadiene
Cy	cyclohexyl
d	doublet
DABCO	1,4-diazabicyclo[2.2.2]octane
dba	dibenzylidene acetone
DCE	1,2-dichloroethane
dd	doublet of doublets
ddd	doublet of doublet of doublets
DEPT	distortionless enhancement by polarization transfer
DMAP	dimethylaminopyridine
DMF	dimethylformamide
DMP	Dess-Martin periodinane

DMS	dimethylsulfide
DMSO	dimethylsulfoxide
dppf	1,1'-bis(diphenylphosphino)ferrocene
dq	doublet of quartets
dr	diastereomeric ratio
dt	doublet of triplets
E	*trans*
EDG	electron donating group
equiv	equivalent(s)
ESI	electrospray ionization
Et	ethyl
EWG	electron withdrawing group
FT	Fourier transform
h	hour(s)
HMBC	heteronuclear multiple bond coherence
HMDS	hexamethyldisilazide
HOMO	highest occupied molecular orbital
HRMS	high resolution mass spectrometry
HSQC	heteronuclear single quantum coherence
Hz	hertz
IR	infrared
$^{n}J_{XX'}$	*n* bond coupling constant between atom X and atom X'
KIE	kinetic isotope effect
LA	Lewis acid
LDA	lithium diisopropyl amide
LUMO	lowest unoccupied molecular orbital
m	multiplet
Me	methyl

min	minute(s)
MHz	megahertz
MOC	methyloxycarbonyl
mol	mole(s)
mp	melting point
Ms	methanesulfonyl
NOE	nuclear Overhauser effect
NMR	nuclear magnetic resonance
ORTEP	Oak Ridge thermal ellipsoid plot
PG	protecting group
Ph	phenyl
PMP	*para*-methoxyphenyl
ppm	parts per million
i-Pr	*iso*-propyl
n-Pr	*normal*-propyl
PTP	*para*-(trifluoromethyl)phenyl
q	quartet
QTAIM	quantum theory of atoms in molecules
rt	room temperature
s	singlet
SOMO	singly occupied molecular orbital
TBS	*tert*-butyldimethylsilyl
t	triplet
td	triplet of doublets
TEA	triethylamine
Tf	trifluoromethanesulfonyl
TFA	trifluoroacetic acid
THF	tetrahydrofuran

TIPS	triisopropylsilyl
TLC	thin layer chromatography
TMEDA	tetramethylethylenediamine
TMP	2,4,6-trimethoxyphenyl
TMS	trimethylsilyl
TOF	time-of-flight
tq	triplet of quartets
Ts	toluenesulfonyl
p-TSA	*para*-toluenesulfonic acid
UV	ultraviolet
Z	*cis*

ACKNOWLEDGMENTS

First and foremost, I'd like to thank my advisor, Dr. Jean Burnell. Dr. Burnell allowed me essentially unlimited intellectual freedom in my projects, and yet his door was always open when I needed to discuss any particular topic, no matter how random or obscure. Dr. Burnell also allowed me significant personal freedom, especially with respect to my often odd working hours, and for that I am also extremely grateful. I was encouraged to attend many conferences, where I was not only able to culture a broader knowledge of organic chemistry, but I like to believe that I also obtained a more grounded perspective of the chemical sciences as a whole. Finally, Dr. Burnell was very supportive of essentially any decision I chose to make, with regards to both chemistry and life, and was always able and willing to dispense with his advice on the matter. Thank you for making it a pleasure to come in to work every day. I would not be the chemist, and person, I am today without your mentorship.

Secondly I'd like to thank my co-workers, both past and present: Giselle Ardagh, Owen Chauhan, Jeremy Hughes, Yonghoon Kwon, François LeFort, Frank MacDonald, Tim Morgan, Jon Moulins, Steve Newmann, Maneesha Rajora, Craig Stamp, Rhonda Stoddard, and Paul Thornton. The equal parts of both crazy antics and stimulating conversation that could always be found made the lab a second home. Craig especially, thank you so much for your mentorship and guidance over the years - you have been like a big brother to me, you kept my ego in check, and after living with you, I think I can live with anyone.

François LeFort and Rhonda Stoddard are especially thanked for their assistance with parts of the experimental work that is included in this thesis (see Experimental Section, General Considerations, Chapters 2 – 4). As a pair, you were truly exceptional undergraduate students, and I feel honoured to have had the opportunity to be your mentor.

The computed data in this thesis was performed by Gavin-Heverly Coulson of the Boyd group. Gavin, thank you for being such an excellent collaborator, your consultation in this area has been invaluable.

Acknowledgement is made to Dr. Mike Lumsden (NMR-3, Dalhousie) for assistance with NMR experiments (specifically in the acquisition of *J*-HMBC spectra), Mr. Xiao Feng (Dalhousie) for collecting mass-spectrometry data, and Dr. Stanley Cameron (Dalhousie) for the collection and interpretation of X-ray data. I would also like to thank the members of my thesis committee, Dr. David Jakeman, Dr. Ian Pottie, and Dr. Laura Turculet, for their willingness to offer both their advice and support throughout the course of my doctoral work.

I would like to extend thanks to the members of the Stradiotto and Turculet groups, for their help when highly air-sensitive technique was necessary. I would like to especially thank Dr. Laura Turculet for assistance with the sublimation of air-sensitive solids, and Erin Morgan for assistance with hydrogenation experiments. Jean D'Amour Twibanire of the Grindley group is also thanked for assistance with ozonolysis experiments.

Kelly Resmer and Erin Morgan were awesome people to have had by my side throughout my graduate school career. Thank you for being there throughout both the good times and the bad, always with an honest opinion and/or word of encouragement.

I will limit myself to acknowledging Rylan Lundgren on a professional level. Thank you for constantly challenging me intellectually, and broadening my perspective of chemistry by forcing me to occasionally think outside of my line of work. Also, thank you for your patience when my projects wern't working, and your invariable willingness to assist in any way you could, both from an intellectual and experimental standpoint.

The Natural Sciences and Engineering Research Council (NSERC) of Canada, the Killam Trusts, and the Sumner Foundation are thanked for providing funding throughout the course of my graduate research.

CHAPTER 1. INTRODUCTION

1.1 New Reaction Discovery

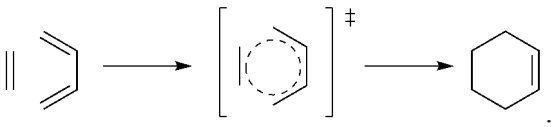
Organic synthesis has come a long way in the past century. With the advent of increasingly sophisticated instruments as tools for both synthesis and characterization, chemists are now able to conduct and analyze a plethora of chemical transformations in rapid succession. This has facilitated the discovery of new reagents and catalysts that can now essentially conduct any imagined transformation. As a result, our understanding of chemical reactivity and reaction mechanism has increased drastically, culminating in the invention of a multitude of new reactions and allowing for the synthesis of the most complex of molecular targets.[1]

Though the wide range of synthetic transformations available today is impressive, many reaction processes are far from perfect. Ideally, the synthesis of a single complex target would be accomplished in high yield and a minimal number of steps through the selection of a series of chemo-, regio-, and stereoselective transformations, with readily available starting materials using inexpensive and non-toxic reagents. However, several important transformations continue to rely on expensive and/or toxic reagents for optimal results. Furthermore chemo-, regio-, and stereoselectivity issues often necessitate the use of a lengthy sequence in order obtain a specific molecular target. Finally, in many instances a particular transformation will consistently result in low yield, or fail entirely, for a particular substrate class. Thus, much research in organic chemistry is still devoted to *new reaction discovery*, which can then be applied to the synthesis of complex molecular targets in a more rapid and efficient manner.[1]

1.2 Pericyclic Reactions

Pericyclic reactions are among the most powerful and best understood chemical transformations available to the synthetic chemist, mainly as a result that many reactions will predictably lead to products in high levels of regio-, chemo-, and diastereoselectivity. Hence, pericyclic reactions have long been exploited in the construction of complex ring systems.

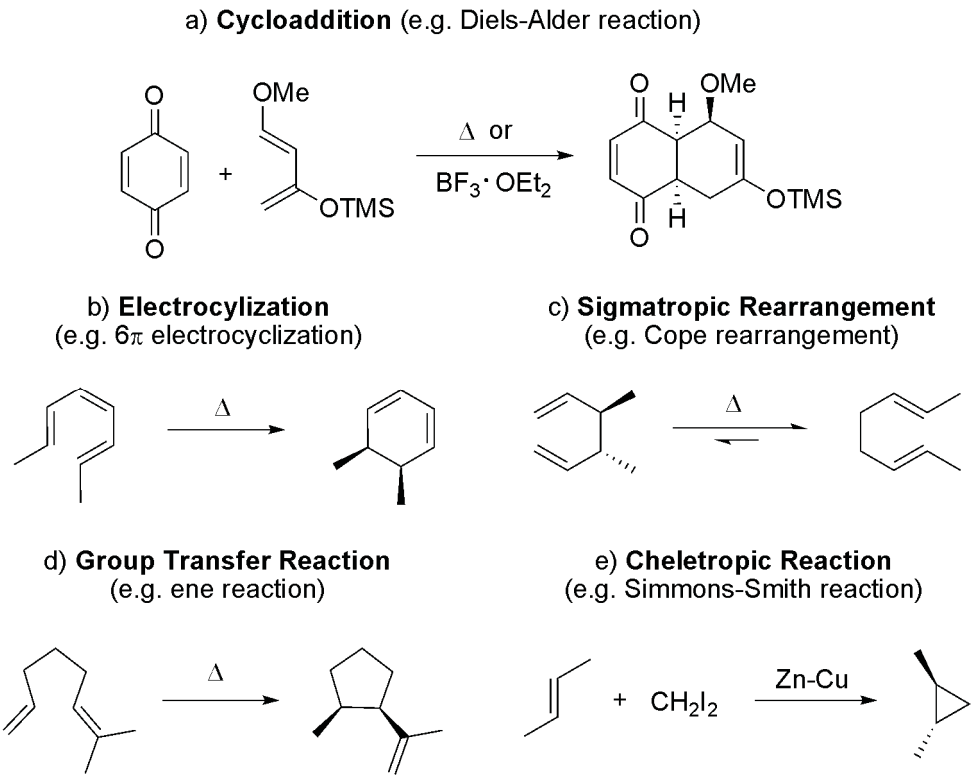
The defining feature of pericyclic reactions is that the reorganization of chemical bonds that occurs as a result of a starting material being converted into a product occurs in a concerted manner through a cyclic transition state, and thus unlike most chemical transformations, pericyclic reactions do not involve any intermediates (Scheme 1).



Scheme 1 Pericyclic reactions are concerted, involve π–electrons, and proceed through a cyclic transition state.

Pericyclic reactions may be categorized according to five sub-divisions: cycloadditions, electrocyclizations, sigmatropic rearrangements, group-transfer reactions, and cheletropic reactions (Scheme 2). Cycloadditions result in the formation of two or more σ-bonds between the termini of two or more conjugated systems, electrocyclizations result in the formation of one σ-bond between the termini of a conjugated system, sigmatropic rearrangements result in the conversion of one σ-bond into another σ-bond as a substituent migrates across a π-system, group-transfer reactions result in the conversion of one π-bond into one σ-bond as a substituent migrates, and

cheletropic reactions result in the conversion of a lone pair and a π-bond into two σ-bonds. An example of each is given in Scheme 2.



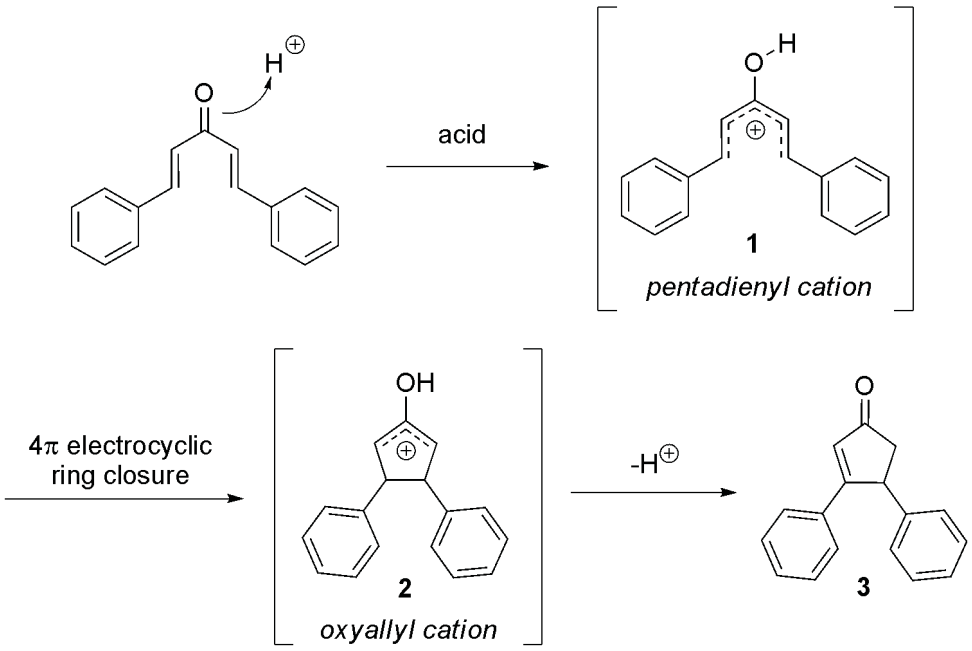
Scheme 2 The five sub-divisions of pericyclic reactions.

With the advent of chiral catalysts, many pericyclic reactions have been developed to favour a high degree of enantioselectivity. Thus, pericyclic reactions continue to have an important role in the synthesis of complex natural products.

1.3 The Nazarov Reaction

A pericyclic reaction that is rapidly gaining popularity for the formation of five-membered rings is the Nazarov reaction, a 4π electrocyclization that traditionally yields cyclopent-2-enones from divinyl ketones (Scheme 3).[2,3] This reaction is usually initiated

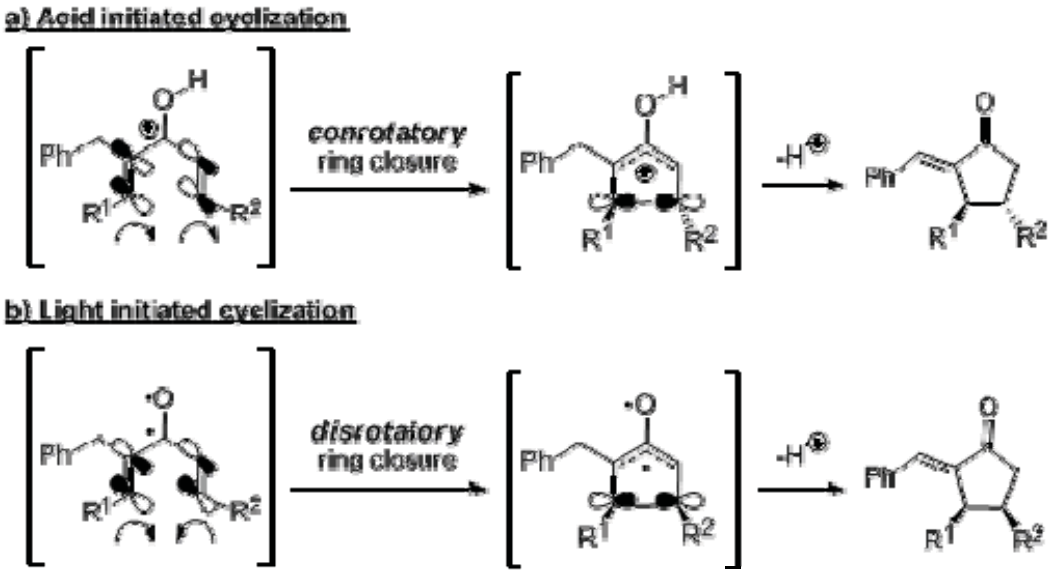
by a Brønsted or Lewis acid, generating a pentadienyl cation (**1**) that undergoes ring closure to generate a cyclic oxyallyl carbocation (**2**), which undergoes deprotonation to yield a cyclopent-2-enone (**3**).



Scheme 3 Mechanism of the Nazarov reaction.

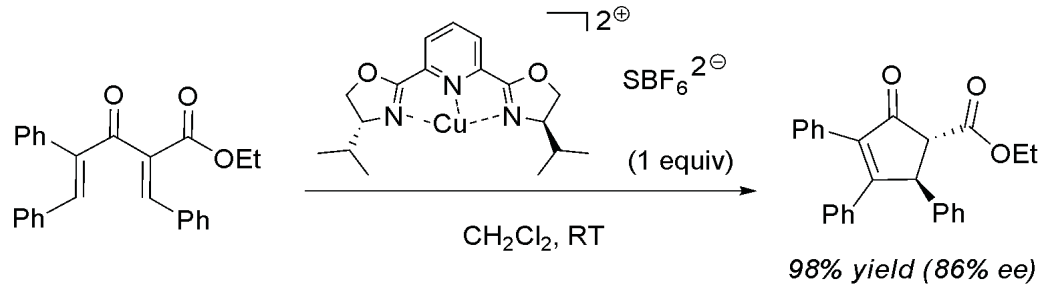
1.3.1 Stereoselectivity in the Nazarov Reaction

Ring closure of the Nazarov reaction is diastereospecific, and is governed by the Woodward-Hoffman rules. When the reaction is initiated by an acid catalyst, the HOMO is involved, and thus the substituents at both termini rotate in the same direction (conrotation) (Scheme 4a). The reaction can also be photochemically initiated, in which case the SOMO (generated by the promotion of a HOMO electron to the LUMO) is involved, and thus the substituents at both termini rotate in opposite directions (disrotation) (Scheme 4b).



Scheme 4 Diastereospecificity in the Nazarov cyclization for both a) thermal and b) photochemical processes.

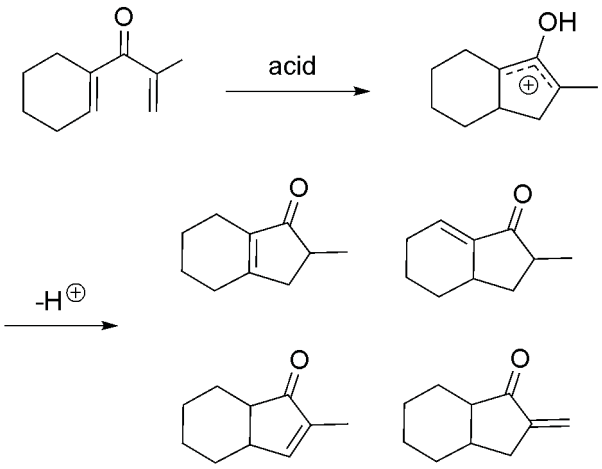
Furthermore, the electrocyclization step may proceed in either a clockwise or counterclockwise manner (termed torquoselectivity), generating a mixture of enantiomers. Many recent efforts have been directed towards the achievement of an enantioselective Nazarov reaction using chiral Lewis acids that promote torquoselectivity and generate a single enantiomer (Scheme 5).[4]



Scheme 5 Enantioselective Nazarov cyclization promoted by a chiral Lewis acid.

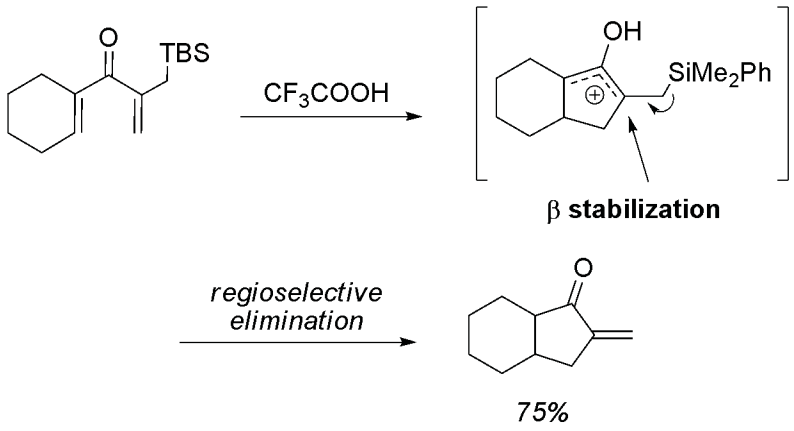
1.3.2 Regioselectivity in the Nazarov Reaction

One drawback of the Nazarov reaction, however, is that the regioselectivity of the proton elimination step is often poor, which can generate a mixture of products in some cases (Scheme 6).



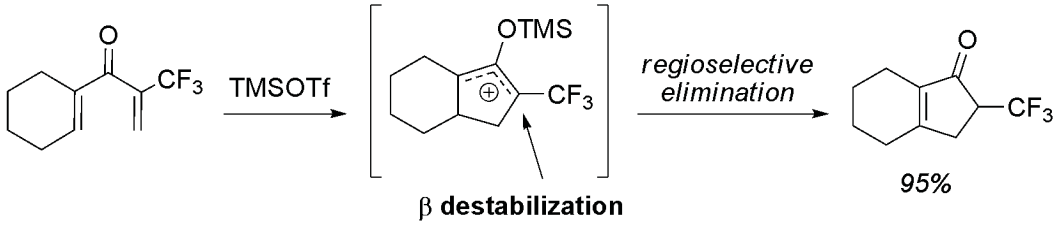
Scheme 6 Nazarov reactions often give non-regioselective elimination.

A general solution to this problem was introduced by Denmark and co-workers with the introduction of a trialkylsilyl group,[5] which ensures controlled collapse of the cyclopentadienyl cation due to the stabilization associated with the positive charge β to the silicon atom (Scheme 7).[6]



Scheme 7 Silicon-directed Nazarov reactions give regioselective elimination.

Following the success of the silicon-directed Nazarov cyclizations, Ichikawa and co-workers have recently pioneered fluorine-directed Nazarov cyclizations,[7] which take advantage of the β-destabilization of a positive charge by fluorine atoms to ensure regioselective elimination (Scheme 8).[8]



Scheme 8 Fluorine-directed Nazarov reactions give regioselective elimination.

1.3.3 Steric Influence of α-Substituents in the Nazarov Reaction

Another drawback of the Nazarov reaction is that often very strong acids are required to promote cyclization. However, cyclization efficiency can be greatly increased with the introduction of one or more alkyl substituents α to the carbonyl group (Figure

1).[2] This is largely attributed to an increase in the population of *s-trans* enone conformers, which are predominantly in the orientation required for cyclization.

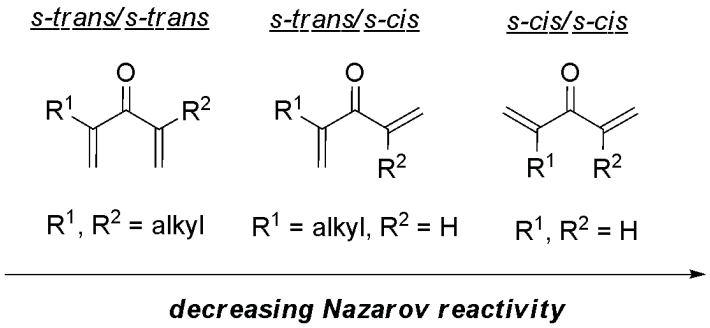
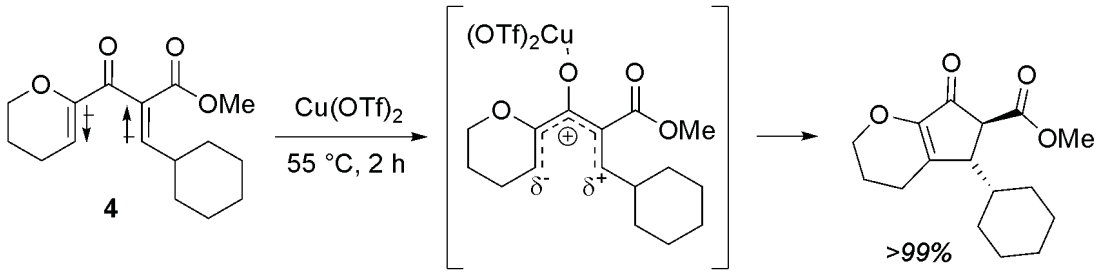


Figure 1 Nazarov reactivity increases with α-substitution.

When there are no α-substituents, the divinyl ketone will prefer to adopt an *s-cis*/*s-cis* conformation to minimize steric interactions between the two sets of methylene protons. However, when α-substituents are introduced, the unfavourable steric interactions experienced in the *s-cis* conformation are much greater than those experienced by the methylene protons, and thus the *s-trans* conformation is favoured.

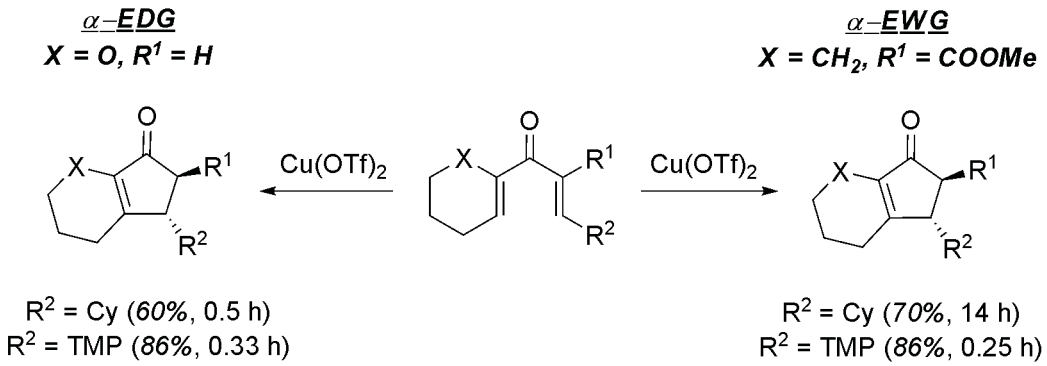
1.4 The Polarized Nazarov Reaction

The rate of the Nazarov reaction is also sensitive to electronic factors. This was first investigated systematically by Frontier and co-workers, who designed divinyl ketones containing one electron-rich double bond (*vinyl nucleophile*) and one electron-poor double bond (*vinyl electrophile*), which allowed for a "push/pull" mechanism (Scheme 9).[9]



Scheme 9 Rationale behind the design of the polarized Nazarov reaction.

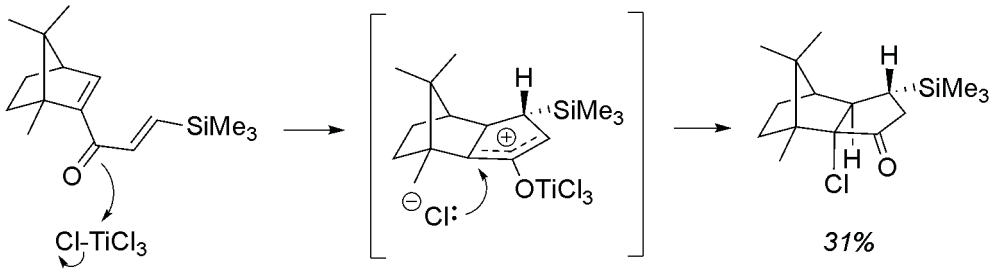
Frontier and co-workers noted a tremendous acceleration in the reaction rate with such polarized substrates – reaction times of only two hours were required to effect quantitative conversion of substrates such as **4** using a mild Lewis acid such as $Cu(OTf)_2$. As an additional advantage, the elimination step was regioselective, regenerating the "nucleophilic" double bond due to stabilization of the α-positive charge by the electron donating group (or similarly destabilization of the positive charge by the electron withdrawing group). Furthermore, Frontier and co-workers noted that the addition of only one electron-donating or electron-withdrawing group at either α-position was necessary for good reactivity, although the addition of the electron-rich 2,4,6-trimethoxyphenyl at one β-position was needed to achieve higher yields (Scheme 10).[9]



Scheme 10 The polarized Nazarov reaction with only one "polar" α-subsituent.

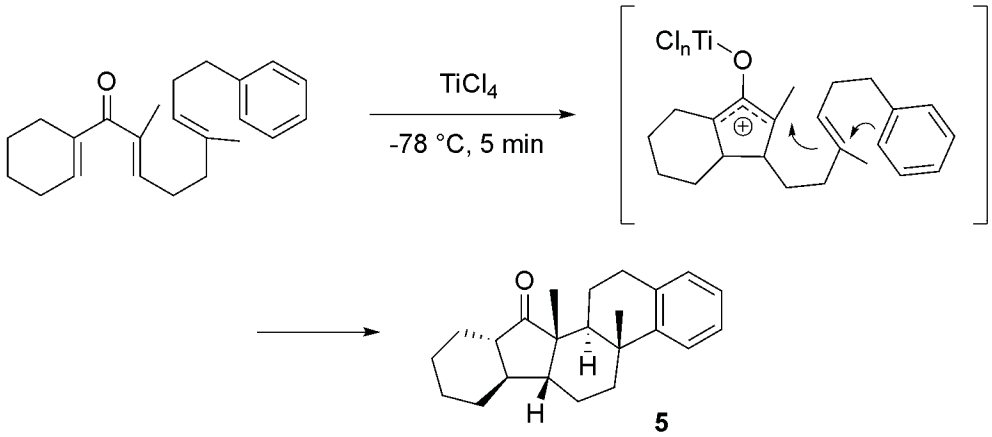
1.5 The Interrupted Nazarov Reaction

West and co-workers have shown that the oxyallyl cationic intermediate of the Nazarov reaction can undergo trapping by a suitable nucleophile in lieu of the elimination step (Scheme 11), and this group has since coined reactions of this type as "interrupted" Nazarov reactions.[10]



Scheme 11 The interrupted Nazarov reaction.

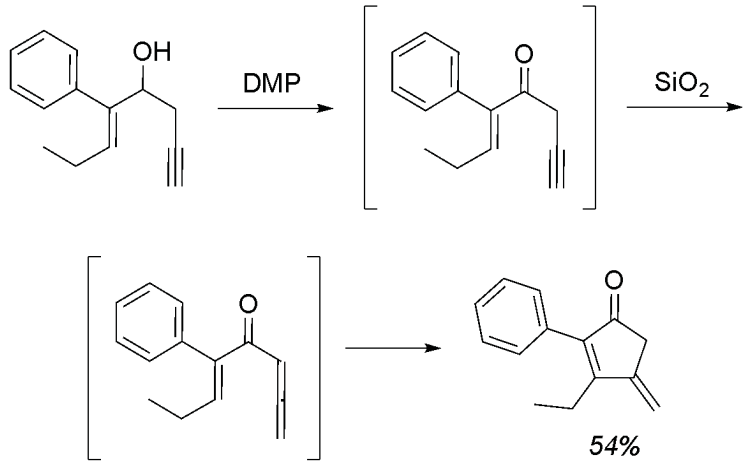
The source of the nucleophile can be from the acid itself, as shown in Scheme 11, or can be present in the reaction mixture. West has shown this reaction to be highly successful with many nucleophilic species such as alkenes,[11] arenes,[12] halides,[13] and hydride.[14] The West group has even demonstrated that an intramolecular cascade process involving internal alkenes can be initiated, forming a complex ring system (Scheme 12).[15] In the case of **5**, six new stereocenters have been formed diastereoselectively in one step!



Scheme 12 An intramolecular Nazarov reaction.

1.6 The Nazarov Reaction of Allenyl Vinyl Ketones

The Hashmi group was the first to report that when one of the alkenes of a divinyl ketone is replaced by an allene, a significant rate enhancement is observed, and that allenyl vinyl ketones undergo Nazarov cyclization spontaneously during silica gel chromatography to generate their corresponding cyclopent-2-enones (Scheme 13).[16]



Scheme 13 Hashmi's approach to the Nazarov cyclization of allenyl vinyl ketones.

It has been postulated that the increase in reactivity seen with allenyl vinyl ketones with respect to their divinyl ketone analogues is twofold. The first is a result of the alleviation of the steric strain of the sp-hybridized central carbon upon cyclization. The second is conformational in nature. A higher number of molecules might prefer to adopt the reactive *s-trans* conformation required for Nazarov cyclization, as steric interactions would be at a minimum (Figure 2).[2a]

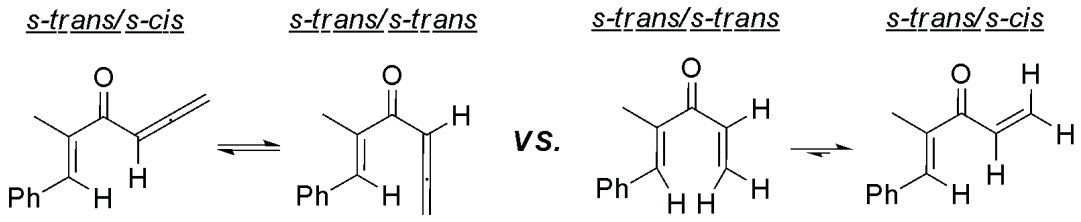
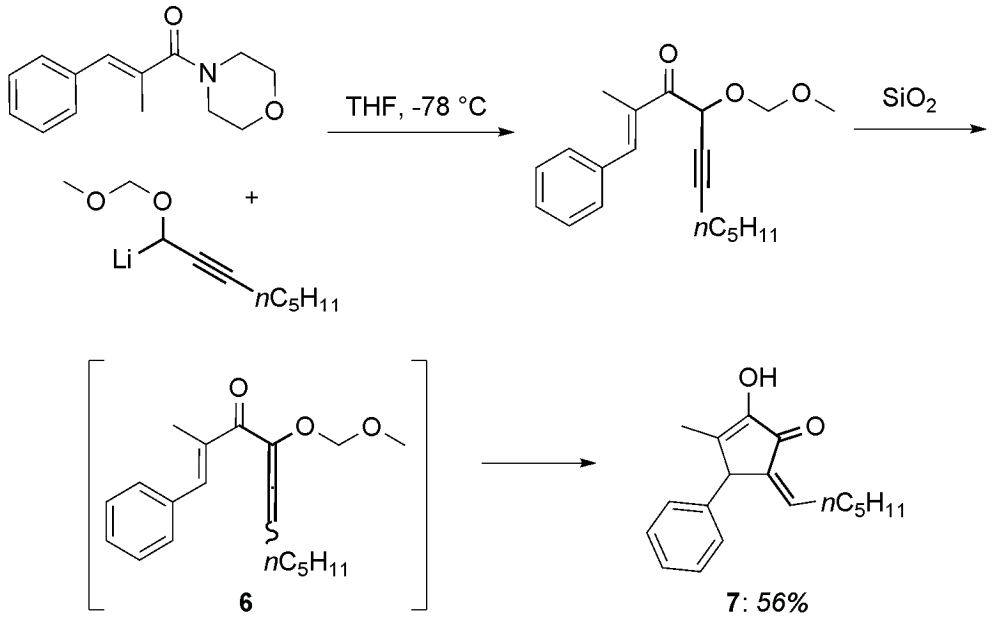


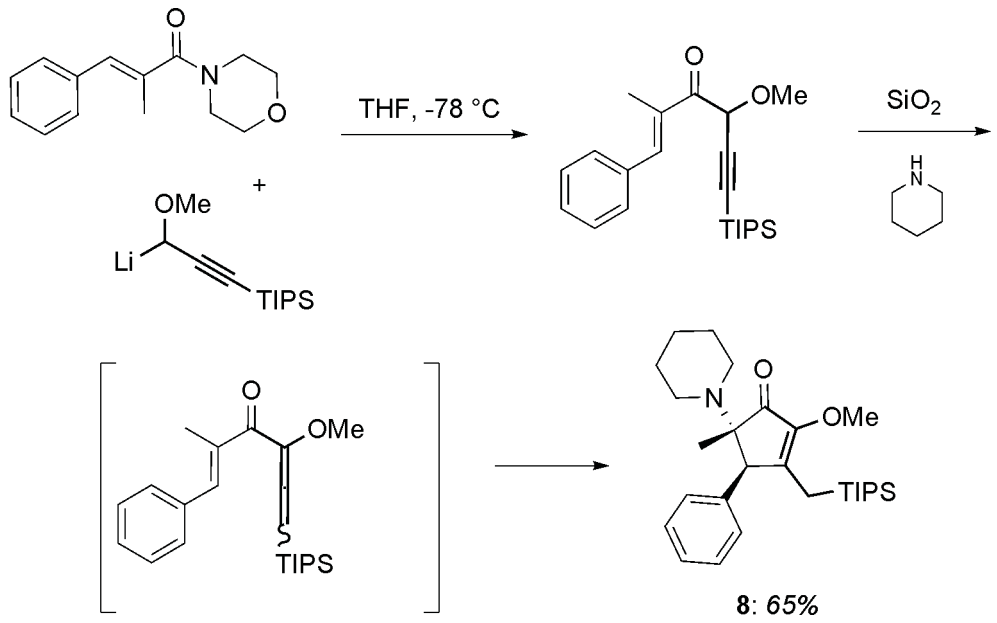
Figure 2 Steric rationale behind increased reactivity of allenyl vinyl ketones.

However, the results of Hashmi and co-workers did not seem general (3 examples, 24%, 54%, and 59% yield),[16] and it was not until extensive work by the Tius group with allenyl ethers that allenyl vinyl ketones were popularized as substrates.[17] Allenyl ethers (**6**) have been shown by Tius and co-workers to be extremely reactive – these molecules are not usually isolable, as following their formation they cyclize spontaneously on work-up to generate the corresponding Nazarov-cyclized products (Scheme 14).[18]



Scheme 14 Tius' approach to the Nazarov cyclization of allenyl vinyl ketones.

It is noteworthy that the elimination product is not observed in this case – the major product is usually a 5-alkylidene-2-hydroxycyclopent-2-enone (**7**) (Scheme 14), though the Tius group has also shown that if an amine is present in the reaction mixture, 4-amino-2-methoxycyclopent-2-ones (**8**) can be generated as well (Scheme 15).[19] The Tius group has recently shown that similar products can also be generated via trapping with indoles.[20]



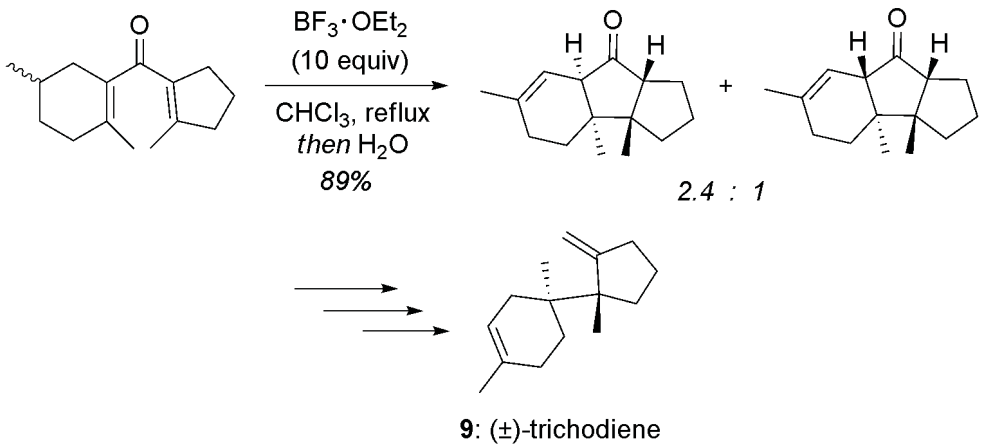
Scheme 15 Allenyl ethers undergo amine-intercepted interrupted Nazarov reactions.

1.7 Synthetic Applications of the Nazarov Reaction

The power of any synthetic methodology is demonstrated in its successful application to the synthesis of a complex natural product. Hence, selected total syntheses utilizing variants of the Nazarov reaction that have been previously discussed are listed below.

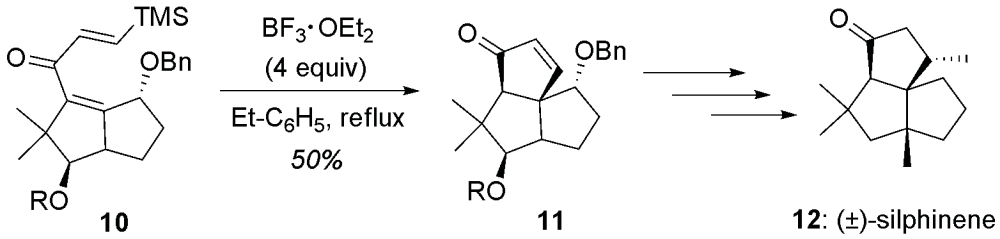
1.7.1 Use of the "Normal" Nazarov Reaction in Synthesis

Harding and co-workers synthesized racemic trichodiene (**9**) in 1990, using the Nazarov reaction as a key step.[21] The Nazarov reaction was chosen as the natural product contains two adjacent quaternary stereocenters, and the diastereospecific nature of the Nazarov reaction would ensure total *trans* selectivity (Scheme 16).



Scheme 16 Total synthesis of racemic trichodiene.

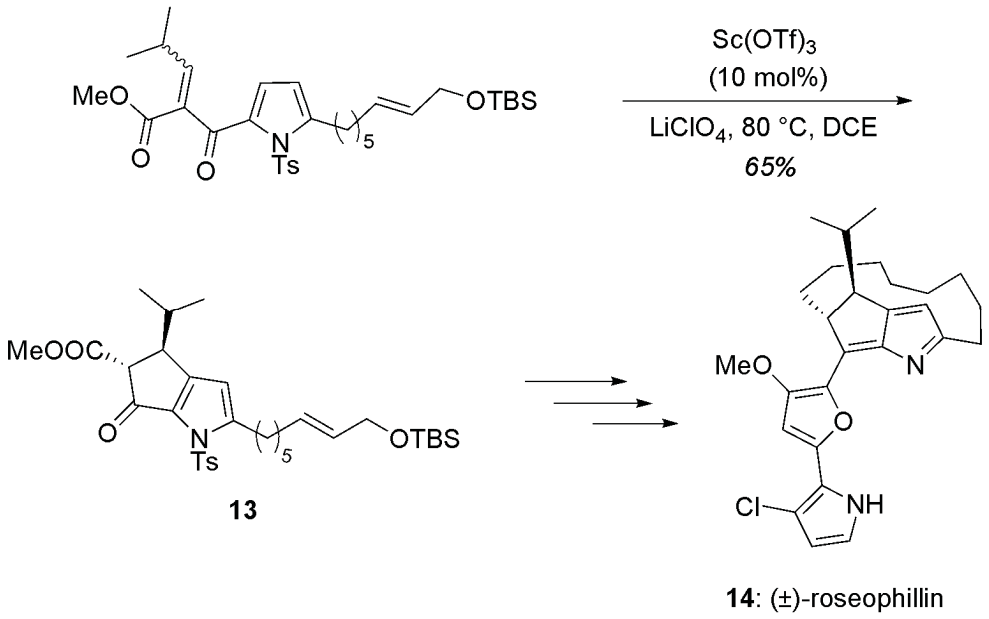
Miesch and co-workers utilized the silicon-directed Nazarov cyclization to synthesize the core of racemic silphinene (**12**) in 1997.[22] The benzyl group of **10** ensured counterclockwise conrotation generating the desired diastereomer (**11**), and the TMS group of **10** directed regioselective elimination (Scheme 17).



Scheme 17 Total synthesis of racemic siliphinene.

1.7.2 Use of the Polarized Nazarov Reaction in Synthesis

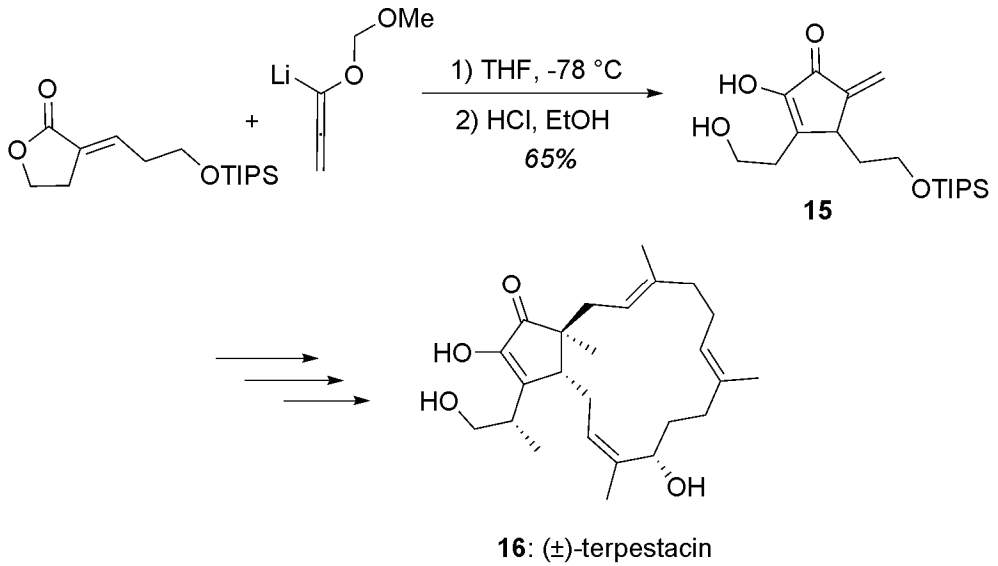
Frontier and co-workers recently utilized the polarized Nazarov cyclization to assemble the substituted pyrrole core (**13**) of racemic roseophilin (**14**) diastereoselectively (Scheme 18).[3b]



Scheme 18 Total synthesis of racemic roseophilin.

1.7.3 Use of the Nazarov Cyclization of Allenyl Ethers in Synthesis

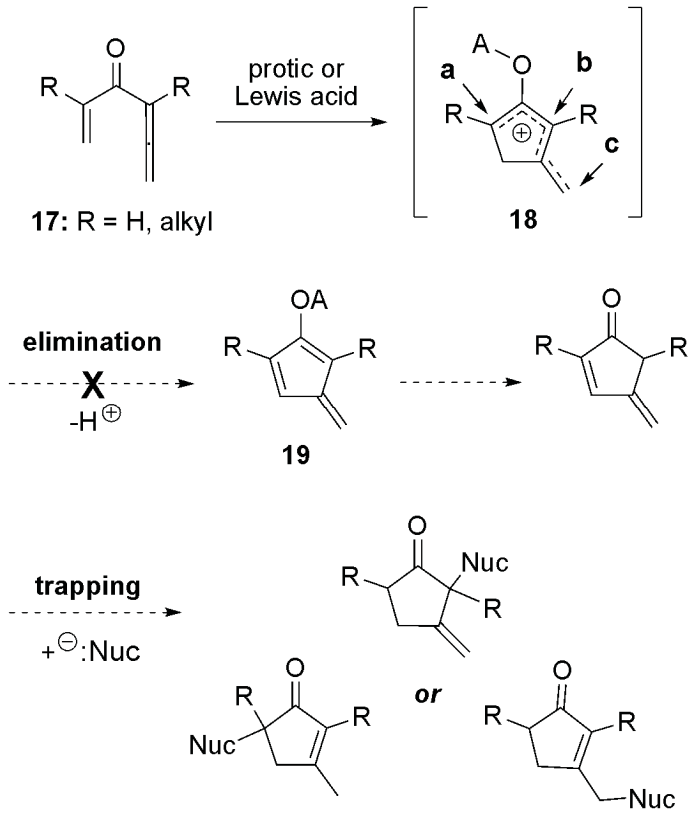
Tius and co-workers have used the Nazarov cyclization of allenyl ethers to assemble the core 2-hydroxycyclopent-2-enone unit (**15**) in their total synthesis of racemic terpestacin (**16**) (Scheme 19).[23]



Scheme 19 Total synthesis of racemic terpestacin.

1.8 Proposed Exploitation of Allenyl Vinyl Ketones in Interrupted Nazarov Reactions

We hypothesized that allenyl vinyl ketones (AVKs) of the general type **17** might be particularly well suited to undergo interrupted Nazarov reactions, due to the proposed longevity of oxyallyl cation **18**, as a result of the increased resonance stabilization provided by the allene unit. In addition, the alternative elimination pathway generating a cyclopent-2-enone necessitates the intermediacy of fulvene **19**, and is thus likely disfavoured. Furthermore, the oxyallyl cation **18** generated from AVKs has, theoretically, three positions to which a nucleophile might add, and thus such a process has the potential to rapidly generate a diverse set of cyclopent-2-enone containing compounds in one step, depending on reaction conditions, from a single, simple, starting material (Scheme 20).



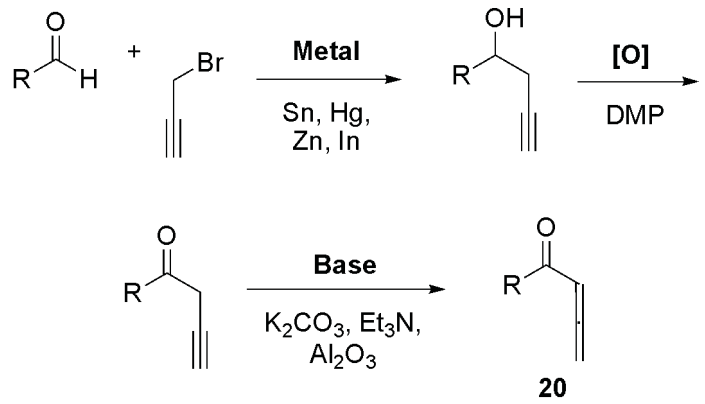
Scheme 20 Hypothetical interrupted Nazarov reaction of allenyl vinyl ketones.

CHAPTER 2. SYNTHESIS OF ALLENYL VINYL KETONES

2.1 Introduction

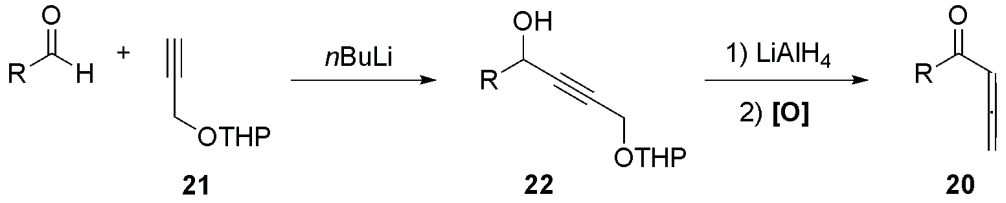
The synthesis of the starting AVKs (**17**) will be discussed initially. They are interesting compounds in themselves, as at the initiation of this project there had been no general route reported for their preparation, isolation, and characterization. Based on the studies conducted by the Hashmi group (Section 1.4), it was anticipated that a route could indeed be developed to obtain isolable compounds, but reaction conditions would likely need to be chosen carefully to avoid silica gel chromatography of the final products, as the Hashmi group has shown that they do not survive this purification step (Scheme 13).

The allenyl ketone functionality itself is relatively stable, and there exist numerous traditional methods for its preparation.[24] For allenyl ketones bearing a hydrogen atom on the allene unit adjacent to the carbonyl (**20**), the most commonly utilized method employs oxidation of a homopropargyl alcohol to the corresponding homopropargyl ketone (Scheme 21). These homopropargyl alcohols are easily synthesized via a Barbier coupling[25] of a terminal propargyl-metal species with an aldehyde (metal = tin, mercury, zinc, or indium), and oxidized using the Dess-Martin periodinane (DMP).[26] Base-induced isomerization yields the allenyl ketone. This isomerization happens in an extremely facile manner with weak bases, generally carbonate or tertiary amine bases, or aluminum oxide. Indeed, terminal homopropargyl ketones are often difficult to isolate as isomerization takes place very readily, even in the presence of silica gel, and thus the allenyl ketone is often obtained quantitatively following chromatography.[24]



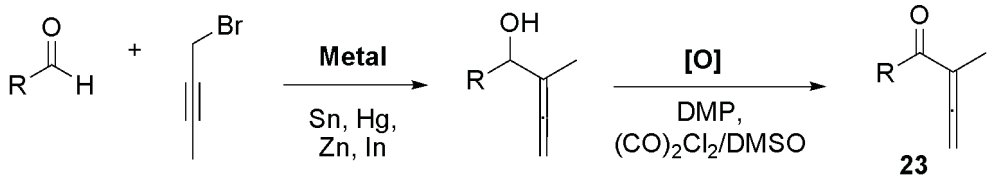
Scheme 21. Synthetic route to access allenyl ketones **20**.

An alternative, well-used method for the synthesis of AVKs **20**, is through the S_N2' displacement of an alkoxide from propargyl alcohols **22** by hydride (Scheme 22).[24] Propargyl alcohols **22** are easily accessed through the addition of the alkynyl lithium derived from **21** to an aldehyde.



Scheme 22 Alternative synthetic route to access allenyl ketones **20**.

Allenyl ketones bearing an alkyl group on the allene unit adjacent to the carbonyl (**23**), on the other hand, are often generated via oxidation of the corresponding allenyl alcohols (Scheme 23); the Swern protocol (DMSO/oxallyl chloride)[27] or Dess-Martin periodinane (DMP) have been shown to be equally effective in this instance. The allenyl alcohols are readily available via a Barbier coupling of an alkyl-substituted propargyl-metal species with an aldehyde (metal = tin, mercury, zinc, or indium).

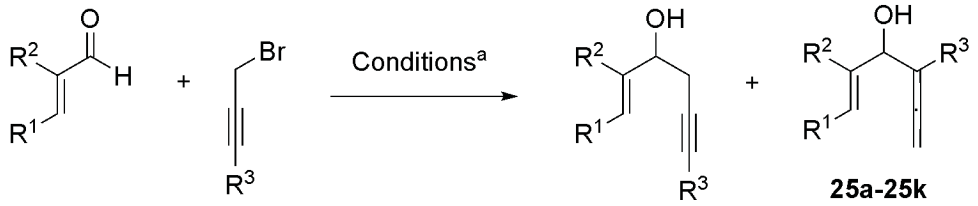


Scheme 23 General synthetic route to access AVKs **23**.

2.2 Allenyl Vinyl Ketone Synthesis

A series of homopropargyl and allenyl alcohols were synthesized through a Barbier-type coupling procedure (as described in 2.1), using indium[28] or zinc[29] metal (Table 1). In general, indium metal provided higher overall yields of product. In the case of terminal propargyl-metal species however (entries 3, 5, 15), it is noteworthy that the reaction proceeds with low regioselectivity using indium metal, generating both homopropargyl and allenyl alcohols in a 1.5:1 ratio, respectively. Zinc metal, on the other hand provides homopropargyl alcohols exclusively, albeit in low yield (entries 4, 6, 16). Choice of solvent in both cases also proved important. For reactions mediated by indium, the addition of less methanol, switching from methanol to THF, or switching from saturated aqueous NH_4Cl to water, results in unconsumed starting material. For reactions mediated by zinc, the MeOH/NH_4Cl ratio proved important – the addition of less saturated aqueous NH_4Cl results in unconsumed starting material.

Table 1 Synthesis of homopropargyl and allenyl vinyl alcohols.

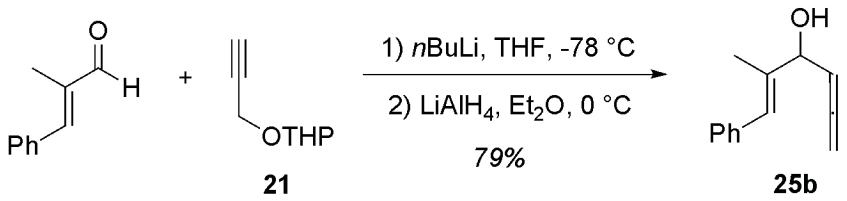


24a-24k

Entry	R^1	R^2	R^3	Conditions[a]	Compound	Yield (%)[b]
1	Ph	H	Me	A	**25a**	88
2	Ph	H	Me	B	**25a**	25
3	Ph	Me	H	A	**24b** + **25b**	79 (1.8:1)
4	Ph	Me	H	B	**24b**	37
5	Ph	H	H	A	**24c** + **25c**	78 (1.6:1)
6	Ph	H	H	B	**24c**	76
7	Ph	Me	Me	A	**25d**	84
8	Ph	Me	Me	B	**25d**	30
9	H	H	Me	A	**25e**	58
10	Me	H	Me	A	**25f**	90
11	*i*Pr	H	Me	A	**25g**	85
12	*p*-OMePh	H	Me	A	**25h**	74
13	*p*-CF_3Ph	H	Me	A	**25i**	91
14	2-Furyl	H	Me	A	**25j**	65
15	-$(CH_2)_4$-		H	A	**24k** + **25k**	64 (1.5:1)
16	-$(CH_2)_4$-		H	B	**24k**	13

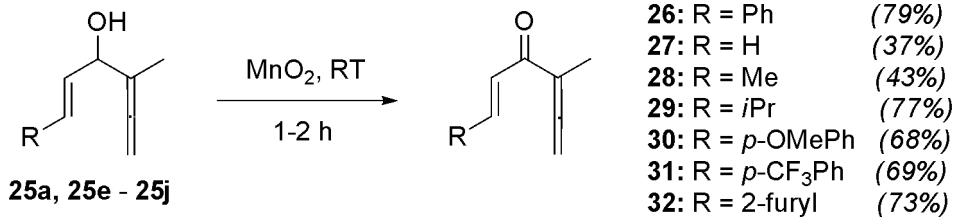
[a] Conditions: **A** = indium powder (1.1 equiv), aldehyde (1 equiv), propargyl bromide (1.1 equiv), NH_4Cl/MeOH (1:3). **B** = zinc dust (3.3 equiv), aldehyde (1 equiv), propargyl bromide (1.3 equiv), NH_4Cl/MeOH (5:1), [b] isolated yields.

In order to obtain the allenyl alcohol exclusively as well, the propargyl alcohol derived from α-methylcinnamylaldehyde and propargyl ether **21** was subjected to $LiAlH_4$ (as described in 2.1), resulting in compound **25b** in high yield (Scheme 24).



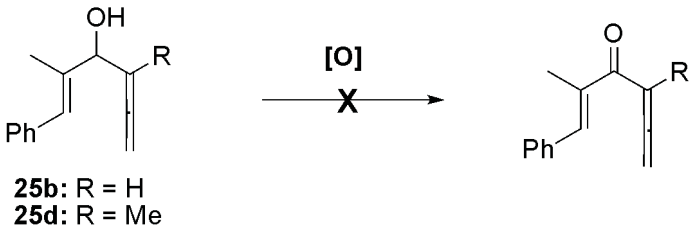
Scheme 24 Regioselective synthesis of alcohol **25b**.

Oxidation of the allenyl alcohols proved more challenging. "Standard" protocols utilized for similar substrates such as the Swern oxidation or DMP (see Section 2.1) failed, as did other mild reagents such as tetrapropylammonium perruthenate/*N*-morpholine-*N*-oxide,[30] *o*-iodoxybenzoic acid,[31] and DMP buffered with $NaHCO_3$ or pyridine. In all cases the starting material was decomposed. However, success was obtained utilizing MnO_2. For allenyl alcohols bearing an alkyl substituent on the allene unit adjacent to the carbonyl and a hydrogen atom on the alkene unit (**25a**, **25e** – **25f**), oxidation to the corresponding allenyl ketones proceeded smoothly in 37 – 79% yield (Scheme 25). It is noteworthy that these yields are *isolated yields following chromatography on silica gel.* This is in contrast to the compounds synthesized by the Hashmi group, which bear a hydrogen atom on the allene unit adjacent to the carbonyl and an alkyl substituent on the alkene unit. Hashmi's compounds do not survive chromatography on silica gel (section 1.4).[16]



Scheme 25 Synthesis of AVKs **26** – **32**.

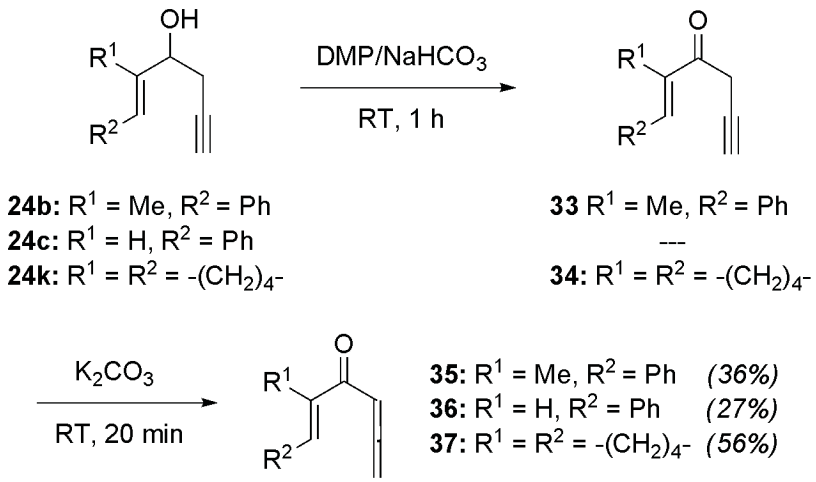
Unfortunately, this protocol was not amenable to allenyl alcohols bearing an alkyl substitutent on the alkene unit adjacent to the carbonyl (Scheme 26), as these derivatives were resistant to oxidation under these conditions resulting in the near quantitative recovery of starting material, even when the more aggressive $BaMnO_4$ was used as the oxidant.



Scheme 26 Attempted oxidation of alcohols **25b** and **25d** was unsuccessful.

However, allenyl vinyl ketones bearing a hydrogen atom on the allene unit adjacent to the carbonyl and an alkyl substituent on the alkene unit (**35** and **37**), were able to be synthesized from their corresponding homopropargyl alcohols in a two-step oxidation/isomerization sequence (Scheme 27), in 36 – 56% yield. Use of DMP, buffered with $NaHCO_3$, as oxidant in the first step proved essential.[32] Use of DMP alone failed, as did the Swern protocol, *o*-iodoxybenzoic acid, and Jones reagent (CrO_3/H_2SO_4),[33] all of which resulted in decomposition of the starting material. Although oxidations with MnO_2 and $BaMnO_4$[34] were also attempted, as seen with the allenyl alcohols **25b** and **25d**, starting material was recovered. For the second, base-mediated isomerization step, triethylamine and K_2CO_3 powder were equally effective, but $NaHCO_3$, Na_2CO_3, or basic Al_2O_3 all resulted in the decomposition of **33**. The yields of this two-step process were determined by ^1H NMR spectroscopy (using 1,3,5-trimethoxybenzene as an internal standard), as attempted purification by silica gel chromatography results only in the

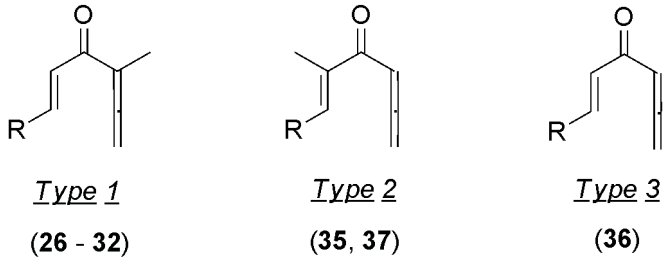
isolation of products of Nazarov cyclization, as observed by the Hashmi group for similar derivatives (Section 1.4).[16] Finally, this method is also amenable to the synthesis of the unsubstituted derivative **36**, which bears a hydrogen atom at both positions α to the carbonyl, although in this case the second base-mediated isomerization step is unnecessary; oxidation of the homopropargyl alcohol **24c** provides AVK **36** directly. Furthermore, this is an *isolated yield following purification by column chromatography*, which parallels the reactivity of allenyl vinyl ketones bearing a hydrogen atom on the allene unit adjacent to the carbonyl and an alkyl substituent on the alkene unit (Scheme 25).



Scheme 27 Synthesis of AVKs **35** – **37**.

For simplicity, AVKs bearing an alkyl substituent on the allene unit adjacent to the carbonyl and a hydrogen atom on the alkene unit will henceforth be categorized as *Type 1 AVKs*, AVKs bearing a hydrogen atom on the allene unit adjacent to the carbonyl and an alkyl substituent on the alkene unit will be henceforth categorized as *Type 2*

AVKs, and AVKs bearing a hydrogen atom at both positions α to the carbonyl will be referred to as *Type 3 AVKs* (Figure 3).



Type 1 (**26** - **32**) *Type 2* (**35**, **37**) *Type 3* (**36**)

Figure 3. Type 1, Type 2, and Type 3 AVKs.

2.3 Summary

Two general methods have been developed for the synthesis and isolation of a variety of allenyl vinyl ketones. Type 1 AVKs were prepared in two steps from commercially available materials, through oxidation of their corresponding allenyl alcohol, in overall yields ranging from 21 – 70%. Type 1 AVKs were found to be fairly stable, as they could be subjected to purification by silica gel chromatography and subsequently stored for prolonged periods. Type 2 AVKs were prepared in three steps from commercially available materials, through oxidation of their corresponding propargyl ketones, in overall yields of 13 - 23%. Type 2 AVKs were found to be much less stable than Type 1 AVKs, and could not be chromatographed or stored for prolonged periods. Type 3 AVKs were prepared in a similar manner as Type 2 AVKs. In contrast to Type 2 AVKs, but similar to Type 1 AVKs, these were amenable to chromatographic purification and could be stored for prolonged periods.

2.4 Experimental Section

2.4.1 General Considerations

All non-aqueous reactions were conducted using oven-dried glassware under an N_2 atmosphere. Reagents were used as received from a commercial supplier without further purification. *p*-Trifluoromethyl-*trans*-cinnamylaldehyde[35] and 1-bromo-2-butyne[36] were prepared according to literature procedures. Ms. Rhonda Stoddard is thanked for assistance with the preparation of compounds **24b**, **24c**, **33**, **35**, and **36**.

Dichloromethane was used freshly distilled from calcium hydride. Tetrahydrofuran and diethyl ether were used freshly distilled from sodium/benzophenone. Ethyl acetate and hexanes were distilled prior to use for column chromatography. All other solvents were used as received.

Thin layer chromatography was conducted using pre-coated silica plates with plastic backing (EMD chemicals, silica gel 60 F_{254}), using UV light (254 nm) as a visualizing agent and potassium permanganate in aqueous KOH and heat, or *o*-vanillin in ethanol/H_2SO_4 and heat, as developing agents. Column chromatography was carried out on silica gel purchased from Silicycle (40 – 63 μm particle size, 230 – 240 mesh).

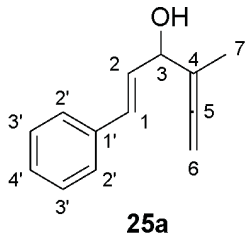
Melting points are uncorrected, and were acquired using a Fisher-Johns apparatus. ^{1}H NMR spectra were recorded at 500 MHz on a Bruker Avance spectrometer with $CDCl_3$ as solvent (7.24 ppm) and TMS as internal reference (0.00 ppm). ^{13}C NMR spectra were recorded at 125 MHz on a Bruker Avance spectrometer with $CDCl_3$ as solvent. ^{19}F NMR spectra were recorded at 225 MHz on a Bruker Avance spectrometer. Infrared spectra were recorded from thin films on a Bruker VECTOR 22 FT-IR instrument using

CsI plates. High resolution mass spectra were acquired by Mr. Xiao Feng, on a Bruker microTOF Focus orthogonal ESI-TOF mass spectrometer.

The carbon and hydrogen atoms of select compounds were assigned following detailed analysis of their one dimensional (^{1}H, ^{13}C, and DEPT-135) and two dimensional (COSY, HSQC, and HMBC) NMR spectral data. The ^{1}H and ^{13}C NMR spectra of all compounds may be found in Appendix A.

2.4.2 Preparation and Characterization Data

(*E*)-4-Methyl-1-phenylhexa-1,4,5-trien-3-ol (25a)



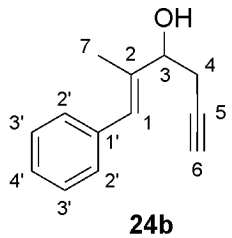
25a

Procedure 1: A saturated aqueous solution of ammonium chloride (30 mL) was added to a methanolic (10 mL) solution of 1-bromo-2-butyne (1.35 mL, 13 mmol) and *trans*-cinnamylaldehyde (1.7 mL, 13 mmol), and the mixture was cooled to 0°C. Indium powder (100 mesh) (1.7 g, 15 mmol) was then added in four portions (over twenty minutes), and the solution was stirred vigourously for 1 h. The solution was then diluted with diethyl ether, filtered through a pad of Celite, added to a separatory funnel containing a saturated aqueous solution of NaCl, and extracted with diethyl ether (×2). The combined extracts were dried with anhydrous $MgSO_4$, concentrated, and the product was purified by column chromatograpy (10% diethyl ether in pentanes) to provide **25a** (2.2 g, 88%) as a colourless oil: IR (film) 3356, 1959, 1600 (w) cm^{-1}; ^{1}H NMR δ: 7.38

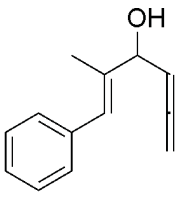
(2H, m, H3'), 7.30 (2H, m, H2'), 7.23 (1H, m, H4'), 6.62 (1H, d, *J* = 16.0 Hz, H1), 6.21 (1H, dd, *J* = 16.0, 6.8 Hz, H2), 4.86 (2H, dq, *J* = 3.1, 3.1 Hz, H6), 4.67 (1H, m, H3), 2.11 (1H, br s, *OH*), 1.74 (3H, t, *J* = 3.1 Hz, H7); ^{13}C NMR δ: 204.7 (C5), 136.5 (C1'), 131.4 (C1), 129.7 (C2), 128.5 (2C, C2'), 127.7 (C4'), 126.5 (2C, C3'), 101.6 (C4), 77.7 (C6), 73.2 (C3), 14.7 (C7); HRMS (ESI): 209.0937, $[C_{13}H_{14}ONa]^+$ requires 209.0937. NMR data matches lit.[37, 38]

Procedure 2: A saturated aqueous solution of ammonium chloride (130 mL) was added to a methanol (25 mL) solution of *trans*-cinnamylaldehyde (7.5 mL, 60 mmol) and 1-bromobut-2-yne (6.8 mL, 78 mmol). The mixture was cooled in an ice bath and vigourously stirred as zinc dust (15 g, 0.22 mol) was added in 4 portions over 30 min at 0 °C. Stirring was continued for 1 h at rt. The solution was filtered through a pad of Celite, and extracted with diethyl ether (×2). The combined ether extracts were washed with brine, dried over $MgSO_4$, and concentrated. The residue was subjected to flash chromatography (10% diethyl ether in pentanes) to provide **25a** (2.8 g, 25%) as a pale yellow oil.

(*E*)-2-Methyl-1-phenylhex-1-en-5-yn-3-ol (24b) and (*E*)-2-methyl-1-phenylhexa-1,4,5-trien-3-ol (25b)



24b



25b

According to *Procedure 1* for **25a**: indium powder (2.0 g, 17 mmol), propargyl bromide (2.0 g, 17 mmol) and α-methyl-*trans*-cinnamaldehyde (2.2 mL, 16 mmol)

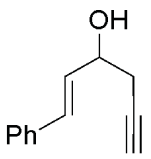
yielded **24b** (1.5 g, 51%) and **25b** (0.82 g, 28%) as colourless oils; for **24b**: IR (film) 3380, 3297, 2128, 1605 cm^{-1}; ^{1}H NMR δ: 7.34 (2H, m, H3'), 7.23 (2H, m, H2'), 7.11 (1H, m, H4'), 6.60 (1H, m, H1), 4.37 (1H, m, H3), 2.58 (2H, m, H4), 2.19 (1H, d, *J* = 3.7 Hz, *OH*), 2.09 (1H, t, *J* = 2.7 Hz, H6), 1.89 (3H, d, *J* = 1.4 Hz, H7); ^{13}C NMR δ: 138.4 (C2), 137.2 (C1'), 129.0 (2C, C2'), 128.1 (2C, C3'), 126.6 (C4'), 126.5 (C2), 80.6 (C5), 75.5 (C6), 70.9 (C3), 26.1 (C4), 13.5 (C7); HRMS (ESI) 209.0941, $[C_{13}H_{14}ONa]^{+}$ requires 209.0937. NMR data matches lit.[39,40] For **25b**: IR 3370, 1958, 1605 (w) cm^{-1}; ^{1}H NMR δ: 7.33 (2H, m), 7.29 (2H, m), 7.22 (1H, m), 6.59 (1H, m), 5.34 (1H, q, *J* = 6.5 Hz), 4.96 (2H, d, *J* = 6.6, 2.7 Hz), 4.74 (1H, m), 2.01 (1H, br s), 1.89 (3H, d, *J* = 1.4 Hz); ^{13}C NMR δ: 207.4, 139.0, 137.6, 129.2 (2C), 128.3 (2C), 126.8, 126.1, 93.8, 78.5, 75.3, 13.9; HRMS (ESI) 209.0929, $[C_{13}H_{14}ONa]^{+}$ requires 209.0937. ^{1}H NMR data matches lit.[41]

According to *Procedure 2* for **25a**: zinc dust (17 g, 0.26 mol), propargyl bromide (12 g, 0.10 mol) and α-methyl-*trans*-cinnamaldehyde (10 mL, 0.08 mol) yielded **24b** (5.5 g, 37%) as a colourless oil.

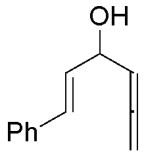
Procedure 3: A 2.5 M solution of *n*-butyllithium in hexanes (34 mL, 0.086 mol) was added to a -78 °C solution of tetrahydro-2-(2-propynyloxy)-2*H*-pyran (10 mL, 0.071 mol) in THF (100 mL), stirred for 1 h, and then α-methyl-*trans*-cinnamaldehyde (10 mL, 0.071 mol) was added. The reaction was stirred at rt overnight, and then diluted with ether. The organic layer was washed with water, brine, dried with $MgSO_4$, then concentrated. The crude residue was dissolved in Et_2O (50 mL), added dropwise to a slurry of $LiAlH_4$ (5.0 g, 0.13 mol) in Et_2O (125 mL) at 0 °C, and stirred for 1 h. Water (15 mL), 10% NaOH (aq) (15 mL), and additional water (15 mL) were then added

successively, and the mixture was stirred at rt for 1 h until a white precipitate formed. Anhydrous $MgSO_4$ was then added, and the mixture was filtered, then concentrated. The residue was subjected to flash chromatography (25% diethyl ether in pentanes) to provide **25b** (10.4 g, 79%) as a colourless oil.

(*E*)-1-Phenylhex-1-en-5-yn-3-ol (24c) and (*E*)-1-phenylhexa-1,4,5-trien-3-ol (25c)



24c

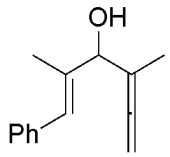


25c

According to *Procedure 1* for **25a**: indium powder (2.0 g, 17 mmol), propargyl bromide (2.0 g, 17 mmol) and *trans*-cinnamaldehyde (2.0 mL, 16 mmol) yielded **24c** (1.3 g, 48%) and **25c** (0.81 g, 30%) as colourless oils; for **24c**: IR (film) 3391, 3296, 2128, 1605 cm^{-1}; ^1H NMR δ: 7.39 (2H, m), 7.32 (2H, m), 7.28 (1H, m), 6.66 (1H, d, J = 16 Hz), 6.28 (1H, dd, J = 16, 6.3 Hz), 4.48 (1H, m), 2.58 (1H, ddd, J = 17, 5.9, 2.7 Hz), 2.52 (1H, ddd, J = 17, 6.0, 2.7 Hz), 2.16 (1H, br s), 2.09 (1H, t, J = 2.7 Hz); ^{13}C NMR δ: 136.3, 131.3, 129.9, 128.6, 127.9, 126.6, 80.2, 71.1, 70.7, 27.7; HRMS (ESI) 195.0788, $[C_{12}H_{12}ONa]^+$ requires 195.0780. NMR data matches lit.[37, 40, 42] For **25c**: IR 3406, 1963, 1605 (w) cm^{-1}; ^1H NMR δ: 7.39 (2H, m), 7.32 (2H, m), 7.25 (1H, m), 6.64 (1H, d, J = 16 Hz), 6.27 (1H, d, J = 16 Hz), 5.37 (1H, q, J = 6.5 Hz), 4.93 (2H, d, J = 6.6, 2.4 Hz), 4.87 (1H, m), 1.13 (1H, d, J = 6.3 Hz); ^{13}C NMR δ: 207.3, 136.5, 130.7, 130.4, 128.6 (2C), 127.9, 126.6 (2C), 93.9, 78.3, 70.5; HRMS (ESI) 195.0772, $[C_{12}H_{12}ONa]^+$ requires 195.0780. NMR data matches lit.[42]

According to *Procedure 2* for **25a**: zinc dust (35 g, 0.53 mol), propargyl bromide (25 g, 0.21 mol) and *trans*-cinnamaldehyde (20 mL, 0.16 mmol) yielded **24c** (21 g, 76%) as a yellow oil.

(*E*)-2,4-Dimethyl-1-phenylhexa-1,4,5-trien-3-ol (25d)

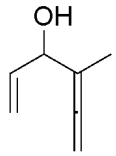


25d

According to *Procedure 1* for **25a**: indium powder (2.0 g, 17 mol), 1-bromo-2-butyne (1.5 ml, 17 mmol) and α-methyl-*trans*-cinnamaldehyde (2.2 mL, 16 mmol) yielded **31** (2.7 g, 84%) as a colourless oil; IR 3406, 1963, 1605 (w) cm^{-1}; ^{1}H NMR δ: 7.34 (2H, m), 7.30 (2H, m), 7.23 (1H, m), 6.56 (1H, m), 4.95 (2H, m), 4.54 (1H, m), 2.07 (1H, d, J = 2.2 Hz), 1.82 (3H, d, J = 1.3 Hz), 1.67 (3H, t, J = 3.2 Hz); ^{13}C NMR δ: 204.6, 137.8, 137.6, 129.2 (2C), 128.3 (2C), 127.7, 126.8, 101.4, 78.7, 78.1, 15.1, 13.1; HRMS (ESI) 223.1083, $[C_{14}H_{16}ONa]^{+}$ requires 223.1093.

According to *Procedure 2* for **25a**: zinc dust (1.4 g, 22 mmol), 1-bromo-2-butyne (0.85 ml, 8.9 mmol) and α-methyl-*trans*-cinnamaldehyde (0.95 mL, 6.8 mmol) yielded **25d** (0.41 g, 30%) as a colourless oil.

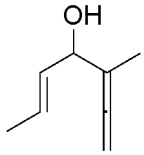
4-Methylhexa-1,4,5-trien-3-ol (25e)



25e

According to *Procedure 1* for **25a**: acrolein (1.8 mL, 27 mmol), indium powder (1.7 g, 15 mmol), and 1-bromo-2-butyne (1.4 mL, 15 mmol) yielded **25e** (0.95 g, 58%) as a colourless oil: IR (film) 3444, 1960 cm^{-1}; ^{1}H NMR δ: 5.86 (1H, ddd, *J* = 17.1, 10.4, 6.3 Hz), 5.31 (1H, dd, *J* = 17.1, 1.3 Hz), 5.19 (1H, dd, *J* = 10.4, 1.3 Hz), 4.84 (2H, dq, *J* = 3.2, 3.2 Hz), 4.50 (1H, m), 1.93 (1H, br s), 1.70 (3H, t, *J* = 3.2 Hz); ^{13}C NMR δ: 204.6, 138.4, 115.8, 101.3, 77.5, 73.5, 14.5; HRMS (ESI): 133.0632, $[C_7H_8ONa]^+$ requires 133.0624.

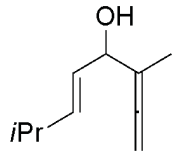
(*E*)-3-Methylhepta-1,2,5-trien-4-ol (25f)



25f

According to *Procedure 1* for **25a**: *trans*-crotonaldehyde (1.1 mL, 13 mmol), indium powder (1.7 g, 15 mmol), and 1-bromo-2-butyne (1.4 mL, 15 mmol) yielded **25f** (1.5 g, 90%) as a colourless oil: IR (film) 3357, 1959 cm^{-1}; ^{1}H NMR δ: 5.73 (1H, dq, *J* = 15.3, 6.7 Hz), 5.50 (1H, dd, *J* = 15.3, 7.4 Hz), 4.83 (2H, m), 4.42 (1H, m), 2.09 (1H, br s), 1.72 (3H, d, *J* = 6.7 Hz), 1.68 (3H, t, *J* = 3.1 Hz); ^{13}C NMR δ: 204.3, 131.4, 128.0, 101.9, 77.5, 73.2, 17.6, 14.7; HRMS (ESI): 147.0789, $[C_8H_{12}ONa]^+$ requires 147.0780.

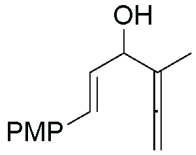
(*E*)-3,7-Dimethylocta-1,2,5-trien-4-ol (25g)



25g

According to *Procedure 1* for **25a**: *trans*-4-methyl-2-pentenal (1.55 mL, 13 mmol), indium powder (1.7 g, 15 mmol), and 1-bromo-2-butyne (1.4 mL, 15 mmol) yielded **25g** (1.7 g, 85%) as a colourless oil: IR (film) 3375, 1960 cm^{-1}; ^1H NMR δ: 5.67 (1H, dd, *J* = 15.6, 6.6 Hz), 5.41 (1H, dd, *J* = 15.6, 6.9 Hz), 4.78 (2H, dq, *J* = 3.1, 3.1 Hz), 4.43 (1H, m), 2.46 (1H, br s), 2.31 (1H, m), 1.67 (3H, t, *J* = 3.1 Hz), 1.00 (6H, d, *J* = 6.8 Hz); ^{13}C NMR δ: 204.5, 139.5, 127.2, 101.7, 77.3, 73.0, 30.5, 22.0 (2C), 14.4; HRMS (ESI): 175.1087, $[C_{10}H_{16}ONa]^+$ requires 175.1093.

(*E*)-1-(4-Methoxyphenyl)-4-methylhexa-1,4,5-trien-3-ol (25h)

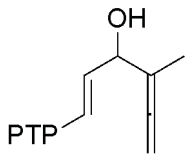


25h

According to *Procedure 1* for **25a**: *p*-methoxy-*trans*-cinnamylaldehyde (2.2 g, 13 mmol), indium powder (1.7 g, 15 mmol), and 1-bromo-2-butyne (1.4 mL, 15 mmol) yielded **25h** (2.1 g, 74%) as a colourless oil: IR (film) 3386, 1958, 1607 cm^{-1}; ^1H NMR δ: 7.32 (2H, d, *J* = 8.8 Hz), 6.85 (2H, d, *J* = 8.8 Hz), 6.58 (1H, d, *J* = 15.8 Hz), 6.07 (1H, dd, *J* = 15.8, 6.9 Hz), 4.86 (2H, dq, *J* = 3.1, 3.1 Hz), 4.64 (1H, m), 3.82 (3H, s), 1.97 (1H, br s), 1.74 (3H, t, *J* = 3.1 Hz); ^{13}C NMR δ: 204.6, 159.3, 130.9, 129.3, 127.8 (2C), 127.5,

114.0 (2C), 101.8, 77.7, 73.4, 55.3, 14.8; HRMS (ESI): 239.1034, $[C_{14}H_{16}O_2Na]^+$ requires 239.1043.

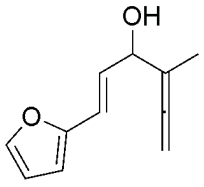
(*E*)-4-Methyl-1-(4-(trifluoromethyl)phenyl)hexa-1,4,5-trien-3-ol (25i)



25i

According to *Procedure 1* for **25a**: *p*-trifluoromethyl-*trans*-cinnamylaldehyde (1.9 g, 9.7 mmol), indium powder (1.2 g, 11 mmol), and 1-bromo-2-butyne (1.0 mL, 11 mmol) yielded **25i** (2.2 g, 91%) as a colourless oil: IR (film) 3384, 1960, 1616, 1327 cm^{-1}; ^1H NMR δ: 7.57 (2H, d, J = 8.3 Hz), 7.48 (2H, d, J = 8.3 Hz), 6.68 (1H, d, J = 15.9 Hz), 6.32 (1H, dd, J = 15.9, 6.4 Hz), 4.89 (2H, dq, J = 3.1, 3.1 Hz), 4.71 (1H, m), 2.22 (1H, br s), 1.75 (3H, t, J = 3.1 Hz); ^{13}C NMR δ: 204.8, 140.1, 132.4, 129.6, 129.5 (q, J = 33 Hz), 126.7 (2C), 125.5 (2C, q, J = 3.6 Hz), 124.1 (q, J = 270 Hz), 101.3, 77.8, 73.0, 14.6; ^{19}F NMR δ: −63.8 (s); HRMS (ESI): 277.0799, $[C_{14}H_{13}F_3ONa]^+$ requires 277.0811.

(*E*)-1-(Furan-2-yl)-4-methylhexa-1,4,5-trien-3-ol (25j)

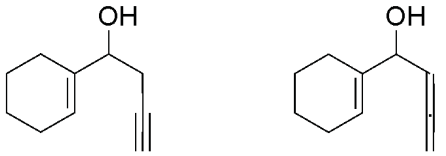


25j

According to *Procedure 1* for **25a**: *trans*-3-(2-furyl)acrolein (1.6 g, 13 mmol), indium powder (1.7 g, 15 mmol), and 1-bromo-2-butyne (1.4 mL, 15 mmol) yielded **25j**

(1.5 g, 65%) as a yellow oil: IR (film) 3383, 1959 cm^{-1}; ^1H NMR δ: 7.34 (1H, d, *J* = 1.6 Hz), 6.46 (1H, d, *J* = 15.8 Hz), 6.36 (1H, dd, *J* = 3.3, 1.8 Hz), 6.25 (1H, d, *J* = 3.3 Hz), 6.17 (1H, dd, *J* = 15.8, 6.5 Hz), 4.85 (2H, dq, *J* = 3.1, 3.1 Hz), 4.65 (1H, m), 2.06 (1H, br s), 1.73 (3H, t, *J* = 3.1 Hz); ^{13}C NMR δ: 204.7, 152.3, 142.0, 128.2, 119.3, 111.3, 108.2, 101.4, 77.6, 72.9, 14.5; HRMS (ESI): 199.0739, $[C_{11}H_{12}O_2Na]^+$ requires 199.0730.

(*E*)-1-Cyclohexenylbut-3-yn-1-ol (24k) and (*E*)-1-cyclohexenylbuta-2,3-dien-1-ol (25k)

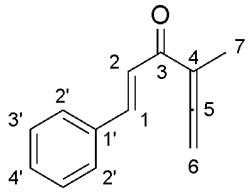


24k **25k**

According to *Procedure 1* for **25a**: indium powder (2.0 g, 17 mmol), propargyl bromide (2.0 g, 17 mmol) and 1-cyclohexene-1-carboxaldehyde (1.8 mL, 16 mmol) yielded **24k** (0.93 g, 39%) and **25k** (0.60 g, 25%) as colourless oils; for **24k**: IR 3308, 2124 (w) cm^{-1}; ^1H NMR δ: 5.75 (1H, m), 4.15 (1H, m), 2.46 (2H, m), 2.04 (4H, m), 1.99 (1H, m), 1.94 (1H, m), 1.61 (4H, m); ^{13}C NMR δ: 138.3, 124.1, 81.4, 74.3, 70.7, 26.0, 25.1, 24.0, 22.7, 22.6; HRMS (ESI) 173.0948, $[C_{10}H_{14}ONa]^+$ requires 173.0937. NMR data matches lit.[43] For **25k**: IR 3366, 1958 cm^{-1}; ^1H NMR δ: 5.76 (1H, m), 5.26 (1H, q, *J* = 6.4 Hz), 4.90 (2H, dd, *J* = 6.7, 2.7 Hz), 4.54 (1H, m), 2.02 (4H, m), 1.81 (1H, br s), 1.61 (4H, m); ^{13}C NMR δ: 207.2, 139.0, 123.6, 93.9, 78.1, 73.9, 25.2, 24.1, 22.7 (2C); HRMS (ESI) 173.0941, $[C_{10}H_{14}ONa]^+$ requires 173.0937.

According to *Procedure 2* for **25a**: zinc dust (23 g, 0.35 mol), propargyl bromide (18 g, 0.15 mol) and 1-cyclohexene-1-carboxaldehyde (13 mL, 0.11 mol) yielded **24k** (2.1 g, 13%) as a colourless oil.

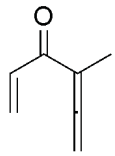
(*E*)-4-Methyl-1-phenylhexa-1,4,5-trien-3-one (26)



26

Activated MnO_2 (19 g, 0.21 mol) was added in four portions (over one hour) to a vigourously stirring solution of allenyl vinyl alcohol **25a** (2.0 g, 11 mmol) in dichloromethane (110 mL) at room temperature. The solution was stirred for 3 h, filtered through a pad of Celite, concentrated, and the product was purified via column chromatography to provide **26** (1.55 g, 79%) as an off-white solid: mp 64–67 °C; IR (film) 1958, 1929, 1660, 1607 cm^{-1}; ^{1}H NMR δ: 7.63 (1H, d, J = 15.8 Hz, H1), 7.54 (2H, m, H3'), 7.40 (1H, d, J = 15.8 Hz, H2), 7.36 (3H, m, H2', H4'), 5.24 (2H, q, J = 3.0 Hz, H6), 1.91 (3H, t, J = 3.0 Hz, H7); ^{13}C NMR δ: 216.2 (C5), 189.2 (C3), 141.6 (C1), 134.9 (C1'), 130.0 (C4'), 128.7 (2C, C2'), 128.2 (2C, C3'), 121.7 (C2), 105.0 (C4), 78.9 (C6), 13.4 (C7); HRMS (ESI): 207.0784, $[C_{13}H_{12}ONa]^{+}$ requires 207.0780.

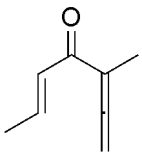
4-Methylhexa-1,4,5-trien-3-one (27)



27

According to the procedure for **26**: allenyl vinyl alcohol **4a** (0.50 g, 4.5 mmol) and MnO_2 (7.9 g, 0.090 mol) yielded **27** (0.18 g, 37%) as a colourless oil: IR (film) 1959, 1934, 1685, 1651 cm^{-1}; ^1H NMR δ: 7.05 (1H, dd, J = 17, 11 Hz), 6.29 (1H, d, J = 17 Hz), 5.61 (1H, d, J = 11 Hz), 5.21 (2H, q, J = 3.0 Hz), 1.86 (3H, t, J = 3.0 Hz); ^{13}C NMR δ: 216.5, 189.5, 131.3, 126.9, 104.2, 78.8, 13.0; HRMS (ESI): 131.0473, $[C_7H_8ONa]^+$ requires 131.0467.

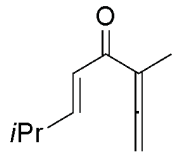
(*E*)-3-Methylhepta-1,2,5-trien-4-one (28)



28

According to the procedure for **26**: allenyl vinyl alcohol **4b** (1.3 g, 10 mmol) and MnO_2 (18 g, 0.20 mol) yielded **28** (0.55 g, 43%) as a colourless oil: IR (film) 1954, 1935, 1673, 1628 cm^{-1}; ^1H NMR δ: 6.89 (1H, dq, J = 15.4, 6.8 Hz), 6.78 (1H, d, J = 15.4 Hz), 5.17 (2H, q, J = 3.0 Hz), 1.88 (3H, d, J = 6.8 Hz), 1.84 (3H, t, J = 3.0 Hz); ^{13}C NMR δ: 214.8, 188.0, 140.1, 125.3, 102.8, 75.5, 16.5, 11.9; HRMS (ESI): 145.0626, $[C_8H_{10}ONa]^+$ requires 145.0624. NMR data matches lit.[44]

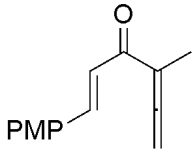
(*E*)-3,7-Dimethylocta-1,2,5-trien-4-one (29)



29

According to the procedure for **26**: allenyl vinyl alcohol **4c** (1.3 g, 8.7 mmol) and MnO_2 (15 g, 0.17 mol) yielded **29** (1.0 g, 77%) as a colourless oil: IR (film) 1959, 1935, 1671, 1625 cm^{-1}; ^1H NMR δ: 6.86 (1H, dd, *J* = 15.5, 6.8 Hz), 6.71 (1H, d, *J* = 15.5 Hz), 5.17 (2H, q, *J* = 3.0 Hz), 2.46 (1H, m), 1.85 (3H, t, *J* = 3.0 Hz), 1.06 (6H, d, *J* = 6.8 Hz); ^{13}C NMR δ: 216.2, 190.0, 152.7, 122.3, 104.5, 78.6, 31.1, 21.4 (2C), 13.4; HRMS (ESI): 173.0935, $[C_{10}H_{14}ONa]^+$ requires 173.0937.

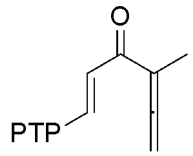
(*E*)-1-(4-Methoxyphenyl)-4-methylhexa-1,4,5-trien-3-one (30)



30

According to the procedure for **26**: allenyl vinyl alcohol **4e** (1.9 g, 9.0 mmol) and MnO_2 (16 g, 0.18 mol) yielded **30** (1.3 g, 68%) as a yellow solid: mp 56–58 °C; IR (film) 1961, 1933, 1653, 1594 cm^{-1}; ^1H NMR δ: 7.60 (1H, d, *J* = 16 Hz), 7.51 (2H, d, *J* = 8.8 Hz), 7.29 (1H, d, *J* = 16 Hz), 6.89 (2H, d, *J* = 8.8 Hz), 5.23 (2H, q, *J* = 3.0 Hz), 3.83 (3H, s), 1.91 (3H, t, *J* = 3.0 Hz); ^{13}C NMR δ: 216.0, 189.3, 161.3, 141.5, 129.9 (2C), 127.7, 119.6, 114.2 (2C), 105.0, 78.8, 55.3, 13.5; HRMS (ESI): 237.0886, $[C_{14}H_{14}O_2Na]^+$ requires 237.0891.

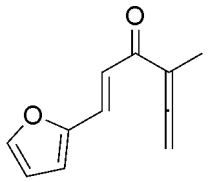
(*E*)-4-Methyl-1-(4-(trifluoromethyl)phenyl)hexa-1,4,5-trien-3-one (31)



31

According to the procedure for **26**: allenyl vinyl alcohol **4f** (2.2 g, 8.6 mmol) and MnO_2 (15 g, 0.17 mol) yielded **31** (1.5 g, 69%) as an off-white solid: mp 57–59 °C; IR (film) 1963, 1930, 1663, 1610, 1325 cm^{-1}; ^1H NMR δ: 7.62 (5H, m), 7.46 (1H, d, J = 16 Hz), 5.29 (2H, q, J = 3.0 Hz), 1.92 (3H, t, J = 3.0 Hz); ^{13}C NMR δ: 216.4, 188.8, 139.6, 138.4, 131.4 (q, J = 33 Hz), 128.2 (2C), 125.6 (2C, q, J = 3.6 Hz), 123.8 (q, J = 270 Hz), 123.8, 105.1, 79.2, 13.3; ^{19}F NMR δ: -63.8 (s); HRMS (ESI): 275.0646, $[C_{14}H_{11}F_3ONa]^+$ requires 275.0654.

(*E*)-1-(Furan-2-yl)-4-methylhexa-1,4,5-trien-3-one (32)

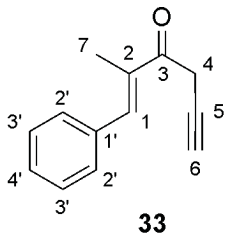


32

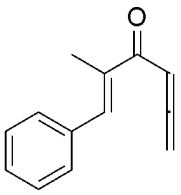
According to the procedure for **26**: allenyl vinyl alcohol **4e** (1.5 g, 8.7 mmol) and MnO_2 (15 g, 0.17 mmol) yielded **32** (1.1 g, 73%) as a yellow solid: mp 67–68 °C; IR (film) 1972, 1938, 1655, 1599 cm^{-1}; ^1H NMR δ: 7.47 (1H, d, J = 1.8 Hz), 7.38 (1H, d, J = 16 Hz), 7.27 (1H, d, J = 16 Hz), 6.64 (1H, d, J = 3.4 Hz), 6.47 (1H, dd, J = 3.4, 1.8 Hz), 5.25 (2H, q, J = 3.0 Hz), 1.90 (3H, t, J = 3.0 Hz); ^{13}C NMR δ: 216.1, 189.2, 151.6, 144.4,

128.0, 119.5, 115.4, 112.4, 105.0, 79.0, 13.4; HRMS (ESI): 197.0565, $[C_{11}H_{10}O_2Na]^+$ requires 197.0573.

(*E*)-2-Methyl-1-phenylhex-1-en-5-yn-3-one (33) and (*E*)-2-methyl-1-phenylhexa-1,4,5-trien-3-one (35)



33

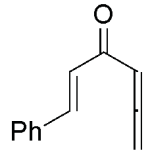


35

Dess-Martin periodinane (1.5 g. 3.5 mmol) was added to a vigourously stirring solution of propargyl alcohol **24b** (0.5 g, 2.7 mmol) and sodium bicarbonate (2.3 g, 27 mmol) in CH_2Cl_2 (25 mL) at rt. After 45 min saturated aqueous solutions of sodium bicarbonate and sodium thiosulfate were added (25 mL each), as well as a small amount of diethyl ether, and the mixture was stirred until both layers went clear. The mixture was extracted thoroughly with CH_2Cl_2, and the organic layer was washed with brine, dried over $MgSO_4$, and concentrated under vacuum, yielding **33** as a pale yellow oil: IR (film) 1641 cm^{-1}; ^1H NMR δ: 7.58 (1H, q, *J* = 1.4 Hz, H1), 7.43 (4H, m, H2', H3'), 7.37 (1H, m, H4'), 3.74 (2H, d, *J* = 2.8 Hz, H4), 2.29 (1H, t, *J* = 2.8 Hz, H6), 2.10 (3H, d, *J* = 1.4 Hz, H7); ^{13}C NMR δ: 194.8 (C3), 140.5 (C1), 135.8 (C2), 135.4 (C1'), 129.8 (2C, C2'), 128.8 (C4'), 128.5 (2C, C3'), 77.3 (C5), 72.9 (C6), 29.7 (C4), 13.3 (C7); HRMS (ESI) 207.0781, $[C_{13}H_{12}ONa]^+$ requires 207.0780. Without further purification, propargyl ketone **33** was dissolved in CH_2Cl_2 (25 mL), and potassium carbonate (0.41 g, 3.0 mmol) was added. After stirring at rt for 20 min, the solution was filtered and concentrated under vacuum, yielding **35** as a red oil (0.18 g, 36%): IR (film) 1967, 1943, 1650, 1601 cm^{-1};

^{1}H NMR δ 7.50 (1H, m), 7.41 (5H, m), 6.34 (1H, t, J = 6.6 Hz), 5.21 (2H, d, J = 6.6 Hz), 2.12 (3H, d, J = 1.9 Hz); ^{13}C NMR δ 215.8, 193.0, 139.3, 137.2, 135.7, 133.2, 129.7, 128.4, 92.5, 78.5, 13.9; HRMS (ESI) 185.0968, $[C_{13}H_{13}ONa]^+$ requires 185.0961. Note: the yield of AVK **35** in the crude reaction mixture was determined by ^{1}H NMR, using 1,3,5-trimethoxybenzene as an internal standard, and was used without further purification.

(*E*)-1-Phenylhexa-1,4,5-trien-3-one (36)

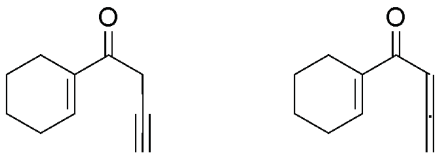


36

Dess-Martin periodinane (3.2 g, 7.5 mmol) was added to a vigourously stirring, room temperature solution of propargyl alcohol **24c** (1.0 g, 5.8 mmol) and sodium bicarbonate (4.9 g, 58 mmol) in CH_2Cl_2 (60 mL). After 45 min, saturated aqueous solutions of sodium bicarbonate (60 mL) and sodium thiosulfate (60 mL) were added, as well as diethyl ether (*ca.* 30 mL), and the mixture was stirred until both layers were clear. The mixture was extracted thoroughly with CH_2Cl_2, and the combined organic layers were washed with brine, dried over $MgSO_4$, and concentrated under vacuum. Flash chromatography of the residue (10% diethyl ether in pentane) provided **36** (0.27 g, 27%) as a yellow oil: IR (film) 1958, 1931, 1664, 1606 cm^{-1}; ^{1}H NMR δ: 7.57 (1H, d, J = 16 Hz), 7.39 (2H, m), 7.26 (3H, m), 7.21 (1H, d, J = 16 Hz), 6.03 (1H, t, J = 6.5 Hz), 5.34 (2H, d, J = 6.5 Hz); ^{13}C NMR δ: 216.5, 188.5, 142.7, 134.6, 130.4, 128.9, 128.4, 121.8,

97.5, 79.8; HRMS (ESI) 193.0632, $[C_{12}H_{10}ONa]^+$ requires 193.0624. NMR data matches lit.[45]

(*E*)-1-Cyclohexenylbut-3-yn-1-one (34) and *(E)*-1-cyclohexenylbuta-2,3-dien-1-one (37)



34 **37**

According to the procedure for **33**: Dess-Martin periodinane (2.4 g, 5.6 mmol), propargyl alcohol **24k** (0.65 g, 4.3 mmol) and sodium bicarbonate (3.6 g, 43 mmol) yielded **34** as a pale yellow oil; IR 1677, 1641 cm^{-1}; ^1H NMR δ: 6.97 (1H, m), 3.56 (2H, d, J = 2.8 Hz), 2.27 (4H, m), 2.23 (1H, t, J = 2.8 Hz), 1.64 (4H, m); ^{13}C NMR δ: 293.6, 142.0, 138.0, 72.6, 29.0, 26.2, 23.2, 21.8, 21.4; HRMS (ESI) 171.0786, $[C_{10}H_{12}ONa]^+$ requires 171.0780. According to the procedure for **35**: crude **34** and potassium carbonate (0.65 g, 4.7 mmol) yielded **37** as a red oil (0.36 g, 56%); IR 1963, 1936, 1641 cm^{-1}; ^1H NMR δ: 6.91 (1H, m), 6.25 (1H, t, J = 6.5 Hz), 5.16 (2H, d, J = 6.5 Hz), 2.27 (4H, m), 1.64 (4H, m); ^{13}C NMR δ: 215.5, 191.2, 140.8, 139.4, 91.7, 78.6, 26.1, 23.6, 21.9, 21.6; HRMS (ESI) 171.0782, $[C_{10}H_{12}ONa]^+$ requires 171.0780. Note: the yield of allenyl vinyl ketone **37** in the crude reaction mixture was determined by ^1H NMR, using 1,3,5-trimethoxybenzene as an internal standard, and was used without further purification.

CHAPTER 3. THE INTERRUPTED NAZAROV CYCLIZATION OF ALLENYL VINYL KETONES WITH HETEROATOM NUCLEOPHILES

3.1 Introduction

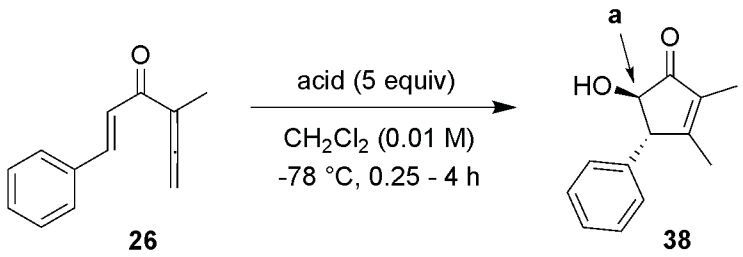
Although it had been documented that AVKs could undergo Nazarov cyclization in the presence of silica gel (Section 1.6), the reactivity of AVKs in the presence of protic or Lewis acids had remained unexplored. Hence, the behavior of AVKs in the presence of Lewis and protic acids well known to promote Nazarov cyclizations will be discussed initially. We chose AVK **26** as a test substrate, as it was hypothesized that the phenyl ring would decrease its susceptibility to side reactions, such as Michael additions or polymerization products. Furthermore, **26** should also yield simpler NMR spectra, resulting in more facile interpretation of NMR spectra of crude reaction products.

3.2 Initial Screening Conditions for Interrupted Nazarov Cyclizations

AVK **26** was exposed to a variety of Lewis and protic acids, as outlined in Table 2. The only cyclized product isolated in each case was interrupted Nazarov product **38**, as a single regioisomer in which interception of the intermediate oxyallyl cation solely occurred at position *a*. In all cases, the double bond from the end of the allene unit had migrated into the ring. No product with an exocyclic double bond was isolated. Furthermore, no cyclopent-2-enone product resulting from the elimination of a proton was detected. Trifluoroacetic acid was clearly the best acid for the formation of **38** (entry 1). It is interesting to note that when the Lewis acids $BF_3{\cdot}Et_2O$, $Cu(OTf)_2$, and $TiCl_4$ were utilized, only intractable material resulted. This may have been the result of a strong associative interaction between the counterion and the metal center, resulting in a lack of

suitable nucleophilic species present to trap the intermediate oxyallyl cation, leading to alternative pathways resulting in the decomposition of **26**.

Table 2 Screening for suitable promoters for the Nazarov reaction of AVK **26**.

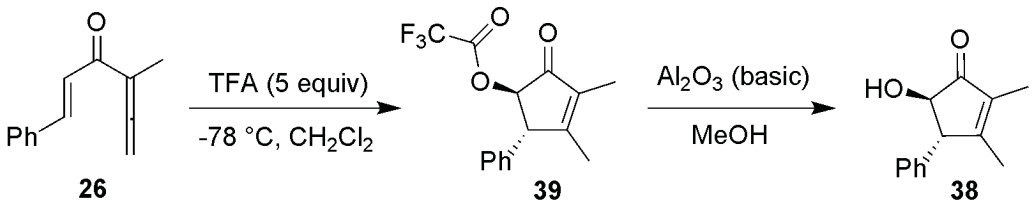


26 **38**

Entry	acid[a]	yield of **38** (%)[b]
1	TFA[c]	96
2	Amberlyst-15	30
3	*p*-TSA	71
4	HCl	0[d]
5	$BF_3{\cdot}Et_2O$	0[e]
6	$Cu(OTf)_2$	0[e]
7	$Sc(OTf)_3$	54
8	$Yb(OTf)_3$	70[f]
9	$TiCl_4$	0[e]

[a]All reactions were slowly warmed from –78 °C until completion by TLC, [b]isolated yields, [c]initial product was the TFA adduct, [d]isolated Michael addition products, [e]resulted in intractable material, [f]resulted in a 1:1 mixture of *cis* and *trans* isomers.

The origin of the alcohol oxygen was from the initially formed trifluoroacetyl or sulfonyl esters. This was obvious from the NMR spectra of the crude cyclization product from the reaction of AVK **26** with TFA. The major signals were attributable to the ester **39**, and its solvolysis must have occurred readily during chromatography on basic alumina (Scheme 28).



Scheme 28 Origin of alcohol oxygen is from TFA-trapped intermediate **39**.

With the exception of $Yb(OTf)_3$ (entry 8), which produced **38** along with its *cis* diastereomer as a 1:1 mixture, all other acids produced compound **38** as a single *trans* diastereomer. The *trans* stereochemistry of **38** was confirmed by X-ray crystallography (Figure 4). The relative stereochemistry was established prior to hydrolysis of the TFA-ester **39**, because the relative stereochemistry of **39** was also *trans*, as was confirmed by comparison of its ^{1}H NMR coupling constants with those of compound **38**. This was likely a result of steric interactions of the incoming nucleophile with the substituent at C4.

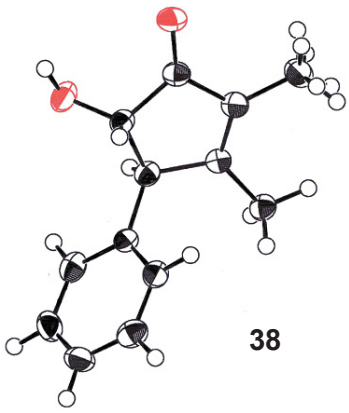
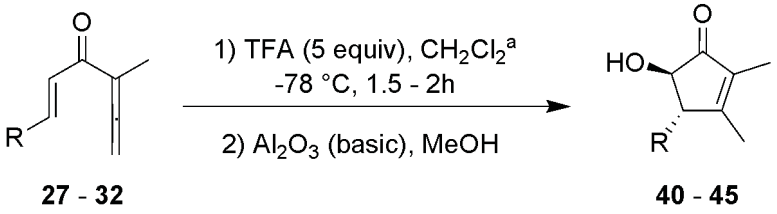


Figure 4 X-ray crystal structure (ORTEP) of compound **38**.

3.3 Scope of Trifluoroacetic Acid-Mediated Interrupted Nazarov Cyclizations

The substrate scope of the TFA-mediated Nazarov reaction was initially evaluated with the remainder of the Type 1 AVKs **27 – 32**, as shown below in Table 3.

Table 3 Scope of the TFA-initiated Nazarov reaction of AVKs.



27 - 32 **40 - 45**

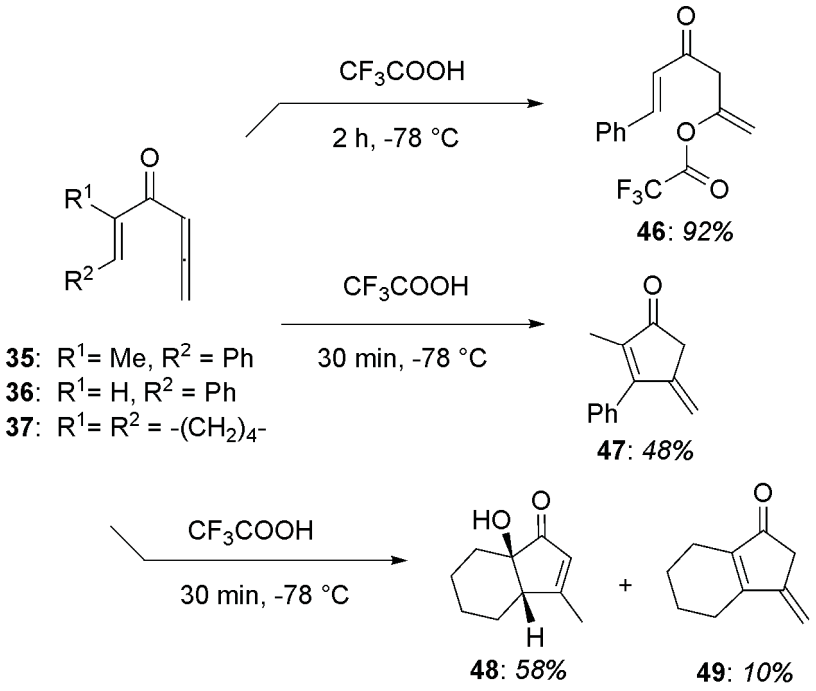
Yield (%)[b]		
40: *89*	**41a** = *trans* **41b** = *cis* (*88, dr 3:1*)	**42**: *90*
43: *>99*	**44**: *64*	**45**: *58*

[a]0.01 M, [b]isolated yields.

The reaction appeared to be general when the enone moiety of the starting ketone was substituted at the ß-position by hydrogen, alkyl, aromatic, or activated aromatic groups. It was unclear why yields were lower when deactivated aromatic and

heteroaromatic derivatives were utilized. It is probable that this was due to the increased likelihood of oligomerization through decomposition pathways, such as those initiated by Michael addition reactions for example, as a result of the increased reaction times. All cyclized products (except **41**) showed complete *trans* selectivity. This relative stereochemistry was confirmed by the magnitude of the ^{1}H NMR coupling constants with those of compound **38**. The ratio of the diastereomers of **41** was determined by integration of the corresponding signals in the ^{1}H NMR spectrum. That only **28** gave a significant amount of *cis* alcohol **41b** further implies that the stereochemistry of the trapping reaction is a sole result of steric interactions of the incoming nucleophile with the substituent at C4.

The reaction was then evaluated with the Type 2 AVKs **35** and **37**, and the Type 3 AVK **36** (Scheme 29). Type 2 and Type 3 AVKs clearly exhibited divergent reactivity



Scheme 29 Reactions of AVKs **35** – **37** in the presence of trifluoroacetic acid.

from Type 1 AVKs. For example, although Type 3 AVK **36** reacted cleanly in the presence of TFA, the product **46** was the result of conjugate addition to the allene. Type 2 AVK **35** also reacted readily in the presence of TFA; however the Nazarov elimination product **47** was the sole product isolated, in 48% yield. Type 2 AVK **37** gave mainly **48**, which represented an intercepted Nazarov product where the oxygen nucleophile had attacked position *a*, with parallel regio- and stereoselectivity to AVKs of Type 1. The relative stereochemistry of **48** was confirmed by X-ray crystallographic analysis of its 3,5-dinitrobenzoate **50** (Figure 5).

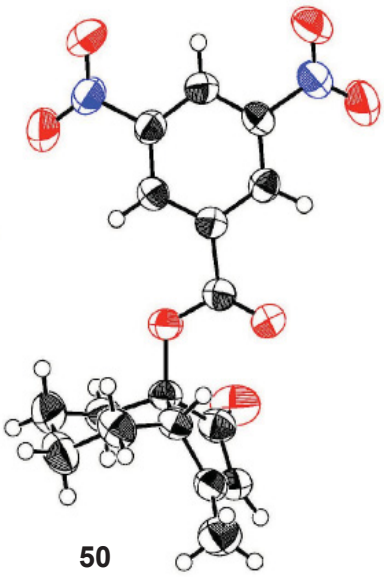
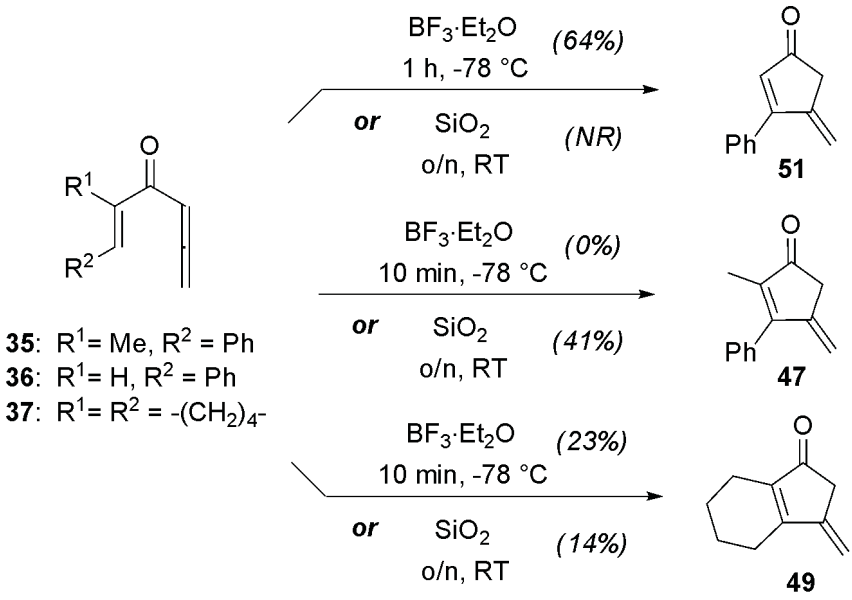


Figure 5 X-ray crystal structure (ORTEP) of compound **50**.

3.4 Reactivity of AVKs of Type 2 and Type 3 in the Absence of Nucleophilic Species

The susceptibility of Type 2 AVKs **35** and **37**, and Type 3 AVK **36**, to undergo a traditional Nazarov cyclization, resulting in elimination of a proton from the oxyallyl cationic intermediate, was briefly probed. It was necessary to choose acid

promoters that do not generate nucleophilic species, which might compete with proton elimination to trap the oxyallyl cation or pre-emptively add to the allene's central carbon prior to Nazarov cyclization. Thus, silica gel and $BF_3{\cdot}Et_2O$ were chosen for the task (Scheme 30).



Scheme 30 Reactions of AVKs **35** – **37** in the presence of $BF_3{\cdot}Et_2O$ and SiO_2.

In the presence of silica gel, AVKs **35** and **37** produced some of the corresponding Nazarov elimination products **47** (41%) and **49** (14%). This observation paralleled the reactivity observed by Hashmi for AVKs with this substitution pattern.[16] Conversely, AVK **36** remained unreacted in the presence of silica gel. This result paralleled the reactivity observed with AVK **26**, which also does not bear an alkyl substituent on the alkene unit. Treatment of **35** and **37** with $BF_3{\cdot}Et_2O$ at -78 °C for 10 minutes led to complex mixtures, although 23% of the Nazarov product **49** was isolated following the reaction of the latter. On the other hand, **36** was much more tolerant of the acid, and after one hour the Nazarov product

51 was obtained in 64% yield. There had been no evidence of a cyclized product following reaction of AVK **26** with $BF_3 \cdot Et_2O$; only intractable material resulted (*cf.* Table 2).

3.5 Mechanistic Rationale for the Reactivity Differences of AVKs of Type 1, Type 2, and Type 3

The differences in reactivity of AVKs of Type 1, Type 2, and Type 3 can be rationalized as a subtle interplay between steric and electronic factors. An alkyl substituent on the allene, such as in AVKs of Type 1, is clearly beneficial by inhibiting alternative allene reactions. It is proposed that an alkyl group on the allene attenuates the reactivity at the central carbon of the allene, by electron donation and/or by steric hindrance, allowing the Nazarov pathway to dominate. Furthermore, it is hypothesized that an alkyl group on the alkene or the allene accelerates the Nazarov reaction. In addition, calculations[†] revealed that the alkyl group on the alkene exerts a significant influence on the conformation, and thus the reactivity, of the AVK (Figure 6). An *s-trans-s-trans* arrangement must resemble the transition state geometry for the Nazarov cyclization. The *s-trans-s-trans* conformation is more than 12 $kJ \cdot mol^{-1}$ higher in energy than an *s-cis-s-trans* conformation for AVK's **26** and **36**. In contrast, the *s-trans-s-trans* conformation is the lowest-energy conformation for AVK **35**.

[†]Calculations were performed by Gavin Heverly-Coulson, using the Q-Chem 3.1[46] and AIMAll (Version 10.03.25)[47] software packages.

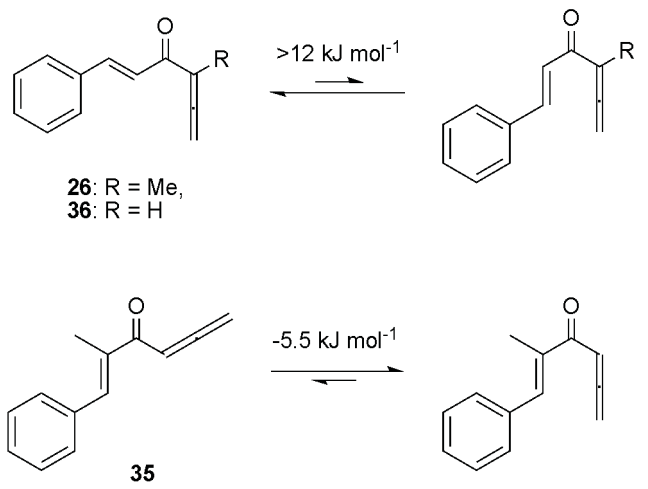


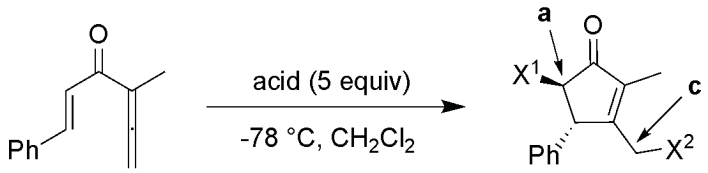
Figure 6 Conformations of AVKs, as calculated by QTAIM[48] methods (RI-MP2/cc-pvdz).[49]

Thus, the role of the alkyl group in AVKs of Type 1 (**26**) appears to be to allow Nazarov reactions to predominate through the inhibition of alternative allene reactions, likely through both steric and electronic means. The role of the alkyl group in AVKs of Type 3 (**35**) appears to be to allow Nazarov reactions to predominate not by the inhibition of alternative allene reactions, but through conformational acceleration of the Nazarov reaction. Although AVKs of Type 2, which bear no α-alkyl substituents, are clearly capable of cyclization as evidenced by the formation of **51**, attempts to elicit an interrupted Nazarov process would be likely to be pre-empted by a more rapid acid-mediated reaction of the allene. The production of cyclopent-2-enone products resulting from elimination of a proton, as sole or major by-products in addition to interrupted Nazarov products, from Type 3 AVKs **35** and **37** is likely a result of the retarded rate of the interrupted Nazarov process due to the steric hindrance imparted by the alkyl group at position *a* of the intermediate oxyallyl cation.

3.6 Screening of Other Lewis Acids for the Interrupted Nazarov Cyclization

Treatment of AVK **26** with $TiCl_4$ had led to the rapid destruction of the substrate (Table 2). However, White and West have observed the trapping of a Nazarov intermediate by chloride when a cyclization had been promoted by $TiCl_4$ (Scheme 11).[13] In the same study, the West group had also observed trapping by fluoride, bromide, and iodide ion when TiF_4, $TiBr_4$, or TiI_4 had been used, respectively. Thus, we decided to evaluate the Nazarov reactions of an AVK with other titanium-based Lewis acids as well as with other Lewis acids bearing halogen counterions. The hope was that interrupted Nazarov reactions of the AVK might produce halogenated cyclopent-2-enones (Table 4).

Table 4 Screening of other halogen-bearing Lewis acids for the interrupted Nazarov cyclization of AVK **26**.



26 **52 - 57**

Entry	Acid	Compound	X^1	X^2	Yield (%)[a]
1	$InCl_3$	**52**	H	Cl	35
2	$InBr_3$	**53**	H	Br	29
3	InI_3	**54**	H	I	32
4	$AlCl_3$	--	---	---	0[b]
5	$FeCl_3$	--	---	---	0[b]
6	$AuCl_3$	**55**	Cl	H	32
7	$TiBr_4$	**56**	Br	H	80
8	TiI_4	**57**	H	H	90
9	$TiCl_3$	--	---	---	0[c]

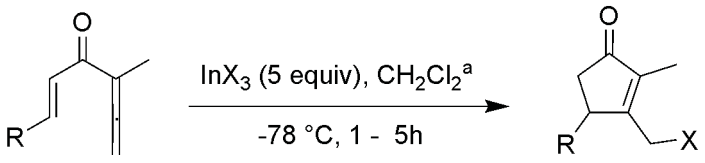
[a]Isolated yields, [b]intractable material, [c]isolated Michael addition products.

In the presence of TiI_4, AVK **26** provided cyclopent-2-enone **57** as the sole product (entry 9). This represented not only a Nazarov cyclization but also a reduction. It seemed likely that **57** was derived from an iodinated cyclopentenone by de-iodination, a process for which there is precedence in work by West.[13] Halogenated cyclopent-2-enones in which the oxyallyl cation had been intercepted at position *a* exclusively were produced in 80% yield using $TiBr_4$ (entry 7) and 32% using $AuCl_3$ (entry 6). The *trans* stereochemistry of **56** and **57** was confirmed by the magnitude of the ^{1}H NMR coupling constants to those of compound **38**. Conversely, indium-based Lewis acids (entries 1 - 3) yielded products trapped at position *c*, only. This could be a consequence of the large effective size of indium, in addition to the long In-O bond, which might block attack of the nucleophile at position *a* of the oxyallyl cation intermediate.

3.7 Scope of Indium-Mediated Interrupted Nazarov Cyclizations

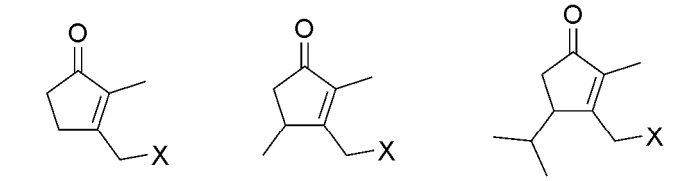
The substrate scope of the indium-initiated interrupted Nazarov reaction was evaluated with AVKs **27 - 32** as shown below in Table 5. In all cases, products trapped at position *c* were obtained exclusively. No products of trapping at position *a* were ever detected, although yields of the interrupted Nazarov products were consistently low. It is interesting to note that AVK **30** (R = *p*-OMePh) gave none of the anticipated interrupted Nazarov product when $InCl_3$ was used as a promoter. The dimer **67** was isolated instead. This must have been due to one molecule of **30** undergoing a Nazarov cyclization, followed by trapping of the oxyallyl cation by another molecule of **30** in a [3+2] fashion (Scheme 31). What is curious about this result is that the cycloaddition involved position *a* of the oxyallyl cation, whereas all other indium-mediated reactions involved position *c*.

Table 5 Scope of indium-mediated Nazarov reaction of AVKs.



27 - 31 **58 - 66**

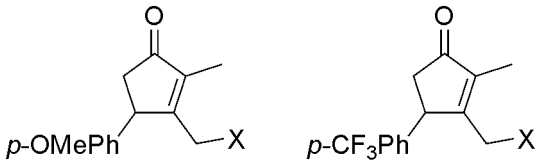
Yield (%)[b]



58: X = Cl (*31*)
59: X = I (*34*)

60: X = Cl (*20*)
61: X = I (*9*)

62: X = Cl (*21*)
63: X = I (*9*)



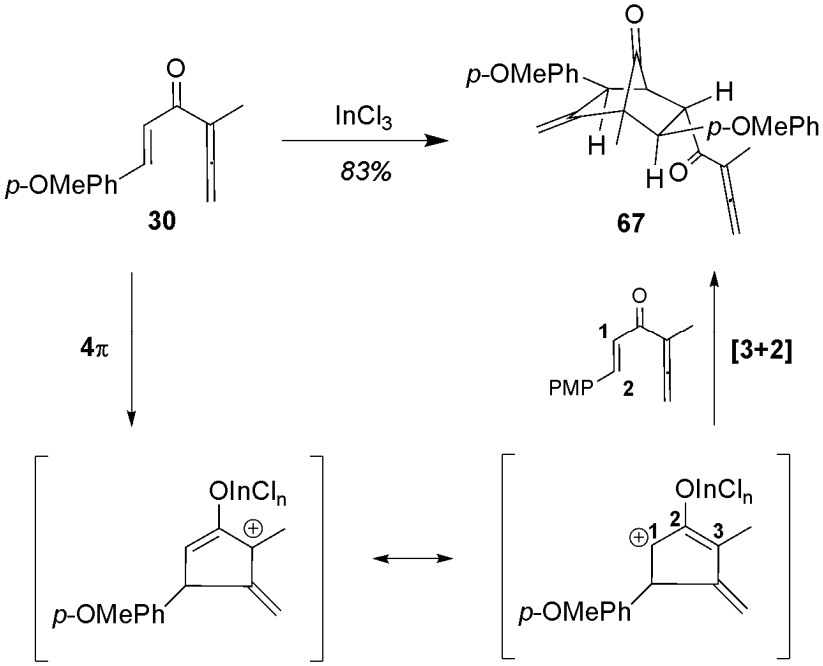
64: X = I (*26*)

65: X = Cl (*23*)
66: X = I (*13*)

[a]0.01 M, [b]isolated yields.

Although interception of an oxyallyl cation by electron-rich alkenes had been reported by West,[11] this type of dimerization had not been reported before. It is particularly interesting to note the high yield of this reaction (83% at 0.01 M). The structure of **67** was confirmed by X-ray crystallography (Figure 7). The complete retention of stereochemistry of the alkene double bond suggested that the mechanism of the [3 + 2] reaction might be a concerted process. This result offered significant promise

for the use of AVKs in tandem reactions involving first a Nazarov cyclization followed by a [4+3] or [3+2] cycloaddition, with dienes and/or activated alkene derivatives.



Scheme 31 Proposed mechanism for formation of **67** from **30** in presence of $InCl_3$.

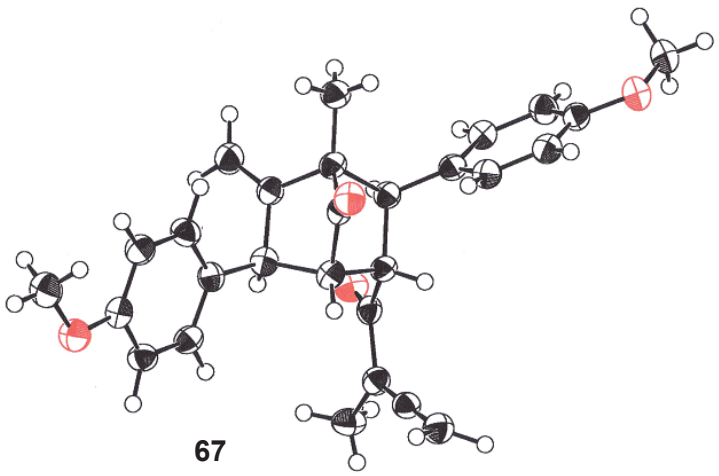
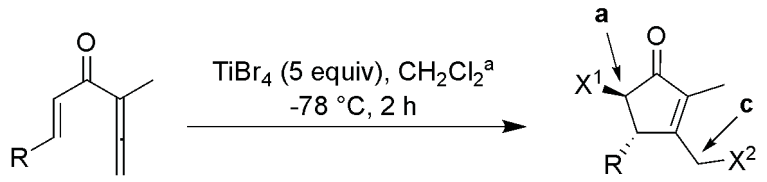


Figure 7 X-ray crystal structure (ORTEP) of compound **67**.

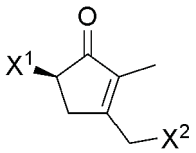
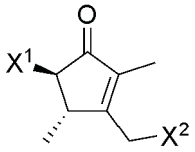
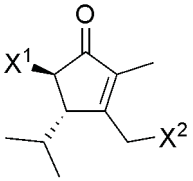
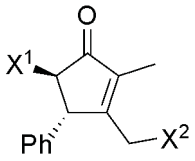
3.8 Scope of Titanium-Mediated Interrupted Nazarov Cyclizations

The substrate scope of the $TiBr_4$-mediated interrupted Nazarov reaction was evaluated with AVKs **26 – 32**, as shown below in Table 6.

Table 6 Scope of $TiBr_4$-mediated Nazarov reaction of AVKs.



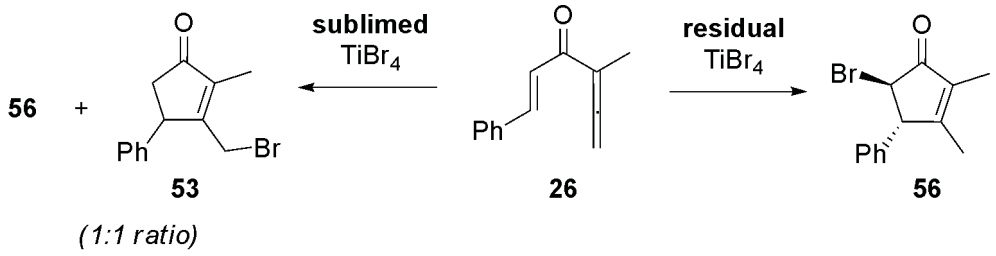
26 - 29 **53, 56, 68 - 73**

Yield (%)[b]	
	
68: X^1 = Br, X^2 = H *(16)* **69**: X^1 = H, X^2 = Br *(16)*	**70**: X^1 = Br, X^2 = H *(19)* **71**: X^1 = H, X^2 = Br *(19)*
	
72: X^1 = Br, X^2 = H *(18)* **73**: X^1 = H, X^2 = Br *(18)*	**56**: X^1 = Br, X^2 = H *(23)* **53**: X^1 = H, X^2 = Br *(23)*

[a]0.01 M, [b]isolated yields.

Unfortunately, the excellent yields and regioselectivity noted in Table 4 for AVK **26** proved irreproducible, on average producing a 1:1 ratio of products trapped at position *a* and position *c* of the oxyallyl cationic intermediate (the *trans* stereochemistry of

compounds substituted at C4 was determined through analysis of ^{1}H NMR coupling constants). Reactions with TiI_4 yielded similar results, in addition to a number of products resulting from the abstraction of iodide, amounts of which also proved irreproducible. These discrepancies showed a high dependence on the exact batch of the commercially acquired reagent. In an attempt to rectify this issue, five grams of newly acquired $TiBr_4$ was carefully sublimed. Upon re-subjection of AVK **26** to both the newly sublimed $TiBr_4$, as well as the impure residue, we were surprised to find that while the purified $TiBr_4$ reproduced the poor regioselectivity noted in Table 6, the residual $TiBr_4$ resulted in the sole formation of the trapped product **56** (Scheme 32). The reason for this disturbing result is unknown at this time.

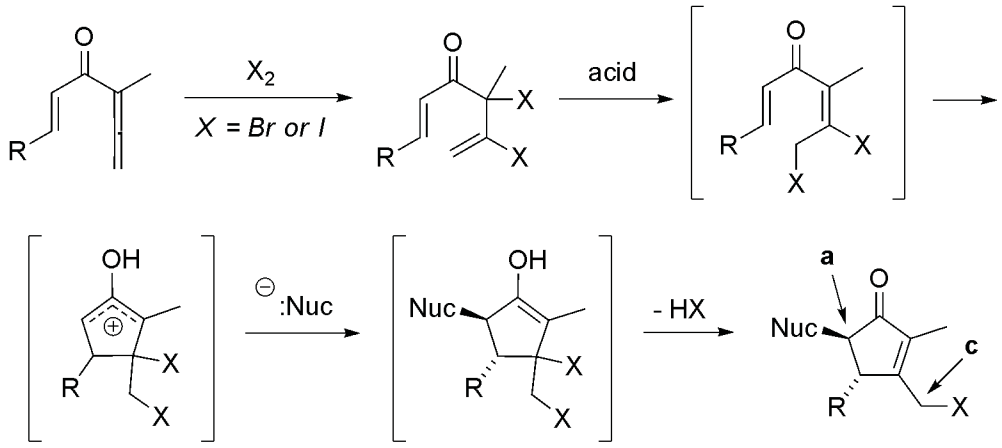


Scheme 32 Comparison of sublimed and residual $TiBr_4$.

3.9 Synthesis of Doubly Functionalized Cyclopent-2-enones via the Initial Addition of Bromine or Iodine

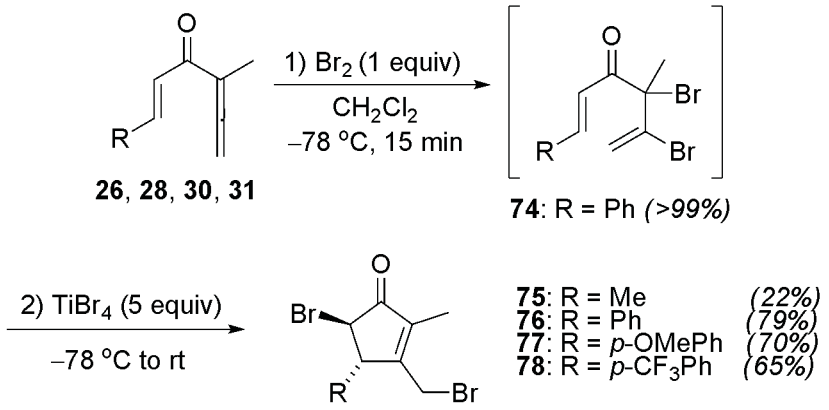
We were inspired to attempt the synthesis of doubly functionalized cyclopent-2-enones, in which a nucleophile had formally added to both positions *a* and *c* of the intermediate oxyallyl cation. Theoretically, this could be achieved by initial halogenation of the conjugated end of the allene unit of the AVK with bromine or iodine. Then, protic or Lewis acid-induced isomerization should provide a halogenated divinyl ketone, which

could then undergo a Nazarov cyclization. Interception of the intermediate oxyallyl cation with a suitable nucleophile followed by elimination of HBr (or HI) would then provide a cyclopent-2-enone functionalized at positions *a* and *c* (Scheme 33).



Scheme 33 Proposed mechanism for the synthesis of multifunctionalized cyclopent-2-enones from AVKs.

AVK **26** (R = Ph) was first treated with Br_2 and then $TiBr_4$ at -78 °C, which led to the doubly brominated cyclopentenone **76** in good overall yield (Scheme 34). This reaction was normally conducted in one-pot, although the intermediate dibromide **74** could be isolated, in quantitative yield, if necessary. The reaction was equally effective for AVKs **30** and **31** (R = *p*-PhOMe and *p*-$PhCF_3$), less effective for AVK **28** (R = Me), and did not result in any cyclized product for AVKs **27** and **29** (R = H and *i*-Pr). This was mainly a result of competing bromination of the alkene double-bond for AVKs **27** - **39**, as careful inspection of the ^{1}H and ^{13}C NMR spectra of the crude products revealed.

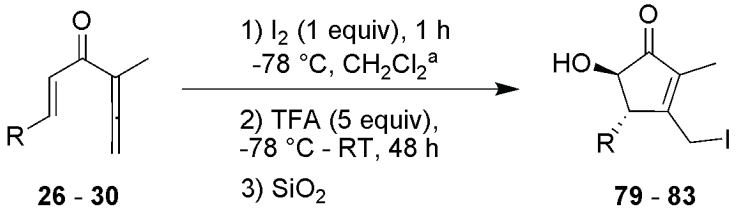


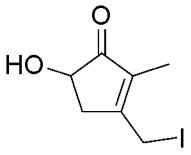
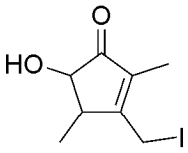
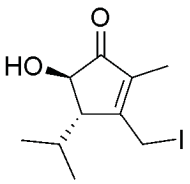
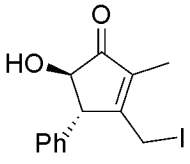
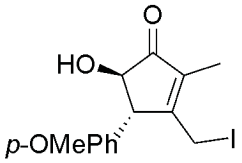
Scheme 34 Scope of $Br_2/TiBr_4$-mediated Nazarov reaction of AVKs.

$TiCl_4$ and $TiBr_4$ were less effective at producing doubly functionalized cyclopent-2-enones. $TiCl_4$ produced mixtures of diastereomers, whereas TiI_4 resulted in a significant amount of dehalogenated byproduct as a result of iodide abstraction. Finally, products substituted at position *c* by iodine as a result of prior addition of I_2 also failed to be produced in reasonable yield when titanium-based Lewis acids were used. In this case, complex mixtures of cyclopent-2-enone species were produced as a result of significant amounts of iodide abstraction.

Trifluoroacetic acid, however, proved to be a more effective promoter when iodine was added initially (Table 7), with the remainder of the material largely being the intermediate iodinated divinyl ketone, as determined by careful inspection of the ^1H NMR spectra of the crude reaction product. In this case, silica gel chromatography was utilized to hydrolyze the intermediate TFA-ester instead of basic alumina, in order to preserve the sensitive allyl-iodide functionality.

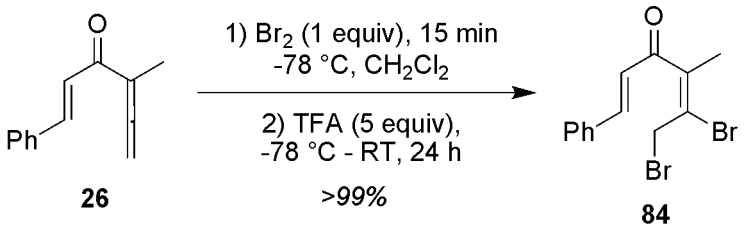
Table 7 Scope of I_2/TFA-mediated Nazarov reaction of AVKs.



Yield (%)[b]		
		
79 *(18)*	**80a** = *trans* **80b** = *cis* *(40, dr 3:1)*	**81** *(45)*
		
82 *(61)*	**83** *(32)*	

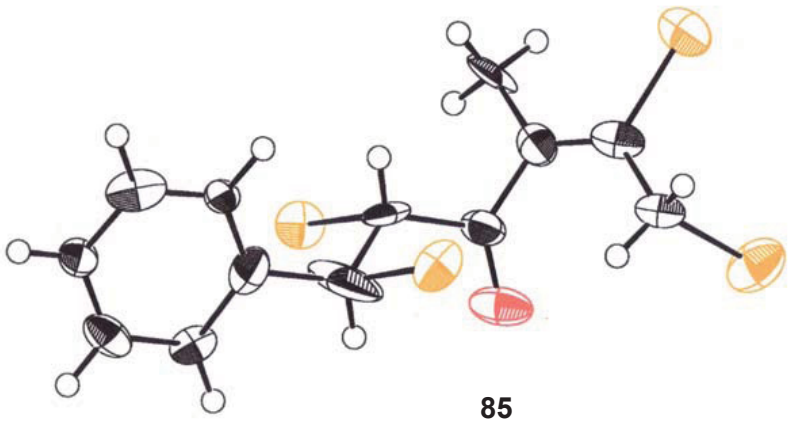
[a]0.01 M, [b]isolated yields.

Unfortunately, this reaction failed to produce brominated cyclopent-2-enone species when bromine was added prior to TFA. Only the halogenated divinyl ketone **84** was recovered after 24 hours (Scheme 35), even with stirring for prolonged reaction times. The (*E*)-stereochemistry of the brominated double bond was confirmed via the X-ray crystal structure of the tetrabrominated derivative **85** (Figure 8).



26 **84**

Scheme 35 Reaction of AVK **26** with Br_2/TFA.



85

Figure 8 X-ray structure (ORTEP) of compound **85**.

3.10 Summary

A variant of the Nazarov cyclization has been presented in which the intermediate oxyallyl cation derived from an allenyl vinyl ketone has been trapped by trifluoroacetate. Al_2O_3-promoted solvolysis then provided a 5-hydroxycyclopent-2-enone. When there was a substituent at C4 in the product, then the predominant or exclusive stereochemistry of the product was *trans*. This intermolecular trapping of a Nazarov cyclization by an oxygen nucleophile offers an opportunity for the production of a variety of cyclopent-2-enones bearing oxygen functionality at the 5-position in good to excellent yield.

We have also ascertained that AVKs can undergo Nazarov cyclizations in which the intermediate carbocation can be trapped by a halogen at either position *a* or position *c* of the oxyallyl cationic intermediate. However, the efficiency of this process is highly dependent on the Lewis acid and the substituent on the alkene, with yields ranging from very good to essentially zero. The AVK bearing a simple phenyl substituent (**26**) was generally the best substrate. We observed the first instance of a formal [3+2] cycloaddition involving a carbocation intermediate being captured by unreacted substrate to generate the dimeric product. This offers significant promise for AVKs as future candidates for tandem Nazarov/[3+2] (or [4+3]) reactions with other alkene or diene partners.

Finally, the presence of an alkyl group α to the ketone on either the alkene or the allene of an AVK has a very significant impact on the efficacy of Nazarov reactions and interrupted Nazarov reactions. An alkyl substituent on the allene is beneficial by inhibiting alternative allene reactions and likely by accelerating the Nazarov reaction. An alkyl substituent on the alkene accelerates the Nazarov reaction, but interception of the intermediate oxyallyl cation by a nucleophile is retarded by steric hindrance.

3.11 Experimental Section

3.11.1 General Considerations

All reactions were conducted using oven-dried glassware under an N_2 atmosphere. Reagents were used as received from a commercial supplier without further purification. Titanium bromide (*ca*. 1 M in dichloromethane) and titanium iodide (*ca*. 0.5 M in dichloromethane) solutions were prepared within an mBraun glovebox apparatus.

Dichloromethane was used freshly distilled from calcium hydride. Ethyl acetate and hexanes were distilled prior to use for column chromatography.

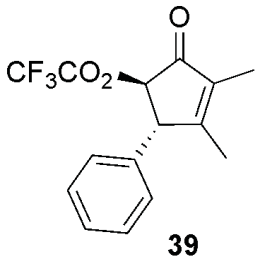
Thin layer chromatography was conducted using pre-coated silica plates with plastic backing (EMD chemicals, silica gel 60 F_{254}), using UV light (254 nm) as a visualizing agent and potassium permanganate in aqueous KOH and heat, or *o*-vanillin in ethanol/H_2SO_4 and heat, as developing agents. Column chromatography was carried out on silica gel purchased from Silicycle (40 – 63 μm particle size, 230 – 240 mesh).

Melting points are uncorrected, and were acquired using a Fisher-Johns apparatus. ^{1}H NMR spectra were recorded at 500 MHz on a Bruker Avance spectrometer with $CDCl_3$ as solvent (7.24 ppm) and TMS as internal reference (0.00 ppm). ^{13}C NMR spectra were recorded at 125 MHz on a Bruker Avance spectrometer with $CDCl_3$ as solvent. ^{19}F NMR spectra were recorded at 235 MHz on a Bruker Avance spectrometer. Infrared spectra were recorded from thin films on a Bruker VECTOR 22 FT-IR instrument using CsI plates. High resolution mass spectra were acquired by Mr. Xiao Feng, on a Bruker microTOF Focus orthogonal ESI-TOF mass spectrometer.

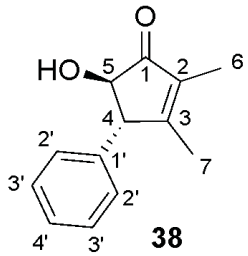
The carbon and hydrogen atoms of select compounds were assigned following detailed analysis of their one dimensional (^{1}H, ^{13}C, and DEPT-135) and two dimensional (COSY, HSQC, and HMBC) NMR spectral data. The ^{1}H and ^{13}C NMR spectra of all compounds may be found in Appendix A, the Cartesian coordinates (including additional computed data) for compounds **26**, **35**, and **36** may be found in Appendix B, and the X-ray crystallographic data for compounds **38**, **50**, **67**, and **85** may be found in Appendix C.

3.11.2 Preparation and Characterization Data

***(trans*)-3,4-Dimethyl-2-oxo-5-phenylcyclopent-3-enyl trifluoroacetate (39) and *(trans*)-5-hydroxy-2,3-dimethyl-4-phenylcyclopent-2-enone (38)**



39

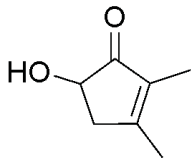


38

Trifluoroacetic acid (0.20 mL, 2.8 mmol) was added dropwise to a solution of AVK **26** (0.10 g, 0.56 mmol) in CH_2Cl_2 (50 mL) at -78 °C, and the solution was stirred for 2 h. The solution was washed with saturated aqueous $NaHCO_3$, the aqueous layer was re-extracted with CH_2Cl_2 (×2), and the combined CH_2Cl_2 layers were dried with Na_2SO_4 and concentrated to provide crude **39** as a yellow oil: IR (film) 1793, 1719, 1603 (w), 1151 cm^{-1}; ^1H NMR δ: 7.35 (3H, m), 7.13 (2H, m), 5.31 (1H, d, J = 3.2 Hz), 3.89 (1H, br d, J = 3.2 Hz), 1.86 (6H, s); ^{13}C NMR δ: 199.1, 169.0, 156.8 (q, J = 43 Hz), 138.0, 136.1, 129.1 (2C), 127.9, 127.7 (2C), 114.4 (q, J = 285 Hz), 81.9, 54.5, 15.5, 8.4; ^{19}F NMR δ: -75.5 (s); HRMS (ESI): 321.0685, $[C_{15}H_{13}F_3O_3Na]^+$ requires 321.0709. The ester **39** was loaded onto a column of Al_2O_3 (activated, basic) with 20% ethyl acetate in hexanes, and the column was flushed with this solvent. Then, elution of the column with MeOH provided **38** (0.11 g, 96%) as colourless needles: mp 78–79 °C; IR (film) 3406, 1702, 1638, 1602 (w) cm^{-1}; ^1H NMR δ: 7.33 (2H, m, H3'), 7.27 (1H, m, H4'), 7.13 (2H, m, H2'), 4.11 (1H, br t, $J \approx 3$ Hz, H5), 3.78 (1H, br s, *OH*), 3.67 (1H, br d, $J \approx 3$ Hz, H4), 1.81 (3H, s, H7), 1.79 (3H, s, H6); ^{13}C NMR δ: 207.9 (C1), 169.4 (C3), 139.8 (C1'),

134.9 (C2), 128.8 (2C, C3'), 127.9 (2C, C2'), 127.2 (C4'), 80.2 (C5), 57.7 (C4), 15.4 (C7), 8.2 (C6); HRMS (ESI): 225.0873, $[C_{13}H_{14}O_2Na]^+$ requires 225.0886.

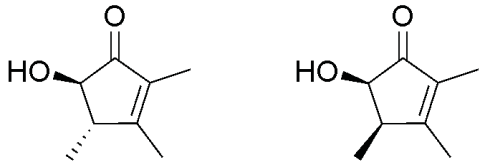
5-Hydroxy-2,3-dimethylcyclopent-2-enone (40)



40

According to the procedure for **38**: AVK **27** (0.060 g, 0.56 mmol) was reacted with trifluoroacetic acid (0.20 mL, 2.8 mmol) for 3 h to yield **40** (0.062 g, 89%) as a colourless solid: mp 48–49 °C (lit.[50] *rac*-**40** <30 °C; lit.[51] (-)-**40** 40-45 °C); IR (film) 3397, 1701, 1638 cm^{-1}; ^1H NMR δ: 4.22 (1H, dd, *J* = 6.7, 3.0 Hz), 3.15 (1H, br s), 2.88 (1H, dd, *J* = 18.0, 6.7 Hz), 2.45 (1H, br dd, *J* = 18.0, 3.0 Hz), 2.06 (3H, s), 1.72 (3H, s); ^{13}C NMR δ: 209.2, 168.1, 133.7, 71.3, 40.3, 17.2, 7.8; HRMS (ESI): 149.0585, $[C_7H_{10}O_2Na]^+$ requires 149.0573.

(*trans*)-5-Hydroxy-2,3,4-trimethylcyclopent-2-enone (41a) and (*cis*)-5-hydroxy-2,3,4-trimethylcyclopent-2-enone (41b)

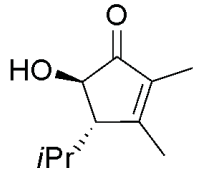


41a **41b**

According to the procedure for **38**: AVK **28** (0.070 g, 0.57 mmol) was reacted with trifluoroacetic acid (0.20 mL, 2.8 mmol) for 2 h to yield 0.070 g (88%) of a 3:1 mixture of **41a**/**41b** (as determined by integration of the ^1H NMR spectrum), colourless

oil: IR (film) 3398, 1700, 1638 cm^{-1}; HRMS (ESI): 163.0726, $[C_8H_{12}O_2Na]^+$ requires 163.0730; the following NMR data were taken from the spectra of the mixture: for **41a**: ^1H NMR δ: 3.76 (1H, d, *J* = 3.1 Hz), 2.91 (1H, m), 2.60 (1H, br s), 2.00 (s, 3H), 1.72 (s, 3H), 1.31 (d, 3H, *J* = 7.2 Hz); ^{13}C NMR δ: 207.6, 170.8, 133.3, 79.3, 45.4, 16.1, 14.5, 8.1; for **41b**: ^1H NMR δ: 4.21 (1H, d, *J* = 6.5 Hz), 2.90 (2H, m), 2.04 (3H, s), 1.72 (3H, s), 1.08 (3H, d, *J* = 7.2 Hz); ^{13}C NMR δ: 208.8, 173.0, 132.3, 74.0, 42.8, 15.5, 14.4, 7.8.

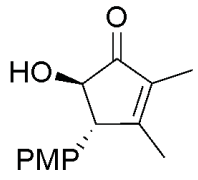
(*trans)*-5-Hydroxy-4-isopropyl-2,3-dimethylcyclopent-2-enone (42)



42

According to the procedure for **38**: AVK **29** (0.090 g, 0.60 mmol) was reacted with trifluoroacetic acid (0.22 mL, 3.0 mmol) for 2 h to yield **42** (0.091 g, 90%) as a colourless solid: mp 73–74 °C; IR (film) 3396, 1691, 1638 cm^{-1}; ^1H NMR δ: 3.91 (1H, d, *J* = 2.8 Hz), 3.68 (1H, br s), 2.59 (1H, br d, *J* = 2.8 Hz), 2.56 (1H, m), 2.00 (3H, s), 1.72 (3H, s), 1.16 (3H, d, *J* = 6.9 Hz), 0.72 (3H, d, *J* = 6.9 Hz); ^{13}C NMR δ: 208.6, 170.8, 134.6, 71.1, 56.1, 26.6, 21.1, 16.2, 14.9, 7.9; HRMS (ESI): 191.1033, $[C_{10}H_{16}O_2Na]^+$ requires 191.1043.

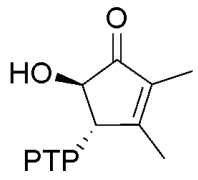
(*trans*)-5-Hydroxy-4-(4-methoxyphenyl)-2,3-dimethylcyclopent-2-enone (43)



43

According to the procedure for **38**: AVK **30** (0.12 g, 0.56 mmol) was reacted with trifluoroacetic acid (0.20 mL, 2.8 mmol) for 1.5 h to yield **43** (0.13 g, 99%) as a colourless solid: mp 101–102 °C; IR (film) 3406, 1701, 1638, 1612 cm^{-1}; ^1H NMR δ: 7.05 (2H, d, J = 8.8 Hz), 6.88 (2H, d, J = 8.8 Hz), 4.07 (1H, d, J = 3.0 Hz), 3.81 (3H, s), 3.62 (1H, br d, J = 3.0 Hz), 3.27 (1H, br s), 1.81 (3H, s), 1.80 (3H, s); ^{13}C NMR δ: 207.9, 169.6, 158.8, 134.7, 131.8, 128.9 (2C), 114.3 (2C), 80.4, 56.8, 55.2, 15.3, 8.2; HRMS (ESI): 255.0989, $[C_{14}H_{16}O_3Na]^+$ requires 255.0992.

(*trans*)-5-Hydroxy-2,3-dimethyl-4-(4-(trifluoromethyl)phenyl)cyclopent-2-enone (44)

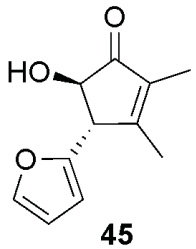


44

According to the procedure for **38**: AVK **31** (0.14 g, 0.56 mmol) was reacted with trifluoroacetic acid (0.20 mL, 2.8 mmol) for 4 h to yield **44** (0.096 g, 64%) as a colourless solid: mp 146–147 °C; IR (film) 3242, 1699, 1642, 1617, 1421 cm^{-1}; ^1H NMR δ: 7.63 (2H, d, J = 8.2 Hz), 7.28 (2H, d, J = 8.2 Hz), 4.09 (1H, br t, J = 2.7 Hz), 3.75 (1H, br s), 3.36 (1H, d, J = 2.7 Hz), 1.84 (3H, s), 1.83 (3H, s); ^{13}C NMR δ: 207.1, 168.0, 144.0, 135.6, 129.8 (q, J = 33 Hz), 128.4 (2C), 126.0 (2C, q, J = 3.5 Hz), 124.0 (q, J = 273 Hz),

80.3, 57.3, 15.4, 8.3; ^{19}F NMR δ: -63.5 (s); HRMS (ESI): 293.0754, $[C_{14}H_{13}F_3O_2Na]^+$ requires 293.0760.

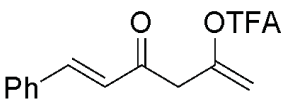
(*trans*)-4-(Furan-2-yl)-5-hydroxy-2,3-dimethylcyclopent-2-enone (45)



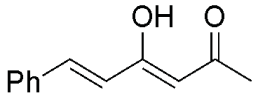
45

According to the procedure for **38**: AVK **32** (0.10 g, 0.57 mmol) was reacted with trifluoroacetic acid (0.20 mL, 2.8 mmol) for 3 h to yield **45** (0.061 g, 56%) as an off-white solid: mp 52–53 °C; IR (film) 3406, 1704, 1642 cm^{-1}; ^{1}H NMR δ: 7.37 (1H, d, *J* = 1.9 Hz), 6.36 (1H, dd, *J* = 3.2, 1.9 Hz), 6.29 (1H, d, *J* = 3.2 Hz), 4.35 (1H, t, *J* = 2.9 Hz), 3.81 (1H, br d, *J* = 2.9 Hz), 3.23 (1H, br s), 1.87 (3H, s), 1.79 (3H, s); ^{13}C NMR δ: 206.8, 166.6, 152.0, 142.4, 134.4, 110.4, 108.2, 76.7, 50.7, 15.2, 8.2; HRMS (ESI): 215.0677, $[C_{11}H_{12}O_3Na]^+$ requires 215.0679.

(*E*)-4-Oxo-6-phenylhexa-1,5-dien-2-yl 2,2,2-trifluoroacetate (46) and (3*Z*,5*E*)-4-hydroxy-6-phenylhexa-3,5-dien-2-one (46a)



46

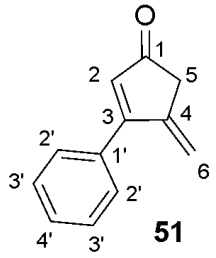


46a

Trifluoroacetic acid (0.16 mL, 2.1 mmol) was added to a solution of AVK **36** (0.070 g, 0.41 mmol) in CH_2Cl_2 (40 mL) at -78 °C, and stirred for 2 h. The mixture was poured into a separatory funnel containing a saturated solution of sodium bicarbonate, the

organic layer was removed, and additional CH_2Cl_2 (×2) was used to extract the aqueous layer. The organic layers were combined and concentrated under vacuum to yield **46** (0.11 g, 92%) as a yellow oil which was not subjected to further purification: ^{1}H NMR δ: 7.62 (1H, d, *J* = 16 Hz), 7.55 (2H, m), 7.41 (3H, m), 6.79 (1H, d, *J* = 16 Hz), 5.28 (1H, d, *J* = 2.9 Hz), 5.14 (1H, d, *J* = 2.9 Hz), 3.67 (2H, s); ^{13}C NMR δ: 193.4, 155.2 (q, *J* = 43 Hz), 148.6, 144.7, 134.0, 131.1, 129.1 (2C), 128.6 (2C), 124.6, 114.4 (q, *J* = 290 Hz), 107.2, 44.7; ^{19}F NMR δ: -75.9 (s). Within 24 h **46** hydrolyzed to **46a**: ^{1}H NMR δ: 7.62 (1H, d, *J* = 16 Hz), 7.52 (2H, m), 7.38 (3H, m), 6.48 (1H, d, *J* = 16 Hz), 5.69 (1H, s), 2.21 (3H, s); ^{13}C NMR δ: 199.4, 177.4, 141.0, 135.0, 130.4, 129.1 (2C), 128.2 (2C), 122.4, 101.5, 27.3. NMR data of **46a** matches lit.[52]

4-Methylene-3-phenylcyclopent-2-enone (51)

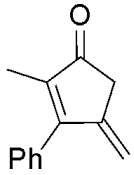


51

$BF_3{\cdot}OEt_2$ (0.070 mL, 0.60 mmol) was added to a -78 °C solution of AVK **36** (0.070 g, 0.41 mmol) in CH_2Cl_2 (40 mL). The solution was stirred for 1 h, and then poured into a separatory funnel containing a saturated solution of sodium bicarbonate. The organic layer was removed, and additional CH_2Cl_2 (×2) was used to extract the aqueous layer. The combined organic layers were concentrated under vacuum. Flash chromatography of the residue (10 to 20% EtOAc in hexanes) provided **51** (0.045 g, 64%) as a yellow oil: IR (film) 1721, 1695, 1610 (w) cm^{-1}; ^{1}H NMR δ: 7.47 (5H, m, H2',

H3', H4'), 6.37 (1H, m, H2), 5.51 (1H, m, H6a), 5.43 (1H, m, H6b), 3.22 (2H, m, H5); ^{13}C NMR δ: 204.5 (C1), 170.6 (C3), 143.6 (C1'), 133.4 (C4), 133.3 (C2), 130.1 (C4') , 128.9 (2C, C3'), 128.4 (2C, C2'), 113.8 (C6), 41.5 (C5); HRMS (ESI) 193.0628, $[C_{12}H_{10}ONa]^+$ requires 193.0624. ^{1}H NMR data matches lit.[53]

2-Methyl-4-methylene-3-phenylcyclopent-2-enone (47)



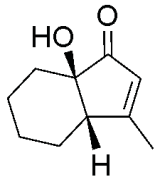
47

Procedure 1: trifluoroacetic acid (0.20 mL, 2.6 mmol) was added to a solution of AVK **35** (0.010 g, 0.54 mmol) in CH_2Cl_2 (55 mL) at -78 °C, and stirred for 30 min. The mixture was poured into a separatory funnel containing a saturated solution of sodium bicarbonate, the organic layer was removed, and additional CH_2Cl_2 (×2) was used to extract the aqueous layer. The organic layers were combined and concentrated under vacuum to yield **47** (0.048 g, 48%) as a yellow oil following flash chromatography (20% EtOAc in hexanes): IR (film) 1703, 1612 cm^{-1}; ^{1}H NMR δ: 7.47 (3H, m), 7.34 (2H, m), 5.29 (1H, s), 5.22 (1H, s), 3.19 (2H, s), 1.88 (3H, s); ^{13}C NMR δ: 205.2, 164.5, 143.7, 141.1, 133.2, 128.8, 128.5 (4C), 110.9, 39.7, 9.4; HRMS (ESI) 185.0962, $[C_{13}H_{13}O]^+$ requires 185.0961.

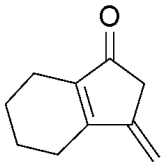
Procedure 2: SiO_2 (0.12 g, 2.7 mmol) was added to a solution of AVK **35** (0.10 g, 0.54 mmol) in CH_2Cl_2 (5 mL) at rt, and this was stirred overnight. The mixture was filtered and concentrated under vacuum, and flash chromatography (10 to 20% EtOAc in

hexanes) of the residue yielded **47** (0.041 g, 41%) as a yellow oil.

***(3aR*,7aS*)*-7a-Hydroxy-3-methyl-3a,4,5,6,7,7a-hexahydro-1*H*-inden-1-one (48) and 3-methylene-2,3,4,5,6,7-hexahydro-1*H*-inden-1-one (49)**



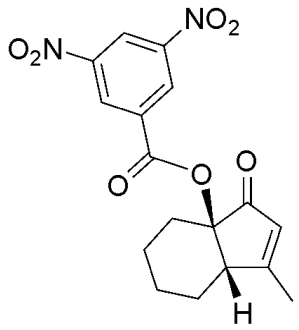
48



49

Trifluoroacetic acid (0.20 mL, 2.6 mmol) was added to a solution of AVK **35** (0.080 g, 0.54 mmol) in CH_2Cl_2 (55 mL) at -78 °C, and this was stirred for 30 min. The mixture was poured into a separatory funnel containing a saturated solution of sodium bicarbonate, the organic layer was removed, and additional CH_2Cl_2 (×2) was used to extract the aqueous layer. The organic layers were combined and concentrated under vacuum. The crude product was then subjected to column chromatography (Al_2O_3, basic, activated, using 20% EtOAc in hexanes then MeOH), which provided **48** (0.052 g, 58%) and **49** (0.009 g, 10%) as yellow oils. For **48**: IR (film) 3437, 1695, 1610 cm^{-1}; ^1H NMR δ: 5.94 (1H, m), 2.76 (1H, m), 2.64 (1H, br s), 2.10 (3H, t, J = 1.3 Hz), 1.89 (1H, m), 1.72 (1H, m), 1.61 (4H, m), 1.46 (1H, m), 1.27 (1H, m); ^{13}C NMR δ: 210.9, 179.1, 126.9, 78.1, 50.3, 32.3, 22.9, 20.7, 18.8, 17.7; HRMS (ESI) 189.0884, $[C_{10}H_{14}O_2Na]^+$ requires 189.0886. For **49**: IR 1704, 1641 cm^{-1}; ^1H NMR δ: 5.24 (1H, s), 5.11 (1H, s), 2.98 (2H, s), 2.45 (2H, m), 2.26 (2H, m), 1.76 (2H, m), 1.70 (2H, m); ^{13}C NMR δ: 204.9, 165.7, 43.9, 143.1, 107.1, 40.1, 23.1, 22.0, 21.8, 20.6; HRMS (ESI) 171.0785, $[C_{10}H_{12}ONa]^+$ requires 171.0780.

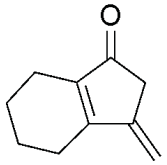
(3a*R,7a*S**)-3-Methyl-1-oxo-3a,4,5,6,7,7a-hexahydro-1*H*-inden-7a-yl-3,5-dinitrobenzoate (50)**



50

Triethylamine (1 mL, 7.2 mmol) and then 3,5-dinitrobenzoylchloride (0.48, 2.1 mmol) were added to solution of **48** (0.17 g, 1.0 mmol) and DMAP (0.13 g, 1.1 mmol) in CH_2Cl_2 (25 mL) at rt. The solution was stirred for 18 h, diluted with ethyl acetate, and washed successively with aqueous solutions of 1 M HCl, 10% NaOH, saturated $NaHCO_3$, and brine. The solution was dried over Na_2SO_4 and concentrated under vacuum. Flash chromatography of the residue (10 to 25% EtOAc in hexanes) provided **50** (0.24 g, 67%), as a peach-coloured solid: mp 176–179 °C; IR (film) 1720, 1619 cm^{-1}; ^1H NMR δ: 9.24 (1H, m), 9.12 (2H, m), 6.14 (1H, s), 3.39 (1H, m), 2.18 (3H, s), 2.14 (1H, m), 1.87 (2H, m), 1.70 (4H, m), 1.42 (1H, m); ^{13}C NMR δ: 203.3, 176.1, 161.4, 148.8, 133.8, 129.8 (2C), 128.3, 122.8, 85.6, 47.0, 30.0, 22.4, 20.5, 18.8, 17.7; HRMS (ESI) 383.0847, $[C_{17}H_{16}N_2O_7Na]^+$ requires 383.0850.

3-Methylene-2,3,4,5,6,7-hexahydro-1*H*-inden-1-one (49)

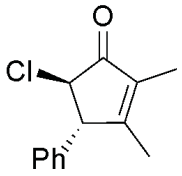


49

According to the procedure for **51**: $BF_3{\cdot}OEt_2$ (0.070 mL, 0.60 mmol) was reacted with AVK **37** (0.080 g, 0.54 mmol) to yield **49** (0.018 g, 23%) as a yellow oil.

According to *Procedure 2* for **47**: SiO_2 (0.12 g, 2.7 mmol) was reacted with AVK **37** (0.080 g, 0.54 mmol) to yield **49** (0.011 g, 14%) as a yellow oil.

(*trans*)-5-Chloro-2,3-dimethyl-4-phenylcyclopent-2-enone (55)

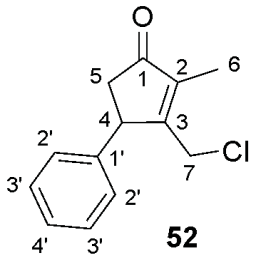


55

Gold trichloride (0.27 g, 0.70 mmol) was added at once to a solution of AVK **26** (0.025 g, 0.14 mmol) in CH_2Cl_2 (15 mL) at -78 °C, and the mixture was stirred for 15 min. The black mixture was washed with saturated aqueous $NaHCO_3$, the aqueous layer was extracted with CH_2Cl_2 (×2), and the combined CH_2Cl_2 layers were dried with Na_2SO_4 and concentrated under vacuum. The residue was purified by column chromatography on silica gel (10% EtOAc in hexanes) to provide **55** as a colourless oil (0.010 g, 32%): IR (film) 1717, 1645, 1603 (w) cm^{-1}; ^1H NMR δ: 7.35 (3H, m), 7.13 (2H, m), 4.10 (1H, d, J = 2.8 Hz), 3.91 (1H, br d, J = 2.8 Hz), 1.87 (6H, s); ^{13}C NMR δ: 201.1,

169.0, 138.8, 135.9, 129.2 (2C), 127.9, 127.6 (2C), 61.8, 60.1, 15.6, 8.6; HRMS (ESI): 243.0529, $[C_{13}H_{13}ClONa]^+$ requires 243.0547.

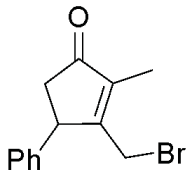
3-(Chloromethyl)-2-methyl-4-phenylcyclopent-2-enone (52)



52

A solution of AVK **26** (0.10 g, 0.56 mmol) in CH_2Cl_2 (50 mL) was cooled to –78 °C, and indium trichloride (0.60 g, 2.8 mmol) was added. The mixture was allowed to warm slowly until completion of the reaction, as evidenced by TLC (3.5 h). The reaction mixture was then poured into a separatory funnel containing saturated aqueous sodium bicarbonate, and shaken vigourously. Additional dichloromethane was added, the aqueous layer was extracted (×2), and the combined organic layers were dried with Na_2SO_4, concentrated, and the product was purified by column chromatography (10% EtOAc in hexanes) to provide **52** (0.040 g, 35%) as a colourless oil: IR (film) 1711, 1652, 1602 (w) cm^{-1}; ^1H NMR δ: 7.33 (2H, m, H3'), 7.28 (1H, m, H4'), 7.14 (2H, m, H2'), 4.34 (1H, d, J = 12 Hz, H7a), 4.24 (1H, m, H4), 3.81 (1H, d, J = 12 Hz, H7b), 2.98 (1H, dd, J = 19, 2.3 Hz, H5a), 2.47 (1H, dd, J = 19, 2.3 Hz, H5b), 1.88 (3H, s, H6); ^{13}C NMR δ: 208.7 (C1), 166.2 (C3), 140.7 (C1'), 139.2 (C2), 129.1 (2C, C3'), 127.5 (3C, C2', C4'), 44.9 (C4), 44.2 (C5), 38.0 (C7), 8.3 (C6); HRMS (ESI): 243.0547, $[C_{13}H_{13}ClONa]^+$ requires 243.0533.

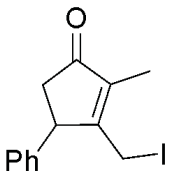
3-(Bromomethyl)-2-methyl-4-phenylcyclopent-2-enone (53)



53

According to the procedure for **52**: AVK **26** (0.10 g, 0.56 mmol) was reacted with indium tribromide (1.0 g, 2.8 mmol) for 2 h to yield **53** (0.040 g, 29%) as a colourless oil: IR (film) 1710, 1647, 1602 (w) cm^{-1}; ^{1}H NMR δ: 7.34 (2H, m) 7.28 (1H, m), 7.14 (2H, m), 4.28 (1H, m), 4.20 (1H, d, *J* = 10 Hz), 3.69 (1H, d, *J* = 10 Hz), 3.01 (1H, dd, *J* = 19, 7.3 Hz), 2.51 (1H, dd, *J* = 19, 2.4 Hz), 1.85 (3H, s); ^{13}C NMR δ: 208.7, 166.6, 140.7, 139.0, 129.1 (2C), 127.5 (3C), 45.1, 44.2, 24.7, 8.4; HRMS (ESI): 287.0034, $[C_{13}H_{13}BrONa]^{+}$ requires 287.0042.

3-(Iodomethyl)-2-methyl-4-phenylcyclopent-2-enone (54)

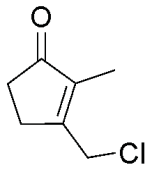


54

According to the procedure for **52**: AVK **26** (0.10 g, 0.56 mmol) was reacted with indium triiodide (1.4 g, 2.8 mmol) for 1.5 h to yield **54** (0.055 g, 32%) as a colourless oil: IR (film) 1707, 1641, 1602 (w) cm^{-1}; ^{1}H NMR δ: 7.38 (2H, m), 7.31 (1H, m), 7.14 (2H, m), 4.36 (1H, m), 4.13 (1H, d, *J* = 9.3 Hz), 3.66 (1H, d, *J* = 9.3 Hz), 3.03 (1H, dd, *J* = 19, 7.4 Hz), 2.56 (1H, dd, *J* = 19, 2.4 Hz), 1.74 (3H, s); ^{13}C NMR δ: 208.7, 168.5, 140.9,

137.5, 129.2 (2C), 127.5, 127.4 (2C), 45.4, 44.2, 8.5, -2.8; HRMS (ESI): 334.9881, $[C_{13}H_{13}IONa]^+$ requires 334.9903.

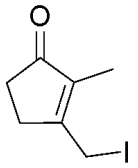
3-(Chloromethyl)-2-methylcyclopent-2-enone (58)



58

According to the procedure for **52**: AVK **27** (0.060 g, 0.56 mmol) was reacted with indium trichloride (0.60 g, 2.8 mmol) for 5 h to yield **58** (0.025 g, 31%) as a colourless oil: IR (film) 1704, 1654 cm^{-1}; ^1H NMR δ: 4.36 (2H, s), 2.69 (2H, m), 2.46 (2H, m), 1.77 (3H, s); ^{13}C NMR δ: 209.4, 164.3, 138.7, 40.2, 34.0, 27.6, 8.0; HRMS (ESI): 167.0231, $[C_7H_9ClONa]^+$ requires 167.0234.

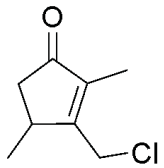
3-(Iodomethyl)-2-methylcyclopent-2-enone (59)



59

According to the procedure for **52**: AVK **27** (0.060 g, 0.56 mmol) was reacted with indium triiodide (1.4 g, 2.8 mmol) for 2 h to yield **59** (0.045 g, 34%) as a colourless oil: IR (film) 1694, 1639 cm^{-1}; ^1H NMR δ: 4.16 (2H, s), 2.76 (2H, m), 2.52 (2H, m), 1.66 (3H, s); ^{13}C NMR δ: 209.5, 166.5, 137.4, 34.1, 28.2, 8.1, -1.2; HRMS (ESI): 258.9570, $[C_7H_9IONa]^+$ requires 258.9590.

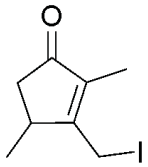
3-(Chloromethyl)-2,4-dimethylcyclopent-2-enone (60)



60

According to the procedure for **52**: AVK **28** (0.070 g, 0.57 mmol) was reacted with indium trichloride (0.60 g, 2.8 mmol) for 4 h to yield **60** (0.018 g, 20%) as a colourless oil: IR (film) 1708, 1650 cm^{-1}; ^{1}H NMR δ: 4.42 (1H, d, *J* = 12 Hz), 4.33 (1H, d, *J* = 12 Hz), 3.10 (1H, m), 2.71 (1H, dd, *J* = 19, 6.5 Hz), 2.05 (1H, dd, *J* = 19, 2.2 Hz), 1.77 (3H, s), 1.23 (1H, d, *J* = 7.2 Hz); ^{13}C NMR δ: 208.4, 168.1, 138.6, 42.8, 37.8, 33.8, 18.7, 8.2; HRMS (ESI): 181.0385, $[C_8H_{11}ClONa]^+$ requires 181.0391.

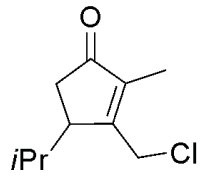
3-(Iodomethyl)-2,4-dimethylcyclopent-2-enone (61)



61

According to the procedure for **52**: AVK **28** (0.060 g, 0.57 mmol) was reacted with indium triiodide (1.4 g, 2.8 mmol) for 2 h to yield **61** (0.012 g, 8%) as a colourless oil: IR (film) 1703, 1638 cm^{-1}; ^{1}H NMR δ: 4.18 (1H, d, *J* = 9.4 Hz), 4.14 (1H, d, *J* = 9.4 Hz), 3.18 (1H, m), 2.73 (1H, dd, *J* = 19, 6.8 Hz), 2.11 (1H, dd, *J* = 19, 2.4 Hz), 1.65 (3H, s), 1.21 (3H, d, *J* = 7.2 Hz); ^{13}C NMR δ: 208.4, 170.2, 137.3, 42.9, 34.3, 19.0, 8.3, -3.8; HRMS (ESI): 272.9723, $[C_8H_{11}IONa]^+$ requires 272.9747.

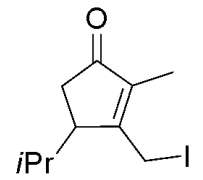
3-(Chloromethyl)-4-isopropyl-2-methylcyclopent-2-enone (62)



62

According to the procedure for **52**: AVK **29** (0.090 g, 0.6 mmol) was reacted with indium trichloride (0.66 g, 3.0 mmol) for 4.5 h to yield **62** (0.023 g, 21%) as a colourless oil: IR (film) 1707, 1650 cm^{-1}; ^{1}H NMR δ: 4.43 (1H, d, J = 12 Hz), 4.22 (1H, d, J = 12 Hz), 3.11 (1H, m), 2.35 (1H, dd, J = 19, 6.8 Hz), 2.23 (2H, m), 1.79 (3H, s), 1.33 (3H, d, J = 6.9 Hz), 0.62 (3H, d, J = 6.9 Hz); ^{13}C NMR δ: 208.8, 166.4, 139.9, 44.7, 38.1, 34.8, 27.3, 21.7, 14.9, 8.1; HRMS (ESI): 209.0693, $[C_{10}H_{15}ClONa]^{+}$ requires 209.0704.

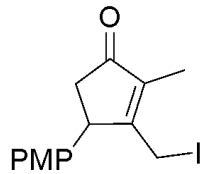
3-(Iodomethyl)-4-isopropyl-2-methylcyclopent-2-enone (63)



63

According to the procedure for **52**: AVK **29** (0.090 g, 0.60 mmol) was reacted with indium triiodide (1.5 g, 3.0 mmol) for 2.5 h to yield **63** (0.015 g, 9%) as a colourless oil: IR (film) 1702, 1638 cm^{-1}; ^{1}H NMR δ: 4.21 (1H, d, J = 9.5 Hz), 4.08 (1H, d, J = 9.5 Hz), 3.23 (1H, m), 2.38 (1H, dd, J = 19, 6.8 Hz), 2.26 (1H, dd, J = 19, 2.4 Hz), 2.16 (1H, m), 1.65 (3H, s), 1.03 (3H, d, J = 6.8 Hz), 0.62 (3H, d, J = 6.8 Hz); ^{13}C NMR δ: 208.8, 168.5, 138.6, 45.1, 34.8, 27.5, 21.6, 14.7, 8.2, -3.3; HRMS (ESI): 301.0044, $[C_{10}H_{15}IONa]^{+}$ requires 301.0060.

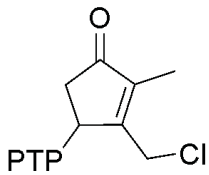
3-(Iodomethyl)-4-(4-methoxyphenyl)-2-methylcyclopent-2-enone (64)



64

According to the procedure for **52**: AVK **30** (0.12 g, 0.56 mmol) was reacted with with indium triiodide (1.4 g, 2.8 mmol) for 1 h to yield **64** (0.049 g, 26%) as a colourless oil: IR (film) 1702, 1639, 1610 cm^{-1}; ^{1}H NMR δ: 7.05 (2H, d, *J* = 8.7 Hz), 6.86 (2H, d, *J* = 8.7 Hz), 4.31 (1H, m), 4.12 (1H, d, *J* = 9.3 Hz), 3.80 (3H, s), 3.67 (1H, d, *J* = 9.3 Hz), 3.01 (1H, dd, *J* = 19, 7.2 Hz), 2.52 (1H, dd, *J* = 19, 2.5 Hz), 1.73 (3H, s); ^{13}C NMR δ: 208.9, 168.7, 158.9, 137.2, 132.8, 128.4 (2C), 114.5 (2C), 55.3, 44.6, 44.3, 8.5, - 2.7; HRMS (ESI): 365.0009, $[C_{14}H_{15}IO_2Na]^+$ requires 365.0014.

3-(Chloromethyl)-2-methyl-4-(4-(trifluoromethyl)phenyl)cyclopent-2-enone (65)

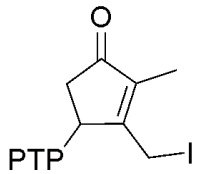


65

According to the procedure for **52**: AVK **31** (0.14 g, 0.56 mmol) was reacted with indium trichloride (0.60 g, 2.8 mmol) for 5 h to yield **65** (0.037 g, 23%) as a colourless oil: IR (film) 1712, 1654, 1620, 1327 cm^{-1}; ^{1}H NMR δ: 7.60 (2H, d, *J* = 8.2 Hz), 7.28 (2H, d, *J* = 8.2 Hz), 4.37 (1H, d, *J* = 12 Hz), 4.33 (1H, m), 3.79 (1H, d, *J* = 12 Hz), 3.01 (1H, dd, *J* = 19, 7.3 Hz), 2.44 (1H, dd, *J* = 19, 2.4 Hz), 1.89 (3H, s); ^{13}C NMR δ: 207.8, 165.2, 144.9, 139.9, 129.9 (q, *J* = 33 Hz), 128.0 (2C), 126.1 (2C, q, *J* = 3.5 Hz), 124.0 (q,

J = 270 Hz), 44.7, 43.9, 37.9, 8.4; ^{19}F NMR δ: -63.5 (s); HRMS (ESI): 289.0603, $[C_{14}H_{12}F_3ClOH]^+$ requires 289.0602.

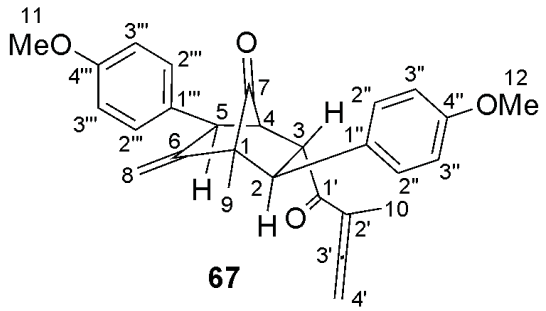
3-(Iodomethyl)-2-methyl-4-(4-(trifluoromethyl)phenyl)cyclopent-2-enone (66)



66

According to the procedure for **52**: AVK **31** (0.14 g, 0.56 mmol) was reacted with with indium triiodide (1.4 g, 2.8 mmol) for 3 h to yield **66** (0.028 g, 13%) as a colourless oil: IR (film) 1705, 1642, 1619, 1326 cm^{-1}; ^{1}H NMR δ: 7.61 (2H, d, *J* = 8.2 Hz), 7.28 (2H, d, *J* = 8.2 Hz), 4.45 (1H, m), 4.44 (1H, d, *J* = 9.5 Hz), 3.61 (1H, d, *J* = 9.5 Hz), 3.06 (1H, dd, *J* = 19, 7.4 Hz), 2.53 (1H, dd, *J* = 19, 2.5 Hz), 1.76 (3H, s); ^{13}C NMR δ: 207.8, 167.4, 145.1, 138.2, 130.0 (q, *J* = 33 Hz), 127.9 (2C), 126.2 (2C, q, *J* = 3.5 Hz), 126.1 (q, *J* = 270 Hz), 45.2, 43.9, 8.6, -3.3; ^{19}F NMR δ: -63.5 (s); HRMS (ESI): 402.9754, $[C_{14}H_{12}F_3IONa]^+$ requires 402.9777.

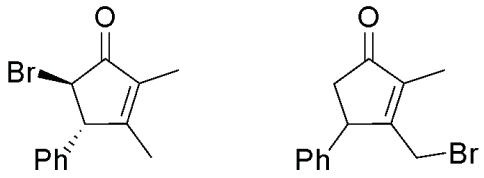
2,5-Bis(4-methoxyphenyl)-1-methyl-3-(2-methylbuta-2,3-dienoyl)-6-methylene bicyclo[2.2.1]heptan-7-one (67)



67

According to the procedure for **52**: AVK **30** (0.12 g, 0.56 mmol) was reacted with indium trichloride (0.60 g, 2.8 mmol) for 3 h to yield **67** (0.049 g, 82%) as a white solid: mp 115 – 117 °C; IR (film) 1958, 1932, 1769, 1673, 1610 cm^{-1}; ^{1}H NMR δ: 6.99 (2H, d, *J* = 8.8 Hz, H2’’’), 6.98 (2H, d, *J* = 8.8 Hz, H2’’), 6.82 (2H, d, *J* = 8.8 Hz, H3’’’), 6.81 (2H, d, *J* = 8.8 Hz, H3’’), 5.16 (1H, dq, *J* = 15, 3.0 Hz, H4’a), 5.13 (1H, d, *J* = 2.3 Hz, H8a), 5.10 (1H, dq, *J* = 15, 3.0 Hz, H4’b), 4.81 (1H, d, *J* = 2.3 Hz, H8b), 3.84 (1H, dd, *J* = 6.7, 4.4 Hz, H3), 3.78 (6H, s, H11, H12), 3.72 (1H, t, *J* = 2.3 Hz, H5), 3.70 (1H, d, *J* = 6.7 Hz, H2), 2.72 (1H, d, *J* = 4.4 Hz, H4), 1.83 (3H, t, *J* = 3.0 Hz, H10), 0.83 (3H, s, H9); ^{13}C NMR δ: 216.2 (C3’), 213.3 (C7), 198.1 (C1’), 158.7 (C4’’’), 158.4 (C4’’), 152.1 (C6), 134.8 (C1’’’), 133.6 (C1’’), 129.3 (2C, C2’’), 128.5 (2C, C2’’’), 114.1 (2C, C3’’), 114.0 (2C, C3’’’), 107.9 (C8), 103.8 (C2’), 79.8 (C4’), 55.2 (2C, C11, C12), 54.4 (C1), 53.6 (C4), 51.1 (C3), 47.0 (C2), 45.0 (C5), 13.5 (C10), 9.9 (C9); HRMS (ESI): 451.1854, $[C_{28}H_{28}O_4Na]^+$ requires 451.1880.

(*trans*)-5-Bromo-2,3-dimethyl-4-phenylcyclopent-2-enone (56) and 3-(bromomethyl)-2-methyl-4-phenylcyclopent-2-enone (53)



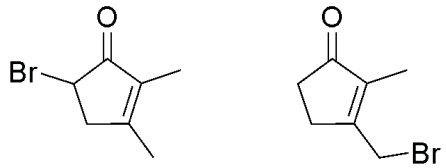
56 **53**

Procedure 1: A solution of AVK **26** (0.10 g, 0.56 mmol) in CH_2Cl_2 (50 mL) was cooled to –78 °C, and a solution of titanium bromide (1.0 M in CH_2Cl_2) (2.8 mL, 2.8 mmol) was added dropwise. The mixture was allowed to warm to warm slowly for 2 h, then poured into a separatory funnel containing saturated aqueous sodium bicarbonate, and shaken vigourously. Additional dichloromethane was added, the aqueous layer was extracted (×2), and the combined organic layers dried with Na_2SO_4. The product was purified by column chromatograpy (10% EtOAc in hexanes) to yield **56** (0.12 g, 80%) as a colourless oil: IR (film) 1714, 1644, 1602 (w) cm^{-1}; ^1H NMR δ: 7.38 (3H, m), 7.12 (2H, m), 4.19 (1H, d, J = 2.5 Hz), 4.03 (1H, br d, J = 2.5 Hz), 1.88 (3H, s), 1.87 (3H, s); ^{13}C NMR δ: 201.5, 169.1, 138.9, 135.8, 129.2 (2C), 128.0, 127.4 (2C), 60.7, 50.4, 15.7, 8.7; HRMS (ESI): 287.0042, $[C_{13}H_{13}BrONa]^+$ requires 287.0047.

Procedure 2: A solution of AVK **26** (0.10 g, 0.56 mmol) in CH_2Cl_2 (50 mL) was cooled to –78 °C, and a solution of freshly sublimed titanium bromide (1.0 M in CH_2Cl_2) (2.8 mL, 2.8 mmol) was added dropwise. The mixture was allowed to warm to warm slowly for 2 h, then poured into a separatory funnel containing saturated aqueous sodium bicarbonate, and shaken vigourously. Additional dichloromethane was added, the aqueous layer was extracted (×2), and the combined organic layers dried with Na_2SO_4.

The product was purified by column chromatograpy (10% EtOAc in hexanes) to yield **56** (0.030 g, 23%) and **53** (0.030 g, 23%) as colourless oils.

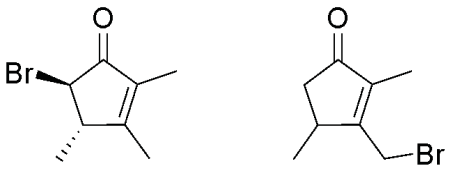
5-Bromo-2,3-dimethylcyclopent-2-enone (68) and 3-(bromomethyl)-2-methylcyclopent-2-enone (69)



68 **69**

According to *Procedure 2* for **56** and **53**: AVK **27** (0.045 g, 0.42 mmol) was reacted with titanium tetrabromide (2.1 mL, 2.1 mmol) to yield **68** (0.013 g, 16%) and **69** (0.013 g, 16%) as colourless oils. For **68**: IR (film) 1711, 1648 cm^{-1}; ^{1}H NMR δ: 4.35 (1H, dd, J = 2.2, 6.8 Hz), 3.19 (1H, dd, J = 6.8, 19 Hz), 2.82 (1H, br dd, J = 2.2, 19 Hz), 1.77 (3H, s), 1.56 (3H, s); ^{13}C NMR δ: 202.3, 167.3, 134.5, 43.1, 41.4, 17.2, 8.3; HRMS (ESI): 188.9907, $[C_7H_{10}BrO]^+$ requires 188.9910. For **69**: IR (film) 1698, 1640 cm^{-1}; ^{1}H NMR δ: 4.22 (2H, s), 2.70 (2H, m), 2.49 (2H, m), 1.76 (3H, s); ^{13}C NMR δ: 209.5, 164.5, 138.8, 34.1, 28.0, 26.7, 8.1; HRMS (ESI): 210.9734, $[C_7H_9BrONa]^+$ requires 210.9729.

(*trans*)-5-Bromo-2,3,4-trimethylcyclopent-2-enone (70) and 3-(bromomethyl) -2,4-dimethylcyclopent-2-enone (71)

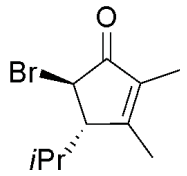


70 **71**

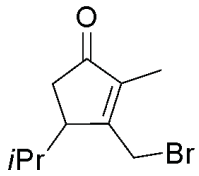
According to *Procedure 2* for **56** and **53**: AVK **28** (0.060 g, 0.56 mmol) was

reacted with titanium tetrabromide (2.8 mL, 2.8 mmol) to yield **70** (0.022 g, 19%) and **71** (0.022 g, 19%) as colourless oils. For **70**: IR (film) 1711, 1645 cm^{-1}; ^{1}H NMR δ: 3.92 (1H, d, *J* = 2.5 Hz), 2.97 (1H, m), 1.76 (3H, s), 2.02 (3H, s), 1.28 (3H, d, *J* = 7.3 Hz); ^{13}C NMR δ: 201.0, 171.2, 134.2, 50.0, 49.1, 16.9, 14.9, 8.5; HRMS (ESI): 224.9873, $[C_8H_{11}BrONa]^+$ requires 224.9885. For **71**: IR (film) 1702, 1641 cm^{-1}; ^{1}H NMR δ: 4.26 (1H, d, *J* = 11 Hz), 4.18 (1H, d, *J* = 11 Hz), 3.13 (1H, m), 2.72 (1H, dd, *J* = 6.7, 19 Hz), 2.07 (1H, dd, *J* = 2.2, 19 Hz), 1.65 (3H, s), 1.22 (3H, d, *J* = 7.2 Hz); ^{13}C NMR δ: 208.4, 168.3, 138.7, 42.9, 34.1, 24.2, 18.7, 18.0, 8.2; HRMS (ESI): 224.9870, $[C_8H_{11}BrONa]^+$ requires 224.9885.

(*trans*)-5-Bromo-4-isopropyl-2,3-dimethylcyclopent-2-enone (72) and 3-(bromomethyl)-4-isopropyl-2-methylcyclopent-2-enone (73)



72

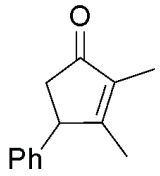


73

According to *Procedure 2* for **56** and **53**: AVK **29** (0.090 g, 0.60 mmol) was reacted with titanium tetrabromide (3.0 mL, 3.0 mmol) to yield **72** (0.025, 18%) and **73** (0.025 g, 18%) as colourless oils. For **72**: IR (film) 1711, 1645 cm^{-1}; ^{1}H NMR δ: 4.10 (1H, d, *J* = 1.9 Hz), 3.01 (1H, m), 2.25 (1H, m), 2.00 (3H, s), 1.77 (3H, s), 1.17 (3H, d, *J* = 6.9 Hz), 0.64 (3H, d, *J* = 6.9 Hz); ^{13}C NMR δ: 201.9, 170.2, 135.4, 59.9, 42.5, 27.9, 21.2, 15.4 (2C), 8.4; HRMS (ESI): 253.0183, $[C_{10}H_{15}BrONa]^+$ requires 253.0198. For **73**: IR (film) 1702, 1638 cm^{-1}; ^{1}H NMR δ: 4.28 (1H, d, *J* = 10 Hz), 4.11 (1H, d, *J* = 10 Hz), 3.15 (1H, m), 2.37 (1H, dd, *J* = 6.7, 19 Hz), 2.23 (1H, dd, *J* = 2.3, 19 Hz), 2.21 (1H, m),

1.77 (3H, s), 1.03 (3H, d, J = 6.9 Hz), 0.62 (3H, d, J = 6.9 Hz); ^{13}C NMR δ: 208.8, 166.7, 139.9, 44.9, 34.8, 27.3, 24.5, 21.7, 14.9, 8.1; HRMS (ESI): 253.0202, $[C_{10}H_{15}BrONa]^+$ requires 253.0198.

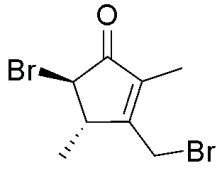
2,3-Dimethyl-4-phenylcyclopent-2-enone (57)



57

According to *Procedure 1* for **56**: AVK **26** (0.10 g, 0.56 mmol) was reacted with titanium tetraiodide (0.5 M in CH_2Cl_2) (5.6 mL, 2.8 mmol) for 48 h to yield **57** (0.090 g, 90%) as a colourless oil: IR (film) 1702, 1649, 1602 (w) cm^{-1}; ^{1}H NMR δ: 7.35 (2H, m), 7.28 (1H, m), 7.12 (2H, m), 3.81 (1H, m), 2.89 (1H, dd, J = 19, 7.1 Hz), 2.36 (1H, dd, J = 19, 2.3 Hz), 1.82 (3H, s), 1.79 (3H, s); ^{13}C NMR δ (ppm): 208.9, 171.4, 142.1, 137.1, 128.9, 127.3, 127.0, 49.1, 44.5, 15.5, 8.2; HRMS (ESI): 209.0937, $[C_{13}H_{14}ONa]^+$ requires 209.0942.

(*trans*)-5-Bromo-3-(bromomethyl)-2,4-dimethylcyclopent-2-enone (75)

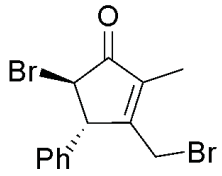


75

A solution of AVK **28** (0.070 g, 0.56 mmol) in CH_2Cl_2 (50 mL) was cooled to –78 °C, and a solution of bromine (1M in CH_2Cl_2) (0.56 mL, 0.56 mmol) was added

dropwise. After stirring for 15 min, a solution of titanium bromide (1M in dichloromethane) (2.8 mL, 2.8 mmol) was added dropwise. The mixture was allowed to warm slowly and stirred at room temperature for 10 h. The reaction mixture was then poured into a separatory funnel containing saturated aqueous sodium bicarbonate, and shaken vigourously. Additional dichloromethane was added, the aqueous layer was extracted (×2), and the combined organic layers were dried with Na_2SO_4, concentrated, and the product purified by column chromatograpy (10% EtOAc in hexanes) to yield **75** (0.034 g, 22%) as a colourless oil: IR (film) 1712, 1633 cm^{-1}; ^1H NMR δ: 4.24 (1H, d, J = 11 Hz), 4.13 (1H, d, J = 11 Hz), 4.03 (1H, d, J = 2.9 Hz), 3.28 (1H, m), 1.83 (3H, s), 1.35 (3H, d, J = 7.3 Hz); ^{13}C NMR δ: 200.8, 165.7, 136.9, 49.8, 46.3, 23.3, 16.6, 8.7; HRMS (ESI): 302.8965, $[C_8H_{10}Br_2ONa]^+$ requires 302.8991.

(*trans*)-5-Bromo-3-(bromomethyl)-2-methyl-4-phenylcyclopent-2-enone (76)

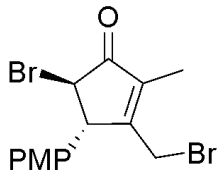


76

According to the procedure for **75**: AVK **26** (0.10 g, 0.56 mmol) was reacted with bromine (0.56 mL, 0.56 mmol) and titanium tetrabromide (2.8 mL, 2.8 mmol) to yield **76** (0.15 g, 79%) as a white solid: mp 84–86 °C; IR (film) 1717, 1642, 1601 (w) cm^{-1}; ^1H NMR δ: 7.37 (3H, m), 7.15 (2H, m), 4.42 (1H, br d, J = 2.7 Hz), 4.33 (1H, d, J = 2.5 Hz), 4.21 (1H, d, J = 11 Hz), 3.69 (1H, d, J = 11 Hz), 1.94 (3H, s); ^{13}C NMR δ: 201.5, 164.2,

137.7, 137.6, 129.5 (2C), 128.4, 127.6 (2C), 57.1, 50.0, 23.9, 8.9; HRMS (ESI): 364.9113, $[C_{13}H_{12}Br_2ONa]^+$ requires 364.9147.

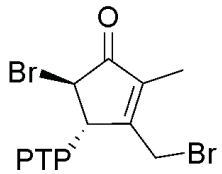
(*trans*)-5-Bromo-3-(bromomethyl)-4-(4-methoxyphenyl)-2-methylcyclopent-2-enone (77)



77

According to the procedure for **75**: AVK **30** (0.12 g, 0.56 mmol) was reacted with bromine (0.56 mL, 0.56 mmol) and titanium tetrabromide (2.8 mL, 2.8 mmol) to yield **77** (0.15 g, 70%) as a colourless oil: IR (film) 1717, 1642, 1601 (w) cm^{-1}; ^1H NMR δ: 7.07 (2H, d, J = 9.0 Hz), 6.90 (2H, d, J = 9.0 Hz), 4.36 (1H, br d, J = 2.6 Hz), 4.29 (1H, d, J = 2.6 Hz), 4.19 (1H, d, J = 11 Hz), 3.81 (3H s), 3.70 (1H, d, J = 11 Hz), 1.92 (3H, s); ^{13}C NMR δ: 201.5, 164.3, 159.6, 137.4, 129.5 (2C), 128.7 (2C), 114.8, 56.4, 55.3, 50.3, 23.9, 8.9; HRMS (ESI): 394.9251, $[C_{14}H_{14}Br_2O_2Na]^+$ requires 394.9253.

(*trans*)-5-Bromo-3-(bromomethyl)-2-methyl-4-(4-(trifluoromethyl)phenyl)cyclopent-2-enone (78)

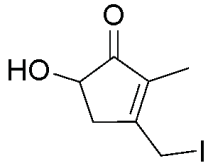


78

According to the procedure for **75**: AVK **31** (0.10 g, 0.56 mmol) was reacted with bromine (0.56 mL, 0.56 mmol) and titanium tetrabromide (2.8 mL, 2.8 mmol) to yield **78**

(0.15 g, 65%) as a colourless oil: IR (film) 1705, 1642, 1619, 1326 cm^{-1}; ^{1}H NMR δ: 7.67 (2H, d, *J* = 8.2 Hz), 7.32 (2H, d, *J* = 8.2 Hz), 4.49 (1H, br d, *J* = 2.8 Hz), 4.31 (1H, d, *J* = 2.8 Hz), 4.24 (1H, d, *J* = 11 Hz), 3.67 (1H, d, *J* = 11 Hz), 1.96 (3H, s); ^{13}C NMR δ: 200.6, 163.1, 141.8, 138.4, 130.8 (q, *J* = 33 Hz), 128.2 (2C), 126.5 (2C, q, *J* = 3.8 Hz), 123.7 (q, *J* = 270 Hz), 56.9, 49.7, 23.7, 9.0; ^{19}F NMR δ: -63.8 (s); HRMS (ESI): 432.8989, $[C_{14}H_{11}Br_2F_3ONa]^+$ requires 432.9021.

5-Hydroxy-3-(iodomethyl)-2-methylcyclopent-2-enone (79)

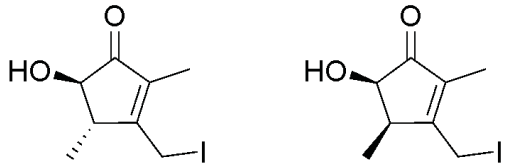


79

A solution of AVK **27** (0.060 g, 0.56 mmol) in CH_2Cl_2 (50 mL) was cooled to –78 °C, and iodine (0.14 g, 0.56 mmol) was added. After stirring for 1 h, the solution was re-cooled to –78 °C, and trifluoroacetic acid (0.20 mL, 2.8 mmol) was added dropwise. The mixture was allowed to warm to room temperature and stirred for 48 h. The reaction mixture was then poured into a separatory funnel containing saturated aqueous sodium bicarbonate, and shaken vigourously. Additional dichloromethane was added, and the aqueous layer was extracted (×2). The combined organic layers were washed with a 10% aqueous solution of sodium thiosulfate, then dried with Na_2SO_4 and concentrated. The intermediate trifluoroacetate ester was hydrolyzed via SiO_2 chromatograpy by loading the product with 10% EtOAc in hexanes, and after one hour commencing elution (10%, then 20%, EtOAc in hexanes) to yield **79** (0.025 g, 18%) as an orange wax: IR (film) 3385,

1702, 1632 cm^{-1}; ^1H NMR δ: 4.34 (1H, dd, *J* = 6.9, 3.0 Hz), 4.17 (1H, d, *J* = 9.3 Hz), 4.11 (1H, d, *J* = 9.3 Hz), 3.11 (1H, dd, *J* = 17, 6.9 Hz), 2.80 (1H, br s), 2.68 (1H, br dd, *J* = 17, 3.0 Hz), 1.69 (3H, s) ; ^{13}C NMR δ: 208.9, 164.5, 134.6, 71.6, 37.1, 8.1, -2.0; HRMS (ESI): 274.9536, $[C_7H_9IO_2Na]^+$ requires 274.9539.

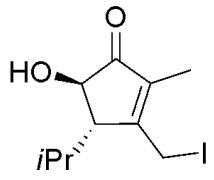
(*trans*)-5-Hydroxy-3-(iodomethyl)-2,4-dimethylcyclopent-2-enone (80a) and (*cis*)-5-hydroxy-3-(iodomethyl)-2,4-dimethylcyclopent-2-enone (80b)



80a **80b**

According to the procedure for **79**: AVK **28** (0.070 g, 0.56 mmol) was reacted with iodine (0.14 g, 0.56 mmol) and trifluoroacetic acid (0.20 mL, 2.8 mmol) to yield 0.062 g (40%) of a 2.5:1 mixture of **80a**/**80b** (as determined by integration of the ^1H NMR spectrum), yellow oil: IR (film) 3397, 1704, 1627 cm^{-1}; HRMS (ESI): 288.9684, $[C_8H_{11}IO_2Na]^+$ requires 288.9696; the following NMR data were taken from the spectra of the mixture: for **80a**: ^1H NMR δ: 4.16 (1H, d, *J* = 9.5 Hz), 4.12 (1H, d, *J* = 9.5 Hz), 3.96 (1H, d, *J* = 3.1 Hz), 3.06 (1H, br s), 3.01 (1H, m), 1.68 (3H, s), 1.37 (3H, d, *J* = 7.2 Hz); ^{13}C NMR δ: 207.2, 167.0, 134.7, 79.5, 42.8, 15.6, 8.3, -4.9; for **80b**: ^1H NMR δ: 4.26 (1H, d, *J* = 7.2 Hz), 4.23 (1H, d, *J* = 9.5 Hz), 4.08 (1H, d, *J* = 9.5 Hz), 2.95 (1H, br s), 3.31 (1H, s), 1.70 (3H, s), 1.13 (3H, d, *J* = 7.2 Hz); ^{13}C NMR δ: 209.0, 169.3, 133.4, 74.4, 40.0, 14.7, 8.1, -3.6.

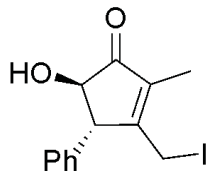
(*trans*)-5-Hydroxy-3-(iodomethyl)-4-isopropyl-2-methylcyclopent-2-enone (81)



81

According to the procedure for **79**: AVK **29** (0.090 g, 0.60 mmol) was reacted with iodine (0.15 g, 0.60 mmol) and trifluoroacetic acid (0.22 mL, 3.0 mmol) to yield **81** (0.080 g, 45%) as a yellow oil: IR (film) 3424, 1706, 1628 cm^{-1}; ^{1}H NMR δ: 4.24 (1H, d, J = 9.5 Hz), 4.14 (1H, d, J = 2.9 Hz), 4.04 (1H, d, J = 9.5 Hz), 3.07 (1H, m), 2.77 (1H, br s), 2.48 (1H, m), 1.68 (3H, s), 1.19 (3H, d, J = 6.9 Hz), 0.77 (3H, d, J = 6.9 Hz); ^{13}C NMR δ: 208.1, 167.2, 136.1, 71.8, 53.0, 26.5, 21.4, 16.5, 8.6, -4.0; HRMS (ESI): 316.9992, $[C_{10}H_{15}IO_2Na]^+$ requires 317.0009.

(*trans*)-5-Hydroxy-3-(iodomethyl)-2-methyl-4-phenylcyclopent-2-enone (82)

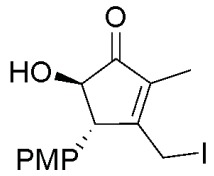


82

According to the procedure for **79**: AVK **26** (0.10 g, 0.56 mmol) was reacted with iodine (0.14 g, 0.56 mmol) and trifluoroacetic acid (0.20 mL, 2.8 mmol) to yield **82** (0.11 g, 61%) as an orange wax: IR (film) 3418, 1698, 1635, 1602 cm^{-1}; ^{1}H NMR δ: 7.38 (2H, m), 7.33 (1H, m), 7.21 (2H, m), 4.36 (1H, d, J = 3.0 Hz), 4.18 (1H, br d, J = 3.0 Hz), 4.14 (1H, d, J = 9.5 Hz), 3.65 (1H, d, J = 9.5 Hz), 2.81 (1H, br s), 1.77 (3H, s); ^{13}C NMR δ:

206.9, 166.0, 138.6, 135.6, 129.2, 128.1 (2C), 127.9 (2C), 80.6, 54.1, 8.7, -3.8; HRMS (ESI): 350.9823, $[C_{13}H_{13}IO_2Na]^+$ requires 350.9852.

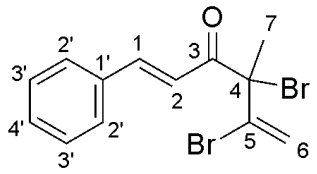
(*trans*)-5-Hydroxy-3-(iodomethyl)-4-(4-methoxyphenyl)-2-methylcyclopent-2-enone (83)



83

According to the procedure for **79**: AVK **30** (0.12 g, 0.56 mmol) was reacted with iodine (0.14 g, 0.56 mmol) and trifluoroacetic acid (0.20 mL, 2.8 mmol) to yield **83** (0.065 g, 32%) as an orange wax: IR (film) 3422, 1704, 1630, 1611 cm^{-1}; ^1H NMR δ: 7.13 (2H, d, J = 8.7 Hz), 6.91 (2H, d, J = 8.7 Hz), 4.33 (1H, br t, J = 2.5 Hz), 4.12 (1H, d, J = 9.2 Hz), 3.82 (3H, s), 3.66 (1H, d, J = 9.2 Hz), 2.82 (1H, d, J = 2.5 Hz), 1.76 (3H, s); ^{13}C NMR δ: 207.0, 166.2, 159.2, 135.3, 130.4, 129.1 (2C), 114.6 (2C), 80.6, 55.3, 53.4, 8.7, -3.7; HRMS (ESI): 380.9929, $[C_{14}H_{15}IO_3Na]^+$ requires 380.9958.

(1*E*)-4,5-Dibromo-4-methyl-1-phenylhexa-1,5-dien-3-one (74)

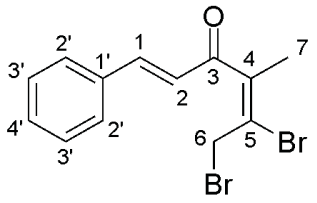


74

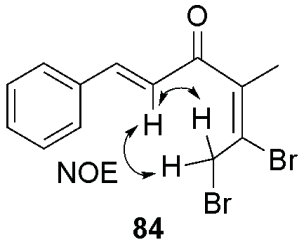
A -78 °C CH_2Cl_2 (14 mL) solution of AVK **26** (0.025 g, 0.14 mmol) was reacted with bromine (0.14 mL, 1 M solution in CH_2Cl_2), and was stirred for 15 min. The reaction mixture was then concentrated, and the product purified by column

chromatograpy (10% EtOAc in hexanes) to yield **74** (0.040, 99%) as a colourless oil: IR (film) 1694, 1611 cm^{-1}; ^{1}H NMR δ: 7.82 (1H, d, *J* = 16 Hz, H1), 7.58 (2H, m, H3'), 7.40 (3H, m, H2', H4'), 7.11 (1H, d, *J* = 16 Hz, H2), 6.59 (1H, d, *J* = 3.0 Hz, H6a), 5.98 (1H, d, *J* = 3.0 Hz, H6b), 2.12 (3H, s, H7); ^{13}C NMR δ: 189.4 (C3), 145.2 (C1), 134.4 (C1'), 130.8 (C4'), 130.5 (C5), 128.9 (2C, C2'), 128.7 (2C, C3'), 123.0 (C6), 120.1 (C2), 68.4 (C4), 27.4 (C7); HRMS (ESI): 364.9113, $[C_{13}H_{12}Br_2ONa]^+$ requires 364.9147.

(1*E*,4*E*)-5,6-Dibromo-4-methyl-1-phenylhexa-1,4-dien-3-one (84)



84

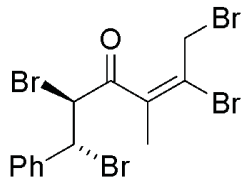


84

A -78 °C CH_2Cl_2 (14 mL) solution of AVK **26** (0.025 g, 0.14 mmol) was reacted with bromine (0.14 mL, 1 M solution in CH_2Cl_2), and after 15 minutes trifluoroacetic acid (0.70 mmol, 0.10 mL) was added, and the mixture was let to warm to room temperature overnight. The mixture was then washed with saturated aqueous sodium bicarbonate, and the aqueous layer back-extracted with dichloromethane. The combined organic layers were dried with Na_2SO_4, concentrated, and the product purified by column chromatograpy (10% EtOAc in hexanes) to yield **84** (0.038, 99%) as a colourless oil: IR (film) 1650, 1617, 1605 cm^{-1}; ^{1}H NMR δ: 7.62 (1H, d, *J* = 16 Hz, H1), 7.61 (2H, m, H3'), 7.44 (3H, m, H2', H4'), 6.83 (1H, d, *J* = 16 Hz, H2), 4.34 (2H, s, H6), 2.12 (3H, s, H7); ^{13}C NMR δ: 194.8 (C3), 148.1 (C1), 141.3 (C4), 133.8 (C1'), 131.4 (C4'), 129.1 (2C,

C2'), 128.8 (2C, C3'), 125.1 (C5), 124.3 (C2), 36.0 (C6), 21.7 (C7); HRMS (ESI): 364.9129, $[C_{13}H_{12}Br_2ONa]^+$ requires 364.9147.

(1*S,2*R**,4*E*)-1,2,5,6-Tetrabromo-4-methyl-1-phenylhex-4-en-3-one (85)**



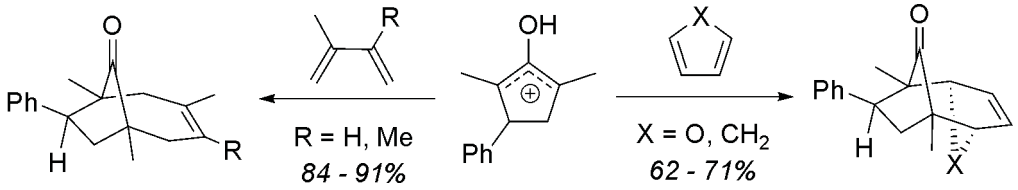
85

A -78 °C CH_2Cl_2 (14 mL) solution of AVK **26** (0.025 g, 0.14 mmol) was reacted with bromine (0.28 mL, 1 M solution in CH_2Cl_2), and after 15 minutes trifluoroacetic acid (0.70 mmol, 0.10 mL) was added, and the mixture was warmed to room temperature and stirred for 18 h. The mixture was then washed with saturated aqueous sodium bicarbonate, and the aqueous layer back-extracted with dichloromethane. The combined organic layers were dried with Na_2SO_4, concentrated, and the product purified by column chromatograpy (10% EtOAc in hexanes) to yield **85** (0.070, 99%) as a colourless solid: mp 85–87 °C; IR (film) 1702, 1603 cm^{-1}; ^1H NMR δ: 7.41 (5H, m), 5.47 (1H, d, J = 12 Hz), 5.31 (1H, d, J = 12 Hz), 4.60 (1H, d, J = 11 Hz), 4.55 (1H, d, J = 11 Hz), 2.30 (3H, s); ^{13}C NMR δ: 192.3, 137.8, 137.5, 134.1, 129.5, 128.9 (2C), 128.2 (2C), 49.5, 49.4, 35.1, 21.3; HRMS (ESI): 522.7469, $[C_{13}H_{12}Br_4ONa]^+$ requires 522.7514.

CHAPTER 4. THE INTERRUPTED NAZAROV CYCLIZATION OF ALLENYL VINYL KETONES WITH CARBON-CARBON BOND FORMATION

4.1 Introduction

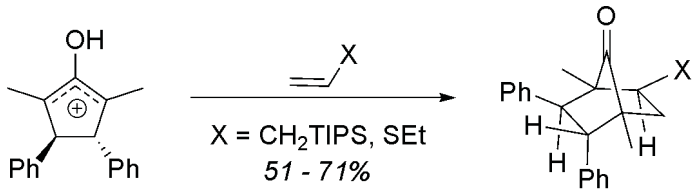
Oxyallyl cations are intermediates in the Nazarov cyclization, but they are also integral in the synthesis of seven-membered carbocycles via [4 + 3] cyclizations with 1,3-dienes.[54] The intermolecular reaction has been shown to proceed efficiently with furan and cyclopentadiene, but the analogous reaction with acyclic dienes has remained underexplored likely because this process can be complicated by alternative [4 + 2] and [3 + 2] cyclizations and by competing decomposition pathways.[55] Recently, the cyclic oxyallyl cations generated by Nazarov cyclization have been shown to be effective partners in intermolecular [4 + 3] cyclizations with furan, cyclopentadiene, and a few acyclic dienes (Scheme 36).[11d] The reaction is highly facially selective, as evidenced by the orientation of the phenyl substituent, which is in an *exo* position. Furthermore, the reaction also takes place with high diastereoselctivity via a compact transition state, as evidenced by the reaction with furan and cyclopentadiene, in which "*endo*"-products are formed exclusively.



Scheme 36 Tandem Nazarov/[4 + 3] reaction.

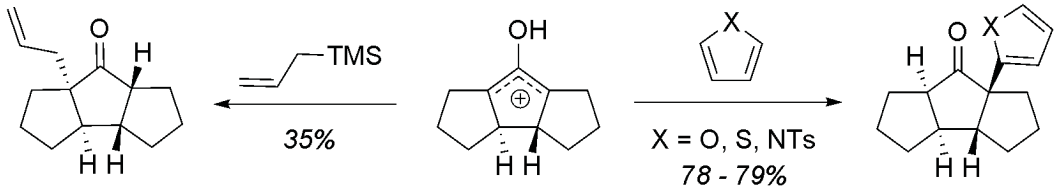
Furthermore, there are two reports of Nazarov cyclizations being followed by intramolecular [3 + 2] cyclizations (Scheme 37).[11a, b,56] This reaction is highly

diastereoselective for products in which the substituents are oriented in an *exo* position.



Scheme 37 Tandem Nazarov/[3 + 2] reaction.

There are also some examples in which, instead of the expected [4 + 3] or [3 + 2] reactions, compounds in which only a single carbon-carbon bond had been formed were produced as the sole or major product (Scheme 38).[11a,12]



Scheme 38 Nazarov reaction followed by single carbon-carbon bond formation.

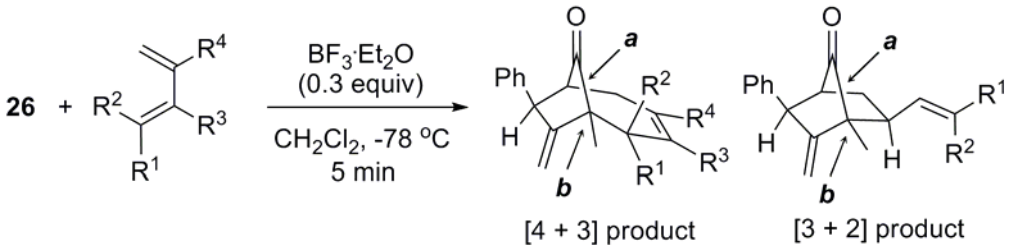
Based on our studies with trapping the oxyallyl cationic intermediate derived from the Nazarov cyclization of an AVK with heteroatom nucleophiles, there are at least four reasons why an AVK presents an especially well suited coupling partner for subsequent cyclization reactions: *1.* An AVK is a particularly reactive substrate for the Nazarov reaction, cyclizing rapidly under acidic conditions to generate the oxyallyl cation. *2.* The oxyallyl cation is stabilized by extra conjugation, and simple loss of a proton to generate a double bond might be unfavourable as the product would be a fulvene. Thus, the oxyallyl cation would be more likely to be trapped. *3.* The products resulting from either [4 + 3] or [3 + 2] cyclizations would contain an exocyclic methylene

unit, providing a good synthetic handle for further transformations. *4.* The oxyallyl cation has two unencumbered positions to which a nucleophile might add readily, which would allow for the production of diverse cyclopentenone-containing ring systems.

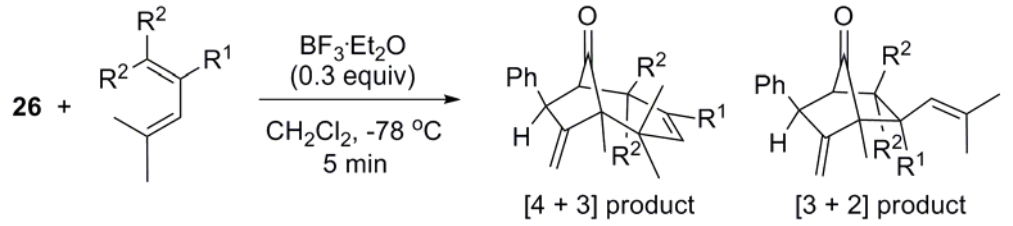
4.2 Synthesis of Bicyclic Ketones by Reaction with Substituted Butadiene Derivatives

AVK **26** was treated with $BF_3{\cdot}Et_2O$ in the presence of various methyl-substituted butadienes (Table 8). Reactions were rapid (5 min at –78 °C) and yielded products of [4 + 3] and [3 + 2] cyclizations onto positions *a* and *b* of the oxyallyl cationic intermediate. $BF_3{\cdot}Et_2O$ was chosen as the acid for most reactions because no nucleophilic species, which might compete with a carbon-nucleophile to trap the oxyallyl cation derived from **26**, had been seen to be generated from this Lewis acid (Table 2). Furthermore, whereas $BF_3{\cdot}Et_2O$ elicited the quantitative formation of **90** (entry 4) in 5 min, $InCl_3$ and $Cu(OTf)_2$ gave **90** more slowly (2 h) and in yields of only 59% and 68%, respectively. Although $InCl_3$ is known to give the product of trapping with chloride at position *c*, the reaction with the diene must be much faster because chlorinated products were not observed when the diene was added. This was true of other experiments involving alkenes with $InCl_3$ (*vide infra*). It is interesting to note that the much more electron-rich *trans*-1-methoxy-3-trimethylsilyloxy-1,3-butadiene did not yield any Nazarov product with **26** (entry 5).

Table 8 Reactions of AVK **26** with butadiene derivatives.



entry	diene	[4 + 3]	[3 + 2]	yield (%)[a] product ratio
1	R^1 = Me, R^2 = H, R^3 = H, R^4 = H	**86a**	**87**	51 **86a**/**87** 1:2.7
2	R^1 = H, R^2 = Me, R^3 = H, R^4 = H	–	**88**	54
3	R^1 = H, R^2 = H, R^3 = Me, R^4 = H	**89a**,**b**[b]	–	56 **89a**/**89b** 1:2.8
4	R^1 = H, R^2 = H, R^3 = Me, R^4 = Me	**90**	–	99
5	R^1 = OMe, R^2 = H, R^3 = H, R^4 = OTMS	–	–	–[c]



entry	diene	[4 + 3]	[3 + 2]	yield (%) product ratio
6	R^1 = H, R^2 = H	–	**91a**	85
7	R^1 = Me, R^2 = H	**92**	**93a**,**b**[d]	71 **92**/**93a**,**b** 1:2
8	R^1 = H, R^2 = Me	–	**94a**,**b**[e]	49

[a]Isolated yields, [b] **89a** R^3 = Me, R^4 = H; **89b** R^3 = H, R^4 = Me, [c] intractable material, [d] **93a** R^1 endo, **93b** R^1 exo, ratio 1:1, [e] **94a** R^1 endo, **94b** R^1 exo, ratio 5:1.

The regioselectivity of all cyclizations (with the exception of entry 3), as determined by detailed analysis of the 2D NMR data of the products, was high. The X-ray crystal structure of **90** showed that the phenyl group was in an *exo* position (Figure 9), and NOE measurements showed that every product had the phenyl group in an *exo* position, indicating a high degree of facial selectivity. As the only [4 + 3] product using *trans*-piperylene was **86a** (entry 1), this reaction also exhibits a high degree of "*exo"*-diastereoselectivity, suggesting that the reaction proceeds through an extended transition state. This is in contrast to similar experiments by the West group with oxyallyl cations derived from divinyl ketones, in which *"endo"*-products had been obtained exclusively (*cf.* Scheme 36).[11d]

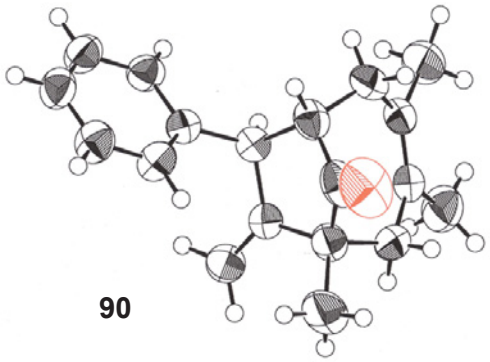
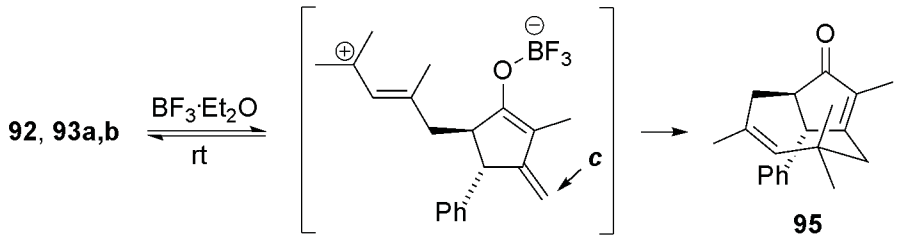


Figure 9 X-ray crystal structure of compound **90**.

All products were stable with $BF_3{\cdot}Et_2O$ at –78 °C, but with $BF_3{\cdot}Et_2O$ at room temperature over a period of hours some compounds equilibrated. One may presume that this much slower process involved ring cleavage to give the enolate and the delocalized cation, which then re-cyclized. The [3 + 2] product **87** equilibrated to a 2.2:1 mixture of the [4 + 3] compound **86a** and the epimer **86b**. On the other hand, compound **88**

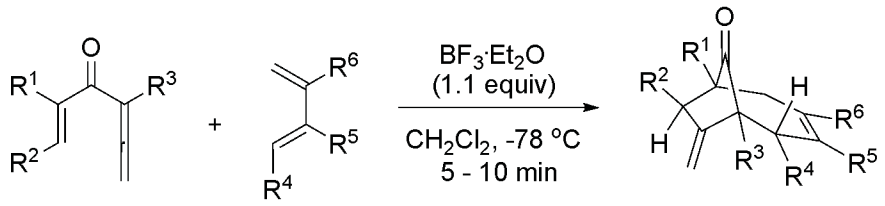
remained unchanged in the presence of $BF_3{\cdot}Et_2O$. Re-subjecting the mixture of **92** and **93a**,**b** to $BF_3{\cdot}Et_2O$ provided **95** in 75% yield. This remarkable outcome indicated that each compound underwent ring-opening, and then reclosure of the enolate onto position *c* (Scheme 39). Compound **95** represented the product of a formal [5 + 4] cyclization of the oxyallyl cation with the diene. Hence, in every instance in Table 8 where the reaction products were mixtures of different sized ring-systems, addition of more $BF_3{\cdot}Et_2O$ to the mixture resulted in confluence to a single ring-system.



Scheme 39 Proposed equilibration of bicyclic ketones to a single ring system via ring opening to a zwitterionic intermediate.

The reaction was also evaluated with other Type 1 AVKs, **27** and **29**, as well as Type 2 AVKs **35** and **37** (Table 9). NOE measurements showed that every product had the phenyl group in an *exo* position, indicating a high degree of facial selectivity. All reactions proceeded with high regio- and stereoselectivity, producing products with similar connectivity to that of AVK **26**. As the only [4 + 3] products using *trans*-piperylene were **98** (entry 3) and **101** (entry 6) for AVKs **35** and **37** respectively, this reaction also exhibits a high degree of "*exo"*-diastereoselectivity. The stereo- and regiochemistry of the reactions was determined by NOE measurements and analysis of the 2D NMR spectra (COSY, HSQC, and HMBC) of the products.

Table 9 Reactions of AVKs **27**, **29**, **35**, and **37** with butadiene derivatives.

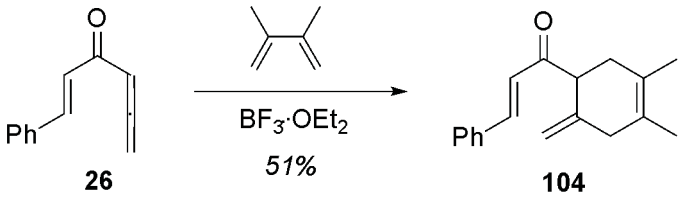


27, **29**, **35**, **37** **96** - **103**

entry	AVK	diene	yield (%)[a] product ratio
1	R^1 = H, R^2 = H, R^3 = Me	R^4 = H, R^5 = Me, R^6 = Me	71 **96**
2	R^1 = H, R^2 = *i*-Pr, R^3 = Me	R^4 = H, R^5 = Me, R^6 = Me	64 **97**
3	R^1 = Me, R^2 = Ph, R^3 = H	R^4 = Me, R^5 = H, R^6 = H	50 **98**
4	R^1 = Me, R^2 = Ph, R^3 = H	R^4 = H, R^5 = Me, R^6 = Me	79 **99**
5	R^1 = Me, R^2 = Ph, R^3 = H	R^4 = H, R^5 = H, R^6 = Me	73 **100a/100b** 1:4[b]
6	R^1, R^2 = -$(CH_2)_4$-, R^3 = H	R^4 = Me, R^5 = H, R^6 = H	48 **101**
7	R^1, R^2 = -$(CH_2)_4$-, R^3 = H	R^4 = H, R^5 = Me, R^6 = Me	74 **102**
8	R^1, R^2 = -$(CH_2)_4$-, R^3 = H	R^4 = H, R^5 = H, R^6 = Me	65 **103a/103b** 1:1.3[c]

[a] Isolated yields, [b] **100a** R^5 = Me, R^6 = H; **100b** R^5 = H, R^6 = Me,
[c] **103a** R^5 = Me, R^6 = H; **103b** R^5 = H, R^6 = Me.

The only product of Type 3 AVK **36** and 2,3-dimethylbutadiene in the presence of $BF_3{\cdot}Et_2O$ was the Diels-Alder adduct **104**, the result of a [4 + 2] reaction across the allene unit (Scheme 40). This result again highlighted the key role of an alkyl group at either α-position of the carbonyl group of the AVK, in order to facilitate Nazarov reactions at the expense of side reactions initiated via additions to the allenyl central carbon, as discussed in Section 3.3.

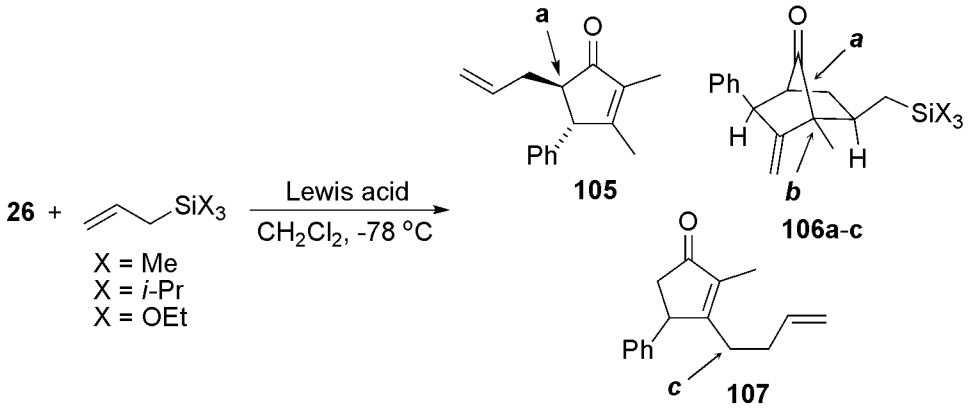


Scheme 40 Reaction of AVK **36** with 2,3-dimethylbutadiene.

4.3 Synthesis of Bicyclic Ketones and/or Cyclopent-2-enones by Reaction with Activated Alkenes

AVK **26** was also treated with either $BF_3{\cdot}Et_2O$, $Cu(OTf)_2$, or $InCl_3$ in the presence of various allylsilanes (Table 10). When $BF_3{\cdot}Et_2O$ was added to **26** and allyltrimethylsilane, two Nazarov products formed very rapidly. One (**105**) was the product of addition to position *a* of the oxyallyl cation, but the major product was the [3 + 2] product **106a**. The relative stereochemistry was determined by measurement of NOEs and the magnitude of the ^1H NMR coupling constants, and the regiochemistry was determined by analysis of the 2D NMR spectra (COSY, HSQC, and HMBC) of the products. When $Cu(OTf)_2$ was employed as the Lewis acid, the reaction was slower and three products were obtained: **105**, **106a**, and **107**, of which **107** was the result of capture at position *c*. With $InCl_3$ the reaction had approximately the same rate as with $Cu(OTf)_2$, **107** was the major product, and there was none of the [3 + 2] product. Utilization of a more robust silane, allyltriisopropylsilane, resulted in an increased proportion of the [3 + 2] product **106b** in the presence of either $BF_3{\cdot}Et_2O$ or $InCl_3$. Allyltriethoxysilane with $BF_3{\cdot}Et_2O$ gave a poor yield of the [3 + 2] product **106c**, but no other Nazarov product was detected.

Table 10 Reactions of AVK **26** with allylsilanes.

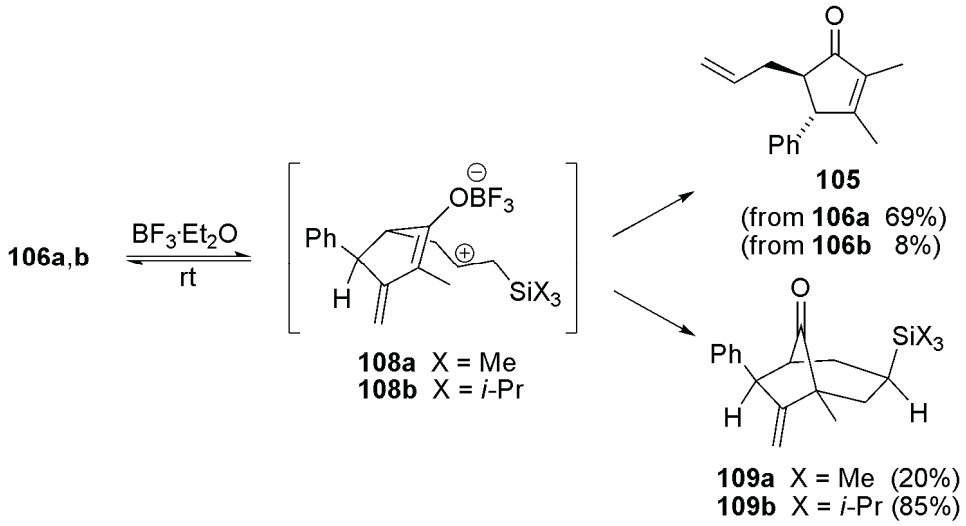


entry	X	Lewis acid	time	yields (%)[a]		
				105	**106a-c**	**107**
1	Me	$BF_3{\cdot}Et_2O$[b]	5 min	27	54 (**106a**)	–
2	Me	$Cu(OTf)_2$[c]	1.5 h	20	10 (**106a**)	42
3	Me	$InCl_3$[c]	2 h	22	–	56
4	*i*-Pr	$BF_3{\cdot}Et_2O$[b]	5 min	19	57 (**106b**)	–
5	*i*-Pr	$InCl_3$[c]	2 h	27	28 (**106b**)	13
6	OEt	$BF_3{\cdot}Et_2O$[b]	5 min	–	15 (**106c**)	–

[a] Isolated yields, [b] 2 equiv of allylsilane, 1.1 equiv of $BF_3{\cdot}Et_2O$,
[c] 5 equiv of allylsilane, 5 equiv of Lewis acid.

The trimethylsilyl [2.2.1]-compound **106a** could be converted in 5 h to **105** in moderate yield in the presence of $BF_3{\cdot}Et_2O$ at room temperature, but a minor product was the trimethylsilyl [3.2.1]-compound **109a** (Scheme 41). This minor compound would have been the result of cyclization of intermediate **108a** in concert with a shift of the silyl group. This sort of process had been anticipated, but not observed, by West in their study of interception of Nazarov reactions with allylsilanes.[11a] When the more robust triisopropylsilyl [2.2.1]-compound **106b** was stirred with $BF_3{\cdot}Et_2O$ at room temperature,

not only was the analogous recyclization of **108b** evident, it led to the triisopropylsilyl [3.2.1]-compound **109b** in very good yield.



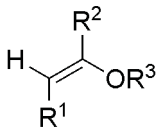
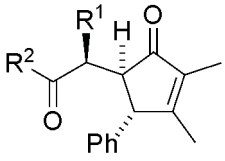
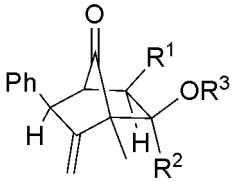
Scheme 41 Ring-opening of silyl-substituted [3 + 2] products at room temperature.

Alternatively, exposure of the crude mixture of **105** and **106a**, obtained following work-up of the reaction of AVK **26** with allyltrimethylsilane and $BF_3{\cdot}Et_2O$, gave similar results as in Scheme 41. However, the addition of excess $BF_3{\cdot}Et_2O$ to the initial mixture of AVK **26** and allyltrimethylsilane, prior to work-up, led to poorer results: whilst **106a** was completely consumed upon warming to room temperature, **105** was obtained in only 33% overall yield following chromatography.

Oxygen-substituted alkenes intercepted the oxyallyl cation with high facial selectivity by nucleophilic attack at position *a* or by the formation of [3 + 2] products (Table 11). The relative stereochemistry was determined by measurement of NOEs and the magnitude of the ^{1}H NMR coupling constants, and the regiochemistry was determined by analysis of the 2D NMR spectra (COSY, HSQC, and HMBC) of the

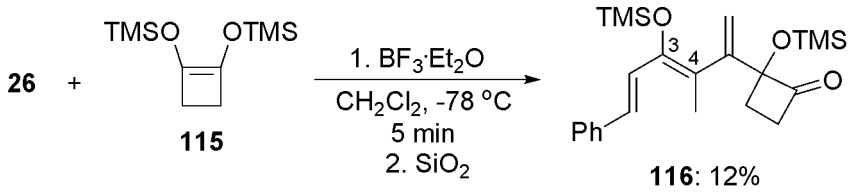
products. A silyl enol ether and an enol acetate (entries 1 and 2) trapped the oxyallyl cation inefficiently to give low yields of **110** and **111**, respectively. The enol ether, *n*-propoxyethene, gave two types of products, **110** and **112**, in high overall yield (entry 3). However, the [3 + 2] product **112**, in contrast with **106a,b**, simply decomposed when treated with $BF_3{\cdot}Et_2O$ at room temperature. Further substitution of the double bond, as in entries 4 and 5, led to products of trapping at position *a*, and **113** and **114** were not accompanied by [3 + 2] products. The [3 + 2] product **112** was obtained as an epimeric mixture, but it is important to note that the formation of **113** was stereoselective. The relative stereochemistry of compound **113** was established by a *J*-correlated NMR method.[57,58]

Table 11 Reactions of AVK **26** with electron-rich alkenes.[a]

entry	alkene	products and yields[b]	
			
1	R^1 = H, R^2 = H, R^3 = TMS	**110** (35%)	–
2	R^1 = H, R^2 = H, R^3 = Ac	–	**111** (18%)
3	R^1 = H, R^2 = H, R^3 = *n*Pr	**110** (59%)	**112** (41%)[c]
4	R^1 = Me, R^2 = H, R^3 = Et	**113** (86%)[d]	–
5	R^1 = H, R^2 = Me, R^3 = Me	**114** (60%)[e]	–

[a] 2 equiv alkene, 1.1 equiv $BF_3{\cdot}Et_2O$, [b] isolated yields,
[c] ether group exo/endo 5:1, [d] *ca.* 90% the isomer shown,
[e] included an inseparable by-product from subsequent reaction of **114**.

In the light of the entries 1 and 4 in Table 11, it was somewhat surprising that introduction of neither the *tert*-butyldimethylsilyl enol ether derived from cyclopentanone nor a cyclic enol ether, dihydropyran, gave any trapped Nazarov product. Also, *N*-vinylpyrrolidinone, as well as the enamine derived from cyclopentanone and pyrrolidine, failed to produce any isolable interrupted Nazarov product – only intractable material was obtained. It is probable that if the alkene or diene is too electron-rich, it will add via a Michael reaction to the central allenic carbon of the AVK before the AVK has undergone the Nazarov reaction. Evidence for this comes from an attempted reaction with an excess of the electron-rich cyclobutene derivative **115** (Scheme 42). The ^{1}H NMR spectrum of the initial product mixture showed signals mainly for the Michael product **116** and residual **115**. The stereochemistry of the C3-C4 double bond was determined by observation of NOEs. Although the isolated yield of **116** following flash chromatography was low, it was subsequently established that **116** decomposed rapidly on silica gel.

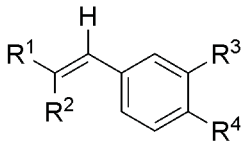
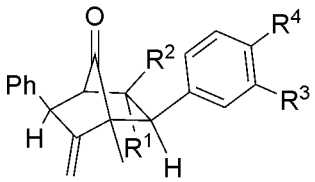


Scheme 42 Attempted interrupted Nazarov reaction of AVK **26** with **113**.

Styrenes afforded only [3 + 2] products as single diastereomers (Table 12). The relative stereochemistry was confirmed by NOE measurements, and the regiochemical outcome was determined by analysis of the 2D NMR spectra of the products. Styrene itself (entry 1) gave a poor yield of **117**, and an electron-poor derivative (entry 2) did not trap the oxyallyl cation at all. On the other hand, electron-donation was clearly

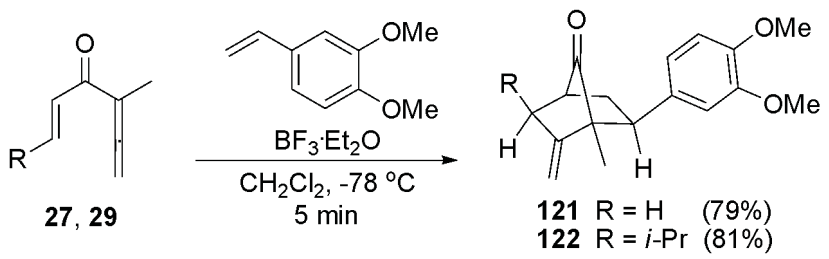
advantageous (entries 3-5). Reaction of **26** with the *trans*-isomer provided **120** in a yield that was slightly higher (entry 5) than the yield from the less substituted styrene (entry 3), but the corresponding *cis*-isomer failed to trap the oxyallyl cation (entry 6). This curious result may reflect reduced electron-donation by the methoxyphenyl group into the alkene moiety in the *cis* isomer,[59] and it is consistent with a hypothesis that the kinetic route to the [3 + 2] products might be concerted, or at least very rapid, at –78 °C because bond rotation in an intermediate carbocation could have given **120** from the *cis* isomer.

Table 12 Reactions of AVK **26** with styrenes.[a]

entry	styrene	product and yield[b]
		
1	R^1, R^2, R^3, R^4 = H	**117** (15%)
2	R^1, R^2, R^3 = H; R^4 = CF_3	–
3	R^1, R^2, R^3 = H; R^4 = OMe	**118** (52%)
4	R^1, R^2 = H; R^3, R^4 = OMe	**119** (76%)
5	R^1 = Me; R^2, R^3 = H; R^4 = OMe	**120** (59%)
6	R^1, R^3 = H; R^2 = Me; R^4 = OMe	–

[a] 2 equiv styrene, 1.1 equiv $BF_3 \cdot Et_2O$, [b] isolated yields.

The reaction was also briefly evaluated with AVKs **27** and **29** (Scheme 43). In the presence of 3,4-dimethoxystyrene, AVKs **27** and **29** rapidly formed the [3 + 2] products **121** and **122**. In both cases, only the *exo*-diastereomer was produced, as confirmed by NOE measurements.



Scheme 43 Reactions of AVKs **27** and **29** with 3,4-dimethoxystyrene.

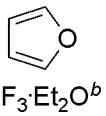
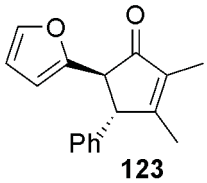
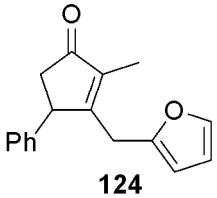
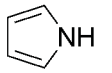
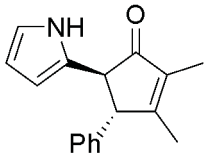
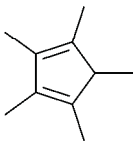
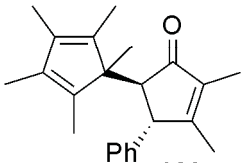
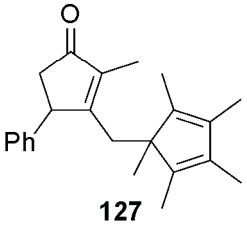
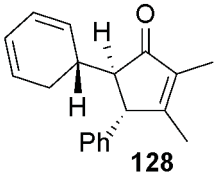
The reactions of allyltrimethylsilane and *p*-methoxystyrene were also evaluated with Type 2 and Type 3 AVKs **35** – **37**, however complex mixtures were obtained. NMR analysis of the product mixtures suggested that the bulk of the material had reacted directly with the allene moiety of the AVK.

4.4 Synthesis of Functionalized Cyclopent-2-enones by Reaction With Cyclic Dienes

When some cyclic dienes were mixed with AVK **26** and $BF_3{\cdot}Et_2O$, the Nazarov reactions were interrupted readily by the cyclic dienes, but it was surprising that no products of [4 + 3] cyclization were detected. Only one carbon-carbon bond formed (Table 13), and the relative stereochemistry of the products was determined by comparison of ^1H NMR coupling constants.

Furan, which has been used in a number of [4 + 3] cyclizations with oxyallyl cations,[54] trapped only at position *a* to provide **123** when the reaction was mediated by $BF_3{\cdot}Et_2O$ (entry 1). Whilst the use of $Cu(OTf)_2$ elicited similar results to $BF_3{\cdot}Et_2O$, $InCl_3$ promoted the formation of a minor amount of **124** via capture at position *c* (entry 2). Reaction with thiophene led to intractable material, however pyrrole provided **125** as a single compound, trapped at position *a*, in 54% yield (entry 3). Intractable material was

Table 13 Reactions of AVK **26** with cyclic dienes.

entry	diene Lewis acid	products		yield (%)[a] product ratio
1	 $BF_3{\cdot}Et_2O$[b]	 **123**	–	64[c]
2	 $InCl_3$[d]	**123**	 **124**	69 **123**/**124** 3.5:1
3	 $BF_3{\cdot}Et_2O$[e]	 **125**	–	54
4	 $BF_3{\cdot}Et_2O$[e]	 **126**	 **127**	72[f] **126**/**127** 1:5.5
5	 $BF_3{\cdot}Et_2O$[e]	 **128**	–	70

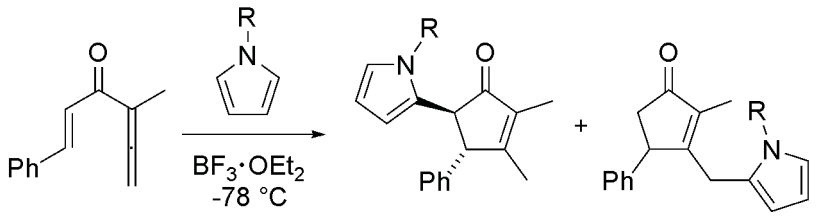
[a] Isolated yields, [b] 10 equiv furan, 1.1 equiv $BF_3{\cdot}Et_2O$, 5 min, [c] in addition, there was 10% of a product where one furan added to two of **123** at position *a*,[12a] [d] 5 equiv furan, 5 equiv $InCl_3$, 2 h, [e] 2 equiv diene, 1.1 equiv $BF_3{\cdot}Et_2O$, 5 min, [f] in addition, there was 8% of the product of the Diels–Alder reaction of the diene with the allene of **26**.

obtained when cyclopentadiene or 6,6-dimethylfulvene were added, but addition of 1,2,3,4,5-pentamethylcyopentadiene led to the formation of a minor product **126**, by

interception at position *a* of the oxyallyl cation intermediate, and a major product **127**, by capture at the less sterically hindered position *c* (entry 4). Using 1,3-cyclohexadiene to trap the oxyallyl cation provided only **128**, as a single diastereomer (entry 5). The relative stereochemistry of **128** was established by a *J*-correlated NMR method.[57,58]

A series of *N*-substituted pyrroles was then evaluated under the reaction conditions (Table 14). The relative stereochemistry of the products substituted at C4 was determined by the magnitude of their ^{1}H NMR coupling constants. As with pyrrole itself, the predominant Nazarov product with *N*-alkyl-, *N*-aryl-, and *N*-silyl-pyrroles involved carbon-carbon bond formation at position *a* of the oxyallyl cation (entries 1–5). The modest yields of Nazarov products in these cases were mostly a result of a competing Michael addition pathway, generating products such as **140** (Scheme 44). The ratio of Nazarov product **125** to Michael adduct **140**, for example, was 3:1 by integration of the ^{1}H NMR spectrum of the crude reaction mixture. Interception of the Nazarov reaction was also attempted with 2-ethyl-, 3,4-diethyl-, and 3-ethyl-2,4-dimethylpyrrole, but these compounds failed to be incorporated into any cyclopent-2-enone product. It appeared by ^{1}H NMR spectroscopy of the crude product mixtures that **26** was reacting mainly by Michael reactions with the pyrroles. Utilization of different Lewis acids, such as $Sc(OTf)_3$ or $InCl_3$, led to no Nazarov product. Only the Michael adduct **140** was isolated (Scheme 43); observation of NOEs established the (*Z*)-geometry. No Michael product was detected for pyrroles with electron-withdrawing groups on the nitrogen atom however (entries 6–9), and much, or all, of the Nazarov product arose by interception at position *c*. With *N*-mesyl and *N*-tosyl pyrrole, the low yields obtained with $BF_3{\cdot}OEt_2$

Table 14 Reactions of AVK **26** with *N*-substituted pyrroles.[a]

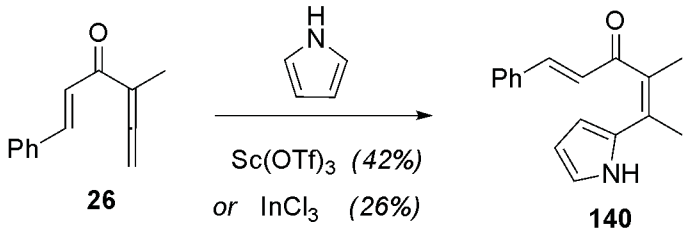


26 **129-135** **136-139**

entry	pyrrole R	product(s)	yield (%)[b]
1	Me	**129**	32
2	Bn	**130**	50
3	Ph	**131**	67
4	PMP	**132**	41
5	TIPS	**133**	31
6	MOC	**134/136** (1:1)[c]	23
7	BOC	**135/137** (1.4:1)[c]	33
8	Ms	**138**	11 (41)[d]
9	Ts	**139**	10 (44)[d]

[a] 2 equiv pyrrole, 1.1 equiv $BF_3 \cdot Et_2O$, [b] isolated yields, [c] determined by integration of the ^1H NMR spectra of the crude reaction products, [d] yields in parentheses were obtained when $InCl_3$ (2 equiv) was used as the Lewis acid.

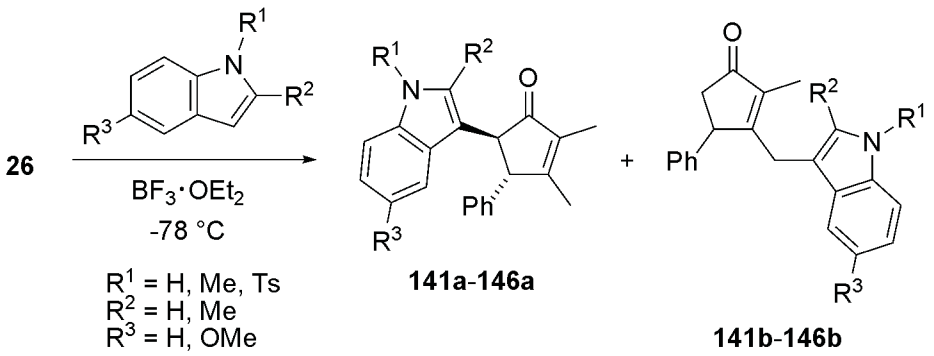
were improved fourfold by using $InCl_3$ as the Lewis acid (entries 8-9), and Michael-addition products were not detected with these pyrroles. The reason for this increase in yield using $InCl_3$ is as yet unclear.



Scheme 44 Michael reactions of AVK **26** with pyrrole.

A series of substituted indoles was then evaluated under the reaction conditions (Table 15). The relative stereochemistry of the products substituted at C4 was determined by comparison of their ^{1}H NMR coupling constants. Interrupted Nazarov reactions mediated by $BF_3{\cdot}OEt_2$ took place in higher yield with indoles than with pyrroles. Michael products made up less than 10% of the product mixtures, and cyclopent-2-enones could be produced in good to excellent yield. The regioselectivity for the trapping, i.e., positions *a* versus *c* of the oxyallyl cation, was modest. Notably, methyl substitution at C2 of the indole (entries 4 and 5) led to a greater proportion of the Nazarov product that had been trapped at position *c*. Although trapping with a more electron-rich derivative, 5-methoxyindole (entry 2), did not affect the yield or selectivity of the reaction, *N*-tosylindole (entry 6), a more electron-poor analogue, failed to generate any trapped product under the same reaction conditions. However, when $InCl_3$ was employed, Nazarov products **146a** and **146b** were obtained (1:1 ratio).

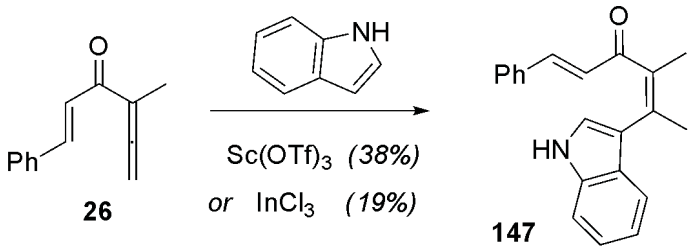
Table 15 Reactions of AVK **26** with substituted indoles.[a]



entry	products	ratio of product(s)[b]	combined yield (%)[c]
1	**141a,b** (R^1, R^2, R^3 = H)	2.3-3.7:1	88-93
2	**142a,b** (R^1, R^2 = H, R^3 = OMe)	2.5-3.9:1	71-92
3	**143a,b** (R^1= Me, R^2, R^3 = H)	3.2-3.6:1	88-90
4	**144a,b** (R^1, R^3 = H, R^2 = Me)	1.1-1.6:1	58-60
5	**145a,b** (R^1, R^2 = Me, R^3 = H)	1.2-1.4:1	87-90
6	**146a,b** (R^1 = Ts, R^2, R^3 = H)	1:1	0(49)[d]

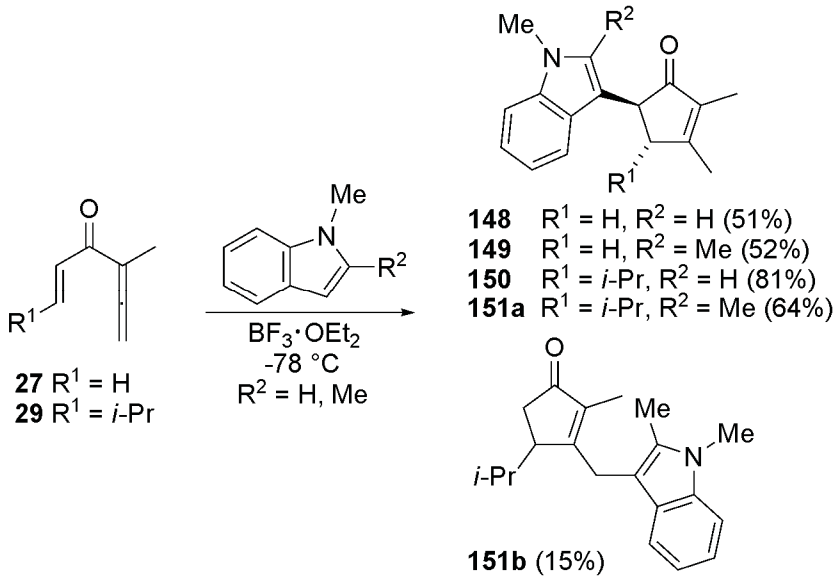
[a] 2 equiv indole, 1.1 equiv $BF_3{\cdot}Et_2O$, [b] range from three trials, determined by integration of the ^{1}H NMR spectra of the crude reaction products, [c] isolated yields, range from two trials, [d] yields in parentheses were obtained when $InCl_3$ (2 equiv) was used as the Lewis acid.

As with pyrrole, when the reaction was assessed with $Sc(OTf)_3$ the Michael adduct **147** was obtained in 38% yield and no Nazarov product was observed, whereas use of $InCl_3$ led to Michael adduct **147** in only 19% yield (Scheme 45). Observation of NOEs established the (*Z*)-geometry of **147**.



Scheme 45 Michael reactions of AVK **26** with indole.

Replacement of the phenyl group of AVK **26** with a hydrogen, as in AVK **27**, or an isopropyl group, as in AVK **29**, might be expected to be significant in terms of the reactivity of the AVKs and the regioselectivity of the Nazarov reactions with substituted indoles (Scheme 46). Similarly to AVK **26**, the less substituted AVK **27** reacted rapidly with *N*-methyl- and 1,2-dimethylindole, but the regioselectivity was much improved. Only the products of trapping at the position corresponding to *a* (**148** and **149**) were obtained. The reactions of AVK **29** were also rapid and much more regioselective than those of AVK **26**, with **150** being the only significant Nazarov product with



Scheme 46 Reactions of AVKs **27** and **29** with *N*-methylindole and 2,3-dimethylindole.

N-methylindole, and **151a** and **151b** being produced in a ratio of 4.3:1 with 1,2-dimethylindole.

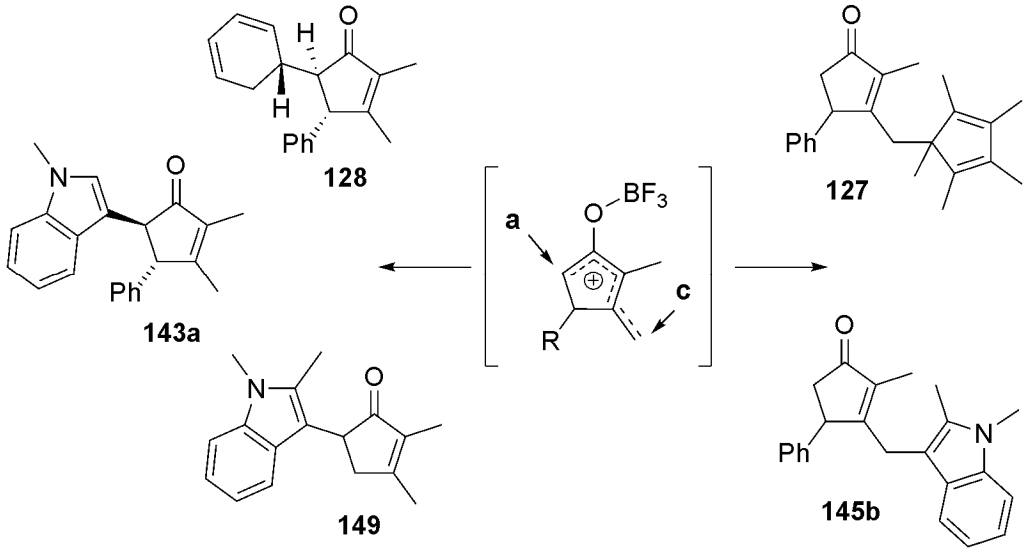
The interrupted Nazarov reaction with cyclic dienes does not appear to be amenable to AVKs of Type 2 or Type 3, however. When AVKs **35** – **37** were reacted with a variety of cyclic dienes (furan, 1,3-cyclohexadiene, *N*-phenylpyrrole, 5-methoxyindole) in the presence of $BF_3 \cdot OEt_2$, complex mixtures were obtained. NMR analysis of the product mixtures suggested that the bulk of the material had reacted directly with the allene moiety of the AVK.

4.5 Mechanistic Rationale for the Observed Regio- and Stereoselectivity in Interrupted Nazarov Reactions of Allenyl Vinyl Ketones

In general, most interrupted Nazarov reactions of AVKs proceeded with high or exclusive regio- and stereoselectivity. For single bond formation, position *a* of the oxyallyl cation intermediate appeared to be the preferred site of bond formation, although in certain cases products at trapped position *c* predominated. When three new stereocenters were formed, the reaction also appeared to be highly stereoselective. In the cases where two bonds are formed simultaneously, as with butadiene derivatives, the less hindered end of the diene also reacted regioselectively at position *a*. Furthermore, the reaction was also highly stereoselective for the formation of products in which the substituents are oriented in an *exo* position. We wished to develop a mechanistic rationale for the observed regio- and stereoselectivity in the Nazarov reaction of AVKs, in order to allow further generalizations to be made in terms of reactivity and selectivity.

4.5.1 Implications of Regioselectivity of Interrupted Nazarov Reactions of AVKs with Cyclic Dienes

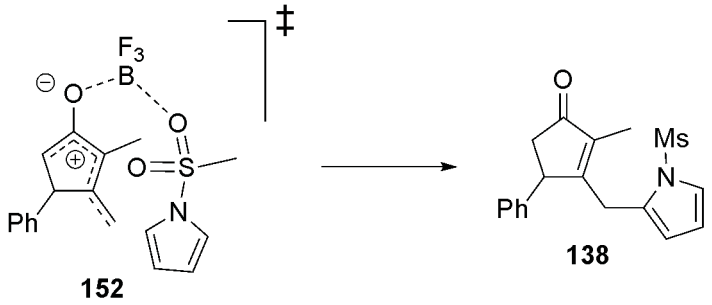
Sterically unhindered substrates such as furan, *N*-substituted pyrroles, indole, *N*-methylindole, and 1,3-cyclohexadiene trapped predominantly at position *a*, whereas dienes with increasing substitution near the reacting carbons, such as indoles substituted at the 2-position and 1,2,3,4,5-pentamethylcyclopentadiene, provided competitive or selective amounts of product trapped at position *c* (Scheme 47). A substitutent at the β-alkenyl position of the AVK also showed a strong influence on the regioselectivity of the trapping process, with unsubstituted AVK **27** and isopropyl-substituted AVK **29** yielding increased or exclusive formation of products trapped at position *a* relative to the phenyl-substituted AVK **26** (Scheme 47). Hence, the regioselectivity of the trapping process showed a strong dependence upon the substitution pattern present in both reacting partners, and regioselectivity became worse with increasing substitution near the reacting



Scheme 47 Bulkier reagents favour products trapped at position *c*.

carbons. These results suggested that position *a* is the electronically preferred trapping site, whereas position *c* becomes favoured for sterically encumbered substrates.

The observed tendancy of *N*-substituted pyrroles bearing MOC, BOC, mesyl, or tosyl groups to produce increasing or exclusive amounts of products trapped at position *c* in the presence of $BF_3{\cdot}OEt_2$ might be explained by invoking a transition state similar to **152**, which might direct attack of the pyrrole to position *c* in these cases (Scheme 48).



Scheme 48 Proposed transition state model leading to **138**.

4.5.2 Computational Investigation of the Oxyallyl Cationic Intermediate

The atomic charge on each atom of the oxyallyl cations **153** – **155**, derived from AVKs **26**, **35**, and **36** respectively, was determined computationally‡ using QTAIM[48] (Figure 10a). There were no significant differences in the lengths of the bonds between adjacent sp^2 carbons for **153** – **155** (Figure 10b). The lengths of the bonds between adjacent sp^2 carbons were all approximately 1.43 Å, except the exocyclic bond was always shorter (*ca.* 1.37 Å). However, important differences were revealed in the delocalization indices (Figure 10c),[60] which are estimates of bond population by pairs of

‡Calculations were performed by Gavin Heverly-Coulson, using the Q-Chem 3.1[46] and AIMAll (Version 10.03.25)[47] software packages.

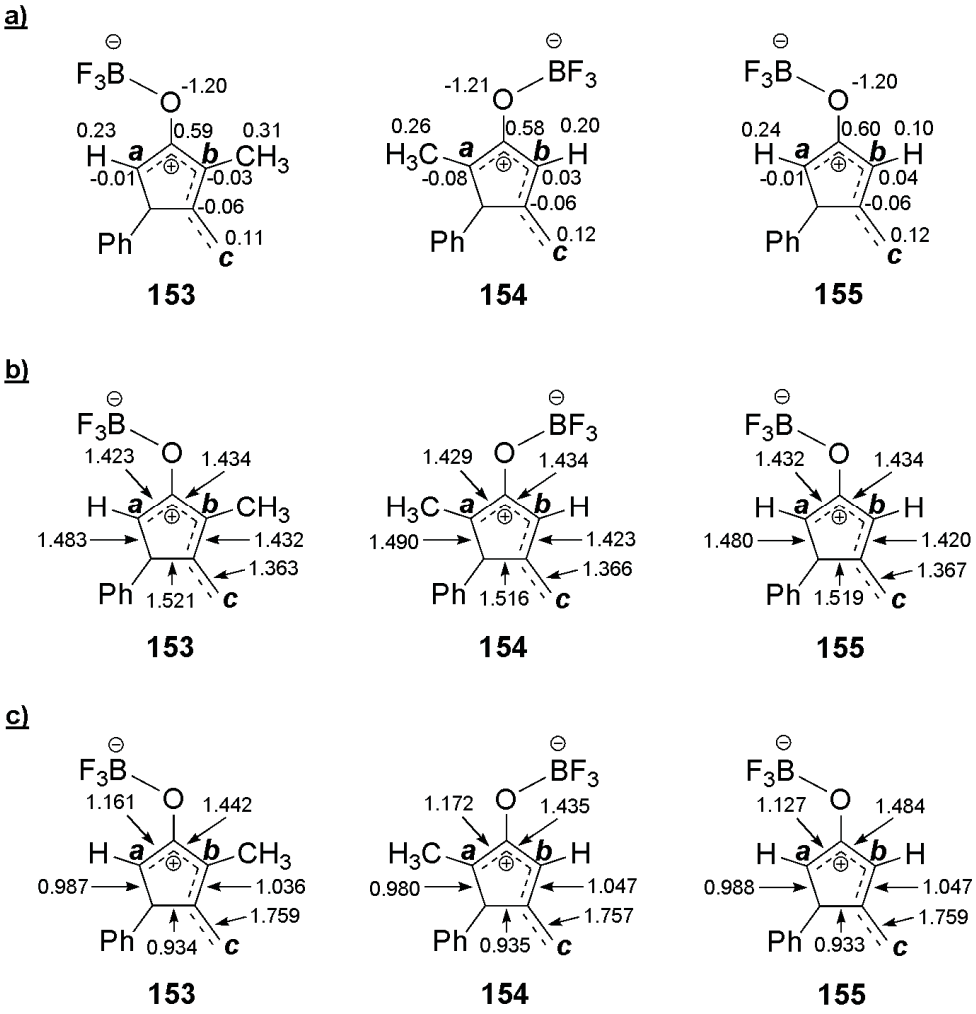
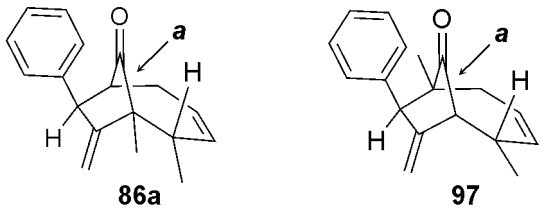


Figure 10 a) Selected atomic charges, b) bond lengths, and c) delocalization indices for the oxyallyl cations **153** -**155**, in their lowest-energy conformations, as calculated using RI-MP2/cc-pvdz.[49]

electrons. Regardless of the presence or the position of the methyl group, the bond from the oxygen-bearing carbon to *b* and the carbon-carbon bond to *c* had larger indices than the bond from the oxygen-bearing carbon to *a*, which pointed to position *a* as the most electrophilic carbon in all three oxyallyl cations. Hence, the computational results suggest that position *a* of the oxyallyl cation derived from AVKs is indeed the electronically preferred site of trapping in interrupted Nazarov cyclizations.

4.5.3 Implications of Regioselectivity of Interrupted Nazarov Reactions of AVKs with Butadiene Derivatives

The regioselectivity of all cyclizations of AVK **26** with butadienes (Table 8), with the exception of entry 3, was high, and this could be rationalized as arising from the most reactive cationic site in the oxyallyl cation **153** being *a* and significant amounts of charge in the diene moieties at the transition states. More importantly, Nazarov reactions of both AVKs **26** and **35** in the presence of *trans*-piperylene gave **86a** and **97** as the only [4 + 3] products. The regioselectivity of these cyclizations was the same. In both cases, the unsubstituted end of the diene reacted at position *a* of the oxyallyl cation (Figure 11). This is further experimental corroboration of the computational result that the electronic bias in the oxyallyl cations derived from AVK's **26** and **35**, i.e., **153** and **154**, is position *a*, regardless of the position of the alkyl substituent.



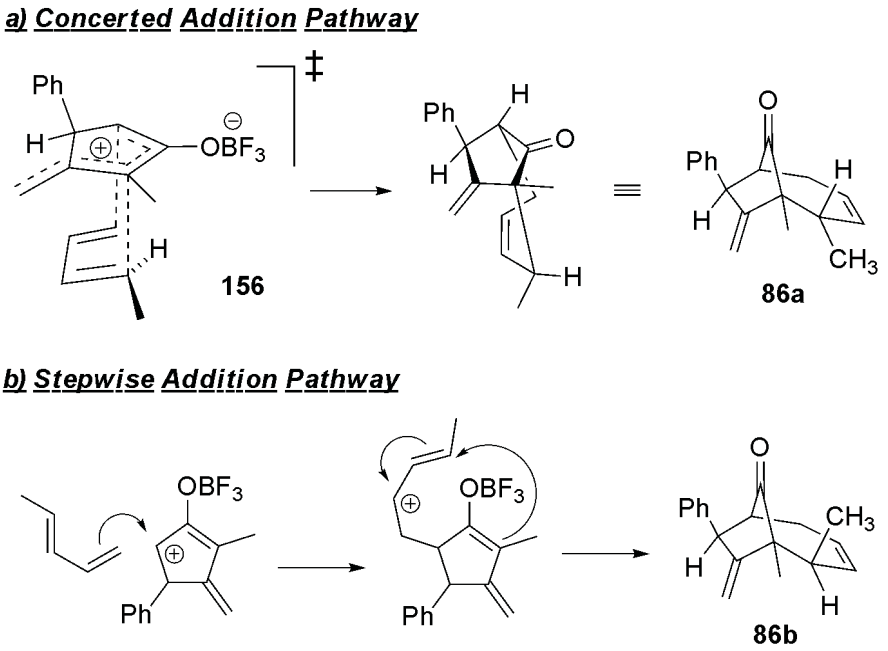
86a **97**

Figure 11 Reactions of AVKs **26** and **35** with *trans*-piperylene occur with the same regioselectivity.

4.5.4 Implications of Stereoselectivity of Interrupted Nazarov Reactions of AVKs with Butadiene Derivatives

Nazarov reactions of AVKs **26** and **35** in the presence of *trans*-piperylene also gave the [4 + 3] products **86a** and **97**, as single stereoisomers.

Calculations[§] showed that the epimer of **86a**, **86b**, is 3.0 kJ·mol^{-1} lower in energy. These findings would be consistent with a concerted, but asynchronous, cycloaddition mechanism via an extended geometry similar to **156** for the formation of the [4 + 3] products (Scheme 49a), in lieu of a stepwise one which might be expected to generate **86b** preferentially (Scheme 49b).



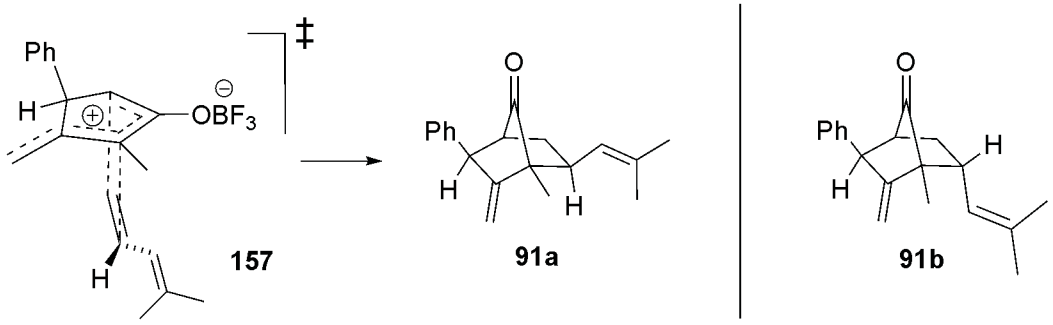
Scheme 49. a) Geometry of cycloaddition that would lead to [4 + 3] product **86a**, and b) Alternative stepwise pathway that would lead to the undetected epimer **86b**.

This was consistent with a computational study involving the reaction of butadiene with a metal-bound acyclic oxyallyl species, which had suggested a concerted pathway to be lower in energy than a stepwise one for adducts resulting from extended transition states.[62] Although cyclic oxyallyl cations generally proceed through a compact

[§]Calculations were performed by Gavin Heverly-Coulson, HF/6-31G//HF/6-311G(d,p) using Gaussian 03, Revision C.02.[61]

geometry in intermolecular [4 + 3] reactions with dienes,[54] extended transition states might be more energetically accessible for oxyallyl cations derived from AVKs as the methylene unit would relieve some of the steric crowding that would be present otherwise.

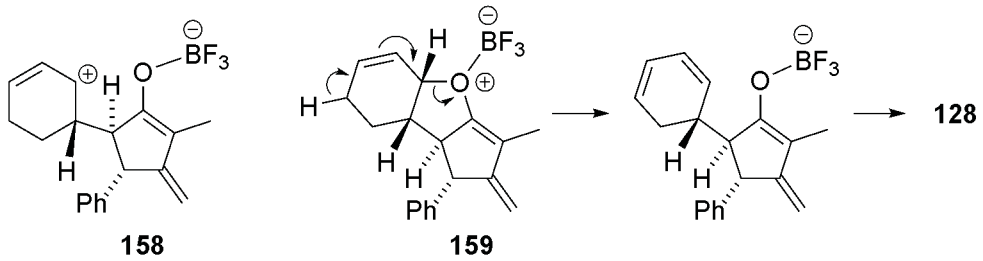
A concerted reaction would require the diene to assume an *s*-cis conformation. s-*Cis* conformations would be disfavoured for the dienes in entries 2, 6, and 8 (Table 8), and these dienes gave no [4 + 3] products, but provided [3 + 2] products, only, in moderate to good yield. In contrast, the dienes in entries 1, 3, 4, and 7 (Table 8) have more accessible s-*cis* conformers, and these dienes did afford [4 + 3] products. It was significant that **87**, **88**, and **91a** were the only [3 + 2] products in entries 1, 2, and 6, indicating a high degree of stereoselectivity in this cyclization, also. This might be expected for a cycloaddition via a geometry similar to **157** (Scheme 50) or a very rapid stepwise reaction, although the stepwise formation of [3 + 2] products might be considered a 5-(enolendo)-exo-trig closure, a disfavoured process.[63] The product **91a** in entry 6 was compared with its (undetected) epimer **91b** computationally,§ and it was **91b** that was lower in energy by 2.2 kJ·mol^{-1}, suggesting that **91a** formed as the result of a concerted reaction.



Scheme 50 Geometry of cycloaddition that would lead to [4 + 3] product **91a**.

4.5.5 Implications of Stereoselectivity of Interrupted Nazarov Reactions of AVK 26 with 1,3-Cyclohexadiene and *(Z)*-Ethylpropenylether

The interrupted Nazarov reaction of AVK **26** with (*Z*)-ethylpropenylether and 1,3-cyclohexadiene led to the stereoselective production of compounds **113** and **128**, respectively (*cf.* Tables 11 and 13). The position of the diene moiety in **128** is intriguing because loss of a proton from a putative intermediate **158** should be expected to lead to a more substituted diene. However, a dipolar [3 + 2] cyclization involving the enol oxygen would give **159** as an intermediate,[15] and conjugate elimination/ring opening during work-up would result in the preferential formation of **128** (Scheme 51). The formation of **113** from **26** might also take place in a similar manner, through the formation of a transient intermediate analogous to **159**, produced by a [3 + 2] process involving the enol oxygen. It has been suggested by the calculations of Cramer and Barrows[62] that a dipolar [3 + 2] cycloaddition can be comparable, or even lower, in energy to all-carbon [3 + 2] and [4 + 3] cycloadditions, depending on the nature of the oxyallyl cation and the diene involved. In the case of the reactions of AVK **26** with (*Z*)-ethylpropenylether and 1,3-cyclohexadiene, it is plausible that the direct formation of [4 + 3] or all-carbon [3 + 2] products would suffer from considerable steric hindrance in transition state geometries



Scheme 51 Formation of compound **128** via a dipolar [3 + 2]/ring opening process.

similar to **156** and **157** (*cf.* Schemes 49a and 50), which might disfavour these pathways relative to a dipolar [3 + 2] cycloaddition pathway.

4.6 Summary

In summary, it has been shown that an AVK is a versatile source of cyclic molecules via a cascade reaction sequence beginning with a Lewis acid-mediated Narazov cyclization and then interception of the intermediate oxyallyl cation by various acyclic dienes, cyclic dienes, electron-rich alkenes, and styrenes by the formation of an additional ring by a [4 + 3] and/or [3 + 2] cyclization or by the formation of one additional carbon-carbon bond. The bicyclic compounds generated in this way are densely substituted, and would be difficult to access as succinctly in other ways. The products of these interrupted Nazarov reactions generally reflect excellent regio- and stereoselectivity in the trapping reaction. In some instances, equilibrating conditions were shown to enhance the proportion of one product at the expense of another or to provide a different carbon skeleton. This process is amenable to unsubstituted, alkyl-substituted, or aromatic-substituted allenyl vinyl ketones.

In general, the trapping process was regioselective for interception of the oxyallyl cation at position *a*, regardless of the placement of the α-substituent of the AVK. Computational data showed that this is likely a result of position *a* being the electronically preferred site for trapping. In the formation of single carbon-carbon bonds, the regioselectivity of the trapping process showed a strong dependence upon the substitution pattern present in both reacting partners, and the regioselectivity became worse with increasing substitution near the reacting carbons. This suggested that,

although position *a* is the electronically preferred trapping site, position *c* is the sterically preferred trapping site.

The process was also determined to be highly stereoselective, especially with respect to the formation of the bicyclic ketones. Preliminary data suggest that this result might be the outcome of a concerted, but highly asynchronous, reaction. The high stereoselectivity noted in the formation of the cyclopent-2-enone containing products was proposed to arise as a result of a dipolar [3 + 2] cyclization, or a very rapid stepwise reaction involving the enol oxygen, followed by conjugate ring opening of the resultant cyclic enol ether.

The results of this study contribute to a more complete understanding of the interrupted Nazarov cyclization of allenyl vinyl ketones, and should allow for further generalizations to be made in terms of reactivity and regioselectivity, with respect to related substrate classes. These findings will be invaluable in the design of feasible synthetic approaches involving Nazarov cyclizations of allenyl vinyl ketones, particularly in the stereocontrolled generation of bicyclo[4.2.1]nonenones.

4.7 Experimental Section

4.7.1 General Considerations

All reactions were conducted using oven-dried glassware under an N_2 atmosphere. Reagents were used as received from a commercial supplier without further purification. 1-(Methanesulfonyl)pyrrole,[64,65] and 1-(toluenesulfonyl)pyrrole[64-66] were prepared according to the literature procedures. Mr. François LeFort is thanked for assistance with the preparation of compounds **125**, **129** – **133**, **135**, **137**, and **139**. Ms.

Rhonda Stoddard is thanked for assistance with the preparation of compounds **98 - 100**.

Dichloromethane was used freshly distilled from calcium hydride. Ethyl acetate and hexanes were distilled prior to use for column chromatography.

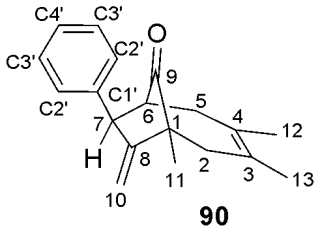
Thin layer chromatography was conducted using pre-coated silica plates with plastic backing (EMD chemicals, silica gel 60 F_{254}), using UV light (254 nm) as a visualizing agent and potassium permanganate in aqueous KOH and heat, or *o*-vanillin in ethanol/H_2SO_4 and heat, as developing agents. Column chromatography was carried out on silica gel purchased from Silicycle (40 – 63 μm particle size, 230 – 240 mesh).

Melting points are uncorrected, and were acquired using a Fisher-Johns apparatus. ^{1}H NMR spectra were recorded at 500 MHz on a Bruker Avance spectrometer with $CDCl_3$ as solvent (7.24 ppm) and TMS as internal reference (0.00 ppm). ^{13}C NMR spectra were recorded at 125 MHz on a Bruker Avance spectrometer with $CDCl_3$ as solvent. Infrared spectra were recorded from thin films on a Bruker VECTOR 22 FT-IR instrument using CsI plates. High resolution mass spectra were acquired by Mr. Xiao Feng, on a Bruker microTOF Focus orthogonal ESI-TOF mass spectrometer.

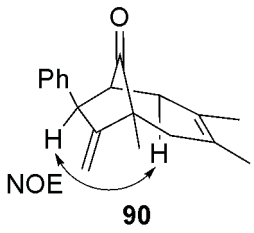
The carbon and hydrogen atoms of select compounds were assigned following detailed analysis of their one dimensional (^{1}H, ^{13}C, and DEPT-135) and two dimensional (COSY, HSQC, and HMBC) NMR spectral data. The ^{1}H and ^{13}C NMR spectra of all compounds, and the DEPT-135, COSY, HSQC, HMBC, and *J*-HMBC spectra (including detailed analysis of the *J*-HMBC spectra) for compounds **113** and **128**, may be found in Appendix A. The Cartesian coordinates (including additional computed data) for compounds **86a**, **86b**, **91a**, **91b**, and **153 - 155**, may be found in Appendix B, and the X-ray crystallographic data for compound **90** can be found in Appendix C.

4.7.2 Preparation and Characterization Data

(1*R,6*S**,7*R**)-1,3,4-Trimethyl-8-methylene-7-phenylbicyclo[4.2.1]non-3-en-9-one (90)**



90



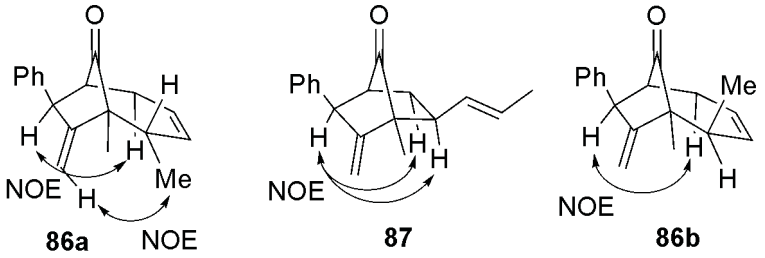
90

Procedure 1: A solution of AVK **26** (0.050 g, 0.28 mmol) and 2,3-dimethyl-1,3-butadiene (0.060 mL, 0.56 mmol) in CH_2Cl_2 (25 mL) was cooled to –78 °C, and $BF_3{\cdot}OEt_2$ (0.01 mL, 0.08 mmol) was added. The mixture was stirred for 5 min, then poured into a separatory funnel containing saturated aqueous sodium bicarbonate. The CH_2Cl_2 layer was removed, and additional CH_2Cl_2 (×2) was used to re-extract the aqueous layer. The combined organic layers were dried over Na_2SO_4 and then concentrated under reduced pressure. Flash chromatography of the residue (SiO_2 using 2.5% EtOAc in hexanes) provided **90** (0.075 g, 99%) as a colourless solid: mp 101–103 °C; IR (film) 1738, 1601 (w) cm^{-1}; ^1H NMR δ: 7.26 (2H, m, H3'), 7.17 (1H, m, H4'), 7.00 (2H, m, H2'), 5.05 (1H, d, *J* = 2.1 Hz, H10a), 4.83 (1H, d, *J* = 2.3 Hz, H10b), 3.61 (1H, br s, H7), 2.66 (1H, m, H6), 2.48 (1H, br d, *J* = 16 Hz, H5a), 2.42 (1H, dd, *J* = 16, 6.3 Hz, H5b), 2.31 (1H, d, *J* = 16 Hz, H2a), 2.04 (1H, d, *J* = 16 Hz, H2b), 1.80 (3H, s, H13), 1.78 (3H, s, H12), 1.27 (3H, s, H11); ^{13}C NMR δ: 222.7 (C9), 157.4 (C8), 146.4 (C1'), 128.7 (2C, C3'), 127.7 (C4), 127.2 (2C, C2'), 126.2 (C4'), 125.6 (C3), 109.2 (C10), 55.3 (C6), 53.9 (C1), 51.0 (C7), 50.8 (C2), 39.9 (C5), 23.8 (2C, C12, C13), 20.8 (C11); HRMS (ESI) 289.1557, $[C_{19}H_{22}ONa]^+$ requires 289.1563.

Procedure 2: A solution of AVK **26** (0.025 g, 0.14 mmol) and 2,3-dimethyl-1,3-butadiene (0.080 mL, 0.70 mmol) in CH_2Cl_2 (15 mL) was cooled to –78 °C, and $Cu(OTf)_2$ (0.25 g, 0.70 mmol) was added. The mixture was stirred for 2 h, then poured into a separatory funnel containing saturated aqueous sodium bicarbonate. The CH_2Cl_2 layer was removed, and additional CH_2Cl_2 (×2) was used to re-extract the aqueous layer. The combined organic layers were dried over Na_2SO_4 and then concentrated under reduced pressure. Flash chromatography of the residue (SiO_2 using 2.5% EtOAc in hexanes) provided **90** (0.025 g, 68%) as a colourless solid.

Procedure 3: A solution of AVK **26** (0.025 g, 0.14 mmol) and 2,3-dimethyl-1,3-butadiene (0.16 mL, 1.4 mmol) in CH_2Cl_2 (15 mL) was cooled to –78 °C, and $InCl_3$ (0.31 g, 1.4 mmol) was added. The mixture was stirred for 2 h, then poured into a separatory funnel containing saturated aqueous sodium bicarbonate. The CH_2Cl_2 layer was removed, and additional CH_2Cl_2 (×2) was used to re-extract the aqueous layer. The combined organic layers were dried over Na_2SO_4 and then concentrated under reduced pressure. Flash chromatography of the residue (SiO_2 using 2.5% EtOAc in hexanes) provided **90** (0.045 g, 59%) as a colourless solid.

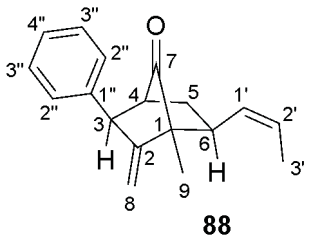
(1*R,2*S**,6*S**,7*R**)-1,2-Dimethyl-8-methylene-7-phenylbicyclo[4.2.1]non-3-en-9-one (86a), (1*R**,3*R**, 4*S**,6*S**)-1-methyl-2-methylene-3-phenyl-6-((*E*)-prop-1-enyl)bicyclo[2.2.1]-heptan-7-one (87), and (1*R**,2*R**,6*S**,7*R**)-1,2-dimethyl-8-methylene-7-phenylbicyclo[4.2.1]non-3-en-9-one (86b)**



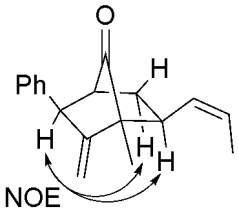
Following *Procedure 1* for **90**: AVK **26** (0.050 g, 0.28 mmol) and *trans*-piperylene (0.060 mL, 0.60 mmol) were reacted with $BF_3{\cdot}OEt_2$ (0.01 mL, 0.08 mmol) to yield **86a** (0.012 g, 17%) and **87** (0.024 g, 34%) as colourless oils. For **86a**: IR (film) 1742, 1604 (w) cm^{-1}; ^1H NMR δ: 7.27 (2H, m), 7.21 (1H, m), 7.07 (2H, m), 5.53 (1H, m), 5.47 (1H, m), 5.00 (1H, d, *J* = 2.4 Hz), 4.79 (1H, d, *J* = 2.4 Hz), 3.62 (1H, br s), 2.75 (1H, m), 2.43 (2H, m), 2.13 (1H, m), 1.26 (3H, s), 1.06 (3H, dd, *J* = 6.7, 1.5 Hz); ^{13}C NMR δ: 222.0, 154.5, 145.7, 135.0, 128.6 (2C), 128.1 (2C), 126.4, 124.0, 112.2, 57.5, 55.2, 51.9, 40.0, 33.1, 19.7, 16.7; HRMS (ESI) 275.1405, $[C_{18}H_{20}ONa]^+$ requires 275.1406. For **87**: IR (film) 1771, 1604 (w) cm^{-1}; ^1H NMR δ: 7.26 (2H, m), 7.19 (1H, m), 7.09 (2H, m), 5.44 (1H, dq, *J* = 15, 6.6 Hz), 5.10 (1H, m), 5.08 (1H, d, *J* = 2.1 Hz), 4.82 (1H, d, *J* = 2.1 Hz), 3.78 (1H, br s), 2.44 (1H, td, *J* = 10, 4.6 Hz), 2.25 (1H, d, *J* = 4.6 Hz), 2.19 (1H, dd, *J* = 13, 10 Hz), 1.74 (1H, dt, *J* = 13, 4.6 Hz), 1.67 (3H, d, *J* = 6.5 Hz), 1.03 (3H, s); ^{13}C NMR δ: 215.5, 153.5, 143.3, 131.9, 128.6 (2C), 127.3 (2C), 126.8, 126.6, 107.9, 52.7, 52.3, 47.9, 44.8, 32.5, 17.8, 9.7; HRMS (ESI) 275.1400, $[C_{18}H_{20}ONa]^+$ requires 275.1406.

Compound **87** (0.009 g, 0.04 mmol) was dissolved in CH_2Cl_2 (4 mL) at rt, and $BF_3{\cdot}OEt_2$ (0.2 mmol, 0.03 mL) was added. The mixture was stirred for 8 h, diluted with CH_2Cl_2, and washed with saturated $NaHCO_3$. After re-extraction with CH_2Cl_2, the combined organic layers were dried over Na_2SO_4, and concentrated. Purification by flash chromatography (2.5% EtOAc in hexanes) yielded 0.005 g (56%) of a 2.2:1 mixture of **86a** and **86b** (as determined by integration of the ^{1}H NMR spectrum). The following NMR data for **86b** were taken from the spectra of the mixture: ^{1}H NMR δ: 7.27 (2H, m), 7.18 (1H, m), 7.04 (2H, m), 5.72 (1H, m), 5.56 (1H, m), 5.05 (1H, d, *J* = 2.3 Hz), 4.89 (1H, d, *J* = 2.3 Hz), 3.67 (1H, br s), 2.72 (1H, m), 2.40 (1H, overlapped), 2.34 (1H, m), 2.23 (1H, m) 1.31 (3H, s), 0.95 (3H, d, *J* = 7.0 Hz); ^{13}C NMR δ: 220.1, 160.1, 146.7, 135.0, 128.7 (2C), 127.0 (2C), 126.3, 122.9, 109.6, 55.8, 55.2, 51.9, 45.6, 31.1, 20.3, 15.3.

(1*R,3*R**,4*S**,6*S**)-1-Methyl-2-methylene-3-phenyl-6-((*Z*)-prop-1-enyl)bicyclo [2.2.1]heptan-7-one (88)**



88

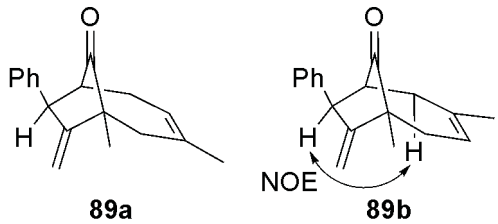


88

According to *Procedure 1* for **90**: AVK **26** (0.050 g, 0.28 mmol) and *cis*-piperylene (0.060 mL, 0.60 mmol) were reacted with $BF_3{\cdot}OEt_2$ (0.01 mL, 0.08 mmol) to yield **88** (0.038 g, 54%) as a colourless solid: mp 72–75 °C; IR (film) 1773, 1602 (w) cm^{-1}; ^{1}H NMR δ: 7.26 (2H, m, H3''), 7.19 (1H, m, H4''), 7.09 (2H, m, H2''), 5.54 (1H,

dq, *J* = 11, 6.8 Hz, H2'), 5.12 (1H, d, *J* = 1.9 Hz, H8a), 5.07 (1H, tq, *J* = 11, 1.9 Hz, H1'), 4.85 (1H, d, *J* = 1.9 Hz, H8b), 3.82 (1H, br s, H3), 2.87 (1H, td, *J* = 11, 4.7 Hz, H6), 2.27 (1H, d, *J* = 4.7 Hz, H4), 2.22 (1H, dd, *J* = 13, 11 Hz, H5a), 1.69 (1H, dt, *J* = 13, 4.7 Hz, H5b), 1.63 (3H, dd, *J* = 6.8, 1.9 Hz, H3'), 1.06 (3H, s, H9); ^{13}C NMR δ: 215.1 (C7), 153.5 (C2), 143.3 (C1''), 131.4 (C1'), 128.6 (2C, C3''), 127.3 (2C, C2''), 126.7 (C4''), 125.2 (C1'), 108.0 (C8), 52.8 (C3), 52.1 (C1), 47.9 (C4), 38.5 (C6), 32.8 (C5), 13.0 (C3'), 9.1 (C9); HRMS (ESI) 275.1398, $[C_{18}H_{20}ONa]^+$ requires 275.1406.

(1*R,6*S**,7*R**)-1,4-Dimethyl-8-methylene-7-phenylbicyclo[4.2.1]non-3-en-9-one (89a) and (1*R**,6*S**,7*R**)-1,3-dimethyl-8-methylene-7-phenylbicyclo[4.2.1]non-3-en-9-one (89b)**

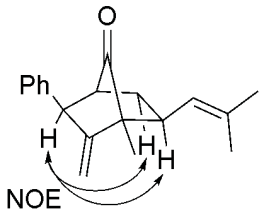


89a **89b**

According to *Procedure 1* for **90**: AVK **26** (0.050 g, 0.28 mmol) and isoprene (0.060 mL, 0.60 mmol) reacted in the presence of $BF_3{\cdot}OEt_2$ (0.01 mL, 0.08 mmol) to yield 0.040 g (56%) of a 1:2.8 mixture of **89a** and **89b** (as determined by integration of the ^{1}H NMR spectrum); IR (film) 1745, 1602 (w) cm^{-1}; HRMS (ESI) 275.1403, $[C_{18}H_{20}ONa]^+$ requires 275.1406. The following NMR data were taken from the spectra of the mixture: for **89a**: ^{1}H NMR δ: 7.26 (2H, m), 7.19 (1H, m), 7.03 (2H, m), 5.43 (1H, m), 5.07 (1H, d, *J* = 2.2 Hz), 4.83 (1H, d, *J* = 2.2 Hz), 3.65 (1H, br s), 2.76 (1H, m), 2.39 (1H, br d, *J* = 17 Hz), 2.30 (1H, dd, *J* = 17, 4.9 Hz), 2.20 (1H, br d, *J* = 16 Hz), 2.15 (1H, dd, *J* = 16, 6.0 Hz), 1.81 (3H, s), 1.30 (3H, s); ^{13}C NMR δ: 221.8, 158.2, 146.3, 132.6,

128.7 (2C), 127.3 (2C), 126.3, 121.8, 109.6, 55.0, 54.6, 51.8, 43.7, 36.7, 28.2, 21.0; for **89b**: ^{1}H NMR δ: 7.26 (2H, m), 7.19 (1H, m), 7.03 (2H, m), 5.47 (1H, m), 5.07 (1H, d, *J* = 2.1 Hz), 4.87 (1H, d, *J* = 2.2 Hz), 3.70 (1H, m), 2.76 (1H, m), 2.47 (1H, m), 2.41 (1H, m), 2.18 (1H, overlapped), 1.98 (1H, d, *J* = 16 Hz), 1.72 (3H, s), 1.31 (3H, s); ^{13}C NMR δ: 222.3, 157.8, 146.4, 134.5, 128.7 (2C), 121.2 (2C), 126.3, 120.3, 109.4, 55.9, 53.2, 51.7, 47.4, 33.1, 28.4, 21.6.

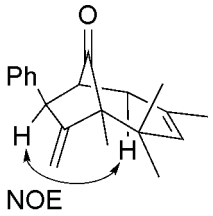
(1*R,3*R**,4*S**,6*S**)-1-Methyl-2-methylene-6-(2-methylprop-1-enyl)-3-phenylbicyclo [2.2.1]heptan-7-one (91a)**



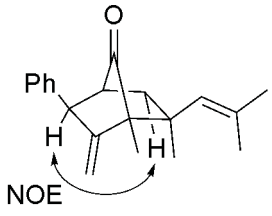
91a

According to *Procedure 1* for **90**: AVK **26** (0.050 g, 0.28 mmol) and 4-methyl-1,3-pentadiene (0.065 mL, 0.56 mmol) reacted in the presence of $BF_3{\cdot}OEt_2$ (0.01 mL, 0.08 mmol) to yield **91a** (0.064 g, 85%) as a colourless solid: mp 68–70 °C; IR (film) 1771, 1604 (w) cm^{-1}; ^{1}H NMR δ: 7.26 (2H, m), 7.19 (1H, m), 7.09 (2H, m), 5.10 (1H, d, *J* = 2.4 Hz), 4.83 (1H, d, *J* = 2.4 Hz), 4.81 (1H, d, *J* = 10 Hz), 3.80 (1H, br s), 2.74 (1H, td, *J* = 10, 4.5 Hz), 2.23 (1H, d, *J* = 4.5 Hz), 2.21 (1H, dd, *J* = 10, 13 Hz), 1.71 (3H, br d, *J* = 0.9 Hz), 1.67 (1H, dt, *J* = 13, 4.5 Hz), 1.62 (3H, br d, *J* = 1.2 Hz), 1.03 (3H, s); ^{13}C NMR δ: 215.5, 153.7, 143.3, 133.4, 128.5 (2C), 127.3 (2C), 126.6, 126.0, 107.8, 52.7, 52.4, 47.9, 39.9, 33.2, 25.7, 18.1, 9.1; HRMS (ESI) 289.1557, $[C_{19}H_{22}ONa]^{+}$ requires 289.1563.

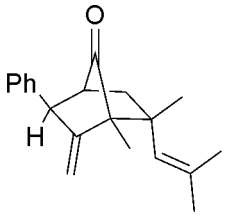
(1*R,6*S**,7*R**)-1,2,2,4-Tetramethyl-8-methylene-7-phenylbicyclo[4.2.1]non-3-en-9-one (92), (1*R**,2*R**,4*R**,5*S**)-1,2-dimethyl-6-methylene-2-(2-methylprop-1-enyl)-5-phenylbicyclo[2.2.1]heptan-7-one (93a), and (1*R**,2*S**,4*R**,5*S**)-1,2-dimethyl-6-methylene-2-(2-methylprop-1-enyl)-5-phenyl-bicyclo[2.2.1]heptan-7-one (93b)**



92



93a

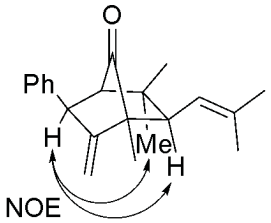


93b

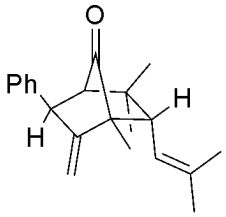
According to *Procedure 1* for **90**: AVK **26** (0.050 g, 0.28 mmol) and 2,4-dimethyl-1,3-pentadiene (0.070 mL, 0.56 mmol) reacted in the presence of $BF_3{\cdot}OEt_2$ (0.01 mL, 0.08 mmol) to provide 0.055 g (71%) of a 1.2:1.1:1.0 mixture of **10**, **11a**, and **11b** respectively (as determined by integration of the ^{1}H NMR spectrum), as an inseparable mixture; IR (film) 1773, 1739, 1602 (w) cm^{-1}; HRMS (ESI) 303.1724, $[C_{20}H_{24}ONa]^+$ requires 303.1719. The following NMR data were taken from the spectra of the mixture: for **92**: ^{1}H NMR δ: 7.26 (2H, m), 7.18 (1H, m), 7.03 (2H, m), 5.27 (1H, br s), 5.02 (1H, d, *J* = 2.4 Hz), 4.81 (1H, d, *J* = 2.4 Hz), 3.56 (1H, m), 2.64 (1H, m), 2.43 (1H, br d, *J* = 17 Hz), 2.25 (1H, overlapped), 1.79 (3H, s), 1.21 (3H, s), 1.12 (3H, s), 0.94 (3H, s); ^{13}C NMR δ: 221.1, 157.1, 146.6, 136.5, 128.9, 128.6 (2C), 127.8 (2C), 126.3, 112.9, 59.7, 55.1, 51.4, 40.3, 36.6, 28.8, 25.8, 24.6, 17.0; for **93a**: ^{1}H NMR δ: 7.26 (2H, m), 7.18 (1H, m), 7.09 (2H, m), 5.29 (1H, br s), 5.13 (1H, d, *J* = 2.1 Hz), 5.01 (1H, d, *J* = 2.1 Hz), 3.61 (1H, br s), 2.64 (1H, m), 2.35 (1H, dd, *J* = 12, 5.4 Hz), 2.13 (1H, m), 1.79 (1H, d, *J* = 12 Hz), 1.71 (3H, s), 1.67 (3H, s), 1.28 (3H, s), 1.14 (3H, s); ^{13}C NMR δ: 221.1, 157.1, 146.6, 136.5, 128.9, 128.6 (2C), 127.8 (2C), 126.3, 112.9, 59.7, 55.1, 51.4, 40.3, 36.6, 28.8, 25.8, 24.6, 17.0; for **93b**: ^{1}H NMR δ: 7.26 (2H, m), 7.18 (1H, m),

7.09 (2H, m), 5.32 (1H, br s), 5.12 (1H, d, *J* = 2.1 Hz), 4.95 (1H, d, *J* = 2.1 Hz), 3.61 (1H, br s), 2.25 (2H, m), 2.13 (1H, m), 1.71 (3H, s), 1.70 (3H, s), 1.09 (3H, s), 1.07 (3H, s); ^{13}C NMR δ: 215.2, 150.3, 143.5, 132.2, 129.9, 128.5 (2C), 127.4 (2C), 126.6, 111.7, 57.0, 53.0, 48.4, 42.8, 38.7, 26.7, 26.0, 19.9, 8.1.

(1*R,2*R**,4*R**,5*R**)-1,3,3-Trimethyl-6-methylene-2-(2-methylprop-1-enyl)-5-phenyl bicyclo[2.2.1]-heptan-7-one (94a) and (1*R**,2*S**,4*R**,5*R**)-1,3,3-trimethyl-6-methylene-2-(2-methylprop-1-enyl)-5-phenylbicyclo[2.2.1]heptan-7-one (94b)**



94a

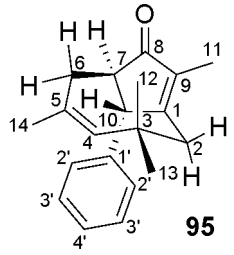


94b

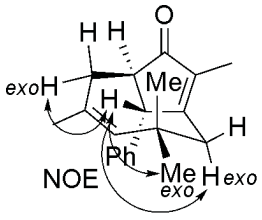
According to *Procedure 1* for **90**: AVK **26** (0.050 g, 0.28 mmol) and 2,5-dimethyl-2,4-hexadiene (0.080 mL, 0.56 mmol) reacted in the presence of $BF_3{\cdot}OEt_2$ (0.01 mL, 0.08 mmol) to yield 0.040 g (49%) of a 5:1 mixture of **94a** and **94b** (as determined by integration of the ^{1}H NMR spectrum); IR (film) 1771, 1603 (w) cm^{-1}; HRMS (ESI) 317.1876, $[C_{21}H_{26}ONa]^+$ requires 317.1876. The following NMR data were taken from the spectra of the mixture: for **94a**: ^{1}H NMR δ: 7.26 (2H, m), 7.18 (1H, m), 7.10 (2H, m), 5.07 (1H, d, *J* = 2.3 Hz), 4.83 (1H, d, *J* = 11 Hz), 4.82 (1H, d, *J* = 2.3 Hz), 4.15 (1H, br s), 2.45 (1H, d, *J* = 11 Hz), 1.89 (1H, m), 1.75 (3H, br d, *J* = 1.0 Hz), 1.62 (3H, br d, *J* = 1.2 Hz), 1.28 (3H, s), 0.97 (3H, s), 0.87 (3H, s); ^{13}C NMR δ: 215.0, 154.1, 143.4, 134.4, 128.6 (2C), 127.5 (2C), 126.5, 121.4, 107.0, 60.3, 55.1, 52.7, 46.2, 36.4, 26.9, 26.0, 25.2, 17.9, 9.6; for **94b**: ^{1}H NMR δ: 7.26 (2H, m), 7.18 (1H, m), 7.10 (2H, m), 5.13 (1H, m), 5.02 (2H, m), 4.01 (1H, br s), 2.29 (1H, d, *J* = 10 Hz), 1.89 (1H, m), 1.79 (3H, br d, *J* =

0.9 Hz), 1.63 (3H, br d, *J* = 1.2 Hz), 1.09 (3H, s), 1.05 (3H, s), 1.00 (3H, s); ^{13}C NMR δ: 215.0, 147.8, 143.4, 136.3, 128.6 (2C), 127.5 (2C), 126.5, 120.0, 111.3, 60.4, 56.9, 49.5, 46.5, 36.6, 31.7, 26.3, 21.1, 18.5, 11.2.

(7*R,10*S**,4*Z*)-3,3,5,9-Tetramethyl-10-phenylbicyclo[5.2.1]deca-1(9),4-dien-8-one (95)**



95

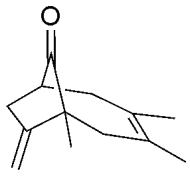


95

A mixture of **92**, **93a**, and **93b** (1.2:1.1:1.0, respectively) (0.008 g, 0.03 mmol) was dissolved in CH_2Cl_2 (3 mL) at rt, and $BF_3{\cdot}OEt_2$ (0.2 mmol, 0.03 mL) was added. The mixture was stirred for 3 h, diluted with CH_2Cl_2, and washed with saturated $NaHCO_3$. After re-extraction with CH_2Cl_2, the combined organic layers were dried over Na_2SO_4, and concentrated. Purification by flash chromatography (10% EtOAc in hexanes) yielded **95** (0.006 g, 75%) as a colourless oil; IR (film) 1705, 1637, 1601 (w) cm^{-1}; ^{1}H NMR δ: 7.26 (2H, m, H3'), 7.21 (1H, m, H4'), 7.14 (2H, m, H2'), 5.49 (1H, br q, *J* = 1.4 Hz, H4), 4.12 (1H, s, H10), 2.78 (1H, t, *J* = 6.0 Hz, H7), 2.56 (1H, d, *J* = 12 Hz, H2a), 2.52 (1H, d, *J* = 12 Hz, H2b), 2.46 (1H, dd, *J* = 13, 6.0 Hz, H6a), 2.42 (1H, dd, *J* = 13, 6.0 Hz, H6b), 1.74 (3H, s, H11), 1.73 (3H, d, *J* = 1.4 Hz, H14), 1.35 (3H, s, H13), 1.13 (3H, s, H12); ^{13}C NMR δ: 211.4 (C8), 176.1 (C1), 142.5 (C1'), 135.5 (C4), 135.3 (C5), 132.3 (C9), 128.7 (2C, C3'), 127.3 (2C, C2'), 126.8 (C4'), 56.7 (C10), 54.4 (C7), 45.3 (C2), 41.4

(C3), 36.2 (C6), 33.4 (C13), 30.4 (C14), 28.2 (C12), 9.5 (C11); HRMS (ESI) 303.1717, $[C_{20}H_{24}ONa]^+$ requires 303.1719.

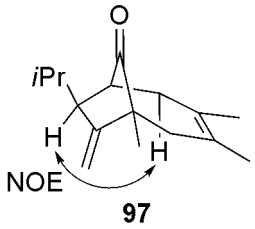
(1*R,6*S**)-1,3,4-Trimethyl-8-methylenebicyclo[4.2.1]non-3-en-9-one (96)**



96

According to *Procedure 1* for **90**: AVK **27** (0.025 g, 0.23 mmol) and 2,3-dimethyl-1,3-butadiene (0.050 mL, 0.44 mmol) reacted in the presence of $BF_3{\cdot}OEt_2$ (0.01 mL, 0.08 mmol) to yield **96** (0.031 g, 71%) as a colourless oil; IR (film) 1747 cm^{-1}; ^1H NMR δ: 4.92 (1H, t, *J* = 2.1 Hz), 4.90 (1H, t, *J* = 2.1 Hz), 2.63 (2H, m), 2.40 (1H, br d, *J* = 16 Hz), 2.32 (1H, m), 2.23 (2H, m), 1.94 (1H, d, *J* = 16 Hz), 1.73 (3H, s), 1.65 (3H, s), 1.16 (3H, s); ^{13}C NMR δ: 222.9, 152.4, 127.5, 125.4, 106.1, 53.0, 50.7, 45.4, 39.8, 32.5, 23.8 (2C), 20.0; HRMS (ESI) 213.1254, $[C_{13}H_{18}ONa]^+$ requires 213.1250.

(1*R,6*S**,7*R**)-7-Isopropyl-1,3,4-trimethyl-8-methylenebicyclo[4.2.1]non-3-en-9-one (97)**

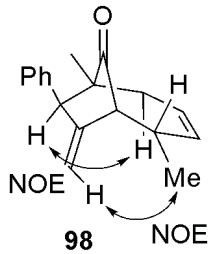


97

According to *Procedure 1* for **90**: AVK **29** (0.040 g, 0.27 mmol) and 2,3-dimethyl-1,3-butadiene (0.060 mL, 0.56 mmol) reacted in the presence of $BF_3{\cdot}OEt_2$ (0.01

mL, 0.08 mmol) to yield **97** (0.040 g, 64%) as a colourless oil; IR 1747; ^{1}H NMR δ: 4.98 (2H, m), 2.43 (2H, m), 2.36 (1H, m), 2.19 (2H, m), 1.95 (1H, d, *J* = 16 Hz), 1.86 (1H, m), 1.72 (3H, s), 1.63 (3H, s), 1.16 (3H, s), 0.89 (3H, d, *J* = 6.9 Hz), 0.65 (3H, d, *J* = 6.9 Hz); ^{13}C NMR δ: 224.0, 157.0, 127.3, 125.8, 106.2, 53.8, 51.1, 50.9, 48.3, 40.4, 33.6, 23.8 (2C), 20.4, 20.1, 17.2; HRMS (ESI) 255.1710, $[C_{16}H_{24}ONa]^{+}$ requires 255.1719.

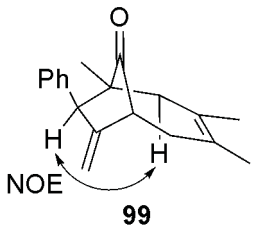
(1*R,5*R**,6*S**,8*S**)-1,5-Dimethyl-7-methylene-8-phenylbicyclo[4.2.1]non-3-en-9-one (98)**



98

According to the procedure for **99**: AVK **35** (0.10 g, 0.54 mmol) and *trans*-piperylene (0.30 mL, 3.0 mmol) were reacted with $BF_3{\cdot}OEt_2$ (0.070 mL, 0.60 mmol) to yield **98** (0.068 g, 50%) as a colourless oil: IR (film) 1741, 1601 cm^{-1}; ^{1}H NMR δ: 7.25 (3H, m), 7.00 (2H, m), 5.65 (1H, m), 5.47 (1H, m), 5.15 (1H, t, *J* = 2.0 Hz), 4.92 (1H, t, *J* = 2.0 Hz), 3.76 (1H, m), 3.10 (1H, m), 2.59 (1H, m), 2.34 (1H, dd, *J* = 17, 7.5 Hz), 2.11 (1H, m), 1.30 (3H, d, *J* = 7.5 Hz), 0.68 (3H, s); ^{13}C NMR δ: 222.5, 149.4, 144.0, 135.1, 129.5, 128.1, 126.4, 125.3, 113.6, 60.0, 58.2, 53.8, 43.2, 36.1, 20.7, 20.4; HRMS (ESI) 275.1400, $[C_{18}H_{20}ONa]^{+}$ requires 275.1406.

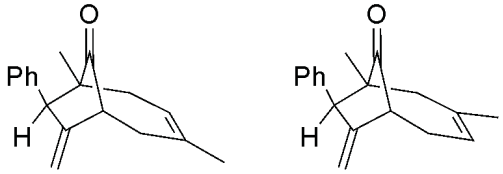
***(1R*,6S*,8S*)*-1,3,4-Trimethyl-7-methylene-8-phenylbicyclo[4.2.1]non-3-en-9-one (99)**



99

$BF_3{\cdot}OEt_2$ (1.1 equiv) was added to a solution of AVK **35** (0.10 g, 0.54 mmol) and 2,3-dimethylbutadiene (0.30 mL, 2.7 mol) in CH_2Cl_2 (55 mL) at -78 °C. The solution was stirred for 10 min, and it was poured into a separatory funnel containing a saturated solution of sodium bicarbonate. The aqueous layer was extracted thoroughly with CH_2Cl_2. The combined organic solutions were dried over $MgSO_4$ and concentrated under vacuum. Flash chromatography of the residue (2.5% EtOAc in hexanes) yielded **99** (0.11 g, 79%) as a colourless oil: IR (film) 1743, 1597 cm^{-1}; ^1H NMR δ: 7.22 (2H, m), 7.17 (1H, m), 6.92 (2H, m), 5.11 (1H, t, *J* = 1.9 Hz), 4.87 (1H, t, *J* = 1.9 Hz), 3.63 (1H, m), 3.24 (1H, m), 2.54 (1H, br d, *J* = 16 Hz), 2.42 (1H dd, *J* = 16, 7.7 Hz), 2.25 (1H, d, *J* = 16 Hz), 2.18 (1H, d, *J* = 16 Hz), 1.81 (3H, s), 1.72 (3H, s), 0.68 (3H, s); ^{13}C NMR δ: 222.9, 152.1, 144.5, 129.1, 128.6, 128.1, 126.7, 126.5, 111.1, 57.9, 54.9, 53.4, 50.6, 41.7, 24.6, 23.9, 20.3; HRMS (ESI) 289.1556, $[C_{19}H_{22}ONa]^+$ requires 289.1563.

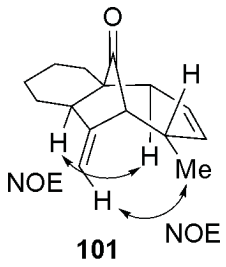
(1*R,6*S**,8*S**)-1,3-Dimethyl-7-methylene-8-phenylbicyclo[4.2.1]non-3-en-9-one (100a) and (1*R**,6*S**,8*S**)-1,4-dimethyl-7-methylene-8-phenylbicyclo[4.2.1]non-3-en-9-one (100b)**



100a **100b**

According to the procedure for **99**: AVK **35** (0.10 g, 0.54 mmol) and isoprene (0.30 mL, 3.0 mmol) were reacted with $BF_3{\cdot}OEt_2$ (0.070 mL, 0.60 mmol) to yield 0.098 g (73%) of a 4:1 mixture of **100a** and **100b** (as determined by integration of the ^{1}H NMR spectrum); IR (film) 1748, 1605 (w) cm^{-1}; HRMS (ESI) 275.1398, $[C_{18}H_{20}ONa]^+$ requires 275.1406. The following NMR data were taken from the spectra of the mixture: for **100a**: ^{1}H NMR δ: 7.24 (2H, m), 7.18 (1H, m), 6.94 (2H, m), 5.47 (1H, m), 5.13 (1H, m), 4.93 (1H, m), 3.73 (1H, m), 3.32 (1H, m), 2.48 (1H, *overlapped*), 2.29 (2H, m), 2.10 (1H, *overlapped*), 1.74 (3H, s), 0.72 (3H, s); ^{13}C NMR δ: 222.3, 152.2, 144.5, 134.5, 128.8 (2C), 128.5 (2C), 126.6, 121.1, 110.9, 58.8, 55.4, 52.5, 43.5, 38.3, 28.2, 20.7; for **100b**: ^{1}H NMR δ: 7.24 (1H, m), 7.18 (2H, m), 6.94 (2H, m), 5.47 (1H, m), 5.15 (1H, m), 4.92 (1H, m), 3.73 (1H, m), 3.32 (1H, m), 2.48 (2H, m), 2.10 (1H, *overlapped*), 1.98 (1H, m), 1.81 (3H, s), 0.71 (3H, s); ^{13}C NMR δ: 222.1, 152.5, 144.2, 133.3, 128.8 (2C), 128.5 (2C), 126.6, 121.5, 111.3, 58.7, 54.1, 53.7, 47.6, 35.1, 29.0, 20.2.

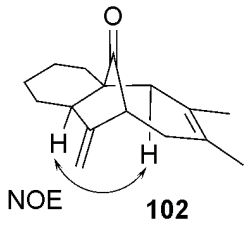
(1*R,3*R**,8*S**,12*S**)-12-Methyl-2-methylenetricyclo[6.4.1.0^{3,8}]triscadec-10-en-13-one (101)**



101

According to the procedure for **99**: AVK **37** (0.080 g, 0.54 mmol) and *trans*-piperylene (0.30 mL, 3.0 mmol) were reacted with $BF_3{\cdot}OEt_2$ (0.070 mL, 0.60 mmol) to yield **101** (0.053 g, 48%) as a colourless oil: IR (film) 1748 cm^{-1}; ^1H NMR δ: 5.46 (1H, m), 5.24 (1H, m), 5.02 (1H, m), 4.97 (1H, m), 2.93 (1H, m), 2.58 (1H, m), 2.40 (1H, m), 2.13 (2H, m), 1.94 (1H, m), 1.82 (1H, m), 1.59 (2H, m), 1.29 (3H, d, *J* = 7.5 Hz), 1.14 (3H, m), 0.94 (1H, m); ^{13}C NMR δ: 221.4, 151.4, 132.6, 125.2, 108.2, 56.0, 53.0, 49.4, 42.2, 36.6, 34.4, 30.5, 23.6, 22.6, 20.7; HRMS (ESI) 239.1397, $[C_{15}H_{20}ONa]^+$ requires 239.1406.

(1*R,3*R**,8*S**)-10,11-Dimethyl-2-methylenetricyclo[6.4.1.0^{3,8}]triscadec-10-en-13-one (102)**

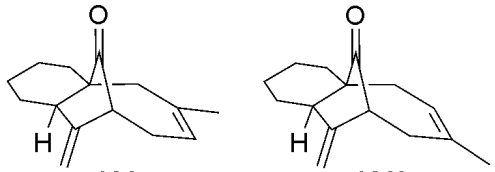


102

According to the procedure for **99**: AVK **37** (0.080 g, 0.54 mmol) and 2,3-dimethyl-1,3-butadiene (0.30 mL, 2.7 mmol) were reacted with $BF_3{\cdot}OEt_2$ (0.070 mL, 0.60 mmol) to yield **102** (0.089 g, 74%) as a colourless oil: IR (film) 1746 cm^{-1}; ^1H NMR δ:

4.94 (1H, m), 4.86 (1H, m), 2.99 (1H, m), 2.55 (1H, br d, *J* = 17 Hz), 2.40 (1H, dd, *J* = 13, 6.3 Hz), 2.33 (1H, dd, *J* = 17, 6.3 Hz), 2.17 (1H, m), 2.03 (1H, m), 1.89 (1H, m), 1.63 (3H, s), 1.60 (3H, s), 1.58 (2H, m), 1.13 (3H, m), 0.86 (1H, m); ^{13}C NMR δ: 220.9, 152.7, 125.5, 124.8, 105.3, 54.0, 49.8 (2C), 49.4, 40.8, 33.9, 30.9, 24.3, 23.7, 23.2, 22.7; HRMS (ESI) 253.1553, $[C_{16}H_{22}ONa]^+$ requires 253.1563.

(1*R,3*R**,8*S**)-10-Methyl-2-methylenetricyclo[6.4.1.0^{3,8}]triscadec-10-en-13-one (103a) and (1*R**,3*R**,8*S**)-11-methyl-2-methylenetricyclo[6.4.1.0^{3,8}]triscadec-10-en-13-one (103b)**

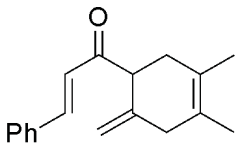


103a **103b**

According to the procedure for **99**: AVK **37** (0.080 g, 0.54 mmol) and isoprene (0.30 mL, 3.0 mmol) were reacted with $BF_3{\cdot}OEt_2$ (0.070 mL, 0.60 mmol) to yield 0.072 g (65%) of a 1.3:1 mixture of **103a** and **103b** (as determined by integration of the ^{1}H NMR spectrum); IR (film) 1748 cm^{-1}; HRMS (ESI) 239.1393, $[C_{15}H_{20}ONa]^+$ requires 239.1406. The following NMR data were taken from the spectra of the mixture: for **103a**: ^{1}H NMR δ: 5.24 (1H, m), 4.99 (1H, m), 4.88 (1H, m), 3.07 (1H, m), 2.41 (2H, m), 2.21 (1H, dd, *J* = 18, 5.4 Hz), 2.17 (1H, m), 2.09 (1H, dd, *J* = 17, 5.7 Hz), 1.95 (1H, m), 1.81 (1H, m), 1.64 (3H, s), 1.59 (3H, m), 1.14 (3H, m), 0.89 (1H, m); ^{13}C NMR δ:. 220.3, 152.9, 131.4, 121.3, 105.3, 54.7, 50.5, 48.6, 42.4, 36.8, 34.0, 30.6, 27.3, 24.3, 23.2; for **103b**: ^{1}H NMR δ: 5.19 (1H, m), 4.99 (1H, m), 4.89 (1H, m), 3.07 (1H, m), 2.50 (1H, br d, *J* = 17 Hz), 2.41 (2H, *overlapped*), 2.17 (1H, m), 1.95 (1H, m), 1.86 (1H, br d, *J* = 17

Hz), 1.81 (1H, m), 1.66 (3H, s), 1.59 (3H, m), 1.14 (3H, m), 0.89 (1H, m); ^{13}C NMR δ: 220.2, 152.8, 132.7, 119.7, 105.9, 53.5, 50.5, 49.4, 46.4, 33.9, 33.8, 30.9, 28.5, 24.2, 23.1.

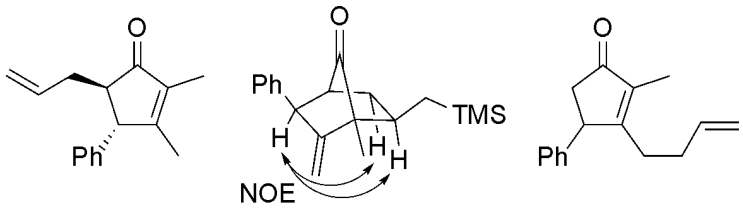
(*E*)-1-(3,4-Dimethyl-6-methylenecyclohex-3-enyl)-3-phenylprop-2-en-1-one (104)



104

$BF_3{\cdot}OEt_2$ (1.1 equiv) was added to a solution of AVK **36** (0.070 g, 0.41 mmol) and 2,3-dimethylbutadiene (0.25 mL, 2.2 mol) in CH_2Cl_2 (40 mL) at -78 °C. The solution was stirred for 1 h, and it was poured into a separatory funnel containing a saturated solution of sodium bicarbonate. The aqueous layer was extracted thoroughly with CH_2Cl_2. The combined organic solutions were dried over $MgSO_4$ and concentrated under vacuum. Flash chromatography of the residue (2.5% EtOAc in hexanes) yielded **104** (0.051 g, 51%) as an off-white solid: mp 71–74 °C; IR (film) 1695, 1614 cm^{-1}; ^{1}H NMR δ: 7.63 (1H, d, *J* = 16 Hz), 7.55 (2H, m), 7.38 (3H, m), 6.97 (1H, d, *J* = 16 Hz), 4.98 (1H, m), 4.86 (1H, m), 3.57 (1H, t, *J* = 5.7 Hz), 2.74 (1H, d, *J* = 19 Hz), 2.69 (1H, d, *J* = 19 Hz), 2.63 (1H, br d, *J* = 19 Hz), 1.65 (1H, br d, *J* = 19 Hz), 1.68 (3H, s), 1.62 (3H, s); ^{13}C NMR δ: 199.4, 144.8, 142.6, 134.9, 130.6, 129.1 (2C), 128.6 (2C), 124.8, 124.3, 124.1, 110.9, 54.2, 39.6, 34.4, 19.0, 18.9; HRMS (ESI) 275.1403, $[C_{18}H_{20}ONa]^+$ requires 275.1406.

(*trans*)-5-Allyl-2,3-dimethyl-4-phenylcyclopent-2-enone (105), (1*R,3*R**,4*S**,6*R**)-1-methyl-2-methylene-3-phenyl-6-((trimethylsilyl)methyl)bicyclo[2.2.1]heptan-7-one (106a), and 3-(but-3-enyl)-2-methyl-4-phenylcyclopent-2-enone (107)**



105 **106a** **107**

Procedure 1: A solution of AVK **26** (0.050 g, 0.28 mmol) and allyltrimethylsilane (0.090 mL, 0.56 mmol) in CH_2Cl_2 (25 mL) was cooled to –78 °C, and $BF_3{\cdot}OEt_2$ (0.040 mL, 0.31 mmol) was added. The mixture was stirred for 5 min, then poured into a separatory funnel containing saturated aqueous sodium bicarbonate. The CH_2Cl_2 layer was removed, and additional CH_2Cl_2 (×2) was used to re-extract the aqueous layer. The combined organic layers were dried over Na_2SO_4 and then concentrated under reduced pressure. Flash chromatography of the residue (2.5%, then 10%, EtOAc in hexanes) provided **105** (0.020 g, 27%) and **106a** (0.045 g, 54%). For **105**: colourless oil; IR (film) 1702, 1650, 1604 (w) cm^{-1}; ^1H NMR δ: 7.31 (2H, m), 7.24 (1H, m), 7.07 (2H, m), 5.70 (1H, m), 5.10 (1H, d of narrow m, J = 17 Hz), 5.02 (1H, d of narrow m, J = 10 Hz), 3.50 (1H, br d, $J \approx 3$ Hz), 2.58 (1H, m), 2.40 (1H, m), 2.28 (1H, ddd, J = 8.9, 4.3, 2.5 Hz), 1.80 (6H, s); ^{13}C NMR δ: 210.1, 170.3, 141.8, 136.3, 135.6, 128.8 (2C), 127.9 (2C), 126.9, 117.0, 55.3, 54.7, 35.6, 15.5, 8.3; HRMS (ESI) 249.1242, $[C_{16}H_{18}ONa]^+$ requires 249.1250. For **106a**: colourless solid; mp 78–79 °C; IR (film) 1763, 1603 (w) cm^{-1}; ^1H NMR δ: 7.27 (2H, m), 7.19 (1H, m), 7.09 (2H, m), 5.05 (1H, d, J = 2.2 Hz), 4.79 (1H, d, J = 2.2 Hz), 3.76 (1H, br s), 2.22 (1H, d, J = 4.7 Hz), 2.15 (1H, dd, J = 13, 10 Hz), 1.95 (1H, m), 1.53 (1H, dd, J = 13, 4.9 Hz), 1.10 (3H, s), 0.76 (1H, dd, J = 14, 2.5 Hz), 0.27

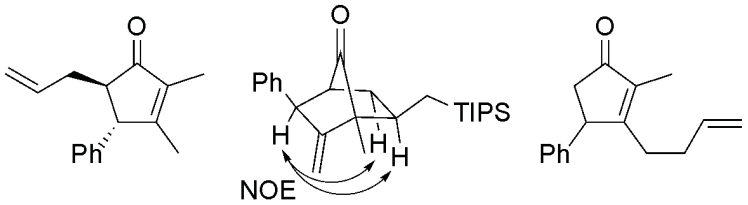
(1H, t, J = 14 Hz), 0.03 (9H, s); ^{13}C NMR δ: 215.5, 154.4, 143.4, 128.6 (2C), 127.3 (2C), 126.6, 107.4, 53.1, 52.5, 48.2, 37.9, 34.4, 20.8, 9.3, -0.6 (3C); HRMS (ESI) 321.1644, $[C_{19}H_{26}OSiNa]^+$ requires 321.1645.

Procedure 2: A solution of AVK **26** (0.025 g, 0.14 mmol) and allyltrimethylsilane (0.11 mL, 0.070 mmol) in CH_2Cl_2 (15 mL) was cooled to –78 °C, and $Cu(OTf)_2$ (0.25 g, 0.070 mmol) was added. The mixture was stirred for 2 h, then poured into a separatory funnel containing saturated aqueous sodium bicarbonate. The CH_2Cl_2 layer was removed, and additional CH_2Cl_2 (×2) was used to re-extract the aqueous layer. The combined organic layers were dried over Na_2SO_4 and then concentrated under reduced pressure. Flash chromatography of the residue (2.5%, then 10%, EtOAc in hexanes) provided **105** (0.008 g, 20%), **106a** (0.003 g, 10%), and **105** (0.013 g, 42%). For **107**: colourless oil; IR (film) 1702, 1643, 1602 (w) cm^{-1}; ^{1}H NMR δ: 7.32 (2H, m), 7.25 (1H, m), 7.09 (2H, m), 5.70 (1H, m), 4.98 (1H, d of narrow m, J = 15 Hz), 4.95 (1H, d of narrow m, J = 7.4 Hz), 3.94 (1H, m), 2.90 (1H, dd, J = 19, 7.0 Hz), 2.51 (1H, m), 2.36 (1H, dd, J = 19, 2.2 Hz), 2.18 (1H, m), 2.09 (2H, m), 1.80 (3H, s); ^{13}C NMR δ: 209.3, 174.1, 142.0, 137.5, 137.1, 129.0 (2C), 127.4 (2C), 127.1, 115.6, 47.0, 44.7, 31.2, 28.5, 8.4; HRMS (ESI) 249.1244, $[C_{16}H_{18}ONa]^+$ requires 249.1250.

Procedure 3: A solution of AVK **26** (0.025 g, 0.14 mmol) and allyltrimethylsilane (0.23 mL, 1.4 mmol) in CH_2Cl_2 (15 mL) was cooled to –78 °C, and $InCl_3$ (0.31 g, 1.4 mmol) was added. The mixture was stirred for 2 h, then poured into a separatory funnel containing saturated aqueous sodium bicarbonate. The CH_2Cl_2 layer was removed, and additional CH_2Cl_2 (×2) was used to re-extract the aqueous layer. The combined organic

layers were dried over Na_2SO_4 and then concentrated under reduced pressure. Flash chromatography of the residue (10% EtOAc in hexanes) provided **105** (0.014 g, 22%) and **107** (0.036 g, 56%).

(*trans*)-5-Allyl-2,3-dimethyl-4-phenylcyclopent-2-enone (105), (1*R,3*R**,4*S**,6*R**)-1-methyl-2-methylene-3-phenyl-6-((triisopropylsilyl)methyl)bicyclo[2.2.1]heptan-7-one (106b), and 3-(but-3-enyl)-2-methyl-4-phenylcyclopent-2-enone (107)**

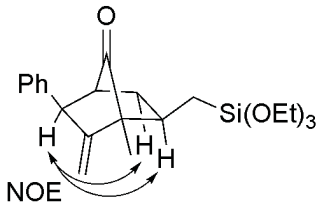


105 **106b** **107**

According to *Procedure 1* for **105** and **106a**: AVK **26** (0.050 g, 0.28 mmol) and allyltriisopropylsilane (0.13 mL, 0.56 mmol) were reacted in the presence of $BF_3{\cdot}OEt_2$ (0.040 mL, 0.31 mmol) to yield **105** (0.012 g, 19%) and **106b** (0.061 g, 57%). For **106b**: colourless oil; IR (film) 1771, 1603 (w) cm^{-1}; ^1H NMR δ: 7.26 (2H, m), 7.18 (1H, m), 7.09 (2H, m), 5.07 (1H, d, *J* = 2.2 Hz), 4.80 (1H, d, *J* = 2.2 Hz), 3.76 (1H, br s), 2.24 (1H, d, *J* = 4.8 Hz), 2.19 (1H, dd, *J* = 12, 10 Hz), 2.06 (1H, m), 1.59 (1H, dt, *J* = 12, 4.6 Hz), 1.16 (3H, s), 1.05 (21H, m), 0.89 (1H, dd, *J* = 14, 1.9 Hz), 0.30 (1H, t, *J* = 14 Hz); ^{13}C NMR δ: 215.3, 154.5, 143.3, 128.6 (2C), 127.3 (2C), 126.6, 107.5, 53.4, 52.6, 48.2, 37.8, 34.6, 18.8 (6C), 13.1, 11.4 (3C), 9.4; HRMS (ESI) 405.2587, $[C_{25}H_{38}OSiNa]^+$ requires 405.2584.

According to *Procedure 3* for **105** and **107**: AVK **26** (0.050 g, 0.28 mmol) and allyltriisopropylsilane (0.34 mL, 1.4 mmol) were reacted with $InCl_3$ (0.31 g, 1.4 mmol) to yield **105** (0.018 g, 27%), **106b** (0.030 g, 28%), and **107** (0.008 g, 13%).

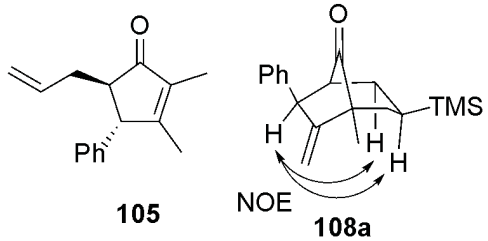
(1*R,3*R**,4*S**,6*R**)-1-Methyl-2-methylene-3-phenyl-6-((triethoxysilyl)methyl)bicyclo [2.2.1]heptan-7-one (106c)**



106c

According to *Procedure 1* for **105** and **106a**: AVK **26** (0.050 g, 0.28 mmol) and allyltriethoxysilane (0.13 mL, 0.56 mmol) were reacted in the presence of $BF_3{\cdot}OEt_2$ (0.040 mL, 0.31 mmol) to yield **106c** (0.016 g, 15%) as a colourless oil; IR (film) 1770, 1604 (w) cm^{-1}; ^1H NMR δ: 7.26 (2H, m), 7.18 (1H, m), 7.08 (2H, m), 5.06 (1H, d, *J* = 2.2 Hz), 4.80 (1H, d, *J* = 2.2 Hz), 3.82 (6H, q, *J* = 7.0 Hz), 3.77 (1H, br s), 2.20 (2H, m), 2.07 (1H, m), 1.73 (1H, dt, *J* = 13, 4.7 Hz), 1.23 (9H, t, *J* = 7.0 Hz), 0.84 (1H, dd, *J* = 15, 2.7 Hz), 0.32 (1H, dd, *J* = 15, 13 Hz); ^{13}C NMR δ: 215.6, 154.2, 143.4, 128.5 (2C), 127.3 (2C), 126.6, 107.7, 58.5 (3C), 52.9, 52.5, 48.2, 36.3, 33.6, 18.3 (3C), 14.7, 9.2; HRMS (ESI) 411.1955, $[C_{22}H_{32}O_4SiNa]^+$ requires 411.1962.

(*trans*)-5-Allyl-2,3-dimethyl-4-phenylcyclopent-2-enone (105) and (1*R,3*R**,5*S**,6*R**) -1-methyl-7-methylene-6-phenyl-3-(trimethylsilyl)bicyclo[3.2.1]octan-8-one (108a)**

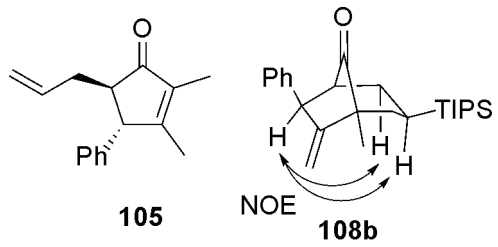


105 **108a**

Compound **106a** (0.025 g, 0.083 mmol) was dissolved in CH_2Cl_2 (8 mL) at rt, and $BF_3{\cdot}OEt_2$ (0.4 mmol, 0.05 mL) was added. The mixture was stirred for 5 h, diluted with

CH_2Cl_2, and washed with saturated $NaHCO_3$. After re-extraction with CH_2Cl_2, the combined organic layers were dried over Na_2SO_4, and concentrated. Purification by flash chromatography (2.5%, then 10% EtOAc in hexanes) yielded **105** (0.013 g, 69%) and **108a** (0.005 g, 20%). For **108a**: colourless solid, mp 141–143 °C; IR (film) 1738, 1603 (w) cm^{-1}; ^1H NMR δ: 7.24 (2H, m), 7.17 (1H, m), 7.01 (2H, m), 5.08 (1H, d, J = 2.1 Hz), 4.97 (1H, d, J = 2.1 Hz), 3.80 (1H, br s), 2.56 (1H, m), 2.18 (1H, m), 1.96 (1H, td, J = 14, 2.5 Hz), 1.79 (2H, m), 1.41 (1H, m), 1.19 (3H, s), -0.02 (9H, s); ^{13}C NMR δ: 222.3, 155.4, 145.7, 128.7 (2C), 127.2 (2C), 126.3, 109.3, 55.3 (2C), 50.5, 50.4, 39.5, 18.3, 16.6, 3.3 (3C); HRMS (ESI) 321.1646, $[C_{19}H_{26}OSiNa]^+$ requires 321.1645.

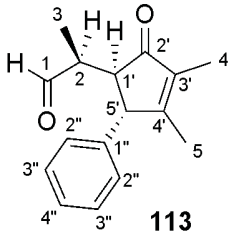
(*trans*)-5-Allyl-2,3-dimethyl-4-phenylcyclopent-2-enone (105) and (1*R,3*R**,5*S**,6*R**) -1-methyl-7-methylene-6-phenyl-3-(triisopropylsilyl)bicyclo[3.2.1]octan-8-one (108b)**



Compound **106b** (0.020 g, 0.052 mmol) was dissolved in CH_2Cl_2 (5 mL) at rt, and $BF_3{\cdot}OEt_2$ (0.2 mmol, 0.03 mL) was added. The mixture was stirred for 3 h, diluted with CH_2Cl_2, and washed with saturated $NaHCO_3$. After re-extraction with CH_2Cl_2, the combined organic layers were dried over Na_2SO_4, and concentrated. Purification by flash chromatography (2.5%, then 10% EtOAc in hexanes) yielded **105** (0.001 g, 8%) and **108b** (0.018 g, 85%). For **108b**: colourless solid: mp 79–81 °C; IR (film) 1742, 1603 (w) cm^{-1}; ^1H NMR δ: 7.24 (2H, m), 7.17 (1H, m), 7.01 (2H, m), 5.08 (1H, d, J = 2.1 Hz),

5.00 (1H, d, J = 2.1 Hz), 3.74 (1H, br s), 2.58 (1H, m), 2.23 (2H, m), 2.05 (1H, dd, J = 14, 13 Hz), 1.83 (2H, m), 1.19 (3H, s), 1.09 (21H, m); ^{13}C NMR δ: 221.8, 155.3, 145.5, 128.7 (2C), 127.1 (2C), 126.3, 109.1, 55.8, 55.7, 51.2, 50.5, 40.2, 19.1 (6C), 16.7, 15.4, 11.2 (3C); HRMS (ESI) 405.2575, $[C_{25}H_{38}OSiNa]^+$ requires 405.2584.

(1'*R,2*R**,5'*R**)-2-(3,4-Dimethyl-2-oxo-5-phenylcyclopent-3-enyl)propanal (113)**

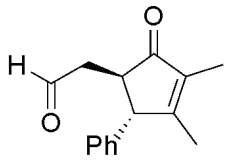


113

A solution of AVK **26** (0.050 g, 0.28 mmol) and 1-ethoxypropene (3:1 *cis*/*trans* mixture) (0.060 mL, 0.54 mmol) in CH_2Cl_2 (25 mL) was cooled to –78 °C, and $BF_3{\cdot}OEt_2$ (0.040 mL, 0.31 mmol) was added. The mixture was stirred for 5 min, then poured into a separatory funnel containing saturated aqueous sodium bicarbonate. The CH_2Cl_2 layer was removed, and additional CH_2Cl_2 (×2) was used to re-extract the aqueous layer. The combined organic layers were dried over Na_2SO_4 and then concentrated under reduced pressure. Flash chromatography of the residue (10% EtOAc in hexanes) provided **113** (0.057 g, 76%) as a colourless oil: IR (film) 1724, 1701, 1602 (w) cm^{-1}; ^{1}H NMR δ: 9.57 (1H, br d, J = 0.6 Hz, H1), 7.32 (2H, m, H3''), 7.26 (1H, m, H4''), 7.02 (2H, m, H2''), 3.45 (1H, br d, $J \approx$ 3 Hz, H5'), 3.04 (1H, m, H2), 2.83 (1H, dd, J = 4.2, 3.2 Hz, H1'), 1.82 (3H, s, H5), 1.81 (3H, s, H4), 1.01 (3H, d, J = 7.0 Hz, H3); ^{13}C NMR δ: 208.1 (C2'), 202.9 (C1), 171.1 (C4'), 140.9 (C1''), 137.2 (C3'), 129.1 (2C, C3''), 127.7 (2C, C2''),

127.3 (C4''), 55.0 (C1'), 51.9 (C5'), 47.4 (C2), 15.5 (C5), 8.9 (C3), 8.3 (C4); HRMS (ESI) 265.1202, $[C_{16}H_{18}O_2Na]^+$ requires 265.1199.

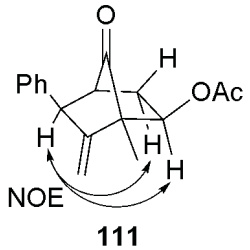
2-((*trans*)-3,4-Dimethyl-2-oxo-5-phenylcyclopent-3-enyl)acetaldehyde (110)



110

According to the procedure for **113**: AVK **26** (0.050 g, 0.28 mmol) and (trimethylsilyl)oxyethene (0.16 g, 0.56 mmol) were reacted with $BF_3{\cdot}OEt_2$ (0.040 mL, 0.32 mmol) to yield **110** (0.022 g, 35%) as a colourless oil; IR (film) 1724, 1701, 1602 (w) cm^{-1}; ^1H NMR δ: 9.72 (1H, br t, J = 1.3 Hz), 7.34 (2H, m), 7.28 (1H, m), 7.08 (2H, m), 3.48 (1H, br d, $J \approx 2.5$ Hz), 2.94 (1H, m), 2.73 (1H, m), 2.71 (1H, m), 1.83 (3H, s), 1.82 (3H, s); ^{13}C NMR δ: 208.3, 200.4, 169.9, 140.8, 136.3, 129.0 (2C), 127.6 (2C), 127.3, 55.9, 50.4, 44.1, 15.4, 8.4; HRMS (ESI) 251.1046, $[C_{15}H_{16}O_2Na]^+$ requires 251.1043.

1-Methyl-6-methylene-7-oxo-5-phenylbicyclo[2.2.1]heptan-2-yl acetate (111)

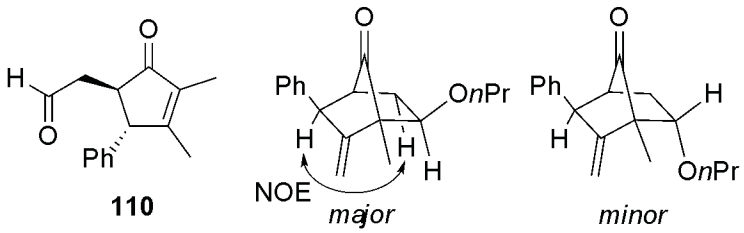


111

According to the procedure for **113**: AVK **26** (0.050 g, 0.28 mmol) and vinyl

acetate (0.050 mL, 0.54 mmol) were reacted with $BF_3{\cdot}OEt_2$ (0.040 mL, 0.32 mmol) to yield **111** (0.014 g, 18%) as a colourless oil; IR (film) 1779, 1743, 1603 (w) cm^{-1}; ^1H NMR δ: 7.26 (2H, m), 7.21 (1H, m), 7.09 (2H, m), 5.32 (1H, d, *J* = 2.4 Hz), 5.08 (1H, d, *J* = 2.4 Hz), 4.94 (1H, dd, *J* = 8.4, 2.4 Hz), 3.75 (1H, br s), 2.46 (1H, dd, *J* = 15, 8.4 Hz), 2.38 (1H, d, *J* = 5.1 Hz), 2.06 (3H, s), 1.96 (1H, m), 1.19 (3H, s); ^{13}C NMR δ: 213.1, 170.3, 147.4, 142.2, 128.7 (2C), 127.2 (2C), 127.0, 112.9, 72.4, 53.1, 52.4, 47.4, 35.4, 21.0, 7.7; HRMS (ESI) 293.1143, $[C_{17}H_{18}O_3Na]^+$ requires 293.1148.

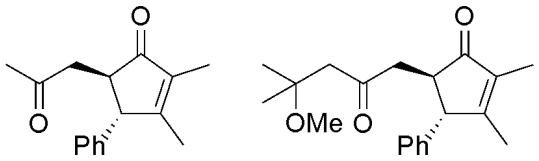
2-((*trans*)-3,4-Dimethyl-2-oxo-5-phenylcyclopent-3-enyl)acetaldehyde (110) and (1*R,3*S**,4*R**,6*S**)- and (1*R**,3*S**,4*R**,6*R**)-1-methyl-2-methylene-3-phenyl-6-propoxybicyclo[2.2.1]heptan-7-one (112)**



According to the procedure for **113**: AVK **26** (0.050 g, 0.28 mmol) and *n*-propoxyethene (0.060 mL, 0.54 mmol) were reacted in the presence of $BF_3{\cdot}OEt_2$ (0.040 mL, 0.32 mmol) to give **110** (0.037 g, 58%) as a colourless oil and 0.031 g (41%) of **112** as a 5:1 mixture of inseparable epimers (as determined by integration of the ^1H NMR spectrum). For **112**: IR (film) 1779, 1603 (w) cm^{-1}; HRMS (ESI) 293.1511, $[C_{18}H_{22}O_2Na]^+$ requires 293.1512; the following NMR data are taken from the spectra of the mixture: *major isomer*: ^1H NMR δ: 7.26 (2H, m), 7.19 (1H, m), 7.09 (2H, m), 5.22 (1H, d, *J* = 2.5 Hz), 4.97 (1H, d, *J* = 2.5 Hz), 3.69 (1H, br s), 3.49 (1H, m), 3.45 (1H, m), 3.30 (1H, m), 2.32 (1H, d, *J* = 5.0 Hz), 2.24 (1H, dd, *J* = 13, 7.7 Hz), 1.98 (1H, ddd, *J* =

13, 5.0, 2.2 Hz), 1.55 (2H, m), 1.23 (3H, s), 0.90 (3H, t, J = 7.5 Hz); ^{13}C NMR δ: 214.4, 149.3, 142.8, 128.5 (2C), 127.3 (2C), 126.7, 111.0, 78.2, 70.8, 54.8, 52.6, 47.5, 35.6, 23.0, 10.7, 7.8; *minor isomer*: ^{1}H NMR δ: 7.26 (2H, m), 7.19 (1H, m), 7.09 (2H, m), 5.12 (1H, d, J = 2.5 Hz), 4.96 (1H, d, J = 2.5 Hz), 3.80 (1H, m), 3.70 (1H, overlapped), 3.49 (1H, overlapped), 3.45 (1H, overlapped), 2.43 (1H, m), 2.35 (1H, d, J = 4.8 Hz), 1.76 (1H, d, J = 14, 3.2 Hz), 1.55 (2H, m), 1.29 (3H, s), 0.93 (3H, t, J = 7.5 Hz); ^{13}C NMR δ: 212.7, 146.4, 143.4, 128.5 (2C), 127.4 (2C), 126.6, 111.2, 76.9, 71.7, 56.6, 52.5, 49.0, 35.5, 23.1, 10.9, 10.6.

(*trans*)-2,3-Dimethyl-5-(2-oxopropyl)-4-phenylcyclopent-2-enone (114) and by-product

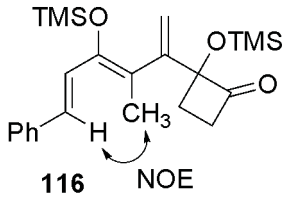


114 by-product (tentative)

According to the procedure for **113**: AVK **26** (0.050 g, 0.28 mmol) and 2-methoxypropene (0.050 mL, 0.52 mmol) were reacted with $BF_3{\cdot}OEt_2$ (0.040 mL, 0.32 mmol) to yield **114** and a by-product (tentative structure above) with the mass of **114** plus 2-methoxypropene (0.031 g, 60%) as an inseparable mixture (3.3:1, respectively, as determined by integration of the ^{1}H NMR spectrum); the following NMR data were taken from the spectra of the mixture: for **114**: ^{1}H NMR δ: 7.35 (2H, m), 7.28 (1H, m), 7.10 (2H, m), 3.52 (1H, narrow m), 2.92 (1H, dd, J = 17, 4.4 Hz), 2.73 (1H, dd, J = 17, 7.7 Hz), 2.60 (1H, m), 2.10 (3H, s), 1.81 (3H, s), 1.80 (3H, s); ^{13}C NMR δ: 208.9, 206.9, 169.8, 141.2, 136.2, 128.9 (2C), 127.7 (2C), 127.1, 55.7, 51.6, 43.5, 29.8, 15.4, 8.4; for

the by-product: ^{1}H NMR (diagnostic signals only) δ: 3.20 (3H, s), 1.23 (3H, s), 1.22 (3H, s); ^{13}C NMR δ: 209.2, 207.7, 169.4, 141.4, 136.2, 128.8 (2C), 127.7 (2C), 127.0, 74.4, 52.5, 51.7, 49.3, 44.4, 24.9, 24.8, 15.4, 8.4; HRMS (ESI) for **114**: 265.1202, $[C_{16}H_{18}O_2Na]^+$ requires 265.1199; for the by-product: 337.1774, $[C_{20}H_{26}O_3Na]^+$ requires 337.1774.

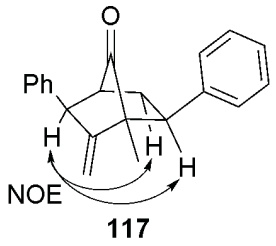
Trimethyl((1*E*,3*Z*)-4-methyl-1-phenyl-5-(1-(trimethylsilyloxy)cyclobutyl)hexa-1,3,5-trien-3-yloxy)silane (116)



116

According to the procedure for **113**: AVK **26** (0.050 g, 0.28 mmol) and 1,2-bis(trimethylsiloxy)cyclobutene (0.36 mL, 1.4 mmol) reacted in the presence of $BF_3{\cdot}OEt_2$ (0.040 mL, 0.31 mmol) to yield **34** (0.014 g, 12%) as a yellow oil after silica gel chromatography (10% EtOAc in hexanes); IR (film) 1787, 1601 (w) cm^{-1}; ^{1}H NMR δ: 7.32 (4H, m), 7.21 (1H, m), 6.97 (1H, d, *J* = 16 Hz), 6.68 (1H, d, *J* = 16 Hz), 2.85 (1H, dd, *J* = 16, 11 Hz), 2.77 (1H, dd, *J* = 16, 11, 5.3), 2.37 (1H, td, *J* = 11, 5.3), 2.08 (1H, t, *J* = 5.3 Hz), 1.91 (3H, s), 0.29 (9H, s), 0.18 (9H, s); ^{13}C NMR δ: 207.7, 147.6, 147.0, 137.2, 128.6 (2C), 128.1, 128.0, 127.4, 126.5 (2C), 123.9, 122.1, 118.1, 94.8, 40.2, 27.6, 18.1, 1.6, 0.8; HRMS (ESI): 437.1932, $[C_{23}H_{34}Si_2O_3Na]^+$ requires 437.1939.

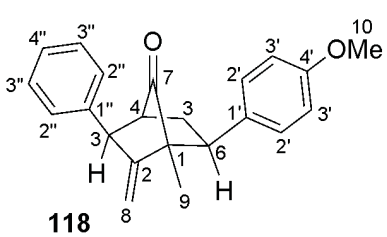
(1*R,3*R**,4*S**,6*S**)-1-Methyl-2-methylene-3,6-diphenylbicyclo[2.2.1]heptan-7-one (35)**



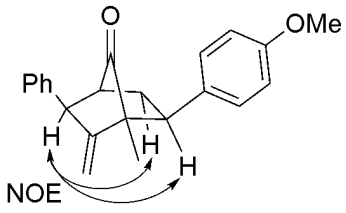
117

According to the procedure for **113**: AVK **26** (0.050 g, 0.28 mmol) and styrene (0.065 mL, 0.56 mmol) reacted in the presence of $BF_3{\cdot}OEt_2$ (0.01 mL, 0.08 mmol) to yield **117** (0.012 g, 15%) as a colourless oil; IR (film) 1764, 1601 (w) cm^{-1}; ^1H NMR δ: 7.29 (4H, m), 7.23 (2H, m), 7.14 (2H, m), 7.06 (2H, m), 5.15 (1H, d, *J* = 2.5 Hz), 4.86 (1H, d, *J* = 2.5 Hz), 3.91 (1H, br s), 3.12 (1H, dd, *J* = 11, 5.8 Hz), 2.46 (2H, m), 2.25 (1H, dt, *J* = 13, 5.2 Hz), 0.79 (3H, s); ^{13}C NMR δ: 215.7, 153.3, 143.2, 143.0, 128.6 (4C), 128.0 (2C), 127.4 (2C), 127.0, 126.7, 108.1, 53.2, 52.6, 48.6, 47.4, 34.1, 9.8; HRMS (ESI) 311.1400, $[C_{21}H_{20}ONa]^+$ requires 311.1406.

(1*R,3*R**,4*S**,6*S**)-6-(4-Methoxyphenyl)-1-methyl-2-methylene-3-phenylbicyclo [2.2.1]heptan-7-one (118)**



118

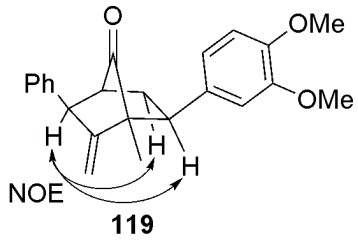


118

According to the procedure for **113**: AVK **26** (0.050 g, 0.28 mmol) and *p*-vinylanisole (0.060 mL, 0.56 mmol) were reacted in the presence of $BF_3{\cdot}OEt_2$ (0.01 mL, 0.08 mmol) to yield **118** (0.047 g, 52%) as a colourless solid: mp 131–133 °C; IR (film)

1772, 1611 cm^{-1}; ^1H NMR δ: 7.28 (2H, m, H3''), 7.21 (1H, m, H4''), 7.13 (2H, m, H2''), 6.97 (2H, br d, *J* = 8.7 Hz, H2'), 6.84 (2H, br d, *J* = 8.7 Hz, H3'), 5.13 (1H, d, *J* = 2.2 Hz, H8a), 4.85 (1H, d, *J* = 2.2 Hz, H8b), 3.89 (1H, br s, H3), 3.80 (3H, s, H10), 3.08 (1H, dd, *J* = 11, 5.8 Hz, H6), 2.45 (2H, m, H3a, H4), 2.20 (1H, dt, *J* = 13, 5.1 Hz, H3b), 0.78 (3H, s, H9); ^{13}C NMR δ: 215.9 (C7), 158.5 (C4'), 153.4 (C2), 143.2 (C1''), 135.0 (C1'), 128.9 (2C, C2'), 128.6 (2C, C3''), 127.4 (2C, C2''), 126.7 (C4''), 113.9 (2C, C3'), 107.8 (C8), 55.2 (C10), 53.3 (C1), 52.5 (C3), 48.6 (C4), 46.7 (C6), 34.3 (C3), 9.8 (C9); HRMS 341.1507, $[C_{22}H_{22}O_2Na]^+$ requires 341.1512.

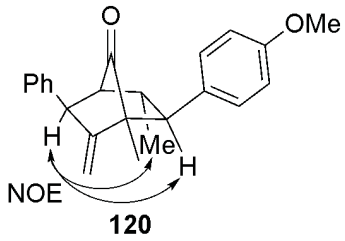
(1*R,3*R**,4*S**,6*S**)-6-(3,4-Dimethoxyphenyl)-1-methyl-2-methylene-3-phenylbicyclo [2.2.1]heptan-7-one (119)**



119

According to the procedure for **113**: AVK **26** (0.050 g, 0.28 mmol) and 3,4-dimethoxystyrene (0.080 mL, 0.54 mmol) reacted in the presence of $BF_3{\cdot}OEt_2$ (0.01 mL, 0.08 mmol) to yield **119** (0.074 g, 76%) as a colourless solid: mp 113–116 °C; IR (film) 1771, 1611 (w) cm^{-1}; ^1H NMR δ: 7.29 (2H, m), 7.21 (1H, m), 7.13 (2H, m), 6.80 (1H, d, *J* = 8.3 Hz), 6.61 (1H, dd, *J* = 8.3, 2.1 Hz), 6.56 (1H, d, *J* = 2.1 Hz), 5.14 (1H, d, *J* = 2.2 Hz), 4.86 (1H, d, *J* = 2.2 Hz), 3.89 (1H, br s), 3.87 (6H, s), 3.06 (1H, dd, *J* = 11, 5.5 Hz), 2.46 (2H, m), 2.22 (1H, dt, *J* = 13, 5.1 Hz), 0.81 (3H, s); ^{13}C NMR δ: 216.0, 153.3, 148.8, 147.9, 143.2, 135.6, 128.6 (2C), 127.3 (2C), 126.7, 120.0, 111.0, 110.8, 108.0, 55.8, 53.3, 52.5, 48.6, 47.1, 34.3, 9.7; HRMS 371.1617, $[C_{23}H_{24}O_3Na]^+$ requires 371.1618.

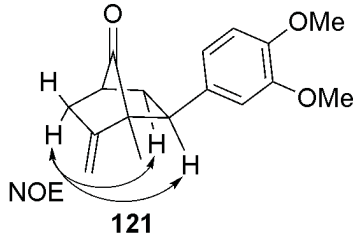
(1*R,2*S**,3*R**,4*S**,5*S**)-2-(4-Methoxyphenyl)-1,3-dimethyl-6-methylene-5-phenyl bicyclo[2.2.1]-heptan-7-one (120)**



120

According to the procedure for **113**: AVK **26** (0.050 g, 0.28 mmol) and *trans*-anethole (0.080 mL, 0.53 mmol) were reacted with $BF_3{\cdot}OEt_2$ (0.01 mL, 0.08 mmol) to yield **120** (0.055 g, 59%) as a colourless solid: mp 129–131 °C; IR (film) 1768, 1611 cm^{-1}; ^1H NMR δ: 7.29 (2H, m), 7.21 (1H, m), 7.16 (2H, m), 6.98 (2H, d, *J* = 8.7 Hz), 6.83 (2H, d, *J* = 8.7 Hz), 5.08 (1H, d, *J* = 2.1 Hz), 4.81 (1H, d, *J* = 2.1 Hz), 4.15 (1H, br s), 3.79 (3H, s), 2.49 (1H, d, *J* = 7.1 Hz), 2.41 (1H, m), 2.36 (1H, d, *J* = 4.0 Hz), 1.27 (3H, d, *J* = 6.8 Hz), 0.78 (3H, s); ^{13}C NMR δ: 215.5, 158.6, 154.0, 143.3, 134.0, 129.3 (2C), 128.6 (2C), 127.6 (2C), 126.6, 113.9 (2C), 107.0, 56.8, 55.3, 55.2, 54.1, 44.0, 38.6, 16.0, 9.9; HRMS (ESI) 355.1659, $[C_{23}H_{24}O_2Na]^+$ requires 355.1669.

(1*R,2*S**,4*S**)-2-(3,4-Dimethoxyphenyl)-1-methyl-6-methylenebicyclo[2.2.1]heptan-7-one (121)**

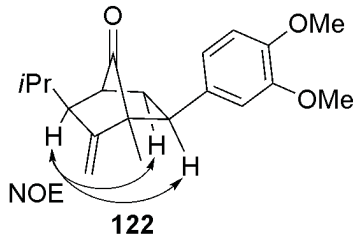


121

According to the procedure for **113**: AVK **27** (0.025 g, 0.23 mmol) and 3,4-dimethoxystyrene (0.070 mL, 0.47 mmol) were reacted in the presence of $BF_3{\cdot}OEt_2$ (0.01

mL, 0.08 mmol) to yield **121** (0.049 g, 79%) as a colourless oil; IR (film) 1772, 1611 (w) cm^{-1}; ^1H NMR δ: 6.77 (1H, d, *J* = 8.3 Hz), 6.57 (1H, dd, *J* = 8.3, 2.1 Hz), 6.51 (1H, d, *J* = 2.1 Hz), 4.97 (1H, t, *J* = 2.3 Hz), 4.90 (1H, d, *J* = 2.3 Hz), 3.86 (3H, s), 3.85 (3H, s), 2.93 (1H, dd, *J* = 11, 5.3 Hz), 2.74 (1H, m), 2.54 (1H, dt, *J* = 16, 2.2 Hz), 2.42 (1H, t, *J* = 4.5 Hz), 2.25 (1H, dd, *J* = 13, 11 Hz), 2.14 (1H, m), 0.73 (3H, s); ^{13}C NMR δ: 216.2, 148.8, 148.7, 147.8, 135.8, 119.9, 110.9, 110.6, 105.4, 55.8 (2C), 52.8, 47.6, 40.8, 35.0, 34.2, 9.5; HRMS 295.1305, $[C_{17}H_{20}O_3Na]^+$ requires 295.1305.

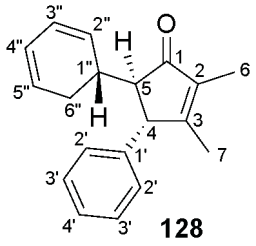
(1*R,3*R**,4*S**,6*S**)-6-(3,4-Dimethoxyphenyl)-3-isopropyl-1-methyl-2-methylene bicyclo[2.2.1]heptan-7-one (122)**



122

According to the procedure for **113**: AVK **29** (0.040 g, 0.27 mmol) and 3,4-dimethoxystyrene (0.080 mL, 0.54 mmol) reacted in the presence of $BF_3{\cdot}OEt_2$ (0.01 mL, 0.08 mmol) to yield **122** (0.068 g, 81%) as a colourless oil; IR (film) 1773, 1610 cm^{-1}; ^1H NMR δ: 6.77 (1H, d, *J* = 8.3 Hz), 6.57 (1H, dd, *J* = 8.2, 2.1 Hz), 6.52 (1H, d, *J* = 2.1 Hz), 5.05 (1H, d, *J* = 2.2 Hz), 4.96 (1H, d, *J* = 2.2 Hz), 3.85 (6H, s), 2.91 (1H, dd, *J* = 11, 5.3 Hz), 2.57 (1H, m), 2.34 (1H, d, *J* = 4.6 Hz), 2.20 (1H, dd, *J* = 13, 11 Hz), 2.13 (1H, dt, *J* = 13, 5.3 Hz), 1.88 (1H, m), 1.02 (3H, d, *J* = 6.9 Hz), 0.77 (3H, d, *J* = 6.9 Hz), 0.72 (3H, s); ^{13}C NMR δ: 217.4, 153.8, 148.7, 147.8, 135.7, 120.1, 110.9, 110.7, 104.7, 55.8 (2C), 53.6, 53.4, 47.7, 42.3, 34.0, 31.9, 21.4, 17.8, 9.5; HRMS 371.1768, $[C_{20}H_{26}O_3Na]^+$ requires 337.1774.

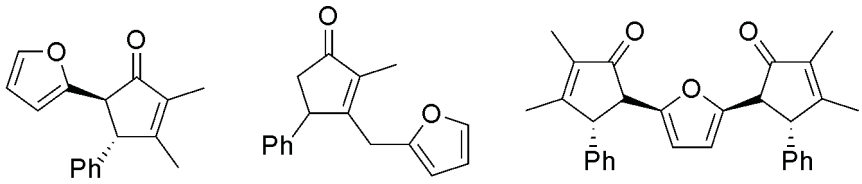
***(1''R*,4S*,5R*)*-5-(Cyclohexa-2,4-dienyl)-2,3-dimethyl-4-phenylcyclopent-2-enone (128)**



128

A solution of AVK **26** (0.050 g, 0.28 mmol) and 1,3-cyclohexadiene (0.055 mL, 0.56 mmol) in CH_2Cl_2 (25 mL) was cooled to –78 °C, and $BF_3{\cdot}OEt_2$ (0.01 mL, 0.08 mmol) was added. The mixture was stirred for 5 min, then poured into a separatory funnel containing saturated aqueous sodium bicarbonate. The CH_2Cl_2 layer was removed, and additional CH_2Cl_2 (×2) was used to re-extract the aqueous layer. The combined organic layers were dried over Na_2SO_4 and then concentrated under reduced pressure. Flash chromatography of the residue (2.5%, then 10%, EtOAc in hexanes) provided **128** (0.043 g, 58%) as a colourless oil; IR (film) 1697, 1645, 1601 (w) cm^{-1}; ^1H NMR δ: 7.30 (2H, m, C3'), 7.24 (1H, m, C4'), 7.08 (2H, m, C2'), 5.88 (2H, m, H3'', H4''), 5.71 (1H, m, H5''), 5.53 (1H, dd, J = 9.2, 3.2 Hz, H2''), 3.84 (1H, br d, $J \approx$ 2.5 Hz, C4), 3.07 (1H, m, C1''), 2.51 (1H, dd, J = 4.9, 2.5 Hz, C5), 2.11 (1H, m, H6''a), 1.98 (1H, m, H6''b), 1.81 (6H, s, H6, H7); ^{13}C NMR δ: 209.8 (C1), 171.2 (C3), 142.1 (C1'), 137.6 (C2), 128.9 (C2''), 128.8 (2C, C3'), 127.8 (2C, C2'), 126.8 (C4'), 125.7 (C5''), 124.7 (C3''), 123.7 (C4''), 58.7 (C5), 53.1 (C4), 34.5 (C1''), 24.3 (C6''), 15.5 (C7), 8.2 (C6); HRMS (ESI) 287.1396, $[C_{19}H_{20}ONa]^+$ requires 287.1406.

(*trans*)-5-(Furan-2-yl)-2,3-dimethyl-4-phenylcyclopent-2-enone (123), 3-(furan-2-ylmethyl)-2-methyl-4-phenylcyclopent-2-enone (124), and (*trans*,*trans*)-5,5'-(furan-2,5-diyl)bis(2,3-dimethyl-4-phenyl-cyclopent-2-enone) (160)



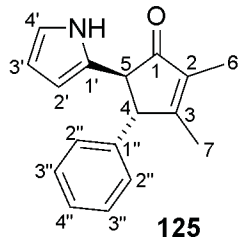
123 **124** **160** (two diastereomers)

Procedure 1: A solution of AVK **26** (0.050 g, 0.28 mmol) and furan (0.20 mL, 2.8 mmol) in CH_2Cl_2 (25 mL) was cooled to –78 °C, and $BF_3{\cdot}OEt_2$ (0.040 mL, 0.31 mmol) was added. The mixture was stirred for 5 min, then poured into a separatory funnel containing saturated aqueous sodium bicarbonate. The CH_2Cl_2 layer was removed, and additional CH_2Cl_2 (×2) was used to re-extract the aqueous layer. The combined organic layers were dried over Na_2SO_4 and then concentrated under reduced pressure. Flash chromatography of the residue (10%, then 25%, EtOAc in hexanes) provided **123** (0.038 g, 54%) and **160** (0.013 g, 22%). For **123**: colourless oil; IR (film) 1708, 1649, 1601 (w) cm^{-1}; ^1H NMR δ: 7.38 (3H, m), 7.31 (1H, m), 7.12 (2H, m), 6.31 (1H, dd, J = 3.2, 2.0 Hz), 6.16 (1H, d, J = 3.2 Hz), 4.01 (1H, br d, J = 3.2 Hz), 3.58 (1H, d, J = 3.2 Hz), 1.89 (3H, s), 1.86 (3H, s); ^{13}C NMR δ: 205.0, 170.3, 151.1, 142.0, 140.9, 136.2, 129.0 (2C), 127.5 (2C), 127.3, 110.3, 107.3, 55.8, 55.2, 15.6, 8.5; HRMS (ESI) 253.1224, $[C_{17}H_{17}O_2]^+$ requires 253.1223. For **160** (1.8:1 inseparable mixture of diastereomers): IR (film) 1708, 1648, 1602 (w) cm^{-1}; HRMS (ESI) 459.1931, $[C_{30}H_{28}O_3Na]^+$ requires 459.1931; the following NMR data are taken from spectra of the mixture: *major isomer*: ^1H NMR δ: 7.32 (4H, m), 7.27 (2H, m), 7.08 (4H, m), 6.07 (2H, s), 3.94 (2H, br d, $J \approx$ 2.5 Hz), 3.53 (2H, overlapped), 1.87 (6H, s), 1.86 (6H, s); ^{13}C NMR δ: 204.9, 170.0,

150.6, 140.9, 136.3, 129.0 (4C), 127.6 (4C), 127.2, 107.8, 55.9, 55.3, 15.6, 8.5; *minor isomer*: ^{1}H NMR δ: 7.32 (4H, m), 7.27 (2H, m), 7.08 (4H, m), 6.07 (2H, s), 3.94 (2H, br d, $J \approx 2.5$ Hz), 3.53 (2H, overlapped), 1.87 (6H, s), 1.86 (6H, s); ^{13}C NMR δ: 205.0, 170.2, 150.8, 140.9, 136.3, 128.9 (4C), 127.7 (4C), 127.2, 107.4, 56.1, 55.2, 15.6, 8.5.

Procedure 2: A solution of AVK **26** (0.025 g, 0.14 mmol) and furan (0.10 mL, 1.4 mmol) in CH_2Cl_2 (15 mL) was cooled to –78 °C, and $InCl_3$ (0.31 g, 1.4 mmol) was added. The mixture was stirred for 2 h, then poured into a separatory funnel containing saturated aqueous sodium bicarbonate. The CH_2Cl_2 layer was removed, and additional CH_2Cl_2 (×2) was used to re-extract the aqueous layer. The combined organic layers were dried over Na_2SO_4 and then concentrated under reduced pressure. Flash chromatography of the residue (10% EtOAc in hexanes) provided **123** (0.039 g, 54%) and **124** (0.011 g, 15%). For **124**: colourless oil; IR (film) 1707, 1651, 1601 (w) cm^{-1}; ^{1}H NMR δ: 7.31 (3H, m), 7.25 (1H, m), 7.07 (2H, m), 6.27 (1H, dd, J = 3.1, 1.9 Hz), 5.90 (1H, d, J = 3.1 Hz), 3.89 (1H, m), 3.72 (1H, d, J = 16 Hz), 3.27 (1H, d, J = 16 Hz), 2.89 (1H, dd, J = 19, 7.1 Hz), 2.39 (1H, dd, J = 19, 2.2 Hz), 1.85 (3H, s); ^{13}C NMR δ: 209.1, 169.5, 150.4, 141.8, 141.7, 138.2, 128.9 (2C), 127.5 (2C), 127.1, 110.4, 107.1, 46.9, 44.5, 28.0, 8.2; HRMS (ESI) 275.1050, $[C_{17}H_{16}O_2Na]^+$ requires 275.1043.

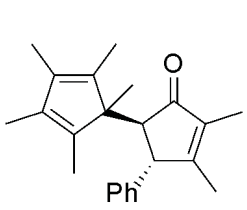
(*trans*)-2,3-Dimethyl-4-phenyl-5-(1*H*-pyrrol-2-yl)cyclopent-2-enone (125)



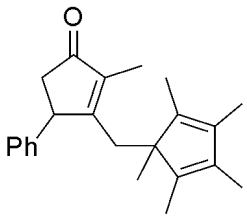
125

A solution of AVK **26** (0.10 g, 0.56 mmol) and pyrrole (0.080 mL, 1.1 mmol) in CH_2Cl_2 (25 mL) was cooled to –78 °C, and $BF_3{\cdot}OEt_2$ (0.080 mL, 0.62 mmol) was added. The mixture was stirred for 5 min at –78 °C before it was poured into a separatory funnel containing saturated aqueous $NaHCO_3$. The CH_2Cl_2 layer was removed, and additional CH_2Cl_2 (×2) was used to re-extract the aqueous layer. The combined organic layers were dried over Na_2SO_4 and then concentrated under reduced pressure. Flash chromatography (10% EtOAc in hexanes with 2.5% triethylamine, and then 25% EtOAc in hexanes with 2.5% triethylamine) of the residue provided **125** (0.093 g, 66%) as a yellow oil: IR (film) 3374, 1697, 1645, 1601 cm^{-1}; ^1H NMR δ: 9.18 (1H, br s, *N*H), 7.39 (2H, m, H3''), 7.32 (1H, m, H4''), 7.25 (1H, m. H2''), 6.74 (1H, m, H4'), 6.13 (1H, dd, J = 6.0, 2.8 Hz, H3'), 6.08 (1H, m, H2'), 4.08 (1H, br d, $J \approx 3$ Hz, H5), 3.57 (1H, d, J = 2.8 Hz, H4), 1.86 (3H, s, H7), 1.81 (3H, br s, H6); ^{13}C NMR δ: 208.2 (C1), 171.6 (C3), 141.3 (C1''), 136.0 (C2), 129.3 (2C, C3''), 128.1 (C1'), 128.0 (2C, C2''), 127.7 (C4''), 117.8 (C4'), 108.2 (C3'), 105.0 (C2'), 56.3 (C5), 53.8 (C4), 15.9 (C7), 8.7 (C6); HRMS (ESI) 274.1190, $[C_{17}H_{17}NONa]^+$ requires 274.1202.

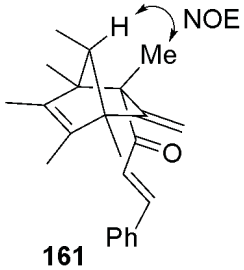
(*trans)*-4-Methyl-5-(1,2,3,4,5-pentamethylcyclopenta-2,4-dienyl)-1-phenylhexa-1,5-dien-3-one (126), 2-methyl-3-((1,2,3,4,5-pentamethylcyclopenta-2,4-dienyl)methyl)-4-phenylcyclopent-2-enone (127), and (1'*R,2'*R**,4'*S**,6'*R**,7'*S**)-1-(1,2,4,5,6,7-hexamethyl-3-methylenebicyclo[2.2.1]hept-5-en-2-yl)-3-phenylprop-2-en-1-one (161)**



126



127

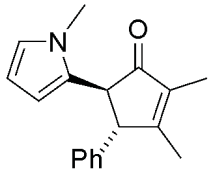


161

According to the procedure for **128**: AVK **26** (0.050 g, 0.28 mmol) and 1,2,3,4,5-pentamethylcyclopentadiene (0.090 mL, 0.56 mmol) were reacted in the presence of $BF_3{\cdot}OEt_2$ (0.040 mL, 0.31 mmol) to provide **126** (0.018 g, 11%), **127** (0.11 g, 61%), and the Diels–Alder adduct **161** (0.011 g, 8%). For **126**: colourless solid, mp 91–93 °C; IR (film) 1698, 1655, 1604 (w) cm^{-1}; ^1H NMR δ: 7.22 (2H, m), 7.19 (1H, m), 6.84 (2H, m), 2.47 (1H, br d, J = 2.3 Hz), 2.30 (1H, d, J = 2.3 Hz), 1.82 (3H, s), 1.80 (3H, s), 1.75 (3H, s), 1.63 (3H, s), 1.52 (3H, s), 1.22 (3H, s), 1.15 (3H, s); ^{13}C NMR δ: 211.3, 169.5, 142.4, 142.1, 138.5, 136.4, 136.0, 133.7, 128.3 (2C), 127.8 (2C), 126.5, 58.6, 57.3, 52.4, 18.3, 15.3, 11.3, 11.0, 10.9, 9.9, 8.1; HRMS (ESI) 343.2032, $[C_{23}H_{28}ONa]^+$ requires 343.2032. For **127**: colourless solid, mp 105–107 °C; IR (film) 1701, 1633, 1601 (w) cm^{-1}; ^1H NMR δ: 7.26 (2H, m), 7.20 (1H, m), 6.85 (2H, m), 3.41 (1H, m), 2.71 (1H, d, J =14 Hz), 2.63 (1H, dd, J = 19, 7.0 Hz), 2.31 (1H, d, J = 14 Hz), 1.97 (1H, dd, J = 19, 2.0 Hz), 1.85 (3H, s), 1.83 (3H, s), 1.75 (3H, s), 1.65 (3H, s), 1.15 (3H, s), 0.90 (3H, s); ^{13}C NMR δ: 209.7, 173.1, 143.1, 141.1, 140.1, 137.7, 134.5, 134.1, 128.6 (2C), 127.2 (2C), 126.4, 56.1, 45.7, 45.3, 33.5, 23.5, 11.3, 11.0, 10.2, 9.7, 9.1; HRMS (ESI) 343.2041, $[C_{23}H_{28}ONa]^+$ requires 343.2032. For **161**: colourless solid, mp 68–70 °C; IR (film) 1964,

1936, 1671, 1602 cm^{-1}; ^1H NMR δ: 7.41 (3H, m), 7.33 (3H, m), 6.68 (1H, d, J = 16 Hz), 5.00 (1H, s), 4.80 (1H, s), 1.82 (1H, q, J = 6.4 Hz), 1.56 (3H, s), 1.32 (3H, s), 1.28 (3H, s), 1.17 (3H, s), 1.03 (3H, s), 0.68 (3H, d, J = 6.4 Hz); ^{13}C NMR δ: 202.9, 160.4, 140.5, 136.0, 135.5, 132.5, 129.7, 128.8 (2C), 128.1 (2C), 123.9, 103.4, 62.5, 60.2, 58.8, 58.4, 21.9, 12.1, 11.9, 10.2, 9.9, 7.1; HRMS (ESI) 321.2221, $[C_{23}H_{29}O]^+$ requires 321.2213.

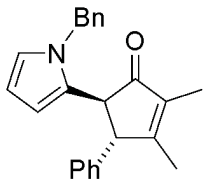
(*trans*)-2,3-Dimethyl-5-(1-methyl-1*H*-pyrrol-2-yl)-4-phenylcyclopent-2-enone (129)



129

According to the procedure for **125**: AVK **26** (0.10 g, 0.56 mmol) and 1-methylpyrrole (0.10 mL, 1.1 mmol) reacted in the presence of $BF_3{\cdot}OEt_2$ (0.080 mL, 0.62 mmol) to yield **129** (0.048 g, 32%) as a pale yellow solid: mp 170–173 °C; IR (film) 1698, 1650, 1605 cm^{-1}; ^1H NMR δ: 7.33 (2H, m), 7.27 (1H, m), 7.13 (2H, m), 6.55 (1H, m), 6.06 (1H, t, J = 3.3 Hz), 5.88 (1H, dd, J = 3.3, 1.8 Hz), 3.89 (1H, br d, $J \approx$ 3 Hz), 3.57 (1H, d, J = 2.5 Hz), 3.46 (3H, s), 1.87 (3H, s), 1.84 (3H, br s); ^{13}C NMR δ: 206.8, 169.9, 141.3, 135.6, 129.8, 129.0 (2C), 127.6 (2C), 127.3, 122.7, 106.9, 105.4, 57.7, 53.9, 34.4, 15.6, 8.6; HRMS (ESI) 288.1354, $[C_{18}H_{19}NONa]^+$ requires 288.1359.

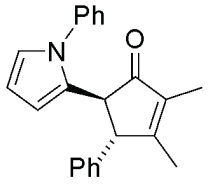
(*trans*)-2,3-Dimethyl-5-(1-benzyl-1*H*-pyrrol-2-yl)-4-phenylcyclopent-2-enone (130)



130

According to the procedure for **125**: AVK **26** (0.10 g, 0.56 mmol) and 1-benzylpyrrole (0.18 g, 1.1 mmol) reacted in the presence of $BF_3{\cdot}OEt_2$ (0.080 mL, 0.62 mmol) to give **7** (0.095 g, 50%) as a colourless solid: mp 137–139 °C; IR (film) 1702, 1648, 1602 cm^{-1}; ^1H NMR δ: 7.22 (3H, m), 7.13 (3H, m), 6.95 (2H, m), 6.76 (2H, m), 6.60 (1H, dd, J = 2.7, 1.8 Hz), 6.14 (1H, dd, J = 3.5, 2.7 Hz), 5.96 (1H, dd, J = 3.5, 1.8 Hz), 5.07 (1H, d, J = 16 Hz), 4.87 (1H, d, J = 16 Hz), 3.82 (1H, br d, $J \approx 3$ Hz), 3.46 (1H, d, J = 3.1 Hz), 1.81 (6H, br s); ^{13}C NMR δ: 206.8, 170.0, 141.1, 138.2, 135.7, 130.0, 129.1 (2C), 128.7 (2C), 127.6 (2C), 127.4, 127.3, 126.5 (2C), 122.6, 107.6, 106.4, 57.9, 54.0, 51.0, 15.7, 8.7; HRMS (ESI) 364.1671, $[C_{24}H_{23}NONa]^+$ requires 364.1672.

(*trans*)-2,3-Dimethyl-4-phenyl-5-(1-phenyl-1*H*-pyrrol-2-yl)cyclopent-2-enone (131)

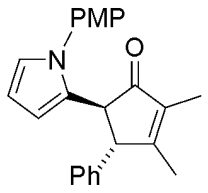


131

According to the procedure for **125**: AVK **26** (0.10 g, 0.56 mmol) and 1-phenylpyrrole (0.16 g, 1.1 mmol) were reacted in the presence of $BF_3{\cdot}OEt_2$ (0.080 mL, 0.62 mmol) to yield **131** (0.13 g, 67%) as a pale yellow solid: mp 132–133 °C; IR (film) 1705, 1650, 1599 cm^{-1}; ^1H NMR δ: 7.18 (6H, m), 7.12 (2H, m), 6.88 (2H, m), 6.74 (1H,

dd, J = 3.2, 1.7 Hz), 6.24 (1H, t, J = 3.2 Hz), 6.00 (1H, dd, J = 3.2, 1.7 Hz), 3.77 (1H, br d, $J \approx 3$ Hz), 3.55 (1H, d, J = 2.9 Hz), 1.78 (3H, br s), 1.77 (3H, s); ^{13}C NMR δ: 207.4, 170.1, 141.1, 139.9, 135.9, 131.4, 129.1 (2C), 129.0 (2C), 127.6 (4C), 127.3, 127.1, 123.0, 108.7, 107.1, 59.7, 53.9, 15.7, 8.8; HRMS (ESI) 350.1513, $[C_{23}H_{21}NONa]^+$ requires 350.1515.

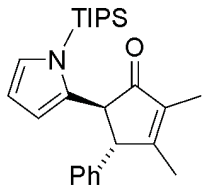
(*trans*)-5-(1-(4-Methoxyphenyl)-1*H*-pyrrol-2-yl)-2,3-dimethyl-4-phenyl-cyclopent-2-enone (132)



132

According to the procedure for **125**: AVK **26** (0.10 g, 0.56 mmol) and 1-(4-methoxyphenyl)pyrrole (0.19 g, 1.1 mmol) reacted in the presence of $BF_3{\cdot}OEt_2$ (0.080 mL, 0.62 mmol) to yield **132** (0.082 g, 41%) as an off-white solid: mp 115–117 °C; IR (film) 1705, 1649, 1605 cm^{-1}; ^{1}H NMR δ: 7.20 (3H, m), 7.03 (2H, d, J = 8.9 Hz), 6.89 (2H, m), 6.69 (3H, m), 6.21 (1H, t, J = 3.2 Hz), 5.98 (1H, dd, J = 3.5, 1.7 Hz), 3.75 (3H, s), 3.75 (1H, *overlapped*), 3.51 (1H, d, J = 2.8 Hz), 1.78 (3H, br s), 1.77 (3H, s); ^{13}C NMR δ: 207.5, 170.1, 159.0, 141.2, 135.9, 132.9, 131.6, 129.0 (2C), 128.4 (2C), 127.7 (2), 127.2, 123.2, 114.1 (2C), 108.3, 106.7, 59.6, 55.7, 53.9, 15.7, 8.8; HRMS (ESI) 380.1623, $[C_{24}H_{23}NO_2Na]^+$ requires 380.1621.

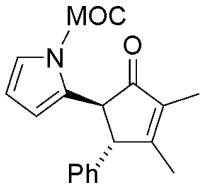
(*trans*)-2,3-Dimethyl-4-phenyl-5-(1-(triisopropylsilyl)-1*H*-pyrrol-2-yl)cyclopent-2-enone (133)



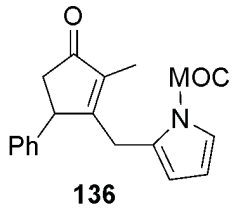
133

According to the procedure for **125**: AVK **26** (0.10 g, 0.56 mmol) and 1-(triisopropylsilyl)pyrrole (0.25 mL, 1.1 mmol) reacted in the presence of $BF_3{\cdot}OEt_2$ (0.080 mL, 0.62 mmol) to yield **133** (0.070 g, 31%) as a pale yellow oil: IR (film) 1706, 1652, 1609 cm^{-1}; ^1H NMR δ: 7.31 (2H, m), 7.26 (1H, m), 7.12 (2H, m), 6.70 (1H, t, J = 2.4 Hz), 6.63 (1H, m), 6.13 (1H, m), 3.80 (1H, br d, $J \approx 3$ Hz), 3.46 (1H, d, J = 2.8 Hz), 1.84 (6H, m), 1.40 (3H, m), 1.07 (18H, m); ^{13}C NMR δ: 209.1, 169.6, 142.3, 136.5, 129.2 (2C), 128.0 (2C), 127.2, 124.7, 122.8, 122.1, 109.4, 59.5, 55.0, 18.2, 15.8, 12.0, 8.9; HRMS (ESI) 430.2535, $[C_{26}H_{37}NOSiNa]^+$ requires 430.2537.

Methyl-2-((*trans*)-3,4-dimethyl-2-oxo-5-phenylcyclopent-3-enyl)-1*H*-pyrrole-1-carboxylate (134) and methyl-2-((2-methyl-3-oxo-5-phenylcyclopent-1-enyl)methyl)-1*H*-pyrrole-1-carboxylate (136)



134

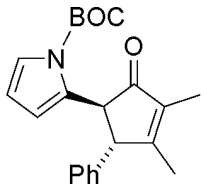


136

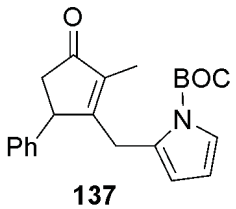
According to the procedure for **125**: AVK **26** (0.10 g, 0.56 mmol) and methyl pyrrole-1-carboxylate (0.13 mL, 1.1 mmol) reacted in the presence of $BF_3{\cdot}OEt_2$ (0.080 mL, 0.62 mmol) to yield 0.038 g (23%) of an inseparable 1:1 mixture of **134** and **136** (as

determined by integration of the ^{1}H NMR spectrum); IR (film) 1748, 1704, 1656, 1602 cm^{-1}; HRMS (ESI) 332.1249, $[C_{19}H_{19}NO_3Na]^+$ requires 332.1257. The following NMR data were taken from the spectra of the mixture: for **134**: ^{1}H NMR δ: 7.32 (1H, m), 7.26 (2H, m), 7.18 (1H, dd, *J* = 3.3, 1.6 Hz), 7.08 (2H, m), 6.10 (1H, t, *J* = 3.3 Hz), 5.90 (1H, m), 3.95 (2H, *overlapped*), 3.70 (3H, br s), 1.87 (3H, s), 1.85 (3H, br s); for **136**: ^{1}H NMR δ: 7.32 (1H, m), 7.26 (3H, m), 7.08 (2H, m), 6.08 (1H, t, *J* = 3.3 Hz), 5.75 (1H, s), 3.98 (1H, d, *J* = 17 Hz), 3.95 (4H, *overlapped*), 3.64 (1H, d, *J* = 17 Hz), 2.89 (1H, dd, *J* = 19, 7.2 Hz), 2.33 (1H, dd, *J* = 19, 2.2 Hz), 1.77 (3H, s); ^{13}C NMR δ: 209.7, 206.0, 171.7, 168.1, 151.3, 151.2, 142.2, 141.3, 138.3, 136.3, 130.3 (2C), 129.0 (4C), 128.1 (2C), 127.6 (2C), 127.3, 127.1, 122.4, 121.5, 114.1, 111.1, 111.0, 57.3, 54.0 (2C), 53.9, 47.4, 45.1, 29.3, 15.6, 8.8, 8.4.

tert-Butyl-2-((_trans_)-3,4-dimethyl-2-oxo-5-phenylcyclopent-3-enyl)-1_H_-pyrrole-1-carboxylate (135) and _tert_-butyl-2-((2-methyl-3-oxo-5-phenylcyclopent-1-enyl)methyl)-1_H_-pyrrole-1-carboxylate (137)



135

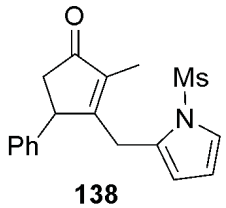


137

According to the procedure for **125**: AVK **26** (0.10 g, 0.56 mmol) and *tert*-butyl pyrrole-1-carboxylate (0.19 mL, 1.1 mmol) reacted in the presence of $BF_3{\cdot}OEt_2$ (0.080 mL, 0.62 mmol) to yield 0.064 g (33%) of an inseparable 1.4:1 mixture of **135** and **137** (as determined by integration of the ^{1}H NMR spectrum); IR (film) 1744, 1707, 1651, 1601 cm^{-1}; HRMS (ESI) 374.1722, $[C_{22}H_{25}NO_3Na]^+$ requires 374.1727; the following

NMR data were taken from the spectra of the mixture: for **135**: ^{1}H NMR δ: 7.29 (2H, m), 7.24 (1H, m), 7.15 (1H, dd, *J* = 3.3, 1.7 Hz), 7.01 (2H, m), 6.04 (1H, t, *J* = 3.3 Hz), 5.73 (1H, m), 3.94 (1H, d, *J* = 17 Hz), 3.92 (1H, *overlapped*), 3.62 (1H, d, *J* = 17 Hz), 2.90 (1H, dd, *J* = 19, 7.1 Hz), 2.36 (1H, dd, *J* = 19, 2.0 Hz), 1.76 (3H, s), 1.46 (9H, s); for **137**: ^{1}H NMR δ: 7.29 (2H, m), 7.24 (1H, m), 7.20 (1H, dd, *J* = 3.3, 1.8 Hz), 7.09 (2H, m), 6.06 (1H, t, *J* = 3.3 Hz), 5.91 (1H, s), 3.91 (1H, *overlapped*), 3.86 (1H, m), 1.84 (6H, s), 1.50 (9H, s); ^{13}C NMR δ: 209.8, 206.1, 172.2, 167.8, 149.6, 149.4, 142.4, 141.5, 138.5, 136.2, 130.2 (2C), 129.1 (4C), 128.2 (2C), 127.7 (2C), 127.3, 127.2, 122.6, 121.6, 113.3, 110.3, 110.2, 84.0, 83.8, 57.4 (2C), 47.6, 45.1, 29.3, 28.2, 28.1, 15.7, 8.9, 8.5.

2-Methyl-3-((1-(methylsulfonyl)-1*H*-pyrrol-2-yl)methyl)-4-phenylcyclopent-2-enone (138)



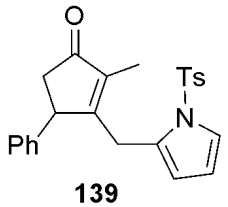
138

Procedure 1: A solution of AVK **26** (0.10 g, 0.56 mmol) and 1-(methanesulfonyl)pyrrole (0.16 g, 1.1 mmol) in CH_2Cl_2 (25 mL) was cooled to –78 °C, and $BF_3{\cdot}OEt_2$ (0.080 mL, 0.62 mmol) was added. The mixture was stirred for 5 min at -78 °C before it was poured into a separatory funnel containing saturated aqueous $NaHCO_3$. The CH_2Cl_2 layer was removed, and additional CH_2Cl_2 (×2) was used to re-extract the aqueous layer. The combined organic layers were dried over Na_2SO_4 and then concentrated under reduced pressure. Flash chromatography (25% EtOAc in hexanes with 2.5% triethylamine, then 50% EtOAc in hexanes with 2.5% triethylamine) of the

residue provided **138** (0.021 g, 11%) as a pale yellow oil: IR (film) 1700, 1645, 1602 cm^{-1}; ^1H NMR δ: 7.26 (4H, m), 7.09 (1H, dd, *J* = 3.3, 1.7 Hz), 7.02 (2H, m), 6.21 (1H, t, *J* = 3.3 Hz), 5.86 (1H, m), 3.99 (1H, m), 3.92 (1H, d, *J* = 17 Hz), 3.50 (1H, d, *J* = 17 Hz), 2.94 (1H, dd, *J* = 19, 7.1 Hz), 2.78 (3H, s), 2.39 (1H, dd, *J* = 19, 2.3 Hz), 1.83 (3H, s); ^{13}C NMR δ: 209.0, 169.8, 141.8, 139.5, 129.2 (6C), 127.4 (4C), 127.5 (2C), 122.5, 114.5, 111.9, 47.0, 44.9, 42.5, 27.7, 8.7; HRMS (ESI) 352.0992, $[C_{18}H_{19}NO_3SNa]^+$ requires 352.0978.

Procedure 2: A solution of AVK **26** (0.10 g, 0.56 mmol) and 1-(methanesulfonyl)pyrrole (0.16 g, 1.1 mmol) in CH_2Cl_2 (25 mL) was cooled to –78 °C, and $InCl_3$ (0.24 g, 1.1 mmol) was added. The mixture was stirred for 2 h before it was poured into a separatory funnel containing saturated aqueous $NaHCO_3$. The CH_2Cl_2 layer was removed, and additional CH_2Cl_2 (×2) was used to re-extract the aqueous layer. The combined organic layers were dried over Na_2SO_4 and then concentrated under reduced pressure. Flash chromatography (25% EtOAc in hexanes with 2.5% triethylamine, then 50% EtOAc in hexanes with 2.5% triethylamine) of the residue provided **138** (0.075 g, 41%) as a pale yellow oil.

2-Methyl-4-phenyl-3-((1-(*para*-toluenesulfonyl)-1*H*-pyrrol-2-yl)methyl)cyclopent-2-enone (139)



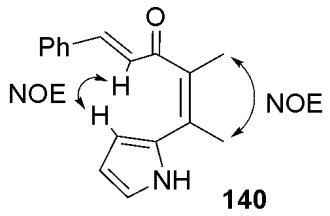
139

According to *Procedure 1* for **138**: AVK **26** (0.10 g, 0.56 mmol) and 1-(*p*-

toluenesulfonyl)pyrrole (0.25 g, 1.1 mmol) were reacted in the presence of $BF_3{\cdot}OEt_2$ (0.080 mL, 0.62 mmol) to yield **139** (0.022 g, 10%) as a pale yellow oil: IR (film) 1703, 1648, 1597 cm^{-1}; ^1H NMR δ: 7.50 (2H, m), 7.35 (1H, m), 7.26 (5H, m), 6.94 (2H, m), 6.21 (1H, t, *J* = 3.3 Hz), 5.72 (1H, m), 3.88 (1H, d, *J* = 17 Hz), 3.66 (1H, m), 3.40 (1H, d, *J* = 17 Hz), 2.70 (1H, dd, *J* = 19, 7.1 Hz), 2.44 (3H, s), 2.29 (1H, dd, *J* = 19, 2.1 Hz), 1.75 (3H, s); ^{13}C NMR δ: 209.0, 169.8, 145.0, 141.6, 139.0, 136.1, 130.0 (2C), 129.2, 128.9 (2C), 127.4 (2C), 127.1, 126.5 (2C), 123.3, 114.6, 111.3, 47.0, 44.6, 27.6, 21.7, 8.4; HRMS (ESI) 428.1279, $[C_{24}H_{23}NO_3SNa]^+$ requires 428.1291.

According to *Procedure 2* for **138**: AVK **26** (0.10 g, 0.56 mmol) and 1-(*p*-toluenesulfonyl)pyrrole (0.25 g, 1.1 mmol) were reacted in the presence of $InCl_3$ (0.24 g, 1.1 mmol) to yield **139** (0.099 g, 44%) as a pale yellow oil.

(1*E*,4*Z*)-4-Methyl-1-phenyl-5-(1*H*-pyrrol-2-yl)hexa-1,4-dien-3-one (140)



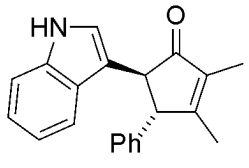
140

Procedure 1: A solution of AVK **26** (0.025 g, 0.14 mmol) and pyrrole (0.020 mL, 0.28 mmol) in CH_2Cl_2 (7 mL) was cooled to –78 °C, and $Sc(OTf)_3$ (0.14 g, 0.28 mmol) was added at once. The mixture was stirred for 45 min, then poured into a separatory funnel containing a saturated aqueous solution of $NaHCO_3$. Following addition of CH_2Cl_2, the aqueous layer was re-extracted with additional CH_2Cl_2 (×2). The combined organic extracts were dried over Na_2SO_4 and concentrated under reduced pressure, and

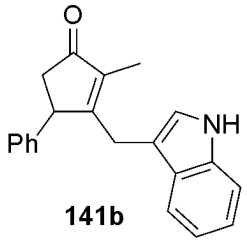
the product was purified by flash chromatography (10% ethyl acetate in hexanes, and then 25% ethyl acetate in hexanes) to yield **140** (0.015 g, 42%) as an orange oil: IR (film) 3334, 1650, 1591, 1578 cm^{-1}; ^1H NMR δ: 9.20 (1H, br s), 7.49 (1H, d, J = 16 Hz), 7.39 (2H, m), 7.32 (3H, m), 6.73 (1H, m), 6.57 (1H, d, J = 16 Hz), 6.36 (1H, m), 6.20 (1H, m), 2.21 (3H, s), 2.07 (3H, s); ^{13}C NMR δ: 198.6, 142.4, 135.0, 133.2, 132.3, 130.8, 130.2, 128.8 (2C), 128.2 (2C), 126.0, 119.4, 110.4, 109.7, 20.1, 17.6; HRMS (ESI) 274.1203, $[C_{17}H_{17}NONa]^+$ requires 274.1202.

Procedure 2: A solution of AVK **26** (0.025 g, 0.14 mmol) and pyrrole (0.020 mL, 0.28 mmol) in CH_2Cl_2 (7 mL) was cooled to –78 °C, and $InCl_3$ (0.060 g, 0.28 mmol) was added at once. The mixture was stirred for 2 h, then poured into a separatory funnel containing a saturated aqueous solution of $NaHCO_3$. Following addition of CH_2Cl_2, the aqueous layer was re-extracted with additional CH_2Cl_2 (×2). The combined organic extracts were dried over Na_2SO_4 and concentrated under reduced pressure, and the product was purified by flash chromatography (10% ethyl acetate in hexanes, and then 25% ethyl acetate in hexanes) to yield **140** (0.009 g, 26%) as an orange oil.

(*trans*)-5-(1*H*-Indol-3-yl)-2,3-dimethyl-4-phenylcyclopent-2-enone (141a) and 3-((1*H*-indol-3-yl)methyl)-2-methyl-4-phenylcyclopent-2-enone (141b)



141a

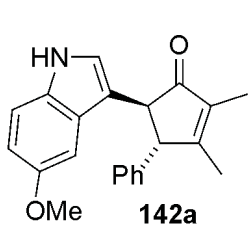


141b

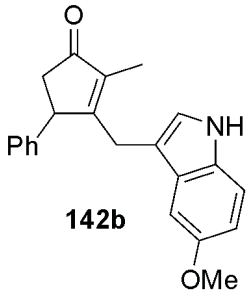
A solution of AVK **26** (0.10 g, 0.56 mmol) and indole (0.13 g, 1.1 mmol) in CH_2Cl_2 (25 mL) was cooled to –78 °C, and $BF_3{\cdot}OEt_2$ (0.080 mL, 0.62 mmol) was added.

The mixture was stirred for 5 min at –78 °C before it was poured into a separatory funnel containing saturated aqueous $NaHCO_3$. The CH_2Cl_2 layer was removed, and additional CH_2Cl_2 (×2) was used to re-extract the aqueous layer. The combined organic layers were dried over Na_2SO_4 and then concentrated under reduced pressure provided a mixture of **141a** and **141b** (3.7:1, respectively, (as determined by integration of the crude ^{1}H NMR spectrum). Flash chromatography (10%, then 35%, EtOAc in hexanes) of the residue yielded **141a** (0.11 g, 68%), still contaminated with < 10% **141b**, as a pale orange solid, and 0.030 g (20%) of a sample containing a mixture of **141a** and **141b**. For **141a**: IR (film) 3302, 1692, 1648, 1598 cm^{-1}; ^{1}H NMR δ: 8.09 (1H, br s), 7.31 (4H, m), 7.13 (4H, m), 7.00 (1H, m), 6.91 (1H, s), 3.93 (1H, br d, $J \approx 3$ Hz), 3.74 (1H, d, $J = 2.8$ Hz), 1.94 (3H, br s), 1.90 (3H, s); ^{13}C NMR δ: 209.1, 170.4, 142.0, 136.8, 129.1 (2C), 127.9 (2C), 127.3, 126.6, 122.6, 122.4, 119.7, 119.4, 113.8, 111.5, 58.9, 54.5, 15.8, 8.8; HRMS (ESI) 324.1361, $[C_{21}H_{19}NONa]^+$ requires 324.1359. The following data for **141b** were taken from spectra of a mixture of **141a** and **141b**: ^{1}H NMR δ: 8.11 (1H, *overlapped*), 7.31 (4H, *overlapped*), 7.13 (4H, *overlapped*), 7.01 (2H, *overlapped*), 3.93 (1H, *overlapped*), 3.80 (1H, m), 3.35 (1H, d, $J = 16$ Hz), 2.80 (1H, dd, $J = 19$, 7.1 Hz), 2.33 (1H, dd, $J = 19$, 2.3 Hz), 2.04 (3H, s); ^{13}C NMR δ: 209.9, 173.9, 142.4, 137.1, 136.4, 129.0 (2C), 127.8 (2C), 127.2, 124.9, 122.9, 122.5, 119.8, 118.7, 111.5, 111.3, 46.5, 44.9, 25.3, 8.9.

(*trans*)-5-(5-Methoxy-1*H*-indol-3-yl)-2,3-dimethyl-4-phenylcyclopent-2-enone (142a) and 3-((5-methoxy-1*H*-indol-3-yl)methyl)-2-methyl-4-phenylcyclopent-2-enone (142b)



142a

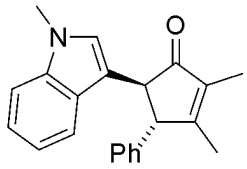


142b

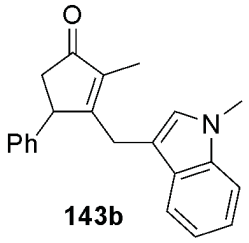
Following the procedure for **141a** and **141b**: AVK **26** (0.10 g, 0.56 mmol) and 5-methoxyindole (0.16 g, 1.1 mmol) were reacted in the presence of $BF_3{\cdot}OEt_2$ (0.080 mL, 0.62 mmol) to yield a 3.8:1 mixture of **142a** and **142b** (ratios determined by integration of crude ^{1}H NMR spectrum). Flash chromatography gave a sample of **142a** (0.095 g, 53%), contaminated with < 10% **19b**, as a yellow solid, and 0.022 g (39%) of a sample containing a mixture of **142a** and **142b**. For **142a**: IR (film) 3347, 1694, 1644, 1602 cm^{-1}; ^{1}H NMR δ: 8.08 (1H, br s), 7.30 (3H, m), 7.16 (3H, m), 6.86 (1H, m), 6.79 (1H, m), 6.52 (1H, s), 3.87 (1H, br d, $J \approx 3$ Hz), 3.76 (1H, d, $J = 2.9$ Hz), 3.63 (3H, s), 1.93 (3H, br s), 1.88 (3H, s); ^{13}C NMR δ: 209.1, 170.4, 154.0, 142.1, 136.8, 131.9, 129.1 (2C), 129.0, 128.0 (2C), 127.8, 127.4, 123.0, 112.4, 112.2, 101.3, 59.1, 55.8, 54.3, 15.7, 8.8; HRMS (ESI) 354.1463, $[C_{22}H_{21}NO_2Na]^+$ requires 354.1465. The following data for **142b** were taken from spectra of a mixture of **142a** and **142b**: ^{1}H NMR δ: 8.01 (1H, *overlapped*), 7.31 (3H, *overlapped*), 7.25 (1H, m), 7.03 (2H, m), 6.86 (1H, s), 6.75 (1H, m), 6.74 (1H, m), 3.89 (1H, *overlapped*), 3.87 (1H, *overlapped*), 3.83 (3H, s), 3.31 (1H, d, $J = 16$ Hz), 2.81 (1H, dd, $J = 19$, 7.2 Hz), 2.33 (1H, dd, $J = 19$, 2.3 Hz), 2.04 (3H, s); ^{13}C NMR δ: 209.9, 173.8, 154.3, 142.5, 137.0, 131.5, 129.0 (2C), 127.8 (2C), 127.2,

123.6, 112.7, 112.2, 111.0, 100.4, 56.0, 46.5, 44.9, 25.2, 8.9.

(*trans*)-2,3-Dimethyl-5-(1-methyl-1*H*-indol-3-yl)-4-phenylcyclopent-2-enone (143a) and 2-methyl-3-((1-methyl-1*H*-indol-3-yl)methyl)-4-phenylcyclopent-2-enone (143b)



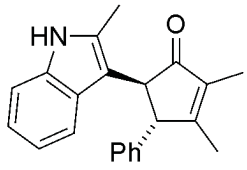
143a



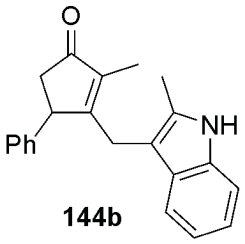
143b

Following the procedure for **141a** and **141b**: AVK **26** (0.10 g, 0.56 mmol) and 1-methylindole (0.14 mL, 1.1 mmol) were reacted in the presence of $BF_3{\cdot}OEt_2$ (0.080 mL, 0.62 mmol) to yield a 3.2:1 mixture of **143a** and **143b** (ratios determined by integration of crude ^{1}H NMR spectrum). Flash chromatography gave a sample of **143a** (0.10 g, 56%), contaminated with < 10% **143b**, as a yellow oil, and 0.060 g (33%) of a sample containing a mixture of **143a** and **143b**. For **143a**: IR (film) 1703, 1648, 1602 cm^{-1}; ^{1}H NMR δ: 7.33 (2H, m), 7.27 (2H, m), 7.19 (1H, m), 7.12 (3H, m), 6.99 (1H, m), 6.83 (1H, s), 3.92 (1H, br d, $J \approx 3$ Hz), 3.73 (1H, d, $J = 2.5$ Hz), 3.71 (3H, s), 1.93 (3H, br s), 1.89 (3H, s); ^{13}C NMR δ: 209.2, 170.3, 142.0, 137.6, 136.8, 129.1 (2C), 127.9 (2C), 127.3, 127.2, 127.0, 121.9, 119.5, 119.2, 112.2, 109.6, 59.2, 54.4, 32.9, 15.8, 8.8; HRMS (ESI) 338.1505, $[C_{22}H_{21}NONa]^+$ requires 338.1515. The following data for **143b** were taken from spectra of a mixture of **143a** and **143b**: ^{1}H NMR δ: 7.31 (4H, *overlapped*), 7.20 (1H, m), 7.09 (1H, m), 7.01 (3H, m), 6.61 (1H, s), 3.92 (1H, *overlapped*), 3.83 (1H, m), 3.74 (3H, s), 3.34 (1H, d, $J = 15$ Hz), 2.81 (1H, dd, $J = 19$, 7.1 Hz), 2.34 (1H, dd, $J = 19$, 2.1 Hz), 2.04 (3H, s); ^{13}C NMR δ: 209.9, 174.0, 142.5, 137.2, 137.0, 129.0 (2C), 127.8 (2C), 127.5, 127.2, 122.0, 119.3, 118.9, 109.7, 109.5, 46.5, 44.9, 25.1, 8.9.

(*trans*)-2,3-Dimethyl-5-(2-methyl-1*H*-indol-3-yl)-4-phenylcyclopent-2-enone (144a) and 2-methyl-3-((2-methyl-1*H*-indol-3-yl)methyl)-4-phenylcyclopent-2-enone (144b)



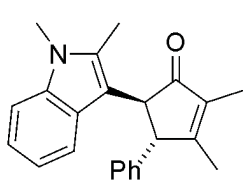
144a



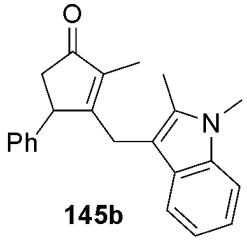
144b

According to the procedure for **141a** and **141b**: AVK **26** (0.10 g, 0.56 mmol) and 2-methylindole (0.14 g, 1.1 mmol) were reacted in the presence of $BF_3{\cdot}OEt_2$ (0.080 mL, 0.62 mmol) to yield **144a** (0.059 g, 37%) and **144b** (0.037 g, 23%). For **144a**: pale yellow solid, mp 175–178 °C; IR (film) 3336, 1695, 1644, 1602 cm^{-1}; ^1H NMR δ: 7.94 (1H, br s), 7.30 (2H, m), 7.25 (1H, m), 7.21 (1H, m), 7.05 (3H, m), 6.96 (2H, m), 3.90 (1H, br d, $J \approx 3$ Hz), 3.60 (1H, d, $J = 3.1$ Hz), 1.97 (3H, br s), 1.94 (3H, s), 1.91 (3H, s); ^{13}C NMR δ: 209.3, 170.2, 142.0, 137.5, 135.8, 133.4, 129.1 (2C), 127.7 (2C), 127.2, 127.1, 121.2, 119.5, 118.2, 110.7, 108.8, 58.4, 54.5, 15.7, 11.8, 8.9; HRMS (ESI) 338.1507, $[C_{22}H_{21}NONa]^+$ requires 338.1515. For **144b**: pale yellow solid, mp 190–193 °C; IR (film) 3343, 1690, 1638, 1602 cm^{-1}; ^1H NMR δ: 7.79 (1H, br s), 7.31 (3H, m), 7.26 (1H, m), 7.16 (2H, m), 7.05 (1H, m), 6.92 (2H, m), 3.94 (1H, d, $J = 16$ Hz), 3.68 (1H, m), 3.37 (1H, d, $J = 16$ Hz), 2.81 (1H, dd, $J = 19$, 7.2 Hz), 2.28 (1H, dd, $J = 19$, 2.2 Hz), 2.08 (3H, s), 1.89 (3H, s); ^{13}C NMR δ: 209.9, 174.5, 142.6, 137.3, 135.4, 132.6, 128.9 (2C), 128.7, 127.7 (2C), 127.0, 121.5, 119.7, 118.0, 110.5, 106.8, 46.3, 45.1, 24.7, 11.4, 8.9; HRMS (ESI) 338.1515, $[C_{22}H_{21}NONa]^+$ requires 338.1515.

(*trans*)-5-(1,2-Dimethyl-1*H*-indol-3-yl)-2,3-dimethyl-4-phenylcyclopent-2-enone (145a) and 3-((1,2-dimethyl-1*H*-indol-3-yl)methyl)-2-methyl-4-phenylcyclopent-2-enone (145b)



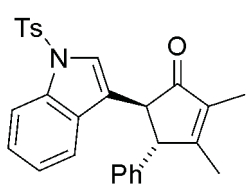
145a



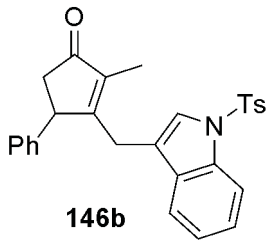
145b

According to the procedure for **141a** and **141b**: AVK **26** (0.10 g, 0.56 mmol) and 1,2-dimethylindole (0.16 g, 1.1 mmol) were reacted in the presence of $BF_3{\cdot}OEt_2$ (0.080 mL, 0.62 mmol) to yield **145a** (0.11 g, 62%) and **145b** (0.052 g, 28%). For **145a**: pale yellow solid, mp 164–166 °C; IR (film) 1702, 1648, 1602 cm^{-1}; ^1H NMR δ: 7.31 (2H, m), 7.25 (2H, m), 7.12 (1H, m), 7.06 (2H, m), 6.97 (2H, m), 3.90 (1H, br d, $J \approx 3$ Hz), 3.65 (1H, d, $J = 3.2$ Hz), 3.61 (3H, s), 2.03 (3H, s), 1.97 (3H, br s), 1.94 (3H, s); ^{13}C NMR δ: 209.3, 169.9, 142.1, 137.4, 137.2, 135.0, 129.1 (2C), 127.7 (2C), 127.1, 126.1, 120.9, 119.1, 118.2, 109.0, 108.0, 58.6, 54.9, 29.8, 15.7, 10.5, 8.9; HRMS (ESI) 352.1667, $[C_{23}H_{23}NONa]^+$ requires 352.1672. For **145b**: pale yellow solid, mp 199–201 °C; IR (film) 1698, 1641, 1602 cm^{-1}; ^1H NMR δ: 7.25 (4H, m), 7.16 (1H, m), 7.12 (1H, m), 7.01 (1H, m), 6.86 (2H, m), 3.92 (1H, d, $J = 16$ Hz), 3.62 (1H, m), 3.61 (3H, s), 3.37 (1H, d, $J = 16$ Hz), 2.74 (1H, dd, $J = 19$, 7.4 Hz), 2.24 (1H, dd, $J = 19$, 2.2 Hz), 2.04 (3H, s), 1.85 (3H, s); ^{13}C NMR δ: 209.9, 174.5, 142.7, 137.1, 136.8, 134.4, 128.9 (2C), 127.8, 127.6 (2C), 127.0, 121.0, 119.2, 118.0, 108.8, 105.9, 46.2, E45.1, 29.8, 25.0, 10.0, 8.9; HRMS (ESI) 352.1676, $[C_{23}H_{23}NONa]^+$ requires 352.1672.

(*trans*)-2,3-Dimethyl-4-phenyl-5-(1-tosyl-1*H*-indol-3-yl)cyclopent-2-enone (146a) and 2-methyl-4-phenyl-3-((1-tosyl-1*H*-indol-3-yl)methyl)cyclopent-2-enone (146b).



146a

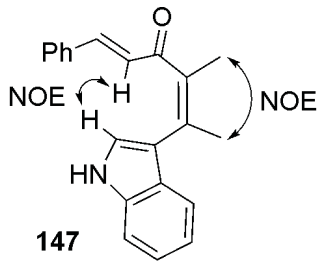


146b

A solution of AVK **26** (0.10 g, 0.56 mmol) and 1-(toluenesulfonyl)indole (0.30 g, 1.1 mmol) in CH_2Cl_2 (25 mL) was cooled to –78 °C, and $InCl_3$ (0.24 g, 1.1 mmol) was added. The mixture was stirred for 2 h before it was poured into a separatory funnel containing saturated aqueous $NaHCO_3$. The CH_2Cl_2 layer was removed, and additional CH_2Cl_2 (×2) was used to re-extract the aqueous layer. The combined organic layers were dried over Na_2SO_4 and then concentrated under reduced pressure. Flash chromatography (20%, then 33%, EtOAc in hexanes) of the residue provided **146a** (0.064 g, 25%) and **146b** (0.061 g, 24%). For **146a**: colourless solid, mp 76–78 °C; IR (film) 1708, 1650, 1605 cm^{-1}; ^1H NMR δ: 7.94 (1H, m), 7.74 (2H, d, J = 8.5 Hz), 7.33 (4H, m), 7.27 (1H, m), 7.22 (2H, d, J = 8.5 Hz), 7.08 (3H, m), 7.03 (1H, m), 3.80 (1H, br d, $J \approx 3$ Hz), 3.67 (1H, d, J = 3.0 Hz), 2.34 (3H, s), 1.92 (3H, br s), 1.89 (3H, s); ^{13}C NMR δ: 207.1, 170.4, 145.1, 141.2, 136.9, 135.6, 135.3, 130.1 (3C), 129.3 (2C), 127.8 (2C), 127.6, 127.1 (2C), 125.0, 123.8, 120.2, 120.1, 113.9, 58.1, 53.7, 21.8, 15.8, 8.8; HRMS (ESI) 478.1424, $[C_{28}H_{25}NO_3SNa]^+$ requires 478.1447. For **146b**: colourless solid, mp 61–63 °C; IR (film) 1704, 1650, 1601 cm^{-1}; ^1H NMR δ: 8.01 (1H, m), 7.75 (2H, d, J = 8.4 Hz), 7.31 (4H, m), 7.25 (2H, d, J = 8.4 Hz), 7.19 (2H, m), 7.08 (1H, s), 6.93 (2H, m), 3.79 (1H, d, J = 16 Hz), 3.67 (1H, m), 3.28 (1H, d, J = 16 Hz), 2.82 (1H, dd, J = 19, 7.2 Hz), 2.36 (s, 3H), 2.34 (1H, dd, J = 19, 2.1 Hz), 1.92 (3H, s); ^{13}C NMR δ: 209.3, 171.1, 145.3, 141.8, 138.1,

135.5, 135.4, 130.5, 130.1 (2C), 129.2 (2C), 127.7 (2C), 127.5, 127.0 (2C), 125.2, 124.4, 123.5, 119.3, 117.9, 114.1, 46.7, 44.8, 25.2, 21.8, 8.9; HRMS (ESI) 478.1431, $[C_{28}H_{25}NO_3SNa]^+$ requires 478.1447.

(1*E*,4*Z*)-5-(1*H*-Indol-3-yl)-4-methyl-1-phenylhexa-1,4-dien-3-one (147)

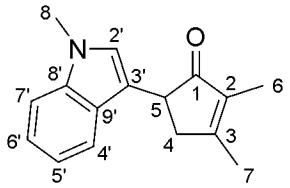


147

According to *Procedure 1* for **140**: AVK **26** (0.025 g, 0.14 mmol) and indole (0.032 g, 0.28 mmol) were reacted with $Sc(OTf)_3$ (0.14 g, 0.28 mmol) to yield **147** (0.016 g, 38%) as a yellow oil: IR (film) 3325, 1646, 1596, 1578 cm^{-1}; ^1H NMR δ: 8.21 (1H, br s), 7.73 (1H, m), 7.29 (1H, m), 7.23 (4H, m), 7.13 (2H, m), 6.89 (1H, d, J = 2.5 Hz), 6.75 (2H, m), 6.14 (1H, d, J = 16 Hz), 2.35 (3H, s), 2.08 (3H, s); ^{13}C NMR δ: 198.0, 138.5, 137.0, 136.8, 136.6, 135.4, 129.2, 127.7 (2C), 127.2 (2C), 126.1, 122.8, 120.6, 120.1, 119.3, 111.6 (2C), 20.7, 16.3; HRMS (ESI) 324.1358, $[C_{21}H_{19}NONa]^+$ requires 324.1359.

According to *Procedure 2* for **140**: AVK **26** (0.025 g, 0.14 mmol) and indole (0.032 g, 0.28 mmol) were reacted with $InCl_3$ (0.060 g, 0.28 mmol) to yield **147** (0.008 g, 19%) as a yellow oil.

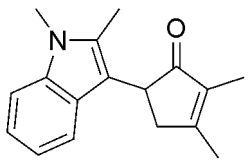
2,3-Dimethyl-5-(1-methyl-1*H*-indol-3-yl)cyclopent-2-enone (148)



148

According to the procedure for **141a** and **141b**: AVK **27** (0.075 g, 0.69 mmol) and 1-methylindole (0.17 mL, 1.4 mmol) were reacted in the presence of $BF_3{\cdot}OEt_2$ (0.090 mL, 0.76 mmol) to yield **148** (0.084 g, 51%), as a colourless oil: IR (film) 1697, 1654 cm^{-1}; ^1H NMR δ: 7.37 (1H, m, H4'), 7.28 (1H, m, H7'), 7.20 (1H, m, H6'), 7.05 (1H, m, H5'), 6.95 (1H, s, H2'), 3.84 (1H, dd, *J* = 7.3, 2.7 Hz, H5), 3.72 (3H, s, H8), 3.12 (1H, dd, *J* = 18, 7.3 Hz, H4a), 3.12 (1H, br dd, *J* = 18, ~3 Hz, H4b), 2.11 (3H, s, H7), 1.81 (3H, s, H6); ^{13}C NMR δ: 209.8 (C1), 168.6 (C3), 137.5 (C8'), 135.7 (C2), 127.2 (C9'), 126.8 (C2'), 121.9 (C6'), 119.2 (C4'), 119.1 (C5'), 112.9 (C3'), 109.6 (C7'), 43.1 (C5), 41.2 (C4), 32.8 (C8), 17.3 (C7), 8.4 (C6); HRMS (ESI) 262.1190, $[C_{16}H_{17}NONa]^+$ requires 262.1202.

5-(1,2-Dimethyl-1*H*-indol-3-yl)-2,3-dimethylcyclopent-2-enone (149)

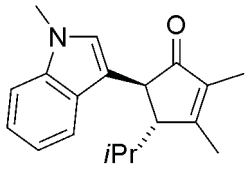


149

According to the procedure for **141a** and **141b**: AVK **27** (0.075 g, 0.69 mmol) and 1,2-dimethylindole (0.20 g, 1.4 mmol) were reacted in the presence of $BF_3{\cdot}OEt_2$ (0.12 mL, 0.84 mmol) to yield **149** (0.091 g, 52%), as a yellow oil (contained <10% of an

inseparable product that likely arose by trapping at position *c*): IR (film) 1704, 1650 cm^{-1}; ^1H NMR δ: 7.22 (1H, m), 7.10 (1H, m), 7.02 (1H, m), 6.95 (1H, m), 3.76 (1H, dd, *J* = 7.3, 3.0 Hz), 3.65 (3H, s), 3.01 (1H, dd, *J* = 18, 7.3 Hz), 2.71 (1H, br dd, *J* = 18, 3 Hz), 2.36 (3H, s), 2.15 (3H, s), 1.84 (3H, s); ^{13}C NMR δ: 210.4, 168.6, 137.0, 136.2, 134.3, 126.2, 120.9, 119.1, 118.0, 109.2, 109.0 43.2, 40.8, 29.8, 17.4, 10.8, 8.6; HRMS (ESI) 276.1362, $[C_{17}H_{19}NONa]^+$ requires 276.1359.

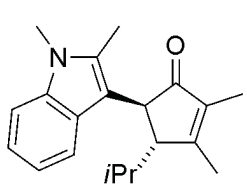
(*trans*)-4-Isopropyl-2,3-dimethyl-5-(1-methyl-1*H*-indol-3-yl)cyclopent-2-enone (150)



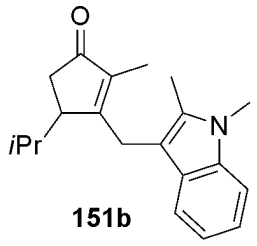
150

According to the procedure for **141a** and **141b**: AVK **29** (0.10 g, 0.67 mmol) and 1-methylindole (0.17 mL, 1.4 mmol) reacted in the presence of $BF_3{\cdot}OEt_2$ (0.090 mL, 0.76 mmol) to yield **150** (0.15 g, 81%), as a white solid (contained <10% of an inseparable product that likely arose by trapping at position *c*): IR (film) 1704, 1654 cm^{-1}; ^1H NMR δ: 7.26 (2H, m), 7.18 (1H, m), 7.01 (1H, m), 6.89 (1H, s), 3.72 (3H, s), 3.51 (1H, d, *J* = 2.6 Hz), 3.01 (1H, m), 2.28 (1H, m), 2.09 (3H, s), 1.82 (3H, s), 1.01 (3H, d, *J* = 6.9 Hz), 0.77 (3H, d, *J* = 6.9 Hz); ^{13}C NMR δ: 209.3, 171.4, 137.6, 136.5, 127.4, 126.7, 121.8, 119.4, 119.1, 113.8, 109.6, 57.1, 44.6, 32.8, 28.7, 21.6, 16.1, 15.6, 8.5; HRMS (ESI) 304.1661, $[C_{19}H_{23}NONa]^+$ requires 304.1672.

(*trans*)-5-(1,2-Dimethyl-1*H*-indol-3-yl)-4-isopropyl-2,3-dimethylcyclopent-2-enone (151a) and 3-((1,2-dimethyl-1*H*-indol-3-yl)methyl)-4-isopropyl-2-methylcyclopent-2-enone (151b)



151a



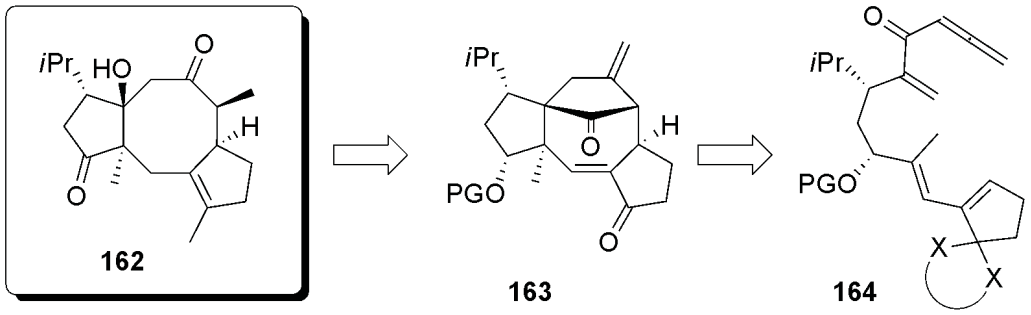
151b

According to the procedure for **141a** and **141b**: AVK **29** (0.10 g, 0.67 mmol) and 1,2-dimethylindole (0.19 g, 1.3 mmol) reacted in the presence of $BF_3{\cdot}OEt_2$ (0.090 mL, 0.76 mmol) to yield a 3.9:1 mixture of **151a** and **151b** (ratios determined by integration of crude ^{1}H NMR spectrum). Flash chromatography afforded a sample of **151a** (0.095 g, 53%), still contaminated with < 10% of **151b**, as a yellow solid, and 0.060 g (26%) of a sample containing a mixture of **151a** and **151b**. For **151a**: IR (film) 1700, 1654 cm^{-1}; ^{1}H NMR δ: 7.21 (1H, m), 7.09 (1H, m), 7.02 (1H, m), 6.93 (1H, m), 3.63 (3H, s), 3.44 (1H, d, *J* = 2.8 Hz), 3.04 (1H, m), 2.38 (3H, s), 2.26 (1H, m), 2.11 (3H, s), 1.83 (3H, s), 0.92 (3H, d, *J* = 6.9 Hz), 0.81 (3H, d, *J* = 6.9 Hz); ^{13}C NMR δ: 209.9, 171.3, 137.1, 137.0, 134.0, 126.5, 120.7, 118.9, 118.1, 109.9, 109.0, 56.8, 44.0, 29.8, 28.3, 21.4, 16.2, 15.5, 11.0, 8.6; HRMS (ESI) 318.1835, $[C_{20}H_{25}NONa]^+$ requires 318.1828. The following data for **151b** were taken from spectra of a mixture of **151a** and **151b**: ^{1}H NMR δ: 7.31 (1H, m), 7.26 (1H, m), 7.16 (1H, m), 7.04 (1H, m), 3.98 (1H, d, *J* = 16 Hz), 3.68 (3H, s), 3.59 (1H, d, *J* = 16 Hz), 2.62 (1H, m), 2.36 (3H, s), 2.11 (2H, *overlapped*), 2.00 (3H, s), 0.85 (3H, d, *J* = 7.0 Hz), 0.64 (3H, d, *J* = 7.0 Hz); ^{13}C NMR δ: 210.4, 175.0, 136.8, 136.7, 133.8, 127.8, 121.1, 119.4, 117.9, 108.9, 106.5, 45.4, 34.9, 29.9, 27.8, 24.8, 22.0, 14.8, 10.7, 8.6.

CHAPTER 5. PROGRESS TOWARDS THE TOTAL SYNTHESIS OF (+)-ROSEADIONE

5.1 Introduction

(+)-Roseadione (**162**), a tricyclic diterpene with a dicyclopenta[*a,d*]cyclooctanoid skeleton, was isolated from the leaves and stems of the tropical shrub *Hypoestes rosea*, collected near Akure, Nigeria.[67] Besides the interest inspired by its molecular complexity, roseadione and molecules of its structural family also have significance in terms of their broad-ranging biological activity.[68] Although there have been studies directed towards the total synthesis of other natural products containing the dicyclopenta[*a,d*]cyclooctanoid framework, to date (+)-roseadione has yet to succumb to total synthesis. The tandem Nazarov/[4 + 3] cascade of allenyl vinyl ketones provides a unique manner in which to access the tricyclic core of this cyclooctanoid natural product. With this in mind, we postulated that the [5,8,5]-tricylic core could be accessed via compound **163**, which could be constructed via a regio- and doubly diastereoselective tandem Nazarov cylization/[4 + 3] cycloaddition strategy from AVK **164** (Scheme 52). The requisite facial and *endo* selectivity for the [4 + 3] cyclization of the oxyallyl cation derived from AVK **164** has moderate precedent, based on work by Harmata and co-workers (Section 5.1.1).

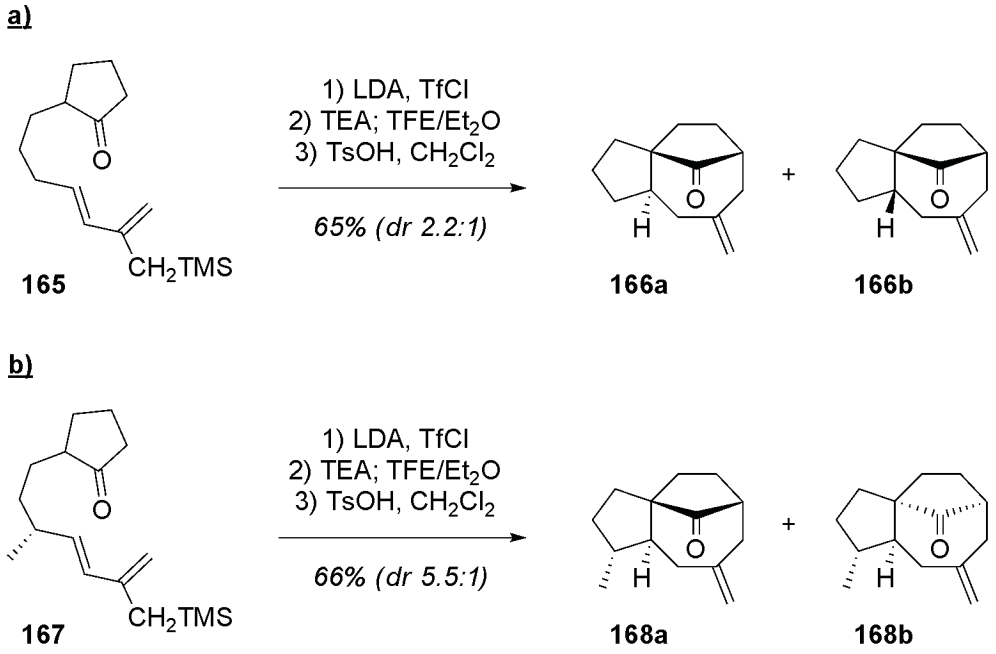


Scheme 52 Retrosynthetic disconnection of (+)-roseadione (**162**) leading to AVK **164**.

5.1.1 Intramolecular [4 + 3] Cyclization of Cyclic Oxyallyl Cations for the Synthesis of Eight-Membered Ring Systems

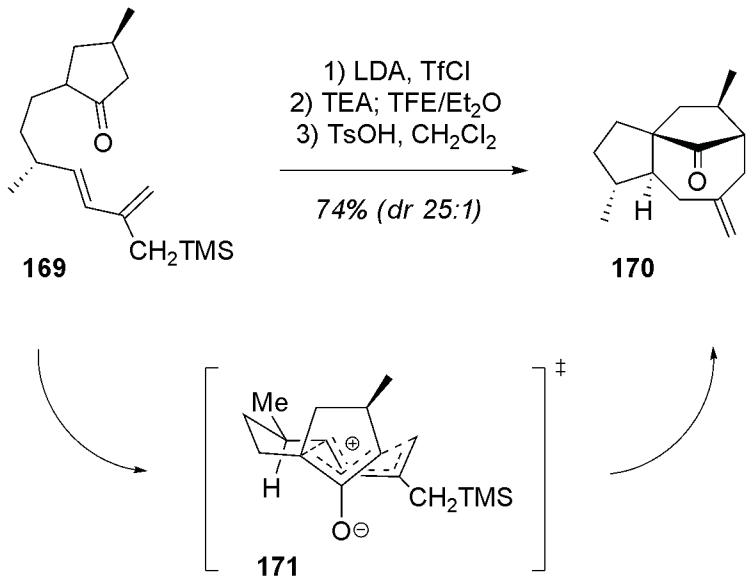
Although the [4 + 3] cyclization of an oxyallyl cation and a diene is a common strategy for the synthesis of seven-membered ring systems, when a five-membered ring oxyallyl cation is utilized the cyclization can be a powerful means in which to generate an eight-membered carbocycle via a formal [4 + 4] process.[54] As previously mentioned (Section 4.1), intermolecular reactions are generally limited to the utilization of furan and cyclopentadiene as diene partners. However, the intramolecular variant appears to be more general, and cyclized products can be produced in high yields for a variety of diene partners under a number of different reaction conditions.[54] Unfortunately, despite the high overall yields commonly reported, the diastereoselectivity of the reaction is often quite poor. However, in an elegant study *en route* to their total synthesis of dactylol,[69] and inspired by the work of Giguere on the diastereoselectivity of [4 + 3] cyclizations of allylic cations derived from allylsilanes,[70] Harmata and co-workers noted that careful placement of stereocenters in the system can result in high levels of stereoselectivity. For example, reaction of substrate **165** proceeded with modest selectivity for the *endo* product **166a** over the *exo* product **166b** (Scheme 53a), but with substitution adjacent to

the diene unit as in **167**, the reaction resulted in a significant increase in selectivity for the *endo* product **168a** (Scheme 53b).[69]



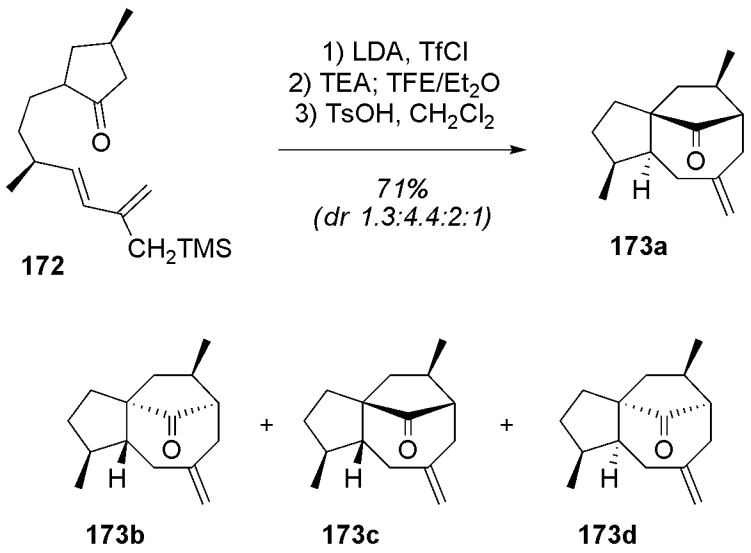
Scheme 53 Intramolecular [4 + 3] cyclizations in which the tether was a) unsubstituted, or b) substituted, at the dienylic position.

In the reaction of compound **167**, the formation of the *exo* product **168b** was the result of addition to the opposite face of the oxyallyl cation, with respect to the formation of *endo* product **168a**. An appropriately placed substituent on the five-membered ring should effectively block that face of the oxyallyl cation, resulting in an increase in *endo* selectivity. Such was indeed the case with compound **169**, which provided the *endo* product **170** almost exclusively (Scheme 54).[69]



Scheme 54 Intramolecular [4 + 3] cyclization in which substitution at the dienylic position of the tether and on the five-membered ring results was "matched".

The high facial and *endo*/*exo* selectivity in the reaction of compound **169** was postulated to be a result of a conformational preference, due to a minimization of steric interactions, for the transition state **171** involving the oxyallyl cation derived from **169**, which led to compound **170**. It is important to recognize, however, that this example is representative of a "matched" case. In an alternative scenario where the stereocenter adjacent to the diene and the stereocenter on the five-membered ring are mismatched, multiple products are formed. Such was the case with the epimer of **169**, compound **172**, which produced roughly equal amounts of all four possible [4 + 3] products **173a-d** (Scheme 55).[69]

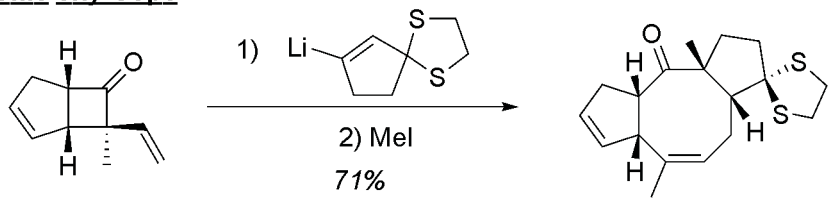


Scheme 55 Intramolecular [4 + 3] cyclization in which substitution at the dienylic position of the tether and on the five-membered ring results was "mismatched".

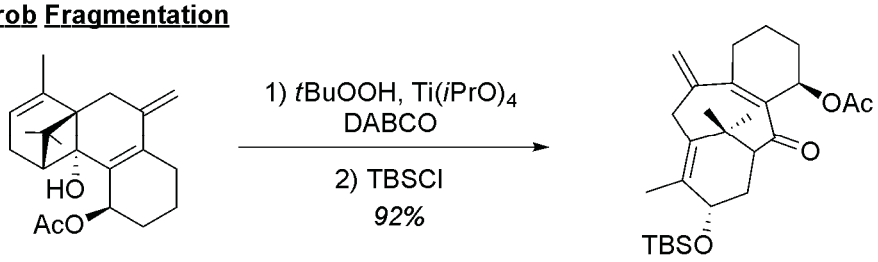
5.1.2 Alternative Methods for the Synthesis of Eight-Membered Ring Systems

The synthesis of eight-membered ring systems is not only valuable from the context of the synthesis of cyclooctanoid natural products, but also as a result of their ability to be subsequently transformed into other useful products through various ring expansion, contraction, or cleavage reactions. Thus, in addition to the [4 + 3] cyclization of cyclopentenyl cations, there exist a number of strategies for the synthesis of cyclooctanoid ring systems, with the consequence that there are several reviews devoted to the subject.[68, 71] Some of these strategies are depicted below in Scheme 56. More traditional approaches invoke a 3,3-sigmatropic rearrangement and/or ring expansion of smaller ring systems, through reactions such as the anionic oxy-Cope process (Scheme 56a)[72] or the Grob fragmentation (Scheme 56b),[73] and have been well-studied. Metal–mediated cyclizations, such as a palladium-catalyzed allylic substitution (Scheme 56c),[74]

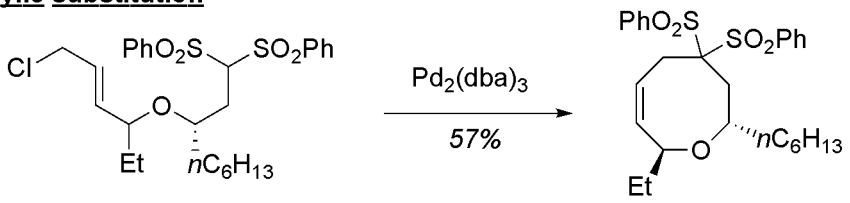
a) **Anionic oxy-Cope**



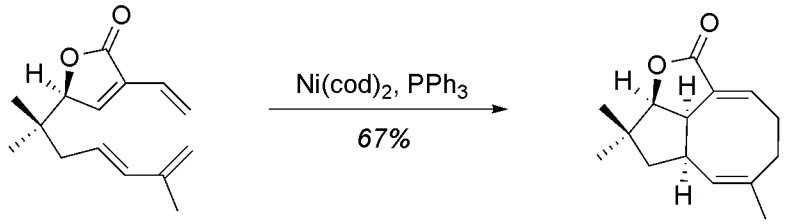
b) **Grob Fragmentation**



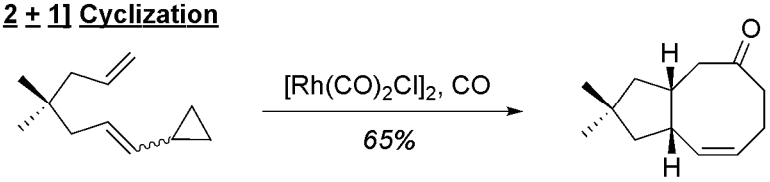
c) **Allylic substitution**



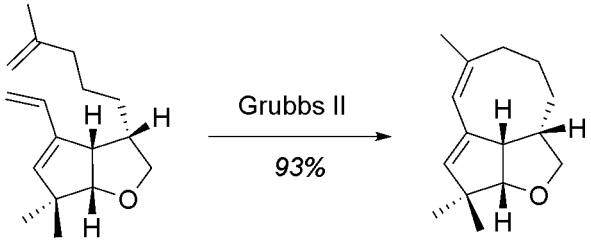
d) **[4 + 4] Cyclization**



e) **[5 + 2 + 1] Cyclization**



f) **Ring-closing metathesis**

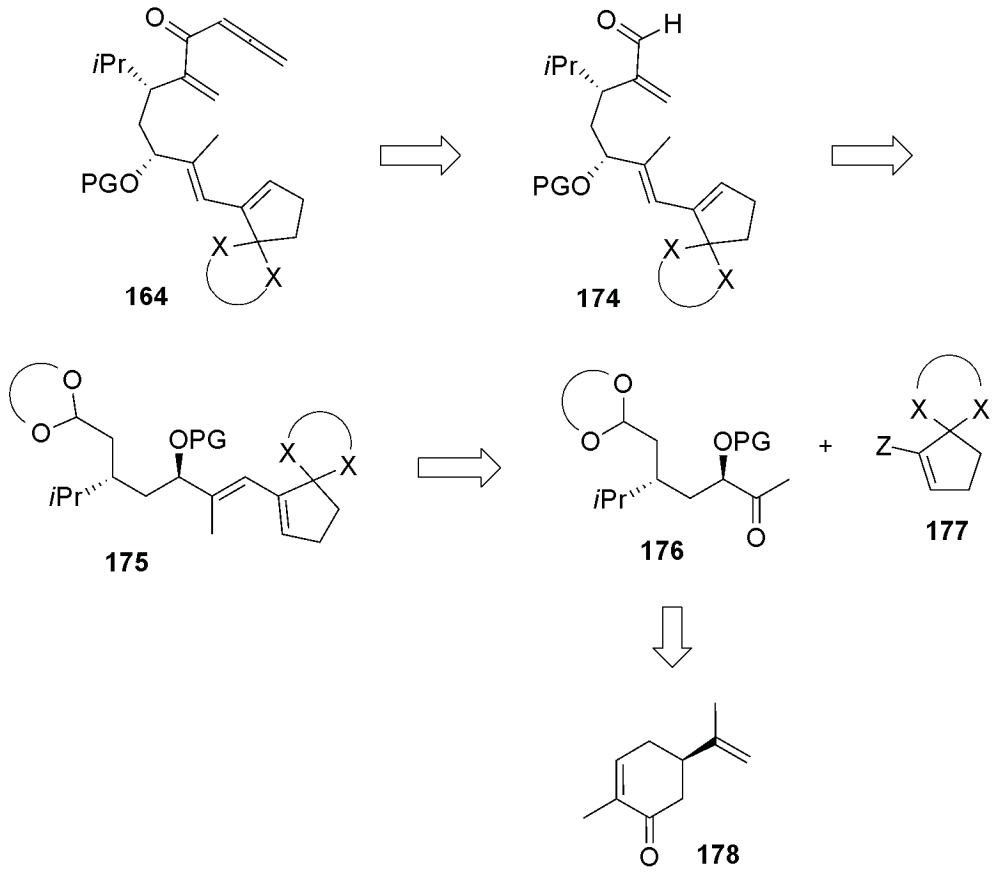


Scheme 56 Some alternative methods for the construction of eight-membered ring systems.

a nickel-catalyzed [4 + 4] cyclization (Scheme 56d),[75] a rhodium-catalyzed [5 + 2 + 1] cyclization (Scheme 56e),[76] and a ruthenium-catalyzed ring-closing metathesis strategy (Scheme 56f),[77] are more recent developments and continue to garner increasing attention both in the context of methodology development and their use in synthesis. It is worth mentioning that each of the examples highlighted in Scheme 56 was utilized as the key step in the synthesis of a cyclooctanoid natural product.

5.2 Retrosynthetic Disassembly of AVK 164

The retrosynthetic strategy devised for AVK **164** is outlined below in Scheme 57. Briefly, AVK **164** could be accessed from Barbier coupling of propargyl bromide with aldehyde **174**, followed by oxidation with the use of DMP, through the method discussed previously in Section 2.2. Aldehyde **174** would be accessed via deprotection of acetal **175**, followed by aldolization with formaldehyde. Acetal **175** could theoretically be derived by the union of ketone **176** and an organometallic species derived from protected cyclopentenone **177**. Ketone **176** should be attainable in enantiopure form from (-)-carvone (**178**).

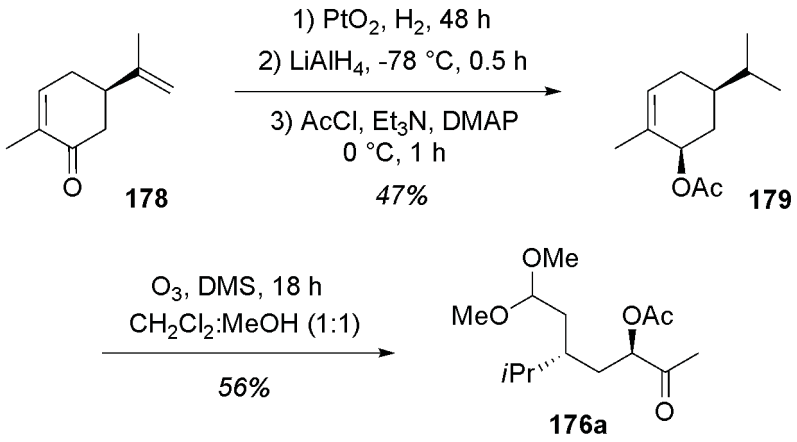


Scheme 57 Retrosynthetic disassembly of AVK **164**.

5.3 Progress Towards the Synthesis of the First Key Intermediate, Acetal 175

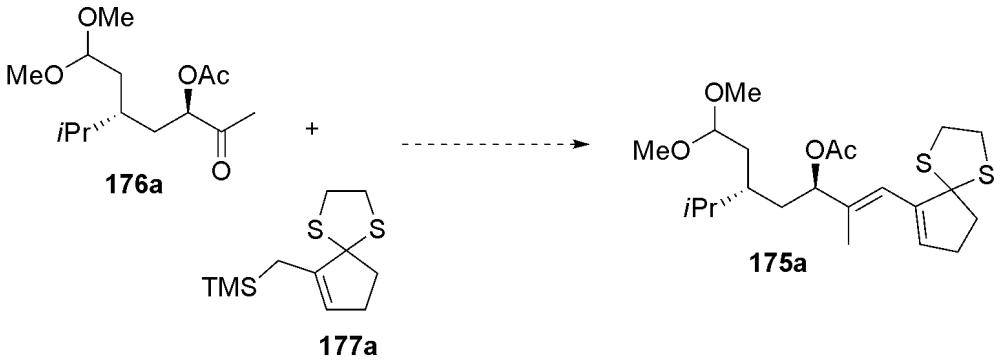
The synthesis of ketone **176a** was accomplished as depicted in Scheme 58 below. (-)-Carvone (**178**) was transformed into its acetate **179** in 47% overall yield via a three-step procedure proceeding through a chemoselective hydrogenation of the exocyclic double bond using Adam's catalyst,[78] a stereo- and regioselective $LiAlH_4$-mediated reduction of the enone carbonyl,[79] and protection of the resultant alcohol with acetyl chloride. *cis*-Carvotanacetol acetate (**179**) was then transformed into ketone **176a** via ozonolysis in 56% yield, which proceeded with simultaneous chemoselective protection

of the aldehyde functionality in one-pot as its dimethyl acetal. It was necessary to use acetate-protected *cis*-carvotanacetol **179** for the ozonolysis step – when benzyl and *tert*-butyldimethylsilyl derivatives were utilized, only decomposition of the starting material resulted.



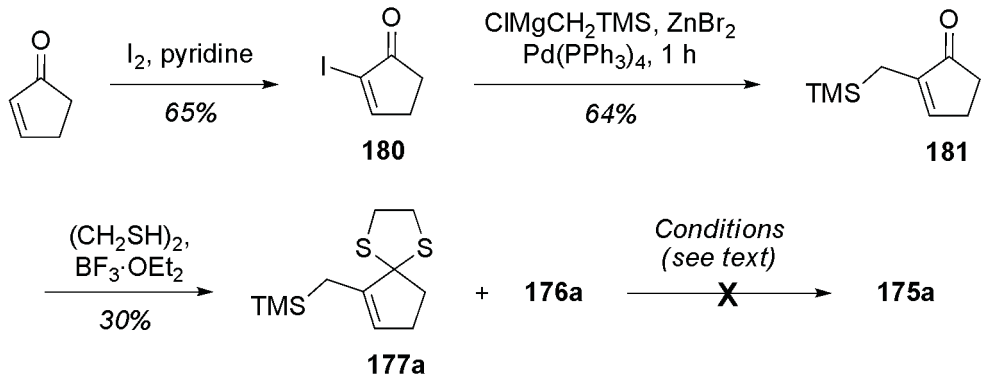
Scheme 58. Synthesis of ketone **176a**.

Initially, we envisioned coupling fragments **176a** and **177a** through a Petersen olefination strategy (Scheme 59). This procedure was chosen as it is notable for its overall high (*E*)/(*Z*) selectivity, and conditions can be carefully chosen in which to yield either the (*E*)- or the (*Z*)-isomer.[80] This method offers considerable advantages over more traditional carbonyl olefination methods, such as Wittig[81] or Julia[82] reactions, which typically give poor (*E*)/(*Z*)-selectivity with ketones.



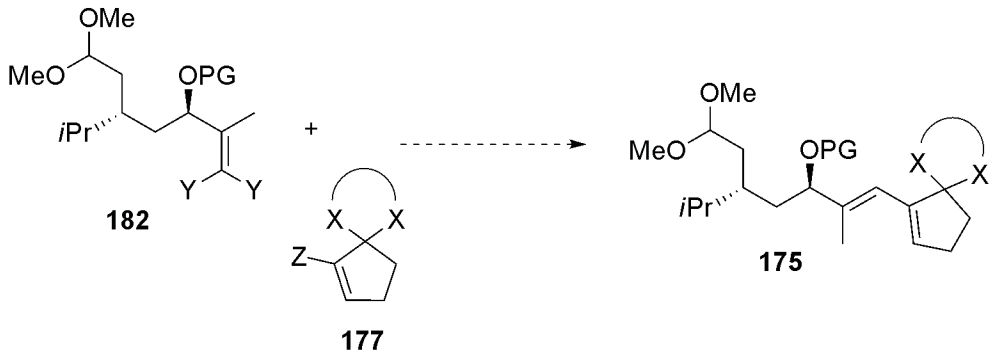
Scheme 59 Proposed Petersen olefination strategy for the synthesis of thioacetal **175a**.

Compound **177a** was readily available from iodinated cyclopent-2-enone **180**,[83] which was transformed into its TMS-derivative **181** through a Negishi cross-coupling with methyltrimethylsilylmagnesium chloride,[84] which was subsequently converted into its dithiolane derivative **177a** with ethanedithiol in 12% overall yield (Scheme 60). Although transformation into its dioxolane derivative was also attempted, compound **184** decomposed in the presence of ethylene glycol, or its trimethylsilyl protected derivative. Unfortunately, in subsequent reactions, compound **177a** did not react with ketone **176a**, returning both starting materials intact under most circumstances. This was later determined to be a result of our failure to deprotonate **177a**, under all conditions attempted (LDA, *n*BuLi, *n*BuLi/TMEDA, *n*BuLi/HMPA, *t*BuLi, *n*BuLi/*t*BuOK).



Scheme 60 Synthesis of dithiane **177a** , with failed elaboration into thioacetal **175a**.

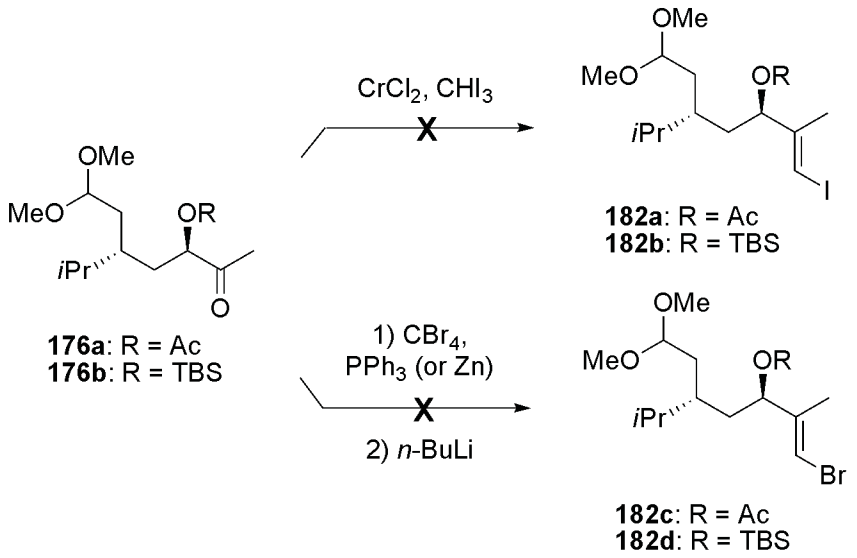
A strategy involving the union of alkene **182** and compound **177b** was then envisioned, which could theoretically be stereoselectivity joined through a variety of palladium-mediated cross-coupling reactions, to generate acetal **175** (Scheme 61).



Scheme 61 Second-generation proposal for the synthesis of acetal **175**.

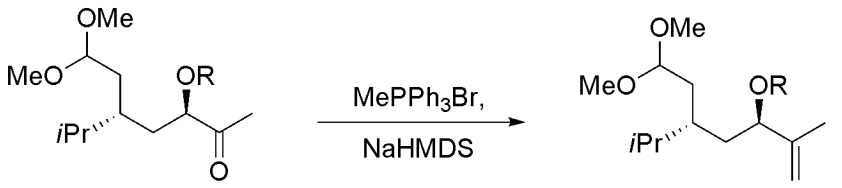
It was initially proposed to employ compound **177** in a Negishi cross-coupling reaction[85] with vinyl iodide **182a** or vinyl bromide **182c** (Scheme 62). However, attempts to prepare either substrate by a Takai olefination procedure[86] (**182a**), or a Corey-Fuchs reaction[87] followed by a stereoselective dehalogenation[88] (**182c**), failed. In the former case, multiple alkene-containing products were produced, as determined by careful analysis of the crude ^{1}H NMR spectrum, whereas in the latter case only decomposition of

the starting material resulted upon treatment with either CBr_4/PPh_3 or CBr_4/Zn. Similarly, exposure of the *tert*-butyldimethylsilyl protected derivative **176b**, which was obtained from acetate **176a** in 36% yield, to the reaction conditions mentioned above also failed to produce **182b** or **182d**. Marginal success did result upon exposure of **176b** to chromium(II)chloride and iodoform in the presence of 2,6-(di-*t*-butyl)pyridine for three hours,[89] however the yield was unacceptably low (ratio of **182d** to **176b** was only 1:7 as determined by integration of crude ^{1}H NMR spectrum), and prolonged reaction times only led to degradation of the product.



Scheme 62 Failed attempts at the synthesis of vinyl halides **182a-d**.

It was next decided to join compound **177** to compound **182** via a Heck cross-coupling protocol.[90] Fortunately, the requisite alkenes **182e** and **182f** were able to be produced in good yields via a Wittig reaction with methyltriphenylphosphonium bromide (Scheme 63).

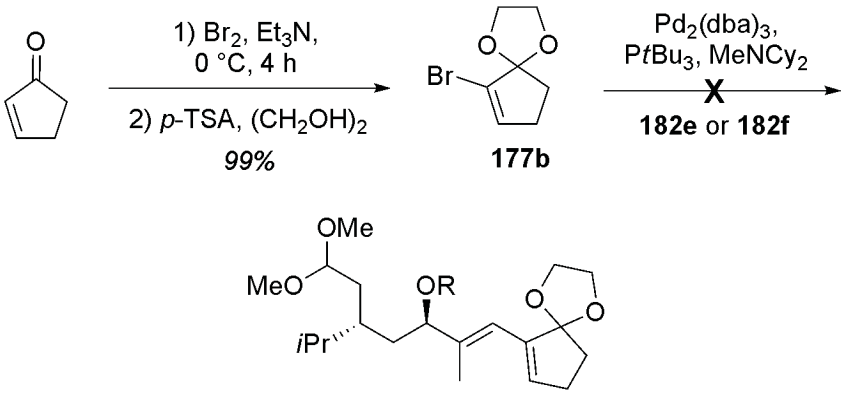


176a: R = Ac
176b: R = TBS

182e: R = Ac *(76%)*
182f: R = TBS *(71%)*

Scheme 63 Synthesis of alkenes **182e** and **182f**.

Compound **177b**, which was readily available via bromination of cyclopent-2-enone followed by protection with ethyleneglycol,[91] was then exposed to $Pd_2(dba)_3$/P*t*Bu_3 and *N*-methyldicyclohexyalmine in the presence of alkenes **182e** and **182f** (Scheme 64). This particular catalyst system and base were chosen as it has been reported that this particular combination has exceptional activity with regards to both sterically hindered and electronically deactivated substrates.[92] Unfortunately, no reaction resulted and only starting material was recovered following several days of stirring at room temperature.



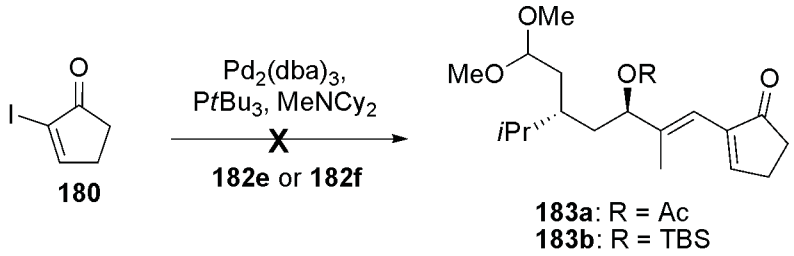
177b

175b: R = Ac
175c: R = TBS

Scheme 64 Synthesis of ketal **177b**, with failed elaboration into acetals **175b-c**.

Reasoning that the failed production of compounds **175b** and **175c** was a result of the failure of the palladium catalyst to undergo oxidative addition with ketal **177b** as a

result of steric hindrance about the bromine atom, alkenes **182e** and **182f** were then exposed to Pd(*t*Bu)$_4$ and *N*-methyldicyclohexyalmine in the presence of iodocyclopent-2-enone (**180**) (Scheme 65). Unfortunately, once again no reaction resulted and starting material was recovered, along with some dimerized **180**, following several days of stirring at room temperature.



Scheme 65 Unsuccessful synthesis of dienones **183a-b**.

5.4 Summary

A strategy for the total synthesis of the cyclooctane natural product (+)-roseadione (**162**), utilizing the tandem Nazarov/[4 + 3] cyclization of allenyl vinyl ketones, has been presented. Unfortunately, although a number of direct precursors to the first key intermediate **175** have been synthesized, a successful route has yet to be developed for the preparation of acetal **175**.

5.5 Experimental Section

5.5.1 General Considerations

All reactions were conducted using oven-dried glassware under an N_2 atmosphere. Reagents were used as received from a commercial supplier without further purification.

Dichloromethane and benzene were used freshly distilled from calcium hydride. Tetrahydrofuran and diethyl ether were used freshly distilled from sodium/benzophenone. Anhydrous methanol was purchased from Sigma-Aldrich and used as received. Ethyl acetate and hexanes were distilled prior to use for column chromatography.

Thin layer chromatography was conducted using pre-coated silica plates with plastic backing (EMD chemicals, silica gel 60 F_{254}), using UV light (254 nm) as a visualizing agent and potassium permanganate in aqueous KOH and heat, or *o*-vanillin in ethanol/H_2SO_4 and heat, as developing agents. Column chromatography was carried out on silica gel purchased from Silicycle (40 – 63 μm particle size, 230 – 240 mesh).

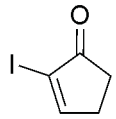
Melting points are uncorrected, and were acquired using a Fisher-Johns apparatus. ^{1}H NMR spectra were recorded at 500 MHz on a Bruker Avance spectrometer with $CDCl_3$ as solvent (7.24 ppm) and TMS as internal reference (0.00 ppm). ^{13}C NMR spectra were recorded at 125 MHz on a Bruker Avance spectrometer with $CDCl_3$ as solvent. Infrared spectra were recorded from thin films on a Bruker VECTOR 22 FT-IR instrument using CsI plates. High resolution mass spectra were acquired by Mr. Xiao Feng, on a Bruker microTOF Focus orthogonal ESI-TOF mass spectrometer.

The carbon and hydrogen atoms of select compounds were assigned following detailed analysis of their one dimensional (^{1}H, ^{13}C, and DEPT-135) and two dimensional

(COSY, HSQC, and HMBC) NMR spectral data. The ^{1}H and ^{13}C NMR spectra of all compounds may be found in Appendix A.

5.5.2 Preparation and Characterization Data

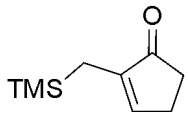
2-Iodocyclopent-2-enone (180)



180

Iodine (54 g, 0.20 mol) was added to a 1:1 solution of pyridine and Et_2O (160 mL), and stirred for 20 min. Cyclopent-2-enone (2 mL, 0.025 mol) was added dropwise, the solution was cooled to 0 °C, and additional cyclopent-2-enone (6.2 mL, 0.075 mmol) was then added dropwise. The solution was brought to rt, stirred for 2 h, then washed successively with 1 M HCl (aq) (×2), 10% $Na_2S_2O_3$ (aq) (×3), and brine. The Et_2O layer was then dried with $MgSO_4$, filtered, and concentrated to provide **180** (10 g, 65%) as a yellow solid: mp 69–71 °C (lit.[93] 70-71 °C); ^{1}H NMR δ: 8.06 (1H, t, J = 2.8 Hz), 2.82 (2H, m), 2.51 (2H, m); ^{13}C NMR δ: 203.8, 169.7, 102.4, 31.0, 30.7.

2-((Trimethylsilyl)methyl)cyclopent-2-enone (181)

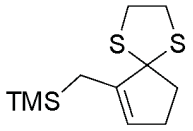


181

A 1 M solution of (trimethylsilyl)methylmagnesium chloride in THF (34 mL, 0.034 mol) was added dropwise to a –78 °C solution of flame-dried $ZnBr_2$ (7.6 g, 0.034

mol) in THF (300 mL), and warmed to rt over 1 h. A solution of **180** (3.5 g, 0.017 mol) and $Pd(PPh_3)_4$ (0.60 g, 0.51 mmol) in DMF/THF (80 mL, 1:1) was then added rapidly by cannula, and stirred 1 h. The mixture was then diluted with ether/hexanes (1:1), washed with saturated NH_4Cl (aq) (×3), water (×2), brine, dried with $MgSO_4$, and concentrated. Flash chromatography of the residue (SiO_2 using 10% EtOAc in hexanes) provided **181** (1.8 g, 64%) as a yellow oil; IR (film) 1711, 1649 cm^{-1}; ^1H NMR δ: 7.12 (1H, m), 2.55 (2H, m), 2.38 (2H, m), 1.66 (2H, d, J = 1.2 Hz), -0.01 (9H, s); ^{13}C NMR δ: 210.0, 154.5, 144.1, 34.2, 26.4, 14.6, -1.5 (3C). HRMS (ESI) 191.0863 $[C_9H_{16}OSiNa]^+$ requires 191.0863.

(1,4-Dithiaspiro[4.4]non-6-en-6-ylmethyl)trimethylsilane (177a)

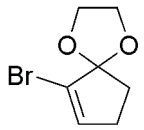


177a

A solution of **181** (1.6 g, 9.1 mmol) and 1,2-ethanedithiol (1.0 mL, 12 mmol) in MeOH (35 mL) was cooled to 0 °C, and $BF_3{\cdot}OEt_2$ (1.5 mL, 12 mmol) was added. The mixture was stirred for 2 h, then warmed to rt, and stirred for an additional 18 h. The solution was diluted with EtOAc, washed with saturated $NaHCO_3$ (aq), then brine, dried with $MgSO_4$, and concentrated. Flash chromatography of the residue (SiO_2 using hexanes) provided **177a** (0.65 g, 30%) as a yellow oil; ^1H NMR δ: 5.42 (1H, br s), 3.29 (4H, m), 2.48 (2H, t, J = 6.3 Hz), 2.30 (2H, m), 1.63 (2H, d, J = 2.8 Hz), 0.07 (9H, s); ^{13}C NMR δ: 143.1,

125.8, 79.6, 46.8, 40.7 (2C), 30.4, 15.8, -0.6 (3C). HRMS (ESI) 245.0851 $[C_{11}H_{21}S_2SiNa]^+$ requires 245.0848.

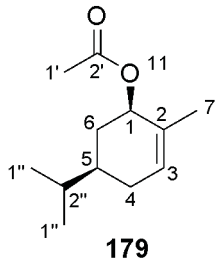
6-Bromo-1,4-dioxaspiro[4.4]non-6-ene (177b)



177b

A solution of Br_2 (1.6 mL, 0.13 mol) in CH_2Cl_2 (20 mL) was added dropwise, over 1 h, to a 0 °C solution of cyclopent-2-enone (2.5 mL, 0.030 mol) in CH_2Cl_2 (20 mL). Then a solution of Et_3N (6 mL, 0.045 mol) in CH_2Cl_2 (20 mL) was added dropwise over 1 h, while the solution was maintained at a 0 °C. The solution was then stirred for 2 h at rt, filtered, and washed successively with 1 M HCl (aq) (×2), saturated $NaHCO_3$ (aq), water, and brine. The CH_2Cl_2 layer was dried over $MgSO_4$, and concentrated. The crude residue was then dissolved in benzene (350 mL). Ethylene glycol (5 mL, 0.090 mol) and *p*-TSA (0.050g, 0.26 mmol) were added, and the solution was heated at reflux for 24 h, with azeotropic removal of water. The solution was cooled to room temperature, dried with K_2CO_3, and filtered over a pad of SiO_2 to provide **177b** (12 g, 99%) as a yellow oil; ^{1}H NMR δ: 6.18 (1H, t, J = 2.8 Hz), 4.19 (2H, m), 3.99 (2H, m), 2.37 (2H, m), 2.17 (2H, t, J = 6.2 Hz); ^{13}C NMR δ: 36.8, 123.9, 117.7, 65.9, 34.4, 28.7; NMR data matches lit.[91]

(1*R*,5*R*)-5-Isopropyl-2-methylcyclohex-2-enyl acetate (179)

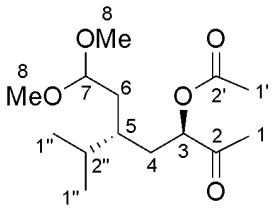


179

PtO_2 (0.15 g, 0.67 mmol), then (-)-carvone (10 mL, 0.066 mol), were added to a dry 100 mL flask. The flask was then evacuated and backfilled with hydrogen gas (×3), and stirred for 48 h under a balloon filled with H_2 (until ^{1}H NMR of a small aliquot showed complete reduction of the exocyclic double bond). The mixture was then diluted with Et_2O, filtered through a short pad of SiO_2, and concentrated. The crude residue was then dissolved in Et_2O (50 mL), added dropwise to a –78 °C solution of $LiAlH_4$ (1.3 g, 0.034 mol) in Et_2O (50 mL), and stirred for 30 min. Water (3 mL), 10% NaOH (3 mL), and additional water (3 mL) were then added successively, and the mixture was then stirred at rt for 1 h until a white precipitate formed. Anhydrous $MgSO_4$ was then added, and the mixture was filtered, then concentrated. The crude residue was then dissolved in CH_2Cl_2 (600 mL), and cooled to 0 °C. DMAP (8.1 g, 0.066 mol), Et_3N (70 mL, 0.5 mol), and acetyl chloride (0.92 mL, 0.013 mol) were then added successively. The mixture was stirred for 1 h, diluted with CH_2Cl_2, and then washed successively with 1 M HCl (aq) (×3), 10% NaOH (aq), saturated $NaHCO_3$ (aq), and brine. The CH_2Cl_2 layer was then dried with Na_2SO_4, concentrated, and purification by column chromatography (SiO_2 with 5% EtOAc in hexanes) provided **179** (6.1 g, 47%) as a colourless oil; IR (film) 1736 cm^{-1}; ^{1}H NMR δ: 5.59 (1H, m, H3), 5.41 (1H, m, H1), 2.12 (1H, m, H6a), 2.08 (3H, s,

H1'), 1.99 (1H, m, H4a), 1.78 (1H, m, H4b), 1.62 (3H, q, *J* = 1.3 Hz, H7), 1.49 (2H, m, H5, H2''), 1.25 (1H, m, H6b), 0.88 (1H, d, *J* = 6.6 Hz, H1''a), 0.87 (1H, d, *J* = 6.6 Hz, H1''b); ^{13}C NMR δ: 171.3 (C2'), 133.1 (C2), 126.6 (C3), 73.8 (C1), 39.4 (C5''), 33.0 (C6), 32.3 (C2''), 29.0 (C4), 21.5 (C1'), 19.9 (C1''a), 19.6 (C1''b), 19.0 (C7); HRMS (ESI) 219.1352 $[C_{12}H_{20}O_2Na]^+$ requires 219.1356.

(3*R*,5*S*)-5-Isopropyl-7,7-dimethoxy-2-oxoheptan-3-yl acetate (176a)

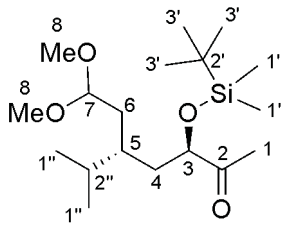


176a

A solution of **179** (5.7 g, 0.029 mol) in CH_2Cl_2/MeOH (600 mL, 1:1) was cooled to –70 °C. Ozone was bubbled through the solution for 1 h, and then excess ozone was removed by bubbling N_2 through the solution for 30 min. DMS (40 mL) was then added, the solution was allowed to slowly warm to rt, and was stirred for 18 h. The mixture was concentrated, and the crude residue was dissolved in EtOAc, washed with water (×3), then brine. The EtOAc layer was then dried with Na_2SO_4, concentrated, and purified by column chromatography (SiO_2 with 10%, then 20%, EtOAc in hexanes) to provide **176a** (4.5 g, 56%) as a colourless oil; IR (film) 1745, 1731 cm^{-1}; ^{1}H NMR δ: 5.03 (1H, dd, *J* = 10, 2.8 Hz, H3), 4.41 (1H, t, *J* = 5.4 Hz, H7), 3.31 (3H, s, H8a), 3.30 (3H, s, H8b), 2.17 (3H, s, C1), 2.14 (3H, s, C1'), 1.78 (1H, m, C2''), 1.60 (5H, m, H4, H5, H6), 0.88 (3H, d, *J* = 6.8 Hz, H1''a), 0.85 (3H, d, *J* = 6.8 Hz, H1''b); ^{13}C NMR δ: 205.9 (C2), 170.8 (C2'), 103.7 (C7), 77.7 (C3), 53.0 (2C, C8), 36.3 (C5), 33.9 (C6), 31.5 (C4), 30.4 (C2''), 26.2

(C1), 20.9 (C1'), 19.5 (C1''a), 18.4 (C1''b); HRMS (ESI) 297.1662 $[C_{14}H_{26}O_5Na]^+$ requires 297.1672.

(3*R*,5*S*)-3-(*tert*-Butyldimethylsilyloxy)-5-isopropyl-7,7-dimethoxyheptan-2-one (176b)

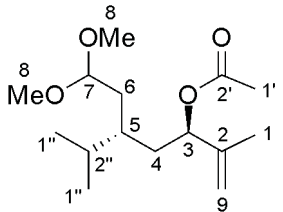


176b

A solution of saturated aqueous potassium carbonate (2.5 mL) was added to a solution of **176a** (1.5 g, 6.0 mmol) in methanol (50 mL). After stirring for 30 min at rt, the reaction mixture was diluted with diethyl ether, and the organic layer was washed with saturated NH_4Cl (aq) (×2), then brine, dried with $MgSO_4$, and concentrated. The crude residue was then dissolved in CH_2Cl_2 (50 mL), cooled to 0 °C, and DMAP (0.045 g, 0.37 mmol), imidazole (0.54 g, 7.9 mmol), and *tert*-butyldimethylsilyl chloride (0.95 g, 6.3 mmol) were added successively. The reaction mixture was stirred at rt for 18 h, then washed with water, brine, dried with Na_2SO_4, and concentrated. Purification by column chromatography (SiO_2 with 10% EtOAc in hexanes) provided **176b** (0.75 g, 36%) as a colourless oil; IR (film) 1715 cm^{-1}; ^1H NMR δ: 4.42 (1H, t, J = 5.8 Hz, H7), 4.0 (1H, dd, J = 7.9, 5.0 Hz, H3), 3.32 (3H, s, H8a), 3.28 (3H, s, H8b), 2.15 (3H, s, C1), 1.81 (1H, m, C2''), 1.61 (1H, m, H6a), 1.57 (1H, m, H4a), 1.51 (1H, m, H6b), 1.46 (1H, m, H4b), 1.39 (1H, m, H5), 0.92 (9H, s, H3'), 0.84 (3H, d, J = 6.9 Hz, H1''a), 0.82 (3H, d, J = 6.9 Hz, H1''b), 0.08 (3H, s, H1'a), 0.04 (3H, s, H1'b); ^{13}C NMR δ: 212.3 (C2), 103.7 (C7), 73.0

(C3), 53.6 (C8a), 52.0 (C8b), 36.1 (C5), 35.8 (C4), 33.8 (C6), 29.5 (C2''), 26.0 (3C, C3'), 24.7 (C1), 18.8 (C1''a), 18.6 (C1''b), 18.2 (C2'), -4.7 (C1'a), -4.8 (C1'b); HRMS (ESI) 369.2432 $[C_{18}H_{38}O_4SiNa]^+$ requires 369.2432.

(3*R*,5*S*)-5-Isopropyl-7,7-dimethoxy-2-methylhept-1-en-3-yl acetate (182e)

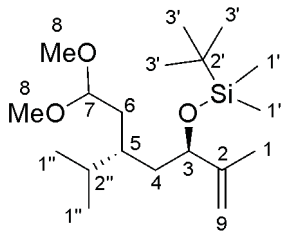


182e

A solution of methyltriphenylphosphonium bromide (0.25g, 0.66 mmol) in THF (1 mL) was cooled to 0 °C, and a 1 M solution of NaHMDS in THF (0.70 mL, 0.70 mmol) was added dropwise. The resultant bright yellow solution was stirred at rt for 30 min, and then a solution of **176a** (0.12 g, 0.44 mmol) in THF (1 mL) was added. The mixture was stirred for 1 h, diluted with diethyl ether, and the organic layer was washed with saturated NH_4Cl (aq) (×2), then brine (×2). The organic layer was then dried with $MgSO_4$ and concentrated, and purification of the residue by column chromatography (SiO_2 with 10% EtOAc in hexanes) provided **182e** (0.085 g, 71%) as a colourless oil; IR (film) 1741 cm^{-1}; ^1H NMR δ: 5.22 (1H, dd, *J* = 8.0, 6.2 Hz, H3), 4.96 (1H, m, H9a), 4.89 (1H, m, H9b), 4.42 (1H, t, *J* = 5.6 Hz, H7), 3.30 (6H, s, H8), 2.05 (3H, s, H1'), 1.80 (1H, m, H2''), 1.73 (3H, s, H1), 1.63 (2H, m, H4a, H6a), 1.44 (3H, m, H4b, H5, H6b), 0.86 (3H, d, *J* = 6.8 Hz, H1''a), 0.84 (3H, d, *J* = 6.8 Hz, H1''b); ^{13}C NMR δ: 170.6 (C2'), 143.7 (C2), 113.1 (C9), 103.7 (C7), 76.3 (C3), 52.7 (2C, C8), 36.1 (C5), 34.1 (C6), 33.3

(C4), 29.3 (C2''), 21.5 (C1'), 19.1 (C1''a), 18.5 (C1''b), 18.1 (C1); HRMS (ESI) 295.1873 $[C_{15}H_{28}O_4Na]^+$ requires 295.1880.

((3*R*,5*S*)-5-Isopropyl-7,7-dimethoxy-2-methylhept-1-en-3-yloxy)*tert*-butyl dimethylsilane (182f)



182f

According to the procedure for **182e**: methyltriphenylphosphonium bromide (0.39 g, 1.1 mmol), NaHMDS (1.2 mL, 1.2 mmol), and **176b** (0.25 g, 0.72 mmol) were reacted to yield **182f** (0.19 g, 76%) as a colourless oil; IR (film) cm^{-1}; ^1H NMR δ: 4.83 (1H, m, H9a), 4.75 (1H, m, H9b), 4.42 (1H, dd, *J* = 6.2, 5.3 Hz, H7), 4.07 (1H, dd, *J* = 7.1, 5.7 Hz, H3), 3.32 (3H, s, H8a), 3.30 (3H, s, H8b), 1.79 (1H, m, H2''), 1.68 (3H, s, H1), 1.58 (1H, m, H6a), 1.51 (1H, m, H4a), 1.42 (2H, m, H5, H6b), 1.24 (1H, m, H4b), 0.88 (9H, s, H3'), 0.84 (3H, d, *J* = 6.8 Hz, H1''a), 0.82 (3H, d, *J* = 6.8 Hz, H1''b), 0.05 (3H, s, H1'a), 0.00 (3H, s, H1'b); ^{13}C NMR δ: 148.4 (C2), 111.0 (C9), 104.0 (C7), 75.8 (C3), 53.3 (C8a), 52.4 (C8b), 37.8 (C4), 36.0 (C5), 33.8 (C6), 29.3 (C2''), 26.1 (3C, C3'), 18.9 (C1''a), 18.6 (C1''b), 18.4 (C2'), 16.8 (C1), -4.4 (C1'a), -4.8 (C1'b); HRMS (ESI) 367.2645 $[C_{19}H_{40}O_3SiNa]^+$ requires 367.2639.

CHAPTER 6. CONCLUSIONS

6.1 Summary of the Thesis

The results detailed in Chapter 2 of this thesis described general synthetic pathways for the synthesis of a variety of α-functionalized allenyl vinyl ketones. Chapter 3 of this thesis divulged initial studies for the use of these compounds as substrates for the interrupted Nazarov cyclization. Considerable success in the trapping of heteroatom nucleophiles was noted, with the best results obtained with AVKs bearing an alkyl group on the allene unit, and it was determined that α-substitution plays a significant role in the reactivity patterns of AVKs. It is likely that an alkyl group on the allene attenuates the reactivity at the central carbon of the allene, by electron donation and/or by steric hindrance, allowing the intramolecular Nazarov pathway to dominate. For AVKs not bearing an alkyl group on the allene unit, it was discovered that an alkyl group on the alkene unit was necessary to achieve an interrupted Nazarov cyclization, which was rationalized, and confirmed computationally, to be a result of conformational acceleration of the Nazarov reaction. AVKs bearing no α-substituents did not cyclize under interrupted Nazarov conditions, and only participated in alternative allene reactions.

The results detailed in Chapter 4 of this thesis expanded this methodology to carbon-carbon formation. A variety of cyclopent-2-enones or bicyclic ketones were produced from a range of reaction partners, including acyclic dienes, cyclic dienes, aza-heterocycles, electron-rich alkenes, or styrenes, with the type of product formed dependent on the nucleophilic species employed. In most cases, the products were formed in very high regio- and stereoselectivity. A combined computational and experimental

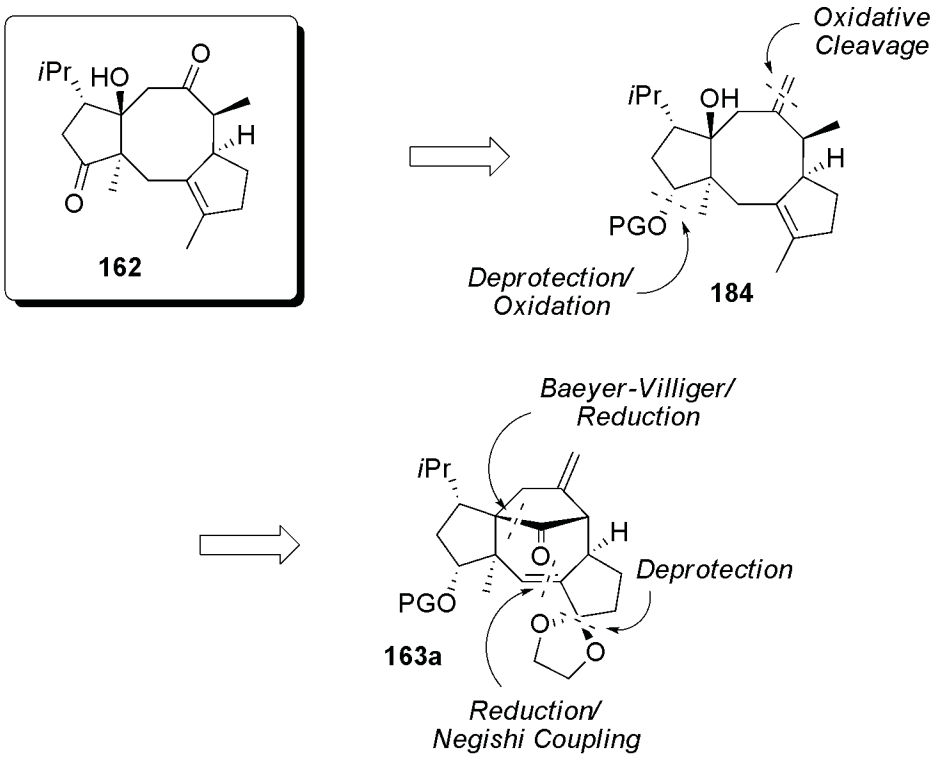
investigation implied that the regiochemical outcome of the reaction was predominantly a result of an electronic bias in the intermediate oxyallyl cation, which resulted in the preferential formation of cyclopent-2-enones substituted at the 5-position, or bicyclic ketones in which initial bond formation had occurred at the same position. The high stereoselectivity in the formation of the bicyclic ketones from acyclic dienes was investigated through a comparison of the relative energies of the products formed, and it was determined that this was likely a result of a highly organized transition state derived from a concerted reaction, which would take place through an extended (or "*exo*") geometry.

The results of this thesis should allow for further generalizations to be made, in terms of reactivity and regioselectivity with respect to related substrate classes, for the interrupted Nazarov reaction of allenyl vinyl ketones. As a result, the interrupted Nazarov cyclization of allenyl vinyl ketones has potential as a useful alternative to other synthetic approaches utilized for the stereocontrolled synthesis of cyclooctanoid natural products. The results described in Chapter 5 of this thesis are the beginning of the realization of this aim.

6.2 Future Work

The results detailed in Chapter 5 of this thesis summarize the current progress towards the total synthesis of (+)-roseadione, which would showcase the interrupted Nazarov cyclization of allenyl vinyl ketones for the construction of the cyclooctanoid ring system. As described in Chapter 5, progress towards the successful implementation of the key Nazarov step is ongoing. However, following its successful application for the

production of compound **163a**, the synthesis of (+)-roseadione is proposed to be completed in a manner in agreement with the retrosynthetic analysis devised in Scheme 66 below. Briefly, lactonization then reductive ring opening of the tricyclic ketone **163a**, followed by a deketalization, then 1,4-reduction of the revealed enone with *in situ* triflation of the resultant enolate, and finally a Negishi cross-coupling with methylmagnesium bromide would yield advanced intermediate **184**. It is envisioned that compound **184** could then be transformed into (+)-roseadione through a chemoselective oxidative cleavage of the exocyclic alkene, followed by deprotection and oxidation of the secondary alcohol unit.



Scheme 66 Retrosynthetic disconnection of (+)-roseadione (**162**) leading to ketone **163a**.

Finally, it is also worth developing a firmer mechanistic rationale for the [4 + 3] and [3 +2] cyclizations discussed in Chapter 4. Of particular interest is elucidation of whether the reactions are concerted or stepwise, for both the acyclic dienes, and activated alkene derivatives. This can in principle be accomplished through determination of the magnitude of the ^{13}C and ^{2}H KIEs of the reacting atoms, for instance positions *a* and *b* in compounds **185** - **187** (Figure 12).[94] The measured KIEs can then be compared to theoretical KIEs, calculated for both a concerted and stepwise process, to determine which is the better fit with the experimental data. The ^{13}C and ^{2}H KIE data of compounds **185** – **187** would be obtained by NMR methods, at natural abundance.

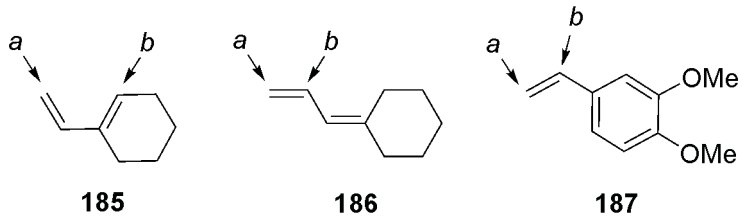


Figure 12 Magnitude of KIEs of atoms at position(s) *a* and/or *b* of **185** – **187** could discriminate between concerted and stepwise mechanisms in reactions with AVKs.

REFERENCES

1. Nicolaou, K. C.; Vourloumis, D.; Winssinger, N.; Baran, P. S. *Angew. Chem. Int. Ed.* **2000,** *39* (1), 44-122.

2. For reviews on the Nazarov reaction see: [a] Frontier, A. J.; Collison, C. *Tetrahedron* **2005,** *61* (32), 7577-7606; [b] Habermas, K. L.; Denmark, S. E.; Jones, T. K., In *Organic Reactions*, John Wiley and Sons: Hoboken, 1994; Vol. 45, pp 1-158; [c] Nakanishi, W.; West, F. G. *Curr. Opin. Drug Discovery Dev.* **2009,** *12* (6), 732-751; [d] Pellissier, H. *Tetrahedron* **2005,** *61* (27), 6479-6517; [e] Tius, M. A. *Eur. J. Org. Chem.* **2005,** (11), 2193-2206.

3. For some recent examples of the development of Nazarov reaction methodology and applications in synthesis: [a] Basak, A. K.; Shimada, N.; Bow, W. F.; Vicic, D. A.; Tius, M. A. *J. Am. Chem. Soc.* **2010,** *132* (24), 8266-8267; [b] Bitar, A. Y.; Frontier, A. J. *Org. Lett.* **2009,** *11* (1), 49-52; [c] Bow, W. F.; Basak, A. K.; Jolit, A.; Vicic, D. A.; Tius, M. A. *Org. Lett.* **2010,** *12* (3), 440-443; [d] Cao, P.; Deng, C.; Zhou, Y. Y.; Sun, X. L.; Zheng, J. C.; Xie, Z. W.; Tang, Y. *Angew. Chem. Int. Ed.* **2010,** *49* (26), 4463-4466; [e] Churruca, F.; Fousteris, M.; Ishikawa, Y.; Rekowski, M. V.; Hounsou, C.; Surrey, T.; Giannis, A. *Org. Lett.* **2010,** *12* (9), 2096-2099; [f] Kawatsura, M.; Kajita, K.; Hayase, S.; Itoh, T. *Synlett* **2010,** (8), 1243-1246; [g] Lazarski, K. E.; Hu, D. X.; Stern, C. L.; Thomson, R. J. *Org. Lett.* **2010,** *12* (13), 3010-3013; [h] Malona, J. A.; Cariou, K.; Frontier, A. J. *J. Am. Chem. Soc.* **2009,** *131* (22), 7560-7561; [i] Rieder, C. J.; Winberg, K. J.; West, F. G. *J. Am. Chem. Soc.* **2009,** *131* (22), 7504-7505; [j] Shimada, N.; Ashburn, B. O.; Basak, A. K.; Bow, W. F.; Vicic, D. A.; Tius, M. A. *Chem. Commun.* **2010,** *46* (21), 3774-3775; [k] Singh, R.; Parai, M. K.; Panda, G. *Org. Biomol. Chem.* **2009,** *7* (9), 1858-1867; [l] Spencer, W. T.; Levin, M. D.; Frontier, A. J. *Org. Lett.* **2011,** *13* (3), 414-417; [m] Vaidya, T.; Atesin, A. C.; Herrick, I. R.; Frontier, A. J.; Eisenberg, R. *Angew. Chem. Int. Ed.* **2010,** *49* (19), 3363-3366; [n] Vaidya, T.; Manbeck, G. F.; Chen, S.; Frontier, A. J.; Eisenberg, R. *J. Am. Chem. Soc.* **2011,** *133* (10), 3300-3303.

4. Aggarwal, V. K.; Beffield, A. J. *Org. Lett.* **2003,** *5* (26), 5075-5078.

5. Denmark, S. E.; Jones, T. K. *J. Am. Chem. Soc.* **1982,** *104* (9), 2642-2645.

6. Barbero, A.; Castreno, P.; Garcia, C.; Pulido, F. J. *J. Org. Chem.* **2001,** *66* (23), 7723-7728.

7. Ichikawa, J.; Miyazaki, S.; Fujiwara, M.; Minami, T. *J. Org. Chem.* **1995,** *60* (8), 2320-2321.

8. Ichikawa, J.; Fujiwara, M.; Okauchi, T.; Minami, T. *Synlett* **1998,** (8), 927-929.

9. [a] He, W.; Herrick, I. R.; Atesin, T. A.; Caruana, P. A.; Kellenberger, C. A.; Frontier, A. J. *J. Am. Chem. Soc.* **2008,** *130* (3), 1003-1011; [b] He, W.; Sun, X. F.; Frontier, A. J. *J. Am. Chem. Soc.* **2003,** *125* (47), 14278-14279.

10. For a review on the interrupted Nazarov reaction see: Grant, T. N.; Rieder, C. J.; West, F. G. *Chem. Commun.* **2009,** (38), 5676-5688.

11. [a] Giese, S.; Kastrup, L.; Stiens, D.; West, F. G. *Angew. Chem. Int. Ed.* **2000,** *39* (11), 1970-1973; [b] Mahmoud, B.; West, F. G. *Tetrahedron Lett.* **2007,** *48* (29), 5091-5094; [c] Wang, Y.; Arif, A. M.; West, F. G. *J. Am. Chem. Soc.* **1999,** *121* (4), 876-877; [d] Wang, Y.; Schill, B. D.; Arif, A. M.; West, F. G. *Org. Lett.* **2003,** *5* (15), 2747-2750.

12. [a] Rieder, C. J.; Fradette, R. J.; West, F. G. *Chem. Commun.* **2008,** (13), 1572-1574; [b] Rieder, C. J.; Fradette, R. J.; West, F. G. *Heterocycles* **2010,** *80* (2), 1413-1427.

13. White, T. D.; West, F. G. *Tetrahedron Lett.* **2005,** *46* (34), 5629-5632.

14. Giese, S.; West, F. G. *Tetrahedron* **2000,** *56* (52), 10221-10228.

15. Bender, J. A.; Blize, A. E.; Browder, C. C.; Giese, S.; West, F. G. *J. Org. Chem.* **1998,** *63* (8), 2430-2431.

16. Hashmi, A. S. K.; Bats, J. W.; Choi, J.-H.; Schwarz, L. *Tetrahedron Lett.* **1998,** *39* (41), 7491-7494.

17. Tius, M. A. *Acc. Chem. Res.* **2003,** *36* (4), 284-290.

18. Forest, J.; Bee, C.; Cordaro, F.; Tius, M. A. *Org. Lett.* **2003,** *5* (22), 4069-4072.

19. Dhoro, F.; Tius, M. A. *J. Am. Chem. Soc.* **2005,** *127* (36), 12472-12473.

20. Basak, A. K.; Tius, M. A. *Org. Lett.* **2008,** *10* (18), 4073-4076.

21. Harding, K. E.; Clement, K. S.; Tseng, C. Y. *J. Org. Chem.* **1990,** *55* (14), 4403-4410.

22. Miesch, M.; Miesch-Gross, L.; Franck-Neumann, M. *Tetrahedron Lett.* **1997,** *53* (6), 2103-2110.

23. Berger, G. O.; Tius, M. A. *J. Org. Chem.* **2007,** *72* (17), 6473-6480.

24. Krause, N.; Hashmi, A. S. K., *Modern Allene Chemistry*. Wiley-VCH: Weinheim, 2004; Vol. 1.

25. Barbier, P. *Compt. Rend.* **1899,** *128*, 110-111.

26. Dess, D. B.; Martin, J. C. *J. Org. Chem.* **1983,** *48* (22), 4155-4156.

27. Omura, K.; Swern, D. *Tetrahedron* **1978,** *34* (11), 1651-1660.

28. [a] Alcaide, B.; Almendros, P.; Rodriguez-Acebes, R. *J. Org. Chem.* **2005,** *70* (8), 3198-3204; [b] Isaac, M. B.; Chan, T.-H. *J. Chem. Soc., Chem. Commun.* **1995,** (10), 1003-1004.

29. Alcaide, B.; Almendros, P.; Aragoncillo, C. *Chem. Eur. J.* **2002,** *8* (7), 1719-1729.

30. Griffith, W. P.; Ley, S. V.; Whitcombe, G. P.; White, A. D. *J. Chem. Soc., Chem. Commun.* **1987,** (21), 1625-1627.

31. Frigerio, M.; Santagostino, M. *Tetrahedron Lett.* **1994,** *35* (43), 8019-8022.

32. Marshall, J. A.; Schaaf, G. M. *J. Org. Chem.* **2001,** *66* (23), 7825-7831.

33. Bowden, K.; Heilbron, I. M.; Jones, E. R. H.; Weedon, B. C. L. *J. Chem. Soc.* **1946**, 39-45.

34. Firouzabadi, H.; Seddighi, M.; Mottaghinejad, E.; Bolourchian, M. *Tetrahedron* **1990,** *46* (19), 6869-6878.

35. Prepared based on a procedure for (*E*)-3-(2-nitro-4-(trifluoromethyl)phenyl)propenal: Chatfield, D. C.; Augsten, A.; D'Cunha, C.; Lewandowska, E.; Wnuk, S. F. *Eur. J. Org. Chem.* **2004,** (2), 313-322.

36. Zhao, L. G.; Lu, X. Y.; Xu, W. *J. Org. Chem.* **2005,** *70* (10), 4059-4063.

37. Zhang, L.; Huang, Y.; Huang, Z. *Tetrahedron Lett.* **1991,** *32* (45), 6579-6582.

38. Masuyama, Y.; Watabe, A.; Ito, A.; Kurusu, Y. *Chem. Commun.* **2000,** (20), 2009-2010.

39. Maddess, M. L.; Lautens, M. *Org. Lett.* **2005,** *7* (16), 3557-3560.

40. Ma, X.; Wang, J.-X.; Li, S.; Wang, K.-H.; Huang, D. *Tetrahedron* **2009,** *65* (42), 8683-8689.

41. Xia, G. Y.; Yamamoto, H. *J. Am. Chem. Soc.* **2007,** *129* (3), 496-497.

42. Fu, F.; Hoang, K. L. M.; Loh, T. P. *Org. Lett.* **2008,** *10* (16), 3437-3439.

43. Menz, H.; Binder, J. T.; Crone, B.; Duschek, A.; Haug, T. T.; Kirsch, S. F.; Klahn, P.; Liebert, C. *Tetrahedron* **2009,** *65* (9), 1880-1888.

44. Larock, R. C.; Chow, M. S.; Smith, S. J. *J. Org. Chem.* **1986,** *51* (13), 2623-2624.

45. Hashmi, A. S. K.; Ruppert, T. L.; Knofel, T.; Bats, J. W. *J. Org. Chem.* **1997,** *62* (21), 7295-7304.

46. Shao, Y.; Fusti-Molnar, L.; Jung, Y.; Kussmann, J.; Ochsenfeld, C.; Brown, S. T.; Gilbert, A. T. B.; Slipchenko, L. V.; O'Neill, D. P.; DiStasio, R. A.; Lochan, R. C.; Wang, T.; Beran, G. J. O.; Besley, N. A.; Herbert, J. M.; Lin, C. Y.; Van Voorhis, T.; Chien, S. H.; Sodt, A.; Steele, R. P.; Rassolov, V. A.; Maslen, P. E.; Korambath, P. P.; Adamson, R. D.; Austin, B.; Baker, J.; Byrd, E. F. C.; Dachsel, H.; Doerksen, A.; Dreuw, A.; BDunietz, B. D.; Dutoi, A. D.; Furlani, T. R.; Gwaltney, S. R.; Heyden, A.; Hirata, S.; Hsu, C.-P.; Kedziora, G.; Khalliulin, R. Z.; Klunzinger, P.; Lee, A. M.; Lee, M. S.; Liang, W.; Lotan, I.; Nair, N.; Peters, B.; Proynov, E. I.; Pieniazek, P. A.; Rhee, Y. M.; Ritchie, J.; Rosta, E.; Sherrill, C. D.; Simmonett, A. C.; Subotnik, J. E.; Woodcook, H. L.; Zhang, W.; Bell, A. T.; Chakraborty, A. K.; Chipman, D. M.; Keil, F. J.; Warshel, A.; Hehre, W. J.; Schaefer, H. F.; Kong, J.; Krylov, A. I.; Gill, P. M. W.; Head-Gordon, M. *Q-Chem*, 3.1; Q-Chem, Inc.: Pittsburgh, 2007.

47. Keith, T. A. *AIMAll*, 10.03.25; 2010.

48. [a] Bader, R. F., *Atoms in Molecules - A Quantum Theory*. Oxford University Press: Oxford, 1990; [b] Matta, C. F.; Boyd, R. J., *The Quantum Theory of Atoms in Molecules*. Wiley-VCH: Weinhem, 2007.

49. [a] Distasio, R. A.; Steele, R. P.; Rhee, Y. M.; Shao, Y. H.; Head-Gordon, M. *J. Comp. Chem.* **2007,** *28* (5), 839-856; [b] Feyereisen, M.; Fitzgerald, G.; Komornicki, A. *Chem. Phys. Lett.* **1993,** *208* (5-6), 359-363; [c] Weigand, F.; Haser, M. *Theor. Chem. Acc.* **1997,** *97* (1-4), 324-330.

50. Matoba, K.; Maeda, T.; Nagase, K.; Yamazaki, T. *Chem. Pharm. Bull.* **1976,** *24* (1), 165-168.

51. Weidler, M.; Rether, J.; Anke, T.; Erkel, G.; Sterner, O. *J. Antibiot.* **2001,** *54* (8), 679-681.

52. Yu, Z. X.; Aumann, R.; Frohlich, R.; Roths, K.; Hecht, J. *J. Organometal. Chem.* **1997,** *541* (1-2), 187-198.

53. Aumann, R.; Weidenhaupt, H. J. *Chem. Ber.* **1987,** *120* (1), 23-27.

54. For reviews see: [a] Harmata, M. *Acc. Chem. Res.* **2001,** *34* (7), 595-605; [b] Harmata, M. *Chem. Commun.* **2010,** *46* (47), 8886-8903; [c] Harmata, M. *Chem. Commun.* **2010,** *46* (47), 8904-8922; [d] Harmata, M.; Rashatasakhon, P. *Tetrahedron* **2003,** *59* (14), 2371-2395; [e] Hosomi, A.; Tominagi, Y., In *Comprehensive Organic Synthesis*, Pergamon: Oxford, 1991; Vol. 5, pp 593-615; [f] Mann, J. *Tetrahedron* **1986,** *42* (17), 4611-4659; [g] Noyori, R. *Acc. Chem. Res.* **1979,** *12* (2), 61-66.

55. [a] Fohlisch, B.; Korfant, H.; Meining, H.; Frey, W. *Eur. J. Org. Chem.* **2000,** (7), 1335-1344; [b] Fujita, M.; Oshima, M.; Okuno, S.; Sugimura, T.; Okuyama, T. *Org. Lett.* **2006,** *8* (18), 4113-4116; [c] Sasaki, T.; Ishibashi, Y.; Ohno, M.

Tetrahedron Lett. **1982,** *23* (16), 1693-1696; [d] Takaya, H.; Makino, S.; Hayakawa, Y.; Noyori, R. *J. Am. Chem. Soc.* **1978,** *100* (6), 1765-1777.

56. Regarding [3 + 2] cyclizations see: references 54a, 54d, 55b, and [a] Hardinger, S. A.; Bayne, C.; Kantorowski, E.; McClellan, R.; Larres, L.; Nuesse, M.-A. *J. Org. Chem.* **1995,** *60* (5), 1104-1105; [b] Hayakawa, Y.; Yokoyama, K.; Noyori, R. *J. Am. Chem. Soc.* **1978,** *100* (6), 1799-1806; [c] Lee, T. V.; Boucher, R. J.; Porter, J. R.; Taylor, D. A. *Tetrahedron* **1988,** *44* (13), 4233-4242; [d] Lee, T. V.; Porter, J. R.; Roden, F. S. *Tetrahedron* **1991,** *47* (1), 139-148; [e] Lee, T. V.; Richardson, K. A.; Taylor, D. A. *Tetrahedron* **1986,** *27* (41), 5021-5024; [f] Masuya, K.; Domon, K.; Tanino, K.; Kuwajima, I. *J. Am. Chem. Soc.* **1998,** *120* (8), 1724-1731; [g] Mizuno, H.; Domon, K.; Masuya, K.; Tanino, K.; Kuwajima, I. *J. Org. Chem.* **1999,** *64* (8), 2648-2656; [h] Nakamura, E.; Yamago, S. *Acc. Chem. Res.* **2002,** *35* (10), 867-877.

57. Matsumori, N.; Kaneno, D.; Murata, M.; Nakamura, H.; Tachibana, K. *J. Org. Chem.* **1999,** *64* (3), 866-876.

58. [a] Bifulco, G.; Dambruoso, P.; Gomez-Paloma, L.; Riccio, R. *Chem. Rev.* **2007,** *107* (9), 3744-3779; [b] Kwan, E. E.; Huang, S. G. *Eur. J. Org. Chem.* **2008,** (16), 2671-2688.

59. [a] Mayr, H.; Foerner, W.; von Rague Schleyer, P. *J. Am. Chem. Soc.* **1979,** *101* (20), 6032-6040; [b] Overberger, C. G.; Tanner, D.; Pearce, E. M. *J. Am. Chem. Soc.* **1958,** *80* (17), 4566-4568; [c] Schmid, G. H. *Can. J. Chem.* **1968,** *46* (23), 3757-3758.

60. Matta, C. F.; Hernandez-Trujillo, J. *J. Phys. Chem. A.* **2003,** *107* (38), 7496-7504.

61. Frisch, M. J.; Trucks, G. W.; Schlegel, H. B.; Scuseria, G. E.; Robb, M. A.; Cheeseman, J. R.; Montgomery, J. A.; Vreven, T.; Kudin, K. N.; Burant, J. C.; Millam, J. M.; Iyengar, S. S.; Tomasi, J.; Barone, V.; Mennucci, B.; Cossi, M.; Scalmani, G.; Rega, N.; Petersson, G. A.; Nakatsuji, H.; Hada, M.; Ehara, M.; Toyota, K.; Fukuda, R.; Hasegawa, J.; Ishida, M.; Nakajima, T.; Honda, Y.; Kitao, O.; Nakai, H.; Klene, M.; Li, X.; Knox, J. E.; Hratchian, H. P.; Cross, J. B.; Adamo, C.; Jaramillo, J.; Gomperts, R.; Stratmann, R. E.; Yazyev, O.; Austin, A. J.; Cammi, R.; Pomelli, C.; Ochterski, J. W.; Ayala, P. Y.; Morokuma, K.; Voth, G. A.; Salvador, P.; Dannenberg, J. J.; Zakrzewski, V. G.; Dapprich, S.; Daniels, A. D.; Strain, M. D.; Farkas, O.; Malick, D. K.; Rabuck, A. D.; Raghavachari, K.; Foresman, J. B.; Ortiz, J. V.; Cui, Q.; Baboul, A. G.; Clifford, S.; Cioslowski, J.; Stefanov, B. B.; Liu, G.; Liashenko, A.; Piskorz, P.; Komaromi, I.; Martin, R. L.; Fox, D. J.; Keith, T.; Al-Laham, M. A.; Peng, C. Y.; Nanayakkara, A.; Challacombe, M.; Gill, P. M. W.; Johnson, B.; Chen, W.; Wong, M. W.; Gonzalez, C.; Pople, J. A. *Gaussian 03*, C.02; Gaussian, Inc.: Wallingford, 2004.

62. [a] Cramer, C. J.; Barrows, S. E. *J. Org. Chem.* **1998,** *63* (16), 5523-5532; [b] Cramer, C. J.; Barrows, S. E. *J. Phys. Org. Chem.* **2000,** *13* (3), 176-186.

63. Baldwin, J. E.; Lusch, M. J. *Tetrahedron* **1982,** *38* (19), 2939-2947.

64. Prinzback, H.; Kaupp, G.; Fuchs, R.; Joyeux, M.; Kitzing, R.; Markert, J. *Chem. Ber.* **1973,** *106* (12), 3824-3849.

65. Abid, M.; Landge, S. M.; Torok, B. *Org. Prep. Proced. Int.* **2006,** *38* (5), 495-500.

66. [a] Kakushima, M.; Frenette, R. *J. Org. Chem.* **1984,** *49* (11), 2025-2027; [b] Zonta, C.; Fabris, F.; De Lucchi, O. *Org. Lett.* **2005,** *7* (6), 1003-1006.

67. Adesomoju, A. A.; Okogun, J. I.; Cava, M. P.; Carroll, P. J. *Phytochemistry* **1983,** *22* (11), 2535-2536.

68. Mehta, G.; Singh, V. *Chem. Rev.* **1999,** *99* (3), 881-930.

69. Harmata, M.; Rashatasakhon, P.; Barnes, C. L. *Can. J. Chem.* **2006,** *84* (10), 1456-1469.

70. Giguere, R. J.; Tassely, S. M.; Rose, M. I. *Tetrahedron Lett.* **1990,** *31* (32), 4577-4580.

71. [a] Evans, P. A., *Modern Rhodium-Catalyzed Organic Reactions*. Wiley-VCH: Weinhem, 2005; [b] Evans, P. A.; Baum, E. W.; Fazal, A. N.; Lai, K. W.; Robinson, J. E.; Sawyer, J. R. *ARKIVOC.* **2006,** (7), 338-358; [c] Michaut, A.; Rodriguez, J. *Angew. Chem. Int. Ed.* **2006,** *45* (35), 5740-5750; [d] Yet, L. *Chem. Rev.* **2000,** *100* (8), 2963-3007; [e] Yu, Z. X.; Wang, Y.; Wang, Y. Y. *Chem. Asian J.* **2010,** *5* (5), 1072-1088.

72. Paquette, L. A.; Colapret, J. A.; Andrews, D. R. *J. Org. Chem.* **1985,** *50* (2), 201-205.

73. Wender, P. A.; Floreancig, P. E.; Glass, T. E.; Natchus, M. G.; Shuker, A. J.; Sutton, J. C. *Tetrahedron Lett.* **1995,** *36* (28), 4939-4942.

74. Hoffmann, H. M. R.; Brandes, A. *Tetrahedron* **1995,** *51* (1), 155-164.

75. Wender, P. A.; Ihle, N. C.; Correia, C. R. D. *J. Am. Chem. Soc.* **1988,** *110* (17), 5904-5906.

76. [a] Fan, X. H.; Tang, M. X.; Zhuo, L. G.; Tu, Y. Q.; Yu, Z. X. *Tetrahedron Lett.* **2009,** *50* (2), 155-157; [b] Fan, X. H.; Zhuo, L. G.; Tu, Y. Q.; Yu, Z. X. *Tetrahedron* **2009,** *65* (24), 4709-4713.

77. Paquette, L. A.; Tae, J. S.; Arrington, M. P.; Sadoun, A. H. *J. Am. Chem. Soc.* **2000,** *122* (12), 2742-2748.

78. Shipe, W. D.; Sorensen, E. J. *J. Am. Chem. Soc.* **2006,** *128* (21), 7025-7035.

79. Dhulut, S.; Bourin, A.; Lannou, M. I.; Fleury, E.; Lensen, N.; Chelain, E.; Pancrazi, A.; Ardisson, J.; Fahy, J. *Eur. J. Org. Chem.* **2007,** (31), 5235-5243.

80. Ager, D. J., In *Organic Reactions*, John Wiley and Sons: Hoboken, 1990; Vol. 38, pp 1-223.

81. Wittig, G.; Schollkopf, U. *Chem. Ber.* **1954,** *87* (9), 1318-1330.

82. Julia, M.; Paris, J. M. *Tetrahedron Lett.* **1973,** (49), 4833-4836.

83. Ruel, F. S.; Braun, M. P.; Johnson, C. R. *Org. Synth.* **1998,** *75*, 69-77.

84. Barriault, L.; Thomas, J. D. O.; Clement, R. *J. Org. Chem.* **2003,** *68* (6), 2317-2323.

85. Negishi, E.; King, A. O.; Okukado, N. *J. Org. Chem.* **1977,** *42* (10), 1821-1823.

86. Takai, K.; Nitta, K.; Utimoto, K. *J. Am. Chem. Soc.* **1986,** *108* (23), 7408-7410.

87. Corey, E. J.; Fuchs, P. L. *Tetrahedron Lett.* **1972,** *13* (36), 3769-3772.

88. Harada, T.; Katsuhira, T.; Oku, A. *J. Org. Chem.* **1992,** *57* (22), 5805-5807.

89. Smith, A. B.; Foley, M. A.; Dong, S. Z.; Orbin, A. *J. Org. Chem.* **2009,** *74* (16), 5987-6001.

90. Heck, R. F.; Nolley, J. P. *J. Org. Chem.* **1972,** *37* (14), 2320-2322.

91. Smith, A. B.; Branca, S. J.; Guaciaro, M. A.; Wovkulich, P. M.; Korn, A. *Org. Synth.* **1983,** *61*, 65-70.

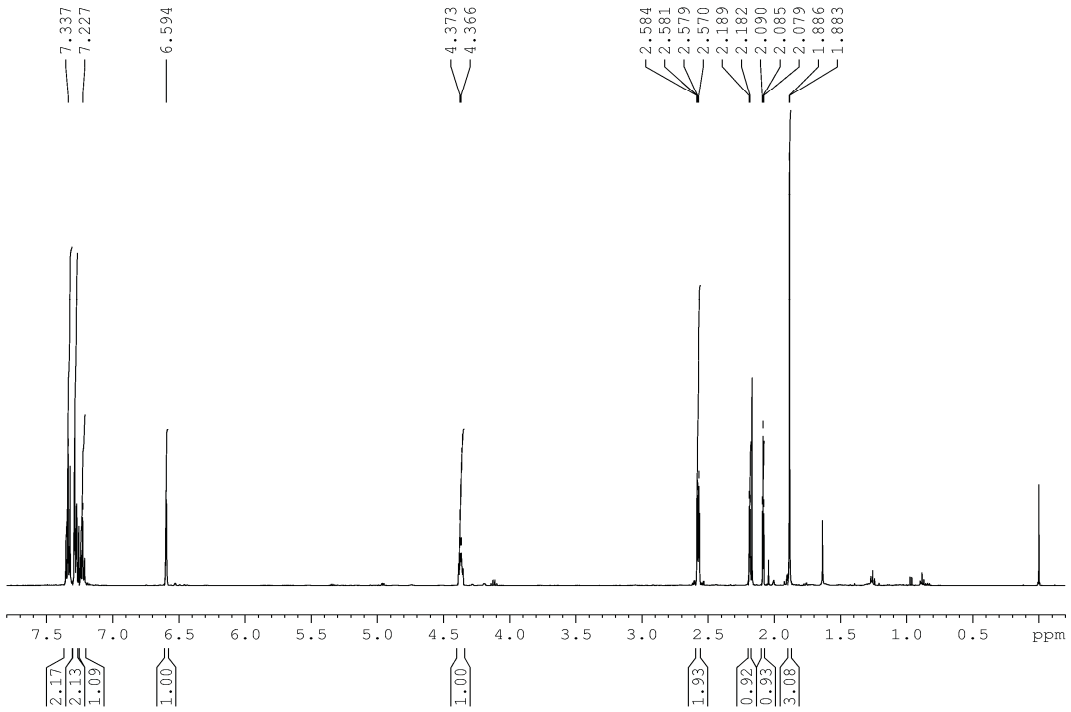
92. Littke, A. F.; Fu, G. C. *J. Am. Chem. Soc.* **2001,** *123* (29), 6989-7000.

93. Smith, A. B.; Kurti, L.; Davulcu, A. H. *Org. Lett.* **2006,** *8* (10), 2167-2170.

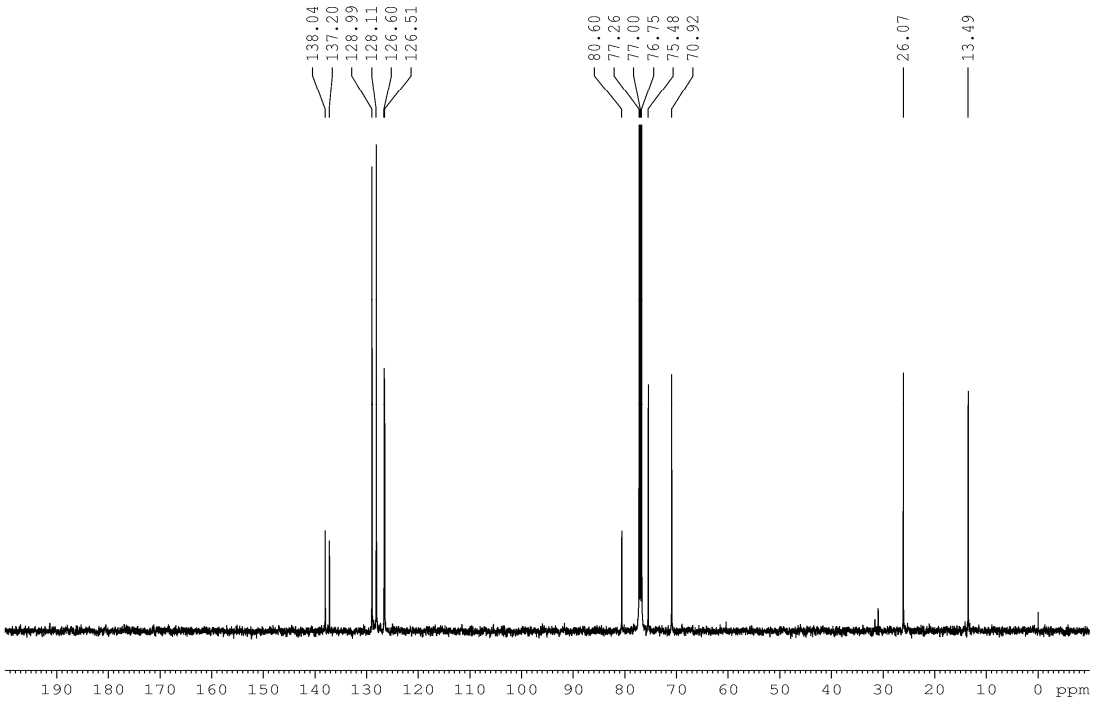
94. Singleton, D. A.; Thomas, A. A. *J. Am. Chem. Soc.* **1995,** *117* (36), 9357-9358.

APPENDIX A. NMR Spectral Data

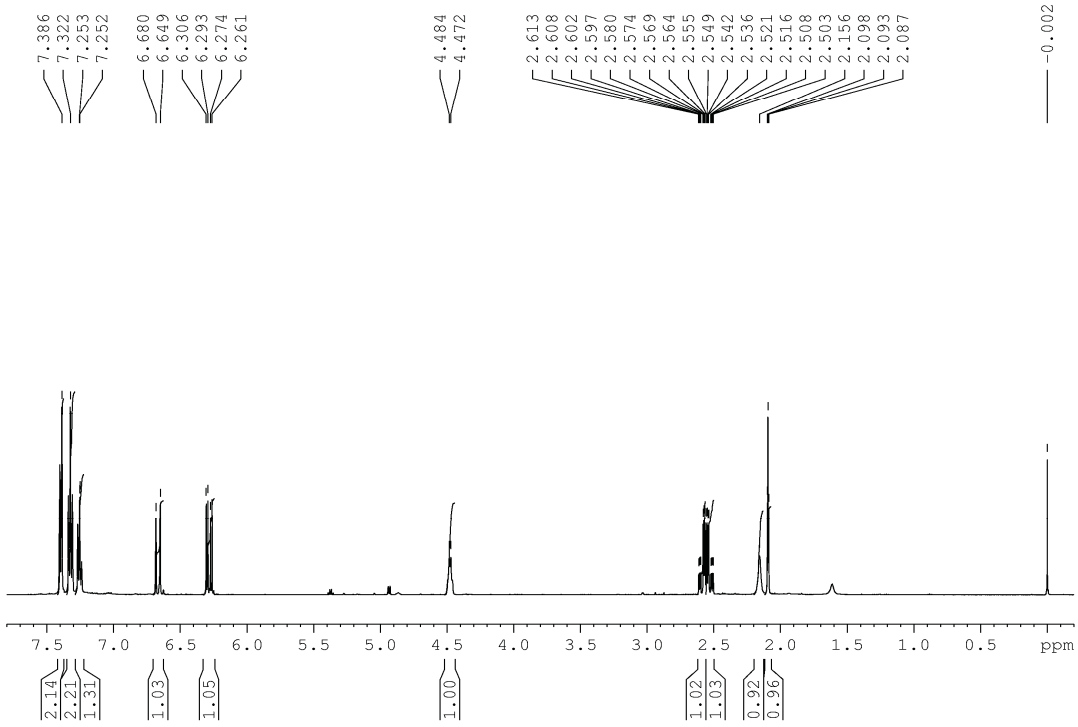
^{1}H NMR (500 MHz, $CDCl_3$) of (*E*)-2-methyl-1-phenylhex-1-en-5-yn-3-ol (24b)



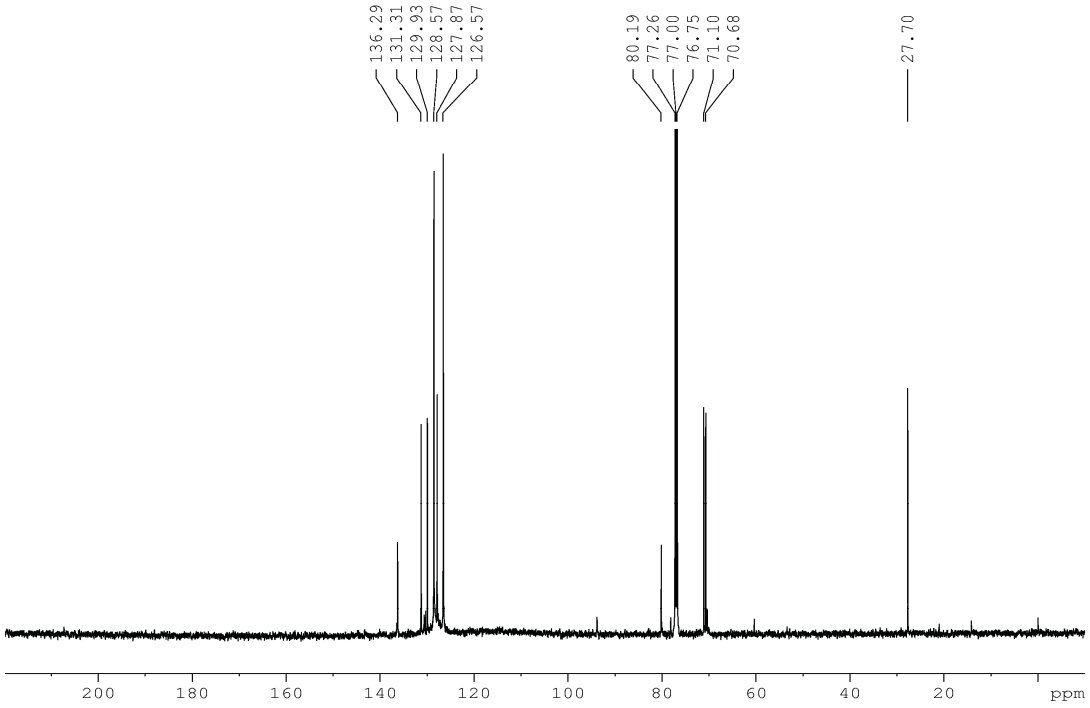
^{13}C NMR (125 MHz, $CDCl_3$) of (*E*)-2-methyl-1-phenylhex-1-en-5-yn-3-ol (24b)



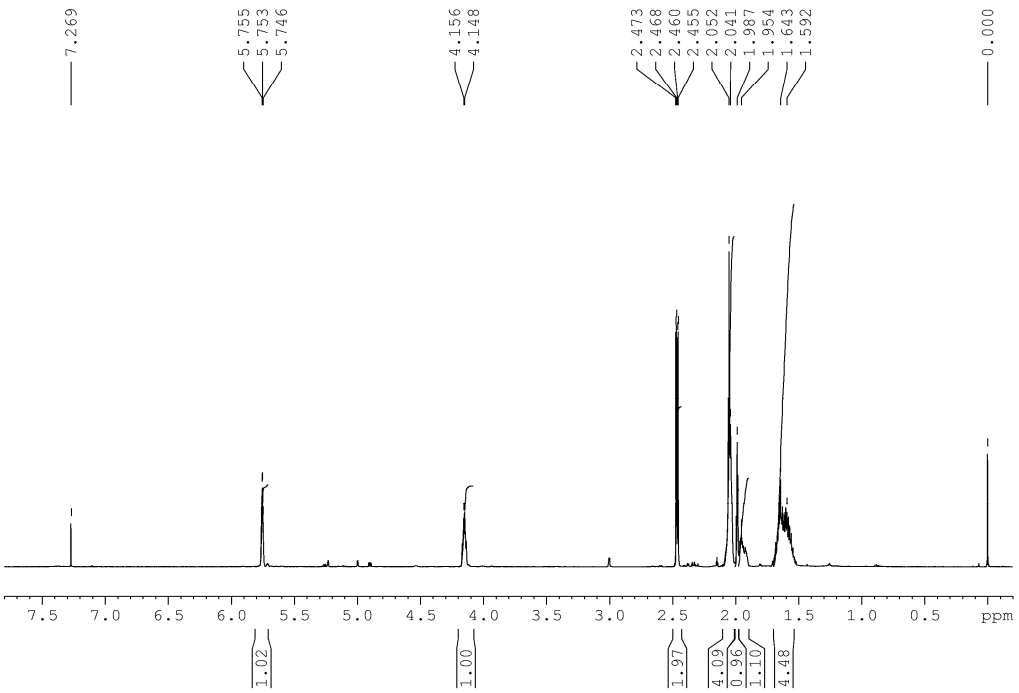
^{1}H NMR (500 MHz, $CDCl_3$) of (*E*)-1-phenylhex-1-en-5-yn-3-ol (24c)



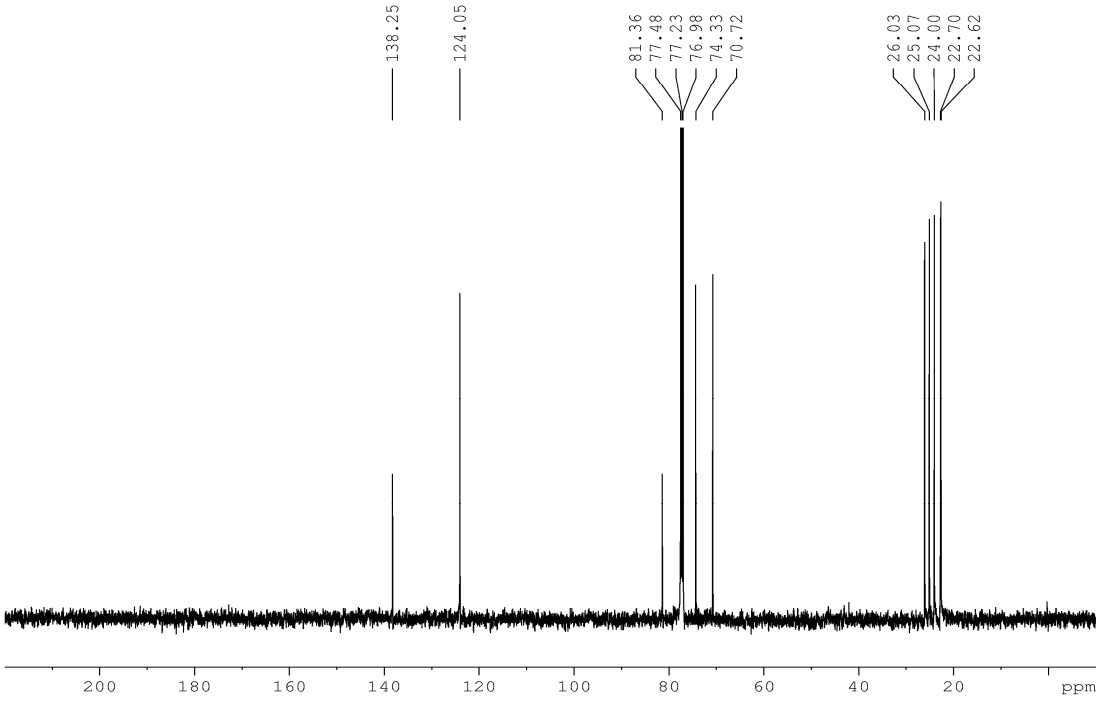
^{13}C NMR (125 MHz, $CDCl_3$) of (*E*)-1-phenylhex-1-en-5-yn-3-ol (24c)



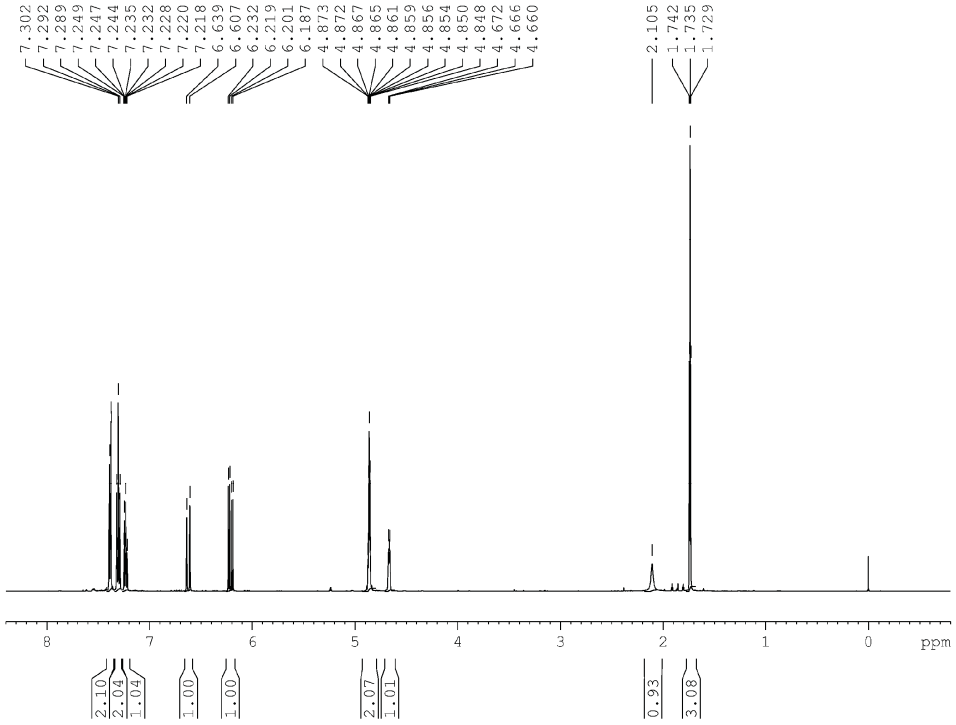
^{1}H NMR (500 MHz, $CDCl_3$) of *(E)*-1-cyclohexenylbut-3-yn-1-ol (24k)



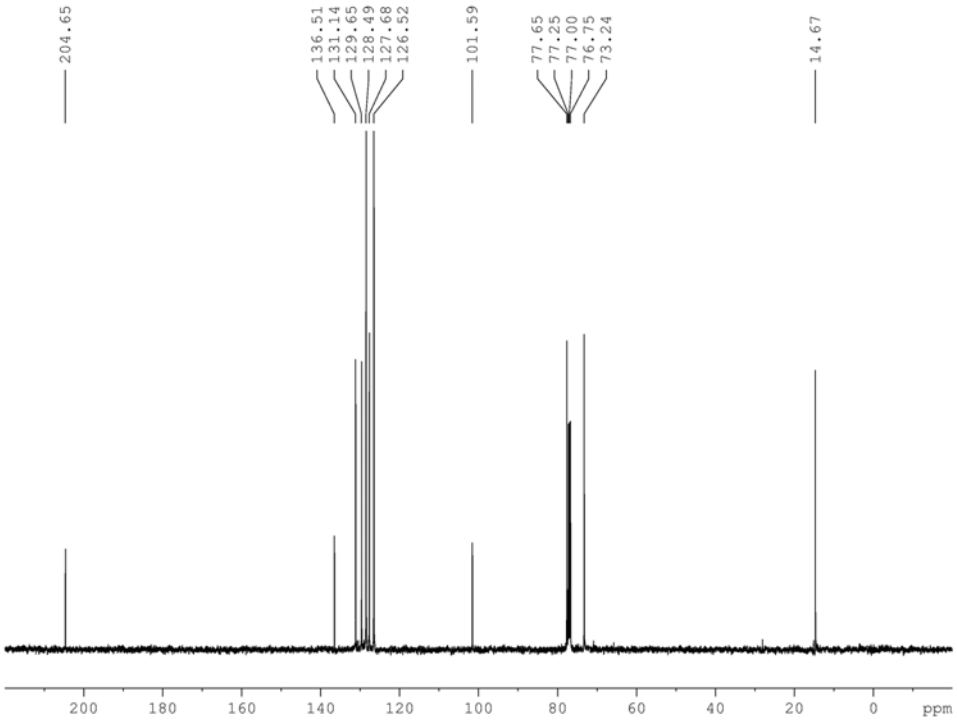
^{13}C NMR (125 MHz, $CDCl_3$) of *(E)*-1-cyclohexenylbut-3-yn-1-ol (24k)



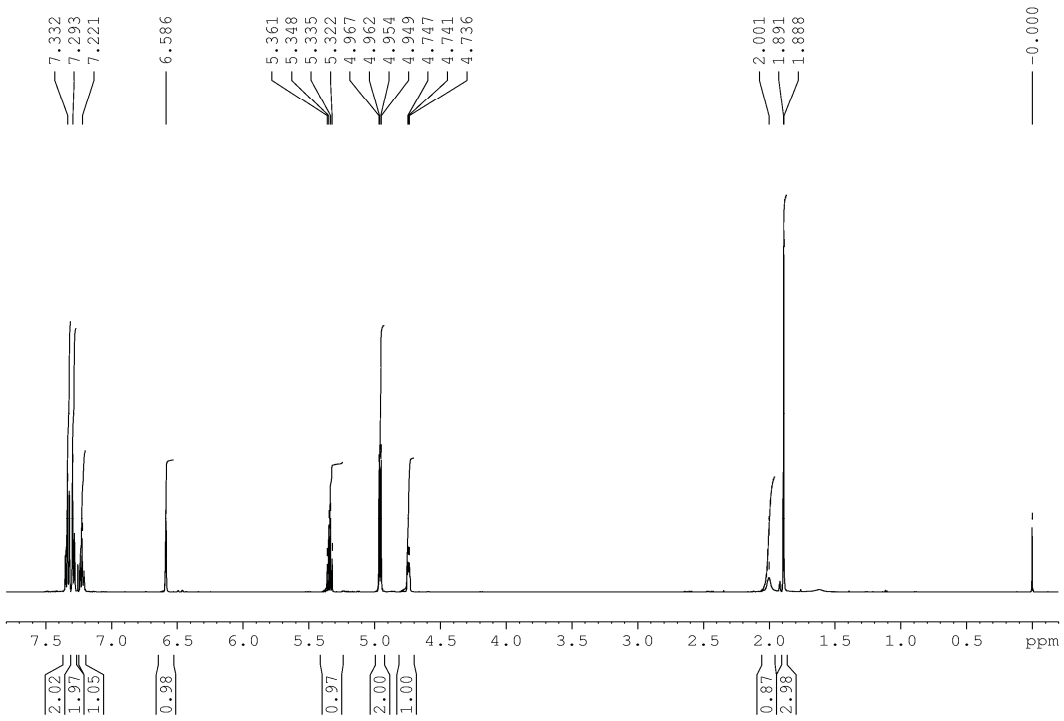
^{1}H NMR ($CDCl_3$, 500 MHz) spectrum of (*E*)-4-methyl-1-phenylhexa-1,4,5-trien-3-ol (25a)



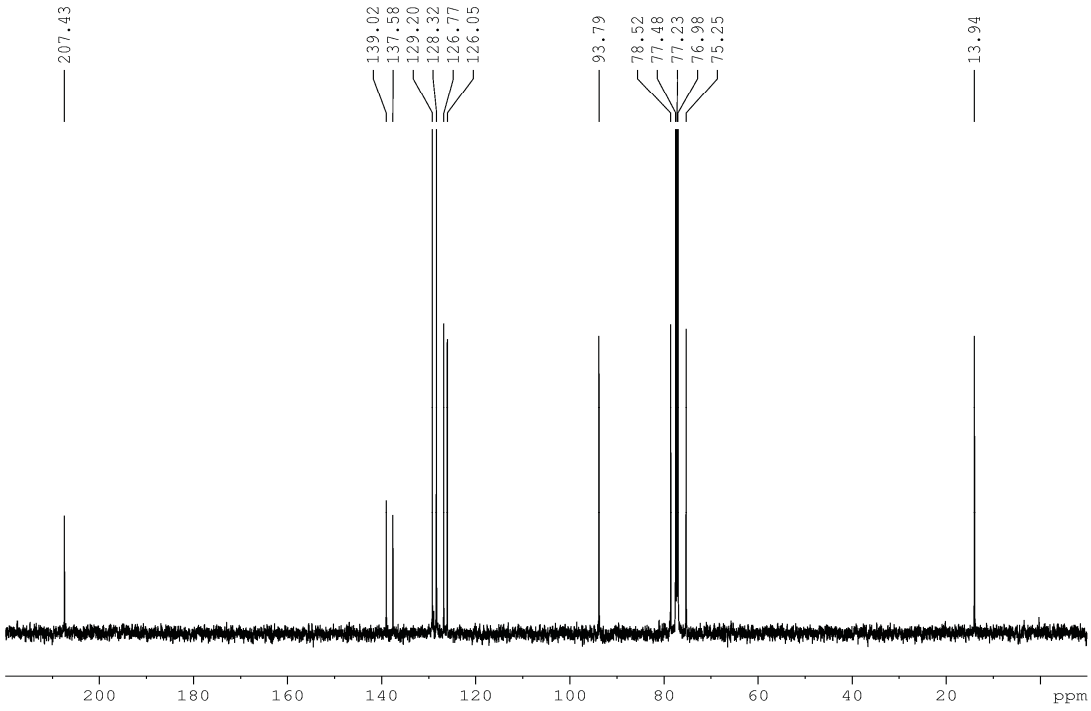
^{13}C NMR ($CDCl_3$, 125 MHz) spectrum of (*E*)-4-methyl-1-phenylhexa-1,4,5-trien-3-ol (25a)



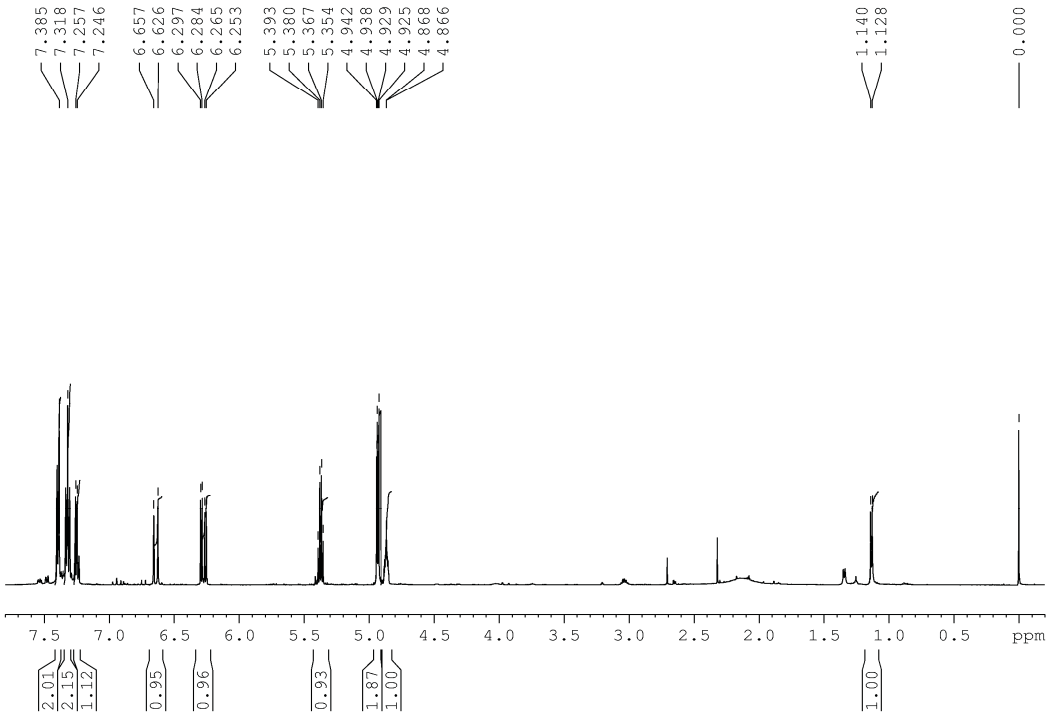
^{1}H NMR (500 MHz, $CDCl_3$) of (*E*)-2-methyl-1-phenylhexa-1,4,5-trien-3-ol (25b)



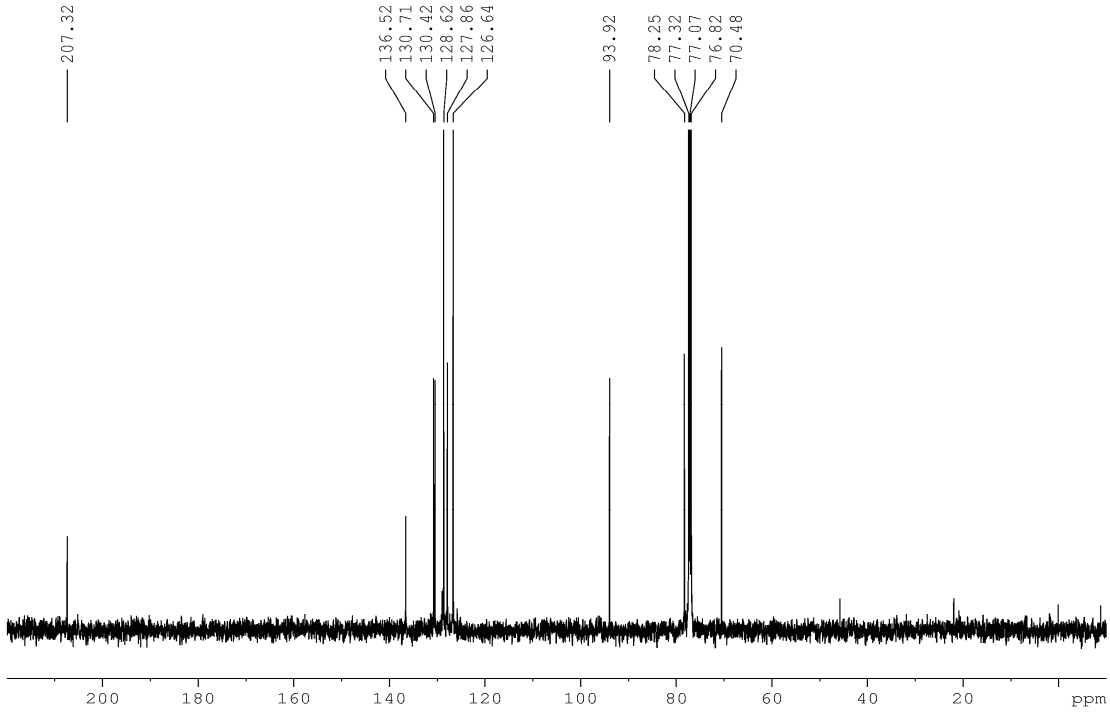
^{13}C NMR (125 MHz, $CDCl_3$) of (*E*)-2-methyl-1-phenylhexa-1,4,5-trien-3-ol (25b)



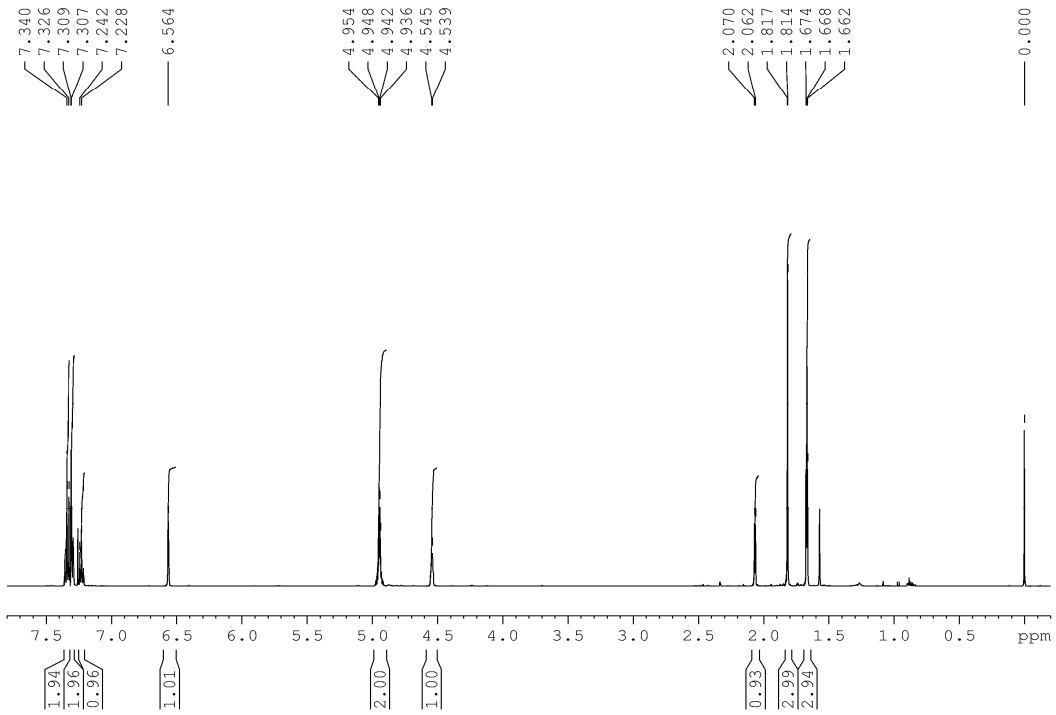
^{1}H NMR (500 MHz, $CDCl_3$) of (*E*)-1-phenylhexa-1,4,5-trien-3-ol (25c)



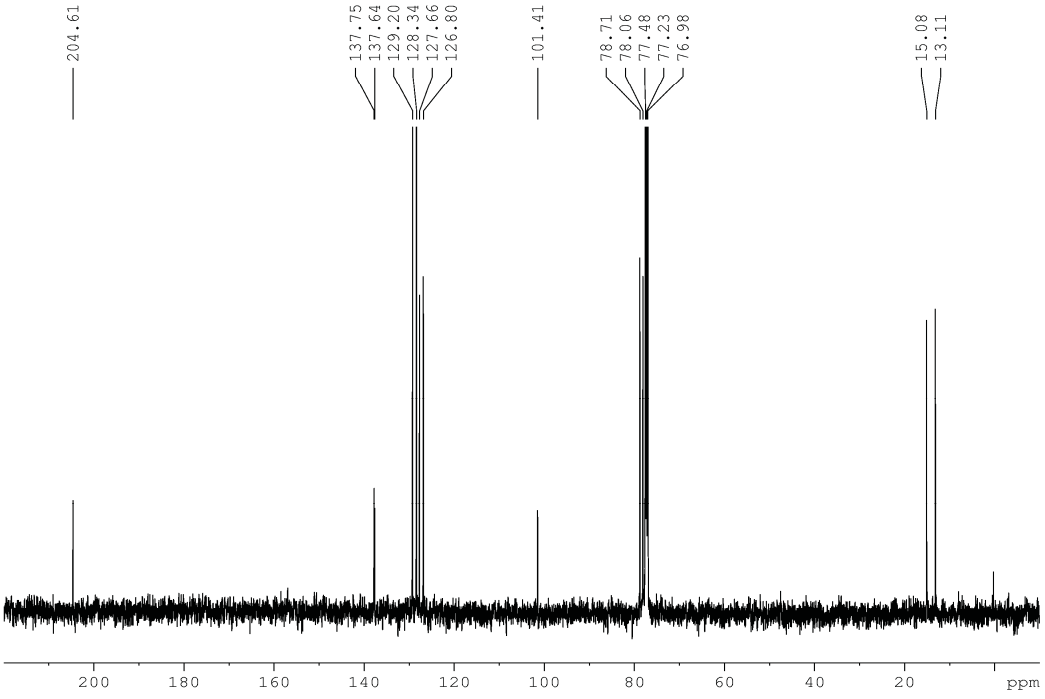
^{13}C NMR (125 MHz, $CDCl_3$) of (*E*)-1-phenylhexa-1,4,5-trien-3-ol (25c)



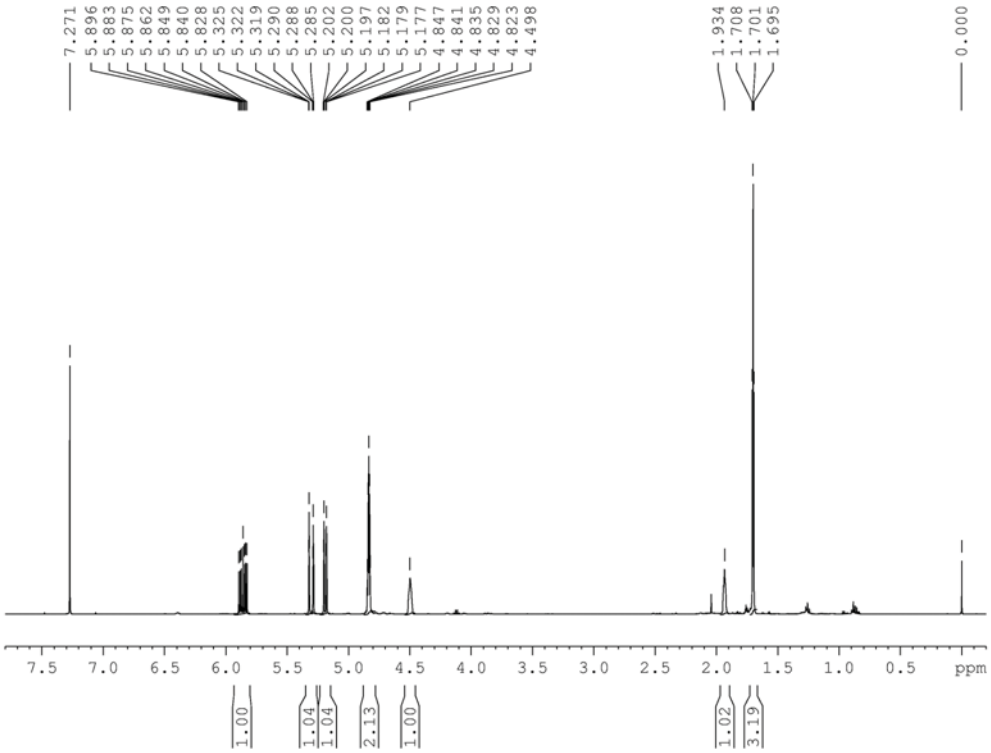
^{1}H NMR (500 MHz, $CDCl_3$) of (*E*)-2,4-dimethyl-1-phenylhexa-1,4,5-trien-3-ol (25d)



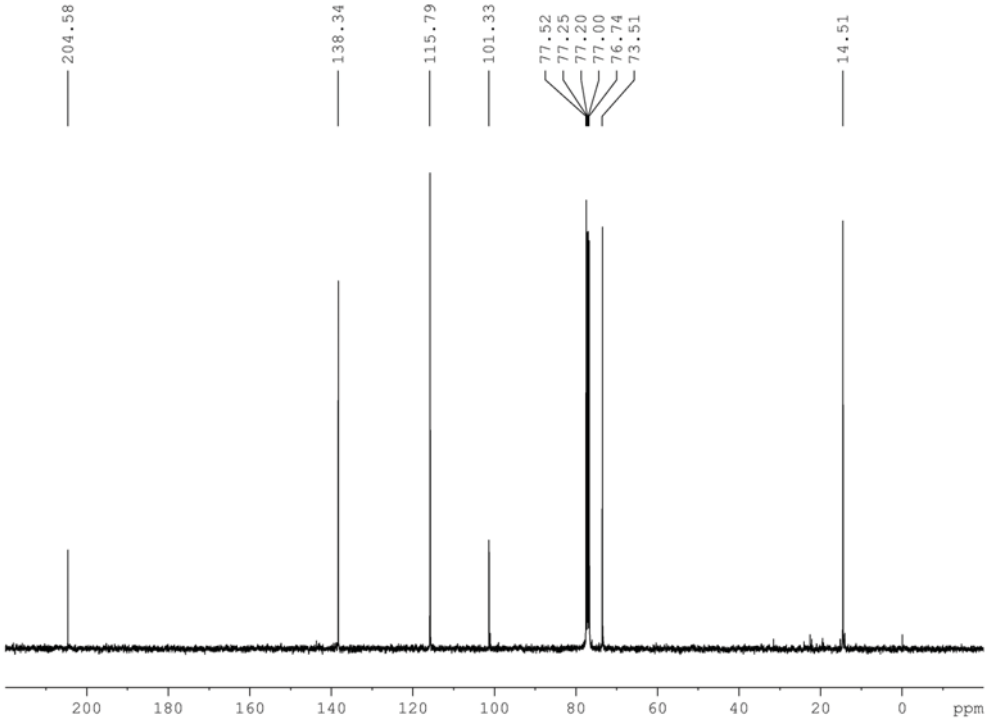
^{13}C NMR (125 MHz, $CDCl_3$) of (*E*)-2,4-dimethyl-1-phenylhexa-1,4,5-trien-3-ol (25d)



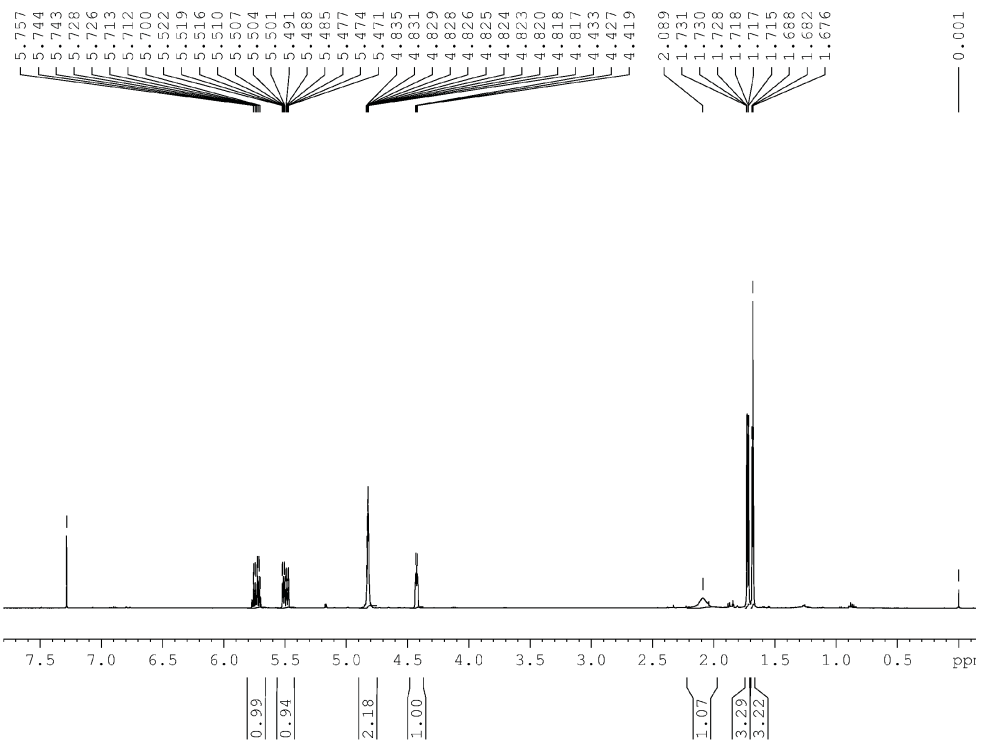
^{1}H NMR ($CDCl_3$, 500 MHz) spectrum of 4-methylhexa-1,4,5-trien-3-ol (25e)



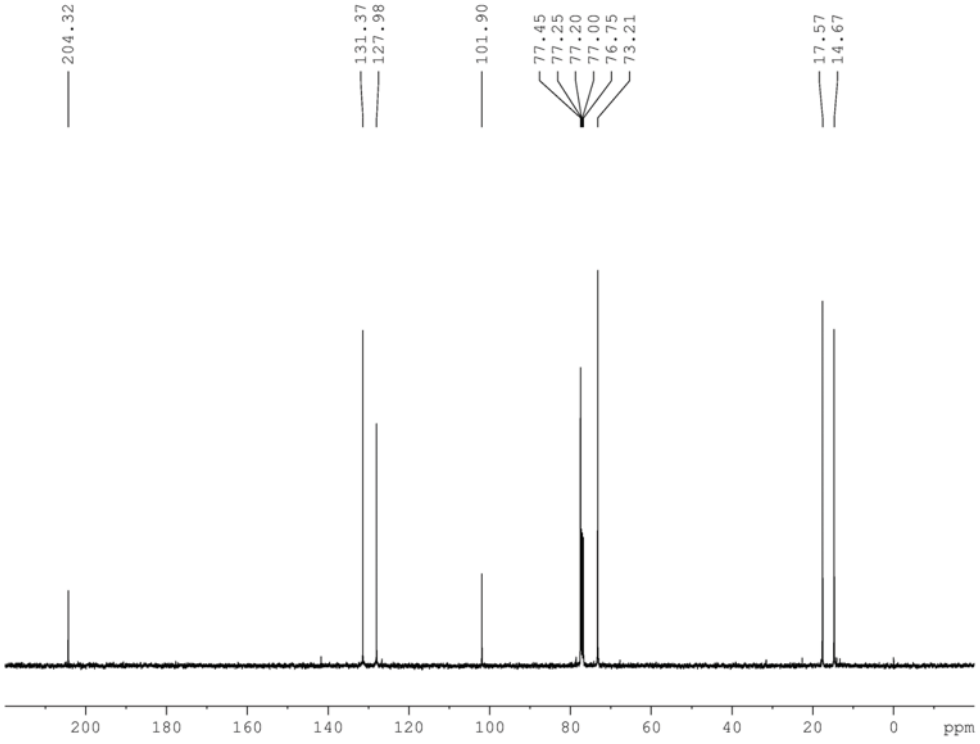
^{13}C NMR ($CDCl_3$, 125 MHz) spectrum of 4-methylhexa-1,4,5-trien-3-ol (25e)



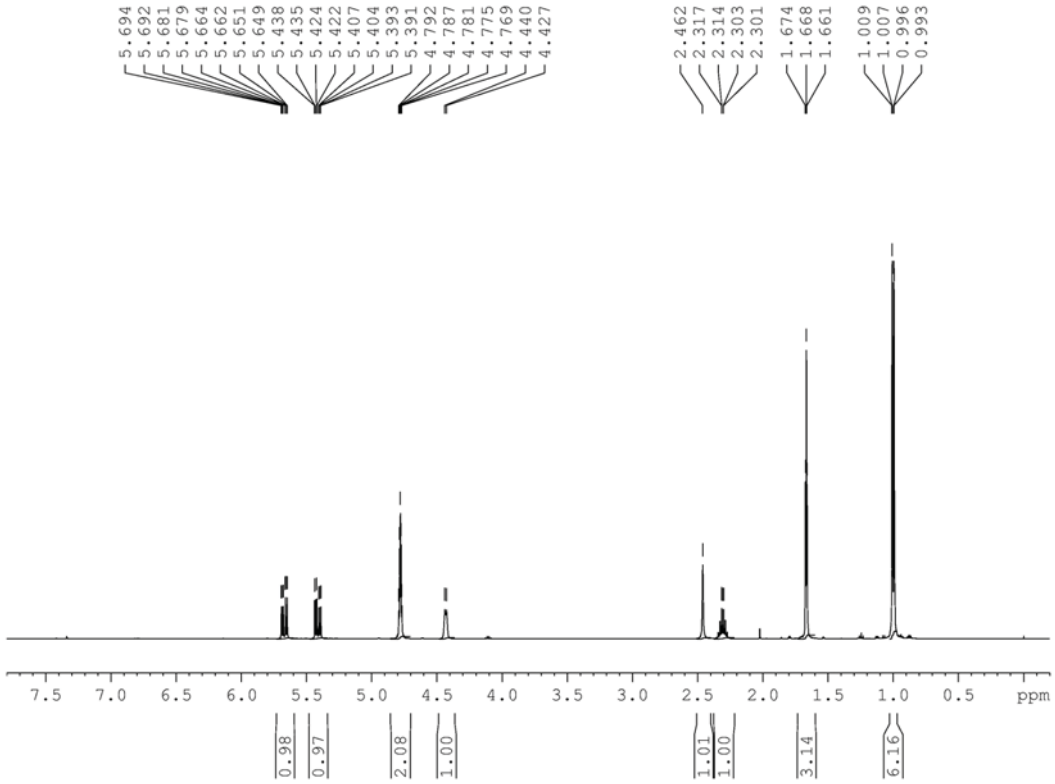
^{1}H NMR ($CDCl_3$, 500 MHz) spectrum of (*E*)-3-methylhepta-1,2,5-trien-4-ol (25f)



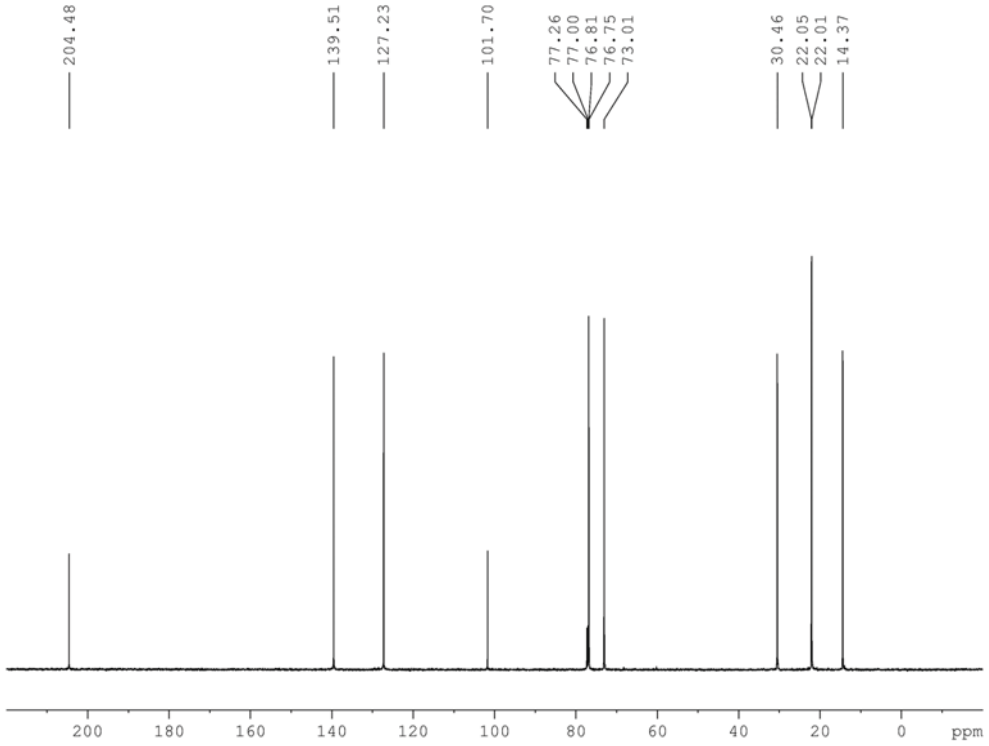
^{13}C NMR ($CDCl_3$, 125 MHz) spectrum of (*E*)-3-methylhepta-1,2,5-trien-4-ol (25f)



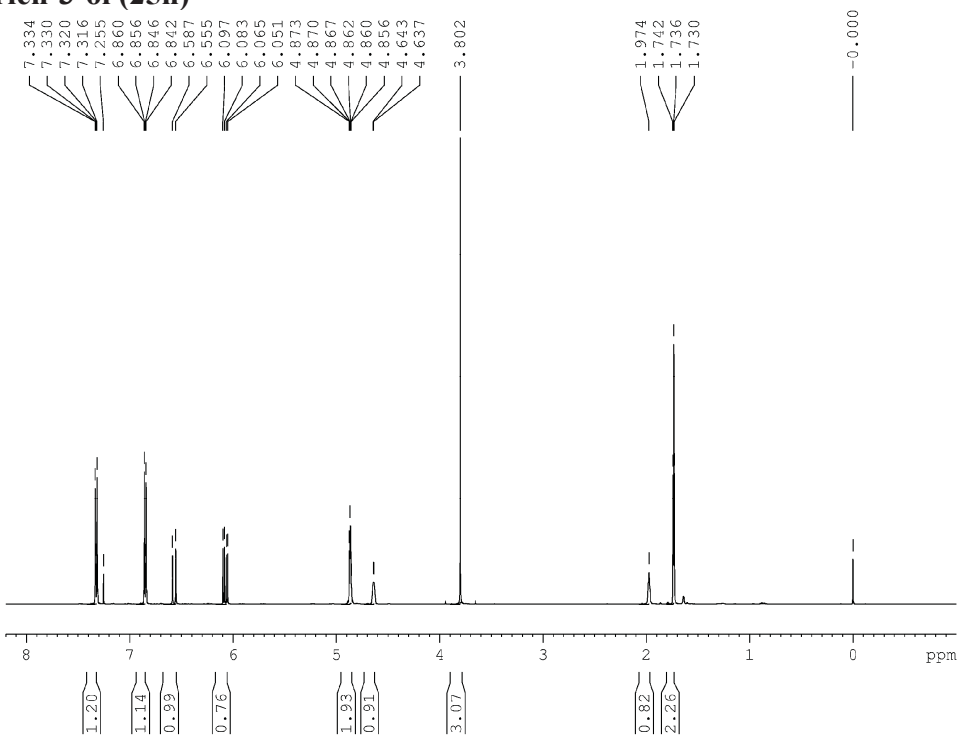
^{1}H NMR ($CDCl_3$, 500 MHz) spectrum of (*E*)-3,7-dimethylocta-1,2,5-trien-4-ol (25g)



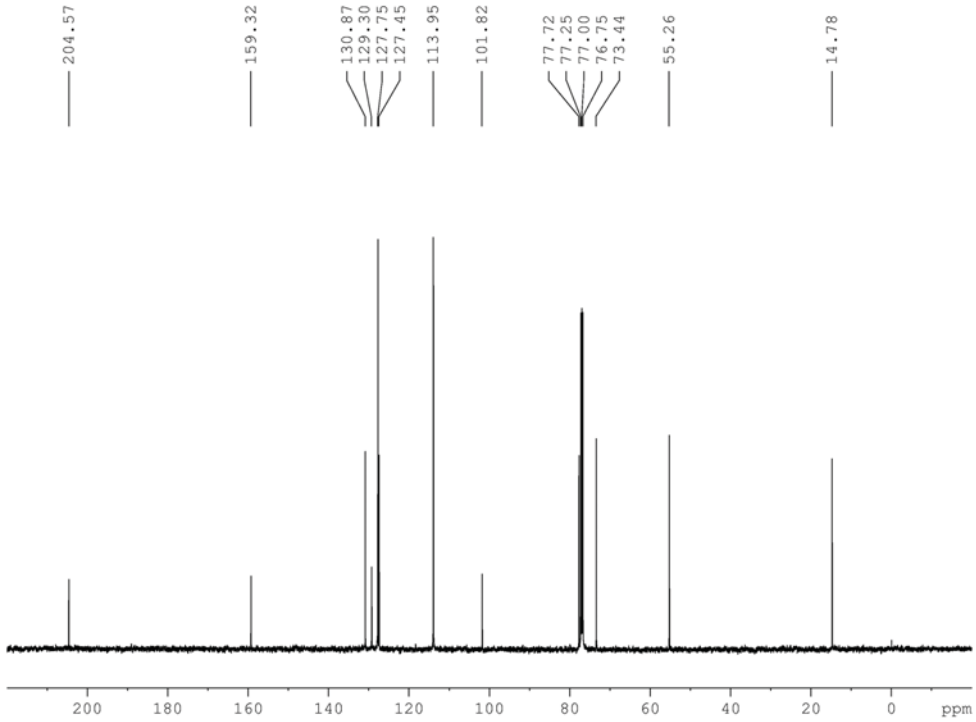
^{13}C NMR ($CDCl_3$, 125 MHz) spectrum of (*E*)-3,7-dimethylocta-1,2,5-trien-4-ol (25g)



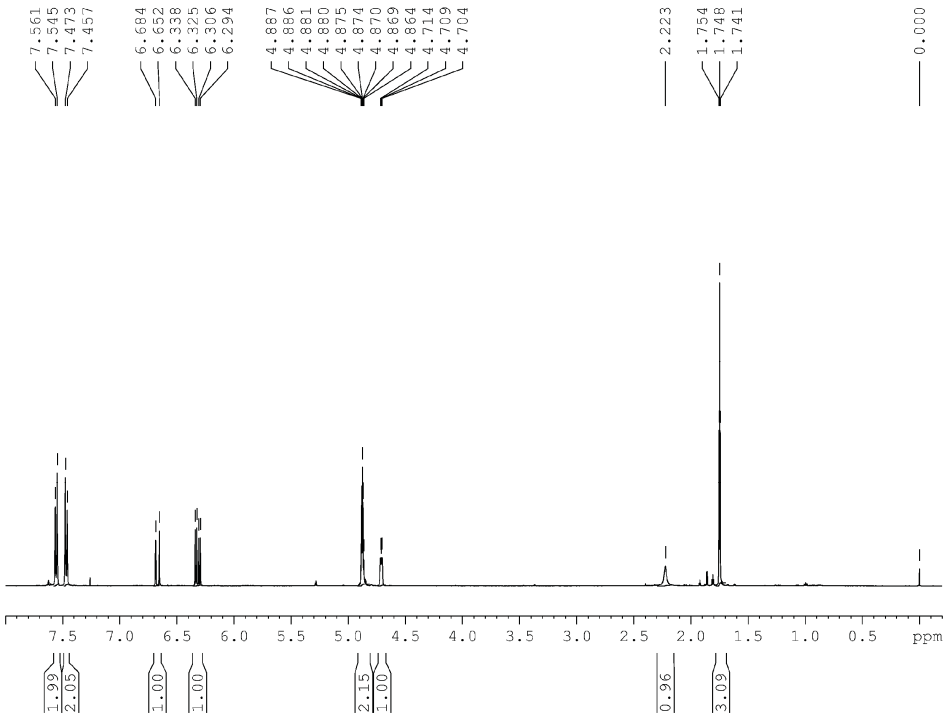
^{1}H NMR ($CDCl_3$, 500 MHz) spectrum of (*E*)-1-(4-methoxyphenyl)-4-methylhexa-1,4,5-trien-3-ol (25h)



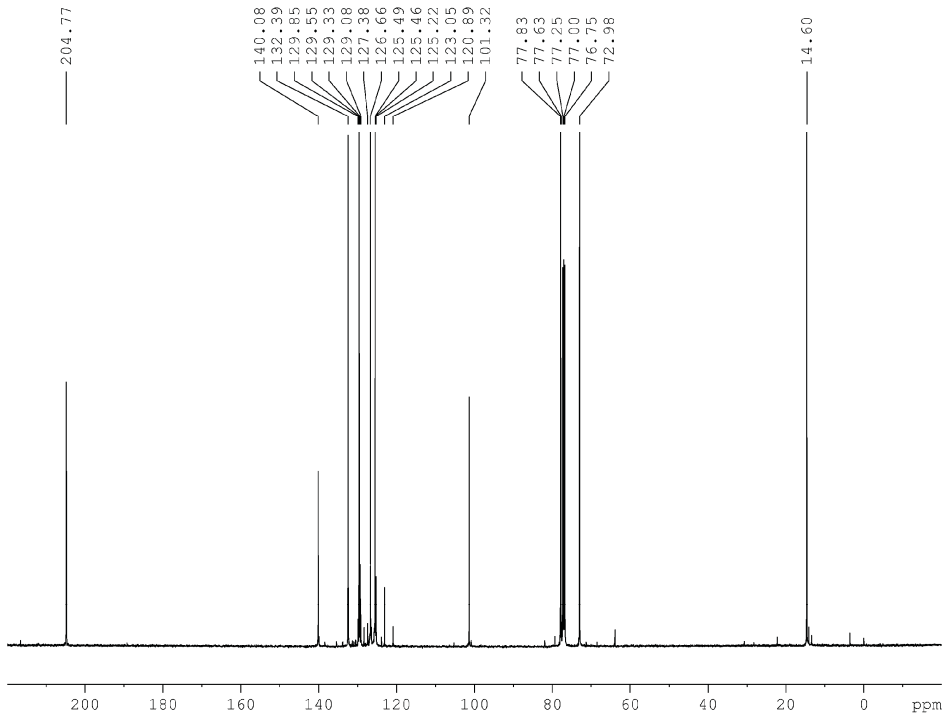
^{13}C NMR ($CDCl_3$, 125 MHz) spectrum of (*E*)-1-(4-methoxyphenyl)-4-methylhexa-1,4,5-trien-3-ol (25h)



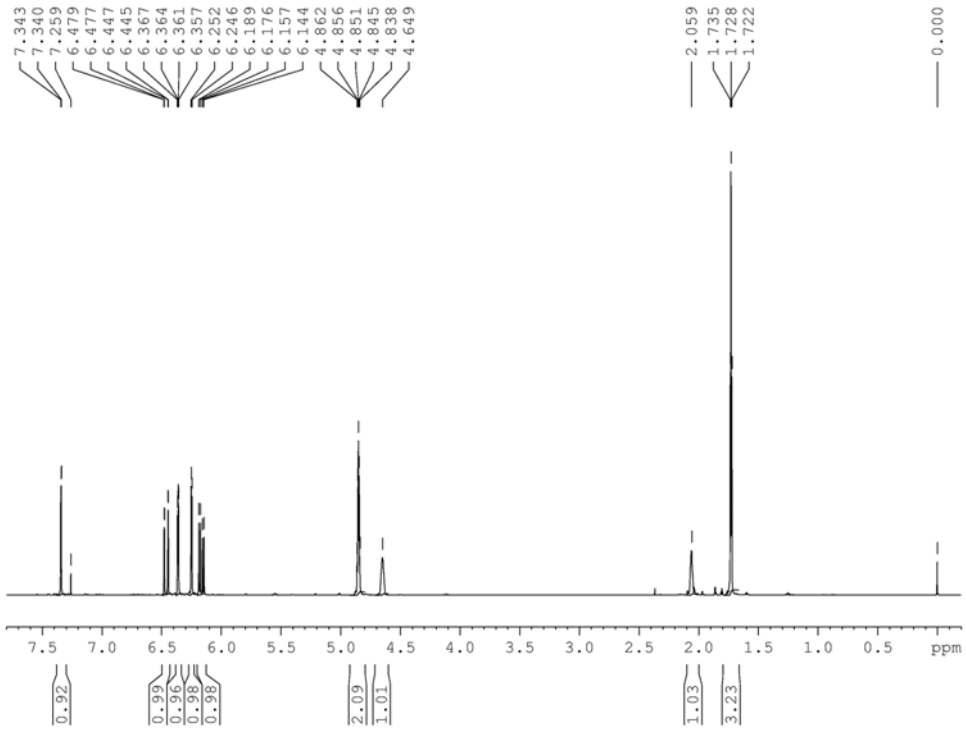
^{1}H NMR ($CDCl_3$, 500 MHz) spectrum of (*E*)-4-methyl-1-(4-(trifluoromethyl)phenyl)hexa-1,4,5-trien-3-ol (25i)



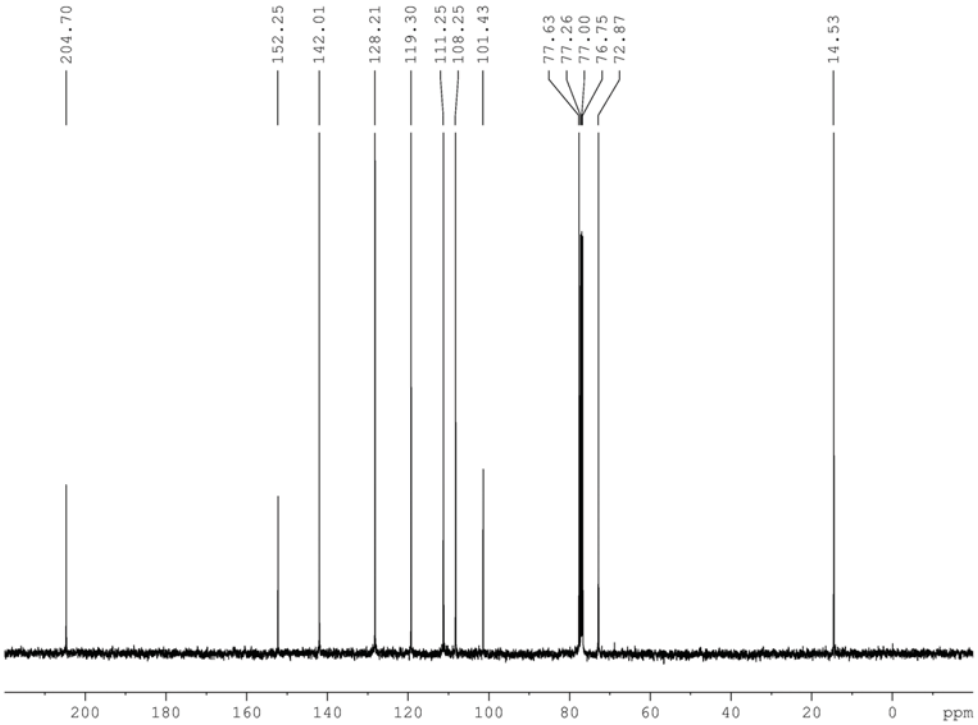
^{13}C NMR ($CDCl_3$, 125 MHz) spectrum of (*E*)-4-methyl-1-(4-(trifluoromethyl)phenyl)hexa-1,4,5-trien-3-ol (25i)



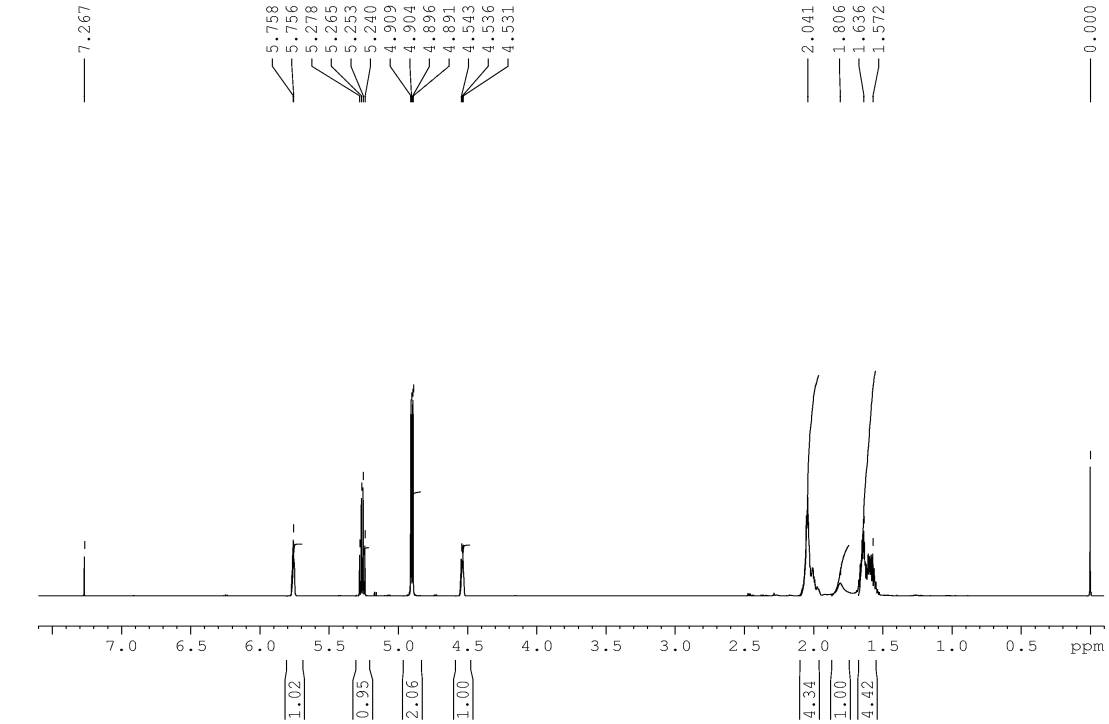
^{1}H NMR ($CDCl_3$, 500 MHz) spectrum of (*E*)-1-(furan-2-yl)-4-methylhexa-1,4,5-trien-3-ol (25j)



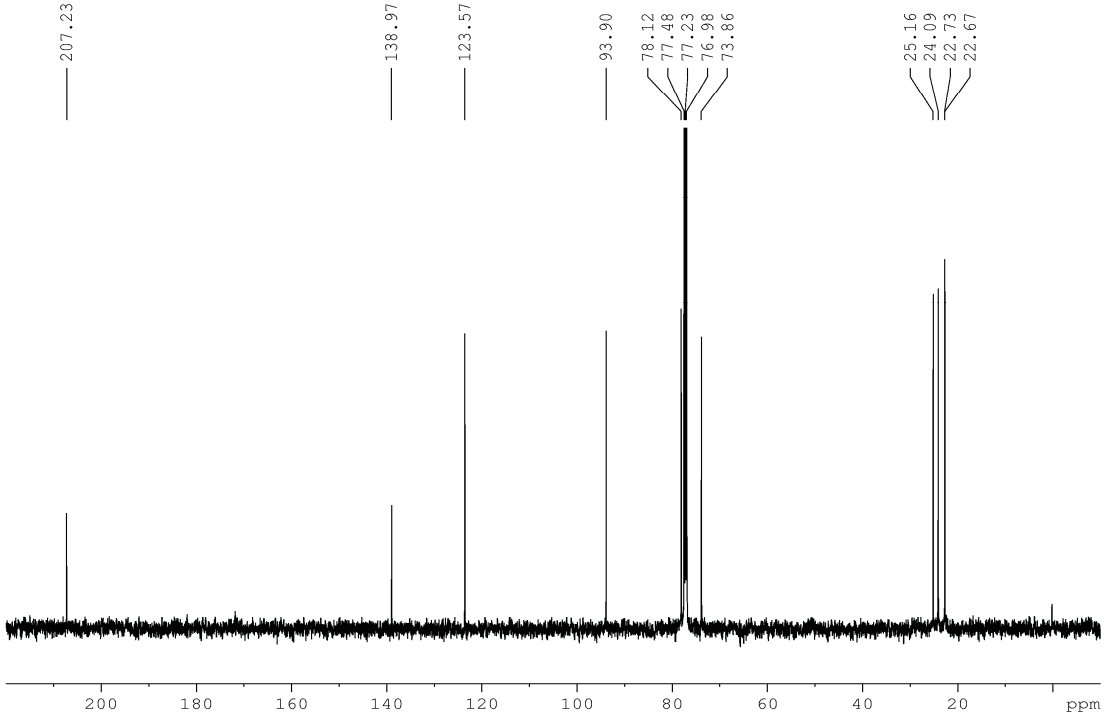
^{13}C NMR ($CDCl_3$, 125 MHz) spectrum of (*E*)-1-(furan-2-yl)-4-methylhexa-1,4,5-trien-3-ol (25j)



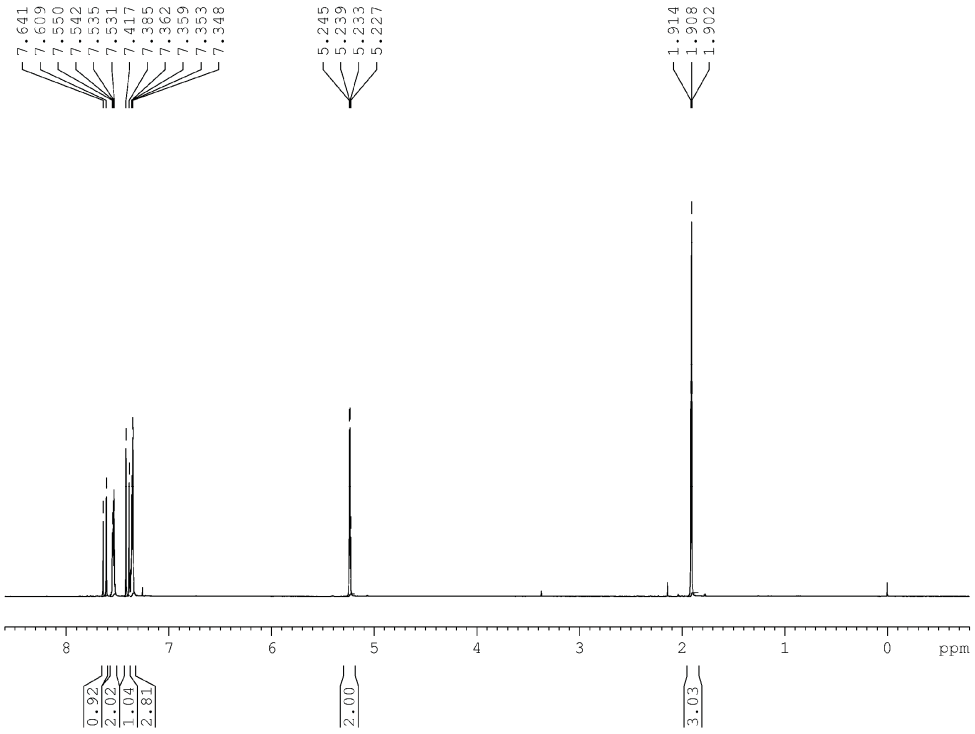
^{1}H NMR (500 MHz, $CDCl_3$) of (*E*)-1-cyclohexenylbuta-2,3-dien-1-ol (25k)



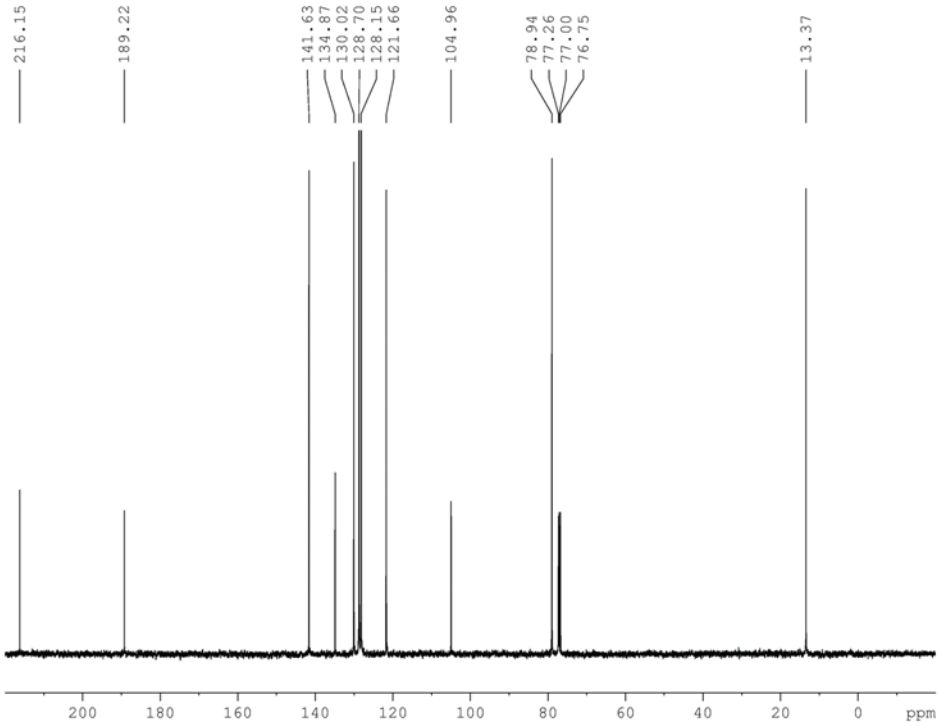
^{13}C NMR (125 MHz, $CDCl_3$) of (*E*)-1-cyclohexenylbuta-2,3-dien-1-ol (25k)



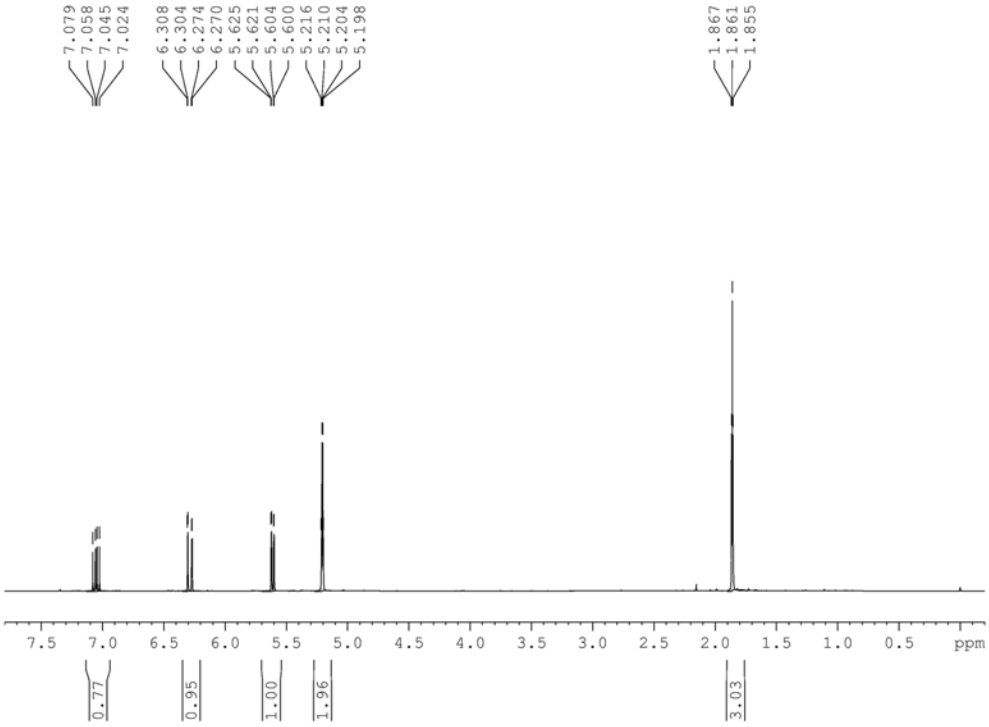
^{1}H NMR ($CDCl_3$, 500 MHz) spectrum of (*E*)-4-methyl-1-phenylhexa-1,4,5-trien-3-one (26)



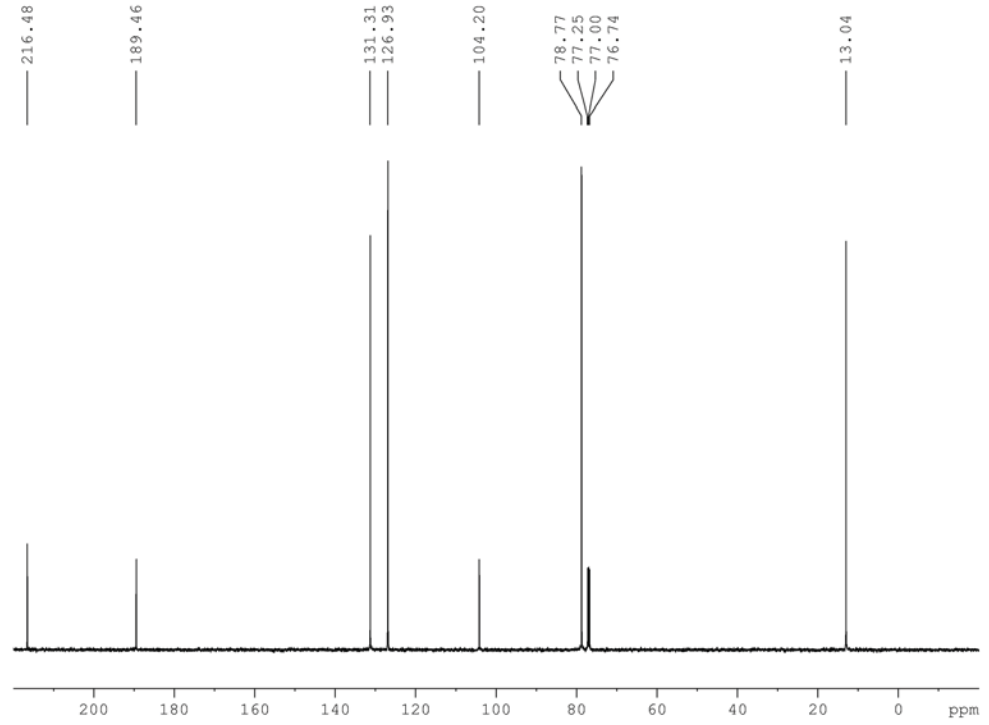
^{13}C NMR ($CDCl_3$, 125 MHz) spectrum of (*E*)-4-methyl-1-phenylhexa-1,4,5-trien-3-one (26)



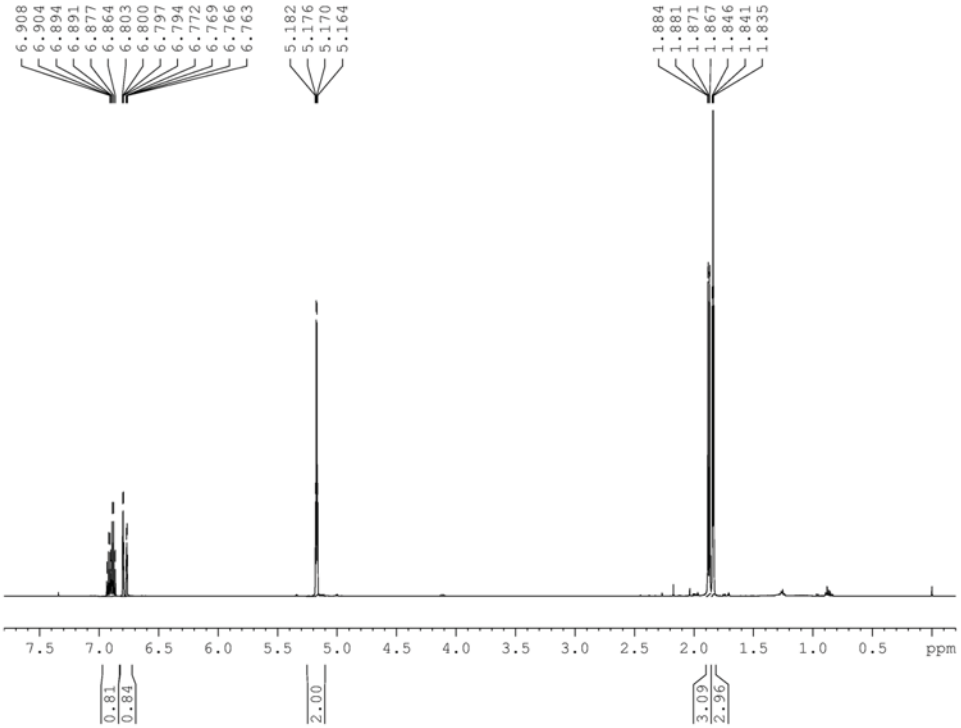
^{1}H NMR ($CDCl_3$, 500 MHz) spectrum of 4-methylhexa-1,4,5-trien-3-one (27)



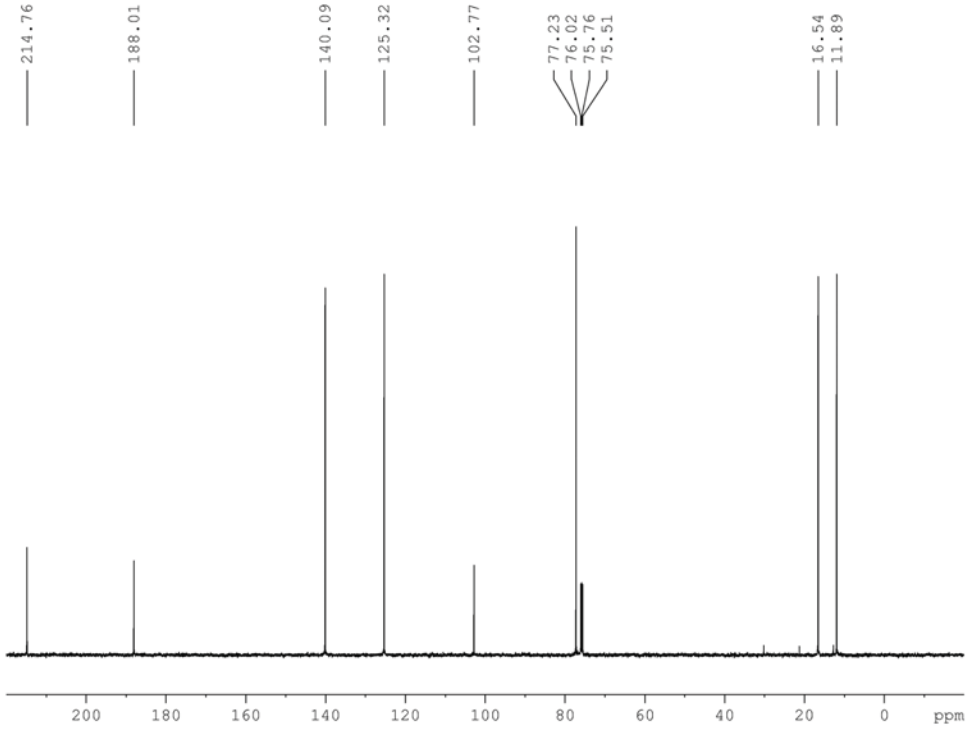
^{13}C NMR ($CDCl_3$, 125 MHz) spectrum of 4-methylhexa-1,4,5-trien-3-one (27)



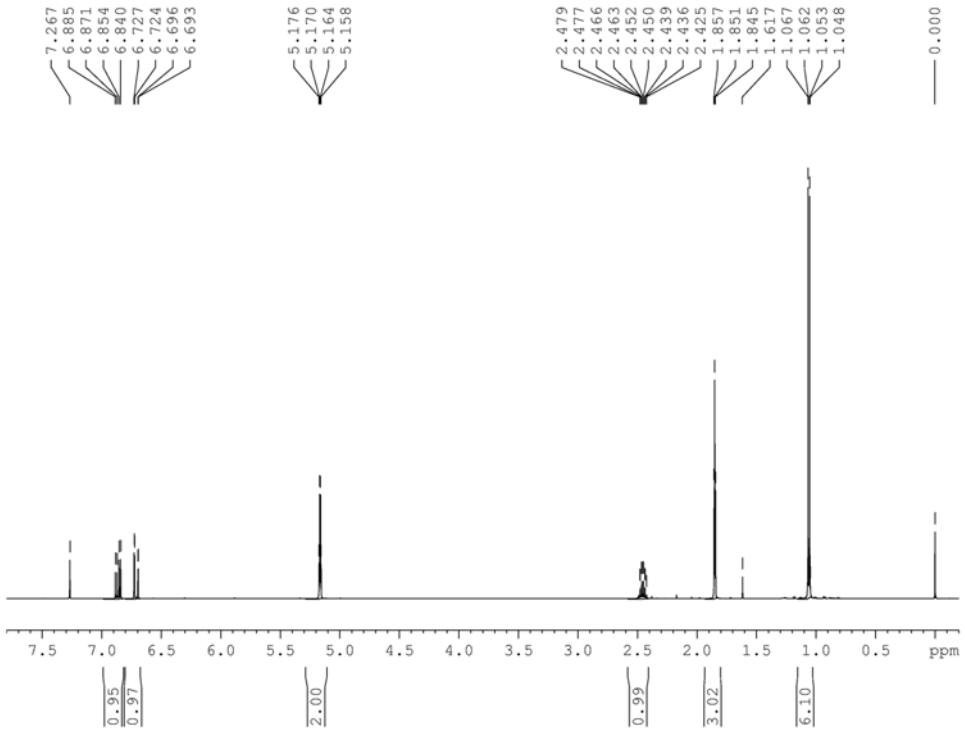
^{1}H NMR ($CDCl_3$, 500 MHz) spectrum of (*E*)-3-methylhepta-1,2,5-trien-4-one (28)



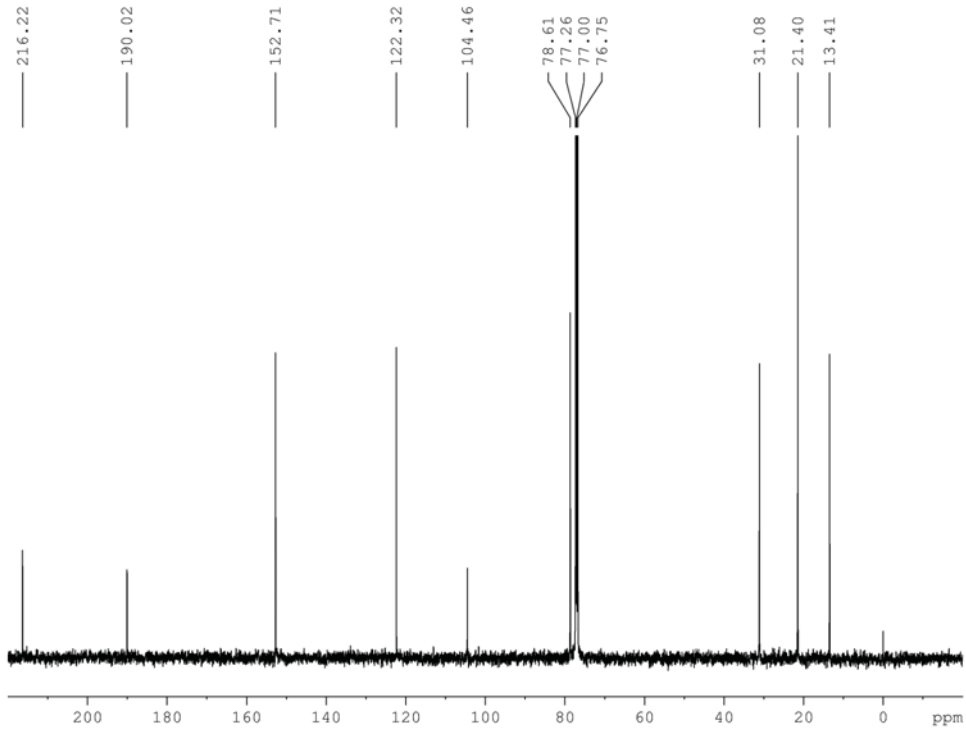
^{13}C NMR ($CDCl_3$, 125 MHz) spectrum of (*E*)-3-methylhepta-1,2,5-trien-4-one (28)



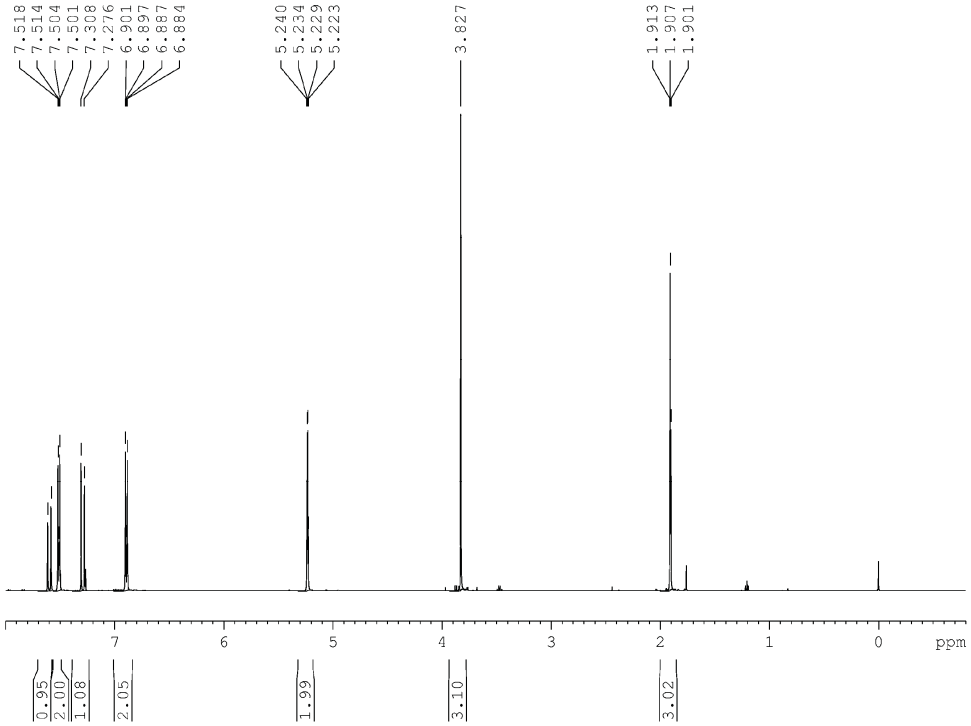
^{1}H NMR ($CDCl_3$, 500 MHz) spectrum of (*E*)-3,7-dimethylocta-1,2,5-trien-4-one (29)



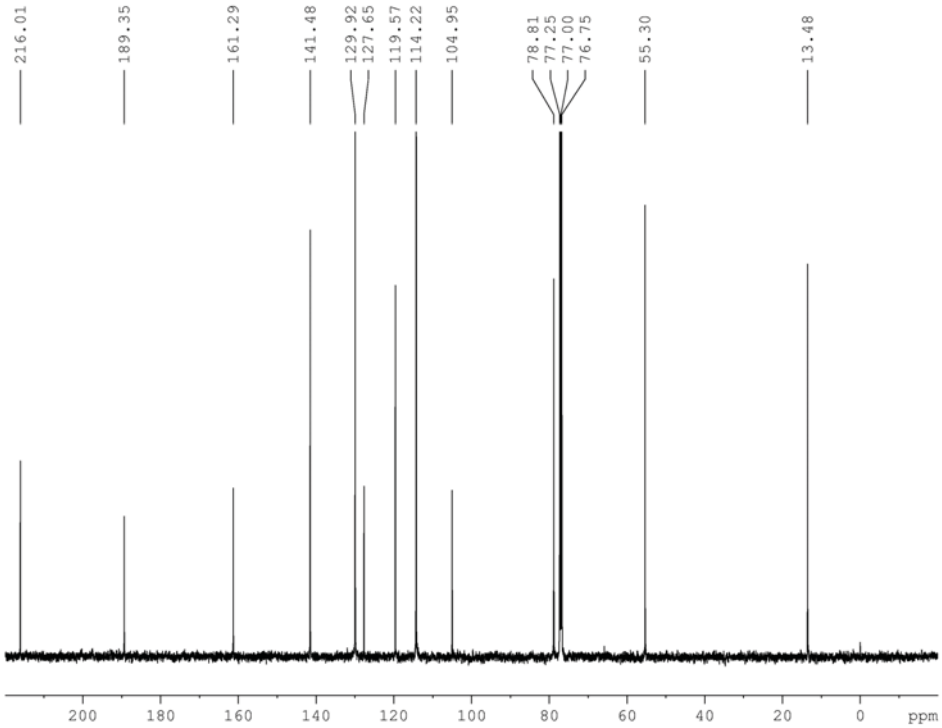
^{13}C NMR ($CDCl_3$, 125 MHz) spectrum of (*E*)-3,7-dimethylocta-1,2,5-trien-4-one (29)



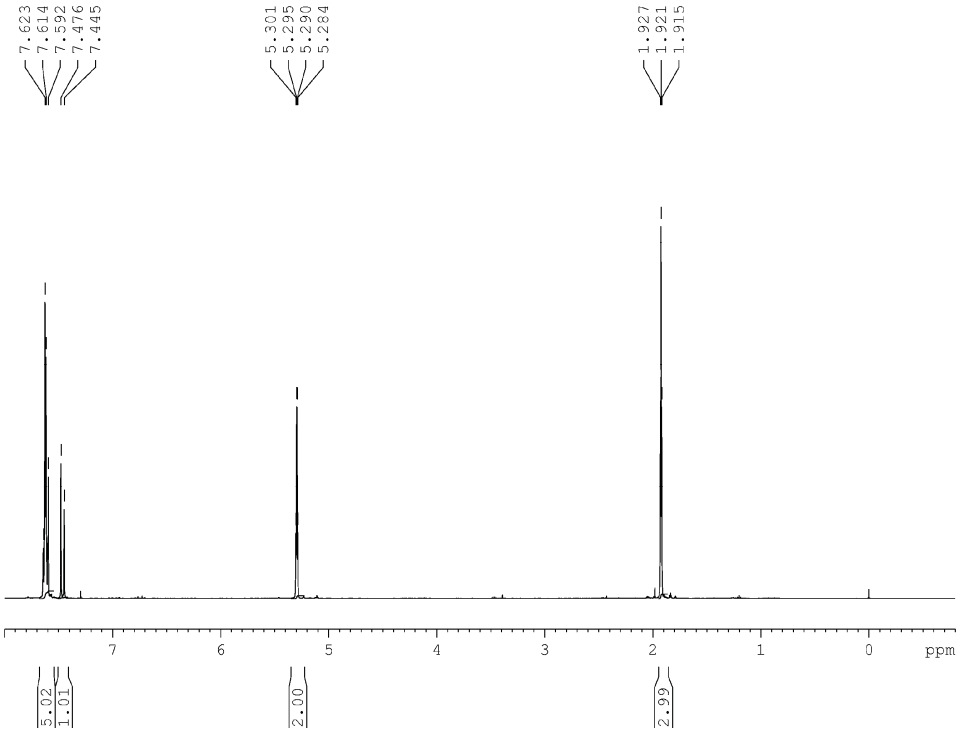
^{1}H NMR ($CDCl_3$, 500 MHz) spectrum of (*E*)-1-(4-methoxyphenyl)-4-methylhexa-1,4,5-trien-3-one (30)



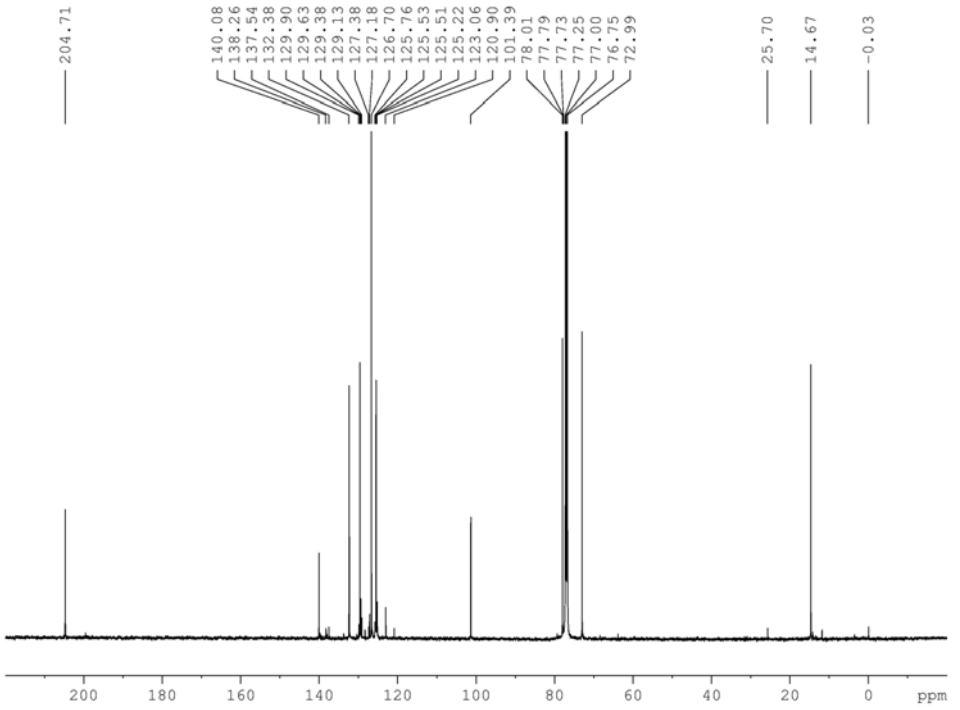
^{13}C NMR ($CDCl_3$, 125 MHz) spectrum of (*E*)-1-(4-methoxyphenyl)-4-methylhexa-1,4,5-trien-3-one (30)



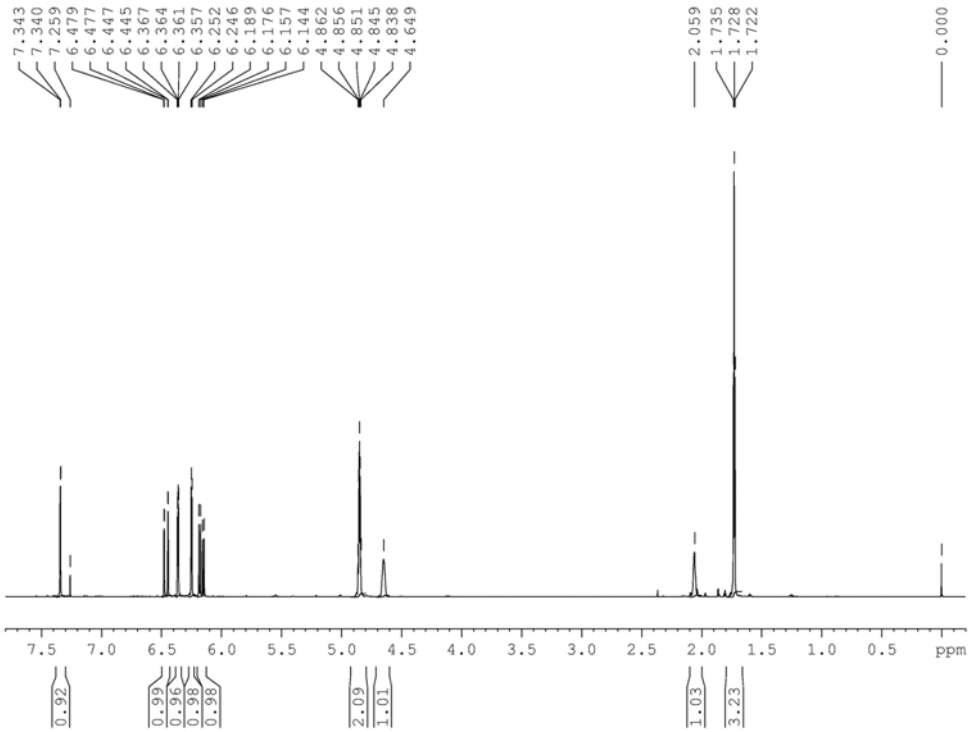
^{1}H NMR ($CDCl_3$, 500 MHz) spectrum of (*E*)-4-methyl-1-(4-(trifluoromethyl)phenyl)hexa-1,4,5-trien-3-one (31)



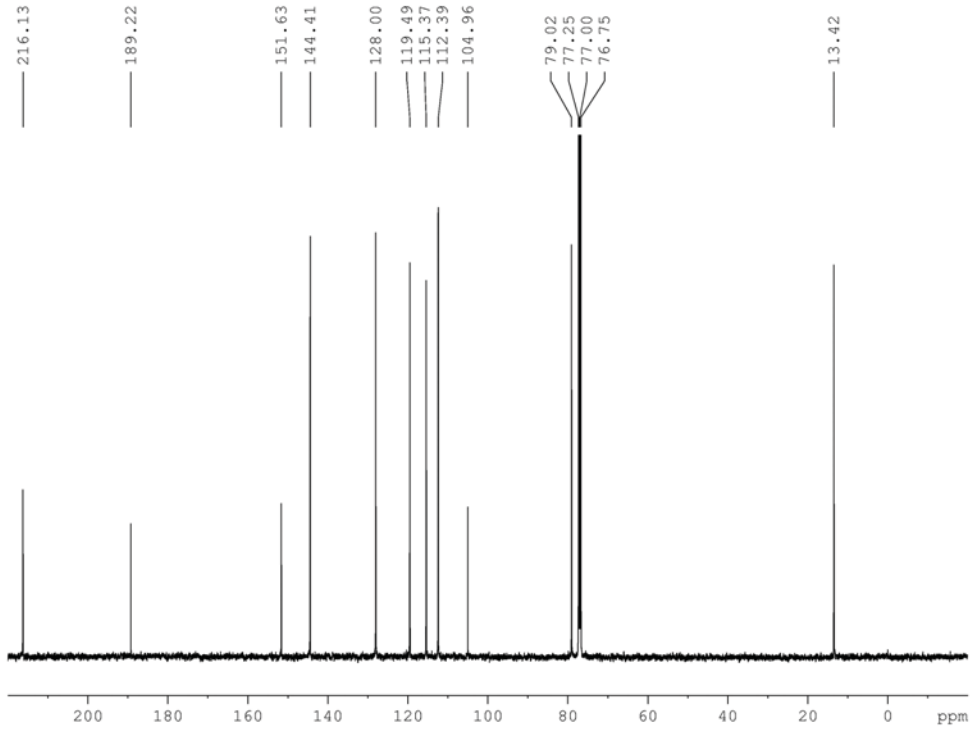
^{13}C NMR ($CDCl_3$, 125 MHz) spectrum of (*E*)-4-methyl-1-(4-(trifluoromethyl)phenyl)hexa-1,4,5-trien-3-one (31)



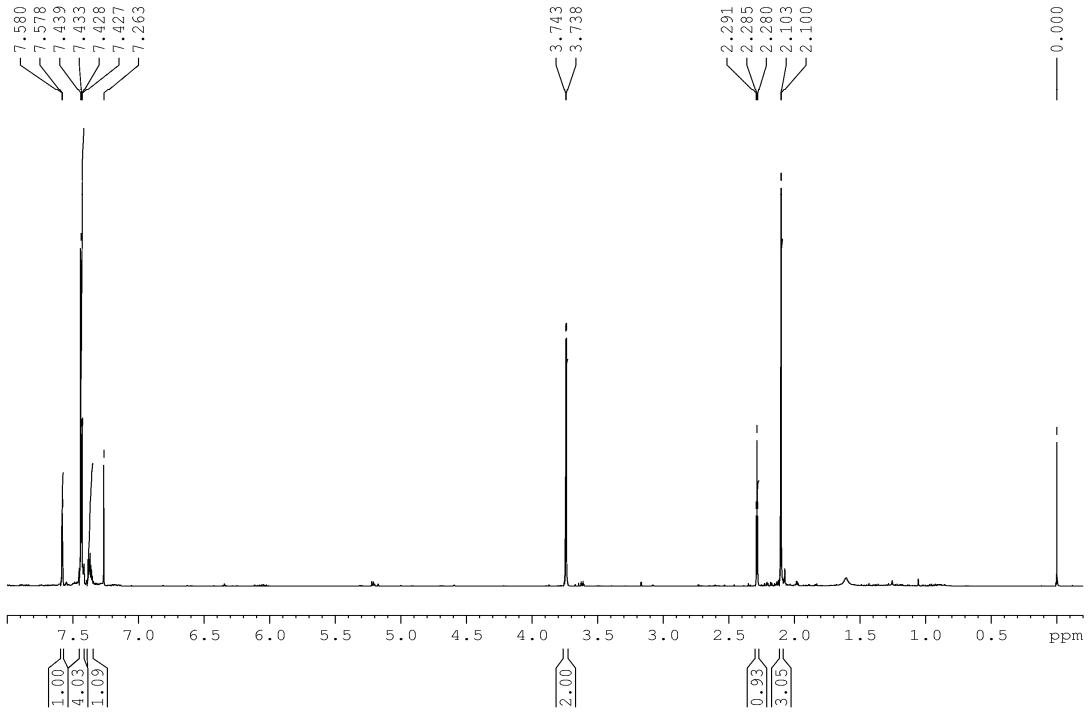
^{1}H NMR ($CDCl_3$, 500 MHz) spectrum of (*E*)-1-(furan-2-yl)-4-methylhexa-1,4,5-trien-3-one (32)



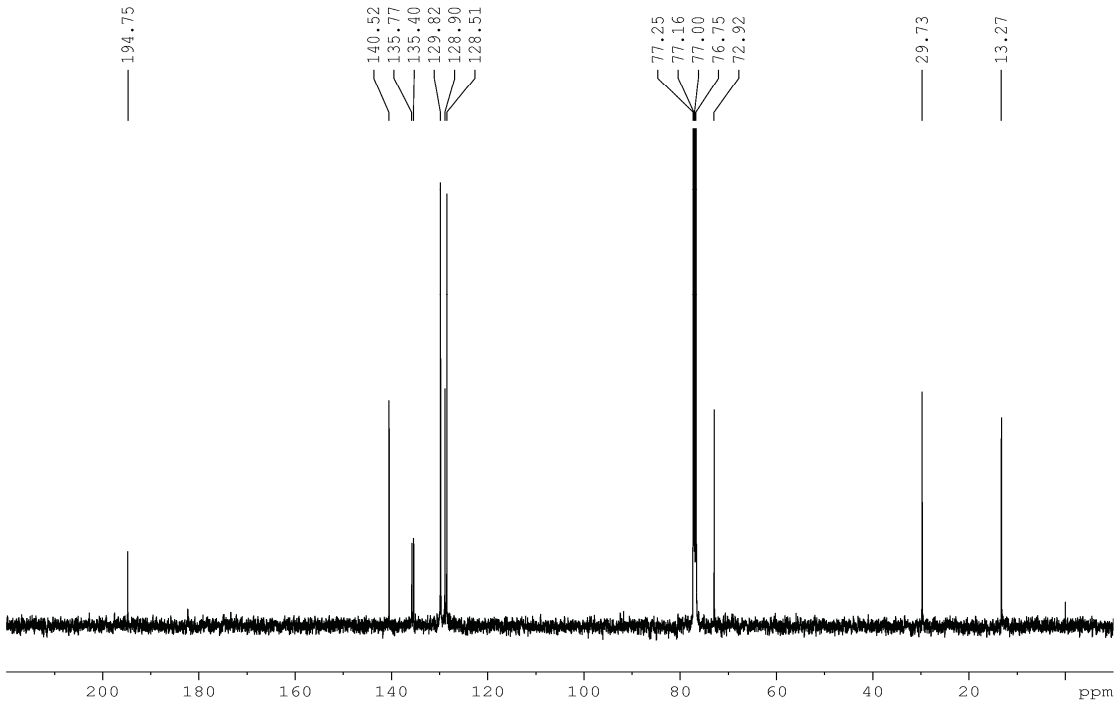
^{13}C NMR ($CDCl_3$, 125 MHz) spectrum of (*E*)-1-(furan-2-yl)-4-methylhexa-1,4,5-trien-3-one (32)



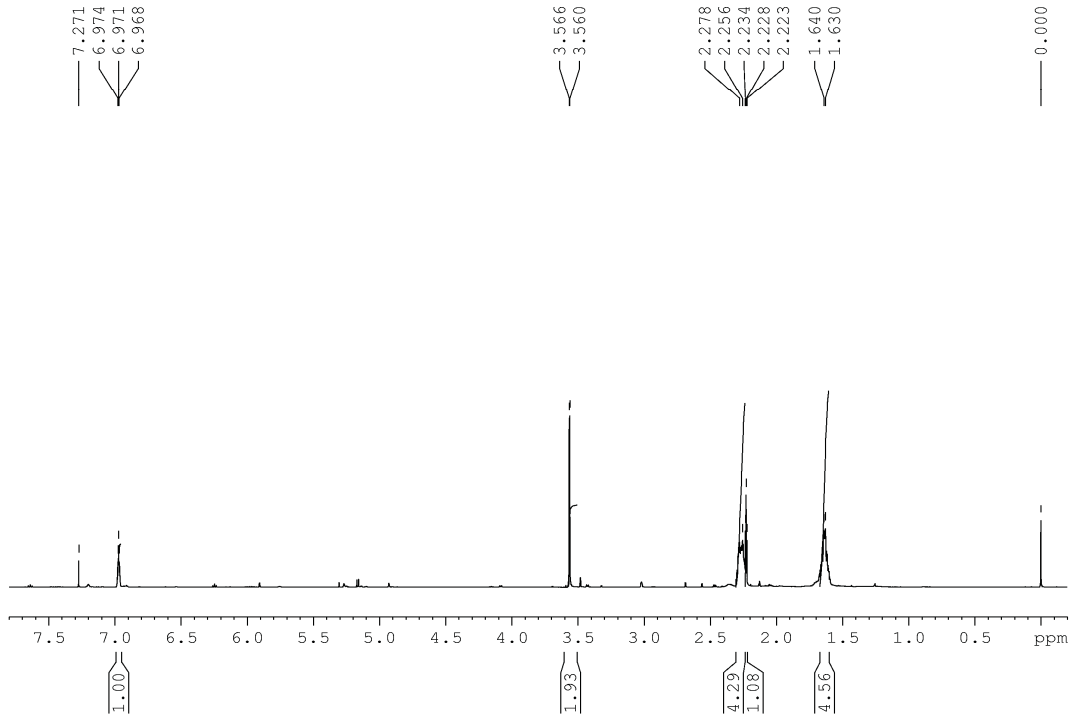
^{1}H NMR (500 MHz, $CDCl_3$) of (*E*)-2-methyl-1-phenylhex-1-en-5-yn-3-one (33)



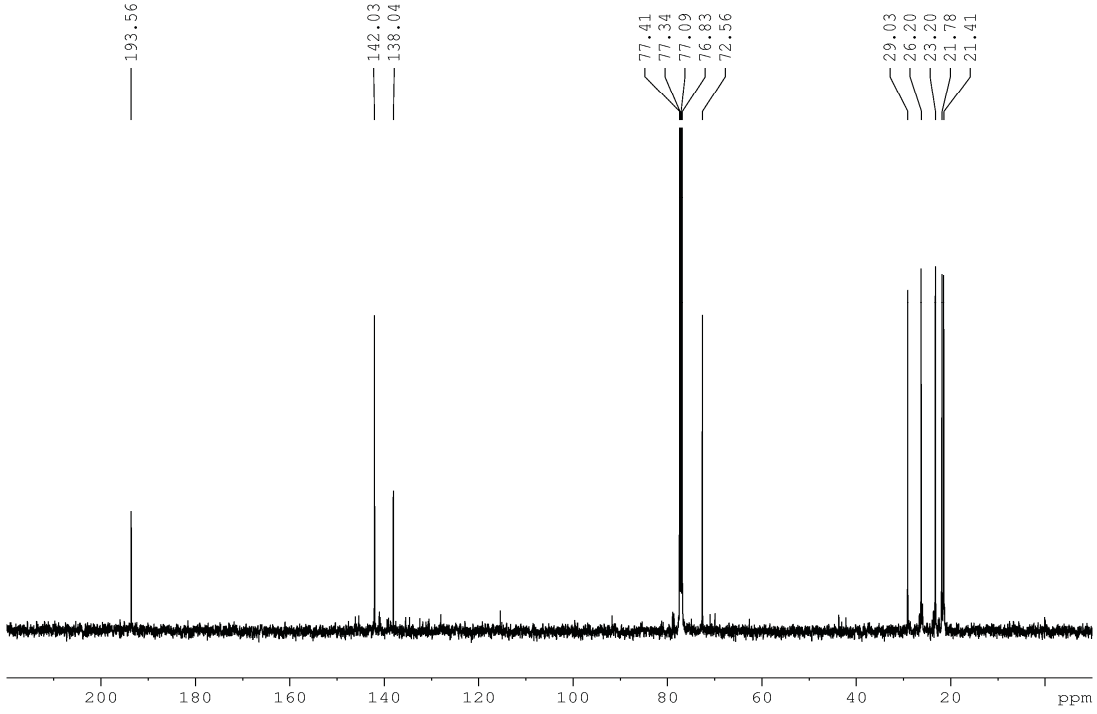
^{13}C NMR (125 MHz, $CDCl_3$) of (*E*)-2-methyl-1-phenylhex-1-en-5-yn-3-one (33)



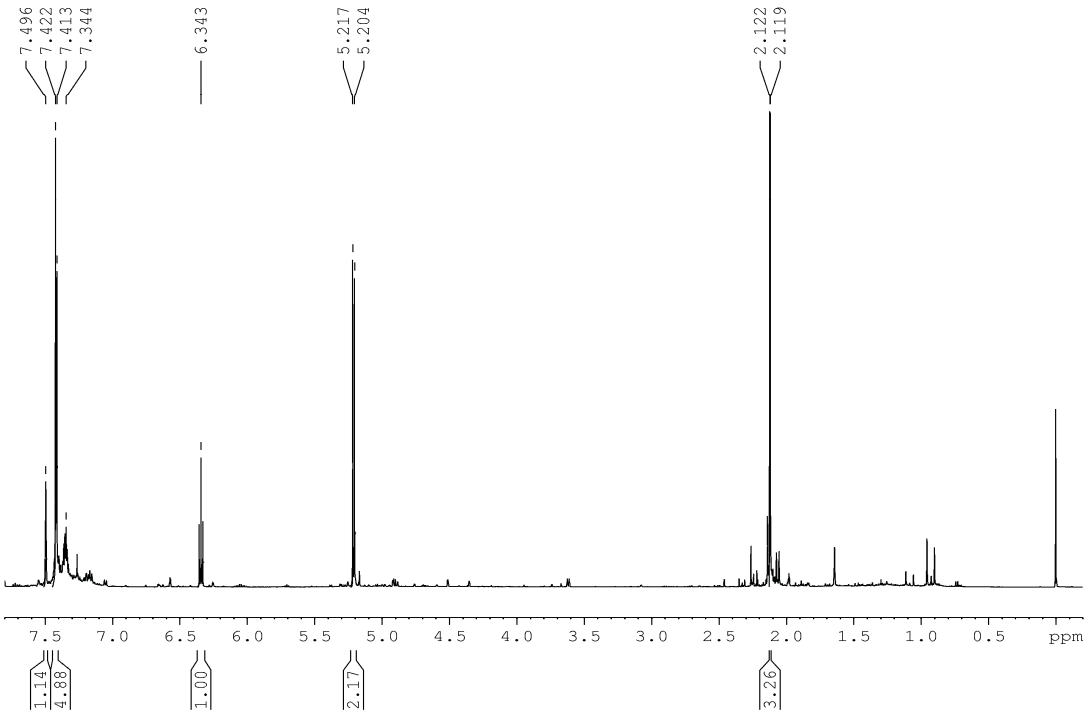
^{1}H NMR (500 MHz, $CDCl_3$) of (*E*)-1-cyclohexenylbut-3-yn-1-one (34)



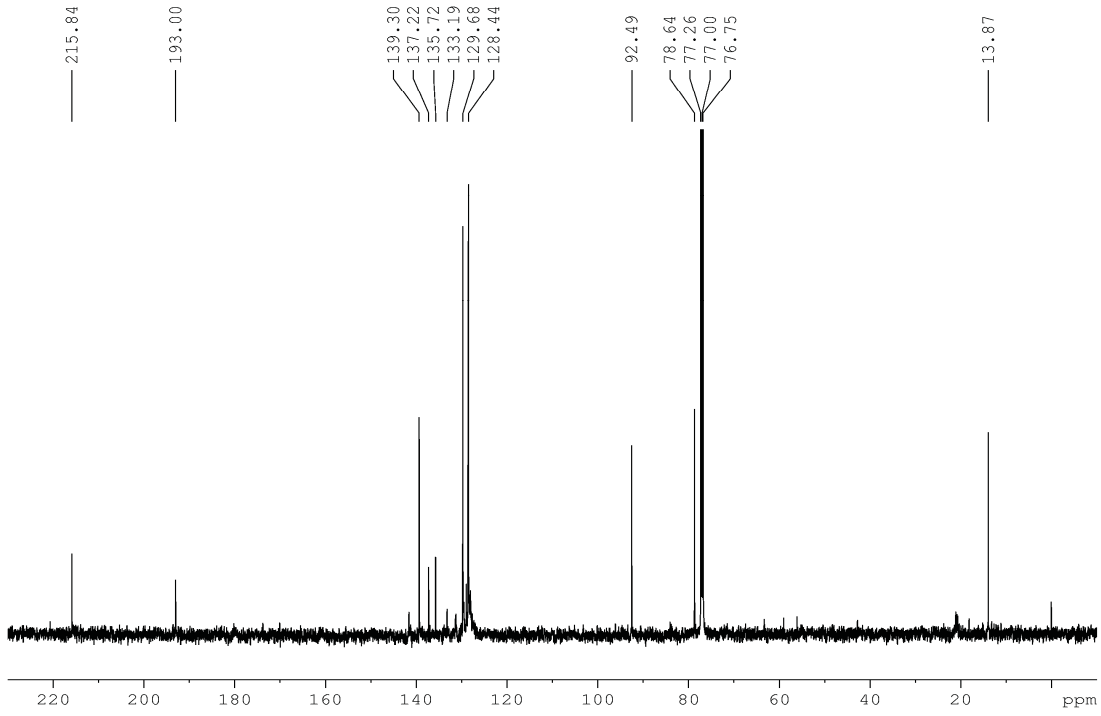
^{13}C NMR (125 MHz, $CDCl_3$) of (*E*)-1-cyclohexenylbut-3-yn-1-one (34)



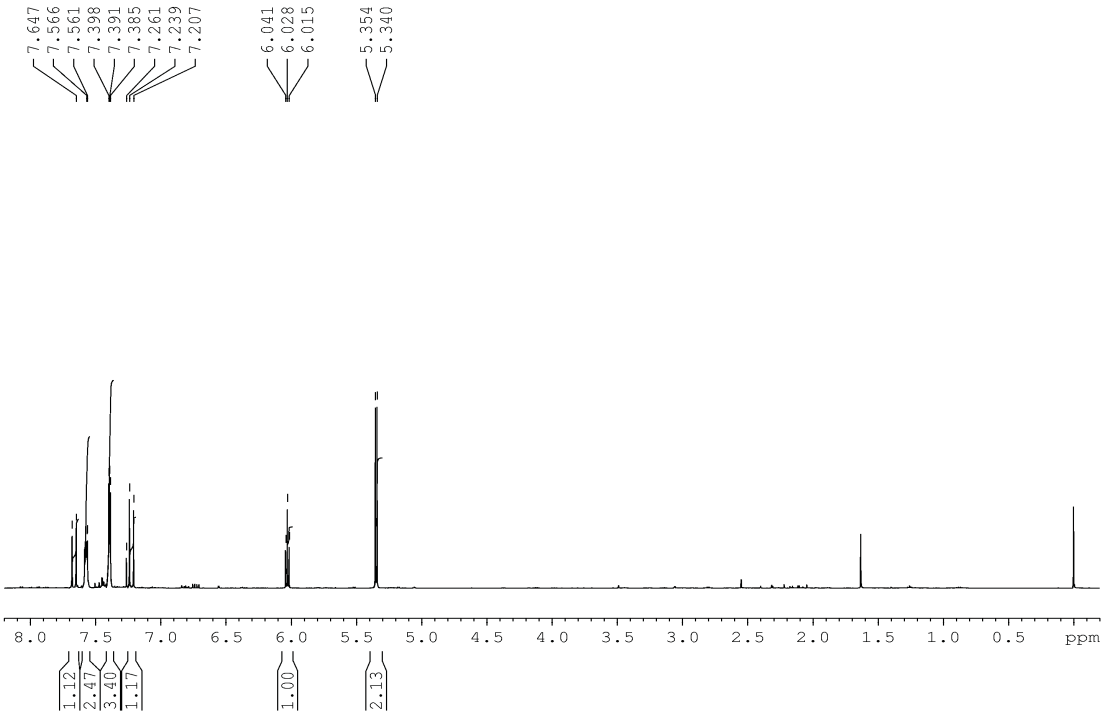
^{1}H NMR (500 MHz, $CDCl_3$) of (*E*)-2-methyl-1-phenylhexa-1,4,5-trien-3-one (35)



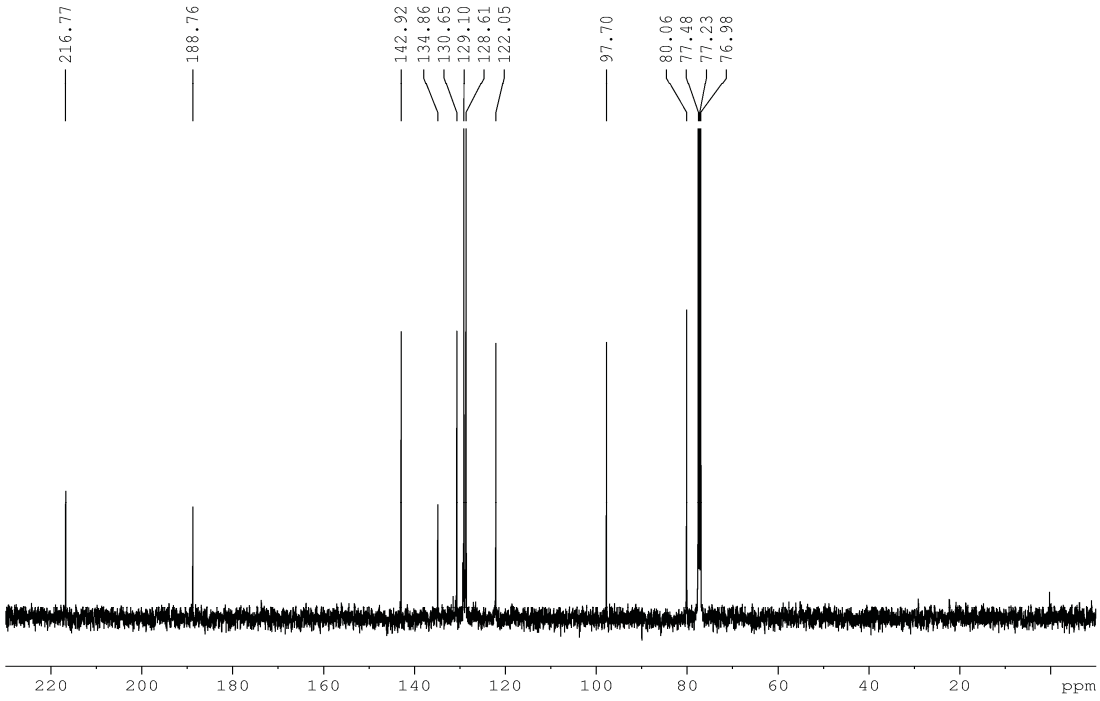
^{13}C NMR (125 MHz, $CDCl_3$) of (*E*)-2-methyl-1-phenylhexa-1,4,5-trien-3-one (35)



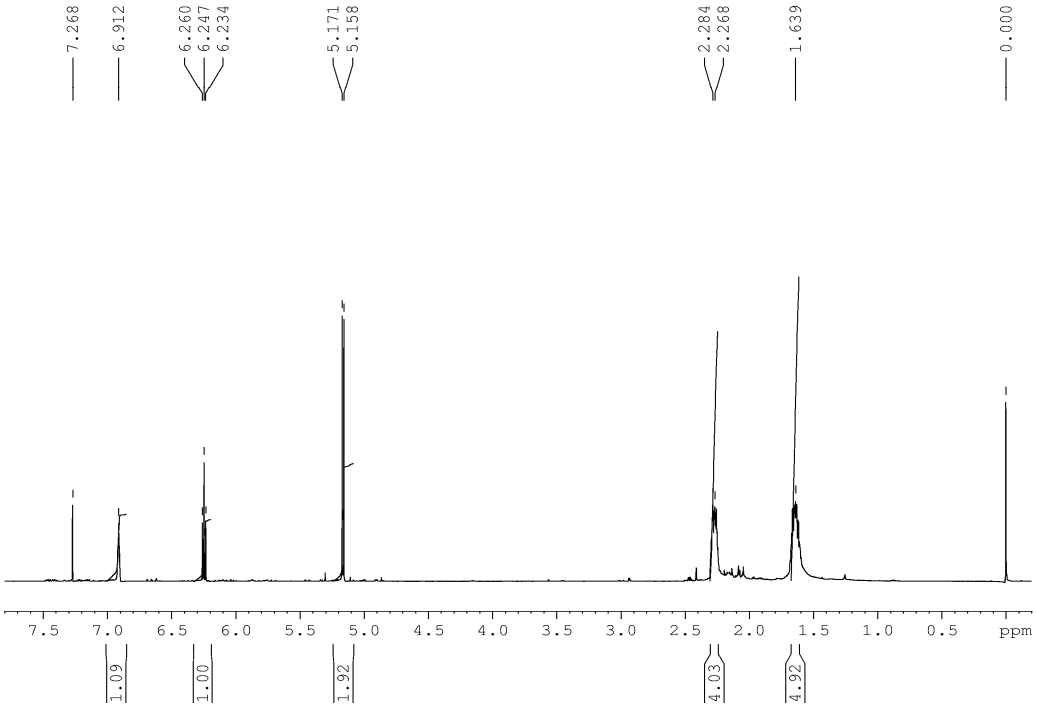
^{1}H NMR (500 MHz, $CDCl_3$) of (*E*)-1-phenylhexa-1,4,5-trien-3-one (36)



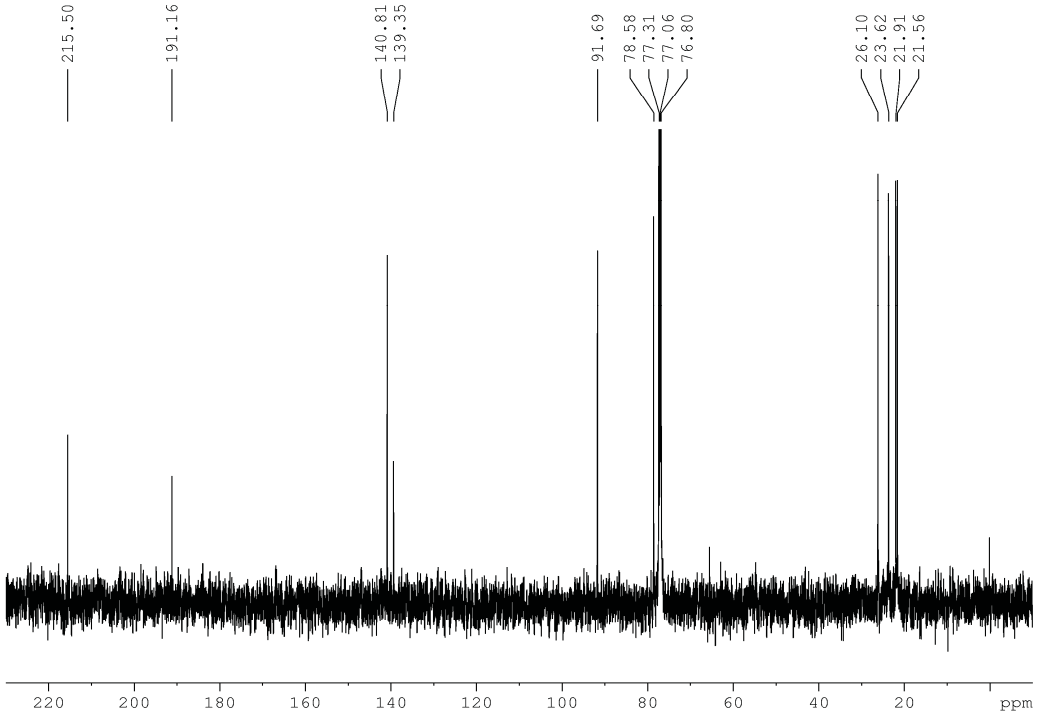
^{13}C NMR (125 MHz, $CDCl_3$) of (*E*)-1-phenylhexa-1,4,5-trien-3-one (36)



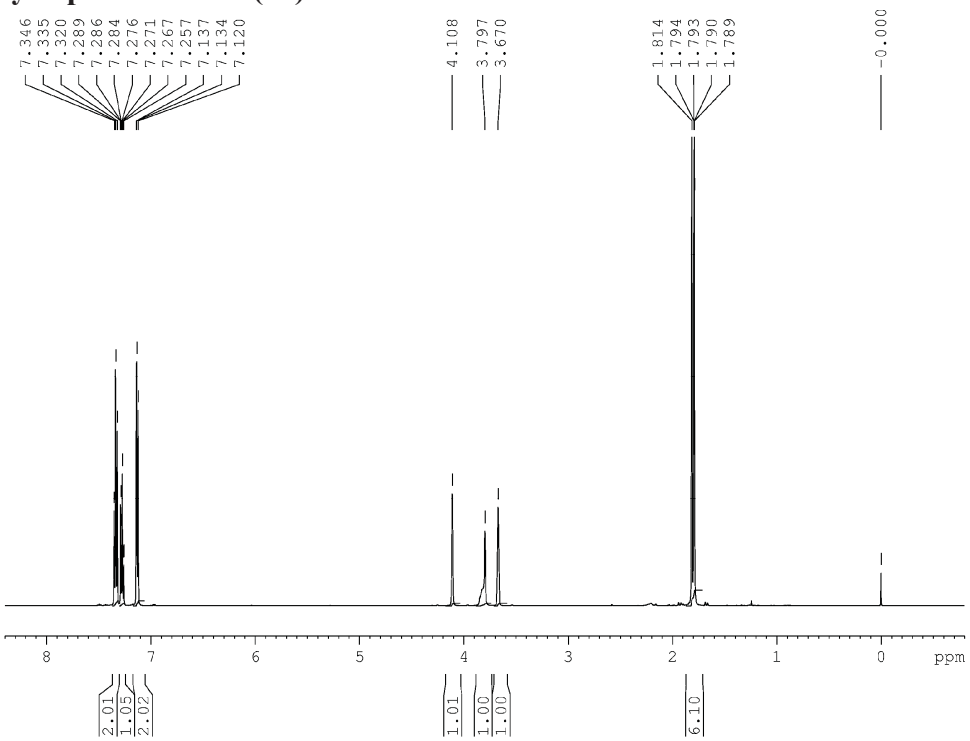
^{1}H NMR (500 MHz, $CDCl_3$) of *(E)*-1-cyclohexenylbuta-2,3-dien-1-one (37)



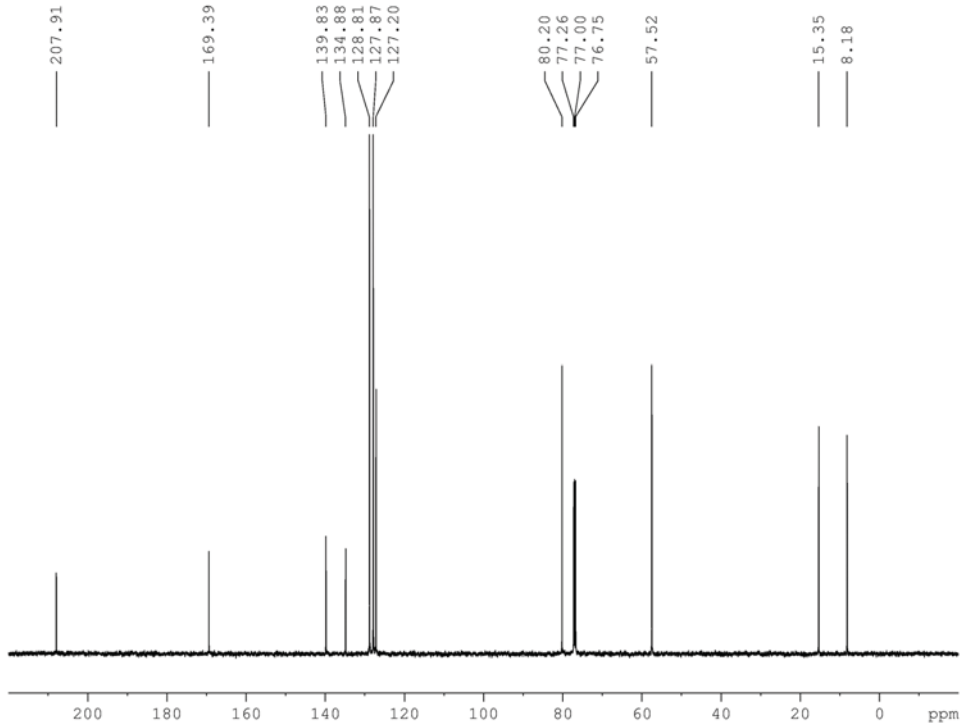
^{13}C NMR (125 MHz, $CDCl_3$) of *(E)*-1-cyclohexenylbuta-2,3-dien-1-one (37)



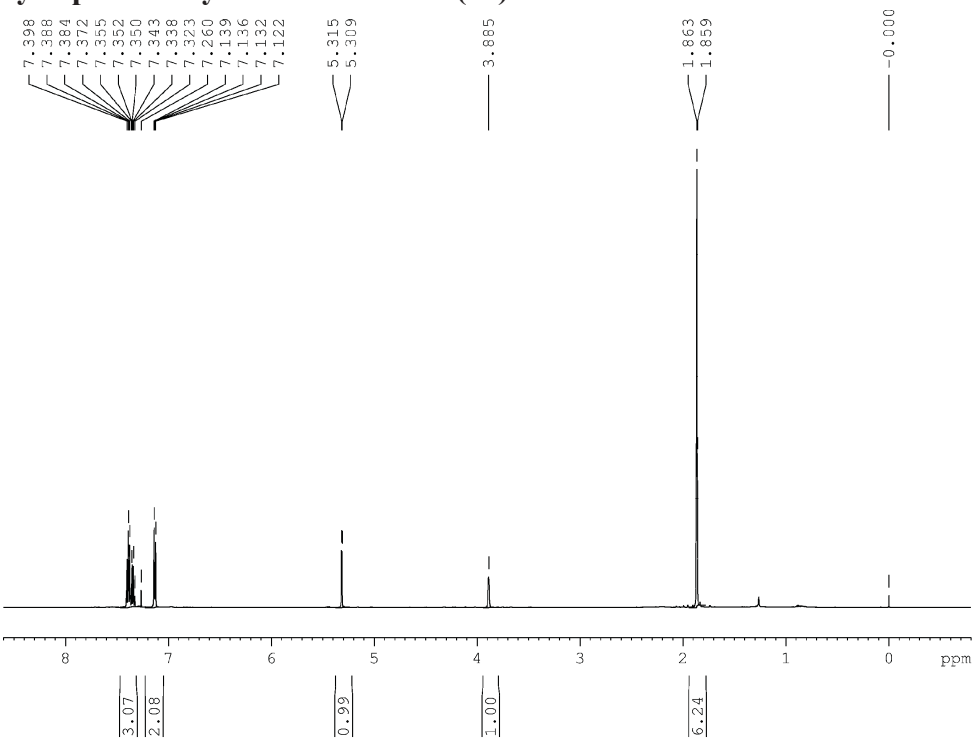
^{1}H NMR ($CDCl_3$, 500 MHz) spectrum of (*trans*)-5-hydroxy-2,3-dimethyl-4-phenylcyclopent-2-enone (38)



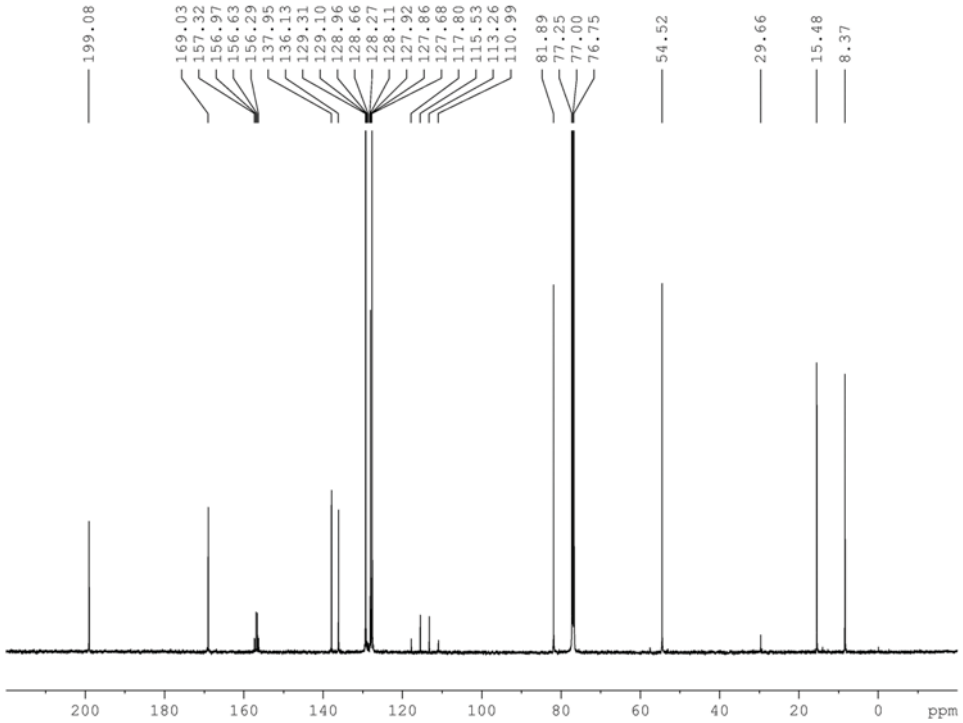
^{13}C NMR ($CDCl_3$, 125 MHz) spectrum of (*trans*)-5-hydroxy-2,3-dimethyl-4-phenylcyclopent-2-enone (38)



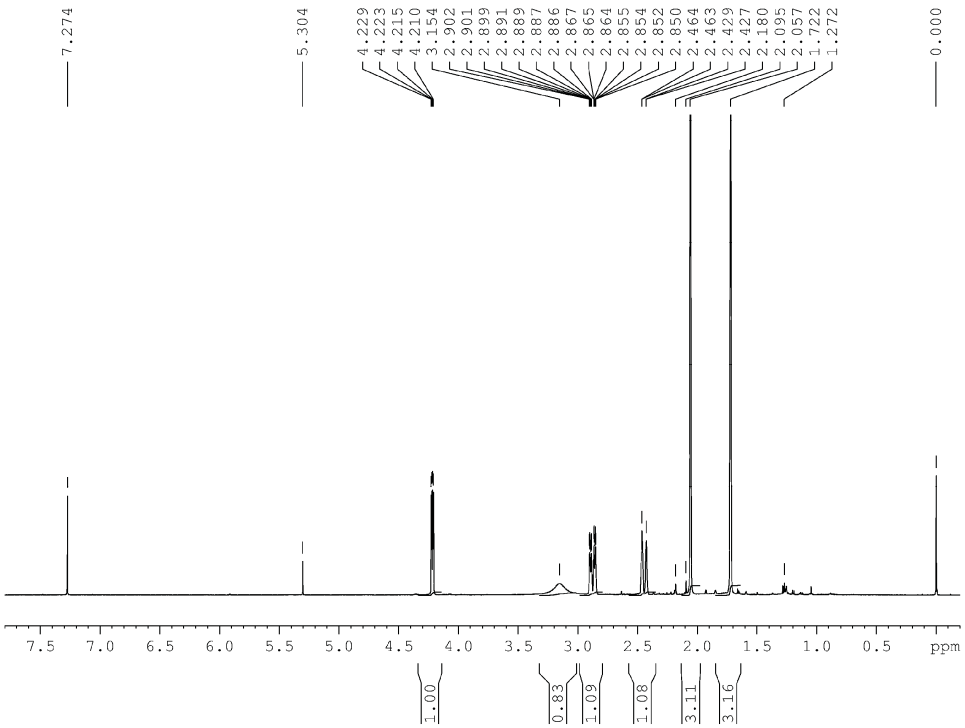
^{1}H NMR ($CDCl_3$, 500 MHz) spectrum of (*trans*)-3,4-dimethyl-2-oxo-5-phenylcyclopent-3-enyl trifluoroacetate (39)



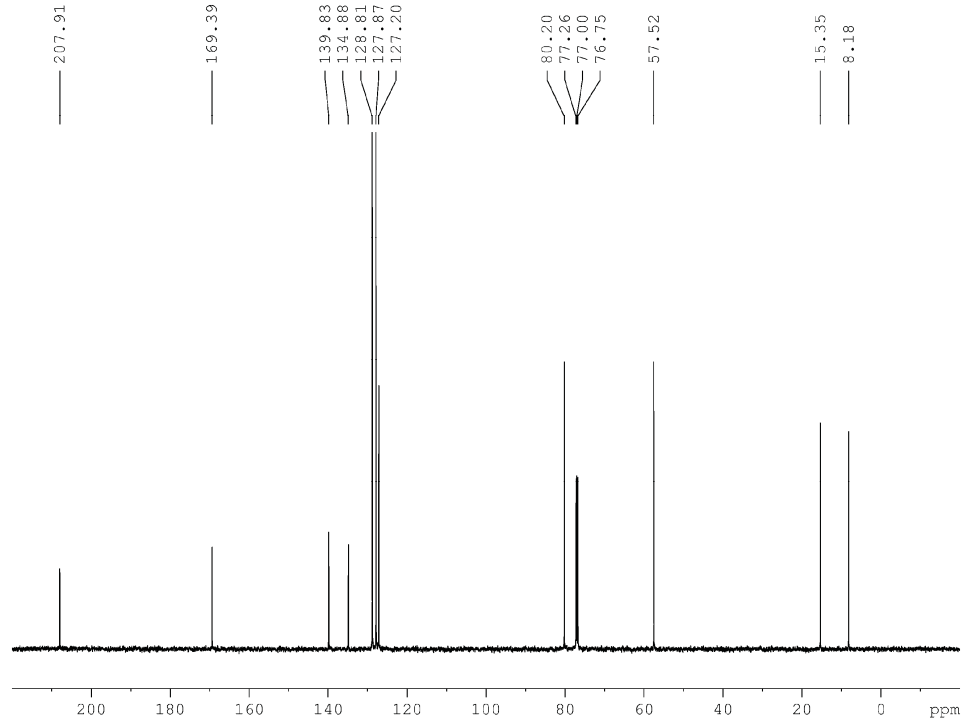
^{13}C NMR ($CDCl_3$, 125 MHz) spectrum of (*trans*)-3,4-dimethyl-2-oxo-5-phenylcyclopent-3-enyl trifluoroacetate (39)



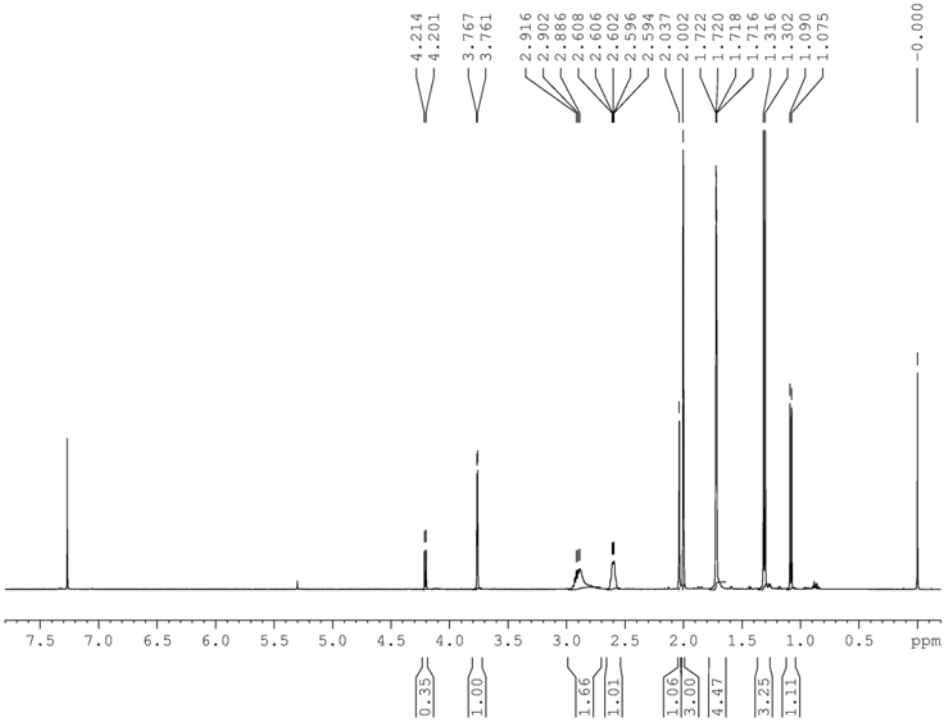
^{1}H NMR ($CDCl_3$, 500 MHz) spectrum of 5-hydroxy-2,3-dimethylcyclopent-2-enone (40)



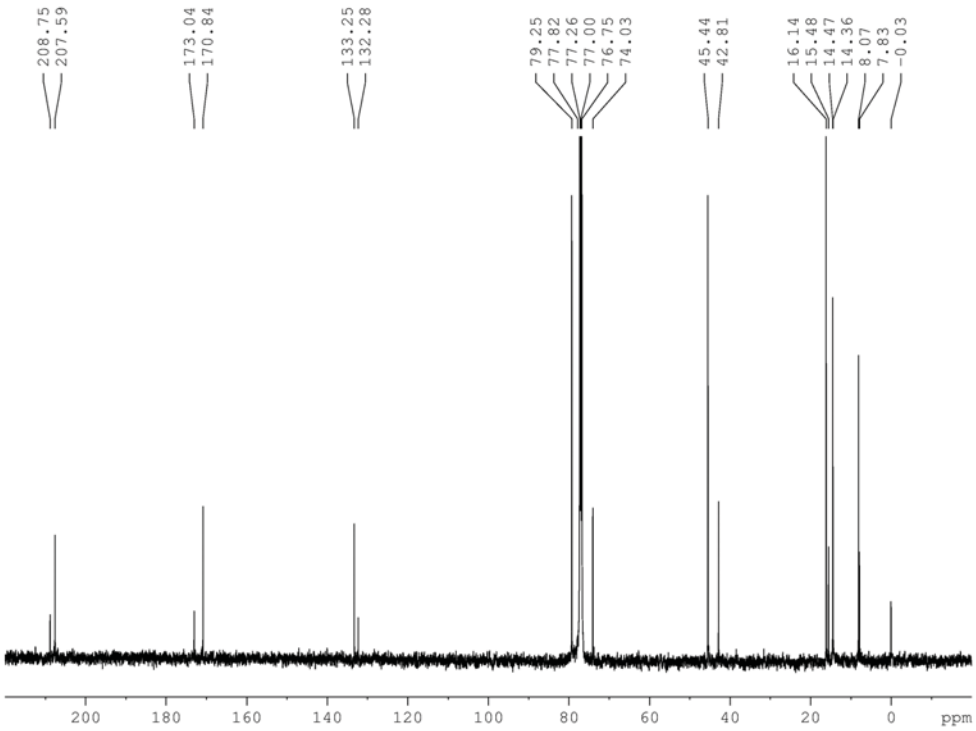
^{13}C NMR ($CDCl_3$, 125 MHz) spectrum of 5-hydroxy-2,3-dimethylcyclopent-2-enone (40)



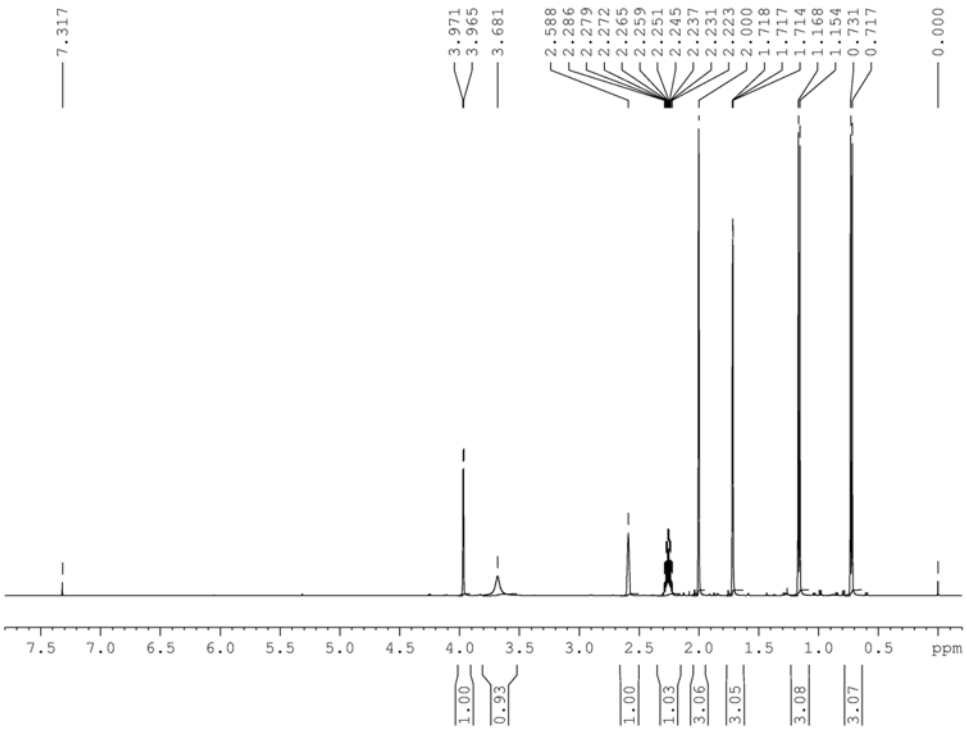
^{1}H NMR ($CDCl_3$, 500 MHz) spectrum of (*trans*)- (41a) and (*cis*)-5-hydroxy-2,3,4-trimethylcyclopent-2-enone (41b)



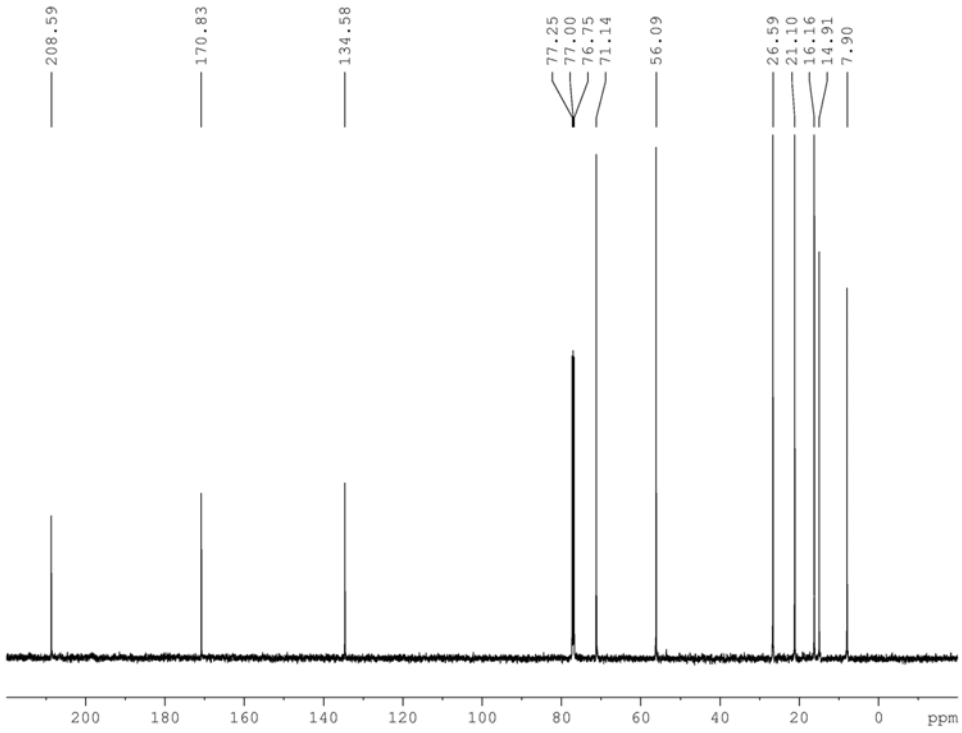
^{13}C NMR ($CDCl_3$, 125 MHz) spectrum of (*trans*)- (41a) and (*cis*)-5-hydroxy-2,3,4-trimethylcyclopent-2-enone (41b)



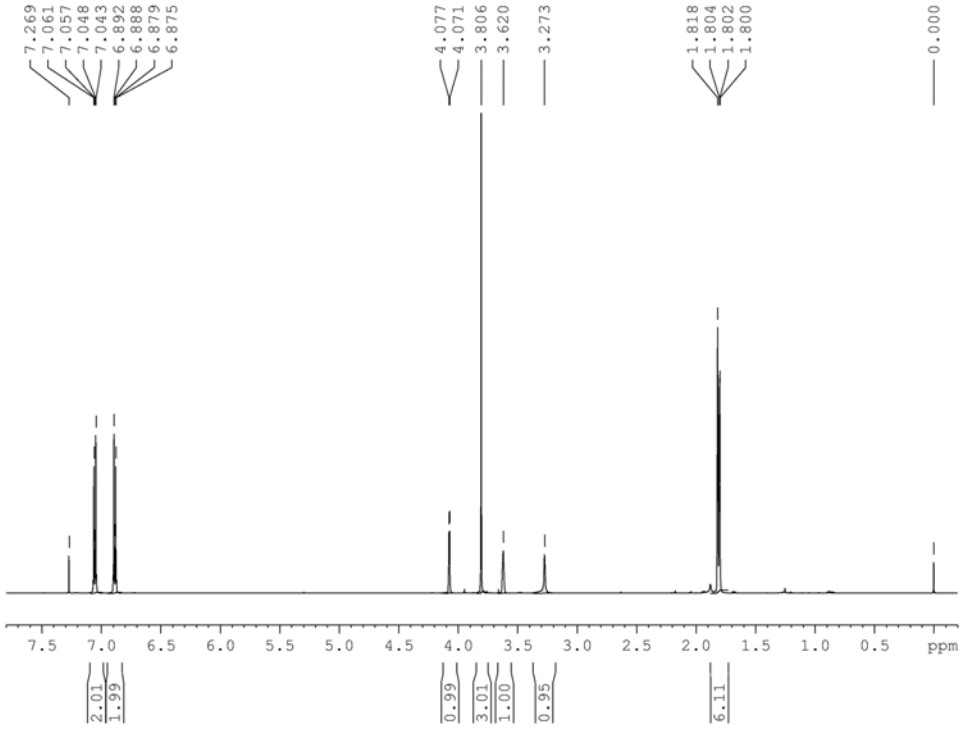
^{1}H NMR ($CDCl_3$, 500 MHz) spectrum of (*trans*)-5-hydroxy-4-isopropyl-2,3-dimethylcyclopent-2-enone (42)



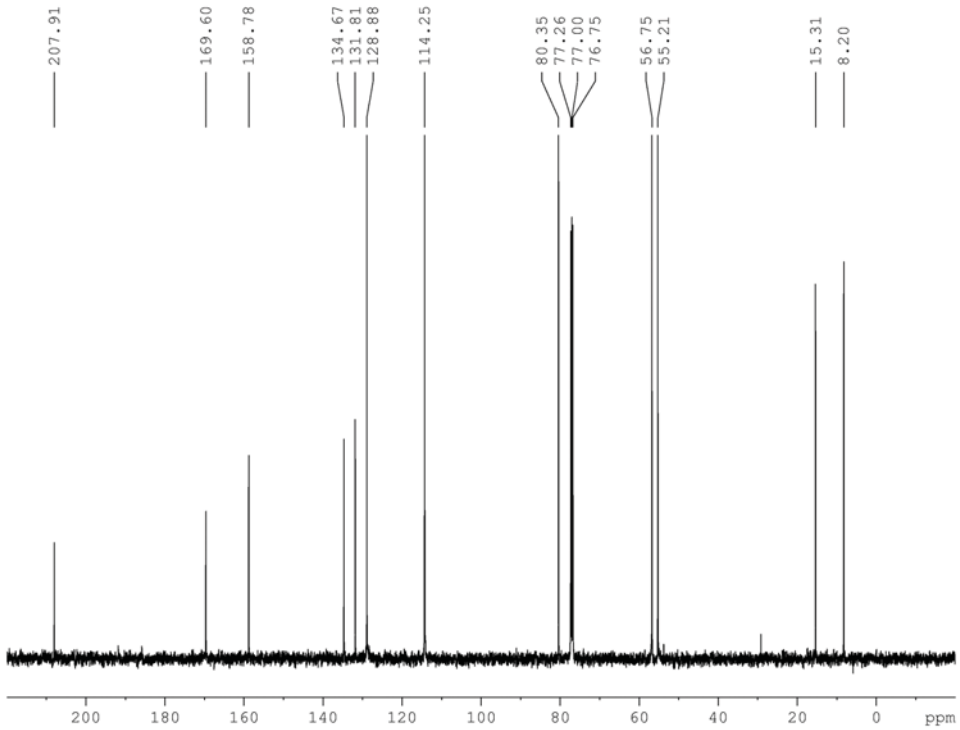
^{13}C NMR ($CDCl_3$, 125 MHz) spectrum of (*trans*)-5-hydroxy-4-isopropyl-2,3-dimethylcyclopent-2-enone (42)



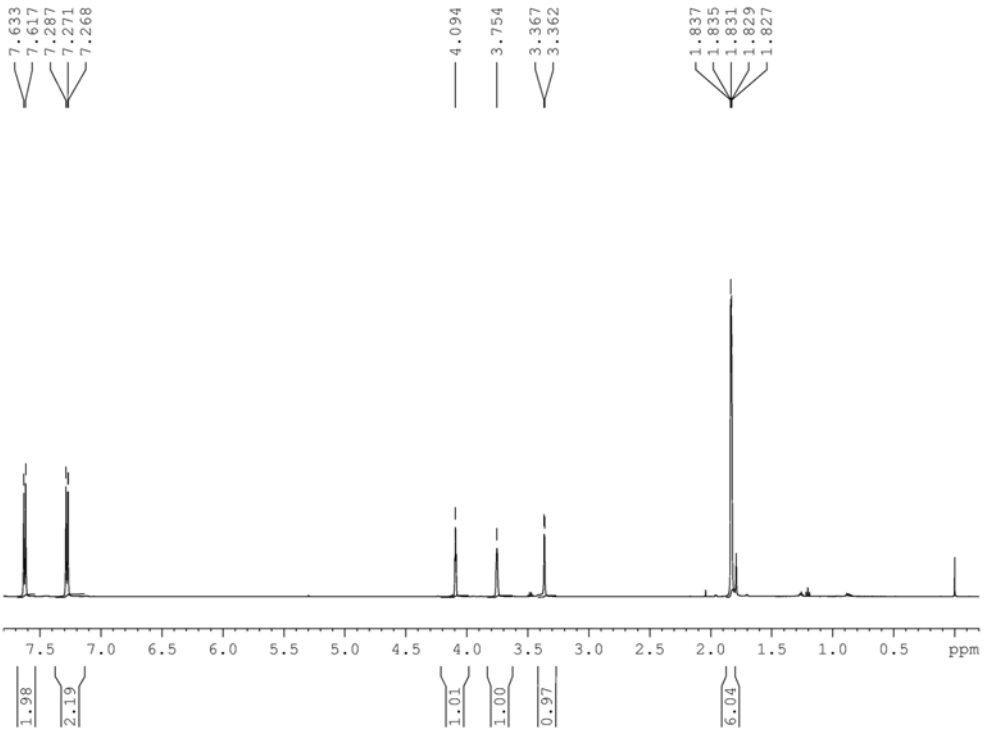
^{1}H NMR ($CDCl_3$, 500 MHz) spectrum of (*trans*)-5-hydroxy-4-(4-methoxyphenyl)-2,3-dimethylcyclopent-2-enone (43)



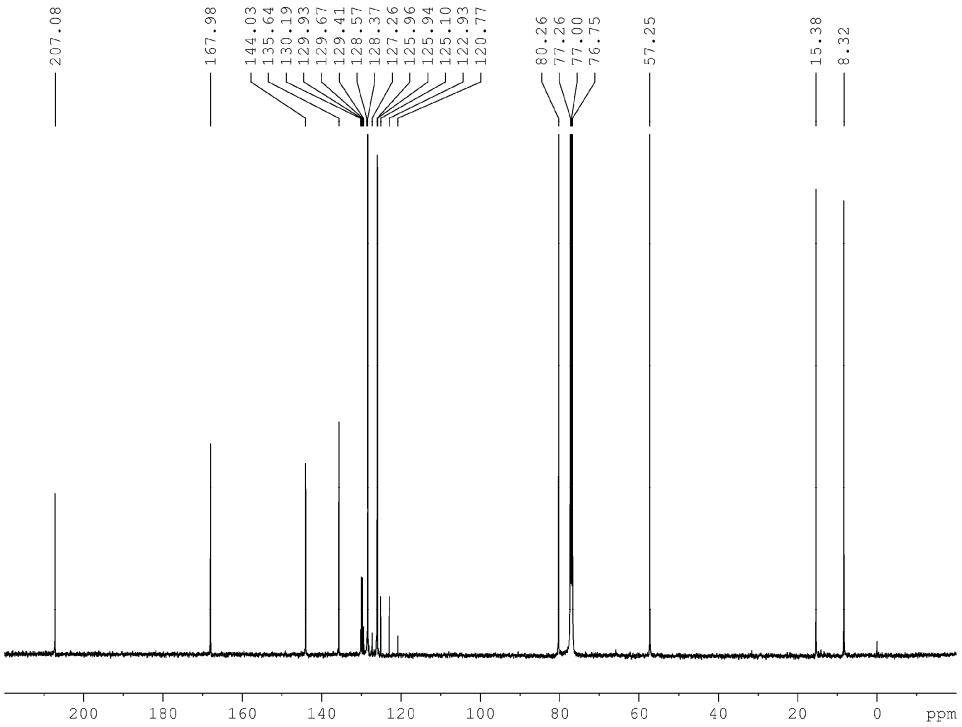
^{13}C NMR ($CDCl_3$, 125 MHz) spectrum of (*trans*)-5-hydroxy-4-(4-methoxyphenyl)-2,3-dimethylcyclopent-2-enone (43)



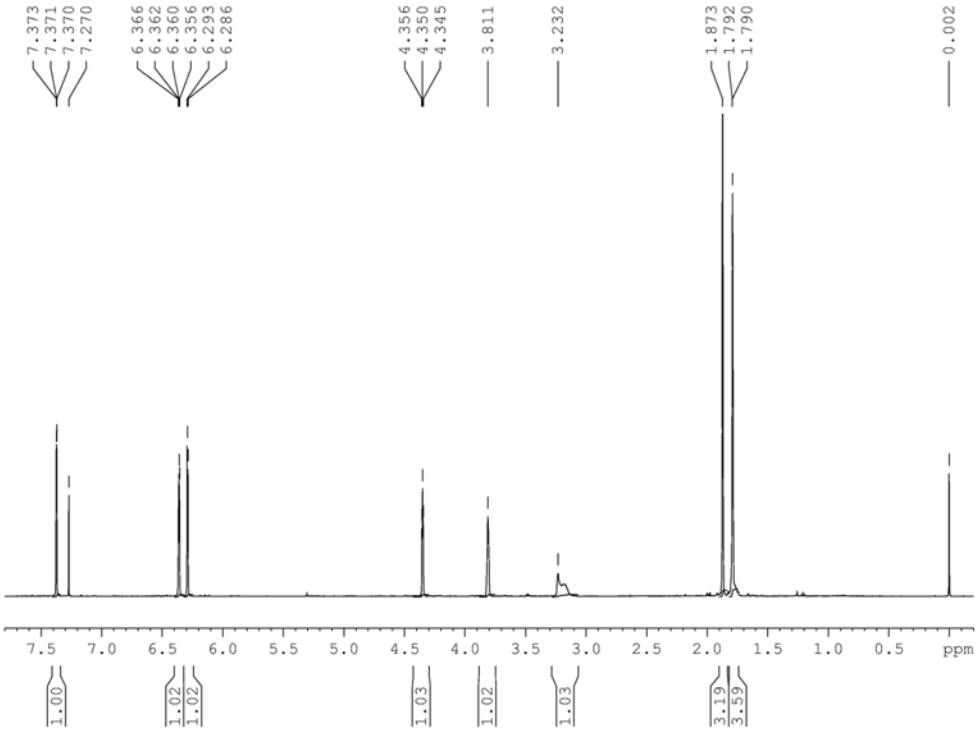
^{1}H NMR ($CDCl_3$, 500 MHz) spectrum of (*trans*)-5-hydroxy-2,3-dimethyl-4-(4-(trifluoromethyl)-phenyl)cyclopent-2-enone (44)



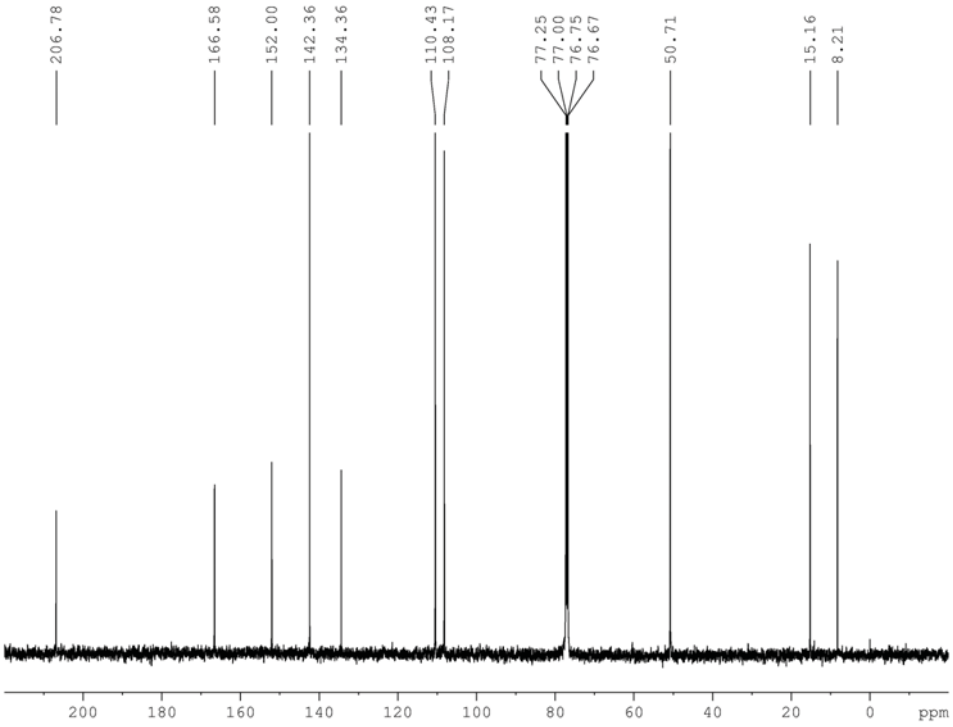
^{13}C NMR ($CDCl_3$, 125 MHz) spectrum of (*trans*)-5-hydroxy-2,3-dimethyl-4-(4-(trifluoromethyl)-phenyl)cyclopent-2-enone (44)



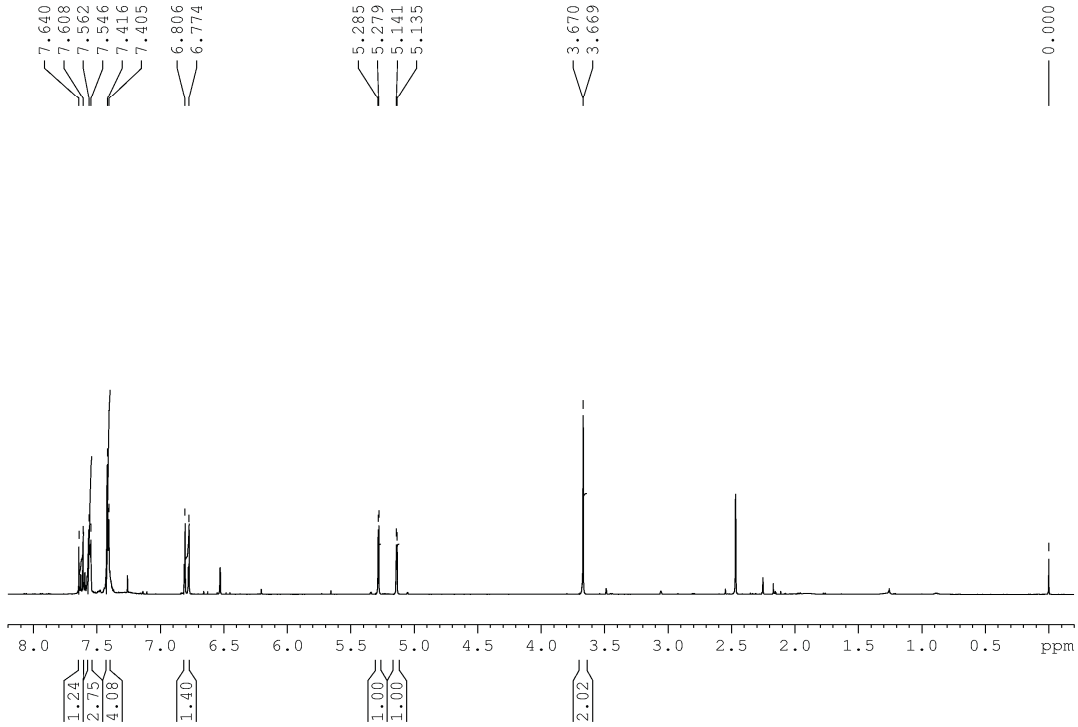
^{1}H NMR ($CDCl_3$, 500 MHz) spectrum of (*trans*)-4-(furan-2-yl)-5-hydroxy-2,3-dimethylcyclopent-2-enone (45)



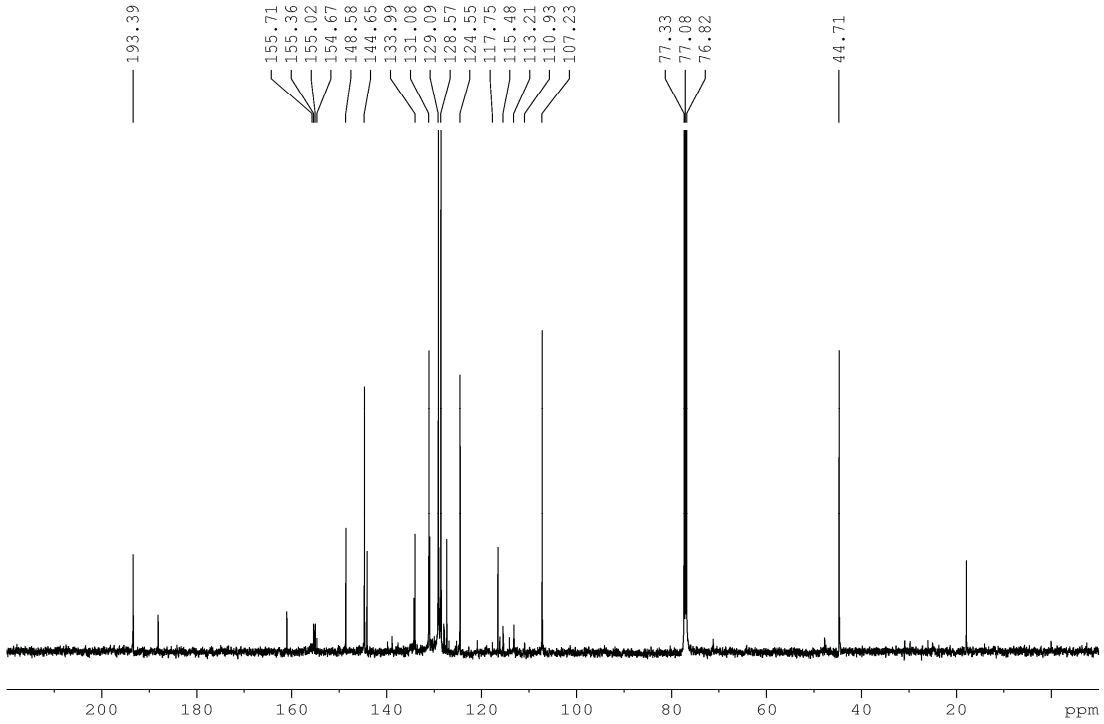
^{13}C NMR ($CDCl_3$, 125 MHz) spectrum of (*trans*)-4-(furan-2-yl)-5-hydroxy-2,3-dimethylcyclopent-2-enone (45)



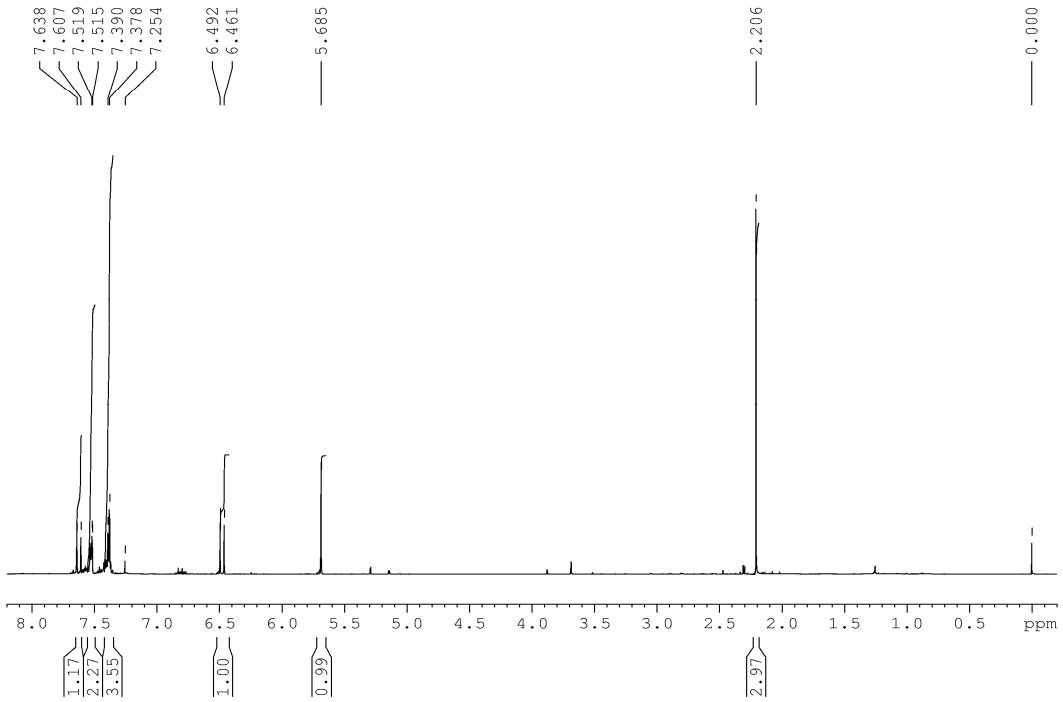
^{1}H NMR (500 MHz, $CDCl_3$) of (*E*)-4-oxo-6-phenylhexa-1,5-dien-2-yl 2,2,2-trifluoroacetate (46)



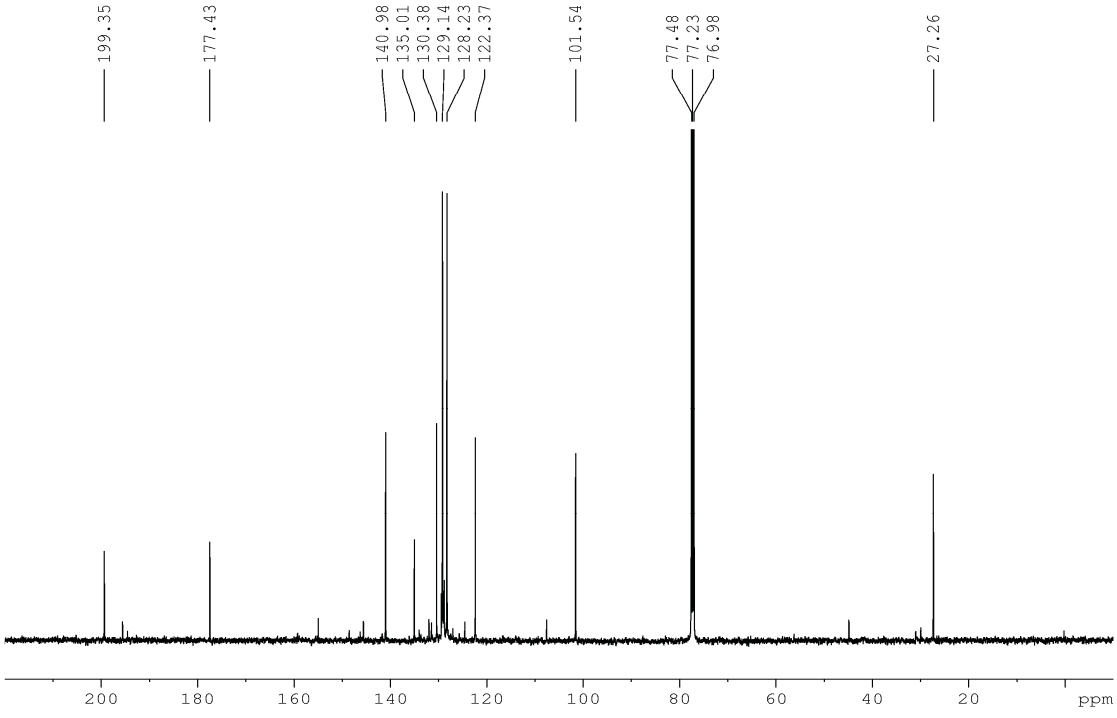
^{13}C NMR (125 MHz, $CDCl_3$) of (*E*)-4-oxo-6-phenylhexa-1,5-dien-2-yl 2,2,2-trifluoroacetate (46)



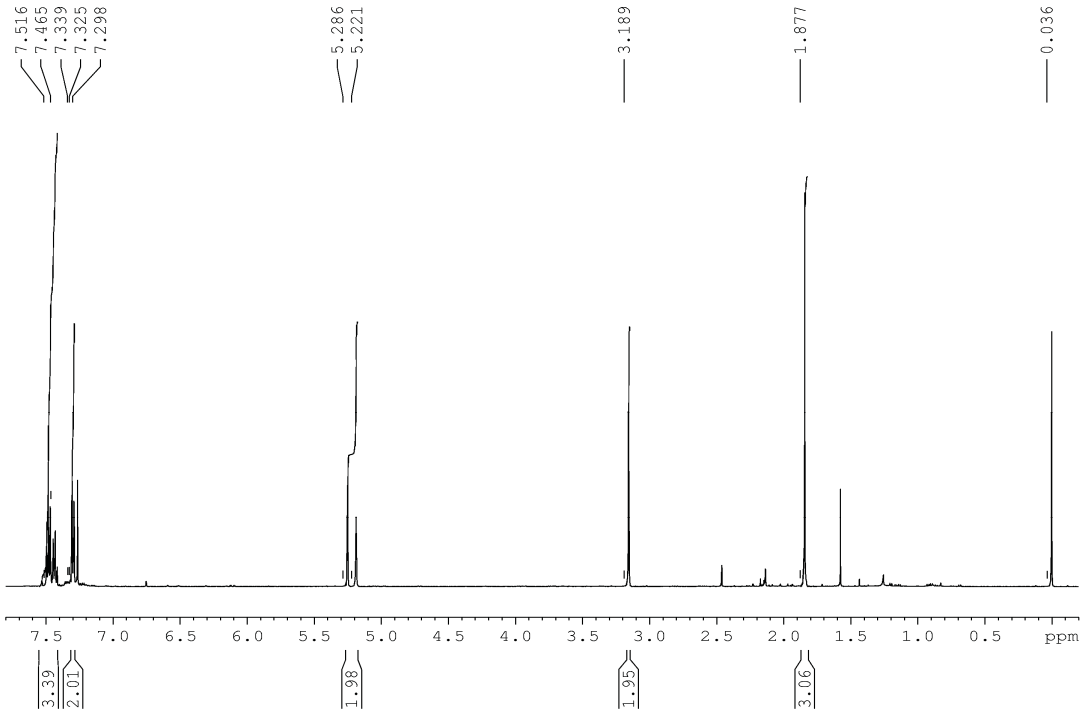
^{1}H NMR (500 MHz, $CDCl_3$) of (3*Z*, 5*E*)-4-hydroxy-6-phenylhexa-3,5-dien-2-one (46a)



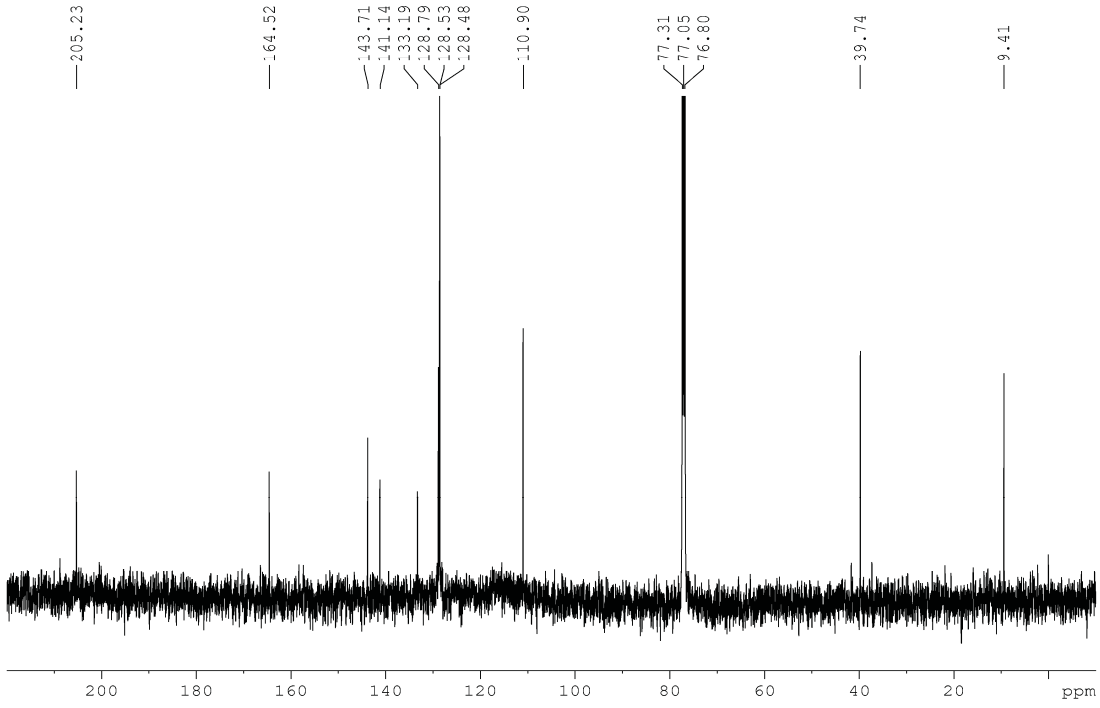
^{13}C NMR (125 MHz, $CDCl_3$) of (3*Z*, 5*E*)-4-hydroxy-6-phenylhexa-3,5-dien-2-one (46a)



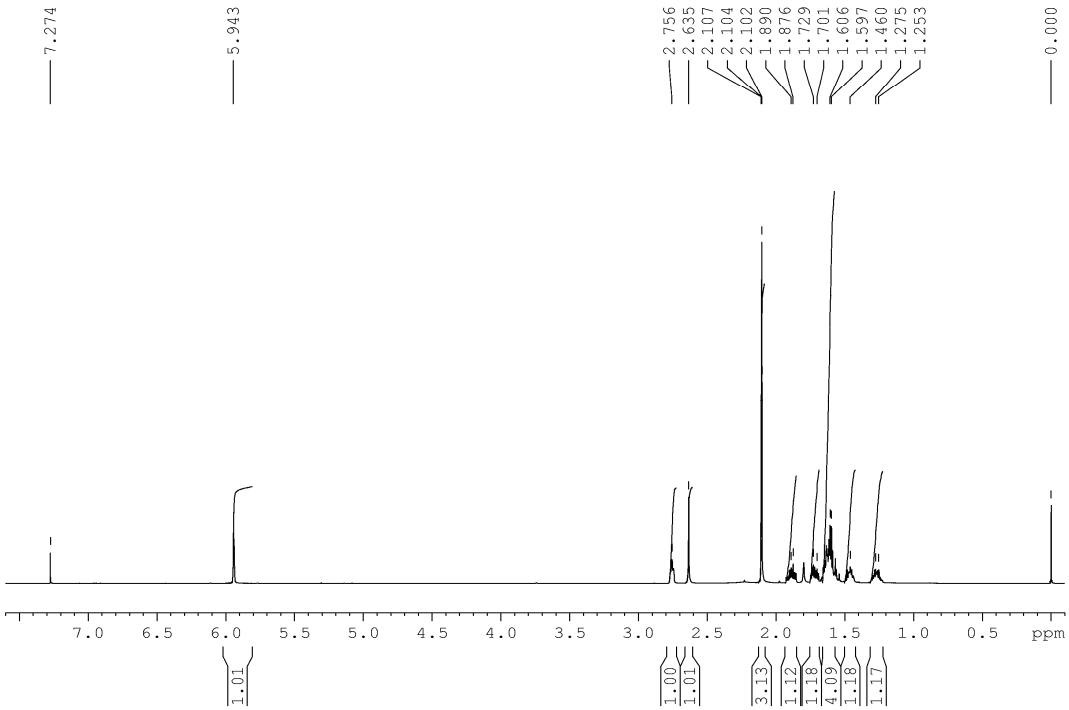
^{1}H NMR (500 MHz, $CDCl_3$) of 2-methyl-4-methylene-3-phenylcyclopent-2-enone (47)



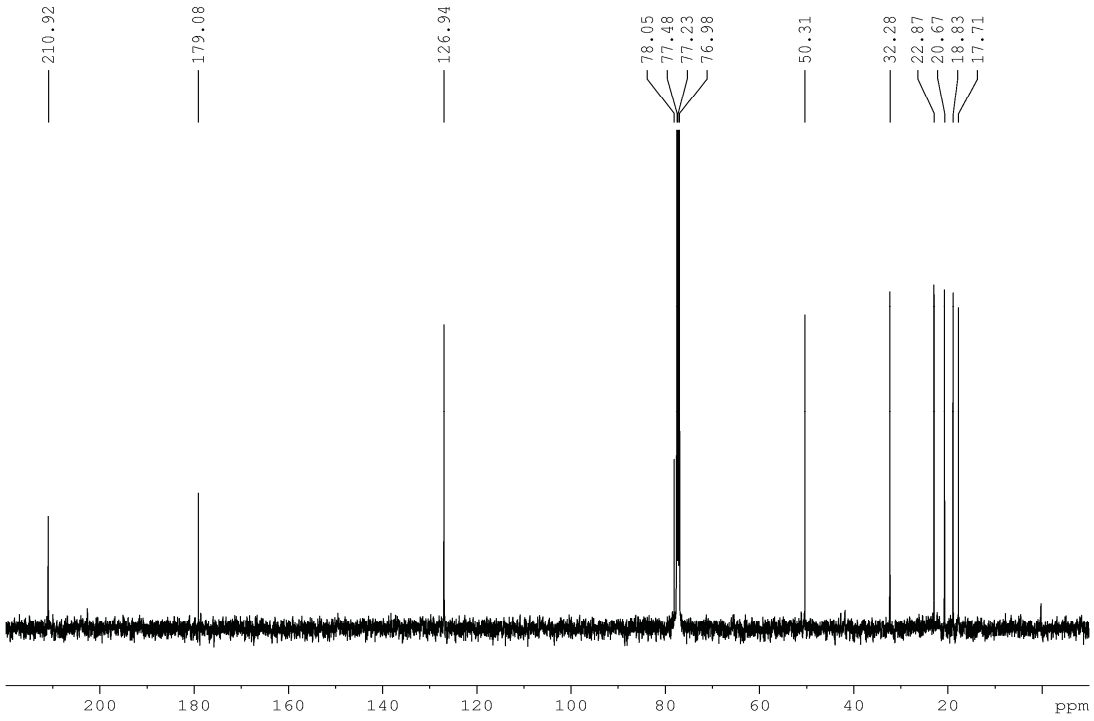
^{13}C NMR (125 MHz, $CDCl_3$) of 2-methyl-4-methylene-3-phenylcyclopent-2-enone (47)



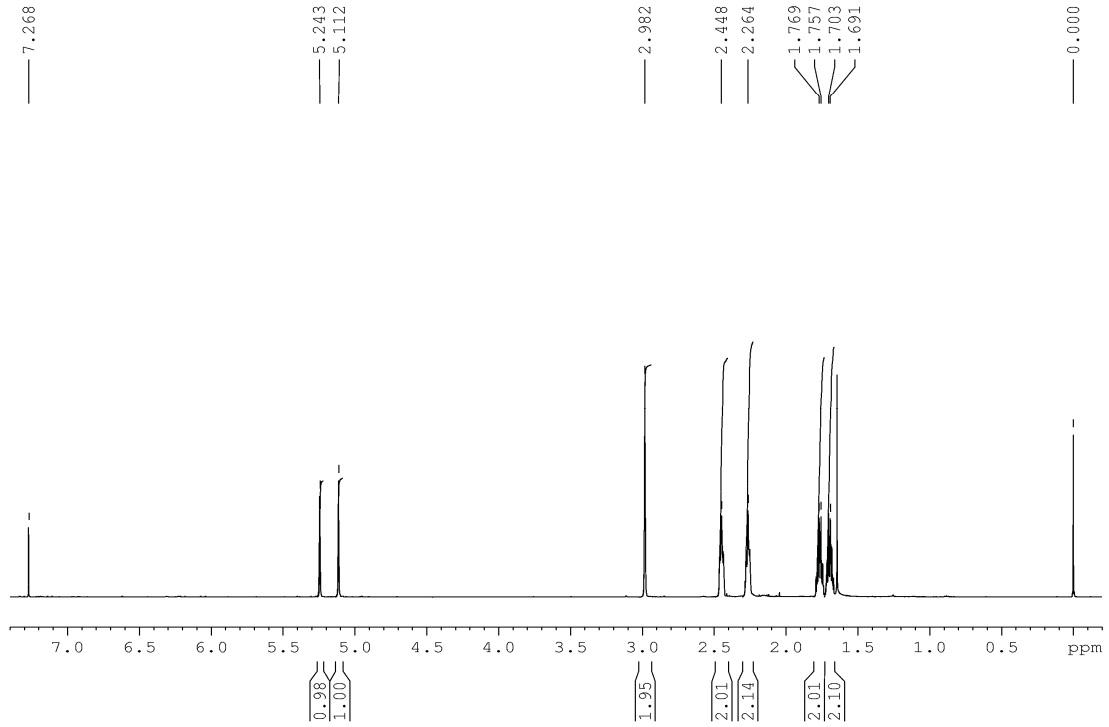
^{1}H NMR (500 MHz, $CDCl_3$) of (3a*R,7a*S**)-7a-hydroxy-3-methyleneoctahydro-1*H*-inden-1-one (48)**



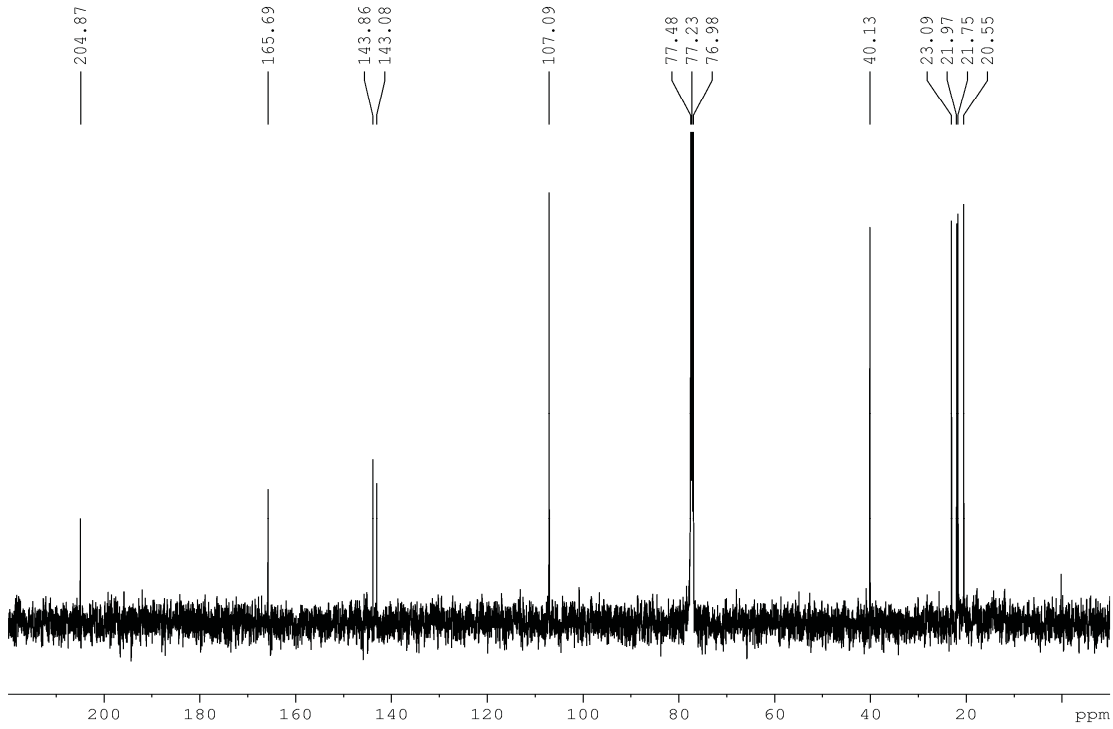
^{13}C NMR (125 MHz, $CDCl_3$) of (3a*R,7a*S**)-7a-hydroxy-3-methyleneoctahydro-1*H*-inden-1-one (48)**



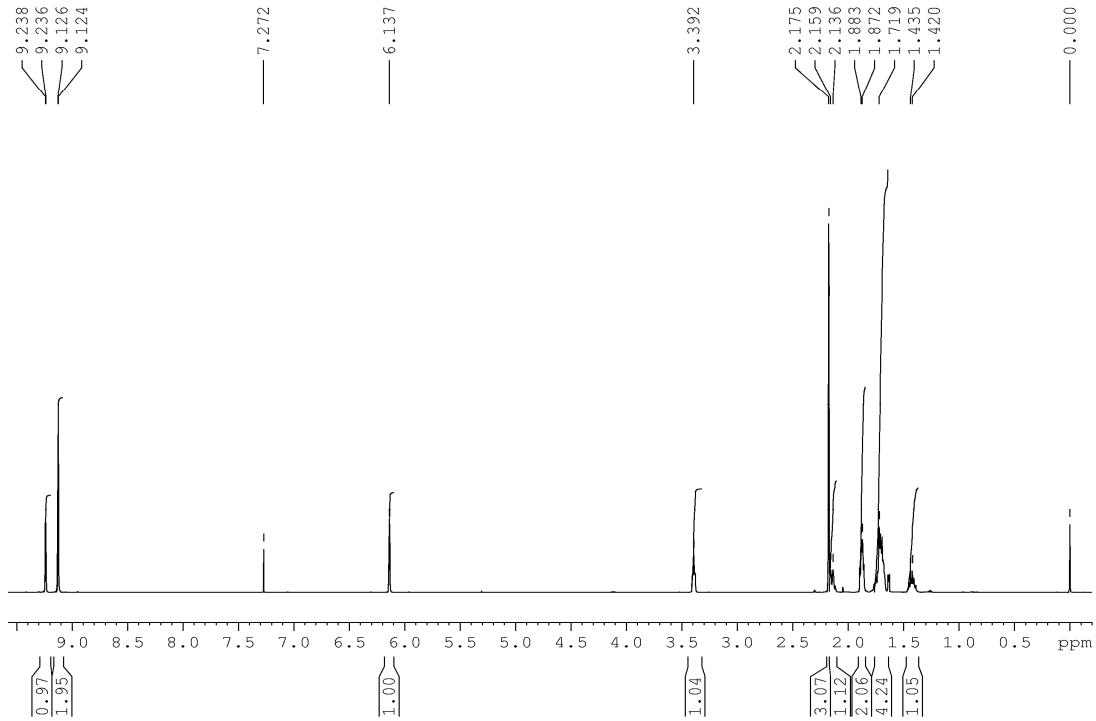
^{1}H NMR (500 MHz, $CDCl_3$) of 3-methylene-2,3,4,5,6,7-hexahydro-1*H*-inden-1-one (49)



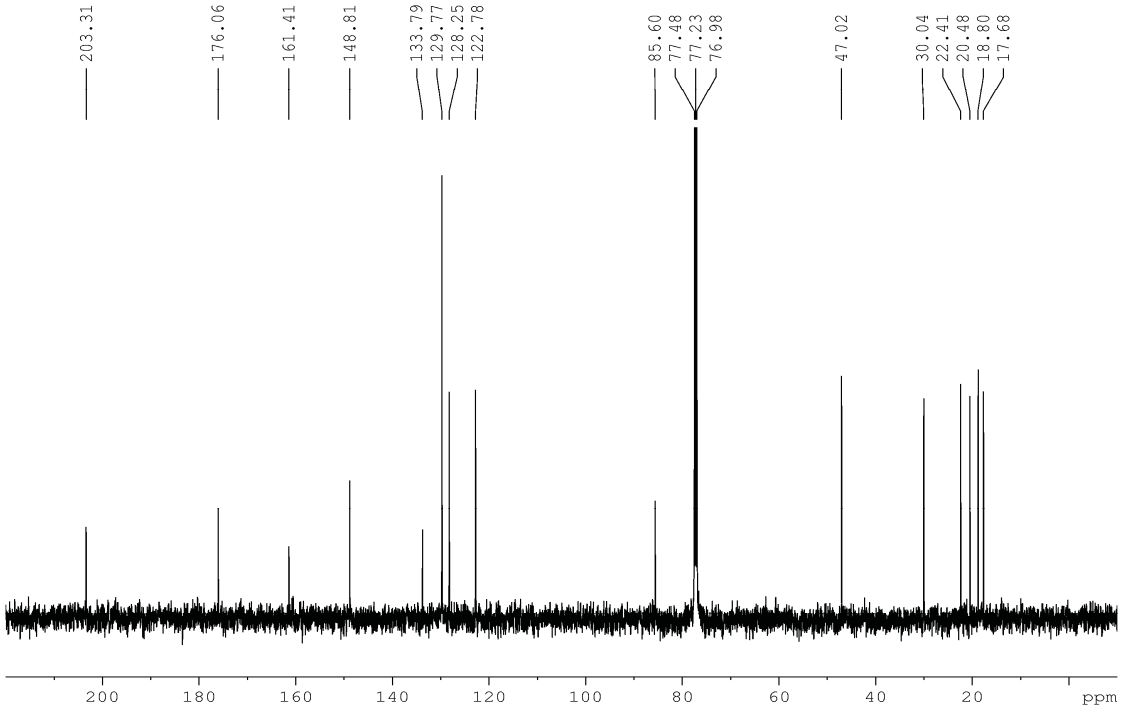
^{13}C NMR (125 MHz, $CDCl_3$) of 3-methylene-2,3,4,5,6,7-hexahydro-1*H*-inden-1-one (49)



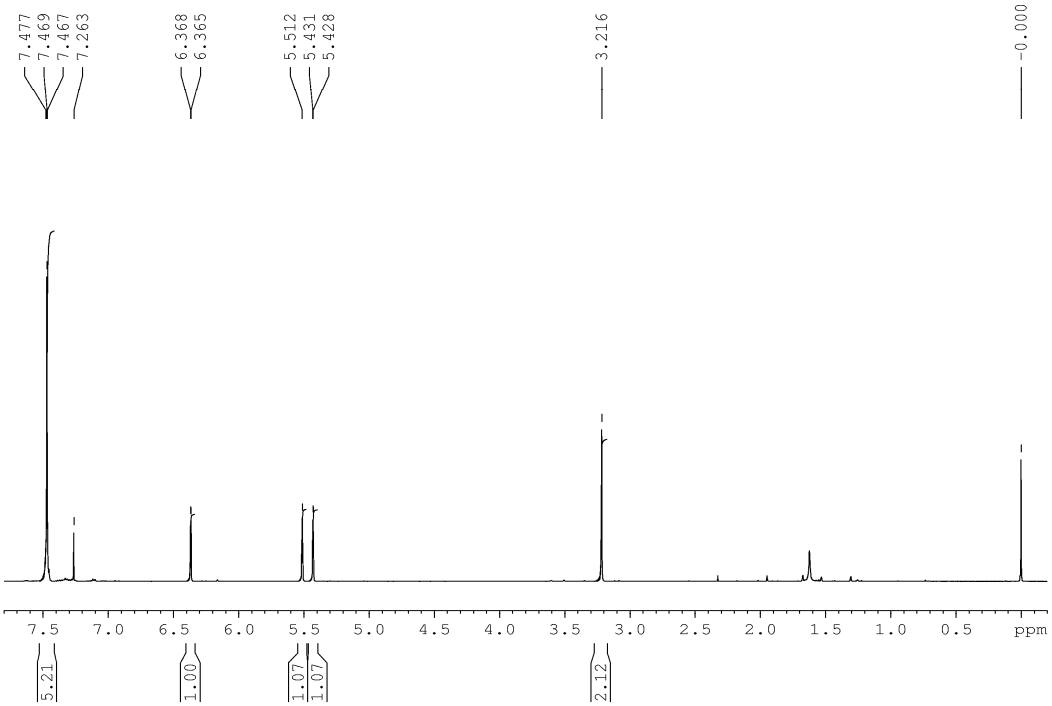
^{1}H NMR (500 MHz, $CDCl_3$) of (3a*R,7a*S**)-1-methylene-3-oxooctahydro-1*H*-inden-3a-yl 3,5-dinitrobenzoate (50)**



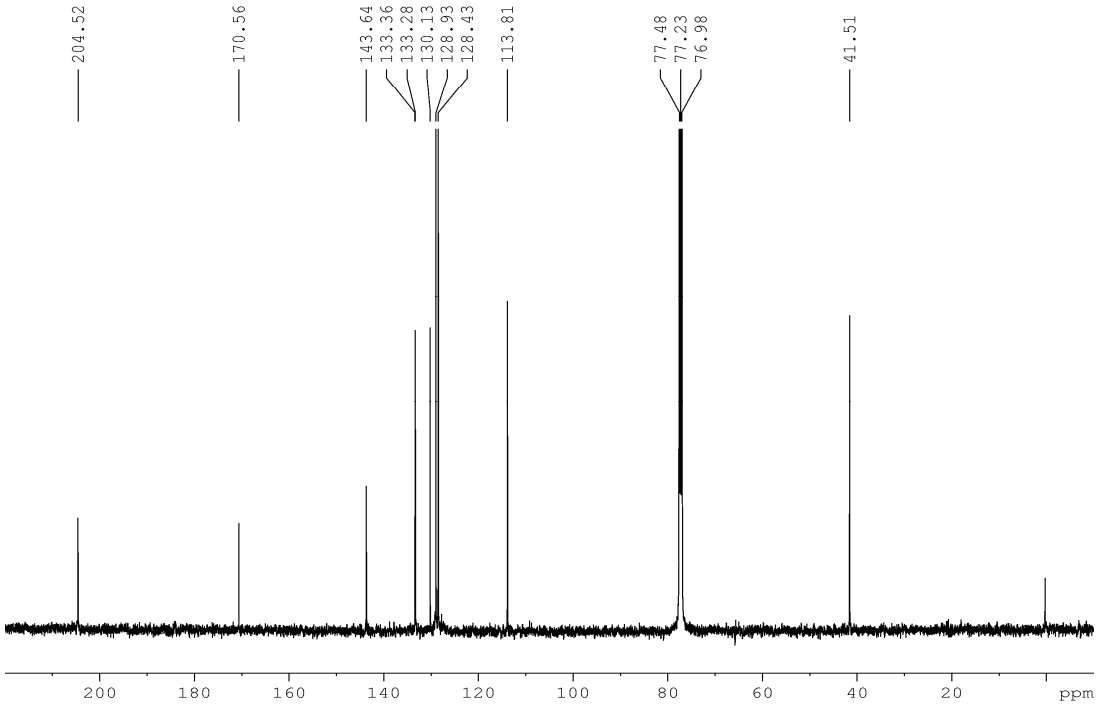
^{13}C NMR (125 MHz, $CDCl_3$) of (3a*R,7a*S**)-1-methylene-3-oxooctahydro-1*H*-inden-3a-yl 3,5-dinitrobenzoate (50)**



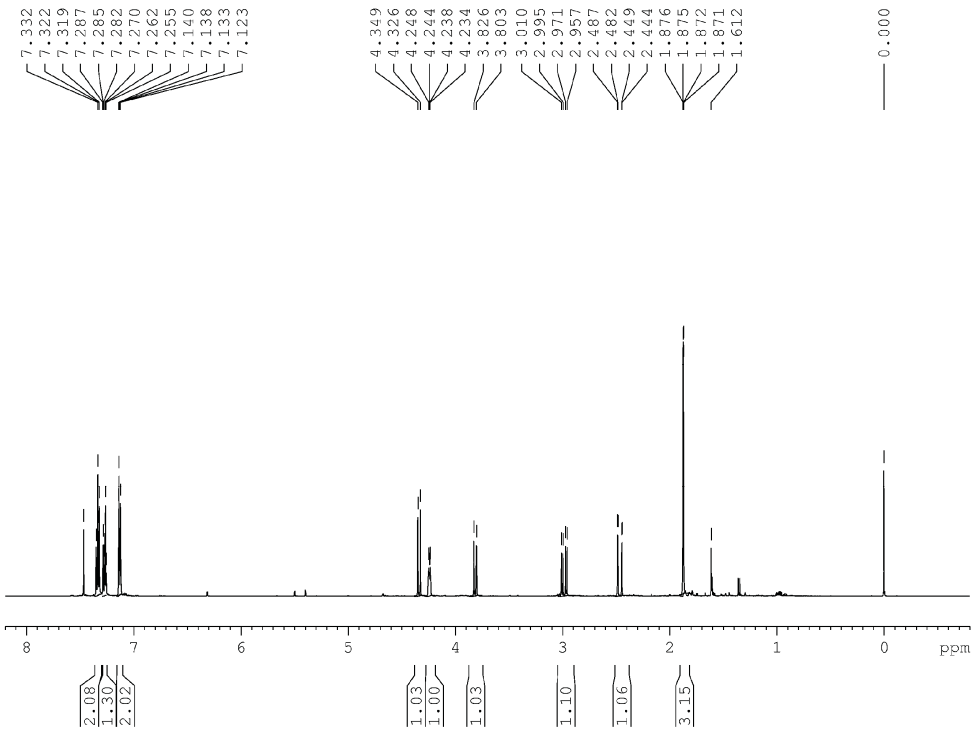
^{1}H NMR (500 MHz, $CDCl_3$) of 4-methylene-3-phenylcyclopent-2-enone (51)



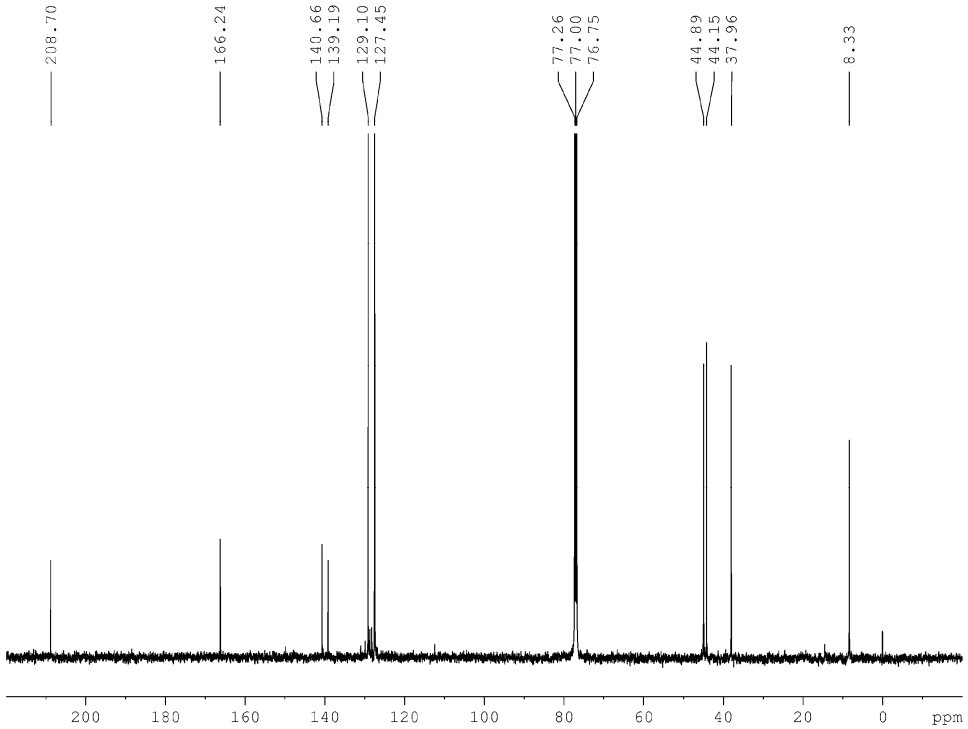
^{13}C NMR (125 MHz, $CDCl_3$) of 4-methylene-3-phenylcyclopent-2-enone (51)



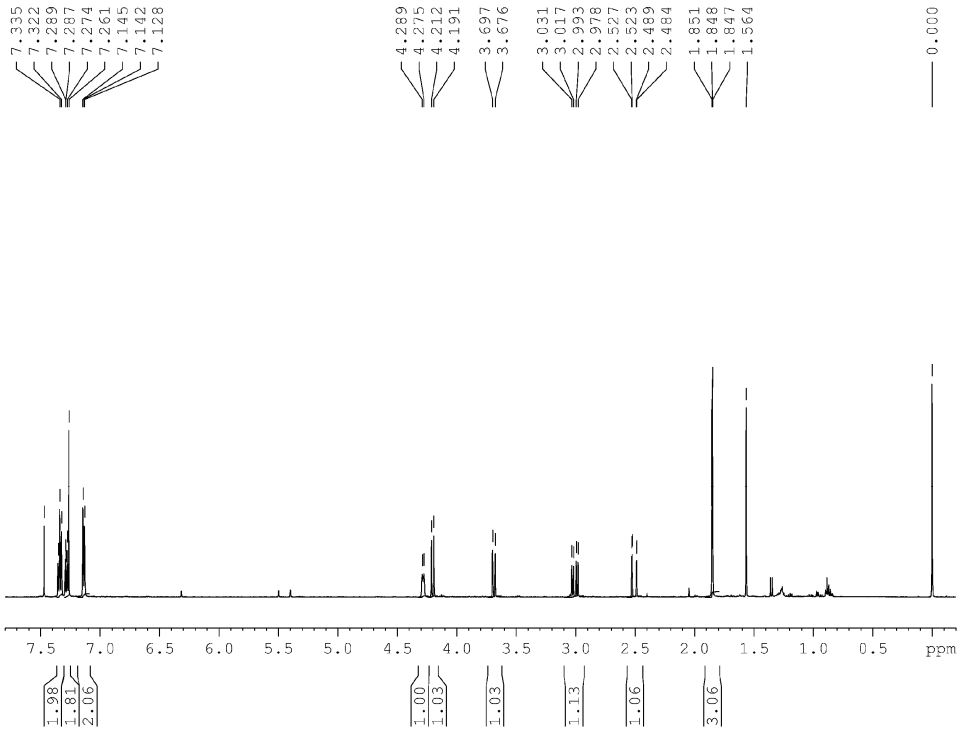
^{1}H NMR ($CDCl_3$, 500 MHz) spectrum of 3-(chloromethyl)-2-methyl-4-phenylcyclopent-2-enone (52)



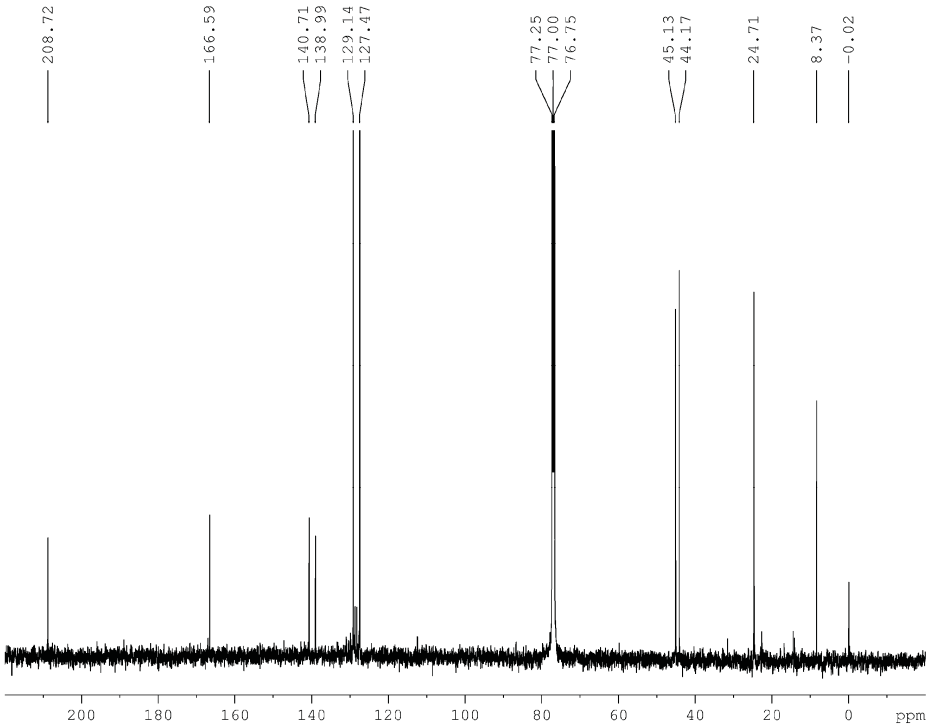
^{13}C NMR ($CDCl_3$, 125 MHz) spectrum of 3-(chloromethyl)-2-methyl-4-phenylcyclopent-2-enone (52)



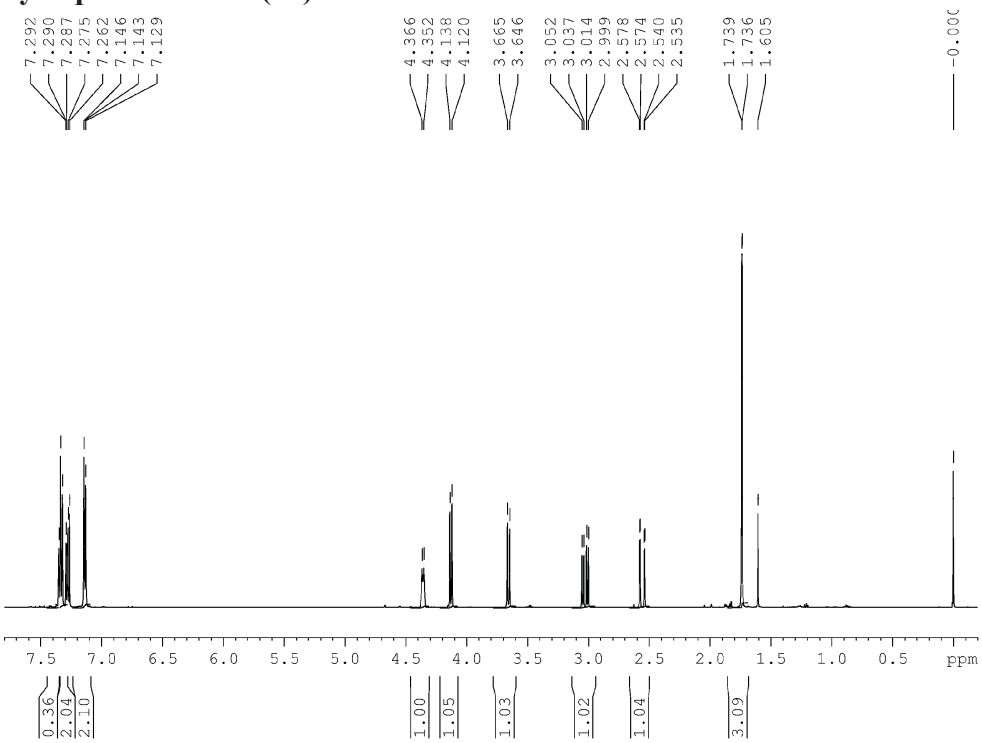
^{1}H NMR ($CDCl_3$, 500 MHz) spectrum of 3-(bromomethyl)-2-methyl-4-phenylcyclopent-2-enone (53)



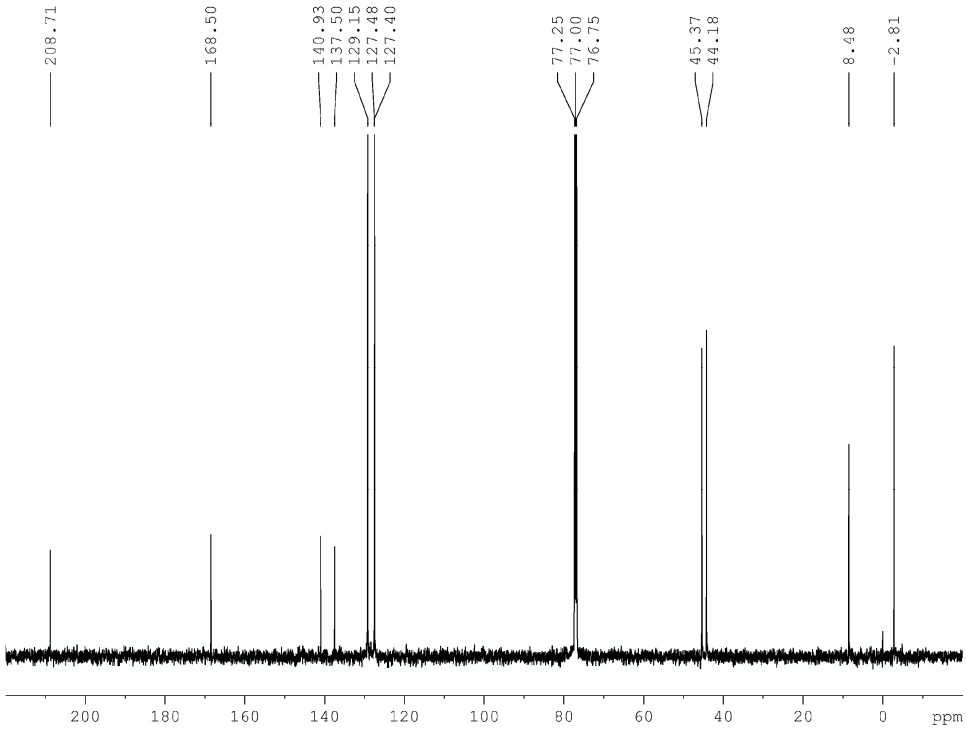
^{13}C NMR ($CDCl_3$, 125 MHz) spectrum of 3-(bromomethyl)-2-methyl-4-phenylcyclopent-2-enone (53)



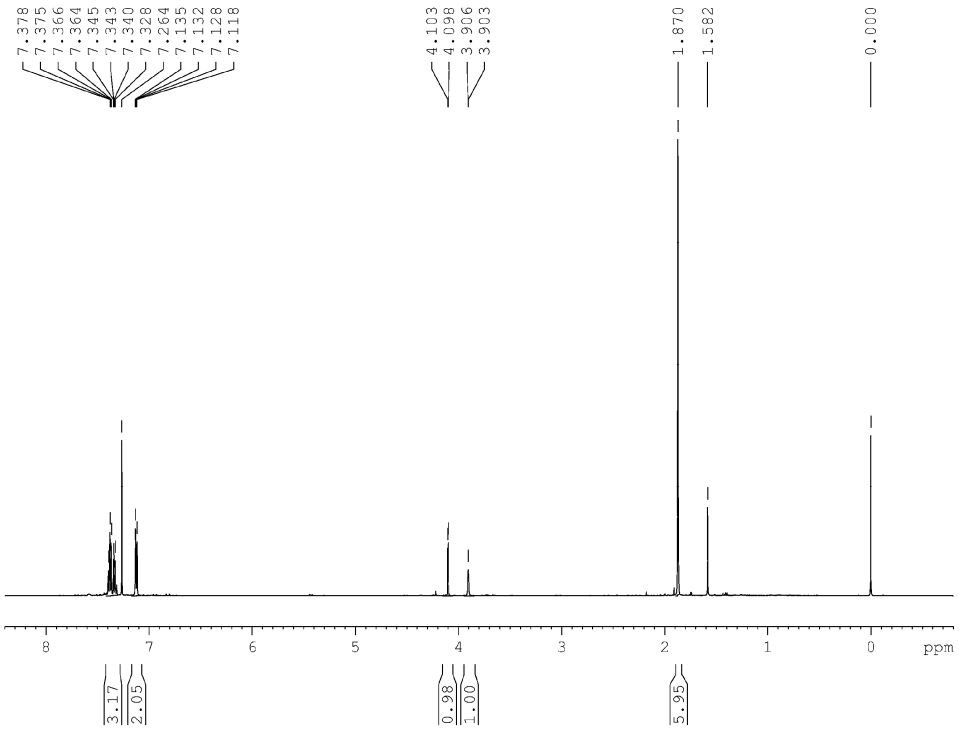
^{1}H NMR ($CDCl_3$, 500 MHz) spectrum of 3-(iodomethyl)-2-methyl-4-phenylcyclopent-2-enone (54)



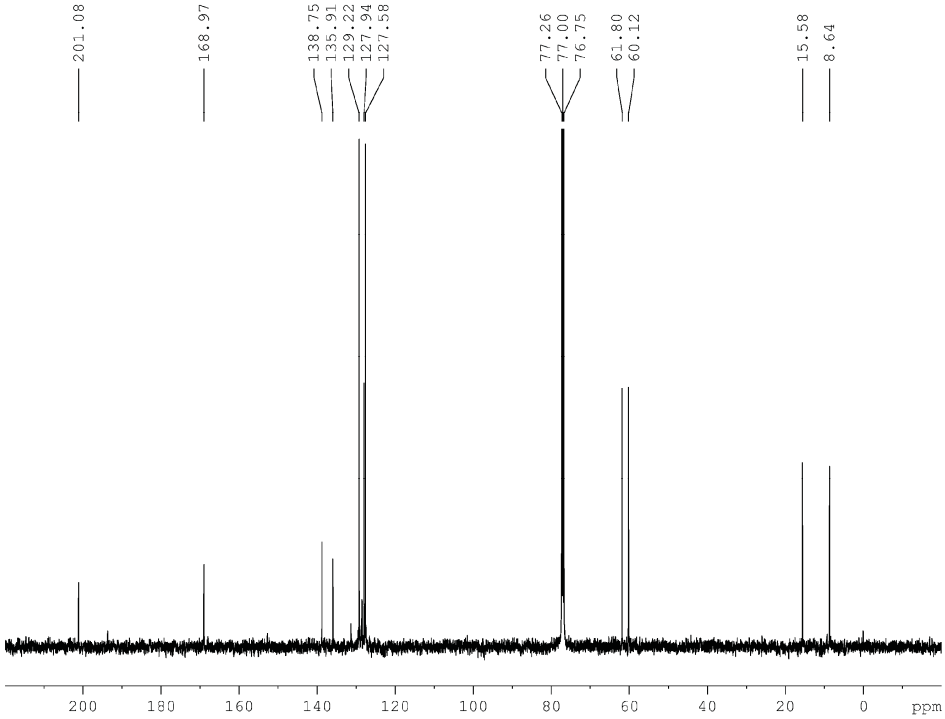
^{13}C NMR ($CDCl_3$, 125 MHz) spectrum of 3-(iodomethyl)-2-methyl-4-phenylcyclopent-2-enone (54)



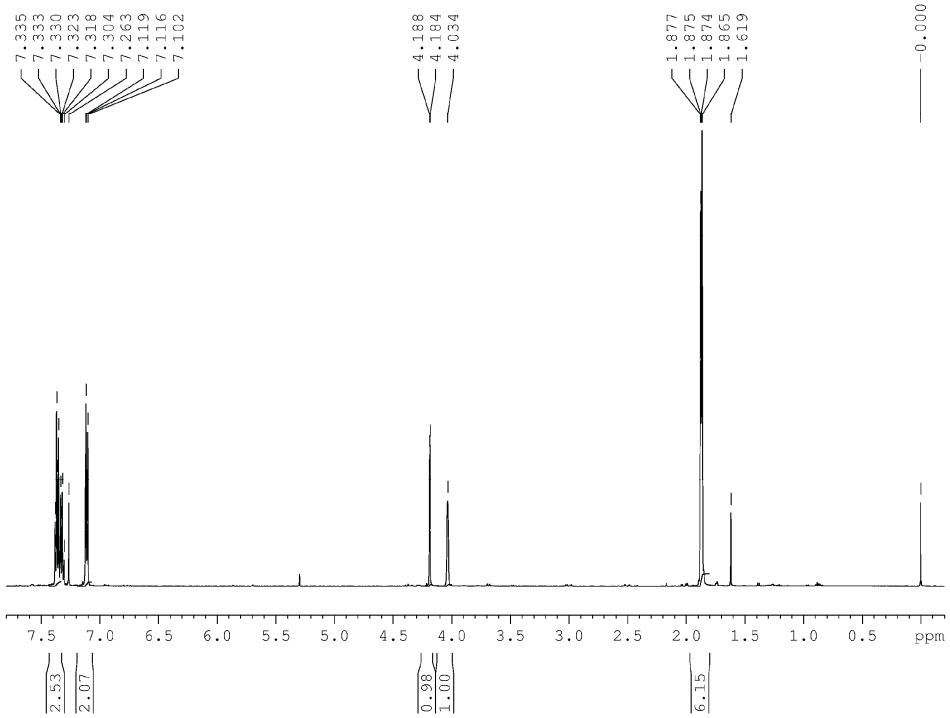
^{1}H NMR ($CDCl_3$, 500 MHz) spectrum of (*trans*)-5-chloro-2,3-dimethyl-4-phenylcyclopent-2-enone (55)



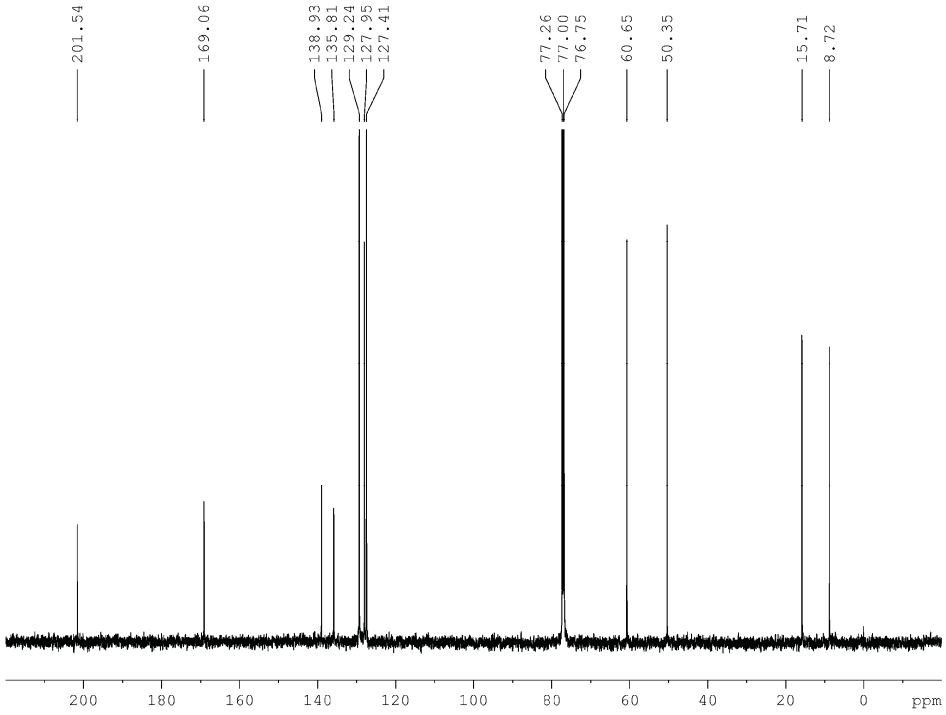
^{13}C NMR ($CDCl_3$, 125 MHz) spectrum of (*trans*)-5-chloro-2,3-dimethyl-4-phenylcyclopent-2-enone (55)



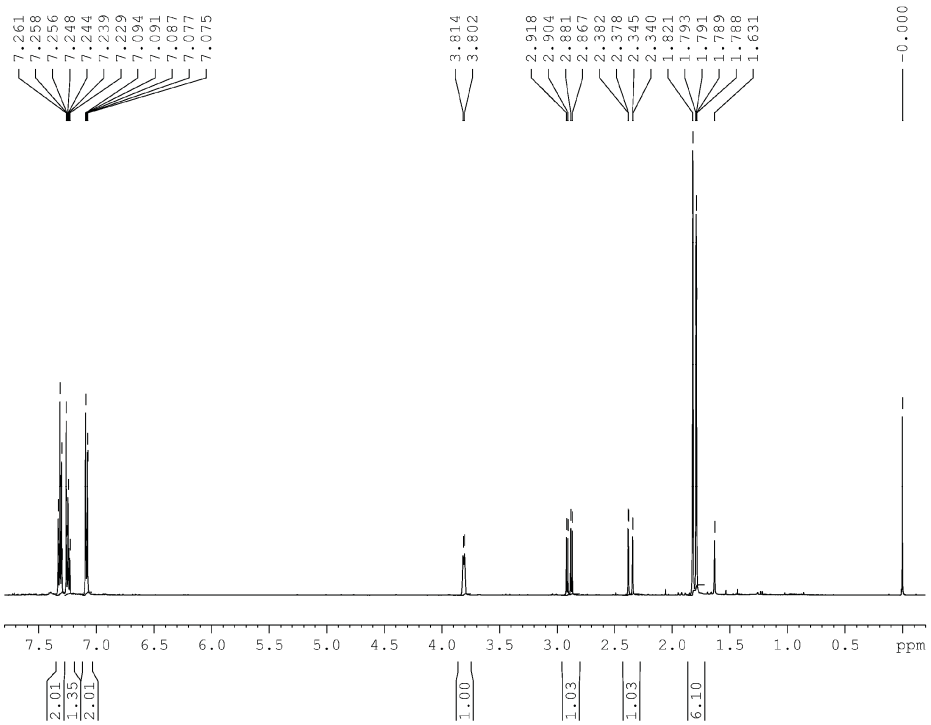
^{1}H NMR ($CDCl_3$, 500 MHz) spectrum of *trans*-5-bromo-2,3-dimethyl-4-phenylcyclopent-2-enone (56)



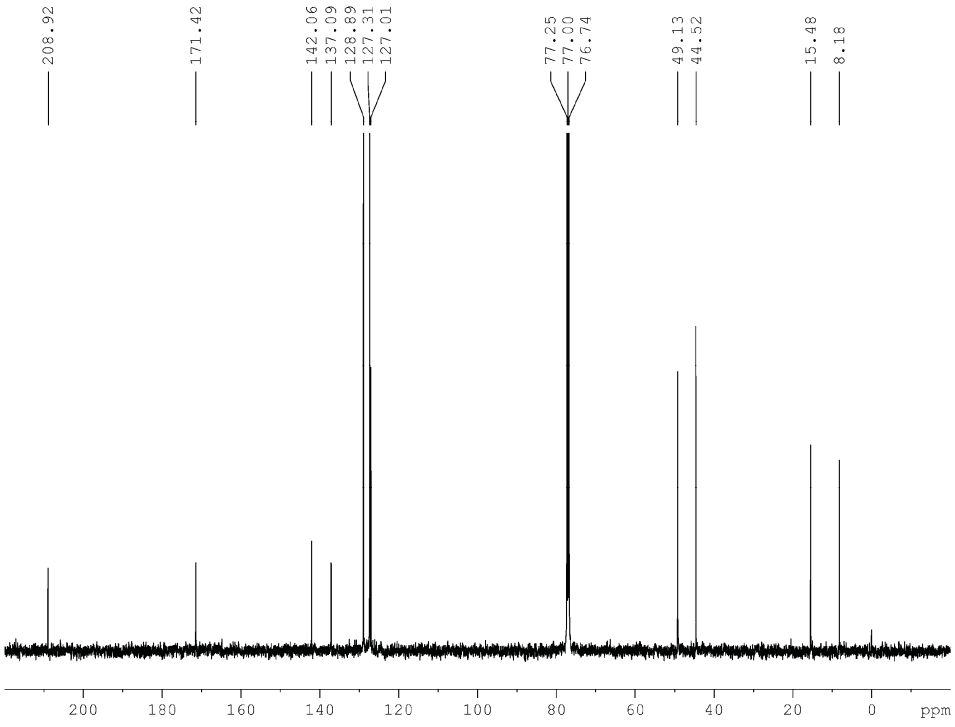
^{13}C NMR ($CDCl_3$, 125 MHz) spectrum of *trans*-5-bromo-2,3-dimethyl-4-phenylcyclopent-2-enone (56)



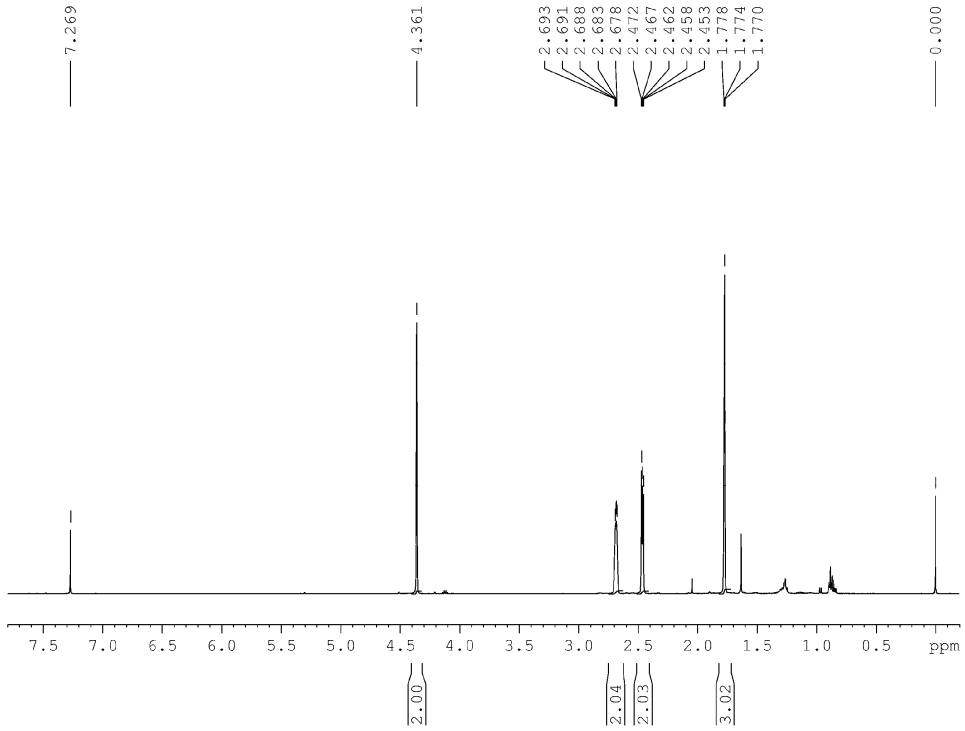
^{1}H NMR ($CDCl_3$, 500 MHz) spectrum of 2,3-dimethyl-4-phenylcyclopent-2-enone (57)



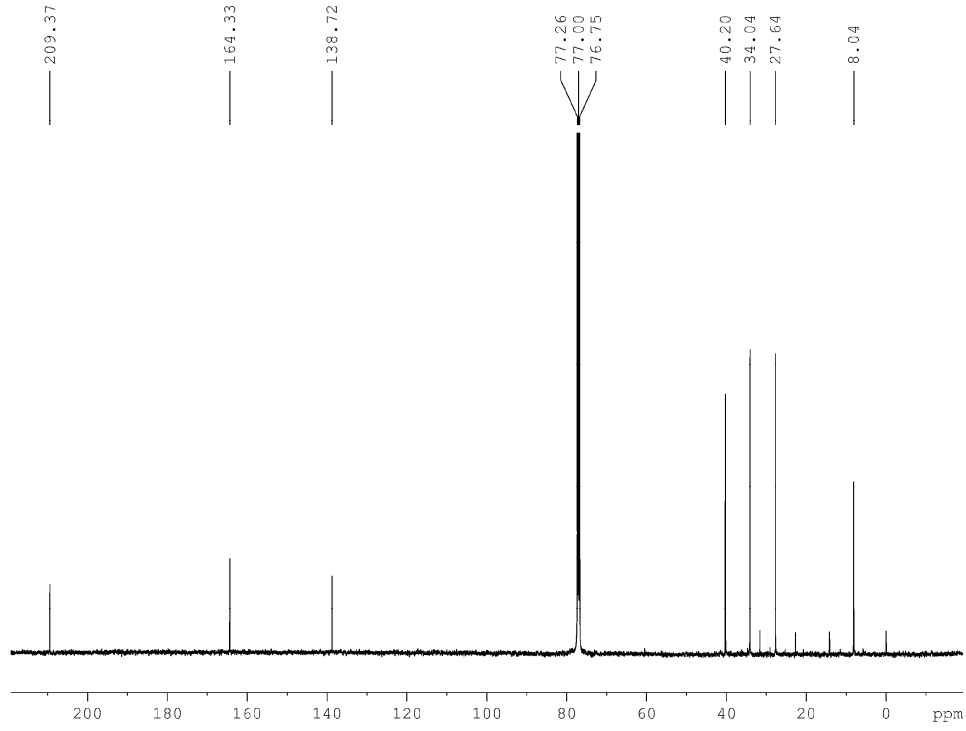
^{13}C NMR ($CDCl_3$, 125 MHz) spectrum of 2,3-dimethyl-4-phenylcyclopent-2-enone (57)



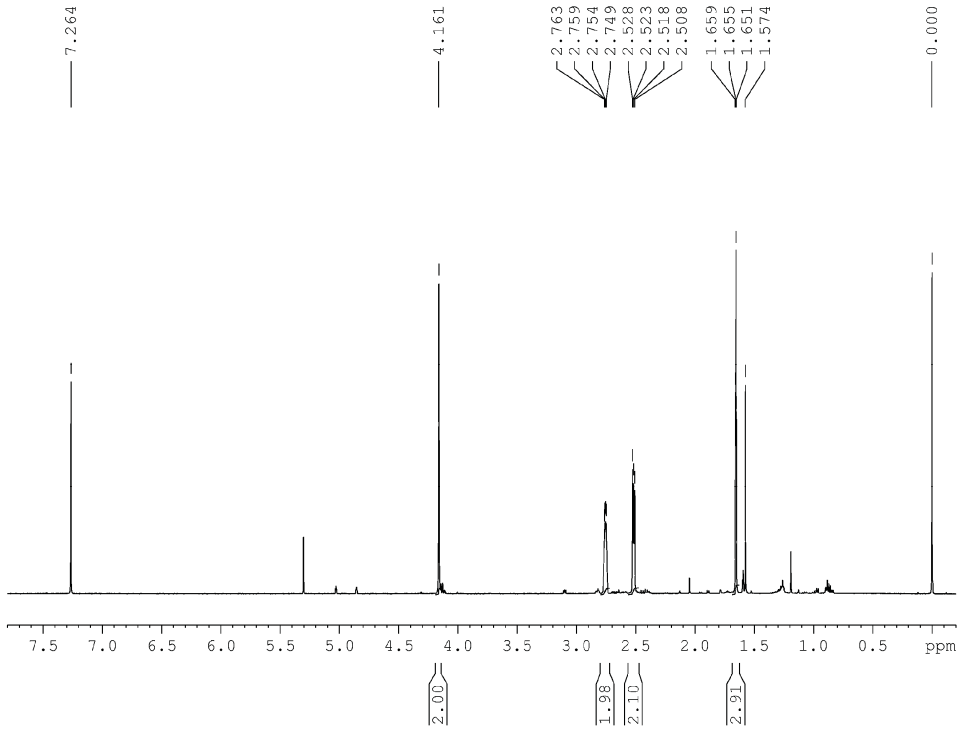
^{1}H NMR ($CDCl_3$, 500 MHz) spectrum of 3-(chloromethyl)-2-methylcyclopent-2-enone (58)



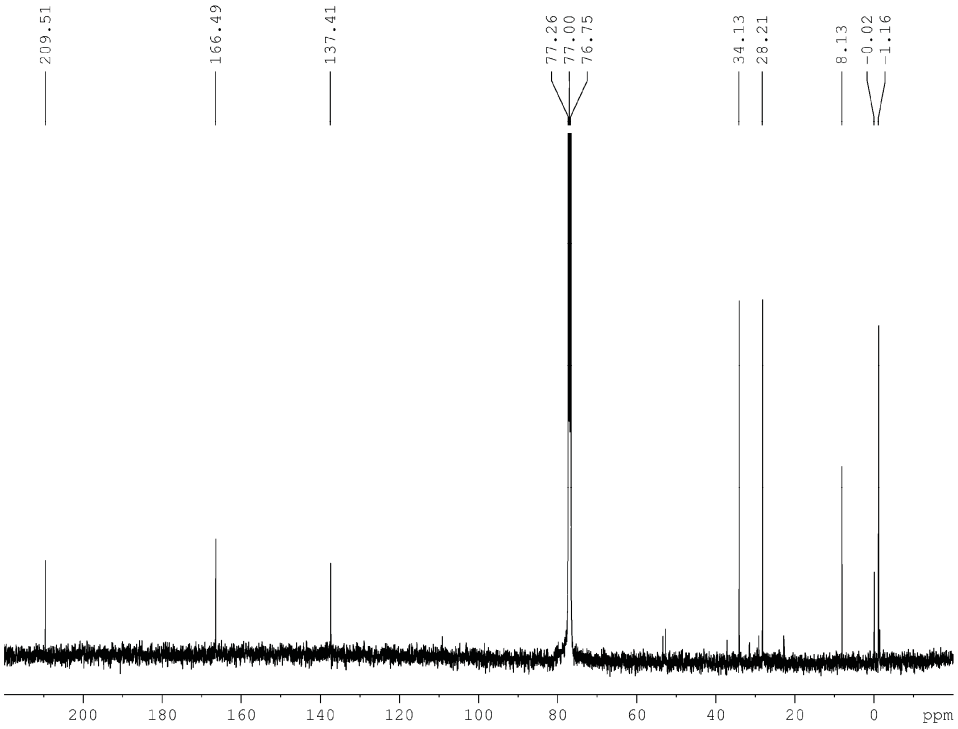
^{13}C NMR ($CDCl_3$, 125 MHz) spectrum of 3-(chloromethyl)-2-methylcyclopent-2-enone (58)



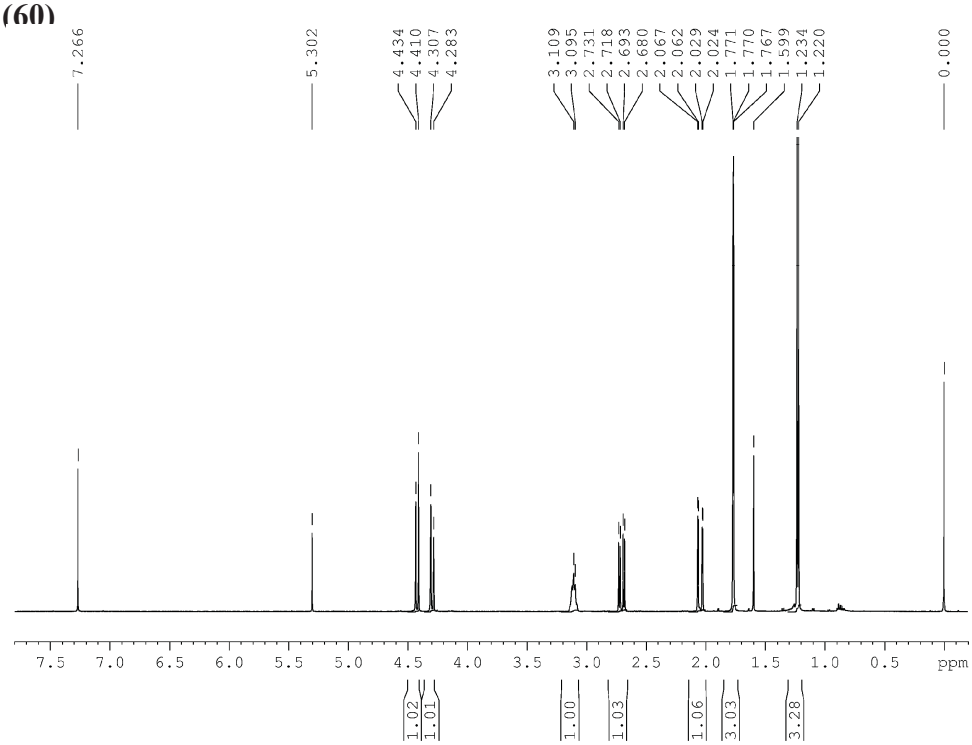
^{1}H NMR ($CDCl_3$, 500 MHz) spectrum of 3-(iodomethyl)-2,4-dimethylcyclopent-2-enone (59)



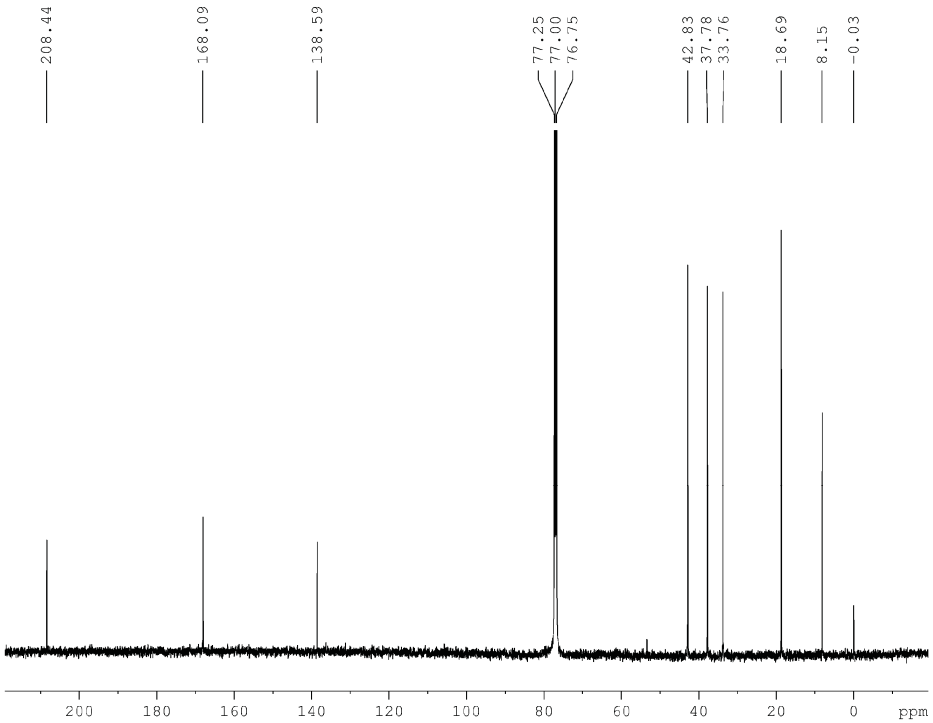
^{13}C NMR ($CDCl_3$, 125 MHz) spectrum of 3-(iodomethyl)-2,4-dimethylcyclopent-2-enone (59)



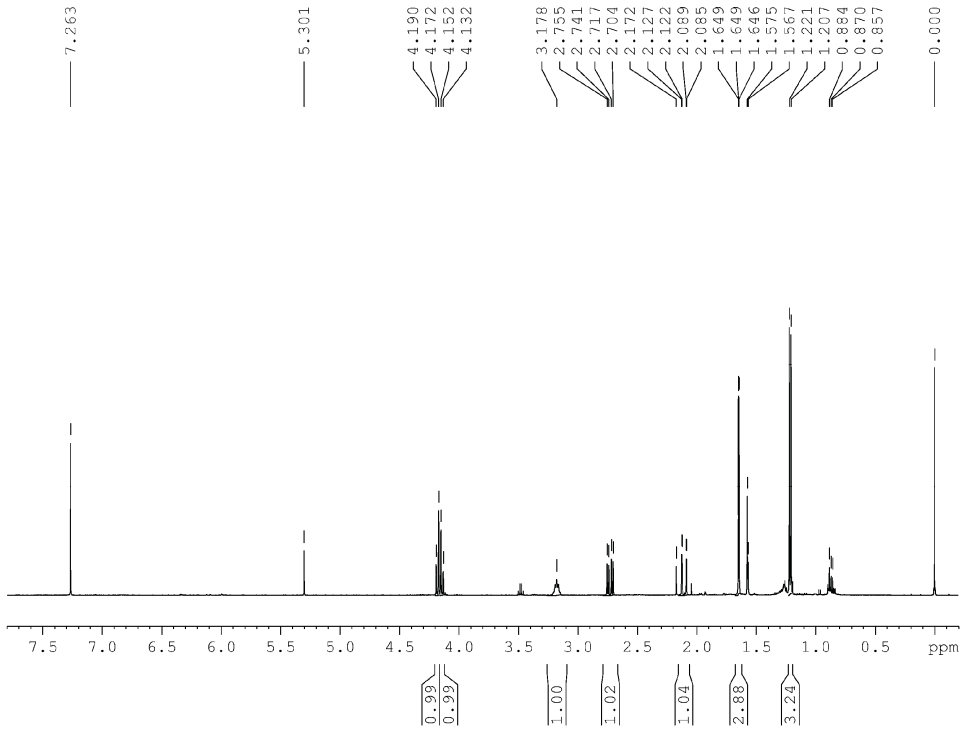
^{1}H NMR ($CDCl_3$, 500 MHz) spectrum of 3-(chloromethyl)-2,4-dimethylcyclopent-2-enone (60)



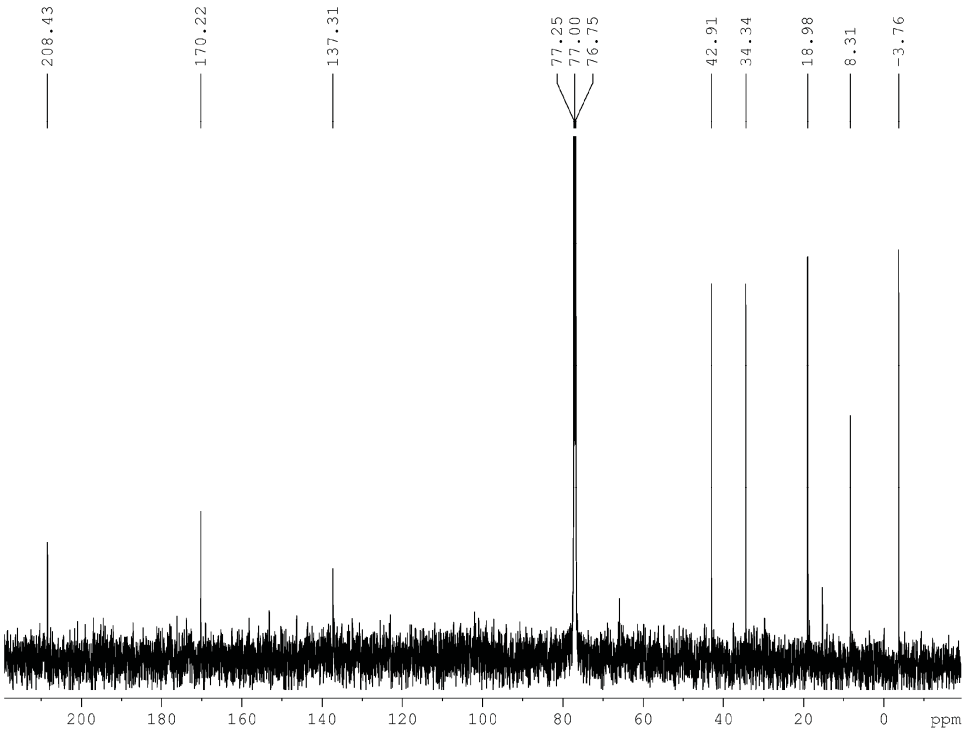
^{13}C NMR ($CDCl_3$, 125 MHz) spectrum of 3-(chloromethyl)-2,4-dimethylcyclopent-2-enone (60)



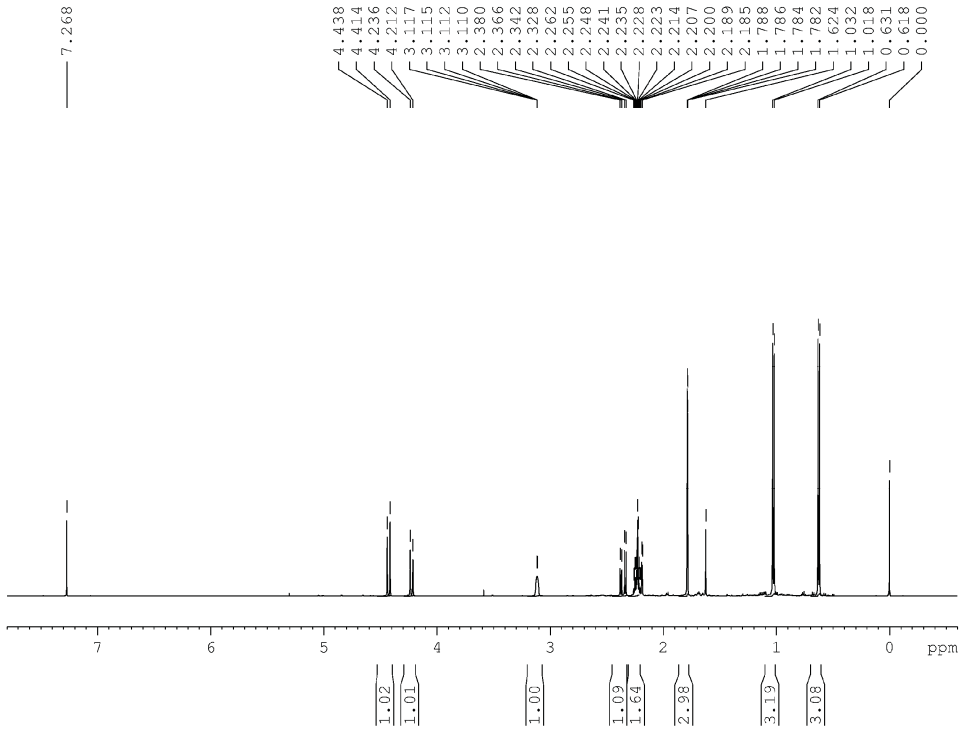
^{1}H NMR ($CDCl_3$, 500 MHz) spectrum of 3-(iodomethyl)-2,4-dimethylcyclopent-2-enone (61)



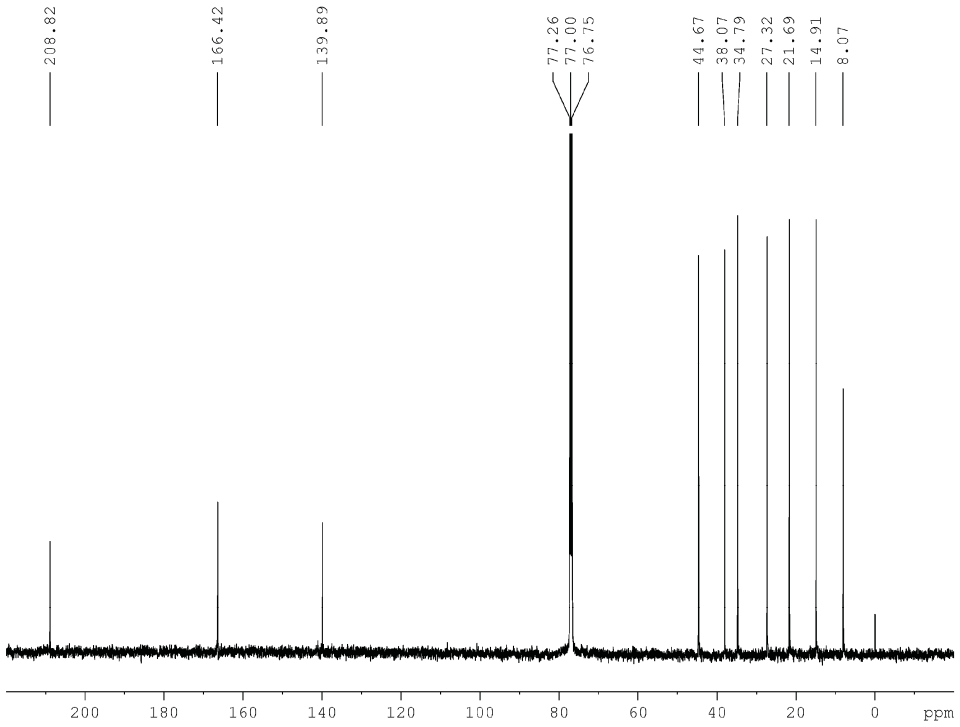
^{13}C NMR ($CDCl_3$, 125 MHz) spectrum of 3-(iodomethyl)-2,4-dimethylcyclopent-2-enone (61)



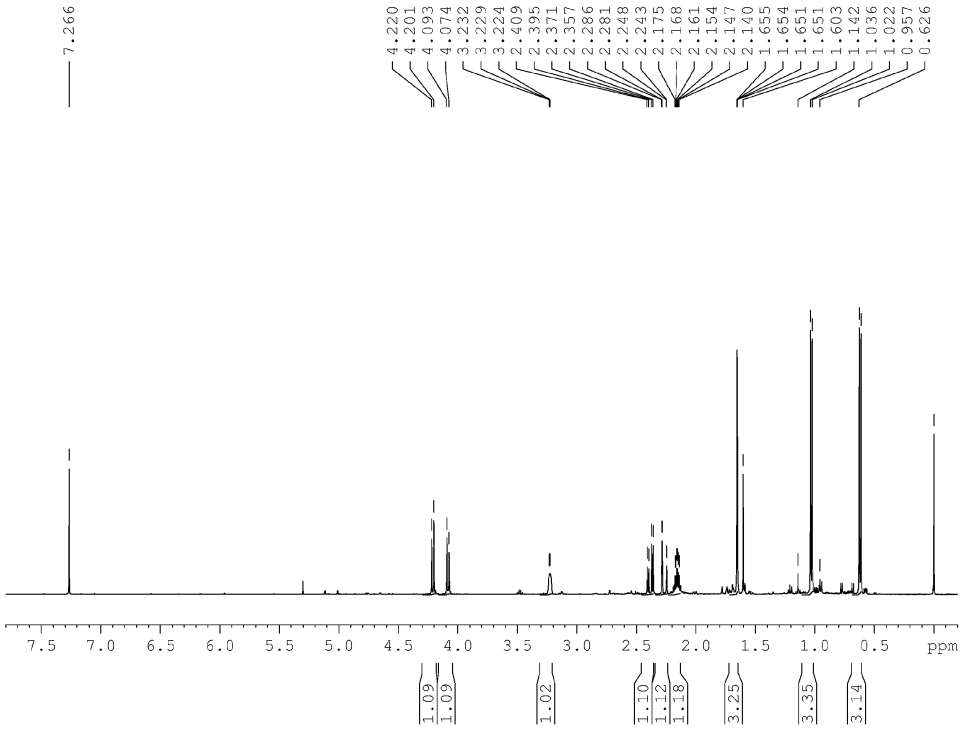
^{1}H NMR ($CDCl_3$, 500 MHz) spectrum of 3-(chloromethyl)-4-isopropyl-2-methylcyclopent-2-enone (62)



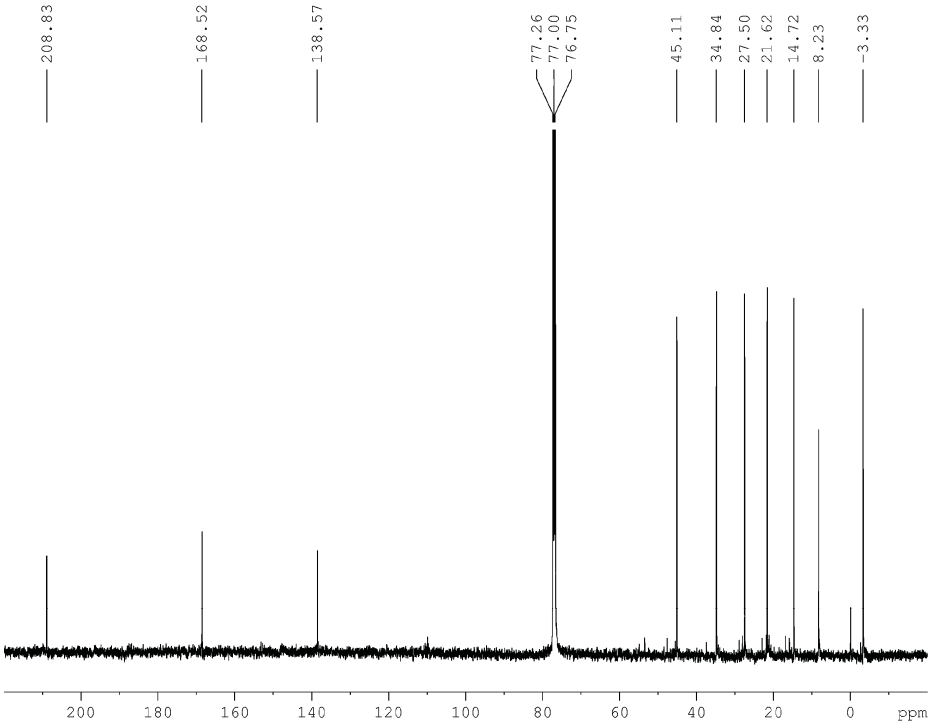
^{13}C NMR ($CDCl_3$, 125 MHz) spectrum of 3-(chloromethyl)-4-isopropyl-2-methylcyclopent-2-enone (62)



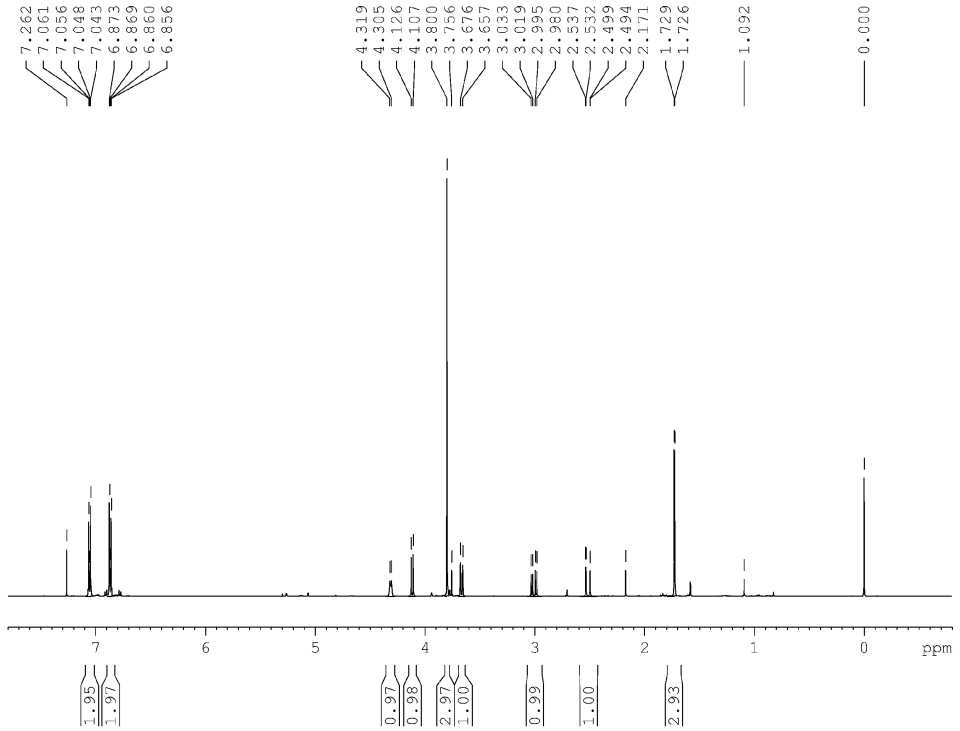
^{1}H NMR ($CDCl_3$, 500 MHz) spectrum of 3-(iodomethyl)-4-isopropyl-2-methylcyclopent-2-enone (63)



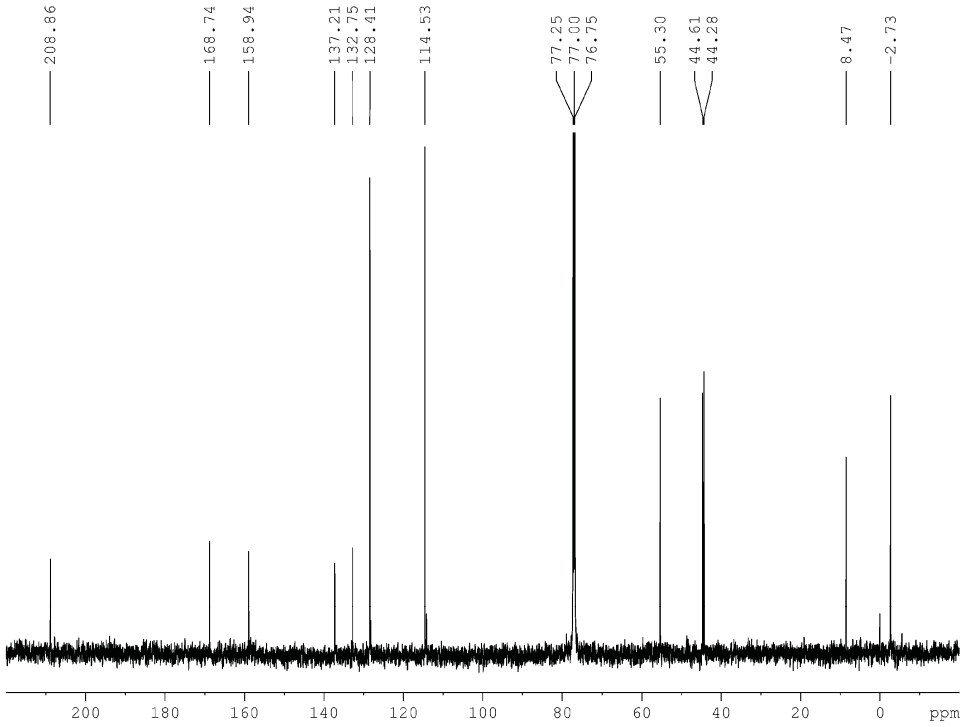
^{13}C NMR ($CDCl_3$, 125 MHz) spectrum of 3-(iodomethyl)-4-isopropyl-2-methylcyclopent-2-enone (63)



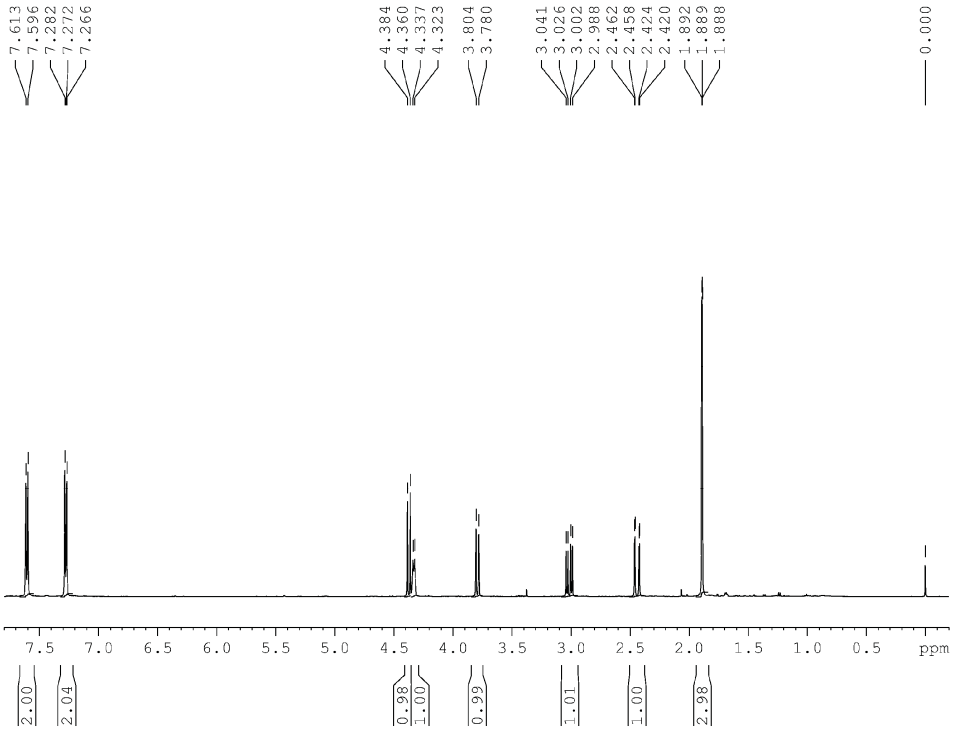
^{1}H NMR ($CDCl_3$, 500 MHz) spectrum of 3-(iodomethyl)-4-(4-methoxyphenyl)-2-methyl-cyclopent-2-enone (64)



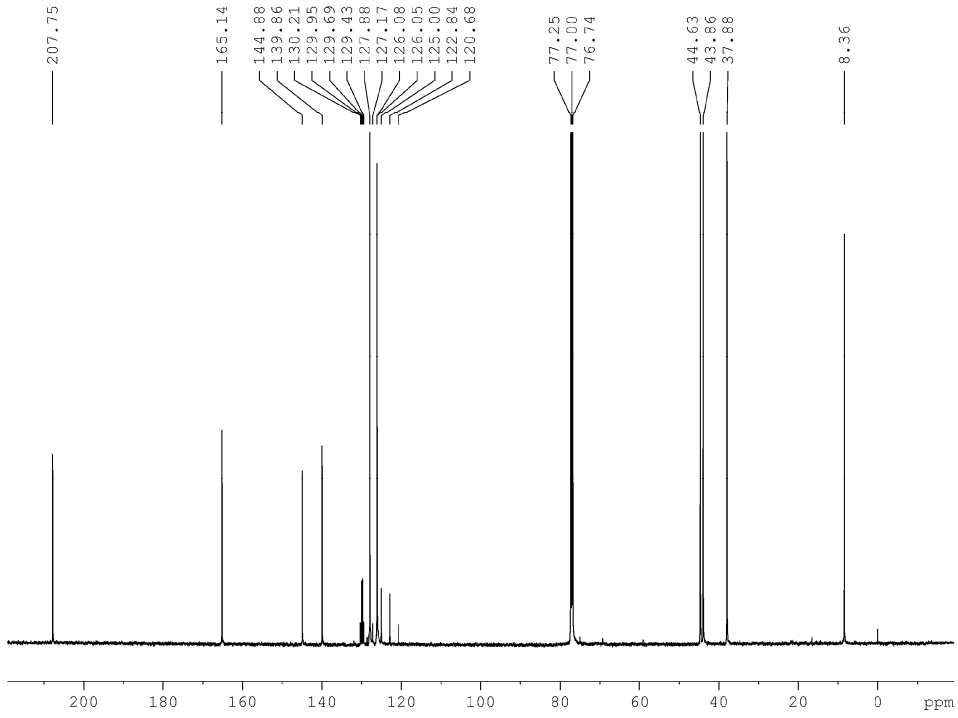
^{13}C NMR ($CDCl_3$, 125 MHz) spectrum of 3-(iodomethyl)-4-(4-methoxyphenyl)-2-methyl-cyclopent-2-enone (64)



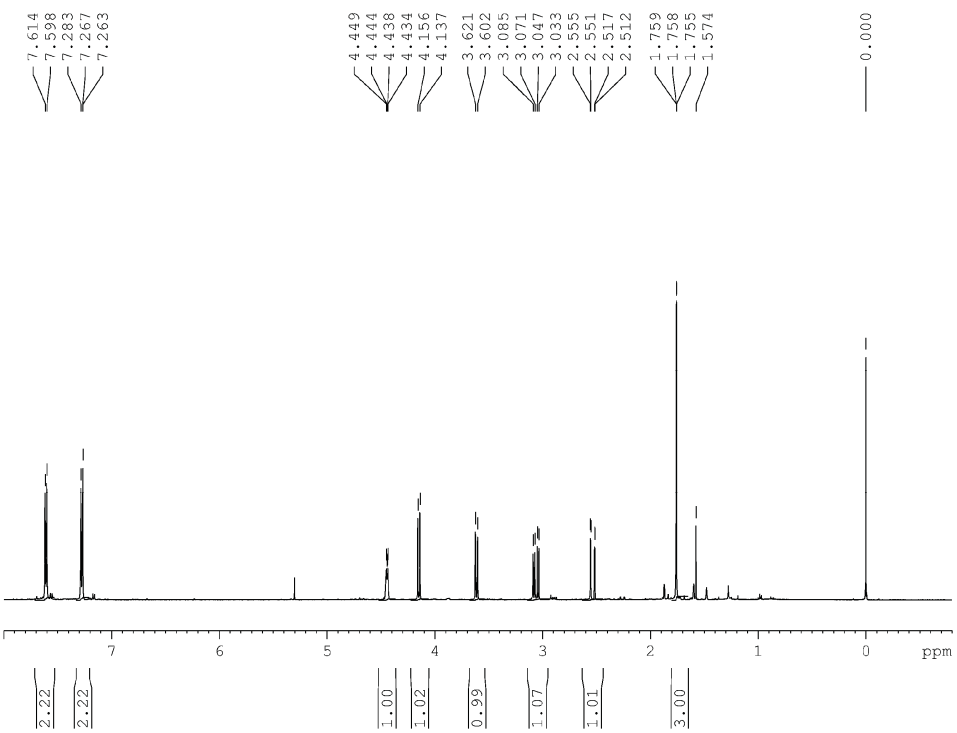
^{1}H NMR ($CDCl_3$, 500 MHz) spectrum of 3-(chloromethyl)-2-methyl-4-(4-(trifluoromethyl)-phenyl)cyclopent-2-enone (65)



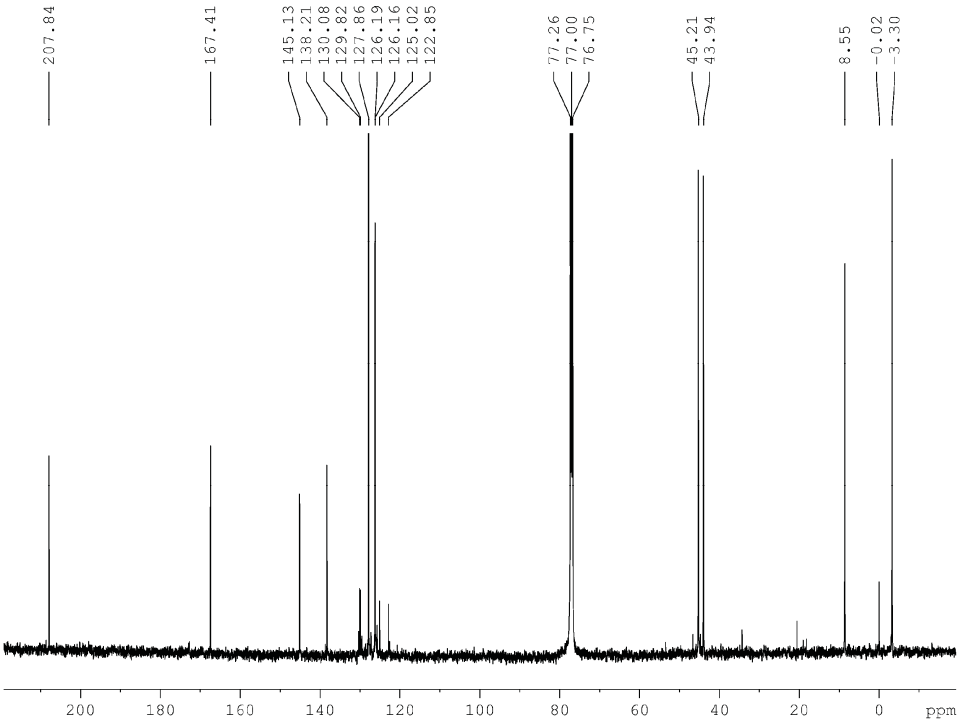
^{13}C NMR ($CDCl_3$, 125 MHz) spectrum of 3-(chloromethyl)-2-methyl-4-(4-(trifluoromethyl)-phenyl)cyclopent-2-enone (65)



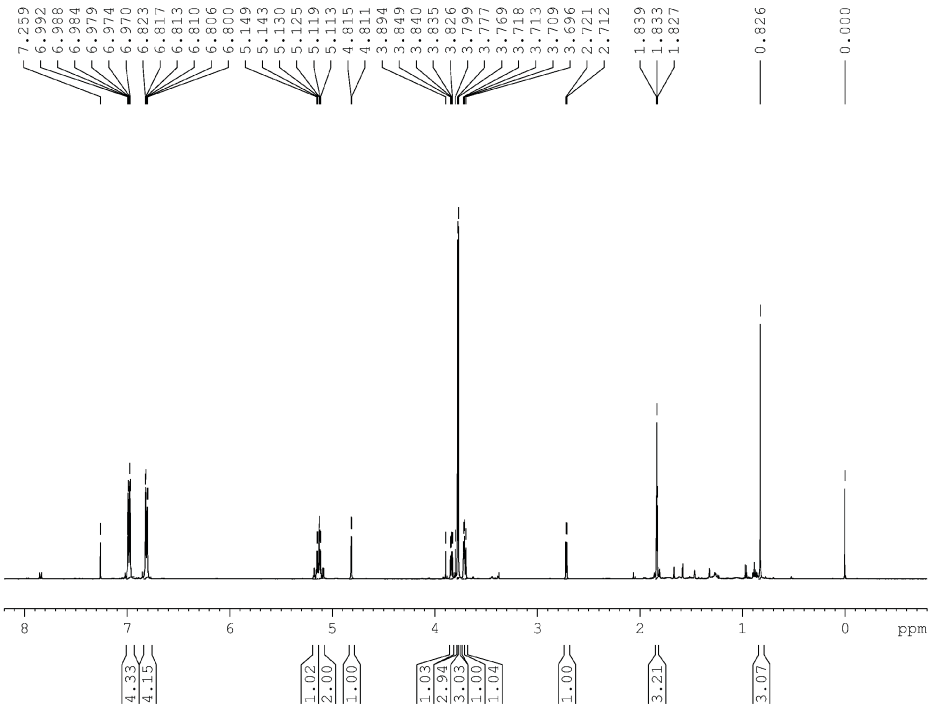
^{1}H NMR ($CDCl_3$, 500 MHz) spectrum of 3-(iodomethyl)-2-methyl-4-(4-(trifluoromethyl)-phenyl)cyclopent-2-enone (66)



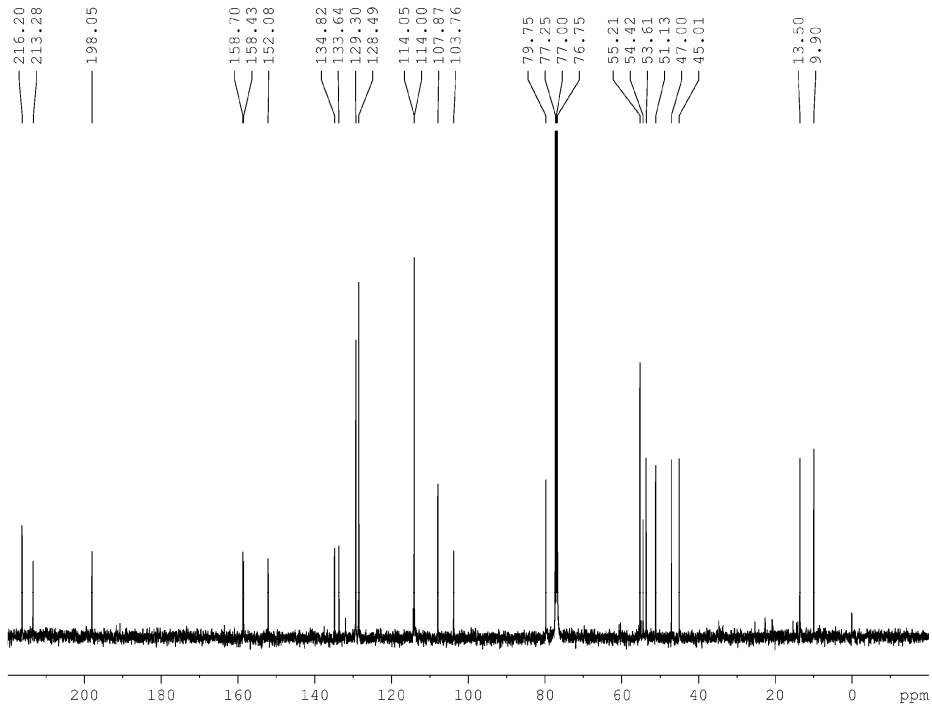
^{13}C NMR ($CDCl_3$, 125 MHz) spectrum of 3-(iodomethyl)-2-methyl-4-(4-(trifluoromethyl)-phenyl)cyclopent-2-enone (66)



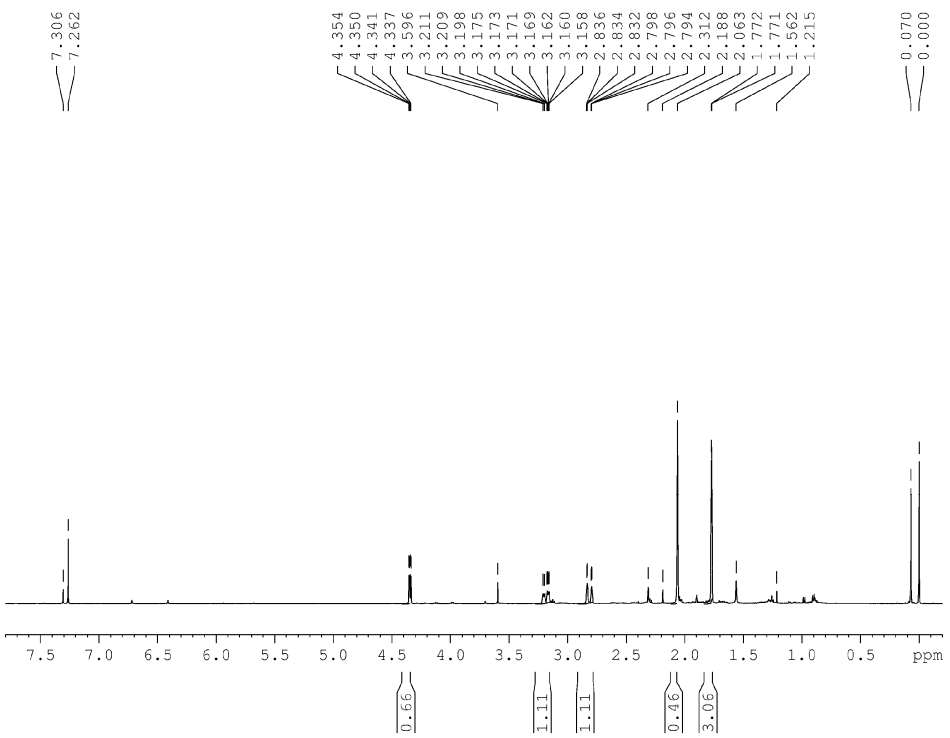
^{1}H NMR ($CDCl_3$, 500 MHz) spectrum of (1*R,2*S**,3*R**,4*R**,5*R**)-2,5-bis(4-methoxyphenyl)-1-methyl-3-(2-methylbuta-2,3-dienoyl)-6-methylenebicyclo[2.2.1] heptan-7-one (67)**



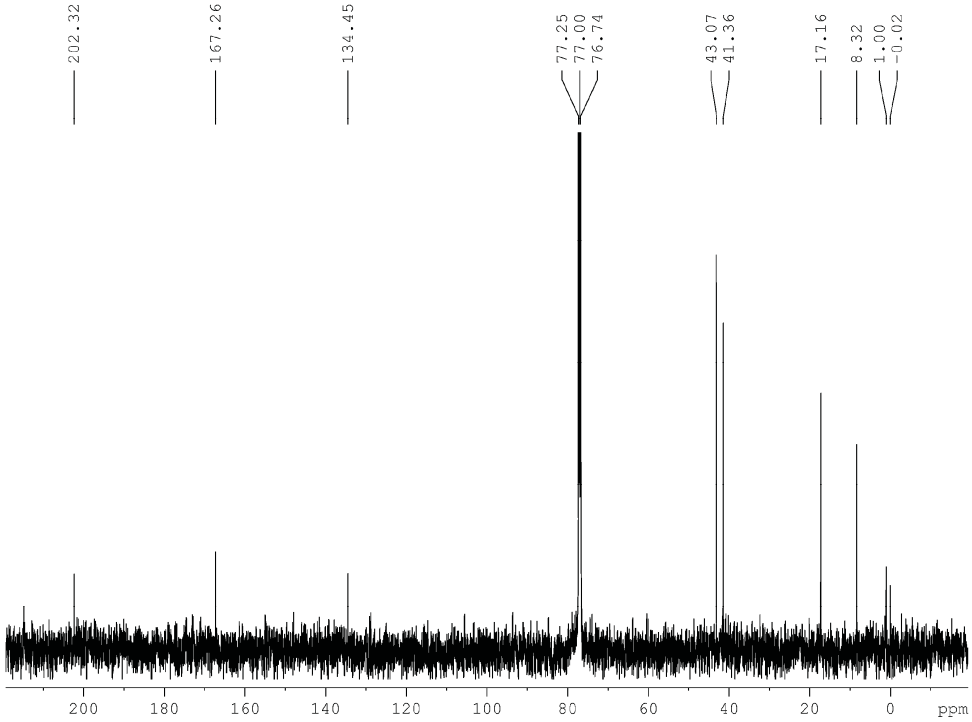
^{13}C NMR ($CDCl_3$, 125 MHz) spectrum of (1*R,2*S**,3*R**,4*R**,5*R**)-2,5-bis(4-methoxyphenyl)- 1-methyl-3-(2-methylbuta-2,3-dienoyl)-6-methylenebicyclo[2.2.1] heptan-7-one (67)**



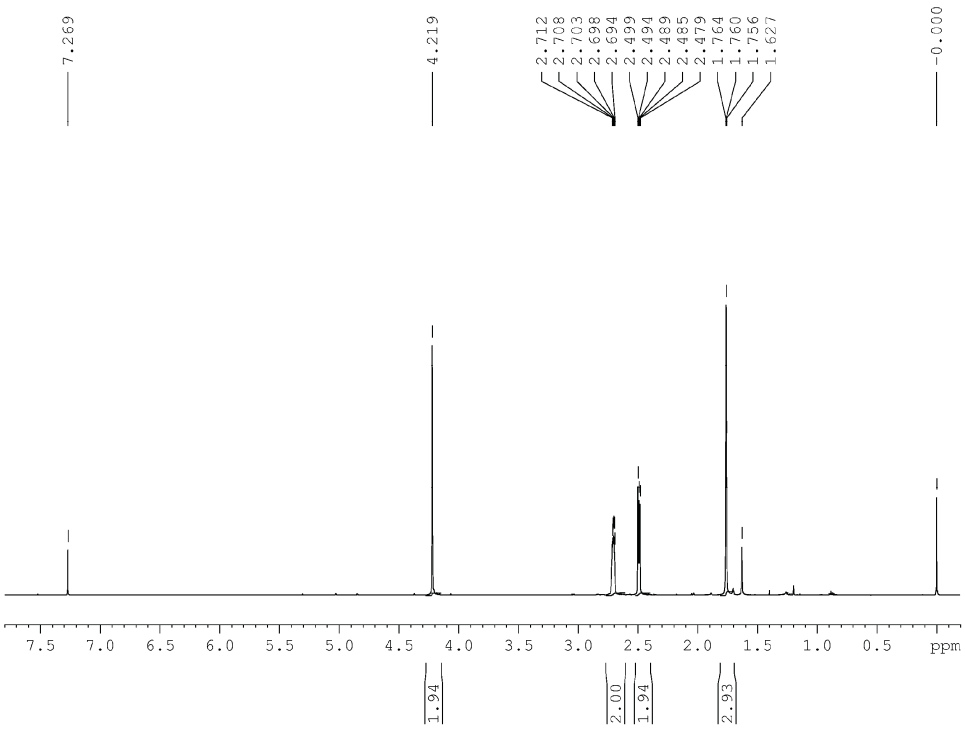
^{1}H NMR ($CDCl_3$, 500 MHz) spectrum of 5-bromo-2,3-dimethylcyclopent-2-enone (68)



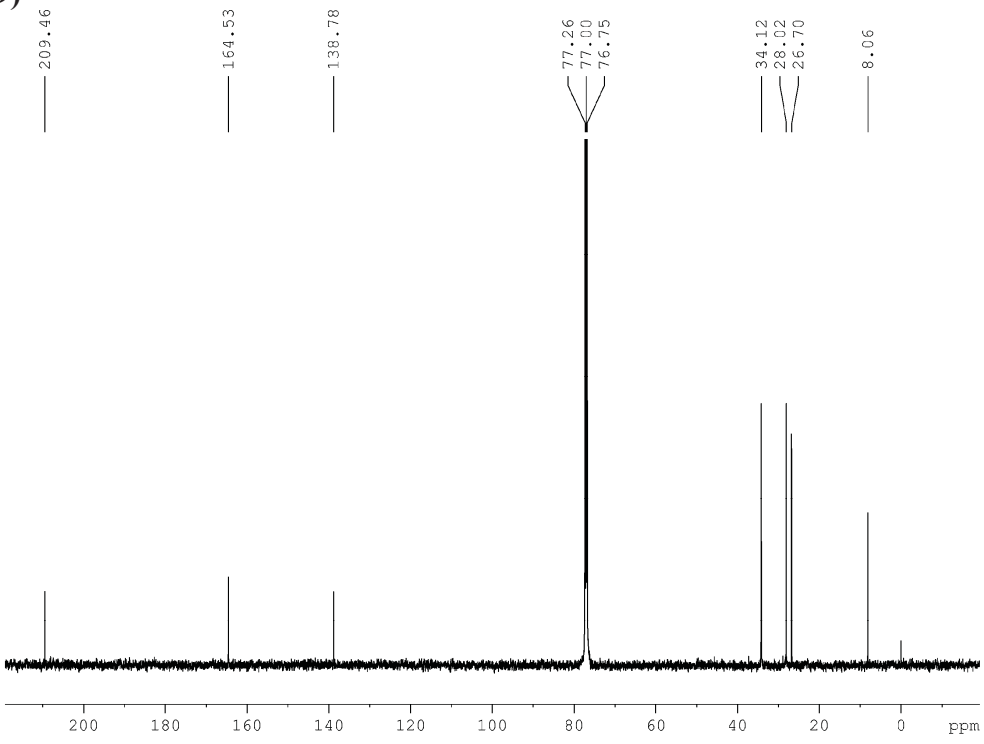
^{13}C NMR ($CDCl_3$, 125 MHz) spectrum of 5-bromo-2,3-dimethylcyclopent-2-enone (68)



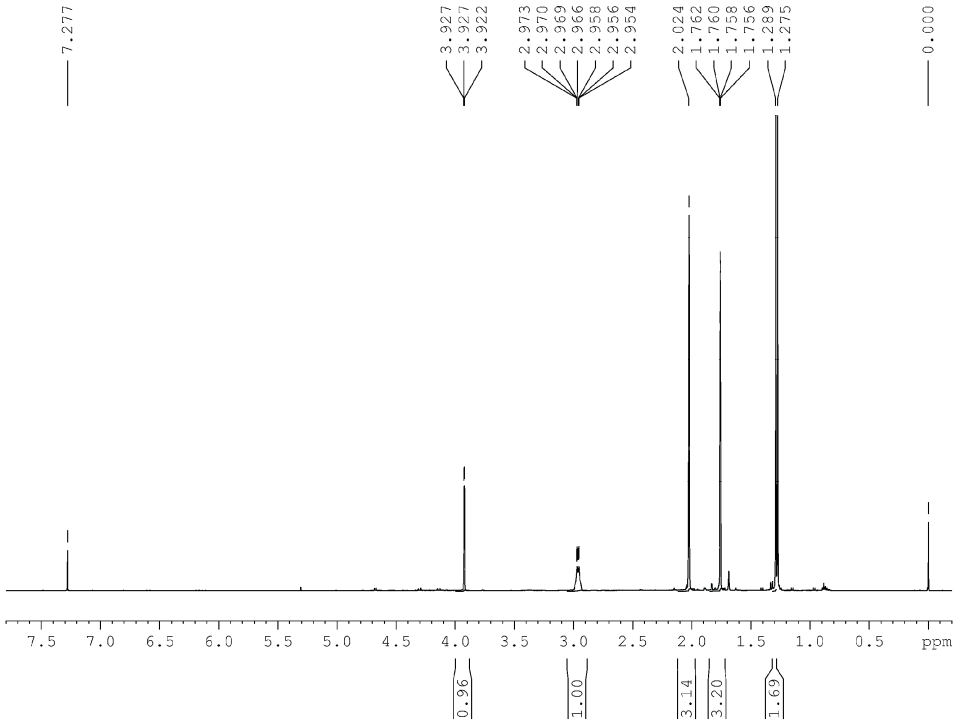
^{1}H NMR ($CDCl_3$, 500 MHz) spectrum of 3-(bromomethyl)-2-methylcyclopent-2-enone (69)



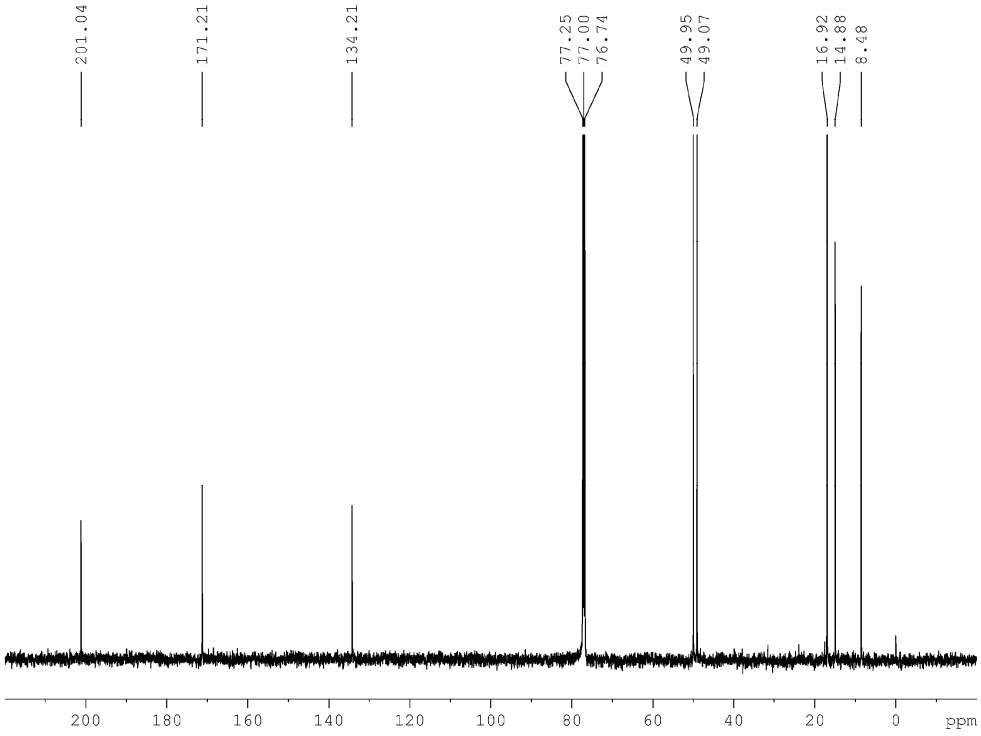
^{13}C NMR ($CDCl_3$, 125 MHz) spectrum of 3-(bromomethyl)-2-methylcyclopent-2-enone (69)



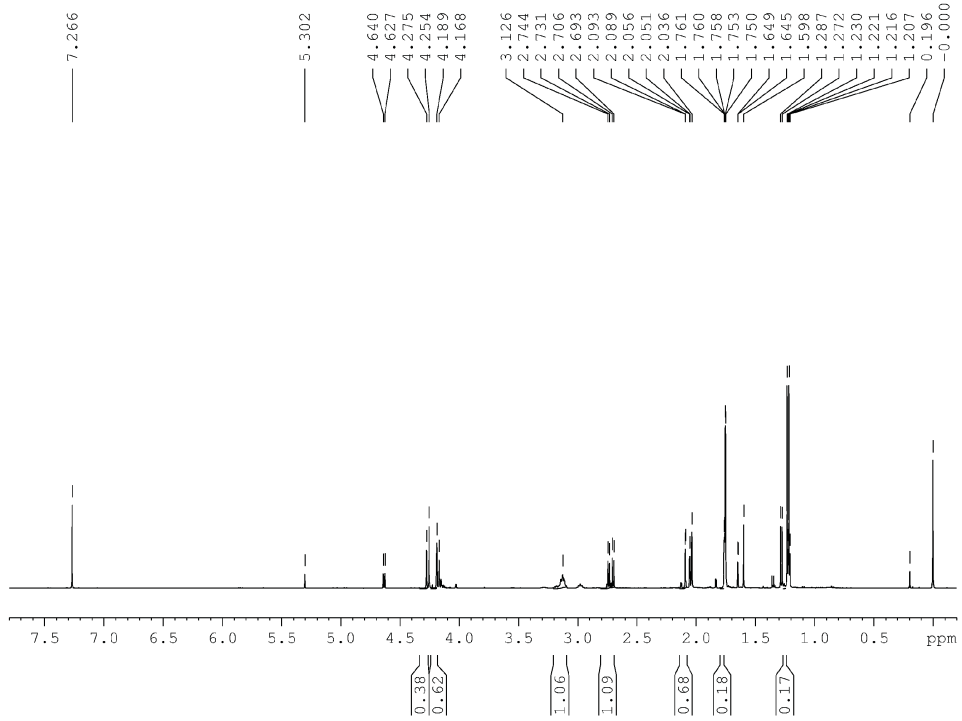
^{1}H NMR ($CDCl_3$, 500 MHz) spectrum of *trans*-5-bromo-4-methyl-2,3-dimethylcyclopent-2-enone (70)



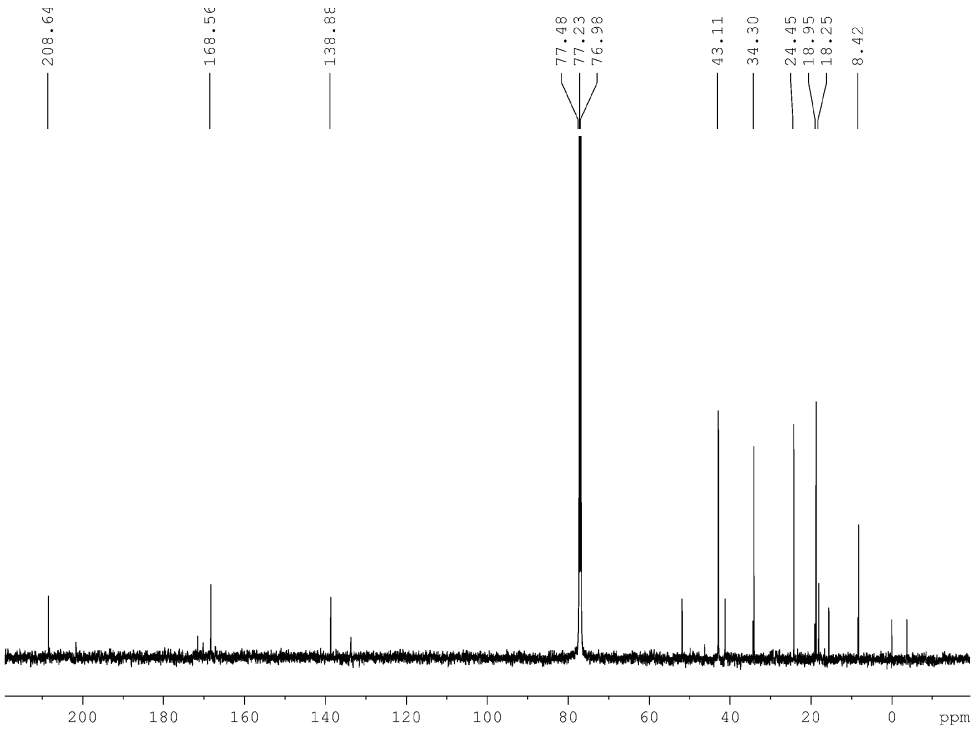
^{13}C NMR ($CDCl_3$, 125 MHz) spectrum of *trans*-5-bromo-4-methyl-2,3-dimethylcyclopent-2-enone (70)



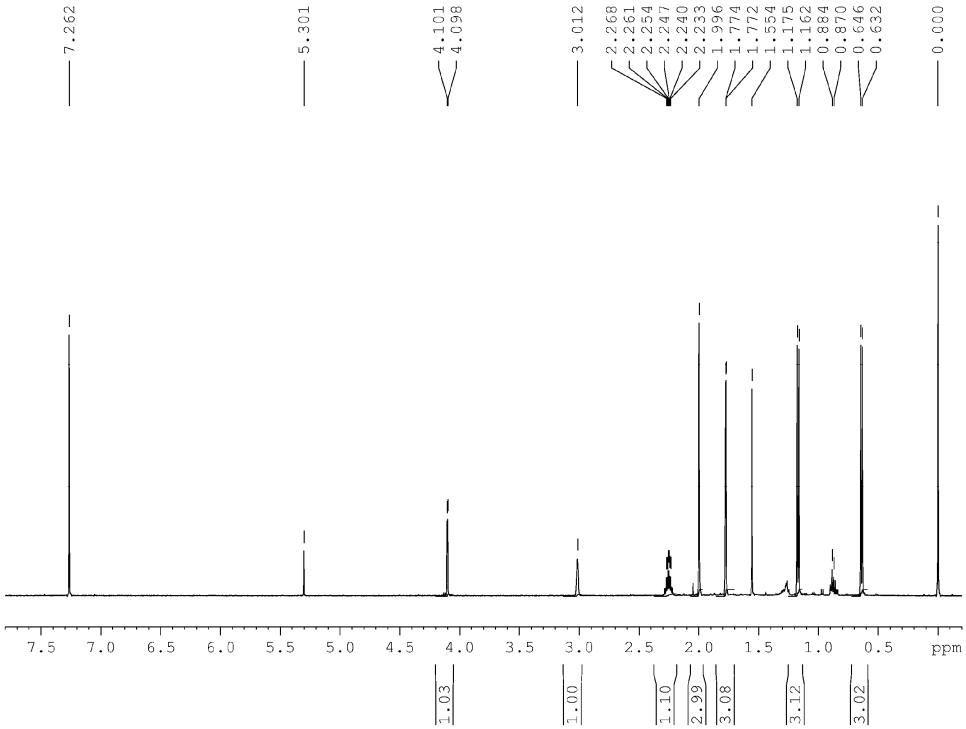
^{1}H NMR ($CDCl_3$, 500 MHz) spectrum of 3-(bromomethyl)-2,4-dimethylcyclopent-2-enone (71)



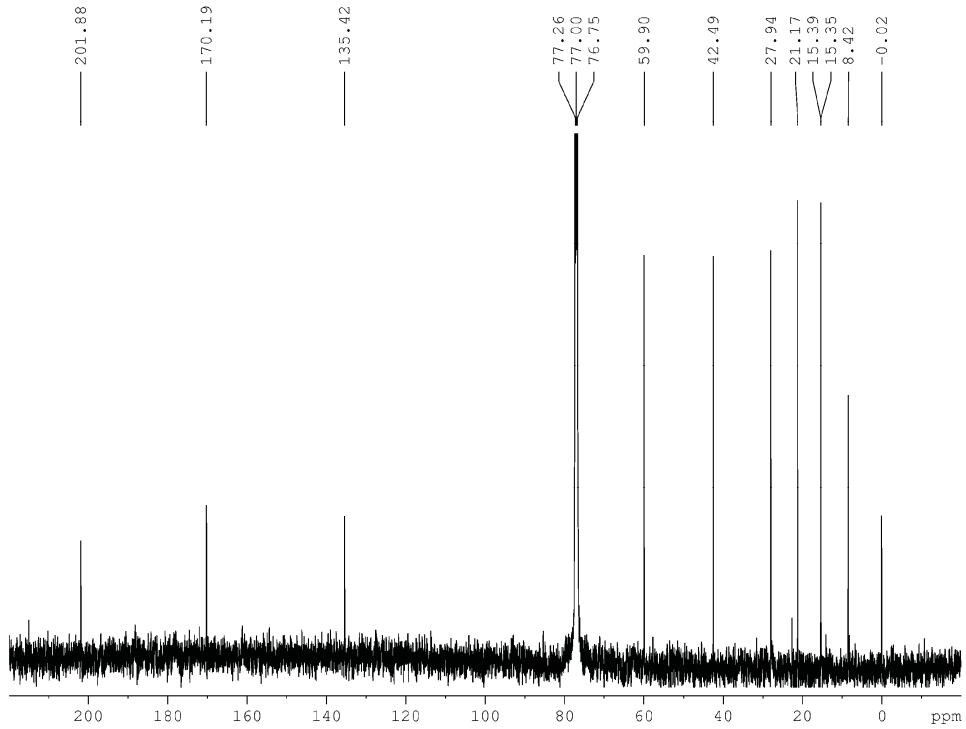
^{13}C NMR ($CDCl_3$, 125 MHz) spectrum of 3-(bromomethyl)-2,4-dimethylcyclopent-2-enone (71)



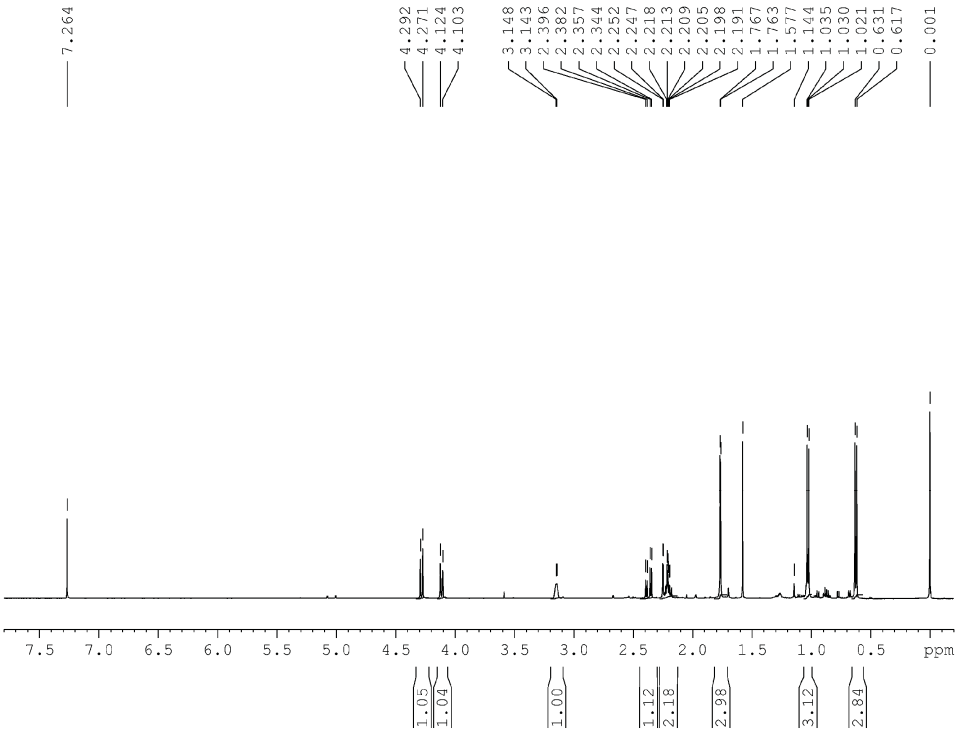
^{1}H NMR ($CDCl_3$, 500 MHz) spectrum of *trans*-5-bromo-4-isopropyl-2,3-dimethylcyclopent-2-enone (72)



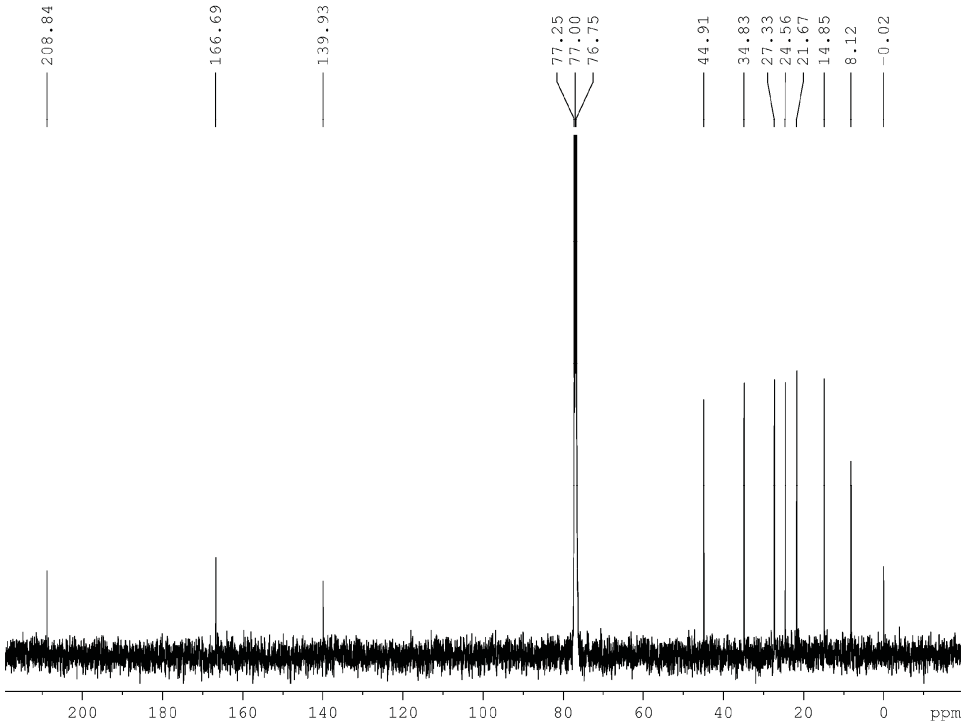
^{13}C NMR ($CDCl_3$, 125 MHz) spectrum of *trans*-5-bromo-4-isopropyl-2,3-dimethylcyclopent-2-enone (72)



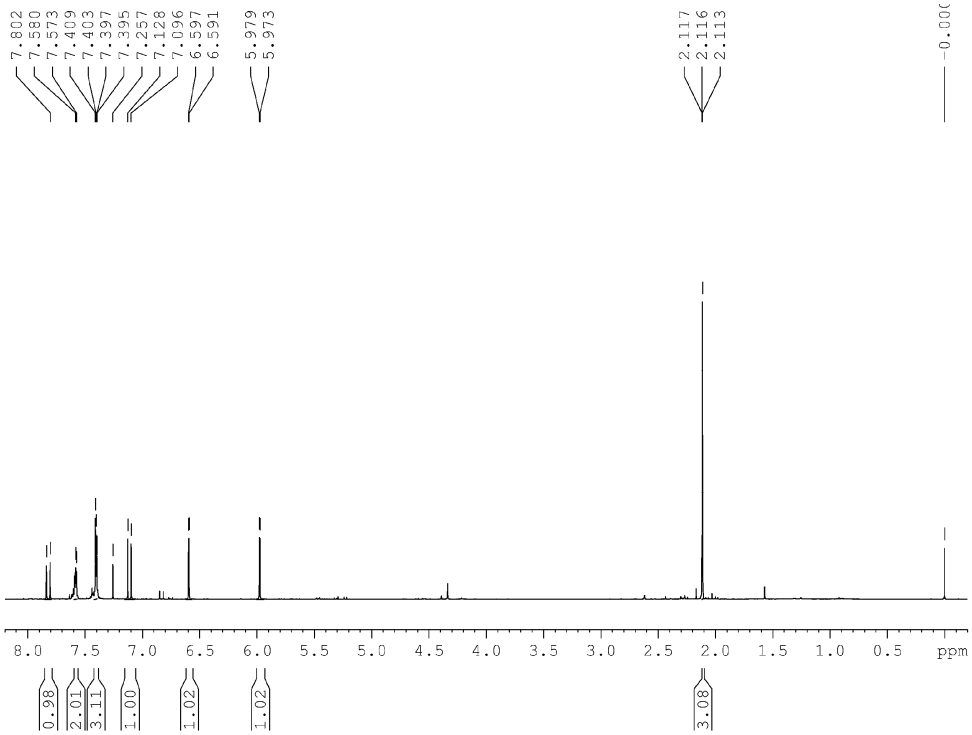
^{1}H NMR ($CDCl_3$, 500 MHz) spectrum of 3-(bromomethyl)-4-isopropyl-2-methylcyclopent-2-enone (73)



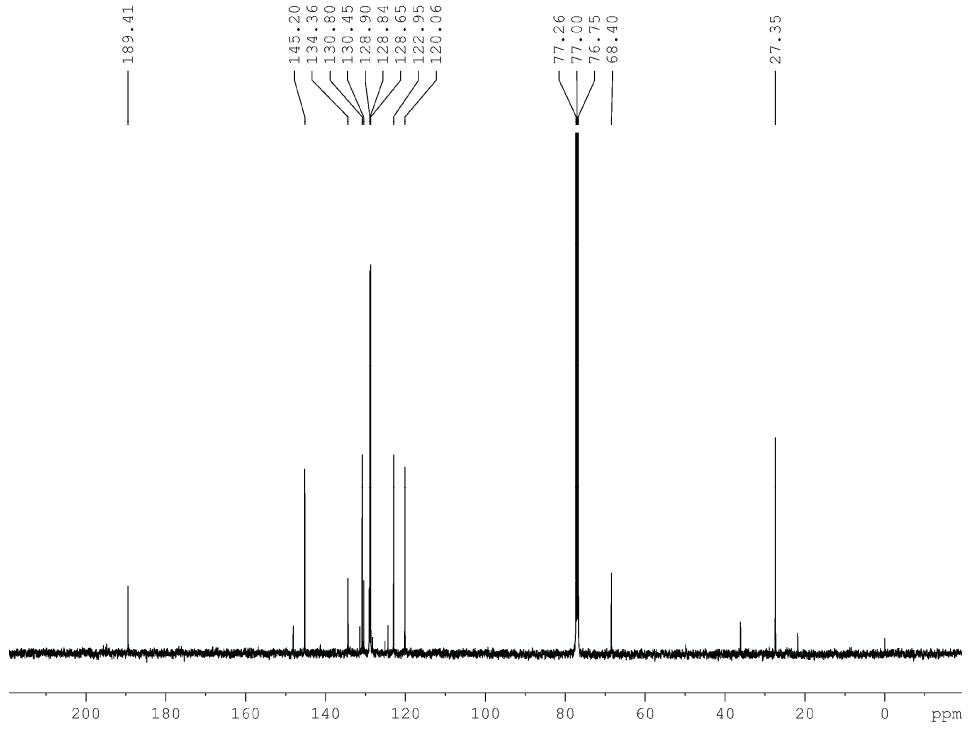
^{13}C NMR ($CDCl_3$, 125 MHz) spectrum of 3-(bromomethyl)-4-isopropyl-2-methylcyclopent-2-enone (73)



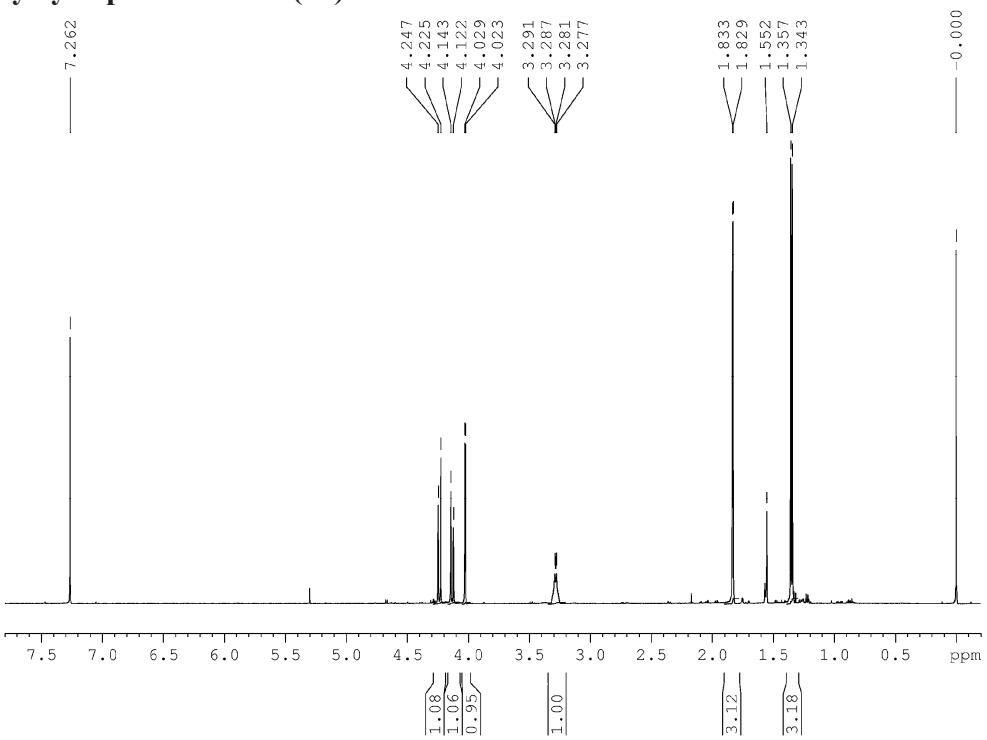
^{1}H NMR ($CDCl_3$, 500 MHz) spectrum of (*E*)-4,5-dibromo-4-methyl-1-phenylhexa-1,5-dien-3-one (74)



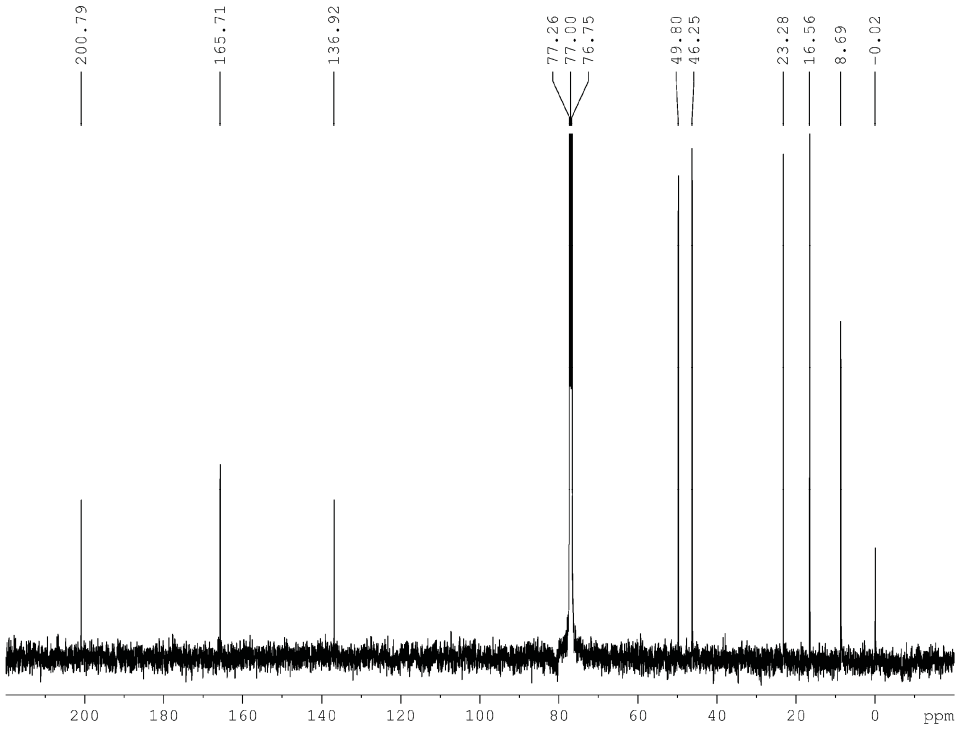
^{13}C NMR ($CDCl_3$, 125 MHz) spectrum of (*E*)-4,5-dibromo-4-methyl-1-phenylhexa-1,5-dien-3-one (74)



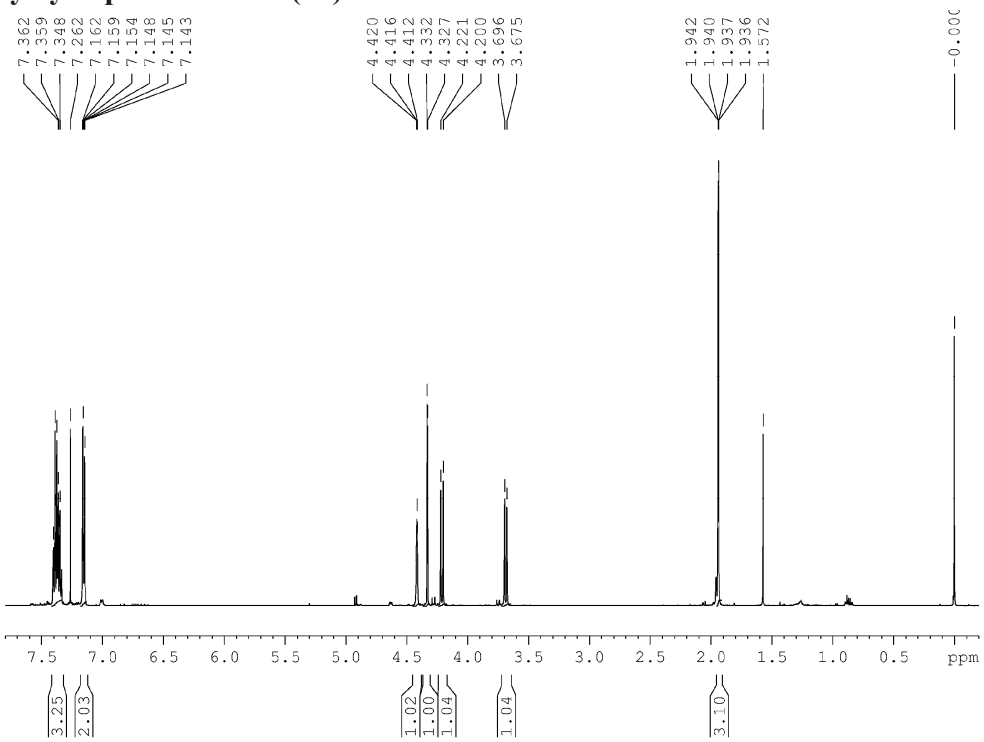
^{1}H NMR ($CDCl_3$, 500 MHz) spectrum of *trans*-5-bromo-3-(bromomethyl)-2,4-dimethylcyclopent-2-enone (75)



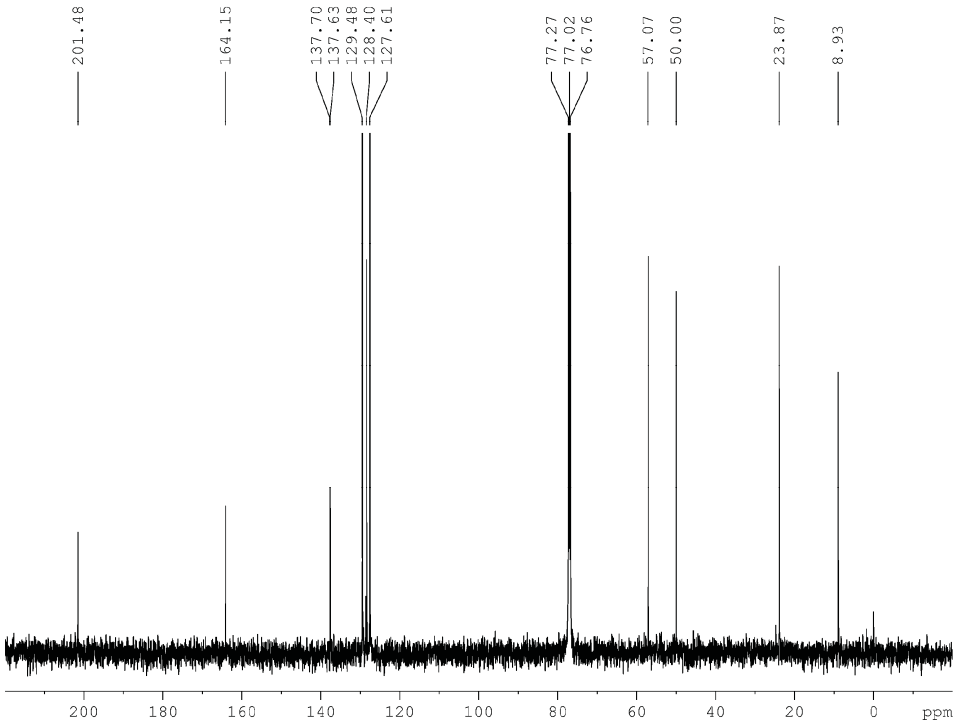
^{13}C NMR ($CDCl_3$, 125 MHz) spectrum of *trans*-5-bromo-3-(bromomethyl)-2,4-dimethylcyclopent-2-enone (75)



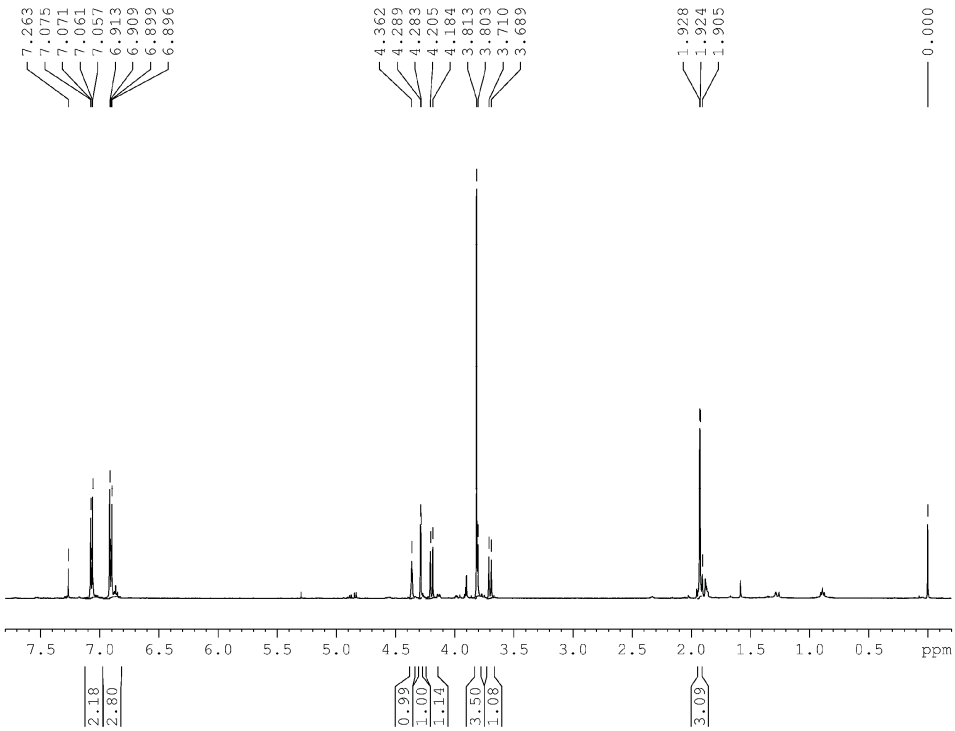
^{1}H NMR ($CDCl_3$, 500 MHz) spectrum of *trans*-5-bromo-3-(bromomethyl)-2-methyl-4-phenylcyclopent-2-enone (76)



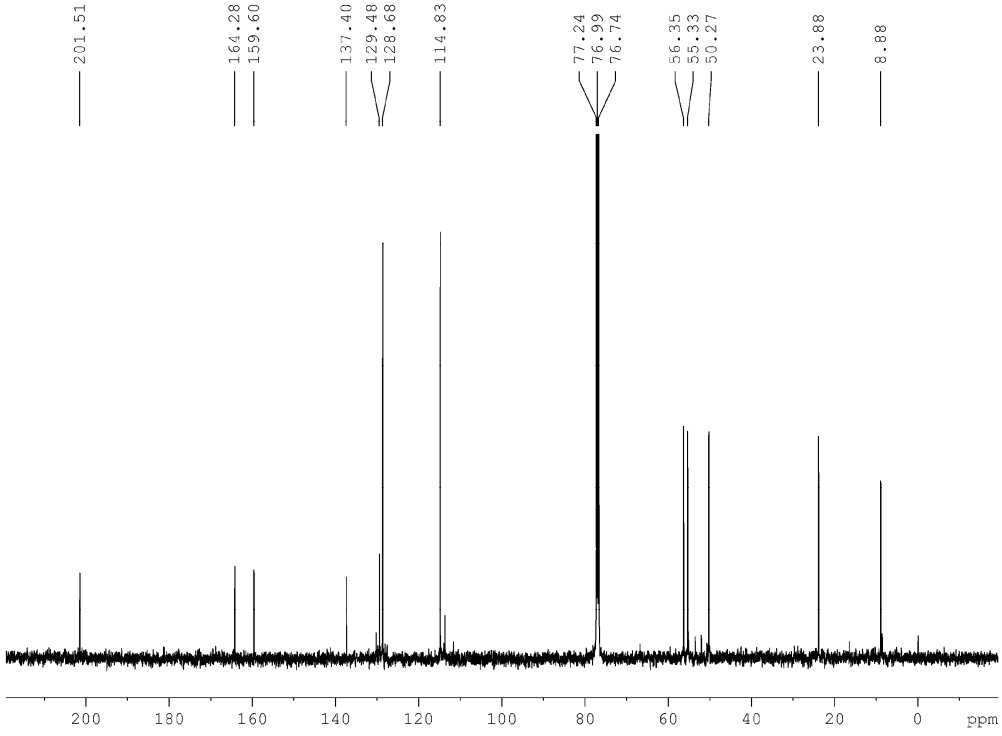
^{13}C NMR ($CDCl_3$, 125 MHz) spectrum of *trans*-5-bromo-3-(bromomethyl)-2-methyl-4-phenylcyclopent-2-enone (76)



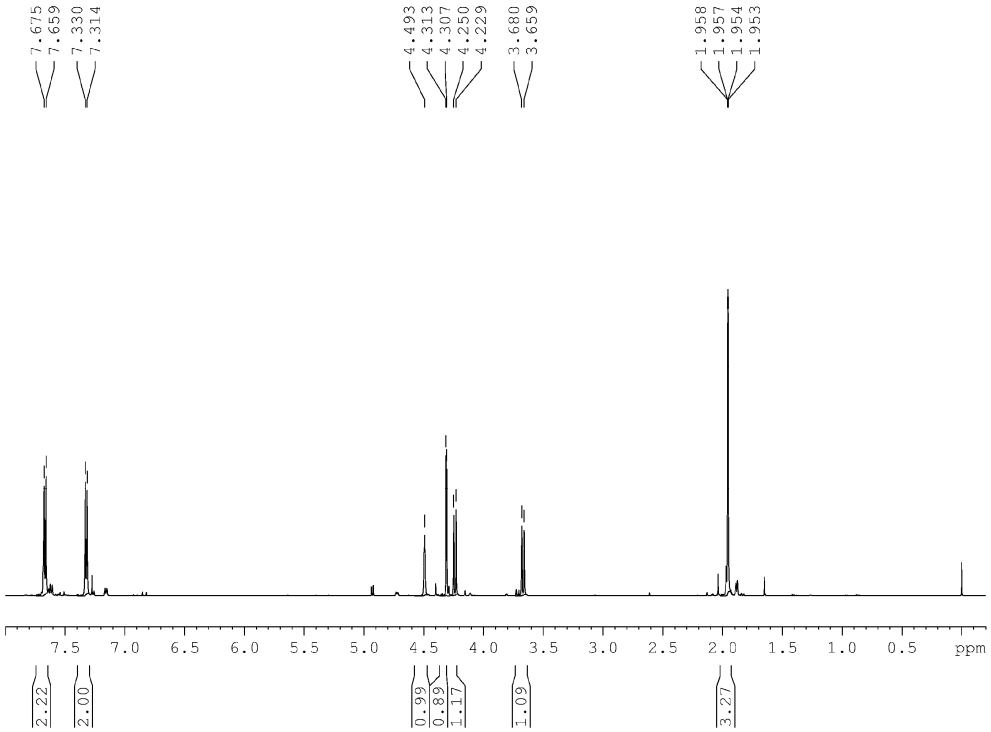
^{1}H NMR ($CDCl_3$, 500 MHz) spectrum of *trans*-5-bromo-3-(bromomethyl)-4-(4-methoxy-phenyl)-2-methylcyclopent-2-enone (77)



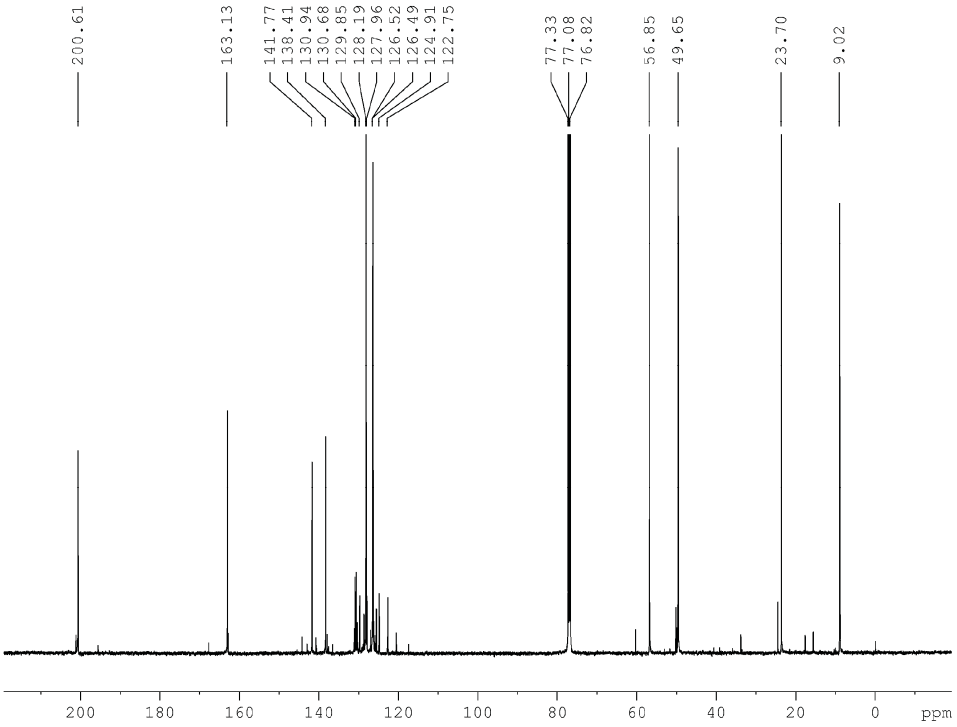
^{13}C NMR ($CDCl_3$, 125 MHz) spectrum of *trans*-5-bromo-3-(bromomethyl)-4-(4-methoxy-phenyl)-2-methylcyclopent-2-enone (77)



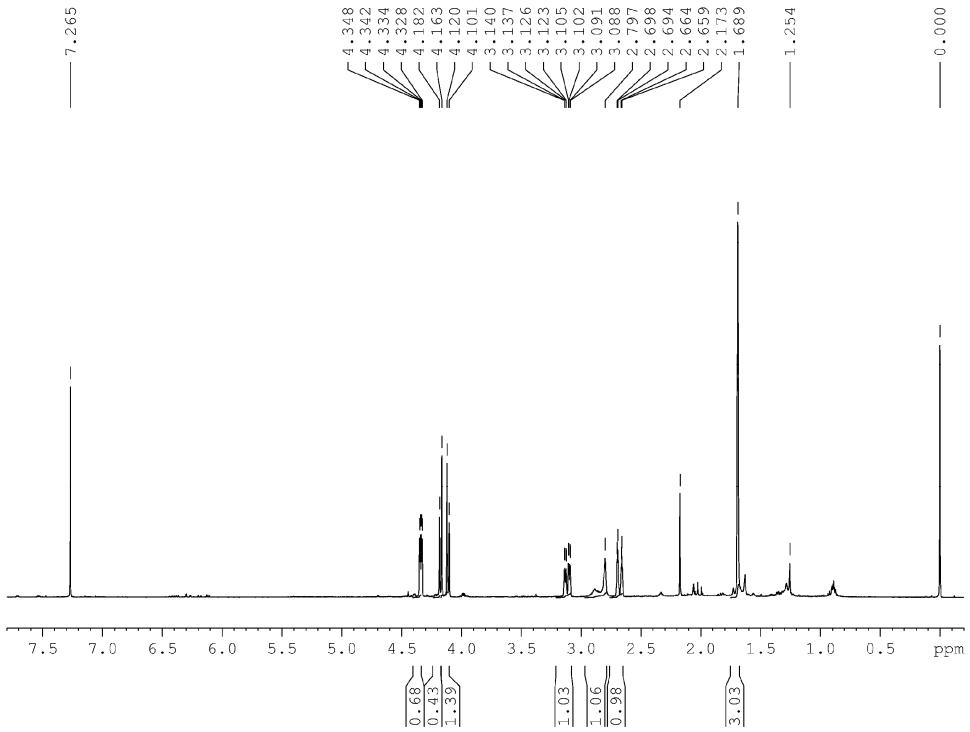
^{1}H NMR ($CDCl_3$, 500 MHz) spectrum of *trans*-5-bromo-3-(bromomethyl)-2-methyl-4-(4- (trifluoromethyl)phenyl)cyclopent-2-enone (78)



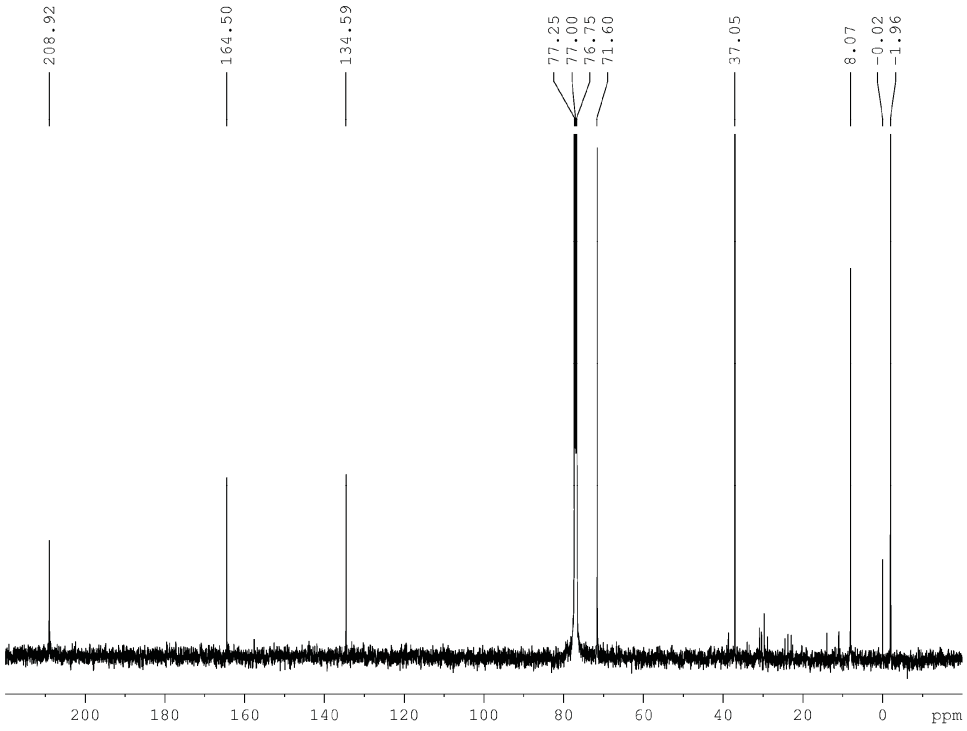
^{13}C NMR ($CDCl_3$, 125 MHz) spectrum of *trans*-5-bromo-3-(bromomethyl)-2-methyl-4-(4- (trifluoromethyl)phenyl)cyclopent-2-enone (78)



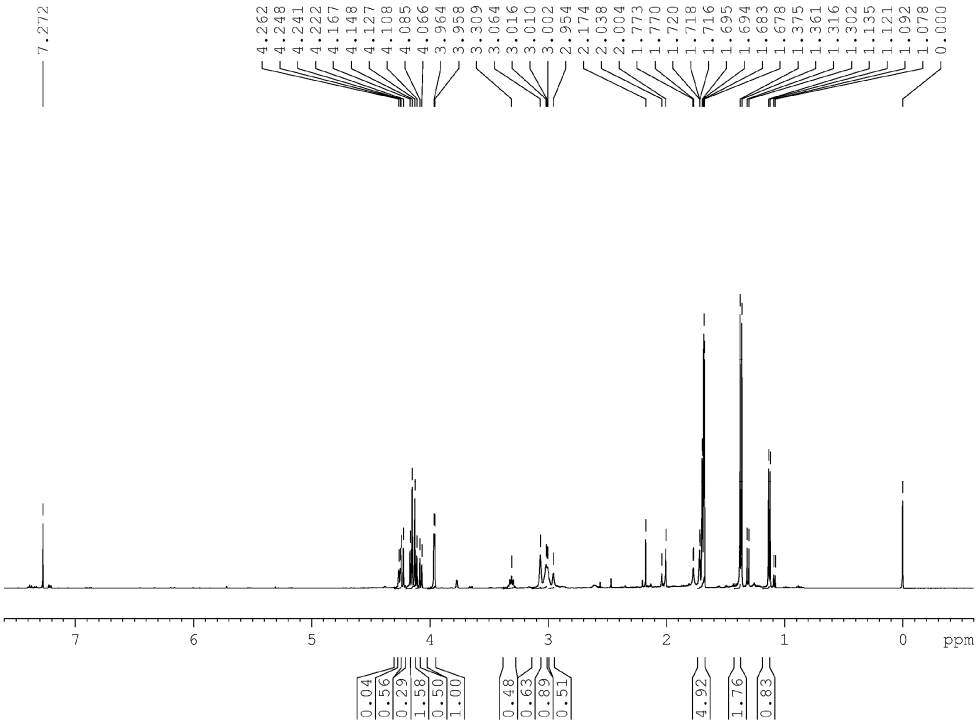
^{1}H NMR ($CDCl_3$, 500 MHz) spectrum of 5-hydroxy-3-(iodomethyl)-2-methylcyclopent-2-enone (79)



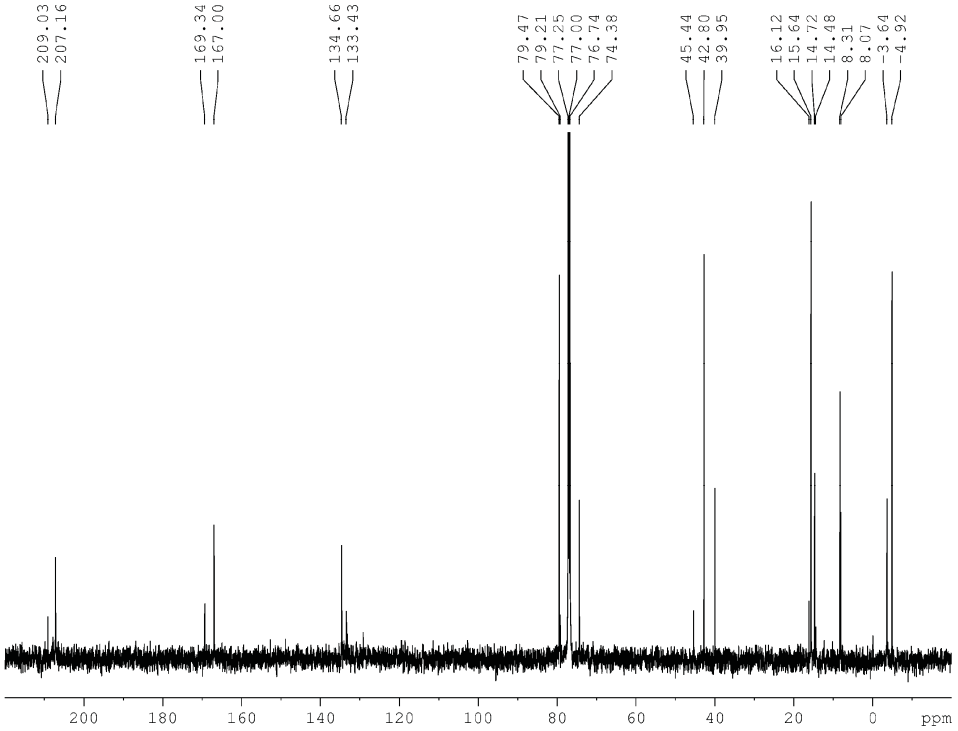
^{13}C NMR ($CDCl_3$, 125 MHz) spectrum of 5-hydroxy-3-(iodomethyl)-2-methylcyclopent-2-enone (79)



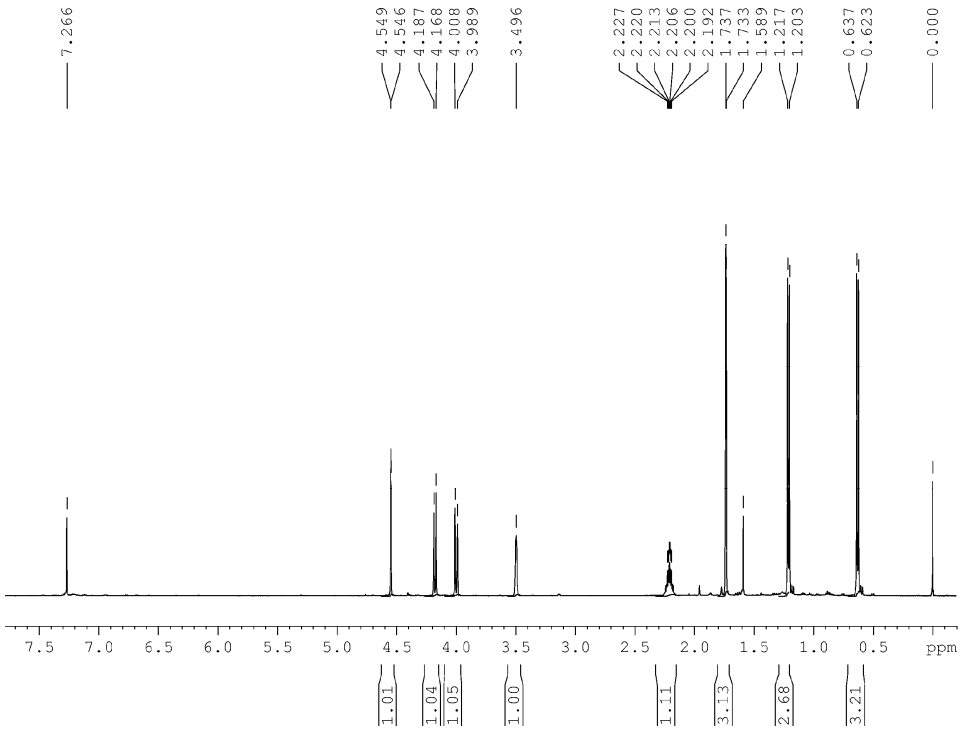
^{1}H NMR ($CDCl_3$, 500 MHz) spectrum of *trans*- (80a) and *cis*-5-hydroxy-3-(iodomethyl)-2,4-dimethylcyclopent-2-enone (80b)



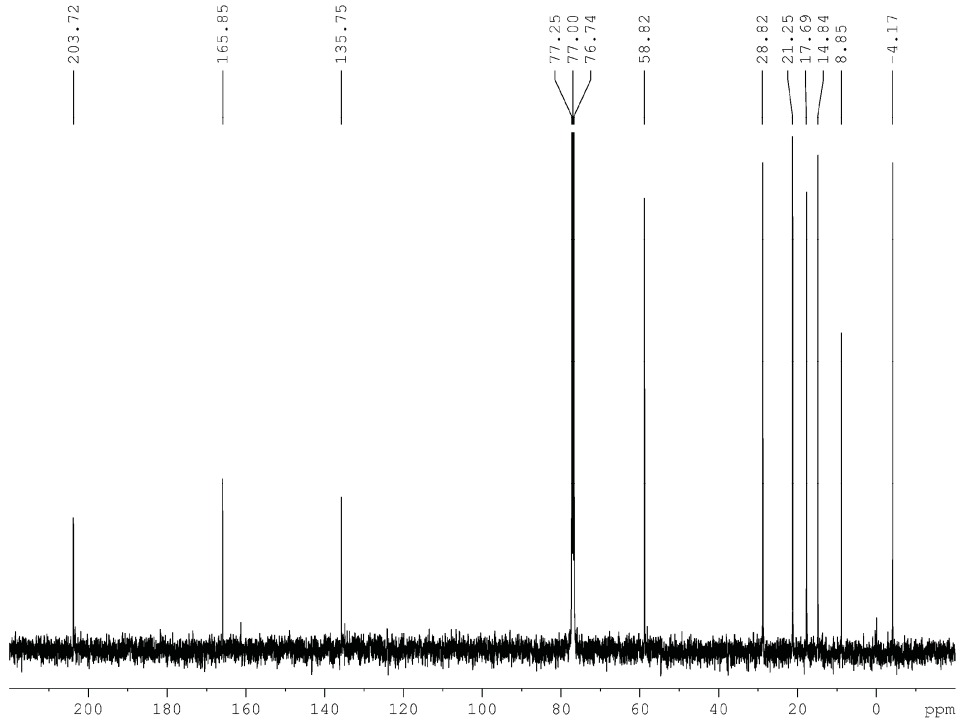
^{13}C NMR ($CDCl_3$, 125 MHz) spectrum of *trans*- (80a) and *cis*-5-hydroxy-3-(iodomethyl)-2,4-dimethylcyclopent-2-enone (80b)



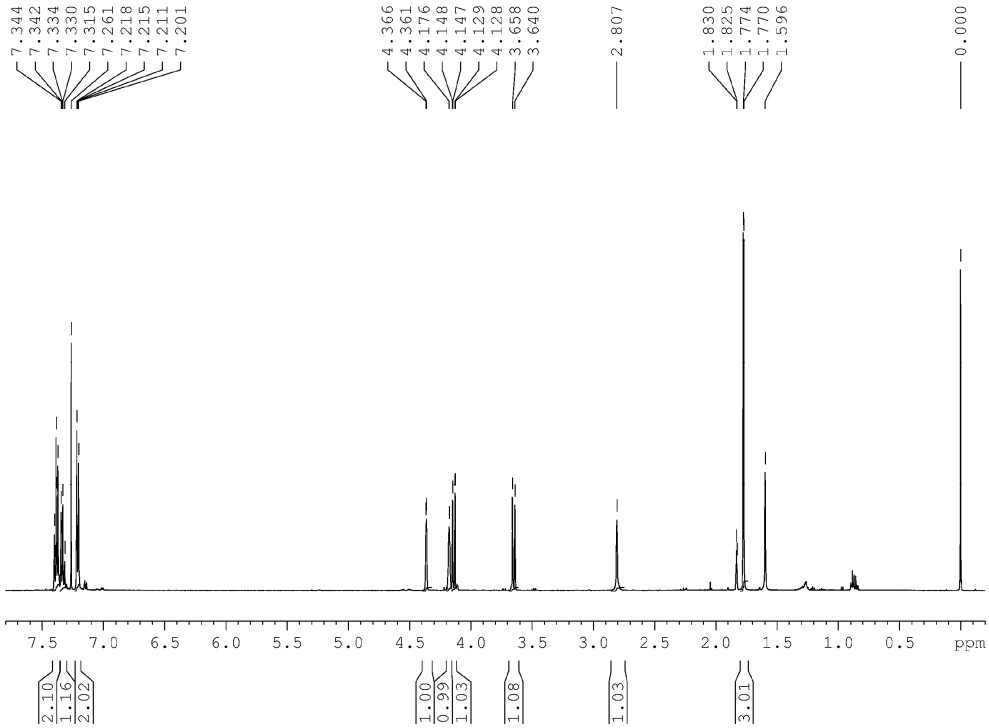
^{1}H NMR ($CDCl_3$, 500 MHz) spectrum of *trans*-5-hydroxy-3-(iodomethyl)-4-isopropyl-2-methylcyclopent-2-enone (81)



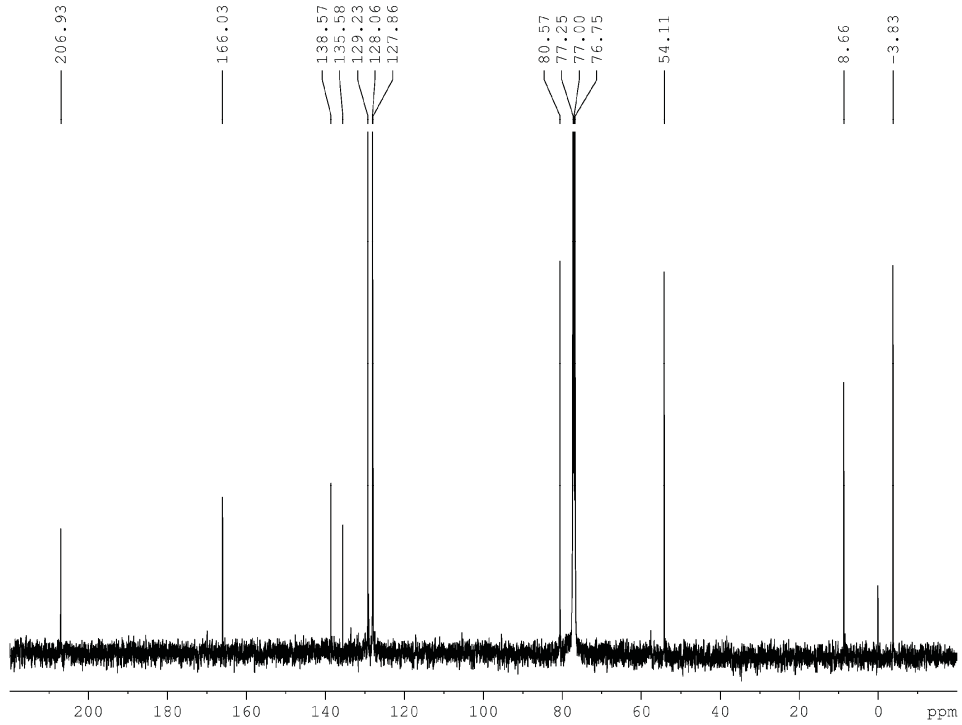
^{13}C NMR ($CDCl_3$, 125 MHz) spectrum of *trans*-5-hydroxy-3-(iodomethyl)-4-isopropyl-2-methylcyclopent-2-enone (81)



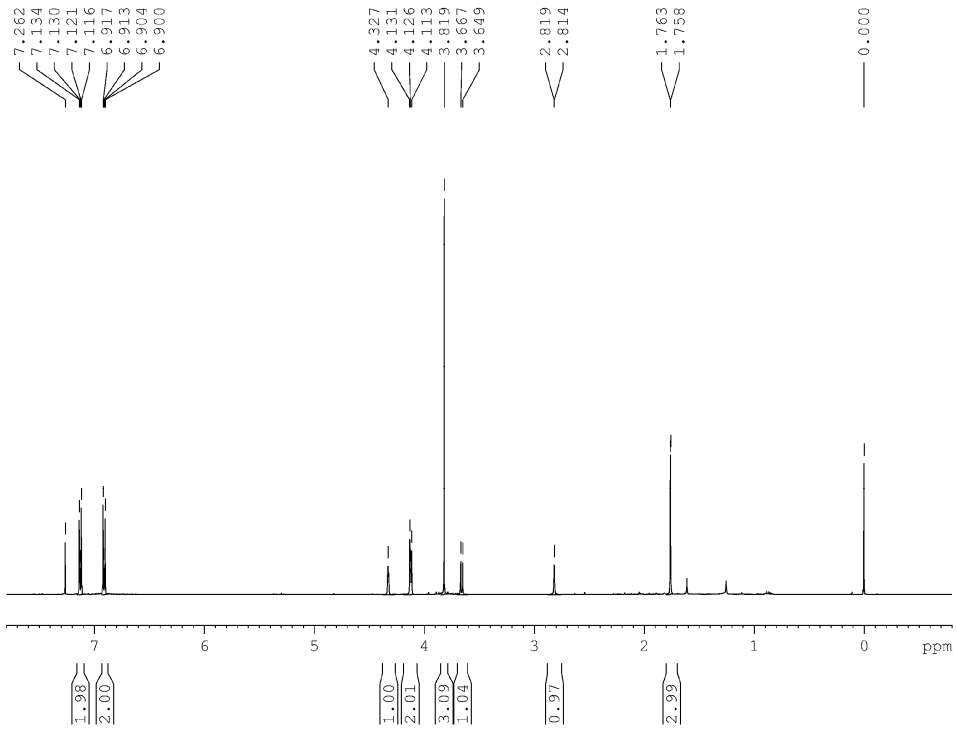
^{1}H NMR ($CDCl_3$, 500 MHz) spectrum of *trans*-5-hydroxy-3-(iodomethyl)-2-methyl-4-phenylcyclopent-2-enone (82)



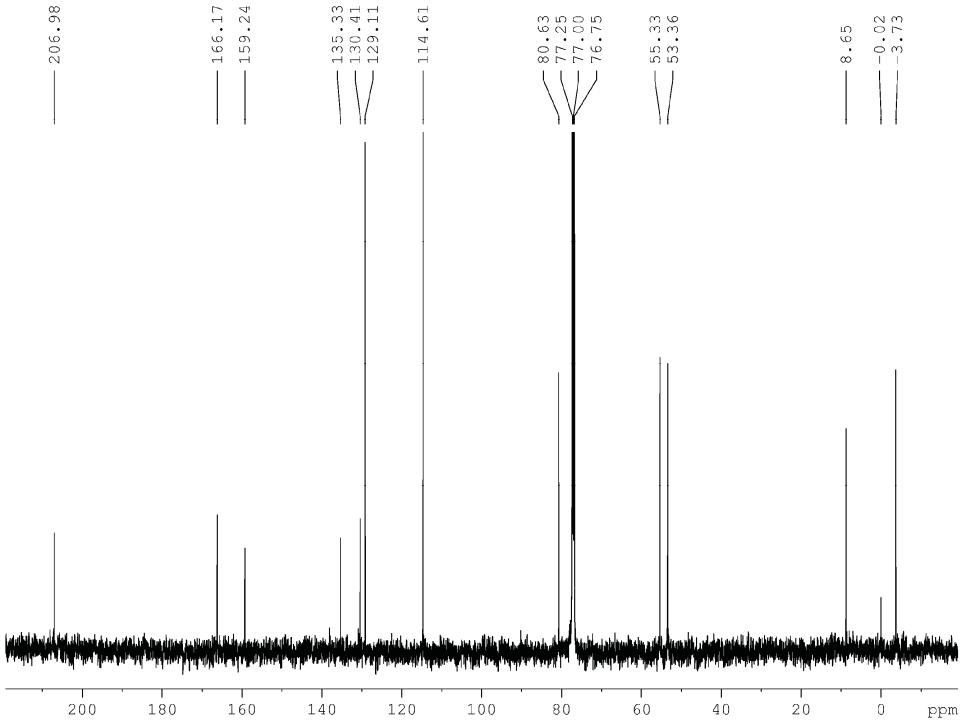
^{13}C NMR ($CDCl_3$, 125 MHz) spectrum of *trans*-5-hydroxy-3-(iodomethyl)-2-methyl-4-phenylcyclopent-2-enone (82)



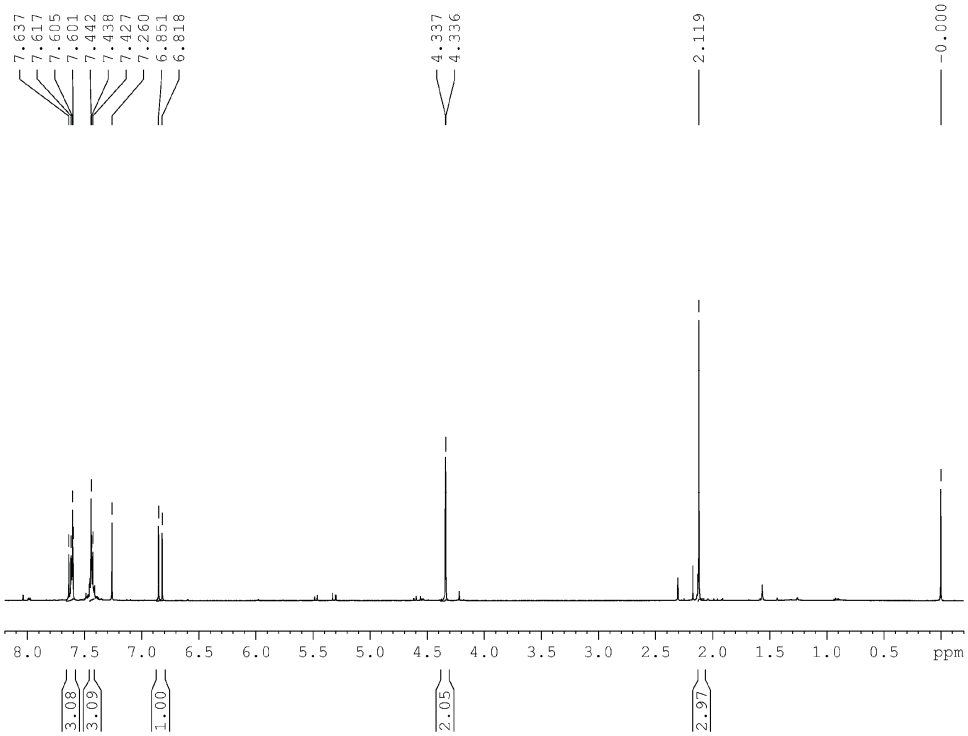
^{1}H NMR ($CDCl_3$, 500 MHz) spectrum of *trans*-5-hydroxy-3-(iodomethyl)-4-(4-methoxy-phenyl)-2-methylcyclopent-2-enone (83)



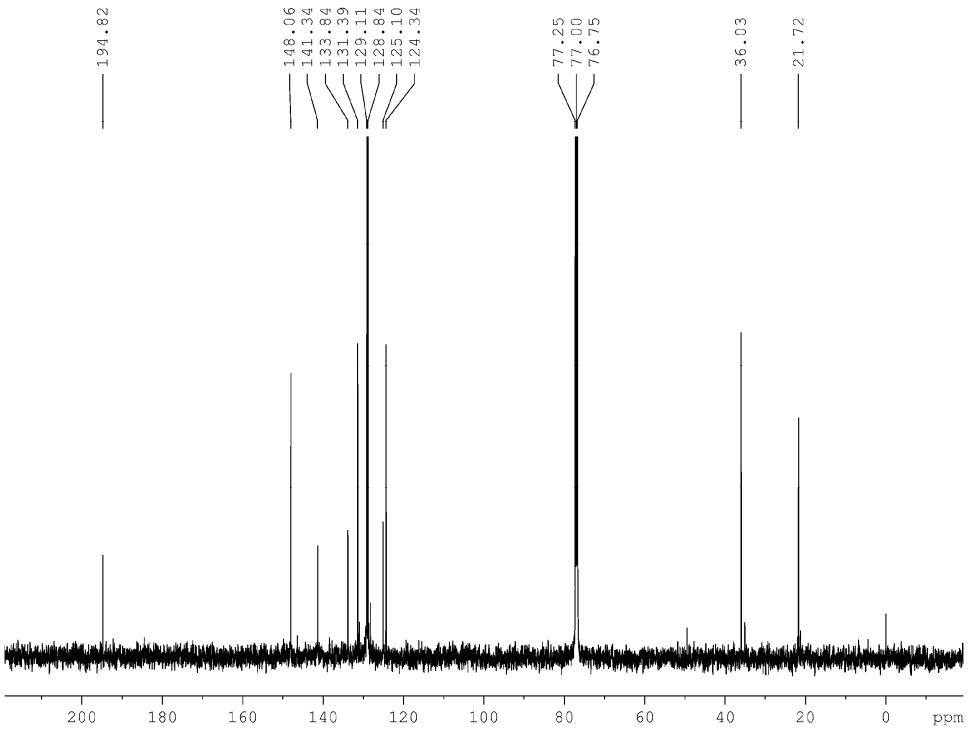
^{13}C NMR ($CDCl_3$, 125 MHz) spectrum of *trans*-5-hydroxy-3-(iodomethyl)-4-(4-methoxy-phenyl)-2-methylcyclopent-2-enone (83)



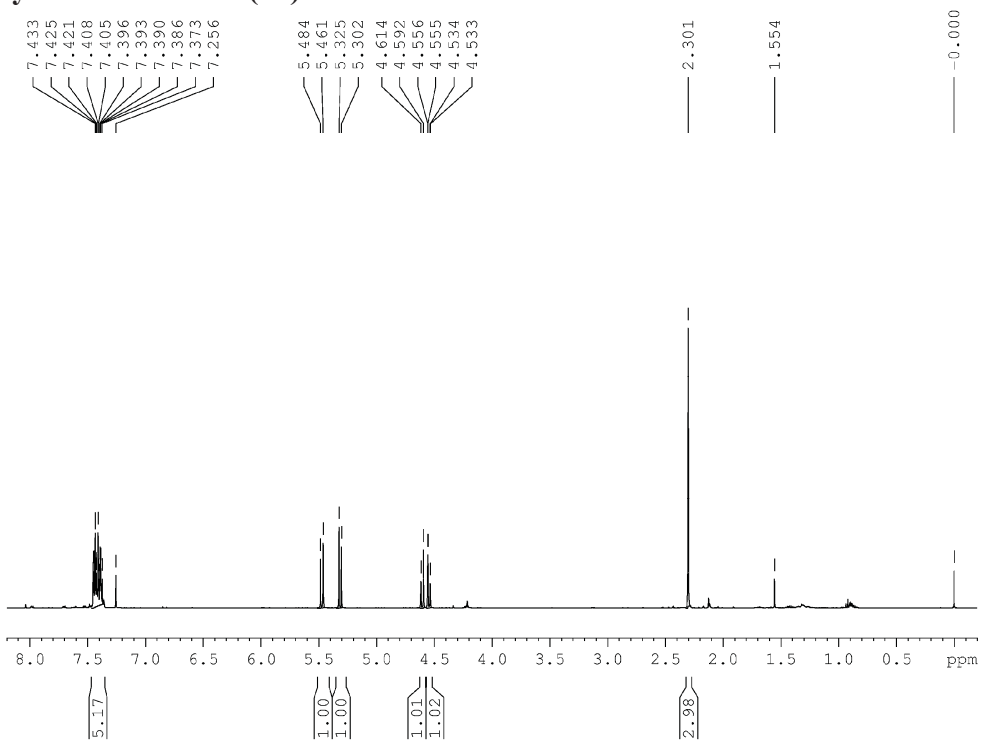
^{1}H NMR ($CDCl_3$, 500 MHz) spectrum of (1*E*,4*E*)-5,6-dibromo-4-methyl-1-phenylhexa-1,4-dien-3-one (84)



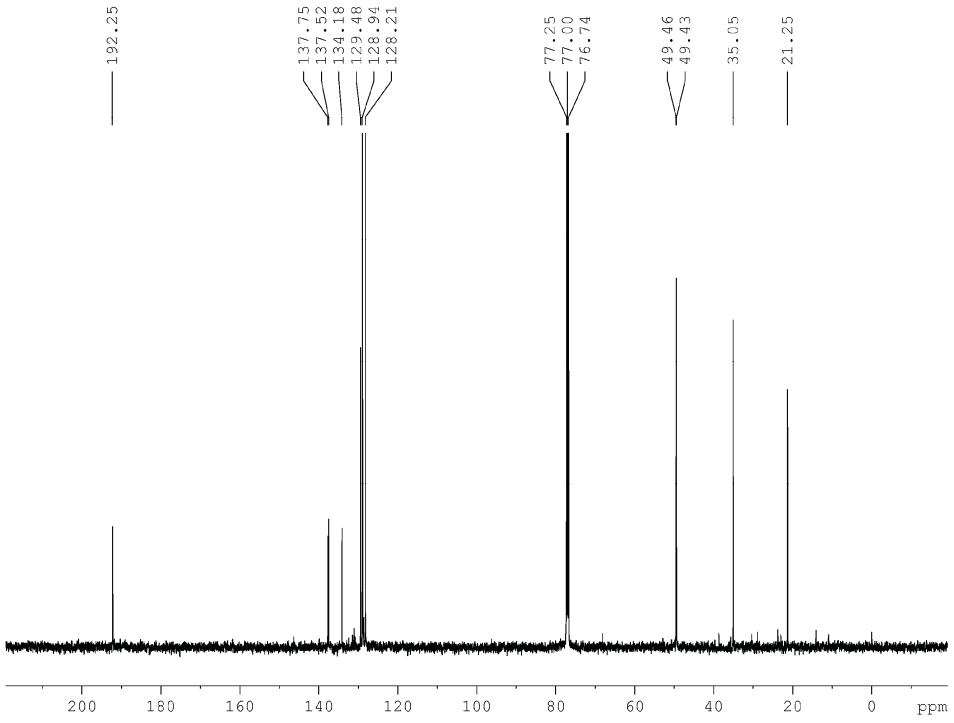
^{13}C NMR ($CDCl_3$, 125 MHz) spectrum of (1*E*,4*E*)-5,6-dibromo-4-methyl-1-phenylhexa-1,4-dien-3-one (84)



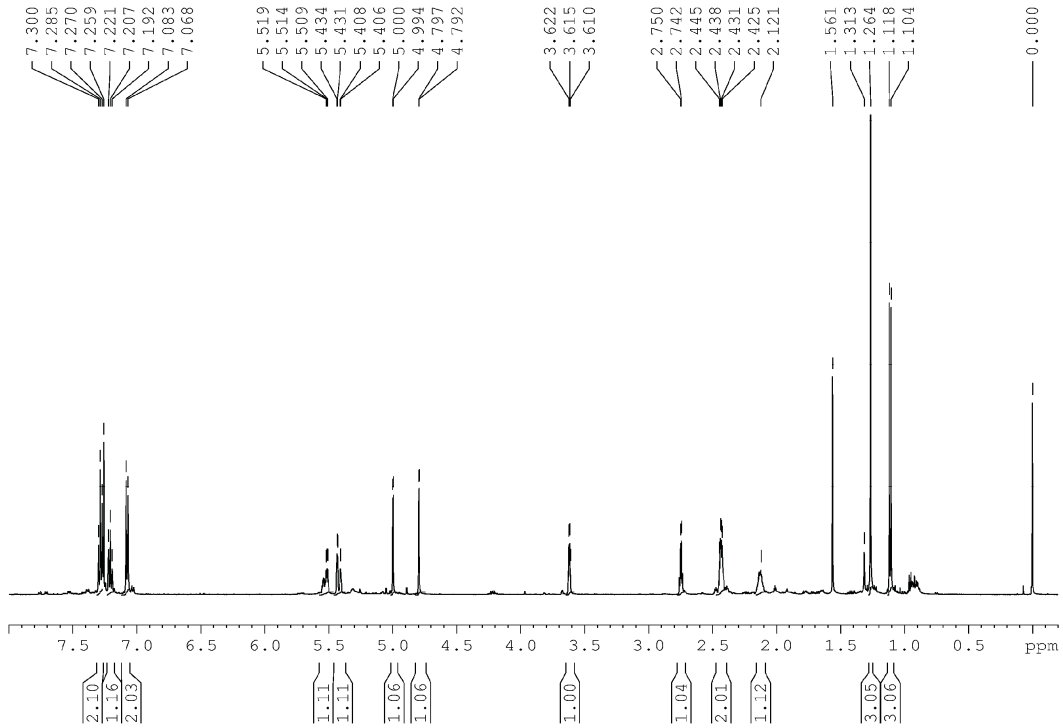
^{1}H NMR ($CDCl_3$, 500 MHz) spectrum of (*erythro*,4*E*)-1,2,5,6-tetrabromo-4-methyl-1-phenylhex-4-en-3-one (85)



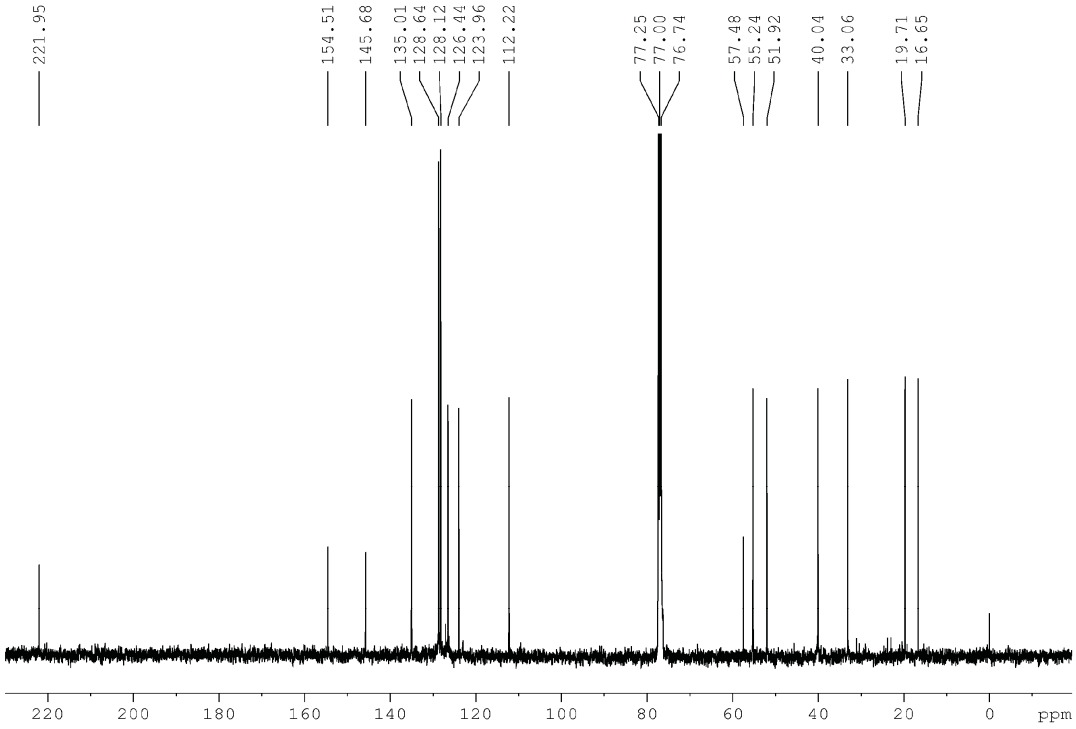
^{13}C NMR ($CDCl_3$, 120 MHz) spectrum of (*erythro*,4*E*)-1,2,5,6-tetrabromo-4-methyl-1-phenylhex-4-en-3-one (85)



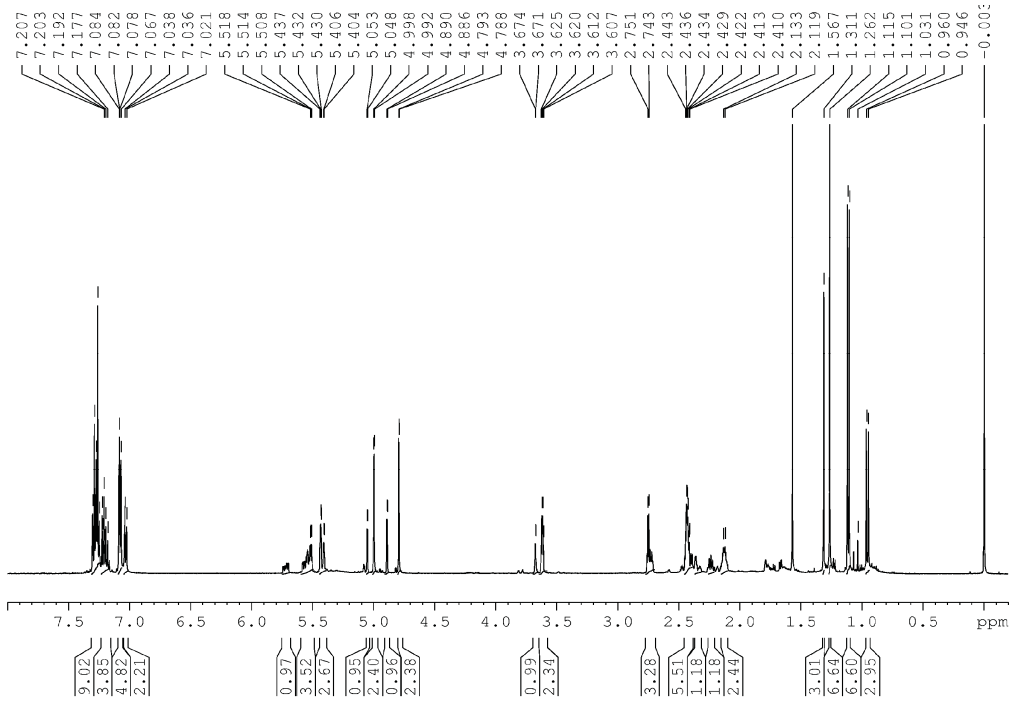
^{1}H NMR ($CDCl_3$, 500 MHz) spectrum of (1*R,2*S**,6*S**,7*R**)-1,2-dimethyl-8-methylene-7-phenylbicyclo[4.2.1]non-3- en-9-one (86a)**



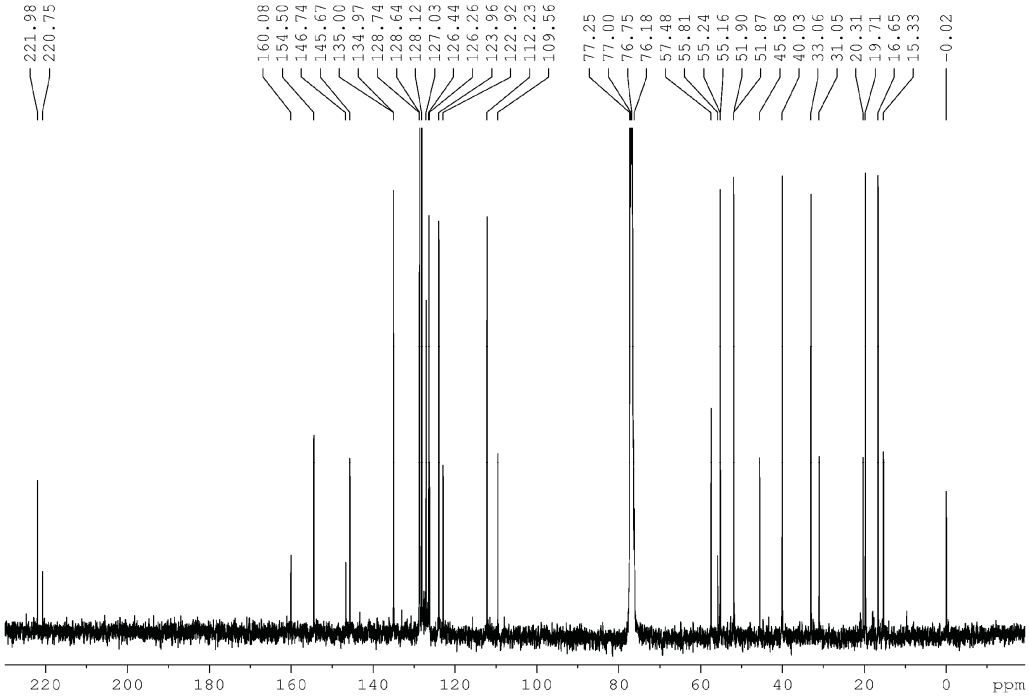
^{13}C NMR ($CDCl_3$, 125 MHz) spectrum of (1*R,2*S**,6*S**,7*R**)-1,2-dimethyl-8-methylene-7-phenylbicyclo[4.2.1]non-3- en-9-one (86a)**



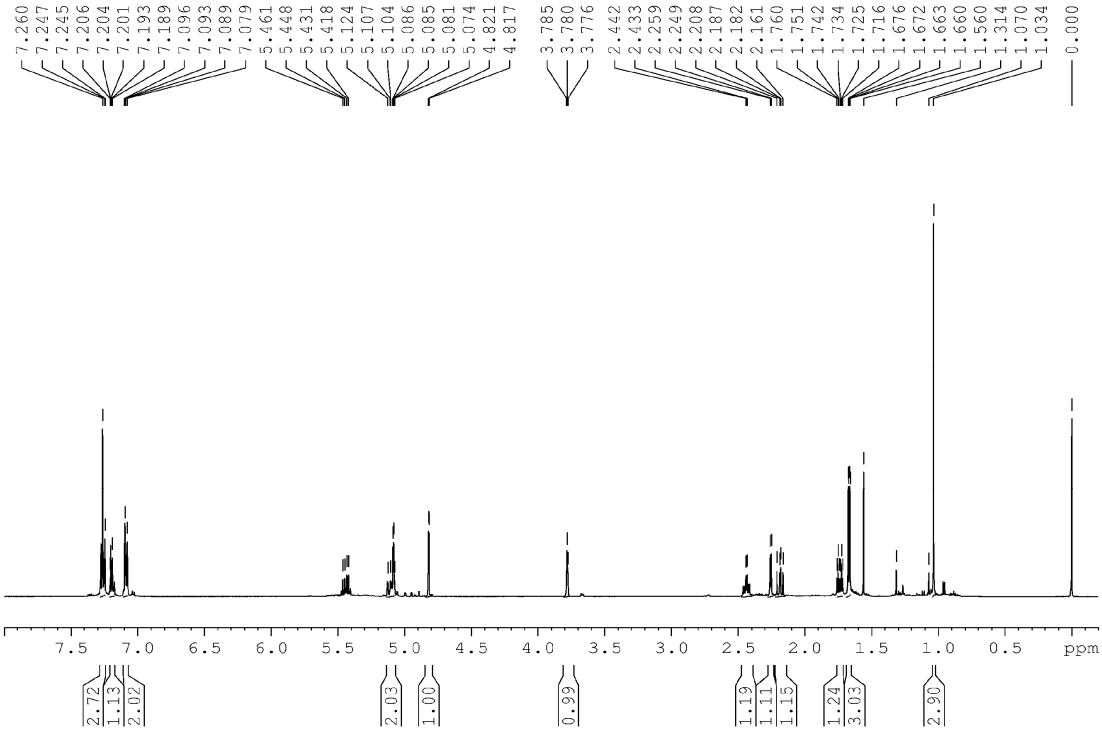
^{1}H NMR ($CDCl_3$, 500 MHz) spectrum of (1*R,2*S**,6*S**,7*R**)-1,2-dimethyl-8-methylene-7-phenylbicyclo[4.2.1]non-3-en-9-one (86a), and (1*R**,2*R**,6*S**,7*R**)-1,2-dimethyl-8-methylene-7-phenylbicyclo[4.2.1]non-3-en-9-one (86b)**



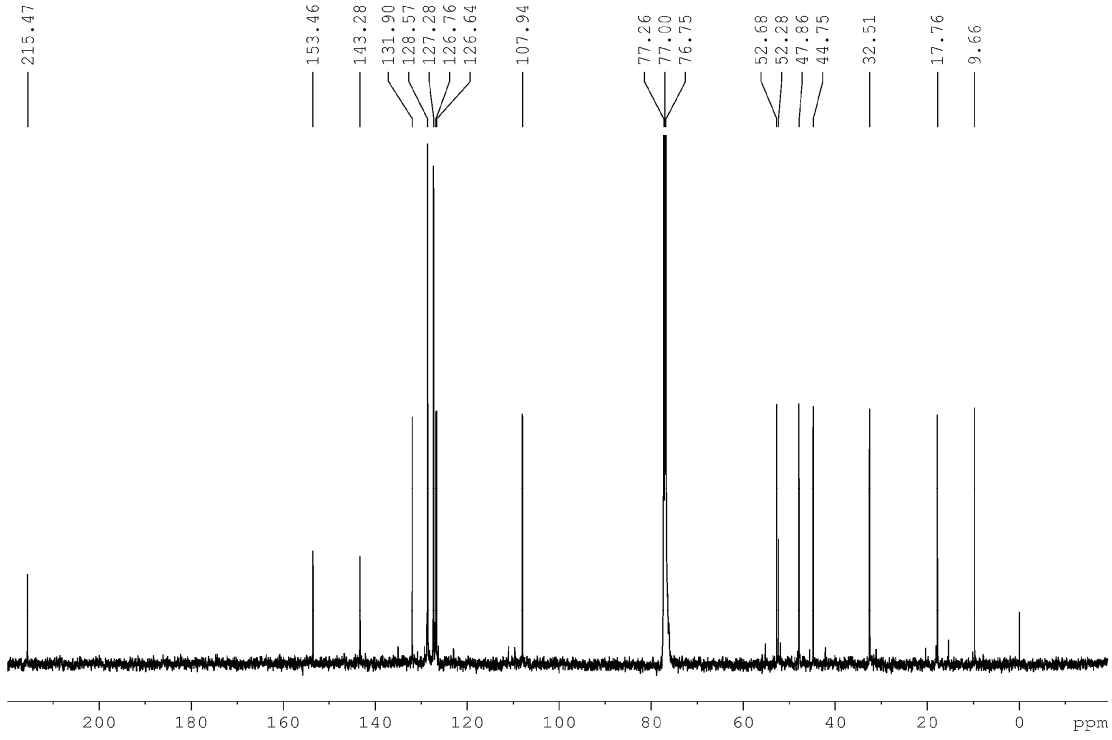
^{13}C NMR ($CDCl_3$, 125 MHz) spectrum of (1*R,2*S**,6*S**,7*R**)-1,2-dimethyl-8-methylene-7-phenylbicyclo[4.2.1]non-3-en-9-one (86a), and (1*R**,2*R**,6*S**,7*R**)-1,2-dimethyl-8-methylene-7-phenylbicyclo[4.2.1]non-3-en-9-one (86b)**



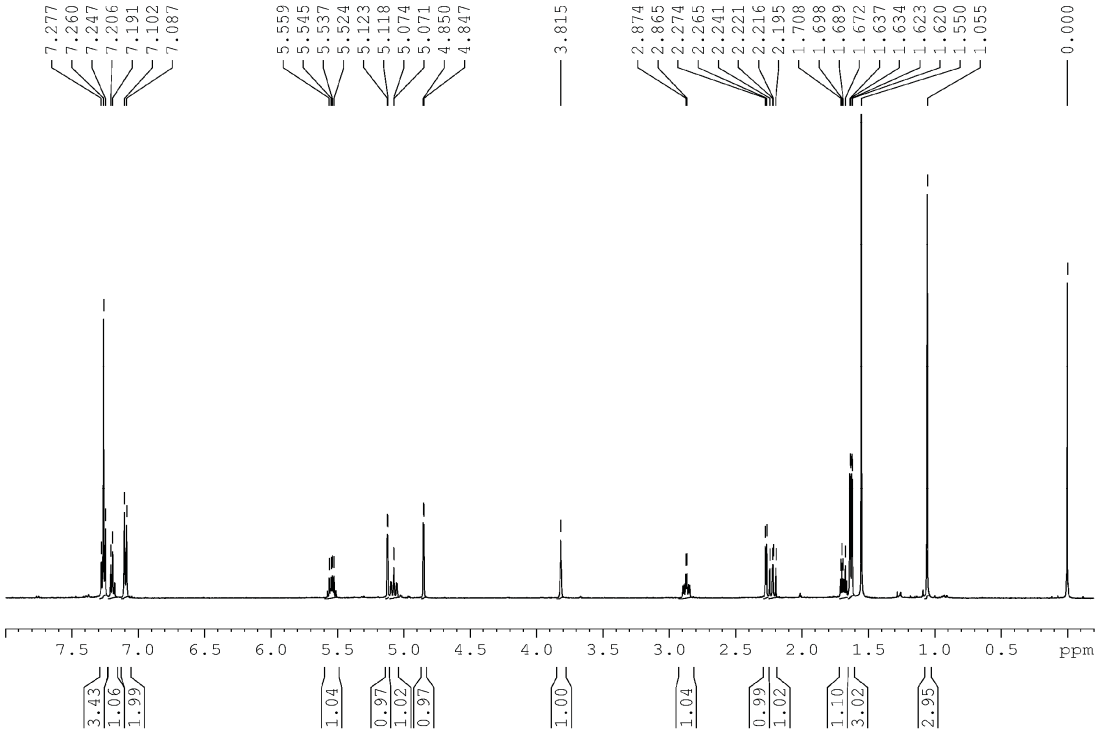
^{1}H NMR ($CDCl_3$, 500 MHz) spectrum of (1*R,3*R**, 4*S**,6*S**)-1-methyl-2-methylene-3-phenyl-6-((*E*)-prop-1-enyl)bicyclo[2.2.1]heptan-7-one (87)**



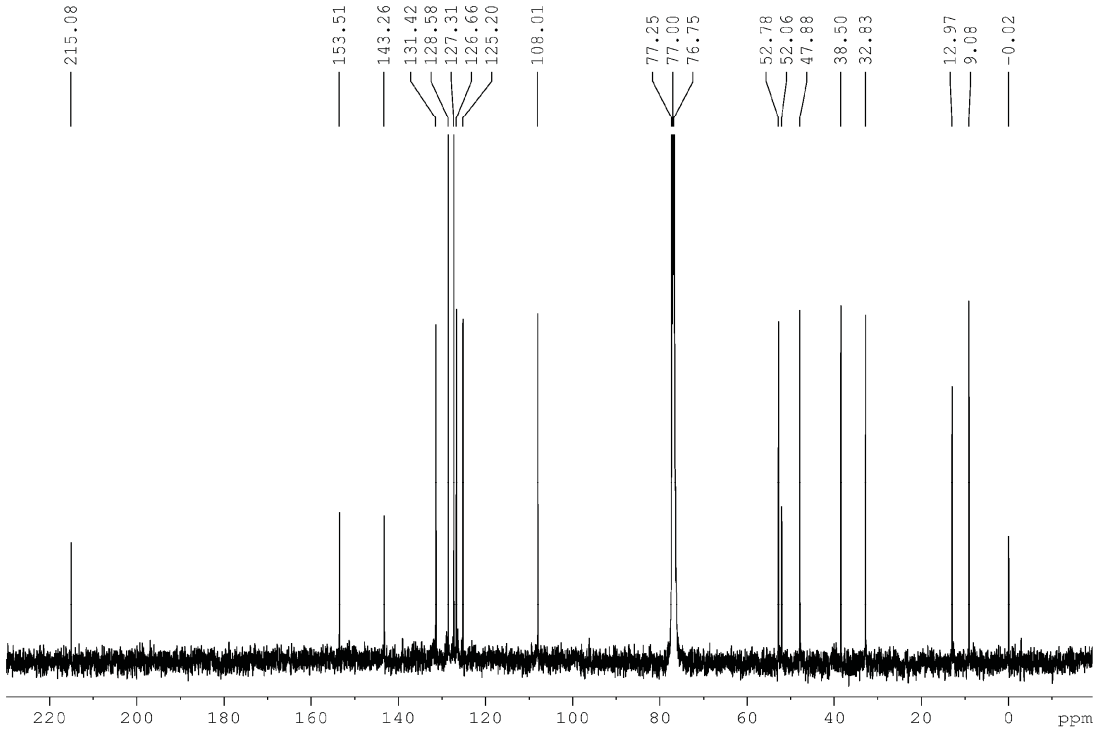
^{13}C NMR ($CDCl_3$, 125 MHz) spectrum of (1*R,3*R**, 4*S**,6*S**)-1-methyl-2-methylene-3-phenyl-6-((*E*)-prop-1-enyl)bicyclo[2.2.1]heptan-7-one (87)**



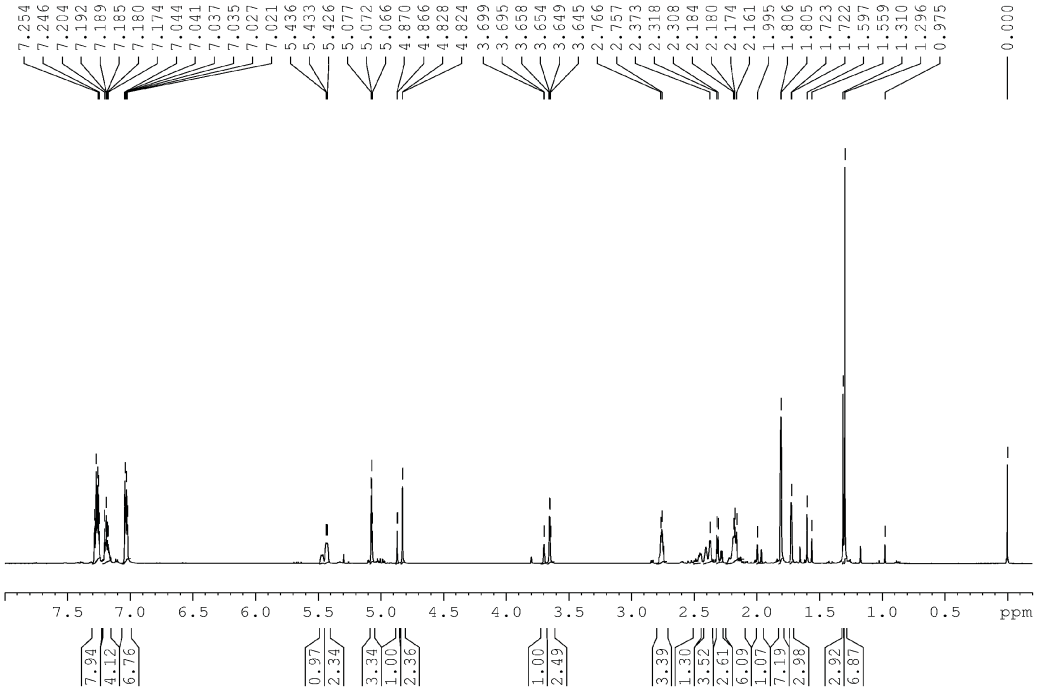
^{1}H NMR ($CDCl_3$, 500 MHz) spectrum of (1*R,3*R**,4*S**,6*S**)-1-methyl-2-methylene-3-phenyl-6-((*Z*)-prop-1-enyl)bicyclo[2.2.1]heptan-7-one (88)**



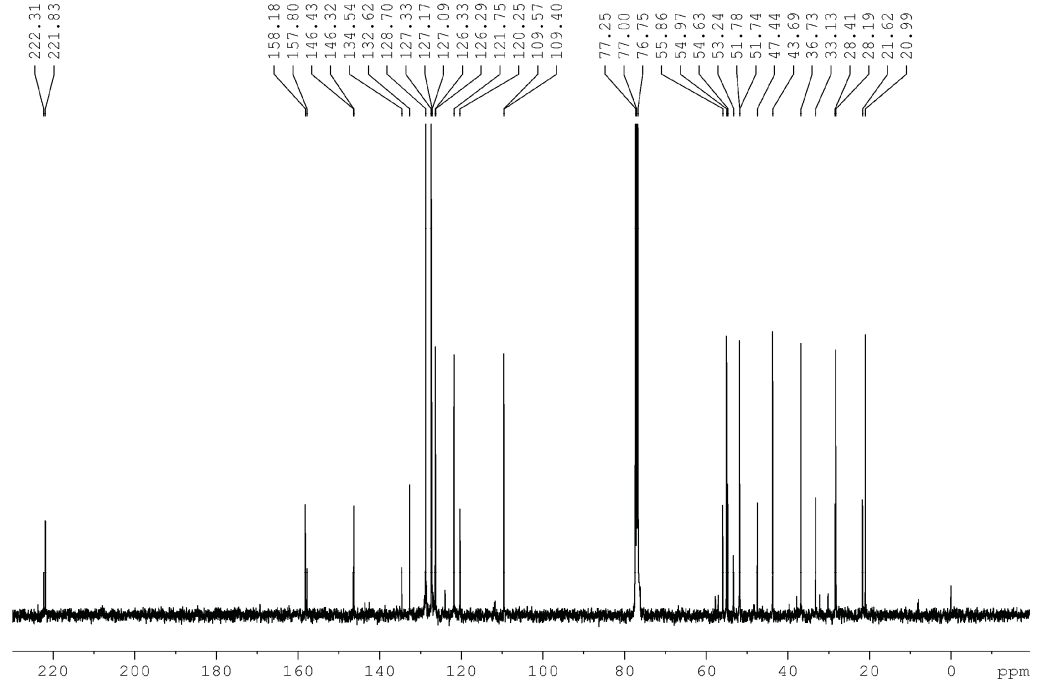
^{13}C NMR ($CDCl_3$, 125 MHz) spectrum of (1*R,3*R**,4*S**,6*S**)-1-methyl-2-methylene-3-phenyl-6-((*Z*)-prop-1-enyl)bicyclo[2.2.1]heptan-7-one (88)**



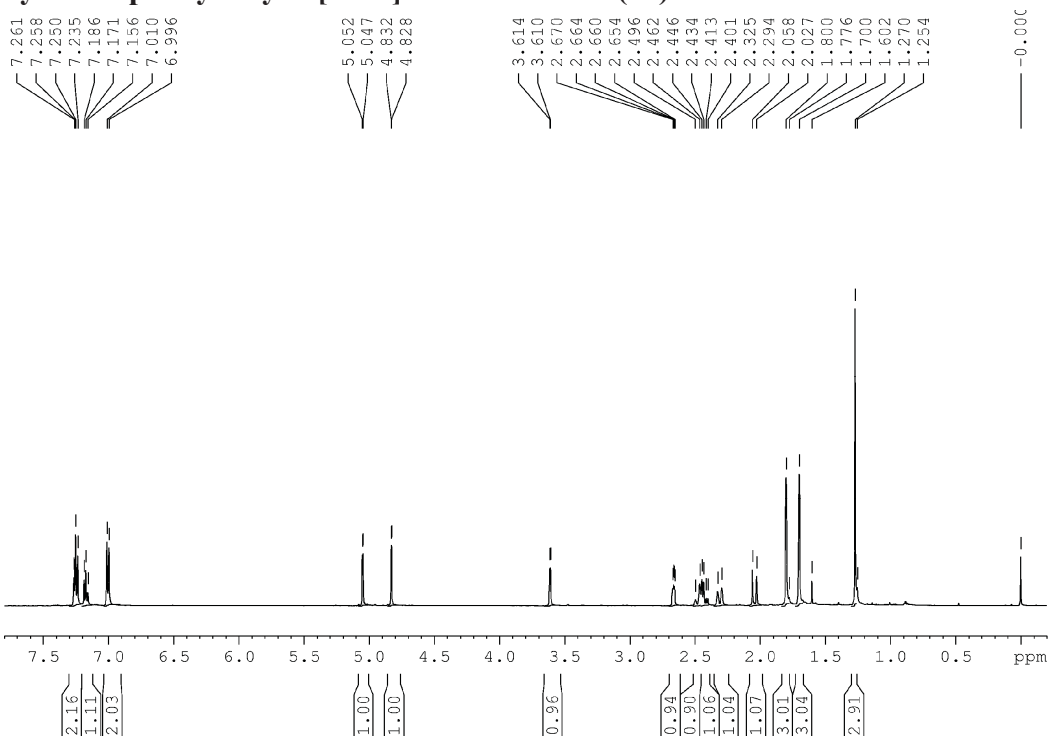
^{1}H NMR ($CDCl_3$, 500 MHz) spectrum of (1*R,6*S**,7*R**)-1,4-dimethyl-8-methylene-7-phenylbicyclo[4.2.1]non-3-en-9-one (89a) and (1*R**,6*S**, 7*R**)-1,3-dimethyl-8-methylene-7-phenylbicyclo[4.2.1]non-3-en-9-one (89b)**



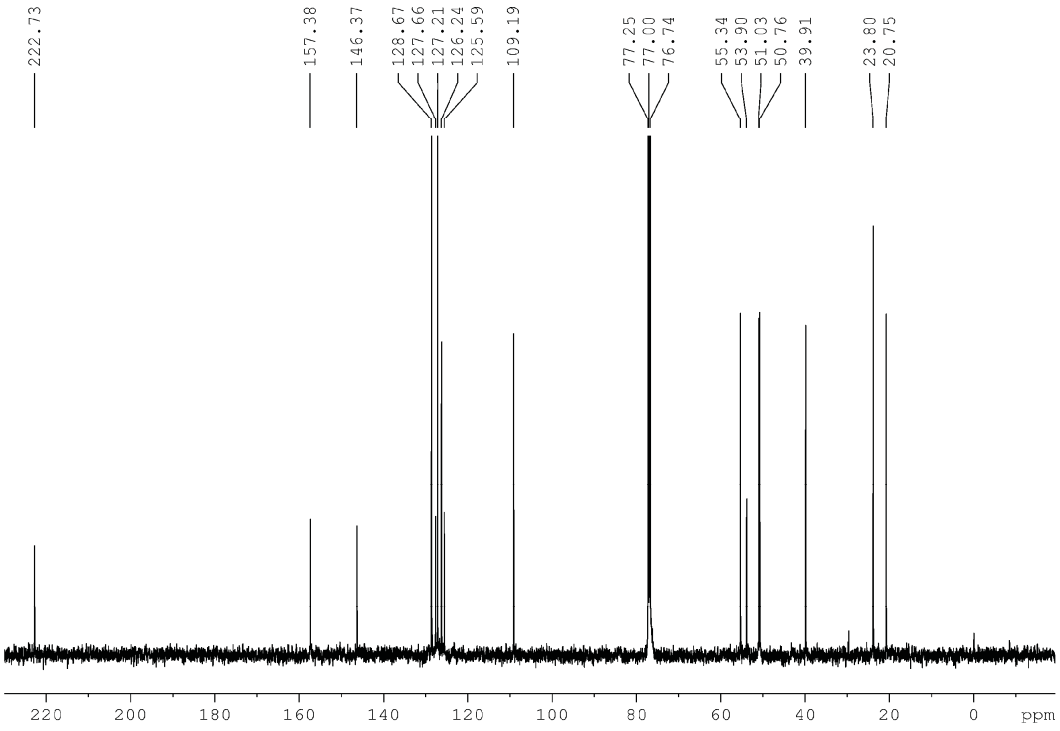
^{13}C NMR ($CDCl_3$, 125 MHz) spectrum of (1*R,6*S**,7*R**)-1,4-dimethyl-8-methylene-7-phenylbicyclo[4.2.1]non-3-en-9-one (89a) and (1*R**,6*S**, 7*R**)-1,3-dimethyl-8-methylene-7-phenylbicyclo[4.2.1]non-3-en-9-one (89b)**



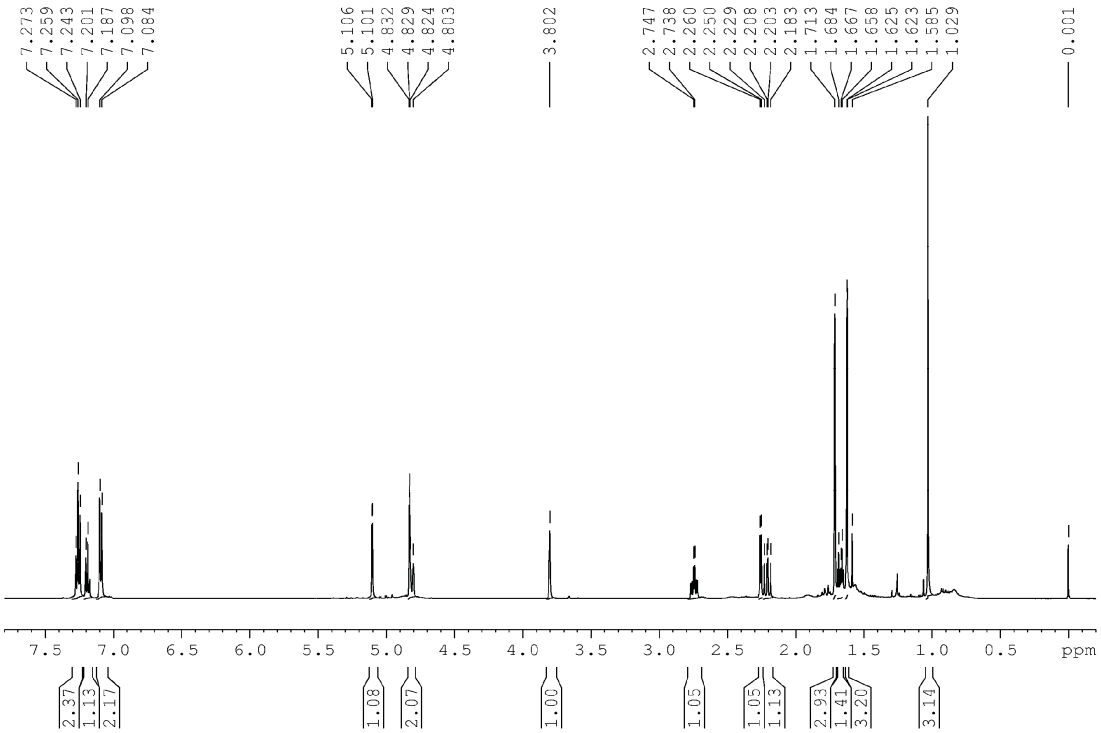
^{1}H NMR ($CDCl_3$, 500 MHz) spectrum of (1*R,6*S**,7*R**)-1,3,4-trimethyl-8-methylene-7-phenylbicyclo[4.2.1]non-3-en-9-one (90)**



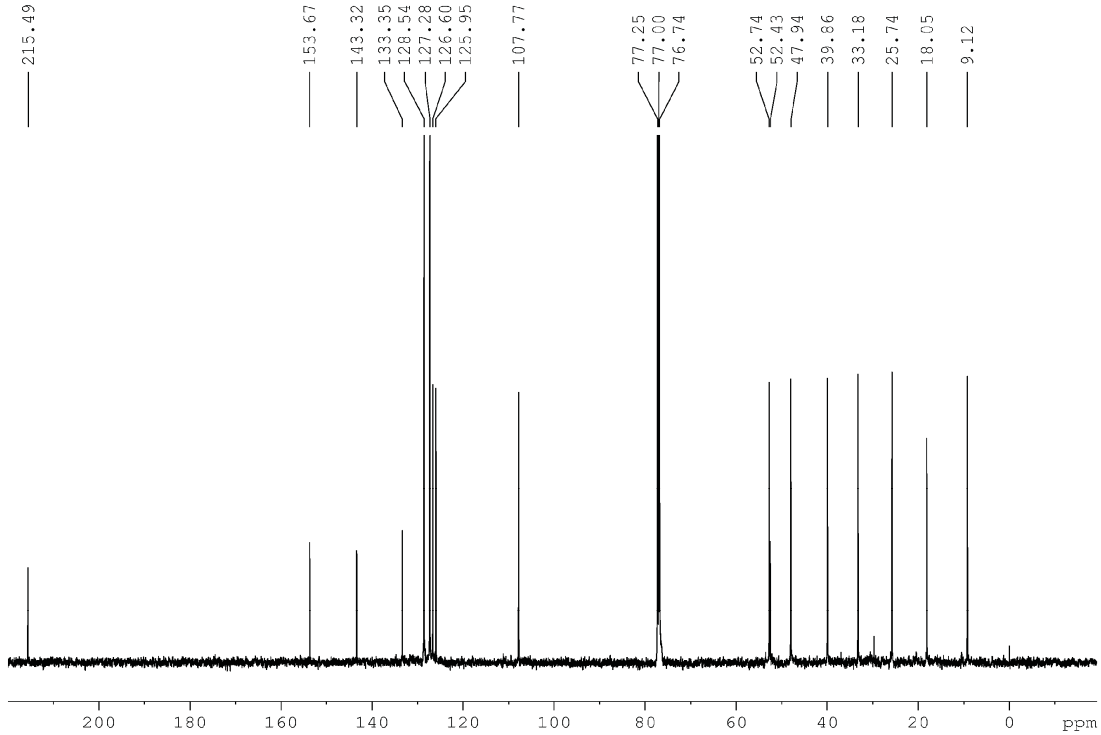
^{1}H NMR ($CDCl_3$, 500 MHz) spectrum of (1*R,6*S**,7*R**)-1,3,4-trimethyl-8-methylene-7-phenylbicyclo[4.2.1]non-3-en-9-one (90)**



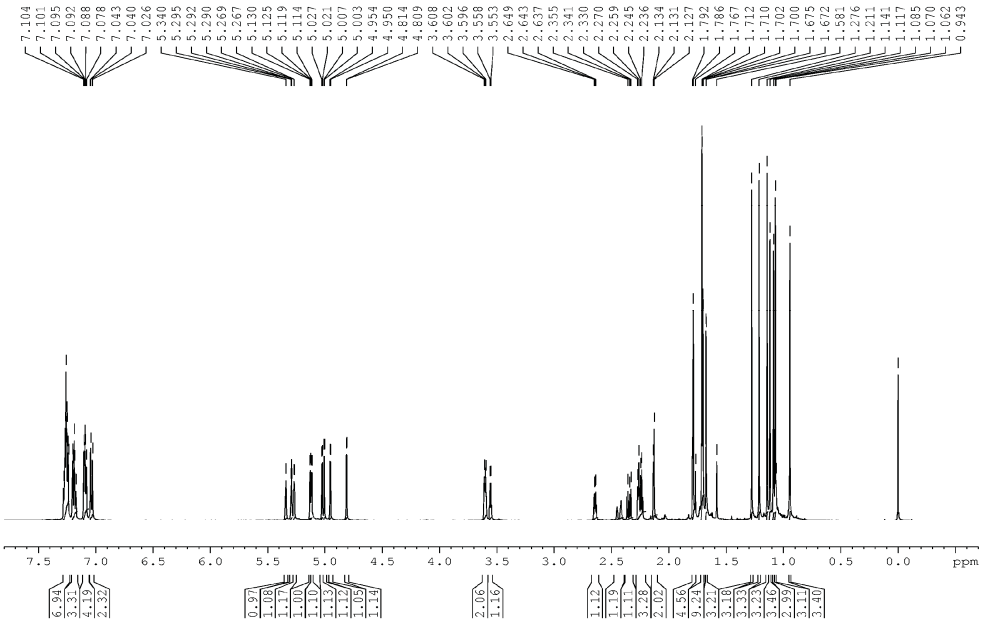
^{1}H NMR ($CDCl_3$, 500 MHz) spectrum of (1*R,3*R**,4*S**,6*S**)-1-methyl-2-methylene-6-(2-methylprop-1-enyl)-3-phenylbicyclo[2.2.1]heptan-7-one (91a)**



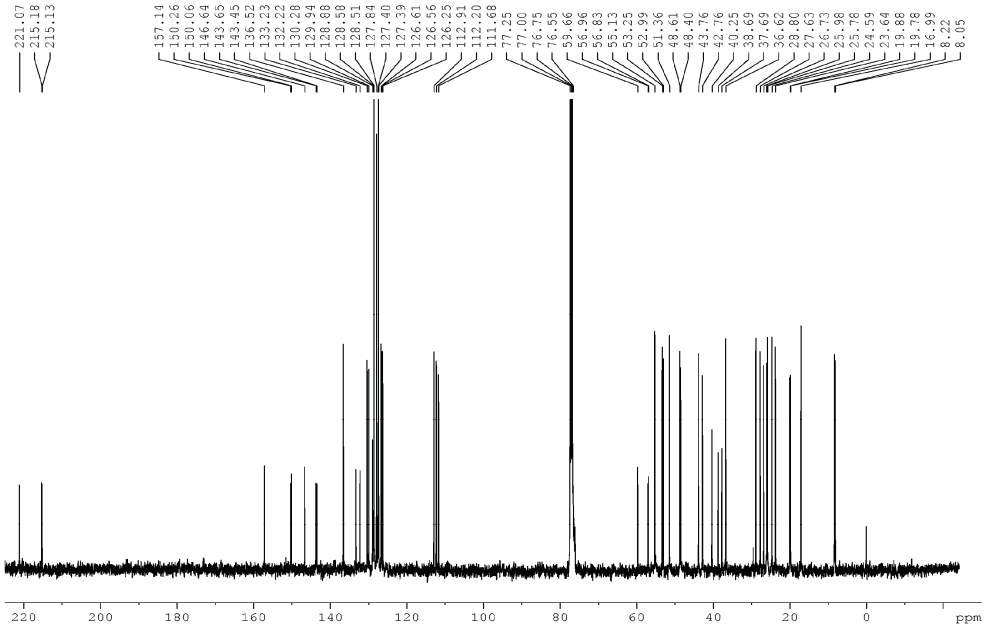
^{13}C NMR ($CDCl_3$, 125 MHz) spectrum of (1*R,3*R**,4*S**,6*S**)-1-methyl-2-methylene-6-(2-methylprop-1-enyl)-3-phenylbicyclo[2.2.1]heptan-7-one (91a)**



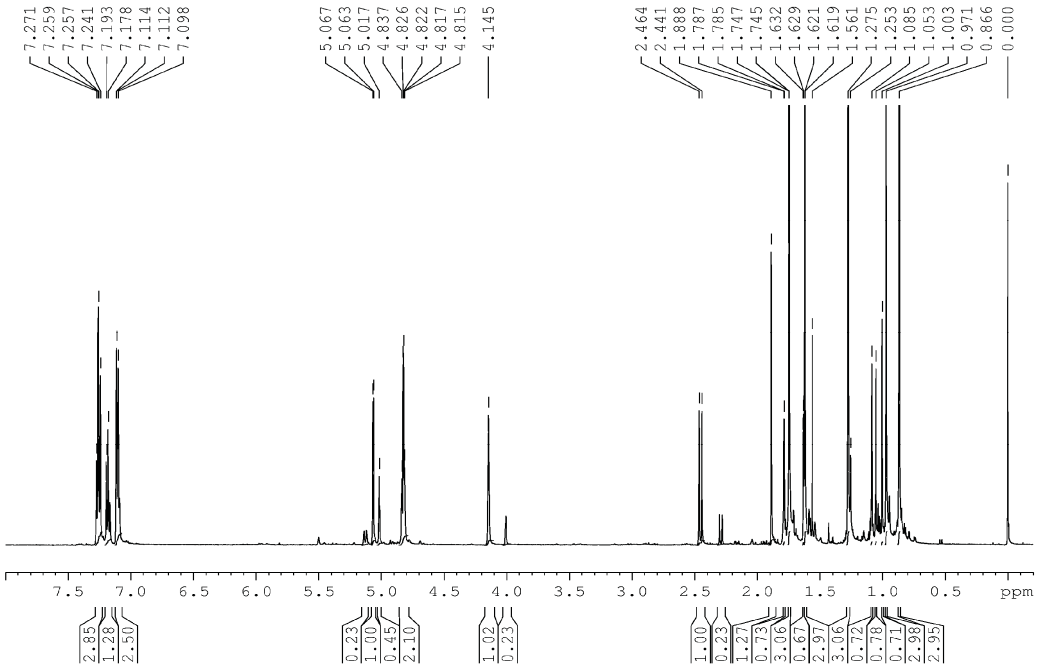
^{1}H NMR ($CDCl_3$, 500 MHz) spectrum of (1*R,6*S**,7*R**)-1,2,2,4-tetramethyl-8-methylene-7-phenylbicyclo[4.2.1]non-3-en-9-one (92), (1*R**, 2*R**,4*R**,5*S**)-1,2-dimethyl-6-methylene-2-(2-methylprop-1-enyl)-5-phenylbicyclo[2.2.1]heptan-7-one (93a), and (1*R**,2*S**,4*R**,5*S**)-1,2-dimethyl-6-methylene-2-(2-methylprop-1-enyl)-5-phenyl-bicyclo[2.2.1]heptan-7-one (93b)**



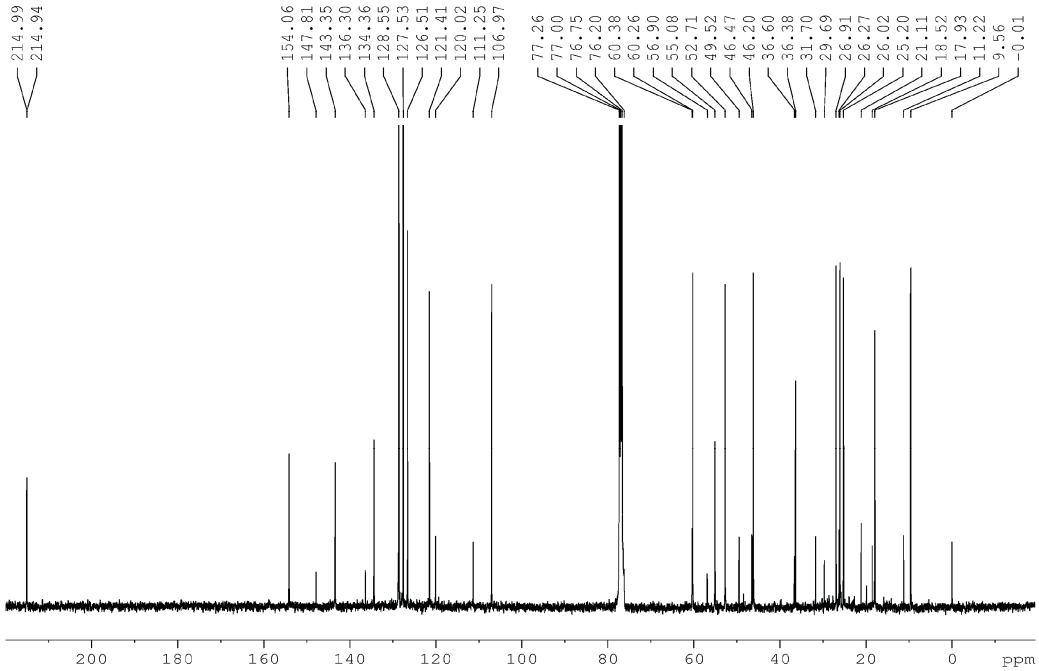
^{13}C NMR ($CDCl_3$, 125 MHz) spectrum of (1*R,6*S**,7*R**)-1,2,2,4-tetramethyl-8-methylene-7-phenylbicyclo[4.2.1]non-3-en-9-one (92), (1*R**, 2*R**,4*R**,5*S**)-1,2-dimethyl-6-methylene-2-(2-methylprop-1-enyl)-5-phenylbicyclo[2.2.1]heptan-7-one (93a), and (1*R**,2*S**,4*R**,5*S**)-1,2-dimethyl-6-methylene-2-(2-methylprop-1-enyl)-5-phenyl-bicyclo[2.2.1]heptan-7-one (93b)**



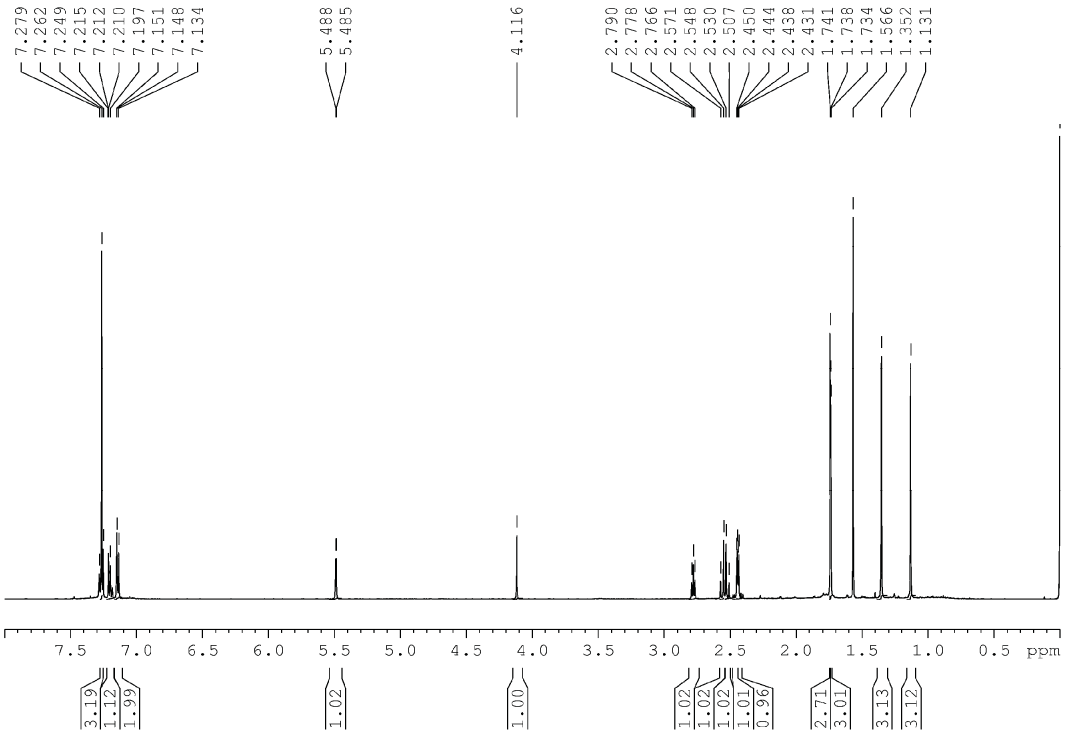
^{1}H NMR ($CDCl_3$, 500 MHz) spectrum of (1*R,2*R**,4*R**,5*R**)-1,3,3-trimethyl-6-methylene-2-(2-methylprop-1-enyl)-5-phenylbicyclo[2.2.1]-heptan-7-one (94a) and (1*R**,2*S**,4*R**,5*R**)-1,3,3-trimethyl-6-methylene-2-(2-methylprop-1-enyl)-5-phenylbicyclo[2.2.1]heptan-7-one (94b)**



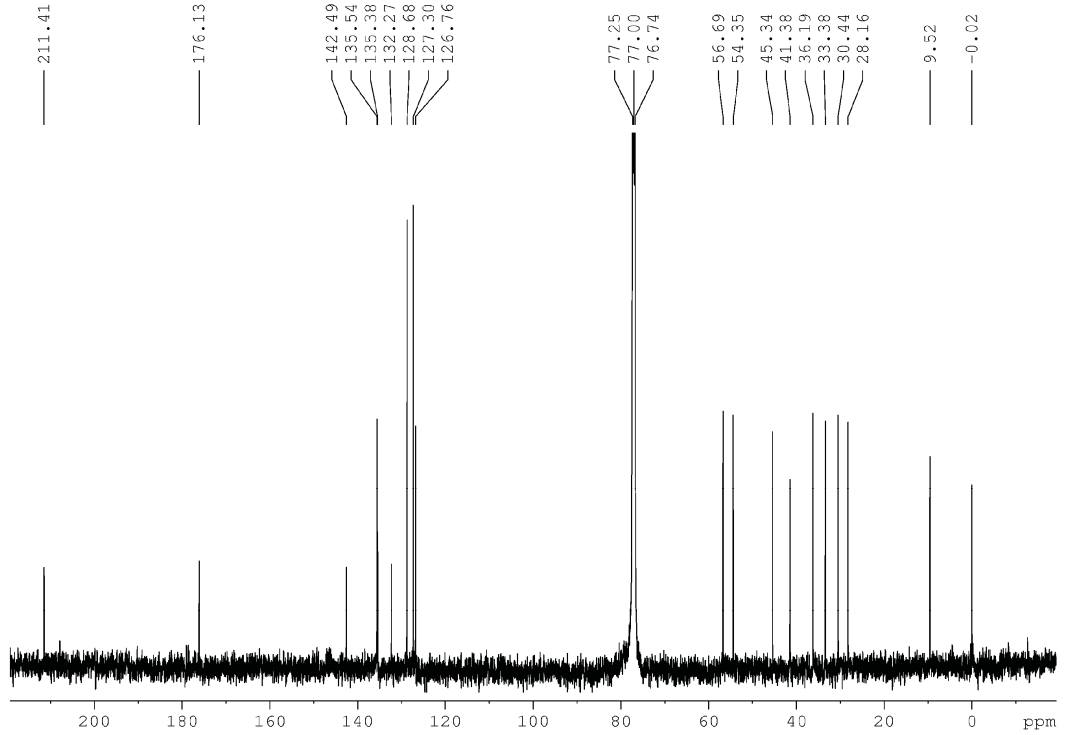
^{13}C NMR ($CDCl_3$, 125 MHz) spectrum of (1*R,2*R**,4*R**,5*R**)-1,3,3-trimethyl-6-methylene-2-(2-methylprop-1-enyl)-5-phenylbicyclo[2.2.1]-heptan-7-one (94a) and (1*R**,2*S**,4*R**,5*R**)-1,3,3-trimethyl-6-methylene-2-(2-methylprop-1-enyl)-5-phenylbicyclo[2.2.1]heptan-7-one (94b)**



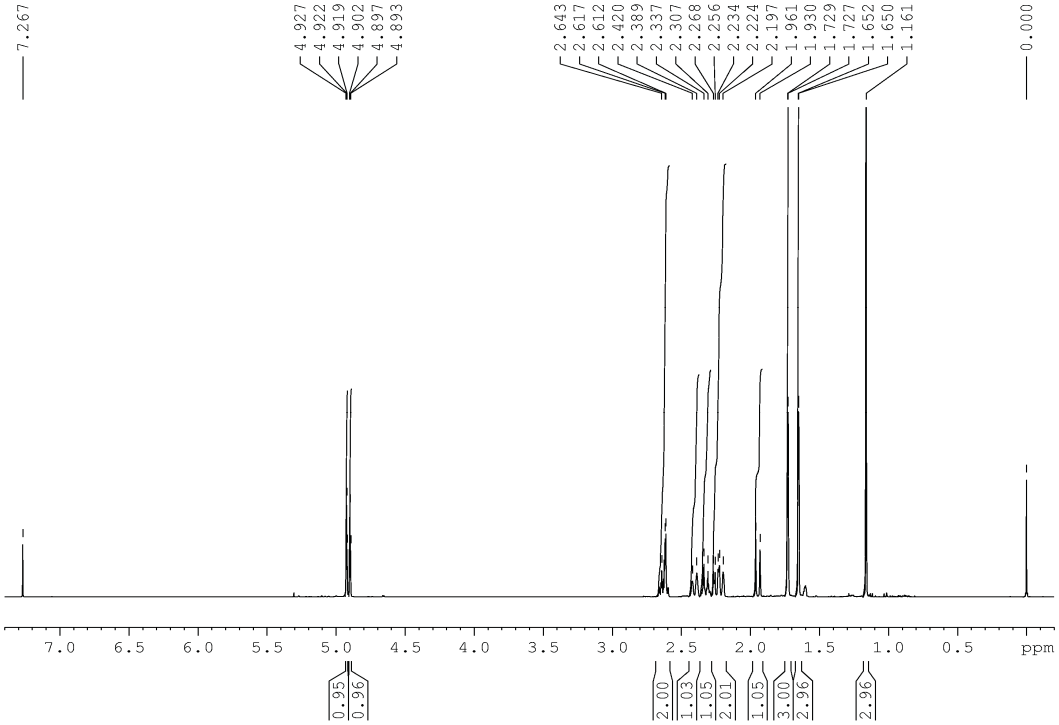
^{1}H NMR ($CDCl_3$, 500 MHz) spectrum of (7*R,10*S**)-3,3,5,9-tetramethyl-10-phenylbicyclo[5.2.1]deca-1(9),4-dien-8-one (95)**



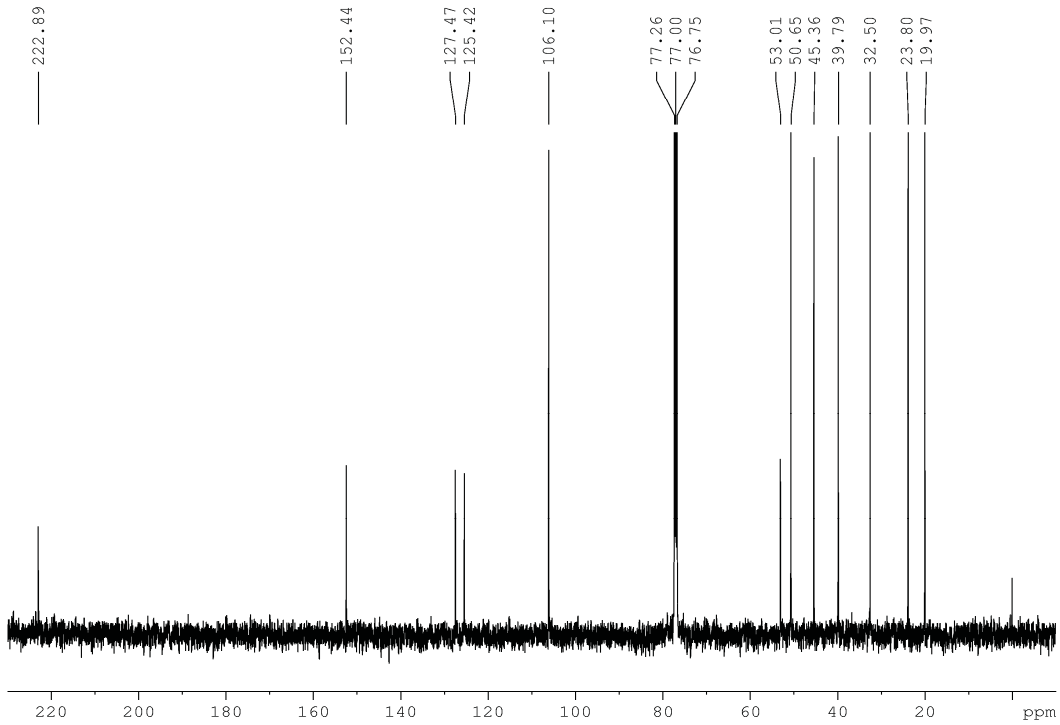
^{13}C NMR ($CDCl_3$, 125 MHz) spectrum of (7*R,10*S**)-3,3,5,9-tetramethyl-10-phenylbicyclo[5.2.1]deca-1(9),4-dien-8-one (95)**



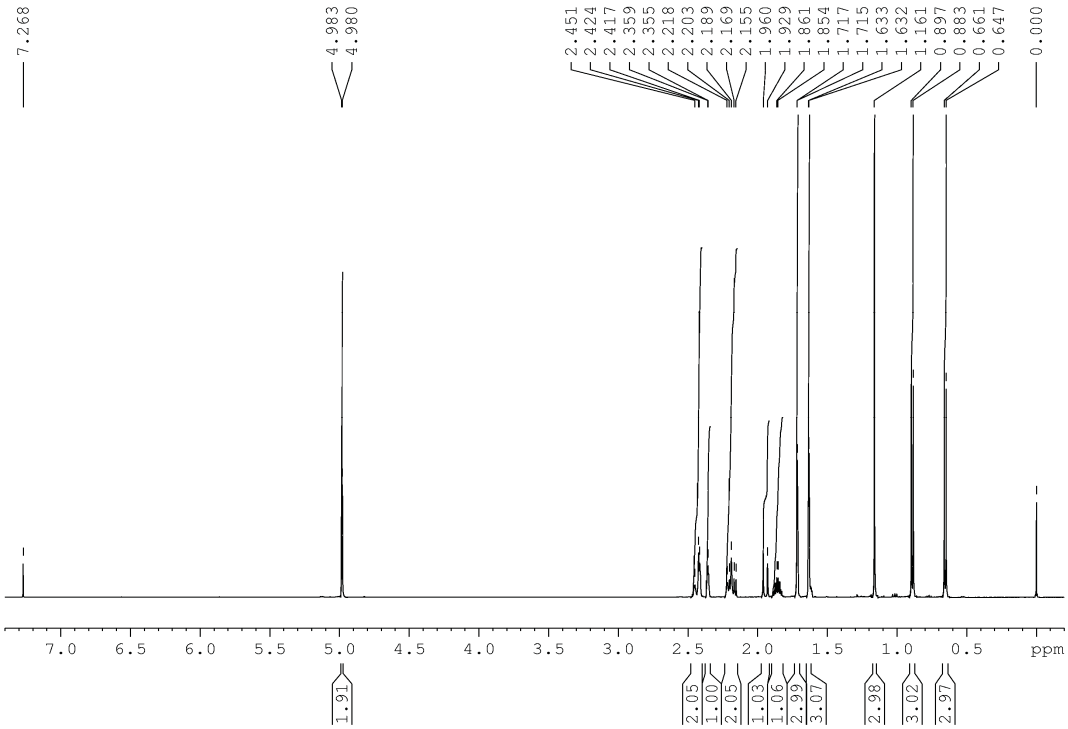
^{1}H NMR ($CDCl_3$, 500 MHz) spectrum of (1*R,6*S**)-1,3,4-trimethyl-8-methylenebicyclo[4.2.1]non-3-en-9-one (96)**



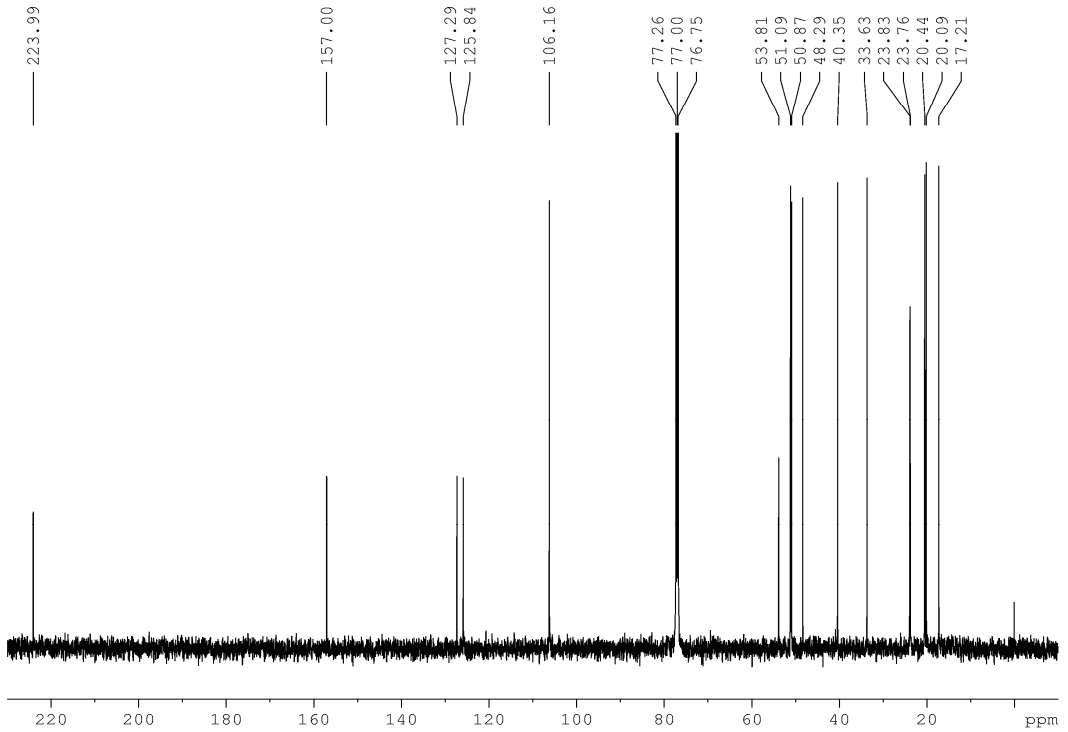
^{13}C NMR ($CDCl_3$, 125 MHz) spectrum of (1*R,6*S**)-1,3,4-trimethyl-8-methylenebicyclo[4.2.1]non-3-en-9-one (96)**



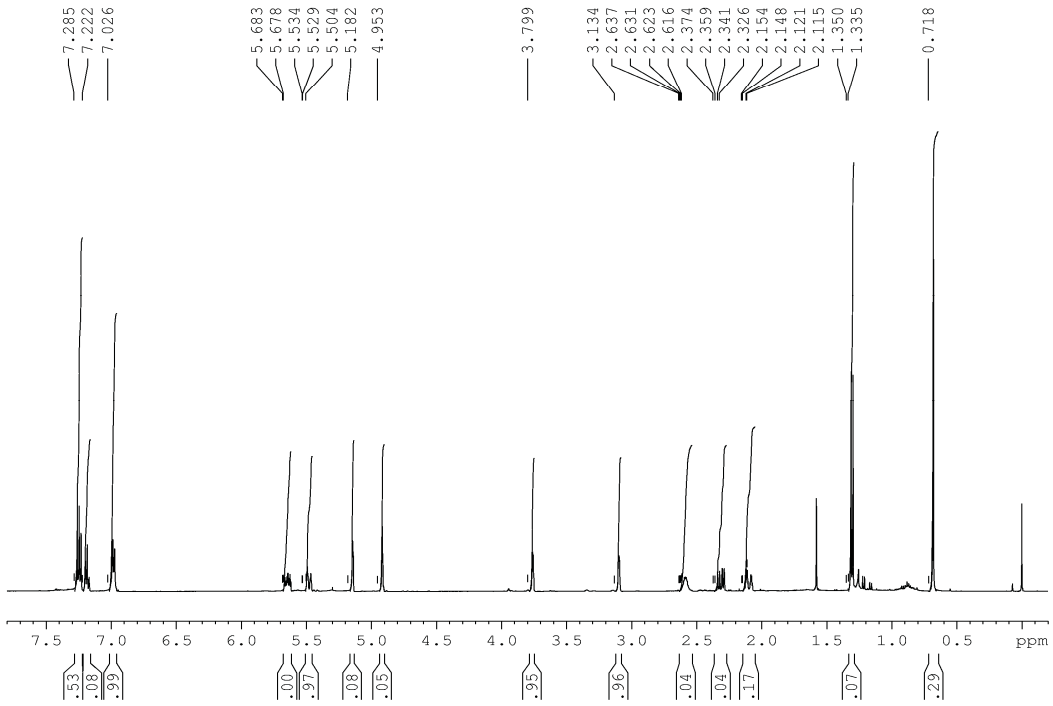
^{1}H NMR ($CDCl_3$, 500 MHz) spectrum of (1*R,6*S**,7*R**)-7-isopropyl-1,3,4-trimethyl-8-methylenebicyclo[4.2.1]non-3-en-9-one (97)**



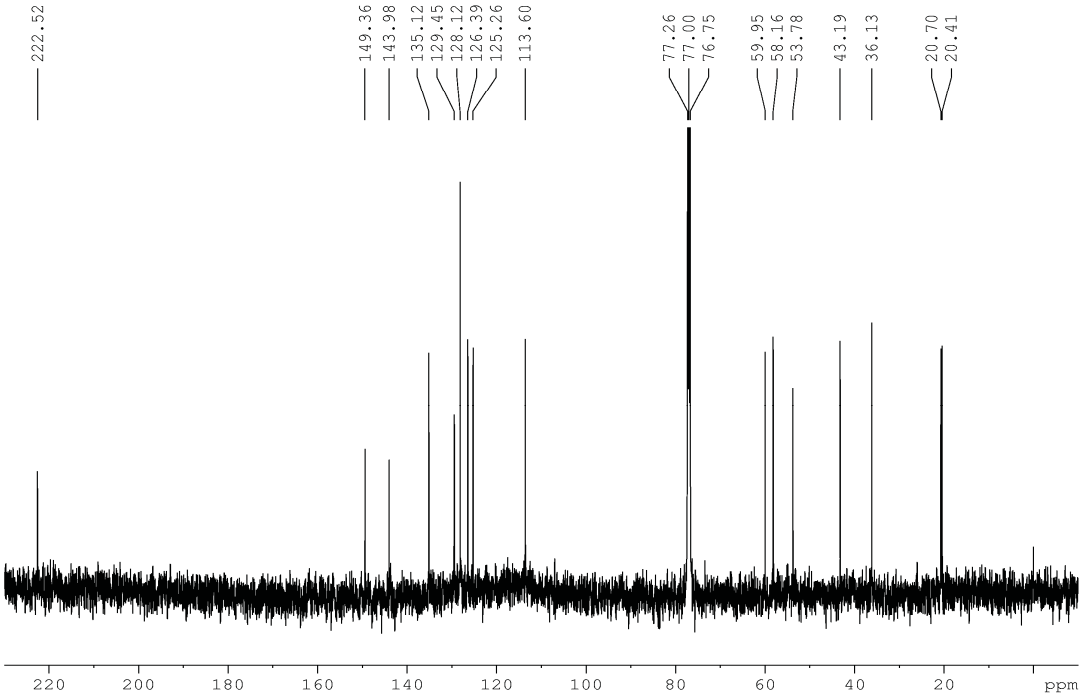
^{13}C NMR ($CDCl_3$, 125 MHz) spectrum of (1*R,6*S**,7*R**)-7-isopropyl-1,3,4-trimethyl-8-methylenebicyclo[4.2.1]non-3-en-9-one (42)**



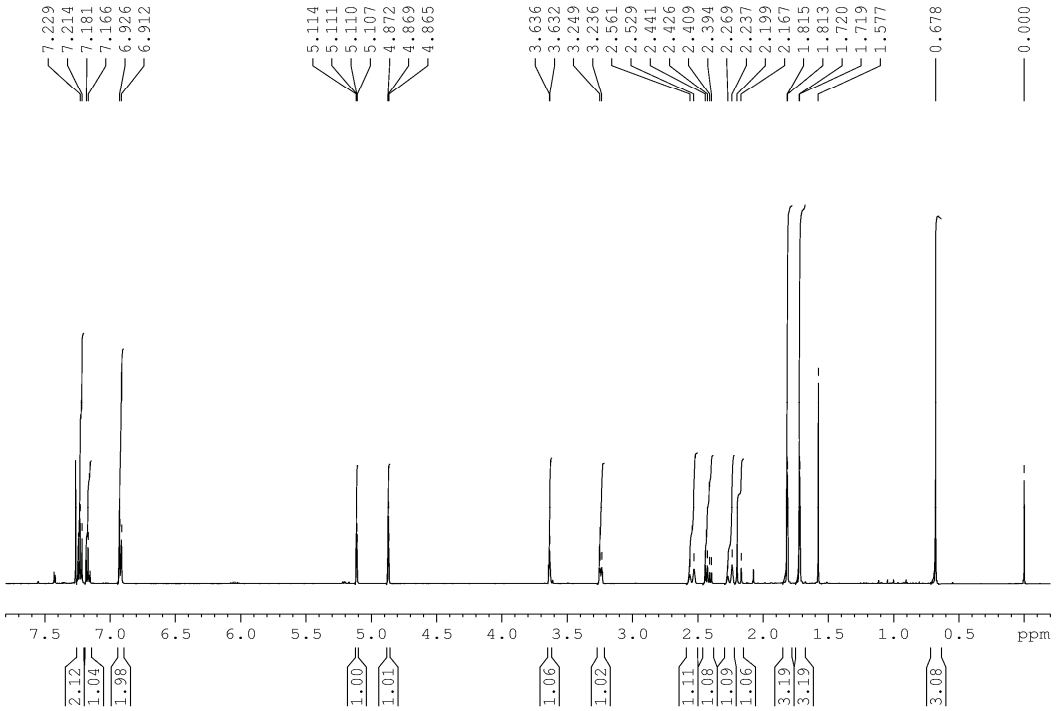
^{1}H NMR (500 MHz, $CDCl_3$) of (1*R,5*R**,6*S**,8*S**)-1,5-dimethyl-7-methylene-8-phenylbicyclo[4.2.1]non-3-en-9-one (98)**



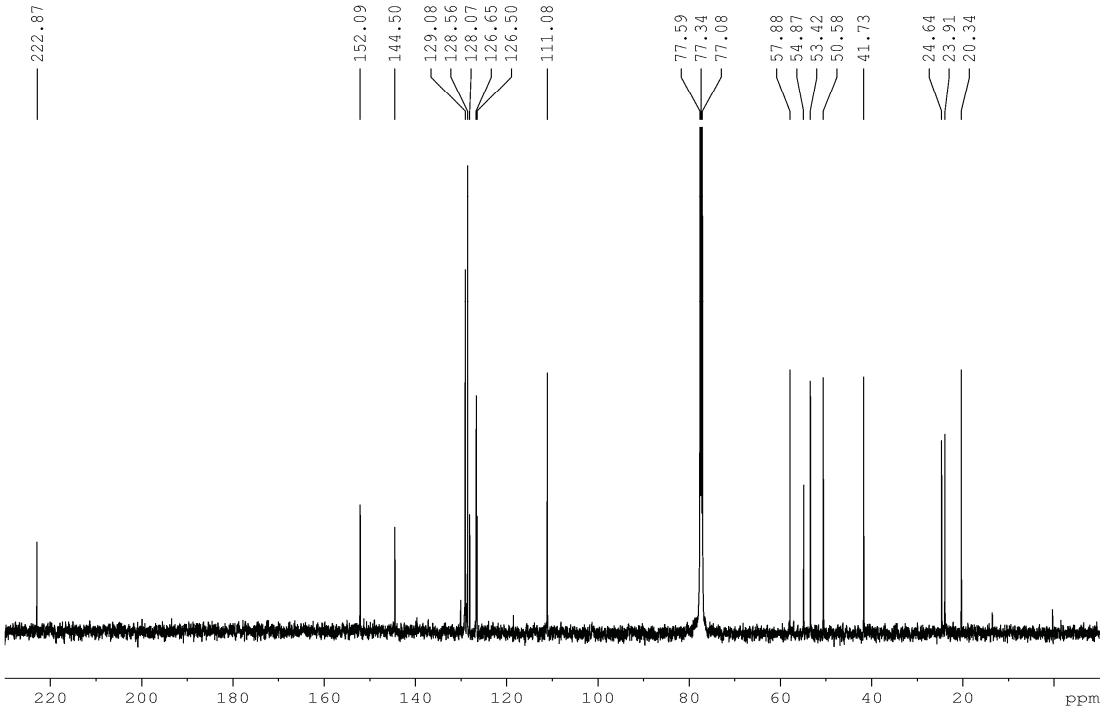
^{13}C NMR (125 MHz, $CDCl_3$) of (1*R,5*R**,6*S**,8*S**)-1,5-dimethyl-7-methylene-8-phenylbicyclo[4.2.1]non-3-en-9-one (98)**



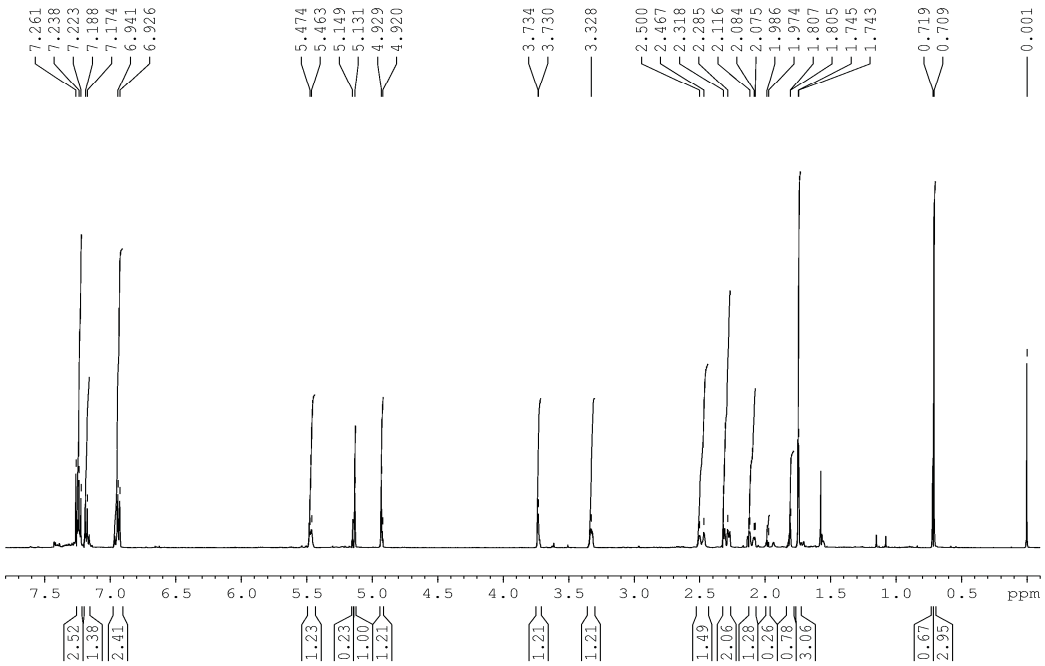
^{1}H NMR (500 MHz, $CDCl_3$) of (1*R,6*S**,8*S**)-1,3,4-trimethyl-7-methylene-8-phenylbicyclo[4.2.1]non-3-en-9-one (99)**



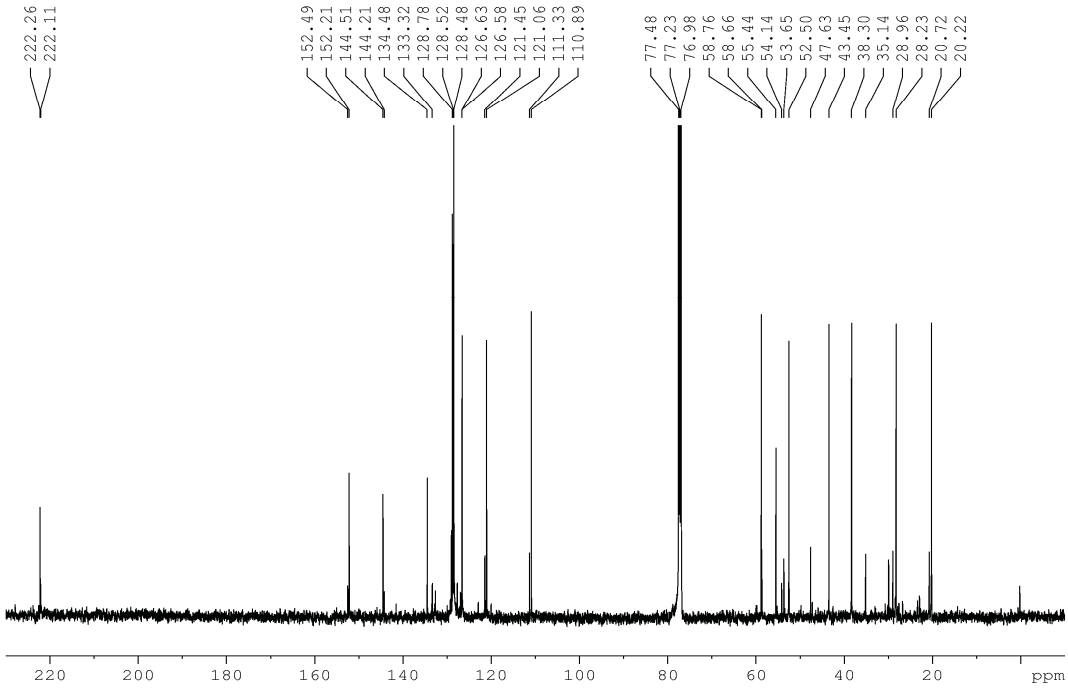
^{13}C NMR (125 MHz, $CDCl_3$) of (1*R,6*S**,8*S**)-1,3,4-trimethyl-7-methylene-8-phenylbicyclo[4.2.1]non-3-en-9-one (99)**



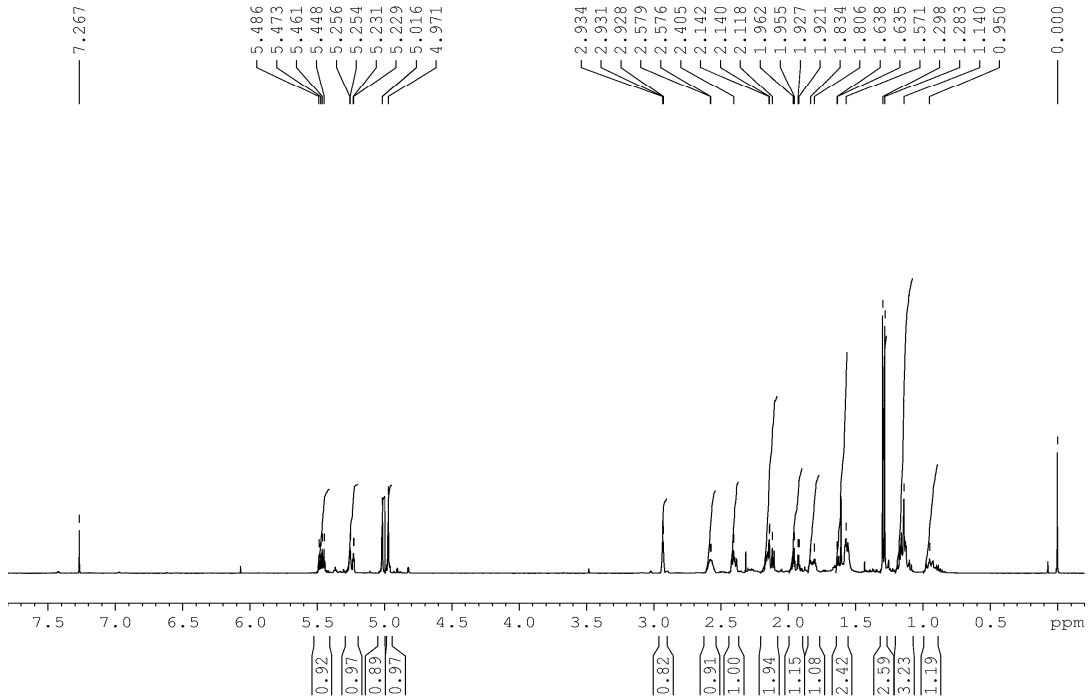
^{1}H NMR (500 MHz, $CDCl_3$) of (1*R,6*S**,8*S**)-1,3-dimethyl-7-methylene-8-phenylbicyclo[4.2.1]non-3-en-9-one (100a) and (1*R**,6*S**,8*S**)-1,4-dimethyl-7-methylene-8-phenylbicyclo[4.2.1]non-3-en-9-one (100b)**



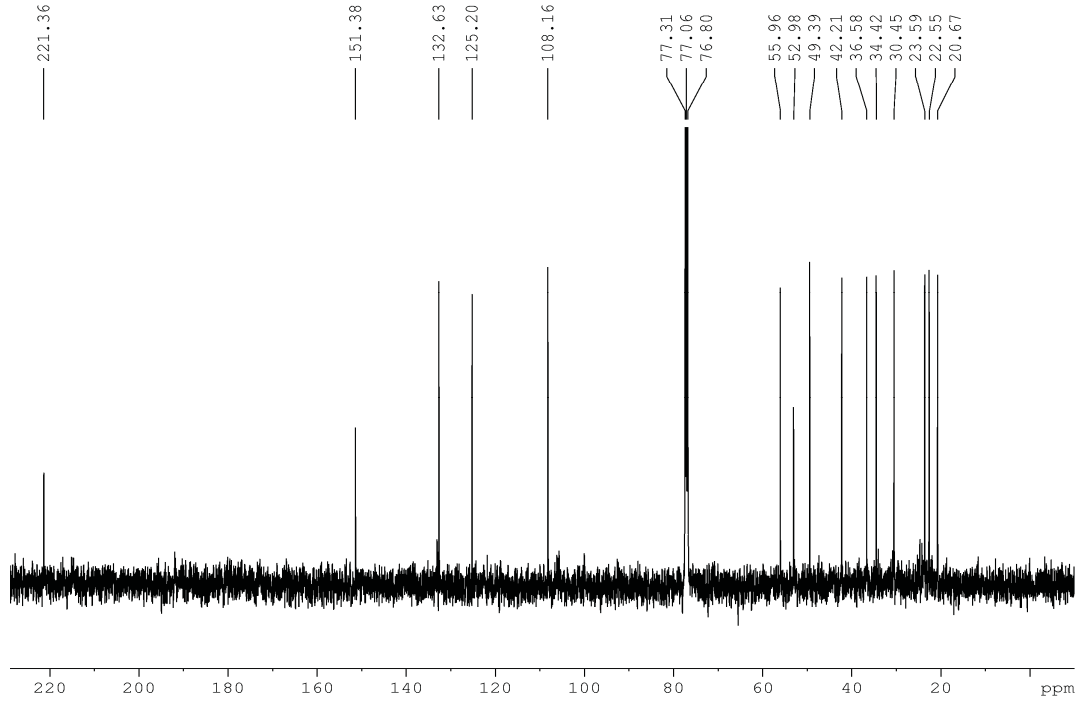
^{13}C NMR (125 MHz, $CDCl_3$) of (1*R,6*S**,8*S**)-1,3-dimethyl-7-methylene-8-phenylbicyclo[4.2.1]non-3-en-9-one (100a) and (1*R**,6*S**,8*S**)-1,4-dimethyl-7-methylene-8-phenylbicyclo[4.2.1]non-3-en-9-one (100b)**



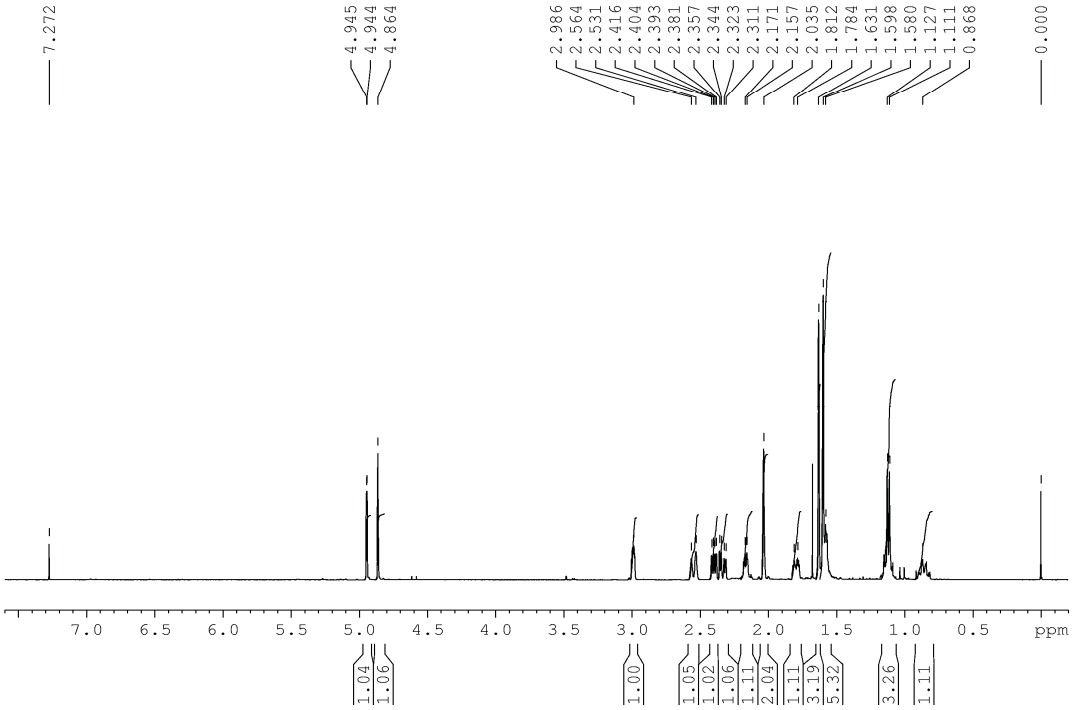
^{1}H NMR (500 MHz, $CDCl_3$) of (1*R,3*R**,8*S**,12*S**)-12-methyl-2-methylenetricyclo[6.4.1.0^{3,8}]triscadec-10-en-13-one (101)**



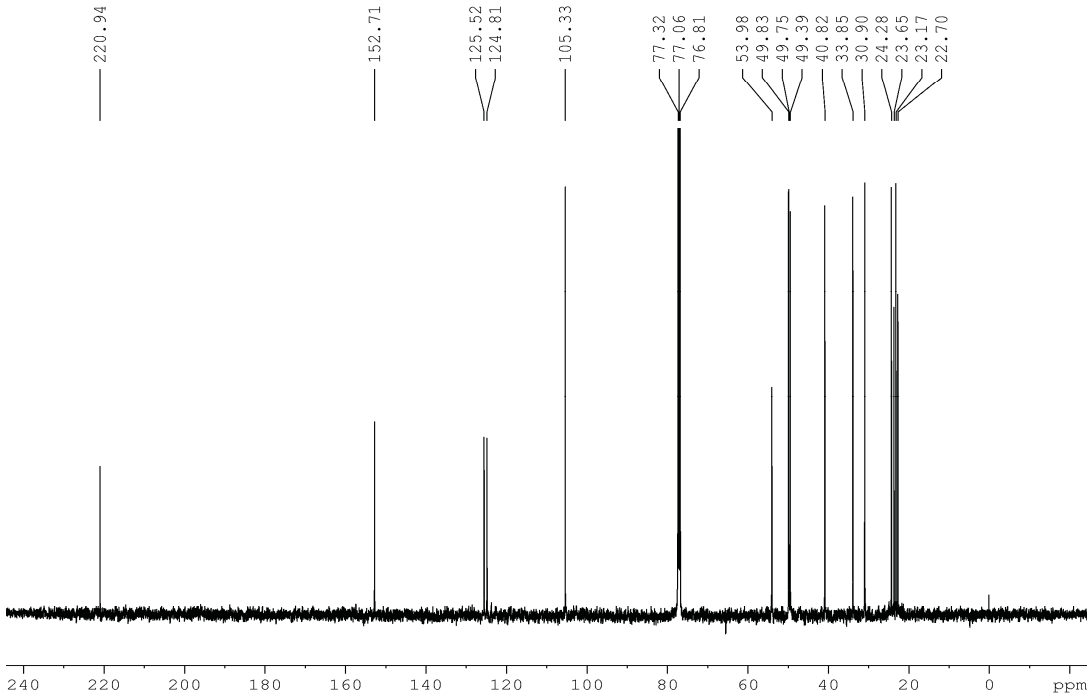
^{13}C NMR (125 MHz, $CDCl_3$) of (1*R,3*R**,8*S**,12*S**)-12-methyl-2-methylenetricyclo[6.4.1.0^{3,8}]triscadec-10-en-13-one (101)**



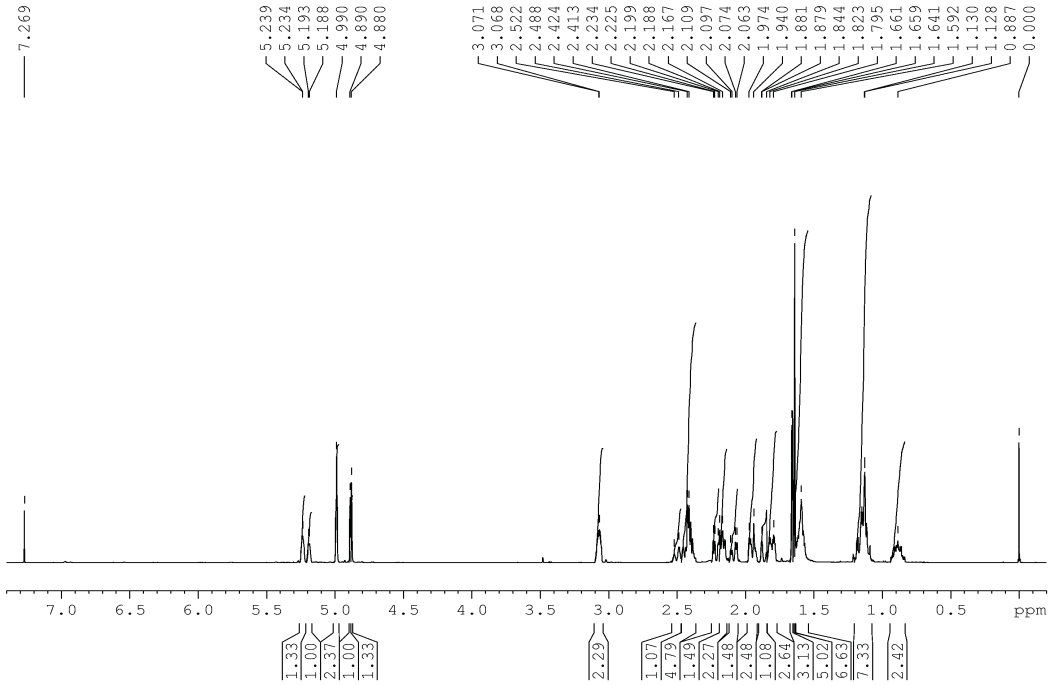
^{1}H NMR (500 MHz, $CDCl_3$) of (1*R,3*R**,8*S**)-10,11-dimethyl-2-methylenetricyclo[6.4.1.0^{3,8}]triscadec-10-en-13-one (102)**



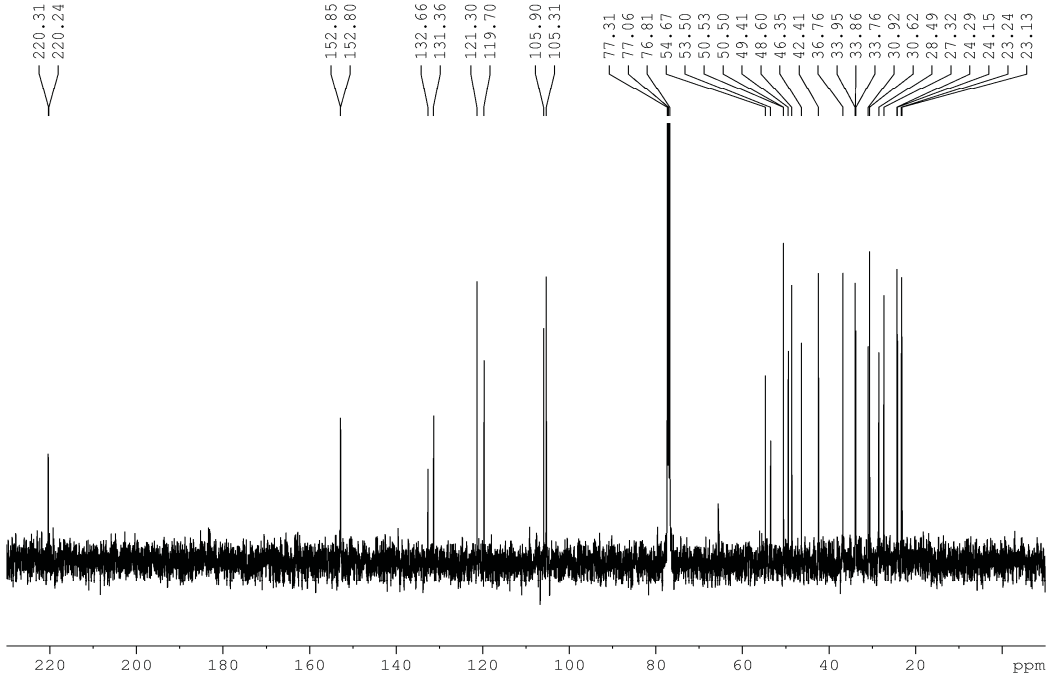
^{13}C NMR (125 MHz, $CDCl_3$) of (1*R,3*R**,8*S**)-10,11-dimethyl-2-methylenetricyclo[6.4.1.0^{3,8}]triscadec-10-en-13-one (102)**



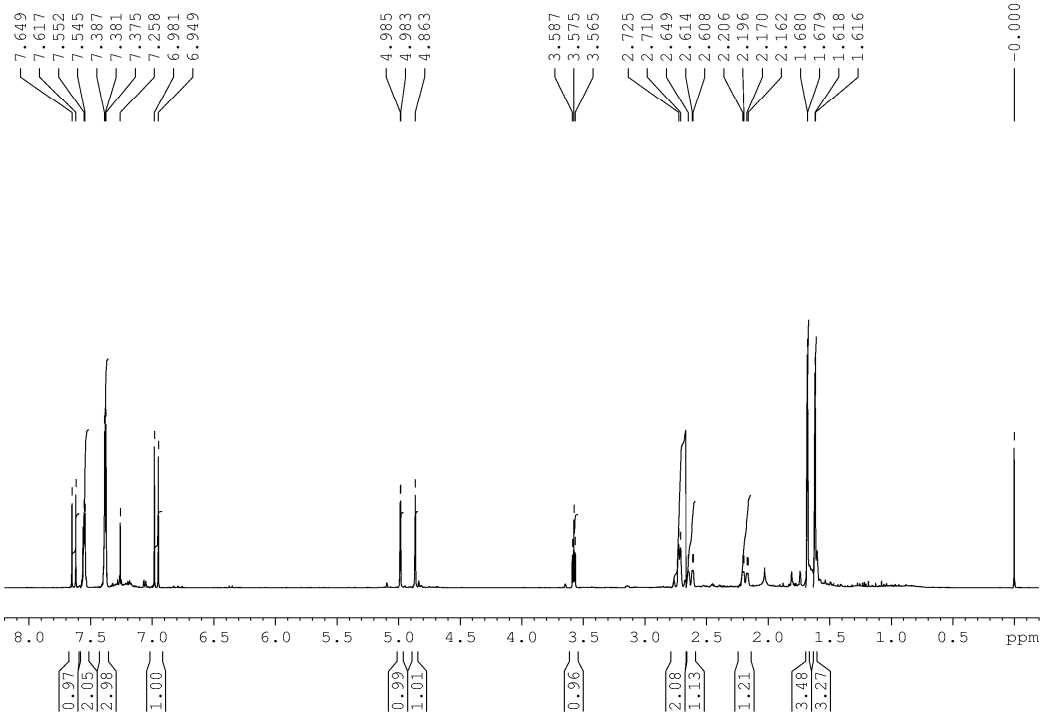
^{1}H NMR (500 MHz, $CDCl_3$) of (1*R,3*R**,8*S**)-10-methyl-2-methylenetricyclo[6.4.1.0^{3,8}]triscadec-10-en-13-one (103a) and (1*R**,3*R**,8*S**)-11-methyl-2-methylenetricyclo[6.4.1.0^{3,8}]triscadec-10-en-13-one (103b)**



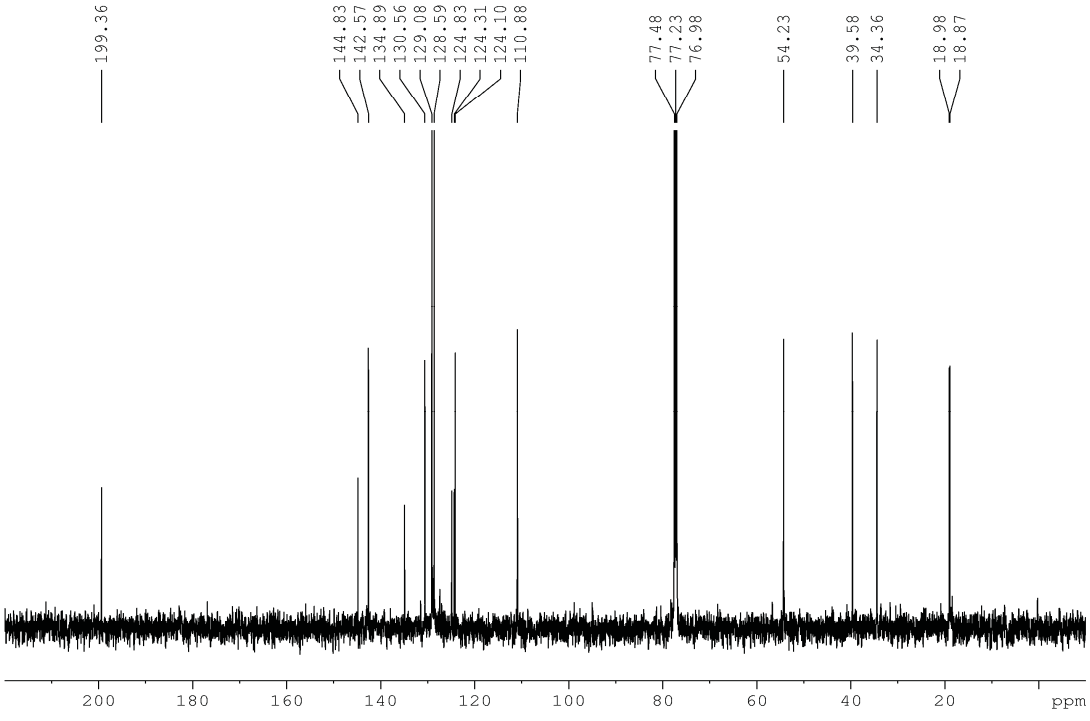
^{13}C NMR (125 MHz, $CDCl_3$) of (1*R,3*R**,8*S**)-10-methyl-2-methylenetricyclo[6.4.1.0^{3,8}]triscadec-10-en-13-one (103a) and (1*R**,3*R**,8*S**)-11-methyl-2-methylenetricyclo[6.4.1.0^{3,8}]triscadec-10-en-13-one (103b)**



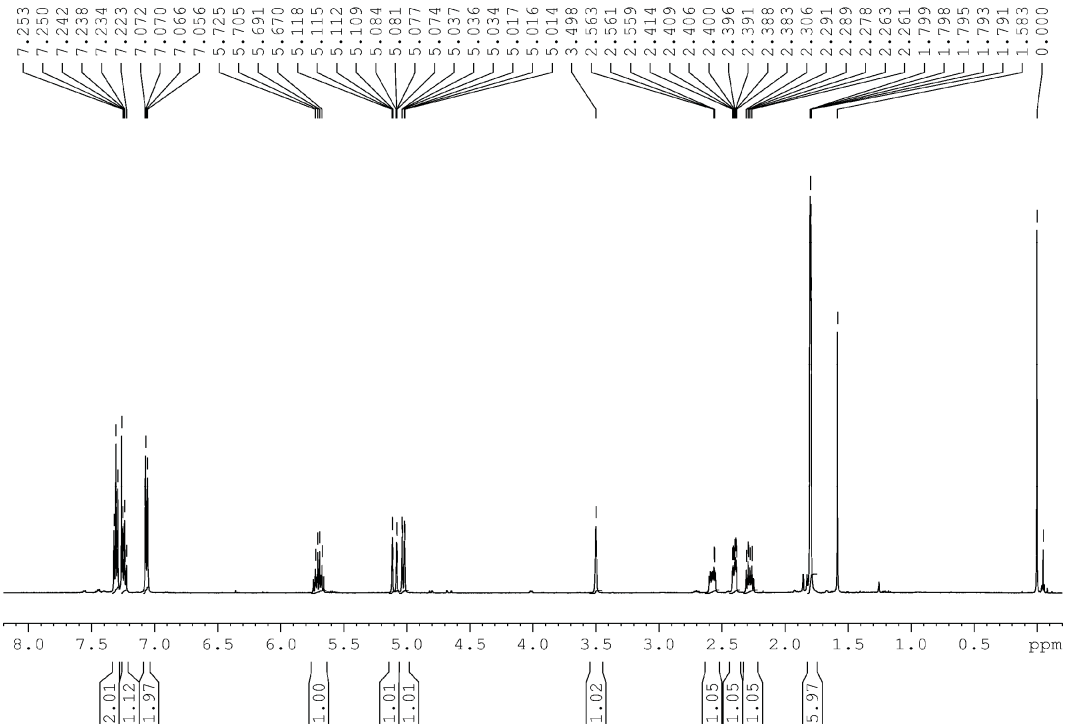
^{1}H NMR (500 MHz, $CDCl_3$) of (*E*)-1-(3,4-dimethyl-6-methylenecyclohex-3-enyl)-3-phenylprop-2-en-1-one (104)



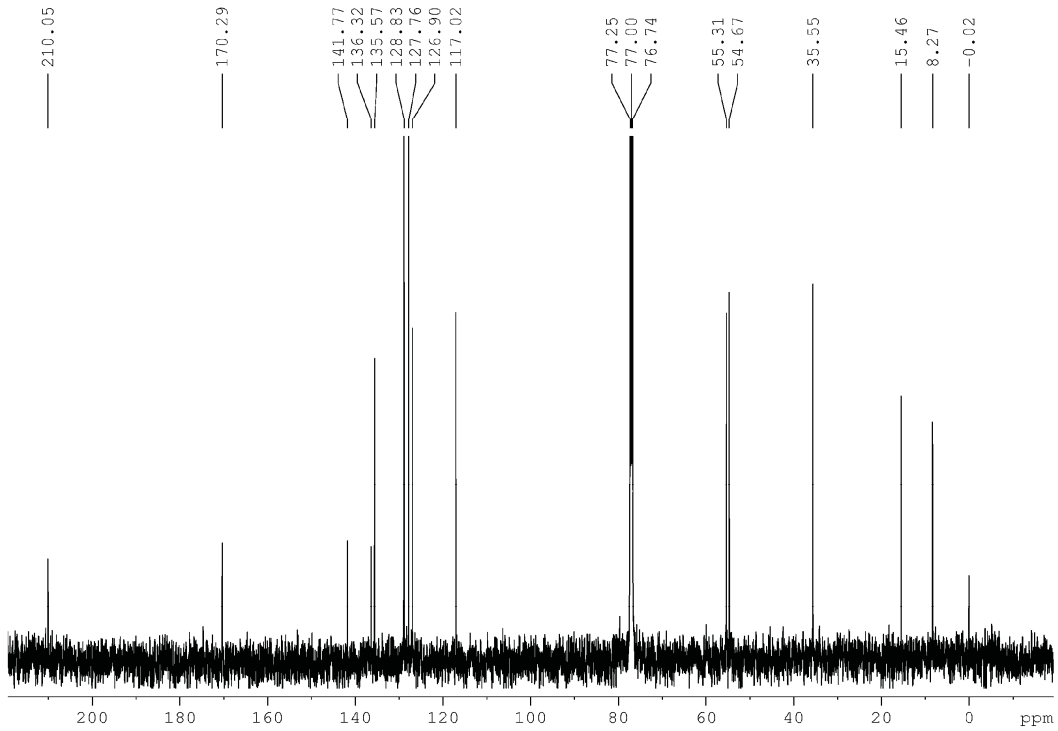
^{13}C NMR (125 MHz, $CDCl_3$) of (*E*)-1-(3,4-dimethyl-6-methylenecyclohex-3-enyl)-3-phenylprop-2-en-1-one (104)



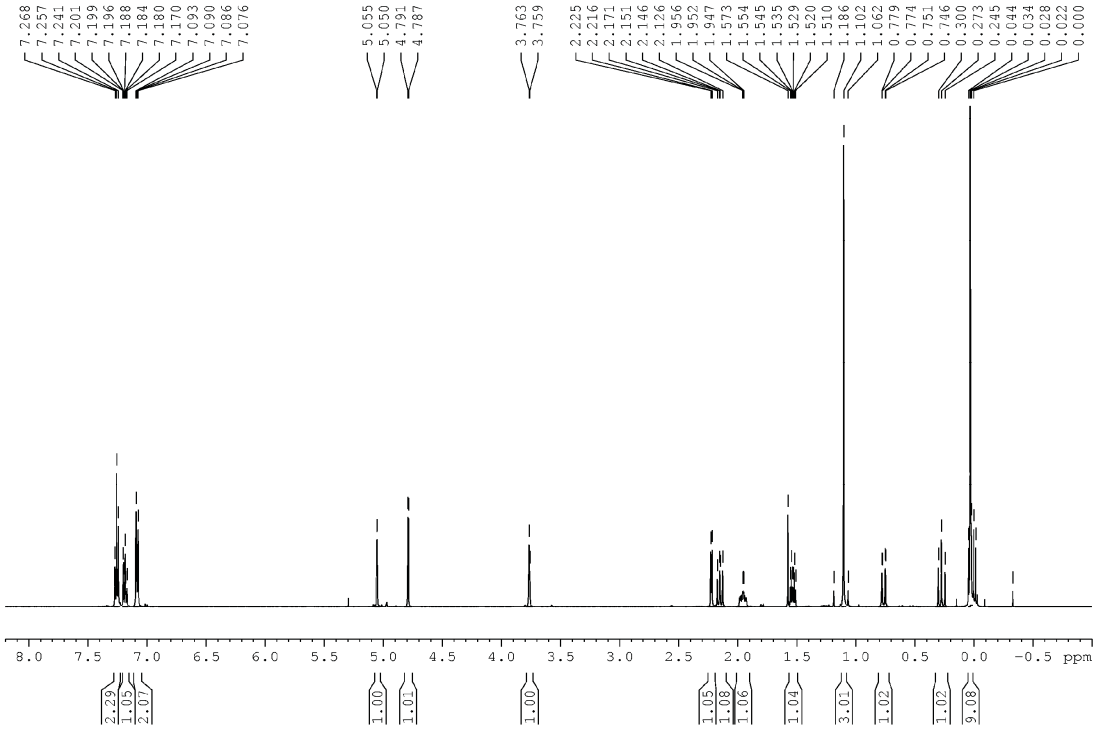
^{1}H NMR ($CDCl_3$, 500 MHz) spectrum of (*trans*)-5-allyl-2,3-dimethyl-4-phenylcyclopent-2-enone (105)



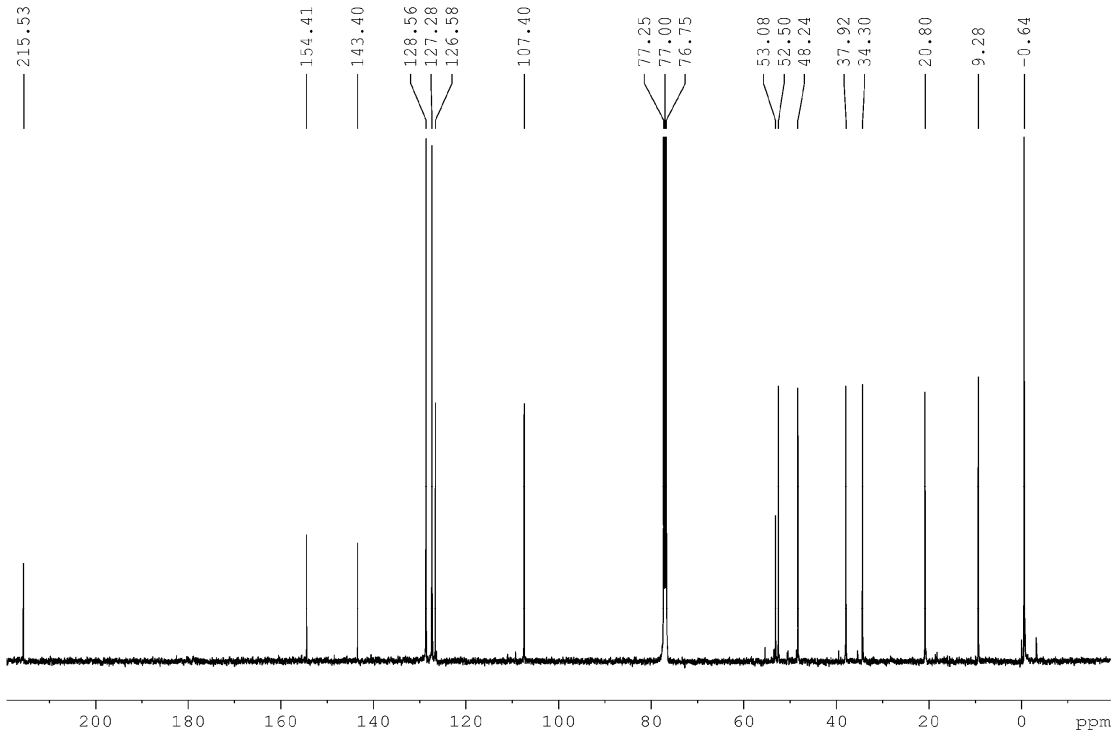
^{13}C NMR ($CDCl_3$, 125 MHz) spectrum of (*trans*)-5-allyl-2,3-dimethyl-4-phenylcyclopent-2-enone (105)



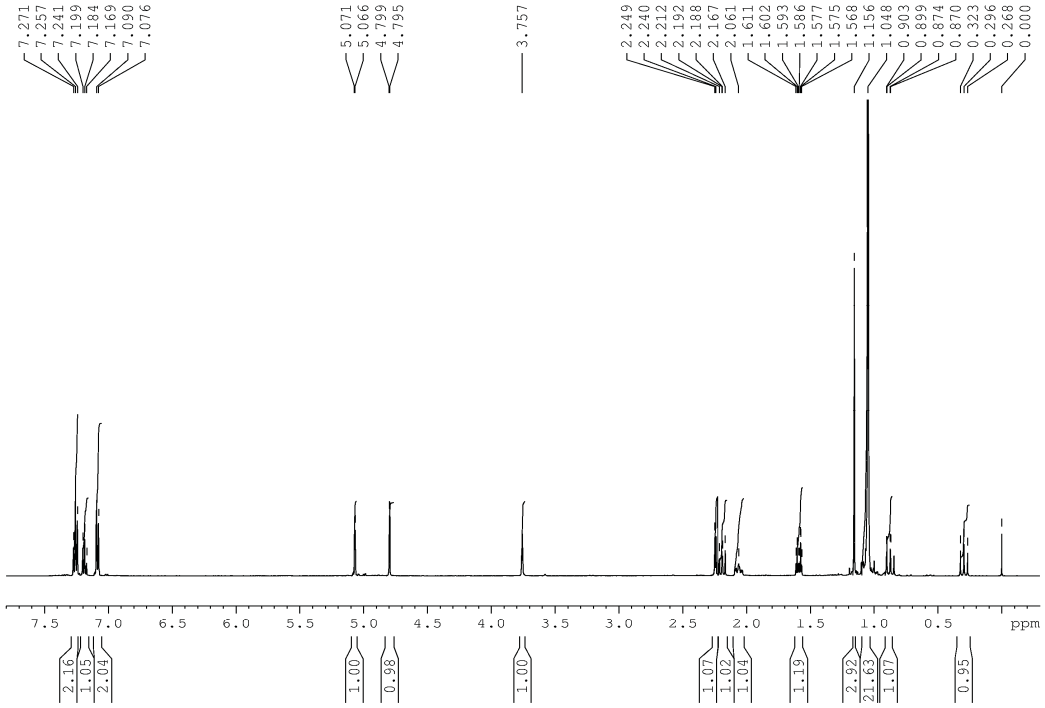
^{1}H NMR ($CDCl_3$, 500 MHz) spectrum of (1*R,3*R**,4*S**,6*R**)-1-methyl-2-meth-ylene-3-phenyl-6-((trimethylsilyl)methyl)bicyclo[2.2.1]-heptan-7-one (106a)**



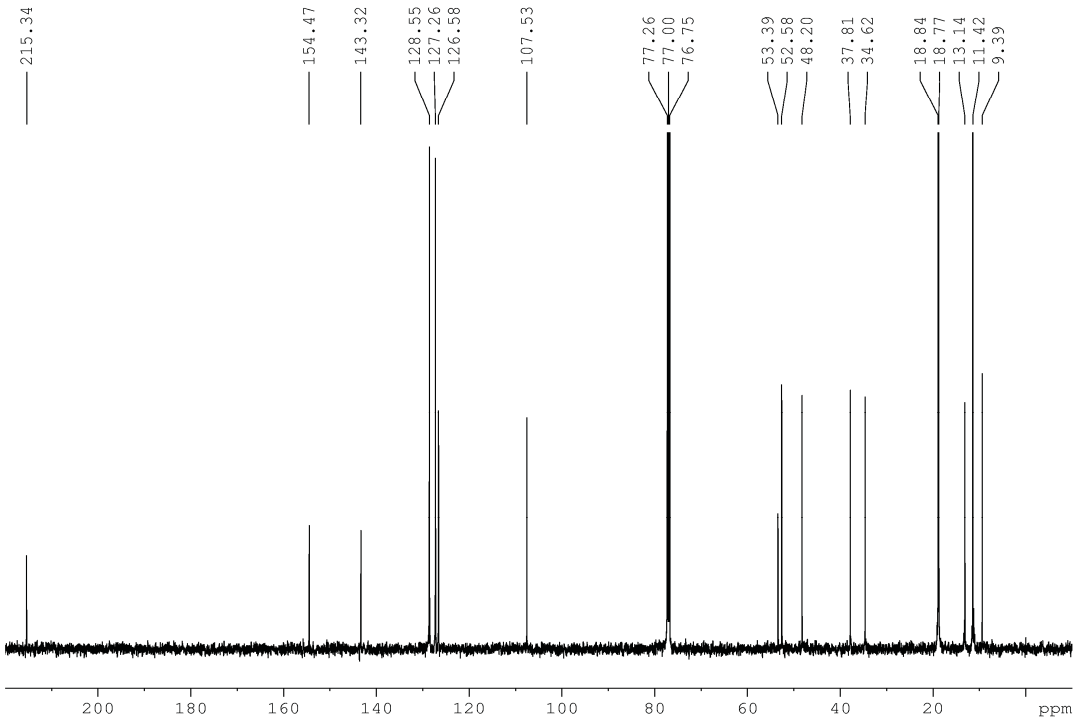
^{13}C NMR ($CDCl_3$, 125 MHz) spectrum of (1*R,3*R**,4*S**,6*R**)-1-methyl-2-meth-ylene-3-phenyl-6-((trimethylsilyl)methyl)bicyclo[2.2.1]-heptan-7-one (106a)**



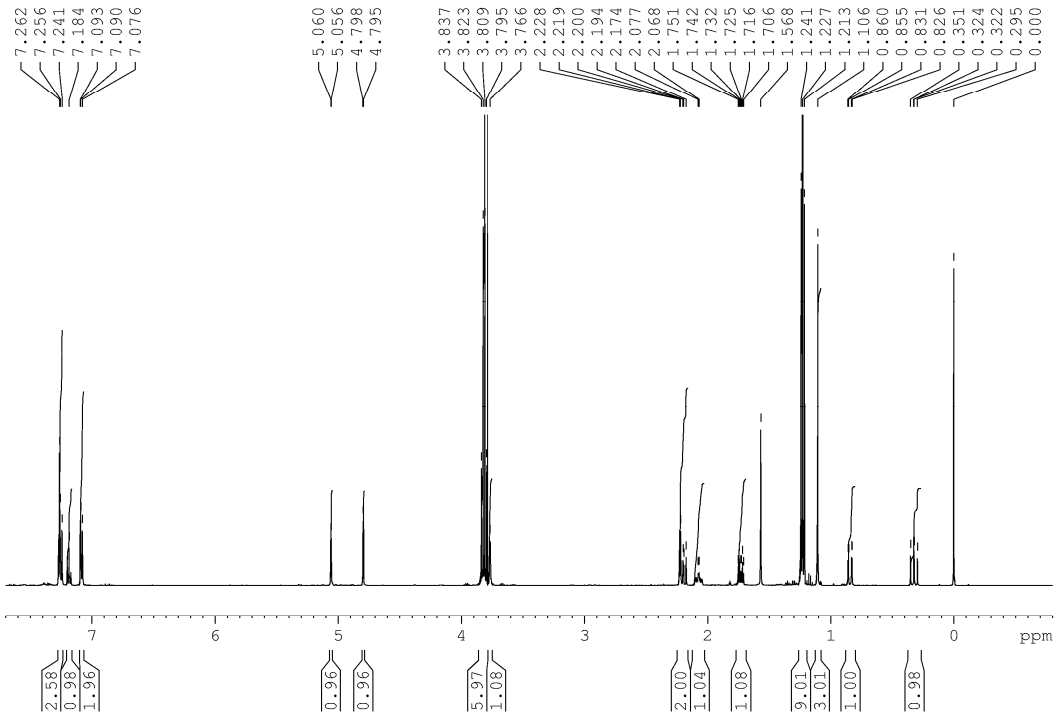
^{1}H NMR ($CDCl_3$, 500 MHz) spectrum of (1*R,3*R**,4*S**,6*R**)-1-methyl-2-methylene-3-phenyl-6-((triisopropylsilyl)methyl) bicycle[2.2.1] -heptan-7-one (106b)**



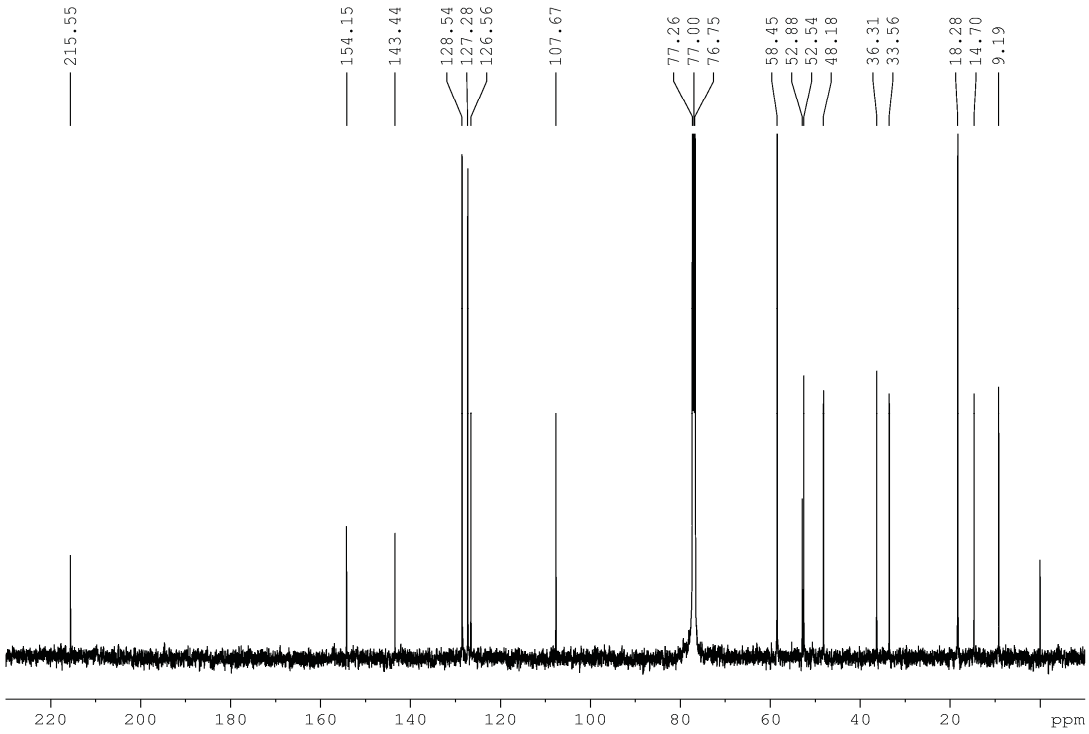
^{13}C NMR ($CDCl_3$, 125 MHz) spectrum of (1*R,3*R**,4*S**,6*R**)-1-methyl-2-methylene-3-phenyl-6-((triisopropylsilyl)methyl) bicyclo[2.2.1]-heptan-7-one (106b)**



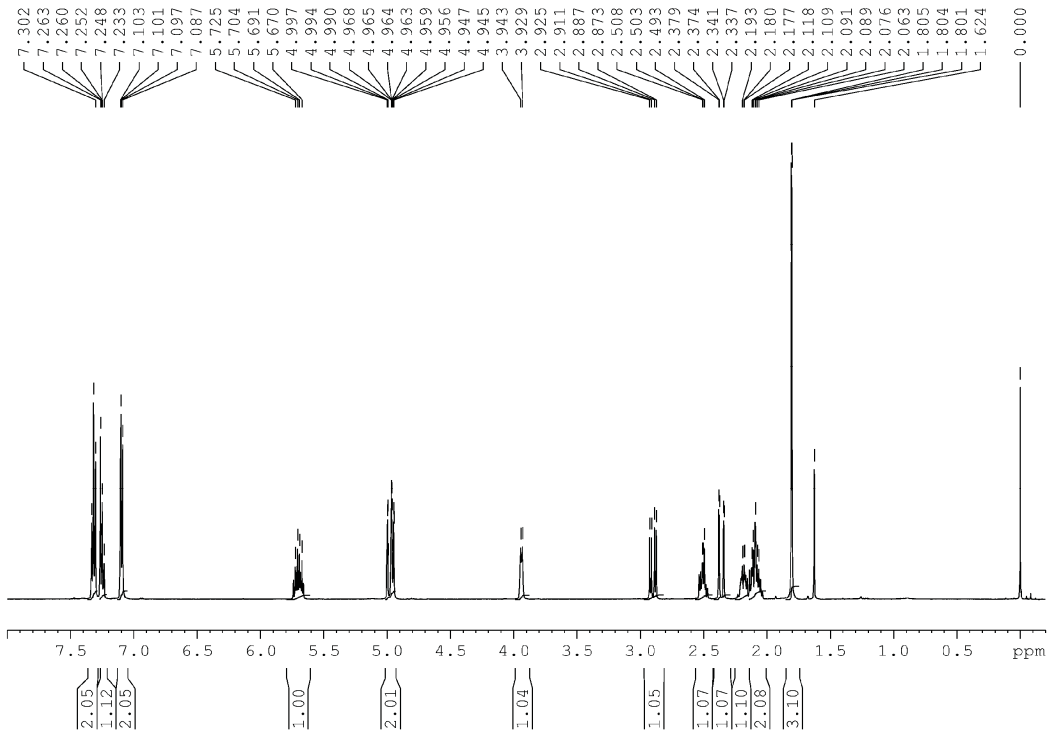
^{1}H NMR ($CDCl_3$, 500 MHz) spectrum of (1*R,3*R**,4*S**,6*R**)-1-methyl-2-methylene-3-phenyl-6-((triethoxysilyl)methyl)bicyclo[2.2.1] heptan-7-one (106c)**



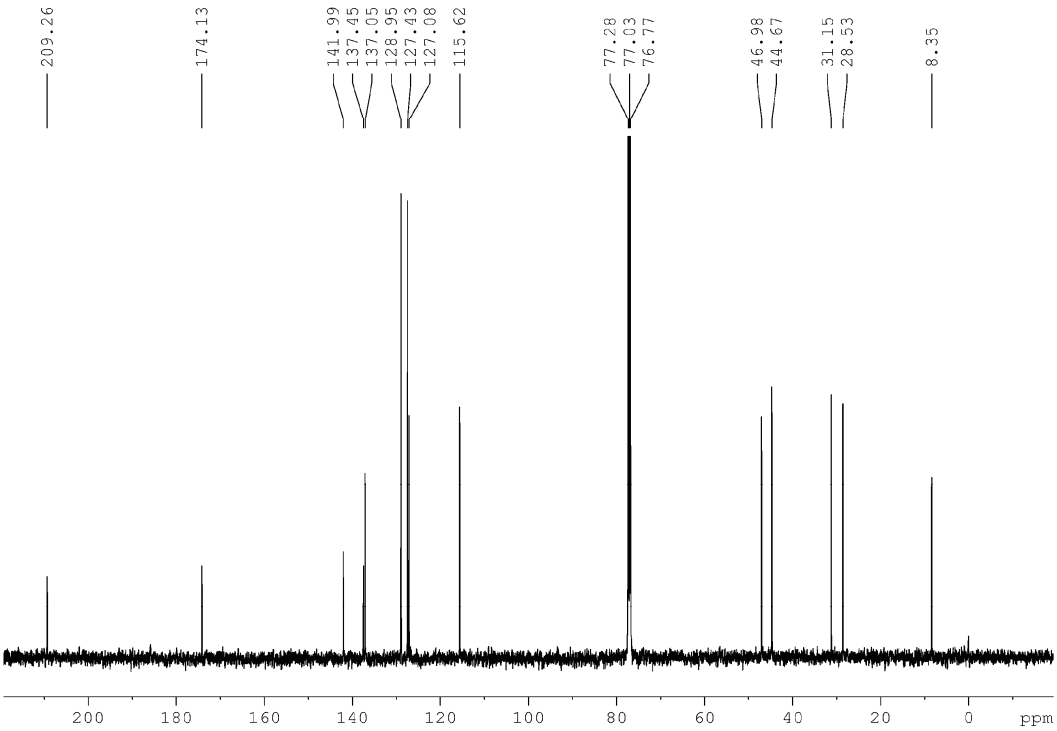
^{13}C NMR ($CDCl_3$, 125 MHz) spectrum of (1*R,3*R**,4*S**,6*R**)-1-methyl-2-methylene-3-phenyl-6-((triethoxysilyl)methyl)bicyclo[2.2.1]heptan-7-one (106c)**



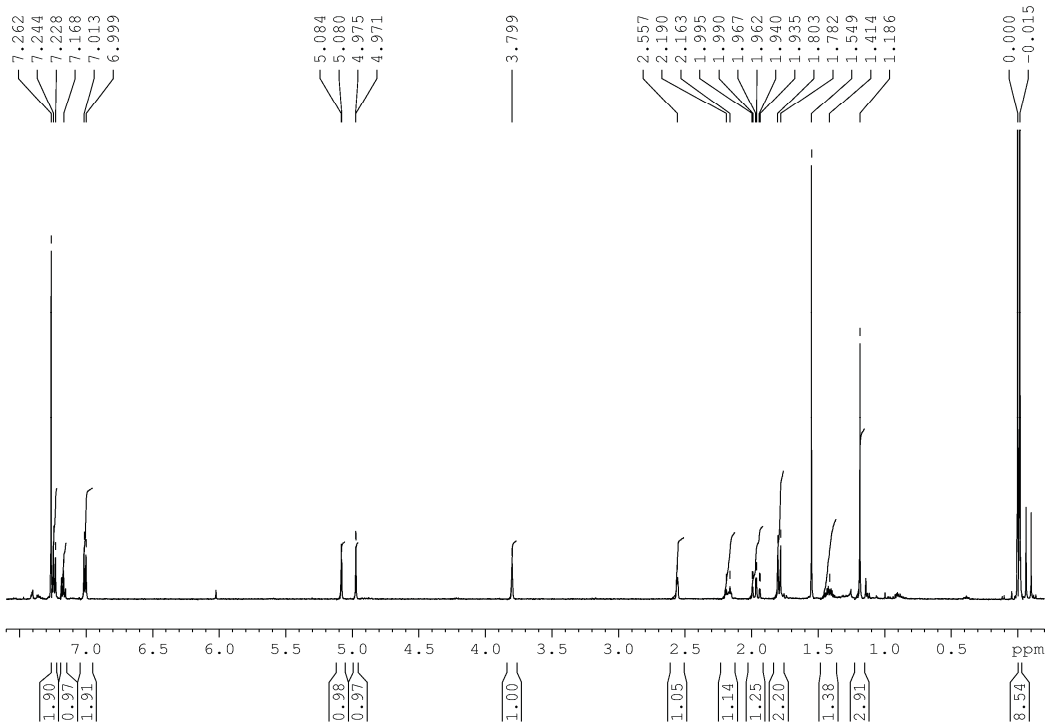
^{1}H NMR ($CDCl_3$, 500 MHz) spectrum of 3-(but-3-enyl)-2-methyl-4-phenylcyclopent-2-enone (107)



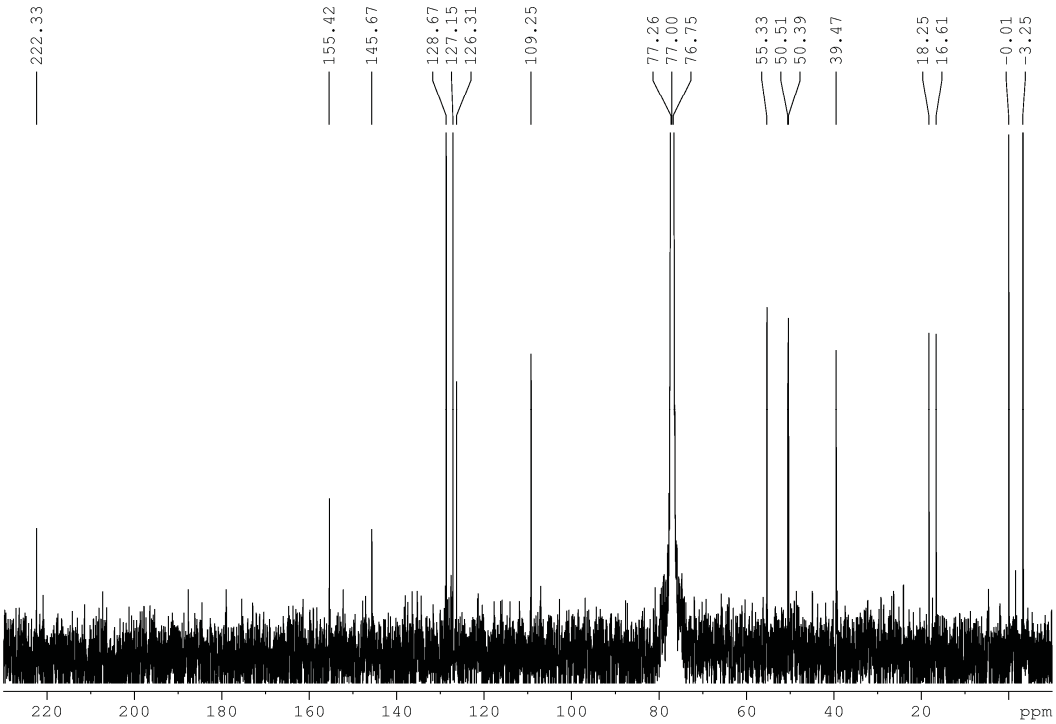
^{13}C NMR ($CDCl_3$, 125 MHz) spectrum of 3-(but-3-enyl)-2-methyl-4-phenylcyclopent-2-enone (107)



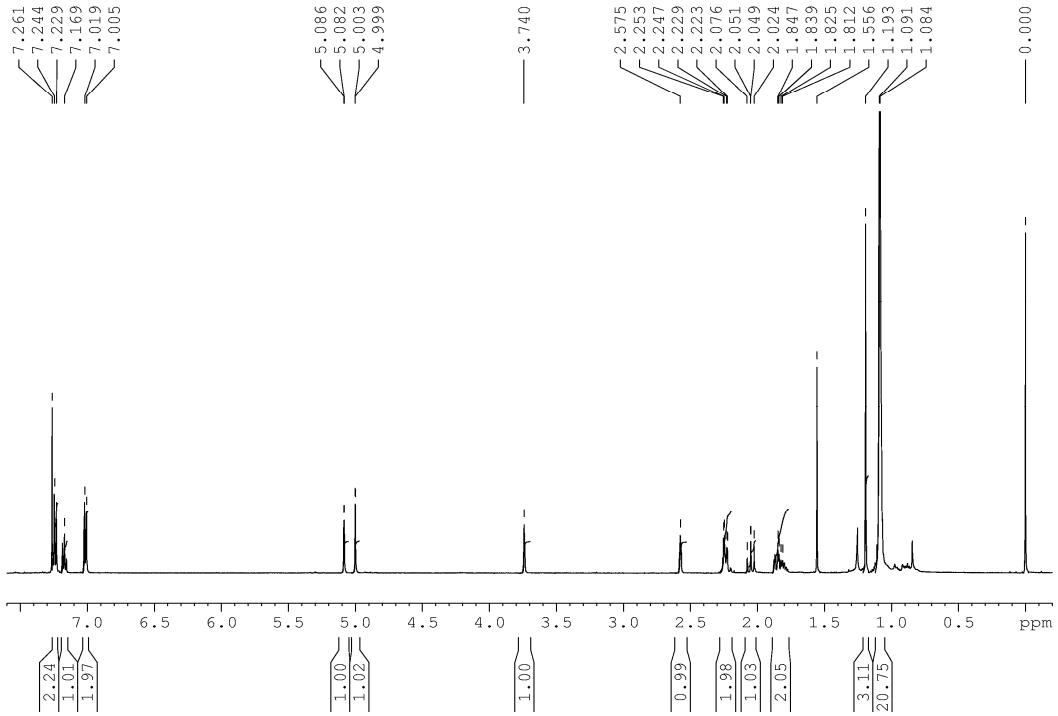
^{1}H NMR ($CDCl_3$, 500 MHz) spectrum of (1*R,3*R**,5*S**,6*R**)-1-methyl-7-methylene-6-phenyl-3-(trimethylsilyl)bicyclo[3.2.1]octan-8-one (109a)**



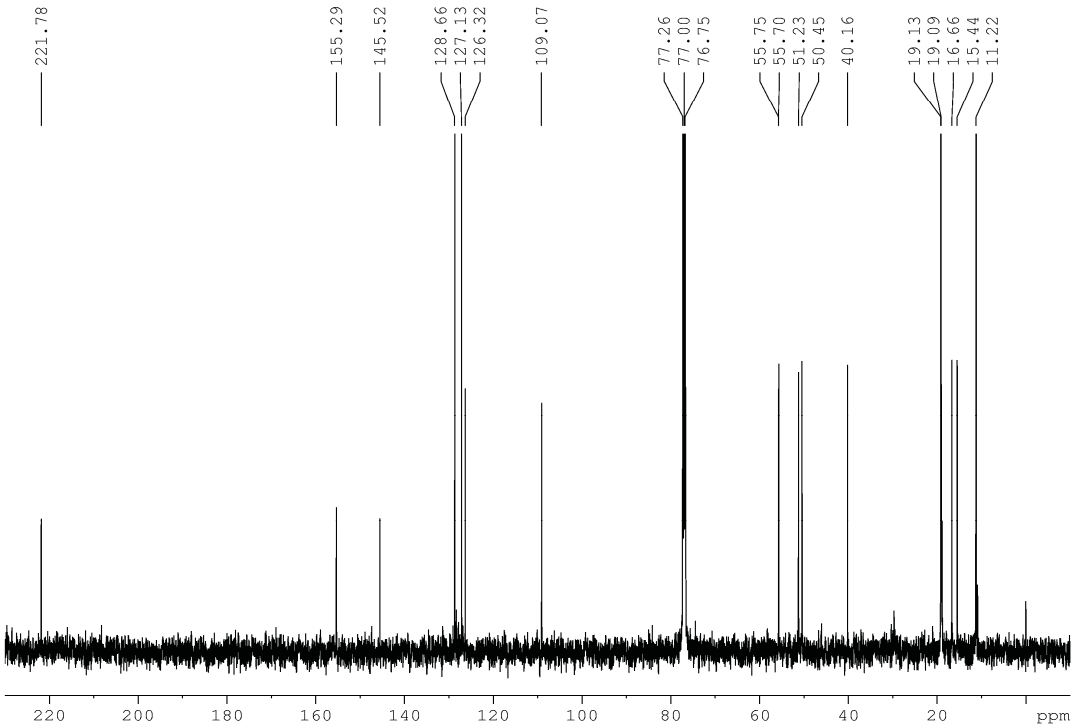
^{13}C NMR ($CDCl_3$, 125 MHz) spectrum of (1*R,3*R**,5*S**,6*R**)-1-methyl-7-methylene-6-phenyl-3-(trimethylsilyl)bicyclo[3.2.1]octan-8-one (109a)**



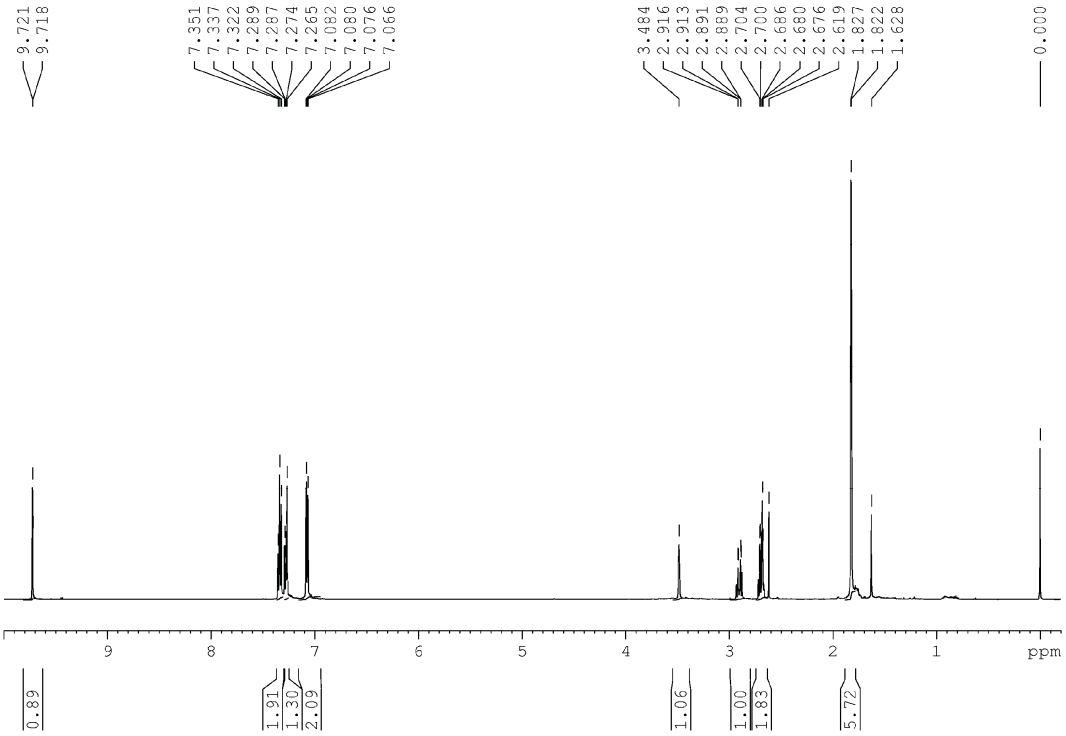
^{1}H NMR ($CDCl_3$, 500 MHz) spectrum of (1*R,3*R**,5*S**,6*R**)-1-methyl-7-methylene-6-phenyl-3-(triisopropylsilyl)bicyclo[3.2.1]octan-8-one (109b)**



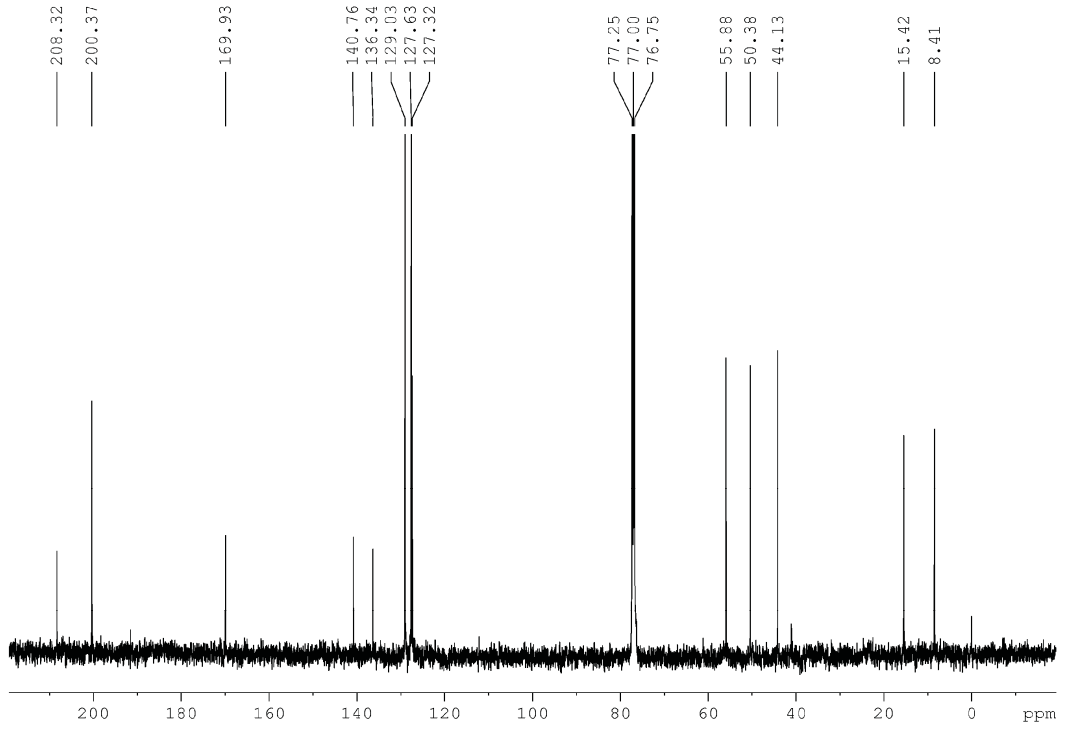
^{13}C NMR ($CDCl_3$, 125 MHz) spectrum of (1*R,3*R**,5*S**,6*R**)-1-methyl-7-methylene-6-phenyl-3-(triisopropylsilyl)bicyclo[3.2.1]octan-8-one (109b)**



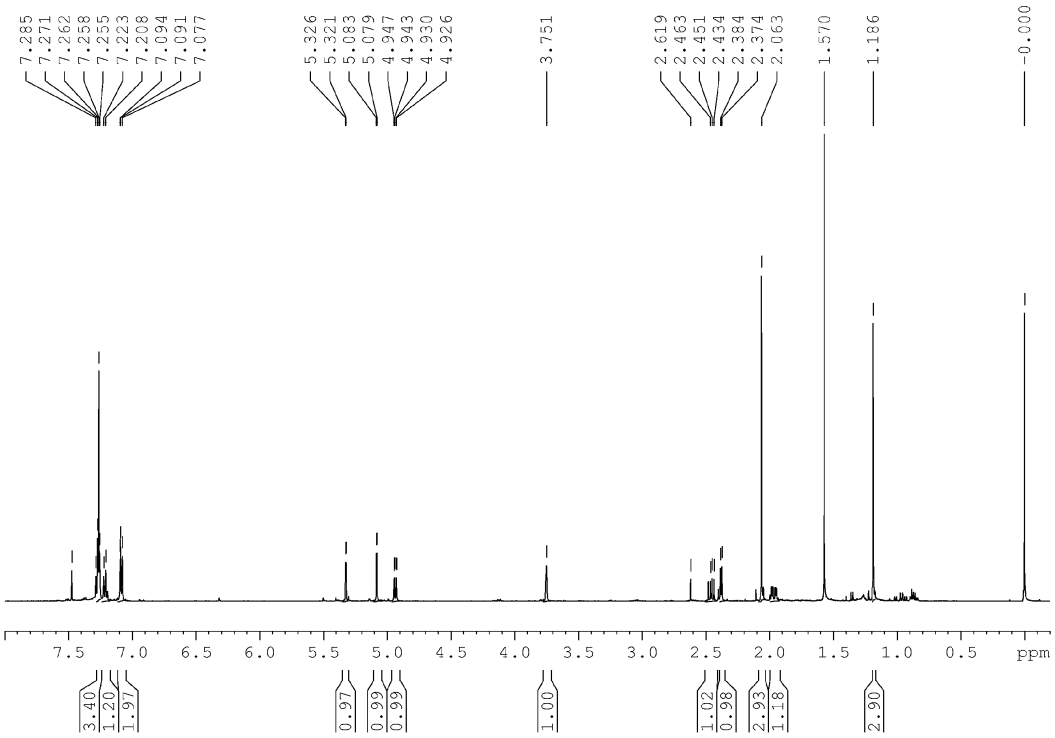
^{1}H NMR ($CDCl_3$, 500 MHz) spectrum of 2-((*trans*)-3,4-dimethyl-2-oxo-5-phenylcyclopent-3-enyl)acetaldehyde (110)



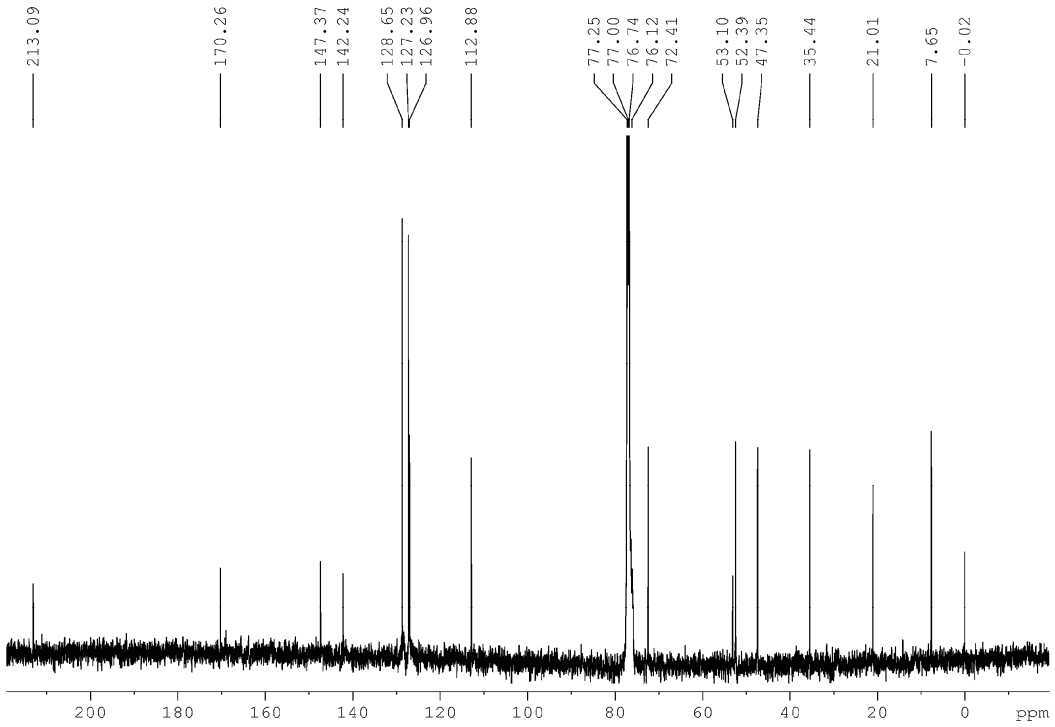
^{13}C NMR ($CDCl_3$, 125 MHz) spectrum of 2-((*trans*)-3,4-dimethyl-2-oxo-5-phenylcyclopent-3-enyl)acetaldehyde (110)



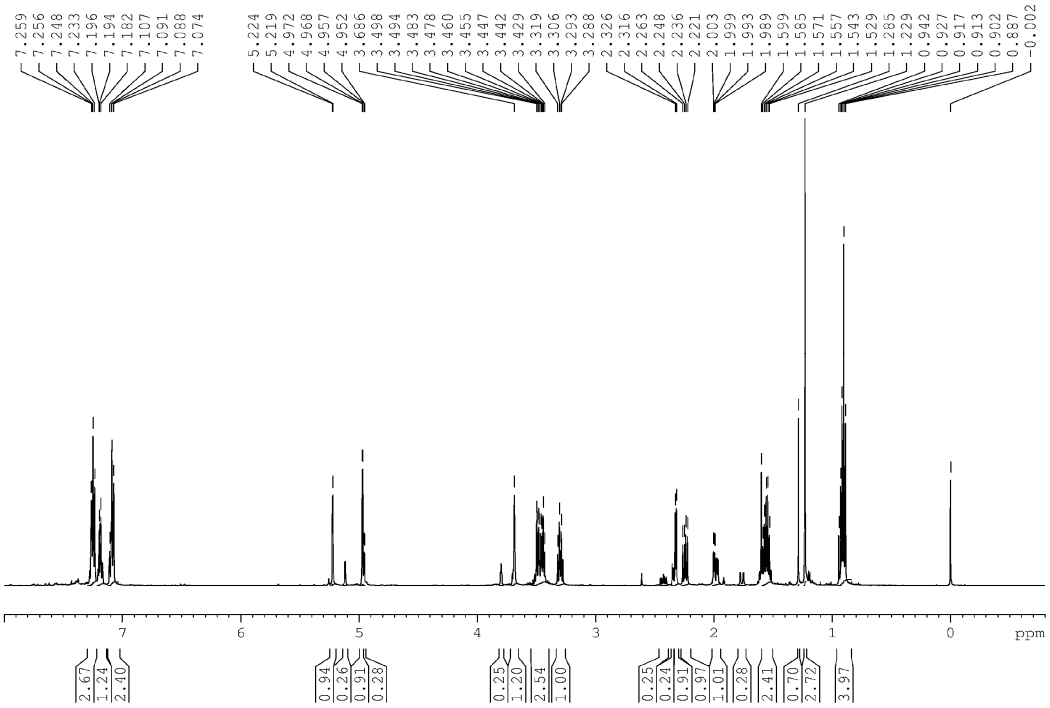
^{1}H NMR ($CDCl_3$, 500 MHz) spectrum of 1-methyl-6-methylene-7-oxo-5-phenylbicyclo[2.2.1]heptan-2-yl acetate (111)



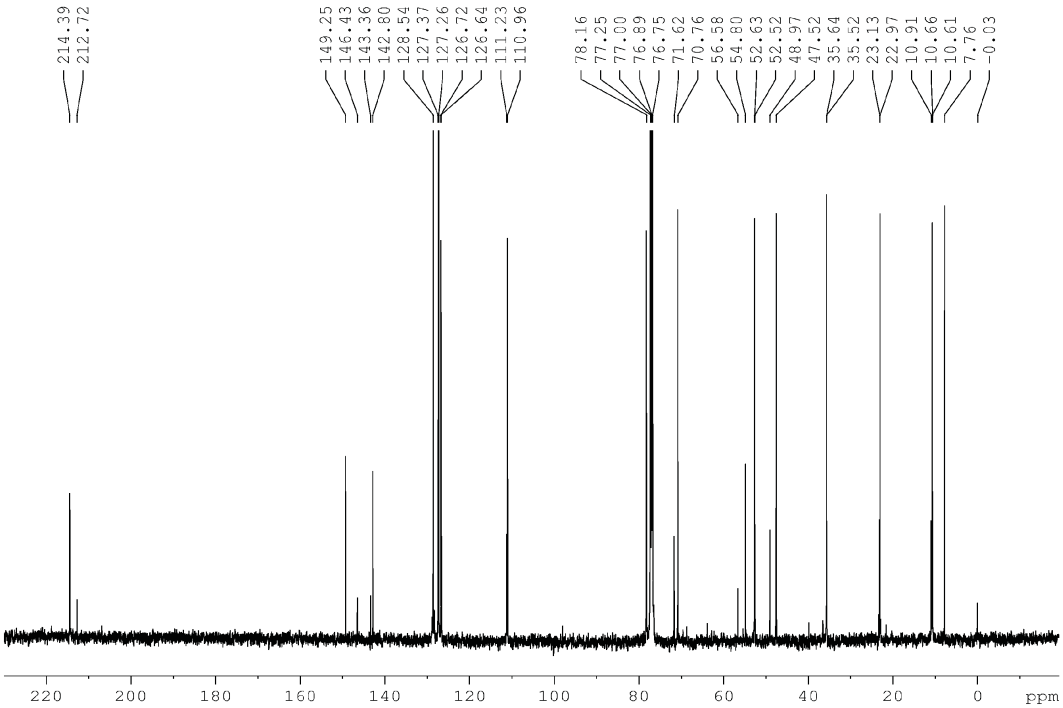
^{13}C NMR ($CDCl_3$, 125 MHz) spectrum of 1-methyl-6-methylene-7-oxo-5-phenylbicyclo[2.2.1]heptan-2-yl acetate (111)



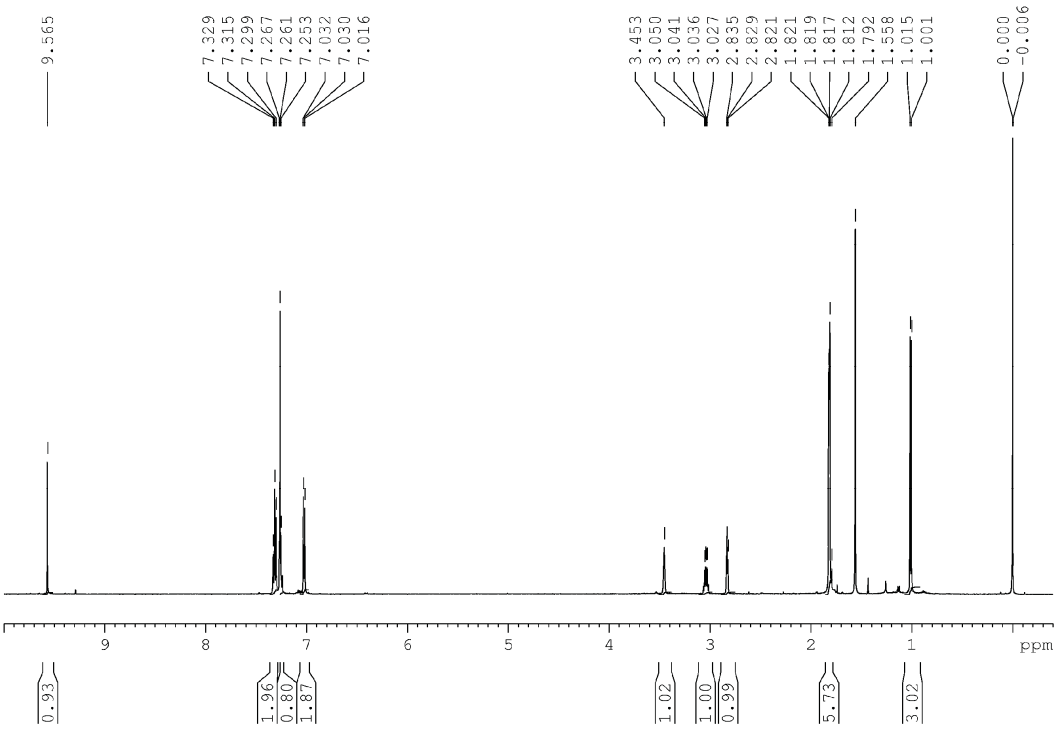
^{1}H NMR ($CDCl_3$, 500 MHz) spectrum of (1*R,3*S**,4*R**,6*S**)- and (1*R**,3*S**,4*R**,6*R**)-1-methyl-2-methylene-3-phenyl-6-propoxybicyclo-[2.2.1]heptan-7-one (112)**



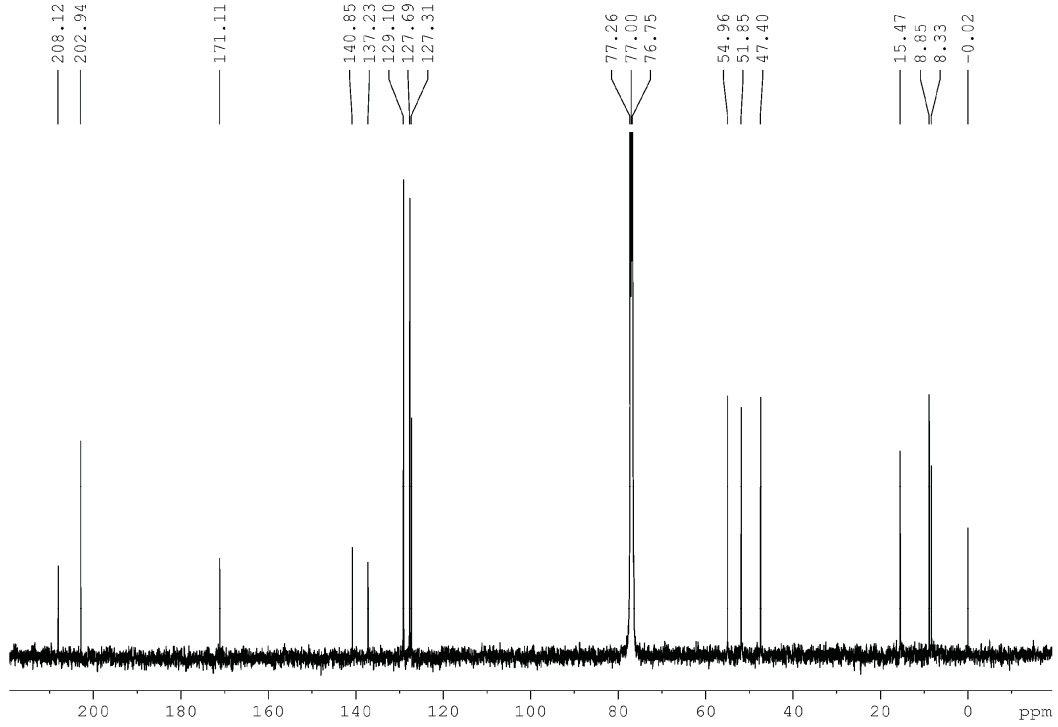
^{13}C NMR ($CDCl_3$, 125 MHz) spectrum of (1*R,3*S**,4*R**,6*S**)- and (1*R**,3*S**,4*R**,6*R**)-1-methyl-2-methylene-3-phenyl-6-propoxybicyclo- [2.2.1]heptan-7-one (112)**



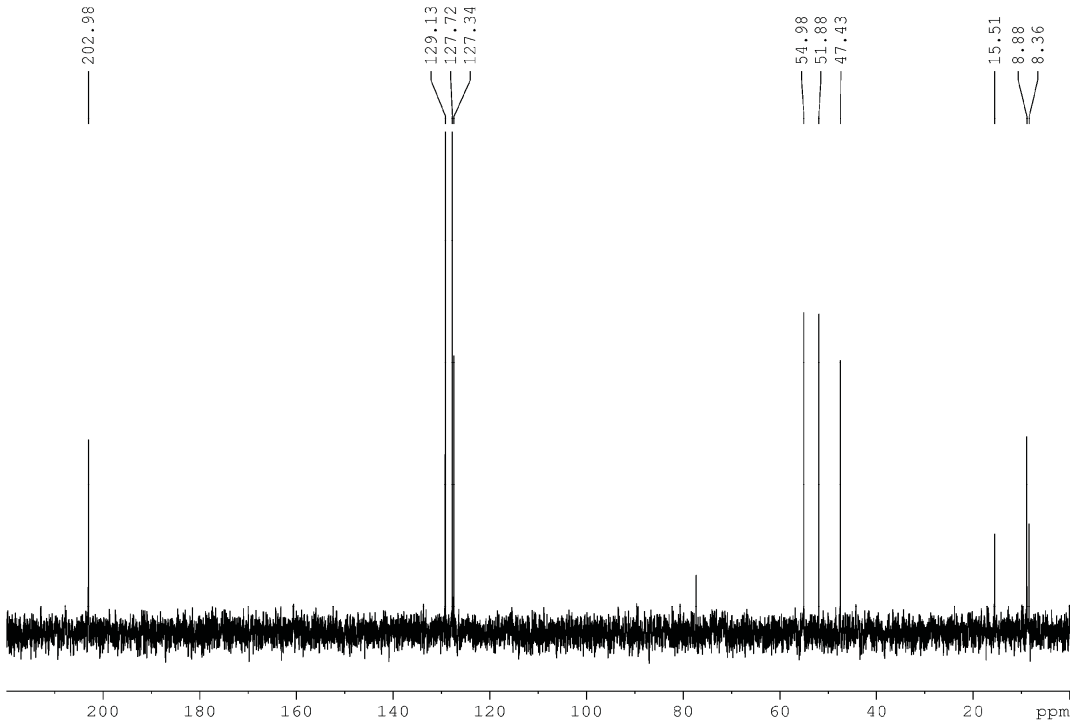
^{1}H NMR ($CDCl_3$, 500 MHz) spectrum of (1'*R,2*S**,5'*R**)-2-(3,4-dimethyl-2-oxo-5-phenylcyclopent-3-enyl)propanal (113)**



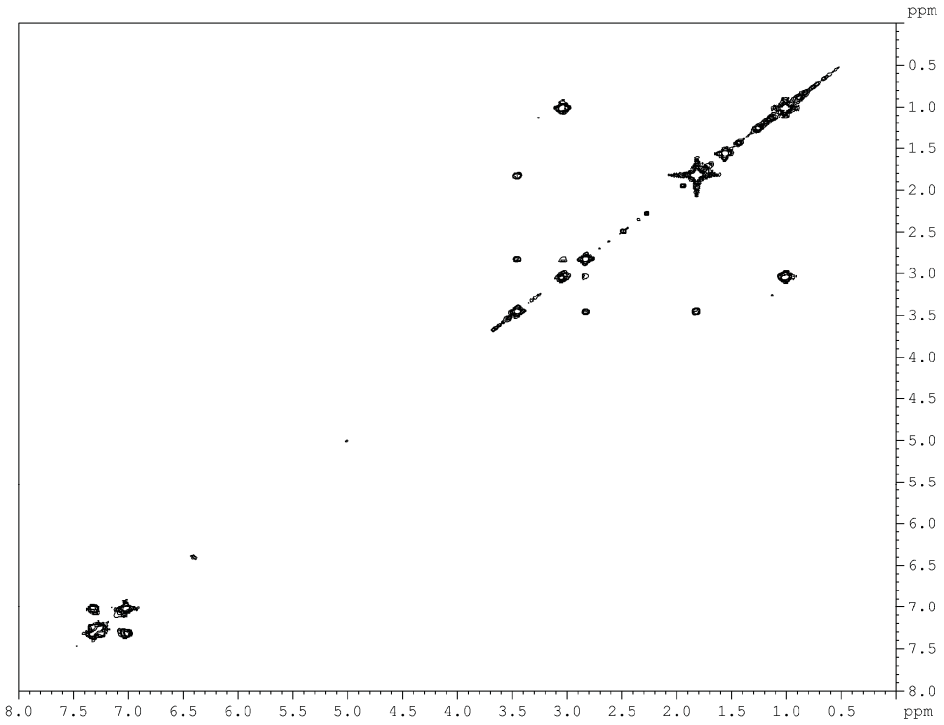
^{13}C NMR ($CDCl_3$, 125 MHz) spectrum of (1'*R,2*S**,5'*R**)-2-(3,4-dimethyl-2-oxo-5-phenylcyclopent-3-enyl)propanal (113)**



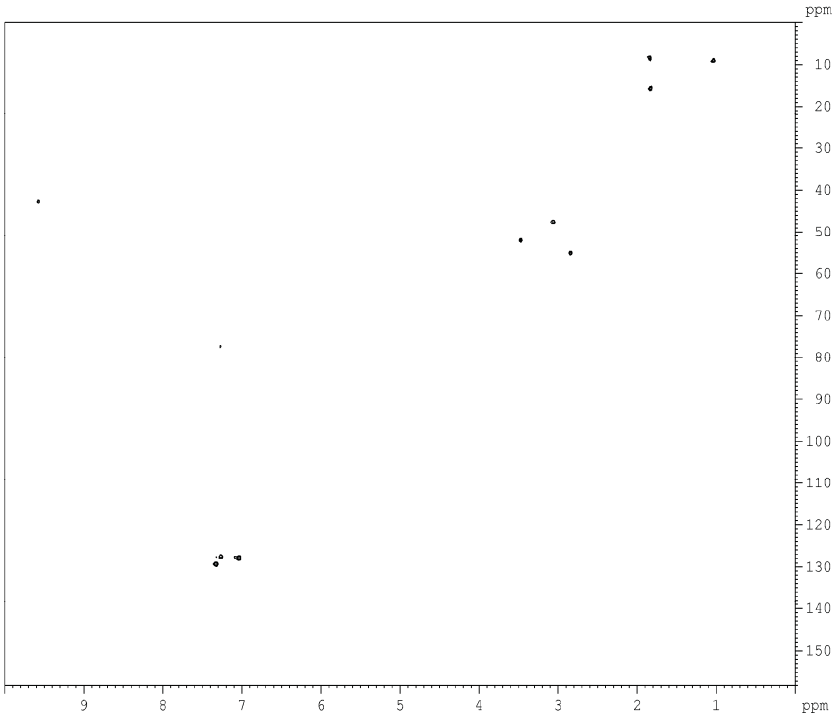
DEPT-135 spectrum of (1'*R,2*S**,5'*R**)-2-(3,4-dimethyl-2-oxo-5-phenylcyclopent-3-enyl)propanal (113)**



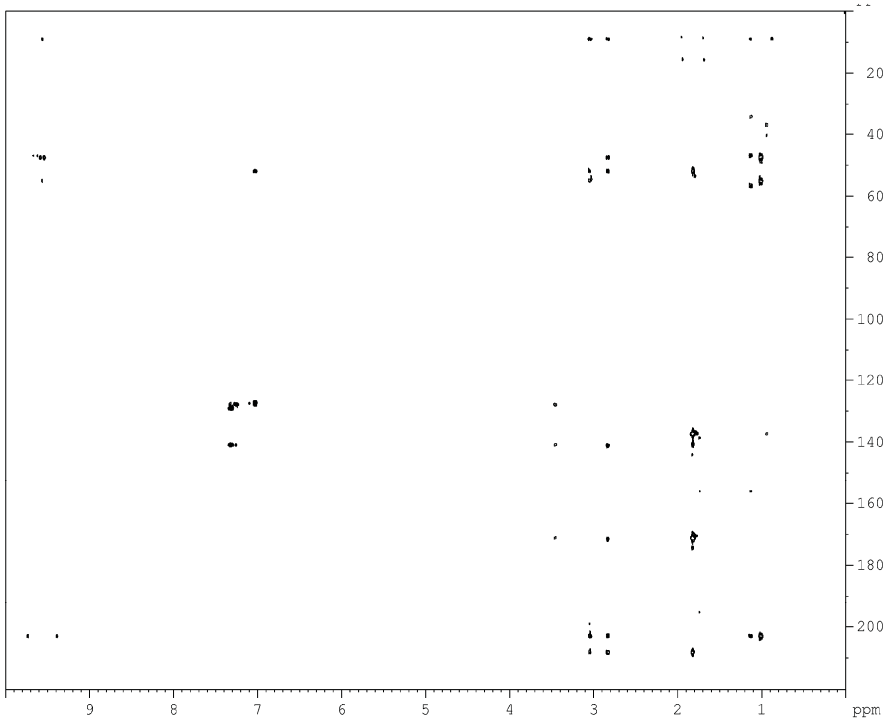
COSY spectrum of (1'*R,2*S**,5'*R**)-2-(3,4-dimethyl-2-oxo-5-phenylcyclopent-3-enyl)propanal (113)**



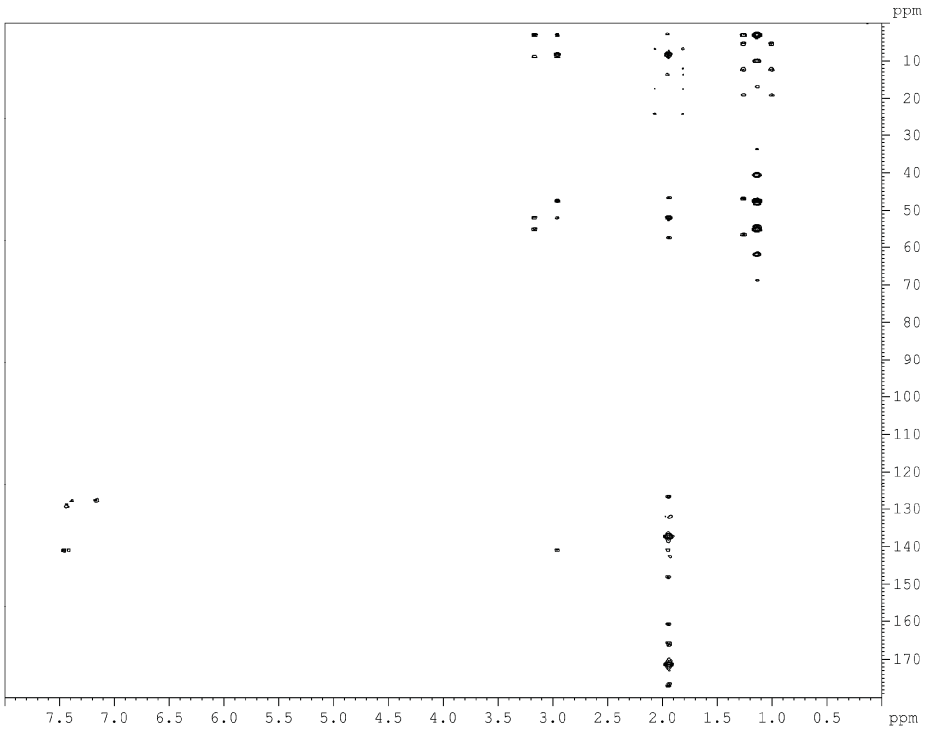
HSQC spectrum of (1'*R,2*S**,5'*R**)-2-(3,4-dimethyl-2-oxo-5-phenylcyclopent-3-enyl)propanal (113)**



HMBC spectrum of (1'*R,2*S**,5'*R**)-2-(3,4-dimethyl-2-oxo-5-phenylcyclopent-3-enyl)propanal (113)**

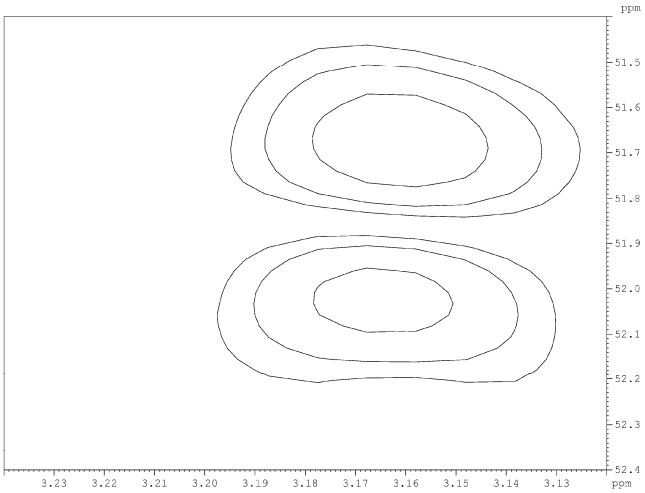


***J*-HMBC spectrum of (1'*R**,2*S**,5'*R**)-2-(3,4-dimethyl-2-oxo-5-phenylcyclopent-3-enyl)propanal (113)**

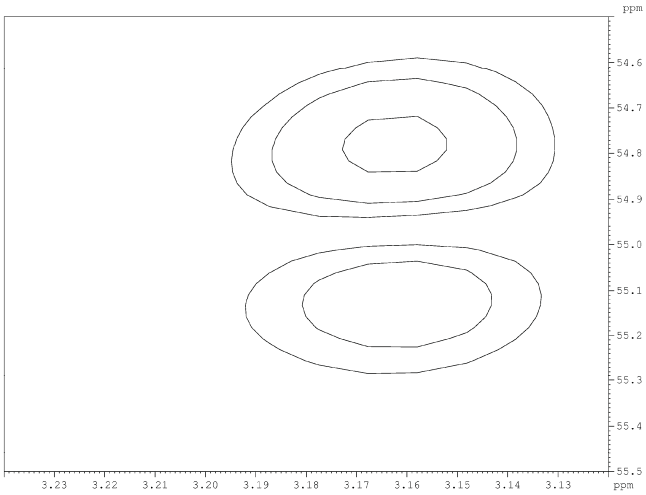


Details of *J*-HMBC spectrum of (1'*R,2*S**,5'*R**)-2-(3,4-dimethyl-2-oxo-5-phenylcyclopent-3-enyl)propanal (113)**

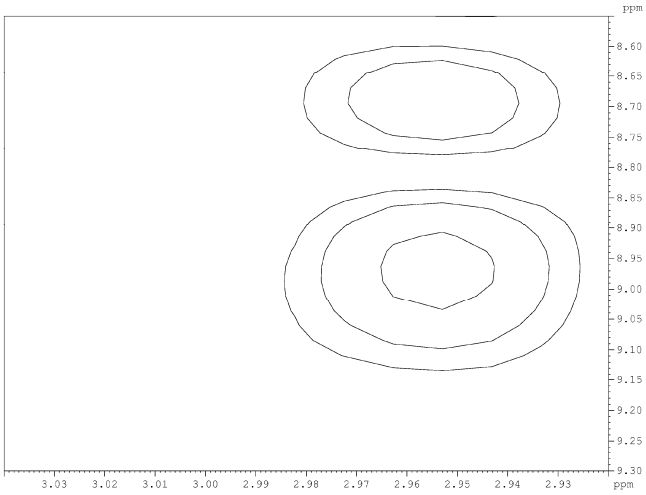
^{2}J H2-C5'



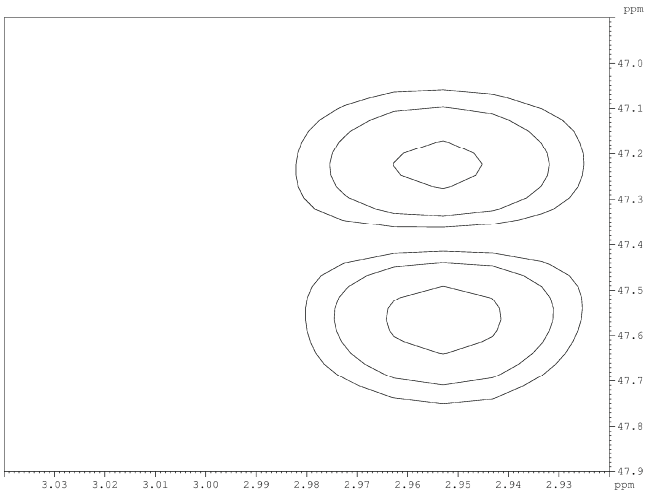
^{2}J H2-C1'



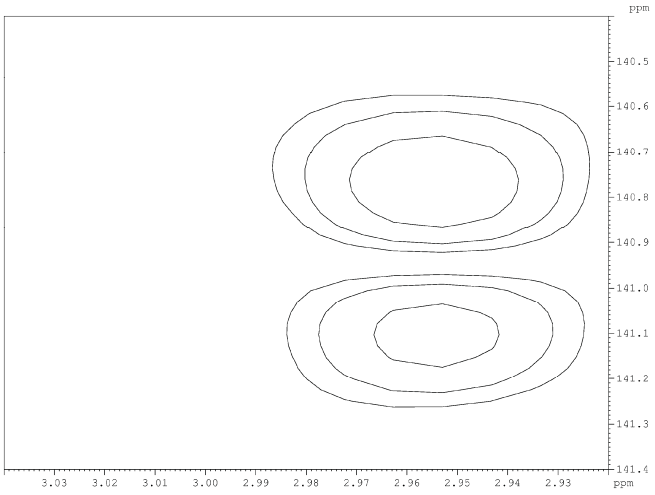
^{3}J H1'-C3



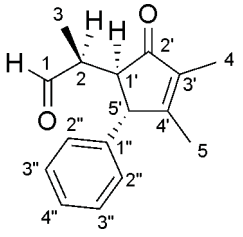
^{2}J H1'-C2

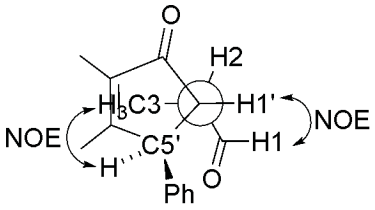


^{3}J H1'-C1"



Critical data from *J*-HMBC spectrum of (1'*R,2*S**,5'*R**)-2-(3,4-dimethyl-2-oxo-5-phenylcyclopent-3-enyl)propanal (113)**





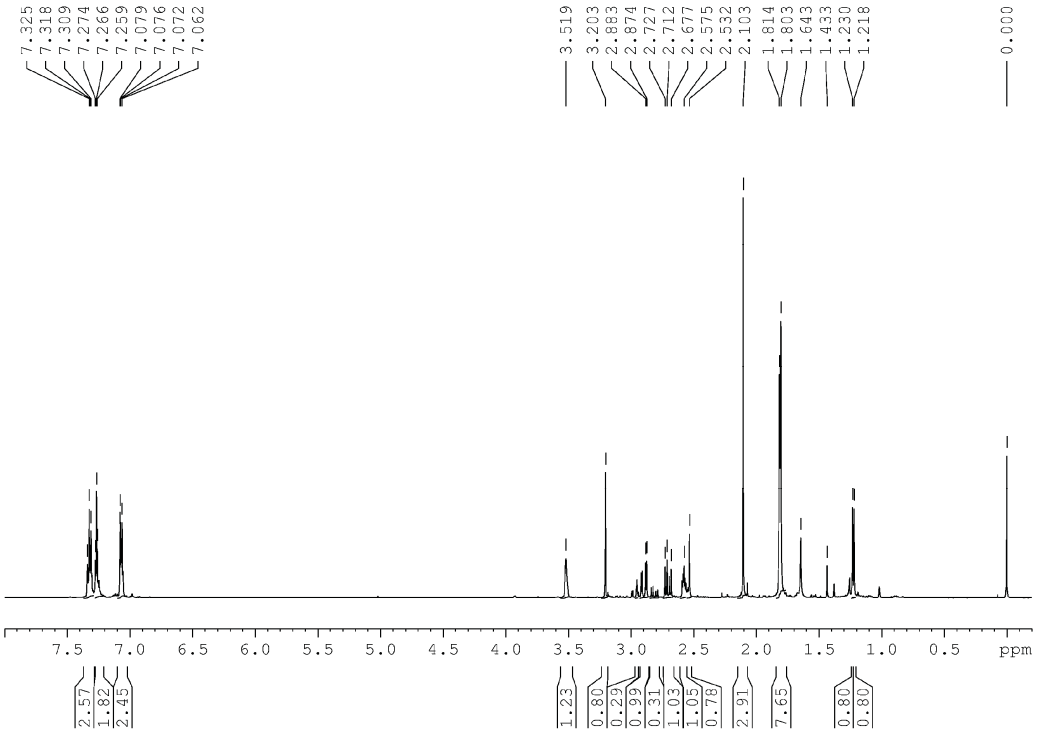
Measured $^{3}J_{H,H}$ and $^{2,3}J_{C,H}$ with respect to the C2-C1' segment in compound **113**

$^{2,3}J_{H,X}$	nuclei	measured value (Hz)	magnitude estimation	stereorelation
$^{3}J_{H,H}$	H2-H1'	4.2	small	*gauche*
$^{3}J_{C,H}$	H2-C5'	7.4	large	*anti*
	H1'-C3	5.9	large	*anti*
$^{2}J_{C,H}$	H2-C1'	7.2	large	*gauche to C2'*
	H1'-C2	7.1	large	*gauche to C1*

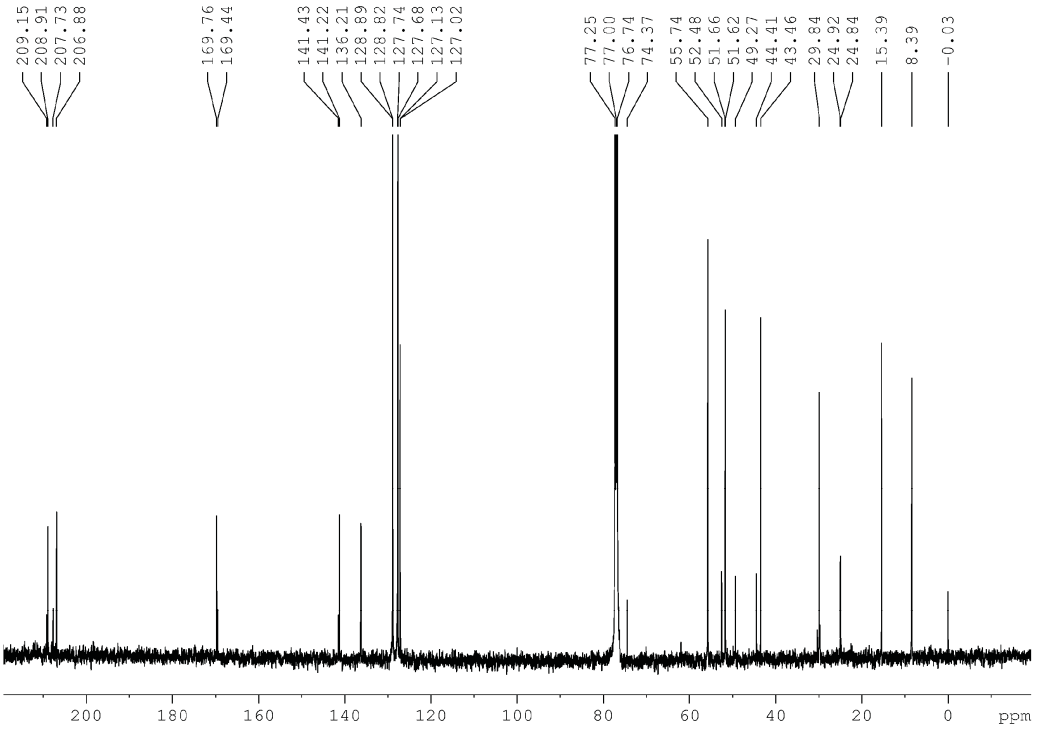
Measured $^{3}J_{H,H}$ and $^{2,3}J_{C,H}$ with respect to the C1'-C5' segment in compound **113**

$^{2,3}J_{H,X}$	nuclei	measured value (Hz)	magnitude estimation	stereorelation
$^{3}J_{H,H}$	H1'-H5'	3.2	small	*anticlinal*
$^{3}J_{C,H}$	H1'-C1''	7.0	large	*synclinal*

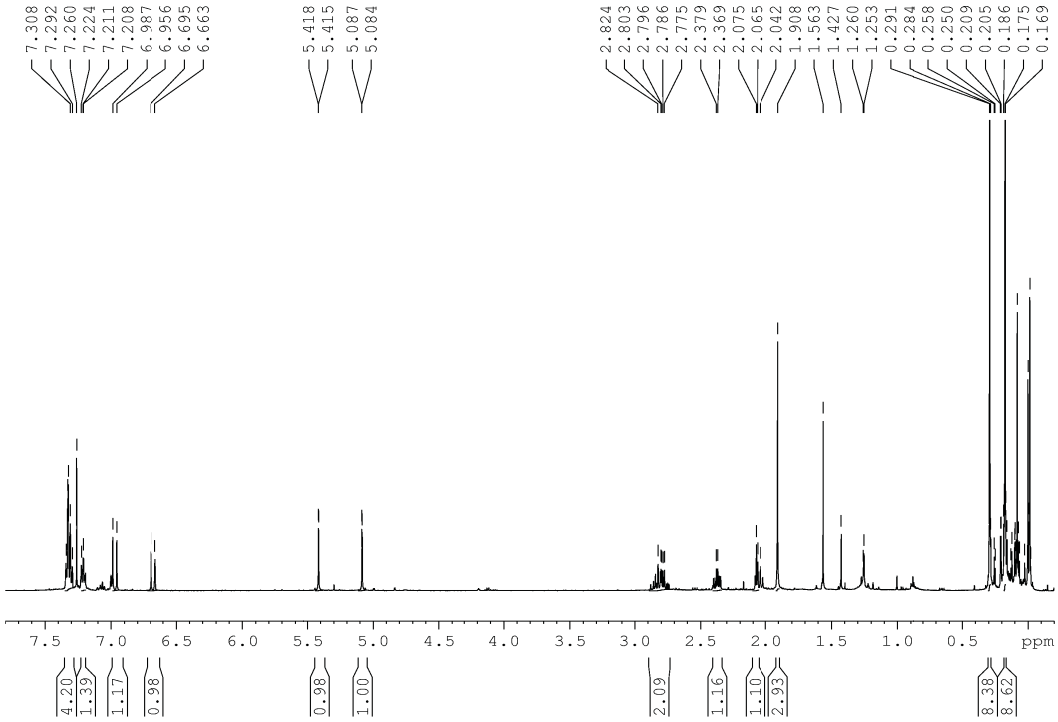
^{1}H NMR ($CDCl_3$, 500 MHz) spectrum of (*trans*)-2,3-dimethyl-5-(2-oxopropyl)-4-phenylcyclopent-2-enone (114) and by-product



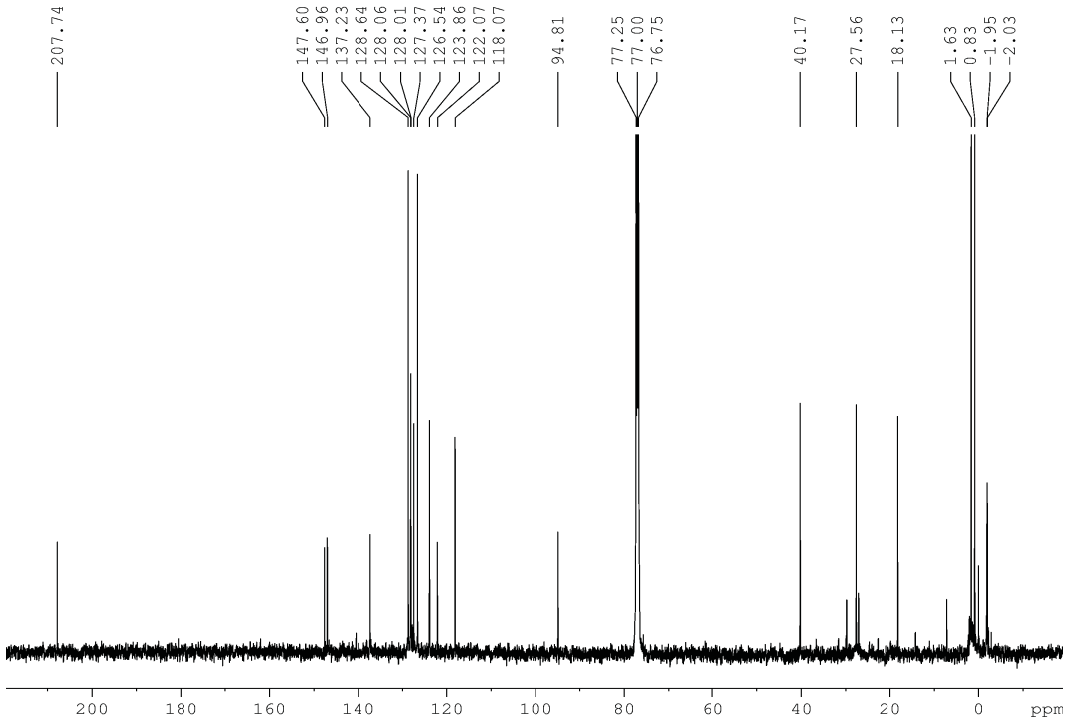
^{13}C NMR ($CDCl_3$, 125 MHz) spectrum of (*trans*)-2,3-dimethyl-5-(2-oxopropyl)-4-phenylcyclopent-2-enone (114) and by-product



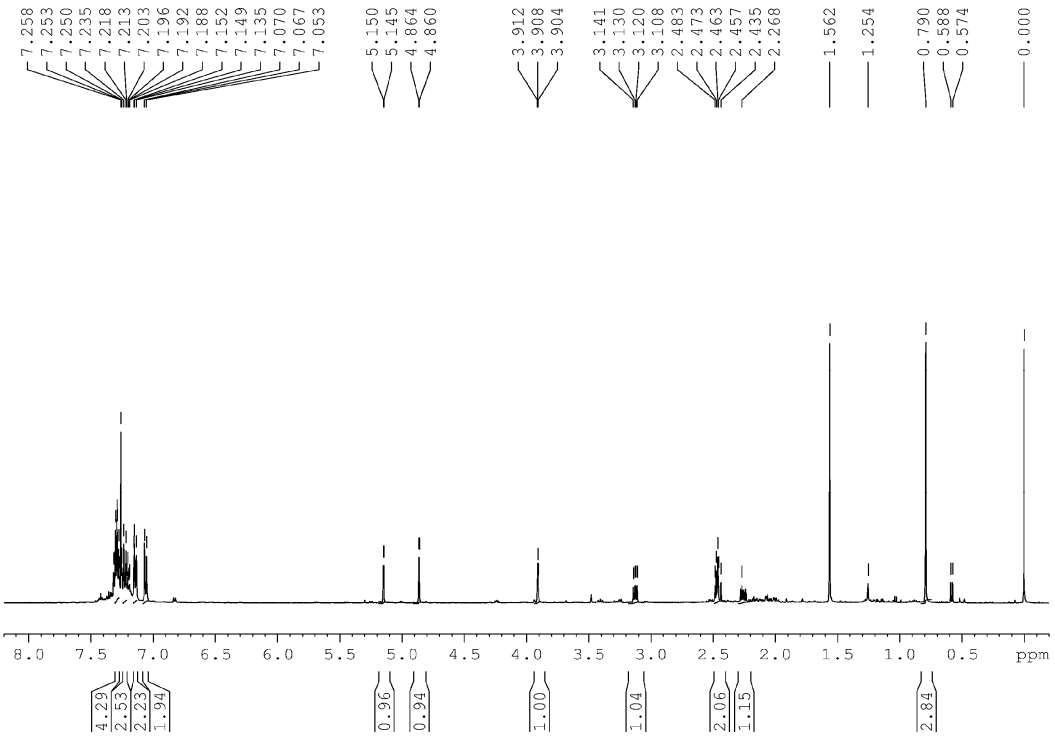
^{1}H NMR ($CDCl_3$, 500 MHz) spectrum of trimethyl((1*E*,3*Z*)-4-methyl-1-phenyl-5-(1-(trimethylsilyloxy)cyclobutyl)hexa-1,3,5-trien-3-yloxy)silane (116)



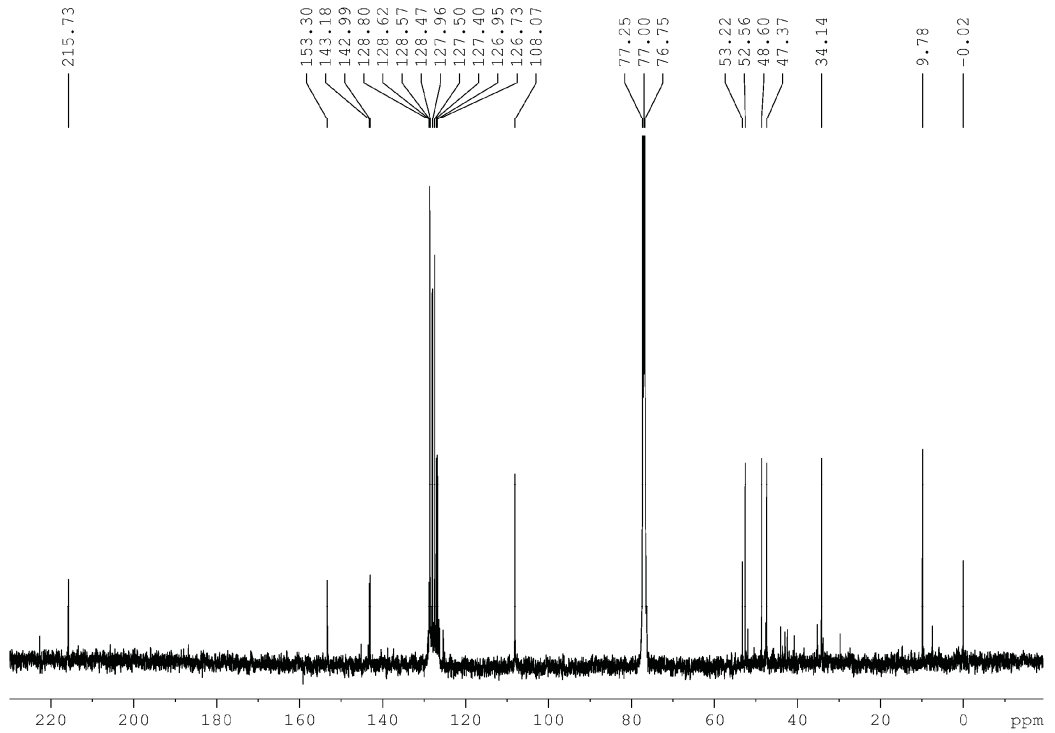
^{13}C NMR ($CDCl_3$, 125 MHz) spectrum of trimethyl((1*E*,3*Z*)-4-methyl-1-phenyl-5-(1-(trimethylsilyloxy)cyclobutyl)hexa-1,3,5-trien-3-yloxy)silane (116)



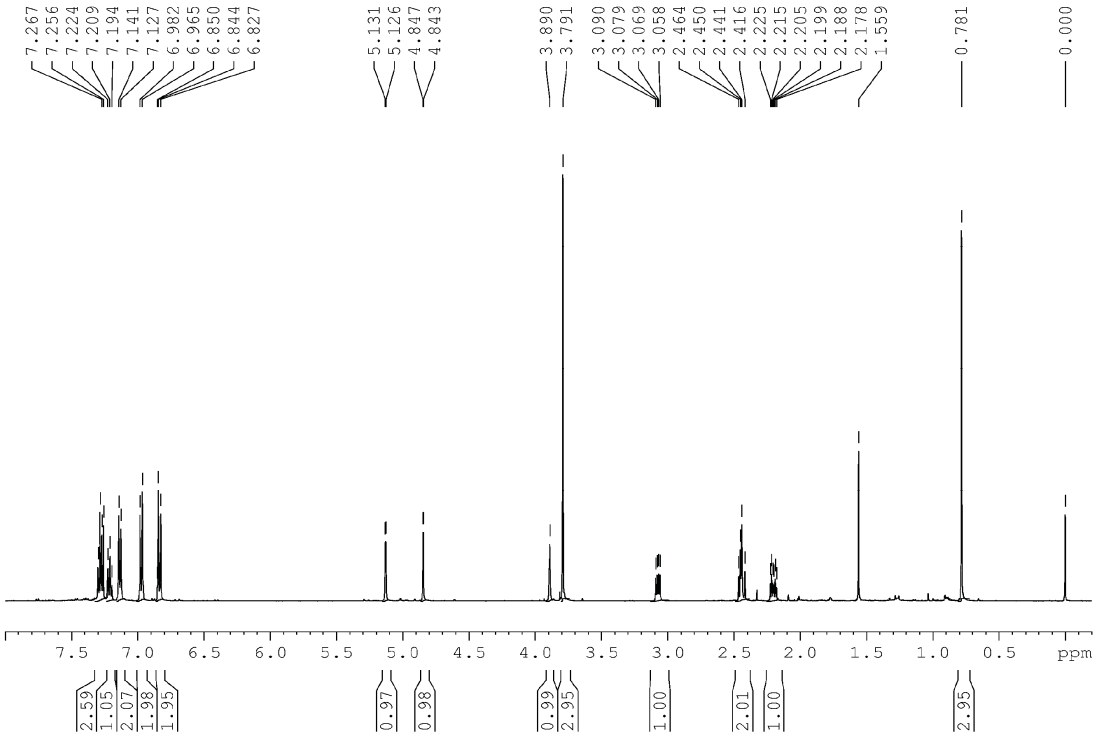
^{1}H NMR ($CDCl_3$, 500 MHz) spectrum of (1*R,3*R**,4*S**,6*S**)-1-methyl-2-methylene-3,6-diphenylbicyclo[2.2.1]heptan-7-one (117)**



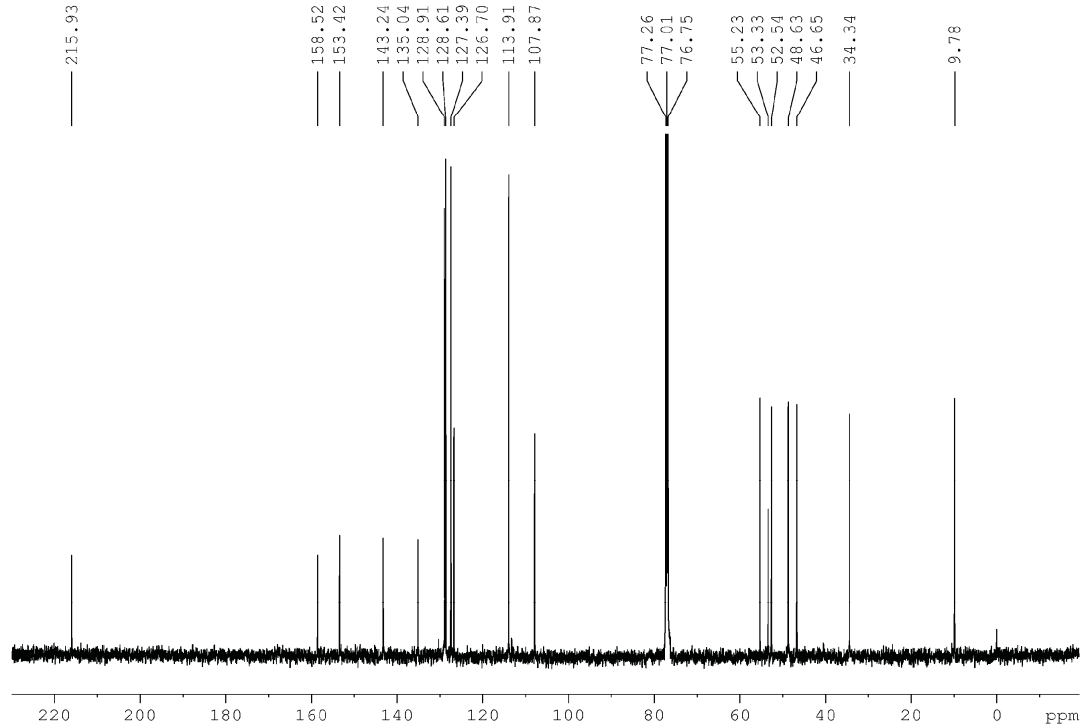
^{13}C NMR ($CDCl_3$, 125 MHz) spectrum of (1*R,3*R**,4*S**,6*S**)-1-methyl-2-methylene-3,6-diphenylbicyclo[2.2.1]heptan-7-one (117)**



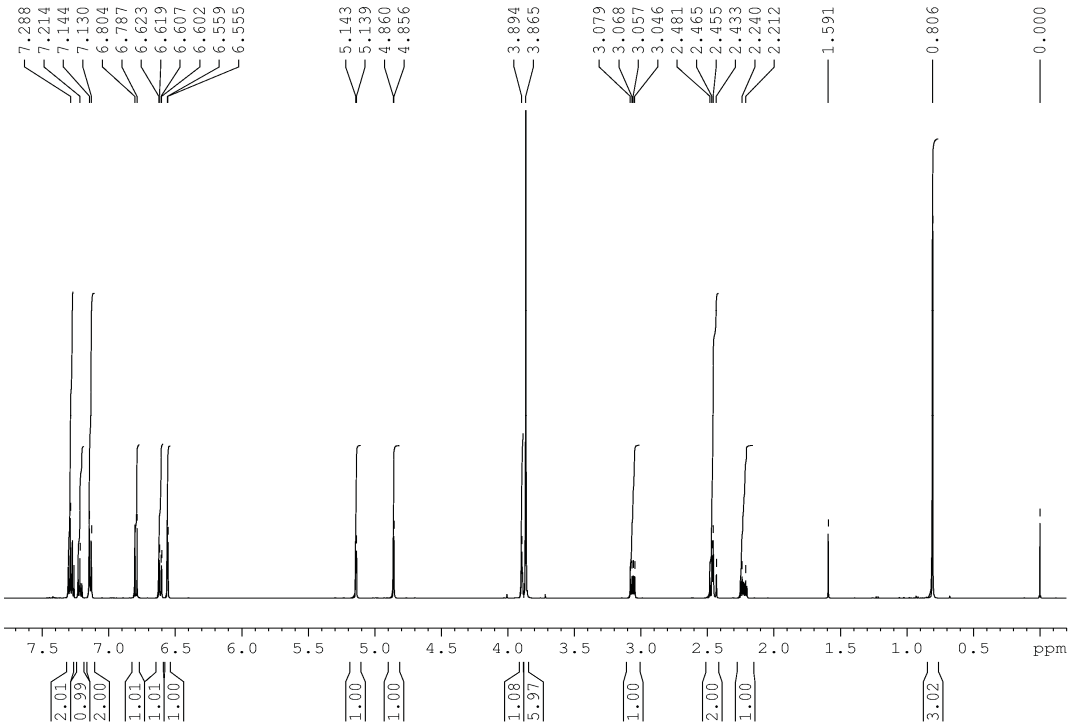
^{1}H NMR ($CDCl_3$, 500 MHz) spectrum of (1*R,3*R**,4*S**,6*S**)-6-(4-methoxyphenyl)-1-methyl-2-methylene-3-phenylbicyclo[2.2.1]heptan-7-one (118)**



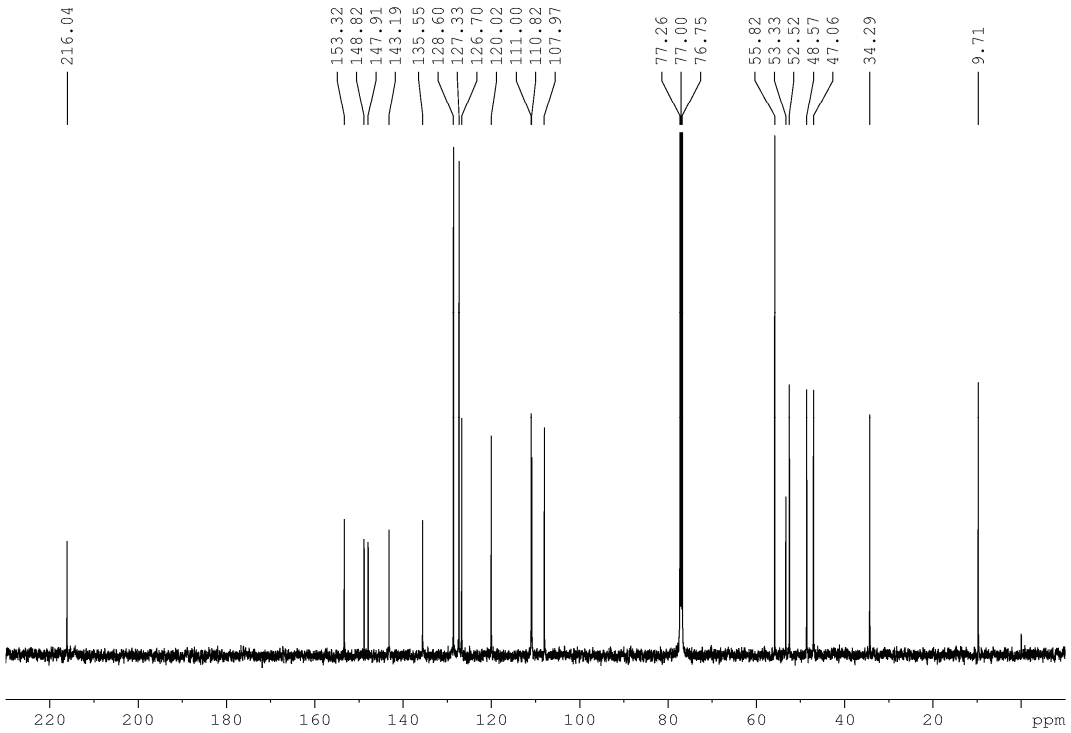
^{13}C NMR ($CDCl_3$, 125 MHz) spectrum of (1*R,3*R**,4*S**,6*S**)-6-(4-methoxyphenyl)-1-methyl-2-methylene-3-phenylbicyclo[2.2.1]heptan-7-one (118)**



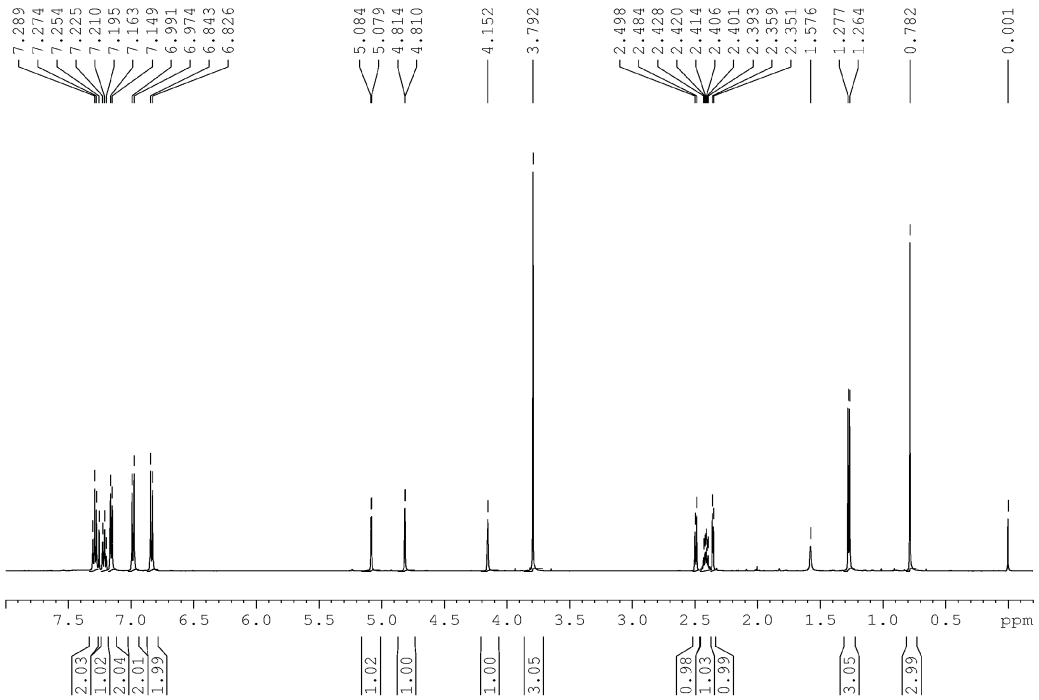
^{1}H NMR ($CDCl_3$, 500 MHz) spectrum of (1*R,3*R**,4*S**,6*S**)- 6-(3,4-dimethoxyphenyl)-1-methyl-2-methylene-3-phenylbicyclo[2.2.1]-heptan-7-one (119)**



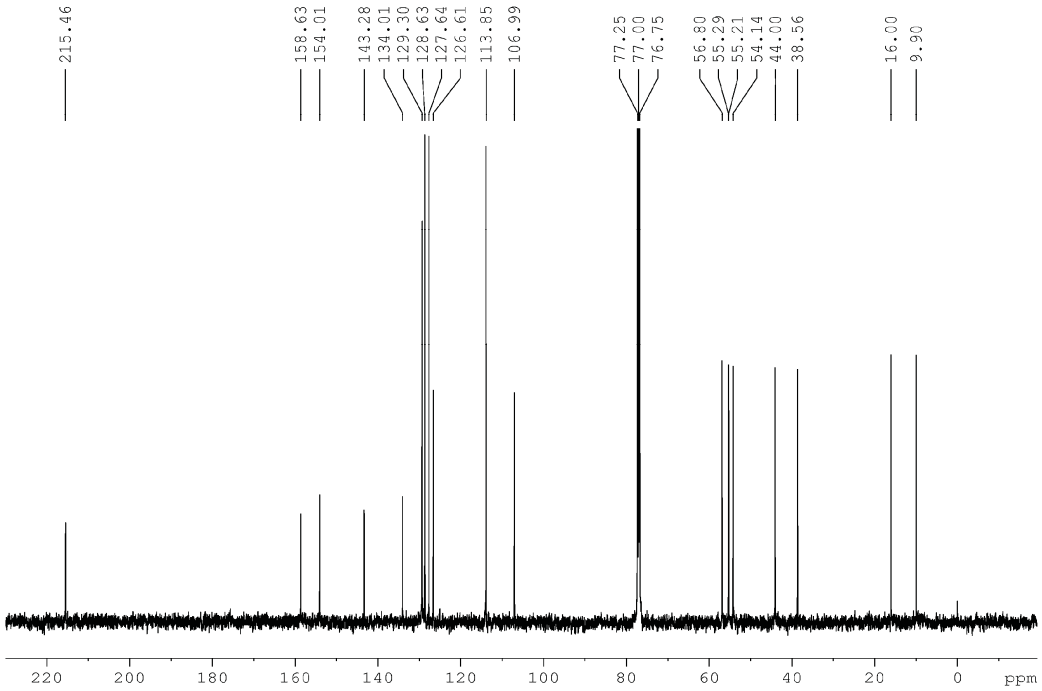
^{13}C NMR ($CDCl_3$, 125 MHz) spectrum of (1*R,3*R**,4*S**,6*S**)- 6-(3,4-dimethoxyphenyl)-1-methyl-2-methylene-3-phenylbicyclo[2.2.1]-heptan-7-one (119)**



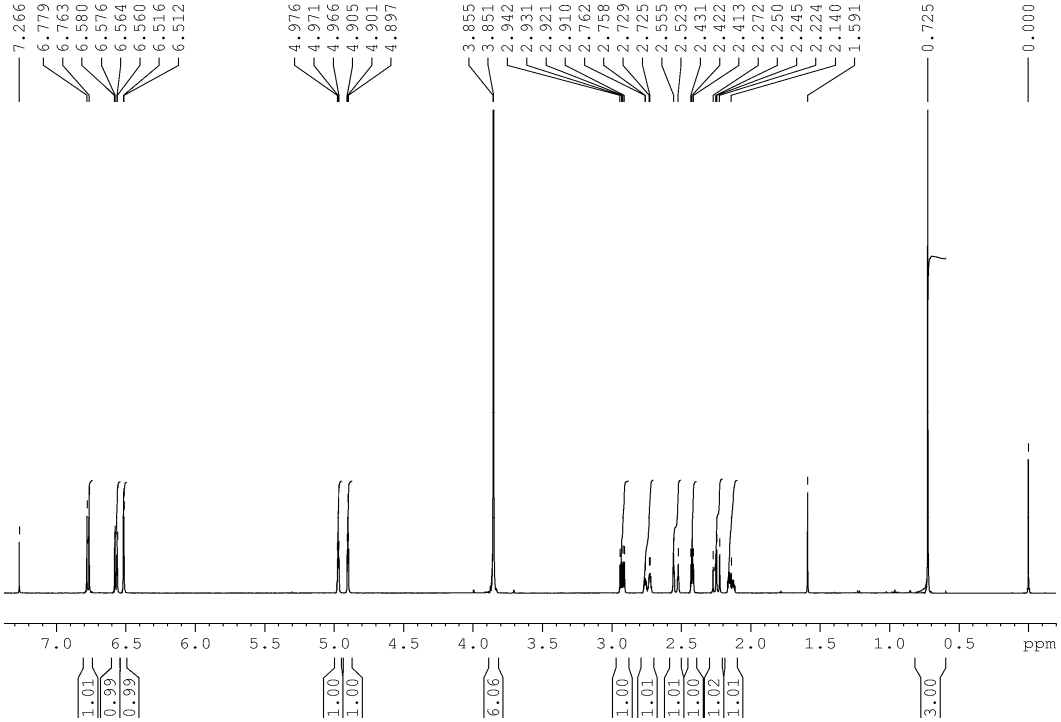
^{1}H NMR ($CDCl_3$, 500 MHz) spectrum of (1*R,2*S**,3*R**,4*S**,5*S**)-2-(4-methoxyphenyl)-1,3-dimethyl-6-methylene-5-phenylbicyclo[2.2.1]- heptan-7-one (120)**



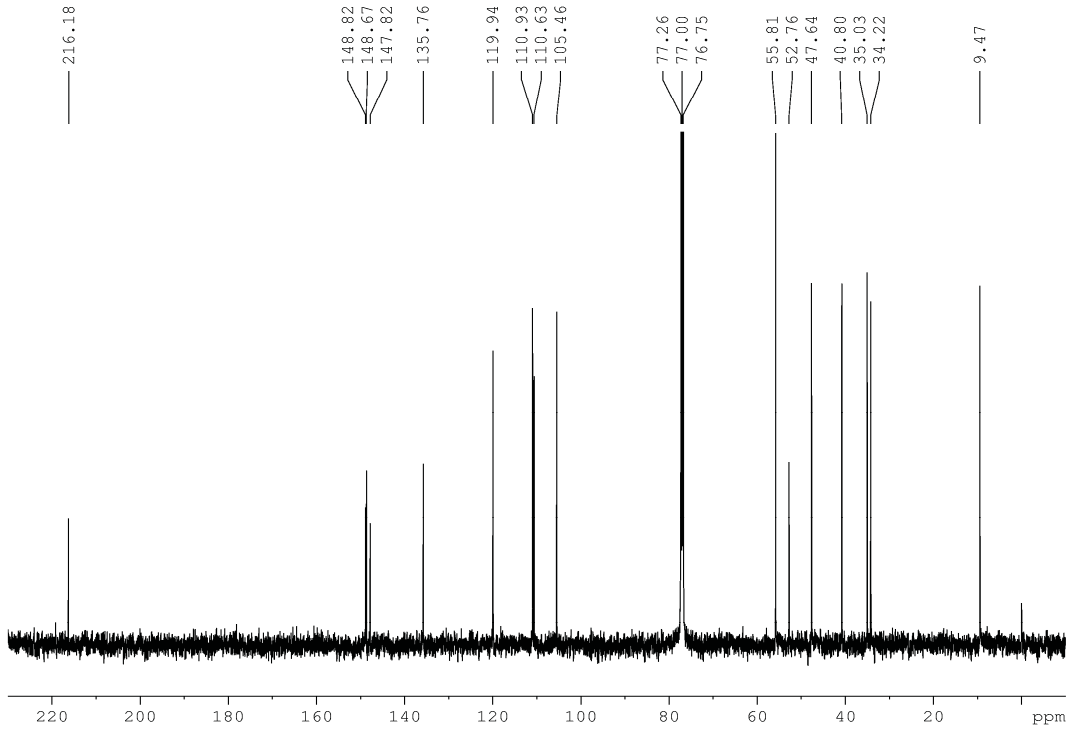
^{13}C NMR ($CDCl_3$, 125 MHz) spectrum of (1*R,2*S**,3*R**,4*S**,5*S**)-2-(4-methoxyphenyl)-1,3-dimethyl-6-methylene-5-phenylbicyclo[2.2.1]- heptan-7-one (120)**



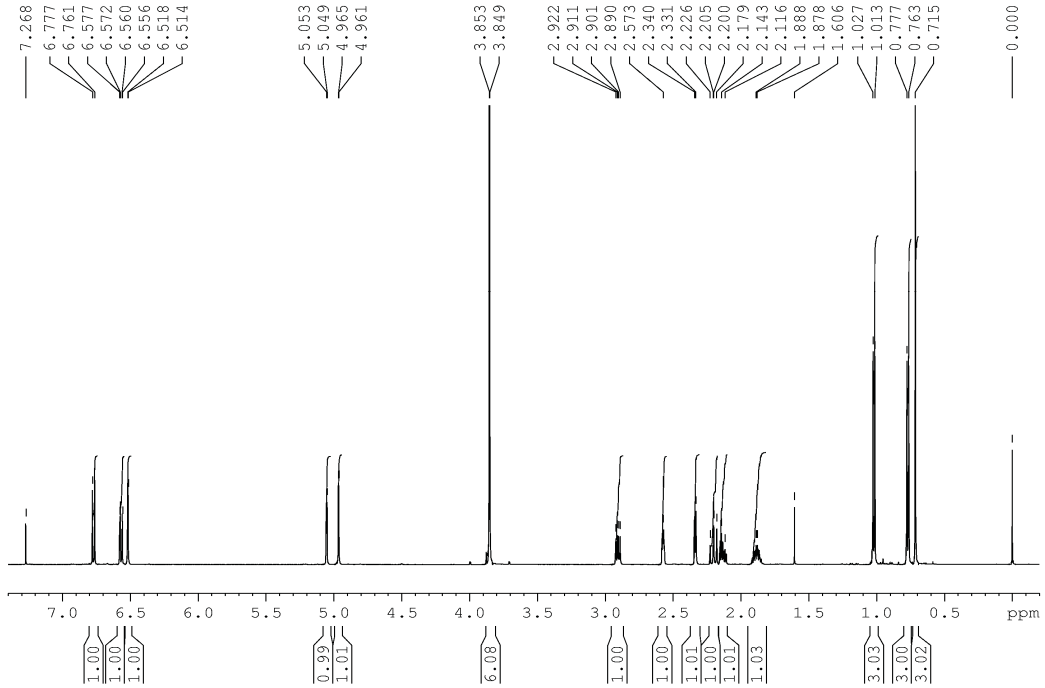
^{1}H NMR ($CDCl_3$, 500 MHz) spectrum of (1*R,2*S**,4*S**)-2-(3,4-dimethoxyphenyl)-1-methyl-6-methylenebicyclo[2.2.1]heptan-7-one (121)**



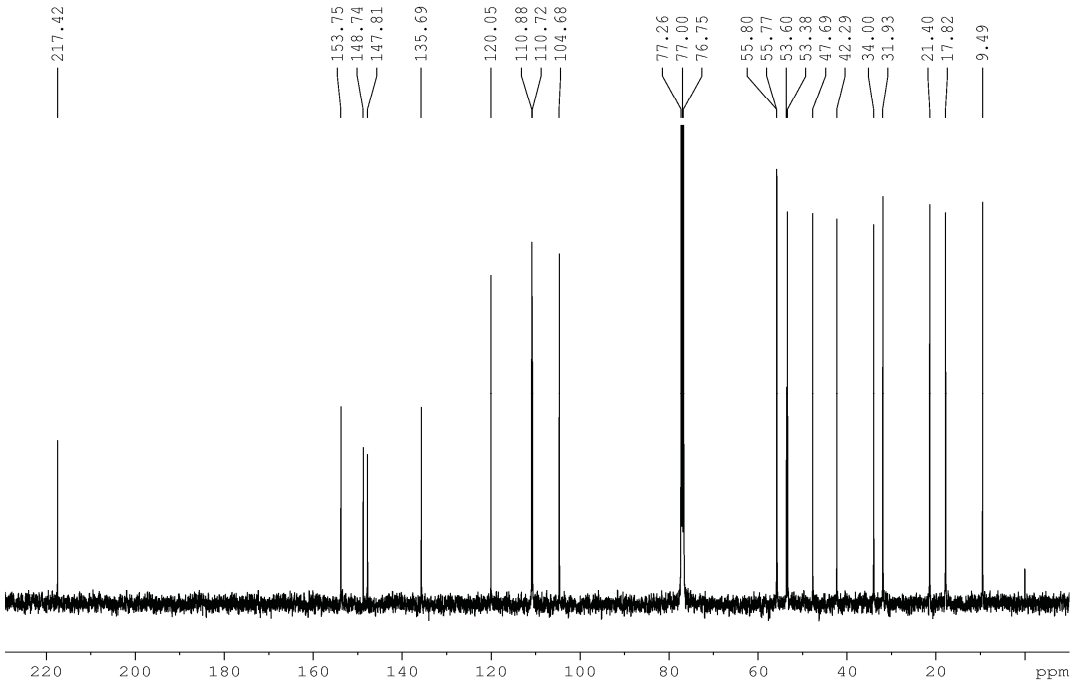
^{13}C NMR ($CDCl_3$, 125 MHz) spectrum of (1*R,2*S**,4*S**)-2-(3,4-dimethoxyphenyl)-1-methyl-6-methylenebicyclo[2.2.1]heptan-7-one (121)**



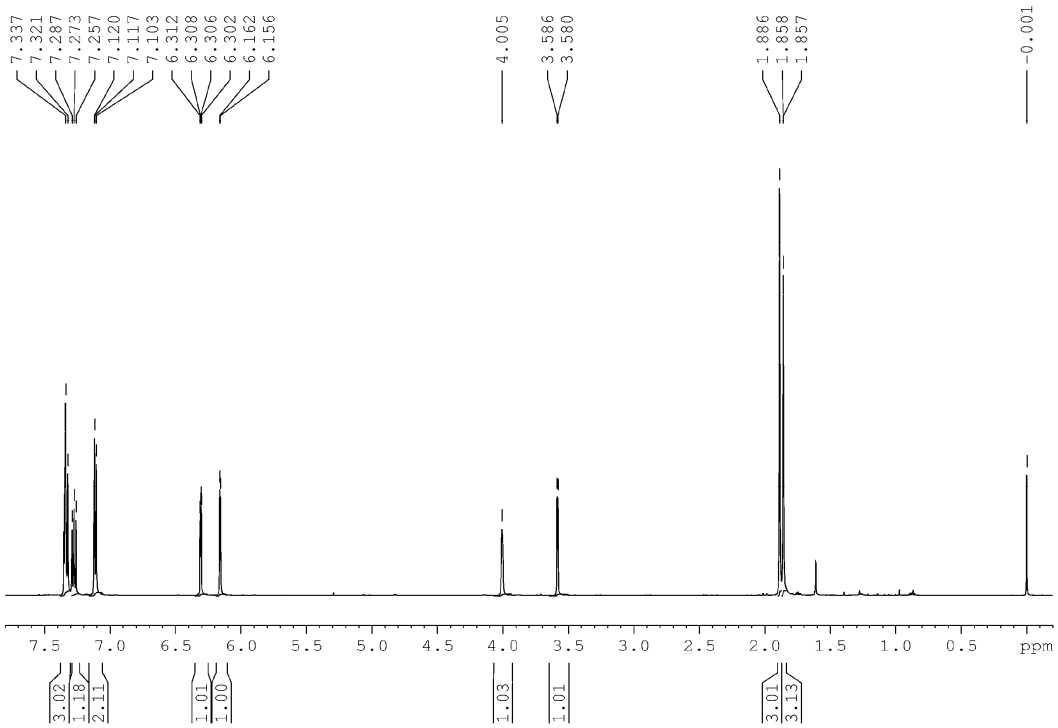
^{1}H NMR ($CDCl_3$, 500 MHz) spectrum of (1*R,3*R**,4*S**,6*S**)-6-(3,4-dimethoxyphenyl)-3-isopropyl-1-methyl-2-methylenebicyclo[2.2.1]-heptan-7-one (122)**



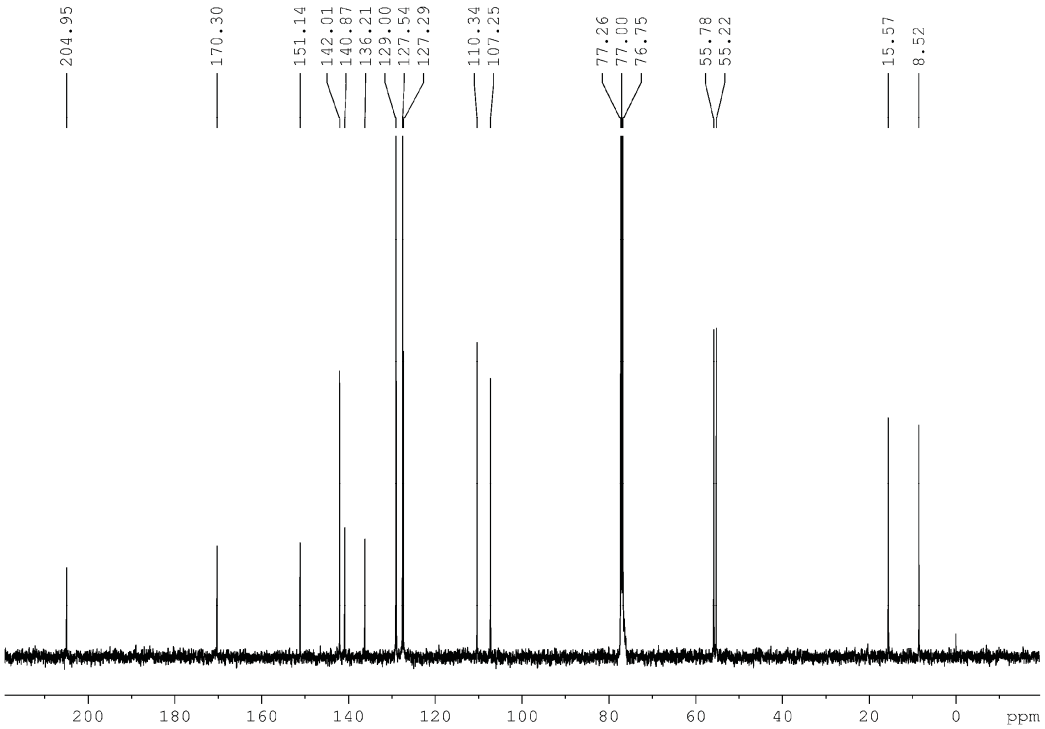
^{13}C NMR ($CDCl_3$, 125 MHz) spectrum of (1*R,3*R**,4*S**,6*S**)-6-(3,4-dimethoxyphenyl)-3-isopropyl-1-methyl-2-methylenebicyclo[2.2.1]-heptan-7-one (122)**



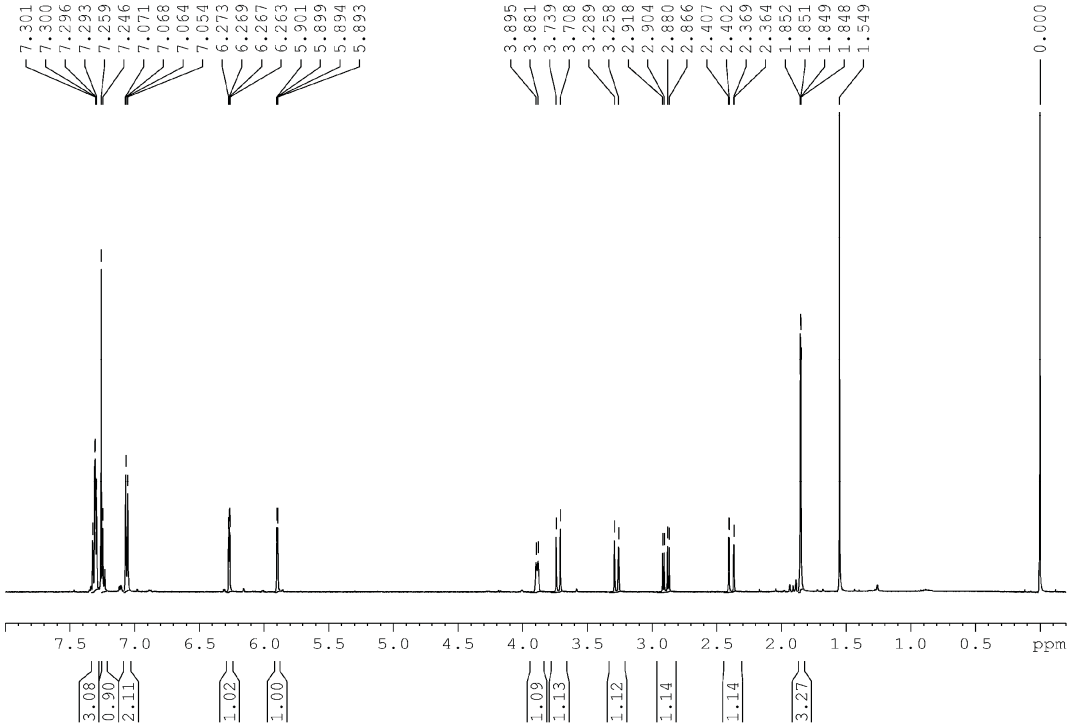
^{1}H NMR ($CDCl_3$, 500 MHz) spectrum of (*trans*)-5-(furan-2-yl)-2,3-dimethyl-4-phenylcyclopent-2-enone (123)



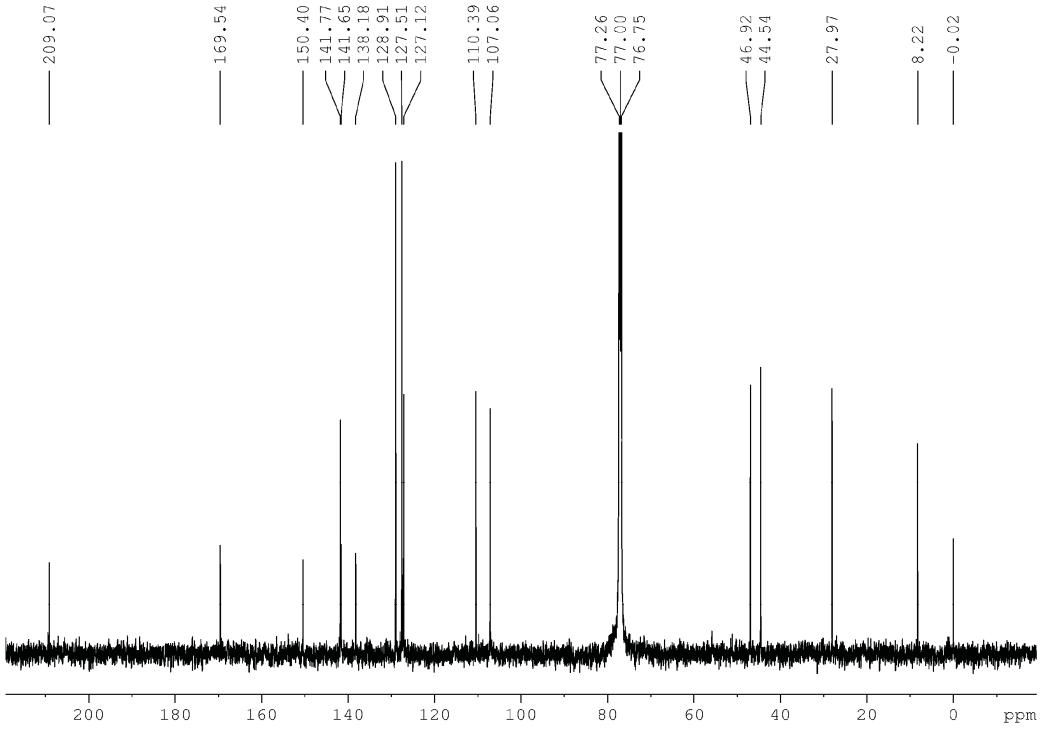
^{13}C NMR ($CDCl_3$, 125 MHz) spectrum of (*trans*)-5-(furan-2-yl)-2,3-dimethyl-4-phenylcyclopent-2-enone (123)



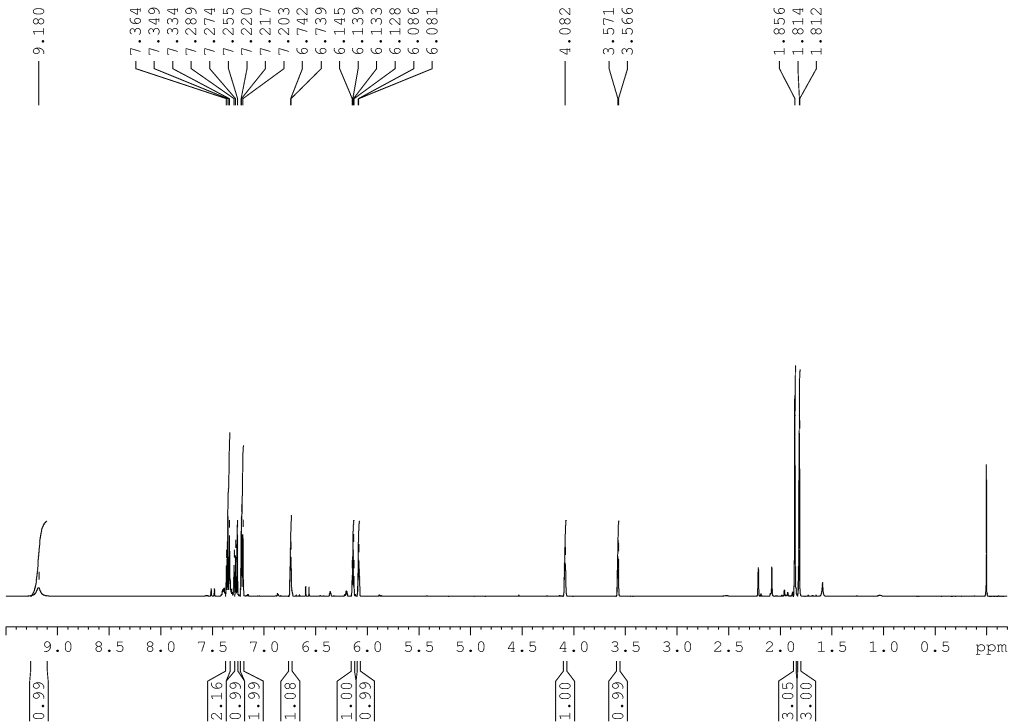
^{1}H NMR ($CDCl_3$, 500 MHz) spectrum of 3-(furan-2-ylmethyl)-2-methyl-4-phenylcyclopent-2-enone (124)



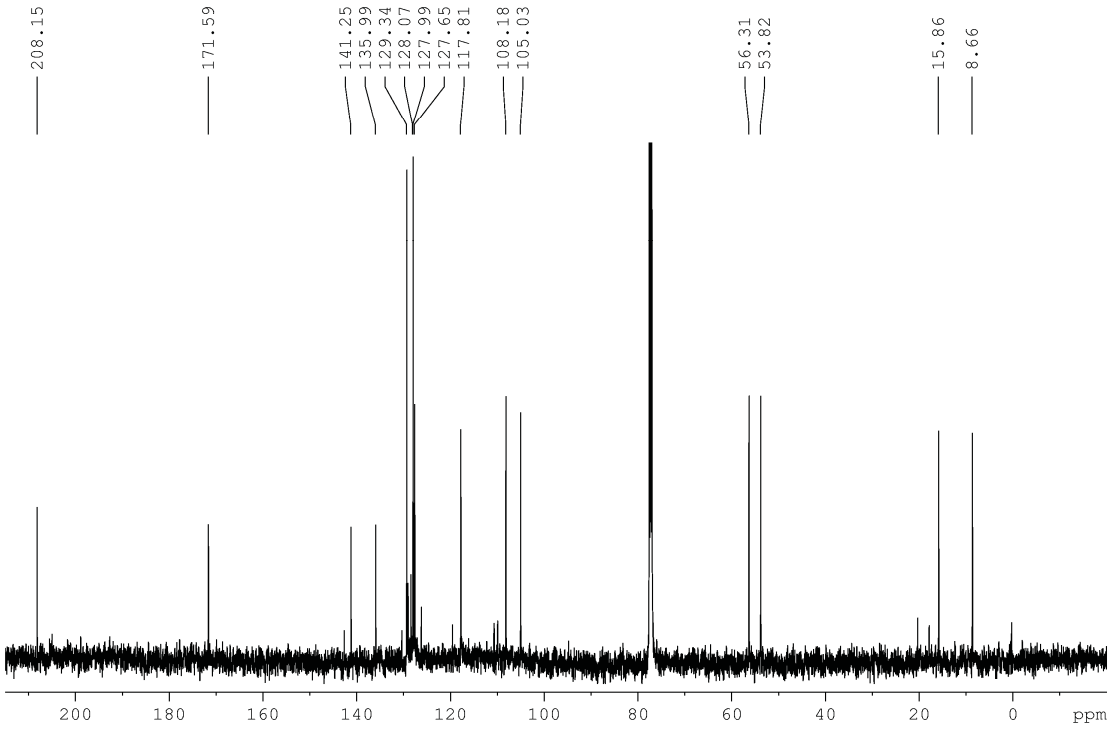
^{13}C NMR ($CDCl_3$, 125 MHz) spectrum of 3-(furan-2-ylmethyl)-2-methyl-4-phenylcyclopent-2-enone (124)



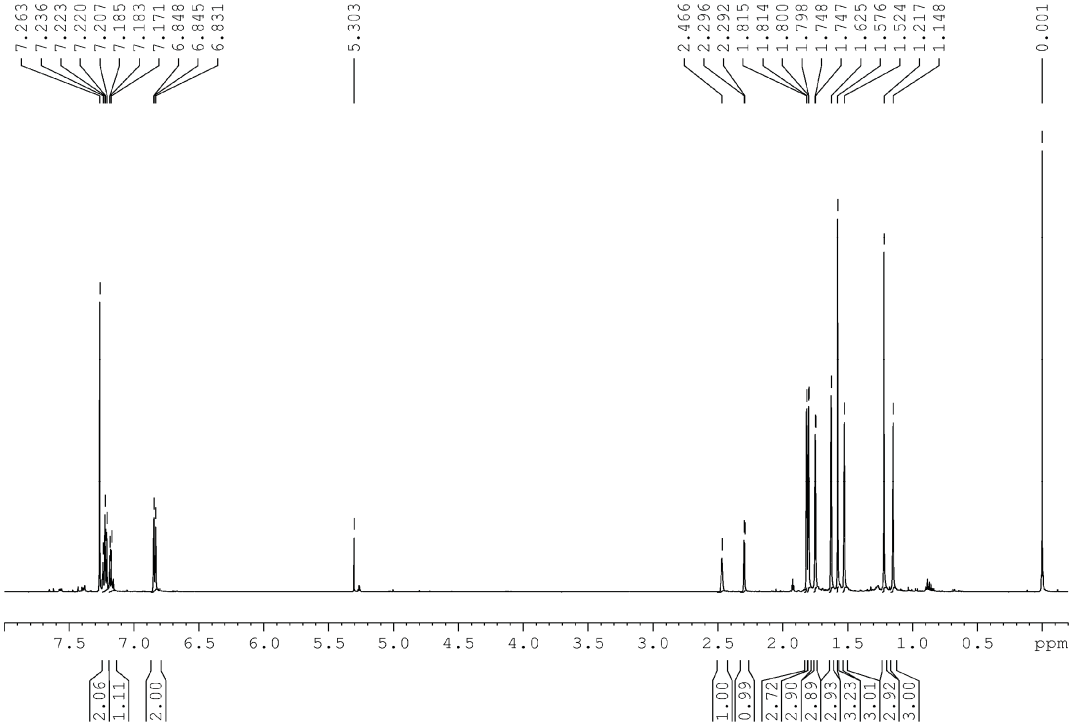
^{1}H NMR ($CDCl_3$, 500 MHz) spectrum of (*trans*)-2,3-dimethyl-4-phenyl-5-(1*H*-pyrrol-2-yl)cyclopent-2-enone (125)



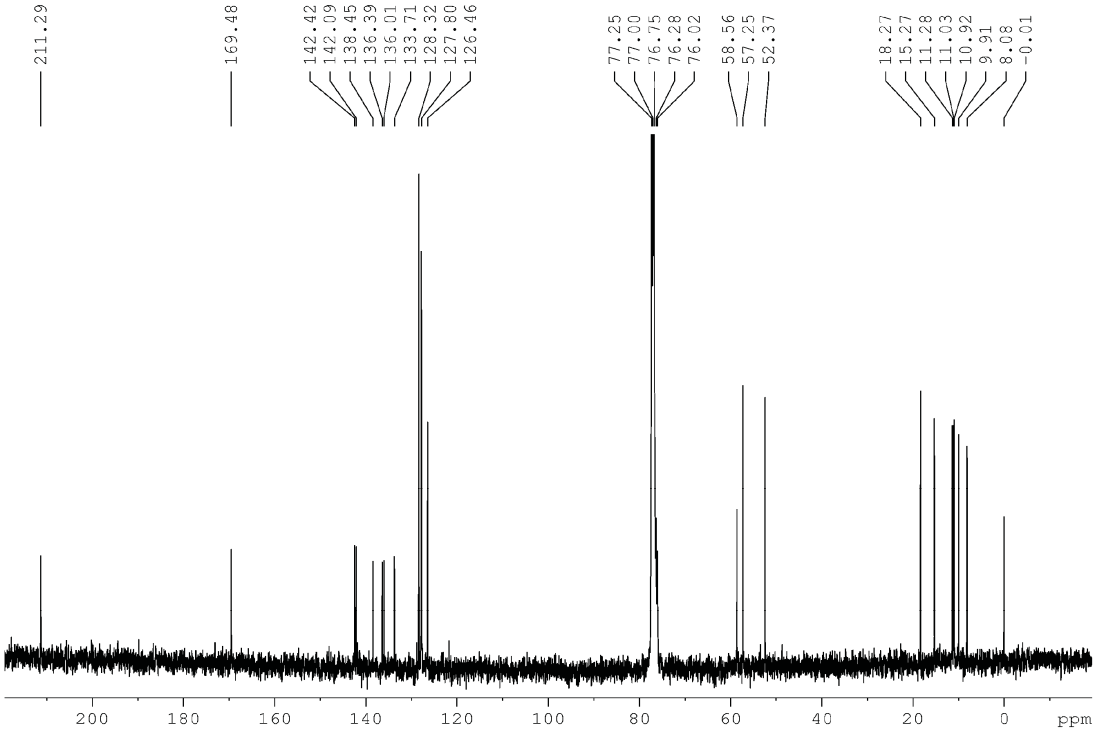
^{13}C NMR ($CDCl_3$, 125 MHz) spectrum of (*trans*)-2,3-dimethyl-4-phenyl-5-(1*H*-pyrrol-2-yl)cyclopent-2-enone (125)



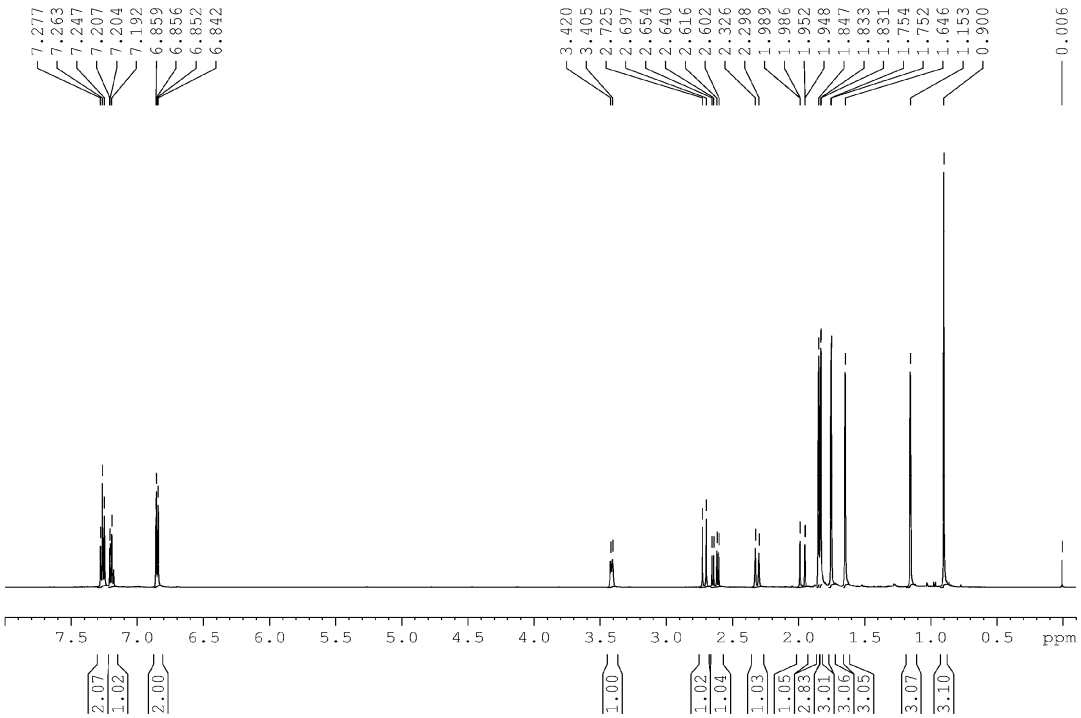
^{1}H NMR ($CDCl_3$, 500 MHz) spectrum of (*trans)*-4-methyl-5-(1,2,3,4,5-pentamethylcyclopenta-2,4-dienyl)-1-phenylhexa-1,5-dien-3-one (126)



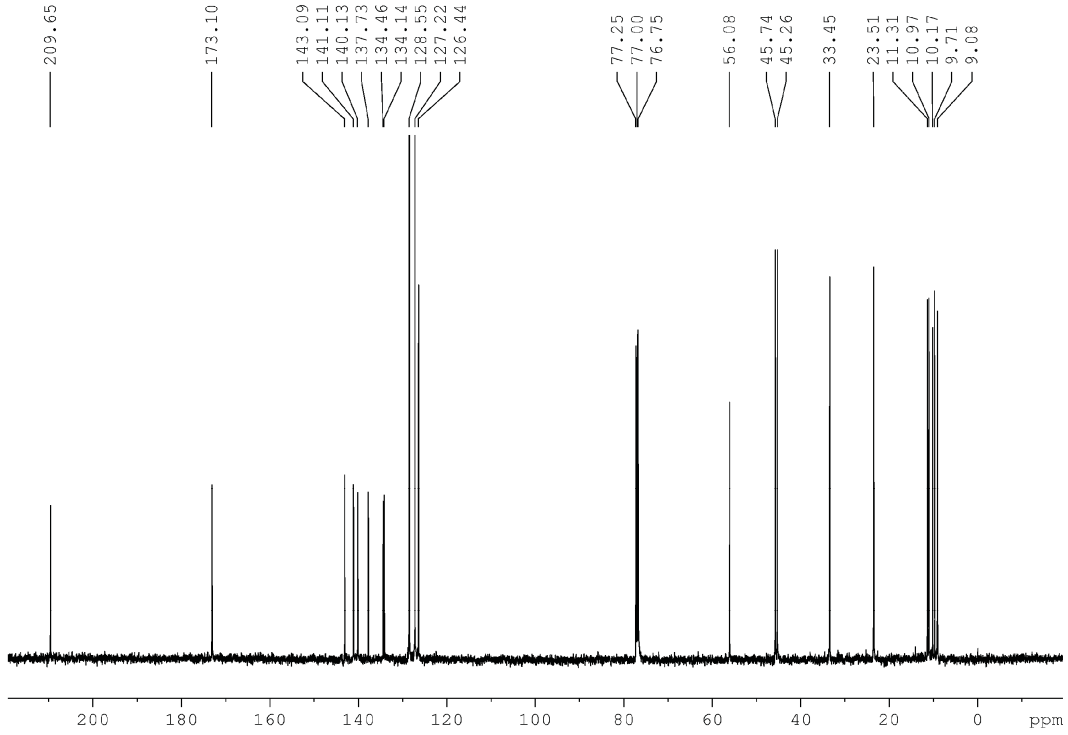
^{13}C NMR ($CDCl_3$, 125 MHz) spectrum of (*trans)*-4-methyl-5-(1,2,3,4,5-pentamethylcyclopenta-2,4-dienyl)-1-phenylhexa-1,5-dien-3-one (126)



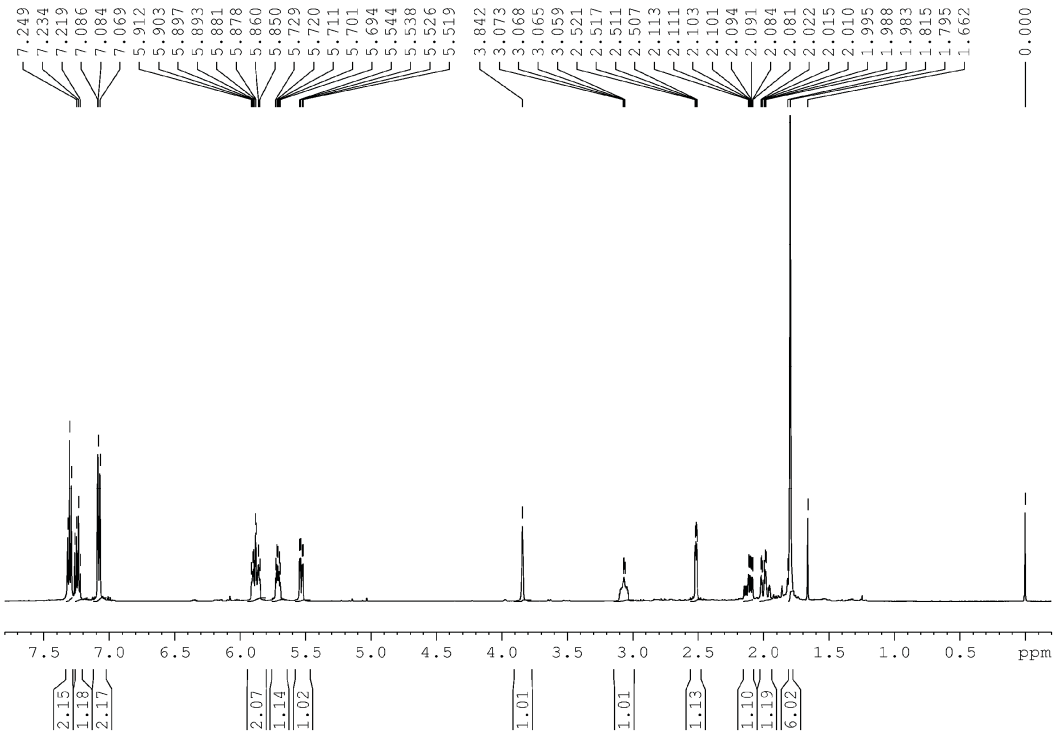
^{1}H NMR ($CDCl_3$, 500 MHz) spectrum of 2-methyl-3-((1,2,3,4,5-pentamethylcyclopenta-2,4-dienyl)methyl)-4-phenylcyclopent-2-enone (127)



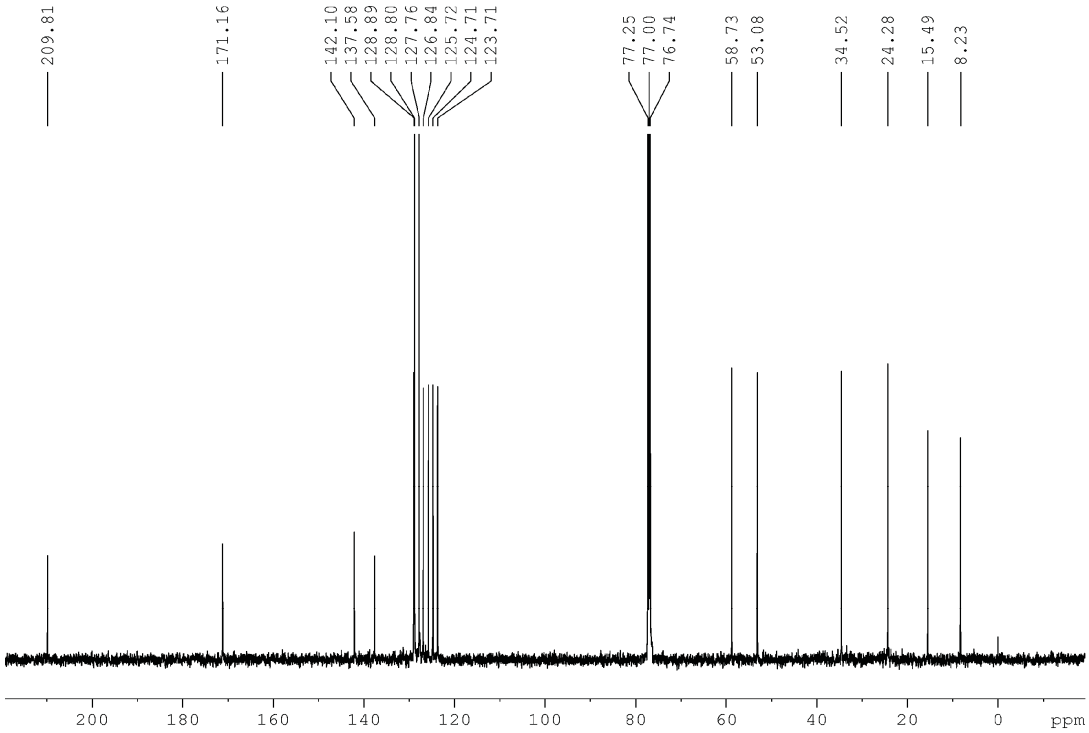
^{13}C NMR ($CDCl_3$, 125 MHz) spectrum of 2-methyl-3-((1,2,3,4,5-pentamethylcyclopenta-2,4-dienyl)methyl)-4-phenylcyclopent-2-enone (127)



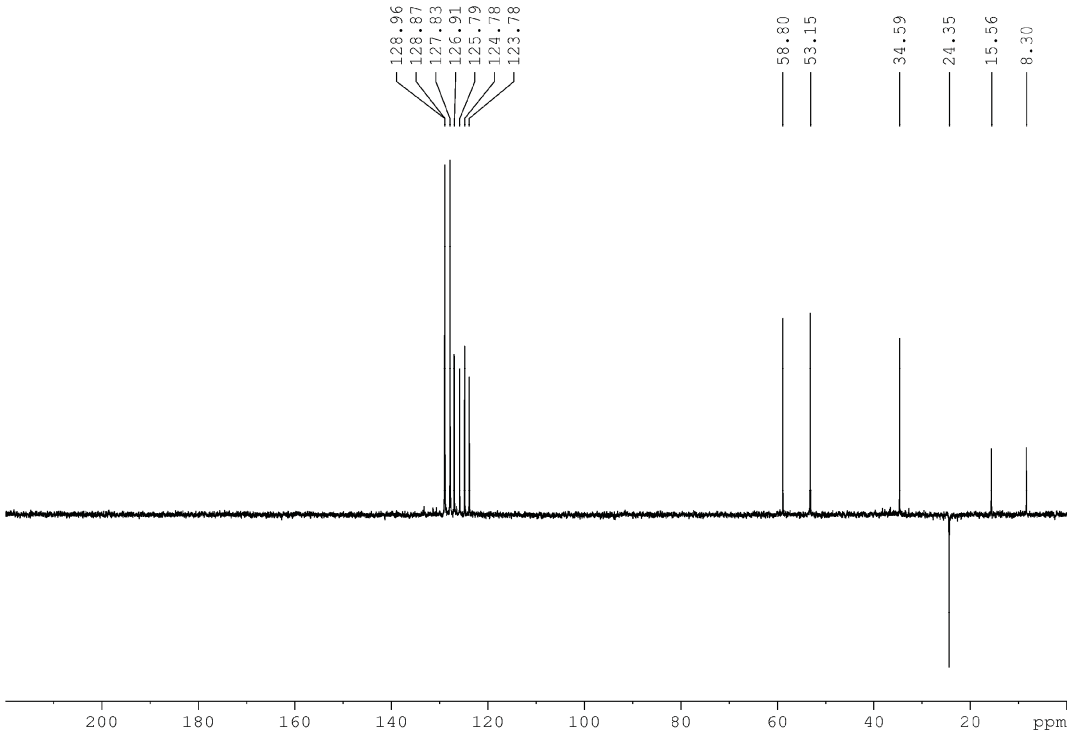
^{1}H NMR ($CDCl_3$, 500 MHz) spectrum of *(1''R*,4S*,5R*)*-5-(cyclohexa-2,4-dienyl)-2,3-dimethyl-4-phenylcyclopent-2-enone (128)



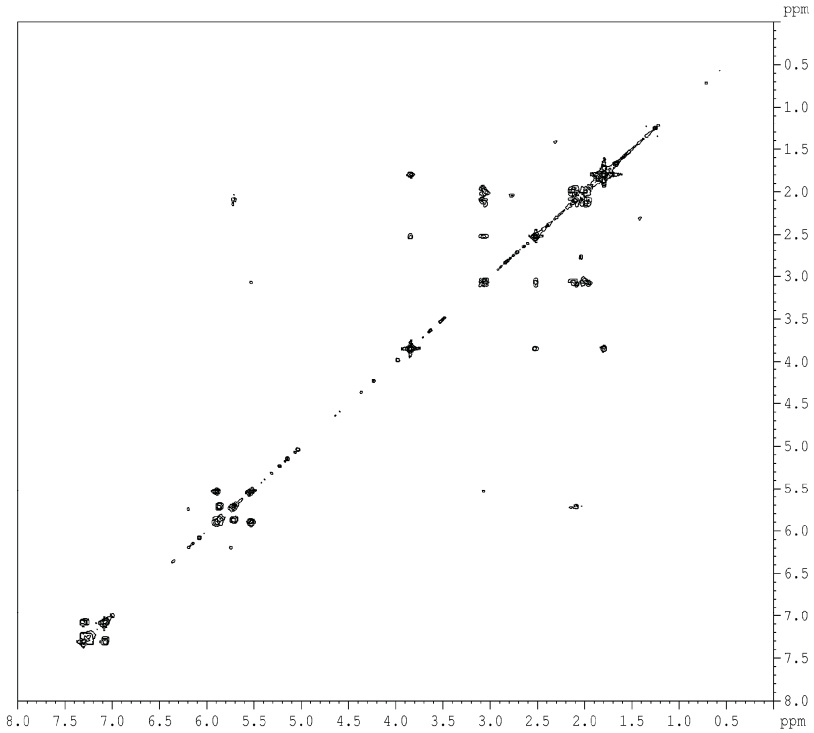
^{13}C NMR ($CDCl_3$, 125 MHz) spectrum of *(1''R*,4S*,5R*)*-5-(cyclohexa-2,4-dienyl)-2,3-dimethyl-4-phenylcyclopent-2-enone (128)



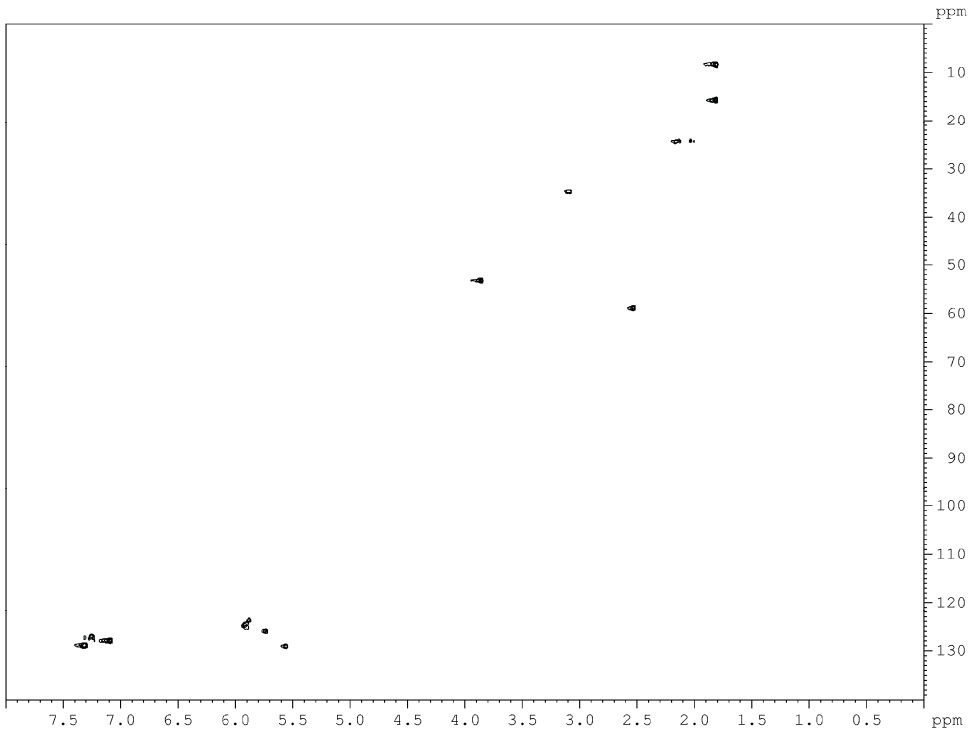
DEPT-135 spectrum of *(1''R*,4S*,5R*)*-5-(cyclohexa-2,4-dienyl)-2,3-dimethyl-4-phenylcyclopent-2-enone (128)



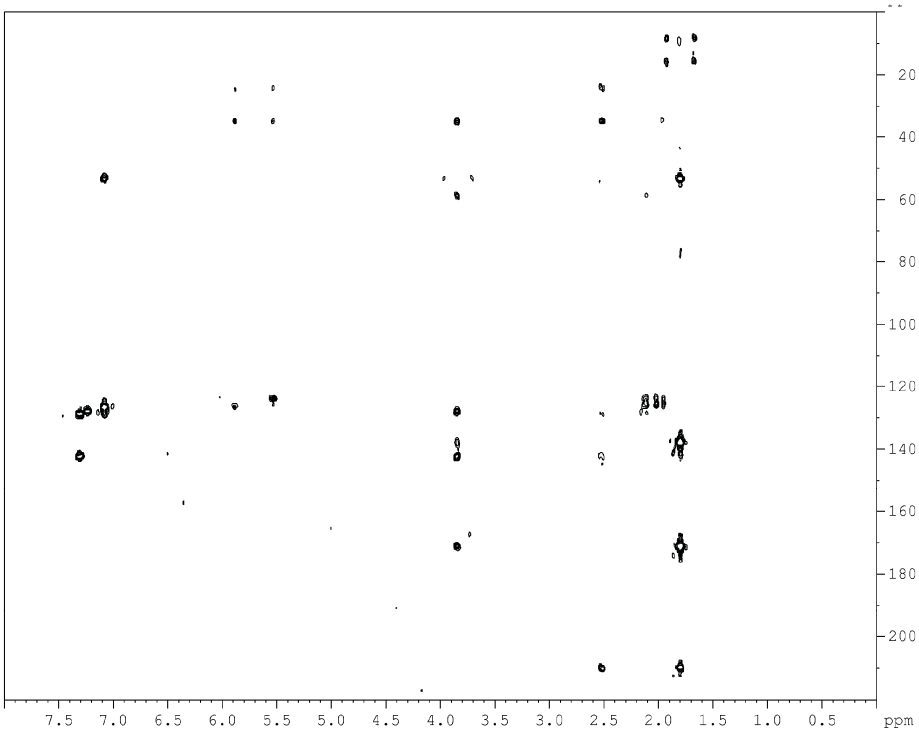
COSY spectrum of *(1''R*,4S*,5R*)*-5-(cyclohexa-2,4-dienyl)-2,3-dimethyl-4-phenylcyclopent-2-enone (128)



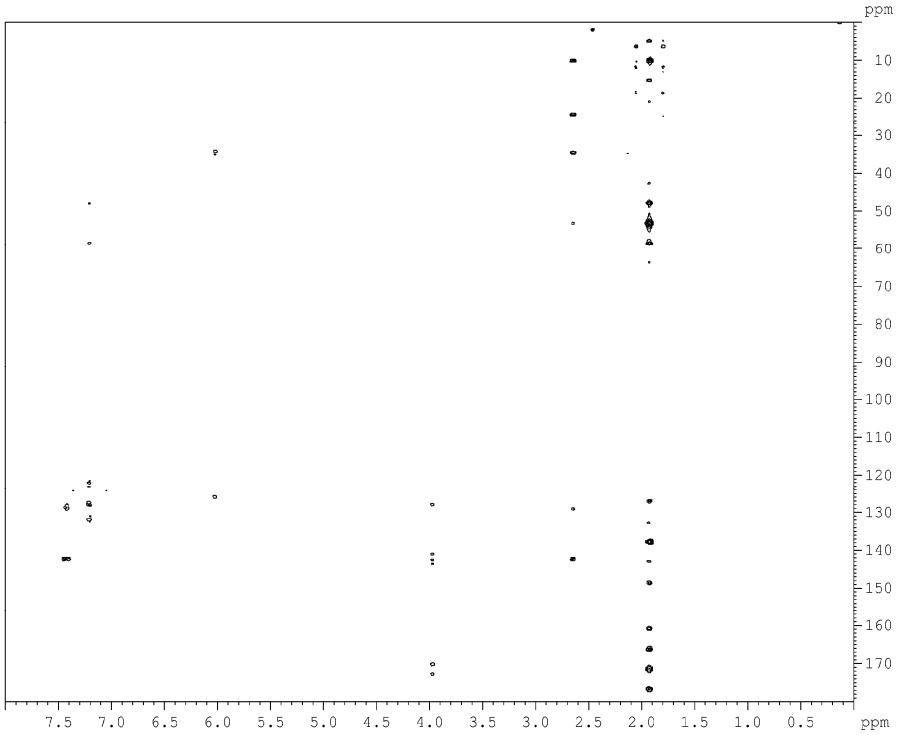
HSQC spectrum of *(1''R*,4S*,5R*)*-5-(cyclohexa-2,4-dienyl)-2,3-dimethyl-4-phenylcyclopent-2-enone (128)



HMBC spectrum of *(1''R*,4S*,5R*)*-5-(cyclohexa-2,4-dienyl)-2,3-dimethyl-4-phenylcyclopent-2-enone (128)

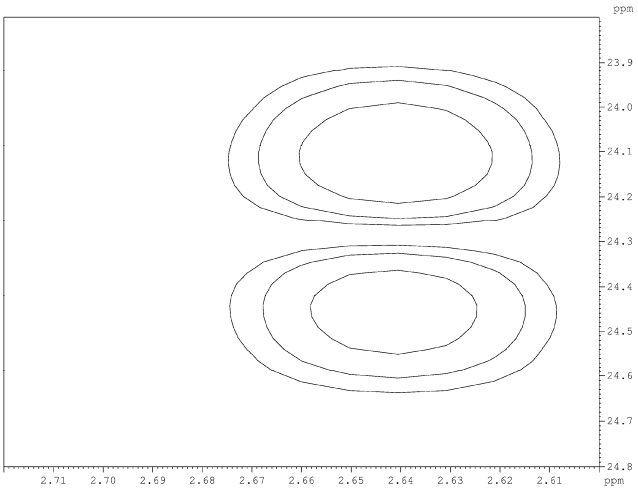


***J*-HMBC spectrum of *(1''R*,4S*,5R*)*-5-(cyclohexa-2,4-dienyl)-2,3-dimethyl-4-phenylcyclopent-2-enone (128)**

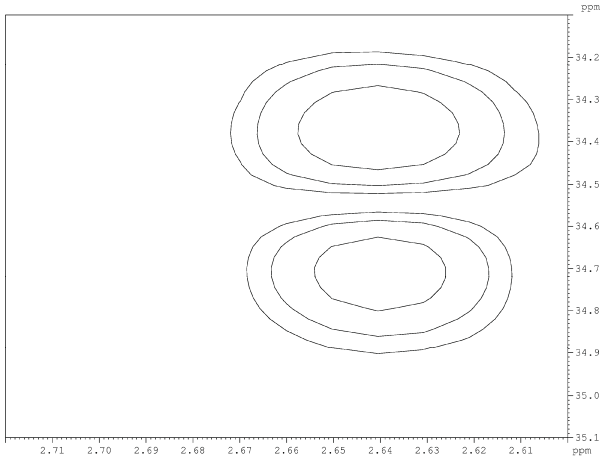


Details of *J*-HMBC spectrum of *(1''R*,4S*,5R*)*-5-(cyclohexa-2,4-dienyl)-2,3-dimethyl-4-phenylcyclopent-2-enone (128)

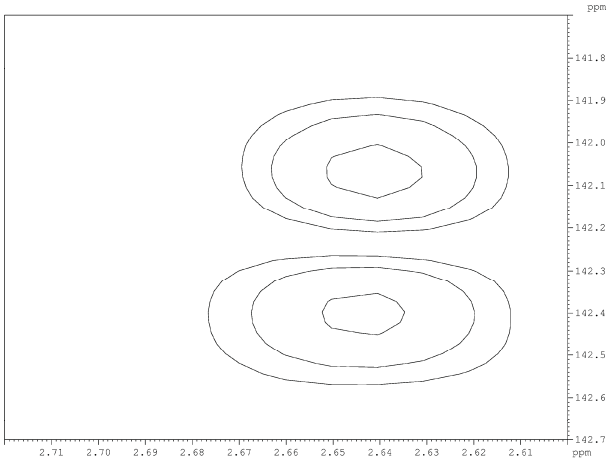
^{3}J H5-C6"



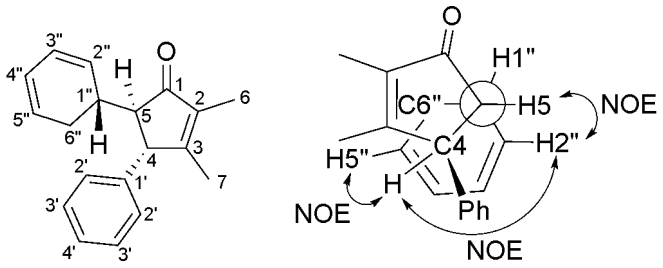
^{2}J H5-C1"



^{3}J H5-C1'



Critical data from *J*-HMBC spectrum of *(1''R*,4S*,5R*)*-5-(cyclohexa-2,4-dienyl)-2,3-dimethyl-4-phenylcyclopent-2-enone (128)



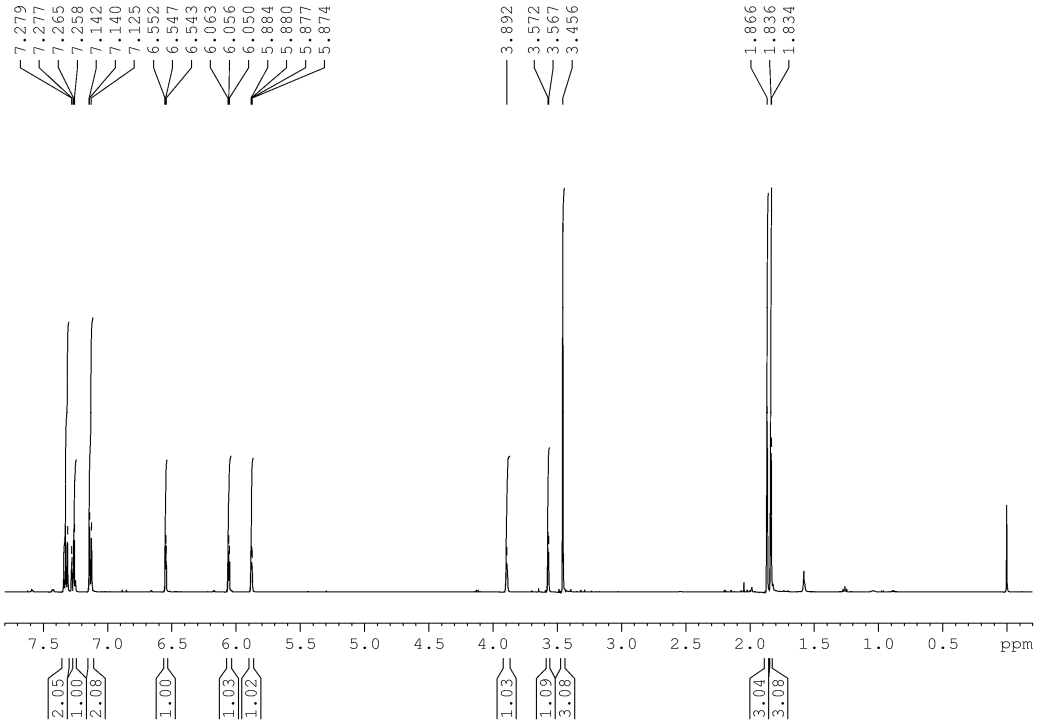
Measured $^{3}J_{H,H}$ and $^{2,3}J_{C,H}$ with respect to the C5-C1" segment in compound **128**

$^{2,3}J_{H,X}$	nuclei	measured value (Hz)	magnitude estimation	stereorelation to H5
$^{3}J_{H,H}$	H5–H1"	4.9	small	*gauche*
$^{3}J_{C,H}$	H5–C6"	7.4	large	*anti*
$^{2}J_{C,H}$	H5–C1"	7.2	large	*gauche to C2"*

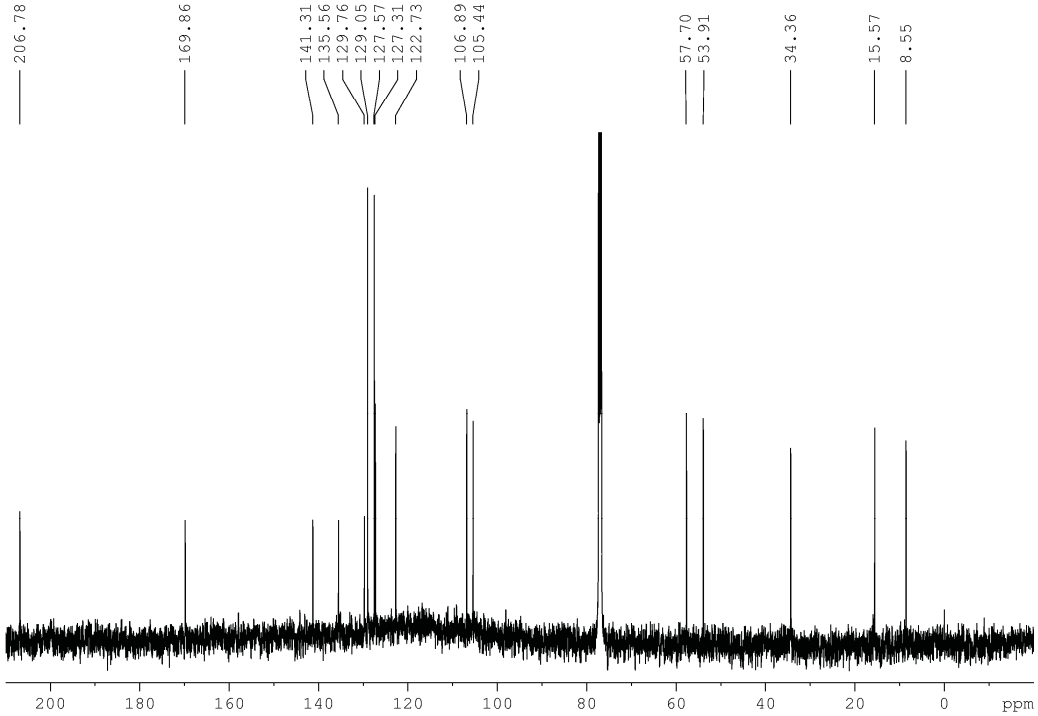
Measured $^{3}J_{H,H}$ and $^{2,3}J_{C,H}$ with respect to the C5-C4 segment in compound **128**

$^{2,3}J_{H,X}$	nuclei	measured value (Hz)	magnitude estimation	stereorelation to H5
$^{3}J_{H,H}$	H5–H4	2.5	small	*anticlinal*
$^{3}J_{C,H}$	H5–C1'	7.0	large	*synclinal*

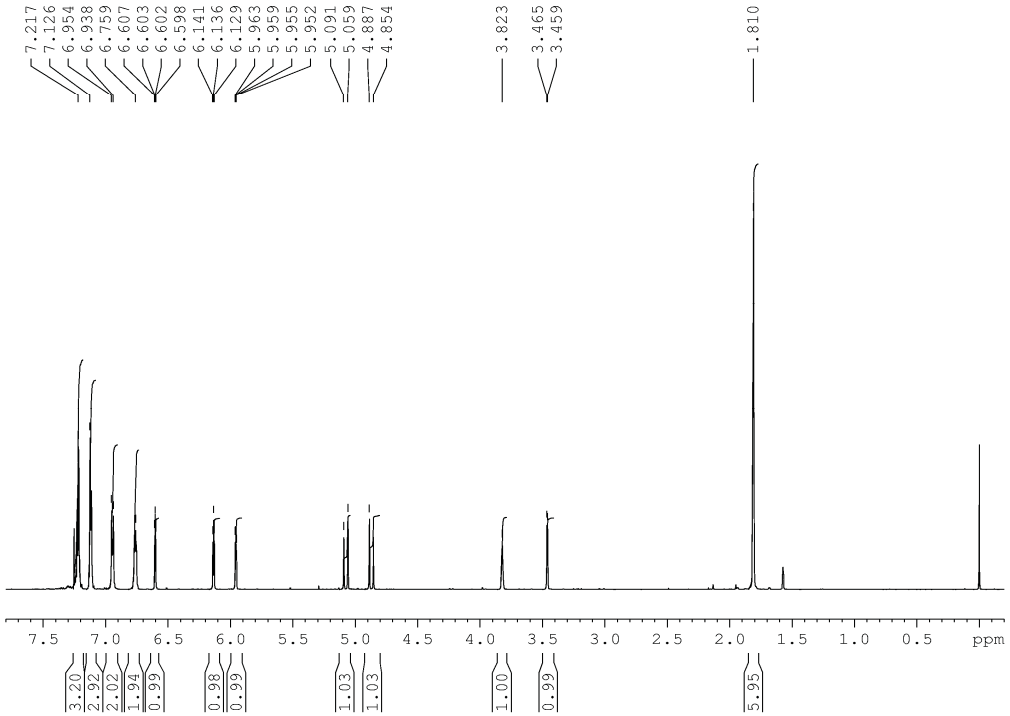
^{1}H NMR ($CDCl_3$, 500 MHz) spectrum of (*trans*)-2,3-dimethyl-5-(1-methyl-1*H*-pyrrol-2-yl)-4-phenylcyclopent-2-enone (129)



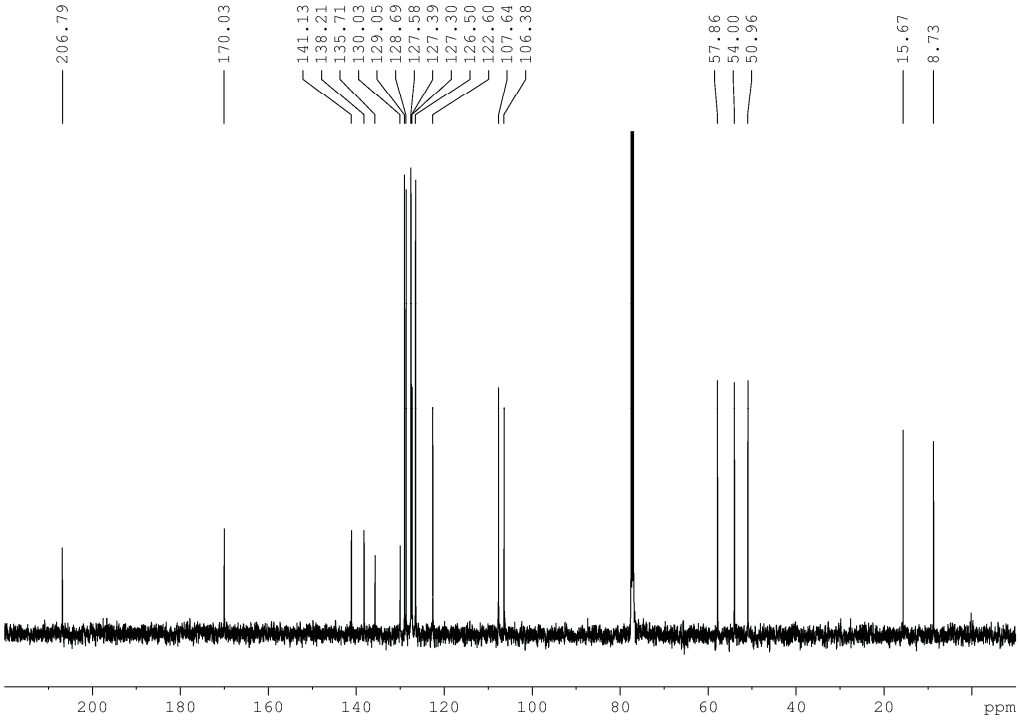
^{13}C NMR ($CDCl_3$, 125 MHz) spectrum of (*trans*)-2,3-dimethyl-5-(1-methyl-1*H*-pyrrol-2-yl)-4-phenylcyclopent-2-enone (129)



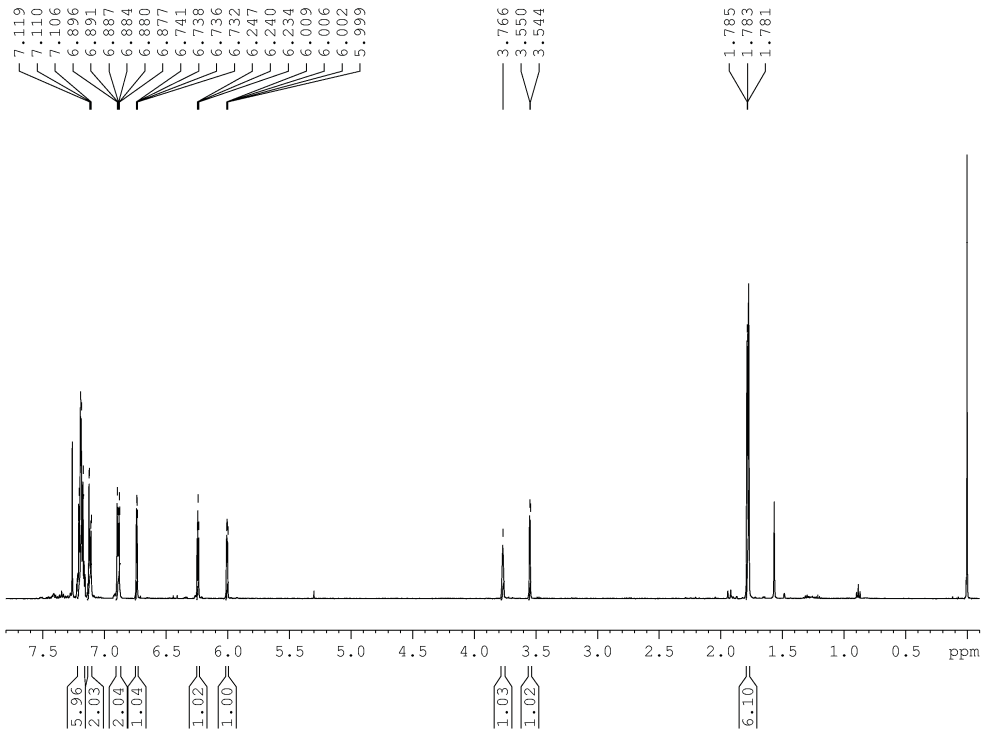
^{1}H NMR ($CDCl_3$, 500 MHz) spectrum of (*trans*)-2,3-dimethyl-5-(1-benzyl-1*H*-pyrrol-2-yl)-4-phenylcyclopent-2-enone (130)



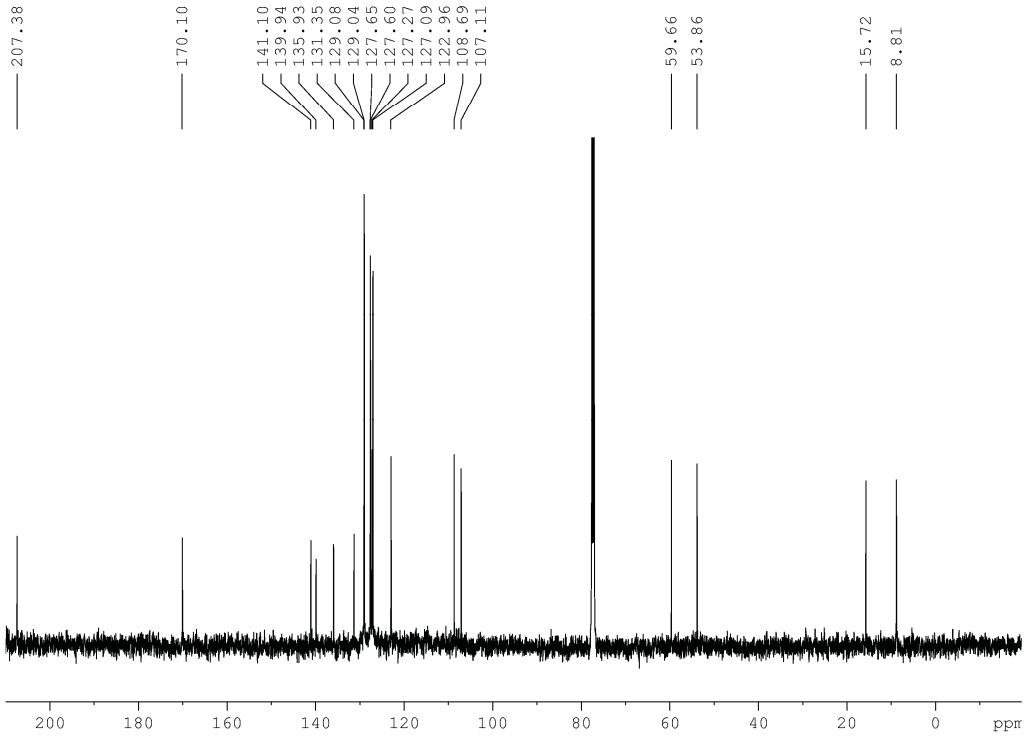
^{13}C NMR ($CDCl_3$, 125 MHz) spectrum of (*trans*)-2,3-dimethyl-5-(1-benzyl-1*H*-pyrrol-2-yl)-4-phenylcyclopent-2-enone (130)



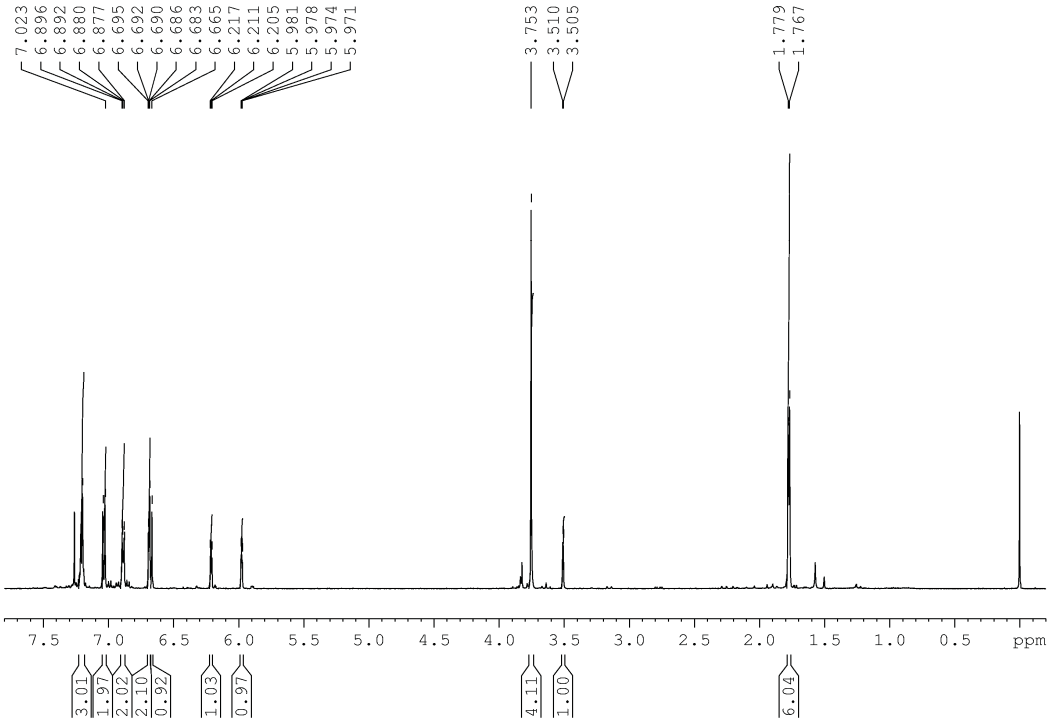
^{1}H NMR ($CDCl_3$, 500 MHz) spectrum of (*trans*)-2,3-dimethyl-4-phenyl-5-(1-phenyl-1*H*-pyrrol-2-yl)cyclopent-2-enone (131)



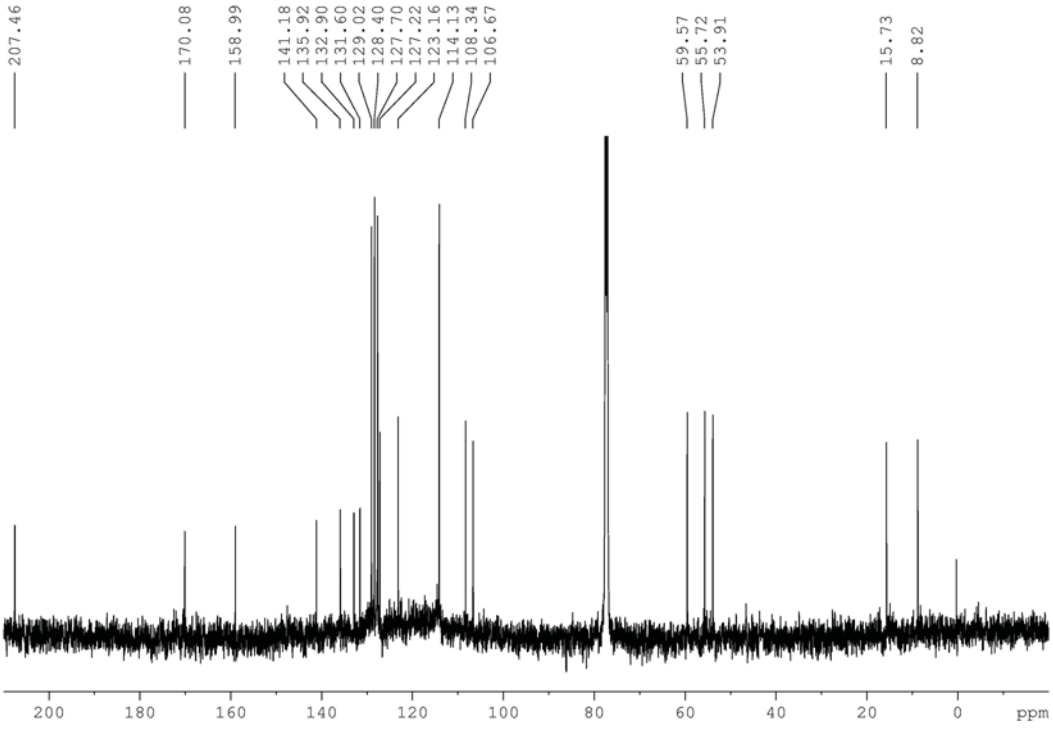
^{13}C NMR ($CDCl_3$, 125 MHz) spectrum of (*trans*)-2,3-dimethyl-4-phenyl-5-(1-phenyl-1*H*-pyrrol-2-yl)cyclopent-2-enone (131)



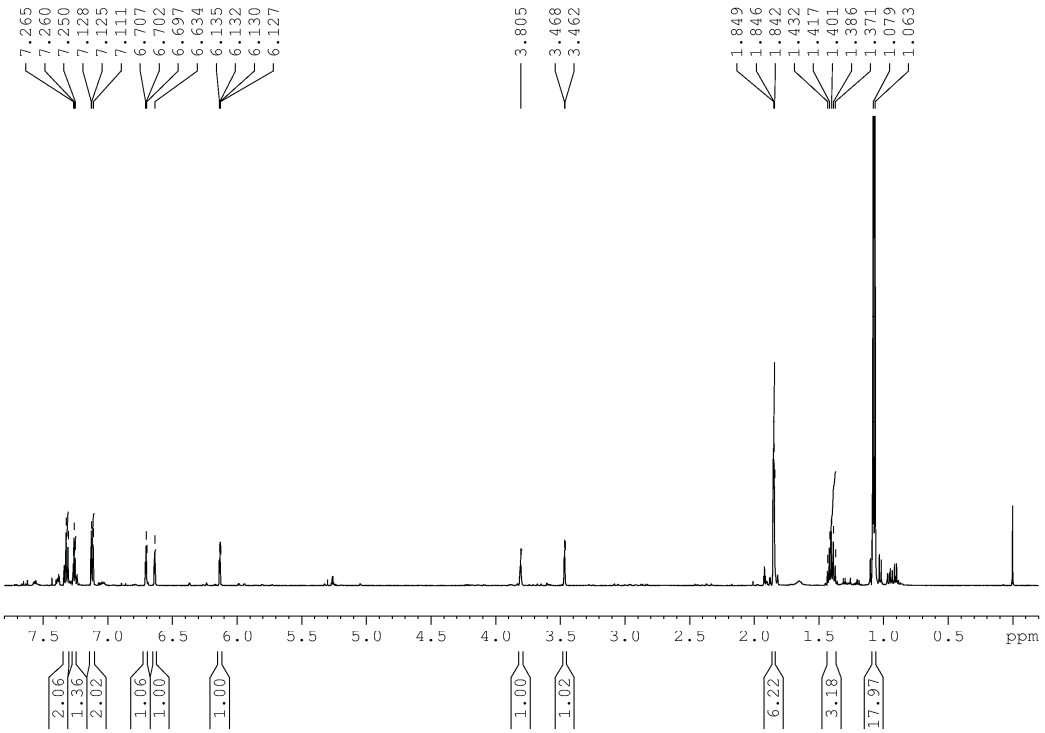
^{1}H NMR ($CDCl_3$, 500 MHz) spectrum of (*trans*)-5-(1-(4-methoxyphenyl)-1*H*-pyrrol-2-yl)-2,3-dimethyl-4-phenyl-cyclopent-2-enone (132)



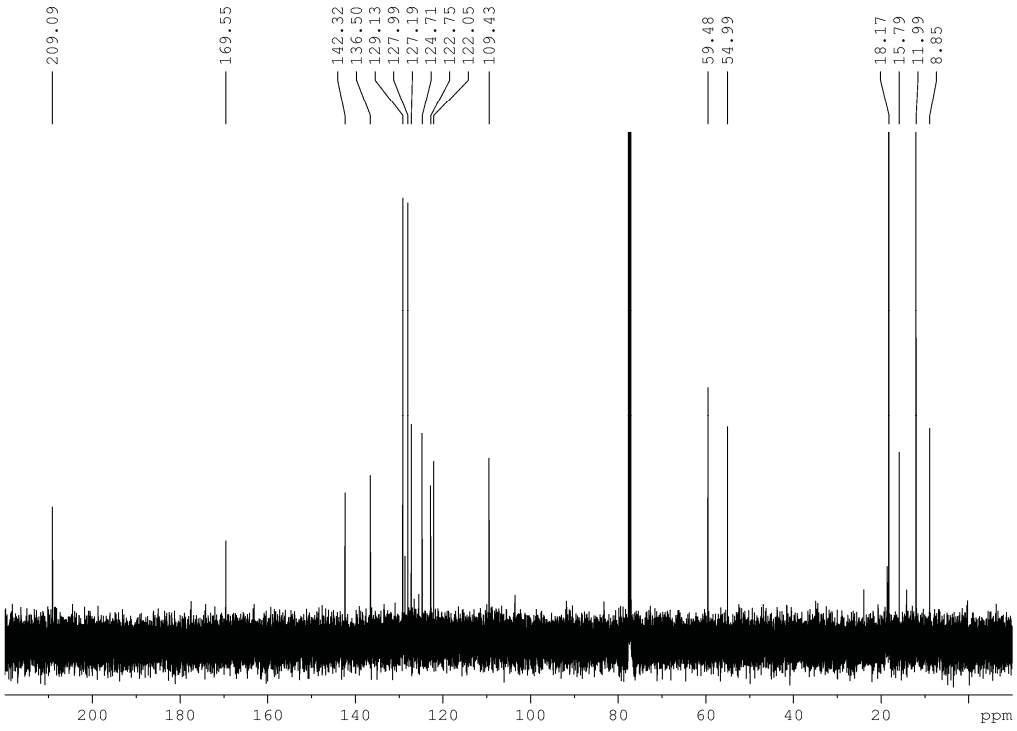
^{13}C NMR ($CDCl_3$, 125 MHz) spectrum of (*trans*)-5-(1-(4-methoxyphenyl)-1*H*-pyrrol-2-yl)-2,3-dimethyl-4-phenyl-cyclopent-2-enone (132)



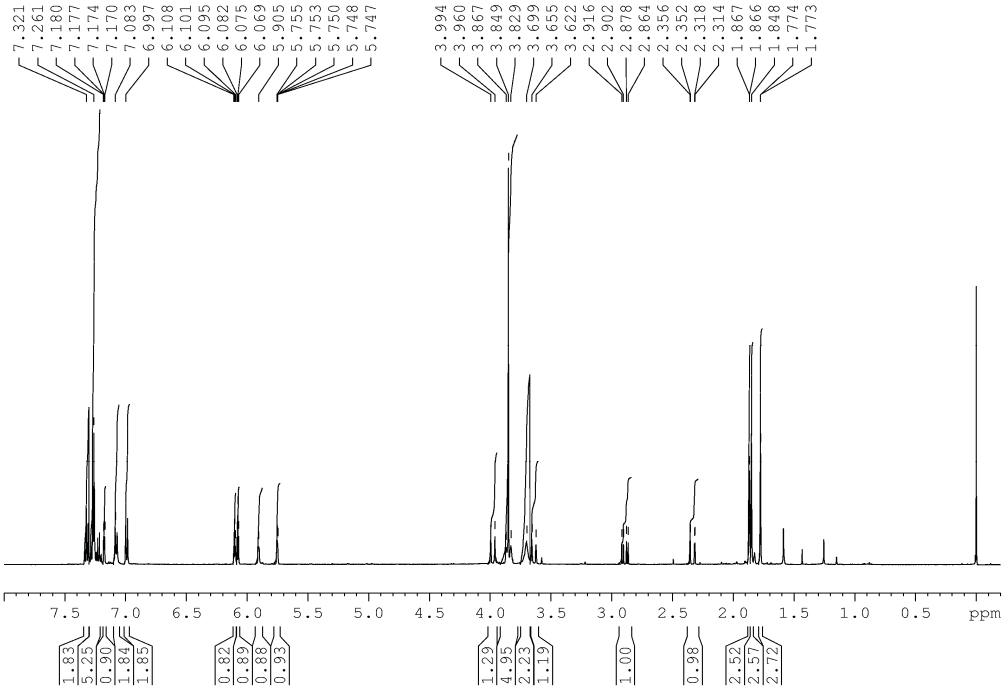
^{1}H NMR ($CDCl_3$, 500 MHz) spectrum of (*trans*)-2,3-dimethyl-4-phenyl-5-(1-(triisopropylsilyl)-1*H*-pyrrol-2-yl)cyclopent-2-enone (133)



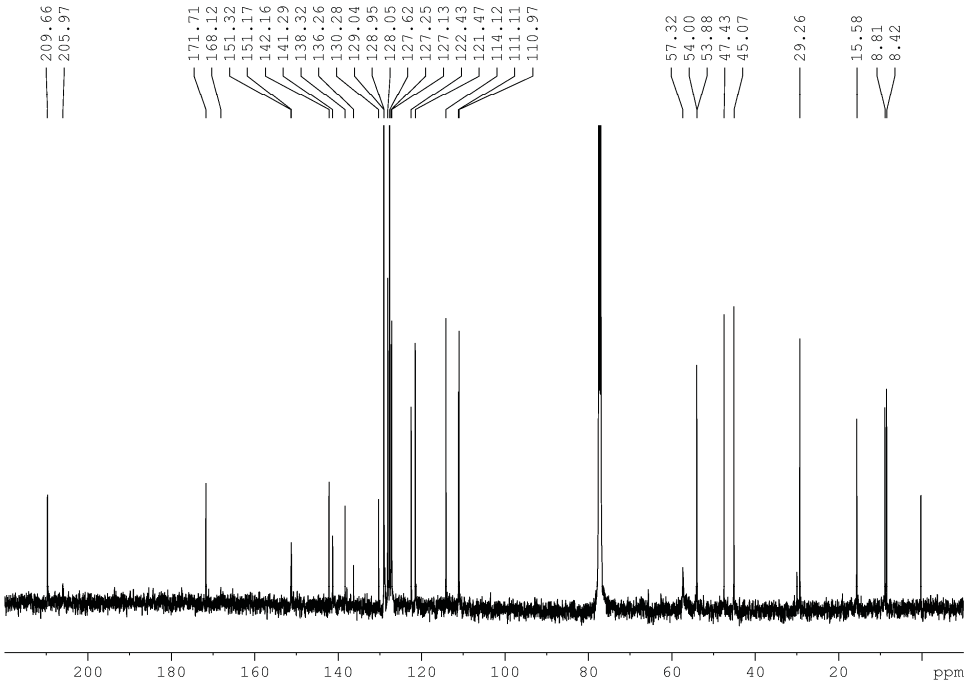
^{13}C NMR ($CDCl_3$, 125 MHz) spectrum of (*trans*)-2,3-dimethyl-4-phenyl-5-(1-(triisopropylsilyl)-1*H*-pyrrol-2-yl)cyclopent-2-enone (133)



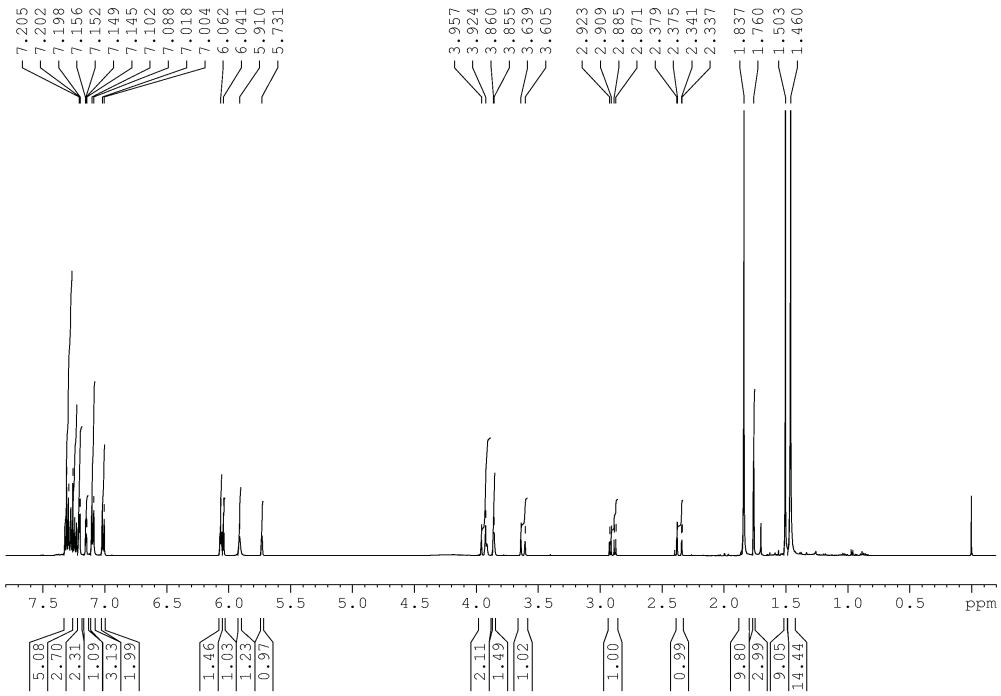
^{1}H NMR ($CDCl_3$, 500 MHz) spectrum of methyl 2-((*trans*)-3,4-dimethyl-2-oxo-5-phenylcyclopent-3-enyl)-1*H*-pyrrole-1-carboxylate (134) and methyl 2-((2-methyl-3-oxo-5-phenylcyclopent-1-enyl)methyl)-1*H*-pyrrole-1-carboxylate (136)



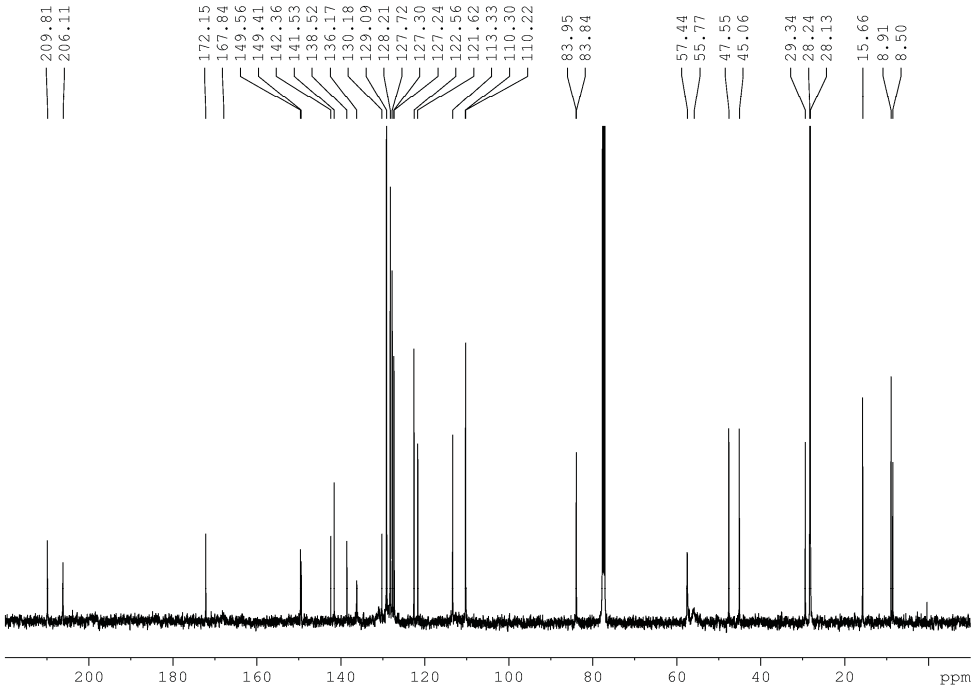
^{13}C NMR ($CDCl_3$, 125 MHz) spectrum of methyl 2-((*trans*)-3,4-dimethyl-2-oxo-5-phenylcyclopent-3-enyl)-1*H*-pyrrole-1-carboxylate (134) and methyl 2-((2-methyl-3-oxo-5-phenylcyclopent-1-enyl)methyl)-1*H*-pyrrole-1-carboxylate (136)



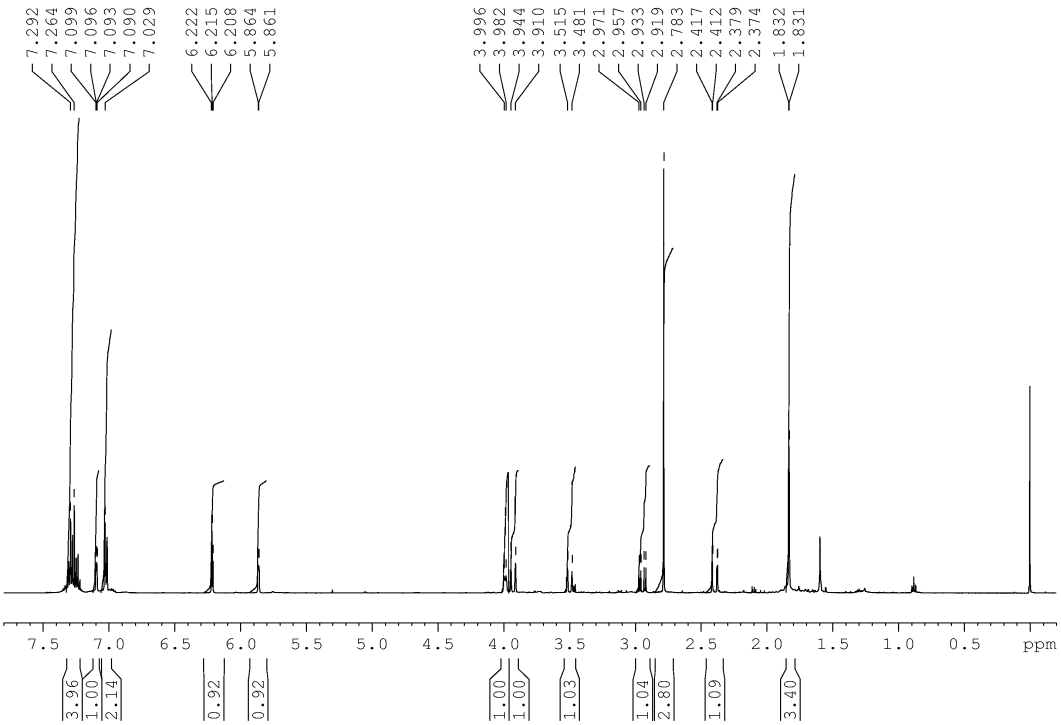
^{1}H NMR ($CDCl_3$, 500 MHz) spectrum of *tert*-butyl 2-((*trans*)-3,4-dimethyl-2-oxo-5-phenylcyclopent-3-enyl)-1*H*-pyrrole-1-car-boxylate (135) and *tert*-butyl 2-((2-methyl-3-oxo-5-phenylcyclopent-1-enyl)methyl)-1*H*-pyrrole-1-carboxylate (137)



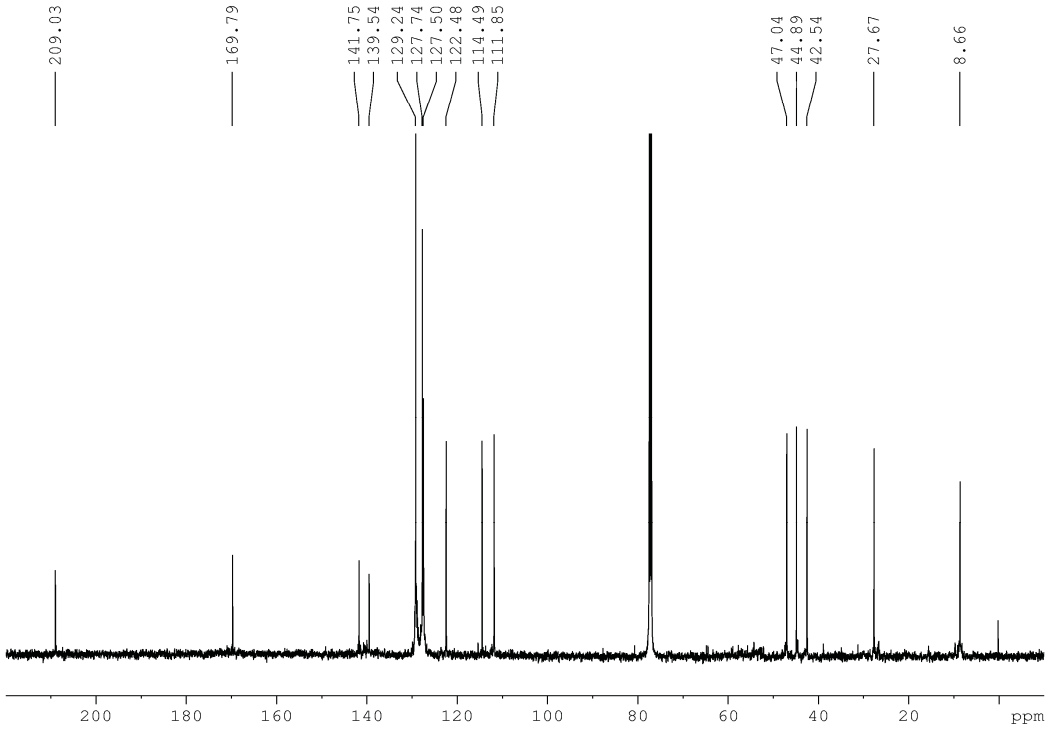
^{13}C NMR ($CDCl_3$, 125 MHz) spectrum of *tert*-butyl 2-((*trans*)-3,4-dimethyl-2-oxo-5-phenylcyclopent-3-enyl)-1*H*-pyrrole-1-car-boxylate (135) and *tert*-butyl 2-((2-methyl-3-oxo-5-phenylcyclopent-1-enyl)methyl)-1*H*-pyrrole-1-carboxylate (137)



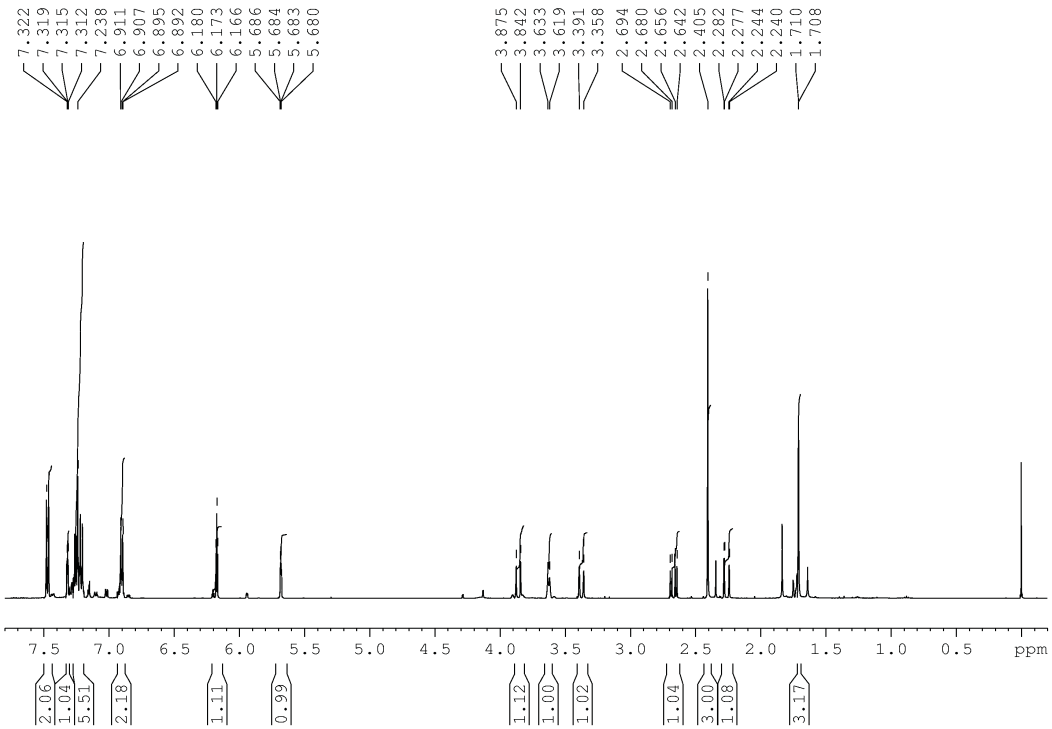
^{1}H NMR ($CDCl_3$, 500 MHz) spectrum of 2-methyl-3-((1-(methylsulfonyl)-1*H*-pyrrol-2-yl)methyl)-4-phenylcyclopent-2-enone (138)



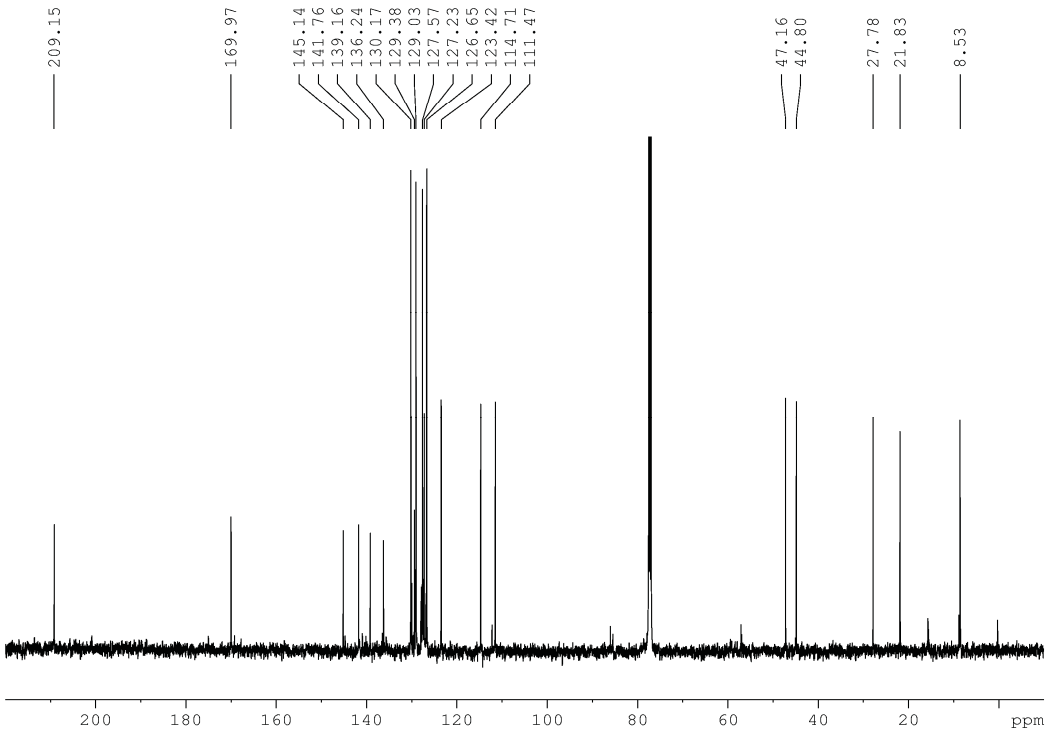
^{13}C NMR ($CDCl_3$, 125 MHz) spectrum of 2-methyl-3-((1-(methylsulfonyl)-1*H*-pyrrol-2-yl)methyl)-4-phenylcyclopent-2-enone (138)



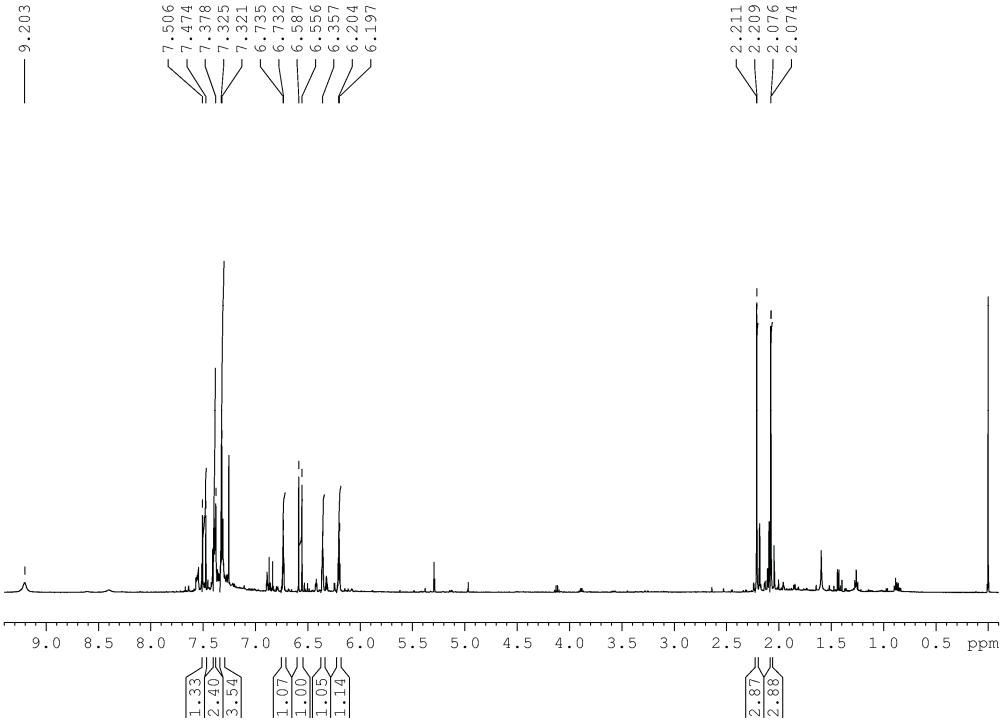
^{1}H NMR ($CDCl_3$, 500 MHz) spectrum of 2-methyl-4-phenyl-3-((1-(*para*-toluenesufonyl)-1*H*-pyrrol-2-yl)methyl)cyclopent-2-enone (139)



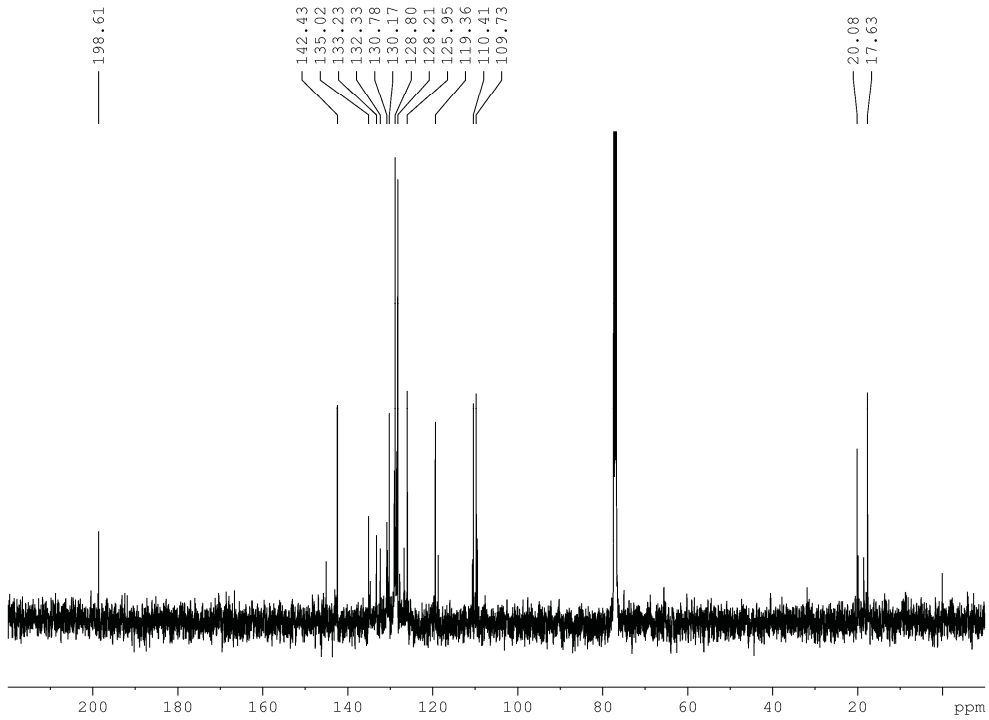
^{13}C NMR ($CDCl_3$, 125 MHz) spectrum of 2-methyl-4-phenyl-3-((1-(*para*-toluenesufonyl)-1*H*-pyrrol-2-yl)methyl)cyclopent-2-enone (139)



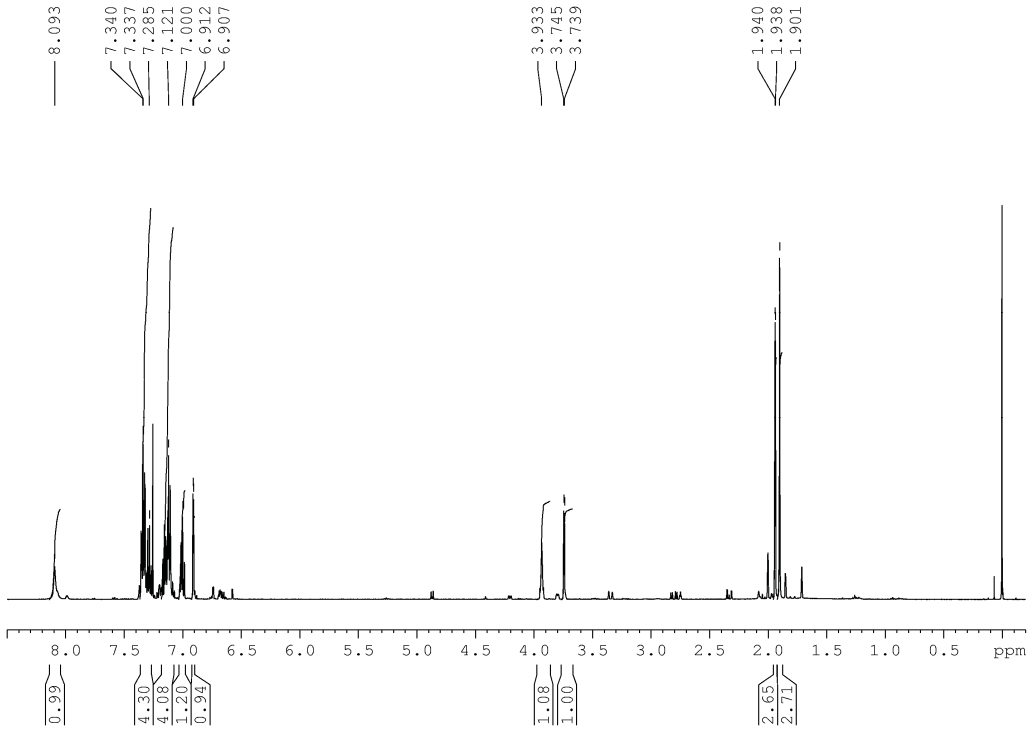
^{1}H NMR ($CDCl_3$, 500 MHz) spectrum of (1*E*,4*Z*)-4-methyl-1-phenyl-5-(1*H*-pyrrol-2-yl)hexa-1,4-dien-3-one (140)



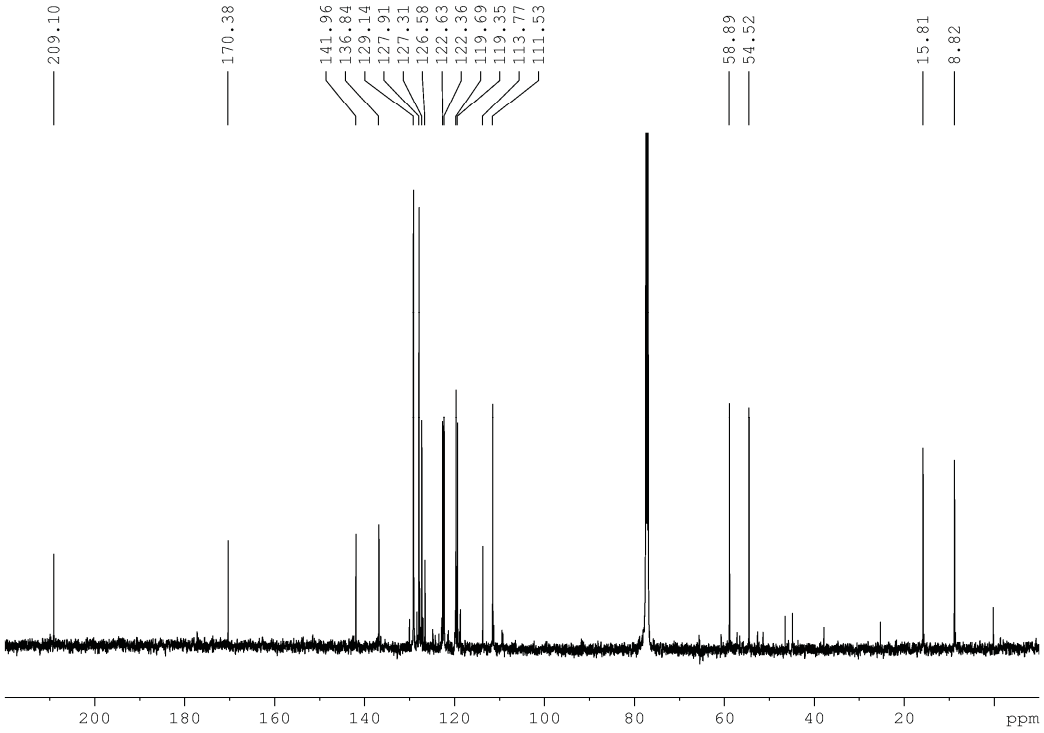
^{13}C NMR ($CDCl_3$, 125 MHz) spectrum of (1*E*,4*Z*)-4-methyl-1-phenyl-5-(1*H*-pyrrol-2-yl)hexa-1,4-dien-3-one (140)



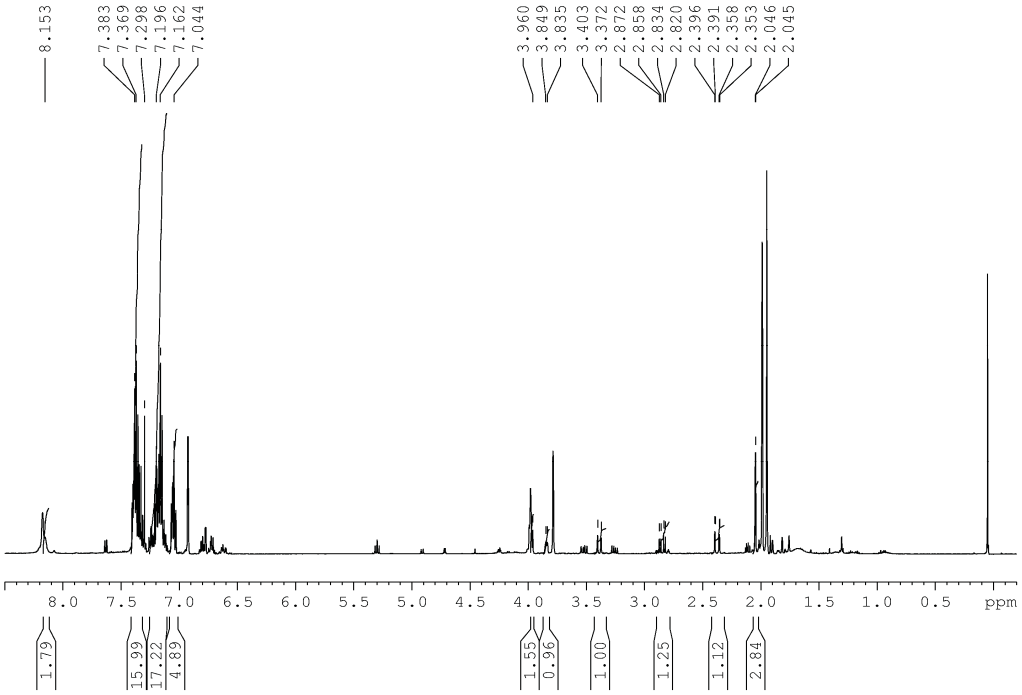
^{1}H NMR ($CDCl_3$, 500 MHz) spectrum of (*trans*)-5-(1*H*-indol-3-yl)-2,3-dimethyl-4-phenylcyclopent-2-enone (141a)



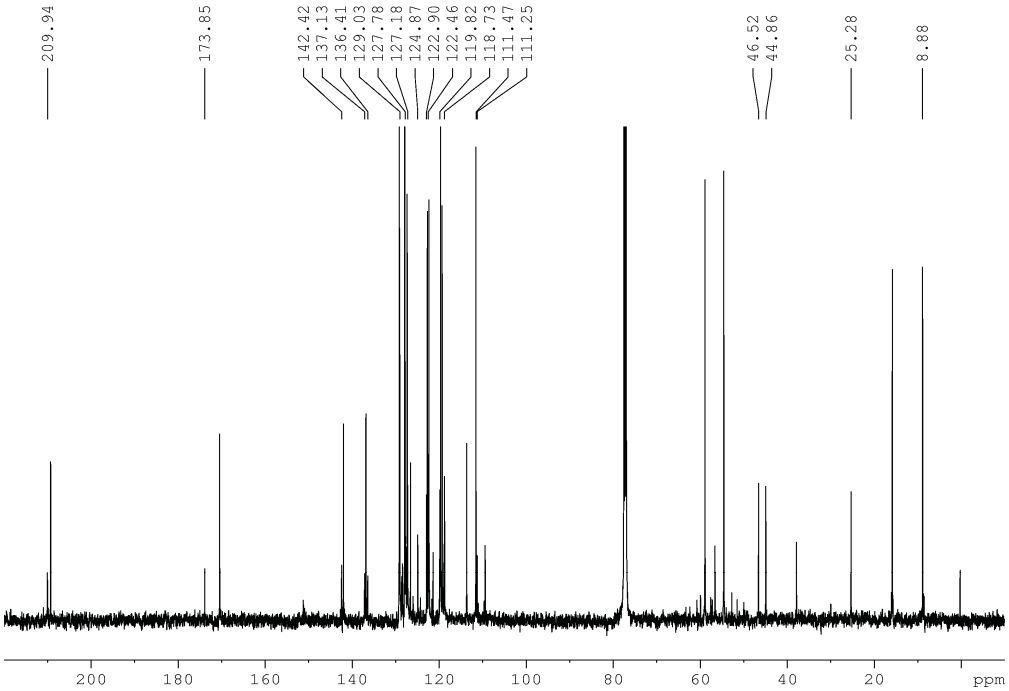
^{13}C NMR ($CDCl_3$, 125 MHz) spectrum of (*trans*)-5-(1*H*-indol-3-yl)-2,3-dimethyl-4-phenylcyclopent-2-enone (141a)



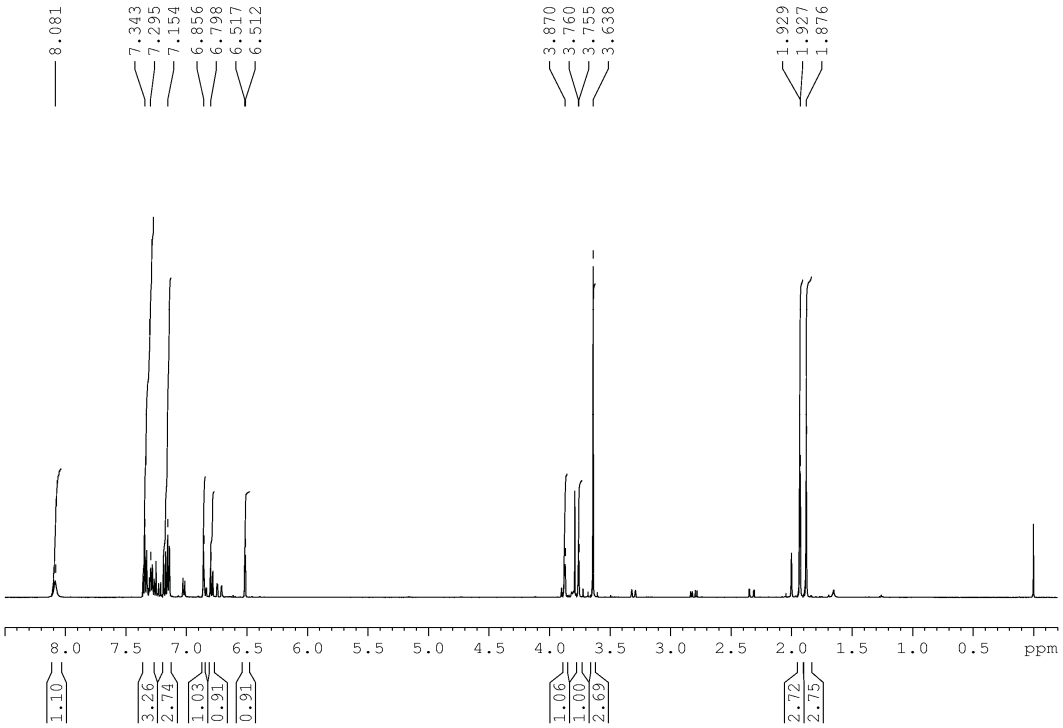
^{1}H NMR ($CDCl_3$, 500 MHz) spectrum of (*trans*)-5-(1*H*-indol-3-yl)-2,3-dimethyl-4-phenylcyclopent-2-enone (141a) and 3-((1*H*-indol-3-yl)methyl)-2-methyl-4-phenylcyclopent-2-enone (141b)



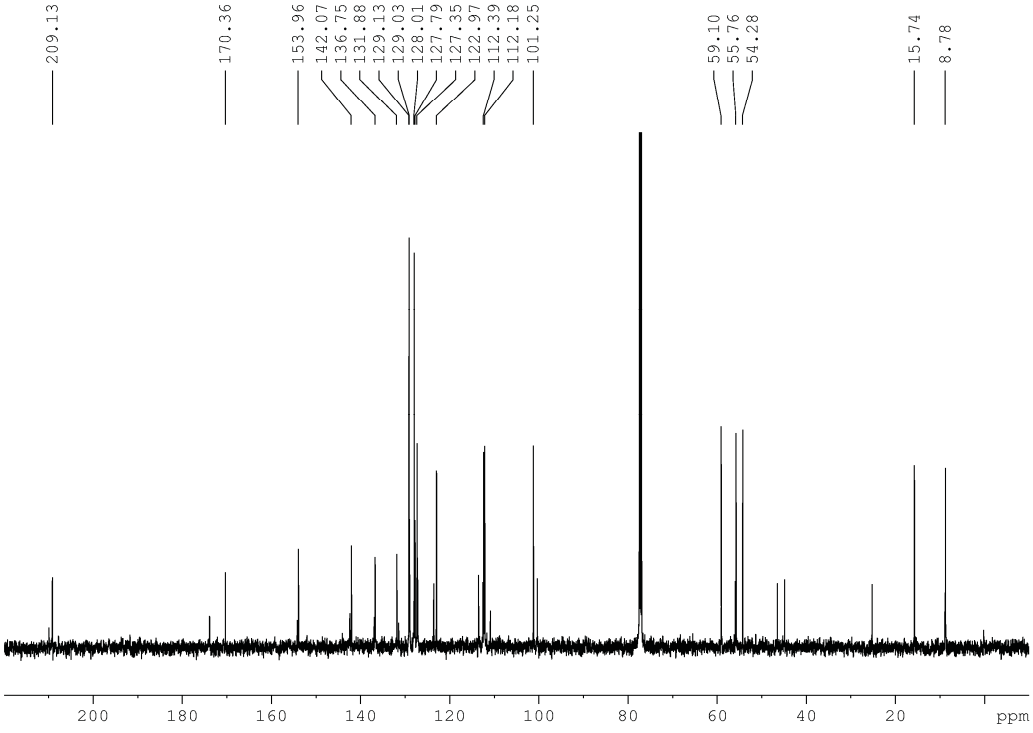
^{13}C NMR ($CDCl_3$, 125 MHz) spectrum of (*trans*)-5-(1*H*-indol-3-yl)-2,3-dimethyl-4-phenylcyclopent-2-enone (141a) and 3-((1*H*-indol-3-yl)methyl)-2-methyl-4-phenylcyclopent-2-enone (141b)



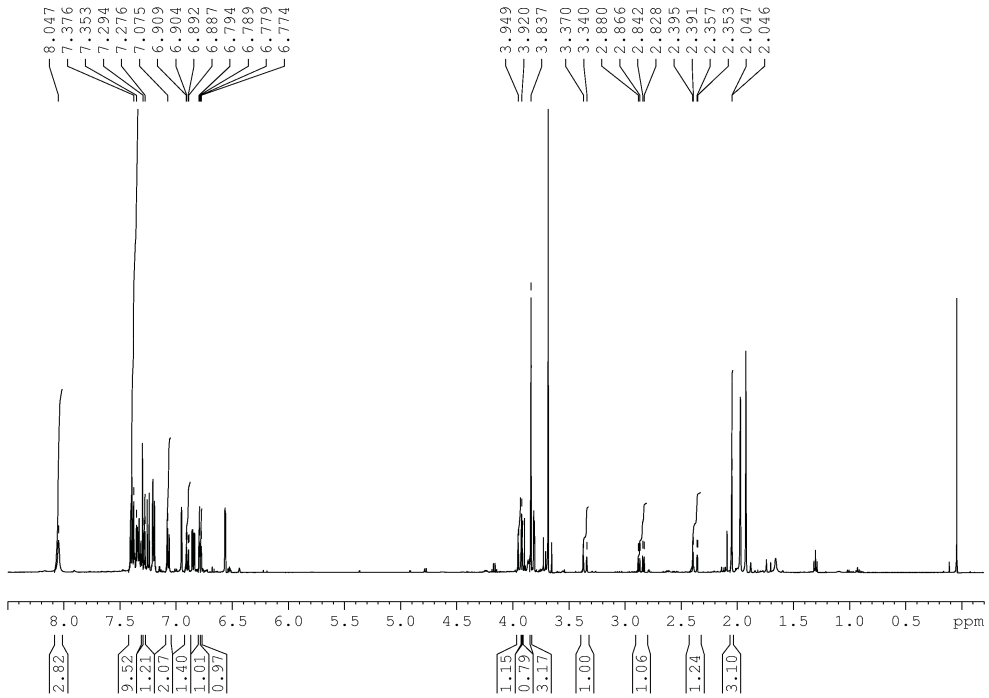
^{1}H NMR ($CDCl_3$, 500 MHz) spectrum of (*trans*)-5-(5-methoxy-1*H*-indol-3-yl)-2,3-dimethyl-4-phenylcyclopent-2-enone (142a)



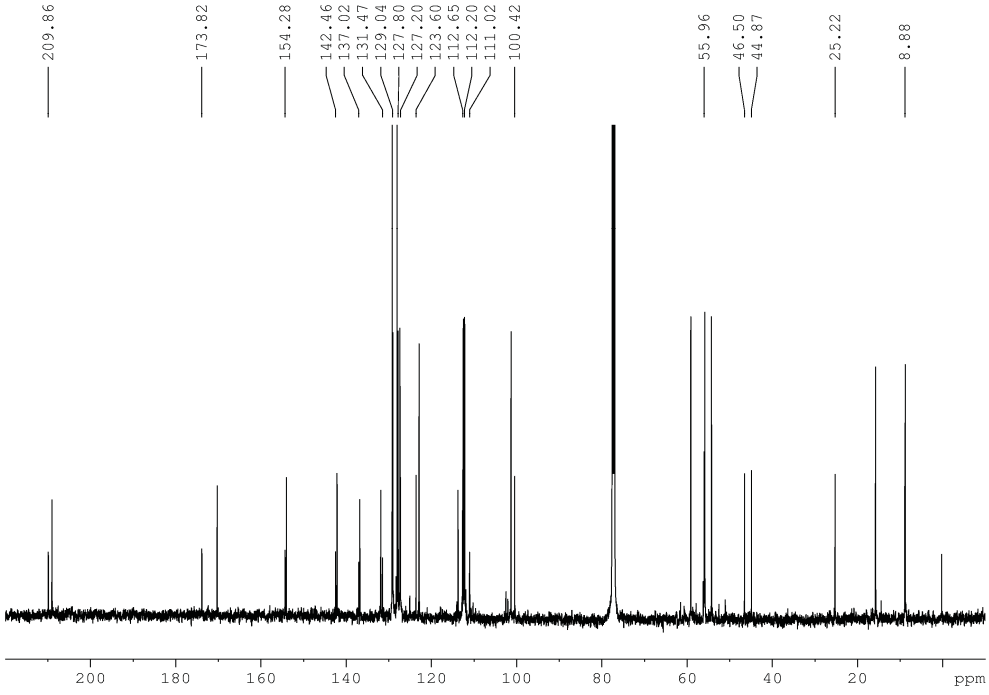
^{13}C NMR ($CDCl_3$, 125 MHz) spectrum of (*trans*)-5-(5-methoxy-1*H*-indol-3-yl)-2,3-dimethyl-4-phenylcyclopent-2-enone (142a)



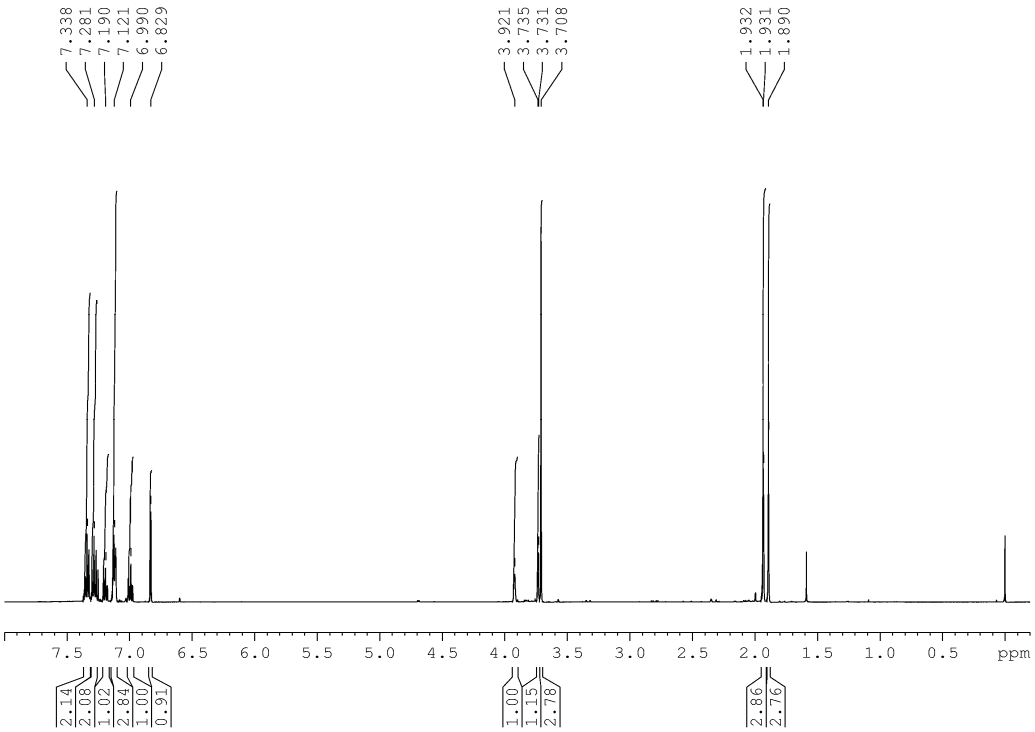
^{1}H NMR ($CDCl_3$, 500 MHz) spectrum of (*trans*)-5-(5-methoxy-1*H*-indol-3-yl)-2,3-dimethyl-4-phenylcyclopent-2-enone (142a) and 3-((5-methoxy-1*H*-indol-3-yl)methyl)-2-methyl-4-phenylcyclopent-2-enone (142b)



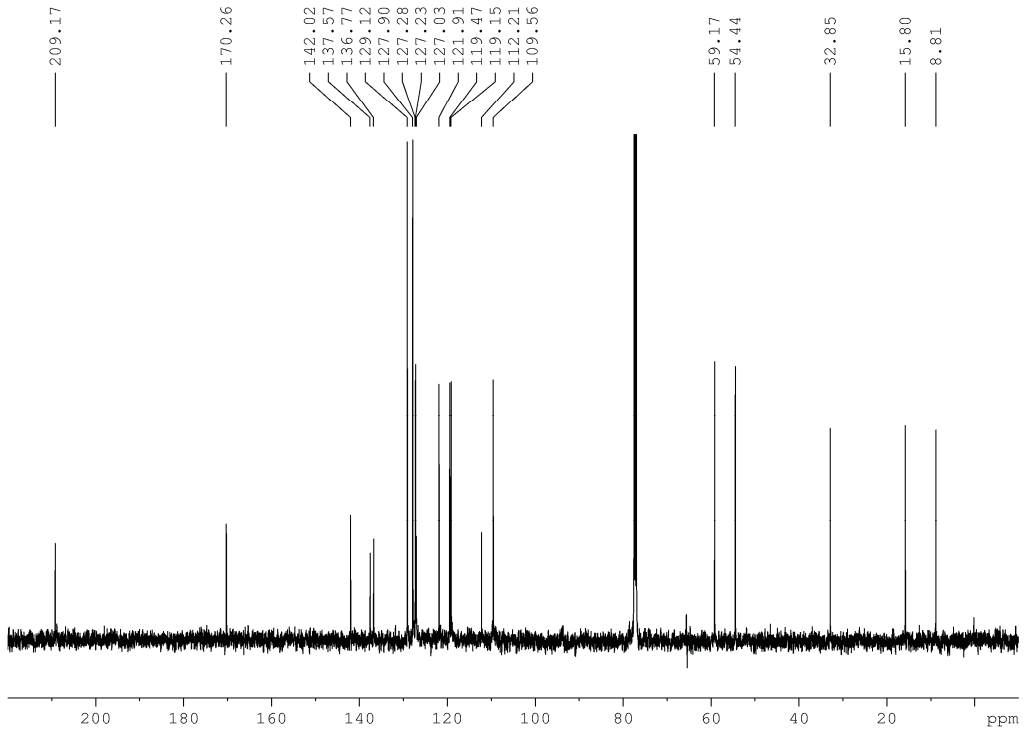
^{13}C NMR ($CDCl_3$, 125 MHz) spectrum of (*trans*)-5-(5-methoxy-1*H*-indol-3-yl)-2,3-dimethyl-4-phenylcyclopent-2-enone (142a) and 3-((5-methoxy-1*H*-indol-3-yl)methyl)-2-methyl-4-phenylcyclopent-2-enone (142b)



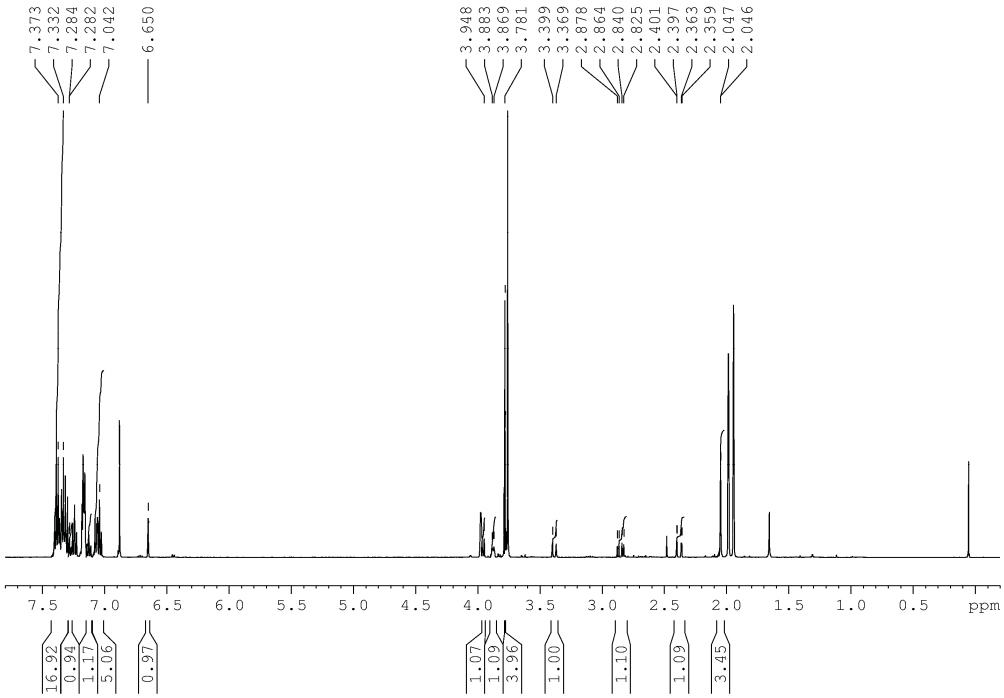
^{1}H NMR ($CDCl_3$, 500 MHz) spectrum of (*trans*)-2,3-dimethyl-5-(1-methyl-1*H*-indol-3-yl)-4-phenylcyclopent-2-enone (143a)



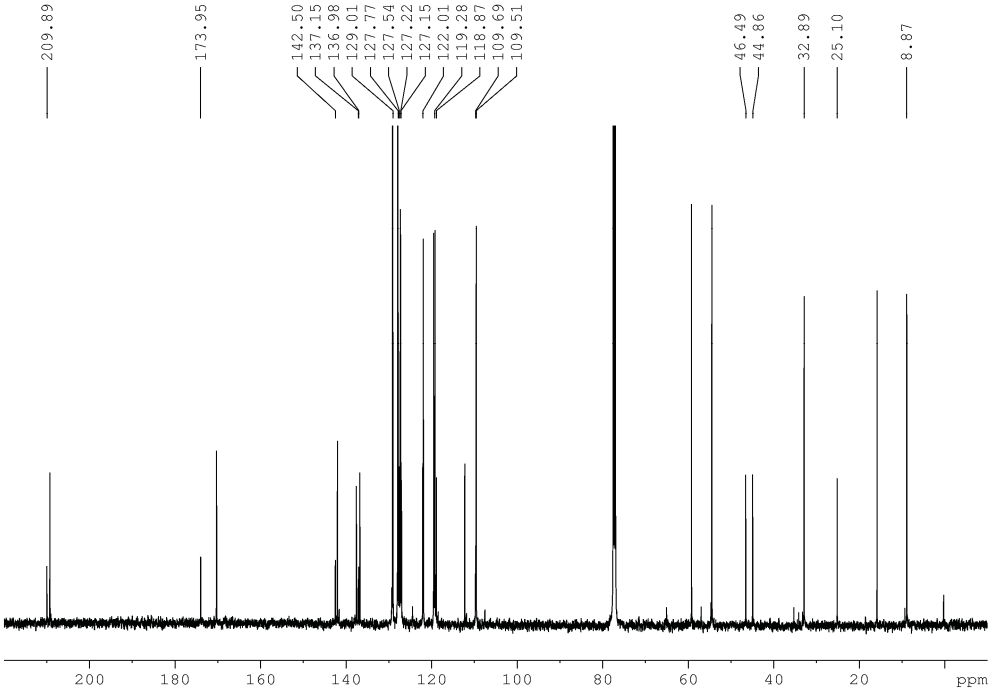
^{13}C NMR ($CDCl_3$, 125 MHz) spectrum of (*trans*)-2,3-dimethyl-5-(1-methyl-1*H*-indol-3-yl)-4-phenylcyclopent-2-enone (143a)



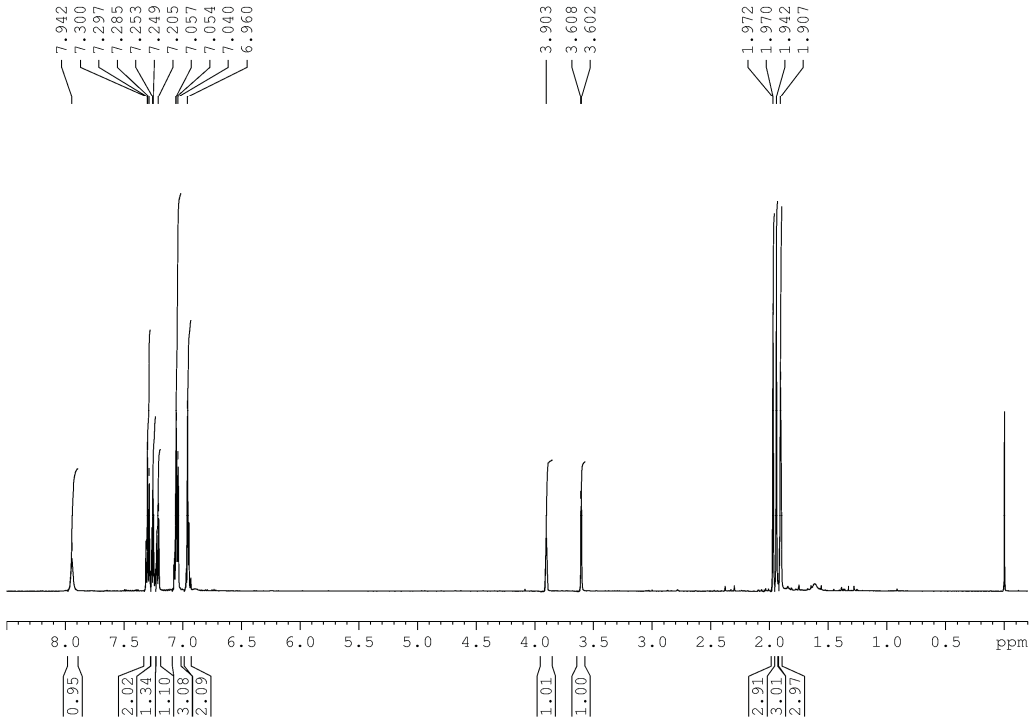
^{1}H NMR ($CDCl_3$, 500 MHz) spectrum of (*trans*)-2,3-dimethyl-5-(1-methyl-1*H*-indol-3-yl)-4-phenylcyclopent-2-enone (143a) and 2-methyl-3-((1-methyl-1*H*-indol-3-yl)methyl)-4-phenylcyclopent-2-enone (143b)



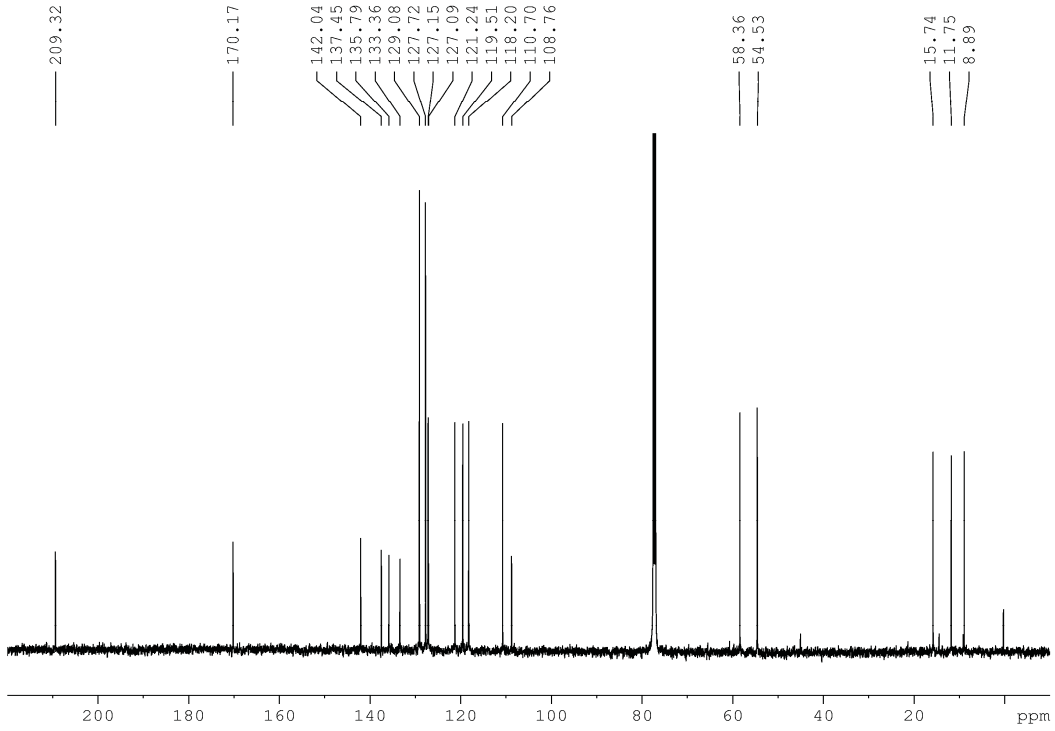
^{13}C NMR ($CDCl_3$, 125 MHz) spectrum of (*trans*)-2,3-dimethyl-5-(1-methyl-1*H*-indol-3-yl)-4-phenylcyclopent-2-enone (143a) and 2-methyl-3-((1-methyl-1*H*-indol-3-yl)methyl)-4-phenylcyclopent-2-enone (143b)



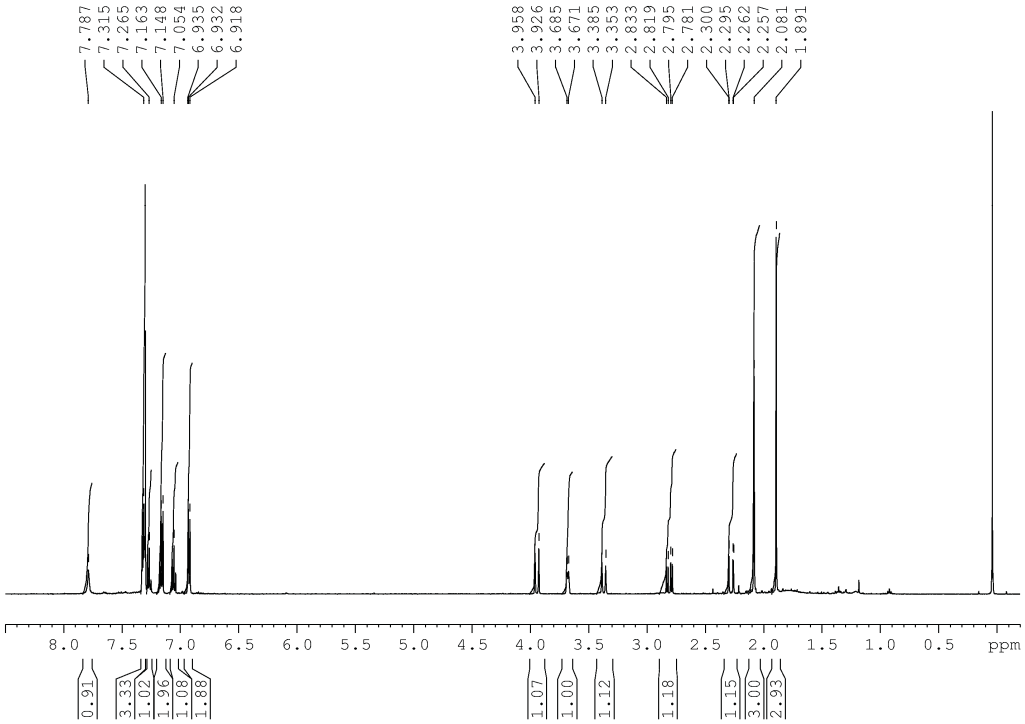
^{1}H NMR ($CDCl_3$, 500 MHz) spectrum of (*trans*)-2,3-dimethyl-5-(2-methyl-1*H*-indol-3-yl)-4-phenylcyclopent-2-enone (144a)



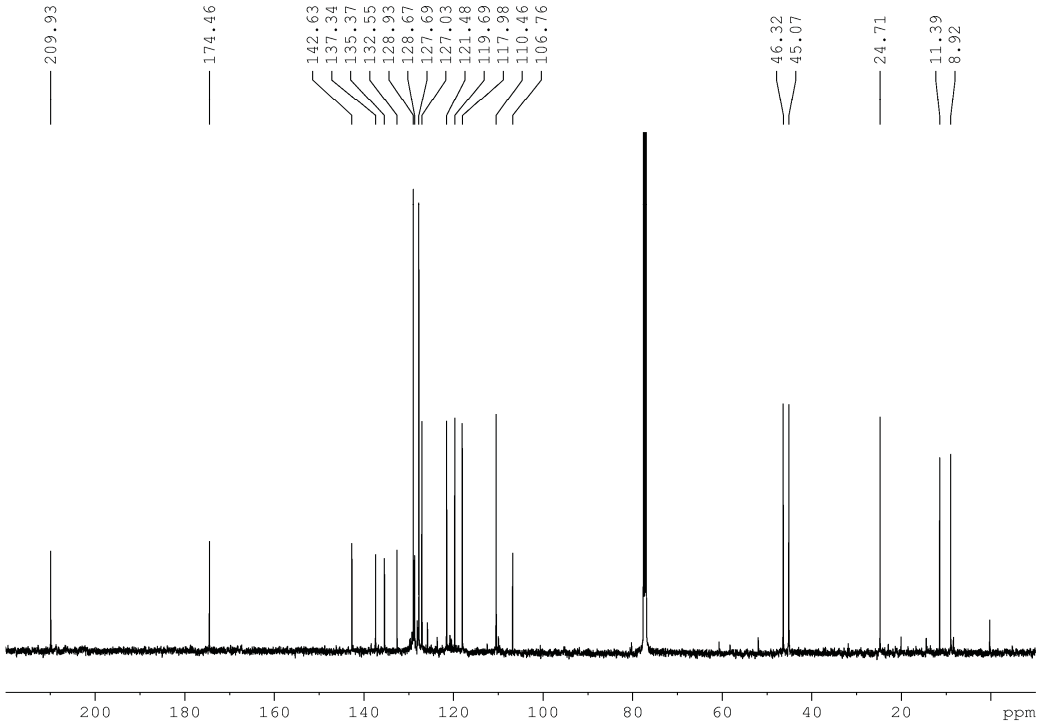
^{13}C NMR ($CDCl_3$, 125 MHz) spectrum of (*trans*)-2,3-dimethyl-5-(2-methyl-1*H*-indol-3-yl)-4-phenylcyclopent-2-enone (144a)



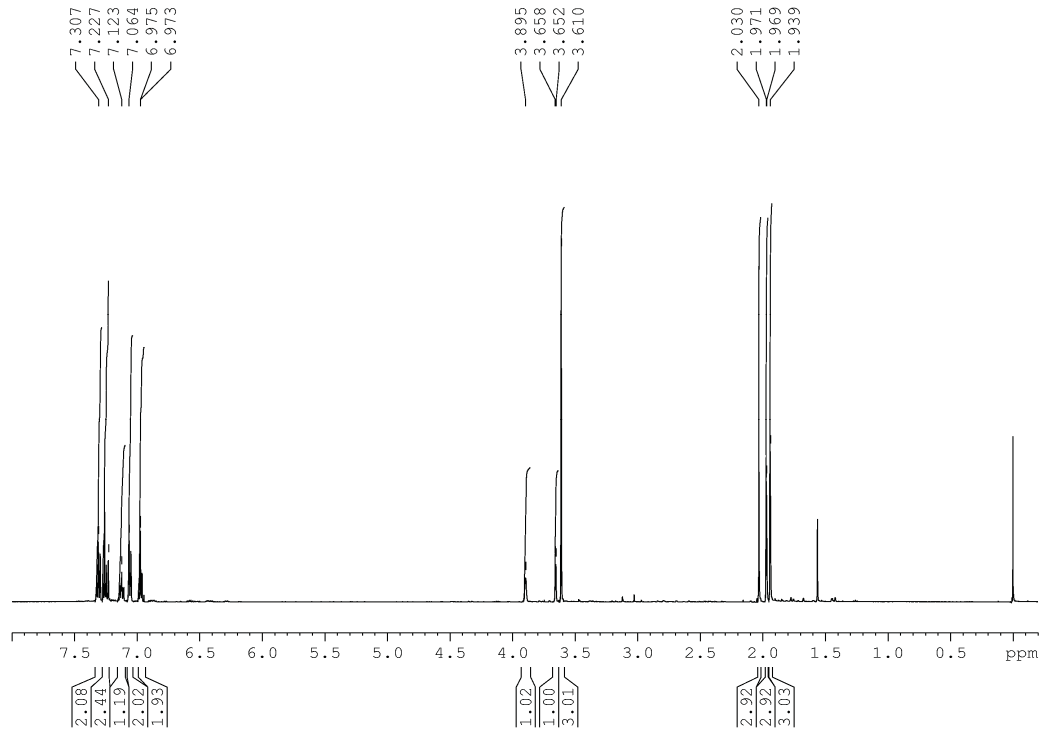
^{1}H NMR ($CDCl_3$, 500 MHz) spectrum of 2-methyl-3-((2-methyl-1*H*-indol-3-yl)methyl)-4-phenylcyclopent-2-enone (144b)



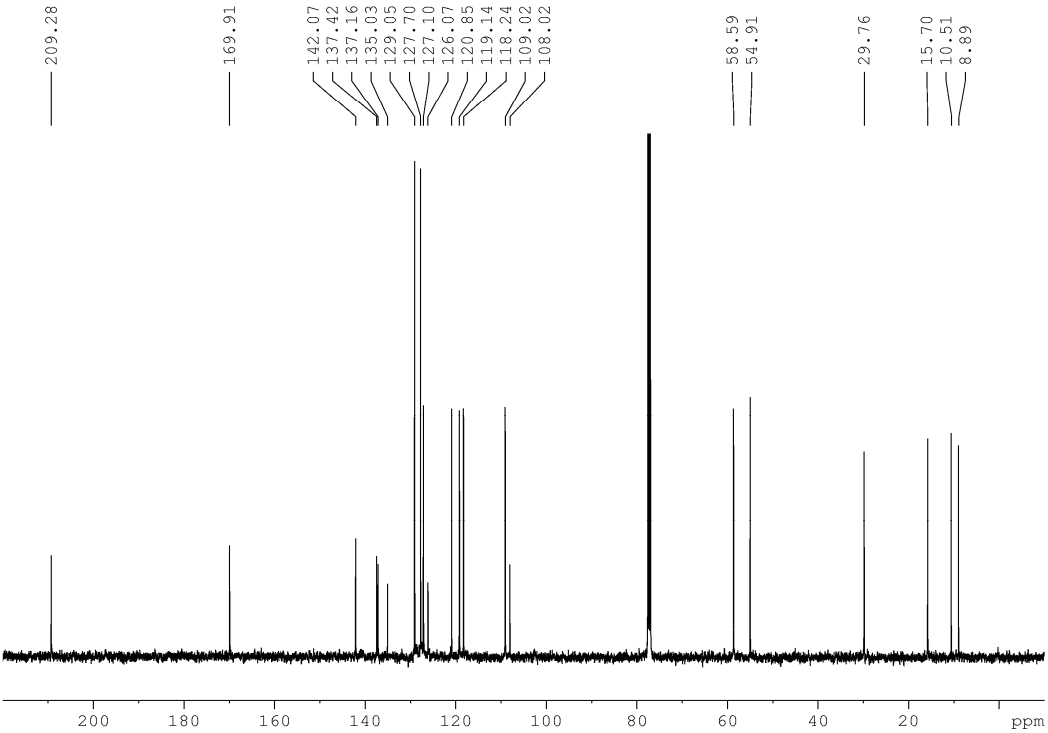
^{13}C NMR ($CDCl_3$, 125 MHz) spectrum of 2-methyl-3-((2-methyl-1*H*-indol-3-yl)methyl)-4-phenylcyclopent-2-enone (144b)



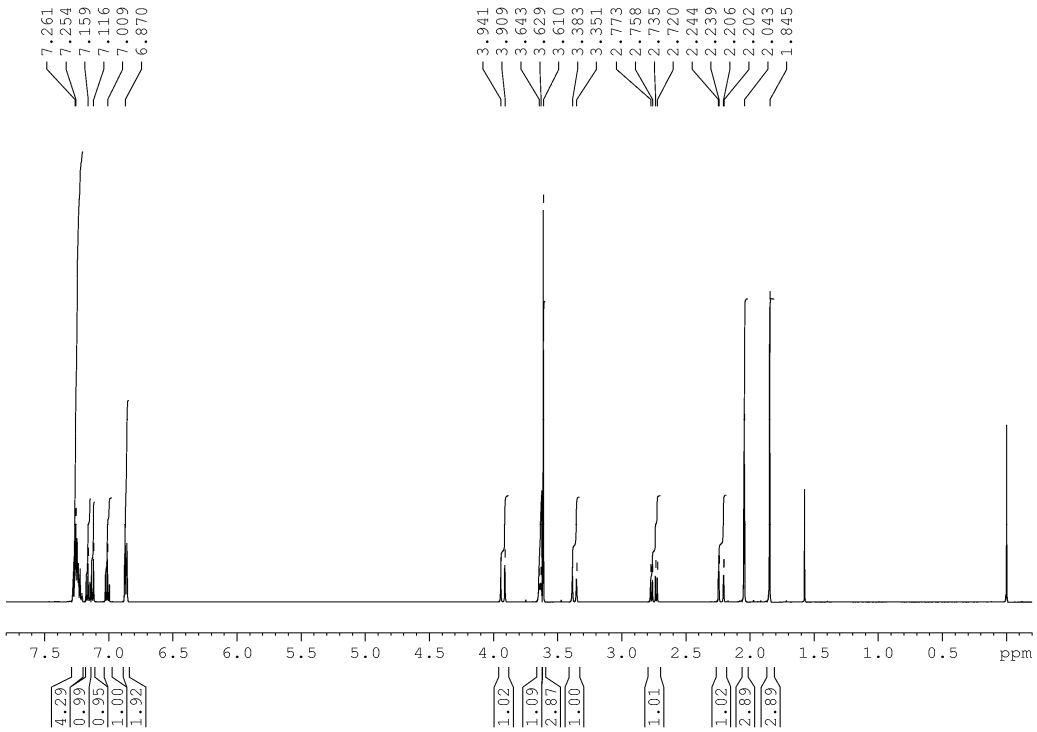
^{1}H NMR ($CDCl_3$, 500 MHz) spectrum of (*trans*)-5-(1,2-dimethyl-1*H*-indol-3-yl)-2,3-dimethyl-4-phenylcyclopent-2-enone (145a)



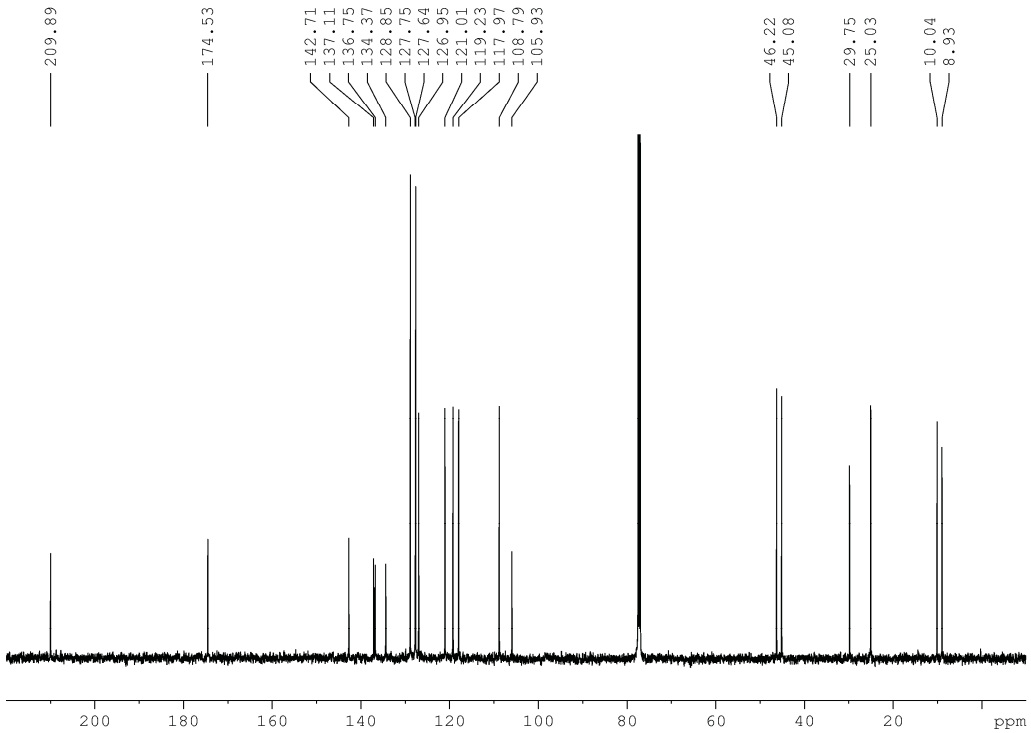
^{13}C NMR ($CDCl_3$, 125 MHz) spectrum of (*trans*)-5-(1,2-dimethyl-1*H*-indol-3-yl)-2,3-dimethyl-4-phenylcyclopent-2-enone (145a)



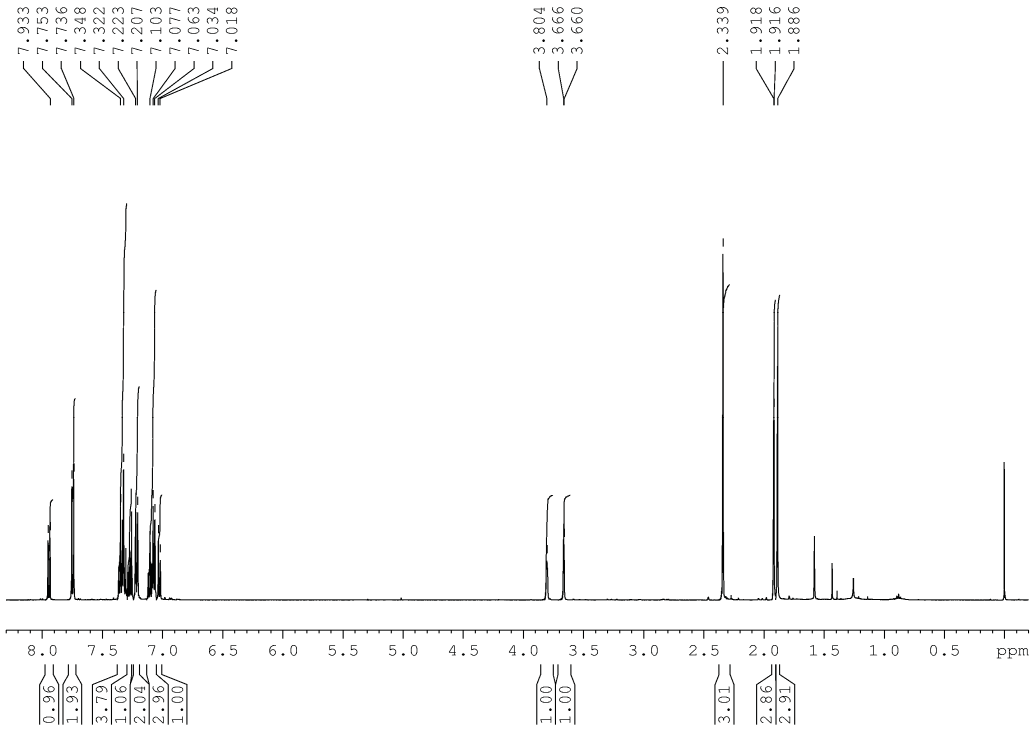
^{1}H NMR ($CDCl_3$, 500 MHz) spectrum of 3-((1,2-dimethyl-1*H*-indol-3-yl)methyl)-2-methyl-4-phenylcyclopent-2-enone (145b)



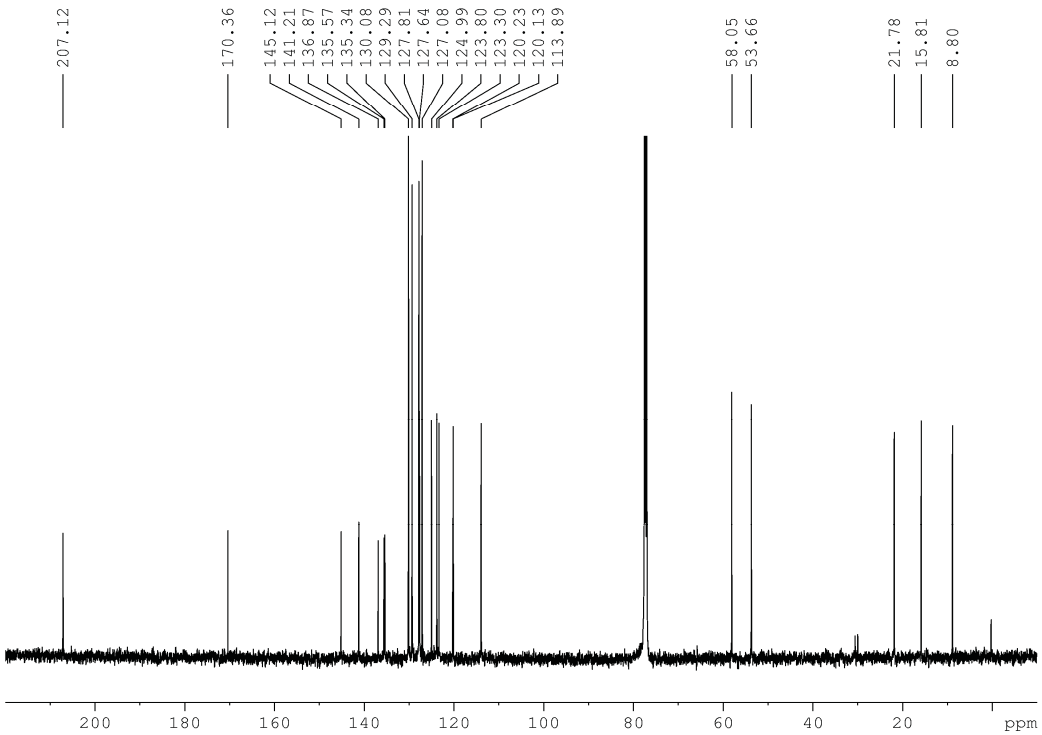
^{13}C NMR ($CDCl_3$, 125 MHz) spectrum of 3-((1,2-dimethyl-1*H*-indol-3-yl)methyl)-2-methyl-4-phenylcyclopent-2-enone (145b)



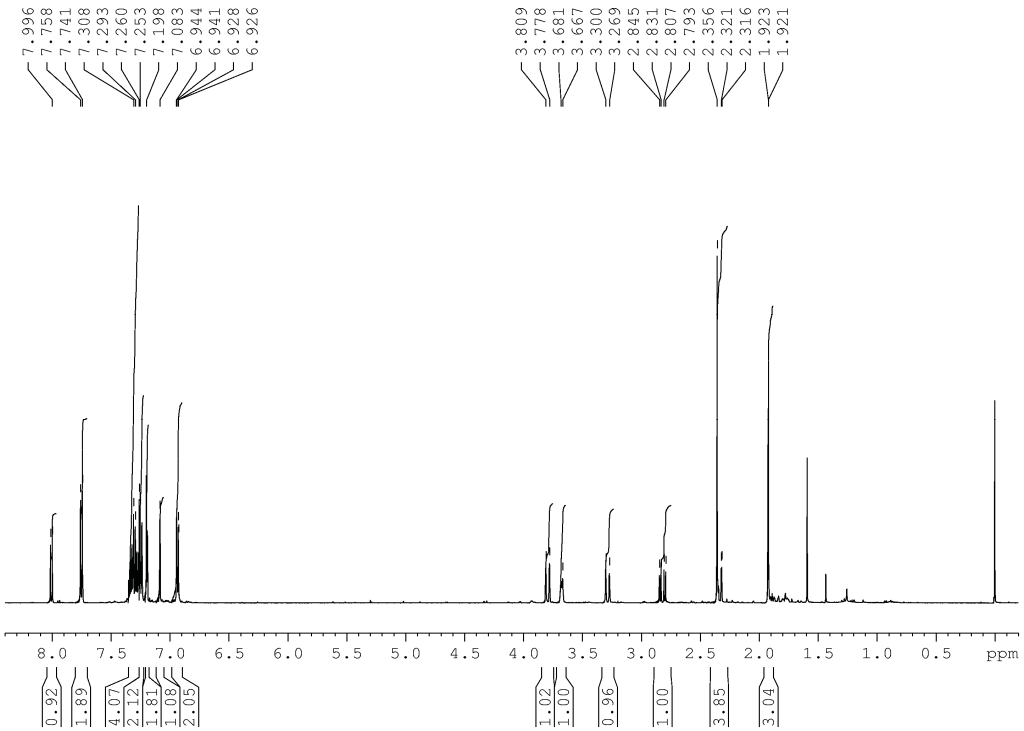
^{1}H NMR ($CDCl_3$, 500 MHz) spectrum of (*trans*)-2,3-dimethyl-4-phenyl-5-(1-tosyl-1H-indol-3-yl)cyclopent-2-enone (146a)



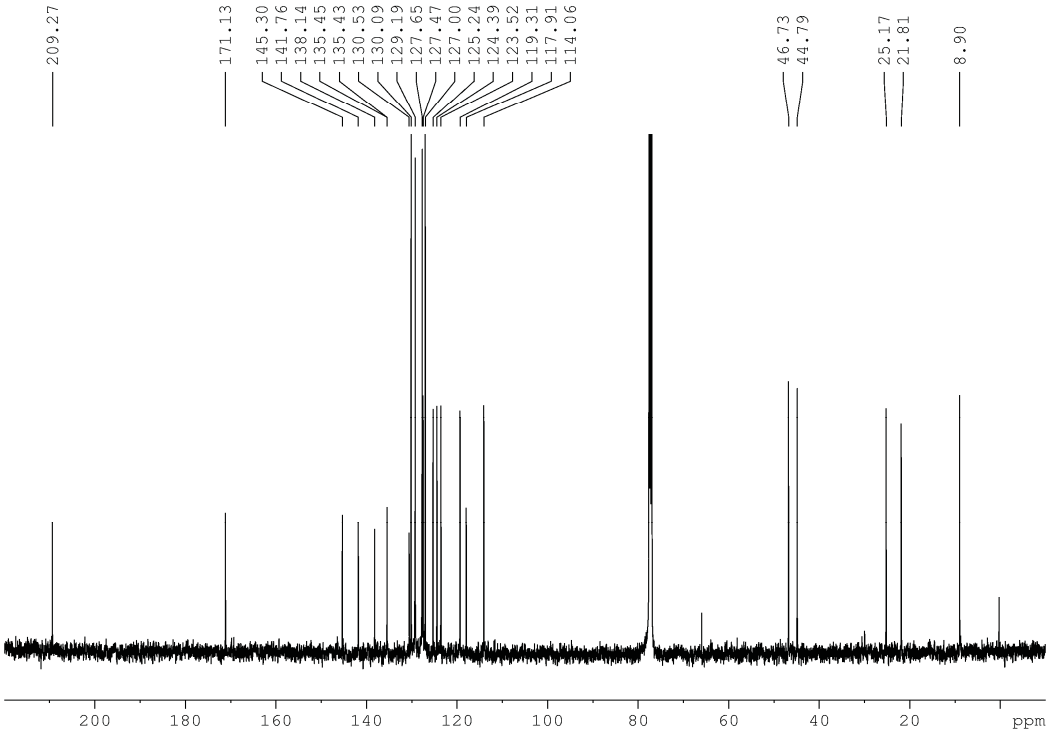
^{13}C NMR ($CDCl_3$, 125 MHz) spectrum of (*trans*)-2,3-dimethyl-4-phenyl-5-(1-tosyl-1H-indol-3-yl)cyclopent-2-enone (146a)



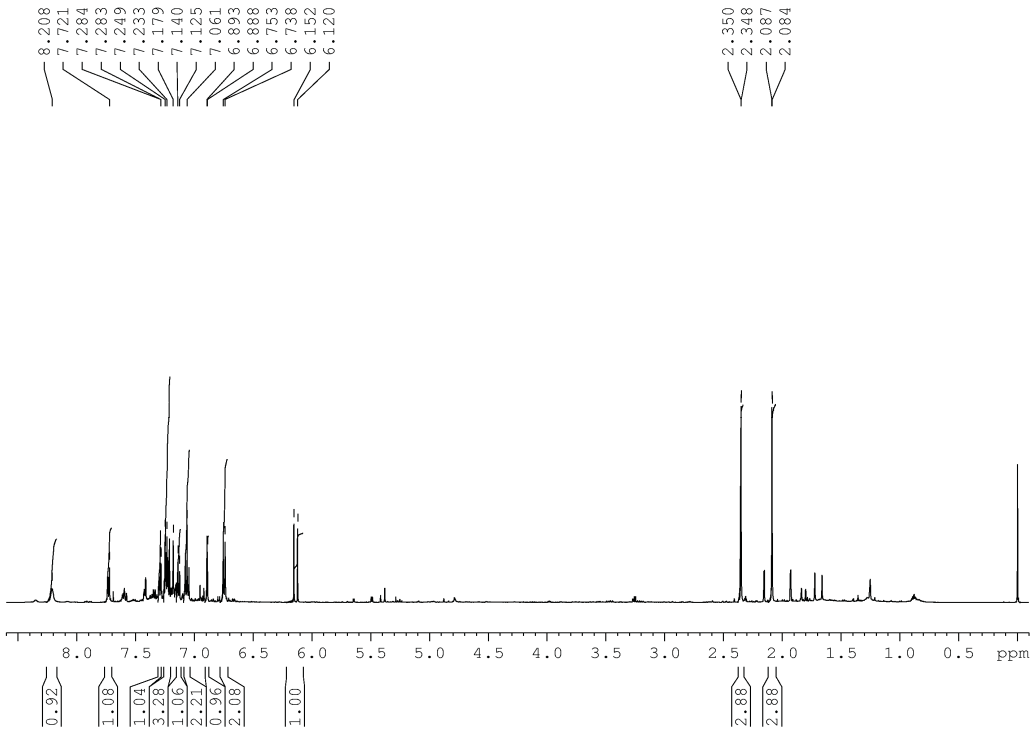
^{1}H NMR ($CDCl_3$, 500 MHz) spectrum of 2-methyl-4-phenyl-3-((1-tosyl-1H-indol-3-yl)methyl)cyclopent-2-enone (146b)



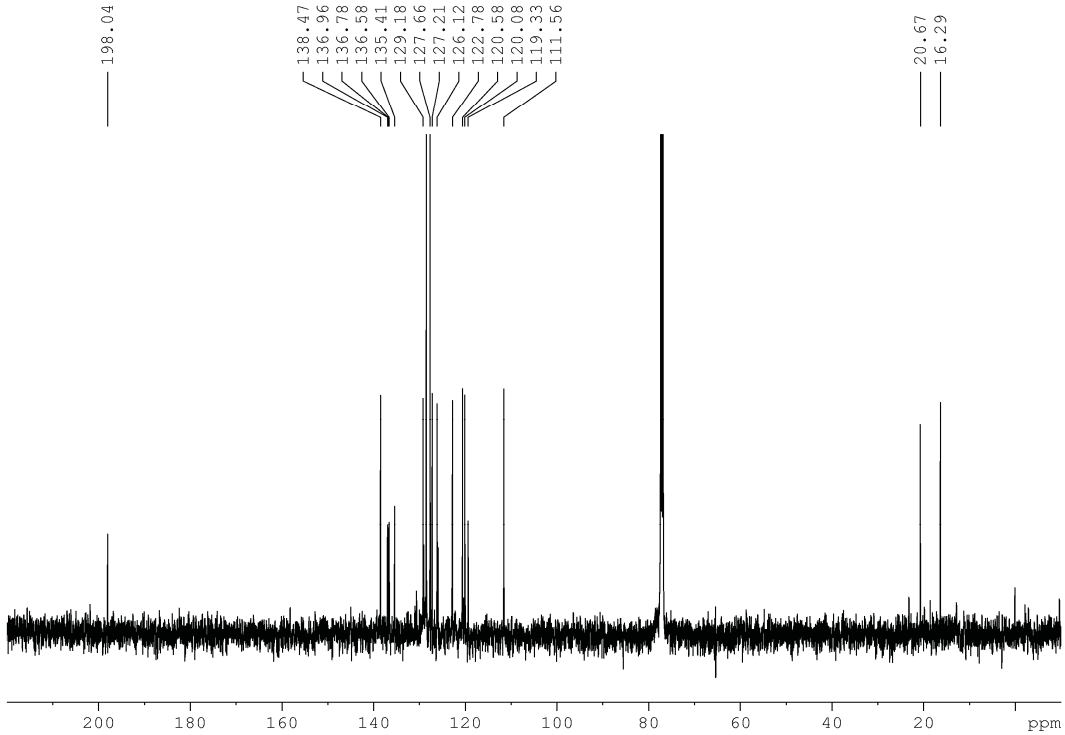
^{13}C NMR ($CDCl_3$, 125 MHz) spectrum of 2-methyl-4-phenyl-3-((1-tosyl-1H-indol-3-yl)methyl)cyclopent-2-enone (146b)



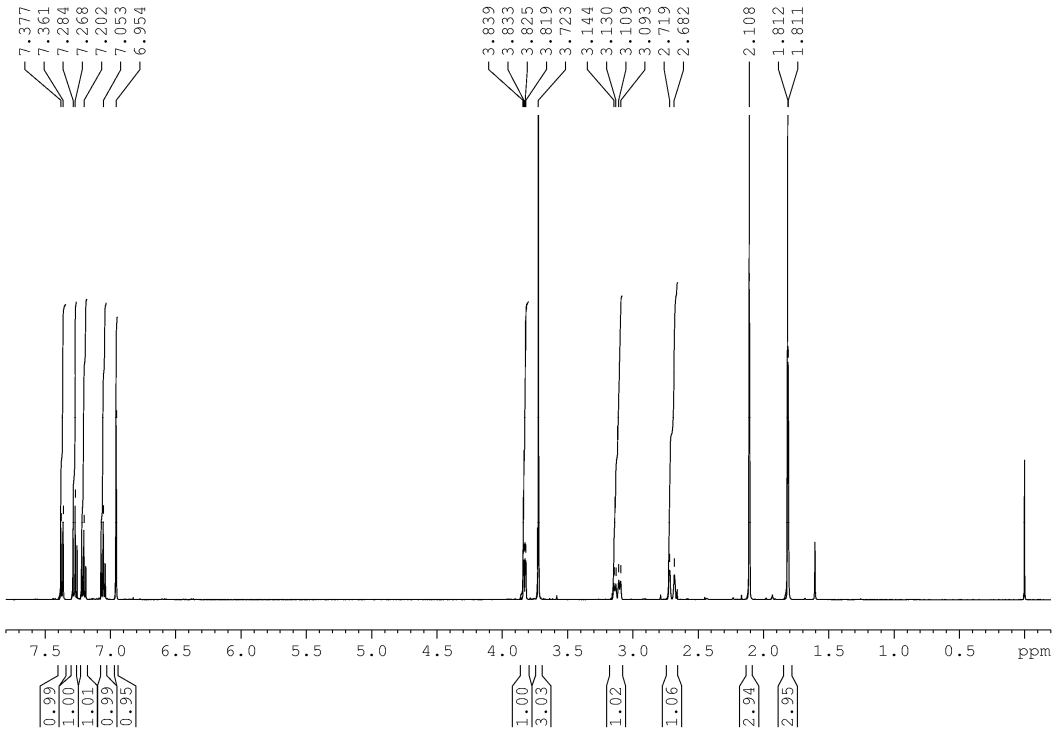
^{1}H NMR ($CDCl_3$, 500 MHz) spectrum of (1*E*,4*Z*)-5-(1*H*-indol-3-yl)-4-methyl-1-phenylhexa-1,4-dien-3-one (147)



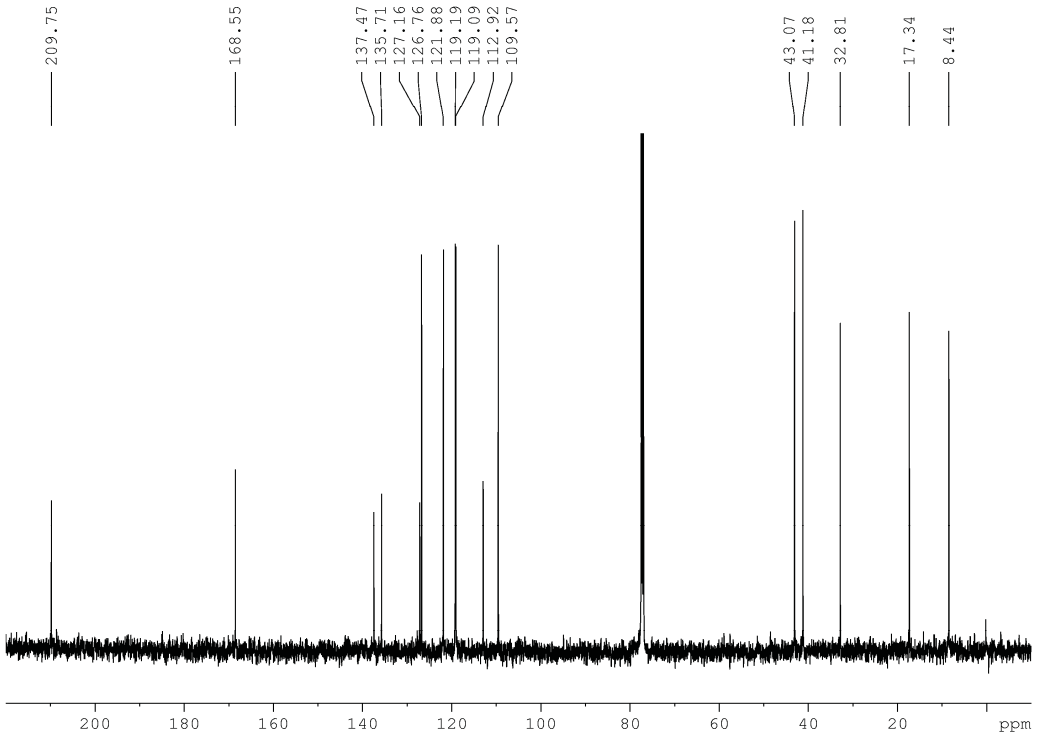
^{13}C NMR ($CDCl_3$, 125 MHz) spectrum of (1*E*,4*Z*)-5-(1*H*-indol-3-yl)-4-methyl-1-phenylhexa-1,4-dien-3-one (147)



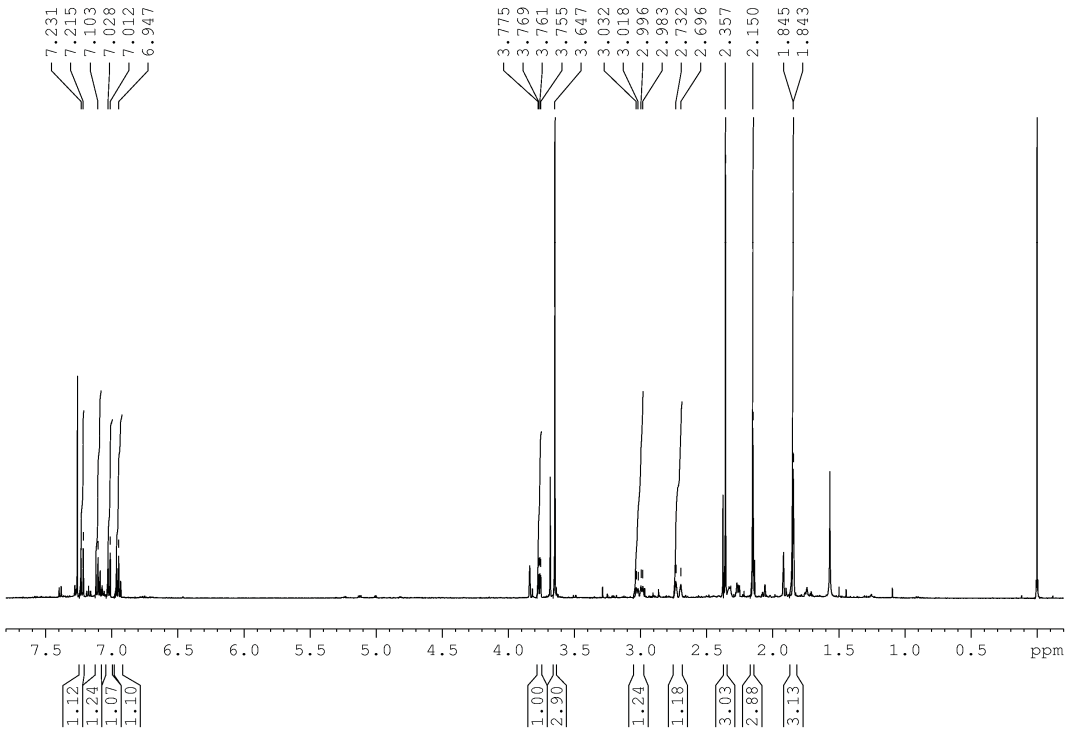
^{1}H NMR ($CDCl_3$, 500 MHz) spectrum of 2,3-dimethyl-5-(1-methyl-1*H*-indol-3-yl)cyclopent-2-enone (148)



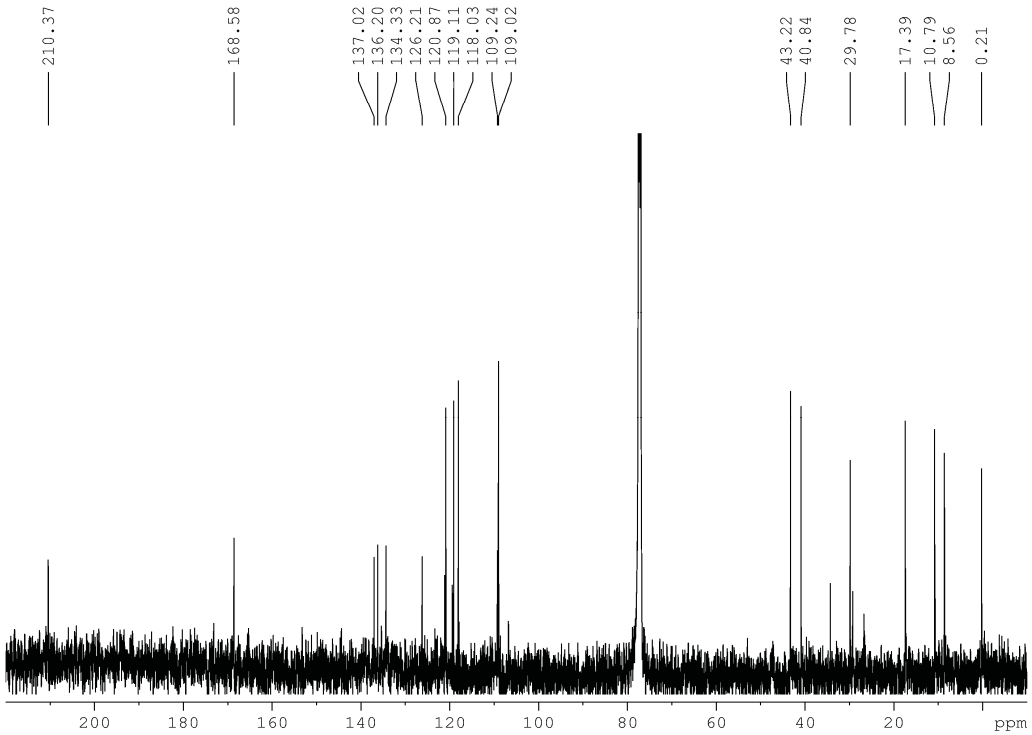
^{13}C NMR ($CDCl_3$, 125 MHz) spectrum of 2,3-dimethyl-5-(1-methyl-1*H*-indol-3-yl)cyclopent-2-enone (148)



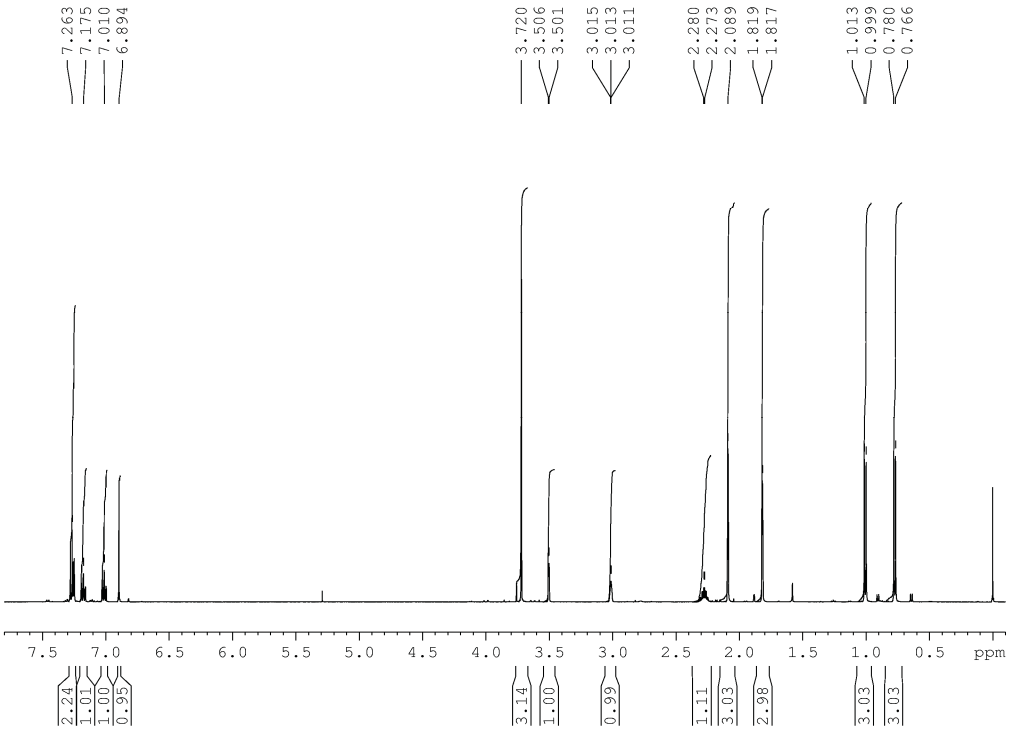
^{1}H NMR ($CDCl_3$, 500 MHz) spectrum of 5-(1,2-dimethyl-1*H*-indol-3-yl)-2,3-dimethylcyclopent-2-enone (149)



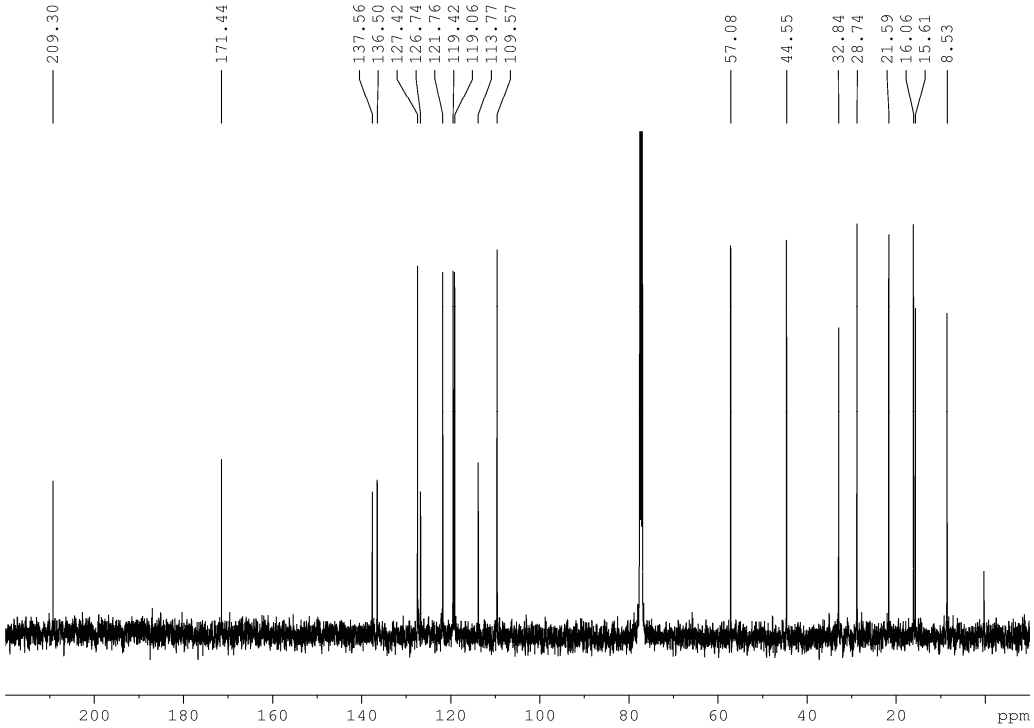
^{13}C NMR ($CDCl_3$, 125 MHz) spectrum of 5-(1,2-dimethyl-1*H*-indol-3-yl)-2,3-dimethylcyclopent-2-enone (149)



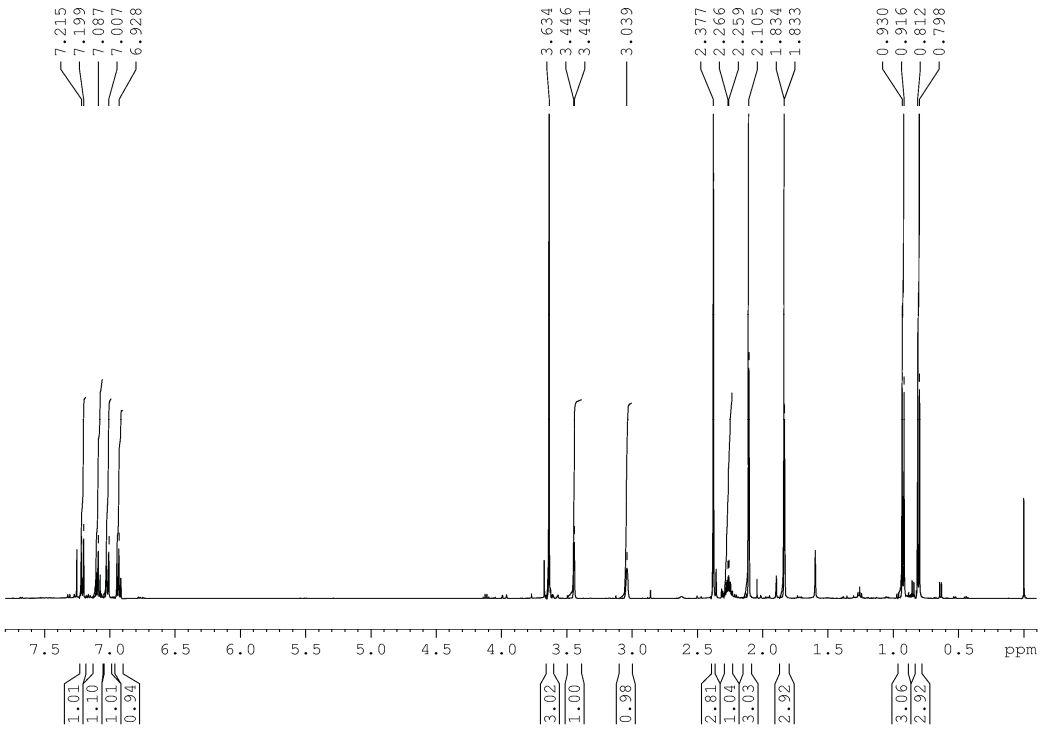
^{1}H NMR ($CDCl_3$, 500 MHz) spectrum of (*trans*)-4-isopropyl-2,3-dimethyl-5-(1-methyl-1*H*-indol-3-yl)cyclopent-2-enone (150)



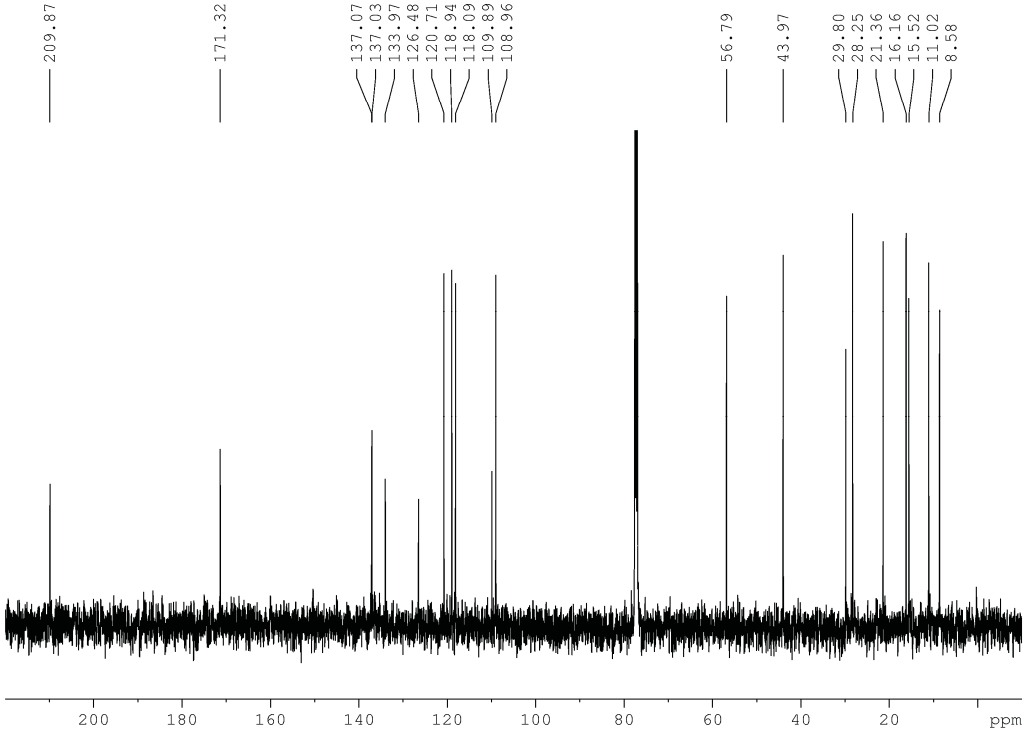
^{13}C NMR ($CDCl_3$, 125 MHz) spectrum of (*trans*)-4-isopropyl-2,3-dimethyl-5-(1-methyl-1*H*-indol-3-yl)cyclopent-2-enone (150)



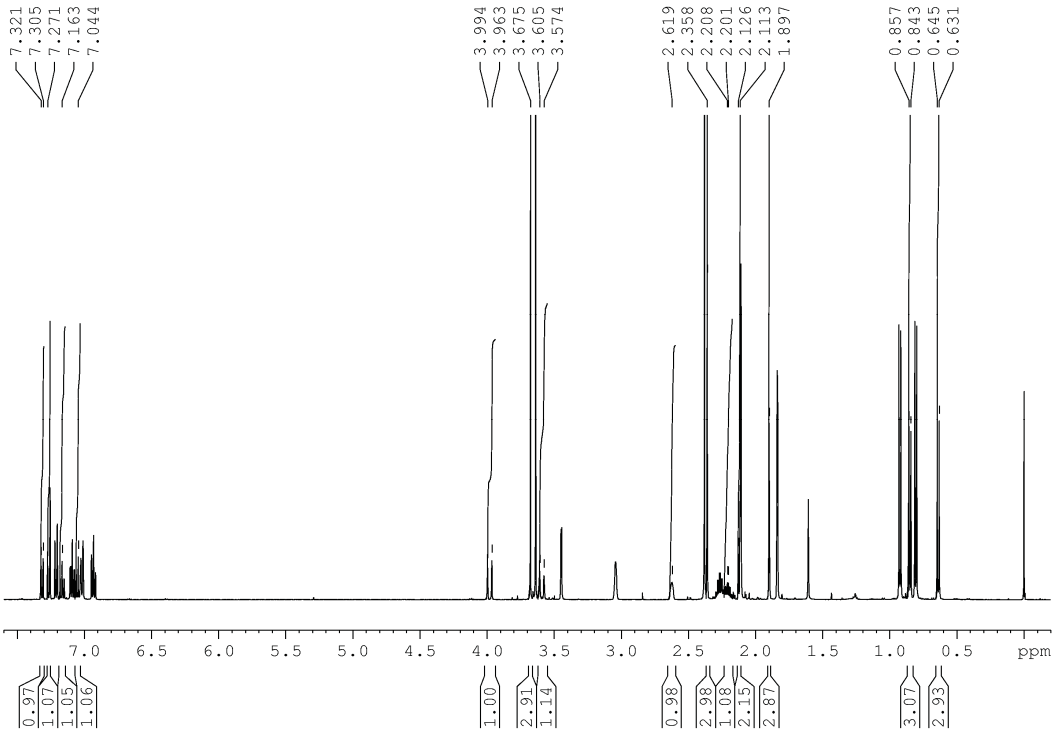
^{1}H NMR ($CDCl_3$, 500 MHz) spectrum of (*trans*)-5-(1,2-dimethyl-1*H*-indol-3-yl)-4-isopropyl-2,3-dimethylcyclopent-2-enone (151a)



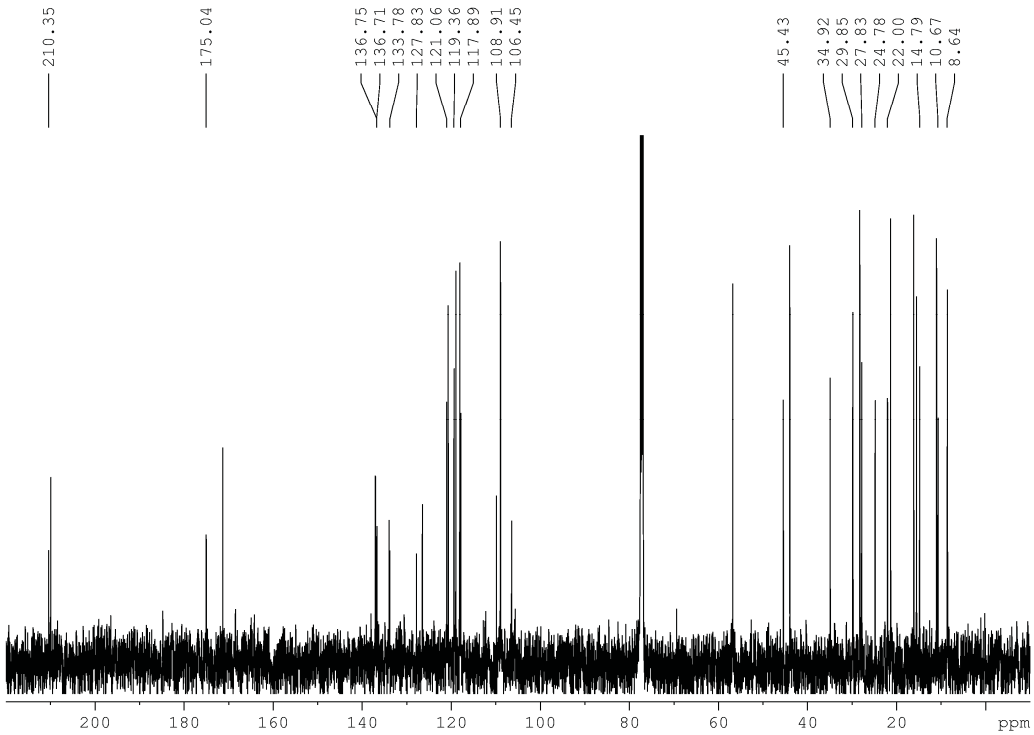
^{13}C NMR ($CDCl_3$, 125 MHz) spectrum of (*trans*)-5-(1,2-dimethyl-1*H*-indol-3-yl)-4-isopropyl-2,3-dimethylcyclopent-2-enone (151a)



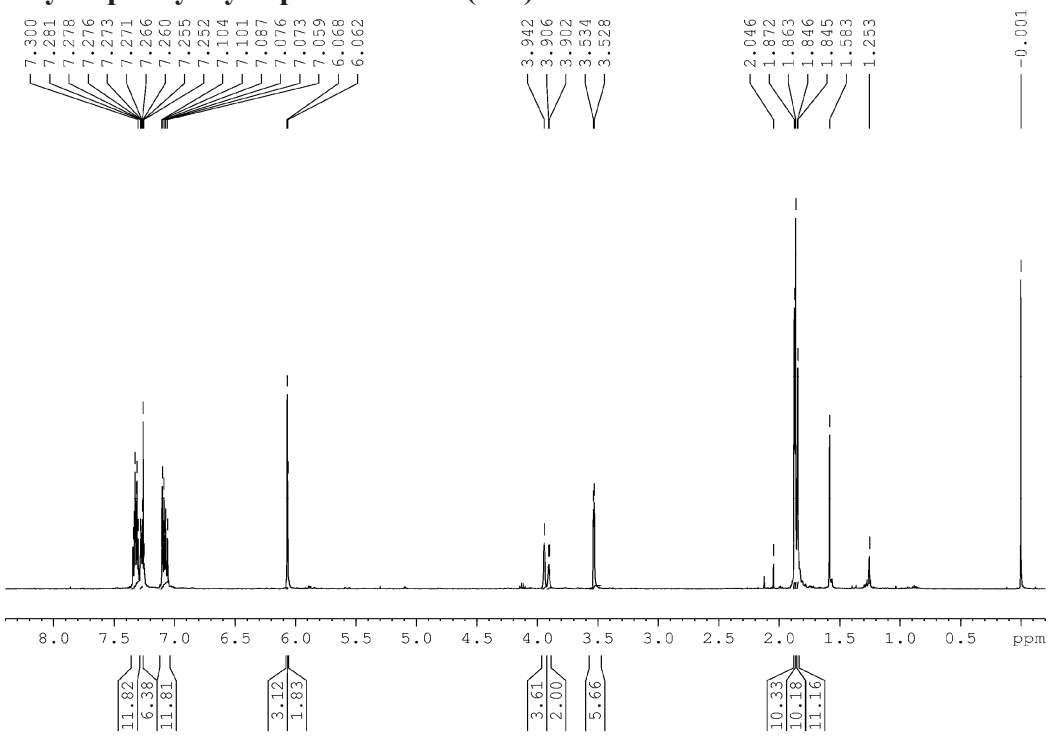
^{1}H NMR ($CDCl_3$, 500 MHz) spectrum of 3-((1,2-dimethyl-1*H*-indol-3-yl)methyl)-4-isopropyl-2-methylcyclopent-2-enone (151b)



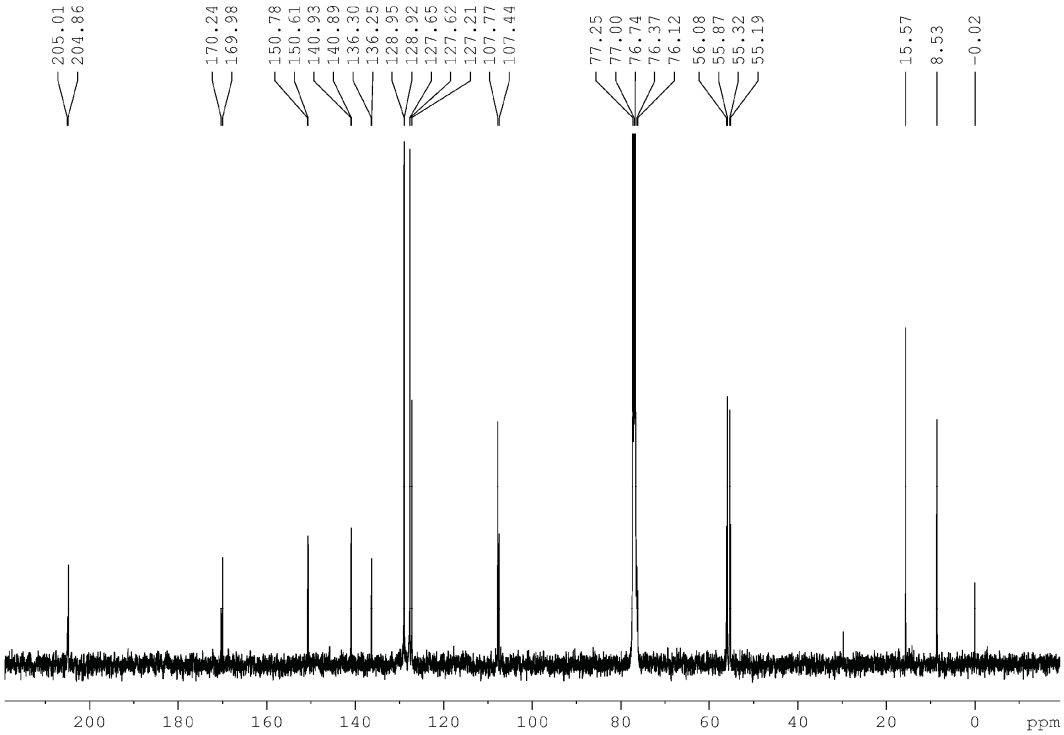
^{13}C NMR ($CDCl_3$, 125 MHz) spectrum of 3-((1,2-dimethyl-1*H*-indol-3-yl)methyl)-4-isopropyl-2-methylcyclopent-2-enone (151b)



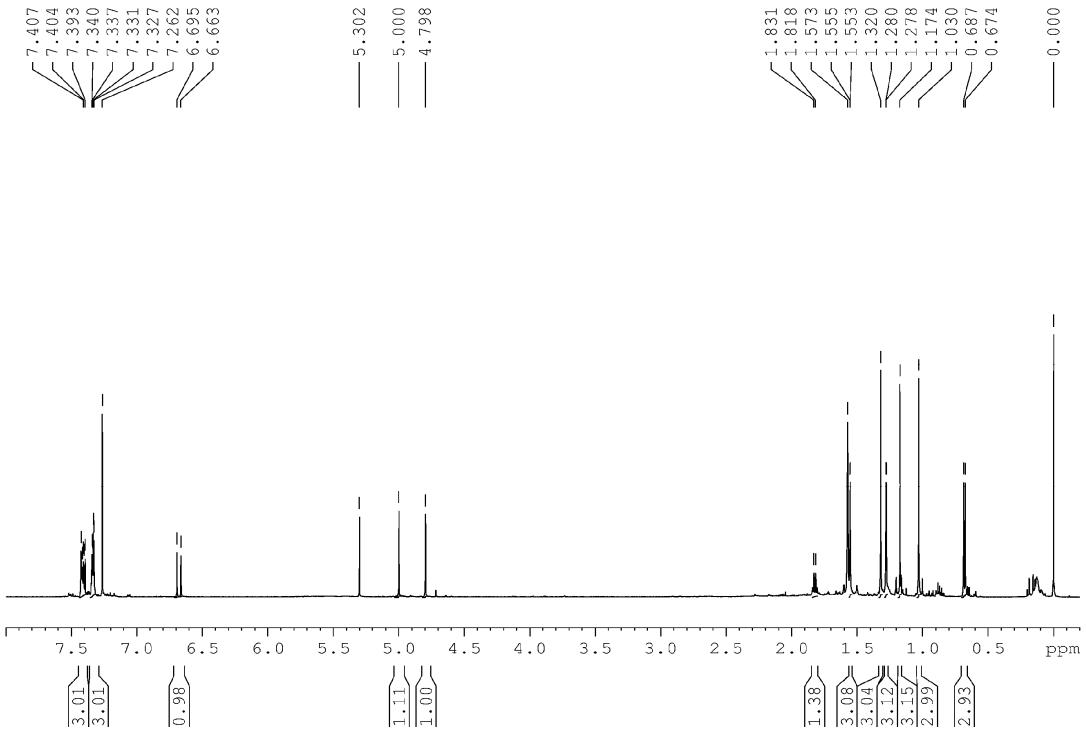
^{1}H NMR ($CDCl_3$, 500 MHz) spectrum of (*trans*,*trans*)-5,5'-(furan-2,5-diyl)bis(2,3-dimethyl-4-phenyl-cyclopent-2-enone (160)



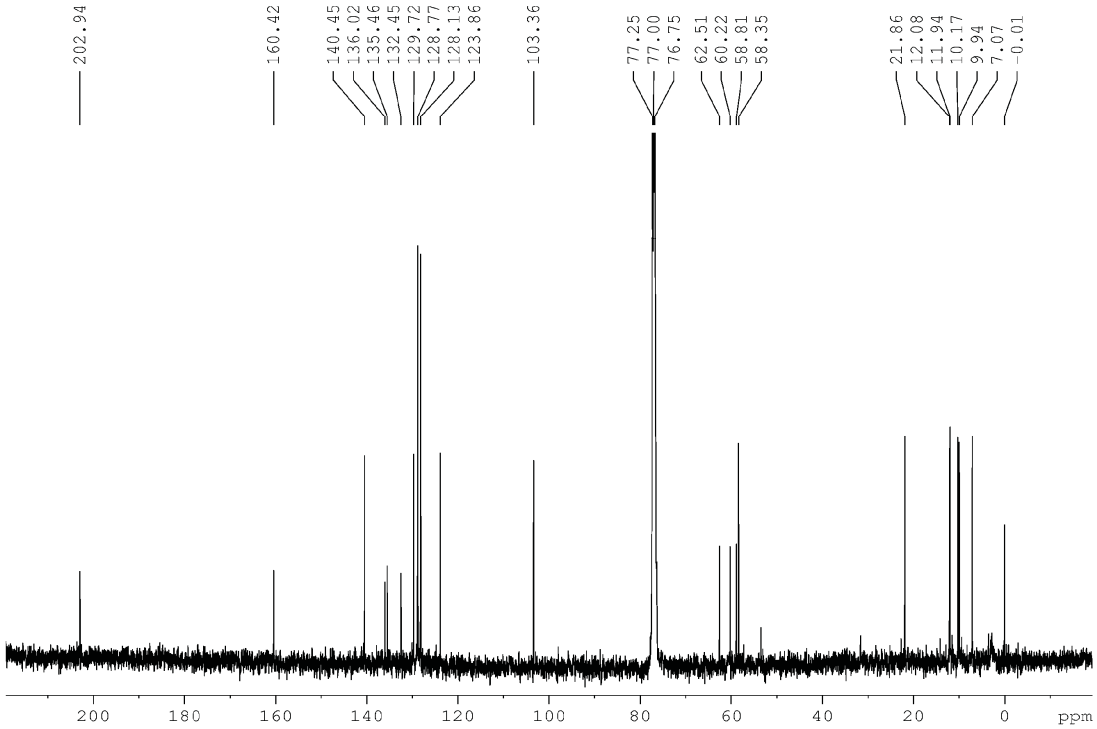
^{13}C NMR ($CDCl_3$, 125 MHz) spectrum of (*trans*,*trans*)-5,5'-(furan-2,5-diyl)bis(2,3-dimethyl-4-phenyl-cyclopent-2-enone (161)



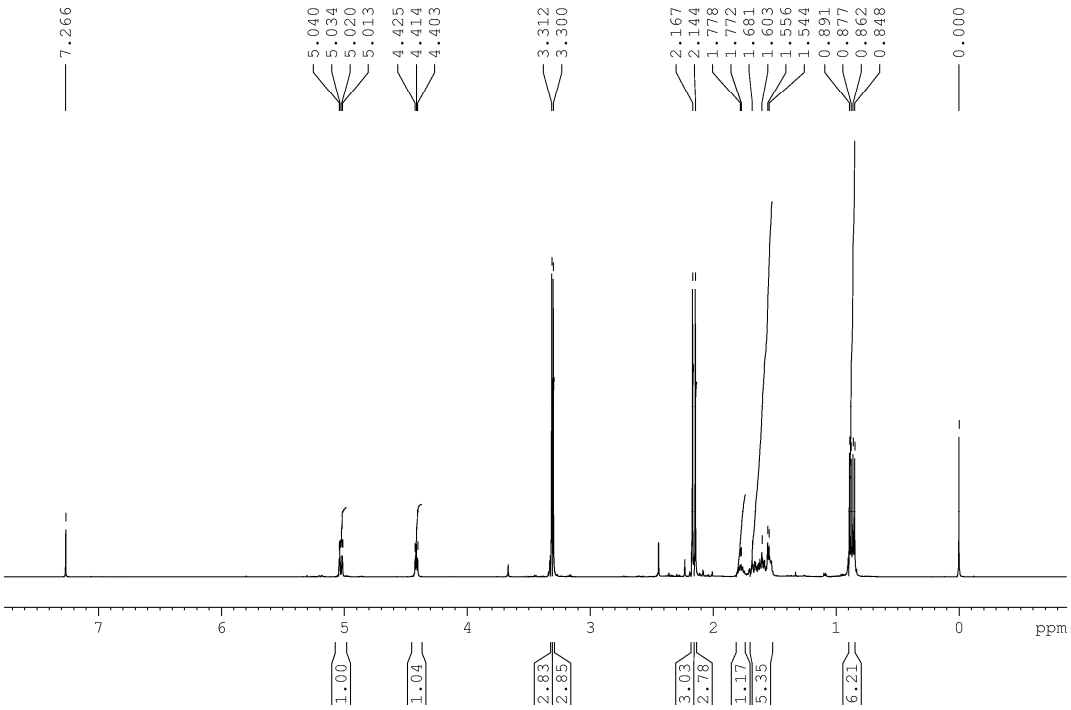
^{1}H NMR ($CDCl_3$, 500 MHz) spectrum of (1'*R,2'*R**,4'*S**,6'*R**,7'*S**)-1-(1,2,4,5,6,7-hexamethyl-3-methylenebicyclo[2.2.1]hept-5-en-2-yl)-3-phenylprop-2-en-1-one (162)**



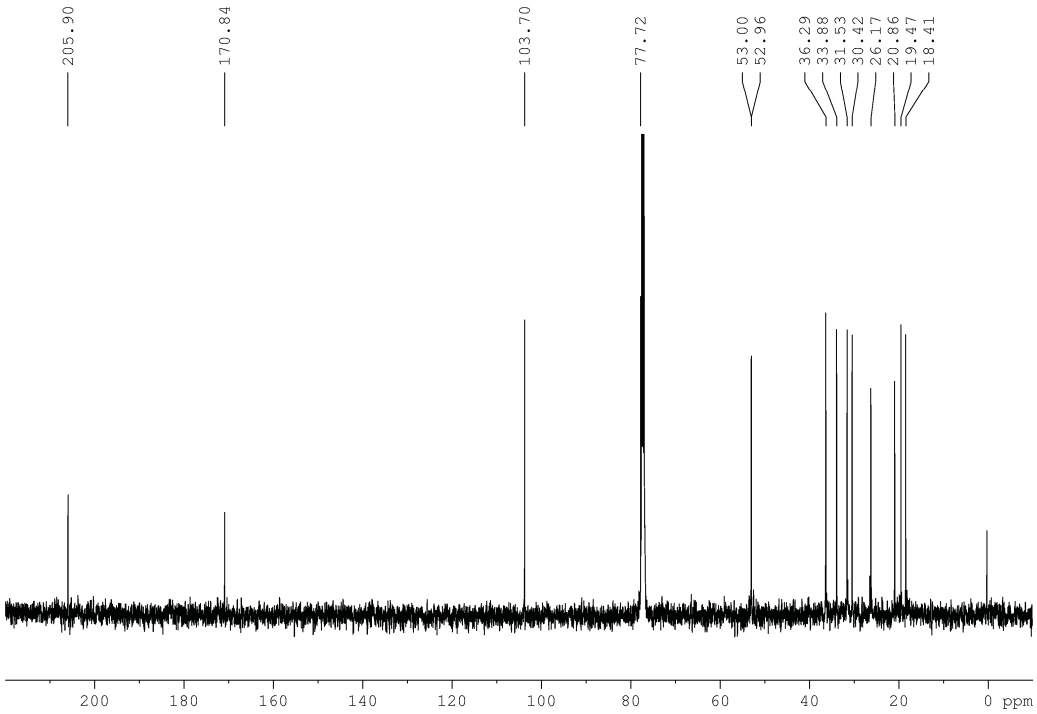
^{13}C NMR ($CDCl_3$, 125 MHz) spectrum of (1'*R,2'*R**,4'*S**,6'*R**,7'*S**)-1-(1,2,4,5,6,7-hexamethyl-3-methylenebicyclo[2.2.1]hept-5-en-2-yl)-3-phenylprop-2-en-1-one (162)**



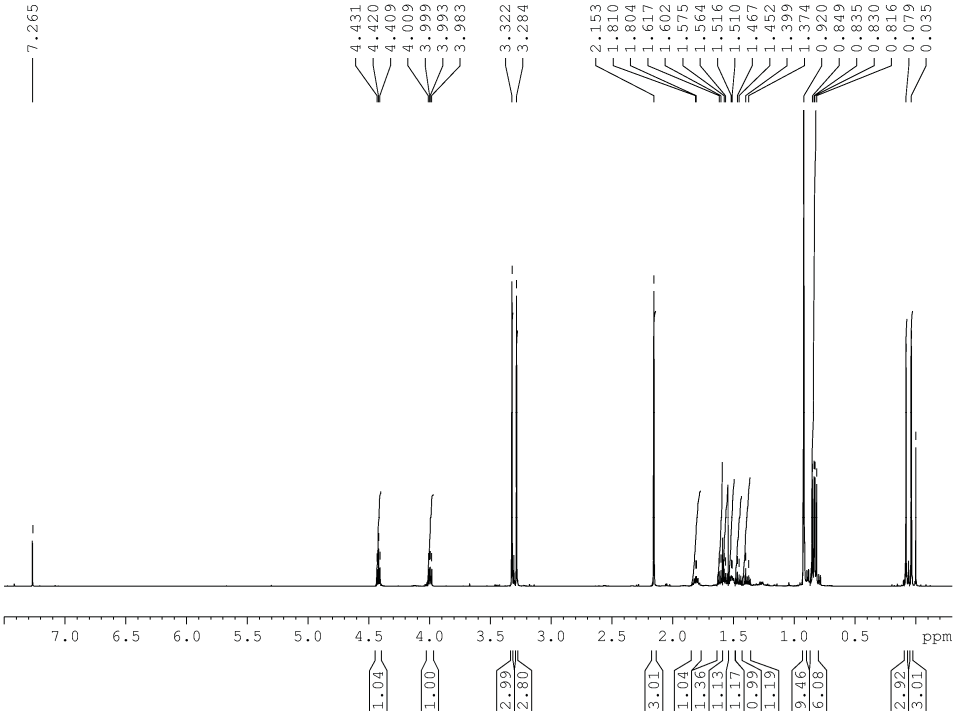
^{1}H NMR ($CDCl_3$, 500 MHz) spectrum of (3*R*,5*S*)-5-isopropyl-7,7-dimethoxy-2-oxoheptan-3-yl acetate (176a)



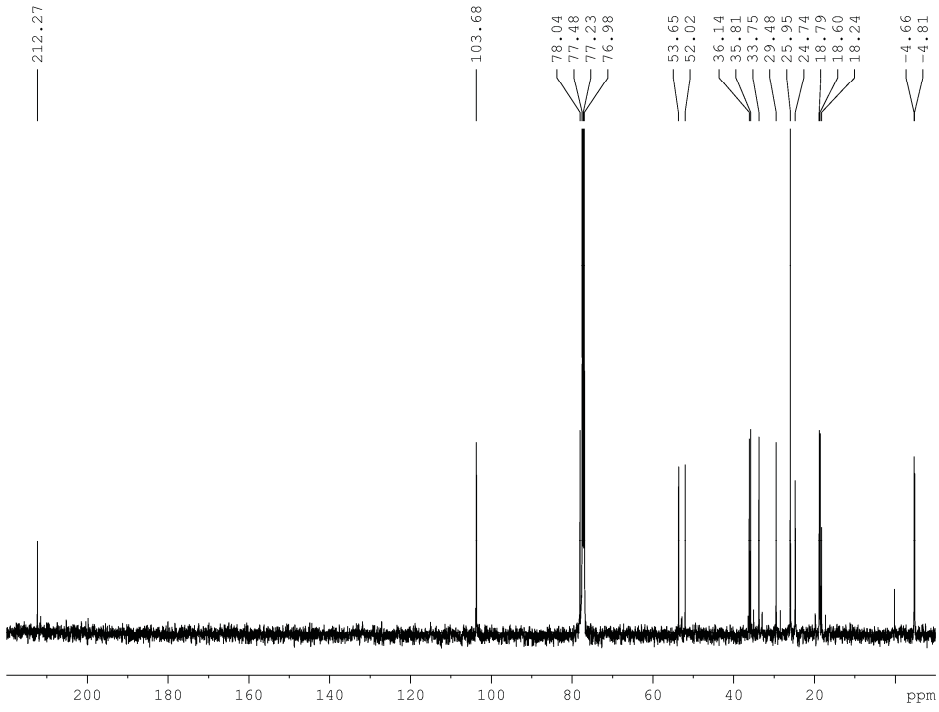
^{13}C NMR ($CDCl_3$, 125 MHz) spectrum of (3*R*,5*S*)-5-isopropyl-7,7-dimethoxy-2-oxoheptan-3-yl acetate (176a)



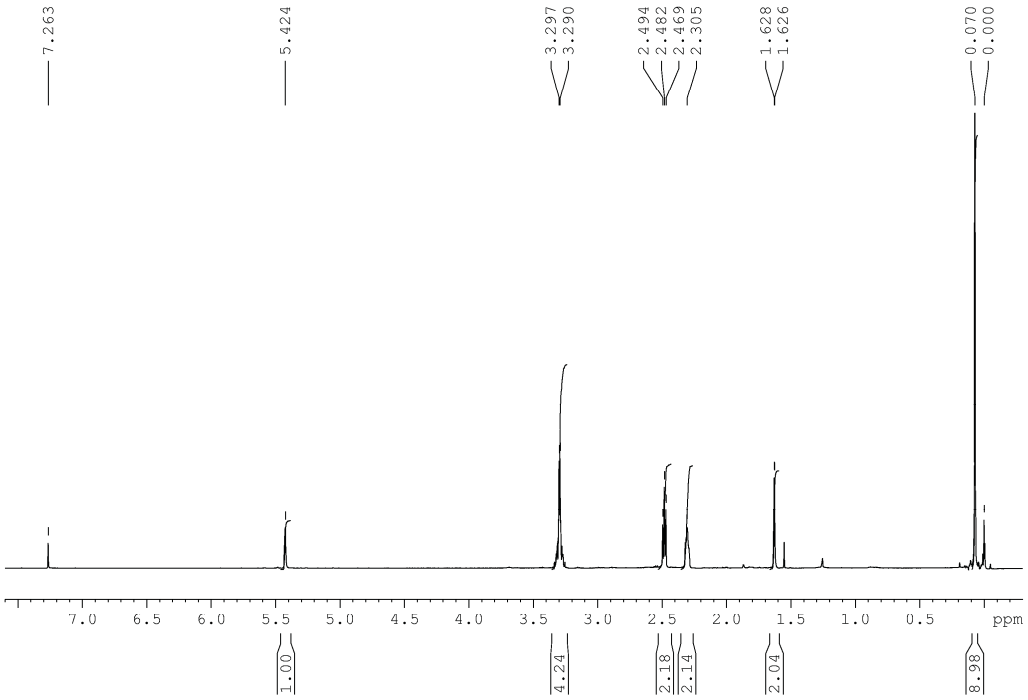
^{1}H NMR ($CDCl_3$, 500 MHz) spectrum of (3*R*,5*S*)-3-(*tert*-butyldimethylsilyloxy)-5-isopropyl-7,7-dimethoxyheptan-2-one (176b)



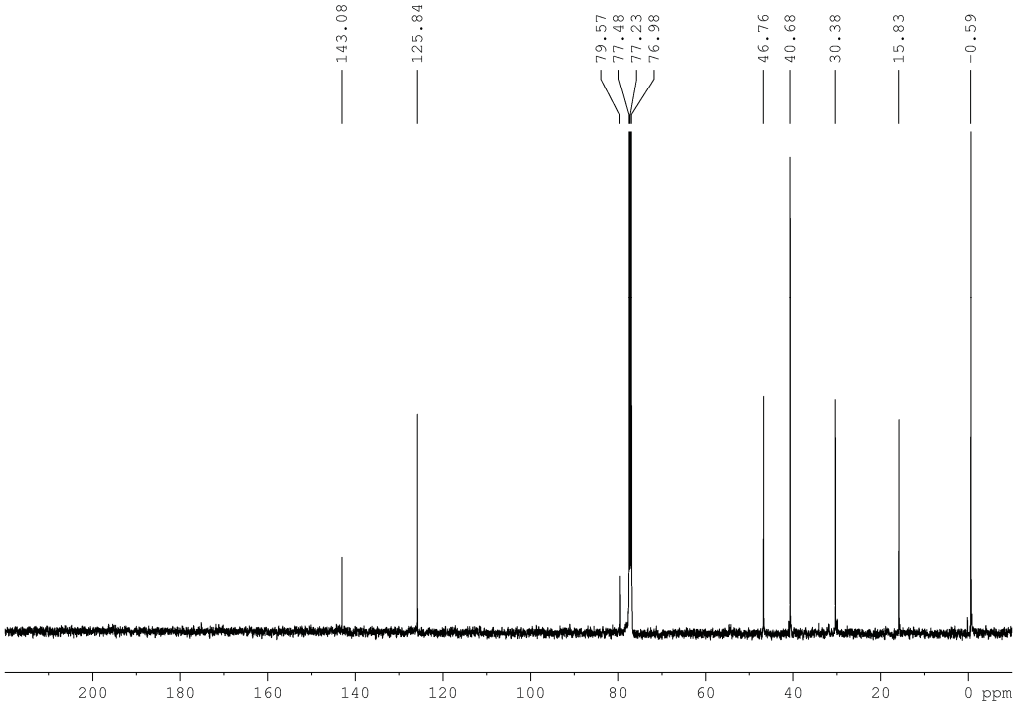
^{13}C NMR ($CDCl_3$, 125 MHz) spectrum of (3*R*,5*S*)-3-(*tert*-butyldimethylsilyloxy)-5-isopropyl-7,7-dimethoxyheptan-2-one (176b)



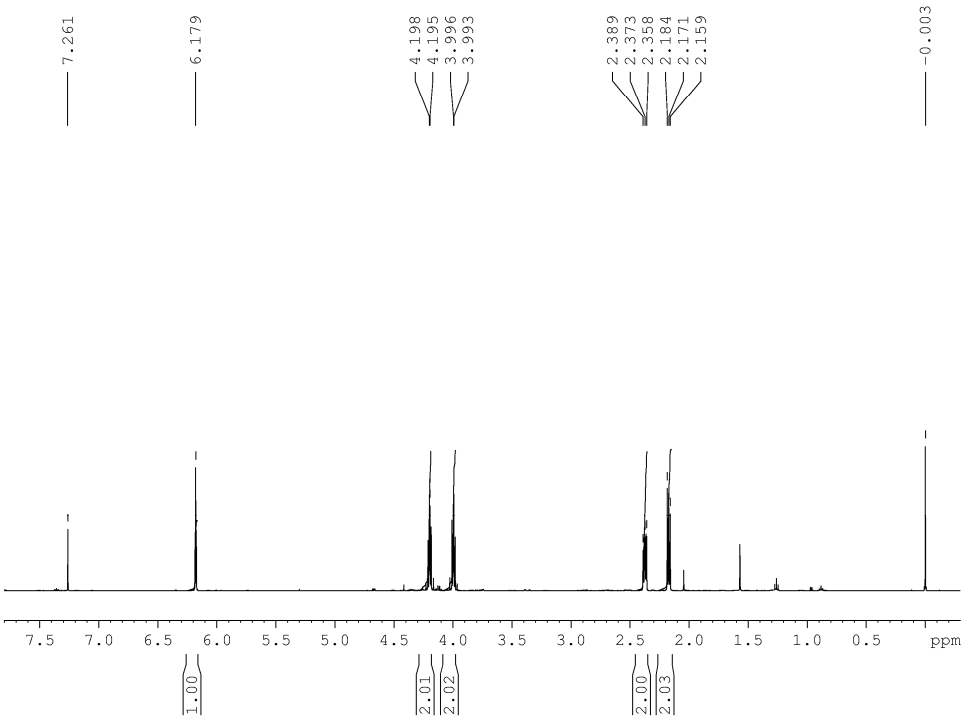
^{1}H NMR ($CDCl_3$, 500 MHz) spectrum of (1,4-dithiaspiro[4.4]non-6-en-6-ylmethyl)trimethylsilane (177a)



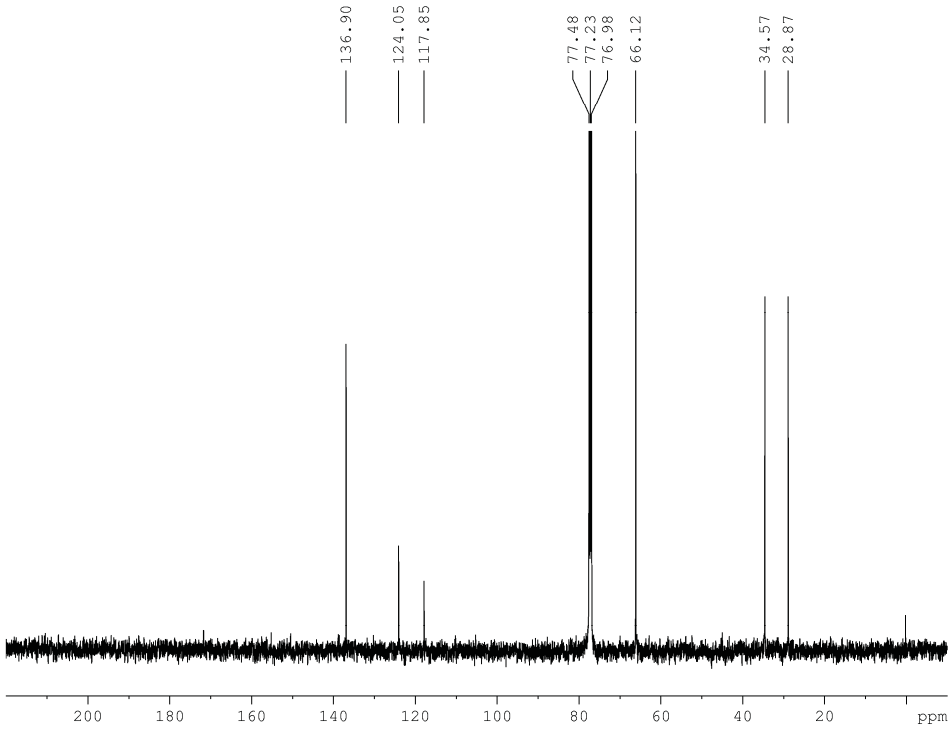
^{13}C NMR ($CDCl_3$, 125 MHz) spectrum of (1,4-dithiaspiro[4.4]non-6-en-6-ylmethyl)trimethylsilane (177a)



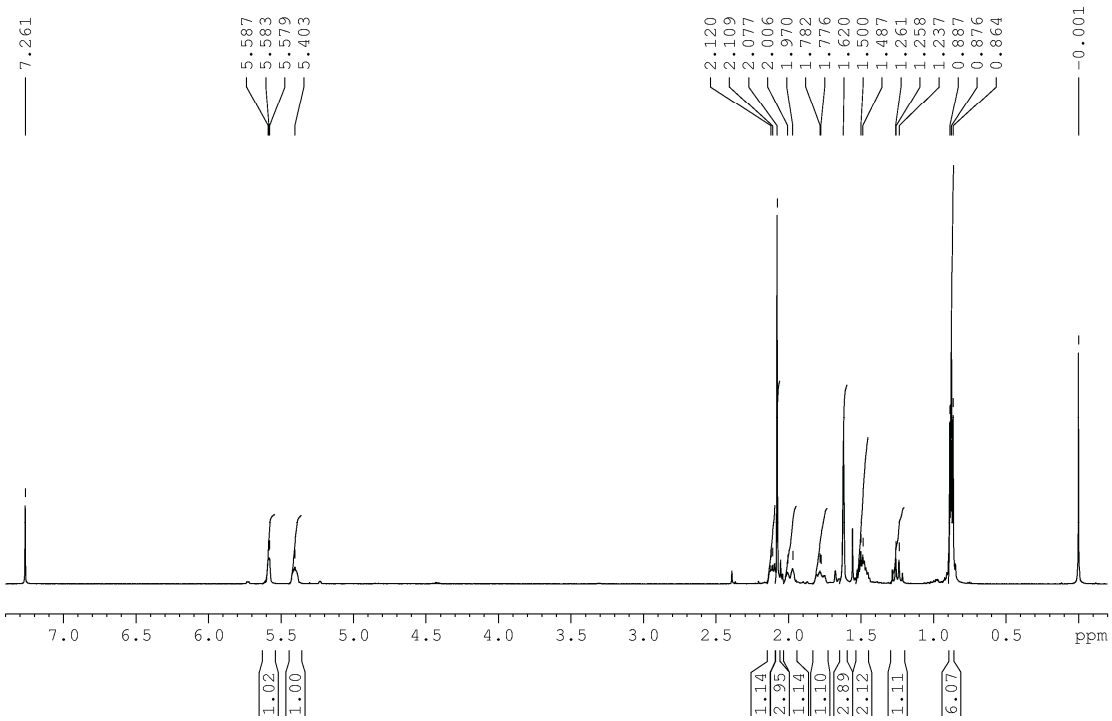
^{1}H NMR ($CDCl_3$, 500 MHz) spectrum of 6-bromo-1,4-dioxaspiro[4.4]non-6-ene (177b)



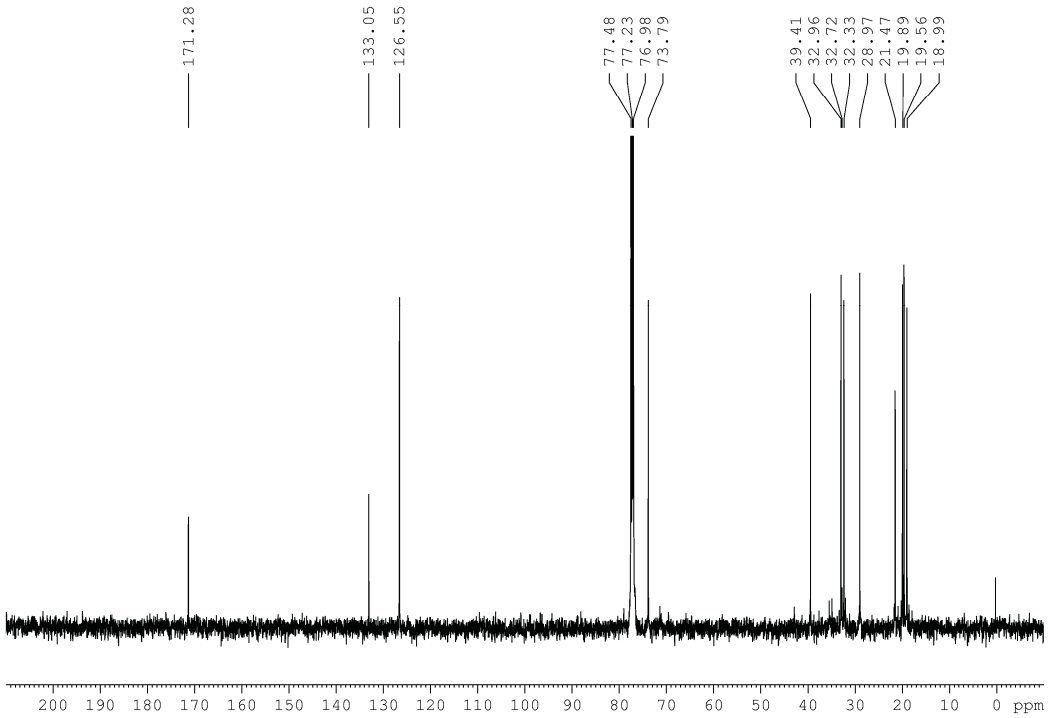
^{13}C NMR ($CDCl_3$, 125 MHz) spectrum of 6-bromo-1,4-dioxaspiro[4.4]non-6-ene (177b)



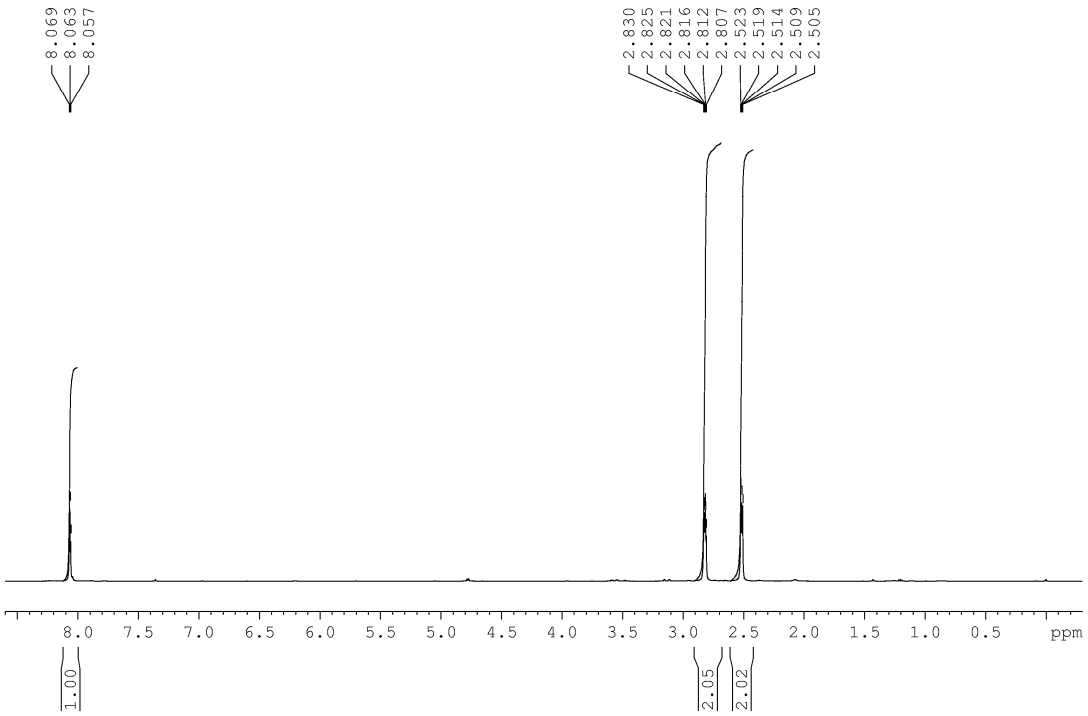
^{1}H NMR ($CDCl_3$, 500 MHz) spectrum of (1*R*,5*R*)-5-isopropyl-2-methylcyclohex-2-enyl acetate (179)



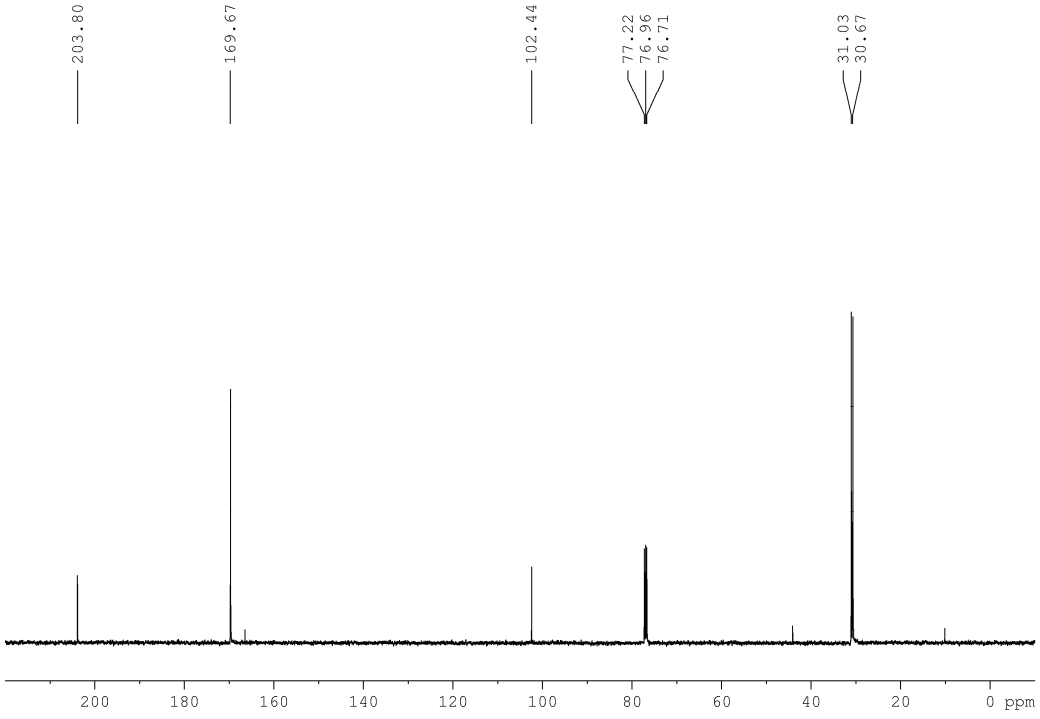
^{13}C NMR ($CDCl_3$, 125 MHz) spectrum of (1*R*,5*R*)-5-isopropyl-2-methylcyclohex-2-enyl acetate (179)



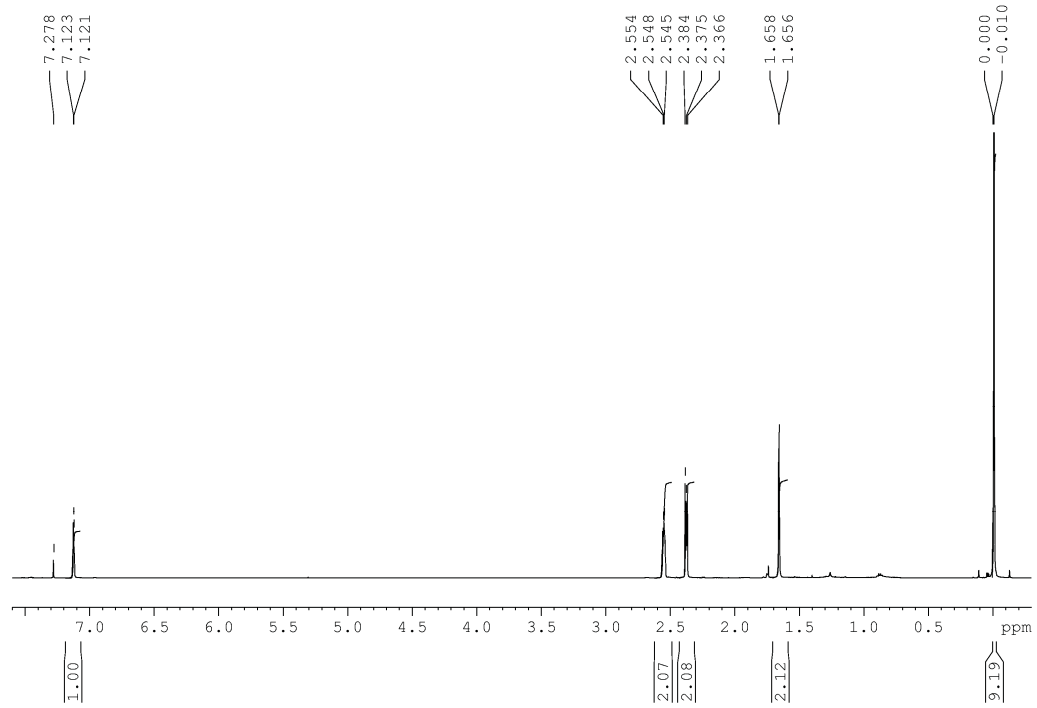
^{1}H NMR ($CDCl_3$, 500 MHz) spectrum of 2-iodocyclopent-2-enone (180)



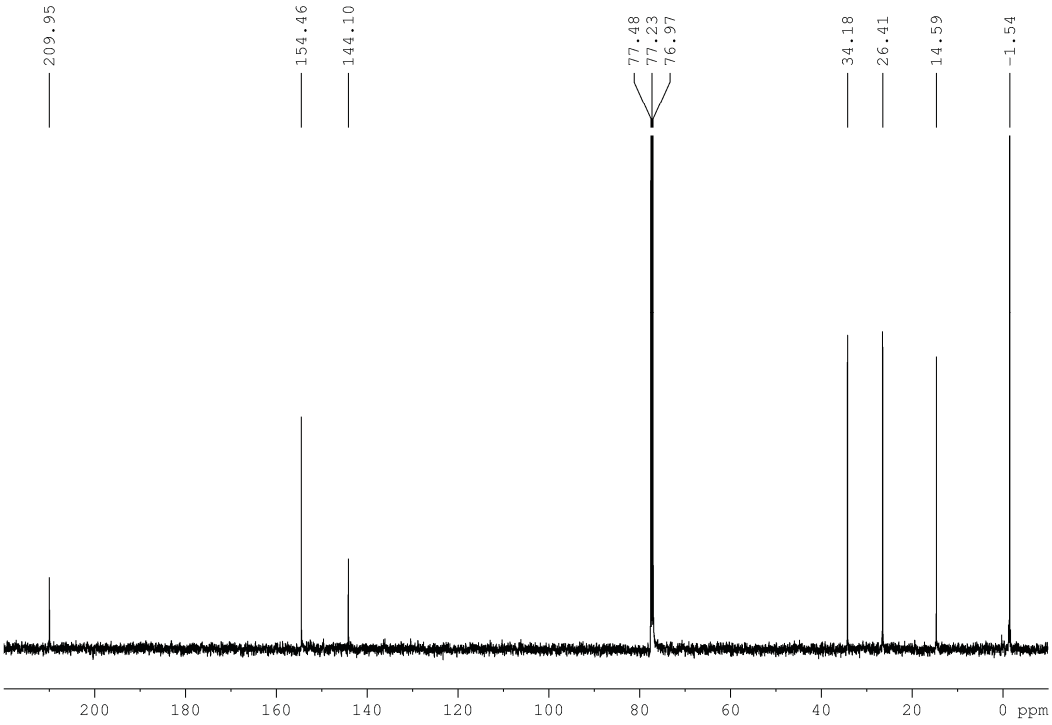
^{13}C NMR ($CDCl_3$, 125 MHz) spectrum of 2-iodocyclopent-2-enone (180)



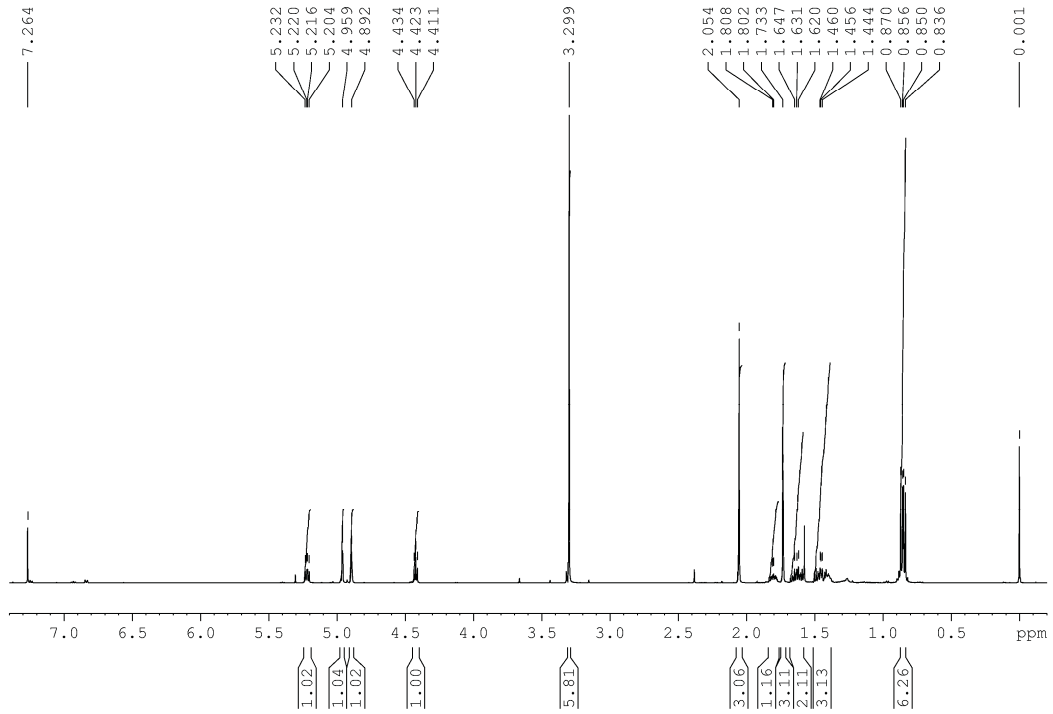
^{1}H NMR ($CDCl_3$, 500 MHz) spectrum of 2-((trimethylsilyl)methyl)cyclopent-2-enone (181)



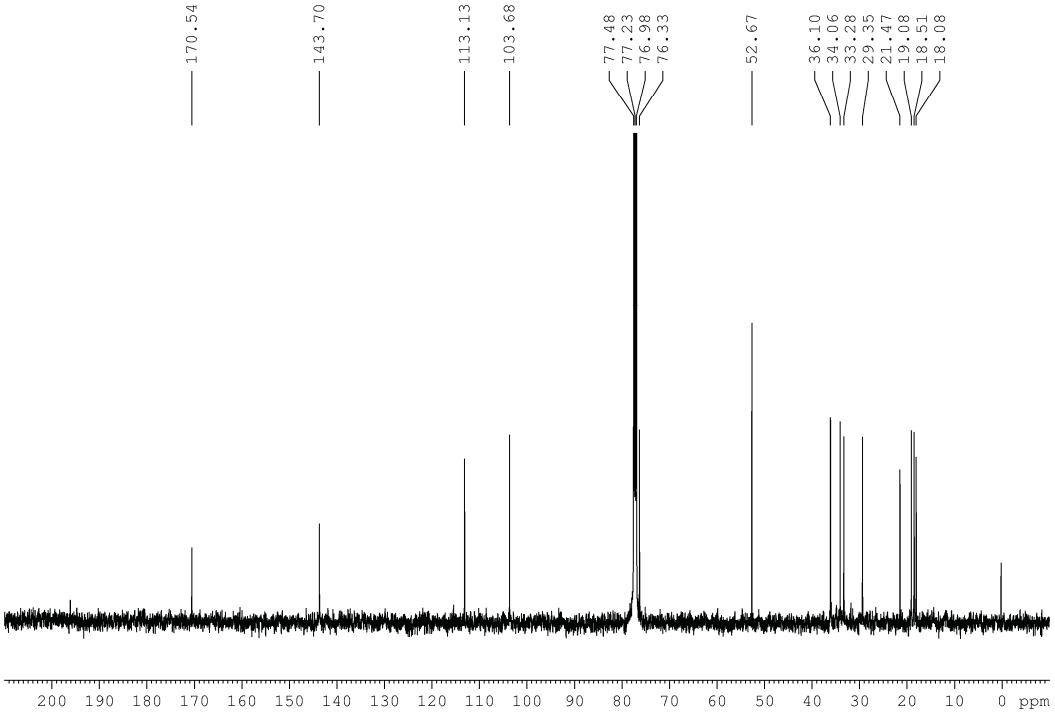
^{13}C NMR ($CDCl_3$, 125 MHz) spectrum of 2-((trimethylsilyl)methyl)cyclopent-2-enone (181)



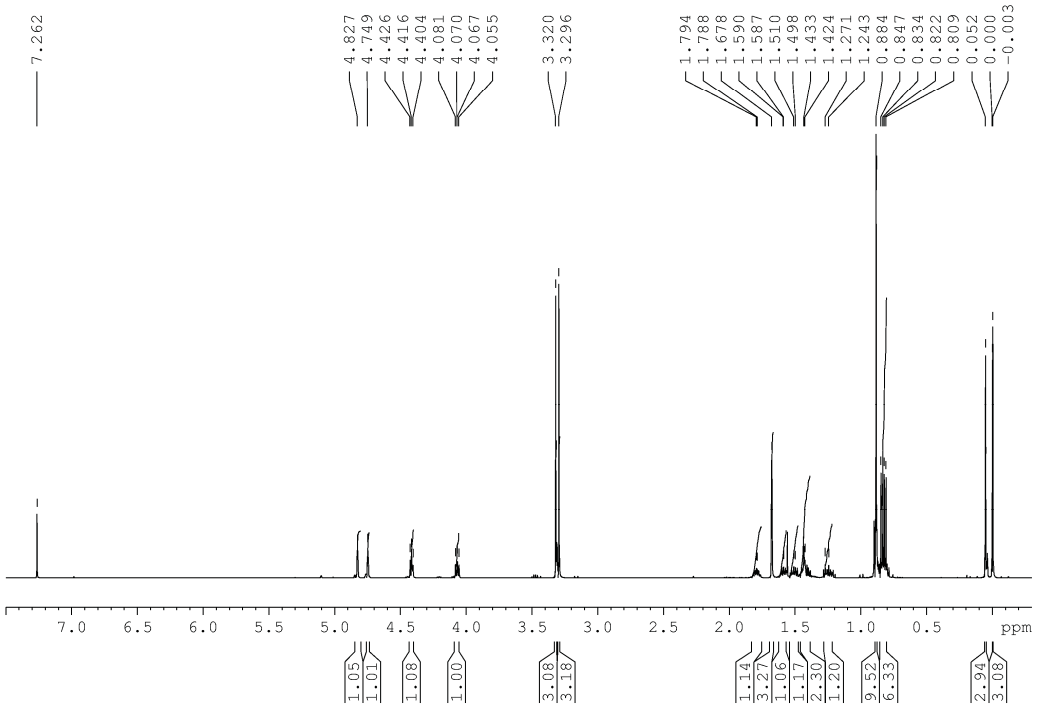
^{1}H NMR ($CDCl_3$, 500 MHz) spectrum of 3*R*,5*S*)-5-isopropyl-7,7-dimethoxy-2-methylhept-1-en-3-yl acetate (182e)



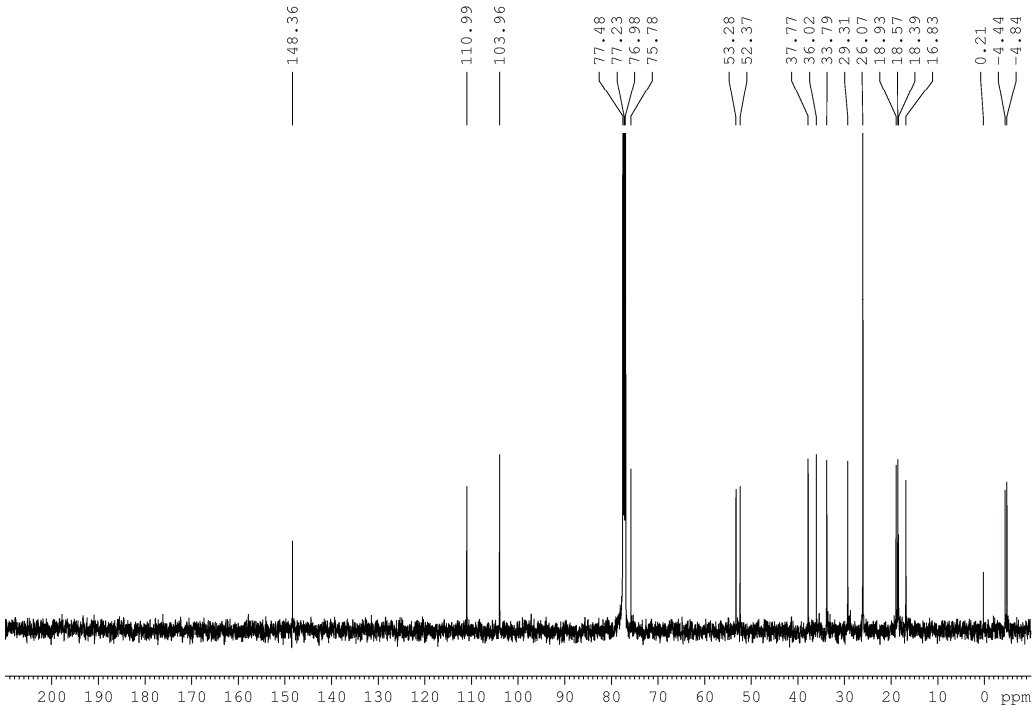
^{13}C NMR ($CDCl_3$, 125 MHz) spectrum of (3*R*,5*S*)-5-isopropyl-7,7-dimethoxy-2-methylhept-1-en-3-yl acetate (182e)



^{1}H NMR ($CDCl_3$, 500 MHz) spectrum of ((3*R*,5*S*)-5-isopropyl-7,7-dimethoxy-2-methylhept-1-en-3-yloxy)*tert*-butyl dimethylsilane (182f)



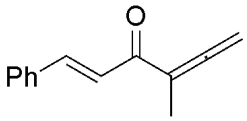
^{13}C NMR ($CDCl_3$, 125 MHz) spectrum of ((3*R*,5*S*)-5-isopropyl-7,7-dimethoxy-2-methylhept-1-en-3-yloxy)*tert*-butyl dimethylsilane (182f)



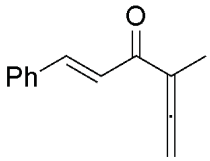
APPENDIX B. Additional Computational Data and Cartesian Coordinates

Summary of relative energies of the conformations of 26, 36, and 37[46-49]

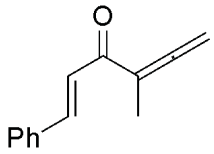
For **26**:



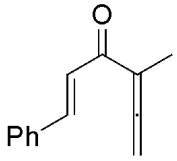
21.5 kJ mol^{-1}



0 kJ mol^{-1}

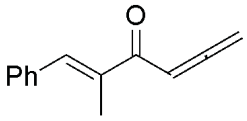


no local minimum

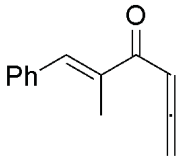


12.7 kJ mol^{-1}

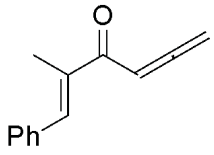
For **35**:



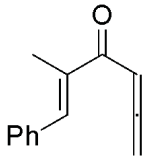
9.0 kJ mol^{-1}



6.9 kJ mol^{-1}

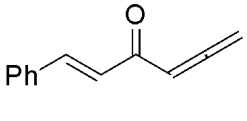


5.5 kJ mol^{-1}

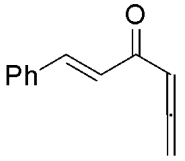


0 kJ mol^{-1}

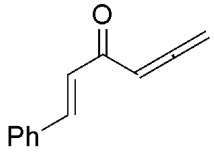
For **36**:



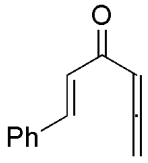
10.5 kJ mol^{-1}



0 kJ mol^{-1}



15.9 kJ mol^{-1}



12.3 kJ mol^{-1}

Cartesian coordinates for 26, *s-cis-s-cis* conformation[46-49]

Atom	x	y	z
C	1.860837	-0.457602	0.017778
C	0.494141	0.146244	0.00354
H	0.389501	1.232777	-0.025209

C	-0.595732	-0.663701	0.028176
H	-0.393601	-1.742334	0.059471
C	-2.00503	-0.25609	0.020741
C	-2.418903	1.095233	-0.037941
C	-2.997358	-1.261008	0.074497
C	-3.779561	1.424313	-0.040685
H	-1.673081	1.894103	-0.0832
C	-4.359958	-0.931233	0.071883
H	-2.686719	-2.310077	0.119206
C	-4.756785	0.414082	0.014421
H	-4.082115	2.474765	-0.086773
H	-5.11222	-1.724424	0.114451
H	-5.818898	0.676005	0.011796
O	2.026245	-1.674996	0.058406
C	3.030274	0.49808	-0.018995
C	4.252008	-0.029855	0.018948
C	5.462354	-0.554137	0.058704
H	5.964873	-0.735334	1.014117
H	5.984394	-0.832299	-0.862311
C	2.828453	1.998074	-0.096034
H	2.263082	2.276313	-1.00044
H	2.27132	2.369416	0.779684
H	3.799965	2.511344	-0.126961

Energy = -576.019759448 au

Cartesian coordinates for 26, *s-cis-s-trans* conformation[46-49]

Atom	x	Y	z
C	-1.962983	0.812838	0.020266
C	-0.65091	0.111747	0.008038
H	-0.651507	-0.981015	0.012699
C	0.498533	0.833268	-0.007637
H	0.385519	1.925417	-0.009185
C	1.86993	0.311685	-0.021018
C	2.16774	-1.070953	-0.033352
C	2.943378	1.230749	-0.021699
C	3.495863	-1.513494	-0.044795
H	1.356105	-1.804273	-0.034979
C	4.273339	0.787294	-0.033066
H	2.722722	2.303317	-0.012808
C	4.555041	-0.587946	-0.044541
H	3.708529	-2.586748	-0.054461
H	5.090105	1.51519	-0.033147
H	5.591328	-0.938344	-0.053655
O	-2.061592	2.041296	0.017345
C	-3.210773	-0.021244	0.036766
C	-3.152898	-1.350975	0.039229
C	-3.114186	-2.672946	0.039596
H	-3.10845	-3.235349	-0.899954

H	-3.086461	-3.234651	0.979143
C	-4.516963	0.737884	0.050218
H	-4.558235	1.39322	0.934009
H	-4.578881	1.388803	-0.83565
H	-5.374353	0.050858	0.061889

Energy = -576.027957914 au

Cartesian coordinates for 26, *s-trans-s-trans* conformation[46- 49]

Atom	x	y	z
C	2.14042	1.07286	0.02447
C	0.66876	1.05831	-0.16012
H	0.26324	2.00334	-0.5374
C	-0.15055	0.0465	0.22949
H	0.30037	-0.8378	0.69297
C	-1.61709	0.0368	0.13455
C	-2.34326	0.98813	-0.61821
C	-2.33412	-0.97248	0.81522
C	-3.74164	0.93768	-0.66976
H	-1.81031	1.76326	-1.17628
C	-3.73431	-1.02227	0.76436
H	-1.78095	-1.71901	1.39527
C	-4.44411	-0.06524	0.022
H	-4.28809	1.6804	-1.25868
H	-4.27135	-1.80918	1.30225

H	-5.53649	-0.10194	-0.02286
O	2.74164	2.14507	0.12065
C	2.9189	-0.21162	0.09307
C	2.48076	-1.32792	-0.48403
C	2.09657	-2.44477	-1.07863
H	1.52885	-3.20862	-0.53717
H	2.32731	-2.62541	-2.13353
C	4.29572	-0.11168	0.71146
H	4.88239	0.64937	0.17495
H	4.21858	0.21735	1.76031
H	4.81704	-1.07816	0.67182

Energy = -576.023106175 au

For **36**, the *s-trans-s-cis* conformation converged to the *s-trans-s-trans* conformation.

Cartesian coordinates for 36, *s-cis-s-cis* conformation[46-49]

Atom	x	y	z
C	2.12884	-0.222195	-0.005369
C	0.736881	0.315138	0.004245
H	0.602764	1.40112	0.027072
C	-0.318804	-0.537963	-0.01355
H	-0.069436	-1.607188	-0.031068
C	-1.744495	-0.192488	-0.007255
C	-2.216063	1.140884	-0.019972

C	-2.692249	-1.240718	0.011859
C	-3.589697	1.410764	-0.010759
H	-1.505575	1.972255	-0.039684
C	-4.067739	-0.970141	0.021331
H	-2.336654	-2.276351	0.0202
C	-4.522259	0.358011	0.01038
H	-3.937331	2.448113	-0.021347
H	-4.784961	-1.796078	0.036814
H	-5.594667	0.573785	0.017104
O	2.373087	-1.425552	-0.029373
C	3.210515	0.817426	0.016892
H	2.929852	1.876371	0.037551
C	4.495175	0.479382	0.012582
C	5.764596	0.121905	0.008739
H	6.299506	-0.05234	0.947086
H	6.303606	-0.015308	-0.93348

Energy = -536.833441146 au

Cartesian coordinates for 36, *s-cis-s-trans* conformation[46-49]

Atom	x	y	z
C	2.293707	-1.050732	0.045586
C	1.029143	-0.265596	0.021609
H	1.100731	0.825284	0.016409

C	-0.163734	-0.912201	0.007571
H	-0.119312	-2.009256	0.016062
C	-1.500011	-0.306514	-0.016231
C	-1.711365	1.091729	-0.040177
C	-2.628194	-1.157409	-0.015281
C	-3.00942	1.615646	-0.061411
H	-0.855929	1.773435	-0.043076
C	-3.928023	-0.632481	-0.036468
H	-2.474518	-2.241484	0.002649
C	-4.123826	0.757435	-0.05952
H	-3.155172	2.699891	-0.079978
H	-4.788343	-1.308319	-0.035136
H	-5.136357	1.171257	-0.076283
O	2.318699	-2.281141	0.053314
C	3.579224	-0.287017	0.061505
H	4.488753	-0.898195	0.078454
C	3.662914	1.038727	0.0557
C	3.74357	2.357741	0.05333
H	3.794496	2.914296	-0.887726
H	3.765409	2.918635	0.992969

Energy = -536.837427503 au

Cartesian coordinates for 36, *s-trans-s-cis* conformation[46-49]

Atom	x	y	z
C	2.181167	0.748744	-0.09058
C	0.698764	0.837517	-0.103815
H	0.331546	1.869262	-0.117312
C	-0.159	-0.213908	-0.029897
H	0.253249	-1.227966	0.033303
C	-1.627091	-0.141133	0.000314
C	-2.340772	1.070141	-0.150873
C	-2.359227	-1.33507	0.186505
C	-3.740164	1.080682	-0.110321
H	-1.800286	2.007696	-0.307471
C	-3.760516	-1.323943	0.228124
H	-1.817126	-2.279791	0.302417
C	-4.456998	-0.114252	0.080277
H	-4.276771	2.026477	-0.230459
H	-4.308444	-2.259327	0.375117
H	-5.550372	-0.100547	0.110706
O	2.85385	1.766501	0.066737
C	2.81467	-0.599484	-0.277783
H	2.214285	-1.44986	-0.614287
C	4.113013	-0.772922	-0.060325
C	5.403355	-0.929814	0.162929

H	6.131059	-0.766125	-0.637532
H	5.770699	-1.216306	1.152828

Energy = -536.831524358 au

Cartesian coordinates for 36, *s-trans-s-trans* conformation[46-49]

Atom	x	y	z
C	2.567684	0.864327	0.329771
C	1.104803	0.974001	0.110454
H	0.778572	1.98131	-0.169852
C	0.205796	-0.01659	0.34916
H	0.5761	-0.978813	0.718879
C	-1.253196	0.089063	0.206186
C	-1.881864	1.165679	-0.460501
C	-2.063759	-0.933185	0.748286
C	-3.277319	1.222429	-0.561796
H	-1.275261	1.955181	-0.913249
C	-3.460939	-0.875624	0.647754
H	-1.58652	-1.775801	1.260114
C	-4.073514	0.204554	-0.007084
H	-3.747889	2.061484	-1.082896
H	-4.071507	-1.674757	1.078427
H	-5.163194	0.252006	-0.090523
O	3.247276	1.874821	0.513891

C	3.241954	-0.473918	0.321033
H	4.233111	-0.489883	0.789953
C	2.804979	-1.551816	-0.320547
C	2.406934	-2.626714	-0.977837
H	1.806203	-3.39815	-0.486027
H	2.664434	-2.762644	-2.032708

Energy = -536.832720606 au

Cartesian coordinates for 37, *s-cis-s-cis* conformation[46-49]

Atom	x	y	z
C	2.046518	-0.321831	-0.092256
C	0.665306	0.266415	0.069481
C	-0.369947	-0.587493	-0.171133
H	-0.083285	-1.623338	-0.39352
C	-1.810183	-0.295808	-0.115336
C	-2.365458	0.917225	-0.583333
C	-2.68623	-1.286814	0.385051
C	-3.748821	1.142293	-0.519937
H	-1.714917	1.669602	-1.037186
C	-4.06625	-1.056193	0.460429
H	-2.270185	-2.240109	0.727539
C	-4.603044	0.162432	0.011272
H	-4.161888	2.083265	-0.895974

H	-4.725897	-1.831062	0.862507
H	-5.681158	0.341088	0.061847
O	2.235594	-1.529828	-0.204188
C	3.190797	0.651576	-0.135998
C	4.447547	0.219976	-0.150637
C	5.688722	-0.225974	-0.159378
H	6.236238	-0.378027	0.77556
H	6.189879	-0.460463	-1.103317
C	0.516162	1.698294	0.519371
H	0.688682	2.415547	-0.301812
H	-0.492322	1.878464	0.917891
H	1.243467	1.928375	1.314296
H	3.000218	1.727872	-0.173283

Energy = -576.017821916 au

Cartesian coordinates for 37, *s-cis-s-trans* conformation[46-49]

Atom	x	y	z
C	2.15351	1.069551	0.146505
C	0.897139	0.247622	0.286792
C	-0.238621	0.853837	-0.164824
H	-0.113333	1.878814	-0.535886
C	-1.610862	0.328022	-0.160216
C	-1.919046	-1.039883	-0.343883

C	-2.680114	1.240839	-0.001004
C	-3.251149	-1.479828	-0.336733
H	-1.116405	-1.75592	-0.534553
C	-4.009179	0.798655	0.019849
H	-2.455263	2.305898	0.118758
C	-4.300213	-0.566371	-0.144471
H	-3.470722	-2.540801	-0.490314
H	-4.820378	1.520101	0.156437
H	-5.3377	-0.913303	-0.136204
O	2.129201	2.29618	0.061756
C	3.484391	0.383785	0.080858
C	3.681871	-0.87062	-0.306922
C	3.900796	-2.111099	-0.706118
H	3.992904	-2.925525	0.019342
H	3.989825	-2.348205	-1.770794
C	0.93926	-1.094489	0.97623
H	-0.017885	-1.285227	1.485741
H	1.126463	-1.924408	0.27638
H	1.745258	-1.114919	1.725502
H	4.347013	1.042208	0.238638

Energy = -576.018650048 au

Cartesian coordinates for 37, *s-trans-s-cis* conformation[46-49]

Atom	x	y	z
C	2.16768	0.5662	0.17196
C	0.68122	0.73643	0.25526
C	-0.14772	-0.316	-0.00496
H	0.30942	-1.2961	-0.18403
C	-1.62017	-0.30379	-0.05967
C	-2.356	0.76118	-0.62679
C	-2.32768	-1.42609	0.42919
C	-3.75757	0.71686	-0.66947
H	-1.82684	1.60888	-1.06878
C	-3.72797	-1.46415	0.39765
H	-1.76777	-2.2682	0.85002
C	-4.44901	-0.38924	-0.14943
H	-4.31119	1.54646	-1.11945
H	-4.25784	-2.33587	0.79311
H	-5.54204	-0.41973	-0.18184
O	2.89127	1.5559	0.07168
C	2.74566	-0.82006	0.22239
C	4.00168	-1.03987	-0.14833
C	5.24907	-1.2443	-0.52548
H	5.487	-1.5102	-1.5597
H	6.07062	-1.14186	0.18986
C	0.23321	2.13993	0.5693

H	0.30075	2.78431	-0.32292
H	-0.80054	2.15834	0.9412
H	0.90465	2.58046	1.32101
H	2.14919	-1.6562	0.5983

Energy = -576.019173599 au

Cartesian coordinates for 37, *s-trans-s-trans* conformation[46-49]

Atom	x	y	z
C	2.53222	0.72033	0.35385
C	1.07579	0.89101	0.04596
C	0.19903	-0.09688	0.39266
H	0.60094	-0.96806	0.9217
C	-1.26069	-0.08811	0.20735
C	-1.87707	0.44878	-0.94593
C	-2.08059	-0.6834	1.1935
C	-3.2721	0.41873	-1.08959
H	-1.25708	0.8577	-1.74783
C	-3.47477	-0.70292	1.05479
H	-1.61304	-1.12093	2.08211
C	-4.07651	-0.14797	-0.08746
H	-3.7321	0.83174	-1.99244
H	-4.0931	-1.1569	1.83498
H	-5.16437	-0.1679	-0.201
O	3.25926	1.68973	0.57366

C	3.13837	-0.64994	0.36927
C	2.67402	-1.69526	-0.30677
C	2.2426	-2.73775	-0.99396
H	1.57524	-3.47529	-0.53752
H	2.53683	-2.87817	-2.03857
C	0.69774	2.24138	-0.50295
H	0.85973	2.28981	-1.59368
H	-0.35396	2.48431	-0.29653
H	1.35197	2.99724	-0.04396
H	4.10672	-0.7194	0.87912

Energy = -576.021265102 au

Cartesian coordinates for oxyallyl cation 153[46-49]

Atom	x	y	z
C	0.85414	-0.72177	-1.01984
C	-0.76992	-1.91744	0.27268
C	-1.39398	-0.70012	-0.15879
C	-0.46584	-0.0451	-1.0155
H	1.14547	-1.01503	-2.04827
H	-0.69285	0.87022	-1.56658
C	0.58462	-1.96742	-0.19005
C	1.498	-2.94448	0.0742
H	1.23474	-3.82961	0.65982
H	2.52826	-2.85122	-0.28103

C	1.95523	0.15116	-0.43078
C	3.28393	0.00053	-0.86863
C	1.65283	1.08529	0.58084
C	4.31031	0.76104	-0.28651
H	3.51382	-0.70313	-1.67659
C	2.68171	1.84888	1.15344
H	0.61506	1.24175	0.89582
C	4.01066	1.68338	0.72936
H	5.341	0.63954	-0.63277
H	2.44018	2.58121	1.92923
H	4.80848	2.28193	1.17833
O	-2.5802	-0.36073	0.20187
B	-2.9321	1.15561	-0.06049
F	-2.95765	1.32832	-1.44895
F	-4.13635	1.37102	0.55915
F	-1.86094	1.87793	0.5058
C	-1.50846	-2.89286	1.10963
H	-1.81887	-2.38755	2.04122
H	-2.44671	-3.16664	0.59761
H	-0.9313	-3.79562	1.34639

Cartesian coordinates for oxyallyl cation 154[46-49]

Atom	x	y	z
C	0.7833	-1.00165	-0.79709

C	-0.7095	-2.09846	0.69593
C	-1.44988	-1.01033	0.12682
C	-0.58082	-0.42932	-0.85182
H	1.06837	-1.42796	-1.78035
H	-1.1319	-2.79658	1.42642
H	-0.8897	0.36665	-1.53311
C	0.62708	-2.12189	0.21642
C	1.61134	-2.9859	0.60829
H	1.4031	-3.78629	1.32454
H	2.63152	-2.88064	0.22811
C	1.83328	0.02683	-0.39101
C	3.15908	-0.10709	-0.843
C	1.48764	1.08991	0.46771
C	4.14234	0.80246	-0.42292
H	3.41967	-0.91526	-1.53554
C	2.47364	2.00088	0.87705
H	0.44882	1.22677	0.78814
C	3.80125	1.85537	0.44179
H	5.17125	0.69356	-0.77835
H	2.1988	2.83147	1.53354
H	4.56517	2.56886	0.76363
O	-2.64207	-0.6818	0.45594
B	-3.08885	0.75114	-0.04491
F	-3.15761	0.68332	-1.44054

F	-4.28487	1.00469	0.57158
F	-2.04382	1.61125	0.35462

Cartesian coordinates for oxyallyl cation 155[46-49]

Atom	x	y	z
C	0.97269	0.58561	0.9986
C	-1.10524	1.2415	0.01645
C	-1.28402	-0.10437	0.47893
C	-0.05276	-0.49152	1.09167
H	1.26898	0.92253	2.01259
C	0.21666	1.69296	0.29021
C	0.73467	2.91557	-0.02933
H	0.12316	3.66664	-0.53769
H	1.77589	3.15943	0.20185
C	2.21452	0.11346	0.25891
C	3.47813	0.14312	0.87339
C	2.0899	-0.37759	-1.05645
C	4.61338	-0.30586	0.17692
H	3.57446	0.52048	1.89721
C	3.22295	-0.82468	-1.74921
H	1.1057	-0.40173	-1.53804
C	4.48708	-0.79083	-1.13374
H	5.59423	-0.27714	0.66049
H	3.11988	-1.20296	-2.77044

H	5.36985	-1.14181	-1.67569
O	-2.30271	-0.88054	0.40879
B	-3.53276	-0.30411	-0.40478
F	-3.02291	0.01386	-1.67139
F	-4.47157	-1.30413	-0.40867
F	-3.92891	0.8567	0.27152
C	0.14241	-1.81797	1.71592
H	-0.43763	-1.8585	2.65771
H	-0.29143	-2.59743	1.06684
H	1.20006	-2.02788	1.92696
H	-1.88944	1.82875	-0.46495

Cartesian coordinates for (1*R,2*S**,6*S**,7*R**)-1,2-dimethyl-8-methylene-7-phenylbicyclo[4.2.1]non-3-en-9-one (86a)**[61]

Basis set for geometry optimization: RH/6-31G; Number of imaginary frequencies: 0

Center Number	Atomic Number	Forces (Hartrees/Bohr) X	Y	Z
1	6	0.000006399	0.000002037	0.000006084
2	6	0.000001136	0.000004417	-0.000004467
3	6	-0.000001984	-0.000001870	0.000004386
4	6	-0.000003081	0.000004661	-0.000008133
5	1	0.000000220	-0.000001813	0.000000910
6	6	0.000003416	-0.000004856	0.000002920
7	6	0.000003239	-0.000000585	-0.000002520
8	1	-0.000000609	-0.000001366	0.000001040
9	6	-0.000004938	0.000003008	0.000001528
10	1	0.000000937	-0.000000238	0.000000252
11	1	0.000000675	0.000000974	0.000000358
12	1	-0.000002000	0.000000766	0.000000249
13	8	-0.000003756	0.000001355	-0.000004622
14	6	0.000003976	0.000007009	0.000005090
15	1	0.000000379	-0.000002428	-0.000002034
16	1	-0.000000072	-0.000003326	-0.000002769
17	6	-0.000003950	-0.000000886	0.000006079
18	6	0.000003394	-0.000002653	-0.000004756
19	6	0.000000543	-0.000002476	0.000000408

20	6	-0.000001450	0.000003779	-0.000003909
21	6	-0.000002763	-0.000004998	-0.000002703
22	6	-0.000001609	-0.000004123	0.000000944
23	1	-0.000000524	-0.000000153	0.000000983
24	6	0.000000182	0.000003571	-0.000004099
25	1	0.000000226	-0.000000160	0.000001310
26	6	0.000002808	0.000000911	0.000005865
27	1	0.000000260	0.000000466	0.000000194
28	1	0.000000242	0.000000103	0.000000358
29	1	-0.000000495	0.000000147	-0.000000301
30	6	0.000001244	0.000000873	-0.000001546
31	1	-0.000000487	0.000001411	0.000001975
32	1	-0.000000683	-0.000001411	0.000000952
33	1	-0.000001226	-0.000000669	-0.000000823
34	6	0.000004998	-0.000002282	0.000000224
35	1	-0.000001442	0.000001380	0.000000223
36	1	-0.000001963	-0.000001900	-0.000000343
37	1	-0.000001179	0.000001189	0.000001364
38	1	0.000000286	0.000000077	-0.000000181
39	1	-0.000000348	0.000000058	-0.000000489

Energy HF/6-31G//HF/6-311G(d,p): –768.2692219 Hartrees

Cartesian coordinates for (1*R,2*R**,6*S**,7*R**)-1,2-dimethyl-8-methylene-7-phenylbicyclo[4.2.1]non-3-en-9-one (86b)**[61]

Basis set for geometry optimization: RH/6-31G; Number of imaginary frequencies: 0

Center Number	Atomic Number	Forces (Hartrees/Bohr) X	Y	Z
1	6	-0.000009137	-0.000001500	0.000000619
2	6	0.000002834	-0.000010801	0.000001809
3	6	-0.000012272	0.000014197	-0.000009063
4	6	0.000010418	0.000005243	0.000006328
5	1	-0.000000138	-0.000005589	-0.000001419
6	6	0.000007367	-0.000001754	-0.000002007
7	6	0.000000745	0.000003143	0.000005854
8	6	0.000003363	-0.000009945	0.000003867
9	1	-0.000000074	0.000000650	-0.000001643
10	1	-0.000001206	0.000001021	-0.000000801
11	1	0.000001868	-0.000000750	0.000001732
12	8	-0.000001864	0.000000168	-0.000004007
13	6	0.000000473	0.000003421	0.000007291
14	1	0.000000813	-0.000001435	-0.000002444
15	1	0.000001129	-0.000000908	-0.000001845
16	6	-0.000006870	0.000000014	-0.000010176
17	6	0.000000633	0.000001299	0.000004871
18	6	0.000006681	-0.000000081	0.000006863
19	6	-0.000003128	0.000002612	-0.000000239
20	6	-0.000005824	-0.000004415	-0.000000932

21	6	-0.000002490	-0.000000635	0.000000757
22	1	0.000000208	-0.000000635	-0.000000507
23	6	-0.000002912	0.000001065	-0.000002760
24	1	0.000001698	0.000000661	-0.000003134
25	6	0.000004433	0.000000057	0.000001793
26	1	0.000000538	-0.000000790	-0.000000129
27	1	0.000001319	-0.000000290	0.000000382
28	1	-0.000000870	-0.000000061	0.000000218
29	6	0.000002967	0.000000638	-0.000003904
30	1	-0.000000602	0.000000490	0.000001296
31	1	-0.000002406	-0.000000866	-0.000000273
32	1	-0.000001410	0.000001581	0.000002928
33	1	0.000000315	0.000001806	-0.000000531
34	1	0.000003048	-0.000000122	0.000000867
35	1	-0.000000585	-0.000000115	-0.000000787
36	6	0.000001786	-0.000002138	-0.000000005
37	1	-0.000001506	0.000001897	-0.000001222
38	1	0.000001054	0.000002892	-0.000000643
39	1	-0.000000396	-0.000000021	0.000000996

Energy HF/6-31G//HF/6-311G(d,p): –768.270356 Hartrees

Cartesian coordinates for (1*R,3*R**,4*S**,6*S**)-1-methyl-2-methylene-6-(2-methylprop-1-enyl)-3-phenylbicyclo[2.2.1]heptan-7-one (91a)**[61]

Basis set for geometry optimization: RH/6-31G; Number of imaginary frequencies: 0

Center Number	Atomic Number	Forces (Hartrees/Bohr) X	Y	Z
1	6	0.000004042	-0.000005565	-0.000000412
2	6	-0.000002464	-0.000000651	0.000009417
3	6	0.000003339	-0.000003854	0.000001136
4	6	-0.000005675	0.000012027	-0.000007331
5	1	-0.000001068	-0.000003149	0.000001392
6	6	-0.000001901	0.000002654	-0.000002675
7	6	0.000007430	-0.000004393	0.000000274
8	6	0.000000851	0.000002431	0.000001268
9	1	-0.000000473	-0.000000159	0.000000948
10	1	-0.000000925	-0.000002243	0.000001023
11	1	-0.000001199	0.000001549	0.000002975
12	8	0.000001326	0.000000414	-0.000000968
13	6	-0.000004731	0.000005610	-0.000001577
14	1	-0.000000305	-0.000002839	-0.000002385
15	1	-0.000001948	-0.000001404	-0.000000818
16	6	0.000006595	-0.000002713	0.000007602
17	6	-0.000002193	0.000000324	-0.000001264
18	6	-0.000002269	0.000002100	-0.000003315
19	6	-0.000000902	-0.000000189	-0.000000670
20	1	-0.000000080	-0.000000661	-0.000000366
21	6	-0.000001075	-0.000001732	-0.000000903
22	1	-0.000000204	-0.000001843	0.000000992

23	6	0.000002797	0.000001071	0.000001848
24	1	0.000000228	-0.000000024	0.000000191
25	1	0.000000294	0.000000350	0.000000218
26	1	-0.000000719	-0.000000245	-0.000000607
27	6	0.000006779	-0.000000219	-0.000004093
28	1	0.000000758	0.000001408	0.000000248
29	1	0.000000082	-0.000000816	0.000000059
30	1	-0.000000387	-0.000000295	0.000001131
31	1	-0.000001504	0.000003782	-0.000001346
32	6	-0.000004731	0.000004286	-0.000005205
33	1	0.000000453	0.000002159	-0.000000201
34	6	0.000002859	-0.000004243	0.000007291
35	6	-0.000002667	0.000000816	0.000000931
36	1	0.000000666	-0.000002142	0.000000092
37	1	-0.000000590	-0.000001393	-0.000001791
38	1	-0.000000264	-0.000001462	-0.000000683
39	6	-0.000004037	0.000004998	-0.000005302
40	1	0.000000412	-0.000000469	0.000000754
41	1	0.000001368	-0.000001017	0.000001066
42	1	0.000002033	-0.000002257	0.000001058

Energy HF/6-31G//HF/6-311G(d,p): –807.3094439 Hartrees

Cartesian coordinates for (1*R,3*R**,4*S**,6*R**)-1-methyl-2-methylene-6-(2-methylprop-1-enyl)-3-phenylbicyclo[2.2.1]heptan-7-one (91b)**[61]

Basis set for geometry optimization: RH/6-31G; Number of imaginary frequencies: 0

Center Number	Atomic Number	Forces (Hartrees/Bohr) X	Y	Z
1	6	0.000007995	-0.000004314	-0.000004782
2	6	-0.000000637	0.000017314	-0.000002648
3	6	-0.000002088	0.000006533	-0.000016218
4	6	0.000000562	-0.000005621	0.000021882
5	1	-0.000000402	0.000001428	0.000000906
6	6	0.000007859	-0.000020162	0.000006459
7	6	0.000012461	-0.000009892	0.000014868
8	6	-0.000001879	0.000005383	0.000000674
9	1	0.000004718	0.000001594	0.000003293
10	1	0.000000308	0.000001892	0.000004771
11	1	-0.000001097	-0.000001388	-0.000000206
12	8	-0.000000463	0.000009455	0.000009798
13	6	-0.000011649	-0.000012912	-0.000013483
14	1	0.000000594	0.000005176	0.000004117
15	1	0.000001138	0.000004469	0.000002594
16	6	-0.000017564	0.000004744	-0.000008564
17	6	0.000015347	0.000015828	-0.000012813
18	6	0.000008790	-0.000027871	0.000004511
19	6	0.000005090	-0.000021745	-0.000000554
20	1	-0.000003503	-0.000000708	0.000002199

21	6	0.000011249	0.000021405	-0.000010141
22	1	-0.000003630	0.000002991	-0.000001108
23	6	-0.000017919	0.000006757	0.000013390
24	1	-0.000001000	0.000002689	0.000000018
25	1	-0.000001231	-0.000001057	0.000000183
26	1	0.000002646	-0.000000454	-0.000000419
27	6	0.000000620	-0.000002483	0.000004530
28	1	-0.000001582	-0.000000661	-0.000000108
29	1	-0.000001586	0.000001076	-0.000000832
30	1	0.000001126	0.000002460	-0.000004460
31	6	-0.000005641	0.000008537	-0.000019986
32	1	-0.000005304	-0.000004318	-0.000000431
33	6	-0.000005678	0.000003555	0.000018223
34	6	-0.000008343	0.000001321	-0.000001281
35	1	0.000001053	0.000004167	0.000001523
36	1	0.000008018	0.000003940	-0.000003482
37	1	0.000002862	-0.000003427	-0.000001393
38	6	-0.000004878	-0.000012930	-0.000009007
39	1	0.000001276	0.000000392	0.000001727
40	1	-0.000000419	-0.000002274	-0.000000885
41	1	0.000004424	0.000002566	-0.000000725
42	1	-0.000001645	-0.000003455	-0.000002136

Energy HF/6-31G//HF/6-311G(d,p): –807.3102898 Hartrees

APPENDIX C. X-ray Crystallographic Data

(*trans*)-5-hydroxy-2,3-dimethyl-4-phenylcyclopent-2-enone (38)

Crystal Data

Empirical Formula	$C_{13}H_{14}O_2$
Formula Weight	202.25
Crystal Colour, Habit	colourless, needle
Crystal Dimensions	0.38 X 0.23 X 0.12 mm
Crystal System	monoclinic
Lattice Type	C-centered
Indexing Images	4 oscillations @ 300.0 seconds
Detector Position	127.40 mm
Pixel Size	0.100 mm
Lattice Parameters	a = 18.7028(14) Å b = 5.9021(2) Å c = 20.8680(12) Å β = 106.022(3) ° V = 2214.0(2) Å^3
Space Group	C2/c (#15)
Z value	8
D_{calc}	1.213 g/cm^3
F_{000}	864.00

μ(MoKα)	0.805 cm^{-1}
<u>Intensity Measurements</u>	
Diffractometer	Rigaku RAXIS-UNKNOWN
Radiation	MoKα(λ = 0.71070 Å) graphite monochromated
Data Images	60 exposures
ω oscillation Range	20.0 - 140.0°
Exposure Rate	456.0 sec./°
ω oscillation Range	20.0 - 200.0°
Exposure Rate	456.0 sec./°
Detector Position	127.40 mm
Pixel Size	0.100 mm
$2\theta_{max}$	144.7°
No. of Reflections Measured	Total: 41835 Unique: 18822 (R_{int} = 0.035)
Corrections	Lorentz-polarization Absorption (trans. factors: 0.819 - 0.990) Secondary Extinction (coefficient: 1.47210e+001)
<u>Structure Solution and Refinement</u>	
Structure Solution	Direct Methods (SHELX97)

Refinement	Full-matrix least-squares on F
Function Minimized	Σ w (|Fo| - |Fc|)^2
Least Squares Weights parameters	Chebychev polynomial with 3 9.8132,5.0194,6.4664,
$2\theta_{max}$ cutoff	52.0^o
Anomalous Dispersion	All non-hydrogen atoms
No. Observations (I>3.00σ (I))	1841
No. Variables	178
Reflection/Parameter Ratio	10.34
Residuals: R (I>3.00σ (I))	0.0634
Residuals: Rw (I>3.00σ (I))	0.0795
Goodness of Fit Indicator	1.076
Max Shift/Error in Final Cycle	0.004
Maximum peak in Final Diff. Map	0.51 e$^-$/Å^3
Minimum peak in Final Diff. Map	-0.25 e$^-$/Å^3

(3a*R,7a*S**)-3-Methyl-1-oxo-3a,4,5,6,7,7a-hexahydro-1*H*-inden-7a-yl-3,5-dinitrobenzoate (50)**

Crystal Data

Empirical Formula	$C_{17}H_{16}O_7N_2$
Formula Weight	360.32

Crystal Colour, Habit	colourless, plate
Crystal Dimensions	0.27 X 0.13 X 0.09 mm
Crystal System	triclinic
Lattice Type	Primitive
Indexing Images	4 oscillations @ 300.0 seconds
Detector Position	127.40 mm
Pixel Size	0.100 mm
Lattice Parameters	a = 10.9142(12) Å b = 11.9957(12) Å c = 13.3277(7) Å α = 87.550(11) ° β = 76.214(11) ° γ = 89.882(15) ° V = 1693.0(3) Å^3
Space Group	P-1 (#2)
Z value	4
D_{calc}	1.414 g/cm^3
F_{000}	752.00
μ(MoKα)	1.114 cm^{-1}
<u>Intensity Measurements</u>	
Diffractometer	Rigaku RAXIS-UNKNOWN
Radiation	MoKα(λ = 0.71070 Å) graphite monochromated

Detector Aperture	0 mm x 0 mm
Data Images	45 exposures
ω oscillation Range	160.0 - 190.0°
Exposure Rate	300.0 sec./°
ω oscillation Range	113.8 - 188.8°
Exposure Rate	300.0 sec./°
ω oscillation Range	51.0 - 175.0°
Exposure Rate	300.0 sec./°
Detector Position	127.40 mm
Pixel Size	0.100 mm
$2\theta_{max}$	71.2°
No. of Reflections Measured	Total: 23233 Unique: 12273 (R_{int} = 0.042)
Corrections	Lorentz-polarization Absorption (trans. factors: 0.809 - 0.990)

Structure Solution and Refinement

Structure Solution	Direct Methods (SHELX97)
Refinement	Full-matrix least-squares on F
Function Minimized	Σ w $(\|Fo\| - \|Fc\|)^2$

Least Squares Weights	Chebychev polynomial with 3 parameters 8.7104,-1.0291,6.8722,
$2\theta_{max}$ cutoff	60.0^{o}
Anomalous Dispersion	All non-hydrogen atoms
No. Observations (I>3.00σ (I))	4429
No. Variables	470
Reflection/Parameter Ratio	9.42
Residuals: R (I>3.00σ (I))	0.0496
Residuals: Rw (I>3.00σ (I))	0.0529
Goodness of Fit Indicator	1.161
Max Shift/Error in Final Cycle	0.000
Maximum peak in Final Diff. Map	0.31 $e^{-}/Å^{3}$
Minimum peak in Final Diff. Map	-0.20 $e^{-}/Å^{3}$

2,5-Bis(4-methoxyphenyl)-1-methyl-3-(2-methylbuta-2,3-dienoyl)-6-methylene bicyclo[2.2.1]heptan-7-one (67)

Crystal Data

Empirical Formula	$C_{28}H_{28}O_{4}$
Formula Weight	428.53
Crystal Colour, Habit	colourless, needle-plate
Crystal Dimensions	0.34 X 0.13 X 0.04 mm

Crystal System	monoclinic
Lattice Type	Primitive
Indexing Images	4 oscillations @ 300.0 seconds
Detector Position	127.40 mm
Pixel Size	0.100 mm
Lattice Parameters	a = 13.1142(11) Å b = 11.7261(11) Å c = 14.7870(13) Å β = 90.486(6) ° V = 2273.8(3) Å^3
Space Group	$P2_1/a$ (#14)
Z value	4
D_{calc}	1.252 g/cm^3
F_{000}	912.00
μ(MoKα)	0.825 cm^{-1}

<u>Intensity Measurements</u>

Diffractometer	Rigaku RAXIS-UNKNOWN
Radiation	MoKα(λ = 0.71070 Å) graphite monochromated
Detector Aperture	0 mm x 0 mm
Data Images	24 exposures
ω oscillation Range	40.0 - 164.0°

Exposure Rate	600.0 sec./^{o}
Detector Position	127.40 mm
Pixel Size	0.100 mm
$2\theta_{max}$	72.8^{o}
No. of Reflections Measured	Total: 17805 Unique: 9087 (R_{int} = 0.059)
Corrections	Lorentz-polarization

Structure Solution and Refinement

Structure Solution	Direct Methods (SHELX97)
Refinement	Full-matrix least-squares on F
Function Minimized	Σ w (|Fo| - |Fc|)^2
Least Squares Weights parameters	Chebychev polynomial with 3 14.0989,-6.7772,10.5568,
$2\theta_{max}$ cutoff	54.0^{o}
Anomalous Dispersion	All non-hydrogen atoms
No. Observations (I>3.00σ (I)) No. Variables	2883 317
Reflection/Parameter Ratio Residuals: R (I>3.00σ (I))	9.09 0.0552
Residuals: Rw (I>3.00σ (I))	0.0612
Goodness of Fit Indicator	1.143

Max Shift/Error in Final Cycle	0.000
Maximum peak in Final Diff. Map	0.28 $e^-/Å^3$
Minimum peak in Final Diff. Map	-0.23 $e^-/Å^3$

(1*S,2*R**,4*E*)-1,2,5,6-Tetrabromo-4-methyl-1-phenylhex-4-en-3-one (85)**

Crystal Data

Empirical Formula	$C_{13}H_{12}Br_4O$
Formula Weight	503.85
Crystal Colour, Habit	colourless, plate
Crystal Dimensions	0.25 X 0.17 X 0.03 mm
Crystal System	monoclinic
Lattice Type	Primitive
Indexing Images	4 oscillations @ 1500.0 seconds
Detector Position Pixel Size	127.40 mm 0.100 mm
Lattice Parameters	a = 11.619(3) Å b = 5.6336(14) Å c = 13.014(4) Å β = 115.711(11) ° V = 767.5(4) $Å^3$
Space Group	$P2_1$ (#4)
Z value	2

D_{calc}	2.180 g/cm^3
F_{000}	476.00
μ(MoKα)	105.037 cm^{-1}

Intensity Measurements

Diffractometer	Rigaku RAXIS-UNKNOWN
Radiation	MoKα (λ = 0.71070 Å) graphite monochromated
Data Images	33 exposures
ω oscillation Range	30.0 - 60.0^o
Exposure Rate	480.0 sec./^{o}
ω oscillation Range	53.8 - 188.8^o
Exposure Rate	480.0 sec./^{o}
Detector Position	127.40 mm
Pixel Size	0.100 mm
$2\theta_{max}$	145.9^o
No. of Reflections Measured	Total: 15882 Unique: 13242 (R_{int} = 0.086) Friedel pairs: 3455
Corrections	Lorentz-polarization Absorption (trans. factors: 0.185 - 0.730) Secondary Extinction (coefficient: 3.93220e+001)

Structure Solution and Refinement

Structure Solution	Direct Methods (SHELX97)
Refinement	Full-matrix least-squares on F^2
Function Minimized	Σ w $(Fo^2 - Fc^2)^2$
Least Squares Weights parameters	Chebychev polynomial with 3 14515.5000,19188.5000,0.0000,
$2\theta_{max}$ cutoff	60.0^o
Anomalous Dispersion	All non-hydrogen atoms
No. Observations (I>3.60σ(I))	1905
No. Variables	175
Reflection/Parameter Ratio	10.89
Residuals: R1 (I>3.60σ(I))	0.0892
Residuals: wR2 (I>3.60σ(I))	0.0844
Goodness of Fit Indicator	1.275
Flack Parameter (Friedel pairs = 3455)	0.22(4)
Max Shift/Error in Final Cycle	0.015
Maximum peak in Final Diff. Map	1.91 $e^-/Å^3$
Minimum peak in Final Diff. Map	-1.82 $e^-/Å^3$

(1*R,6*S**,7*R**)-1,3,4-Trimethyl-8-methylene-7-phenylbicyclo[4.2.1]non-3-en-9-one (90)**

Crystal Data

Empirical Formula	$C_{19}H_{22}O$
Formula Weight	266.38
Crystal Colour, Habit	colourless, plate
Crystal Dimensions	0.36 X 0.24 X 0.13 mm
Crystal System	monoclinic
Lattice Type	Primitive
Indexing Images	4 oscillations @ 300.0 seconds
Detector Position	127.40 mm
Pixel Size	0.100 mm
Lattice Parameters	a = 12.3808(5) Å b = 7.1865(2) Å c = 17.5078(8) Å β = 98.452(2) ° V = 1540.83(10) Å^3
Space Group	$P2_1/a$ (#14)
Z value	4
D_{calc}	1.148 g/cm^3
F_{000}	576.00
μ(MoKα)	0.686 cm^{-1}

Intensity Measurements

Diffractometer	Rigaku RAXIS-RAPID

Radiation	MoKα(λ = 0.71070 Å) graphite monochromated
Data Images	51 exposures
ω oscillation Range	70.0 - 198.0°
Exposure Rate	360.0 sec./°
ω oscillation Range	72.5 - 202.5°
Exposure Rate	360.0 sec./°
Detector Position	127.40 mm
Pixel Size	0.100 mm
$2\theta_{max}$	71.5°
No. of Reflections Measured	Total: 23169 Unique: 5766 (R_{int} = 0.019)
Corrections	Lorentz-polarization

Structure Solution and Refinement

Structure Solution	Direct Methods (SHELX97)
Refinement	Full-matrix least-squares on F
Function Minimized	$\Sigma w (\|Fo\| - \|Fc\|)^2$
Least Squares Weights	Chebychev polynomial with 3 parameters
	7.9587,5.3376,5.8881,
$2\theta_{max}$ cutoff	60.0°
Anomalous Dispersion	All non-hydrogen atoms
No. Observations (I>3.00σ((I))	3007
No. Variables	203
Reflection/Parameter Ratio	14.81

Residuals: R (I>3.00σ((I))	0.0526
Residuals: Rw (I>3.00σ((I))	0.0693
Goodness of Fit Indicator	1.078
Max Shift/Error in Final Cycle	0.000
Maximum peak in Final Diff. Map	0.23 $e^-/Å^3$
Minimum peak in Final Diff. Map	-0.22 $e^-/Å^3$