University of Alberta

Exploring New Aspects of the Nazarov Cyclization

by

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Abstract

The five-membered carbocyclic framework is a prevailing structural motif found in natural products and bioactive compounds. Over the years, the Nazarov reaction has been continuously refined as a versatile protocol to access cyclopentanoid products. In this dissertation, several projects built on Nazarov chemistry will be detailed.

Recent research activities regarding umpolung reactivity at the carbonyl α-carbon, a relatively underemphasized carbonyl umpolung, is discussed in Chapter 1. The cationic intermediates generated during the Nazarov cyclization have been shown to participate in domino or cascade sequences, thus providing a convenient entry to expeditiously increase molecular complexity from relatively simple precursors. Chapter 2 describes a comprehensive investigation of new bond-forming reactions initiated by the Nazarov reaction wherein umpolung reactivity at the α-carbon of cyclopentanones was achieved through the interception of 2-oxidocyclopentenyl cations derived from the initial electrocyclization with an array of carbon nucleophiles.

Alternative substrates to the key pentadienyl cation intermediate in the Nazarov reaction, potentially offering access to unconventional substitution patterns or milder conditions, have recently attracted considerable interest. Chapter 3 discusses the use of vinyl silyloxyallenes, which function as dienone surrogates through Brønsted acid activation, to effect the Nazarov cyclization. Additionally, a novel extension of the vinyl allene version of the Nazarov

reaction, involving an interrupted Nazarov reaction employing pendent aromatic traps will be presented.

Chapter 4 recounts a novel, two-step, modular synthesis of α-amidoindanones. This process is based upon the Nazarov cyclization of 2-amido-1,4-pentadien-3-ones that were in turn prepared via a novel coupling process between α,β-unsaturated aldehydes and an α-lithiated allenamide. As supported by a deuterium labelling study, the mechanism of the coupling entails sequential carbonyl addition and 1,3-sigmatropic rearrangement.

Acknowledgements

I would like to express my deepest gratitude to Professor F. G. West for all the support and insightful discussions along the way. Thank you for encouraging us to freely explore our own ideas and always providing your valuable feedback to our research projects.

Also, I would like to acknowledge past and present West group members who made my graduate study so rewarding, not only in the field of chemistry but also for the life experiences as an international student. Whiteboard problem sets, safety meetings, Avenue...oh I even learned how to shotgun a beer from Owen.

The department is equipped with prestigious research facilities. I must appreciate the assistant of the support staff within the department who made the work described herein possible.

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Table of Contents

Chapter 1

Chapter 2

Chapter 3

Chapter 4

List of Tables

Chapter 1

Chapter 2

Chapter 3

Chapter 4

List of Figures

Chapter 1

Chapter 2

Chapter 3

Chapter 4

List of Schemes

Chapter 1

Chapter 2

Chapter 3

Chapter 4

List of Symbols and Abbreviations

^{1}H	proton
^{13}C	carbon-13
Å	Angstrom
Ac	acetyl
acac	acetylacetonate
app.	apparent (spectral)
aq	aqueous solution
Ar	aryl
atm	atmosphere
Bn	benzyl
br	broad (spectral)
Bu	butyl
ºC	degrees celsius
calcd	calculated
CAN	ceric ammonium nitrate
cat.	indicates that the reagent was used in a catalytic amount
cm^{-1}	wave numbers
COSY	H-H correlation spectroscopy
conc.	concentrated
Cy	cyclohexyl
d	day(s); doublet (spectral)

DBU	1,8-diazabicyclo[5.4.0]undec-7-ene
dd	doublet of doublets (spectral)
ddd	doublet of doublet of doublets (spectral)
DIBAL-H	diisobutylaluminum hydride
DMAP	4-dimethylaminopyridine
DMDO	dimethyldioxirane
DME	1,2-dimethoxyethane
DMF	*N,N*-dimethylformamide
DMSO	dimethylsulfoxide
DMP	Dess-Martin periodinane
dr	diastereomeric ratio
dt	doublet of triplets (spectral)
E^+	an unspecified electrophile
EDG	electron-donating group
EI	electron impact (mass spectrometry)
er	enantiomeric ratio
ESI	electrospray ionization (mass spectrometry)
Et	ethyl
EtOAc	ethyl acetate
equiv.	equivalent(s)
EWG	electron-withdrawing group
g	gram(s)
h	hour(s)

Hex	hexyl
HMBC	heteronuclear multiple bond coherence (spectral)
HOMO	highest occupied molecular orbital
HSQC	heteronuclear single quantum coherence (spectral)
HPLC	high performance liquid chromatography
HRMS	high resolution mass spectrometry
$h\nu$	light
Hz	hertz
IPr	1,3-bis(diisopropylphenyl)imidazol-2-ylidene
i-Pr	isopropyl
IR	infrared
J	coupling constant
kcal	kilocalories
L	liter(s)
LA	Lewis acid
LAH	lithium aluminum hydride
LDA	lithium diisopropylamide
LHMDS	lithium hexamethyldisilazide
LUMO	lowest unoccupied molecular orbital
M	molar
m	multiplet (spectral)
M^+	generalized Lewis acid or protic acid; molecular ion
m-CPBA	*meta-chloroperbenzoic* acid

Me	methyl
mg	milligram(s)
MHz	megahertz
min	minute(s)
mL	milliliter(s)
mmol	millimole(s)
mol	mole(s)
mp	melting point
MS	molecular sieves
Ms	methanesulfonyl
m/z	mass to charge ratio
NBS	*N*-bromosuccinimide
NIS	*N*-iodosuccinimide
NMR	nuclear magnetic resonance
Nu	an unspedified nucleophile
ORTEP	Oak Ridge thermal-ellipsoid plot
PCC	pyridinium chlorochromate
Ph	phenyl
ppm	parts per million
Pr	propyl
R	generalized alkyl group of substituent
R_f	retention factor (in chromatography)
rOe	rotating-frame Overhauser enhancement

rt	room temperature
s	singlet (spectral)
RVC	reticulated vitreous carbon
t	triplet (spectral)
T	temperature
TBS	*tert*-butyldimethylsilyl
t-Bu	*tert*-butyl
TES	triethylsilyl
Tf	trifluoromethanesulfonyl
TFA	trifluoroacetic acid
THF	tetrahydrofuran
THP	2-tetrahydropyranyl
TIPS	triisopropylsilyl
TLC	thin layer chromatography
TMS	trimethylsilyl
Tol	tolyl
TROESY	transverse rotating-frame Overhauser enhancement spectroscopy
Ts	*p*-toluenesulfonyl
TsOH	*p*-toluenesulfonic acid
δ	chemical shift

Chapter 1

Harvesting Umpolung Reactivity at the Carbonyl α-Carbon

1.1 Background

The mainstream of synthetic chemistry has historically entailed the manipulation of functional groups to access desired structural motifs.[1] Functional groups typically consist of groups of atoms and possess characteristic reactivity and physical properties. In general, heteroatoms within functional groups whose electronegativities are greater than carbon's can impose a certain degree of polarity alternation along the backbone of carbogenic molecules.[2] As bonding electrons are withdrawn by the heteroatom, the adjacent carbon assumes a more electropositive state, and alternates the polarity of neighboring carbons respectively. Hence the carbons along the chain can be simply differentiated into two kinds based on their relative electronic nature per previous discussions. The more electron-rich carbons are arbitrarily assigned as the donor (d), and the more electron-deficient ones are coined as the acceptor (a). A representative example of such an alternating pattern is shown in Figure 1, wherein the heteroatom (X) is a donor center (d^0), itself, and the successive carbons are labeled as corresponding a^{2n+1} and d^{2n}.

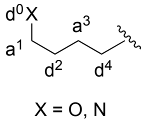


Figure 1. General Reactivity Patterns of Heteroatom-containing Substrates

As most of organic reactions between functionalities are more or less polar in nature, thermodynamically favored chemical transformations ought to entail the mutual interactions of two reaction centers bearing opposite polarity. While innate reactivity of functional groups can be readily appreciated by polarity alternation (*vide supra*), this consideration merely reflects one possible pathway for combining two molecular fragments (Figure 2).

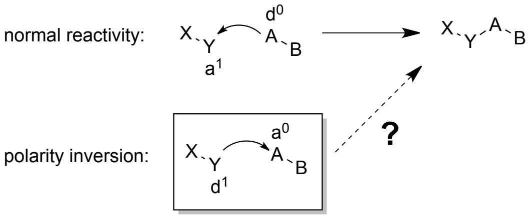


Figure 2. Two Potential Bond Disconnections

In the 1950s, several pioneering research groups began to explore the seemingly counterintuitive paradigm of inversed polarity-driven reactivity.[3] In the early 1970s, Seebach suggested the German word, umpolung, be used as a concise expression of the methods for the construction of organic molecules involving the interchange of the donor/acceptor reactivity of an atom.[4] In principle, the umpolung protocol doubles the possibilities of forming a strategic bond. This alternative view of synthetic assembly not only expands the dimension of choosing appropriate precursors in the design plan of synthesis, but also allows chemists to garner new modes of reactivity though such polarity-inversion methods. Presently, the strategy has been popularized and has resulted in the development of numerous novel methodologies;[5] in particular, research efforts to access carbonyl umpolung associated with acyl anions[6] and homoenolates[7] have acquired certain success (Figure 3). However, it is noteworthy that chemistry related to another subclass of carbonyl umpolung, α-electrophiles, remained underemphasized until very recently. Some recent advances of reactions pertaining to carbonyl α cation intermediates will be discussed as follows.

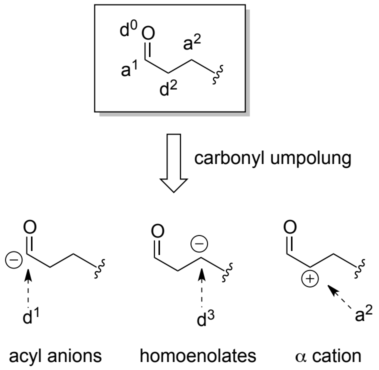
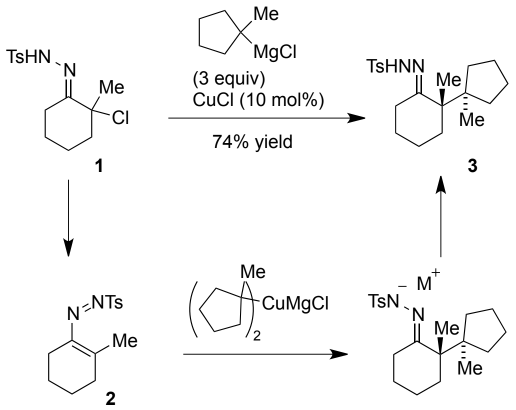


Figure 3. Umpolung Reactivity of Carbonyl Groups

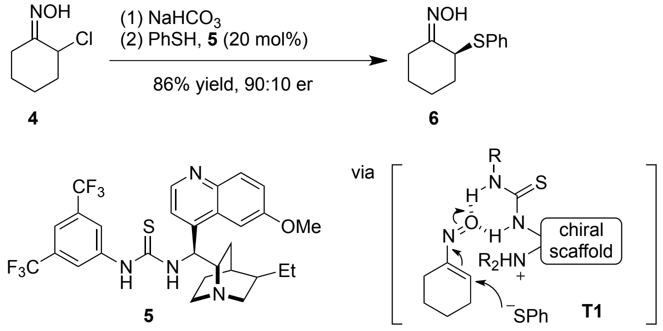
1.2 α-Functionalization of Umpoled Carbonyl Derivatives

Hatcher and Coltart described an unconventional catalytic alkylation procedure involving Cu(I)-catalyzed addition of Grignard reagents to *in situ*-generated azoalkene intermediates (Scheme 1).[8] At least one equivalent of the Grignard reagent served as a base to convert chlorine-substituted hydrazone **1** into the corresponding vinyl azo compound **2** that set the stage for the subsequent umpolung reaction. The following conjugate addition would occur at the carbon that was originally α to the parent hydrazone functionality. This novel alkylation method allows for the construction of highly sterically congested compounds that would be inaccessible employing traditional enolate or aza-enolate synthons.



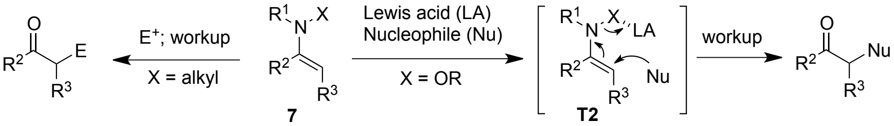
Scheme 1. Cu(I)-catalyzed Grignard Umpolung Addition

The Coltart group recently reported an elegant extension of their umpolung strategy, in which a heteroatom nucleophile was asymmetrically introduced at the α-carbon of an oxime group (Scheme 2).[9] Racemic α-chloro oxime **4** was first transformed into a nitrosoalkene upon treatment with base. Amino thiourea **5,** acting as a bifunctional catalyst, mediated the bond-forming event between the activated unsaturated nitroso species and the thiolate as shown in transition state **T1**. This asymmetric organocatalytic sulfenylation sequence offered a new opportunity of bond disconnection obviating the common need for electrophilic sulfur reagents.



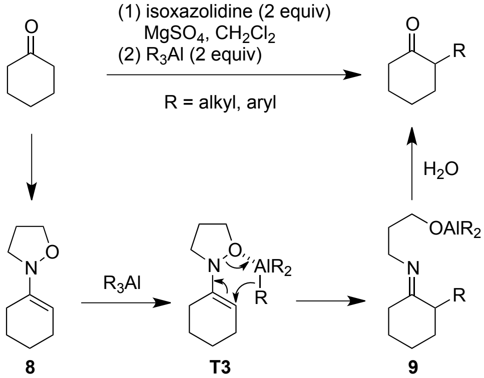
Scheme 2. Organocatalytic Umpolung Sulfenylation

Miyata and co-workers developed a new protocol for umpolung α-functionalization of carbonyls through enamine intermediate **7** (Scheme 3).[10] In general, enamines tend to react with electrophilic agents furnishing the corresponding 2-substituted ketones. The authors anticipated that when the nitrogen end of an enamine possessed a heteroatom substituent, a formal α-electrophile could be generated by coordination with a Lewis acid, allowing subsequent attack of nucleophiles in an S_N2' mode on the polarity-inversed position (transition state **T2**).



Scheme 3. Umpolung Strategy Employing Enamine Intermediate

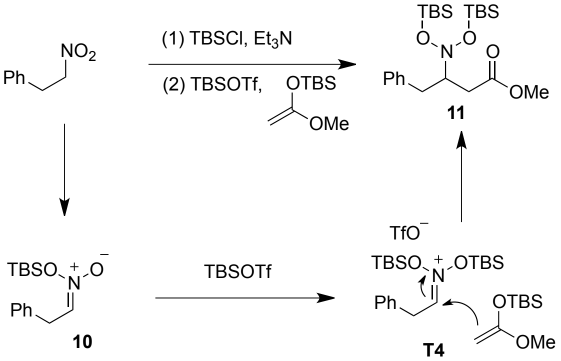
Miyata's proposal was realized by initial conversion of a ketone into an alkenyl isoxazolidine **8**. Subsequent addition of organoaluminum reagents then promoted a conjugate displacement of **8** via transition state **T3** giving the alkoxy imine **9** that was eventually hydrolyzed to the ketone product upon aqueous workup. Notably, both α-alkylation and α-arylation could be achieved by the use of the according aluminum reagents.



Scheme 4. Polarity Inversion of *N*-Alkoxyenamines

Smirnov *et al.* demonstrated that the normal reactivity of acyclic nitroalkanes could be altered though sequential silylation activations (Scheme

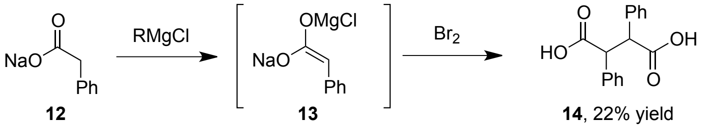
5).[11] In the presence of a silyl triflate, the coupling between nitronates **10** and ketene acetals yielded bis-silylated nitroso acetals **11** via transition state **T4**. As demonstrated by the authors, an obvious synthetic value of compound **11** is its potential as a convenient precursor of β-amino acid derivatives through chemoselective reductions.



Scheme 5. Umpolung Reactivity of Aliphatic Nitro Substrates

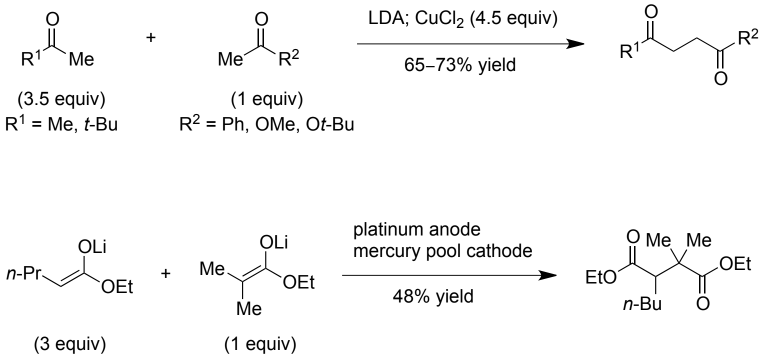
1.3 Oxidative Coupling of Enols, Enolates and Enamines with Electron-rich π-Systems

Well before the concept of umpolung was introduced, the oxidative dimerization of sodium carboxylates **12** was disclosed by Ivanoff and Spassoff in 1935.[12] In this early investigation, two carboxylate dianions **13** were merged together at the innate nucleophilic carbons via a net two-electron oxidation yielding the substituted succinic acid **14**. Although not fully appreciated until several decades later, the fundamental idea of this prototypical enolate coupling experienced a renaissance in the 1970s and became an active field of research.[13]



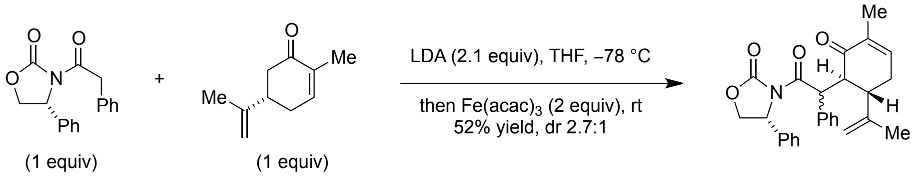
Scheme 6. Intermolecular Oxidative Enolate Homocoupling by Ivanoff

While the intermolecular homocoupling of enolate derivatives has became a practical method, analogous heterocoupling processes employing two carbonyl subunits, without superfluous prefunctionalization, remain extremely challenging. Saegusa and co-workers first showed such a reaction sequence using simple deprotonated carbonyl species, mediated by $CuCl_2$, was possible by using three-fold excess of one of the monomers, resulting in the formation of unsymmetrical succinate products in synthetically useful yields (Scheme 7).[14] In the same year, Itoh and co-workers demonstrated a cross-coupling reaction between two different lithium enolates under electrolytic conditions, again relying on a stoichiometric advantage in order to obtain the heterodimer in an efficient manner (Scheme 7).[15]



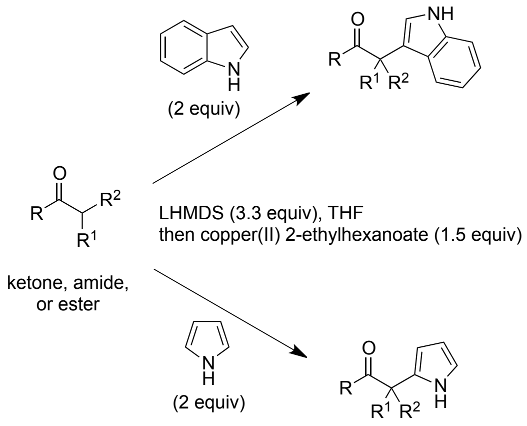
Scheme 7. Early Studies in Oxidative Heterocoupling of Enolates

More recently, the Baran group thoroughly investigated the heterocoupling of enolate intermediates, both in intra- and intermolecular variants, with particular focus placed on understanding the mechanistic details.[16] By systematically examining the reaction parameters (solvent, temperature, concentration, etc.), Baran and co-workers developed reliable and scalable methods for the union of monomeric starting materials using soluble copper(II) or iron(III) salts as oxidants; significantly selective heterocouplings, utilizing only one equivalent of each coupling partner, could be achieved under the Fe(III)-mediated coupling system (Eq 1).[17]



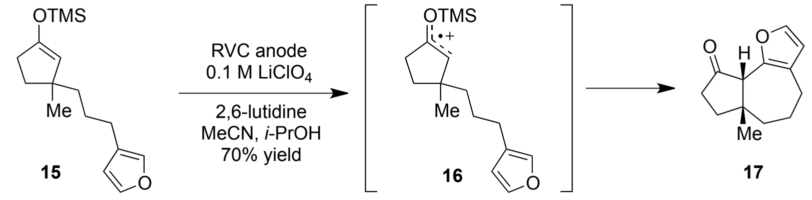
(1)

Baran and co-workers attempted to generalize the oxidative heterocoupling strategy of two distinct anionic modalities so that no preprogramming of the coupling partners was required. In Baran's system, the direct couplings of simple indoles and pyrroles to carbonyl derivatives were accomplished (Scheme 8).[18] Additionally, all-carbon quaternary centers could be readily installed at the α position.



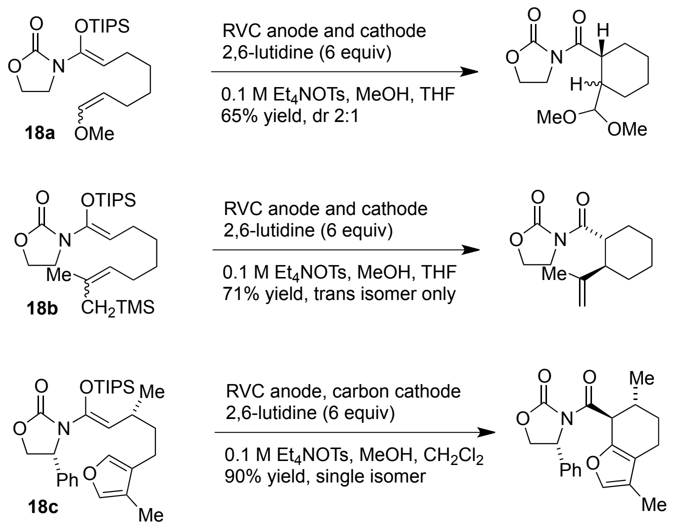
Scheme 8. Direct Indole and Pyrrole Couplings at the Carbonyl α Carbon

Electrochemistry constitutes a powerful means for the selective removal or addition of electrons from functional groups.[19] The nucleophilic addition to radical cation intermediates derived from electrochemical oxidation of normally nucleophilic alkenes involves umpolung reactivity. An early example by Itoh has been shown in Scheme 7. Recently, Sperry and Wright showed that an anodic oxidation of heteroaryl-terminated enol ether **15** leads to the initial generation of radical cation **16** that is then captured in a notable seven-membered ring closure to give tricyclic products **17**, whereby two innately nucleophilic sp^2 carbons were forged under relatively neutral conditions (Scheme 9).[20] The groups of Moeller and Trauner adopted this anodic annulation strategy in their synthetic studies toward alliacol A[21] and guanacastepene E[22] respectively.



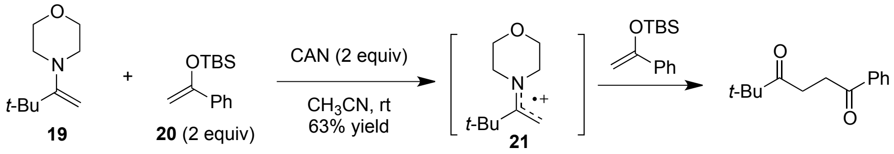
Scheme 9. Intramolecular Anodic Olefin Coupling Reaction

Moeller and co-workers have expanded the scope of coupling groups used in the electrochemical reactions, wherein the unified theme is to fuse two nucleophilic moieties in an intramolecular fashion.[23] Oxazolidinone-derived ketene acetals **18** were found to be superior reaction partners for the carbon-carbon bond formation in the anodic olefin coupling methods. The radical cation generated from the electrolysis of ketene *N*,*O*-acetals **18a–b** could be trapped by a broad range of tethered carbon nucleophiles (Scheme 10).[24]



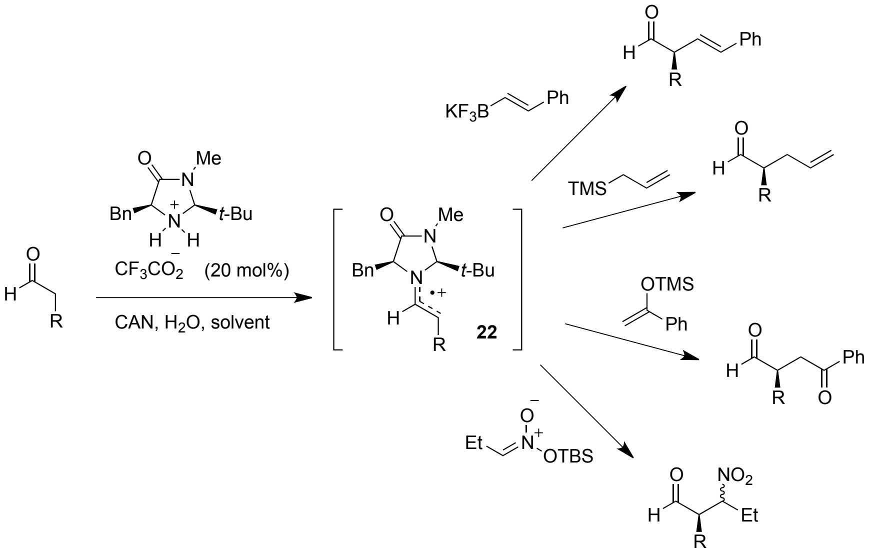
Scheme 10. Selected Anodic Umpolung Reactions by the Moeller Group

In 1992, Narasaka *et al.* used CAN (ceric ammonium nitrate) as the oxidant to affect the coupling of two nucleophiles, pinacolone enamine **19** and silyl enol ether **20** (Scheme 11).[25] Although the generality of this process was not further examined, this single example showcased a novel enamine umpolung. The authors also presumed that the reaction mechanism involves nucleophilic attack onto enamine cation radical **21**.



Scheme 11. Synthesis of 1,4-Dicarbonyl Compounds via Enamine Umpolung

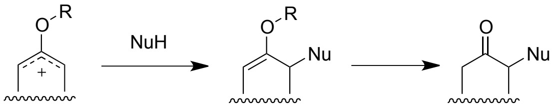
MacMillan and co-workers brought the concept of enamine umpolung to a more sophisticated level, wherein they developed an elegant enantioselective organocatalytic approach to functionalize the α carbon of aldehydes through the combination of enamine catalysis and singly occupied molecular orbital (SOMO) activation. In the presence of CAN, the intermediate enamine can be converted to a now electrophilic radical cation **22** that can be captured by a variety of trapping agents (Scheme 12).[26] The intramolecular variants of asymmetric umpolung bond forming reactions proceeded equally well under SOMO activation.[27] Further mechanistic investigations of SOMO organocatalysis offered proof for the appearance of the putative enamine radical cation intermediate.[28]



Scheme 12. Enantioselective Umpolung Reactions via Oxidative Organocatalysis

1.4 Polar Addition to 2-Oxidoallyl Cationic Intermediates

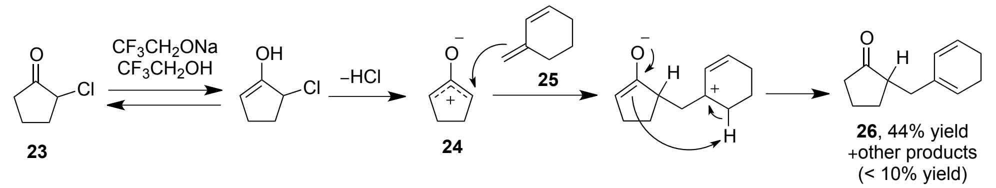
2-Oxyallyl cation intermediates have been invoked in various types of reaction mechanisms.[29] The synthetic potential of these oxyallyl cations has been greatly explored in the context of cycloaddition reactions, particularly in a [4+3] mode with dienes.[30] Conversely, direct nucleophilic attacks on the oxyallyl cations, which can be considered as a formal α-electrophile (Scheme 13), shows limited generality and applicability in respect to the substrate scope and reaction yields.



Scheme 13. Carbonyl α Carbon Umpolung via 2-Oxyallyl Cation

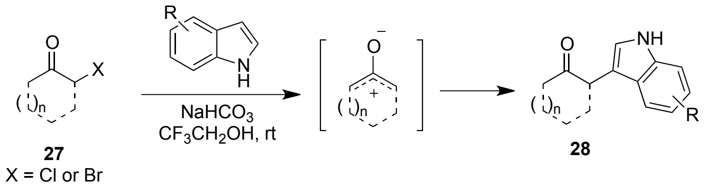
One traditional approach to access the reactive oxyallyl species involves sequential enolization and ionization of 2-chloroketones (e.g. **23**) by the action of bases in polar solvents (Föhlisch conditions).[31] While [4+3] cycloadditions under

Föhlisch conditions are a prevailing reaction type,[32] Leitich and Heise hypothesized alternative reactivity might be possible and examined the addition of the zwitterionic 2-oxyallyl cation **24** to several monoenes and dienes, which cannot adopt the requisite s-*cis* conformation for the homologous Diels-Alder cycloaddition.[33] In general, those substrates incapable of participating in the [4+3] cycloaddition furnished complicated product mixtures. A notable exception is that when 3-methylenecyclohexene (**25**) was used as the trap, α-addition product **26** was obtained as the predominant component, presumably via an ene-type process (Scheme 14).



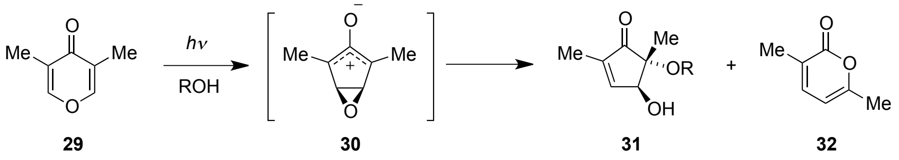
Scheme 14. Unpolung Bond Formation Under the Föhlisch Condition

More recently, Chi and co-workers demonstrated an application of Föhlisch's method for the direct coupling of unprotected indole nucleophiles and structurally diverse α-halo ketones **27** (Scheme 15).[34] In sharp contrast to the olefin nucleophiles tested by Leitich and Heise, indole substrates displayed excellent trapping reactivity to the oxyallyl intermediates giving the desired products in good to quantitative yields. Moreover, this simple and mild method to access indolyl ketones **28** is complementary to Baran's protocol using strong base and oxidant (Scheme 8).



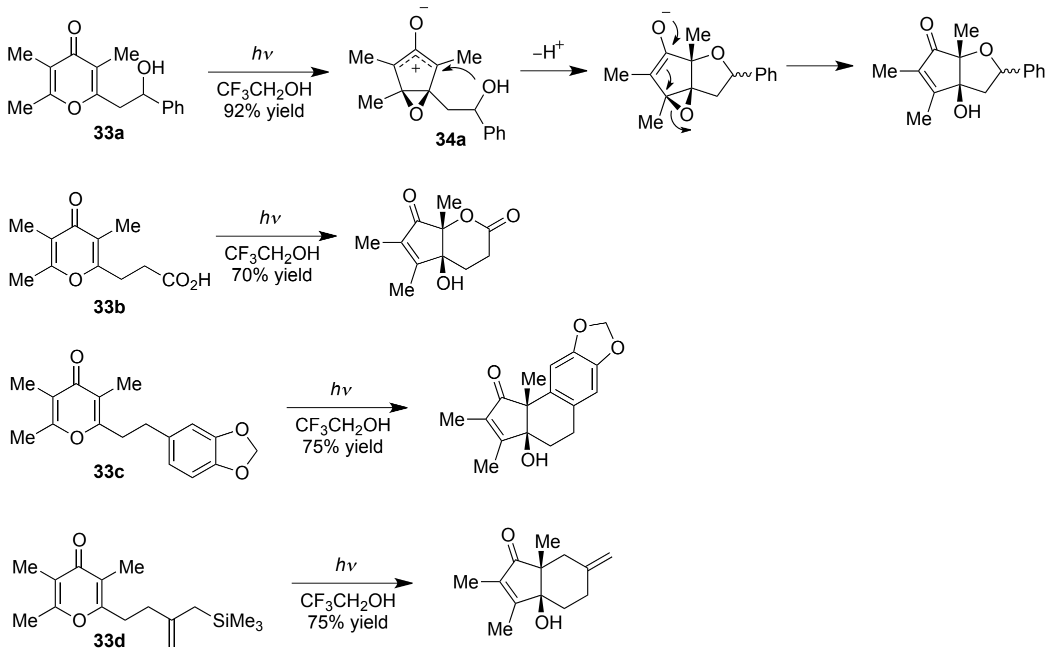
Scheme 15. Facile Access to α-Indole Carbonyl Compounds

Under photolysis conditions, the groups of Pavlik[35] and Barltrop[36] independently reported that 4-pyrones **29** underwent ring contraction to afford zwitterionic oxyallyls **30**, which could be captured by alcoholic solvents resulting in α-alkoxy carbonyl products **31**; typically, the reactions were accompanied by a competing unimolecular photoisomerization leading to the corresponding 2-pyrones **32** (Scheme 16).[37]



Scheme 16. Photochemistry of 4-Pyrones

West and co-workers envisaged that the intramolecular interception of photochemically generated oxyallyl intermediates could be more efficient than the bimolecular trapping event noted above. Upon irradiation of 4-pyrones **33a–d** with pendent trapping groups, the resulting zwitterionic intermediates (e.g. **34a**) generated from the initial electrocyclization were attacked at the α-carbon by a variety of the tethered nucleophiles, including hydroxy groups,[38] carboxylic acids,[39] aromatic systems,[40] and alkenes,[41] followed by the eliminative opening of the epoxide to give polycyclic products with an angular hydroxy group in good yields and excellent stereoselectivities (Scheme 17).



Scheme 17. Intramolecular Trapping of Photochemically Induced Oxyallyls

1.5 Conclusion

Umpolung reactivity of the carbonyl α carbon clearly offers a powerful tactic to prepare highly substituted carbonyl derivatives that are difficult to access through traditional enolate chemistry. Our laboratory has described that oxyallyl intermediates derived from the photolytic rearrangement of 4-pyrones could function as a formal α cation (Scheme 17). However, this photochemical transformation was found to be quite restricted within the range of trapping modalities, and could only be performed in highly polar but non-nucleophilic solvents. In order to conquer the generality issue, West and co-workers took an alternative path and consequently demonstrated that the oxyallyl cation intermediates generated from thermal, acid-mediated Nazarov cyclizations could be intercepted by a variety of functional groups (For details, please refer to Section 2.1).

Intrigued by the Nazarov reaction, standing as a versatile annulation process and beyond, the goal of this thesis is devoted to study several facets of

Nazarov-related chemistry. In Chapter 2, a comprehensive survey of umpolung reactivity initiated by the Nazarov reaction will be presented.

Protonation-initiated Nazarov reactions of silyloxy vinyl allenes, along with an extension using an unconventional Nazarov precursor in domino processes again involving α carbon umpolung will be discussed in chapter 3.

Additionally, a novel and concise approach to prepare amido-substituted 1,4-pentadien-3-ones will be described followed by a systematically investigation into their Nazarov cyclizations (Chapter 4).

1.6 References

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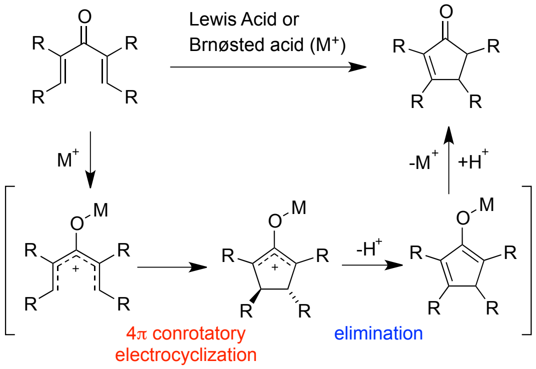
Chapter 2

Interrupting the Nazarov Reactions with Electron-Rich π-Systems[1]

2.1 Interrupted Nazarov Reactions

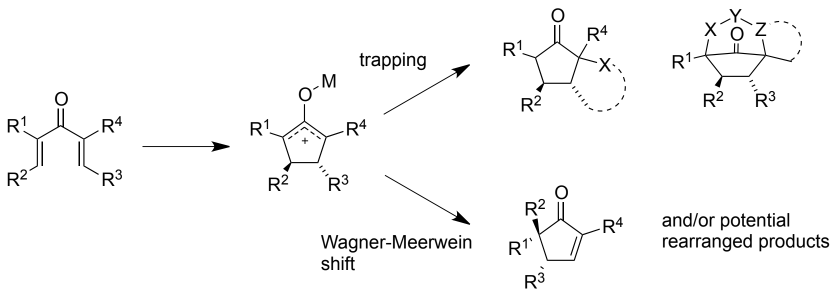
The Nazarov reaction,[2] named after the eminent Russian chemist Ivan Nikolaevich Nazarov,[3] is a widely employed cyclopentannulation protocol that, in its typical manifestation, converts a cross-conjugated dienone into a cyclopentenone (Scheme 1).



Scheme 1. The Nazarov cyclization

While its mechanistic nature is a pericyclic process,[4] the Nazarov reaction is a unique example of electrocyclization subject to Lewis or Brønsted acid activation. While eliminative termination is a common fate of the cyclized

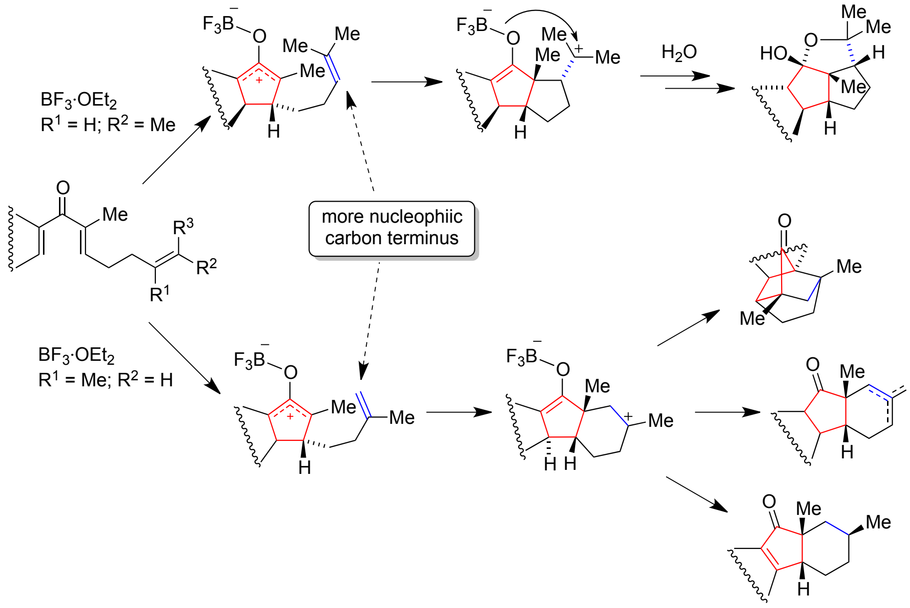
Nazarov intermediate, the appearance of an oxyallyl cation intermediate in the reaction pathway provides the potential for additional bond-forming events or skeletal rearrangements (Scheme 2). West and co-workers have coined this new aspect of diverting the Nazarov reaction from its conventional path as the interrupted Nazarov reaction.[5] The following section highlights advances in domino or cascade processes where the cationic intermediate derived from the thermal Nazarov reaction was attacked by intra- or intermolecular nucleophilic traps; skeletal rearrangements of the Nazarov intermediate through Wagner-Meerwein shifts will not be discussed herein.[6]



Scheme 2. Interrupted Nazarov Processes

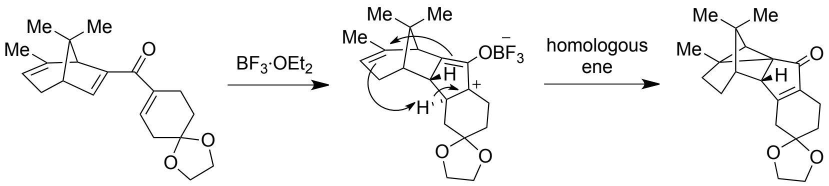
2.1.1. Intramolecular Trapping of the Nazarov Intermediate

West and co-workers described the first deliberate interception of the cationic Nazarov intermediate with a tethered alkene. Initial reports of this intramolecular Prins-type process indicated that 5-*exo* or 6-*endo* cyclization were dictated by the substitution pattern of the alkene nucleophile (Scheme 3). On the one hand, a formal [3+2] cycloaddition, consisting of capture of oxyallyl in a 5-*exo* fashion and attack by proximal enolate oxygen, furnished the strained enol ether that, upon workup, gave the corresponding diquinane product.[7] On the other hand, 6-*endo* closure provided a hydrindan tertiary carbocation, which could then suffer from three terminations resulting in products in varying ratios: (1) addition onto the enolate intermediate to give a bridged system, (2) loss of a proton to give regioisomeric alkenes, and (3) hydride shift assisted by enolate to yield conjugated enone.[8]



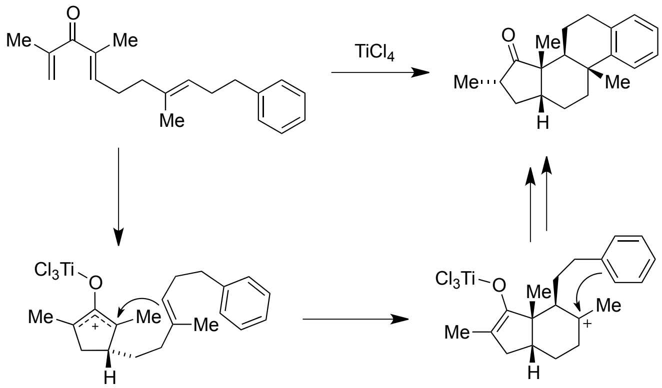
Scheme 3. Cation-Olefin Cyclization Sequence

Participation of an alkene held nearby the pentadienyl system has been observed by West and co-workers during their synthetic study toward taxane skeleton (Scheme 4).[9] The initial electrocyclization of facially biased bicyclic trienone proceeded with high *endo*-selectivity. The isolated olefin then participated in a homologous-ene process furnishing a cyclopropyl ketone as the exclusive product.



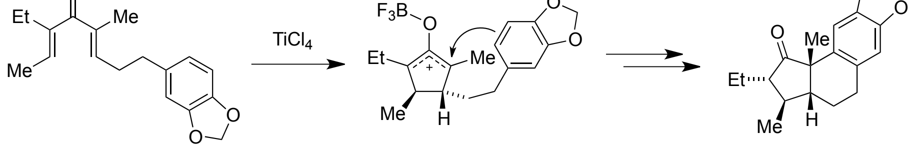
Scheme 4. Participation of an Isolated Olefin during Nazarov Cyclization

A cationic cascade sequence initiated by Nazarov reaction was realized with aryl-terminated trienones (Scheme 5).[10] In this case, the use of the stronger Lewis acid $TiCl_4$, which may prolong the lifetime of the cationic intermediates, was mandatory for the polycyclization to occur with high efficiency. Notably, tetracyclic systems were generated in a single step with the establishment of five new stereocenters.



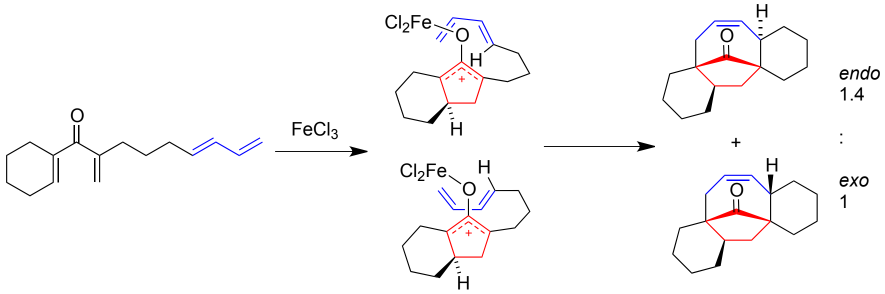
Scheme 5. Polyene Cyclization Sequence

Similarly, tethered arenes could function as immediate traps in the interrupted Nazarov process (Scheme 6).[11] A variety of aryl-substituted dienones could be converted to the corresponding benzohydrindenones in good yields and diasteroselectvities. However, one limitation was seen that electrophilic aromatic substitution of less electron-rich traps such as simple phenyl group were uncompetitive with the elimination pathway.



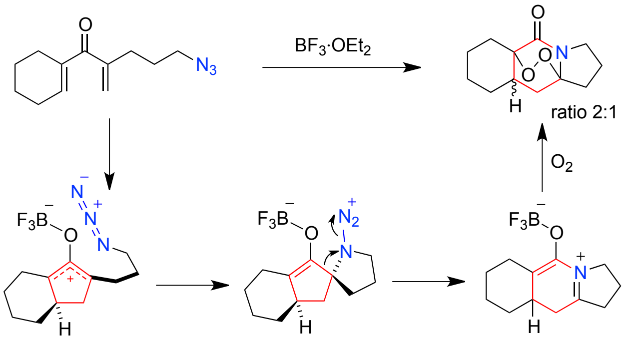
Scheme 6. Arene Trapping of the Oxyallyl Cation

The oxyallyl intermediate derived from the Nazarov cyclization could serve as a dienophile in a [4+3] cycloaddition with a tethered 1,3-diene.[12] West and co-workers found that ferric(III) chloride is an effective Lewis acid catalyst for this particular sequence. While the diene approached exclusively from the more accessible face of the bicyclic carbocation was seen, products originated from both *endo* and *exo* transition states were observed (Scheme 7). Although efficient conversion to novel cycloadducts was generally seen, the mode of trapping ([3+2] versus [4+3]) and stereoselectivity in this series were heavily dependent upon substitution patterns of the dienone substrates.



Scheme 7. [4+3] Cycloaddition with the Oxyallyl Cation

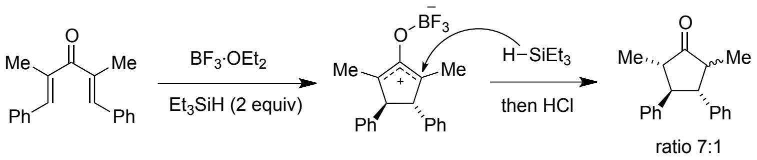
West and co-workers disclosed the use of azides to capture the Nazarov intermediates, where initial studies were focused on intramolecular variant of azide-tethered substrates (Scheme 8).[13] Exposure of the azidodienones to $BF_3 \cdot OEt_2$ at low temperature provided a mixture of diastereomeric endoperoxides. The proposed mechanism involved initial Schmidt-type process of cyclopentenyl cation followed by an aerobic oxidation of a 1,4-betaine intermediate.



Scheme 8. Endoperoxides Derived from Intramolecular Azide Trapping

2.1.2. Intermolecular Trapping of the Nazarov Intermediate

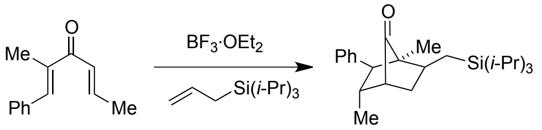
Although early research activity devoted to interrupted Nazarov chemistry primarily centered on intramolecular trapping, recent investigations by West and others revealed that bimolecular processes constituted an extremely fruitful area of developing new bond-forming reactions. In 1999, Giese and West reported a one-step synthesis of cyclopentanones through in situ reduction of cationic Nazarov intermediate by trialkylsilane.[14] This initial example was critical at that time as it suggested that intermolecular trapping can occur at a rate competitive with eliminative termination.



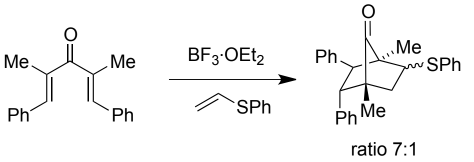
Scheme 9. Reductive Nazarov Reaction

West and colleagues demonstrated an intermolecular version of interrupted Nazarov process with π-nucleophiles where allyltrimethylsilane was first examined;[15] the reaction typically afforded a diastereomeric mixture of α-allylated cyclopentanones along with bicyclo[2.2.1]heptanone products derived from formal [3+2] cycloaddition (in-depth discussion are provided in Section

2.2.1). Further studies showed that formation of the [3+2] product could be maximized by employing the more robust triisopropylsilyl group (Eq 1). Analogously, vinyl sulfides have been shown to display [3+2] reactivity with the Nazarov intermediate in intermolecular trapping events (Eq 2).[16]

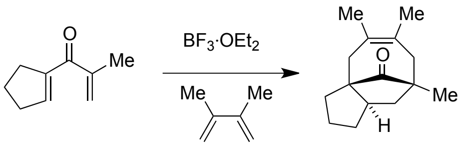


(1)



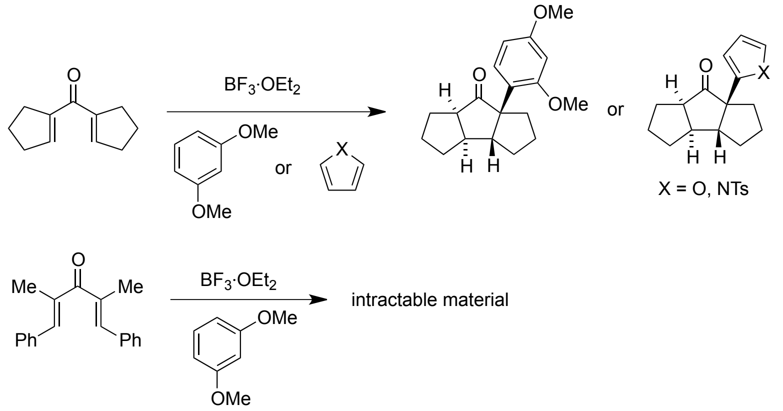
(2)

Interception of the cationic oxyallyl intermediate, generated during the Nazarov reaction, with pendent dienes showcased its synthetic utility to function as an effective dienophile. The analogous intermolecular process was surprisingly efficient and excellent stereoselectivity was seen, in that keto-bridged medium carbocycles could be readily constructed (Eq 3).[17] More recently, Burnell and co-workers showed that similar chemistry could be applied to allenyl vinyl ketones.[18]



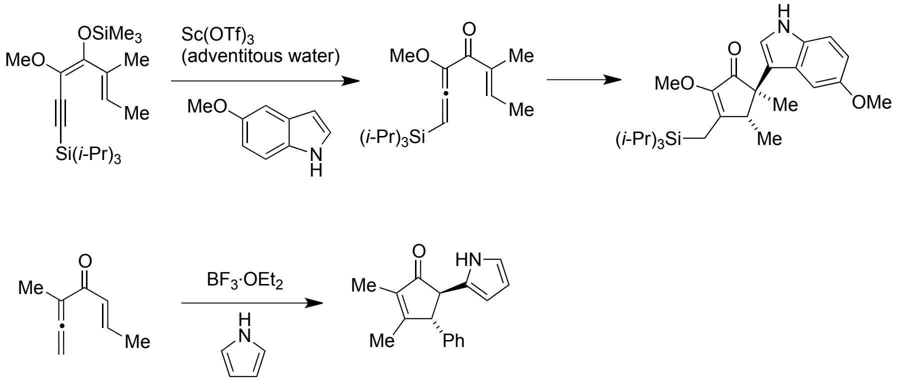
(3)

Bimolecular trapping of oxyallyls by aromatic systems does not occur as readily as the intramolecular version. Although the reaction using acyclic 1,4-pentadien-3-ones inevitably furnished intractable material, West and co-workers found that dienones whose alkenes were encased in rings offered the desired α-arylation profiles (Scheme 10);[19] heterocycles were also shown to be effective traps.



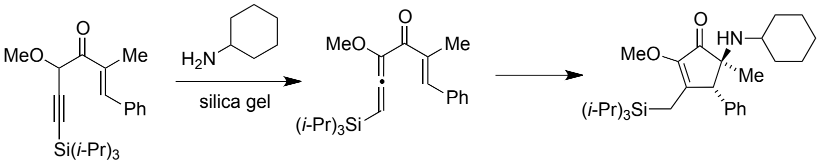
Scheme 10. Intermolecular Trapping with Electron-rich Arenes

Following the results disclosed by the West laboratories, Tius[20] and Burnell[21] individually developed conceptually related interrupted Nazarov processes of allene substrates employing nitrogen heterocycles as the aromatic nucleophiles (Scheme 11). Notably, These examples circumvented the substrate limitation seen by West and co-workers, namely efficient intermolecular trapping by electrophilic aromatic substitution occurred without the need to constrain part of the π-system within a preexisting ring.



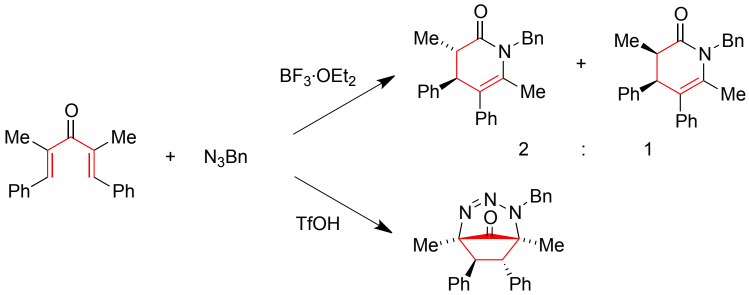
Scheme 11. Intermolecular Trapping Utilizing Allenyl Vinyl Ketones

In 2005, Dhoro and Tius developed a novel interrupted Nazarov protocol making use of primary or secondary amines as traps (Scheme 12).[22] Under solvent-free condition, the cyclization of allene ethers, isomerized from the corresponding propargylic ketones, was triggered by silica gel; interestingly, the amine then functioned as a nucleophile rather than base toward the cationic oxyallyl species yielding amino-substituted cyclopentenones. Subsequently, an asymmetric version of this process using a camphor-derived auxiliary was demonstrated by the same group.[23]



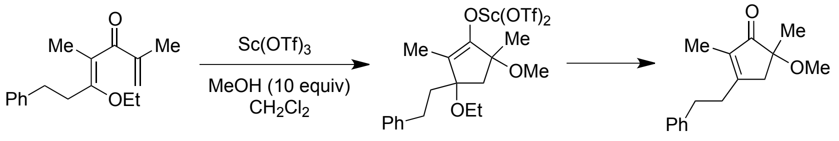
Scheme 12. Interrupting the Nazarov Cyclization with Amines

West and co-workers have utilized alkyl azides to capture the Nazarov intermediates intermolecularly. In the intermolecular variants mediated by $BF_3{\cdot}OEt_2$, the 1,4-dipolar intermediate derived from domino Nazarov/Schmidt rearrangement sequence simply underwent proton-transfer pathway furnishing epimeric dihydropyridones (Scheme 13).[24] Interestingly, the reactivity seen in the bimolecular trapping contrasts from one noted in intramolecular cases where peroxy-bridged products were produced predominantly (Scheme 8). Additionally, [3+3] reactivity between the azide and the oxyallyl cation was possible giving unusual bridged bicyclic triazenes when triflic acid was used as the promoter.[25]



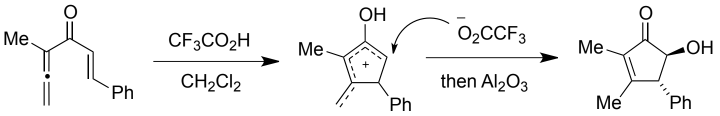
Scheme 13. Intermolecular Azide Capture

Shindo and co-workers studied the interrupted Nazarov process of β-alkoxydienones using aliphatic alcohols as trapping agents (Scheme 14).[26] The authors found that β-alkoxy substitution was essential for the overall efficiency of this catalytic process, which also directed the regioselective formation of the conjugated alkene.



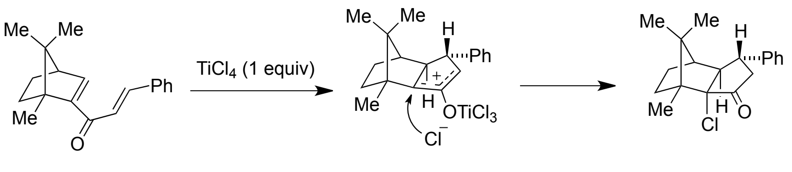
Scheme 14. Intermolecular Alcohol Trapping

Marx and Burnell reported the cyclization of allenyl vinyl ketones in the presence of trifluoroacetic acid that functioned first as a promoter then a nucleophile to give trifluoroacetate-trapped products (Scheme 15).[27] The resulting esters were immediately hydrolyzed to yield α-hydroxycyclopentenones upon elution through basic alumina.



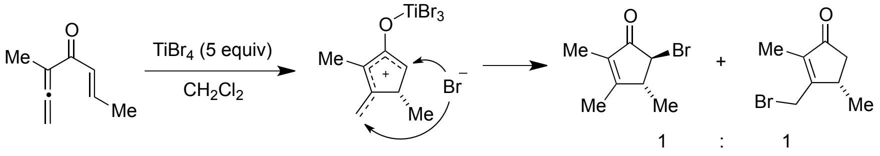
Scheme 15. Intermolecular Trapping with Trifluoroacetate

White and West found that the Nazarov intermediate could be intercepted by halides derived from Ti(IV)-based Lewis acids (Scheme 16).[28] However, this reactivity appeared to be limited to bridged bicyclic dienone substrates.



Scheme 16. Halide-Interrupted Nazarov Reaction

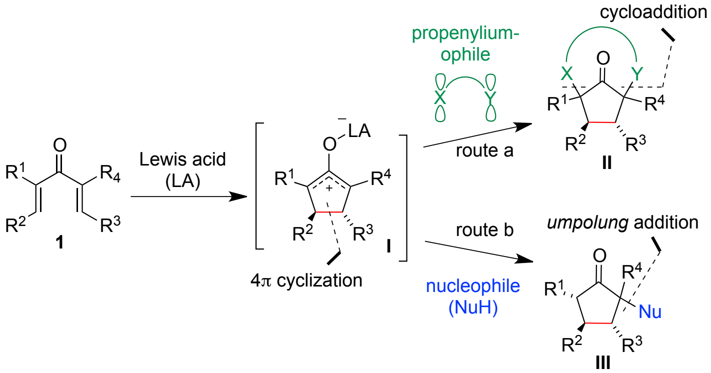
Burnell and co-workers explored the feasibility of halide capture following the Nazarov cyclization of allenyl vinyl ketones (Scheme 17).[29] When titanium(IV) bromide was used, low to moderate yields of regioisomeric mono-brominated cyclopentenones were obtained.



Scheme 17. Interrupted Nazarov Process of Allenyl Vinyl Ketones with Halides

2.2 Results and Discussions

The West group and others showed that cationic oxyallyl species generated during the Nazarov cyclization could be intercepted by various inter- or intramolecular nucleophiles by diversion from the typical eliminative termination. Intermolecular capture of the Nazarov intermediate with suitable trapping reagents is arguably more attractive as it expeditiously increases molecular complexity from two relatively simple precursors. In that regard, the oxyallyl species derived from the 4π-electrocyclization has been shown to be an excellent reaction partner notably in cycloaddition chemistry (Scheme 18, route a).



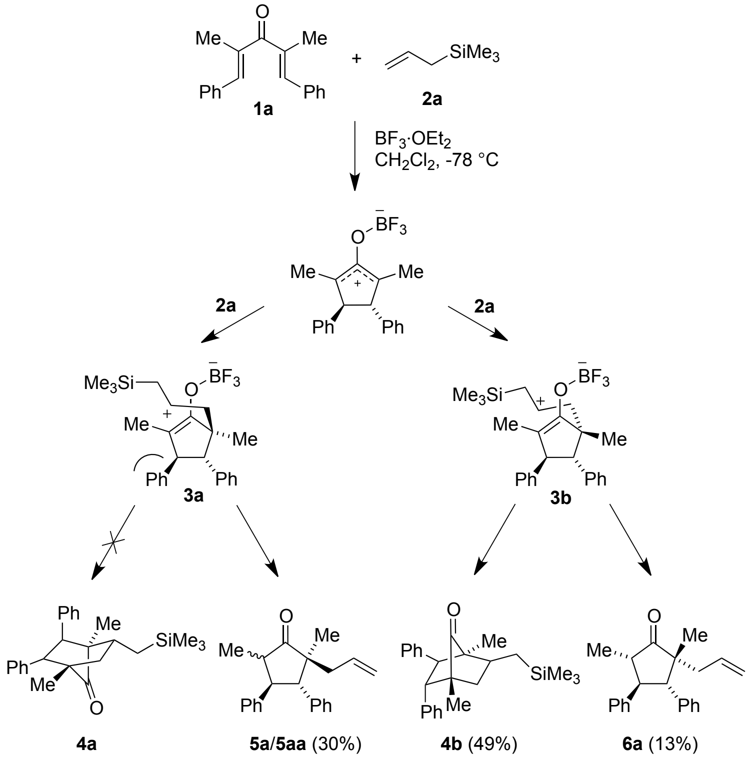
Scheme 18. Intercepting the Nazarov Intermediate with Intermolecular Traps

While bridged bicycles **II** could be constructed through that chemistry, selective functionalization at one terminus of the cyclized allylic cation, yielding α-functionalized ketones **III**, most often has involved heteroatom nucleophiles. Inspired by this concern, we sought to explore a type of interrupted Nazarov reactions in which electrocyclic ring closure was followed by polar addition of carbon-based nucleophiles. In such a reaction cascade, 2-oxyallyl cation **I** could be viewed as an electroyclization-initiated umpolung[30] of carbon α to carbonyl (Scheme 18, route b). The newly incorporated carbon motif adjacent to ketone would serve as a useful synthetic handle for further derivatization. We present herein our comprehensive investigation, exploiting the Nazarov cyclization as a springboard for new carbon-carbon bond-forming processes that allowed facile access to a variety of α-functionalized cyclopentanoid products in a one-step operation.

2.2.1. Intermolecular Trapping of the Nazarov Intermediate with Allyl Donors

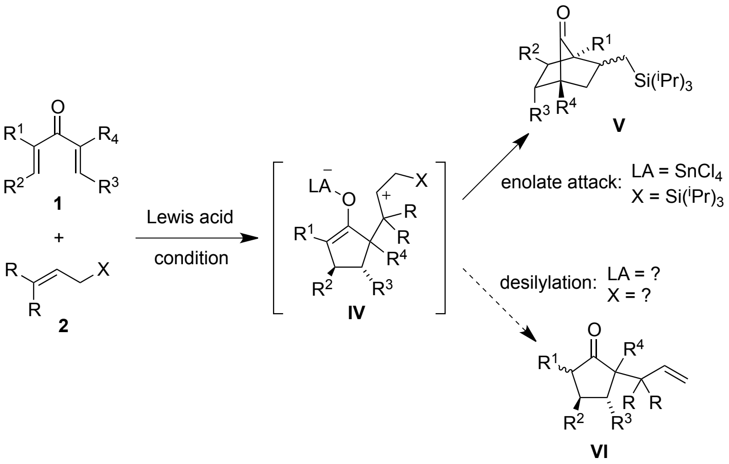
West and co-workers reported the first example of intermolecular interception of the cyclized oxyallyl cation by a cabon-based trap, namely allylsilanes,[31] in the context of the "interrupted Nazarov" reaction. Initial experiments employing cross-conjugated dienone **1a** and allyltrimethylsilane **2a** resulted in the predominant production of densely substituted bicyclo[2.2.1]cycloheptanone **4b** along with a diastereomeric mixture of α-allylated cyclopentanones **5a**, **5aa** and **6a**[32] (Scheme 19).

It is notable that none of the bicyclic product **4a** resulting from intermediate **3a** was isolated, possibly because repulsive nonbonded interactions exerted from *syn*–phenyl substitution prevented the enolate cyclization. Alternatively, zwitterion **3b**, which was derived from the allylsilane attacking from the same face as the adjacent phenyl group, primarily underwent ring closure sequence furnishing bridged bicyclic product **4b**. Although the selectivity of the reaction is poor, distributing a series of interrupted Nazarov products, we were pleased to find none of product arisen from either conventional Nazarov cyclization of **1a** or the Hosomi–Sakurai reaction[33] of **2a** with **1a**. Significantly, this result demonstrated that the electrocyclization could be coupled with an intermolecular trapping event in a well-controlled manner.



Scheme 19. Divergent Reaction Pathway

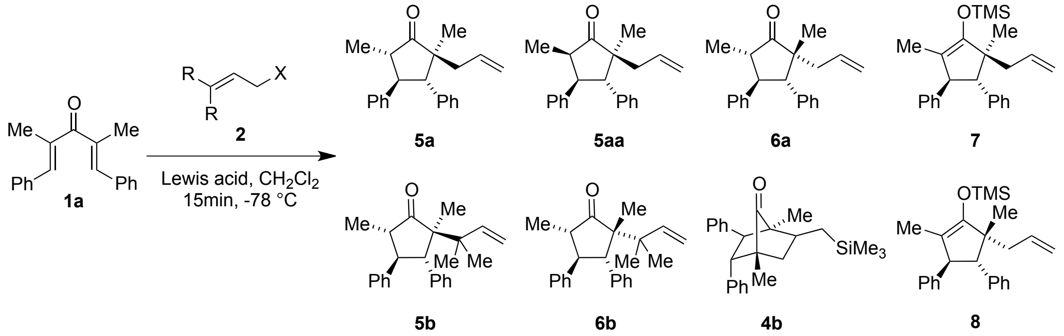
Alternatively, the utilization of more robust allyltriisopropylsilane in the reaction mediated by $SnCl_4$ with several divinyl ketones uniformly furnished bridged bicycles **V** in good yields (Scheme 20; Eq 1). The desilylation process of intermediate **IV** was surely suppressed by bulky substituents on the silicon atom.[34] While compound **V** represents an unusual structure type, there is no convenient entry to functionalize the appended trialkylsilyl group. As such, we envisioned that 2-allylcyclopentanones would be more useful synthetic building blocks for other elaborated targets. Therefore, we sought to identify ideal conditions that will promote exclusive conversion of **IV** into the allylated product **VI** through facile loss of "X" as the termination step.



Scheme 20. Design Plan (I)

We commenced to determine the optimal Lewis acids for promoting the domino electrocyclization/Hosomi–Sakurai allylation process using dienone **1a** (Table 1, entries 1–5). When $SnCl_4$ was employed, a similar product distribution as in the case of $BF_3{\cdot}OEt_2$ was found with diminished overall yield. With TMSOTf, the diastereofacial selectivity is significantly increased albeit the undesired [3+2] cycloaddition could not be precluded. Interestingly, the reaction utilizing $TiCl_4$ exclusively furnished the allylation products with high diastereofacial control (entry 4). In this case, we presumed that halide transfer from titanium Lewis acid during the Nazarov cyclization served an essential role in assisting β-silyl elimination. The effect of the Brønsted acid was also studied as protonated oxyallyl species may perform differently from the Lewis acid–bound counterpart. For the model reaction employing **1a** and **2a**, the use of triflic acid offered inferior chemo- and stereoselectivity.

Table 1. Survey of the Variations on Allyl Donors **2** and Lewis Acids[a]



Entry	2, X/R	Lewis acid	Allylated products	[3+2] adducts	Product ratio[b]	Facial selectivity	Combined yield (%)[c]
1	**2a**, $SiMe_3$/H	BF_3·OEt_2	**5a**/**5aa**/**6a**	**4b**	2:1:1:5	1:2	92
2	**2a**, $SiMe_3$/H	$SnCl_4$	**5a**/**5aa**/**6a**	**4b**	2:1:1:4	1:1.7	58
3	**2a**, $SiMe_3$/H	TMSOTf	**5a**/**6a**	**4b**	1:5:4	1:9	ND[e]
4	**2a**, $SiMe_3$/H	$TiCl_4$	**5a**/**6a**	–	1:9	1:9	90
5	**2a**, $SiMe_3$/H	TfOH	**5a**/**6a**	**4b**	1:2:2	1:4	ND[e]
6	**2b**, B(pin)/H	TMSOTf	–	–	n/a	n/a	n/a
7	**2c**, BF_3K/H	$TiCl_4$	–	–	n/a	n/a	n/a
8	**2d**, $SnBu_3$/H	BF_3·OEt_2	**5a**/**6a**	–	1:2	1:2	30
9	**2d**, $SnBu_3$/H	$TiCl_4$	**5a**/**6a**	–	1:3	1:3	76
10	**2d**, $SnBu_3$/H	TMSOTf	**7**/**8**	–	1:5	1:5	82
11[d]	**2d**, $SnBu_3$/H	TMSOTf	**5a**/**6a**	–	1:5	1:5	81
12[d]	**2e**, $SnBu_3$/Me	TMSOTf	**5b**/**6b**	–	1:1	1:1	95

[a]Standard procedure: To a stirred solution of dienone **1a** and **2** (2 equiv) in CH_2Cl_2 (0.2 M in **1**) at –78 °C was added Lewis acid (1.1 equiv). After 15 min, the reaction mixture was quenched with sat. aq $NaHCO_3$, followed by extraction with CH_2Cl_2, drying over $MgSO_4$, and chromatographic purification. [b]Determined by integration of ^1H NMR signals. [c]Isolated yield. [d]The reaction was quenched with TsOH instead of sat. aq $NaHCO_3$. [e]ND = Not determined.

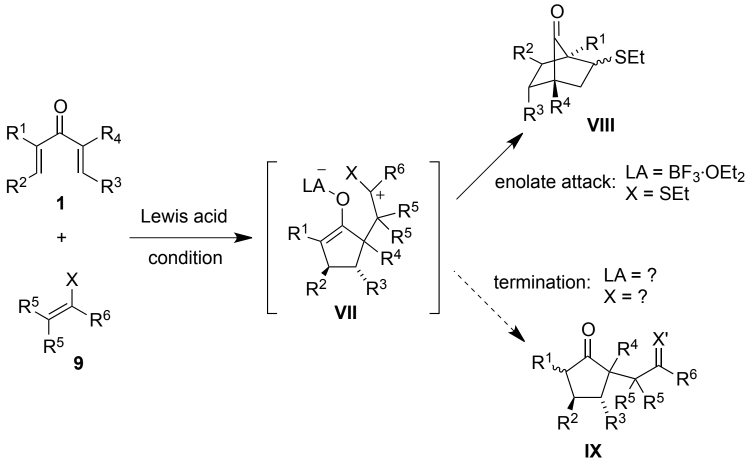
Next, we probed allyl traps other than the silicon-based one in this process. While allylborane and allyltrifluoroborates are widely used in several types of allylation processes,[35] reaction of **1a** with either allylB(pin) or potassium allyltrifluoroborate, however, resulted in intractable material at the expense of the dienone substrate. When allylstannane **2d**, a stronger nucleophilie than allylsilane,[36] was employed, we found that its reaction with **1a** in the presence of BF_3·OEt_2 provided a diastereomeric mixture of allylation products, and notably tributyltin-appended [3+2] adducts were not formed to any extent (entry 1 vs.

entry 8). This case indicated that the elimination of the tributyltin moiety following allylstannane addition to the Nazarov intermediate (intermediate **IV**, X = $SnBu_3$) occurred rapidly in analogy to the Keck–type allylation.[37] With this encouraging result in hand, $TiCl_4$ was then employed as the Lewis acid as it gave an excellent reaction profile in the previous example using allylsilane as the trapping agent. While the yield for $TiCl_4$-mediated reaction of **1a** and **2d** was improved (entry 8 vs. entry 9), the diastereofacial selectivity of allylation unexpectedly remained low. Interestingly, cyclization of **1a** under treatment with **2d** and TMSOTf gave a diastereomeric mixture (ca. 1:5) of silyl enol ethers **7** and **8** in good combined yield. Compound **7** and **8** displayed an unusual stability against typical workup procedure and silica gel chromatography; the same product type was not isolated in related interrupted Nazarov reactions using other carbon-based nucleophiles together with TMSOTf (vide infra). Instead of workup with basic aqueous solution, the same reaction could be quenched with strong acid such as TsOH releasing homoallyl ketones **5a** and **6a** in one pot (entry 11). Use of the sterically more demanding trisubstituted stannane **2e** furnished the analogous prenylated products **5b** and **6b** in surprisingly good yields, generating adjacent quaternary carbon centers in the process (entry 12).

We have demonstrated selective production of either α–allylated cyclopentanones or [3+2] adducts could be achieved by varying Lewis acid and/or allyl donor. However, there are still demands for further improvement on diastereofacial selectivity of the allylation step.[38] Also, synthetic implication of **7/8** for intercepting additional electrophilic reagents in tandem would be an interest of further investigation.

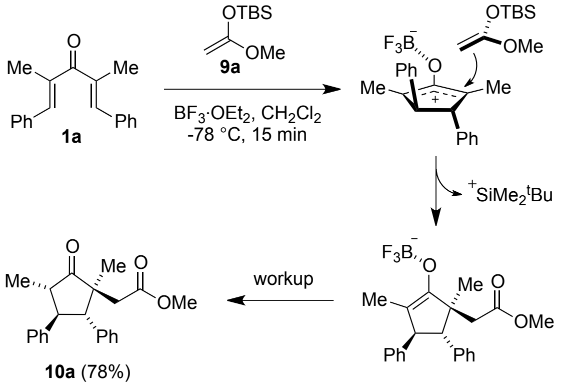
2.2.2. Intermolecular Trapping of the Nazarov Intermediate with Silyloxyalkenes

Mahmoud and West reported that vinyl sulfide underwent [3+2] trapping with the Nazarov intermediate (Eq 2). This observation prompted us to investigate the use of other heteroatom-substituted alkenes with higher nucleophilicity; we envisaged such change might increase the propensity of making simple α–attack products (Scheme 21).



Scheme 21. Design Plan (II)

A model reaction of dienone **1a** and silyl ketene acetal **9a** was carried out in the presence of $BF_3{\cdot}OEt_2$ furnishing keto ester **10a** as a single diastereomer (Scheme 22); its structure was unambiguously determined by X–ray diffraction analysis. This synthetic sequence resulting in two carbonyl groups in a 1,4-relationship can be considered as a homologous Mukaiyama reaction.[39] The relative configuration of **10a** implied that **9a** attacked on the Nazarov intermediate from the face opposite to the adjacent phenyl ring, and a highly stereoselective protonation of the resulting boron enolate secured the 1,4-dicarbonyl product **10a**.[40] We again experimentally validated our proposal, i.e. the evolution of the Nazarov intermediate could be controlled by the selection of trapping modalities residing on two extremes of the nucleophlic scale (Scheme 21).[41]

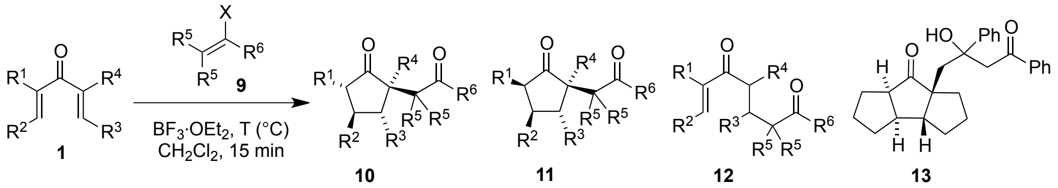


Scheme 22. Interrupted Nazarov Reaction of **1a** with Silyl Ketene Acetal **9a**

The scope of this domino process with dienones **1a**-**1e** and various oxygenated alkenes **9a**-**9f** was examined (Table 2). Using prototypical dienone **1a**, dimethyl ketene acetal **9b**, *S*,*O*–ketene acetal **9c**, and silyl enol ethers **9d**,**e** were successfully applied as trapping reagents to yield the corresponding ester **10b**, thioester **10c**, ketone **10d**, and aldehydes **10e**/**11e** (entries 2–5).[42] Utilization of methoxypropene **9f** as the π-trap, however, gave a complex mixture, in which neither homologous Mukaiyama adducts nor simple cyclopentenones could be identified. Presumably, it was a result of lacking favorable termination event of intermediate **VI** (X = OMe). As in the case of **1a**, interrupted Nazarov reactions of **1b** with **9b–d** proceeded smoothly to give densely substituted cyclopentanones (entries 7–9).

The reaction of dienones **1c** and **1d** were studied to test the regioselectivity of the trapping event where unsymmetrically substituted oxyallyls were derived. While Mukaiyama-Michael reaction of dienone **1d** with ketene acetal **9a** was unavoidable under various conditions (entry 10), complete regioselective attack of weaker nucleophiles **9c**,**d** on the less substituted terminus of the cyclopentenyl cation originated from **1c** gave **10j** and **10k** respectively in good yields (entries 11 and 12). With monocyclic dienone substrate **1d**, selective addition of **9c** at the bridgehead carbon of cyclized cationic intermediate furnished **10l** and undesired conjugate adduct **12l** (entry 13). On the other hand, interrupted Nazarov reaction of **1d** in the presence of silyl enol ether **9d** did not result in any premature

Table 2. Scope of Homologous Mukaiyama Reactions[a]



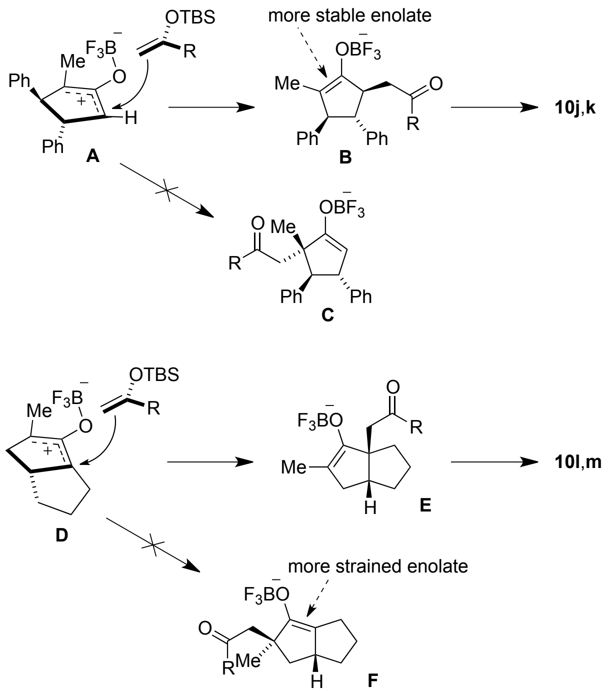
1b: $R^1 = R^2 = R^3 = R^4 = Me$
1c: $R^1 = Me; R^2 = R^3 = Ph; R^4 = H$
1d: $R^1 = Me; R^2 = H; R^3 = R^4 = (CH_2)_3$
1e: $R^1 = R^2 = (CH_2)_3; R^3 = R^4 = (CH_2)_3$

Entry	Dienone	Alkene	R^5	R^6	X	T (°C)	Products (yield %)[b]
1	**1a**	**9a**	H	OMe	OTBS	−78	**10a** (78)
2	**1a**	**9b**	Me	OMe	OTMS	−78	**10b** (87)
3	**1a**	**9c**	H	S*t*-Bu	OTBS	−78	**10c** (98)
4	**1a**	**9d**	H	Ph	OTBS	−78	**10d** (78)
5	**1a**	**9e**	Me	H	OTMS	−78	**10e** (44)/**11e** (19)
6	**1a**	**9f**	H	Me	OMe	−78	complex mixture
7	**1b**	**9b**	Me	OMe	OTMS	rt	**10f** (59)
8	**1b**	**9c**	H	S*t*-Bu	OTBS	0	**10g** (64)
9	**1b**	**9d**	H	Ph	OTBS	0	**10h** (66)
10	**1c**	**9a**	H	OMe	OTBS	0	**12i** (67)
11	**1c**	**9c**	H	S*t*-Bu	OTBS	0	**10j** (71)
12	**1c**	**9d**	H	Ph	OTBS	0	**10k** (66)
13	**1d**	**9c**	H	S*t*-Bu	OTBS	0	**10l/12l** (67; 7:1)[c]
14	**1d**	**9d**	H	Ph	OTBS	0	**10m/11m** (66; 25:1)[d]
15	**1e**	**9c**	H	S*t*-Bu	OTBS	rt	**10n/12n** (78; 3:1)[c]
16	**1e**	**9d**	H	Ph	OTBS	rt	**13** (62)[e]

[a] Standard procedure: $BF_3·OEt_2$ (1.1 equiv) was added to a solution of dienone **1** and alkene trap (2 equiv) in CH_2Cl_2 (0.05 M in **1**) at the indicated temperature. After 15 min, the reaction was quenched with satd aq $NaHCO_3$, followed by extraction, drying ($MgSO_4$) and chromatographic purification. [b] Isolated yield. [c] Inseparable mixture; the ratio was determined by integration of ^1H NMR signals (*t*-butyl groups). [d] Inseparable mixture; the ratio was determined by integration of ^1H NMR signals (angular methyl groups). [e] A mixture of two diastereomers (ca. 20:1). The minor product was inferred to be isomeric at the carbinol carbon.

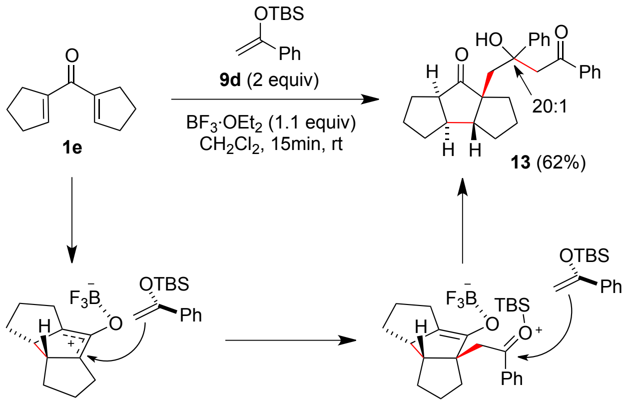
Michael addition, instead yielding angular-substituted diquinanes **10m/11m** (entry 14). The high regioselectivity seen with substrate **1c**,**d** merits some comments (Scheme 23). For the nucleophilic attack of differentially substituted cyclic oxyallyl cation **A**, the less substituted end would be more accessible; also, incipient formation of more substituted enolate **B** rather than **C** may be favored.

Alternatively, selective attack at the bridgehead carbon of cation **D** may be accounted for by the reduced strain encountered by enolate **E** in respect to **F**.



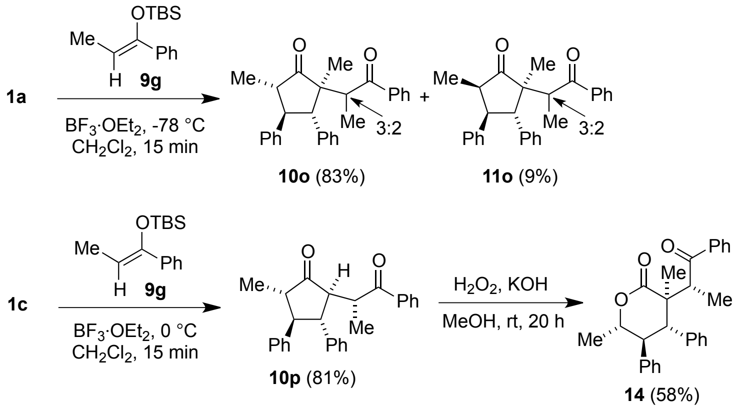
Scheme 23. Rationale for Observed Regioselectivity

In the case of less reactive Nazarov substrate **1e** with **9c**, it was necessary to perform the reactions at higher temperature; however the formation of **10n** was still accompanied by significant proportion of Michael adduct **12n** (entry 15). Intriguingly, bicyclic dienone **1e** reacted with silyl enol ether **9d** in the presence of $BF_3{\cdot}OEt_2$ to afford a higher-order adduct **13** containing a hydroxy group and two phenyl rings. A plausible mechanism that accounts for the formation of **13** is shown in Scheme 24; the overall process represents a novel multicomponent coupling sequence initiated by the Nazarov cyclization.



Scheme 24. Domino Electrocyclization/Homologous Mukaiyama Addition/Mukaiyama Aldol Sequence

We aimed to probe the viability of stereocontrol adjacent to the exocyclic carbonyl group through the employment of (*Z*)-silyl enol ether **9g** (Scheme 25). Under standard conditions, **1a** reacted with **9g** to give diketones **10o** and **11o**, each comprising a pair of diastereomers (ca. 3:2 ratio). Conversion of **11o** into **10o** was readily achieved by treatment with catalytic amount of DBU; nevertheless, no epimerization took place at the branched carbon on the side chain. In contrast to this disappointing level of selectivity, the related reaction with **9g** employing dienone **1c** furnished a single stereoisomer **10p**, in which five contiguous stereocenters were established in a single operation.



Scheme 25. Stereoselective Interrupted Nazarov Reaction with a (*Z*)-Enol Silyl Ether

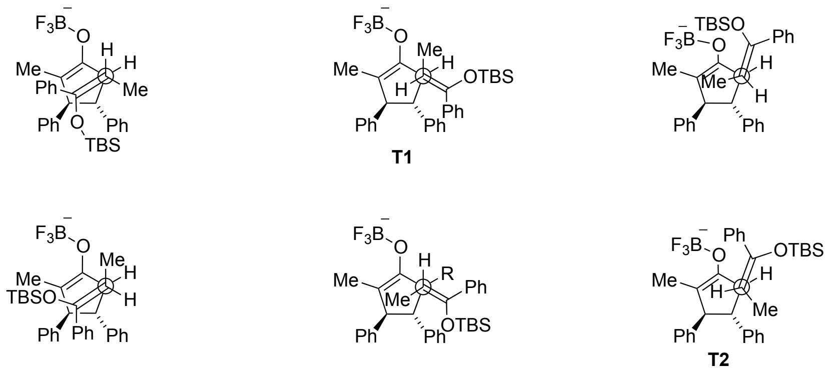
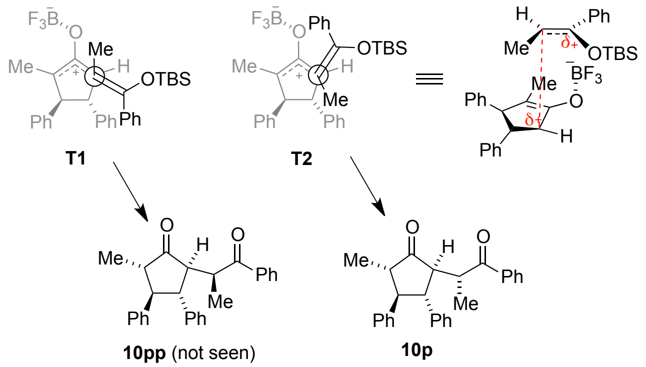


Figure 1. Six Possible Nucleophile Approaches



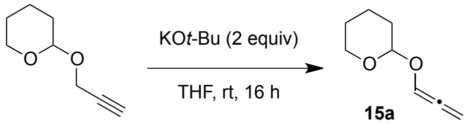
Scheme 26. Two Open Transition States with less anticipated steric demand for the Reaction of (*Z*)–**9g**

Although it was not feasible to fully resolve the relative configuration of **10p** by NMR technique,[43] subsequent X-ray diffraction analysis of its chemical derivative **14**, obtained from a highly chemo- and regioselective Baeyer-Villiger oxidation, allowed unambiguous assignment of relative configuration. The excellent diastereoselectivity observed in the reaction of **1c** and **9g**, in stark contrast to that of **1a** and **9g**, marked the significant stereochemical influence of the C2-substituent of the dienone substrate. We attempted to rationalize the high level of stereocontrol by estimating relative energy of potential transition states. As shown in Figure 1, **T1** and **T2** were anticipated to have relatively small steric demand among several possibilities. Of these two, **T2**, which will ultimately lead to relative configuration shown for **10p**, may acquire additional stabilization through interactions of developing partial charges (Scheme 26). On the other hand, replacement of the C2–hydrogen with a methyl group, as in **1a**, increases the steric demand around the reaction center corresponding to **T1** and **T2**, therefore rendering other possible transition structures to compete, and leading to the minimal selectivity observed.

2.2.3. Intermolecular Trapping of the Nazarov Intermediate with Alkoxyallenes

We have demonstrated that the interrupted Nazarov reaction of enol-type nucleophiles, effectively a homologous Mukaiyama reaction, is general and efficient in making diverse 1,4-dicarbonyl products. We sought to extend the scope of polar addition by electron-rich π-nucleophiles. Use of oxygenated allenes as traps was proposed, with the expected conjugated enal products resembling homologous Morita-Baylis-Hillman-type [44] (MBH–type) adducts through trapping by a formal α-acylvinyl anion equivalent.[45]

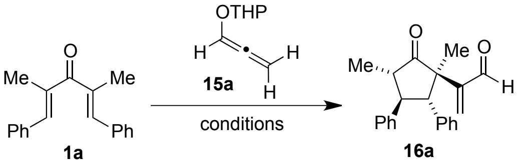
Preliminary experiments showed that silyl allenol ethers were very prone to hydrolysis upon purification. On the other hand, the THP-protected counterpart **15a**, prepared via base-catalyzed isomerization of the corresponding propargyl ether,[46] is more durable respective to purification and handling, so it was carried forward in following studies (Eq 4).



(4)

Treatment of **1a** and **15a** with the optimized conditions for the homologous Mukaiyama reactions yielded the desired α-(2-propenalyl) cyclopentanone **16a** in modest yield together with a fair amount of unidentifiable material (Table 3, entry 1). Fortunately, the structural assignment of **16a** was

Table 3. Optimization of the Interrupted Nazarov Reaction Using Allenol Ether **15a** as a Trap[a]



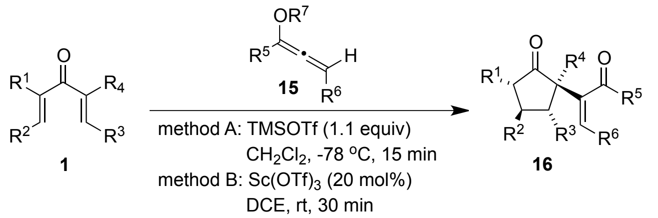
Entry	Reaction conditions	Yield % of **16a**[b]
1	$BF_3 \cdot OEt_2$ (1.1 equiv), CH_2Cl_2, −78 °C, 15 min	24
2	TMSOTf (1.1 equiv), CH_2Cl_2, −78 °C, 15 min	63
3	$Cu(OTf)_2$ (20 mol%), $(CH_2Cl)_2$, rt, 30 min	15
4	$Zn(OTf)_2$ (20 mol%), $(CH_2Cl)_2$, rt, 30 min	47
5	$Sc(OTf)_3$ (20 mol%), $(CH_2Cl)_2$, rt, 30 min	58

[a]Dienone **1a** and **15a** were stirred with Lewis acid at the indicated temperature. [b]Isolated yield.

ascertained by X–ray diffraction analysis. Not unexpectedly, a similar stereochemical outcome to that seen previously with oxygenated alkenes, arising from approach of the trapping reagent from the face opposite the adjacent bulkyl substituent, was observed. Research efforts were then focused on determining the optimal conditions for the reaction (Table 3). When TMSOTf was employed as the Lewis acid, domino electrocyclization/formal MBH reaction proceeded smoothly giving **16a** in good yield. We also examined the effect of catalytic amount of metal Lewis acids, including $Cu(OTf)_2$, $Zn(OTf)_2$ and $Sc(OTf)_3$, and found that higher temperature and longer reaction time were crucial for those cyclizations (Table 3, entries 3–5). With $Cu(OTf)_2$, a complex mixture was produced in which **16a** could only be isolated in low yield. While zinc Lewis acid is relatively unexplored in Nazarov chemistry, the reaction of **1a** and **15a** catalyzed by $Zn(OTf)_2$ gave the desired product in 47% yield. Utilization of $Sc(OTf)_3$ as catalyst led to the formation of **16a** in a yield comparable to the example using stoichiometric amount of TMSOTf.

The scope of this process with other dienone substrates and allenol ethers was then evaluated, where both TMSOTf and $Sc(OTf)_3$ were tested as the Lewis acid promoter (Table 4). In the presence of TMSOTf, symmetrical dienones **1f**,**g**

Table 4. Scope of Formal Morita-Baylis-Hillman Reactions

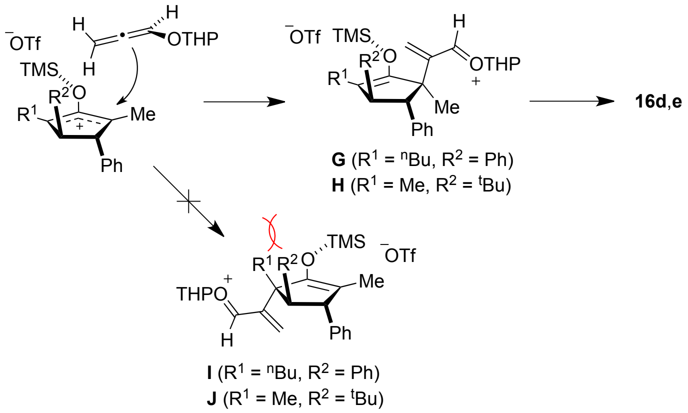


1f: $R^1 = R^4 = Me$; $R^2 = R^3 =$ 4-OMePh
1g: $R^1 = R^4 = Me$; $R^2 = R^3 =$ 4-ClPh
1h: $R^1 =$ *n*-Pr; $R^2 = R^3 = Ph$; $R^4 = Me$
1i: $R^1 = R^4 = Me$; $R^2 =$ *t*-Bu; $R^3 = Ph$

Entry	Dienone	Allene	R^5	R^6	R^7	Method[a]	Product (yield %)[b]
1	**1a**	**15a**	H	H	THP	A	**16a** (63)
2	**1f**	**15a**	H	H	THP	A	**16b** (37)
3	**1g**	**15a**	H	H	THP	A	**16c** (58)
4	**1h**	**15a**	H	H	THP	A	**16d** (63)
5	**1i**	**15a**	H	H	THP	A	**16e** (42)
6	**1a**	**15b**	Ph	H	TBS	A	**16f** (23)
7	**1a**	**15c**	H	Ph	THP	A	**16g** (46)
8	**1h**	**15c**	H	Ph	THP	A	**16h** (51)
9	**1a**	**15a**	H	H	THP	B	**16a** (58)
10	**1f**	**15a**	H	H	THP	B	**16b** (55)
11	**1g**	**15a**	H	H	THP	B	**16c** (47)
12	**1h**	**15a**	H	H	THP	B	**16d** (51)
13	**1i**	**15a**	H	H	THP	B	**16e** (33)

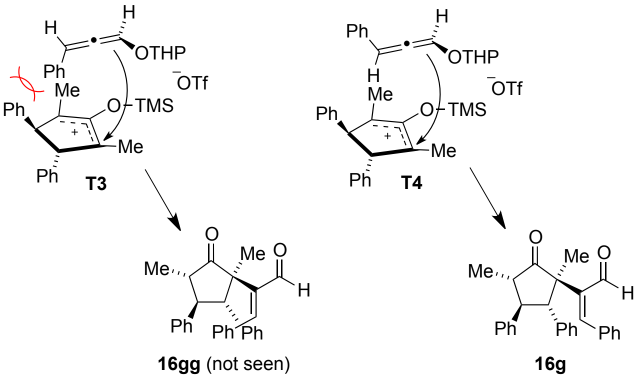
[a] Method A: TMSOTf (1.1 equiv) was added to a solution of dienone **1** and allene trap (2 equiv) in CH_2Cl_2 (0.1 M in **1**) at –78 °C. After 15 min, the reaction was quenched with satd aq $NaHCO_3$, followed by extraction, drying ($MgSO_4$) and chromatographic purification; Method B: $Sc(OTf)_3$ (0.2 equiv) was added to a solution of dienone **1** and allene trap (2 equiv) in 1,2–dichloroethane (0.1 M in **1**) at rt. After 30 min, the reaction was quenched with satd aq $NaHCO_3$, followed by extraction (CH_2Cl_2), drying ($MgSO_4$) and chromatographic purification. [b] Isolated yield.

reacted with **15a** to give single α-addition products **16b** and **16c** respectively (entries 2 and 3). In the examples of unsymmetrically substituted dienones **1h** and **1i**, excellent regioselectivity in the trapping event was observed giving in each case single products **16d** and **16e** (entries 4 and 5). It is surprising to realize that the β-substituent, which should ultimately reside on the opposite face to the incoming nucleophile, plays a critical role in regiochemical control. Such high level of selectivity may originate from avoiding non-bonded repulsion built up between R^1 and R^2 as the reaction progressed toward intermediate **I** or **J** (Scheme 27).



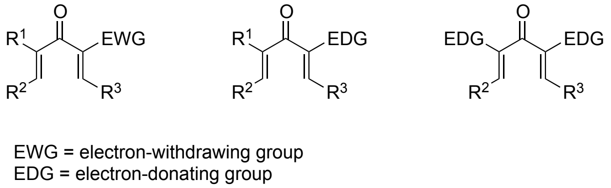
Scheme 27. Regioselective Capture of the Nazarov Intermediate by allene **15a**

TMSOTf-mediated interrupted Nazarov reaction of **1a** and 1-phenyl siloxy allene **15b** was less efficient (entry 6) possibly owing to the instability of **15b** in acidic media. Utilizing 3-phenyl allenyl ether **15c** furnished a single adduct **16g** (entry 7) whose stereochemical assignment was supported by 2D TROESY experiment; notably, the reaction has complete control over the alkene geometry thus introducing a 2-(*cis*-cinnamaldehyde) segment at the α-carbon of cyclic ketone. In addition, unsymmetrical dienone **1h** reacted with **15c** cleanly to give **16h** with excellent regio- and diastereoselectivity (entry 8). Regarding the high level of *cis*-selectivity, approach of axially chiral allene **15c** to the Nazarov intermediate should favor a trajectory that can alleviate non-bonded interactions resulting in the production of *cis*-alkene (**T3** vs. **T4**, Scheme 28).



Scheme 28. Diastereoselective Capture of the Nazarov Intermediate by allene **15c**

A catalytic version of the interrupted Nazarov reaction using dienone **1a**,**f**–**i** and allene **15a** with $Sc(OTf)_3$ was pursued (entries 9–13). In general, excellent stereoselectivity and moderate yields were observed in parallel to the results with the use of full equivalent of TMSOTf. As noted by Frontier and Eisenberg, the catalytic Nazarov process was typically limited to strongly polarized substrates (Figure 2).[47] We believed that the function of trapping agents is essential to the success of the present work utilizing relatively unactivated dienones with catalytic promoter.[48] Presumably, the products being intercepted by intermolecular nucleophiles experience greater steric crowding, and are therefore less likely to remain bound to the catalyst and inhibit turnover.

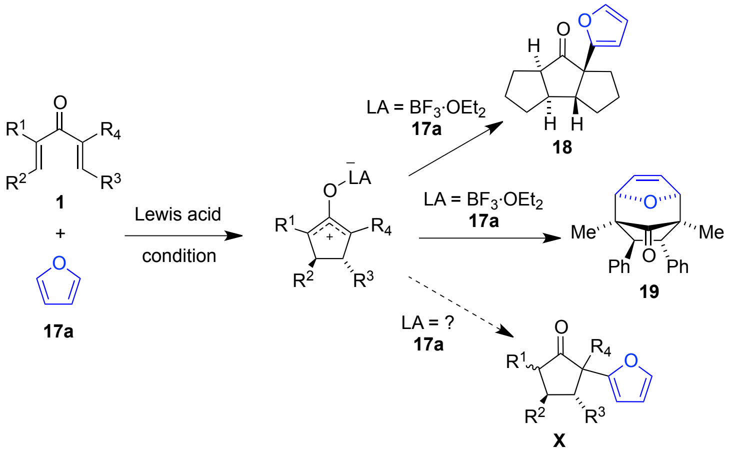


EWG = electron-withdrawing group
EDG = electron-donating group

Figure 2. Polarized Nazarov Substrates

2.2.4. Intermolecular Trapping of the Nazarov Intermediate with Heterocycles

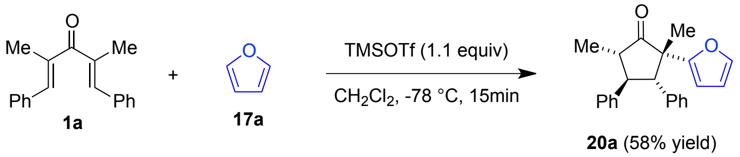
Oxyallyl cations, which have been invoked in various reaction pathways, have been shown to be particularly effective partners in [4+3] cycloadditions with furan and simple 1,3-dienes.[49] Our laboratory has described that acyclic divinyl ketone **1a** and furan reacted in the presence of $BF_3 \cdot OEt_2$ furnishing keto-bridged cycloadducts **19** through a domino electrocyclization/[4+3] cycloaddition sequence (Scheme 29). On the other hand, upon treatment with $BF_3 \cdot OEt_2$, Nazarov cyclization of bis(cyclopentenyl) ketone **1e** was followed by Friedel-Crafts-type reaction with furan yielding α-furyl triquinane **18** in good yield and excellent diastereoselectivity (Scheme 29). Rieder *et al.* attributed the distinct reaction pathway of **1a** and **1e** with furan to the conformational effects associated with the Nazarov intermediate following electrocyclization. More specifically, the oxyallyl derived from **1e** may not be able to undergo [4+3] cycloaddition owing to severe steric demand likely encountered in the compact transition state; also, simple eliminative termination may be impeded as a result of diminished conformational mobility in tricyclic framework therefore the cationic intermediate may persist long enough to be intercepted by intermolecular arene traps.



Scheme 29. Design Plan (III)

We considered that introduction of an aryl functionality α to a ketone is a highly valuable transformation.[50] In line with the theme for this work, we questioned that whether the scope of umpoled Friedel-Crafts trapping seen with **1e** could be extended to simple acyclic dienones, so a wide range of α-aryl cyclopentanones **X** could be synthesized via a general interrupted Nazarov strategy (Scheme 29).[51] It is known that the electrophilicity of oxyallyl cations is dictated by the degree of covalency between Lewis acid center and oxygen atom. As such, the course of reaction with furan may be controlled, wherein by increasing electrophilic character associated with oxyallyls, stepwise bond-forming mechanism can be favored over concerted cycloaddition.[52] By employing a suitable Lewis acid, we envisioned that electrophilic aromatic substitution of furan could be a dominant pathway, followed by loss of a proton to yield furylation products.

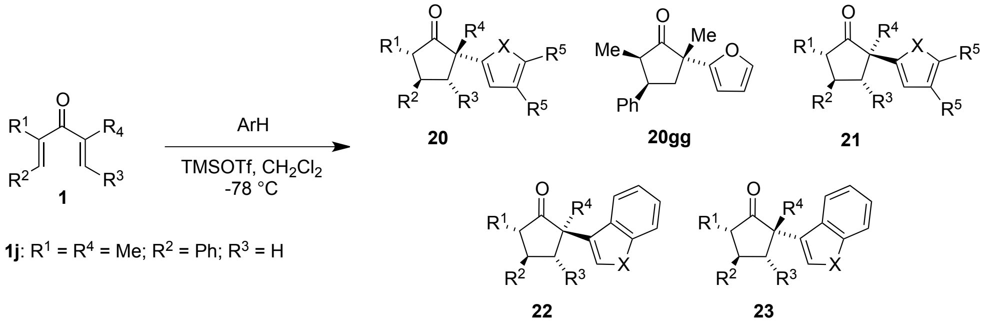
Serendipitously, we found that dienone **1a** and furan reacted in the presence of TMSOTf to give a single diastereomer **20a**, and no keto-bridged product **19** derived from [4+3] cycloaddition was observed (Eq 5). Later the structure of **20a** was confirmed through single crystal X–ray diffraction analysis. It is worthy to note that α-furyl substituent was installed *syn* to the adjacent phenyl ring that is in contrast to the aforementioned results with oxygenated alkenes and allenes.[53]



(5)

With the new scenario disclosed, we proceeded to examine the generality of the α-arylation protocol with other acyclic dienones and heteroaromatic nucleophiles (Table 5). When dienone **1a** was treated with disubstituted furan **17b**, the desired product **20b** was obtained in good yield. Trapping of **1a** with pyrrole **17c** was very efficient, but the diastereofacial selectivity of electrophilic

Table 5. Domino Electrocyclization/Friedel-Crafts-Type Reaction Sequences[a]



1j: $R^1 = R^4 = Me$; $R^2 = Ph$; $R^3 = H$

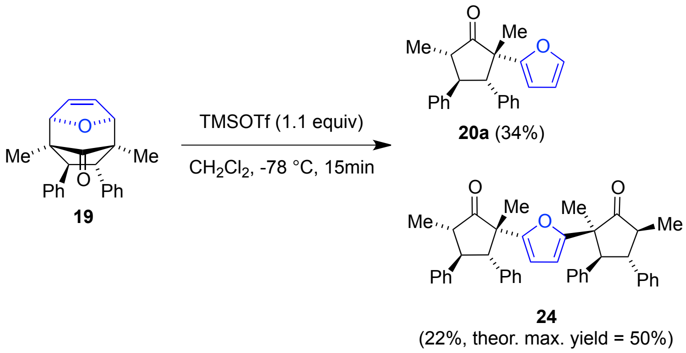
Entry	Dienone	ArH	X	R^5	Products (yield %)[b]
1	**1a**	furan (**17a)**	O	H	**20a** (58)
2	**1a**	2,3–dimethylfuran (**17b**)	O	Me	**20b** (90)
3	**1a**	1–methylpyrrole (**17c**)	NMe	H	**20c**/**21c** (98; 3:1)[c]
4	**1a**	thiophene (**17d**)	S	H	intractable material
5	**1a**	1,3–dimethoxybenzene (**17e**)	n/a	n/a	intractable material
6	**1c**	furan (**17a**)	O	H	**21d** (69)
7	**1c**	2,3–dimethylfuran (**17b**)	O	Me	**21e** (39)
8	**1h**	furan (**17a)**	O	H	**20f** (66)
9	**1j**	furan (**17a)**	O	H	**20g**/**20gg** (61; 3:1)[d]
10	**1a**	indole (**17f**)	NH	n/a	**22a** (48)/**23a** (7)
11	**1a**	1–tosyllindole (**17g**)	NTs	n/a	intractable material
12	**1a**	1–methylindole (**17h**)	NMe	n/a	**22b** (40)/**23b** (32)
13	**1a**	1–benzylindole (**17i**)	NBn	n/a	**22c** (92)
14	**1h**	1–benzylindole (**17i**)	NBn	n/a	**22d** (83)
15	**1j**	1–benzylindole (**17i**)	NBn	n/a	**23e** (74)

[a] Standard procedure: TMSOTf (1.1 equiv) was added to a solution of dienone **1** and heteroarene trap (2 equiv) in CH_2Cl_2 (0.05 M in **1**) at –78 ºC. Once the dienone was completely consumed according to TLC analysis (generally less than 30 min), the reaction was quenched with satd aq $NaHCO_3$, followed by extraction, drying ($MgSO_4$) and chromatographic purification. [b] Isolated yield. [c] Inseparable mixture; the ratio was determined by integration of ^1H NMR signals (pyrrole methyls) [d] Inseparable mixture; the ratio was determined by integration of ^1H NMR signals (singlet methyls).

aromatic substitution was modest. On the other hand, the employment of thiophene and 1,3-dimethoxybenzene as the trap gave intractable material (entries 4 and 5). Three unsymmetrically substituted dienones **1c**,**h**,**j** were also examined in order to probe the regioselectivity of this process (entries 6–9). In the event, complete regioselective capture of the cationic intermediate was seen in each case providing α-(2-furyl) cyclopentanone in moderate to good yields.[54] Interestingly, 1D NOESY studies of trapped products derived from divinyl ketone **1c** suggested an all-*trans* stereochemistry for **21d** and **21e** (entries 6 and 7); based on other trapping examples (ex. **20a**), we had expected predominant or exclusive attack *syn* to the adjacent phenyl substituent. We attributed the reversed face selectivity to the degree of substitution of the Nazarov oxyallyl that could be an important factor for its electrophilicity and reactivity.

As noted in the previous report, arene capture of the Nazarov intermediate derived from bicyclic ketone **1e** with thiophene (**18d**) and 1,3-dimethoxybenzene (**18e**) was exceptionally effective. However, the reactions of acyclic dienone **1a** with **18d** and **18e** respectively gave intractable material. The fact that we could not isolate arylation product was puzzling and prompted us to reconsider whether the process truly entails an electrophilic-aromatic-substitution mechanism. In the case of **1a** with furan, one may presume that inceptive formation of [4+3] adduct **19** was followed by an acid-mediated ring cleavage,[55] in a highly stereoselective fashion, to give α-furyl cyclopentanones **20a**. If it is the case, failure to observe any trapping event of **1a** with **17d**,**e** might be accounted by two factors: (1) dimethoxybenzene and thiophene, possessing higher degree of aromaticity relative to furan and pyrrole,[56] were incompatible cycloaddition partners in the first place, and (2) the oxyallyl cation derived from the acyclic dienone did not persist long enough to undergo intermolecular Fridel-Crafts trapping.

To gain more insights into the mechanism, we first prepared the [4+3] adduct **19** following the procedure reported by Wang *et al.*,[17a] and we fortuitously verified its structural assignment by single crystal X-ray diffraction analysis. When we treated compound **19** with TMSOTf at –78 °C for 15 min, **19** was completely consumed, and **20a** was isolated in 34% yield along with an atypical product **24** having two pieces of cyclopentanyl moiety linked through the 2,5–positions of a furan ring (Scheme 30). The structural assignment of **24** was unequivocally determined based on X-ray diffraction analysis, which clearly showed the C2-symmetry of **24** (Figure 3).



Scheme 30. Mechanistic Studies

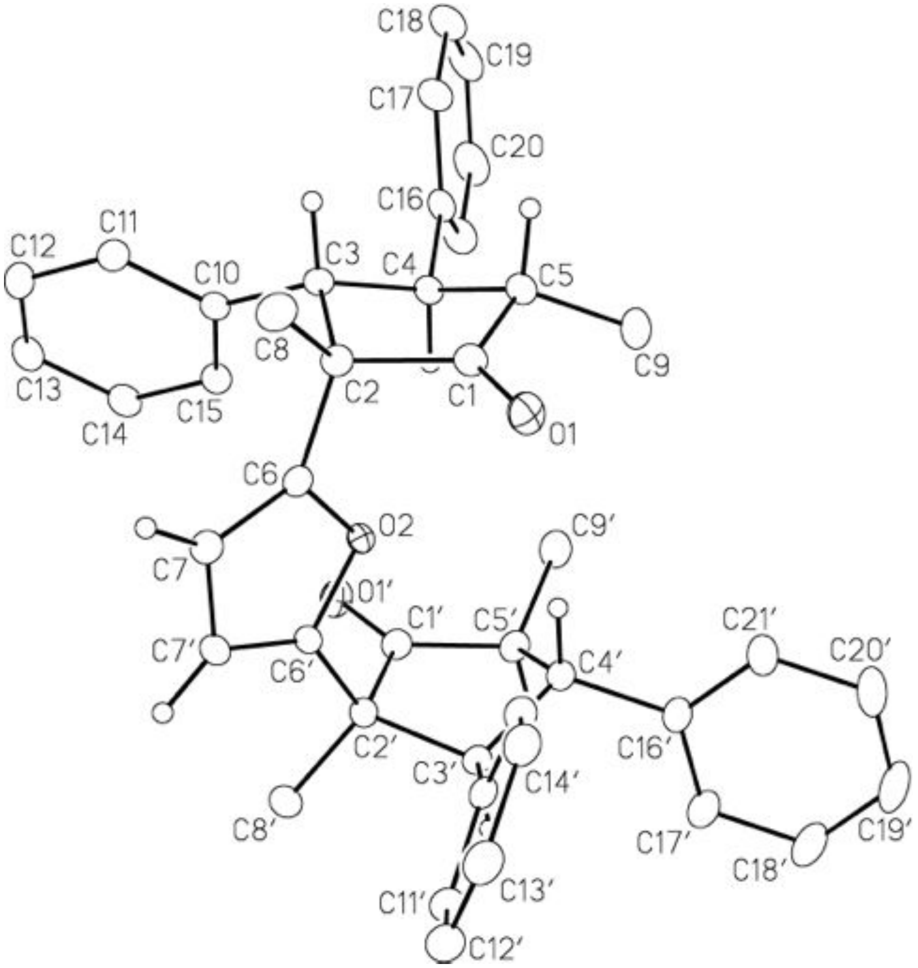
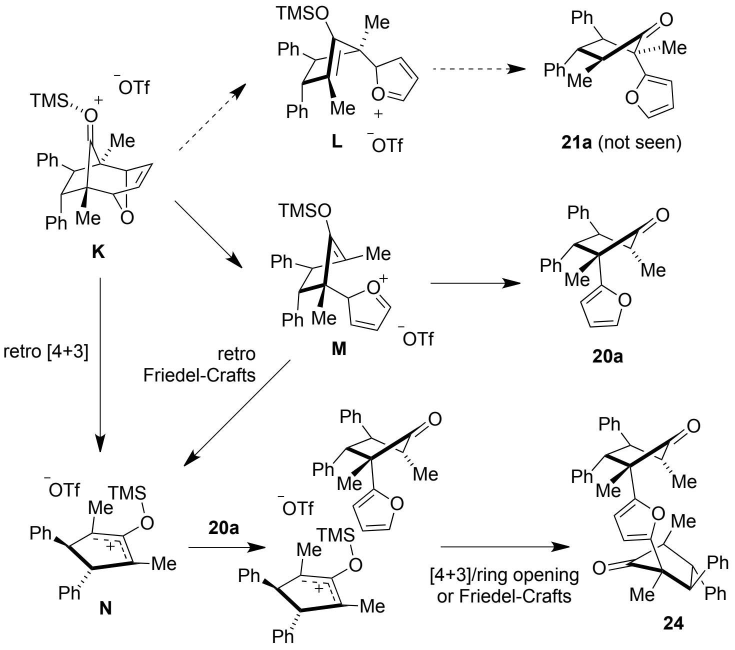


Figure 3. ORTEP Drawing of **24**



Scheme 31. Proposed Mechanism

It is noteworthy that Grob-type fragmentation of TMSOTf/**19** complex **K** only produced intermediate **M**, in lieu of **L**, where the carbon-carbon bond antiperiplanar to the phenyl substitution was selectively cleaved (Scheme 31). This remarkable selectivity may be rationalized by subtle stereoelectronic effects imposed by the *exo*-phenyl group.[57] In general, bond strength is inversely proportional to bond length.[58] The bond-weakening effect of C5–C6 in comparison to C1–C2 is evident in crystallographic data of compound **19**, in that the interatomic distance of C5–C6 (1.5773Å) is longer than the one of C1–C2 (1.5646Å) (Figure 4). As for the formation of **24**, we hypothesized that silyloxyallyl cation **N** may arise from either **K** via a retro-[4+3] cycloaddition or **M** via a retro-Friedel-Crafts reaction; subsequently intermediate **N** could be captured by the furan of ring-opened product **20a** providing C2-symmetrical bis(cyclopentanyl) furan **24** (Scheme 31). More intriguingly, the fact that we could not detect any meso isomer implied the occurrence of matched/mismatched interactions between enantiomers of racemate **20a** and rac-intermediate **N**.

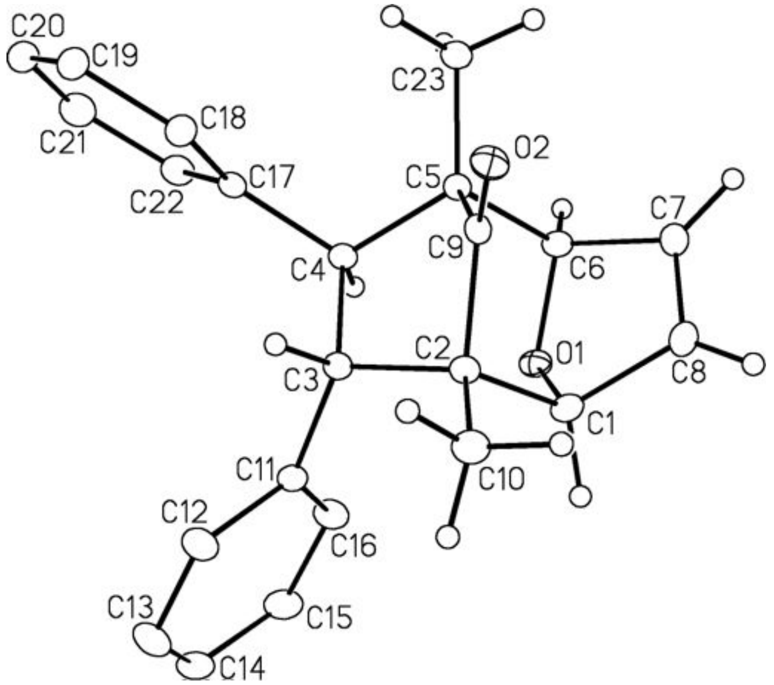


Figure 4. ORTEP Drawing of [4+3] Adduct **19**

Although we have experimentally demonstrated that [4+3] adduct **19** could be an intermediary species for the furylation process giving **20a**, further computational investigations are in demand to fully understand the mechanistic details for the apparent domino electrocyclization/Fridel-Crafts reaction sequence.

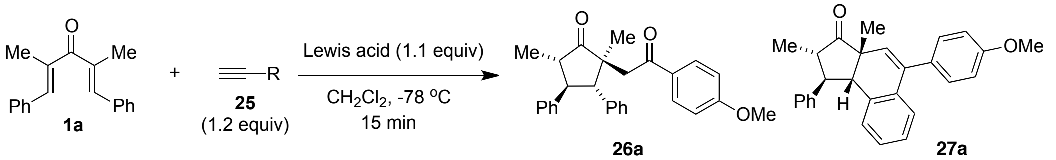
Finally, another class of nitrogen heterocycles, indole,[59] was studied (Table 5, entries 10–15).[60] The TMSOTf-mediated reaction of **1a** and indole **17f** provided the diastereomeric trapped products **22a** and **23a** (ca. 7:1) together with several unidentifiable compounds. We envisioned that utilization of protected indoles as the trapping agents may offer cleaner reaction profiles. As such, tosylindole **17g** was first examined and later concluded as an incompetent nucleophile excluding further investigations on the use of electron–withdrawing protecting groups. Treatment of **1a** with methylindole **17h** in the presence of TMSOTf gave **22b** and **23b** in a 4:3 ratio, where the diastereofacial selectivity of indole addition was unfortunately low. However, interrupting the Nazarov cyclization of **1a** with benzylindole **17i** took place efficiently, furnishing a single interrupted Nazarov product, the structure of which was analyzed by X–ray diffraction analysis in which the relative stereochemistry of **22c** indicated **17i** approached *anti* to the adjacent phenyl substitution. The stereochemical outcome is in close analogy to the cases using enol-type traps, but is opposed to cases using furans. As **17i** was empirically determined as a superior indole donor in this process, we applied it to the reaction of other dienone substrates. With **1h**, indole-trapped product **22d** was produced in good yield and excellent regioselectivity. In the case of using less substituted dienone **1j**, the formation of **23e** was highly selective, as the site and face for trapping were less sterically encumbered.

2.2.5. Intermolecular Trapping of the Nazarov Intermediate with Alkynes

The use of carbon nucleophile in the interrupted Nazarov reactions permitted facile installation of carbon fragments onto cyclopentanoid skeleton where molecular complexity can be increased in a highly step-economic fashion. While the survey of the carbon-based traps engaged in interrupted Nazarov chemistry appears comprehensive (*vide supra*), it is noteworthy that the competence of alkynes to capture the Nazarov intermediate, to the best of our knowledge, remains unknown.[61] The relatively low nucleophilicity of alkyne, in comparison with its alkene counterpart,[36] can be a significant concern for its potential applications to the cationic cascade reaction, especially for an intermolecular version. However, given precedents of utilizing triple bond to intercept intermolecular carbon electrophiles,[62] we set out to investigate the feasibility of trapping cyclopentenyl cation with acetylene derivatives. During this study, a novel domino process initiated by the Nazarov reaction was disclosed, where the participation of alkyne diverted the initial electrocyclization to an unusual Kucherov-type alkylative hydration sequence[63] furnishing 1,4-diketone products.[64]

We commenced to examine the reaction between dienone **1a** and selected alkynes **25** in the presence of $BF_3{\cdot}OEt_2$ (Table 6, entries 1–4). Preliminary experiments indicated that silyl and alkyl substituted alkynes were not compatible

Table 6. A Brief Survey of Lewis Acids and Alkynes[a]

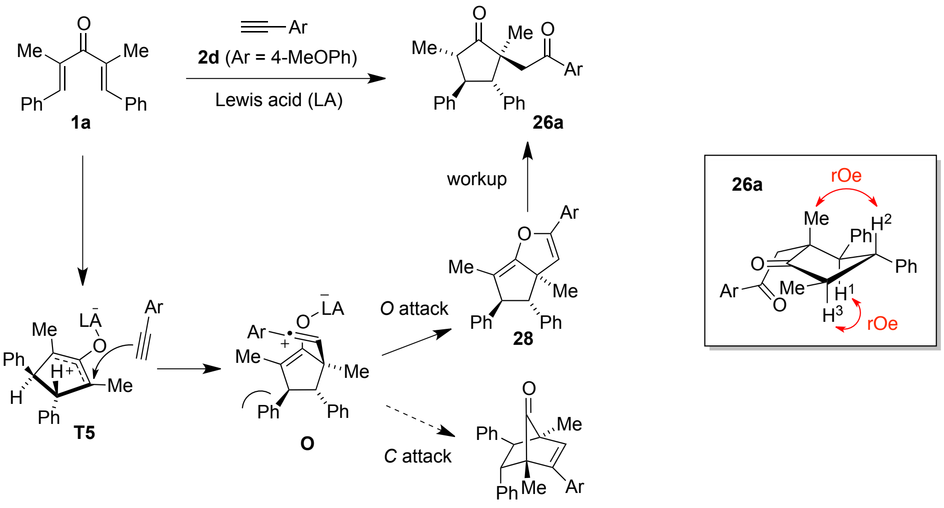


Entry	Alkyne	R	Lewis acid	Product(s)	Yield (%)[b]
1	**25a**	$SiMe_3$	$BF_3{\cdot}OEt_2$	–	n/a
2	**25b**	*n*-Bu	$BF_3{\cdot}OEt_2$	–	n/a
3	**25c**	Ph	$BF_3{\cdot}OEt_2$	–	n/a
4	**25d**	PMP[c]	$BF_3{\cdot}OEt_2$	**26a**	97
5	**25d**	PMP[c]	$AlCl_3$	**26a**	92
6	**25d**	PMP[c]	$FeCl_3$	**26a**	85
7	**25d**	PMP[c]	$TiCl_4$	**26a**	7[d]
8	**25d**	PMP[c]	$SnCl_4$	**26a** + **27a**	91 (3:2)

[a]Standard procedure: To a stirred solution of **1a** and alkyne (1.2 equiv) in CH_2Cl_2 (0.2 M in **1a**) at −78 °C was added Lewis acid (1.1 equiv). After 15 min, the reaction mixture was quenched with sat. aq $NaHCO_3$, followed by extraction with CH_2Cl_2, drying over $MgSO_4$, and chromatographic purification. [b]Isolated yield. [c]PMP = 4-MeOPh. [d]complex product mixture.

reaction partners yielding intractable material with complete consumption of the starting dienone. We directed our interests to apply aryl-terminated acetylenes as the nucleophilicity of triple bond could be easily tuned by varying aromatic substituents. Though phenylacetylene (**25c**) was an incompetent trapping agent, we were delighted to find that more electron-rich 4-ethynyl anisole (**25d**) did provoke the interception of the cyclized oxyallyl cation resulting in a type of interrupted Nazarov product, the structure of which was fully characterized and assigned as α-phenacyl cyclopentanone **26a**. It is worthy to emphasize that while 1,4-diketone is a common structural element existing in natural products and medicinal agents, an efficient synthesis of this motif is not so trivial in laboratories.

The mechanism for the formation of **26a** merits some discussions (Scheme 32). We presumed that the cationic Nazarov intermediate was initially intercepted by **25d** from the opposite face of the nearby phenyl group as shown in the transition state **T5**. The resulting vinyl cation **O** was then attacked by internal oxygen to give dihydrofuran **28** that was eventually hydrolyzed to **26a** during workup procedure. Of particular interest is that alkyne served as a latent enolate in the overall transformation. Notably, we did not observe any bridged bicyclic compound **29a** via formal [3+2] cycloaddtion of **25d** with the oxyallyl cation, presumably the productive interaction between sp^2 cation and oxygen end of the enolate is guided by HSAB (hard and soft acids and bases) principle.[65] In addition, potential nonbonded repulsion exerted from β' phenyl substitution (see intermediate **O**) can hamper the *C*-vinylation pathway.



Scheme 32. Proposed Mechanism for the formation of **26a** and assignment of its relative configuration based on 2D TROESY

Other metal chlorides (MCl_n) were surveyed in an attempt to divert the putative vinyl cation intermediate **O** through chloride transfer (Table 6, entries 5–8). In the event, aluminum(III) chloride and ferric(III) chloride both are effective promoters providing **26a** in good yields. On the other hand, titanium(IV) chloride that has been previously shown to deliver chloride in the Nazarov cyclization produced a complex product mixture in that **26a** could only be isolated in poor yield. When tin(IV) chloride was employed, a single diastereomer **27a**, an apparent interrupted Nazarov product possessing only one keto functionality, was formed along with regular product **26a**. Provisional structural assignment of **27a** was based on a series of spectral analyses (Figure 5). In addition, a notable spectroscopic feature of **27a** is the appearance of a long-range coupling between vinyl proton and the benzylic proton adjacent to the α quartenary center. Compound **27a** may arise from an intramolecular Friedel-Crafts reaction of cationic intermediate **P** that originated from alkyne attack from the same face as the β-phenyl substitution (Scheme 33, pathway a).[66] The distinctive reaction progress of diastereomerically trapped intermediates **P** and **Q** yielding **27a** and **26a** respectively is obscure. Nevertheless, this unusual result seen only with $SnCl_4$ appealed further investigation.

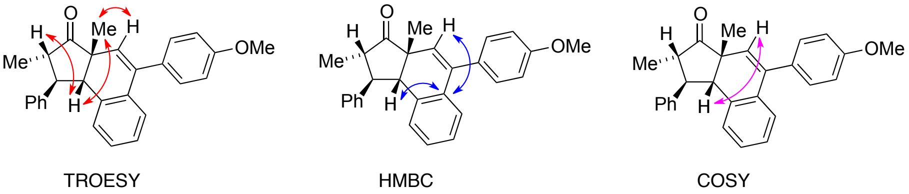
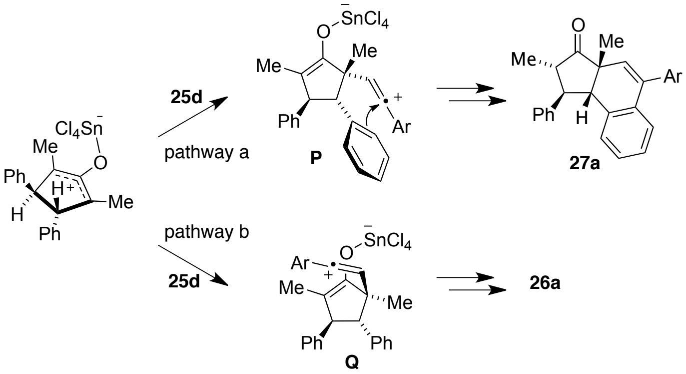
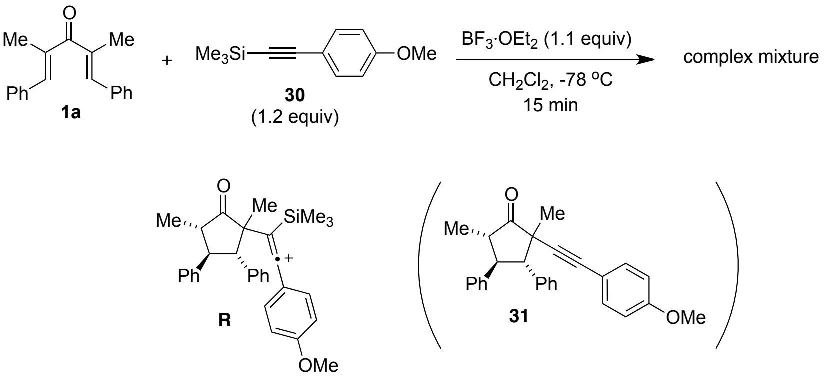


Figure 5. Diagnostic 2D NMR correlations of **27a**



Scheme 33. Divergent Reaction Pathways

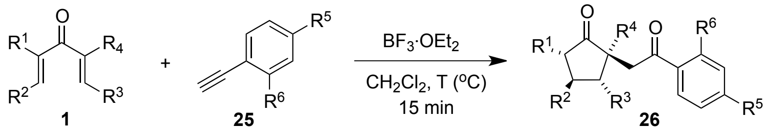
We sought to directly introduce alkynyl functionality at the α-carbon by employing trimethylsilyl-capped aryl acetylene **30** as the trap for the Nazarov intermediate (Scheme 34). We thought that elimination of silyl moiety from intermediate **R** would occur readily providing the desired product **31** if the trapping was successful. However, preliminary experiment was fruitless resulting in intractable material at the expense of dienone **1a**.



Scheme 34. Attempted Installation of Alkynyl Functionality at the α-Carbon

In order to probe the scope of this domino electrocyclization/Kucherov-type reaction sequence, various dienones along with alkynes were subjected to the optimized conditions noted above (Table 7). The influence of increasing steric impendence around the triple bond to the overall process was first tested. To our delight, reaction using alkyne trap **25e** with additional *ortho* methyl group proceeded smoothly thus allowing potential variation of substitution pattern at this position (entry 2). To ascertain the importance of the *para* substitution (R^5 of **25**), electronic nature of the aryl alkyne was altered by replacing the methoxy group to a methyl, a weaker electron-donating group. Although the yield of reaction involving **25f** is apparently lower (entry 3), it exhibited that a simple *para* alkyl substituent could provide sufficient stabilization to the presumed vinyl cation **O**. Symmetrical dienones **1g**,**k** reacted with alkynes to give the corresponding alkylative hydration products **26d–g** in moderate to good yields (entries 4–7). Considering alkyne is a relatively small nucleophile, the regioselectivity of the trapping event for unsymmetrical dienones was an issue to be addressed. In the use of dienone substrates **1i** and **1h**, complete regioselective capture of the oxyallyls with **25e** furnished single diastereomers **26h** and **26i** respectively. The regiochemical assignment of **26h** was based on the 2D HMBC experiment. Such

Table 7. Intermolecular Trapping of Nazarov Intermediates with Terminal Alkynes[a]



1k: $R^1 = R^4 = Me$; $R^2 = R^4 = i\text{-}Pr$

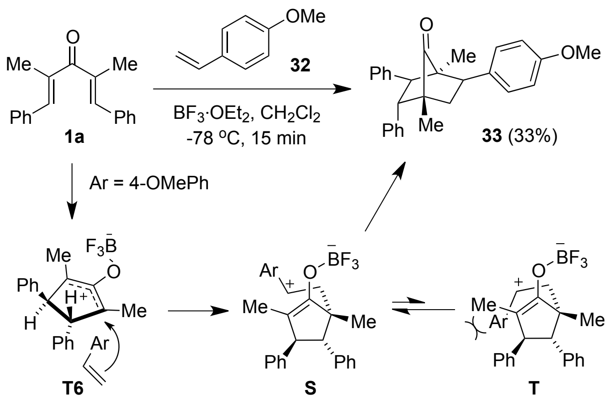
Entry	Dienone	Alkyne	R^5	R^6	T (°C)	Product	Yield (%)[b]
1	**1a**	**25d**	OMe	H	−78	**26a**	97
2	**1a**	**25e**	OMe	Me	−78	**26b**	95
3	**1a**	**25f**	Me	H	−78	**26c**	62
4	**1g**	**25d**	OMe	H	−40	**26d**	92
5	**1g**	**25e**	OMe	Me	−40	**26e**	84
6	**1g**	**25f**	Me	H	−40	**26f**	61
7	**1k**	**25f**	Me	H	−12	**26g**	30
8	**1i**	**25e**	OMe	Me	−40	**26h**	32
9	**1h**	**25e**	OMe	Me	−78	**26i**	62

[a] Standard procedure: To a stirred solution of **1** and alkyne **2** (1.2 equiv) in CH_2Cl_2 (0.2 M in **1a**) at the indicated temperature was added BF_3·OEt_2 (1.1 equiv). After 15 min, the reaction mixture was quenched with sat. aq $NaHCO_3$, followed by extraction with CH_2Cl_2, drying over $MgSO_4$, and chromatographic purification. [b] Isolated yield.

high level of selectivity seen with **1i**,**h** is noted in the previous section employing allenyl ethers as intermolecular traps.

While the Nazarov reaction was readily interrupted by alkyne nucleophile (**2d**) showcasing a novel-trapping pathway, it is of our interest to examine the reactivity of its reduced analogue 4-vinyl anisole (**32**) under the same reaction condition (the reaction is not optimized for comparison purpose). Interestingly, BF_3·OEt_2-mediated reaction of **1a** with **32** furnished aryl-substituted bicyclo[2.2.1]heptanone **33** as a single diastereomer (Scheme 35). The structure of **33**, a crystalline solid, was unambiguously determined by X–ray diffraction analysis. The formation of formal [3+2] adduct **33** could be accounted by a stepwise mechanism where initial *syn*-to-phenyl addition by distal carbon of vinyl anisole on 2-oxidocyclopentenyl cation (**T6**→**S**) was followed by a highly stereoselective ring closure (**S**→**33** rather than **T**→**33** for steric considerations).

This result is closely analogous to previous interrupted Nazarov studies involving allylsilanes and vinyl sulfides as trapping reagents; hence the distinct reactivity seen with alkyne nucleophiles is particularly intriguing. However, the origin of reversal in facial selectivity (**T5** versus **T6**) is far from clear at this moment and demands further computational investigations.



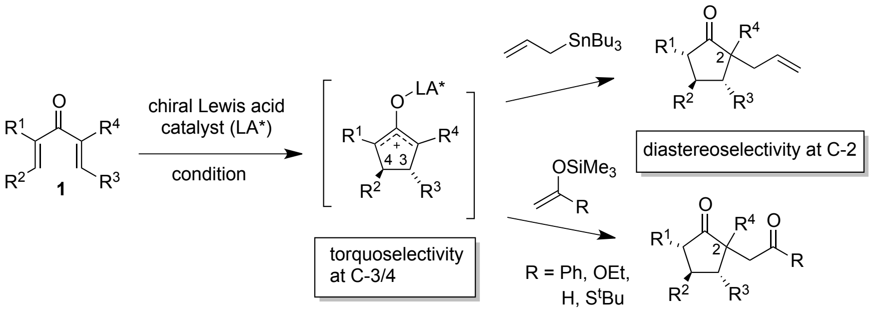
Scheme 35. Formal [3+2] cycloaddition of 4-vinylanisole **9** with the Nazarov intermediate

2.3 Conclusion

We have described a modular synthetic approach toward α-functionalized cyclopentanoid products in that a variety of structurally simple dienones and easily accessible carbon nucleophiles including allylstannanes, allylsilanes, oxygenated alkenes and allenes, and heterocycles were assembled via interrupted Nazarov chemistry. We validated that the propensity of the oxyallyl cation undergoing cycloaddition or single carbon–carbon bond formation is governed by the identity of Lewis acid-promoter and the nucleophilicity of trapping agents. Mechanistically, the domino reaction sequence disclosed herein was triggered by an electrocyclic ring closure of the dienone giving a stereodefined cyclopentenyl cation that was then attacked by suitable π-traps on one terminus of the oxyallyl intermediate furnishing densely substituted cyclopentanones with the establishment of up to five new streocenters. As the introduction of a carbon nucleophile α to a carbonyl group must involve a polarity inversion in the retrosynthetic perspective, the Nazarov intermediate can be viewed as an electrocyclization-initiated umpolung in the context of this work. In terms of diastereofacial selectivity, the major products observed in the cases using allylsilanes, allylstannanes, pyrroles, and furans as the trap predominantly resulted from nucleophilic addition *syn* to the β-substitution, but opposite diastereofacial selectivity was seen with examples using enol-type traps and indole derivatives. The origins of reversal of selectivity found in those examples are obscure and demand further experimental and computational investigations. Lastly, we have demonstrated the first example of intermolecular capture of the Nazarov intermediate with alkyne species, providing access to highly substituted α-phenacyl cyclopentanones in good yields. The transformation entails the Kucherov-type alkylative hydration of aryl acetylene with the oxyally cation in a highly stereo- and regioselective manner. Overall, we showed that the Nazarov reaction, beyond its conventional practice, served as an initiation for new bond-forming processes.

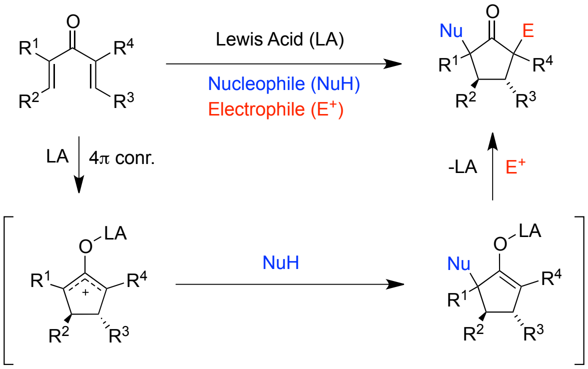
2.4 Future Directions

Significant research efforts during the past decade have been devoted to controlling the absolute sense of Nazarov cyclization through internal or external asymmetric inductions;[2b] typically, one of the newly formed tetrahedral carbon carrying absolute stereochemical information would be lost during the eliminative termination. To date limited examples of asymmetric interrupted Nazarov process have been described, where the direction of initial conrotation were guided by chiral auxiliaries or pre-existing stereocenters within dienone substrates.[67]



Scheme 36. Asymmetric Interrupted Nazarov Reactions

We envisioned that application of asymmetric catalysis in the interrupted Nazarov process would be an attractive alternative (Scheme 36). Optimization of chiral Lewis acid promoters for efficient enantioselective cyclization of non-polarized dienones would be the major challenge of this work,[2b] however, new breakthrough has been recently made by the Rawal group at the University of Chicago.[68] Subsequent attacks of the traps described in this chapter onto the putative intermediate would result in valuable enantiomerically-enriched cyclopentanoid building blocks. Whether the diastereoselectivity of trapping events would remain the same as the racemic variant employing simple Lewis acids is another critical topic to be addressed.



Scheme 37. Nazarov Three-component Coupling Reaction

A novel concept (Scheme 37), that the intermediates derived from the Nazarov cyclization could be sequentially captured by nucleophiles and electrophiles, has been preliminarily examined. Further investigations to generalize such multicomponent process in respect to the choice of nucleophilic and electrophilic trapping agents will be pursued.

2.5 Experimental

General Information. Reactions were carried out in flame-dried glassware under a positive argon atmosphere unless otherwise stated. Transfer of anhydrous solvents and reagents was accomplished with oven-dried syringes or cannulae. Solvents were distilled before use: methylene chloride from calcium hydride, tetrahydrofuran, diethylether and benzene from sodium/benzophenone ketyl, toluene from sodium metal. All other solvents and commercially available reagents were either purified by standard procedures or used without further purification. Thin layer chromatography was performed on glass plates precoated with 0.25 mm silica gel; the stains for TLC analysis were conducted with 2.5% *p*-anisaldehyde in AcOH-H_2SO_4-EtOH (1:3:85) and further heating until development of color. Flash chromatography was performed on 230-400 mesh silica gel with the indicated eluents. Nuclear magnetic resonance (NMR) spectra were recorded in indicated deuterated solvents and are reported in ppm in the presence of TMS as internal standard and coupling constants (*J*) are reported in Hertz (Hz). Infrared (IR) spectra were recorded neat and reported in cm^{-1}. Mass spectra were recorded by using EI or ESI as specified in each case.

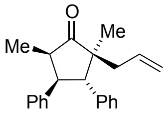
Preparation of 1,4-Dien-3-ones.

Dienones **1a**-**j** were synthesized by previously described procedures:

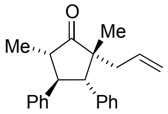
Dienones **1a** and **1e**: Giese, S.; West, F. G. *Tetrahedron* **2000**, *56*, 10221-10228. **1b**: DeVries, L. *J. Org. Chem.* **1960**, *25,* 1838. **1c**: Arnold, A.; Markert, M.; Mahrwald, R. *Synthesis* **2006**, 1099-1102. **1d** and **1j**: Wang, Y.; Schill, B. D.; Arif, A. M.; West, F. G. *Org. Lett.* **2003,** *5*, 2747-2750. **1f**,**h**,**i**: Scadeng, O.; Ferguson, M. J.; West, F. G. *Org. Lett.* **2011**, *13*, 114-117. **1g**: Rieder, C. J.; Winberg, K. J.; West, F. G. *J. Org. Chem.* **2011**, *76*, 50-56.

Standard Procedure (A) for the interrupted Nazarov reaction with allyl nucleophiles.

Dienone (0.50 mmol) and the allyl donor (1.00 mmol, 2.0 equiv) were dissolved in dichloromethane (2.5 mL, 0.2 M in dienone) under argon and cooled to −78 °C (acetone/dry ice bath). Lewis acid (0.55 mmol, 1.1 equiv) was added dropwise. The reaction mixture was stirred at the same temperature for 15 min. The reaction was quenched with saturated aqueous sodium bicarbonate (5 mL) and warmed to room temperature. The aqueous layer was extracted with dichloromethane (2 x 10 mL), the combined organic layers were washed with brine solution (1 x 15 mL) and dried over anhydrous magnesium sulfate. After filtration, the solvent was removed by rotary evaporation providing a crude residue that was purified by flash column chromatography (silica gel) to provide the desired product.

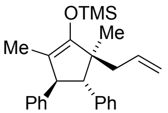


5a

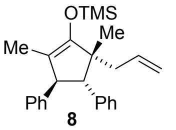


6a

Reaction of 1,5-diphenyl-2,4-dimethyl-1,4-pentadien-3-one with various allyl donors in the presence of different Lewis acid was performed under the standard procedure (A) giving various ratio of **5a** and **6a**; **5a**: mp 68 °C; IR (film) 3030, 2965, 1736, 1602, 1452, 1372 cm^{-1}; ^{1}H NMR (500 MHz, CDCl$_3$) d 7.27-7.24 (m, 6H), 7.21-7.14 (m, 4H), 5.83 (dddd, *J* = 19.0, 10.5, 9.0, 5.5 Hz, 1H), 5.30-5.25 (m, 2H), 3.70 (d, *J* = 12.0 Hz, 1H), 3.28 (app. t, *J* = 12 Hz, 1H) 2.56 (dddd, *J* = 14.0, 6.0, 1.5, 1.5 Hz, 1H), 2,90 (dq, *J* = 12.0, 7.0 Hz, 1H), 2.14 (dd, *J* = 14.0, 9.0 Hz, 1H), 1.16 (d, *J* = 7.0 Hz, 3H), 0.79 (s, 3H); ^{13}C NMR (125 MHz, CDCl$_3$) δ 221.2, 140.7, 137.2, 134.4, 129.3, 128.6, 128.1, 127.7, 126.8, 126.6, 119.3, 53.3, 53.2, 52.7, 50.7, 41.1, 20.4, 13.0; HRMS (EI, M$^+$) for C$_{22}$H$_{24}$O calcd. 304.1827, found: m/z 304.1826. **6a**: mp 78 °C; IR (film) 3029, 2962, 1734, 1602, 1452, 1373 cm^{-1}; ^{1}H NMR (500 MHz, CDCl$_3$) d 7.30-7.15 (m, 10H), 5.54 (dddd, *J* = 17.5, 10.5, 7.5, 7.5 Hz, 1H), 5.00 (dddd, *J* = 10.0, 2.0, 1.0, 1.0 Hz, 1H), 4,89 (dddd, *J* = 17.0, 1.5, 1.5, 1.5 Hz, 1H), 3.47-3.46 (m, 2H), 2.44-2.37 (m, 1H), 2.16 (dd, *J* = 14.0, 7.0 Hz, 1H), 1.74 (ddd, *J* = 14.5, 7.5, 1.0 Hz, 1H), 1.25 (s, 3H), 1.22 (d, *J* = 7.0 Hz, 3H); ^{13}C NMR (125 MHz, CDCl$_3$) δ 220.5, 140.9, 136.6, 133.5, 129.3, 128.6, 128.1, 127.7, 126.9, 126.8, 118.0, 58.8, 53.0, 52.1, 50.3, 37.7, 22.0, 13.5; HRMS (EI, M^+) for $C_{22}H_{24}O$ calcd. 304.1827, found: m/z 304.1830.

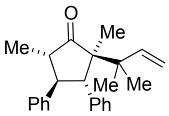


7

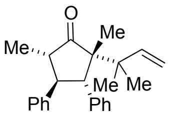


8

Reaction was performed with allyltributylstannane in the presence of TMSOTf under the standard procedure (A). Flash chromatography (19:1 hexane:EtOAc) gave **7** and **8** (50 mg, 82%; **7**:**8** = 1:5) as an inseparable mixture: IR (film) 3027, 2961, 1679, 1602, 1495, 1452 cm^{-1}; Partial ^1H and ^{13}C NMR data of **7**: ^1H NMR (500 MHz, $CDCl_3$) d 5.91 (dddd, *J* = 19.5, 10.5, 9.5, 5.0 Hz, 1H), 5.18-5.15 (m, 1H), 5.14-5.10 (m, 1H), 3.96 (dq, *J* = 9.0, 1.0 Hz, 1H), 3.21 (d, *J* = 9.0 Hz, 1H), 2.29 (dddd, *J* = 14.0, 5.0, 1.5, 1.5 Hz, 1H), 1.41 (d, *J* = 1.5 Hz, 3H), 0.72 (s, 3H), 0.29 (s, 9H); ^{13}C NMR (125 MHz, $CDCl_3$) d 153.7, 144.1, 139.0, 136.2, 115.9, 112.8, 64.5, 53.5, 49.4, 40.8, 24.1, 11.7, 1.19; Partial ^1H and ^{13}C NMR data of **8**: ^1H NMR (500 MHz, $CDCl_3$) d 5.46 (dddd, *J* = 17.0, 10.0, 7.0, 7.0 Hz, 1H), 4.81-4.78 (m, 1H), 4.77-4.73 (m, 1H), 4.05 (dq, *J* = 9.5, 1.0 Hz, 1H), 2.98 (d, *J* = 9.5 Hz, 1H), 2.06-2.02 (m, 1H), 1.76-1.71 (m, 1H), 1.43 (d, *J* = 1.5 Hz, 1H), 1.11 (s, 3H), 0.30 (s, 9H); ^{13}C NMR (125 MHz, $CDCl_3$) d 152.5, 144.3, 140.0, 136.5, 117.4, 112.3, 58.1, 54.1, 49.8, 41.9, 22.2, 11.7, 1.30; HRMS (EI, M^+) for $C_{25}H_{32}OSi$ calcd. 376.2222, found: m/z 376.2223.



5b

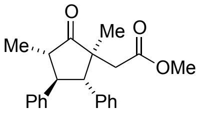


6b

Dienone (0.20 mmol) and allyltributylstannane (0.40 mmol, 2.0 equiv) were dissolved in dichloromethane (1.5 mL) under argon and cooled to −78 °C (acetone/dry ice bath). TMSOTf (0.22 mmol, 1.1 equiv) was added dropwise. The reaction mixture was stirred at the same temperature for 15 min. The reaction was quenched with 3 mL of *p*-toluenesulfonic acid monohydrate (0.02 mmol, 0.1 equiv) in MeOH/CH_2Cl_2 (1:1) and allowed to warm to room temperature. The aqueous layer was extracted with dichloromethane (2 x 10 mL), the combined organic layers were washed with brine solution (1 x 15 mL) and dried over anhydrous magnesium sulfate. After filtration, the solvent was removed by rotary evaporation providing a crude residue that was purified by flash column chromatography (silica gel) to provide **5b** and **6b** (63 mg, 95%; **5b**:**6b** = 1:5) as an inseparable mixture: IR (film) 3062, 2969, 2931, 1729, 1601, 1498, 1452, 1371 cm^{-1}; ^{1}H NMR (500 MHz, CDCl$_3$) d 7.28-7.26 (m, 2H), 7.22-7.04 (m, 18H), 5.93 (dd, *J* = 17.0, 10.5 Hz, 1H), 5.73 (dd, *J* = 17.5, 11.0 Hz, 1H), 5.15-5.10 (m, 2H), 4.85 (dd, *J* = 10.5, 1.0 Hz, 1H), 4.74 (dd, 17.0, 1.0 Hz, 1H), 3.75 (dd, *J* = 13.0, 11.5 Hz, 1H), 3.68 (d, *J* = 12.0 Hz, 1H), 3.61 (d, *J* = 13.0 Hz, 1H), 2.86 (app. t, *J* = 12.5 Hz, 1H), 2.54 (dq, *J* = 13.0, 7.0 Hz, 1H), 2.23 (dq, *J* = 11.5, 7.0 Hz, 1H), 1.50 (s, 3H), 1.18 (s, 3H), 1.16 (d, *J* = 7.0 Hz, 3H), 1.10 (s, 3H), 1.03 (s, 3H), 1.01 (d, *J* = 6.5 Hz, 3H), 0.96 (s, 3H), 0.61 (s, 3H); ^{13}C NMR (125 MHz, CDCl$_3$) δ 222.7, 220.8, 145.5, 141.7, 140.8, 139.8, 137.9, 131.0, 128.5, 128.3, 127.9, 127.6, 127.5, 127.4, 126.7, 126.6, 126.3, 113.2, 111.7, 59.8, 58.7, 56.6, 54.9, 54.5, 53.0, 52.2, 50.5, 43.3, 43.0, 25.5, 23.6, 23.5, 23.4, 22.7, 16.3, 12.2, 12.2; HRMS (EI, M$^+$) for $C_{24}H_{28}O$ calcd. 332.2140, found: m/z 332.2144.

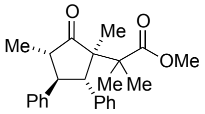
Standard Procedure (B) for the interrupted Nazarov reaction with silyloxyalkenes.

Dienone (0.10 mmol) and silyl ketene acetal (0.20 mmol, 2.0 equiv) were dissolved in dichloromethane (2.0 mL, 0.05 M) under argon and cooled to the indicated temperature. Boron trifluoride etherate (14 μL, 0.11 mmol, 1.1 equiv) was added dropwise. The reaction mixture was stirred at the same temperature for 15 min. The reaction was quenched with saturated aqueous sodium bicarbonate (5 mL) and warmed to room temperature. The aqueous layer was extracted with dichloromethane (2 x 10 mL), the combined organic layers were washed with brine solution (1 x 15 mL) and dried over anhydrous magnesium sulfate. After filtration, the solvent was removed by rotary evaporation providing a crude residue that was purified by flash column chromatography (silica gel) to provide the desired product.



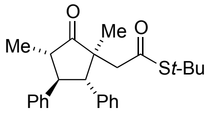
10a

Reaction carried out at −78 °C (acetone/dry ice bath) was performed under the standard procedure. Flash chromatography (10:1 hexane:EtOAc) gave **10a** (23mg, 78%) as a white solid: mp 152-153 °C; IR (film) 3029, 2966, 1737, 1661, 1602, 1452 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) d 7.34-7.32 (m, 2H), 7.28-7.25 (m, 4H), 7.21-7.15 (m, 4H), 3.92 (d, *J* = 12.0 Hz, 1H), 3.81 (s, 3H), 3.33 (app. t, *J* = 12.0 Hz, 1H), 2.88 (d, *J* = 17.5 Hz, 1H), 2.79 (dq, *J* = 12.0, 7.0 Hz, 1H), 2.48 (d, *J* = 17.0 Hz, 1H), 1.20 (d, *J* = 7.0 Hz, 3H), 0.75 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) d 220.3, 172.0, 140.9, 136.7, 129.1, 128.5, 128.2, 127.8, 126.9, 126.8, 53.4, 51.9, 51.8, 50.7, 50.6, 40.4, 19.8, 13.2; HRMS (EI, M$^+$) for $C_{22}H_{24}O_3$ calcd. 336.1726, found: m/z 336.1727.



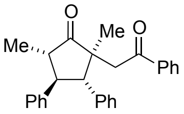
10b

Reaction carried out at −78 °C (acetone/dry ice bath) was performed under the standard procedure. Flash chromatography (10:1 hexane:EtOAc) gave **10b** (116.7 mg, 87%) as a pale yellow oil: IR (film) 3029, 2980, 1732, 1663, 1602, 1453 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) d 7.17-7.05 (m, 10H), 3.55 (s, 3H), 3.54 (d, *J* = 13.5 Hz, 1H), 2.94 (app. t, *J* = 12.2 Hz, 1H), 2.71 (dq, *J* = 12.5, 6.5 Hz, 1H), 1.42 (s, 3H), 1.19 (s, 3H), 1.31 (s, 3H). 1.06 (d, *J* = 7.0 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) d 219.7, 177.1, 140.5, 138.8, 130.6, 128.4, 127.6, 127.5, 126.7, 126.6, 56.3, 55.4, 54.3, 51.6, 51.3, 49.5, 23.0, 21.7, 16.2, 12.9; HRMS (EI, M$^+$) for $C_{24}H_{28}O_3$ calcd. 364.2039, found: m/z 364.2033.



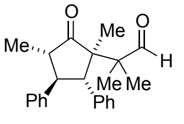
10c

Reaction carried out at –78 °C (acetone/dry ice bath) was performed under the standard procedure. Flash chromatography (8:1 hexane:EtOAc) gave **10c** (146.5 mg, 98%) as a colorless oil: IR (film) 3022, 2966, 1730, 1666, 1602, 1452 cm^{-1}; ^{1}H NMR (500 MHz, CDCl$_3$) d 7.28-7.12 (m, 10H), 3.80 (d, *J* = 12.5 Hz, 1H), 3.26 (app. t, *J* = 12.0 Hz, 1H), 3.03 (d, *J* = 16.5 Hz, 1H), 2.82 (dq, *J* = 11.7, 7.0 Hz, 1H), 2.66 (d, *J* = 17.0 Hz, 1H), 1.55 (s, 9H), 1.16 (d, *J* = 7.0 Hz, 3H), 0.66 (s, 3H); ^{13}C NMR (125 MHz, CDCl$_3$) d 219.7, 198.7, 141.0, 136.8, 129.2, 128.6, 128.2, 127.8, 126.8, 126.7, 53.0, 51.7, 51.5, 50.7, 50.6, 48.7, 29.9, 19.8, 13.1; HRMS (EI, M$^+$) for $C_{25}H_{30}O_2S$ calcd. 394.1967, found: m/z 394.1967.

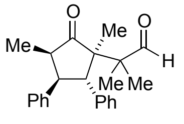


10d

Reaction carried out at –78 °C (acetone/dry ice bath) was performed under the standard procedure. Flash chromatography (6:1 hexane:EtOAc) gave **10d** (101.3 mg, 78%) as a pale yellow oil: IR (film) 3028, 2967, 1737, 1683, 1599, 1498, 1450 cm^{-1}; ^{1}H NMR (500 MHz, CDCl$_3$) d 8.01 (d, *J* = 8.5 Hz, 2H), 7.63-7.59 (m, 1H), 7.51-7.48 (m, 2H), 7.37 (d, *J* = 8.0 Hz, 2H), 7.26-7.25 (m, 2H), 7.22-7.19 (m, 2H), 7.16-7.12 (m, 2H), 7.07 (d, *J* = 8.0 Hz, 2H), 4.06 (d, *J* = 12.0 Hz, 1H), 3.39 (d, *J* = 19.0 Hz, 1H), 3.37 (app. t, *J* = 12.0 Hz, 1H), 3.32 (d, *J* = 19.0 Hz, 1H), 3.14 (dq, *J* = 12.8, 7.0 Hz, 1H), 1.21 (d, *J* = 7.0 Hz, 3H), 0.83 (s, 3H); ^{13}C NMR (125 MHz, CDCl$_3$) d 221.0, 198.0, 141.3, 137.3, 136.7, 133.5, 129.2, 128.7, 128.5, 128.2, 128.1, 128.0, 126.8, 126.7, 53.2, 51.6, 51.1, 50.4, 45.4, 20.1, 13.5; HRMS (EI, M$^+$) for $C_{27}H_{26}O_2$ calcd. 382.1933, found: m/z 382.1932.

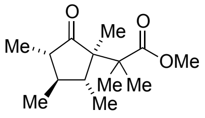


10e



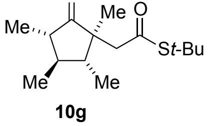
11e

Reaction carried out at –78 °C (acetone/dry ice bath) was performed under the standard procedure. Flash chromatography (20:1 hexane:EtOAc) gave **10e** (57.6 mg, 48%) and **11e** (22.6 mg, 19%): **10e**: IR (film) 3029, 2973, 2932, 2875, 2723, 1732, 1602, 1498, 1453 cm^{-1}; ^{1}H NMR (500 MHz, CDCl$_3$) d 9.60 (s, 1H), 7.20-7.08 (m, 10H), 3.65 (d, J = 12.0 Hz, 1H), 3.04 (app. t, J = 12.0 Hz, 1H), 2.66 (dq, J = 12.4, 7.0 Hz, 1H), 1.22 (s, 3H), 1.18 (s, 3H), 1.12 (s, 3H), 1.09 (d, J = 7.0 Hz, 3H); ^{13}C NMR (125 MHz, CDCl$_3$) d 220.6, 204.5, 140.2, 138.2, 130.7, 128.4, 127.9, 127.5, 126.8, 126.8, 56.0, 55.1, 54.2, 51.9, 51.8, 19.3, 18.6, 16.4, 13.0; HRMS (EI, M$^+$) for $C_{23}H_{26}O_2$ calcd. 334.19327, found: m/z 334.19307. **11e**: IR (film) 3029, 2974, 2936, 2877, 2734, 1731, 1602, 1497, 1453, 1373 cm^{-1}; ^{1}H NMR (500 MHz, CDCl$_3$) d 9.71 (s, 1H), 7.28-7.07 (m, 10H), 4.09 (d, J = 12.5 Hz, 1H), 4.03 (dd, J = 12.7, 8.2 Hz, 1H), 2.80 (app. quintet, J = 8.0 Hz, 1H), 1.38 (s, 3H), 1.28 (s, 3H), 0.96 (s, 3H), 0.81 (d, J = 8.0 Hz, 3H); ^{13}C NMR (125 MHz, CDCl$_3$) d 222.7, 204.2, 137.9, 137.5, 130.5, 128.9, 128.2, 128.1, 127.1, 126.5, 58.8, 50.2, 48.7, 48.0, 45.5, 20.0, 18.5, 15.8, 12.5; HRMS (EI, [M-CO]$^+$) for $C_{22}H_{26}O$ calcd. 306.1984, found: m/z 306.1976.



10f

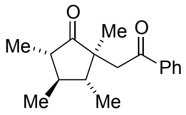
Reaction carried out at rt was performed under the standard procedure. Flash chromatography (10:1 hexane:EtOAc) gave **10f** (76.1 mg, 59%) as a pale yellow oil: IR (film) 2963, 2875, 1729, 1464, 1373 cm^{-1}; ^{1}H NMR (500 MHz, CDCl$_3$) d 3.64 (s, 3H), 1.90-1.81 (m, 2H), 1.29 (s, 3H), 1.23 (s, 3H), 1.12-1.11(m, 4H), 1.02 (d, J = 7.0 Hz, 3H), 0.94 (s, 3H), 0.91 (d, J = 6.5 Hz, 3H); ^{13}C NMR (125 MHz, CDCl$_3$) d 222.1, 176.6, 53.7, 51.7, 51.5, 48.1, 43.1, 42.7, 22.1, 21.4, 17.0, 14.1, 13.9, 12.4; HRMS (EI, M$^+$) for $C_{14}H_{24}O_3$ calcd. 240.1726, found: m/z 240.1727.



10g

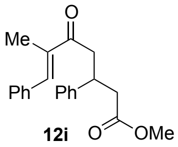
Reaction carried out at 0 °C (water/ice bath) was performed under the standard procedure. Flash chromatography (8:1 hexane:EtOAc) gave **10g** (129.0 mg, 64%) as a pale yellow oil: IR (film) 2963, 2929, 2875, 1741, 1683, 1456, 1365 cm^{-1}; ^{1}H

NMR (400 MHz, $CDCl_3$) d 2.86 (d, *J* = 16.0 Hz, 1H), 2.58 (d, *J* = 15.6 Hz, 1H), 1.99 (dq, *J* = 11.6, 7.0 Hz, 1H), 1.79 (dq, *J* = 10.8, 6.8 Hz, 1H), 1.43 (s, 9H), 1.38-1.30 (m, 1H), 1.13 (d, *J* = 6.4 Hz, 3H), 1.11 (d, *J* = 7.2 Hz, 3H), 0.98 (d, *J* = 7.2 Hz, 3H), 0.81 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) d 222.4, 198.4, 60.0, 50.7, 50.6, 48.5, 43.0, 42.8, 30.0, 18.4, 17.0, 13.1, 11.9; HRMS (EI, M^+) for $C_{15}H_{26}O_2S$ calcd. 270.1653, found: m/z 270.1646.



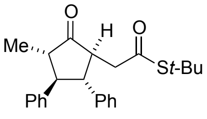
10h

Reaction carried out at 0 °C (water/ice bath) was performed under the standard procedure. Flash chromatography (6:1 hexane:EtOAc) gave **10h** (95.8 mg, 66%) as a colorless oil: IR (film) 2962, 2929, 2874, 1736, 1686, 1597, 1449, 1351 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) d 7.92-7.89 (m, 2H), 7.56-7.52 (m, 1H), 7.45-7.42 (m, 2H), 3.30 (d, *J* = 18.5 Hz, 1H), 3.26 (d, *J* = 18.0 Hz, 1H), 2.36 (dq, *J* = 11.7, 7.2 Hz, 1H), 1.98 (dq, *J* = 10.7, 6.7 Hz, 1H), 1.40 (ddq, *J* = 12.5, 11.5, 6.3 Hz, 1H), 1.16 (d, *J* = 6.5 Hz, 3H), 1.13 (d, *J* = 7.0 Hz, 3H), 0.94 (d, *J* = 7.0 Hz, 3H), 0.89 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) d 223.7, 197.6, 136.8, 133.2, 128.5, 127.9, 50.5, 49.1, 45.3, 43.0, 42.4, 18.6, 16.8, 13.2, 11.7; HRMS (EI, M^+) for $C_{17}H_{22}O_2$ calcd. 258.1620, found: m/z 258.1614.



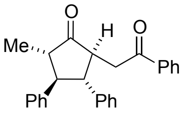
12i

Reaction carried out at 0 °C (water/ice bath) was performed under the standard procedure. Flash chromatography (5:1 hexane:EtOAc) gave **10i** (25.9 mg, 67%) as a pale yellow oil: IR (film) 3060, 3028, 2952, 1737, 1667, 1625, 1495, 1437 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) d 7.46 (br s, 1H), 7.41-7.19 (m, 10H), 3.82 (app. quintet, *J* = 7.2 Hz, 1H), 3.60 (s, 3H), 3.22-3.18 (m, 2H), 2.79 (dd, *J* = 15.5, 7.0 Hz, 1H), 2.68 (dd, *J* = 15.5, 7.5 Hz, 1H), 1.99 (d, *J* = 1.0 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) d 200.3, 172.4, 143.5, 138.9, 137.5, 135.8, 129.7, 128.6, 128.5, 128.4, 127.3, 126.8, 51.6, 43.7, 40.6, 38.2, 13.1; HRMS (EI, M$^+$) for $C_{21}H_{22}O_3$ calcd. 322.1569, found: m/z 322.1569.



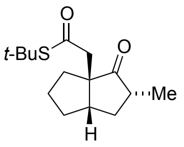
10j

Reaction carried out at 0 °C (water/ice bath) was performed under the standard procedure. Flash chromatography (8:1 hexane:EtOAc) gave **10j** (88.2 mg, 71%) as a pale yellow oil: IR (film) 3062, 3029, 2964, 1741, 1679, 1602, 1497, 1454, 1364 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) d 7.24-7.07 (m, 10H), 3.25 (app. t, *J* = 11.5 Hz, 1H), 2.94-2.88 (m, 2H), 2.79-2.66 (m, 3H), 1.40 (s, 9H), 1.13 (d, *J* = 7.0 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) d 217.1, 198.0, 140.0, 139.6, 128.5, 128.5, 127.7, 127.6, 127.0, 126.9, 56.9, 53.3, 53.2, 51.3, 48.4, 42.3, 29.7, 12.7; HRMS (EI, M$^+$) for $C_{24}H_{28}O_2S$ calcd. 380.1810, found: m/z 380.1819.

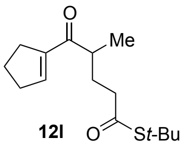


10k

Reaction carried out at 0 °C (water/ice bath) was performed under the standard procedure. Flash chromatography (8:1 hexane:EtOAc) gave **10k** (63.7 mg, 66%) as a pale yellow oil: IR (film) 3062, 3029, 2965, 1739, 1684, 1598, 1497, 1449 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) d 7.91-7.89 (m, 2H), 7.57-7.53 (m, 1H), 7.45-7.41 (m, 2H), 7.25-7.13 (m, 8H), 7.06-7.05 (m, 2H), 3.52 (app. t, *J* = 10.7 Hz, 1H), 3.48 (dd, *J* = 18.4, 5.0 Hz, 1H), 3.28 (dd, *J* = 18.4, 4.0 Hz, 1H), 3.04-2.95 (m, 2H), 2.82 (ddd, *J* = 11.0, 4.2, 4.2 Hz, 1H), 1.17 (d, *J* = 6.5 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) d 218.2, 197.5, 140.3, 140.1, 136.5, 133.3, 128.6, 128.5, 128.1, 128.1, 127.7, 127.7, 126.9, 126.8, 57.5, 52.7, 52.5, 51.4, 36.4, 12.8; HRMS (EI, M$^+$) for $C_{26}H_{24}O_2$ calcd. 368.1776, found: m/z 368.1775.

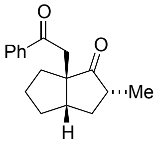


10l

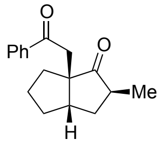


12l

Reaction carried out at 0 °C (water/ice bath) was performed under the standard procedure. Flash chromatography (8:1 hexane:EtOAc) gave an inseparable mixture of **10l** and **12l** (143.8 mg, 67%) as a pale yellow oil: **10l**: IR (film) 2960, 2870, 1737, 1682, 1476, 1456, 1364 cm^{-1}; ^{1}H NMR (500 MHz, CDCl$_3$) δ 2.93 (d, *J* = 15.4 Hz, 1H), 2.60-2.52 (m, 2H), 2.57 (d, *J* = 15.9 Hz, 1H), 2.31 (ddd, *J* = 13.0, 9.5, 8.5 Hz, 1H), 1.88-1.83 (m, 1H), 1.75-1.58 (m, 4H), 1.50-1.45 (m, 1H), 1.42 (s, 9H), 1.09 (d, *J* = 7.0 Hz, 3H), 1.00 (ddd, *J* = 12.5, 12.5, 10.0 Hz, 1H); ^{13}C NMR (125 MHz, CDCl$_3$) δ 222.6, 198.2, 58.5, 50.5, 48.4, 44.2, 43.2, 35.5, 35.4, 31.9, 29.8, 23.7, 14.6; HRMS (EI, M$^+$) for $C_{15}H_{24}O_2S$ calcd. 268.1497, found: m/z 268.1499. (The minor product could not be isolated in pure form, but was tentatively assigned as **12l**.)

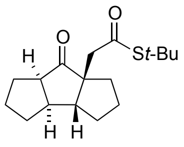


10m

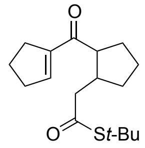


11m

Reaction carried out at 0 °C (water/ice bath) was performed under the standard procedure. Flash chromatography (6:1 hexane:EtOAc) gave an inseparable mixture of **10m** and **11m** (138.0 mg, 66%; **10m**:**11m** = 30:1) as a pale yellow oil: **10m**: IR (film) 3061, 2956, 2870, 1730, 1686, 1597, 1449, 1353 cm^{-1}; ^{1}H NMR (500 MHz, CDCl$_3$) d 7.91-7.89 (m, 2H), 7.55-7.52 (m, 1H), 7.44-7.41 (m, 2H), 3.50 (d, *J* = 18.5 Hz, 1H), 3.26 (d, *J* = 18.5 Hz, 1H), 2.91 (ddq, *J* = 11.7, 9.5, 7.2 Hz, 1H), 2.65-2.60 (m, 1H), 2.42 (ddd, *J* = 12.2, 8.7, 8.7 Hz, 1H), 1.89-1.66 (m, 4H), 1.65-1.56 (m, 2H), 1.15 (d, *J* = 7.0 Hz, 3H), 1.14-1.11 (m, 1H); ^{13}C NMR (125 MHz, CDCl$_3$) d 224.2, 198.2, 136.7, 133.2, 128.5, 128.0, 57.7, 45.8, 44.2, 44.0, 35.9, 35.6, 31.6, 23.7, 15.3; HRMS (EI, M$^+$) for $C_{17}H_{20}O_2$ calcd. 256.1463, found: m/z 256.1465. (The minor product could not be isolated in pure form, but was tentatively assigned as **11m**.)

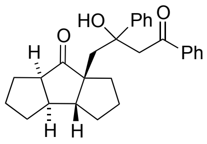


10n



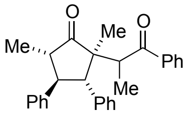
12n

The standard procedure carried out at rt was used to yield 140.1 mg (78%) of an inseparable mixture (**10n**:**12n** = 3:1) as a colorless oil: The following NMR data were taken from the spectra of the mixture: partial spectral data of **10n**: ^{1}H NMR (500 MHz, $CDCl_3$) δ 2.87 (d, *J* = 15.4 Hz, 1H), 2.81 (ddd, *J* = 10.0, 10.0, 4.0 Hz, 1H), 2.55 (d, *J* = 15.4 Hz, 1H), 2.57-2.52 (m, 2H), 2.30-2.28 (m, 1H), 2.18 (dddd, *J* = 9.5, 7.5, 4.5, 4.5 Hz, 1H), 1.42 (s, 9H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 223.8, 198.0, 60.8, 52.3, 50.9, 48.8, 48.2, 46.3, 37.4, 34.3, 34.2, 29.7, 25.8, 24.6, 22.7; partial spectral data of **12n**: ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.71-6.70 (m, 1H), 3.16-3.12 (m, 1H), 2.69-2.65 (m, 1H), 2.50 (dd, *J* = 14.4, 6.5 Hz, 1H), 2.39 (dd, *J* = 14.4, 8.0 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 200.7, 199.3, 146.0, 143.3, 52.4, 49.2, 47.9, 40.0, 34.0, 32.3, 31.3, 30.9, 29.8, 29.7, 24.7; HRMS (EI, M^+) for $C_{17}H_{26}O_2S$ calcd. 294.1653, found: m/z 294.1660.

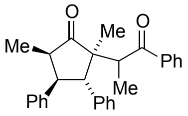


13

Reaction carried out at rt was performed under the standard procedure. Flash chromatography (8:1 hexane:EtOAc) gave **13** (160.1 mg, 62%) as a pale yellow oil: IR (film) 3462 (br), 3058, 2953, 1690, 1598, 1448, 1357, 1209 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.94-7.91 (m, 2H), 7.56-7.52 (m, 3H), 7.46-7.43 (m, 2H), 7.34-7.30 (m, 2H), 7.27-7.23 (m, 1H), 4.52 (br s, 1H), 3.47 (d, *J* = 17.5 Hz, 1H), 3.16 (d, *J* = 17.5 Hz, 1H), 2.39 (ddd, *J* = 14.5, 9.0, 9.0 Hz, 1H), 2.22-2.13 (m, 3H), 2.04-1.58 (m, 10H), 1.36-1.32 (m, 1H), 1.27-1.18 (m, 1H), 0.86-0.82 (m, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 229.3, 197.7, 144.5, 137.1, 133.1, 128.6, 128.0, 127.7, 126.9, 126.7, 76.5, 70.0, 60.2, 50.6, 50.2, 44.7, 35.5, 33.7, 32.7, 31.6, 27.7, 23.9, 23.8; HRMS (ESI, $[M+Na]^+$ for $C_{27}H_{30}NaO_3$ calcd. 425.2087, found: m/z 425.2085.

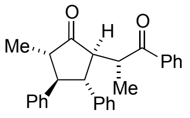


10o



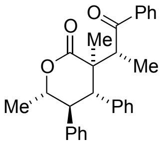
11o

The standard procedure carried out at −78 °C (acetone/dry ice bath) was used to yield 184.5 mg (92%) of an inseparable mixture (**10o**:**11o** = 9:1) as a colorless oil: **10o** (two diastereomers, **10o’** and **10o’’** in 3:2 ratio): partial spectral data of **10o’**: ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.03-8.01 (m, 2H), 7.66-7.62 (m, 1H), 7.57-7.53 (m, 2H), 7.02-7.01 (m, 2H), 3.76 (q, *J* = 7.5 Hz, 1H), 3.26-3.16 (m, 2H), 1.50 (d, *J* = 8.0 Hz, 3H), 1.16 (d, *J* = 6.5 Hz, 3H), 0.93 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 220.9, 203.6; partial spectral data of **10o’’**: ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.94-7.92 (m, 2H), 7.57-7.53 (m, 1H), 7.48-7.45 (m, 2H), 7.29-7.27 (m, 2H), 4.53 (d, *J* = 12.5 Hz, 1H), 3.91 (q, *J* = 7.8 Hz, 1H), 3.13 (app. t, *J* = 12 Hz, 1H), 2.76 (dq, *J* = 12.3, 7.0 Hz, 1H), 1.20 (s, 3H), 1.09 (d, *J* = 7.0 Hz, 3H), 1.06 (d, *J* = 8.0 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 222.8, 205.3; HRMS (EI, M^+) for $C_{28}H_{28}O_2$ calcd. 396.2089, found: m/z 396.2077. **11o** (two diastereomers, **11o’** and **11o’’** in 3:2 ratio): partial spectral data of **11o’**: ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.99-7.95 (m, 2H), 7.65-7.61 (m, 1H), 7.55-7.51 (m, 2H), 4.17 (dd, *J* = 12.8, 9.3 Hz, 1H), 3.89 (d, *J* = 13.0 Hz, 1H), 3.68 (q, *J* = 7.8 Hz, 1H), 2.89 (app. quintet, *J* = 8.0 Hz, 1H), 1.52 (d, *J* = 7.5 Hz, 3H), 1.11 (d, *J* = 8.0 Hz, 3H), 1.07 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 222.7, 202.3; partial spectral data of **11o’’**: ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.99-7.95 (m, 2H), 7.47-7.44 (m, 2H), 7.41-7.39 (m, 2H), 4.98 (d, *J* = 12,5 Hz, 1H), 4.03 (dd, *J* = 12.8, 9.3 Hz, 1H), 3.96 (q, *J* = 8.0 Hz, 1H), 2.81 (app. quintet, *J* = 8.0 Hz, 1H), 1.28 (s, 3H), 1.00 (d, *J* = 8.0 Hz, 3H), 0.73 (d, *J* = 8.0 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 223.3, 205.2; HRMS (EI, M^+) for $C_{28}H_{28}O_2$ calcd. 396.2089, found: m/z 396.2089.



10p

Reaction carried out at 0 °C (water/ice bath) was performed under the standard procedure. Flash chromatography (8:1 hexane:EtOAc) gave **10p** (164.0 mg, 81%) as a pale yellow oil: IR (film) 3029, 2973, 2931, 1737, 1680, 1597, 1497, 1453 cm^{-1}; ^{1}H NMR (500 MHz, CDCl$_3$) d 7.70-7.68 (m, 2H), 7.53-7.50 (m, 1H), 7.40-7.37 (m, 2H), 7.26-7.17 (m, 2H), 7.15-7.11 (m, 4H), 7.06-7.04 (m, 2H), 6.94-6.92 (m, 2H), 3.87 (qd, *J* = 7.5, 4.0 Hz, 1H), 3.24-3.16 (m, 1H), 2.86-2.80 (m, 3H), 1.37 (d, *J* = 7.0 Hz, 3H), 1.13-1.11 (m, 3H); ^{13}C NMR (125 MHz, CDCl$_3$) δ 217.9, 202.0, 140.2, 139.9, 136.1, 132.8, 128.6, 128.4, 128.4, 128.2, 127.8, 127.5, 126.8, 57.6, 57.5, 52.2, 51.7, 42.3, 15.2, 12.5 [one sp^2 carbon signal is missing due to peak overlap.]; HRMS (EI, M$^+$) for C$_{27}$H$_{26}$O$_2$ calcd. 382.1933, found: m/z 382.1931.



14

Compound **10p** (15.1 mg) and hydrogen peroxide (30 wt. % in water; 1.96 mmol, 222 μL) were dissolved in methanol (1 mL). Potassium hydroxide (0.20 mmol, 11.0 mg) was added at room temperature. The reaction mixture was stirred at the same temperature for 20 h. The mixture was diluted with dichloromethane (4 mL). The organic layer was washed with brine solution (4 mL) and dried over anhydrous magnesium sulfate. After filtration, the solvent was removed by rotary evaporation providing a crude residue that was purified by flash column chromatography (silica gel, 10:1 hexane:EtOAc) to provide the desired lactone **14** (9.2 mg, 58%): mp 173-174 °C; IR (film) 3027, 2980, 2916, 1718, 1673, 1597, 1493, 1452 cm^{-1}; ^{1}H NMR (500 MHz, CDCl$_3$) δ 7.54-7.35 (m, 2H), 7.58-7.45 (m, 1H), 7.43-7.39 (m, 2H), 7.11-7.04 (m, 6H), 6.90-6.86 (m, 4H), 4.98 (dq, *J* = 10.5, 6.5 Hz, 1H), 3.83 (qd, *J* = 7.3, 2.5 Hz, 1H), 3.12 (app. t, *J* = 11.0 Hz, 1H), 3.06

(dd, *J* = 10.3, 2.3 Hz, 1H), 2.91 (app. t, *J* = 10.8 Hz, 1H), 1.57 (d, *J* = 7.5 Hz, 3H), 1.22 (d, *J* = 6.5 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 202.2, 172.2, 140.7, 138.4, 136.0, 133.1, 128.7, 128.5, 128.5, 128.3, 128.1, 127.0, 127.0, 79.3, 54.3, 50.6, 49.5, 44.8, 20.3, 17.3 [one sp^2 carbon signal is missing due to peak overlap.]; HRMS (EI, M$^+$) for $C_{27}H_{26}O_3$ calcd. 398.1882, found: m/z 398.1885.

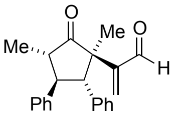
Standard Procedure (C) and (D) for the interrupted Nazarov reaction with allenol ether.

Standard Procedure (C)−With *stoichiometric* Lewis acid:

Dienone (0.50 mmol) and the allenol ether trap (1.00 mmol, 2.0 equiv) were dissolved in dichloromethane (5 mL, 0.1 M in dienone) under argon and cooled to −78 °C (acetone/dry ice bath). Lewis acid (0.55 mmol, 1.1 equiv) was added dropwise. The reaction mixture was stirred at the same temperature for 15 min. The reaction was quenched with saturated aqueous sodium bicarbonate (5 mL) and warmed to room temperature. The aqueous layer was extracted with dichloromethane (2 x 10 mL), the combined organic layers were washed with brine solution (1 x 15 mL) and dried over anhydrous magnesium sulfate. After filtration, the solvent was removed by rotary evaporation providing a crude residue that was purified by flash column chromatography (silica gel) to provide the desired product.

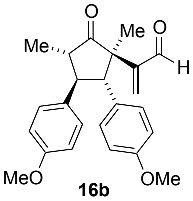
Standard Procedure (D)−With *catalytic* Lewis acid:

Dienone (0.50 mmol) and the allenol ether trap (1.00 mmol, 2.0 equiv) were dissolved in 1,2-dichloroethane (5 mL, 0.1 M in dienone) under argon at rt. Lewis acid (0.10 mmol, 0.2 equiv) was added. The reaction mixture was stirred at the same temperature for 30 min. The reaction was quenched with saturated aqueous sodium bicarbonate (5 mL) and warmed to room temperature. The aqueous layer was extracted with dichloromethane (2 x 10 mL), the combined organic layers were washed with brine solution (1 x 15 mL) and dried over anhydrous magnesium sulfate. After filtration, the solvent was removed by rotary evaporation providing a crude residue that was purified by flash column chromatography (silica gel) to provide the desired product.



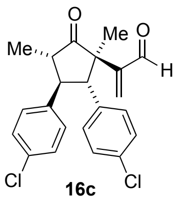
16a

Reaction was performed under the standard procedure (C) or (D). Flash chromatography (8:1 hexane:EtOAc) gave **16a** as a white solid: mp 136-137 °C; IR (film) 3088, 3029, 2966, 2872, 2711, 1740, 1689, 1623, 1601, 1499, 1452 cm^{-1}; ^{1}H NMR (500 MHz, CDCl$_3$) d 9.62 (s, 1H), 7.36-7.32 (m, 2H), 7.26-7.22 (m, 2H), 7.20-7.11 (m, 4H), 7.00-6.96 (m, 2H), 6.31 (s, 1H), 6.11 (s, 1H), 3.97 (d, *J* = 12.1 Hz, 1H), 3.39 (app. t, *J* = 11.9 Hz, 1H), 3.10 (dq, *J* = 11.6, 7.1 Hz, 1H), 1.19 (d, *J* = 7.1 Hz, 3H), 0.88 (s, 3H); ^{13}C NMR (125 MHz, CDCl$_3$) d 218.4, 194.0, 151.9, 140.9, 138.5, 136.3, 129.1, 128.6, 127.9, 127.8, 126.8, 126.8, 54.7, 54.2, 51.9, 51.1, 16.3, 13.6; HRMS (EI, M$^+$) for $C_{22}H_{22}O_2$ calcd. 318.1620, found: m/z 318.1621.



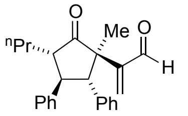
16b

Reaction was performed under the standard procedure (C) or (D). Flash chromatography (8:1 hexane:EtOAc) gave **16b** as a colorless oil: IR (film) 3034, 2958, 1739, 1689, 1612, 1583, 1514, 1463 cm^{-1}; ^{1}H NMR (500 MHz, CDCl$_3$) d 9.60 (s, 1H), 7.25-7.21 (m, 2H), 6.91-6.87 (m, 2H), 6.80-6.75 (m, 2H), 6.74-6.70 (m, 2H), 6.28 (s, 1H), 6.10 (s, 1H), 3.84 (d, *J* = 12.1 Hz, 1H), 3.73 (s, 3H), 3.72 (s, 3H), 3.27 (app. t, *J* = 11.9 Hz, 1H), 3.03 (dq, *J* = 11.7, 7.1 Hz, 1H), 1.17 (d, *J* = 7.1 Hz, 3H), 0.86 (s, 3H); ^{13}C NMR (125 MHz, CDCl$_3$) d 218.8, 194.0, 158.4, 158.4, 152.1, 138.3, 133.0, 130.1, 128.7, 128.4, 114.0, 113.3, 55.1, 55.1, 54.8, 53.8, 51.9, 50.7, 16.2, 13.6; HRMS (EI, M$^+$) for $C_{24}H_{26}O_4$ calcd. 378.1831, found: m/z 378.1831.



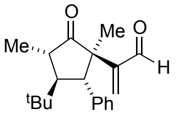
16c

Reaction was performed under the standard procedure (C) or (D). Flash chromatography (8:1 hexane:EtOAc) gave **16c** as a colorless oil: IR (film) 3053, 2936, 1742, 1694, 1635, 1594, 1493, 1454 cm^{-1}; ^{1}H NMR (500 MHz, CDCl$_3$) d 9.60 (s, 1H), 7.26-7.20 (m, 4H), 7.19-7.15 (m, 2H), 6.91-9.87 (m, 2H), 6.32 (s, 1H), 6.13 (s, 1H), 3.87 (d, *J* = 12.1 Hz, 1H), 3.30 (app. t, *J* = 11.9 Hz, 1H), 3.05 (dq, *J* = 11.6, 7.1 Hz, 1H), 1.17 (d, *J* = 7.1 Hz, 3H), 0.87 (s, 3H); ^{13}C NMR (125 MHz, CDCl$_3$) d 217.3, 194.0, 151.5, 139.0, 138.7, 134.5, 132.9, 132.7, 130.2, 129.0, 128.9, 128.3, 54.5, 53.8, 51.6, 50.8, 16.2, 13.5; HRMS (EI, M$^+$) for C$_{22}$H$_{20}$Cl$_2$O$_2$ calcd. 386.0841, found: m/z 386.0850.



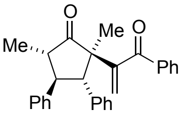
16d

Reaction was performed under the standard procedure (C) or (D). Flash chromatography (8:1 hexane:EtOAc) gave **16d** as a colorless oil: IR (film) 3060, 3028, 3005, 1738, 1689, 1623, 1498, 1452 cm^{-1}; ^{1}H NMR (500 MHz, CDCl$_3$) d 9.62 (s, 1H), 7.36-7.33 (m, 2H), 7.25-7.20 (m, 2H), 7.20-7.15 (m, 2H), 7.15-7.10 (m, 2H), 7.00-6.96 (m, 2H), 6.28 (s, 1H), 6.09 (s, 1H), 3.90 (d, *J* = 12.0 Hz, 1H), 3.56 (app. t, *J* = 11.8 Hz, 1H), 3.15 (app. p, *J* = 5.8 Hz, 1H), 1.73-1.57 (m, 2H), 1.44-1.33 (m, 1H), 1.27-1.15 (m, 1H), 0.87 (s, 3H), 0.82 (t, *J* = 7.3 Hz, 3H); ^{13}C NMR (125 MHz, CDCl$_3$) d 218.1, 194.0, 151.9, 141.6, 138.4, 36.3, 129.2, 128.5, 127.9, 127.8, 126.8, 126.7, 56.2, 55.0, 54.8, 48.7, 31.2, 20.0, 15.9, 14.2; HRMS (ESI, [M+Na]$^+$) for C$_{24}$H$_{26}$NaO$_2$ calcd. 369.1825, found: m/z 369.1828.



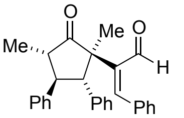
16e

Reaction was performed under the standard procedure (C) or (D). Flash chromatography (8:1 hexane:EtOAc) gave **16e** as a colorless oil: IR (film) 3061, 3028, 2961, 1739, 1692, 1630, 1601, 1498, 1454 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) d 9.52 (s, 1H), 7.33-7.29 (m, 2H), 7.22-7.15 (m, 2H), 6.72-6.68 (m, 1H), 6.19 (s, 1H), 5.90 (s, 1H), 3.47 (d, *J* = 11.0 Hz, 1H), 2.67 (dq, *J* = 8.8, 7.3 Hz, 1H), 2.34 (dd, 11.0, *J* = 11.0, 8.8 Hz, 1H), 1.44 (d, *J* = 7.3 Hz, 3H), 0.84 (s, 9H), 0.83 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) d 221.4, 193.3, 152.0, 139.8, 137.6, 130.7, 128.3, 128.0, 127.3, 126.5, 55.5, 54.4, 50.9, 44.8, 34.3, 29.3, 21.1, 17.8; HRMS (EI, M^{+}) for $C_{20}H_{26}O_2$ calcd. 298.1933, found: m/z 298.1929.



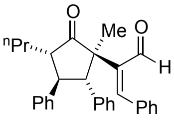
16f

Reaction was performed under the standard procedure (C). Flash chromatography (8:1 hexane:EtOAc) gave **16f** (30 mg, 23%) as a colorless oil: IR (film) 3062, 3029, 2964, 1736, 1652, 1599, 1498, 1452 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) d 7.83-7.80 (m, 2H), 7.61-7.57 (m, 1H), 7.52-7.47 (m, 2H), 7.36-7.33 (m, 2H), 7.25-7.19 (m, 4H), 7.17-7.10 (m, 2H), 7.10-7.07 (m, 2H), 6.00 (s, 1H), 5.78 (s, 1H), 4.12 (d, *J* = 12.0 Hz, 1H), 3.40 (app. t, *J* = 11.9 Hz, 1H), 3.18 (dq, *J* = 11.7, 7.0 Hz, 1H), 1.21 (d, *J* = 7.0 Hz, 3H), 0.98 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) d 218.4, 198.0, 149.7, 141.1, 138.1, 136.8, 132.5, 131.4, 129.7, 129.3, 128.6, 128.4, 127.9, 127.9, 126.8, 126.8, 56.9, 55.1, 51.7, 51.4, 17.4, 13.7; HRMS (ESI, [M+Na]$^{+}$) for $C_{28}H_{26}NaO_2$ calcd. 417.1825, found: m/z 417.1823.



16g

Reaction was performed under the standard procedure (C). Flash chromatography (8:1 hexane:EtOAc) gave **16g** (63 mg, 46%) as a colorless oil: IR (film) 3060, 3028, 3060, 2965, 1738, 1670, 1601, 1498, 1452 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) d 9.87 (s, 1H), 7.44-7.40 (m, 3H), 7.39-7.35 (m, 2H), 7.34-7.30 (m, 2H), 7.28-7.22 (m, 3H), 7.22-7.17 (m, 2H), 7.17-7.11 (m, 2H), 7.07-7.02 (m, 2H), 4.03 (d, *J* = 12.1 Hz, 1H), 3.42 (app. t, *J* = 11.8 Hz, 1H), 3.18 (dq, *J* = 11.6, 7.1 Hz, 1H), 1.22 (d, *J* = 7.1 Hz, 3H), 0.94 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) d 218.8, 192.4, 149.5, 143.3, 141.2, 136.5, 133.8, 130.0, 129.4, 129.3, 128.6, 128.5, 127.9, 127.9, 126.8, 126.8, 55.7, 55.2, 51.7, 51.2, 16.4, 13.8; HRMS (EI, M$^+$) for $C_{28}H_{26}O_2$ calcd. 394.1933, found: m/z 394.1940.

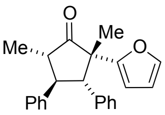


16h

Reaction was performed under the standard procedure (C). Flash chromatography (8:1 hexane:EtOAc) gave **16h** (30 mg, 51%) as a colorless oil: IR (film) 3060, 3028, 2958, 1737, 1670, 1601, 1498, 1452 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) d 9.86 (s, 1H), 7.43-7.40 (m, 3H), 7.40-7.36 (m, 2H), 7.33-7.28 (m, 2H), 7.25-7.21 (m, 3H), 7.21-7.16 (m, 2H), 7.15-7.10 (m, 2H), 7.06-7.02 (m, 2H), 3.97 (d, *J* = 11.9 Hz, 1H) 3.59 (app. t, *J* = 11.8 Hz, 1H), 3.23 (app. p, *J* = 5.8 Hz, 1H), 1.77-1.68 (m, 1H), 1.68-1.58 (m, 1H), 1.47-1.35 (m, 1H), 1.29-1.17 (m, 1H), 0.93 (s, 3H), 0.83 (t, *J* = 7.3 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) d 218.6, 192.5, 149.5, 143.3, 141.9, 136.5, 133.9, 130.0, 129.3, 128.5, 128.5, 128.0, 127.8, 126.8, 126.7, 56.0, 56.0, 55.9, 48.8, 31.5, 20.1, 16.0, 14.3 [one sp^2 carbon signal is missing due to peak overlap.]; HRMS (EI, M$^+$) for $C_{30}H_{30}O_2$ calcd. 422.2246, found: m/z 422.2253.

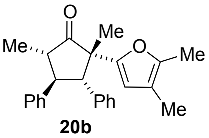
Standard Procedure (E) for the interrupted Nazarov reaction with heterocycles.

Dienone (0.50 mmol) and the heterocycle trap (1.00 mmol, 2.0 equiv) were dissolved in dichloromethane (2.5 mL, 0.2 M in dienone) under argon and cooled to −78 °C (acetone/dry ice bath). TMSOTf (0.55 mmol, 1.1 equiv) was added dropwise. The reaction mixture was allowed to warm to rt over 15 min. The reaction was quenched with saturated aqueous sodium bicarbonate (5 mL) and warmed to room temperature. The aqueous layer was extracted with dichloromethane (2 x 10 mL), the combined organic layers were washed with brine solution (1 x 15 mL) and dried over anhydrous magnesium sulfate. After filtration, the solvent was removed by rotary evaporation providing a crude residue that was purified by flash column chromatography (silica gel) to provide the desired product.



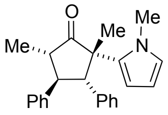
20a

Reaction was performed under the standard procedure (E). Flash chromatography (8:1 hexane:EtOAc) gave **20a** (59 mg, 58%) as a white solid: mp 116-118 °C; IR (film) 3062, 3029, 2971, 1745, 1601, 1500, 1452 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) d 7.33-7.31 (m, 1H), 7.24-7.19 (m, 4H), 7.16-7.10 (m, 1H), 7.07-7.03 (m, 3H), 6.80-6.76 (m, 2H), 6.17 (dd, *J* = 3.3, 1.8 Hz, 1H), 5.72 (d, *J* = 3.3 Hz, 1H), 3.73 (app. t, *J* = 12.0 Hz, 1H), 3.40 (d, *J* = 12.5 Hz, 1H), 2.58 (dq, *J* = 11.4, 6.9 Hz, 1H), 1.54 (s, 3H), 1.31 (d, *J* = 7.0 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) d 218.5, 154.5, 140.5, 137.0, 128.6, 128.5, 127.7, 127.7, 126.8, 126.8, 110.0, 107.8, 61.2, 55.8, 52.0, 52.0, 20.9, 12.9 [one sp^2 carbon signal is missing due to peak overlap.]; HRMS (EI, M^+) for $C_{23}H_{22}O_2$ calcd. 330.1620, found: m/z 330.1621.

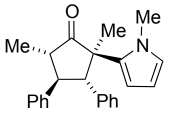


20b

Reaction was performed under the standard procedure (E). Flash chromatography (8:1 hexane:EtOAc) gave **20b** (91 mg, 90%) as a colorless oil: IR (film) 3062, 3028, 2972, 1745, 1602, 1498, 1452 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) d 7.29-7.22 (m, 4H), 7.18-7.06 (m, 4H), 6.89-6.84 (m, 2H), 5.54 (s, 1H), 3.76 (app. t, *J* = 11.9 Hz, 1H), 3.39 (d, *J* = 12.5 Hz, 1H), 2.58 (dq, *J* = 11.4, 6.9 Hz, 1H), 2.18 (s, 3H), 1.83 (s, 3H), 1.51 (s, 3H), 1.34 (d, *J* = 7.0 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) d 219.0, 151.0, 146.2, 140.8, 137.3, 128.8, 128.5, 127.7, 127.6, 126.7, 126.6, 114.1, 111.1, 61.1, 55.9, 52.1, 52.0, 20.7, 13.1, 11.4, 9.8; HRMS (EI, M$^+$) for $C_{25}H_{26}O_2$ calcd. 358.1933, found: m/z 358.1939.

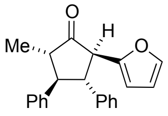


20c



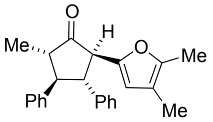
21c

Reaction was performed under the standard procedure (E). Flash chromatography (8:1 hexane:EtOAc) gave **20c** and **21c** (57 mg, 98%; **20c**: **21c** = 3:1) as an inseparable mixture: IR (film) 3061, 3028, 2964, 1738, 1602, 1498, 1452 cm^{-1}; Partial ^{1}H and ^{13}C NMR data of **20c**: ^{1}H NMR (500 MHz, $CDCl_3$) d 6.34 (app. t, *J* = 2.5 Hz, 1H), 5.79 (app. t, *J* = 2.0 Hz, 1H), 5.79 (app. t, *J* = 2.0 Hz, 1H), 5.23 (dd, *J* = 2.5, 2.0 Hz, 1H), 3.48 (s, 3H), 3.45 (d, *J* = 12.0 Hz, 1H), 3.30 (app. t, *J* = 12.0 Hz, 1H), 2.48 (dq, *J* = 11.5, 7.0 Hz, 1H), 1.52 (s, 3H), 1.27 (d, *J* = 7.0 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) d 221.8, 60.1, 55.1, 52.3, 51.0, 36.1, 24.5, 12.8; Partial ^{1}H and ^{13}C NMR data of **21c**: ^{1}H NMR (500 MHz, $CDCl_3$) d 6.66 (app. t, *J* = 2.5 Hz, 1H), 6.05 (dd, *J* = 4.0, 2.5 Hz, 1H), 5.77 (dd, *J* = 4.0, 2.0 Hz, 1H), 3.94 (d, *J* = 12.5 Hz, 1H), 3.68 (s, 3H), 3.51 (app. t, *J* = 12.0 Hz, 1H), 2.68 (dq, *J* = 11.5, 7.0 Hz, 1H), 1.31 (d, *J* = 7.0 Hz, 3H), 1.10 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) d 219.4, 55.9, 54.8, 52.7, 49.8, 36.3, 18.0, 14.3; HRMS (EI, M$^+$) for $C_{24}H_{25}NO$ calcd. 343.1936, found: m/z 343.1935.



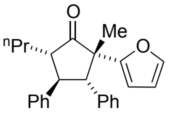
21d

Reaction was performed under the standard procedure (E). Flash chromatography (8:1 hexane:EtOAc) gave **21d** (69 mg, 86%) as a colorless oil: IR (film) 3063, 3030, 2968, 1748, 1602, 1498, 1453 cm^{-1}; ^{1}H NMR (500 MHz, C_6D_6) d 7.27-7.26 (m, 1H), 7.22-7.17 (m, 2H), 7.17-7.11 (m, 3H), 7.11-7.06 (m, 1H), 7.04-6.99 (m, 4H), 6.26 (d, *J* = 3.2 Hz, 1H), 6.22 (dd, *J* = 1.9, 3.1 Hz, 1H), 3.82 (app. t, *J* = 11.3 Hz, 1H), 3.77 (d, *J* = 11.7 Hz, 1H), 2.88 (app. t, *J* = 11.5 Hz, 1H), 2.65 (dq, *J* = 12.3, 6.8 Hz, 1H), 1.27 (d, *J* = 6.9 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) d 213.4, 150.2, 139.5, 139.5, 128.7, 128.5, 127.6, 127.5, 127.1, 127.0, 110.4, 108.3, 56.4, 55.9, 53.6, 52.1, 12.5 [one sp^2 carbon signal is missing due to peak overlap.]; HRMS (EI, M$^+$) for $C_{22}H_{20}O_2$ calcd. 316.1463, found: m/z 316.1475.



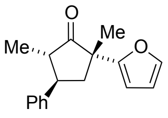
21e

Reaction was performed under the standard procedure (E). Flash chromatography (8:1 hexane:EtOAc) gave **21e** (29 mg, 39%) as a colorless oil: IR (film) 3062, 3029, 2969, 1748, 1603, 1497, 1453 cm^{-1}; ^{1}H NMR (500 MHz, CDCl$_3$) d 7.28-7.23 (m, 2H), 7.21-7.15 (m, 5H), 7.15-7.10 (m, 1H), 7.07-7.03 (m, 2H), 5.88 (s, 1H), 3.70 (app. t, *J* = 11.5 Hz, 1H), 3.61 (d, *J* = 11.7 Hz, 1H), 2.98 (app. t, *J* = 11.7 Hz, 1H), 2.71 (dq, *J* = 12.2, 6.8 Hz, 1H), 2.15 (s, 1H), 1.84 (s, 1H), 1.15 (d, *J* = 6.9 Hz, 1H); ^{13}C NMR (125 MHz, CDCl$_3$) d 214.0, 147.2, 146.9, 139.7, 139.7, 128.6, 128.3, 127.6, 127.5, 127.0, 126.8, 114.6, 111.6, 56.4, 55.9, 53.4, 51.9, 12.5, 11.4, 9.8; HRMS (EI, M$^+$) for $C_{24}H_{24}O_2$ calcd. 344.1764, found: m/z 344.1772.

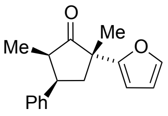


20f

Reaction was performed under the standard procedure (E). Flash chromatography (8:1 hexane:EtOAc) gave **20f** (69 mg, 66%) as a colorless oil: IR (film) 3062, 3029, 2961, 1742, 1602, 1499, 1453 cm^{-1}; ^{1}H NMR (500 MHz, CDCl$_3$) d 7.34-7.33 (m, 1H), 7.24-7.17 (m, 4H), 7.14-7.08 (m, 1H), 7.07-7.02 (m, 3H), 6.79-6.74 (m, 2H), 6.18 (dd, *J* = 3.3, 1.8 Hz, 1H), 5.73 (dd, *J* = 3.3, 0.8 Hz, 1H), 3.87 (app. t, *J* = 11.9 Hz, 1H), 3.30 (d, *J* = 12.4 Hz, 1H), 2.65 (dt, *J* = 11.7, 5.9 Hz, 1H), 1.91-1.82 (m, 1H), 1.78-1.67 (m, 1H), 1.52 (s, 3H), 1.49-1.37 (m, 1H), 1.37-1.24 (m, 1H), 0.82 (t, *J* = 7.3 Hz, 3H); ^{13}C NMR (125 MHz, CDCl$_3$) d 218.4, 154.6, 141.3, 137.0, 128.6, 128.5, 127.7, 127.7, 126.7, 126.7, 110.0, 107.8, 62.3, 56.1, 55.8, 50.6, 31.5, 21.0, 20.5, 14.2 [one sp^2 carbon signal is missing due to peak overlap.]; HRMS (EI, M$^+$) for $C_{25}H_{26}O_2$ calcd. 358.1933, found: m/z 358.1939.

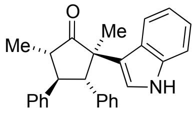


20g

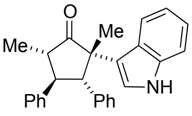


20gg

Reaction was performed under the standard procedure (E). Flash chromatography (8:1 hexane:EtOAc) gave **20g** and **20gg** (72 mg, 61%; **20g**: **20gg** = 3:1) as an inseparable mixture: IR (film) 3062, 3029, 2968, 1743, 1602, 1499, 1454 cm^{-1}; **20g**: ^1H NMR (500 MHz, $CDCl_3$) d 7.20-7.34 (m, 3H), 7.30-7.27 (3H), 6.35 (dd, *J* = 3.0, 1.5 Hz, 1H), 6.14 (dd, *J* = 3.5, 1.0 Hz, 1H), 3.06 (ddd, *J* = 12.5, 6.5, 6.5 Hz, 1H), 2.85 (dd, *J* = 13.0, 6.0 Hz, 1H), 2.44 (dq, *J* = 12.0, 7.0 Hz, 1H), 2.04 (app. t, *J* = 12.5 Hz, 1H), 1.54 (s, 3H), 1.13 (d, *J* = 7.0 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) d 218.0, 155.4, 142.1, 128.8, 127.2, 126.9, 110.2, 105.9, 50.9, 50.7, 47.7, 43.8, 23.4, 13.4 [one sp^2 carbon signal is missing due to peak overlap.]; Partial ^1H and ^{13}C NMR data of **20gg**: ^1H NMR (500 MHz, $CDCl_3$) d 6.16 (dd, *J* = 3.0, 0.5 Hz, 1H), 3.79 (ddd, *J* = 12.5, 8.0, 6.5 Hz, 1H), 2.88-2.82 (m, 2H), 2.34 (app. t, *J* = 12.5 Hz, 1H), 1.56 (s, 3H), 0.82 (d, *J* = 7.5 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) d 218.0, 155.3, 142.1, 140.1, 128.4, 128.1, 126.5, 110.3, 105.7, 50.8, 47.7, 43.8, 41.8, 23.8, 12.3; HRMS (EI, M^+) for $C_{17}H_{18}O_2$ calcd. 254.1307, found: m/z 254.1307.

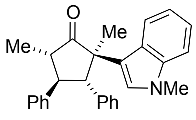


22a

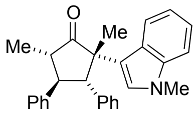


23a

Reaction was performed under the standard procedure (E). Flash chromatography (4:1 hexane:EtOAc) gave **22a** (24 mg, 48%) and **23a** (4 mg, 7%); **22a**: IR (film) 3409(br), 3029, 2967, 1735, 1619, 1498, 1453 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) d 8.11 (br s, 1H), 7.60 (d, *J* = 8.0 Hz, 1H), 7.46 (d, *J* = 8.0 Hz, 1H), 7.42 (d, *J* = 7.5 Hz, 1H), 7.34-7.27 (m, 3H), 7.23-7.20 (m, 2H), 7.13-7.08 (m, 3H), 6.83-6.79 (m, 3H), 4.35 (d, *J* = 12.5 Hz, 1H), 3.59 (app. t, *J* = 12.0 Hz, 1H), 2.95 (dq, *J* = 12.0, 7.0 Hz, 1H), 1.38 (d, *J* = 7.0 Hz, 3H), 1.19 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 220.3, 141.0, 137.2, 136.6, 129.1, 128.8, 127.8, 127.5, 126.9, 126.5, 124.9, 123.6, 122.2, 119.8, 119.4, 118.3, 111.9, 56.1, 53.9, 53.4, 50.2, 17.6, 14.1; HRMS (ESI, [M+Na]$^{+}$) for $C_{27}H_{25}NNaO$ calcd. 402.1828, found: m/z 402.1830. **23a**: IR (film) 3411(br), 3029, 2968, 1734, 1619, 1498, 1452 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) d 7.99 (br s, 1H), 7.29-7.12 (m, 6H), 7.05-7.00 (m, 2H), 6.93 (app. t, *J* = 7.5 Hz, 2H), 6.81 (d, *J* = 7.0 Hz, 2H), 6.69 (app. t, *J* = 7.0 Hz, 1H), 6.56 (d, *J* = 2.5 Hz, 1H), 6.46 (d, *J* = 8.0 Hz, 1H), 3.56 (d, *J* = 12.0 Hz, 1H), 3.41 (app. t, *J* = 12.5 Hz, 1H), 2.67 (dq, *J* = 12.5, 6.5 Hz, 1H), 1.81 (s, 3H), 1.39 (d, *J* = 7.0 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 221.8, 140.3, 137.6, 136.0, 129.5, 128.5, 127.8, 127.6, 126.7, 126.6, 126.5, 122.6, 121.4, 121.0, 119.0, 115.3, 110.8, 61.0, 55.9, 52.2, 51.5, 23.9, 12.8; HRMS (ESI, [M+Na]$^{+}$) for $C_{27}H_{25}NNaO$ calcd. 402.1828, found: m/z 402.1817.

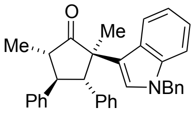


22b



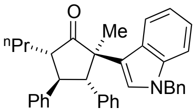
23b

Reaction was performed under the standard procedure (E). Flash chromatography (6:1 hexane:EtOAc) gave **22b** (35 mg, 40%) and **23b** (28 mg, 32%); **22b**: IR (film) 3028, 2967, 1738, 1601, 1451, 1376 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) d 7.60 (d, *J* = 8.0 Hz, 1H), 7.42 (d, *J* = 8.0 Hz, 1H), 7.35-7.30 (m, 3H), 7.23-7.20 (m, 2H), 7.12-7.10 (m, 3H), 6.84-6.82 (m, 2H), 6.72 (s, 1H), 4.37 (d, *J* = 12.0 Hz, 1H), 3.77 (s, 3H), 3.56 (app. t, *J* = 12 Hz, 1H), 2.95 (dq, *J* = 12.0, 7.0 Hz, 1H), 1.38 (d, *J* = 6.5 Hz, 1H), 1.20 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) d 220.3, 141.1, 138.0, 136.8, 129.1, 128.8, 128.4, 127.8, 127.5, 126.9, 126.5, 125.4, 121.7, 119.5, 119.3, 116.7, 109.9, 56.2, 53.9, 53.3, 50.2, 32.9, 17.7, 14.1; HRMS (EI, M^{+}) for $C_{28}H_{27}NO$ calcd. 393.2093, found: m/z 393.2098. **23b**: IR (film) 3028, 2965, 1737, 1601, 1452, 1370 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) d 7.23-7.20 (m, 5H), 7.15-7.13 (m 1H), 7.08-7.05 (m, 1H), 7.04-7.01 (m, 1H), 6.95-6.92 (m, 2H), 6.83 (d, *J* = 5.0 Hz, 2H), 6.68-6.65 (m, 1H), 6.39 (s, 1H), 6.36 (d, *J* = 8.0 Hz, 1H), 3.71 (s, 3H), 3.56 (d, *J* = 12.5 Hz, 1H), 3.39 (app. t, *J* = 12.0 Hz, 1H), 2.65 (dq, *J* = 12.0, 7.0 Hz, 1H), 1.79 (s, 3H), 1.40 (d, *J* = 7.0 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) d 221.9, 140.4, 137.7, 136.8, 129.6, 128.5, 127.8, 127.6, 127.4, 127.1, 126.7, 126.6, 121.1, 120.9, 118.5, 113.3, 108.8, 60.9, 56.1, 52.2, 51.4, 32.7, 24.0, 12.9; HRMS (EI, M^+) for $C_{28}H_{27}NO$ calcd. 393.2093, found: m/z 393.2089.



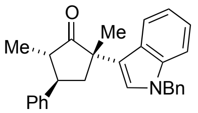
22c

Reaction was performed under the standard procedure (E). Flash chromatography (6:1 hexane:EtOAc) gave **22c** (154 mg, 92%) as a white solid: mp 178-179 °C; IR (film) 3062, 3029, 2963, 1737, 1603, 1497, 1452 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) d 7.62-7.58 (m, 1H), 7.44-7.38 (m, 2H), 7.36-7.16 (m, 9H), 7.12-7.03 (m, 5H), 6.83-6.78 (m, 2H), 6.77 (s, 1H), 5.35 (d, *J* = 16.2 Hz, 1H), 5.21 (d, *J* = 16.3 Hz, 1H), 4.33 (d, *J* = 12.5 Hz, 1H), 3.59 (app. t, *J* = 11.9 Hz, 1H), 2.95 (dq, *J* = 11.3, 7.0 Hz, 1H), 1.38 (d, *J* = 6.9 Hz, 3H), 1.16 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) d 220.1, 141.1, 137.7, 137.6, 136.6, 129.1, 128.8, 128.8, 128.0, 127.8, 127.6, 127.5, 127.0, 126.6, 126.6, 125.6, 122.1, 119.7, 119.6, 117.4, 110.5, 56.3, 54.0, 53.4, 50.1, 49.9, 17.6, 14.2; HRMS (ESI, $[M+Na]^+$) for $C_{34}H_{31}NNaO$ calcd. 492.2298, found: m/z 492.2291.



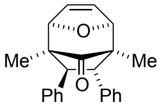
22d

Reaction was performed under the standard procedure (E). Flash chromatography (6:1 hexane:EtOAc) gave **22d** (101 mg, 83%) as a pale yellow oil: IR (film) 3061, 3029, 2960, 1736, 1603, 1496, 1452 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) d 7.61-7.57 (m, 1H), 7.42-7.38 (m, 2H), 7.33-7.14 (m, 9H), 7.10-7.02 (m, 5H), 6.80-6.75 (m, 2H), 6.73 (s, 1H), 5.33 (d, *J* = 16.3 Hz, 1H), 5.20 (d, *J* = 16.3 Hz, 1H), 4.21 (d, *J* = 12.3 Hz, 1H), 3.74 (app. t, *J* = 11.8 Hz, 1H), 2.99 (dt, *J* = 11.3, 5.6 Hz, 1H), 1.88-1.74 (m, 2H), 1.58-1.44 (m, 1H), 1.38-1.25 (m, 1H), 1.13 (s, 3H), 0.89 (t, *J* = 7.3 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) d 219.7, 141.8, 137.6, 137.5, 136.5, 129.1, 128.7, 128.7, 127.8, 127.5, 127.4, 126.8, 126.5, 126.5, 125.6, 122.0, 119.7, 119.5, 117.4, 110.4, 57.7, 57.2, 54.1, 49.9, 47.5, 31.7, 20.2, 17.0, 14.3; HRMS (EI, M$^+$) for $C_{36}H_{35}NO$ calcd. 497.2719, found: m/z 497.2719.



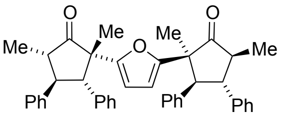
23e

Reaction was performed under the standard procedure (E). Flash chromatography (6:1 hexane:EtOAc) gave **23e** (151 mg, 74%) as a colorless oil: IR (film) 3061, 3029, 2964, 1734, 1603, 1496, 1453 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) d 7.83-7.80 (m, 1H), 7.34-7.26 (m, 6H), 7.26-7.15 (m, 4H), 7.13-7.08 (m, 3H), 6.77 (s, 1H), 5.30 (d, *J* = 16.1 Hz, 1H), 5.26 (d, *J* = 16.1 Hz, 1H), 3.10 (dd, *J* = 12.7, 5.7 Hz, 1H), 2.80 (td, *J* = 12.0, 5.6 Hz, 1H), 2.37 (dq, *J* = 11.6, 7.0 Hz, 1H), 2.13 (app. t, *J* = 12.5 Hz, 1H), 1.66 (s, 3H), 1.09 (d, *J* = 7.0 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) d 220.6, 142.4, 137.9, 137.4, 128.8, 128.6, 127.7, 127.3, 126.7, 126.7, 126.1, 125.9, 122.0, 120.9, 119.2, 115.7, 110.2, 50.8, 50.5, 50.1, 47.4, 44.6, 24.8, 14.1; HRMS (EI, M$^+$) for $C_{28}H_{27}NO$ calcd. 393.2093, found: m/z 393.2094.



19

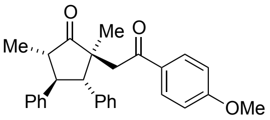
Prepared by the literature procedure (see ref. 17a). Flash chromatography (8:1 hexane:EtOAc) gave **19** (171 mg, 75%) as a white solid: mp 172-173 °C; IR (film) 3027, 2960, 1741, 1601, 1451, 1379 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) d 7.57-7.56 (m, 2H), 7.32-7.29 (m, 2H), 7.25-7.19 (m, 3H), 7.16-7.13 (m, 1H), 7.01-7.00 (m, 2H), 6.42 (dd, *J* = 6.0, 1.5 Hz, 1H), 6.37 (d, *J* = 6.0, 1.5 Hz, 1H), 4.71 (s, 1H), 4.30 (s, 1H), 4.04 (d, *J* = 7.5 Hz, 1H), 2.99 (d, *J* = 7.5 Hz, 1H), 1.11 (s, 3H), 0.72 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) d 212.3, 142.1, 137.2, 135.4, 134.3, 130.0, 128.7, 128.4, 128.2, 126.9, 126.7, 88.3, 84.6, 59.7, 59.5, 57.8, 53.7, 13.5, 12.4; HRMS (EI, M$^+$) for $C_{23}H_{22}O_2$ calcd. 330.1620, found: m/z 330.1618.



24

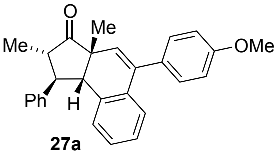
TMSOTf (0.14 mmol) was added to a stirred solution of **19** (0.13 mmol) in CH_2Cl_2 (3 mL) at −78 °C (acetone/dry ice bath). After 15 min, the reaction was quenched with saturated aqueous sodium bicarbonate (3 mL) and warmed to room temperature. The aqueous layer was extracted with dichloromethane (2 x 5 mL), the combined organic layers were washed with brine solution (1 x 10 mL) and dried over anhydrous magnesium sulfate. After filtration, the solvent was removed by rotary evaporation providing a crude residue that was purified by flash column chromatography (silica gel) to provide **24** (17 mg, 22%; theoretical maximum yield = 50%) and **20a** (14 mg, 34%) as a white solid respectively; **24**: mp >235 °C; IR (film) 3029, 2970, 1743, 1602, 1452, 1372 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) d 7.28-7.24 (m, 4H), 7.18-7.13 (m, 3H), 7.09-7.05 (m, 1H), 6.83-6.81 (m, 2H), 5.42 (s, 1H), 3.69 (app. t, *J* = 12.0 Hz, 1H), 3.41 (d, *J* = 12.0 Hz, 1H), 2.78 (dq, *J* = 12.0, 7.0 Hz, 1H), 1.52 (s, 3H), 1.43 (d, *J* = 7.0 Hz, 3H); HRMS (ESI, $[M+Na]^+$) for $C_{42}H_{40}NaO_3$ calcd. 615.2870, found: m/z 615.2871.

Standard Procedure. Dienone (0.40 mmol) and alkyne (0.48 mmol, 1.2 equiv) were dissolved in dichloromethane (2.0 mL, 0.2 M) under argon and cooled to the indicated temperature. Boron trifluoride etherate (56 μL, 0.44 mmol, 1.1 equiv) was added dropwise. The reaction mixture was stirred at the same temperature for 15 min. The reaction was quenched with saturated aqueous sodium bicarbonate (5 mL) and warmed to room temperature. The aqueous layer was extracted with dichloromethane (2 x 10 mL), the combined organic layers were washed with brine solution (1 x 15 mL) and dried over anhydrous magnesium sulfate. After filtration, the solvent was removed by rotary evaporation providing a crude residue that was purified by flash column chromatography (silica gel) to provide the desired product.



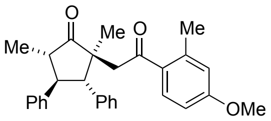
26a

Reaction carried out at –78 °C (acetone/dry ice bath) was performed under the standard procedure with various Lewis acids. **26a**: IR (film) 3006, 2930, 1733, 1674, 1661, 1600 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) d 8.03-8.00 (m, 2H), 7.41-7.39 (m, 2H), 7.29-7.25 (m, 2H), 7.23-7.7.22 (m, 2H), 7.19-7.15 (m, 2H), 7.10-7.09 (m, 2H), 7.01-6.98 (m, 2H), 4.09 (d, *J* = 12.0 Hz, 1H), 3.93 (s, 3H), 3.38 (app. t, *J* = 12.0 Hz, 1H), 3.37 (d, *J* = 18.5 Hz, 1H), 3.30 (d, *J* = 18.5 Hz, 1H), 3.16 (dq, *J* = 12.0, 7.0 Hz, 1H), 1.22 (d, *J* = 6.5 Hz, 3H), 0.84 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 221.1, 196.4, 163.8, 141.3, 137.4, 130.4, 129.8, 129.3, 128.5, 128.1, 128.0, 126.7, 126.6, 113.8, 55.5, 53.2, 51.6, 51.1, 50.4, 45.1, 20.1, 19.5; HRMS (ESI, $[M+Na]^+$) for $C_{28}H_{28}NaO_3$ calcd. 435.1931, found: m/z 435.1926.



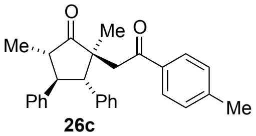
27a

Reaction carried out at –78 °C (acetone/dry ice bath) was performed under the standard procedure with $SnCl_4$ as Lewis acid. Flash chromatography (10:1 hexane:EtOAc) gave **26a** (51 mg, 56%) and **27a** (31 mg, 35%) as a colorless oil respectively. **27a**: IR (film) 3028, 2961, 1740, 1607, 1510, 1453 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) d 7.32-7.24 (m, 5H), 7.14-7.07 (m, 4H), 6.95-6.92 (m, 3H), 6.46-6.44 (m, 1H), 5.45 (d, *J* = 1.5 Hz, 1H), 3.85 (s, 3H), 3.09 (dd, *J* = 11.5, 1.5 Hz, 1H), 2.82 (app. t, *J* = 11.5 Hz, 1H), 2.58 (dq, *J* = 11.5, 7.0 Hz, 1H), 1.24 (s, 3H), 1.03 (d, *J* = 7.0 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 220.5, 159.2, 140.4, 138.8, 133.9, 132.1, 131.4, 130.0, 129.7, 128.5, 128.2, 127.3, 127.0, 126.9, 126.3, 126.2, 113.7, 55.4, 54.7, 54.5, 52.6, 49.3, 21.9, 12.8; HRMS (ESI, $[M+Na]^+$) for $C_{28}H_{26}NaO_2$ calcd. 417.1825, found: m/z 417.1819.



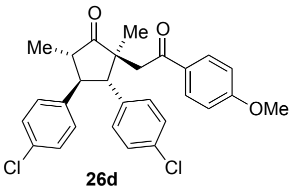
26b

Reaction carried out at −78 °C (acetone/dry ice bath) was performed under the standard procedure. Flash chromatography (10:1 hexane:EtOAc) gave **26b** (232 mg, 95%) as a colorless oil: IR (film) 3028, 2966, 1736, 1671, 1602, 1567 cm^{-1}; ^{1}H NMR (500 MHz, CDCl$_3$) d 7.80 (d, *J* = 8.5 Hz, 1H), 7.40 (d, *J* = 8.0 Hz, 2H), 7.27 (d, *J* = 7.5 Hz, 2H), 7.24 (d, *J* = 7.5 Hz, 2H), 7.19-7.16 (m, 2H), 7.11 (d, *J* = 7.5 Hz, 2H), 6.84-6.80 (m, 2H), 4.07 (d, *J* = 12.5 Hz, 1H), 3.89 (s, 3H), 3.38 (app. t, *J* = 12.0 Hz, 1H), 3.35 (d, *J* = 18.5 Hz, 1H), 3.27 (d, *J* = 18.5 Hz, 1H), 3.18 (dq, *J* = 12.0, 7.0 Hz, 1H), 2.62 (s, 3H), 1.21 (d, *J* = 7.0 Hz, 3H), 0.79 (s, 3H); ^{13}C NMR (125 MHz, CDCl$_3$) δ 221.2, 199.5, 162.1, 142.3, 141.5, 137.5, 131.6, 129.8, 129.3, 128.5, 128.2, 128.0, 126.7, 126.7, 117.7, 110.8, 55.4, 53.3, 51.6, 51.2, 50.8, 47.7, 22.6, 20.1, 13.5; HRMS (ESI, [M+Na]$^+$) for $C_{29}H_{30}NaO_3$ calcd. 449.2087, found: m/z 449.2077.



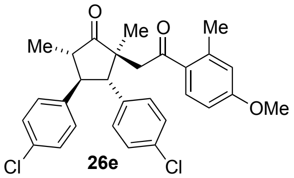
26c

Reaction carried out at −78 °C (acetone/dry ice bath) was performed under the standard procedure. Flash chromatography (10:1 hexane:EtOAc) gave **26c** (43 mg, 62%) as a colorless oil: IR (film) 3029, 2966, 1737, 1678, 1606 cm^{-1}; ^{1}H NMR (500 MHz, CDCl$_3$) d 7.95-7.93 (m, 2H), 7.41-7.39 (m, 2H), 7.34-7.32 (m, 2H), 7.28-7.22 (m, 4H), 7.19-7.15 (m, 2H), 7.10-7.08 (m, 2H), 4.08 (d, *J* = 12.0 Hz, 1H), 3.40 (d, *J* = 18.5 Hz, 1H), 3.39 (app. t, *J* = 12.0 Hz, 1H), 3.33 (d, *J* = 19.0 Hz, 1H), 3.16 (dq, *J* = 11.5, 7.0 Hz, 1H), 2.47 (s, 3H), 1.24 (d, *J* = 7.0 Hz, 3H), 0.84 (s, 3H); ^{13}C NMR (125 MHz, CDCl$_3$) δ 221.1, 197.6, 144.4, 141.3, 137.3, 134.2, 129.4, 129.3, 128.5, 128.3, 128.2, 128.0, 126.7, 126.7, 53.2, 51.6, 51.1, 50.4, 45.3, 21.7, 20.1, 13.5; HRMS (ESI, [M+Na]$^+$) for $C_{28}H_{28}NaO_2$ calcd. 419.1982, found: m/z 419.1976.



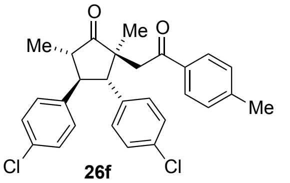
26d

Reaction carried out at –40 °C (acetonitrile/dry ice bath) was performed under the standard procedure. Flash chromatography (10:1 hexane:EtOAc) gave **26d** (100 mg, 92%) as a colorless oil: IR (film) 3025, 2966, 1737, 1671, 1599 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) d 8.01-7.98 (m, 2H), 7.31-7.29 (m, 2H), 7.26-7.21 (m, 4H), 7.01-6.98 (m, 4H), 4.02 (d, *J* = 12.0 Hz, 1H), 3.93 (s, 3H), 3.39 (d, *J* = 18.5 Hz, 1H), 3.29 (app. t, *J* = 12.0 Hz, 1H), 3.23 (d, *J* = 18.5 Hz, 1H), 3.10 (dq, *J* = 12.0, 7.0 Hz, 1H), 1.22 (d, *J* = 7.0 Hz, 3H), 0.84 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 220.1, 196.3, 164.0, 139.5, 135.6, 132.8, 132.6, 130.4, 129.6, 129.2, 128.8, 128.5, 113.9, 55.6, 52.8, 51.4, 50.8, 50.3, 45.0, 19.9, 13.4 [one sp^2 carbon signal is missing due to peak overlap.]; HRMS (ESI, $[M+Na]^+$) for $C_{28}H_{26}Cl_2NaO_3$ calcd. 503.1151, found: m/z 503.1149.



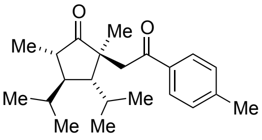
26e

Reaction carried out at –40 °C (acetonitrile/dry ice bath) was performed under the standard procedure. Flash chromatography (10:1 hexane:EtOAc) gave **26e** (103 mg, 84%) as a colorless oil: IR (film) 2966, 2930, 1737, 1669, 1602, 1567 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) d 7.78 (d, *J* = 8.5 Hz, 1H), 7.30-7.22 (m, 6H), 7.03-7.01 (m, 2H), 6.83-6.79 (m, 2H), 3.99 (d, *J* = 12.0 Hz, 1H), 3.90 (s, 3H), 3.35 (d, *J* = 18.5 Hz, 1H), 3.28 (app. t, *J* = 12.0 Hz, 1H), 3.20 (d, *J* = 18.0 Hz, 1H), 3.12 (dq, *J* = 12.0, 7.0 Hz, 1H), 2.64 (s, 3H), 1.22 (d, *J* = 7.0 Hz, 3H), 0.81 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 220.1, 199.2, 162.3, 142.5, 139.6, 135.7, 132.8, 132.5, 131.6, 130.4, 129.4, 129.2, 128.8, 128.5, 117.7, 110.8, 55.4, 52.9, 51.3, 50.9, 50.6, 47.5, 22.7, 19.9, 13.4; HRMS (ESI, $[M+Na]^+$) for $C_{29}H_{28}Cl_2NaO_3$ calcd. 517.1308, found: m/z 517.1299.



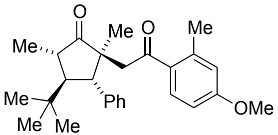
26f

Reaction carried out at −40 °C (acetonitrile/dry ice bath) was performed under the standard procedure. Flash chromatography (10:1 hexane:EtOAc) gave **26f** (55 mg, 61%) as a colorless oil: IR (film) 3030, 2966, 1737, 1677, 1607 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) d 7.90-7.87 (m, 2H), 7.31-7.17 (m, 8H), 6.98-6.95 (m, 2H), 3.98 (d, *J* = 12.3 Hz, 1H), 3.38 (d, *J* = 18.9 Hz, 1H), 3.26 (app. t, *J* = 12.0 Hz, 1H), 3.22 (d, *J* = 18.6 Hz, 1H), 3.07 (dq, *J* = 11.4, 6.9 Hz, 1H), 2.44 (s, 3H), 1.19 (d, *J* = 7.2 Hz, 3H), 0.81 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 220.0, 197.5, 144.6, 139.5, 135.6, 134.0, 132.9, 132.6, 130.4, 129.5, 129.2, 128.8, 128.5, 128.2, 52.8, 51.4, 50.9, 50.3, 452, 21.7, 19.9, 13.4; HRMS (ESI, $[M+Na]^+$) for $C_{28}H_{26}Cl_2O_2$ calcd. 487.1202, found: m/z 487.1199.



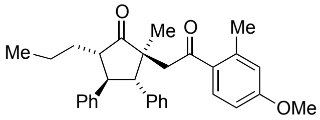
26g

Reaction carried out at −12 °C (ethylene glycol/dry ice bath) was performed under the standard procedure. Flash chromatography (10:1 hexane:EtOAc) gave **26g** (27 mg, 30%) as a colorless oil: IR (film) 2962, 2933, 1735, 1682, 1608 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) d 7.85-7.83 (m, 2H), 7.27-7.25 (m, 2H), 3.38 (d, *J* = 18.5 Hz, 1H), 3.27 (d, *J* = 18.0 Hz, 1H), 2.60 (dq, *J* = 10.5, 7.0 Hz, 1H), 2.43 (s, 3H), 2.20 (dd, *J* = 11.5, 2.5 Hz, 1H), 2.10 (qqd, *J* = 7.0, 7.0, 2.0 Hz, 1H), 1.90 (qqd, *J* = 7.0, 7.0, 2.0 Hz, 1H), 1.85 (ddd, *J* = 11.0, 11.0, 2.5 Hz, 1H), 1.26 (d, *J* = 7.0 Hz, 3H), 1.12 (d, *J* = 7.0 Hz, 3H), 1.04 (d, *J* = 7.0 Hz, 3H), 1.02 (d, *J* = 7.5 Hz, 3H), 1.01 (d, *J* = 6.5 Hz, 3H), 1.00 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 224.2, 197.4, 143.9, 134.6, 129.2, 128.1, 50.5, 48.9, 46.3, 45.9, 43.3, 28.2, 26.4, 24.4, 23.3, 21.6, 19.9, 19.6, 17.5, 15.9; HRMS (EI, M^+) for $C_{22}H_{32}O_3$ calcd. 328.2402, found: m/z 328.2403.



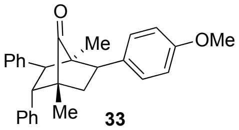
26h

Reaction carried out at −40 °C (acetonitrile/dry ice bath) was performed under the standard procedure. Flash chromatography (10:1 hexane:EtOAc) gave **26h** (20 mg, 32%) as a colorless oil: IR (film) 3026, 2963, 1734, 1672, 1603, 1568 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) d 7.70-7.67 (m, 1H), 7.35-7.32 (m, 2H), 7.23-7.20 (m, 2H), 6.86-6.85 (m, 1H), 6.75-6.71 (m, 2H), 3.85 (s, 3H), 3.58 (d, *J* = 11.4 Hz, 1H), 3.17 (d, *J* = 18.3 Hz, 1H), 3.01 (d, *J* = 18.3 Hz, 1H), 2.70 (dq, *J* = 9.0, 7.2 Hz, 1H), 2.54 (s, 3H), 2.28 (dd, *J* = 11.1, 8.7 Hz, 1H), 1.43 (d, *J* = 7.5 Hz, 3H), 0.86 (s, 9H), 0.71 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 224.1, 199.0, 161.9, 142.1, 141.2, 131.3, 130.5, 130.0, 128.7, 128.4, 127.6, 126.4, 117.5, 110.6, 55.3, 54.3, 51.4, 49.7, 47.4, 44.6, 34.3, 29.5, 22.4, 21.4, 20.8; HRMS (ESI, $[M+Na]^+$) for $C_{27}H_{37}NaO_3$ calcd. 429.2400, found: m/z 429.2389.



26i

Reaction carried out at −78 °C (acetone/dry ice bath) was performed under the standard procedure. Flash chromatography (10:1 hexane:EtOAc) gave **26i** (24 mg, 62%) as a colorless oil: IR (film) 3027, 2962, 1735, 1670, 1602 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) d 7.77 (d, *J* = 8.5 Hz, 1H), 7.41-7.39 (m, 2H), 7.27-7.19 (m, 4H), 7.18-7.15 (m, 2H), 7.13-7.10 (m, 2H), 6.83-6.78 (m, 2H), 4.00 (d, *J* = 12.0 Hz, 1H), 3.89 (s, 3H), 3.54 (app. t, *J* = 12.0 Hz, 1H), 3.32 (d, *J* = 18.5 Hz, 1H), 3.20 (d, *J* = 18.0 Hz, 1H), 3.23-3.19 (m, 1H), 2.65 (s, 3H), 1.79-1.63 (m, 2H), 1.48-1.40 (m, 1H), 1.30-1.22 (m, 1H), 0.87 (app. t, *J* = 7.5 Hz, 3H), 0.80 (s, 3H), ; ^{13}C NMR (125 MHz, $CDCl_3$) δ 220.9, 119..6, 162.0, 142.2, 142.2, 137.5, 131.5, 129.9, 129.3, 128.4, 128.1, 128.0, 126.7, 126.5, 117.6, 110.7, 55.9, 55.4, 54.1, 50.8, 48.7, 47.6, 31.3, 22.5, 20.2, 19.6, 14.3; HRMS (ESI, $[M+Na]^+$) for $C_{31}H_{34}NaO_3$ calcd. 477.2400, found: m/z 477.2390.



33

1,5-Diphenyl-2,4-dimethyl-1,4-pentadien-3-one **1a** (69 mg, 0.26 mmol) and 4-vinylanisole (0.31 mmol, 1.2 equiv) were dissolved in dichloromethane (1.5 mL) under argon and cooled to −78 °C (acetone/dry ice bath). Boron trifluoride etherate (36 μL, 0.29 mmol, 1.1 equiv) was added dropwise. The reaction mixture was stirred at the same temperature for 15 min. The reaction was quenched with saturated aqueous sodium bicarbonate (4 mL) and warmed to room temperature. The aqueous layer was extracted with dichloromethane (2 x 8 mL), the combined organic layers were washed with brine solution (1 x 15 mL) and dried over anhydrous magnesium sulfate. After filtration, the solvent was removed by rotary evaporation providing a crude residue that was purified by flash column chromatography (silica gel) to provide the desired product **33** (34 mg, 33%) as a white solid: mp 140-141 °C; IR (film) 3030, 2925, 1755, 1610, 1514 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) d 7.45-7.41 (m, 4H), 7.35-7.32 (m, 1H), 7.28-7.25 (m, 2H), 7.21-7.18 (m, 1H), 7.11-7.09 (m, 2H), 7.03-7.01 (m, 2H), 6.87-6.85 (m, 2H), 3.82 (s, 3H), 3.48 (d, *J* = 7.0 Hz, 1H), 3.25-3.22 (m, 2H), 2.53 (dd, *J* = 13.5, 10.5 Hz, 1H), 1.58 (ddd, *J* = 14.0, 5.0, 2.0 Hz, 1H), 1.19 (s, 3H), 0.40 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 219.6, 158.4, 143.1, 137.9, 136.2, 129.4, 128.9, 128.5, 128.4, 128.3, 127.2, 126.9, 113.9, 56.0, 55.4, 55.2, 51.7, 49.4, 48.6, 34.4, 14.0, 11.2; HRMS (ESI, $[M+Na]^+$) for $C_{28}H_{28}NaO_3$ calcd. 419.1982, found: m/z 419.1968.

2.6 References

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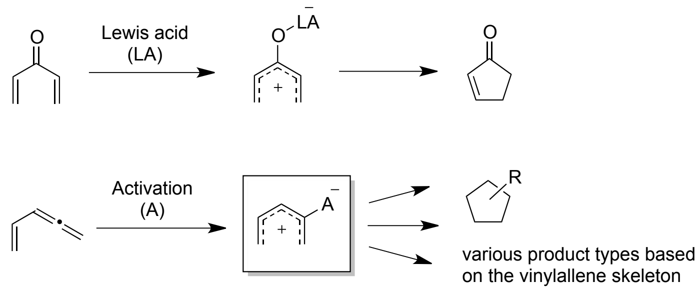
Chapter 3

Nazarov Chemistry of Vinylallenes[1]

3.1 Accessing the Nazarov Pentadienyl Intermediate from Vinylallenes

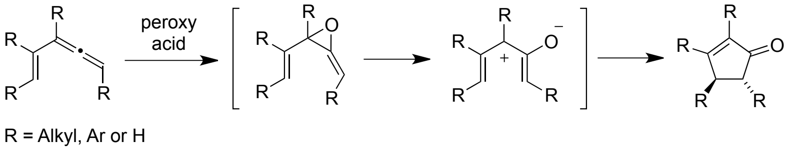
The Nazarov cyclization, among various approaches for cyclopentannulation reactions, is arguably one of the most prominent protocols.[2] In its traditional format, a pentadienyl cation is first generated through the acid activation of a cross-conjugated dienone, which then cyclizes to give the corresponding cyclopentenone. However, alternative routes to access the requisite pentadienyl system are possible, offering opportunities to expand the substrate scope and applications of the Nazarov-type cyclization. In particular, cycloisomerization of vinylallenes leading to five-membered carbocycles has been recently investigated under different sets of activation conditions (Scheme 1).



Scheme 1. Nazarov-type Cyclization Using Vinylallenes

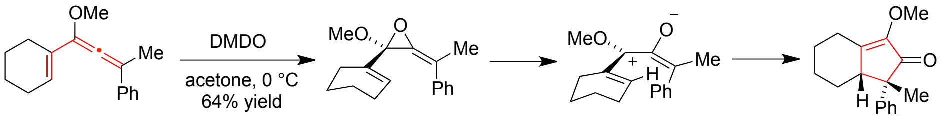
3.1.1. Oxidation-Initiated Cyclization of Vinylallenes

In the biosynthesis of jasmonates in plants, allene oxide synthase (AOS) and allene oxide cyclase (AOC) have been identified in the enzymatic conversion of a polyunsaturated fatty acid into a cyclopentenone intermediate, wherein the vinylallene oxide moiety derived from the metabolic oxidation of a vinylallene rearranges into a carbocyclic core.[3] Oxidative transformation of simple vinylallenes into cyclopentenone products has been conducted in the laboratory (Scheme 2).[4] However, the regioselectivity of the epoxidation step could be problematic resulting in side products.



Scheme 2. Cyclopentenone Formation via an Allene Oxide

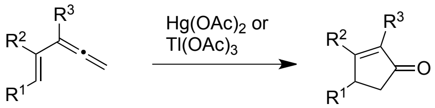
More recently, Frontier and co-workers developed the oxidation-initiated cyclization of alkoxy-substituted vinylallenes under relatively mild conditions.[5] The synthetic utility of such approach has also been exemplified in the total synthesis of (±)-rocaglamide.[6] The epoxidation with dimethyldioxirane (DMDO) occurred regioselectively on the electronically biased internal C=C bond of the allene, also from the less sterically demanding face (Scheme 3). The pentadienyl cation was unveiled from ring opening of the strained epoxide, and underwent conrotatory electrocyclization to give highly functionalized cyclopentenones.



Scheme 3. Oxidation-initiated Nazarov Cyclization

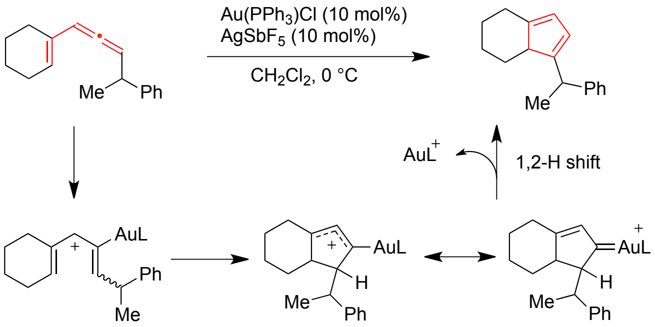
3.1.2. Transition Metal-Catalyzed Cyclization of Vinylallenes

Electrophilic activation of allenes with π-Lewis acids represents a major field of recent research focus.[7] Nevertheless, some early examples have shown that mercury(II) and thallium(III) acetate promote the oxidative conversion of vinylallenes into cyclopentenones (Scheme 4).[8] The proposed mechanism was presumed to involve acetate trapping of the allyl cation intermediate followed by a demetalation sequence.

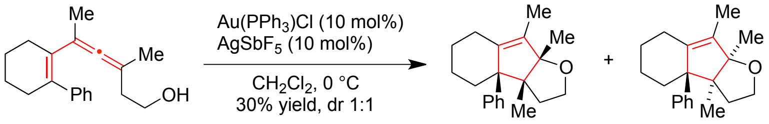


Scheme 4. Early Examples of Oxidative Cycloisomerization of Vinylallenes

More recently, Lee and Toste described a gold(I)-catalyzed cycloisomerization of 1,2,4-trienes for the synthesis of cyclopentadienes (Scheme 5).[9] Coordination of a cationic gold(I)-phosphine complex to the allene moiety furnished a pentadienyl cation intermediate that underwent electrocyclization to give the allyl cation. The gold(I)-carbenoid intermediate then collapsed through an 1,2-hydrongen shift yielding a single regioisomer of the cyclopentadiene. The authors also demonstrated that a tethered hydroxy group could intercept the vinyl gold-carbenoid to provide tetrahydrofuran products (Eq 1).

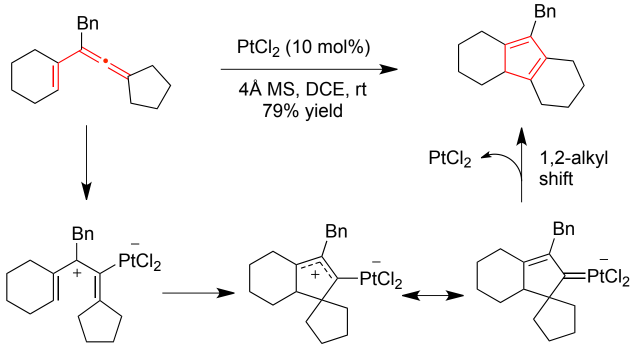


Scheme 5. Gold(I)-catalyzed Cyclopentadiene Synthesis



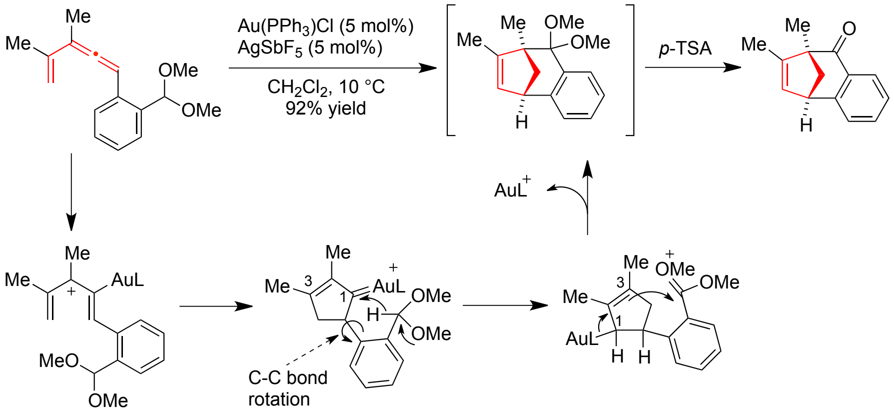
(1)

Published back to back with Toste,[9] Iwasawa and co-workers found that treatment of vinylallenes with platinum(II) chloride resulted in the formation of substituted cyclopentadienes in good yields.[10] With 1,1-disubstituted 1,2,4-trienes, a 1,2-alkyl shift following annulation proceeded smoothly to give a tricyclic diene (Scheme 6).



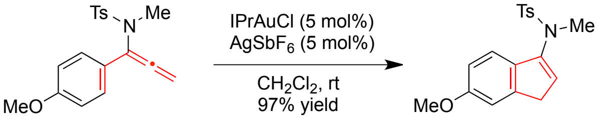
Scheme 6. Pt(II)-catalyzed Cyclopentadiene Synthesis

In 2008, Bhunia and Liu disclosed a novel cascade sequence initiated by the annulation reaction of 1,2,4-trienes in the presence of a gold(I) catalyst.[11] Conjugated gold(I)-carbenoids, which were derived from the cycloisomerization of vinylallenes appended with a ketal functionality, induced an unconventional mode of C–H activation to give bridged bicyclic products (Scheme 7). From the deuterium-labeling and crossover experiments, the authors presumed that the 1,3-addition of $C(sp^3)$–H bond to vinylcarbenoid species proceeded through an intramolecular fashion. No simple cyclopentadiene products were observed in Liu's system, highlighting the competitiveness of the hydride transfer, likely assisted by oxygenation on the hydride donor carbon.



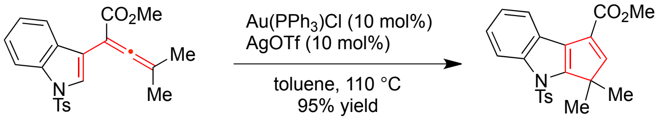
Scheme 7. Gold(I)-catalyzed Synthesis of Bridged Bicycles

Hsung and co-workers described a formal imino-Nazarov cyclization where a variety of α-aryl allenamides were converted into sulfoamide-substituted indenes through gold(I) activation (Eq 2).[12] This result represents an elegant solution to the challenge of establishing the cyclization of C-3 nitrogenated pentadienyl cations.[13]



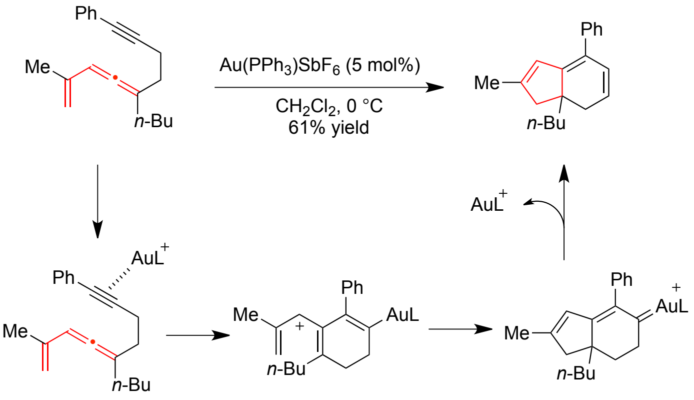
(2)

Similarly, gold-catalyzed cyclizations of 3-allenyl indoles led to the formation of indole-fused cyclopentenes (Eq 3).[14] Notably, the presence of electron-withdrawing groups at the internal allene carbon was found to be critical to the success of this transformation.



(3)

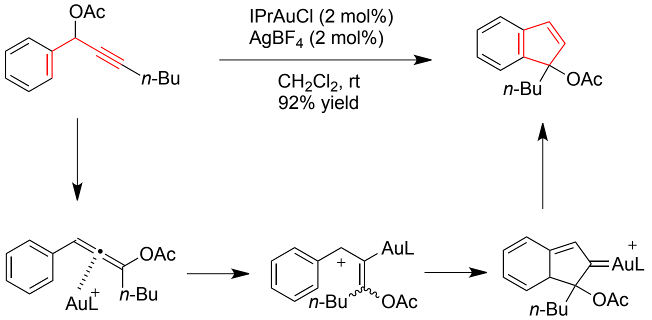
Liu and co-workers developed a catalytic annulation cascade of 1,6-allenynes, wherein a 6-*endo* cyclization of Au(I)-π-alkyne complexes was followed by a Nazarov-type reaction.[15] A notable feature of this work is that the cyclization of vinylallenes was triggered by a tethered gold-activated π-system, resulting in an additional carbon–carbon bond forming event.



Scheme 8. Gold-catalyzed Double Annulation of 1,6-Allenynes

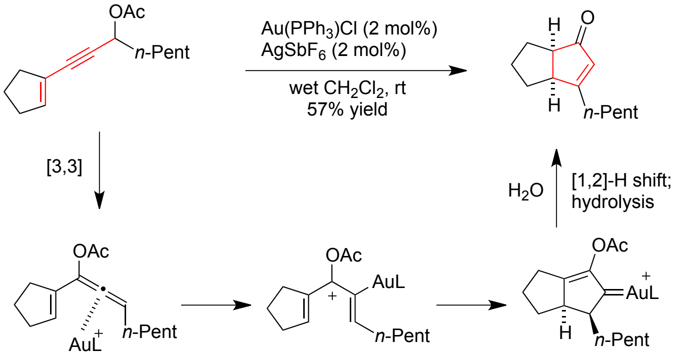
3.1.3. Tandem Vinyallene Formation/Cyclization Sequence

In 2006, Nolan and co-workers described a novel type of gold-catalyzed synthesis of oxygenated indenes from aryl propargyl acetates (Scheme 9).[16] The initial 1,3-migration of the acetate moiety gave an aryl allene intermediates which was presumably facilitated by activation of the alkyne with a cationic gold species. The gold center that is mandatorily proximal to the allene moiety subsequently promoted the ring closure event.



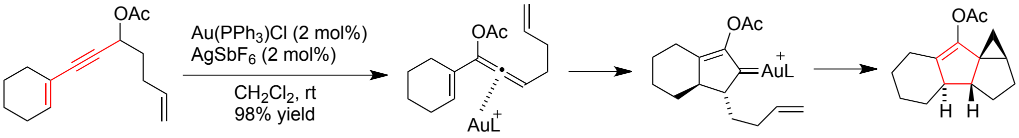
Scheme 9. Gold(I)-catalyzed Indene Synthesis

Conceptually related to Nolan's report,[16] Zhang and Wang reported that enynyl acetates could function as an alternative Nazarov precursor under gold catalysis (Scheme 10).[17] Gold(I) activation of the 3-acetoxy vinylallene, derived from the rearrangement of the propargylic acetate, furnished the cationic pentadienyl intermediate that then underwent Nazarov-type cyclization to give the cyclopentenone product. Interestingly, an increase in rate and yield was seen when the reaction was performed in wet dichloromethane as opposed to in anhydrous conditions; on the basis of a DFT study, the effect of water was presumed to involve assistance of the 1,2-hydrogen shift of the vinyl gold carbenoid, facilitating catalyst turnover.[18]



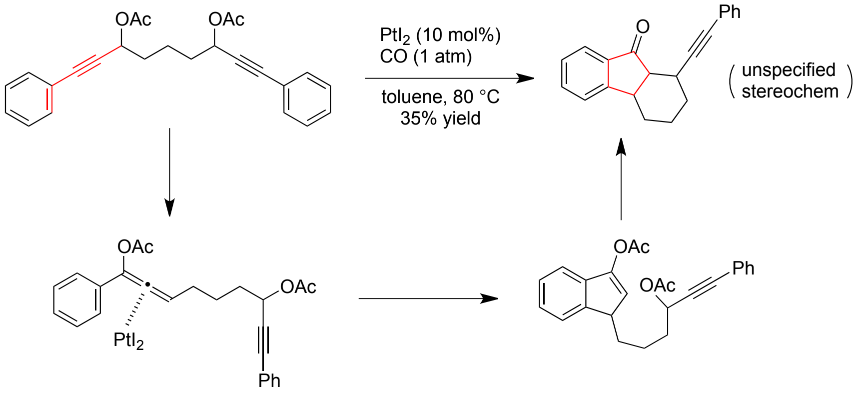
Scheme 10. Gold(I)-catalyzed Cyclopentenone Synthesis

Following the work by the Zhang group,[17] Malacria and co-workers devised an even more sophisticated domino process employing propargyl acetates appended with a remote olefin (Scheme 11).[19] Intriguingly, the reaction was terminated by an electrophilic cyclopropanation, where the Au(I)-cyclopentenylidene intermediates originated from the cycloisomerization were captured by the pendent alkene moiety, furnishing polycyclic compounds.



Scheme 11. Gold(I)-catalyzed Polycarbocycle Synthesis

For the cycloisomerization of arylpropargylic esters, She and co-workers found that various gold catalyst were, unexpectedly, ineffective to induce the formation of indanone derivatives.[20] However, optimal results could be obtained employing platinum(II) iodide under one atmosphere of carbon monoxide. An alternative trapping mode, in which the cycloisomerization product reacts with electrophiles, has been realized affording tricyclic frameworks in moderate yield (Scheme 12).

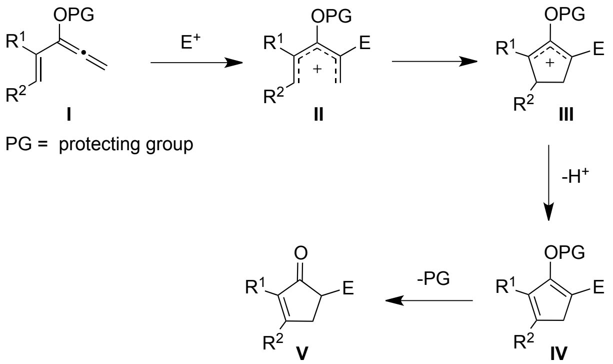


Scheme 12. Pt(II)-catalyzed Polycarbocycle Synthesis

3.2 Results and Discussions

Recently there has been considerable interest in alternative precursors to the key pentadienyl cation intermediate in the Nazarov reaction, potentially offering access to unusual substitution patterns or milder activation conditions. Notable examples include allenyl vinyl ketones, α-diketones, vinyl dichlorocyclopropanes, and cross-conjugated trienes.[2c] Additionally, several transition metal-catalyzed cycloisomerization approaches have been documented; in such variants of the Nazarov cyclization, activation of vinylallenes with gold(I) or platinum(II) species constitutes a major advance in the field, along the line with what has been discussed in Section 3.1. However, we were surprised to note that Brønsted acid activation of vinylallenes for the construction of cyclopentenoid compounds is unprecedented in the literature.

We sought to generalize a process of electrophilic activation of C-3 oxygenated vinylallenes **I**, to what would amount to a novel addition to alternative Nazarov chemistry.[2c] While conventional Nazarov sequences require Lewis acid-coordination on C-3 keto functionality to promote the cyclization (Scheme 1), the reaction of substrate **I** demands a bond-forming event at C-2 position which is activated by the C-3 oxygen substitution by resonance donating effect. In theory, addition of any electrophile would be expected to occur at the allene central carbon to directly furnish the desired pentadienyl intermediate **II**. Electrocyclization to cyclopentenyl cation **III** and termination via loss of a proton would then provide cyclopentenones, or alternatively **III** could be interecepted by a variety of traps in an "interrupted Nazarov" reaction.[2d] Here we describe the results of a preliminary study using Brønsted acid activation, in which protonation of readily prepared 3-silyloxy vinyl allenes effects their conversion to cyclopentenones under simple and mild conditions. Also, preliminary investigations of interrupted Nazarov reactions using arene-tethered vinylallenes will be discussed.

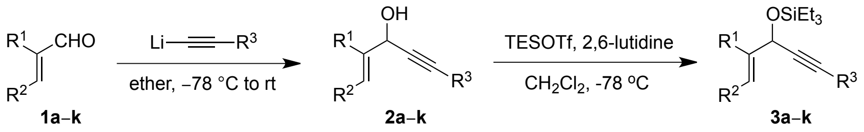


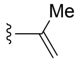
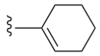
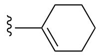
Scheme 13. Electrophilic Activation of Vinylallenes

3.2.1. Brønsted Acid-Mediated Nazarov Cyclizations of Vinylallenes

The proposed strategy required a reliable and efficient method for preparation of the oxygenated vinylallene substrates. We settled on a

Table 1. Preparation of Silyloxy Enynes[a]



Entry	R^1	R^2	R^3	Product of step 1 (Yield %)[b]	Product of step 2 (Yield %)[b]
1	Me	Ph	Ph	**2a** (86)	**3a** (96)
2	Me	Ph	*n*-Hex	**2b** (83)	**3b** (99)
3	Me	Ph		**2c** (90)	**3c** (95)
4	Me	Me	Ph	**2d** (91)	**3d** (72)
5	Me	Me	*n*-Hex	**2e** (94)	**3e** (95)
6	Me	Me		**2f** (95)	**3f** (77)
7	Me	$(CH_2)_2Ph$	Ph	**2g** (91)	**3g** (91)
8	H	Ph	Ph	**2h** (84)	**3h** (96)
9	$(CH_2)_4$		Ph	**2i** (92)	**3i** (95)
10	$(CH_2)_4$		*n*-Hex	**2j** (92)	**3j** (94)
11	$(CH_2)_3$			**2k** (98)	**3k** (73)

[a]General procedures are given in the experimental section. [b]Isolated yields.

straightforward approach employing base-catalyzed isomerization[21] of suitably protected allyl propargyl alcohols **3**, which should be readily available from acetylide addition into enals, followed by installation of the protecting group. In the event, a variety of unsaturated aldehydes were subjected to 1,2-addition of lithium acetylides to afford alcohols **2a**-**k** in high yields (Table 1).

The next task was to identify a suitable protecting group (PG, see Scheme 13) for the following alkyne/allene isomerization and Nazarov-type reaction. Initially, we envisioned that a robust protecting group would be essential for the electrophilic activation of allene substrates, as a premature deprotection, leading to simple divinyl ketone, was thought to be detrimental to the cyclization step. In the event, the corresponding triisopropylsilyl ethers could be prepared in high yields, but the subsequent isomerization step failed to go to completion. This failure with the use of a bulkier protecting group prompted us to screen other relatively small protecting groups (e.g. triethylsilyl group, Figure 1). The alcohols were then cleanly protected as triethylsilyl ethers **3a**-**k** by treatment with Et_3SiOTf at low temperature in the presence of 2,6-lutidine (Table 1).

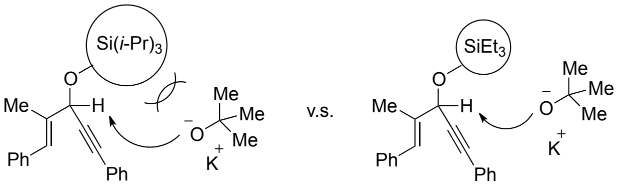
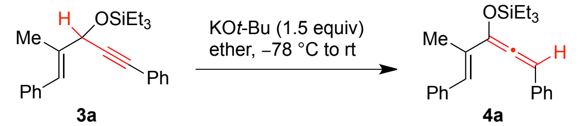


Figure 1. Steric Effects of the Protecting Group

Substrate **3a** was chosen to examine the feasibility of the desired process. First, isomerization of the enyne **3a** to vinyl allene **4a** was explored; several basic conditions including NaH/catalytic EtOH in THF, KOH in EtOH, and *n*-BuLi in THF did not offer a clean reaction profile for the allene/alkyne isomerization. However, the reaction proceeded smoothly upon treatment with 1.5 equiv KO*t*-Bu at –78 °C, followed by warming to room temperature (Scheme 14).[22] On the other hand, use of catalytic amounts (10 mol %) of KO*t*-Bu resulted in poor conversion and unacceptably slow reactions. While the desired vinyl allene **4a** was present as the principal component of the crude reaction mixture according to the diagnostic spectral data of the crude material (Scheme 14), it decomposed during attempted chromatographic purification. Therefore, conditions to effect the Nazarov reaction were evaluated with the unpurified **4a**.



3a

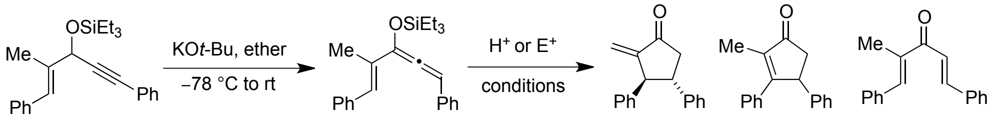
IR: 2203 cm^{-1}
^1H NMR: 5.21 ppm
^{13}C NMR: 89.2, 85.0 ppm

4a

IR: 1912 cm^{-1}
^1H NMR: 7.10 ppm
^{13}C NMR: 202.2 ppm

Scheme 14. Alkyne/Allene Isomerization and Diagnostic Spectral Data

Table 2. A Screening for the Electrophilic Activation of Vinylallenes



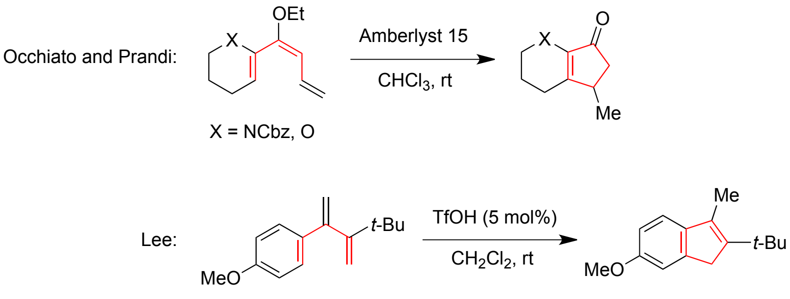
3a **4a** **5a** **6a** **7a**

Entry	H^+ or E^+	Solvent	T (°C)	Time (h)	Products (% yield over 2 steps)[e]
1[a]	H_3PO_4	CH_3CN	rt	4	**7a** (63)
2[a]	HCl	CH_3CN	rt	4	intractable mixture
3[a]	AcOH	CH_2Cl_2	rt	4	**7a** (45)
4[a]	$HClO_4$	CH_3CN	rt	4	**6a** (17)
5[a]	CF_3CO_2H	CH_2Cl_2	rt	4	**5a** (51) + **6a** (47)
6[b]	$BF_3{\cdot}OEt_2$	CH_2Cl_2	−78	0.5	intractable mixture
7[b]	$TiCl_4$	CH_2Cl_2	−78	0.5	intractable mixture
8[c]	$Sc(OTf)_3$/PhCHO	CH_2Cl_2	rt	4	**6a** (30)
9[c]	$BF_3{\cdot}OEt_2$/PhCHO	CH_2Cl_2	rt	4	**6a** (25)
10[d]	PhSeCl	CH_2Cl_2	reflux	8	intractable mixture
11[d]	NBS	CH_2Cl_2	rt	14	**7a** (trace)
12[d]	NIS	CH_2Cl_2	rt	14	**7a** (50)
13[d]	I_2	CH_2Cl_2	rt	14	**6a** (32)

[a] **4a** was stirred with Brønsted acid (3 equiv) in the indicated solvent for 4 h at rt. [b] **4a** was stirred with Lewis acid (1.1 equiv) in CH_2Cl_2 for 30 min at −78 °C. [c] **4a** and benzaldehyde (1.1 equiv) were stirred with Lewis acid (1.1 equiv) in CH_2Cl_2 for 4 h at rt. [d] **4a** was stirred with the indicated electrophilic agent (1.1 equiv) in CH_2Cl_2 for 14 h at rt. [e] Isolated yields.

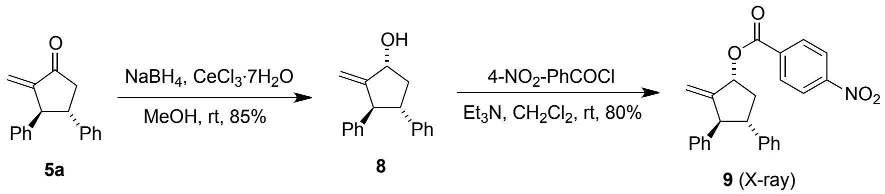
A number of Brønsted acids commonly applied to the Nazarov cyclization were initially tested (Table 2). Stronger mineral acids such as H_3PO_4 or HCl at room temperature resulted in destruction of **4a** or simple hydrolysis to give dienone **7a**, as was also the case with AcOH (entries 1–3). Perchloric acid in CH_3CN did furnish small amounts of the desired cyclopentenone **6a** (entry 4), butthe optimal conditions were found to be trifluoroacetic acid (TFA) in CH_2Cl_2, which afforded a nearly 1:1 mixture of **6a** and methylidene cyclopentanone **5a** in near quantitative yield (entry 5). Treatment of **4a** with strong Lewis acid led to decomposition of the starting material implying the cyclization has to be triggered by a protonation event (entries 6 and 7). Preliminary investigations into a domino aldol/Nazarov reaction sequence using a Lewis acid-activated aldehyde electrophile resulted in the formation of simple cyclopentenone **6a** in low yield (entries 8 and 9); we postulated that **6a** might be formed via a retro-aldol reaction of the aldehyde-trapped product, or some trace of water activated by the Lewis acid offered an alternative proton source for the Brønsted acid-mediated cyclization. Activations of allenes using heteroatom electrophiles were examined (entries 10–13), however no fruitful results were obtained under those conditions. When iodine was employed, **6a** presumably results from deiodination of the initially formed α-iodo ketone by additional iodide.[23]

Conceptually related to our work, protonation of isomeric trienes with strong Brønsted acids have been executed furnishing Nazarov-type products (Scheme 15).[24] Although surprisingly, in the latter example the authors did not postulate an electrocyclization mechanism for the trasformation.



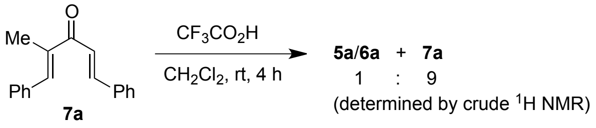
Scheme 15. Other Examples of Protonation-initiated Nazarov Process

The *trans* relative stereochemistry was unambiguously assigned to the product **5a** on the basis of single crystal X-ray diffraction analysis of a reduced derivative **9**. Compound **9** was prepared via a two-step sequence, in which compound **5a** was reduced under Luche conditions[25] to give the corresponding allylic alcohol **8** in a highly stereoselective fashion, and then the alcohol was capped with a nitrobenzoyl moiety furnishing a crystalline solid (Scheme 16).



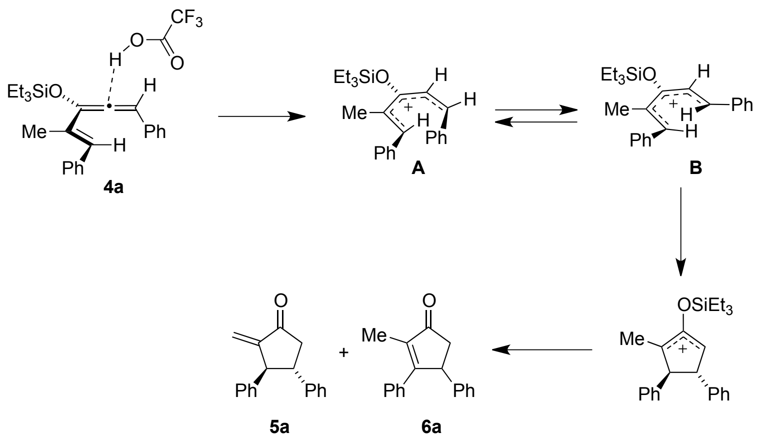
Scheme 16. Two-step Derivatization of **5a**

When dienone **7a** was subjected to the standard Brønsted acid activation (TFA/$\mathrm{CH_2Cl_2}$/4 h), a minor amount of cyclized products was formed (Eq 4), however the overall efficiency is inferior to the reaction involving vinylallene **4a** (Table 2, entry 5). Therefore, we discount an alternative mechanism invoking initial deprotection of the silyloxy allene, furnishing the conventional Nazarov precursor, the divinyl ketone, followed by electrocyclic ring closure.



(4)

With the above mechanistic study and the information of stereochemistry of **5a** in hand, we proposed a mechanism to account for the cycloisomerization of **4a** triggered by simple protonation. Assuming the usual conrotatory electrocyclization pathway, a *trans* relationship for the phenyl groups demands the intermediacy of (*E,E*)-pentadienyl cation **B** (Scheme 17). However, we presume initial protonation of the allenol silyl ether from the less hindered side, affording (*E,Z*)-pentadienyl cation **A**. If this is the case, an isomerization from **A** to **B** must take place prior to electrocyclization.[26]

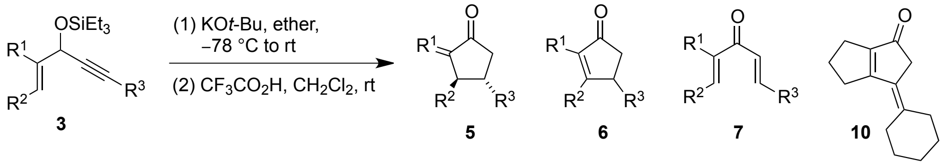


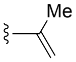
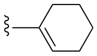
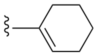
Scheme 17. Possible Pentadienyl Intermediate

In order to examine the scope of this process, the remaining substrates **3b–k** were then subjected to the standard conditions optimized for **3a** (Table 3). In general, the conversion of enynes **3** to the regioisomeric cyclized products **5**/**6** progressed swiftly with moderate to good overall yields (Table 3). In general, the substrate scope was broad with respect to the nature of substituent (R^3) attached to the alkyne moiety (alkyl, vinyl, or phenyl group). However, less-substituted substrate **3h** failed to undergo the desired annulation reaction, conforming to a general trend that cyclizations of pentadienyl systems lacking both 2- and 4-substituents are extremely sluggish.

For most acyclic substrates (entries 1−7), the termination of the Nazarov process by proton loss predominently led to cyclopentenone **6**, in contrast to the preferential formation of exocyclic olefins **5** for six-membered cyclic precursors (entries 9−10). In the case of **3k** (entry 11), the remote olefin within the resulting cyclized product isomerized under the acidic reaction conditions to give fully conjugated dienone **10** along with trace amount of hydrolyzed product **7k**. Moreover, **7k** was unreactive under the reaction conditions, indicating that the dienone is not an intermediate in the cyclization process. It is notable that all cyclopentenone products **6** were formed with complete regioselectivity in favor of the more substituted alkene isomer. Moreover, no evidence was seen of trapping of the cyclopentenyl cation by trifluoroacetate, in contrast to the recent report by

Table 3. Isomerization and Cyclization of Enynes[a]

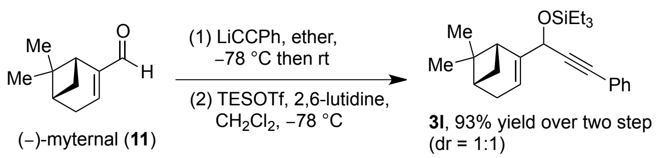


Entry	Substrate	R^1	R^2	R^3	Product(s) (% yield)[b]
1	**3a**	Me	Ph	Ph	**5a** (51) + **6a** (47)
2	**3b**	Me	Ph	*n*-Hex	**6b** (82)
3	**3c**	Me	Ph		**6c** (35)
4	**3d**	Me	Me	Ph	**5d** (10) + **6d** (30)
5	**3e**	Me	Me	*n*-Hex	**6e** (45)
6	**3f**	Me	Me		**6f** (45)
7	**3g**	Me	$(CH_2)_2Ph$	Ph	**5g** (28) + **6g** (39)
8	**3h**	H	Ph	Ph	**7h** (70)
9	**3i**	$(CH_2)_4$		Ph	**5i** (65) + **6i** (14)
10	**3j**	$(CH_2)_4$		*n*-Hex	**5j** (33) + **6j** (20)
11	**3k**	$(CH_2)_3$			**7k** (2) + **10** (28)

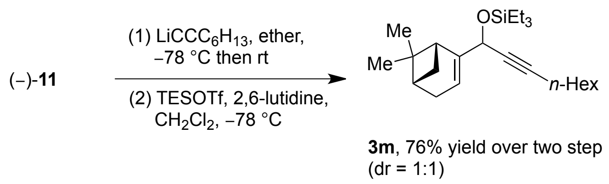
[a]General procedures are given in the experimental section. [b]Isolated yields.

Marx and Burnell.[27] A possible explanation for this difference is a longer-lived cyclopentenyl cation in allenyl vinyl ketone cases studied by Marx and Burnell due to greater conjugative stabilization.

To further explore the potential of this protocol, we then examined two examples in which the pentadienyl framework would be part of a rigid, bridged bicyclic system with preexisting stereogenic centers. Related dienone systems had displayed significant levels of diastereoselectivity in either silyl-directed Nazarov cyclizations[28] or halide trapping processes.[29] Enynes **3l** and **3m** were readily prepared from (–)-myrtenal (**11**) via the usual method (Eqs 5 and 6).

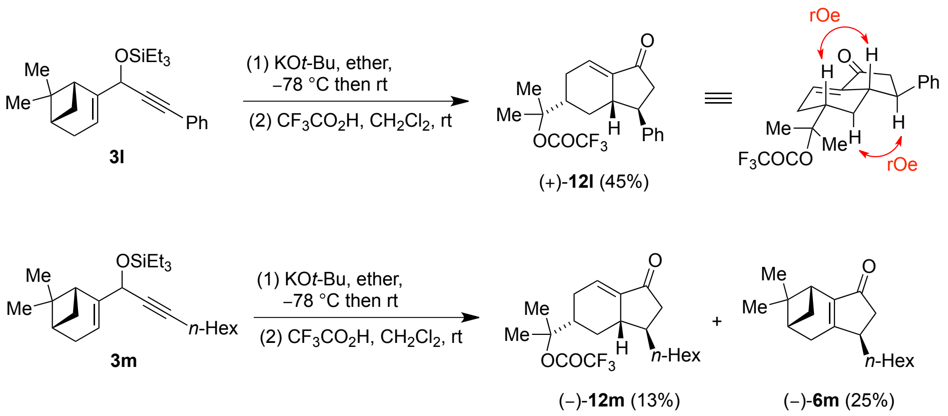


(5)



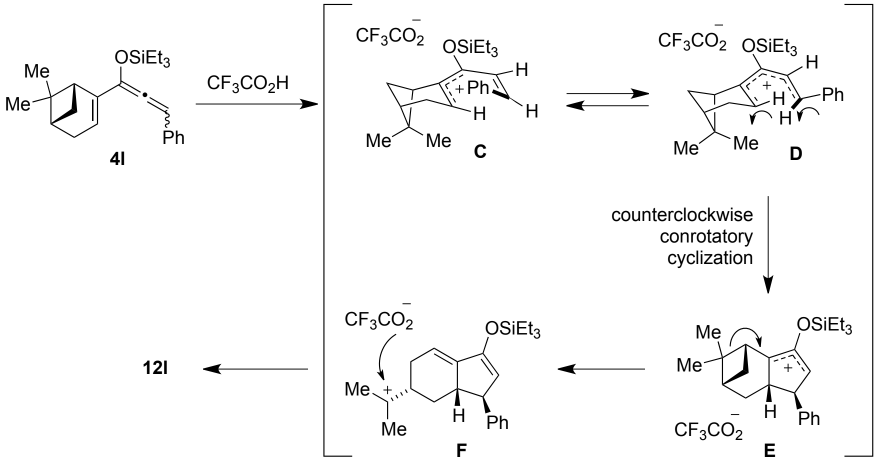
(6)

In the event, when **3l** was subjected to the typical conditions, the normal cyclized product was not observed to any extent. Instead, hydrindenone **12l** was obtained in moderate yield as a single diastereomer, with the relative configuration assigned based upon the indicated TROESY correlations (Scheme 18). Likewise, substrate **3m** also furnished hydrindenone **12m**, albeit less efficiently, along with greater amounts of compound **6m** arising from usual eliminative termination.



Scheme 18. Fragmentation of Bridged Bicyclic Substrates

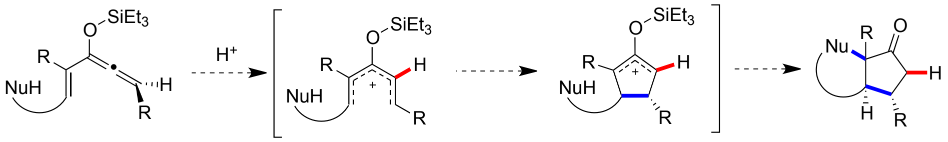
Product **12l** is presumed to result from bond cleavage of the strained cyclobutylcarbinyl cation **E** formed after electrocyclization (Scheme 19). The resulting tertiary cation would then undergo capture by trifluoroacetate. As with the simpler monocyclic product **5a**, the relative stereochemistry at the two centers in **12l** corresponding to the former termini of the pentadienyl indicates an isomerization of the initially formed (*E*,*Z*)-isomer to the (*E*,*E*) isomer prior to cylization. Notably, the relationship between the tertiary trifluoroacetate side-chain and the bridgehead proton indicates that cyclization of this cation appears to occur from the same face as the geminal dimethyl bridge (**D** to **E**). The complete facial selectivity observed in this case is somewhat unexpected; presumably, the counterclockwise torquoselectivity of the electrocyclization from that face is energetically favorable, as the alternate clockwise rotation would move the phenyl substituent into steric conflict with the hindered quaternary carbon of the bridge.



Scheme 19. Proposed Mechanism for the Formation of **12l**

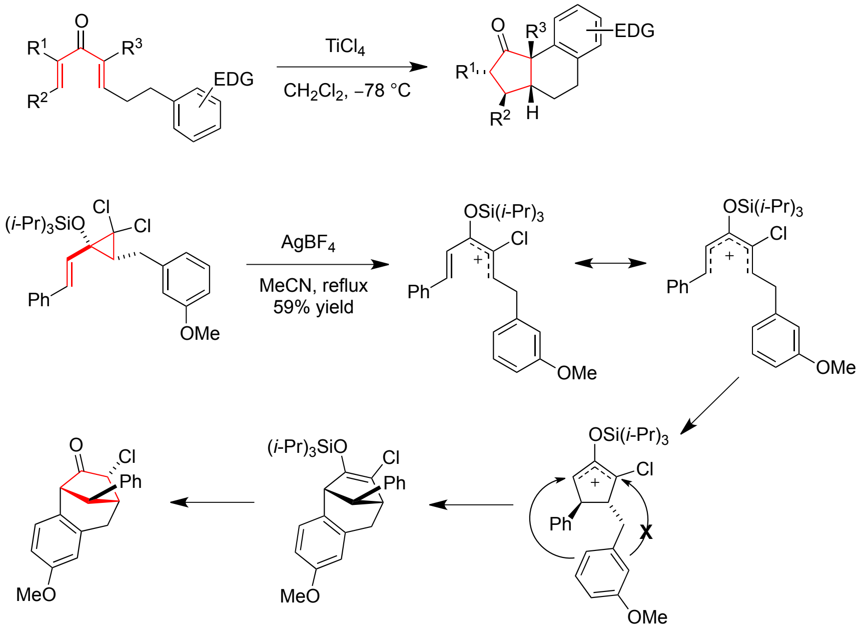
3.2.2. Intramolecular Arene Trapping of Oxyallyl Cations Derived from Vinylallenes

With the results discussed in the above section, we sought to explore an extension of the vinylallene version of the Nazarov reaction, involving an interrupted Nazarov process[2d] employing intramolecular nucleophilic traps (Scheme 20). The proposed domino reaction, initiated by simple protonation, would furnish valuable bicyclic building blocks from acyclic precursors.



Scheme 20. Proposed Interrupted Nazarov Reaction Using Vinylallenes

Previously, West and co-workers have demonstrated intramolecular arene trapping in traditional Nazarov reactions furnishing benzohydrindenones in good yields and with the establishment of up to four new stereocenters (Scheme 21).[30] More recently, Grant and West showed that interrupted Nazarov reaction utilizing *gem*-dichlorocyclopropanes as dienone surrogates were feasible, wherein a new mode of arene trapping was discovered in that system.[31] For instance an unusual bridged bicyclic skeleton could be constructed by tethering the arene trap through the cyclopropane unit (Scheme 21).



Scheme 21. Two Possible Arene-trapping Pathways

Since intramolecular capture of Nazarov intermediates with aryl functionality appears to be a facile and general process (both conventional and alternative Nazarov substrates were applicable), we envisioned that investigations into arene-terminated vinylallenes would be a logical starting point (Scheme 19, NuH = Ar). With preliminary results garnered, we shall make comparisons of trapping reactivity between these "interrupted Nazarov" systems (Figure 2).

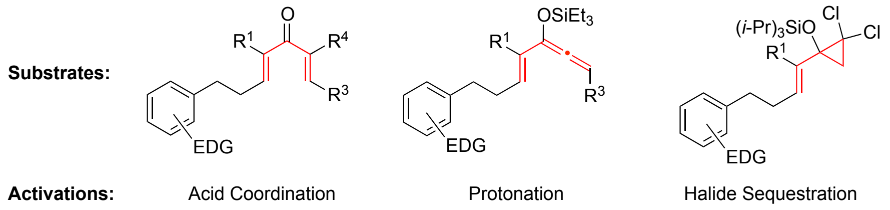
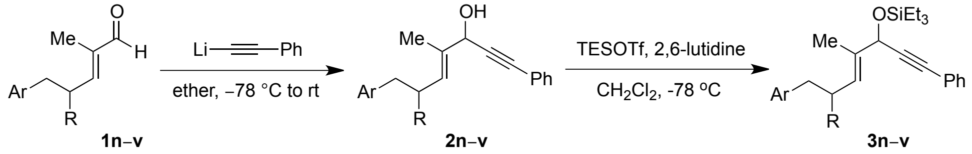


Figure 2. Three Different Modes of Activation for Non-traditional Nazarov Processes

We aimed to examine the effects of aromatic substitution and potential diastereocontrol. We had already shown that the cyclization of phenylethyl-substituted substrate **3g** in the two-step protocol resulted in the formation of regioisomeric cyclopentenone products with no evidence of arene trapping taking place (Table 3). An obvious direction that would lead to the success of our plan is to increase the nucleophilicity of the pendent aromatic trap. Hence substrates studied in this investigation were designed for probing those factors.

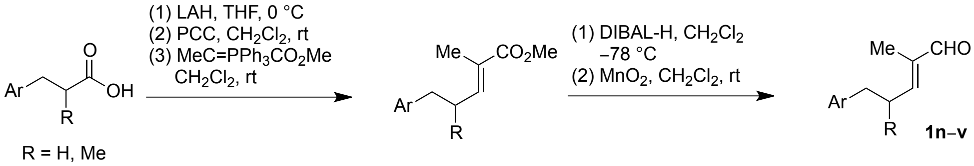
We adopted a previously described two-step strategy to prepare allene precursors from two fragments, terminal alkynes and arylethyl enals (Table 4). In the event, the synthetic route proved robust, wherein silyl-protected enynols **3n–v**, appended with a variety of aromatic groups were obtained in an efficient manner. The preparation of the required arene-tethered unsaturated aldehydes is synthetically trivial (Scheme 22); exhaustive reduction of the corresponding hydrocinnamic acids, followed by a PCC oxidation/Wittig olefination sequence, provided a series of unsaturated esters that were then converted to the desired enals through redox manipulations.

Table 4. Preparation of Arene-tethered Silyloxy Enynes[a]



Entry	Ar	R	Product of step 1 (Yield %)[b]	Product of step 2 (Yield %)[b]
1	3-MePh	H	**2n** (86)	**3n** (96)
2	4-MeOPh	H	**2o** (83)	**3o** (99)
3	3-MeOPh	H	**2p** (98)	**3p** (99)
4	3,4-$(MeO)_2$Ph	H	**2q** (87)	**3q** (91)
5	3,4-OCH_2OPh	H	**2r** (99)	**3r** (88)
6	3,4,5-$(MeO)_3$Ph	H	**2s** (95)	**3s** (66)
7	2-furyl	H	**2t** (99)	**3t** (99)
8	2-thienyl	H	**2u** (98)	**3u** (94)
9	3,4-OCH_2OPh	Me	**2v** (99)	**3v** (97)

[a]General procedures are given in the experimental section. [b]Isolated yields.



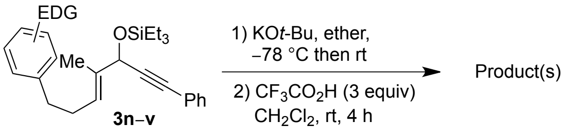
Scheme 22. Synthetic Route to Arylethyl Enals **1n–v**

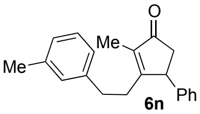
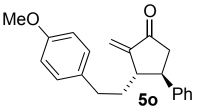
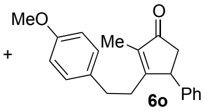
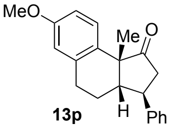
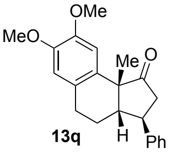
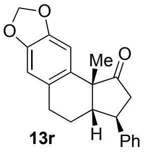
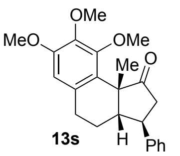
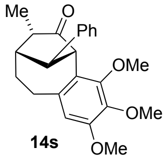
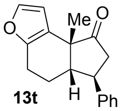
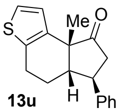
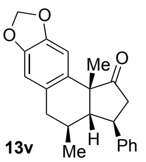
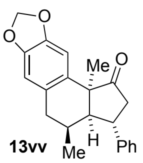
With the enyne substrates **3n–v** in hand, we applied the optimized conditions from the previous study (Section 3.2.1) to examine the protonation-initiated interrupted Nazarov processes wherein the reaction course could be diverted from the usual eliminative termination by electrophilic substitution onto pendent aryl traps (Table 5). We set out to probe the minimal nucleophilicity, which is reflected by the aromatic substitution pattern, required for the trapping to occur. An intramolecular tolyl trap failed to participate in the reaction, wherein only the product of the simple Nazarov reaction, **6n**, was observed (entry 1).

Similarly, reaction of substrate **3o** terminated with a 4-methoxyphenyl group furnished cyclized products derived from an initial electrocyclization and elimination rather than arene trapping (entry 2). In light of this result, we concluded that the *meta* carbon that ought to attack on the tertiary allylic cation might not be sufficiently electron-rich to affect the reaction. With modified substrate **3p**, we were delighted to find that the desired tricyclic compound **13p** was generated in good yield; moreover the arene trapping exclusively occurred at the position *para* to the methoxy substituent, rather than the more sterically demanding *ortho* carbon (entry 3); such a high level of regioselectivity has been noted in previously related studies.[30,31b] Substrates **3q**,**r** bearing arene traps with adequate nucleophilicity were swiftly converted to their corresponding benzohydrindan skeleton under the standard two-step preparations (entries 4 and 5). In the cases of **13p** and **13r**, we were able to unequivocally assign the relative stereochemistry based on X-ray analysis.

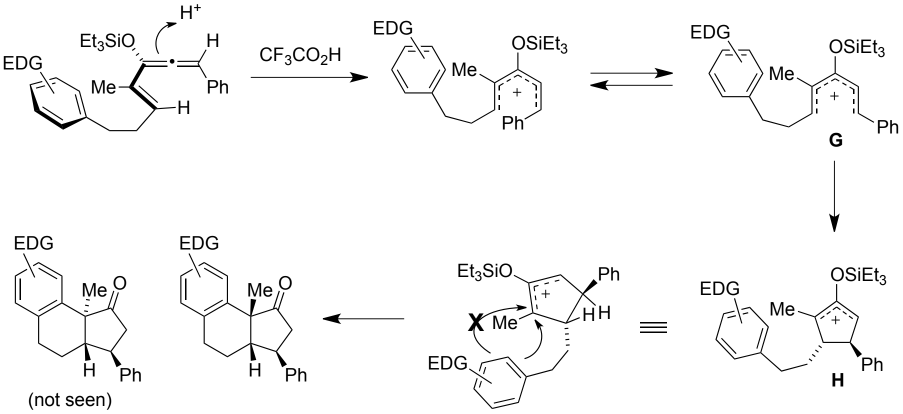
In light of the stereochemical outcome, a mechanism for this domino sequence was proposed as follows (Scheme 23). An initial protonation of the allenol silyl ether from the less hindered side followed by an isomerization gives the (*E*,*E*)-pentadienyl cation **G** which then cyclized in a conrotatory fashion. Subsequently, the aromatic trap approached the resulting oxyallyl cation intermediate **H** from the same face as the pendent side chain affording a *cis*-fused hydrindan product.

Table 5. Protonation-initiated Interrupted Nazarov Reactions[a]



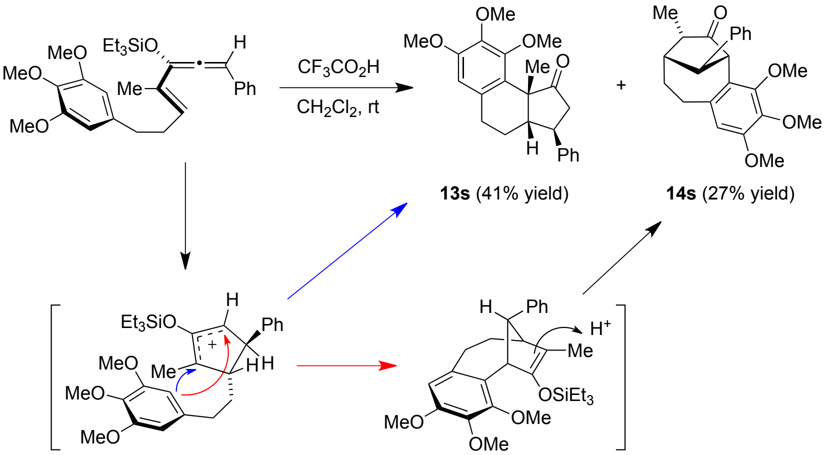
Entry	Substrate	Product(s)	Yield (%)[b]
1	**3n**		**6n** (64)
2	**3o**	 + 	**5o** (29) + **6o** (40)
3	**3p**		**13p** (53)
4	**3q**		**13q** (55)
5	**3r**		**13r** (65)
6	**3s**	 + 	**13s** (41) + **14s** (27)
7	**3t**		**13t** (trace)
8	**3u**		**13u** (60)
9	**3v**	 + 	**13v** + **13vv** (69; ca. 4.5:1)[c]

[a]General procedures are given in the experimental section. [b]Isolated yields. [c]Ratio was determined by ^{1}H NMR intergrations of the angular methyl group.



Scheme 23. Domino Protonation/Electrocyclization/Electrophilic Aromatic Substitution Sequence

When the nucleophilicity of the arene trap was increased by installing an additional methoxy substituent, a new mode of trapping occurred to give unusual bridged carbon frameworks (Table 5, entry 6). Beside the normal interrupted pathway, a novel 7-*exo* trapping by the pendent arene at the remote terminus of the oxyallyl cation led to the formation of an atypical product **14s** (Scheme 24). A provisional structural assignment of **14s** was made based on a series of 2D NMR analyses (Figure 3), indicating the final acidic hydrolysis was highly stereoselective from the convex face of the silyl enol ether intermediate. Although **14s** was generated as a minor component, it is the first instance of an interrupted Nazarov processes that the seven-membered ring formation was observed, overcoming detrimental entropy factor, when 6-*exo* cyclization is also possible. Presumably, both high electron density and steric bulk of the arene nucleophile were essential for this mode of trapping reactivity, allowing for the attack to occur on the less hindered, yet more distant terminus of the allylic cation.



Scheme 24. An Unusual Mode of Arene Trapping

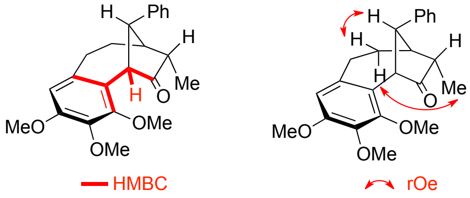
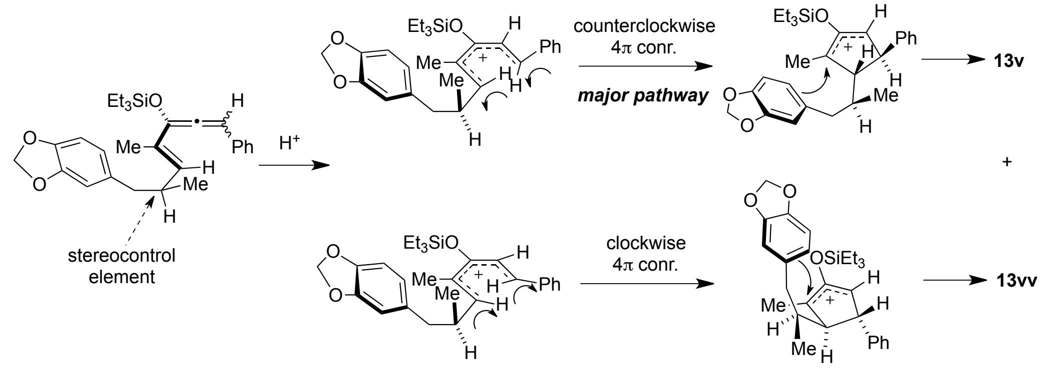


Figure 3. Diagnostic 2D NMR Correlations of **14s**

Reactions involving heterocycles as the terminator were also examined to test the scope of this process (Table 5, entries 7 and 8). Use of furan-containing substate **3t** provided only a trace amount of interrupted product, possibly as a result of the instability of the 2-furyl moiety in the presence of protic acid. On the other hand, the participation of a more robust thienyl group, in the case of **3u**, readily furnished thiophene-fused tricyclic product **13u** in good yield.

Finally, we incorporated a stereocenter within the tether to test whether it could offer any degree of stereocontrol; previously related studies have been focused only on substrates with one or more pre-existing stereocenters on the rigid carbocyclic frameworks. Intriguingly, we found that the presence of the stereogenic center on the rotatable side chain did affect the electrocyclization with a good level of torquoselectivity (entry 9). The structure of the major component **13v** has been validated by X-ray diffraction analysis. Although we have not computationally investigated what rotamer is in action, the relative configuration of **13v** indicated that counterclockwise conrotation, for the specific enantiomeric intermediate depicted in Scheme 25, is an energetically favored process.



Scheme 25. Torquoselectivity of Substrate Possessing a Stereogenic Center on the Side Chain

3.3 Conclusion

We have found that silyl-protected allyl propargyl alcohols can serve as convenient substrates for Nazarov cyclization, via sequential base-catalyzed isomerization to siloxy vinyl allenes, followed by mild activation with trifluoracetic acid. The modular nature of the substrate synthesis allows for substantial diversity in substitution. Notably, two cases possessing remote stereocenters displayed high levels of diastereoselectivity, as well as an intriguing fragmentation/trapping pathway.

Additionally, we describe a novel extension of the vinyl allene version of the Nazarov reaction, involving "interrupted Nazarov" cyclizations employing electron-rich arenes to afford tricyclic products. In one case using a particularly electron-rich trap, a new mode of cycloheptannulation reaction was seen in competition with the conventional 6-*exo* pathway. We also demonstrated that the torquoselectivity could be controlled, to a certain degree, by the stereogenic center resided on the rotatable side chain.

Comparing the trapping reactivity of three different Nazarov precursors (Figure 2), we learned that arene-terminated interrupted Nazarov reactions involving cationic intermediates derived from vinylallenes were, in general, analogous to the examples employing divinyl ketones; on the other hand, the chlorine-substituted oxyallyl intermediates, generated from rearrangements of alkenyl dichlorocyclopropanes, were considered to be more reactive, wherein even an electron-poor aryl moiety could readily participate in the Friedel-Crafts type reaction.

With the results from the above studies in hand, we postulated that the chemical shift of the aryl proton attached to the expected site of electrophilic substitution could be used as an indication of whether the arene nucleophile is sufficiently electron-rich to attack on the cationic Nazarov intermediate under the TFA-activation system (Figure 4). With the current data set, we may confidently predict that if the chemical shift of the proton of interest is greater than 7.02 ppm, the arene trapping pathway will not be able to compete with the simple eliminative termination.

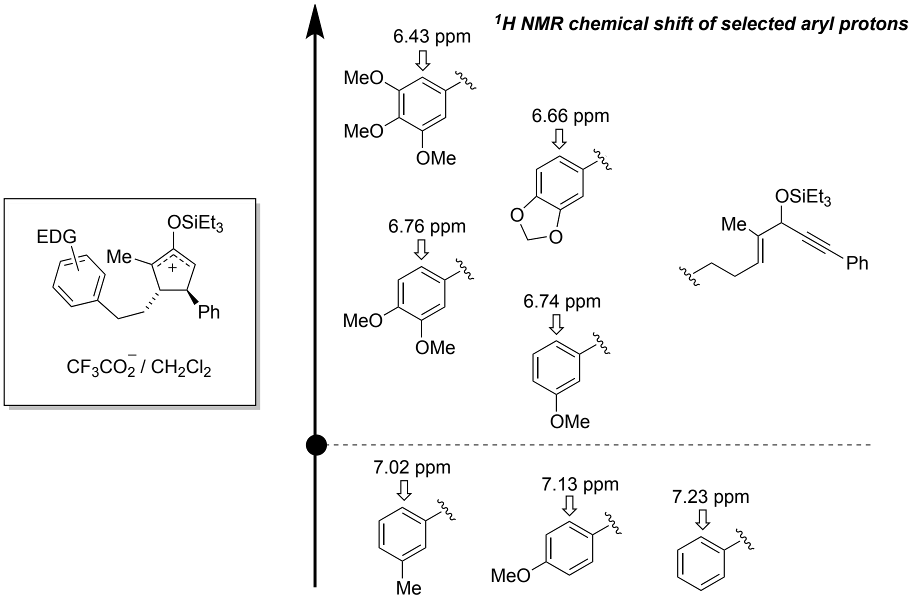
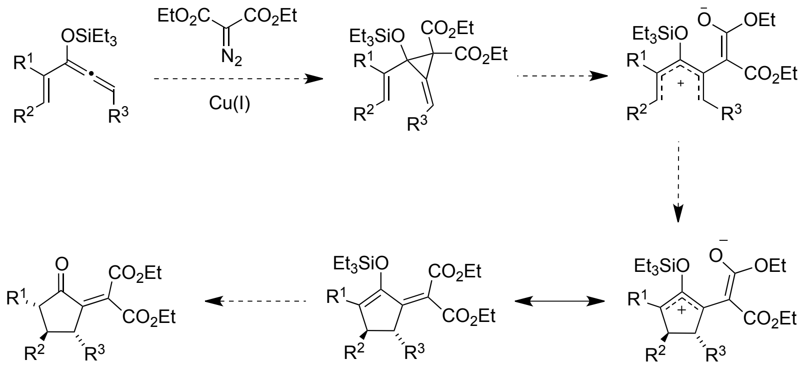


Figure 4. Attempts to Correlate Chemical Shifts and Trapping Reactivity

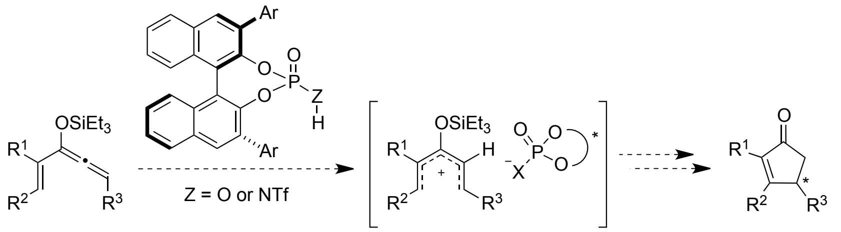
3.4 Future Directions

The use of vinylallene substrates as novel Nazarov precusors creates unique opportunities for accessing cyclopentenoid compounds through actions of various electrophilic reagents. In addition, alternative approaches to activate the allene substrates can potentially lead to the development of novel domino or cascade sequences. For instance, it may be possible to trigger the cyclization of vinylallenes through a cyclopropanation reaction (Scheme 26). The resulting strained push-pull cyclopropane moiety may suffer ring opening to yield a zwitterionic pentadienyl system that then undergoes electrocyclization yielding a keto diester product.



Scheme 26. Potential Cyclopropation-initiated Domino Reaction Sequence

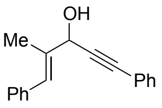
Another interesting direction is to examine asymmetric cyclizations of silyloxy vinyl allenes with chiral Brnøsted acids (Scheme 27).[32] Following delivery of a proton from the acid to the allene carbon, the absoulute sense of rotation of the pentadienyl cation could be affect by the resulting chiral counteranion, thus affording enantiomerically enriched cyclopentenones.



Scheme 27. Proposed Strategy to Prepare Enantiomerically enriched Cyclopentenones

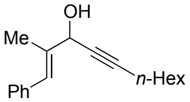
3.5 Experimental

General Information. Reactions were carried out in flame-dried glassware under a positive argon atmosphere unless otherwise stated. Transfer of anhydrous solvents and reagents was accomplished with oven-dried syringes or cannulae. Solvents were distilled before use: methylene chloride from calcium hydride, tetrahydrofuran, diethylether and benzene from sodium/benzophenone ketyl, toluene from sodium metal. All other solvents and commercially available reagents were either purified by standard procedures or used without further purification. Thin layer chromatography was performed on glass plates precoated with 0.25 mm silica gel; the stains for TLC analysis were conducted with 2.5 % *p*-anisaldehyde in AcOH-H_2SO_4-EtOH (1:3:85) and further heating until development of color. Flash chromatography was performed on 230-400 mesh silica gel with the indicated eluents. Nuclear magnetic resonance (NMR) spectra were recorded in indicated deuterated solvents and are reported in ppm in the presence of TMS as internal standard and coupling constants (*J*) are reported in Hertz (Hz). Infrared (IR) spectra were recorded neat and reported in cm^{-1}. Mass spectra were recorded by using EI or ESI as specified in each case.



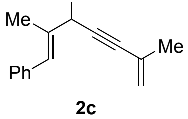
2a

To a flame-dried round bottom flask containing a magnetic stirring bar was added phenylacetylene (3.98 mmol, 406 mg) and ether (8 mL) under Ar. The temperature of the solution was dropped to −78 °C (acetone/dry ice bath). *n*-BuLi (1.60 M solution in hexane, 3.98 mmol, 2.48 mL) was added dropwise and the reaction mixture was stirred at the same temperature for 30 min. The a-methyl-*trans*-cinnamaldehyde (3.98 mmol, 581 mg) was added and the resulting solution was allowed to warm to room temperature. The reaction was quenched with saturated aqueous NH_4Cl and diluted with ether. The separated organic layer was washed with brine, dried over anhydrous $MgSO_4$, filtered and concentrated to provide pure compound **2a** (850 mg, yield 86%): R$_f$ 0.28 (hexane:EtOAc 4:1); IR (film) 3341 (br), 3081, 3056, 3024, 2981, 2917, 2859, 2201, 1664, 1598, 1573, 1489, 1442, 1381, 1361, 1281, 1070, 1008, 998, 756, 691 cm^{-1}; ^{1}H NMR (400 MHz, CDCl$_3$) δ 7.52-7.50 (m, 2H), 7.39-7.30 (m, 7H), 7.29-7.27 (m, 1H), 6.81 (s, 1H), 5.20 (s, 1H), 2.31 (br s, 1H), 2.11 (d, *J* = 1.2 Hz, 3H); ^{13}C NMR (100 MHZ, CDCl$_3$) δ 137.0, 136.7, 131.7, 129.0, 128.5, 128.2, 128.1, 127.2, 126.7, 122.4, 88.0, 86.3, 68.7, 14.1; HRMS (EI, M$^+$) for $C_{18}H_{16}O$ calcd 248.1201, found: m/z 248.1196.



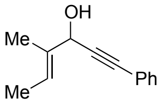
2b

Synthesized according to the previous procedure using a-methyl-*trans*-cinnamaldehyde (5.61 mmol, 819 mg), 1-octyne (5.61 mmol, 619 mg), and *n*-BuLi (5.61 mmol, 3.50 mL) to afford **2b** (1.187g, yield 83%) as a pale yellow oil: R$_f$ 0.50 (hexane:EtOAc 4:1); IR (film) 3354 (br), 3082, 3057, 3025, 2955, 2930, 2858, 2274, 2223, 1682, 1621, 1600, 1492, 1446, 1378, 1304, 1131, 1011, 751, 699 cm^{-1}; ^{1}H NMR (400 MHz, CDCl$_3$) δ 7.36-7.27 (m, 4H), 7.25-7.21 (m, 1H), 6.68 (s, 1H), 4.91 (s, 1H), 2.26 (td, *J* = 7.2, 2.0 Hz, 2H), 1.99 (d, *J* = 1.6 Hz, 3H), 1.92 (br s, 1H), 1.57-1.50 (m, 2H), 1.44-1.36 (m, 2H) 1.34-1.24 (m, 4H), 0.89 (m, 3H); ^{13}C NMR (100 MHz, CDCl$_3$) δ 137.6, 137.5, 129.2, 128.3, 126.9, 126.9, 87.6, 79.4, 68.8, 31.5, 28.8, 22.7, 19.0, 14.2 [Two aliphatic carbon signals are missing due to peak overlap.]; HRMS (EI, M$^+$) for $C_{18}H_{24}O$ calcd 256.1827, found: m/z 256.1826.



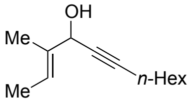
2c

Synthesized according to the previous procedure using a-methyl-*trans*-cinnamaldehyde (4.12 mmol, 601 mg), 2-methylbut-1-en-3-yne (4.12 mmol, 272 mg), and *n*-BuLi (4.12 mmol, 2.57 mL) to afford **2c** (786 mg, yield 90%) as a pale yellow oil: R_f 0.61 (hexane: EtOAC 4:1); IR (film) 3372 (br), 3057, 3025, 2952, 2921, 2856, 2199, 1615, 1446, 1373, 1291, 1073, 1010, 899, 753, 699 cm^{-1}; ^{1}H NMR (400 MHz, CDCl$_3$) δ 7.36-7.29 (m, 4H), 7.25-7.19 (m, 1H), 6.70 (s, 1H), 5.34 (m, 1H), 5.27 (app. quintet, *J* = 1.6 Hz, 1H), 5.04 (s, 1H), 2.01 (d, *J* = 1.2 Hz, 3H), 1.95 (br s, 1H), 1.94 (dd, *J* = 1.4, 1.0 Hz, 3H); ^{13}C NMR (100 MHz, CDCl$_3$) δ 137.3, 137.0, 129.2, 128.3, 127.4, 127.0, 126.4, 122.8, 87.8, 87.2, 68.9, 23.5, 14.3. HRMS (EI, M$^+$) for $C_{15}H_{16}O$ calcd 212.1201, found: m/z 212.1193.



2d

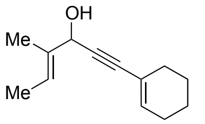
Synthesized according to the previous procedure using (*E*)-2-methylbut-2-enal (2.69 mmol, 226 mg), phenylacetylene (2.69 mmol, 275 mg), and *n*-BuLi (2.69 mmol, 1.68 mL) to afford **2d** (455 mg, yield 91%) as a pale yellow oil: R_f 0.44 (hexane:EtOAc 4:1); IR (microsope) 3353 (br), 3080, 3057, 3033, 2978, 2919, 2860, 2198, 1673, 1598, 1489, 1443, 1380, 1069, 1006, 996, 756, 691 cm^{-1}; ^{1}H NMR (400 MHz, CDCl$_3$) δ 7.49-7.45 (m, 2H), 7.34-7.30 (m, 3H), 5.79 (qq, *J* = 6.6, 0.8 Hz, 1H), 5.01 (s, 1H), 2.56 (br s, 1H), 1.85 (d, *J* = 1.2 Hz, 3H), 1.70 (d, *J* = 6.6 Hz, 3H); ^{13}C NMR (100 MHz, CDCl$_3$) δ 135.3, 131.9, 128.6, 128.5, 122.9, 122.9, 88.9, 86.1, 68.7, 13.5, 12.3; HRMS (EI, M$^+$) for $C_{13}H_{14}O$ calcd 186.1045, found: m/z 186.1045.



2e

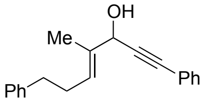
Synthesized according to the previous procedure using (*E*)-2-methylbut-2-enal (4.29 mmol, 360 mg), 1-octyne (4.29 mmol, 473 mg), and *n*-BuLi (4.29 mmol, 2.68 mL) to afford **2e** (779 mg, 94%) as a pale yellow oil: R_f 0.56 (hexane: EtOAc 4:1); IR (microscope) 3347 (br), 2956, 2930, 2859, 2229, 1674, 1456, 1379, 1135, 995 cm^{-1}; ^{1}H NMR (400 MHz, CDCl$_3$) δ 5.68 (qq, *J* = 6.8, 1.2 Hz, 1H), 4.73 (br s, 1H), 2.25 (td, *J* = 7.2, 2.0 Hz, 2H), 1.74 (app t, *J* = 1.2 Hz, 3H), 1.72 (br s, 1H), 1.64 (d, *J* = 6.8 Hz, 3H), 1.54-1.47 (m, 2H), 1.41-1.25 (m, 6H), 0.88 (t, *J* = 7.0

Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 135.5, 122.1, 86.8, 79.5, 68.3, 31.3, 28.5, 28.5, 22.5, 18.7, 14.0, 13.2, 11.8; HRMS (EI, M^+) for $C_{13}H_{22}O$ calcd 194.1671, found: m/z 194.1672.



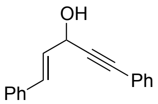
2f

Synthesized according to the previous procedure using (*E*)-2-methylbut-2-enal (4.31 mmol, 362 mg), 1-ethynylcyclohex-1-ene (4.31 mmol, 458 mg), and *n*-BuLi (4.31 mmol, 2.69 mL) to afford **2f** (778 mg, yield 95%) as a pale yellow oil: R_f 0.60 (hexane:EtOAc 4:1); IR (microscope) 3356 (br), 3027, 2930, 2859, 2218, 2184, 1670, 1631, 1436, 1379, 1199, 1003, 918, 841 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.12 (app. quintet, J = 2.0 Hz, 1H), 5.69 (qqd, J = 6.8, 1.2, 1.2 Hz, 1H), 4.85 (s, 1H), 2.13-2.06 (m, 4H), 1.75 (app t, J = 1.0 Hz, 3H), 1.64 (d, J = 7.2 Hz, 3H), 1.61-1.54 (m, 4H) [OH peak is not observed.]; ^{13}C NMR (100 MHz, $CDCl_3$) δ 135.3, 135.2, 122.4, 120.1, 87.8, 85.7, 68.5, 29.1, 25.6, 22.2, 21.4, 13.2, 11.9; HRMS (EI, M^+) for $C_{13}H_{18}O$ calcd 190.1358, found: m/z 190.1354.



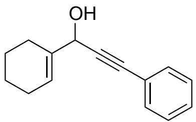
2g

Synthesized according to the previous procedure using (*E*)-2-methyl-5-phenylpent-2-enal (3.18 mmol, 554 mg), phenylacetylene (3.18 mmol, 324 mg), and *n*-BuLi (3.18 mmol, 1.98 mL) to afford **2g** (792 mg, yield 91%) as a pale yellow oil: R_f 0.55 (hexane:EtOAc 4:1); IR (film) 3370 (br), 3083, 3061, 3026, 2925, 2857, 2225, 2203, 1671, 1599, 1489, 1453, 1443, 1302, 1029, 1007, 996, 756, 691 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.47-7.44 (m, 2H), 7.37-7.29 (m, 5H), 7.23-7.19 (m, 3H), 5.77 (tq, J = 7.2, 1.2 Hz, 1H), 4.99 (br s, 1H), 2.73 (t, J = 6.8 Hz, 2H), 2.43 (app q, J = 7.2 Hz, 2H), 1.88 (br s, 1H), 1.78 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 142.0, 135.2, 131.9, 128.7, 128.6, 128.5, 128.5, 127.6, 126.1, 122.8, 88.5, 86.2, 68.7, 35.7, 29.9, 12.6; HRMS (EI, M$^+$) for $C_{20}H_{20}O$ calcd 276.1514, found: m/z 276.1509.



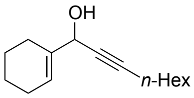
2h

Synthesized according to the previous procedure using cinnamaldehyde (6.00 mmol, 793 mg), phenylacetylene (6.00 mmol, 612 mg), and *n*-BuLi (6.00 mmol, 3.75 mL) to afford **2h** (1167 mg, yield 84%) as a pale yellow oil: IR (microscope) 3143 (br), 3079, 2211, 1597 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.54-7.29 (m, 10H), 6.88 (d, *J* = 16.0, 1H), 6.44 (dd, *J* = 15.6, 6.0 Hz, 1H), 5.33 (d, *J* = 6.0 Hz, 1H), 2.42 (br s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 136.4, 132.4, 132.3, 132.1, 129.1, 128.9, 128.6, 128.4, 127.1, 122.7, 88.3, 86.7, 63.7; HRMS (EI, M$^+$) for $C_{17}H_{14}O$ calcd 234.1045, found: m/z 234.1035.



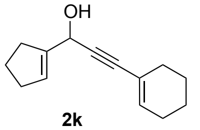
2i

Synthesized according to the previous procedure using cyclohex-1-enecarbaldehyde (2.61 mmol, 287 mg), phenylacetylene (2.61 mmol, 267 mg), and *n*-BuLi (2.61 mmol, 1.63 mL) to afford **2i** (454 mg, yield 82%) as a pale yellow oil: R_f 0.48 (hexane:EtOAc 4:1); IR (microscope) 3406 (br), 3056, 3033, 2930, 2858, 2197, 1714, 1669, 1627, 1489, 1443, 1305, 1029, 1010, 916, 756, 690 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.48-7.46 (m, 2H), 7.34-7.31 (m, 3H), 6.00 (br s, 1H), 4.98 (s, 1H), 2.33-2.26 (m, 1H), 2.22-2.17 (m, 1H), 1.90 (br s, 1H), 2.13-2.09 (m, 2H), 1.75-1.70 (m, 2H), 1.68-1.59 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 137.2, 131.9, 128.6, 128.5, 125.3, 122.9, 88.6, 86.1, 67.5, 25.3, 24.4, 22.7, 22.4; HRMS (EI, M$^+$) for $C_{15}H_{16}O$ calcd 212.1201, found: m/z 212.1199.



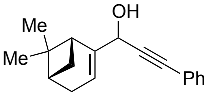
2j

Synthesized according to the previous procedure using cyclohex-1-enecarbaldehyde (3.25 mmol, 357 mg), 1-octyne (3.25 mmol, 357 mg), and *n*-BuLi (3.25 mmol, 2.03 mL) to afford **2j** (652 mg, yield 92%) as a pale yellow oil: R_f 0.58 (hexane:EtOAc 4:1); IR (microscope) 3542 (br), 2930, 2858, 2222, 1636, 1457, 1378, 1136, 992, 847 cm^{-1}; ^{1}H NMR (400 MHz, CDCl$_3$) δ 5.90 (br s, 1H), 4.73 (s, 1H), 2.23 (td, *J* = 7.2, 2.0 Hz, 2H), 2.21-2.18 (m, 1H), 2.16-2.06 (m, 3H), 1.73-1.58 (m, 5H), 1.55-1.49 (m, 2H), 1.44-1.29 (m, 6H), 0.91 (t, *J* = 6.8 Hz, 3H); ^{13}C NMR (100 MHz, CDCl$_3$) δ 137.8, 124.6, 86.9, 79.7, 67.3, 31.5, 28.8, 28.7, 25.2, 24.3, 22.7, 22.7, 22.5, 19.0, 14.2; HRMS (EI, M$^+$) for $C_{15}H_{24}O$ calcd 220.1827, found: m/z 220.1827.



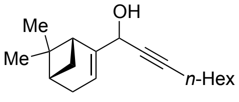
2k

Synthesized according to the previous procedure using cyclopent-1-enecarbaldehyde (4.69 mmol, 450 mg), 1-ethynylcyclohex-1-ene (4.69 mmol, 497 mg), and *n*-BuLi (4.69 mmol, 2.93 mL) to afford **2k** (923 mg, yield 98%) as a pale yellow oil: R_f 0.60 (hexane:EtOAc 4:1); IR (microscope) 3355 (br), 3026, 2931, 2855, 2217, 2185, 1713, 1629, 1436, 1298, 1040, 950, 918 cm^{-1}; ^{1}H NMR (400 MHz, CDCl$_3$) δ 6.12 (tt, *J* = 4.0, 2.0 Hz, 1H), 5.80 (m, 1H), 5.07 (s, 1H), 2.52-2.28 (m, 5H), 2.13-2.06 (m, 4H), 1.94 (quintet, *J* = 7.2 Hz, 2H), 1.66-1.56 (m, 4H); ^{13}C NMR (100 MHz, CDCl$_3$) δ 143.6, 135.4, 127.5, 120.1, 87.1, 85.5, 62.0, 32.2, 31.4, 29.1, 25.5, 23.3, 22.2, 21.4; HRMS (EI, M$^+$) for $C_{14}H_{18}O$ calcd 202.1358, found: m/z 202.1353.



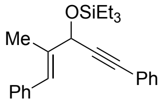
2l

Synthesized according to the previous procedure using (-)-myrtenal (3.59 mmol, 539 mg), phenylacetylene (3.59 mmol, 366 mg), and *n*-BuLi (3.59 mmol, 2.24 mL) to afford **2l** (904 mg, yield 99%) as an inseparable mixture of two diastereomers (dr = 1:1): R_f 0.50 (hexane:EtOAc 4:1); Spectral data for the mixture of isomers: IR (microscope) 3341 (br), 3081, 3054, 3033, 2985, 2915, 2885, 2830, 2226, 1598, 1490, 1443, 1381, 1365, 1264, 1030, 1014, 1030, 957, 755, 690 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.47-7.44 (m, 4H), 7.34-7.30 (m, 6H), 5.77 (td, *J* = 3.0, 1.6 Hz, 1H), 5.75-5.74 (m, 1H), 5.02 (d, *J* = 0.8 Hz, 1H), 4.99 (d, *J* = 1.2 Hz, 1H), 2.53-2.45 (m, 4H), 2.43-2.31 (m, 4H), 2.30-2.20 (m, 2H), 2.17-2.14 (m, 2H), 1.36 (s, 3H), 1.35 (s, 3H), 1.28 (dd, *J* = 8.2, 3.0 Hz, 2H; 2 overlapping 1H signals), 0.92 (s, 3H), 0.91 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 146.9, 146.9, 131.9, 131.9, 128.6, 128.5, 128.5, 122.9, 120.3, 119.4, 88.31, 85.8, 85.6, 65.9, 65.5, 43.2, 42.9, 41.0, 41.0, 38.3, 32.0, 31.9, 31.4, 31.4, 26.3, 21.5, 21.4 [Some carbon signals are missing due to peak overlap.]; HRMS (EI, M^+) for $C_{18}H_{20}O$ calcd 252.1514, found: m/z 252.1513.



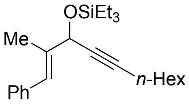
2m

Synthesized according to the previous procedure using (-)-myrtenal (3.14 mmol, 471 mg), 1-octyne (3.14 mmol, 346 mg), and *n*-BuLi (3.14 mmol, 1.96 mL) to afford **2m** (711 mg, yield 87%) as an inseparable mixture of two diastereomers (dr = 1:1): R_f 0.56 (hexane:EtOAc 4:1); Spectral data for the mixture of isomers: IR (microscope) 3365 (br), 2984, 2930, 2871, 2832, 2222, 1614, 1467, 1381, 1365, 1001, 965 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.65-5.63 (m, 2H), 4.74 (d, *J* = 1.2 Hz, 1H), 4.72 (d, *J* = 1.2 Hz, 1H), 2.47-2.36 (m, 4H), 2.33-2.26 (m, 4H), 2.22 (td, *J* = 7.0, 1.5 Hz, 4H), 2.12-2.10 (m, 2H), 1.51 (m, 4H), 1.41-1.33 (m, 4H), 1.32-1.24 (m, 8H), 1.32 (s, 6H), 0.90 (t, *J* = 6.8 Hz, 6H), 0.85 (s, 3H), 0.84 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 147.5, 119.6, 118.9, 86.6, 86.4, 79.2, 79.1, 65.7, 65.3, 43.0, 42.8, 41.0, 41.0, 38.1, 38.1, 32.0, 31.9, 31.5, 31.3, 31.3, 28.8, 28.8, 28.7, 28.7, 26.3, 22.7, 21.4, 21.2, 18.9, 14.2 [Some carbon signals are missing due to peak overlap.]; HRMS (EI, M^+) for $C_{18}H_{28}O$ calcd 260.2140, found: m/z 260.2138.



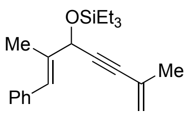
3a

To a flame-dried round bottom flask containing a magnetic stirring bar was sequentially added hydroxyenyne **2a** (1.06 mmol, 264 mg), CH_2Cl_2 (5 mL), and 2,6-lutidine (3.18 mmol, 0.37 mL) under Ar. The temperature of the solution was dropped to −78 °C (acetone/dry ice bath). Triethylsilyl trifluoromethanesulfonate (1.59 mmol, 0.36 mL) was added dropwise and the resulting solution was stirred at the same temperature for 30 min. The reaction mixture was quenched with H_2O and diluted with CH_2Cl_2. The separated organic layer was washed with brine, dried over anhydrous $MgSO_4$, filtered and concentrated. The crude mixture thus obtained was purified by flash column chromatography (silica gel, 2% EtOAc/hexane) to give pure siloxyenyne **3a** (369 mg, yield 96%): R_f 0.80 (hexane:EtOAc 4:1); IR (film) 3081, 3060, 3026, 2956, 2912, 2876, 2203, 1691, 1665, 1490, 1450, 1238, 1060, 1003, 754, 690 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.53-7.50 (m, 2H), 7.43-7.35 (m, 7H), 7.29-7.27 (m, 1H), 6.80 (br s, 1H), 5.21 (s, 1H), 2.11 (d, J = 1.2 Hz, 3H), 1.16-1.06 (m, 9H), 0.86-0.80 (m, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 137.5, 137.5, 131.6, 129.0, 128.2, 128.0, 126.5, 125.7, 123.0, 89.2, 85.0, 68.7, 14.1, 6.8, 4.9 [One sp^2 carbon signal is missing due to peak overlap.]; HRMS (EI, M$^+$) for $C_{24}H_{30}OSi$ calcd 362.2066, found: m/z 362.2063.



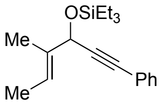
3b

Prepared according to the previous procedure using **2b** (1.95 mmol, 500 mg), 2,6-lutidine (5.85 mmol, 0.68 mL), triethylsilyl trifluoromethanesulfonate (2.93 mmol, 0.66 mL) to afford **3b** (721 mg, yield 99%) as a pale yellow oil: R_f 0.85 (hexane:EtOAc 4:1); IR (microsope) 3062, 3029, 2956, 2932, 2875, 2860, 2211, 1712, 1671, 1601, 1455, 1413, 1379, 1239, 1069, 1005, 745, 700 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.34-7.27 (m, 4H), 7.23-7.18 (m, 1H), 6.62 (s, 1H), 4.89 (br s, 1H), 2.23 (td J = 7.2, 2.0 Hz, 2H), 1.95 (d, J = 1.2 Hz, 3H), 1.56-1.48 (m, 2H), 1.44-1.36 (m, 2H), 1.35-1.24 (m, 4H), 1.00 (t, *J* = 8.0 Hz, 9H), 0.88 (t, *J* = 7.0 Hz, 3H), 0.73-0.66 (m, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 138.5, 137.9, 129.2, 128.2, 126.6, 125.4, 86.0, 80.2, 68.7, 31.5, 28.8, 28.8, 22.8, 19.1, 14.2, 7.0, 5.1 [One aliphatic carbon signal is missing due to peak overlap.]; HRMS (EI, M^+) for $C_{24}H_{38}OSi$ calcd 370.2692, found: m/z 370.2684.



3c

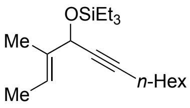
Prepared according to the previous procedure using **2c** (0.92 mmol, 193 mg), 2,6-lutidine (2.76 mmol, 0.32 mL), triethylsilyl trifluoromethanesulfonate (1.38 mmol, 0.31 mL) to afford **3c** (283 mg, yield 95%) as a pale yellow oil: R_f 0.78 (hexane:EtOAc 4:1); IR (film) 3061, 3027, 2956, 2913, 2877, 2204, 1721, 1679, 1616, 1454, 1413, 1239, 1072, 1005, 746, 699 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.35-7.27 (m, 4H), 7.24-7.19 (m, 1H), 6.65 (s, 1H), 5.29 (m, 1H), 5.22 (app. quintet, *J* = 1.6 Hz, 1H), 5.02 (br s, 1H), 1.97 (d, *J* = 1.2 Hz, 3H), 1.90 (dd, *J* = 1.4, 1.0 Hz, 3H), 1.01 (t, *J* = 7.8 Hz, 9H), 0.71 (m, 6H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 137.8, 137.8, 129.2, 128.3, 126.8, 126.7, 125.8, 122.0, 88.4, 86.5, 68.8, 23.5, 14.3, 7.0, 5.1; HRMS (EI, M^+) for $C_{21}H_{30}OSi$ calcd 326.2066, found: m/z 326.2063.



3d

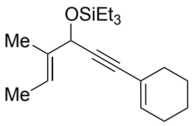
Prepared according to the previous procedure using **2d** (1.38 mmol, 258 mg), 2,6-lutidine (4.14 mmol, 0.48 ml), triethylsilyl trifluoromethanesulfonate (2.07 mmol, 0.47 ml) to afford **3d** (296 mg, yield 72%) as a pale yellow oil: R_f 0.80 (hexane:EtOAc 4:1); IR (film) 3081, 3033, 2955, 2937, 2913, 2876, 2202, 1689,1672, 1632, 1598, 1490, 1458, 1317, 1239, 1055, 1005, 754, 690 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.48-7.44 (m, 2H), 7.35-7.31 (m, 3H), 5.74 (qqd, *J* = 6.4, 1.2, 1.2 Hz, 1H), 5.01 (br s, 1H), 1.82 (app. t, *J* = 1.0 Hz, 3H), 1.70 (dd, *J* =

6.8, 0.8 Hz, 3H), 1.04 (t, *J* = 7.8 Hz, 9H), 0.77-0.71 (m, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 135.8, 131.8, 128.4, 128.3, 123.4, 121.2, 89.9, 85.0, 68.8, 13.5, 12.3, 7.0, 5.1; HRMS (EI, M^+) for $C_{19}H_{28}OSi$ calcd 300.1910, found: m/z 300.1906.



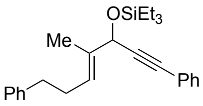
3e

Prepared according to the previous procedure using **2e** (1.46 mmol, 284 mg), 2,6-lutidine (4.38 mmol, 0.50 ml), triethylsilyl trifluoromethanesulfonate (2.19 mmol, 0.49 ml) to afford **3e** (427 mg, 95%) as a pale yellow oil: R_f 0.86 (hexane:EtOAc 4:1); IR (microscope) 2955, 2934, 2876, 2861, 2229, 1458, 1379, 1093, 1045, 1005, 849, 743, 728 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.60 (qqd, *J* = 6.7, 1.4, 1.4 Hz, 1H), 4.72 (br s, 1H), 2.20 (td, *J* = 7.0, 2.0 Hz, 2H), 1.70 (app. t, *J* = 1.0 Hz, 3H), 1.61 (dd, *J* = 7.2, 1.0 Hz, 3H), 1.54-1.47 (m, 2H), 1.42-1.22 (m, 6H), 0.96 (t, *J* = 8.0 Hz, 9H), 0.88 (t, *J* = 7.0 Hz, 3H), 0.68-0.61 (m, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 136.4, 120.5, 85.7, 80.6, 68.5, 31.5, 28.8, 28.8, 22.8, 19.0, 14.2, 13.4, 12.1, 7.0, 5.0; HRMS (EI, M^+) for $C_{19}H_{36}OSi$ calcd 308.2535, found: m/z 308.2541.



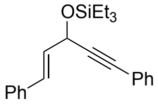
3f

Prepared according to the previous procedure using **2f** (2.42 mmol, 461 mg), 2,6-lutidine (7.26 mmol, 0.84 mL), triethylsilyl trifluoromethanesulfonate (3.63 mmol, 0.82 mL) to afford **3f** (562 mg, yield 77%) as a pale yellow oil: R_f 0.80 (hexane:EtOAc 4:1); IR (microscope) 2953, 2876, 2216, 2188, 1718, 1673, 1457, 1239, 1074, 1006, 842, 742 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.06 (app. quintet, *J* = 2.0 Hz, 1H), 6.62 (qqd, *J* = 6.6, 1.2, 1.2 Hz, 1H), 4.84 (br s, 1H), 2.12-2.04 (m, 4H), 1.71 (app. t, *J* = 1.0 Hz, 3H), 1.62 (dd, *J* = 6.8, 0.8 Hz, 3H), 1.59-1.53 (m, 4H), 0.97 (t, *J* = 7.8 Hz, 9H), 0.69-0.62 (m, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 135.8, 134.4, 120.5, 120.4, 86.7, 86.6, 68.5, 29.0, 25.5, 22.2, 21.5, 13.2, 11.9, 6.80, 4.87; HRMS (EI, M^+) for $C_{19}H_{32}OSi$ calcd 304.2222, found: m/z 304.2220.



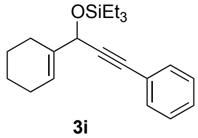
3g

Prepared according to the previous procedure using **2g** (2.83 mmol, 784 mg), 2,6-lutidine (8.49 mmol, 0.98 mL), triethylsilyl trifluoromethanesulfonate (4.25 mmol, 0.96 mL) to afford **3g** (999 mg, yield 91%) as a pale yellow oil: R_f 0.80 (hexane:EtOAc 4:1); IR (film) 3084, 3027, 2955, 2912, 2876, 2202, 1714, 1665, 1602, 1490, 1454, 1239, 1070, 1005, 747, 698 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.45-7.42 (m, 2H), 7.33-7.27 (m, 5H), 7.23-7.19 (m, 3H), 5.69 (t, *J* = 7.2 Hz, 1H), 4.97 (s, 1H), 2.72 (t, *J* = 7.6 Hz, 2H), 2.41 (app. q, *J* = 7.6 Hz, 2H), 1.75 (s, 3H), 1.02 (t, *J* = 8.0 Hz, 9H), 0.74-0.67 (m, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 142.0, 135.5, 131.5, 128.4, 128.2, 128.1, 128.0, 125.7, 125.5, 123.1, 89.6, 84.7, 68.4, 35.5, 29.6, 12.3, 6.8, 4.9; HRMS (EI, M^+) for $C_{26}H_{34}OSi$ calcd 390.2379, found: m/z 390.2380.



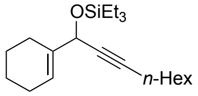
3h

Prepared according to the previous procedure using **2h** (2.28 mmol, 531 mg), 2,6-lutidine (6.83 mmol, 0.790 mL), triethylsilyl trifluoromethanesulfonate (2.73 mmol, 0.62 mL) to afford **3h** (762 mg, yield 96%) as a pale yellow oil: IR (microscope) 3028, 2956, 2211, 1599 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.53-7.46 (m, 4H), 7.40-7.34 (m, 5H), 7.32-7.27 (m, 1H), 6.85 (br d, *J* = 15.6 Hz, 1H), 6.43-6.37 (m, 1H), 5.37-5.35 (m, 1H), 1.13-1.07 (m, 9H), 0.84-0.77 (m, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 136.5, 131.6, 130.5, 129.2, 128.5, 128.3, 128.2, 127.8, 126.7, 122.9, 88.8, 85.5, 63.7, 6.8, 4.9; HRMS (EI, M^+) for $C_{23}H_{28}OSi$ calcd 348.1910, found: m/z 348.1910.



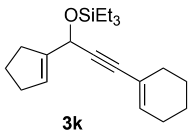
3i

Prepared according to the previous procedure using **2i** (2.25 mmol, 479 mg), 2,6-lutidine (6.75 mmol, 0.785 mL), triethylsilyl trifluoromethanesulfonate (3.38 mmol, 0.76 mL) to afford **3i** (697 mg, yield 95%) as a pale yellow oil: R$_f$ 0.83 (hexane:EtOAc 4:1); IR (microscope) 3060, 2939, 2875, 2201, 1717, 1663, 1598, 1449, 1289, 1115, 1070, 1003, 757, 690 cm^{-1}; ^{1}H NMR (400 MHz, CDCl$_3$) δ 7.48-7.45 (m, 2H), 7.34-7.31 (m, 3H), 5.97 (br s, 1H), 5.00 (br s, 1H), 2.26-2.20 (m, 2H), 2.13-2.10 (m, 2H), 1.76-1.69 (m, 2H), 1.67-1.61 (m, 2H), 1.06 (t, *J* = 8.0 Hz, 9H), 0.78-0.72 (m, 6H); ^{13}C NMR (100 MHz, CDCl$_3$) δ 137.7, 131.8, 128.4, 128.3, 123.6, 123.4, 89.8, 85.1, 67.6, 25.3, 24.5, 22.8, 22.6, 7.1, 5.1; HRMS (EI, M$^+$) for $C_{21}H_{30}OSi$ calcd 326.2066, found: m/z 326.2063.



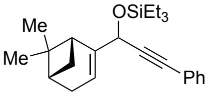
3j

Prepared according to the previous procedure using **2j** (2.95 mmol, 651 mg), 2,6-lutidine (8.85 mmol, 1.0 mL), triethylsilyl trifluoromethanesulfonate (4.43 mmol, 1.0 mL) to afford **3j** (927 mg, yield 94%) as a pale yellow oil: R$_f$ 0.84 (hexane:EtOAc 4:1); IR (microscope) 2954, 2933, 2875, 2859, 2838, 2225, 1644, 1458, 1413, 1326, 1239, 1127, 1057, 1035, 1005, 742, 728 cm^{-1}; ^{1}H NMR (400 MHz, CDCl$_3$) δ 5.83 (br s, 1H), 4.73 (br s, 1H), 2.22 (td, *J* = 6.8, 2.0 Hz, 2H), 2.14-2.11 (m, 2H), 2.07-2.04 (m, 2H), 1.68-1.63 (m, 2H), 1.61-1.55 (m, 2H), 1.53-1.48 (m, 2H), 1.44-1.35 (m, 2H), 1.35-1.26 (m, 4H), 0.99 (t, *J* = 7.8 Hz, 9H), 0.90 (t, *J* = 6.8 Hz, 3H), 0.70-0.63 (m, 6H); ^{13}C NMR (100 MHz, CDCl$_3$) δ 138.3, 122.9, 85.6, 80.4, 67.3, 31.5, 28.8, 28.7, 25.2, 24.3, 22.8, 22.7, 22.6, 19.0 , 14.2, 7.0, 5.1; HRMS (EI, M$^+$) for $C_{21}H_{38}OSi$ calcd 334.2692, found: m/z 334.2688.



3k

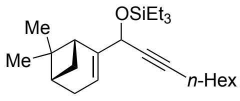
Prepared according to the previous procedure using **2k** (1.81 mmol, 366 mg), 2,6-lutidine (5.43 mmol, 0.63 mL), triethylsilyl trifluoromethanesulfonate (2.72 mmol, 0.61 mL) to afford **3k** (413 mg, yield 73%) as a pale yellow oil: R_f 0.78 (hexane:EtOAc 4:1); IR (microscope) 2952, 2876, 2214, 2188, 1717, 1666, 1436, 1239, 1073, 1005, 742, 728 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.09 (t, *J* = 2.0 Hz, 1H), 5.76 (br s, 1H), 5.10 (br s, 1H), 2.48-2.33 (m, 4H), 2.14-2.07 (m, 4H), 1.93 (app. quintet, *J* = 7.6 Hz, 2H), 1.67-1.56 (m, 4H), 1.00 (t, *J* = 7.8 Hz, 9H), 0.72-0.65 (m, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 144.5, 134.7, 126.6, 120.6, 86.5, 86.5, 62.4, 32.4, 31.8, 29.3, 25.8, 23.6, 22.5, 21.7, 7.0, 5.1; HRMS (EI, M$^+$) for $C_{20}H_{32}OSi$ calcd 316.2222, found: m/z 316.2219.



3l

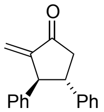
Prepared according to the previous procedure using **2l** (1.99 mmol, 503 mg), 2,6-lutidine (5.97 mmol, 0.69 mL), triethylsilyl trifluoromethanesulfonate (2.99 mmol, 0.67 mL) to afford **3l** (686 mg, yield 94%) as an inseparable mixture of two diastereomers (dr = 1:1): R_f 0.80 (hexane:EtOAc 4:1); Spectral data for the mixture of isomers: IR (microscope) 3081, 3055, 3033, 2986, 2952, 2913, 2876, 2831, 2224, 1598, 1490, 1465, 1381, 1314, 1238, 1125, 1083, 1064, 1051, 1002, 977, 850, 754, 690 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.43-7.40 (m, 4H), 7.33-7.29 (m, 6H), 5.68 (td, *J* = 3.0, 1.4 Hz, 1H), 5.64 (td, *J* = 2.8, 1.2 Hz, 1H), 5.00 (d, *J* = 1.2 Hz, 1H), 4.97 (d, *J* = 1.6 Hz, 1H), 2.48-2.43 (m, 3H), 2.40-2.35 (m, 3H), 2.32-2.25 (m, 2H), 2.14-2.11 (m, 2H), 1.33 (s, 6H), 1.28-1.24 (m, 2H), 1.03 (t, *J* = 7.8 Hz, 9H), 1.02 (t, *J* = 7.8 Hz, 9H), 0.91 (s, 3H), 0.90 (s, 3H), 0.75-0.67 (m, 12H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 147.4, 137.2, 131.8, 131.8, 128.4, 128.4, 128.2, 128.2, 123.5, 123.4, 89.3, 89.3, 84.5, 84.5, 65.9, 65.4, 43.2, 42.9, 41.2, 41.1, 38.3, 38.2, 32.0, 31.8, 31.3, 31.3, 26.5, 26.4, 21.4, 21.3, 7.0, 7.0, 5.2, 5.1

[Some carbon signals are missing due to peak overlap.]; HRMS (EI, M$^+$) for $C_{24}H_{34}OSi$ calcd 366.2379, found: m/z 366.2377.

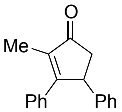


3m

Prepared according to the previous procedure using **1m** (1.53 mmol, 399.1 mg), 2,6-lutidine (4.59 mmol, 0.54 mL), triethylsilyl trifluoromethanesulfonate (2.30 mmol, 0.52 mL) to afford **2m** (500 mg, yield 87%) as an inseparable mixture of two diastereomers (dr = 1:1): R_f 0.90 (hexane:EtOAc 4:1); Spectral data for the mixture of isomers: IR (microscope) 2986, 2953, 2934, 1916, 2876, 2225, 1607, 1466, 1431, 1414, 1238, 1121, 1062, 1050, 1005, 852, 743 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.58-5.54 (m, 2H), 4.75-4.73 (m, 2H), 2.44-2.39 (m, 2H), 2.37-2.33 (m, 2H), 2.32-2.30 (m, 2H), 2.28-2.25 (m, 2H), 2.20 (td, *J* = 7.0, 2.0 Hz, 4H), 2.13-2.08 (m, 2H), 1.53-1.48 (m, 4H), 1.43-1.34 (m, 6H), 1.34-1.25 (m, 6H), 1.31 (s, 6H), 1.20 (t, *J* = 8.4 Hz, 2H), 1.00 (t, *J* = 8.0 Hz, 9H), 0.99 (t, *J* = 8.0 Hz, 9H), 0.91 (t, *J* = 6.8 Hz, 6H), 0.85 (s, 3H), 0.84 (s, 3H), 0.70-0.64 (m, 12H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 147.9, 117.4, 117.1, 85.1, 79.9, 65.5, 65.1, 43.1, 42.9, 41.2, 41.1, 38.2, 38.1, 32.0, 31.8, 31.6, 31.2, 31.2, 28.8, 28.8, 28.7, 26.4, 26.4, 22.8, 21.4, 21.3, 19.0, 19.0, 14.2, 7.1, 7.0, 5.2, 5.1 [Some carbon signals are missing due to peak overlap.]; HRMS (EI, M$^+$) for $C_{24}H_{42}OSi$ calcd 374.3005, found: m/z 374.3008.

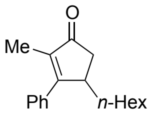


5a



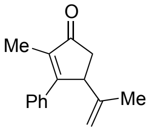
6a

To a flame-dried round bottom flask containing a magnetic stirring bar was added siloxyenyne **3a** (0.044 mmol, 16 mg) and ether (4 mL) under Ar. The temperature of the solution was dropped to −78 °C (acetone/dry ice bath). KO*t*-Bu (0.07 mmol, 7 mg) was added in one portion and the resulting suspension was stirred vigorously followed by the immediate removal of the cooling bath. Upon consumption of **3a** as determined by thin layer chromatography, the reaction was quenched with 15% aqueous NH_4Cl and diluted with ether. The separated organic layer was washed with brine, dried over anhydrous $MgSO_4$, filtered and concentrated to give the crude siloxyallene **4a** which was used for the next step without further purification. The unpurified **4a** thus obtained was dissolved in CH_2Cl_2 (2 mL) and treated with trifluoroacetic acid (3.0 equiv based on **3a**, 0.13 mmol, 10 μL) at room temperature. After stirring for 4 h, the reaction was quenched with saturated aqueous $NaHCO_3$ and diluted with CH_2Cl_2. The separated organic layer was washed with brine, dried over anhydrous $MgSO_4$, filtered and concentrated. The crude mixture was purified by flash column chromatography (silica gel, 10% EtOAc/hexane) to provide the desired products **5a** (5.6 mg, yield 51%) and **6a** (5.1 mg, yield 47%). **5a**: R_f 0.61 (hexane:EtOAc 4:1); IR (film) 3085, 3061, 3028, 2925, 2854, 1718, 1601, 1495, 1453, 1119, 1075, 785, 698 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.29-7.17 (m, 6H), 7.12-7.07 (m, 4H), 6.22 (dd, *J* = 3.3, 0.9 Hz, 1H), 5.04 (dd, *J* = 3.0, 0.8 Hz, 1H), 3.96 (ddd, *J* = 10.6, 3.0, 3.0 Hz, 1H), 3.41 (ddd, *J* = 11.2, 11.2, 7.2 Hz, 1H), 2.91 (ddd, *J* = 18.2, 7.6, 0.8 Hz, 1H), 2.71 (dd, *J* = 18.0, 12.0 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 204.7, 149.6, 141.1, 140.9, 128.9, 128.8, 128.8, 127.4, 127.3, 127.2, 120.0, 56.7, 48.9, 45.8; HRMS (EI, M^+) for $C_{18}H_{16}O$ calcd 248.1201, found: m/z 248.1201. **6a**: R_f 0.50 (hexane:EtOAc 4:1); IR (film) 3060, 3027, 2923, 2853, 1698, 1624,1495, 1454, 1443, 1378, 1342, 1076, 761, 698 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.27-7.02 (m, 10H), 4.43 (ddq, *J* = 7.1, 2.0, 2.0 Hz, 1H), 3.05 (dd, *J* = 19.0, 7.2 Hz, 1H), 2.44 (dd, *J* = 19.0, 2.2 Hz, 1H), 1.97 (d, *J* = 2.0 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 208.9, 169.1, 142.4, 137.7, 135.3, 128.9, 128.7, 128.3, 128.0, 127.3, 126.7, 47.1, 45.1, 9.9; HRMS (EI, M^+) for $C_{18}H_{16}O$ calcd 248.1201, found: m/z 248.1198.



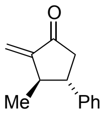
6b

As described for the synthesis of siloxyallene **4a**, compound **3b** (0.18 mmol, 69 mg) in 3 mL ether was reacted with KO*t*-Bu (0.27 mmol, 30 mg) followed by workup as described above to give crude **4b**. The desired Nazarov product was then prepared according to the previous procedure using trifluoroacetic acid (0.54 mmol, 40 μL) to afford **6b** (38 mg, yield 82%) as a pale yellow oil: R_f 0.65 (hexane:EtOAc 4:1); IR (microsope) 3058, 3030, 2955, 2927, 2855, 1702, 1629, 1454, 1379, 1342, 1075, 777, 698 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.48-7.44 (m, 2H), 7.42-7.25 (m, 3H), 3.26 (m, 1H), 2.69 (dd, *J* = 18.8, 6.4 Hz, 1H), 2.22 (dd, *J* = 18.8, 2.0 Hz, 1H), 1.84 (d, *J* = 1.6 Hz, 3H), 1.58-1.51 (m, 2H), 1.28-1.10 (m, 8H), 0.833 (t, *J* = 6.4 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 209.3, 172.0, 136.9, 135.9, 129.1, 128.8, 127.8, 41.2, 40.8, 33.9, 31.8, 29.4, 27.2, 22.7, 14.2, 9.6; HRMS (EI, M$^+$) for $C_{18}H_{24}O$ calcd 256.1827, found: m/z 256.1826.

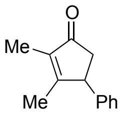


6c

As described for the synthesis of siloxyallene **4a**, compound **3c** (0.57 mmol, 188 mg) in 4 mL ether was reacted with KO*t*-Bu (0.86 mmol, 96 mg) followed by workup as described above to give crude **4c**. The desired Nazarov product was then prepared according to the previous procedure using trifluoroacetic acid (1.71 mmol, 127 μL) to afford **6c** (43 mg, yield 35%) as a pale yellow oil: R_f 0.51 (hexane:EtOAc 4:1); IR (microsope) 3074, 3024, 2924, 2856, 1699, 1648, 1624, 1442, 1377, 1340, 1277, 894, 733, 696 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.43-7.38 (m, 5H),4.83-4.82 (m, 1H), 4.74 (app. quintet, *J* = 1.6 Hz, 1H), 4.01 (dt, *J* = 7.2, 2.0 Hz, 1H), 2.78 (dd, *J* = 19.0, 7.0 Hz, 1H), 2.35 (dd, *J* = 18.8, 2.0 Hz, 1H), 1.94 (d, *J* = 2.0 Hz, 3H), 1.25 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 208.7, 168.7, 144.8, 138.2, 135.6, 129.4, 128.6, 128.2, 114.2, 48.9, 40.9, 18.3, 10.1; HRMS (EI, M$^+$) for $C_{15}H_{16}O$ calcd 212.1201, found: m/z 212.1199.

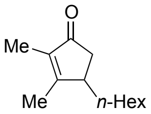


5d



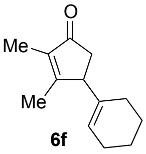
6d

As described for the synthesis of siloxyallene **4a**, compound **3d** (0.56 mmol, 170 mg) in 3 mL ether was reacted with KO*t*-Bu (0.84 mmol, 94 mg) followed by workup as described above to give crude **4d**. The desired Nazarov product was then prepared according to the previous procedure using trifluoroacetic acid (1.68 mmol, 125 μL) to afford **5d** (10 mg, yield 10%) and **6d** (32 mg, yield 30%). **5d**: R_f 0.64 (hexane:EtOAc 4:1); IR (film) 3061, 3029, 2691, 2926, 2874, 2853, 1726, 1641, 1602, 1495, 1454, 1376, 1221, 1169, 1123, 1074, 759, 700 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.40-7.36 (m, 2H), 7.31-7.27 (m, 3H), 6.13 (dd, *J* = 2.8, 0.8 Hz, 1H), 5.29 (d, *J* = 2.4 Hz, 1H), 2.84-2.74 (m, 3H), 2.59-2.51 (m, 1H), 1.18 (d, *J* = 6.0 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 205.5, 150.4, 141.8, 128.9, 127.5, 127.2, 116.6, 48.6, 46.3, 44.2, 16.3; HRMS (EI, M^+) for $C_{13}H_{14}O$ calcd 186.1045, found: m/z 186.1041. **6d**: R_f 0.51 (hexane:EtOAc 4:1); IR (microscope) 3062, 3027, 2961, 2923, 1701, 1648, 1601, 1494, 1454, 1384, 1323, 1073, 764, 702 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.36-7.32 (m, 2H), 7.29-7.25 (m, 1H), 7.12-7.09 (m, 2H), 3.83 (br d, *J* = 6.4 Hz, 1H), 2.92 (dd, *J* = 19.0, 7.0 Hz, 1H), 2.38 (dd, *J* = 18.8, 2.4 Hz, 1H), 1.84 (q, *J* = 0.8 Hz, 3H), 1.81 (q, *J* = 0.8 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 209.2, 171.7, 142.3, 129.1, 129.1, 127.5, 127.2, 49.4, 44.7, 15.7, 8.4; HRMS (EI, M^+) for $C_{13}H_{14}O$ calcd 186.1045, found: m/z 186.1042.



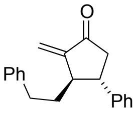
6e

As described for the synthesis of siloxyallene **4a**, compound **3e** (0.58 mmol, 180 mg) in 5 mL ether was reacted with KO*t*-Bu (0.87 mmol, 98 mg) followed by workup as described above to give crude **4e**. The desired Nazarov product was then prepared according to the previous procedure using trifluoroacetic acid (1.74 mmol, 129 μL) to afford **6e** (51 mg, 45%) as a pale yellow oil: R_f 0.58 (hexane:EtOAc 4:1); IR (microscope) 2956, 2927, 2856, 1702, 1648, 1457, 1410, 1384, 1325, 1072 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.64-2.60 (m, 1H), 2.48 (dd, *J* = 18.4, 6.4 Hz, 1H), 2.67 (dd, *J* = 18.6, 1.8 Hz, 1H), 1.98 (s, 3H), 1.78-1.73 (m, 2H), 1.67 (q, *J* = 0.8 Hz, 3H), 1.35-1.21 (m, 8H), 0.88 (t, *J* = 6.8 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 209.0, 172.9, 136.2, 42.7, 40.5, 32.8, 31.7, 9.3, 27.0, 22.5, 15.1, 14.0, 7.9; HRMS (EI, M$^+$) for $C_{13}H_{22}O$ calcd 194.1671, found: m/z 194.1670.

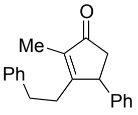


6f

As described for the synthesis of siloxyallene **4a**, compound **3f** (0.48 mmol, 147 mg) in 3 mL ether was reacted with KO*t*-Bu (0.72 mmol, 82 mg) followed by workup as described above to give crude **4f**. The desired Nazarov product was then prepared according to the previous procedure using trifluoroacetic acid (1.44 mmol, 107 μL) to afford **6f** (41 mg, yield 45%) as a pale yellow oil: R$_f$ 0.60 (hexane:EtOAc 4:1); IR (microscope) 2927, 2858, 2837, 1701, 1649, 1573, 1437, 1383, 1072 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.57 (m, 1H), 3.23 (br d, *J* = 6.8 Hz, 1H), 2.51 (dd, *J* = 19.0, 7.0 Hz, 1H), 2.18 (dd, *J* = 19.0, 1.8 Hz, 1H), 2.04-2.02 (m, 2H), 1.89 (s, 3H), 1.70 (q, *J* = 1.2 Hz, 3H), 1.61-1.54 (m, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 209.0, 171.5, 137.2, 136.6, 125.0, 51.2, 40.0, 25.3, 23.7, 22.7, 22.4, 15.1, 8.1; HRMS (EI, M$^+$) for $C_{13}H_{18}O$ calcd 190.1358, found: m/z 190.1358.



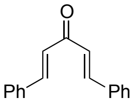
5g



6g

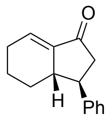
As described for the synthesis of siloxyallene **4a**, compound **3g** (0.31 mmol, 123 mg) in 5 mL ether was reacted with KO*t*-Bu (0.46 mmol, 52 mg) followed by workup as described above to give crude **4g**. The desired Nazarov product was then prepared according to the previous procedure using trifluoroacetic acid (0.93 mmol, 69 μL) to afford **5g** (24 mg, yield 28%) and **6g** (33 mg, 39%). **5g**: R$_f$ 0.53

(hexane:EtOAc 4:1); IR (microscope) 3084, 3061, 3027, 3003, 2927, 2860, 1725, 1637, 1602, 1495, 1453, 1370, 1222, 1171, 1158, 1030, 753, 700 cm^{-1}; ^{1}H NMR (400 MHz, CDCl$_3$) δ 7.37-7.17 (m, 8H), 7.09-7.06 (m, 2H), 6.21 (d, *J* = 2.4 Hz, 1H), 5.40 (d, *J* = 2.4 Hz, 1H), 3.22 (app. q, *J* = 8.7 Hz, 1H), 3.00-2.94 (m, 1H), 2.84 (dd, *J* = 18.4, 7.9 Hz, 1H), 2.64-2.60 (m, 2H), 2.52 (dd, *J* = 18.4, 9.8 Hz, 1H), 2.01-1.94 (m, 2H); ^{13}C NMR (100 MHz, CDCl$_3$) δ 205.41, 148.4, 142.9, 141.6, 128.8, 128.4, 128.2, 127.1, 126.9, 125.9, 117.4, 48.1, 46.2, 45.5, 34.2, 32.7; HRMS (EI, M$^+$) for $C_{20}H_{20}O$ calcd 276.1514, found: m/z 276.1514. **6g**: R$_f$ 0.47 (hexane:EtOAc 4:1); IR (microscope) 3084, 3026, 3002, 2924, 2860, 1700, 1643, 1601, 1494, 1454, 1325, 1076, 756, 701 cm^{-1}; ^{1}H NMR (400 MHz, CDCl$_3$) δ 7.37-7.32 (m, 2H), 7.30-7.25 (m, 3H), 7.23-7.19 (m, 1H), 7.11-7.06 (m, 4H), 3.85 (dd, *J* = 6.8, 1.6 Hz, 1H), 2.89 (dd, *J* = 18.8, 7.0 Hz, 1H), 2.80-2.68 (m, 2H), 2.64-2.56 (m, 1H), 2.39 (dd, *J* = 18.9, 2.3 Hz, 1H), 2.39-2.31 (m, 1H), 1.73 (d, *J* = 1.9 Hz, 3H); ^{13}C NMR (100 MHz, CDCl$_3$) δ 209.1, 173.8, 141.8, 140.6, 137.5, 128.9, 128.4, 128.1, 127.4, 127.1, 126.3, 47.2, 44.5, 33.2, 31.0, 8.1; HRMS (EI, M$^+$) for $C_{20}H_{20}O$ calcd 276.1514, found: m/z 276.1514.

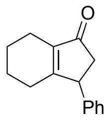


7h

As described for the synthesis of siloxyallene **4a**, compound **3h** (0.07 mmol, 26 mg) in 3 mL ether was reacted with KO*t*-Bu (0.10 mmol, 11 mg) followed by workup as described above to give crude **4h**. The reaction was then performed according to the previous procedure using trifluoroacetic acid to afford **7h** (12 mg, yield 70%): IR (microscope) 3083, 3028, 1651, 1596 cm^{-1}; ^{1}H NMR (400 MHz, CDCl$_3$) δ 7.75 (d, *J* = 16.0 Hz, 2H), 7.63-7.61 (m, 4H), 7.43-7.41 (m, 6H), 7.10 (d, *J* = 16.0 Hz, 2H); ^{13}C NMR (100 MHz, CDCl$_3$) δ 188.9, 143.3, 134.8, 130.5, 129.0, 128.4, 125.4; HRMS (EI, M$^+$) for $C_{17}H_{14}O$ calcd 234.1045, found: m/z 234.1038.

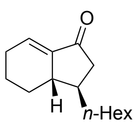


5i

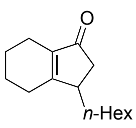


6i

As described for the synthesis of siloxyallene **4a**, compound **3i** (0.06 mmol, 19 mg) in 3 mL ether was reacted with KO*t*-Bu (0.09 mmol, 10 mg) followed by workup as described above to give crude **4i**. The desired Nazarov product was then prepared according to the previous procedure using trifluoroacetic acid (0.18 mmol, 13 μL) to afford **5i** (8 mg, yield 65%) and **6i** (2 mg, 14%). **5i**: R_f 0.52 (hexane:EtOAc 4:1); IR (microscope) 3061, 3028, 2931, 2858, 1719, 1652, 1601, 1453, 1247, 1223, 1187, 930, 749, 700 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.40-7.35 (m, 2H), 7.32-7.27 (m, 3H), 6.81 (app. q, *J* = 2.4 Hz, 1H), 2.83 (ddd, *J* = 12.6, 10.6, 7.0 Hz, 1H), 2.71-2.63 (m, 1H), 2.68 (dd, *J* = 17.8, 7.4 Hz, 1H), 2.55 (dd, *J* = 17.8, 12.6 Hz, 1H), 2.40-.32 (m, 1H), 2.86-2.17 (m, 1H), 2.04 (dq, *J* = 12.0, 3.2 Hz, 1H), 1.92-1.86 (m, 1H), 1.55-1.43 (m, 1H), 1.19-1.09 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 204.7, 141.8, 141.3, 133.2, 128.9, 127.3, 127.1, 48.4, 46.3, 46.0, 27.3, 25.7, 21.8; HRMS (EI, M^+) for $C_{15}H_{16}O$ calcd 212.1201, found: m/z 212.1203. **6i**: R_f 0.48 (hexane:EtOAc 4:1); IR (microscope) 3061, 3027, 2930, 2858, 1698, 1645, 1453, 1390, 1277, 1245, 766, 701 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.37-7.31 (m, 2H), 7.28-7.24 (m, 1H), 7.12-7.10 (m, 2H), 3.85 (br d, *J* = 6.8 Hz, 1H), 2.93 (dd, *J* = 18.8, 7.2 Hz, 1H), 2.38 (dd, *J* = 18.8, 2.4 Hz, 1H), 2.27-2.25 (m, 2H), 2.10-2.07 (m, 2H), 1.72-1.66 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 208.4, 175.4, 142.1, 139.5, 129.1, 127.5, 127.2, 48.2, 45.1, 26.7, 22.4, 21.8, 20.3; HRMS (EI, M^+) for $C_{15}H_{16}O$ calcd 212.1201, found: m/z 212.1197.

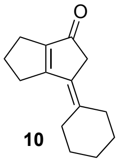


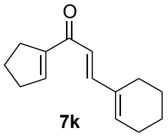
5j



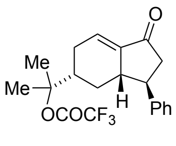
6j

As described for the synthesis of siloxyallene **4a**, compound **3j** (0.28 mmol, 96 mg) in 4 mL ether was reacted with KO*t*-Bu (0.42 mmol, 48 mg) followed by workup as described above to give crude **4j**. The desired Nazarov product was then prepared according to the previous procedure using trifluoroacetic acid (0.84 mmol, 64 μL) to afford **5j** (21 mg, yield 33%) and **6j** (12 mg, yield 20%). **5j**: R_f 0.61 (hexane:EtOAc 4:1); IR (microscope) 2927, 2856, 1720, 1655, 1456, 1248, 1170, 1139 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.67 (br s, 1H), 2.47 (dd, *J* = 17.8, 7.0 Hz, 1H), 2.44-2.38 (m, 1H), 2.33-2.23 (m, 1H), 2.22-2.14 (m, 3H), 1.74-1.44 (m, 6H), 1.36-1.27 (m, 8H), 0.911 (t, *J* = 6.6 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 206.1, 142.0, 132.0, 45.0, 44.7, 42.5, 34.4, 32.0, 29.7, 28.2, 27.8, 25.6, 22.8, 21.9, 14.3; HRMS (ESI, $[M+H]^+$) for $C_{15}H_{25}O$ calcd 221.1900, found: m/z 221.1901. **6j**: R_f 0.57 (hexane:EtOAc 4:1); IR (microscope) 2927, 2856, 1698, 1647, 1457, 1437, 1277, 1169 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.68 (m, 1H), 2.53 (dd, *J* = 18.6, 6.6 Hz, 1H), 2.44-2.36 (m, 1H), 2.22-2.12 (m, 3H), 2.07 (dd, *J* = 18.2, 2.2 Hz, 1H), 1.78-1.59 (m, 6H), 1.34-1.30 (m, 8H), 0.90 (t, *J* = 6.8 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 208.6, 176.7, 138.6, 42.1, 41.3, 33.0, 31.9, 29.6, 27.3, 26.6, 22.8, 22.4, 21.9, 20.2, 14.2; HRMS (ESI, $[M+H]^+$) for $C_{15}H_{25}O$ calcd 221.1900, found 221.1898.


10

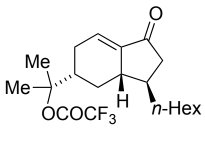

7k

As described for the synthesis of siloxyallene **4a**, compound **3k** (0.63 mmol, 202 mg) in 5 mL ether was reacted with KO*t*-Bu (0.95 mmol, 105 mg) followed by workup as described above to give crude **4k**. The desired Nazarov product was then prepared according to the previous procedure using trifluoroacetic acid (1.89 mmol, 140 μL) to afford **10** (35 mg, yield 28%) and **7k** (2 mg, yield 2%). **10**: R_f 0.65 (hexane:EtOAc 4:1); IR (microscope) 3346, 2929, 2878, 2861, 2818, 1691, 1659, 1635, 1450, 1394, 1277, 1229, 1162, 1098, 1058, 750 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.93-2.88 (m, 4H), 2.38 (t, *J* = 7.0 Hz, 2H), 2.35 (t, *J* = 5.8 Hz, 2H), 2.22-2.19 (m, 2H), 1.80-1.57 (m, 8H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 196.3, 163.2, 154.8, 141.3, 126.1, 35.8, 33.5, 31.7, 27.6, 26.8, 25.2, 22.3, 21.8, 20.2; HRMS (EI, H^+) for $C_{14}H_{18}O$ calcd 202.1358, found: m/z 202.1355. **7k**: R_f 0.70 (hexane:EtOAc 4:1); IR (microscope) 2928, 2856, 1729, 1650, 1620, 1610, 1588, 1449, 1365, 1297, 1168, 1001, 981 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.28 (d, *J* = 16.0 Hz, 1H), 6.78-6.76 (m, 1H), 6.60 (d, *J* = 15.6 Hz, 1H), 6.24 (s, 1H), 2.67-2.57 (m, 4H), 2.24-2.20 (m, 4H), 1.96 (quintet, *J* = 7.6 Hz, 2H), 1.78-1.62 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 188.7, 146.9, 145.7, 142.5, 139.4, 135.3, 119.2, 34.0, 31.1, 29.6, 26.6, 24.3, 22.8, 22.1; HRMS (EI, M^{+}) for $C_{14}H_{18}O$ calcd 202.1358, found: m/z 202.1348.

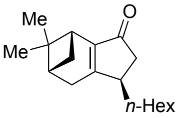


(+)-**12l**

As described for the synthesis of siloxyallene **4a**, compound **3l** (1.41 mmol, 516 mg) in 5 mL ether was reacted with KO*t*-Bu (2.12 mmol, 237 mg) followed by workup as described above to give crude **4l**. The desired Nazarov product was then prepared according to the previous procedure using trifluoroacetic acid (4.23 mmol, 315 μL) to afford **12l** (193 mg, yield 45%): R$_f$ 0.36 (hexane:EtOAc 4:1); IR (microscope) 3062, 3030, 2924, 1776, 1721, 1660, 1602, 1454, 1422, 1392, 1372, 1218, 1166, 1134, 776, 700 cm^{-1}; ^{1}H NMR (400 MHz, CDCl3) δ 7.40-7.37 (m, 2H), 7.31-7.29 (m, 3H), 6.78 (app. q, *J* = 2.0 Hz, 1H), 2.85 (ddd, *J* = 12.6, 10.5, 7.0 Hz, 1H), 2.80-2.77 (m, 1H), 2.72 (dd, *J* = 17.9, 7.0 Hz, 1H), 2.57 (dd, *J* = 18.2, 12.6 Hz, 1H), 2.43 (app. dq, *J* = 19.6, 4.2 Hz, 1H), 2.25 (app. tdd, *J* = 11.9, 4.9, 2.1 Hz, 1H), 2.21-2.15 (m, 1H), 2.03 (ddd, *J* = 11.9, 4.9, 2.1 Hz, 1H), 1.59 (s, 3H), 1.55 (s, 3H), 1.07 (app. td, *J* = 12.6, 11.2 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 203.4, 156.0 (q, *J* = 40.9 Hz), 141.0, 140.0, 131.2, 128.8, 127.0, 127.0, 114.3 (q, *J* = 285.4 Hz), 90.5, 47.8, 46.5, 45.9, 42.7, 28.1, 26.7, 23.3, 22.7; ^{19}F NMR (376 MHz, $CDCl_3$) δ -76.0; HRMS (EI, [M-CF_3CO_2H]$^{+}$) for $C_{18}H_{20}O$ calcd 252.1514, found: m/z 252.1512; [a]$_D^{25}$: +67.16° (c 2.87, $CHCl_3$).

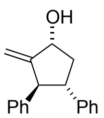


(−)-**12m**



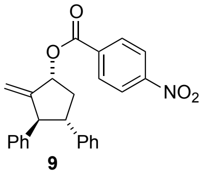
(−)-**6m**

As described for the synthesis of siloxyallene **4a**, compound **3m** (0.14 mmol, 52 mg) in 3 mL ether was reacted with KO*t*-Bu (0.21 mmol, 23 mg) followed by workup as described above to give crude **4m**. The desired Nazarov product was then prepared according to the previous procedure using trifluoroacetic acid (0.42 mmol, 31 μL) to afford **12m** (7 mg, yield 13%) and **6m** (9 mg, yield 25%). **12m**: R_f 0.41 (hexane:EtOAc 4:1); IR (film) 2955, 2926, 2856, 1778, 1722, 1660, 1466, 1372, 1219, 1167, 1125, 1167, 1125, 777 cm^{-1}; ^{1}H NMR (400 MHz, CDCl3) δ 6.63 (dt, *J* = 4.0, 3.0 Hz, 1H), 2.50 (dd, *J* = 18.0, 6.9 Hz, 1H), 2.39-2.30 (m, 1H), 2.27-2.17 (m, 3H), 2.14-2.08 (m, 1H), 1.94 (dd, *J* = 18.0, 12.0 Hz, 1H), 1.71-1.62 (m, 2H), 1.61 (s, 3H), 1.59 (s, 3H), 1.39-1.25 (m, 9H), 1.04-0.94 (m, 1H), 0.89-0.87 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 204.8, 156.1 (q, *J* = 41.2 Hz), 141.8, 130.1, 114.4 (q, *J* = 285.0 Hz), 90.8, 45.0, 44.9, 42.8, 42.0, 34.1, 31.7, 29.4, 28.6, 28.0, 26.8, 22.9, 22.8, 22.5, 14.0; ^{19}F NMR (376 MHz, $CDCl_3$) δ -76.0; HRMS (EI, $[M-CF_3CO_2H]^+$) for $C_{18}H_{28}O$ calcd 260.2140, found: m/z 260.2136; $[a]_D^{25}$: -44.56° (c 0.35, $CHCl_3$). **6m**: R_f 0.50 (hexane:EtOAc 4:1); IR (film) 2954, 2927, 2857, 1695, 1625, 1466, 1416, 1385, 1239, 1168 cm^{-1}; ^{1}H NMR (400 MHz, CDCl3) δ 2.76-2.68 (m, 1H), 2.68-2.61 (m, 2H), 2.54 (app. dt, *J* = 9.0, 2.7 Hz, 1H), 2.47 (br d, *J* = 18.8 Hz, 1H), 2.25 (app. tt, *J* = 5.6, 2.8 Hz, 1H), 2.17 (dd, *J* = 19.2, 2.0 Hz, 1H), 1.82-1.73 (m, 2H), 1.69-1.57 (m, 4H), 1.36 (s, 3H), 1.36-1.26 (m, 5H), 1.05 (d, *J* = 9.0 Hz, 1H), 0.93-0.87 (m, 3H), 0.71 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 205.4, 175.9, 148.8, 42.8, 41.0, 40.6, 37.1, 33.7, 32.4, 31.9, 31.7, 29.3, 28.3, 25.8, 22.5, 20.9, 14.0 [One aliphatic carbon signal is missing due to peak overlap.]; HRMS (EI, M^+) for $C_{18}H_{28}O$ calcd 260.2140, found: m/z 260.2143; $[a]_D^{25}$: -8.62° (c 0.21, $CHCl_3$).



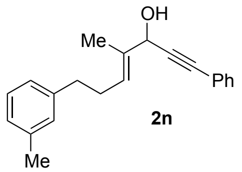
8

To a solution of **5a** (0.06 mmol, 15 mg) and cerium (III) chloride heptahydrate (0.06 mmol, 22 mg) in 3 mL MeOH was added $NaBH_4$ (0.06 mmol, 3 mg) at room temperature. The mixture was stirred for 8 h then quenched by adding saturated NH_4Cl solution. The organic layer was separated and washed with brine, dried over anhydrous $MgSO_4$, filtered and concentrated under reduced pressure. The crude mixture was purified by flash column chromatography (hexane:EtOAc 2:1) to provide the alcohol as a single diastereomer (13 mg, yield 85%): R_f 0.25 (hexane:EtOAc 4:1); IR (microscope) 3411 (br s), 3063, 3028, 2959, 2923, 2857, 1661, 1602, 1469, 1452, 1328, 1211, 1087, 1076, 914, 905, 761, 699 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.26-7.21 (m, 3H), 7.20-7.15 (m, 3H), 7.11-7.08 (m, 2H), 7.05-7.02 (m, 2H), 5.33 (app. t, *J* = 2.4 Hz, 1H), 4.86-4.81 (m, 2H), 3.81 (app. dq, *J* = 10.8, 2.6 Hz, 1H), 3.09 (ddd, *J* = 12.4, 11.2, 6.0 Hz, 1H), 2.61 (ddd, *J* = 12.4, 6.4, 6.4 Hz, 1H), 1.95 (ddd, *J* = 12.4, 12.4, 9.6 Hz, 1H) 1.82 (br s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 158.0, 142.6, 141.9, 128.4, 128.3, 128.2, 127.3, 126.5, 126.3, 110.1, 74.7, 57.2, 50.0, 42.7; HRMS (EI, M^+) for $C_{18}H_{18}O$ calcd 250.1358, found: m/z 250.1358.



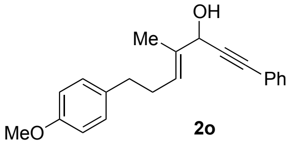
9

To a solution of **8** (0.032 mmol, 8 mg) and triethylamine (0.096 mmol, 13 mL) in 3 mL CH_2Cl_2 was added 4-nitrobenzoyl chloride (0.035 mmol, 7 mg) at room temperature. The mixture was stirred for 8 h then quenched by adding 5 mL water and CH_2Cl_2 (10 mL). The organic layer was separated and washed with brine, dried over anhydrous $MgSO_4$, filtered and concentrated under reduced pressure. The crude mixture was purified by flash column chromatography (hexane:EtOAc 5:1) to provide **9** (10 mg, 80%): mp: 176-177 °C; IR (microscope) 3109, 3085, 3061, 3029, 1724, 1605, 1528, 1347, 1273, 1119, 1103 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.36-8.33 (m, 2H), 8.32-8.29 (m, 2H), 7.30-7.26 (m, 4H), 7.24-7.20 (m, 2H), 7.17-7.11 (m, 4H), 6.11 (app. td, *J* = 7.2, 2.2 Hz, 1H), 5.41 (dd, *J* = 3.0, 2.2 Hz, 1H), 4.92 (t, *J* = 2.6 Hz, 1H), 3.92 (app. dq, *J* = 11.0, 2.6 Hz, 1H), 3.28 (app. td, *J* = 11.6, 6.6 Hz, 1H), 2.88 (app. dt, *J* = 12.8, 7.2 Hz, 1H), 2.21 (app. td, *J* = 12.6, 8.6 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.8, 153.0, 150.8, 141.6, 141.4, 135.9, 131.0, 128.8, 128.7 128.6, 127.5, 127.0, 126.9, 123.8, 113.5, 77.5, 57.5, 50.7, 39.5; HRMS (EI, M$^+$) for $C_{25}H_{21}NO_4$ calcd 399.1471, found: m/z 399.1466.



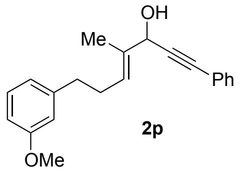
2n

Synthesized according to the previous procedure to afford **2n** (200 mg, yield 83%) as a pale yellow oil: IR (microscope) 3352 (br), 3022, 2921, 2226 cm^{-1}; ^{1}H NMR (400 MHz, CDCl$_3$) δ 7.47-7.45 (m, 2H), 7.36-7.31 (m, 3H), 7.21-7.18 (m, 1H), 7.04-7.02 (m, 3H), 5.77 (t, *J* = 6.8 Hz, 1H), 4.99 (s, 1H), 2.69 (t, *J* = 8.0 Hz, 2H), 2.41 (app. q, *J* = 7.6 Hz, 2H), 2.35 (s, 3H), 1.96 (br s, 1H), 1.81 (s, 3H); ^{13}C NMR (100 MHz, CDCl$_3$) δ 141.8, 137.9, 134.9, 131.7, 129.3, 128.4, 128.3, 128.2, 127.5, 126.6, 125.5, 122.6, 88.4, 86.0, 68.5, 35.4, 29.8, 21.4, 12.4; HRMS (EI, M$^+$) for $C_{21}H_{22}O$ calcd 290.1671, found: m/z 290.1665.



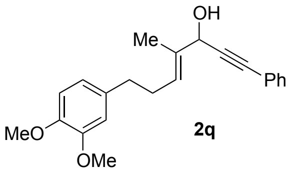
2o

Synthesized according to the previous procedure to afford **2o** (1.187 g, yield 86%) as a pale yellow oil: IR (microscope) 3402 (br), 2203, 1611 cm^{-1}; ^{1}H NMR (400 MHz, CDCl$_3$) δ 7.47-7.45 (m, 2H), 7.35-7.32 (m, 3H),7.15-7.13 (m, 2H), 6.85-6.83 (m, 2H), 5.76 (t, *J* = 7.2 Hz, 1H), 4.99 (s, 1H), 3.80 (s, 3H), 2.68 (t, *J* = 7.6 Hz, 2H), 2.39 (app. q, *J* = 7.2 Hz, 2H), 1.87 (br s, 1H), 1.79 (s, 3H); ^{13}C NMR (100 MHz, CDCl$_3$) δ 158.1, 135.1, 134.1, 132.0, 129.6, 128.7, 128.5, 127.7, 122.9, 114.0, 88.6, 86.3, 68.8, 55.5, 34.8, 30.2, 12.7; HRMS (EI, M$^+$) for $C_{21}H_{22}O_2$ calcd 306.1620, found: m/z 306.1612.



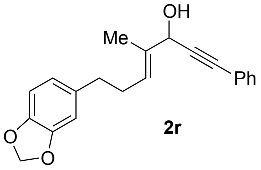
2p

Synthesized according to the previous procedure to afford **2p** (140 mg, yield 98%) as a pale yellow oil: IR (microscope) 3331 (br), 2203 cm^{-1}; ^{1}H NMR (400 MHz, CDCl$_3$) δ 7.45-7.42 (m, 2H), 7.33-7.30 (m, 3H), 7.20 (ddd, *J* = 7.6, 7.6, 0.8 Hz, 1H), 6.81-6.79 (m, 1H), 6.76-6.72 (m, 2H), 5.74 (tqd, *J* = 7.2, 1.2, 1.2 Hz, 1H), 4.97 (br s, 1H), 3.78 (s, 3H), 2.69 (t, *J* = 7.2 Hz, 2H), 2.40 (app. q, *J* = 7.2 Hz, 2H), 1.78 (br s, 3H); ^{13}C NMR (100 MHz, CDCl$_3$) δ 159.6, 143.6, 135.5, 131.6, 129.2, 128.2, 128.1, 125.6, 123.1, 120.9, 114.2, 111.1, 88.6, 84.8, 67.4, 54.1, 36.6, 28.5, 12.4; HRMS (EI, M$^+$) for $C_{21}H_{22}O_2$ calcd 306.1620, found: m/z 306.1612.



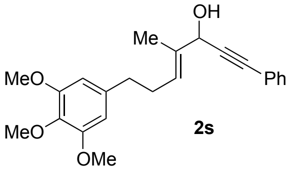
2q

Synthesized according to the previous procedure to afford **2q** (50 mg, yield 87%) as a pale yellow oil: IR (microscope) 3462 (br), 2227 cm^{-1}; ^{1}H NMR (300 MHz, CDCl$_3$) δ 7.46-7.42 (m, 2H), 7.34-7.29 (m, 3H), 6.80-6.72 (m, 3H), 5.74 (tq, *J* = 7.5, 1.2 Hz, 1H), 4.97 (br s, 1H), 3.87 (s, 3H), 3.85 (s, 3H), 2.67 (t, *J* = 7.2 Hz, 2H), 2.38 (app. q, *J* = 7.5 Hz, 2H), 1.93 (br s, 1H), 1.78 (d, *J* = 1.2 Hz, 3H); ^{13}C NMR (100 MHz, CDCl$_3$) δ 148.8, 147.2, 134.9, 134.4, 131.7, 128.4, 128.3, 127.4, 122.6, 120.3, 111.8, 111.2, 88.4, 86.0, 68.5, 55.9, 55.8, 35.0, 29.9, 12.4; HRMS (EI, M$^+$) for $C_{22}H_{24}O_3$ calcd 336.1726, found: m/z 336.1731.



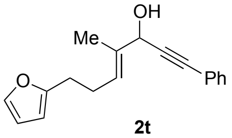
2r

Synthesized according to the previous procedure to afford **2r** (300 mg, yield 99%) as a pale yellow oil: IR (microscope) 3389, 2226 cm^{-1}; ^{1}H NMR (400 MHz, CDCl$_3$) δ 7.54-7.43 (m, 2H), 7.34-7.30 (m, 3H), 6.74-6.70 (m, 2H), 6.66-6.64 (m, 1H), 5.91-5.88 (m, 2H), 5.71 (br t, *J* = 7.2 Hz, 1H), 4.97 (br s, 1H), 2.63 (t, *J* = 7.6 Hz, 2H), 2.38 (app. q, *J* = 7.6 Hz, 2H), 1.85 (br s, 1H), 1.78 (d, *J* = 0.8 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 147.5, 145.6, 135.7, 135.0, 131.7, 128.4, 128.3, 127.2, 122.6, 121.2, 108.9, 108.1, 100.7, 88.4, 86.0, 68.4, 35.2, 30.0, 12.4; HRMS (EI, M^+) for $C_{21}H_{20}O_3$ calcd 320.1412, found: m/z 320.1413.



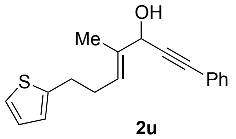
2s

Synthesized according to the previous procedure to afford **2s** (101 mg, yield 95%) as a pale yellow oil: IR (microscope) 3447 (br), 2201, 1590 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.47-7.41 (m, 2H), 7.35-7.30 (m, 3H), 6.42 (s, 2H), 5.75 (br t, *J* = 7.6 Hz, 1H), 4.98 (br s, 1H), 3.85 (s, 3H), 3.82 (s, 6H), 2.66 (t, *J* = 7.6 Hz, 2H), 2.40 (app. q, *J* = 7.6 Hz, 2H), 1.96 (br s, 1H), 1.85 (d, *J* = 1.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 153.1, 137.6, 136.2, 135.0, 131.8, 131.7, 128.4, 127.3, 122.5, 105.4, 88.3, 86.1, 68.4, 60.8, 56.1, 35.8, 29.7, 12.5; HRMS (EI, M^+) for $C_{23}H_{26}O_4$ calcd 366.1831, found: m/z 366.1841.



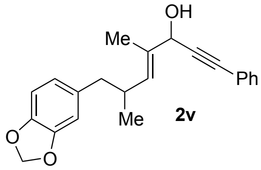
2t

Synthesized according to the previous procedure to afford **2t** (151 mg, yield 99%) as a pale yellow oil: IR (microscope) 3383 (br), 2203, 1490 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.47-7.45 (m, 2H), 7.36-7.31(m, 4H), 6.30 (dd, *J* = 3.2, 2.0 Hz, 1H), 6.03 (dd, *J* = 2.4, 1.2 Hz, 1H), 5.74 (t, *J* = 7.2 Hz, 1H), 4.99 (br s, 1H), 2.75 (br t, *J* = 7.2 Hz, 2H), 2.46 (app. q, *J* = 7.2 Hz, 2H), 1.89 (br s, 1H), 1.83 (d, *J* = 1.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 155.7, 141.2, 135.6, 132.0, 128.7, 128.5, 127.1, 122.8, 110.4, 105.4, 88.5, 86.3, 68.7, 27.9, 26.7, 12.6; HRMS (EI, M^+) for $C_{18}H_{18}O_2$ calcd 266.1307, found: m/z 266.1302.



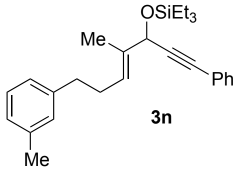
2u

Synthesized according to the previous procedure to afford **2u** (227 mg, yield 98%) as a pale yellow oil: IR (microscope) 3357, 2227, 1490 cm^{-1}; ^{1}H NMR (500 MHz, CDCl$_3$) δ 7.46-7.44 (m, 2H), 7.33-7.31 (m, 3H), 7.13 (d, *J* = 5.0 Hz, 1H), 6.92 (dd, *J* = 5.0, 3.5 Hz, 1H), 6.82 (d, *J* = 3.0 Hz, 1H), 5.76 (t, *J* = 7.3 Hz, 1H), 5.00 (br s, 1H), 2.94 (t, *J* = 7.8 Hz, 2H), 2.48 (app. q, *J* = 7.5 Hz, 2H), 1.88 (br s, 1H), 1.81 (s, 3H); ^{13}C NMR (125 MHz, CDCl$_3$) δ 144.6, 135.6, 132.1, 131.7, 128.5, 128.3, 126.7, 124.4, 123.2, 122.6, 88.4, 86.1, 68.4, 30.0, 29.5, 12.5; HRMS (EI, M$^+$) for $C_{18}H_{18}SO$ calcd 282.1079, found: m/z 282.1073.



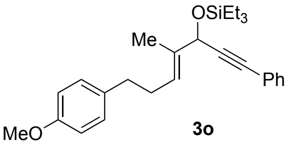
2v

Synthesized according to the previous procedure to afford **2v** (651 mg, yield 99%) as a pale yellow oil: IR (microscope) 3390 (br), 3051, 2958, 2226 cm^{-1}; ^{13}C NMR (125 MHz, CDCl$_3$) δ 147.3, 147.3, 145.6, 134.4, 134.4, 133.6, 133.5, 133.5, 133.4, 131.7, 128.4, 128.3, 122.7, 122.1, 109.6, 109.6, 107.9, 107.9, 100.7, 100.6, 88.4, 85.9, 68.6, 68.5, 43.2, 34.6, 34.6, 20.3, 20.1, 12.6, 12.3 [Several carbon signals are missing due to peak overlap]; HRMS (EI, M$^+$) for $C_{22}H_{22}O_3$ calcd 334.1569, found: m/z 334.1575; Partial ^{1}H NMR spectral data for the major isomer: ^{1}H NMR (500 MHz, CDCl$_3$) δ 5.90-5.89 (m, 2H), 5.53-5.51 (m, 1H), 4.94 (br s, 1H), 1.90 (br s, 1H), 1.68 (d, *J* = 1.0 Hz, 3H), 0.99 (d, *J* = 7.0 Hz, 3H); Partial ^{1}H NMR spectral data for the minor isomer: ^{1}H NMR (500 MHz, CDCl$_3$) δ 5.87-5.86 (m, 1H), 5.83-5.82 (m, 1H), 5.49-5.48 (m, 1H), 4.95 (br s, 1H), 1.90 (br s, 1H), 1.65 (d, *J* = 1.0 Hz, 3H), 1.01 (d, *J* = 7.0 Hz, 3H)



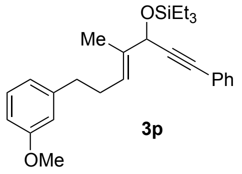
3n

Synthesized according to the previous procedure to afford **3n** (157 mg, yield 96%) as a pale yellow oil: IR (microscope) 3022, 2954, 2226 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.44-7.43 (m, 2H), 7.33-7.31 (m, 3H), 7.20-7.17 (m, 1H), 7.04-7.01 (m, 3H), 5.69 (t, *J* = 7.5 Hz, 1H), 4.98 (s, 1H), 2.68 (t, *J* = 8.0 Hz, 2H), 2.40 (app. q, *J* = 7.5 Hz, 2H), 2.34 (s, 3H), 1.78 (s, 3H), 1.02 (t, *J* = 8.0 Hz, 9H), 0.76-0.66 (m, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 142.0, 137.8, 135.4, 131.6, 131.6, 129.3, 128.2, 128.1, 126.5, 125.8, 125.5, 123.2, 89.6, 84.8, 68.5, 35.5, 29.7, 21.4, 12.4, 6.8, 4.9; HRMS (EI, M^{+}) for $C_{27}H_{36}OSi$ calcd 404.2535, found: m/z 404.2530.



3o

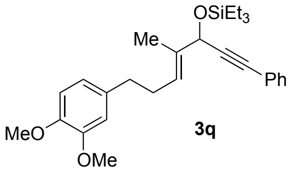
Synthesized according to the previous procedure to afford **3o** (420 mg, yield 99%) as a pale yellow oil: IR (microscope) 3031, 2953, 1612 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.45-7.42 (m, 2H), 7.33-7.31 (m, 3H), 7.15-7.12 (m, 2H), 6.84-6.82 (m, 2H), 5.68 (t, *J* = 7.2 Hz, 1H), 4.97 (s, 1H), 3.80 (s, 3H), 2.66 (t, *J* = 8.0 Hz, 2H), 2.37 (app. q, *J* = 7.6 Hz, 2H), 1.74 (s, 3H), 1.02 (t, *J* = 8.0 Hz, 9H), 0.76-67 (m, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 158.0, 135.7,134.4, 131.8, 129.6, 128.4, 128.3, 125.9, 123.4, 113.9, 89.9, 85.0, 68.7, 55.5, 34.9, 30.1, 12.6, 7.1, 5.1; HRMS (EI, M^{+}) for $C_{27}H_{36}O_2Si$ calcd 420.2485, found: m/z 420.2482.



3p

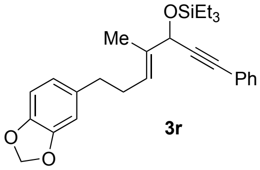
Synthesized according to the previous procedure to afford **3p** (155 mg, yield 99%) as a pale yellow oil: IR (microscope) 3054, 2952, 2224 cm^{-1}; ^{1}H NMR (400 MHz,

$CDCl_3$) δ 7.45-7.43 (m, 2H), 7.33-7.30 (m, 3H), 7.21 (app. t, *J* = 7.8 Hz, 1H), 6.83-6.81 (m, 1H), 6.79-6.74 (m, 2H), 5.70 (tqd, *J* = 7.2, 1.2, 1.2 Hz, 1H), 4.98 (br s, 1H), 3.80 (s, 3H), 2.70 (t, *J* = 7.8 Hz, 2H), 2.41 (app. q, *J* = 7.6 Hz, 2H), 1.78 (d, *J* = 1.2 Hz, 3H), 1.03 (t, *J* = 8.0 Hz, 9H), 0.75-0.68 (m, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.6, 143.6, 135.5, 131.6, 129.2, 128.2, 128.1, 125.6, 123.1, 120.9, 114.2, 111.1, 89.6, 84.8, 68.4, 55.1, 35.6, 29.5, 12.4, 6.8, 4.9; HRMS (ESI, $[M+Na]^+$) for $C_{27}H_{36}O_2Si$ calcd 443.2382, found: m/z 443.2384.



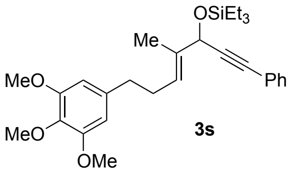
3q

Synthesized according to the previous procedure to afford **3q** (29 mg, yield 91%) as a pale yellow oil: IR (microscope) 3056, 2954, 2226, 1516 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.44-7.39 (m, 2H), 7.34-7.28 (m, 3H), 6.80-6.73 (m, 3H), 5.67 (t, *J* = 7.2 Hz, 1H), 4.96 (br s, 1H), 3.87 (s, 3H), 3.83 (s, 3H), 2.66 (t, *J* = 7.7 Hz, 2H), 2.38 (app. q, *J* = 7.5 Hz, 2H), 1.76 (s, 3H), 1.03 (t, *J* = 8.0 Hz, 9H), 0.76-0.65 (m, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 148.8, 147.2, 135.5, 134.7, 131.6, 128.2, 128.1, 125.7, 123.1, 120.3, 111.8, 111.2, 89.6, 84.8, 68.4, 55.9, 55.8, 35.1, 29.8, 12.4, 6.8, 4.9; HRMS (EI, M^+) for $C_{28}H_{38}O_3Si$ calcd 450.2590, found: m/z 450.2586.



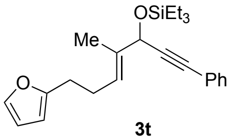
3r

Synthesized according to the previous procedure to afford **3r** (363 mg, yield 88%) as a pale yellow oil: IR (microscope) 2954, 2224, 1490 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.46-7.41 (m, 2H), 7.35-7.29 (m, 3H), 6.74-6.67 (m, 2H), 6.66-6.64 (m, 1H), 5.91-5.88 (m, 2H), 5.66 (br t, *J* = 7.1 Hz, 1H), 4.97 (br s, 1H), 2.63 (t, *J* = 7.6 Hz, 2H), 2.35 (app. q, *J* = 7.2 Hz, 2H), 1.76 (br s, 3H), 1.04 (t, *J* = 7.8 Hz, 9H), 0.78-0.65 (m, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 147.5, 145.6, 135.9, 135.6, 131.6, 128.2, 128.1, 125.4, 123.2, 121.2, 109.0, 108.1, 100.7, 89.6, 84.8, 68.4, 35.3, 29.9, 12.4, 6.8, 4.9; HRMS (EI, M$^+$) for $C_{27}H_{34}O_3Si$ calcd 434.2277, found: m/z 434.2274.



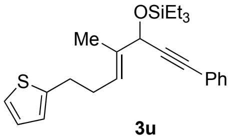
3s

Synthesized according to the previous procedure to afford **3s** (84 mg, yield 66%) as a pale yellow oil: IR (microscope) 3058, 2954, 1590 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.42-7.40 (m, 2H), 7.34-7.30 (m, 3H), 6.43 (s, 2H), 5.68 (t, *J* = 7.6 Hz, 1H), 4.96 (br s, 1H), 3.83 (s, 3H), 3.82 (s, 6H), 2.66 (t, *J* = 7.6 Hz, 2H), 2.40 (app. q, *J* = 7.6 Hz, 2H), 1.78 (d, *J* = 0.8 Hz, 3H), 1.02 (t, *J* = 7.8 Hz, 9H), 0.78-0.65 (m, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 153.0, 137.8, 136.1, 135.5, 131.5, 128.2, 128.1, 125.5, 123.1, 105.3, 89.5, 84.9, 68.4, 60.8, 56.0, 35.8, 29.6, 12.5, 6.8, 4.9; HRMS (EI, M$^+$) for $C_{29}H_{40}O_4Si$ calcd 480.2696, found: m/z 480.2694.



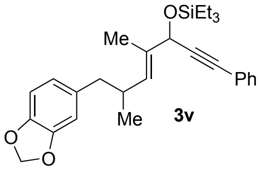
3t

Synthesized according to the previous procedure to afford **3t** (338 mg, yield 99%) as a pale yellow oil: IR (microscope) 3061, 2955, 2203, 1667 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.45-7.43 (m, 2H), 7.34-7.31 (m, 4H), 6.29 (dd, *J* = 3.2, 1.6 Hz, 1H), 6.02 (dd, *J* = 2.0, 0.8 Hz, 1H), 5.67 (br t, *J* = 7.6 Hz, 1H), 4.98 (br s, 1H), 2.74 (t, *J* = 7.6 Hz, 2H), 2.43 (app. q, *J* = 7.6 Hz, 2H), 1.79 (d, *J* = 1.2 Hz, 3H), 1.02 (t, *J* = 7.6 Hz, 9H), 0.78-0.68 (m, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 155.9, 141.1, 136.2, 131.8, 128.5, 128.4, 125.3, 123.4, 110.3, 105.3, 89.8, 85.0, 68.6, 28.0, 26.6, 12.6, 7.1, 5.1; HRMS (EI, M$^+$) for $C_{24}H_{32}O_2Si$ calcd 380.2172, found: m/z 380.2173.



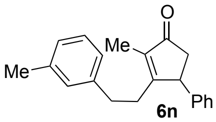
3u

Synthesized according to the previous procedure to afford **3u** (228 mg, yield 94%) as a pale yellow oil: IR (microscope) 3021, 2954, 2226 cm^{-1}; ^{1}H NMR (500 MHz, CDCl$_3$) δ 7.47-7.45 (m, 2H), 7.35-7.33 (m, 3H), 7.14 (dd, *J* = 4.8, 1.2 Hz, 1H), 6.94 (dd, *J* = 5.0, 3.5 Hz, 1H), 6.85 (dd, *J* = 3.5, 1.0 Hz, 1H), 5.73 (tqd, *J* = 7.6, 1.5, 1.5 Hz, 1H), 5.01 (br s, 1H), 2.96 (t, *J* = 7.5 Hz, 2H), 2.50 (app. q, *J* = 8.0 Hz, 2H), 1.82 (br s, 3H), 1.06 (t, *J* = 7.5 Hz, 9H), 0.79-0.70 (m, 6H); ^{13}C NMR (125 MHz, CDCl$_3$) δ 144.8, 136.1, 131.6, 128.2, 128.1, 126.7, 125.0, 125.0, 124.3, 123.2, 89.6, 84.9, 68.4, 30.0, 29.7, 12.5, 6.9, 4.9; HRMS (EI, M$^+$) for $C_{24}H_{32}SiSO$ calcd 396.1943, found: m/z 396.1945.



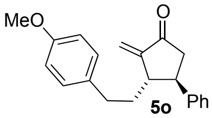
3v

Synthesized according to the previous procedure to afford **3v** (574 mg, yield 97%) as a pale yellow oil: Spectral data for the mixture of isomers: IR (microscope) 3034, 2955, 2219 cm^{-1}; ^{13}C NMR (125 MHz, CDCl$_3$) δ 147.3, 147.3, 145.5, 145.5, 134.6, 134.6, 134.2, 134.0, 131.8, 131.6, 131.6, 128.2, 128.1, 128.1, 128.0, 128.0, 123.2, 122.1, 122.1, 109.6, 109.6, 107.9, 107.8, 100.6, 100.6, 89.7, 84.6, 84.4, 68.6, 68.5, 43.3, 43.2, 34.5, 34.4, 20.2, 20.2, 12.5, 12.2, 6.8, 4.8 [Several carbon signals are missing due to peak overlap]; HRMS (EI, M$^+$) for $C_{28}H_{36}O_3Si$ calcd 448.2434, found: m/z 448.2443; Partial ^{1}H NMR spectral data for the major isomer: ^{1}H NMR (500 MHz, CDCl$_3$) δ 5.89-5.88 (m, 2H), 5.44-5.42 (m, 1H), 4.91 (br s, 1H), 1.90 (br s, 1H), 1.66 (d, *J* = 1.5 Hz, 3H); Partial ^{1}H NMR spectral data for the minor isomer: ^{1}H NMR (500 MHz, CDCl$_3$) δ 5.86-5.85 (m, 1H), 5.82-5.81 (m, 1H), 5.40-5.38 (m, 1H), 4.92 (br s, 1H), 1.90 (br s, 1H), 1.62 (d, *J* = 1.0 Hz, 3H)

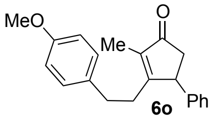


6n

Synthesized according to the previous procedure to afford **6n** (34 mg, yield 64%) as a pale yellow oil: IR (microscope) 3027, 2922, 1701, 1644 cm^{-1}; ^{1}H NMR (400 MHz, CDCl$_3$) δ 7.35-7.31 (m, 2H), 7.28-7.25 (m, 1H), 7.15 (t, *J* = 6.0 Hz, 1H), 7.10-7.07 (m, 2H), 7.02-7.00 (m, 1H), 6.87-6.84 (m, 2H), 3.85-3.81 (m, 1H), 2.87 (dd, *J* = 18.5, 7.0 Hz, 1H), 2.47-2.67 (m, 2H), 2.58-2.52 (m, 1H), 2.40-2.33 (m, 2H), 2.31 (s, 3H), 1.74 (br d, *J* = 1.9 Hz, 3H); ^{13}C NMR (100 MHz, CDCl$_3$) δ 209.2, 174.0, 141.9, 140.6, 138.1, 137.4, 128.9, 128.9, 128.4, 127.5, 127.1, 127.0, 125.2, 47.2, 44.6, 33.2, 31.0, 21.3, 8.2; HRMS (EI, M$^+$) for $C_{21}H_{22}O$ calcd 290.1671, found: m/z 290.1665.

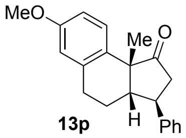


5o



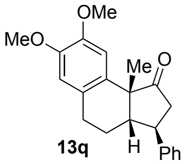
6o

Synthesized according to the previous procedure to afford **5o** (25 g, yield 29%) and **6o** (35 mg, 40%): **5o**: IR (microscope) 3004, 2933, 1726, 1612 cm^{-1}; ^{1}H NMR (400 MHz, CDCl$_3$) δ 7.39-7.36 (m, 2H), 7.30-7.27 (m, 1H), 7.25-7.23 (m, 2H), 7.00-6.97 (m, 2H), 6.82-6.78 (m, 2H), 6.20 (d, *J* = 2.8 Hz, 1H), 5.40 (d, *J* = 2.8 Hz, 1H), 3.80 (s, 3H), 3.10 (app. q, *J* = 9.2 Hz, 1H), 2.98-2.93 (m, 1H), 2.86-2.80 (m, 1H), 2.58-2.48 (m, 3H), 1.97-1.87 (m, 2H); ^{13}C NMR (100 MHz, CDCl$_3$) δ 205.7, 158.1, 148.8, 143.3, 133.9, 129.4, 129.1, 127.5, 127.2, 117.7, 114.1, 55.5, 48.3, 46.5, 45.9, 34.8, 32.1; HRMS (EI, M$^+$) for $C_{21}H_{22}O_2$ calcd 306.1620, found: m/z 306.1617. **6o**: IR (microscope) 3028, 2932, 1701, 1643, 1512 cm^{-1}; ^{1}H NMR (400 MHz, CDCl$_3$) δ 7.37-7.33 (m, 2H), 7.30-7.26 (m, 1H), 7.12-7.09 (m, 2H), 7.00-6.96 (m, 2H), 6.83-6.80 (m, 2H), 3.84 (br d, *J* = 6.8 Hz, 1H), 3.80 (s, 3H), 2.89 (dd, *J* = 19.0, 6.8 Hz, 1H), 2.73-2.65 (m, 2H), 2.56-2.54 (m, 1H), 2.38 (dd, *J* =19.0, 2.0 Hz, 1H), 2.32-2.28 (m, 1H), 1.73 (d, *J* = 1.2 Hz, 3H); ^{13}C NMR (100 MHz, CDCl$_3$) δ 209.5, 174.3, 158.4, 142.2, 137.7, 133.0, 129.4, 129.2, 127.7, 127.4, 114.2, 55.5, 47.5, 44.8, 32.7, 31.5, 8.4; HRMS (EI, M$^+$) for $C_{21}H_{22}O_2$ calcd 306.1620, found: m/z 306.1618.



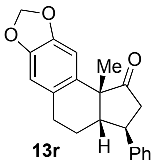
13p

Synthesized according to the previous procedure to afford **13p** (64 mg, yield 53%) as a white solid: mp 156-157 °C; IR (microscope) 3010, 2930, 1729, 1607 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.43 (d, *J* = 8.8 Hz, 1H), 7.37-7.33 (m, 2H), 7.28-7.24 (m, 3H), 6.76 (dd, *J* = 8.8, 2.8 Hz, 1H), 6.65 (d, *J* = 2.8 Hz, 1H), 3.80 (s, 3H), 3.22 (ddd, *J* = 11.6, 11.6, 8.4 Hz, 1H), 2.99 (ddd, *J* = 18.4, 12.8, 6.8, 1H), 2.78-2.70 (m, 2H), 2.43 (dd, *J* = 18.8, 11.6 Hz, 1H), 2.33 (ddd, *J* = 11.6, 3.6, 3.6 Hz, 1H), 1.88-1.79 (m, 1H), 1.77-1.71 (m, 1H), 1.45 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 218.5, 158.2, 142.0, 136.6, 129.8, 128.7, 127.3, 127.0, 126.8, 114.1, 112.8, 55.2, 51.9, 50.4, 45.1, 40.5, 26.6, 24.8, 18.0; HRMS (EI, M^+) for $C_{21}H_{22}O_2$ calcd 306.1620, found: m/z 306.1621.



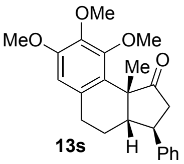
13q

Synthesized according to the previous procedure to afford **13q** (14 mg, yield 55%) as a pale yellow oil: IR (microscope) 3002, 2927, 1733, 1511 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.39-7.34 (m, 2H), 7.30-7.27 (m, 3H), 7.01 (s, 1H), 6.60 (s, 1H), 3.87 (s, 3H), 3.86 (s, 3H), 3.25 (ddd, *J* = 12.8, 12.8, 9.2 Hz, 1H), 3.00-2.91 (m, 1H), 2.76 (dd, *J* = 18.8, 9.2 Hz, 1H), 2.73-2.67 (m, 1H), 2.46 (dd, *J* = 19.2, 12.0 Hz, 1H), 2.34 (ddd, *J* = 12.0, 3.2, 3.2 Hz, 1H), 1.88-1.72 (m, 2H), 1.46 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 218.9, 147.9, 147.7, 142.0, 128.7, 127.4, 127.3, 126.9, 126.6, 111.7, 110.7, 55.9, 55.8, 52.2, 50.3, 45.1, 40.5, 26.5, 24.2, 18.1; HRMS (EI, M^+) for $C_{22}H_{24}O_3$ calcd 336.1726, found: m/z 336.1728.

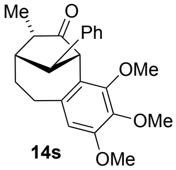


13r

Synthesized according to the previous procedure to afford **13r** (50 mg, yield 65%) as a white solid: mp 168-169 °C; IR (microscope) 3028, 2925, 1735, 1602, 1484 cm^{-1}; ^{1}H NMR (500 MHz, CDCl$_3$) δ 7.38-7.35 (m, 2H), 7.29-7.26 (m, 3H), 7.03 (s, 1H), 6.58 (s, 1H), 3.23 (ddd, *J* = 12.5, 12.5, 9.0 Hz, 1H), 2.94 (ddd, *J* = 18.0, 13.0, 6.5 Hz, 1H), 2.75 (dd, *J* = 18.5, 8.5 Hz, 1H), 2.71-2.67 (m, 1H), 2.45 (dd, *J* = 18.5, 12.0 Hz, 1H), 2.32 (ddd, *J* = 12.0, 3.4 Hz, 1H), 1.85-1.71 (m, 2H), 1.44 (s, 3H); ^{13}C NMR (125 MHz, CDCl$_3$) δ 218.5, 146.5, 146.4, 142.0, 128.8, 128.7, 127.8, 127.3, 126.9, 108.8, 108.1, 52.4, 50.3, 45.0, 40.5, 26.7, 24.8, 18.1; HRMS (EI, M$^+$) for $C_{21}H_{20}O_3$ calcd 320.1412, found: m/z 320.1414.

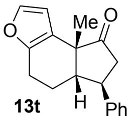


13s



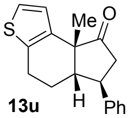
14s

Synthesized according to the previous procedure to afford **13s** (25 g, yield 41%) and **14s** (17 mg, 27%): **13s**: IR (microscope) 3025, 2932, 1739, 1492 cm^{-1}; ^{1}H NMR (500 MHz, CDCl$_3$) δ 7.34-7.31 (m, 2H), 7.25-7.22 (m, 3H), 6.47 (s, 1H), 3.86 (s, 3H), 3.82 (s, 6H), 3.23 (ddd, *J* = 11.2, 11.2, 8.8, 1H), 3.01 (ddd, *J* = 18.4, 11.6, 7.2, 1H), 2.90 (dd, *J* = 18.4, 10.8 Hz, 1H), 2.79 (dd, *J* = 17.6, 5.6 Hz, 1H), 2.30 (dd, *J* = 18.8, 8.4 Hz, 1H), 2.06 (ddd, *J* = 11.2, 3.6, 3.6 Hz, 1H), 1.85-1.82 (m, 1H), 1.75-1.72 (m, 1H), 1.39 (s, 3H); ^{13}C NMR (125 MHz, CDCl$_3$) δ 214.7, 153.1, 152.5, 143.3, 140.5, 131.4, 128.7, 127.5, 126.7, 122.0, 107.8, 60.5, 60.5, 55.8, 52.4, 50.8, 43.7, 39.1, 23.8, 22.2, 17.7; HRMS (EI, M$^+$) for $C_{23}H_{26}O_4$ calcd 366.1831, found: m/z 366.1830.**14s**: IR (microscope) 3016, 2935, 1737, 1494 cm^{-1}; ^{1}H NMR (500 MHz, CDCl$_3$) δ 7.37-7.33 (m, 2H), 7.29-7.22 (m, 3H), 6.47 (s, 1H), 4.46 (br s, 1H), 3.86 (s, 3H), 3.83 (s, 3H), 3.78 (s, 3H), 3.29 (br s, 1H), 2.78-2.70 (m, 3H), 2.58 (ddd, *J* = 16.8, 3.6, 3.6 Hz, 1H), 2.19-2.13 (m, 1H), 2.10-2.02 (m, 1H), 1.18 (d, *J* = 6.4 Hz, 3H); ^{13}C NMR (125 MHz, CDCl$_3$) δ 222.8, 151.3, 151.1, 144.3, 140.4, 134.9, 129.5, 128.5, 126.8, 126.3, 110.3, 61.8, 60.9, 56.0, 54.0, 49.7, 46.7, 45.1, 32.4, 29.9, 8.5; HRMS (EI, M^+) for $C_{23}H_{26}O_4$ calcd 366.1831, found: m/z 366.1828.



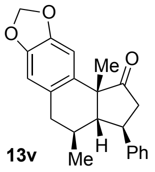
13t

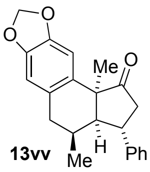
Synthesized according to the previous procedure to afford **13t** (continimated with unidentifiable material, yield <5%): IR (microscope) 3028, 2921, 1739, 1602 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.40-7.33 (m, 6H), 6.39 (d, *J* = 1.8 Hz, 1H), 3.14 (ddd, *J* = 11.7, 11.7, 7.5 Hz, 1H), 2.78-2.66 (m, 3H), 2.49 (dd, *J* = 18.9, 12.0 Hz, 1H), 2.31 (ddd, *J* = 11.4, 3.3, 3.3 Hz, 1H), 1.85-1.81 (m, 2H), 1.39 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 217.8, 149.7, 142.0, 141.3, 128.9, 128.8, 127.3, 127.0, 109.1, 50.5, 49.7, 45.3, 40.7, 23.7, 19.0, 18.9; HRMS (EI, M^+) for $C_{18}H_{18}O_2$ calcd 266.1307, found: m/z 266.1309.



13u

Synthesized according to the previous procedure to afford **13u** (7 mg, yield 60%) as a pale yellow oil: IR (microscope) 3028, 2925, 1737, 1607 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.39-7.36 (m, 2H), 7.30-7.28 (m, 3H), 7.10 (d, *J* = 5.5 Hz, 1H), 7.06 (d, *J* = 5.5 Hz, 1H), 3.21 (ddd, *J* = 12.0, 12.0, 8.0 Hz, 1H), 2.88-2.86 (m, 2H), 2.74 (dd, *J* = 19.0, 8.0 Hz, 1H), 2.49 (dd, *J* = 19.0, 12.5 Hz, 1H), 2.36 (ddd, *J* = 11.5, 3.0, 3.0 Hz, 1H), 1.86-1.83 (m, 2H), 1.44 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 217.9, 142.0, 135.9, 133.7, 128.9, 127.4, 127.0, 126.7, 127.7, 52.2, 50.1, 45.4, 40.7, 25.0, 20.7, 19.3; HRMS (EI, M^+) for $C_{18}H_{18}SO$ calcd 282.1079, found: m/z 282.1080.


13v


13vv

Synthesized according to the previous procedure to afford **13v** and **13vv** (40 mg, ratio ca. 4.5: 1, 69%); Major component **13v** can be obtained in more pure form (**13v**:**13vv** > 20:1) via recrystallization: **13v**: mp 162-163 °C; IR (microscope) 3028, 2965, 1736, 1483 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.38-7.34 (m, 2H), 7.29-7.26 (m, 3H), 7.10 (s, 1H), 6.58 (s, 1H), 5.92-5.90 (m, 2H), 3.10-3.03 (m, 2H), 2.72 (dd, *J* = 18.5, 8.0 Hz, 1H), 2.51 (dd, *J* = 19.0, 12.0 Hz, 1H), 2.46 (dd, *J* = 16.5, 3.5 Hz, 1H), 2.21 (dd, *J* = 11.0, 3.5 Hz, 1H), 2.00-1.98 (m, 1H), 1.53 (s, 3H), 1.01 (d, *J* = 7.5 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 218.7, 146.5, 142.4, 128.8, 128.7, 128.1, 127.6, 127.4, 126.9, 109.4, 107.9, 100.8, 57.3, 51.4, 45.1, 43.5, 33.0, 28.6, 26.7, 21.4; HRMS (EI, M^{+}) for $C_{22}H_{22}O_3$ calcd 334.1569, found: m/z 334.1569; Partial spectral data for **13vv**: ^{1}H NMR (500 MHz, $CDCl_3$) δ 3.33-3.14 (m, 1H), 3.06-3.00 (m, 1H), 2.83 (dd, *J* = 19.0, 9.0 Hz, 1H), 2.34 (dd, *J* = 19.0, 11.0 Hz, 1H), 1.50 (s, 3H), 0.68 (d, *J* = 7.5 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 217.9, 64.1, 47.8, 40.8, 40.1, 39.1, 34.0, 27.5, 26.1, 20.3.

3.6 References

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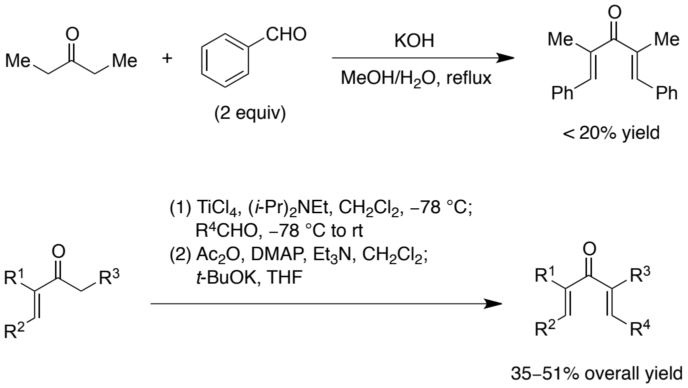
Chapter 4

Construction of α-Amido-Indanones via Formal Allenamide Hydroacylation−Nazarov Cyclization[1]

4.1 Approaches to Prepare Nazarov Precursors, 1,4-Pentadien-3-ones

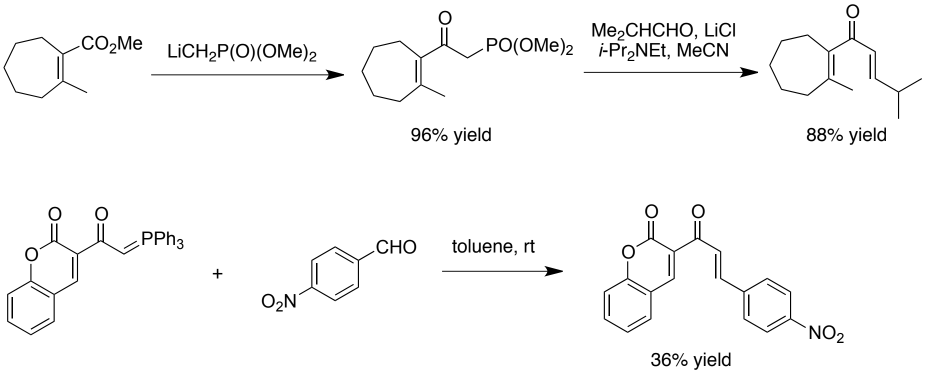
The Nazarov cyclization has become a well-established method for constructing a diverse array of cyclopentanoids, notably since the disclosure of silicon-directed Nazarov reactions by the Denmark group.[2] Upon treatment with Lewis or Brønsted acid, cross-conjugated divinyl ketones can be converted to five-membered carbocycles via a stereospecific electrocyclic ring closure, guided by orbital symmetry.[3] Recent research activity toward expanding the synthetic utility of this process has focused on three main areas: (1) the use of unconventional starting substrates and alternative modes of activation;[4] (2) the development of catalytic and asymmetric variants;[5] and (3) domino or tandem processes triggered by the initial electrocyclization.[6] While advances and innovations in the field of Nazarov chemistry in the past decade are evident,[7] the more fundamental issue regarding the efficiency in terms of step/atom economy[8] for the synthesis of conventional Nazarov precursors, i.e. 1,4-dien-3-ones, remains an underemphasized topic.

Traditionally, the required cross-conjugated dienones have been prepared from simple aliphatic ketones through aldol condensation, however this approach typically requires harsh basic condition or multi-step operation (Scheme 1).[9] In general, the overall sequence, though quite reliable, suffered from low to modest yields. While few modern modifications permitted the reaction being performed under relatively mild conditions, the substrate scopes were still limited.[10]



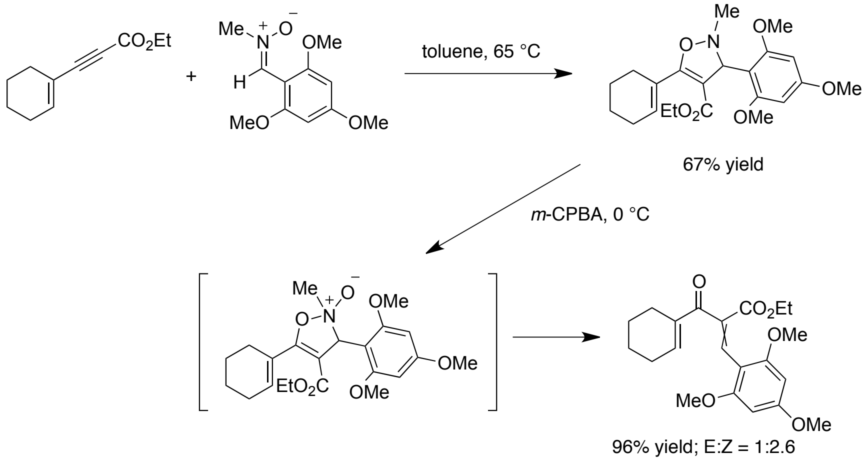
Scheme 1. Dienone Synthesis through Aldol-type Reactions

Horner-Wadsworth-Emmons (HWE) or related Wittig-type olefinations have been employed to install the alkenes conjugated with the ketone (Scheme 2).[11] High control over alkene geometry could often be achieved. However, the stoichiometric production of phosphorus-containing side products is less atom-economical and may cause difficulties in product purification.



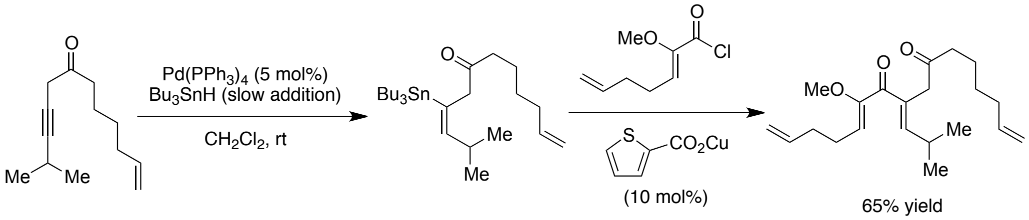
Scheme 2. Dienone Synthesis via HWE[11a] and Wittig[11b] Olefinations

Frontier and co-workers described a two-step sequence for the synthesis of polarized divinyl ketones that entails a [3+2] cycloaddition of electron-deficient alkynes and nitrones followed by an oxidative rearrangement of the corresponding isoxazoline intermediates (Scheme 3).[12] Notably, the olefin geometry of final products is determined in the oxidation/extrusion step. As such, the selectivities of alkene isomers were heavily dependent on the combined steric and electronic effects of substituents, and could range from low to good.



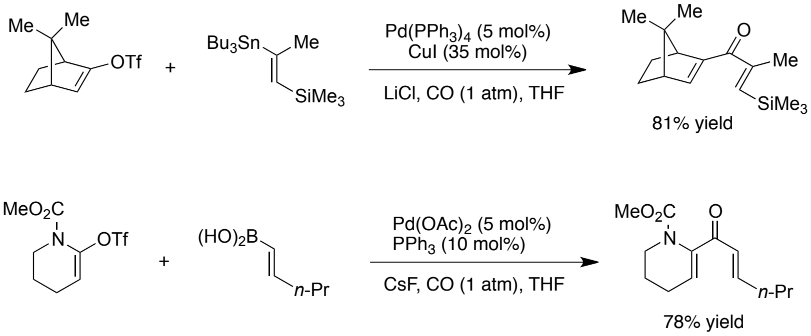
Scheme 3. [3+2]/Oxidation Sequence for the Synthesis of Dienones

Recently, Kerr and Flynn described a concise formal synthesis of (+)-roseophilin where the Nazarov cyclization was central to their strategy.[13] The desired Nazarov precursor was obtained via a reductive coupling sequence in which a vinylstannane intermediate derived from a highly regioselective hydrostannylation of alkyne was subjected to reaction with acyl chloride under catalysis with copper(I) thiophenecarboxylate (CuTC), yielding methoxy-substituted dienone in good yield (Scheme 4).



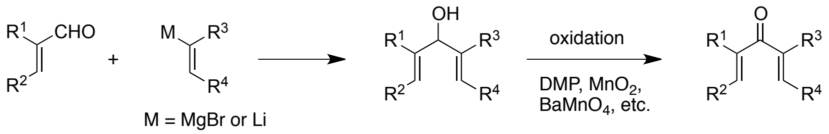
Scheme 4. Reductive Coupling of Alkyne and Acyl chloride

Palladium-catalyzed carbonylative coupling reactions between an array of vinyl donors and supplemental fragments provided a flexible route to cross-conjugated 1,4-dien-3ones with diverse substitution patterns (Scheme 5). West and co-workers found that the inclusion of cocatalytic CuI[14] or CuBr significantly improves the efficiency of the carbonylative Stille coupling between bulky coupling partners, offering access to a series of sterically congested Nazarov substrates.[15] Alternatively, Occhiato and co-workers reported a carbonylative Suzuki-Miyaura coupling reaction of lactam-derived triflates and alkenylboronic acids providing nitrogen-substituted dienones.[16] Although these approaches appeared convenient, the preparation of respective coupling units may be tedious in certain cases.



Scheme 5. Carbonylative Cross-Coupling Reactions

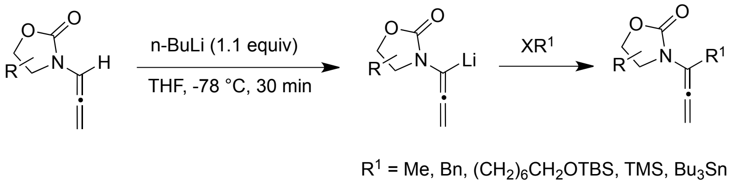
A two-step preparation of divinyl ketones from addition of alkenyl nucleophiles into α,β-unsaturated aldehydes followed by oxidation was also widely employed (Scheme 6).[17] However, the intermediate bis-allylic alcohols can be quite sensitive, which necessitates that the subsequent oxidation be performed under very mild conditions; thus, the conversion can be inefficient.



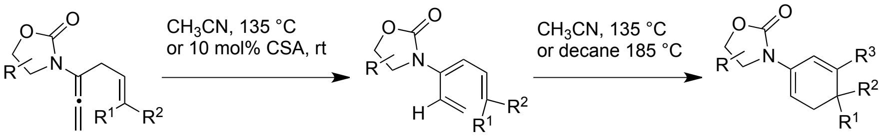
Scheme 6. Nucleophilic Addition/Oxidation Sequence

4.2 Results and Discussions

In 2000, the Hsung group reported α-functionalizations of allenamides with various electrophilic agents including stannyl or silyl chlorides and alkyl halides (Scheme 7).[18] While allyl allenamides could be prepared by the same regioselective deprotonation protocol, Hsung and co-workers demonstrated their use in a tandem isomerization/6π electrocyclization sequence furnishing amido-substituted cyclohexadienes (Scheme 8).[19] The same group has disclosed several new methodologies employing α-substituted allenamides to construct polycyclic carbocycles in a tandem pericyclic reaction sequence.[20]

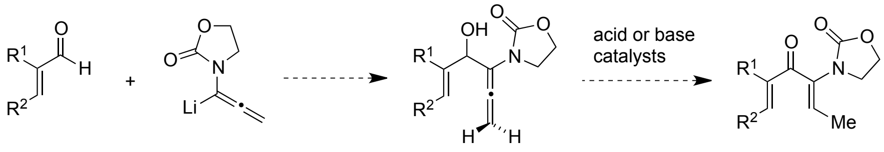


Scheme 7. α-Functionalizations of Allenamides



Scheme 8. Tandem Isomerization/Electrocyclization Sequence

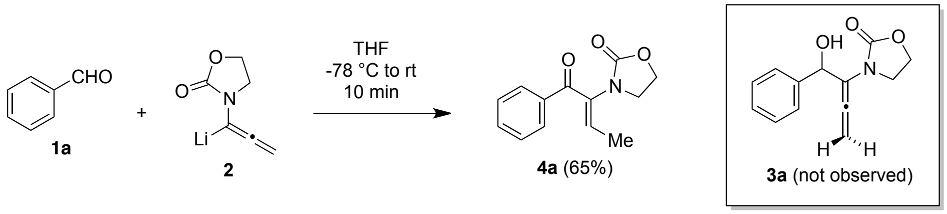
Our continuing interest in the Nazarov reaction prompted us to examine alternative synthetic route to a variety of new Nazarov precursors. Inspired by Hsung's seminal contribution in selective derivatization of allenamides, we envisioned that an unsaturated aldehyde could be used as an electrophilic trap for α-lithiated allenamides, where the resulting allenyl alcohol could be isomerized to the desired 2-amido-1,4-dien-3-one under suitable conditions (Scheme 9).



Scheme 9. Proposed New Approach for Dienone Synthesis

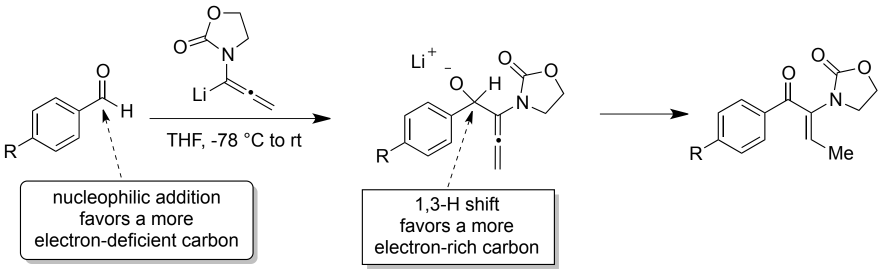
4.2.1. Scope of Formal Allenamide Hydroacylation

We fortuitously discovered that the model reaction between benzaldehyde **1a** and lithiated allenamide **2**[21] produced **4a** in lieu of the expected product **3a** in a one-pot operation (Scheme 10). We set out to examine the scope of this intriguing transformation that constitutes a metal-free formal hydroacylation[22] of the allenamide. In order to gain more insights into this process, we also commenced elucidating its mechanism. Herein, we describe a novel route to α-amidodienones, and the application of the products in the Nazarov reaction.



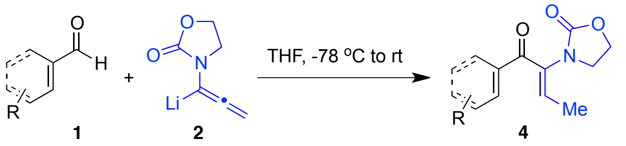
Scheme 10. A One-pot Synthesis of Nazarov Substrates from Aldehydes and Allenamides

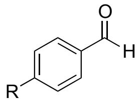
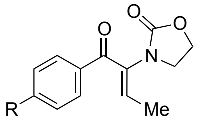
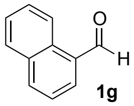
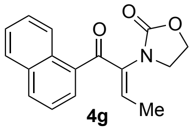
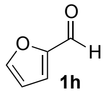
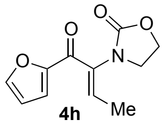
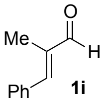
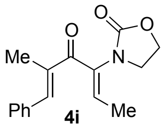
As shown in Table 1 (entries 1–7), α-lithiated allenamide **2** reacted with aromatic aldehydes **1** with distinct *para*-substituents resulting in the formation of aryl vinyl ketones appended with an oxazolidinone group. While the yields were moderate to low, the results clearly showed that strong polarizing groups such as methoxy or carboxylate at the *para* position are baneful to the overall efficiency. As there is no obvious correlation between yields and substituent effects, the electronic factors that favor 1,2-addition and those that favor the subsequent isomerisation may work at cross-purposes (Scheme 11).[23] Additionally, 2-furyl aldehyde **1h** was utilized to trap **2** providing a convenient route to heteroaryl vinyl ketone (entry 8). Furthermore, the reaction could be extended to the use of simple unsaturated aldehyde **1i** yielding the corresponding divinyl ketone **4i** in moderate yield (entry 9). Notably, a single alkene isomer was isolated in all examples, where the geometry of conjugated olefin was suggested by the TROESY correlations between vinyl and aryl protons.



Scheme 11. Potential Effects of Electronic Factors

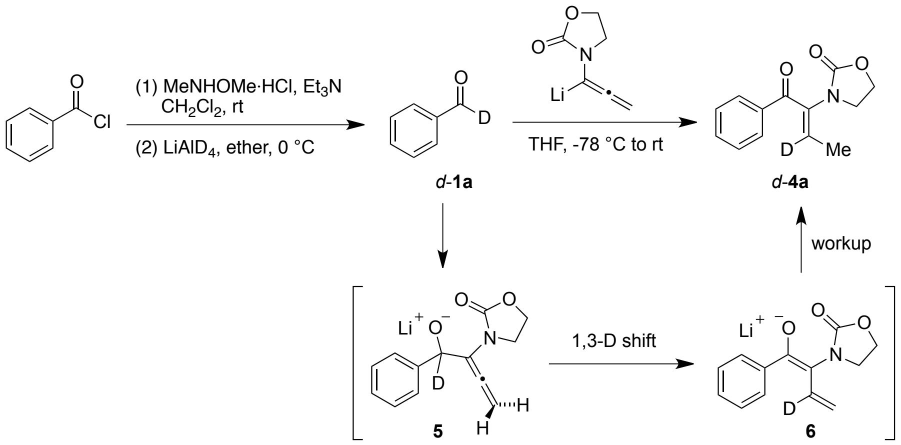
Table 1. The Overall Hydroacylation of Allenamides **2**[a]



Entry	Aldehyde	Product	Yield (%)[b]
			
1	R = H, **1a**	R = H, **4a**	65
2	R = Me, **1b**	R = Me, **4b**	44
3	R = OMe, **1c**	R = OMe, **4c**	18
4	R = SMe, **1d**	R = SMe, **4d**	52
5	R = Cl, **1e**	R = Cl, **4e**	46
6	R = CO_2Me, **1f**	R = CO_2Me, **4f**	14
7	 **1g**	 **4g**	52
8	 **1h**	 **4h**	33
9	 **1i**	 **4i**	35

[a]Standard procedure: To a homogeneous solution of allenamide **2** (0.5 mmol) in anhydrous THF under argon atmosphere, 1.2 equiv *n*-BuLi was added dropwise at -78 °C. After 45 min, freshly distilled aldehyde **1** (1.1 equiv) in THF was added at −78 °C then the the reaction mixture was allowed to warm to rt. The reaction was quenched with sat. aq NH_4Cl, followed by extraction, drying ($MgSO_4$), and chromatographic purification. [b]Isolated yields based on allenamides.

While the substrate scope has been briefly studied, we embarked on an investigation of the reaction mechanism. Deuterated benzaldehyde *d*-**1a** was synthesized and treated with lithiated allenamide **2** to furnish *d*-**4a** as the only identifiable product where the deuterium was selectively incorporated at the sp^2 carbon β to the carbonyl (Scheme 12). This finding strongly supports the hypothesis that a concerted 1,3-deuteride shift is the operating pathway for the generation of *d*-**4a** from allenyl alkoxide **5**, rather than proton shuffling mediated by external acid or base.



Scheme 12. A Deuterium Labeling Experiment

Given that the transition state of 1,3-H shift involves 4n (n = 1) electrons, a thermally allowed 1,3-hydrogen shift for a purely allylic system has to involve an antarafacial transfer (or a Möbius topological transition state) based upon Möbius-Hückel analysis;[24] however, such a process invokes an extremely strained transition state, and therefore it is deemed geometrically impossible (Figure 1).[25] On the other hand, the 1,3-H shift for an allenylic system is relatively more feasible owing to the unique structural feature of the allene group, wherein the orthogonally oriented p-orbital at the central allene carbon is spatially more accessible to participate in the 1,3-shift, and meanwhile the required counts of phase inversion for the Möbius topology is still obeyed.

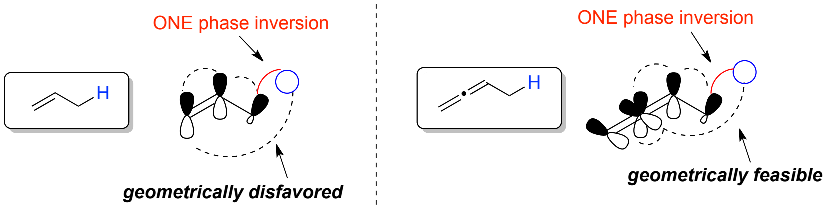
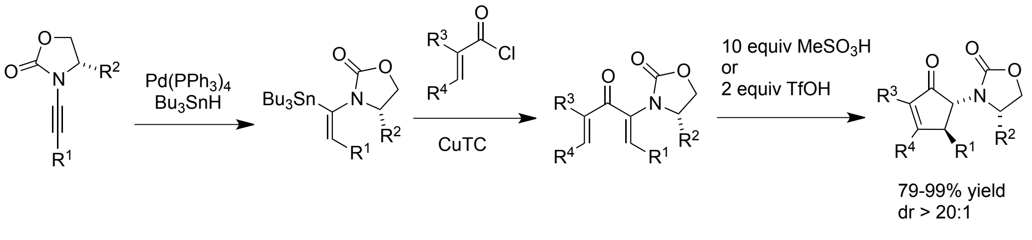


Figure 1. Möbius Orbital Arrays for Four-electron ($2\pi + 2\sigma$) Sigmatropic Shift

Nevertheless, the calculated activation energy of 1,3-H shift in the allenylic system remains high (around 77 kcal/mol).[26] Indeed, as noted previously by Hsung, the isomerization of simple α-allylated allenamides giving triene products did not occur spontaneously and required additional reaction parameters, either heat or acid (Scheme 8).[27] In our system, the facile 1,3-D shift (**5→6**) was presumably facilitated by alkoxide substitution, i.e. an anion-assisted sigmatropic rearrangement.[28] We are aware of ample precedents for the allenylation of unsaturated aldehydes with terminally substituted propargyl-metallic reagents.[29] However, to the best of our knowledge, those reactions effectively provided allenic alcohols with no evidence of the corresponding isomerizations. From this comparison, we infer that the oxazolidinone group functions a promoter for the 1,3-deuteride shift.

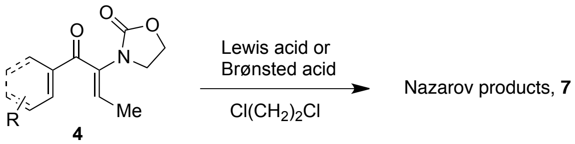
4.2.2. Nazarov Cyclizations of 2-Amido-1,4-dien-3-ones

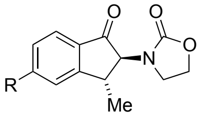
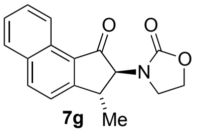
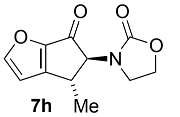
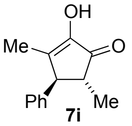
Very recently, Flynn and co-workers described an elegant study on diasteroselective Nazarov cyclization employing Evans' oxazolidinone as a chiral auxiliary, where the Nazarov precursors were prepared via a two-step reductive coupling protocol (Scheme 13).[30] In their work, superstoichiometric Brønsted acid was used as the Lewis acid promoter for the cyclization. More importantly, the authors demonstrated that oxazolidinone-based auxiliary could offer excellent control over the torquoselectivity of the electrocyclization process.



Scheme 13. Flynn's Diastereoselective Nazarov Cyclization

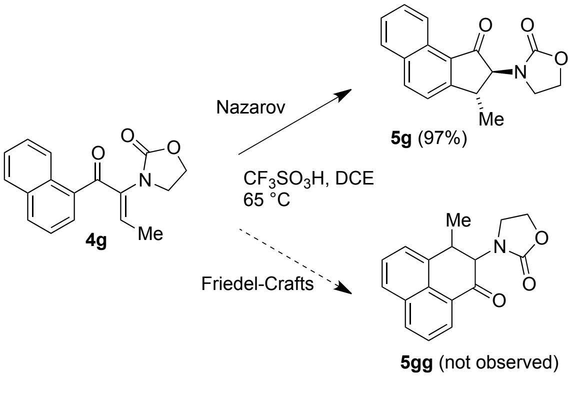
Table 2. Nazarov Cyclization of **4**[a]



Entry	Dienone	Acid (equiv)/T (°C)	Nazarov products	Yield (%)[b] (ratio)[c]
				
1	**4a**	$FeCl_3$ (0.2)/80	R = H, **7a**	NR[d]
2	**4a**	$Sc(OTf)_3$ (0.2)/80	R = H, **7a**	Trace
3	**4a**	$Eu(OTf)_3$ (0.2)/80	R = H, **7a**	NR[d]
4	**4a**	$In(OTf)_3$ (0.2)/80	R = H, **7a**	65 (20:1)
5	**4a**	CF_3SO_3H (5)/65	R = H, **7a**	98 (20:1)
6	**4b**	CF_3SO_3H (5)/65	R = Me, **7b**	87 (20:1)
7	**4c**	CF_3SO_3H (5)/65	R = OMe, **7c**	88 (4:1)
8	**4d**	CF_3SO_3H (5)/65	R = SMe, **7d**	97 (20:1)
9	**4e**	CF_3SO_3H (5)/65	R = Cl, **7e**	94 (20:1)
10	**4f**	CF_3SO_3H (5)/65	R = CO_2Me, **7f**	91 (20:1)
11	**4g**	$In(OTf)_3$ (0.2)/80	 **7g**	76 (20:1)
12	**4g**	CF_3SO_3H (5)/65		97 (20:1)
13	**4h**	$In(OTf)_3$ (0.2)/80	 **7h**	NR[d]
14	**4h**	CF_3SO_3H (5)/65		65 (3:1)
15	**4i**	$Sc(OTf)_3$ (0.2)/80	 **7i**	96
16	**4i**	BF_3OEt_2 (1.1)/−78		81

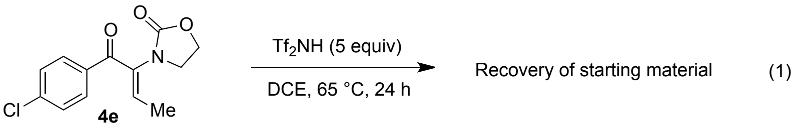
[a] Standard procedure: To a stirred solution of **4** in DCE at the indicated temperature, acid was added. Once the starting material was consumed (based on TLC), the reaction was quenched with sat. aq $NaHCO_3$, followed by extraction, drying ($MgSO_4$) and chromatographic purification. [b] Isolated yields. [C] *Cis*/*trans* isomers were inseparable and the ratios were determined by intergration of ^1H NMR signals (β-methyl groups). [d] NR = No reaction.

We anticipated that the α-amido group would favorably polarize the pentadienyl system thus lowering the activation barriers of the electrocyclic ring closure.[31] With oxazolidinone-substituted cross-conjugated ketones in hand, we sought to explore the Nazarov reactivity of **4** and attempted to identify optimal *catalytic* conditions for triggering their cyclization (Table 2). In the event, a catalyst screening with **4a** showed that only indium(III) triflate was an effective catalytic promoter (DCE, 80 °C), providing cyclized product **7a** in 65% yield. Given a recent observation that $Sc(OTf)_3$ shows superior reactivity in catalyzing the Nazarov cyclization of heteroaromatic substrates,[32] the failure of using $Sc(OTf)_3$ in our system marked the challenge of Nazarov reaction of aromatic substrates.[33] Subsequently, we turned our attention to use commercially available superacids as catalysts. The cyclization of **4a** using substoichiometric amount of triflic acid gave partial conversion of the starting material. After considerable modification, the optimized reaction condition was determined entailing excess TfOH with mild heating (Table 2, entry 5). For *para*-substituted aryl vinyl ketones, $In(OTf)_3$ displayed little to no reactivity, demonstrating that subtle electronic changes exert a large effect on catalysis of the Nazarov reaction. Nevertheless, **4b**-**4f** did undergo efficient cyclization in the presence of triflic acid, with negligible effects of substitution (entries 6–10). Naphthyl substrate **4g** could potentially undergo a competing Friedel-Crafts type cyclization to furnish the phenalan skeleton (Scheme 14);[34] however, exclusive reaction via the Nazarov pathway was observed, using either TfOH or $In(OTf)_3$ (entries 11 and 12).



Scheme 14. Cyclization of **4g**

2-Furyl vinyl ketones have long been considered as unreactive substrates for the Nazarov reaction.[35] However, the cyclization of **4h** proceeded smoothly with triflic acid, though not with indium(III) triflate (entry 13 vs 14). This result is consistent with the report of Flynn's laboratories,[26] wherein the authors attributed cyclization of conventionally inert substrates to the potent activation exerted from the oxazolidinone substitution. However, we found that Nazarov reactions of aryl and 2-furyl ketones **4a–h** are quite sensitive to acid strength; for instance, triflimide (Tf_2NH) failed to mediate the cyclization of **4e** (Eq 1).



Apparently, the oxazolidinone auxiliary is not the sole factor for the success. We propose that the superacid (TfOH) may play an equally critical role, which provokes formation of highly reactive dicationic intermediate **8** or protosolvated species **9** allowing effective electrocyclizations (Figure 2).[36]

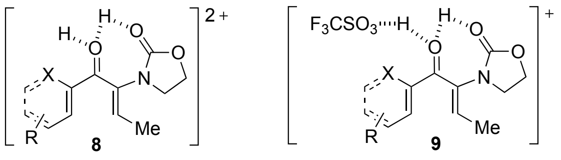
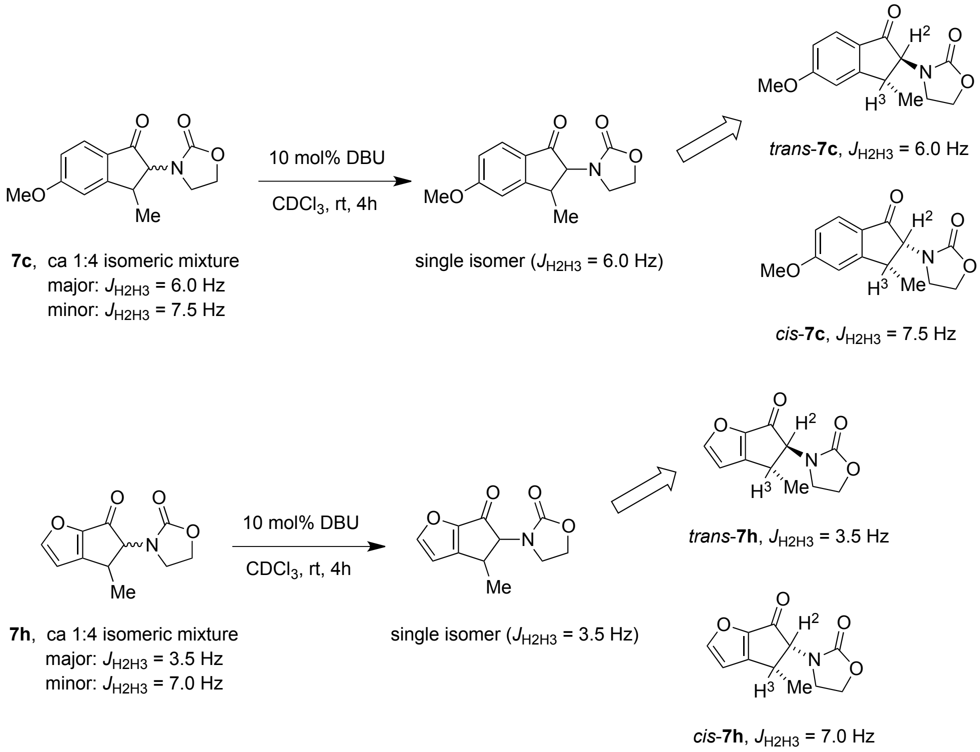


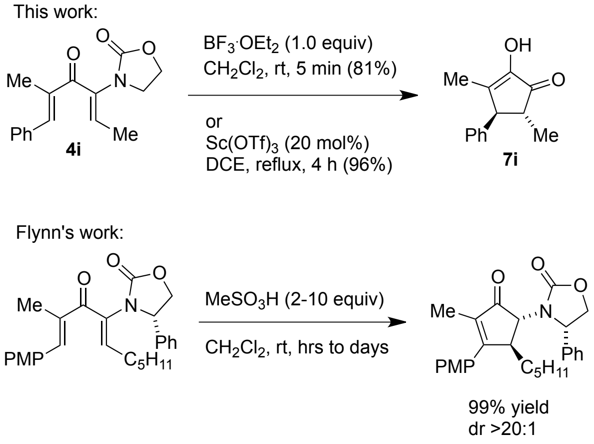
Figure 2. Proposed Superelectrophilic Intermediates

The *trans* isomers of 2,3-substituted-1-indanone were considered to be thermodynamically favored over their *cis* counterparts. In the case of **7c** obtained as isomeric products (ratio ca 1:4), the coupling constant (J) between H2 and H3 for the major isomer is 6.0 Hz and for the minor isomer is 7.5 Hz. That mixture was subjected to 10 mol% DBU in $CDCl_3$ (0.01M to **7c**) at room temperature, where the epimerization was envisioned to be guided by the thermodynamic control (Scheme 15). After 4 h, the minor isomer could no longer be detected by ^1H NMR spectroscopy; thus, it was assigned as *cis*-**7c** and the predominant isomer as *trans*–**7c**. With that, we presumed that J_{H2H3} for *trans* isomers of closely resembled indanones would be similar to the value of 6.0 Hz. Based on the evaluation of J_{H2H3}, **7a**, **7b**, **7d**-**g** were assigned as *trans*. A similar approach was then applied to the stereochemical assignment for heteroaromatic substrate **7h** isolated as a ca 1:3 isomeric mixture, and the *trans* isomer could be readily assigned, whose J_{H2H3} equals 3.5 Hz.



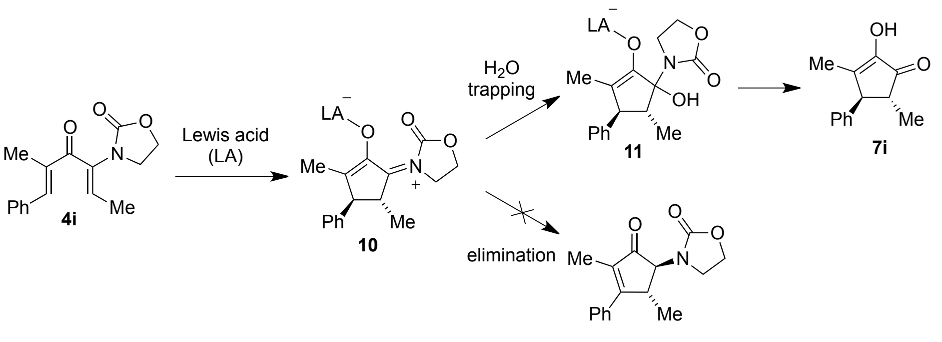
Scheme 15. Stereochemical Assignment of *cis*- and *trans*-Isomers

Finally, we found that Lewis acid-catalyzed cyclization of non-aromatic substrate **4i** deviated from the typical eliminative termination, furnishing α-hydroxy cyclopentenone **7i** (entries 14 and 15), in contrast to the reactivity observed by the Flynn group in related cases (Scheme 16).[26]



Scheme 16. Distinct Reaction Pathways in Flynn's and Our System

Other research groups have observed similar hydrolytic Nazarov reactions of 2-oxygenated 1,4-pentadien-3-ones.[37] A proposed mechanism for the formation of **7i** is shown in Scheme 17. While the reaction was not terminated by loss of a proton in analogy to the cases seen with aryl ketone substrates (Table 2), cyclized eniminium ion **10** was intercepted by water followed by elimination of the oxazolidinone group to give 2-hydroxyenone **7i**. While it is difficult to rationalize the contradictory reaction mode seen in Flynn's example versus ours, we envisioned that, for steric consideration, the additional phenyl group on oxazolidinone moiety might prevent addition of water at the iminium carbon thus favoring simple elimination.



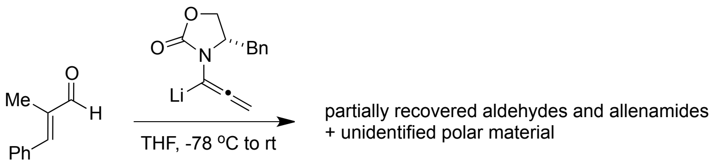
Scheme 17. Mechanism of the Hydrolytic Nazarov Reaction

4.3 Conclusion

We have described a step-economic approach to oxazolidinone-substituted Nazarov precursors through coupling of simple unsaturated aldehydes and a lithiated allenamide. Formally, oxy functionality generated *in situ* was oxidized to ketone by the internal allene moiety. A deuterium-labelling study shed light on the reaction mechanism that appears to entail carbonyl addition/1,3-sigmatropic rearrangement in tandem. As for the Nazarov reaction, triflic acid was found to be an effective promoter for the aromatic or heteroaromatic substrates. Alternatively, the cyclization of divinyl ketone proceeded under a catalytic condition where the oxazolidinone served as a traceless activating group.

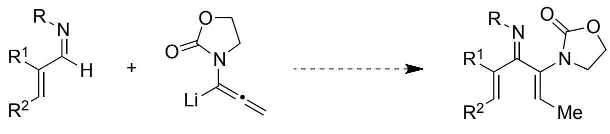
4.4 Future Directions

An expanded study of varying substituents on amino allenes must be pursued in order to establish a more general approach for the purpose of dienone synthesis. Preliminary studies of utilizing chiral oxazolidinone-substituted allene were not fruitful, in which the desired dienone products were not formed for reasons not clear to us (Scheme 18). However, we envisioned that use of the allenes appended with other chrial amide-derived auxilary might offer better reaction profiles. In addition, the effect of additives, known to enhance the reactivity of lithium reagents, has to be examined.

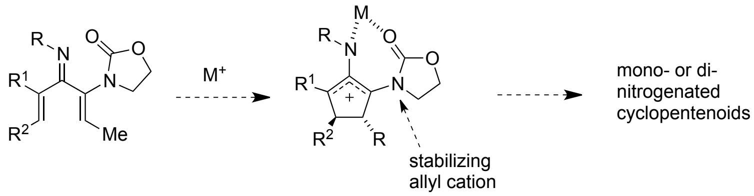


Scheme 18. Attempted Preparation of Chiral Dienone Substrates

It may be feasible to use conjugated imines as alternative trapping agents for the lithiated allenamide (Eq 2). Through this route, a novel structure type, amido-substituted divinyl imine, can be obtained in analogy to the work described in this chapter. It would then allow further investigations into the imino-Nazarov cyclization, a relatively underexplored field of Nazarov chemistry, wherein the oxazolidinone substituent strategically offers an additional stabilization to the cyclized cationic intermediate (Scheme 19); various termination events are possible furnishing cyclic products appended with aza-functional groups.



(2)



stabilizing allyl cation

mono- or di-nitrogenated cyclopentenoids

Scheme 19. Potential Imino-Nazarov Cyclization

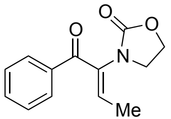
4.5 Experimental

General Information. Reactions were carried out in flame-dried glassware under a positive argon atmosphere unless otherwise stated. Transfer of anhydrous solvents and reagents was accomplished with oven-dried syringes. Solvents were distilled before use: methylene chloride and 1,2-dichloroethane from calcium hydride, tetrahydrofuran from sodium/benzophenone ketyl. All other solvents and commercially available reagents were either purified by standard procedures or used without further purification. Thin layer chromatography was performed on glass plates precoated with 0.25 mm silica gel; the stains for TLC analysis were conducted with 2.5 % *p*-anisaldehyde in AcOH-H_2SO_4-EtOH (1:3:85) and further heating until development of color. Flash chromatography was performed on 230-400 mesh silica gel with the indicated eluents. Nuclear magnetic resonance (NMR) spectra were recorded in indicated deuterated solvents and are reported in ppm in the presence of TMS as internal standard and coupling constants (*J*) are reported in Hertz (Hz). Infrared (IR) spectra were recorded neat and reported in cm^{-1}. Mass spectra were recorded by using EI or ESI as specified in each case.

Standard Procedure for the Synthesis of 4:

To a flame-dried round bottom flask containing a magnetic stirring bar was added allenamide **1** (0.5 mmol) and anhydrous THF (6 mL) under Ar. The temperature of the solution was reduced to -78 °C (acetone/dry ice bath). *n*-BuLi (1.2 equiv, 2.27 M in hexane, 0.26 mL) was added dropwise using 1 mL syringe. After stirring for 45 min, a solution of aldehydes **2** (1.1 equiv, 0.55 mmol) was added. The reaction mixture was stirred at -78 °C for 5 min, then allowed to warm to rt for 10 min. The reaction was quenched with sat. aq NH_4Cl solution. The organic layer was separated and the aqueous layer was extracted with Et_2O (3 x 20 mL). The combined organic layer was washed with brine (1 x 20 mL), dried over anhydrous $MgSO_4$, and then filtered through a pad of cellite. The solvent was removed under reduced pressure and the residue was purified on a silica gel column to afford the desired product.

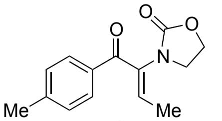
Characterization Data for 4a-i and *d*-4a:



4a

(Z)-3-(1-Oxo-1-phenylbut-2-en-2-yl) oxazolidin-2-one (4a)

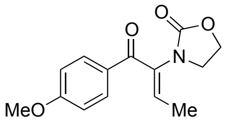
Following the representative procedure, flash chromatography (hexane/EtOAc = 1/1) gave **4a** in 65% yield as a colorless oil: IR (film) 3062, 2960, 2916, 1756, 1654, 1598, 1413, 1247 cm^{-}1; ^{1}H NMR (400 MHz, CDCl$_3$) δ 7.74-7.71 (m, 2H), 7.58-7.53 (m, 1H), 7.47-7.27 (m, 2H), 6.63 (q, *J* = 6.8 Hz, 1H), 4.52-4.48 (m, 2H), 3.86-3.82 (m, 2H), 1.96 (d, *J* = 6.8 Hz, 3H); ^{13}C NMR (100 MHz, CDCl$_3$) δ 192.0, 156.6, 142.0, 137.0, 135.6, 132.0, 128.8, 128.0, 62.5, 45.5, 14.1; HRMS (EI, M$^+$) Calcd for $C_{13}H_{13}NO_3$ 231.0895; found m/z 231.0889.



4b

(Z)-3-(1-Oxo-1-(p-tolyl)but-2-en-2-yl) oxazolidin-2-one (4b)

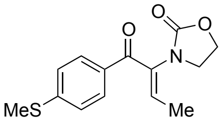
Following the representative procedure, flash chromatography (hexane/EtOAc = 1/1) gave **4b** in 44% yield as a colorless oil: IR (film) 2959, 2921, 2852, 1755, 1653, 1606, 1412, 1246 cm^{-1}; ^{1}H NMR (400 MHz, CDCl$_3$) δ 7.65-7.63 (m, 2H), 7.27-7.23 (m, 2H), 6.60 (q, *J* = 7.2 Hz, 1H), 4.50-4.46 (m, 2H), 3.84-3.80 (m, 2H), 2.41 (s, 3H), 1.95 (d, *J* = 6.8 Hz, 3H); ^{13}C NMR (100 MHz, CDCl$_3$) δ 191.7, 156.5, 142.8, 141.1, 135.5, 134.3, 129.1, 128.7, 62.4, 45.5, 21.2, 14.0; HRMS (EI, M$^+$) Calcd for $C_{14}H_{15}NO_3$ 245.1052; found m/z 245.1050.



4c

(Z)-3-(1-(4-Methoxyphenyl)-1-oxobut-2-en-2-yl) oxazolidin-2-one (4c)

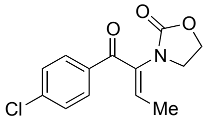
Following the representative procedure, flash chromatography (hexane/EtOAc = 1/1) gave **4c** in 18% yield as a pale yellow oil: IR (film) 2915, 2842, 1755, 1648, 1600, 1510, 1414, 1252 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.78-7.74 (m, 2H), 6.95-6.92 (m, 2H), 6.55 (q, *J* = 6.8 Hz, 1H), 4.50-4.46 (m, 2H), 3.87 (s, 3H), 3.84-3.80 (m, 2H), 1.95 (d, *J* = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 190.7, 162.9, 156.5, 139.7, 135.4, 131.3, 129.4, 113.3, 62.4, 55.1, 45.6, 13.9; HRMS (EI, M$^+$) Calcd for $C_{14}H_{15}NO_4$ 261.1001; found m/z 261.0999.



4d

(Z)-3-(1-(4-(Methylthio) phenyl)-1-oxobut-2-en-2-yl) oxazolidin-2-one (4d)

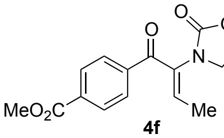
Following the representative procedure, flash chromatography (hexane/EtOAc = 1/1) gave **4d** in 52% yield as a pale yellow oil: IR (film) 2958, 2920, 2850, 1753, 1649, 1589, 1411, 1246 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.71-7.69 (m, 2H), 7.30-7.27 (m, 2H), 6.61 (q, *J* = 7.0 Hz, 1H), 4.53-4.50 (m, 2H), 3.87-3.83 (m, 2H), 2.55 (s, 3H), 1.98 (d, *J* = 7.0 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 191.4, 156.9, 145.4, 141.0, 135.8, 133.4, 129.9, 125.0, 62.8, 46.0, 14.9, 14.4; HRMS (EI, M$^+$) Calcd for $C_{14}H_{15}NO_3S$ 277.0773; found m/z 277.0772.



4e

(Z)-3-(1-(4-Chlorophenyl)-1-oxobut-2-en-2-yl) oxazolidin-2-one (4e)

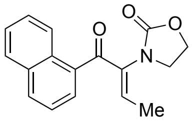
Following the representative procedure, flash chromatography (hexane/EtOAc = 1/1) gave **4e** in 46% yield as a colorless oil: IR (film) 3068, 2960, 2917, 1755, 1657, 1588, 1413, 1247 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.71-7.70 (m, 2H), 7.47-7.44 (m, 2H), 6.61 (q, *J* = 7.0 Hz, 1H), 4.54-4.51 (m, 2H), 3.87-3.84 (m, 2H), 1.99 (d, *J* = 7.0 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 191.3, 157.0, 142.2, 138.9, 135.9, 135.7, 130.7, 128.8, 62.9, 46.0, 14.5; HRMS (EI, M$^+$) Calcd for $C_{13}H_{12}ClNO_3$ 265.0506; found m/z 265.0504.



4f

(Z)-Methyl 4-(2-(2-oxooxazolidin-3-yl) but-2-enoyl) benzoate (4f)

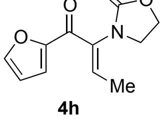
Following the representative procedure, flash chromatography (hexane/EtOAc = 1/1) gave **4f** in 46% yield as a colorless oil: IR (film) 2954, 2916, 1755, 1724, 1659, 1610, 1408, 1281 cm^{-1}; ^{1}H NMR (500 MHz, CDCl$_3$) δ 8.15-8.13 (m, 2H), 7.80-7.77 (m, 2H), 6.65 (q, *J* = 7.0 Hz, 1H), 4.56-4.53 (m, 2H), 3.98 (s, 3H), 3.90-3.87 (m, 2H), 2.00 (d, *J* = 7.0 Hz, 3H); ^{13}C NMR (125 MHz, CDCl$_3$) δ 191.9, 166.2, 156.9, 143.6, 141.2, 136.1, 133.3, 129.6, 129.1, 62.9, 52.5, 45.9, 14.6; HRMS (EI, M$^+$) Calcd for $C_{15}H_{15}NO_5$ 289.0950; found m/z 289.0949.



4g

(Z)-3-(1-(Naphthalen-2-yl)-1-oxobut-2-en-2-yl) oxazolidin-2-one (4g)

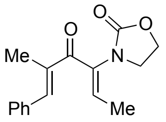
Following the representative procedure, flash chromatography (hexane/EtOAc = 1/1) gave **4g** in 52% yield as a colorless oil: IR (film) 3053, 2960, 2915, 1755, 1662, 1591, 1414, 1246 cm^{-1}; ^{1}H NMR (500 MHz, CDCl$_3$) δ 8.12-8.01 (m, 1H), 7.98 (d, *J* = 8.5 Hz, 1H), 7.91-7.89 (m, 1H), 7.63-7.61 (m, 1H), 7.56-7.54 (m, 2H), 7.52-7.50 (m, 1H), 6.64 (q, *J* = 7.0 Hz, 1H), 4.58-4.55 (m, 2H), 3.98-3.95 (m, 2H), 1.93 (d, *J* = 7.5 Hz, 3H); ^{13}C NMR (125 MHz, CDCl$_3$) δ 194.0, 157.2, 145.5, 138.1, 135.6, 133.6, 131.2, 130.7, 128.4, 127.4, 127.0, 126.6, 125.4, 124.3, 63.0, 46.1, 14.6; HRMS (EI, M$^+$) Calcd for $C_{17}H_{15}NO_3$ 281.1052; found m/z 281.1050.



4h

(Z)-3-(1-(Furan-2-yl)-1-oxobut-2-en-2-yl) oxazolidin-2-one (4h)

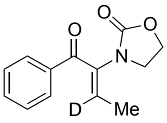
Following the representative procedure, flash chromatography (hexane/EtOAc = 1/1) gave **4h** in 33% yield as a yellow oil: IR (film) 2920, 1754, 1644, 1564, 1466, 1414, 1252 cm^{-1}; ^{1}H NMR (500 MHz, CDCl$_3$) 7.65-7.64 (m, 1H), 7.27-7.26 (m, 1H), 7.12 (q, J = 7.0 Hz, 1H), 6.58-6.57 (m, 1H), 4.54-4.50 (m, 2H), 3.85-3.82 (m, 2H), 2.00 (d, J = 7.5 Hz, 3H); ^{13}C NMR (125 MHz, CDCl$_3$) δ 177.4, 157.0, 151.7, 146.9, 140.9, 135.0, 119.9, 112.3, 62.8, 46.0, 14.5; HRMS (EI, M$^+$) Calcd for $C_{11}H_{11}NO_4$ 221.0688; found m/z 221.0688.



4i

3-((2Z, 5E)-5-Methyl-4-oxo-6-phenylhexa-2, 5-dien-3-yl) oxazolidin-2-one (4i)

Following the representative procedure, flash chromatography (hexane/EtOAc = 1/1) gave **4i** in 35% yield as a colorless oil: IR (neat) 3056, 2985, 2917, 1757, 1642, 1575, 1411, 1243 cm^{-1}; ^{1}H NMR (500 MHz, CDCl$_3$) δ 7.46-7.42 (m, 4H), 7.38-7.36 (m, 1H), 7.29 (s, 1H), 6.67 (q, J = 7.0 Hz, 1H), 4.54-4.50 (m, 2H), 3.87-3.84 (m, 2H), 2.18 (br s, 3H), 1.97 (d, J = 7.0 Hz, 3H); ^{13}C NMR (125 MHz, CDCl$_3$) δ 194.8, 157.1, 139.9, 139.4, 136.2, 135.7, 135.5, 129.7, 128.6, 128.5, 62.9, 46.1, 14.6, 14.3; HRMS (EI, M$^+$) Calcd for $C_{16}H_{17}NO_3$ 271.1209; found m/z 271.1205.



d-**4a**

Deuterated 4a

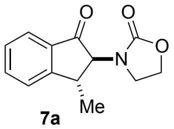
Following the representative procedure, flash chromatography (hexane/EtOAc = 1/1) gave *d*-**4a** in 44% yield as colorless oil: IR (film) 3060, 2958, 2924, 2854, 1756, 1656, 1598, 1411, 1250 cm^{-1}; ^{1}H NMR (500 MHz, CDCl$_3$) δ 7.74-7.70 (m, 2H), 7.58-7.53 (m, 1H), 7.47-7.42 (m, 2H), 4.52-4.48 (m, 2H), 3.86-3.83 (m, 2H), 1.96 (s, 3H); ^{13}C NMR (125 MHz, CDCl$_3$) δ 192.4, 156.9, 142.1 (t, J_{CD} = 23.9

Hz), 137.5, 135.9, 132.4, 129.3, 128.4, 62.8, 45.9, 14.4; HRMS (ESI, $[M+Na]^+$) Calcd for $C_{13}H_{12}DNNaO_3$ 255.0850; found m/z 255.0848.

Standard Procedure for the Synthesis of 7:

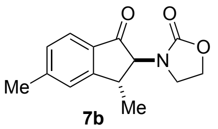
To a stirred solution of **4** (0.1 mmole) in 1,2-dichloroethane (10 mL) at the indicated temperature was added Lewis or Brønsted acid (reagent and equivalent specified below) under argon atmosphere. After starting material was completely consumed as monitored by TLC, the reaction was quenched with sat. aq $NaHCO_3$ (5 mL). The organic layer was separated and the aqueous layer was extracted with dichloromethane (2 x 5 mL). The combined organic layer was washed with brine, dried over anhydrous $MgSO_4$, and then filtered through a pad of cellite. The solvent was removed under reduced pressure and the residue was purified on a silica gel column to afford the desired product.

Characterization Data for 7a-i



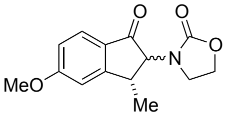
7a

Following the representative procedure using 5 equiv triflic acid at 65 °C (oil bath), flash chromatography (hexane/EtOAc = 1/1) gave **7a** in 98% yield (*cis*:*trans* >20:1): IR (film) 2963, 2924, 1748, 1722, 1607, 1429, 1261, 1207 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.81-7.79 (m, 1H), 7.75-7.71 (m, 1H), 7.57-7.55 (m, 1H), 7.49-7.46 (m, 1H), 4.50 (ddd, *J* = 8.5, 8.5, 7.0 Hz, 1H), 4.45 (ddd, *J* = 9.0, 9.0, 7.0 Hz, 1H), 4.42 (d, *J* = 6.5 Hz, 1H), 3.67 (ddd, *J* = 9.0, 8.0, 7.0 Hz, 1H), 3.52 (ddd, *J* = 9.0, 8.0, 7.0 Hz, 1H), 3.36 (app. quintet, *J* = 6.5 Hz, 1H), 1.64 (d, *J* = 6.5 Hz, 3H)); ^{13}C NMR (125 MHz, $CDCl_3$) δ 199.9, 158.9, 154.8, 135.9, 134.3, 128.2, 124.9, 124.0, 67.0, 62.3, 41.9, 36.6, 17.7; HRMS (EI, M^+) Calcd for $C_{13}H_{13}NO_3$ 231.0895; found m/z 231.0900.



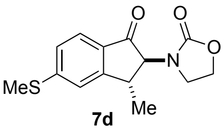
7b

Following the representative procedure using 5 equiv triflic acid at 65 °C (oil bath), flash chromatography (hexane/EtOAc = 1/1) gave **7b** in 87% yield (*cis*:*trans* >20:1); IR (film) 3018, 2966, 2919, 1749, 1719, 1611, 1430, 1263, 1216 cm^{-1}; ^{1}H NMR (500 MHz, CDCl$_3$) δ 7.66 (d, *J* = 8.5 Hz, 1H), 7.31 (br s, 1H), 7.24 (d, *J* = 8.5 Hz, 1H), 4.48-4.39 (m, 2H), 4.37 (d, *J* = 6.0 Hz, 1H), 3.62 (ddd, *J* = 9.5, 8.0, 7.0 Hz, 1H), 3.46 (ddd, *J* = 9.5, 8.0, 7.0 Hz, 1H), 3.26 (app. quintet, *J* = 6.5 Hz, 1H), 2.47 (s, 3H), 1.58 (d, *J* = 6.5 Hz, 3H);); ^{13}C NMR (125 MHz, CDCl$_3$) δ 199.3, 159.0, 155.3, 147.4, 132.0, 129.4, 125.3, 123.8, 67.0, 62.3, 41.8, 36.5, 22.3, 17.6; HRMS (ESI, [M+Na]$^+$) Calcd for $C_{14}H_{15}NNaO_3$ 268.0944; found m/z 268.0941.



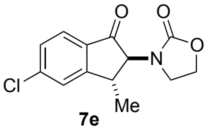
7c, *cis*:*trans* 1:4

Following the representative procedure using 5 equiv triflic acid at 65 °C (oil bath), flash chromatography (hexane/EtOAc = 1/1) gave **7c** in 88% yield (*cis*:*trans* 1:4, inseparable mixture): IR (film) 3019, 2969, 2917, 1750, 1713, 1601, 1429, 1263, 1217 cm^{-1}; trans isomer: ^{1}H NMR (500 MHz, CDCl$_3$) δ 7.70 (d, *J* = 8.5 Hz, 1H), 6.94 (dd, *J* = 8.5, 2.0 Hz, 1H), 6.92 (br s, 1H), 4.48-4.37 (m, 2H), 4.36 (d, *J* = 6.0 Hz, 1H), 3.91 (s, 3H), 3.64-3.59 (m, 1H), 3.48-3.43 (m, 1H), 3.25 (app. quintet, *J* = 7.0 Hz, 1H), 1.57 (d, *J* = 7.0 Hz, 3H); ^{13}C NMR (125 MHz, CDCl$_3$) δ 197.9, 166.3, 158.9, 157.9, 127.6, 125.9, 115.8, 108.5, 66.8, 62.2, 55.8, 41.8, 36.7, 17.7; cis isomer: ^{1}H NMR (500 MHz, CDCl$_3$) δ 7.72 (d, *J* = 8.5 Hz, 1H), 6.94 (dd, *J* = 8.5, 2.5 Hz, 1H), 6.9 (d, *J* = 2.5 Hz, 1H), 4.81 (d, *J* = 7.5 Hz, 1H), 4.45-4.35 (m, 2H), 4.04 (ddd, *J* = 7.5, 7.5, 7.0 Hz, 1H), 3.91 (s, 3H), 3.78 (app. quintet, *J* = 8.0 Hz, 1H), 3.39 (ddd, *J* = 8.5, 8.5, 7.0 Hz, 1H), 1.28 (d, *J* = 7.0 Hz, 3H); ^{13}C NMR (125 MHz, CDCl$_3$) δ 198.3, 166.3, 160.6, 159.2, 126.9, 126.2, 116.2, 109.1, 62.7, 62.0, 43.5, 37.8, 17.6 [one aliphatic carbon is missing due to peak overlapping.]; HRMS (ESI, $[M+Na]^+$) Calcd for $C_{14}H_{15}NNaO_4$ 284.0893; found m/z 284.0889.



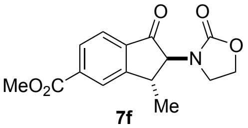
7d

Following the representative procedure using 5 equiv triflic acid at 65 °C (oil bath), flash chromatography (hexane/EtOAc = 1/1) gave **7d** in 97% yield (*cis*:*trans* >20:1): IR (film) 3058, 2965, 2924, 1747, 1713, 1594, 1431, 1262, 1198 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.68 (d, *J* = 8.5 Hz, 1H), 7.31 (br s, 1H), 7.28 (d, *J* = 8.5 Hz, 1H), 4.49 (ddd, *J* = 8.5, 8.5, 6.5 Hz, 1H), 4.44 (ddd, *J* = 9.0, 9.0, 6.5 Hz, 1H), 4.41 (d, *J* = 6.0 Hz, 1H), 3.65 (ddd, *J* = 9.5, 8.0, 6.5 Hz, 1H), 3.51 (ddd, *J* = 9.0, 8.0, 7.0 Hz, 1H), 3.30 (app. quintet, *J* = 6.5 Hz, 1H), 2.59 (s, 3H), 1.62 (d, *J* = 6.5 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 198.5, 158.9, 155.4, 150.1, 130.9, 125.1, 124.0, 120.4, 66.9, 62.3, 41.9, 36.6, 17.6, 14.9; HRMS (ESI, $[M+Na]^+$) Calcd for $C_{14}H_{15}NNaO_3S$ 300.0665; found m/z 300.0660.

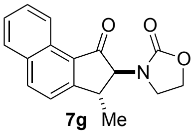


7e

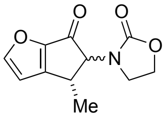
Following the representative procedure using 5 equiv triflic acid at 65 °C (oil bath), flash chromatography (hexane/EtOAc = 1/1) gave **7e** in 94% yield (*cis*:*trans* >20:1): IR (film) 3061, 2965, 2923, 1748, 1725, 1600, 1431, 1259, 1210 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.70 (d, *J* = 8.5 Hz, 1H), 7.51 (br s, 1H), 7.42 (d, *J* = 8.5 Hz, 1H), 4.47 (ddd, *J* = 9.0, 9.0, 7.0 Hz, 1H), 4.42 (ddd, *J* = 8.5, 8.5, 7.0 Hz, 1H), 4.36 (d, *J* = 6.5 Hz, 1H), 3.66-3.61 (m, 1H), 3.53-3.48 (m, 1H), 3.32 (app. quintet, *J* = 6.5 Hz, 1H), 1.59 (d, *J* = 7.0 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 198.5, 158.8, 156.2, 142.6, 132.7, 129.0, 125.4, 125.2, 67.0, 62.3, 42.1, 36.6, 17.5; HRMS (ESI, $[M+Na]^+$) Calcd for $C_{13}H_{12}ClNNaO_3$ 288.0398; found m/z 288.0395.


7f

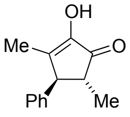
Following the representative procedure using 5 equiv triflic acid at 65 °C (oil bath), flash chromatography (hexane/EtOAc = 1/1) gave **7f** in 91% yield (*cis*:*trans* >20:1): IR (film) 3020, 2955, 2927, 1751, 1726, 1615, 1436, 1262, 1216 cm^{-1}; ^{1}H NMR (500 MHz, CDCl$_3$) δ 8.23 (br s, 1H), 8.14-8.12 (m, 1H), 7.86-7.85 (m, 1H), 4.55-4.46 (m, 2H), 4.44 (d, *J* = 6.5 Hz, 1H), 4.01 (s, 3H), 3.69 (ddd, *J* = 9.0, 8.0, 7.0 Hz, 1H), 3.56 (ddd, *J* = 9.0, 8.0, 7.0 Hz, 1H), 3.41 (app. quintet, *J* = 7.0 Hz, 1H), 1.68 (d, *J* = 7.0 Hz, 3H); ^{13}C NMR (125 MHz, CDCl$_3$) δ 199.6, 166.0, 158.8, 154.5, 137.4, 136.6, 129.3, 126.3, 123.9, 67.4, 62.3, 52.7, 42.2, 36.6, 17.6; HRMS (ESI, [M+Na]$^+$) Calcd for $C_{15}H_{15}NNaO_5$ 312.0842; found m/z 312.0841.


7g

Following the representative procedure using 5 equiv triflic acid at 65 °C (oil bath), flash chromatography (hexane/EtOAc = 1/1) gave **7g** in 97% yield (*cis*:*trans* >20:1): IR (film) 3014, 2966, 2925, 1744, 1704, 1628, 1428, 1269, 1219 cm^{-1}; ^{1}H NMR (500 MHz, CDCl$_3$) δ 9.07 (d, *J* = 8.5 Hz, 1H), 8.20 (d, *J* = 8.5 Hz, 1H), 7.96-7.94 (m, 1H), 7.76-7.73 (m, 1H), 7.65-7.61 (m, 2H), 4.55-4.44 (m, 2H), 4.54 (d, *J* = 5.5 Hz, 1H), 3.71 (ddd, *J* = 9.0, 8.0, 7.0, 1H), 3.55 (ddd, *J* = 9.5, 7.5, 6.5 Hz, 1H), 3.46 (app. quintet, *J* = 6.0 Hz, 1H), 1.70 (d, *J* = 7.0 Hz, 3H); ^{13}C NMR (125 MHz, CDCl$_3$) δ 200.2, 159.1, 157.8, 137.1, 132.8, 129.6, 128.9, 128.8, 128.3, 127.2, 124.3, 121.8, 67.1, 62.3, 42.0, 36.8, 17.9; HRMS (EI, M$^+$) Calcd for $C_{17}H_{15}NO_3$ 281.1052; found m/z 281.1049.


7h, *cis*:*trans* 1:3

Following the representative procedure using 5 equiv triflic acid at 65 °C (oil bath), flash chromatography (hexane/EtOAc = 1/1) gave **7h** in 65% yield (*cis*:*trans* 1:3, inseparable mixture): IR (film) 3059, 2972, 2918, 1749, 1715, 1579, 1426, 1268, 1246 cm^{-1}; trans isomer: ^1H NMR (500 MHz, $CDCl_3$) δ 7.87 (d, *J* = 2.0 Hz, 1H), 6.59 (d, *J* = 2.0 Hz, 1H), 4.52 (d, *J* = 3.5 Hz, 1H), 4.50-4.40 (m, 2H), 3.66-3.61 (m, 1H), 3.57-3.52 (m, 1H), 3.21 (qd, *J* = 7.5, 3.5 Hz, 1H), 1.53 (d, *J* = 7.5 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 182.3, 158.5, 157.6, 154.5, 152.0, 109.2, 70.1, 62.2, 42.2, 33.1, 18.0; cis isomer: ^1H NMR (500 MHz, $CDCl_3$) δ 7.87 (d, *J* = 2.0 Hz, 1H), 6.60 (d, *J* = 2.0 Hz, 1H), 4.50-4.40 (m, 3H), 4.00-3.95 (m, 1H), 3.69 (app. quintet, *J* = 7.0 Hz, 1H), 3.52-3.47 (m, 1H), 1.31 (d, *J* = 7.5 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 181.9, 160.0, 158.7, 154.6, 151.8, 109.6, 65.3, 62.6, 42.1, 33.0, 16.1; HRMS (ESI, $[M+Na]^+$) Calcd for $C_{11}H_{11}NNaO_4$ 244.0580; found m/z 244.0583.



7i

Following the representative procedure using 20 mol% $Sc(OTf)_3$ at 80 °C (oil bath), flash chromatography (hexane/EtOAc = 1/1) gave **7i** in 96% yield: IR (film) 3336 (br), 3027, 2977, 1700, 1656, 1600, 1406, 1360, 1206 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.38-7.35 (m, 2H), 7.32-7.29 (m, 1H), 7.16-7.14 (m, 2H), 5.37 (br s, 1H), 3.32 (app. quintet, *J* = 1.9 Hz, 1H), 2.32 (qdd, *J* = 8.0, 2.2, 0.8 Hz, 1H), 1.82 (dd, *J* = 2.3, 0.8 Hz, 3H), 1.29 (d, *J* = 7.5 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 204.3, 148.2, 143.3, 141.2, 128.9, 127.5, 127.2, 54.7, 48.6, 15.0, 12.5; HRMS (EI, M^+) Calcd for $C_{13}H_{14}O_2$ 202.0994; found m/z 202.0995.

4.6 References

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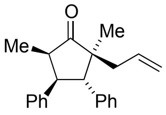
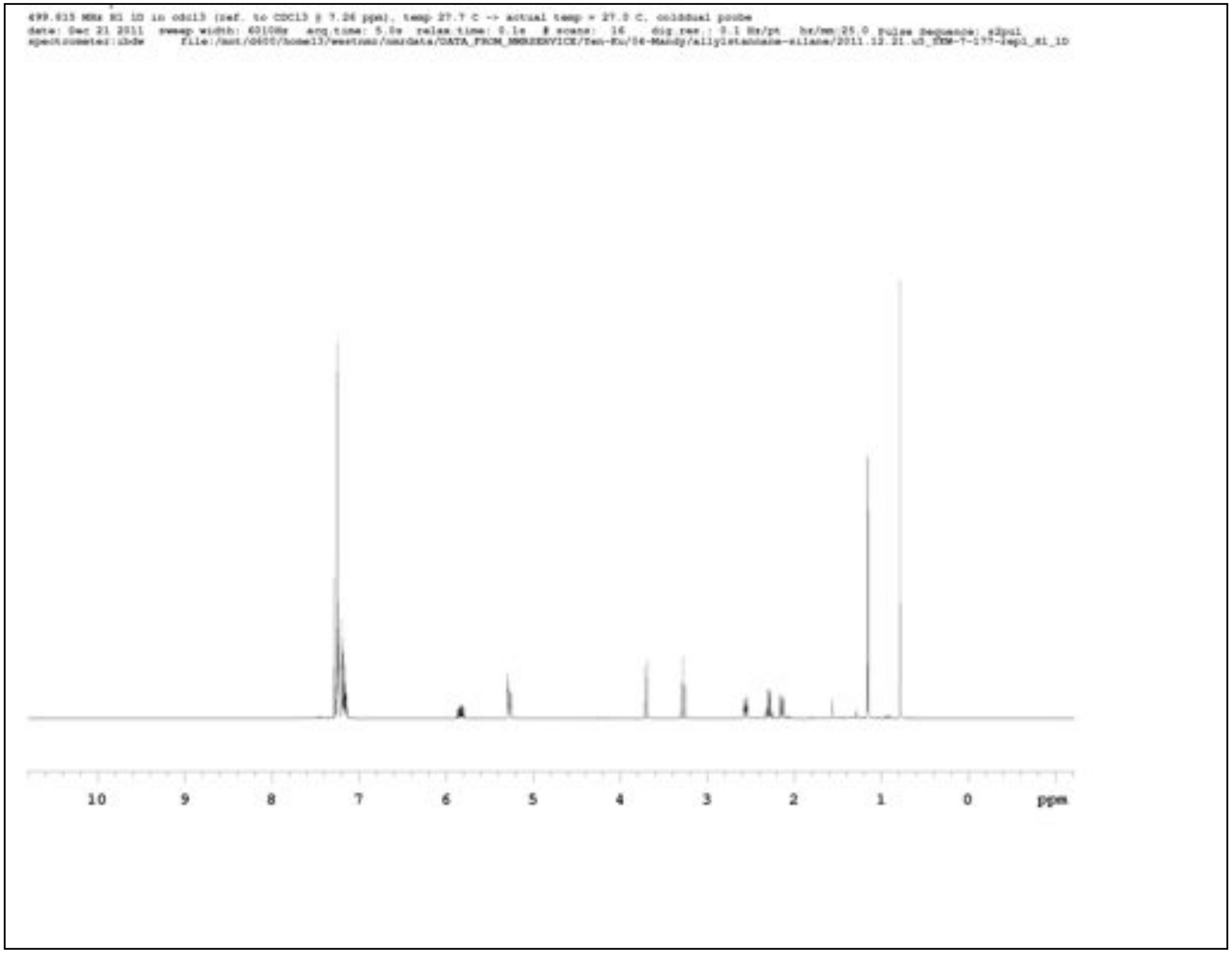
Appendix I:

Selected NMR Spectra (Chapter 2)


5a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date: Dec 21 2011 sweep width: 6010Hz acq.time: 5.0s relax.time: 0.1s # scans: 16 dig.res.: 0.1 Hz/pt hz/mm:25.0 Pulse Sequence: s2pul
spectrometer:ibde file:/mnt/d600/home13/eastman/nmrdata/DATA_FROM_NMRSERVICE/Ten-Xu/06-Mandy/allylstannane-silane/2011.12.21.u5_TXM-7-177-1epi_H1_1D
10
9
8
7
6
5
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3
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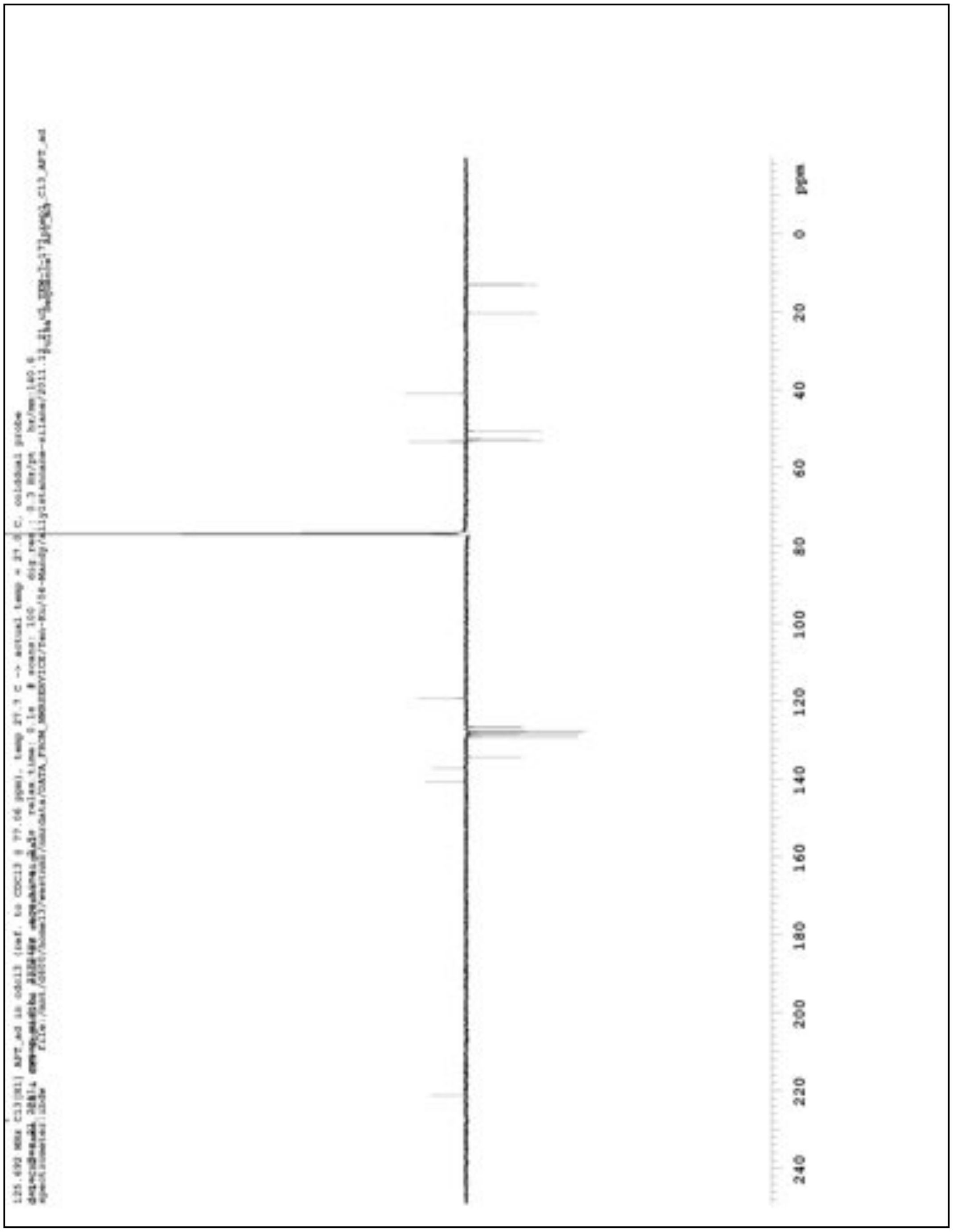
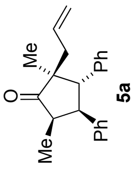
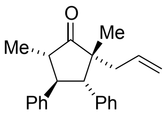
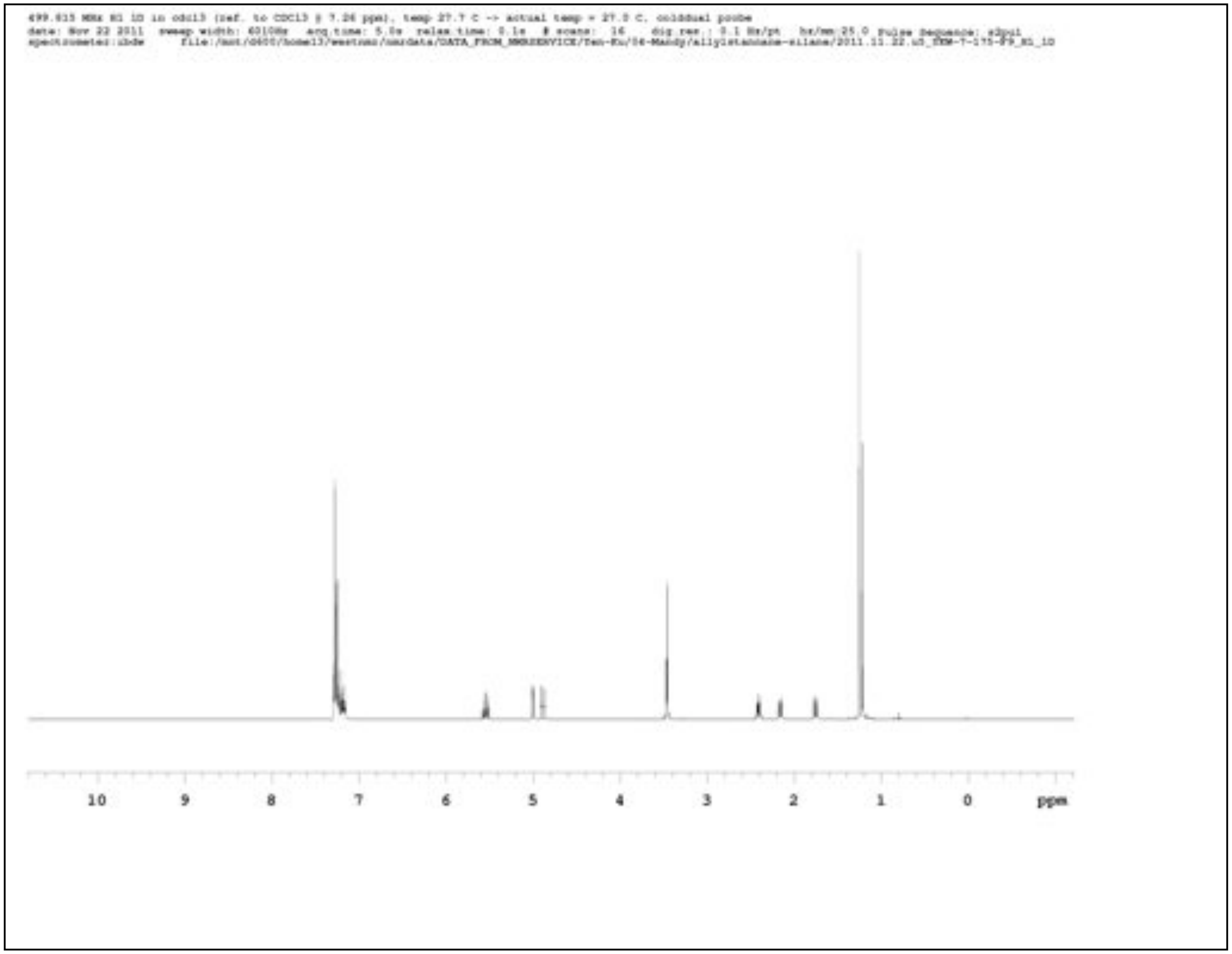


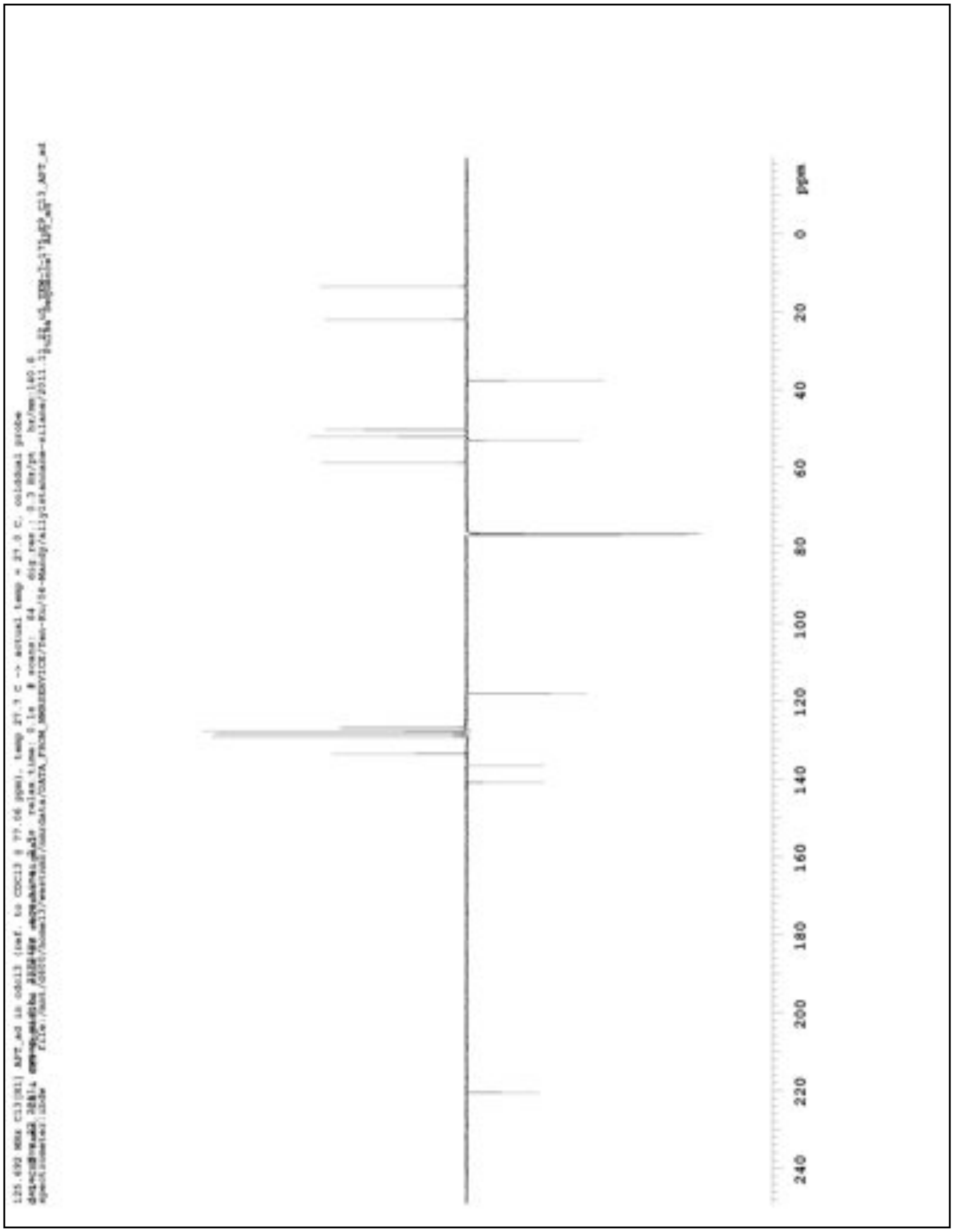


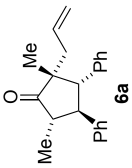
5a


O
Me
Me
Ph
Ph

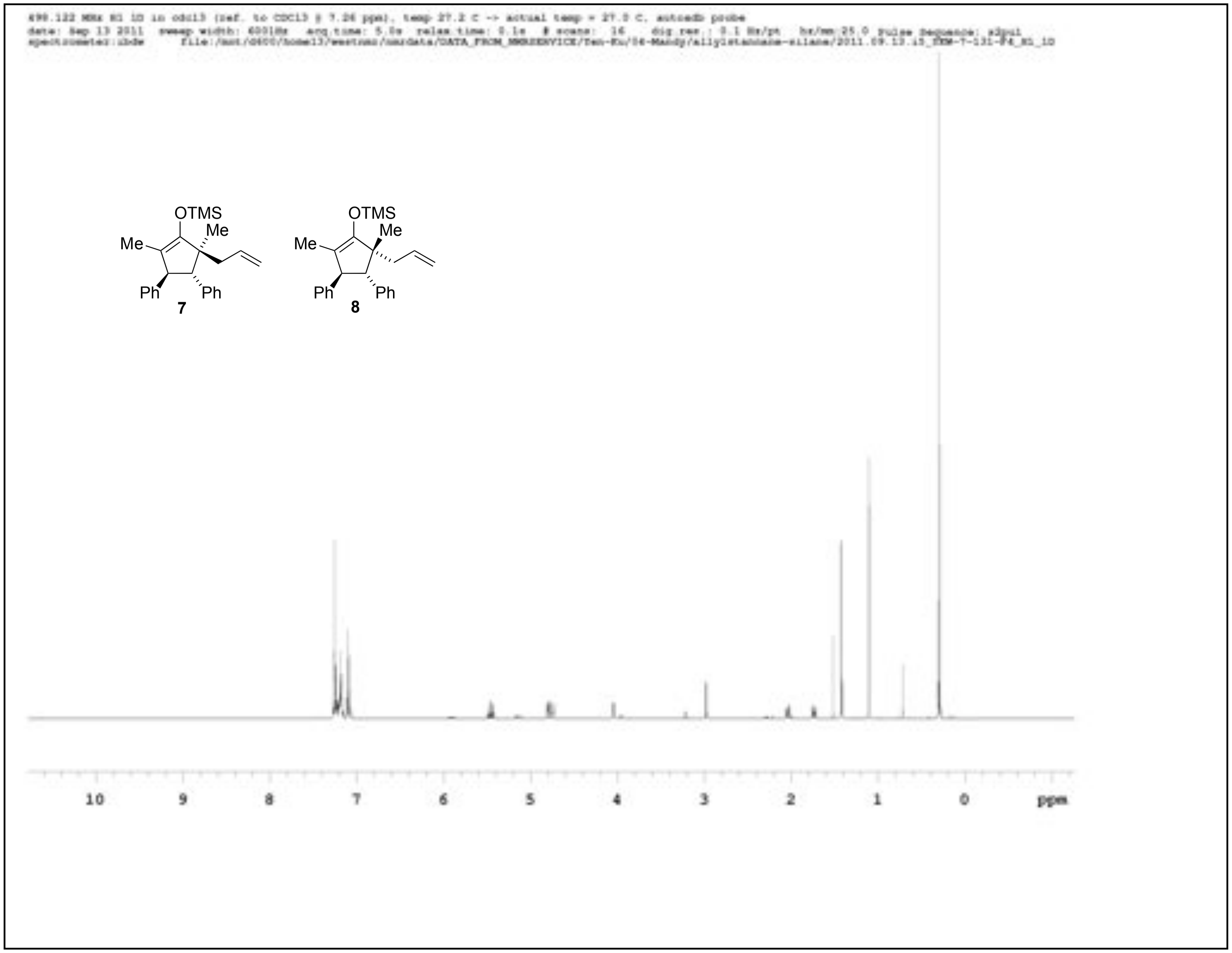
6a

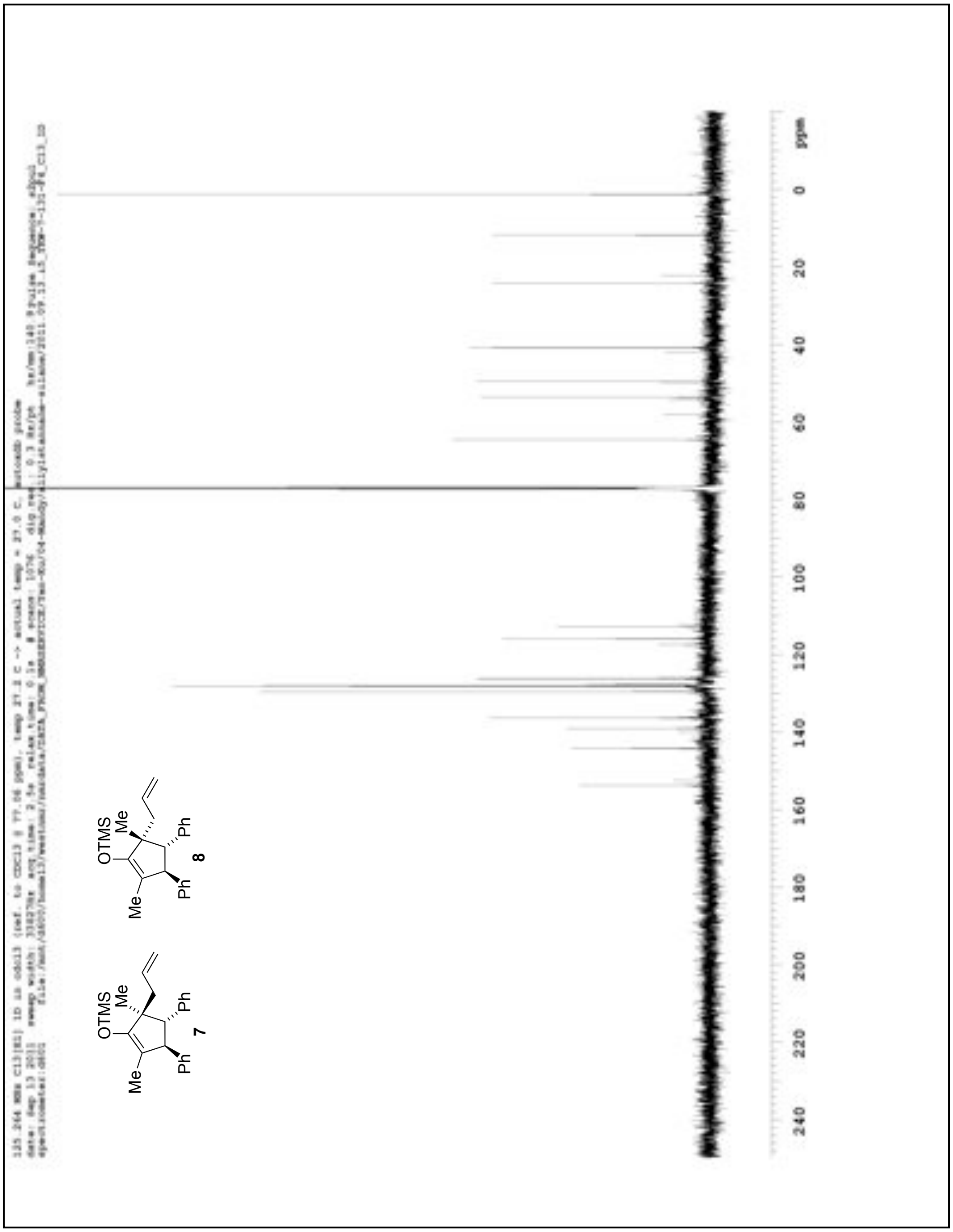

499.815 MHz H1 1D in cdcl3 (ref. to CDCl3 @ 7.26 ppm), temp 27.7 C -> actual temp = 27.0 C, colddual probe
date: Nov 22 2011 sweep width: 6010Hz acq.time: 5.0s relax.time: 0.1s # scans: 16 dig.res.: 0.1 Hz/pt hz/mm:25.0 Pulse Sequence: s2pul
spectrometer:inde file:/mnt/d600/home13/westonc/nmrdata/DATA_FROM_NMRSERVICE/Ten-Ku/06-Mandy/allylstannane-silane/2011.11.22.u5_TKM-7-175-F9_H1_1D
10
9
8
7
6
5
4
3
2
1
0
ppm


125.692 MHz C13[H1] APT_ad in CDCl3 (ref. to CDCl3 @ 77.06 ppm), temp 27.7 C -> actual temp = 27.0 C, colddual probe
ppm
0
20
40
60
80
100
120
140
160
180
200
220
240

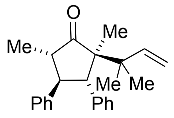

O
Me
Ph
Ph
Me

6a

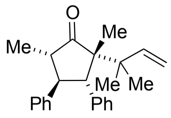

499.122 MHz H1 1D in cdcl3 (ref. to CDCl3 @ 7.26 ppm), temp 27.2 C -> actual temp = 27.0 C, autoxdb probe
date: Sep 13 2011 sweep width: 6001Hz acq time: 5.0s relax time: 0.1s # scans: 16 dig res.: 0.1 Hz/pt hz/mm:25.0 Pulse Sequence: s2pul
spectrometer:i3de file:/mnt/d600/home13/westons/nmrdata/DATA_FROM_NMRSERVICE/Ten-Ku/06-Mandy/allylstannane-silane/2011.09.13.i5_TEM-7-131-F4_H1_1D
OTMS
Me
Me
Ph
Ph
7
OTMS
Me
Me
Ph
Ph
8
10
9
8
7
6
5
4
3
2
1
0
ppm


Me
OTMS
Me
Ph
Ph
7
Me
OTMS
Me
Ph
Ph
8
240
220
200
180
160
140
120
100
80
60
40
20
0
ppm

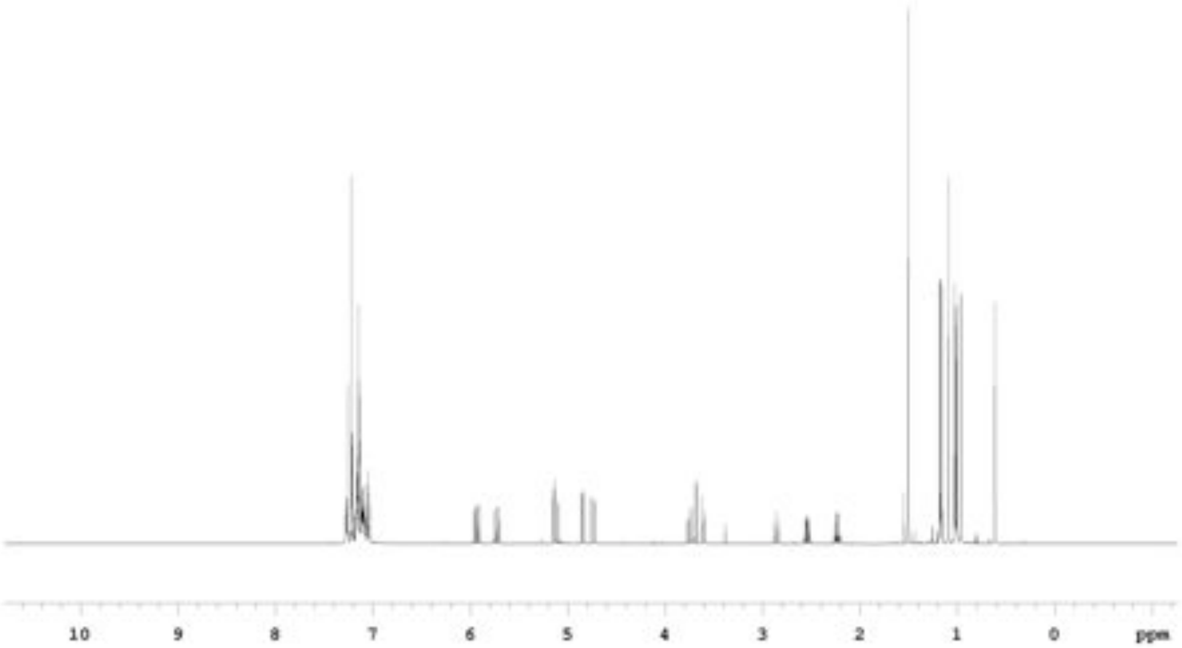
```
499.122 MHz H1 1D in cdcl3 (ref. to CDCl3 δ 7.26 ppm), temp 27.2 C -> actual temp = 27.0 C, autoxdb probe
date: Sep 30 2011  sweep width: 6001Hz  acq.time: 5.0s  relax.time: 0.1s  # scans:  16   dig.res.: 0.1 Hz/pt  hz/mm:25.0  Pulse Sequence: s2pul
spectrometer:i1de     file:/mnt/d600/home13/westonc/nmrdata/DATA_FROM_NMRSERVICE/Tan-Ku/04-Mandy/allylstannane-silane/2011.09.30.i5_TKM-7-155-F45_H1_1D
```

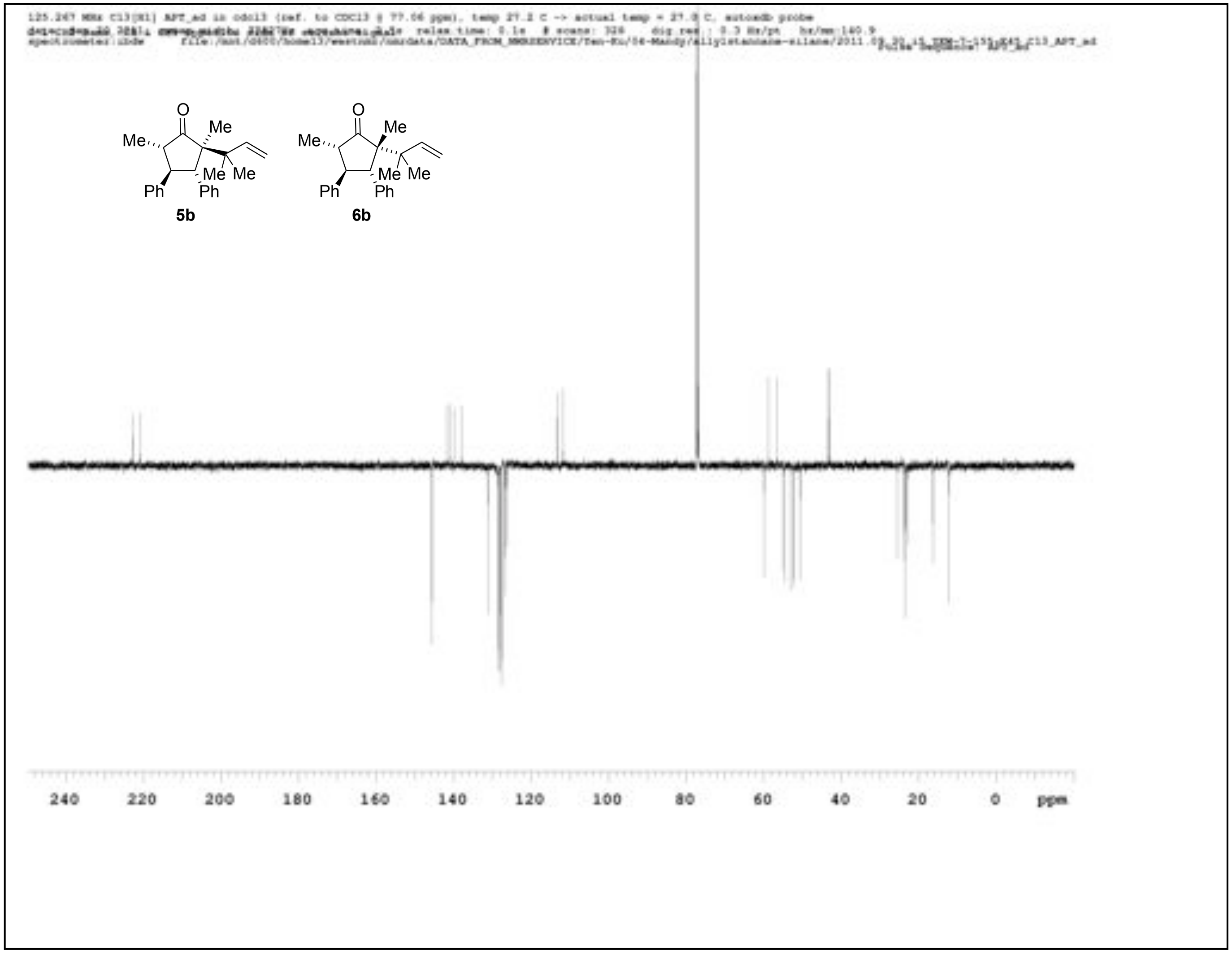


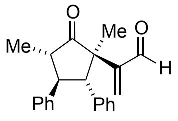
5b



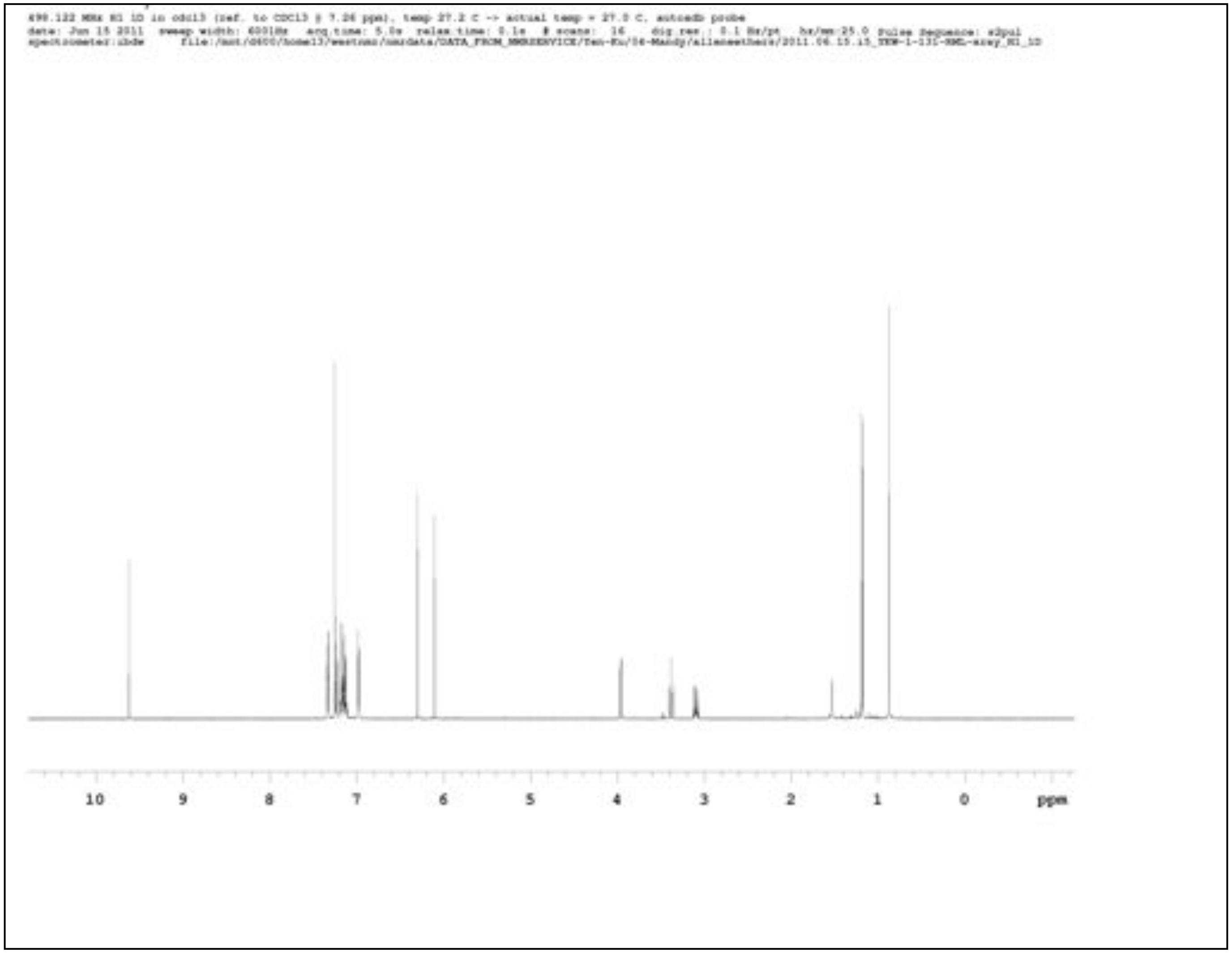
6b

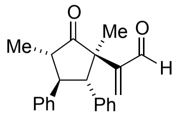



125.247 MHz C13[H1] APT_ad in cdcl3 (ref. to CDCl3 @ 77.06 ppm), temp 27.2 C -> actual temp = 27.0 C, autoxdb probe
relax time: 0.1s # scans: 328 dig res.: 0.3 Hz/pt hz/mm:140.9
O
Me
Me
Me
Me
Ph
Ph
5b
O
Me
Me
Me
Me
Ph
Ph
6b
240
220
200
180
160
140
120
100
80
60
40
20
0
ppm

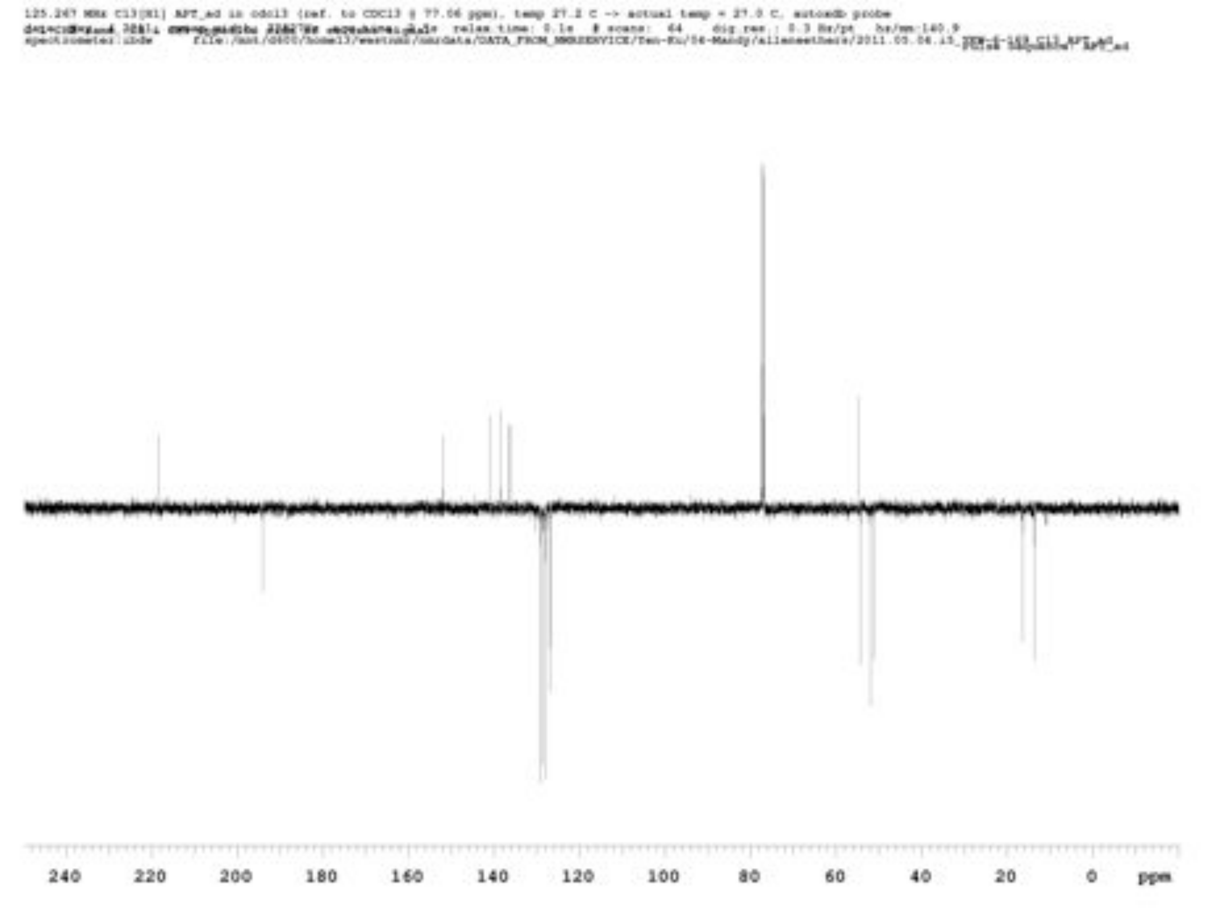


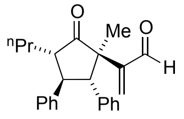
16a


499.122 MHz H1 1D in cdcl3 (ref. to CDCl3 @ 7.26 ppm), temp 27.2 C -> actual temp = 27.0 C, autoxdb probe
date: Jun 15 2011 sweep width: 6001Hz acq time: 5.0s relax time: 0.1s # scans: 16 dig res.: 0.1 Hz/pt hz/mm:25.0 Pulse Sequence: s2pul
spectrometer:ibdw file:/mnt/d600/home13/westumr/nmrdata/DATA_FROM_NMRSERVICE/Tan-Ku/04-Mandy/alleneethers/2011.06.15.i5_TKW-1-131-HML-array_H1_1D
10
9
8
7
6
5
4
3
2
1
0
ppm



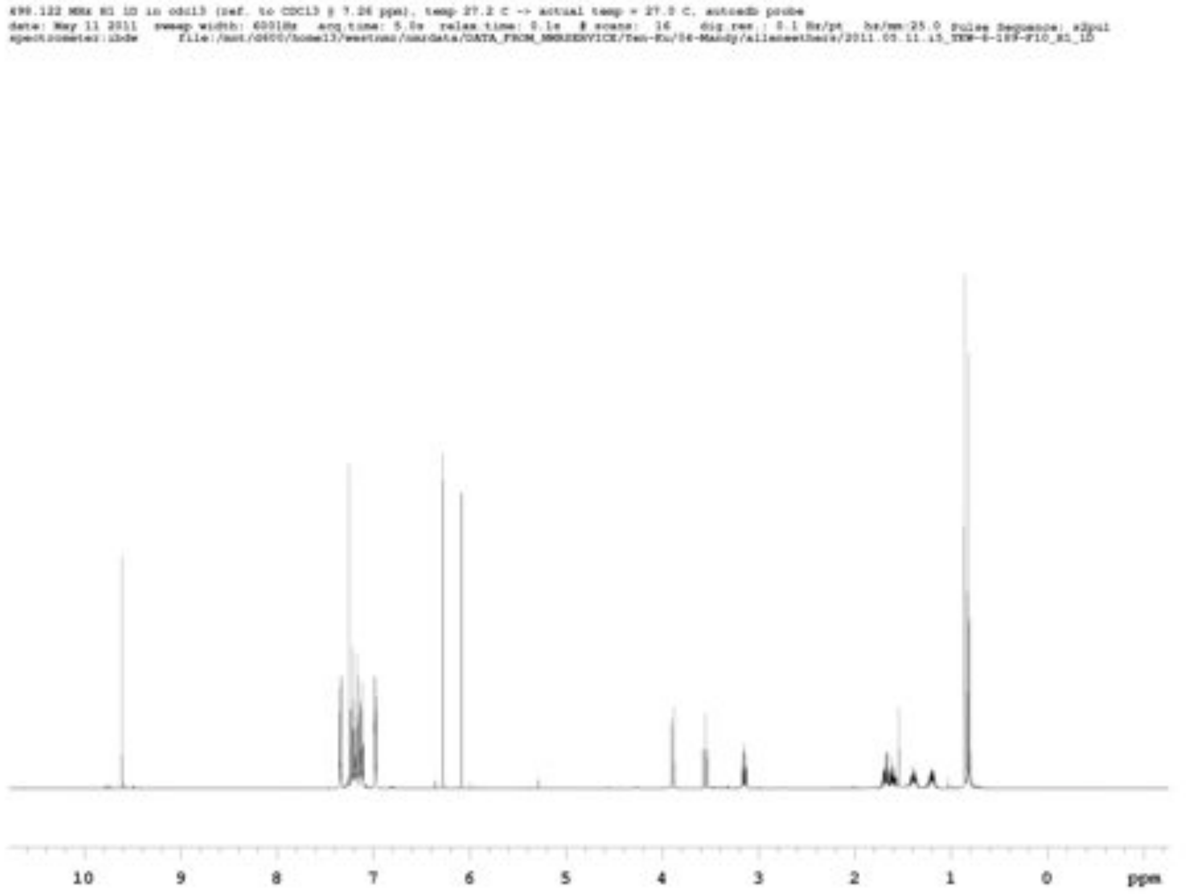
16a


125.267 MHz C13[H1] APT_ad in cdcl3 (ref. to CDCl3 @ 77.06 ppm), temp 27.2 C -> actual temp = 27.0 C, autoxdb probe
relax time: 0.1s # scans: 64 dig res.: 0.3 Hz/pt hz/mm:140.9
240
220
200
180
160
140
120
100
80
60
40
20
0
ppm

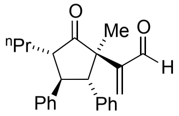


O
ⁿPr
Me
O
H
Ph
Ph

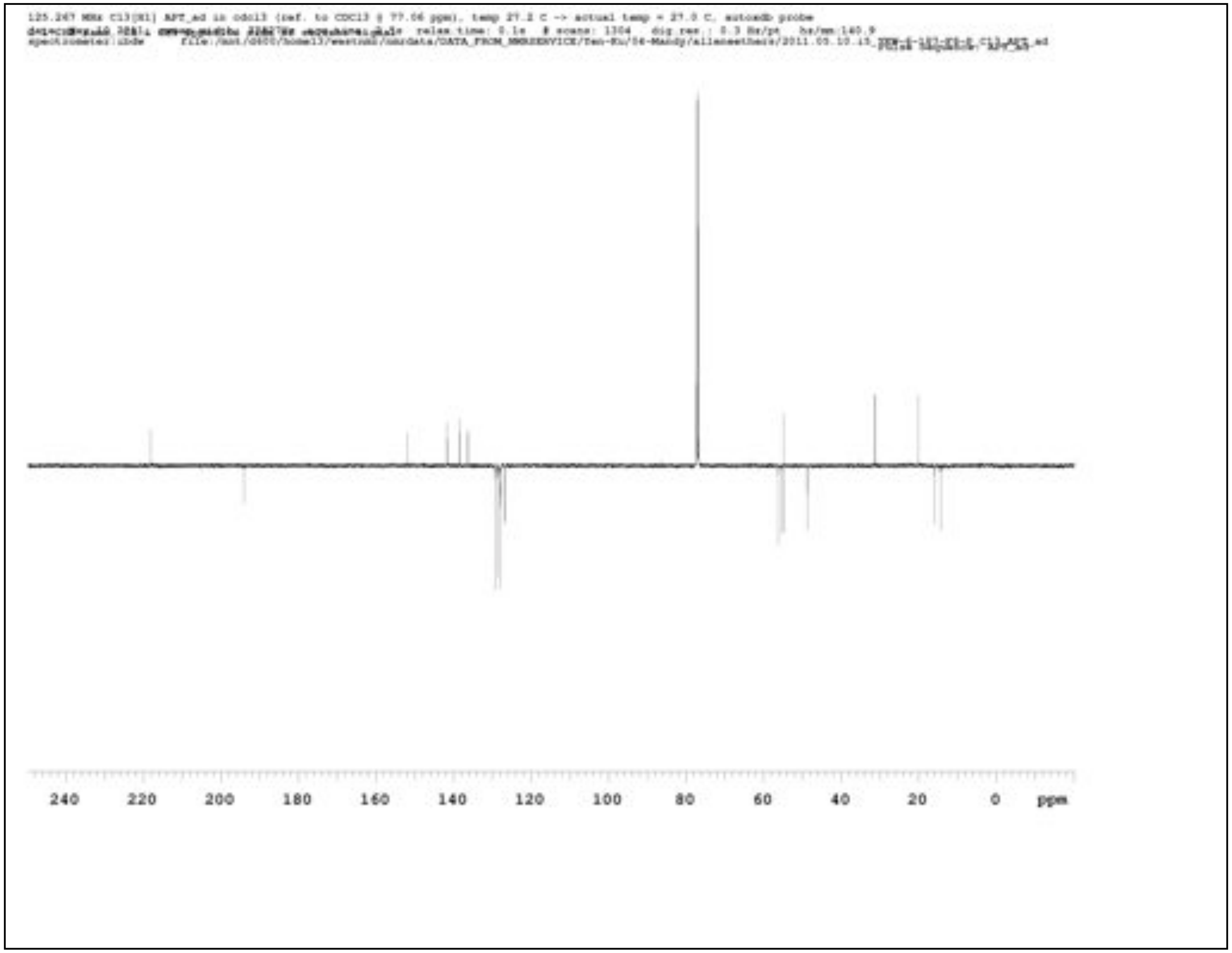
16d

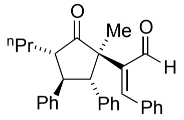


499.122 MHz H1 1D in cdcl3 (ref. to CDCl3 @ 7.26 ppm), temp 27.2 C -> actual temp = 27.0 C, autoxdb probe
date: May 11 2011 sweep width: 6001Hz acq.time: 5.0s relax.time: 0.1s # scans: 16 dig.res.: 0.1 Hz/pt hz/mm:25.0 Pulse Sequence: s2pul
spectrometer:ib4e file:/mnt/d600/home13/westumz/nmrdata/DATA_FROM_NMRSERVICE/Ten-Ku/06-Mandy/alleneethers/2011.05.11.i5_TKW-6-189-F10_H1_1D
10
9
8
7
6
5
4
3
2
1
0
ppm

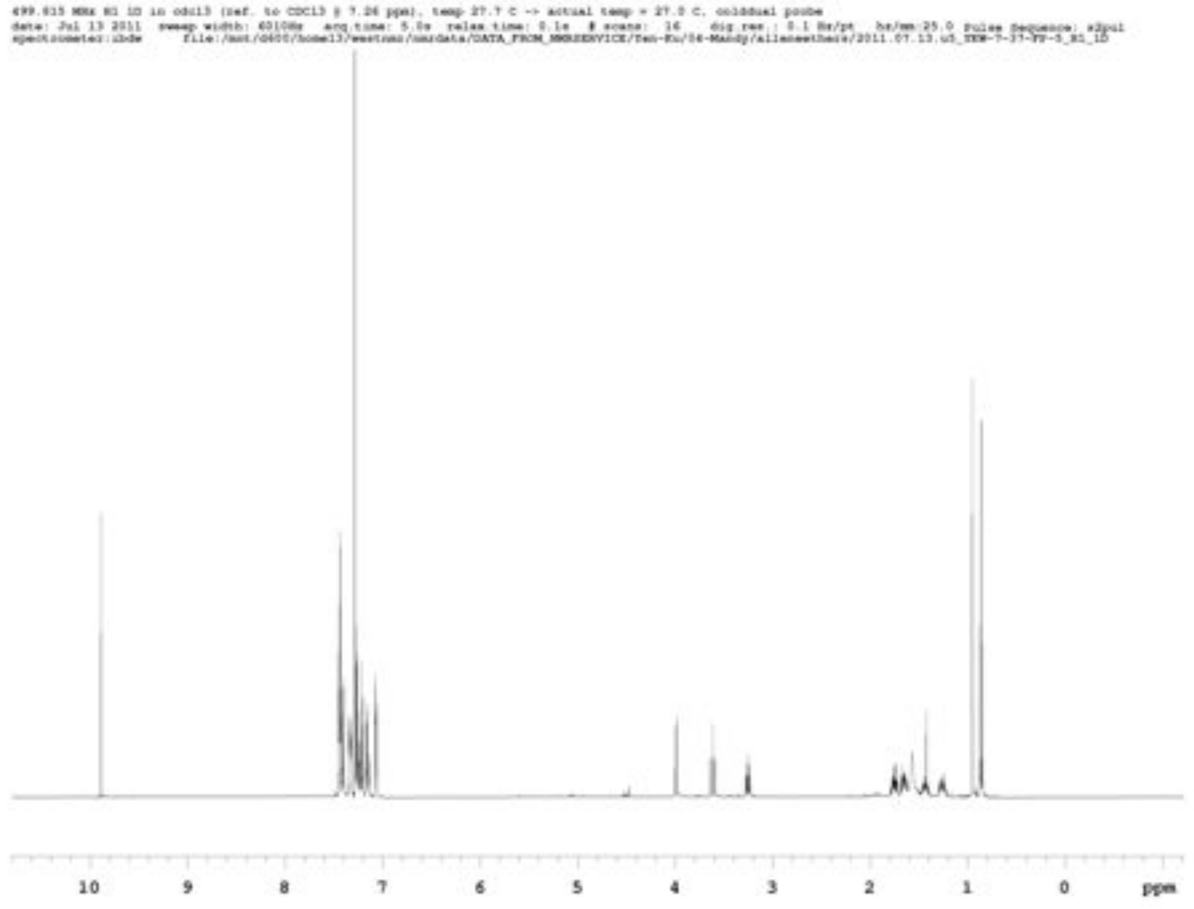

ⁿPr
O
Me
O
H
Ph
Ph

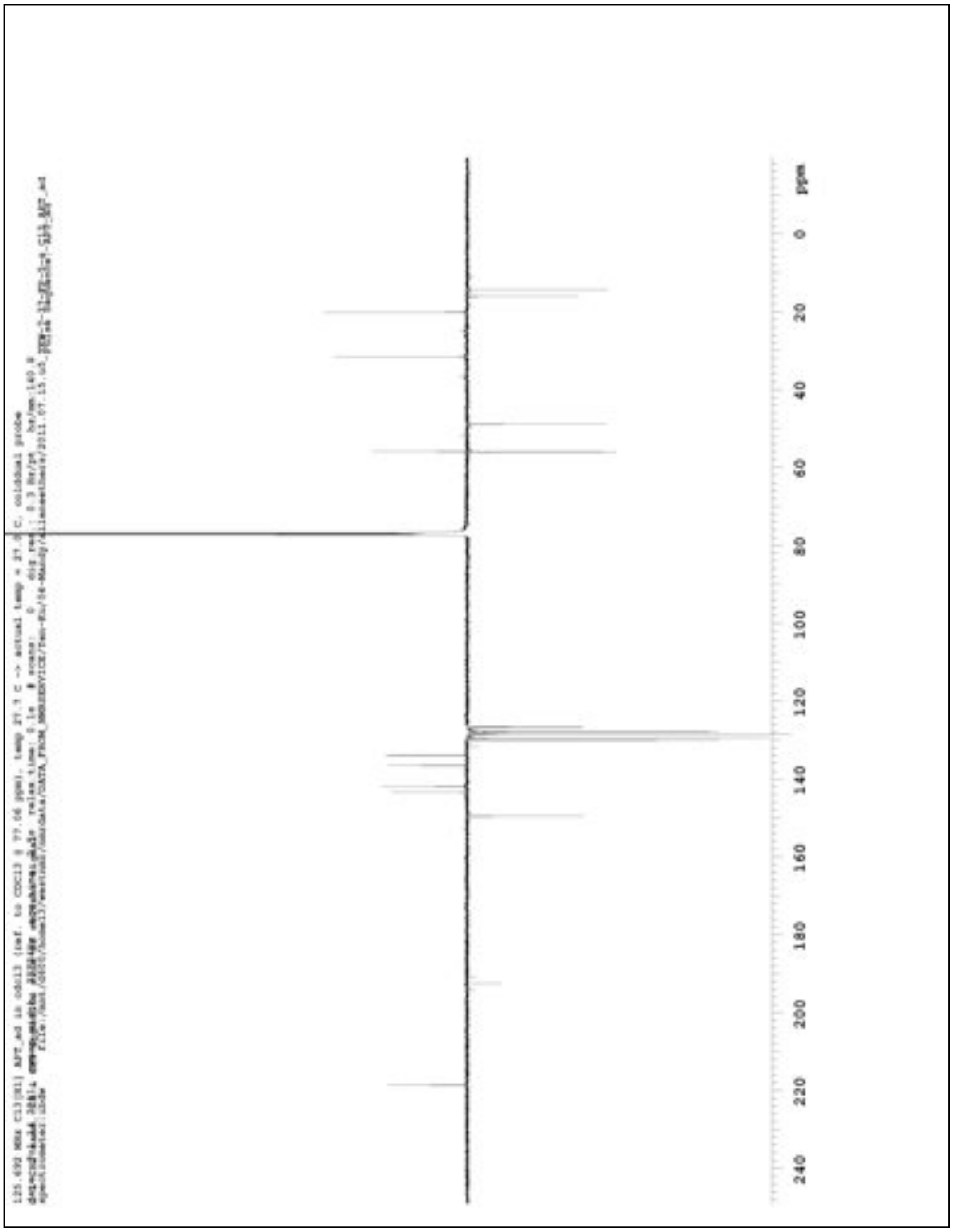
16d

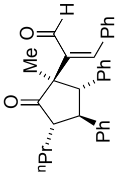

125.267 MHz C13[H1] APT_ad in cdcl3 (ref. to CDCl3 @ 77.06 ppm), temp 27.2 C -> actual temp = 27.0 C, autoxdb probe
relax.time: 0.1s # scans: 1304 dig.res.: 0.3 Hz/pt hz/mm:140.9
240
220
200
180
160
140
120
100
80
60
40
20
0
ppm


O
Me
O
H
ⁿPr
Ph
Ph
Ph

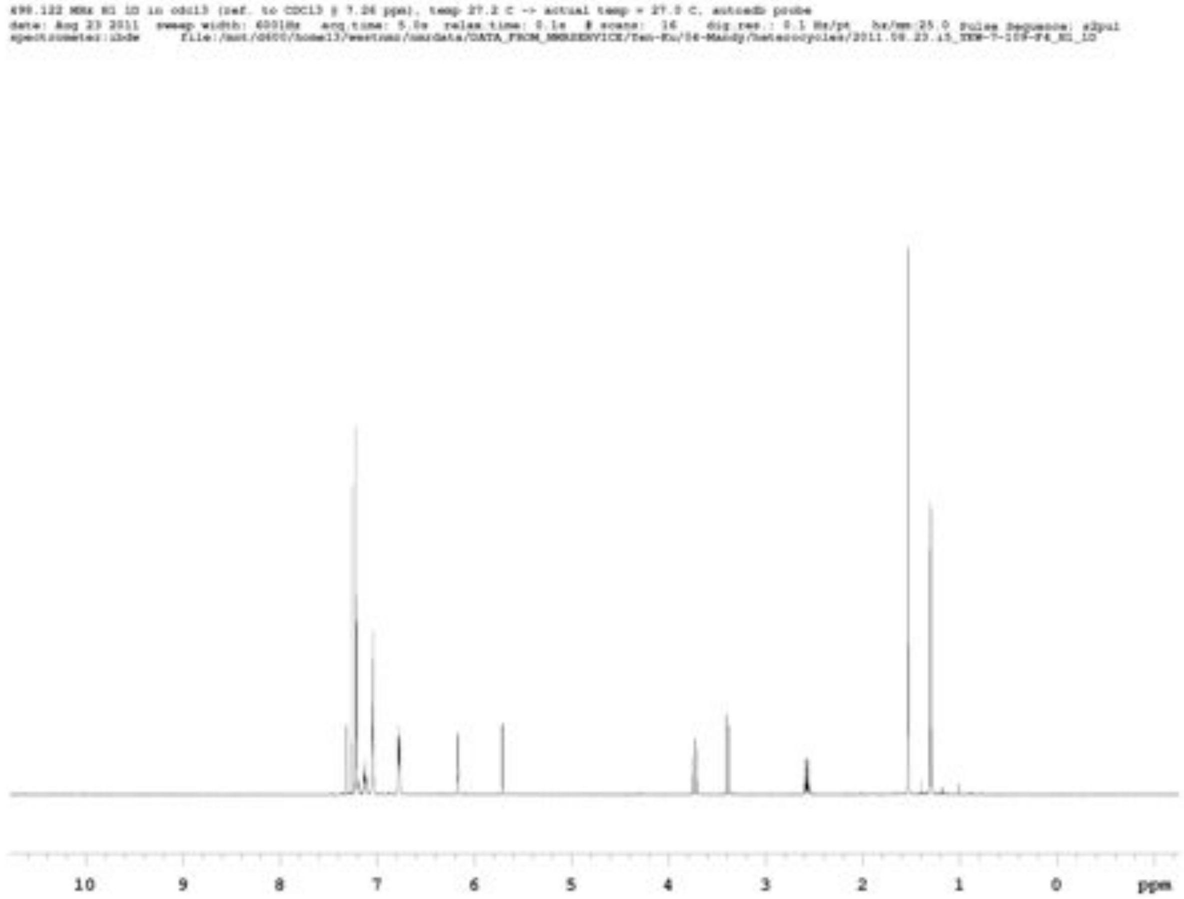
16h

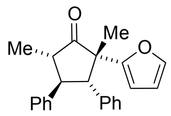

499.815 MHz H1 1D in cdcl3 (ref. to CDCl3 δ 7.26 ppm), temp 27.7 C -> actual temp = 27.0 C, colddual probe
date: Jul 13 2011 sweep width: 6010Hz acq time: 5.0s relax time: 0.1s # scans: 16 dig res.: 0.1 Hz/pt hz/mm:25.0 Pulse Sequence: s2pul
spectrometer:ibdw file:/mnt/d600/home13/eastnmr/nmrdata/DATA_FROM_NMRSERVICE/Tan-Ku/04-Mandy/alleneethers/2011.07.13.u5_TKW-7-37-PF-5_H1_1D
10
9
8
7
6
5
4
3
2
1
0
ppm


240
220
200
180
160
140
120
100
80
60
40
20
0
ppm

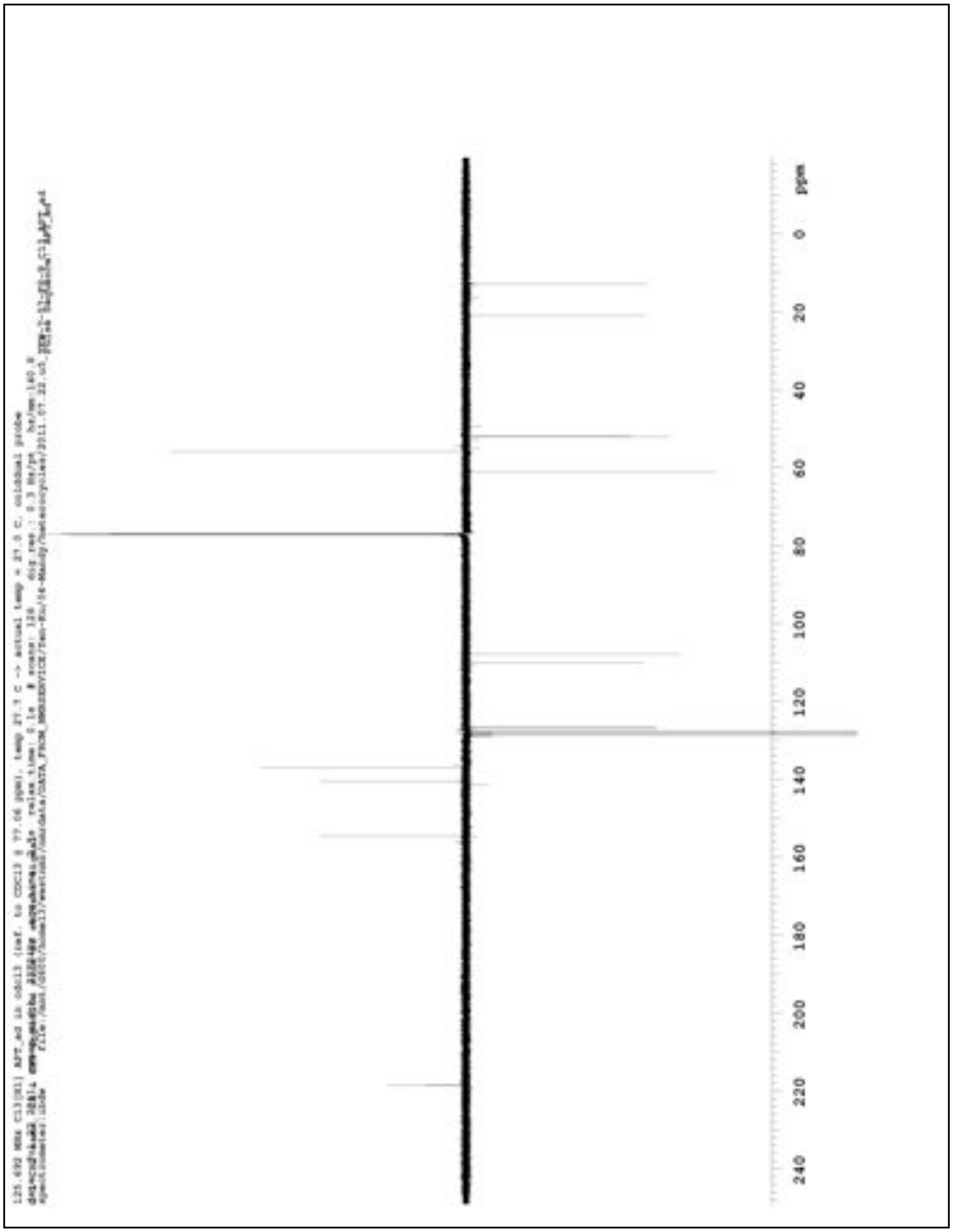

O
Me
O
H
Ph
Ph
Ph
ⁿPr

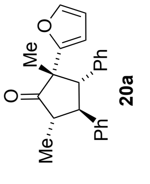
16h


499.122 MHz H1 1D in cdcl3 (ref. to CDCl3 @ 7.26 ppm), temp 27.2 C -> actual temp = 27.0 C, autoxdb probe
date: Aug 23 2011 sweep width: 6001Hz acq time: 5.0s relax time: 0.1s # scans: 16 dig res.: 0.1 Hz/pt hz/mm:25.0 Pulse Sequence: s2pul
spectrometer:ibdw file:/mnt/d600/home13/westnmr/nmrdata/DATA_FROM_NMRSERVICE/Tan-Ku/06-Mandy/heterocycles/2011.08.23.i5_TKW-7-109-F4_H1_1D
10
9
8
7
6
5
4
3
2
1
0
ppm

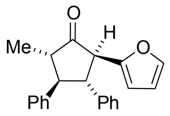

O
Me
Me
O
Ph
Ph

20a

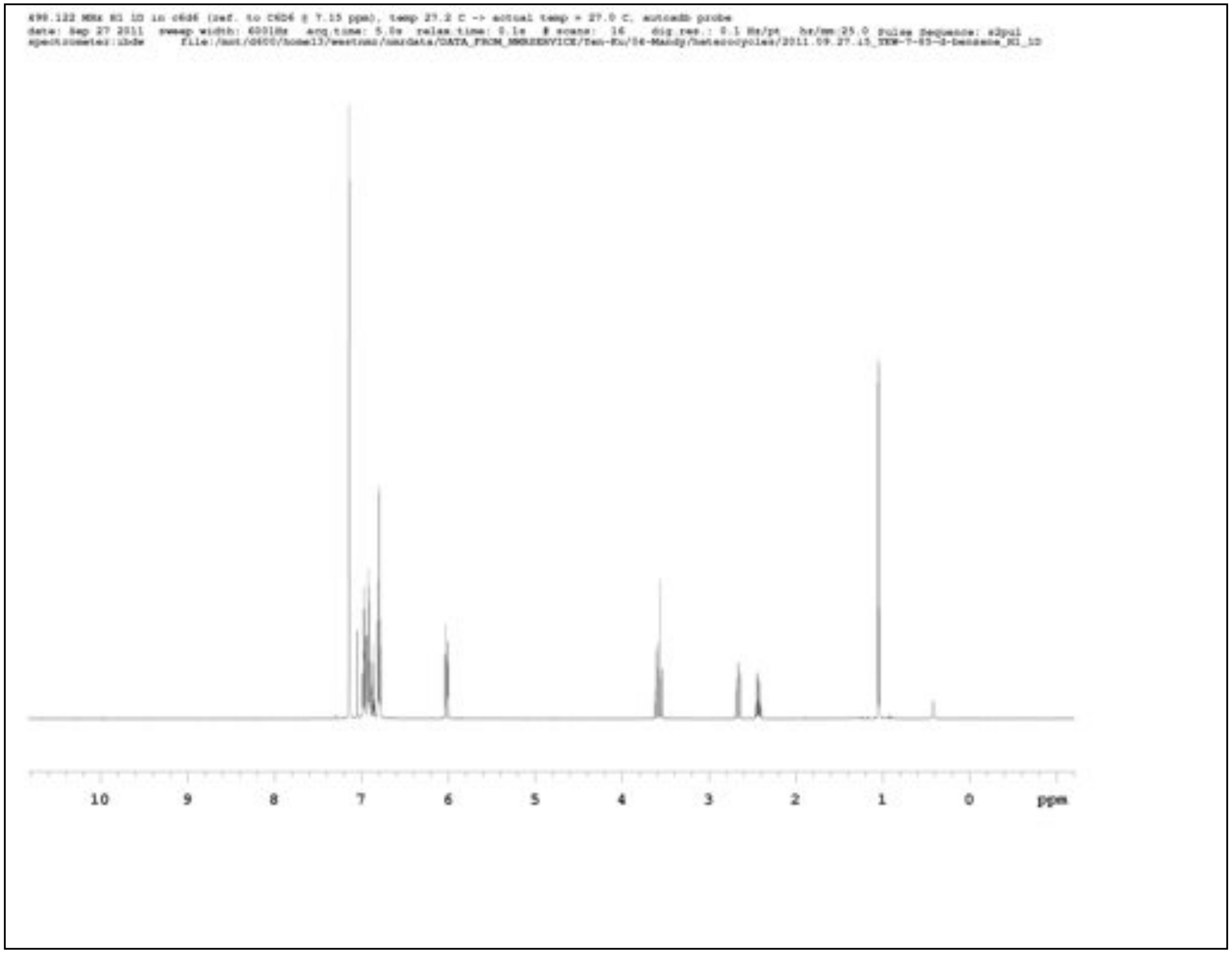


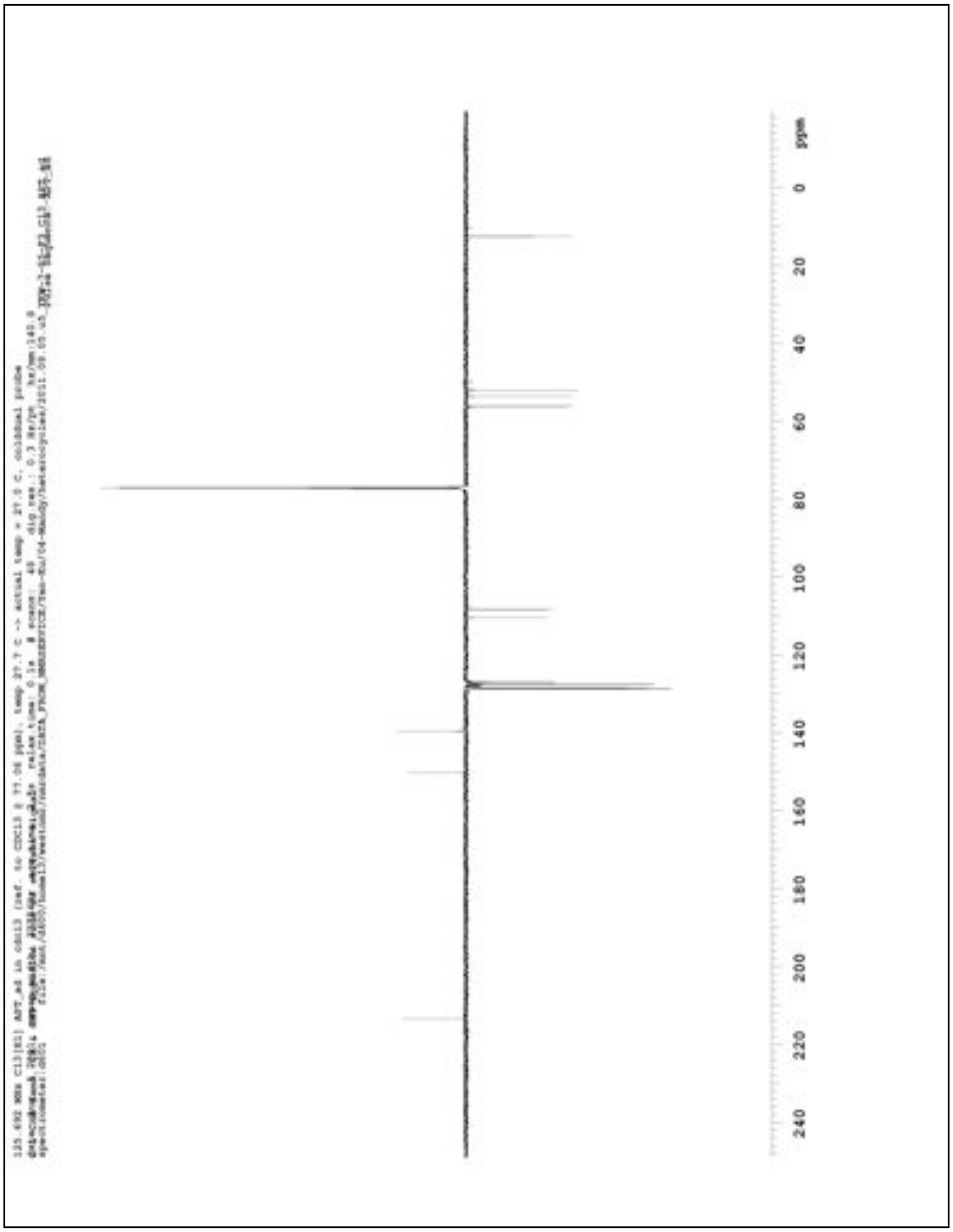


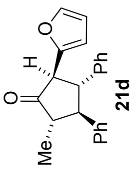
20a


O
H
Me
Ph
Ph

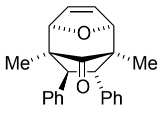
21d


499.122 MHz H1 1D in c6d6 (ref. to C6D6 @ 7.15 ppm), temp 27.2 C -> actual temp = 27.0 C, autoxdb probe
date: Sep 27 2011 sweep width: 6001Hz acq.time: 5.0s relax.time: 0.1s # scans: 16 dig.res.: 0.1 Hz/pt hz/mm:25.0 Pulse Sequence: s2pul
spectrometer:i3de file:/mnt/d600/home13/westnmr/nmrdata/DATA_FROM_NMRSERVICE/Ten-Ru/04-Mandy/heterocycles/2011.09.27.i5_TKW-7-83-2-benzene_H1_1D
10
9
8
7
6
5
4
3
2
1
0
ppm


125.692 MHz C13[H1] APT_s4 in cdcl3 (ref. to CDCl3 @ 77.06 ppm), temp 27.7 C -> actual temp = 27.0 C, colddual probe
240
220
200
180
160
140
120
100
80
60
40
20
0
ppm

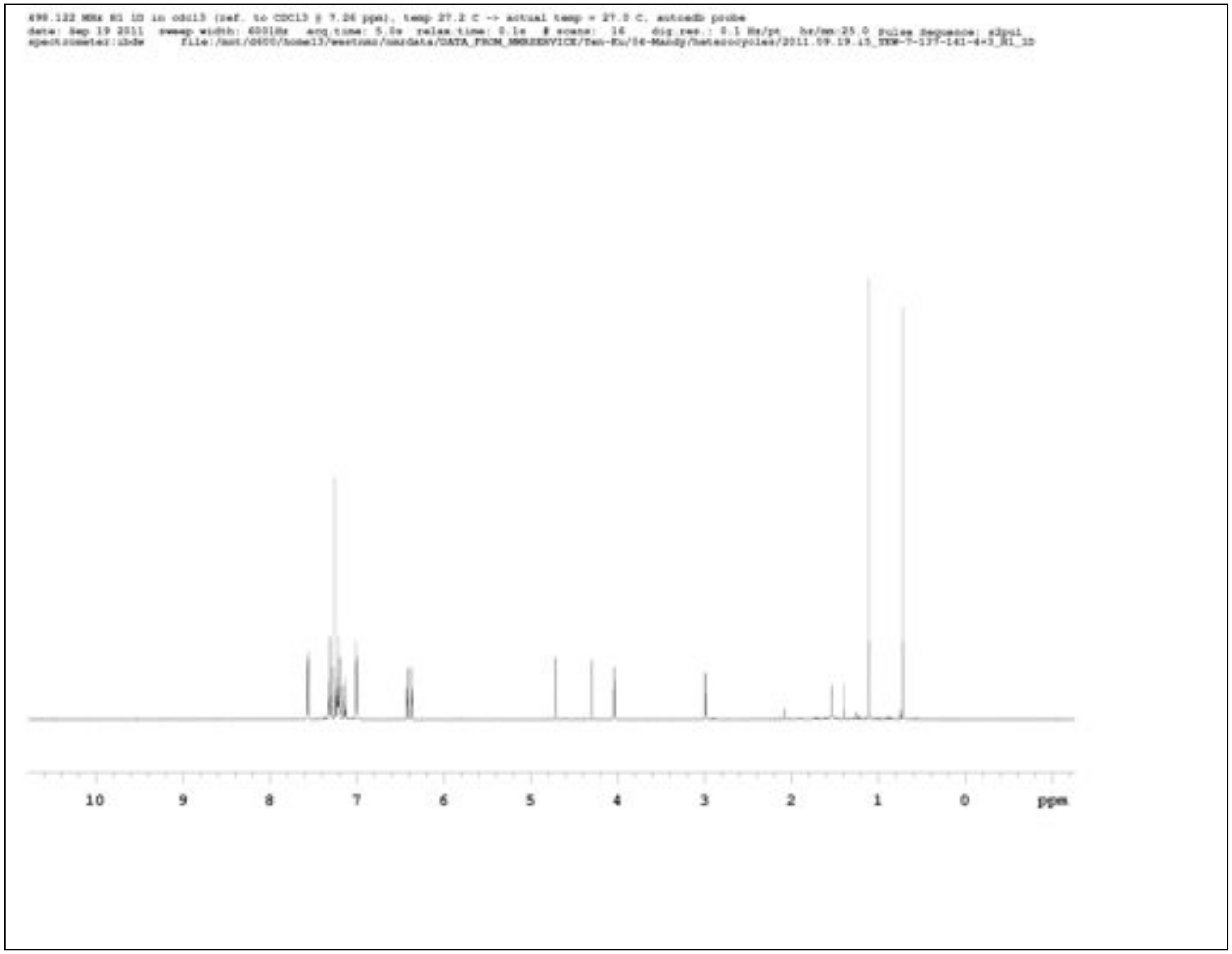

O
H
O
Ph
Ph
Me

21d

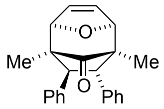


O
Me
Me
Ph
O
Ph

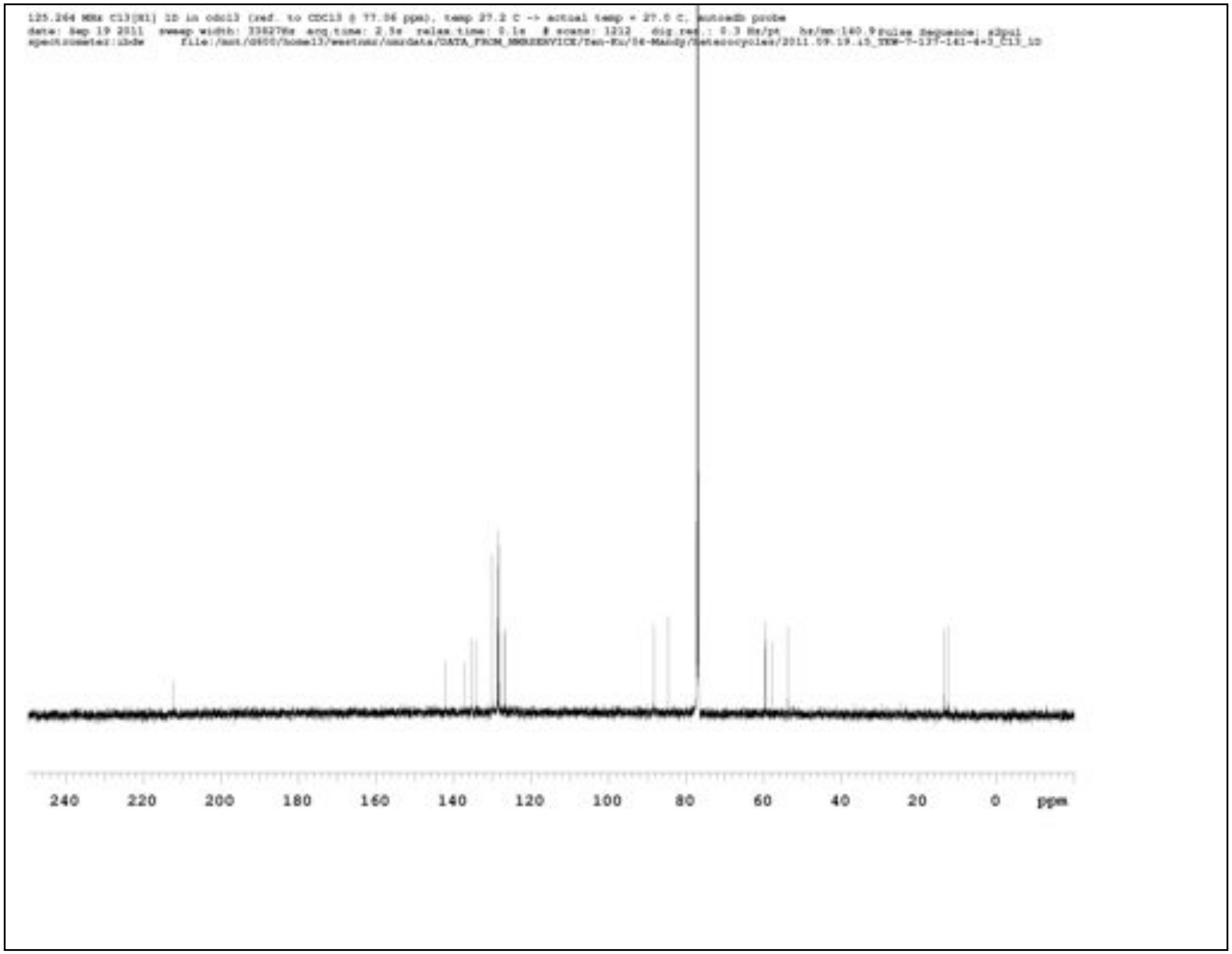
19

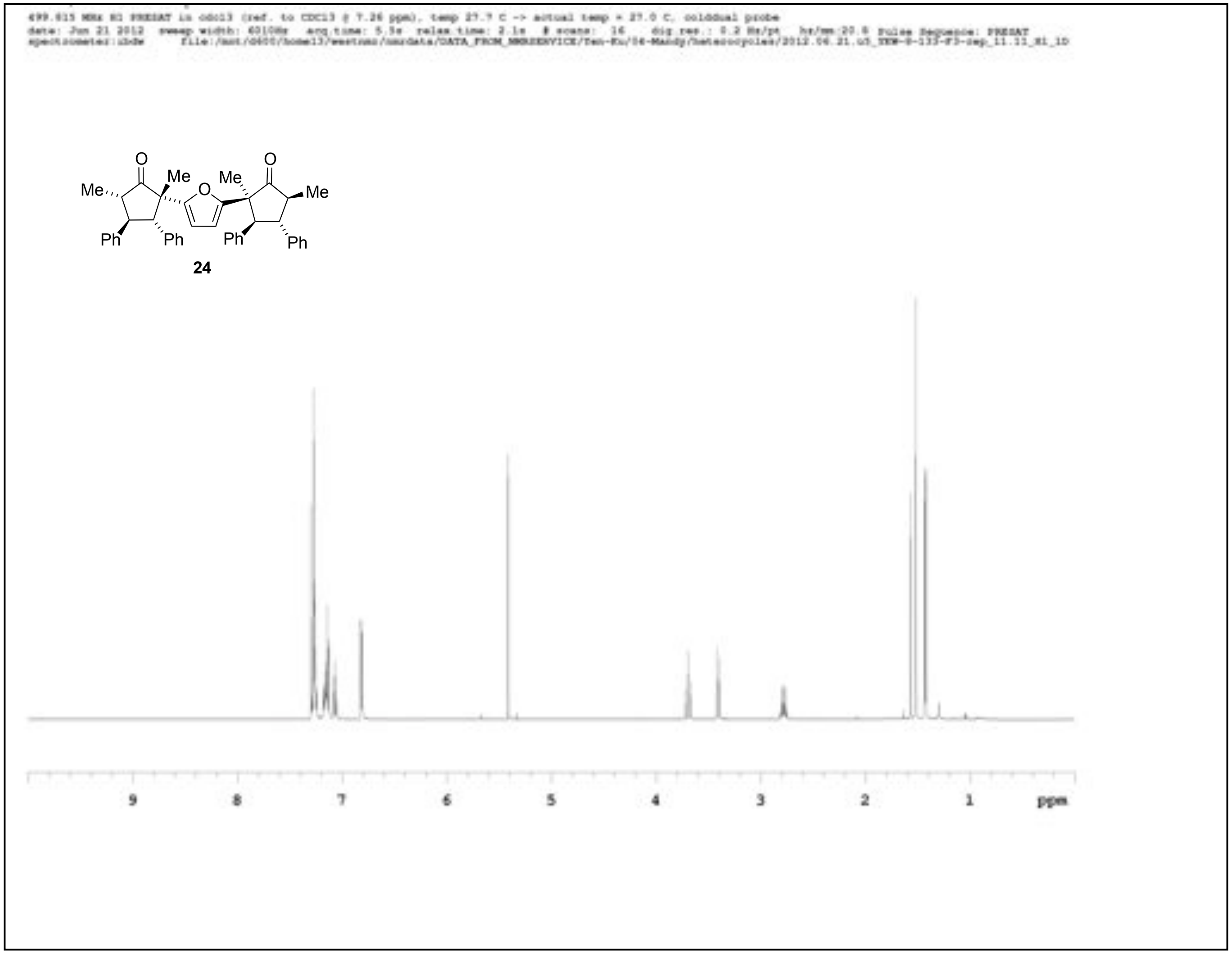


499.122 MHz H1 1D in cdcl3 (ref. to CDCl3 @ 7.26 ppm), temp 27.2 C -> actual temp = 27.0 C, autoxdb probe
date: Sep 19 2011 sweep width: 6001Hz acq time: 5.0s relax time: 0.1s # scans: 16 dig res.: 0.1 Hz/pt hz/mm:25.0 Pulse Sequence: s2pul
spectrometer:i1xde file:/mnt/d600/home13/westnmr/nmrdata/DATA_FROM_NMRSERVICE/Ten-Ku/04-Mandy/heterocycles/2011.09.19.i5_TKW-7-137-141-4+3_H1_1D
10
9
8
7
6
5
4
3
2
1
0
ppm

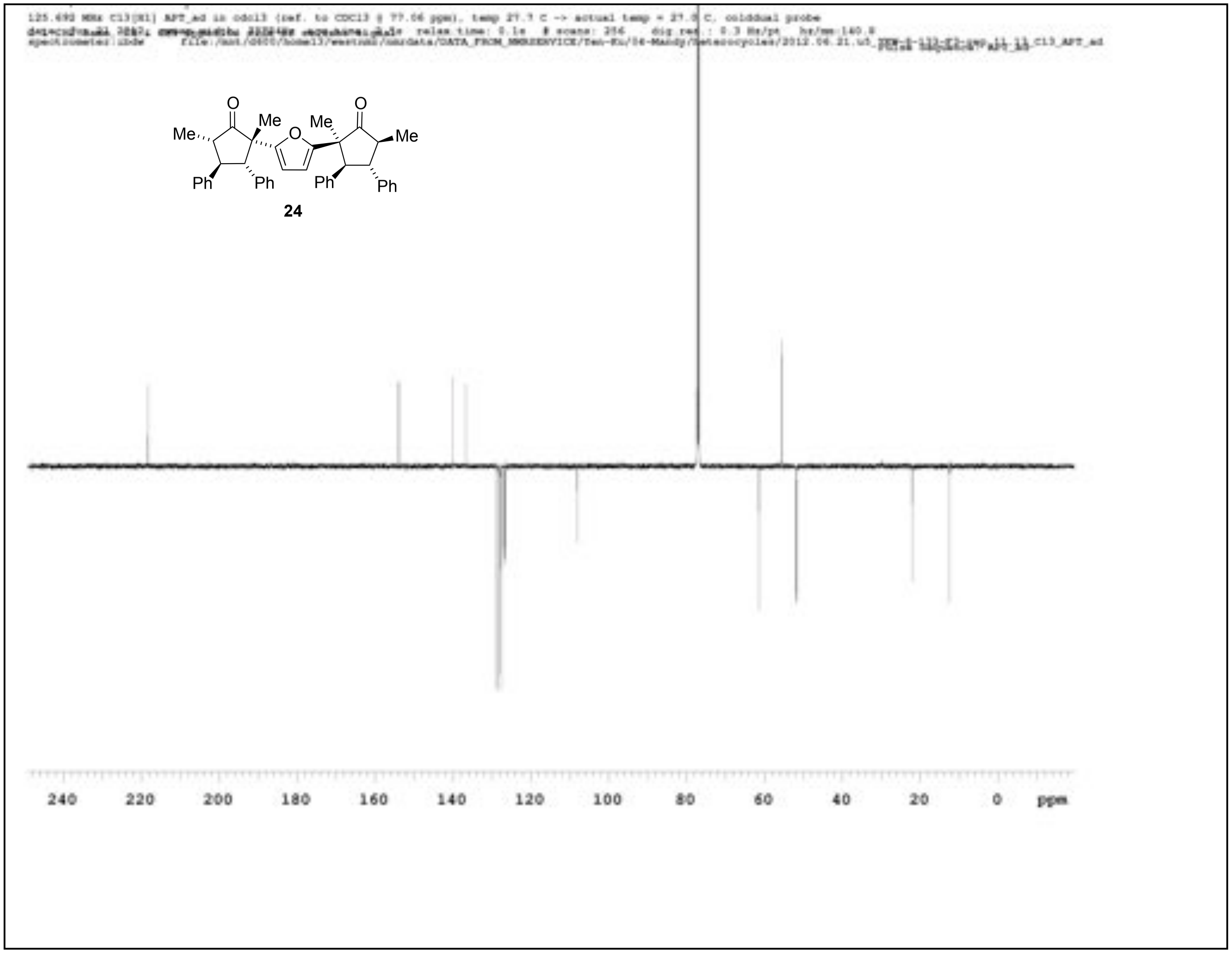

O
Me
Me
Ph
O
Ph

19

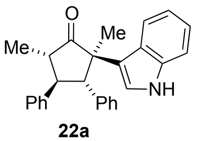

125.264 MHz C13[H1] 1D in cdcl3 (ref. to CDCl3 @ 77.06 ppm), temp 27.2 C -> actual temp = 27.0 C, autoxdb probe
date: Sep 19 2011 sweep width: 33827Hz acq time: 2.5s relax time: 0.1s # scans: 1212 dig res.: 0.3 Hz/pt hz/mm:140.9 Pulse Sequence: s2pul
spectrometer:i3dw file:/mnt/d600/home13/westnmr/nmrdata/DATA_FROM_NMRSERVICE/Ten-Hu/06-Mandy/Heterocycles/2011.09.19.i3_TEW-7-137-141-4-3_C13_1D
240
220
200
180
160
140
120
100
80
60
40
20
0
ppm

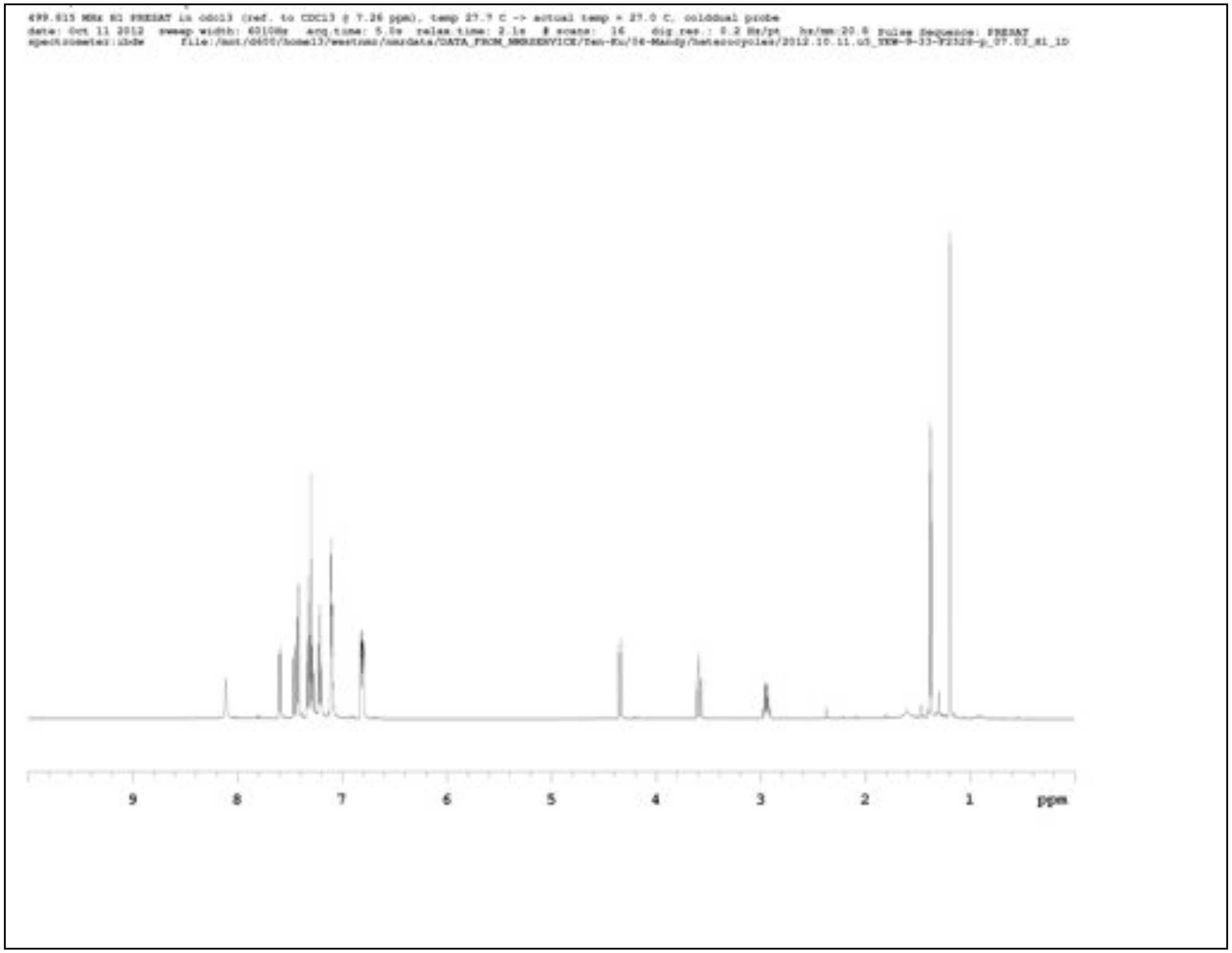

499.615 MHz H1 PRESAT in cdcl3 (ref. to CDCl3 @ 7.26 ppm), temp 27.7 C -> actual temp = 27.0 C, colddual probe
date: Jun 21 2012 sweep width: 6010Hz acq time: 5.3s relax time: 2.1s # scans: 16 dig res.: 0.2 Hz/pt hz/mm: 20.0 Pulse Sequence: PRESAT
spectrometer: i3c8w file: /mnt/d600/home13/westnmr/nmrdata/DATA_FROM_NMRSERVICE/Ten-Ku/04-Mandy/heterocycles/2012.06.21.u5_TKW-0-133-F3-sep_11.11_01_1D
O
Me
Me
O
Me
O
Me
Ph
Ph
Ph
Ph
9
8
7
6
5
4
3
2
1
ppm

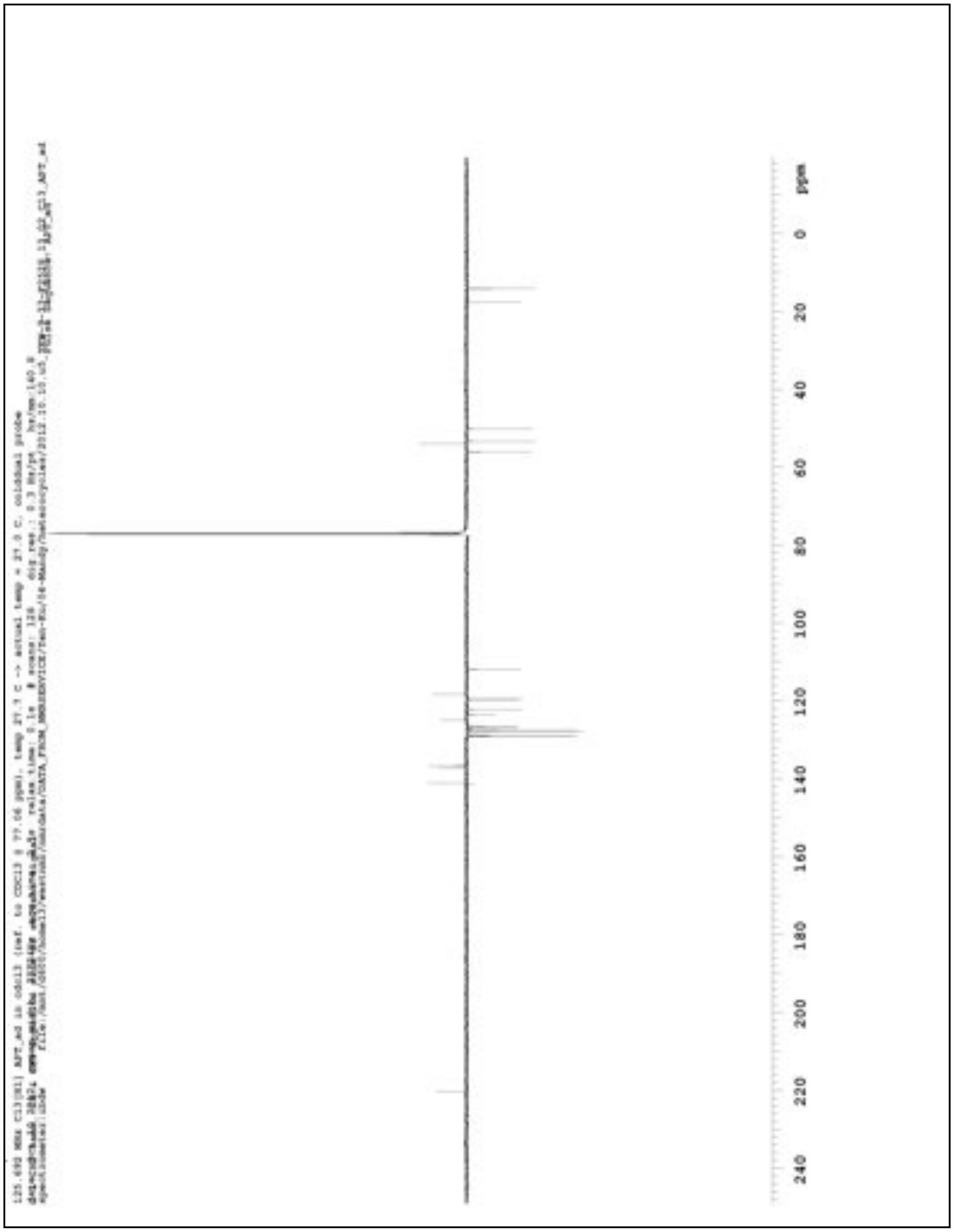
24

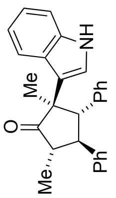

125.692 MHz C13[H1] APT_ad in cdcl3 (ref. to CDCl3 @ 77.06 ppm), temp 27.7 C -> actual temp = 27.0 C, colddual probe
relax. time: 0.1s # scans: 256 dig. res.: 0.3 Hz/pt hz/mm:140.8
O
Me
Me
O
Me
Me
Ph
Ph
Ph
Ph
240
220
200
180
160
140
120
100
80
60
40
20
0
ppm

24

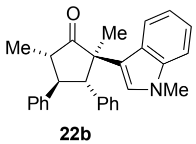

22a


499.815 MHz H1 PRESAT in cdcl3 (ref. to CDCl3 @ 7.26 ppm), temp 27.7 C -> actual temp = 27.0 C, colddual probe
date: Oct 11 2012 sweep width: 6010Hz acq time: 5.0s relax time: 2.1s # scans: 16 dig res.: 0.2 Hz/pt hz/mm: 20.0 Pulse Sequence: PRESAT
9
8
7
6
5
4
3
2
1
ppm

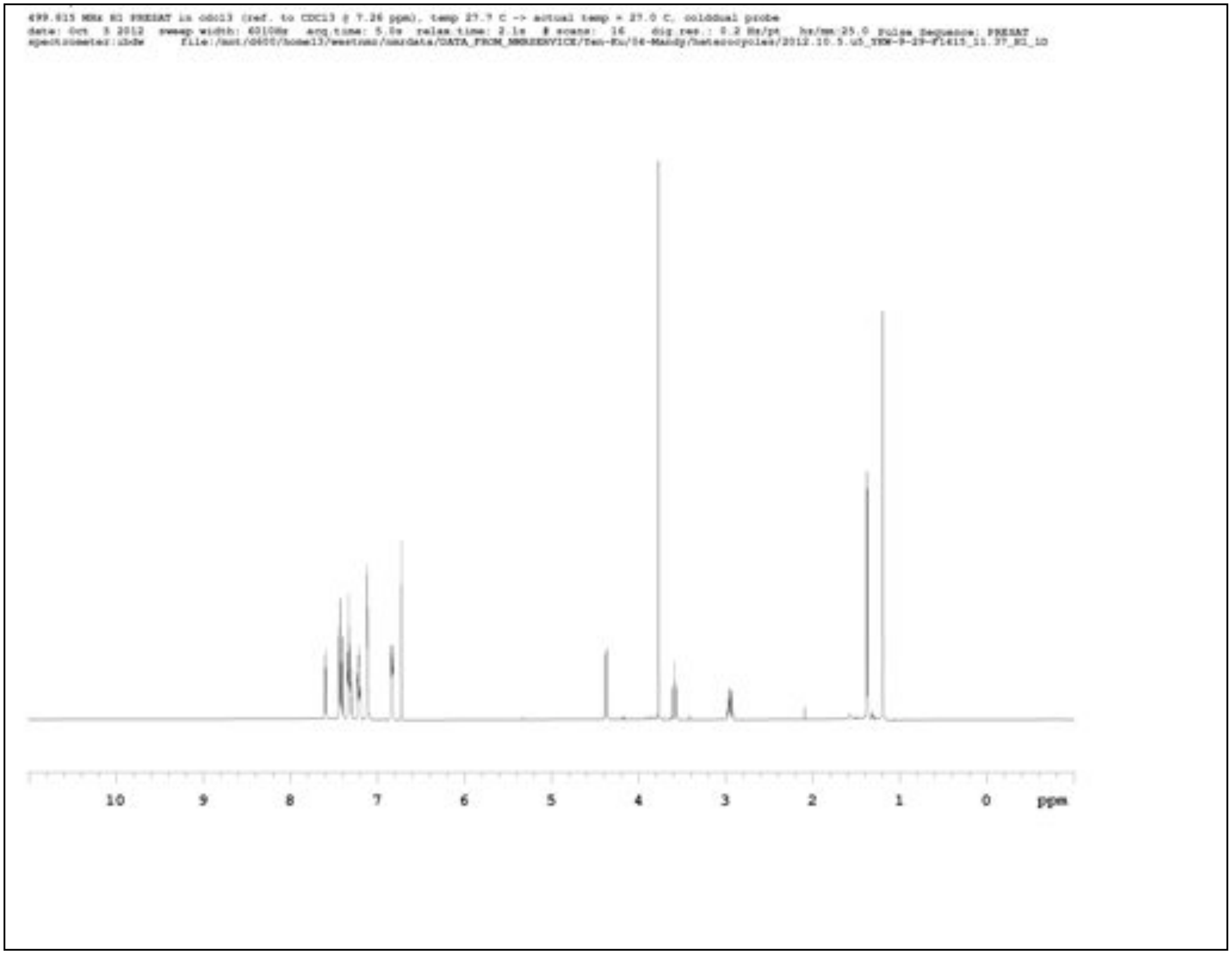

125.692 MHz C13[H1] APT_ad in cdcl3 (ref. to CDCl3 @ 77.06 ppm), temp 27.7 C -> actual temp = 27.0 C, coldual probe
240
220
200
180
160
140
120
100
80
60
40
20
0
ppm

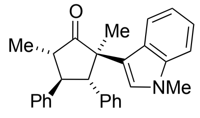

NH
Me
Ph
O
Me
Ph

22a

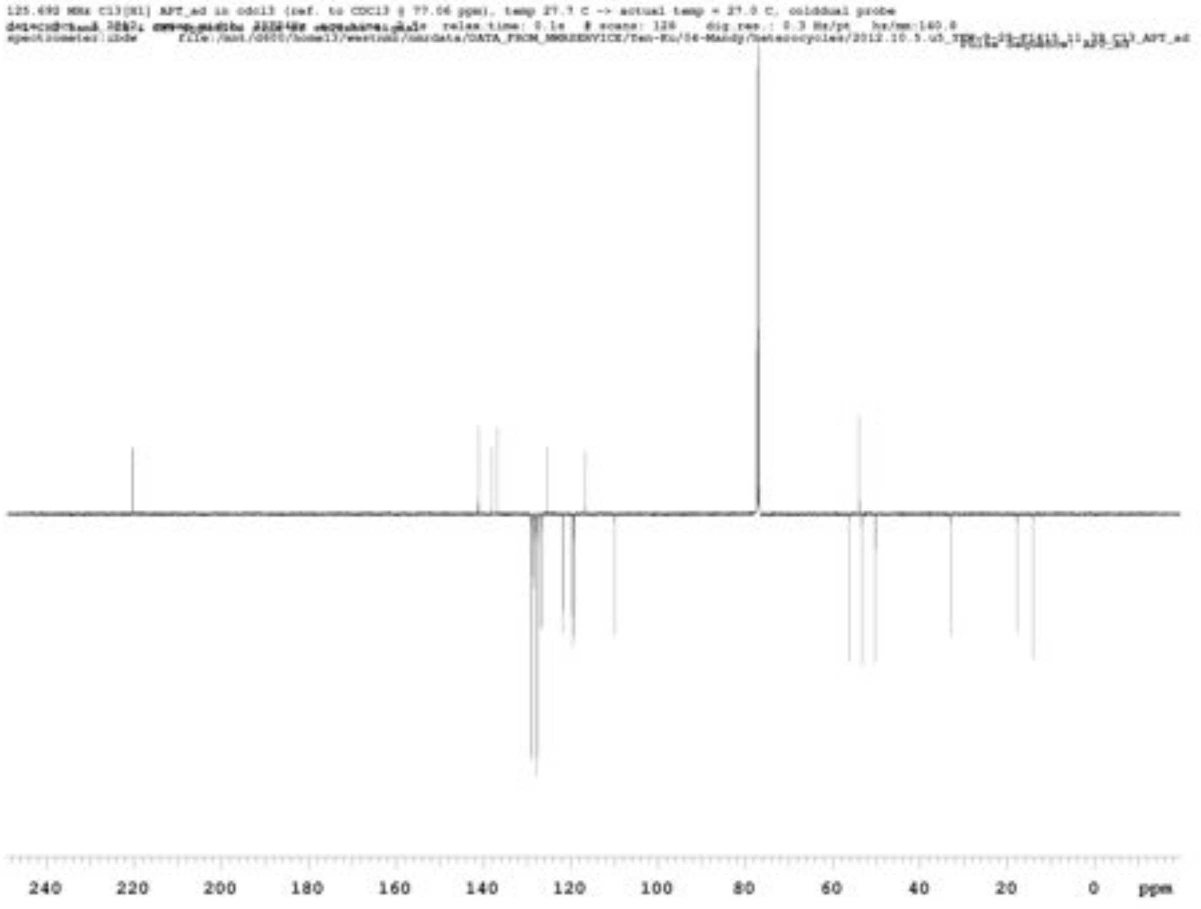

O
Me
Me
Ph
Ph
NMe

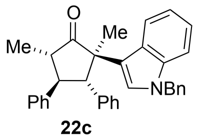
22b


499.815 MHz H1 PRESAT in cdcl3 (ref. to CDCl3 @ 7.26 ppm), temp 27.7 C -> actual temp = 27.0 C, colddual probe
date: Oct 3 2012 sweep width: 6010Hz acq time: 5.0s relax time: 2.1s # scans: 16 dig res.: 0.2 Hz/pt hz/mm:25.0 Pulse Sequence: PRESAT
spectrometer:i3dw file:/mnt/d600/home13/westuma/nmrdata/DATA_FROM_NMRSERVICE/Ten-Ru/36-Mandy/heterocycles/2012.10.5.u5_YEW-9-29-F1613_11.37_H1_1D
10
9
8
7
6
5
4
3
2
1
0
ppm

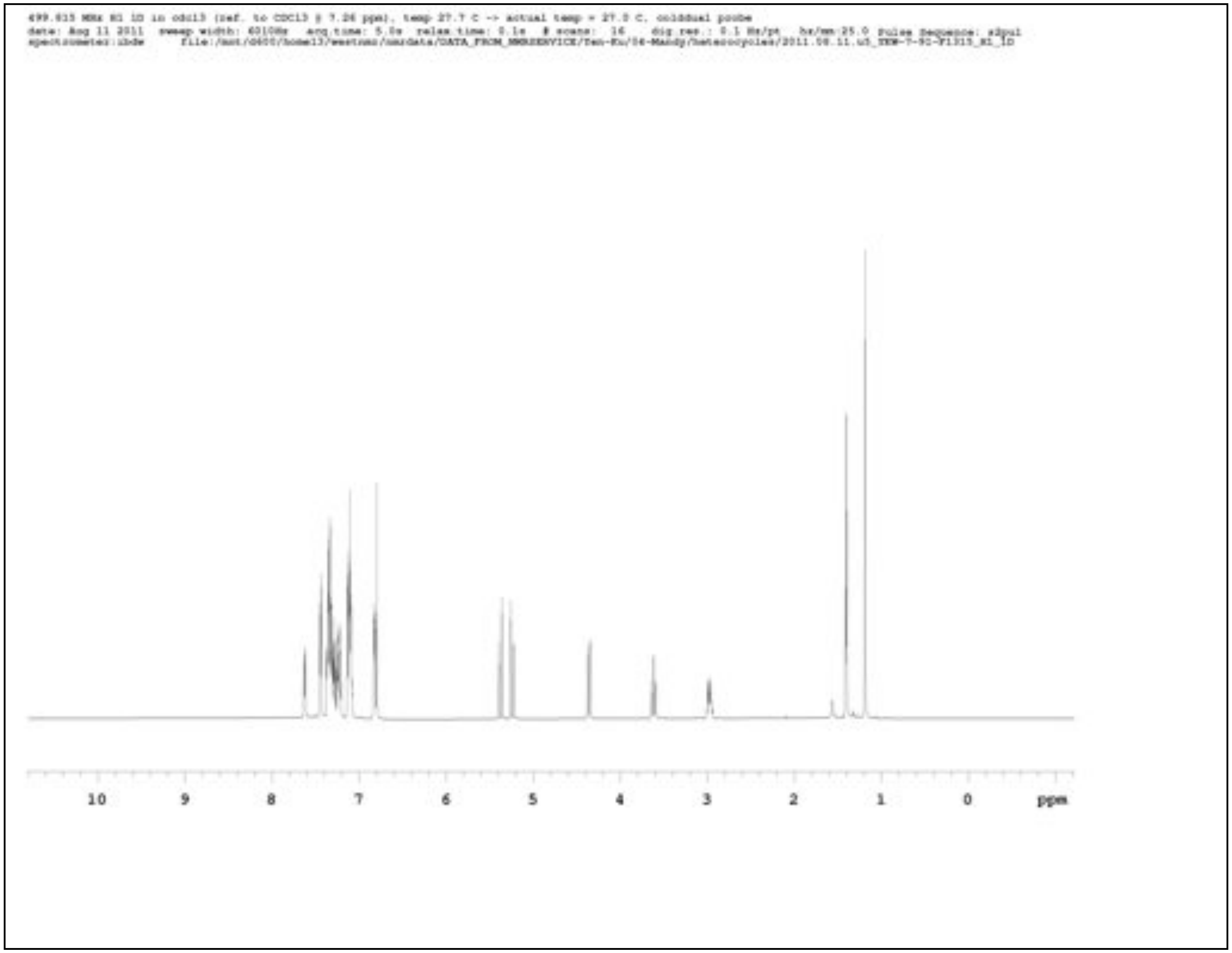


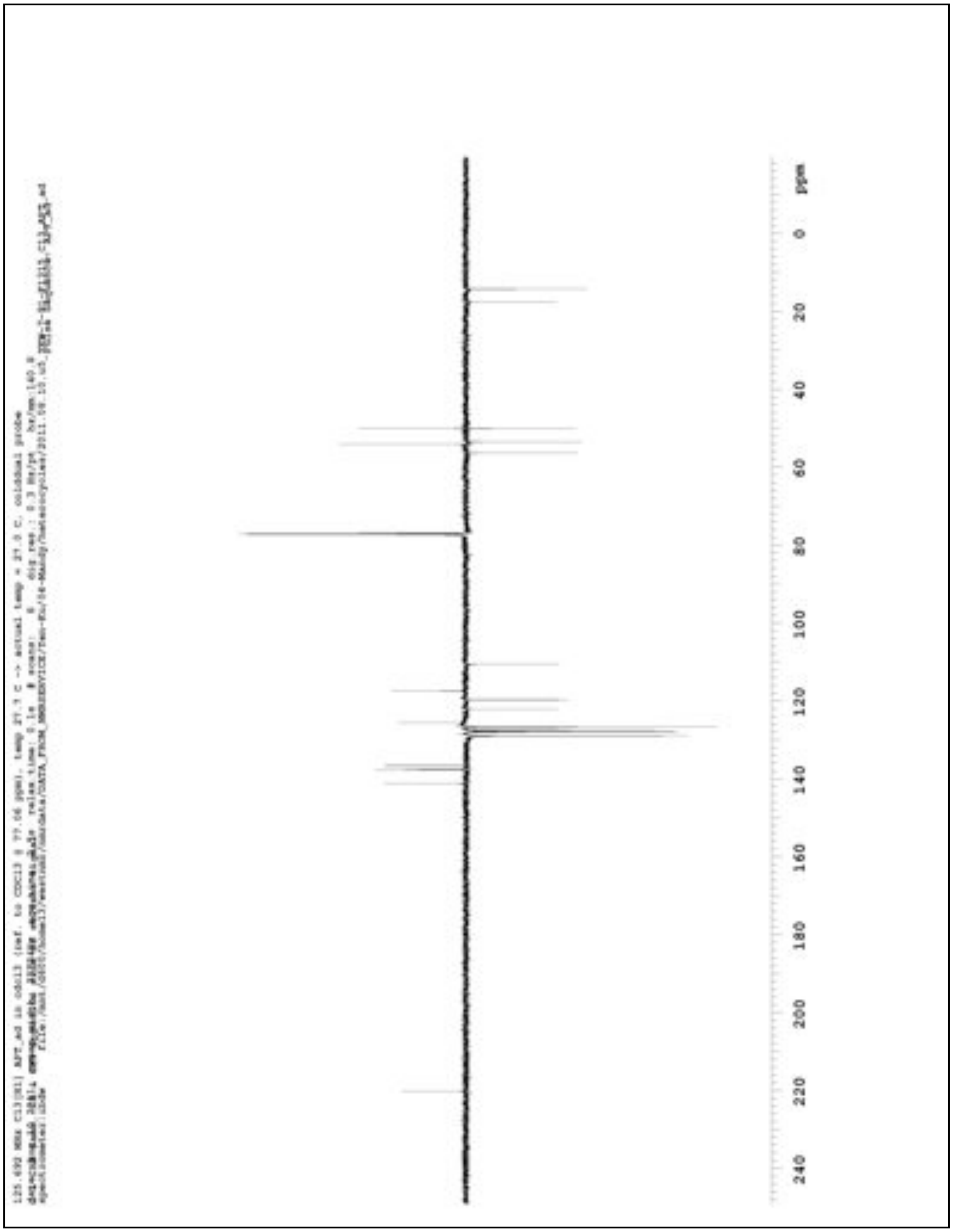
22b

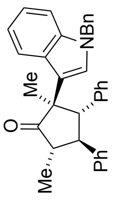

125.692 MHz C13[H1] APT_ad in cdcl3 (ref. to CDCl3 @ 77.06 ppm), temp 27.7 C -> actual temp = 27.0 C, colddual probe
relax time: 0.1s # scans: 128 dig res.: 0.3 Hz/pt hz/mm:140.6
spectrometer:ibdw file:/mnt/d600/home13/westuser/nmrdata/DATA_FROM_NMRSERVICE/Ten-Ku/04-Mandy/heterocycles/2012.10.5.u5_APT_ad
240
220
200
180
160
140
120
100
80
60
40
20
0
ppm


O
Me
Me
NBn
Ph
Ph

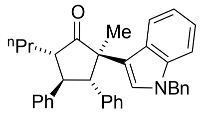
22c


499.815 MHz H1 1D in cdcl3 (ref. to CDCl3 @ 7.26 ppm), temp 27.7 C -> actual temp = 27.0 C, colddual probe
date: Aug 11 2011 sweep width: 6010Hz acq time: 5.0s relax time: 0.1s # scans: 16 dig res.: 0.1 Hz/pt hz/mm:25.0 Pulse Sequence: s2pul
spectrometer:ibdw file:/mnt/d600/home13/westonz/nmrdata/DATA_FROM_NMRSERVICE/Ten-Ku/04-Mandy/heterocycles/2011.08.11.u5_TKW-7-92-F1315_H1_1D
10
9
8
7
6
5
4
3
2
1
0
ppm

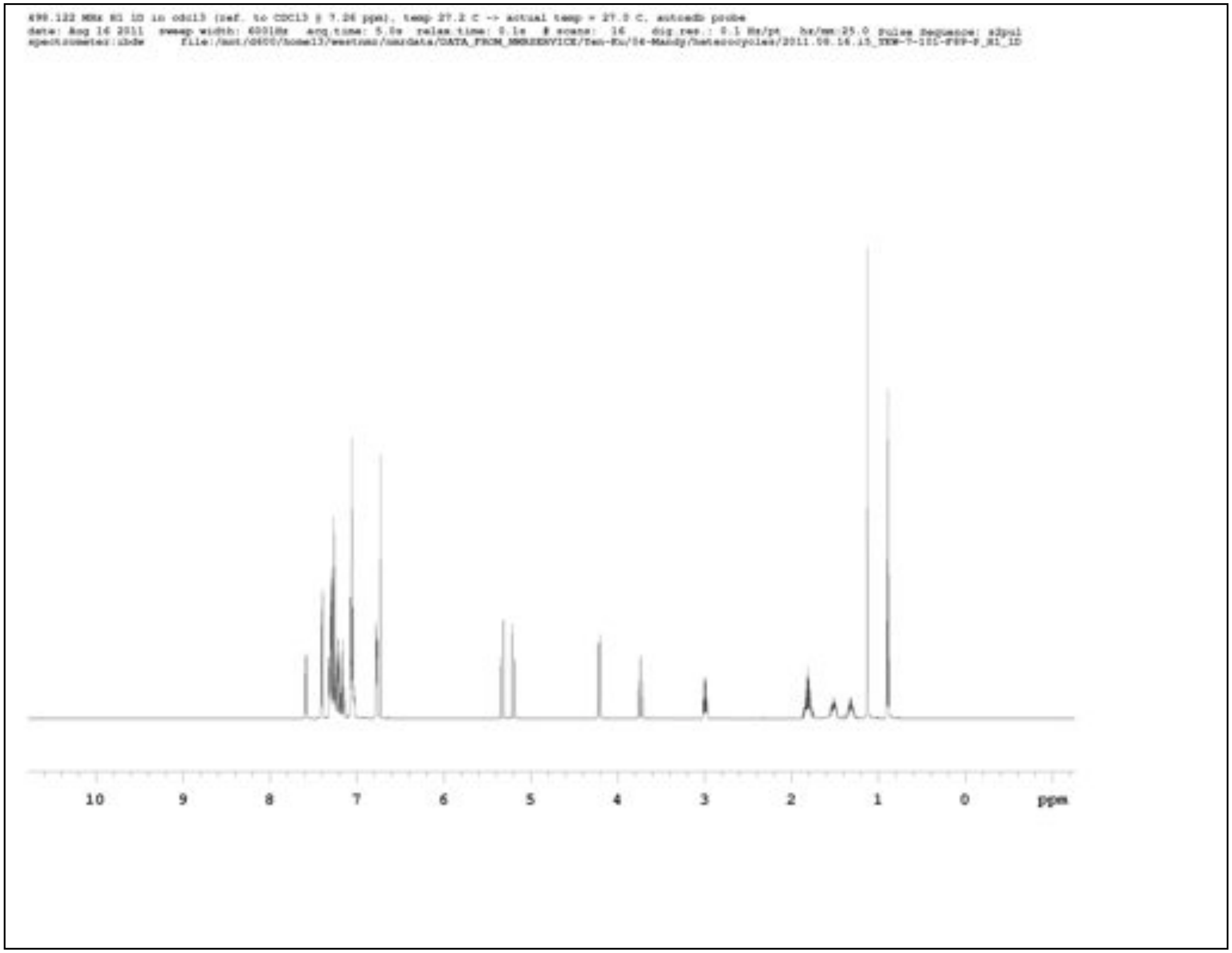


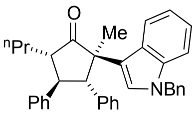


22c


O
Me
ⁿPr
Ph
Ph
NBn

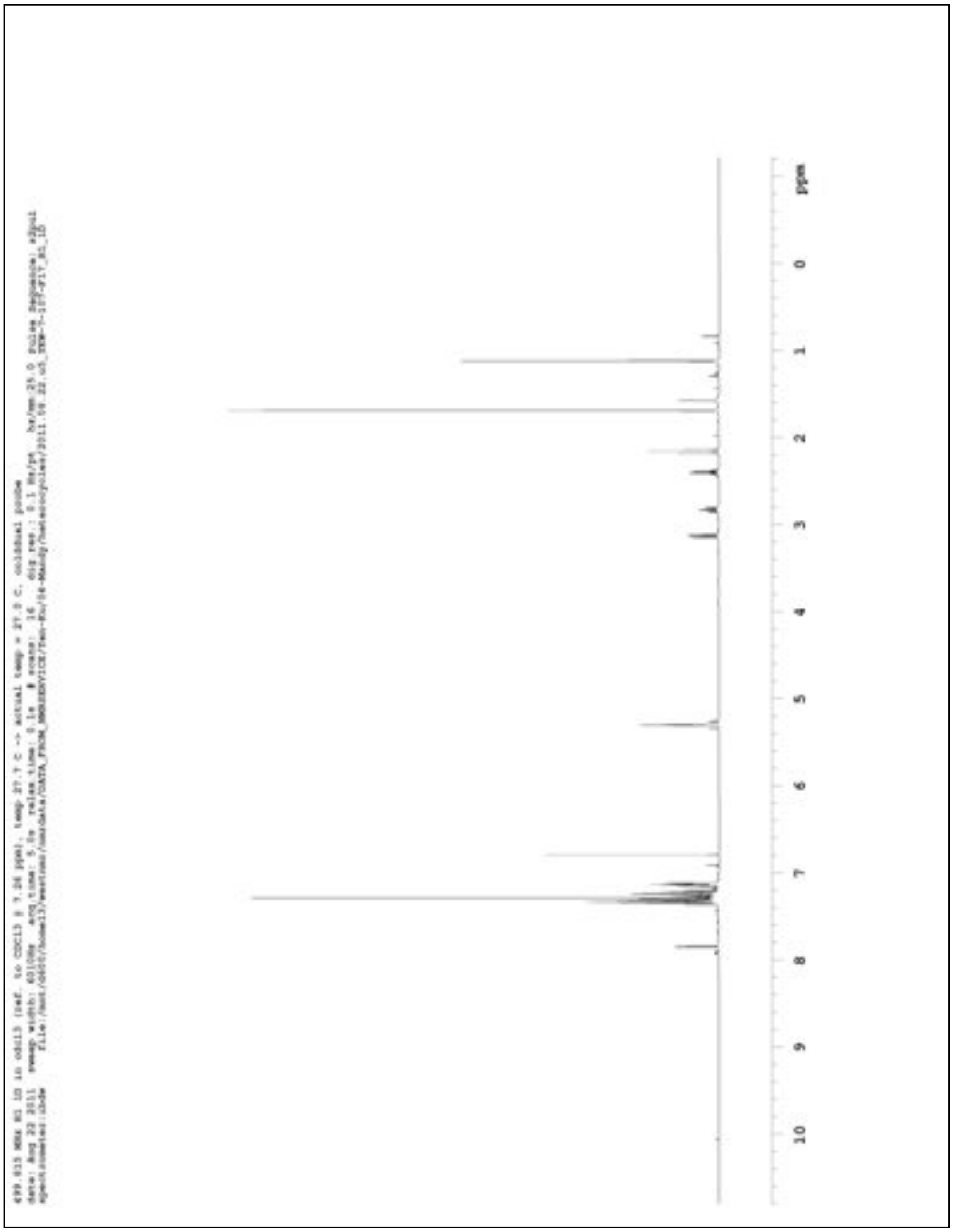
22d

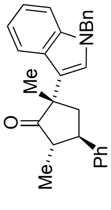

499.122 MHz H1 1D in cdcl3 (ref. to CDCl3 @ 7.26 ppm), temp 27.2 C -> actual temp = 27.0 C, autoxdb probe
date: Aug 16 2011 sweep width: 6001Hz acq.time: 5.0s relax.time: 0.1s # scans: 16 dig.res.: 0.1 Hz/pt hz/mm:25.0 Pulse Sequence: s2pul
spectrometer:ib4w file:/mnt/d600/home13/westums/nmrdata/DATA_FROM_NMRSERVICE/Ten-Ku/06-Mandy/heterocycles/2011.08.16.i5_TKW-7-101-F99-F_H1_1D
10
9
8
7
6
5
4
3
2
1
0
ppm


O
Me
ⁿPr
Ph
Ph
NBn

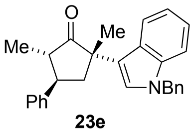
22d


125.692 MHz C13[H1] APT_ad in cdcl3 (ref. to CDCl3 @ 77.06 ppm), temp 27.7 C -> actual temp = 27.0 C, colddual probe
relax time: 0.1s # scans: 44 dig res.: 0.3 Hz/pt hz/mm:140.8
240
220
200
180
160
140
120
100
80
60
40
20
0
ppm

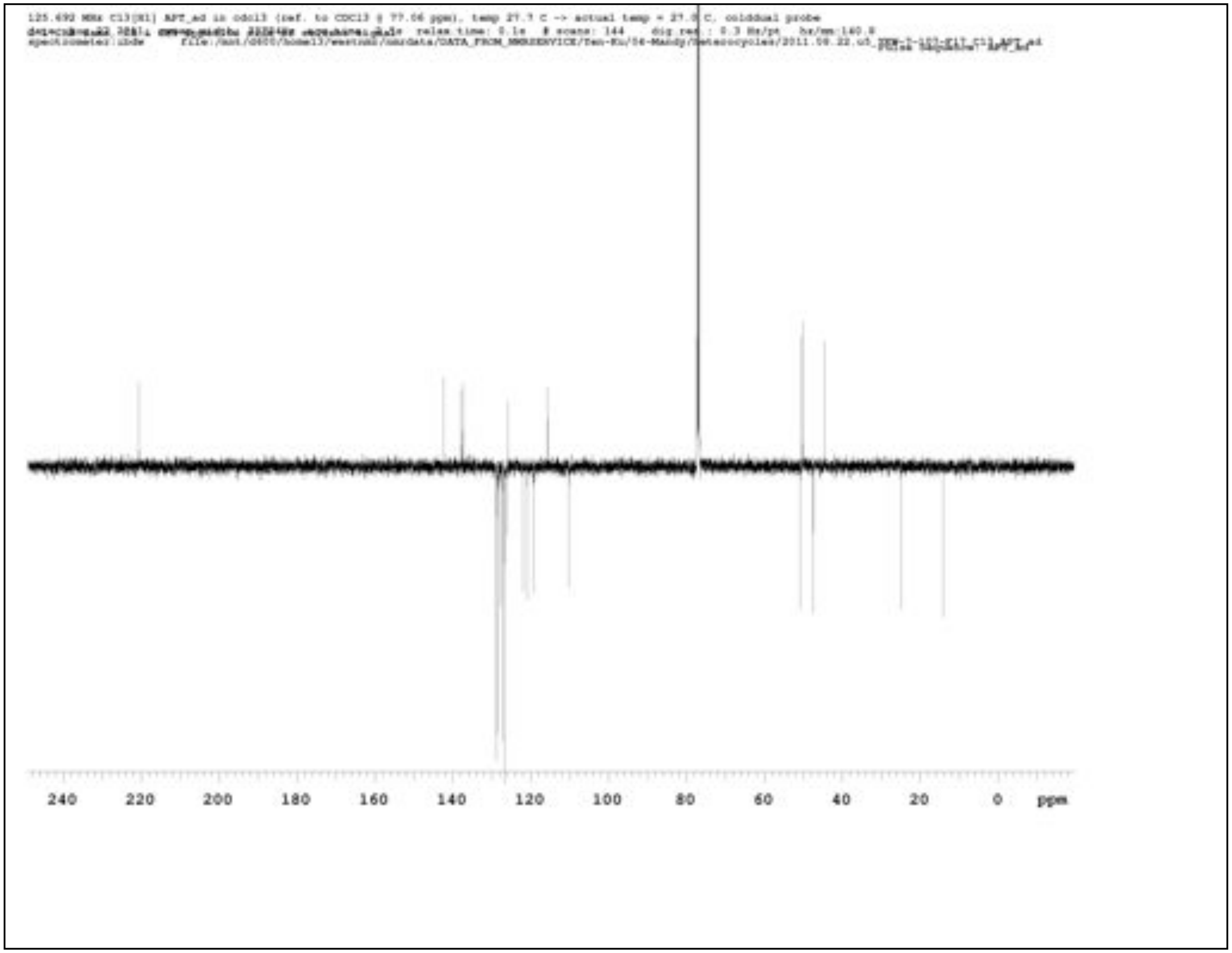

499.815 MHz H1 1D in cdcl3 (ref. to CDCl3 @ 7.26 ppm), temp 27.7 C -> actual temp = 27.0 C, coldual probe
10
9
8
7
6
5
4
3
2
1
0
ppm

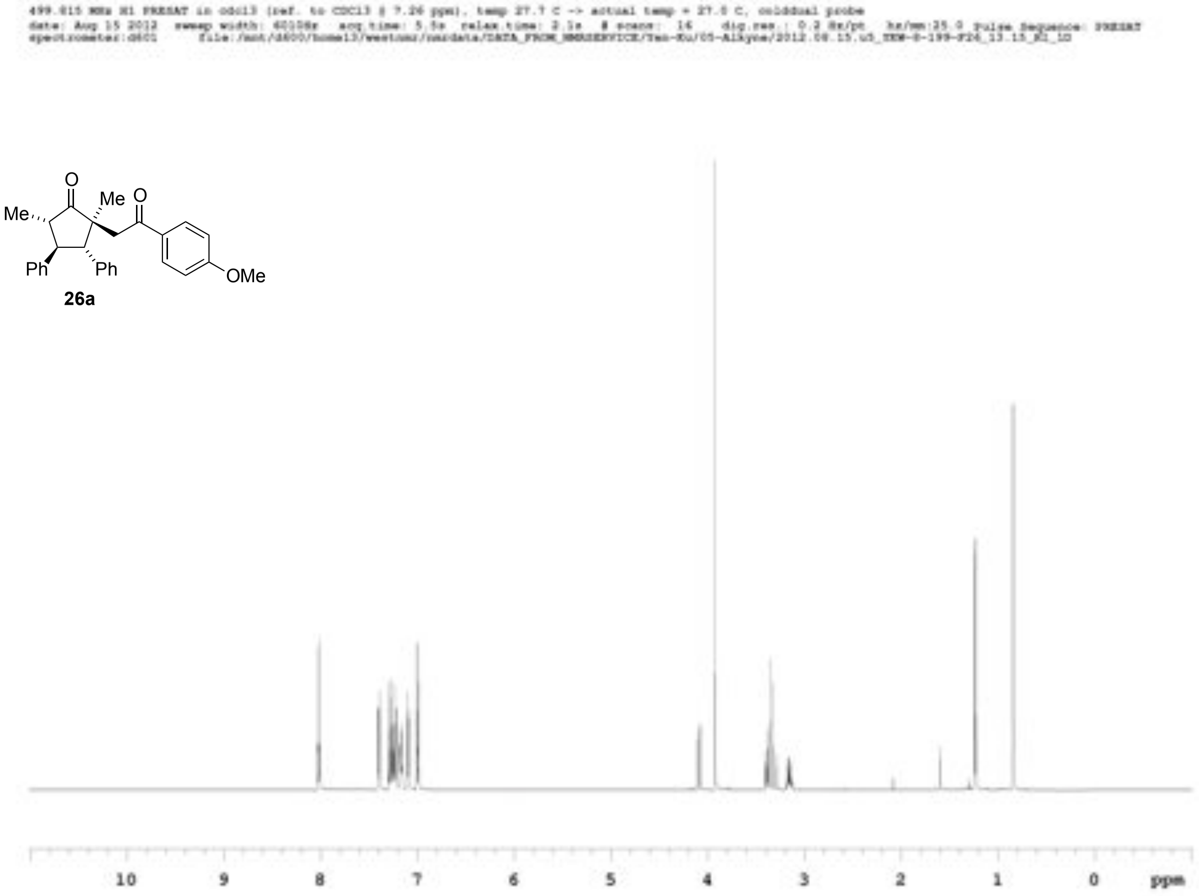

NBn
Me
O
Me
Ph

23e

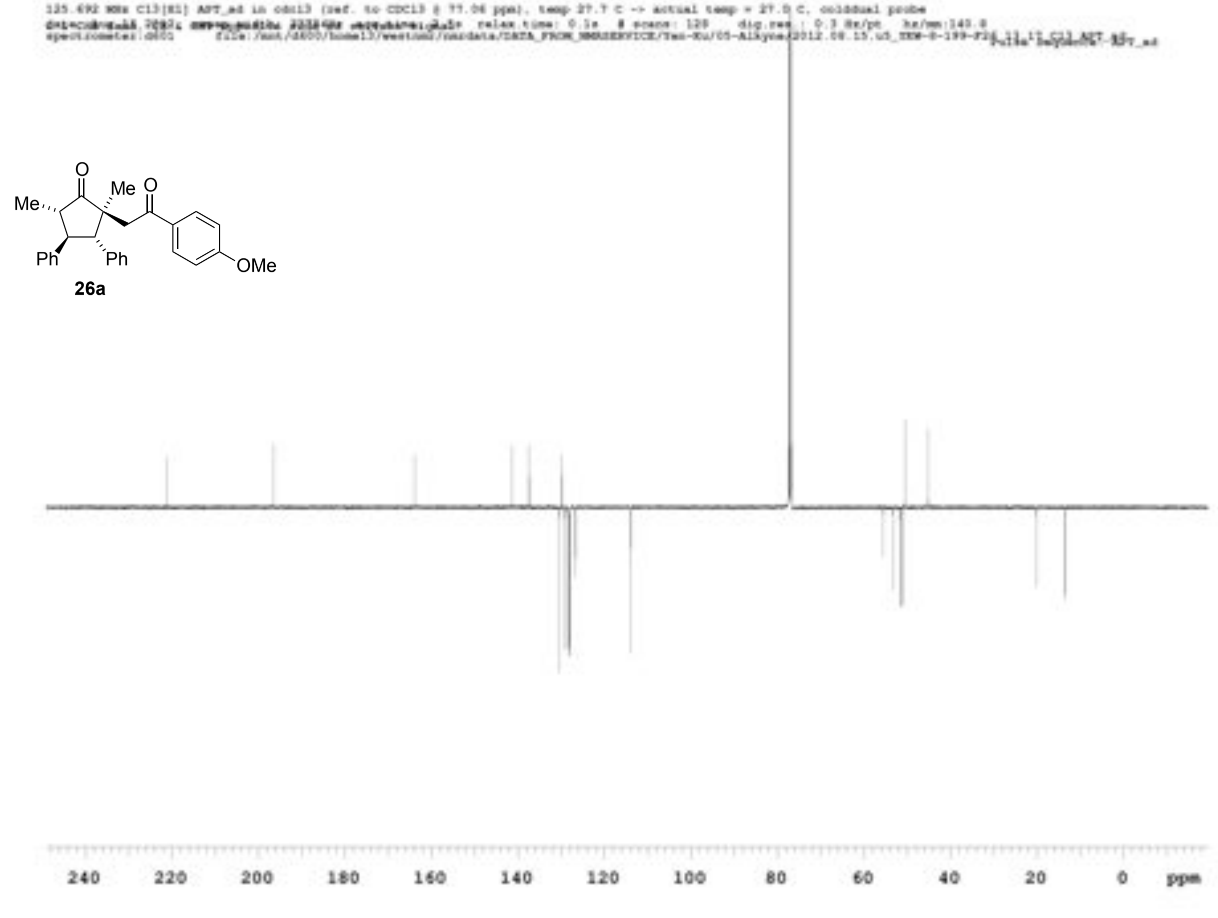

O
Me
Me
Ph
NBn

23e

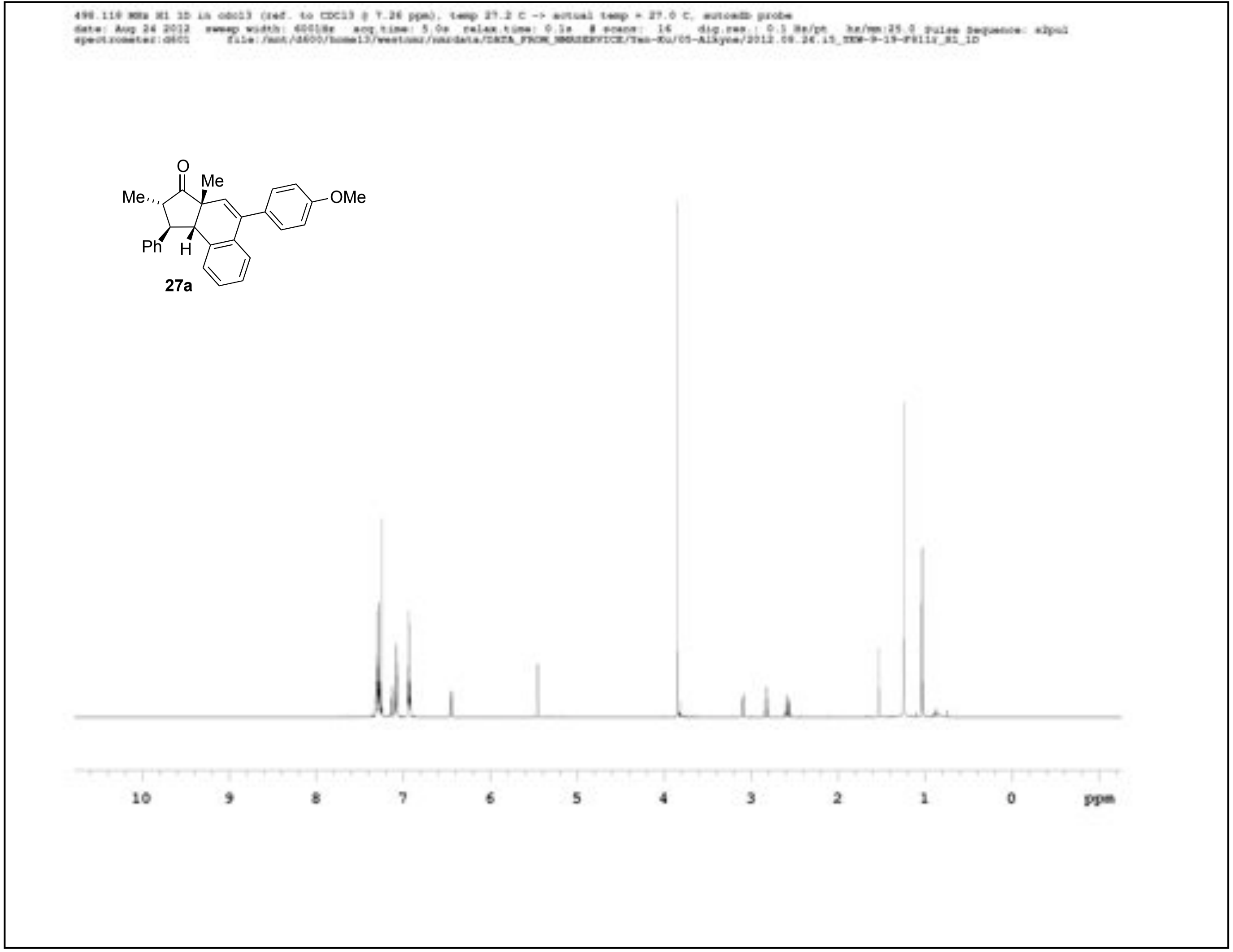

125.692 MHz C13[H1] APT_ad in cdcl3 (ref. to CDCl3 @ 77.06 ppm), temp 27.7 C -> actual temp = 27.0 C, colddual probe
relax time: 0.1s # scans: 144 dig res.: 0.3 Hz/pt hz/mm:140.8
spectrometer:inde file:/mnt/d600/home13/westnmr/nmrdata/DATA_FROM_NMRSERVICE/Tan-Ru/04-Mandy/Heterocycles/2011.08.22.u5
240
220
200
180
160
140
120
100
80
60
40
20
0
ppm


499.815 MHz H1 PRESAT in cdcl3 (ref. to CDCl3 @ 7.26 ppm), temp 27.7 C -> actual temp = 27.0 C, colddual probe
date: Aug 15 2012 sweep width: 4010Hz acq.time: 5.5s relax.time: 2.1s # scans: 16 dig.res.: 0.2 Hz/pt hz/mm:25.0 Pulse Sequence: PRESAT
spectrometer:d601 file:/mnt/d600/home13/westonr/nmrdata/DATA_FROM_NMRSERVICE/Yan-Xu/05-Alkyne/2012.08.15.u5_TXW-8-199-F26_13.15_H1_1D
O
Me
O
Me
Ph
Ph
OMe
10
9
8
7
6
5
4
3
2
1
0
ppm

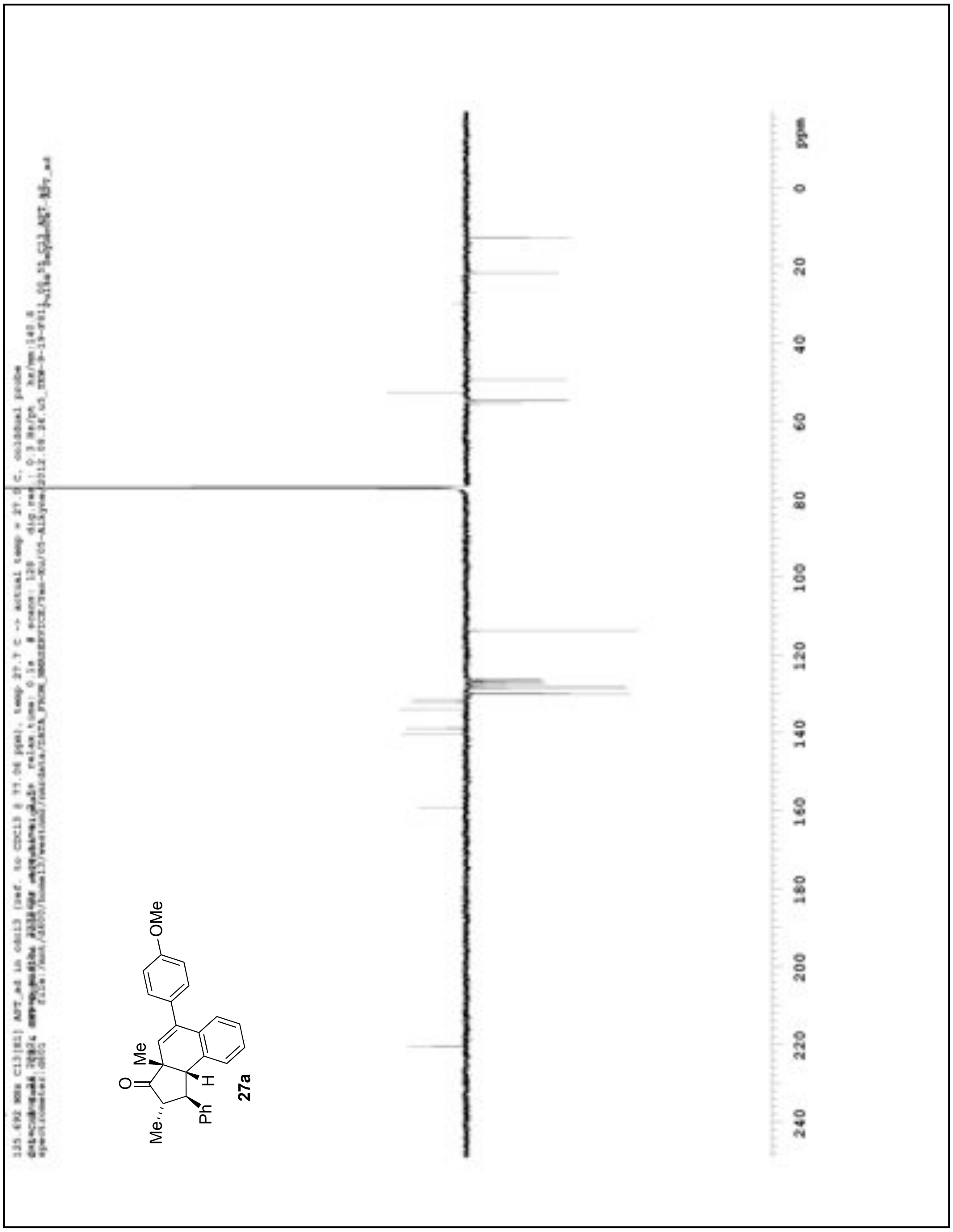
26a


125.692 MHz C13[H1] APT_ad in cdcl3 (ref. to CDCl3 @ 77.06 ppm), temp 27.7 C -> actual temp = 27.0 C, colddual probe
relax.time: 0.1s # scans: 128 dig.res.: 0.3 Hz/pt hz/mm:140.8
spectrometer:d601 file:/mnt/d600/home13/westonl/nmrdata/DATA_FROM_NMRSERVICE/Tan-Xu/05-Alkyne/2012.08.15.u5_TXW-0-199-F2
O
Me
Me
O
Ph
Ph
OMe
240
220
200
180
160
140
120
100
80
60
40
20
0
ppm

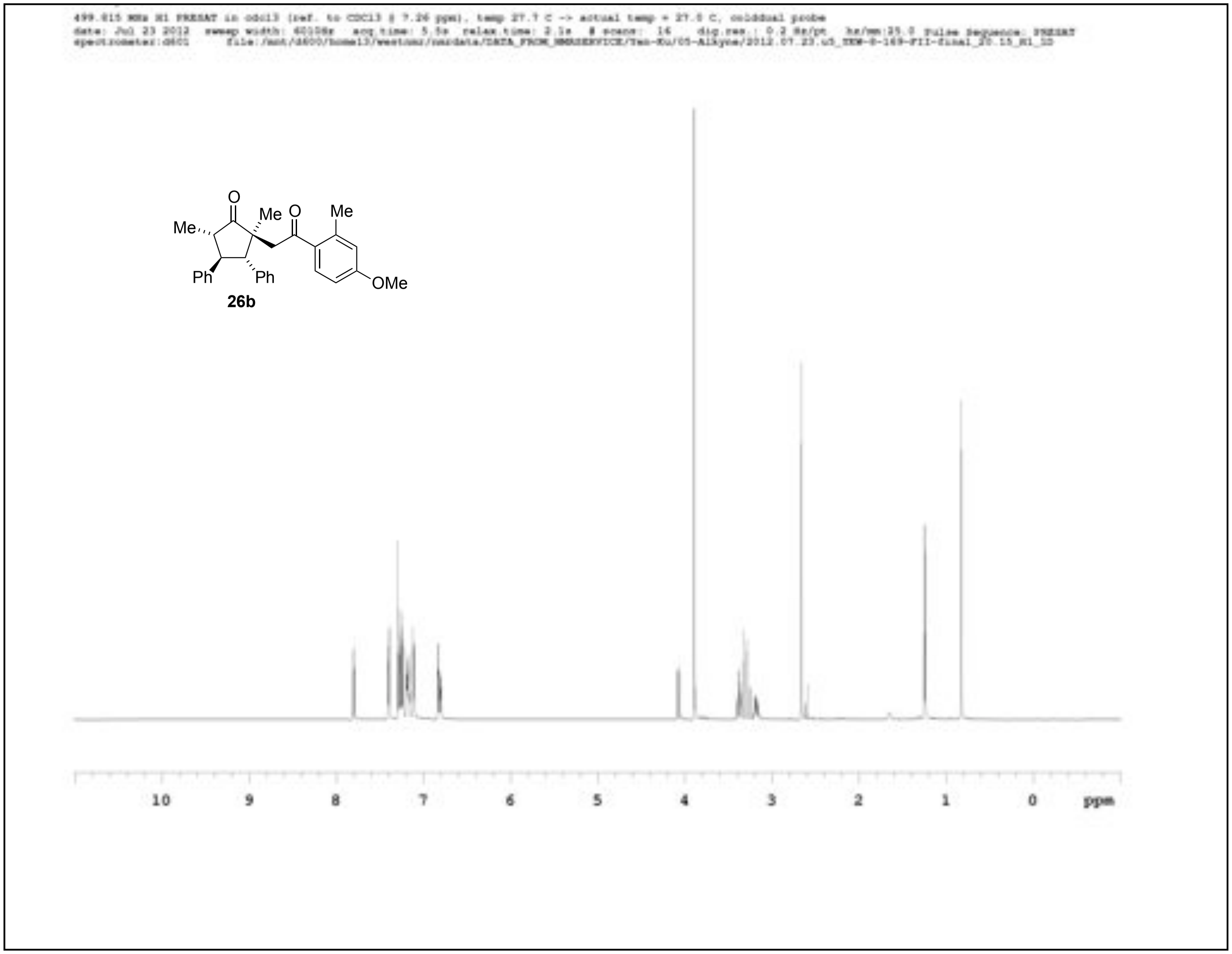
26a


499.110 MHz H1 1D in cdcl3 (ref. to CDCl3 @ 7.26 ppm), temp 27.2 C -> actual temp = 27.0 C, autoxdb probe
date: Aug 24 2012 sweep width: 6001Hz acq.time: 5.0s relax.time: 0.1s # scans: 16 dig.res.: 0.1 Hz/pt hz/mm:25.0 Pulse Sequence: s2pul
spectrometer:d601 file:/mnt/d600/home13/westonz/nmrdata/DATA_FROM_NMRSERVICE/Yan-Xu/05-Alkyne/2012.08.24.15_YXW-9-19-F8112_H1_1D
O
Me
Me
OMe
Ph
H
10
9
8
7
6
5
4
3
2
1
0
ppm

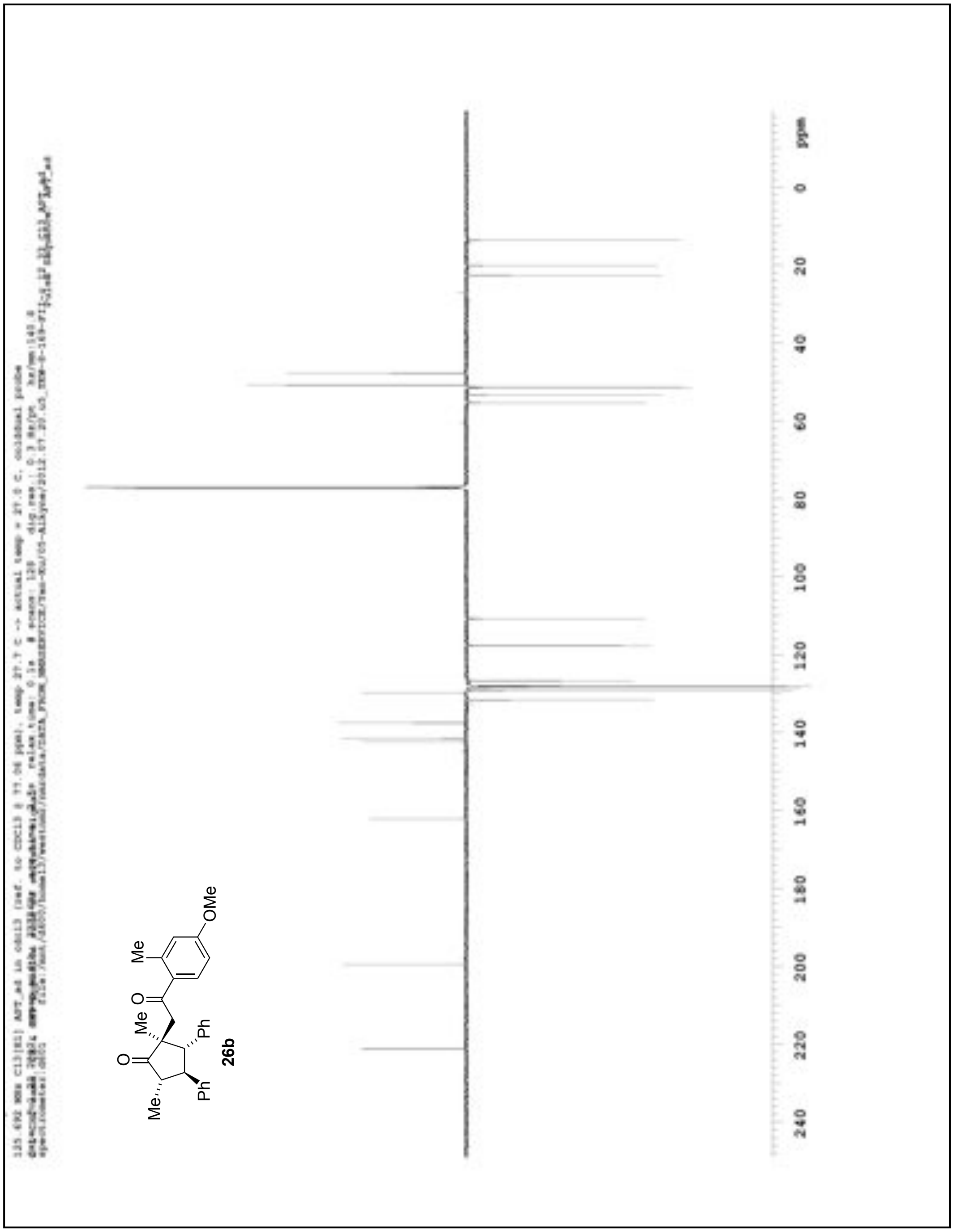
27a



27a

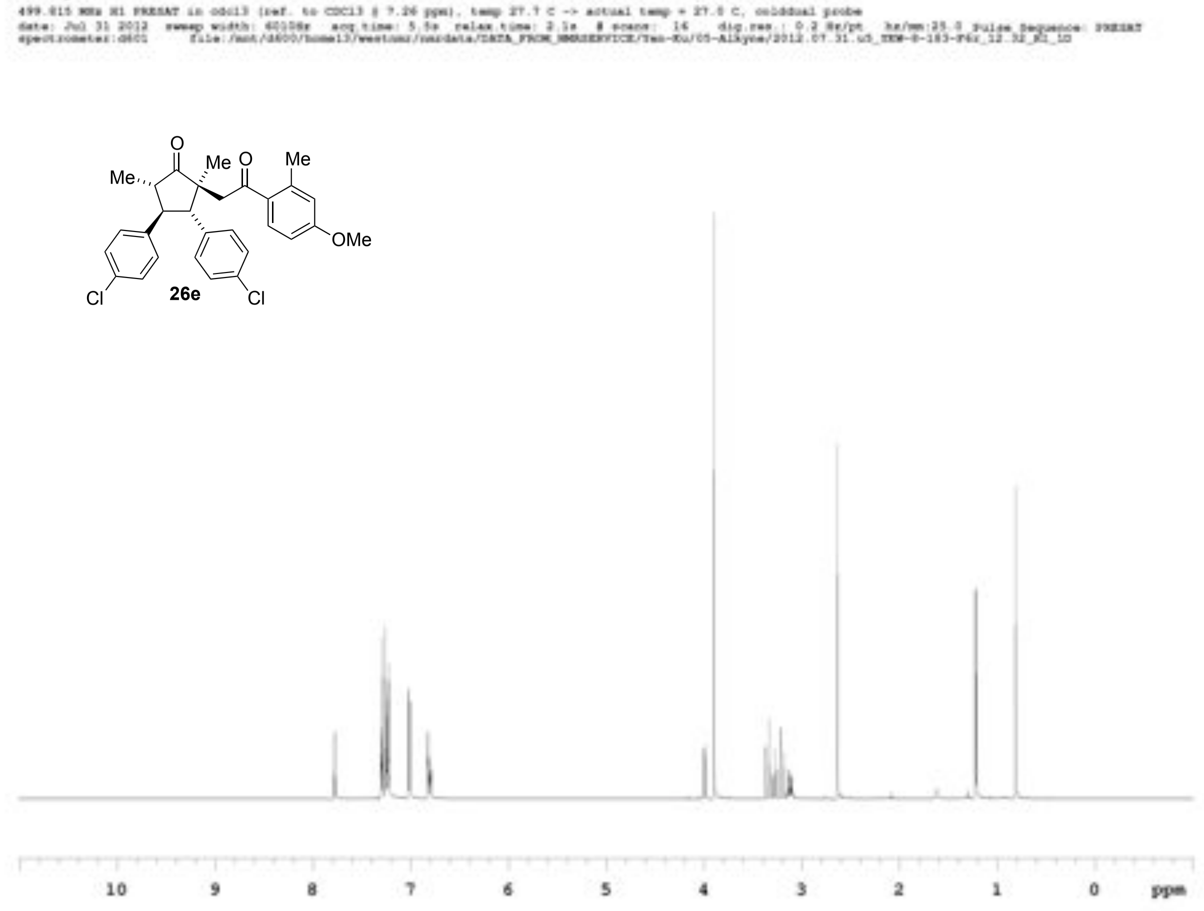

499.815 MHz H1 PRESAT in cdcl3 (ref. to CDCl3 δ 7.26 ppm), temp 27.7 C -> actual temp = 27.5 C, colddual probe
date: Jul 23 2012 sweep width: 6010Hz acq time: 5.5s relax time: 2.1s # scans: 16 dig res.: 0.2 Hz/pt hz/mm:25.0 Pulse Sequence: PRESAT
spectrometer:d601 file:/mnt/d600/home13/westomr/nmrdata/DATA_FROM_NMRSERVICE/Yan-Xu/05-Alkyne/2012.07.23.u5_YXW-8-169-PII-final_20.15_H1_1D
O
Me
Me
O
Me
Ph
Ph
OMe
10
9
8
7
6
5
4
3
2
1
0
ppm

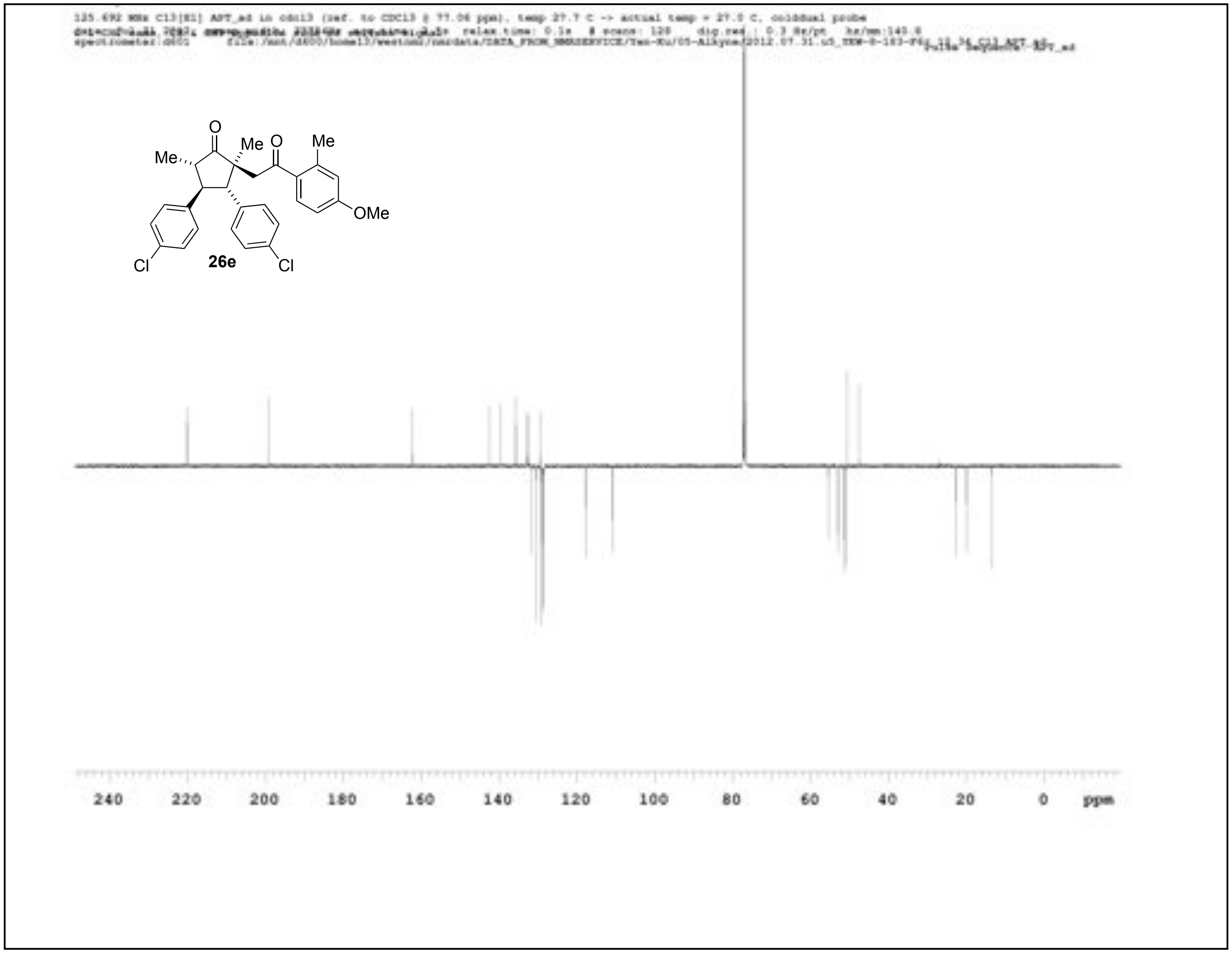
26b



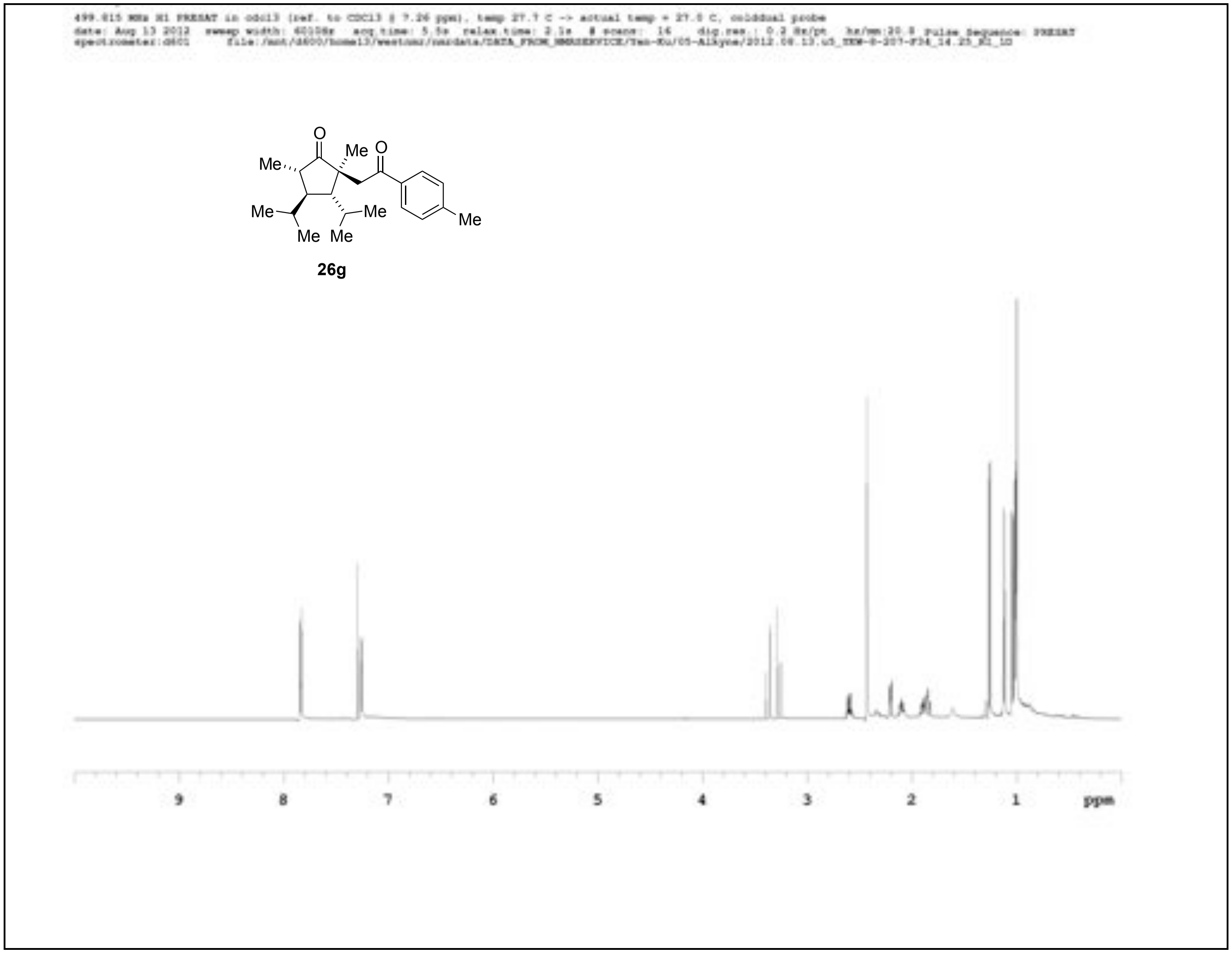
26b

Me
O
Me
O
OMe
Ph
Ph
Me
ppm
0
20
40
60
80
100
120
140
160
180
200
220
240

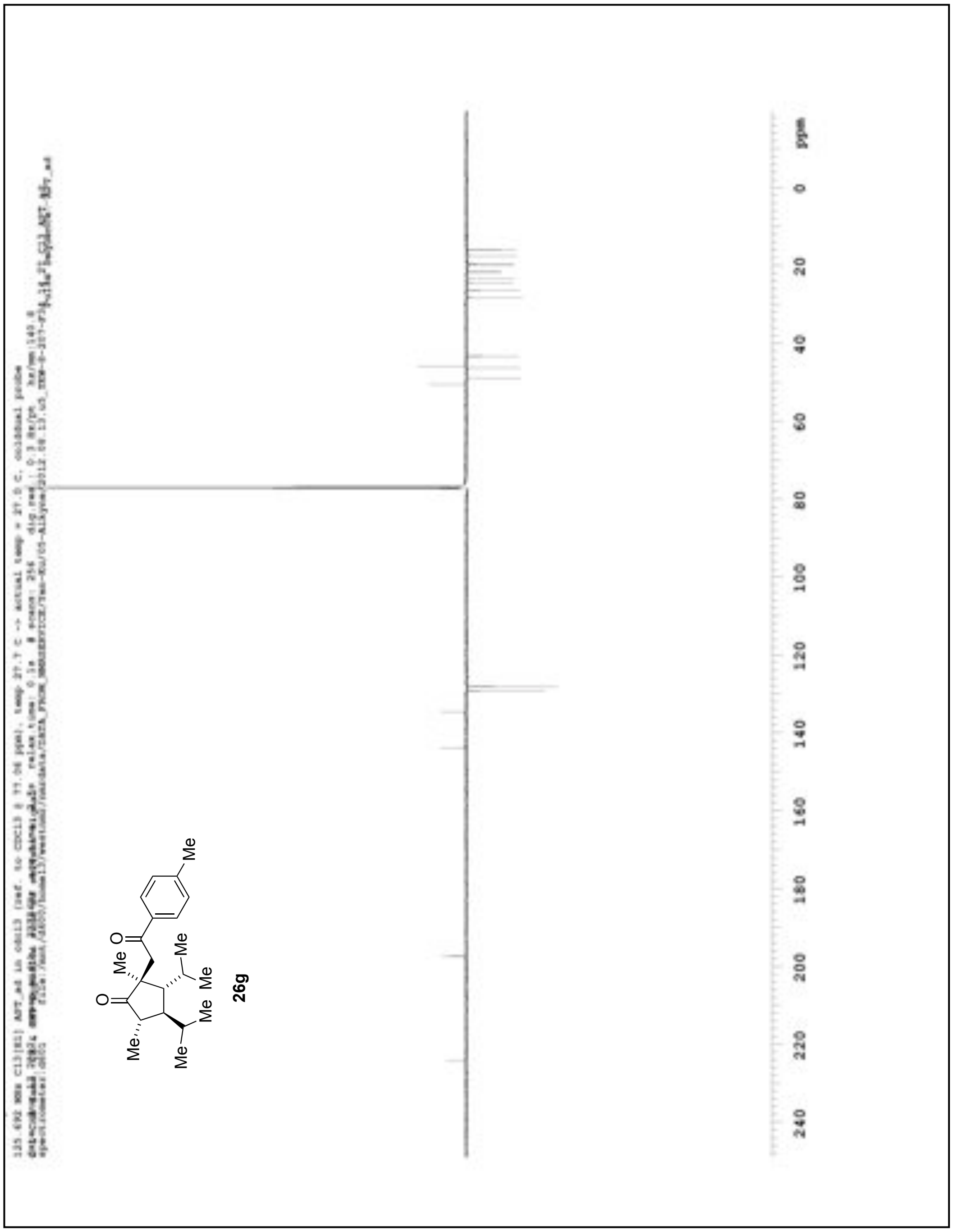

499.815 MHz H1 PRESAT in cdcl3 (ref. to CDCl3 @ 7.26 ppm), temp 27.7 C -> actual temp = 27.0 C, colddual probe
date: Jul 31 2012 sweep width: 6010Hz acq time: 5.5s relax time: 2.1s # scans: 16 dig res.: 0.2 Hz/pt hz/mm:25.0 Pulse Sequence: PRESAT
spectrometer:d601 file:/mnt/d600/home13/westumz/nmrdata/DATA_FROM_NMRSERVICE/Yan-Xu/05-Alkyne/2012.07.31.u5_YXW-8-183-F6r_12.32_H1_1D
O
Me
Me
O
Me
OMe
Cl
26e
Cl
10
9
8
7
6
5
4
3
2
1
0
ppm

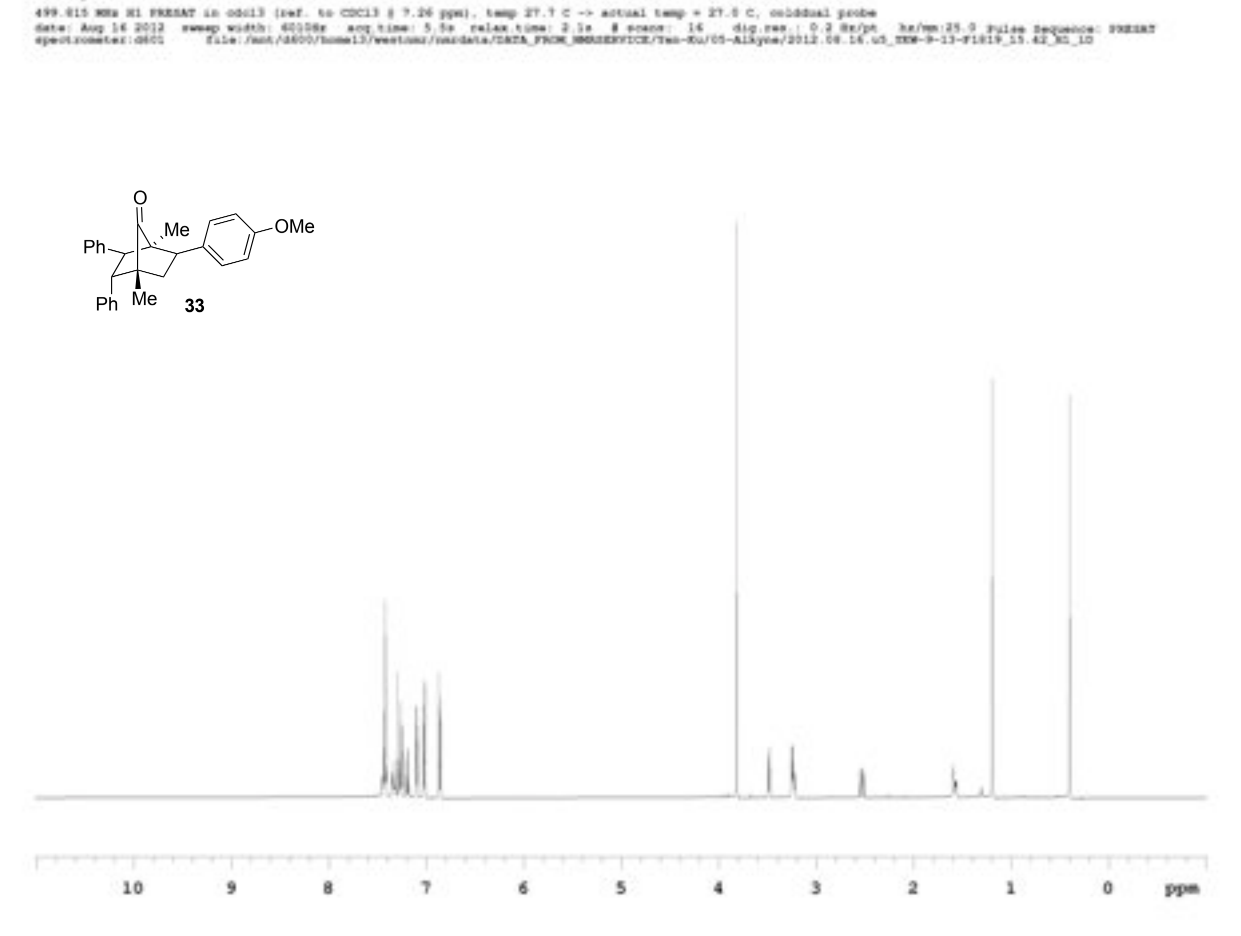

125.692 MHz C13[H1] APT_ad in cdcl3 (ref. to CDCl3 @ 77.06 ppm), temp 27.7 C -> actual temp = 27.0 C, colddual probe
relax.time: 0.1s # scans: 128 dig.res.: 0.3 Hz/pt hz/mm:140.6
spectrometer:d601 file:/mnt/d600/home13/westuml/nmrdata/DATA_FROM_NMRSERVICE/Yan-Xu/05-Alkyne/2012.07.31.u5_ZXW-8-183-F6_11.34_C13_APT_ad
Pulse Sequence: APT_ad
O
Me
Me
O
Me
OMe
Cl
Cl
240
220
200
180
160
140
120
100
80
60
40
20
0
ppm

26e

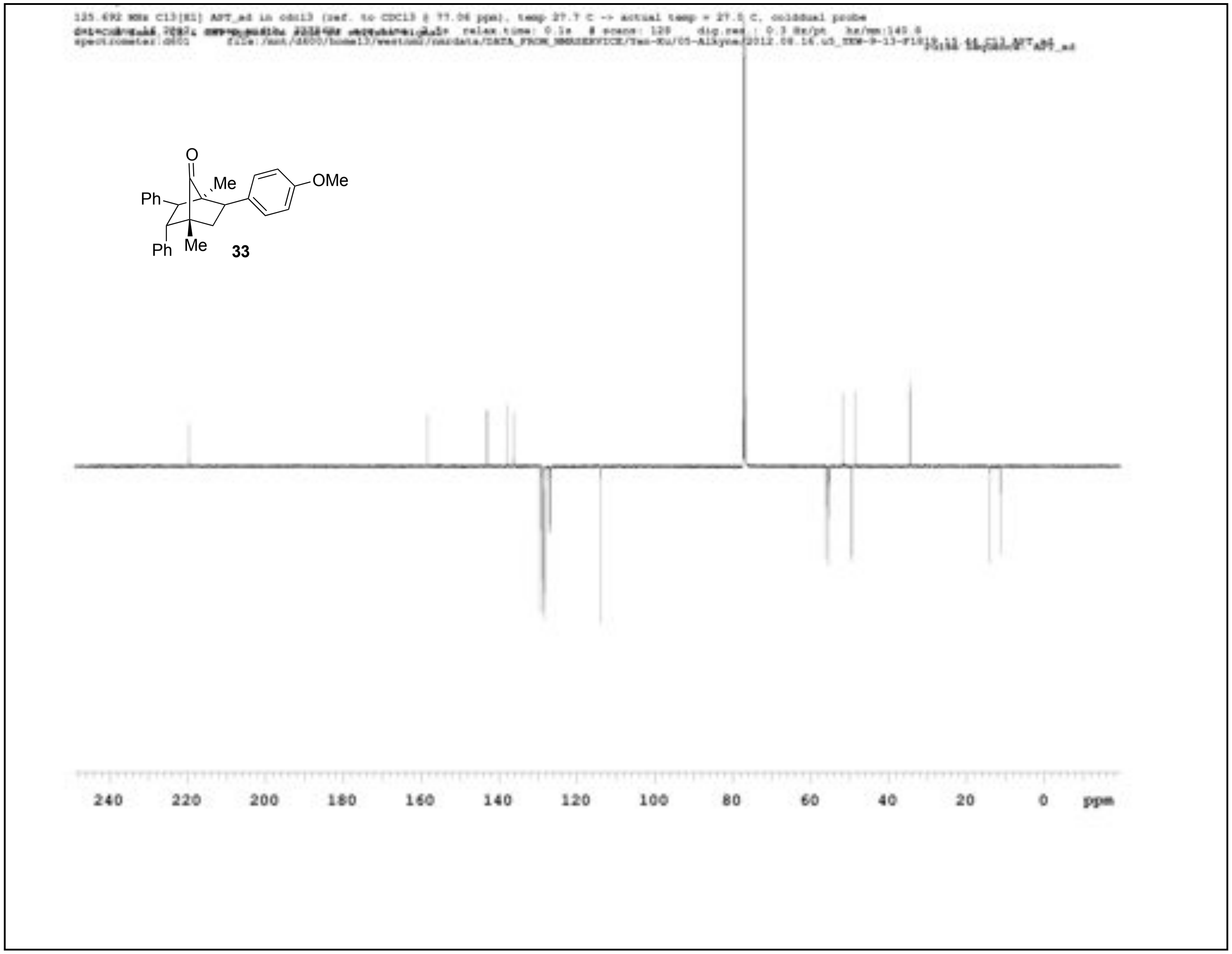

499.815 MHz H1 PRESAT in cdcl3 (ref. to CDCl3 @ 7.26 ppm), temp 27.7 C -> actual temp = 27.5 C, colddual probe
date: Aug 13 2012 sweep width: 6010Hz acq time: 5.5s relax time: 2.1s # scans: 16 dig.res.: 0.2 Hz/pt hz/mm:20.0 Pulse Sequence: PRESAT
spectrometer:d601 file:/mnt/d600/home13/westonz/nmrdata/DATA_FROM_NMRSERVICE/Yan-Xu/05-Alkyne/2012.08.13.u5_YXW-8-207-F34_14.25_H1_1D
O
Me
O
Me
Me
Me
Me
Me
Me
9
8
7
6
5
4
3
2
1
ppm

26g


125.692 MHz C13[H1] APT_ad in cdcl3 (ref. to CDCl3 @ 77.06 ppm), temp 27.7 C -> actual temp = 27.0 C, colddual probe
O
Me
O
Me
Me
Me
Me
Me
Me
26g
0
20
40
60
80
100
120
140
160
180
200
220
240
ppm

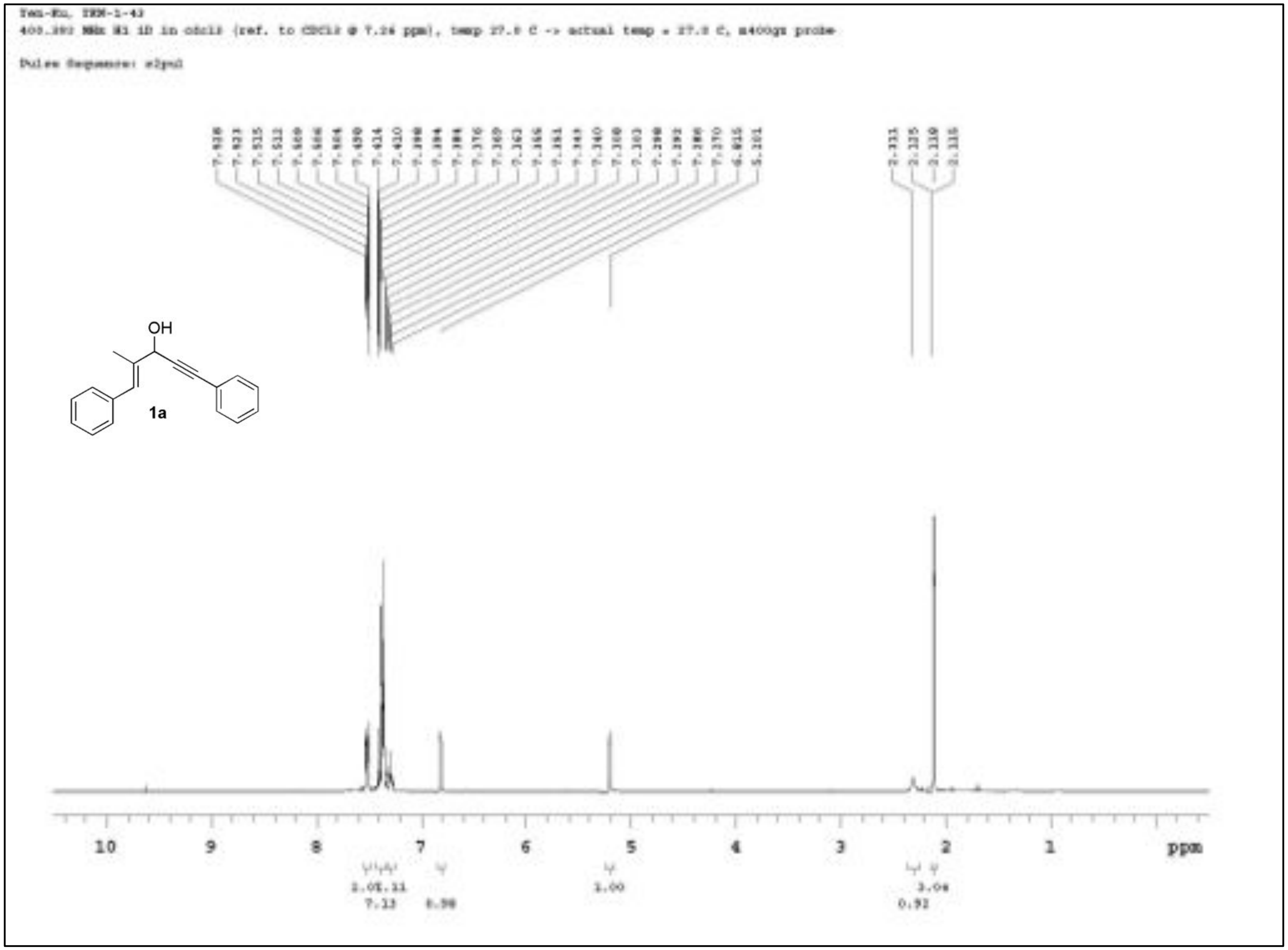


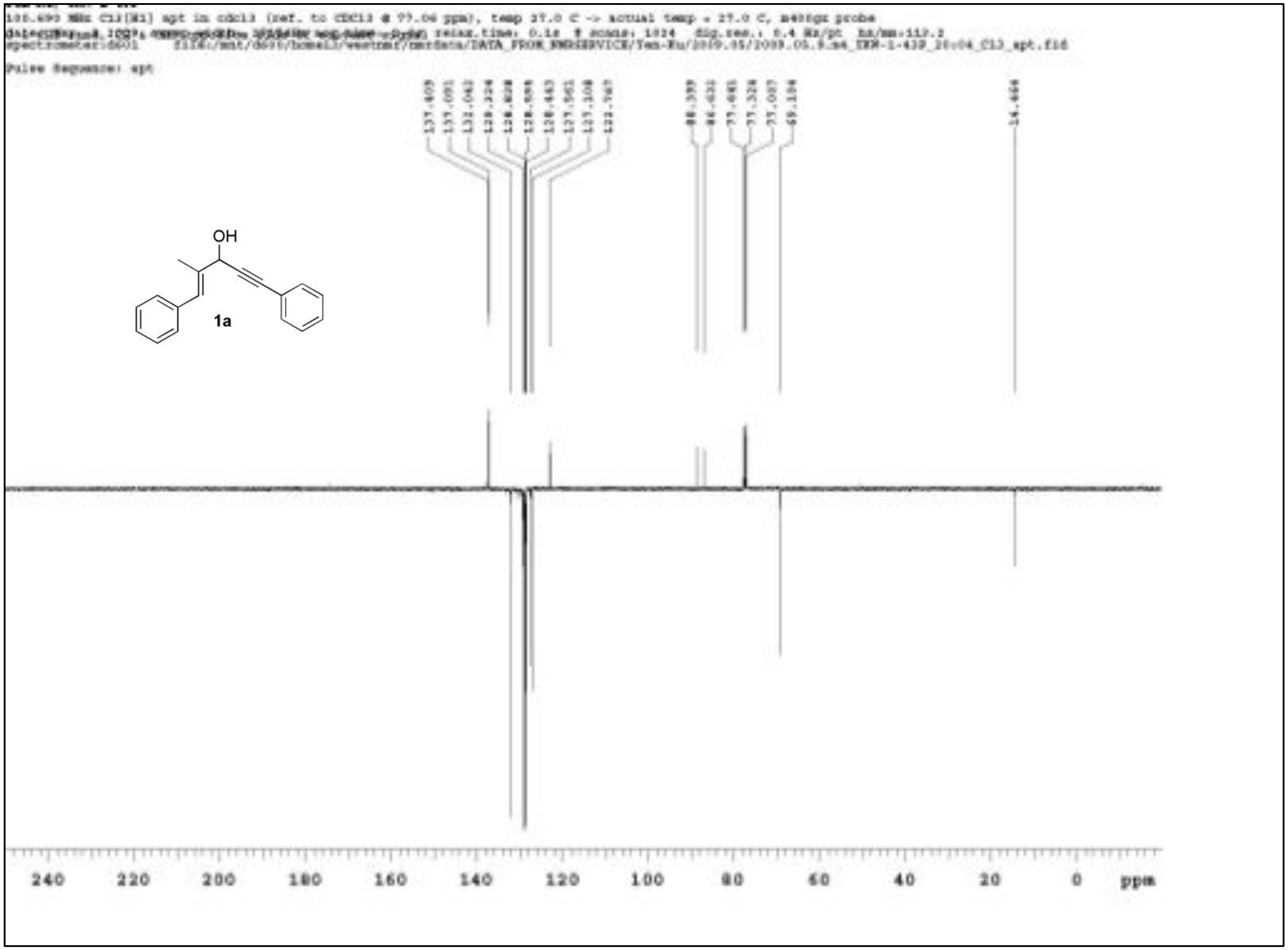
```
499.815 MHz H1 PRESAT in cdcl3 (ref. to CDCl3 @ 7.26 ppm), temp 27.7 C -> actual temp = 27.0 C, colddual probe
date: Aug 16 2012  sweep width: 6010Hz  acq time: 5.5s  relax time: 2.1s  # scans: 16  dig.res.: 0.2 Hz/pt  hz/mm:25.0 Pulse Sequence: PRESAT
spectrometer:d601     file:/mnt/d600/home13/westonr/nmrdata/DATA_FROM_NMRSERVICE/Tan-Ku/05-Alkyne/2012.08.16.u5_TKW-9-13-F1819_15.42_H1_1D
```

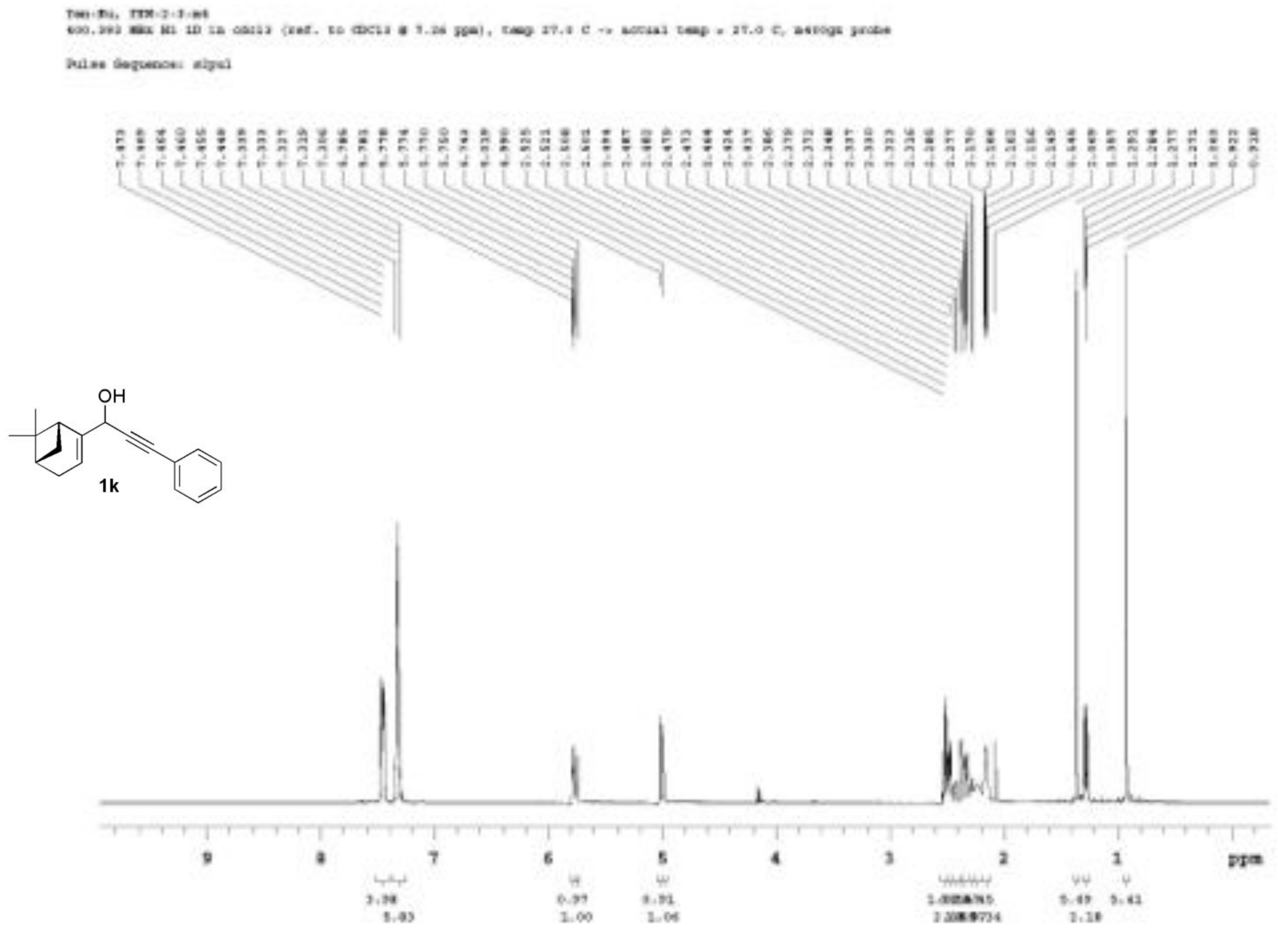

125.692 MHz C13[H1] APT_ad in cdcl3 (ref. to CDCl3 @ 77.06 ppm), temp 27.7 C -> actual temp = 27.5 C, colddual probe
relax.time: 0.1s # scans: 120 dig.res.: 0.3 Hz/pt hz/mm:140.6
spectrometer:d601 file:/mnt/d600/home13/westuml/nmrdata/DATA_FROM_NMRSERVICE/Yan-Xu/05-Alkyne/2012.08.16.u5_TXW-9-13-F1
O
Me
OMe
Ph
Ph
Me
33
240
220
200
180
160
140
120
100
80
60
40
20
0
ppm

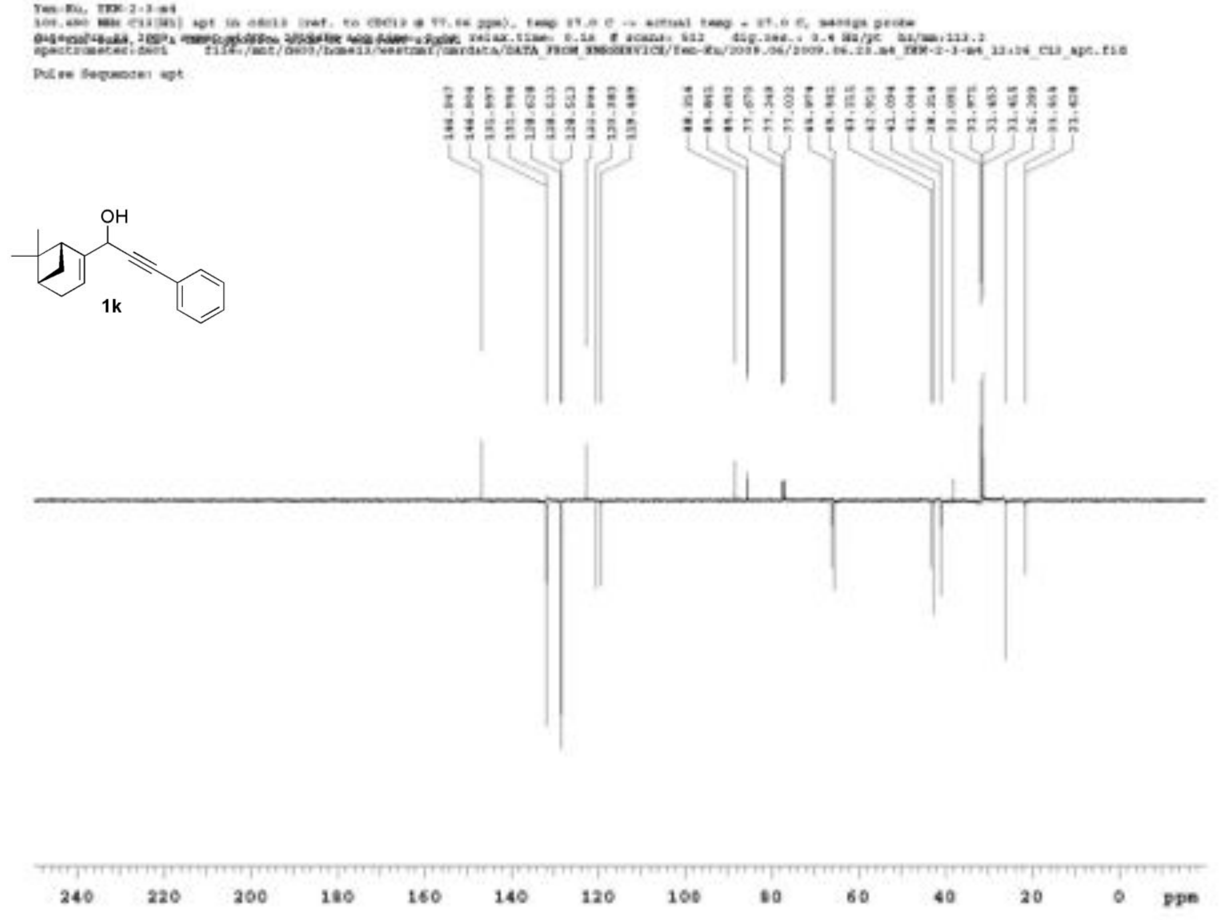
Appendix II:

Selected NMR Spectra (Chapter 3)

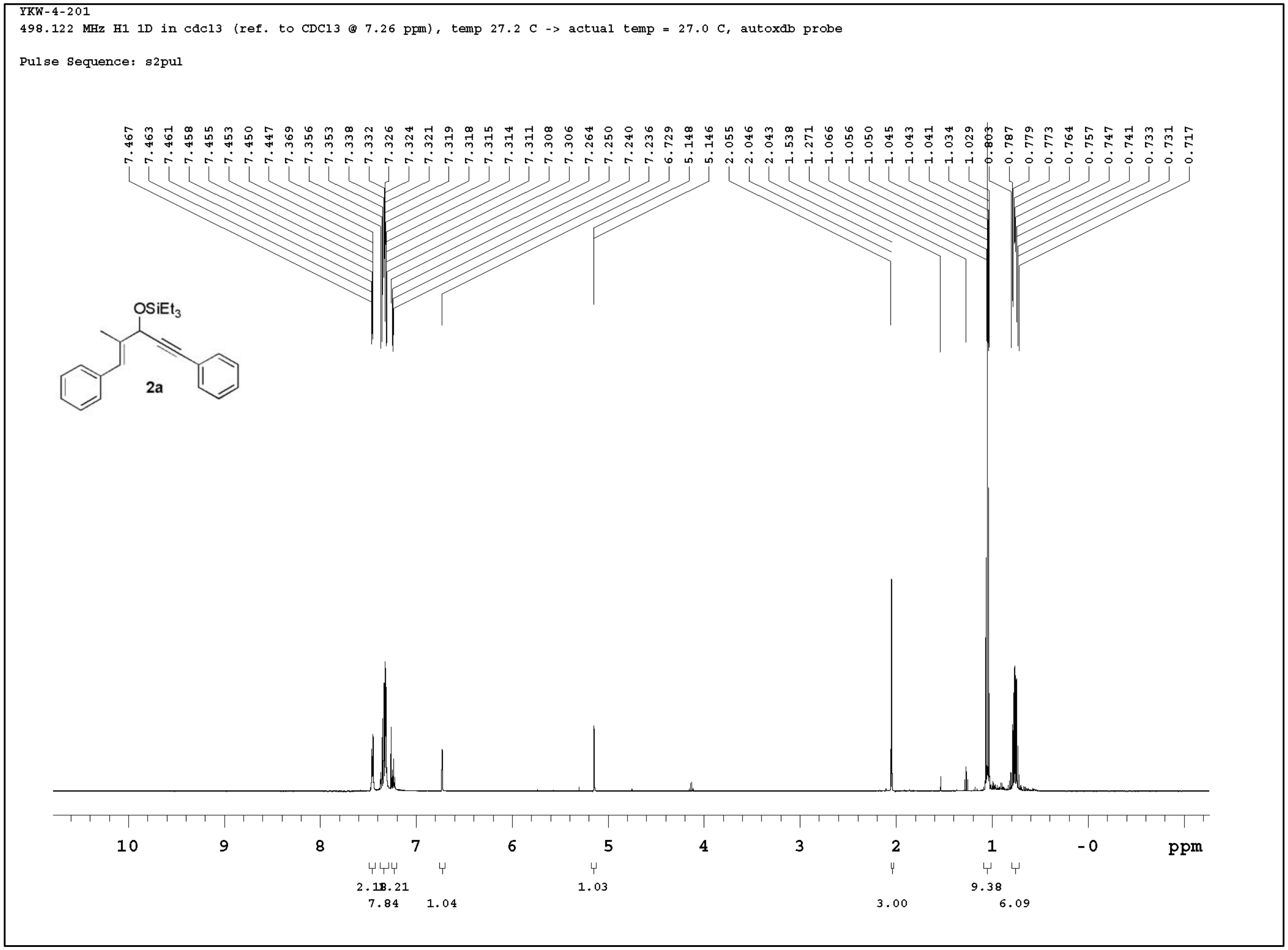

Yen-Ku, YKM-1-43
400.392 MHz H1 1D in cdcl3 (ref. to CDCl3 @ 7.26 ppm), temp 27.0 C -> actual temp = 27.0 C, m400gx probe
Pulse Sequence: s2pul
7.538
7.533
7.515
7.511
7.469
7.466
7.464
7.450
7.434
7.430
7.398
7.394
7.384
7.376
7.369
7.363
7.355
7.351
7.343
7.340
7.308
7.303
7.298
7.292
7.288
7.270
6.815
5.101
2.331
2.325
2.119
2.115
OH
1a
10
9
8
7
6
5
4
3
2
1
ppm
2.05
2.11
7.13
0.98
1.00
3.04
0.92

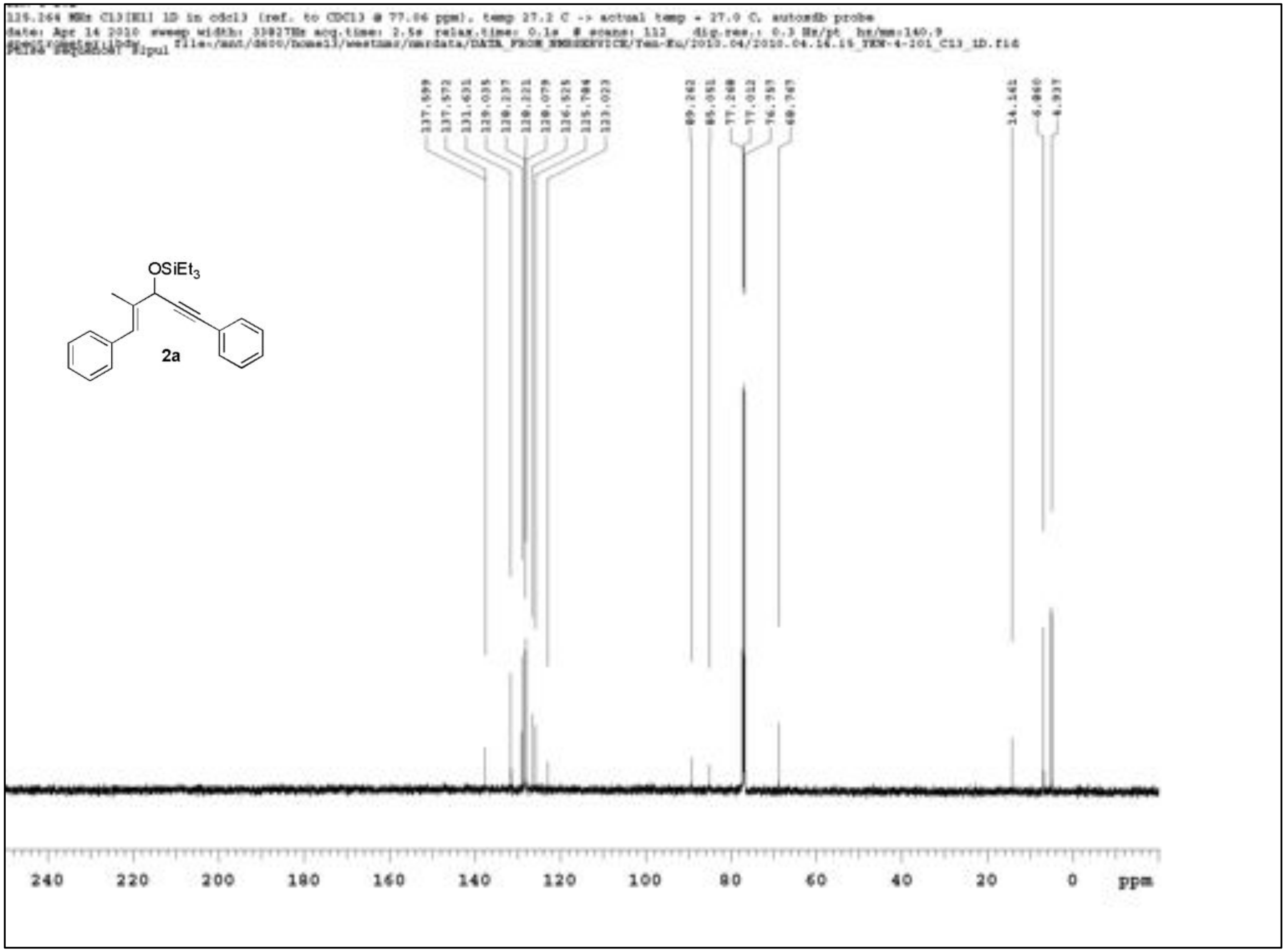

100.690 MHz C13[H1] apt in cdcl3 (ref. to CDCl3 @ 77.06 ppm), temp 27.0 C -> actual temp = 27.0 C, m400gx probe
relax.time: 0.1s # scans: 1024 dig.res.: 0.4 Hz/pt Hz/mm:112.2
spectrometer:d601 file:/mnt/d600/home13/westnmr/nmrdata/DATA_FROM_NMRSERVICE/Ten-Fu/2009.05/2009.05.9.m4_TRN-1-439_20:04_C13_apt.fid
Pulse Sequence: apt
137.409
137.091
132.042
129.324
128.828
128.595
128.443
127.561
127.108
122.767
88.399
86.631
77.648
77.328
77.007
69.108
14.468
OH
1a
240
220
200
180
160
140
120
100
80
60
40
20
0
ppm

400.393 MHz H1 1D in cdcl3 (ref. to CDCl3 @ 7.26 ppm), temp 27.0 C -> actual temp = 27.0 C, probe
Pulse Sequence: s2pul
OH
1k
9
8
7
6
5
4
3
2
1
ppm
3.08
5.03
0.97
1.00
0.91
1.06
2.18
5.49
5.41

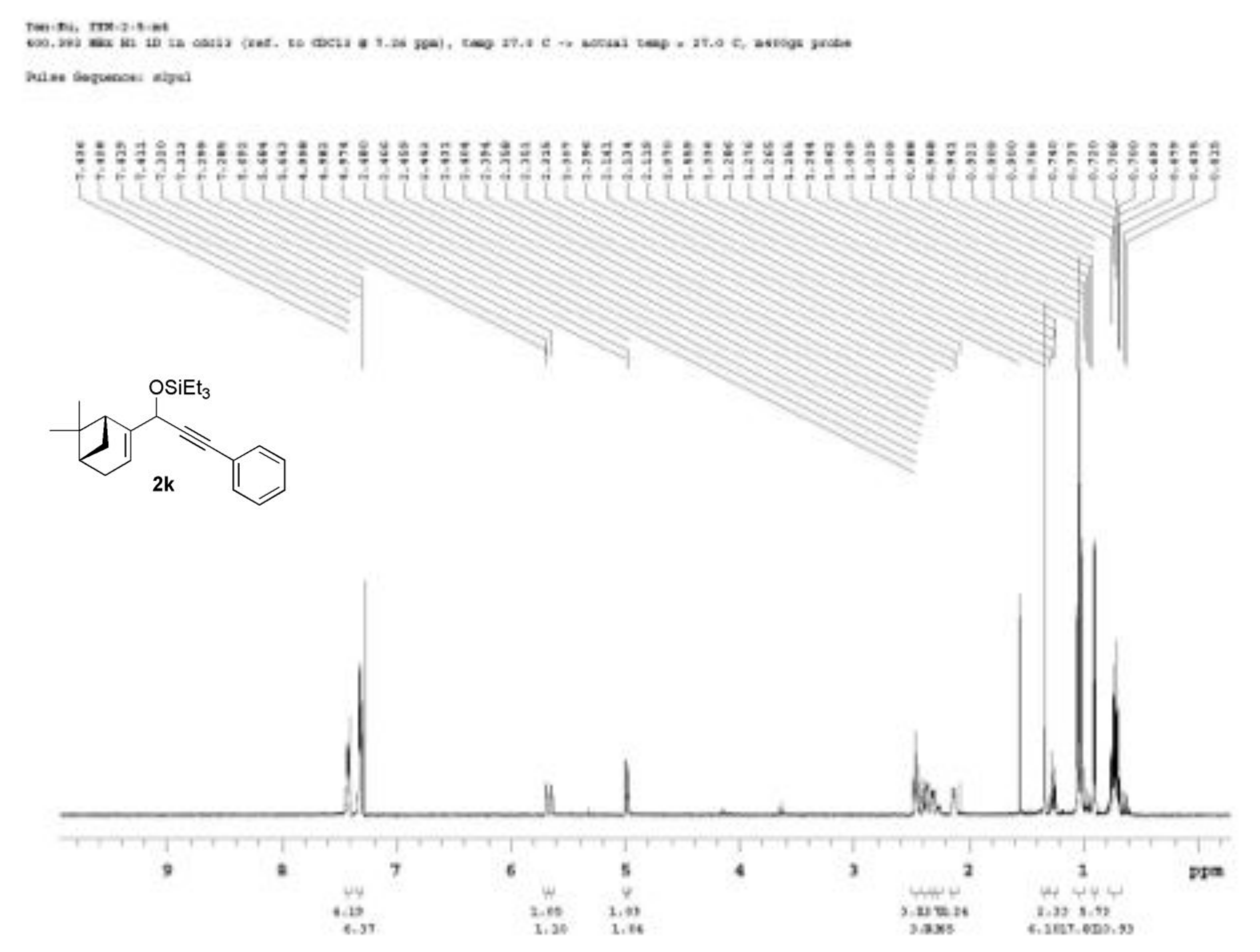

Yen-Ku, TEM-2-3-m4
100.490 MHz C13[H1] apt in cdcl3 (ref. to CDCl3 @ 77.06 ppm), temp 27.0 C -> actual temp = 27.0 C, autoxdb probe
relax.time: 0.1s # scans: 512 dig.res.: 3.4 Hz/pt hz/mm:113.2
spectrometer:dn01 file:/mnt/dn03/home13/westmat/nmrdata/DATA_FROM_NMRSERVICE/Yen-Ku/2009.06/2009.06.23.m4_TEM-2-3-m4_12:26_C13_apt.fid
Pulse Sequence: apt
146.947
146.904
131.997
131.998
128.628
128.513
128.513
122.994
120.383
119.889
88.254
85.861
85.653
77.679
77.349
77.032
65.974
65.945
43.155
42.953
41.094
41.049
38.214
33.091
31.975
31.453
31.455
26.389
21.616
21.639
OH
240
220
200
180
160
140
120
100
80
60
40
20
0
ppm

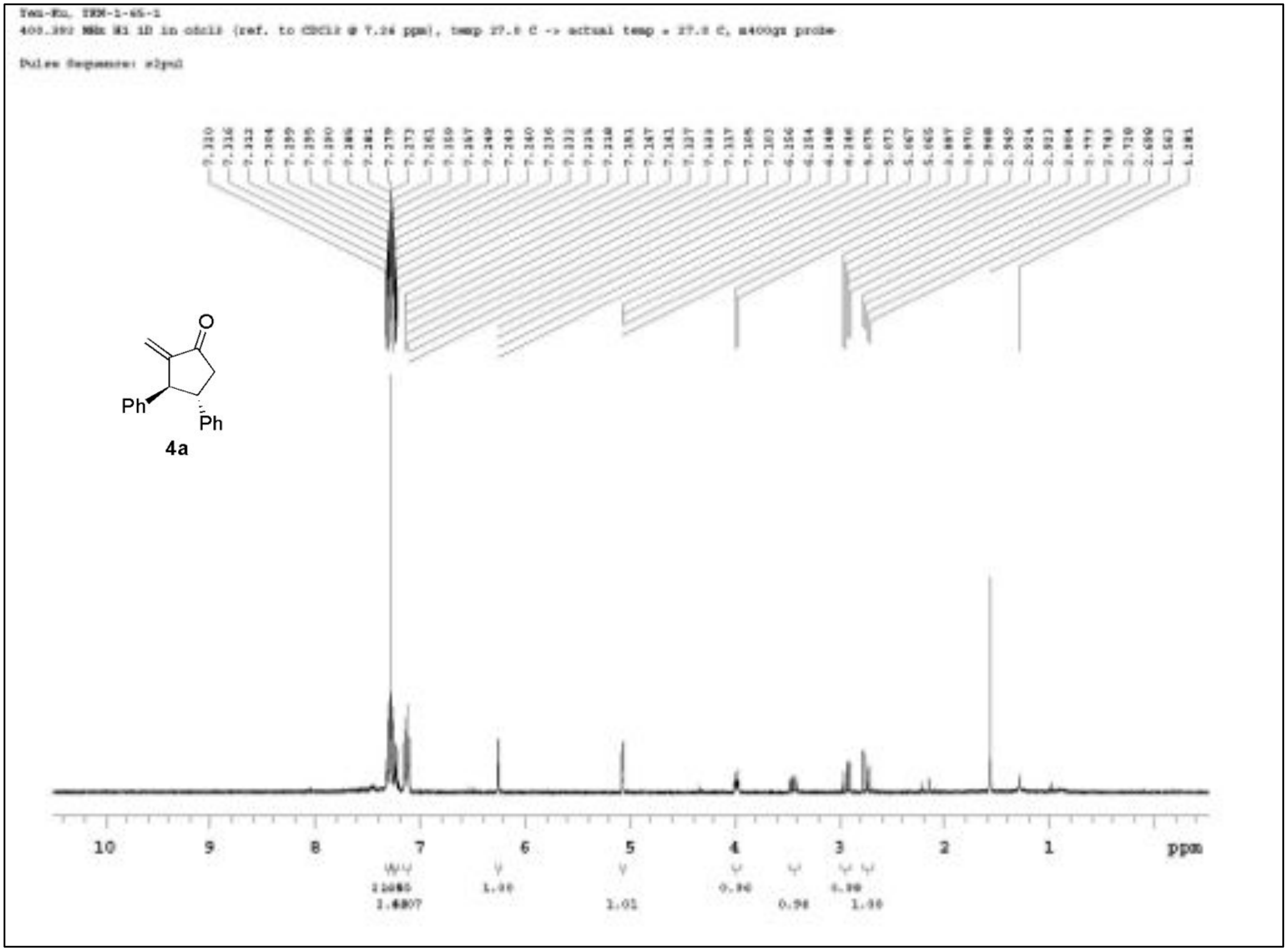
1k


YKW-4-201
498.122 MHz H1 1D in cdcl3 (ref. to CDCl3 @ 7.26 ppm), temp 27.2 C -> actual temp = 27.0 C, autoxdb probe
Pulse Sequence: s2pul
7.467
7.463
7.461
7.458
7.455
7.453
7.450
7.447
7.369
7.356
7.353
7.338
7.332
7.326
7.324
7.321
7.319
7.318
7.315
7.314
7.311
7.308
7.306
7.264
7.250
7.240
7.236
6.729
5.148
5.146
2.055
2.046
2.043
1.538
1.271
1.066
1.056
1.050
1.045
1.043
1.041
1.034
1.029
0.803
0.787
0.779
0.773
0.764
0.757
0.747
0.741
0.733
0.731
0.717
OSiEt3
2a
10
9
8
7
6
5
4
3
2
1
-0
ppm
2.18.21
7.84
1.04
1.03
3.00
9.38
6.09

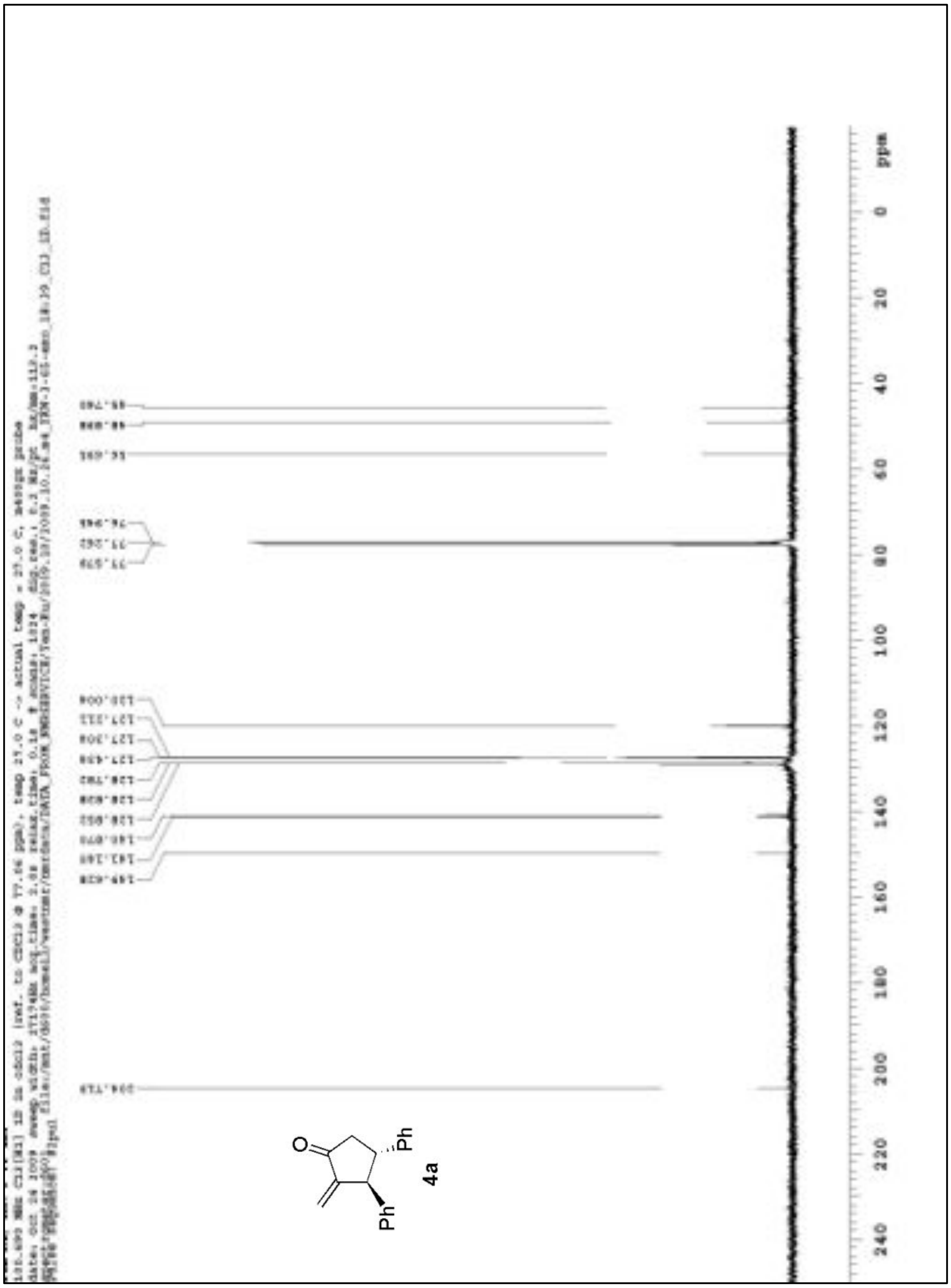


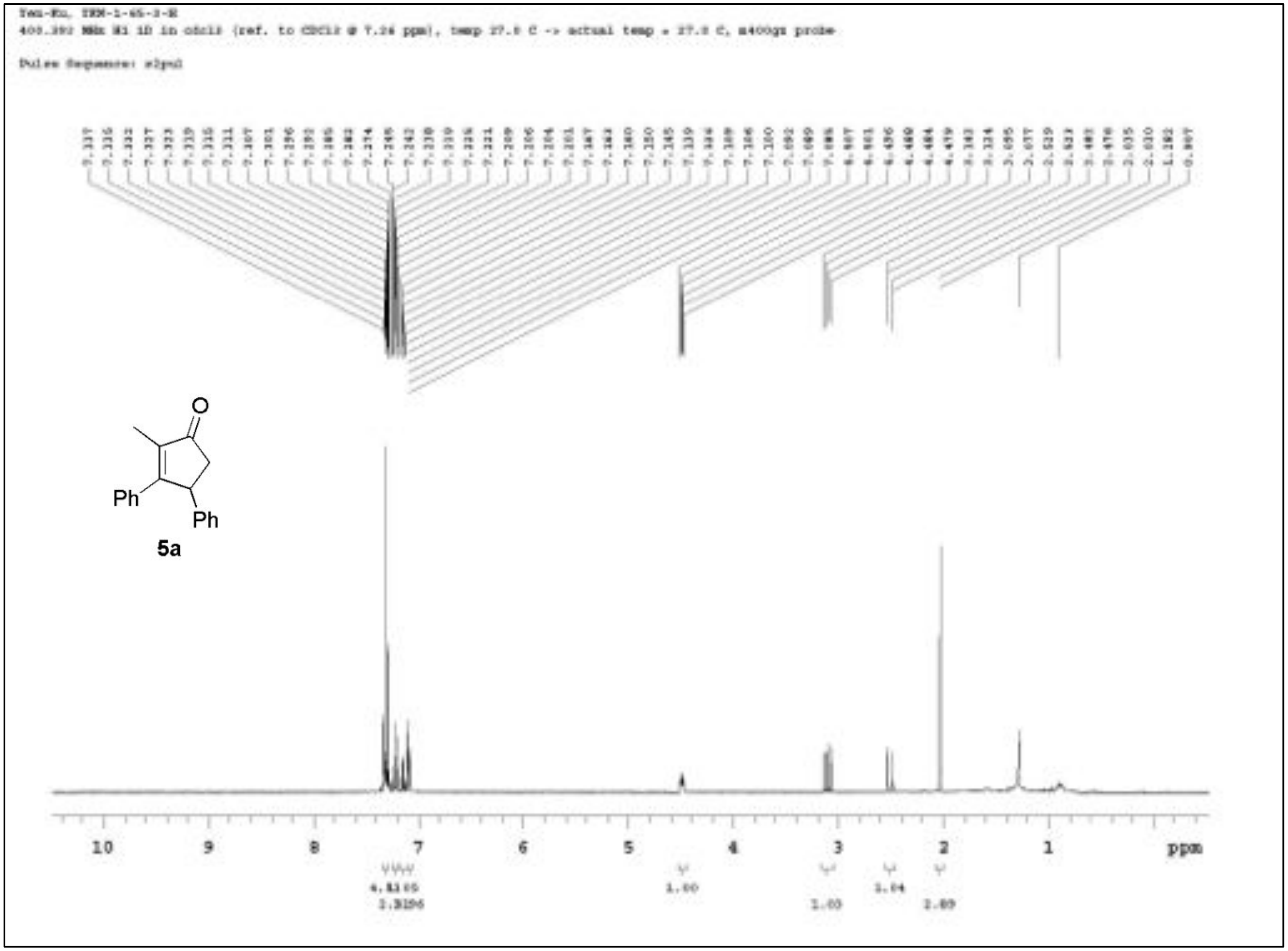
```
125.264 MHz C13[H1] 1D in cdcl3 (ref. to CDCl3 @ 77.06 ppm), temp 27.2 C -> actual temp = 27.0 C, autoxdb probe
date: Apr 14 2010  sweep width: 33827Hz  acq.time: 2.5s  relax.time: 0.1s  # scans: 112    dig.res.: 0.3 Hz/pt  hz/mm:140.9
Pulse Sequence: s2pul  file=/mnt/d600/home13/westnmr/nmrdata/DATA_FROM_NMRSERVICE/Tan-Eu/2010.04/2010.04.14.15_TKN-4-201_C13_1D.fid
```


400.392 MHz H1 1D in cdcl3 (ref. to CDCl3 @ 7.26 ppm), temp 27.0 C -> actual temp = 27.0 C
Pulse Sequence: s2pul
OSiEt3
2k
9
8
7
6
5
4
3
2
1
ppm


Yen-Ku, YKM-1-65-1
400.392 MHz H1 1D in cdcl3 (ref. to CDCl3 @ 7.26 ppm), temp 27.0 C -> actual temp = 27.0 C, m400gx probe
Pulse Sequence: s2pul
7.320
7.316
7.312
7.304
7.299
7.295
7.290
7.286
7.281
7.279
7.273
7.261
7.259
7.257
7.249
7.243
7.240
7.236
7.233
7.226
7.218
7.181
7.147
7.141
7.137
7.133
7.117
7.105
7.103
6.256
6.254
6.248
6.246
5.075
5.073
5.067
5.065
3.987
3.970
2.968
2.949
2.924
2.923
2.904
2.777
2.743
2.720
2.690
1.563
1.281
O
Ph
Ph
10
9
8
7
6
5
4
3
2
1
ppm
11086
1.4807
1.00
1.01
0.96
0.98
0.98
1.00

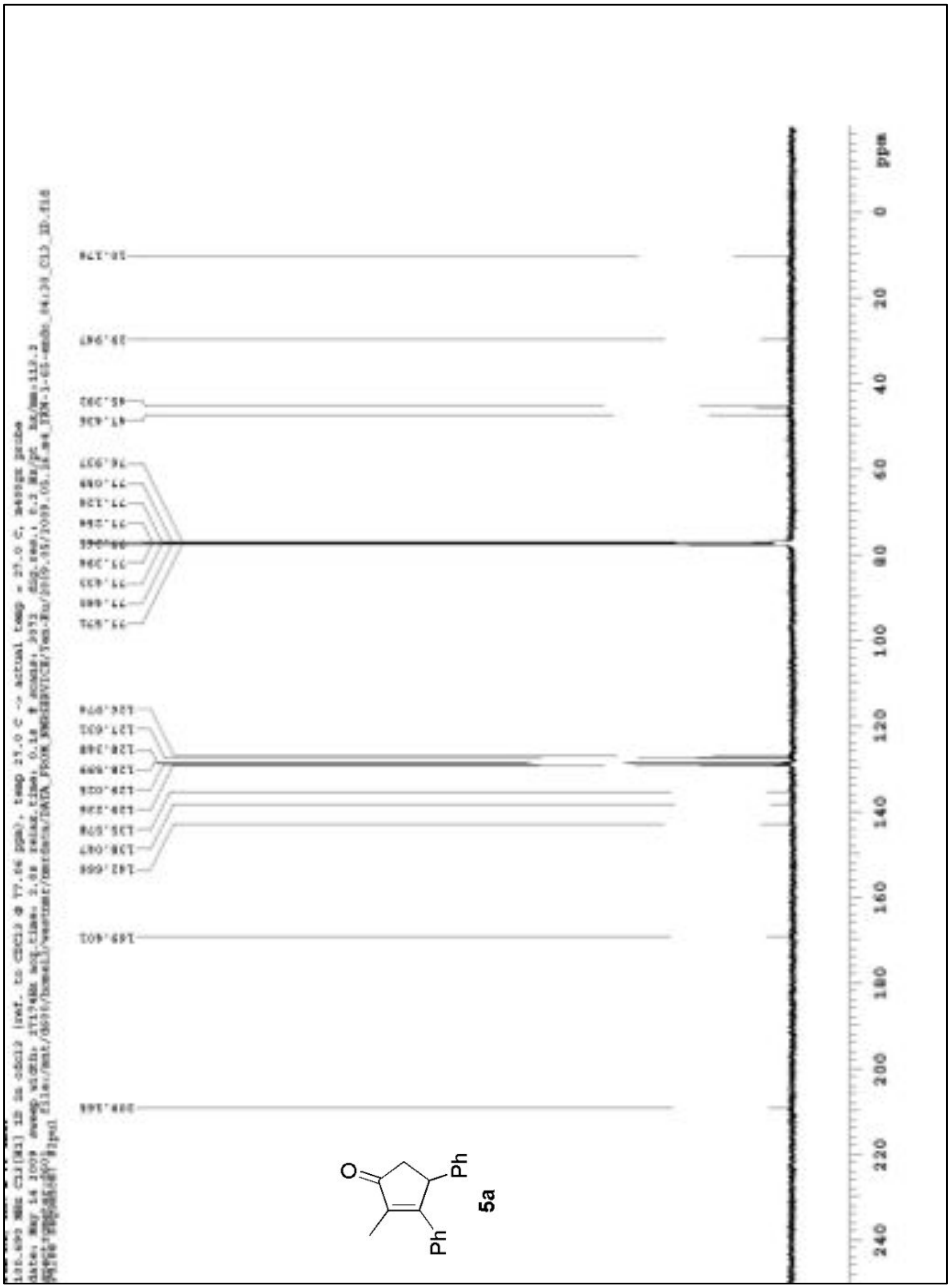
4a


45.760
48.898
56.091
76.946
77.262
77.579
120.008
127.111
127.308
127.458
128.782
128.608
128.852
140.870
141.168
149.628
204.719
O
Ph
Ph
4a
0
20
40
60
80
100
120
140
160
180
200
220
240
ppm

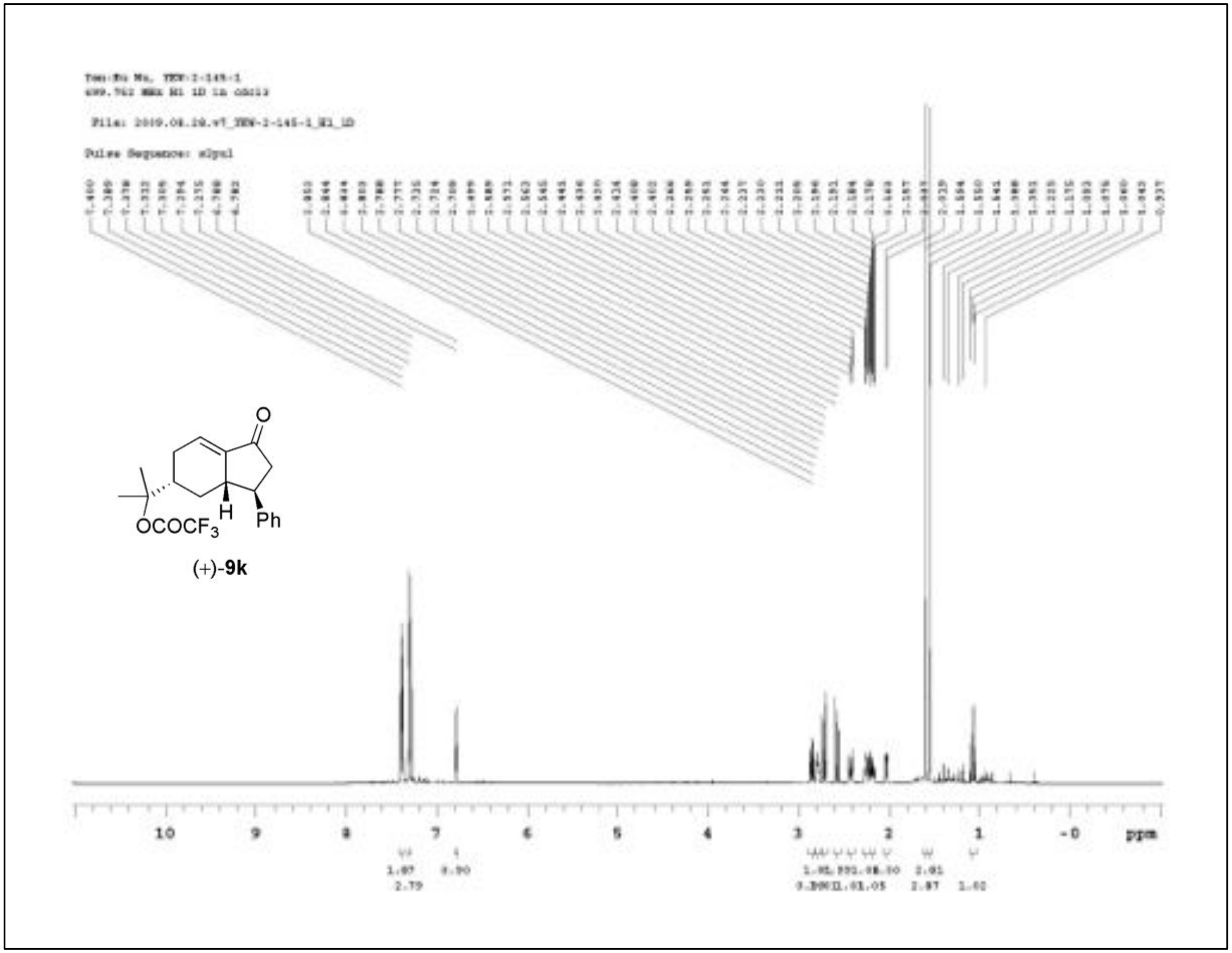


400.392 MHz H1 1D in cdcl3 (ref. to CDCl3 @ 7.26 ppm), temp 27.0 C -> actual temp = 27.0 C, m400gs probe
Pulse Sequence: s2pul
O
Ph
Ph
10
9
8
7
6
5
4
3
2
1
ppm
1.00
1.03
1.04
2.09

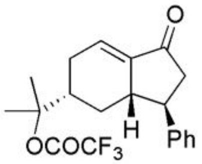
5a



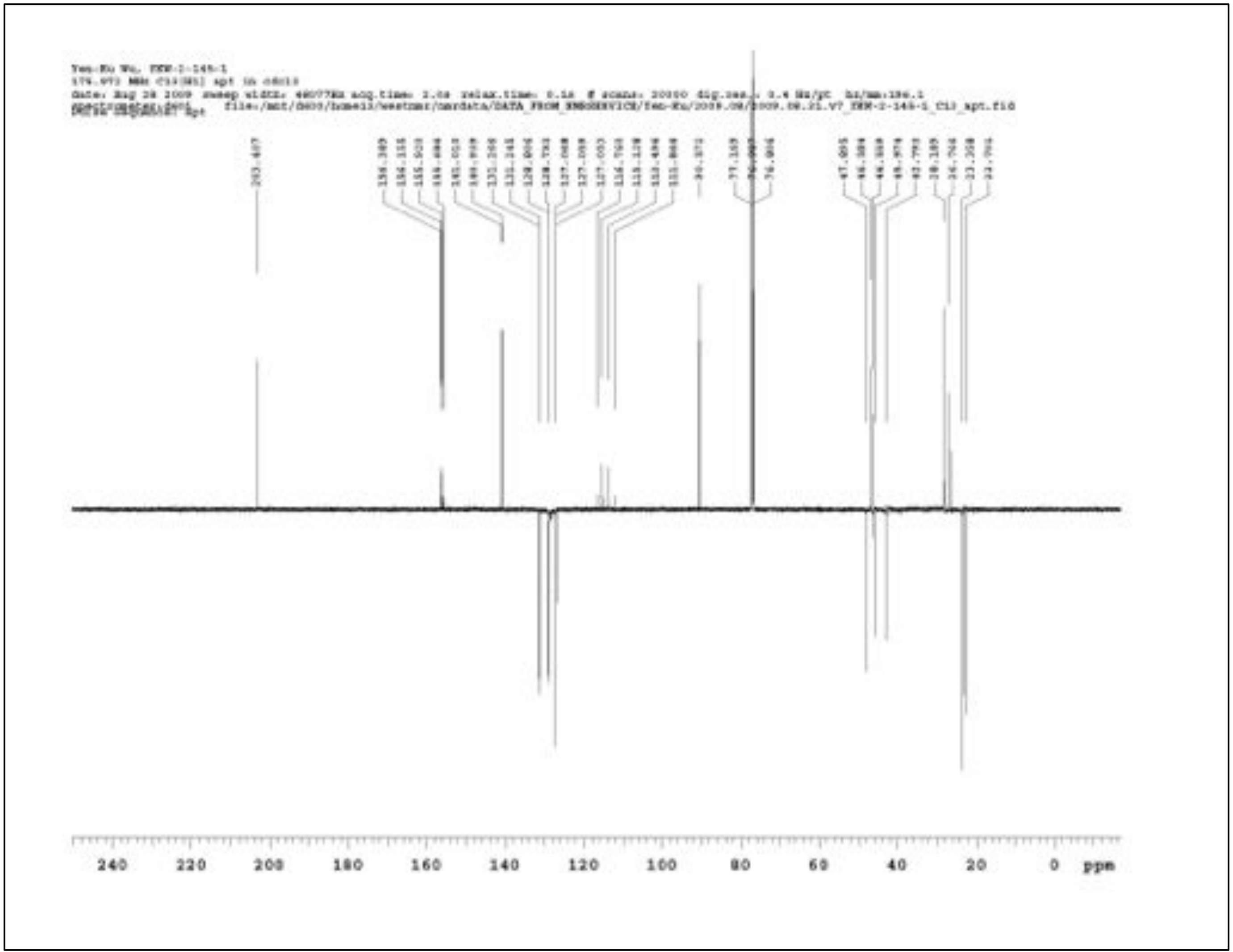
10.178
29.967
45.392
47.636
76.937
77.089
126.974
127.601
128.348
128.609
135.578
138.047
142.668
169.401
209.166
O
Ph
Ph
5a
ppm
0
20
40
60
80
100
120
140
160
180
200
220
240

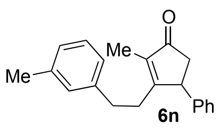


(+)-**9k**



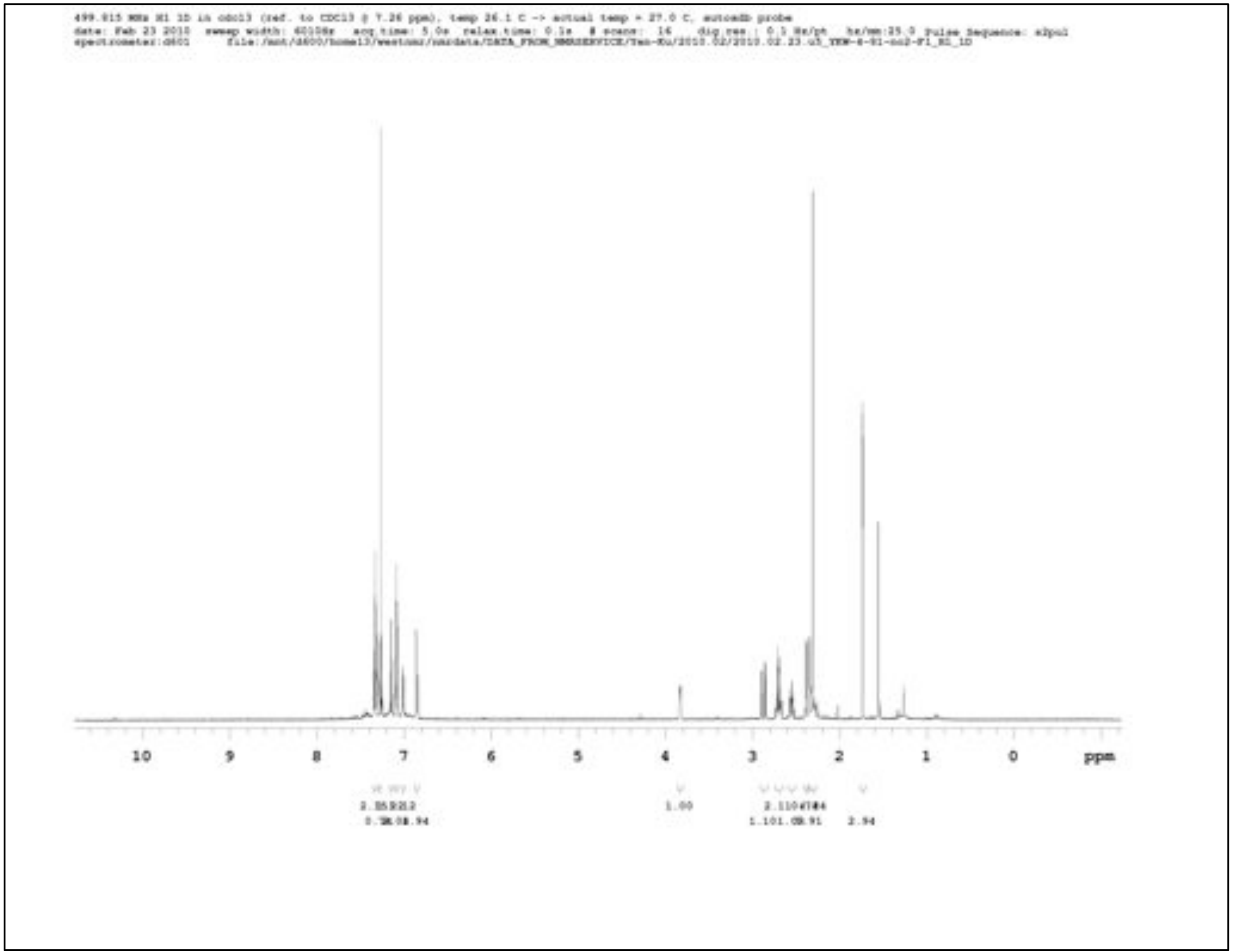
(+)-**9k**

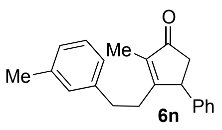

Yen-Ku Wu, YKW-2-145-1
175.973 MHz C13[H1] apt in cdcl3
date: Aug 28 2009 sweep width: 48077Hz acq.time: 2.0s relax.time: 0.1s # scans: 20000 dig.res.: 3.4 Hz/pt hz/mm:196.1
file=/mnt/d600/home13/westmr/nmrdata/DATA_FROM_NMRSERVICE/Yen-Ku/2009.08/2009.08.21.V7_YKW-2-145-1_C13_apt.fid
203.407
156.389
156.145
155.903
155.661
141.053
140.949
131.268
131.148
128.806
128.793
127.068
127.009
117.003
116.760
115.128
113.496
111.866
90.372
77.169
76.987
76.804
47.695
46.384
44.359
42.974
42.793
28.189
26.764
23.358
22.794
240
220
200
180
160
140
120
100
80
60
40
20
0
ppm



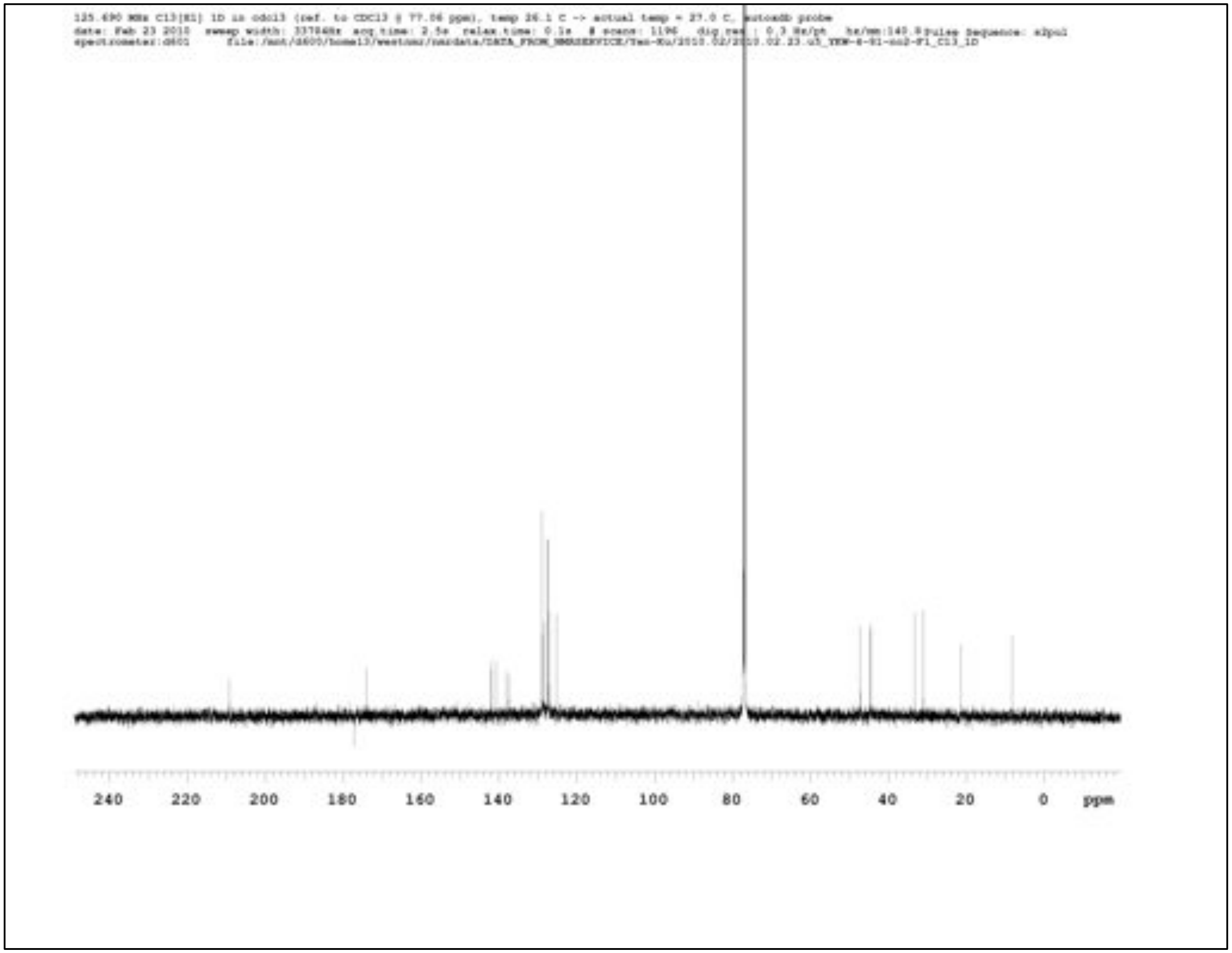
6n

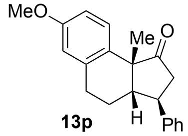
O
Me
Me
Ph


499.815 MHz H1 1D in cdcl3 (ref. to CDCl3 @ 7.26 ppm), temp 26.1 C -> actual temp = 27.0 C, autoxdb probe
date: Feb 23 2010 sweep width: 6010Hz acq.time: 5.0s relax.time: 0.1s # scans: 16 dig.res.: 0.1 Hz/pt hz/mm:25.0 Pulse Sequence: s2pul
spectrometer:d601 file:/mnt/d600/home13/westonr/nmrdata/DATA_FROM_NMRSERVICE/Yan-Xu/2010.02/2010.02.23.u5_YXW-4-91-co2-F1_H1_1D
10
9
8
7
6
5
4
3
2
1
0
ppm
1.00
2.94

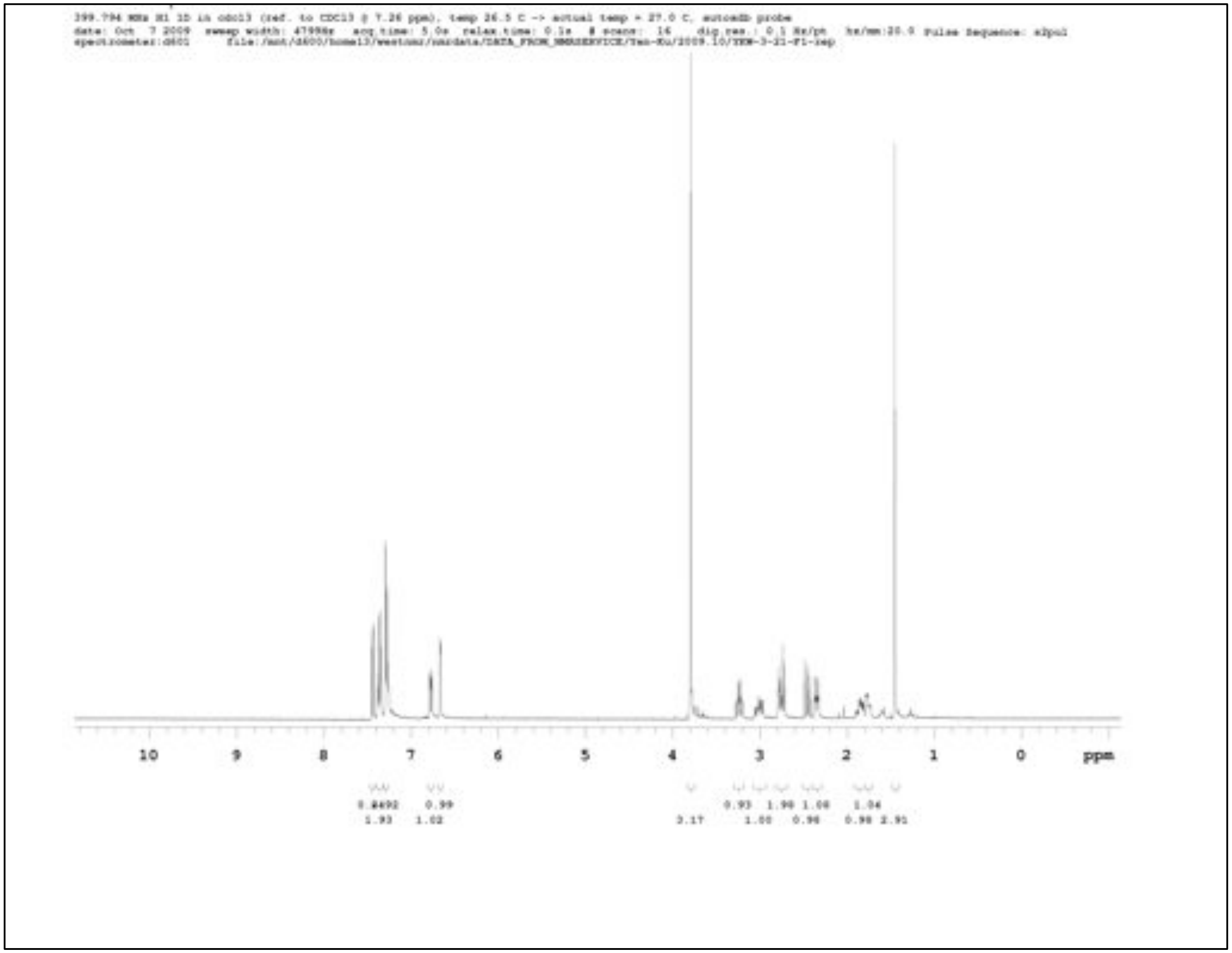


6n

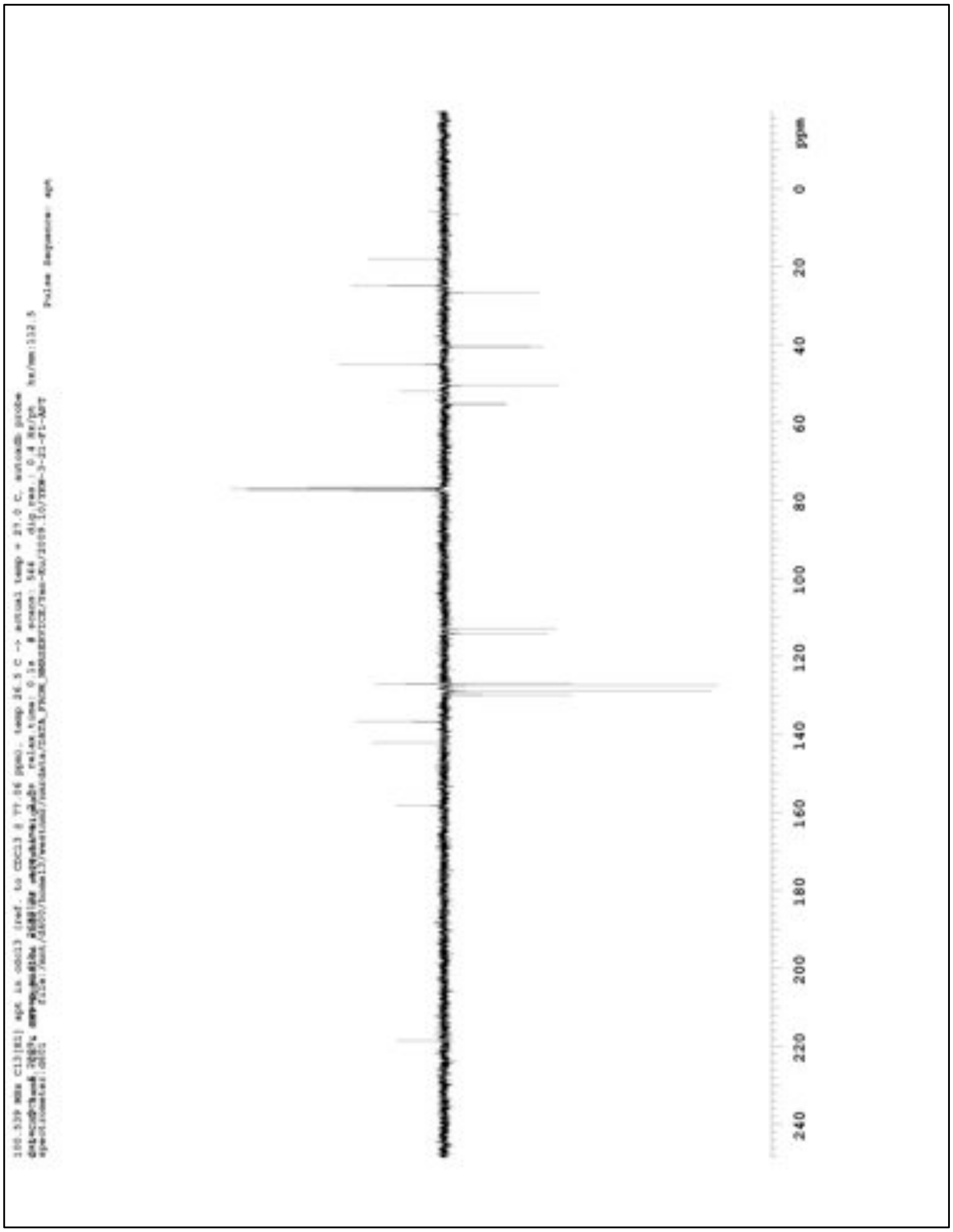

125.690 MHz C13[H1] 1D in cdcl3 (ref. to CDCl3 @ 77.06 ppm), temp 26.1 C -> actual temp = 27.0 C, autoxdb probe
date: Feb 23 2010 sweep width: 33784Hz acq time: 2.5s relax time: 0.1s # scans: 1196 dig res : 0.3 Hz/pt hz/mm:140.8 Pulse Sequence: s2pul
spectrometer:d601 file:/mnt/d600/home13/westonz/nmrdata/DATA_FROM_NMRSERVICE/Yan-Xu/2010.02/2010.02.23.u5_YKW-4-91-co2-F1_C13_1D
240
220
200
180
160
140
120
100
80
60
40
20
0
ppm

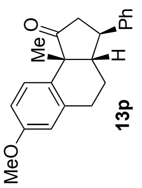


13p

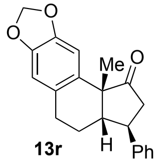


399.794 MHz H1 1D in cdcl3 (ref. to CDCl3 @ 7.26 ppm), temp 26.5 C -> actual temp = 27.0 C, autoxdb probe
date: Oct 7 2009 sweep width: 4799Hz acq.time: 5.0s relax.time: 0.1s # scans: 16 dig.res.: 0.1 Hz/pt hz/mm:20.0 Pulse Sequence: s2pul
spectrometer:d601 file:/mnt/d600/home13/westnmr/nmrdata/DATA_FROM_NMRSERVICE/Yan-Xu/2009.10/YXW-3-21-F1-sep
10
9
8
7
6
5
4
3
2
1
0
ppm
0.8492
1.93
0.99
1.02
3.17
0.93
1.00
1.90
1.08
0.96
1.04
0.98
2.91

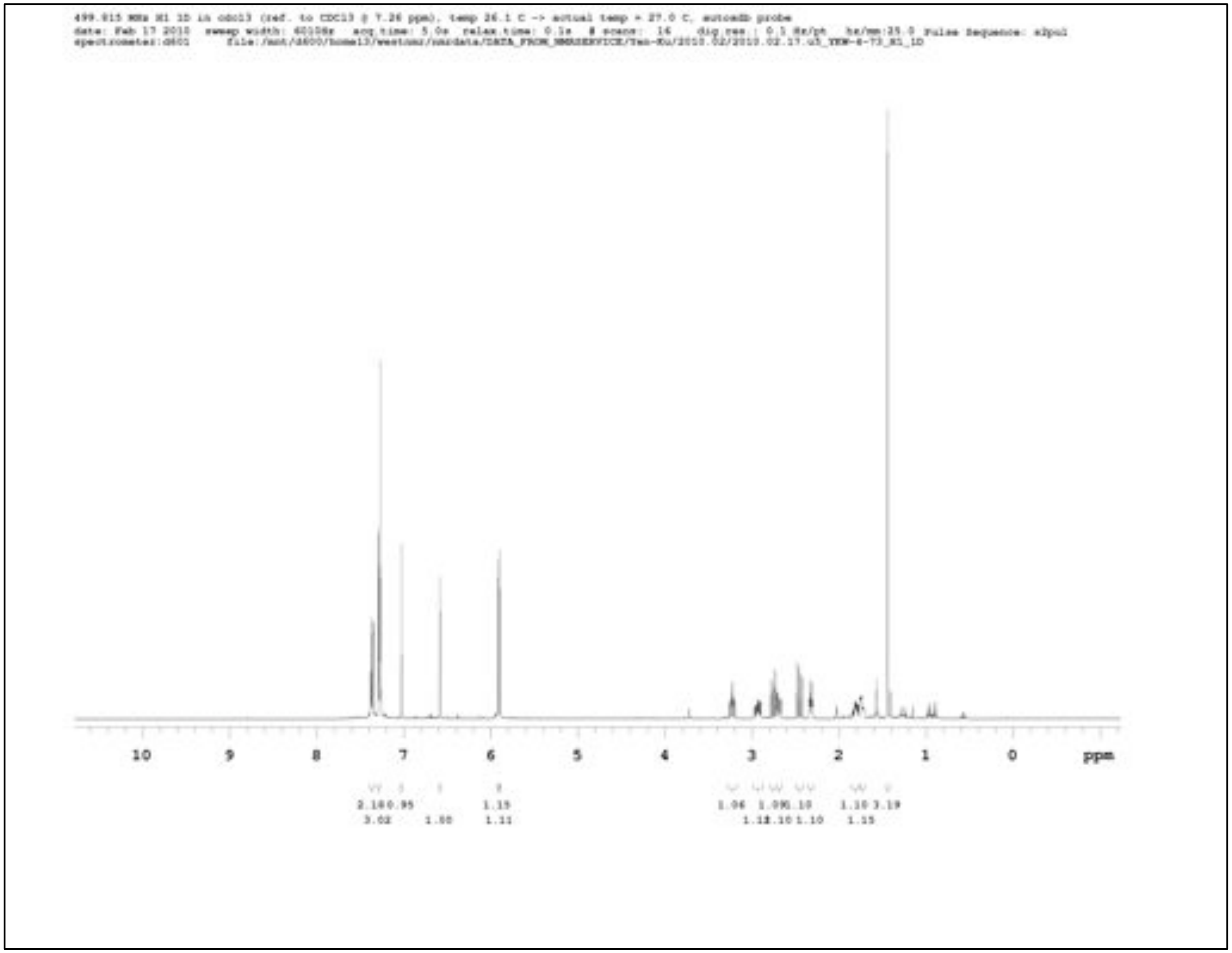

240
220
200
180
160
140
120
100
80
60
40
20
0
ppm
Pulse Sequence: apt

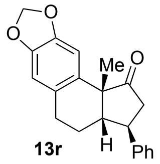

MeO
Me
O
H
Ph

13p


O
O
Me
O
H
Ph

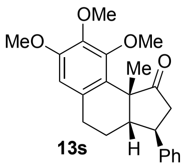
13r


499.815 MHz H1 1D in cdcl3 (ref. to CDCl3 @ 7.26 ppm), temp 26.1 C -> actual temp = 27.0 C, autoxdb probe
date: Feb 17 2010 sweep width: 6010Hz acq.time: 5.0s relax.time: 0.1s # scans: 16 dig.res.: 0.1 Hz/pt hz/mm:25.0 Pulse Sequence: s2pul
spectrometer:d601 file:/mnt/d600/home13/westonz/nmrdata/DATA_FROM_NMRSERVICE/Yan-Xu/2010.02/2010.02.17.u5_YXW-6-73_H1_1D
10
9
8
7
6
5
4
3
2
1
0
ppm
2.10
0.95
3.02
1.00
1.15
1.11
1.06
1.09
1.12
1.10
1.10
1.10
1.10
1.15
3.19

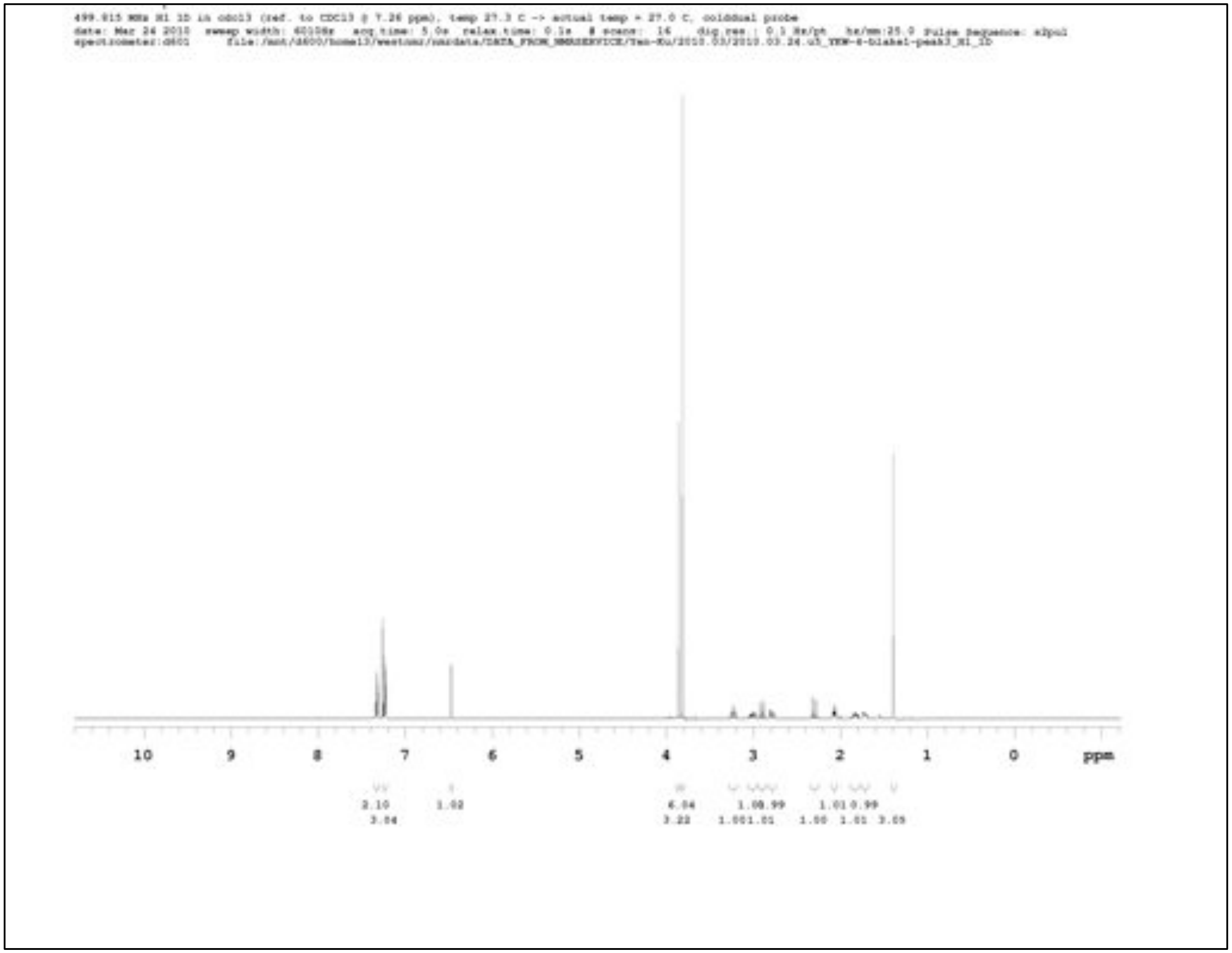

Me
O
O
O
H
Ph

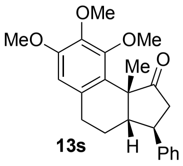
13r


125.690 MHz C13[H1] 1D in cdcl3 (ref. to CDCl3 @ 77.06 ppm), temp 26.1 C -> actual temp = 27.0 C, autoxdb probe
date: Feb 17 2010 sweep width: 33784Hz acq.time: 2.5s relax.time: 0.1s # scans: 188 dig.res.: 0.3 Hz/pt hz/mm:140.9 Pulse Sequence: s2pul
spectrometer:d601 file:/mnt/d600/home13/westonr/nmrdata/DATA_FROM_NMRSERVICE/Yan-Xu/2010.02/2010.02.17.u5_YXW-4-73_C13_1D
240
220
200
180
160
140
120
100
80
60
40
20
0
ppm

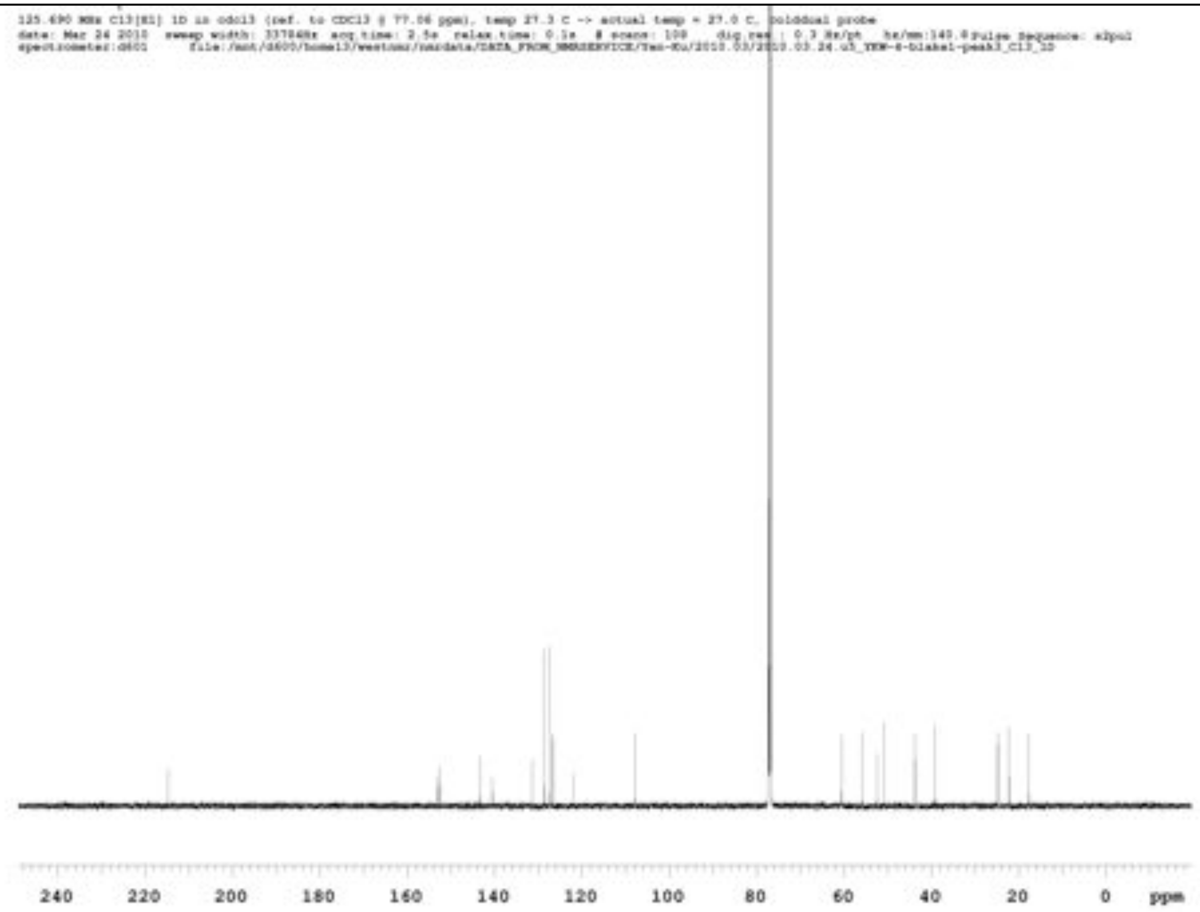


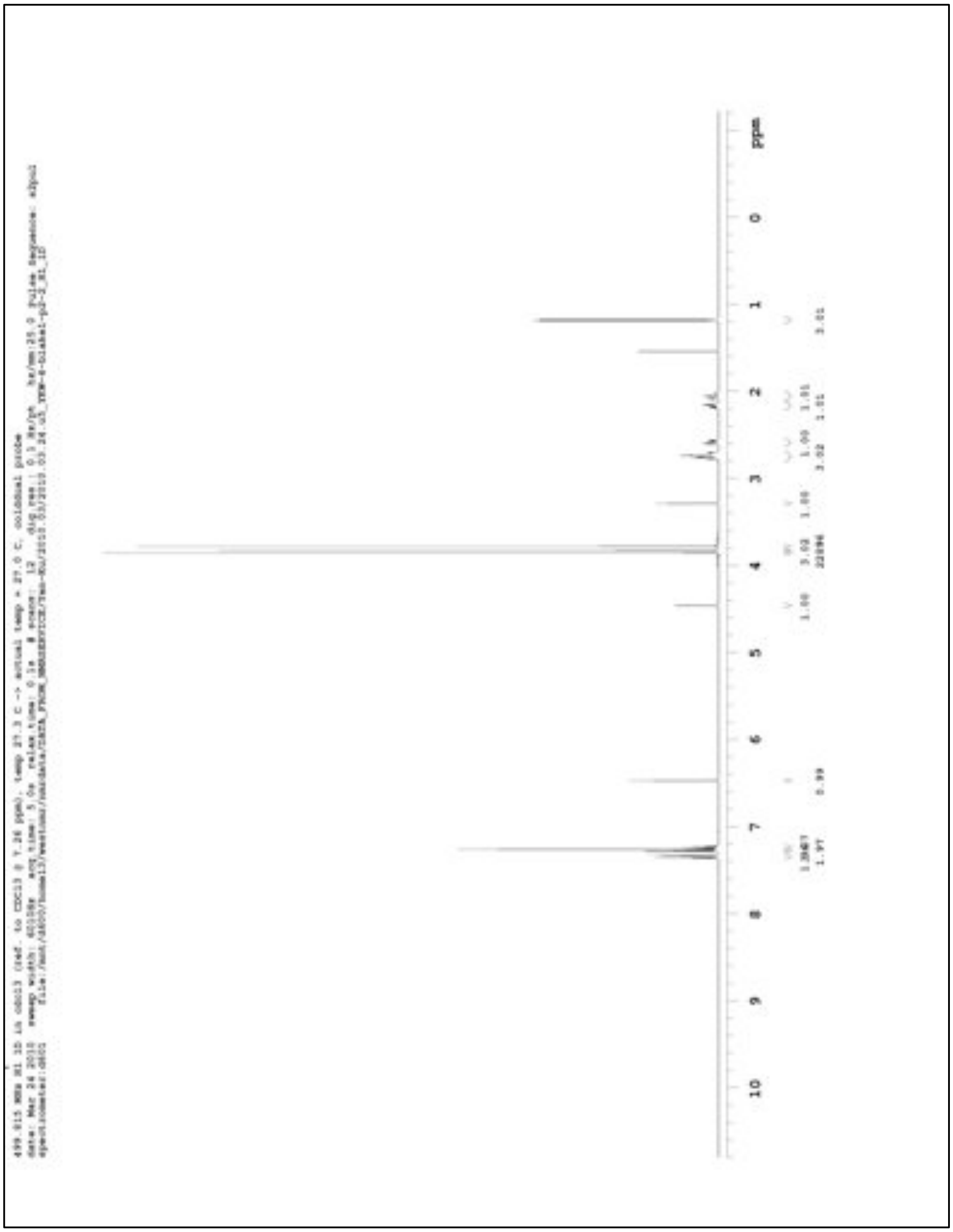
13s

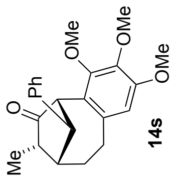

499.815 MHz H1 1D in cdcl3 (ref. to CDCl3 @ 7.26 ppm), temp 27.3 C -> actual temp = 27.0 C, colddual probe
date: Mar 24 2010 sweep width: 4010Hz acq.time: 5.0s relax.time: 0.1s # scans: 16 dig.res.: 0.1 Hz/pt hz/mm:25.0 Pulse Sequence: s2pul
spectrometer:d601 file:/mnt/d600/home13/westumr/nmrdata/DATA_FROM_NMRSERVICE/Yan-Xu/2010.03/2010.03.24.u5_YXW-4-blabel-peak3_H1_1D
10
9
8
7
6
5
4
3
2
1
0
ppm
2.10
3.04
1.02
6.04
3.22
1.00
0.99
1.00
1.01
1.01
0.99
1.00
1.01
3.09



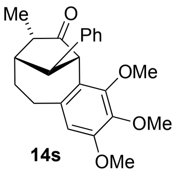
13s


125.690 MHz C13[H1] 1D in cdcl3 (ref. to CDCl3 @ 77.06 ppm), temp 27.3 C -> actual temp = 27.0 C, boldual probe
date: Mar 24 2010 sweep width: 33784Hz acq.time: 2.5s relax.time: 0.1s # scans: 100 dig.res.: 0.3 Hz/pt hz/mm:140.8 Pulse Sequence: s2pul
spectrometer:d601 file:/mnt/d600/home13/westnmr/nmrdata/DATA_FROM_NMRSERVICE/Tao-Xu/2010.03/2010.03.24.u5_TXW-4-blakel-peak3_C13_10
240
220
200
180
160
140
120
100
80
60
40
20
0
ppm


ppm
0
1
2
3
4
5
6
7
8
9
10
1.97
0.99
1.00
3.02
1.00
3.02
1.00
1.01
1.01
3.01

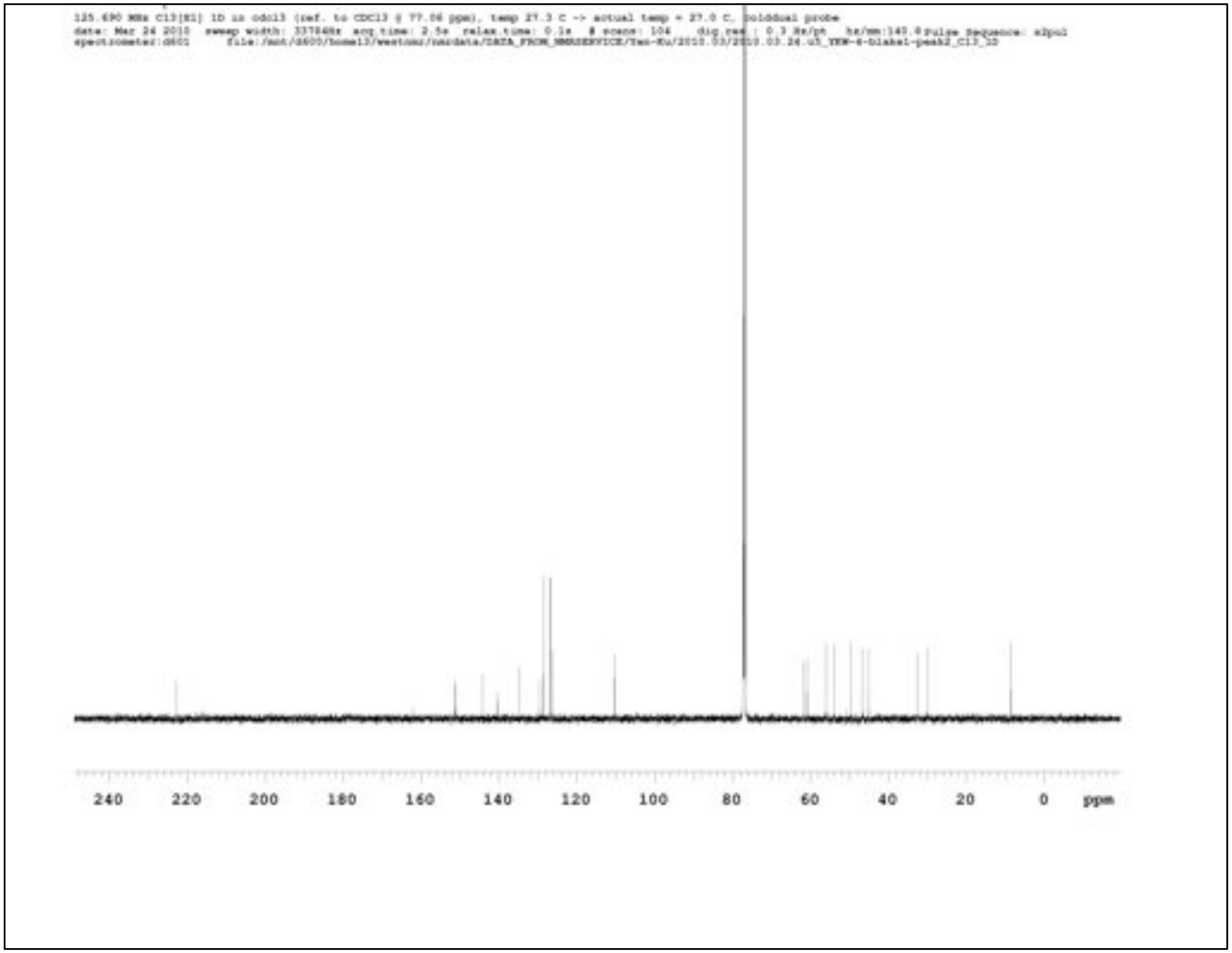

Me
O
Ph
OMe
OMe
OMe

14s

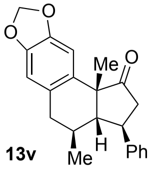


Me
O
Ph
OMe
OMe
OMe

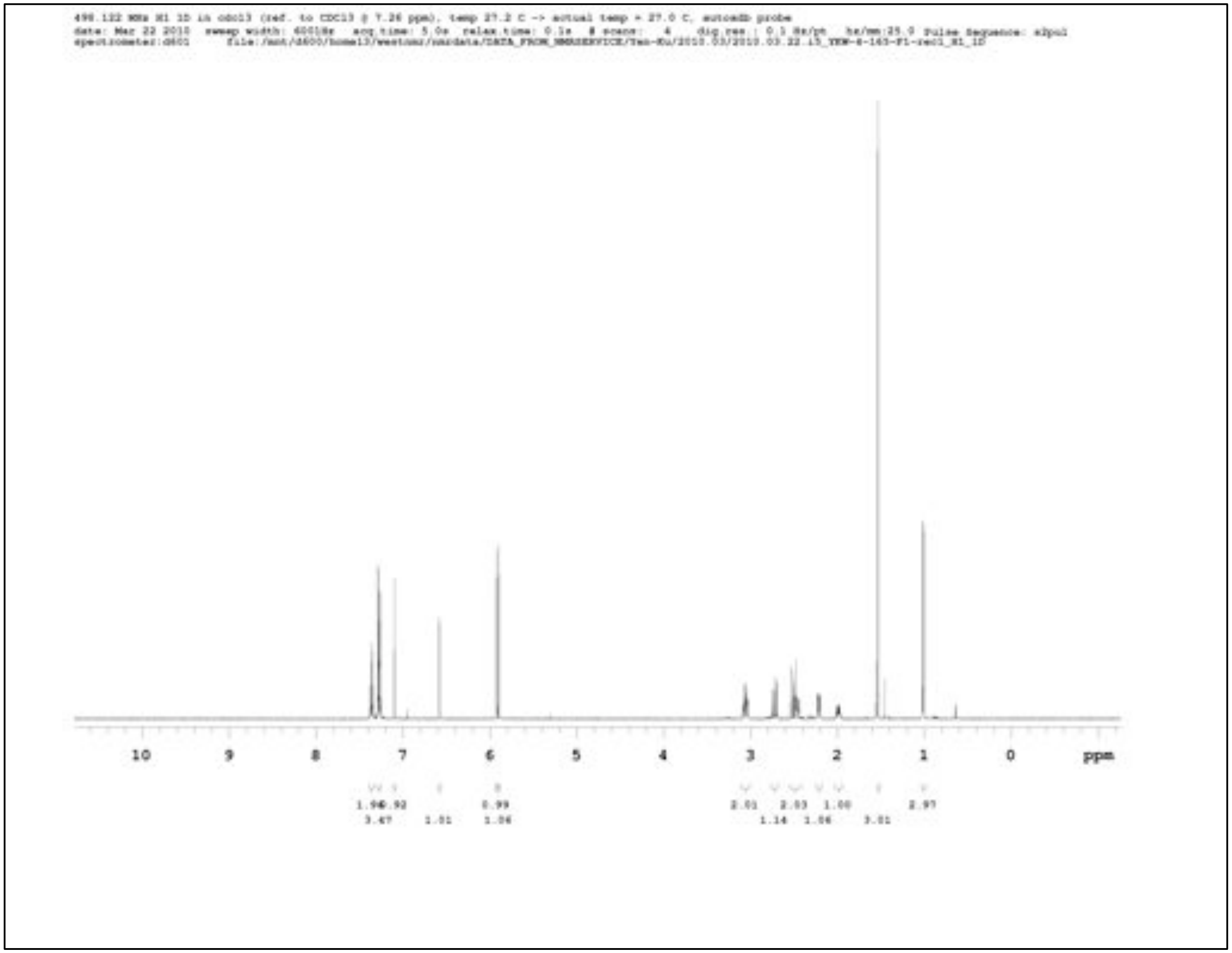
14s

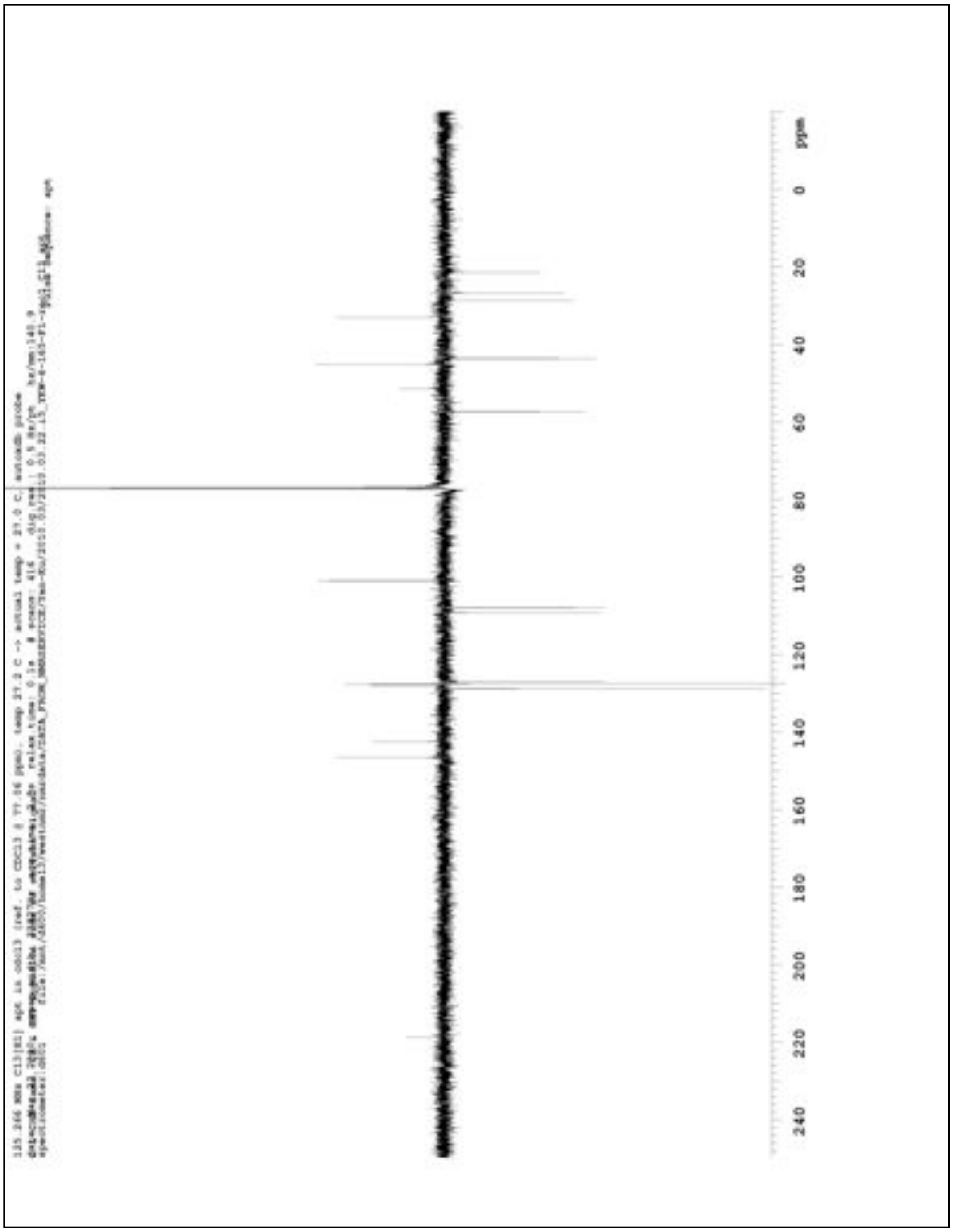


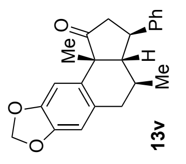
125.690 MHz C13[H1] 1D in cdcl3 (ref. to CDCl3 @ 77.06 ppm), temp 27.3 C -> actual temp = 27.0 C, bolddual probe
date: Mar 24 2010 sweep width: 33784Hz acq.time: 2.5s relax.time: 0.1s # scans: 104 dig.res.: 0.3 Hz/pt hz/mm:140.8 Pulse Sequence: s2pul
spectrometer:d601 file:/mnt/d600/home13/westnmr/nmrdata/DATA_FROM_NMRSERVICE/Yan-Xu/2010.03/2010.03.24.u5_YXW-4-blake1-peak2_C13_10
240
220
200
180
160
140
120
100
80
60
40
20
0
ppm



13v


498.122 MHz H1 1D in cdcl3 (ref. to CDCl3 @ 7.26 ppm), temp 27.2 C -> actual temp = 27.0 C, autoxdb probe
date: Mar 22 2010 sweep width: 6001Hz acq.time: 5.0s relax.time: 0.1s # scans: 4 dig.res.: 0.1 Hz/pt hz/mm:25.0 Pulse Sequence: s2pul
spectrometer:d601 file:/mnt/d600/home13/westomr/nmrdata/DATA_FROM_NMRSERVICE/Yen-Ku/2010.03/2010.03.22.i5_YKW-6-165-F1-recl_H1_1D
10
9
8
7
6
5
4
3
2
1
0
ppm
1.96
0.92
3.47
1.01
0.99
1.06
2.01
1.14
2.03
1.06
1.00
3.01
2.97

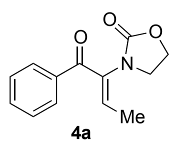




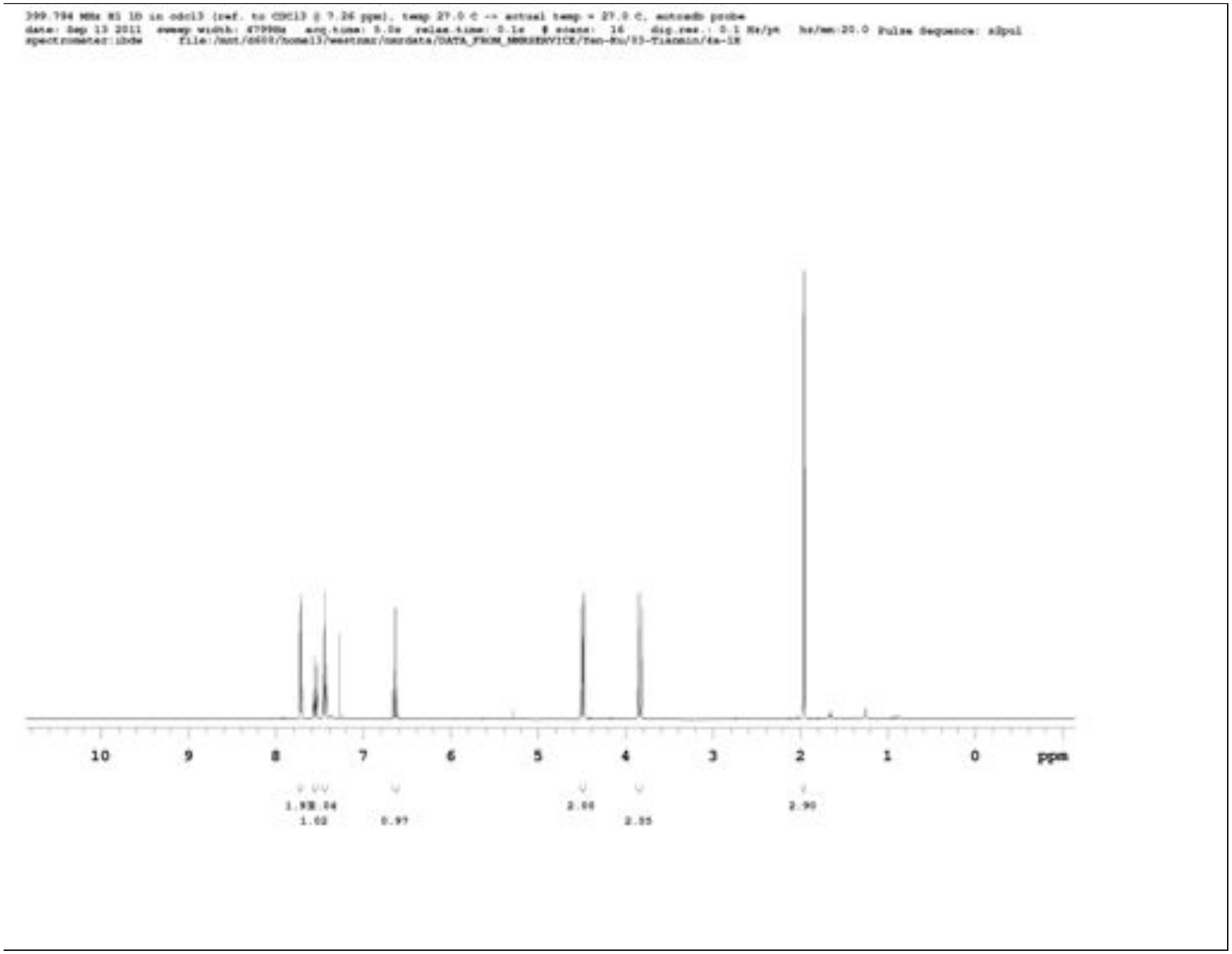
13v

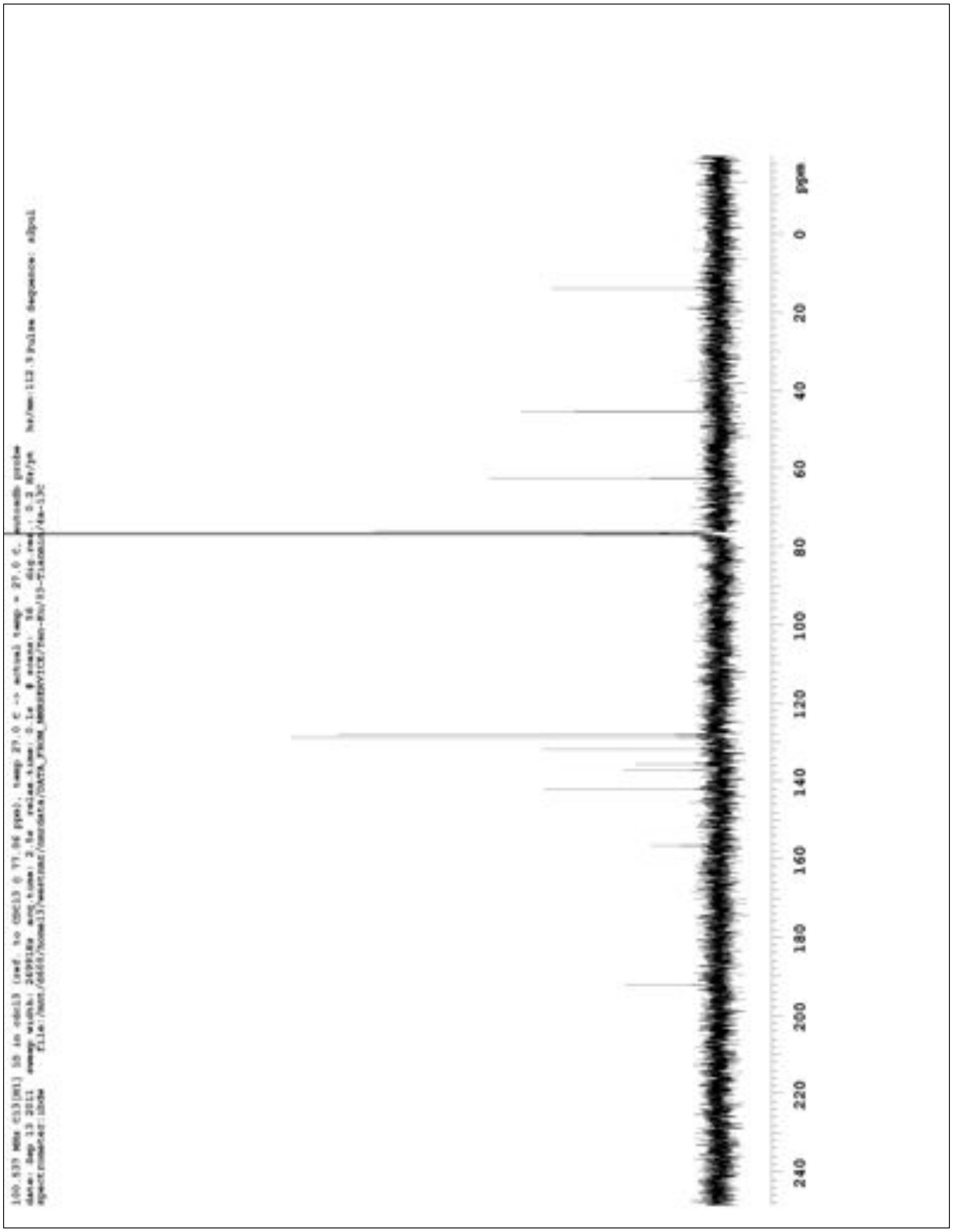
Appendix III:

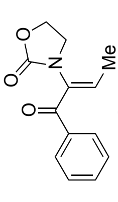
Selected NMR Spectra (Chapter 4)



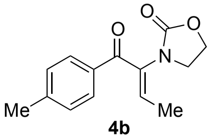
4a


399.794 MHz H1 1D in cdcl3 (ref. to CDCl3 @ 7.26 ppm), temp 27.0 C -> actual temp = 27.0 C, autoxdb probe
date: Sep 13 2011 sweep width: 4799Hz acq.time: 5.0s relax.time: 0.1s # scans: 16 dig.res.: 0.1 Hz/pt hz/mm:20.0 Pulse Sequence: s2pul
spectrometer:ibdw file:/mnt/d600/home13/westnmr/nmrdata/DATA_FROM_NMRSERVICE/Tan-Ru/03-Tianmin/4a-1H
10
9
8
7
6
5
4
3
2
1
0
ppm
1.98
2.04
1.02
0.97
2.08
2.35
2.90

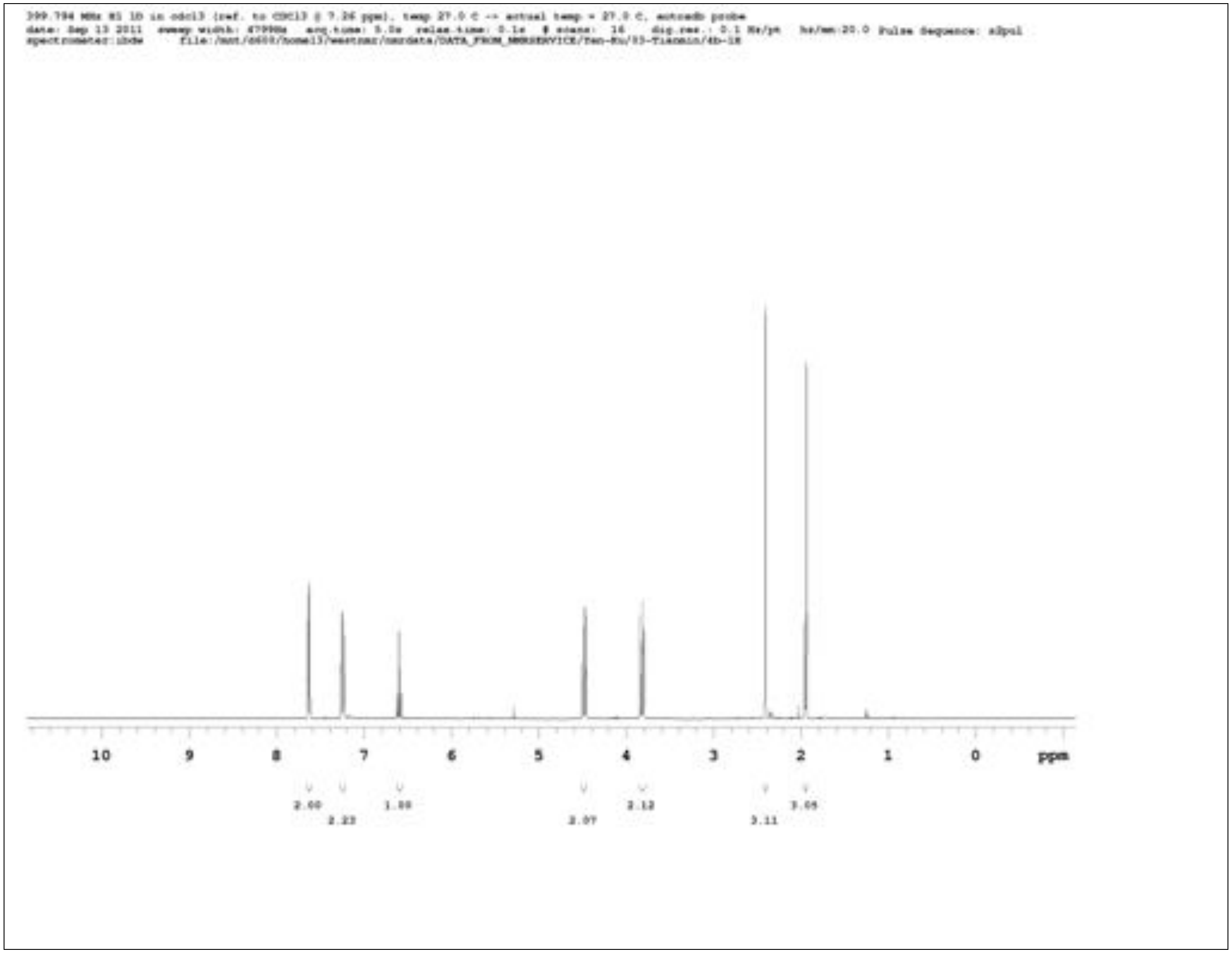


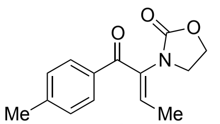


4a

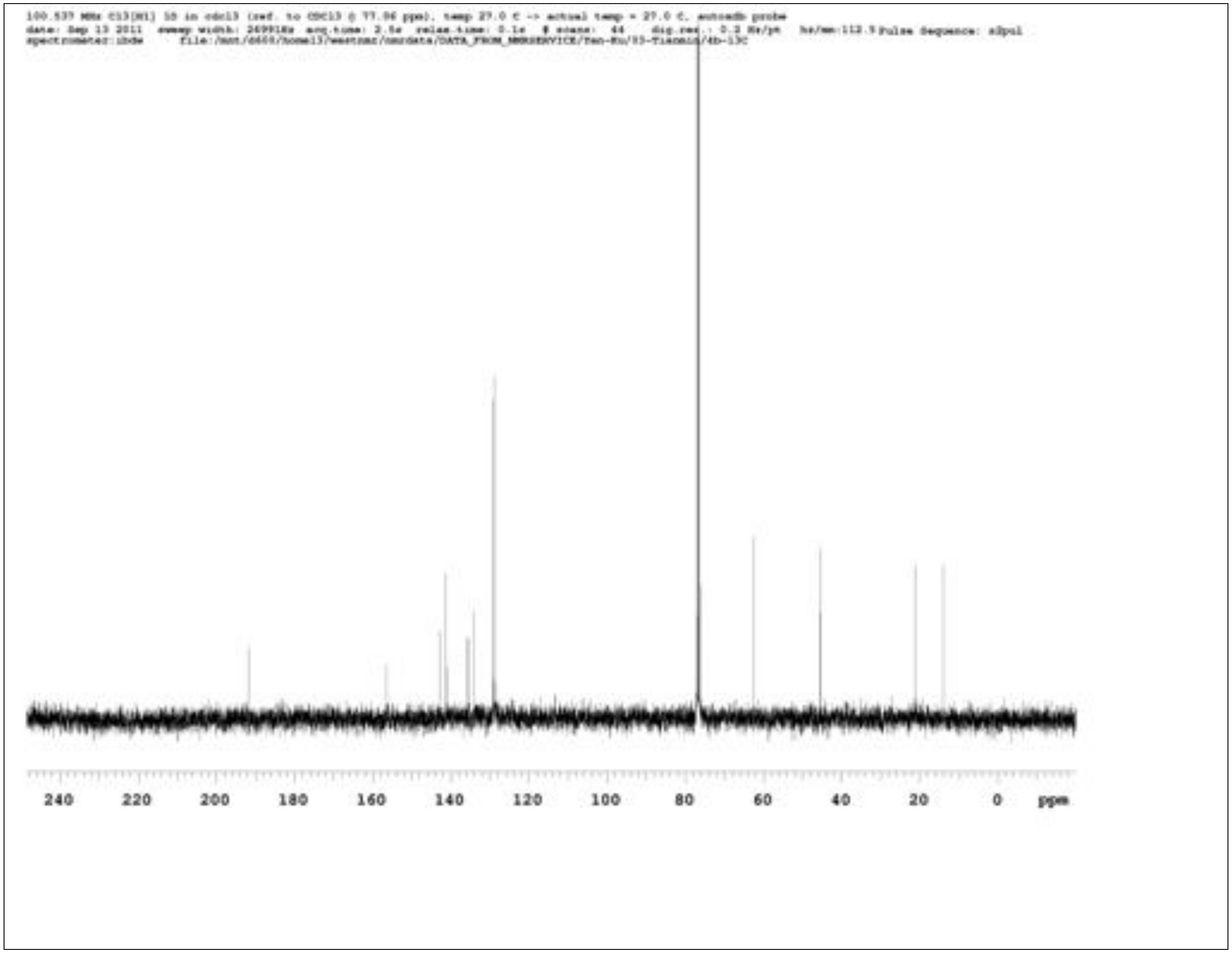

O
O
O
N
Me
Me

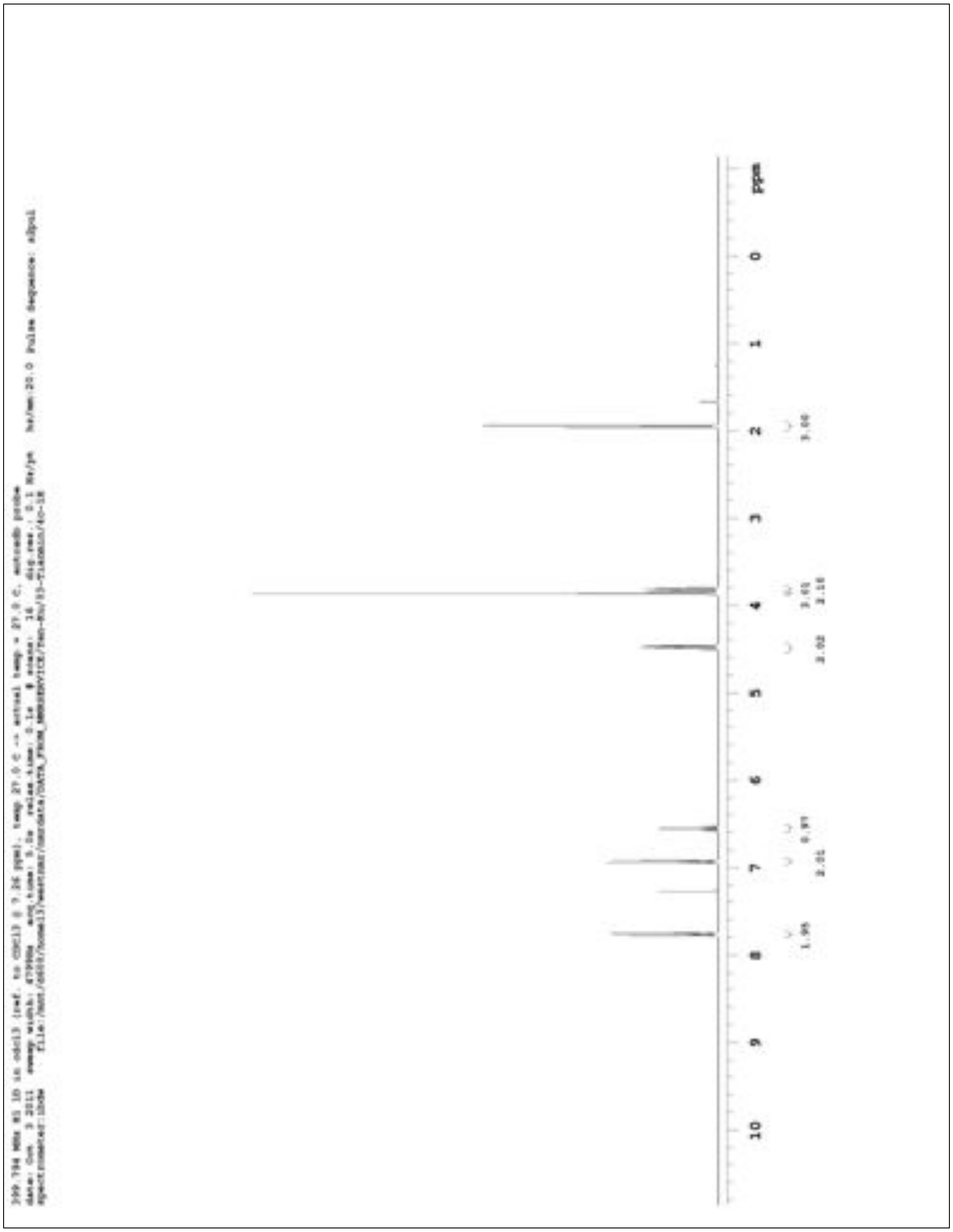
4b

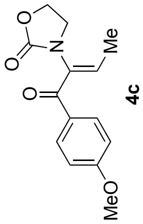

399.794 MHz H1 1D in cdcl3 (ref. to CDCl3 @ 7.26 ppm), temp 27.0 C -> actual temp = 27.0 C, autoxdb probe
date: Sep 13 2011 sweep width: 4799Hz acq.time: 5.0s relax.time: 0.1s # scans: 16 dig.res.: 0.1 Hz/pt hz/mm:20.0 Pulse Sequence: s2pul
spectrometer:ibdw file:/mnt/d600/home13/westnmr/nmrdata/DATA_FROM_NMRSERVICE/Yan-Xu/33-Tianmin/4b-1H
10
9
8
7
6
5
4
3
2
1
0
ppm
2.00
2.23
1.00
2.07
2.12
3.11
3.05



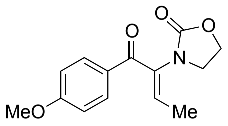
4b


100.537 MHz C13[H1] 1D in cdcl3 (ref. to CDCl3 @ 77.06 ppm), temp 27.0 C -> actual temp = 27.0 C, autoxdb probe
date: Sep 13 2011 sweep width: 24991Hz acq.time: 2.5s relax.time: 0.1s # scans: 44 dig.res.: 0.2 Hz/pt hz/mm:112.5 Pulse Sequence: s2pul
spectrometer:ibdw file:/mnt/d660/home13/westnmr/nmrdata/DATA_FROM_NMRSERVICE/Ten-Hu/33-Tianmin/4b-13C
240
220
200
180
160
140
120
100
80
60
40
20
0
ppm

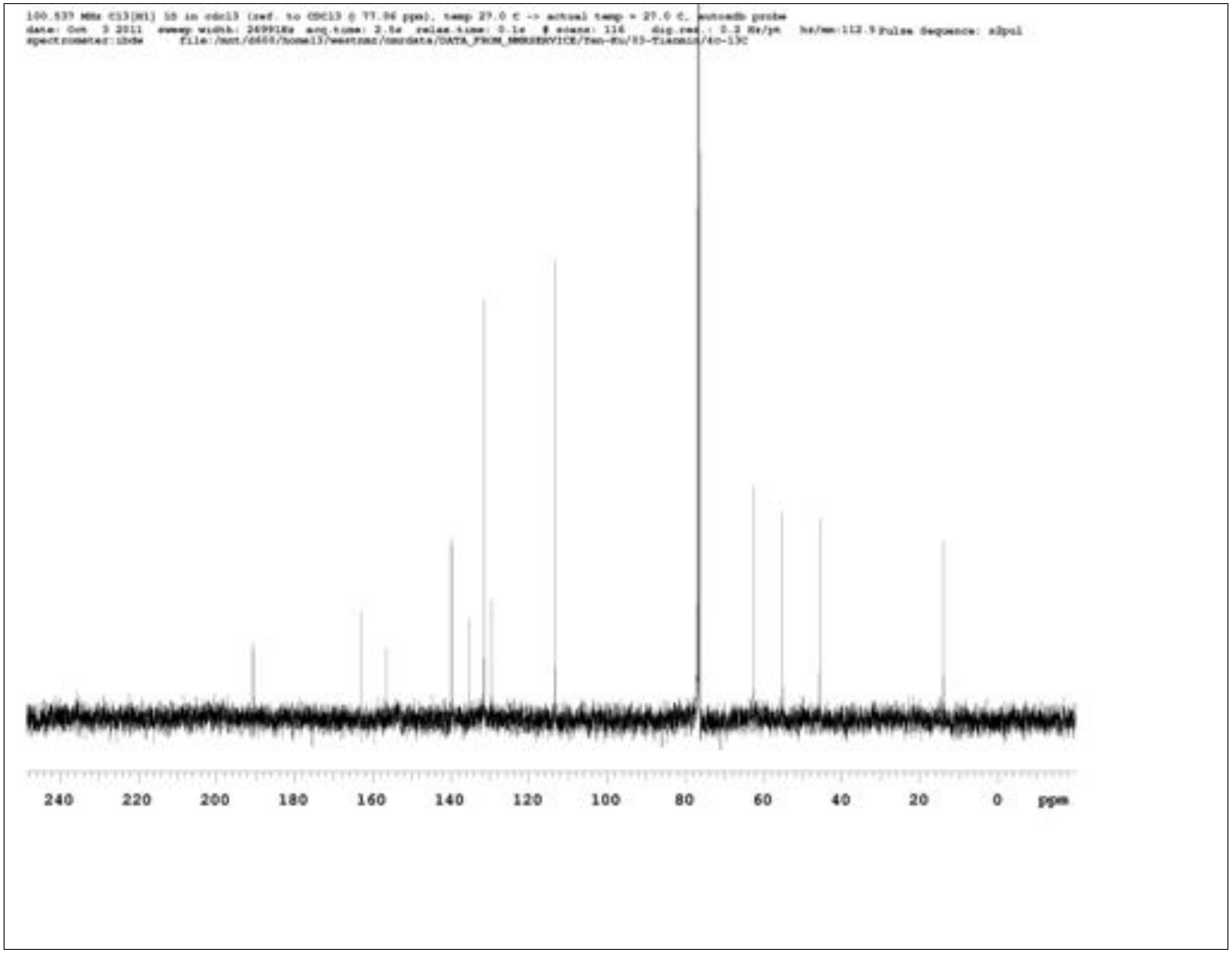


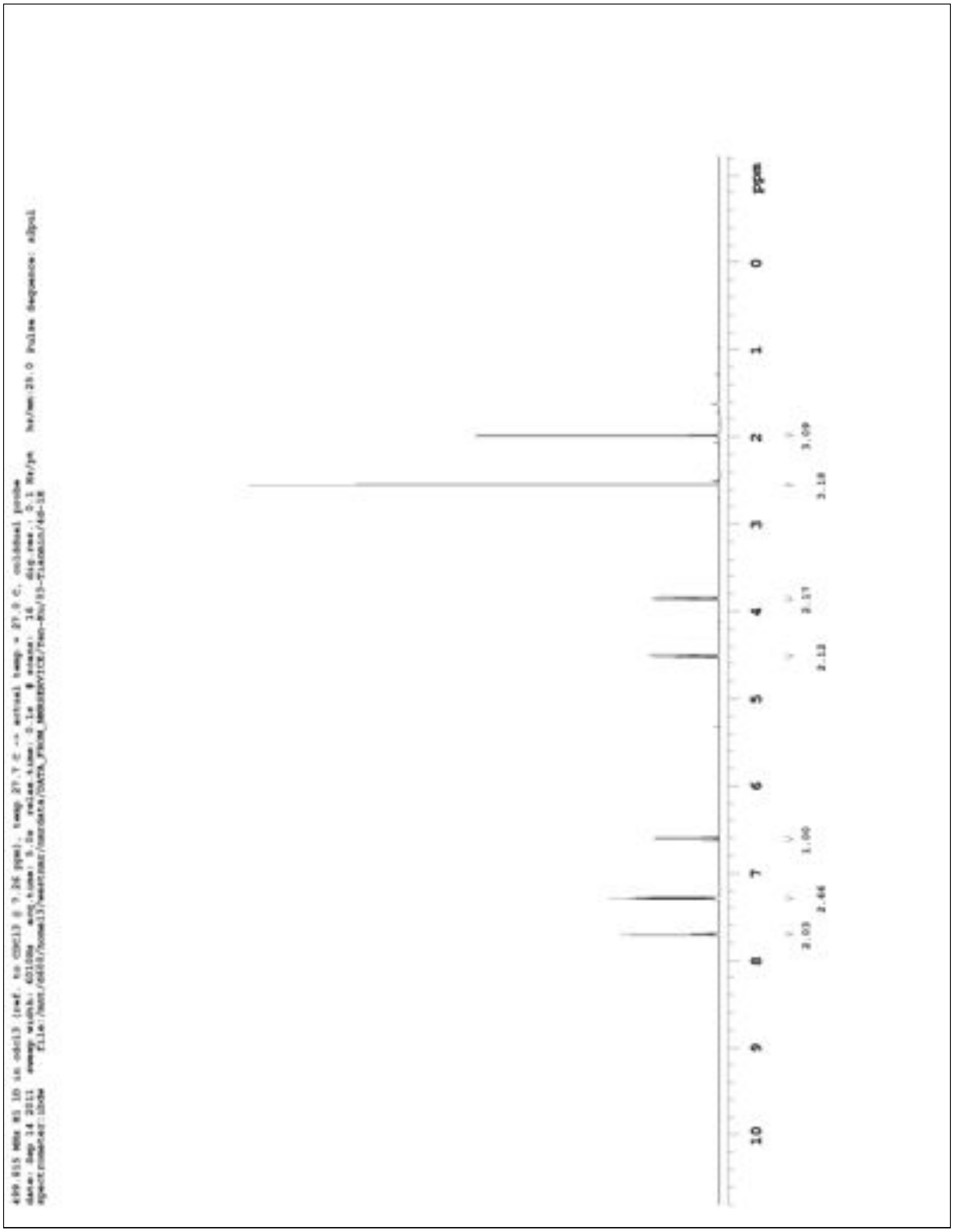


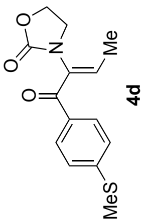
4c



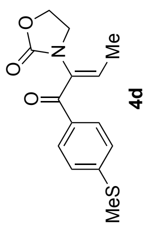
4c


100.537 MHz C13[H1] 1D in cdcl3 (ref. to CDCl3 @ 77.06 ppm), temp 27.0 C -> actual temp = 27.0 C, autoxdb probe
date: Oct 3 2011 sweep width: 26991Hz acq.time: 2.5s relax.time: 0.1s # scans: 116 dig.res.: 0.2 Hz/pt hz/mm:112.5 Pulse Sequence: s2pul
spectrometer:ibdw file:/mnt/d660/home13/westnmr/nmrdata/DATA_FROM_NMRSERVICE/Ten-Hu/03-Tianning/4c-13C
240
220
200
180
160
140
120
100
80
60
40
20
0
ppm

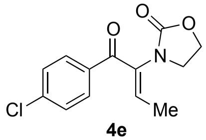




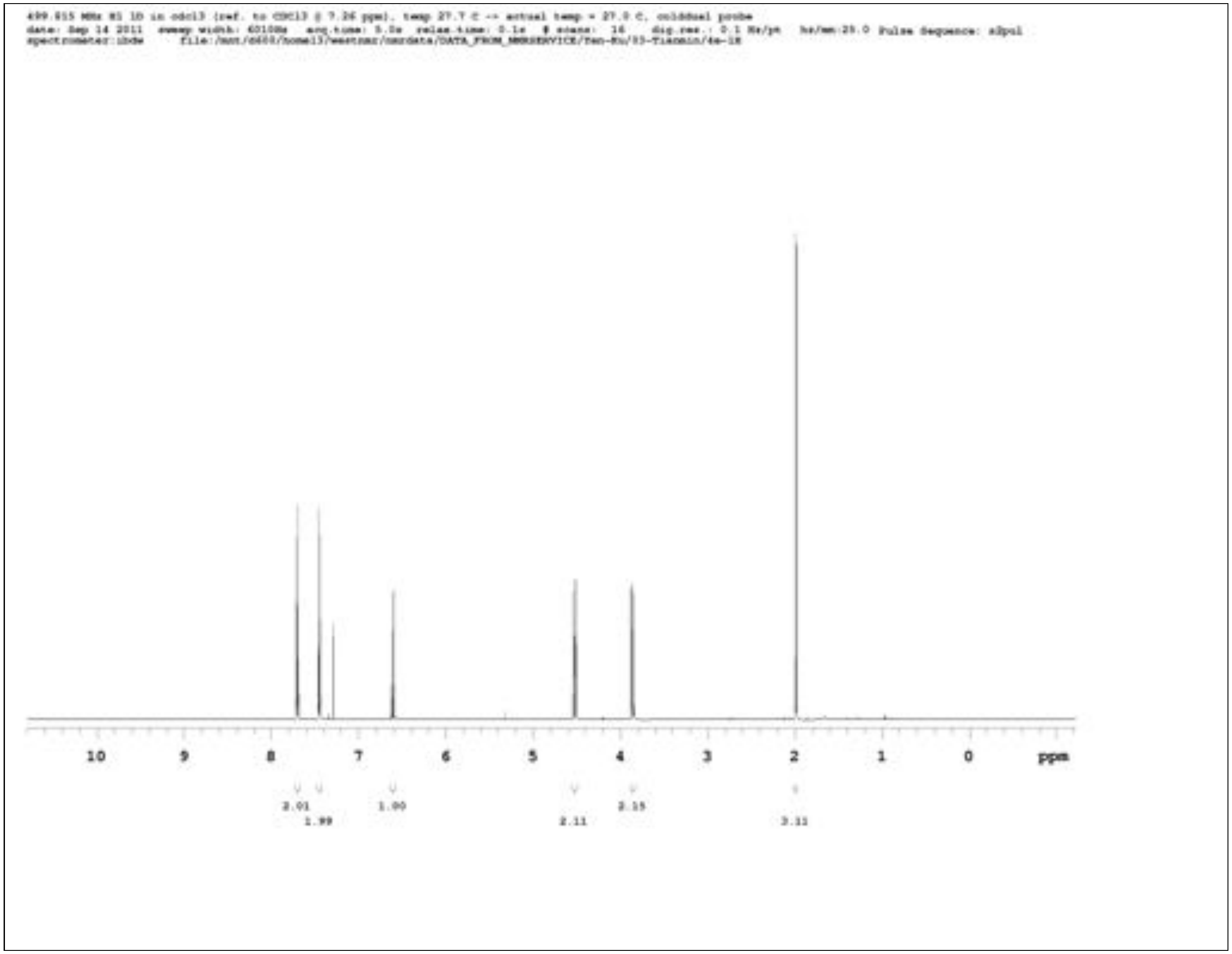
4d

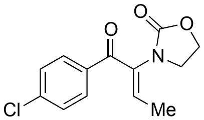


4d

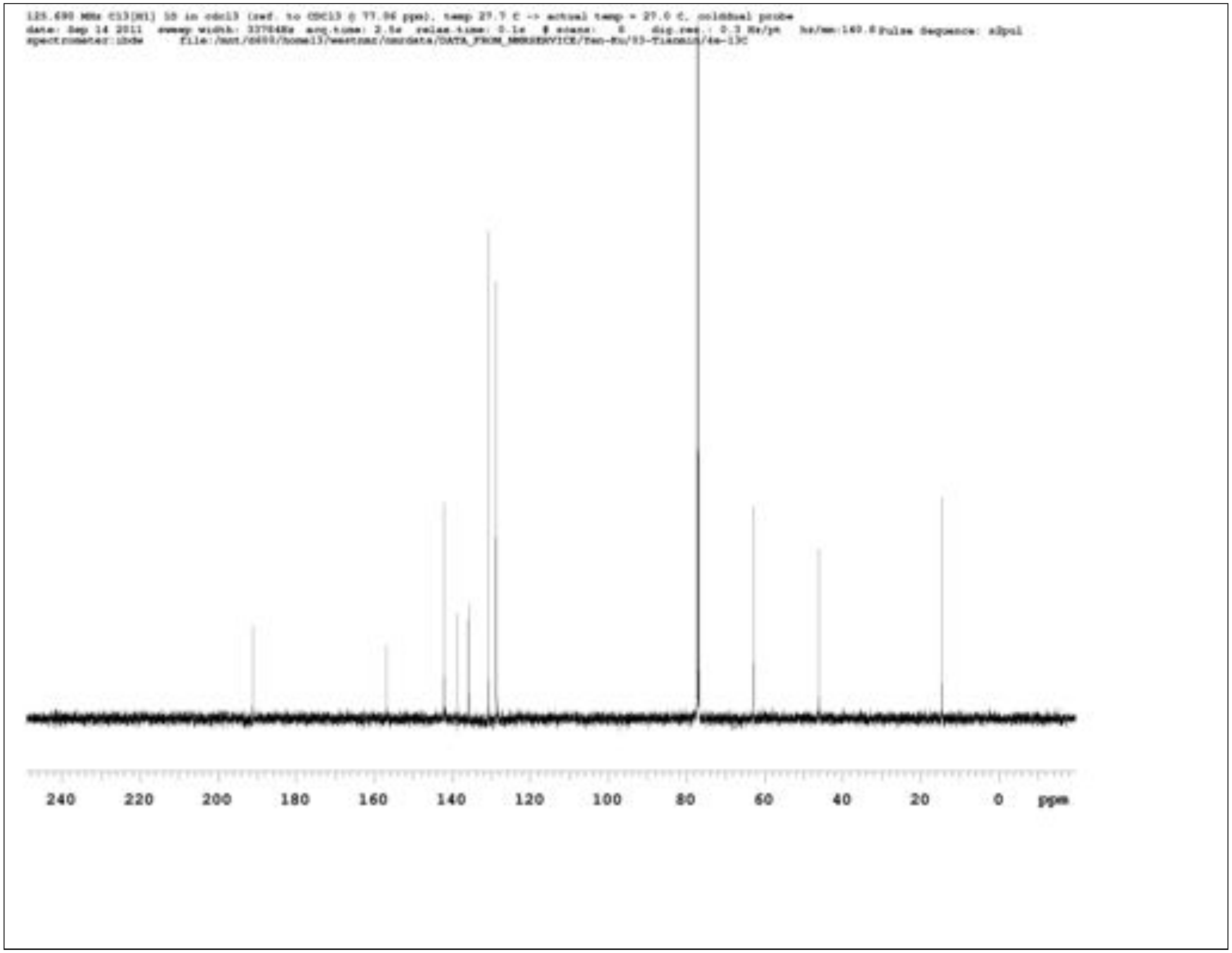

O
O
O
N
Cl
Me

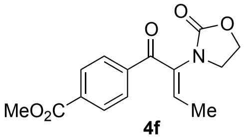
4e


499.815 MHz H1 1D in cdcl3 (ref. to CDCl3 @ 7.26 ppm), temp 27.7 C -> actual temp = 27.0 C, colddual probe
date: Sep 14 2011 sweep width: 6010Hz acq.time: 5.0s relax.time: 0.1s # scans: 16 dig.res.: 0.1 Hz/pt hz/mm:25.0 Pulse Sequence: s2pul
spectrometer:ibdw file:/mnt/d600/home13/westnmr/nmrdata/DATA_FROM_NMRSERVICE/Ten-Hu/33-Tianmin/4e-1H
10
9
8
7
6
5
4
3
2
1
0
ppm
2.01
1.99
1.00
2.11
2.15
3.11

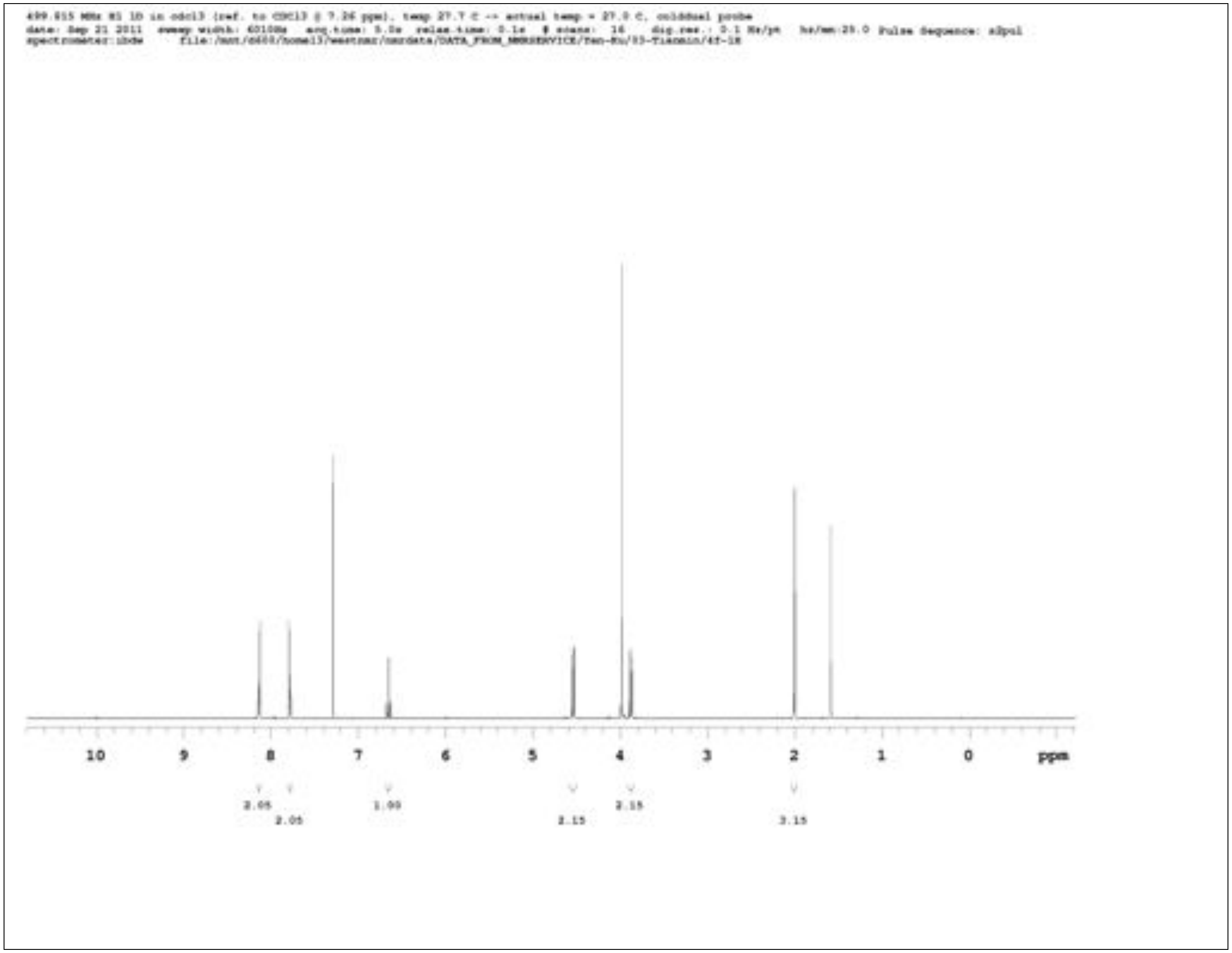

O
O
O
N
Cl
Me

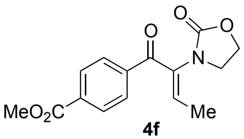
4e


125.690 MHz C13[H1] 1D in cdcl3 (ref. to CDCl3 @ 77.06 ppm), temp 27.7 C -> actual temp = 27.0 C, colddual probe
date: Sep 14 2011 sweep width: 33784Hz acq.time: 2.5s relax.time: 0.1s # scans: 8 dig.res.: 0.3 Hz/pt hz/mm:140.8 Pulse Sequence: s2pul
spectrometer:inde file:/mnt/d600/home13/westnmr/nmrdata/DATA_FROM_NMRSERVICE/Tan-Ru/33-Tianmin/4e-13C
240
220
200
180
160
140
120
100
80
60
40
20
0
ppm

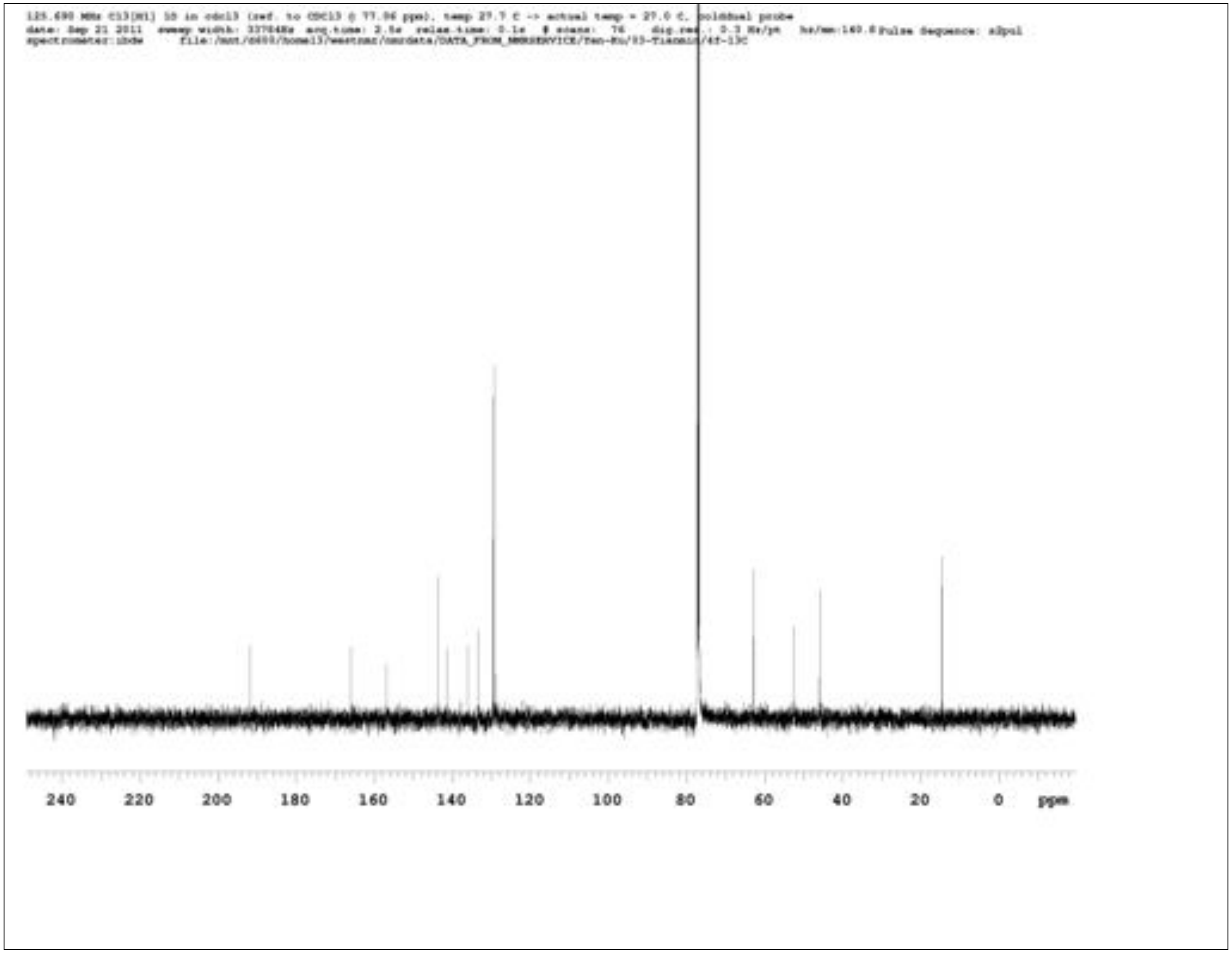

O
O
O
N
MeO2C
Me

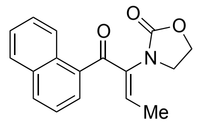
4f


499.815 MHz H1 1D in cdcl3 (ref. to CDCl3 @ 7.26 ppm), temp 27.7 C -> actual temp = 27.0 C, colddual probe
date: Sep 21 2011 sweep width: 6010Hz acq.time: 5.0s relax.time: 0.1s # scans: 16 dig.res.: 0.1 Hz/pt hz/mm:25.0 Pulse Sequence: s2pul
spectrometer:ibdw file:/mnt/d600/home13/westnmr/nmrdata/DATA_FROM_NMRSERVICE/Ten-Bu/03-Tianmin/4f-1H
10
9
8
7
6
5
4
3
2
1
0
ppm
2.05
2.05
1.00
2.15
2.15
3.15

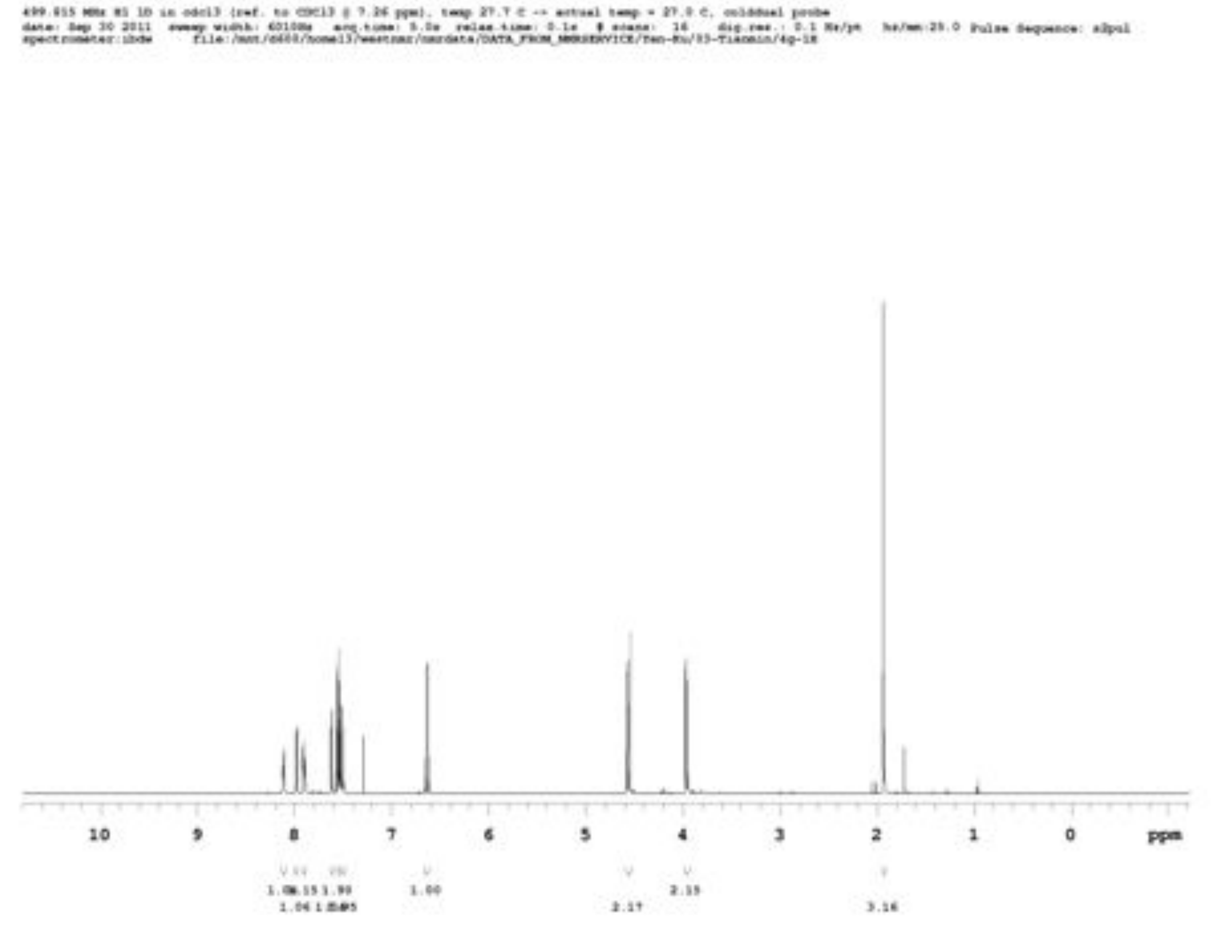


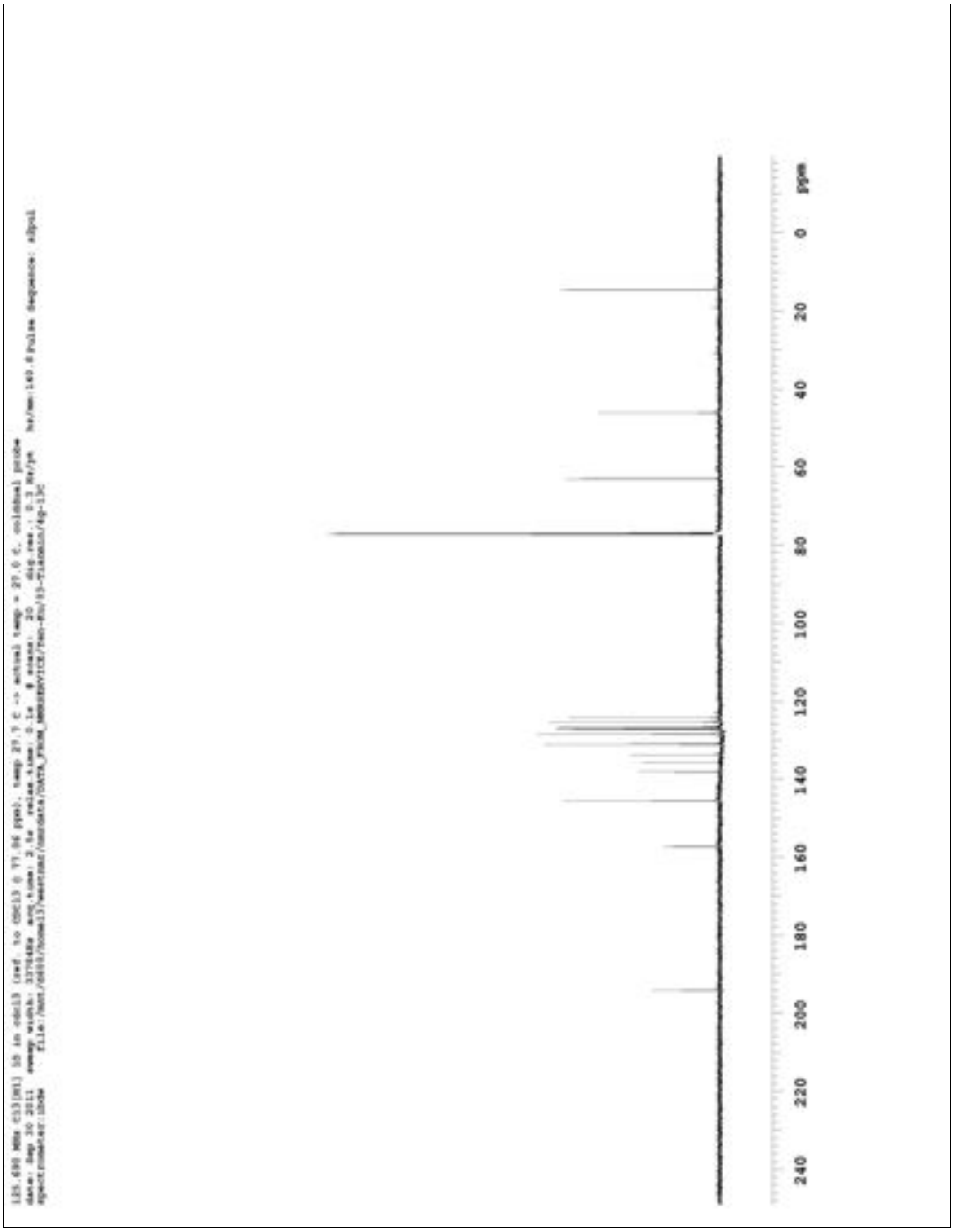
4f

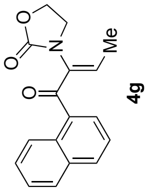

125.690 MHz C13[H1] 1D in cdcl3 (ref. to CDCl3 @ 77.06 ppm), temp 27.7 C -> actual temp = 27.0 C, colddual probe
date: Sep 21 2011 sweep width: 33784Hz acq.time: 2.5s relax.time: 0.1s # scans: 76 dig.res.: 0.3 Hz/pt hz/mm:140.8 Pulse Sequence: s2pul
spectrometer:ibdw file:/mnt/d600/home13/westnmr/nmrdata/DATA_FROM_NMRSERVICE/Tan-Ru/03-Tianning/4f-13C
240
220
200
180
160
140
120
100
80
60
40
20
0
ppm



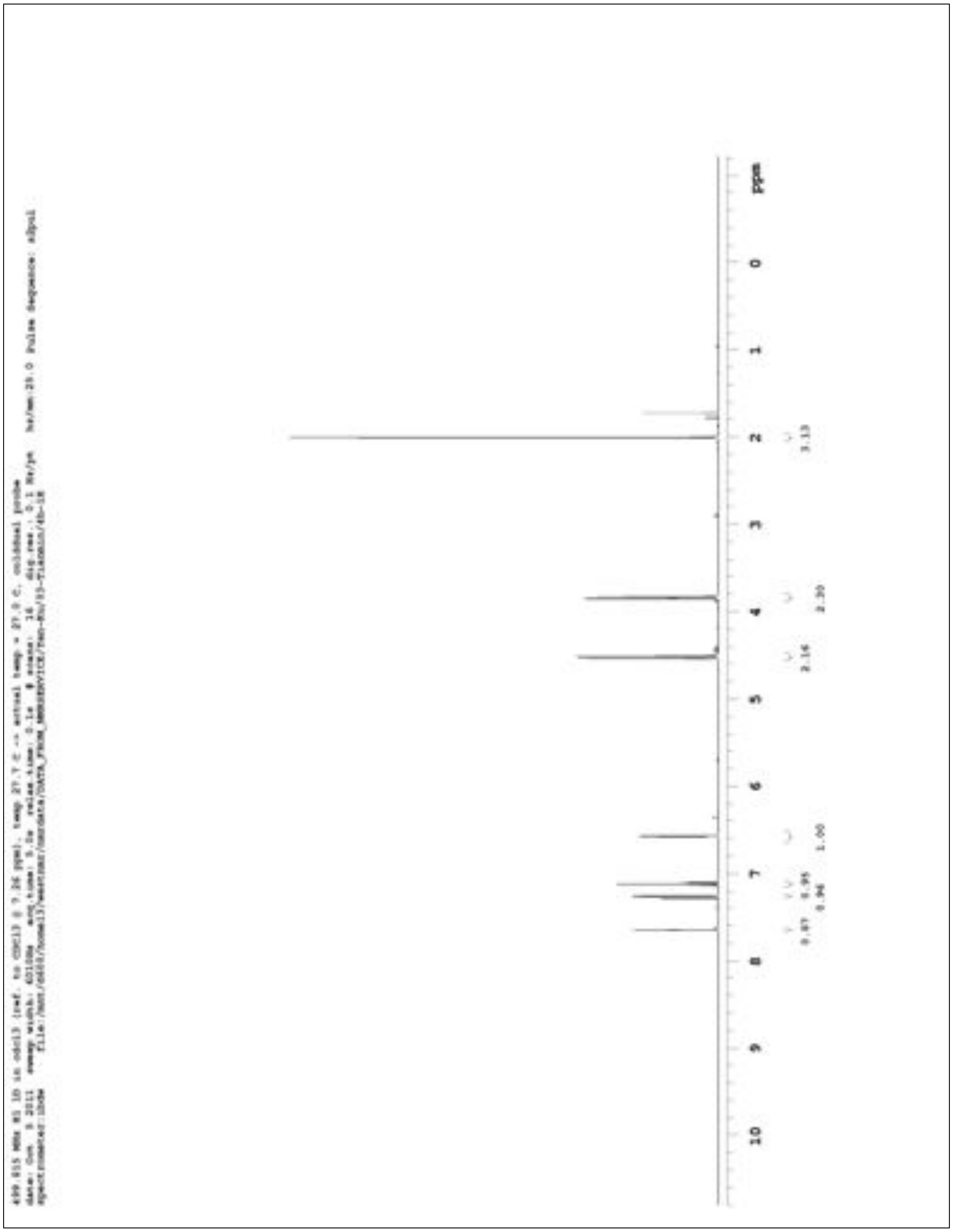
4g

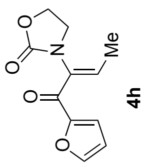

499.815 MHz H1 1D in cdcl3 (ref. to CDCl3 @ 7.26 ppm), temp 27.7 C -> actual temp = 27.0 C, colddual probe
date: Sep 30 2011 sweep width: 6010Hz acq.time: 5.0s relax.time: 0.1s # scans: 16 dig.res.: 0.1 Hz/pt hz/mm:25.0 Pulse Sequence: s2pul
spectrometer:ibdw file:/mnt/d600/home13/eastnmr/nmrdata/DATA_FROM_NMRSERVICE/Yen-Ku/33-Tianmin/4g-1H
10
9
8
7
6
5
4
3
2
1
0
ppm
1.06
1.15
1.99
1.04
1.05
1.00
2.17
2.15
3.16



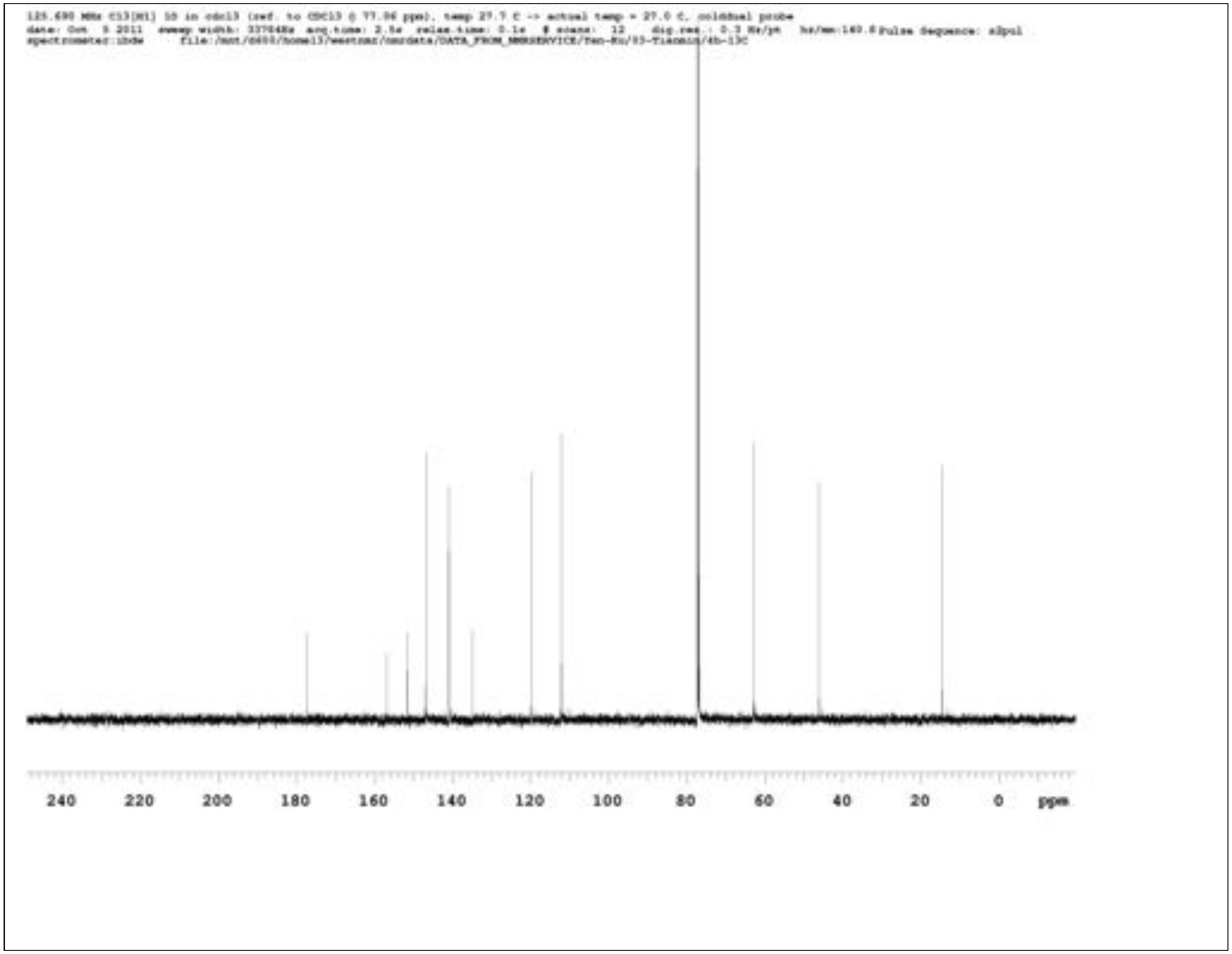


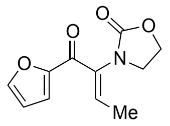
4g



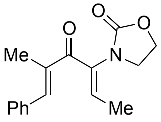


4h

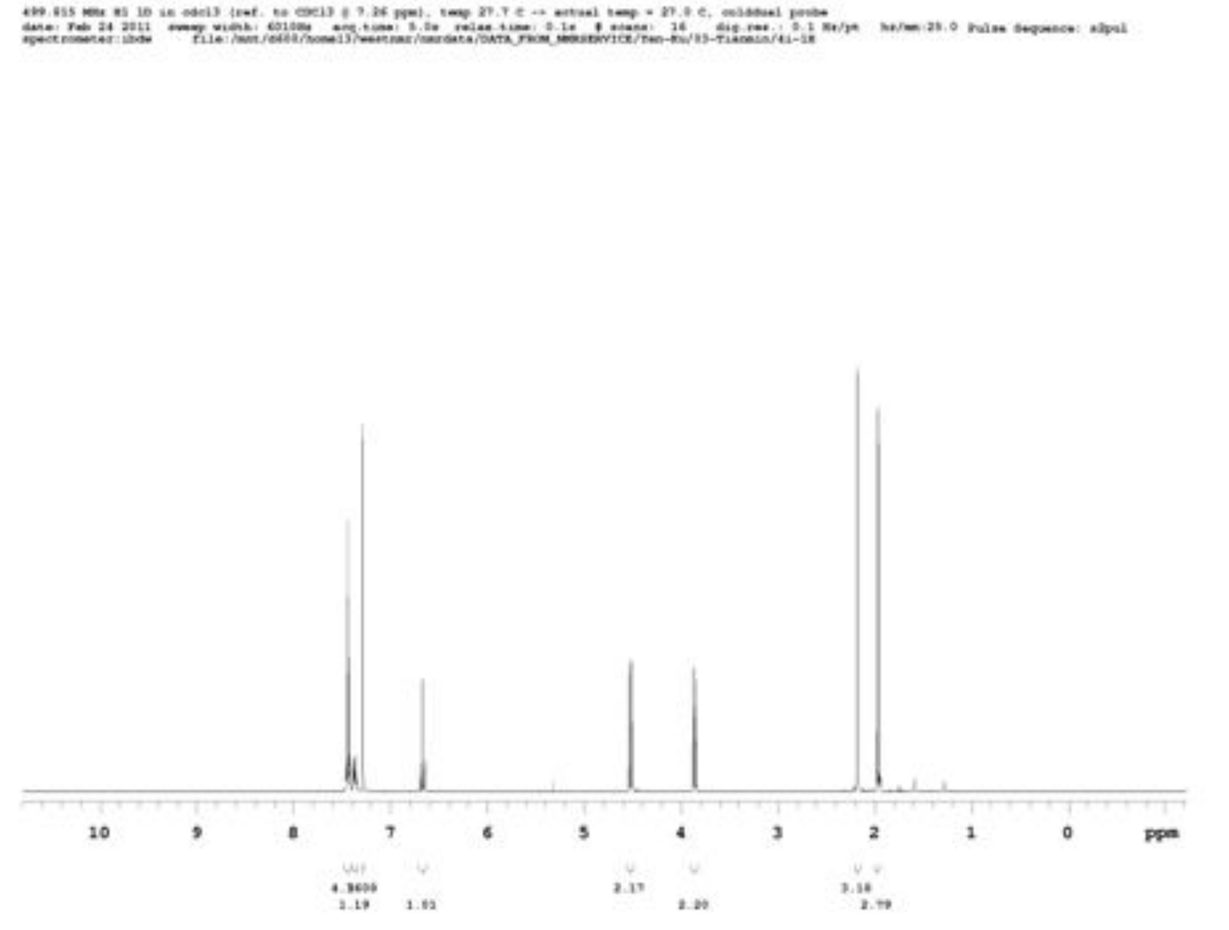

125.690 MHz C13[H1] 1D in cdcl3 (ref. to CDCl3 @ 77.06 ppm), temp 27.7 C -> actual temp = 27.0 C, coldDual probe
date: Oct 5 2011 sweep width: 33784Hz acq.time: 2.5s relax.time: 0.1s # scans: 12 dig.res.: 0.3 Hz/pt hz/mm:140.8 Pulse Sequence: s2pul
spectrometer:ibdw file:/mnt/d600/home13/westsmr/nmrdata/DATA_FROM_NMRSERVICE/Ten-Ru/03-Tianning/4h-13C
240
220
200
180
160
140
120
100
80
60
40
20
0
ppm

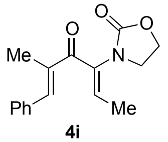

O
O
O
N
O
Me

4h

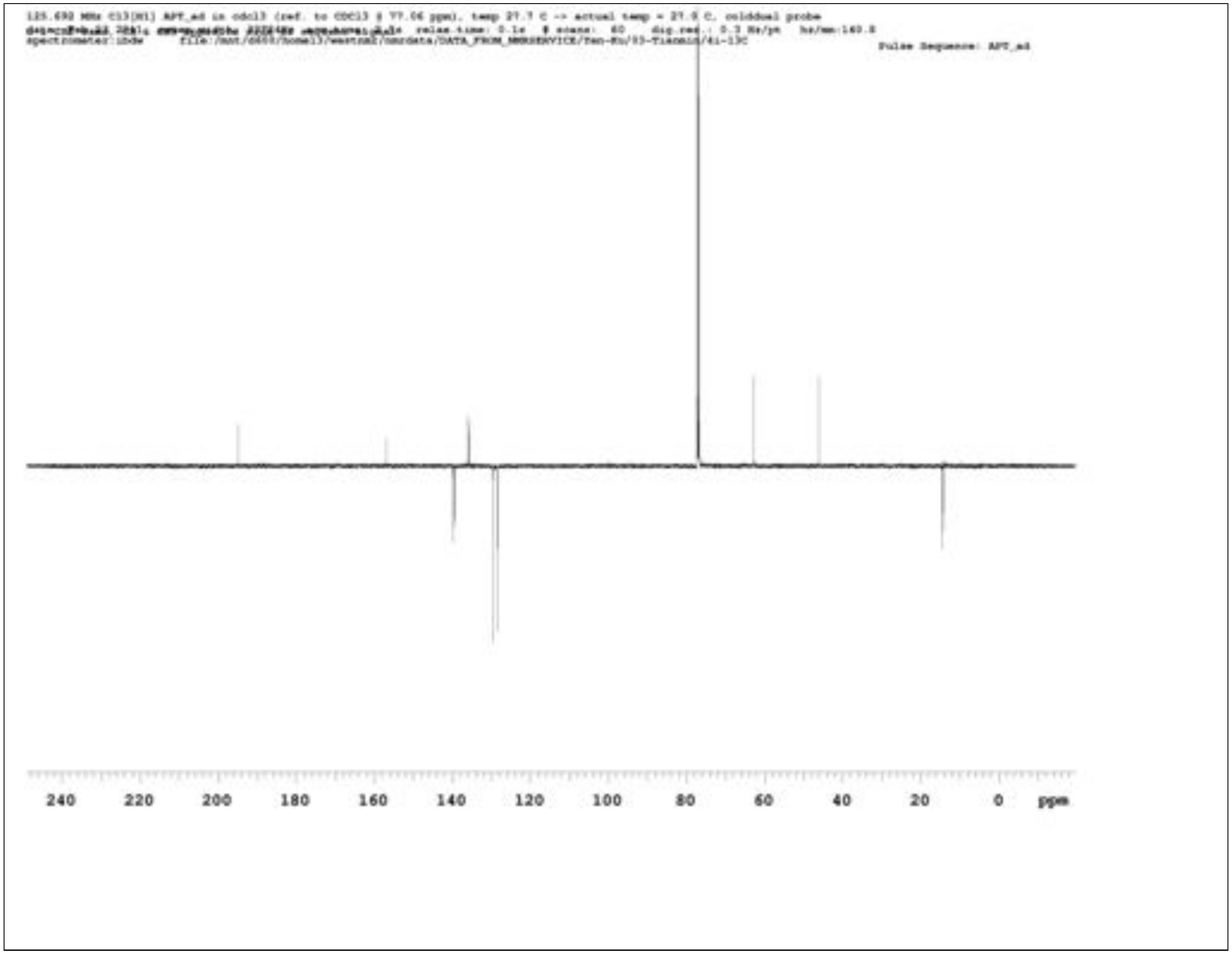


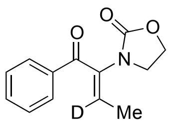
4i


499.615 MHz H1 1D in cdcl3 (ref. to CDCl3 @ 7.26 ppm), temp 27.7 C -> actual temp = 27.0 C, colddual probe
date: Feb 24 2011 sweep width: 6010Hz acq.time: 5.0s relax.time: 0.1s # scans: 16 dig.res.: 0.1 Hz/pt hz/mm:25.0 Pulse Sequence: s2pul
spectrometer:ibdw file:/mnt/d600/home13/westnmr/nmrdata/DATA_FROM_NMRSERVICE/Ten-Ru/03-Tianmin/4i-1H
10
9
8
7
6
5
4
3
2
1
0
ppm
4.3609
1.19
1.01
2.17
2.20
3.18
2.79

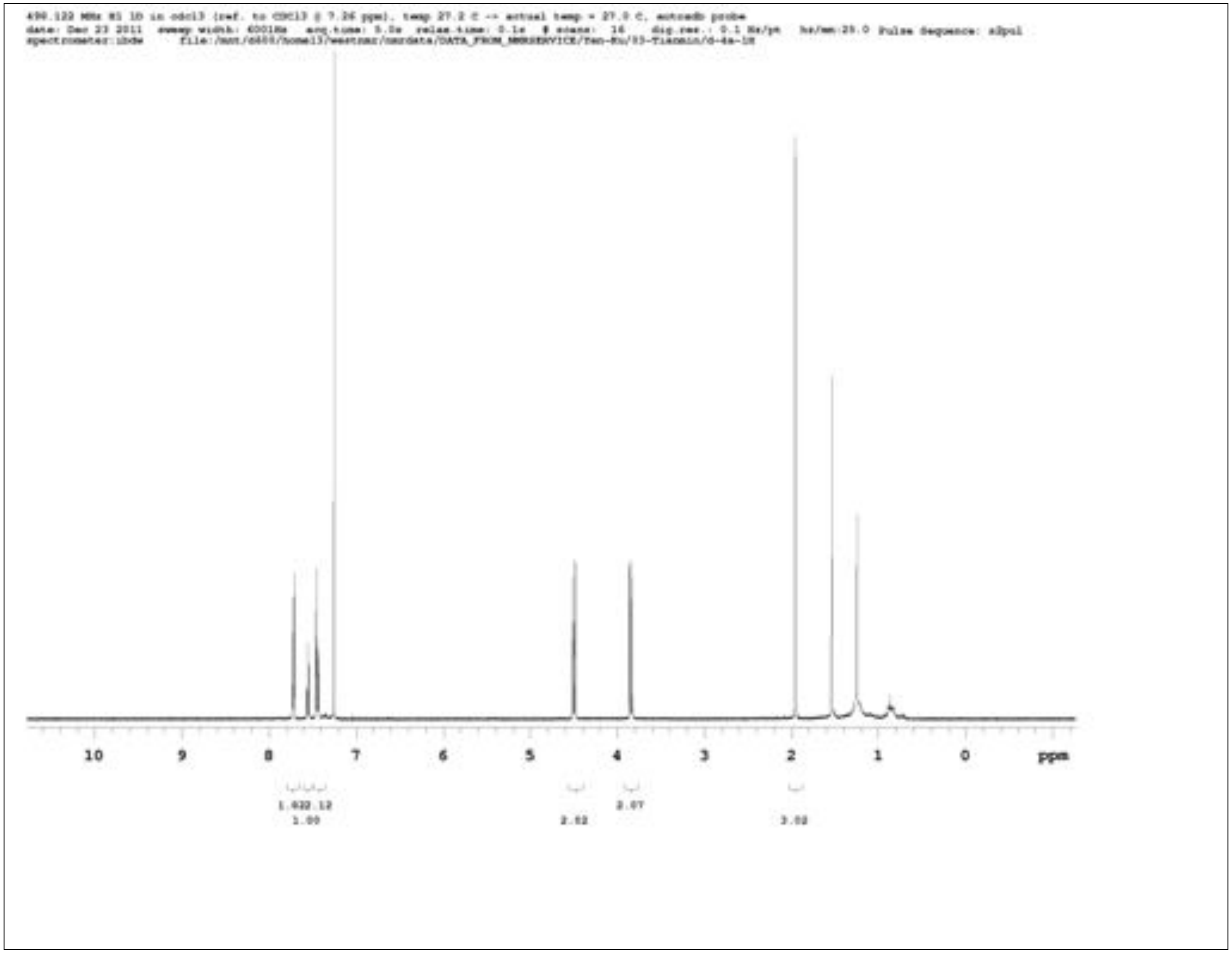

Me
O
O
O
N
Ph
Me

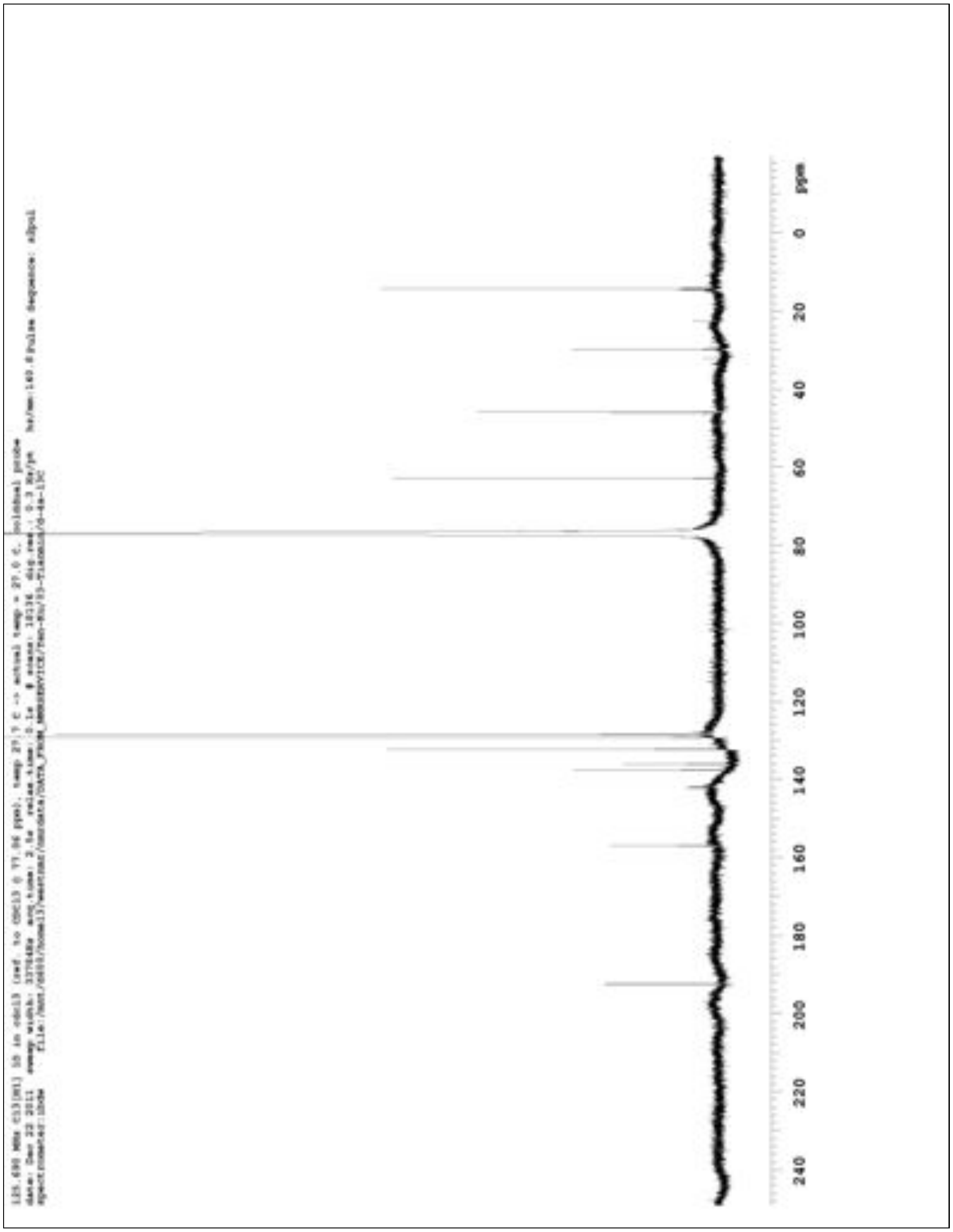
4i

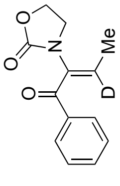

125.692 MHz C13[H1] APT_ad in cdcl3 (ref. to CDCl3 @ 77.06 ppm), temp 27.7 C -> actual temp = 27.0 C, colddual probe
[illegible] relax.time: 0.1s # scans: 60 dig.res.: 0.3 Hz/pt hz/mm:140.8
spectrometer:inds file:/mnt/d600/home13/westrm2/nmrdata/DATA_FROM_NMRSERVICE/Ten-Ru/03-Tianmin/4i-13C
Pulse Sequence: APT_ad
240
220
200
180
160
140
120
100
80
60
40
20
0
ppm


O
O
O
N
D
Me

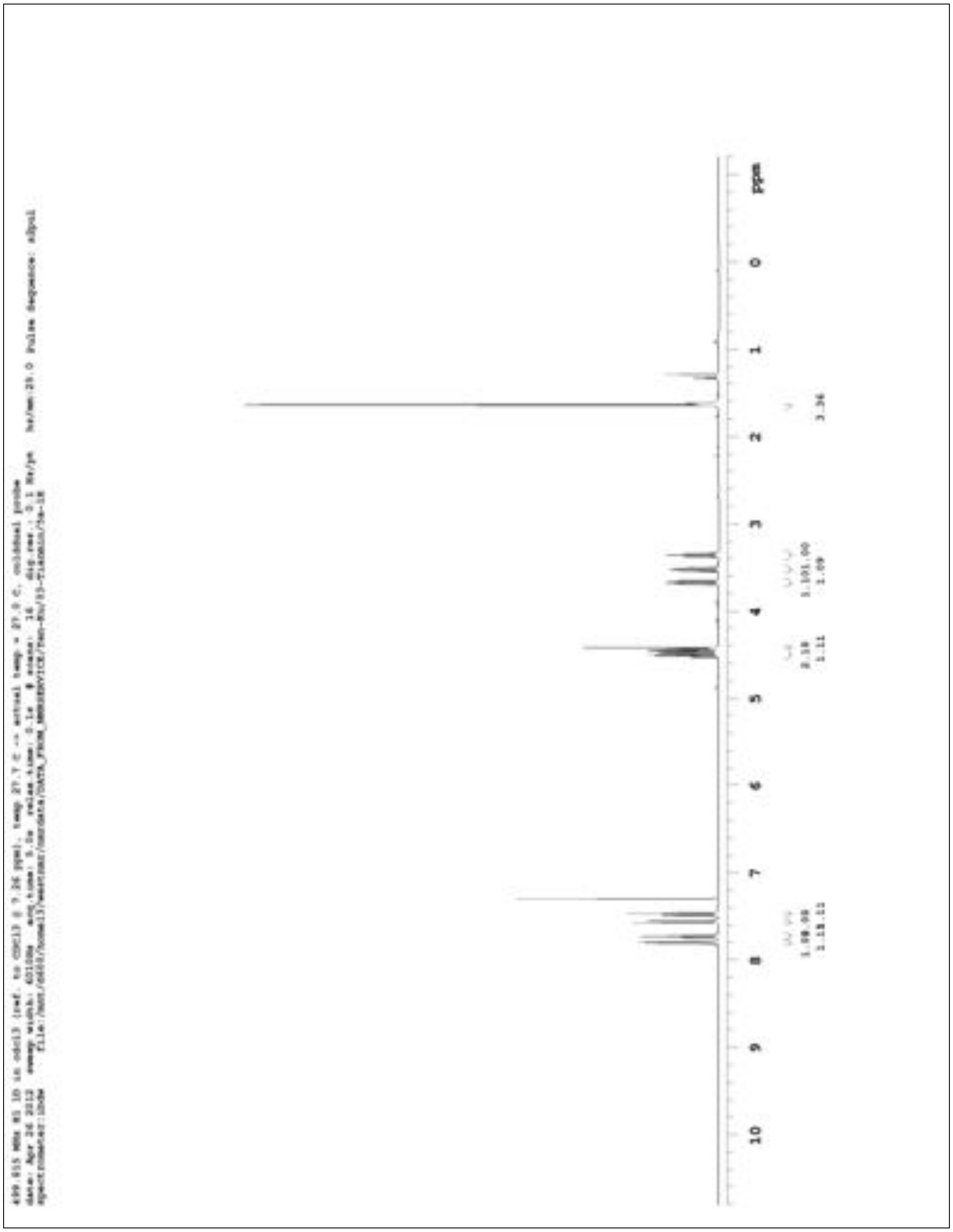
d-**4a**

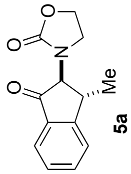

499.122 MHz H1 1D in cdcl3 (ref. to CDCl3 @ 7.26 ppm), temp 27.2 C -> actual temp = 27.0 C, autoxdb probe
date: Dec 23 2011 sweep width: 6001Hz acq.time: 5.0s relax.time: 0.1s # scans: 16 dig.res.: 0.1 Hz/pt hz/mm:25.0 Pulse Sequence: s2pul
spectrometer:ibdw file:/mnt/d600/home13/westnmr/nmrdata/DATA_FROM_NMRSERVICE/Tan-Ru/03-Tianmin/d-4a-1H
10
9
8
7
6
5
4
3
2
1
0
ppm
1.02
2.12
1.00
2.02
2.07
3.02



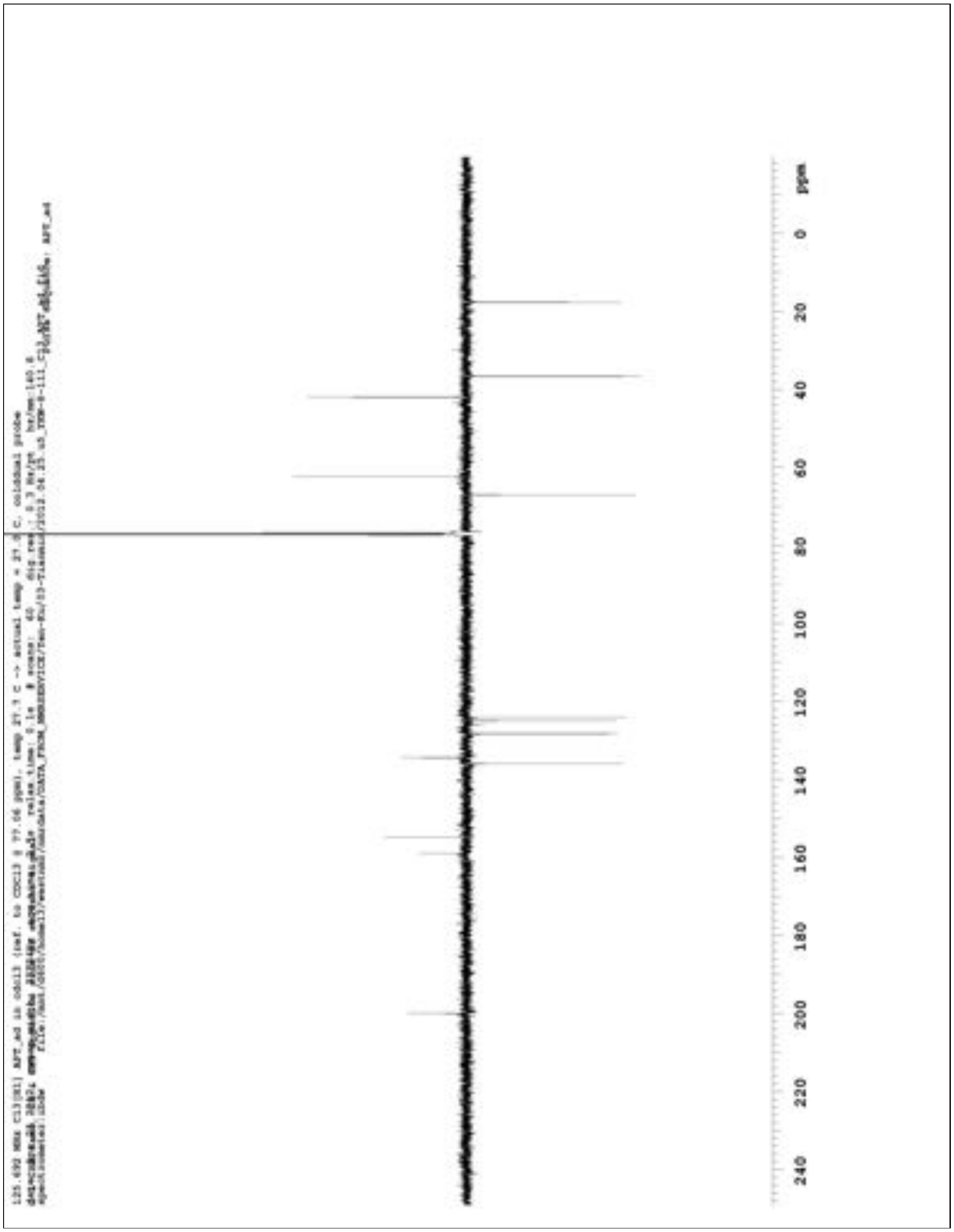


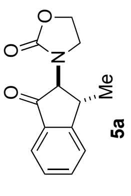
d-**4a**

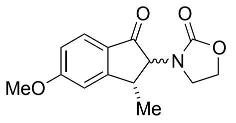




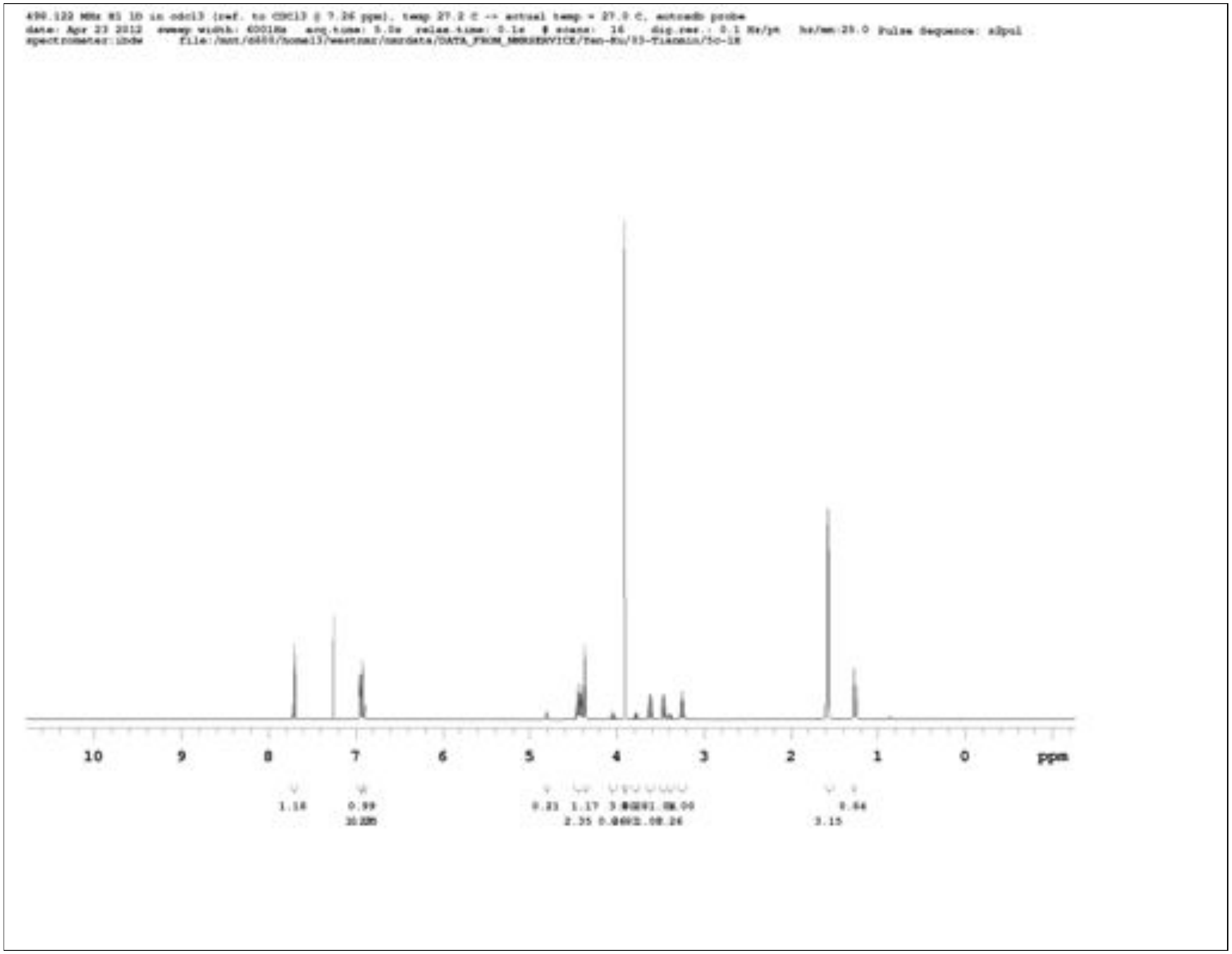
5a

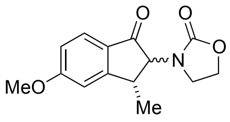



5a

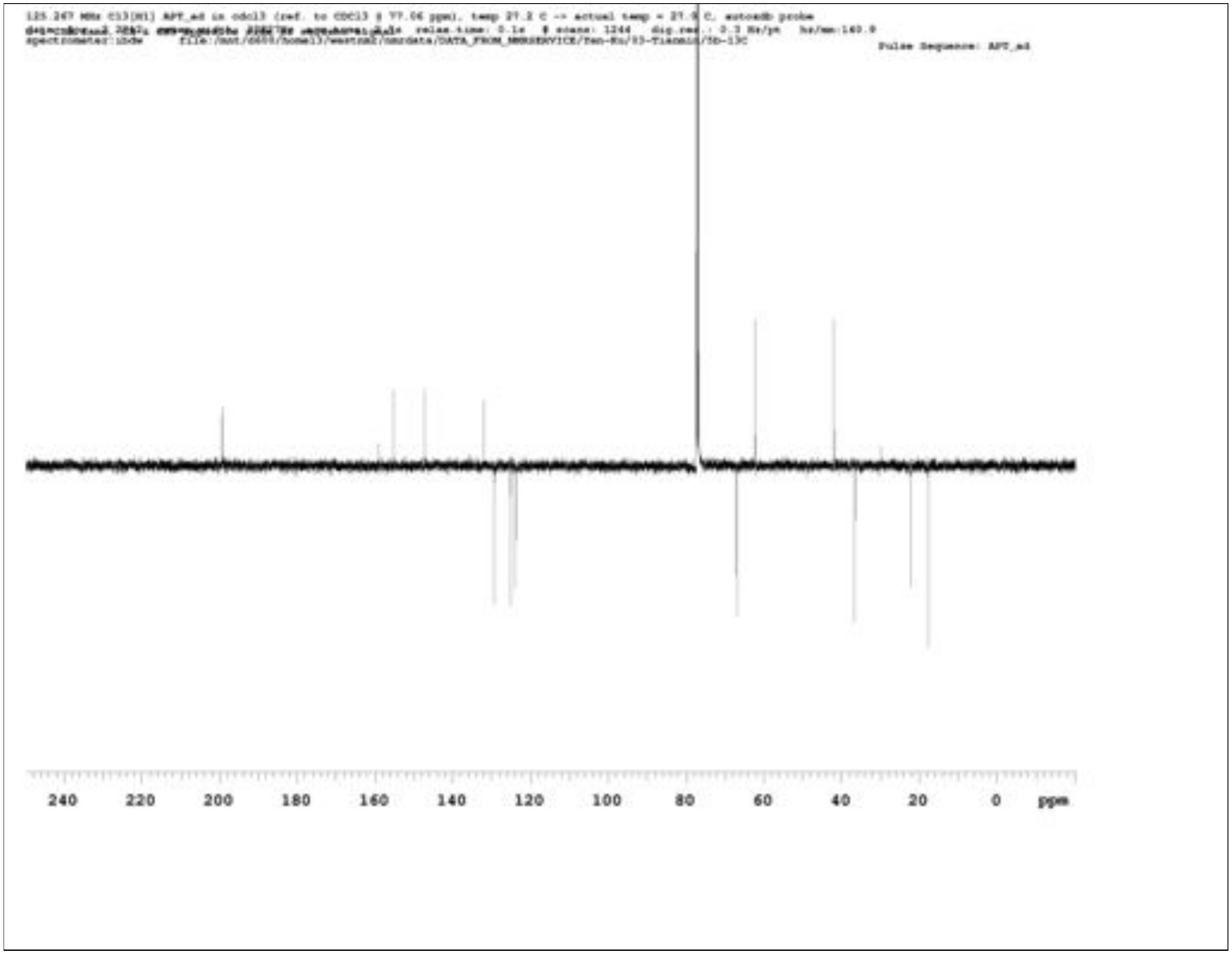


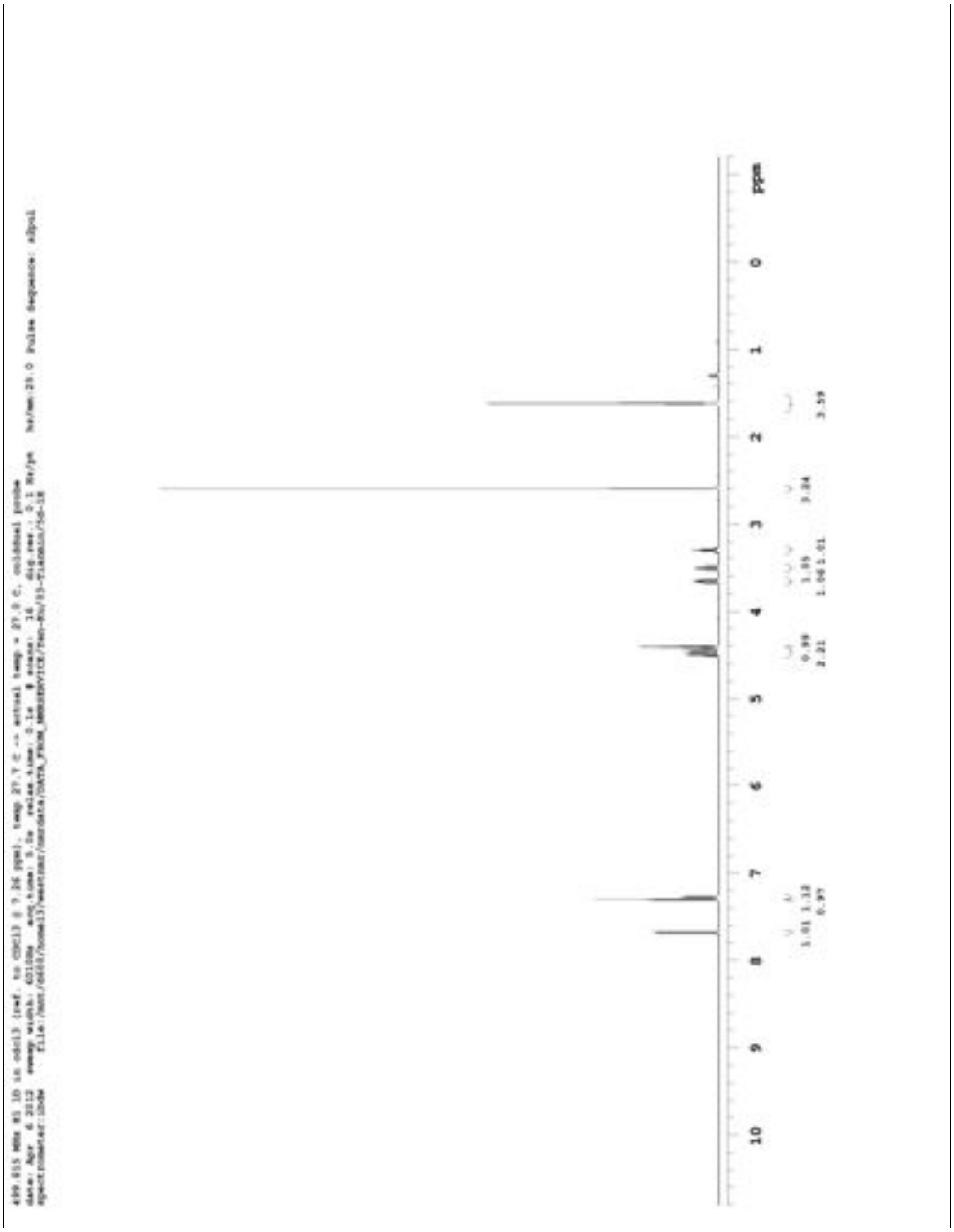
5c, cis:trans 1:4

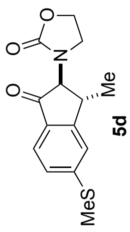




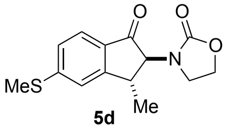
5c, cis:trans 1:4



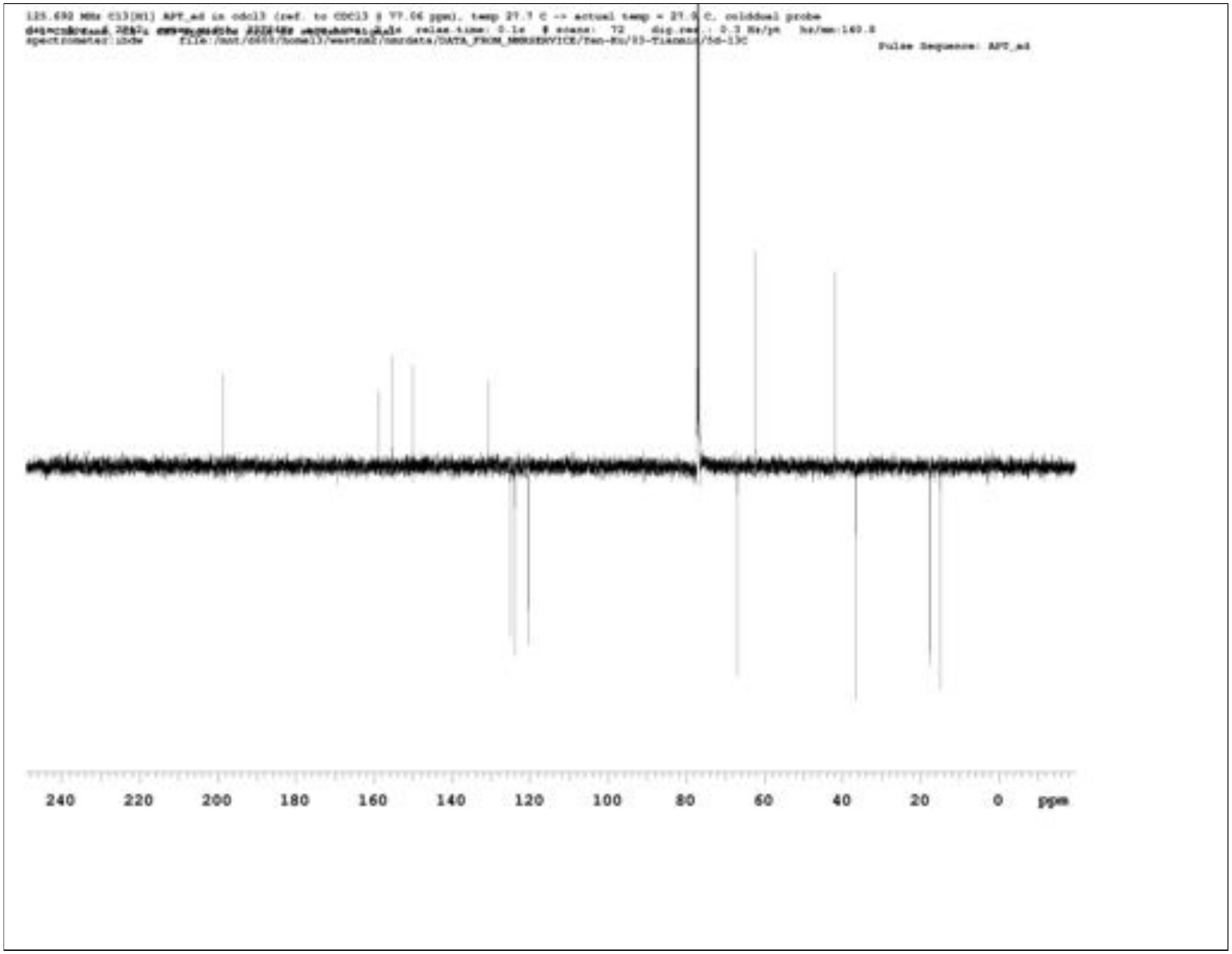

10
9
8
7
6
5
4
3
2
1
0
ppm
1.01 1.12
0.97
0.99
2.21
1.09
1.06 1.01
3.04
3.59

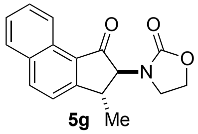

O
O
N
O
Me
MeS

5d



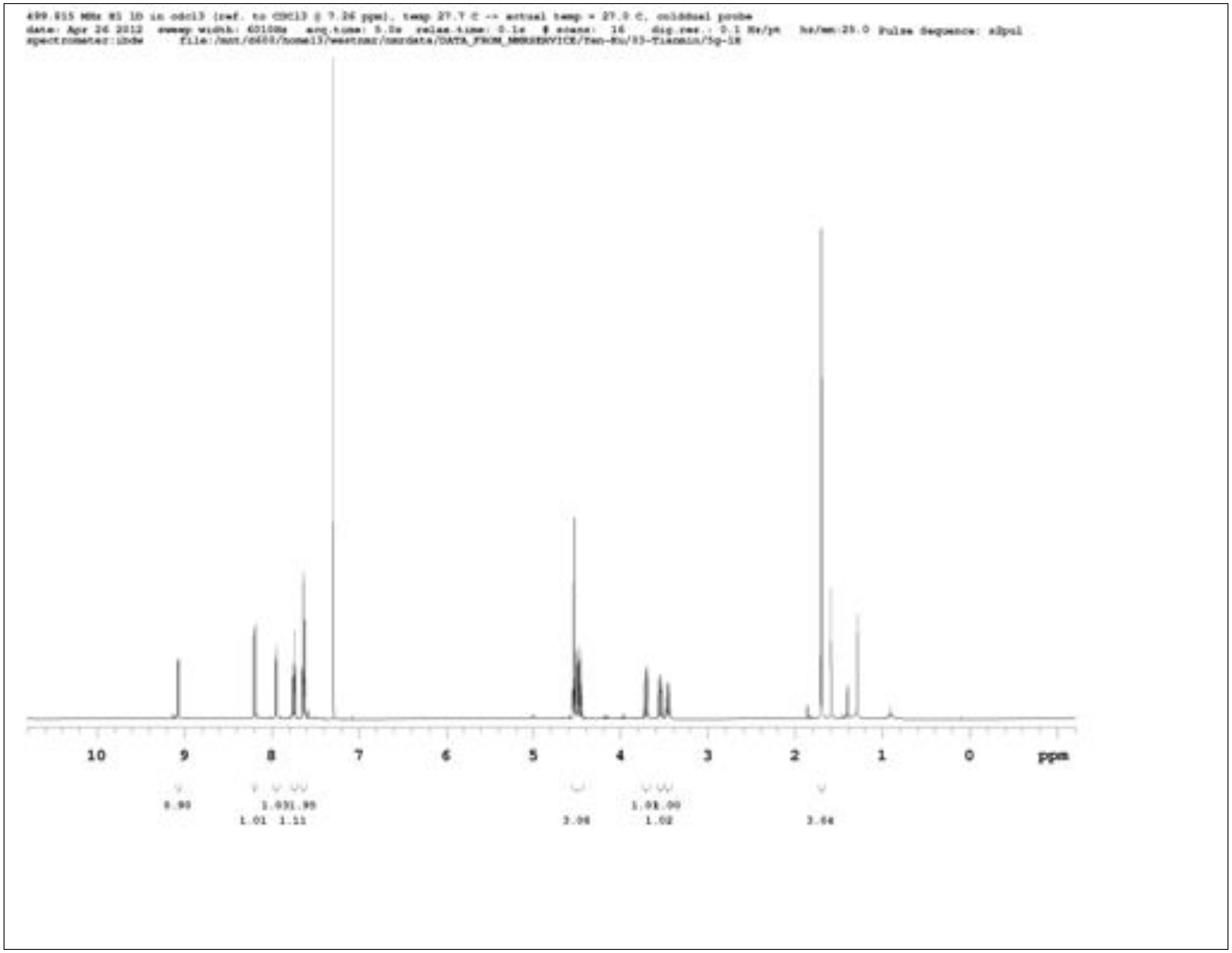
5d


125.690 MHz C13[H1] APT_sd in cdcl3 (ref. to CDCl3 @ 77.06 ppm), temp 27.7 C -> actual temp = 27.9 C, colddual probe
relax.time: 0.1s # scans: 72 dig.res.: 0.3 Hz/pt hz/mm:140.8
spectrometer:inde file:/mnt/d600/home13/westza2/nmrdata/DATA_FROM_NMRSERVICE/Ten-Ru/03-Tianning/5d-13C
Pulse Sequence: APT_sd
240
220
200
180
160
140
120
100
80
60
40
20
0
ppm

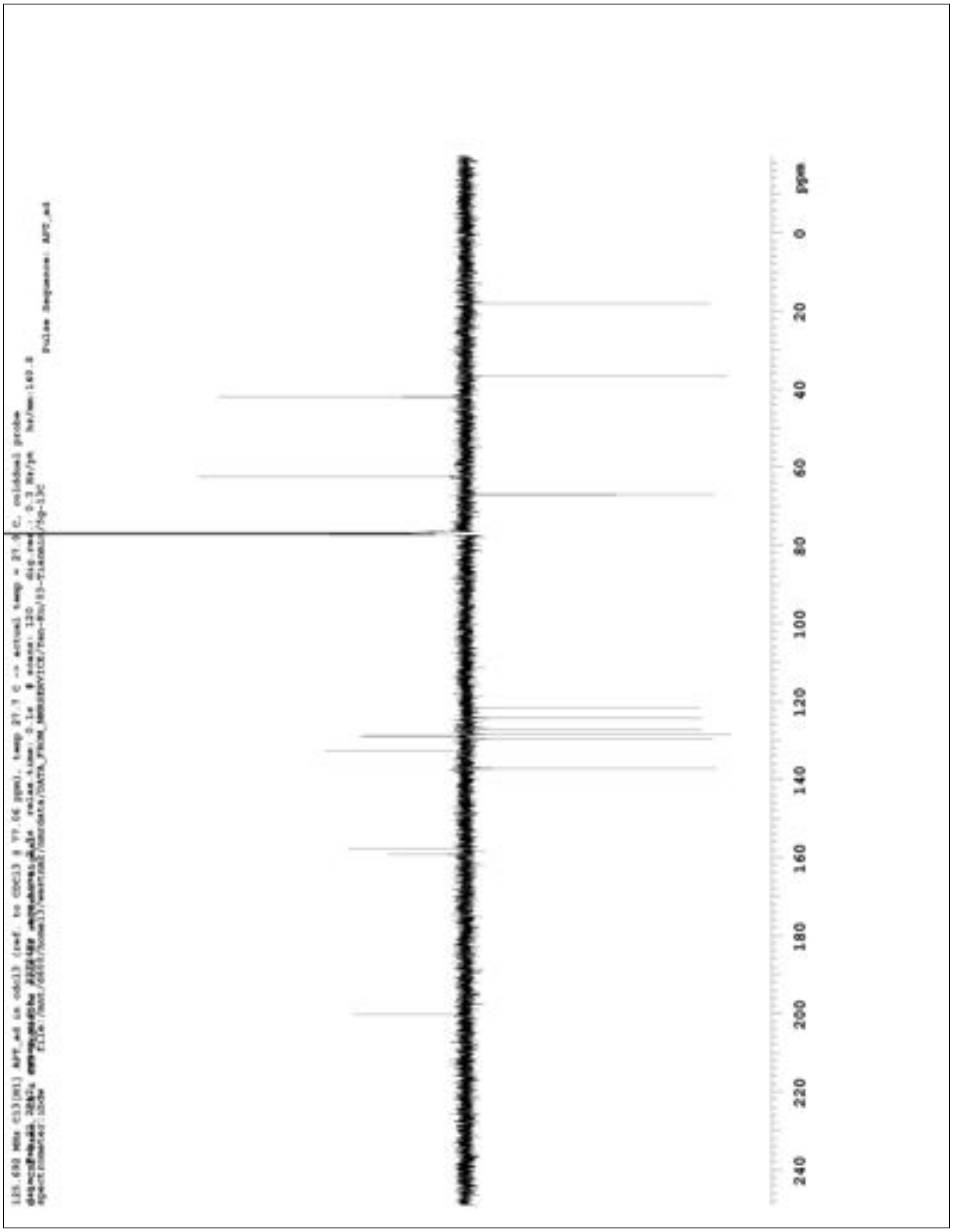


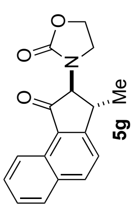
5g

O
O
N
O
Me

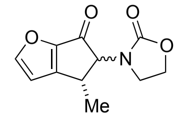


499.815 MHz H1 1D in cdcl3 (ref. to CDCl3 @ 7.26 ppm), temp 27.7 C -> actual temp = 27.0 C, colddual probe
date: Apr 26 2012 sweep width: 6010Hz acq.time: 5.0s relax.time: 0.1s # scans: 16 dig.res.: 0.1 Hz/pt hs/mm:25.0 Pulse Sequence: s2pul
spectrometer:inde file:/mnt/d600/home13/westnmr/nmrdata/DATA_FROM_NMRSERVICE/Yen-Hu/03-Tianmin/5g-1H
10
9
8
7
6
5
4
3
2
1
0
ppm
0.90
1.031.99
1.01 1.11
3.08
1.01.00
1.02
3.04

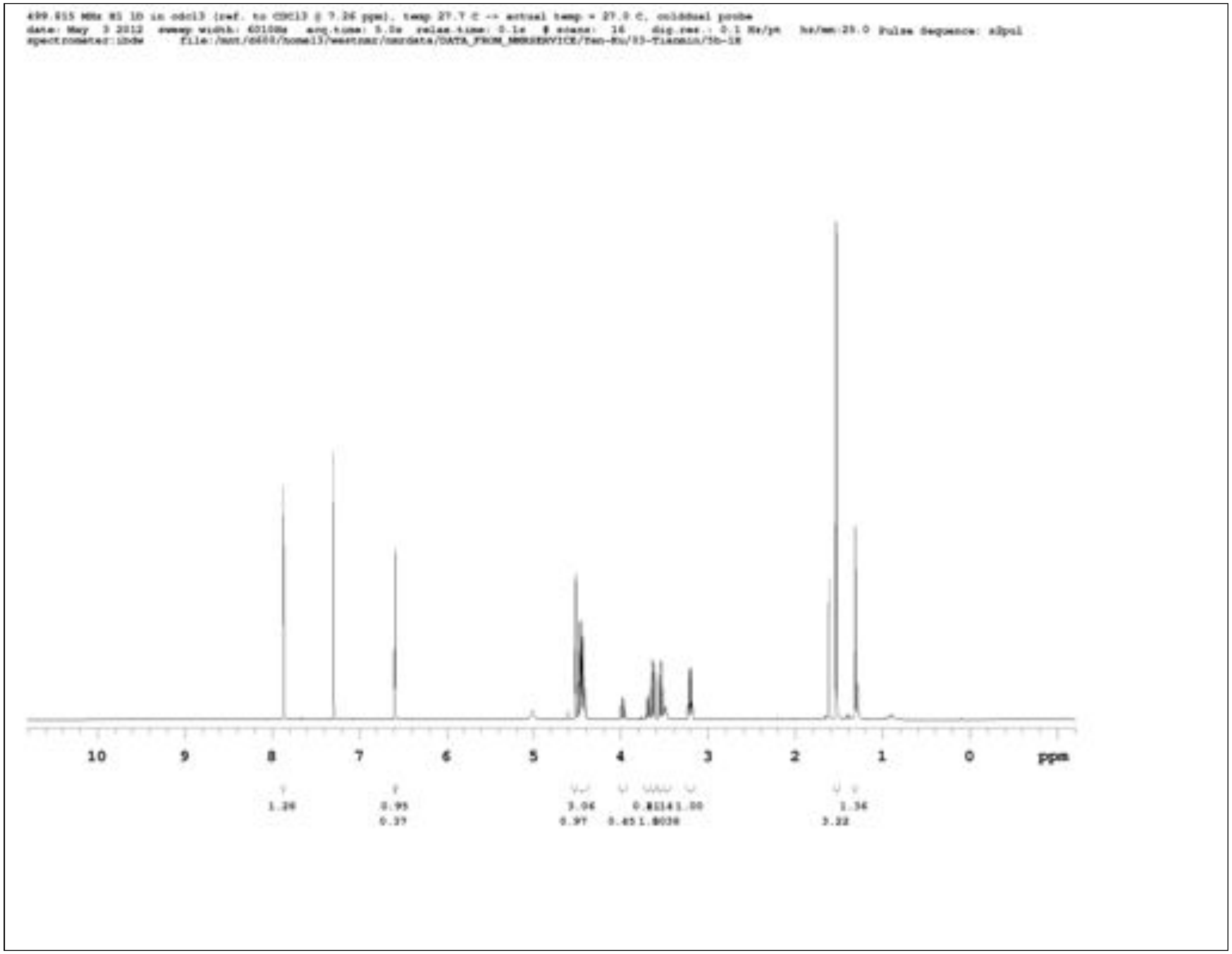

ppm
0
20
40
60
80
100
120
140
160
180
200
220
240
Pulse Sequence: APT_s4

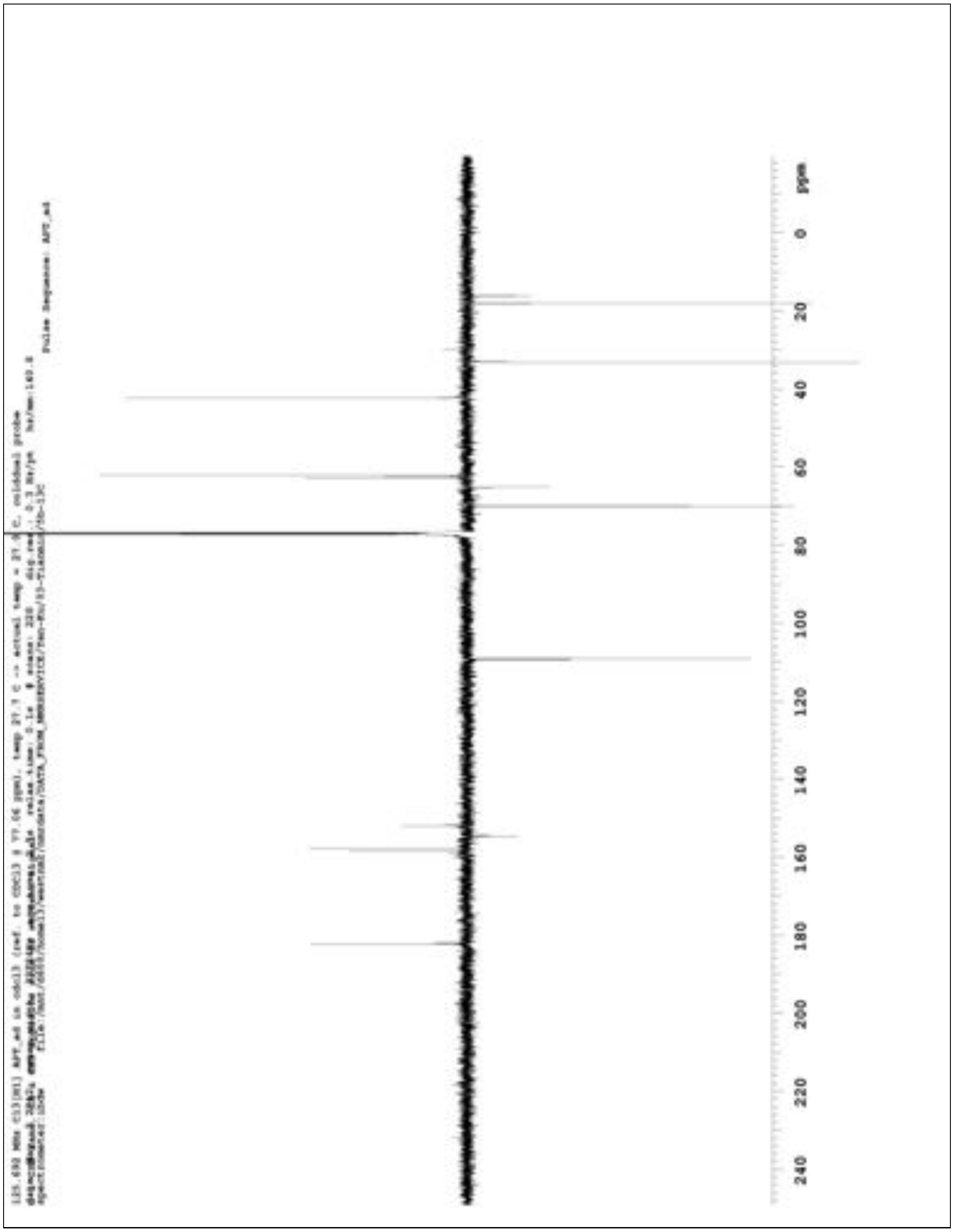

O
O
N
O
Me

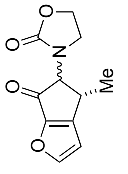
5g



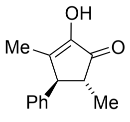
5h, cis:trans 1:3



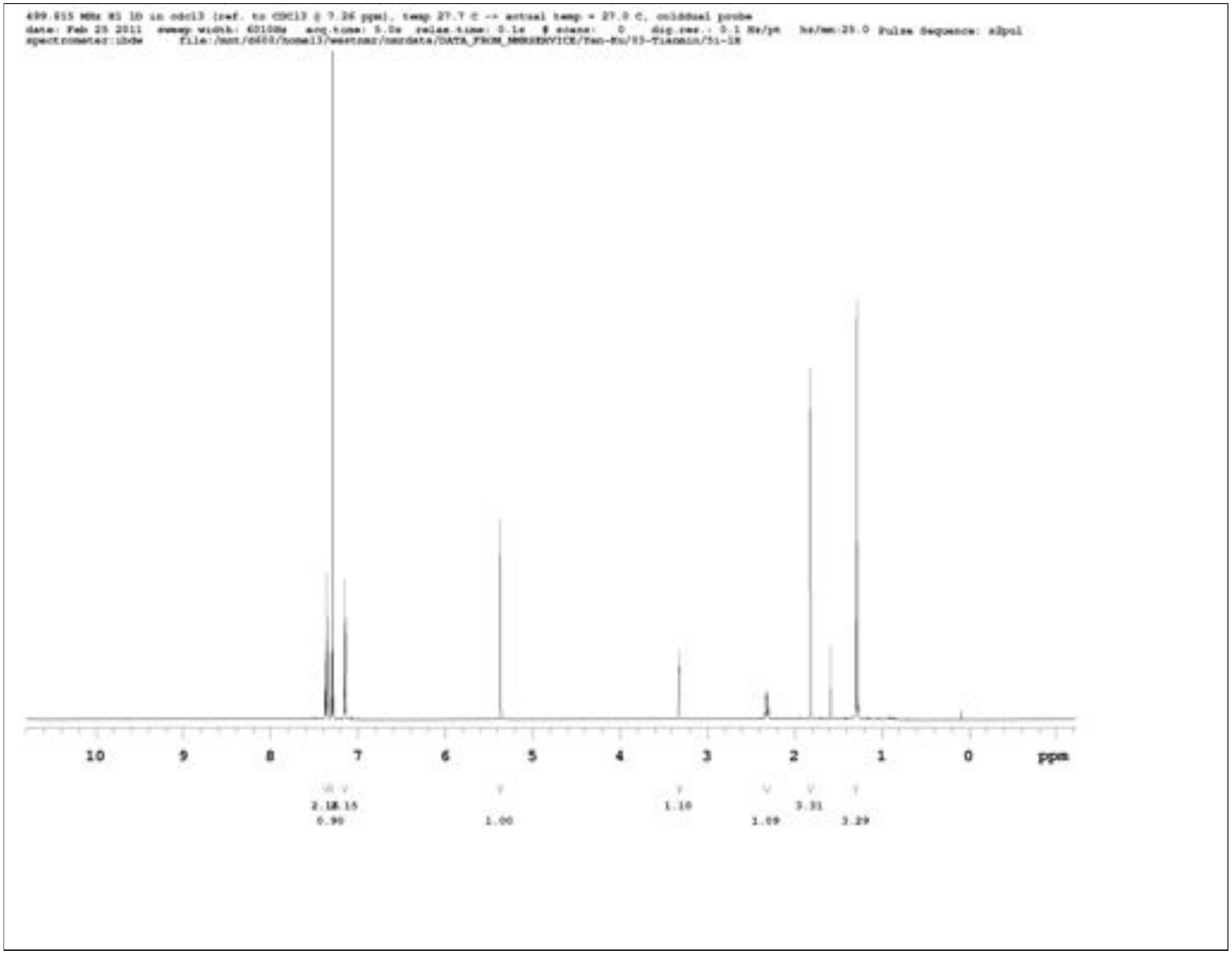


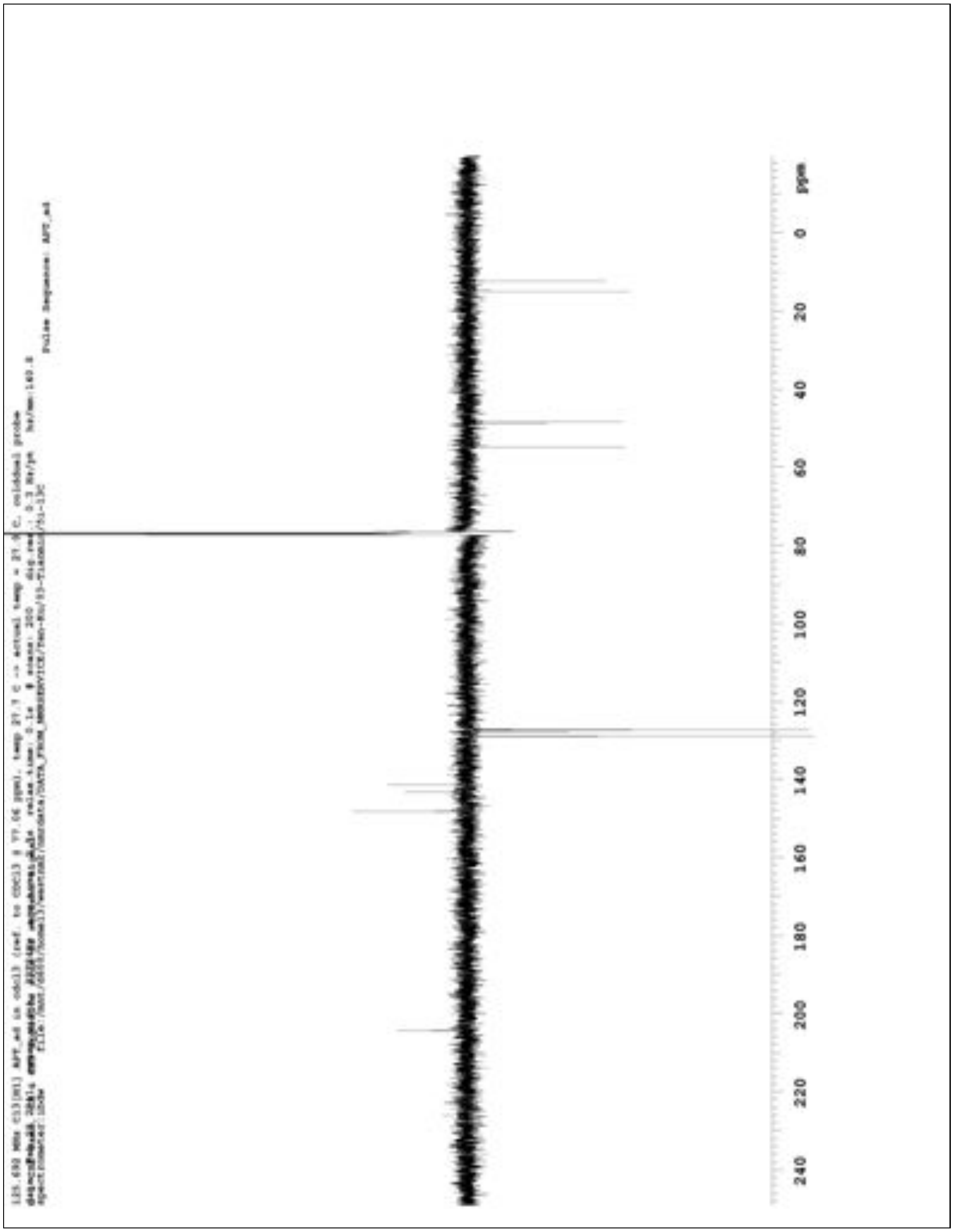


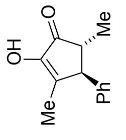
5h, cis:trans 1:3



5i


499.855 MHz H1 1D in cdcl3 (ref. to CDCl3 @ 7.26 ppm), temp 27.7 C -> actual temp = 27.0 C, colddual probe
date: Feb 25 2011 sweep width: 6010Hz acq.time: 5.0s relax.time: 0.1s # scans: 0 dig.res.: 0.1 Hz/pt hz/mm:25.0 Pulse Sequence: s2pul
spectrometer:ibdw file:/mnt/d600/home13/westnmr/nmrdata/DATA_FROM_NMRSERVICE/Ten-Hu/03-Tianmin/5i-1H
10
9
8
7
6
5
4
3
2
1
0
ppm
2.18
2.15
0.90
1.00
1.10
1.09
3.31
3.29





5i

Appendix IV:

X-ray Crystallographic Data for Compounds **6a**, **10a**, **14**, **16a**, **19**, **20a**, **22c**, **24**, and **33** (Chapter 2)

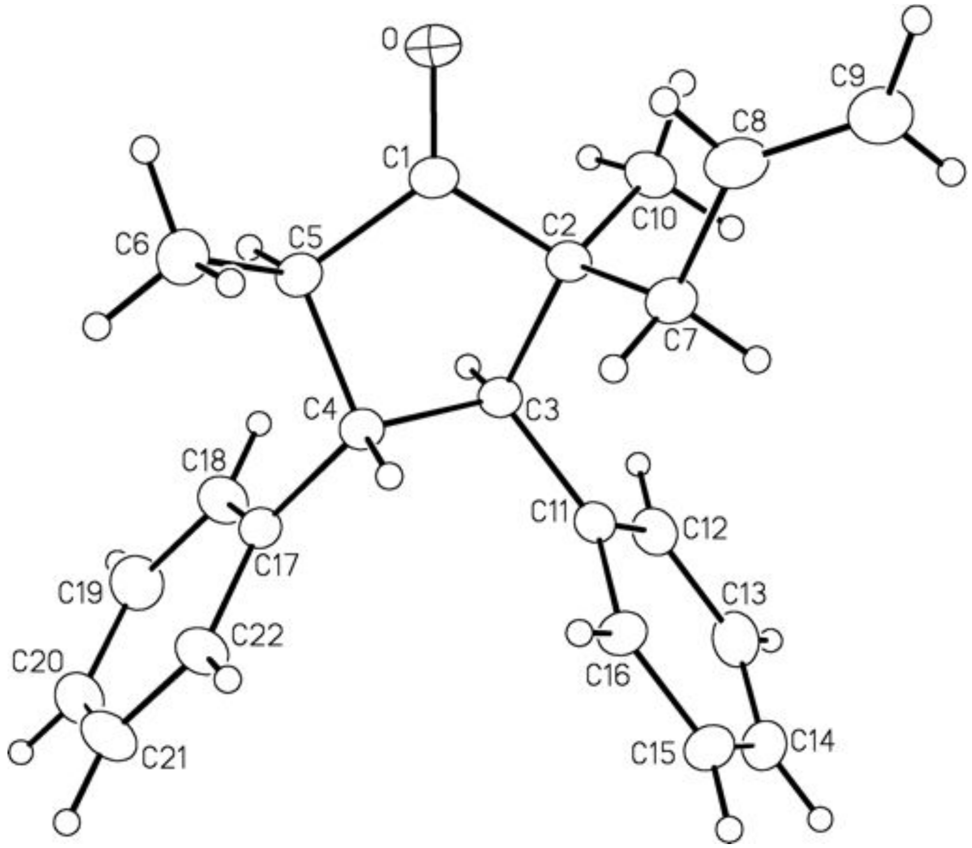
STRUCTURE REPORT

XCL Code: FGW1109 **Date:** 6 December 2011

Compound: 2,5-dimethyl-3,4-diphenyl-2-(prop-2-en-1-yl)cyclopentanone
Formula: $C_{22}H_{24}O$

Supervisor: F. G. West **Crystallographer:**

M. J. Ferguson



Compound **6a**

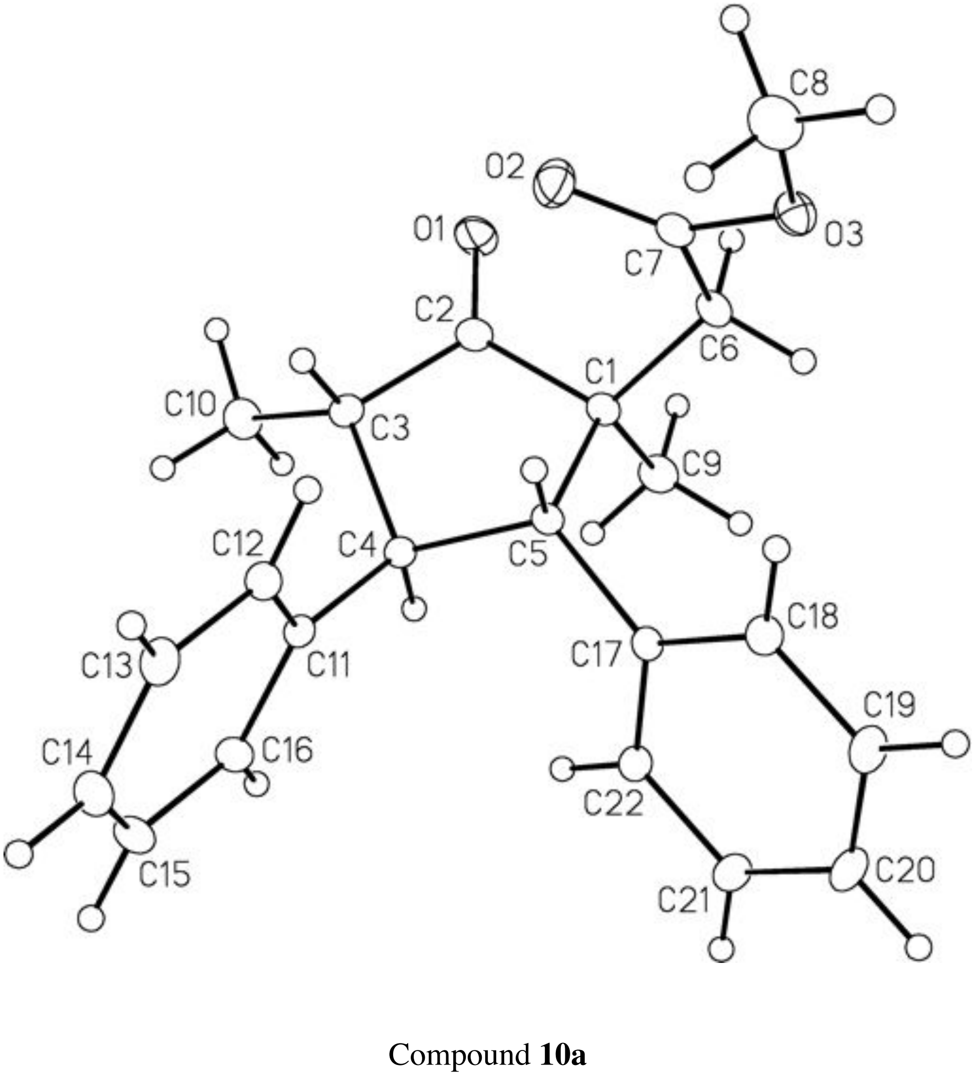
STRUCTURE REPORT

XCL Code: FGW1009 **Date:** 15 September 2010

Compound: Methyl (1,3-dimethyl-2-oxo-4,5-diphenylcyclopentyl)acetate
Formula: $C_{22}H_{24}O_3$

Supervisor: F. G. West **Crystallographer:**

R. McDonald



Compound **10a**

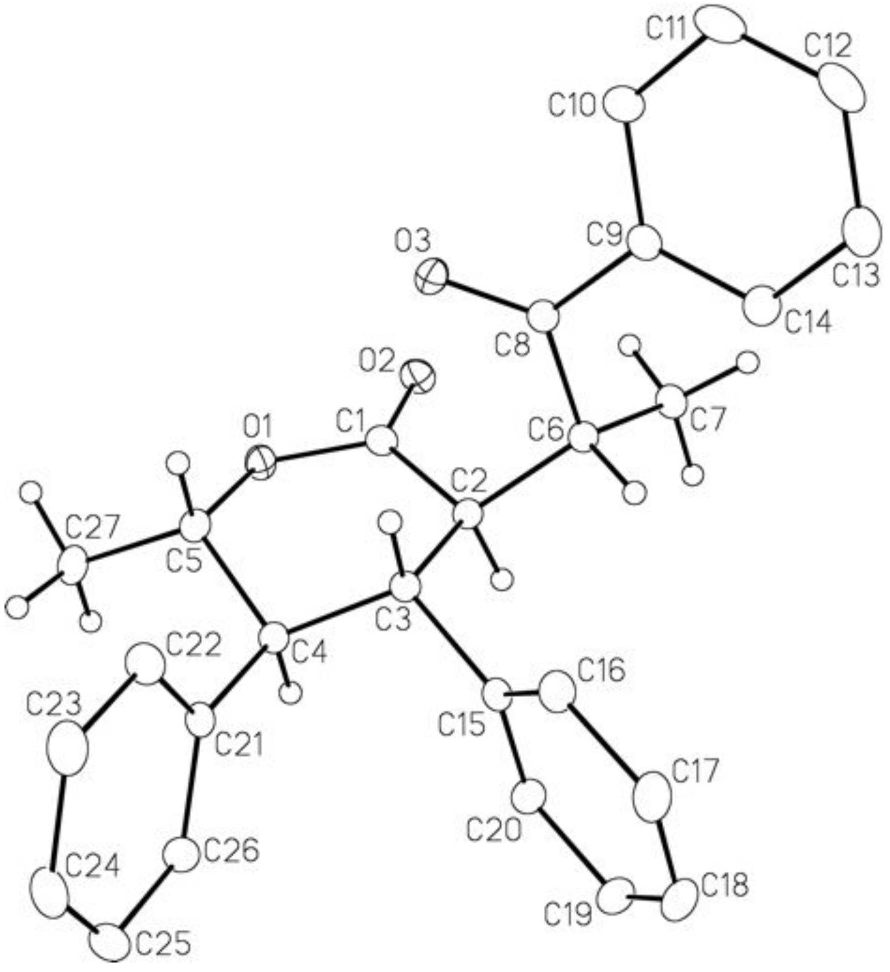
STRUCTURE REPORT

XCL Code: FGW1103 **Date:** 3 June 2011

Compound: 6-Methyl-3-(1-oxo-1-phenylpropan-2-yl)-4,5-diphenyltetrahydro-2*H*-pyran-2-one

Formula: $C_{27}H_{26}O_3$

Supervisor: F. G. West **Crystallographer:** R. McDonald



Compound **14**

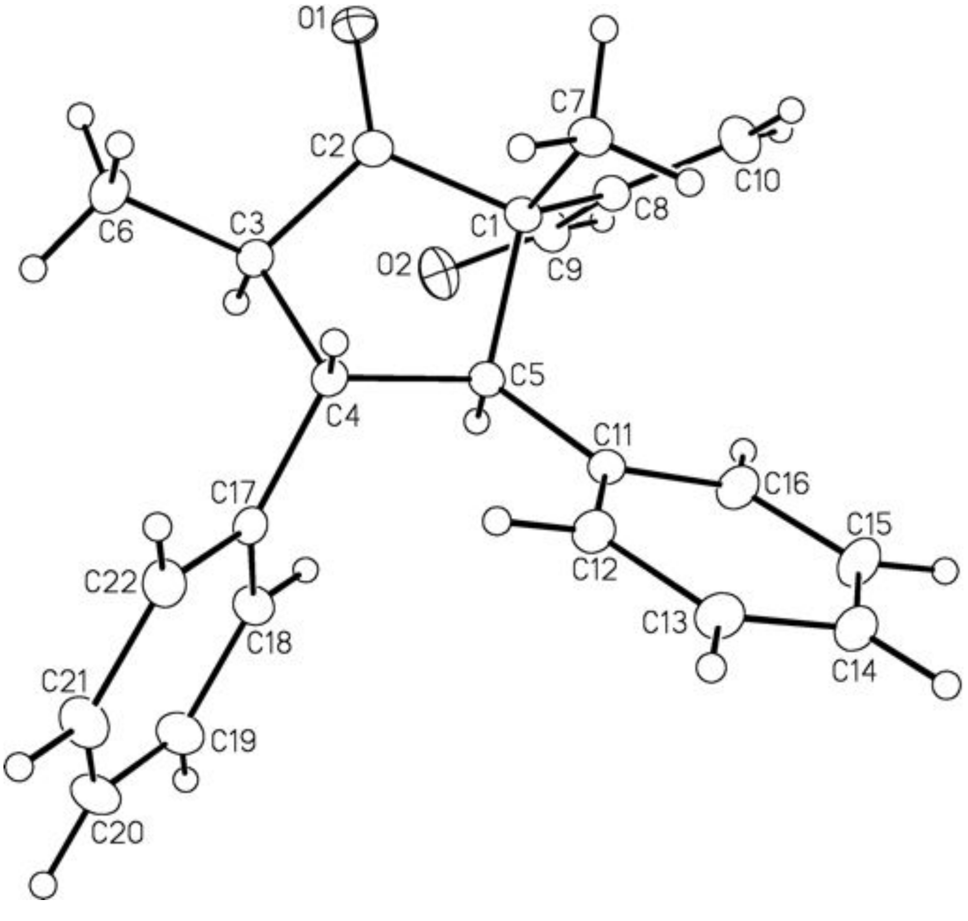
STRUCTURE REPORT

XCL Code: FGW1102 **Date:** 18 April 2011

Compound: 2-(1,3-dimethyl-2-oxo-4,5-diphenylcyclopentyl)prop-2-enal
Formula: $C_{22}H_{22}O_2$

Supervisor: F. G. West **Crystallographer:**

M. J. Ferguson



Compound **16a**

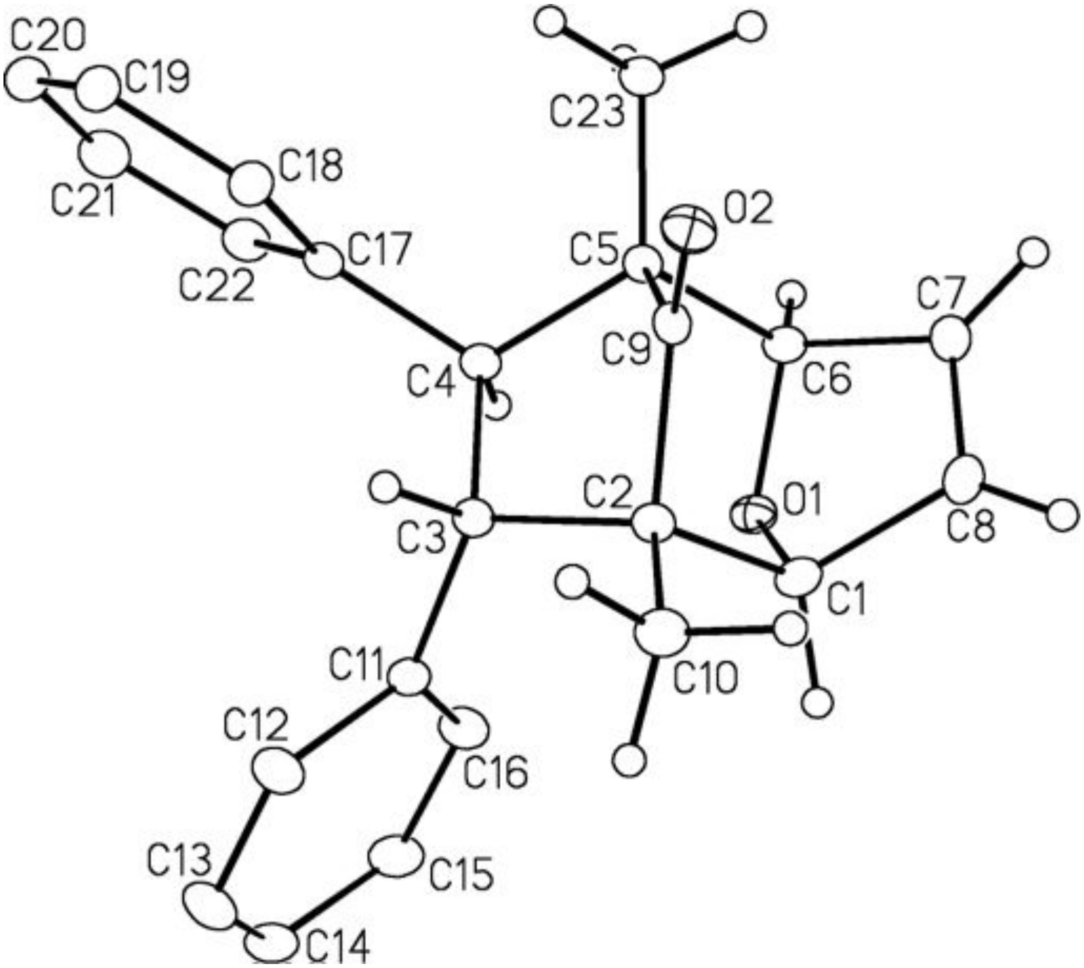
STRUCTURE REPORT

XCL Code:	FGW1203	**Date:**	25 June 2012

Compound: 2,5-Dimethyl-3,4-diphenyl-9-oxatricyclo[4.2.1.$1^{2,5}$]dec-7-en-10-one

Formula: $C_{23}H_{22}O_2$

Supervisor: F. G. West **Crystallographer:** R. McDonald



Compound **19**

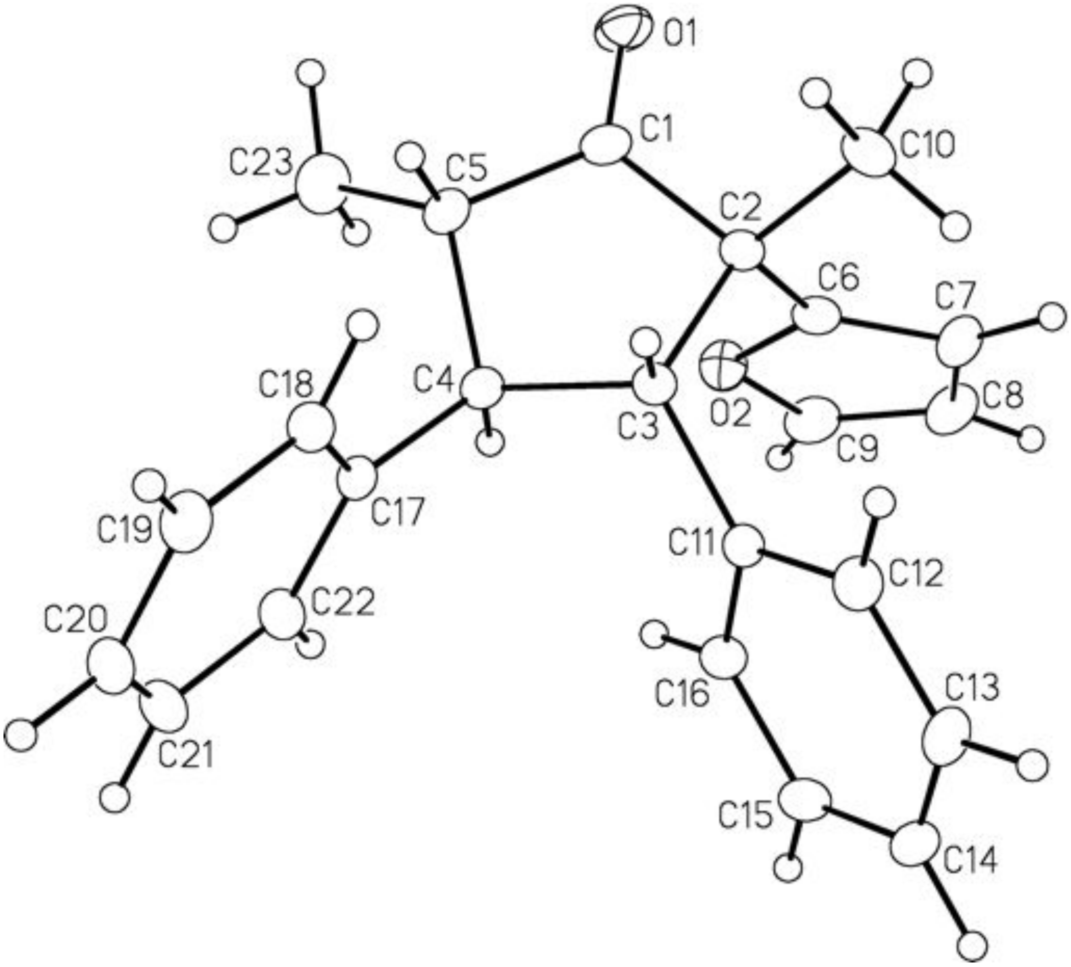
STRUCTURE REPORT

XCL Code: FGW1107 **Date:** 9 September
2011

Compound: 2-(Furan-2-yl)-2,5-dimethyl-3,4-diphenylcyclopentanone
Formula: $C_{23}H_{22}O_2$

Supervisor: F. G. West **Crystallographer:**

R. McDonald



Compound **20a**

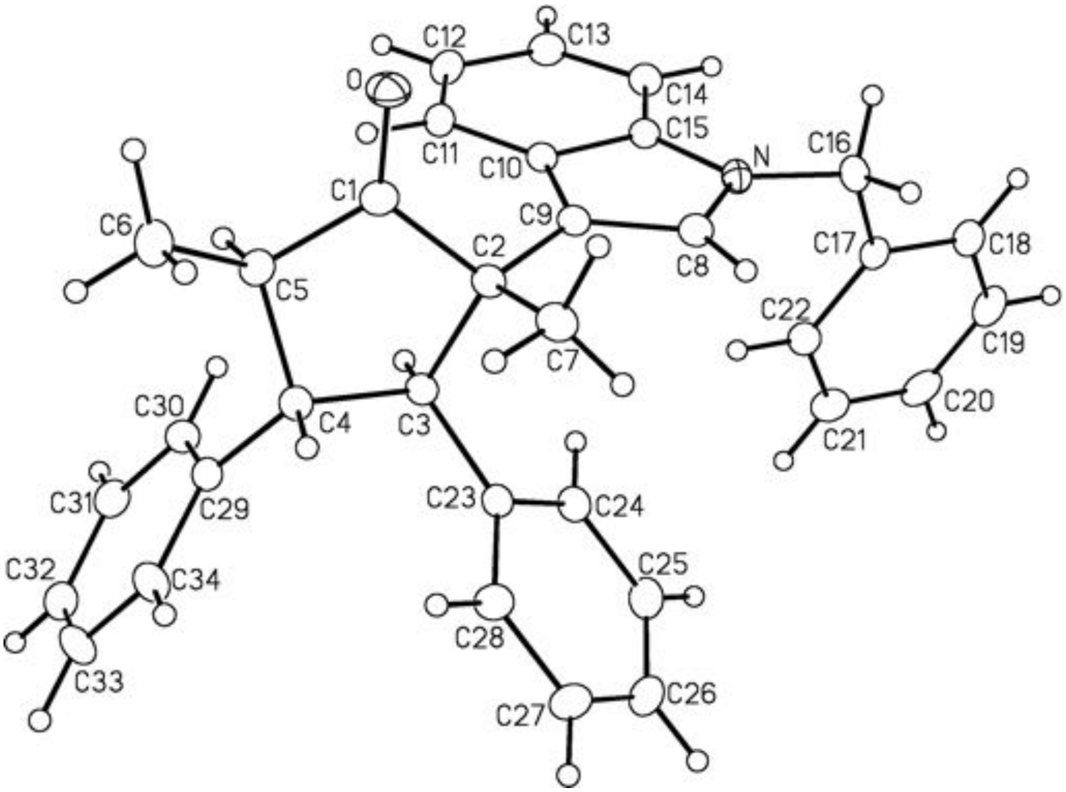
STRUCTURE REPORT

XCL Code: FGW1106 **Date:** 16 August 2011

Compound: 2-(1-benzyl-1*H*-indol-3-yl)-2,5-dimethyl-3,4-diphenylcyclopentanone

Formula: $C_{34}H_{31}NO$

Supervisor: F. G. West **Crystallographer:** M. J. Ferguson



Compound **22c**

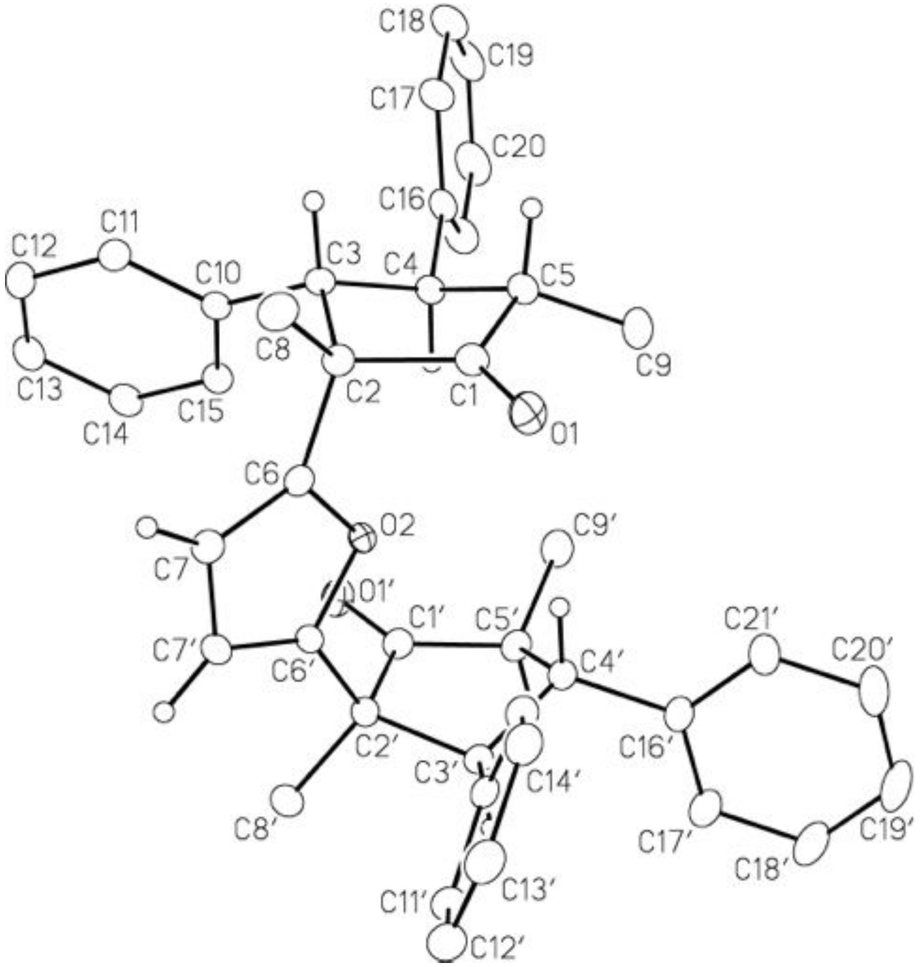
STRUCTURE REPORT

XCL Code: FGW1204 **Date:** 27 June 2012

Compound: 2,2’-Furan-2,5-diylbis(2,5-dimethyl-3,4-diphenylcyclopentanone)
Formula: $C_{42}H_{40}O_3$

Supervisor: F. G. West **Crystallographer:**

R. McDonald



Compound **24**

STRUCTURE REPORT

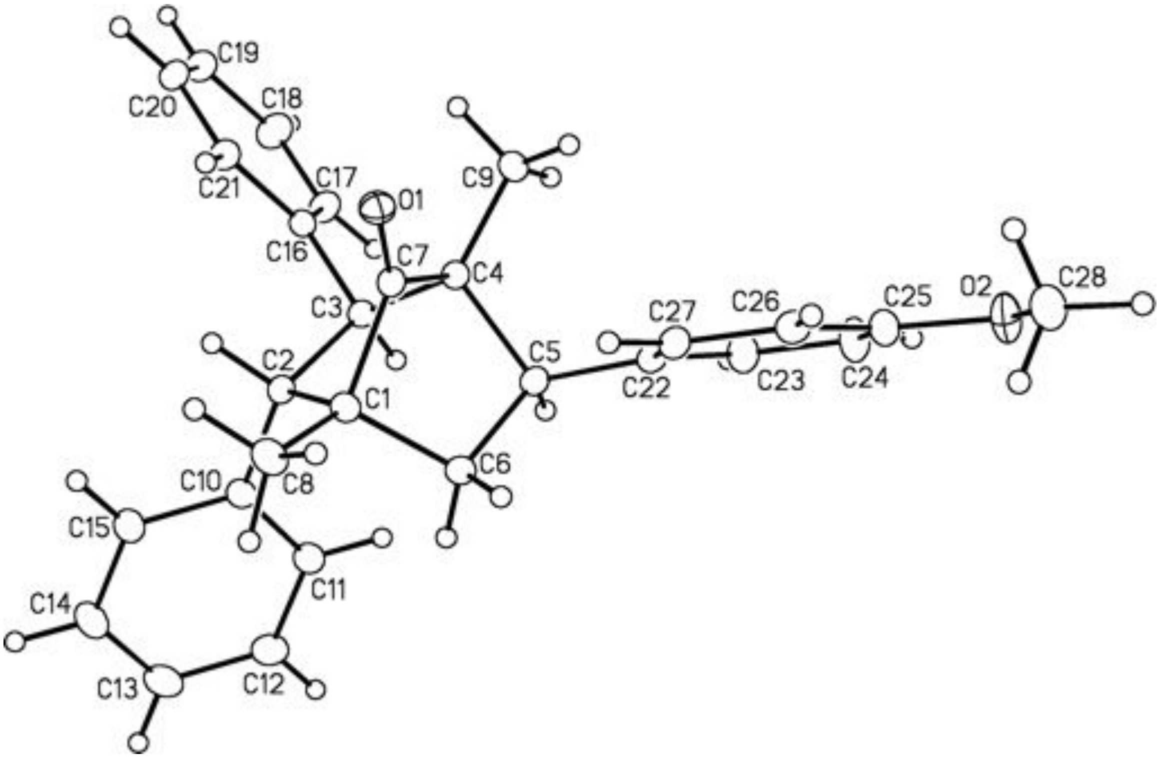
XCL Code: FGW1210 **Date:** 31 August 2012

Compound: 5-(4-methoxyphenyl)-1,4-dimethyl-2,3-diphenylbicyclo[2.2.1]heptan-7-one

Formula: $C_{28}H_{28}O_2$

Supervisor: F. G. West **Crystallographer:**

M. J. Ferguson



Compound **33**

Appendix V:

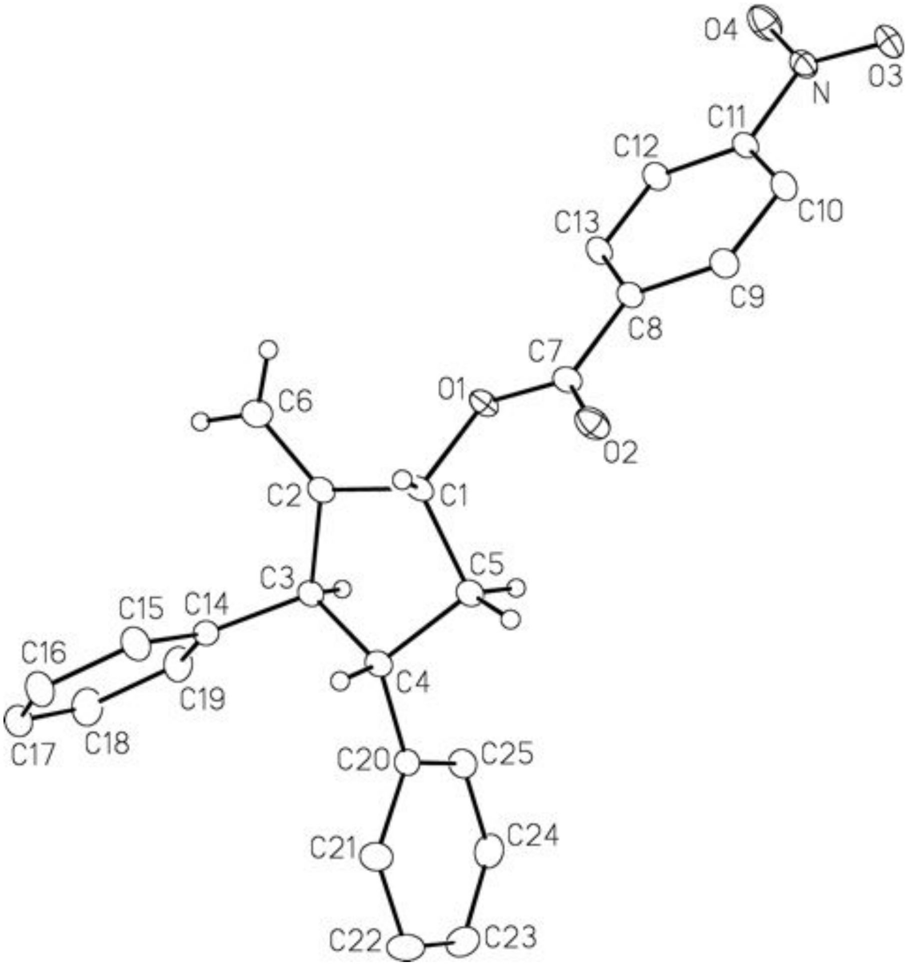
X-ray Crystallographic Data for Compounds **9**, **13p**, **13r**, and **13v** (Chapter 3)

STRUCTURE REPORT

XCL Code: FGW1101 **Date:** 9 March 2011

Compound: 2-methylidene-3,4-diphenylcyclopentyl 4-nitrobenzoate
Formula: $C_{25}H_{21}NO_4$

Supervisor: F. G. West **Crystallographer:** R. McDonald



Compound **9**

STRUCTURE REPORT

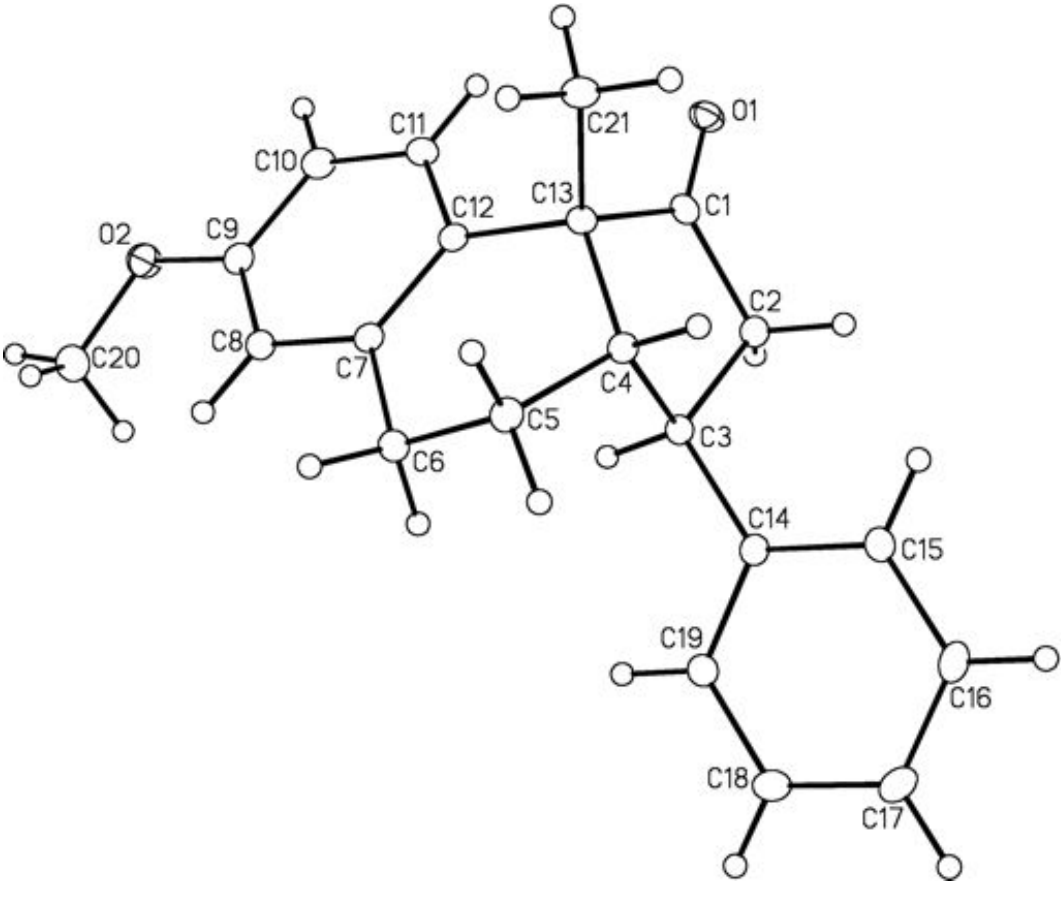
XCL Code: FGW0904 **Date:** 9 October 2009

Compound: 7-methoxy-9b-methyl-3-phenyl-2,3,3a,4,5,9b-hexahydro-1*H*-cyclopenta[a]naphthalen-1-one

Formula: $C_{21}H_{22}O_2$

Supervisor: F. G. West **Crystallographer:**

M. J. Ferguson



Compound **13p**

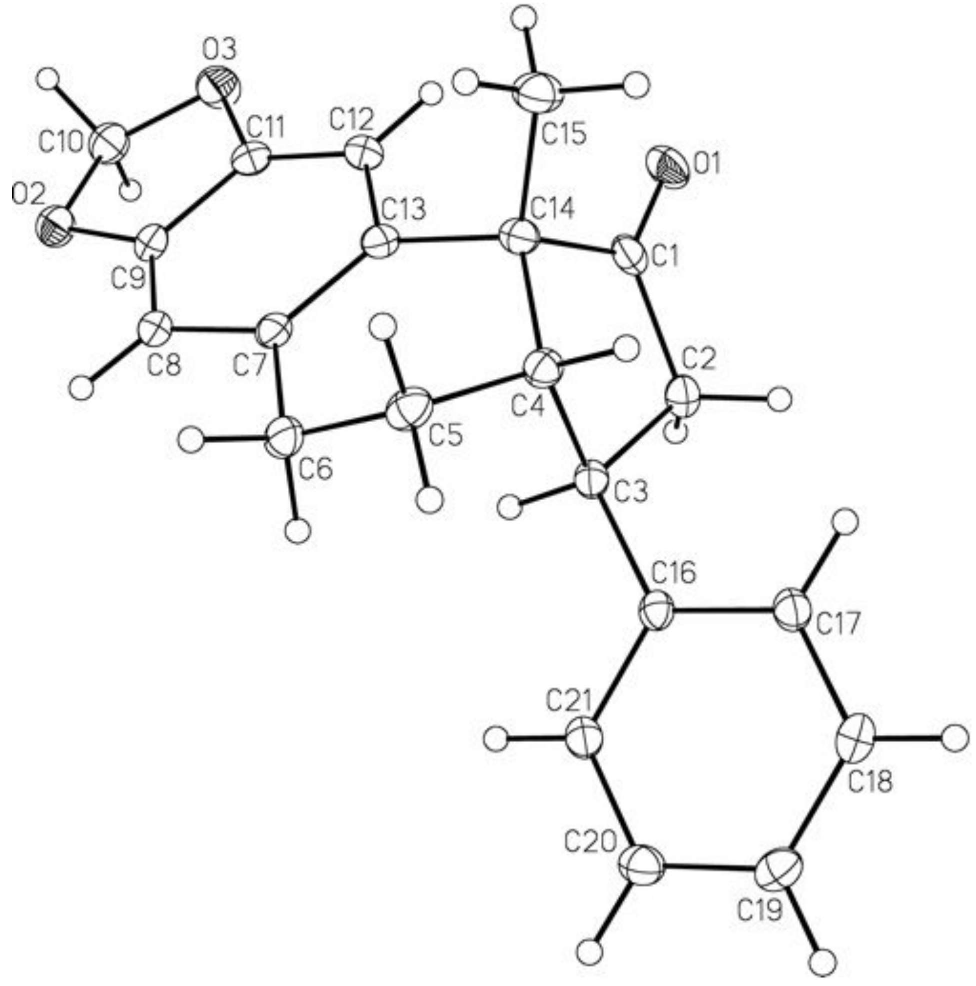
STRUCTURE REPORT

XCL Code: FGW1004 **Date:** 1 March 2010

Compound: 10*b*-methyl-3-phenyl-2,3,3*a*,4,5,10*b*-hexahydro-1*H*-cyclopenta[5,6]naphtho[2,3-*d*][1,3]dioxol-1-one

Formula: $C_{21}H_{20}O_3$

Supervisor: F. G. West **Crystallographer:** M. J. Ferguson



Compound **13r**

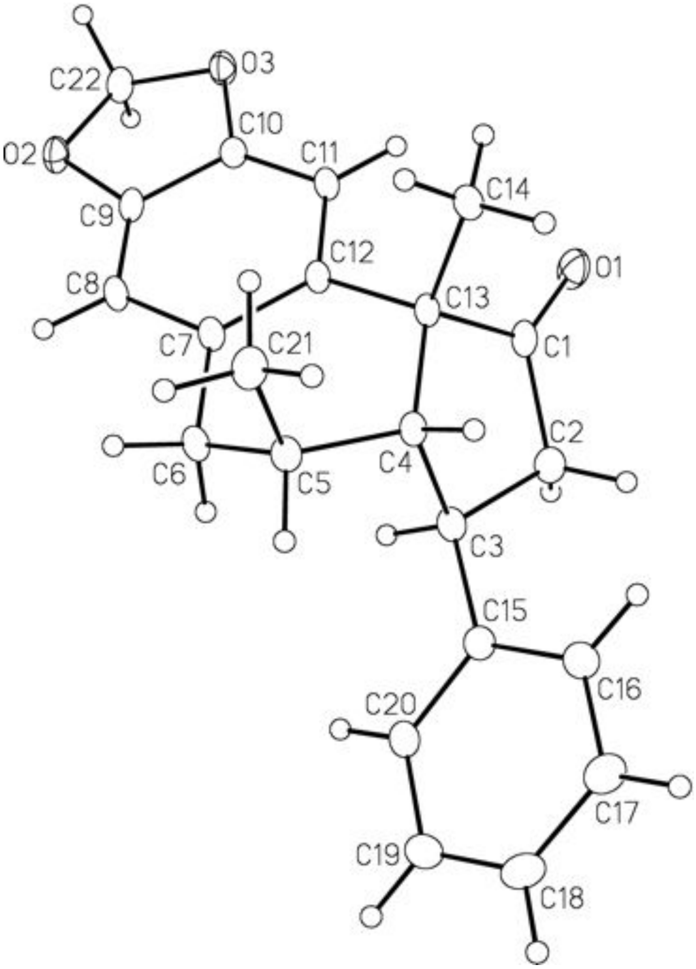
STRUCTURE REPORT

XCL Code: FGW1005 **Date:** 24 March 2010

Compound: 4,10*b*-dimethyl-3-phenyl-2,3,3*a*,4,5,10*b*-hexahydro-1*H*-cyclopenta[5,6]naphtho[2,3-*d*][1,3]dioxol-1-one

Formula: $C_{22}H_{22}O_3$

Supervisor: F. G. West **Crystallographer:** M. J. Ferguson



Compound **13v**