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Part I: Tetrasubstituted Allenyl Ethers
Part II: Triply Convergent Cyclopentannulation

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Finally, in the words of the philosopher Brian McNelis, “that’s the news and I’m out of here.”

ABSTRACT

Part I: A method for the synthesis of tetrasubstituted allene ethers is described. The Brook rearrangement is employed to form key propargyl ether intermediates. The resulting propargyl ethers are isomerized to allenes. The allenes are used in the cyclopentannelation reaction to form β,β -disubstituted cyclopentenones.

Part II: Based on methodology developed by our group, the scope of the triply convergent cyclopentannelation is expanded. Modifications to the existing protocol are described. An expanded set of morpholino enamides are employed.

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LIST OF ABBREVIATIONS

Å	angstrom
Ac	acetyl
anal.	analysis
aq	aqueous
ax	axial
atm	atmospheres
bp	boiling point
br	broadened
Bu	butyl
BuLi	butyl lithium
calcd.	calculated
ca.	circa
cat.	catalytic
Cb	carbamate
COSY	correlation spectroscopy
d	doublet
dd	doublet of doublets
ddd	doublet of doublet of doublets
ddt	doublet of doublet of triplets
δ	chemical shift
DCM	dichloromethane

dm	doublet of multiplets
DMAP	4-(dimethylamino)pyridine
DMF	<i>N,N</i> -dimethylformamide
DMSO	dimethylsulfoxide
dt	doublet of triplets
<i>E</i>	entgegen
E	electrophile
<i>ee</i>	enantiomeric excess
equiv	equivalent(s)
Et	ethyl
Et ₂ O	diethyl ether
g	gram
h	hour
HFIP	hexafluoroisopropanol
HMDS	hexamethyldisilazane
HMPA	hexamethylphosphoramide
HPLC	high performance liquid chromatography
HRMS	high resolution mass spectroscopy
Hz	hertz
IR	infrared spectroscopy
<i>J</i>	coupling constant
L	liter
LA	Lewis Acid

LDA	lithium diisopropylamide
m	multiplet
M	molarity
M ⁺	molecular ion
Me	methyl
MeI	methyl iodide
mg	milligram
MHz	megahertz
min	minute
mL	milliliter
mmol	millimole
MOMCl	methoxymethyl chloride
mp	melting point
μL	microliter
m/z	mass/charge
NCS	<i>N</i> -chlorosuccinimide
nM	nanomolar
NMR	nuclear magnetic resonance
NOE	nuclear Overhauser effect
Ph	phenyl
pH	pondus hydrogenii
PMP	paramethoxyphenyl
ppm	parts per million

Pr	propyl
pyr	pyridine
q	quartet
quint	quintet
R_f	retention factor
rt	room temperature
s	singlet
SAR	structure-activity relationship
t	triplet
TBAF	tetrabutyl ammonium fluoride
TBS	<i>tert</i> -butyldimethylsilyl
TBSCl	<i>tert</i> -butyldimethylsilyl chloride
td	triplet of doublets
TFAA	trifluoroacetic anhydride
TFE	trifluoroethanol
THF	tetrahydrofuran
THP	tetrahydropyran
TIPSCl	triisopropylsilylchloride
TLC	thin-layer chromatography
tm	triplet of multiplets
TMS	trimethylsilyl
TMSCl	trimethylsilyl chloride
TOCSY	totally correlated spectroscopy

tq	triplet of quartets
TrocCl	trichloroethyl chloroformate
tt	triplet of triplets
Z	zusammen

Part I: Tetrasubstituted Allene Ethers; Synthesis and Use in the Nazarov Reaction

A. Introduction

1. The Nazarov Reaction

The five membered ring is a ubiquitous motif in natural products. For this reason, the Nazarov cyclization¹ is often employed as the key step in total synthesis. The Nazarov reaction is a 4- π conrotatory electrocyclicization. It is initiated when a divinyl ketone **1** is exposed to protic acid or Lewis acid and a pentadienyl cation **2** is formed. The cationic intermediate **2** undergoes conrotatory ring closure. The resulting carbocation can be captured with a nucleophile to form cyclopentenone **4**. Alternatively, loss of a proton can occur, whereupon cyclopentanone **3** is formed.

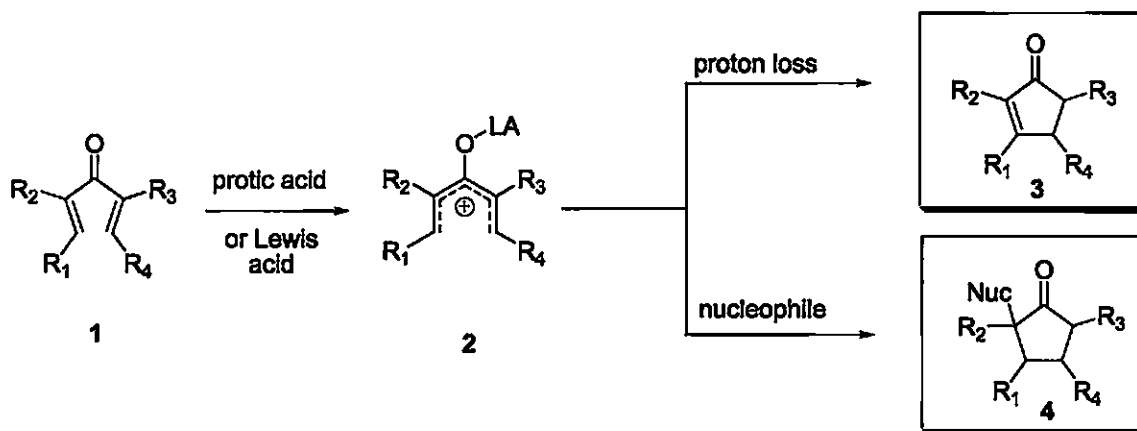


Figure 1. Mechanism of Nazarov Cyclization

The Nazarov cyclization undergoes conrotatory ring closure under thermal conditions or disrotatory ring closure under photochemical conditions.¹ Additionally, the ring closure may proceed in a clockwise or counterclockwise fashion (torquoselectivity). If the starting divinyl ketone contains a chiral center, the reaction will result in the generation of two diastereomers. Torquoselectivity is under steric control of the substituents in the vicinity of the newly formed bonds.¹

2. Cationic Cyclopentannelation of Allene Ethers

The scope of the Nazarov reaction may be expanded if an allenyl vinyl ketone instead of a divinyl ketone is used as a substrate. This variant can be used to produce densely functionalized cross-conjugated cyclopentenones.² The general mechanism for the allenyl-vinyl ketone Nazarov cyclization is shown below in figure 2. Generation of the cation intermediate **5** is followed by a conrotatory ring closure to form cyclopentenone **6**. Loss of methoxymethyl cation results in the formation of cross-conjugated cyclopentenone **7**.

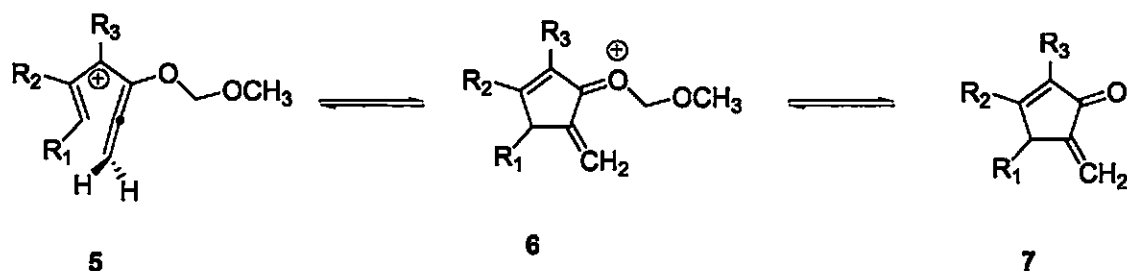
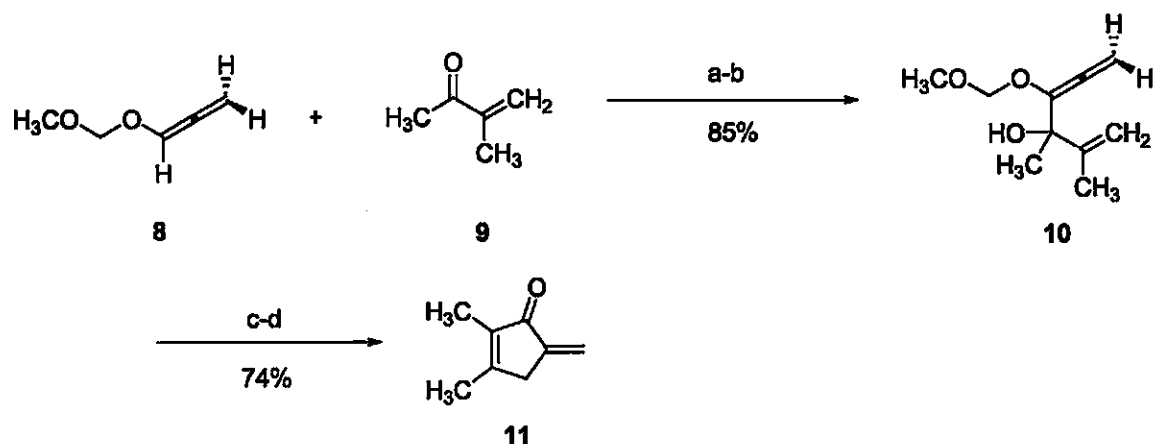


Figure 2. Cationic Cyclopentannelation of Allene Ethers

The first example of cationic cyclopentannulations of allenyl ethers discovered by Tius and co-workers,³ involved the addition of 3-methyl-3-buten-2-one **9** to 1-lithio-1-(methoxy)methoxyallene. Addition of TFAA and 2,6 lutidine in a subsequent step yielded cross-conjugated cyclopentenone, methylenomycin B **11**. The Nazarov cyclization provided a concise, elegant solution for the synthesis of methylenomycin B.



Scheme 1.^a

^aReaction conditions: (a) 4 equiv of **8**, BuLi, THF, Et₂O, -78 °C; (b) 1 equiv of **9**, THF, -78 °C; (c) 3 equiv TFAA; (d) 5 equiv 2,6-lutidine, DCM, -20 °C.

In general, allenyl ethers can be employed to produce compounds of broad structural diversity under mild conditions. Typically, strong mineral acids are used in standard Nazarov procedures. Relief of axial strain of the allene during the cyclization allows the use of mild aqueous acids such as KH₂PO₄ or Lewis acids such as FeCl₃. Furthermore, the methodology is tolerant of a wide variety of substrates as evidenced in Figure 3. For instance, lithio allene **12** can be combined with various α,β -unsaturated

electrophiles **13,14**, and **15** to yield cyclopentenones **16,17**, and **18**. Generation of structurally diverse cyclopentenones **19-21** is also possible utilizing lithio allene **12**.

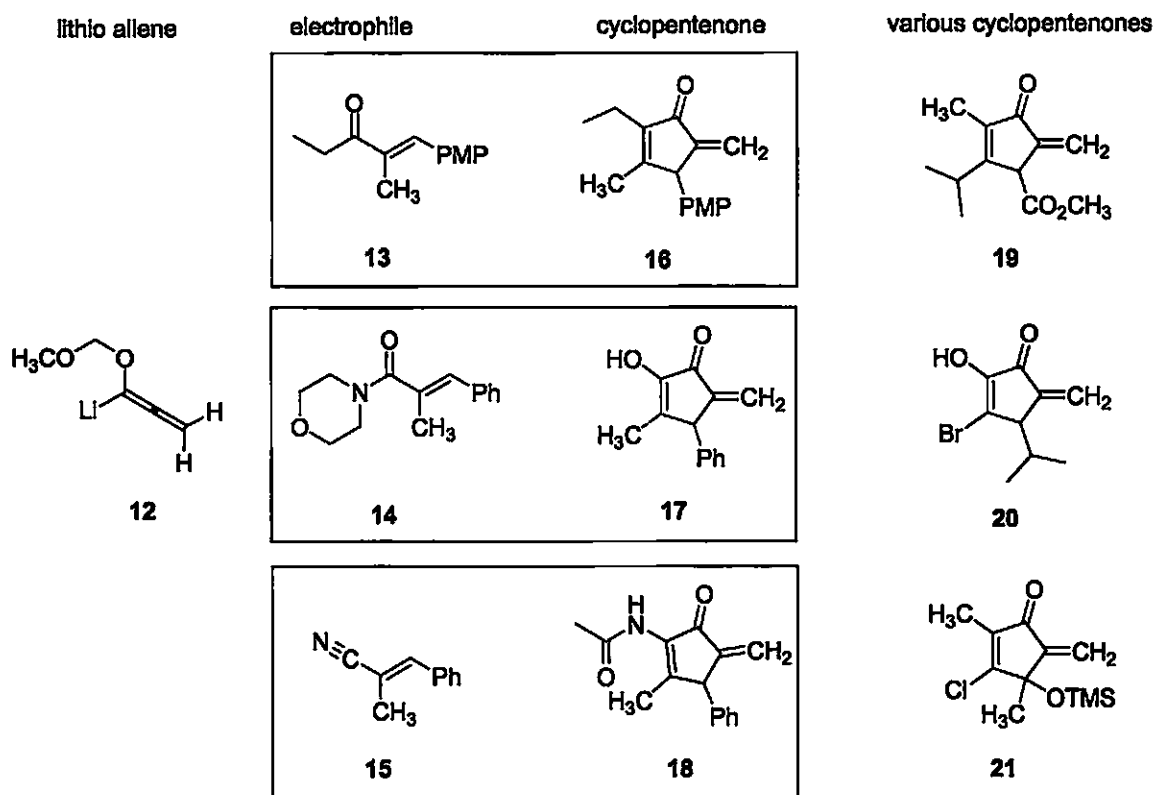


Figure 3. Examples of Cationic Cyclopentannelation Products

3. Limitation of Cyclopentannelation Reaction

However, employing the method in total synthesis revealed a few limitations. While methylenomycin B **11** contains an exocyclic methylene, other total synthesis targets may require addition to the β -carbon of the exocyclic methylene. For example, during the synthesis of roseophilin, it was necessary to functionalize the exocyclic methylene (carbon 6) of α -methylene cyclopentenone **22**,⁴ a transformation accomplished

via a Stetter reaction,⁵ which added a moderate yielding step to the multi-step total synthesis (Figure 4). Additionally, while the Stetter reaction was particularly effective in this synthesis, since the resulting 1,4-diketone was an exploitable intermediate, it is not suitable in all synthetic routes. Therefore, it was necessary to develop a general method for the synthesis of cyclopentenones bearing substitution at the exocyclic methylene.

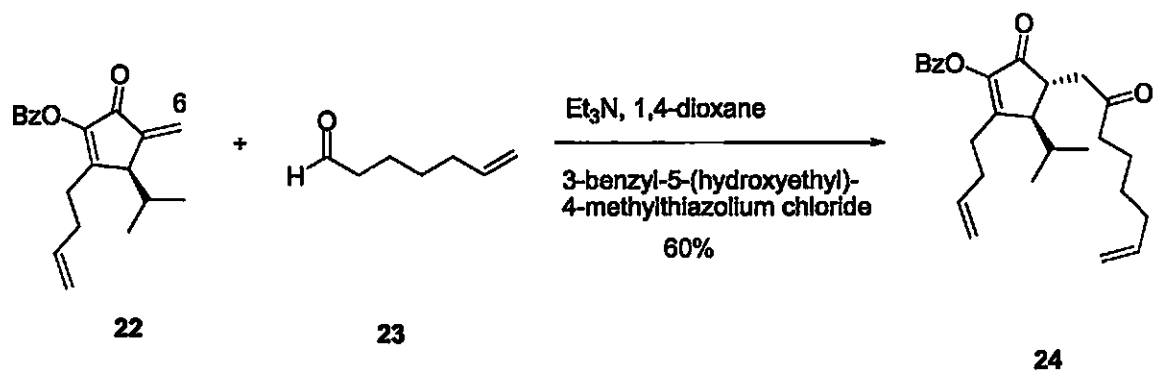


Figure 4. Use of Stetter Reaction in Roseophilin Synthesis

An alternative approach to functionalizing the α,β -unsaturated carbon of the cross-conjugated Nazarov product involved a more convergent strategy. Hu and co-workers⁶ added γ -substituted lithioallene **26** to Weinreb amide **25** at $-78\text{ }^\circ\text{C}$; upon exposure of the reaction mixture to KH_2PO_4 cyclopentenone **27** was formed in 80% yield (Figure 5). Thus, functionalizing the allene prior to cyclization enabled a more convergent approach.

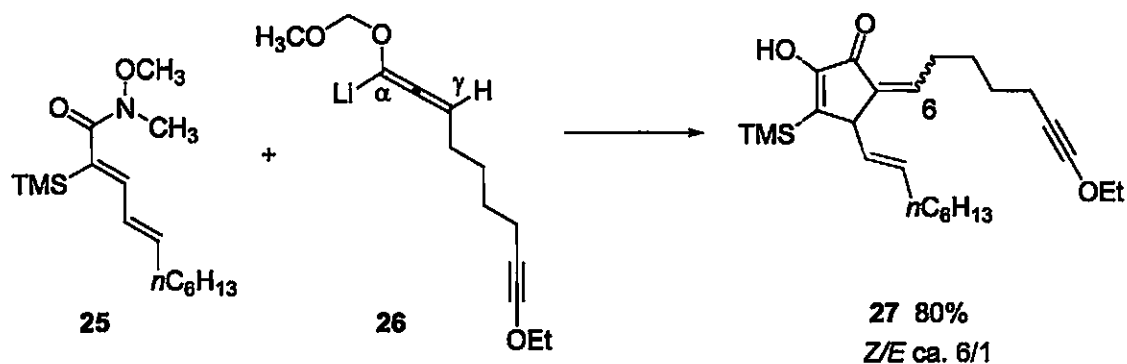


Figure 5. β -Substituted Cyclopentenone

4. γ -Substituted Allenes

Using γ -substituted allenyl ethers in the cyclopentannulation reaction allows a convergent route to C6 substituted cyclopentenones. However, application of existing methodology employed to produce γ -substituted allenyl ethers revealed some limitations. Thus, while (methoxy)methoxyallene **29** was formed in 90% yield by treating the corresponding propargyl ether **28** with catalytic amounts of potassium *tert*-butoxide according to Brandsma's procedure⁷ (Figure 6), the synthesis of γ -substituted allenyl ethers required treatment of propargyl ether **28** with *n*-butyllithium and trapping the intermediate with an alkyl halide. This approach yielded a mixture of allene and acetylene which was difficult to separate. Alternatively, the α -carbon of allenyl ether **29** was lithiated with *n*-butyllithium at -78 °C and trapped with TMSCl.⁸ With the α -position blocked, the resulting allenyl ether **30** was exposed to *sec*-butyllithium and trapped with an alkyl halide. Subsequent desilylation with TBAF yields γ -substituted

allenyl ether **31**. Although the allene was the exclusive product, several steps were required to produce allenyl ether **31**. Moreover, the method is not suitable for the formation of γ,γ -disubstituted allene **32**, as a second γ -deprotonation was not possible. Thus, the preparation of γ -substituted allenyl ethers using existing methodology was not straightforward and limited with respect to scope.

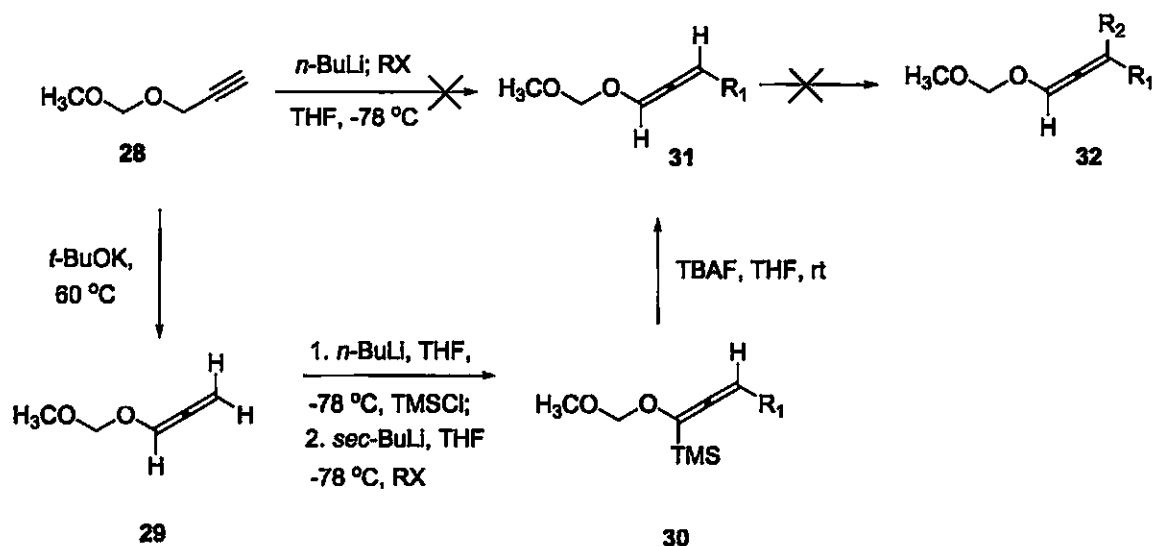


Figure 6. Existing Methodology For γ -Substituted Allene Synthesis

As a result, two strategies were envisioned to address this problem. The first strategy was based on a fortuitous observation. An attempt was made to isomerize tributyl(1-(methoxymethoxy)non-2-ynyl)stannane **33** to γ -substituted allene **34** (Figure 7). While there was NMR evidence to support small amounts of allene product, the unknown product degraded upon standing. It was hypothesized that lithiation of a silyl analogue might improve the stability of the product. Treatment of trimethyl silyl

analogue **35** under similar conditions yielded allene ether **36**. The benefits of this discovery are two-fold: (1) while there are methods to produce tetrasubstituted allenes, to our knowledge there are no known methods to generate tetrasubstituted allene ethers; (2) after hydro-desilylation allene ether **37** can be used in the Nazarov cyclization to form β,β -disubstituted cyclopentenones. Furthermore, it was hoped that this discovery could be developed to lead to allow the synthesis of enantioenriched axially chiral allene ethers.

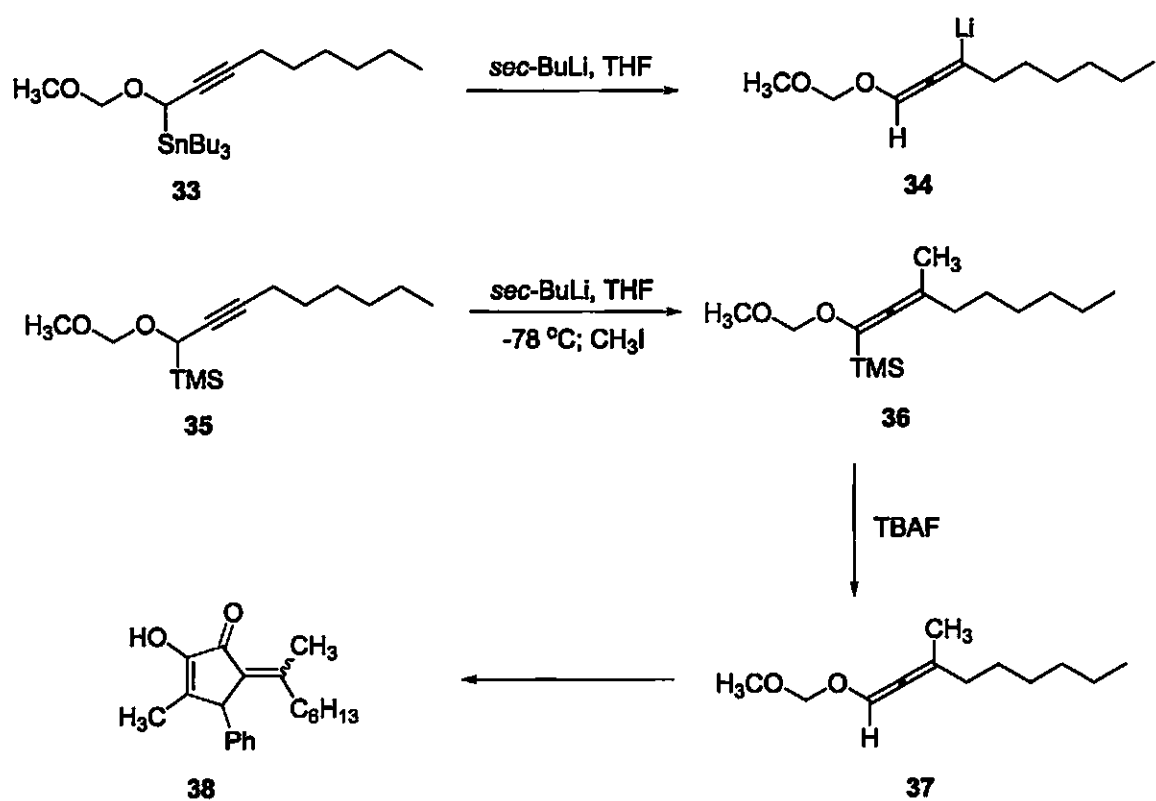


Figure 7. Synthesis of Tetrasubstituted Allenes

5. Potential Routes to Axially Chiral Allene Ethers

During the synthesis of a cross-conjugated prostaglandin analogue,⁶ a preference for the *Z* isomer (ca. 6/1) of the exocyclic double bond was observed in the formation of intermediate **27** (Figure 5). It was postulated that the preference for the *Z* isomer was caused by steric repulsion (torquoselectivity) to favor one of the two possible modes for the conrotatory ring closure of allenyl ether **39** (Figure 8). Therefore, it was hypothesized that chiral non-racemic allenyl ethers could be used to transfer asymmetry to the tetrahedral ring carbon (C4 in **40**).

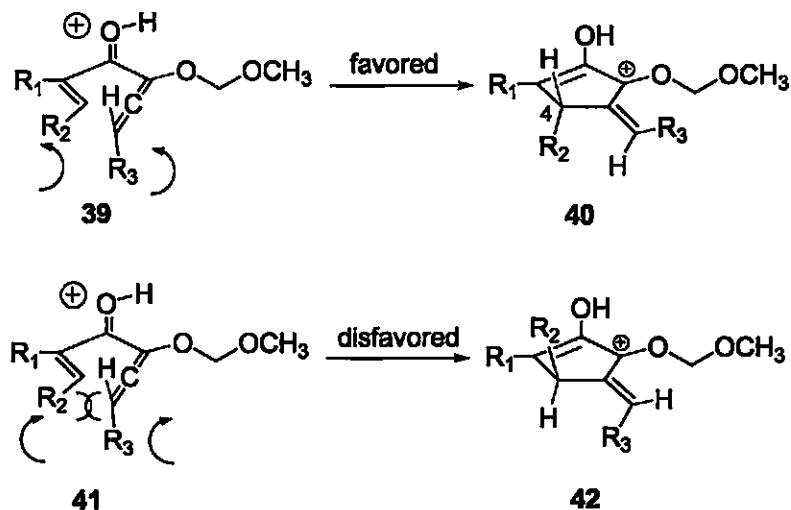


Figure 8. Two Possible Modes of Conrotation for the Cyclopentannulation

Hu and co-workers,¹⁰ prepared chiral non-racemic allene **43** using chiral semi-prep HPLC (Figure 9). Exposure of (+)-**43** (98% *ee*) to vinyl lithium species **44** followed

by acidic workup gave exclusively the *Z* isomer of (-)-45 (95% *ee*, >95% chirality transfer) in 64% yield. However, for this method to be synthetically useful, a more convenient route was needed for the preparation of the axially chiral allenyl ether.

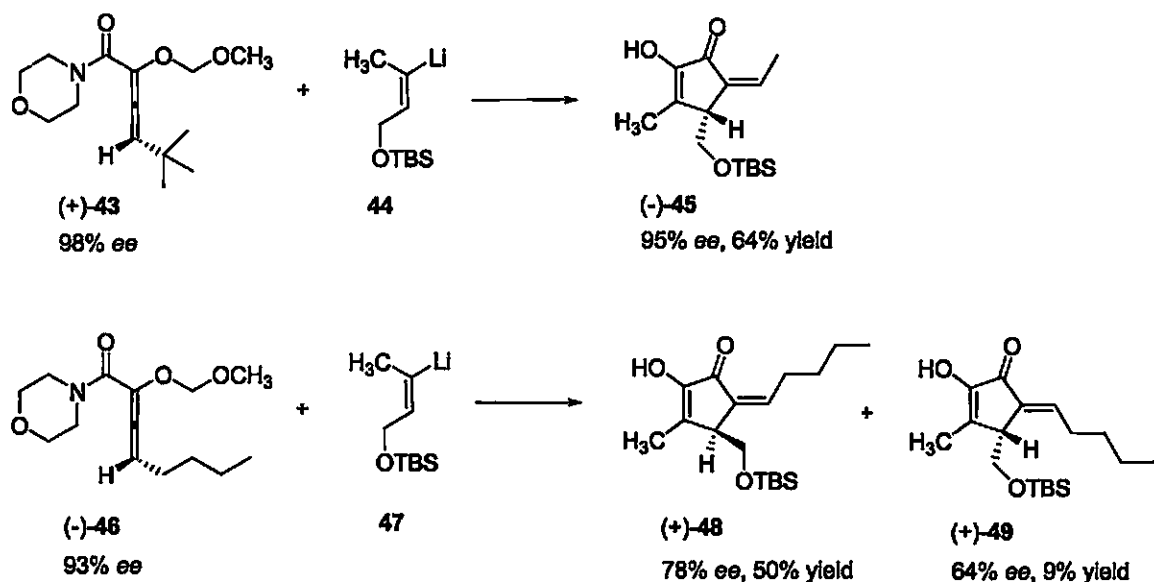


Figure 9. Chirality Transfer in the Nazarov Cyclization

It was envisioned that the preparation of the optically active allene **50** would provide an excellent route to chiral non-racemic allenes (Figure 10). Metallation and isomerization of propargyl ethers has been studied by Leroux *et al.*¹¹ and Corey *et al.*¹² with a limited number of electrophiles. Corey and co-workers¹² performed the metallation of tetrahydropyranyl derivative **51** with *n*-butyllithium to form a propargylic lithio intermediate, which was then quenched with methanol to give, in quantitative yield, a mixture of allene **52** and starting material **51** in a ratio of 70:30. Leroux¹¹ treated

propargyl ether **53** with *n*-butyllithium and trapped with Me₂SO₄ to afford the corresponding allene **54** in 80% yield.

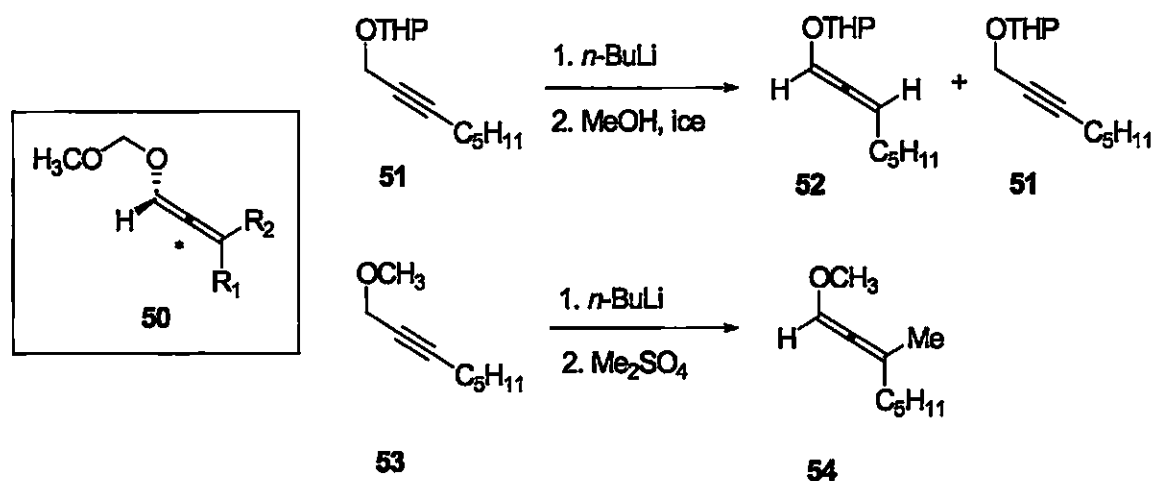


Figure 10. Synthesis of Allenyl Ethers

To date, there is no general route to the tetrasubstituted allene **56**. It was hypothesized that optically active propargyl silane **55**, easily prepared according to known literature procedures,^{13,14} can be isomerized to allene **56** through a stereospecific process involving deprotonation with a base and trapping with an electrophile. Protodesilylation of allene **56** affords axially chiral allenyl ether **57** (Figure 11). Although there was no direct literature precedent to support our hypothesis, we decided to determine the feasibility of the proposed method.*

* Work done by Hoppe and co-workers²² suggests that isomerization of propargyl ethers to the corresponding axially chiral allenes could be accomplished stereospecifically when employing sparteine and *n*-butyllithium.

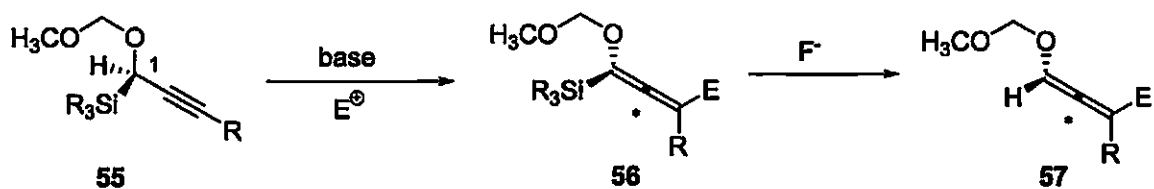


Figure 11. Synthesis of Optically Active Allenes

To maximize transfer of asymmetry during the cyclopentannulation process, it is important that the difference in size between the two groups R and E on allene **57** be as large as possible. As summarized in Figure 9, the cyclization with γ -substituted *tert*-butyl allene **43** proceeded with > 95% chirality transfer while the corresponding *n*-butyl allene **46** showed diminished asymmetry transfer at 84%.

In addition to the transfer of asymmetry during the Nazarov cyclization, allenyl ether **57** would have a second utility: functionalizing the γ -position of the allenyl ether. Doing so would allow for a convergent synthesis of cyclopentenones β,β -disubstituted at the exocyclic double bond. In work done by Bee and co-workers,⁹ the acidic proton of the allenyl ether in the tetrahedral intermediate **58** had been removed by an equivalent of *sec*-butyllithium. Trapping with an electrophile followed by acidic workup gave cyclopentenones **62** monosubstituted at the exocyclic methylene (Figure 12).*

* Improvement to the triply convergent cyclopentannulation process is summarized in Part II.

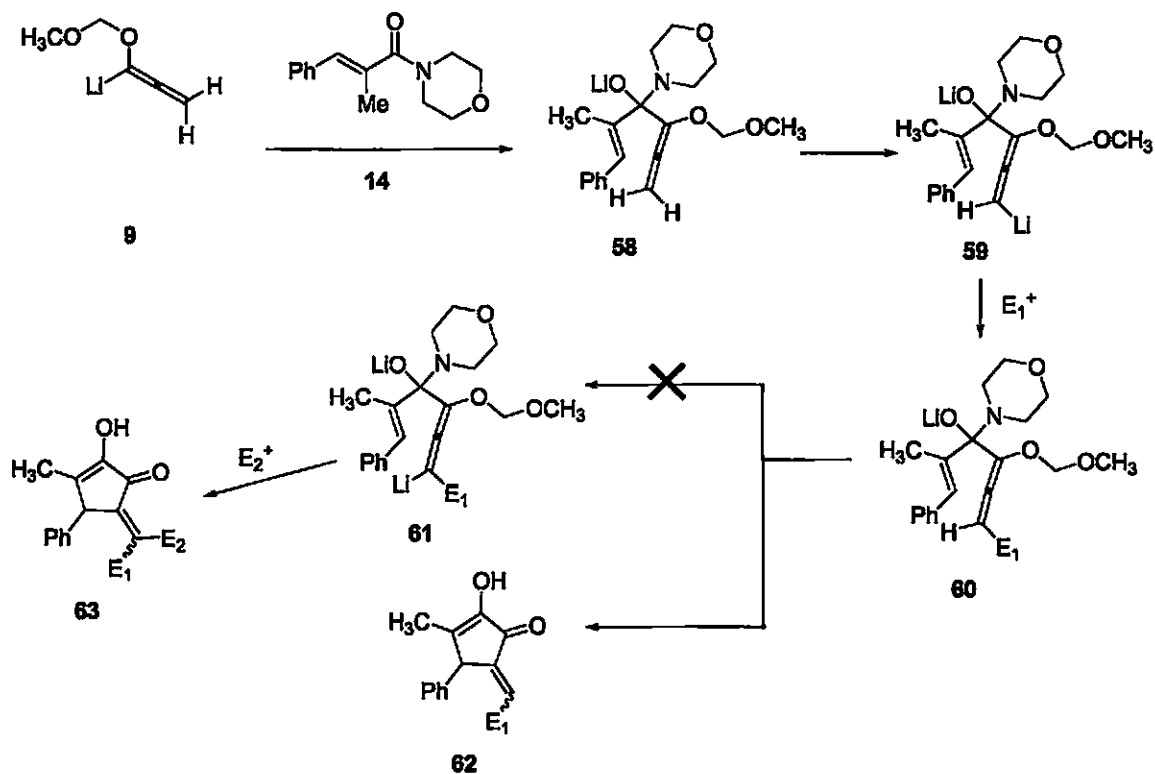


Figure 12. Triply Convergent Cyclopentannulation Process

Attempts at lithiating the remaining γ -proton on intermediate **60** and trapping with a second electrophile were unsuccessful. Thus, only cyclopentenones monosubstituted at the exocyclic double bond could be accessed by this method. Utilizing γ,γ -disubstituted allenyl ethers would allow us to fully functionalize the C6 exocyclic methylene of the cyclopentenone product.

An attempt was made to develop a convenient method for the synthesis of allenyl ethers that will lend itself to asymmetric synthesis. Our overall goals were as follows: (1) to prepare γ,γ -disubstituted allenyl ethers for the synthesis of β,β -disubstituted cyclopentenones and (2) to prepare γ,γ -disubstituted allenyl ethers with a marked difference in size between the two γ -substituents. In the following the preparation of

these γ,γ -disubstituted allenyl ethers and their use in the Nazarov cyclization to produce C6 disubstituted cross-conjugated cyclopentenones will be described.

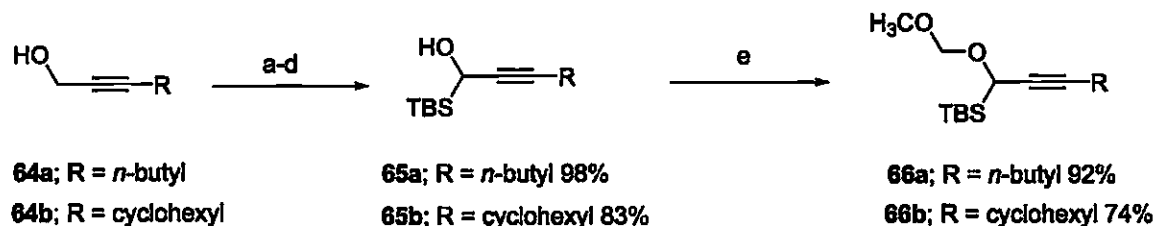
B. Results and discussion

1. Preparation of propargyl silane 66a-b.

The synthesis of intermediates **66a** and **66b** was carried out starting with readily available propargyl alcohols **64a** and **64b** in an elegant one-pot reverse Brook rearrangement,¹⁵ developed by Ohfuné and co-workers,¹³ to obtain propargylsilanes **65a** and **65b** (Scheme 2).

Several minor modifications were made to the existing procedure. First, the purity of the *n*-butyllithium was important to the success of the reaction. Use of aged bottles of alkyl lithium resulted in diminished yields and recovery of propargyl ether. Aged bottles of alkyl lithium contained higher concentrations of LiOH, which could have contributed to appreciable amounts of desilylation resulting in the observed propargyl ether. Second, it was necessary to keep the reaction at $-20\text{ }^{\circ}\text{C}$ after the addition of *tert*-butyldimethylsilyl chloride. The reaction was maintained at $-20\text{ }^{\circ}\text{C}$ for 40 minutes rather than at $-45\text{ }^{\circ}\text{C}$ for 2 hours as described in Ohfuné's general procedure. At $-45\text{ }^{\circ}\text{C}$ substantial amounts of alkynyloxysilane were recovered, while higher temperatures favored the rearrangement. Last, the reaction was quenched at $-20\text{ }^{\circ}\text{C}$ with aqueous NaHCO_3 . If the reaction was quenched at $-45\text{ }^{\circ}\text{C}$, as reported by Ohfuné, appreciable amounts of alkynyloxysilane were recovered. For our substrates, the yields reported by

Ohfune were not reproducible in our hands without using the modified procedure. As a final note, TBS was used preferentially over TMS due to product stability. TBS propargyl ethers were more stable to acid. Finally, protection of the propargylsilane **65a-b** with MOMCl gave the desired methoxymethyl ether **66a-b**.



Scheme 2^a

^aReaction conditions: (a) BuLi, THF, -78 °C; (b) TBSCl; (c) BuLi, -20 °C; (d) aq NaHCO₃; (e) MeOCH₂Cl, *i*-Pr₂NEt, CH₂Cl₂.

2. Synthesis of γ,γ -disubstituted allenyl ethers.

Allenyl ethers were prepared by treating methoxymethyl ether **66a** or **66b** with 1.3 equivalents of *sec*-butyllithium in THF at -78 °C and trapping with various electrophiles. The results are summarized in Table 1. Presumably, the mechanism proceeded as summarized in Figure 13. After deprotonation with *sec*-butyllithium, an equilibrium was reached between the lithio alkyne and the lithio allene. Treatment of the intermediate with methyl iodide yielded allenyl ether **68**.

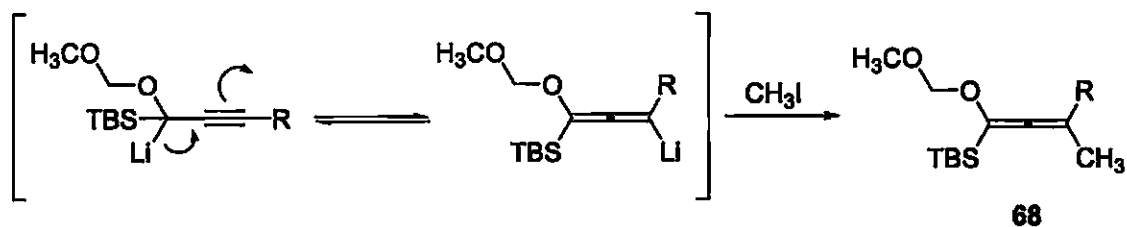


Figure 13. Mechanism of Rearrangement

Use of *sec*-butyllithium was necessary in this transformation as *n*-butyllithium and *tert*-butyllithium gave mixtures of starting material and allene. Product yields varied from good to excellent and the reaction worked with a diverse range of electrophiles including alkyl halides, ketones, amides, and chlorosilanes. Exposure of the allenyl ethers to protic acid resulted in lower yields. As a result, all reactions were quenched with aqueous NaHCO_3 and silica gel column chromatography was run with 1% triethylamine in the eluent. In addition, allenes were stored in flasks pre-treated with HMDS. The resulting allenes were stable over several weeks at 0 °C and showed little to no degradation. However, slow decomposition took place on standing at room temperature.

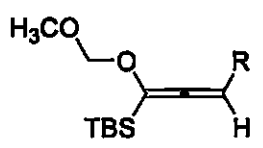
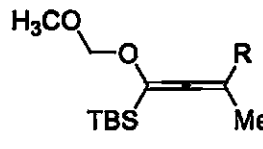
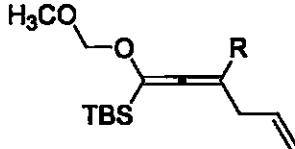
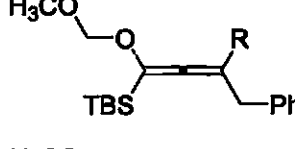
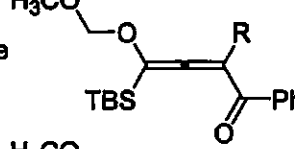
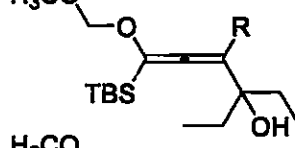
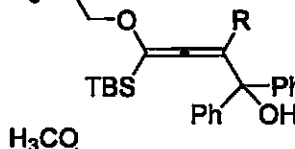
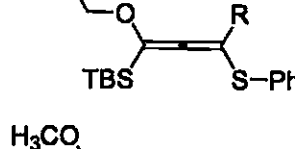
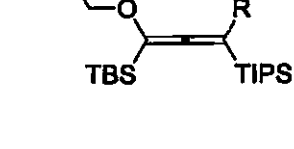
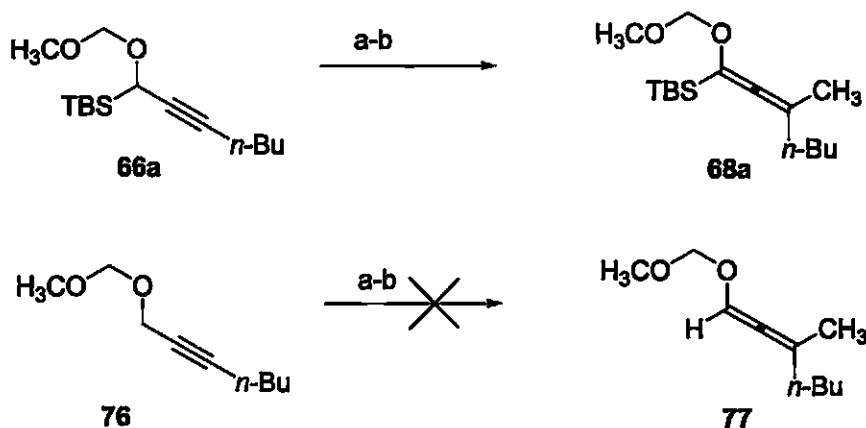
<u>Electrophile</u>	<u>Product</u>	<u>Yield R=<i>n</i>-butyl</u>	<u>R=cyclohexyl</u>
EtOH		67a; 85%	67b; 77%
Mel		68a; 96%	68b; 86%
BrCH ₂ CH=CH ₂		69a; 84%	69b; 85%
BrCH ₂ Ph		70a; 98%	70b; 92%
PhCON(OMe)Me		71a; 93%	71b; 54%
3-pentanone		72a; 61%	72b; 87%
benzophenone		73a; 76%	73b; 61%
PhSOSO ₂ Ph		74a; 93%	74b; 97%
TIPSCI		75a; 95%	75b; 97%

Table 1.

It should be emphasized that the silyl substituent was critical to the success of the facile rearrangement. Under identical reaction conditions, propargyl ether **76** returned starting material. It was hypothesized that the silyl group has an electronic effect, which stabilizes the anion at the γ -carbon on the allene.

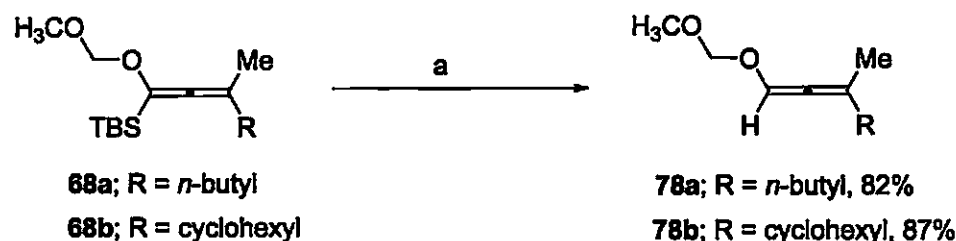


Scheme 3.^a

^aReaction conditions: (a) *sec*-BuLi, THF, $-78\text{ }^{\circ}\text{C}$, 30 min; (b) MeI, 30 min.

Treatment of the tetrasubstituted allenyl ethers **68a-b** with a mixture of 1 equivalent of TBAF and 1 equiv of $\text{LiOH}_{(s)}$ gave the desired desilylated trisubstituted allenes **78a-b** (Scheme 4). Without 1 equivalent of $\text{LiOH}_{(s)}$ the reaction was extremely sluggish and required ca. 8 equivalents of TBAF to proceed to completion. However, in the presence of 1 equivalent of $\text{LiOH}_{(s)}$ only 1 equivalent of TBAF was required for the reaction to proceed to completion in 2 hours at room temperature. At the end of the 2

hours the reaction mixture was completely homogeneous. The role of $\text{LiOH}_{(s)}$ is not fully understood. Because $\text{LiOH}_{(s)}$ is not soluble in THF, homogeneity may imply that the TBAF serves as a phase-transfer catalyst and that LiOH actually performed the protodesilylation. After workup, desilylated products **78a-b** were detected by NMR spectroscopy. Impurities including *tert*-butyldimethylsilanol were easily separated from the product by simple Kugelrohr distillation at reduced pressure to yield the allenes **78a-b** in good yield.



Scheme 4.^a

^aReaction conditions: (a) 1 equiv TBAF, 1 equiv $\text{LiOH}_{(s)}$, THF, r.t.

3. Nazarov cyclizations of γ,γ -disubstituted allenyl ethers.

With the allenyl ethers in hand, we set out to accomplish our second goal: to use the γ,γ -disubstituted allenes in the three broad categories of the cyclopentannulation reaction. Each α,β -unsaturated electrophile gives rise to a different category of cyclopentenones: the morpholino amide **14** yields α -hydroxy cyclopentenones, the nitrile

15 produces α -amino cyclopentenones,¹⁶ and the α,β -unsaturated ketone **13** gives α -alkyl cyclopentenones (Figure 14).

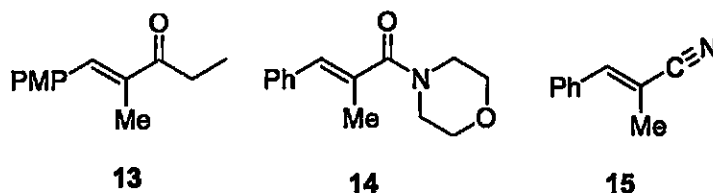
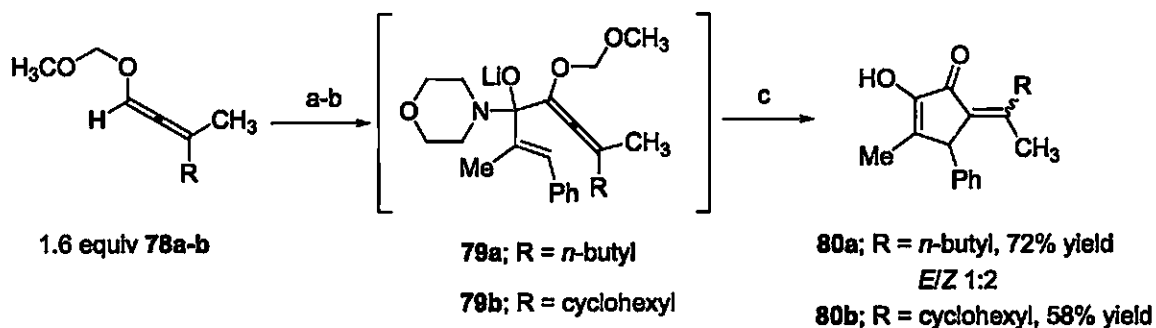


Figure 14. α,β -Unsaturated Electrophiles

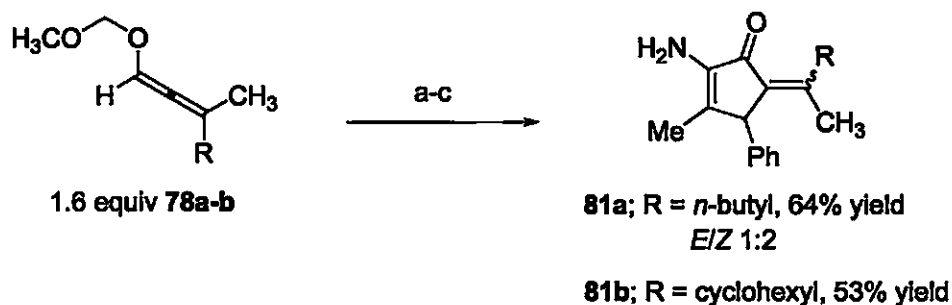
Exposure of allenyl ethers **78a-b** to *n*-butyllithium and subsequent addition of amide **14** produced the presumed tetrahedral intermediates **79a-b** (Scheme 5). The reaction was initiated by transferring the reaction mixture *via* cannula into a solution of FeCl₃ in DCM at room temperature to give cyclopentenones **80a** and **80b** in 72% and 58% yield respectively. Quenching the reaction mixture with ethanolic HCl instead leads to hydrolysis of the excess allene and the resulting aldehyde proved difficult to separate from the cyclopentenone product *via* silica gel chromatography. Experimentation revealed that upon exposure to FeCl₃ in DCM, allenyl ethers **78a-b** are stable at rt for up to 1 h and hydrolysis was not observed. Thus, FeCl₃ was chosen as a mild Lewis acid to induce cyclization and facilitate work up.



Scheme 5.^a

^aReaction conditions: (a) BuLi (1.8 equiv), THF, -78 °C; (b) **14** (1 equiv); (c) FeCl₃, CH₂Cl₂.

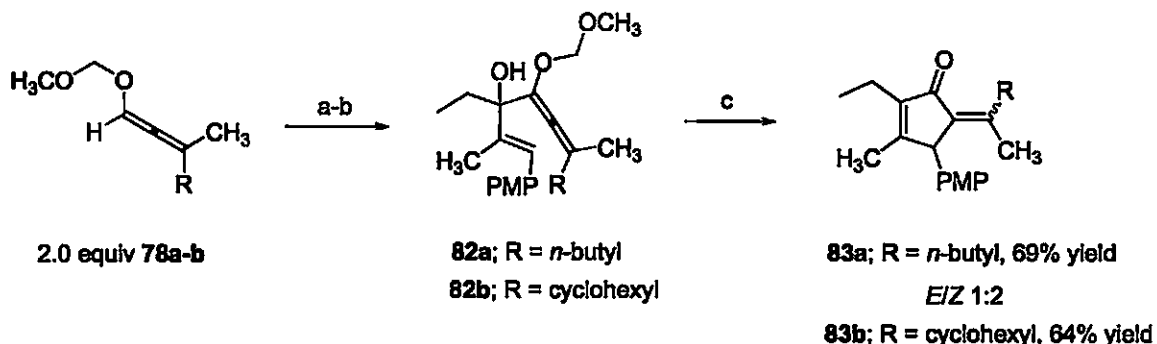
The allenyl ethers were also used to prepare α -amino cyclopentenones (Scheme 6). After lithiation of **78a-b** with *n*-butyllithium, α -methylcinnamionitrile **15** was added to the reaction mixture. The reaction was quenched with FeCl₃ in Et₂O and afforded the α -amino cyclopentenones **81a-b** in acceptable yields.



Scheme 6.^a

^aReaction conditions: (a) BuLi (1.8 equiv), THF, -78 °C; (b) **15** (1.0 equiv); (c) FeCl₃, Et₂O.

γ,γ-Disubstituted allenyl ethers were also used to prepare α-alkyl cyclopentenones (Scheme 7). After exposing allenyl ether **78** to *n*-butyllithium, enone **13** was added to the reaction mixture. The tertiary alcohols **82a-b** were isolated after workup and cyclized in a subsequent step. Treatment of the tertiary alcohol with FeCl₃ in DCM at room temperature gave the desired α-alkyl cyclopentenones **83a** and **83b** in 69% and 64% yield, respectively. It was found that excess enone **15** co-eluted with the cyclopentenone products **83a-b** during silica gel purification. Therefore, 2.0 equivalents of the lithio allene was used to make sure all of the enone **15** was consumed in the reaction.

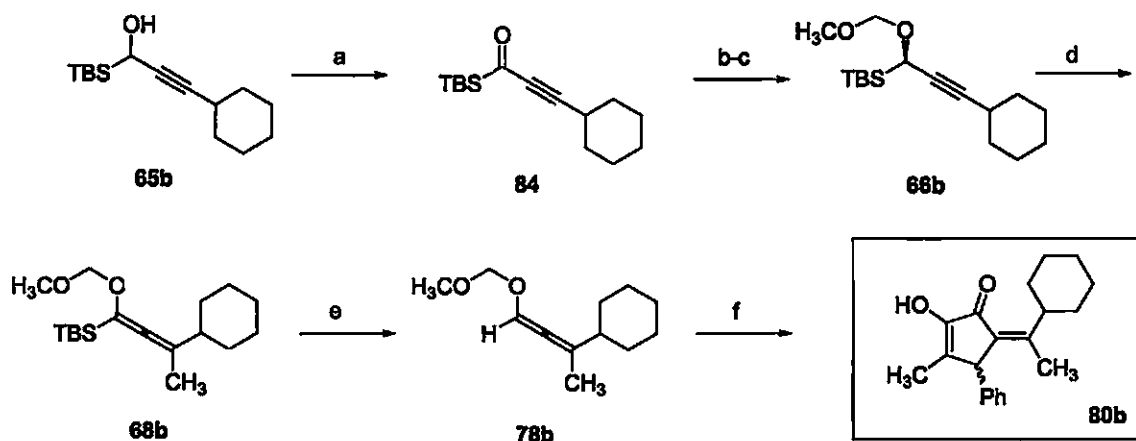


Scheme 7.^a

^aReaction conditions: (a) BuLi (2.05 equiv), THF, -78 °C; (b) **13** (1.0 equiv); (c) FeCl₃, CH₂Cl₂.

4. Axially Chiral Tetrasubstituted Allenes

Our last goal was to determine whether axially chiral tetrasubstituted allenes^{17,18} could be synthesized and whether the asymmetry could be transferred during the cyclopentannulation. Racemic propargyl silane **65b**, was oxidized using the Swern protocol to yield acyl silane **84**. Subsequent reduction with alpine borane gave the optically active propargyl silane (95% *ee*). The resulting alcohol was protected with MOMCl and rearranged to the allene using the aforementioned protocol. After protodesilylation, the allene ether **78b** was used in the Nazarov cyclization. Unfortunately, no optical enrichment in the cyclization product **80b** was detected using chiral chromatography.



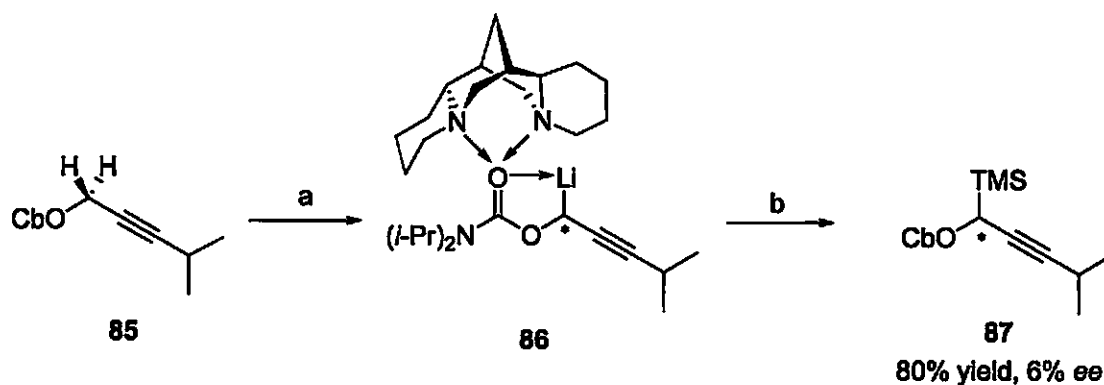
Scheme 8.^a

^aReaction conditions: (a) oxalyl chloride (1.2 equiv), DMSO (2 equiv), NEt₃ (4 equiv), DCM, -60 °C; (b) alpine borane (1.5 equiv), rt; (c) MeOCH₂Cl, *i*-Pr₂NEt, CH₂Cl₂; (d)

sec-BuLi, THF, $-78\text{ }^{\circ}\text{C}$, MeI, 30 min; (e) 1 equiv TBAF, 1 equiv LiOH_(s), THF, rt; (f) BuLi (1.8 equiv), THF, $-78\text{ }^{\circ}\text{C}$; **14** (1 equiv); FeCl₃, CH₂Cl₂.

Lithiated propargylic derivatives are known to exist in two rapidly interconverting tautomeric forms.²² The lithio-propargyl and the allenyllithium species may not be configurationally stable. As a result, although propargyl ether **66b** was enantioenriched, the reaction conditions may have led to the formation of racemic **68b**. However, we did not confirm the *ee* of allene **68b**.

A related experiment by Hoppe and co-workers supports our hypothesis.^{21,22} Propargyl ether **85** was treated with *n*-BuLi and (–)-sparteine. For other substrates, this combination (*n*-BuLi/sparteine) is a highly selective chiral base. However, trapping the lithio anion resulted in the formation of nearly racemic product. Hoppe reports that the low enantioselectivity may be due to a lack of configurational stability of the anion.



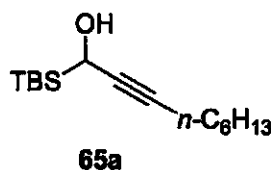
Scheme 9.^a

^aReaction conditions: (a) *n*-BuLi, (–)-sparteine, toluene, $-78\text{ }^{\circ}\text{C}$, 0.5 h; (b) TMSCl.

C. Summary

We successfully developed a method for the synthesis of tetrasubstituted allene ethers. While there are several methods available for the synthesis of tetrasubstituted allenes, prior to this work there were no protocols available for the formation of tetrasubstituted allene ethers. The resulting allene ethers were amenable to the three categories of cyclopentannulation reactions, and the products formed were the first cases of cyclopentenones with β,β -disubstituted exocyclic double bonds. It is hoped that the method can be employed in total synthesis. The method is unsuitable for the synthesis of chiral non-racemic β,β -disubstituted cyclopentenones.

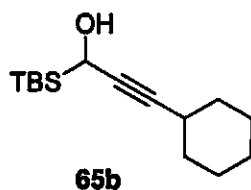
D. Experimental



1-(*tert*-Butyldimethylsilyl)-non-2-yn-1-ol **65a**.

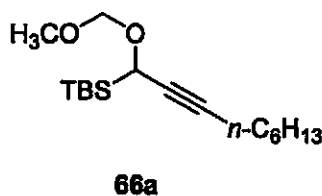
To a solution of alkynol **64a** (6.0 g, 42.8 mmol) in THF (30 mL) at $-78\text{ }^{\circ}\text{C}$ was added BuLi (17.3 mL; 47.1 mmol; 2.7 M solution in hexane). The reaction mixture was warmed to $0\text{ }^{\circ}\text{C}$ and allowed to stir for 30 min. After cooling to $-78\text{ }^{\circ}\text{C}$, TBSCl (7.1 g, 68.5 mmol) in THF (5 mL) was added via cannula. After stirring for 2 h at r.t., the reaction mixture was cooled to $-78\text{ }^{\circ}\text{C}$ and BuLi (25.3 mL; 2.7 M solution in hexane) was added. The mixture was stirred for 40 min at $-20\text{ }^{\circ}\text{C}$, and the reaction mixture was subsequently diluted with aq NaHCO₃ and Et₂O. The aq phase was extracted with Et₂O, the combined organic extracts dried (MgSO₄), and the solvent was removed in vacuo. Column chromatography (silica gel; 5% EtOAc-hexane) gave **65a**. IR (film): 3420 (br), 2940, 1690, 1460, 1250 cm⁻¹; ¹H NMR (300 MHz, CDCl₃): $\delta = 4.20$ (t, 1 H, $J = 2.4$ Hz,

CH), 2.33 (td, 2 H, $J = 6.9, 2.4$ Hz, CH₂), 1.51-1.26 (m, 8 H, CH₂), 0.97 (s, 9 H, CH₃), 0.96-0.86 (m, 3 H, CH₃), 0.10 (s, 3 H, CH₃), 0.07 (s, 3 H, CH₃); ¹³C NMR (75 MHz, CDCl₃): $\delta = 89.0, 81.2, 55.2, 31.6, 29.1, 28.8, 27.1$ (3 C), 22.8, 19.3, 17.2, 14.3, -7.7, -8.4; MS (EI): m/z (%) = 73 (61), 75 (100), 197 (4), 211 (4), 254 (1); HRMS: m/z [M^+] Calcd for C₁₅H₃₀OSi 254.2066. Found 254.2052.



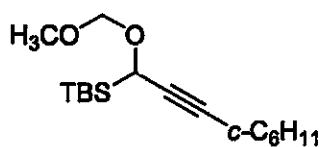
1-(*tert*-Butyldimethylsilyl)-3-cyclohexylprop-2-yn-1-ol **65b**.

IR (film): 3420 (br), 2910, 1690, 1270 cm⁻¹; ¹H NMR (300 MHz, CDCl₃): $\delta = 4.14$ (d, 1 H, $J = 2.1$ Hz, CH), 2.37-2.30 (m, 1 H, CH), 1.79-1.14 (m, 10 H, CH₂), 0.89 (s, 9 H, CH₃), 0.02 (s, 3 H, CH₃), -0.002 (s, 3 H, CH₃); ¹³C NMR (75 MHz, CDCl₃): $\delta = 93.2, 81.1, 55.2, 41.8, 33.1, 29.6, 27.2$ (3 C), 26.1, 25.2, 23.5, 17.2, -7.6, -8.4; MS (EI): m/z (%) = 75 (68), 89 (15), 115 (18), 177 (8), 252 (1); HRMS: m/z [M^+] Calcd for C₁₅H₂₈OSi 252.1909. Found 252.19897.



tert-Butyl-(1-methoxymethoxy-non-2-ynyl)-dimethylsilane **66a**.

To a solution of alkynol **65a** (7.2 g, 28.3 mmol) in CH₂Cl₂ (30 mL) was added Hünig's base (9.9 mL, 56.6 mmol). After cooling to 0 °C, chloromethyl methyl ether (3.7 mL, 48.7 mmol) was added and the mixture was allowed to stir at r.t. for 2 h. The reaction mixture was diluted with aq NaHCO₃ and Et₂O. The aq phase was extracted with Et₂O, the combined organic extracts dried (MgSO₄), and the solvent was removed in vacuo. Column chromatography (silica gel; 0.625% EtOAc-hexane) gave **66a**. IR (film): 2950, 1460, 1250, 1140 cm⁻¹; ¹H NMR (300 MHz, CDCl₃): δ = 4.99 (d, 1 H, *J* = 6.3 Hz, OCH₂O), 4.51 (d, 1 H, *J* = 6.3 Hz, OCH₂O), 4.18 (t, 1 H, *J* = 2.4 Hz, CH), 3.50 (s, 3 H, OCH₃), 2.21 (td, 2 H, *J* = 6.9, 2.4 Hz, CH₂), 1.58-1.23 (m, 8 H, CH₂), 0.99 (s, 9 H, CH₃), 0.98-0.88 (m, 3 H, CH₃), 0.09 (s, 3 H, CH₃), 0.08 (s, 3 H, CH₃); ¹³C NMR (75 MHz, CDCl₃): δ = 94.7, 93.1, 78.0, 57.6, 55.9, 31.6, 29.1, 28.8, 27.1 (3 C), 25.9, 22.8, 19.3, 17.3, -7.5, -8.0; MS (EI): *m/z* (%) = 73 (100), 89 (29), 115 (13), 149 (5), 253 (14), 298 (1); HRMS: *m/z* [M⁺] Calcd for C₁₇H₃₄O₂Si 298.2328. Found 298.2370.

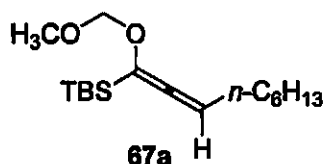


66b

tert-Butyl(3-cyclohexyl-1-(methoxymethoxy)prop-2-ynyl)dimethylsilane **66b**.

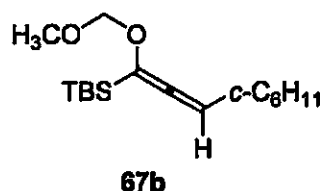
IR (film): 2940, 2760, 1690, 1460, 1250 cm⁻¹; ¹H NMR (300 MHz, CDCl₃): δ = 4.99 (d, 1 H, *J* = 6.3 Hz, OCH₂O), 4.49 (d, 1 H, *J* = 6.3 Hz, OCH₂O), 4.18 (d, 1 H, *J* = 2.1 Hz, CH), 3.34 (s, 3 H, OCH₃), 2.45-2.34 (m, 1 H, CH), 1.82-1.24 (m, 10 H, CH₂), 0.96 (s, 9

H, CH₃), 0.084 (s, 3 H, CH₃), 0.073 (s, 3 H, CH₃); ¹³C NMR (75 MHz, CDCl₃): δ = 94.6, 93.0, 77.9, 57.6, 55.9, 33.0, 29.6, 27.2 (3 C), 26.1 (2C), 25.1 (2 C), 17.3, -7.4, -8.0; MS (EI): *m/z* (%) = 73 (100), 75 (32), 83 (20), 115 (7), 251 (26); HRMS: *m/z* [M-CH₂OCH₃]⁺ Calcd for C₁₅H₂₇OSi 251.1831. Found 251.1842.



tert-Butyl(1-(methoxymethoxy)nona-1,2-dienyl)dimethylsilane **67a**.

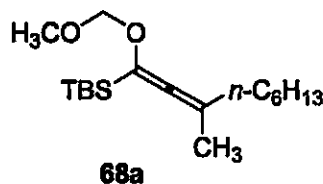
IR (film): 2990, 1910, 1250 cm⁻¹; ¹H NMR (300 MHz, CDCl₃): δ = 5.55 (t, 1 H, *J* = 6.6 Hz, C=C=CH), 4.83 (d, 1 H, *J* = 5.7 Hz, OCH₂O), 4.78 (d, 1 H, *J* = 5.7 Hz, OCH₂O), 3.39 (s, 3 H, OCH₃), 2.03 (m, 2 H, CH₂), 1.48-1.27 (m, 8 H, CH₂), 0.93 (s, 9 H, CH₃), 0.89 (m, 3 H, CH₃) 0.07 (s, 3 H, CH₃), 0.05 (s, 3H, CH₃); ¹³C NMR (75 MHz, CDCl₃): δ = 197.0, 126.0, 102.1, 94.9, 56.3, 31.9, 31.1, 29.2, 29.1, 27.1 (3 C), 22.8, 17.3, 14.3, -6.4, -6.3; MS (EI): *m/z* (%) = 73 (100), 83 (16), 243 (27), 298 (4); HRMS: *m/z* [M⁺] Calcd for C₁₇H₃₄O₂Si 298.2328. Found 298.2342.



tert-Butyl(3-cyclohexyl-1-(methoxymethoxy)propa-1,2-dienyl)dimethylsilane **67b**.

IR (film): 2980, 1930, 1460, 1250 cm⁻¹; ¹H NMR (300 MHz, CDCl₃): δ = 5.53 (d, 1 H, *J* = 5.7 Hz, C=C=CH), 4.81 (d, 1 H, *J* = 4.5 Hz, OCH₂O), 4.78 (d, 1 H, *J* = 4.5 Hz, OCH₂O), 3.38 (s, 3 H, OCH₃), 1.73 (m, 1 H, CH), 1.27-0.97 (m, 10 H, CH₂), 0.94 (s, 9 H, CH₃), 0.05 (s, 6 H, CH₃); ¹³C NMR (75 MHz, CDCl₃): δ = 195.6, 126.9, 107.7, 94.7,

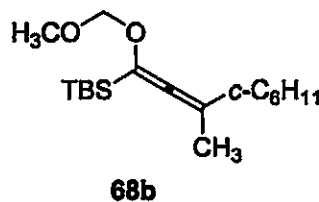
56.3, 39.2, 33.1, 32.9 (2 C), 26.9 (3 C), 26.4 (2 C), 17.4, -6.1, -6.3; MS (EI): m/z (%) = 73 (100), 89 (34), 113 (12), 145 (12), 169 (5), 251 (52); HRMS: m/z [M^+] Calcd for $C_{17}H_{32}O_2Si$ 296.2172. Found 296.2162.



tert-Butyl(1-(methoxymethoxy)-3-methylnona-1,2-dienyl)dimethylsilane **68a**.

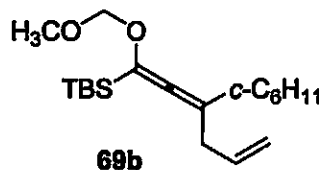
To a solution of methoxymethyl ether **66a** (2.5 g, 8.4 mmol) in THF (3 mL) was added *s*-BuLi (8.4 mL; 10.9 mmol; 1.3 M solution in hexane) at -78 °C. After stirring for 15 min, MeI (0.78 mL, 12.6 mmol) was added. The mixture was allowed to stir for an additional 15 min before dilution with aq NaHCO₃ and Et₂O. The aq phase was extracted Et₂O, the combined organic extracts were dried (MgSO₄), and the solvent was removed in vacuo. Column chromatography (silica gel; 0.625% EtOAc-hexane) gave **68a**.

IR (film): 2980, 1960, 1465 cm⁻¹; ¹H NMR (300 MHz, CDCl₃): δ = 4.77 (s, 2 H, OCH₂O), 3.37 (s, 3 H, OCH₃), 2.01-1.95 (m, 2 H, CH₂), 1.74 (s, 3 H, CH₃), 1.48-1.18 (m, 8 H, CH₂), 0.94 (s, 9 H, CH₃), 0.91-0.85 (m, 3 H, CH₃), 0.04 (s, 3 H, CH₃), 0.03 (s, 3 H, CH₃); ¹³C NMR (75 MHz, CDCl₃): δ = 193.8, 126.8, 110.9, 94.7, 56.1, 35.0, 32.0, 27.9, 27.1 (3 C), 26.8, 22.8, 21.2, 17.1, 14.3, -6.1, -6.4; MS (EI): m/z (%) = 218 (46), 230 (53), 243 (23), 268 (12), 312 (1); HRMS: m/z [M^+] Calcd for $C_{18}H_{36}O_2Si$ 312.2485. Found 312.2477.



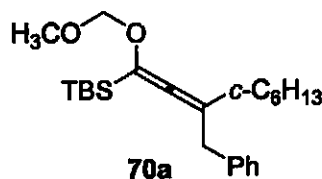
tert-Butyl(3-cyclohexyl-1-(methoxymethoxy)buta-1,2-dienyl)dimethylsilane **68b**.

IR (film): 2980, 1960, 1450, 1240 cm^{-1} ; ^1H NMR (300 MHz, CDCl_3): δ = 4.76 (s, 2 H, OCH_2O), 3.37 (s, 3 H, OCH_3), 1.78-1.62 (m, 1 H, CH), 1.74 (s, 3 H, CH_3), 1.30-1.02 (m, 10 H, CH_2), 0.94 (s, 9 H, CH_3), 0.04 (s, 3 H, CH_3), 0.03 (s, 3 H, CH_3); ^{13}C NMR (75 MHz, CDCl_3): δ = 193.2, 125.6, 115.6, 94.6, 56.1, 43.4, 32.3, 32.1, 31.8, 26.9 (3 C), 26.8, 26.6, 21.2, 17.2, -5.9, -6.3; MS (EI): m/z (%) = 73 (100), 89 (56), 191 (11), 265 (45), 310 (2); HRMS: m/z [M^+] Calcd for $\text{C}_{18}\text{H}_{34}\text{O}_2\text{Si}$ 310.2328. Found 310.2320.



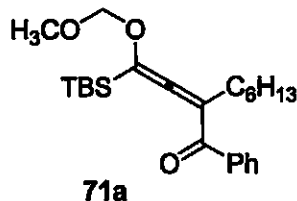
tert-Butyl(3-cyclohexyl-1-(methoxymethoxy)hexa-1,2,5-trienyl)dimethylsilane **69b**.

IR (film): 2980, 2850, 1750, 1640, 1250 cm^{-1} ; ^1H NMR (300 MHz, CDCl_3): δ = 5.80-5.66 (m, 1 H, $\text{HC}=\text{CH}_2$), 4.98-4.88 (m, 2 H, $\text{HC}=\text{CH}_2$), 4.69 (s, 2 H, OCH_2O), 3.34 (s, 3 H, OCH_3), 2.73-2.69 (m, 2 H, CH_2), 2.70-2.58 (m, 1 H, CH), 1.26-0.98 (m, 10 H, CH_2), 0.88 (s, 9 H, CH_3), -0.04 (s, 6 H, CH_3); ^{13}C NMR (75 MHz, CDCl_3): δ = 193.4, 136.7, 127.8, 118.7, 115.6, 94.5, 55.9, 42.0, 38.0, 32.6, 32.4, 27.1 (3 C), 26.8, 26.6, 22.9, 17.2, -5.9, -6.1; MS (EI): m/z (%) = 75 (88), 89 (8), 133 (24), 251 (64), 291 (5), 336 (4); HRMS: m/z [M^+] Calcd for $\text{C}_{20}\text{H}_{36}\text{O}_2\text{Si}$ 336.2485. Found 336.2468.



tert-Butyl(3-benzyl-1-(methoxymethoxy)nona-1,2-dienyl)dimethylsilane **70a**.

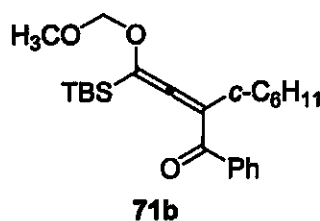
IR (film): 2980, 1930, 1420, 1250 cm^{-1} ; ^1H NMR (300 MHz, CDCl_3): δ = 7.09-6.99 (m, 5 H, Ar), 4.53 (d, 1 H, J = 5.4 Hz, OCH_2O), 4.51 (d, 1 H, J = 5.4 Hz, OCH_2O), 3.15 (s, 3 H, OCH_3), 1.82-1.76 (m, 2 H), 1.24-1.06 (m, 10 H, CH_2) 0.74 (s, 9 H, CH_3), 0.71-0.64 (m, 3 H, CH_3), -0.20 (s, 3 H, CH_3), -0.22 (s, 3 H, CH_3); ^{13}C NMR (75 MHz, CDCl_3): δ = 194.5, 139.9, 129.5, 128.3 (2 C), 126.9, 126.2 (2 C), 114.9, 94.7, 56.0, 41.9, 33.9, 32.0, 31.8, 29.5, 26.9 (3 C), 22.8, 17.2, 14.3, -6.2, -6.1; MS (EI): m/z (%) = 65 (13), 79 (33), 91 (100), 142 (100), 182 (18), 343 (2); HRMS: m/z $[\text{M}-\text{CH}_2\text{OCH}_3]^+$ Calcd for $\text{C}_{22}\text{H}_{35}\text{OSi}$ 343.2457. Found 343.2474.



2-(2-(*tert*-Butyldimethylsilyl)-2-(methoxymethoxy)vinylidene)-1-phenyloctan-1-one **71a**.

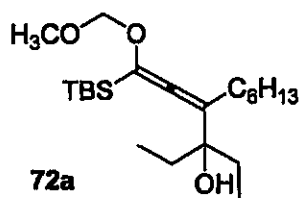
IR (film): 2920, 2880, 1900, 1650, 1470 cm^{-1} ; ^1H NMR (300 MHz, CDCl_3): δ = 7.78-7.59 (m, 5 H, Ar), 4.90 (d, 1 H, J = 6.0 Hz, CH_2), 4.88 (d, 1 H, J = 6.0 Hz, CH_2), 3.40 (s, 3 H, CH_3), 2.56-2.31 (m, 2 H, CH_2), 1.48-1.30 (m, 8 H, CH_2), 0.94-0.86 (m, 3 H, CH_3), 0.75 (s, 9 H, CH_3), -0.015 (s, 3 H, CH_3), -0.13 (s, 3 H, CH_3); ^{13}C NMR (75 MHz, CDCl_3): δ = 207.3, 195.5, 139.4, 131.5, 129.6, 128.9 (2 C), 127.8 (2 C), 116.2, 96.6, 56.3, 31.9, 29.9, 29.5, 28.4, 26.6 (3 C), 22.8, 17.4, 14.3, -6.3, -6.6; MS (EI): m/z (%) = 75 (23), 89

(27), 105 (38), 115 (16), 253 (18), 329 (12), 357 (29), 358 (11), 402 (9); HRMS: m/z $[M^+]$ Calcd for $C_{24}H_{38}O_3Si$ 402.2590. Found 402.2582.



4-(*tert*-Butyldimethylsilyl)-2-cyclohexyl-4-(methoxymethoxy)-1-phenylbuta-2,3-dien-1-one **71b**.

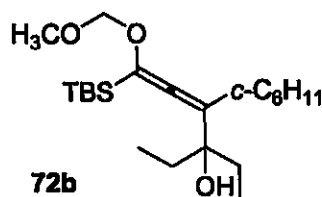
IR (film): 2910, 2850, 1900, 1650, cm^{-1} ; 1H NMR (300 MHz, $CDCl_3$): δ = 7.58-7.26 (m, 5 H, Ar), 4.89 (d, 1 H, J = 5.7 Hz, OCH_2O), 4.87 (d, 1 H, J = 5.7 Hz, OCH_2O), 3.38 (s, 3 H, OCH_3), 2.76 (m, 1 H, CH), 1.79-0.916 (m, 10 H, CH_2), 0.76 (s, 9 H, CH_3), 0.01 (s, 3 H, CH_3), -0.15 (s, 3 H, CH_3); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 206.3, 195.4, 139.7, 133.0, 131.2, 128.5 (2 C), 127.8 (2 C), 121.5, 96.4, 56.3, 42.3, 37.0, 33.4, 32.3, 26.7 (3 C), 26.5, 26.4, 17.5, -6.2, -6.4; MS (EI): m/z (%) = 73 (93), 109 (87), 115 (8), 256 (49), 355 (14), 400 (5); HRMS: m/z $[M^+]$ Calcd for $C_{24}H_{36}O_3Si$ 400.2434. Found 400.2432.



4-(2-(*tert*-Butyldimethylsilyl)-2-(methoxymethoxy)vinylidene)-3-ethyldecan-3-ol **72a**.

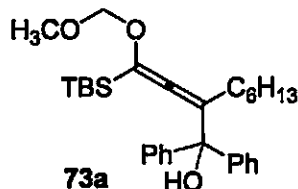
IR (film): 3510, 2980, 1920, 1470, 1360 cm^{-1} ; 1H NMR (300 MHz, $CDCl_3$): δ = 4.93 (d, 1 H, J = 6 H, OCH_2O), 4.69 (d, 1 H, J = 6.0 Hz, OCH_2O), 3.37 (s, 3 H, OCH_3), 2.72 (s, 1 H, OH), 1.93-1.80 (m, 2 H, CH_2), 1.65-1.27 (m, 12 H, CH_2), 0.97 (m, 9 H, CH_3), 0.92-0.85 (m, 9 H, CH_3), 0.08 (s, 6 H, CH_3); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 191.5, 131.9,

123.5, 93.3, 76.5, 55.9, 32.3, 32.0, 31.9, 29.7, 29.5, 28.5, 27.0 (3 C), 22.8, 17.3, 14.3, 8.7, 7.9, -5.8, -5.9; MS (EI): m/z (%) = 73 (100), 89 (32), 115 (20), 179 (58), 253 (7) 366 (8); HRMS: m/z [M-H₂O]⁺ Calcd for C₂₂H₄₂O₂Si 366.2954. Found 366.2948.



6-(*tert*-Butyldimethylsilyl)-4-cyclohexyl-3-ethyl-6-(methoxymethoxy)hexa-4,5-dien-3-ol
72b.

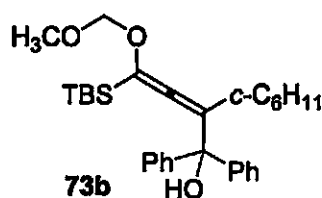
IR (film): 3500, 2980, 1910, 1470, 1360 cm⁻¹; ¹H NMR (300 MHz, CDCl₃): δ = 4.98 (d, 1 H, J = 6.0 Hz, OCH₂O), 4.66 (d, 1 H, J = 6.0 Hz, OCH₂O), 3.38 (s, 3 H, OCH₃), 2.64 (s, 1 H, OH), 1.78 (m, 1 H, CH), 1.84-1.42 (m, 14 H, CH₂), 0.99 (s, 9 H, CH₃), 0.96-0.85 (m, 6 H, CH₃), 0.09 (s, 6 H, CH₃); ¹³C NMR (75 MHz, CDCl₃): δ = 191.8, 132.2, 128.7, 93.1, 78.2, 55.9, 38.8, 34.8, 32.1, 31.8, 31.5, 27.2 (3 C), 26.3, 25.9, 22.5, 17.9, 8.9, 8.4, -5.8 (2 C); MS (EI): m/z (%) = 75 (100), 99 (56), 149 (23), 364 (20); HRMS: m/z [M-H₂O]⁺ Calcd for C₂₂H₄₀O₂Si 364.2798. Found 364.2775.



2-(2-(*tert*-Butyldimethylsilyl)-2-(methoxymethoxy)vinylidene)-1,1-diphenyloctan-1-ol
73a.

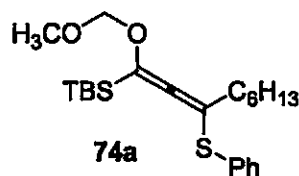
IR (film): 3490 (br), 2800, 1960, 1670, 1610, 1450 cm⁻¹; ¹H NMR (300 MHz, CDCl₃): δ = 7.45-7.23 (m, 10 H, Ar), 4.99 (d, 1 H, J = 6.0 Hz, OCH₂O), 4.76 (d, 1 H, J = 6.0 Hz,

OCH₂O), 3.89 (s, 1 H, OH), 3.38 (s, 3 H, OCH₃), 1.94-1.89 (m, 2 H, CH₂), 1.35-1.19 (m, 8 H, CH₂), 0.95 (s, 9 H, CH₃), 0.87-0.82 (m, 3 H, CH₃), 0.07 (s, 3 H, SiCH₃), 0.04 (s, 3 H, SiCH₃); ¹³C NMR (75 MHz, CDCl₃): δ = 193.0, 146.4, 145.1, 132.5, 130.3, 128.5, 128.2 (2 C), 127.9 (2 C), 127.3 (2 C), 127.2 (2 C), 123.2, 94.0, 81.2, 55.9, 31.9, 29.5, 28.8, 27.0 (3 C), 26.6, 22.8, 17.3, 14.3, -5.9, -6.1; MS (EI): *m/z* (%) = 77 (54), 84 (67), 105 (100), 362 (14), 418 (32), 480 (1); HRMS: *m/z* [*M*⁺] Calcd for C₃₀H₄₄O₂Si 480.3060. Found 480.3069.



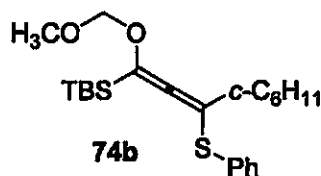
4-(*tert*-Butyldimethylsilyl)-2-cyclohexyl-4-(methoxymethoxy)-1,1-diphenylbuta-2,3-dien-1-ol **73b**.

IR (film): 3490, 2980, 1920, 1660, 1600, 1450 cm⁻¹; ¹H NMR (300 MHz, CDCl₃): δ = 7.83-7.23 (m, 10 H, Ar), 5.00 (d, 1 H, *J* = 6.0 Hz, OCH₂O), 4.72 (d, 1 H, *J* = 6.0 Hz OCH₂O), 3.82 (s, 1 H, OH), 3.35 (s, 3 H, OCH₃), 1.86-1.72 (m, 1 H, CH), 1.59-1.12 (m, 10 H, CH₂), 0.94 (s, 9 H, CH₃), 0.06 (s, 3 H, CH₃), 0.02 (s, 3 H, CH₃); ¹³C NMR (75 MHz, CDCl₃): δ = 192.9, 146.5, 137.8, 133.1, 132.7, 130.3, 128.5, 128.2, 127.8, 127.3 (2 C), 123.2 (2 C), 93.8 (2 C), 81.7 (2 C), 56.0, 40.3, 34.8 (2 C), 34.6 (2 C), 27.1 (3 C), 26.3, 17.3, -5.9, -6.1; MS (EI): *m/z* (%) = 75 (78), 89 (100), 105 (63), 119 (30), 145 (33), 175 (15), 182 (24), 209 (2), 478 (1); HRMS: *m/z* [*M*⁺] Calcd for C₃₀H₄₂O₃Si 478.2903. Found 478.2930.



tert-Butyl(1-(methoxymethoxy)-3-(phenylthio)nona-1,2-dienyl)dimethylsilane **74a**.

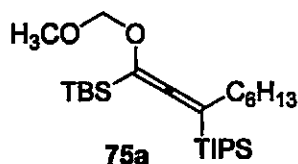
IR (film): 2940, 1910, 1580, 1140 cm^{-1} ; ^1H NMR (300 MHz, CDCl_3): δ = 7.52-7.22 (m, 5 H, Ar), 4.70 (d, J = 5.7 Hz, 1 H, OCH_2O), 4.62 (d, J = 5.7 Hz, 1 H, OCH_2O), 3.33 (s, 3 H, CH_3), 2.22 (m, 2 H, CH_2), 1.56-1.24 (m, 8 H, CH_2), 0.89 (s, 9 H, CH_3), 0.88 (m, 3 H, CH_3), -0.02 (s, 3H, CH_3), -0.04 (s, 3 H, CH_3); ^{13}C NMR (75 MHz, CDCl_3): δ = 192.0, 134.1, 132.1, 130.8, 128.9 (2 C), 127.7 (2 C), 112.9, 95.3, 56.4, 45.1, 35.2, 31.9, 29.1, 28.6, 26.9 (3 C), 20.7, 17.2, -6.3 (2 C); MS (EI): m/z (%) = 73 (100), 77 (28), 107 (34), 115 (8), 163 (12), 198 (4), 183 (11), 207 (58), 406 (3); HRMS: m/z [M^+] Calcd for $\text{C}_{23}\text{H}_{38}\text{O}_2\text{SSi}$ 406.2362. Found 406.2370.



tert-Butyl(3-cyclohexyl-1-(methoxymethoxy)-3-(phenylthio)propa-1,2-dienyl)dimethylsilane **74b**.

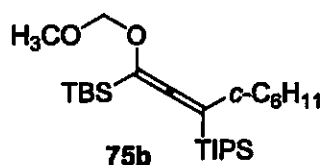
IR (film): 2920, 1910, 1580, 1470 cm^{-1} ; ^1H NMR (300 MHz, CDCl_3): δ = 7.51-7.22 (m, 5 H, Ar), 4.66 (d, 1 H, J = 5.4 Hz), 4.56 (d, 1 H, J = 5.4 Hz), 3.32 (s, 3 H, CH_3), 2.03-1.98 (m, 1 H, CH), 1.77-0.91 (m, 10 H, CH_2), 0.89 (s, 9 H, CH_3), -0.05 (s, 3 H, CH_3), -0.09 (s, 3 H, CH_3); ^{13}C NMR (75 MHz, CDCl_3): δ = 190.9, 134.3, 133.7, 132.0, 129.3, 128.9, 128.0 (2 C), 127.7 (2 C), 118.4, 95.1, 56.3, 43.5, 33.2, 26.9 (3 C), 26.7, 26.4, 17.2, -6.2, -

6.3; MS (EI): m/z (%) = 71 (28), 109 (85), 115 (21), 155 (12), 218 (100), 404 (1); HRMS: m/z [M^+] Calcd for $C_{23}H_{36}O_2SSi$ 404.2205. Found 404.2188.



1-(*tert*-Butyldimethylsilyl)-3-(triisopropylsilyl)-1-(methoxymethoxy)nona-1,2-diene **75a**.

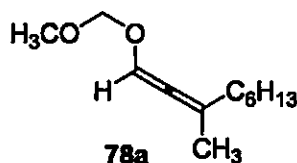
IR (film): 2920, 1695, 1470 cm^{-1} ; 1H NMR (300 MHz, $CDCl_3$): δ = 4.83 (d, 1 H, J = 5.4 Hz, OCH_2O), 4.74 (d, 1 H, J = 5.4 Hz, OCH_2O), 3.37 (s, 3 H, OCH_3), 2.08-1.87 (m, 3 H, CH), 1.62-1.39 (m, 2 H, CH_2), 1.36-1.11 (m, 8 H, CH_2), 1.19-1.11 (m, 18 H, CH_3), 0.98 (s, 9 H, CH_3), 0.89-0.99 (m, 3 H, CH_3), 0.07 (s, 3 H, CH_3), 0.03 (s, 3 H, CH_3); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 202.8, 124.7, 107.9, 94.7, 56.1, 32.3, 32.1, 29.7, 28.7, 27.2 (3 C), 22.8, 19.2, 17.6, 14.3 (3 C), 11.9 (6 C), -5.7, -6.0; MS (EI): m/z (%) = 73 (100), 87 (26), 115 (47), 145 (64), 157 (27), 307 (3), 454 (4); HRMS: m/z [M^+] Calcd for $C_{26}H_{54}O_2Si_2$ 454.3662. Found 454.3668.



(3-(*tert*-Butyldimethylsilyl)-1-(triisopropylsilyl)-3-(methoxymethoxy)propa-1,2-dienyl)cyclohexane **75b**.

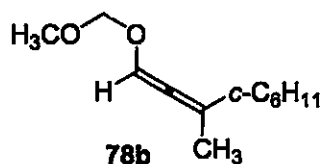
IR (film): 2920, 1695, 1470 cm^{-1} ; 1H NMR (300 MHz, $CDCl_3$): δ = 4.82 (d, 1 H, J = 5.4 Hz, OCH_2O), 4.76 (d, 1 H, J = 5.4 Hz, OCH_2O), 3.38 (s, 3 H, OCH_3), 1.86-1.61 (m, 4 H, CH), 1.24-1.10 (m, 10 H, CH_2), 1.10-1.08 (m, 18 H, CH_3), 0.985 (s, 9 H, CH_3), 0.074 (s, 3 H, CH_3), 0.043 (s, 3 H, CH_3); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 202.9, 135.2, 113.1,

94.8, 56.3, 40.9, 34.2, 27.3 (3 C), 26.7 (2 C), 26.4 (2 C), 19.3 (6 C), 17.6, 12.2 (3 C), -5.5, -6.0; MS (EI): m/z (%) = 73 (11), 77 (86), 98 (7), 117 (16), 208 (34), 407 (5), 452 (2); HRMS: m/z [M^+] Calcd for $C_{26}H_{52}O_2$ 452.3506. Found 452.3489.



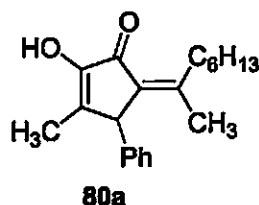
1-(Methoxymethoxy)-3-methynona-1,2-diene **78a**.

To a solution of allene ether **68a** (2.1 g, 6.7 mmol) in THF (10 mL) was added TBAF (2.1 g, 8.1 mmol) and LiOH (0.16 g, 6.7 mmol). After stirring at r.t. for 2 h, the reaction mixture was diluted with aq $NaHCO_3$ and Et_2O . The aq phase was extracted with Et_2O , the combined organic extracts were dried ($MgSO_4$), and the solvent was removed in vacuo. Column chromatography (silica gel; 0.625% $EtOAc$ -hexane) gave **78a**. Yield: 1.1 g (5.7 mmol; 82%); colorless oil. IR (film): 2940, 1920, 1470, 1390 cm^{-1} ; 1H NMR (300 MHz, $CDCl_3$): δ = 6.45 (m, 1 H, $HC=C=C$), 4.77 (s, 2 H, OCH_2O), 3.41 (s, 3 H, OCH_3), 2.02 (m, 2 H, CH_2), 1.79 (d, 3 H, J = 2.1 Hz, CH_3), 1.46-1.23 (m, 8 H, CH_2), 0.905-0.855 (m, 3 H, CH_3); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 189.0, 116.7, 116.0, 94.9, 56.1, 35.9, 32.0, 29.2, 27.6, 22.8, 21.6, 14.3; MS (EI): m/z (%) = 68 (16), 81 (14), 128 (100), 142 (12), 198 (1); HRMS: m/z [M^+] Calcd for $C_{12}H_{22}O_2$ 198.1620. Found 198.1615.



(4-(Methoxymethoxy)buta-2,3-dien-2-yl)cyclohexane **78b**.

IR (film): 2980, 1920, 1470, 1390 cm^{-1} ; ^1H NMR (300 MHz, CDCl_3): δ = 6.47 (m, 1 H, C=C=CH), 4.76 (s, 2 H, OCH_2O), 3.40 (s, 3 H, CH_3), 1.84 (m, 1 H, CH), 1.76-1.11 (m, 10 H, CH_2), 1.79 (d, 3 H, J = 1.8 Hz, CH_3); ^{13}C NMR (75 MHz, CDCl_3): δ = 188.5, 120.9, 117.3, 94.8, 56.1, 43.4, 31.9, 26.6 (2 C), 22.9 (2 C), 14.3; MS (EI): m/z (%) = 67 (14), 79 (10), 100 (18), 128 (14), 142 (100), 151 (11), 196 (3); HRMS: m/z [M^+] Calcd for $\text{C}_{12}\text{H}_{20}\text{O}_2$ 196.1463. Found 196.1466.

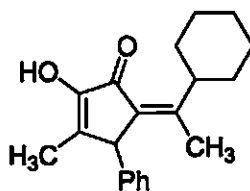


2-Hydroxy-3methyl-5-(octan-2-ylidene)-4-phenylcyclopent-2-enone 80a.

To a solution of allene **78a** (200 mg, 1.01 mmol) in THF (5 mL) was added BuLi (0.45 mL; 1.21 mmol; 2.7 M solution in hexane) at -78 °C. After stirring for 1 h, morpholino enamide **13** (280 mg, 1.21 mmol) in THF (3 mL) was added via cannula. After stirring for 2 h, the reaction was transferred by cannula in to a solution of FeCl_3 (204 mg, 2.00 mmol) in CH_2Cl_2 (10 mL). The reaction mixture was diluted with aq NaHCO_3 and Et_2O . The aq phase was extracted with Et_2O , the combined organic extracts were dried (MgSO_4), and the solvent was removed in vacuo. Column chromatography (silica gel; 5% EtOAc-hexane) gave **80a** as a ca. 1:2 mixture of *E* and *Z* isomers. Yield: 216 mg (0.73 mmol; 72%); yellow oil: *Z*-**80a** IR (film): 3250, 1690, 1640, 1400 cm^{-1} ; ^1H NMR (300 MHz, CDCl_3): δ = 7.31-7.06 (m, 5 H, Ar), 5.79 (s, 1 H, OH), 4.09 (s, 1 H, CH), 2.95-2.70 (m, 2 H, CH_2), 1.71 (d, 3 H, J = 1.2 Hz, CH_3), 1.58 (s, 3 H, CH_3), 1.43-1.25 (m, 8 H, CH_2), 0.91-0.85 (m, 3 H, CH_3); ^{13}C NMR (75 MHz, CDCl_3): δ = 190.2, 163.3,

152.9, 150.5, 139.8, 138.4, 131.7, 128.2 (2 C), 127.1 (2 C), 50.2, 37.3, 31.8, 29.5, 26.8, 22.7, 18.5, 14.3, 11.6; MS (EI): m/z (%) = 67 (15), 77 (15), 185 (45), 214 (6), 228 (19), 242 (37), 298 (72); HRMS: m/z [M^+] Calcd for $C_{20}H_{26}O_2$ 298.1933. Found 298.1952.

E-**80a**: IR (film): 3300, 1680, 1400 cm^{-1} ; 1H NMR (300 MHz, $CDCl_3$): δ = 7.29-7.08 (m, 5 H, Ar), 5.74 (s, 1 H, OH), 4.19 (s, 1 H, CH), 2.29 (s, 3 H, CH_3), 1.98-1.86 (m, 2 H, CH_2), 1.70 (d, 3 H, J = 0.9 Hz, CH_3), 1.28-0.927 (m, 8 H, CH_2), 0.838 (t, 3 H, J = 3.3 Hz, CH_3); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 190.3, 168.2, 150.4, 141.2, 136.6, 131.9, 128.5, 128.0 (2 C), 126.8 (2 C), 50.4, 33.8, 31.9, 29.4, 28.6, 22.8, 21.7, 14.3, 11.7; MS (EI): m/z (%) = 105 (65), 115 (29), 129 (26), 149 (21), 167 (13), 185 (54), 209 (14), 228 (100), 241 (28), 298 (69); HRMS: m/z [M^+] Calcd for $C_{20}H_{26}O_2$ 298.1933. Found 298.1948.

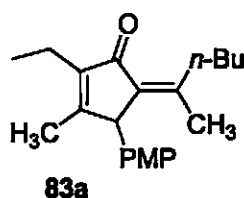


80b

5-(1-Cyclohexylethylidene)-2-hydroxy-3-methyl-4-phenylcyclopent-2-enone **80b**.

IR (film): 2990, 1680, 1650 cm^{-1} ; 1H NMR (300 MHz, $CDCl_3$): δ = 7.30-7.07 (m, 5 H, Ar), 5.72 (s, 1 H, OH), 4.16 (tt, 1 H, J = 11.7 Hz, 3.3 Hz, CH), 4.08 (s, 1 H, CH), 1.76-1.10 (m, 10 H, CH_2), 1.70 (d, 3 H, J = 1.2 Hz, CH_3), 1.52 (s, 3 H, CH_3); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 190.4, 158.6, 150.4, 141.4, 136.6, 131.2, 128.9, 128.1 (2 C), 126.9 (2 C), 68.2, 50.5, 39.7, 30.9 (2 C), 26.3 (2 C), 16.8, 11.7; MS (EI): m/z (%) = 67 (16), 91 (28), 105 (20), 186 (54), 214 (15), 296 (100); HRMS: m/z [M^+] Calcd for $C_{20}H_{24}O_2$ 296.1776. Found 296.1772. *Z*-**80b**: IR (film): 2990, 2880, 1690, 1620 cm^{-1} ; 1H NMR

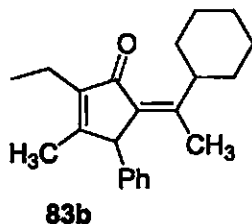
(300 MHz, CDCl₃): δ = 7.42-7.07 (m, 5 H, Ar), 5.80 (s, 1 H, OH), 4.18 (s, 1 H, CH), 2.29 (tt, 1 H, J = 12.0 Hz, 3.3 Hz, CH), 2.21 (s, 3 H, CH₃), 1.68 (d, 3 H, J = 3.3 Hz), 1.58-0.62 (m, 10 H, CH₂); ¹³C NMR (75 MHz, CDCl₃): δ = 191.4, 156.4, 150.5, 141.6, 136.3, 130.7, 128.5, 128.0 (2 C), 126.8 (2 C), 49.9, 44.3, 29.7, 28.6, 26.2, 25.8, 25.6, 13.8, 11.4; MS (EI): m/z (%) = 83 (12), 170 (8), 186 (33), 214 (21), 220 (8), 296 (92); HRMS: m/z [M^+] Calcd for C₂₀H₂₄O₂ 296.1776. Found 296.1770.



2-Ethyl-5-(hexan-2-ylidene)-3-methyl-4-phenylcyclopent-2-enone 83a.

To a solution of allene **78a** (200 mg; 1.01 mmol) in THF (5 mL) was added BuLi (0.45 mL, 1.21 mmol, 2.7 M solution in hexane) at -78 °C. After stirring for 1 h, enone **13** (0.103 g, 0.50 mmol) in THF (3 mL) was added via cannula. After stirring for 2 h, the reaction was diluted with aq NaHCO₃ and Et₂O. The aq phase was extracted with Et₂O, the combined organic extracts dried (MgSO₄), and the solvent was removed in vacuo. To a solution of crude tertiary alcohol **82a** in CH₂Cl₂ (10 mL) was added FeCl₃ (82 mg, 0.50 mmol) at r.t. After stirring at r.t. for 20 min, the reaction mixture was diluted with aq NaHCO₃ and Et₂O. The aq phase was extracted with Et₂O, the combined organic extracts were dried (MgSO₄), and the solvent was removed in vacuo. Column chromatography (silica gel; 5% EtOAc-hexane) gave **23** as a ca. 1:1 mixture of *E* and *Z* isomers. Yield: 118 mg (0.35 mmol; 69%); yellow oil.

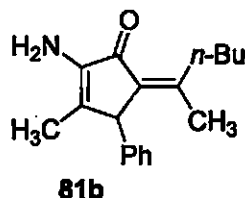
IR (film): 2990, 1695, 1630 cm^{-1} ; ^1H NMR (300 MHz, CDCl_3): δ = 6.99 (d, 4 H, J = 8.7 Hz, Ar), 6.81 (d, 4 H, J = 8.7 Hz, Ar), 4.10 (s, 1 H, CH), 4.06 (s, 1H, CH), 3.78 (s, 3 H, OCH_3), 3.77 (s, 3 H, OCH_3), 2.90 (m, 2 H, CH_2), 2.68 (m, 2 H, CH_2), 2.29 (m, 2 H, CH_2), 2.28 (s, 3 H, CH_3), 2.27 (s, 3 H, CH_3), 1.93 (m, 2 H, CH_2), 1.74 (s, 3 H, CH_3), 1.58 (s, 3 H, CH_3), 1.28-1.06 (m, 16 H, CH_2), 1.05 (m, 3 H, CH_3), 1.03 (m, 3 H, CH_3), 0.84 (m, 3 H, CH_3), 0.82 (m, 3 H, CH_3); ^{13}C NMR (75 MHz, CDCl_3): δ = 191.1, 190.5, 162.8, 162.7, 158.4, 158.3, 150.7, 149.5, 144.0, 143.8, 134.7, 134.1, 133.9, 133.7, 128.9 (4 C), 113.9 (4 C), 55.2 (2 C), 52.8, 52.6, 37.9, 33.6, 32.2, 31.9, 29.9, 29.8, 28.8, 27.2, 26.8 (2 C), 23.1, 22.9, 22.1, 18.2, 16.6 (2 C), 14.1, 14.0, 13.0 (2 C); MS (EI): m/z (%) = 69 (37), 91 (26), 101 (13), 115 (20), 135 (21), 147 (47), 175 (100), 204 (49), 270 (32), 340 (59); HRMS: m/z [M^+] Calcd for $\text{C}_{23}\text{H}_{32}\text{O}_2$ 340.2402. Found 340.2416.



(5Z)-5-(1-Cyclohexylethylidene)-2-ethyl-3-methyl-4-phenylcyclopent-2-enone **83b**.

IR (film): 2980, 1690, 1610 cm^{-1} ; ^1H NMR (300 MHz, CDCl_3): δ = 6.99 (d, 4 H, J = 8.7 Hz, Ar), 6.79 (d, 4 H, J = 8.7 Hz, Ar), 4.22 (m, 1 H, CH), 4.15 (s, 1 H, CH), 4.02 (s, 1 H, CH), 3.79 (s, 3 H, OCH_3), 3.77 (s, 3 H, OCH_3), 3.22 (m, 1 H, CH), 2.27 (m, 2 H, CH_2), 2.19 (s, 3 H, CH_3), 2.11 (m, 2 H, CH_2), 1.90 (s, 3 H, CH_3), 1.74 (s, 3 H, CH_3), 1.57 (s, 3 H, CH_3), 1.46-1.21 (m, 20 H, CH_2), 1.21 (m, 6 H, CH_3); ^{13}C NMR (75 MHz, CDCl_3): δ = 190.4, 190.1, 162.7, 162.5, 158.3, 158.2, 154.4, 153.2, 144.2, 144.1, 133.4, 133.3, 128.9,

128.7, 128.5 (4 C), 113.9 (4 C), 67.2, 55.3 (2 C), 52.7, 44.6, 41.7, 37.5, 33.4, 31.6, 31.4 (2 C), 27.2 (2 C), 26.9 (2 C), 25.4, 22.9, 22.8, 18.1, 15.3, 14.0 (2 C), 13.0 (2 C); MS (EI): m/z (%) = 67 (12), 77 (19), 83 (13), 143 (28), 175 (100), 213 (10), 205 (16), 255 (38), 338 (72); HRMS: m/z [M^+] Calcd for $C_{23}H_{30}O_2$ 338.2246. Found 338.2252.



2-Amino-3-methyl-5-(octan-2-ylidene)-4-phenylcyclopent-2-enone **81b.**

To a solution of allene **78b** (200 mg, 1.01 mmol) in THF (5 mL) was added BuLi (0.45 mL; 1.21 mmol; 2.7 M solution in hexane) -78 °C. After stirring for 1 h, α -methylcinnamionitrile **15** (144 mg, 0.14 mmol) was added *via* cannula. The reaction mixture was warmed to -40 °C and stirred for 1 h. The mixture was then transferred by cannula into a solution of $FeCl_3$ (204 mg, 2.00 mmol) in Et_2O (10 mL). The reaction mixture was diluted with aq $NaHCO_3$ and Et_2O . The aq phase was extracted with Et_2O , the combined organic extracts dried ($MgSO_4$), and the solvent was removed in vacuo. Column chromatography (silica gel; 5% $EtOAc$ -hexane) gave *E*-**20a** and *Z*-**20a** (ca. 1:2). Yield: 195 mg (0.65 mmol; 68% combined yield); orange oils; IR (film): 3490, 3380, 1650, 1560 cm^{-1} ; 1H NMR (300 MHz, $CDCl_3$): δ = 7.28-7.01 (m, 5 H, Ar), 4.07 (s, 1 H, CH), 2.95-2.70 (m, 2 H, CH_2), 1.63 (d, 3 H, J = 1.2 Hz, CH_3), 1.56 (s, 3 H, CH_3), 1.50-1.27 (m, 8 H, CH_2), 0.867 (m, 3 H, CH_3); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 191.9, 150.3, 142.4, 142.3, 134.6, 132.8, 129.7, 128.4 (2 C), 126.5 (2 C), 51.2, 37.3, 31.6, 29.3, 26.6, 22.4, 14.7, 14.1, 12.3; MS (EI): m/z (%) = 185 (67), 241 (34), 255 (8), 297 (92).

HRMS: m/z [M^+] Calcd for $C_{20}H_{27}NO$ 297.2093. Found 297.2083.

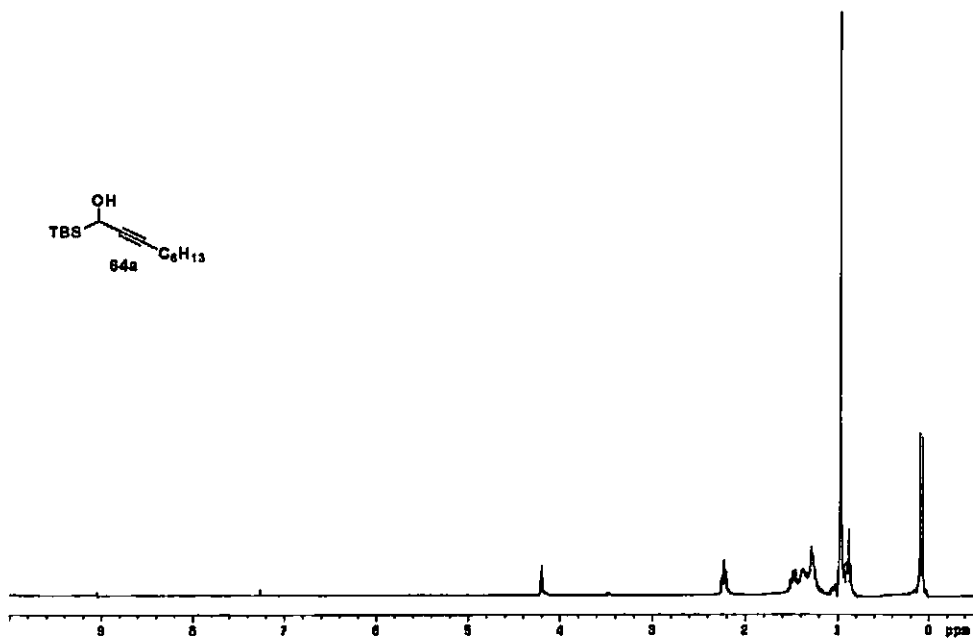
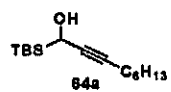
D. References Cited

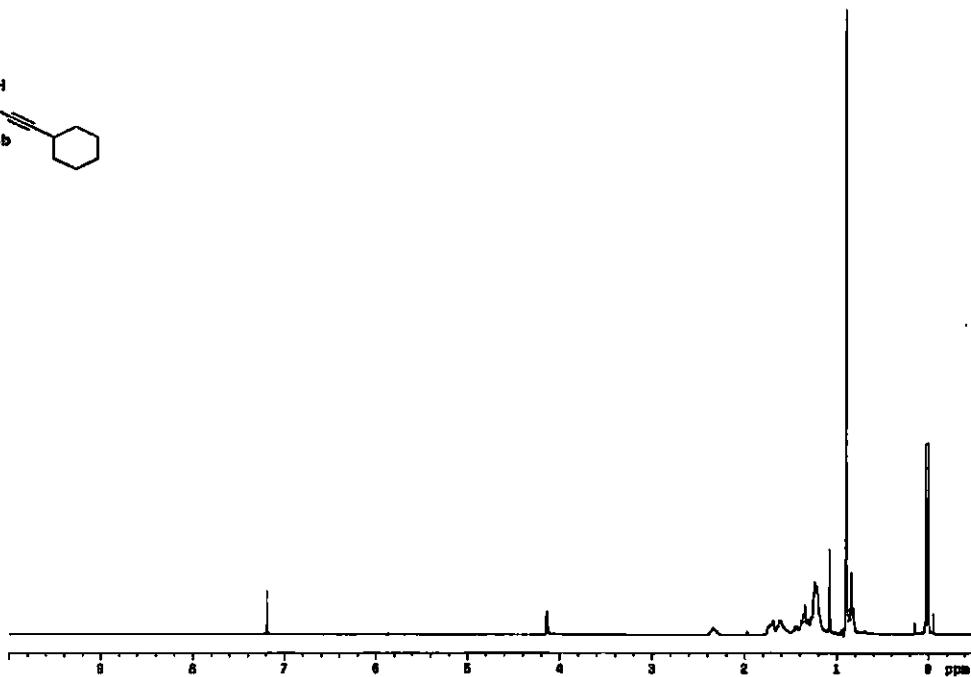
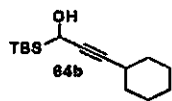
1. (a) For a review of the Nazarov reaction, see: Habermas, K. L.; Denmark, S. Jones, T. K. in *Organic Reactions*, Vol. 45, L. A. Paquette, Ed.; John Wiley & Sons, Inc., New York, 1994; pp 1-158. (b) Pellisier, H. *Tetrahedron* 2005, 61, 6479. (c) Jacobi, P. A.; Armacost, L. M.; Kravitz, J. I.; Martinelli, M. J.; Selnick, H. G. *Tetrahedron Lett.* 1988, 29, 6865. (d) Bender, J. A.; Arif, A. M.; West, F. G. *J. Am. Chem. Soc.* 1999, 121, 7443-

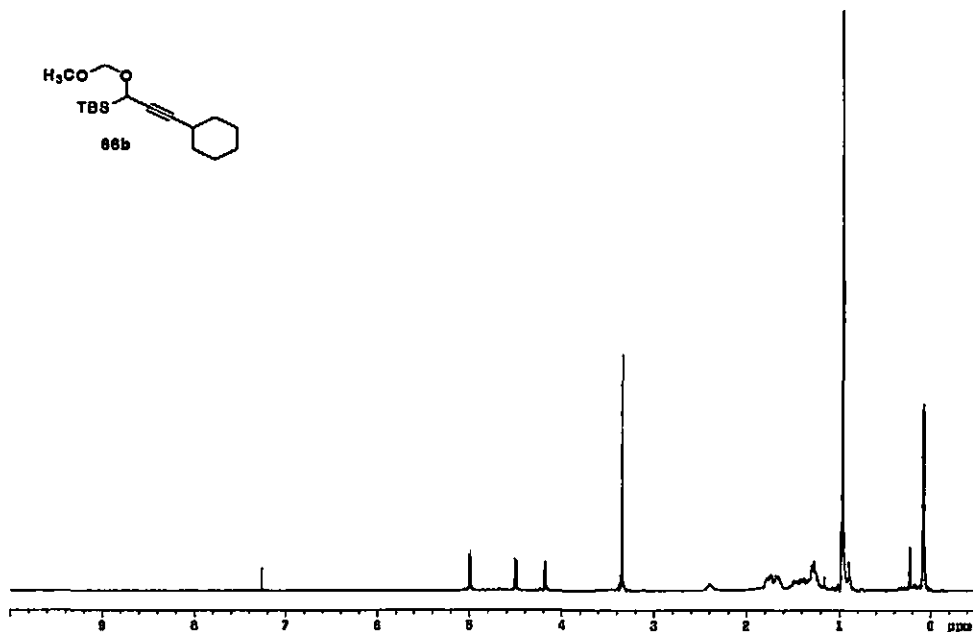
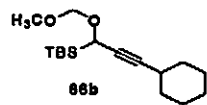
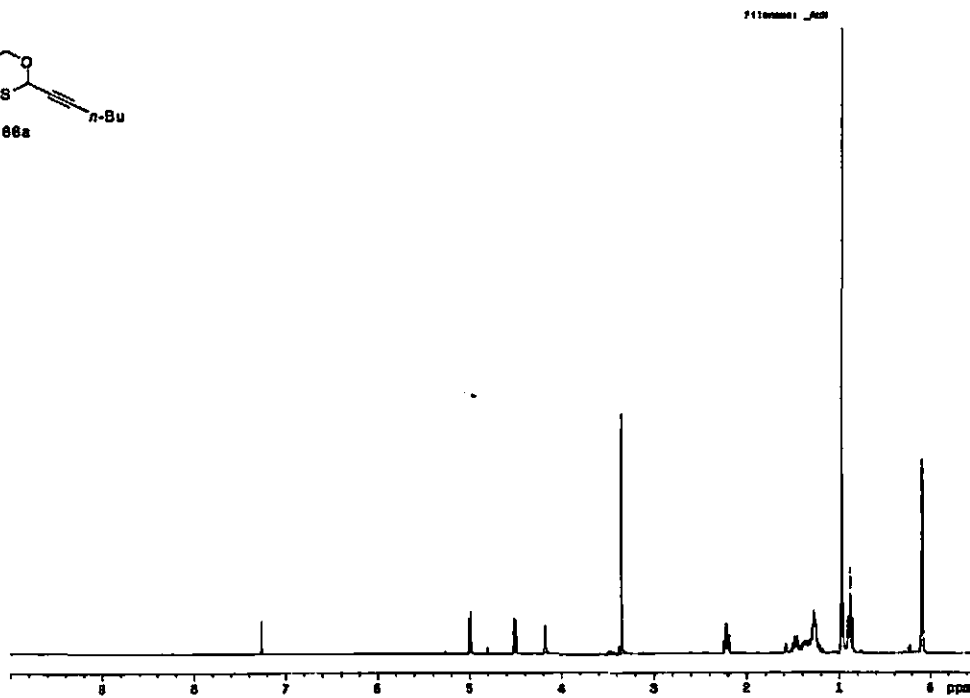
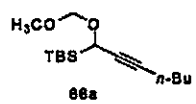
7444. (e) Hashmi, A. S. K.; Bats, J. W.; Choi, J.-H.; Sharz, L. *Tetrahedron Lett.* **1998**, *39*, 7491. (f) Schultz-Fademrecht.; Tius, M.A.; Grimme, S.; Wibbeling, B.; Hoppe, D. *Ang. Chem. Int. Ed.* **2002**, *41*, 1532.
2. For an overview of the group's work in this area: Tius, M. A. *Acc. Chem. Res.* **2003**, *36*, 284.
3. (a) Tius, M. A.; Patterson, G. M. L.; Astrab, D. P. *J. Antibiotics* **1985**, *38*, 1061. (b) Tius, M. A.; Astrab, D. P.; Fauq, A. H.; *J. Am. Chem. Soc.* **1986**, *108*, 3438.
4. Harrington, P. E.; Tius, M. A. *Org. Lett.* **2000**, *2*, 2447.
5. For a review of the Stetter reaction, see: Stetter, H.; Kulmann, H. In *Organic Reactions*; Paquette, L. A., Ed.; John Wiley & Sons: New York, 1991; Vol. 40, pp 407-496. See also: Stetter, H.; Haese, W. *Chem. Ber.* **1984**, *117*, 682.
6. Hu, H.; Tius, M. A. *Tetrahedron Lett.* **1998**, *39*, 5937.
7. Hoff, S.; Brandsma, L.; Arens, J. F. *Recl. Trav. Chim. Pays-Bas* **1968**, *87*, 916.
8. Tius, M. A.; Busch-Petersen, J.; Yamashita, M. *Tetrahedron Lett.* **1998**, *39*, 4219.
9. Bee, C.; Tius, M. A. *Org. Lett.* **2003**, *5*, 1681.
10. Hu, H.; Smith, D.; Cramer, R. E.; Tius, M. A. *J. Am. Chem. Soc.* **1999**, *121*, 9895.
11. Leroux, Y.; Roman, C. *Tetrahedron Lett.* **1973**, *28*, 2585.
12. Corey, E. J.; Terashima, S. *Tetrahedron Lett.* **1972**, *18*, 1815.
13. Sakaguchi, K.; Fujita, M.; Suzuki, H.; Higashino, M.; Ohfuné, Y. *Tetrahedron Lett.* **2000**, *41*, 6589.
14. Yadav, J. S.; Deshpande, P. K.; Sharma, G. V. M. *Tetrahedron* **1990**, *46*, 7033.

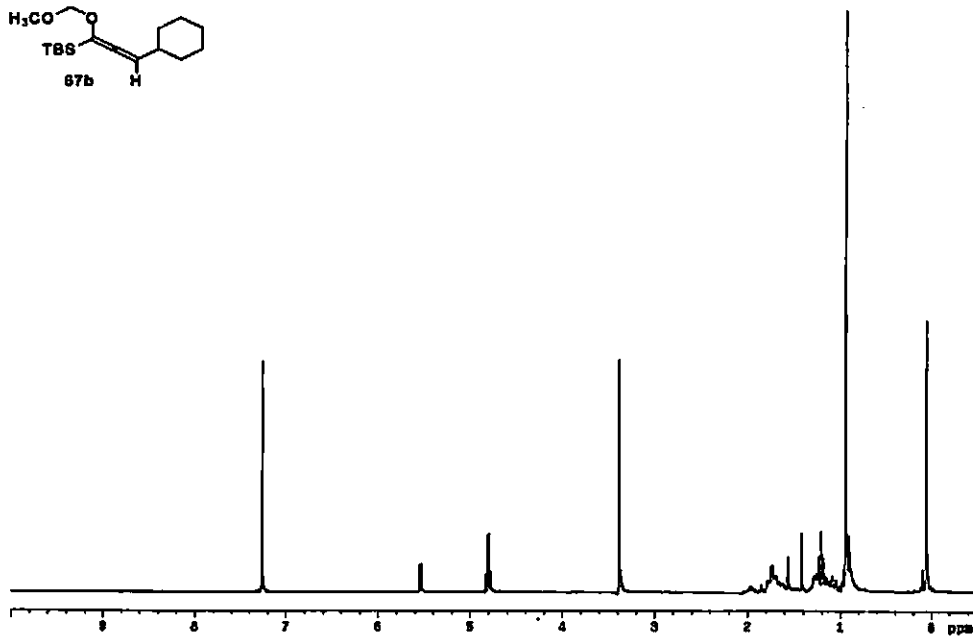
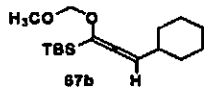
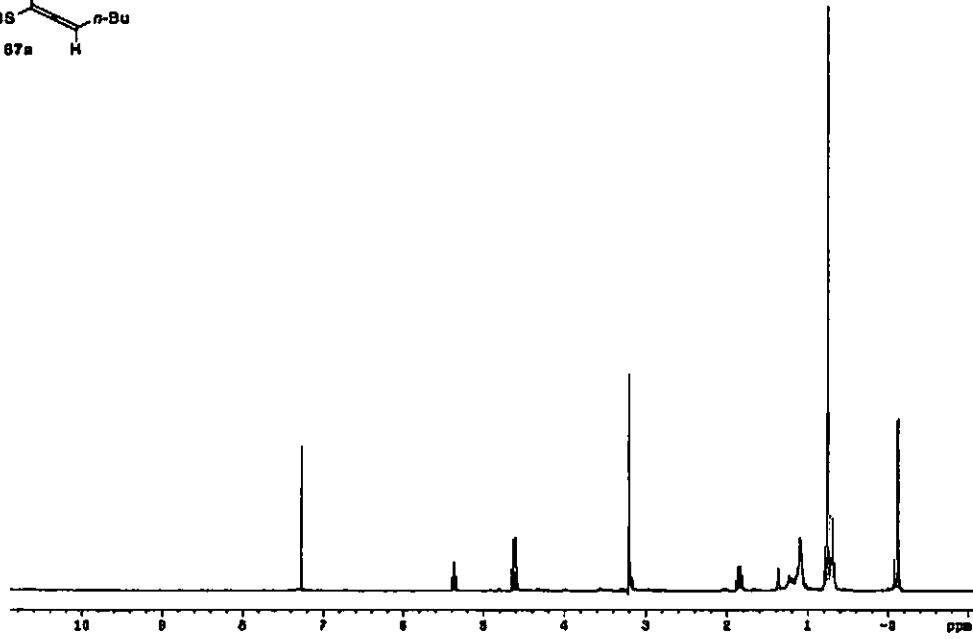
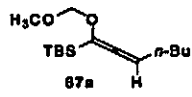
15. (a) Linderman, R. J.; Ghannam, A. *J. Am. Chem. Soc.* **1990**, *112*, 2398. (b) Hoffmann, R.; Brueckner, R. *Chem. Ber.* **1992**, *125*, 1471. (c) Jiang, X.-L.; Bailey, W. F. *Organometallics* **1995**, *14*, 5704-5707.
16. Tius, M. A.; Chu, C. C.; Nieves-Colberg, R. *Tetrahedron Lett.* **2001**, *42*, 2419.
17. For some approaches to the synthesis of allenes, see: (a) Silveira, C. C.; Boeck, P.; Braga, A. L. *Tetrahedron Lett.* **2000**, *41*, 1867. (b) Tius, M. A.; Pal, S. K. *Tetrahedron Lett.* **2001**, *42*, 2605. (c) Hamada, T.; Mizojiri, R.; Urabe, H.; Sato, F.; Prabharasuth, R.; Van Vranken, D. L. *J. Org. Chem.* **2001**, *66*, 5256. (d) Satoh, T.; Sakamoto, T.; Watanabe, M. *Tetrahedron Lett.* **2002**, *43*, 2043. (e) Inoue, H.; Tsubouchi, H.; Nagaoka, Y.; Tomioka, K. *Tetrahedron* **2002**, *58*, 83. (f) Bacci, J. P.; Greenman, K. L.; Van Vranken, D. L. *J. Org. Chem.* **2003**, *68*, 4955. (g) Fukuhara, K.; Okamoto, S.; Sato, F. *Org. Lett.* **2003**, *5*, 2145. (h) Huang, X.; Xiong, Z.-C. *Tetrahedron Lett.* **2003**, *44*, 5913. (i) Huang, X.; Xiong, Z.-C. *J. Chem. Soc., Chem. Commun.* **2003**, 1714.
18. For some approaches to the synthesis of axial chiral allenes, see: (a) Patai, S. *The Chemistry of Ketenes, Allenes, and Related Compounds*; Wiley: Chichester, **1980**. (b) Alexakis, A.; Mangeney, P.; Ghribi, A.; Marek, I.; Sedrani, R.; Guir, C.; Normant, J. F. *Pure Appl. Chem.* **1983**, *60*, 49. (c) Schuster, H. F.; Coppola, G. M. *Allenenes in Organic Synthesis*; Wiley: New York, **1984**. (d) Landor, S. R. *The Chemistry of the Allenenes*; Academic Press: New York, **1982**. (e) Konoike, T.; Araki, Y. *Tetrahedron Lett.* **1992**, *33*, 5093. (f) Hoffman-Röder, A.; Krause, N. *Angew. Chem. Int. Ed.* **2002**, *41*, 2933; *Angew. Chem.* **2002**, *114*, 3057. (g) Frederick, M. O.; Hsung, R. P.; Lambeth, R. H.; Mulder, J. A.; Tracey, M. R. *Org. Lett.* **2003**, *5*, 2663. (h) Ogasawara, M.; Ueyama, K.;

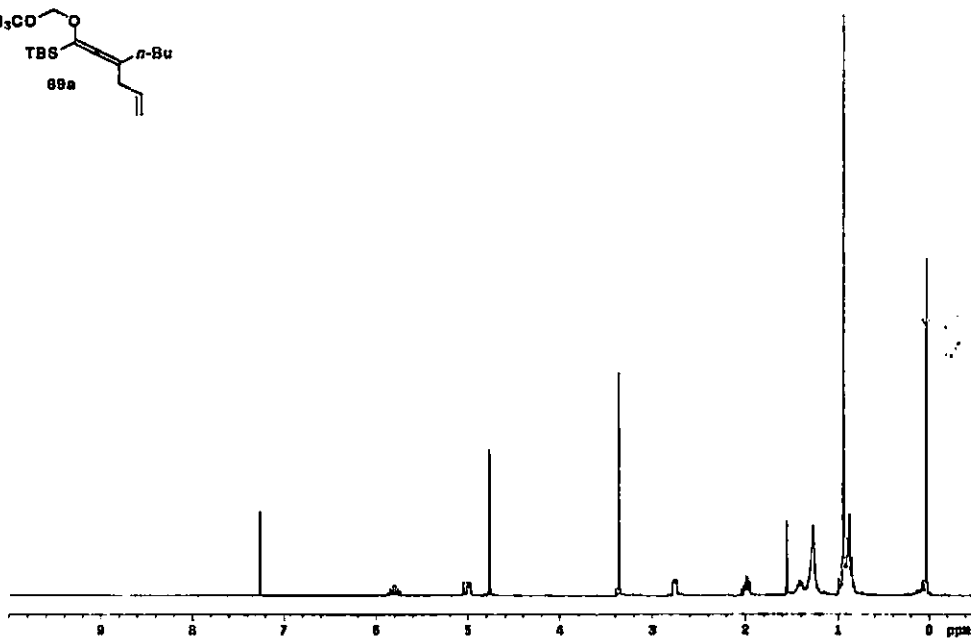
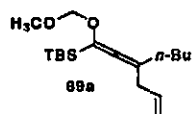
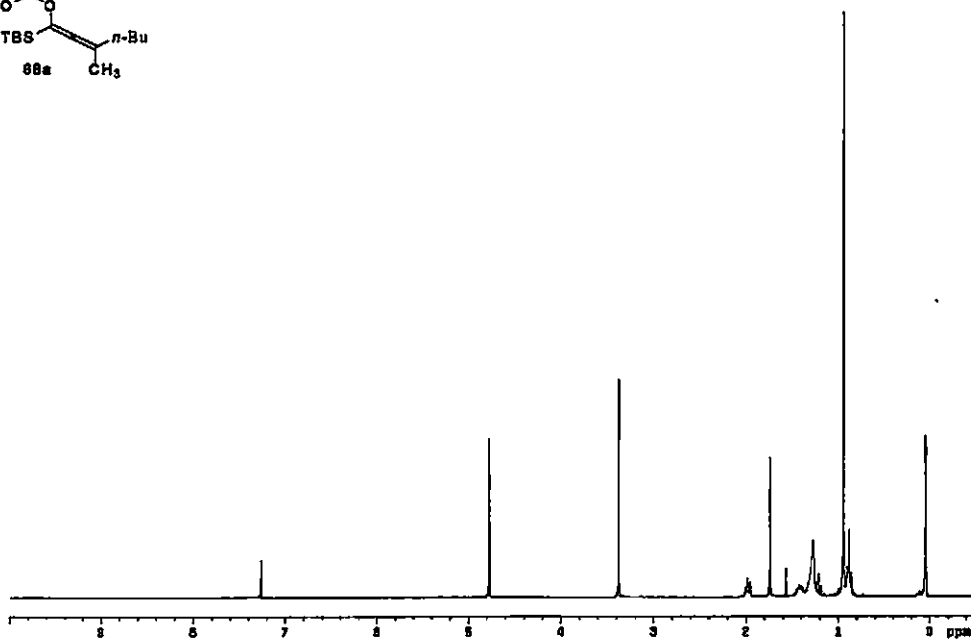
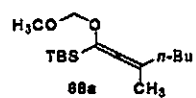
- Nagano, T.; Mizuhata, Y.; Hayashi, T. *Org. Lett.* **2003**, *5*, 217. (i) Sherry, B. D.; Toste, F. D. *J. Am. Chem. Soc.* **2004**, *126*, 15978.
19. (a) Arterburn, J. B. *Tetrahedron* **2001**, *57*, 9765-9788. (b) Huang, S. L.; Omura, K.; Swern, D. *Synthesis* **1978**, 297.
20. (a) Midland, M. M.; McDowell, D. C.; Hatch, R. L. Tramontano, A. *J. Am. Chem. Soc.* **1980**, *102*, 867. (b) Ram Reddy, M. V.; Rearick, J. P.; Hoch, N.; Ramachandran, P. V. *Org. Lett.* **2001**, *3*, 19.
21. (a) Hoppe, D.; Riemenschneider, C. *Angew. Chem., Int. Ed. Engl.* **1983**, *22*, 54. *Angew. Chem.* **1983**, *95*, 64. (b) Hoppe, D.; Gonschorrek, C.; Schmidt, D.; Egert, E. *Tetrahedron* **1987**, *43*, 2457.
22. (a) Dreller, S.; Dyrbusch, M.; Hoppe, D. *Synlett* **1991**, 397. (b) Schultz-Fademrecht, C.; Wibbeling, B.; Frölich, R.; Hoppe, D. *Org. Lett.* **2001**, *3*, 1221.

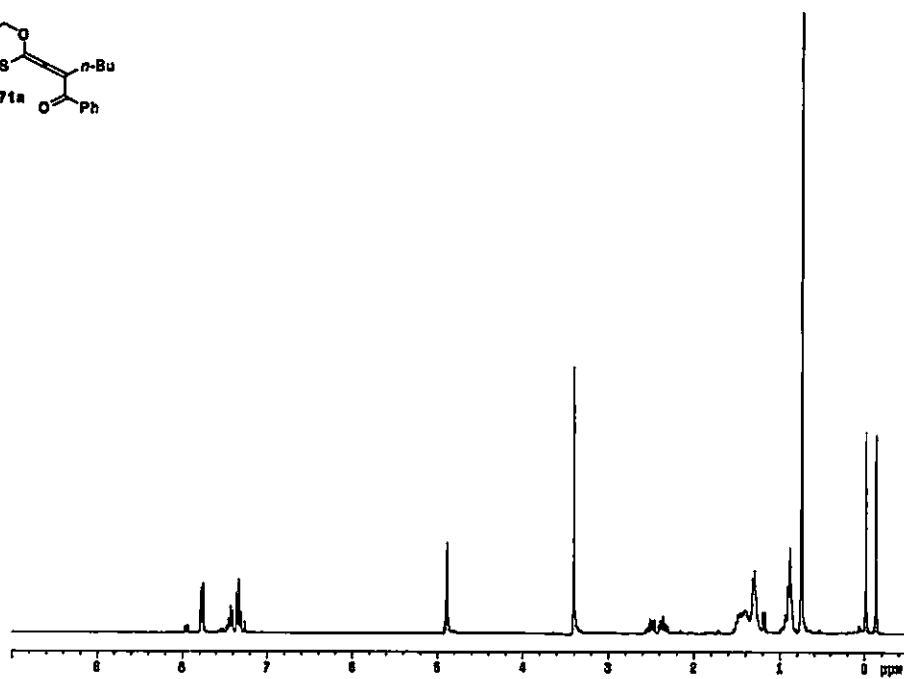
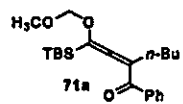
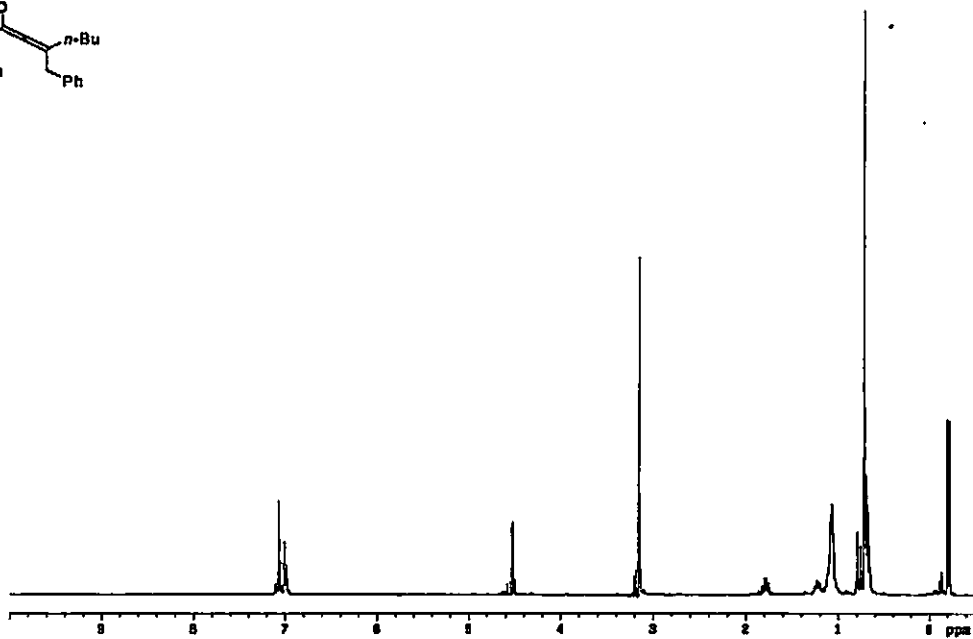
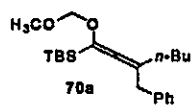


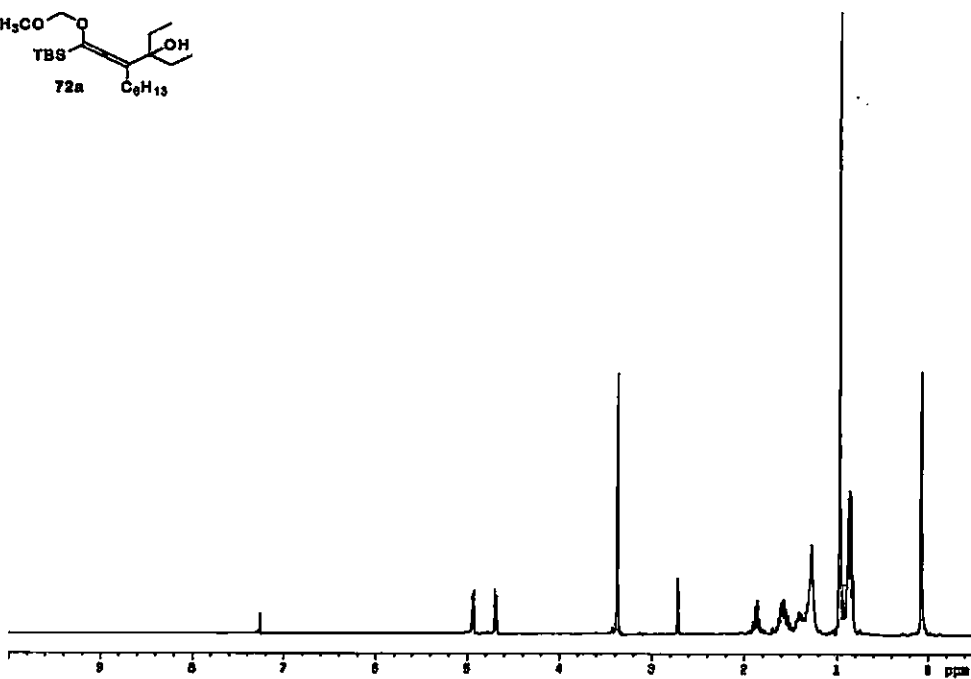
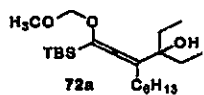
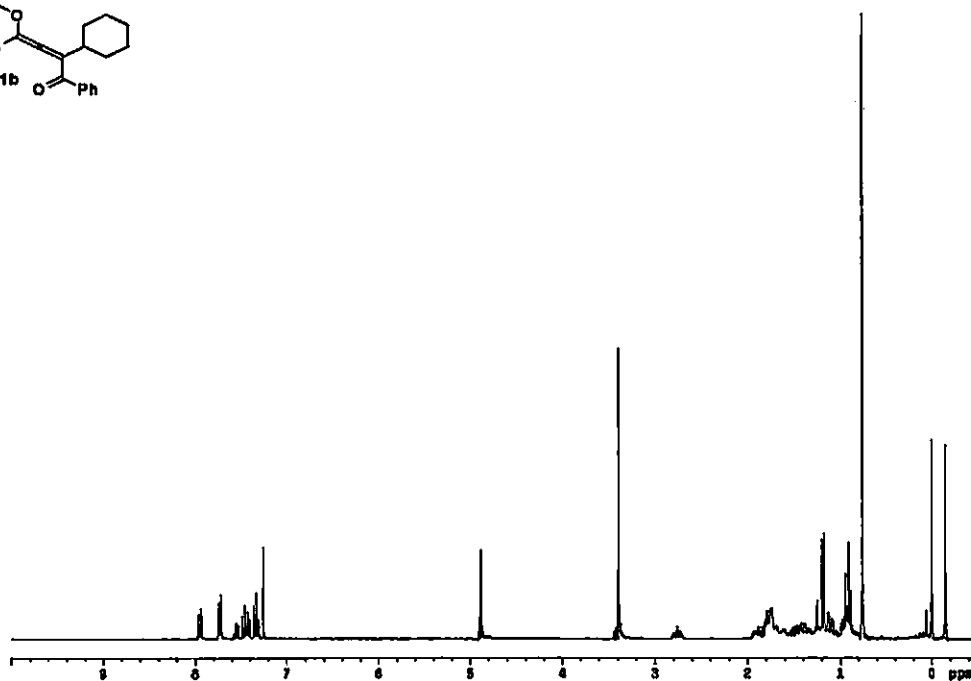
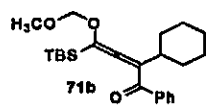


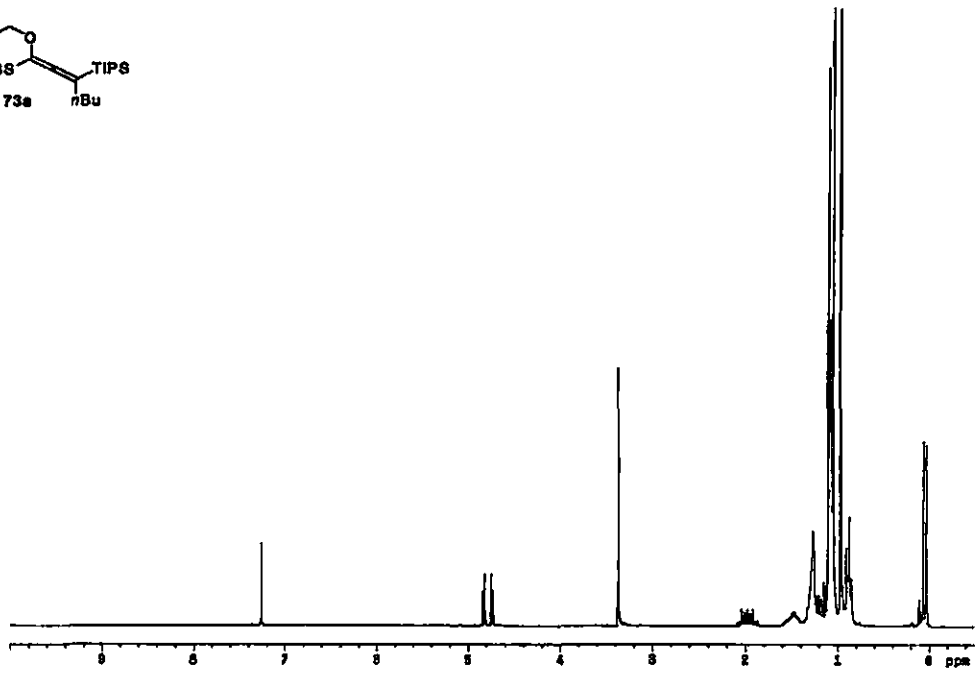
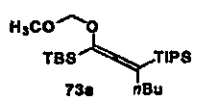
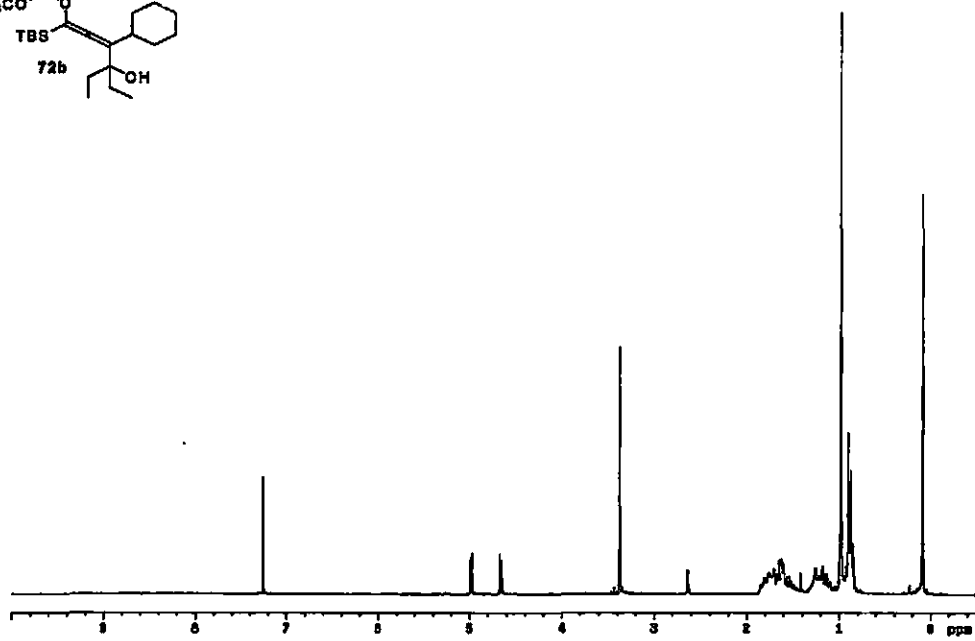
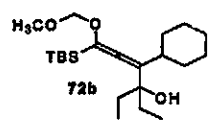


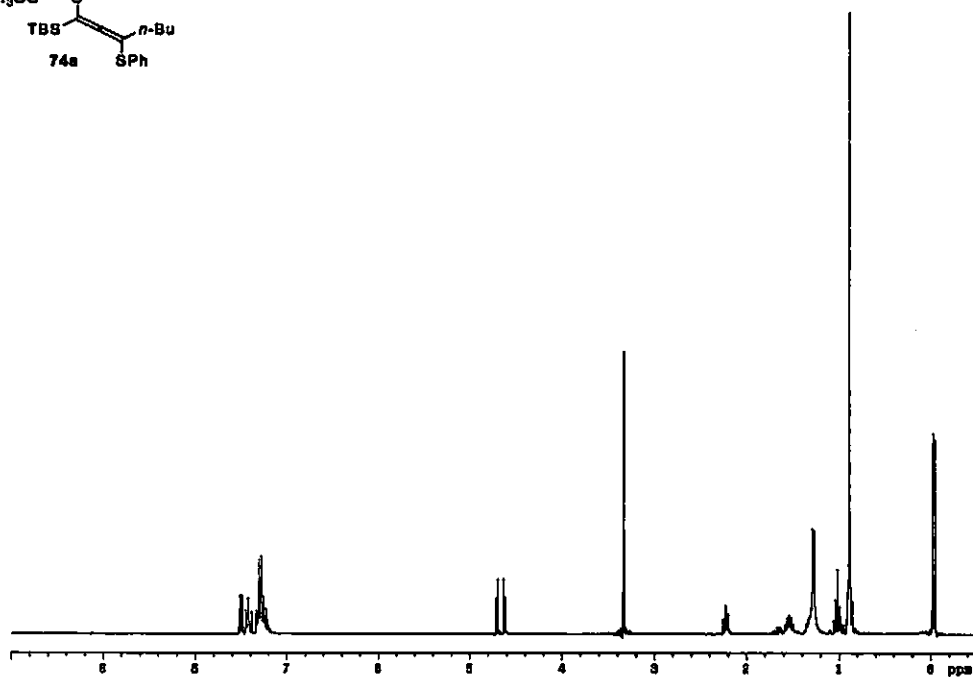
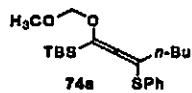
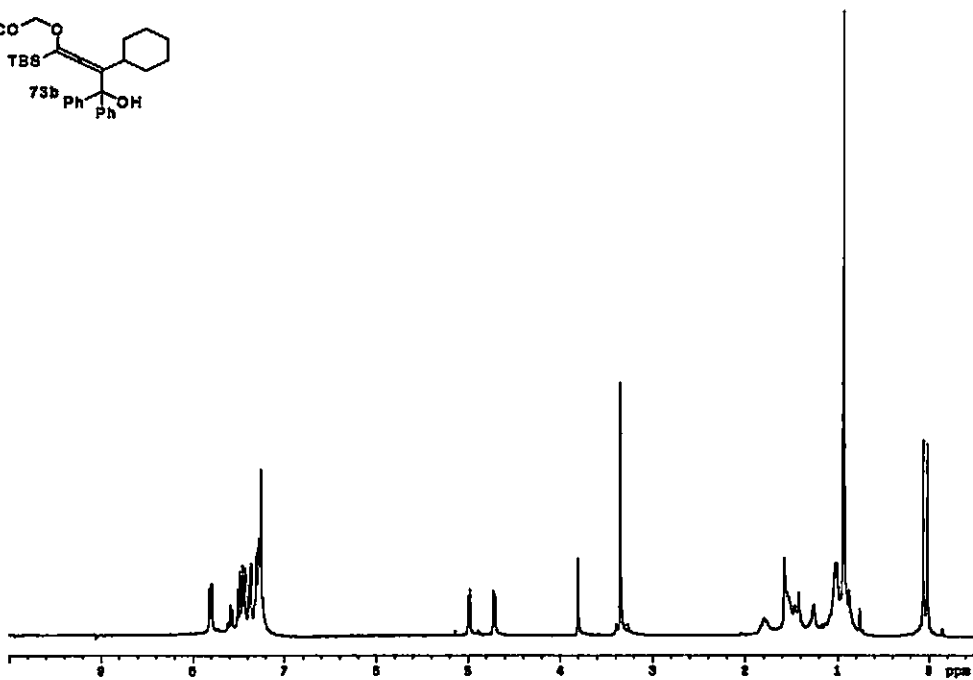
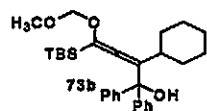


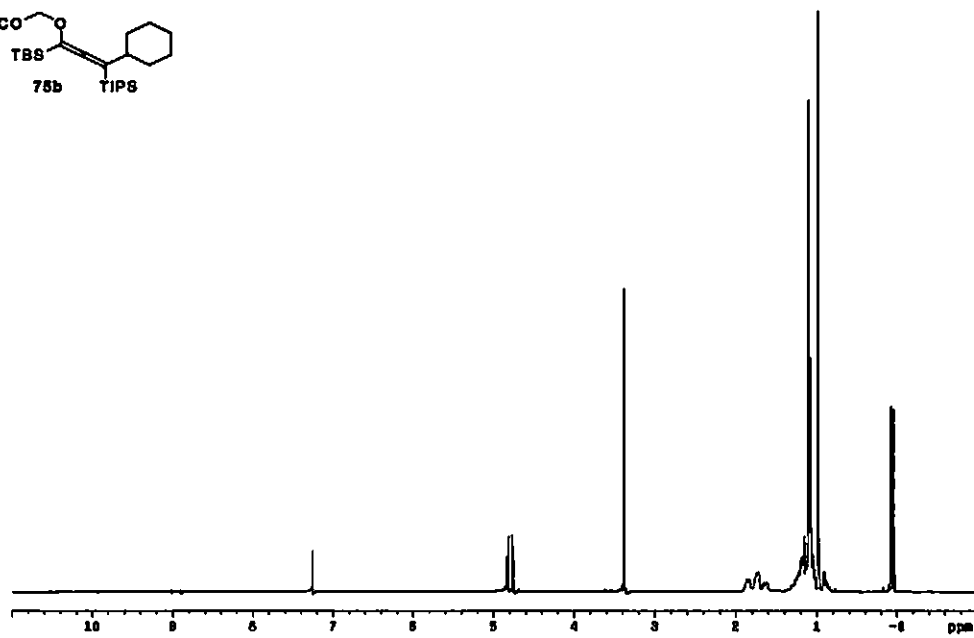
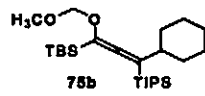
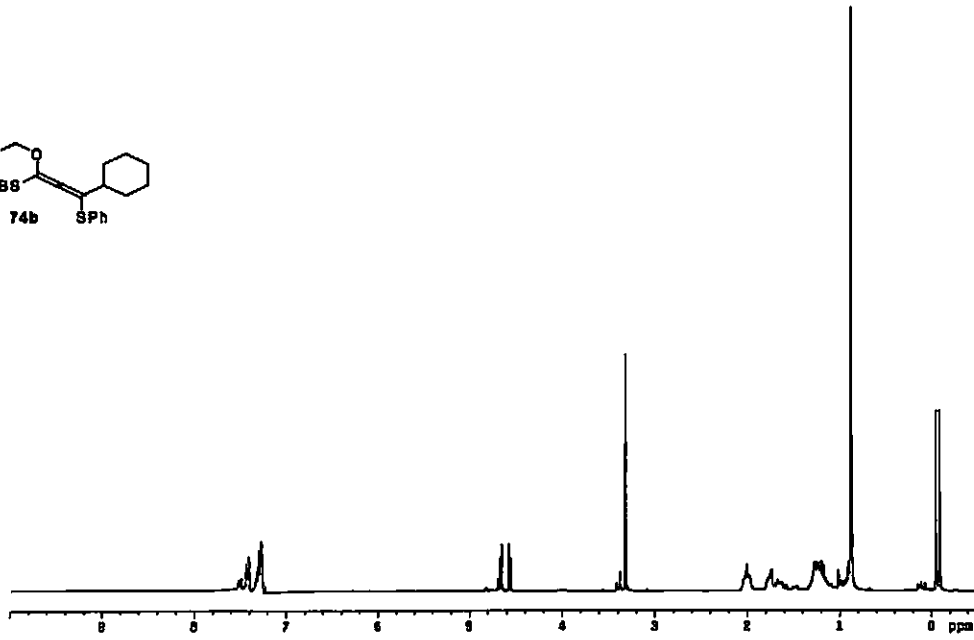
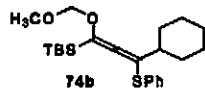


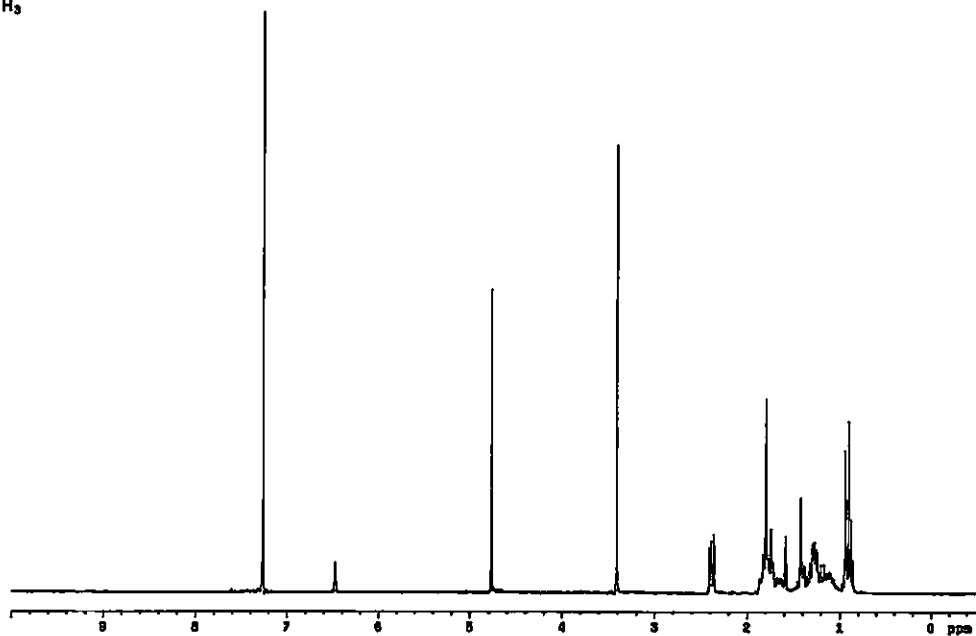
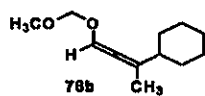
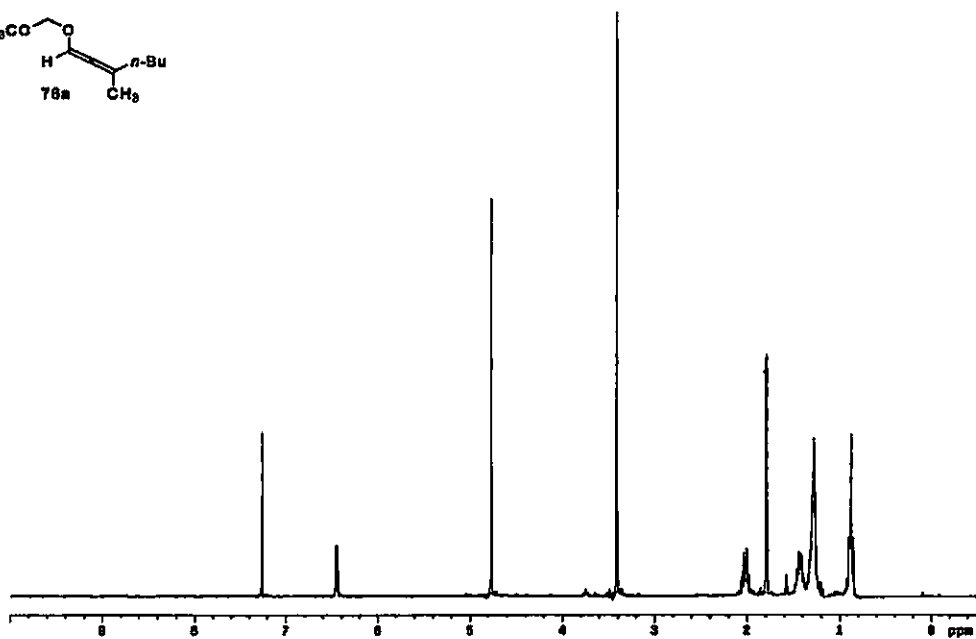
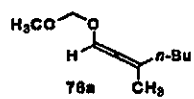


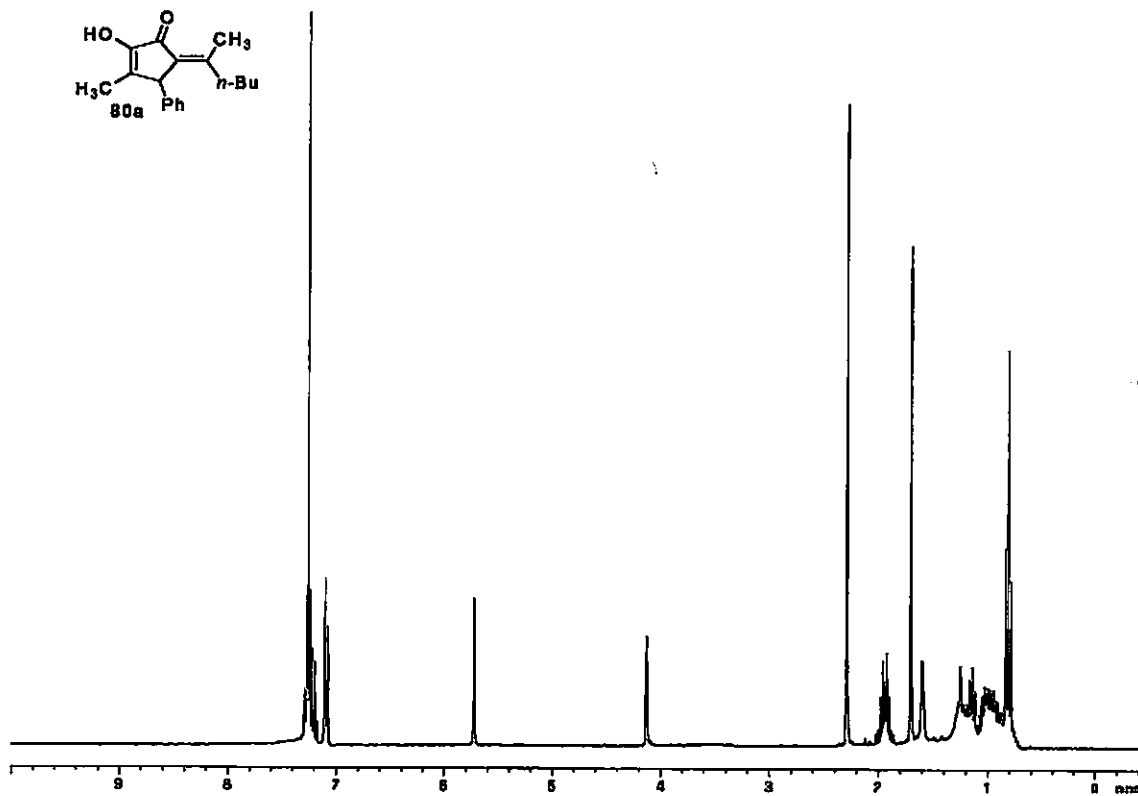
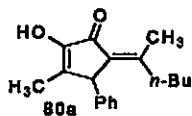
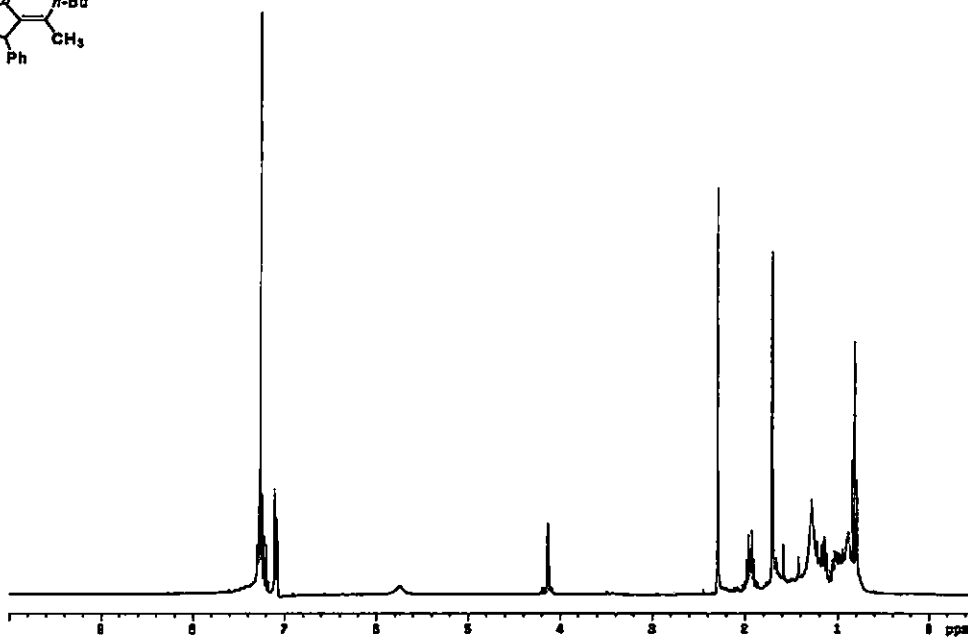
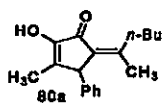


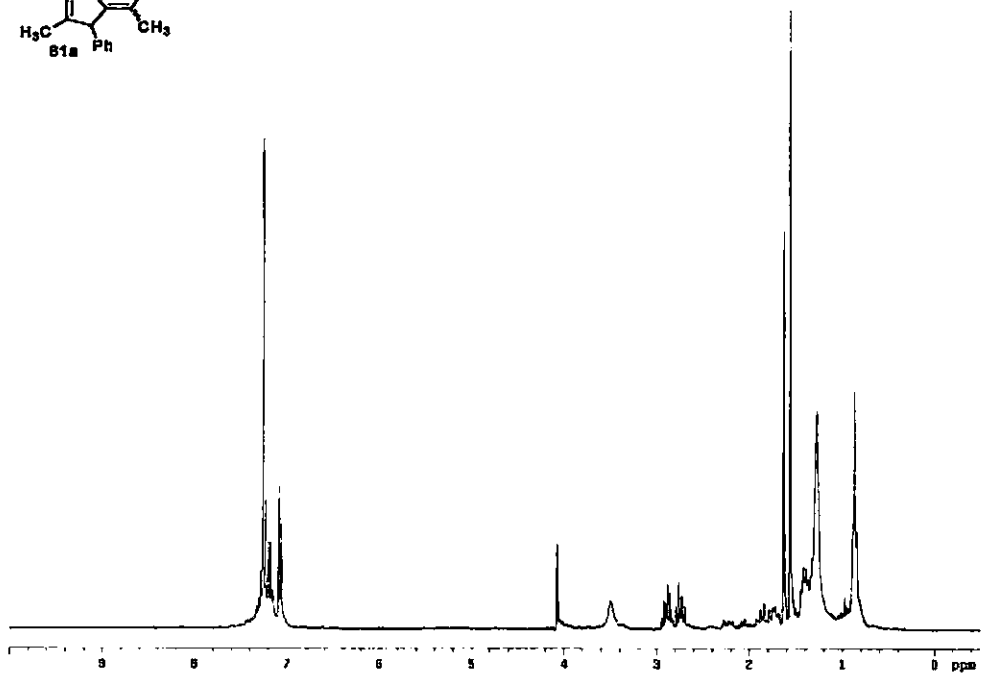
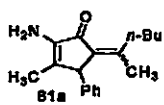
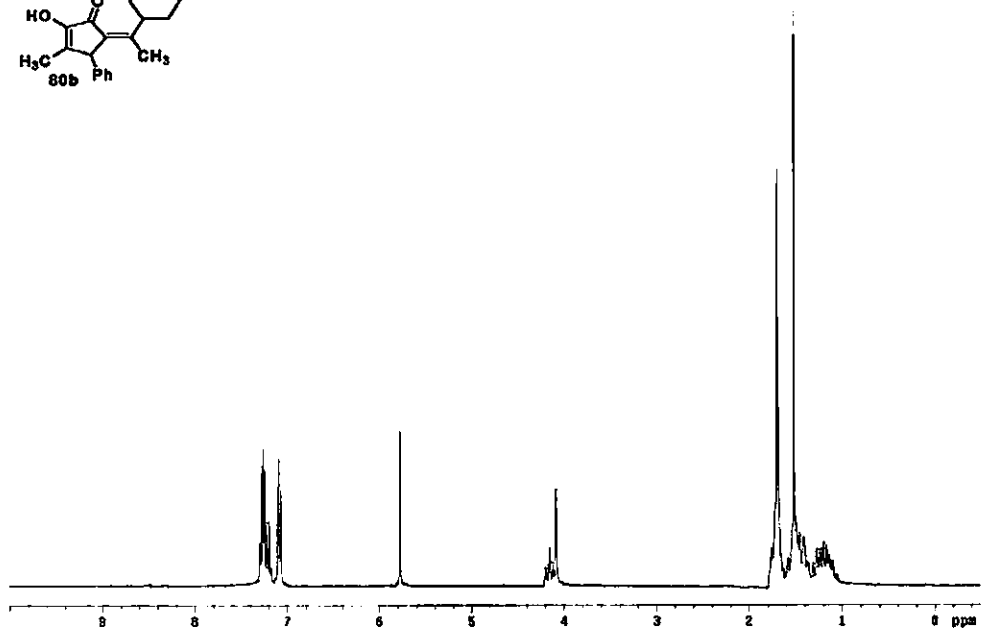
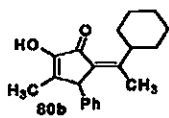


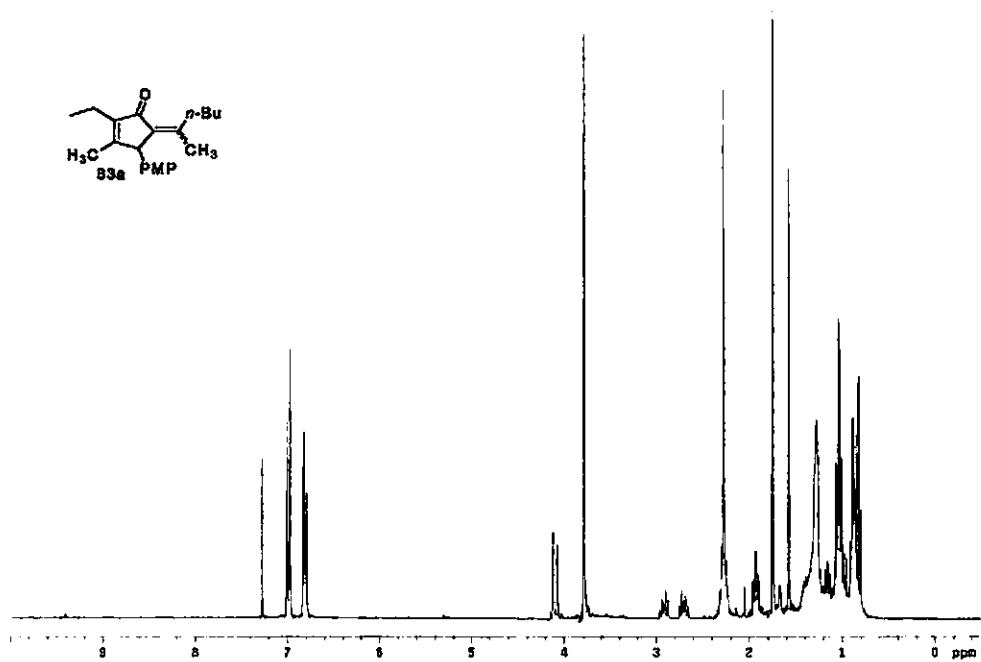
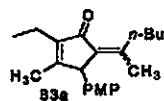
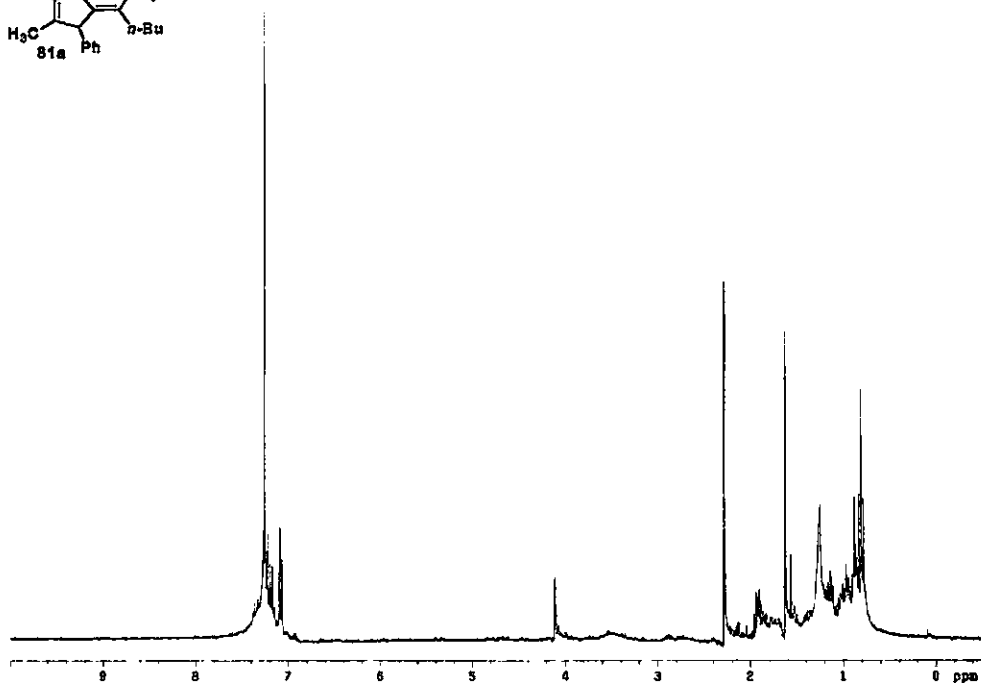
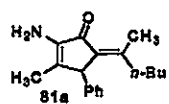












Part II: A Triply Convergent Nazarov Process

A. Introduction

Concurrent research in our group, carried out by Bee and co-workers¹ approached the problem of substituting the C6 exocyclic methylene of the Nazarov product,^{*} using a second strategy. While α -lithiation of allene ether **1** was easily accomplished with *n*-butyllithium, all attempts at a subsequent γ -deprotonation of lithio allene **2** to form α,γ -dilithioallene **3** met with unrestricted failure (Figure 1). Furthermore, while α,γ -dilithioallenes have been reported in the literature,² the dilithio-intermediate required a anion-stabilizing group such as TMS, SPh and Ph at both the α and the γ positions on the allene.

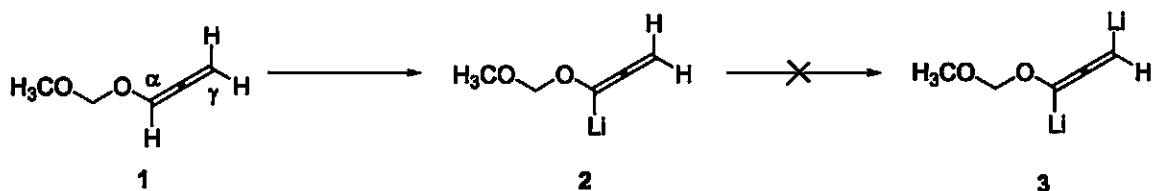


Figure 1. Dilithio Allene Ethers

A simple, elegant solution was proposed by Bee (Figure 2).¹ Addition of lithio allene **2** to morpholine enamide **4** produced putative intermediate **5**. Blocking the α -site of the allene in this way allowed a γ -deprotonation of intermediate **5**. Trapping dilithio intermediate **6** with methyl iodide followed by exposure to ethanolic HCl produced β -substituted cyclopentenone **8**. While the formation of dilithio allene **3** was not possible in our hands, *O,C*-dilithio intermediate **6** was readily accessible.

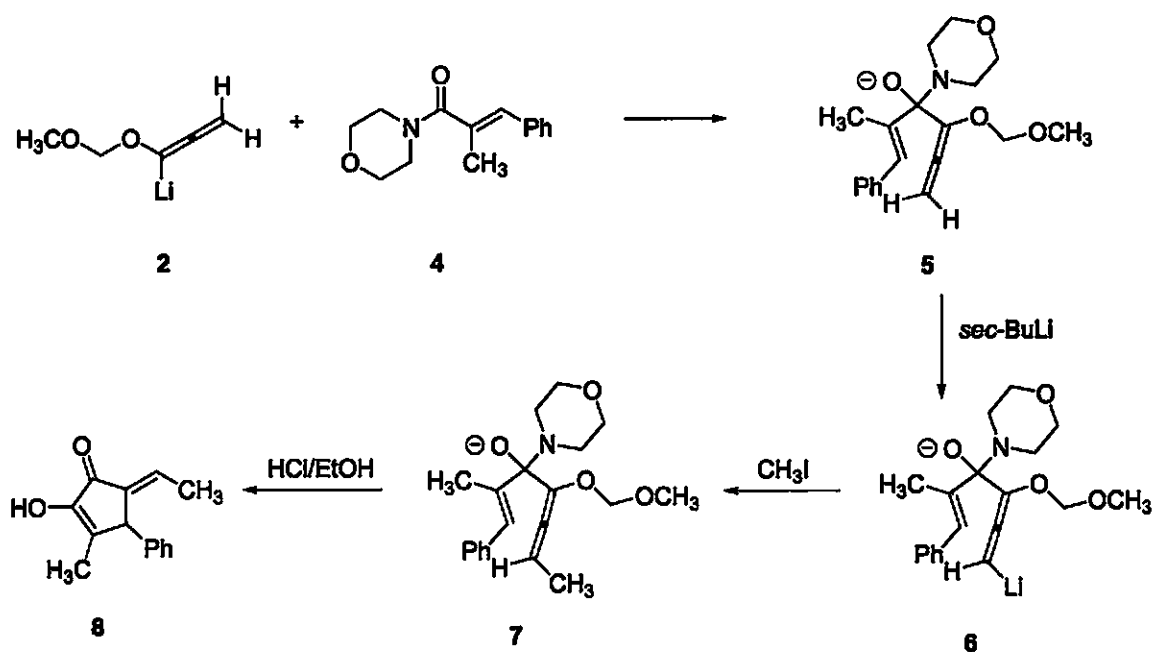


Figure 2. Mechanism of Triply Convergent Cyclopentannulation

This resulting method was considered triply convergent. Three elements, an α,β -unsaturated component 4, lithio allenyl ether 2 and an electrophile (CH_3I) are combined to yield β -substituted cyclopentenones. Varying the α,β -unsaturated component results in three broad categories of cyclopentenones (Figure 3). When ketones 9 are employed, α -alkyl cyclopentenones 12 are formed, while using morpholino enamides 4 results in α -hydroxy cyclopentenones 11. Finally, nitriles of type 10 produce α -amino cyclopentenones 13.³

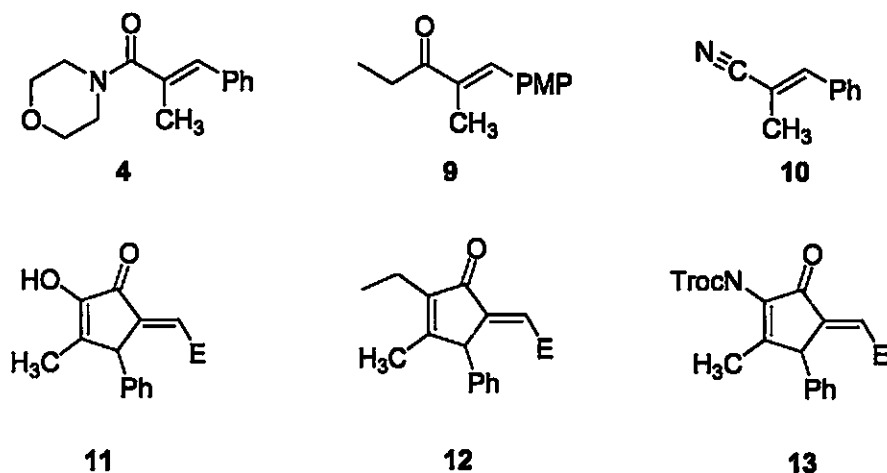
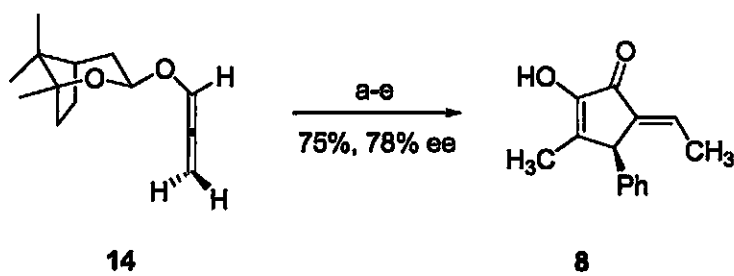


Figure 3. Electrophiles and Corresponding Nazarov Products

Bee also demonstrated that the method was compatible with camphor auxiliary **14**.¹ Utilizing the method developed by Harrington *et al.*,⁴ Bee developed a protocol for the generation of non-racemic cyclopentenones substituted at the exocyclic olefin. Camphor allene **14** was used to generate cyclopentenone (*R*)-**8** in 75% yield and in 78% *ee*.



Scheme 1.^a

^aReaction conditions: (a) 1.2 equiv *n*-BuLi, THF, -78 °C, 20 min; (b) 1.0 equiv **4**, -78 °C to -30 °C, 1 h; (c) 1.7 equiv *sec*-BuLi, -78 °C, 20 min; (d) 3.0 equiv MeI, -78 °C, 30 min, -40 °C, 30 min; (e) HCl/HFIP/TFE.

In order for the “triple convergent” method to be employed in total synthesis we decided to expand the scope of the reaction by using other morpholino enamides and electrophiles. We also hoped to determine the optimum conditions for the reaction. Our progress on our two goals is detailed herein.

2. Results and Discussion

In order to obtain the optimum conditions for the triple convergent cyclopentannulation process we decided to examine an expanded set of morpholino amides (see Figure 4). Alkyl halides, ketones and silyl halides were employed as electrophiles.

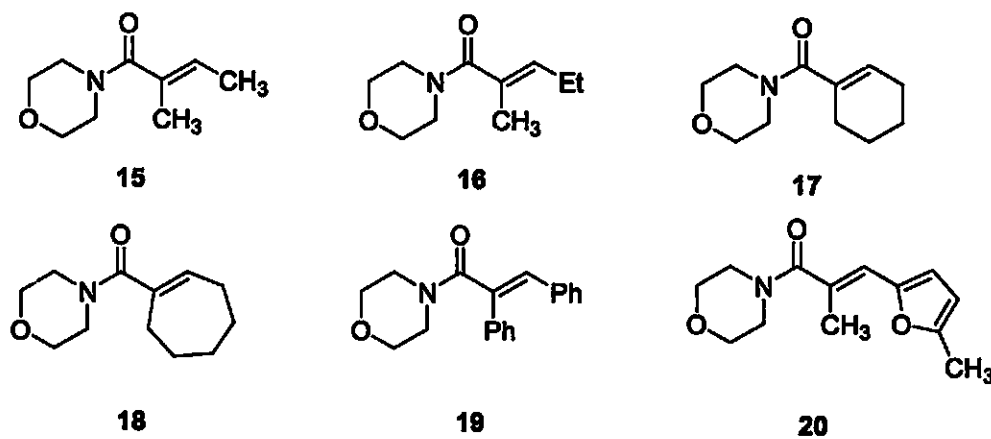


Figure 4. Expanded Set of Morpholino Amides

A number of small modifications were made to the existing procedure developed by Bee and co-workers in order to maximize the yield of the reaction. To ensure inclusive lithiation of tetrahedral intermediate **5**, care must be taken to preclude adventitious proton sources. Failure to do so results in the formation of a mixture of β -substituted cyclopentenone and unsubstituted cyclopentenone after cyclization. Logically, the presence of the undesired side-product results in a decrease of overall yields and complicates purification.

Several steps were taken to minimize adventitious proton sources. First, all amides were dried *via* azeotropic distillation with benzene. The distillation was repeated three times. The resulting amide was stored in THF over activated 4Å molecular sieves in an inert atmosphere for immediate use. As previously mentioned, the isomerization of 3-(methoxymethoxy)prop-1-yne to MOM allene required *t*-BuOK. As a result, trace amounts of *tert*-butyl alcohol were detected in the distilled product. Freshly prepared MOM allene, distilled over KH, limited the amount of *tert*-butyl alcohol introduced in to the reaction mixture. Finally, the reaction was not monitored by TLC to minimize the exposure to atmospheric moisture.

Additionally, the best results were obtained with fresh bottles of alkyllithium. Use of aged bottles of alkyllithium routinely resulted in diminished yields even if titrations were performed immediately prior to use. There are two possible explanations: a reduced titre results in the addition of a larger volume of hydrocarbon solvent, which could change the kinetics of the reaction allowing the formation of undesired side-products. Also, aged

bottles of alkyllithium could have contained appreciable amounts of peroxide. Introduction of peroxide into the reaction mixture may create oxidation products.

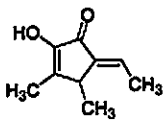
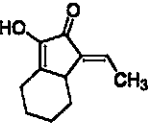
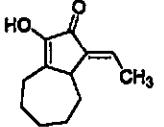
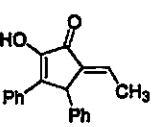
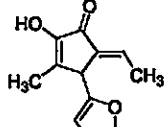

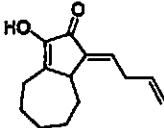
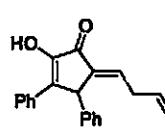
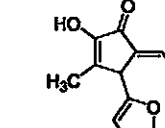
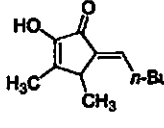
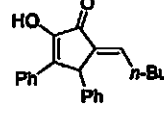
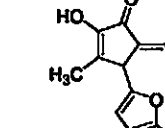

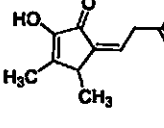
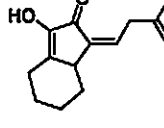
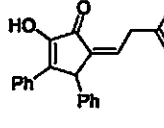
	amide	15	17	18	19	20
alkyl halide						
MeI		 21 70%	 22 62%	 23 63%	 24 64%	 25 70%
				 26 54%	 27 61%	 28 58%
<i>n</i> -BuI		 29 66%			 30 63%	 31 52%
		 32 56%	 33 51%		 34 93%	

Table 1.

Freshly distilled alkyl halide electrophiles were passed through a short column of basic alumina prior to addition. The reactions using allyl bromide, methyl iodide and *n*-butyl iodide as electrophiles required the addition of HMPA and LiI to increase reaction rates. The use of alkyl halide as electrophiles is summarized in Table 1. TBSCl was

sublimed immediately before use. A fresh bottle of TIPSCl was required for the success of the reaction. Using aged bottles of TIPSCl that were redistilled diminished the overall yield of the reaction. Results from silyl electrophiles are summarized in Table 2. All ketone electrophiles were distilled from CaH₂ and stored over activated 4Å molecular sieves prior to use. A summary of the results with ketone electrophiles is listed in Table 3.

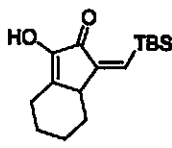
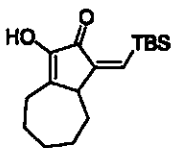
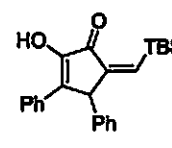
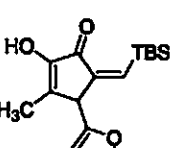
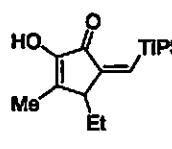
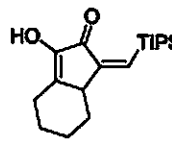
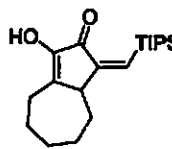
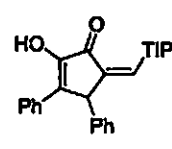
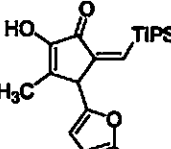
	amide 16	17	18	19	20
silyl halide					
TBSCl		 35 68%	 36 71%	 37 76%	 38 69%
TIPSCl	 39 68%	 40 50%	 41 65%	 42 79%	 43 75%

Table 2.

Proper conditions for the cyclization step were also critical to the success of the reaction. The reaction mixture was quickly transferred in to an equal volume of 5% HCl/EtOH at 0 °C. The solution was stirred for no more than 2 min. The reaction mixture was then neutralized with copious amounts of pH 7 phosphate buffer. If the reaction was stirred for longer than 2 min, diminished yields and unwanted side-products were observed. While some products were stable to prolonged contact with ethanolic HCl, all of the

compounds were cyclized after 2 min. Therefore, as a precaution, all cyclizations were performed within the 2 min time limit.


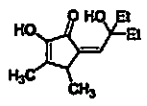
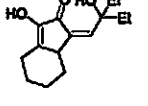
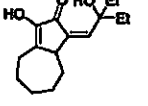
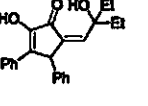
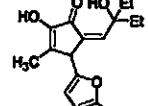

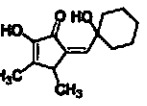
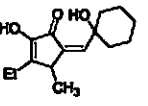
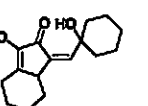
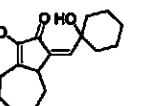
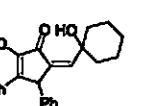
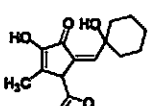
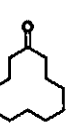
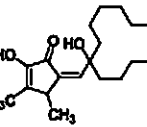
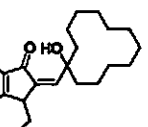
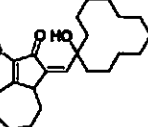
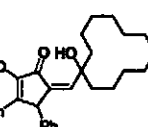
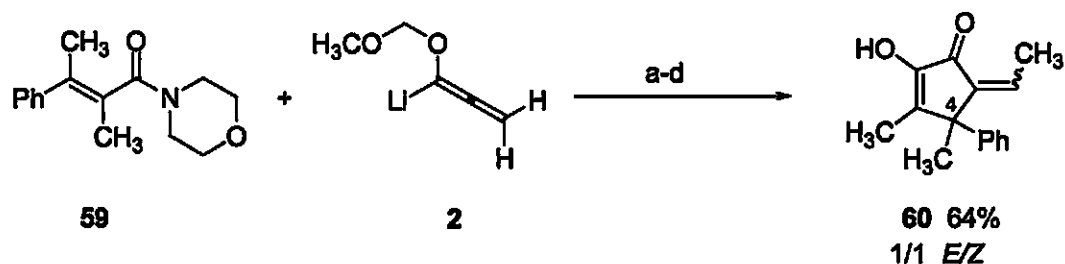
	amide 15	16	17	18	19	20
Ketones						
	 44 59%		 45 60%	 46 51%	 47 76%	 48 48%
	 49 58%	 50 64%	 51 60%	 52 48%	 53 68%	 54 64%
	 55 62%		 56 55%	 57 67%	 58 66%	

Table 3.

While amides 15-20 were monosubstituted at the β carbon, we wanted to determine if the method was also amenable to amides disubstituted at the β carbon. The original protocol was modified to include two major changes: (1) upon addition of the α,β -unsaturated amide 59 to lithio allene 2, the reaction was allowed to stir for 1.5 h; (2) the reaction was warmed to -5 °C. These two changes were critical to the success of the reaction. This may be due to a slow rate of addition of the lithio allene to the morpholino amide. The use of β -disubstituted morpholino amide allowed the formation of cyclopentenone 60, bearing a quaternary carbon at C4.



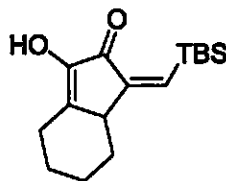
Scheme 2.^a

^aReaction conditions: (a) THF, $-5\text{ }^{\circ}\text{C}$, 90 min; (b) *sec*-BuLi (2.2 equiv), $-78\text{ }^{\circ}\text{C}$, 20 min; (c) MeI (6 equiv), THF, $-78\text{ }^{\circ}\text{C}$, 30 min; (d) 5% HCl/EtOH, $-5\text{ }^{\circ}\text{C}$.

C. Conclusion

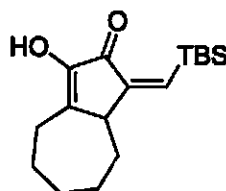
A general protocol has been developed that defines specific parameters for the successful implementation of the triply convergent Nazarov cyclization. Strict adherence to the described protocol allows the formation of densely functionalized β -substituted cyclopentenones in good yields, while alteration of the procedure typically results in degradation of yields. It is hoped that the triply convergent Nazarov process will be used in total synthesis.

D. Experimental



21 (3Z)-3-((tert-butyldimethylsilyl)methylene)-3a,4,5,6-tetrahydro-1-hydroxy-1H-inden-2(4H)-one.

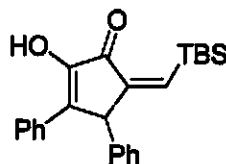
Isolated as a white crystalline solid (140mg, 68%); IR (film): 3326 (br), 2930, 2855, 1686, 1657, 1607, 1401, 1250, 1087, 1070, 860, 825, 768 cm^{-1} ; ^1H NMR (300 MHz, CDCl_3): δ = 6.16 (d, J = 0.9 Hz, 1 H), 6.06 (bs, 1 H), 2.98 (dm, J = 14.2 Hz, 1 H), 2.82 (dd, J = 11.8, 5.3 Hz, 1 H), 2.27-2.21 (m, 1 H), 2.11-1.86 (m, 3 H), 1.48 (qt, J = 13.2, 3.0 Hz, 1 H), 1.29 (qt, J = 12.0, 3.6 Hz, 1 H), 1.01 (qd, J = 9.6, 3.0 Hz, 1 H), 0.92 (s, 9 H), 0.21 (s, 3 H), 0.20 (s, 3 H); ^{13}C NMR (75 MHz, CDCl_3): δ = 189.8, 152.3, 148.0, 143.7, 135.7, 42.3, 32.6, 26.4 (3), 25.3, 25.1, 24.9, 17.0, -5.8, -5.9; MS: m/z (%) = 221 (M^+ - C_4H_9 , 100), 75 (23); HREIMS calcd for $\text{C}_{16}\text{H}_{26}\text{O}_2\text{Si}$ (- C_4H_9) 221.0998, found 221.0999.



22 (3Z)-3-((tert-butyldimethylsilyl)methylene)-3a,4,5,6,7,8-hexahydro-1-hydroxyazulen-2(1H)-one.

Isolated as a white crystalline solid (86 mg, 71% yield): mp 128°-133°C; IR (film): 3339, 2923, 1671, 1601, 1407, 825 cm^{-1} ; ^1H NMR (300 MHz, C_6D_6): δ = 6.83 (s, 1 H), 6.14 (s, 1 H), 2.73-2.69 (m, 1 H), 2.54-2.49 (m, 2 H), 1.92-1.82 (m, 1 H), 1.62-1.40 (m, 3 H), 1.24-

1.14 (m, 2 H), 1.12 (s, 9 H), 1.00-0.80 (m, 2 H), 0.51 (s, 3 H), 0.50 (s, 3 H); ^{13}C NMR (75 MHz, C_6D_6): δ = 189.6, 154.3, 151.9, 148.7, 134.9, 45.5, 35.1, 30.7, 30.1, 28.4, 26.7 (3), 25.8, 17.4, -5.3 (2); HREIMS calcd for $\text{C}_{17}\text{H}_{28}\text{O}_2\text{Si}$ 292.18586, found 292.1875.



23 (5Z)-5-((tert-butyl dimethylsilyl)methylene)-2-hydroxy-3,4-diphenylcyclopent-2-enone.

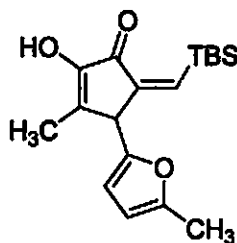
To a solution of allene **2** (44 mg, 0.44 mmol) in 3 mL THF at $-78\text{ }^{\circ}\text{C}$ was added *n*-BuLi (155 μL , 2.91 M in hexanes, 0.45 mmol). After 45 min a solution of amide **11** (106 mg, 0.36 mmol) in 2 mL THF was added at $-78\text{ }^{\circ}\text{C}$ *via* cannula. After 10 min at $-78\text{ }^{\circ}\text{C}$, the reaction mixture was warmed from $-78\text{ }^{\circ}\text{C}$ to $-30\text{ }^{\circ}\text{C}$ over 30 min and stirred further for 30 min at $-30\text{ }^{\circ}\text{C}$. *sec*-BuLi (420 μL , 1.35 M in cyclohexane, 0.57 mmol) was added dropwise at $-78\text{ }^{\circ}\text{C}$. After 45 min, a solution of freshly sublimed *tert*-butyl dimethylsilyl chloride (218 mg, 1.45 mmol) in 2 mL THF was added at $-78\text{ }^{\circ}\text{C}$ *via* cannula. The reaction mixture was warmed from $-78\text{ }^{\circ}\text{C}$ to $-30\text{ }^{\circ}\text{C}$, stirred further for 1.5 hr at $-30\text{ }^{\circ}\text{C}$; then quenched by rapid addition through a large bore cannula to 5% (v/v) aqueous HCl in EtOH (7 mL).

After 10 min, it was neutralized with pH 7 buffer, and extracted with EtOAc (3x). The combined organic extracts were washed with brine (2x) and dried over MgSO_4 .

Purification by flash column chromatography on silica (1% EtOAc in hexanes) gave cyclopentenone **23** as a yellow crystalline solid (107 mg, 76% yield).

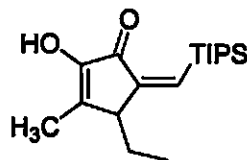
IR (film): 3272 (br), 2927, 1668, 1398 cm^{-1} ; ^1H NMR (300 MHz, CDCl_3): δ = 7.84-7.74 (m, 2 H), 7.40-7.10 (m, 8 H), 6.18 (s, 1 H), 4.76 (s, 1 H), 0.83 (s, 9 H), 0.23 (s, 3 H), 0.20 (s, 3 H); ^{13}C NMR (75 MHz, CDCl_3): δ = 190.2, 152.1, 151.8, 141.6, 140.9, 133.9, 132.6,

129.4 (2), 128.8 (2), 128.5 (2), 128.4 (2), 127.5 (2), 49.4, 26.4 (3), 17.2, -5.6, -5.9; MS: m/z (%) = 361 (M^+ - CH_3 , 3), 343 (1), 319 (100); HREIMS calcd for $C_{24}H_{28}O_2Si$ (M^+ - CH_3) 361.1624, found 361.1604.



24 (5Z)-5-((tert-butyl dimethylsilyl)methylene)-2-hydroxy-3-methyl-4-(5-methylfuran-2-yl)cyclopent-2-enone.

Isolated as a pale yellow wax (65 mg, 52% yield). IR (film): 3400, 1680, 1410 cm^{-1} ; 1H NMR (300 MHz, $CDCl_3$): δ = 6.21 (d, J = 1.2 Hz, 1 H), 5.98 (d, J = 3.0 Hz, 1 H), 5.87 (dt, J = 3.0, 1.2 Hz, 1 H), 5.51 (s, 1 H), 4.23 (bs, 1 H), 2.22 (d, J = 0.9 Hz, 3 H), 1.93 (d, J = 1.2 Hz, 3 H), 0.83 (s, 9 H), 0.21 (s, 3 H), 0.20 (s, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 189.3, 151.9, 151.8, 151.0, 149.0, 138.2, 107.9, 106.1, 94.7, 45.9, 26.3 (3), 17.2, 13.5, 12.1, -5.6, -5.8; HREIMS calcd for $C_{18}H_{26}O_3Si$ 318.1651, found 318.1642.

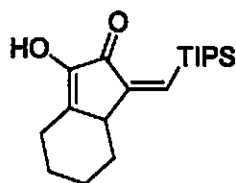


25 (5Z)-4-ethyl-2-hydroxy-5-((triisopropylsilyl)methylene)-3-methylcyclopent-2-enone.

Isolated as a white crystalline solid (150 mg, 68% yield): mp 83-85 $^{\circ}C$; IR (neat): 3316 (br), 2939, 2864, 1684, 1656, 1606 cm^{-1} ; 1H NMR (300 MHz, $CDCl_3$): δ = 6.08 (d, J = 1.2

Hz, 1 H), 5.98 (s, 1 H), 3.16 (m, 1 H), 1.95 (d, $J = 1.2$ Hz, 3 H), 1.71-1.92 (m, 2 H), 1.43 (m, 2 H), 1.04* (d, $J = 7.4$ Hz, 9 H), 1.04 (d, $J = 7.4$ Hz, 9 H), 0.64 (t, $J = 7.4$ Hz, 3 H); ^{13}C NMR (75 MHz, CDCl_3): $\delta = 189.7, 151.7$ (2), 139.4, 133.9, 45.4, 22.7, 19.1 (2)*, 12.3, 11.5, 7.7; HREIMS calcd for $\text{C}_{15}\text{H}_{22}\text{O}_3$ 250.1569, found 250.1590.

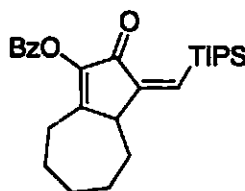
*For this substrate the methyl groups of the isopropyl group displayed unusual asymmetry in the ^1H NMR at 300 & 500 MHz and the ^{13}C NMR at 125 MHz. For this compound, at these field strengths, there are exactly two types of isopropyl methyls. Thus, in the ^1H NMR there are 2 doublets of equal intensity and in the ^{13}C NMR there are 2 signals for the methyl carbons. It had been anticipated that methyl groups on a given isopropyl group would be equivalent and if there was any asymmetry, it would give rise to different types of isopropyl group rather than different types of methyl groups. This, however, was not the case.



26 (3Z)-3a,4,5,6-tetrahydro-1-hydroxy-3-((triisopropylsilyl)methylene)-1H-inden-2(4H)-one.

Isolated as a white crystalline solid (86 mg, 50% yield): mp 128-133 °C. IR (neat): 3373 (br), 2934, 1681, 1402 cm^{-1} ; ^1H NMR (300 MHz, C_6D_6): $\delta = 6.07$ (d, $J = 0.9$ Hz, 1 H), 5.70 (bs, 1 H), 3.00-2.94 (m, 1 H), 2.87 (dd, $J = 11.7, 5.5$ Hz, 1 H), 2.28 (m, 1 H), 2.09 (ddd, $J = 12.7, 5.5, 1.5$ Hz, 1 H), 1.98-1.86 (m, 2 H), 1.53-1.47 (m, 1 H), 1.45-1.36 (m, 3 H), 1.34-1.25 (m, 2 H), 1.05 (d, $J = 3.3$ Hz, 12 H), 1.02 (d, $J = 3.3$ Hz, 6 H); ^{13}C NMR (75 MHz, CDCl_3): $\delta = 189.6, 153.2, 147.9, 143.0, 134.3, 42.8, 33.2, 25.5, 25.4, 25.1, 19.3, 12.4$;

EIMS m/z : 277 (M^+ , $-C_3H_7$, 100), 145 (14), 117 (11), 115 (10), 74 (10), 68 (3); HREIMS calcd for $C_{19}H_{32}O_2Si$ ($M^+ - C_3H_7$) 277.1624, found 277.1618.

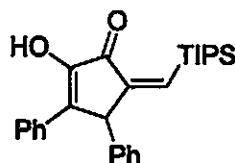


27 (1Z)-1,2,4,5,6,7,8,8a-octahydro-1-(((triisopropylsilyl)methylene)-2-oxoazulen-3-yl benzoate.

To a solution of methoxymethyl allene ether (76 mg, 0.76 mmol) in 2 mL of THF at $-78\text{ }^\circ\text{C}$ was added n -BuLi (0.31 mL, 2.49 M in hexanes, 0.78 mmol). After 30 min, a solution of cycloheptenamide 19 (99 mg, 0.47 mmol) in 2 mL THF was added at $-78\text{ }^\circ\text{C}$ via cannula and the reaction mixture was allowed to warm from $-78\text{ }^\circ\text{C}$ to $-30\text{ }^\circ\text{C}$ over one hour, added with sec -BuLi (0.57 mL, 1.68 M in cyclohexane, 0.95 mmol) and was stirred at $-78\text{ }^\circ\text{C}$ for an additional 30 min. TIPSCl (0.30 mL, 1.40 mmol) in 1 mL THF was then added at $-78\text{ }^\circ\text{C}$ via cannula and the reaction was allowed to warm from $-78\text{ }^\circ\text{C}$ to $-30\text{ }^\circ\text{C}$ over one hour, was quenched with 5% HCl in EtOH, allowed to warm to rt over 20 – 30 min and was then neutralized with pH 7 buffer. The mixture was extracted with EtOAc (3X) and the combined organic extracts were washed with brine, dried over $MgSO_4$. The crude mixture was dissolved into 2 mL of DCM and was followed by the addition of Hünig's base (0.25 mL, 1.42 mmol). The mixture was cooled to $0\text{ }^\circ\text{C}$, benzoyl chloride (0.06 mL, 0.52 mmol) was added dropwise, stirred at rt for one hour, was quenched with $NaHCO_3(aq)$, washed with brine and was isolated via flash column chromatography on

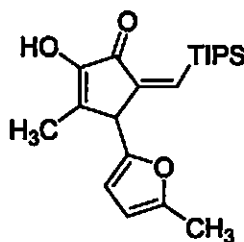
silica gel (1% EtOAc in hexanes) to yield a pale yellow oil (112 mg, 71% yield): $R_f = 0.39$ (3% EtOAc in hexanes).

IR (film): 2929, 1747, 1702, 1608, 1257, 882, 706 cm^{-1} ; ^1H NMR (300 MHz, C_6D_6): $\delta = 8.13$ (d, $J = 8.1$ Hz, 2 H), 7.13-6.95 (m, 3 H), 6.10 (s, 1 H), 2.88 (brd, $J = 9.0$ Hz, 1 H), 2.36-2.28 (m, 2 H), 1.99-1.89 (m, 1 H), 1.70-1.23 (m, 6 H), 1.23-1.14 (m, 20 H), 1.14-0.84 (m, 2 H); ^{13}C NMR (75 MHz, C_6D_6): $\delta = 186.7, 163.0, 162.0, 154.6, 148.2, 133.4, 133.3, 130.5, 129.3, 128.6, 46.7, 35.1, 30.4, 29.7, 28.3, 25.5, 19.5, 12.6$; HREIMS calcd for $\text{C}_{27}\text{H}_{38}\text{O}_3\text{Si}$ ($\text{M}^+ - \text{C}_3\text{H}_8$) 395.2042, found 395.2040.



28 (5Z)-2-hydroxy-5-((triisopropylsilyl)methylene)-3,4-diphenylcyclopent-2-enone.

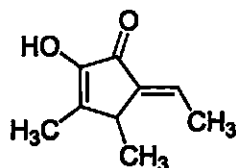
Isolated as an amorphous solid (118 mg, 79% yield); IR (film): 3273 (br), 2948, 1667, 1402 cm^{-1} ; ^1H NMR (300 MHz, CDCl_3): $\delta = 7.96$ -7.88 (m, 2 H), 7.40-7.10 (m, 8 H), 6.10 (bs, 1 H), 6.05 (s, 1 H), 4.83 (s, 1 H), 1.56-1.36 (m, 3 H), 1.20-0.90 (m, 18 H); ^{13}C NMR (75 MHz, CDCl_3): $\delta = 190.6, 152.9, 141.9, 139.9, 134.7, 132.7, 129.4$ (2), 129.0 (2), 128.7 (2), 128.3 (2), 127.3 (2), 126.8, 49.6, 18.5 (6), 17.6 (3); HREIMS calcd $\text{C}_{24}\text{H}_{27}\text{O}_2\text{Si}$ ($\text{M}^+ - \text{C}_3\text{H}_8$) 375.1780, found 375.1761.



29 (5*Z*)-2-hydroxy-5-((triisopropylsilyl)methylene)-3-methyl-4-(5-methylfuran-2-yl)cyclopent-2-enone.

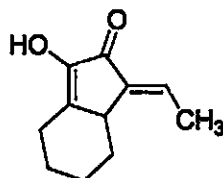
Isolated as a colorless oil (123 mg, 75% yield); IR (neat): 3315, 2935, 1681, 1652 cm^{-1} .

^1H NMR (300 MHz, CDCl_3): δ = 6.10 (d, J = 1.5 Hz, 1 H), 6.01 (d, J = 2.7 Hz, 1 H), 5.86 (dt, J = 3.0, 0.9 Hz, 1 H), 4.75 (bs, 1 H), 2.20 (d, J = 0.9 Hz, 3 H), 1.94 (s, 3 H), 1.38 (m, 3 H), 1.03-1.89 (m, 18 H); ^{13}C NMR (75 MHz, CDCl_3): δ = 189.3, 151.9, 151.7, 151.1, 149.6, 137.8, 108.1, 105.9, 94.4, 45.9, 18.9 (6), 17.7 (3), 13.5, 12.8; HREIMS calcd for $\text{C}_{21}\text{H}_{32}\text{O}_3\text{Si}$ 360.2121, found 360.2134.



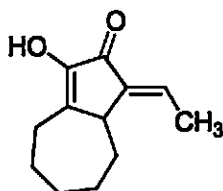
30 (5*E*)-5-ethylidene-2-hydroxy-3,4-dimethylcyclopent-2-enone.

Isolated as a white crystalline solid (106 mg, 70% yield): mp 132-134°C. IR (film): 3270 (br), 1675, 1630, 1405 cm^{-1} ; ^1H NMR (300 MHz, C_6D_6): δ = 7.86 (bs, 1 H), 6.57 (qd, J = 7.2, 1.5 Hz, 1 H), 2.54 (bq, J = 6.9 Hz, 1 H), 1.69 (s, 3 H), 1.34 (d, J = 7.2 Hz, 3 H), 0.77 (d, J = 6.9 Hz, 3 H); ^{13}C NMR (75 MHz, C_6D_6): δ = 189.8, 151.3, 142.5, 139.7, 129.6, 36.7, 17.3, 14.3, 11.5; MS: m/z (%) = 152 (M^+ , 100), 137 (65), 109 (60); HREIMS calcd for $\text{C}_9\text{H}_{12}\text{O}_2$ 152.0837, 152.0868.

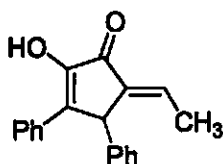


31 (3*E*)-3-ethylidene-3a,4,5,6-tetrahydro-1-hydroxy-1*H*-inden-2(4*H*)-one.

Isolated as a white amorphous solid (111 mg, 62%); IR (film): 3300 (br), 2935, 2856, 1682, 1630, 1444, 1399, 1202, 1119, 1050, 972 cm^{-1} ; ^1H NMR (300 MHz, CDCl_3): δ = 6.64 (dq, J = 7.2, 4.2 Hz, 1 H), 5.95 (bs, 1 H), 3.01 (dd, J = 12.0, 4.5 Hz, 2 H), 2.41-2.35 (dm, 1 H), 2.12-1.83 (m, 6 H), 1.52 (qt, J = 13.2, 3.3 Hz, 1 H), 1.34 (qt, J = 12.6, 3.3 Hz, 1 H), 1.04 (qd, J = 12.9, 3.6 Hz, 1 H); ^{13}C NMR (75 MHz, CDCl_3): δ = 189.4, 107.0, 144.4, 137.5, 130.8, 39.5, 32.7, 26.2 (2), 25.2, 14.6; MS: m/z (%) = 178 (M^+ , 96), 160 (21), 149 (17), 135 (100), 79 (58); HREIMS calcd for $\text{C}_{11}\text{H}_{14}\text{O}_2$ 178.0994, found 178.0996.

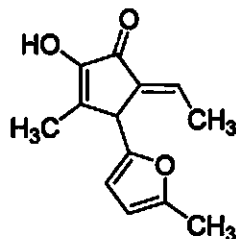


32 (3*E*)-3-ethylidene-3a,4,5,6,7,8-hexahydro-1-hydroxyazulen-2(1H)-one; Isolated as a white crystalline solid (61 mg, 63% yield): decomposition at 73 $^{\circ}\text{C}$; IR (film): 3292 (br), 2927, 1671, 1626, 1404, 953 cm^{-1} ; ^1H NMR (300 MHz, C_6D_6): δ = 7.45 (bs, 1 H), 6.59 (q, J = 7.3 Hz, 1 H), 2.74 (d, J = 9.9 Hz, 1 H), 2.70-2.44 (m, 2 H), 1.89-1.78 (m, 1 H), 1.60-1.44 (m, 2 H), 1.35 (d, J = 7.3, 3 H), 1.30-0.76 (m, 5 H); ^{13}C NMR (75 MHz, C_6D_6): δ = 188.9, 150.5, 147.2, 139.3, 128.6, 41.4, 34.3, 30.3, 29.5, 28.1, 25.5, 14.0; MS: m/z (%) = 192 (M^+ , 100), 174 (20), 164 (10), 149 (85), 135 (20), 107 (20); HREIMS calcd for $\text{C}_{12}\text{H}_{16}\text{O}_2$ 192.1150, found 192.1166.



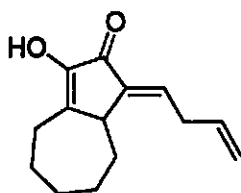
33 (5*E*)-5-ethylidene-2-hydroxy-3,4-diphenylcyclopent-2-enone.

To a solution of allene **2** (43 mg, 0.43 mmol) in 3 mL THF at $-78\text{ }^{\circ}\text{C}$ was added *n*-BuLi (155 μL , 2.91 M in hexanes, 0.45 mmol). After 45 min, a solution of amide **20** (105 mg, 0.36 mmol) in 2 mL THF was added at $-78\text{ }^{\circ}\text{C}$ *via* cannula. After 10 min at $-78\text{ }^{\circ}\text{C}$, the reaction mixture was warmed from $-78\text{ }^{\circ}\text{C}$ to $-30\text{ }^{\circ}\text{C}$ over 30 min, and stirred further for 30 min at $-30\text{ }^{\circ}\text{C}$. *sec*-BuLi (415 μL , 1.35 M in cyclohexane, 0.56 mmol) was added dropwise at $-78\text{ }^{\circ}\text{C}$. After 45 min, MeI (110 μL , 1.77 mmol) in 2 mL THF was added at $-78\text{ }^{\circ}\text{C}$ *via* cannula. The reaction mixture was warmed from $-78\text{ }^{\circ}\text{C}$ to $-30\text{ }^{\circ}\text{C}$ over 15 minutes, and stirred further for 1 hr at $-30\text{ }^{\circ}\text{C}$; then quenched by rapid addition through a large bore cannula to 5% (v/v) aqueous HCl in EtOH (7 mL). After 10 min, it was neutralized with pH 7 buffer, and extracted with EtOAc (3x). The combined organic extracts were washed with brine (2x) and dried over MgSO_4 . Purification by flash column chromatography on silica gel (10% EtOAc in hexanes) gave cyclopentenone **16** as a white crystalline solid (83 mg, 84% yield): mp $196\text{--}198\text{ }^{\circ}\text{C}$; $R_f = 0.32$ (20% EtOAc in hexanes); IR (film): 3222 (br), 3018, 1683, 1655, 1401 cm^{-1} ; $^1\text{H NMR}$ (300 MHz, CDCl_3): $\delta = 7.90\text{--}7.82$ (m, 2 H), 7.36–7.10 (m, 8 H), 6.98 (bs, 1 H), 6.80 (qd, $J = 7.3, 1.3\text{ Hz}$, 1 H), 4.93 (d, $J = 1.3\text{ Hz}$, 1 H), 1.71 (d, $J = 7.3\text{ Hz}$, 3 H); $^{13}\text{C NMR}$ (75 MHz, CDCl_3): $\delta = 190.0, 150.7, 140.6, 138.3, 135.5, 132.7, 132.4, 128.9$ (2), 128.6 (2), 128.4 (2), 128.1 (2), 126.9 (2), 45.8, 14.2; EIMS: m/z (%) = 276 (M^+ , 100), 261 (2), 258 (13), 232 (3), 199 (3); HREIMS calcd for $\text{C}_{19}\text{H}_{16}\text{O}_2$ 276.1150, found 276.1179.



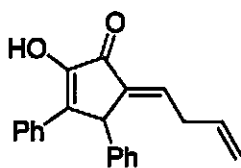
34 (5E)-5-ethylidene-2-hydroxy-3-methyl-4-(5-methylfuran-2-yl)cyclopent-2-enone.

Isolated as a white crystalline solid (97 mg, 70% yield): mp 188 °C; IR (film): 3243, 2980, 1678 cm^{-1} ; ^1H NMR (300 MHz, CDCl_3): δ = 6.67 (qd, J = 8.0, 1.8 Hz, 1 H), 5.95 (d, J = 3.0 Hz, 1 H), 5.85 (dt, J = 3.0, 0.9 Hz, 1 H), 4.30 (bs, 1 H), 2.19 (d, J = 0.9 Hz, 3 H), 1.88 (s, 3 H), 1.75 (d, J = 8.0 Hz, 3 H); ^{13}C NMR (75 MHz, CDCl_3): δ = 189.3, 153.8, 150.6, 150.4, 149.9, 145.7, 137.2, 132.6, 101.1, 43.8, 14.0, 13.2, 11.9; HREIMS calcd for $\text{C}_{13}\text{H}_{14}\text{O}_3$ 218.0943, found 218.0943.



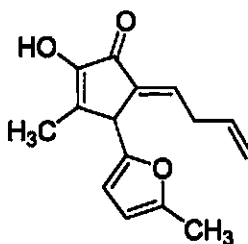
35 (3Z)-3-(but-3-enylidene)-3a,4,5,6,7,8-hexahydro-1-hydroxyazulen-2(1H)-one.

Isolated as a white amorphous solid (75 mg, 54% yield); IR (neat): 3584, 3383 (br), 2924, 1670, 1613, 1407, 1078 cm^{-1} ; ^1H NMR (300 MHz, C_6D_6): δ = 5.60-5.45 (m, 1 H), 5.33 (t, J = 7.6 Hz, 1 H), 4.84-4.68 (m, 2 H) 3.54-3.32 (m, 2 H), 2.40-2.32 (m, 1 H) 2.18-2.10 (m, 2 H), 1.45-1.34 (m, 1 H), 1.34-1.90 (m, 3 H), 0.96-0.55 (m, 5 H); ^{13}C NMR (75 MHz, C_6D_6): δ = 190.1, 151.3, 146.2, 137.2, 136.2, 136.2, 115.9, 43.8, 35.1, 32.0, 30.7, 29.8, 28.1, 25.9; MS: m/z (%) = 218 (M^+ , 25), 105 (10), 91 (10), 84 (100), 70 (10); HREIMS calcd for $\text{C}_{14}\text{H}_{18}\text{O}_2$ 218.1307, found 218.1297.



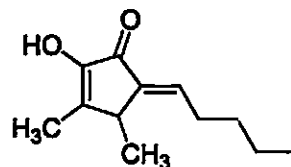
36 (5Z)-5-(but-3-enylidene)-2-hydroxy-3,4-diphenylcyclopent-2-enone.

Isolated as a yellow crystalline solid (65 mg, 61% yield): mp 158-160°C; IR (film): 3248 (br), 2915, 1668, 1398 cm^{-1} ; $^1\text{H-NMR}$ (300 MHz, CDCl_3): δ = 7.90-7.82 (m, 2 H), 7.40-7.10 (m, 8 H), 6.77 (bs, 1 H), 5.93 (t, J = 7.5 Hz, 1 H), 5.80 (m, 1 H), 5.00 (s, 1 H), 4.95 (m, 1 H), 4.78 (s, 1 H), 3.82-3.62 (m, 1 H), 3.52-3.34 (m, 1 H); $^{13}\text{C-NMR}$ (75 MHz, CDCl_3): δ = 190.4, 151.6, 141.6, 140.7, 136.4, 135.2, 133.0, 132.4, 129.2 (2), 128.9 (2), 128.4 (2), 127.4 (2), 127.0 (2), 116.1, 47.5, 32.1; EIMS: m/z (%) = 302 (M^+ , 100), 273 (6), 284 (10), 245 (5); HREIMS calcd for $\text{C}_{21}\text{H}_{18}\text{O}_2$ 302.1307, found 302.1337.



37 (*5E*)-5-(but-3-enylidene)-2-hydroxy-3-methyl-4-(5-methylfuran-2-yl)cyclopent-2-enone.

Isolated as a yellow oil (80 mg, 58% yield); IR (film): 3280, 1673, 1490 cm^{-1} ; $^1\text{H NMR}$ (300 MHz, CDCl_3): δ = 6.64 (m, 1 H), 6.05 (dt, J = 3.0, 0.9 Hz, 1 H), 5.87 (d, 0.9 Hz, 1 H), 5.70-5.59 (m, 1 H), 5.31 (bs, 1 H), 4.98 (d, J = 10.0 Hz, 1 H), 4.89 (d, J = 17.0 Hz, 1 H), 4.35 (bs, 1 H), 2.91-2.80 (m, 2 H), 2.24 (d, J = 0.9 Hz, 3 H), 1.95 (s, 3 H); $^{13}\text{C NMR}$ (75 MHz, CDCl_3): δ = 189.9, 161.3, 153.2, 152.5, 150.2, 146.8, 138.4, 134.8, 116.0, 112.1, 108.2, 44.8, 31.0, 13.7, 12.9; HREIMS calcd for $\text{C}_{15}\text{H}_{16}\text{O}_3$ 244.1099 found 244.1089.

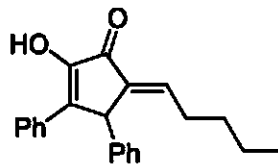


38 (*5E*)-2-hydroxy-3,4-dimethyl-5-pentylidenecyclopent-2-enone.

Product isolated as a light amber oil (57 mg, 29%); IR *Z* isomer: (neat) 3310 (br), 2960, 2930, 2870, 1770, 1680, 1625 cm^{-1} ; Product isolated as an amorphous solid (67 mg, 37%). *E* isomer: (neat) 3310 (br), 2960, 2930, 2870, 1680, 1625, 1410 cm^{-1} ; ^1H NMR (300 MHz, C_6D_6) *Z* isomer: δ = 7.12 (s, 1 H), 5.62 (td, J = 7.8, 0.9 Hz, 1 H), 2.93 (m, 2 H), 2.52 (bq, J = 7.0 Hz, 1 H), 1.64 (s, 3 H), 1.28 (m, 4 H), 1.25 (t, J = 6.9 Hz, 3 H), 0.86 (d, J = 7.0 Hz, 3 H); *E* isomer: δ = 6.61 (td, J = 8.1, 1.5 Hz, 1 H), 2.63 (bq, J = 6.9 Hz, 1 H), 1.89 (m, 2 H), 1.68 (s, 3 H), 1.13 (m, 4 H), 0.83 (d, J = 6.9 Hz, 3 H), 0.80 (m, 3 H). ^{13}C NMR (75 MHz, CDCl_3); *Z* isomer: δ = 190.5, 151.7, 139.8, 139.7, 137.2, 38.4, 31.8, 27.5, 22.6, 17.6, 14.2, 11.1; *E* isomer: δ = 189.4, 150.7, 141.6, 138.2, 134.6, 36.5, 30.9, 28.4, 22.6, 17.3, 13.9, 11.0.

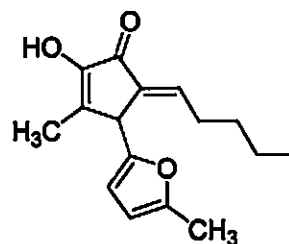
Z isomer HREIMS calcd for $\text{C}_{12}\text{H}_{18}\text{O}_2$ 194.1307, found 194.1297.

E isomer HREIMS calcd for $\text{C}_{12}\text{H}_{18}\text{O}_2$ 194.1307, found 194.1250.



39 (*5E*)-2-hydroxy-5-pentylidene-3,4-diphenylcyclopent-2-enone.

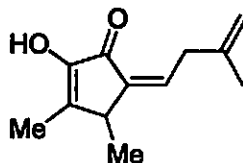
Isolated as a yellow crystalline solid (74 mg, 63% yield): mp 200-202°C; IR (film): 3208 (br), 2958, 1655, 1401 cm^{-1} ; ^1H NMR (300 MHz, CDCl_3): δ = 7.82 (d, J = 7.3 Hz, 2 H), 7.40-7.10 (m, 8 H), 6.82 (bs, 1 H), 6.71 (t, J = 7.9 Hz, 1 H), 4.93 (s, 1 H), 2.25-1.95 (m, 2 H), 1.30-0.90 (m, 4 H), 0.76 (t, J = 7.0 Hz, 3 H); ^{13}C -NMR (75 MHz, CDCl_3): δ = 190.5, 150.9, 141.2, 138.3, 137.4, 135.6, 132.7, 129.2 (2), 128.9 (2), 128.6 (2), 128.4 (2), 127.1 (2), 46.1, 30.3, 28.5, 22.6, 14.0; EIMS: m/z (%) = 318 (M^+ , 100), 300 (13), 289 (10). HREIMS calcd for $\text{C}_{22}\text{H}_{22}\text{O}_2$ 318.1620, found 318.1589.



40 (*5E*)-2-hydroxy-3-methyl-4-(5-methylfuran-2-yl)-5-pentylidenecyclopent-2-enone

Isolated as a pale yellow wax (65 mg, 52% yield); IR (neat): 3300, 2960, 1660 cm^{-1} ;

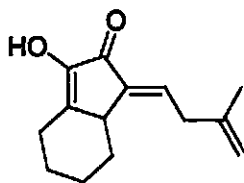
^1H NMR (300 MHz, CDCl_3): δ = 6.57 (td, J = 8.1, 1.8 Hz, 1 H), 5.92 (d, J = 3.0 Hz, 1 H), 5.80 (dt, J = 3.0, 0.9 Hz, 1 H), 4.24 (bs, 1 H), 2.15 (d, J = 0.9 Hz, 3 H), 1.92-2.06 (m, 2 H), 1.82 (s, 3 H), 1.04-1.65 (m, 4 H), 0.75 (t, J = 7.2 Hz, 3 H); ^{13}C NMR (75 MHz, CDCl_3): δ = 188.5, 153.2, 151.5, 150.4, 149.9, 141.4, 138.5, 131.1, 106.1, 42.2, 30.3, 28.2, 22.3, 13.8, 13.5, 11.8; HREIMS calcd for $\text{C}_{16}\text{H}_{20}\text{O}_3$ 260.1412, found 260.1415.



41 (*5Z*)-2-hydroxy-3,4-dimethyl-5-(3-methylbut-3-enylidene)cyclopent-2-enone.

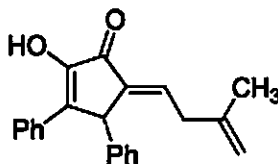
Isolated as an oil (114 mg, 59% yield). IR (neat): 3314, 2967, 2932, 2871, 1679, 1626,

1650, 1409, 1357 cm^{-1} ; ^1H NMR (300 MHz, CDCl_3): δ = 6.02 (td, J = 7.8, 1.2 Hz, 1 H), 4.72 (s, 1 H), 4.76 (s, 1 H), 3.54 (d, J = 7.8 Hz, 2 H), 3.02 (q, J = 7.2 Hz, 1 H), 1.96 (d, J = 1.2 Hz, 3 H), 1.75 (s, 3 H), 1.20 (d, J = 7.2 Hz, 3 H); ^{13}C NMR (75 MHz, CDCl_3): δ = 190.5, 150.9, 148.9, 144.3, 141.0, 137.1, 111.3, 38.6, 35.8, 22.9, 17.9, 11.7; HREIMS calcd for $\text{C}_{12}\text{H}_{16}\text{O}_2$ 192.1150, found 192.1146.



42 (3Z)-3a,4,5,6-tetrahydro-1-hydroxy-3-(3-methylbut-3-enylidene)-1H-inden-2(4H)-one.

Isolated as an oil (104 mg, 51% yield). IR (film): 3315, 2933, 2855, 1687, 1623, 1445, 1400, 1361.2 cm^{-1} ; ^1H NMR (300 MHz, CDCl_3): δ = 6.35 (bs, 1 H), 5.99 (t, J = 7.8 Hz, 1 H), 4.76 (s, 1 H), 4.70 (s, 1 H) 3.53 (d, J = 7.8 Hz, 2 H), 2.97 (dd, J = 13.8, 4.2 Hz, 1 H), 2.82 (dd, J = 11.7, 5.4 Hz, 1 H) 2.26-2.14 (m, 1 H), 2.10-1.80 (m, 3 H), 1.74 (s, 3 H), 1.56-1.38 (m, 1 H), 1.36-1.15 (m, 1 H), 1.15-0.80 (m, 1 H); ^{13}C NMR (75 MHz, CDCl_3): δ = 190.9, 148.1, 144.3, 142.9, 136.8, 136.5, 111.3, 40.9, 35.7, 33.2, 25.5, 25.2, 25.1, 22.9; HREIMS calcd for $\text{C}_{14}\text{H}_{18}\text{O}_2$ 218.2915, found 260.1334.



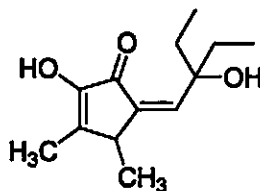
43 (5Z)-2-hydroxy-5-(3-methylbut-3-enylidene)-3,4-diphenylcyclopent-2-enone.

Isolated as a yellow crystalline solid (97 mg, 93% yield): mp 164-166 $^{\circ}\text{C}$.

To a solution of allene 2 (40 mg, 0.40 mmol) in 3 mL THF at -78°C was added *n*-BuLi (140 μL , 2.91 M in hexanes, 0.41 mmol). After 45 min, a solution of amide 20 (97 mg, 0.33 mmol) in 2 mL THF was added at -78°C via cannula. After 10 min at -78°C , the reaction mixture was warmed from -78°C to -30°C over 30 min and stirred further for 30 min at -30°C . *sec*-BuLi (380 μL , 1.35 M in cyclohexane, 0.51 mmol) was added dropwise at -78°C . After 45 min, a solution of methallyl chloride (165 μL , 1.67 mmol), LiI (225 mg, 1.68 mmol), and HMPA (115 μL , 0.66 mmol) in 3 mL THF was added at -78°C via

cannula. The reaction mixture was warmed from $-78\text{ }^{\circ}\text{C}$ to $-30\text{ }^{\circ}\text{C}$ over 15 min and stirred further for 2 hr at $-30\text{ }^{\circ}\text{C}$; then quenched by rapid addition through a large bore cannula to 5% (v/v) aqueous HCl in EtOH (7 mL). After 10 min, it was neutralized with pH 7 buffer and extracted with EtOAc (3x). The combined organic extracts were washed with brine (2x) and dried over MgSO_4 . Purification by crystallization of the crude in 3% EtOAc in hexanes gave cyclopentenone **26** as a yellow crystalline solid (97 mg, 93% yield): mp $164\text{--}166\text{ }^{\circ}\text{C}$; $R_f = 0.58$ (20% EtOAc in hexanes).

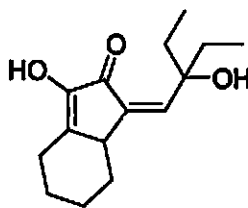
$^1\text{H-NMR}$ (300 MHz, CDCl_3): $\delta = 7.90\text{--}7.82$ (m, 2 H), 7.35–7.14 (m, 8 H), 6.61 (bs, 1 H), 5.95 (t, $J = 7.9$ Hz, 1 H), 4.79 (s, 1 H), 4.70 (s, 1 H), 4.54 (s, 1 H), 3.62 (dd, $J = 15.9, 8.1$ Hz, 1 H), 3.46 (dd, $J = 15.9, 7.8$ Hz, 1 H), 1.67 (s, 3 H); $^{13}\text{C-NMR}$ (75 MHz, CDCl_3): $\delta = 190.4, 151.6, 143.6, 141.7, 141.2, 136.8, 132.8, 132.4, 129.2$ (2), 128.9 (2), 128.4 (2), 127.4 (2), 127.0 (2), 111.3, 47.6, 35.9, 22.8; EIMS: m/z (%) = 316 (M^+ , 100), 301 (30), 298 (7), 287 (4), 259 (3); HREIMS calcd for $\text{C}_{22}\text{H}_{20}\text{O}_2$ 316.1463, found 316.1477.



44 (5Z)-2-hydroxy-5-(2-hydroxy-2-ethylbutylidene)-3,4-dimethylcyclopent-2-enone.

Isolated as a pale yellow oil (70 mg, 59% yield); IR (film): 3306 (br), 2966, 1661, 1616, 797 cm^{-1} ; $^1\text{H NMR}$ (300 MHz, C_6D_6): $\delta = 7.11$ (bs, 1 H), 5.75 (s, 1 H), 5.65 (bs, 1 H), 2.45–2.32 (m, 1 H), 1.86–1.70 (m, 2 H), 1.66–1.52 (m, 2 H), 1.50 (d, $J = 1.2$ Hz, 3 H), 1.12–0.96 (m, 6 H), 0.67 (d, $J = 7.2$ Hz, 3 H); $^{13}\text{C NMR}$ (75 MHz, C_6D_6): $\delta = 190.8, 151.7, 147.6, 143.5, 138.0, 77.0, 38.9, 34.4, 17.5, 11.5, 8.7$.

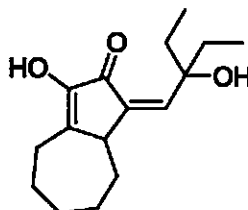
HREIMS calcd for $\text{C}_{13}\text{H}_{20}\text{O}_3$ 224.2961, found 224.1416.



45 (3Z)-3a,4,5,6-tetrahydro-1-hydroxy-3-(2-hydroxy-2-ethylbutylidene)-1H-inden-2(4H)-one.

Isolated as a pale yellow crystalline solid (150mg, 60% yield); IR (film): 3294 (br), 2934, 1664, 1616, 1457, 1403, 1255, 1204, 1095 cm^{-1} ; ^1H NMR (300 MHz, CDCl_3): δ = 6.59 (s, 1 H), 6.05 (s, 1 H), 3.01-2.95 (m, 1 H), 2.87 (dd, J = 12.0, 5.1 Hz, 1 H), 2.21 (m, 1 H), 2.24–1.86 (m, 4 H), 1.74–1.41 (m, 5 H), 1.28 (qt, J = 12.9, 3.9 Hz, 1 H), 1.06 (qd, J = 12.9 Hz, 3.3 Hz, 1 H), 0.92 (t, J = 7.5 Hz, 3 H), 0.90 (t, J = 7.5 Hz, 3 H); ^{13}C NMR (75 MHz, CDCl_3): δ = 190.8, 147.7, 147.6, 145.5, 136.1, 76.7, 41.2, 33.8, 33.8, 33.0, 25.2, 25.1, 24.8, 8.3, 8.2; MS: m/z (%) = 250 (M^+ , 2), 222 (13), 221 (100), 193 (17).

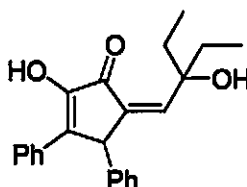
HREIMS calcd for $\text{C}_{15}\text{H}_{22}\text{O}_3$ 250.15689, found 250.1565.



46 (3Z)-3a,4,5,6,7,8-hexahydro-1-hydroxy-3-(2-hydroxy-2-ethylbutylidene)azulen-2(1H)-one.

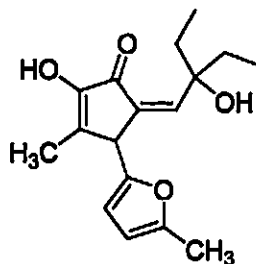
Isolated as a white crystalline solid (135 mg, 51% yield): mp 140-142 $^{\circ}\text{C}$; IR (neat): 3310, 2960, 1715, 1666, 1610, 1457, 1415, 1359 cm^{-1} ; ^1H NMR (300 MHz, CDCl_3): δ = 6.71 (s, 1 H), 6.09 (s, 1 H), 3.19 (dd, J = 10.2, 1.8 Hz, 1 H), 2.82-2.58 (m, 2 H), 2.10 (dd, J = 14.0, 2.7 Hz, 1 H), 2.00-1.80 (m, 3 H), 1.76-1.40 (m, 6 H), 1.38-1.20 (m, 2 H), 0.90 (t, J

= 7.5 Hz, 3 H), 0.91 (t, $J = 7.5$ Hz, 3 H); ^{13}C NMR (75 MHz, CDCl_3): $\delta = 190.0, 150.3, 149.9, 148.5, 137.2, 44.8, 35.6$ (2), 34.2, 34.1, 30.8, 29.9, 28.5, 25.9, 8.5 (2).
 MS: m/z (%) = 264 (M^+ , 2), 246 (9), 235 (100); HREIMS calcd for $\text{C}_{16}\text{H}_{24}\text{O}_3$ 264.1725, found 264.1742.



47 (5*Z*)-2-hydroxy-5-(2-hydroxy-2-ethylbutylidene)-3,4-diphenylcyclopent-2-enone.

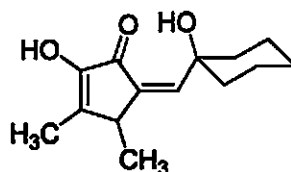
Isolated as a yellow crystalline solid (98 mg, 76% yield): mp 144-145 °C; IR (film): 3321 (br), 2939, 1644, 1405 cm^{-1} ; ^1H -NMR (300 MHz, CDCl_3): $\delta = 7.90$ -7.76 (m, 2 H), 7.40-7.10 (m, 8 H), 6.88 (bs, 1 H), 6.53 (bs, 1 H), 5.94 (s, 1 H), 4.78 (s, 1 H), 1.80-1.38 (m, 4 H), 0.94 (t, $J = 7.5$ Hz, 3 H), 0.57 (t, $J = 7.4$ Hz, 3 H); ^{13}C -NMR (75 MHz, CDCl_3): $\delta = 190.9, 153.0, 151.6, 141.2, 136.7, 135.8, 132.0, 129.5$ (2), 129.0 (2), 128.4 (2), 127.4 (2), 127.2 (2), 77.2, 48.0, 34.0, 33.8, 8.3, 8.0; HREIMS calcd for $\text{C}_{23}\text{H}_{24}\text{O}_3$ 348.1725, found 348.1738.



48 (5*Z*)-2-hydroxy-5-(2-hydroxy-2-ethylbutylidene)-3-methyl-4-(5-methylfuran-2-yl)cyclopent-2-enone.

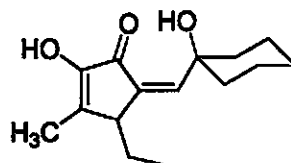
Isolated as a clear oil (143 mg, 64% yield). IR (neat): 3312, 1676, 1482 cm^{-1} ; ^1H NMR (300 MHz, CDCl_3): $\delta = 6.43$ (d, $J = 1.8$ Hz, 1 H), 6.05 (d, $J = 3.0$ Hz, 1 H), 5.86 (dt, $J =$

3.0, 0.9 Hz, 1 H), 4.69 (bs, 1 H), 4.22 (bs, 1 H), 2.20 (d, $J = 0.9$ Hz, 3 H), 1.95 (s, 3 H), 1.41-1.72 (m, 4 H), 1.11 (t, $J = 7.4$ Hz, 3 H), 0.80 (t, $J = 7.4$ Hz, 3 H); ^{13}C NMR (75 MHz, CDCl_3): $\delta = 189.9, 154.0, 152.1, 151.8, 150.7, 139.2, 118.1, 106.6, 104.3, 55.9, 46.2, 38.0, 33.4, 13.6, 12.7, 8.1, 8.0$; HREIMS calcd for $\text{C}_{17}\text{H}_{22}\text{O}_4$ 290.1518, found 290.1522.



49 (5*Z*)-2-hydroxy-5-((1-hydroxycyclohexyl)methylene)-3,4-dimethylcyclopent-2-enone.

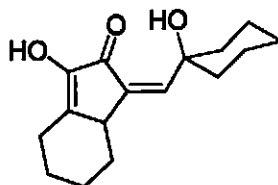
Isolated as a colorless oil (123 mg, 56% yield). IR (film): 3300, 2932, 2855, 1659, 1613, 1446, 1403, 1350 cm^{-1} ; ^1H NMR (300 MHz, C_6D_6): $\delta = 6.64$ (bs, 1 H), 6.14 (bs, 1 H), 5.89 (s, 1 H), 3.24-3.16 (m, 1 H), 3.14-3.06 (m, 1 H), 2.42-2.30 (m, 1 H), 2.08-1.90 (m, 3 H), 1.52 (s, 3 H), 1.50-1.38 (m, 3 H), 1.18-1.15 (m, 2 H), 0.69 (d, $J = 6.9$ Hz, 3 H); ^{13}C NMR (75 MHz, CDCl_3): $\delta = 190.3, 150.8, 148.9, 144.2, 136.6, 71.7, 38.9, 37.9, 37.8, 25.6, 25.4, 22.3, 17.8, 12.0$; HREIMS calcd for $\text{C}_{14}\text{H}_{20}\text{O}_3$ 236.1412, found 236.1440.



50 (5*Z*)-4-ethyl-2-hydroxy-5-((1-hydroxycyclohexyl)methylene)-3-methylcyclopent-2-enone.

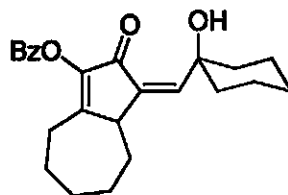
Isolated as a clear oil (107 mg, 64% yield); IR (film): 3329 (br), 2933, 1753, 1659, 1612 cm^{-1} ; ^1H NMR (300 MHz, CDCl_3): $\delta = 6.76$ (s, 1 H), 5.92 (d, $J = 0.9$ Hz, 1 H), 2.52 (m, 1 H), 1.93-2.06 (m, 4 H), 1.54 (d, $J = 1.5$ Hz, 3 H), 1.53-1.20 (m, 8 H), 0.41 (t, $J = 7.4$ Hz, 3 H); ^{13}C NMR (75 MHz, CDCl_3): $\delta = 191.1, 152.8, 147.9, 141.8, 134.2, 71.8, 43.7, 38.1,$

37.9, 25.9, 22.9, 22.3 (2), 11.5, 7.3; HREIMS calcd for C₁₅H₂₂O₃ 250.15689, found 250.15998.



51 (3Z)-3a,4,5,6-tetrahydro-1-hydroxy-3-((1-hydroxycyclohexyl)methylene)-1H-inden-2(4H)-one.

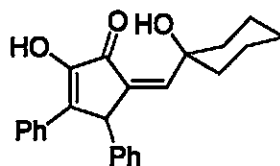
Isolated as a white crystalline solid (157 mg, 60% yield): mp 281-282 °C. IR (neat): 3300, 2932, 2855, 1659, 1613, 1446, 1403, 1350 cm⁻¹; ¹H NMR (300 MHz, CDCl₃): δ = 6.23 (d, *J* = 3 Hz, 1 H), 5.70 (bs, 1 H), 3.05-2.92 (m, 1 H), 2.83 (dd, *J* = 12.0, 5.4 Hz, 1 H), 2.26-1.05 (m, 17 H), 1.05 (qd, *J* = 12.6, 3.3 Hz, 1H); ¹³C NMR (75 MHz, CDCl₃): δ = 190.7, 148.6, 147.9, 146.2, 135.3, 71.8, 41.1, 37.9 (2), 33.0, 25.6, 25.4 (2), 25.1, 22.3 (2); MS: *m/z* (%) = 262 (M⁺, 100), 244 (56), 150 (79); HREIMS calcd for C₁₆H₂₂O₃ 262.1569, found 262.1572.



52 (1Z)-1,2,4,5,6,7,8,8a-octahydro-1-((1-hydroxycyclohexyl)methylene)-2-oxoazulen-3-yl benzoate.

Isolated as a clear oil (88 mg, 46% yield); IR (film): 3442 (br), 2931, 1745, 1681, 1633, 707 cm⁻¹; ¹H NMR (300 MHz, C₆D₆): δ = 8.19 (d, *J* = 8.3 Hz, 2 H), 7.30-6.95 (m, 3 H), 6.72 (bs, 1 H), 6.25 (s, 1 H), 2.67 (d, *J* = 7.5 Hz, 1 H), 2.37-2.16 (m, 2 H), 2.10-1.90 (m, 4

H), 1.74-0.80 (m, 14 H); ^{13}C NMR (75 MHz, CDCl_3): δ = 188.8, 164.5, 163.0, 150.8, 147.4, 139.6, 136.2, 133.6, 132.9, 130.2, 128.5, 126.0, 71.3, 45.1, 38.1, 37.9, 34.6, 30.2, 29.5, 28.4, 25.9, 25.2, 22.2, 20.5; HREIMS calcd for $\text{C}_{24}\text{H}_{28}\text{O}_4$ 380.1988, found 380.1961.

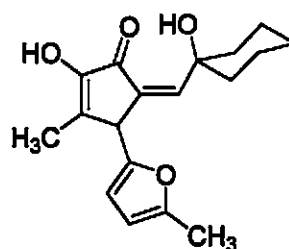


53 (5Z)-2-hydroxy-5-((1-hydroxycyclohexyl)methylene)-3,4-diphenylcyclopent-2-enone

To a solution of allene **2** (44 mg, 0.44 mmol) in 3 mL THF at $-78\text{ }^\circ\text{C}$ was added *n*-BuLi (160 μL , 2.91 M in hexanes, 0.47 mmol). After 45 min a solution of amide **20** (108 mg, 0.37 mmol) in 2 mL THF was added at $-78\text{ }^\circ\text{C}$ via cannula. After 10 min at $-78\text{ }^\circ\text{C}$, the reaction mixture was warmed from $-78\text{ }^\circ\text{C}$ to $-30\text{ }^\circ\text{C}$ over 30 min and stirred further for 30 min at $-30\text{ }^\circ\text{C}$. *sec*-BuLi (430 μL , 1.35 M in cyclohexane, 0.58 mmol) was added dropwise at $-78\text{ }^\circ\text{C}$. After 45 min, a solution of cyclohexanone (170 μL , 1.64 mmol) in 2 mL THF was added at $-78\text{ }^\circ\text{C}$ via cannula. The reaction mixture was warmed from $-78\text{ }^\circ\text{C}$ to $-30\text{ }^\circ\text{C}$ over 15 min, and stirred further for 1 hr at $-30\text{ }^\circ\text{C}$; then quenched by rapid addition through a large bore cannula to 5% (v/v) aqueous HCl in EtOH (7 mL). After 10 min, it was neutralized with pH 7 buffer, and extracted with EtOAc (3x). The combined organic extracts were washed with brine (2x) and dried over MgSO_4 . Purification by flash column chromatography on silica gel (10% EtOAc in hexanes) gave cyclopentenone **53** as a yellow, crystalline solid (90 mg, 68% yield): mp $184\text{--}186\text{ }^\circ\text{C}$; R_f = 0.18 (20% EtOAc in hexanes).

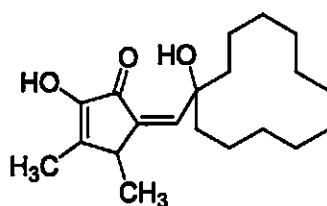
IR (film): 3372 (br), 2938, 1651, 1451 cm^{-1} ; ^1H NMR (300 MHz, CDCl_3): δ = 7.84-7.74 (m, 2 H), 7.40-7.00 (m, 8 H), 6.47 (bs, 1 H), 6.12 (bs, 1 H), 6.04 (s, 1 H), 4.75 (s, 1 H),

1.84-1.10 (m, 10 H); ^{13}C NMR (75 MHz, CDCl_3): δ = 190.6, 153.1, 151.7, 141.0, 136.1, 135.7, 132.1, 129.5 (2), 129.0 (2), 128.4 (2), 127.4 (2), 127.2 (2), 71.9, 47.8, 37.5, 37.2, 25.3, 21.9, 21.8; EIMS: m/z (%) = 360 (M^+ , 100), 342 (57), 248 (47); HREIMS calcd for $\text{C}_{24}\text{H}_{24}\text{O}_3$ 360.1726, found 360.1685.



54 (5Z)-2-hydroxy-5-((1-hydroxycyclohexyl)methylene)-3-methyl-4-(5-methylfuran-2-yl)cyclopent-2-enone.

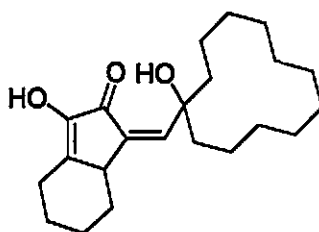
Isolated as a clear oil (143 mg, 64% yield). IR (film): 3316, 1678 cm^{-1} ; ^1H NMR (300 MHz, CDCl_3): δ = 6.15 (d, J = 1.8 Hz, 1 H), 6.02 (d, J = 3.0 Hz, 1 H), 5.88 (dt, J = 3.0, 0.9 Hz, 1 H), 5.40 (bs, 1 H), 4.31 (d, J = 1.8 Hz, 1 H), 2.23 (d, J = 0.8 Hz, 3 H), 1.96 (s, 3 H), 1.82-1.40 (m, 10 H); ^{13}C NMR (75 MHz, CDCl_3): δ = 189.2, 153.4, 152.1, 151.4, 150.2, 138.7, 118.2, 108.0, 106.1, 57.0, 43.4, 33.4, 25.3, 25.2, 20.9, 18.5, 13.2, 11.7; HREIMS calcd for $\text{C}_{18}\text{H}_{22}\text{O}_4$ 302.1518 found 302.1537.



55 (5Z)-2-hydroxy-5-((1-hydroxycyclododecyl)methylene)-3,4-dimethylcyclopent-2-enone.

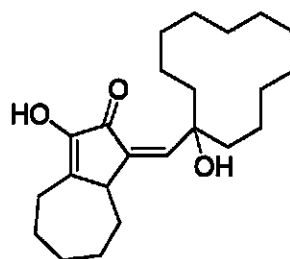
Isolated as a white crystalline solid (198mg, 62%): mp 149-151 $^{\circ}\text{C}$; IR (film): 3340 (br), 2930, 2860, 1680, 1660, 1615, 1110 cm^{-1} ; ^1H NMR (300 MHz, C_6D_6): δ = 6.80 (s, 1 H),

6.50 (bs, 1 H), 5.96 (bs, 1 H), 2.42 (q, $J = 7.0$ Hz, 1 H), 2.05-1.80 (m, 4 H), 1.57 (d, $J = 0.6$ Hz, 3 H), 1.50-1.30 (m, 18 H), 0.75 (d, $J = 7.0$ Hz, 3H); ^{13}C NMR (75 MHz, C_6D_6): $\delta =$ 190.3, 151.6, 148.6, 143.1, 136.2, 75.2, 38.6, 35.4, 35.3, 26.8, 26.4, 22.8, 22.3, 20.3, 20.1, 17.3, 11.3; HREIMS calcd for $\text{C}_{20}\text{H}_{32}\text{O}_3$ 320.2351, found 320.2390.



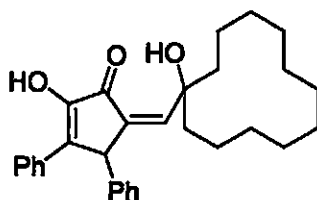
56 (3Z)-3a,4,5,6-tetrahydro-1-hydroxy-3-((1-hydroxycyclododecyl)methylene)-1H-inden-2(4H)-one.

Isolated as a white crystalline solid. (119 mg, 58% yield): mp 154-156 °C. IR (neat): 3310, 2960, 1714, 1665, 1610, 1457, 1414, 1359 cm^{-1} ; ^1H NMR (300 MHz, CDCl_3): $\delta =$ 6.39 (bs, 1 H), 6.19 (s, 1 H), 3.05-2.90 (m, 1 H), 2.81 (dd, $J = 11.7, 5.4$ Hz, 1 H), 2.24-0.80 (m, 29 H); ^{13}C NMR (75 MHz, CDCl_3): $\delta =$ 190.7, 148.8, 147.9, 146.2, 134.9, 75.4, 41.2, 35.1, 35.0, 33.1, 26.6, 26.3, 25.4 (2), 25.1 (2), 22.7 (2), 22.3 (2), 20.2, 19.9; MS: m/z (%) = 346 (M^+ , 100), 328 (51), 150 (86); HREIMS calcd for $\text{C}_{22}\text{H}_{34}\text{O}_3$ 346.2508, found 346.2487.



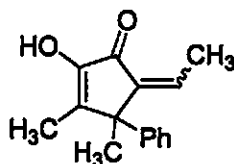
57 (3Z)-3a,4,5,6,7,8-hexahydro-1-hydroxy-3-((1-hydroxycyclododecyl)methylene)azulen-2(1H)-one.

Isolated as a white crystalline solid (120 mg, 67% yield): mp 160-162 °C; IR (neat): 3345, 2927, 2850, 1667, 1610, 1470, 1419 cm^{-1} ; ^1H NMR (300 MHz, CDCl_3): δ = 6.43 (bs, 1 H), 6.24 (s, 1 H), 5.65 (bs, 1 H), 3.14 (d, J = 9.9 Hz, 1 H), 2.82-2.58 (m, 2 H), 2.08 (d, J = 11.7 Hz, 1 H), 2.00-1.71 (m, 5 H), 1.70-1.57 (m, 3 H) 1.50-1.20 (m, 21 H); ^{13}C NMR (75 MHz, CDCl_3): δ = 189.5, 150.2, 149.9, 149.1, 135.5, 75.1, 44.3, 35.1, 34.9, 34.8 (2), 30.6, 29.7, 28.3, 26.4 (2), 26.0, 25.6, 22.5 (2), 22.0, 19.9, 19.8; HREIMS calcd for $\text{C}_{23}\text{H}_{36}\text{O}_3$ 360.2664, found 360.2700.



58 (*5Z*)-2-hydroxy-5-((1-hydroxycyclododecyl)methylene)-3,4-diphenylcyclopent-2-enone.

Isolated as a yellow crystalline solid (106 mg, 66% yield): mp 200-202 °C; IR (film): 3417 (br), 2939, 1665, 1405 cm^{-1} ; ^1H -NMR (300 MHz, CDCl_3): δ = 7.90-7.76 (m, 2 H), 7.40-7.10 (m, 8 H), 6.79 (bs, 1 H), 6.25 (bs, 1 H), 6.08 (s, 1 H), 4.73 (s, 1 H), 1.90-0.80 (m, 22 H); ^{13}C -NMR (75 MHz, CDCl_3): δ = 190.5, 153.6, 151.6, 141.0, 135.0, 135.1, 132.1, 129.5 (2), 129.0 (2), 128.5 (2), 127.4 (2), 127.2 (2), 75.5, 47.8, 34.8, 34.7, 26.3, 26.3, 26.0, 22.4 (2), 22.0, 21.9, 19.5 (2); HREIMS calcd for $\text{C}_{30}\text{H}_{36}\text{O}_3$ 444.2664, found 444.2687.



60 (*5Z*)-5-ethylidene-2-hydroxy-3,4-dimethyl-4-phenylcyclopent-2-enone.

To a solution of methoxymethyl allene ether (88 mg, 0.88 mmol) in 2 mL of THF at

-78 °C was added *n*-BuLi (0.30 mL, 2.78 M in hexanes, 0.83 mmol). After 20 min, a solution of amide **59** (108 mg, 0.44 mmol) in 1 mL THF was added at -78 °C *via* syringe and the reaction mixture warmed to -5 °C and maintained for 90 min. The reaction was then re-cooled to -78 °C, *sec*-BuLi (0.70 mL, 1.33 M in cyclohexane, 0.92 mmol) added and stirred at -78 °C for an additional 20 min. MeI (373 mg, 2.6 mmol) in 3 mL THF was then added at -78 °C *via* cannula and the reaction stirred at -78 °C for 30 min and -30 °C for 30 min and followed by quench with 5% HCl in EtOH at -5 °C. The reaction mixture was allowed to warm to rt over 7 min and was then neutralized with pH 7 buffer. The mixture was extracted with EtOAc (3X) and the combined organic extracts were washed with brine, dried over MgSO₄ and concentrated. The crude residue was purified *via* flash column chromatography on silica gel (10-25% Et₂O in hexanes) to provide **60** (*Z* isomer) as a clear oil and **60** (*E* isomer) as a white crystalline solid (33 mg of *Z* isomer, 26 mg of *E* isomer, 5 mg of a mixture, 64% yield): mp (*E* isomer) 134-136 °C; R_f = 0.42 (*Z*), 0.31 (*E*) (25% Et₂O in Hexanes); IR *Z* isomer: (neat) 3310 (br), 2969, 2932, 1676, 1627 cm⁻¹; *E* isomer: (neat) 3292 (br), 2922, 1679, 1630 cm⁻¹; ¹H NMR (300 MHz, CDCl₃) *Z* isomer: δ = 7.18-7.32 (m, 5 H), 5.84 (q, *J* = 7.4 Hz, 1 H), 2.19 (d, *J* = 7.4, 3 H), 1.69 (s, 3 H), 1.63 (s, 3 H); *E* isomer: δ = 7.18-7.34 (m, 5 H), 6.62 (q, *J* = 7.4 Hz, 1 H), 5.85 (s, 1 H), 1.69 (s, 3 H), 1.65 (s, 3 H), 1.48 (d, *J* = 7.4, 3 H); ¹³C NMR (75 MHz, CDCl₃) *Z* isomer: δ = 191.2, 150.6, 143.7, 143.1, 142.8, 136.7, 128.4, 126.5, 126.5, 48.9, 23.2, 14.3, 9.4; *E* isomer: δ = 189.8, 149.3, 146.4, 143.5, 142.4, 130.7, 128.4, 126.6 (2), 48.2, 21.2, 13.9, 8.9; HREIMS calcd for C₁₅H₁₆O₂ 228.1150 (*E* isomer), found 228.1132.

E. References

1. Bee, C.; Tius, M. A. *Org. Lett.* **2003**, *5*, 1681-1684.
2. (a) Leroux, Y.; Mantione, R. *Tetrahedron Lett.* **1971**, *12*, 591-592. (b) Eisch, J. J.; Behrooz, M.; Galle, J. E. *Tetrahedron Lett.* **1984**, *25*, 4851-4854. (c) Pang, Y.; Petrich, S. S.; Young, V. G., Jr.; Gordon, M. S.; Barton, T. J. *J. Am. Chem. Soc.* **1993**, *115*, 2534-2536. (d) Seyferth, D.; Langer, P.; Döring, M. *Organometallics* **1995**, *14*, 4457-4459. (e) Reich, H. J.; Holladay, J. E.; Walker, T. G.; Thompson, J. L. *J. Am. Chem. Soc.* **1999**, *121*, 9769-9780.
3. Tius, M. A.; Chu, C. C.; Nieves-Colberg, R. *Tetrahedron Lett.* **2001**, *42*, 2419-2422.
4. Harrington, P. E.; Murai, T.; Chu, C.; Tius, M. A. *J. Am. Chem. Soc.* **2002**, *124*, 10091-10100.

