Chapter Three

Allene-Driven Cope Rearrangements

Introduction

The Cope rearrangement refers to [3,3]sigmatropic shift in all-carbon atomic arrays and it is very comparable to its aza and oxa (Claisen rearrangement) variations both in terms of mechanism and synthetic utility.\(^1\)

In the context of allene-driven [3,3]sigmatropic shifts, we envisioned the 1,2-butadiene to 1,3-butadiene conversion functioning as the fuel to pry open six membered carbocycles (Scheme 1).\(^2\) The transformation has potential synthetic utility because the number of known natural products possessing cyclodecene and 1,5-cyclodecadiene core structural motifs is rapidly increasing.\(^3\) The majority of these may be found in the structural family heliangolide. Many of these natural products function in nature as pheromones, antibiotics, and antitumor agents.\(^4\)

The synthesis of 1,5-cyclodecadiene core structures presents a challenge to conventional anionic or electrophilic coupling because developing transannular ring strain\(^5\) in the
transition state of most intramolecular carbon/carbon bond forming reactions hinders the cyclization of carbon chains between eight and fourteen methylene units long.⁶

**Table I.** Strain Energy in Carbocycles

<table>
<thead>
<tr>
<th>Ring Size</th>
<th>$\Delta H_f$ empirical</th>
<th>$\Delta H_f(\text{CH}_2)$</th>
<th>$\Delta H_{\text{strain}}$</th>
</tr>
</thead>
<tbody>
<tr>
<td>6</td>
<td>-29.05</td>
<td>-30.90</td>
<td>1.4</td>
</tr>
<tr>
<td>7</td>
<td>-28.21</td>
<td>-36.05</td>
<td>7.8</td>
</tr>
<tr>
<td>8</td>
<td>-29.73</td>
<td>-41.20</td>
<td>11.5</td>
</tr>
<tr>
<td>9</td>
<td>-31.73</td>
<td>-46.35</td>
<td>14.6</td>
</tr>
<tr>
<td>10</td>
<td>-36.88</td>
<td>-51.50</td>
<td>14.6</td>
</tr>
<tr>
<td>11</td>
<td>-42.87</td>
<td>-56.65</td>
<td>13.8</td>
</tr>
<tr>
<td>12</td>
<td>-55.03</td>
<td>-61.80</td>
<td>6.8</td>
</tr>
<tr>
<td>13</td>
<td>-58.88</td>
<td>-66.95</td>
<td>8.1</td>
</tr>
<tr>
<td>14</td>
<td>-57.13</td>
<td>-72.10</td>
<td>15.0</td>
</tr>
<tr>
<td>15</td>
<td>-72.04</td>
<td>-77.25</td>
<td>5.2</td>
</tr>
<tr>
<td>16</td>
<td>-76.88</td>
<td>-82.40</td>
<td>5.5</td>
</tr>
<tr>
<td>17</td>
<td>-87.07</td>
<td>-87.55</td>
<td>0.5</td>
</tr>
</tbody>
</table>

Table I illustrates the effect of ring size on the heat of formation of carbocycles.⁷ The difference between the $\Delta H_f$ of an idealized acyclic segment possessing only methylene units and the empirical $\Delta H_f$ of the carbocycle is the strain energy. Since the strain energy is a result of nonbonded steric interactions in the ring cavity, the strain should be
alleviated somewhat by the sp² centers in the ring, although good quantitative investigations of this effect in medium sized rings so as to permit generalizations and predict numbers is lacking. Some of the earliest approaches to the synthesis of ten membered carbocycles overcame the thermodynamic problems using fragmentation reaction of bicyclic precursors. Nevertheless, formation of medium sized rings by intramolecular coupling of functionalities has succeeded to varying degrees under conditions of high dilution.

Cope Rearrangement and Ring Expansion

Cope ring expansion occurs with the small highly strained ring systems of divinylcyclopropane\textsuperscript{11} 3.3a (Scheme 2) and 1,2-divinylcyclobutane 3.3b to give cycloheptadienes and cyclooctadienes respectively.\textsuperscript{12} In these cases the equilibrium completely favors the larger rings 3.4 due to the high degree of strain in the starting material. The Cope rearrangement of 3.3a proceeds at -10 °C whereas rearrangement of 3.3b requires warming to 80 °C. It is of interest to note that the facility of the Cope rearrangement does not correlate precisely with strain in these two related cases.
since the strain in both systems is nearly identical. If there were greater bond breaking than bond making in the transition state the four membered ring should rearrange with comparable facility due to the approximate equivalence of release of ring-strain in the two structures. Also, extensive work with substituted acyclic 1,5-dienes reveals that roughly one quarter of the overall exergonicity of the Cope rearrangement is reflected in the rate of the reaction. Thus, increased deformation of the sigma bonds in the cyclopropane ring must exert a stabilizing effect on an advanced transition state.

The Cope rearrangements of 1,2-divinylcarbocycles larger than cyclobutane are usually forbidden by large unfavorable ΔG values. Evans has shown that larger rings can be prepared using the anionic oxy-Cope rearrangement (Scheme 3) wherein the favorable ΔG of enolate formation in 3.6 drives the equilibrium from 3.5 toward the larger ring. Since Evans' discovery, the synthetic utility of the anionic oxy-Cope rearrangement has surfaced many times in the literature. Early work had demonstrated a similar thermodynamic advantage for the
alcohol corresponding to 3.5, but the Evans method has the added advantage of greatly lowering the activation barrier.

In striking contrast to the cope ring expansions in Scheme 2, the equilibrium of the Cope ring expansions of cis-divinylcyclopentane lies heavily in the direction of the smaller five membered ring instead of the nine membered diene. The facility of the Cope ring contraction in these systems depends to a great extent on transition state structure and on the degree of transannular strain in the larger ring. Thus, cis,cis-1,5-cyclononadiene 3.8 requires heating to 220 °C\textsuperscript{16} to establish equilibrium (5:95) between it and 3.7a in favor of the smaller ring. Cis, trans-1,5-nonadiene 3.9 converts completely to 3.7a at 130 °C. To explain the kinetic difference between these two Cope rearrangements, it has been suggested that the conversion of 3.9 involves a chair transition state whereas the conversion of 3.8 has a transition state of boat shaped geometry. Likewise, the rearrangement of 3.10 must pass
through a chair transition state. Cyclic diene 3.10 is known only as a hypothetical intermediate¹⁷ because it rearranges to an 84:16 mixture of cis- and trans-1,2-divinylcyclopentane respectively under conditions in which both 3.8 and 3.9 are stable. Thus, the facility of the conversion of 3.10 to 3.5b must be due to the geometry of the transition state and the transannular strain in the nine membered ring starting material.

**Scheme 5**

In principle, the Cope rearrangement of 1,2-divinyl-cyclohexanes could be applied to the synthesis of 1,5-decadiene ring systems. However, the desired cyclodecadiene is also the unfavored product in a very biased equilibrium, (ΔG = 8–9 kcal mol⁻¹). *Cis,trans*-cyclodecadiene 3.13 in
Scheme 5 rearranges to cis-divinylcyclohexane\(^{18}\) \textbf{3.11} between 120 and 150 °C and the rearrangement is greater than 97% stereoselective.\(^{19}\) Cis,cis-1,5-cyclodecadiene \textbf{3.12} also rearranges\(^{20}\) to \textbf{3.11} although the Cope rearrangement of \textbf{3.12} requires higher temperatures (above 140 °C).

In elegant experimentation, Wharton et. al. have shown that partially resolved trans-1,2-divinylcyclohexane \textbf{3.14} loses optical activity through equilibration with 1,5-cyclodecadiene \textbf{3.15} (Scheme 5).\(^{21}\) The material equilibrates conveniently between 40 °C and 90 °C with an \(E_a\) of 32±1 kcal mol\(^{-1}\) whereas the \(E_a\) of the ring contraction is 25.0 kcal mol\(^{-1}\). The difference between these two numbers, ca 7 kcal mol\(^{-1}\), reflects the difference in energy between the starting material and the product. The \(E_a\) of the degenerate Cope rearrangement of \textbf{3.16} is also 25 kcal mol\(^{-1}\).\(^{22}\) Thus, most of the difference in \(E_a\) of the Cope related system, \textbf{3.15} and \textbf{3.16}, must be attributable to the relative instability of carbocycle \textbf{3.15} compared to the divinylcyclohexane isomer \textbf{3.14}. The authors take the difference in energy between a mono and a 1,2-disubstituted olefin to be 2.5 kcal mol\(^{-1}\). Thus, the difference in energy
between 3.15 and 3.14 is 12 kcal mol⁻¹(2 × 2.5 + 7), when the advantage that 3.15 has in terms of olefinic substitution is taken into account. This energy must be the ring strain in ten membered ring diene 3.15. The authors did not discuss gauche steric interactions in the cyclohexane ring derived from 1,2-divinyl substitution which disappears upon ring expansion. This is worth approximately 1.6 kcal mol⁻¹. ²³ Thus, the strain energy of the 1,5-cyclic diene may be closer to 13.5 kcal mol⁻¹.

**Scheme 6**

![Scheme 6](image)

**Scheme 7**

![Scheme 7](image)

The same selectivity and similar thermodynamic preference for the six membered ring is observed in Cope rearrangements of the natural products with 1,5-cyclodeca-
diene substructures. ²⁴ Germacrene-A 3.17a-c rearranges cleanly to elemene 3.18 upon mild heating (Scheme 6). ²⁵ The high selectivity of the rearrangement is not affected by the presence of more sp² centers in the ring as demonstrated
rearrangement of 3.19 in Scheme 7 to cis-elemene derivative 3.20. However, the rearrangement is sensitive to the geometry of the double bonds involved and to the presence of extraannular rings. Thus, linderalactone 3.22 (Scheme 8) rearranges at 160 °C to a 2:3 equilibrium mixture of iso-linderalactone 3.23 and linderalactone 3.22, however the cis-isomer 3.21 was reported to be thermally stable. The effect of ring fusion is also demonstrated by equilibrium in a related system 3.24 and saussurea lactone 3.25 in Scheme 8. The equilibrium ratio of (1: 2) of 3.24 and 3.25 is established when the sample is warmed to 160 °C.

Scheme 8
The Cope equilibrium of seven-membered 1,2-divinylcycloheptanes favors the seven membered ring. Thus, zerumbone 3.26 rearranges completely to "photozerumbone" 3.27 when heated to 160 °C. However, the trend toward the thermodynamicity of the smaller rings in the 1,2-divinylcycloalkane series appears to end here with the seven-membered rings.

Driven by the transannular ring-strain in the eight membered ring, trans-2,3-divinylcyclooctanone 3.28 undergoes Cope rearrangement 3.28 smoothly at 160 °C to the twelve membered 3.29. Although the authors draw structure 3.29 as a trans, trans-medium ring diene, the experimental (especially the ¹H NMR) gives no spectral evidence for this structure. The double bond geometry was most probably presumed from chair transition state considerations.

Only one report of an unassisted Cope ring expansion
(not an oxy-Cope rearrangement) involving larger rings than seven could be found in the literature. Transannular strain in the medium sized ring 11 membered meta-cyclophane thioether 3.30 drives the equilibrium toward the fifteen membered ring in an exceptionally facile Cope rearrangement which proceeds at 80 °C. The facility of the reaction is probably a composite function of the 3,5- effect of the phenyl substituent and meta-cyclophanyl transannular steric interactions.

**Kinetic Effect of Allene in Cope Rearrangements**

There has been very little work done with the Cope rearrangement of allenes. However, most of the reports contain commentary about moderate increases in reactivity of the sigmatropic shifts involving allenes compared to similar rearrangements involving alkenes. Both of the cyclononatrienes 3.32 and 3.34 should be relatively strain free. However the two structures rearrange at different tempera-

![Scheme 12](image-url)
tures. The Cope rearrangement of 3.32 to 3.33 requires heating to 130-180 °C\textsuperscript{33} whereas the rearrangement of the cis-isomer 3.34 to 3.33 occurs at or below 25 °C.\textsuperscript{34} The argument forwarded again targets transition state geometry. Cis-isomer 3.34 transposes its sigma bonds in a strain-free chair transition state, but geometrical constraints force isomer 3.32, through the more energetic boat transition state. In any case the outcome is thermodynamically counter intuitive because in most medium sized ring systems the trans olefins induce a high degree of strain and it appears that the higher energy structure is converted by a sigmatropic process slower than the lower energy structure.

In a related ring system, germacrene derivatives 3.35 with intraannular allene substructure rearrange to the dehydroelemene derivatives 3.36 upon brief warming to 130 °C.\textsuperscript{35}
In a recent report, anionic oxy-Cope rearrangement is used to expand five, six and seven membered rings with alleny1 substituents.\textsuperscript{36} The authors state that the alleny1 anionic oxy Cope is more facile than its alkenyl counter part because the alleny1 version runs within hours at room temperature. The compounds under study are depicted in Scheme 13. Note that in these systems the mechanism is uncertain. The $\pi$ systems are electronically biased to rearrange by a retro-aldol reaction followed by Michael-type intramolecular cyclization of the resulting extended enolate. Since cyclization to form a 10-membered ring is not likely, the conventional anionic [3,3]sigmatropic rearrangement is the more plausible mechanistic alternative. Regardless of
what the mechanism actually is, these structures are electronically biased for rearrangement. In Evans' original report it is stated that sodium alkoxides accelerate the anionic oxy-Cope rearrangement, however potassium functions better in this capacity.\textsuperscript{37} In many anionic oxy-Cope rearrangements sodium does not produce the desired result at all. The viability of this allenyl anionic oxy-Cope rearrangement at room with sodium as the counter ion could be a function of the allenyl moiety, but this has not been shown conclusively.

In connection with the synthesis of medium ring ketones of commercial importance in the perfume industry, \textbf{3.43} was rearranged to \textbf{3.44} under thermal conditions.\textsuperscript{38} The authors carried out the transformation at 350 °C and did not call much attention to allenic assistance above and beyond what would be expected from an alkenyl variation of this rearrangement. However, the authors did note in the experimental section that \textbf{3.43} rearranges at room temperature while sitting for months.
Stereoselective Cope rearrangement is observed with bridgehead allenyl substituted norbornenes \(^\text{3.45a}\) and \(^\text{3.45b}\) at 160 °C. This observation piques curiosity because the 7-methoxy norbornene isomers \(^\text{3.47}\) and \(^\text{3.48}\) both rearrange to \(^\text{3.49}\) at 250 °C, suggesting homolysis and a common biradical intermediate. It is well known that the methoxy substituent stabilizes \(\alpha\) radicals and would facilitate the cleavage of \(^\text{3.47}\) and \(^\text{3.48}\) to the biradical. Unexpected thermal stability of 7-vinyl-2-norbornene \(^\text{3.50}\) offers further evidence for the biradical nature for the thermolysis of the rearrangement of \(^\text{3.47}\) and \(^\text{3.48}\) in that \(^\text{3.50}\) does not undergo Cope rearrangement at 320 °C.
The authors theorize that through extended overlap of the norbornene double bond with the nonparticipating allenic π bond (depicted in 3.51) the allene moiety in 3.45 offers a lower energy concerted pathway for the Cope rearrangement that is not available to the 7-vinyl and the 7-methoxy-7'-vinyl analogue due to the orthogonal nature of the overlap of the π system, (depicted in 3.52). Similar Möbius interpretations of twisted overlap in allenic structure have been advanced. The Cope rearrangement of 1,2,6-heptatriene is observed when the sample is heated to 160 °C. Unusual facility in the Cope rearrangement of 1,2,6-heptatriene (Scheme 18) has been observed. The authors find the $E_a$ for this rearrangement to be 28.5 kcal mol$^{-1}$ and compare this number in terms of other activation energies of Cope rearrangements involving straight chain alkenes. Observed $E_a$'s for the Cope rearrangement of the 1,5-hexadienes range between 32.5 and 33.5 kcal mol$^{-1}$. This
implies a kinetic effect due to the allenyl substituent of ca -4 kcal mol$^{-1}$.

**Synthesis of the Starting Materials: 1-Allenyl-2-vinyl-cycloalkanes**

In order to realize carbocyclic allene-driven Cope ring expansions, we had need of 1-allenyl-2-vinyl substituted five, six and/or seven membered rings.

Michael addition of the allenyl substituent or Michael addition of a latent allenyl substituent was considered. This synthetic problem was discussed in Chapter 1 so it will not be treated in depth here. Suffice it to say that the compounds we wished to study were not the excellent Michael acceptors discussed in Chapter 1 and 1,4-addition of the propargylic silane failed, except in the case of enone 3.55 wherein Michael addition of the diethylaluminum derivative of propargyldimethylphenylsilane functioned moderately well.$^{44}$
The allene 3.57 was obtained by treatment of Michael adduct 3.56 with TFA. More than one equivalent of freshly distilled TFA was necessary at 25 °C. Protodesilylation yielded allene most efficiently if the reaction was not left to run more than 3-4 h. Invariably, longer exposure to the high acid conditions resulted in decreased yields. Chromatographic separation of the starting propargylic silane 3.56 from keto allene 3.57 was very difficult. In every solvent system tried the two materials coeluted. Nevertheless chloroform elution achieved baseline separation in the tlc by running the chromatogram twice.
Methylenation with the Lombardo reagent at 0 °C gave the benzo-fused six membered ring 3.58 with functionality poised for allenyl Cope ring-expansion. The methylenation step was not optimized. Perhaps better yields than 65-70% should have resulted from this methylenation or perhaps the Lewis acidity of the titaniumtetrachloride recipe resulted in yield limiting destruction of the allene. Quenching the excess reagent after the desired transformation was complete had to be done with care because the quenching step was highly exothermic and haste at this stage resulted in lower yields of the desired product.

Unfortunately, direct methods to transform a carbonyl to a terminal allene have not been reported. There is one such report in the chemical literature involving olefin metathesis through a titanacyclobutane intermediate based on methodology surrounding the development of the Tebbe reagent. Even though the yields reported in the original account were not high (50%) for aliphatic terminal allenes, the directness of the approach would have redeemed some loss in mass. Regrettably this procedure was fruitless in our hands.

Since so many examples of allene syntheses starting with propargylic alcohols and propargylic acetates have been reported, this functionality was chosen
as a synthon for the terminal allenyl substituent.

Clean analysis and spectral interpretation depended on highly cis/trans-selective synthetic procedures for the synthesis of allenylvinylcycloalkanes. Stoichiometric lithium heptynylvinylcuprate was found to be very efficient in this regard for the 1,4-addition of vinyl to 1-acetylcycloalkenes. The stoichiometric lithium divinylcuprate•SMe₂ procedure and the trimethylsilylchloride activated procedure with vinylmagnesium bromide and catalytic CuBr•SMe₂ were less efficient than the method developed here. The afore mentioned procedures for cuprate addition produced a significant amount of 1,2 addition along with the desired vinyl 1,4 adducts, whereas our procedure produced the 1,4-adduct cleanly (less than 4% intervention from 1,2-addition)
In the cyclohexane series, cis-1-acetyl-2-vinyl-cyclohexane 3.61 was available upon kinetic quench of the corresponding copper enolate generated by 1,4 addition of the vinyl cuprate to ketone 3.60 as a 96:4 mixture of ketones 3.61 and 3.67. Trans-2-vinyl-1-acetylcyclohexane (94% diastereomerically pure) was available by acid catalyzed equilibration of cis-ketone 3.61 by mildly heating a
chloroform solution of the ketones in the presence of a catalytic amount of toluenesulfonic acid. In both steps material was recovered in good yield. This procedure had been previously reported and analyzed by the same methods, but more modest claims of diastereoselectivity were made. While both the cis- and trans-material was contaminated by the other diastereomer, further manipulation and purification of the material as the synthetic plan was followed resulted in an improved isomeric ratio. However, isomeric purification was more efficient with cis-substituted 3.61 than with trans-substituted 3.67 and derivatives of the later were not obtained with less than 5% of the cis-diastereomer.

We envisioned carrying the five and the seven membered ring analogues through the same procedure. Even though the vinyl cuprate recipe yielded the 1,4-adduct very efficiently, neither the kinetic quenching of the copper enolate or the equilibration of the ketones was as selective with the five and the seven membered rings as it was for the cyclohexane.

Our procedure for the copper(I) mediated 1,4-addition of vinyl to 1-acetylcyclopentene and 1-acetylcycloheptene efficiently furnished the desired 1,4-vinyl adducts 3.81, 3.82, 3.86 and 3.87 in 85-95% yield with no detectable 1,2-addition (1H NMR). The material was handled in much the same way as
for 3.61, but extra care had to be exercised with the five
membered ring material due to its volatility.

Unfortunately, kinetic quenching of the copper eno-
late of 1-acetyl-2-vinylcyclopentane gave a 1:3 ratio of
diastereomers, 3.81 and 3.82. The same problem was encountered for the copper
enolate of the seven membered ring 3.86 which upon quenching
gave a 1:1 ratio cis:trans of (3.86 and 3.87). The situation
became worse when separation of these materials was
attempted. Neither the cis: trans isomeric mixtures of 3.81
and 3.82 (Scheme 21) or 3.86 and 3.87 (Scheme 22) were
separable chromatographically. Five cycles with a prep HPLC
(Waters500) enabled isolation of a small fraction of trans-
3.86 (70 mg) before band broadening resulted in diminishing
returns.
Equilibration of both the five and the seven membered rings improved the selectivity problem only slightly. The acetylcyclopentane 3.82 reached an equilibrium of 90:10 trans: cis under very mild conditions in the presence of catalytic toluenesulfonic acid, gently heated to 50 °C. Excellent mass recovery was realized after aqueous workup and distillation. The acetylcycloheptanes 3.86 and 3.87 had to be heated to >60 °C at which temperature slow equilibration resulted in an 85:15 ratio of trans:cis with slightly less efficient mass recovery. The equilibrium products of the five and the seven membered ring ketones 3.82 and 3.86 were assumed to be trans-substituted by analogy with the six membered 3.70. This assignment was consistent with the glpc data. The retention time of the more stable isomer was always significantly shorter than the retention time for the other isomer. The assignment was eventually corroborated by the relative reactivity of seven membered vinylallene 3.90 which behaved
much like its corresponding six membered ring analogue.

Midland's procedure for 1,2-addition of lithium acetylide to ketones was used to efficiently make the propargylic alcohols \(3.62, 3.68, 3.80,\) and \(3.68\) from the corresponding ketones. The cis-derived propargylic alcohols were readily separated from one another by chromatography in the case of \(3.62.\) However, the analogous 7-membered adduct \(3.68\) could not be separated unless HPLC purified starting material was used. Acetylide addition to \(3.82\) also occurred smoothly and partial separation of isomers was possible.

**Scheme 23**

![Chemical structures](image)

Similar transformations were performed with benzo-fused ketone \(3.72\) in Scheme 23. The first step was equilibration of isomers with catalytic toluenesulfonic acid. The trans:cis ratio was 98:2, and the material epimerized cleanly
upon mild heating. Greater care was necessary in the addition of acetylide to the trans-isomer of ketone 3.72 in Scheme 23. The conversion was best done using Cl₂CeC≡CSiMe₃ to avoid enolate formation. ⁵² The cerium modification of the reaction conditions allowed for complete 1,2 addition whereas in the absence of the lanthanide salt starting material was always present in the residue after work up. Quantitative deprotection of the silylacetylene to give 3.73 was accomplished by letting the material stand in a solution of 0.2 M MeONa/MeOH.

The propargylic alcohols 3.62, 3.68, 3.73, 3.80 and 3.88 were acylated via the catalytic dimethylaminopyridine protocol of Steglich. ⁵³ This recipe never failed to give the hindered acetate in yields over 80% on all substrates attempted.

**Synthesis of Terminal Allenes**

We chose to study the rearrangement of terminal allenes to avoid characterization of diastereomeric mixtures beyond the cis:trans cycloalkane substitution pattern. 1,3-Disubstituted allenyl moieties would have complicated the spectra by the introduction of axial chirality.

Synthesis of the terminal allenes was problematic. Samarium iodide reduction of propargylic acetates catalyzed
by palladium tetrakistriphenylphosphine \( \text{Pd}\left(\text{P(Ph)}_3\right)_4 \) was employed with limited success. Only low yields of the desired allenes were obtained (40-50%). Unfortunately, no other procedure could be found that competed with this one in terms of purity of the end product. The main competing side reaction in the \( \text{Pd}^0 \) catalyzed procedure produced isomeric olefins that were difficult to identify. Polymeric olefinic material was also isolated. Perhaps the proximity of the vinyl substituent on the six membered ring allowed for competing reactions through intramolecular interception of the \( \pi \) bound transition metal intermediate. No one has ever referenced this procedure for the successful synthesis of allenes after the initial report in 1986. The original paper describes a general procedure providing 90-98% yield. The only other reference to this method in the literature indicated that the procedure was not repeatable.

A recently published recipe involving the interception of a transient allenyl dibutylcopper(III) intermediate at low
temperature\textsuperscript{56} was attempted with acetate 3.63. However, this technique furnished a 1:1 mixture of the desired terminal allene 3.64 and the butylated allene 3.78. The success of the method presumably relies on the ability of the proton source to quench the hypothetical copper(III) intermediate 3.77 before reductive coupling of butyl and allenyl ligands occurs (Scheme 24). The isolation of butylated product 3.78 prompted a temperature threshold study to investigate whether butyl addition could be frozen out. It was discovered that butylation of acetate 3.63 and 3.69 occurred at the same temperature threshold as the desired terminal allene forming reaction. Although the procedure worked moderately well to make 3.79 from an acetate that closely resembles the reported precedent,\textsuperscript{56} the method still could not be applied to the task at hand. The authors stated that their experience with the synthesis of terminal allenes leads them to believe that there are no general solutions to this problem. They also state that the few successful examples are limited to small scale experiments (<1 mmol).\textsuperscript{57}

Efficient transformation of the propargylic alcohols would have obviated the acylation step and produced allenes more directly. We were intrigued by a report by Corey in which an allene was made from Dibal-H reduction of a
propargylic alcohol.\textsuperscript{58} In another report alane was used to carry out the desired synthesis (although competing production of alkynes was also reported).\textsuperscript{59} Neither method was high-yielding with the substrates under study. In some cases mixtures of alkynes and allenes were obtained. In the case of the Corey procedure, the triple bond of the propargylic acetates was reduced to give allylic alcohols accompanied by the desired allenic elimination products. Similar results were obtained with the EtMe\textsubscript{2}N•AlH\textsubscript{3} complex\textsuperscript{60} recently reported for the reduction of various organic functionalities.

In any case, the desired allenes were successfully obtained from the Pd(PPh\textsubscript{3})\textsubscript{4} catalyzed SmI\textsubscript{2} reductive procedure from the corresponding propargylic acetates and via protodesilylation of propargylic silane 3.56. The structures were clear from characteristic IR absorptions (1950–1960 cm\textsuperscript{-1}), \textsuperscript{1}H NMR data, and the \textsuperscript{13}C NMR signal (δ 200–215) for the sp hybridized allenic carbon atom.

**Thermolysis of Allenylvinylcycloalkanes**

We have found that the 1,2-disubstituted cycloalkane systems 3.58, 3.64, 3.70, and 3.75 in synthetic Schemes 19–23 undergo facile Cope rearrangement upon heating in the range of 90 to 140 °C. In the case of trans-substituted 3.64, 3.70
and 3.58 the reactions did not proceed to completion and equilibria favoring the medium sized ring products were observed. The ring expanded products in all cases gave characteristic signals in the $^1$H NMR spectrum at $\delta$ 3.10 - 2.50 for the doubly allylic methylene protons in the ring, and sharp multiplets at $\delta$ 5.20 - 4.80 for the olefinic exocyclic terminal methylenes. These structures were verified with $^{13}$C NMR, and all had the correct carbon count and multiplicity. Geometry at the disubstituted alkene was deduced from the vecinal coupling constant ($^1$H NMR homonuclear decoupling), while the trisubstituted double bond geometry was established using NOE methods as described later.

The benzo-fused six membered ring structure 3.58 established a thermal equilibrium with the ten membered ring 3.59 in a ratio of 2:98 when heated to 120 °C for 2 days (Scheme 25). The rearrangement was exceedingly clean. Unfortunately, the 2% starting material impurity could not be removed from the product using chromatography. As a result the equilibrium could not be approached from the product side to confirm the
equilibrium ratio. The material was quantitatively recovered from toluene-\textit{d8} after the equilibrium had been reached. \textsuperscript{1}H NMR analysis revealed a chiral environment on the NMR time scale producing diastereotopic signals in the \textsuperscript{1}H NMR spectrum from the benzylic, allylic methylene, and the doubly allylic methylene positions in the ten membered ring.

Similar behavior upon thermolysis was observed when the related benzo-fused 3.75 was heated in a degassed NMR solvent. The reaction proceeded smoothly to a 5:95 equilibrium ratio of the starting allene to the ten membered ring product at 120-140 °C. All of the starting mass was recovered quantitatively from pentane elution on silica gel. By carefully shaving chromatographic fractions, ten membered ring material pure enough to study the equilibrium from the product side was obtained ca 99:1, 3.76:3.75 (according to glpc, \textsuperscript{1}H NMR analysis). Resubjecting the purified ten membered ring 3.76 to thermolytic conditions resulted in the reestablishment of the 5:95 equilibrium.

Both of the benzo-fused structures studied (3.75 and 3.58) underwent completely selective, very clean sigmatropic
transposition, but neither reaction went to completion. Detailed evidence to prove the assignment of both of the rearranged structures as E,E-1,5-cyclodecadienes will be presented later.

In contrast, the thermolysis of the parent system 3.70 was less straightforward. Part of the difficulty was that 3.70 was never obtained free of the cis-diastereomer, but there were other complications. Trans-substituted cyclohexane 3.70 equilibrated thermally to a 14:86 ratio of E,E-cyclodecadiene 3.71. The reaction was followed by $^1$H NMR over time at 133 °C as the system approached 86% conversion. Signals from the six membered ring material were replaced by signals assignable to cyclodecadiene derivative 3.71. Further heating did not increase the ratio of product to starting material. Higher temperature thermolysis also had little effect on the outcome. A graph of the time dependence of the ratio of 3.70/[3.70 + 3.71] is presented in Figure 1 on the following page. The thermolysis of 3.70 produced one cyclodecadiene product. This product proved to be isomeric to the

---

**Scheme 27**

![Scheme 27](image)