Silicon Assisted [3+2] Cycloadditions

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Total Synthesis Drives New Methodology

- Discovery of biologically active natural products such as the polyquinanes, steroids, and prostaglandins has prompted many new synthetic methodologies.
- By the early 1980's, much research had gone into the development of new methods to form 5-membered rings.
- There was no synthetic equivalent of the Diels-Alder type reaction for the formation of 5-membered carbocycles.
- In 1981 Danheiser presented a novel silicon assisted [3+2] cyclization to form cyclopentenes.
- This initial discovery has led to the development of many new silicon assisted cyclizations employing silicon, all of which rely on Silicon’s ability to stabilize beta cations.

Dragojlovic, V. *Molecules* 2000, 5, 674
The Beta Effect

- Silicon is a slightly electropositive atom
- Si-C bond stabilizes formed carbocation via hyperconjugation
- Molecular calculations by Jorgensen show the beta carbocation to be stabilized by 38 Kcal/mol (9Kcal/mol for methyl substituent)
- Likewise a Vinyl cation is shown to be stabilized by 29 Kcal/mol (8 Kcal/mol for methyl)

Jorgenson, W. et al. JACS. 1985, 107,1496
[3+2] annulation of an α,β unsaturated ketone and a trimethylsilyl allene

Reaction promoted by 1.5 eq TiCl₄

Relies on trimethylsilyl moiety to stabilize β carbocation, as well as a rearrangement which leads to regioselective formation of the olefin
Proposed Mechanism for Danheiser Annulation
Reactive Substrates: Allenophiles

\[ \text{\(\alpha,\beta\) unsaturated ketone} + \begin{aligned} &\text{H} \\ &\text{H} \\ &\text{SiMe}_3 \end{aligned} \rightarrow \begin{aligned} &\text{CH}_3 \\ &\text{SiMe}_3 \end{aligned} \]

- Ketone: 75%
- Ketone: 65%
- Ketone: 48%
- Ketone: 85%
- Ketone: 90%-94% (83:17, cis:trans)
- Ketone: 66%
- Ketone: 49%
- Ketone: 84%
- Ketone: 86%

Danheiser, R.L. et al. JACS, 1981, 103, 1604
Reactive Substrates: Allenes

Trimethylsilyl allene + cyclohexene $\xrightarrow{\text{TiCl}_4, \text{CH}_2\text{Cl}_2, -75^\circ\text{C}}$ product

\[ \text{H}_2\text{SiMe}_3 \quad \text{H} \quad \text{H} \]

85%

\[ \text{H}_2\text{SiMe}_3 \quad \text{SiMe}_3 \quad \text{H} \quad \text{H} \]

81% - 85%

\[ \text{H}_2\text{SiMe}_3 \quad \text{SiMe}_3 \quad \text{H} \quad \text{H} \]

79% (95-5, exo:endo)

Danheiser, R.L. et al. JACS, 1981, 103, 1604
Stereochemical Consequences...

\[ \text{Attack from Bottom} \]

\[ \text{Attack from Bottom} \]

Stereochemical Consequences

Danheiser, R.L. et al. JACS, 1981, 103, 1604
Limitations of the Danheiser Annulation

- Works Primarily with $\alpha,\beta$ unsaturated ketones
- Does not work with $\alpha,\beta$ unsaturated aldehydes, methacrolein under reaction conditions yields a "complex mixture of products"
- Does not work with nitroolefins
- Reaction of $\alpha,\beta$ unsaturated esters is considerably slow in comparison to the reaction of $\alpha,\beta$ unsaturated ketones (13.5 hrs : 1 hr)
- $\beta,\beta$ disubstituted allenes are unreactive at $-78^\circ\text{C}$, but do react within reasonable times.
- Highly sterically encumbered ketones, such as isophorone, are unreactive
- Substitution at the $\alpha$ position of the allene is a necessity, due to the relative instability of the terminal vinyl cation

Danheiser, R.L. et al. JACS, 1981, 103, 1604
Reaction of Allenylsilanes with Acylysilanes

\[
\text{TBDMS CO} + \text{Me}_3\text{Si} \text{SiMe}_3 \xrightarrow{\text{TiCl}_4, \text{CH}_2\text{Cl}_2, -78^\circ \text{C}} \text{TBDMS CO} \text{SiMe}_3 \xrightarrow{10\% \text{NaOH}, 30\% \text{H}_2\text{O}_2, \text{THF}, 40^\circ \text{C}, 30\text{min}} \text{HO CO} \text{SiMe}_3
\]
72%

\[
\text{Me}_3\text{Si CO} + \text{Me}_3\text{Si SiMe}_3 \xrightarrow{\text{TiCl}_4, \text{CH}_2\text{Cl}_2, -78^\circ \text{C}, 30\text{sec}} \text{Me}_3\text{Si CO} \text{SiMe}_3 \xrightarrow{10\% \text{NaOH}, 30\% \text{H}_2\text{O}_2, \text{THF}, 40^\circ \text{C}, 30\text{min}} \text{HO CO} \text{SiMe}_3
\]
66%

\[
\text{Me}_3\text{Si CO} + \text{Me}_3\text{Si SiMe}_3 \xrightarrow{\text{TiCl}_4, \text{CH}_2\text{Cl}_2, -78^\circ \text{C}, 45\text{min}} \text{Me}_3\text{Si CO} \text{SiMe}_3 \xrightarrow{10\% \text{NaOH}, 30\% \text{H}_2\text{O}_2, \text{THF}, 40^\circ \text{C}, 30\text{min}} \text{HO CO} \text{SiMe}_3
\]
74%

\[
\text{Me}_3\text{Si CO} + \text{Me}_3\text{Si SiMe}_3 \xrightarrow{\text{TiCl}_4, \text{CH}_2\text{Cl}_2, -78^\circ \text{C}, 45\text{min}} \text{Me}_3\text{Si CO} \text{SiMe}_3 \xrightarrow{10\% \text{NaOH}, 30\% \text{H}_2\text{O}_2, \text{THF}, 40^\circ \text{C}, 30\text{min}} \text{HO CO} \text{SiMe}_3
\]
85%

Reaction of Allenylsilanes with Acylsilanes

\[
\begin{align*}
\text{TMS} & \quad \text{SiMe}_3 \quad \text{TiCl}_4, \text{CH}_2\text{Cl}_2, -50^\circ\text{C} \\
\text{H}_3\text{C} & \quad \text{CH}_3 \\
\text{CH}_3 & \quad \text{SiMe}_3
\end{align*}
\]

2 hrs
56%

\[
\begin{align*}
\text{TMS} & \quad \text{SiMe}_3 \quad \text{TiCl}_4, \text{CH}_2\text{Cl}_2, -50^\circ\text{C} \\
\text{H}_3\text{C} & \quad \text{CH}_3 \\
\text{CH}_3 & \quad \text{SiMe}_3 + \text{H}_3\text{C} \quad \text{CH}_3 \\
70:30
\end{align*}
\]

2 hrs
41%

\[
\begin{align*}
\text{TBDMS} & \quad \text{SiMe}_3 \quad \text{TiCl}_4, \text{CH}_2\text{Cl}_2, -78^\circ\text{C} \\
\text{H}_3\text{C} & \quad \text{CH}_3 \\
\text{CH}_3 & \quad \text{SiMe}_3
\end{align*}
\]

2 min
78%

\[
\begin{align*}
\text{TBDMS} & \quad \text{SiMe}_3 \quad \text{TiCl}_4, \text{CH}_2\text{Cl}_2, -78^\circ\text{C} \\
\text{HO} & \quad \text{SiMe}_3
\end{align*}
\]

10% NaOH
30% H_2O_2
THF
40°C, 30 min

Proposed Mechanism for [3+2] 
Cyclopentenannulation with Acylsilanes

Reaction pathway dependent on formation of tertiary carbocation 21
If bulkier Silyl group is used, vinyl shift disfavored due to steric hindrance
Using acyl silanes, cyclopentenyl carboxylic acids and α,β unsaturated

Adaptation of the Danheiser Annulation to the Synthesis of Heterocycles

- Early studies demonstrate annulation reaction conditions with aldehydes and ketones produces homopropargyl alcohols in moderate to high yield
- Chloride anion either assists in desilylation, or is trapped by vinyl cation
- These reactions occur preferentially over cyclization to the dihydrofuran
- Solution: Increase steric bulk around the silicon to depress the rate of desilylation

Danheiser, R.L., Carini, D.J. *JOC*, 1980, 45, 2513
Synthesis of Substituted Dihydrofurans and Alkaloids

$$\text{aldehyde} + \overset{\text{R}_1}{\longrightarrow} \overset{\text{TBDMS}}{\longrightarrow} \text{dihydrofuran}$$

\begin{align*}
\text{R}_1 = \text{H} & \quad \overset{\text{76\%}}{\longrightarrow} \\
\text{Ph} & \quad \overset{\text{70\%}}{\longrightarrow} \\
\text{Bn} & \quad \overset{\text{88\%}}{\longrightarrow} \\
\text{Et} & \quad \overset{\text{(67\%)} \quad \text{1.2:1, cis:trans}}{\longrightarrow} \\
\text{N} & \quad \overset{\text{63\%}}{\longrightarrow} \\
\end{align*}

\text{TBDMS group is difficult to functionalize!}

Danheiser, R.L. et al. JACS, 1985, 107, 7233
Summary of Allene Chemistry

• Excellent regiochemistry imparted by Silicon group
• Predictable stereochemistry due to constraint of the 5-membered ring (usually cis ring juncture)
• Established scope and limitations
• Chiral starting materials lead to chiral products in a predictable fashion
• Functionalization of Silicon group difficult
• Harsh conditions to cleave C-Si bond limit functionality of starting materials
Allylsilanes as Masked 1,3 Dipoles…

\[
\text{SiR}_3 \text{Si} \quad \text{SiR}_3 \quad \text{SiR}_3
\]

Hosomi-Sakurai Reaction (Sakurai allylation)

\[
\text{Cl}_3\text{Ti}^+ \quad \text{O}^+ \quad \text{Cl}_3\text{Ti}\text{O}^+
\]

\[
\text{Cl}_3\text{Ti}^+ \quad \text{O}^+ \quad \text{Cl}_3\text{Ti}\text{O}^+
\]

Knolker’s Observation

Danheiser's Contribution

Chemical reactions and structures are shown with products and reaction conditions.

Danheiser, R.L. et al. JOC, 1992, 57, 6094
Rationalization of Stereochemistry

The Use of Chiral E-crotylsilanes Towards Stereoselective Synthesis of Cyclopentanes

- Addition of chiral crotyl silanes to oxocarbenium ions was studied extensively by Panek
- It was conceived that addition of these nucleophiles to α,β unsaturated ketones would yield the corresponding cyclopentane in high yields and enantiopurity

Panek, J.S., Yang, M. JACS, 1991, 113, 6594
Preparation of Chiral E-crotylsilanes

\[ \text{OH} \xrightarrow{1) \text{Resolution w/ mandelic acid}} \xrightarrow{2) \text{hydrolysis}} \xrightarrow{3) \text{esterification}} \text{OH} \]

\[ \begin{array}{c}
\text{OH} \\
\text{LDA} \\
\text{TMSCl} \\
\text{LHMDS/HMPA} \\
\text{TBSCl} \\
\text{LDA} \\
\text{TMSCl} \\
\text{LDA} \\
\text{TMSCl}
\end{array} \xrightarrow{1. [3,3]} \xrightarrow{2. \text{H}_2\text{O}^+} \xrightarrow{3. \text{MeOH/} \text{SOCl}_2} \]

1. \[ \text{SiMe}_2\text{Ph} \]
2. \[ \text{CO}_2\text{Me} \]
3. \[ \text{80\%} \]

1. \[ \text{SiMe}_2\text{Ph} \]
2. \[ \text{CO}_2\text{Me} \]
3. \[ \text{81\%} \]

1. \[ \text{SiMe}_2\text{Ph} \]
2. \[ \text{CO}_2\text{Me} \]
3. \[ \text{81\%} \]

1. \[ \text{SiMe}_2\text{Ph} \]
2. \[ \text{CO}_2\text{Me} \]
3. \[ \text{69\%} \]

Panek, J.S., Sparks, M.A. JOC, 1991, 56, 3431
Asymmetric Synthesis of Tetrasubstituted Cyclopentanes

Table I. Asymmetric \( [3 + 2] \) Cyclopentane Annulation

<table>
<thead>
<tr>
<th>Crotysilane</th>
<th>( \alpha,\beta )-unsaturated aldehyde/ketone</th>
<th>reaction condns*</th>
<th>major diast**</th>
<th>% yield**</th>
</tr>
</thead>
<tbody>
<tr>
<td>1a</td>
<td>2a</td>
<td>rt/8</td>
<td>3a</td>
<td>93</td>
</tr>
<tr>
<td>1b</td>
<td>2a</td>
<td>rt/12</td>
<td>3b</td>
<td>73</td>
</tr>
<tr>
<td>1c</td>
<td>2a</td>
<td>rt/12</td>
<td>3c</td>
<td>73</td>
</tr>
<tr>
<td>1d</td>
<td>2a</td>
<td>rt/7</td>
<td>3d</td>
<td>65</td>
</tr>
<tr>
<td>1b</td>
<td>2b</td>
<td>rt/5.5</td>
<td>3e</td>
<td>62</td>
</tr>
<tr>
<td>1d</td>
<td>2c</td>
<td>rt/7</td>
<td>3f</td>
<td>51</td>
</tr>
<tr>
<td>1a</td>
<td>2e</td>
<td>rt/7</td>
<td>3g</td>
<td>81</td>
</tr>
<tr>
<td>1a</td>
<td>2d</td>
<td>-10-0/10</td>
<td>3h</td>
<td>56</td>
</tr>
</tbody>
</table>

BF3·OEt2
DCM

cyclopentane

Panek, J.S., Jain, N.F. JOC, 1993, 58, 2345
Stereochemical Rationale

\[
\begin{align*}
\text{(S)-1a} & \quad \text{Me\textsubscript{2}SiPh} \\
\text{BF\textsubscript{3}} & \quad \text{Me\textsubscript{2}SiEt\textsubscript{2}} \\
\end{align*}
\]

\[
\begin{align*}
\text{2a} & \quad \text{MeCHO} \\
\text{Me\textsubscript{2}Si} & \quad \text{Me} \\
\end{align*}
\]

\[
\begin{align*}
\text{3a} & \quad \text{Me\textsubscript{2}Si} \\
\text{Me} & \quad \text{Me} \\
\end{align*}
\]

\[
\begin{align*}
\text{enolate alkylation} & \quad \text{with C1-C2 bond construction} \\
\end{align*}
\]

\[
\begin{align*}
\text{syncinal T.S.} & \quad \text{anti-S\textsubscript{E} addition with asymmetric 4C-5C bond construction} \\
\end{align*}
\]

Masse, C.E., Panek, J.S., CHEMREV, 1995, 95, 1293
Diastereoselective Synthesis of Substituted Furans

<table>
<thead>
<tr>
<th>entry</th>
<th>aldehydes</th>
<th>(E)-crotyllane</th>
<th>reaction cond/Temp/hour</th>
<th>major diastereomer</th>
<th>yield%</th>
<th>4,5-synten%</th>
<th>%de</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>2a</td>
<td>(2S,3S)-1a</td>
<td>-78 °C/15h</td>
<td>3a</td>
<td>85</td>
<td>50</td>
<td>96</td>
</tr>
<tr>
<td>2</td>
<td>2a</td>
<td>(2R,3R)-1b</td>
<td>-78 °C/15h</td>
<td>3b</td>
<td>85</td>
<td>30:1</td>
<td>96</td>
</tr>
<tr>
<td>3</td>
<td>2a</td>
<td>(2R,3S)-1c</td>
<td>-78 °C/15h</td>
<td>3c</td>
<td>80</td>
<td>30:1</td>
<td>96</td>
</tr>
<tr>
<td>4</td>
<td>2a</td>
<td>(2R,3R)-1d</td>
<td>-78 °C/15h</td>
<td>3d</td>
<td>88</td>
<td>30:1</td>
<td>96</td>
</tr>
<tr>
<td>5</td>
<td>2b</td>
<td>1e</td>
<td>-30 °C/15h</td>
<td>3e</td>
<td>85</td>
<td>30:1</td>
<td>96</td>
</tr>
<tr>
<td>6</td>
<td>2b</td>
<td>1d</td>
<td>-30 °C/15h</td>
<td>3f</td>
<td>50</td>
<td>20:1</td>
<td>96</td>
</tr>
</tbody>
</table>

Masse, C.E., Panek, J.S., CHEMREV, 1995, 95, 1293
Panek, J.S., Yang, M. JACS, 1991, 113, 9868
Lewis Acid Control of Diastereoselectivity

\[
\begin{align*}
\text{BnO} & \quad \text{BF}_3\text{OEt}_2 \\
\text{Me} & \quad \text{Me} \\
(2S, 3R)\text{-Silane} & \\
\text{SnCl}_4 & \quad \text{BnO} \\
\text{Me} & \quad \text{Me} \\
(2S, 3R)\text{-Silane} & \\
\end{align*}
\]

2,5-Cis-Tetrahydrofuran
2,5-Trans-Tetrahydrofuran

<table>
<thead>
<tr>
<th>entry</th>
<th>aldehyde</th>
<th>(E)-crotylsilane</th>
<th>reaction condi\textsuperscript{a}</th>
<th>reaction products\textsuperscript{d} (% yield)\textsuperscript{c}</th>
<th>homoallylic alcohol</th>
<th>ratio anti/syn C4/C8 (furan)\textsuperscript{f}</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. 2</td>
<td>OPh &amp; (2S, 3R)-1a</td>
<td>SnCl\textsubscript{4} &amp; -35 °C/12h</td>
<td>Me &amp; OMe</td>
<td>3a (75) &amp; 4a (&lt;5)</td>
<td>&gt;40:1</td>
<td></td>
</tr>
<tr>
<td>2. 2</td>
<td>1a &amp; (2R, 3S)-1b</td>
<td>BF\textsubscript{3}OEt\textsubscript{2} &amp; -25 °C/12h</td>
<td>Me &amp; OMe</td>
<td>3b (50) &amp; 4b (&lt;5)</td>
<td>40:1</td>
<td></td>
</tr>
<tr>
<td>3. 2</td>
<td>(2S, 3R)-1a</td>
<td>BF\textsubscript{3}OEt\textsubscript{2} &amp; -25 °C/12h</td>
<td>Me &amp; OMe</td>
<td>3c (65) &amp; 4c (10)</td>
<td>&gt;40:1</td>
<td></td>
</tr>
<tr>
<td>4. 2</td>
<td>1b &amp; (2S, 3R)-1b</td>
<td>SnCl\textsubscript{4} &amp; -35 °C/12h</td>
<td>Me &amp; OMe</td>
<td>3c (36) &amp; 4c (38)</td>
<td>&gt;40:1</td>
<td></td>
</tr>
</tbody>
</table>
Rationalization of Diastereoselectivity

\[ \text{BnO} \quad (S)\cdot 2 \quad \text{re face addition} \]

\[ \text{Me}_{2}\text{SiPh} \quad \text{(2S,3R)-1a} \]

\[ \text{SnCl}_{4} \]

\[ \text{Me}_{2}\text{SiPh} \quad \text{antiperiplanar} \]

\[ \text{2,5-cis 3b} \]

\[ \text{BnO} \quad (S)\cdot 2 \quad \text{si face addition} \]

\[ \text{Me}_{2}\text{SiPh} \quad \text{synclinal} \]

\[ \text{2,5-trans 3a} \]

Panek, J.S. et al JOC 1993, 58 809
Silylmethyl allylic silanes have rarely been used in organic synthesis. Woerpel and coworkers recognized that, upon reaction with aldehydes, as in the case of Panek's work, a 1,2 silylmigration might occur. If an electron donating group, such as a methylsilyl group was attached, the cation would be doubly stabilized, pushing the reaction to proceed. No general preparation for silylmethyl allylic silanes was known.

Synthesis of Substituted Tetrahydrofurans

<table>
<thead>
<tr>
<th>Entry</th>
<th>Substrate</th>
<th>Lewis Acid (Equiv)</th>
<th>Temperature</th>
<th>Time (h)</th>
<th>Yield (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>(Z)-8</td>
<td>BF₃·OEt₂ (1)</td>
<td>-78 °C → -33 °C</td>
<td>24</td>
<td>No reaction</td>
</tr>
<tr>
<td>2</td>
<td>(Z)-8</td>
<td>BF₃·OEt₂ (1)</td>
<td>0 °C</td>
<td>20</td>
<td>No reaction</td>
</tr>
<tr>
<td>3</td>
<td>(Z)-8</td>
<td>SnBr₄ (1)</td>
<td>-30 °C</td>
<td>20</td>
<td>No reaction</td>
</tr>
<tr>
<td>4</td>
<td>(Z)-8</td>
<td>TiCl₄ (1)</td>
<td>-30 °C</td>
<td>19</td>
<td>Complex mixture</td>
</tr>
<tr>
<td>5</td>
<td>(Z)-8</td>
<td>TiCl₄ (1)</td>
<td>-78 °C</td>
<td>3</td>
<td>25</td>
</tr>
<tr>
<td>6</td>
<td>(Z)-8</td>
<td>TiCl₄ (2)</td>
<td>-90 °C</td>
<td>4</td>
<td>41</td>
</tr>
<tr>
<td>7</td>
<td>(Z)-25</td>
<td>TiCl₄ (2)</td>
<td>-90 °C</td>
<td>4</td>
<td>46</td>
</tr>
</tbody>
</table>

Difference in Reactivities Between E,Z Olefins

Analysis of E-Olefin TS

- For E-olefin there are three approaches that lead to product
- Only anti-periplanar is refuted due to steric factors

Analysis of Z-Olefin TS

- In the case of the Z-olefin, all three transition states are disfavored by steric effects

Diastereoselective Synthesis of Lactones

Scheme 1

\[
\text{R}_3\text{Si} \xrightarrow{\text{ClSO_2-NCO}, \text{CH_2Cl}_2} \text{3a} \xrightarrow{\text{HCl, THF}} \text{5a} \quad (79\%) \quad \text{and} \quad \text{4a} \quad (8\%)
\]

one diastereomer

\[
\begin{align*}
\text{Cl-SO}_2\text{N} & \quad \xrightarrow{\text{-Nu}} \quad \text{Cl-SO}_2\text{NO}_2^- \\
\text{Cl-SO}_2\text{NO} & \quad \xrightarrow{\text{-}} \quad \text{Cl-SO}_2\text{NO}_2^- \\
\end{align*}
\]

Gamma butyrolactones are found in a variety of natural products

Studies to Determine O,N selectivity

Table 1. Annulation Reactions of Allylic Silanes with CISO₂NCO⁺

<table>
<thead>
<tr>
<th>Allylic Silane ²</th>
<th>[Z/M]²</th>
<th>Products</th>
<th>Yields (Diastereomer ratio)³</th>
</tr>
</thead>
<tbody>
<tr>
<td>R₃Si-CH=CHMe</td>
<td>1:6</td>
<td>5b, 4b</td>
<td>16% (95:5), 77% (98:2)</td>
</tr>
<tr>
<td>R₃Si-CH=CHMe</td>
<td>1:2</td>
<td>2c, 5c</td>
<td>30% (98:2), 57% (99:1)</td>
</tr>
<tr>
<td>R₃Si-CH=CHt-Bu</td>
<td>&gt;20:1</td>
<td>2d, 5d</td>
<td>61% (≥99:1), 1%</td>
</tr>
<tr>
<td>R₃Si-CH=CHMe</td>
<td>&gt;20:1</td>
<td>2e, 5e</td>
<td>81% (94:6), 3%</td>
</tr>
<tr>
<td>R₃Si-CH=CHMe</td>
<td>8:1</td>
<td>8f, 5f</td>
<td>82% (≥96:4), 8%</td>
</tr>
<tr>
<td>R₃Si-CH=CHMe</td>
<td>1:1</td>
<td>5g, 4g</td>
<td>37% (91:9), 42% (91:9)</td>
</tr>
</tbody>
</table>

² ²⁵0°C, ¹ ¹, ³ ¹, ⁴ ¹, ⁵ ¹, ⁶ ¹

[1,2]-Si shift

Favored: R¹ = large, R² = small

N-Cyclization

Favored: R¹ = small, R² = large

O-Cyclization

Total Synthesis of Blastomycin

- 13% yield over 13 steps
- 3 contiguous stereocenters set selectively in one step
- Methylsilyl allylsilanes are reactive starting material whose chemistry has yet to be fully explored

Conclusion

• Silicon assisted [3+2] cyclization reactions have been carried out using allenyl, and allyl silanes
• There are predictable, diastereoselective syntheses in the literature for carbocycles as well as heterocycles
• The Danheiser annulation as well as early allyl cyclizations suffer from alkyl silyl groups that are difficult to manipulate
• Later syntheses employ activated silanes that can undergo stereoselective functionalization
• Much work has yet to be accomplished in all examples, primarily in the silyl methyl allylic silanes
• Although well studied, few total syntheses employ this methodology