Silacyclopropanes

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Outline

• History
• Synthesis
• Reactions of Silacyclopropanes
• Applications to Synthesis
• Summary/Conclusion
Prior Attempts

Many attempts to synthesize silacycloprenanes

Failure can be attributed to the excessive ring strain introduced by the silicon atom

First Isolated Silacyclopropane

Prior to Seyferth's work, attempts to synthesize silacyclopropanes were directed toward "lightly" substituted silacyclopropanes.

Wurtz type coupling

Still, the question remains: are all siliranes stable? Is there something special about the dispiro structure? If the dispiro structure was important, was it important due to steric bulk or electronic factors?

Other Isolated Silacyclopropanes

- Stable under an inert atmosphere at room temp for about 9 days
dispiro system has a half life of 7 days at 63 °C

- Seyferth suggests that electronic as well as steric factors are important in making the dispiro silacyclopropanes so stable

- Proposed that the dispiro compound is stabilized considerable by hyperconjugation (overlap of the filled Walsh orbitals of the spiroannelated cyclopropane ring with vacant silicon 3d orbitals

Synthesis of Silacyclop propane s

Metal Mediated Silylene Transfer

short coming: siliranes generated under these conditions are unstable giving rise to isomeric products

Synthesis of Silacyclopropanes

Thermal generation of silylenes

![Chemical structure](image)

Broad functional group tolerance, increased yields
Cannot be used for cyclohexenes or 1,1 disubstituted alkenes

Generation of di-tert-butyilsilenoid by lithium reduction of tBu₂SiCl₂

![Chemical structure](image)

Investigated the influence of an ether substituent on the reaction. Ether functionality does not direct silacyclopropanation. Not as broad of a scope as the thermal reaction.

Reactions of Silacyclopropanes: Insertions


Stereochemically and regiochemically defined insertions of aldehydes
Outcome is dictated by reaction conditions
Further elaborated into 1,3 diols

<table>
<thead>
<tr>
<th>silirane</th>
<th>conditions</th>
<th>1B</th>
<th>1C</th>
<th>1D</th>
<th>1E</th>
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<tbody>
<tr>
<td>trans A</td>
<td>100 °C</td>
<td>75</td>
<td>7</td>
<td>8</td>
<td>10</td>
</tr>
<tr>
<td>cis A</td>
<td>100 °C</td>
<td>48</td>
<td>6</td>
<td>32</td>
<td>14</td>
</tr>
<tr>
<td>trans A</td>
<td>25% KOt-Bu/ 18-crown-6</td>
<td>3</td>
<td>1</td>
<td>13</td>
<td>83</td>
</tr>
<tr>
<td>cis A</td>
<td>10% Of-Bu/ 18-crown-6</td>
<td>69</td>
<td>30</td>
<td>&lt;1</td>
<td>&lt;1</td>
</tr>
</tbody>
</table>

Reactions of Silacyclopropanes: Insertions

One Atom Insertions:

Reactions of Silacyclopropanes: Insertions

Metal catalyzed Insertion reactions of formamides are stereospecific

![Chemical structures](attachment:chemical_structures.png)

Reactions of Silacyclopropanes: Imines

\[ \text{R}^1 = \text{N} \quad \text{R}^2 \]

\[ \text{AgO Tf (5-10 mol\%)} \quad \xrightarrow{4\pi \text{ electrolyzation}} \quad \text{R}^1 = \text{N} \quad \text{R}^2 \]

\[ \text{R}^1 = \text{N} \quad \text{R}^2 = \text{Y} \quad \text{R}^3 \]

\[ \text{AgO Tf (5-10 mol\%)} \quad \xrightarrow{6\pi \text{ electrolyzation}} \quad \text{R}^1 = \text{N} \quad \text{R}^2 = \text{Y} \quad \text{R}^3 \]

\[ \text{PhCHO} \quad \text{AgO Tf (1 mol\%)} \quad \xrightarrow{\text{Bn}} \quad \text{Ph} \]

\[ \text{t-BuNC} \quad \xrightarrow{\text{t-BuNC}} \quad \text{t-BuNC} \]

\[ \text{R}^3 \equiv \text{H} \quad \text{Pd(PPh)}_3 \text{(1 mol\%)} \quad \xrightarrow{} \quad \text{R}^3 \equiv \text{N} \quad \text{R}^2 \]

Reactions of Silacyclopropanes: Imines

Nevarez, Z.; Woerpel, K. *Org. Lett.* 9, 3773.
Interesting Transformations of Silacyclopropanes

Interesting Transformations of Silacyclopropanes

\[
\begin{aligned}
\text{O}_2\text{CCF}_3 (0.5 \text{ mol}) & \quad \rightarrow \\
\text{SiOBn}(\text{tBu})_2 & \quad \rightarrow \\
\text{ClSO}_2\text{NCO}; \text{HCl} & \quad \rightarrow \\
\text{(tBu)}_2\text{BnOSi} & \quad \rightarrow \\
\end{aligned}
\]

Hint:

\[
\begin{aligned}
\text{Si} & \quad \rightarrow \\
\text{tBu} & \quad \rightarrow \\
\text{tBu} & \quad \rightarrow \\
\text{tBu} & \quad \rightarrow \\
\end{aligned}
\]

Interesting Transformations of Silacyclopropanes

Interesting Transformations of Silacyclopropanes

Application To Total Synthesis: (+/-)-Epi-Stegobinone

- Female-produced sex pheromone of the drugstore beetle and the furniture beetle
- Readily isomerizes to epi-stegobinone, which is a repellent to the male species

Synthesis

\[ \text{Me} = \text{Me} \rightarrow \text{AgOCOCF}_3 \text{(1-2 mol %)} \]

\[ \begin{array}{c}
\text{Si} \\
\text{Bn} \\
\hline
\text{Me} \end{array} \]

\[ \text{CHO} \]

\[ \begin{array}{c}
\text{Bn} \\
\text{N} \\
\text{Me} \end{array} \]

\[ \text{Cu} \]

\[ \text{CuSO}_4 \text{(aq), Ac}_2\text{O} \]

74%

\[ \begin{array}{c}
\text{X} \\
\text{Me} \\
\text{Cu} \\
\text{N} \\
\text{Me} \end{array} \]

\[ \text{CHO} \]

\[ \text{Bn} \]

\[ \begin{array}{c}
\text{N} \\
\text{Me} \end{array} \]

\[ \begin{array}{c}
\text{Me} \\
\text{Me} \\
\text{t-Bu} \\
\text{t-Bu} \end{array} \]

\[ \text{OSiMe}_3 \]

\[ \text{Et} \]

\[ \text{Me} \]

\[ \text{Et} \]

\[ \text{Me} \]

\[ \text{Me} \]

97:2:1 dr

1. \text{Ph}_3\text{PCH}_3\text{Br} \\
\text{n-BuLi}, 79%

2. \text{PhMe}_2\text{C(OOH)} \\
\text{KH, CsF}, 94%

Completed Synthesis

1. $t$-Bu$_2$Si(OTf)$_2$, 2,6-lutidine, 80%
2. $O_3$, PPh$_3$

$t$-Bu $t$-Bu

1. Ac$_2$O, 97%
2. HF-pyridine
3. TBDMSCI

58% over 2 steps

R = TBDMS

$i$-Bu$_2$AlH, 93%

Dess-Martin, 48%

Conclusion

• There are several ways to synthesize silacyclopropanes
  – Photochemical trapping of silylenes
  – Metal mediated transfer of silylenoids
  – Thermal generation of silylenes
  – Lithium assisted generation of silenoids through $\alpha$-elimination
• Aldehydes, formamides, isocyanides, and imines all undergo insertion reactions with silycyclopropanes
• Products of insertions between silycyclopropanes can be manipulated to form 1,3 diols, enantioenriched $\alpha$-hydroxy carboxylic acids (with 2 contiguous stereocenters), and various 5 membered rings
• Reactions of silacyclopropanes have been applied to several syntheses including the total synthesis of (+/-)-Epi-Stegobinone
Further Reading

• mini review:

• transition state structures/ explanations for attack on 5-membered ring oxacarbenium ions:

• Ireland Claisen methodology: