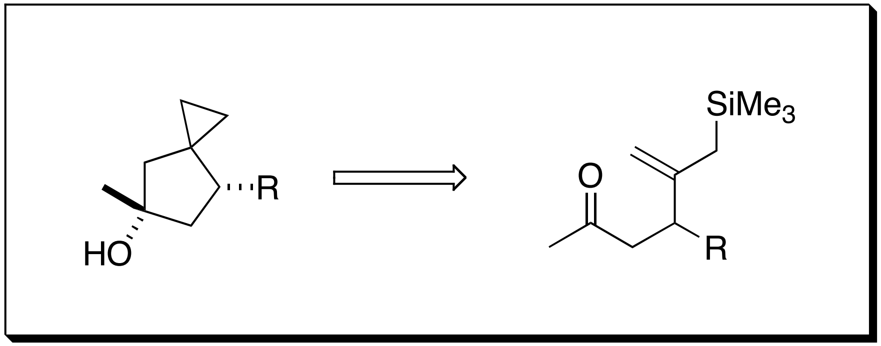
Spiro-Cyclopropanation from Oxoallylsilanes

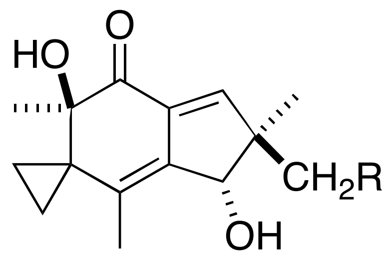
Barbero, A.; Castreno, P.; Pulido, F. J. *JACS*, **2005** *ASAP*

Claire Coleman Current Literature Presentation
June 4 2005



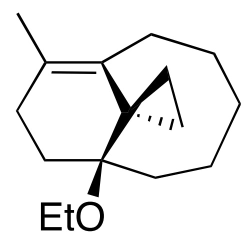
Importance of the Spirocyclopropyl Moiety

Stereoselective synthesis of cyclopropanes important in natural product synthesis
The spirocyclopropyl moiety is present in the skeleton of illudin M and taxane-AB fragment



R = H ***illudin M***

R = OH ***illudin S***



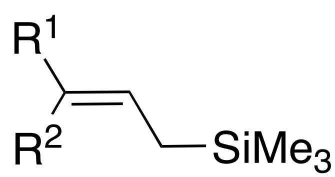
Taxane-AB-Fragment

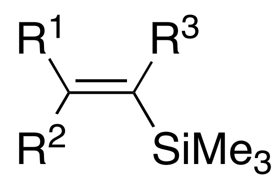
Tett. Lett., *41*, **2000**, 5923-5926.
Synlett, ***2002***, *814*-816.

Organo-Silicon Chemistry – A Cornerstone of Organic Synthesis

Allyl- and vinylsilanes are most useful

- stable towards a wide range of reagents and common FGI's
- useful in cyclization reactions

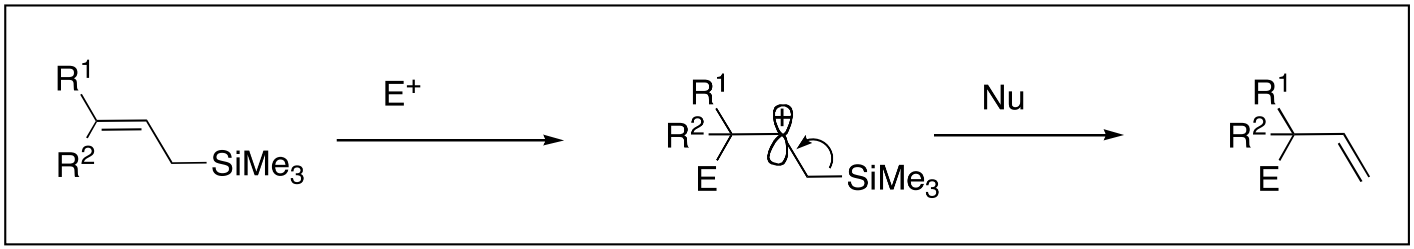




Chem. Rev. **1995**, *95,* 1375-1408.

Allylsilanes

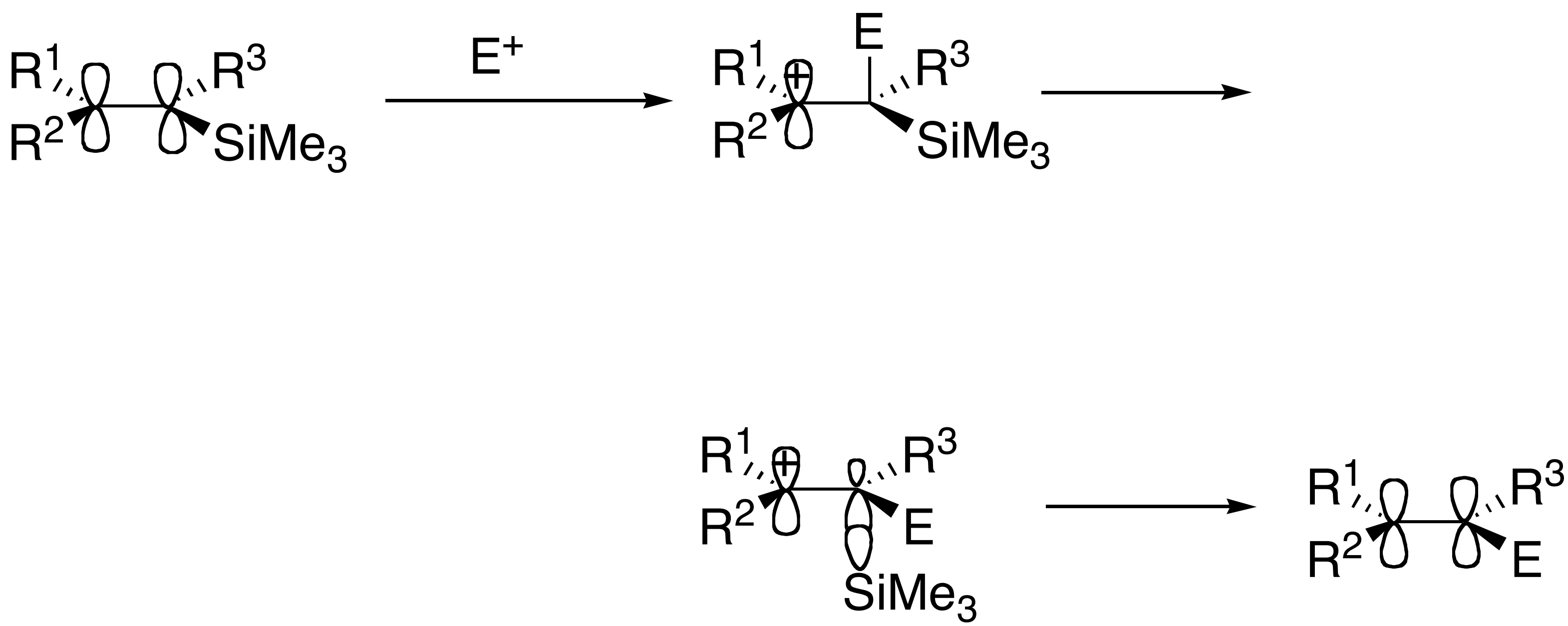
Attack by electrophile at γ-carbon to form β-cation relative to Si
C-Si bond stabilization via σ-π conjugation (β-effect)



Chem. Rev. **1995,** *95*, 1375-1408

Vinyl silanes

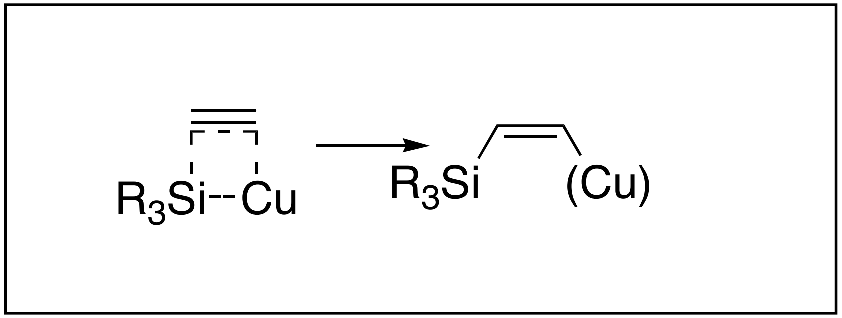
Electrophilic substitution takes place at Si-bearing carbon

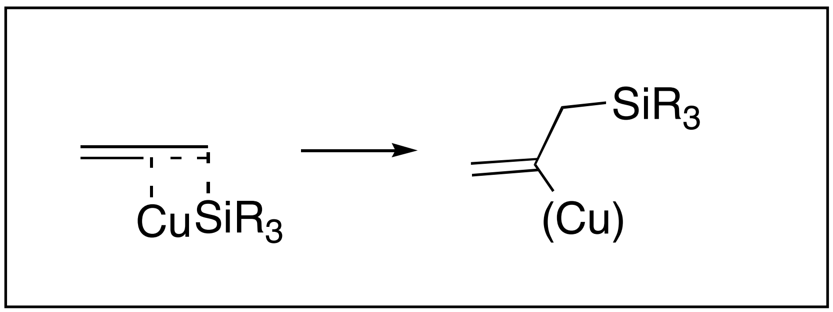


Chem. Rev. **1995,** *95*, 1375-1408

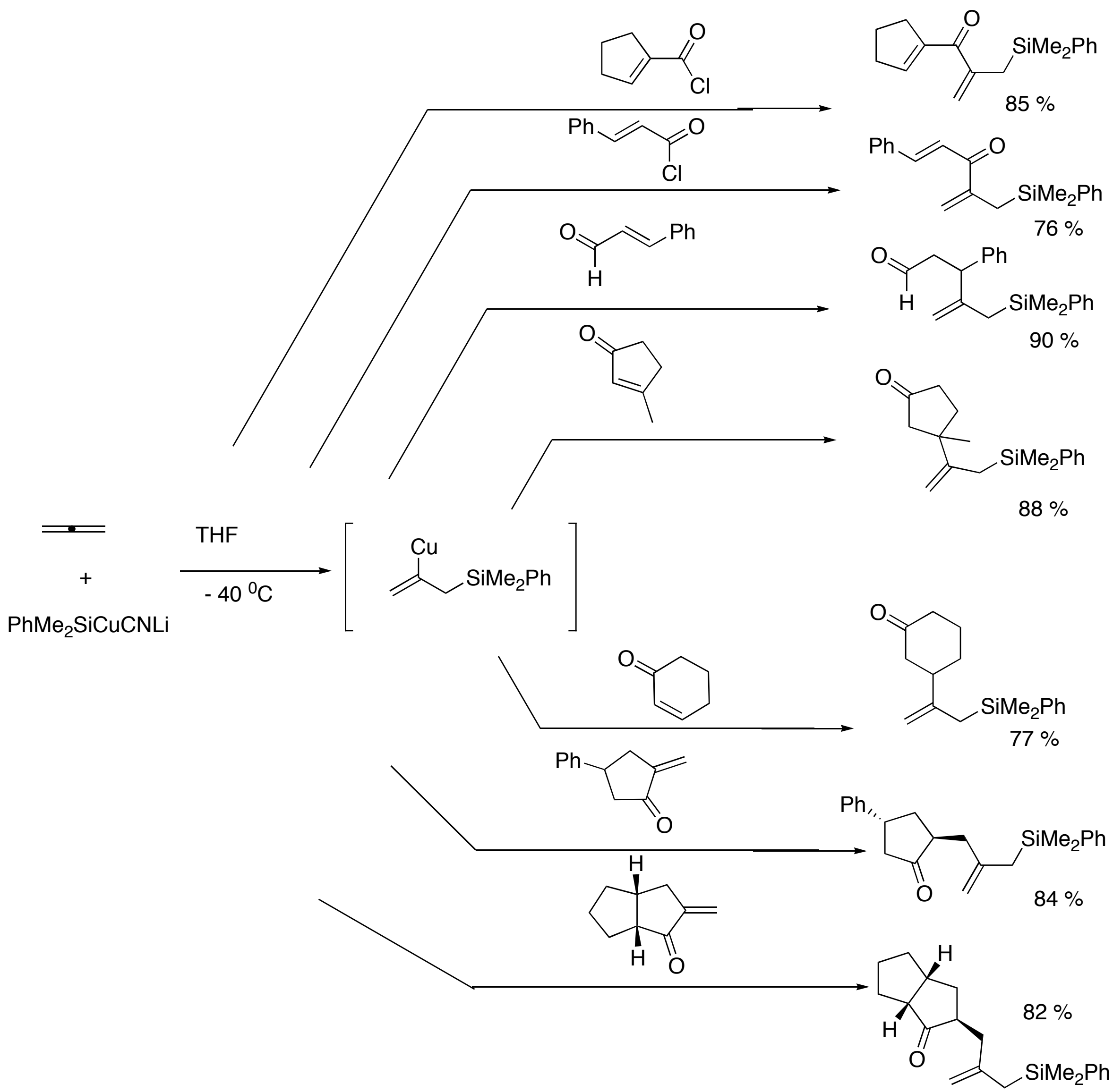
Preparation

Silylmetallation of multiple bonds (allenes and acetylenes)
The intermediate cuprates react with electrophiles to form vinyl- or allylsilanes

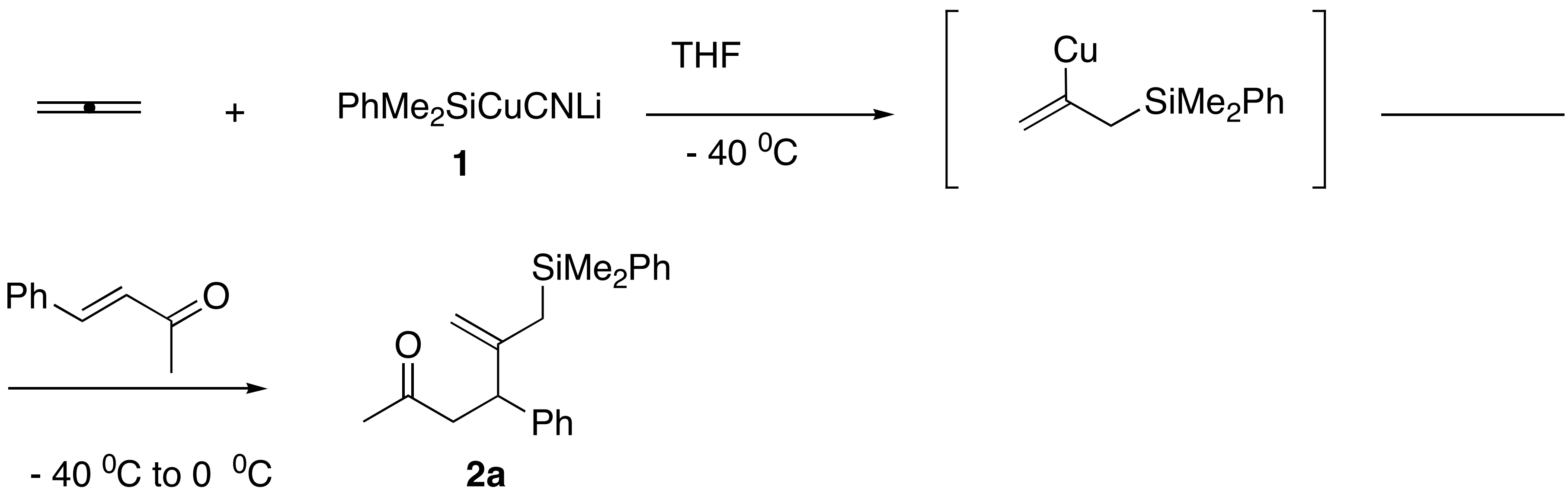




Acc. Chem. Res., **2004**, *37*, 827-825

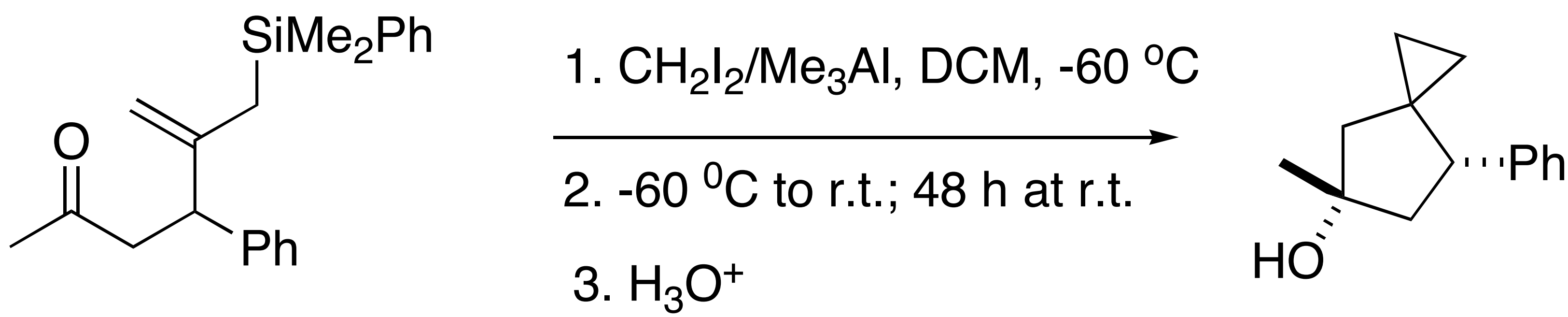

THF
- 40 0C
PhMe2SiCuCNLi
Cu
SiMe2Ph
O
Cl
Ph
H
85 %
76 %
90 %
88 %
77 %
84 %
82 %

Synthesis of starting material Oxoallylsilanes



One pot reaction proceeds under mild conditions

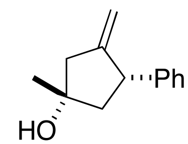
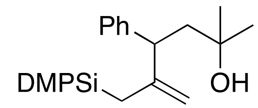
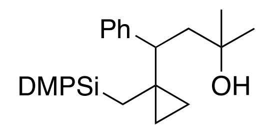
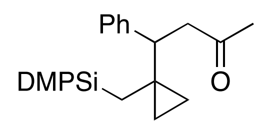
Spirocyclopropanation from oxoallylsilanes (optimized conditions shown)



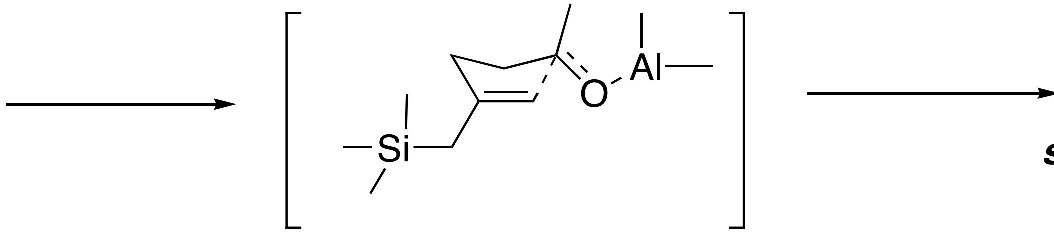
2a **3a**

Optimization included

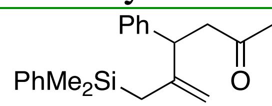
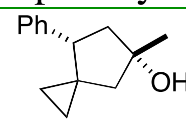
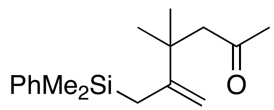
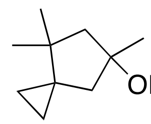
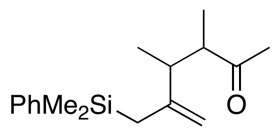
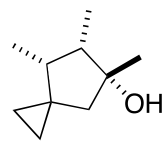
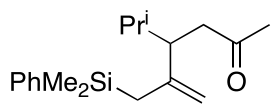
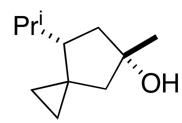
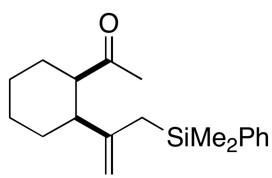
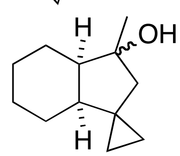
- solvent
- time
- reagent-to-substrate ratio
- use of different organometallics (Al or Zn)

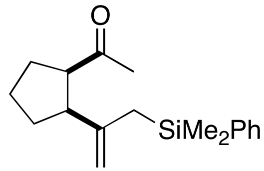
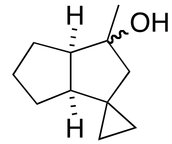
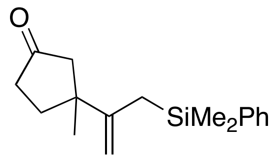
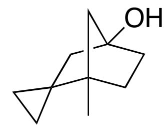
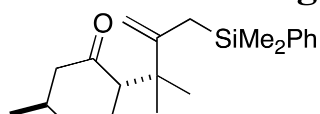
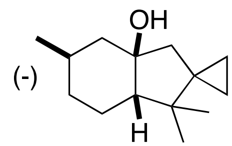
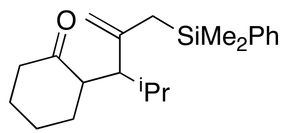
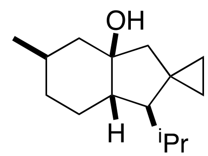
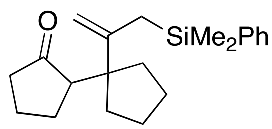
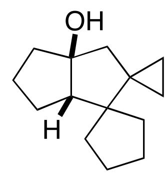
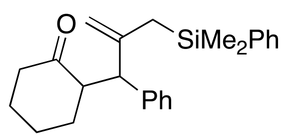
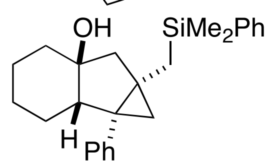
Entry	Comp(1eq.)	Reagent ratio Solvent	T ^{0}C t (h)	Products (yield)
1	**2a**	CH_2I_2/Me_3Al (2:2), DCM	-60 (48)	**3a** (75)
2	**2a**	CH_2I_2/Me_3Al (2:2), DCM	-60 (24)	**3a** (43) (28)  **(4)**
3	**2a**	CH_2I_2/Me_3Al (2:2), DCM	-40 (48)	**3a** (30) + **5** (44)  **(5)**
4	**2a**	CH_2I_2/Me_3Al (2:2), toluene	-60 (48)	**3a** (21) + **5** (46) + **2a** (15)
5	**2a**	CH_2I_2/Me_3Al (2:3), DCM	-60 (48)	**3a** (12) + (70%) **6**  **(6)**
6	**2a**	CH_2I_2/Me_3Al (1:1), DCM	-60 (60)	**3a** (17) + **4** (11) + **5** (33) +**2a** (19)
7	**2a**	CH_2I_2/Et_2Zn (2:2), DCM	-60 (48)	**3a** (43) + **7** (35)  **(7)**
8	**2a**	Me_3Al (2 eq.) DCM	60 (2)	**5** (90)
9	**2a**	$CH_2I_2/Et_2Zn/TFA$ (2:2:2), DCM	0 (4) 4	**7** (88)

2
oxoallylsilane



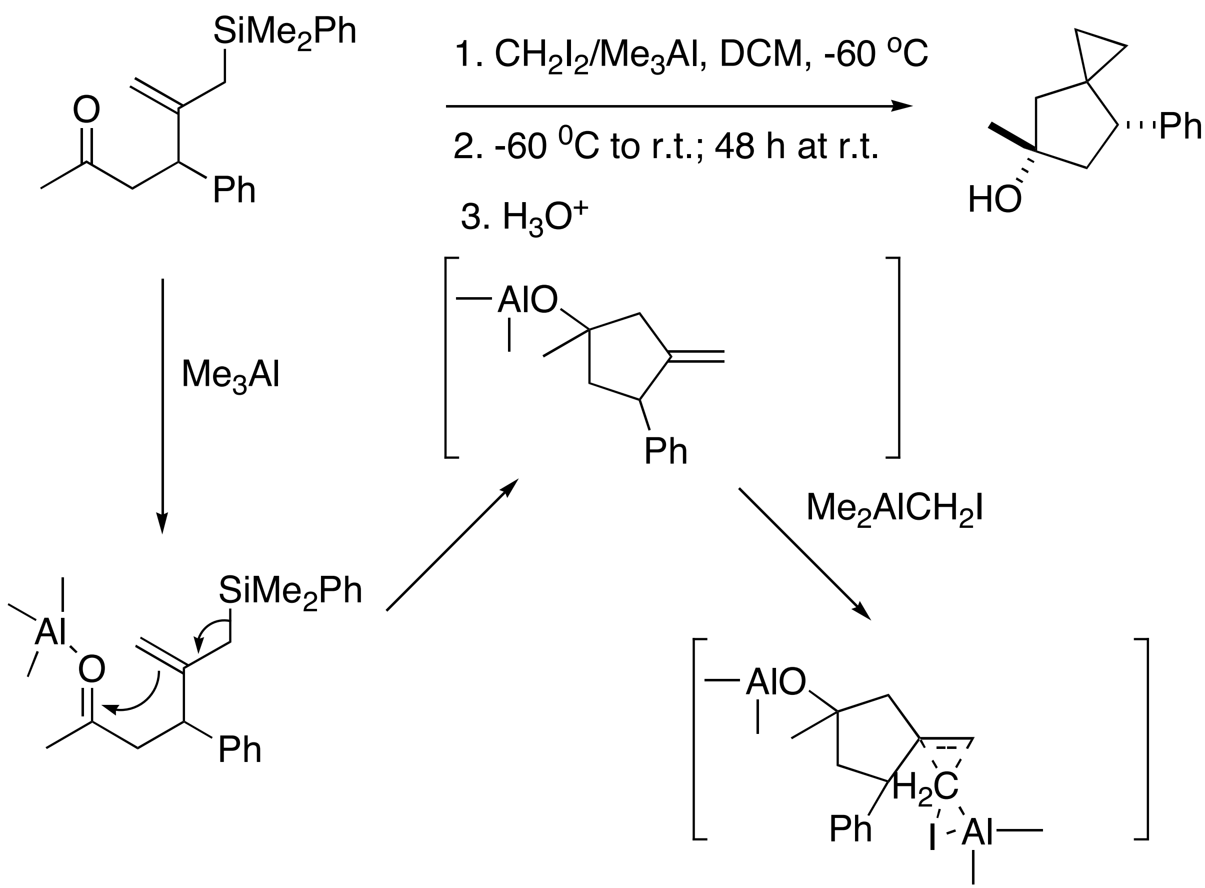
3
spirocyclopropane

Entry	Oxoallylsilane	Spiro-cyclopropane	Yield %[a]
1	 **2a**		75
2	 **2b**		92
3	 **2c**		88
4[b]	 **2d**		52
5	 **2e**		72[c]

6	 **2f**		77[6]
7	 **2g**		58
8	 **2h**		79
9	 **2i**		88
10	 **2j**		80
11	 **2k**		72

[a]Isolated pure compounds
[b]Reagent used: CH_2I_2/Et_2Zn
[c]Epimeric ratio 3:1

Mechanism of Reaction

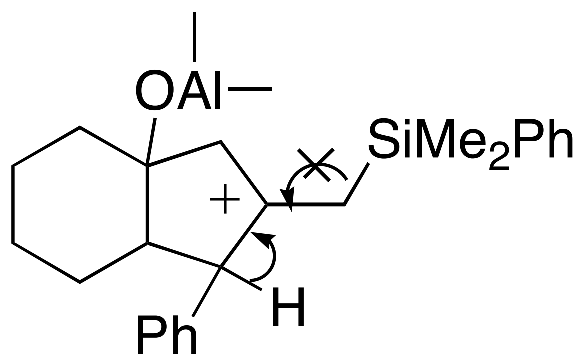


Conclusions

- new spirocyclopropanation from oxoallylsilanes (mild conditions) in one step

Future directions

- Use of methodology in natural product synthesis


OAl
SiMe2Ph
+
Ph
H