DANHEISER CYCLOPENTENE ANNULATION

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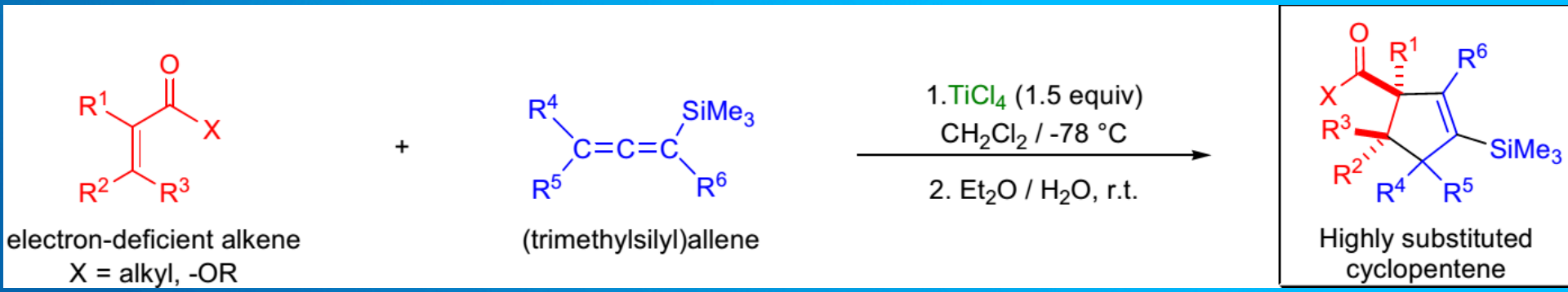
Rick Lane Danheiser
A C Cope Professor of Chemistry， MIT

- Rick Danheiser grew up in New York and California and received his undergraduate education at ***Columbia College***. While working as an undergraduate under the direction ***of Professor Gilbert Stork***, Dr. Danheiser developed a method for the regiospecific alkylation of ß-diketone enol ethers (the "Stork-Danheiser Alkylation") and employed it in a total synthesis of the spiro sesquiterpene ß-vetivone. Professor Danheiser received his Ph.D. at Harvard University in 1978. His doctoral research (under the direction ***of Professor E. J. Corey***) involved the first total synthesis of the diterpene plant growth hormone gibberellic acid.

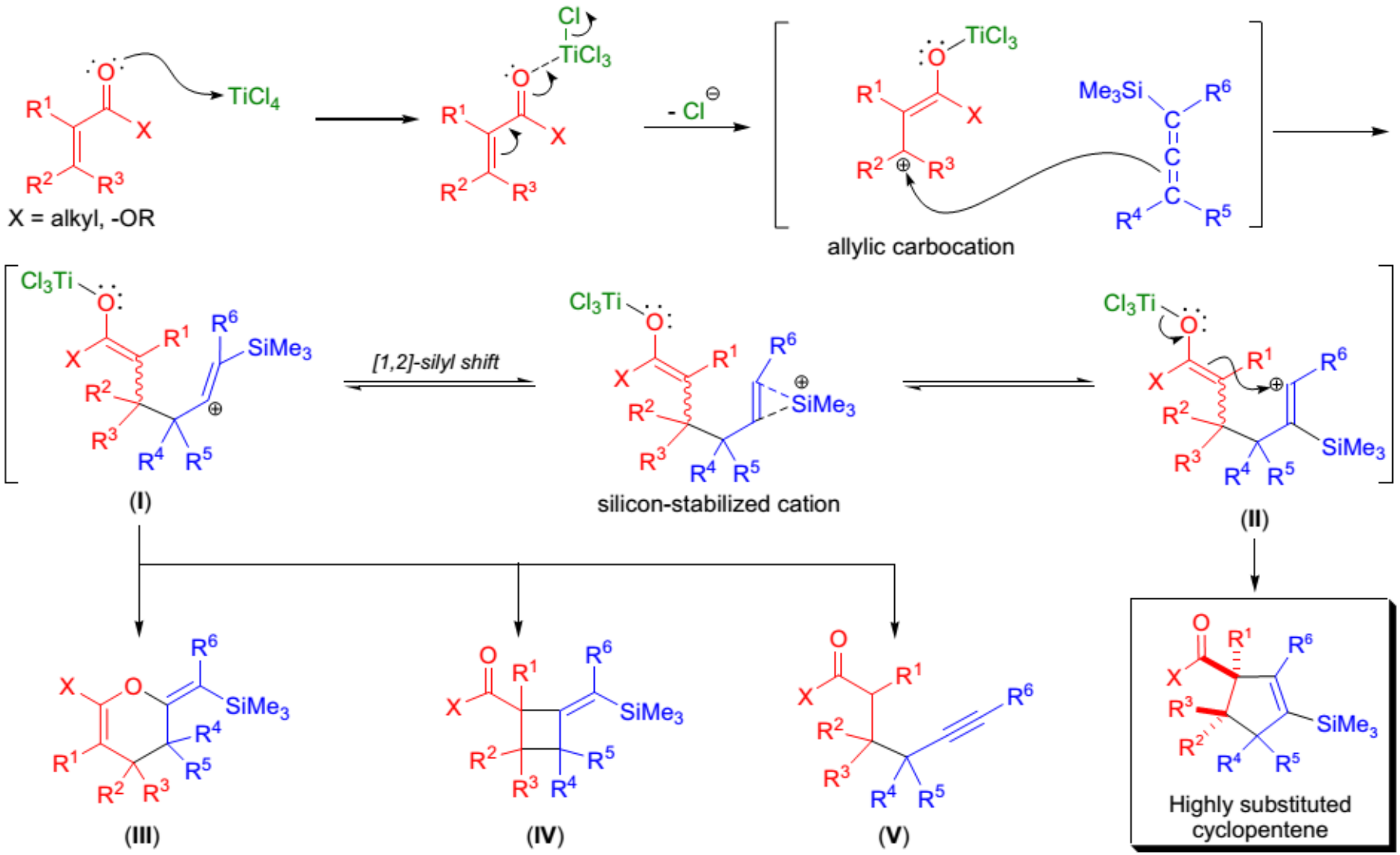
- Dr. Danheiser joined the faculty of the Massachusetts Institute of Technology in 1978 and at present is the Arthur C. Cope Professor of Chemistry.

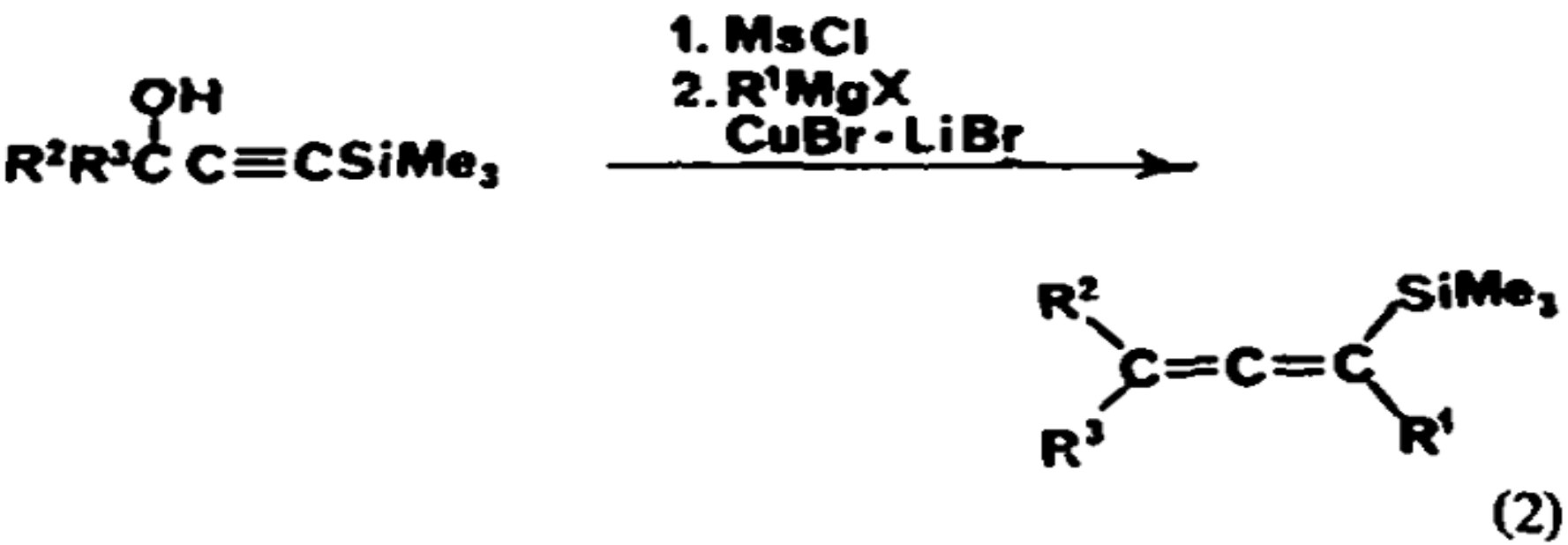
DANHEISER CYCLOPENTENE ANNULATION



- The one-step regio- and stereoselective [3+2] annulation of (trimethylsilyl)allenes and electron-deficient alkenes (allenophiles) in the presence of titanium tetrachloride (TiCl4) to produce highly substituted cyclopentene derivatives is referred to as the ***Danheiser cyclopentene annulation***.

Mechanism


TiCl4
X = alkyl, -OR
- Cl
allylic carbocation
[1,2]-silyl shift
silicon-stabilized cation
(I)
(II)
(III)
(IV)
(V)
Highly substituted cyclopentene



(2)

a $R^1 = Me, \quad R^2, R^3 = H$

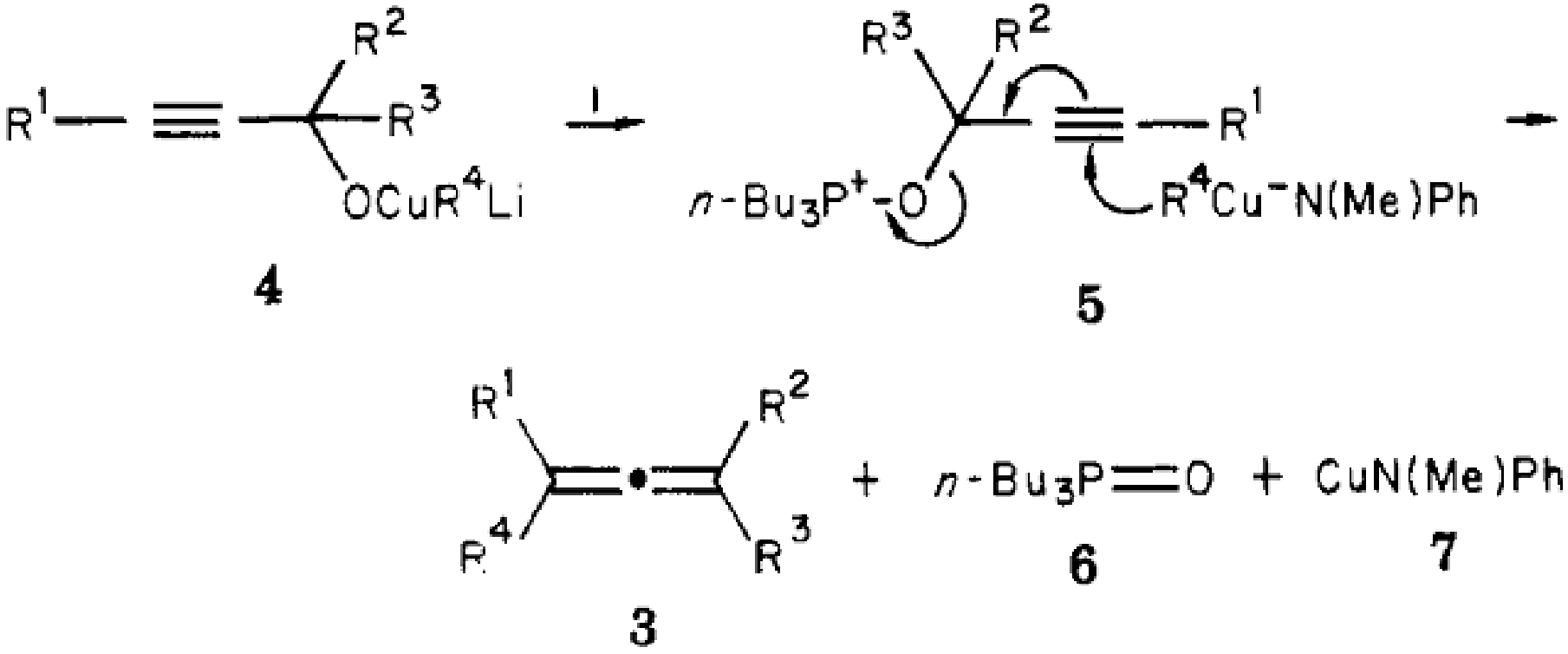
b $R^1 = iPr, \; R^2, R^3 = H$

c $R^1, R^2 = Me, \; R^3 = H$

d $R^1 = Me, \; R^2 = Et, \; R^3 = H$

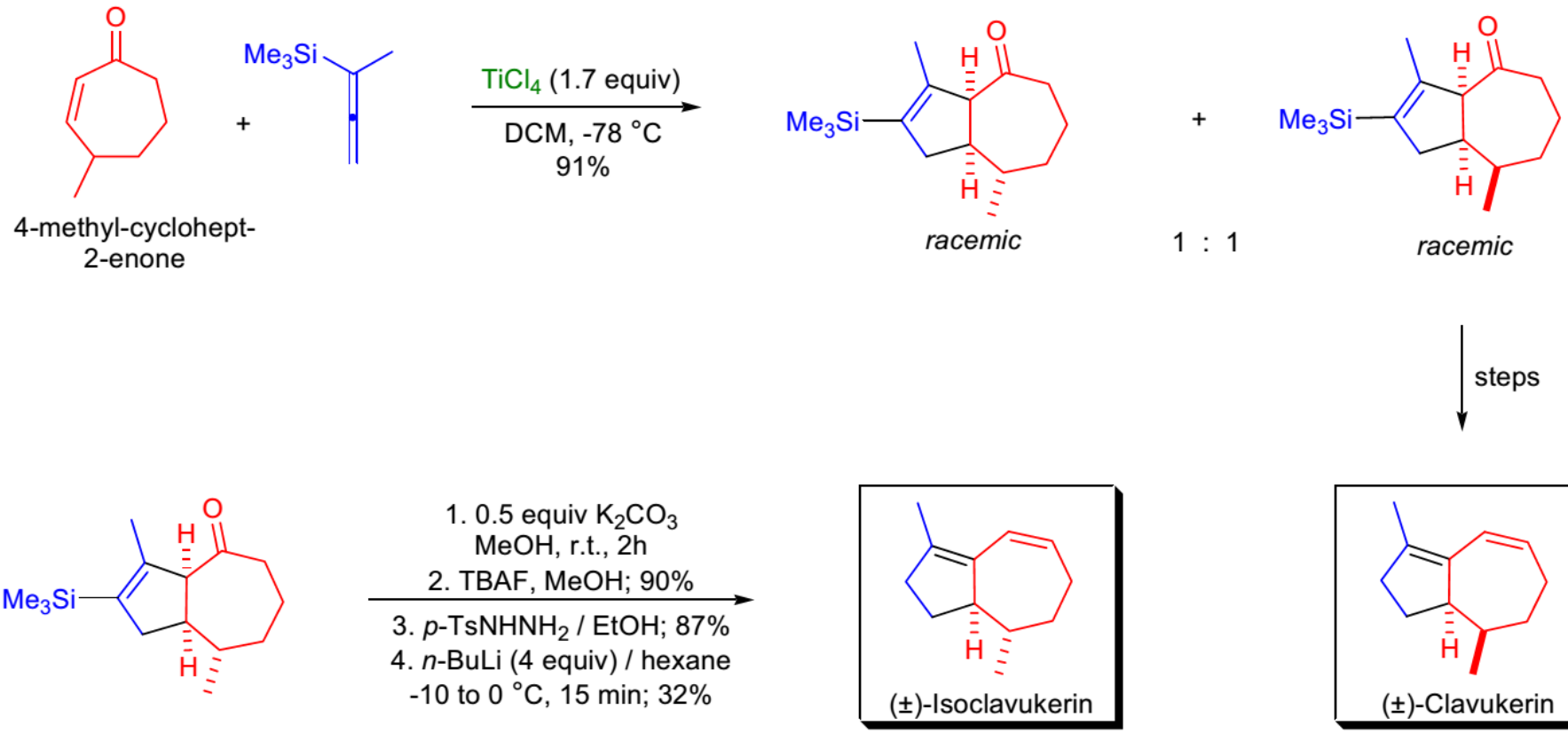
e $R^1, R^2, R^3 = Me$

Mechanism

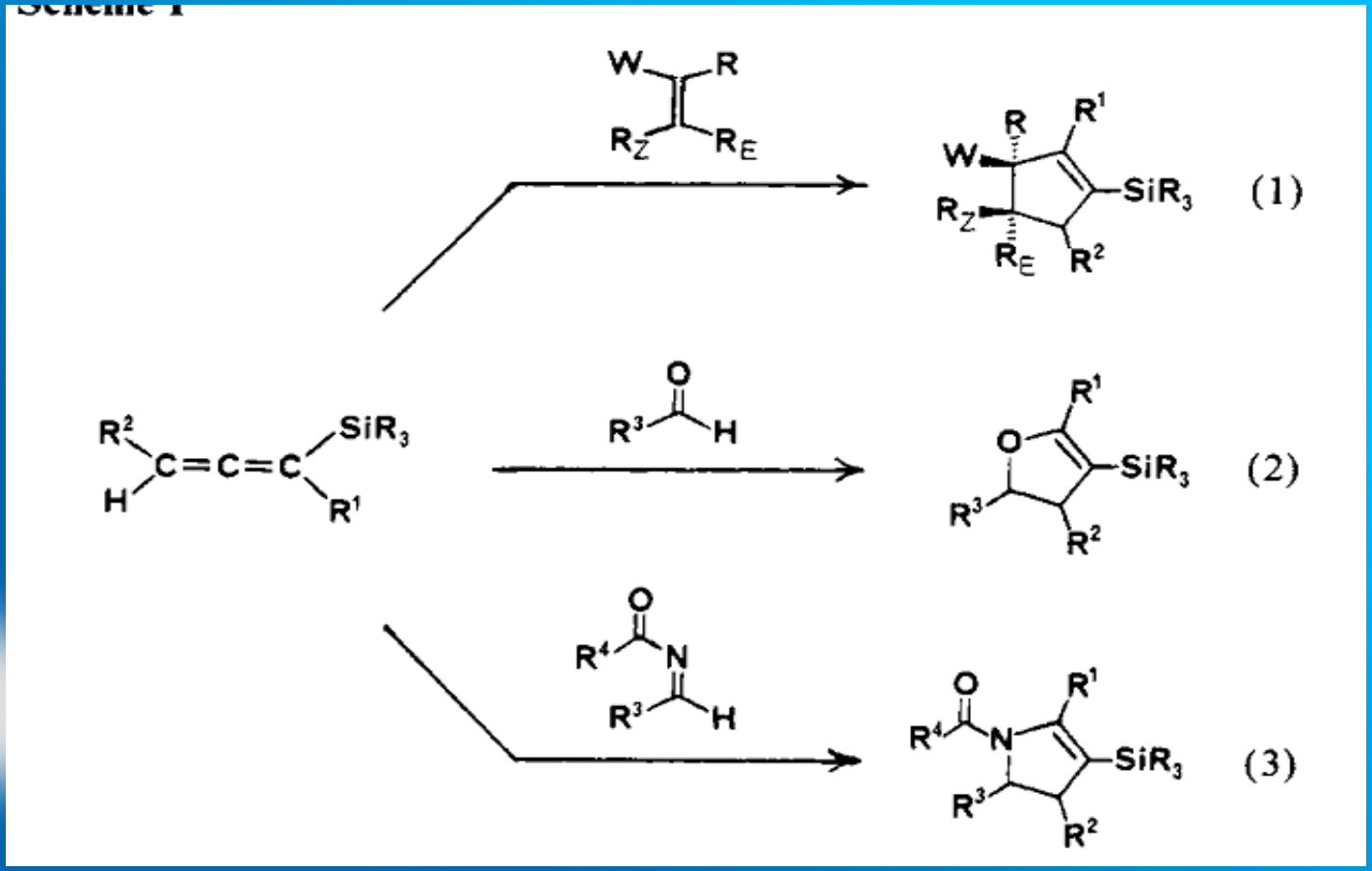


- Hard-Soft-Acid-Base?

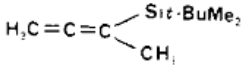
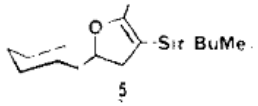
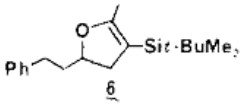
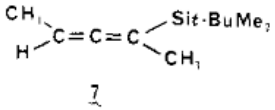
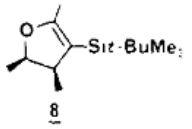
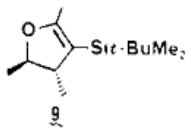
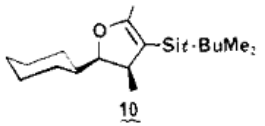
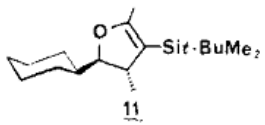
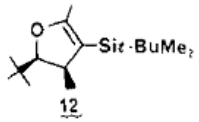
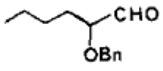
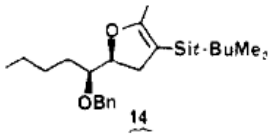
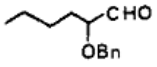
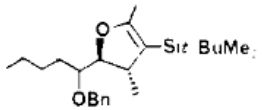
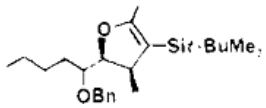
Synthetic Applications



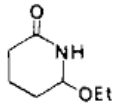
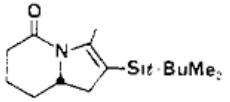
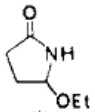
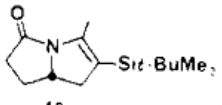
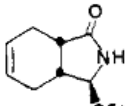
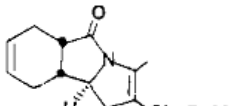
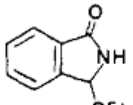
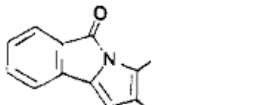
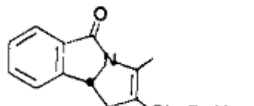
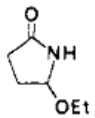
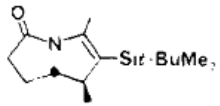
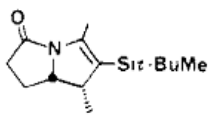
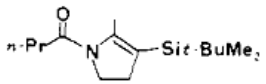
Research in the laboratory of R.L. Danheiser has shown that allenylsilanes can be reacted with electrophiles other than enones, such as aldehydes and N-acyl iminium ions to generate oxygen and nitrogen heterocycles.Aldehydes can function as heteroallenophiles and the reaction of C3 substituted allenylsilane with the achiral cyclohexane carbaldehyde afforded predominantly cis-substituted dihydrofurans



Synthetic Applications

entry	allenophile	allene	annulation product(s)	yield, %[a]
1		 4	 5	76
2	$PhCH_2CH_2CHO$	4	 6	70
3	CH_3CHO	 7	 8  9	78 (1.4:1)
4		7	 10  11	97 (7:1)
5	*t*-BuCHO	7	 12	92
6	 13[b]	4	 14	88
7	 13	7	 15a,b  16	86 (3.5:1)

Synthetic Applications

entry	allenophile	allene	annulation product(s)	yield, %[a]
1	 17[b]	4	 18	67
2	 1[b]	4	 19	63
3	 20[b]	4	 21	76[d]
4	 22[b]	4	 23  24	64 (2.8:1)
5	 1	7	 25  26	60 (1.2:1)[f]
6	n-PrCONHCH$_2$Ot-Bu 27[g]	4	 28	25

- Thank you