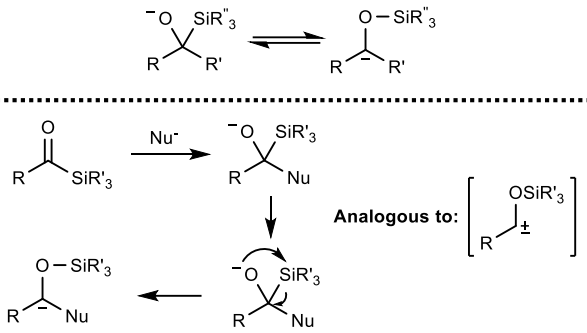
The Brook Rearrangement

General Reaction Scheme



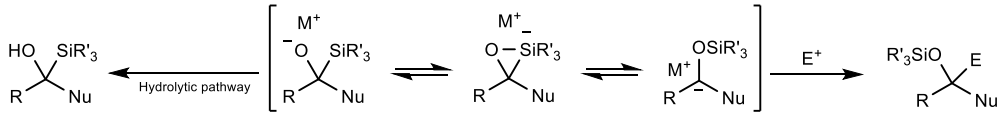
The term “Brook Rearrangement” describes an intramolecular anionic shift of a silyl group from a carbon atom to an oxygen atom.

While originally dubbed in the context of 1,2-silyl shifts, the term has been broadened to encompass 1,*n*-silyl shift from a carbon-silyl bond to an oxygen-silyl bond.

1,2-shifts bear the majority of currently known synthetic utility, as they enable carbonyl carbons to act as 1,1-dipoles when used in conjunction with a nucleophile.

Guiding overview: Sasaki, M.; Takeda, K., *Molecular Rearrangements in Organic Synthesis Ch. 6: Brook Rearrangement*. 2015.

Mechanism



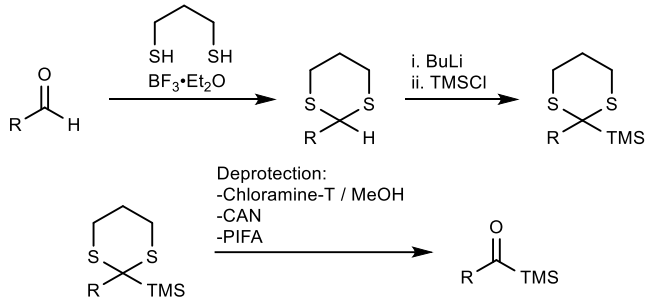
M = Mg
R or Nu = EDG

M = K, Na, Li
R or Nu = EWG or anion-intercepting group

The productive reaction pathway requires the equilibrium to favor the carbanion intermediate over the oxyanion. Strongly coordinating counterions such as Mg retard the productive Brook pathway, whereas more weakly coordinating ions such as Li^+, Na^+, or K^+ will accelerate the rearrangement.

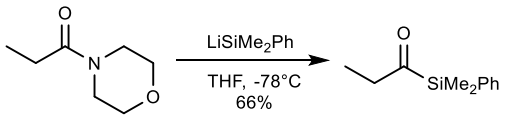
Preparation of acyl silanes:

From aldehydes (Corey-Brook method):



Chem. Soc. Rev., **2013**, *42*, 8540. and references therein. https://doi.org/10.1039/C3CS60185D

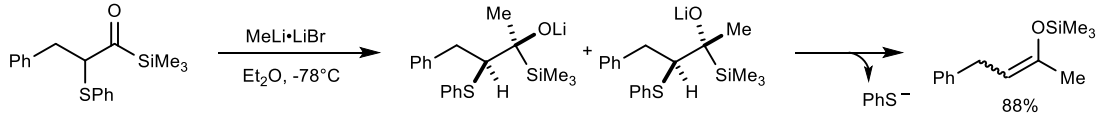
From morpholine amides:



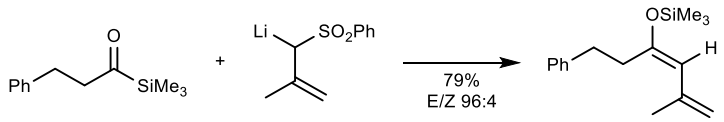
Org. Synth. **2007**, *84*, 22. https://doi.org/10.15227/orgsyn.084.0022

As a method for Olefination:

When a leaving group is present alpha to an acyl silane, sequential nucleophilic addition, rearrangement, and elimination can proceed to form vinyl silanes:

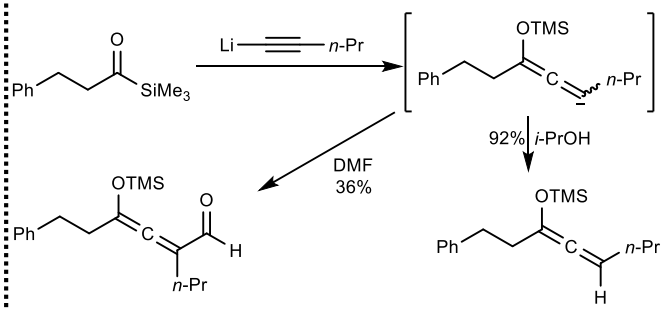


Alternatively, the leaving group can be introduced from the nucleophile:



J. Am. Chem. Soc. **1990**, *112* 5609. https://doi.org/10.1021/ja00170a026

Silyl allenol ethers can be made through a similar approach from the corresponding lithium acetylides:



J. Am. Chem. Soc. **1986**, *108*, 7791. https://doi.org/10.1021/ja00284a051

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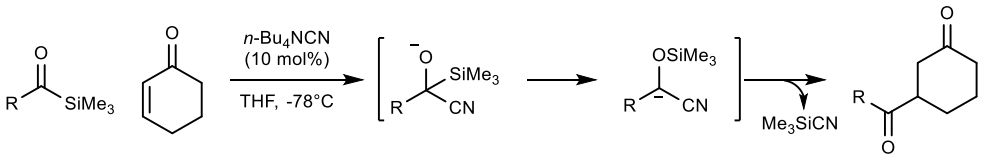
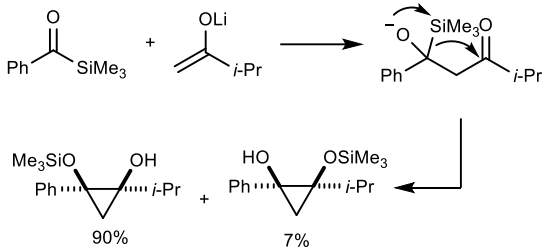
As a method for Nucleophilic Acylation:

The use of catalytic quantities of Bu_4NCN enables for the formation of a stabilized carbanion in the cyanohydrin intermediate, allowing for rearrangement in the absence of a metalation step:



As a method for strained ring formation:

Lithium enolates can act as tandem donor-acceptor pairs with acyl silanes to form strained cyclic systems:

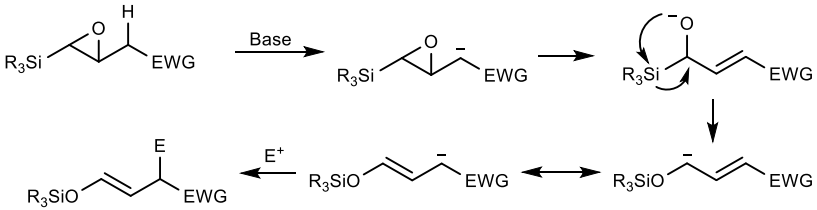


Synlett. **1993**, 841. https://doi.org/10.1055/s-1993-22627

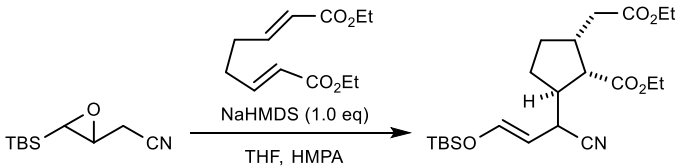
Alternative precursors to silyl alkoxides:

From Epoxysilanes:

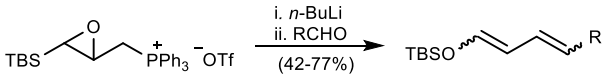
General Mechanism:



Examples:



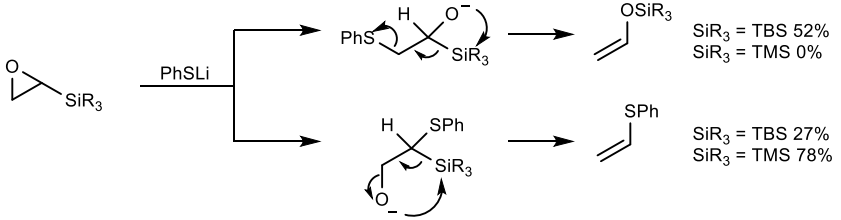
Org. Lett. **2004**, *6*, 4367. https://doi.org/10.1021/ol048100n



R = *n*-C_5H_{11}, *i*-Pr,Cyclohexyl, *t*-Bu

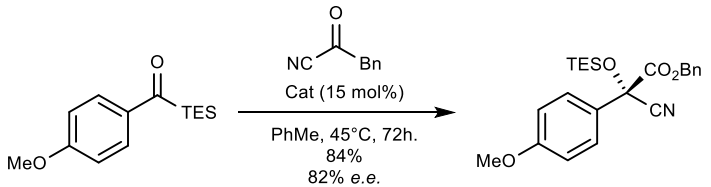
Tetrahedron Lett. **2006**, *47*, 9271. https://doi.org/10.1016/j.tetlet.2006.10.121

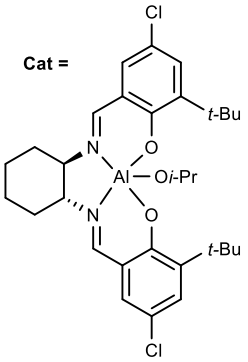
Terminal Epoxysilanes require the use of bulky silyl groups in order to achieve terminal substitution. The nonproductive pathway will result in Peterson-type elimination.



Tetrahedron Lett. **2000**, *41*, 1111. https://doi.org/10.1016/S0040-4039(99)02242-X

Enantioselective Variants of this reaction struggle with racemization of the intermediate carbanion. The Johnson group reported the use of an aluminum salen complex to induce enantioselectivity in the Brook-based synthesis of cyanoformates:





J. Org. Chem **2004**, *69*, 6548. https://doi.org/10.1021/jo049164e

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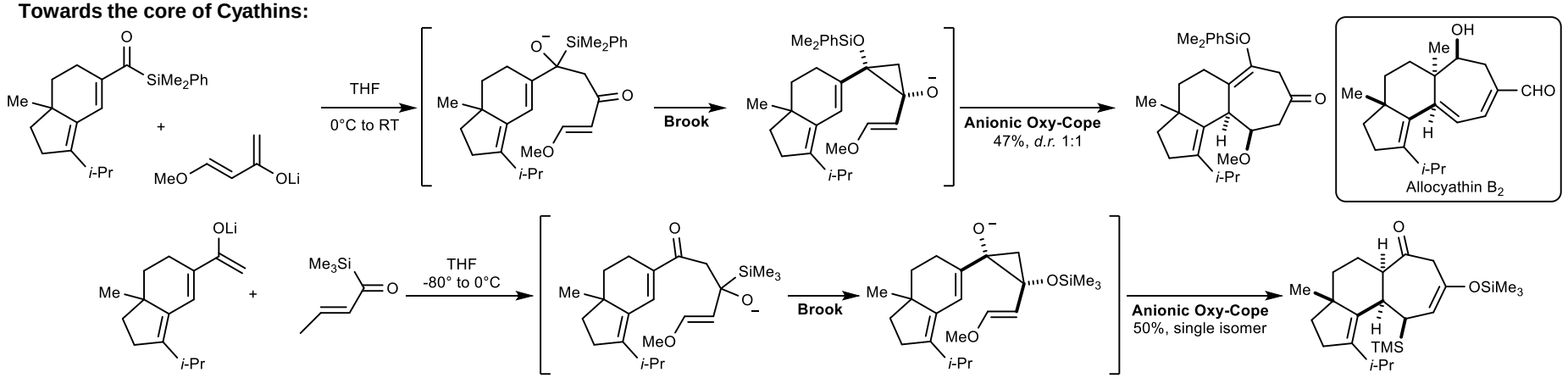
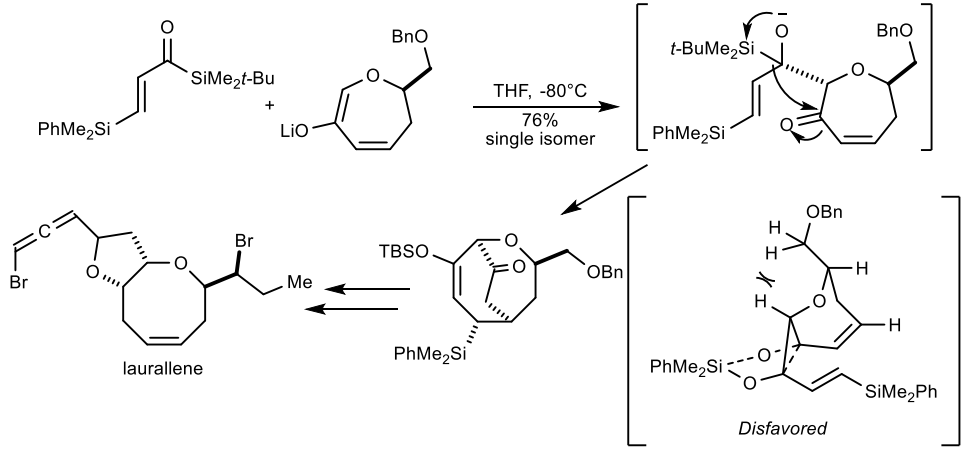
Applications in Total Synthesis:

Towards the core of Cyathins:



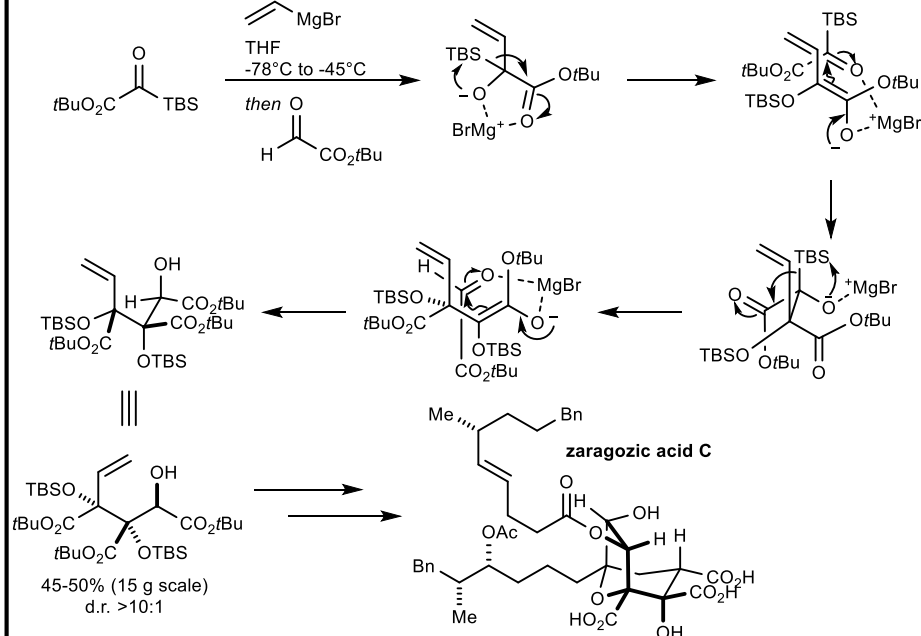
Org. Lett. **2000**, *2*, 1903. https://doi.org/10.1021/ol0059753

In the formal synthesis of laurallene:



Org. Lett. **2008**, *10*, 1803. https://doi.org/10.1021/ol8003595

Towards the core of zaragozic acid C:



J. Am. Chem. Soc. **2008**, *130*, 17281. https://doi.org/10.1021/ja808347q