

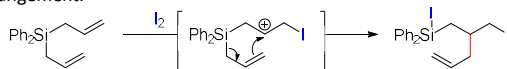
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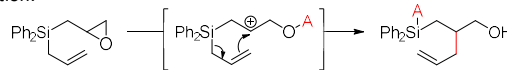
Abstract: Allylsilanes can be regioselectively transformed into the corresponding 3-silylfluorohydrin in good yield using a sequence of epoxidation followed by treatment with $\text{HF}\cdot\text{Et}_3\text{N}$ with or without isolation of the intermediate epoxide. Various silicon-substitution is tolerated, resulting in a range of 2-fluoro-3-silylpropan-1-ol products from this method. Whereas other fluorohydrin syntheses by epoxide opening using $\text{HF}\cdot\text{Et}_3\text{N}$ generally require more forcing conditions (e.g. higher reaction temperature), opening of allylsilane-derived epoxides with this reagent occurs at room temperature. We attribute this rate acceleration along with the observed regioselectivity to a beta-silyl effect that stabilizes a proposed cationic intermediate. The use of enantioenriched epoxides produces similarly enantioenriched fluorohydrins suggestive of an $\text{S}_{\text{N}}2$ -type mechanism.

Background

- Our group has developed an iodine-mediated diallylsilane rearrangement.



- We set out to investigate a similar intramolecular epoxide allylation.



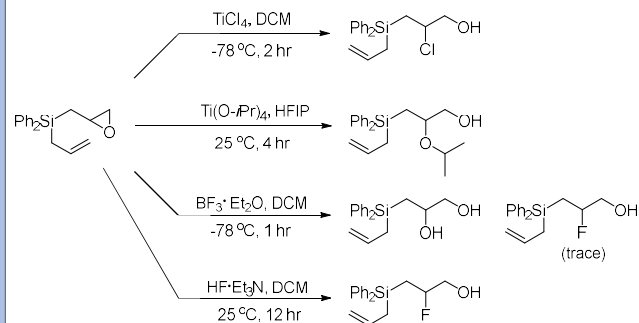
Cummins, E. J., and O'Neil, G. W. *Tetrahedron Lett.* **2017**, 58, 3406-3409.

Myers et al. *Tetrahedron Lett.* **2021**, 82, 153392.

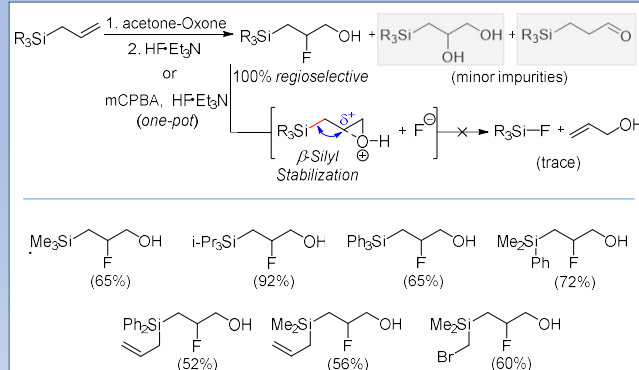
Fomina et al. *Heterocycles* **2022**, 104, DOI: 10.3987/COM-22-14735.

Initial Discovery

- Attempts at an intramolecular epoxide allylation led to trace amounts of a fluorohydrin which are valuable synthetic intermediates.



Fluorohydrin Scope



Clover, A. W., Jones, A. P., and O'Neil, G. W. *ChemRxiv. Cambridge: Cambridge Open Engage*; **2023**.

One-Pot vs Two-Step

- Both one-pot and two-step reactions gave comparable yields.
- The one-pot was preferred for more volatile compounds.
- Using these conditions small amounts of the hydroxyester was formed.

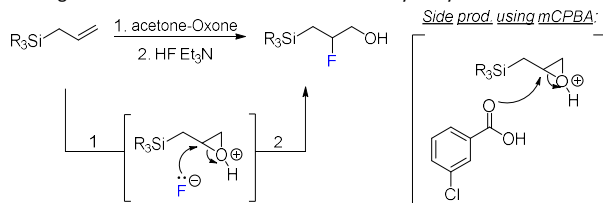
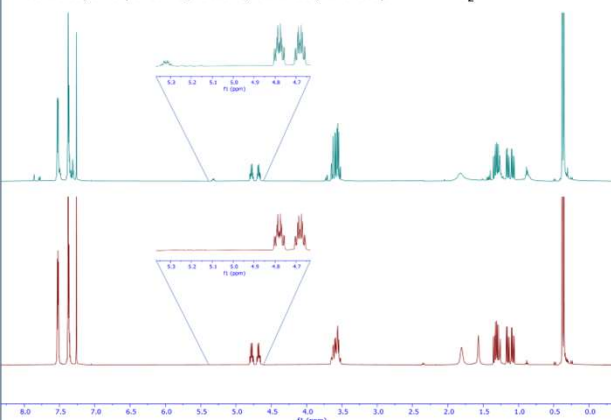
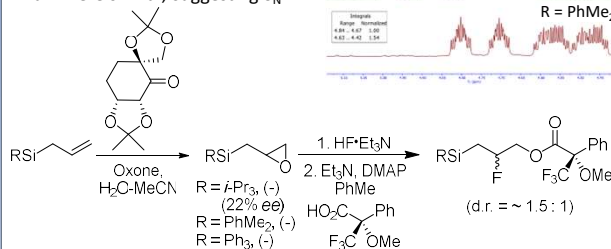


Figure. Stacked ^1H NMR spectrum of dimethylphenylfluorohydrin (top, blue trace) one-pot and (bottom, red trace) two-step. $\text{R} = \text{PhMe}_2$



Shi Epoxidation and Mosher Esterification

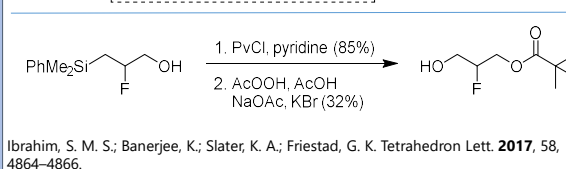
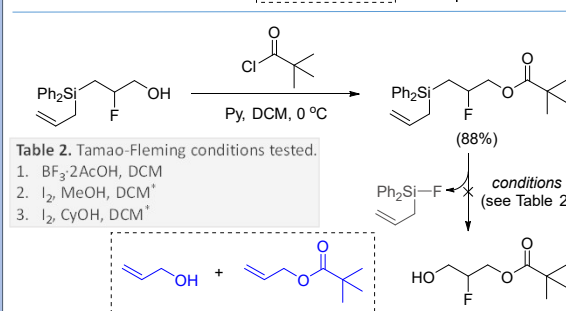
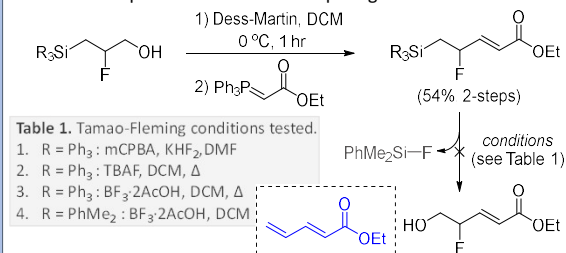
- An enantioselective epoxidation was performed to test whether this mechanism was $\text{S}_{\text{N}}2$ or $\text{S}_{\text{N}}1$.
- The epoxide *ee* and fluorohydrin d.r. were similar, suggesting $\text{S}_{\text{N}}2$.



Wang, Z.-X.; Tu, Y.; Frohn, M.; Zhang, J.-R.; Shi, Y. J. *Am. Chem. Soc.* **1997**, 119, 11224-11235.

Tamao Oxidation

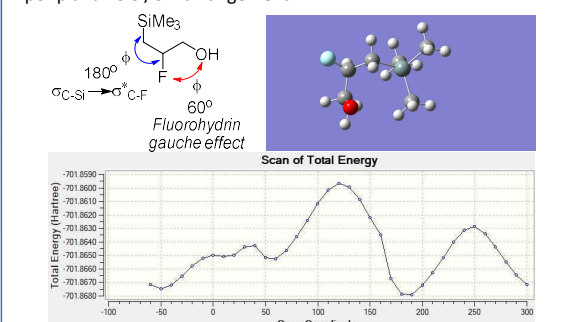
- Initial attempts suffered from a competing elimination.



Ibrahim, S. M. S.; Banerjee, K.; Slater, K. A.; Friestad, G. K. *Tetrahedron Lett.* **2017**, 58, 4864-4866.

Computational Study

- Conformational analysis shows a strong preference for an anti-periplanar C-Si/C-F arrangement.



Compliments of Tomás Nevesely.