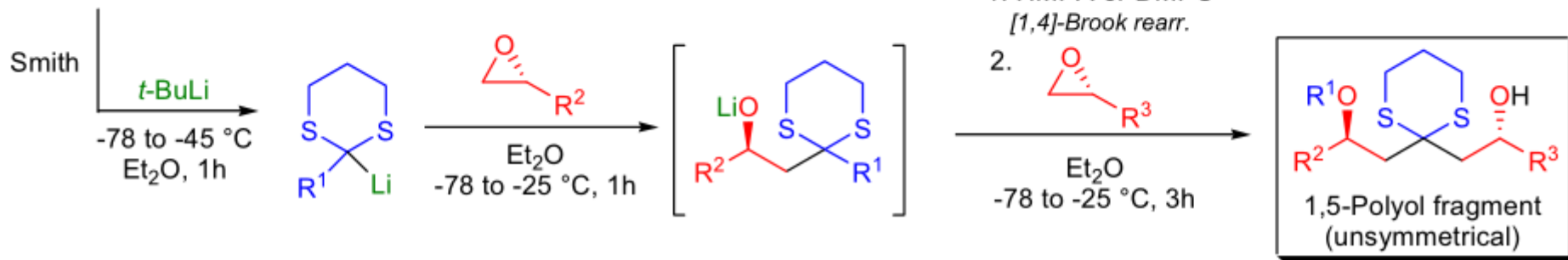
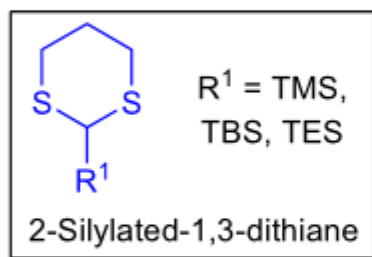
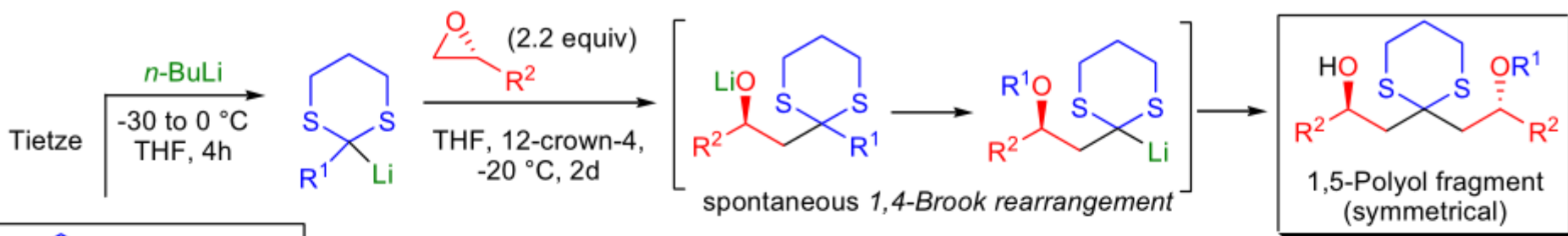


**SMITH-TIETZE MULTICOMPONENT  
DITHIANE LINCHPIN COUPLING**

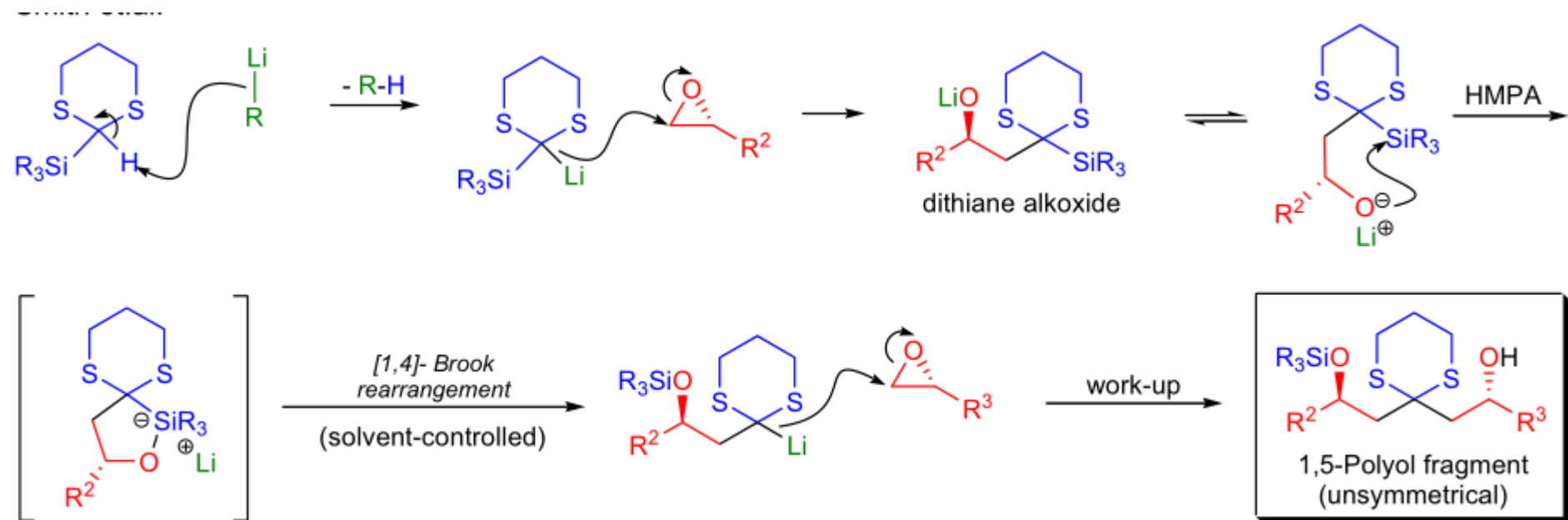
- 1) **The first application of 2-lithio-1,3-dithianes as “carbonyl anion” equivalents** was described by **E.J. Corey and D. Seebach** in the mid-1960s;
- 2) In 1994, **L.F. Tietze** and co-workers successfully synthesized C 2 –symmetrical **enantiopure** 1,5-diols, 3-oxo-1,5-diols and 1,3,5-triols by the symmetrical bis-alkylation of lithiated 2-trialkylsilyl-1,3-dithianes with epoxides;
- 3) **A.B. Smith** et al. used HMPA or DMPU as an additive in the solvent, which significantly **increased the rate of the reaction** and allowed **two different electrophiles** (epoxides) to be coupled with the dithiane in a **one-pot operation**.



## Features:

- 1) The epoxide ring-opening is completely **regioselective**, the nucleophile **attacks on the least substituted carbon**;
- 2) The exact timing of the **Brook rearrangement** is possible by the addition of **HMPA or DMPU** to the reaction mixture (solvent-controlled Brook rearrangement) and the formation of **symmetrical adducts** can be completely **avoided**;
- 3) Altering the absolute configuration of the epoxides and the stereoselective reduction of the ketone moiety after the **removal of the dithiane can give rise to 1,3-polyols of any desired configuration**;
- 4) After the second epoxide has reacted, the resulting unsymmetrical adduct has its hydroxyl groups differentiated by one of them being silylated;
- 5) The use of an enantiopure bis-epoxide as the second epoxide component allows for a one-pot five-component linchpin coupling.

# Mechanism:



## Synthetic Applications:

