

# Recent (and Not-So-Recent) Applications of Geminal Dianions

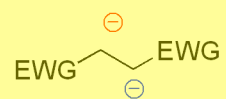
Danielle Jacobs  
Crimmins Group Meeting  
3/7/07

# Carbon-Based Dianions

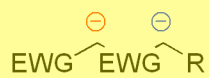
- Important intermediates for carbon-carbon bond forming reactions
- Nomenclature
  - Numbers denote where substitution occurs, despite resonance structures
  - Heteroatom, if applicable, distinguished first – primary deprotonation site
  - Bis-heteroatom dianions are named the same way
  - Often further distinguished by functional groups
  - EWG = C(O)R, SO<sub>n</sub>R, NO<sub>2</sub>, P(O)OR<sub>2</sub>, CN, etc...



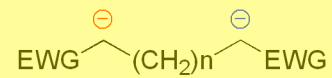
1,1-(C,C)  
geminal  
 $\alpha, \alpha$



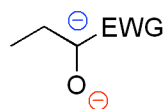
1,2-(C,C)  
vicinal  
 $\alpha, \beta$



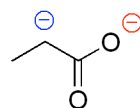
1,3-(C,C)  
 $\alpha, \gamma$



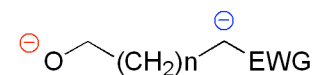
1,Z-(C,C)



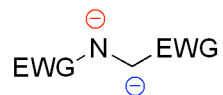
1,2-(O,C)  
vicinal  
 $\alpha, \beta$



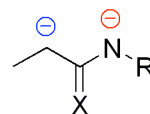
1,3-(O,C)  
 $\alpha, \alpha'$



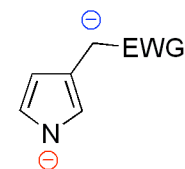
1,Z-(O,C)



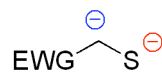
1,2-(N,C)  
vicinal  
 $\alpha, \beta$



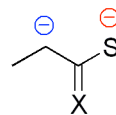
1,3-(N,C)  
 $\alpha, \alpha'$



1,4-(N,C)



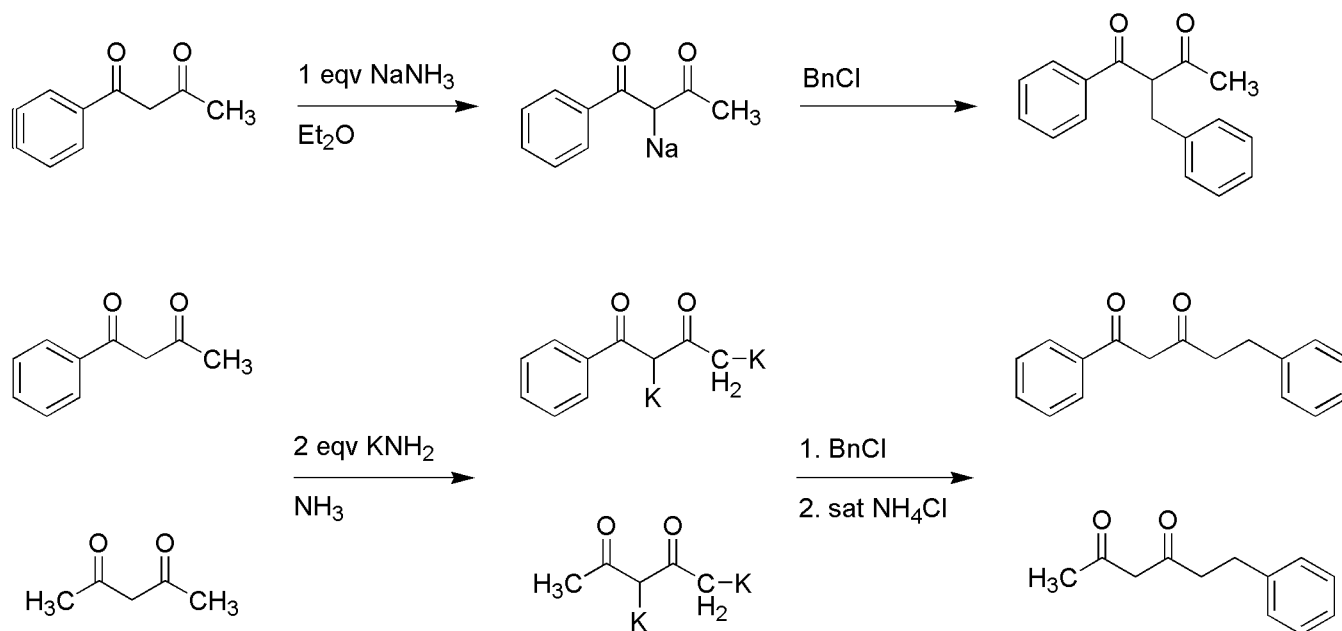
1,2-(S,C)  
vicinal  
 $\alpha, \beta$



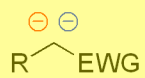
1,3-(S,C)  
 $\alpha, \alpha'$

# History of C,C-Dianions

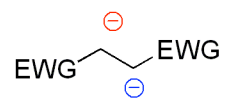
- Hauser & Harris, 1958



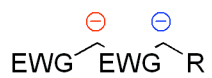
- Base variation (metal amides, hindered organic bases)



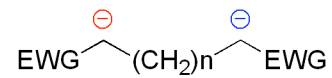
1,1-(C,C)  
geminal  
 $\alpha, \alpha$



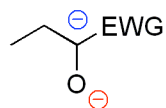
1,2-(C,C)  
vicinal  
 $\alpha, \beta$



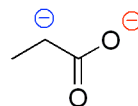
1,3-(C,C)  
 $\alpha, \gamma$



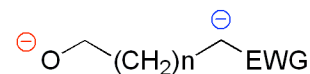
1,Z-(C,C)



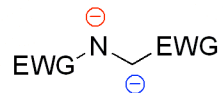
1,2-(O,C)  
vicinal  
 $\alpha, \beta$



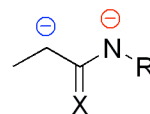
1,3-(O,C)  
 $\alpha, \alpha'$



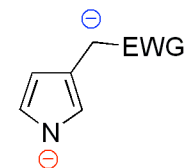
1,Z-(O,C)



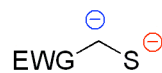
1,2-(N,C)  
vicinal  
 $\alpha, \beta$



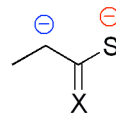
1,3-(N,C)  
 $\alpha, \alpha'$



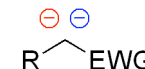
1,4-(N,C)



1,2-(S,C)  
vicinal  
 $\alpha, \beta$



1,3-(S,C)  
 $\alpha, \alpha'$

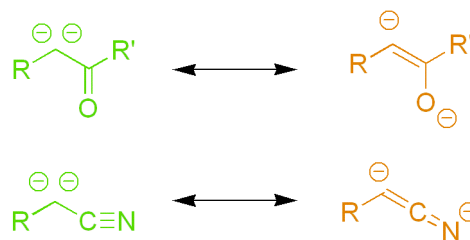


# 1,1-(C,C)-Dianions

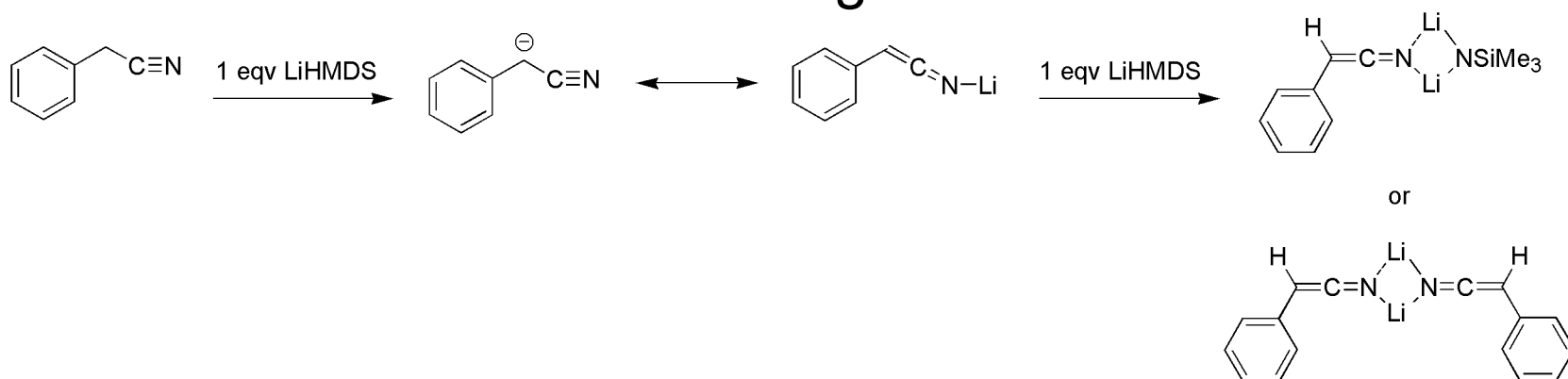
- Also known as *geminal* or  $\alpha,\alpha$  dianions
- Occurs when there is little or no opportunity for deprotonation to occur elsewhere in the molecule
- Benefits
  - Increases sluggish reactivity simple  $\alpha$ -stabilized monoanions
  - One carbon center can react **once** or **twice** with bifunctional electrophiles or two different monofunctional electrophiles
  - EWGs behave as function handles

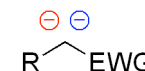
# Possible Forms of Geminal Dianion

- Stabilization by resonance to the 1,3 enolate or heteroenolate dianion to counteract high degree of coulombic repulsion



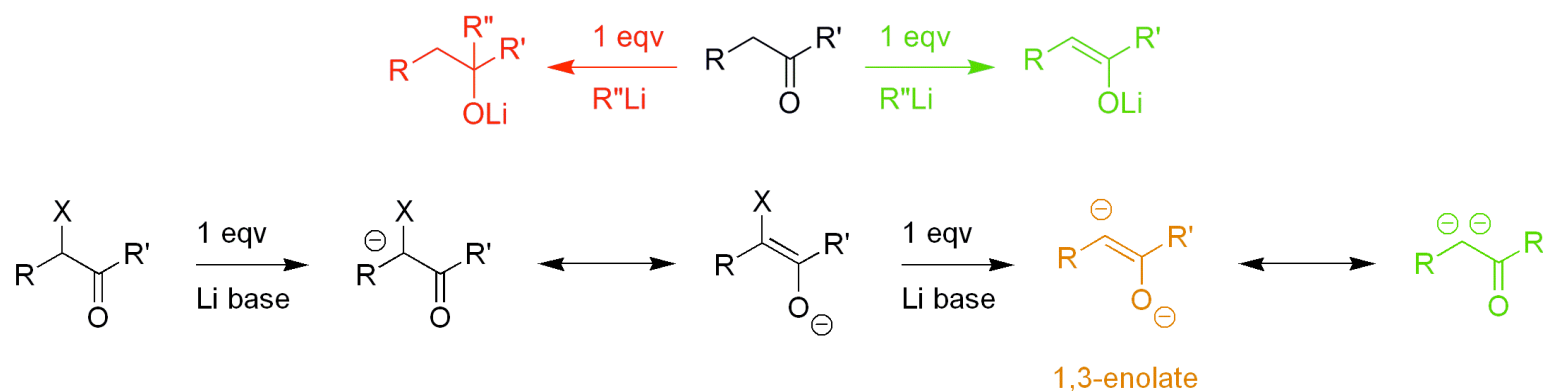
- Evidence for chelated or bridged dimer form



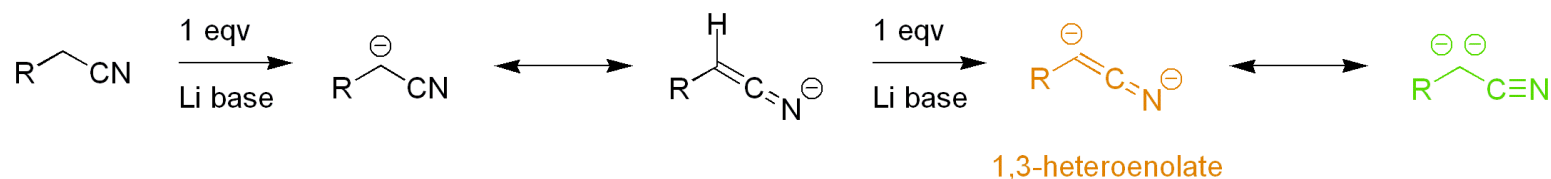


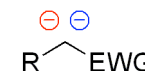
# Traditional Geminal Dianions

- $\alpha$ -Halocarbonyl-stabilized



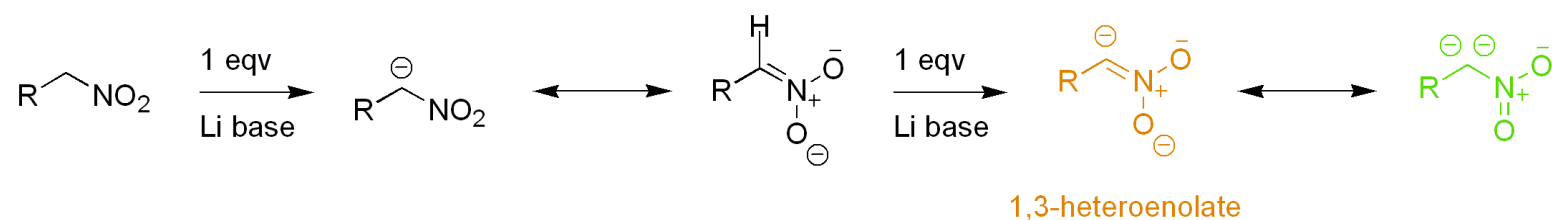
- Nitrile-stabilized



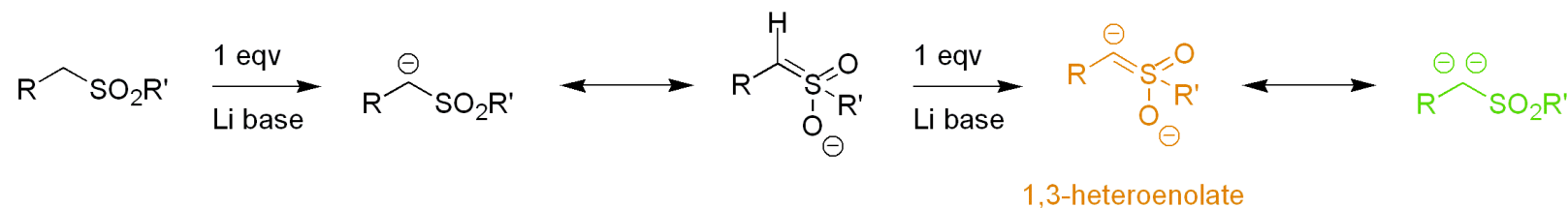


# Traditional Geminal Dianions

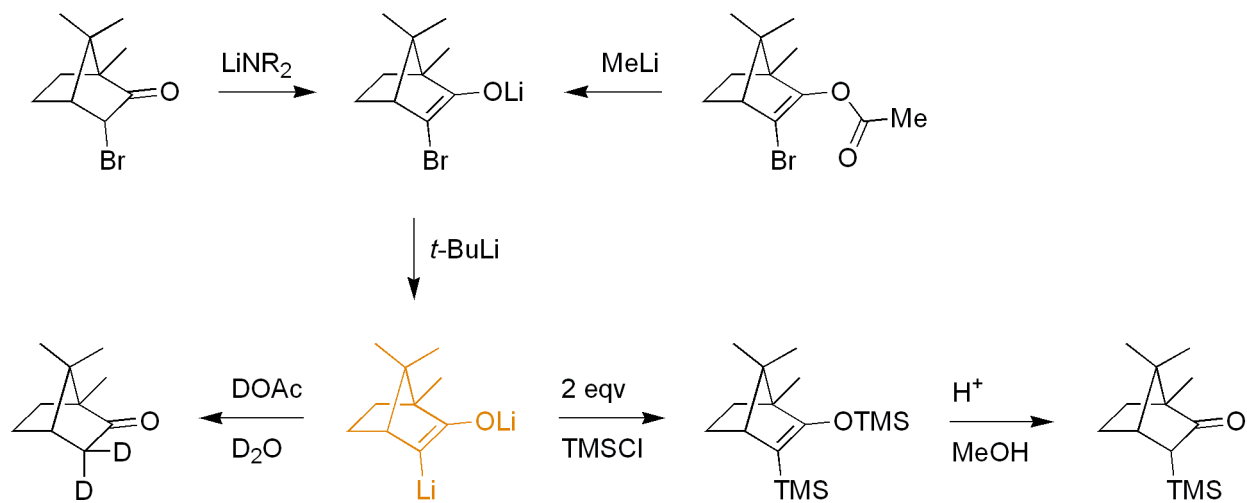
- Nitro-stabilized



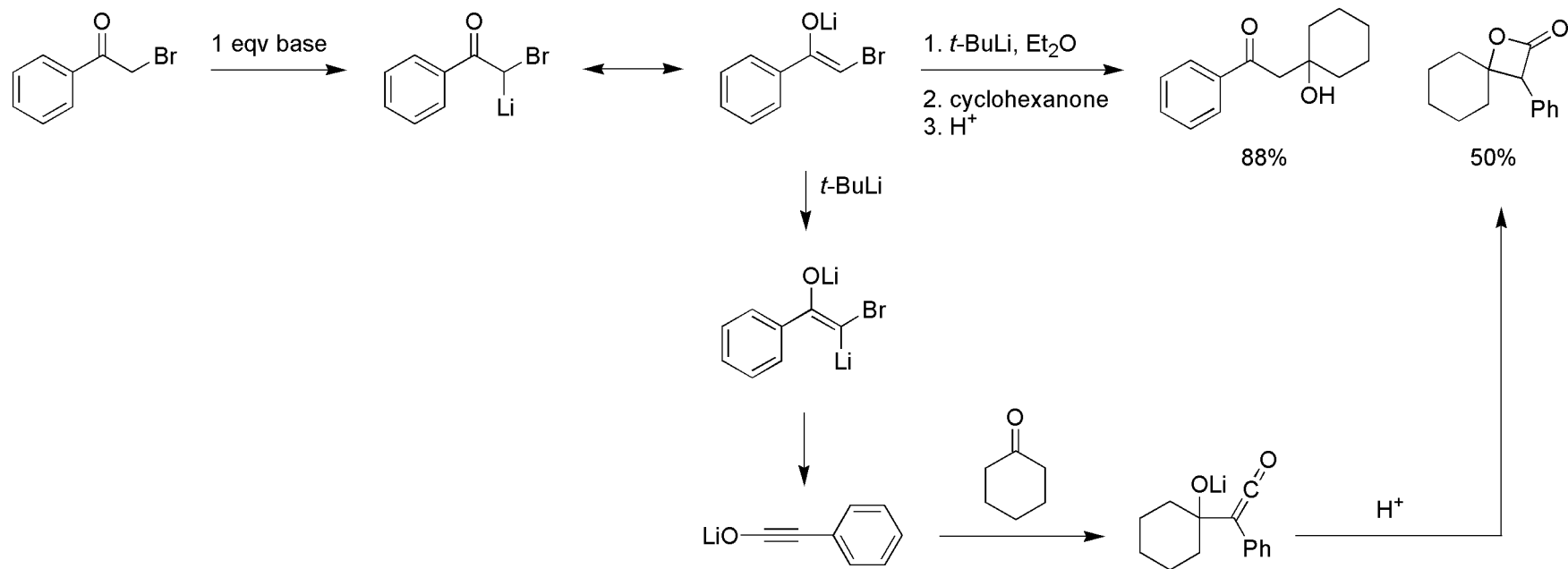
- Sulfone-stabilized



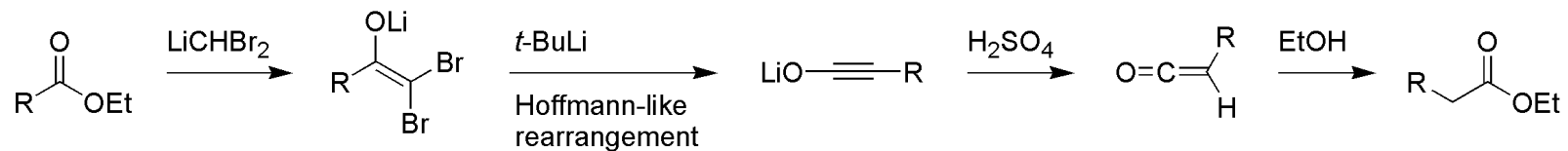
# $\alpha$ -Halocarbonyl Dianions



# $\alpha$ -Halocarbonyl Dianions

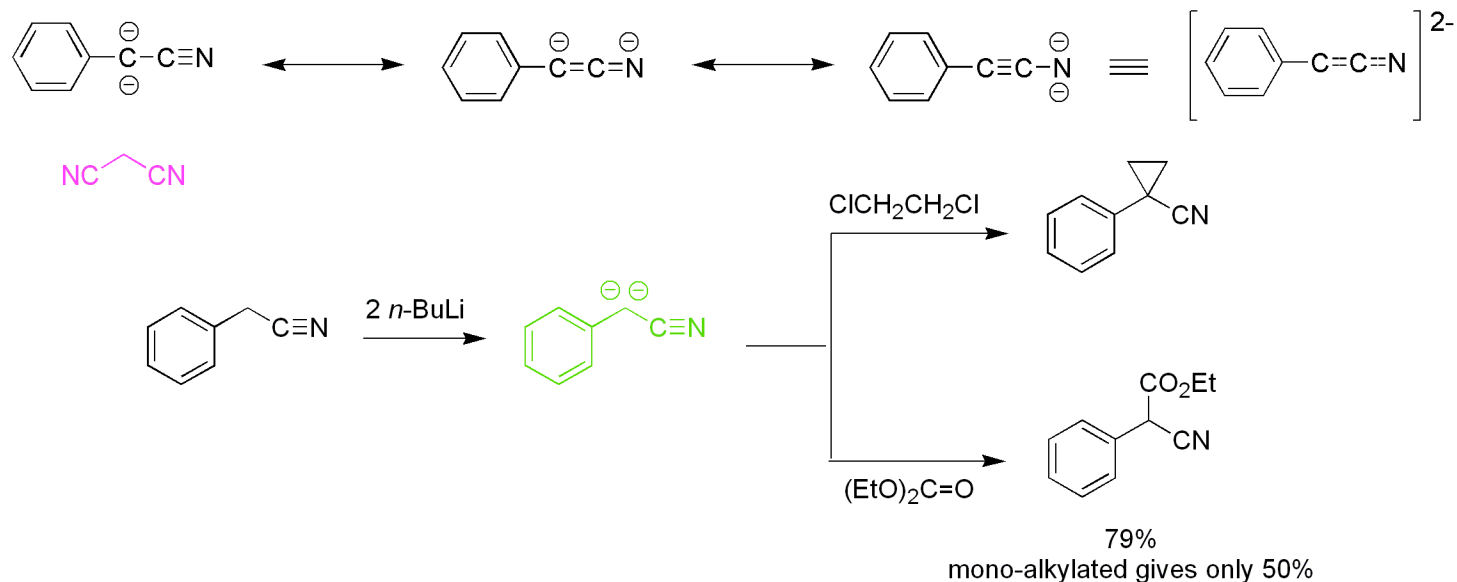


- One-pot homologation of esters



# $\alpha$ -Nitrile Dianions

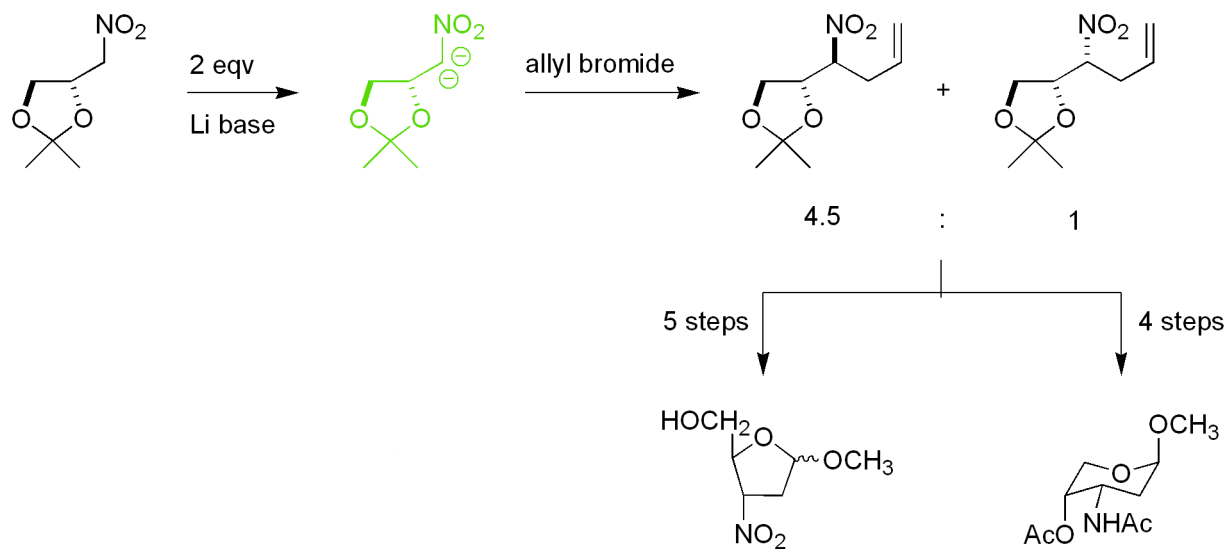
- More reactive than  $\alpha$ -halocarbonyl dianions
- Waning interest due to propensity for bis-alkylation and/or mixed alkylation at  $\alpha$ -carbon and nitrogen
- Dianion stabilized by predicted sesquiazacteylene resonance



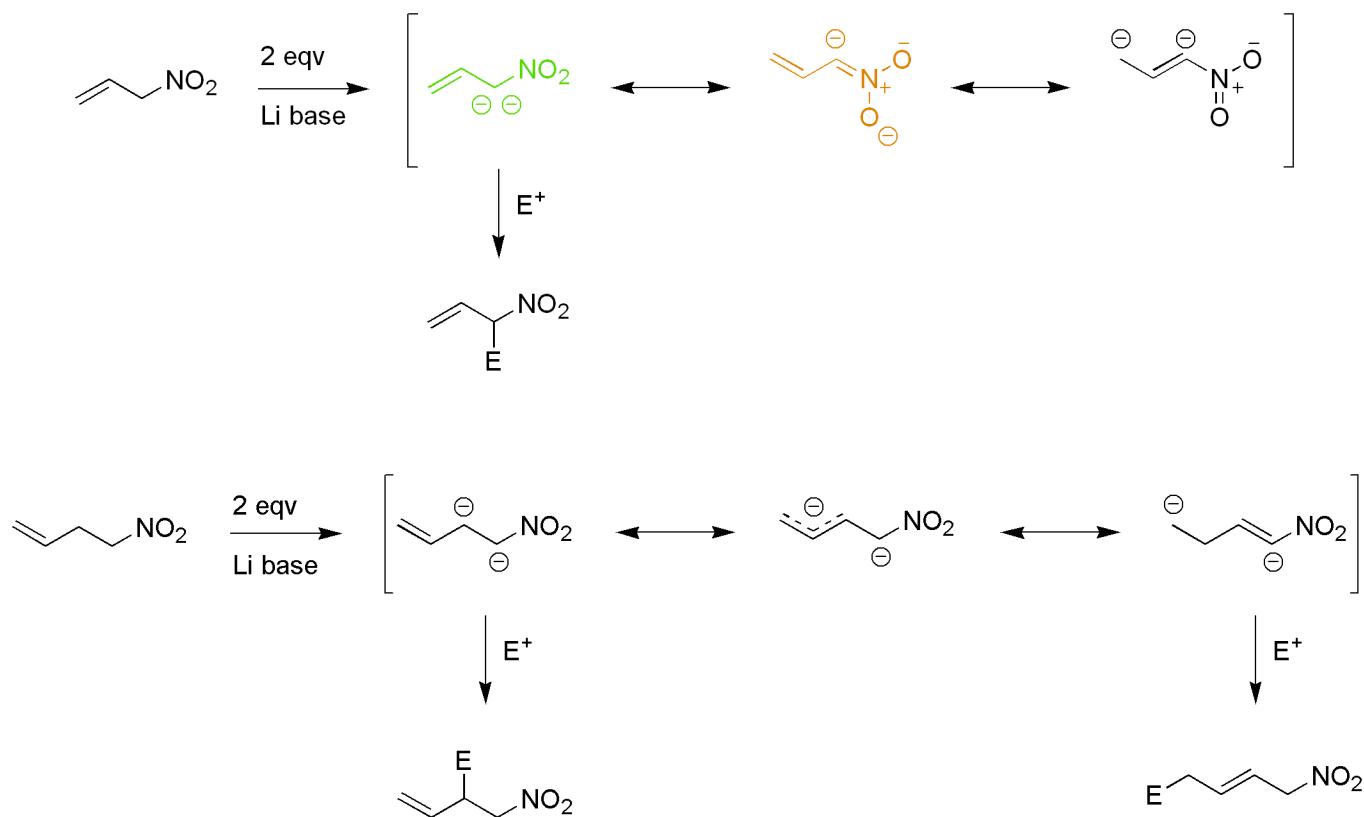
Kaiser, E.M.; Solter, L.E.; Schwarz, R.A.; Beard, R.D.; Hauser, C.R. *J. Am. Chem. Soc.* **1971**, *93*, 4237. Tsai, T-Y.; Shia, K-S.; Liu, H-J. *Synlett* **2003**, 97.

# $\alpha$ -Nitro Dianions

- Higher acidity provides for easier deprotonation but lower nucleophilicity
- Dianion can overcome diminished nucleophilicity
- Facile transformation into amines or ketones

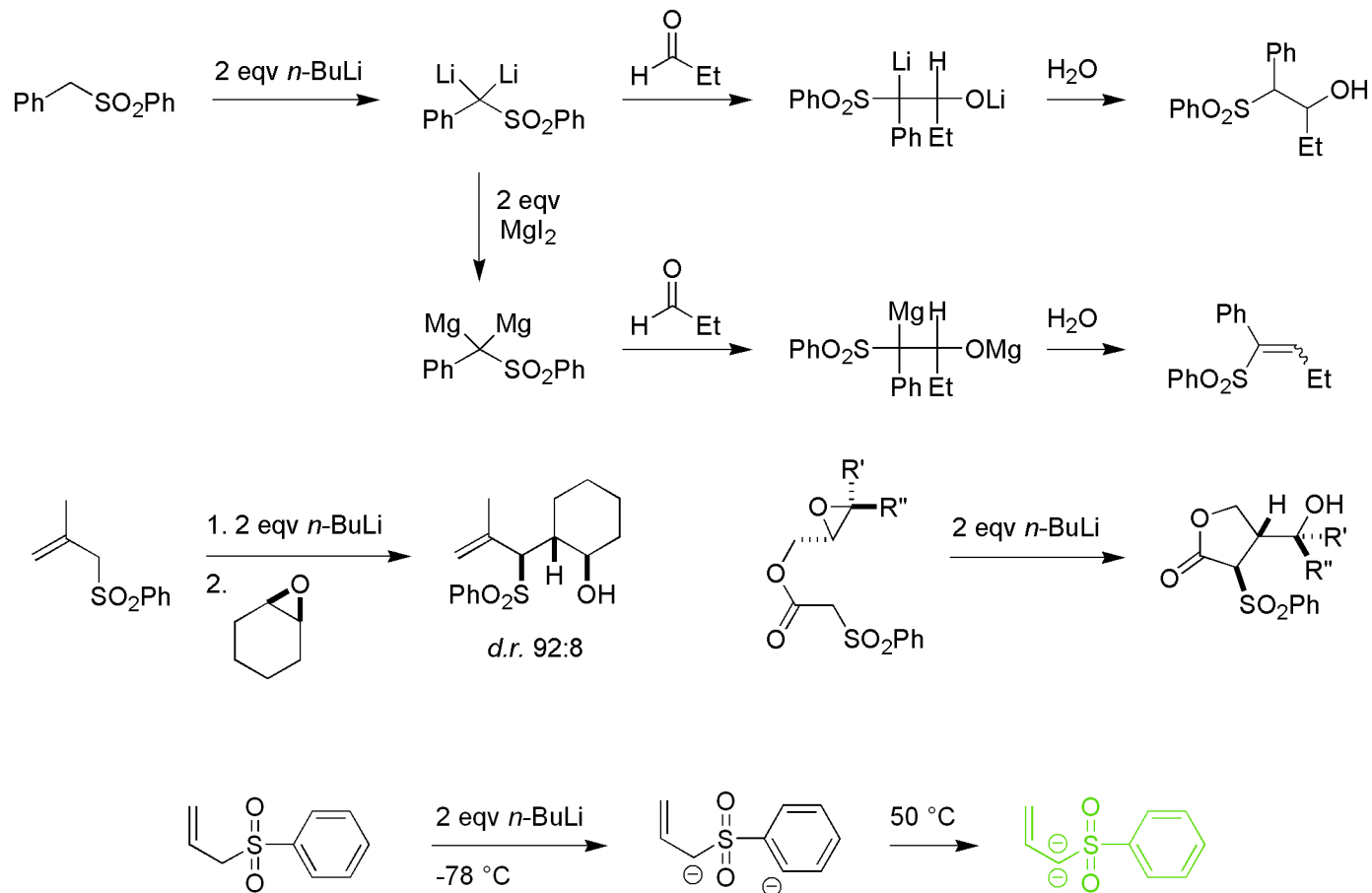


# $\alpha$ -Nitro Dianions



Seebach, D.; Henning, R.; Lehr, F.; Gonnermann, J. *Tetrahedron Lett.* **1977**, 1161. Seebach, D.; Henning, R.; Lehr, F. *Angew Chem.* **1978**, 90, 479.

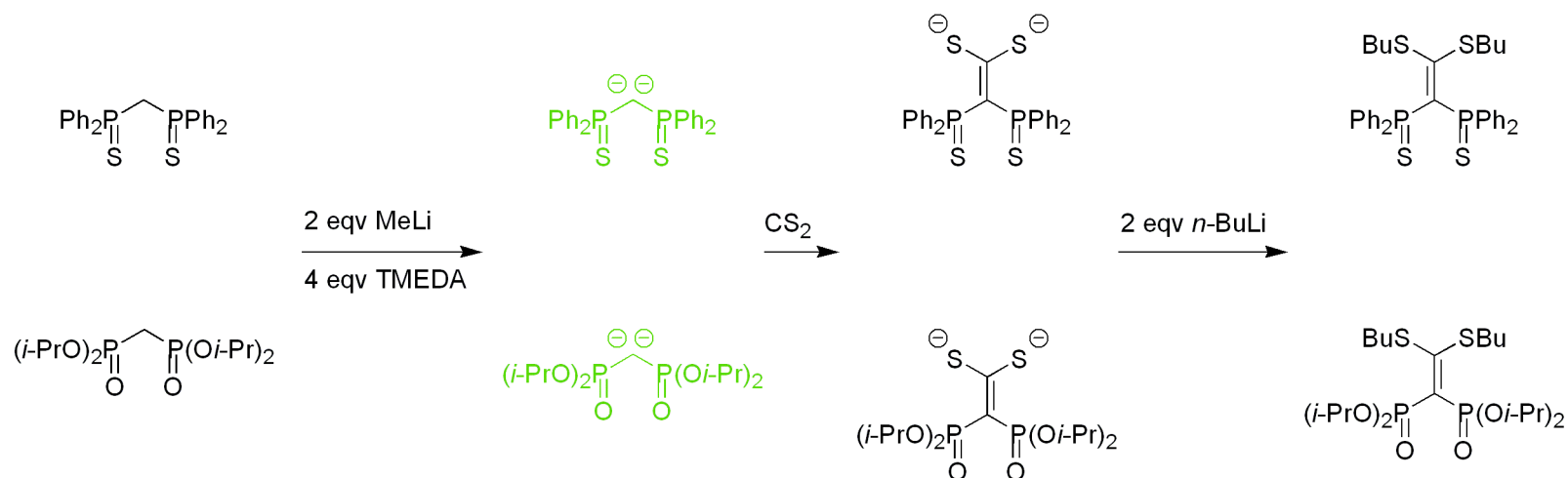
# $\alpha$ -Sulfone Dianion



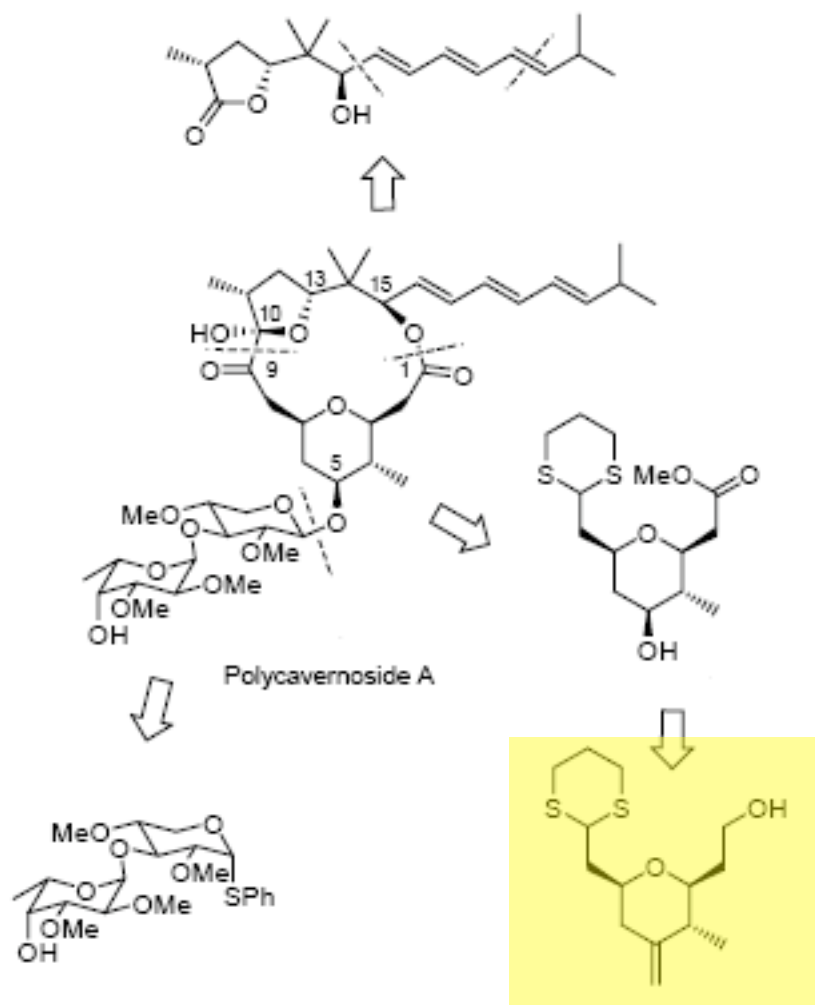
Trost, B.M.; Merlic, C.A. *J. Am. Chem. Soc.* **1988**, *110*, 5216. McCombie, S.W.; Shankar, B.B.; Ganguly, A.K. *Tetrahedron Lett.* **1989**, *30*, 7029. Volhardt, J.; Gais, H-J.; Lukas, K.L. *Angew. Chem. Int. Ed. Engl.* **1985**, *24*, 696. Bonete, P.; Nájera, C. *Tetrahedron* **1996**, *52*, 4111.

# New Additions to $\alpha,\alpha$ -Dianion Arsenal

- Phosphorus-stabilized

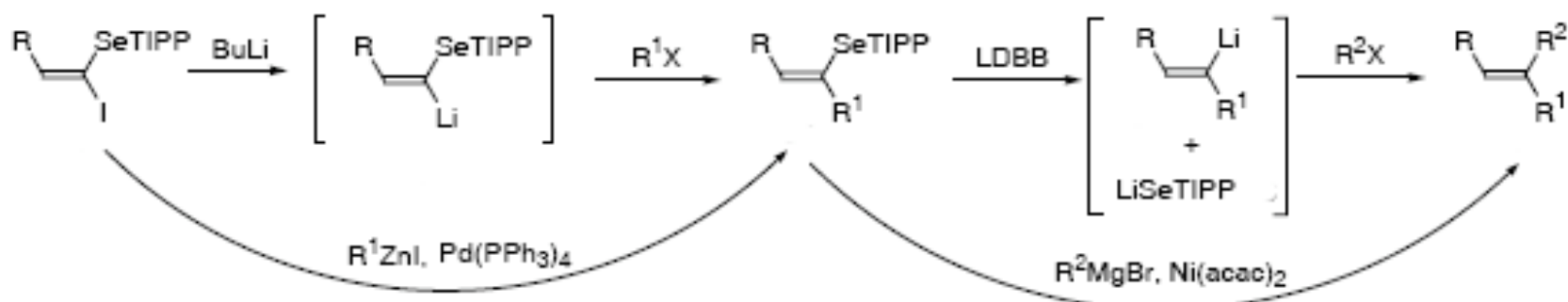
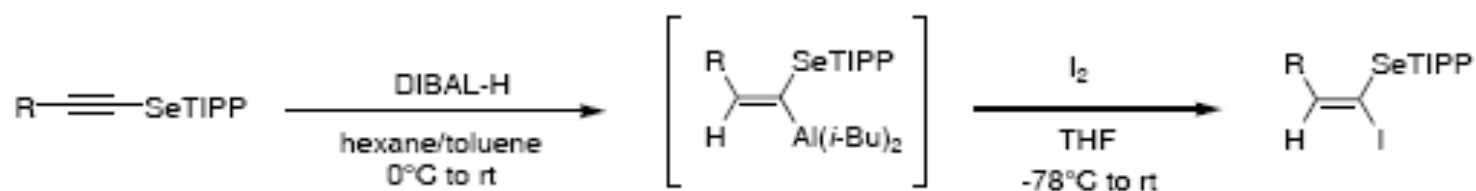


# 1,1-Olefinic Dianion Surrogates

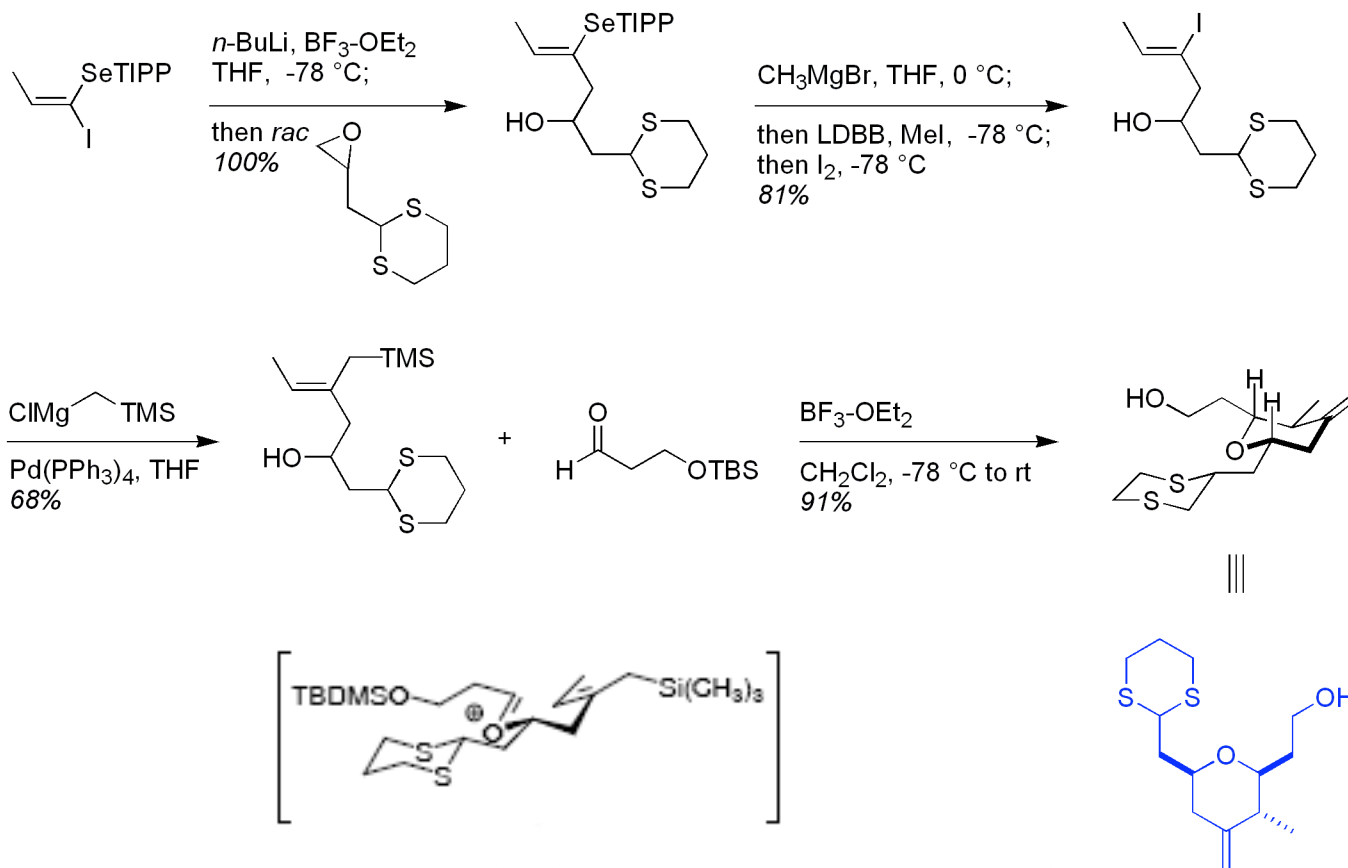


Pérez-Baldado, C.; Markó, I.E. *Tetrahedron* **2006**, 62, 2331. Pérez-Baldado, C.; Markó, I.E. *Tetrahedron Lett.* **2005**, 46, 2887. Pérez-Baldado, C.; Lucaccioni, F.; Markó, I.E. *Tetrahedron Lett.* **2005**, 46, 4883.

# 1,1-Olefinic Dianion Surrogates

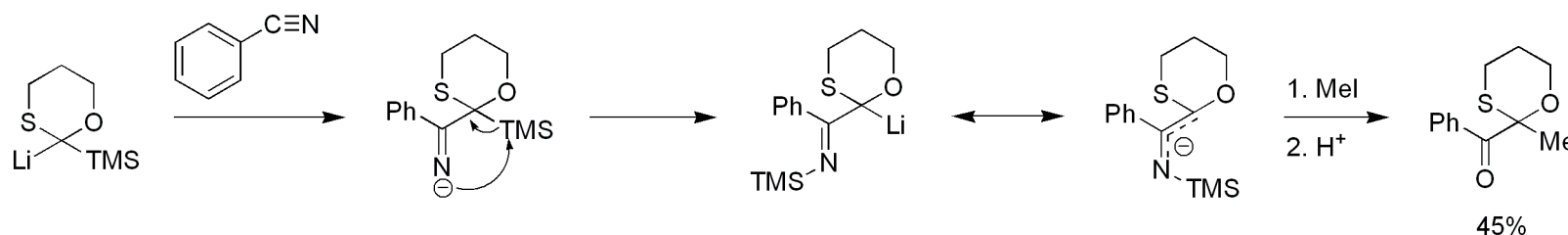


# 1,1-Olefinic Dianion Surrogates

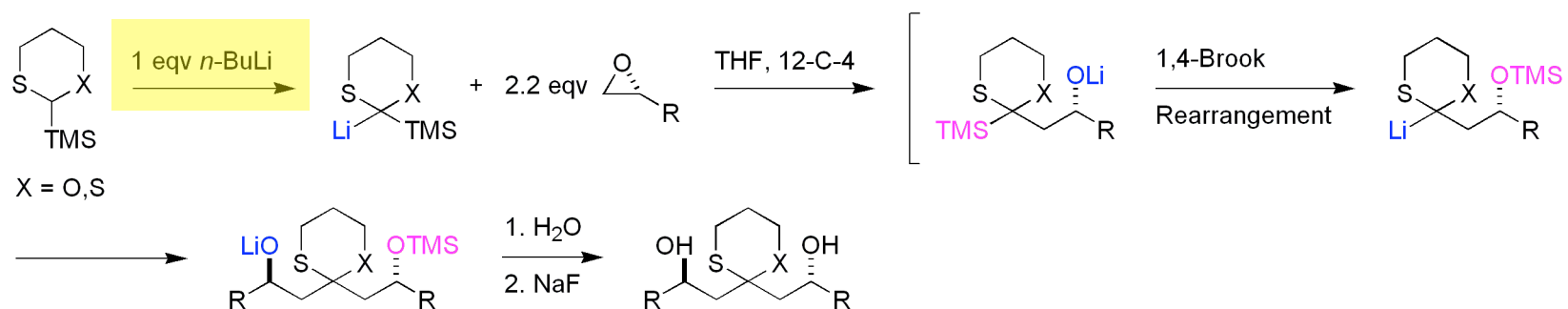


# Dithiane and Oxathian Surrogates

- Silyl oxathian dianion originally reported in 1983 by Fuji and coworkers



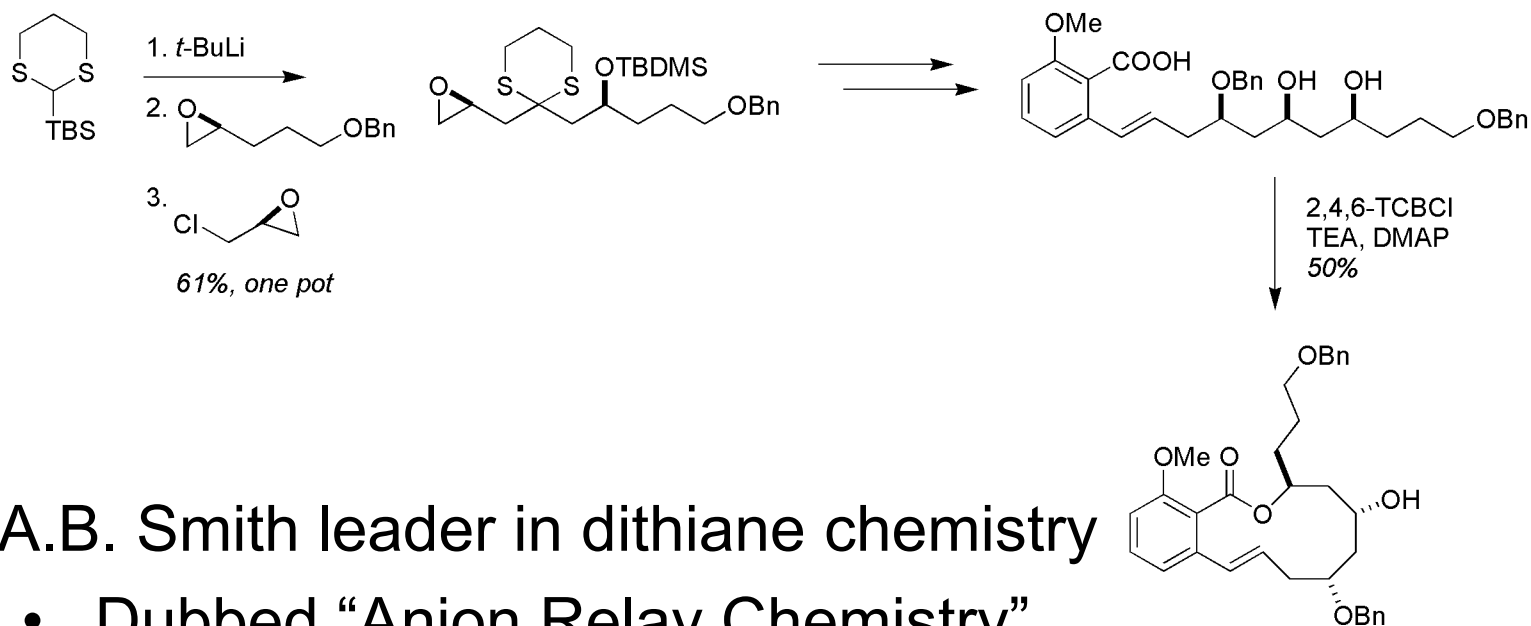
- Tietze later employed domino transformation with dithiane to construct enantiopure 1,5 diols and 1,3,5 triols



Fuji, K.; Ueda, M.; Fujita, E. *J. Chem. Soc. Chem. Commun.* **1983**, 49. Tietze, L.F.; Geissler, H.; Gewert, J.A.; Jakobi, U. *Synlett* **1994**, 511.

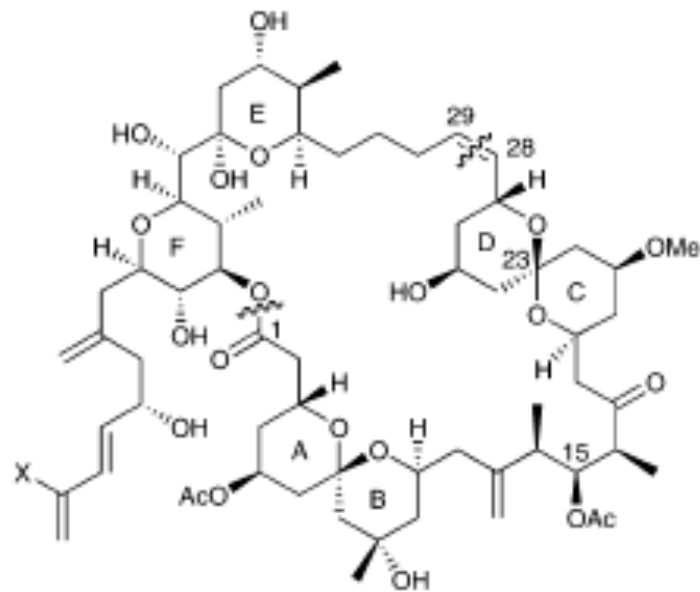
# Dithiane and Oxathian Surrogates

- Asymmetric variant employed by Maier for construction of benzolactone-enamide core natural products



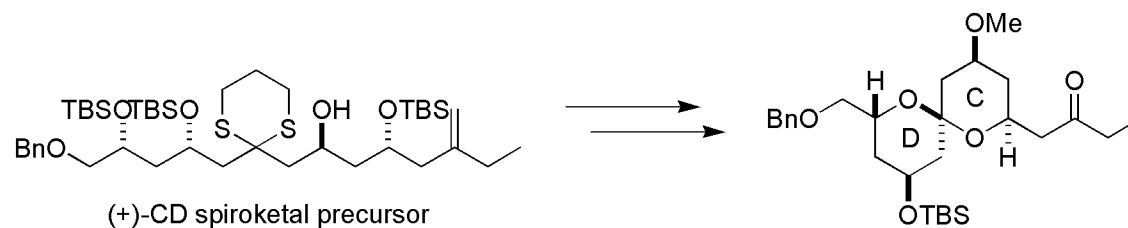
- A.B. Smith leader in dithiane chemistry
  - Dubbed “Anion Relay Chemistry”
  - Pioneered term *linchpin* for silyl-substituted dithiane in this context

# Dithiane and Oxathian Surrogates



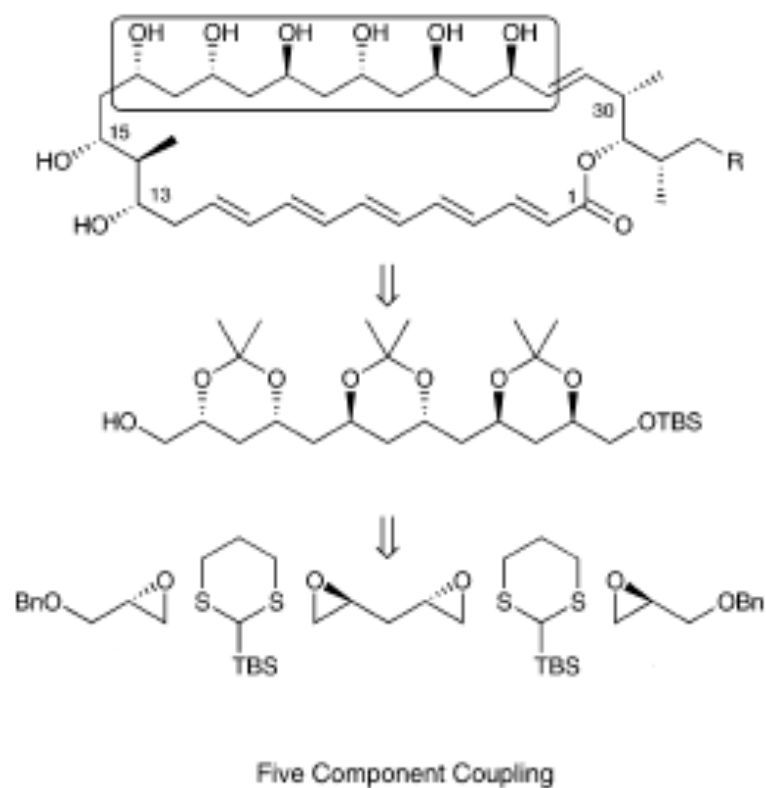
(+)-Spongistatin 1, X = Cl

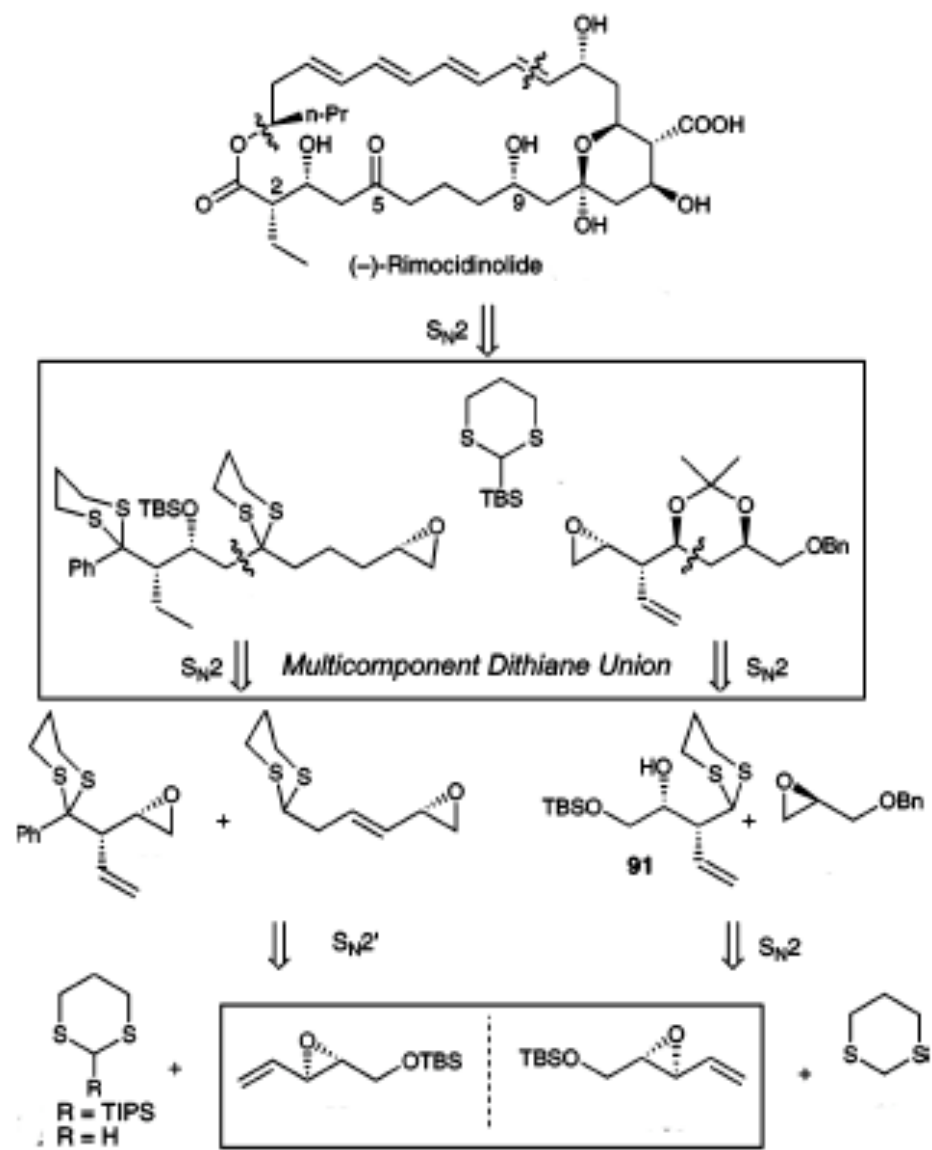
(+)-Spongistatin 2, X = H



# Dithiane and Oxathian Surrogates

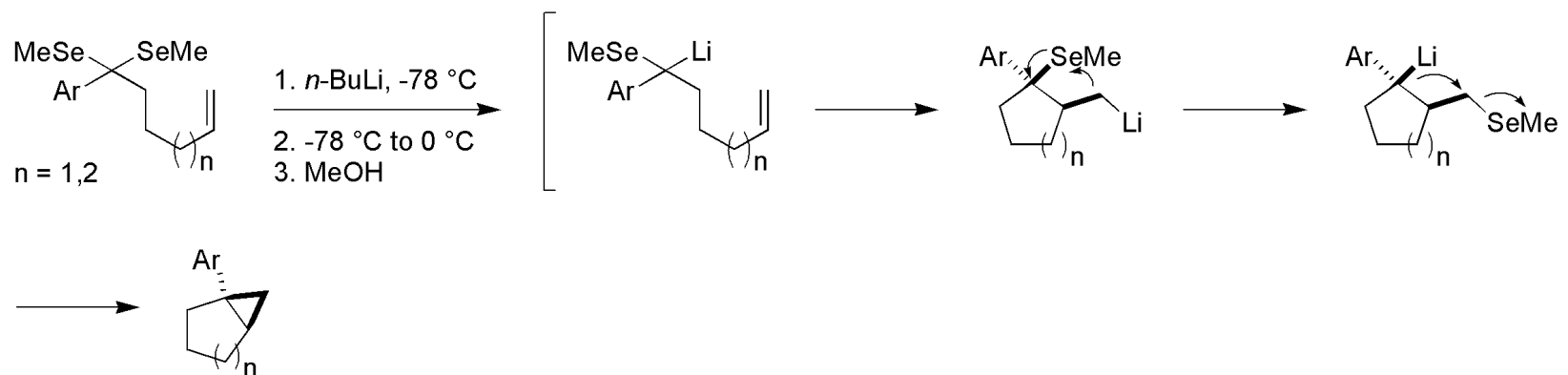
- Formal synthesis of Mycoticin: one-pot 5-component





# Other $\alpha,\alpha$ -Dianion Surrogates

- Selenium-based dianion substitutes
  - No EWG needed
  - Se both stabilizes and undergoes Li/Se exchange to form  $\alpha$ -selanylalkyllithiums
  - SeMe reacts primarily over SePh



# Other $\alpha,\alpha$ -Dianion Surrogates

- Silicon-based dianion substitutes
  - Intramolecular ring closure on bifunctional electrophiles
  - Silyl-substituted silanes
  - Sulfur-substituted silanes

