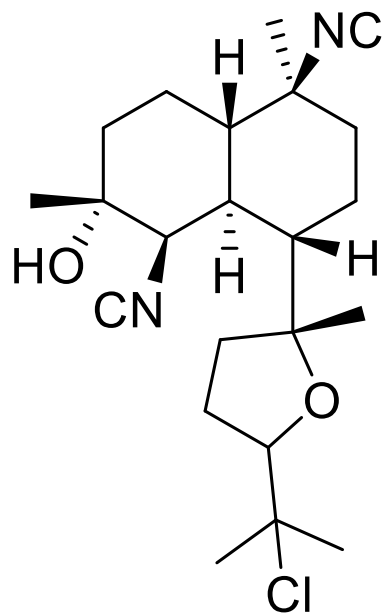


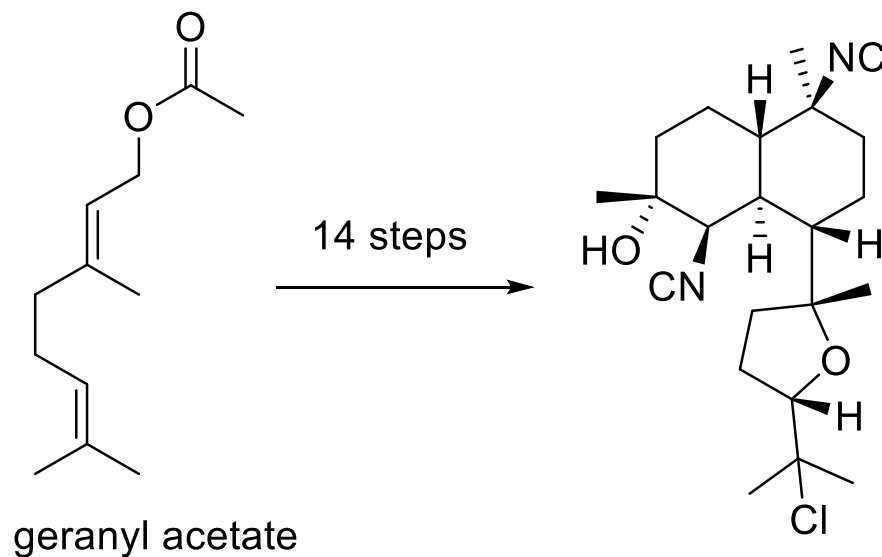
Enantioselective Total Synthesis of (+)-Kalihinol B



Presented by: Grace Hubbell

January 27, 2018

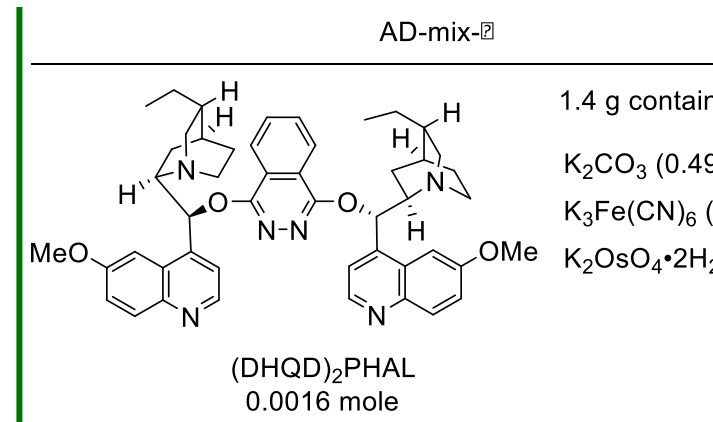
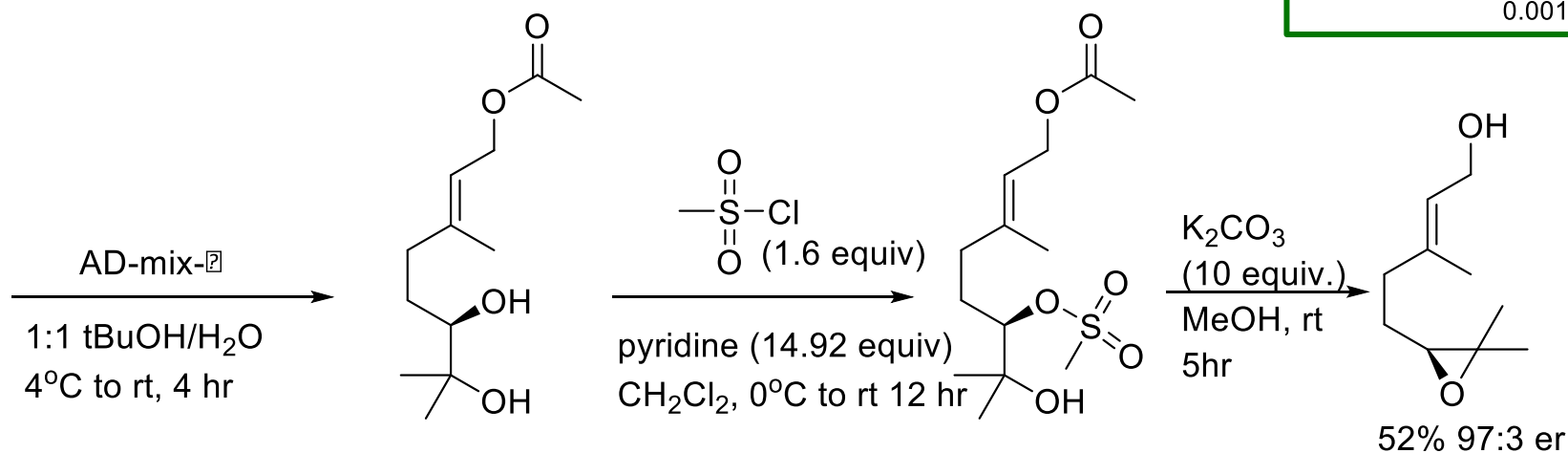
(+)-Kalihinol B Total Synthesis



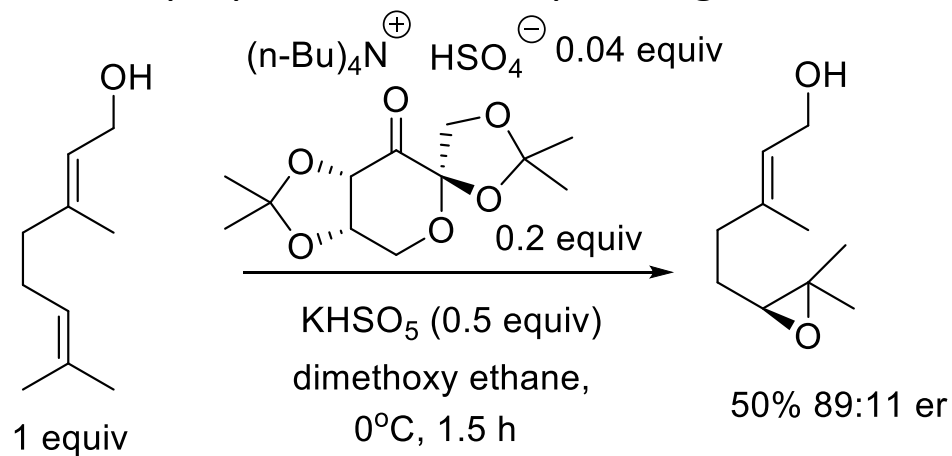
- Diterpenoid isolated from sponge of genus *Acanthella*
- Enantioselective synthesis achieved in 2015 by Vanderwal and coworkers. ¹

Epoxidation

Epoxidation of geranyl acetate via Sharpless Asymmetric dihydroxylation ²



Alternatively, the epoxide can be prepared in one-step from geraniol via Shi Epoxidation: ³

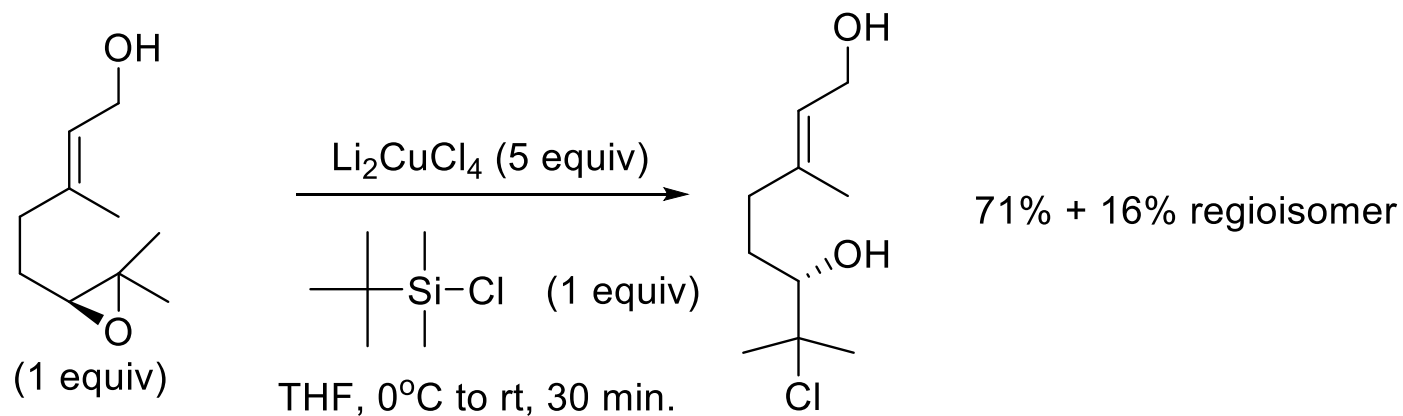


2.) Surendra, J.; Corey, E.J. *J. Am. Chem. Soc.* **125**, 8865.

3.) Wang, Z-X.; Shi, Y. *J. Org. Chem.* **1998**, *63*, 3099.

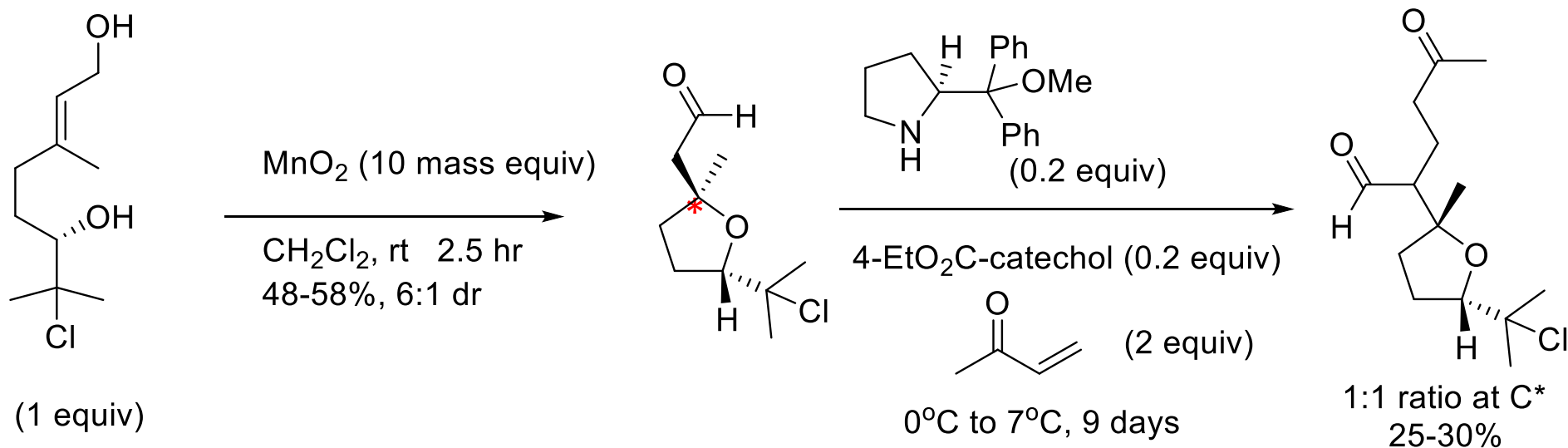
Regioselective Epoxide Chlorinolysis

Regioselective chlorinolysis of the epoxide carried out with lithium tetrachlorocuprate ⁴



Selective Oxidation of Allylic Alcohol

Following oxidation of allylic alcohol, spontaneous cyclization to yield tetrahydrofuran ring occurs

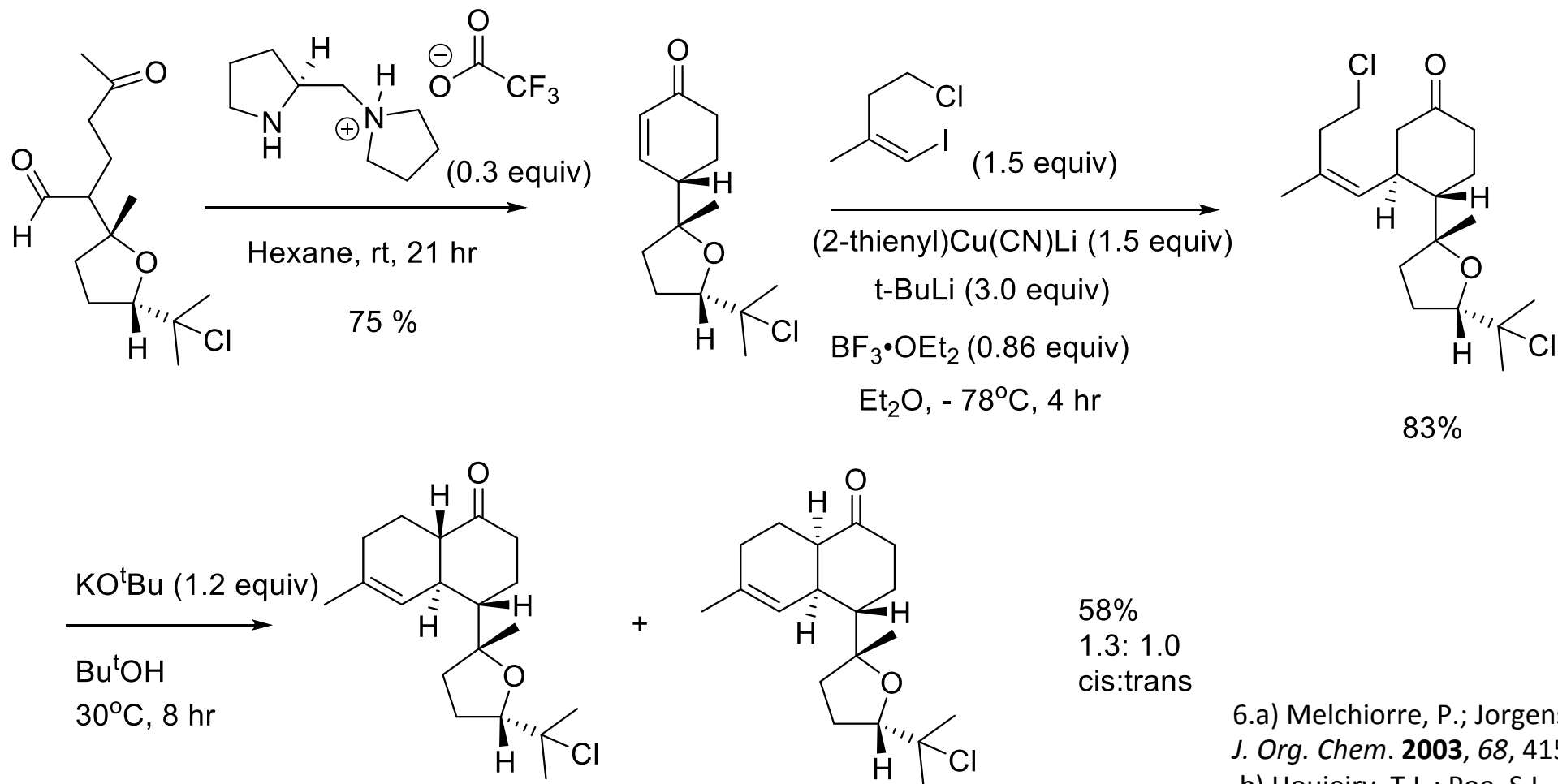


However, incorrect stereochemical configuration at the indicated carbon

Use of Gellman prolinol catalyst in a Michael Addition allowed for partial stereochemical correction ⁵

Decalinone Formation

Michael addition using chiral diamine auxiliary yields α,β -unsaturated cyclohexenone ⁶
Robinson annulation achieved with aid of cyanocuprate reagent, vinyl halide ⁷

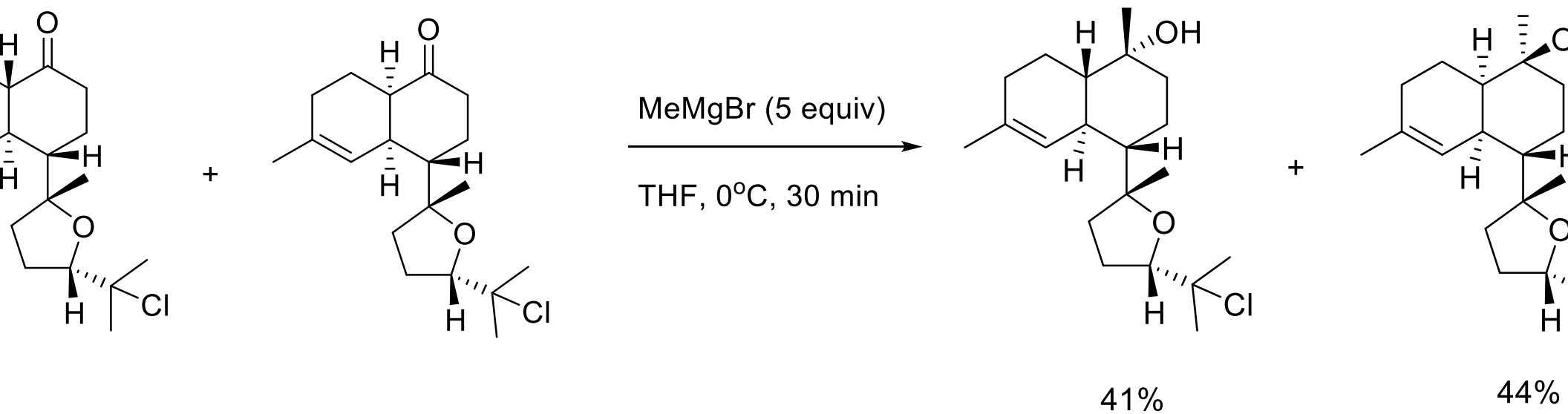


6.a) Melchiorre, P.; Jorgenson, K.
J. Org. Chem. **2003**, *68*, 4151.

b) Houjeiry, T.L.; Poe, S.L. McQuinn
Org. Lett. **2012**, *14*, 4394.

7.) Piers, E. *Pure Appl. Chem.* **198**

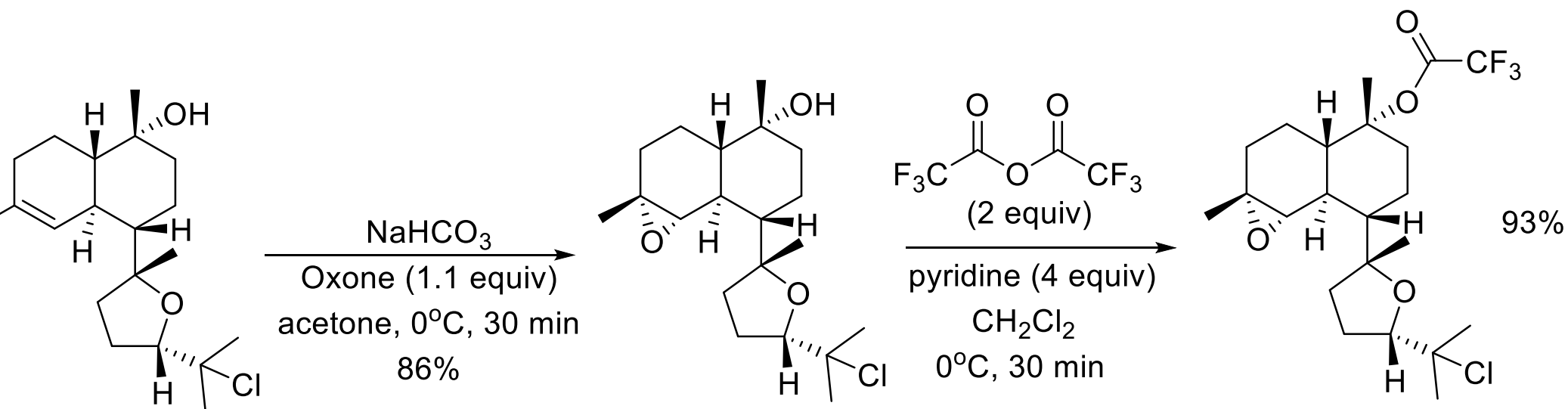
Grignard Addition to Decalinones



Both trans and cis decalinones were subjected to reaction with Grignard Reagent
Desired product isolated in 41 % yield

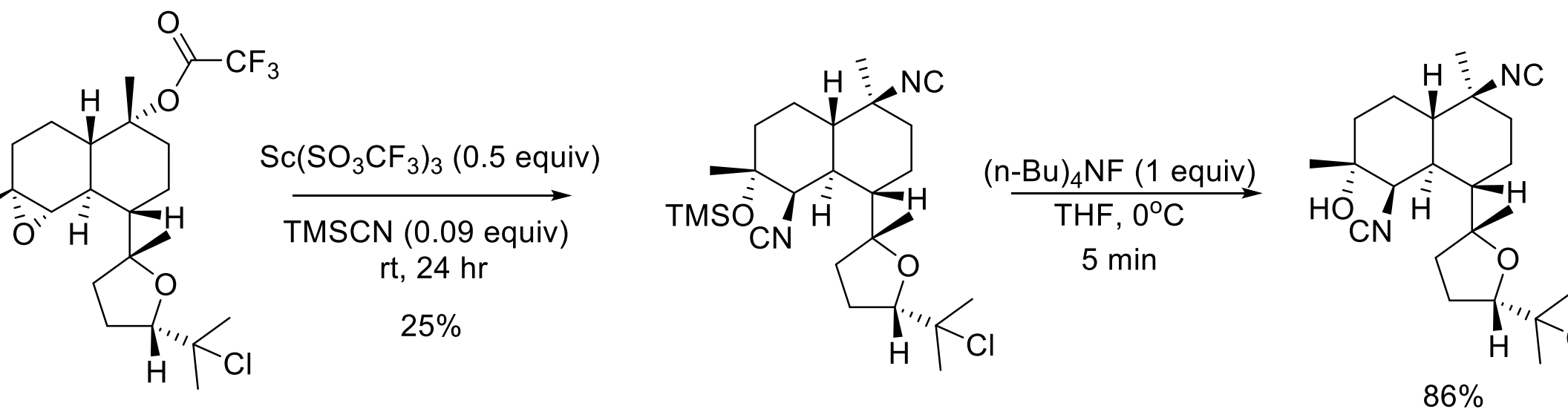
Epoxidation & Triflate Formation

Stereospecific epoxidation of trans-decalin occurs on the bottom face



Triflate formation at tertiary alcohol generates a good leaving group for subsequent reaction

Shenvi's Method of Isocyanation ⁸



Overall Yield: 18%

Isonitrile displacement of triflate mediated with Scandium catalyst results in stereochemical inversion

8.a.) Pronin, S.V.; Reiher, C.A.; Shenvi, R.A.; *Nature*. **2013**, *501*, 195. b.) Pronin, S.V.; Reiher, C.A.; Shenvi, R.A. *J. Am. Chem. Soc.* **2012**, *134*, 19604.

Questions?