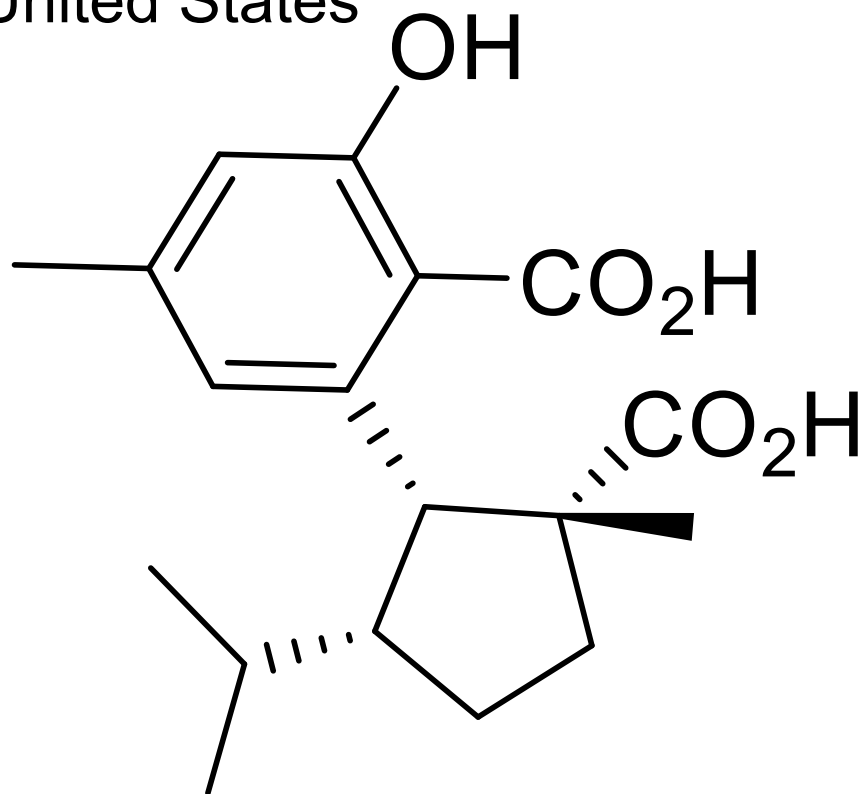


# Total Synthesis of Debromohamigeran E

Thomas P. Blaisdell and James P. Morken: Department of Chemistry, Boston College, Chestnut Hill, Massachusetts, United States

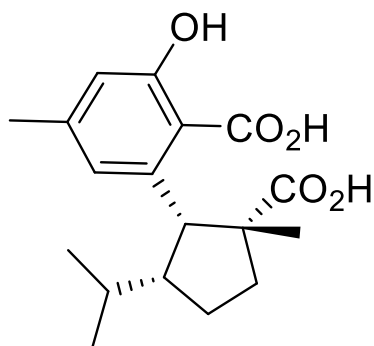


Presented by: Emmanuel W. Maloba

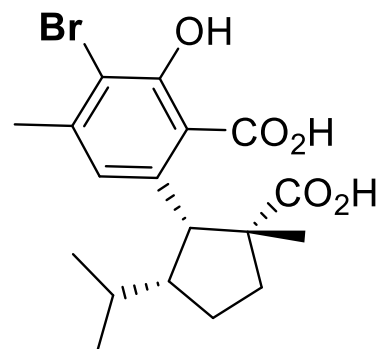
04/07/2018

For: CEM 852

# Why Debromohamigeran E?



**Debromohamigeran E**



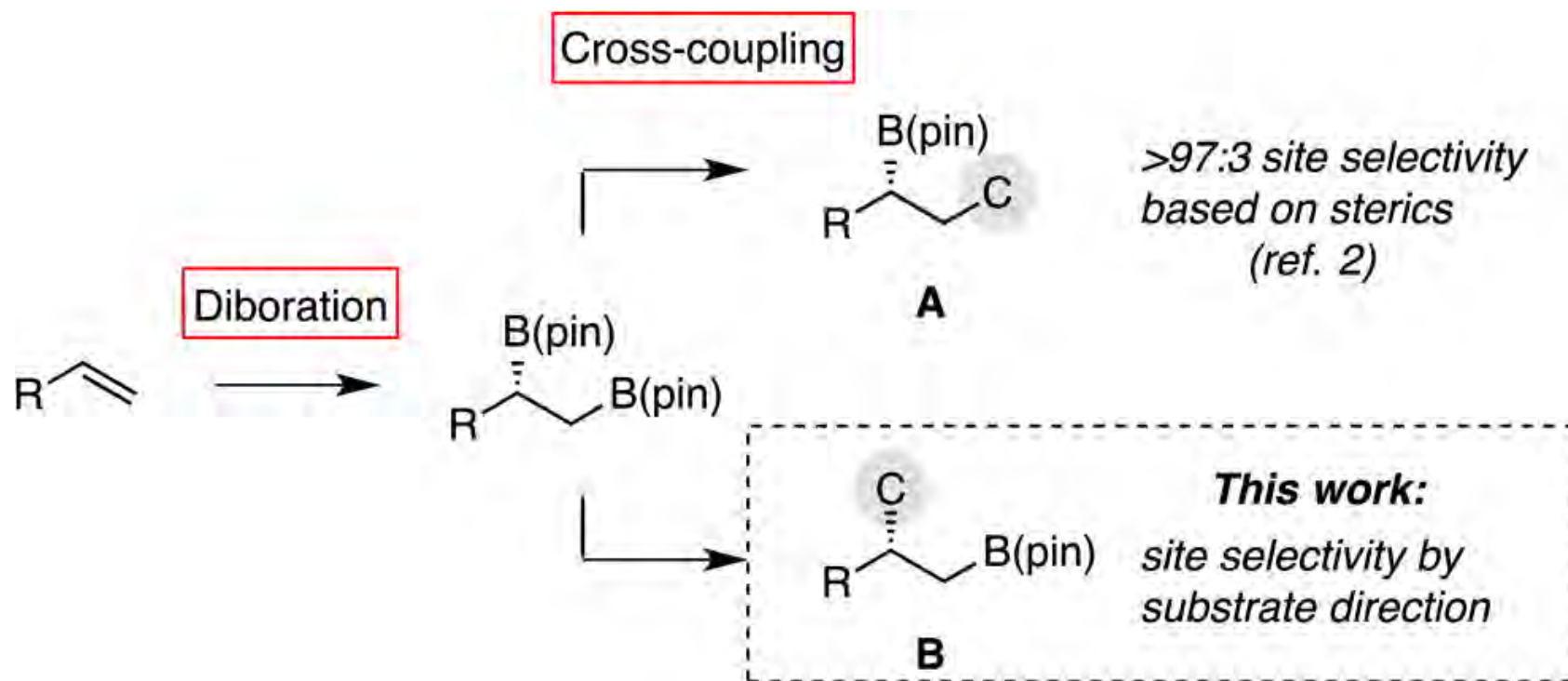
**Hamigeran E**

- ❖ Hamigerans are phenolic compounds with varying degrees of bromination and cyclization isolated from *Hamigera tarangaensis*, a poecilosclerid sponge found predominately around northern New Zealand.
- ❖ The live sponge is orange-red to bright yellow underwater with rippled exterior and large, tented oscules.
- ❖ The reported biological activity of these compounds range from mild cytotoxicity to inhibition of herpes and polio viruses for hamigeran B.

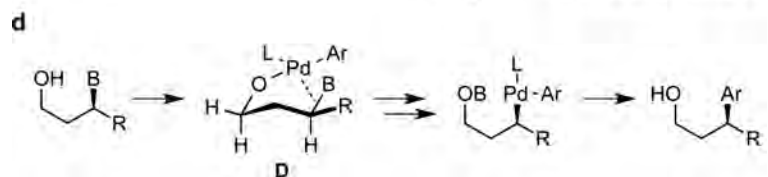
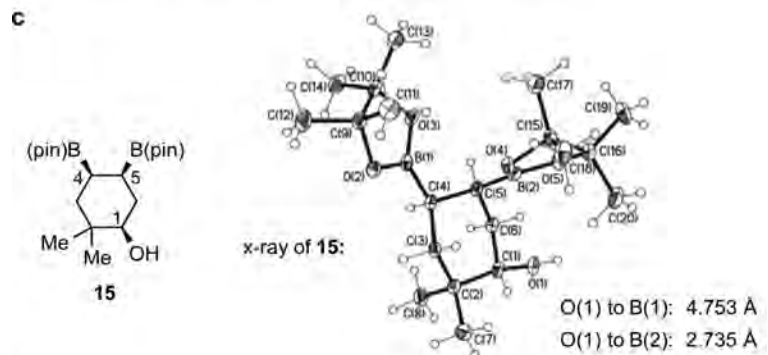
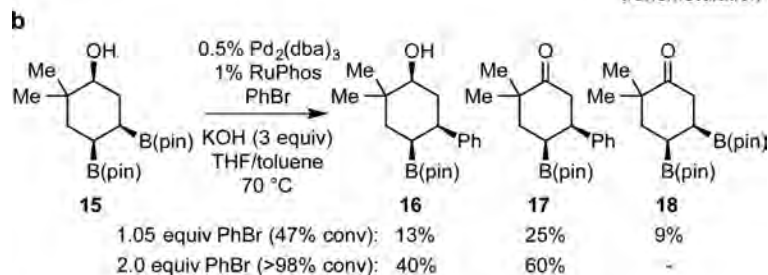
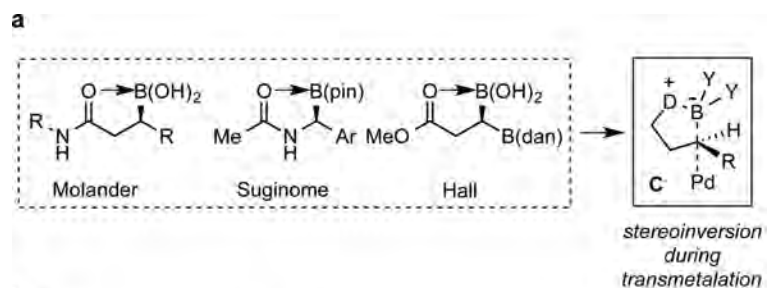
John H. Millera; Peter T. Northcote, *Org. Biomol. Chem.*, **2013**, *11*, 8041–8051

Thomas P. Blaisdell and James P. Morken, *J. Am. Chem. Soc.* **2015**, *137*, 8712

# Hydroxyl-Directed Diborylation followed by Cross-Coupling



# Features of Directed Cross-Coupling Reactions



❖ The reaction exhibits complete selectivity when the B(pin) group is positioned β to the hydroxyl substituent

❖ A plausible mechanism for the directing effect involve:

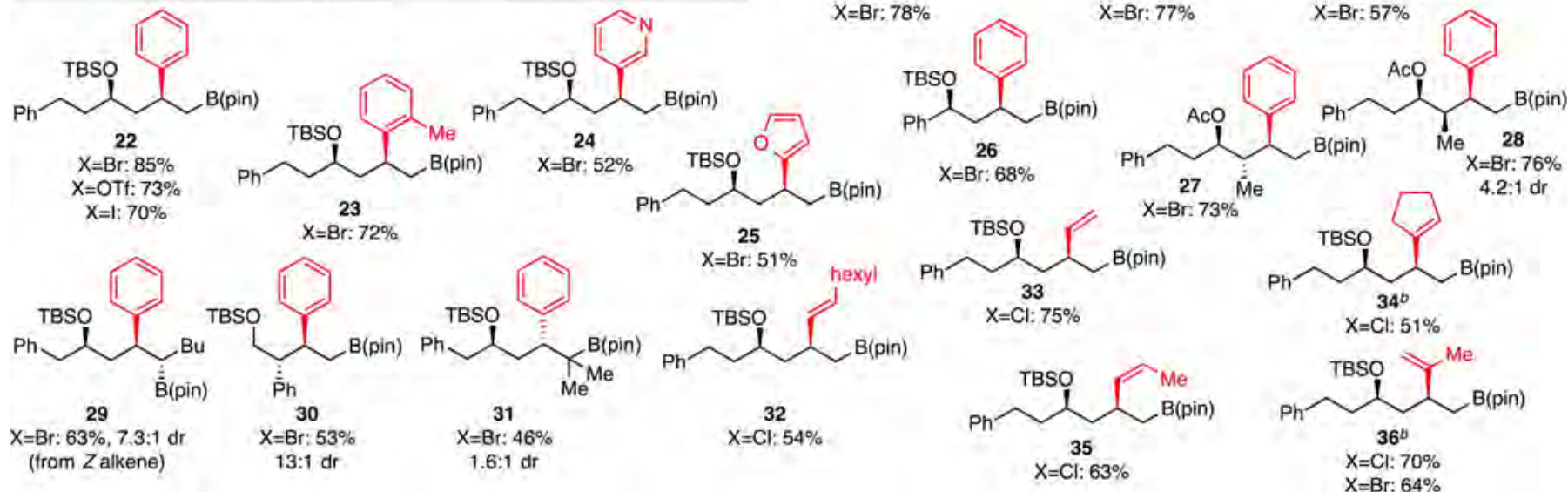
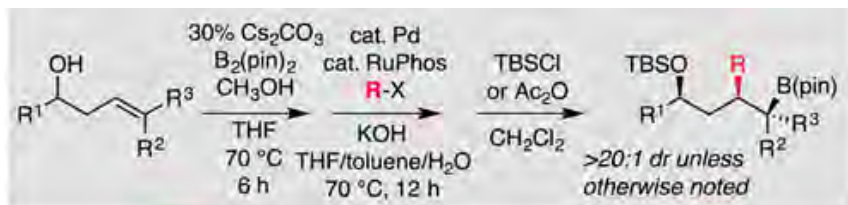
a) binding of the substrate hydroxyl to an LPdAr complex by displacement of a halide;

b) subsequent internal delivery of Pd through a complex such as **D**;

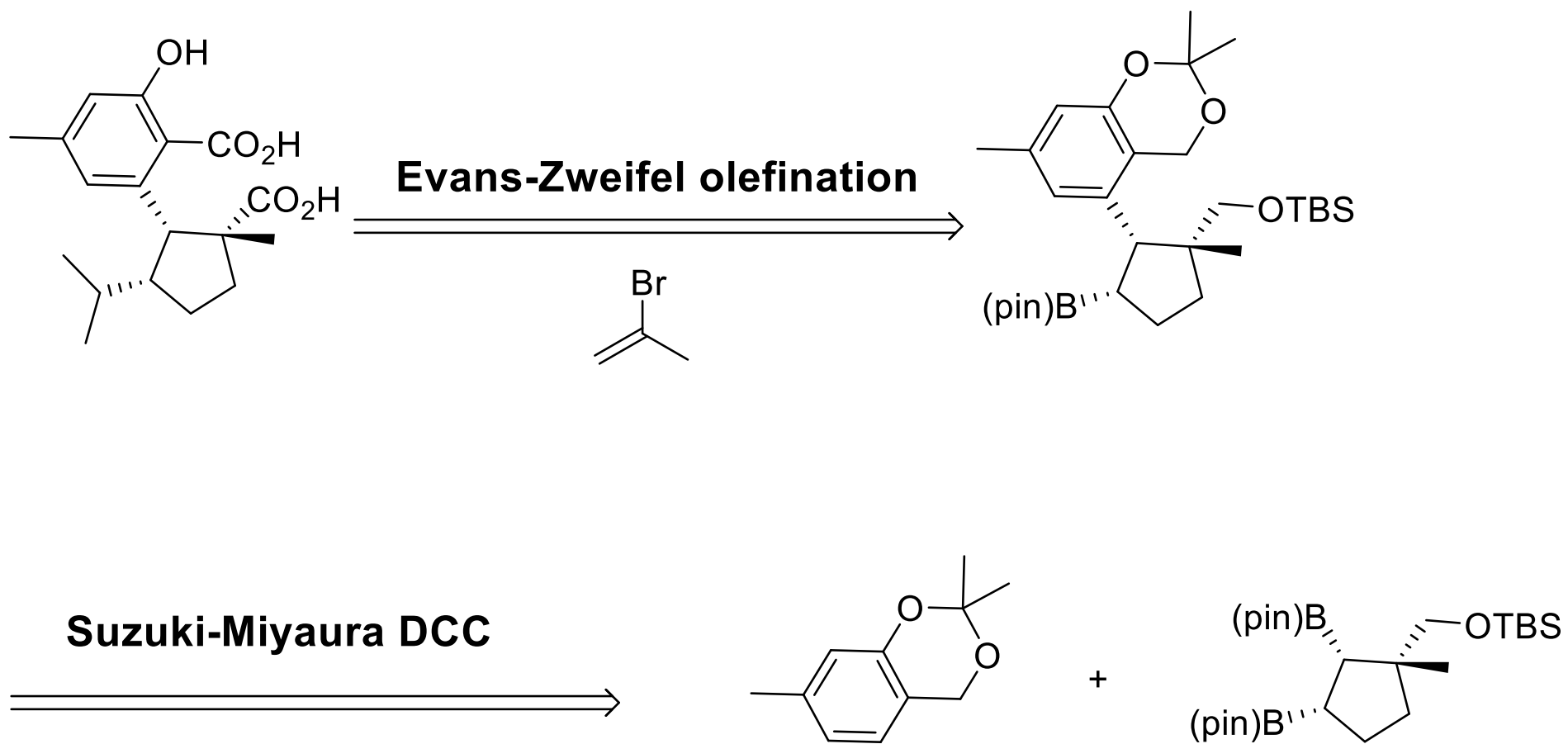
c) Generation of an organopalladium complex through an inner-sphere stereoretentive transmetalation and,

d) Ultimately deliver the corresponding coupling product

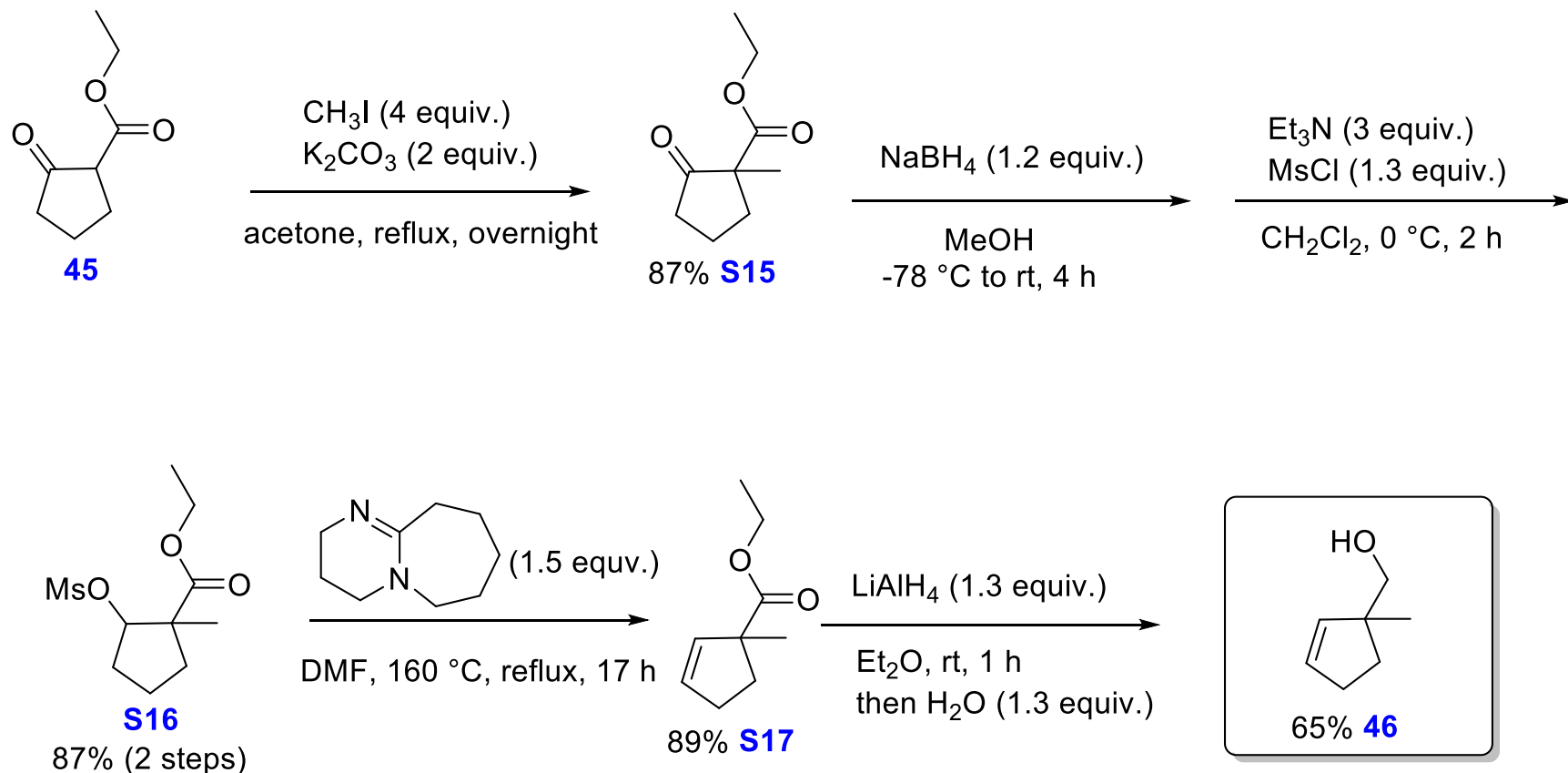
# Survey of Hydroxyl-Directed Cross-Couplings



# Retrosynthesis



# Preparation of Starting Materials

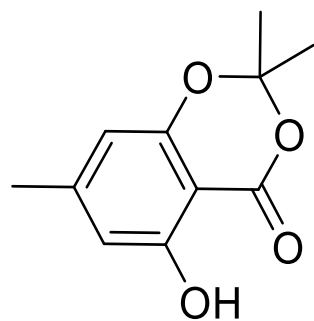
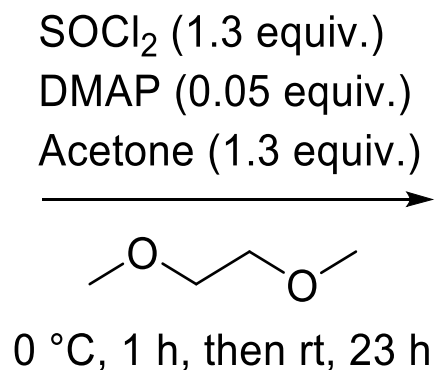
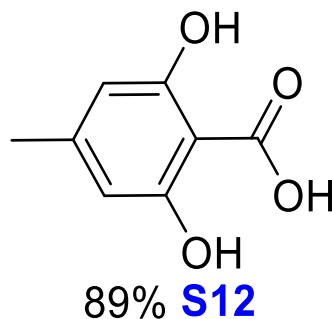
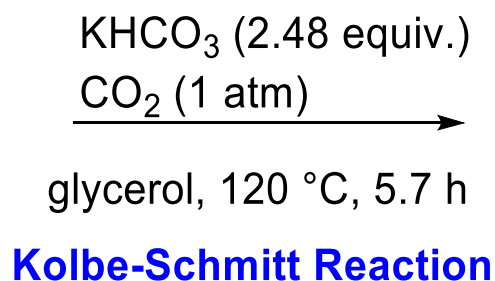
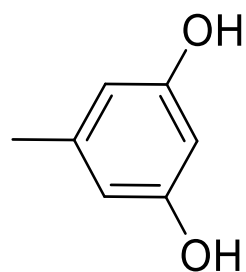


Hausch, Felix; Tiefenbacher, Konrad, *Chem. Eur. J.*, **2017**, 23, 3178 – 3183

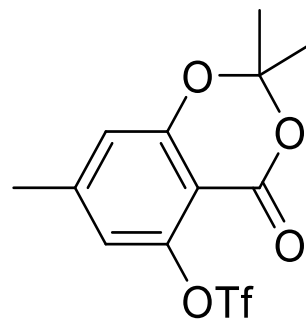
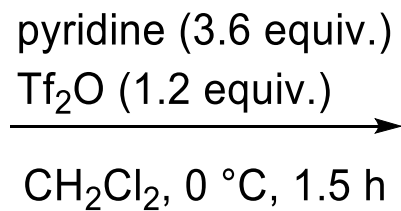
Ruiz, K. Basu, L. A. Paquette, *Tetrahedron*, **2006**, 62, 5178 – 5194

Thomas P. Blaisdell and James P. Morken, *J. Am. Chem. Soc.* **2015**, 137, 8712

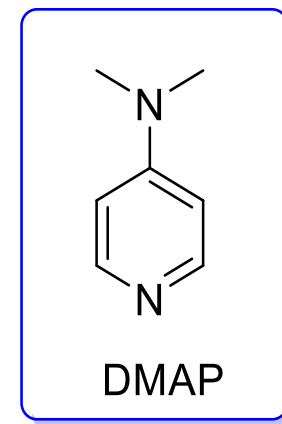
# Preparation of Starting Materials Cont...



71% **S13**

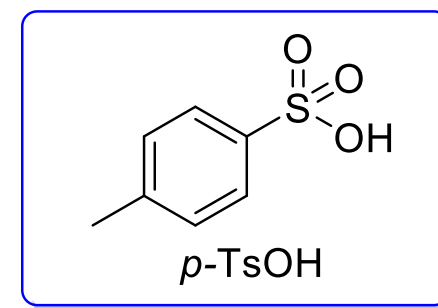
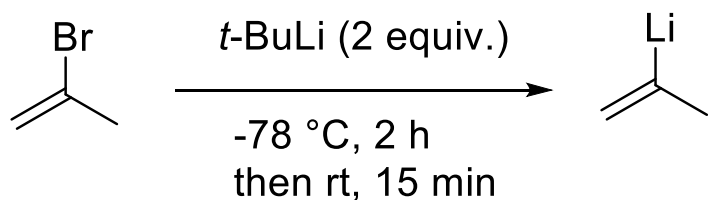
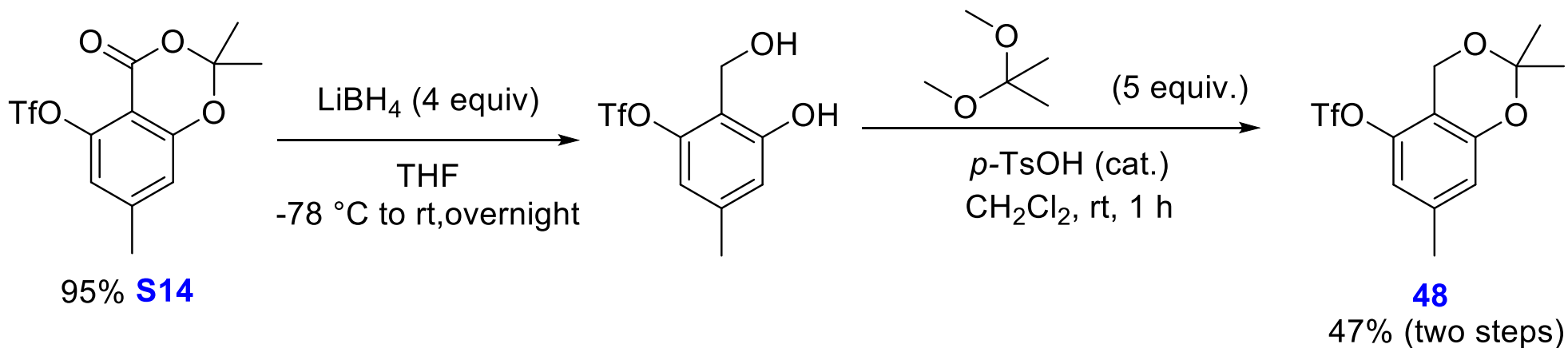


95% **S14**

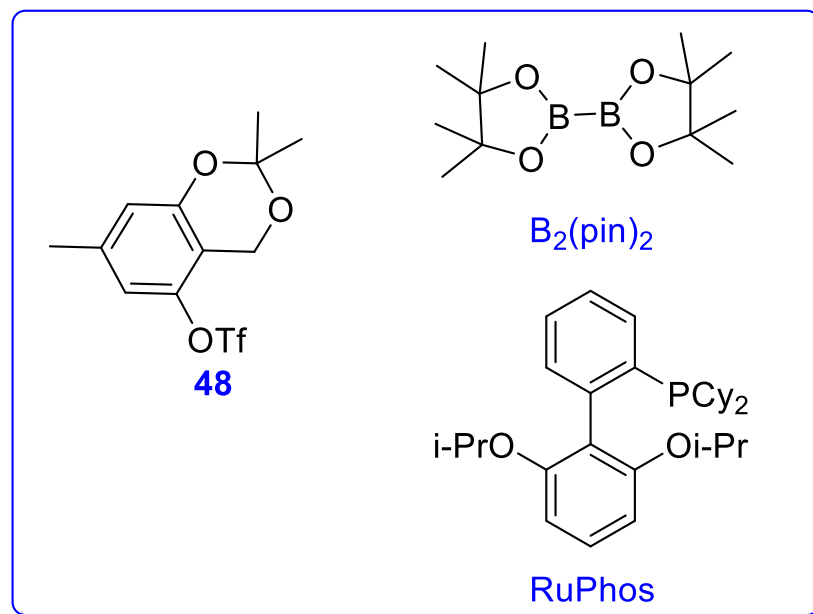
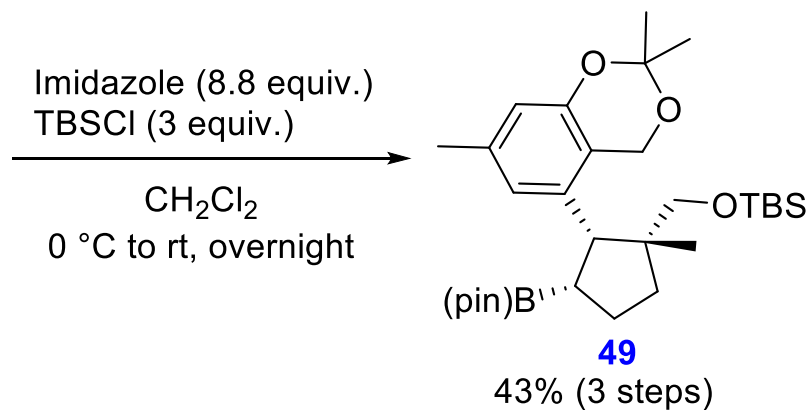
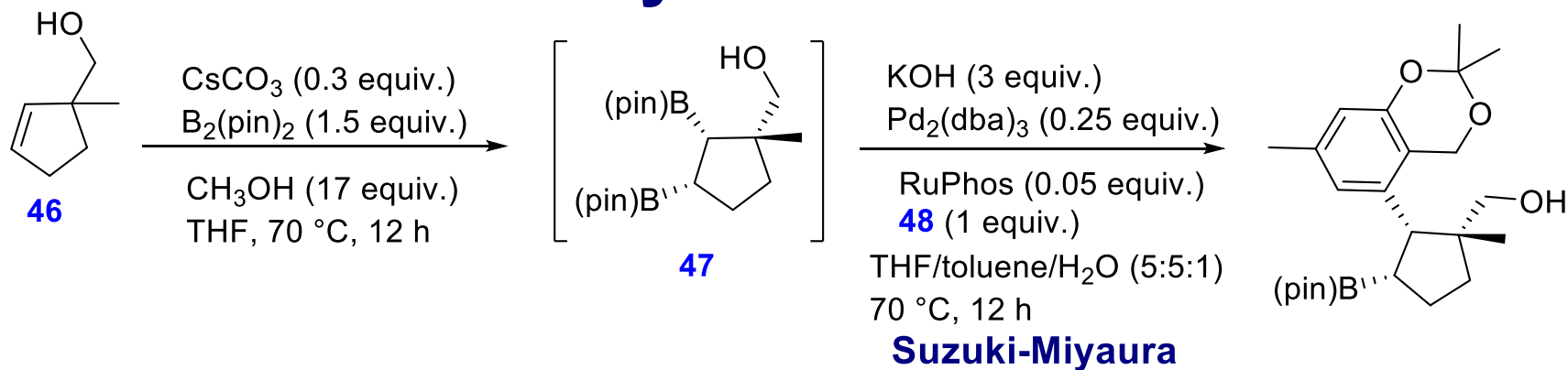


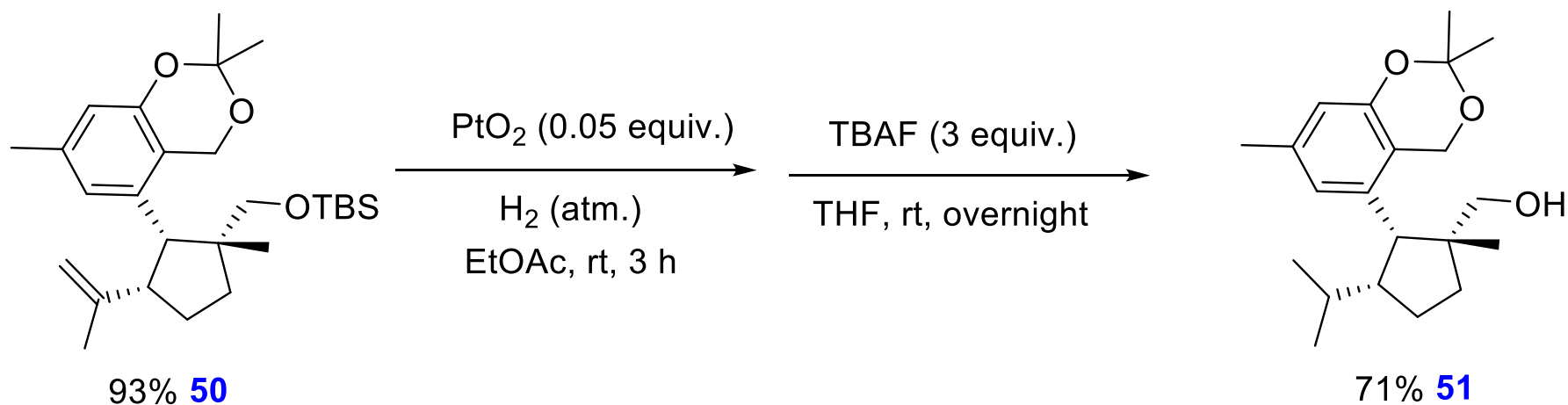
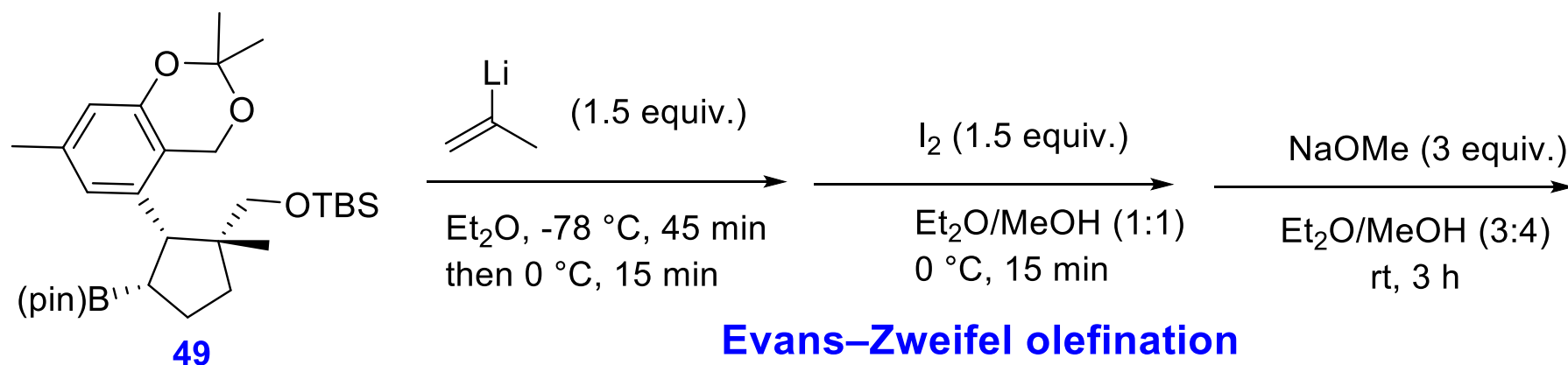


# Preparation of Starting Materials Cont...



# Synthesis

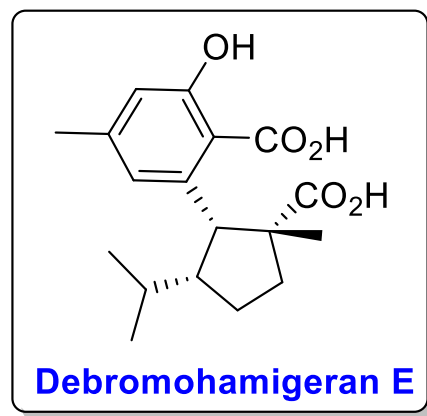
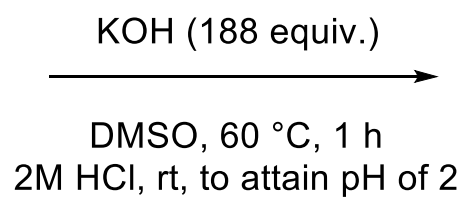
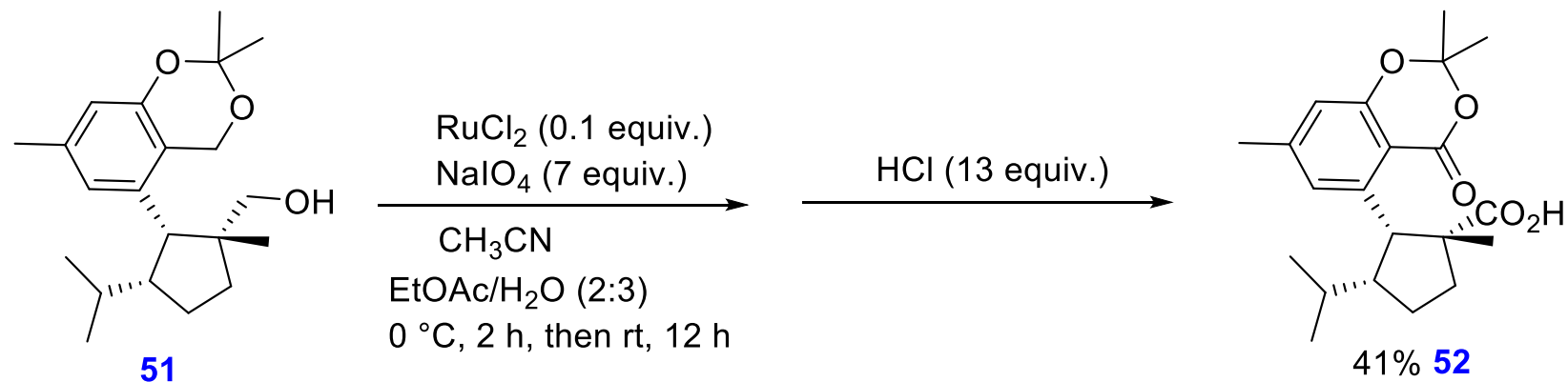




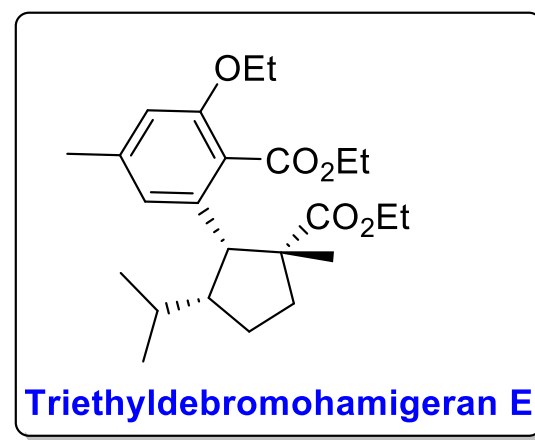
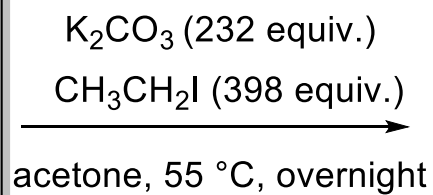
Zweifel, G.; Arzoumanian, H.; Whitney, C. C. *J. Am. Chem. Soc.* **1967**, *89*, 3652

Evans, D. A.; Crawford, T. C.; Thomas, R. C.; Walker, J. A. *J. Org. Chem.* **1976**, *41*, 3947

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93%



64%

**THANK YOU!!**