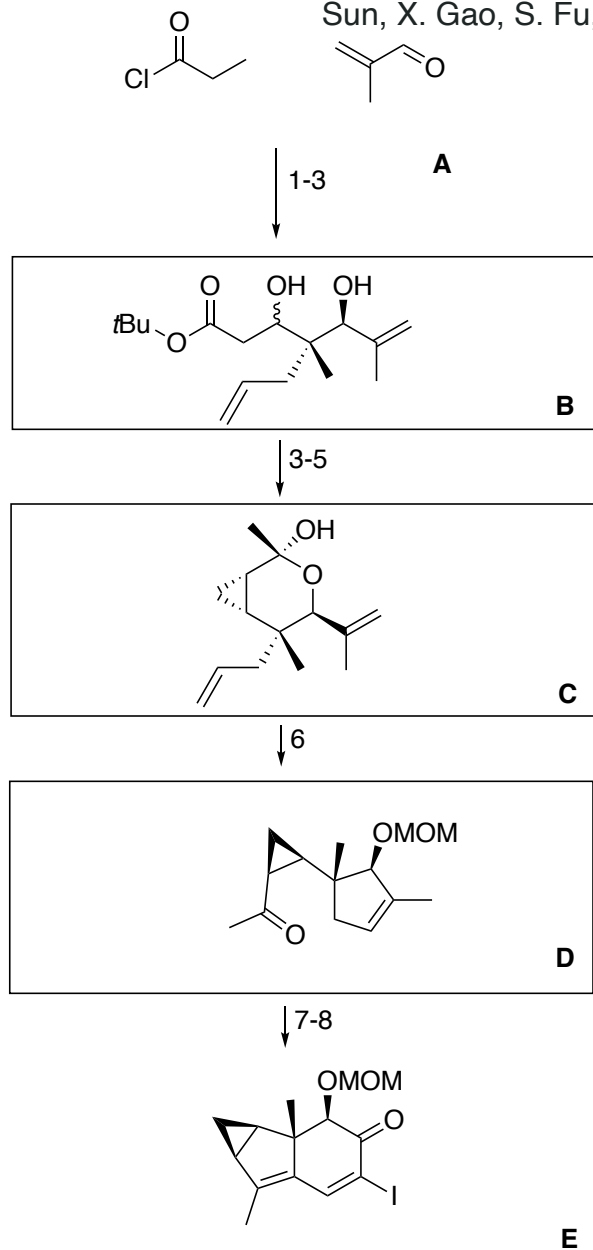


Synthesis Challenge 101

Asymmetric Total Synthesis of Shizukaol J, Trichloranoid C and Trishizukaol A, X. Wang, Z. Wang, X. Ma, Z. Huang, K. Sun, X. Gao, S. Fu, B. Liu, *Angew. Chem. Int. Ed.* **2022**, ASAP: 10.1002/anie.202200258

17.02.2022

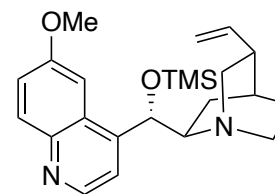


1) **Cat I** (10 mol%), LiI, $i\text{Pr}_2\text{NEt}$, DCM/ Et_2O
 2) LiHMDS (xs), allyl iodide, THF/HMPA;
 then **I**; then conc. aq. HCl, then NaBH_4 , MeOH

3) $p\text{TsOH}\cdot\text{H}_2\text{O}$, PhCH_3 , 70 to 100°C
 4) $\text{CH}_2=\text{S}(\text{O})\text{Me}_2$, DMSO
 5) MeLi, ether, -78 to 0°C

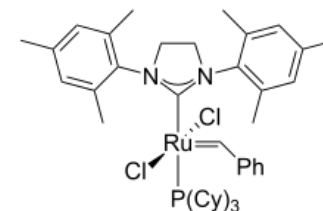
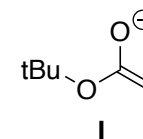
6) 2nd gen. Grubbs cat., DCM, rt
 then $i\text{Pr}_2\text{NEt}$, MOMCl, TBAI

7) O_3 , DCM/ $i\text{PrOH}$, -78°C; then PPh_3 ;
 then piperidine (0.5 eq.) AcOH (1 eq.) rt to 60°C;
 then KOH, MeOH, rt
 8) I_2 , py, DCM, 55°C



Cat I

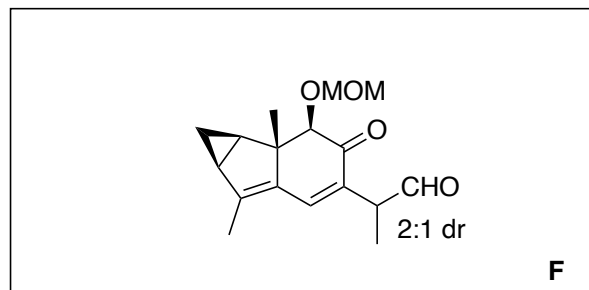
Step 1: via Keten [2+2]
 cycloaddition



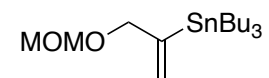
2nd gen. Grubbs cat.

E

↓ 9-11

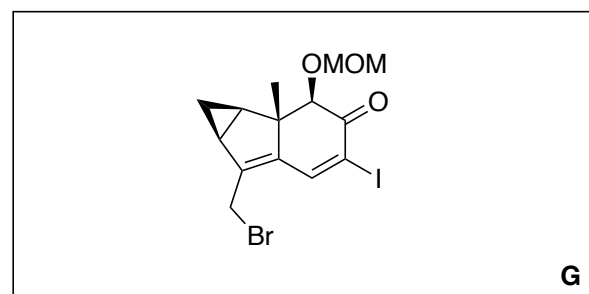


- 9) **II**, CuI, CsF, Pd(PPh₃)₄, DMF, rt
10) DBU, PhCH₃, 130°C
11) TMSCl, MeCN, -45 to -40°C



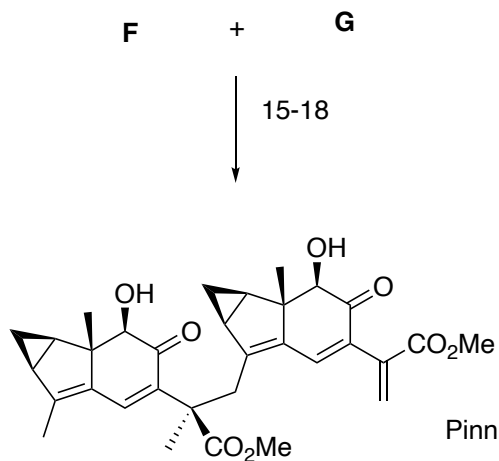
E

↓ 12-14

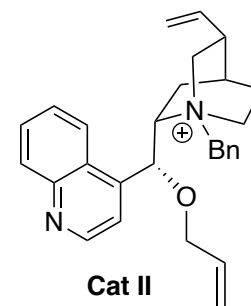


- 12) SeO₂, dioxane, 100°C
13) LiAlH(OtBu)₃, THF, -78°C
14) CBr₄, PPh₃, imidazole, DCM, 0°C

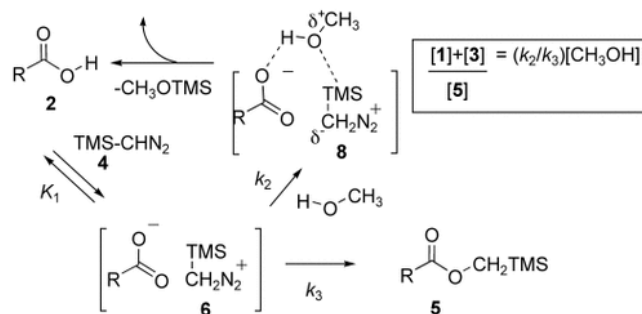
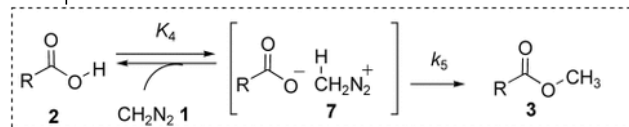
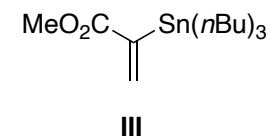
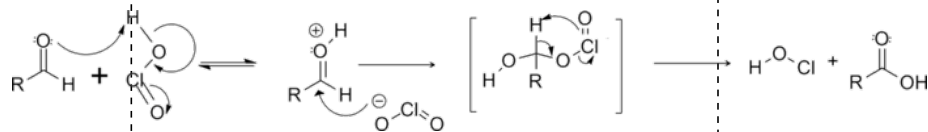
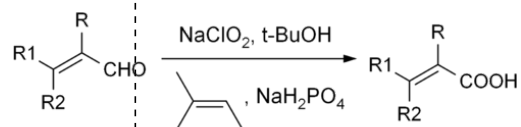
Riley oxidation



- 15) **Cat II** (20 mol%), aq. CsOH, MnSO₄, PhMe
- 16) Pinnick Oxidation; then TMSCHN₂, 0°C
- 17) **III**, Pd(PPh₃)₄, CuI, CsF, DMF, rt
- 18) TMSCl, NaI, MeCN, -40 to -20°C



Pinnick Oxidation (https://en.wikipedia.org/wiki/Pinnick_oxidation):



<https://doi.org/10.1002/anie.200702131>