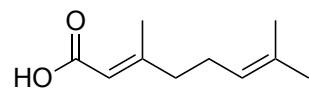
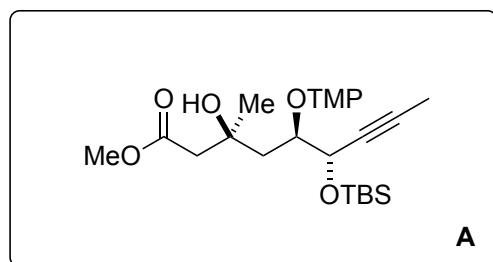


Total Synthesis of (-)-Sinulariadiolide. A Transannular Approach

Zhanchao Meng and Alois Fürstner; *J. Am. Chem. Soc.* **2019**, *141*, 805–809.

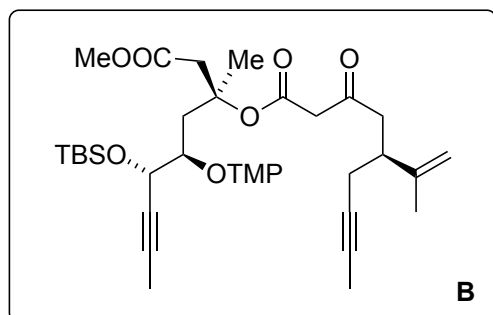


1-6

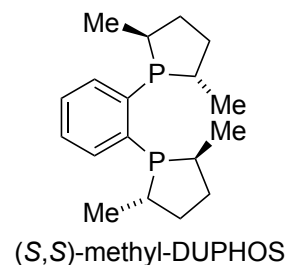
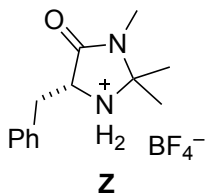


(R)-(-)-carvone

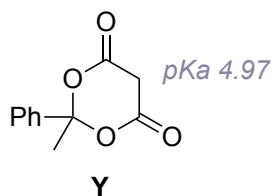
7-10



- 1) Me_2SO_4 , *i*- Pr_2NEt , 0 °C
then O_3 , -78 °C, then PPh_3
- 2) **Z** (25 mol%), CuCl_2 (12 mol%),
TEMPO, MS 4 Å, -10 °C (e.r. 83%)
- 3) propyn-1-ylmagnesium bromide, pentane
- 4) TBSCl, imidazole
- 5) $\text{B}_2(\text{pin})_2$, *t*-BuONa (15 mol%), CuCl (6 mol%),
(*S,S*)-methyl-DUPHOS (6 mol%), MeOH/THF
- 6) $\text{NaBO}_3 \cdot 6\text{H}_2\text{O}$, aq. THF, 90 °C



- 7) aq. H_2O_2 , NaOH
- 8) TsNHNH_2 , HOAc, CH_2Cl_2
- 9) NaClO_2 , NaH_2PO_4 , 2-methylbut-2-ene, *t*-BuOH/ H_2O
- 10) **Y**, DCC, DMAP, Et_3N , CH_2Cl_2 , then **A**, PhMe, 60 °C



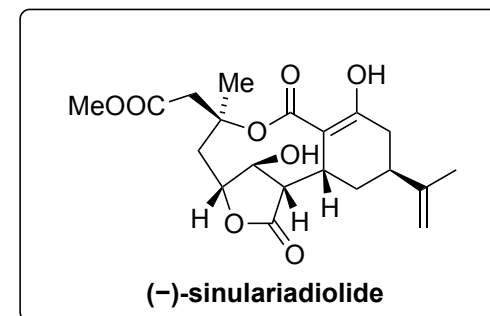
1) Name the starting material. How is this commercially prepared from isoprenol? *Geranic acid*

BASF citral process to geranial followed by oxidation (see below)

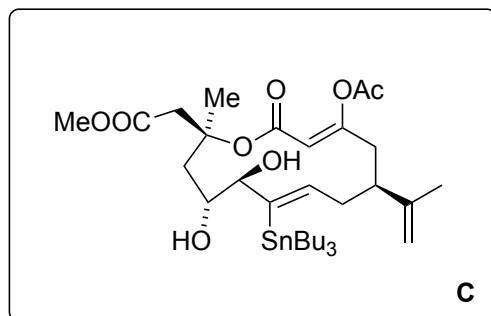
2) Name of the organocatalyst **Z**? How would you prepare it? *Macmillan imidazolidinone organocatalysts (see below)*

5) *copper-catalyzed asymmetric hydroboration: Angew. Chem. Int. Ed.* **2009**, *48*, 6062;
J. Am. Chem. Soc. **2009**, *131*, 3160;
J. Am. Chem. Soc. **2017**, *139*, 1275.

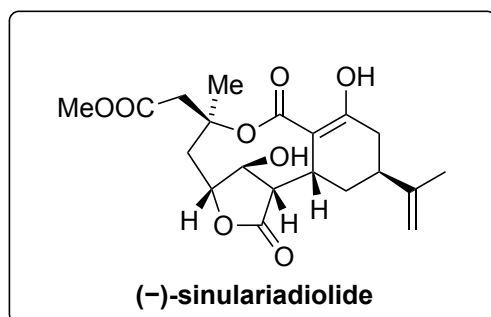
7) *Weitz-Scheffer epoxidation*
8) *Hint: a fragmentation occurs Eschenmoser–Tanabe fragm.*
9) *Pinnick oxidation*



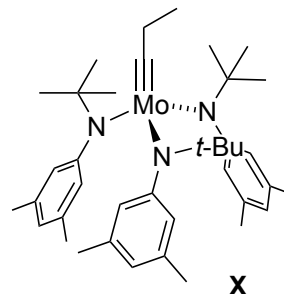
11-15



16-19



- 11) Ac_2O , DMAP (20 mol%), Et_3N , CH_2Cl_2 , $-40\text{ }^\circ\text{C}$;
- 12) aq. HF, THF
- 13) **X** (30 mol%), $\text{PhSi}[\text{CH}_2\text{CH}_2(\text{Ph})_2\text{SiOH}]_3$ (30 mol%)
toluene, $120\text{ }^\circ\text{C}$
- 14) Zn, HOAc, THF/ H_2O
- 15) Bu_3SnH , $[\text{Cp}^*\text{RuCl}]_4$ (11 mol%)



- 16) CO (1 atm), $\text{Pd}(\text{OAc})_2$ (20 mol%), AsPh_3 (40 mol%)
1,4-benzoquinone, TFA (40 mol%), MeOH
- 17) triphosgene, CH_2Cl_2 , pyridine, $0\text{ }^\circ\text{C}$
- 18) Cs_2CO_3 , CH_2Cl_2 , MeOH/ H_2O
- 19) BBr_3 , 2-methyl-2-butene, CH_2Cl_2

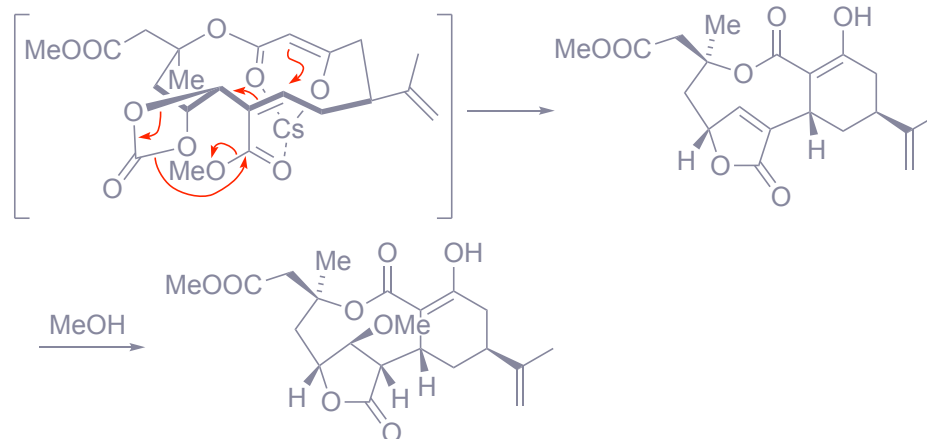
- 11) *Hint*: 1,3-dicarbonyl compounds are not well-tolerated by molybdenum alkylidynes/silanolate catalyst-ligand systems

13) *ring-closing alkyne metathesis (RCAM)*

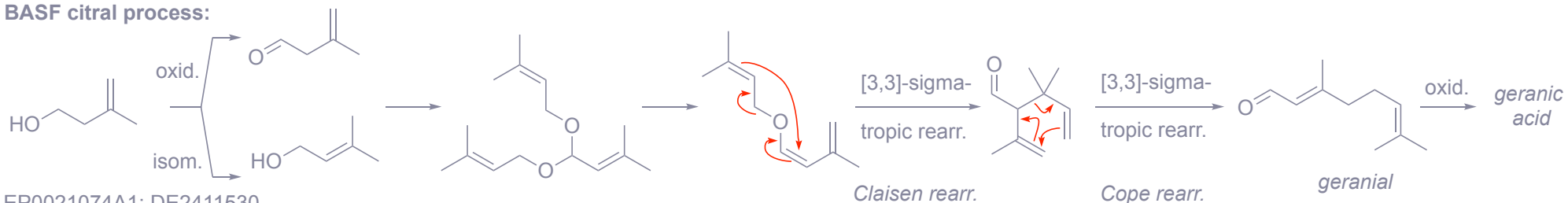
15) Mechanism? *see below*

- 17) *Hint*: numerous attempts to induce ring contraction at this stage failed, hence two hydroxyl groups were functionalized first.

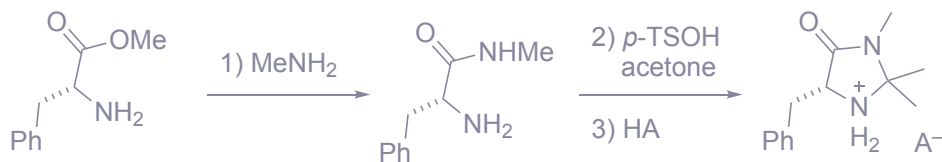
18) Ring Contraction:



BASF citral process:

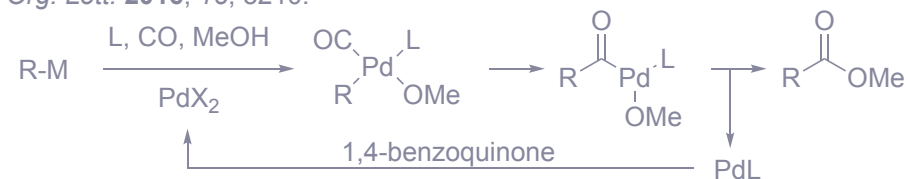


Macmillan Imidazolidinone Organocatalysts:



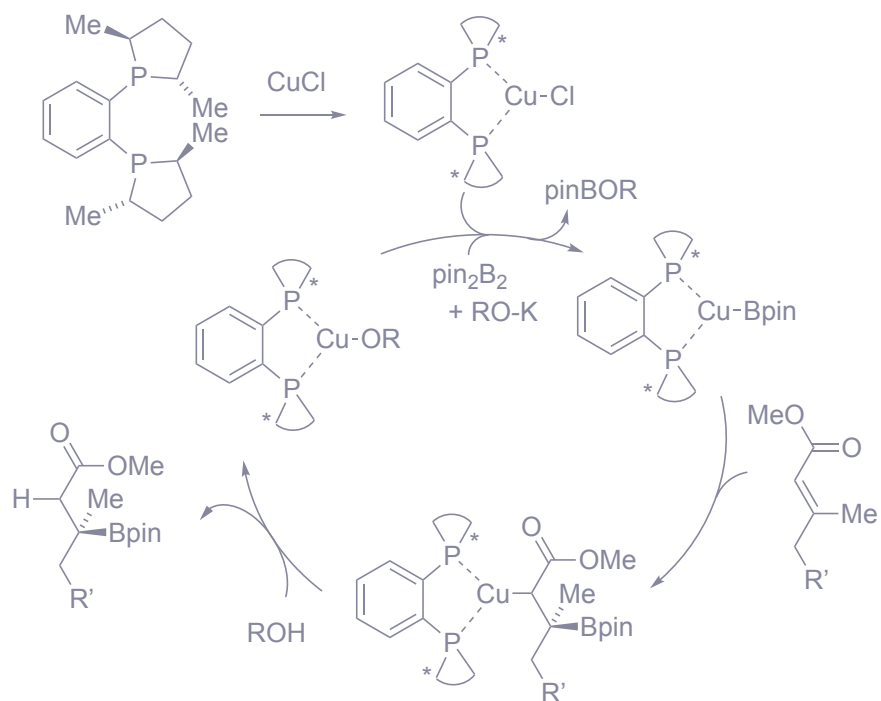
16) Methoxycarbonylation of an Organometallic Substrate

Org. Lett. **2016**, *18*, 3210.



5) Copper-Catalyzed Asymmetric Hydroboration:

proposed mechanism:



15) Ruthenium-Catalyzed *trans*-Selective Hydrostannation of Alkynes:

Angew. Chem. Int. Ed. **2014**, *53*, 3626

