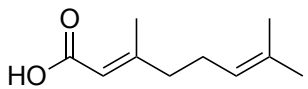
Total Synthesis of (−)-Sinulariadiolide. A Transannular Approach

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



1-6

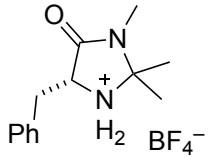
A

(*R*)-(–)-carvone

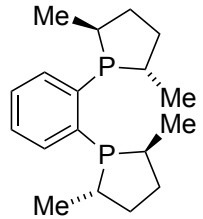
7-10

B

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) $B_2(pin)_2$, *t*-BuONa (15 mol%), CuCl (6 mol%),
(*S*,*S*)-methyl-DUPHOS (6 mol%), MeOH/THF
6) $NaBO_3 \cdot 6H_2O$, aq. THF, 90 °C

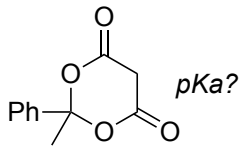


Z



(*S*,*S*)-methyl-DUPHOS

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

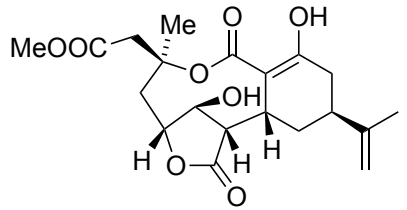


Y

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

2) Name of the organocatalyst **Z**? How would you prepare it?

8) *Hint:* a fragmentation occurs

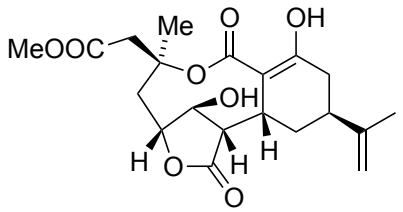


(−)-sinulariadiolide

11-15

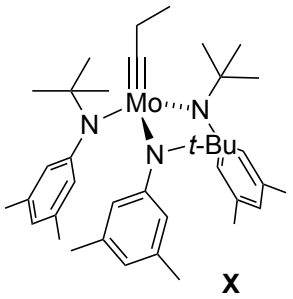
C

16-19



(−)-sinulariadiolide

11) Ac_2O, DMAP (20 mol%), Et_3N, CH_2Cl_2, −40 °C;
12) aq. HF, THF
13) **X** (30 mol%), $PhSi[CH_2CH_2(Ph)_2SiOH]_3$ (30 mol%) toluene, 120 °C
14) Zn, HOAc, THF/H_2O
15) Bu_3SnH, $[Cp^*RuCl]_4$ (11 mol%)



X

16) CO (1 atm), $Pd(OAc)_2$ (20 mol%), $AsPh_3$ (40 mol%) 1,4-benzoquinone, TFA (40 mol%), MeOH
17) triphosgene, CH_2Cl_2, pyridine, 0 °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 the molybdenum alkylidynes/silanolate catalyst-ligand systems

15) Mechanism?

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