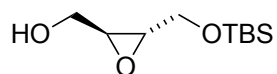
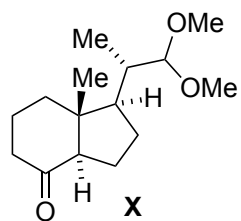
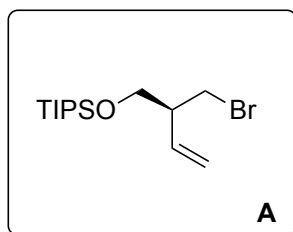


# Asymmetric Total Synthesis of Cyclocitrinol

J. Liu, J. Wu, J.-H. Fan, X. Yan, G. Mei, and C.-C. Li  
*J. Am. Chem. Soc.* **2018**, *140*, 5365–5369

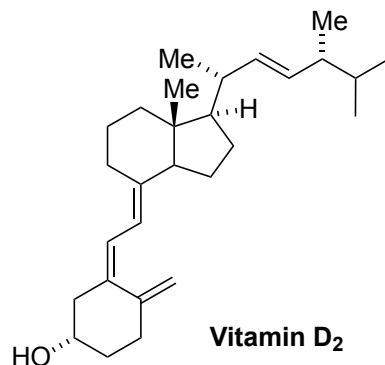


1-6



7-9

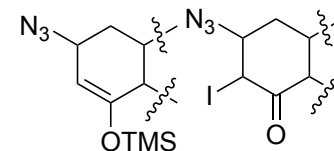
- 1) CuI, vinylMgBr, THF,  $-78\text{ }^{\circ}\text{C}$
- 2) TIPSCl (1.1 equiv.), imidazole
- 3) *p*-TsOH, MeOH
- 4) NaIO<sub>4</sub>
- 5) NaBH<sub>4</sub>
- 6) CBr<sub>4</sub>, PPh<sub>3</sub>



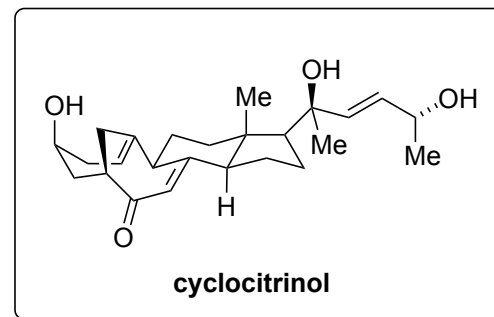
- 7) LDA, TMSCl
- 8) IBX, DMSO
- 9) TMSN<sub>3</sub>, pyridine, I<sub>2</sub>

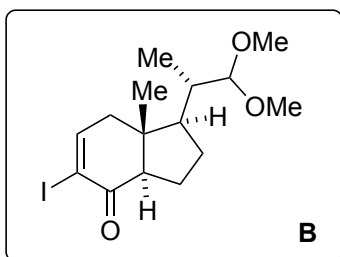
**step 7:** **X** is commercially available. How is it prepared from Vitamin D<sub>2</sub>? *Ozonolysis*

**step 9:** role of TMSN<sub>3</sub>

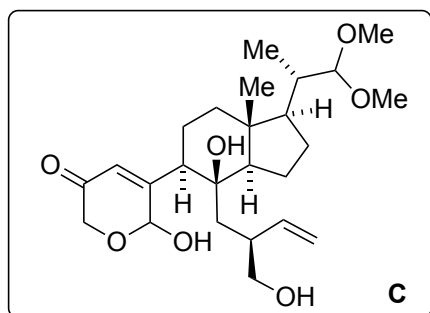


azide as smaller nucleophile  
 for hindered substrates (usually used: DMAP, py)  
 Danishefsky, S. J. and coworkers  
*J. Am. Chem. Soc.* **2008**, *130*, 13765.

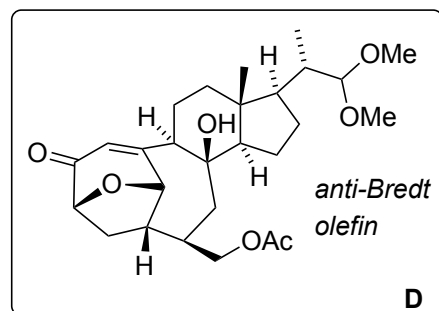




10-13

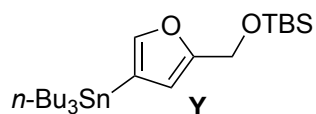


14+15



16-19

- 10) CuTC, LiOAc, NMP, Y
- 11) NaBH<sub>4</sub>, NiCl<sub>2</sub>·H<sub>2</sub>O
- 12) **A**, *t*-BuLi, Et<sub>2</sub>O, -78 °C
- 13) TBAF, then NBS, NaOAc, NaHCO<sub>3</sub>, H<sub>2</sub>O



- 14) Ac<sub>2</sub>O, 2,2,6,6-tetramethylpiperidine (TMP), DMAP
- 15) TMP, MeCN, 155 °C

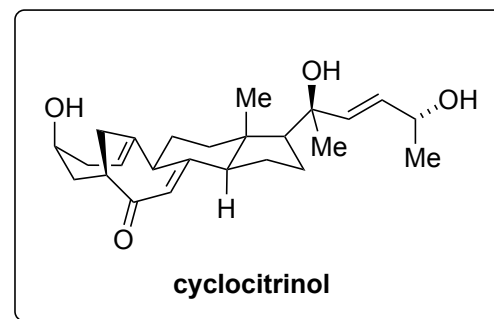
- 16) NaBH<sub>4</sub>
- 17) KHMDS, CS<sub>2</sub>, MeI
- 18) AIBN, *n*-Bu<sub>3</sub>SNH, PhMe, 80 °C
- 19) SOCl<sub>2</sub>, pyridine, 2,4,6-trimethylpyridine, 0 °C

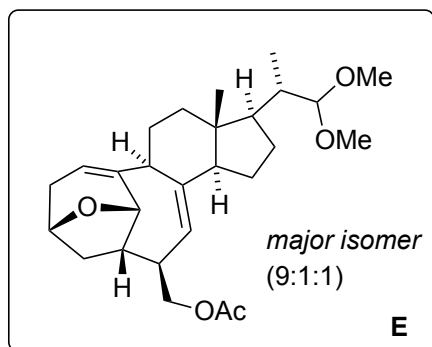
**step 10:** name reaction? *Stille coupling*

**step 13:** name reaction? *Achmatowicz reaction*

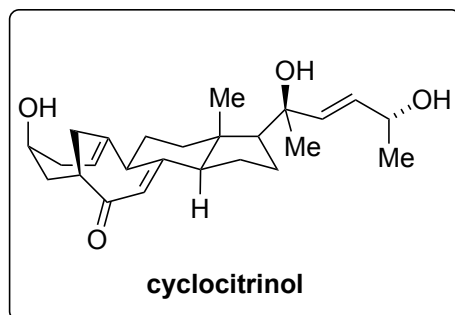
**step 14:** hint: reaction occurs 2x

**step 15:** mechanism? which unusual functionality is introduced? *see below*

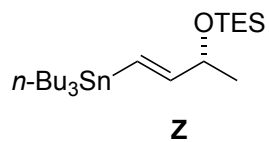




20-24



- 20) Li, EtNH<sub>2</sub>
- 21) TEMPO, NCS, TBACl
- 22) TESOTf
- 23) *t*-BuOK, O<sub>2</sub>, *t*-BuOH
- 24) **Z**, *n*-BuLi, THF, -78 °C, then TBAF



**step 20:** hint: two deprotections occur

Solutions of individual steps:

