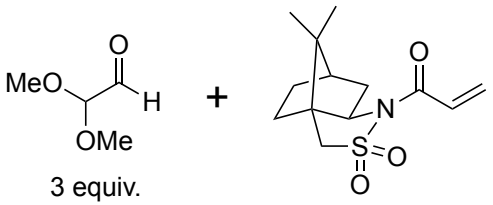
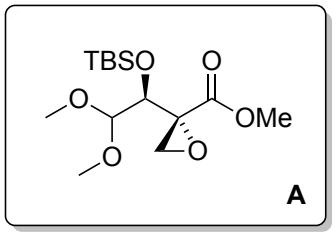
Component-based Synthesis of Trioxacarcin A

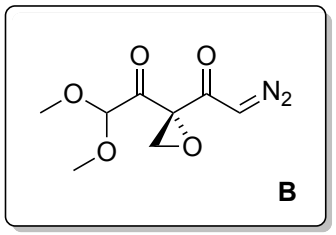
Jakub Švenda, Nicholas Hill, and Andrew G. Myers, *P. Natl. Acad. Sci. USA* **2011**, *108*, 6709–6714.
Thomas Magauer, Daniel J. Smaltz, and Andrew G. Myers, *Nat. Chem.* **2013**, *5*, 886–893.



1–4



5–8

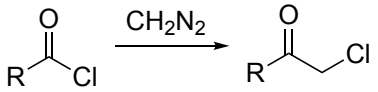


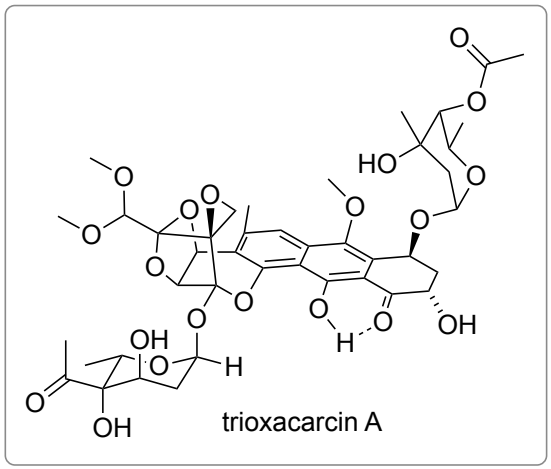
1) DABCO
2) Et_3N, MeOH
3) TBSOTf, DIPEA
4) *t*-BuOOH, *t*-BuOK
anti:syn = 13:1

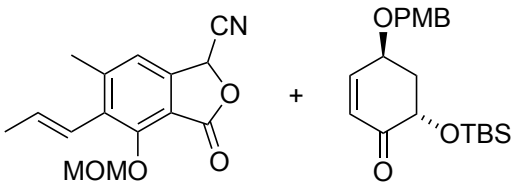
5) LiOH (aq)
6) $ClCO_2i$-Bu, Et_3N, *then* CH_2N_2
7) $Et_3N \cdot 3HF$
8) DMP, aq. $NaHCO_3$

Name the reaction of step 1?
Oppolzer sultam auxiliary-controlled Morita–Baylis–Hillman
Hint: The (*S*)-enantiomer is obtained after step 2
James W. Leahy et al - UC Berkeley
J. Am. Chem. Soc. **1997**, *119*, 18, 4317–4318.

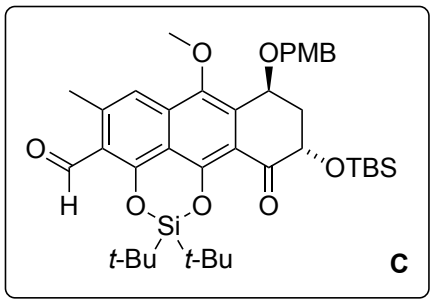
Step 6: Why is it important to form the mixed anhydride as the activated species over an acid chloride?
avoiding the Nierenstein reaction



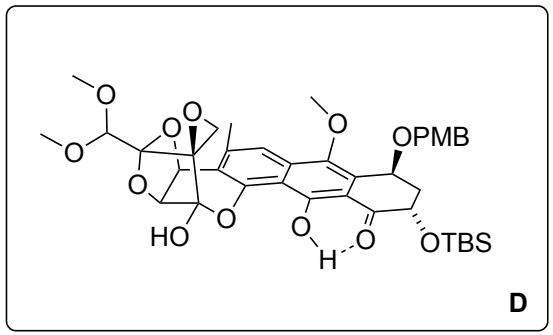




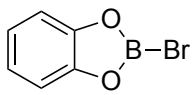
9–12



13, 14



9) *t*-BuOLi (3 equiv.), *then* $(MeO)_2SO_2$
10) K_2OsO_4, $NaIO_4$
11) BrBcat
12) *t*-Bu_2SiCl_2, Et_3N, HOBt

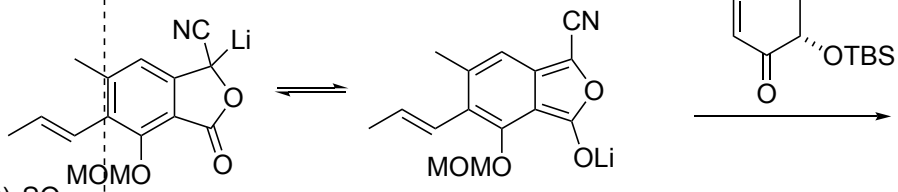


BrBcat

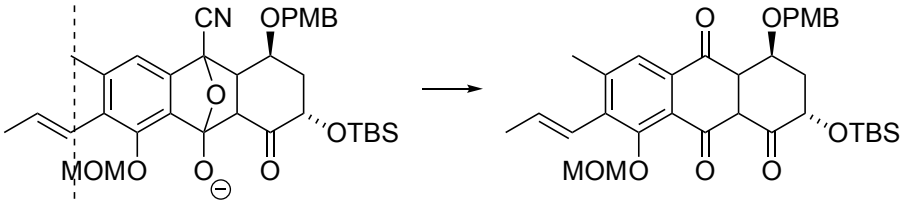
13) **B**, $Rh_2(OAc)_4$
14) Et_3N • 3HF

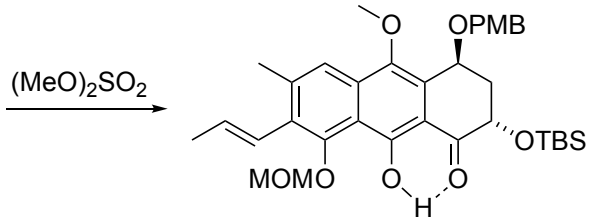
Please provide a mechanism and the name reaction of step 9.

Kraus Sugimoto annulation
also: Hauser Kraus annulation

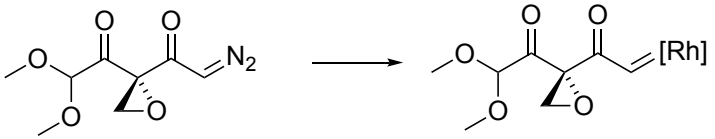


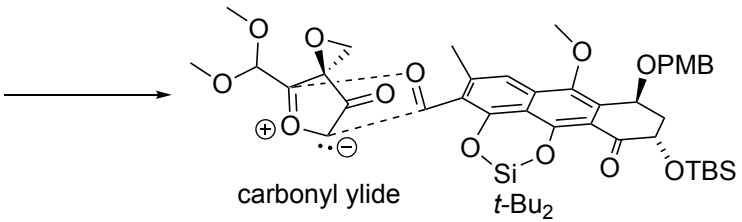
isobenzofuran



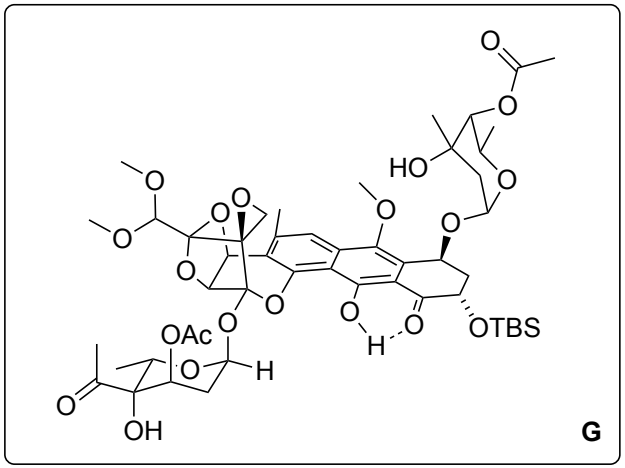


Please provide a mechanism for the key step happening in step 13.
Hint: It's a 1,3-dipolar cycloaddition reaction.



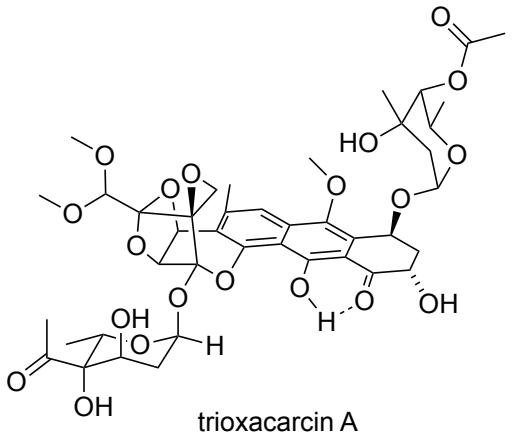


15–17



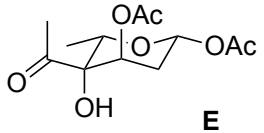
G

18, 19

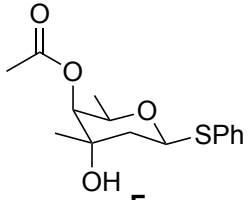


trioxacarcin A

15) **E**, $TMSNTf_2$
16) DDQ
17) **F,** $AgPF_6$

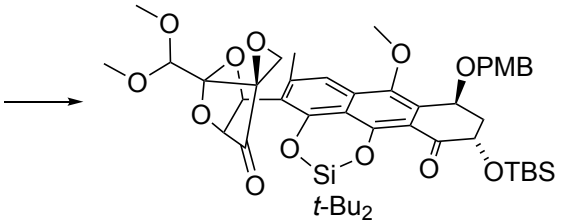


E



F

18) K_2CO_3, MeOH
19) $Et_3N \cdot 3HF$



$Et_3N \cdot 3HF$

D