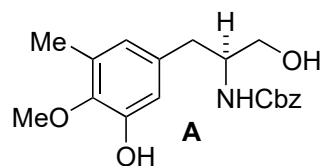
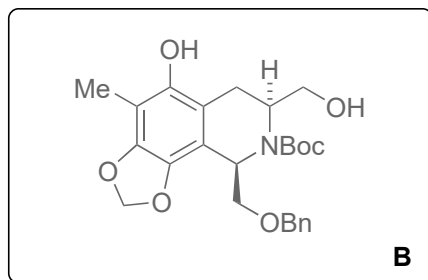


A Scalable Total Synthesis of the Antitumor Agents Et-743 and Lurbinectedin

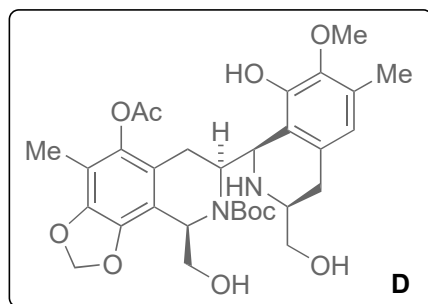
Weiming He, Zhigao Zhang, and Dawei Ma
Angew. Chem. Int. Ed. **2019**, *58*, 1–5.



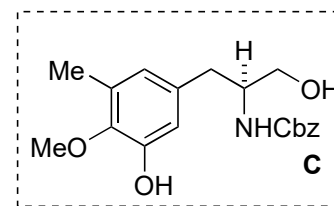
1) – 5)



6) – 8)

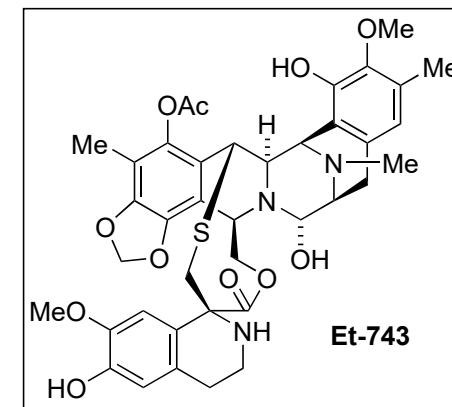
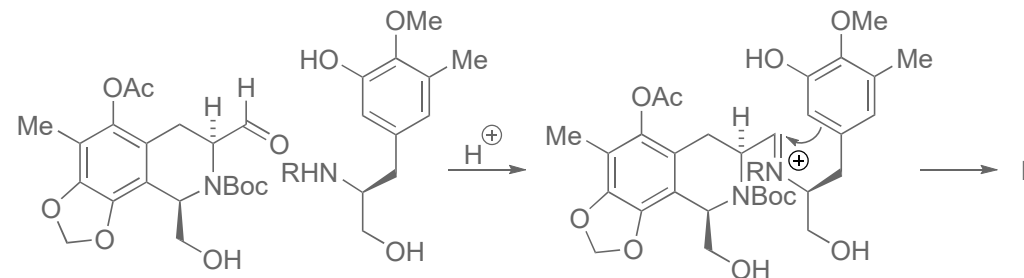


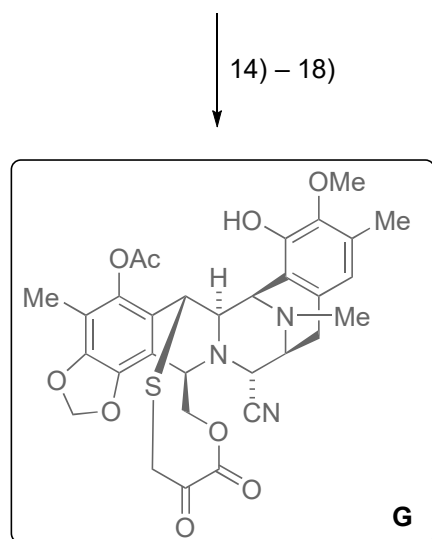
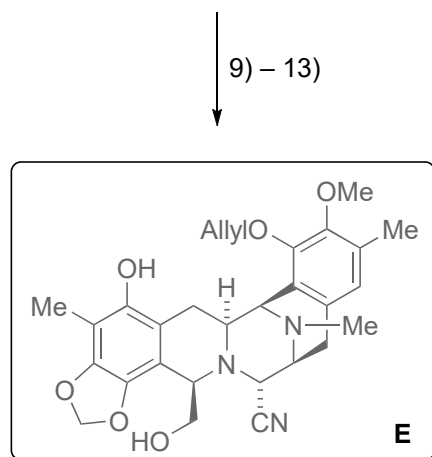
- 1) Pd/C, H₂
- 2) BnOCH₂CHO, AcOH
- 3) Boc₂O
- 4) Salcomine, O₂
- 5) Blue light, THF, room temperature



- 6) BnBr, K₂CO₃
- 7) (COCl)₂, DMSO, DIPEA
- 8) **C**, AcOH

Step 8: Name the reaction and come up with a mechanism.
 [Pictet-Spengler]

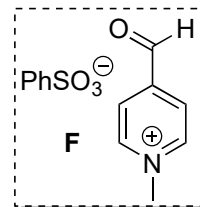




2 steps
Lurbinectedin

2 steps
Et-743 [1.1 g]

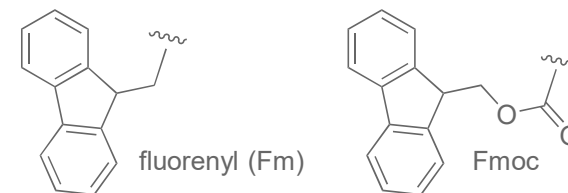
- 9) HCHO, NaBH₃CN, AcOH
- 10) AllylBr, K₂CO₃
- 11) (COCl)₂, DMSO, DIPEA
- 12) TFA *then* TMSCN
- 13) BCl₃ *then* TMSCN



- 14) (PhSeO)₂O
- 15) (R)-N-Alloc-S-Fm-Cys, EDCI, DMAP
- 16) Tf₂O, DMSO, -40 °C *then* DIPEA, 0 °C
then t-BuOH *then* (Me₂N)₂C=NtBu *then* Ac₂O
- 17) Pd(PPh₃)₄, nBu₃SnH, AcOH
- 18) **F** *then* DBU *then* (CO₂H)₂

Step 12: Name the reaction. [intramol. Strecker]
Step 13: Partial hydrolysis occurred.

Step 16: Think about the stability of the Fm-group.
What is the structure and which PG is similar to Fm?



- How would you synthesize the natural products in 2 steps from **G**?
- 19) R-NH₃Cl, NaOAc
[Pictet-Spengler]
 - 20) AgNO₃, H₂O

