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

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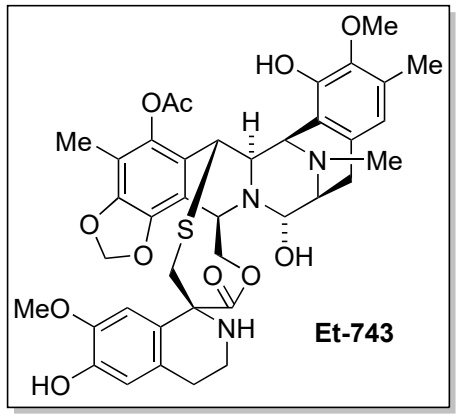
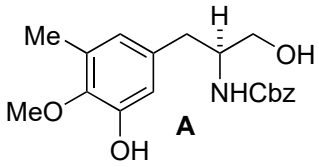


Et-743



A

1) – 5)

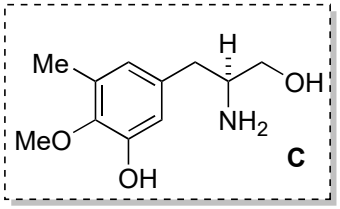
B

6) – 8)

D

1) Pd/C, H_2
2) $BnOCH_2CHO$, AcOH
3) Boc_2O
4) Salcomine, O_2
5) Blue light, THF, room temperature

6) BnBr, K_2CO_3
7) $(COCl)_2$, DMSO, DIPEA
8) **C**, AcOH



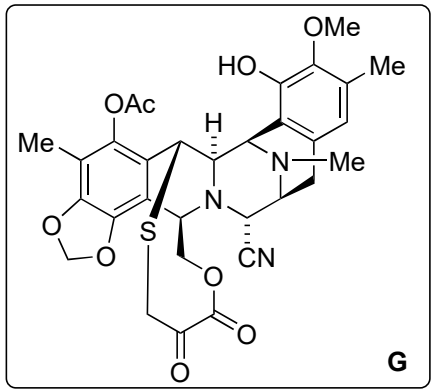
C

Step 8: Name the reaction and come up with a mechanism.

9) – 13)

E

14) – 18)



2 steps

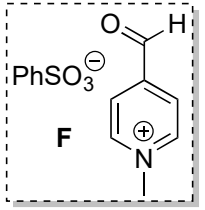
2 steps

Lurbinectedin

Et-743 [1.1 g]

9) HCHO, $NaBH_3CN$, AcOH
10) AllylBr, K_2CO_3
11) $(COCl)_2$, DMSO, DIPEA
12) TFA *then* TMSCN
13) BCl_3 *then* TMSCN

Step 12: Name the reaction.
Step 13: Partial hydrolysis occurred.



14) $(PhSeO)_2O$
15) (R)-N-Alloc-S-Fm-Cys, EDCI, DMAP
16) Tf_2O, DMSO, –40 °C *then* DIPEA, 0 °C *then* t-BuOH *then* $(Me_2N)_2C{=}NtBu$ *then* Ac_2O
17) $Pd(PPh_3)_4$, nBu_3SnH, AcOH
18) **F** *then* DBU *then* $(CO_2H)_2$

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

How would you synthesize the natural products in 2 steps from **G**?