Total Synthesis of Tagetitoxin

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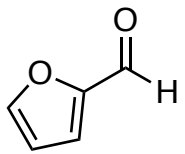
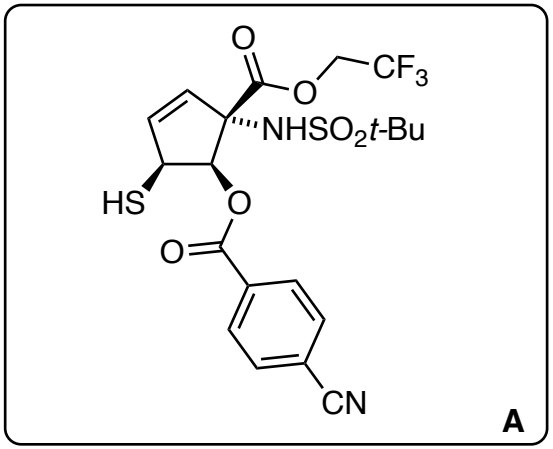
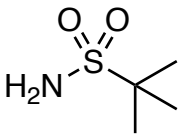


1–7

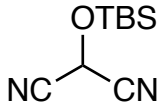


A

8–10

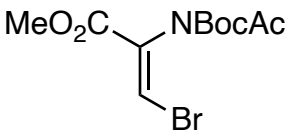


1

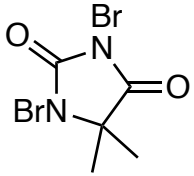


2

1) **1**, amberlyst 15, Δ
2) **2**, Et_3N *then* 2,2,2,trifluoroethanol, TBAF
3) methylene blue, O_2, hν *then* Me_2S, SiO_2
4) 4-cyanobenzoyl chloride, DMAP
5) $CeCl_3 \cdot 7H_2O$, $NaBH_4$
6) 1,1'-thiocarbonyldiimidazole
7) BHT, 115 °C *then* PTSA, H_2O



3

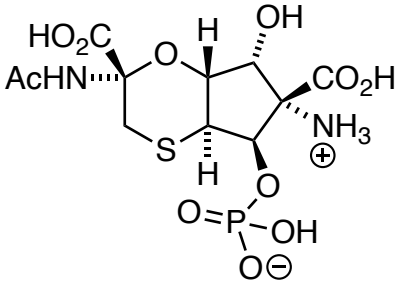


4

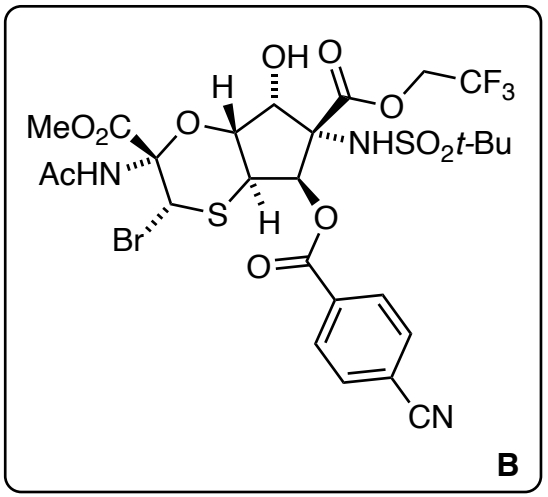
8) **3**, Et_3N
9) OsO_4, NMO, citric acid *then* HCl
10) **4**, AcOH, Δ

3) Please provide a mechanism.
See below
5) Please name the reaction.
Luche reduction
7) Please classify the reaction.
[3,3]-sigmatropic rearrangement

9) Hint: The most labile protective group is lost.

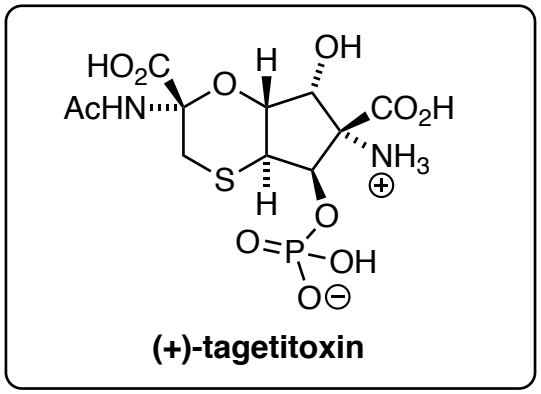


(+)-tagetitoxin

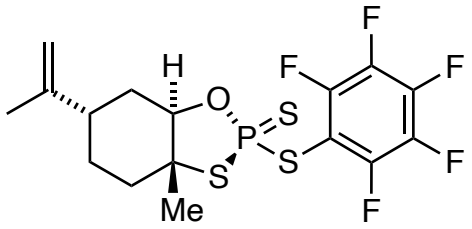


B

11–15



(+)-tagetitoxin



5

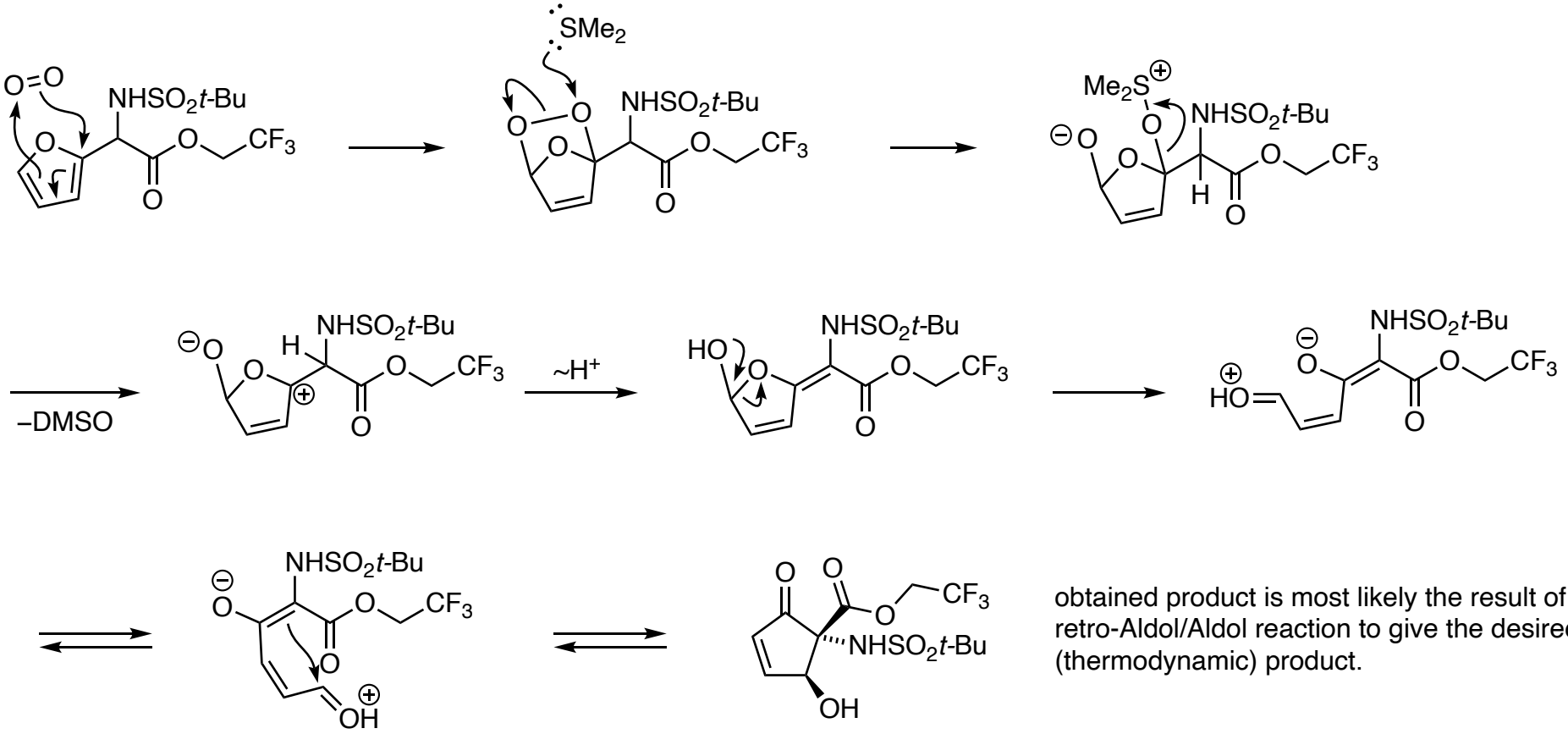
11) TfOH, anisole
12) *n*-Bu_3SnH, AIBN *then* acetone, PTSA
13) MeOH, Et_3N *then* **5**, DBN; separation of diastereomers
14) SeO_2
15) TMSOK, H_2O *then* $MeONH_2$•HCl

11) Hint: Monodeprotection.

13) Hint: 2 eq of MeOH are consumed.

solution to step 3:

overall: Piancatelli-type rearrangement



obtained product is most likely the result of a retro-Aldol/Aldol reaction to give the desired (thermodynamic) product.