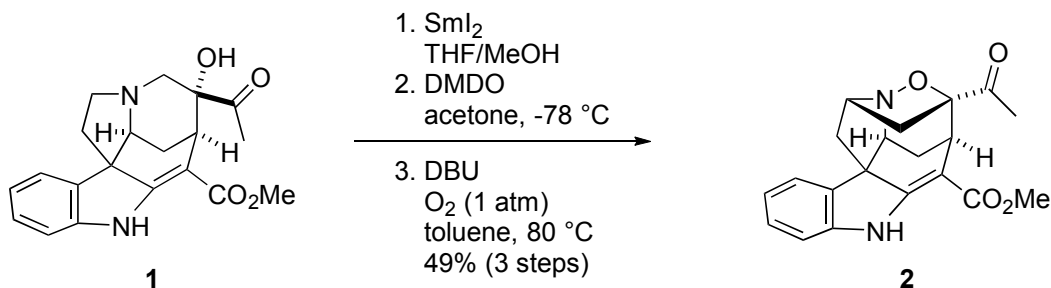


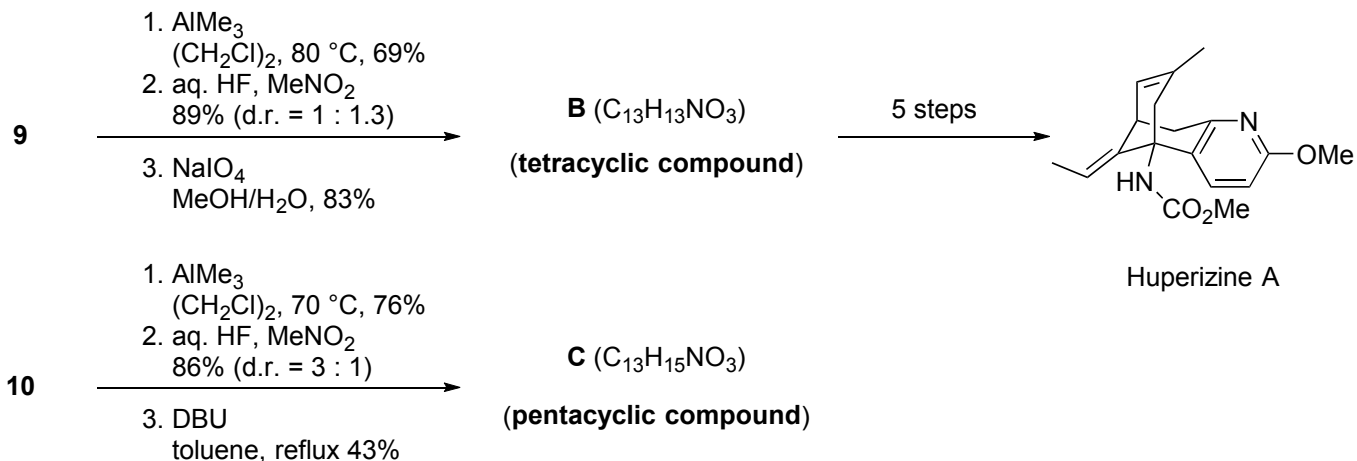
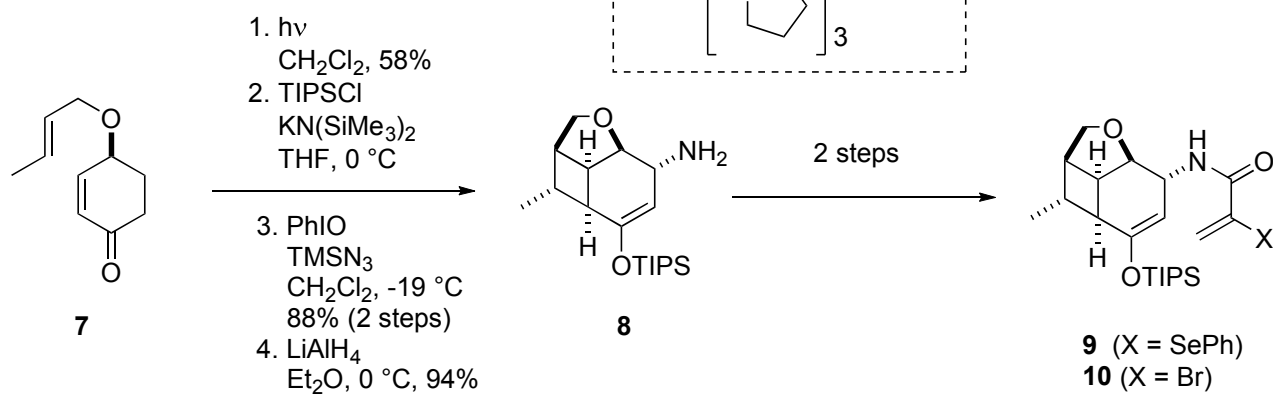
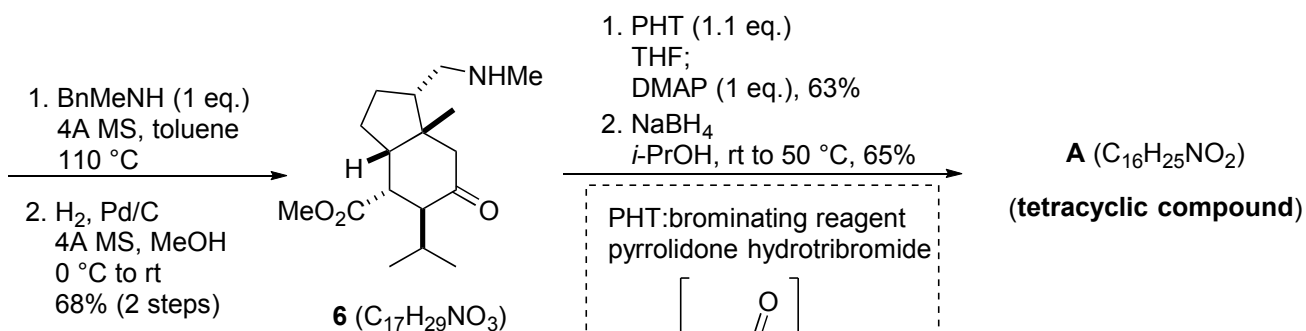
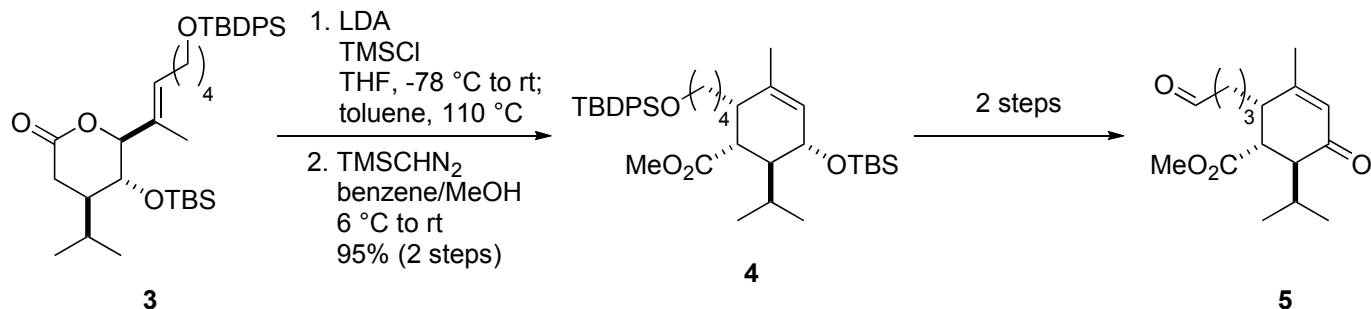
Problem Session (4)

2016/1/14 Hiroki Fujisawa

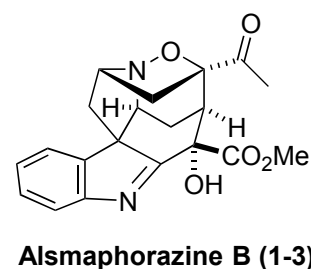
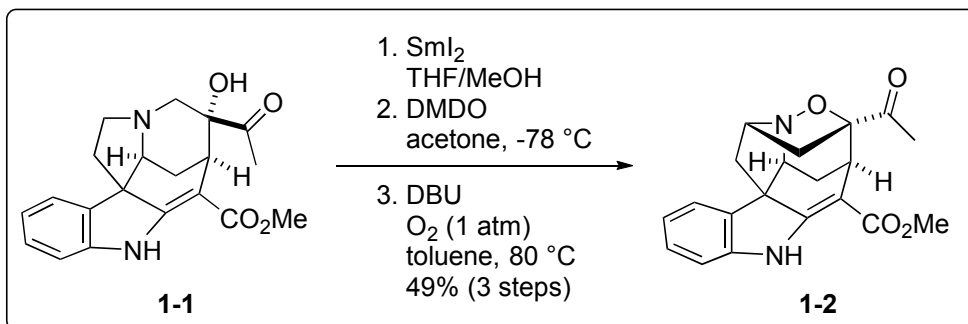
1. Please provide the reasonable reaction mechanisms.



2. Please provide the reasonable reaction mechanism, explain the stereoselectivity and fill in the blank.

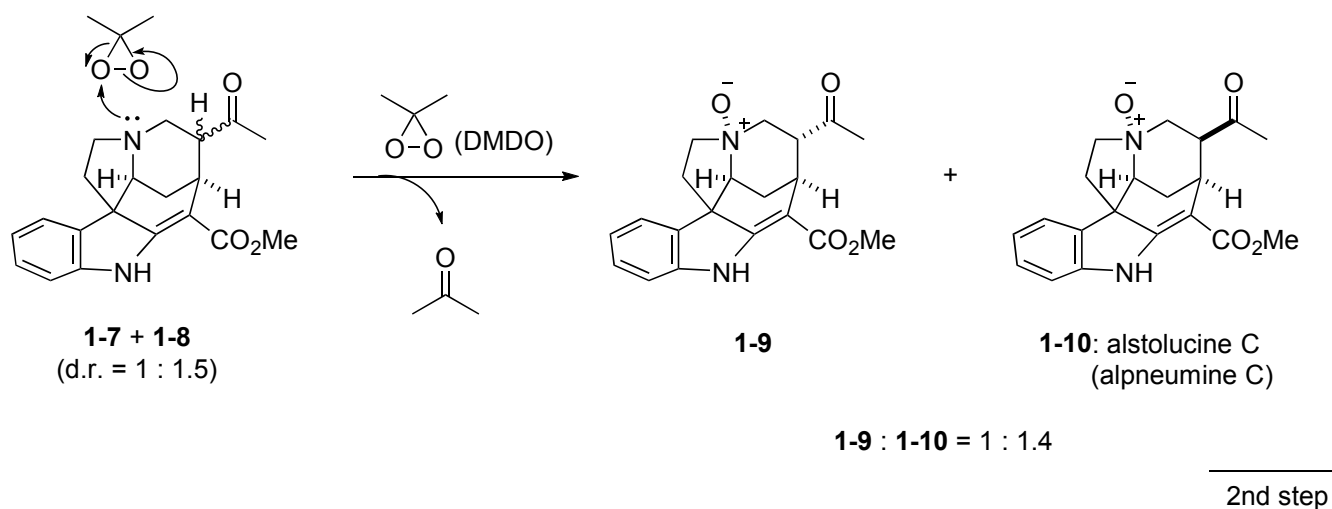
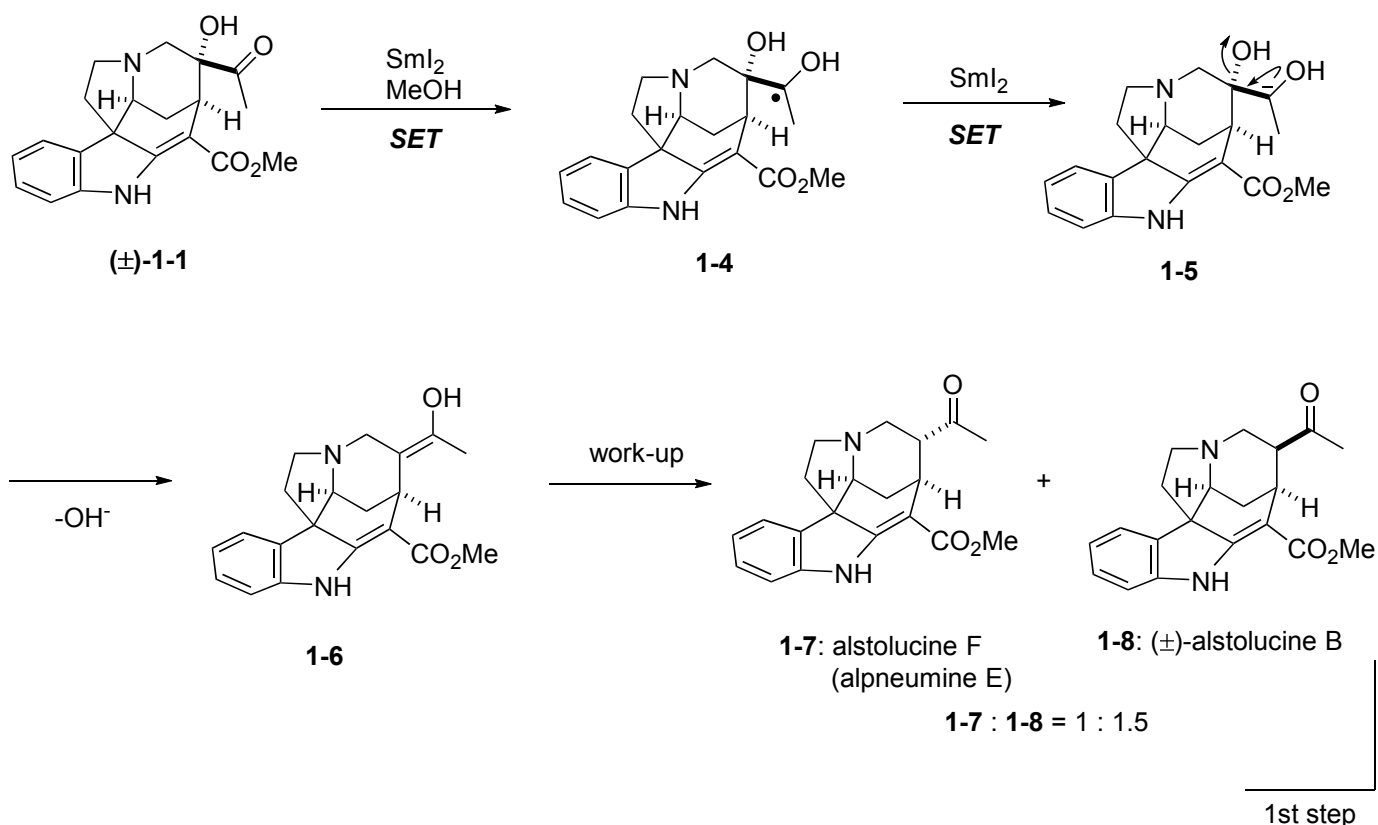


Problem 1: Total synthesis of Alsmaphorazine B

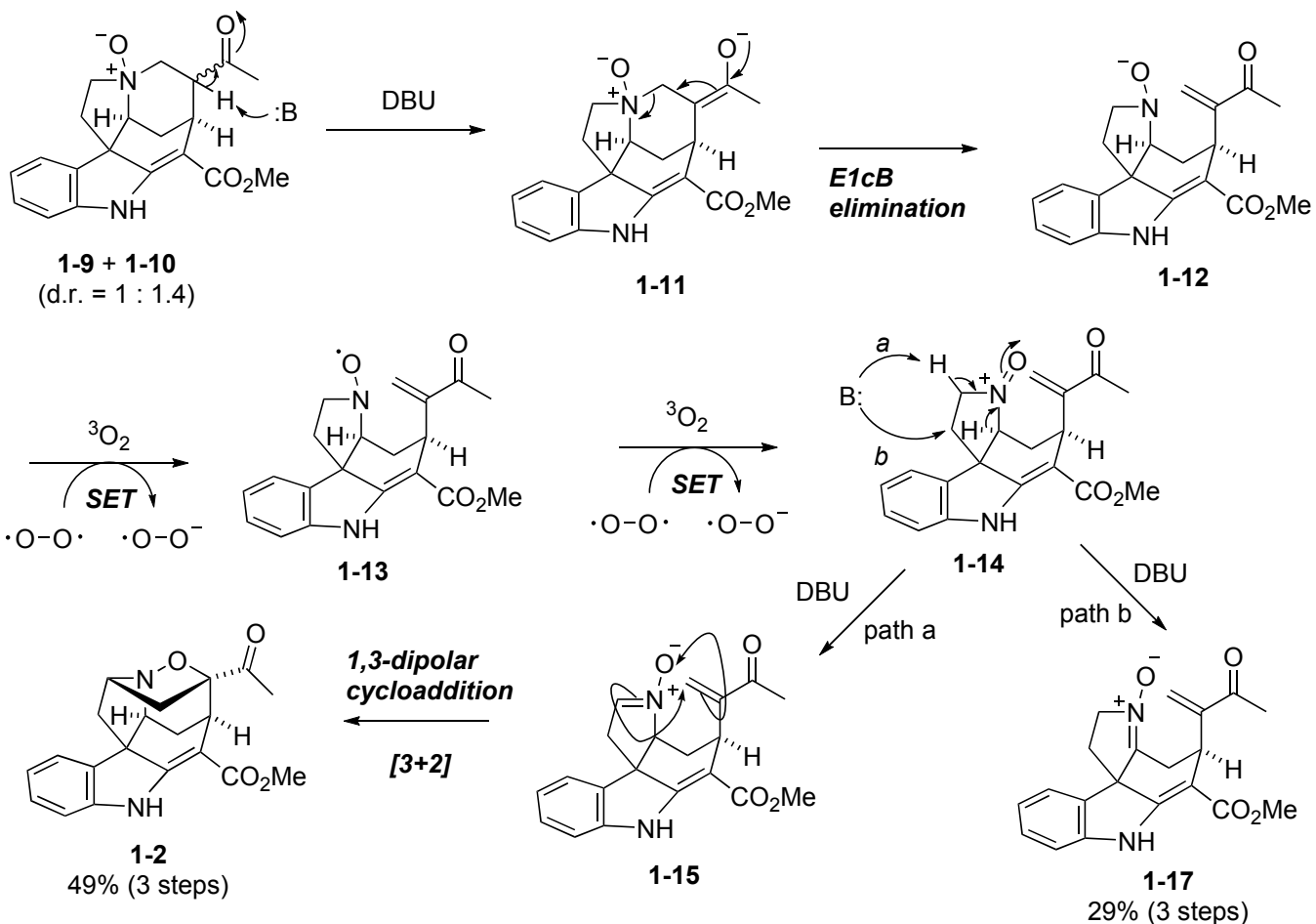


Answer:

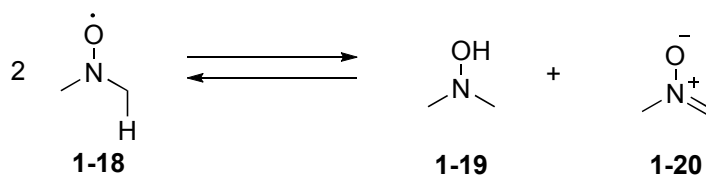
Hong, A. Y.; Vanderwal, C. D. *J. Am. Chem. Soc.* **2015**, *137*, 7306.



The described structures are 'alstolucine' X.
'Alpneumine' Y is the enantiomer of 'alstolucine' X.

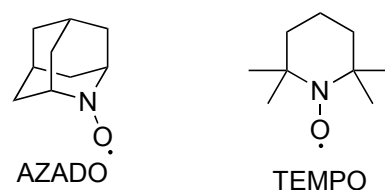


Discussion: Formation of nitron from nitroxy radical.



Nitroxy radical which possesses α -H causes self-reaction.

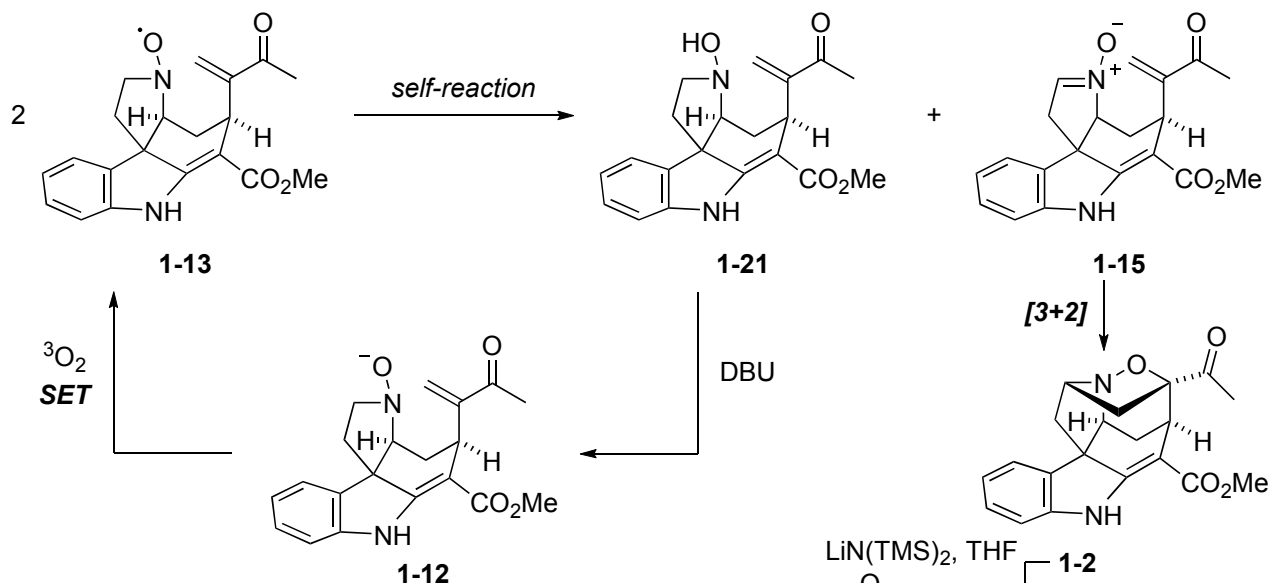
cf. Examples of stable nitroxy radical.



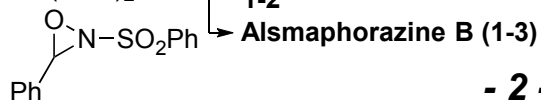
AZADO...Bredt's rule
 TEMPO...no α -H

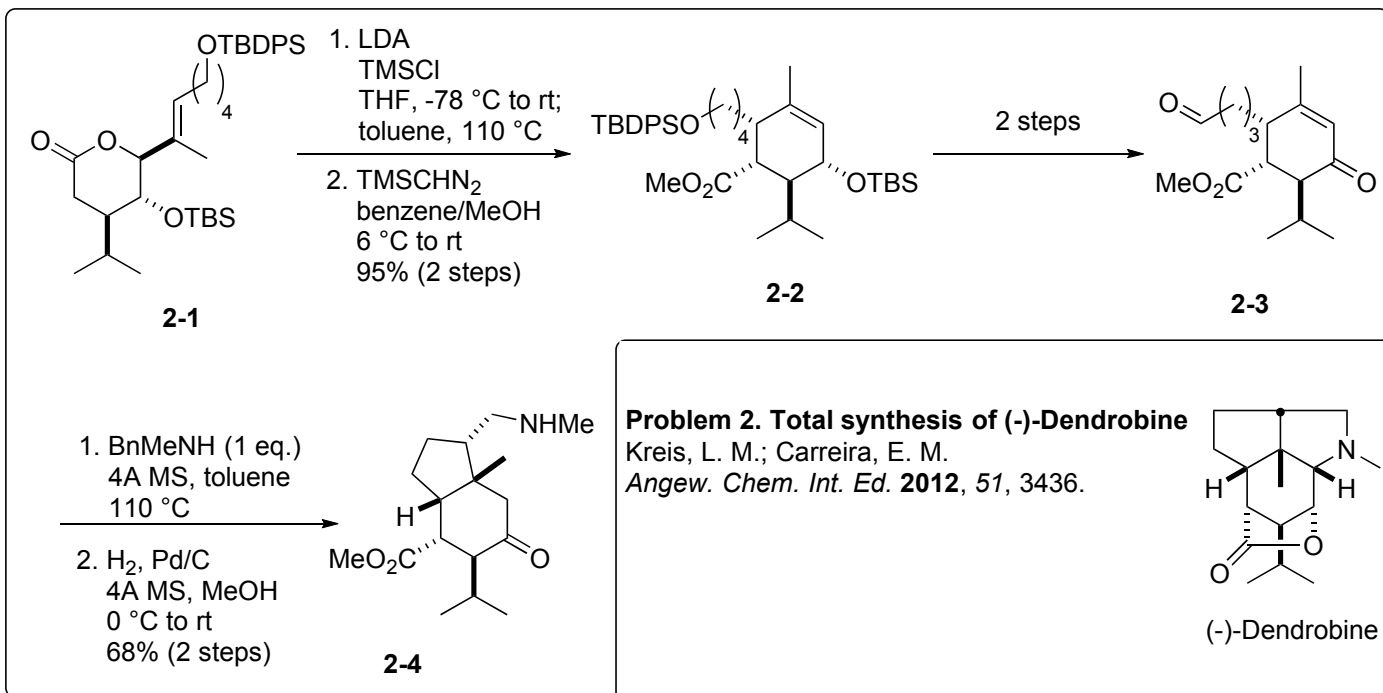
Adamic, K.; Bowman, D. F.; Gillan, T.; Ingold, K. U. *J. Am. Chem. Soc.* **1971**, *93*, 902.

Another possible reaction mechanism (**1-13** \Rightarrow **1-16**)

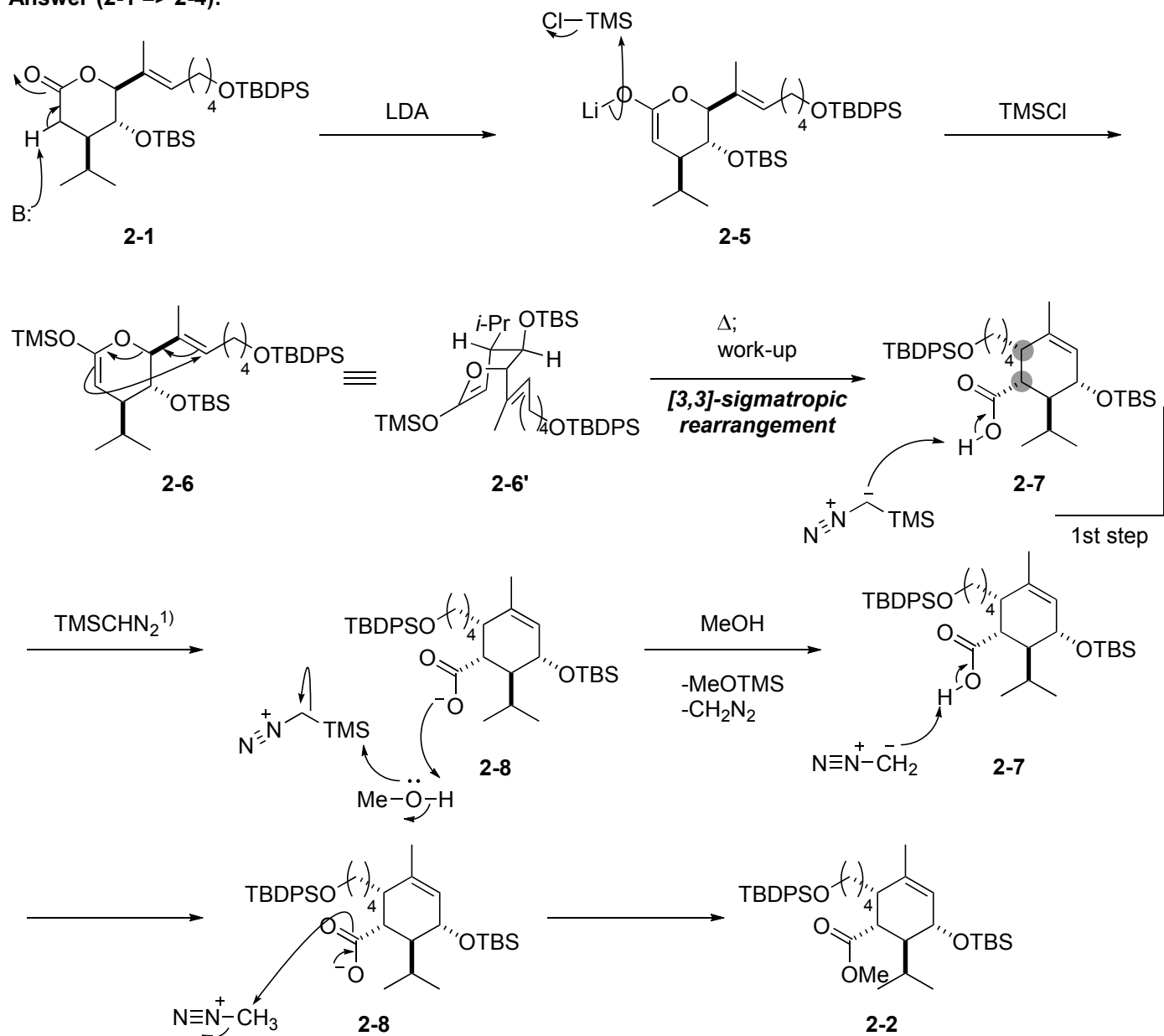


In this case, O_2 was positively added in the reaction mixture. So, I concluded that oxidation of **1-13** with O_2 is reasonable.



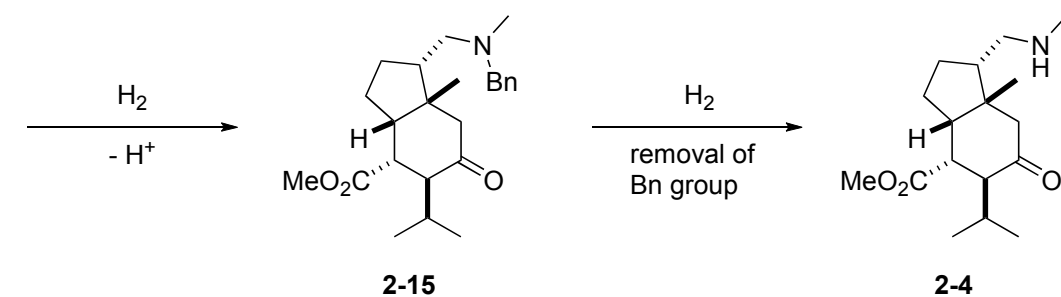
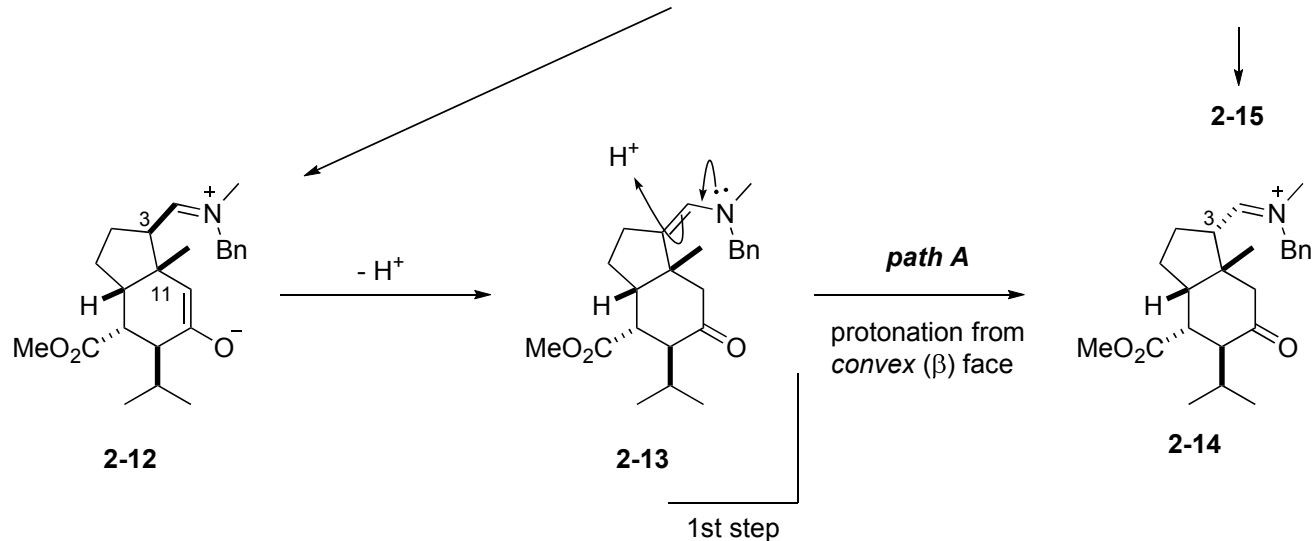
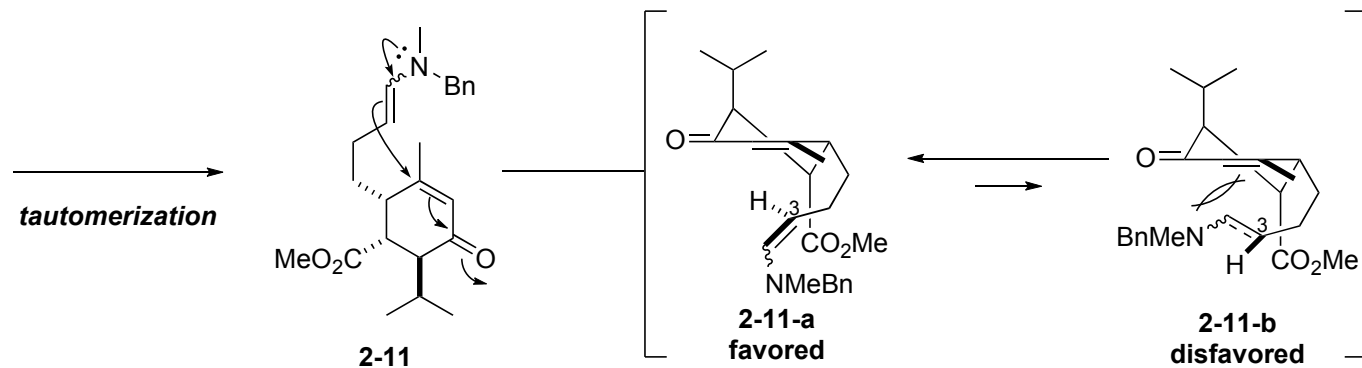
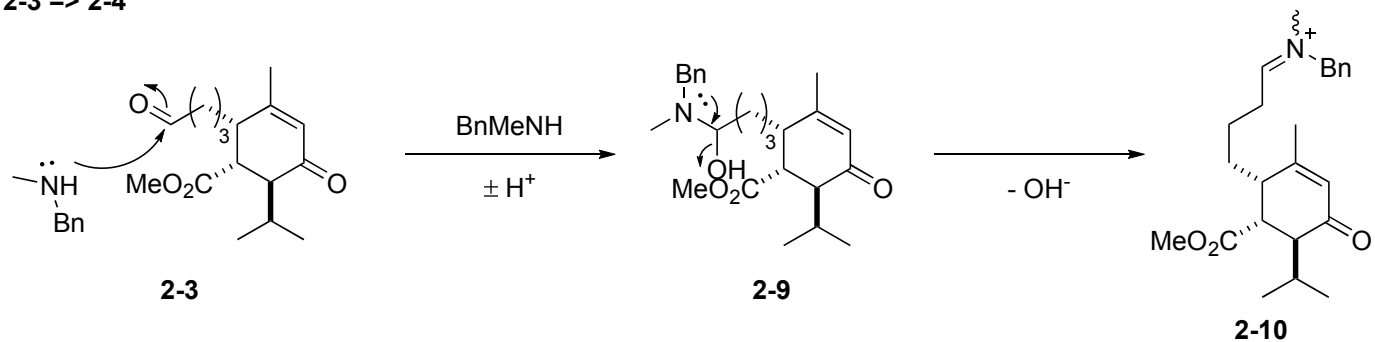


Answer (2-1 => 2-4):

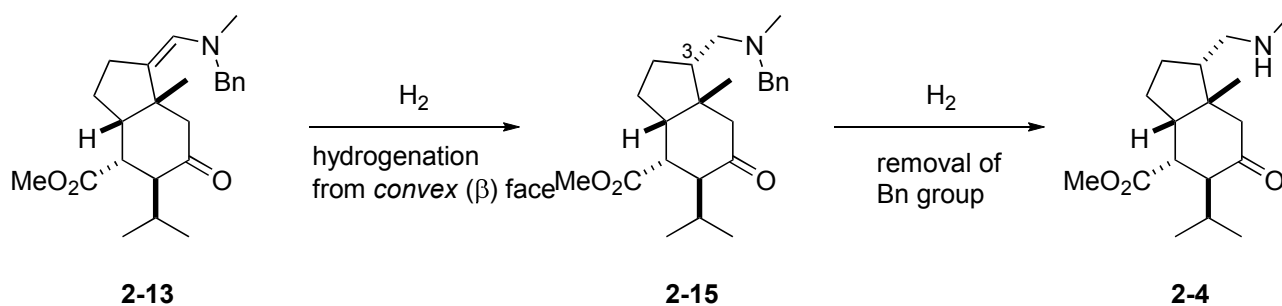


1. Kühnel, E.; Laffen, D. D. P.; Lloyd-Jones, G. C.; Campo, T. M.; Shepperson, I. R.; Slaughter, J. L. *Angew. Chem. Int. Ed.* **2007**, *46*, 7075.

2-3 => 2-4

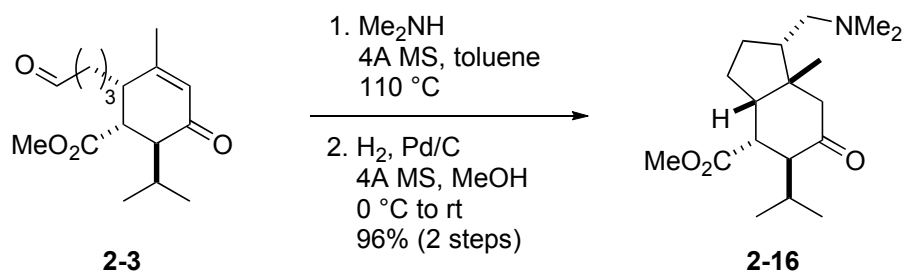


path B

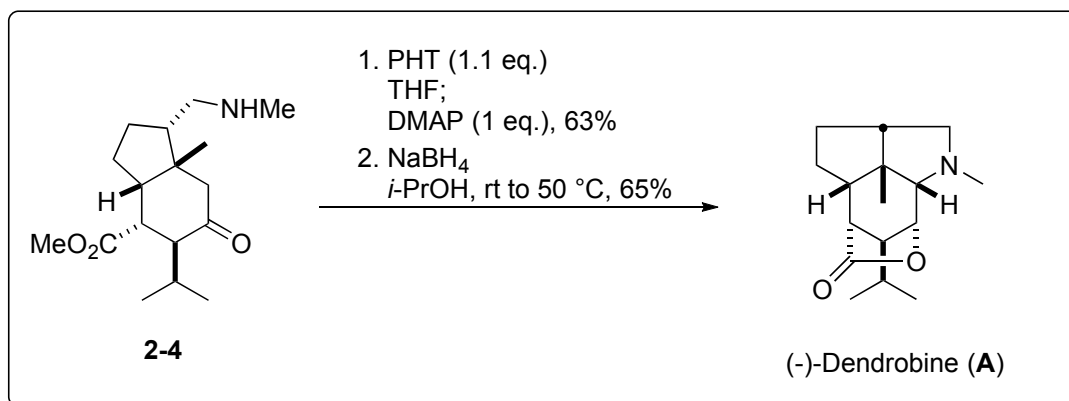


In any case (path A~B), "H" atom was kinetically added at C3 position from convex face.

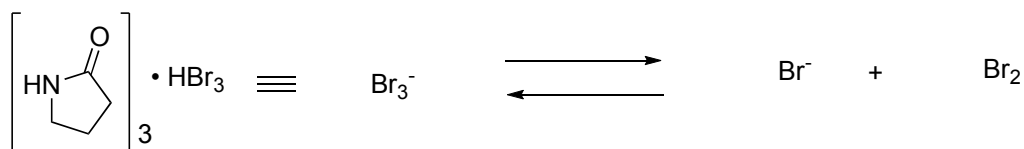
Another example of cyclization/hydrogenation cascade.



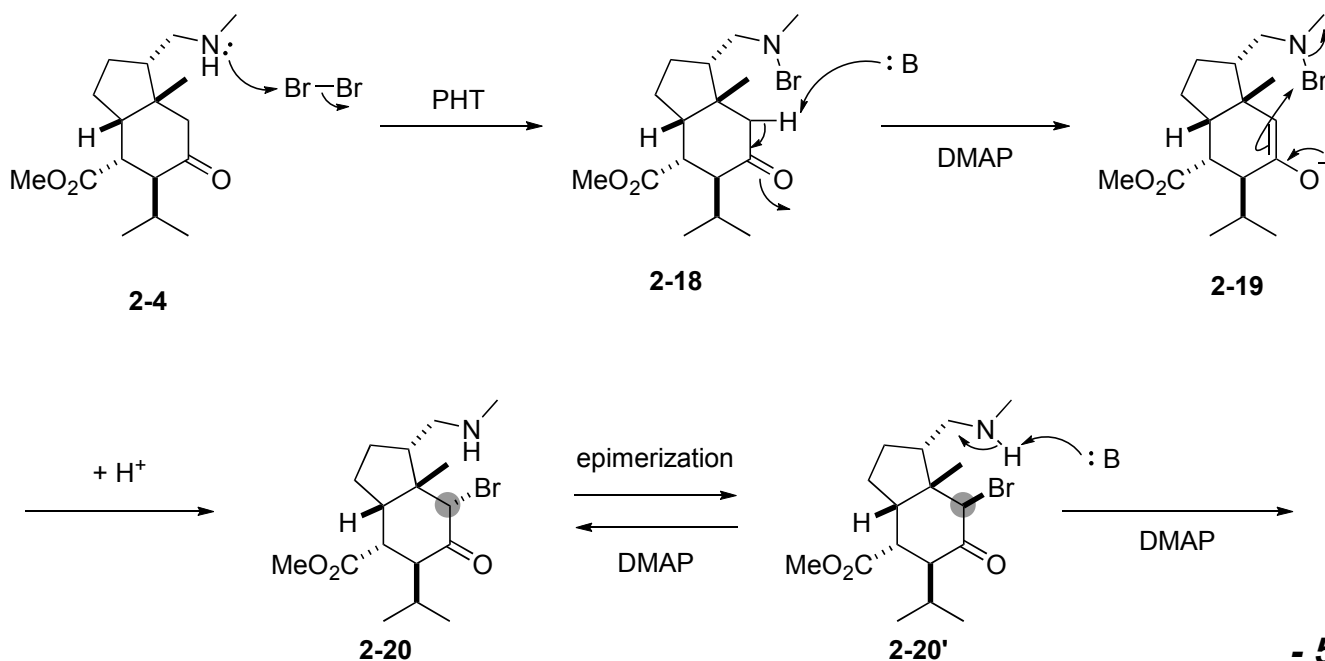
Tertiary amine also can be cleanly synthesized.

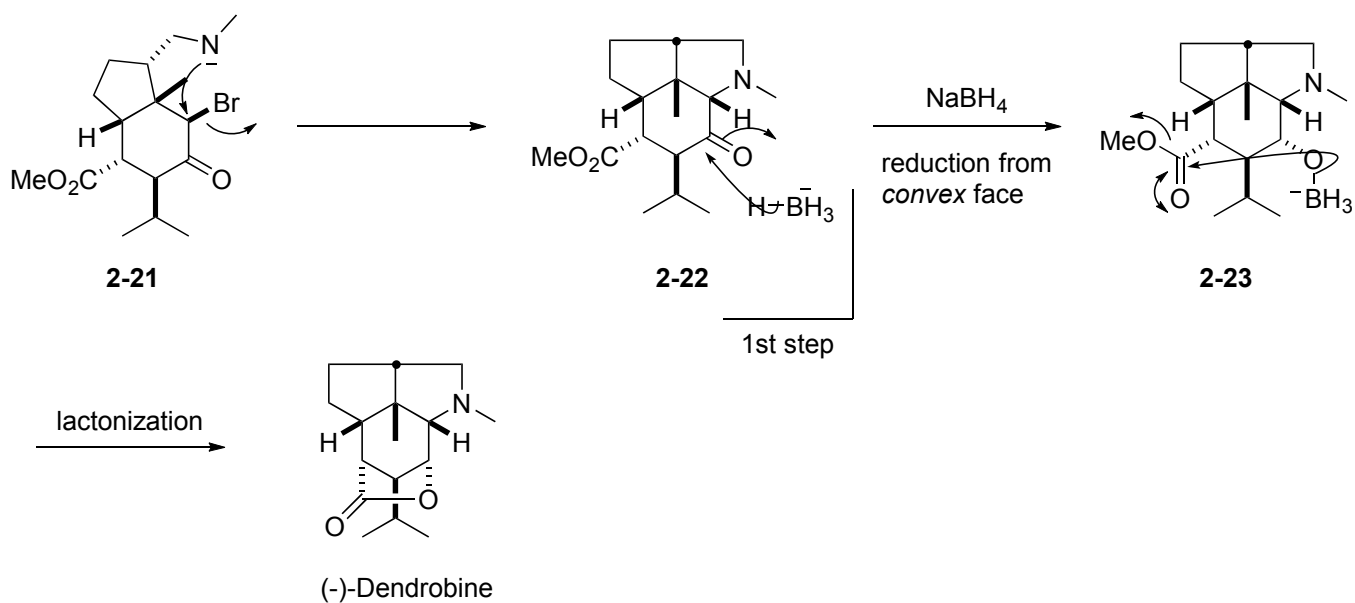


Answer (2-4 => Dendrobine) :



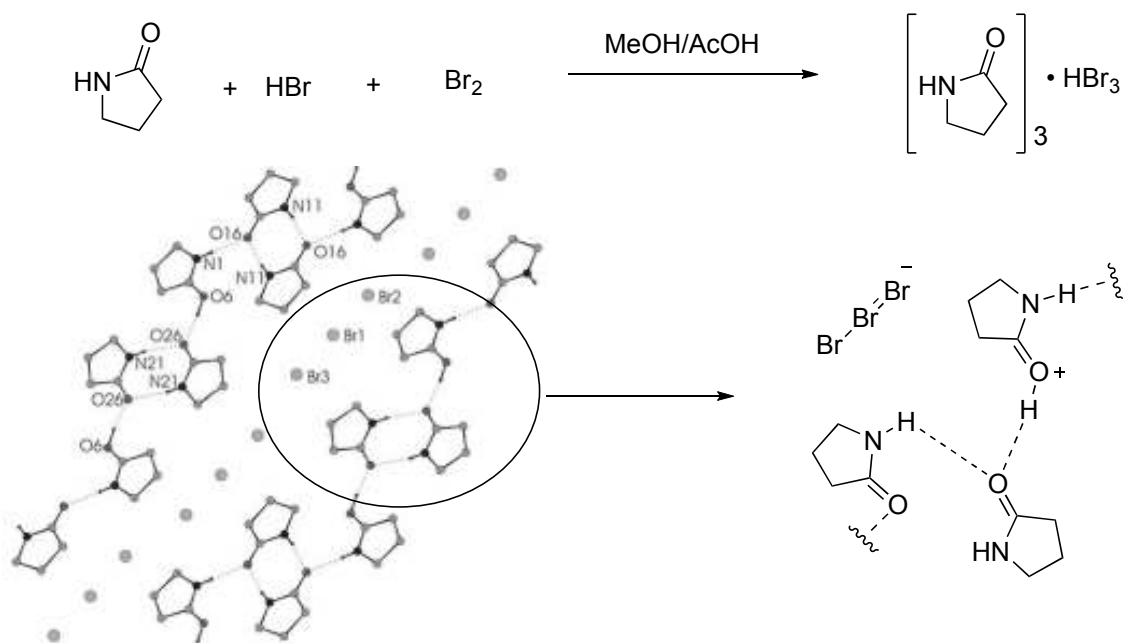
PHT (pyrrolidone hydrotribromide)



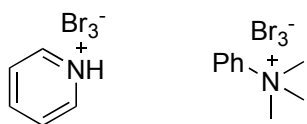


Discussion: About Br_3^- salt

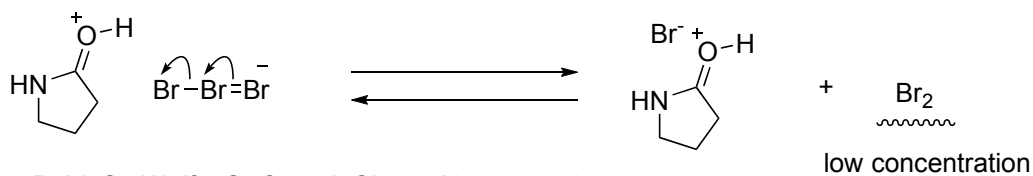
1. Preparation and structure of PHT



example of Br_3^- salt

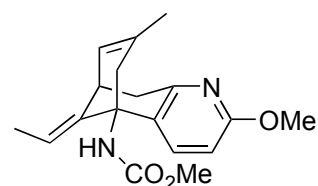
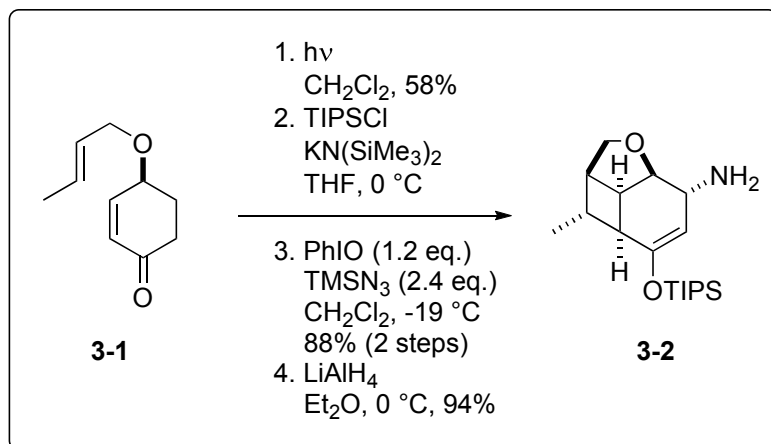


2. Br_3^- salt gradually generates Br_2 . \Rightarrow Br_3^- is mild brominate reagent.



Awang, D. V. C.; Wolfe, S. *Can. J. Chem.* **1969**, 47, 706.

Problem 3: Total synthesis of Huperzine A.

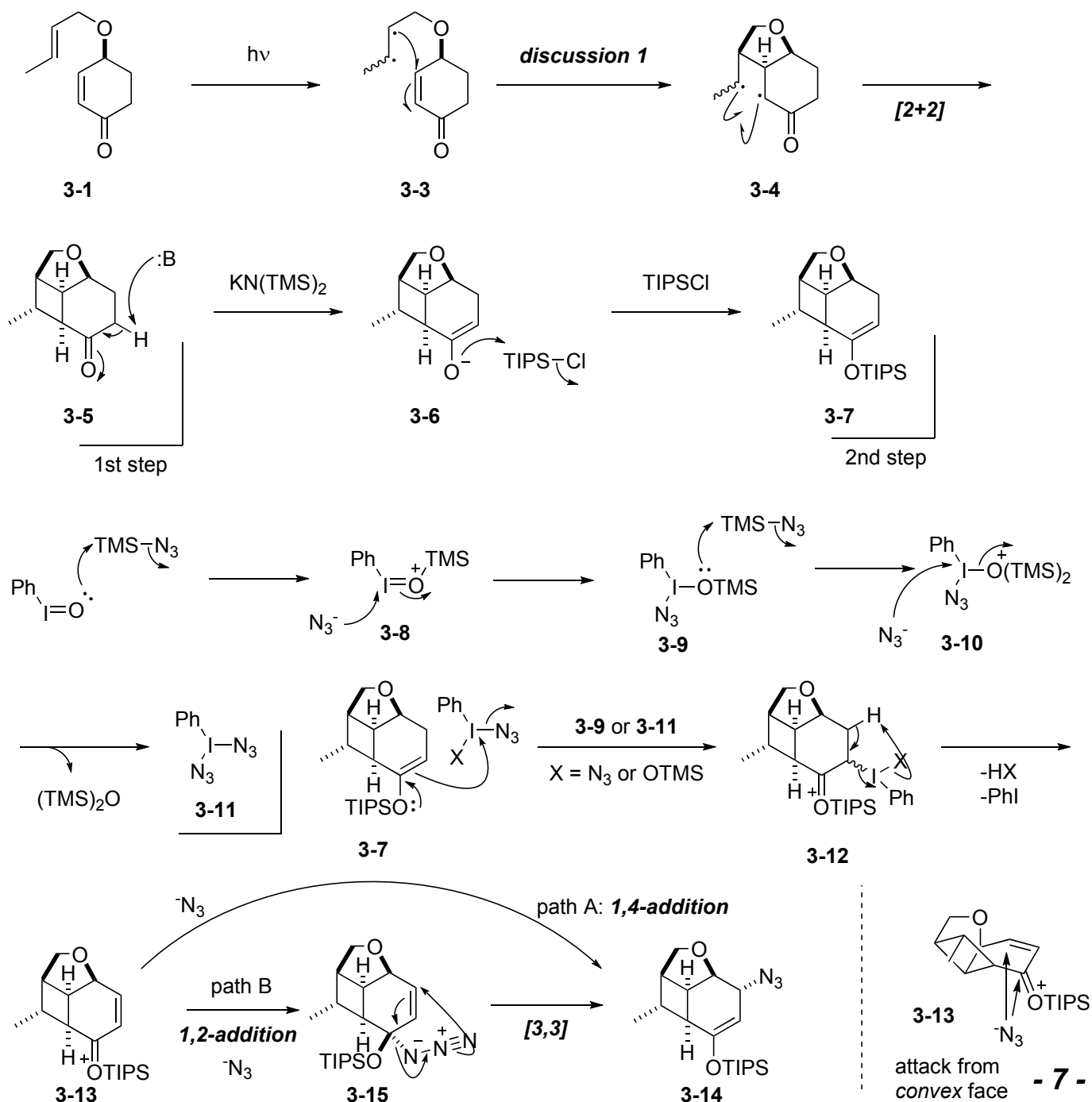


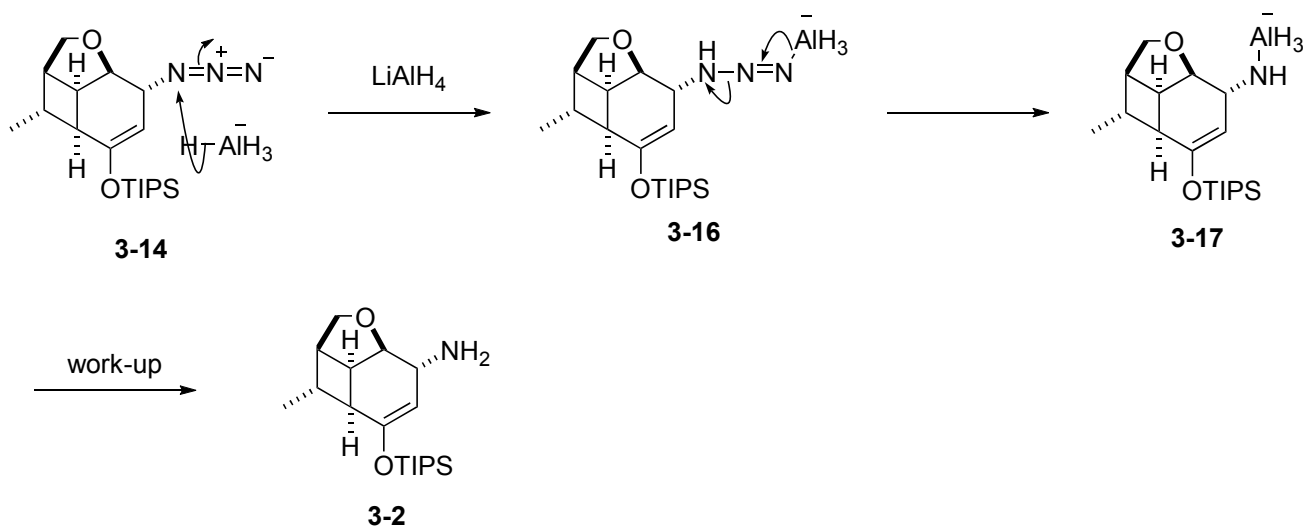
Huperzine A

White, J. D.; Li, Y.; Kim, J.; Terinek, M.
J. Org. Chem. **2015**, *80*, 11806.

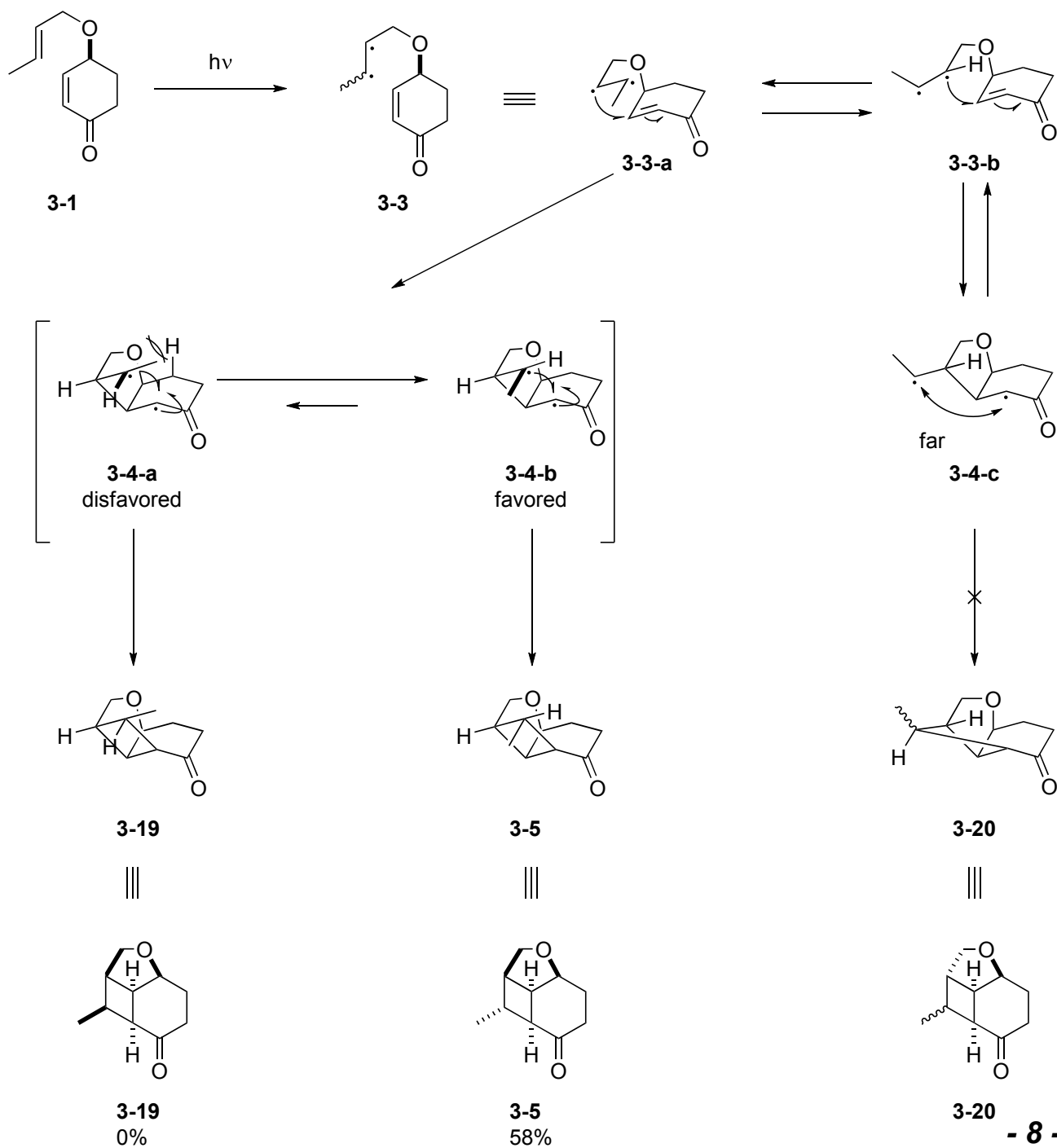
Answer (3-1 => 3-2):

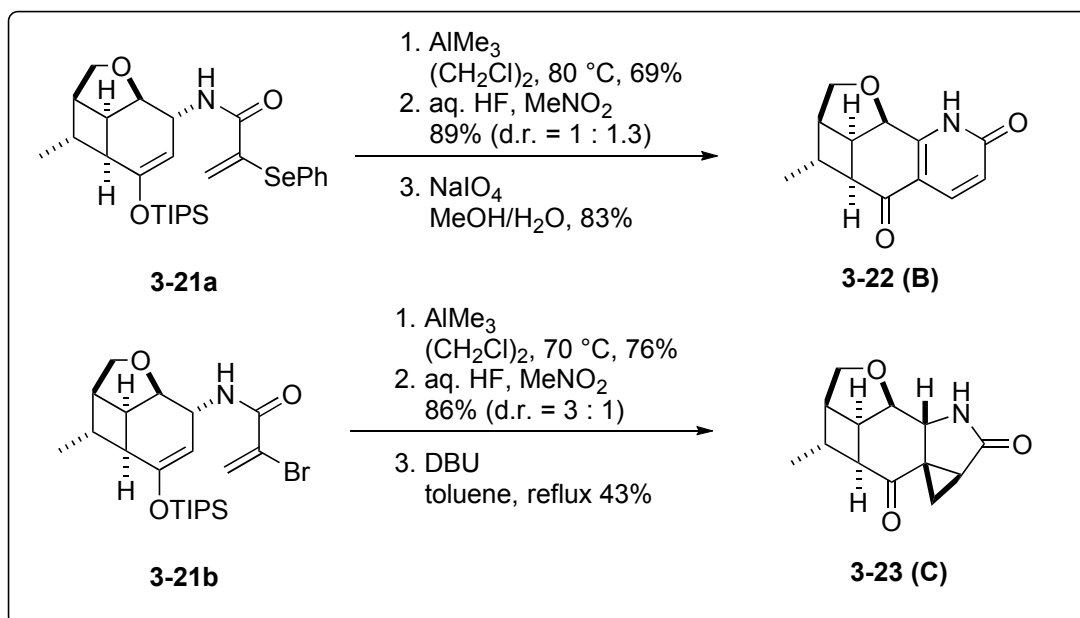
(about the reaction mechanism of γ -azidation: Magnus, P.; Lacour, J. *J. Am. Chem. Soc.* **1992**, *114*, 767.)



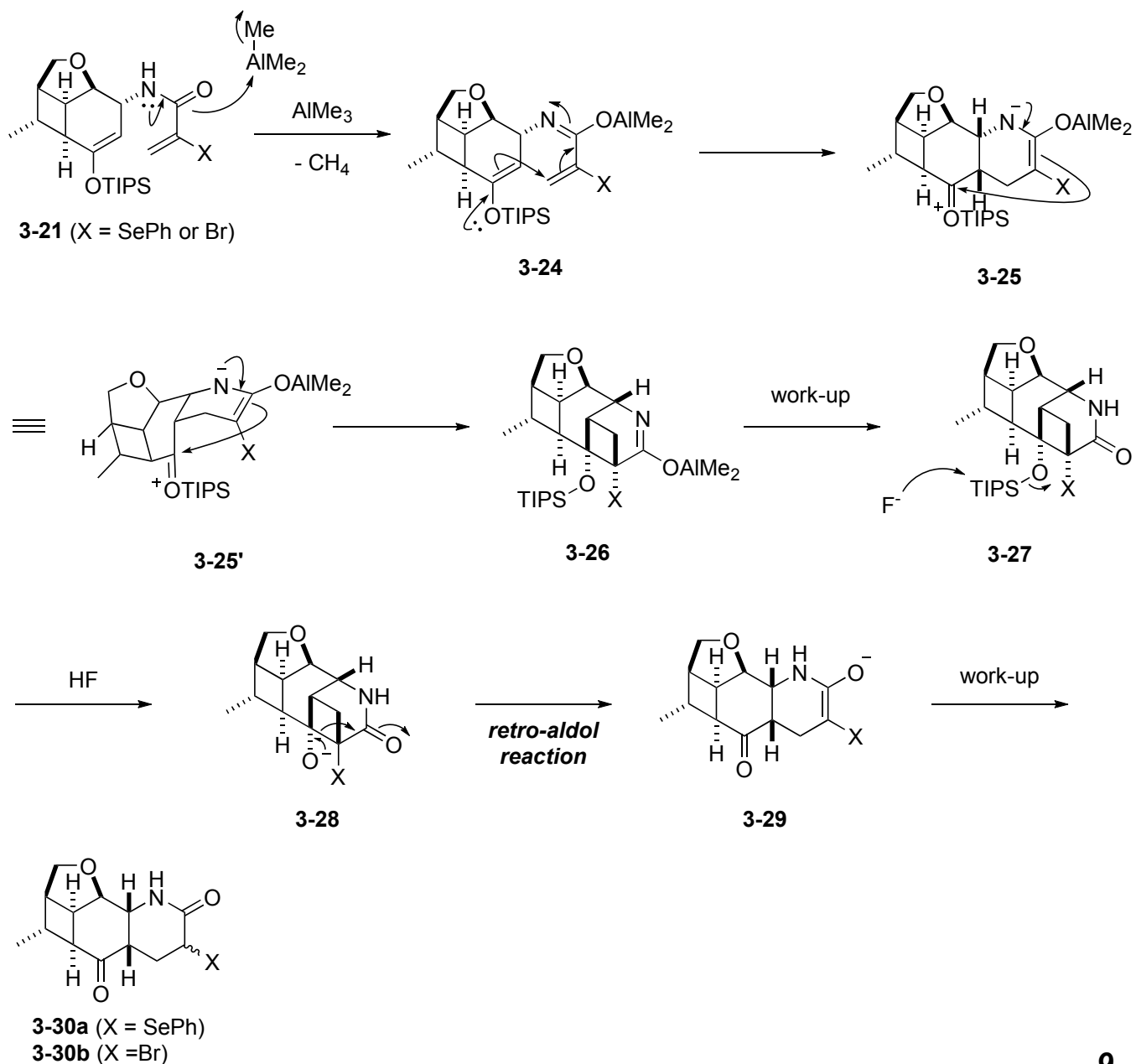


Discussion 1: Stereoselectivity in [2+2]-photocycloaddition

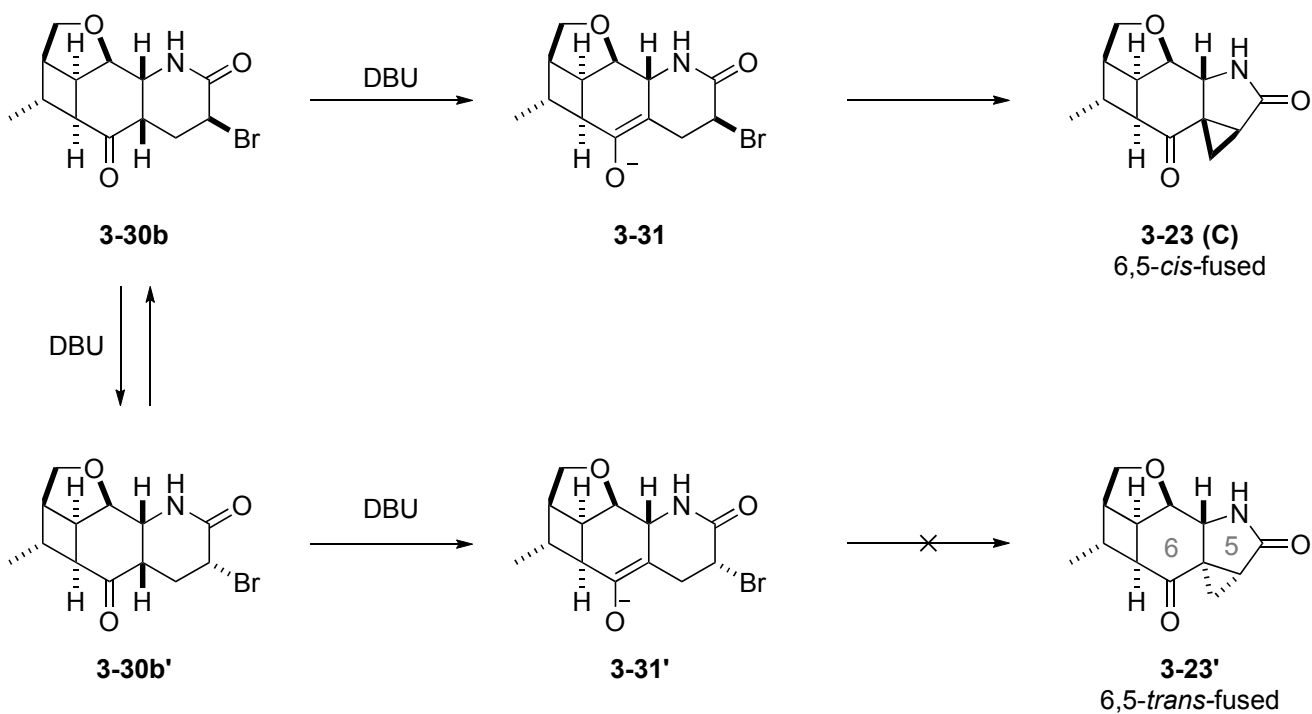




Answer (3-21 => 3-30):



Answer (3-30b => 3-23)



Answer (3-30a => 3-22)

