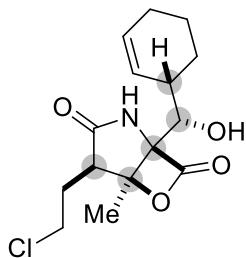


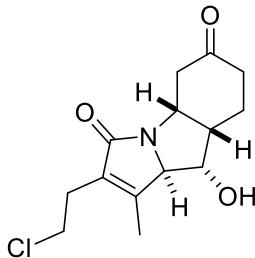
Topic: Total synthesis of salinosporamide A

0. Introduction

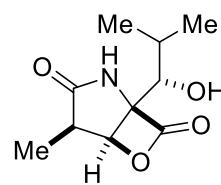
0.1 Structures



salinosporamide A (**0-1**)



salinosporamide C (**0-2**)



omuralide (**0-3**)

* Salinosporamide B, D - K also exist in structures similar to salinosporamide A (**0-1**).

For details please check: Gulder, T. A.; Moore, B. S. *Angew. Chem. Int. Ed.* **2010**, 49, 9346.

0.2 Isolation

from obligate marine bacteria *Salinispora tropica* and *Salinispora arenicola*

Fenical, W. et al. *Angew. Chem. Int. Ed.* **2003**, 42, 355.

0.3 Biological activity

salinosporamide A (**0-1**): potent proteasome inhibitor, about 35 times more potent than omuralide (**0-3**).

0.4 Structural properties

- ◆ [3,2,0]-bicyclic core containing five contiguous stereocenters.
- ◆ High concentration of both electrophilic and nucleophilic functional groups.

0.5 Total syntheses

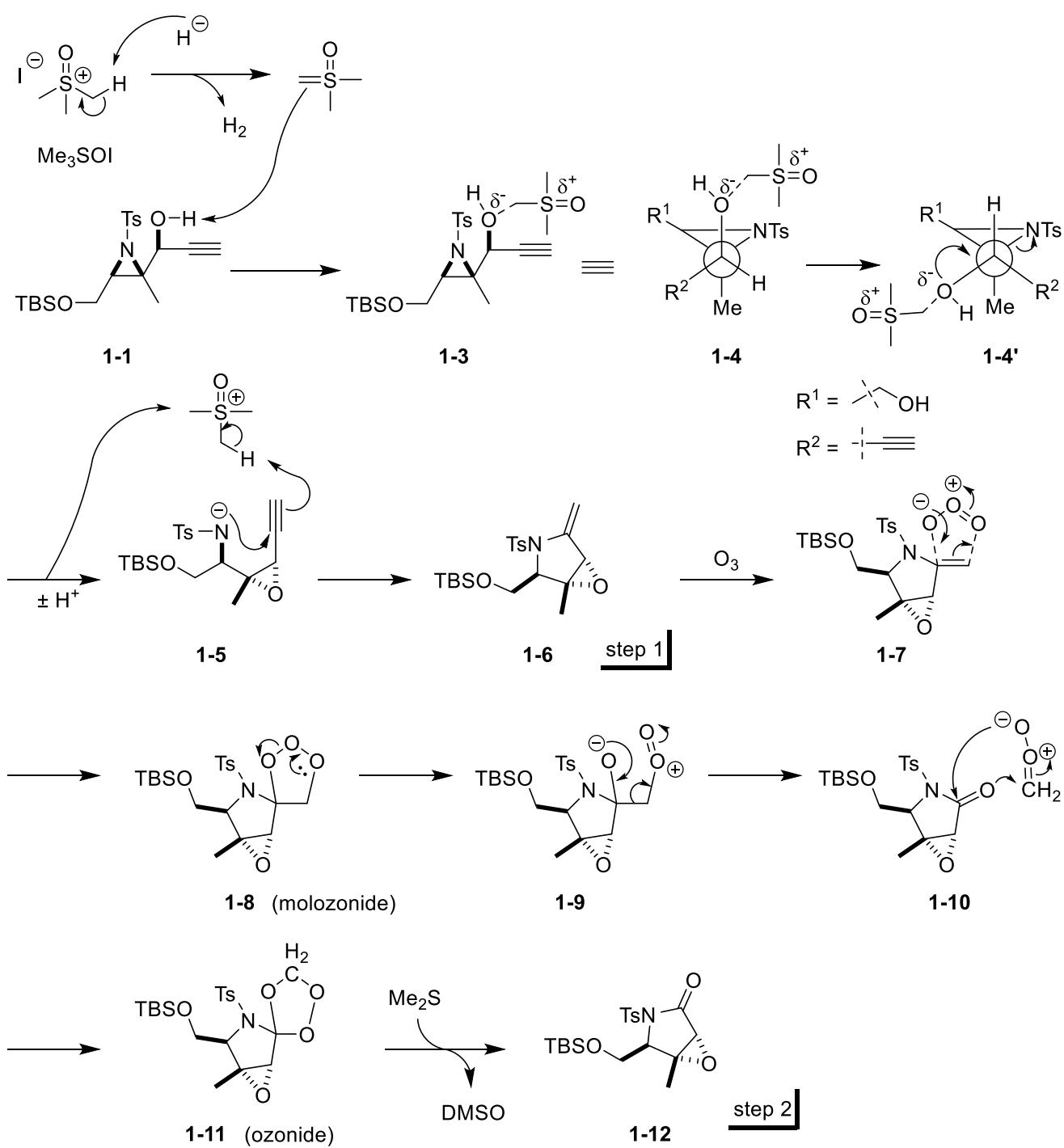
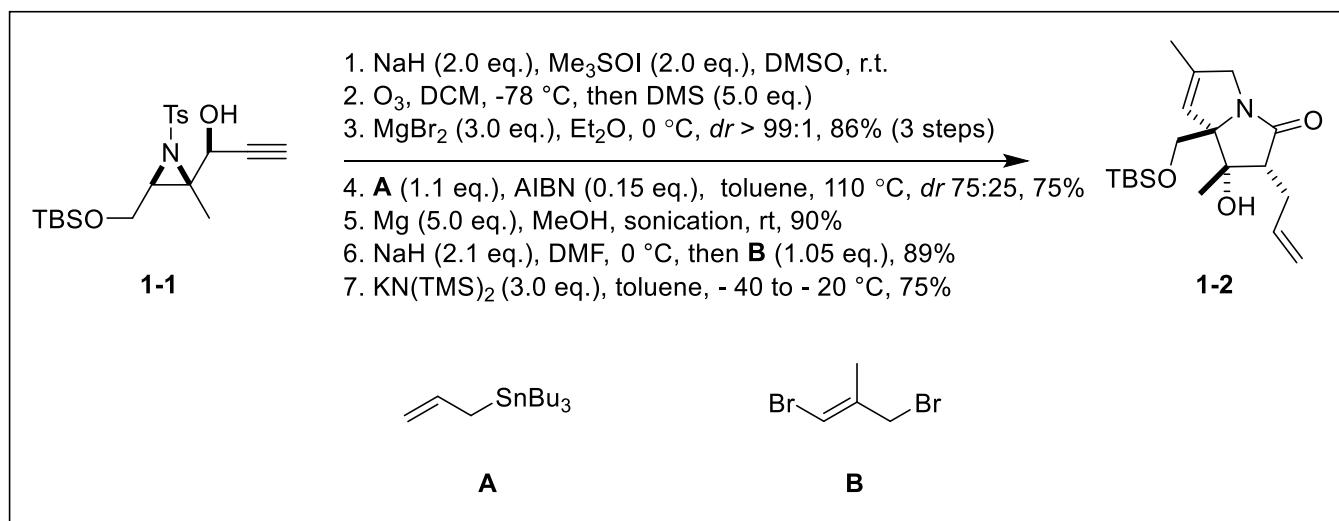
asymmetric syntheses:

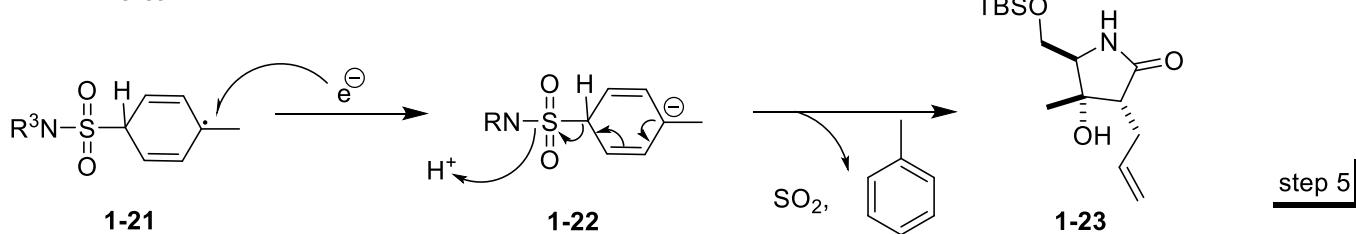
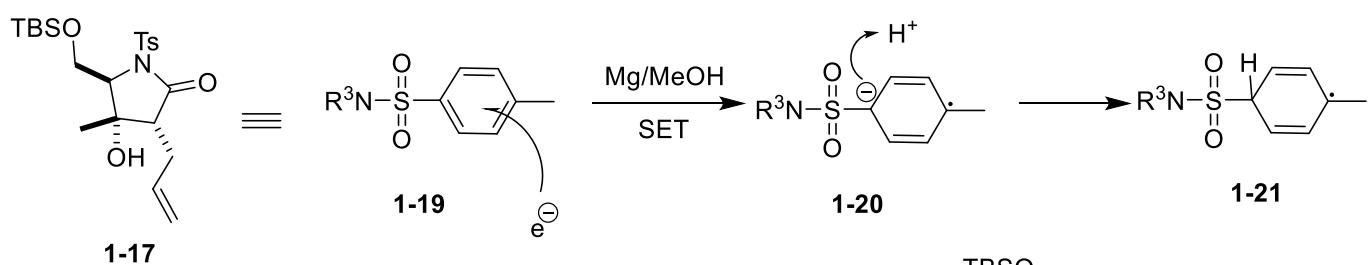
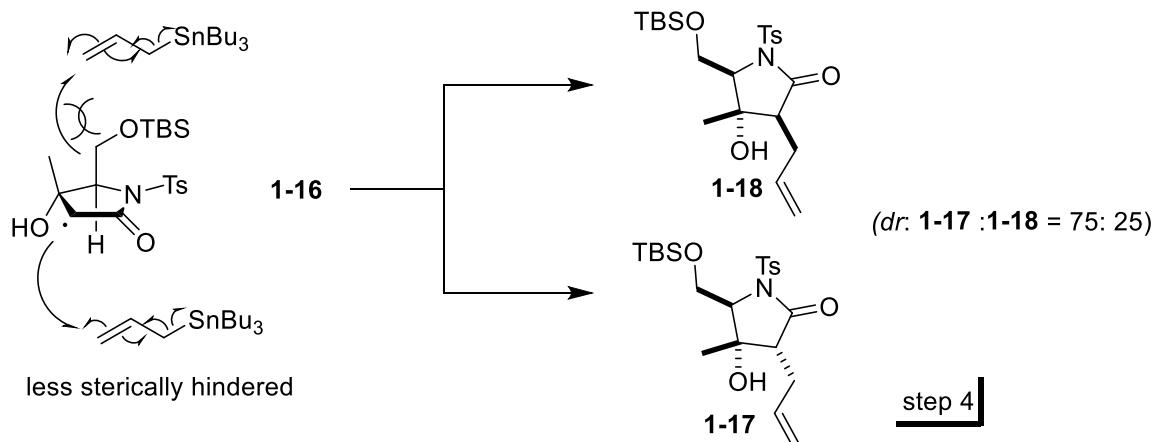
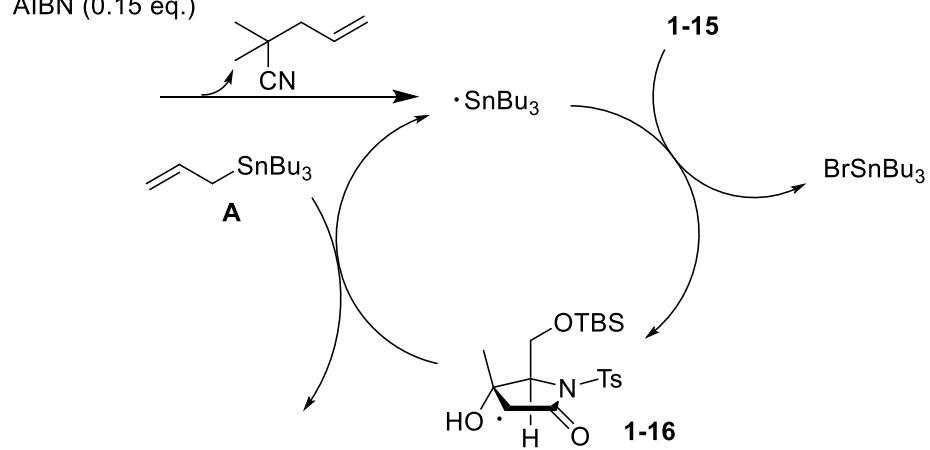
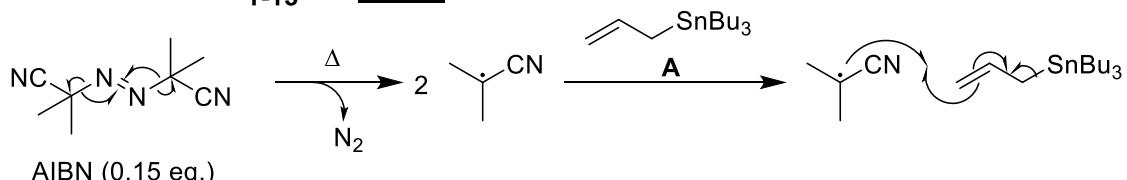
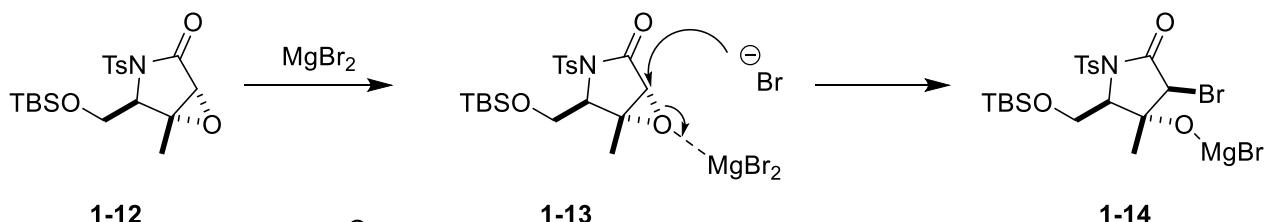
- Corey, E. J. et al. *J. Am. Chem. Soc.* **2004**, 126, 6230.
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 Marx, L. B.; Burton, J. W. *Chem. Eur. J.* **2018**, 24, 6747. (Problem 2)
 Borhan, B. et al. *Angew. Chem. Int. Ed.* **2019**, 58, 10110. (Problem 1)

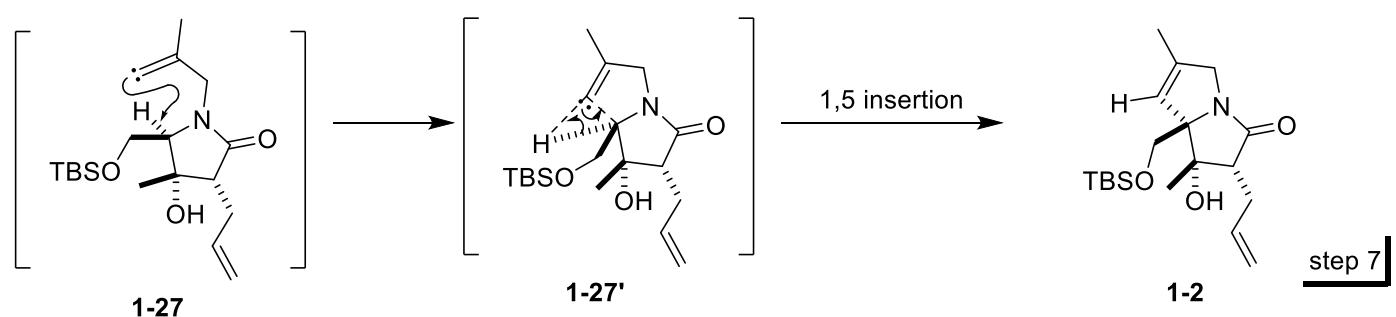
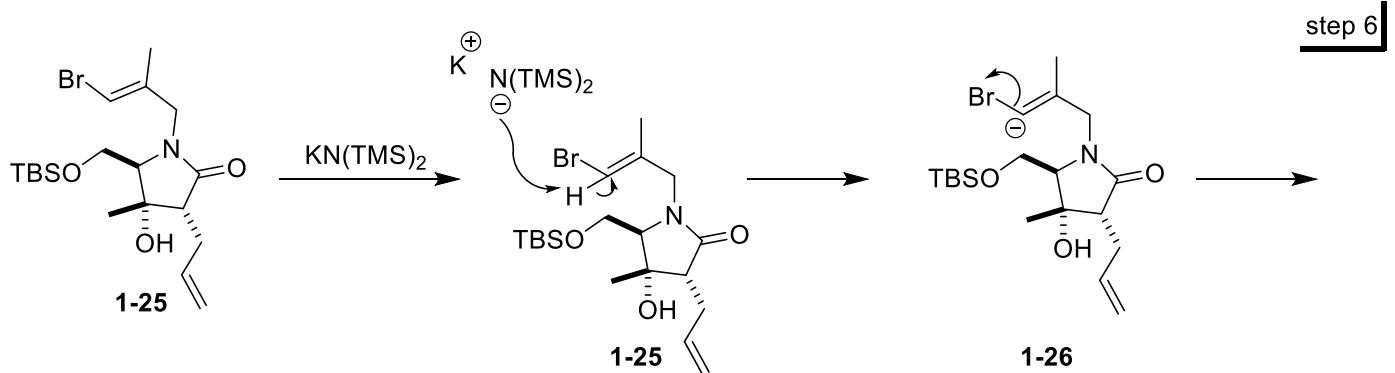
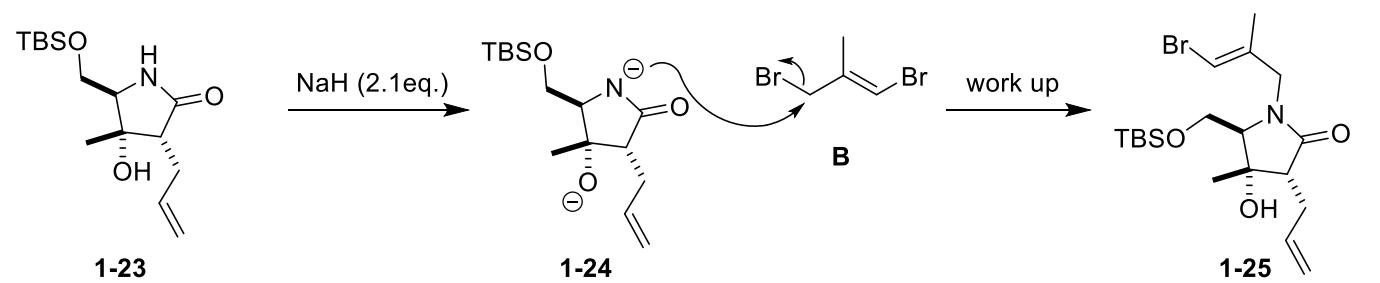
racemic syntheses:

- I. A. S. Walters et al. *Org. Biomol. Chem.* **2006**, 4, 2845.
 D. Romo et al. *Org. Lett.* **2007**, 9, 2143.
 I. A. Walters et al. *Org. Biomol. Chem.* **2008**, 6, 2782.

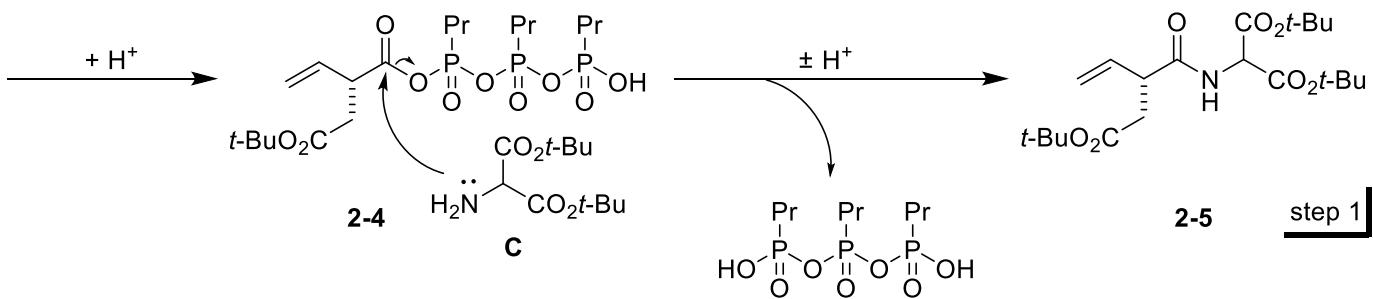
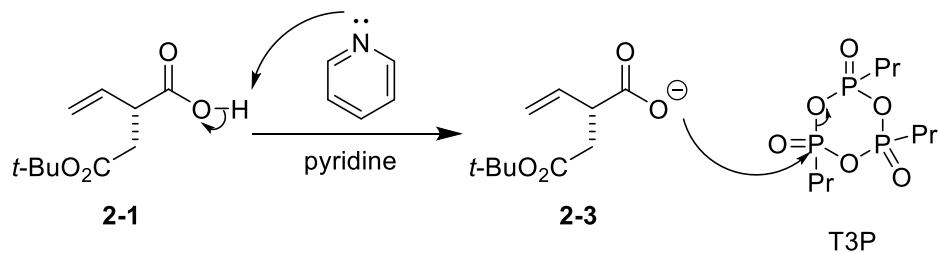
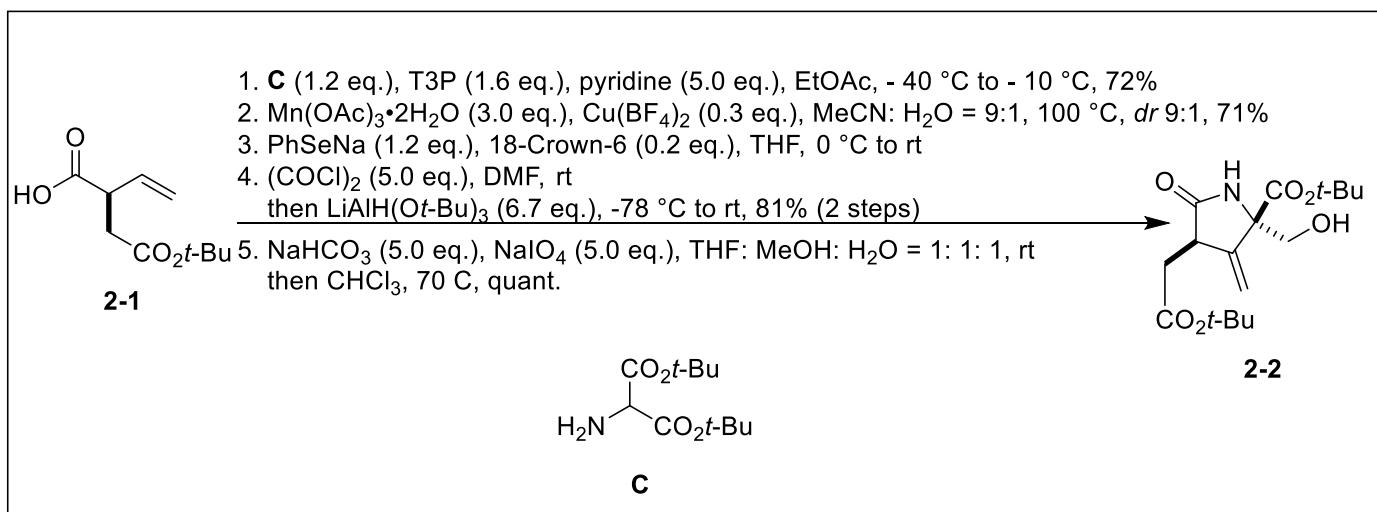
1.1 Reaction and mechanism



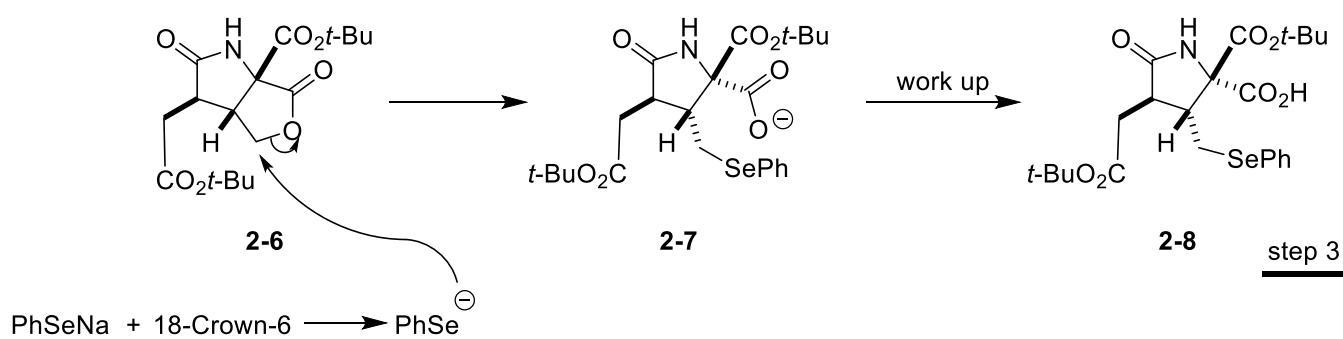
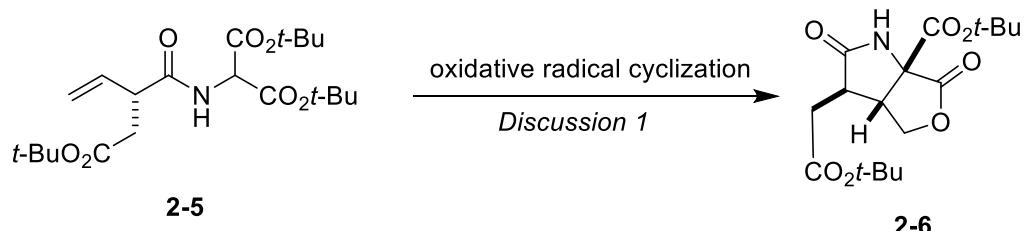


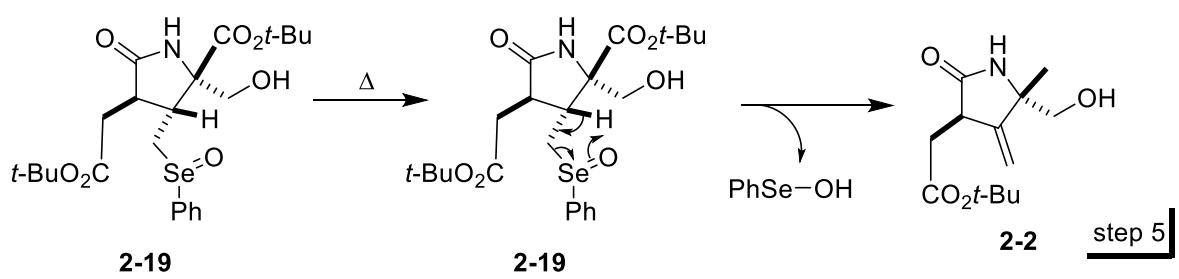
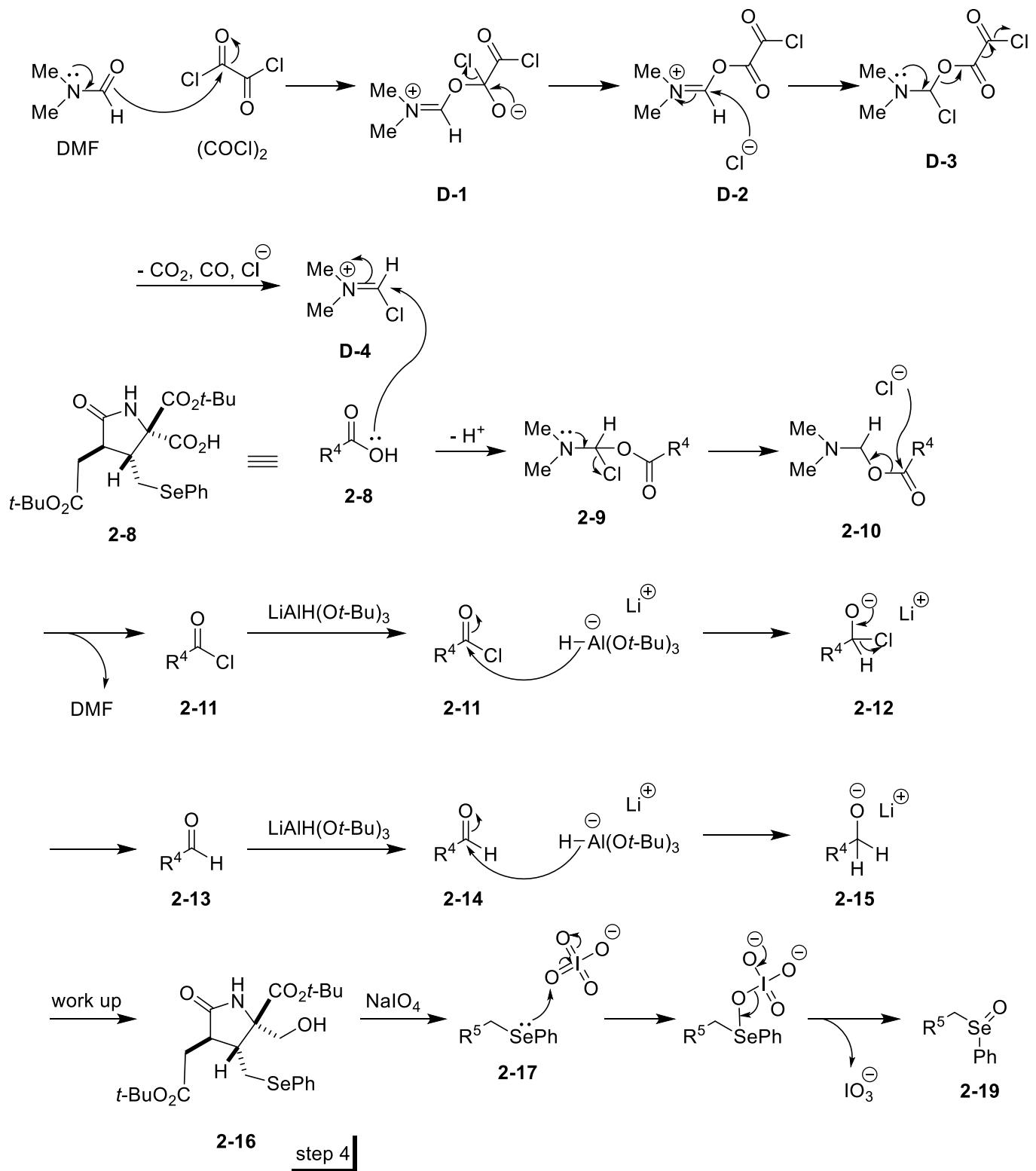


2.1 Reaction and mechanism

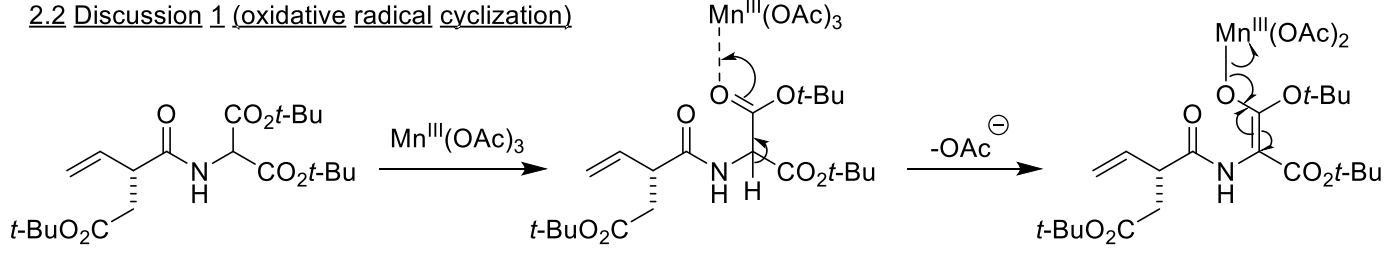


*For more about the mechanisms about other condensing agents, please refer to 140920_PS_Kuranaga.





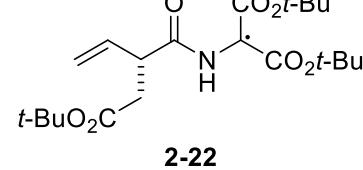
2.2 Discussion 1 (oxidative radical cyclization)



2-5

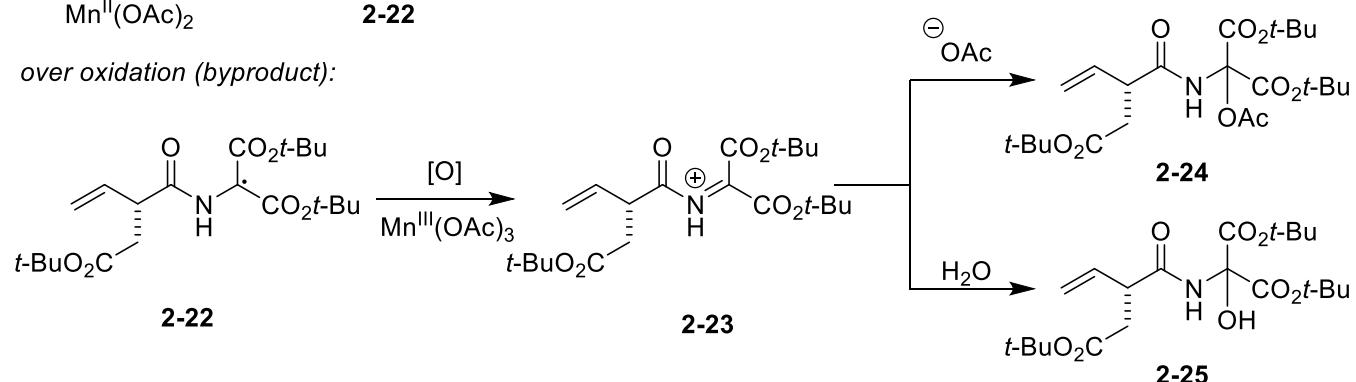
2-20

2-21

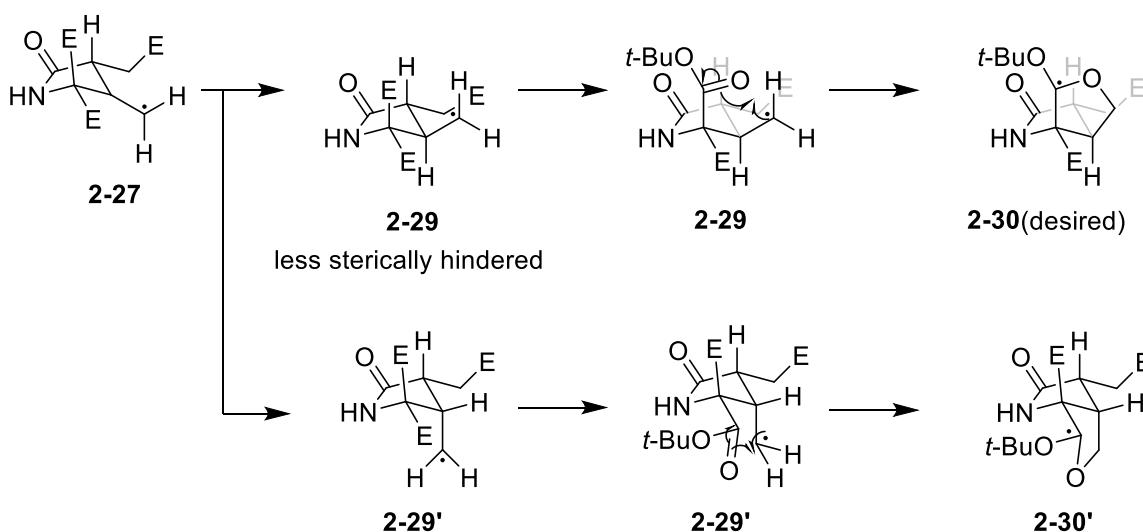
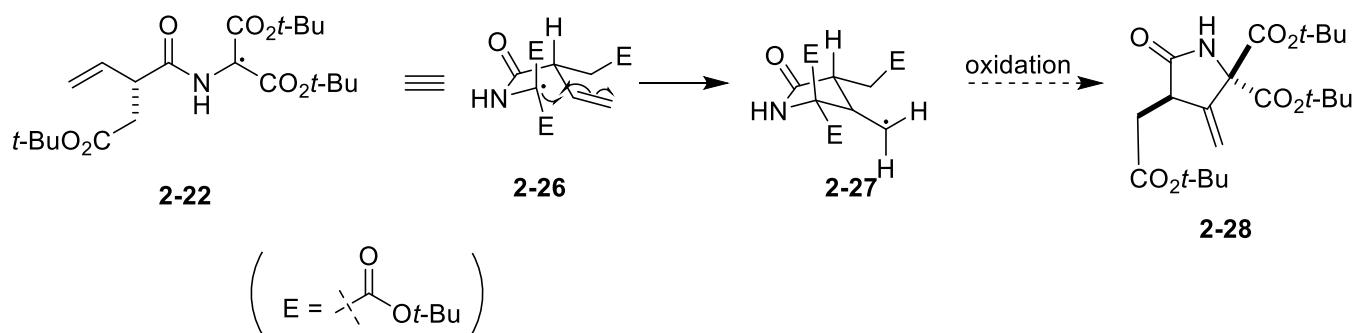


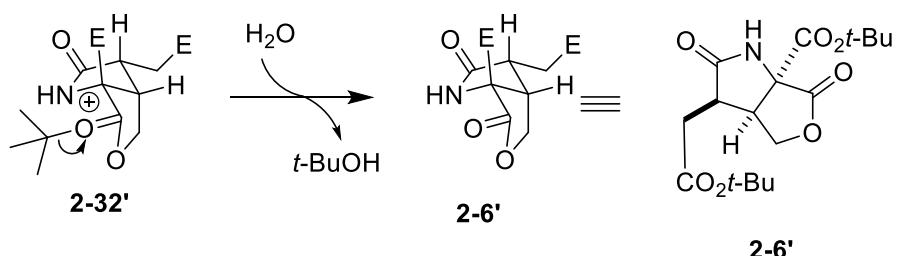
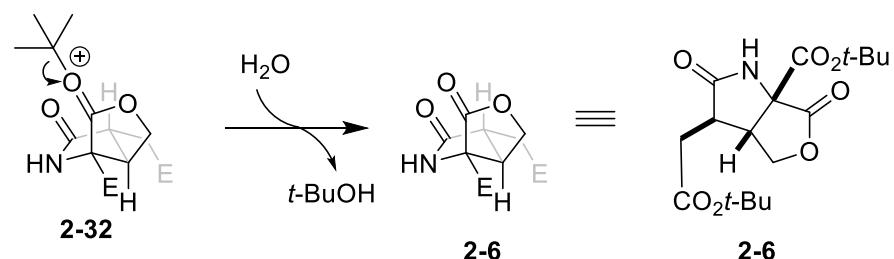
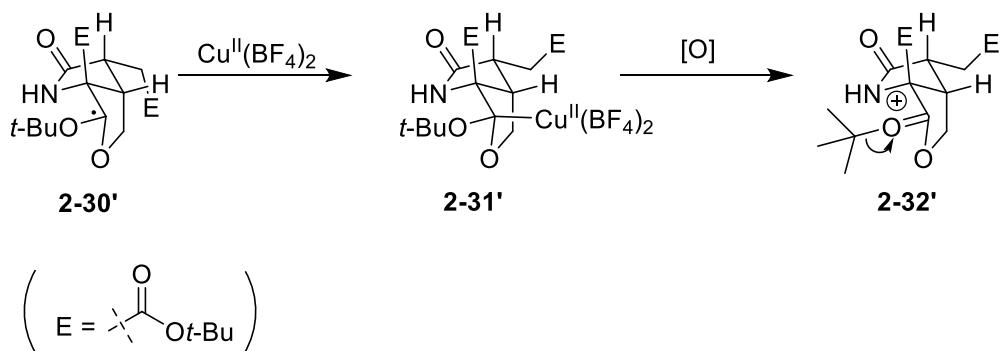
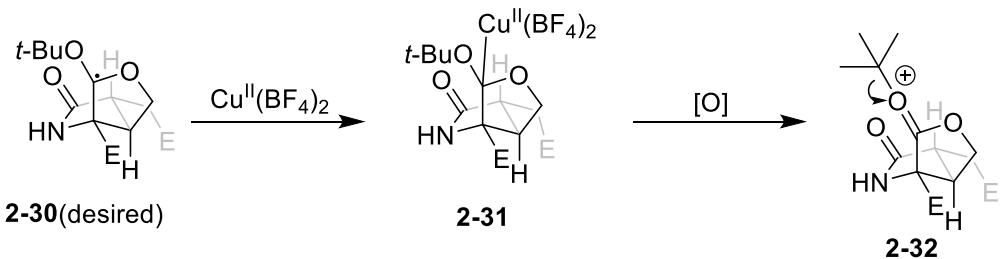
Mn^{II}(OAc)₂

over oxidation (byproduct):



cyclization:





(dr: 2-6: 2-6' = 9:1)