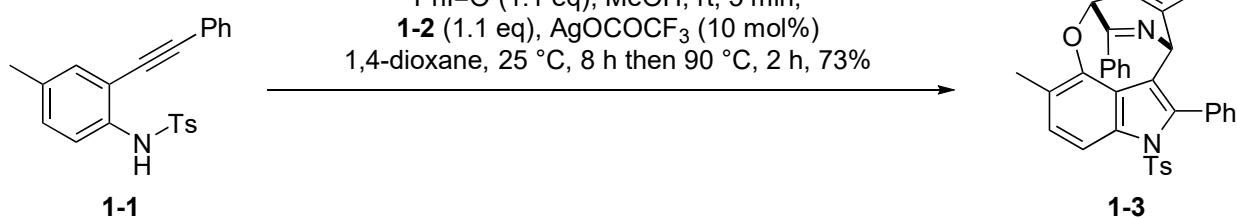


Problem session (2)

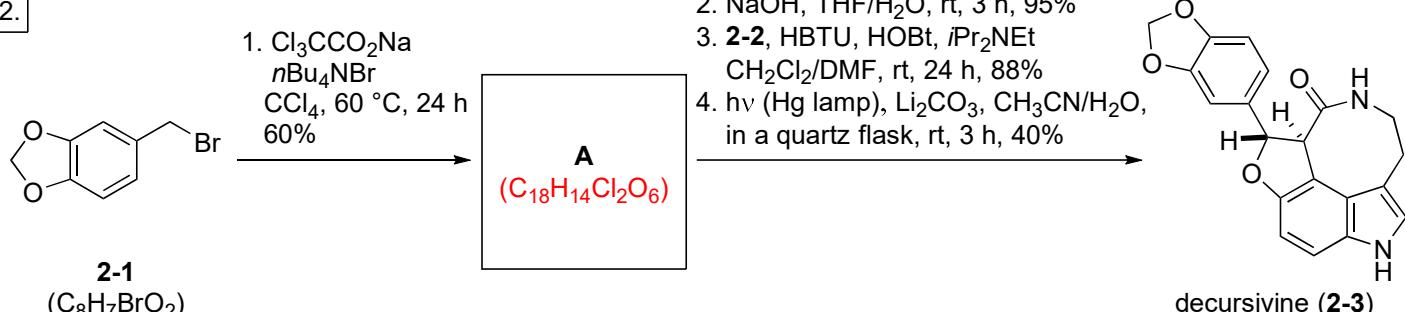
2017.1.21 Daiki Kuwana

Please fill in the blank and explain the reaction mechanisms.

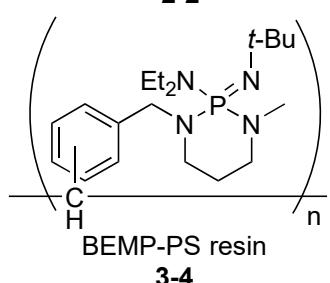
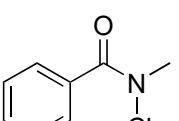
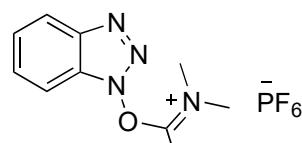
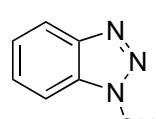
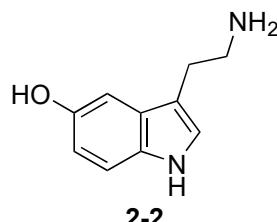
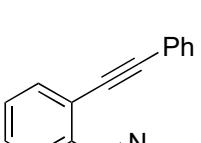
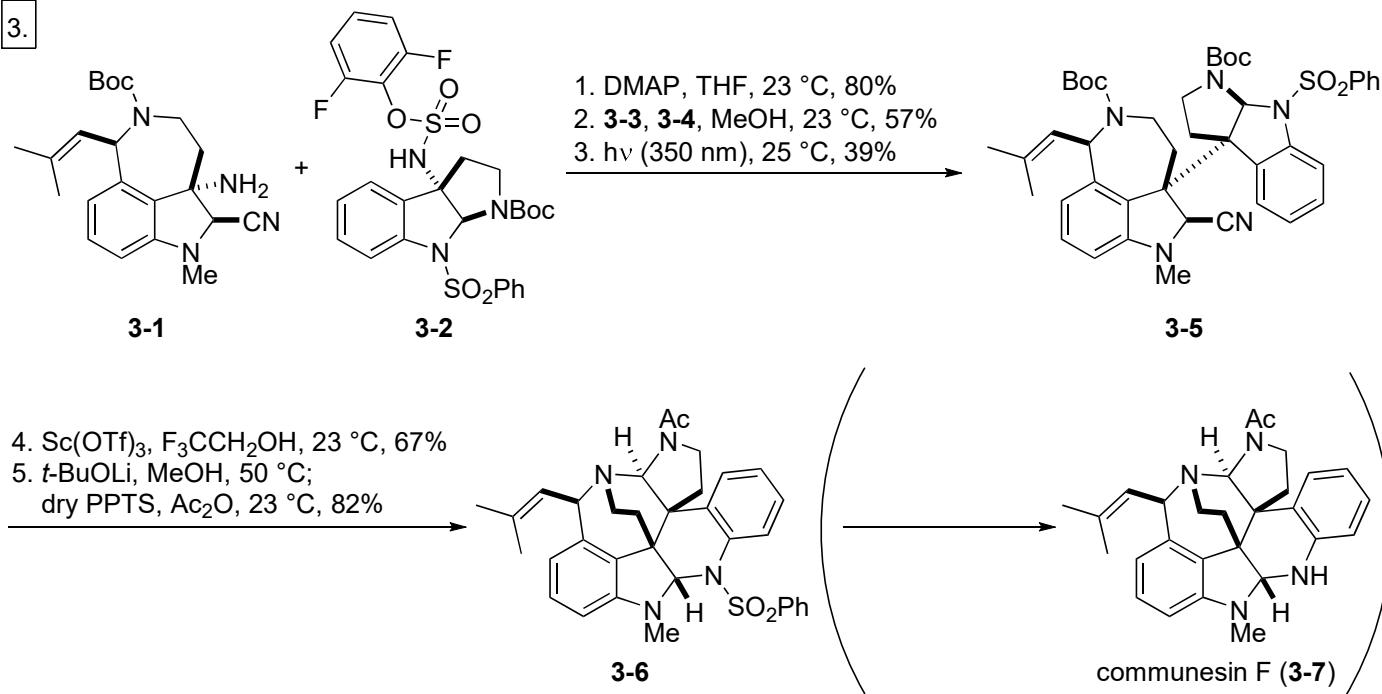
1.



2.



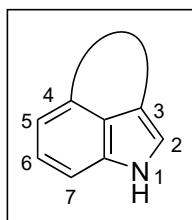
3.



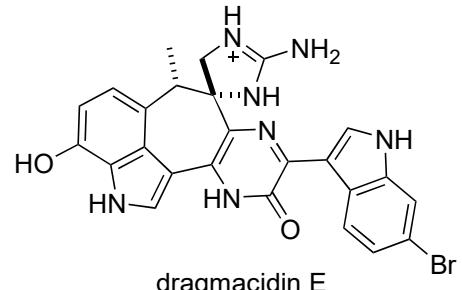
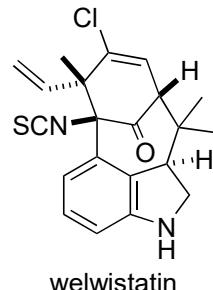
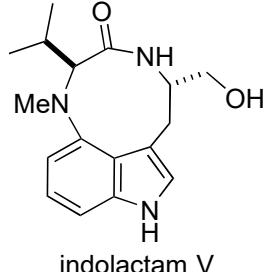
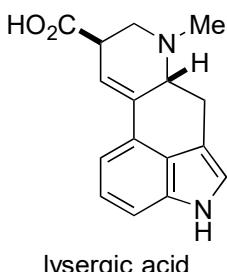
Problem session (2) -Answer-

2017.1.21 Daiki Kuwana

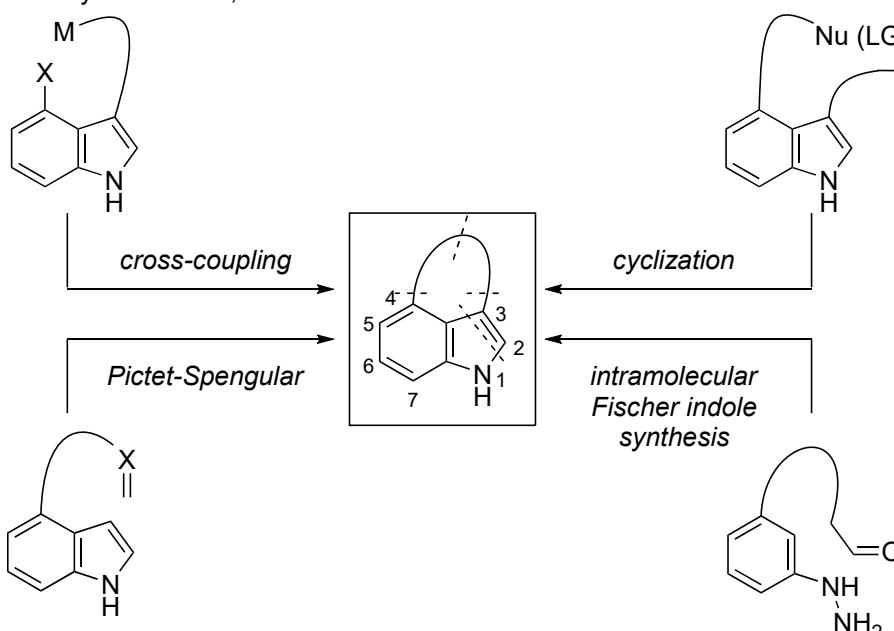
Topics: 3,4-fused indoles



0-1. Examples of 3,4-fused indole alkaloids



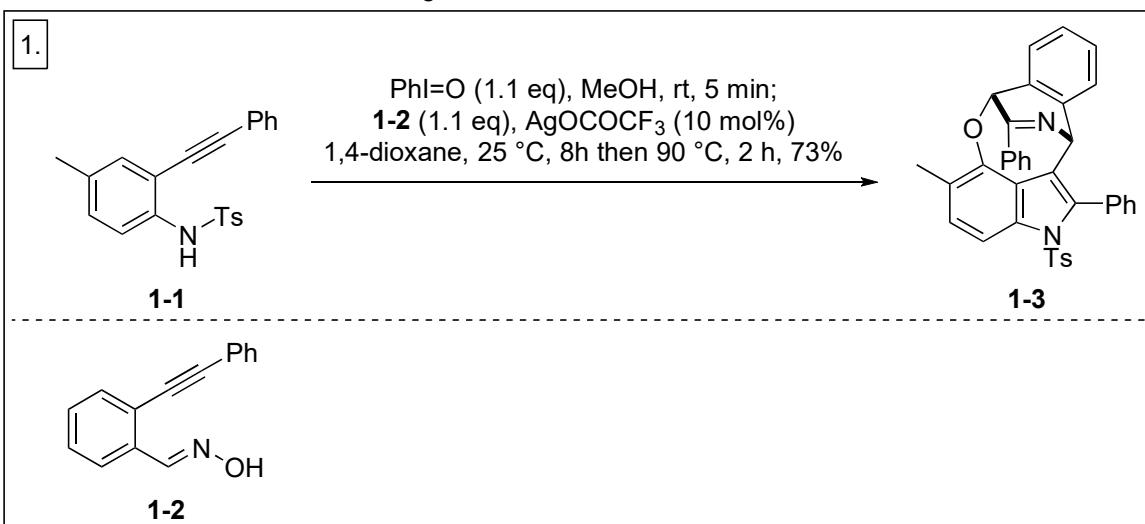
0-2. Synthesis of 3,4-fused indole skeleton



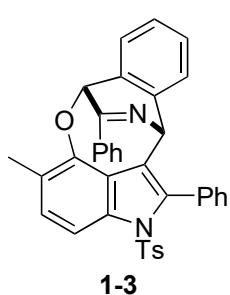
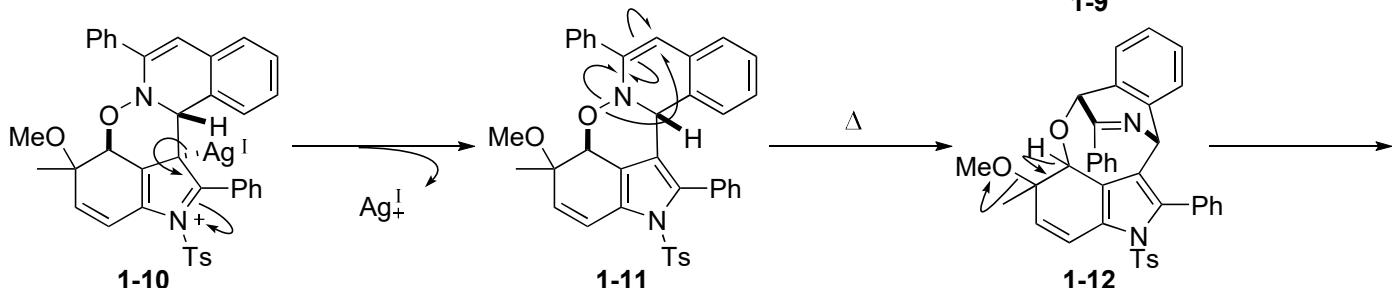
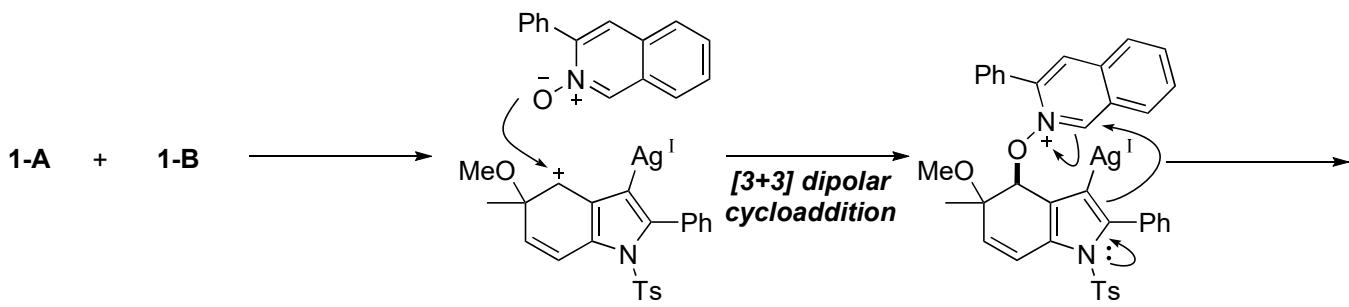
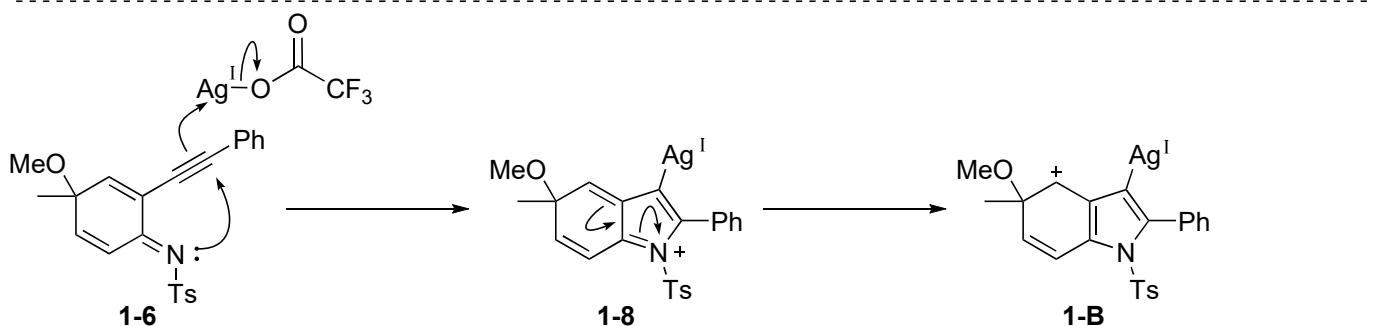
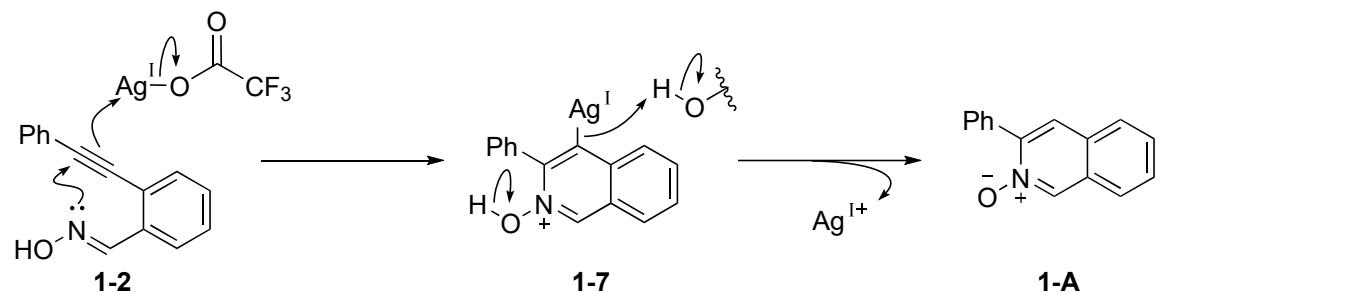
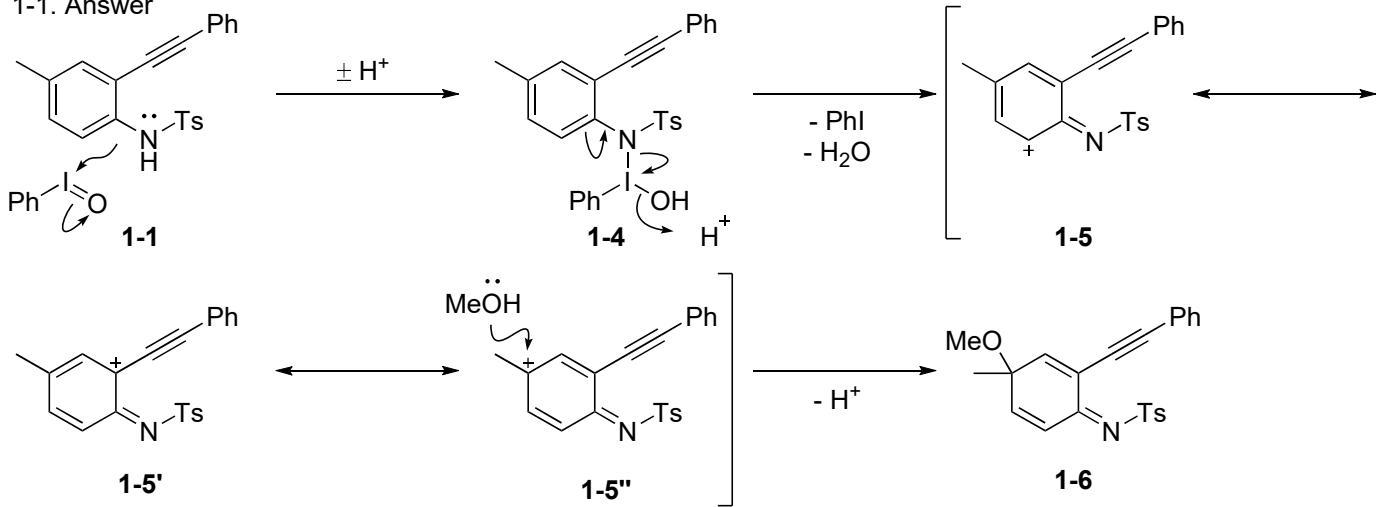
cf. Yoshida-san, PS, 2016/6/25 (indole synthesis)

1. Synthesis of oxocino[4,3,2-cd]indoles

Han, D.; He, Q.; Fan, R. et al. *Angew. Chem.* **2015**, *127*, 14219.

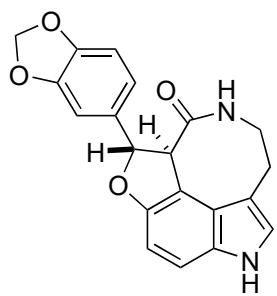


1-1. Answer



2. Total synthesis of decursivine

Hu, W.; Qin, H.; Cui, Y.; Jia, Y. et al. *Chem. Eur. J.* **2013**, *19*, 3139;



Isolation

Rhaphidophora decursiva Fong, H. H. S. et al. *Pharm. Biol.* **2002**, *40*, 221

Bioactivity

antimalarial activity against the D6 and W2 clones of *Plasmodium falciparum*.

Total synthesis

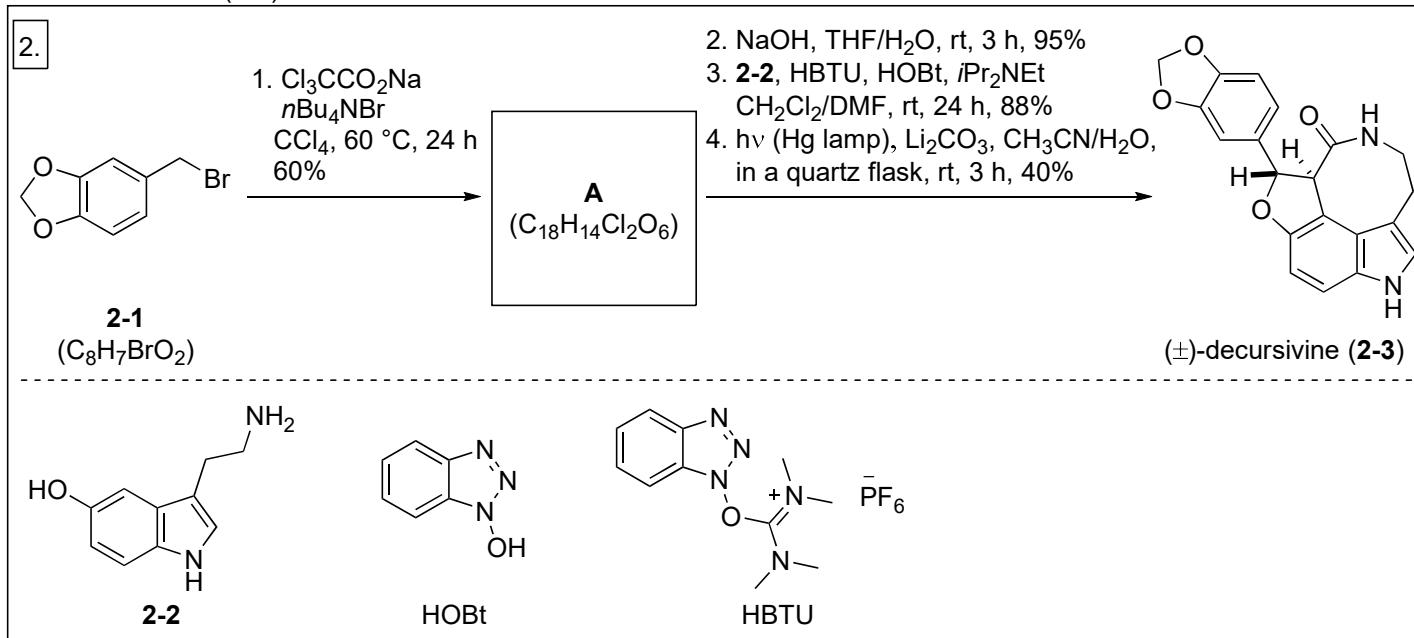
Leduc, A. B.; Kerr, M. A. *Eur. J. Org. Chem.* **2007**, 237.

Mascal, M.; Modes, K. V.; Durmus, A.; *Angew. Chem.* **2011**, *123*, 4539.

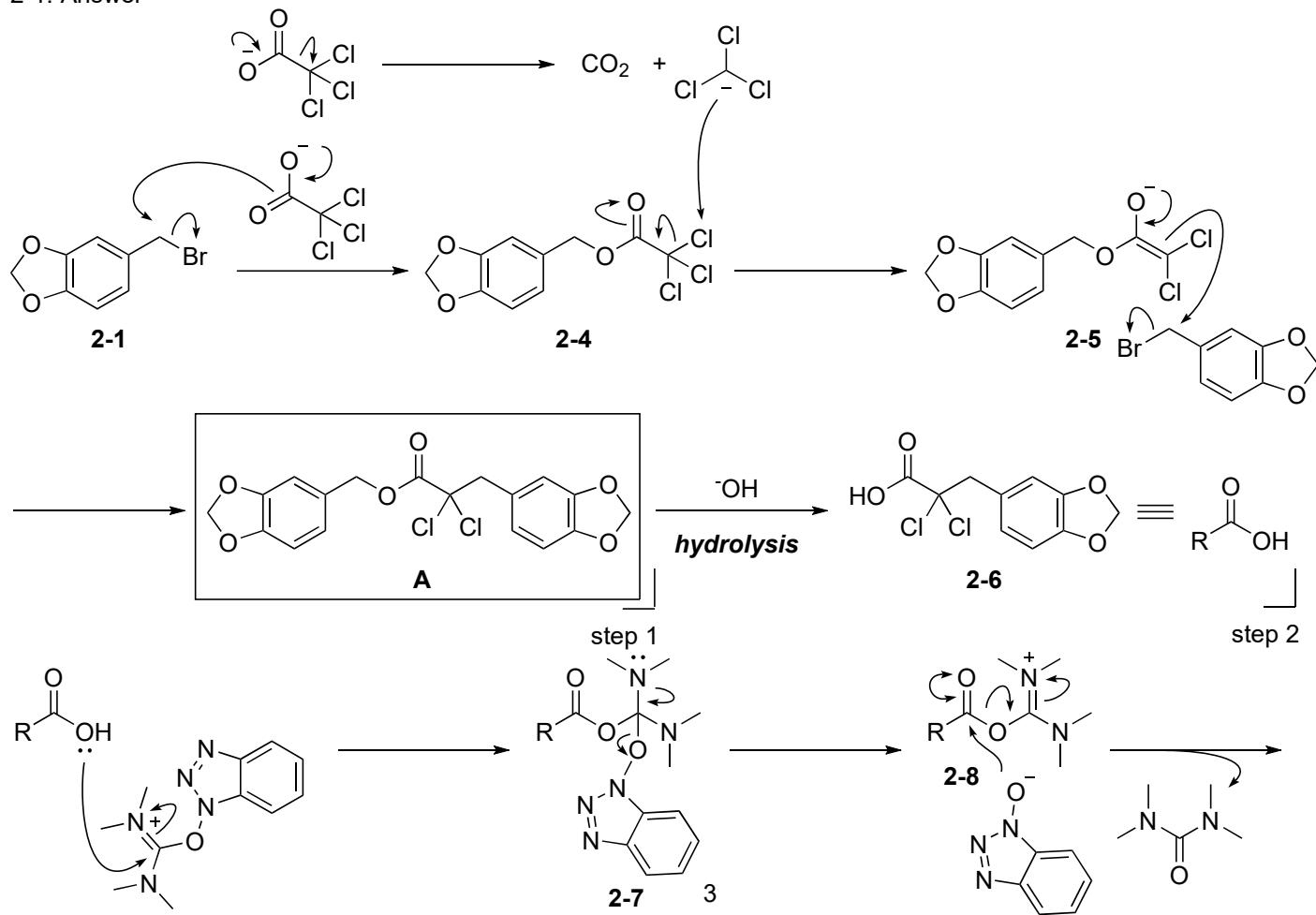
Qin, H.; Xu, Z.; Cui, Y.; Jia, Y. *Angew. Chem. Int. Ed.* **2011**, *50*, 4447.

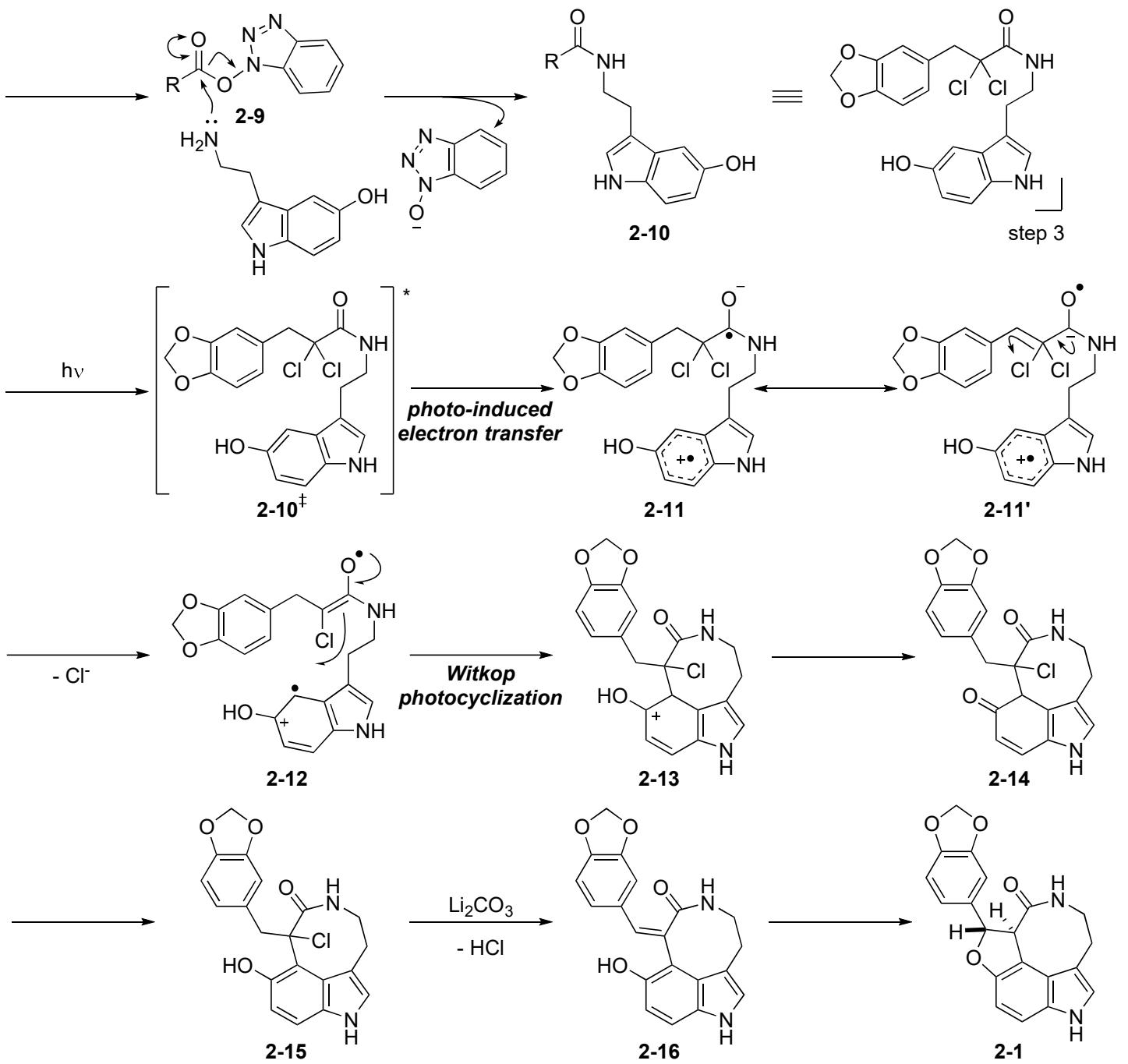
Sun, D.; Zhao, Q.; Li, C. *Org. Lett.* **2011**, *13*, 5302. (asymmetric)

decurvivine (2-3)

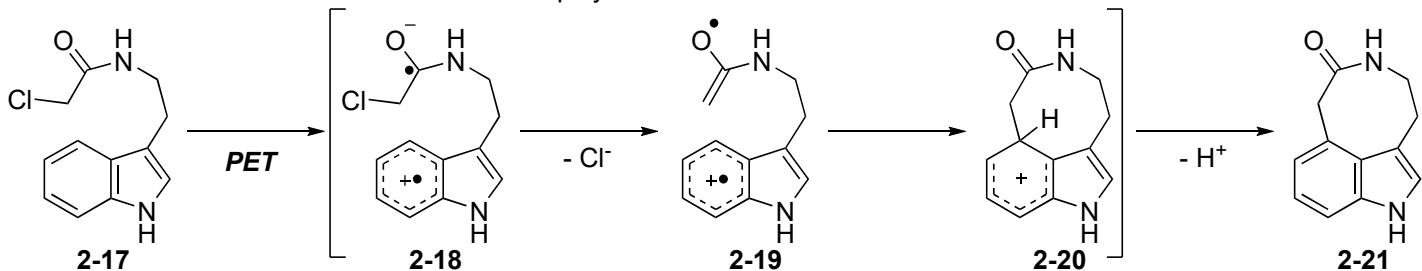


2-1. Answer

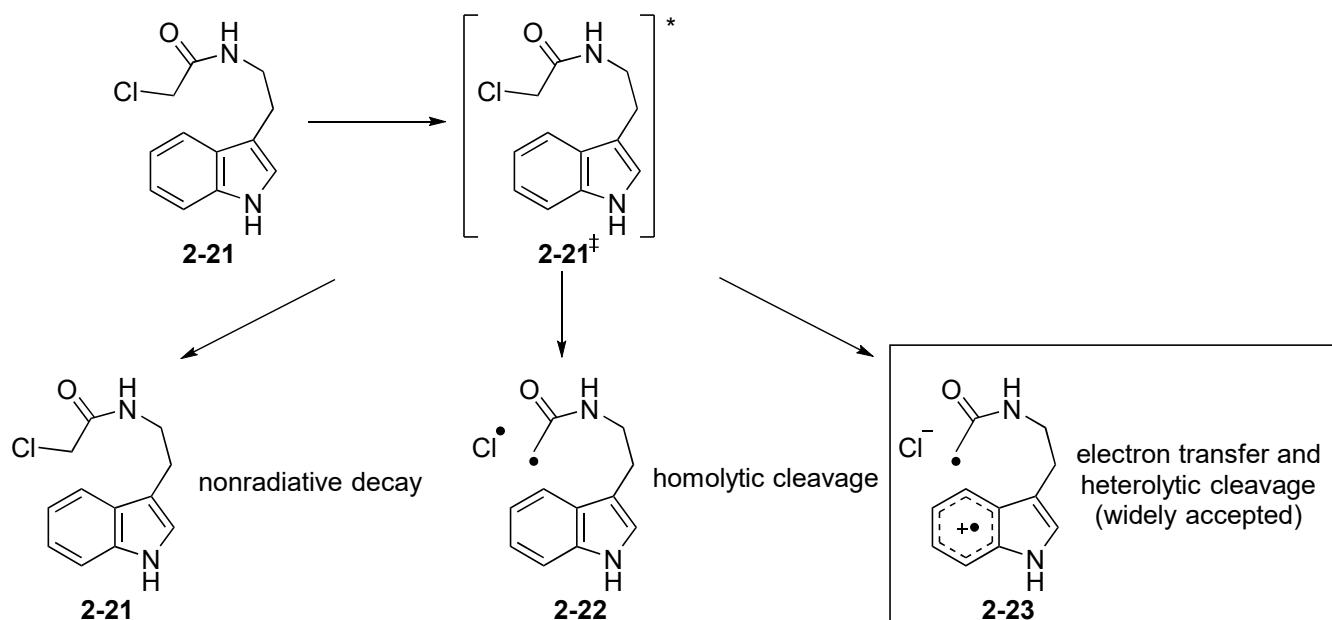




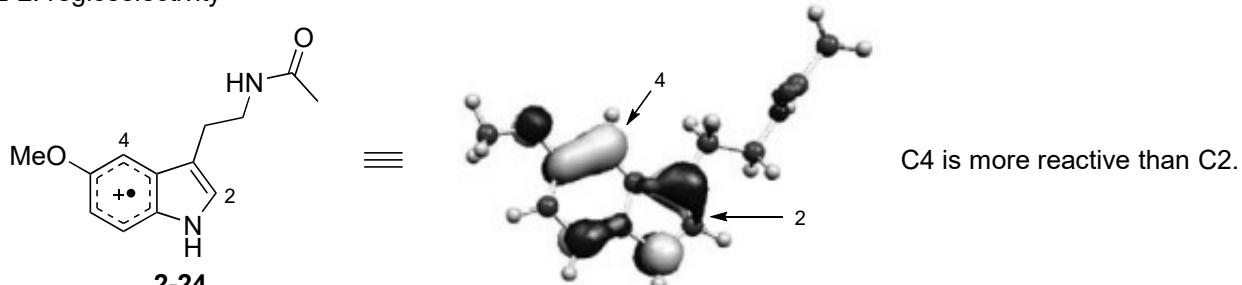
2-2. Discussion : reaction mechanism of Witkop cyclization



2-2-1. Photoexcitation of indole

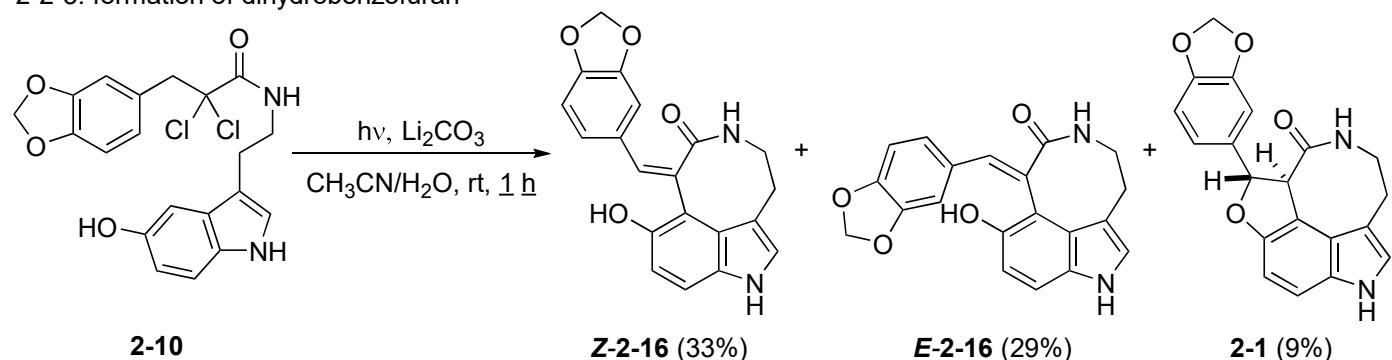


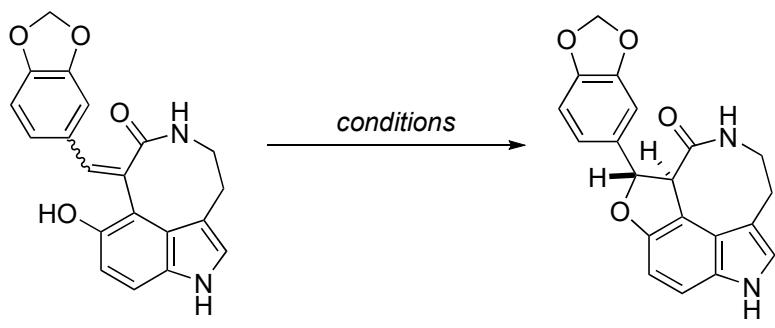
2-2-2. regioselectivity



Crespo, A.; Turjanski, A. G.; Estrin, D. A. *Chem. Psy. Lett.* **2002**, 365, 15-21

2-2-3. formation of dihydrobenzofuran



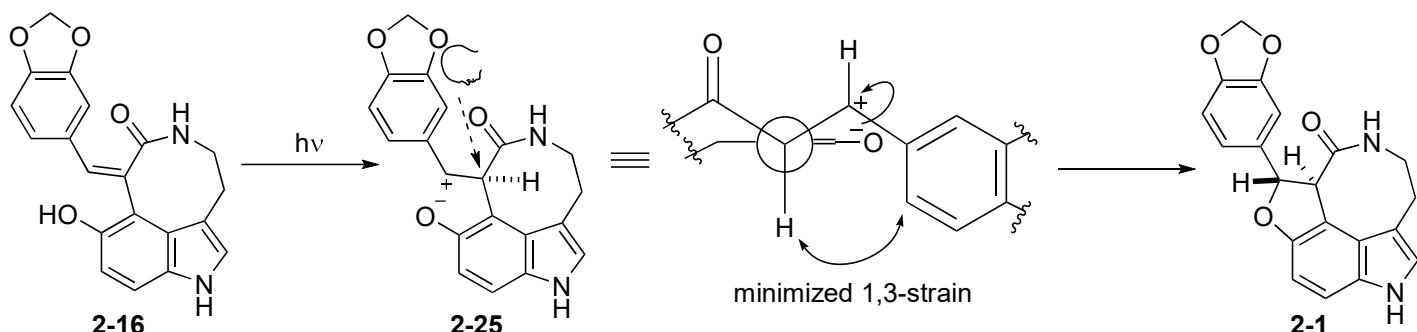


Table

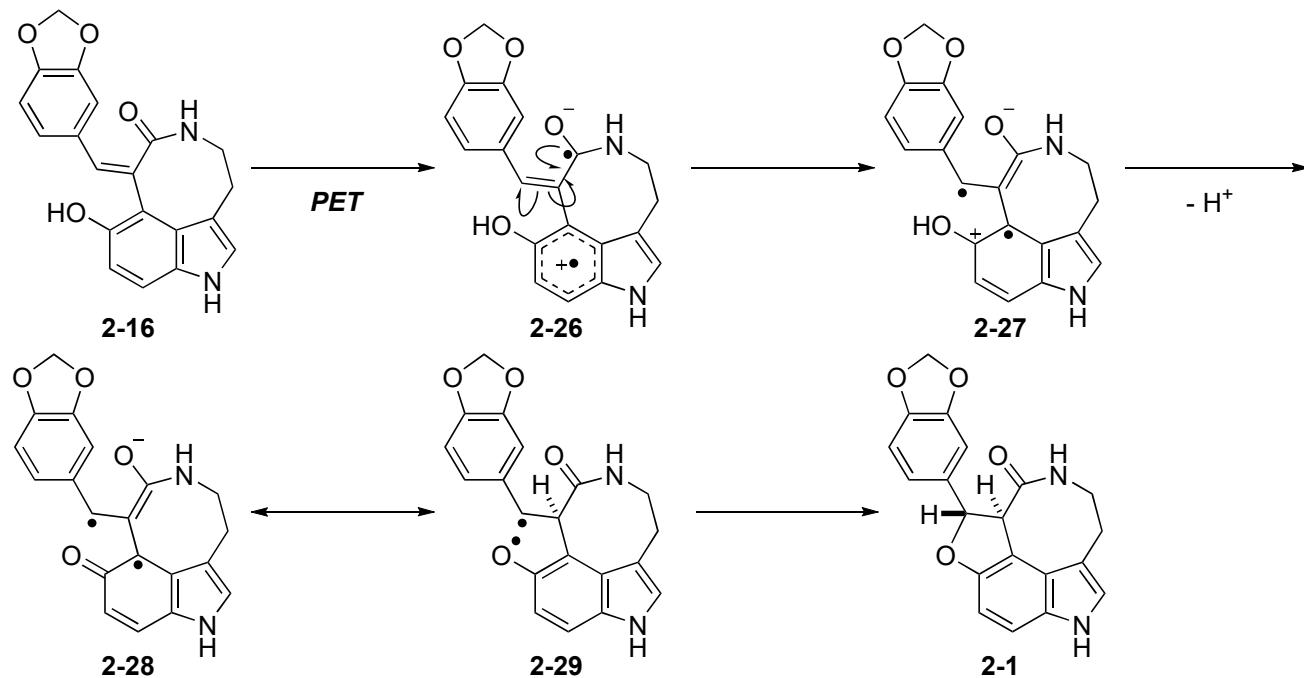
entry	conditions	2-16
1	$\text{h}\nu$, Li_2CO_3 , $\text{CH}_3\text{CN}/\text{H}_2\text{O}$, rt, 3 h	53%
2	$\text{h}\nu$, $\text{CH}_3\text{CN}/\text{H}_2\text{O}$, rt, 3 h	54%
3	$\text{h}\nu$, CH_3CN , rt, 3 h	52%

- Stereochemistry is not determined at the stage of olefin formation.
- Li salt and H_2O are not necessary for the conversion of 2-23 to 2-1.

2-2-3-1. Author's proposal

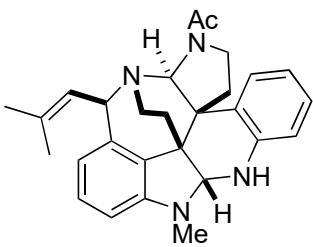


2-2-3-2. My proposal



3. Total synthesis of communesin F

Lathrop, S. P.; Pompeo, M.; Chang, W.-T. T.; Movassaghi, M. *J. Am. Chem. Soc.* **2016**, 138, 7763.



(-)communesin F (3-7)

Isolation

from fungi *Penicillium expansum*

Hayashi, H.; Matsumoto, H.; Akiyama, K. *Biosci., Biotechnol., Biochem.* **2004**, 68, 753.

Bioactivity

insecticidal activity against 3rd instar larvae of silkworms

Total synthesis

Yang, J.; Wu, H.; Shen, Y.; Qin, Y. *J. Am. Chem. Soc.* **2007**, 129, 13794.

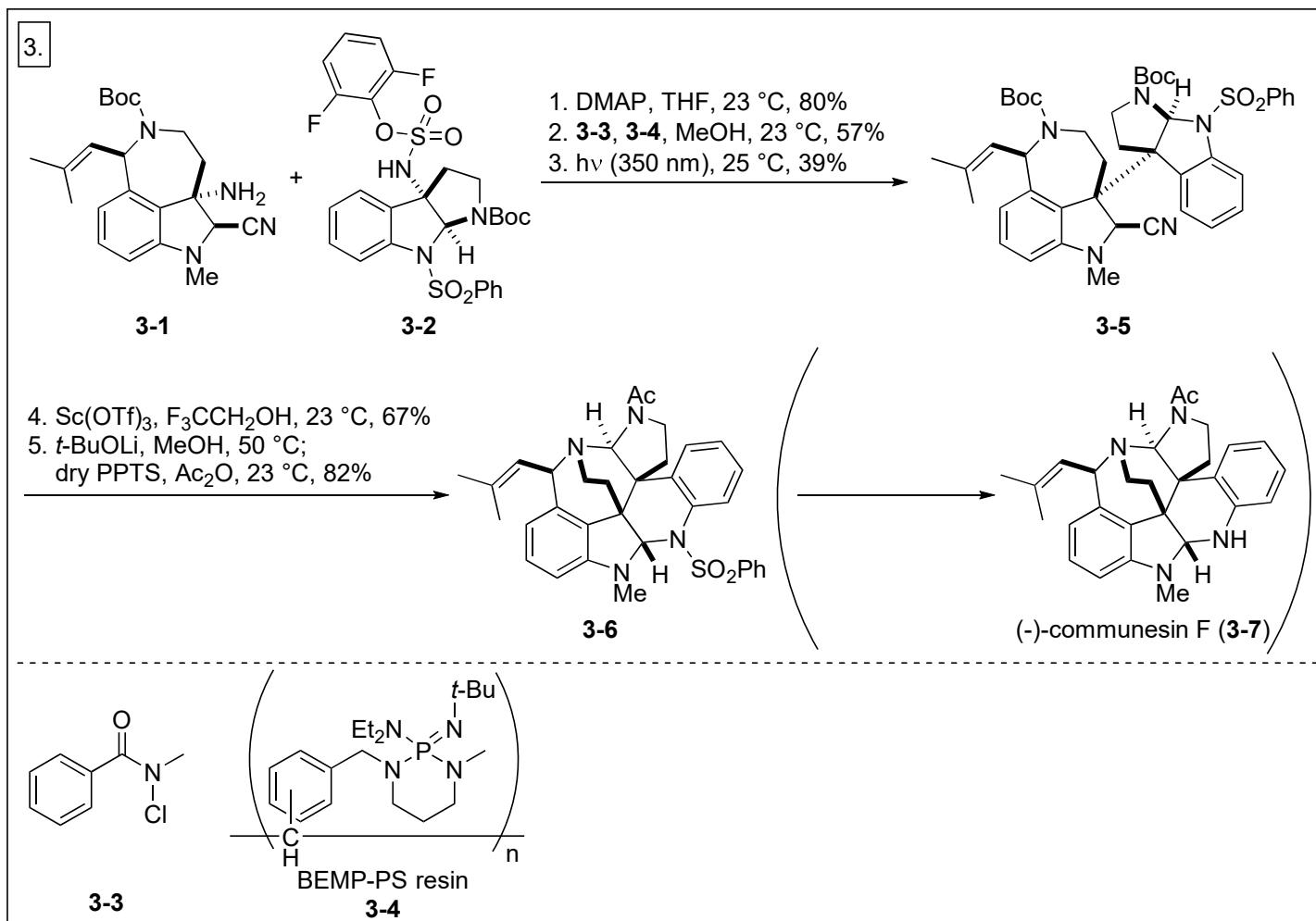
Zuo, Z.; Xie, W.; Ma, D. *J. Am. Chem. Soc.* **2010**, 132, 13226.

Liu, P.; Seo, J. H.; Weinreb, S. M. *Angew. Chem., Int. Ed.* **2010**, 49, 2000.

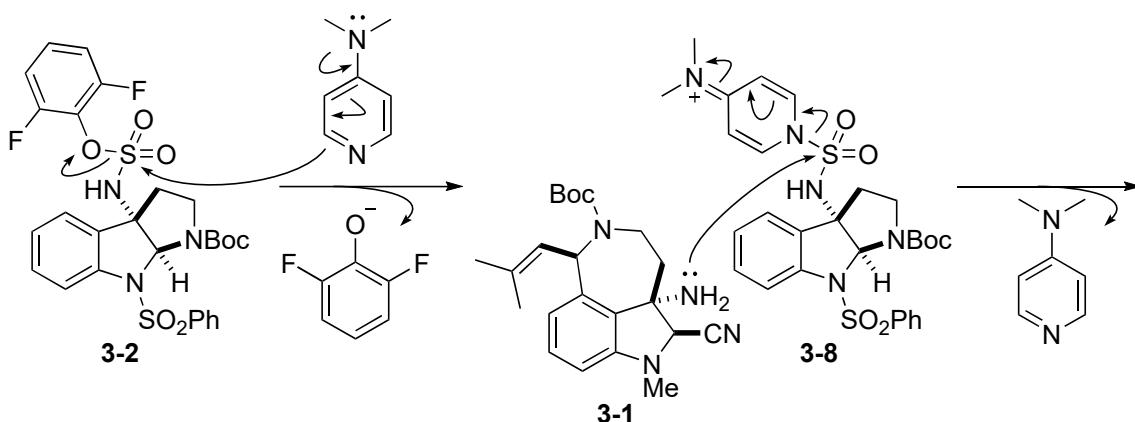
Belmar, J.; Funk, R. L. *J. Am. Chem. Soc.* **2012**, 134, 16941.

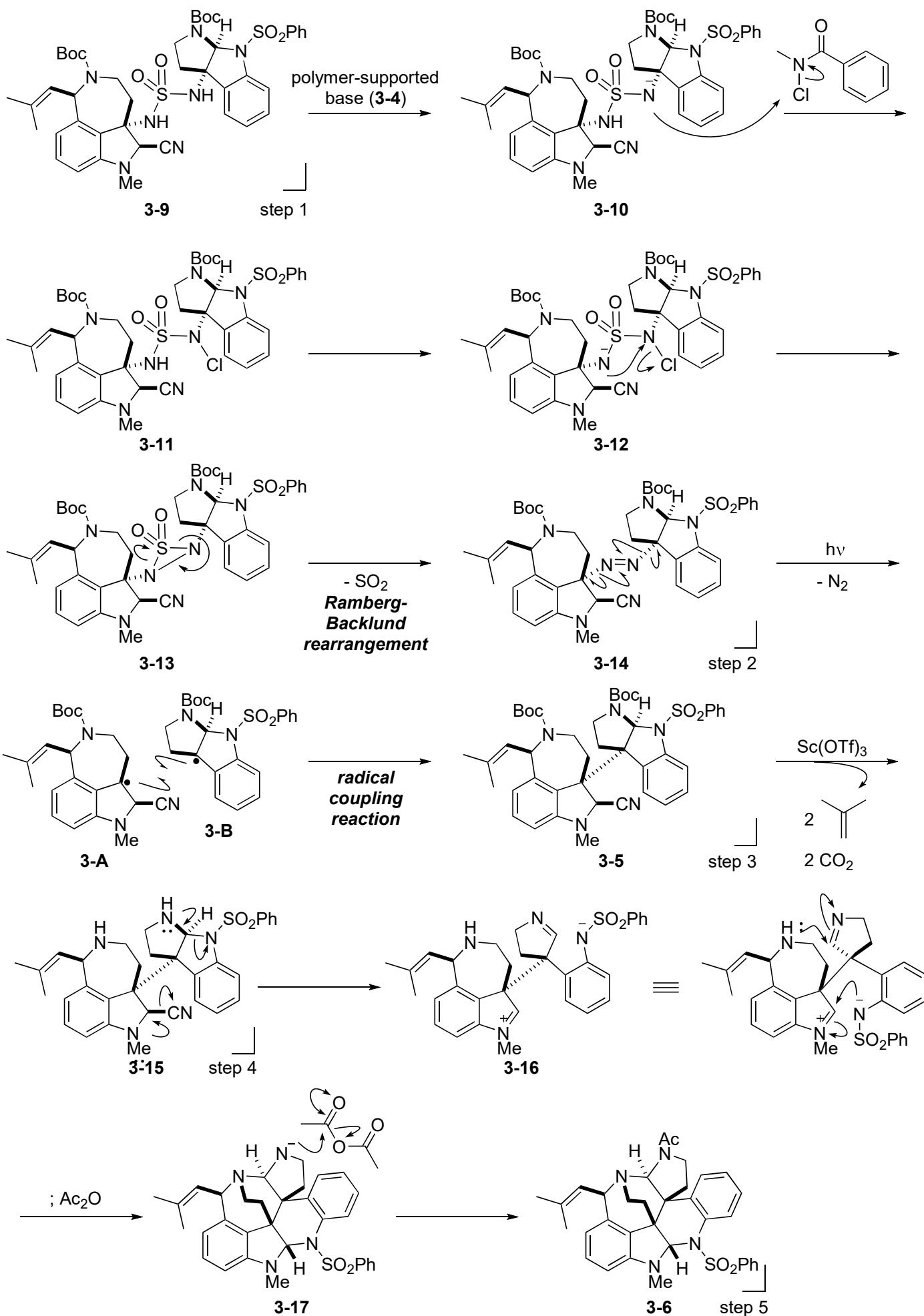
Zuo, Z.; Ma, D. *Angew. Chem., Int. Ed.* **2011**, 50, 12008. (asymmetric)

Han, S.-J.; Vogt, F.; May, J. A.; Krishnan, S.; Gatti, M.; Virgil, S. C.; Stoltz, B. M. *J. Org. Chem.* **2015**, 80, 528. (formal synthesis)



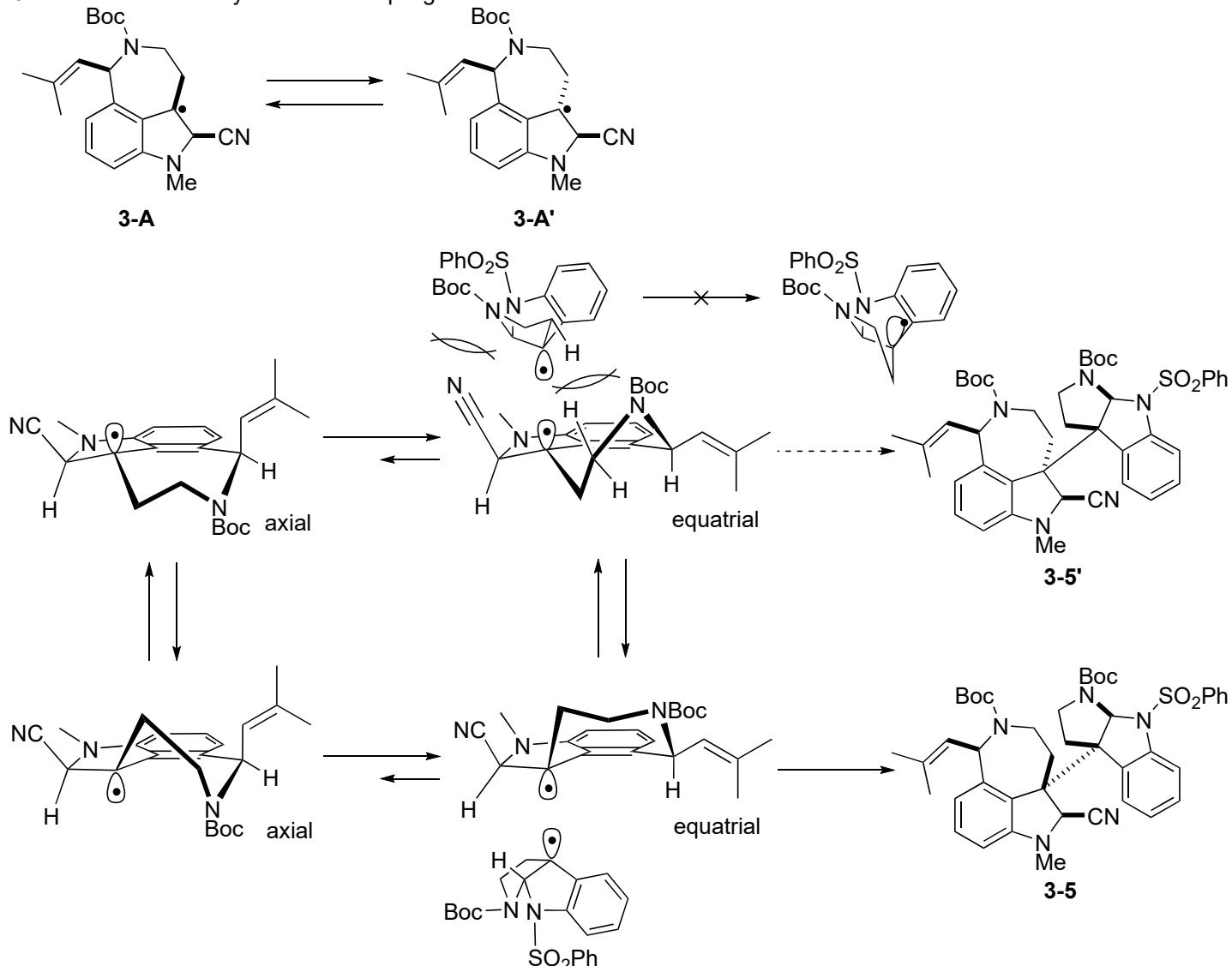
3-1. Answer



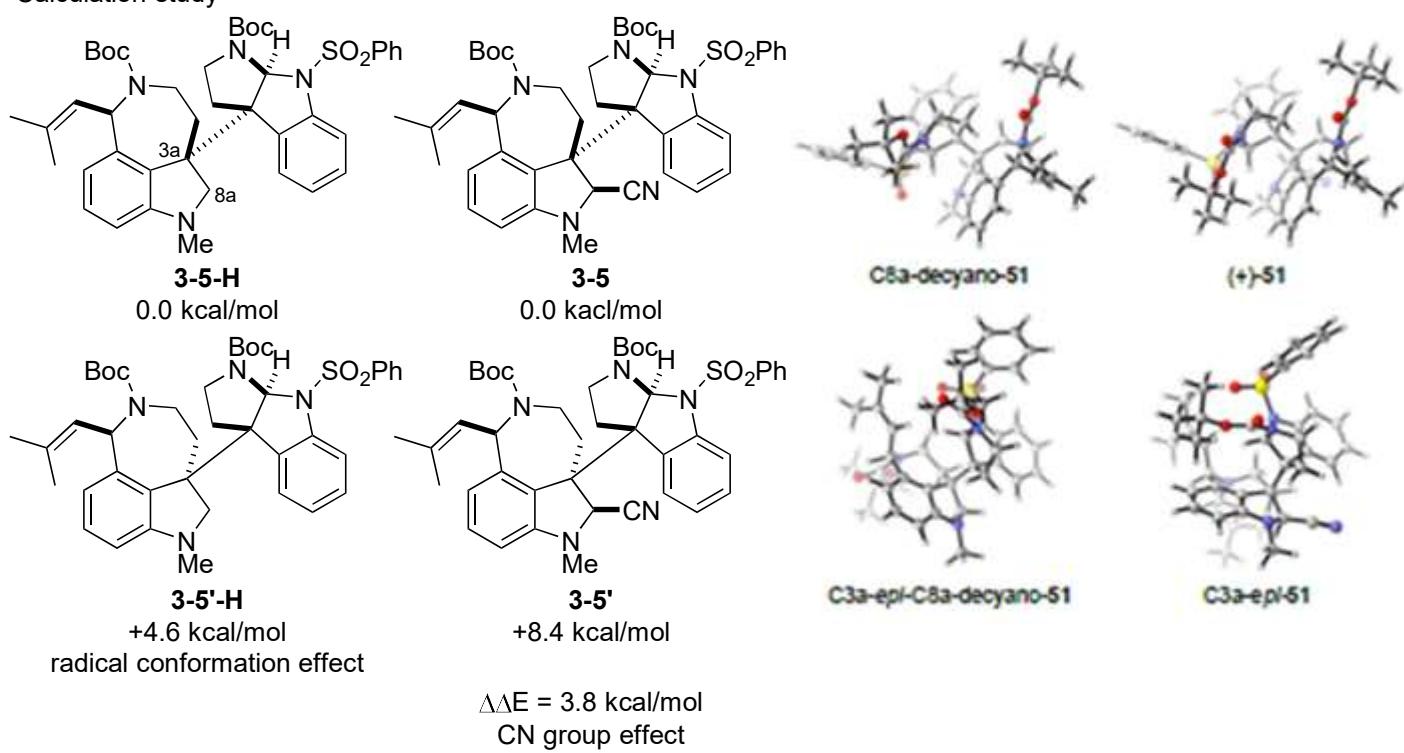


3-2. Discussion

3-2-1: Stereoselectivity at radical coupling reaction



Calculation study



3-3-2. Stereoselectivity at ring reorganization

