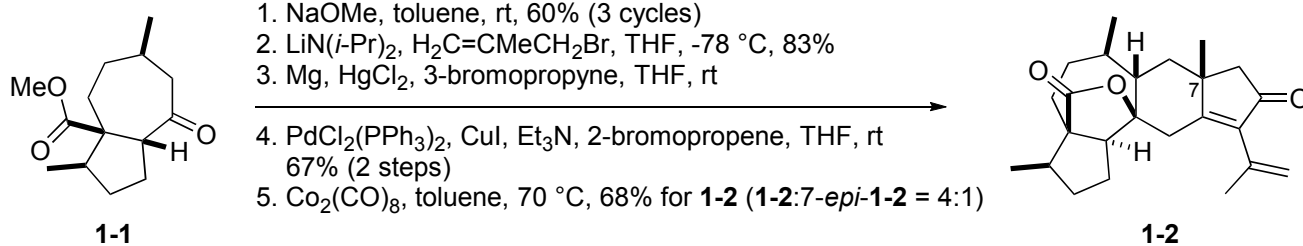


Problem Session (6)

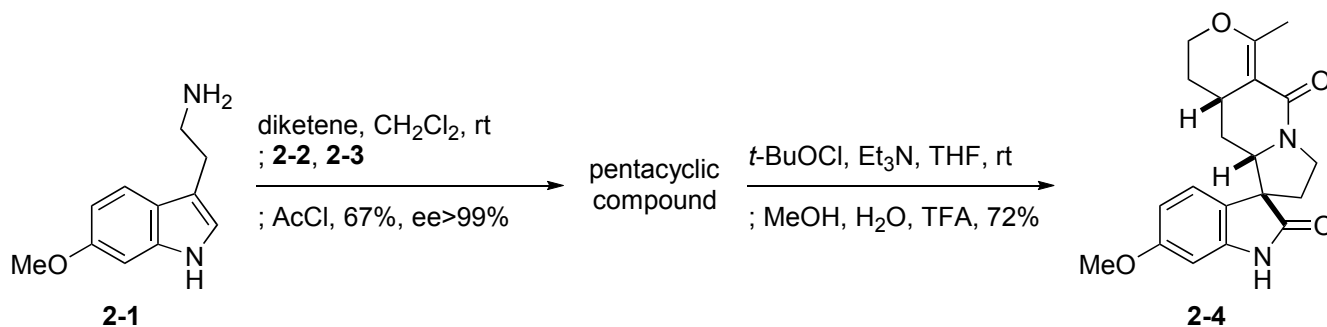
2018.7.28 Hiroyuki Mutoh

Please provide each reaction mechanisms and explain the stereoselectivities.

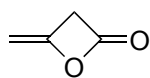
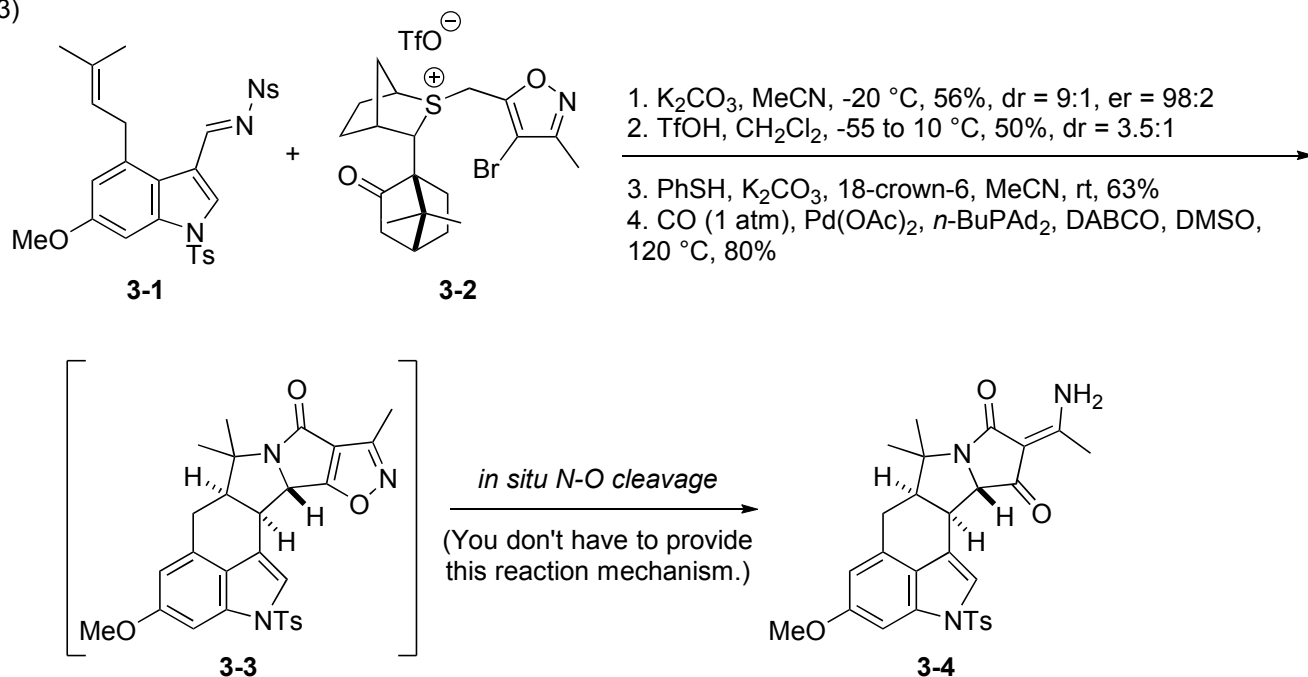
1)



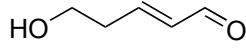
2)



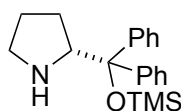
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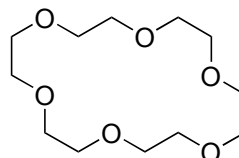
diketene



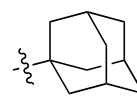
2-2



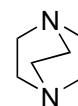
2-3



18-crown-6

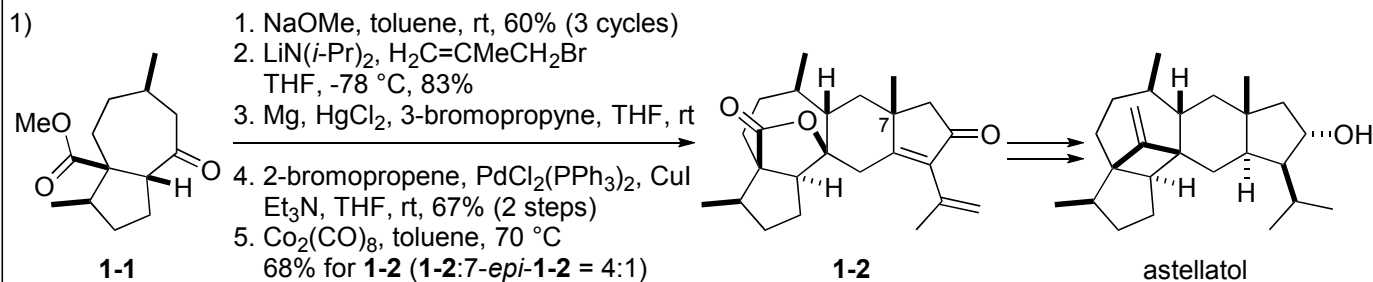


Ad



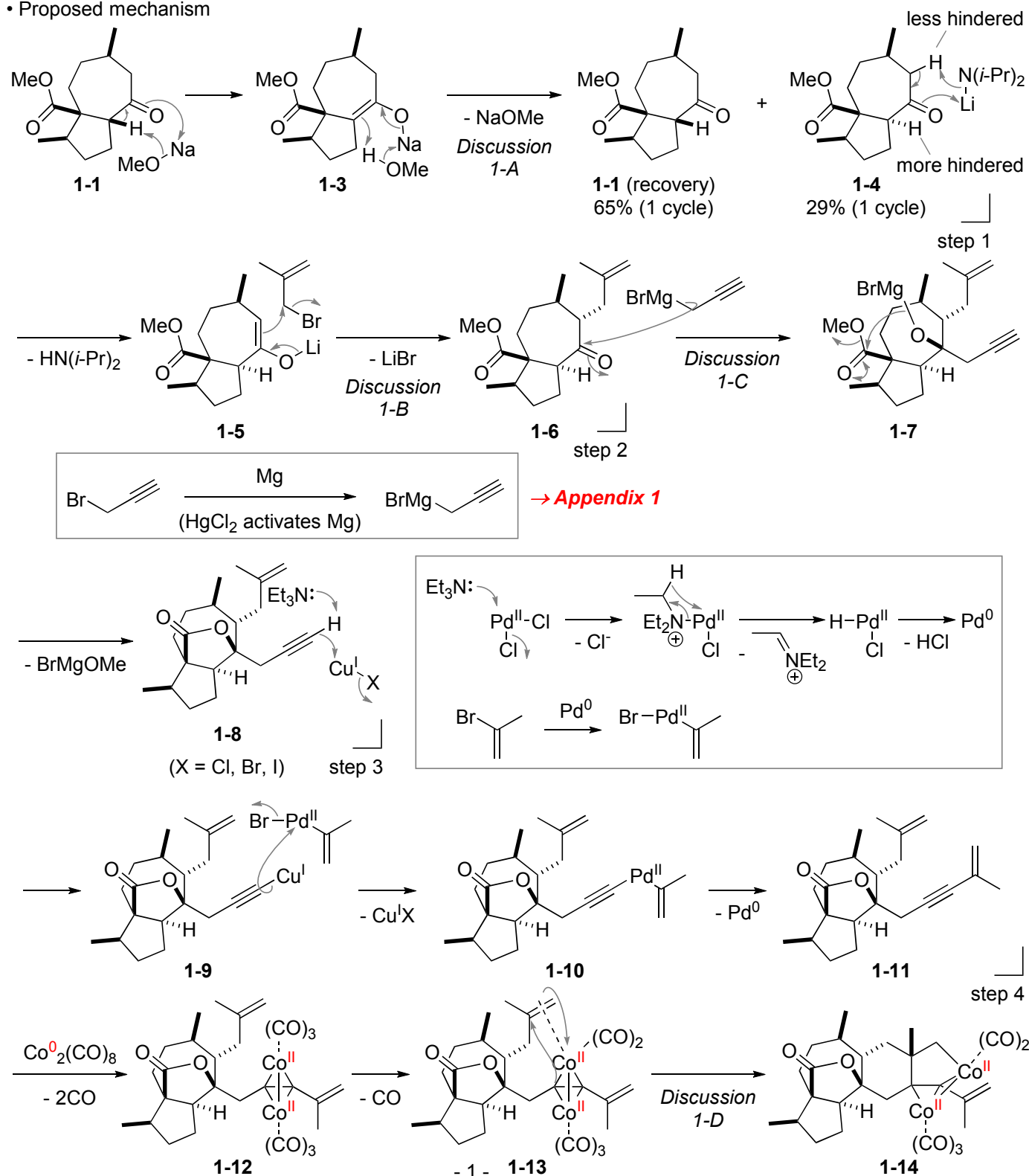
DABCO

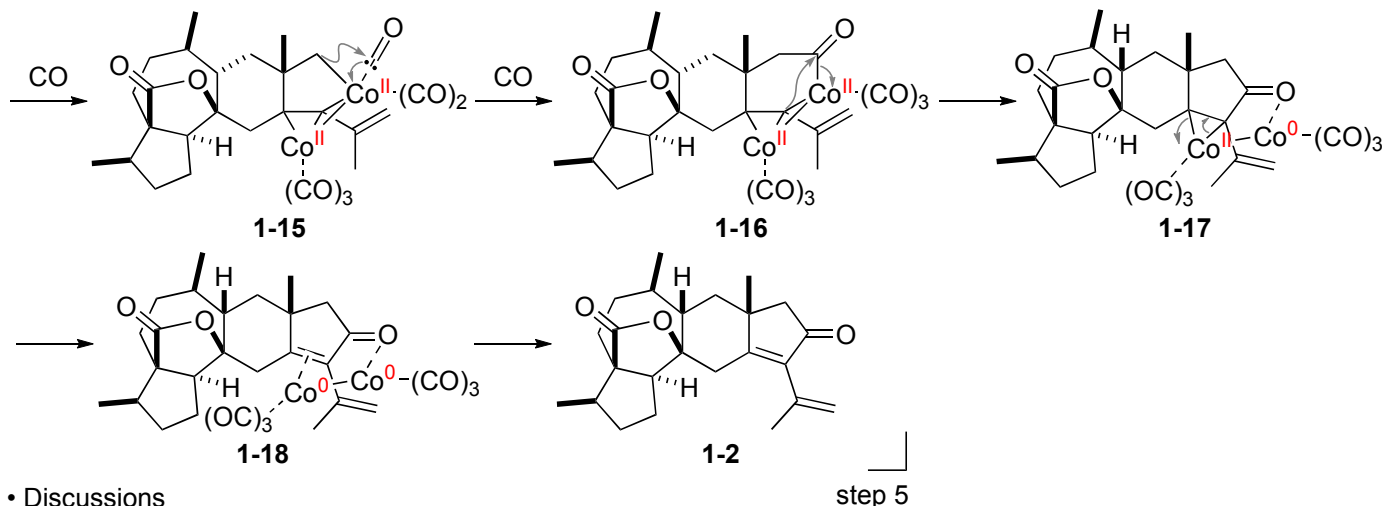
Topic: recent total syntheses



Zhao, N.; Yin, S.; Xie, S.; Yan, H.; Ren, P.; Chen, G.; Chen, F.; Xu, J. *Angew. Chem. Int. Ed.* **2018**, *57*, 3386.

• Proposed mechanism

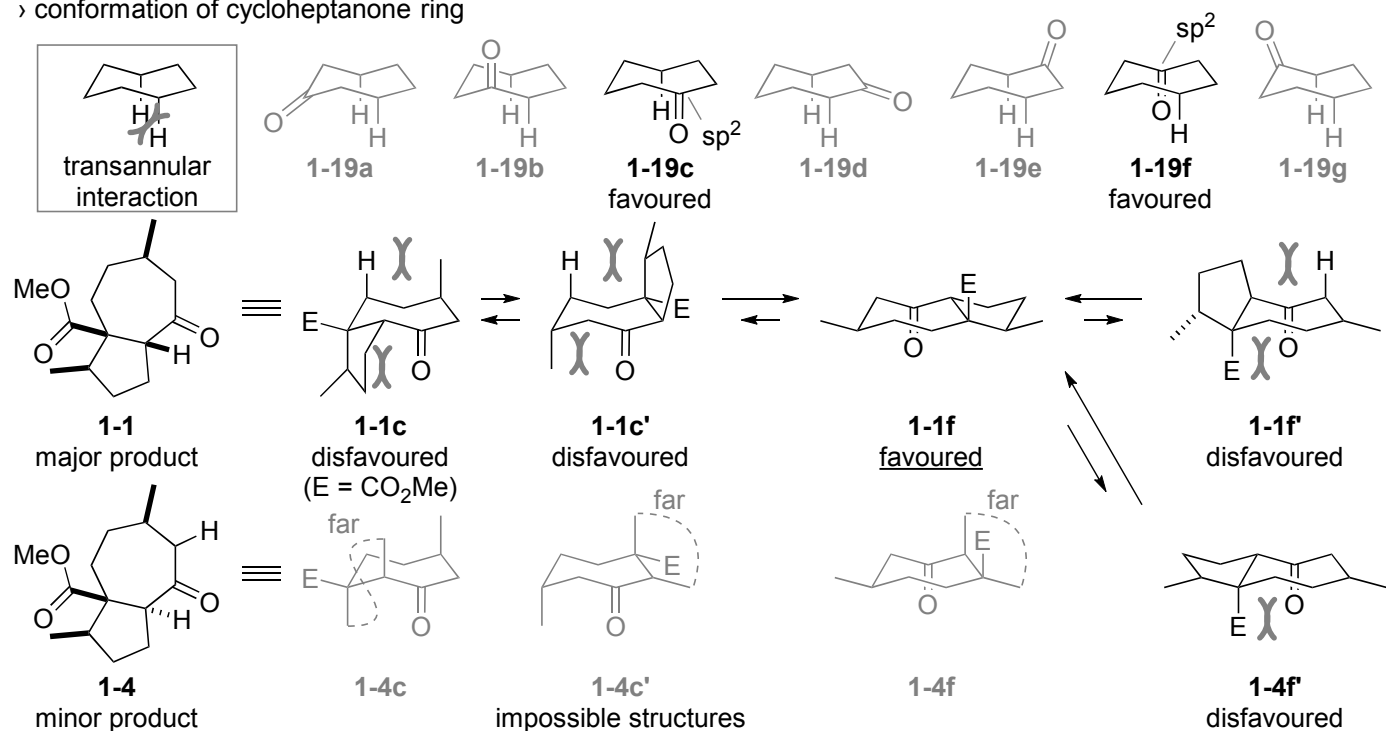




• Discussions

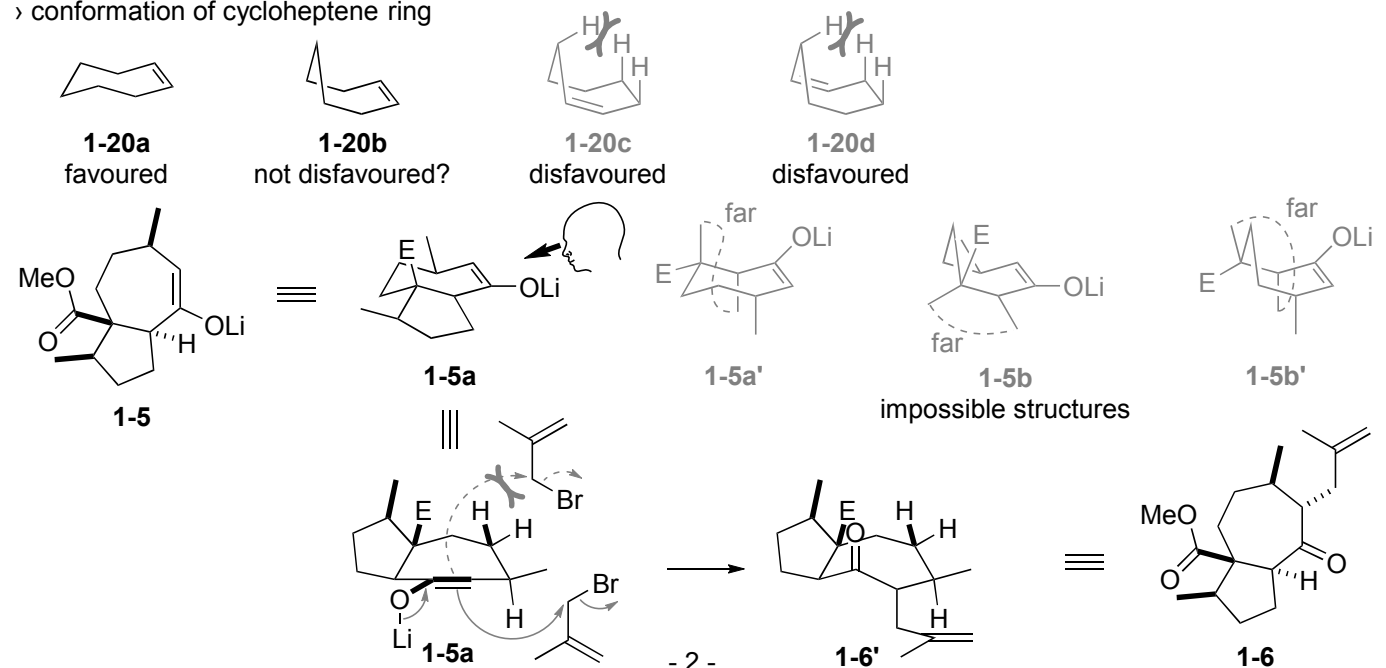
Discussion 1-A: stereoselectivity of thermodynamic epimerization → consider the product stability.

› conformation of cycloheptanone ring



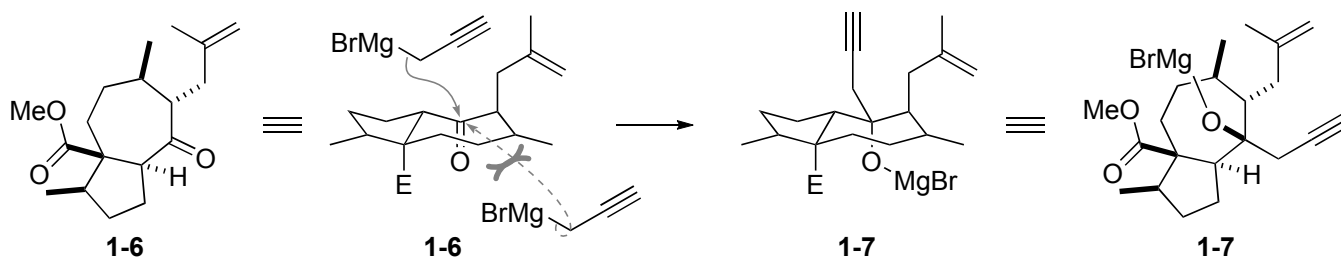
Discussion 1-B: stereoselectivity of alkylation of enolate

› conformation of cycloheptene ring



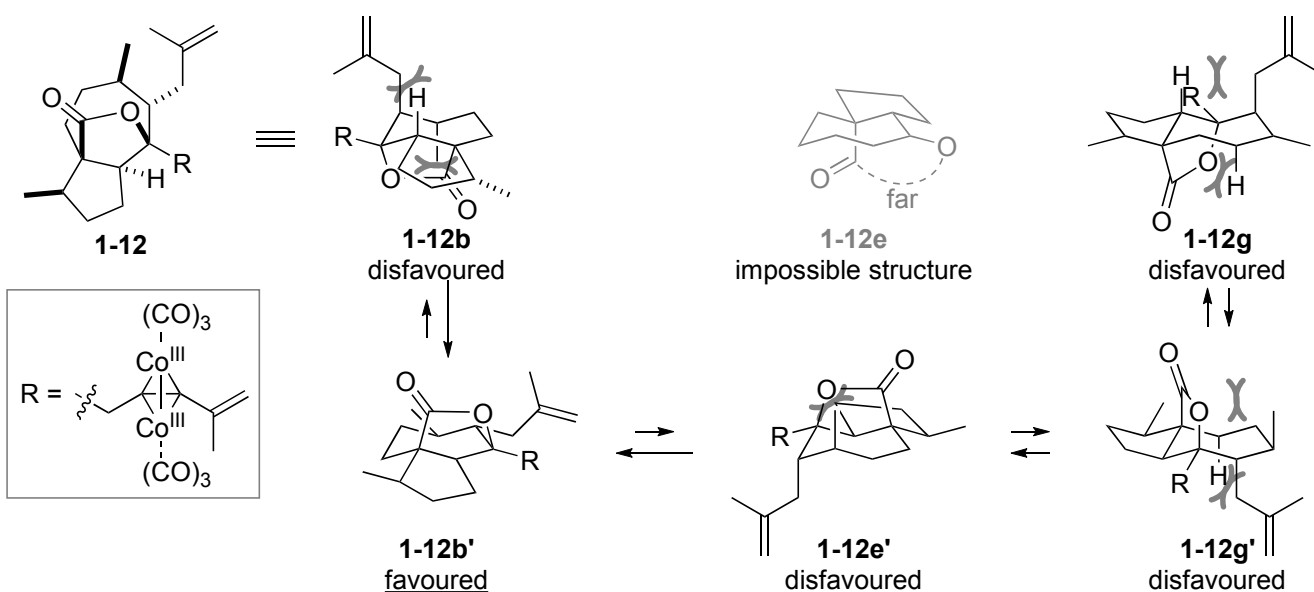
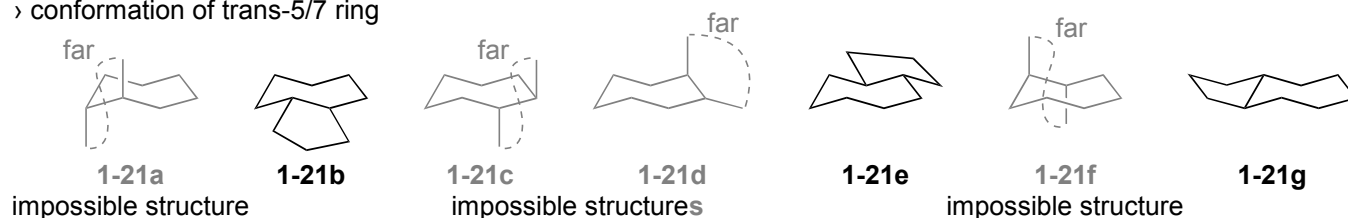
Discussion 1-C: stereoselectivity of 1,2-addition

The favoured conformation of **1-6** can be predicted based on *Discussion 1-A*.

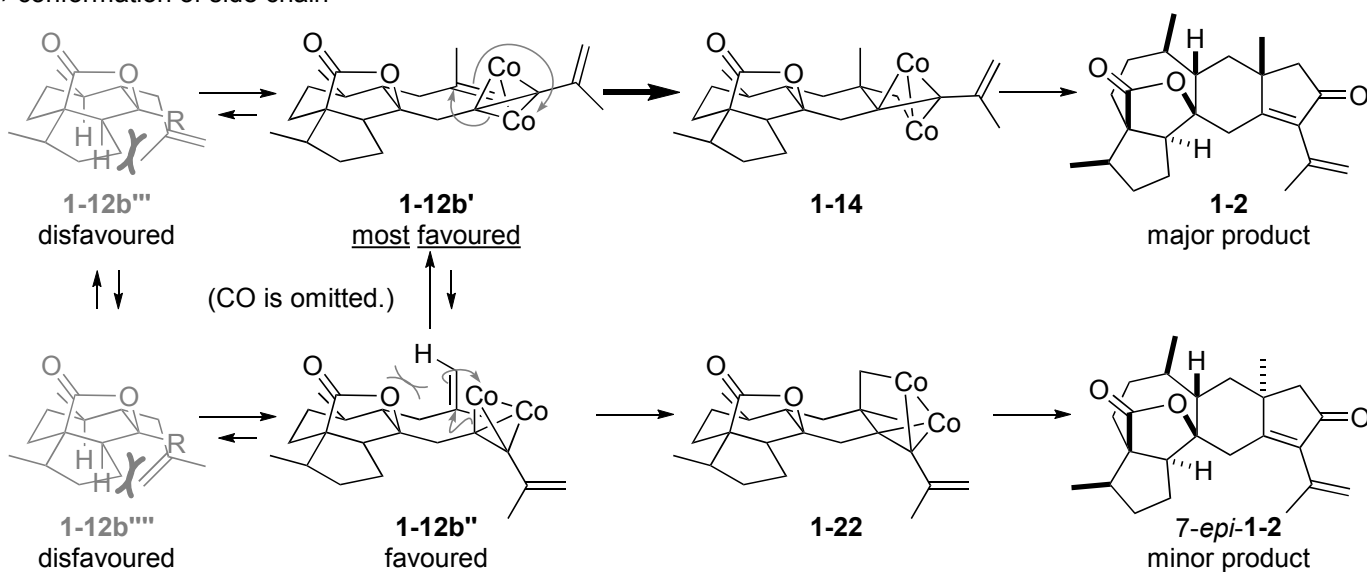


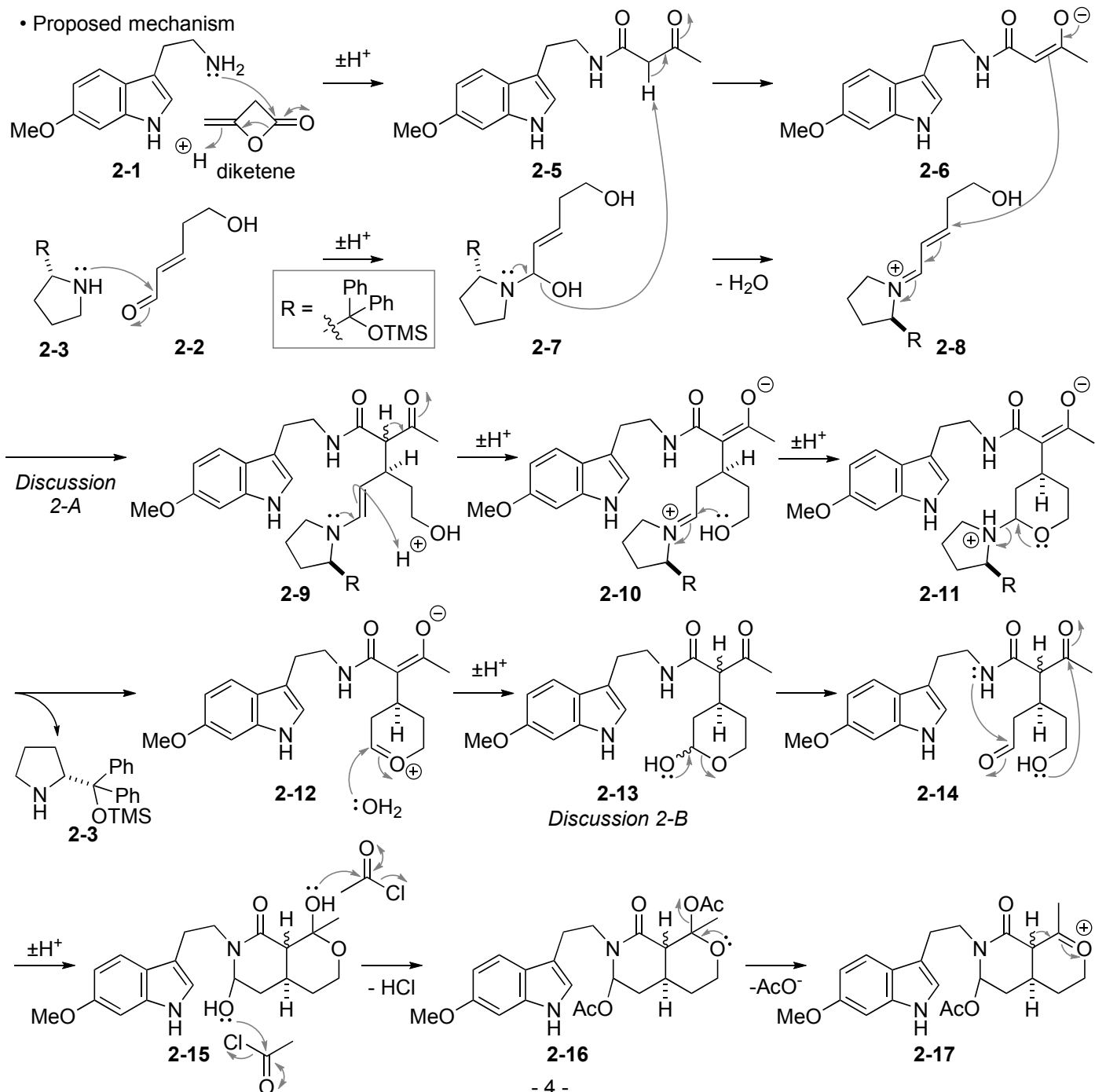
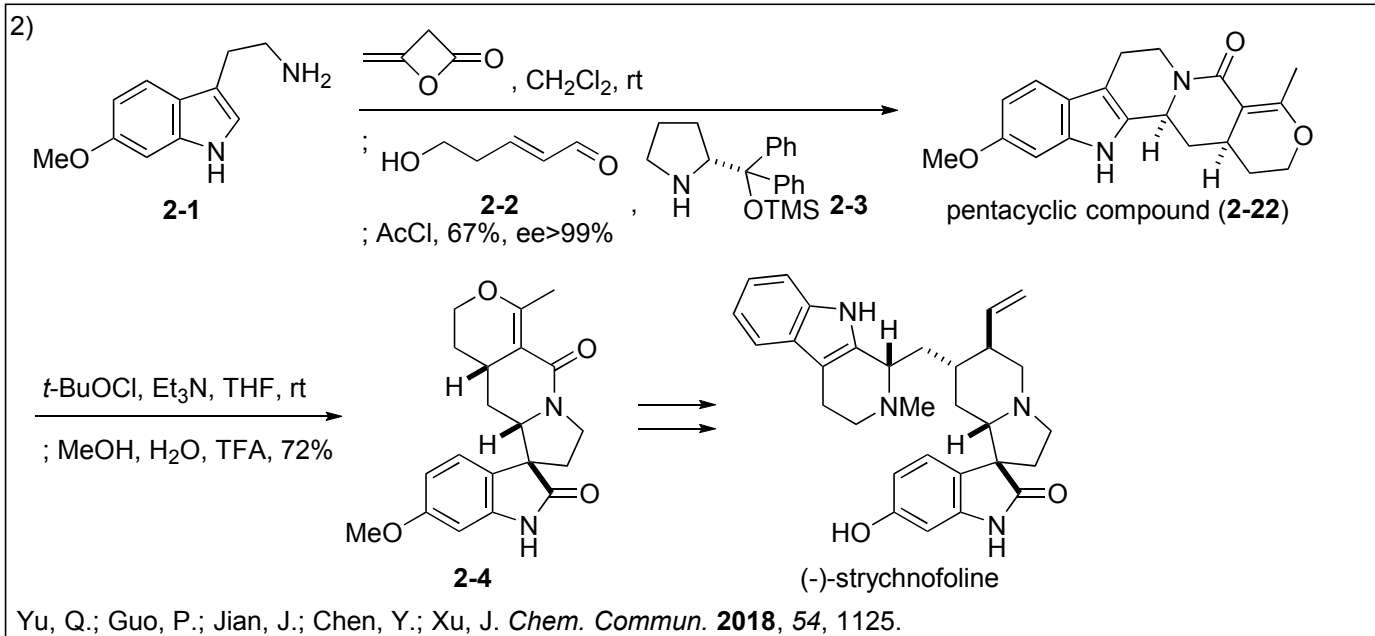
Discussion 1-D: stereoselectivity of Pauson-Khand reaction \rightarrow **Appendix 2**

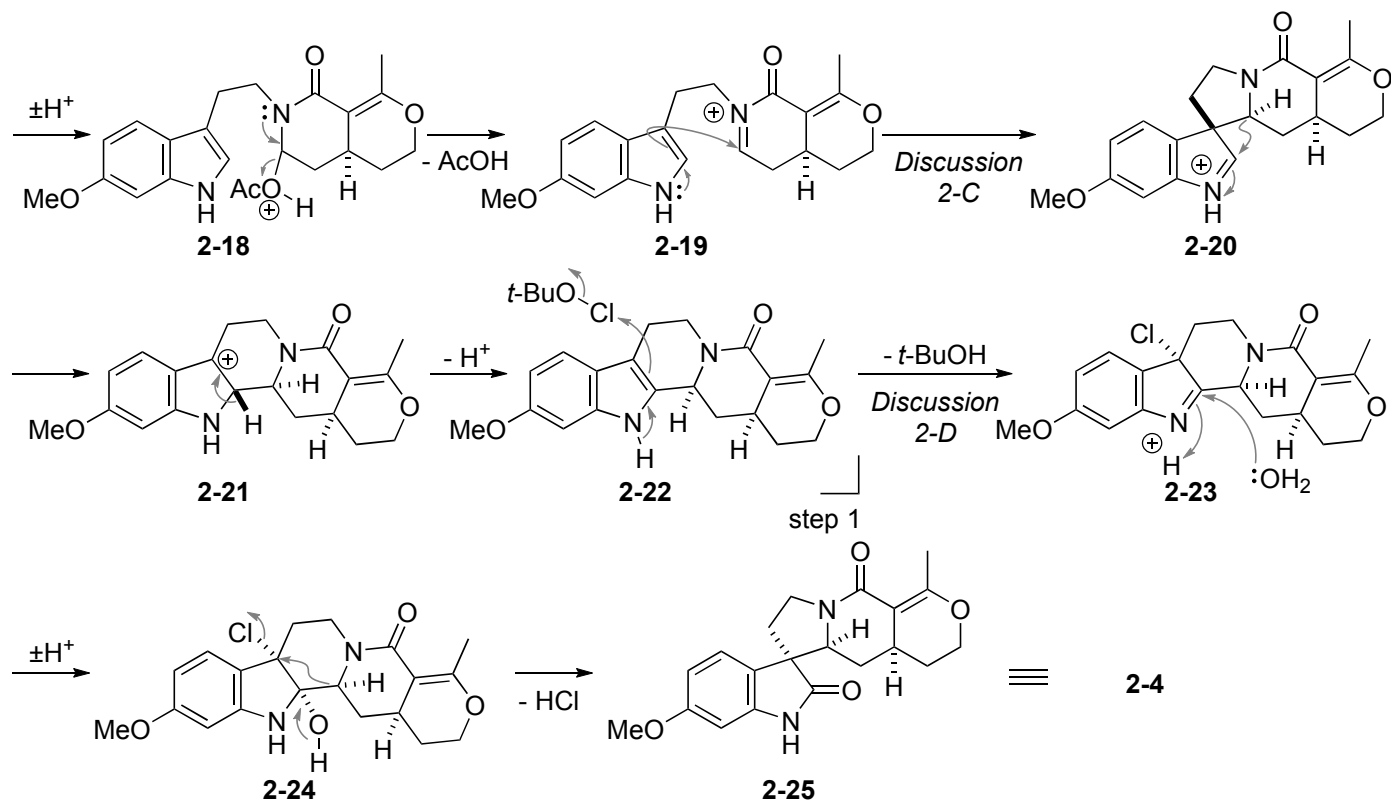
\triangleright conformation of trans-5/7 ring



\triangleright conformation of side chain

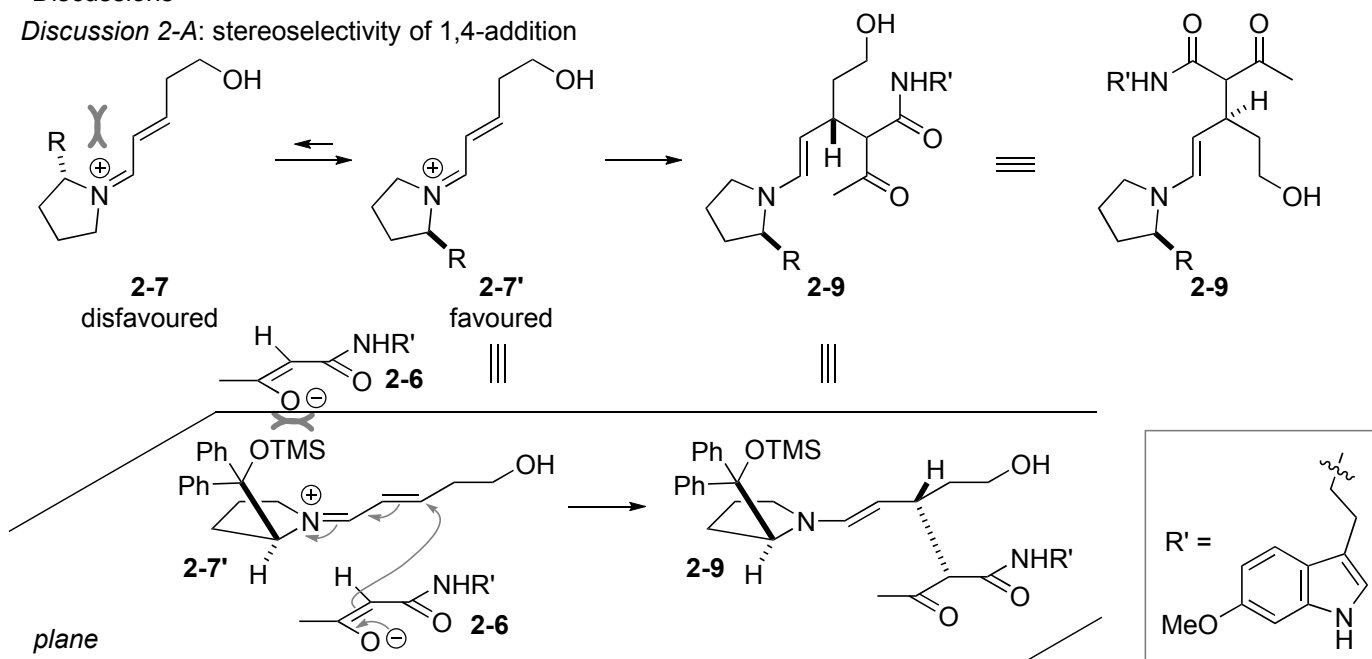




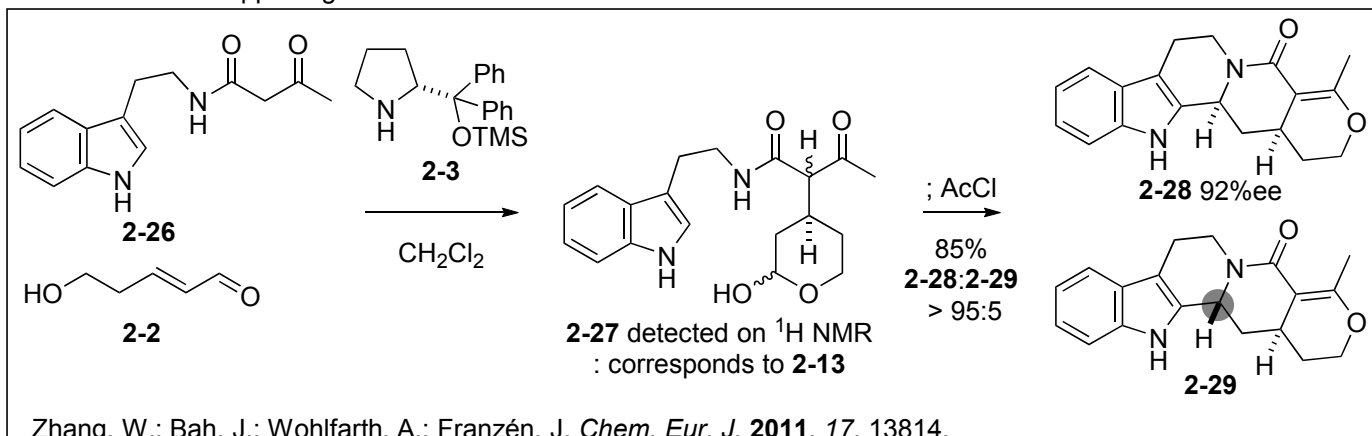


• Discussions

Discussion 2-A: stereoselectivity of 1,4-addition

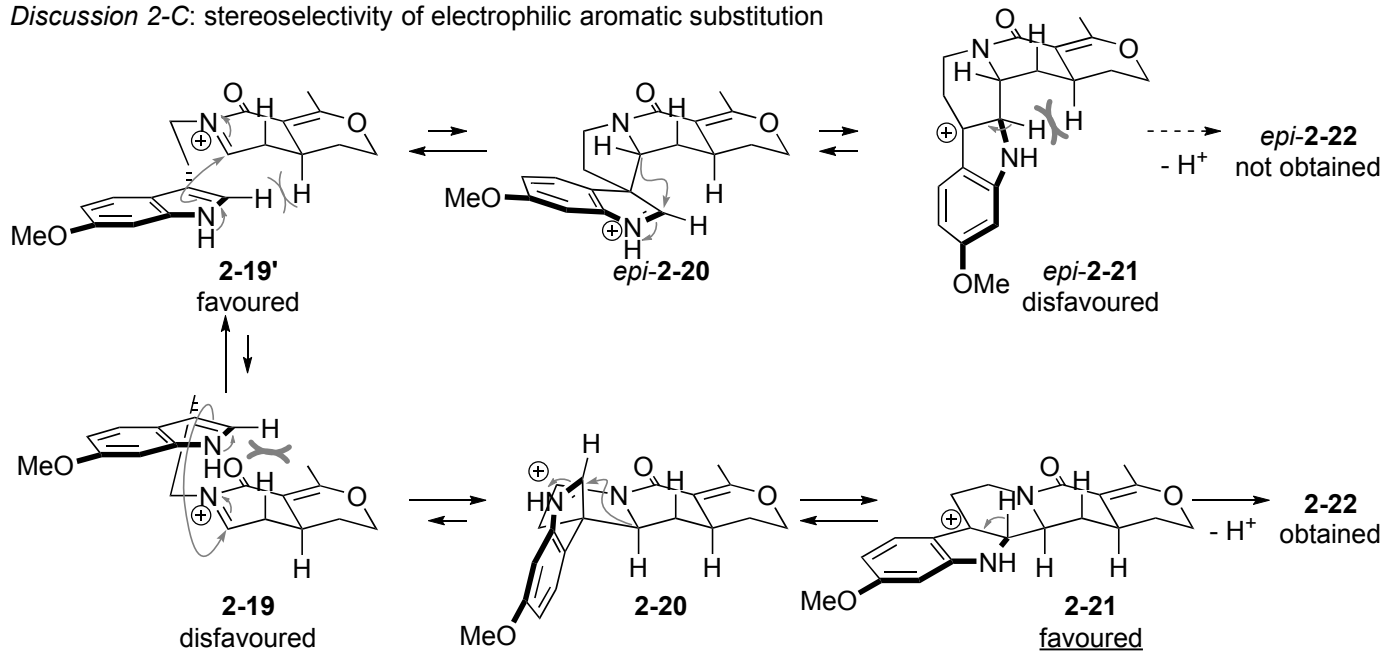


Discussion 2-B: supporting information of reaction intermediate

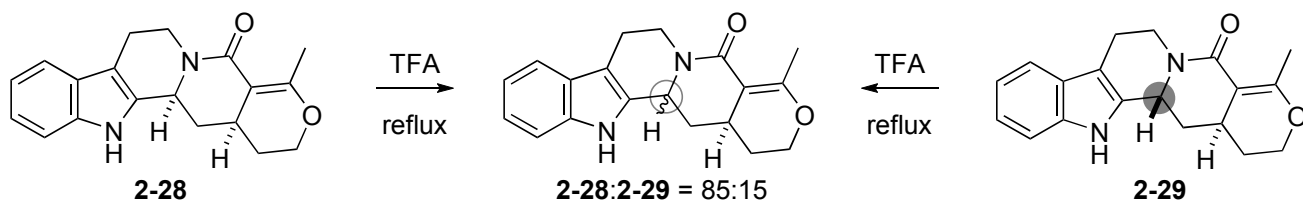


Zhang, W.; Bah, J.; Wohlfarth, A.; Franzén, J. *Chem. Eur. J.* **2011**, *17*, 13814.

Discussion 2-C: stereoselectivity of electrophilic aromatic substitution

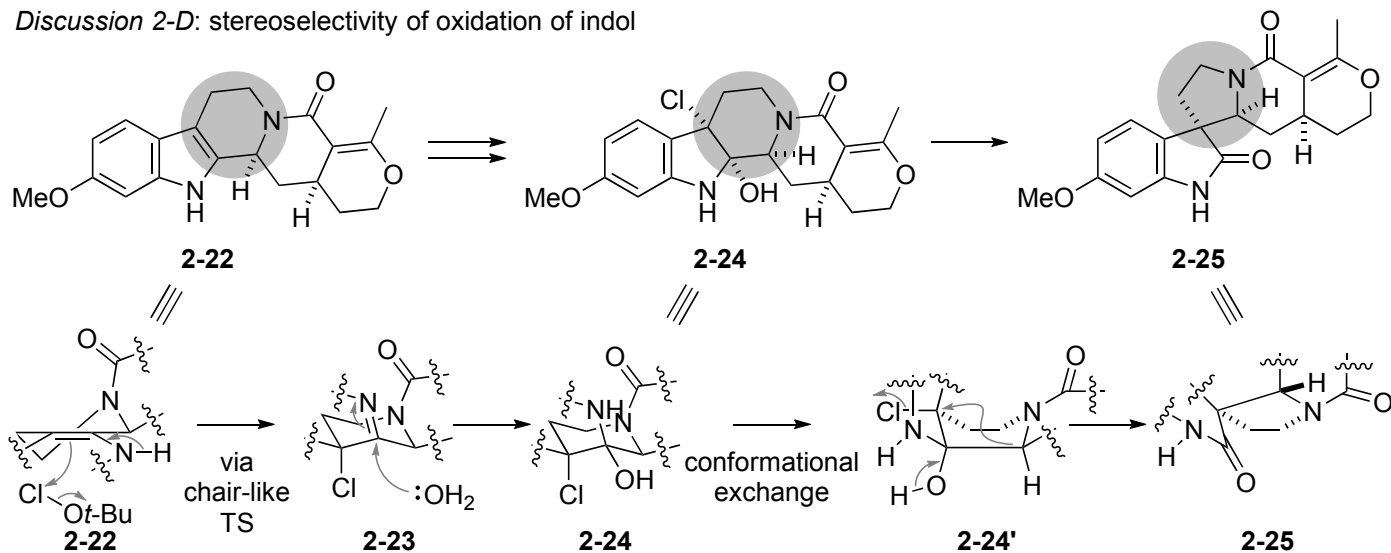


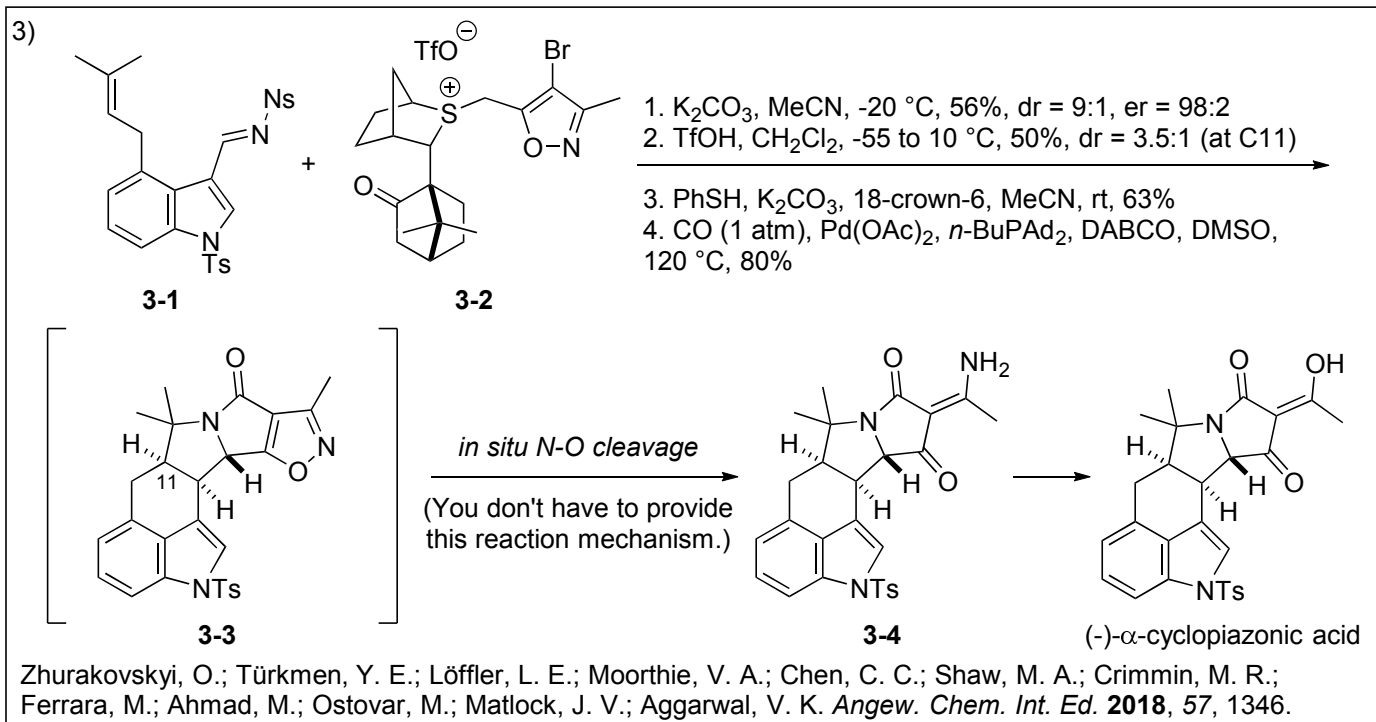
> relative stability of the products



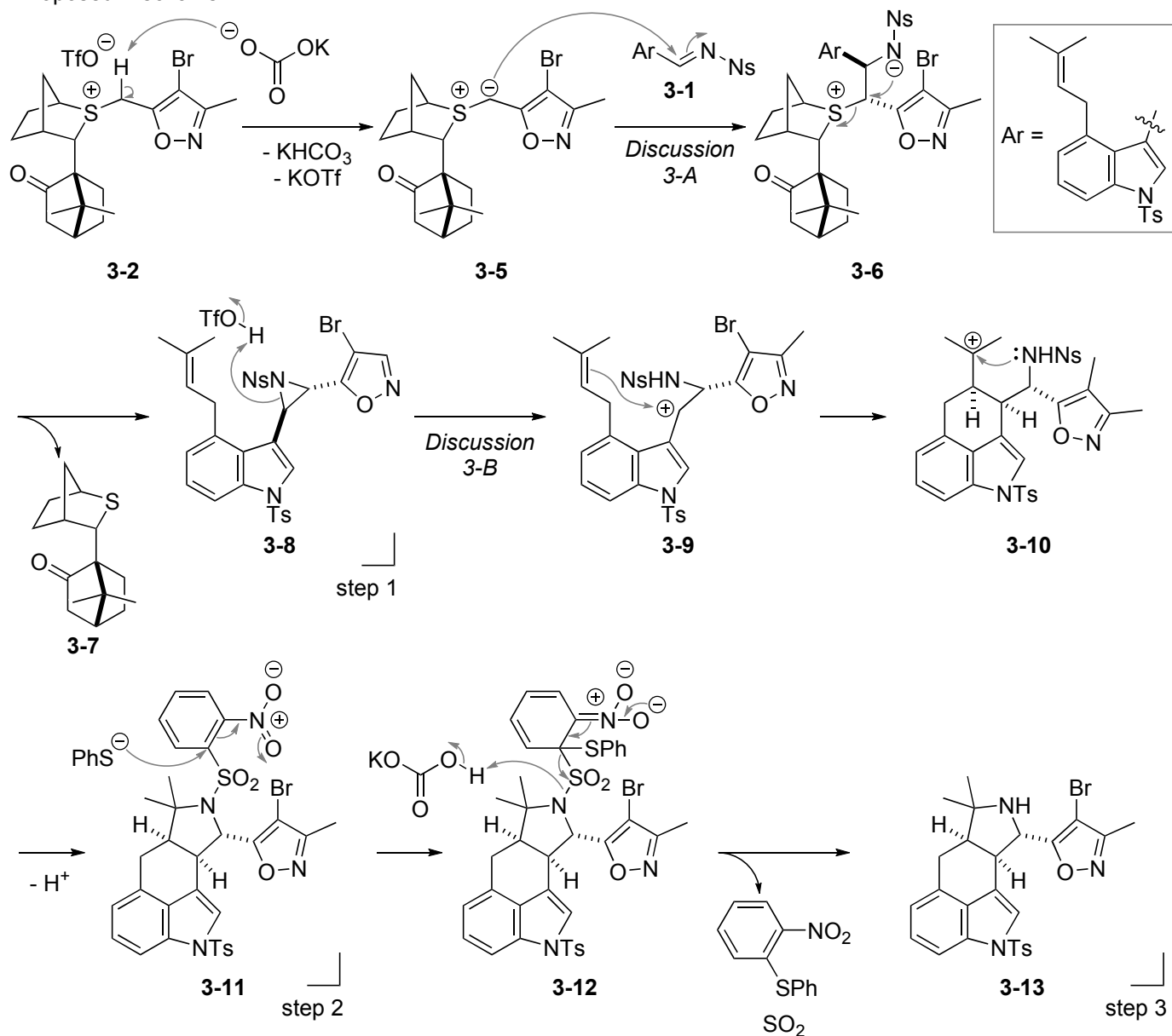
Zhang, W.; Bah, J.; Wohlfarth, A.; Franzén, J. *Chem. Eur. J.* **2011**, *17*, 13814.

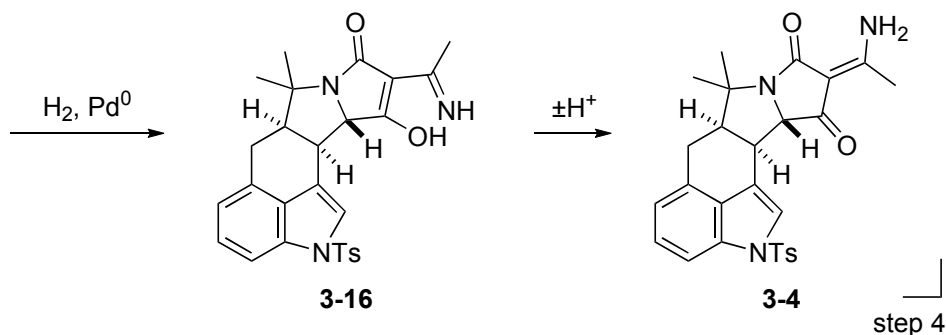
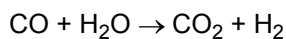
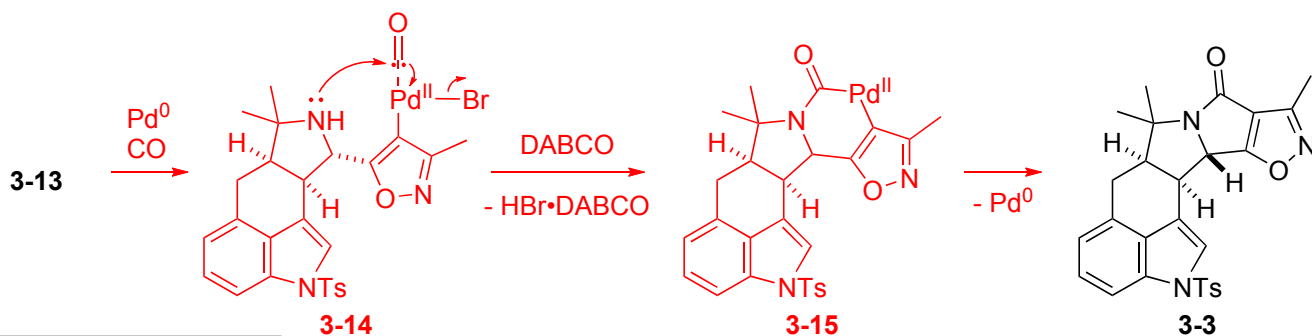
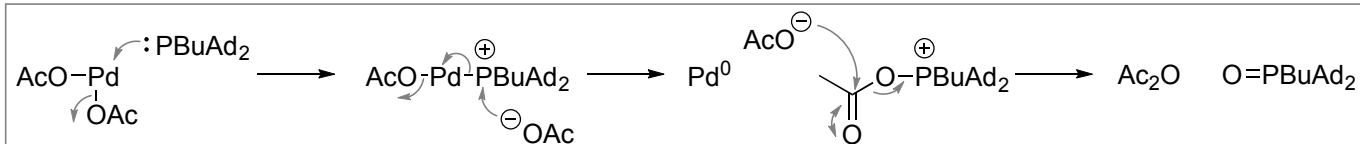
Discussion 2-D: stereoselectivity of oxidation of indol





• Proposed mechanism



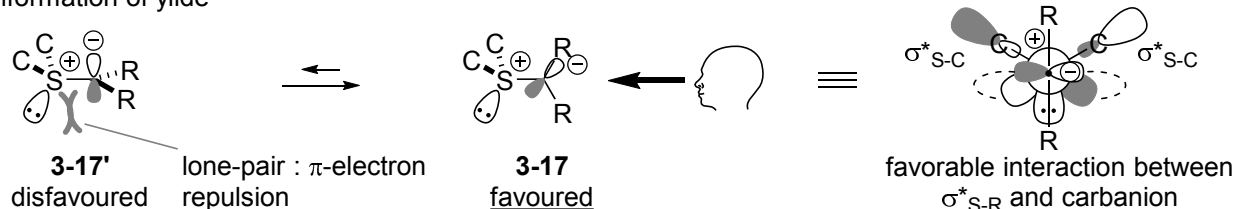


• Discussions

Discussion 3-A: stereoselectivity of aziridine formation

› facial selectivity of sulfonium ylide (enantioselectivity)

• conformation of ylide

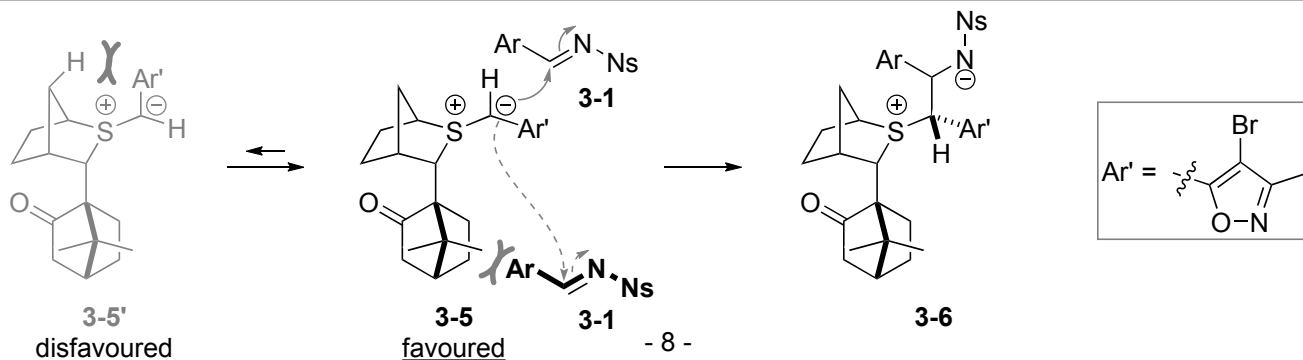


Galloy, J.; Watson, W. H.; Craig, D.; Guidry, C.; Morgan, M.; McKellar, R.; Ternay Jr. A. L.; Martin, G. J. *Heterocyclic Chem.* **1983**, *20*, 399.

• computational study

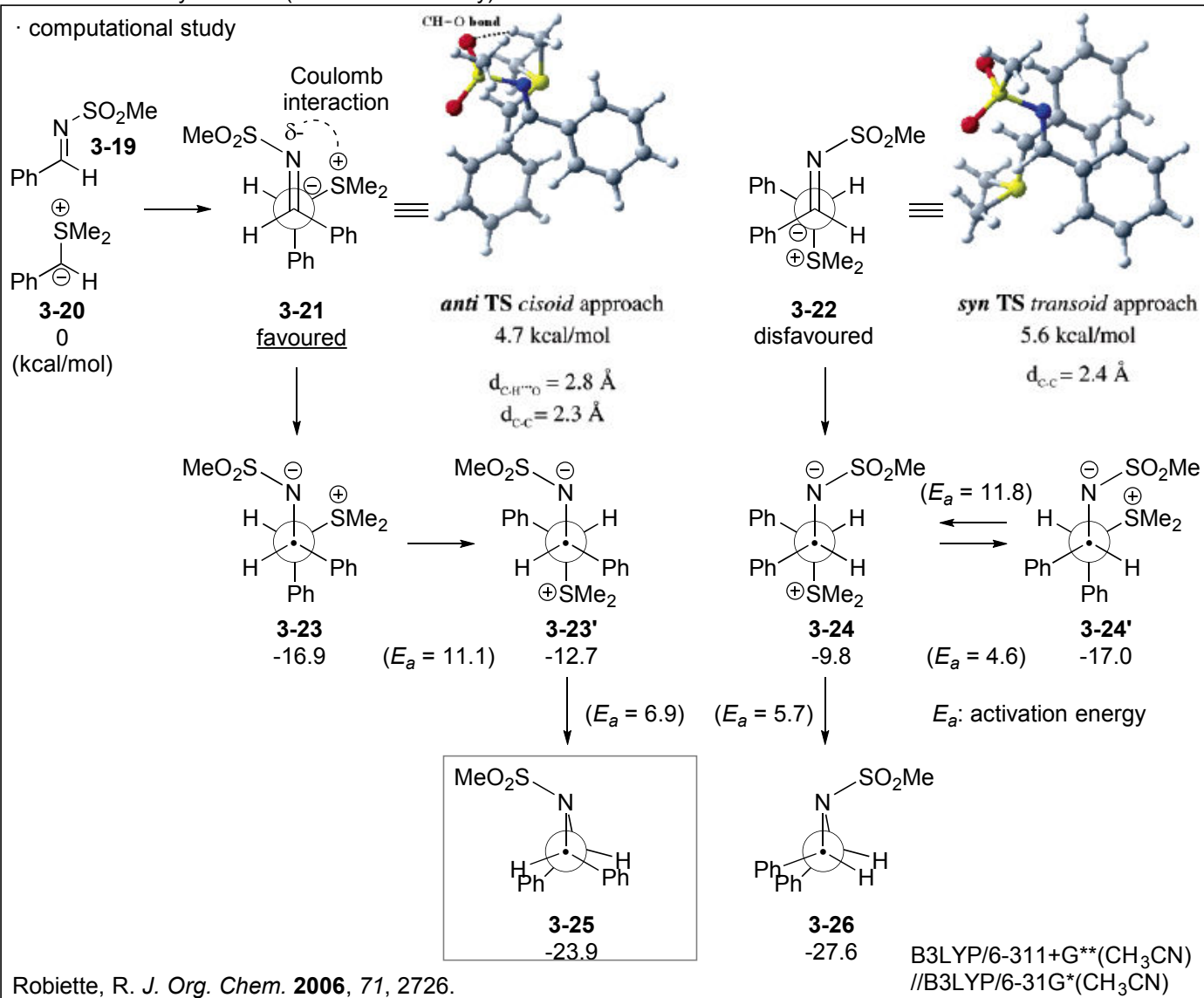


Aggarwal, V. K.; Charmant, J.; Dudin, L.; Porcelloni, M.; Richardson, J. *Proc. Natl. Acad. Sci. USA*, **2004**, *101*, 5467.

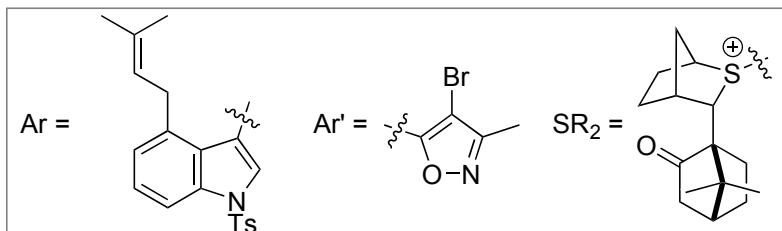
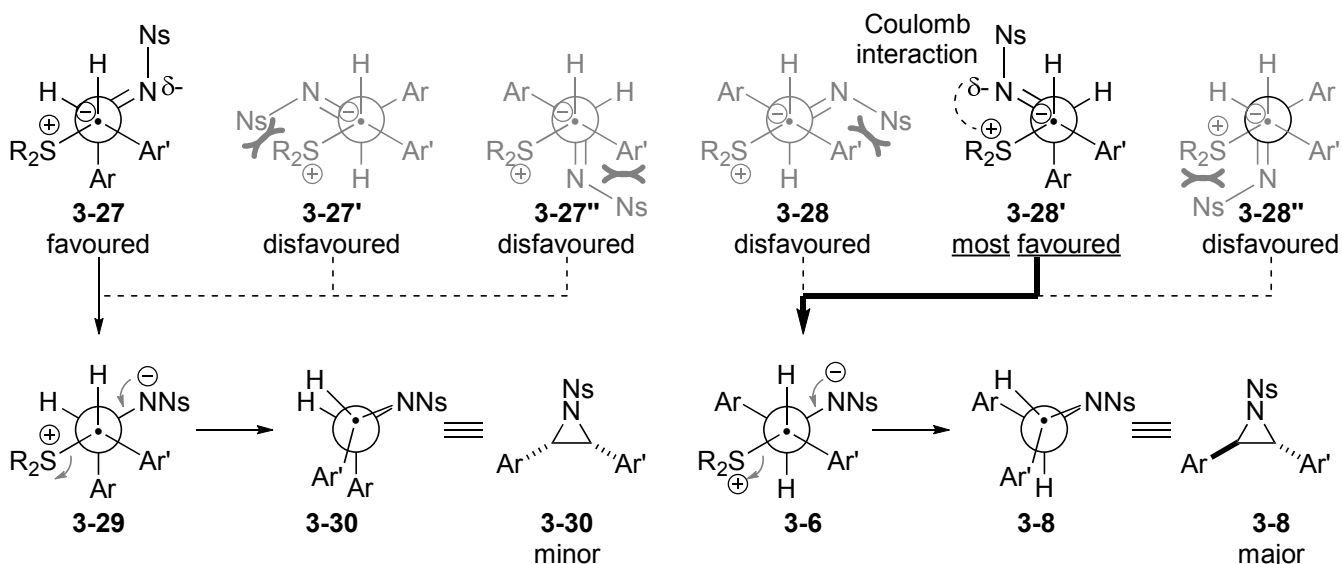


> facial selectivity of imine (diastereoselectivity)

· computational study

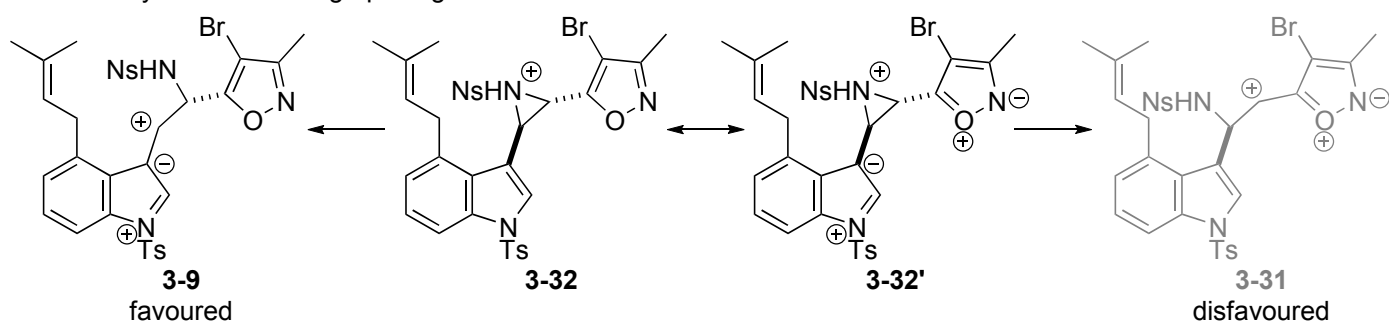


Robiette, R. *J. Org. Chem.* **2006**, *71*, 2726.

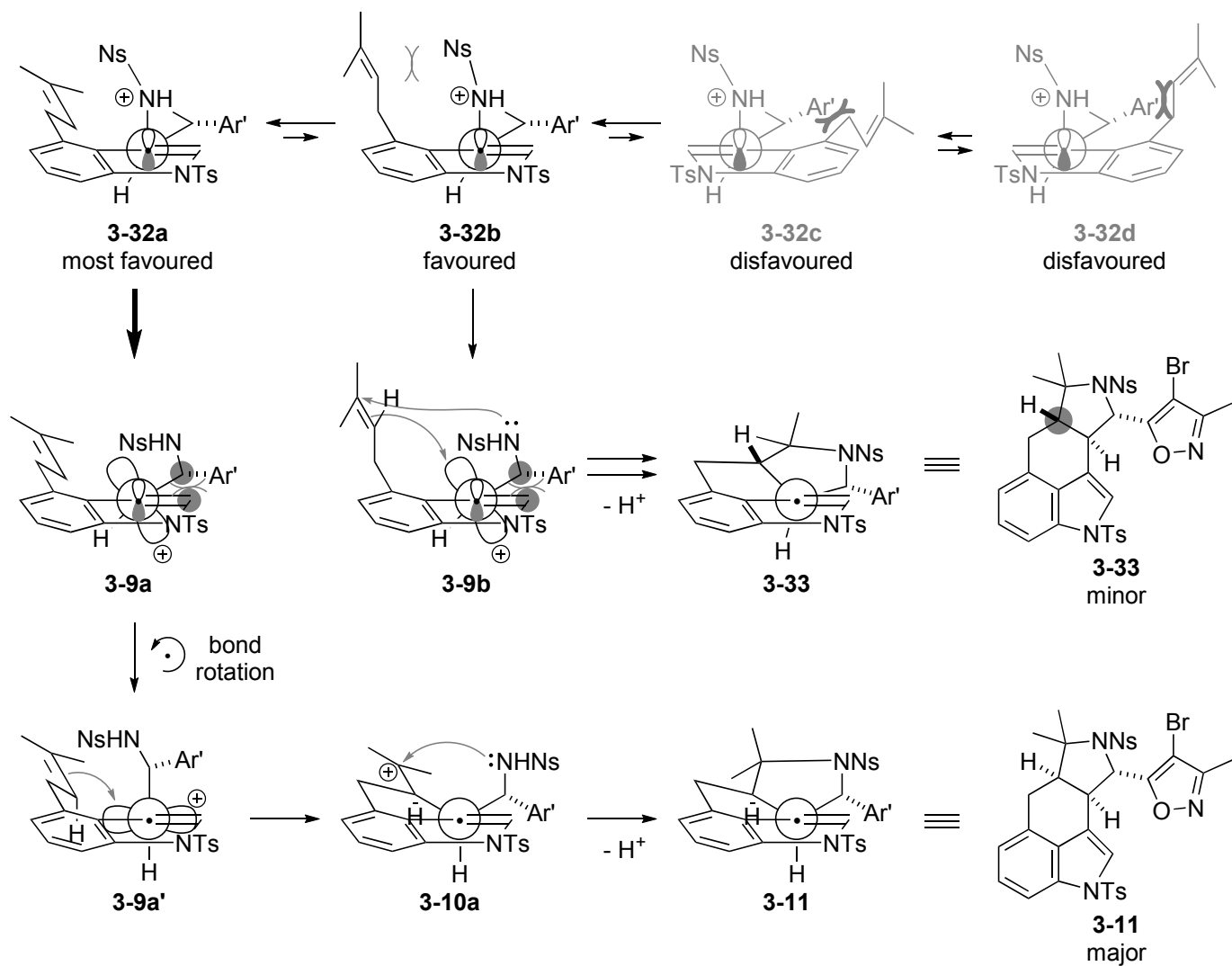


Discussion 3-B: selectivity of pyrrolidine formation

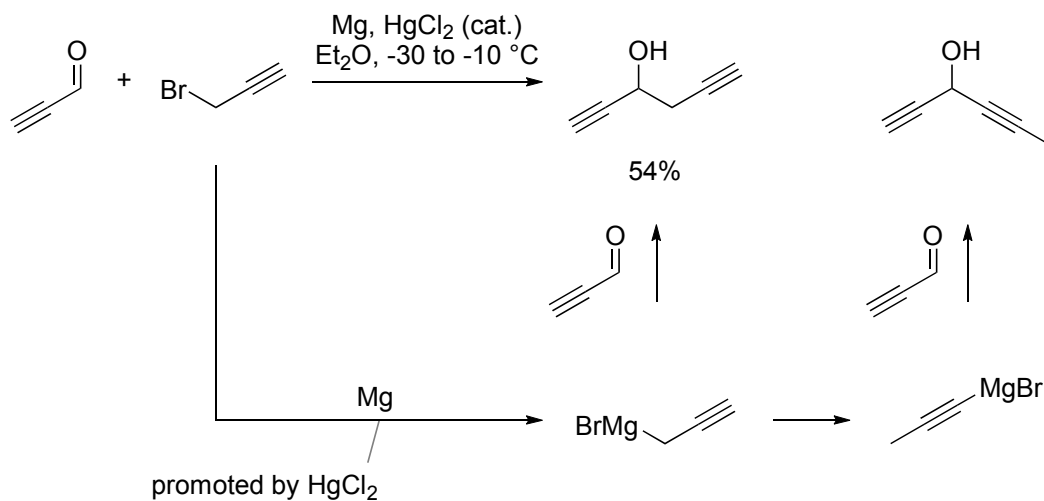
› selectivity of aziridine ring opening



› stereoselectivity of pyrrolidine ring formation



Appendix 1



Yanagisawa, A. *Sci. Synth.* **2004**, 7, 541-547.

Appendix 2

- another possible path

