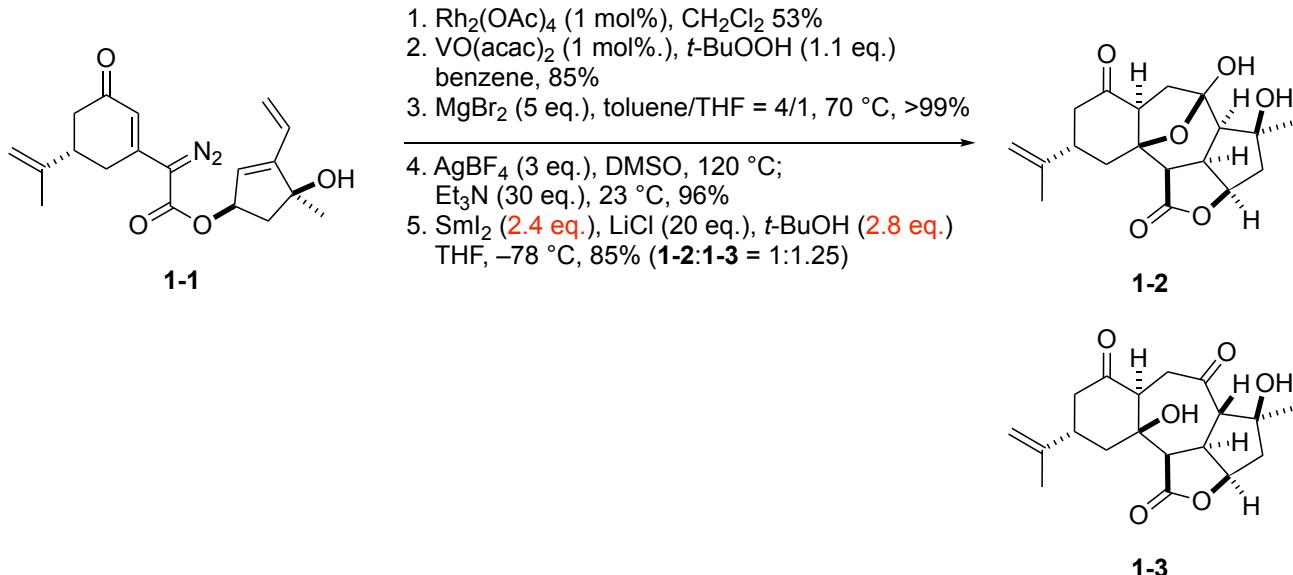


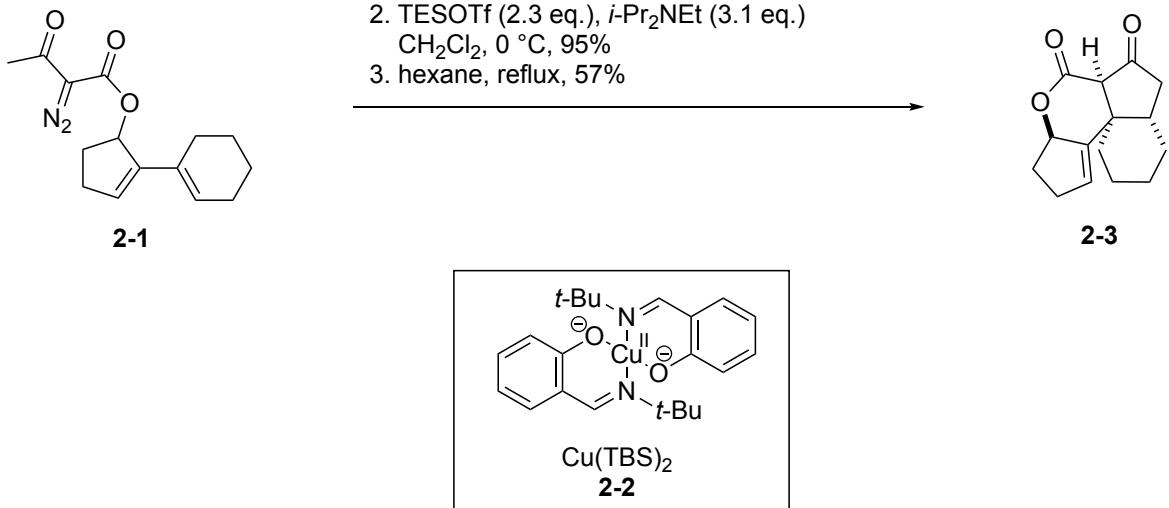
Problem Session (2) -Answer-

2019.05.11 Toshiya Nagai

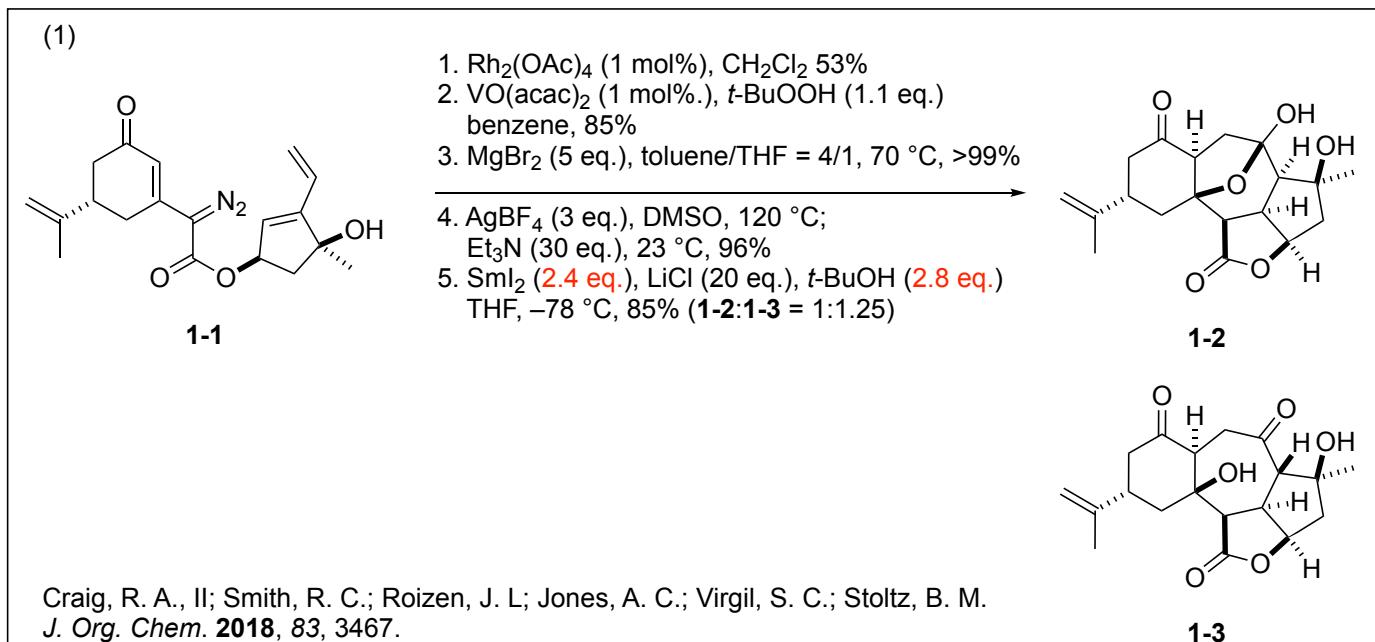
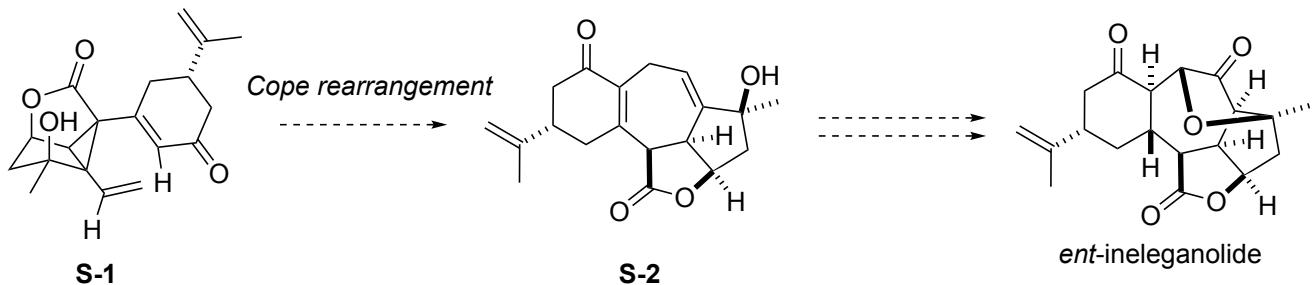
(1)



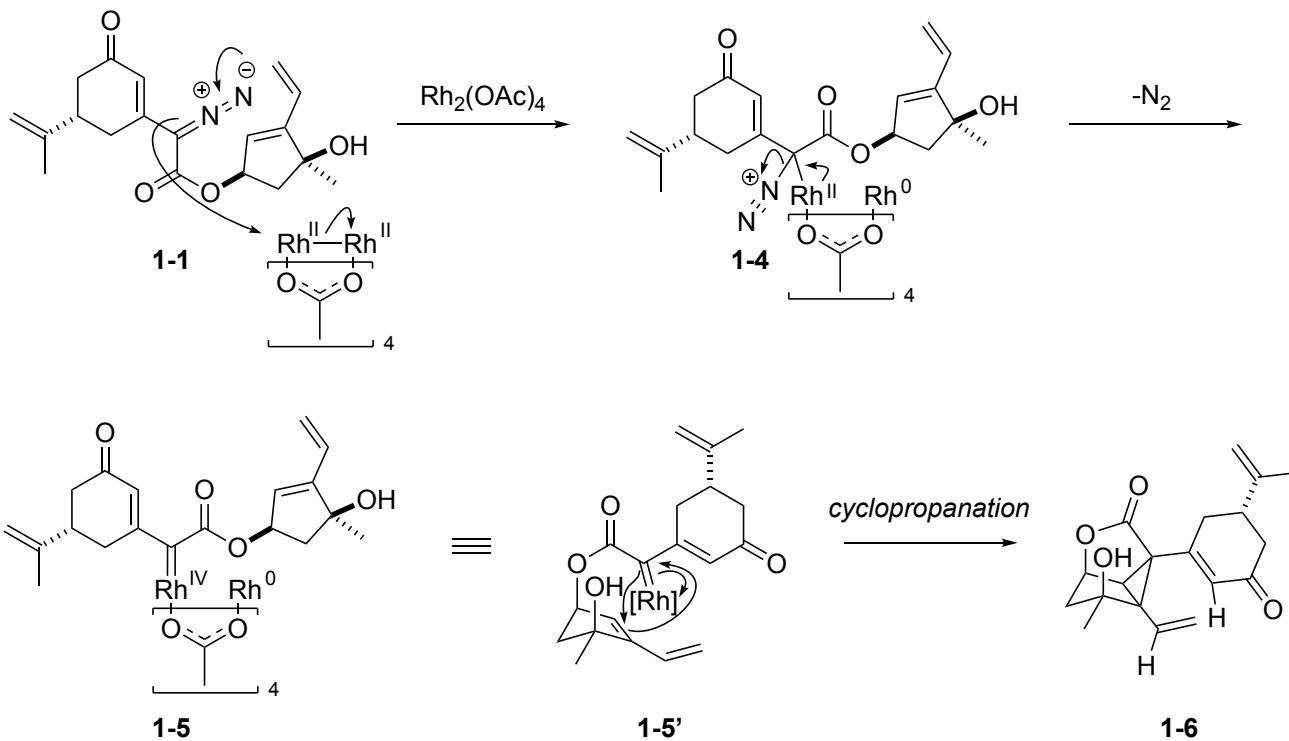
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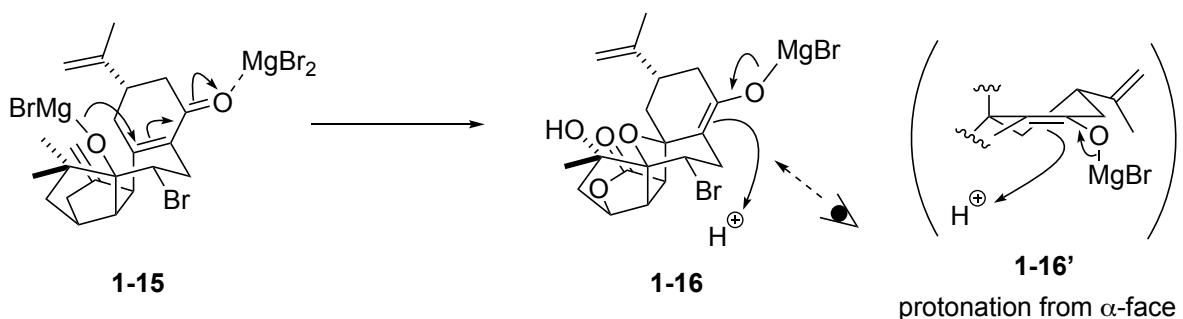
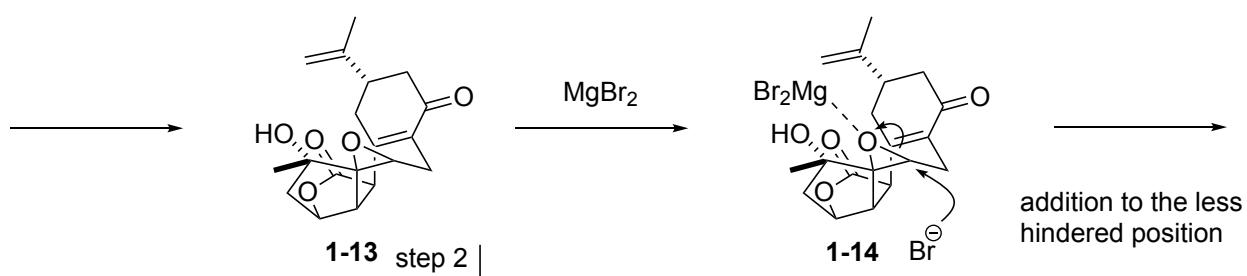
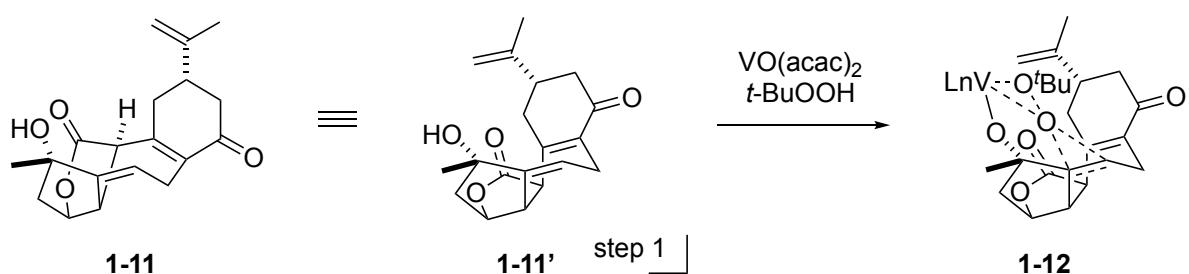
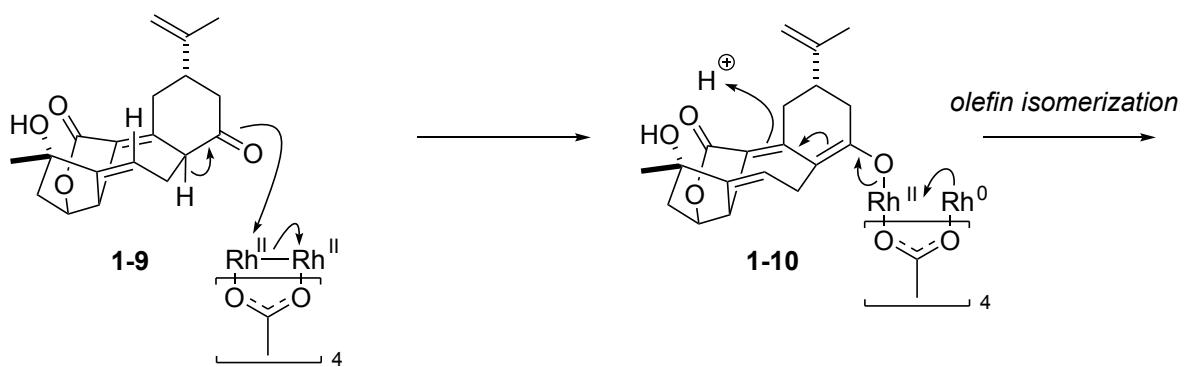
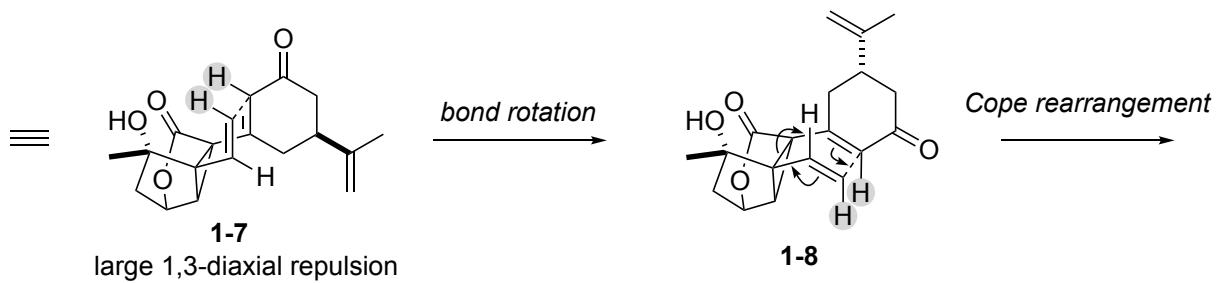


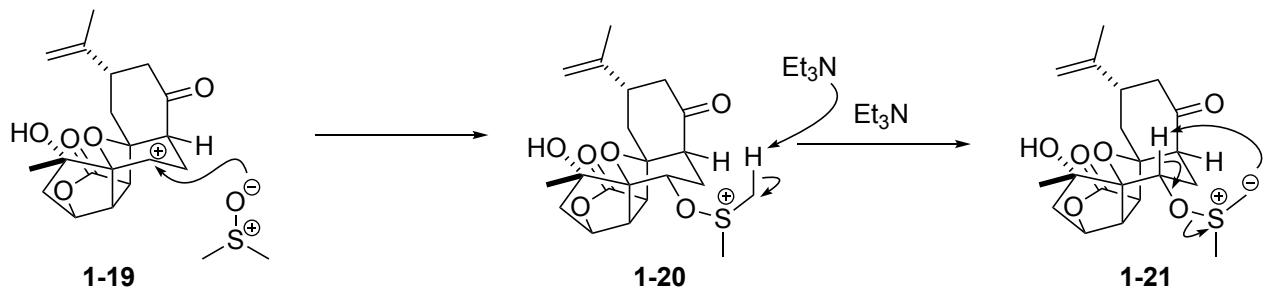
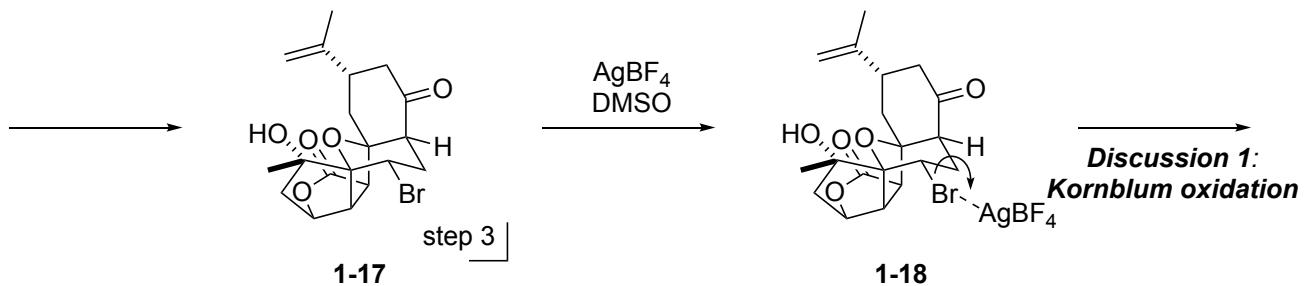
Topic: Synthetic Studies using divinylcyclopropane
Introduction of problem 1 : Synthetic study of *ent*-ineleganolide



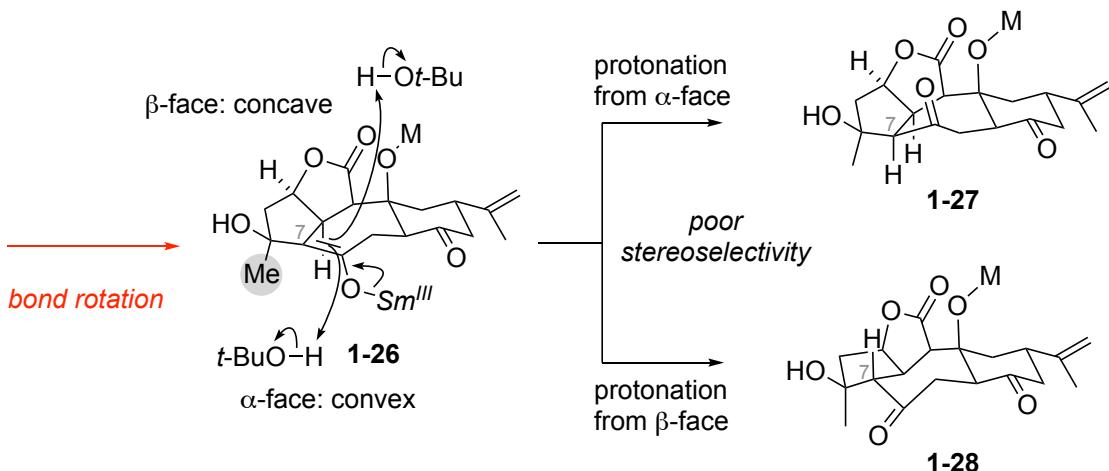
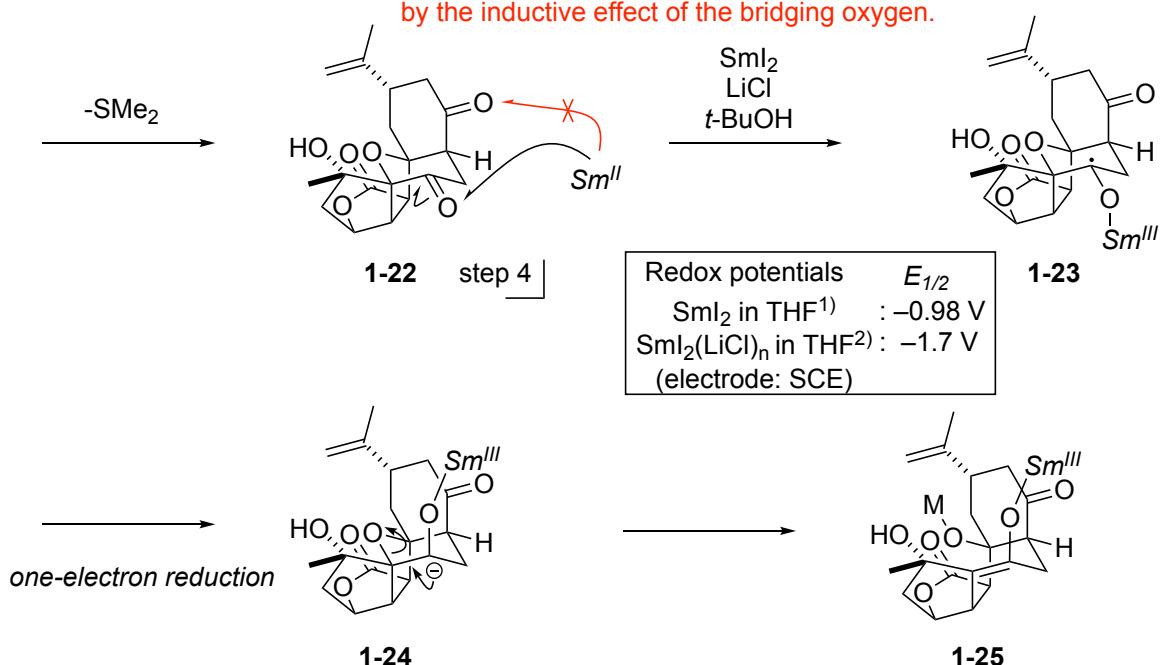
Answer

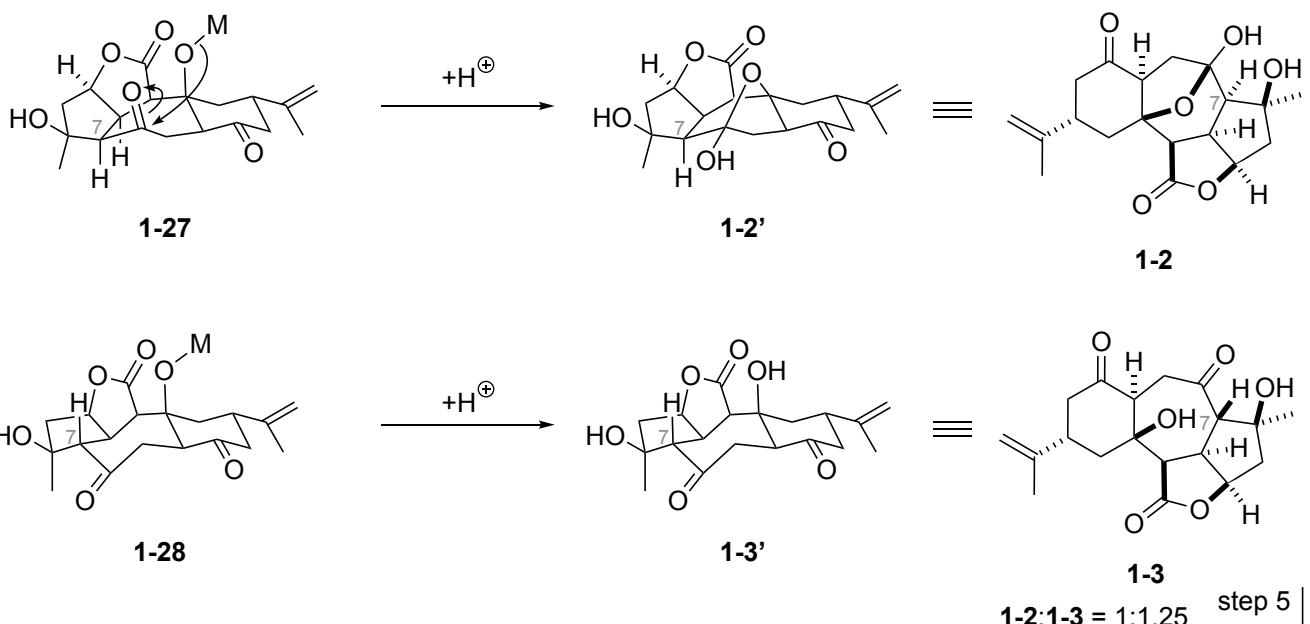






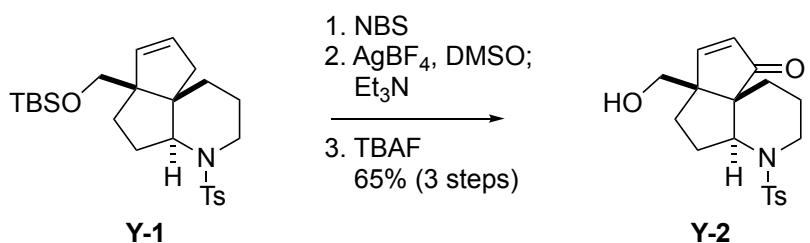
The regio-selectivity of the reduction would be caused by the inductive effect of the bridging oxygen.



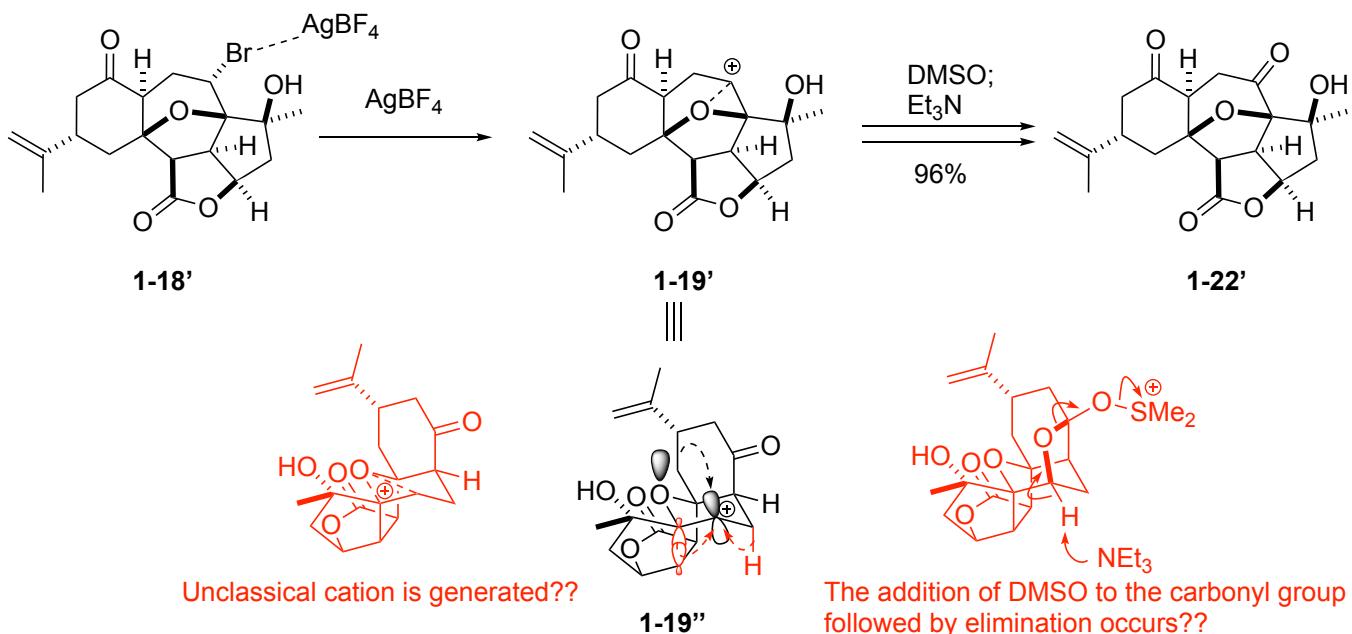


Discussion 1 : Kornblum oxidation

- Yang, Z. et al. Org. Lett. 2017, 19, 2921.

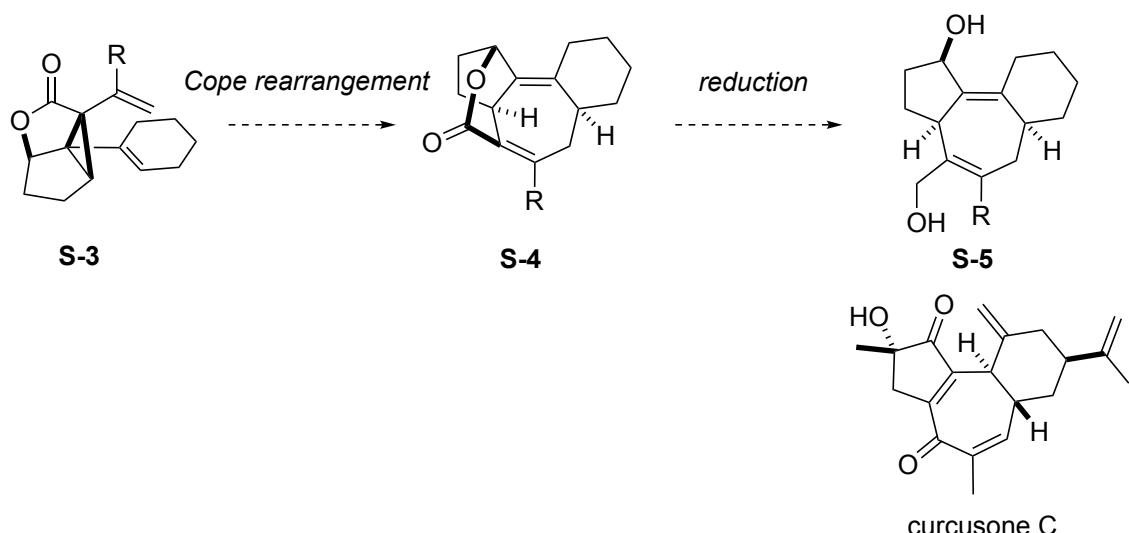


Generally, Kornblum oxidation needs to stabilize the carbocation by olefin or aromatic ring.



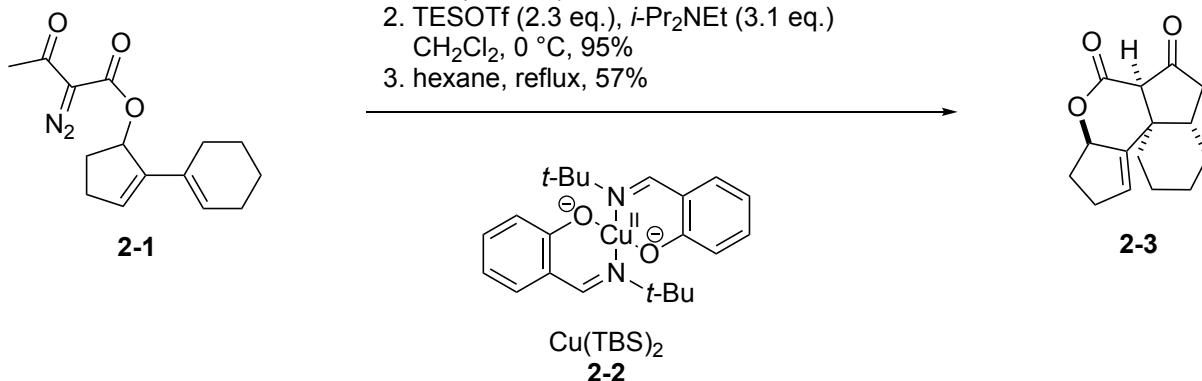
The authors hypothesize that the furyl oxygen bridge allow for the donation of electron density into the vacant p-orbital of the secondary carbocation.

Introduction of problem 2 : Synthetic study of curcusone C



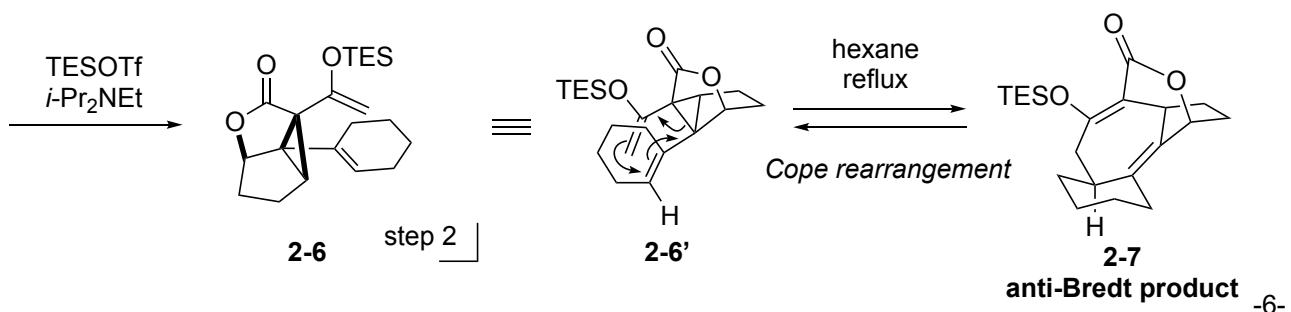
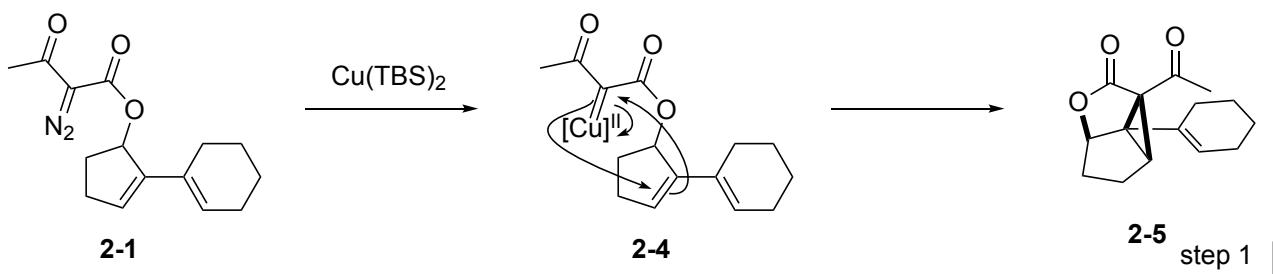
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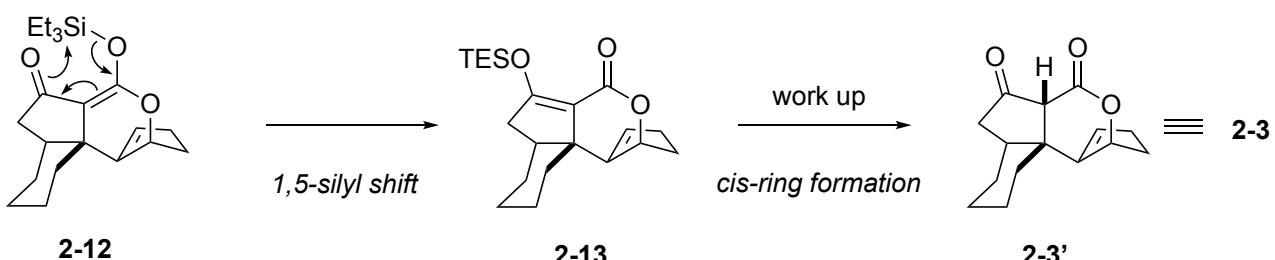
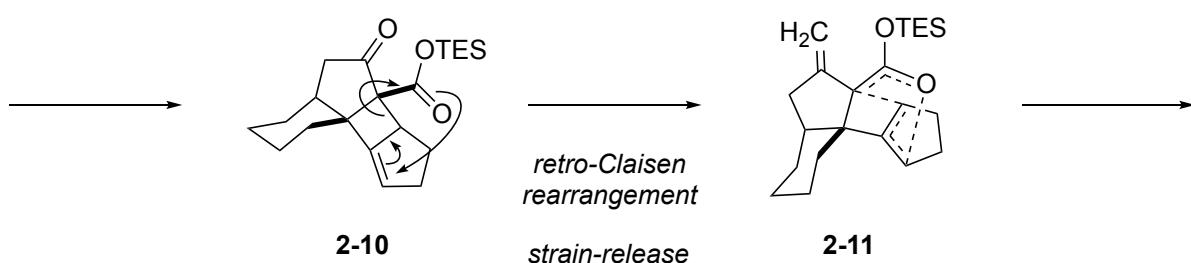
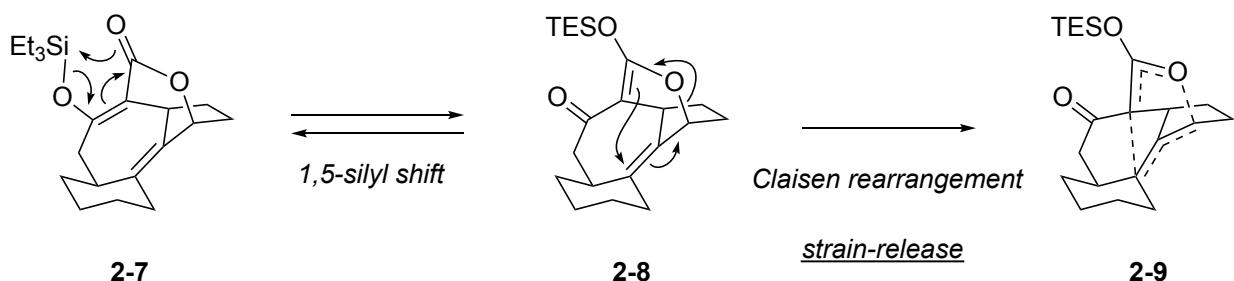
1. **2-2** (5 mol%), toluene, 110 °C, 65%
 2. TESOTf (2.3 eq.), *i*-Pr₂NET (3.1 eq.)
CH₂Cl₂, 0 °C, 95%
 3. hexane, reflux, 57%



Lee, C. W.; Taylor, B. L. H.; Petrova, G. P.; Patel, A.; Morokuma, K.; Houk, K. N.; Stoltz, B. M. *J. Am. Chem. Soc.* **2019**, *141*, 6995.

Answer

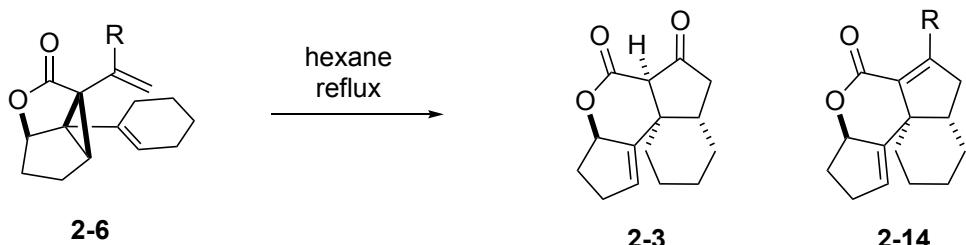




Discussion 2 : Reaction mechanisms of the transformation 2-6 → 2-3

Discussion 2-1 : Validation of the proposed mechanism

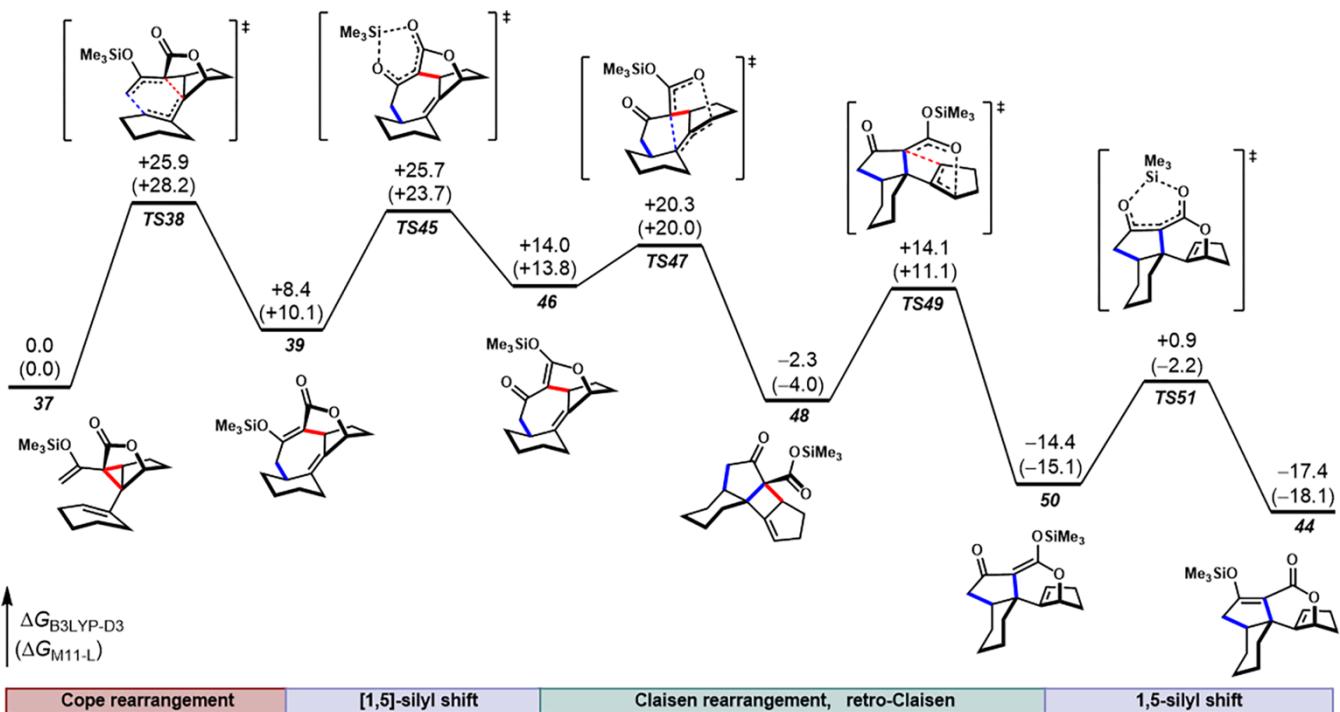
- The effect of the silyl group



| entry | R | 2-3 | 2-14 |
|-------|------|--------------|-------------|
| 1 | OTES | 57% | 0% |
| 2 | OTBS | trace | 50% |
| 3 | Me | not observed | |

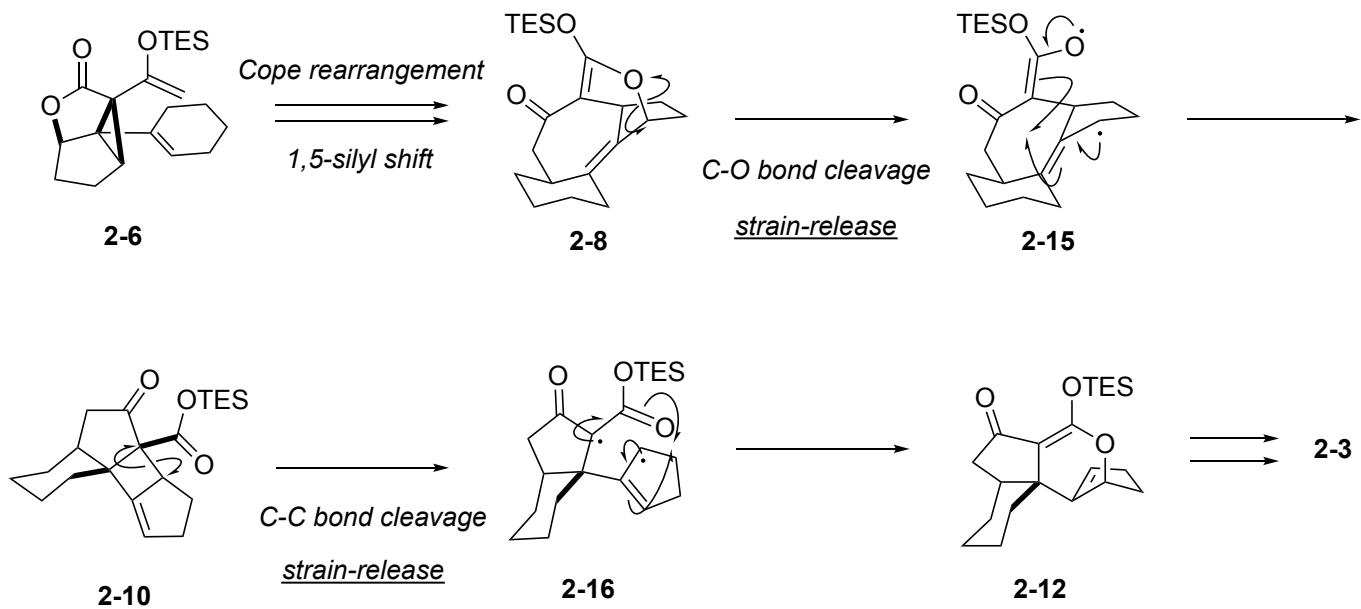
- The silyl group should affect or participate in the transformation.

• Computational study

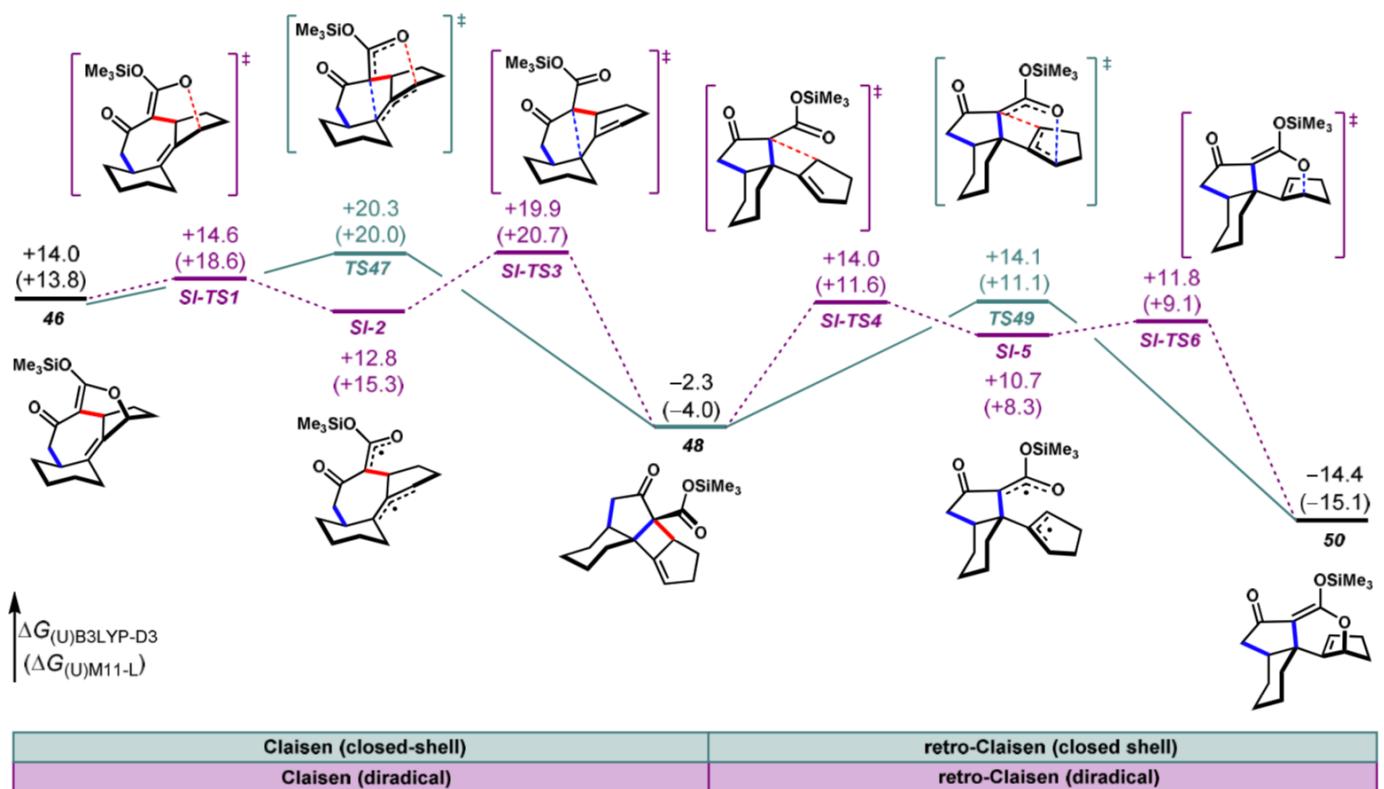


Discussion 2-2 : Other mechanisms

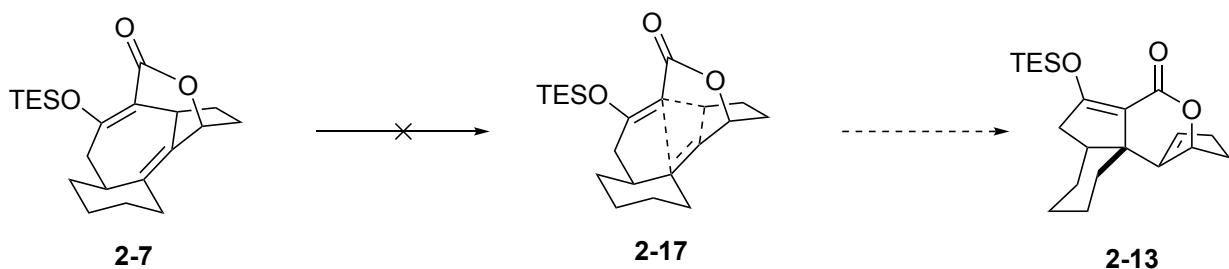
• Diradical pathway



• Computational study of the diradical pathway

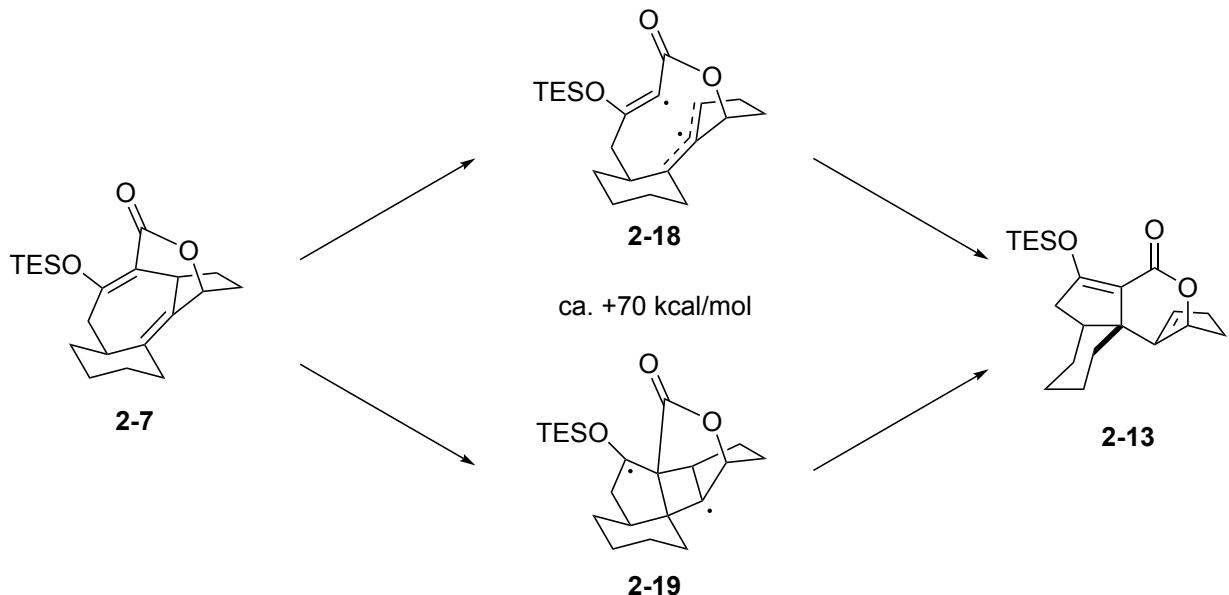


• Formal 1,3-shift (concerted pathway)



The concerted 1,3-shift is thermally forbidden by Woodward-Hoffmann rule.

• Formal 1,3-shift (concerted pathway)



References

- 1) Miller, R. S. et al. *J. Am. Chem. Soc.* **2000**, *122*, 7718.
- 2) Fuchs, J. R. et al. *Tetrahedron Lett.* **1997**, *38*, 8157.