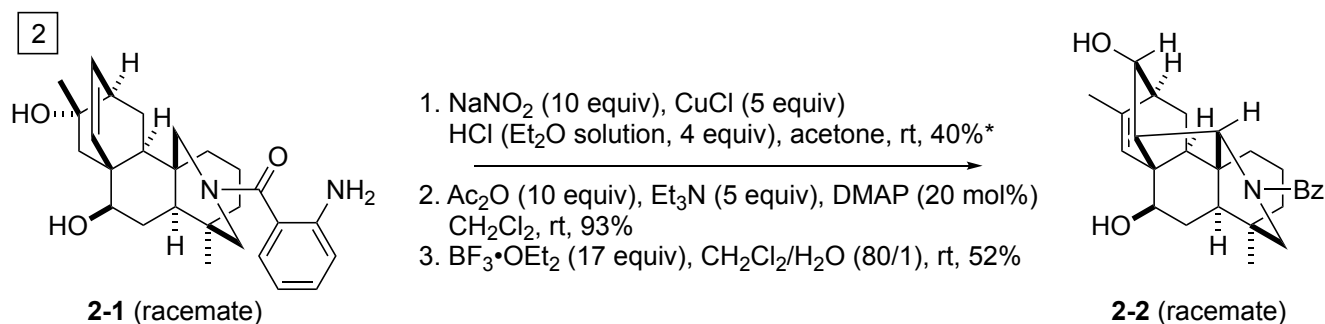
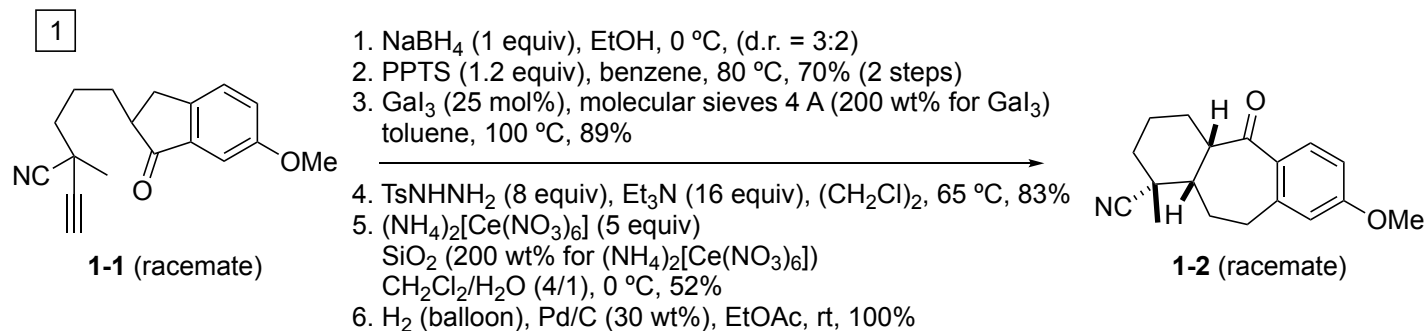


Problem Session (5)

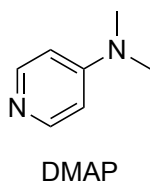
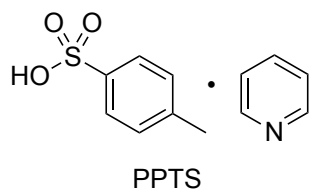
Please provide the reaction mechanisms.

2024.4.6

Hibiki Asai



*byproduct was obtained in 45% yield.



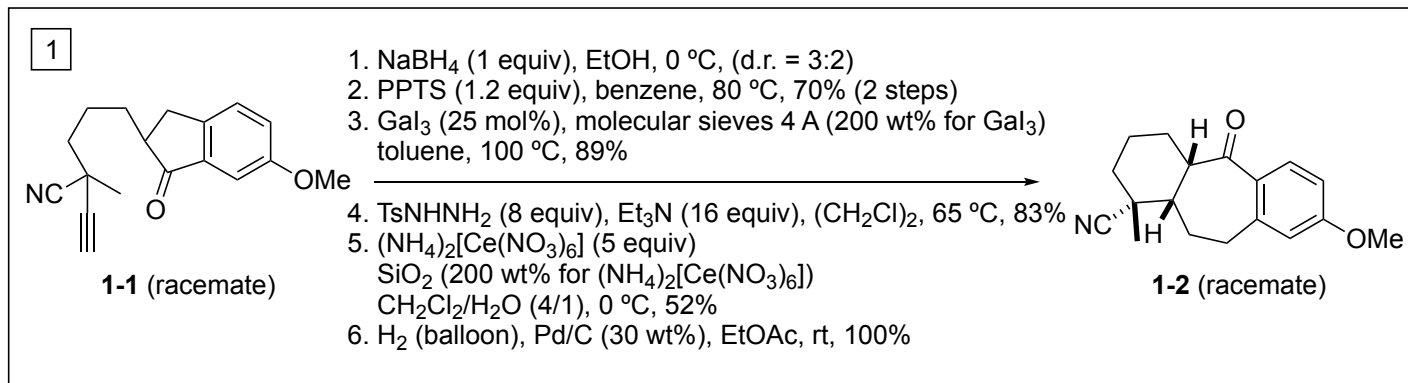
Ts: *p*-toluenesulfonyl
Bz: benzoyl

Problem Session (5)

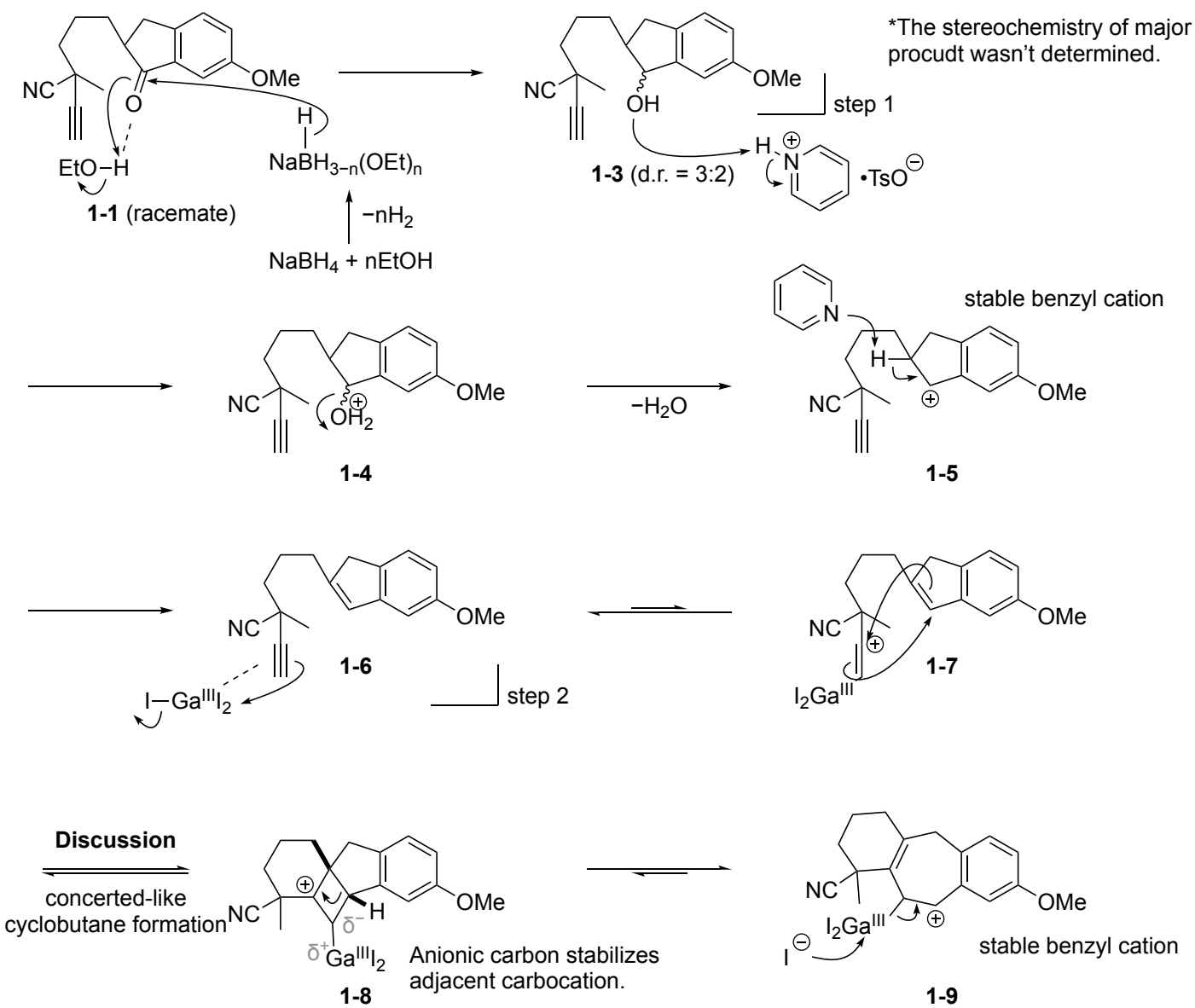
Topic: Synthetic study of C20-diterpenoid alkaloids

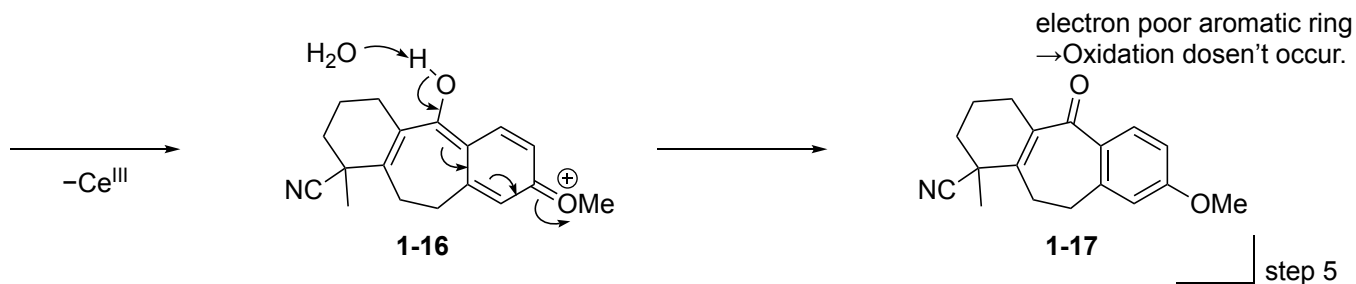
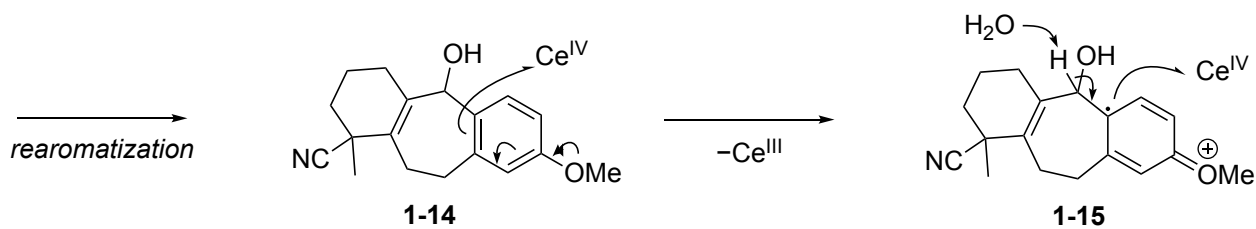
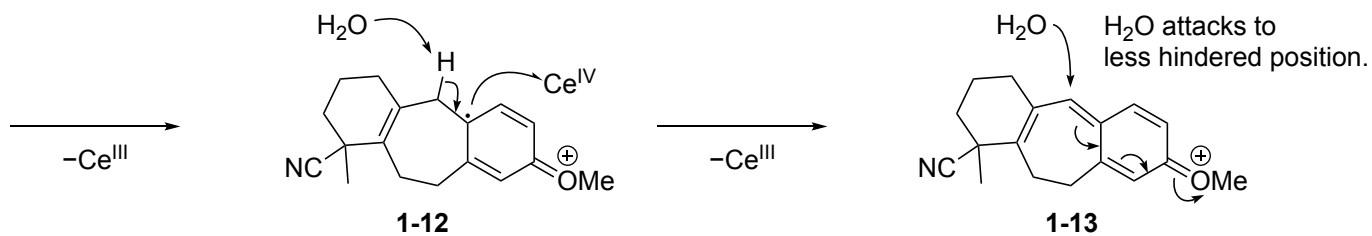
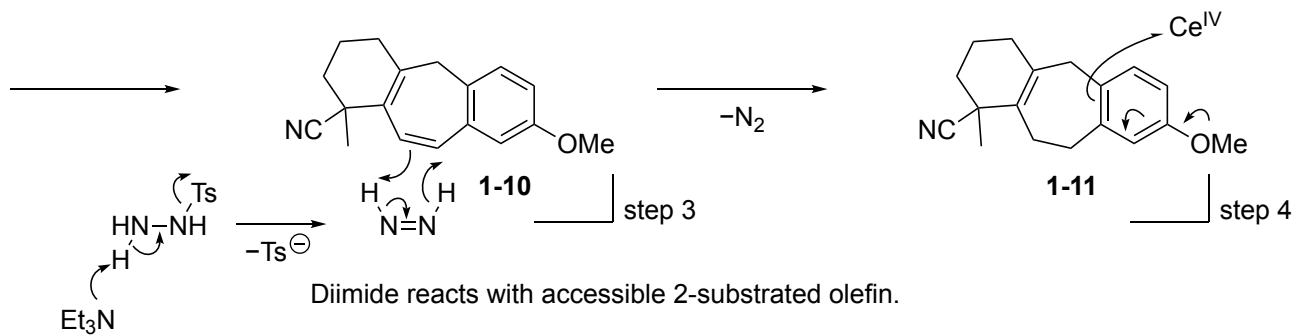
2024.4.6

Hibiki Asai



Hamlin, A. M.; Cortez, F. J.; Lapointe, D.; Sarpong, R. *Angew. Chem. Int. Ed.* **2013**, *52*, 4854–4857.



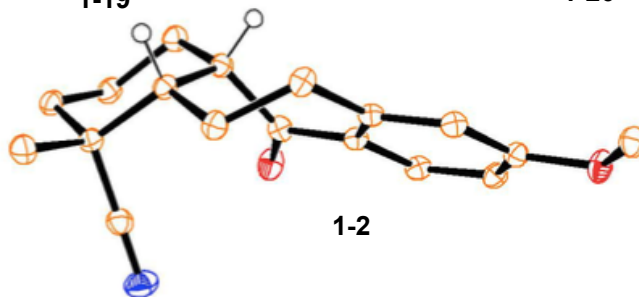
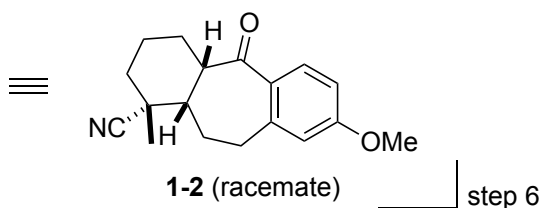
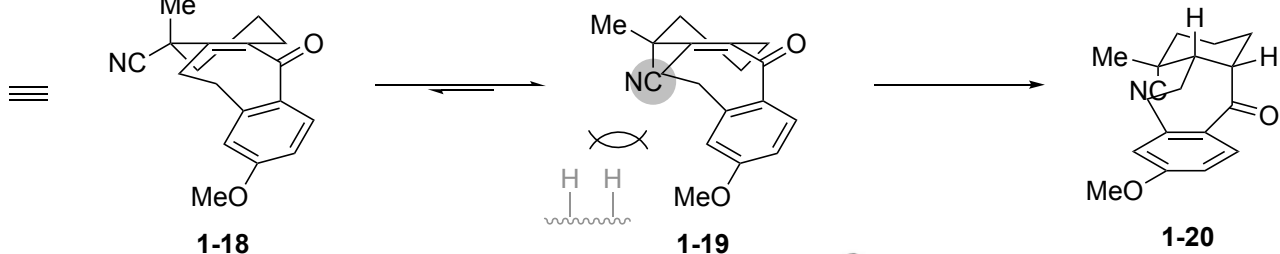


SiO₂ may be added for simplification work-up procedure to absorb Ce reagent.

A values

CN: 0.17

Me: 1.7

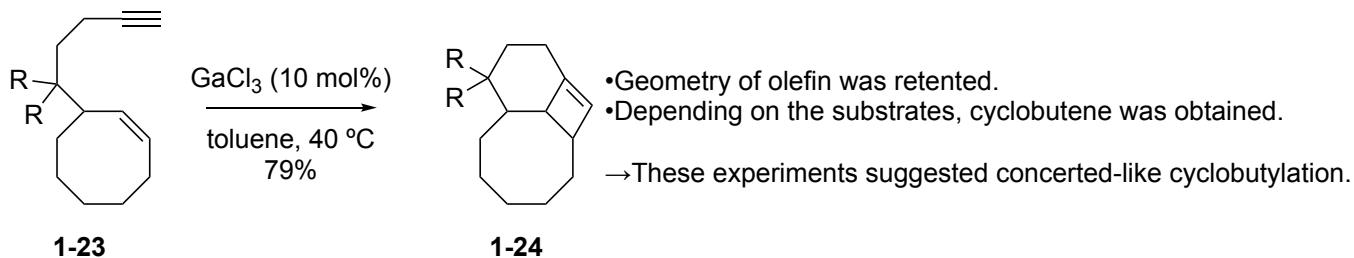
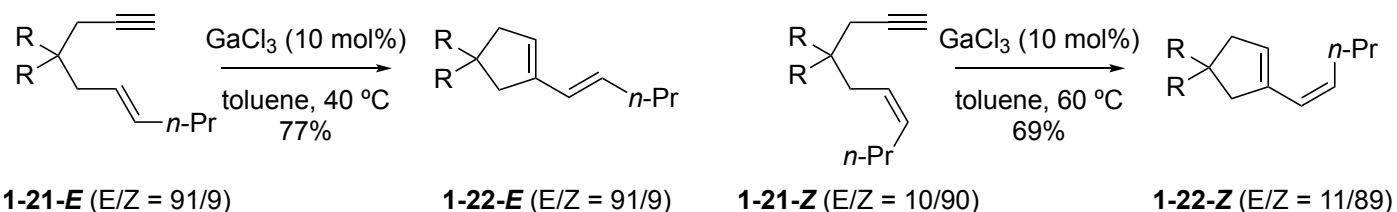


Discussion:

1. Cation cyclization

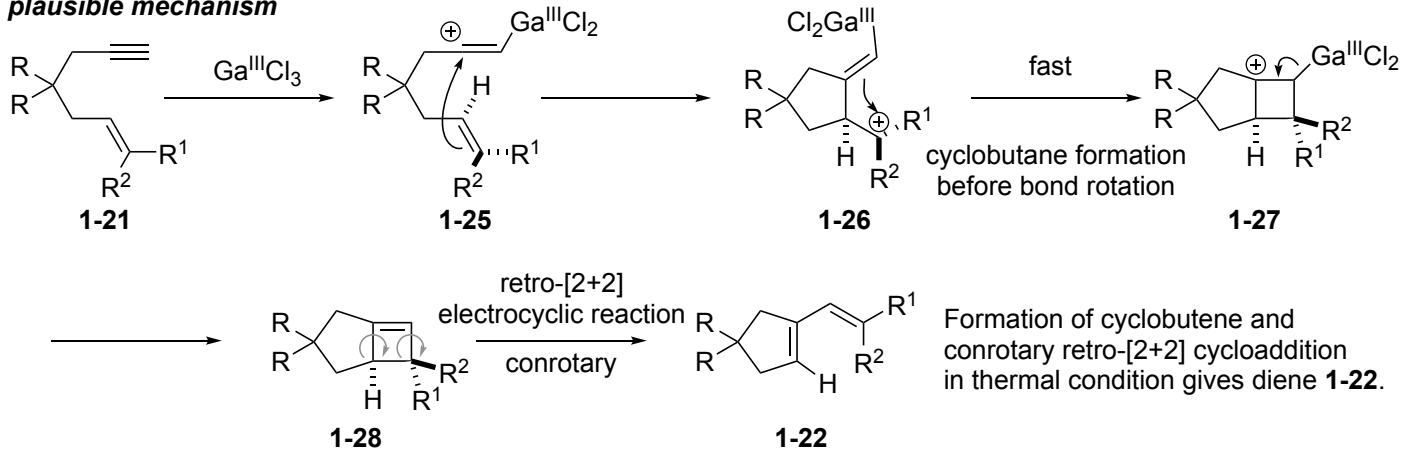
1-1. Concerted-like pass way

a) supports of concerted-like cyclobutylation R = CO₂Et

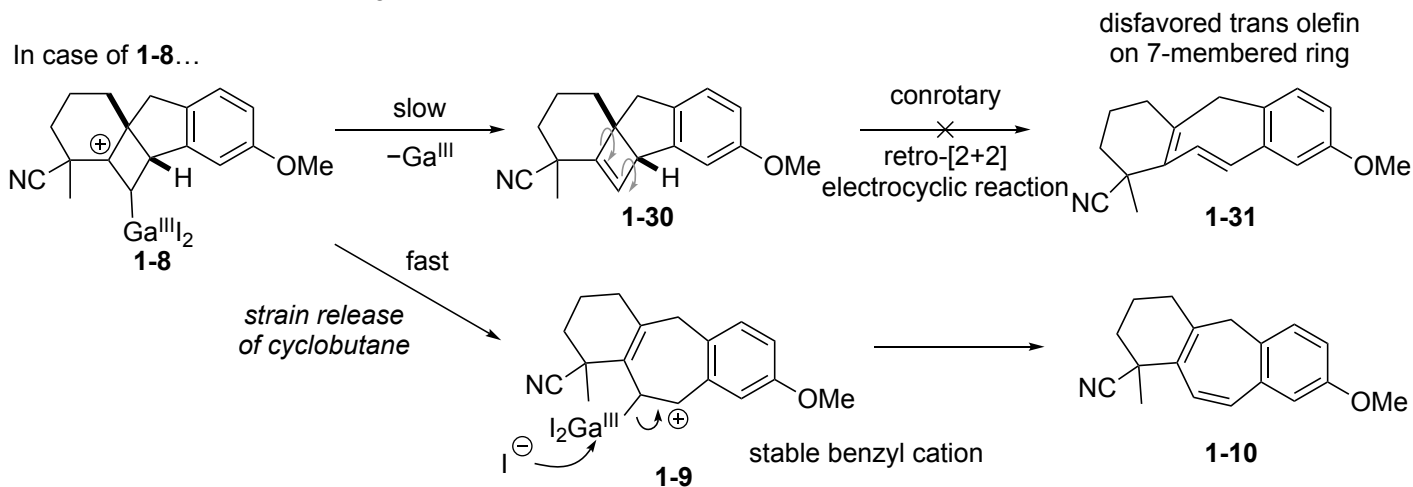


Chatani, N.; Inoue, H.; Kotsuma, T.; Murai, S. *J. Am. Chem. Soc.* **2002**, *124*, 10294–10295.

plausible mechanism



In case of **1-8**...

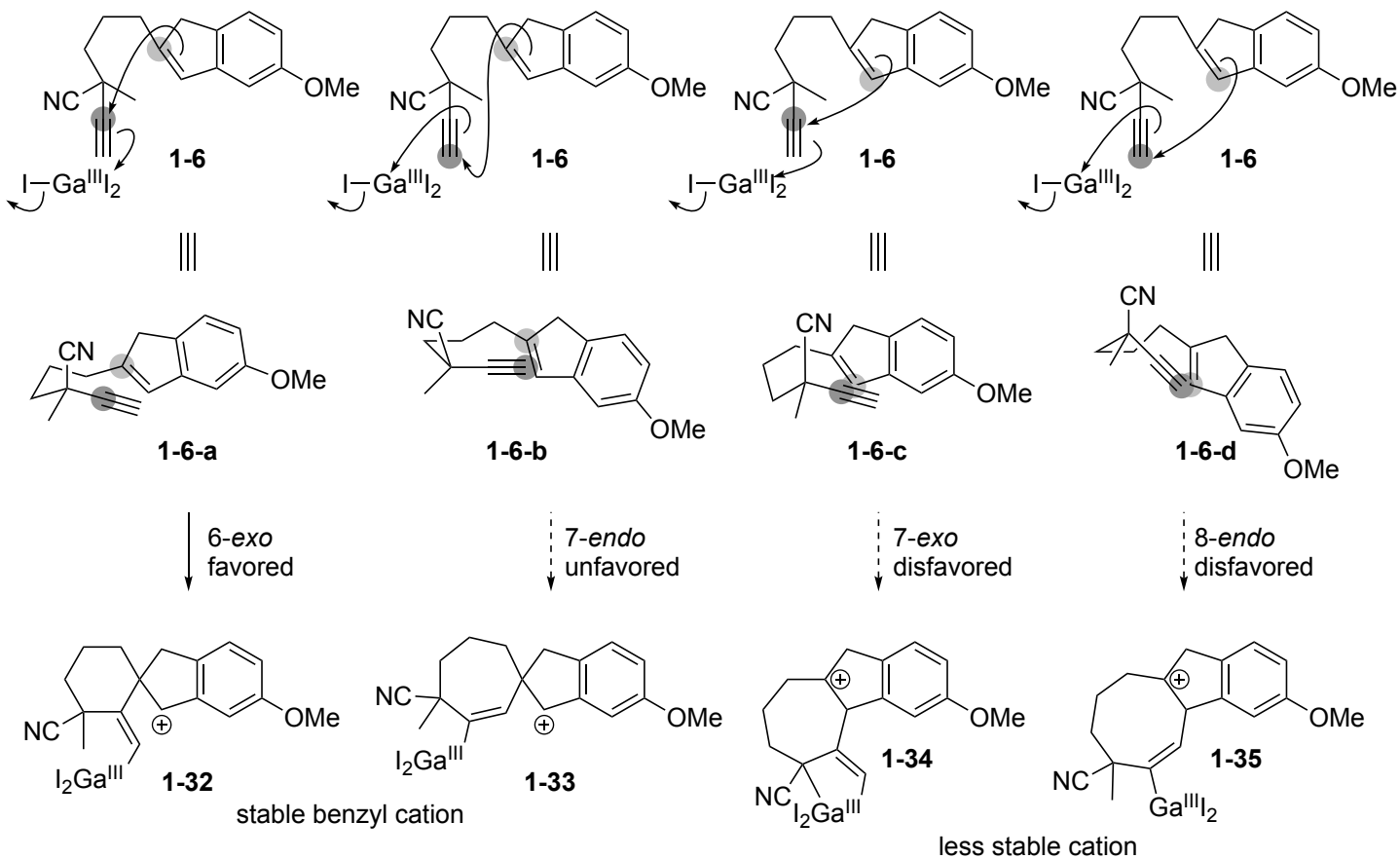


Retro-[2+2] cycloaddition couldn't occur because disfavored trans-olefin on 7-membered ring would be formed. On the other hand, cation **1-9** is stable due to conjugation with aromatic ring. Therefore, ring opening of cyclobutane of **1-8** would be faster.

1-2. Stepwise pass way

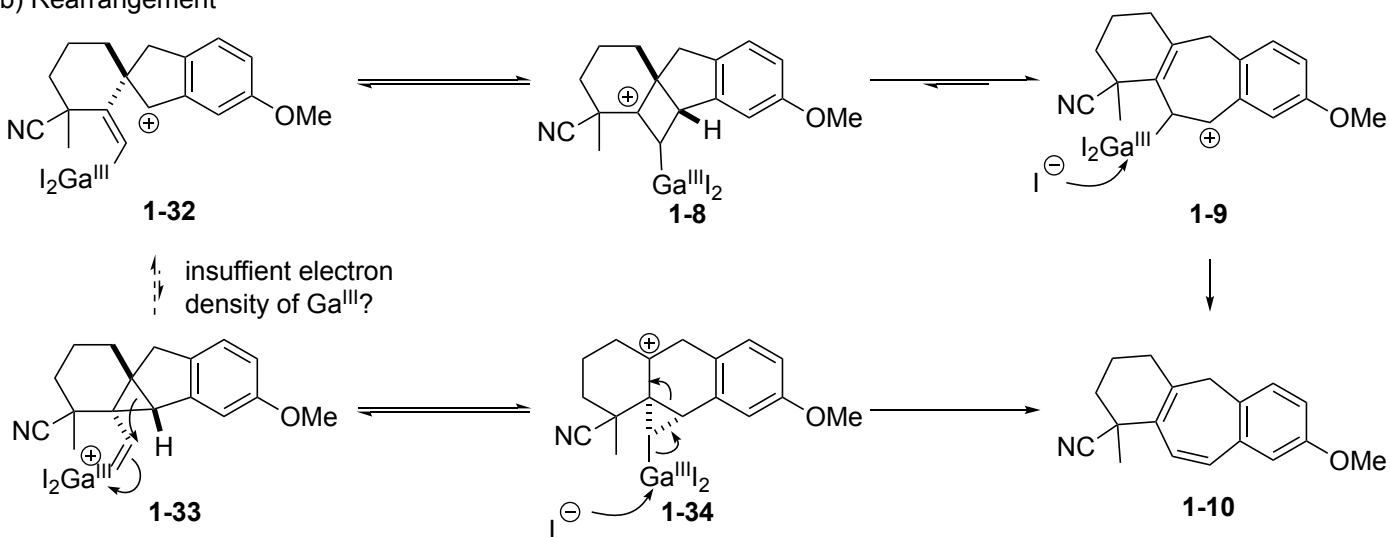
From **1-6**, stepwise pass way might be possible because firstly generated benzyl cation would be stable.

a) First cyclization



Faster 6-exo cyclization is favored.

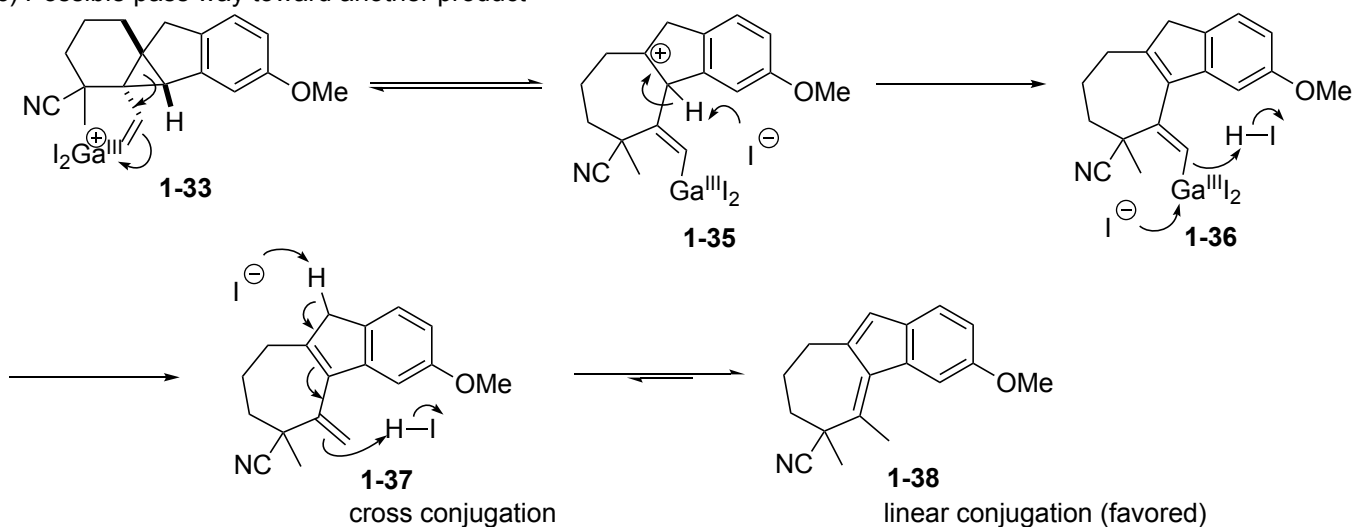
b) Rearrangement



From **1-32**, cyclobutane formation and ring opening give **1-10** likewise.

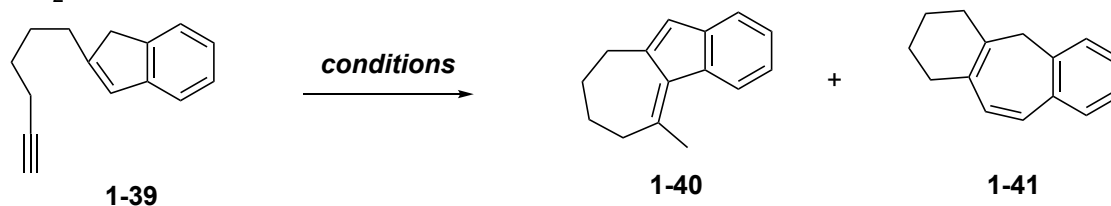
Another pass way from **1-32** to **1-10** is worth being considered, i.e. cyclopropane formation, but this pass way is unfavored because of low electron density of Ga^{III} .

c) Possible pass way toward another product



If cyclopropane was formed, **1-38** would be also obtained, which is unlikely because of unfavored **1-33**.

•cf. PtCl_2 condition



PtCl_2 (10 mol%), toluene, 80 °C

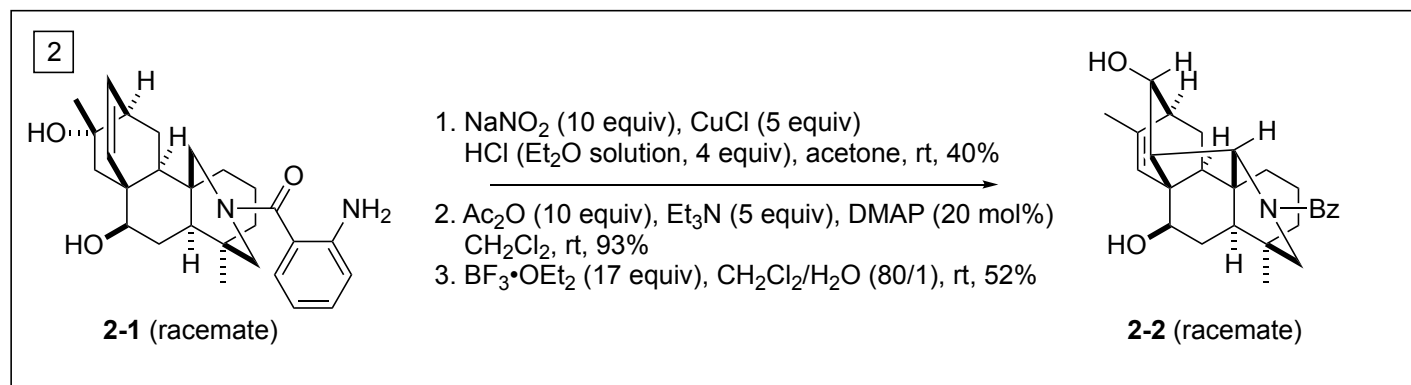
1-40:1-41 = 1:1.1

GaI_3 (10 mol%), toluene, 23 °C

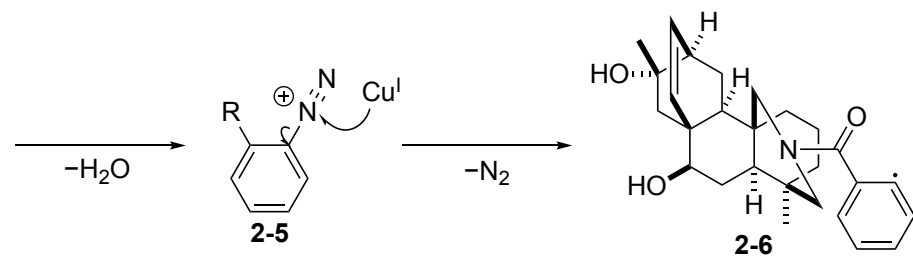
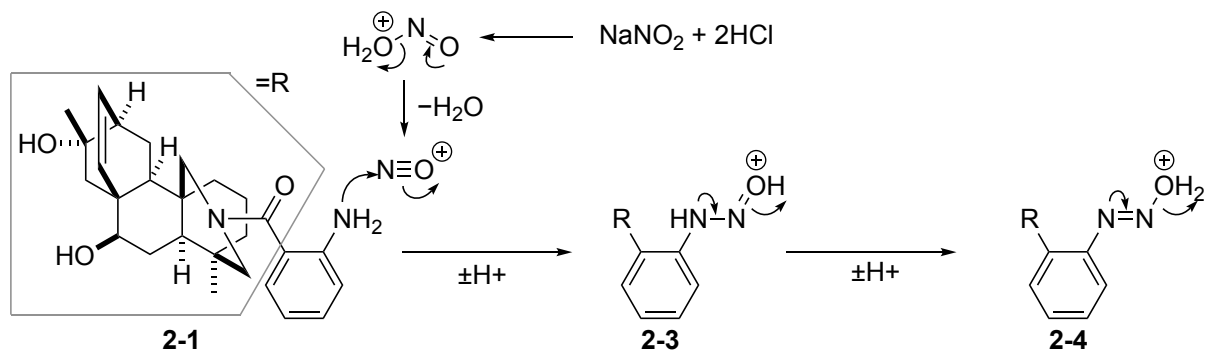
1-40:1-41 = 0:1 *The yields were not mentioned.

Simmons, E. M.; Sarpong, R. *Org. Lett.* **2006**, *8*, 2883–2886.

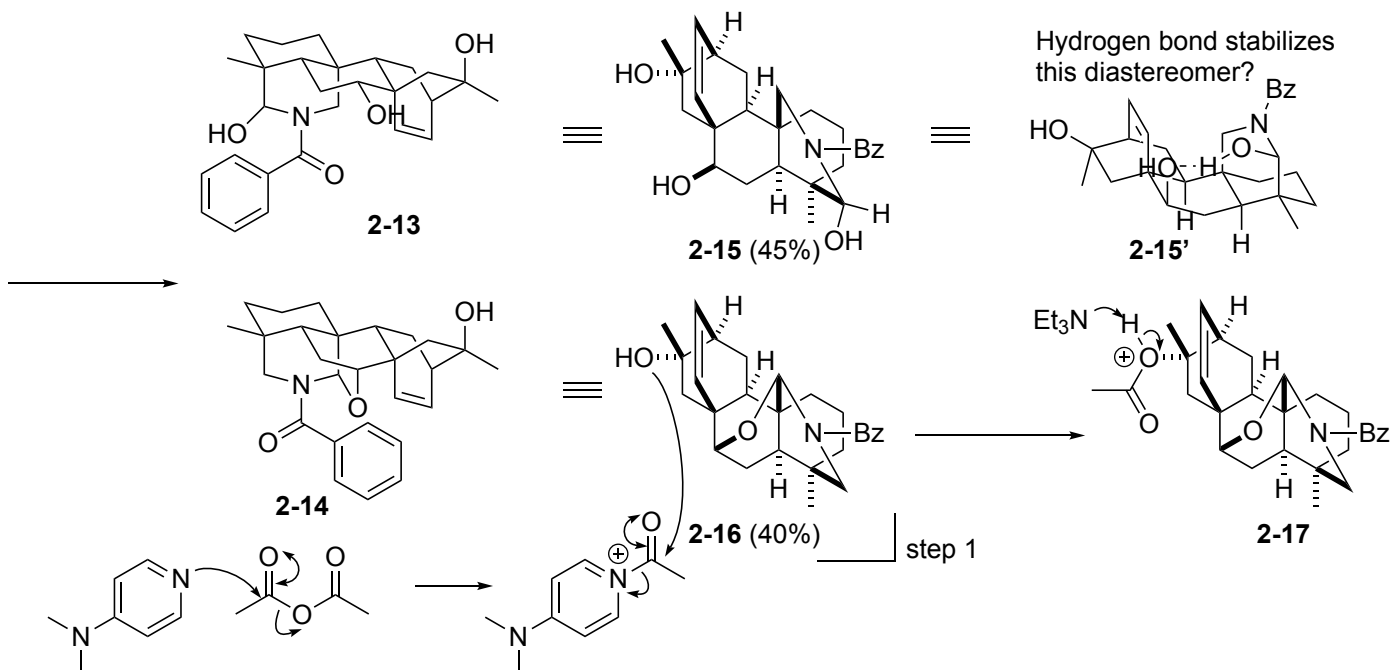
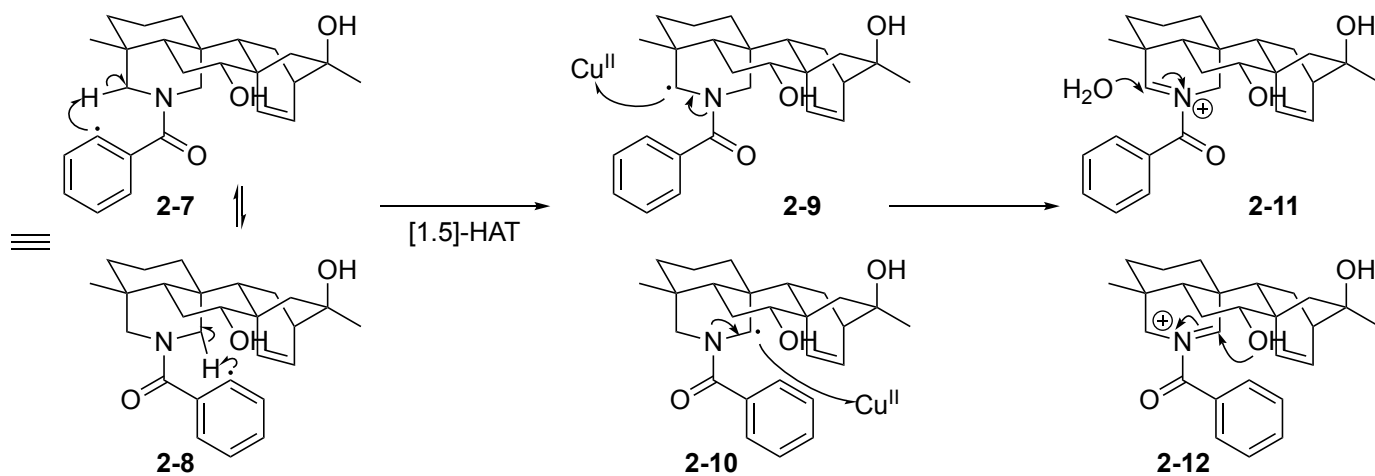
In the condition using PtCl_2 , **1-40** was also obtained. Pt^{II} more easily gives electrons than Ga^{III} , so cyclopropane formation occurred competitively. On the other hand, GaI_3 gave only **1-41**.

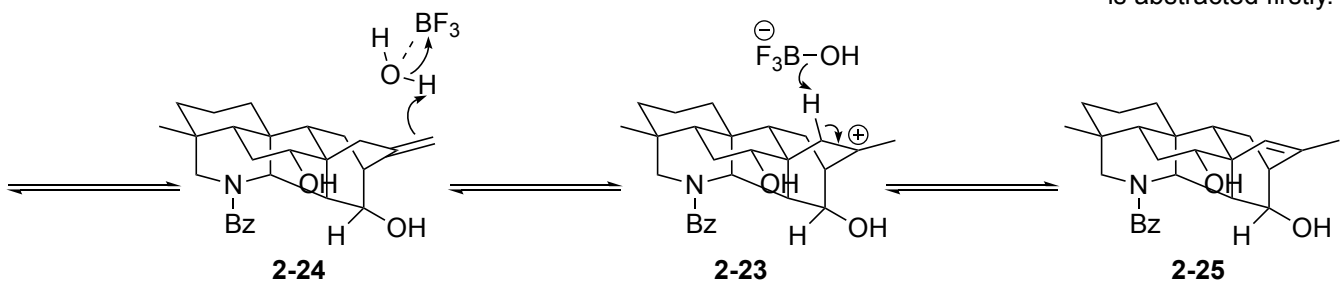
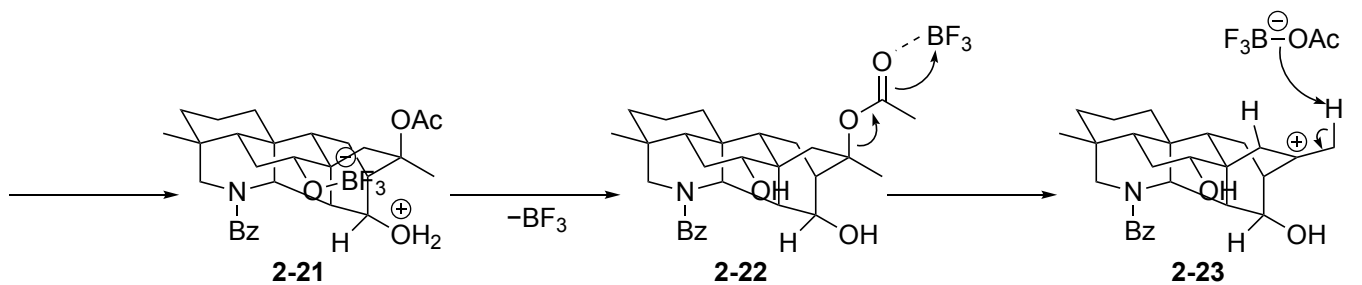
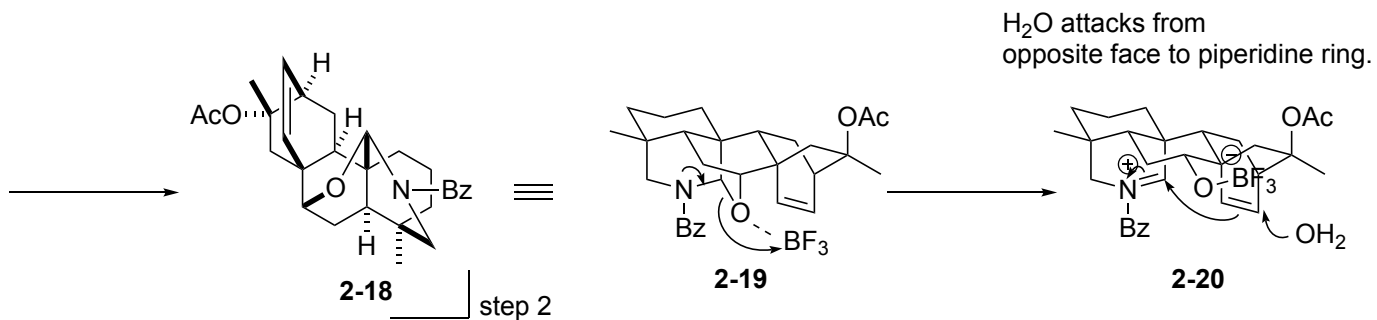


Zhu, M.; Li, X.; Song, X.; Wang, Z.; Liu, X.; Song, H.; Zhang, D.; Wang, F.; Qin, Y.
Chin. J. Chem. **2017**, *35*, 991–1000.

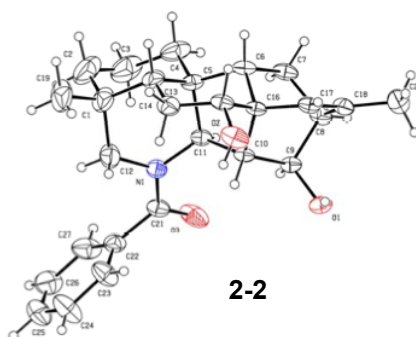
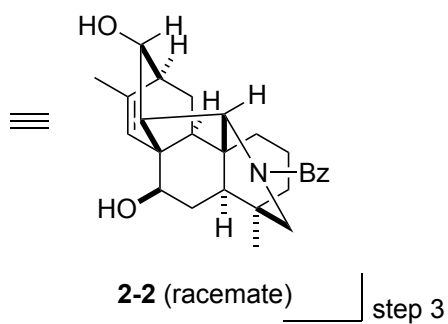


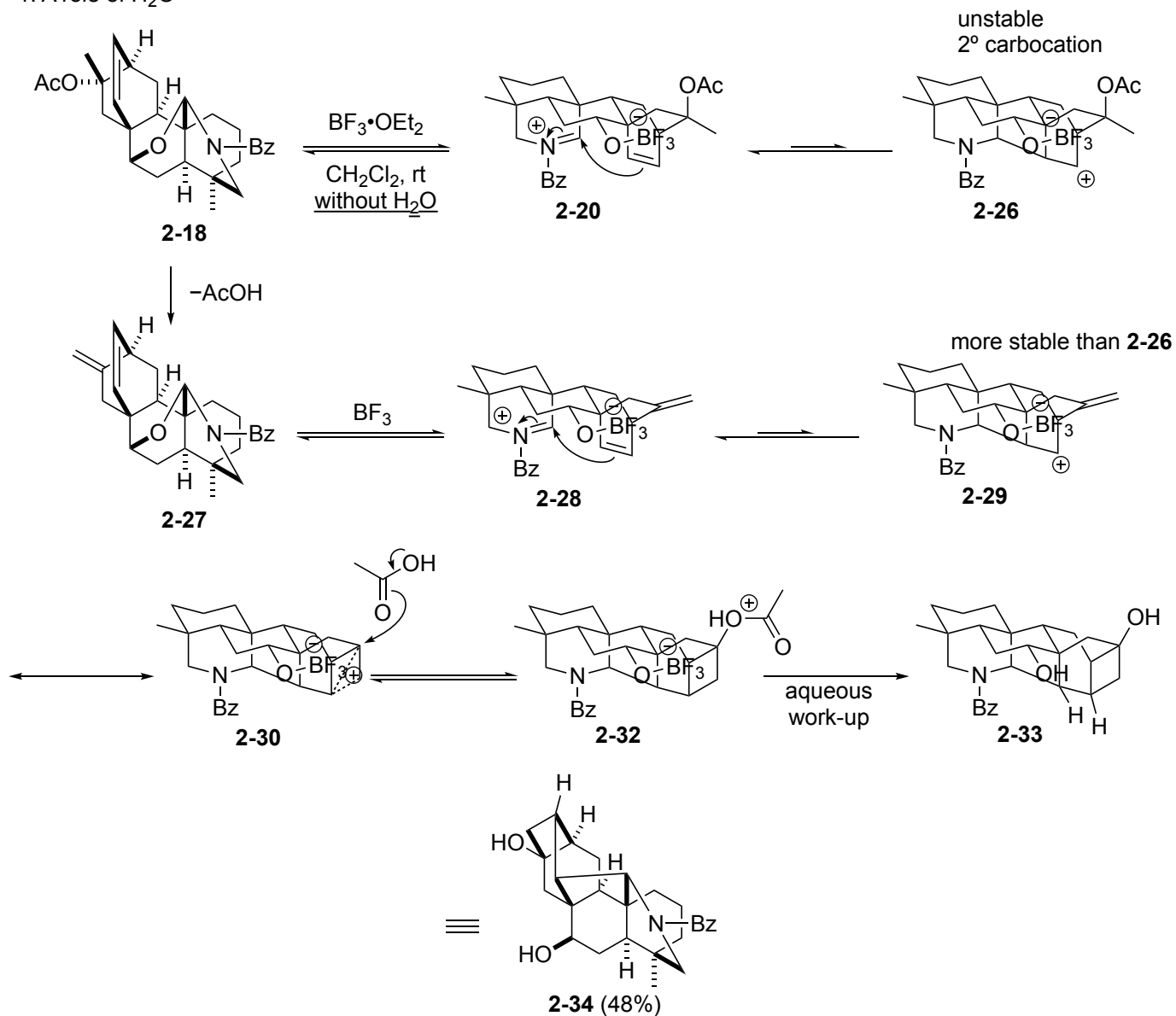
Electron deficient iminium ion is immediately trapped by H_2O .



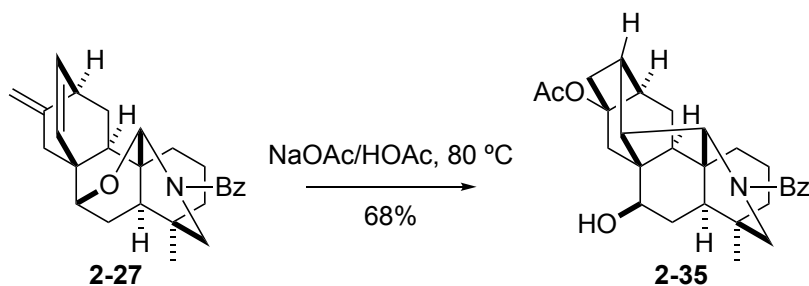


Thermally stable 3-substituted olefin was finally obtained.



Discussion:1. A role of H₂OIn the presence of H₂O, carbocation was smoothly trapped by H₂O.

Without H₂O, unstable 2° carbocation wasn't trapped. Therefore, elimination of AcOH occurred before aza-Prins cyclization to give diene **2-27**, from which undesired cyclobutane formation proceeded.



In addition, cyclobutane was formed from **2-27** in AcOH at high temperature, which indicates **2-27** was an intermediate generated from **2-18**.