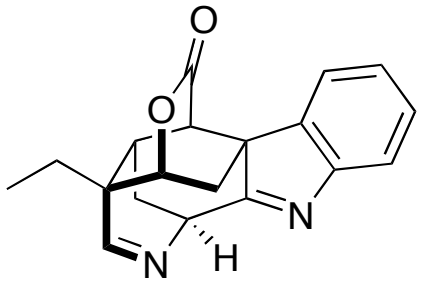

Total Synthesis of (+)-Scholarisine A

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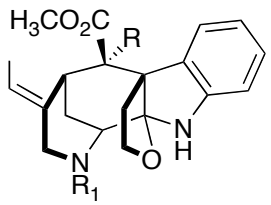
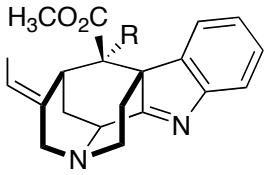
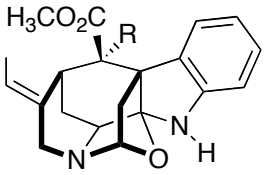
Akuammiline Alkaloids: Scholarisine



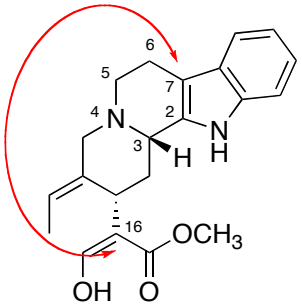
R = H, R_1 = CHO **Aspidophylline A**
R = CH_2OAc, R_1 = H **Aspidodasycarpine**



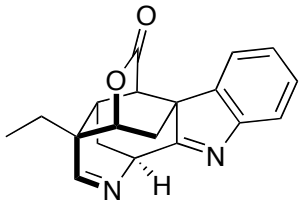
R = H, **Strictamine**
R = CH_2OAc, **Akuammiline**



R = H, **Picrinine**
R = CH_2OAc, **Picraline**



Geissoschizine

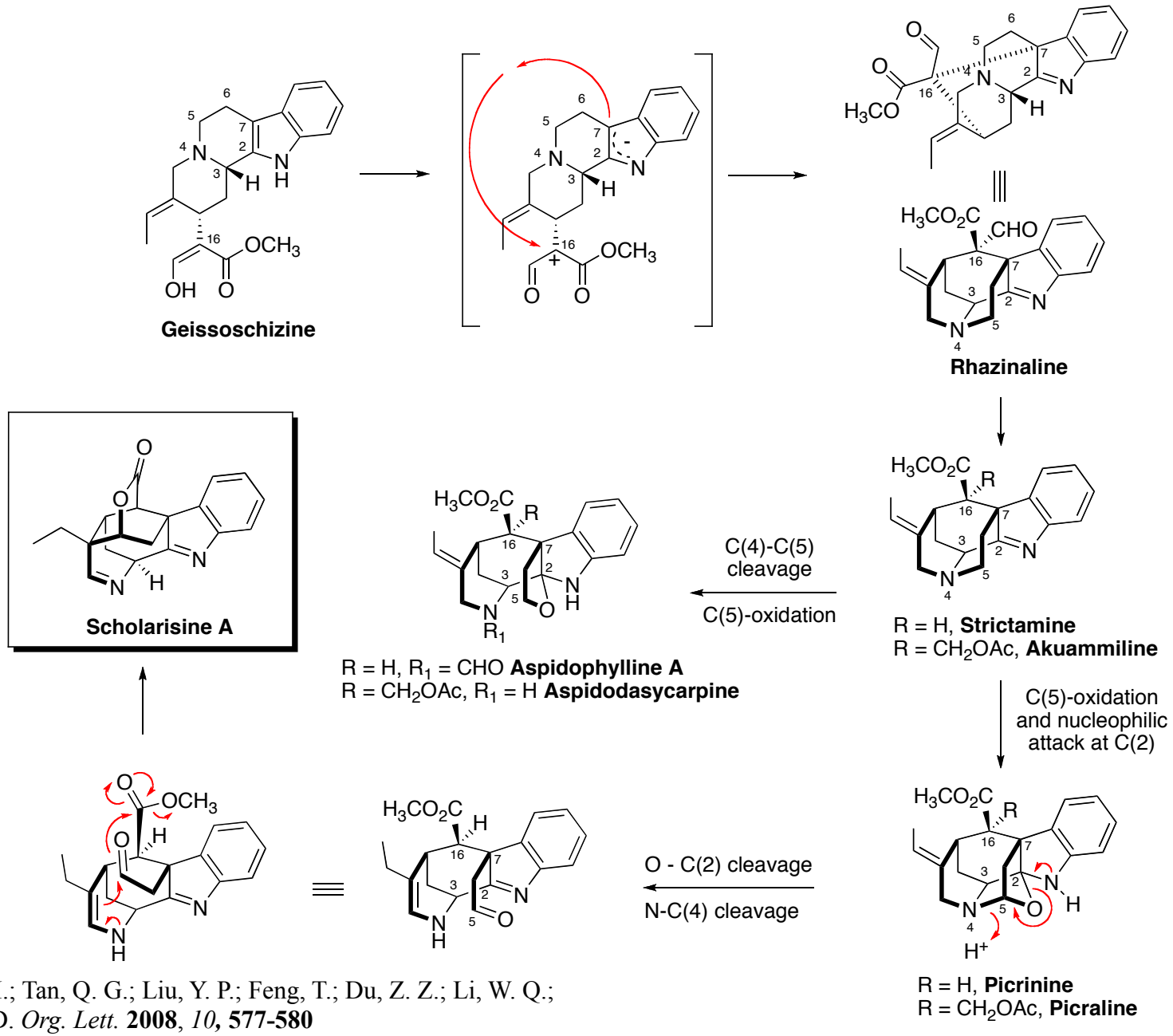


Scholarisine A

- isolated in 2008 from *Alstonia scholaris*
- unprecedented skeleton
- no information on the bioactivity (picraline is a target for type-II diabetes)

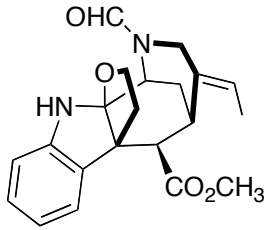
1. Wenkert, E.; Wickberg, B. *J. Am. Chem. Soc.* **1965**, *87*, 1580-1589. 2. Ramirrez, A.; Garcia-Rubio, S. *Curr. Med. Chem.* **2003**, *10*, 1891-1915. 3. Cai, X. H.; Tan, Q. G.; Liu, Y. P.; Feng, T.; Du, Z. Z.; Li, W. Q.; Luo, X. D. *Org. Lett.* **2008**, *10*, **577-580. 4. http://en.wikipedia.org/wiki/Alstonia_scholaris**

Biosynthetic Relationship in the Akuammiline Familiy



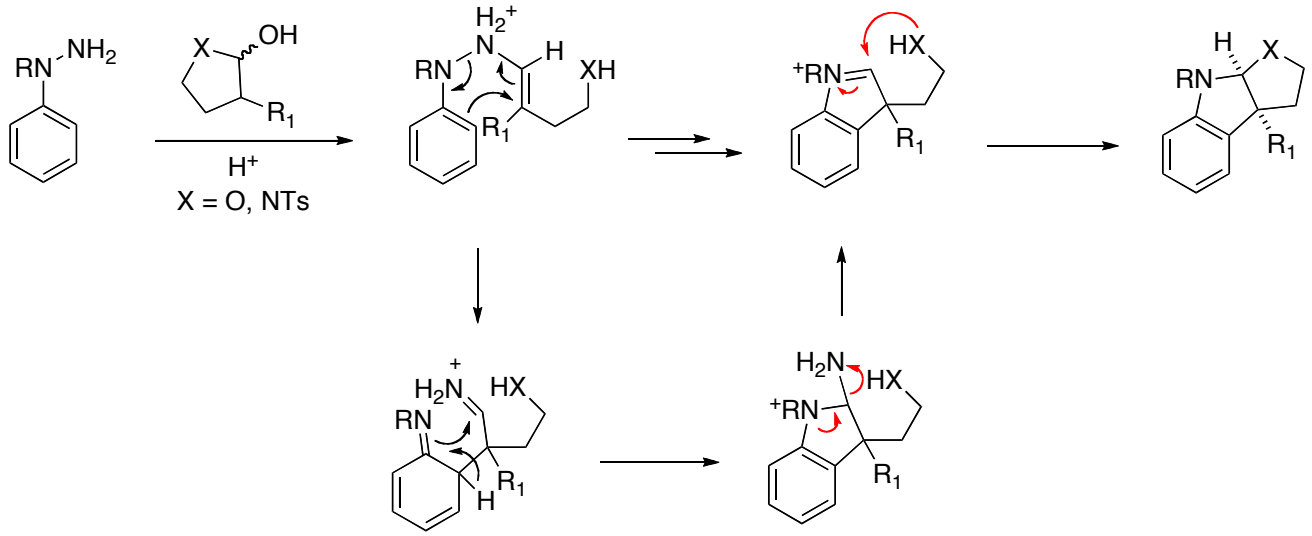
Cai, X. H.; Tan, Q. G.; Liu, Y. P.; Feng, T.; Du, Z. Z.; Li, W. Q.; Luo, X. D. *Org. Lett.* **2008**, *10*, **577-580**

Total Synthesis of Aspidophilline A: First Akuammiline Alkaloid Synthesized



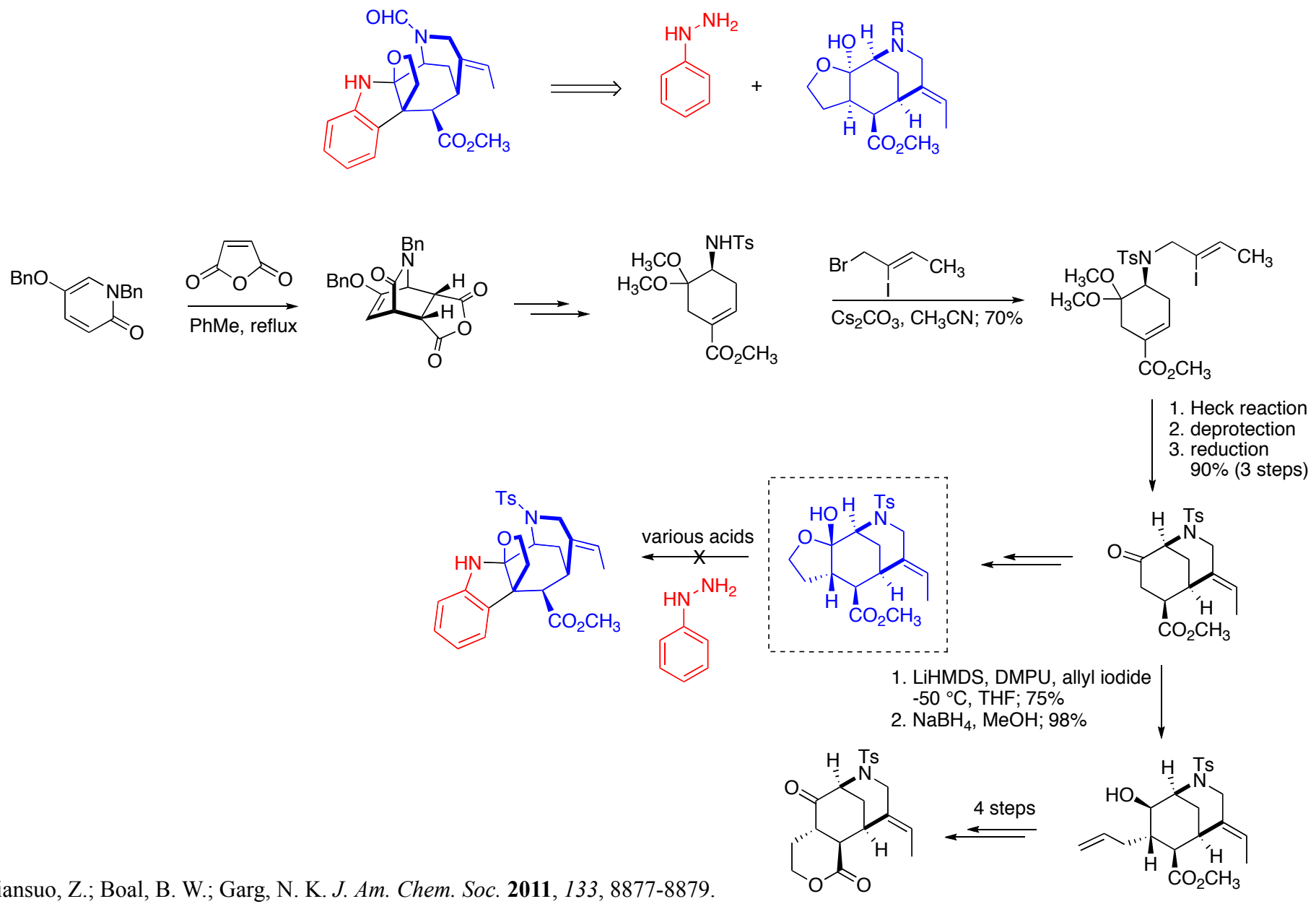
(±)-Aspidophylline A

Interrupted Fisher Indolization Cascade



Liansuo, Z.; Boal, B. W.; Garg, N. K. *J. Am. Chem. Soc.* **2011**, *133*, 8877-8879.

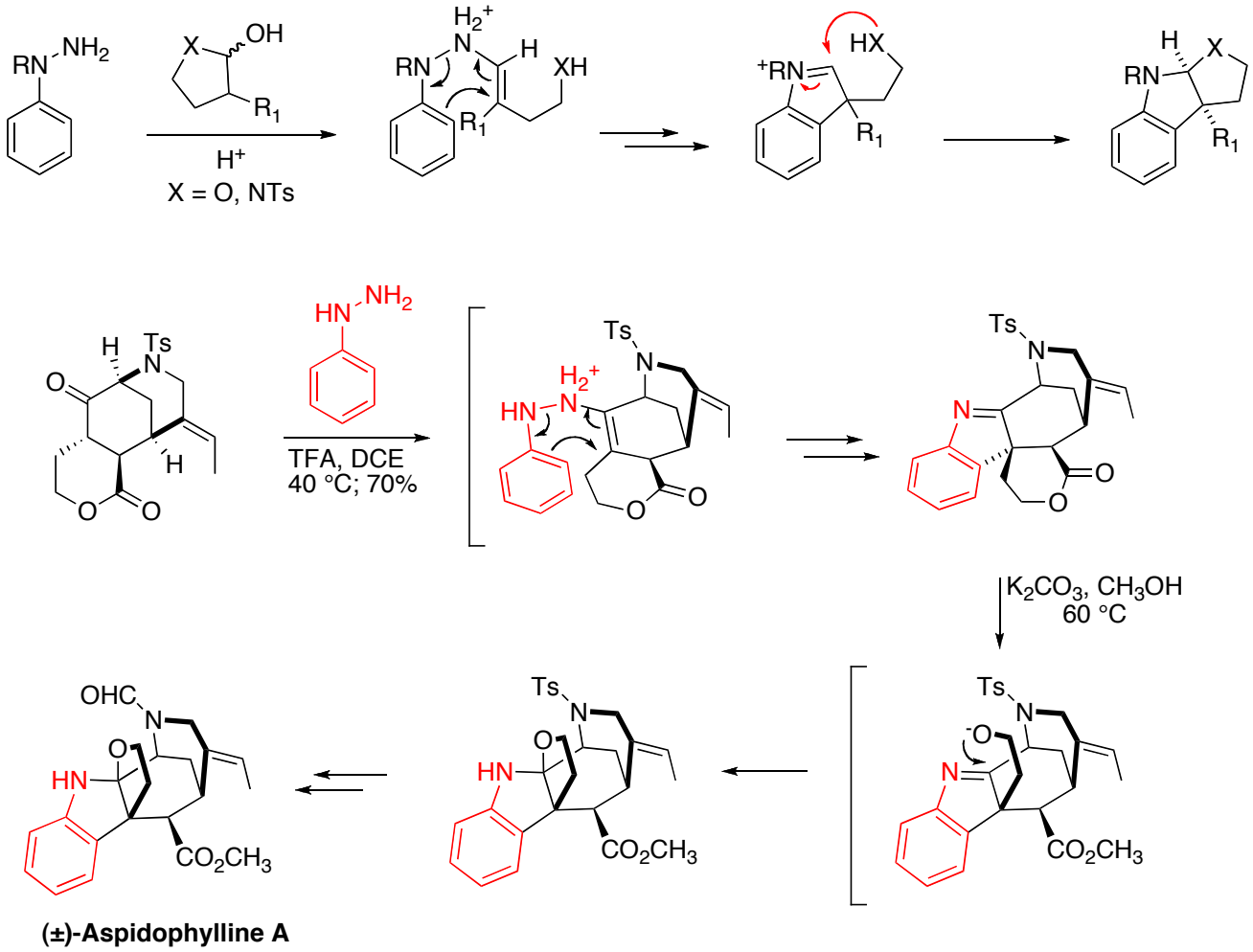
Garg's Approach to Aspidophylline A



Liansuo, Z.; Boal, B. W.; Garg, N. K. *J. Am. Chem. Soc.* **2011**, *133*, 8877-8879.

Garg's Approach to Aspidophylline A: End Game

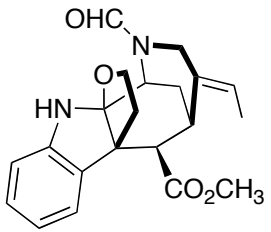
Interrupted Fisher Indolization Cascade



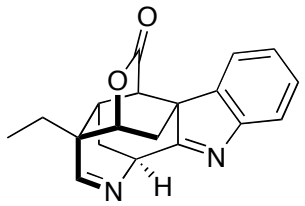
(±)-Aspidophylline A

Liansuo, Z.; Boal, B. W.; Garg, N. K. *J. Am. Chem. Soc.* **2011**, *133*, 8877-8879.

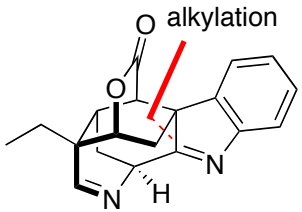
Smith's Approach: Late-stage Retro-Biosynthetic Fragmentation



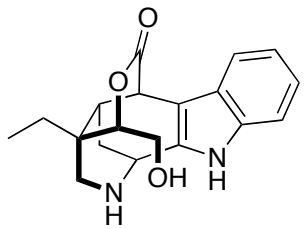
(±)-Aspidophylline A

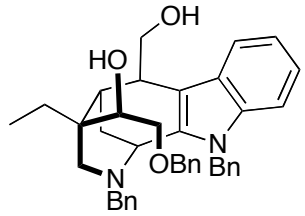


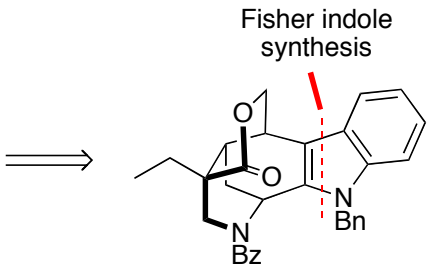
Scholarisine A

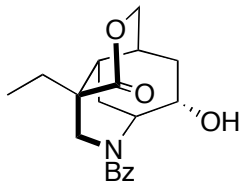


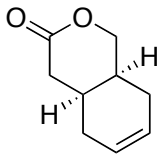
Scholarisine A











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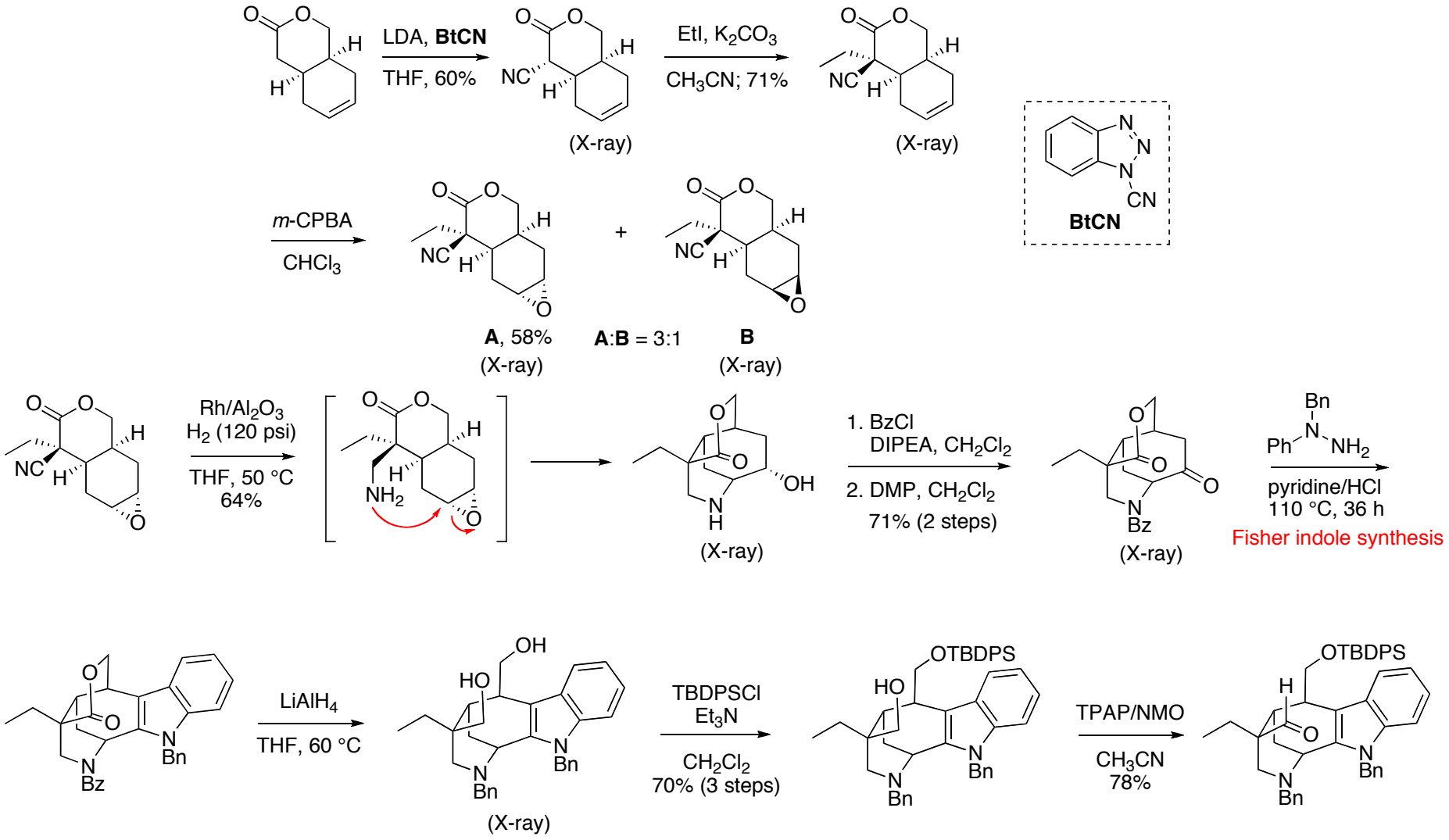
Smith's Approach: Construction of the Tetracyclic Alcohol



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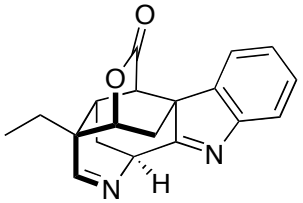
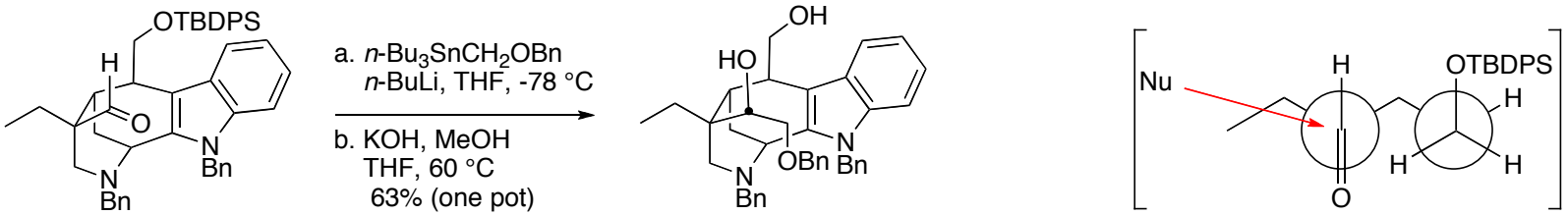
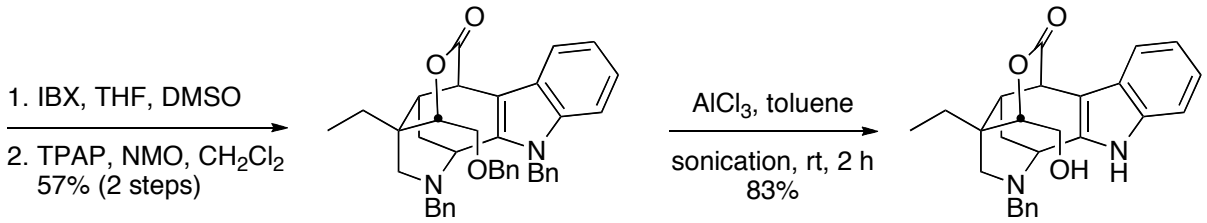
Addition of the Stannane Reagent: Formation of the Lactone



Scholarisine A





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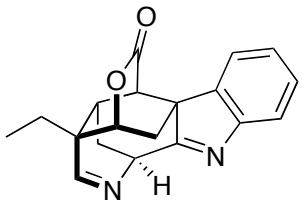
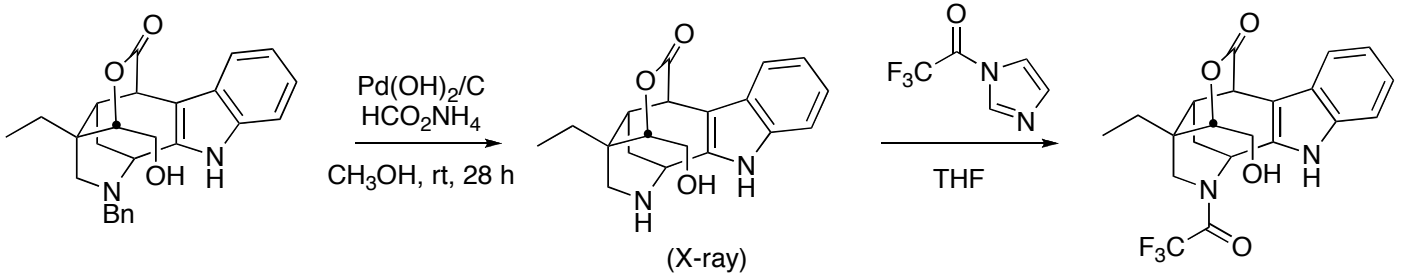
Scholarisine A: End Game

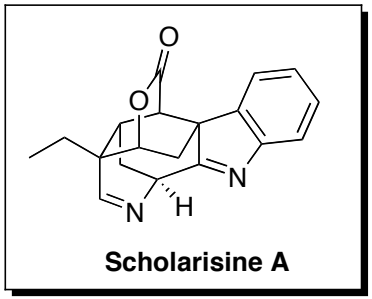


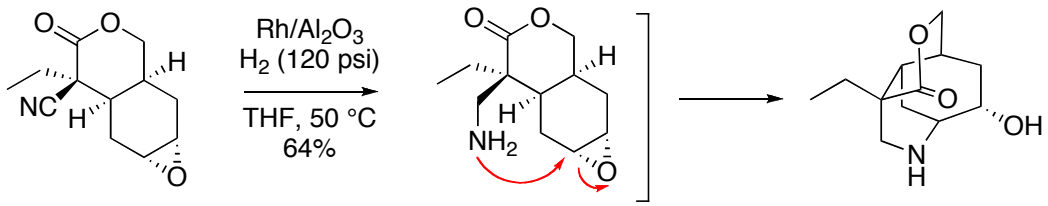
Scholarisine A



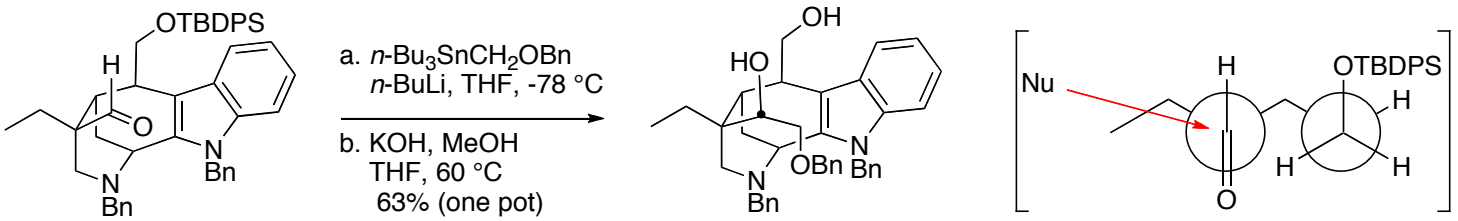
Conclusions

- Effective total synthesis of (+)-Scholarisine A (20 setps)
- Novel route: "retro-biosynthetic" fragmentation
- Nitrile reduction on Rh/Al_2O_3 – epoxide opening cascade





- Facial selectivity in the stannane reaction: model based on NMR-studies



- Intramolecular cyclization leads to the indolenine ring of Scholarisine A