Christian Gloor
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Enantioselective total synthesis of (+)-alsmaphorazine E

K. Yu, B. Gao, Z. Liu and H. Ding
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Isolation, Structure and biological activity

- Alsmaphorazine E was isolated in 2012 from the leaves of *Alstonia pneumatora* among 2 other new biogenetically related compounds.

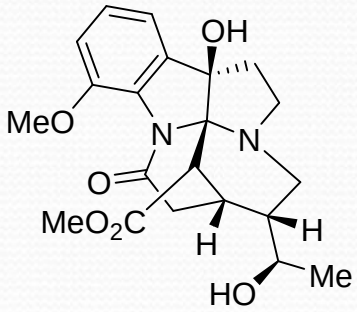
- Extracts of *Alstonia* plants are used in folk medicine for the treatment of various kinds of illnesses such as bleeding, fever, malaria and cancer

- The isolated compounds of *Alstonia* plants are characterized as unique heterocyclic alkaloids containing a monoterpene indole skeleton.

Isolation, Structure and biological activity

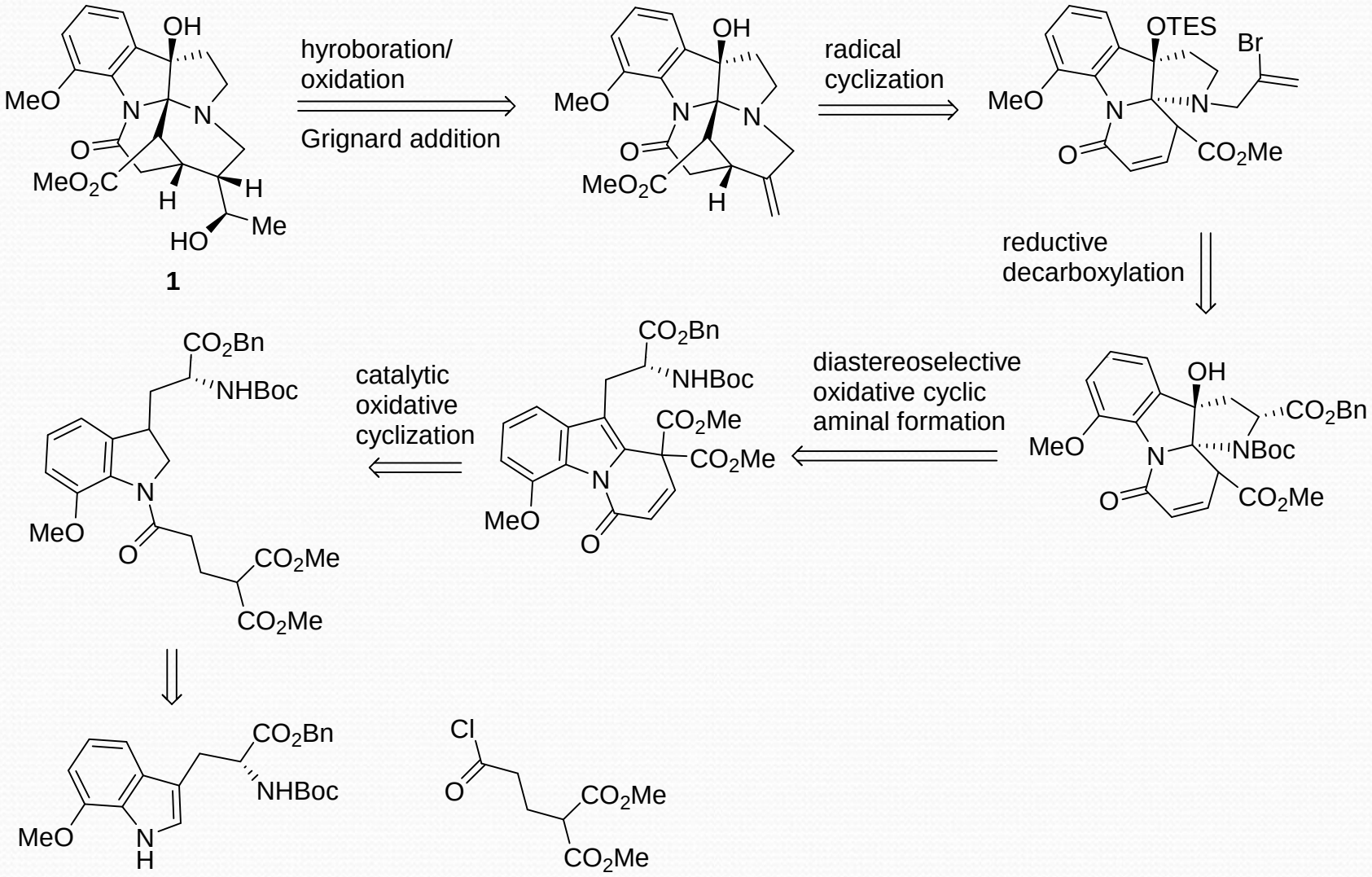
- (+)-alsmaphorazine E is composed of a hexahydropyrrolo[2,3-*b*]pyrrole fused diazabicyclo[3.3.1]nonane

- Six contiguous stereogenic centers and a benzylic tertiary alcohol

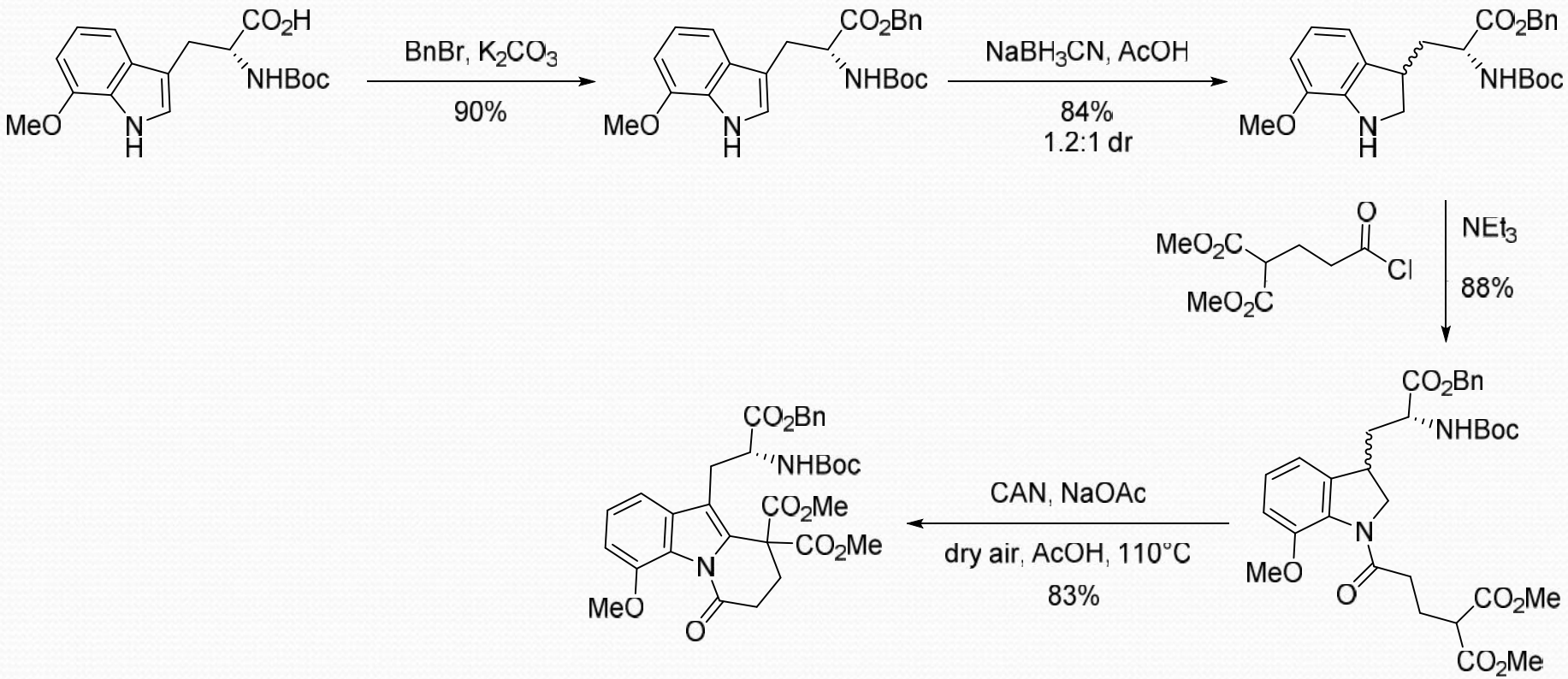


(+)-alsmaphorazine E

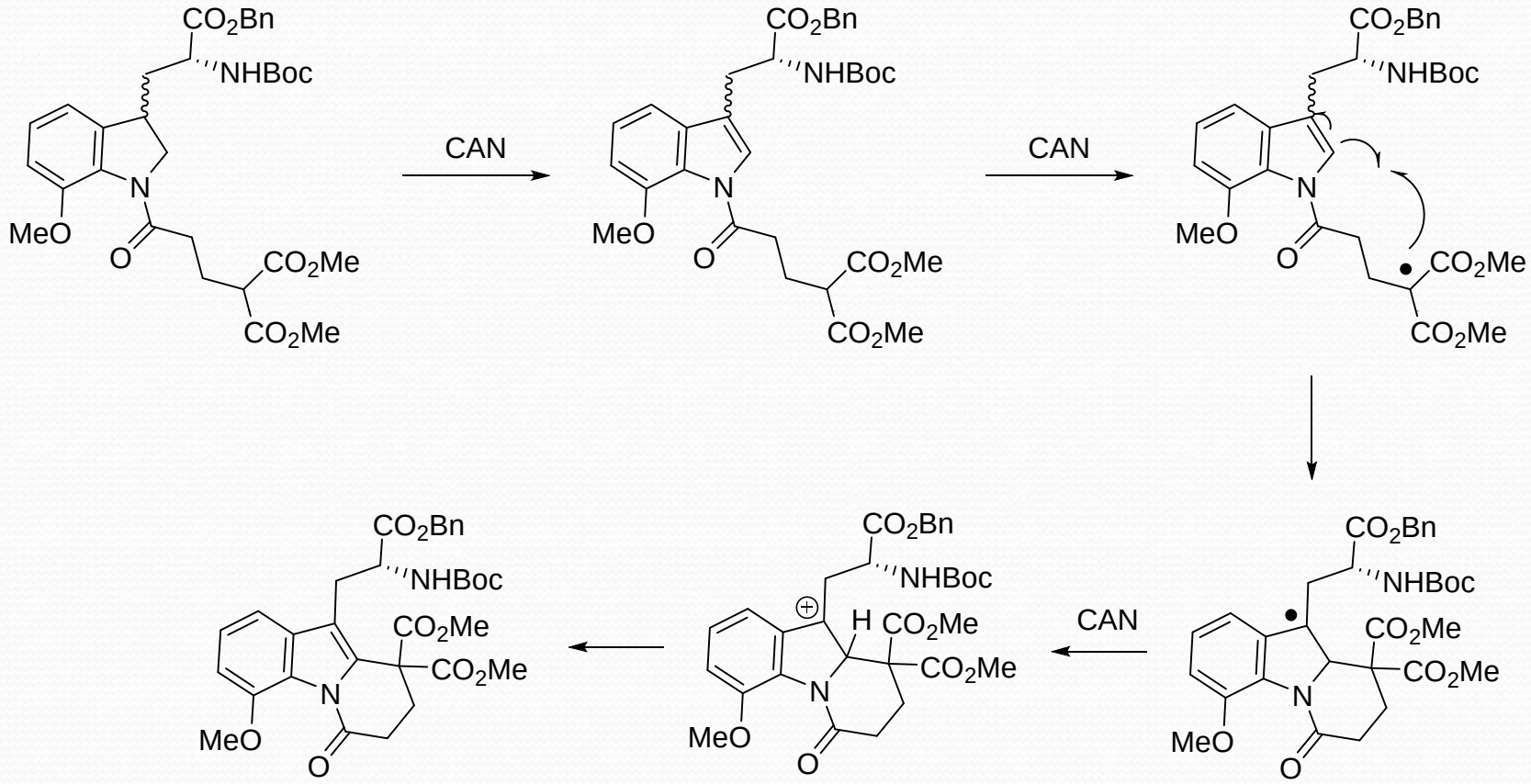
Retrosynthetic analysis



Synthetic approach

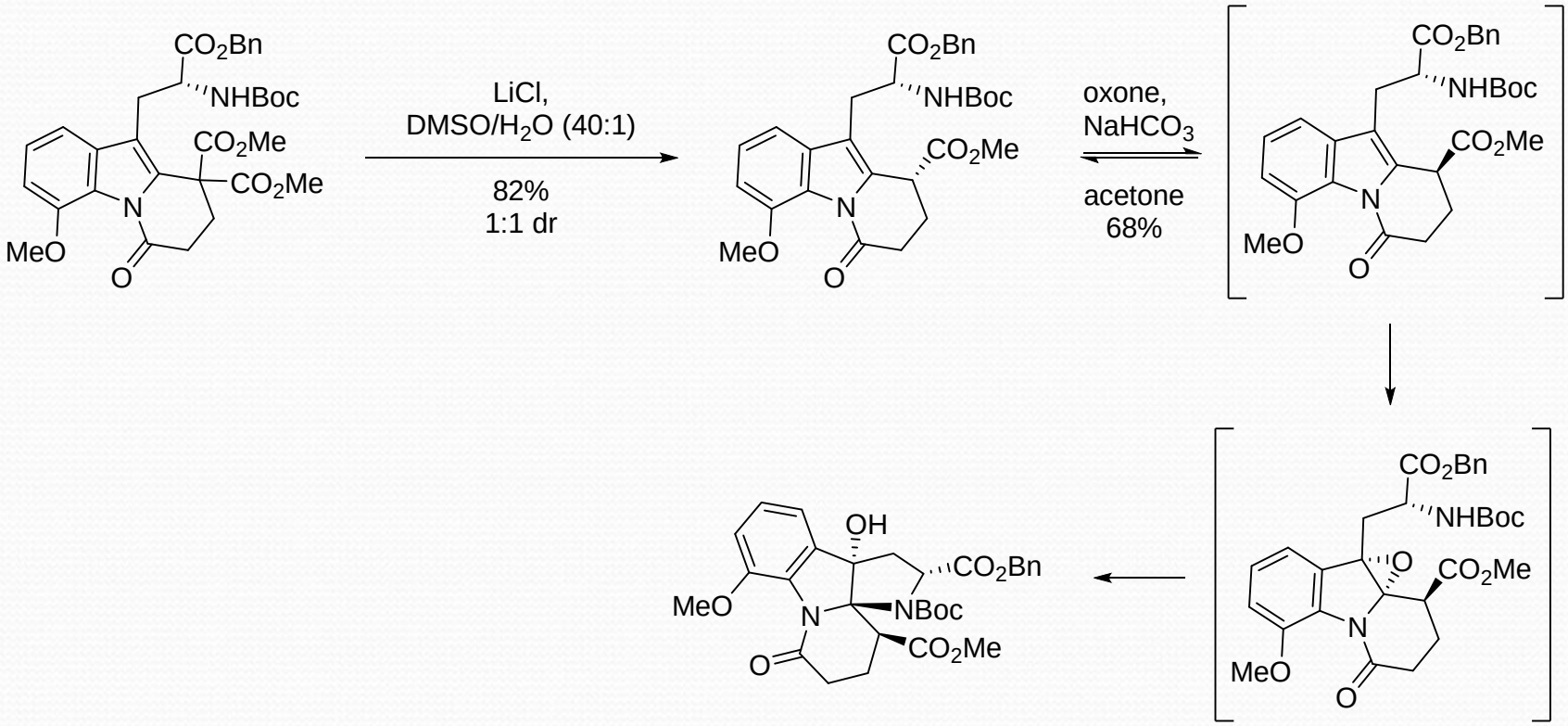


Catalytic tandem indoline oxidation/malonic radical cyclization

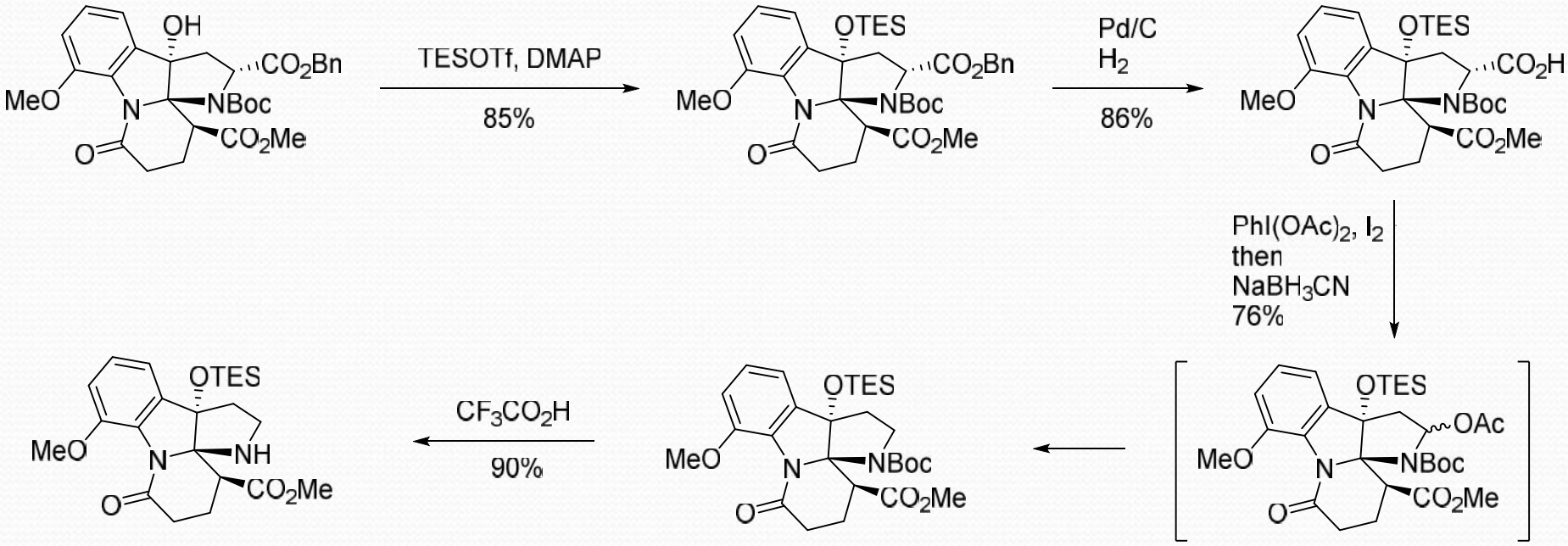


C. Zhu, Z. Liu, G. Chen, K. Zhang, H. Ding, *Angew. Chem. Int. Ed.* **2015**, *54*, 879
J. Magolan, M. A. Kerr, *Org. Lett.* **2006**, *8*, 4561

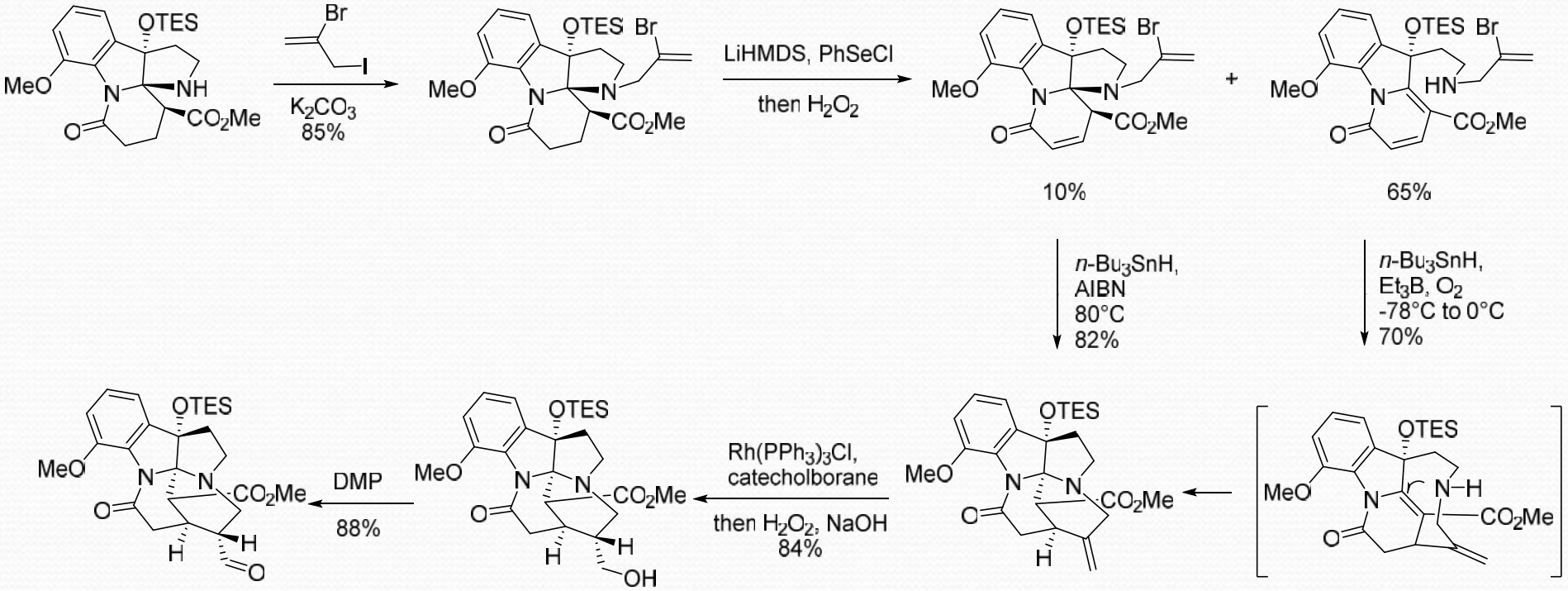
Synthetic approach



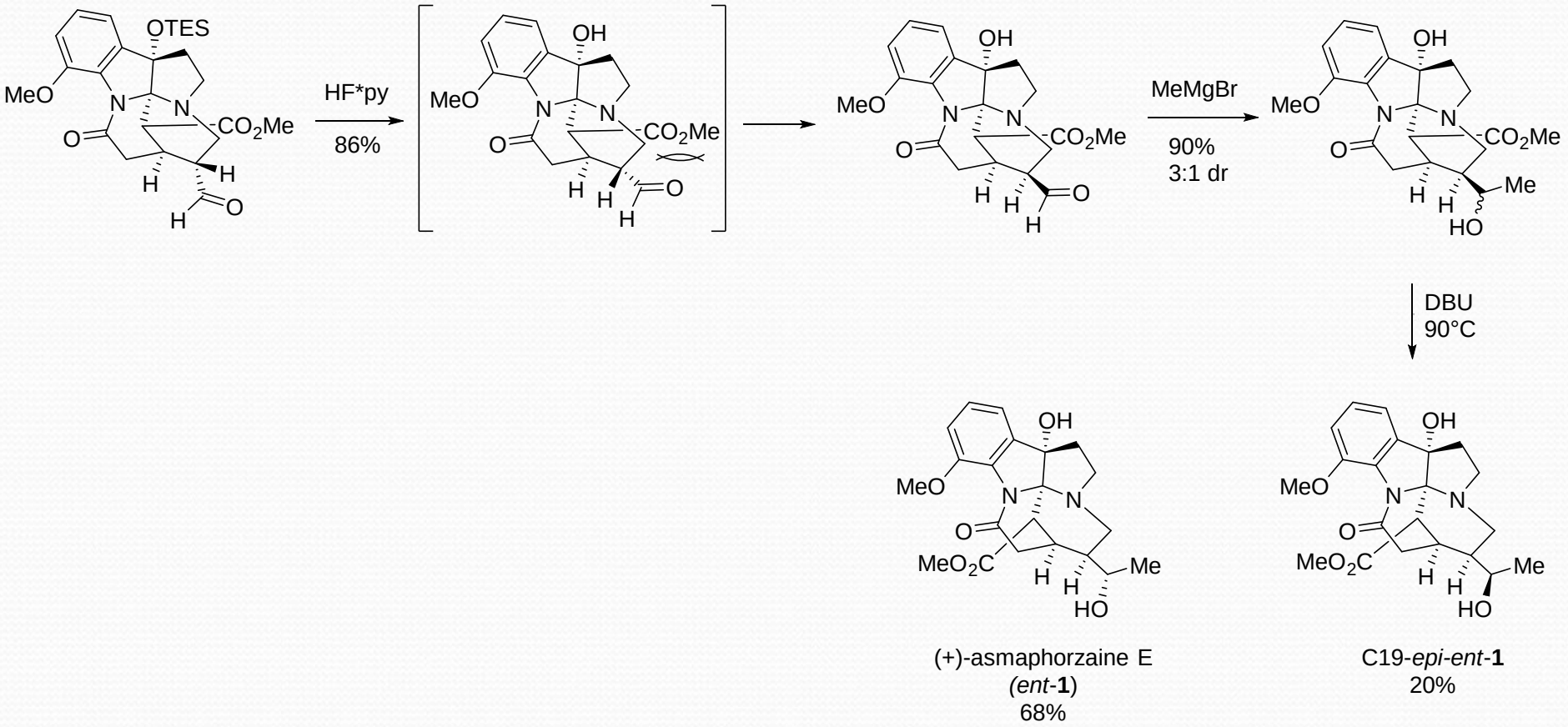
Synthetic approach



Synthetic approach



Synthetic approach



(+)-asmaphorzaine E
(*ent*-**1**)
68%

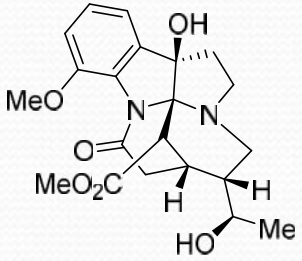
C19-*epi*-*ent*-**1**
20%

Conclusion

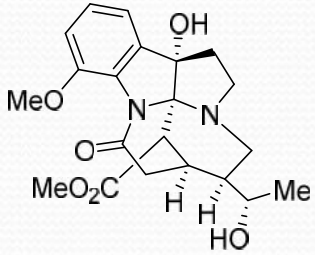
total synthesis was achieved with 14 steps and an overall yield of 1.2%

Key steps are :
- CAN-catalyzed intramolecular oxidative cyclization
- Diastereoselective oxidative cyclic aminal formation
- radical cyclization/transannular aza-Michael addition cascade

The synthesis led to a structural reassignement of the natural product



original proposed structure



(+)-asmaphorzaine E

Thank you for your attention