

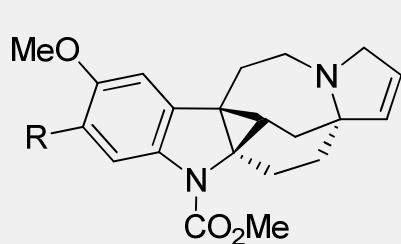
# Total Synthesis of (±)-Lundurine B

M. Hoshi, O. Kaneko, M. Nakajima, S. Arai, A. Nashida *Org. Lett.* **2014**, *16*, 768-771.

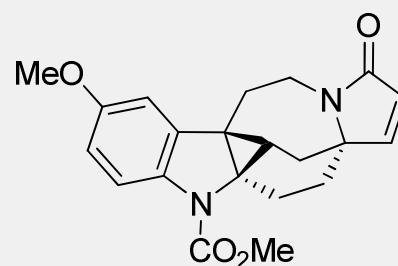
# Introduction

## Lundurines

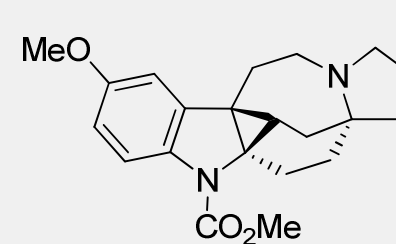
- Isolated from *Kopsia Tenuis* By Kam *et al.* in 1995



R = H: Lundurine B  
R = OMe: Lundurine D



Lundurine A



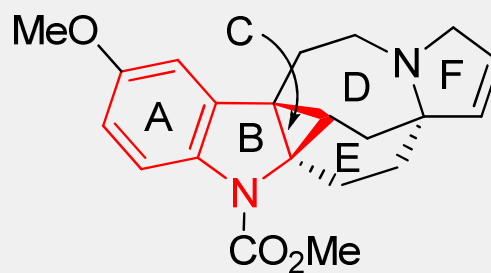
Lundurine C

- Biological activities: toxicity against B16 melanoma cells and reverse multidrug resistance in vincristine-resistant KB cells
- No other synthesis reported to date

# Introduction

## (±)-Lundurine B

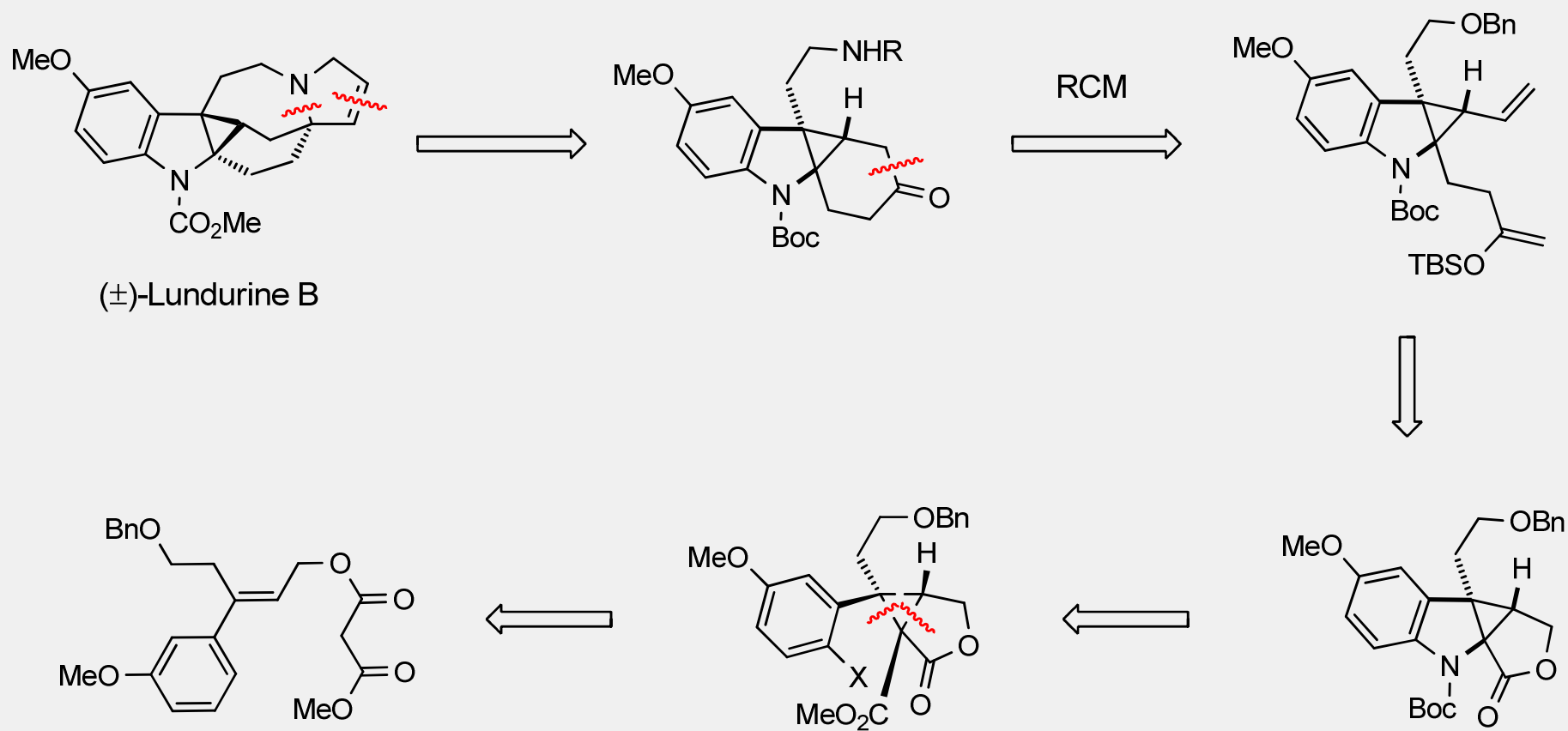
- Unique polycyclic skeleton:
  - Hexacyclic framework
  - Cyclopropane-fused indoline



Lundurine B

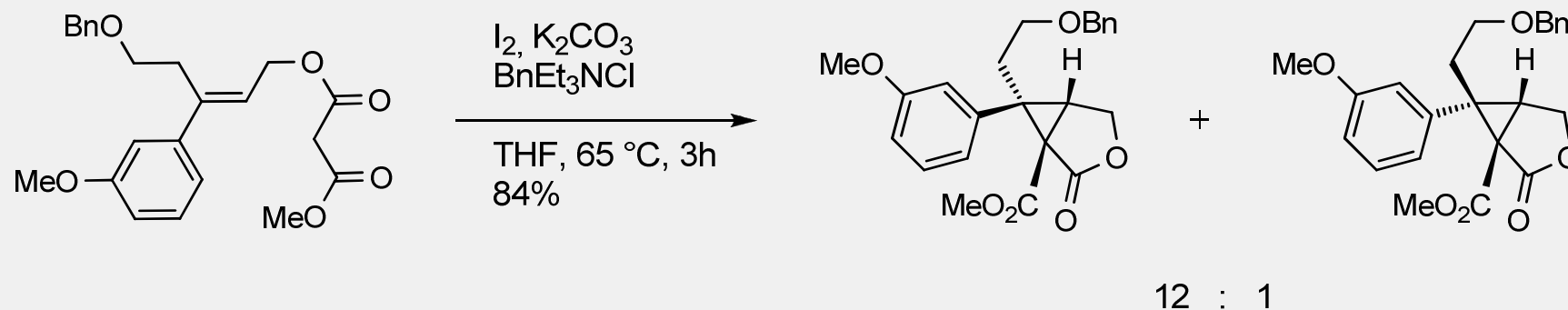
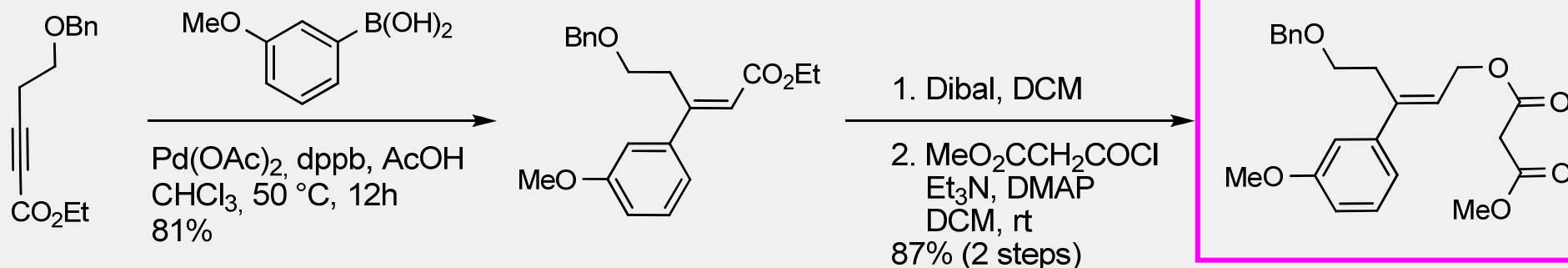
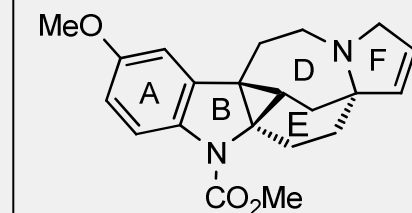
# Synthetic strategy

## Retrosynthesis



# Synthesis of ( $\pm$ )-Lundurine B

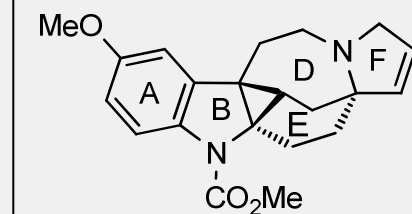
## Preparation of the cyclopropane-fused Indoline



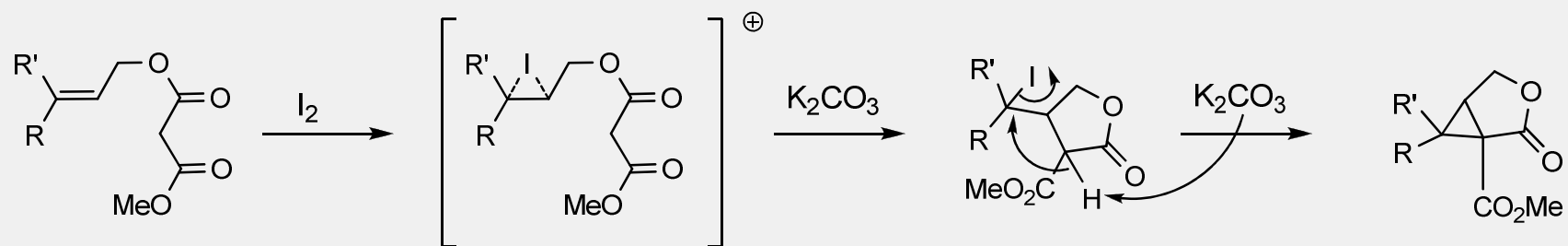
4

# Synthesis of ( $\pm$ )-Lundurine B

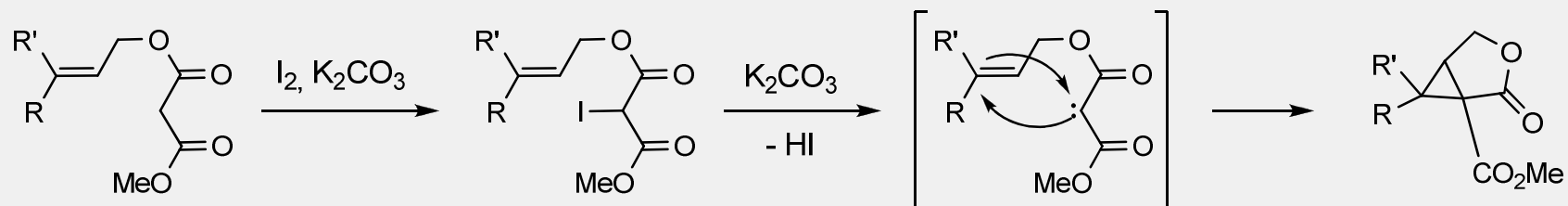
## Mechanism for the iodine-mediated cyclopropanation



### ➤ Ionic pathway

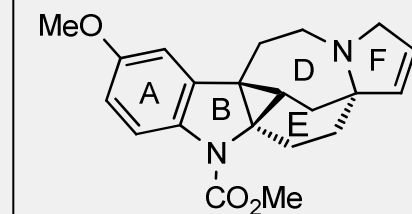


### ➤ « Triplet carbene » pathway

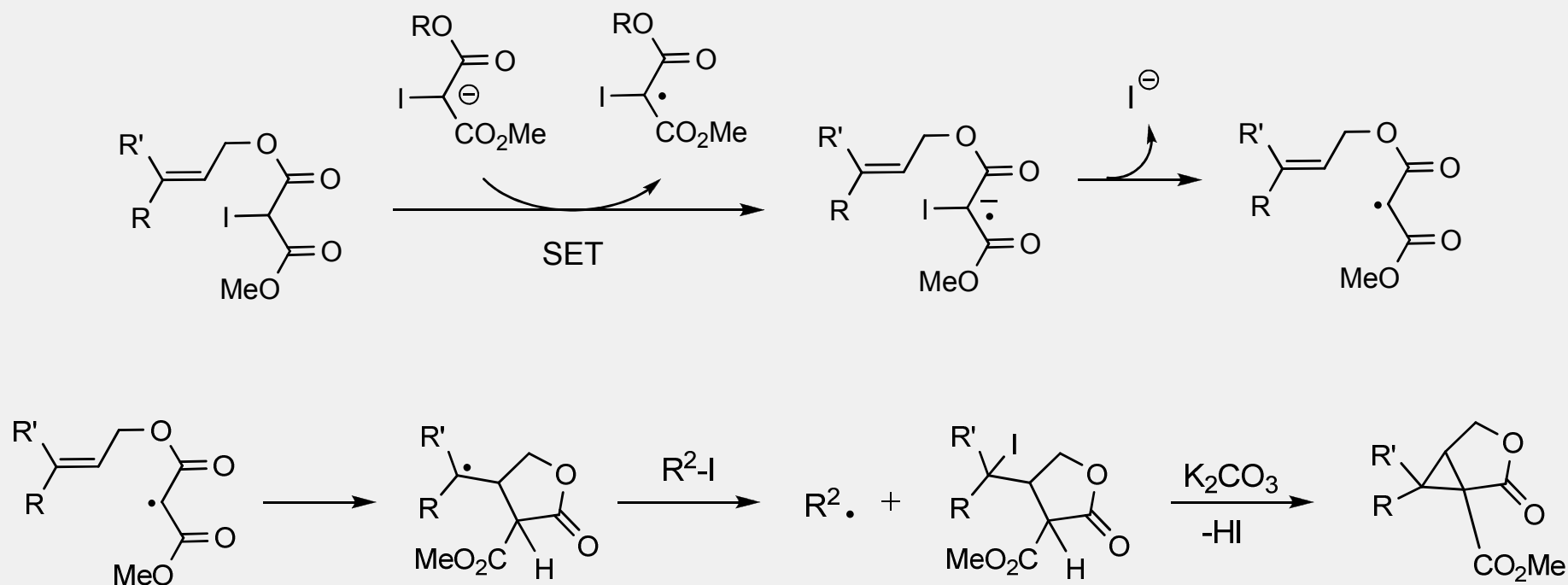


# Synthesis of ( $\pm$ )-Lundurine B

## Mechanism for the iodine-mediated cyclopropanation

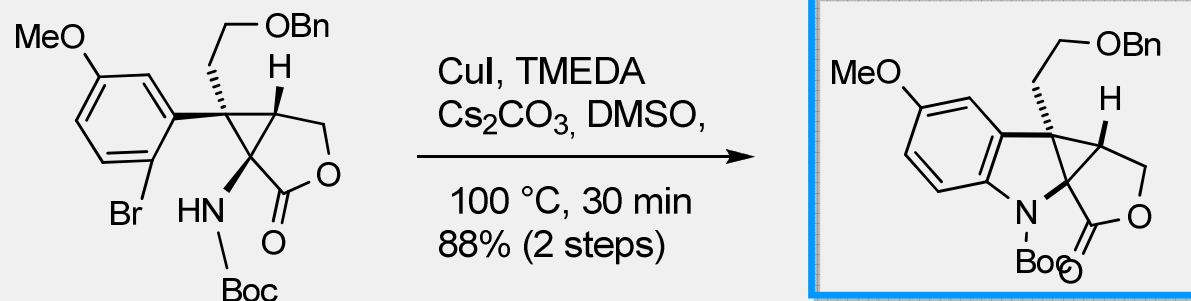
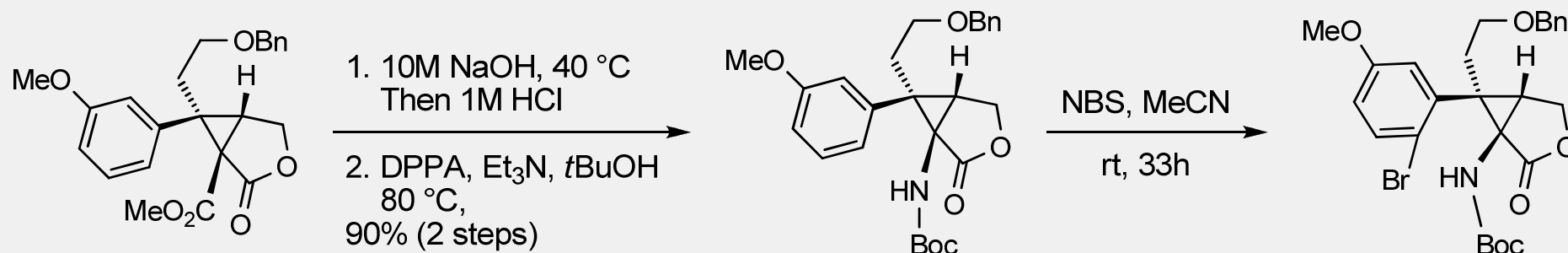
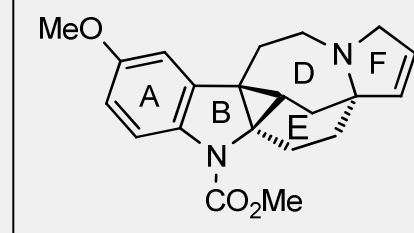


### ➤ Radical pathway



# Synthesis of ( $\pm$ )-Lundurine B

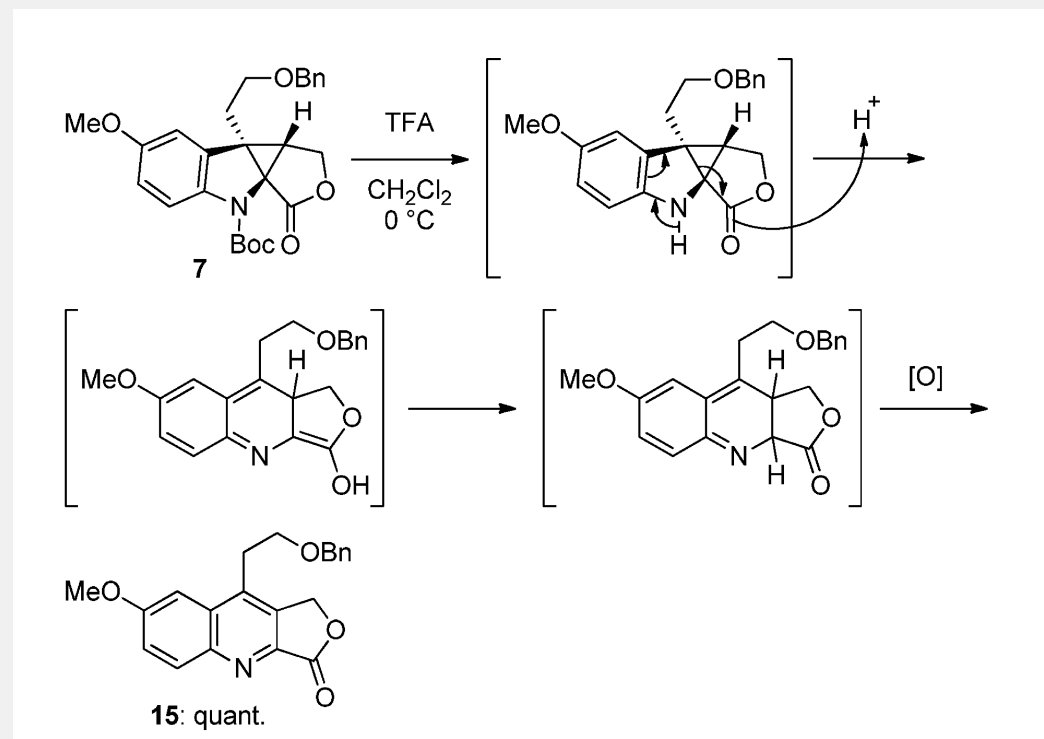
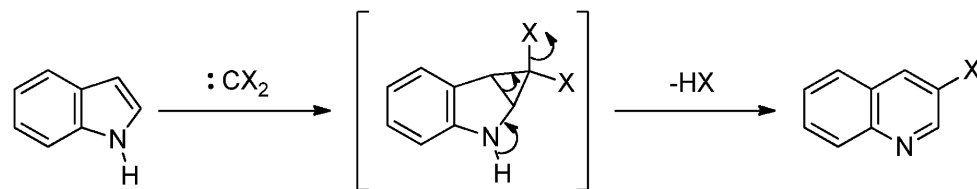
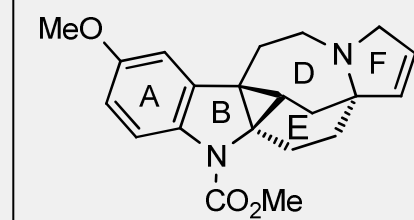
## Preparation of the cyclopropane-fused Indoline





# Synthesis of ( $\pm$ )-Lundurine B

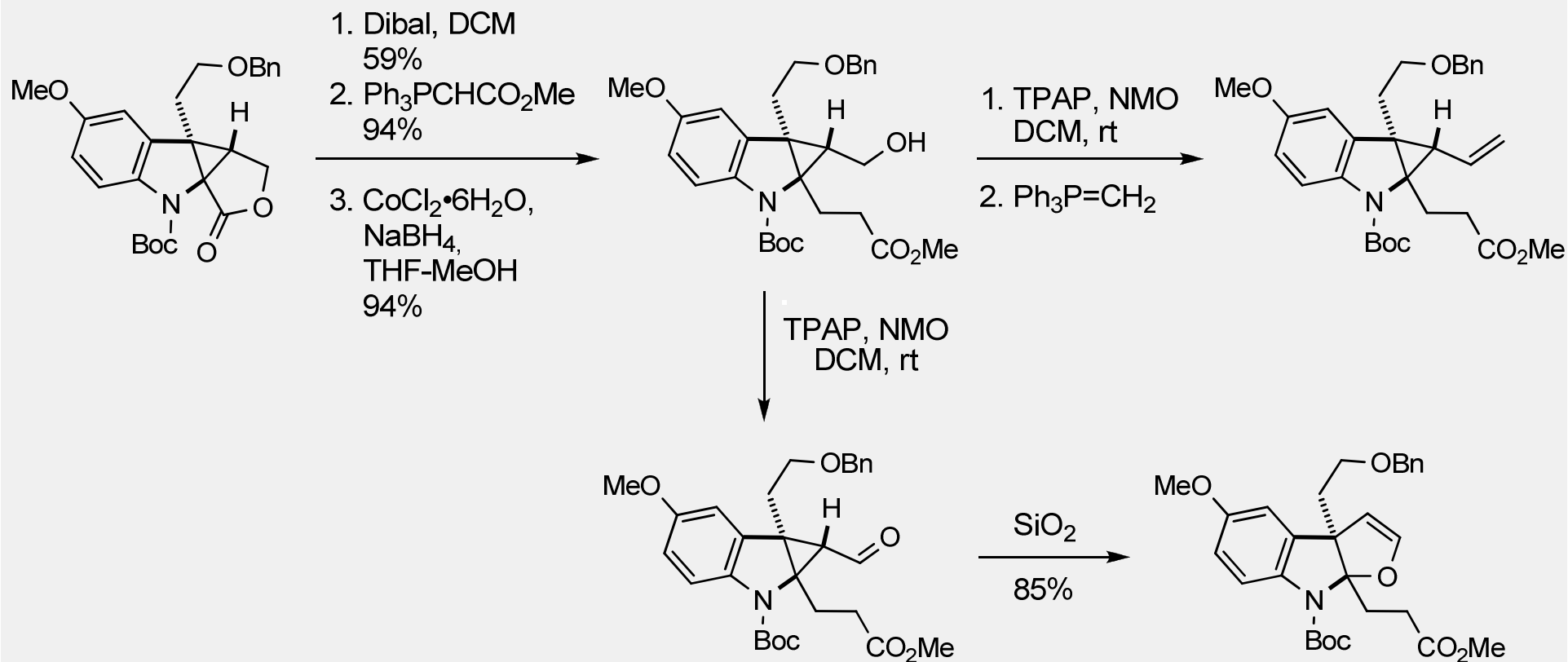
## Rearrangement of cyclopropane-fused Indolines



➤ Removal of the Boc group = rearrangement

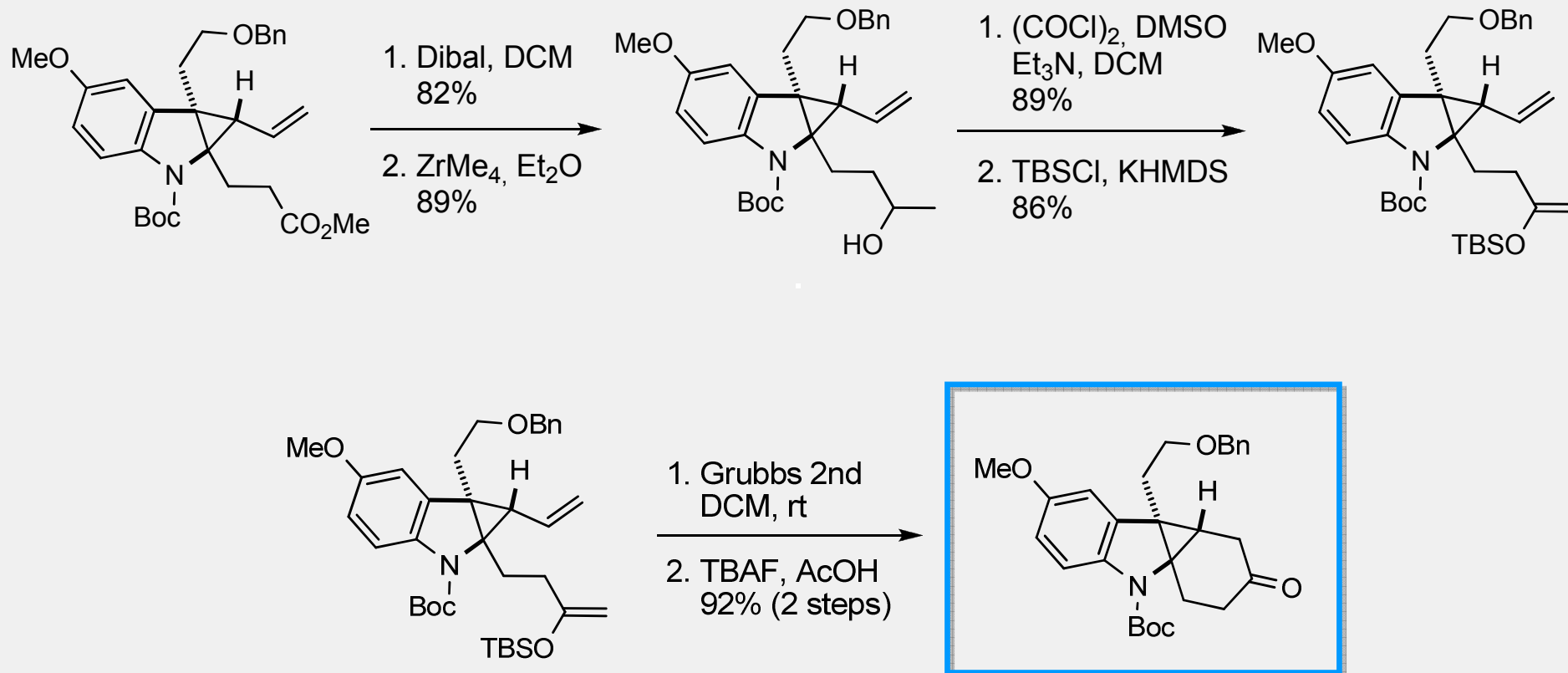
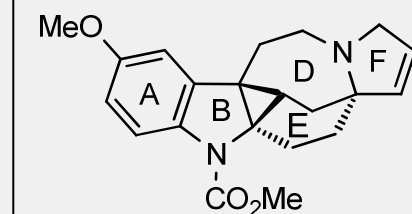
# Synthesis of ( $\pm$ )-Lundurine B

## Synthesis of ABCE-Core



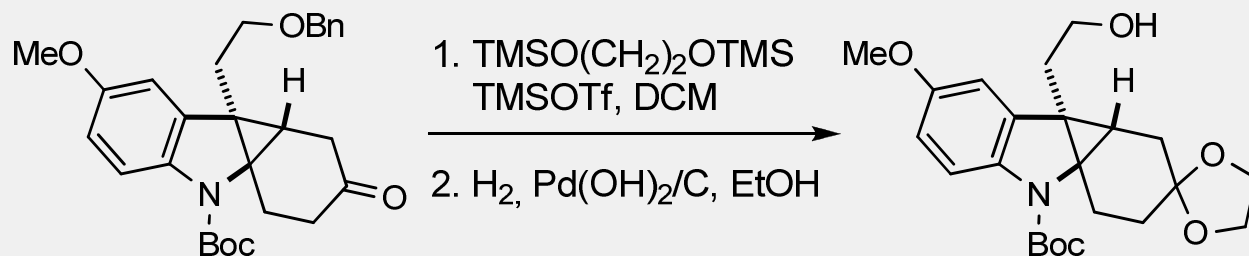
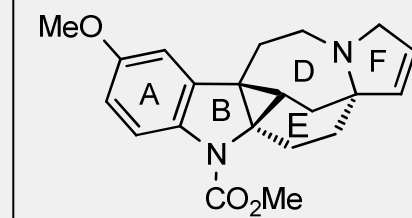
# Synthesis of ( $\pm$ )-Lundurine B

## Synthesis of ABCE-Core

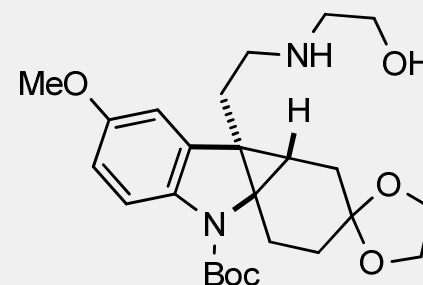
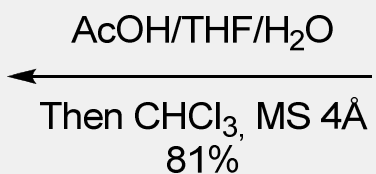
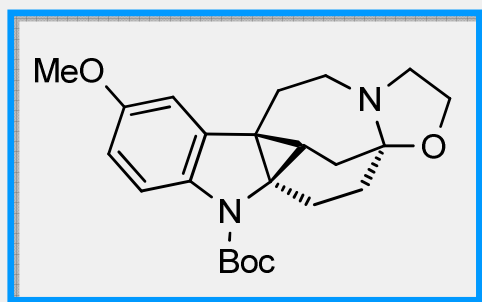


# Synthesis of ( $\pm$ )-Lundurine B

## Formation of the D and F rings

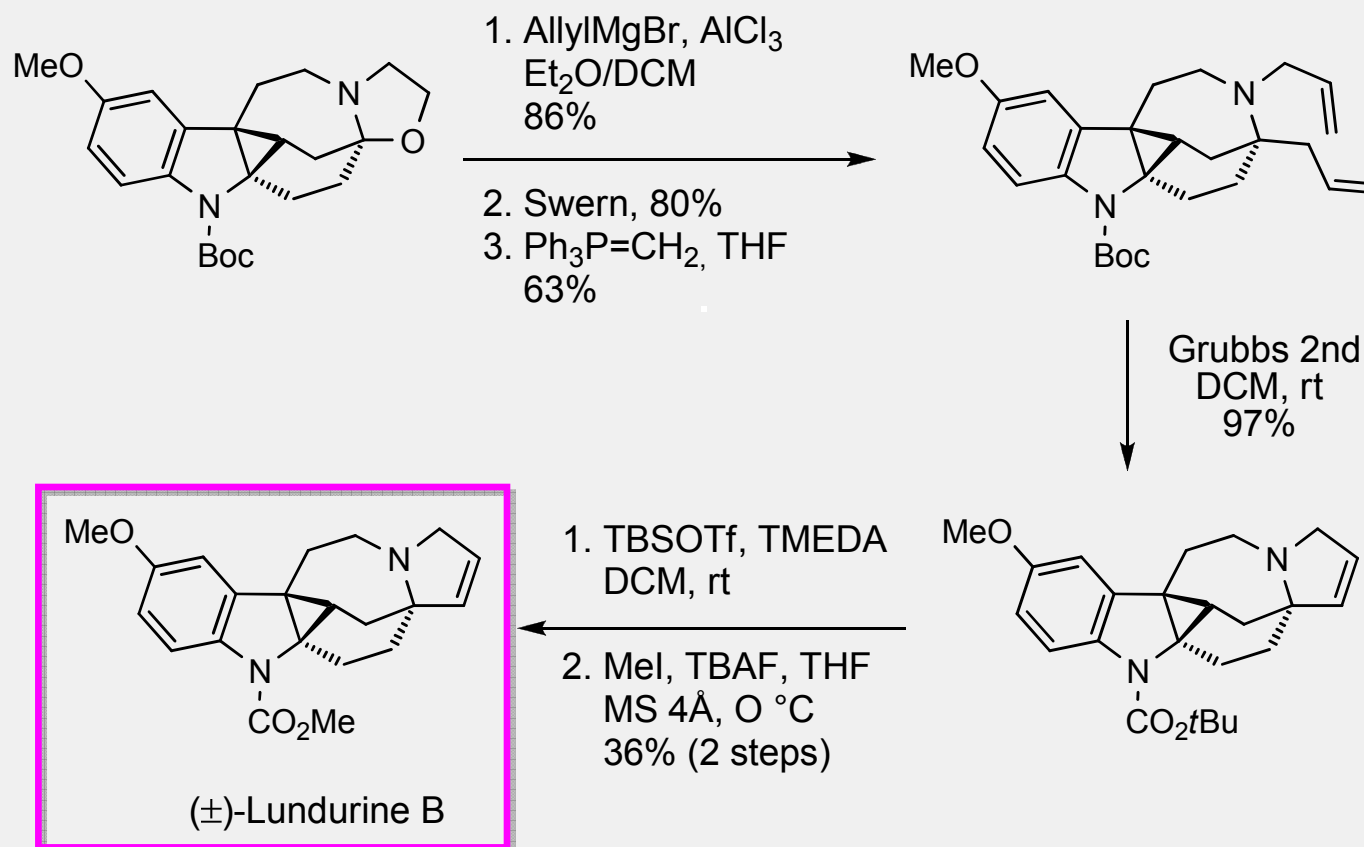
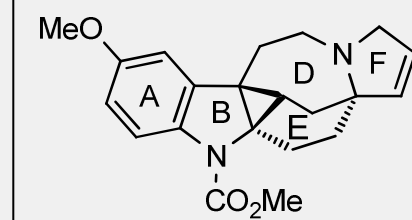


3. Swern [O]  
83% (3 steps)
4. 2-aminoethanol, MeOH  
Then NaBH<sub>4</sub>



# Synthesis of ( $\pm$ )-Lundurine B

## Formation of the D and F rings



# Conclusion

- Fused indole-Cyclopropane skeleton formation
- avoid acidic rearrangement to quinoline
- Low conversion for the last step, but interesting transcarbamation

Thanks for your attention