

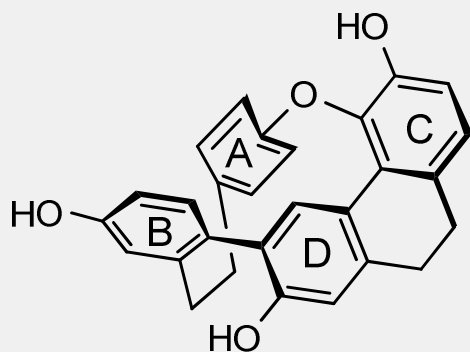
# Synthesis of Cavicularin by a Symmetrization/Assymetrization Approach

K. Suzuki *et al.*, *Angew. Chem., Int. Ed.* **2013**, 52, Early View.

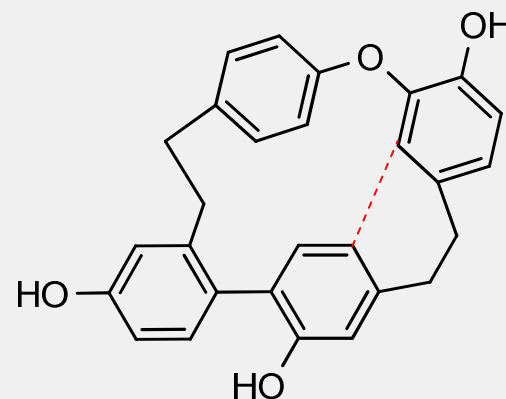
# Introduction

## Cavicularin

- Isolated from the *Cavicularia densa* by Asakawa and coworkers in 1996



Cavicularin



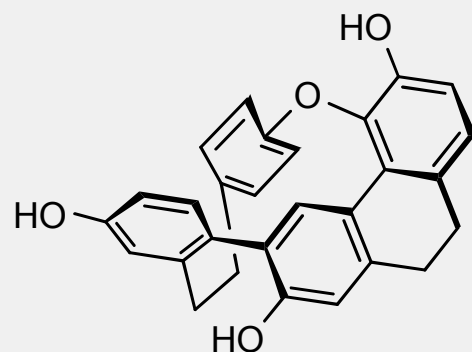
Riccardin C

- No asymmetric carbon, optical activity only derived from atropisomerism
- Polycyclophane ring, highly strained
- Riccardin C is a biosynthetic precursor of Cavicularin

# Introduction

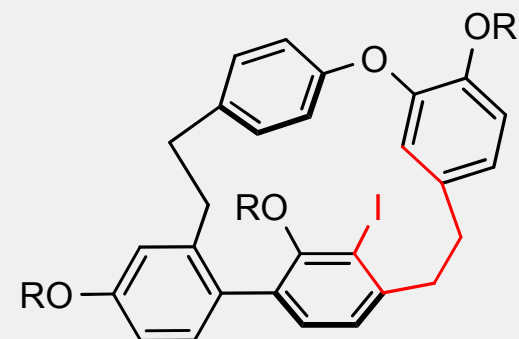
## Cavicularin

- 2 previously reported total syntheses:



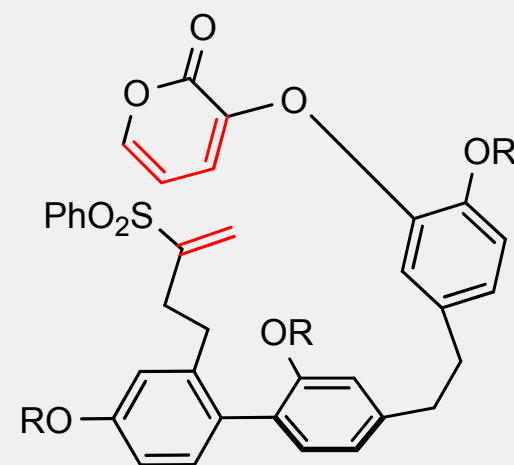
Harrowven

radical-induced  
transannular  
ring contraction



Beaudry

Pyrone  
Diels-Alder  
Reaction

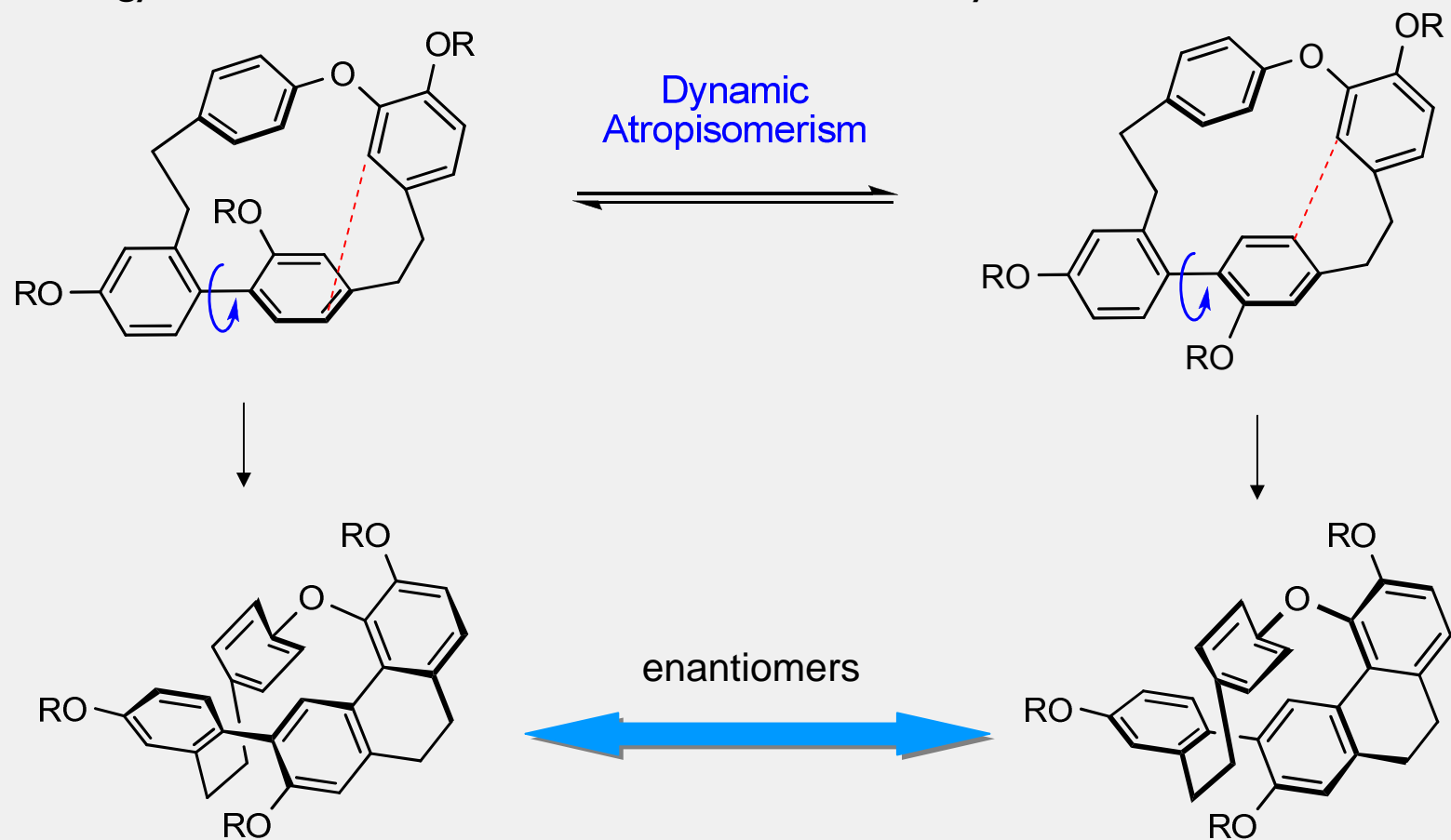


- No Asymmetric synthesis

# Introduction

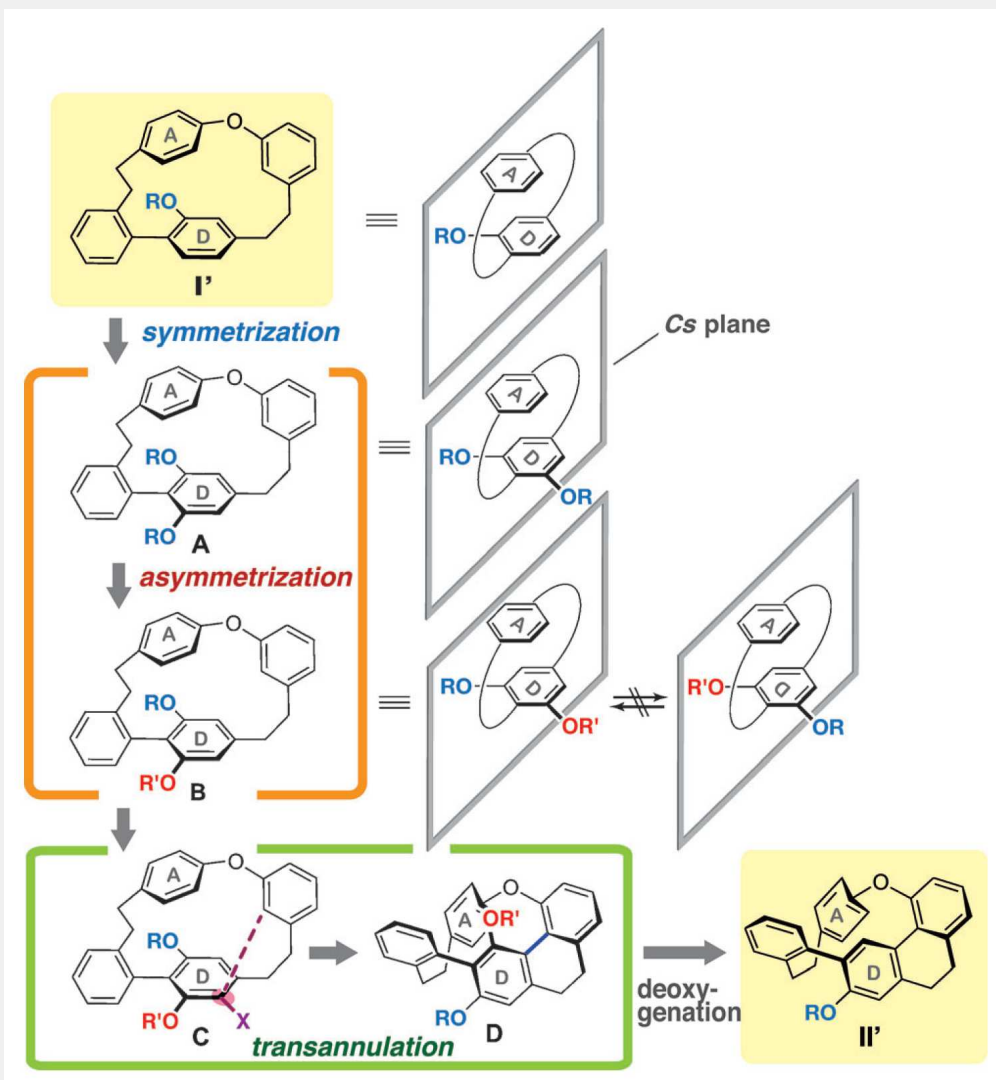
## Asymmetric synthesis by transannulation

- Strategy: Transannulation from Riccardin-like macrocycle



# Synthetic strategy

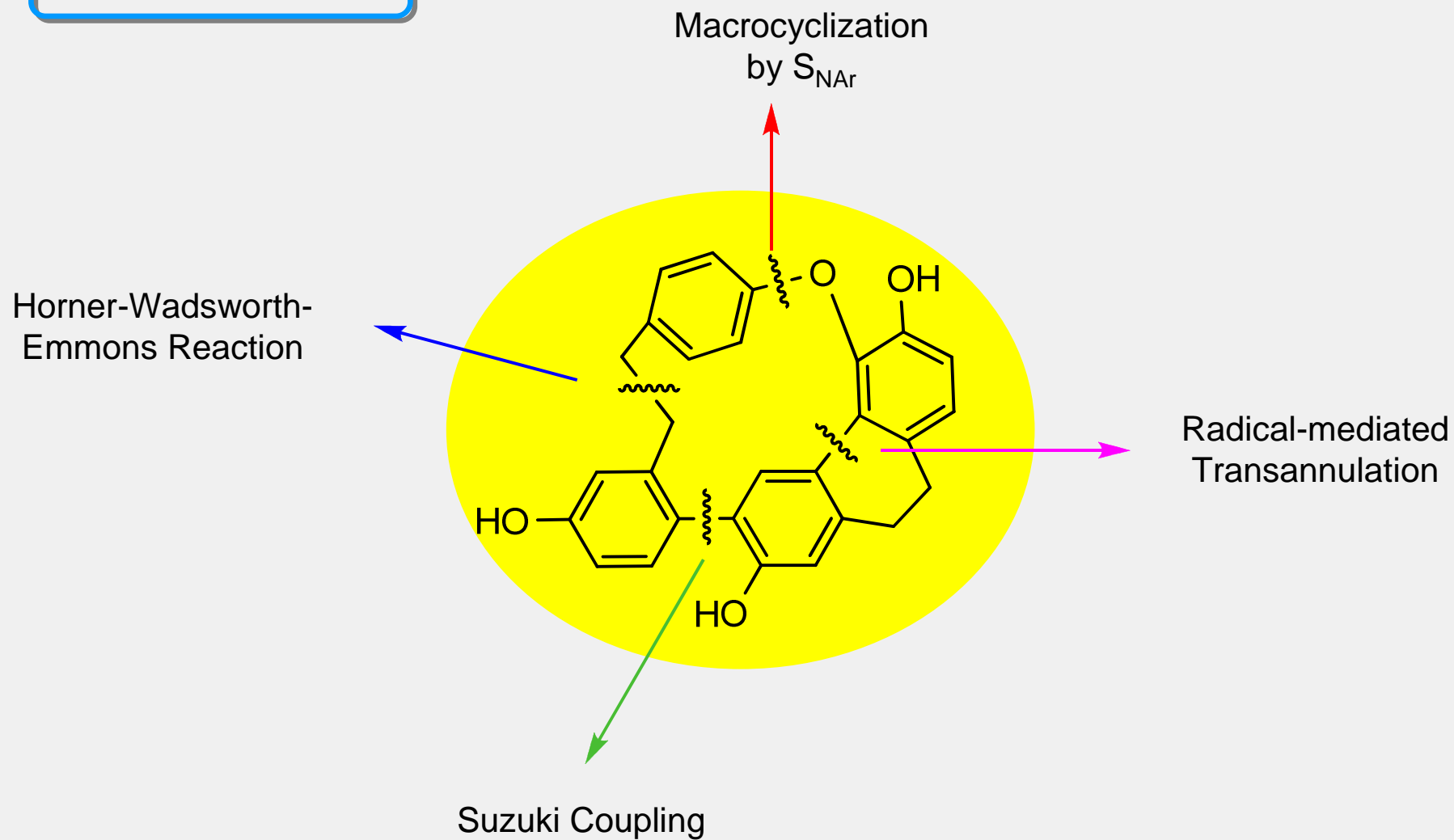
## Symmetrization/Asymmetrization strategy



1. Addition of an extra oxy-function
2. Induction of planar chirality
3. Introduction of X group to control regioselectivity
4. Transannulation
5. Removal of the extra oxy-function

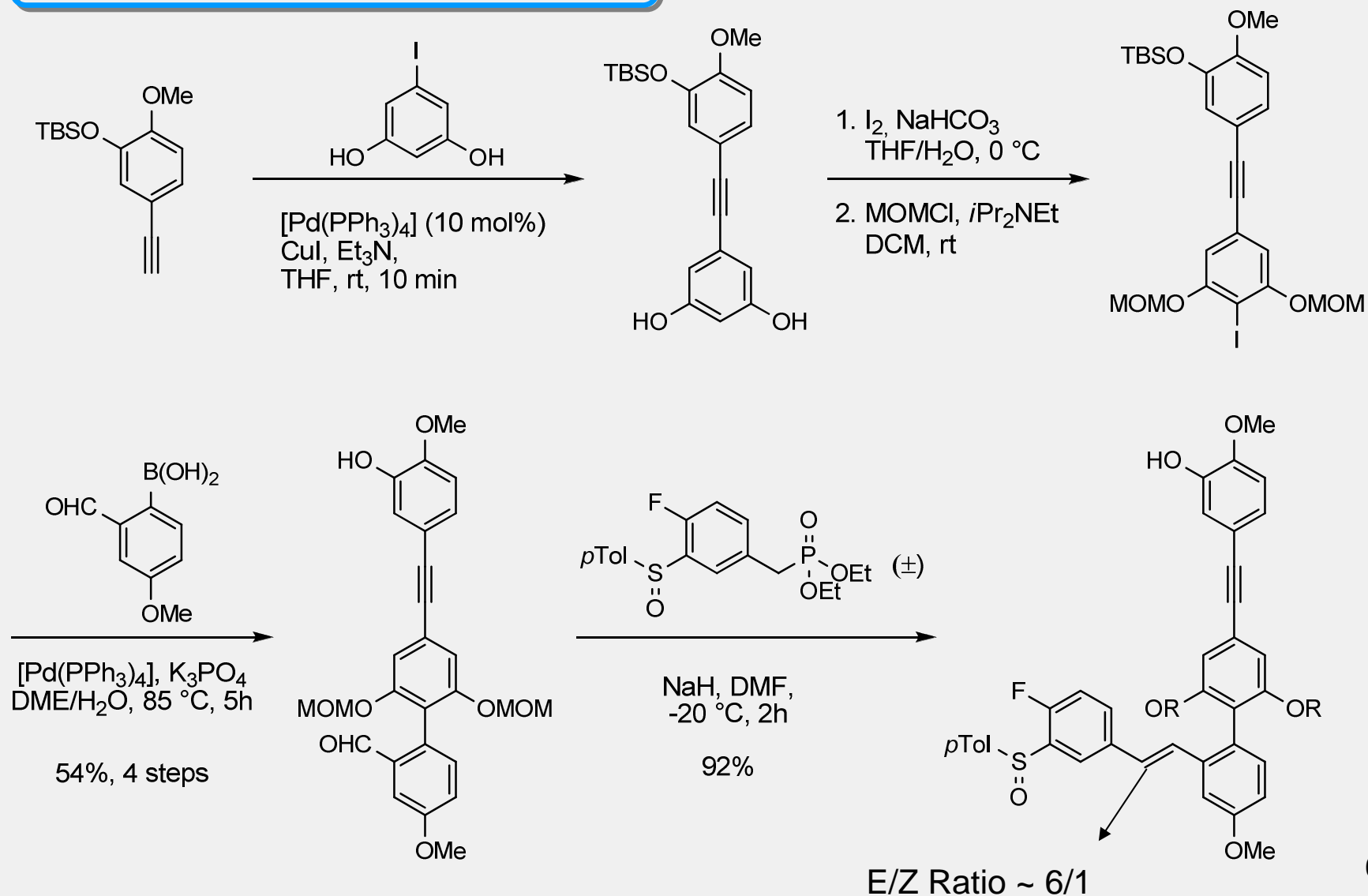
# Synthetic strategy

## Key disconnections



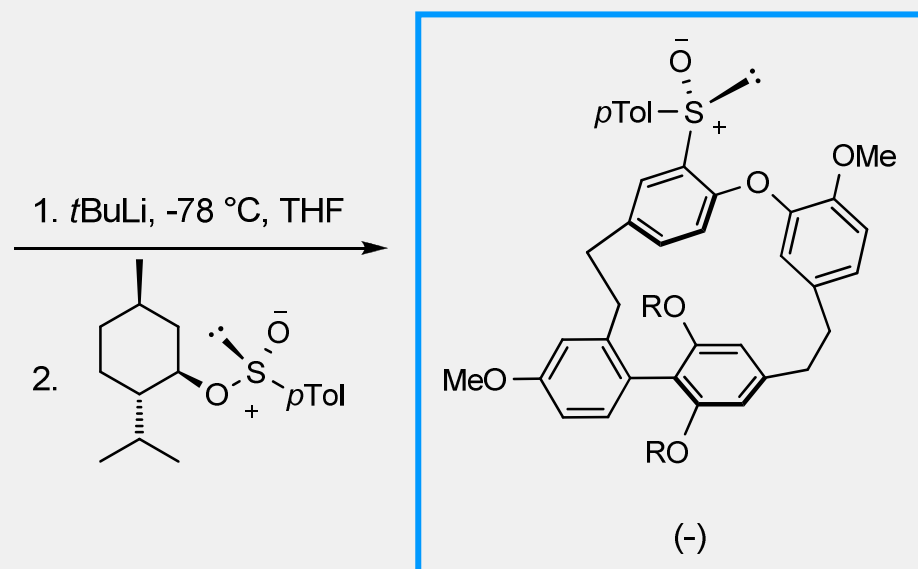
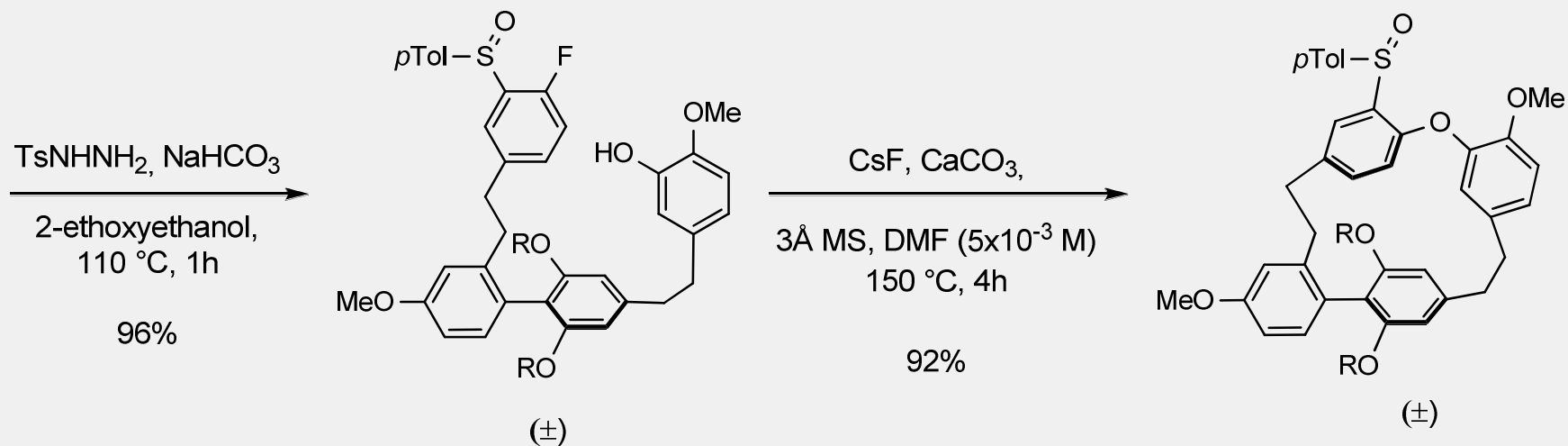
# Synthesis of (-)-Cavicularin

## Synthesis of the Riccardin-like Core



# Synthesis of (-)-Cavicularin

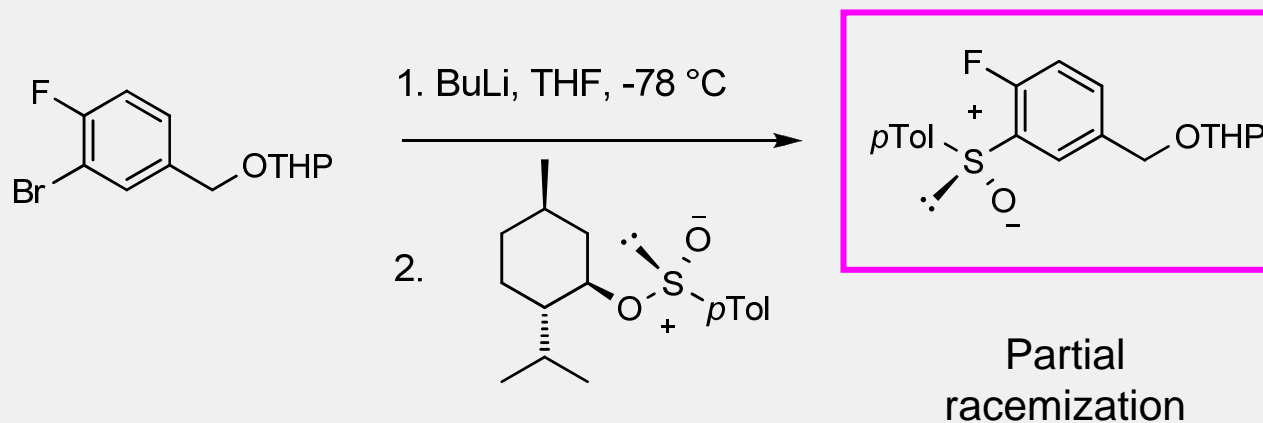
## Synthesis of the Riccardin-like Core





# Synthesis of (-)-Cavicularin

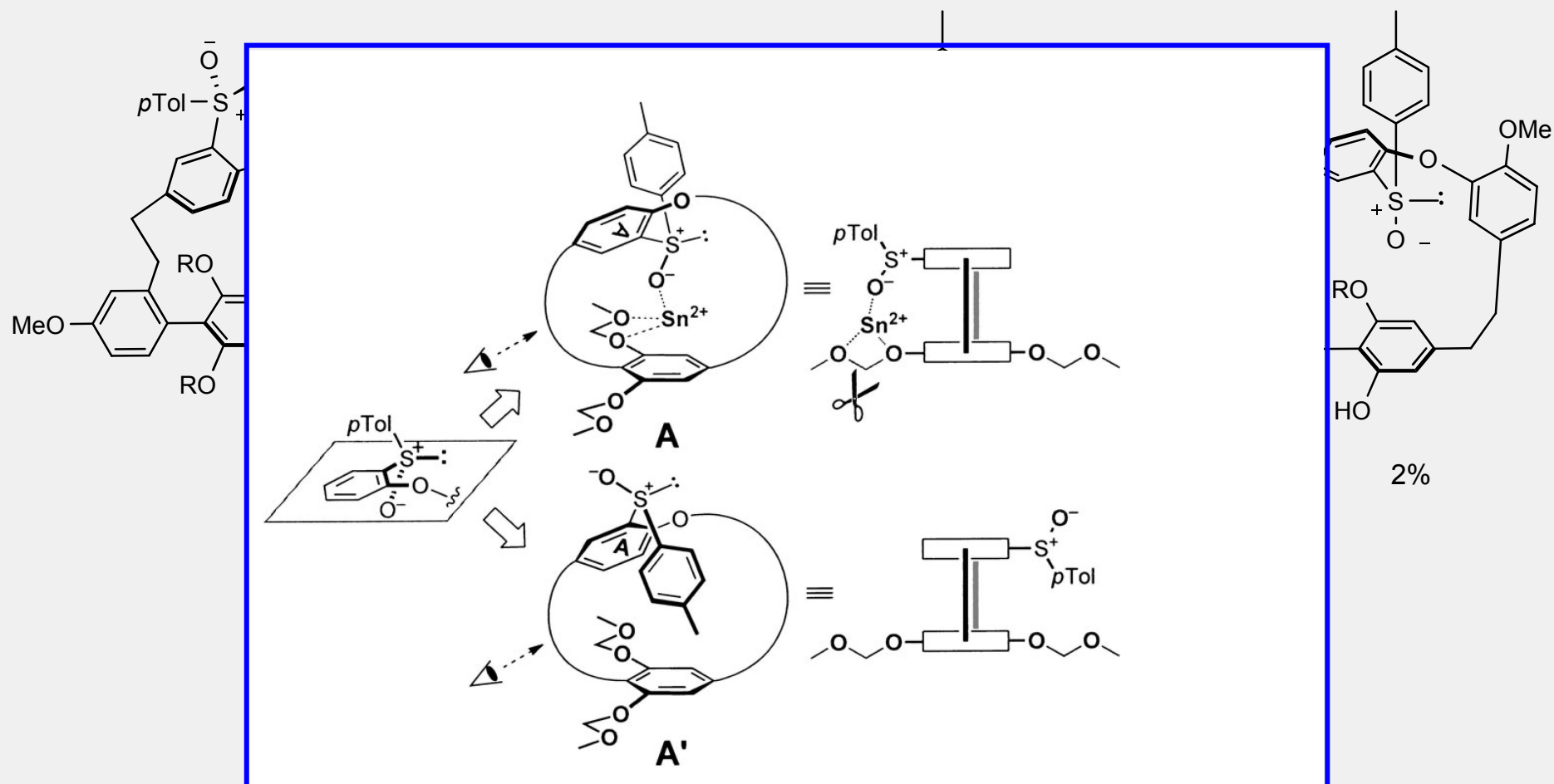
## Introduction of the chiral sulfoxide



Late-stage introduction

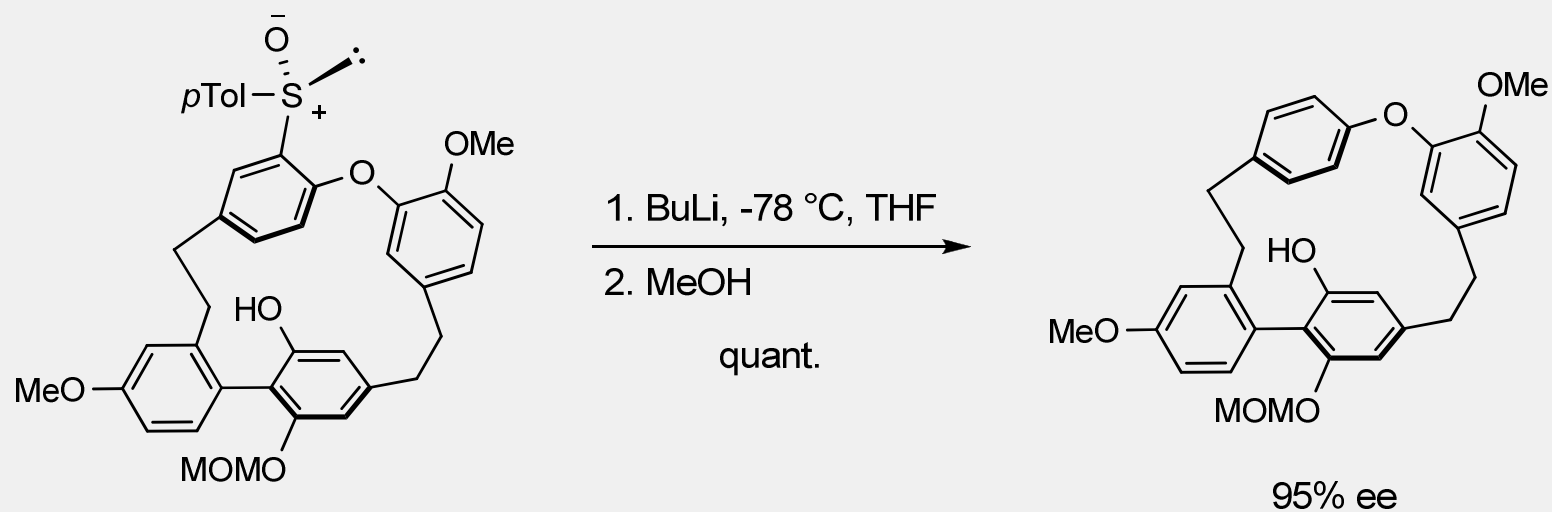
# Synthesis of (-)-Cavicularin

## Selective acetal cleavage



# Synthesis of (-)-Cavicularin

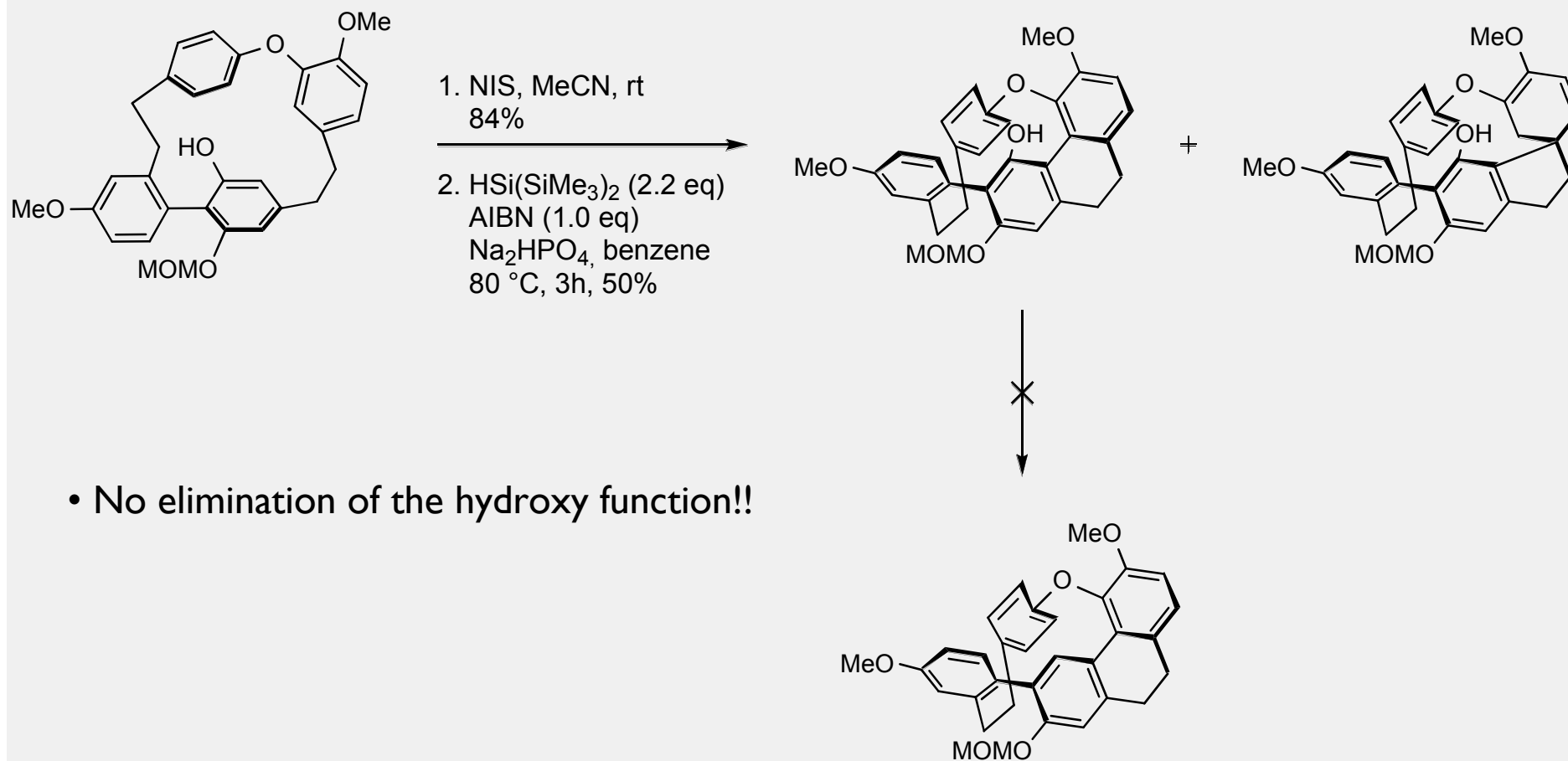
Removal of the chiral sulfinyl group



- No epimerization at 80 °C
- Only partial epimerization at 110 °C

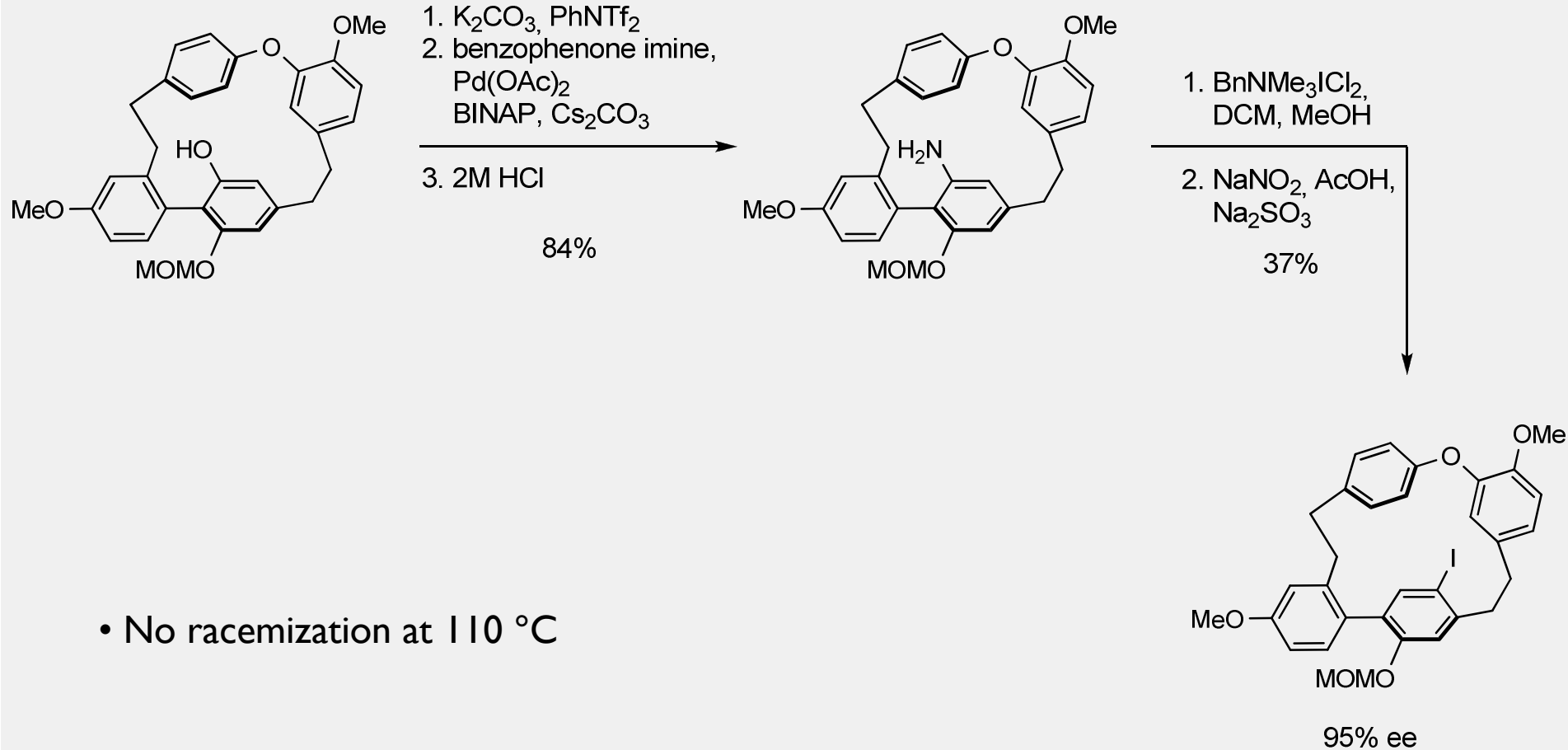
# Synthesis of (-)-Cavicularin

## Radical transannulation



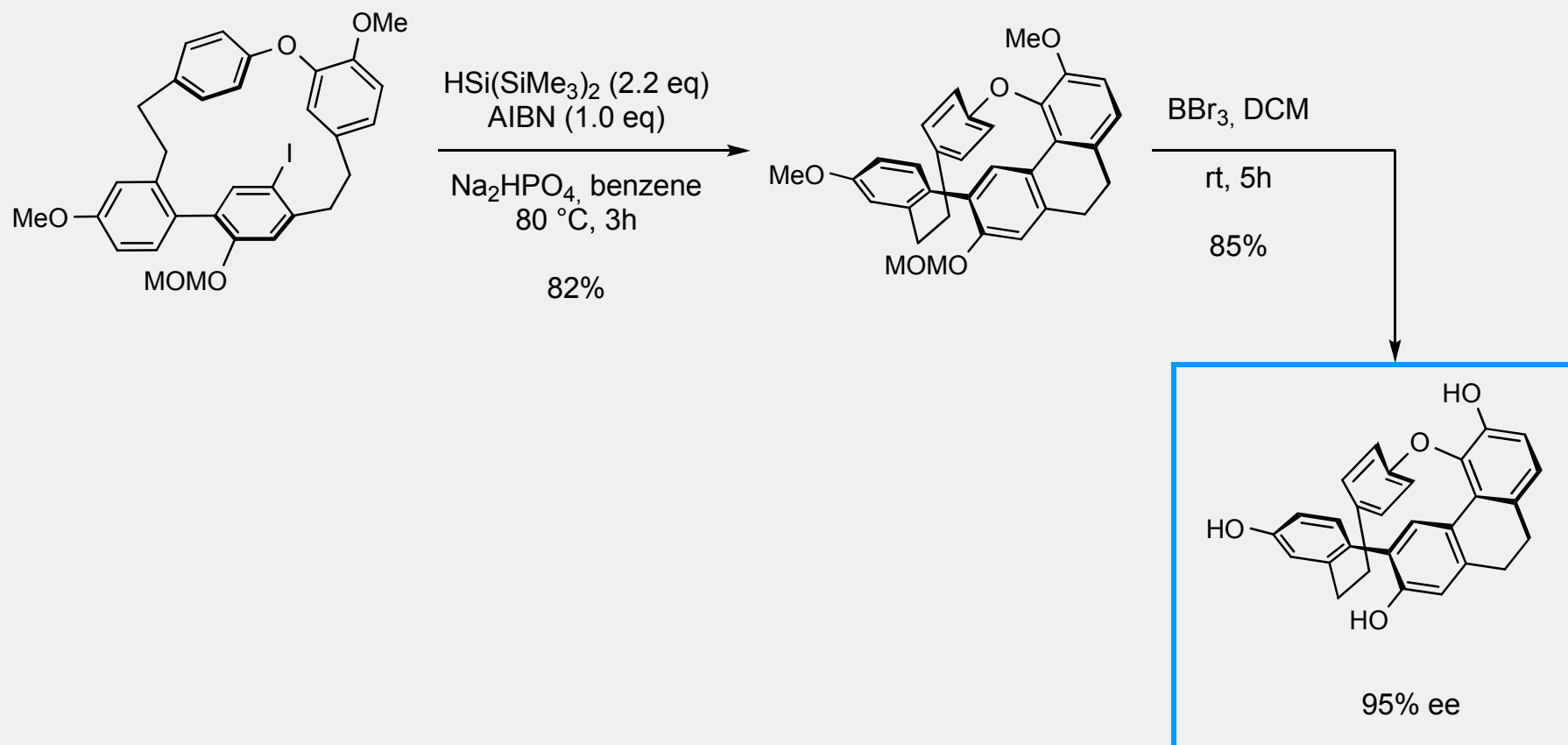
# Synthesis of (-)-Cavicularin

## Radical transannulation (2)



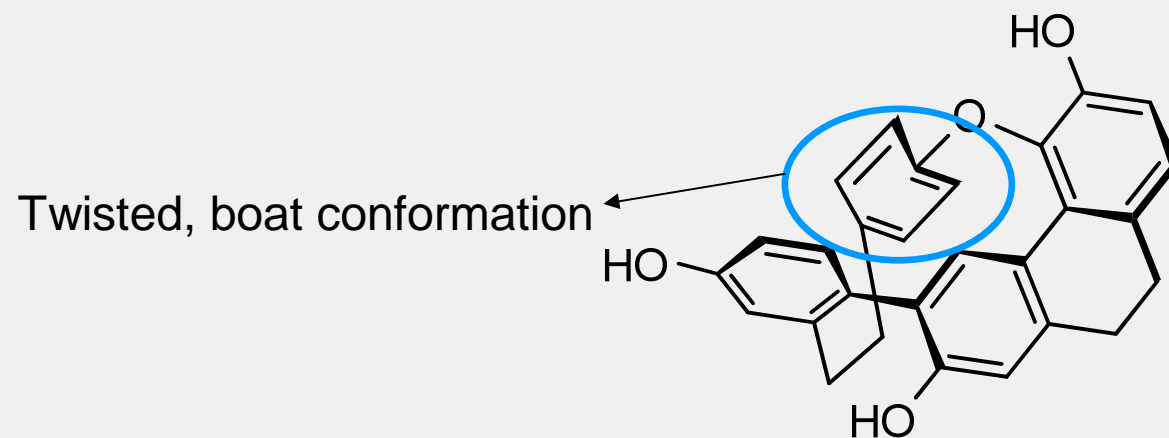
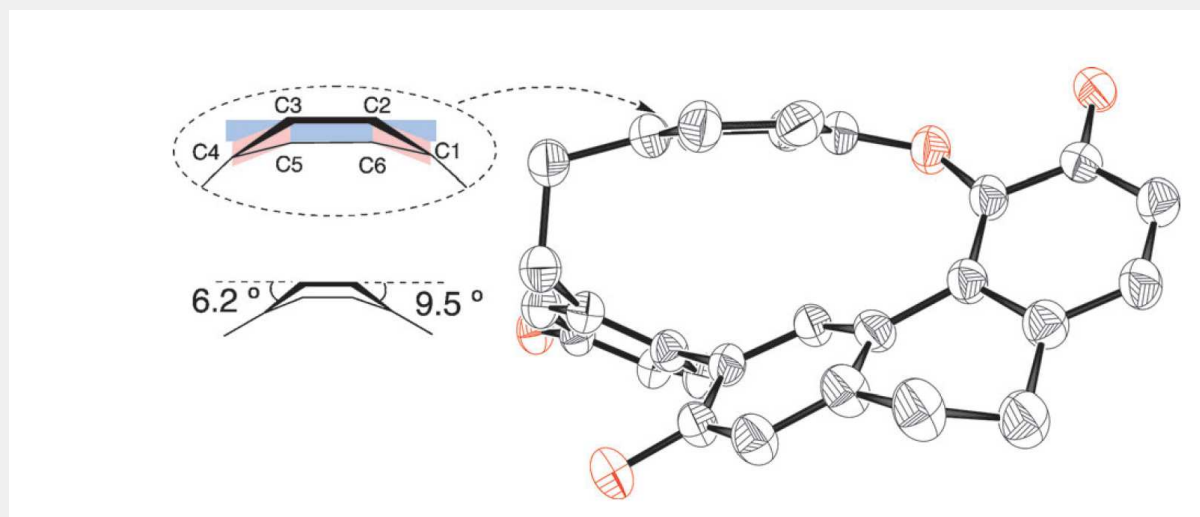
# Synthesis of (-)-Cavicularin

## Radical transannulation (2)



# Synthesis of (-)-Cavicularin

X Ray diffraction



# Conclusion

- First asymmetric synthesis of (-)-Cavicularin
- Very efficient symmetrization/asymmetrization strategy using chiral sulfoxide
- Change of strategy in the end resulting in low conversion
- Confirmation of the boat-like conformation of ring A by XRay crystallography

Thanks for your attention