

# Reserpine

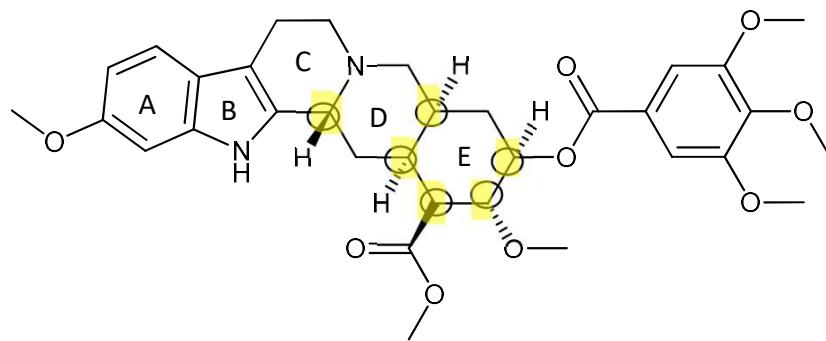
Total Synthesis  
Chapter 4

R.B. Woodward - 1958

Nicolaou, K. C.; Chakraborty, T. K.; Piscopio, A. D.; Minowa, N.; Bertinato, P. J. Am. Chem. Soc. 1993, 115, 4419.

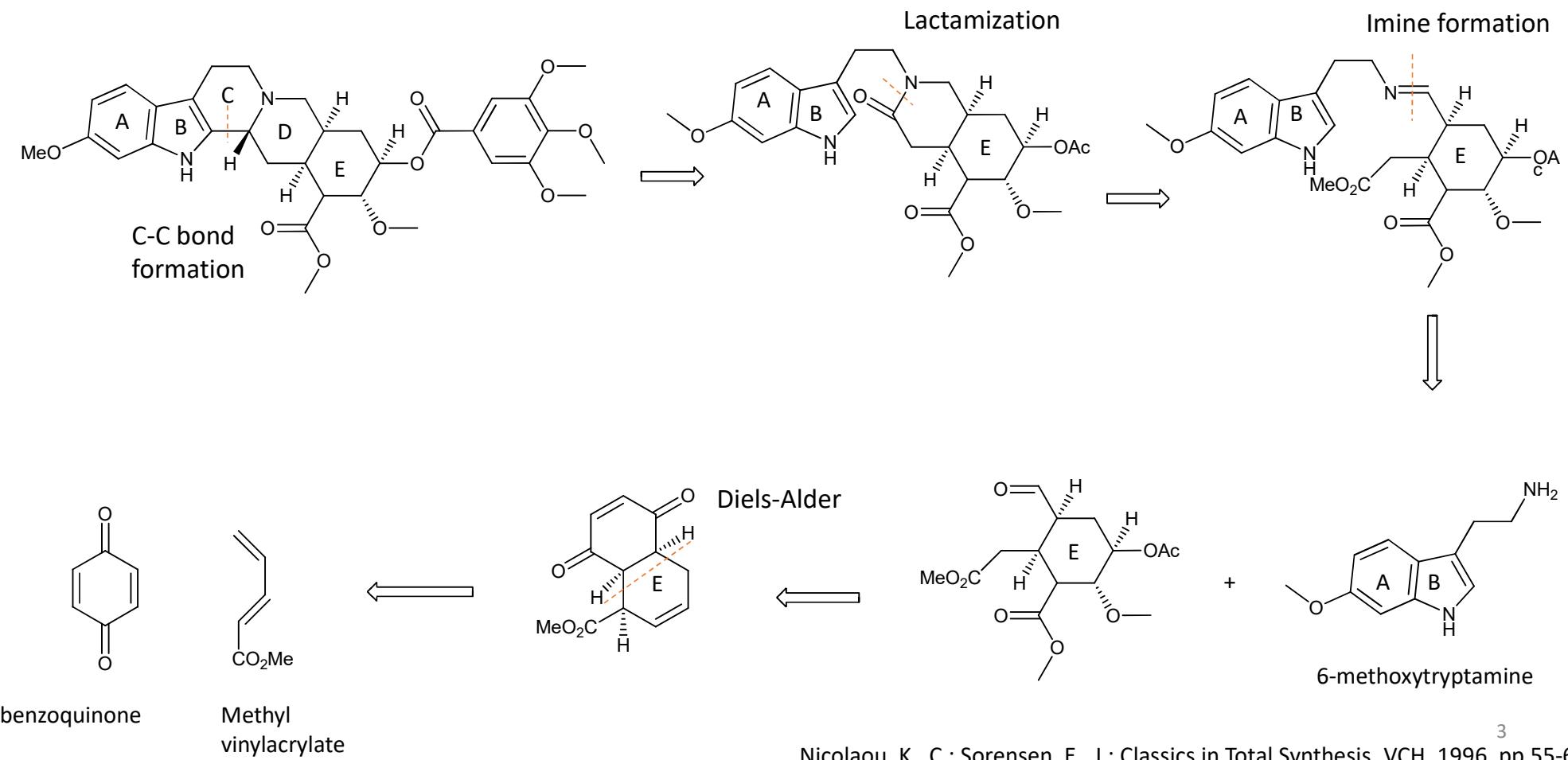
# (-)-Reserpine

- Found in Indian snakeroot *Rauwolfia Serpentina* Benth.
- First isolated by Schlittler *et al.* in 1952.
- Absolute confirmation found in 1955.
- Treats hypertension, nervous and mental disorders.
- Five out of six stereocenters located adjacent in ring E.

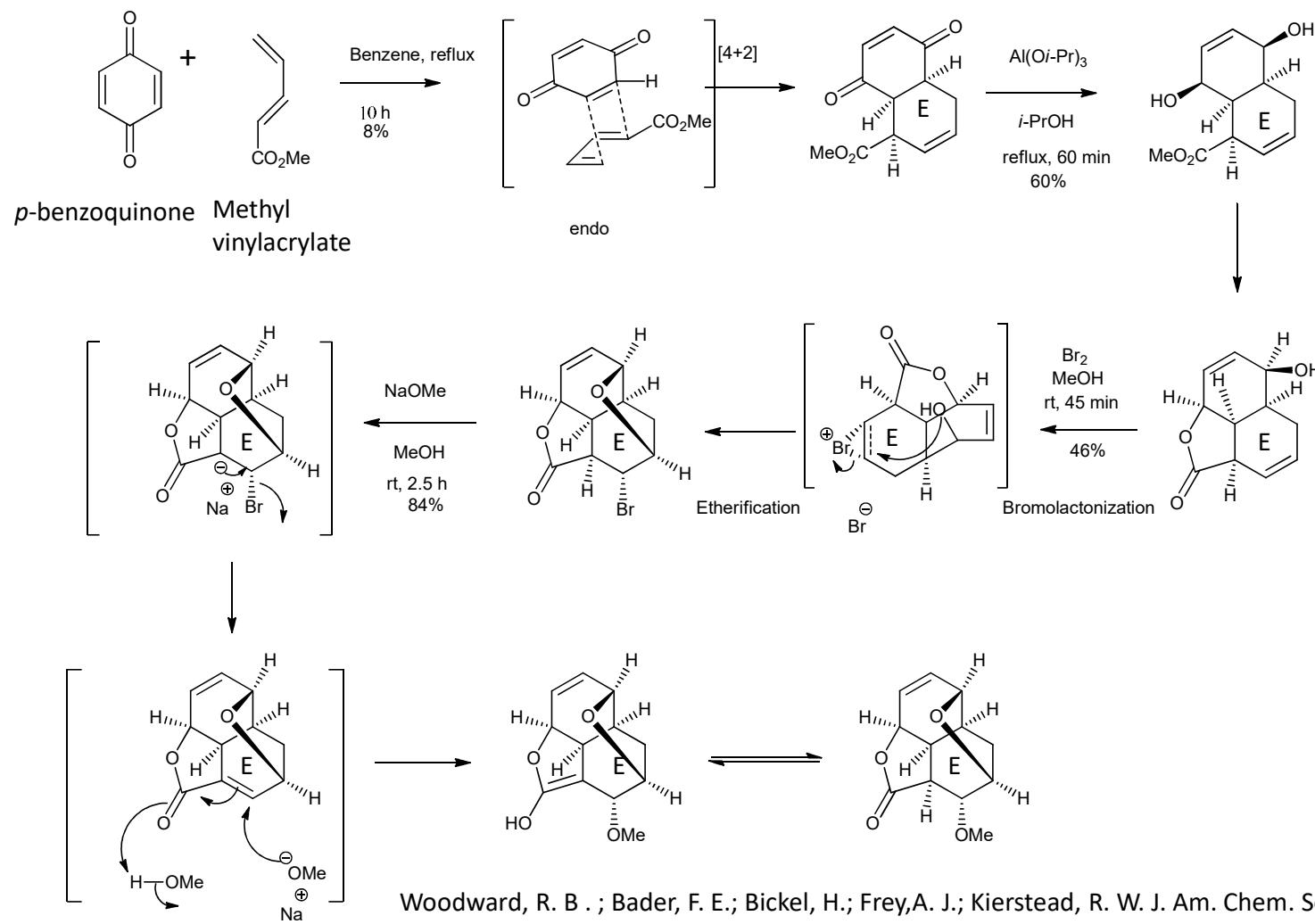


Scriabine, A. In Pharmacology of Antihypertensive Drugs; Scriabine, A., Ed., Raven Press: New York, 1980, p. 119. 2  
Muller, J. M . ; Schlittler, E.; Bein, H . J. Experientia 1952, 8,338 .

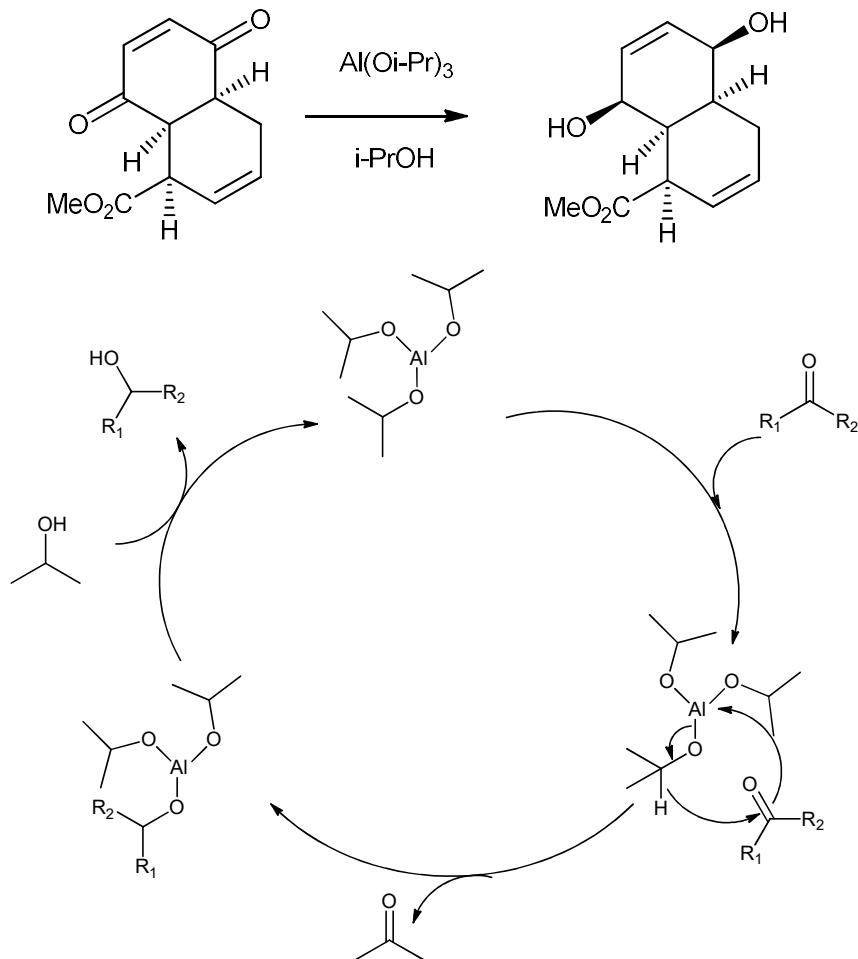
# Retrosynthesis and strategy for total synthesis



# Synthesis of Ring E

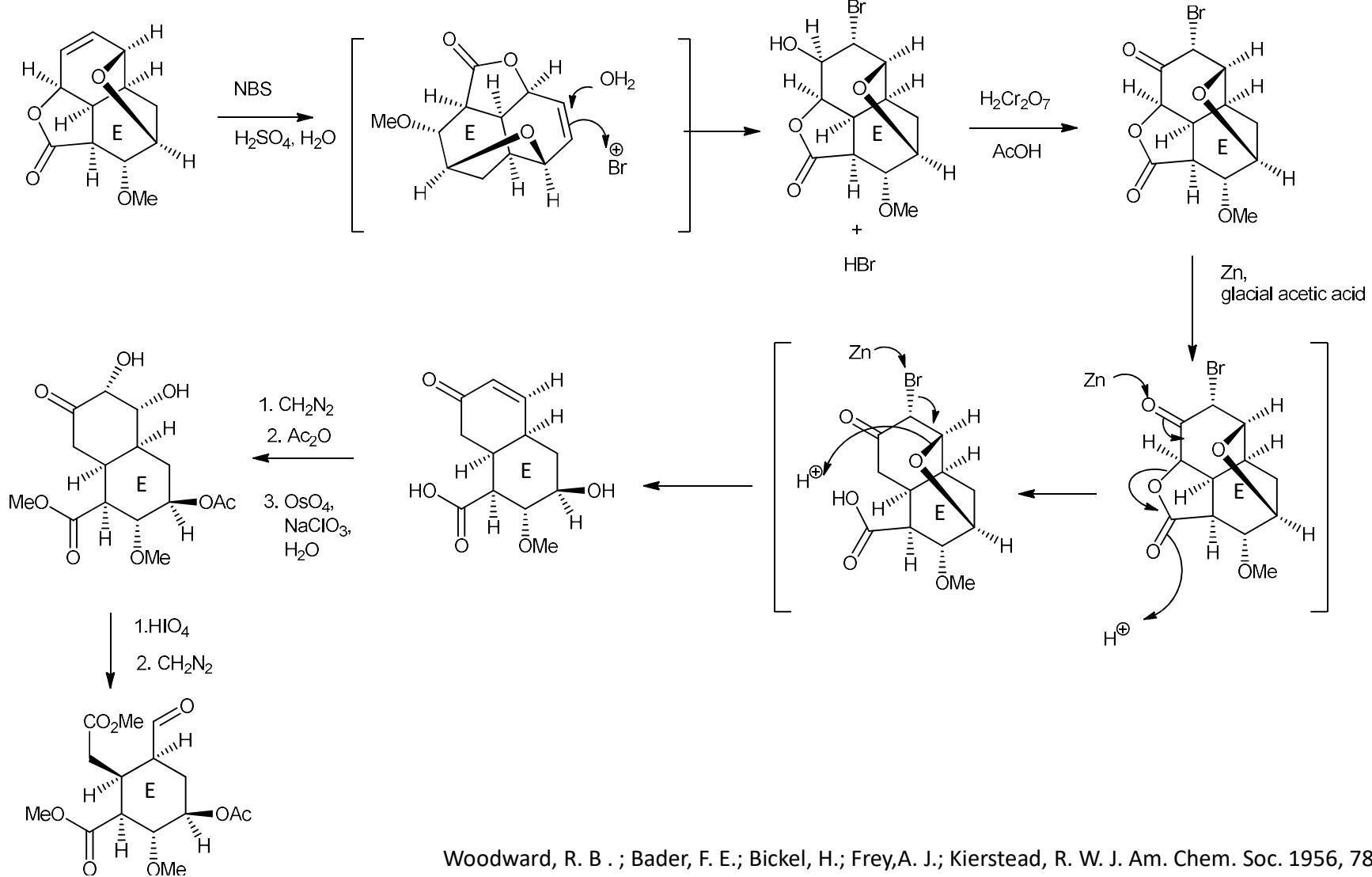


# Meerwein-Ponndorff-Verley Reduction

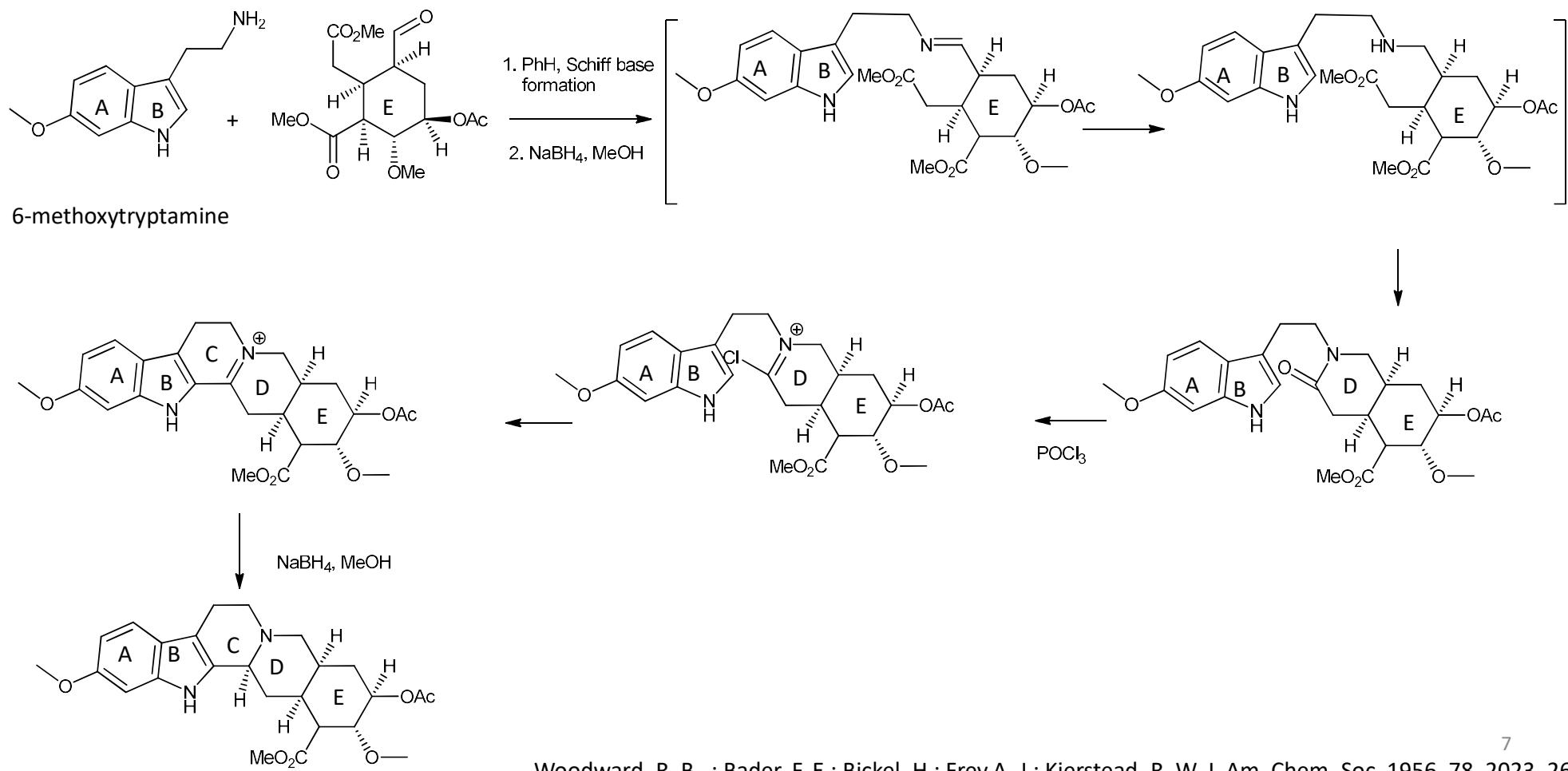


H. Meerwein, R. Schmidt, Justus Liebigs Ann. Chem. 1925, 444, 221–238

# Synthesis of Ring E

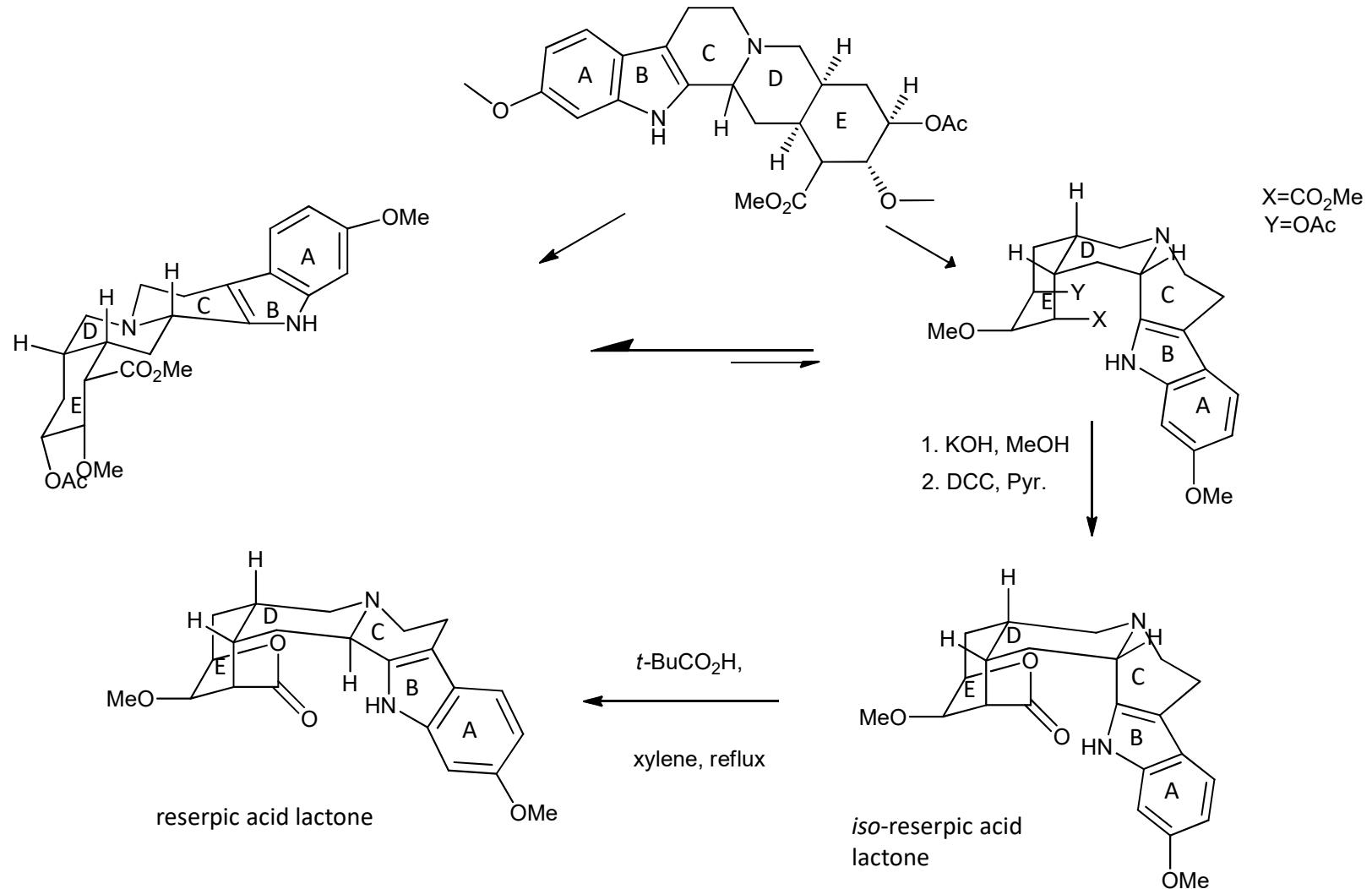


# Synthesis of Ring C and D

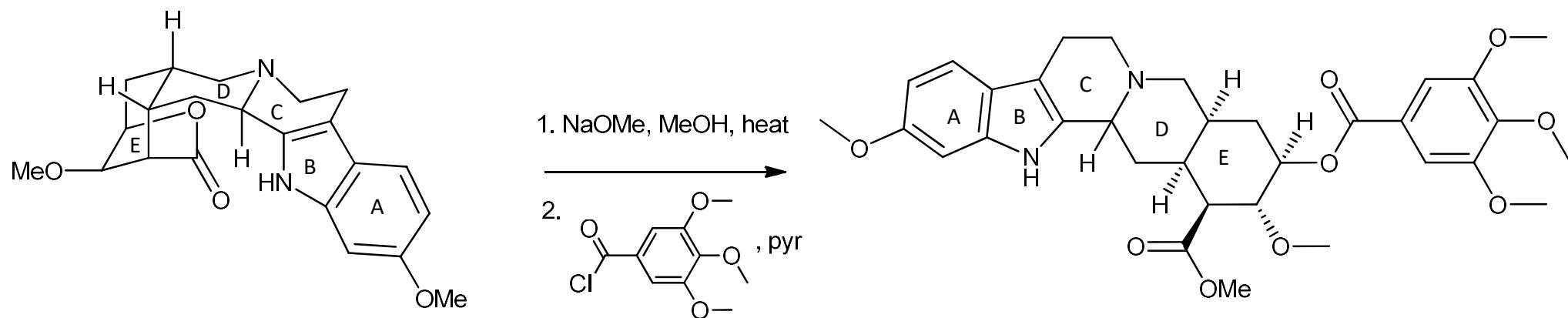


Woodward, R. B. ; Bader, F. E.; Bickel, H.; Frey,A. J.; Kierstead, R. W. J. Am. Chem. Soc. 1956, 78, 2023, 2657

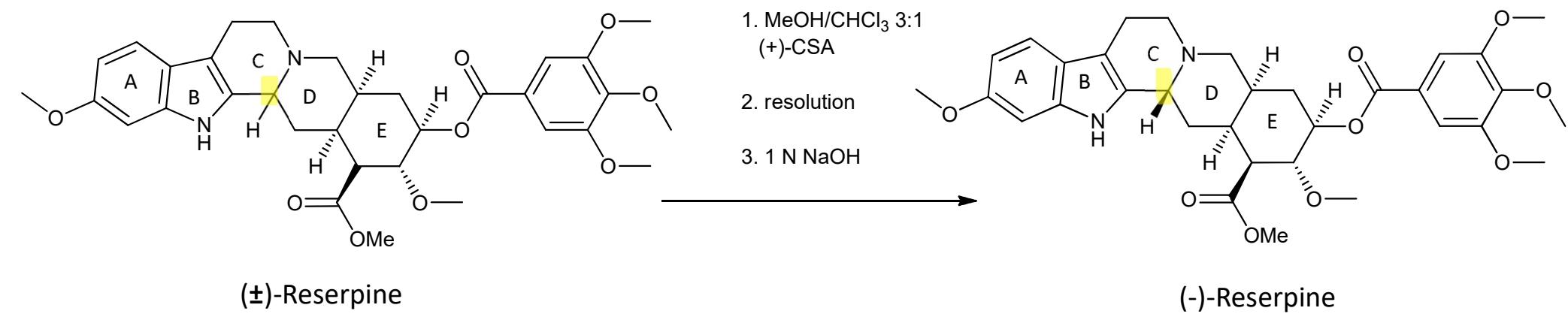
# Synthesis of ( $\pm$ )-Reserpine



# Synthesis of ( $\pm$ )-Reserpine



## ( $\pm$ )-Reserpine to (-)-Reserpine



# Conclusion

- Highly functionalized 6 membered ring formed by a Diels-Alder reaction.
- Epimerization as a crucial step to generate the good enantiomer.
- It is described as Woodward's one the greatest contribution.

