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The Total Synthesis of Reserpine
J. Am. Chem. Soc. **1956**, *78*, 2023–2025, DOI: 10.1021/ja01590a079.
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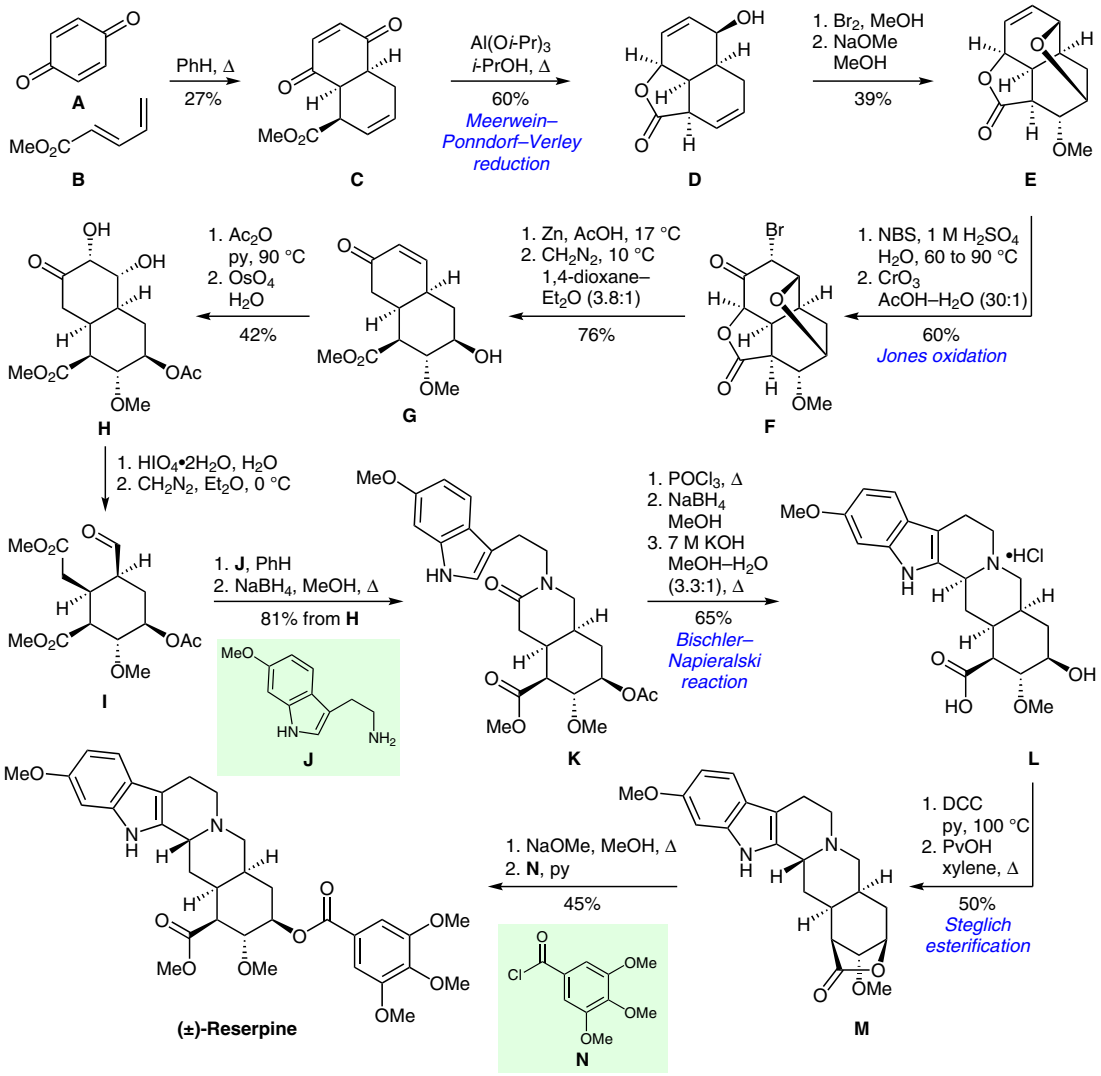
Tetrahedron **1958**, *2*, 1–57, DOI: 10.1016/0040-4020(58)88022-9.

Total Synthesis of (±)-Reserpine



Significance: (±)-Reserpine was isolated from *Rauvolfia serpentina*, a flower from the *Apocynaceae* family. Today it is used as a drug for the treatment of high blood pressure. The configuration was elucidated in 1955 by the Ciba group. In 1956, Woodward and co-workers disclosed the first total synthesis, which completed (±)-reserpine in 21 steps.

Comment: Lactone **D** is obtained through a Diels–Alder reaction of quinone **A** with diene **B** and subsequent reduction. Functional group interconversions lead to aldehyde **I** bearing five stereocenters. Reductive amination of **I** and indole derivative **J**, followed by lactamization forms **K**. Subsequent Bischler–Napieralski reaction completes the carbon skeleton of (±)-reserpine.

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Synthesis of Natural Products and Potential Drugs

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(±)-reserpine
indole alkaloids
Meerwein–Ponndorf–Verley reduction
Jones oxidation
Bischler–Napieralski reaction
Steglich esterification