W. OPPOLZER*, E. FRANCOTTE, K. BÄTTIG (UNIVERSITY OF GENEVA, SWITZERLAND)
Total Synthesis of (±)-Lysergic Acid by an Intramolecular Imino-Diels–Alder Reaction
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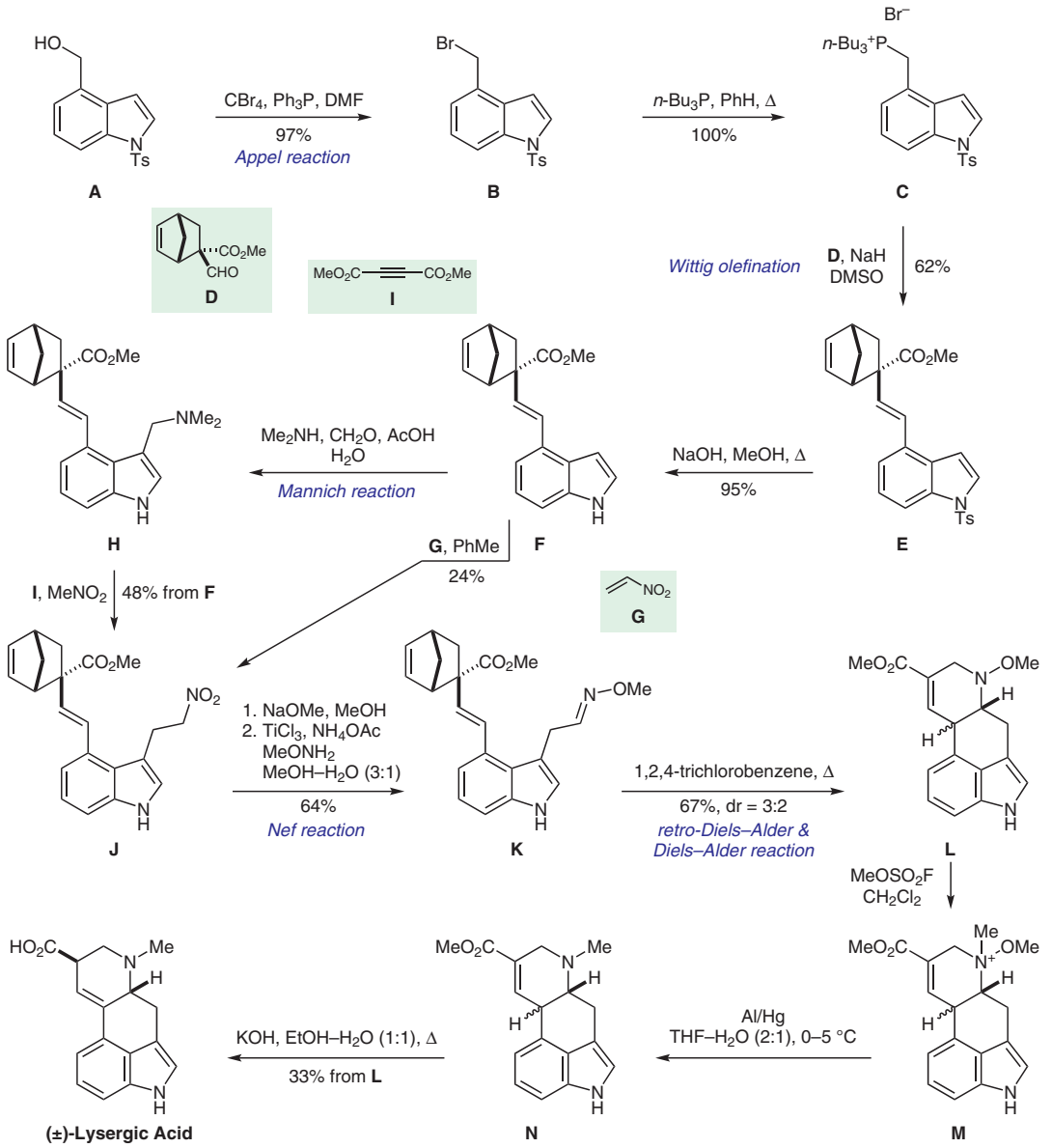
Total Synthesis of (±)-Lysergic Acid



Significance: In 1981, Oppolzer and co-workers reported a concise synthesis of (±)-lysergic acid, a precursor for many ergoline alkaloids. Their synthesis improved upon earlier approaches in terms of efficiency and length by utilizing a Diels–Alder cycloaddition as the key step.

Comment: Intermediate **F** was accessed from 4-hydroxymethyl-1-tosylindole (**A**) in four steps and was converted to **J** either directly by treatment with **G**, or more efficiently over two steps. Nef reaction gave rise to **K**, which underwent retro-Diels–Alder followed by Diels–Alder cycloaddition in one pot at 200 °C. Three more steps gave (±)-lysergic acid.

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Nef reaction
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