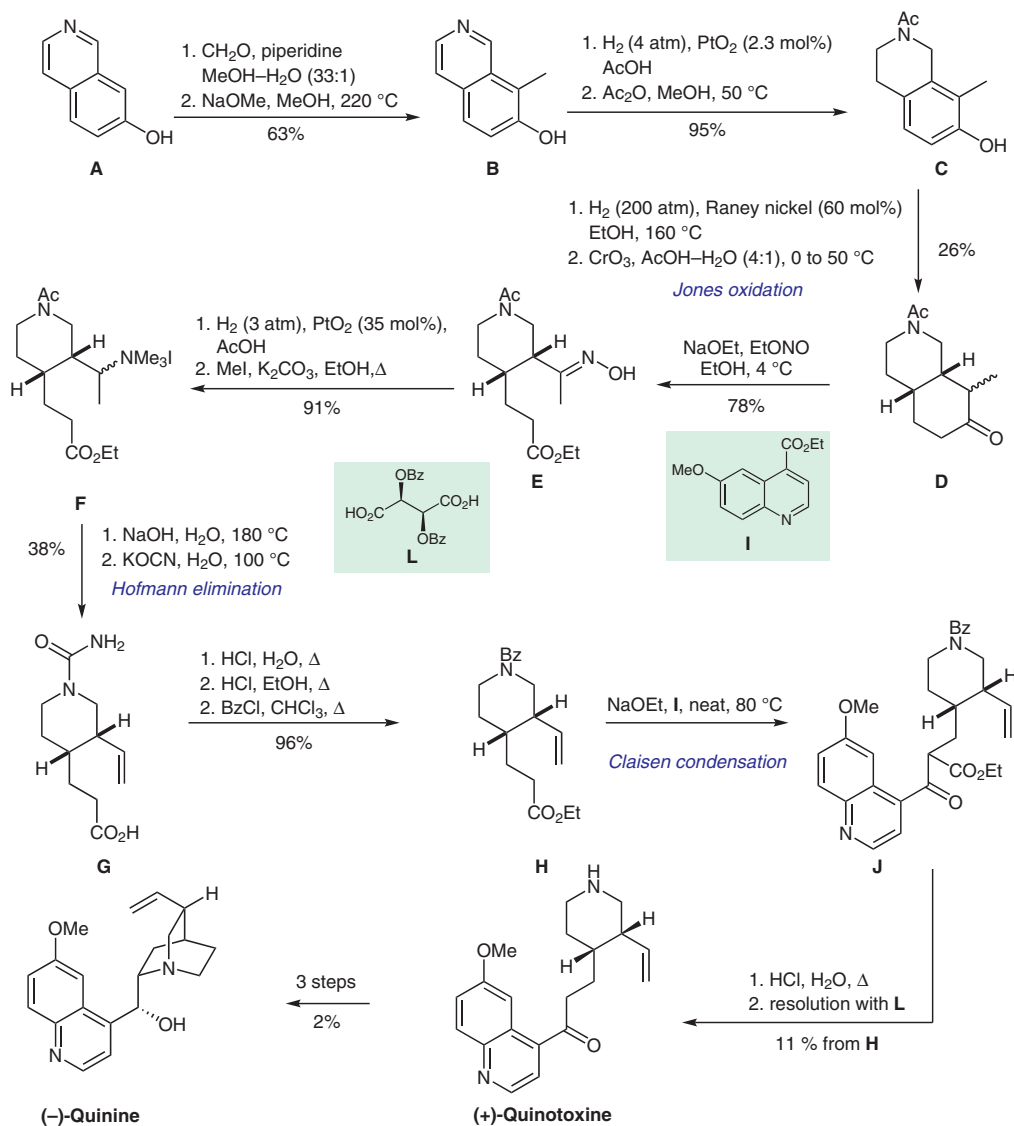


Formal Synthesis of (-)-Quinine



Significance: Quinine, a natural product isolated from the chinchona tree, displays anti malaria properties. The alkaloid has been used in medicine for centuries. Since the seminal report by Woodward, several groups achieved the total synthesis of quinine, among them Uskoković (1970), Stork (2001), and Jacobsen (2004).

Comment: Isoquinoline **A** was converted into ketone **D**, which fragmented to oxime **E** upon treatment with EtONO . Reduction and Hofmann elimination led to acid **G**. Protection of the acid and the amine gave rise to **H** that underwent Claisen condensation. Deprotection and resolution gave (+)-quinotoxine, which Rabe and Kindler (1918) and later Williams (2008) have transformed to (-)-quinine.