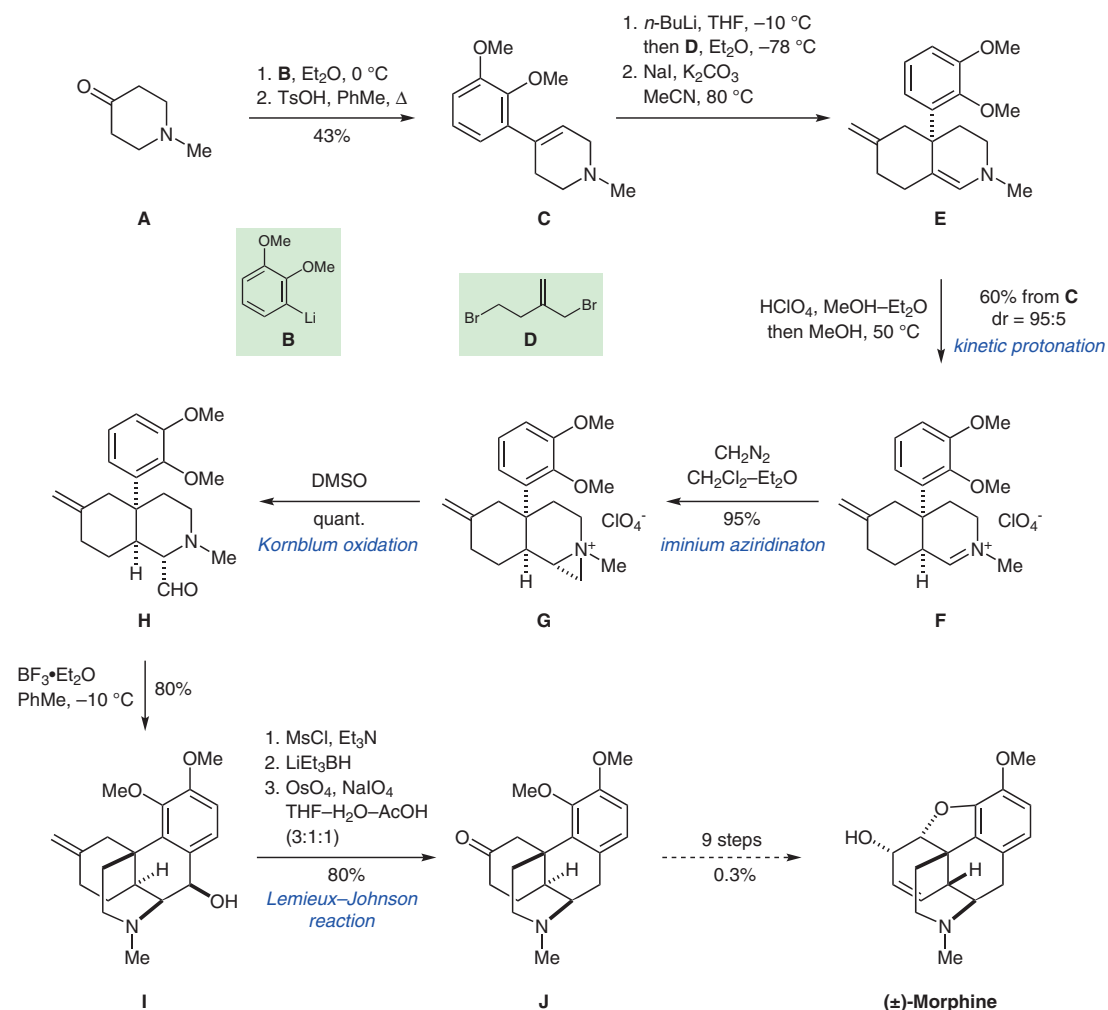


A Formal Synthesis of (\pm)-Morphine



Significance: In 1982, Evans and Mitch disclosed an elegant route to access the core of morphine alkaloids. Their synthetic route provides access to an intermediate from Gates' seminal morphine synthesis (*J. Am. Chem. Soc.* **1956**, 78, 1380). Evans' formal synthesis, which features an unusual Kornblum oxidation as its centerpiece, accesses known tetra-cycle **J**, which can be transformed into the natural product in nine additional steps.

Comment: Metalation and double alkylation of **C** affords enamine **E** which is, under kinetic conditions, transformed into the *cis*-configured iminium **F**. A subsequent aziridination and Kornblum oxidation sequence gives rise to α -amino aldehyde **H**. A Friedel-Crafts-type reaction of **H** affords tetra-cycle **I**, which is then elaborated into known intermediate **J**, thereby completing the formal synthesis of (\pm)-morphine.