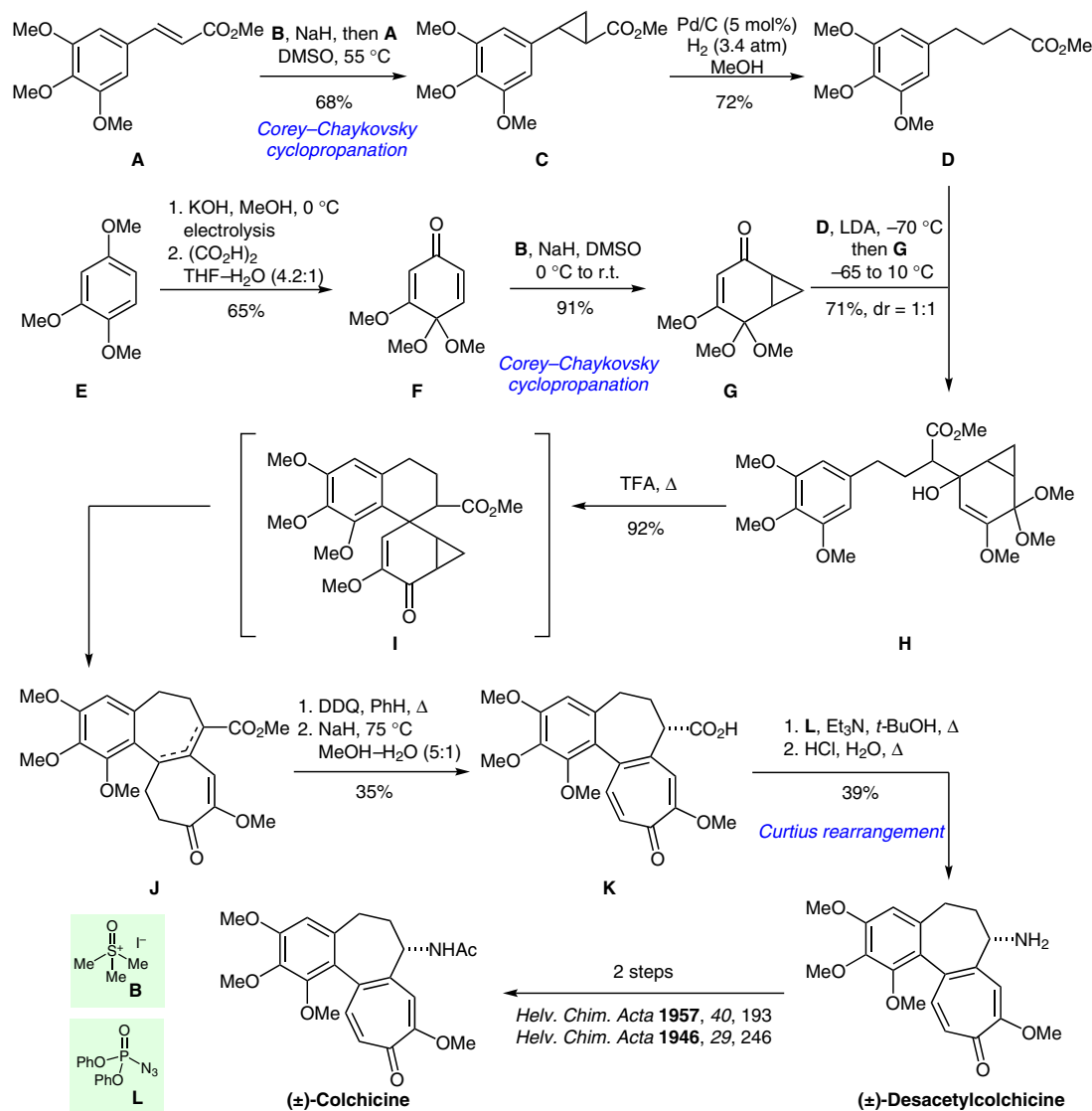


Total Synthesis of (±)-Desacetamidocolchicine and Formal Synthesis of (±)-Colchicine



Significance: In 1981, Evans and co-workers reported the total synthesis of colchicine, a natural product that attracted the interest of chemists for decades. Their route featured a highly convergent approach, giving quick access to the tropolone scaffold present in colchicine. The approach furthermore solved the problem of introducing the amido side chain via a Curtius rearrangement.

Comment: Saturated ester **D** and ketal **G** are coupled via an aldol reaction to yield aldol adduct **H** as a 1:1 mixture of diastereomers. Acid-induced spirocyclization followed by in situ rearrangement yielded the desired tropolone **J**, from which (±)-desacetamidocolchicine was accessible by a Curtius rearrangement.