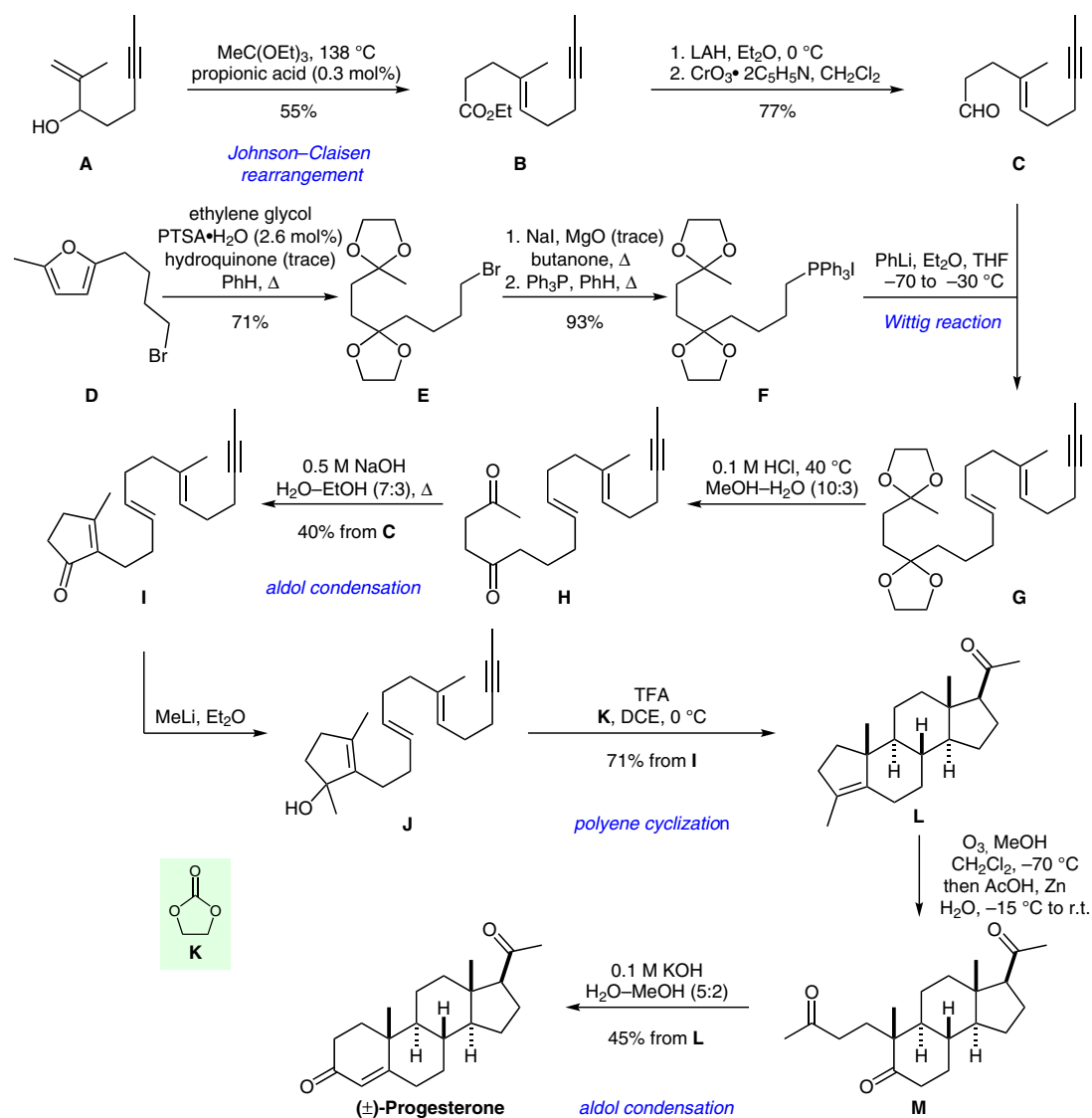


Total Synthesis of (±)-Progesterone



Significance: In 1971, Johnson and co-workers published the total synthesis of racemic progesterone relying on a biomimetic, cationic polyene-cyclization. Similar polyene cyclizations have been used frequently in the total synthesis of various natural products ever since Johnson's seminal studies.

Comment: The synthesis relies on a convergent coupling of aldehyde **C** and Wittig reagent **F** to yield diketal **G**. Elaboration into cyclization precursor **J** enables the key acid-mediated polyene cyclization forging three rings and setting six stereocenters with excellent diastereocontrol. Ozonolysis of olefin **L** followed by aldol condensation yields racemic progesterone.