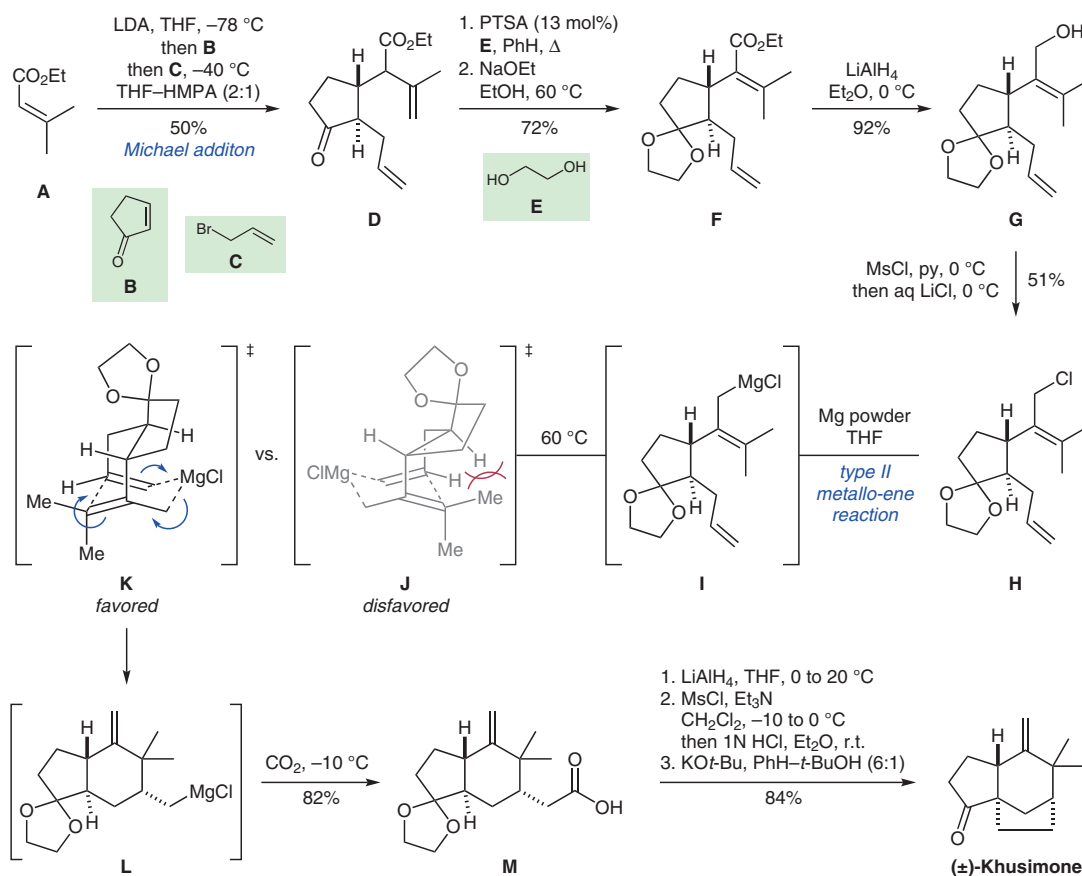


## Total Synthesis of (±)-Khusimone



**Significance:** Oppolzer and Pitteloud report a racemic total synthesis of the norsesquiterpenoid (±)-khusimone. The bicyclic (3.2.1)octane motif can be found in other sesquiterpenes such as zizanoic acid and zizane. Khusimone and these related natural products have found application in perfumery due to their woody, aromatic and earthy flavor. Oppolzer accomplished the total synthesis in nine steps, featuring a type II metallo-ene cyclization, which to date has found little application.

**Comment:** The synthesis commenced with  $\gamma$ -deprotonation of **A**, which underwent Michael addition onto cyclopentenone **B**. The resulting enolate was quenched with allyl bromide to give **D** in 50% yield. Subsequent transformation of the  $\gamma,\delta$ -unsaturated ester **D** to the allylic chloride **H** sets the stage for the type II metallo-ene reaction. In situ formation of Grignard species **I** resulted in cyclization to Grignard reagent **L** via transition state **K**. The excellent diastereoselectivity of this cyclization is noteworthy and was rationalized by flagpole repulsion in alternative transition state **J**.