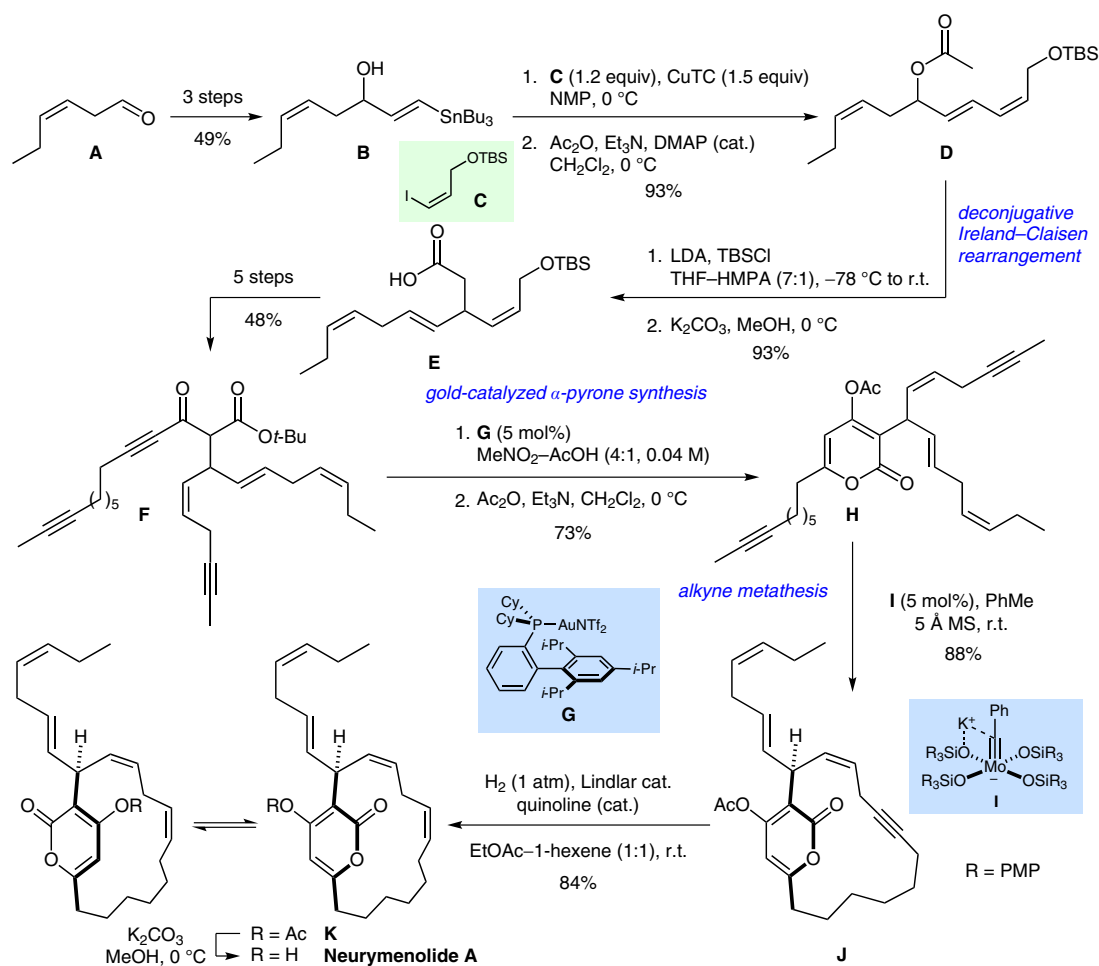


## Total Synthesis of Neurymenolide A



**Significance:** Neurymenolide A is an unusual  $\alpha$ -pyrone macrolide that was isolated in 2009 from the Fijian red alga *Neurymenia fraxinifolia*, exhibiting a broad scope of biological activity. This work represents the first total synthesis of the natural product and features a series of remarkably selective transition metal-catalyzed transformations to build up the highly sensitive cyclophane scaffold.

**Comment:** The route is based on a novel gold-catalyzed pyrone synthesis that allowed for selective alkyne activation within intermediate **F**.  $\alpha$ -Pyrone **H** was subjected to efficient alkyne metathesis to construct macrocycle **J**. Neurymenolide A acetate (**K**) exists as a mixture of interchanging atropisomers and the synthetic material obtained was identical to a sample derived from natural sources. Deprotection of **K** led to rapid degradation.