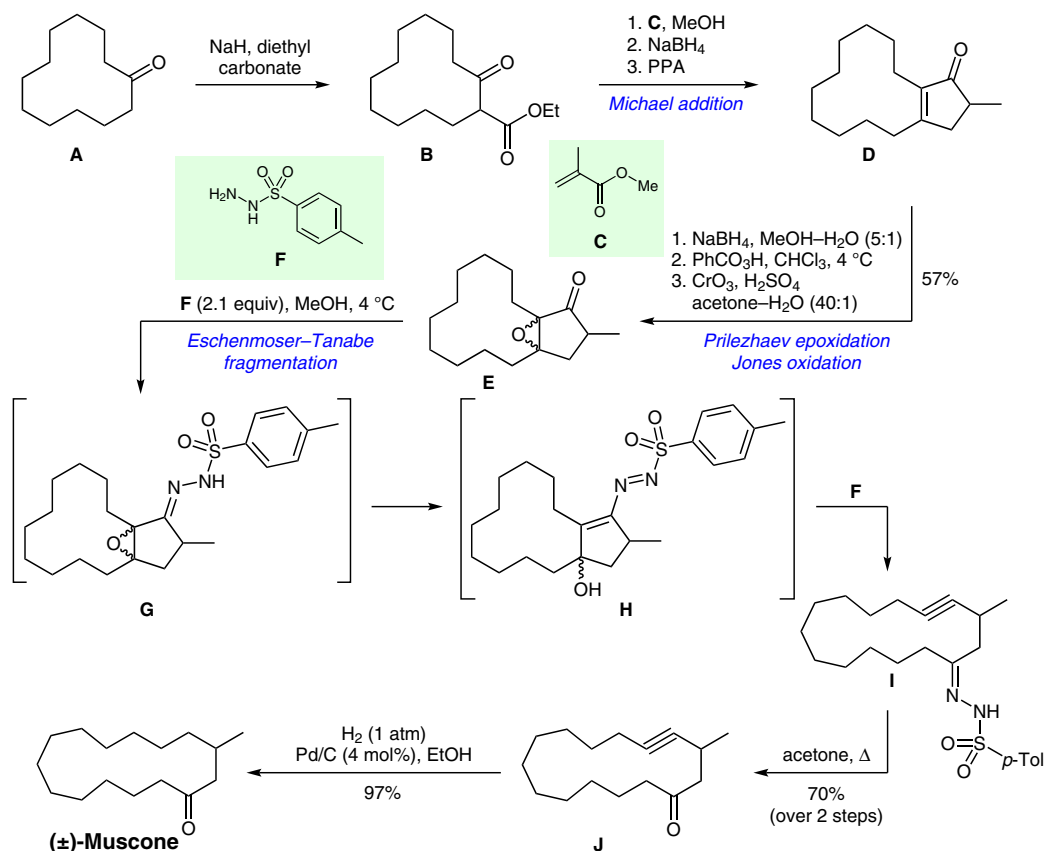


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$\alpha,\beta$ -Epoxyketon  $\rightarrow$  Alkinon-Fragmentierung I: Synthese von Exalton und *rac*-Muscon aus Cyclododecanon über synthetische Methoden, 3. Mitteilung

*Helv. Chim. Acta* **1971**, 54, 2896–2912, DOI: 10.1002/hlca.19710540855.

## Total Synthesis of (±)-Muscone



**Significance:** First reported as part of a communication in 1967 (*Helv. Chim. Acta* **1967**, 50, 708), Eschenmoser, Ohloff, and co-workers reported a total synthesis of the cyclopentadecanone (±)-muscone. (–)-Muscone is the main odorant of musk, a glandular secretion of the male musk deer. Owing to its characteristic smell, muscone has found wide use in many products of the fragrance industry. The highlighted 1971 article includes synthetic details and further examples of the classic  $\alpha,\beta$ -epoxyketone fragmentation reaction which can result in macrocyclic alkyne products. This reaction is today known as the Eschenmoser–Tanabe fragmentation; for an independent report of the fragmentation reaction by Tanabe et al., see: *Tetrahedron Lett.* **1967**, 8, 3943.

**Comment:** The synthesis commenced with acylation of cyclododecanone **A** which is industrially accessed via trimerization of butadiene for the synthesis of dodecanedioic acid and laurilactam. Keto ester **B** was subjected to Michael addition with methyl methacrylate **C**. Reduction and annulation under concomitant decarboxylation with PPA generated enone **D**. Epoxidation of **D** proved difficult; therefore, the enone was reduced to the allylic alcohol, epoxidized, and re-oxidized to epoxyketone **E** which was set up for fragmentation. Addition of two equivalents of tosyl hydrazide **F** led to direct formation of hydrazone fragmentation product **I**. Cleavage of the hydrazone in refluxing acetone followed by hydrogenation gave access to target compound (±)-muscone.