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One-Pot Synthesis of (+)-Nootkatone via Photooxidation of (+)-Valencene

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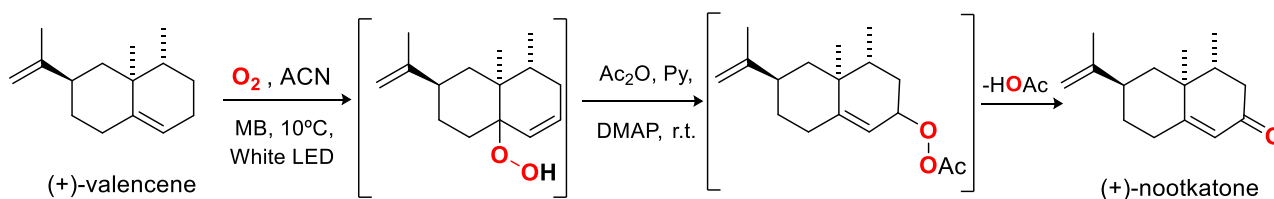
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ABSTRACT

(+)-Nootkatone is a high-value compound, very regarded in the flavoring and fragrance industry for its characteristic grapefruit aroma and low perception threshold. Additionally, (+)-nootkatone is used as a food additive and possesses insecticidal activity¹, which highlights its versatility and contributes to its significant commercial value, especially given its low natural abundance. Herein, we describe the semi-synthesis of (+)-nootkatone from commercial (+)-valencene using a one-pot photooxygenation followed by an allylic rearrangement and E₂ elimination.

Our protocol involves the photooxidation of (+)-valencene with O₂ and methylene blue (MB), followed by the Schenk rearrangement, acetylation of the hydroperoxides and HOAc elimination for the formation of (+)-nootkatone (Scheme 1), using an adapted methodology previously developed in our laboratory.² To date, we have succeeded in obtaining (+)-nootkatone in overall yields up to 13% in batch. We are currently optimizing this protocol in batch to evaluate the initial reaction conditions, and subsequently translate this to continuous flow conditions.



Scheme 1. (+)-Nootkatone synthesis.

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