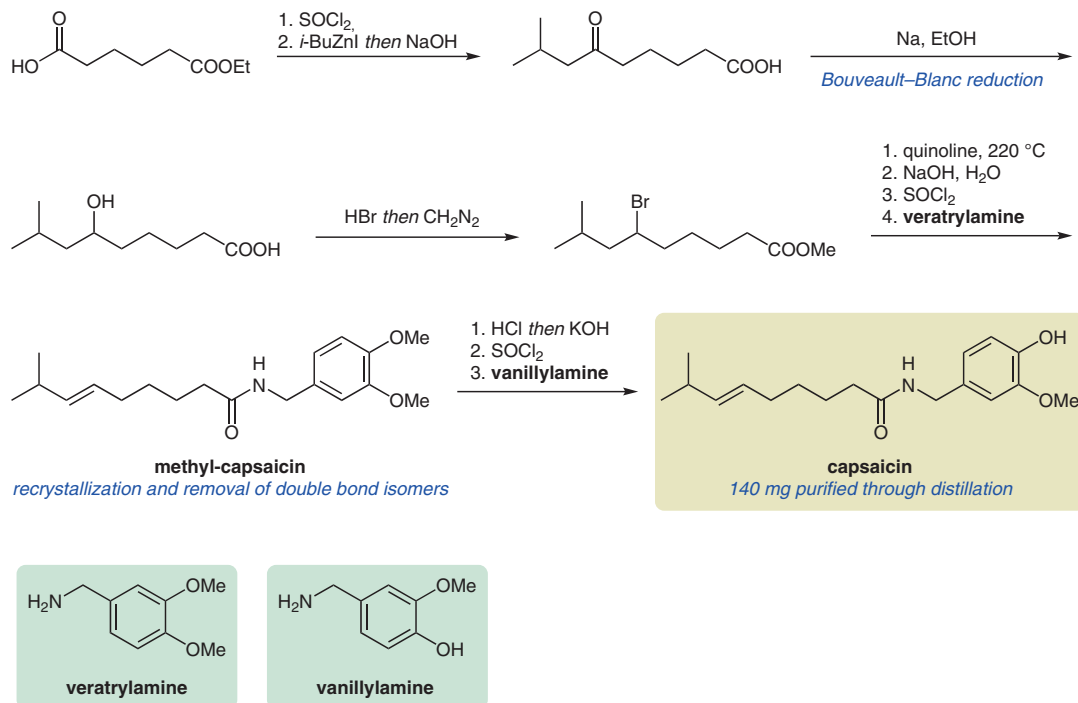


A Spicy Total Synthesis



Significance: Capsaicin is an irritant that produces a sensation of burning when in contact with tissues. It is also the active component of chili peppers responsible for their pungency. As a member of the vanilloid family, capsaicin binds and stimulates the vanilloid receptor subtype 1 (TRPV1). This leads to a physiological sensation of heat, stinging and irritation. Creams, lotions, and patches containing low concentrations of capsaicin are widely sold and used as local analgesics to relieve pain.

Comment: After the synthesis of the hydrophobic chain of capsaicin, methyl-capsaicin was formed for ease of purification. The amide was crystalline and enabled the removal of various double bond isomers. Subsequent hydrolysis and amide bond formation with vanillylamine furnished 140 mg of capsaicin after purification through distillation. Due to the irritant nature of this natural product, the authors warn that: “working with this substance is only somehow bearable if any atomization is carefully avoided.”