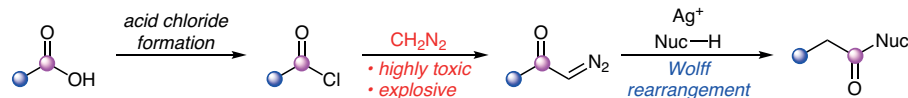
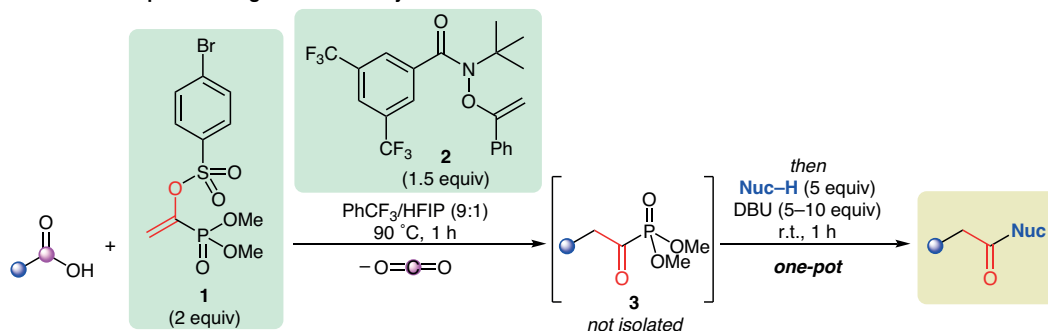


One-Pot Homologation of Aliphatic Carboxylic Acids

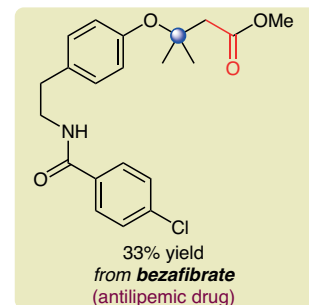
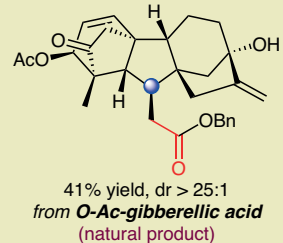
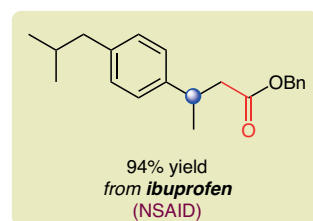
Arndt–Eistert homologation:



Alexanian's one-pot homologation of carboxylic acids:



Examples of homologated drugs and natural products:



Significance: Carboxylic acids are omnipresent, decorating natural products as well as drug and building block libraries. They are involved in the most fundamental and well-developed reactions, such as the amide or ester bond coupling. In contrast, a simple one-carbon extension of carboxylic acids remains a challenging three-step transformation (Arndt–Eistert reaction). In collaboration with Abbvie, Alexanian's group reports a novel one-pot homologation of aliphatic carboxylic acids to form the corresponding one-carbon-extended carboxylic acid derivatives. The new methodology is operationally simpler and safer than the Arndt–Eistert procedure.

Comment: The Arndt–Eistert homologation strategy is based on the stereospecific Wolff rearrangement. Conceptually independent, Alexanian's approach relies on a HAT-induced radical decarboxylation (mediated by **2**), followed by a diastereoselective radical capture with the two-carbon unit **1**, to form activated carboxylic acid derivative **3** (an acyl phosphonate). Subsequent capture by a nucleophile in one pot furnishes the homologated products. However, whereas the Arndt–Eistert method is preceded for both aliphatic and aromatic carboxylic acids, the authors of this manuscript do not comment on the reaction outcomes with aromatic carboxylic acids.