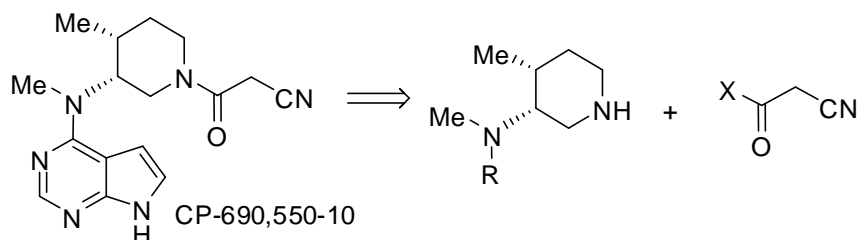
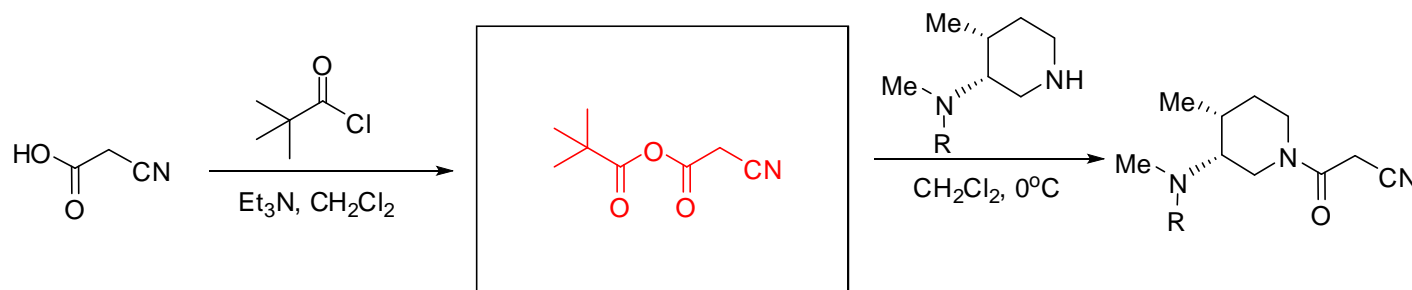


1. Pfizer Pharmaceutical Company chemists were recently trying to synthesize a new drug for the treatment of rheumatoid arthritis and psoriasis. The drug has the company name CP-690,550-10 and the structure is shown below. In a just published 'ASAP' article entitled "Mild and Efficient DBU-Catalyzed Amidation of Cyanoacetates", they reported a more efficient reaction to synthesize the amide bond in the molecule.



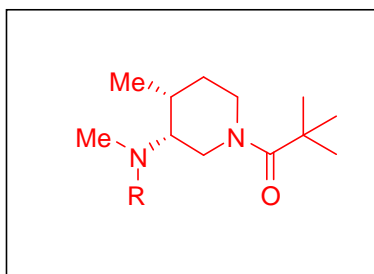
a) The old procedure is the two step reaction shown below. Complete the sequence by providing the intermediate product in the two step process.



b) Provide the most specific name that we used to describe the functional group formed in the intermediate product.

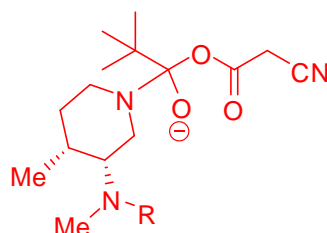
The reaction between the acid chloride and the acid makes a mixed or unsymmetrical acid anhydride.

c) Actually the reaction in part a can potentially form two amide products, but the desired product (depicted) is the major product. Draw the second amide product and provide a reason it is not formed to an appreciable extent. (Hint: You might consider the structure of the tetrahedral intermediate.)



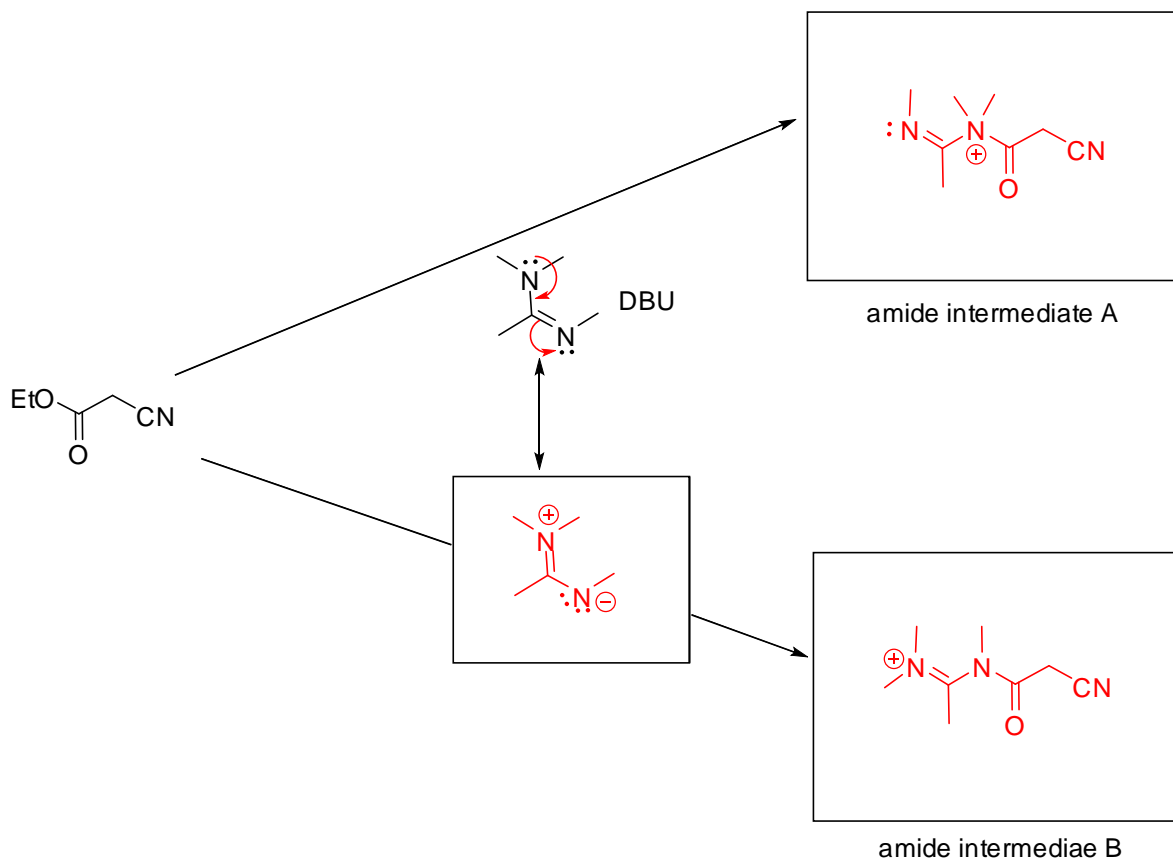
other potential amide product

This product is not formed because the tert-butyl group makes nucleophilic attack on the carbonyl less likely due to the steric congestion in the tetrahedral intermediate:



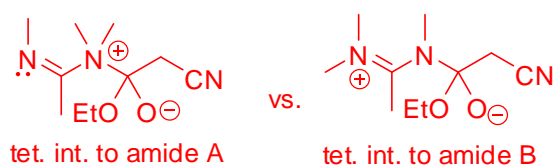
Notice there are two quaternary carbon centers right next to each other.

d) The Pfizer researchers report an improved one pot procedure which uses DBU (shown below in abbreviated form) to catalyze the reaction with an ethyl ester. DBU has two nitrogen atoms and both can react. The second one reacts as a resonance form of the first. Draw the resonance form and the two possible amide intermediates, A and B.

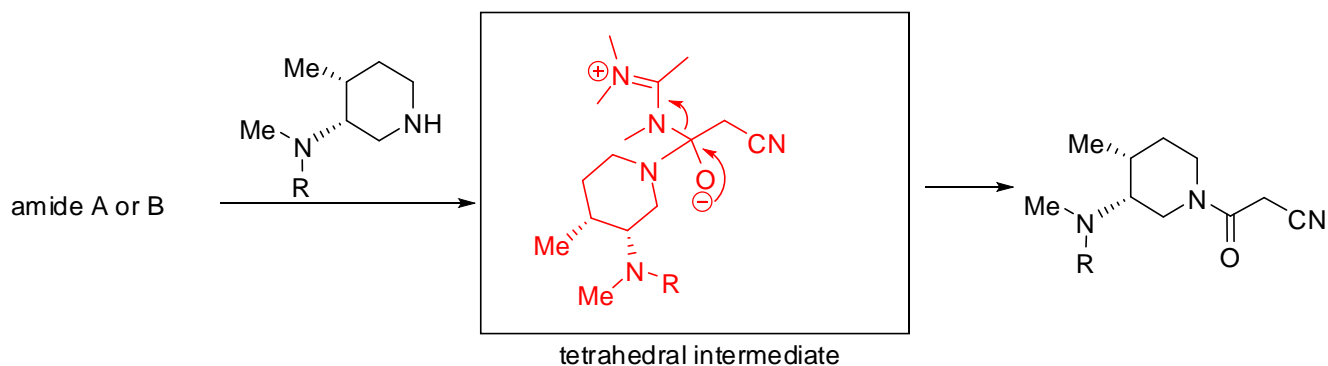


e) Which amide do you think is favored? Why? (Hint: the answer is consistent with part c)

Amide B is favored because this amide is less sterically crowded; it does not have a quaternary atom next to the carbonyl. The tetrahedral intermediate precursor would be crowded, just like in question c, with two quaternary centers next to each other:

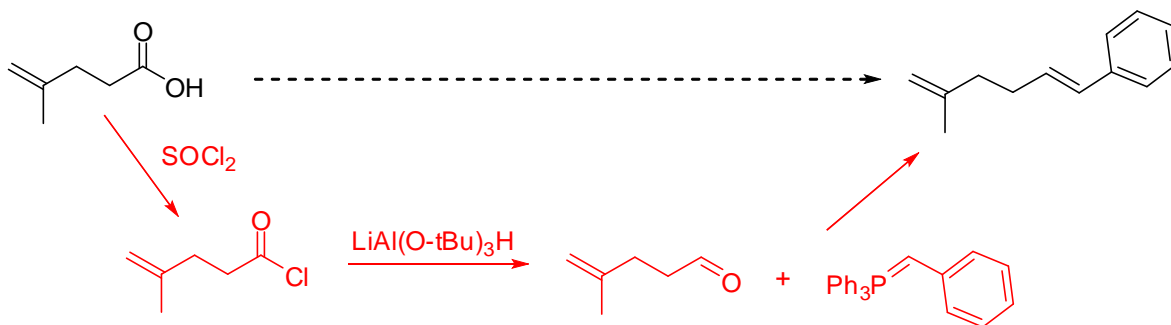


f) In the final stage of this one pot reaction, the amine reacts with amide A/B to afford the desired final product. Draw the tetrahedral intermediate that leads to the final product.

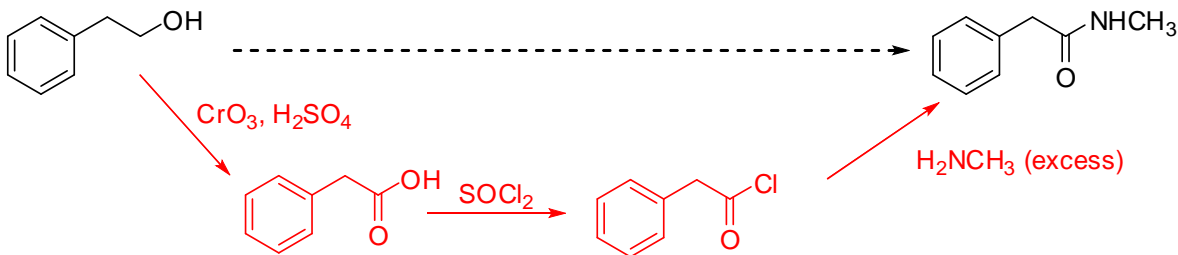


2. Complete the following syntheses by converting the starting material on the left to the product on the right. You may use any organic or inorganic reagent. All transformations can be conducted in three steps or less.

a)



b)



c)

