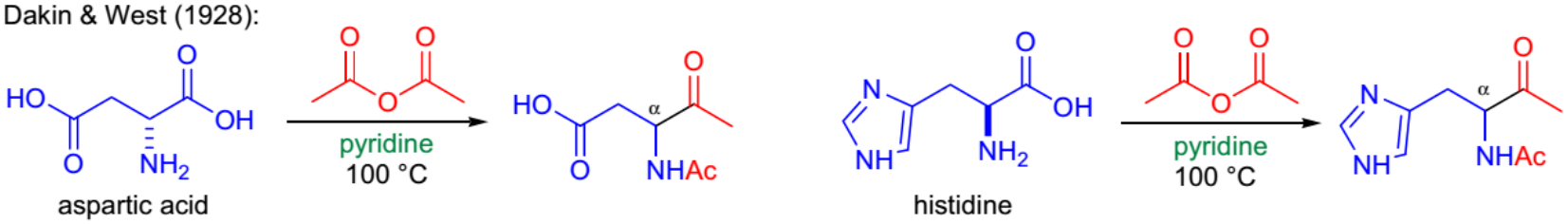
DAKIN-WEST REACTION

—H.D. Dakin and R. West

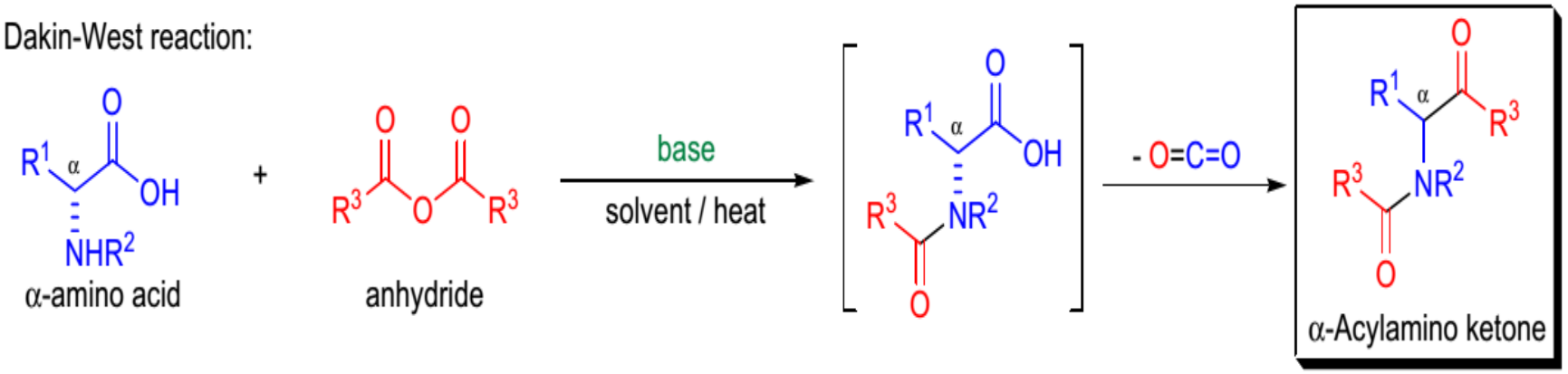
Importance

In 1928, H.D. Dakin and R. West reported that when certain amino acids, such as aspartic acid and histidine,were heated in acetic anhydride in the presence of pyridine, the corresponding α-acetamido methyl ketones were formed in high yield. The formation of α-acylamino alkyl ketones from α-amino acids and symmetrical carboxylic acid anhydrides in the presence of a base is known as the Dakin-West reaction.



Importance

Dakin-West reaction:



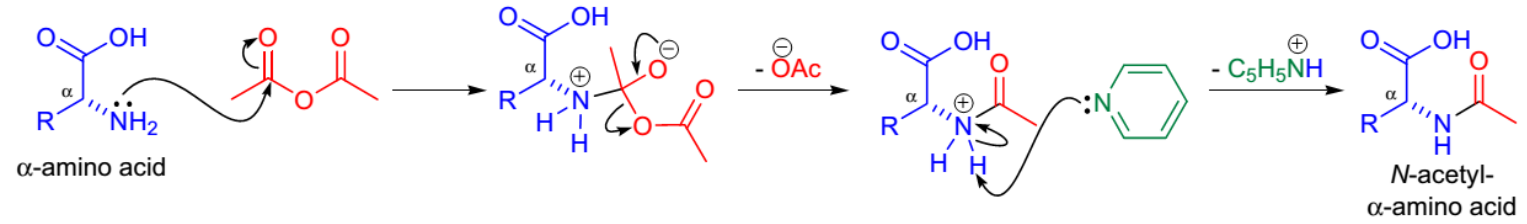
R^1 = H, alkyl, substituted alkyl; R^2 = H, alkyl, substituted alkyl, aryl, heteroaryl; R^3 = Me, Et, *n*-Pr; base: pyridine, alkylpyridine, NaOAc; solvent: pyridine, Et_3N

features

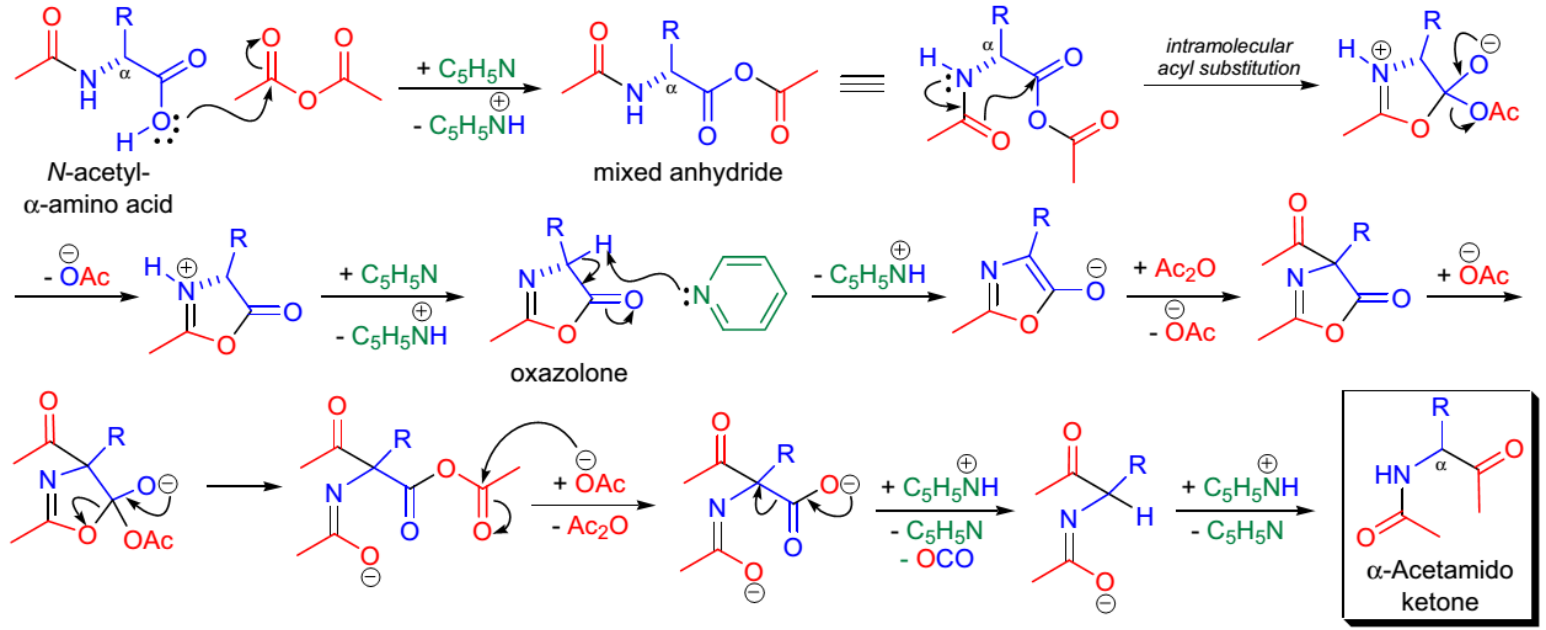
- Both primary and secondary α-amino acids undergo this transformation, but β-amino acids only afford the corresponding N-acylated derivatives.
- The α-amino acids need to have a proton at their α-position,otherwise they simply undergo N-acylation.
- The anhydride component is most often acetic anhydride, but other anhydrides such as propionic anhydride can also be used.
- When acetic anhydride is used, the product is an α-acetylamino methyl ketone, whereas with propionic anhydride the corresponding α-propionylamino ethyl ketone is obtained.
- The base is usually pyridine, but various alkylpyridines and sodium acetate have been successfully employed.
- Primary α-amino acids react with anhydrides at around 100 ° C, but secondary α-amino acids require significantly higher reaction temperatures.
- The addition of a nucleophilic catalyst such as DMAP allows the reaction to take place at room temperature

Mechanism

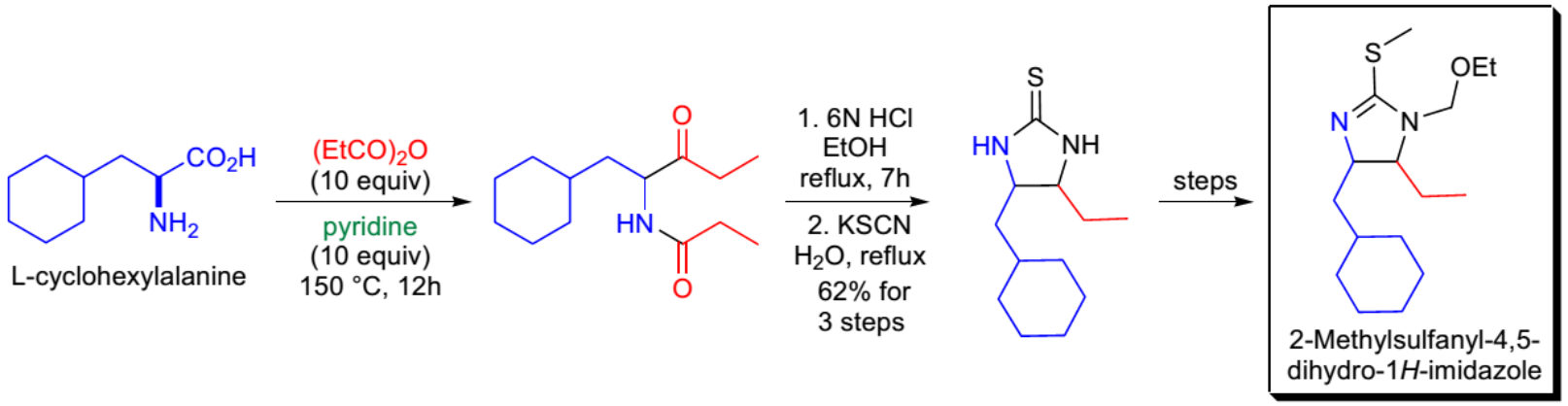
Formation of *N*-acetyl-α-amino acid:



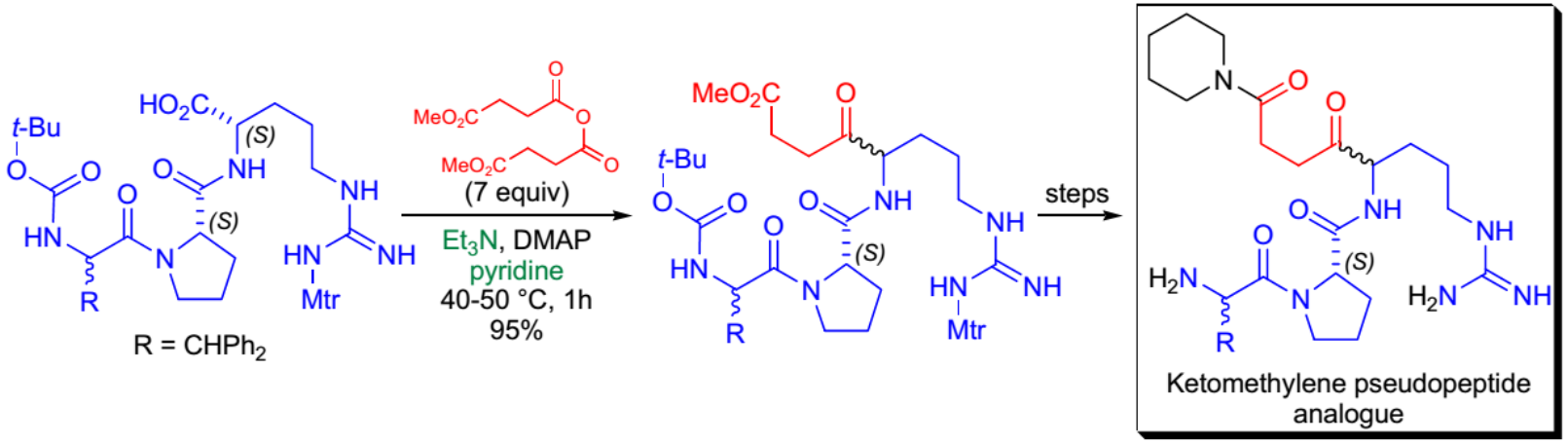
Formation of α-acetamido ketone from *N*-acetyl-α-amino acid:



Synthetic Applications

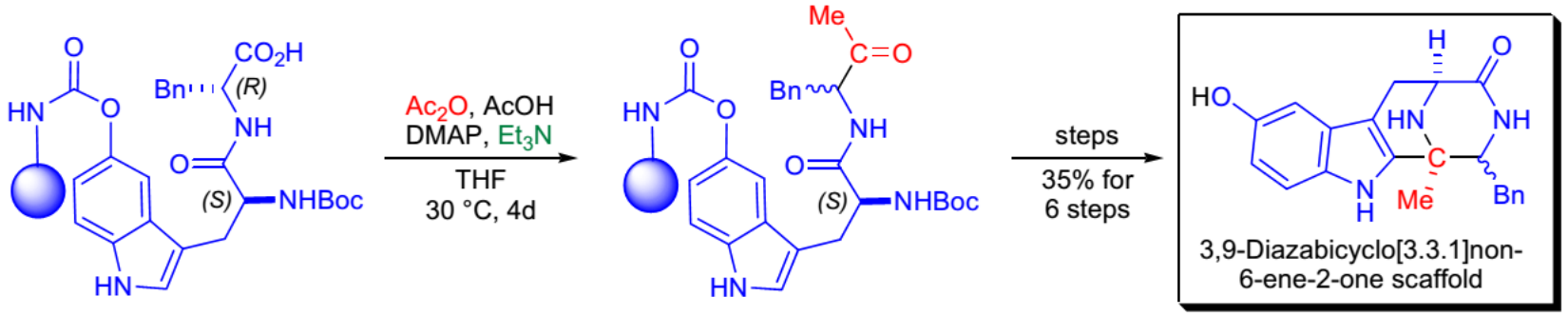


Synthetic Applications

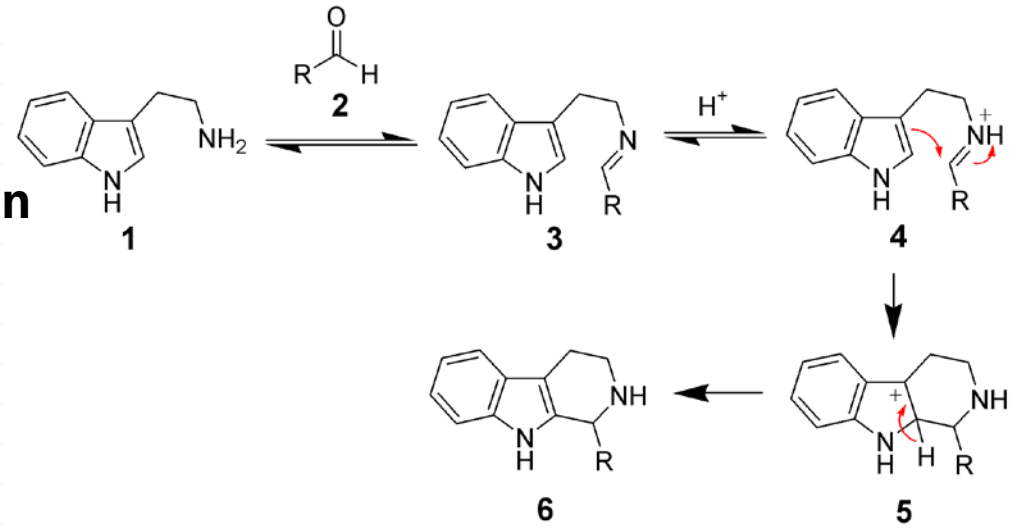


Synthetic Applications

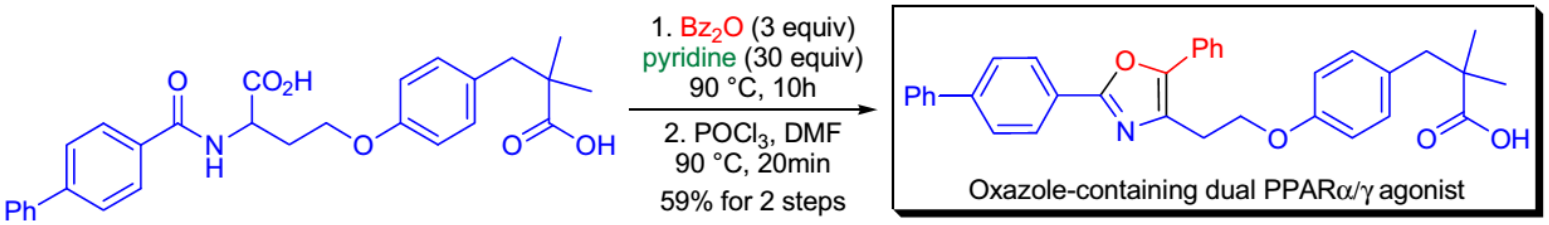
A novel sequential Dakin-West reaction



Pictet–Spengler reaction



Synthetic Applications



Thanks