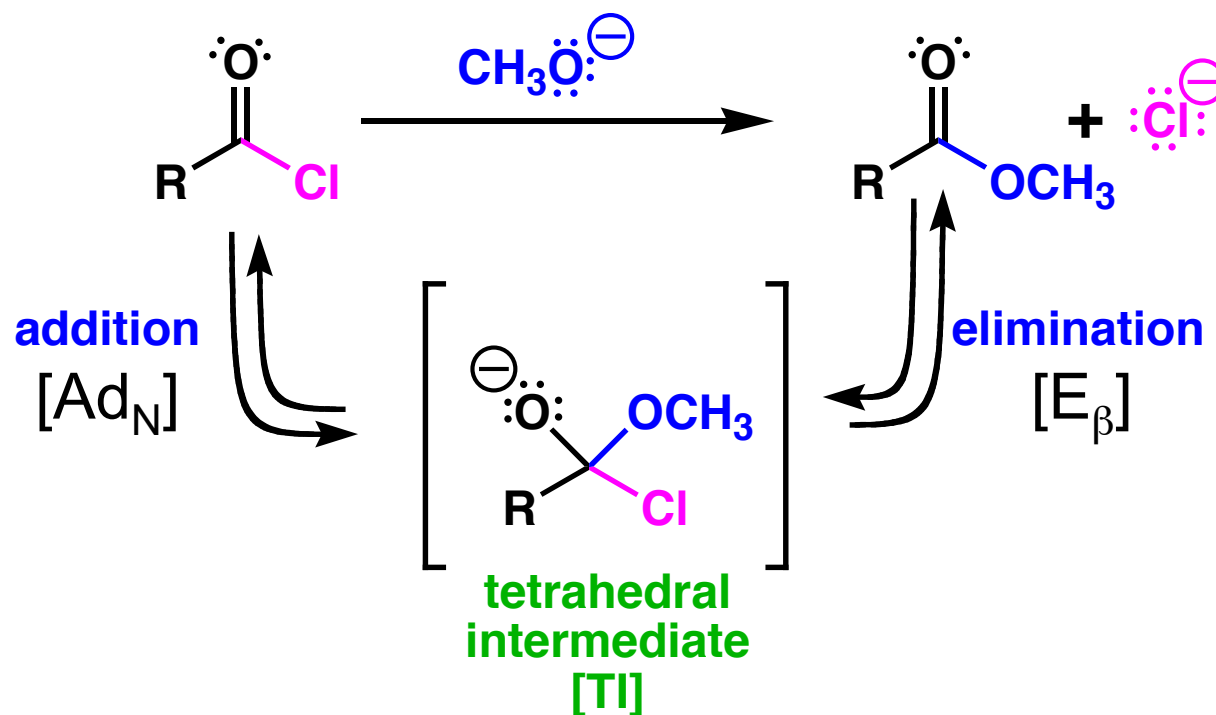


Nucleophilic Acyl Substitution: Addition-Elimination Through a Tetrahedral Intermediate



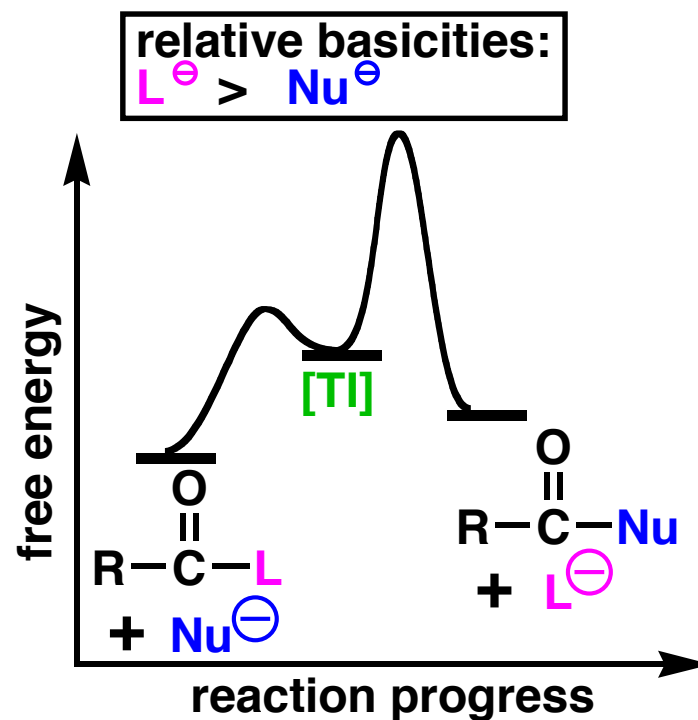
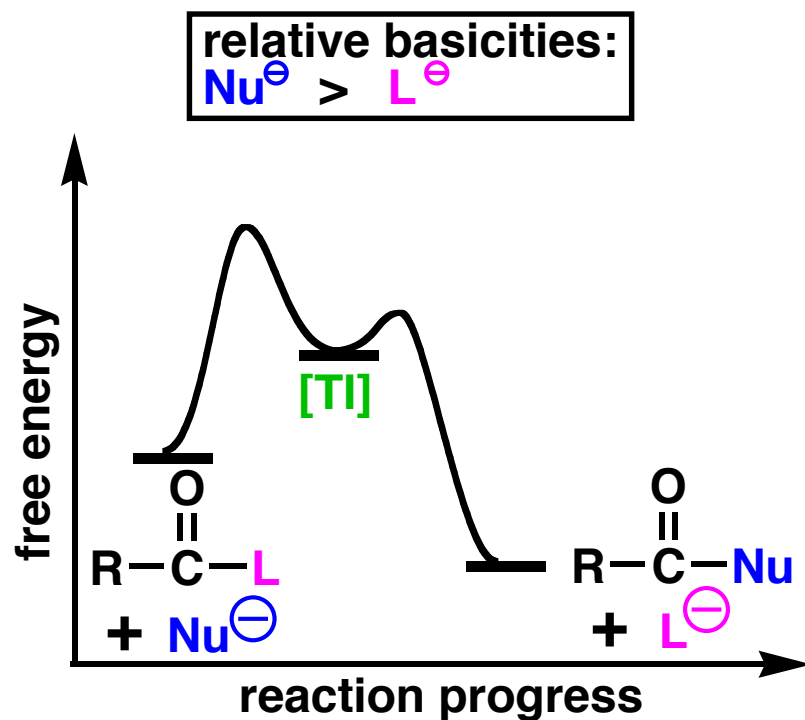
C=O nucleophilic addition	▶
C=O nucleophilic substitution	▶ Ester hydrolysis/formation - acid catalysis
C=O addition - loss of carbonyl oxygen	▶ Amide formation from acid chloride
Conjugate addition	▶

Here's a related mechanism on the formation of amides via acid chlorides.

<http://www.chemtube3d.com/>

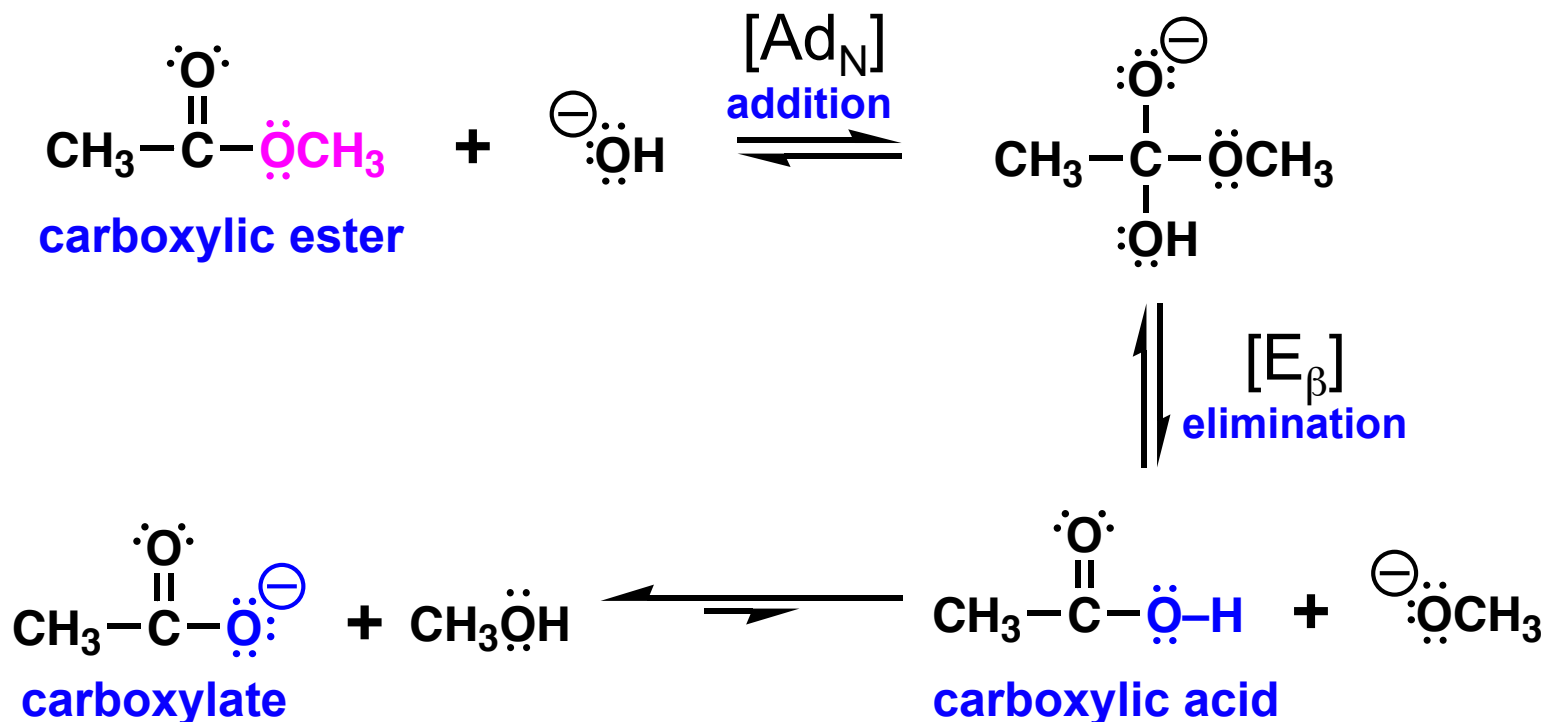


Equilibrium Position and the RDS Depend on Relative Basicity of Nu and X



best	leaving group (conjugate acid pK_a)	$\text{:}\ddot{\text{Cl}}\text{:}^\ominus$ (-2.2)	$\text{:}\ddot{\text{O}}\text{:}^\ominus-\text{C}(=\ddot{\text{O}})-\text{R}$ (4.8)	$\text{:}\ddot{\text{O}}\text{:}^\ominus\text{H}$ (15.7)	$\text{:}\ddot{\text{O}}\text{:}^\ominus-\text{R}$ (16)	$\text{:}\ddot{\text{N}}\text{H}_2^\ominus$ (35)	worst
	derivative	$\text{R}-\text{C}(=\ddot{\text{O}})-\ddot{\text{Cl}}\text{:}$ acyl chloride	$\text{R}-\text{C}(=\ddot{\text{O}})-\ddot{\text{O}}-\text{C}(=\ddot{\text{O}})-\text{R}$ acid anhydride	$\text{R}-\text{C}(=\ddot{\text{O}})-\ddot{\text{O}}\text{H}$ acid	$\text{R}-\text{C}(=\ddot{\text{O}})-\ddot{\text{O}}-\text{R}$ ester	$\text{R}-\text{C}(=\ddot{\text{O}})-\ddot{\text{N}}\text{H}_2$ amide	

Base-Catalyzed Ester Hydrolysis



Note that under **basic** conditions, all intermediates are either neutral or negatively charged. All steps are reversible, but the last step lies very far to the side of the carboxylate. This nearly irreversible step makes formation the reverse process (formation of esters from acids under basic conditions) nearly impossible.