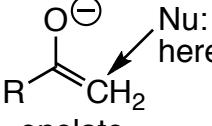
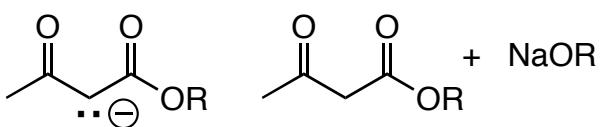


# CHM 422 Organic Synthesis, Dr. Laurie S. Starkey

## Electrophiles and Nucleophiles

Most organic reactions result from the union of an electron-rich Nucleophile ( $\text{Nu:}$ ) with an electron-poor Electrophile ( $\text{E}^+$ ). Shown below are several  $\text{Nu:}$  and  $\text{E}^+$  that are commonly utilized in organic synthesis.

Nucleophiles ( $\text{Nu:}$ )	Reagents/ notes	Electrophiles ( $\text{E}^+$ )	Notes
$\text{RO}^-$	$\text{ROH} + \text{NaH}$	$\left[ \begin{array}{c}   \\ \text{C}^+ \\   \\ \text{R}-\text{C} \\   \\ \text{R} \end{array} \right]$	Can't put this in a bottle! Instead, our $\text{E}^+$ reagents will have $\delta^+$ sites.
$\text{RNH}_2$	( $\text{RNH}^-$ is a strong base, not a $\text{Nu:}$ )	$\delta^+ \text{R}-\text{X} \delta^-$	$\text{R}-\text{Cl}, \text{R}-\text{Br}, \text{R}-\text{I}$ ( $\text{Br}-\text{Br}$ )
$\text{NO}_2^-, \text{N}_3^-$	$\text{NaNO}_2, \text{NaN}_3 \rightarrow$ amine synthesis	$\delta^+ \text{O} \delta^-$	$\text{Nu}-\text{CH}_2-\text{OH}$
$\text{I}^-$	$\text{NaI}$ (best halide $\text{Nu:}$ )	$\delta^+ \text{C}_3\text{H}_5 \delta^+$	
$\text{H:}^-$	$\text{LiAlH}_4$ or $\text{NaBH}_4$	$\delta^+ \text{C}_2\text{H}_5 \delta^-$	
$\text{R:}^-$	$\left\{ \begin{array}{l} \text{RX} + \text{Mg} \rightarrow \text{RMgX} \\ \text{RX} + \text{Li} \rightarrow \text{RLi} \\ 2 \text{RLi} + \text{Cu} \rightarrow \text{R}_2\text{CuLi} \end{array} \right.$	$\delta^+ \text{C}_2\text{H}_5 \delta^-$ (ketone/aldehyde)	
$\text{N}\equiv\text{C:}^-$	$\text{NaCN}$	$\delta^+ \text{C}_2\text{H}_5 \delta^-$	
$\text{RC}\equiv\text{C:}^-$	$\text{RC}\equiv\text{CH} + \text{NaNH}_2$	$\delta^+ \text{C}_2\text{H}_5 \delta^-$	
	$\text{R}-\text{C}(=\text{O})-\text{CH}_2^- + \text{LDA} \rightarrow \text{R}-\text{C}(=\text{O})-\text{CH}_2 + \text{LDAs}^-$	$\delta^+ \text{C}_2\text{H}_5 \delta^-$	
$\text{NO}_2-\text{CH}_2^-$	"EWG"- $\text{CH}_3 + \text{LDA}$	$\delta^+ \text{C}_2\text{H}_5 \delta^-$	
$\text{NC}-\text{CH}_2^-$	(enolate-like $\text{Nu:}$ 's)	$\delta^+ \text{C}_2\text{H}_5 \delta^-$	
	$\delta^+ \text{C}_2\text{H}_5 \delta^-$	$\delta^+ \text{C}_2\text{H}_5 \delta^-$	
 $\text{acetoacetate enolate} \xrightarrow{\text{alkylation}} \text{ester}$	$\delta^+ \text{C}_2\text{H}_5 \delta^-$	$\delta^+ \text{C}_2\text{H}_5 \delta^-$	
	$\xrightarrow{\text{1)NaOH, H}_2\text{O}}$	$\delta^+ \text{C}_2\text{H}_5 \delta^-$	
	$\xrightarrow{\text{2) H}_3\text{O}^+}$	$\delta^+ \text{C}_2\text{H}_5 \delta^-$	
	$\beta\text{-ketoacid}$	$\delta^+ \text{C}_2\text{H}_5 \delta^-$	
	$\xrightarrow{\Delta}$	$\delta^+ \text{C}_2\text{H}_5 \delta^-$	
	$\xrightarrow{-\text{CO}_2}$	$\delta^+ \text{C}_2\text{H}_5 \delta^-$	
	$\text{enol} \longrightarrow \text{ketone}$	$\delta^+ \text{C}_2\text{H}_5 \delta^-$	
		$\delta^+ \text{C}_2\text{H}_5 \delta^-$	carboxylic acid derivatives generally add 2 eq. of C or H $\text{Nu:}$ (addn/elim mech)
		$\delta^+ \text{C}_2\text{H}_5 \delta^-$	$\text{Nu}-\text{CH}_2-\text{OH}$

Note: The enolate of acetoacetate is often used as a *synthetic equivalent* of the acetone enolate, since acetone itself typically gives poor yields. The extra C is lost by hydrolysis/decarboxylation.

