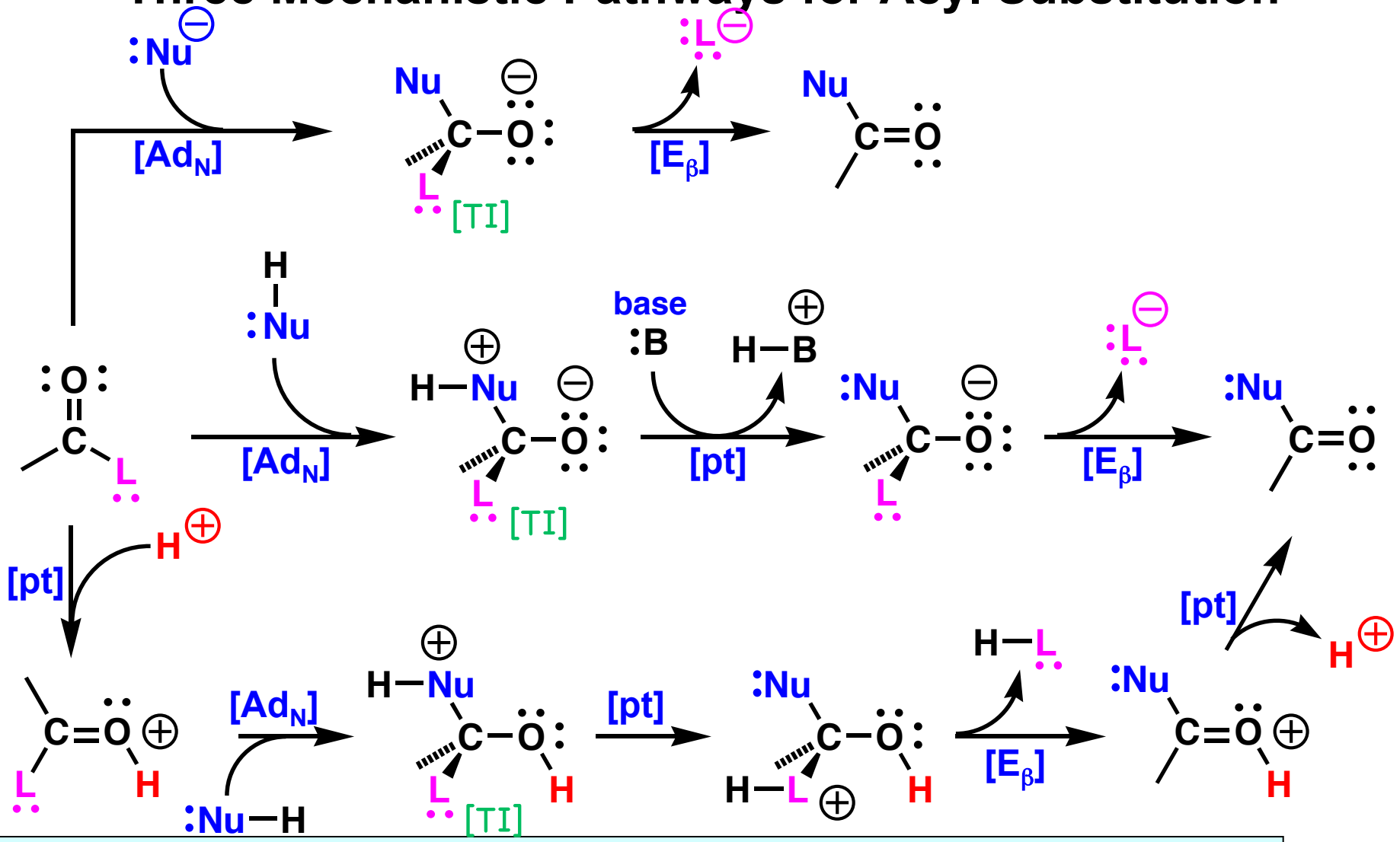
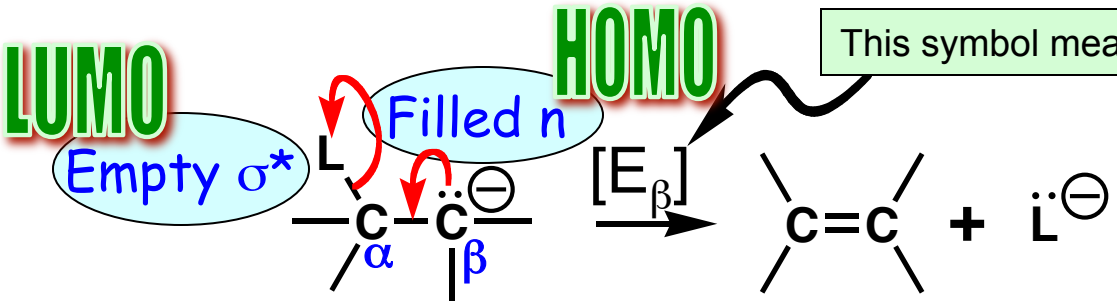
# Three Mechanistic Pathways for Acyl Substitution




All three pathways include [Ad$_N$] and subsequently [E$_\beta$] steps (i.e., addition followed by elimination, proceeding through tetrahedral intermediate [TI]). The three paths differ by the role of [pt]. Which pathway is best will depend on the pH, the nucleophile strength, and the leaving group quality. A rough generalization is that the top pathway is for basic, the middle for neutral, and the bottom for acidic conditions. Slight variations on these pathways will be encountered.

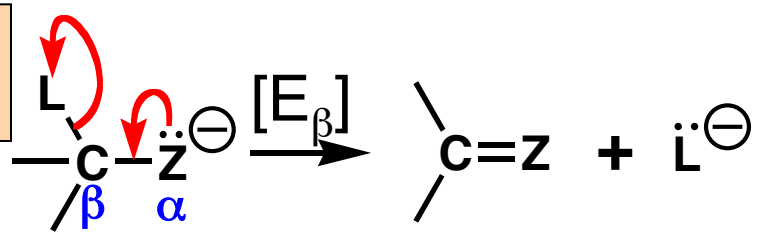
# Acyl Substitution Requires a Variation of the [$E_\beta$] Step: Beta Elimination Across the C-Z: Bond




This symbol means beta elimination

[$E_\beta$] involves
π-bond making
σ-bond breaking

-L is a LG;
Z: is O or N




**[$E_\beta$] is an *n* → σ* *π-type* interaction**

We first encountered [$E_\beta$] when we studied the [E1cb] elimination pathway (top equation). In the second equation, [$E_\beta$] is now shown for the generalized case where Z: may be an oxygen or nitrogen atom. Many leaving groups (-L) participate in [$E_\beta$], even poor ones (e.g., -OH). **This step is the reverse of [$Ad_N$].**

**Curved Arrows Imply the Frontier Orbitals**

Curved arrows indicate the HOMO-LUMO pair (Frontier Orbitals) involved in this elementary step. The tail of the first arrow implies that the filled orbital (HOMO) is a nonbonded electron pair, *n*. The head of the first arrow points between C-Z: suggesting a new π-bond. An empty, low-lying σ*-orbital from the adjacent C-L bond is available to accommodate this electron pair suggesting the LUMO is σ*. The HOMO (*n*) is beside (and nearly parallel to) the LUMO (σ*) allowing for a π-type interaction.

| empty / filled | σ* | a | π* |
|---|---|---|---|
| σ | σ→σ* | σ→a | σ→π* |
| n | n→σ* | n→a | n→π* |
| π | π→σ* | π→a | π→π* |