

# Direct Addition vs Conjugate Addition

## The Nature of the Nucleophile

| Attribute                    | Direct Addition                                   | Conjugate Addition                                                |
|------------------------------|---------------------------------------------------|-------------------------------------------------------------------|
| Base strength of nucleophile | Nucleophiles that are stronger bases              | Nucleophiles that are weaker bases                                |
| Carbanion nucleophiles       | Organolithium (RLi) and Grignard reagents (RMgBr) | Organocopper reagents ( $R_2CuLi$ )<br>Cyanide (NaCN)<br>Enolates |
| Hetero nucleophiles          | Amines ( $RNH_2$ )                                | Thiols (RSH)                                                      |
| Hydride Nucleophiles         | Lithium aluminium hydride ( $LiAlH_4$ )           | Copper hydride (CuH)                                              |

# Conjugate Addition Reactions

## Reactions with Enolates: The Rationale

Enolate nucleophiles can undergo conjugate addition, but they have exactly the same opportunity to attack the carbonyl group directly as do simple nucleophiles.

Thermodynamic control leads to conjugate addition, but kinetic control leads to direct attack.

Success in conjugate addition is pegged on the direct addition (an Aldol reaction) being reversible. This enables the conjugate addition to compete and, as its product is more stable (thermodynamically stable), it eventually become the sole product.