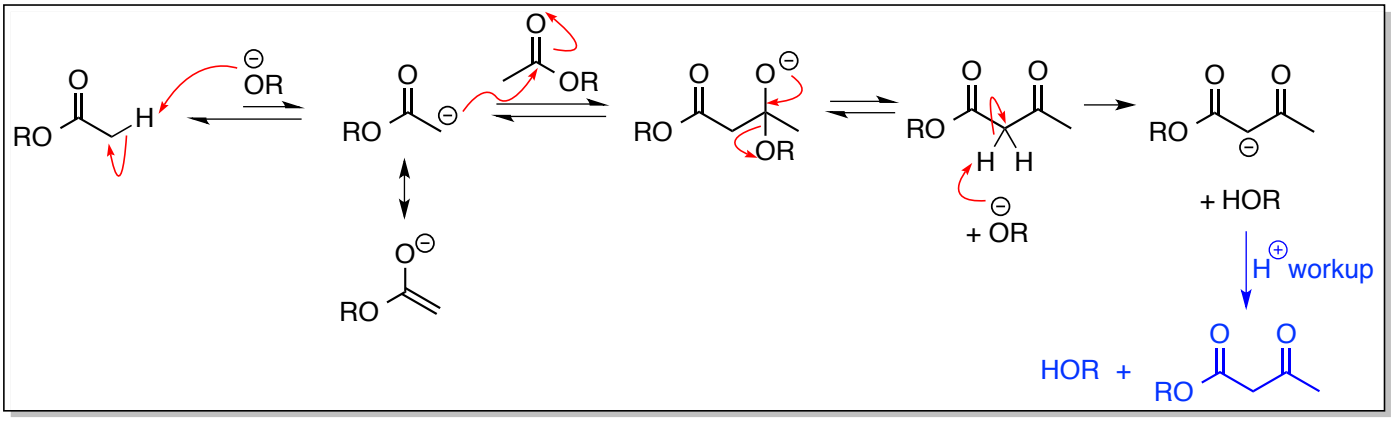
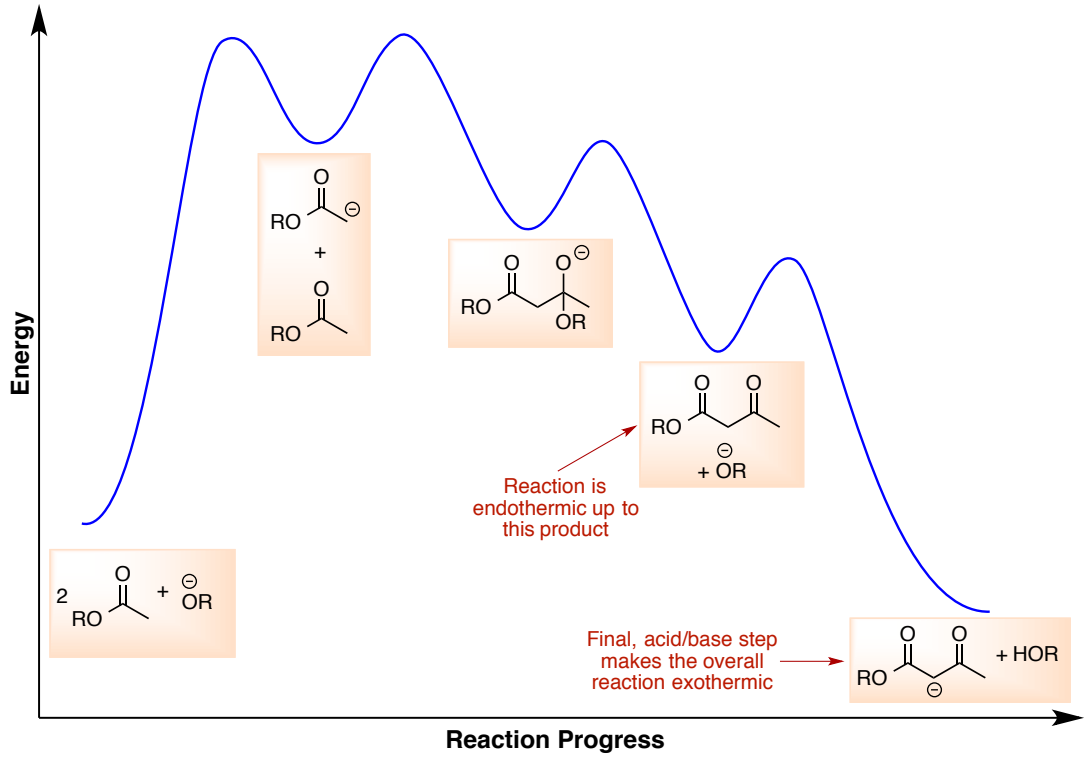
Energetic Considerations for the Claisen Reaction

General Mechanism



Reaction Coordinate



Features

- The first step (enolate formation) is endothermic. The α-H's on the ester have a pKa of ~25 while the pKa of HOR is ~16 making this acid base reaction unfavorable. At equilibrium there will be a few molecules of enolate, which is enough to carry through with the reaction.
- Formation of the β-ketoester in the third step is still not thermodynamically favored. This compound is higher in energy than the two ester starting materials. Each of the two ester starting materials are stabilized by resonance while there is only one ester in the β-ketoester that has resonance stabilization (two is better than one).
- The thermodynamic driving force for the reaction happens in the final step. The alkoxide quickly reacts with one of the α-H's of the β-ketoester (pKa~11) to give the resonance stabilized enolate plus the alcohol (pKa~16).