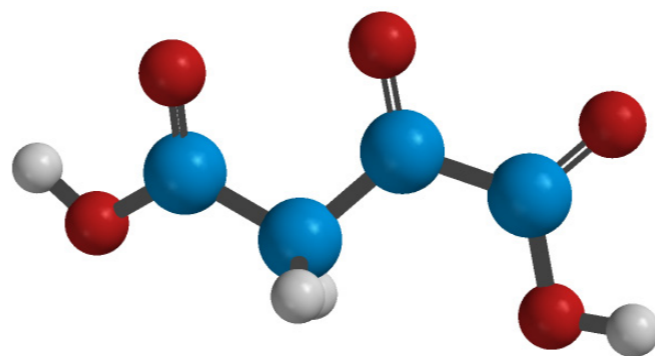


22

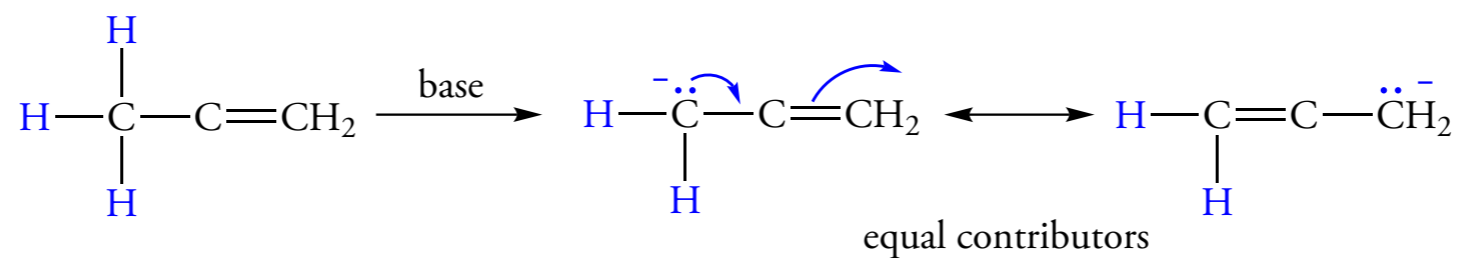
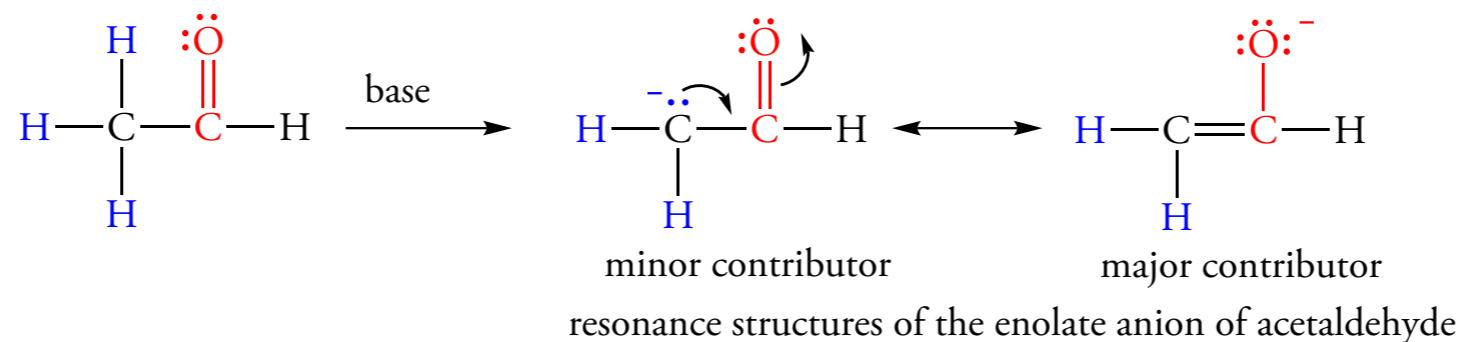
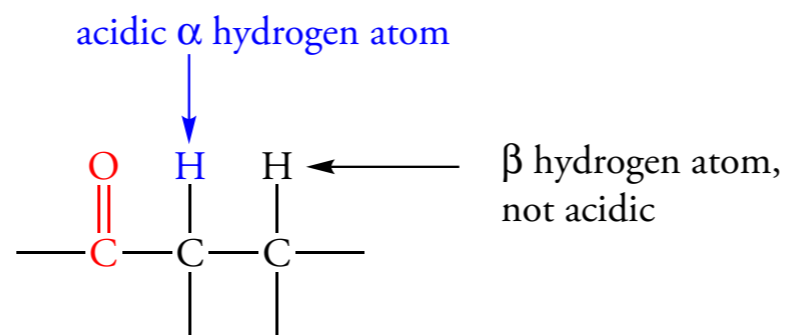
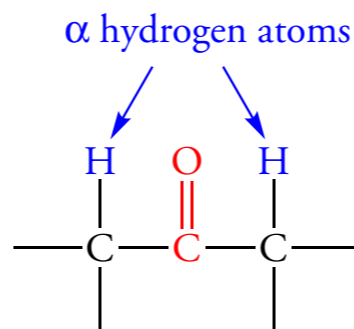
# CONDENSATION REACTIONS OF CARBONYL COMPOUNDS



Oxaloacetic acid

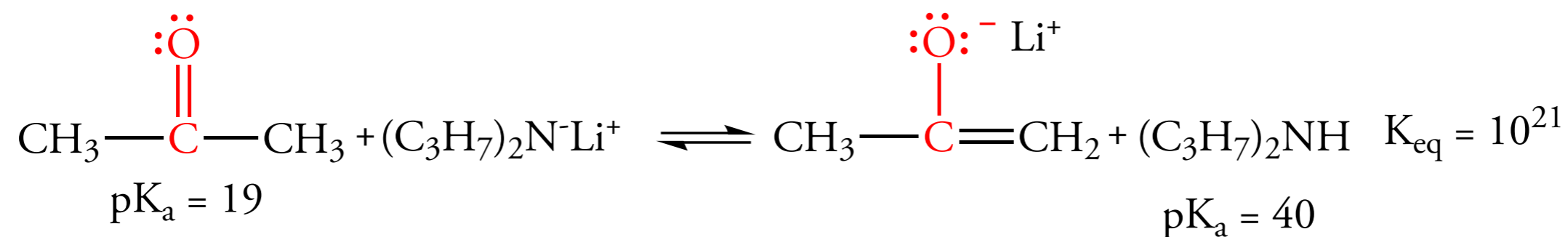
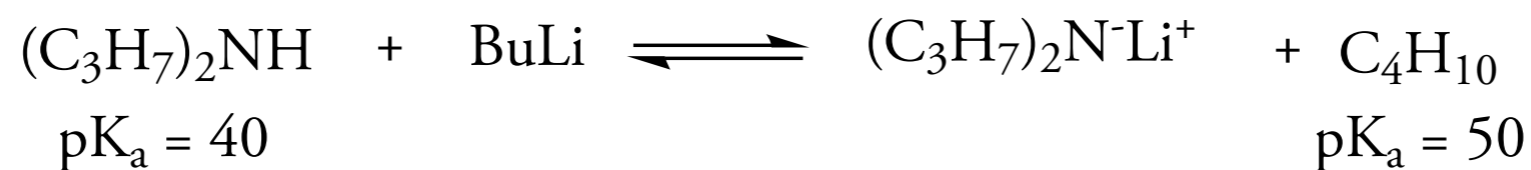
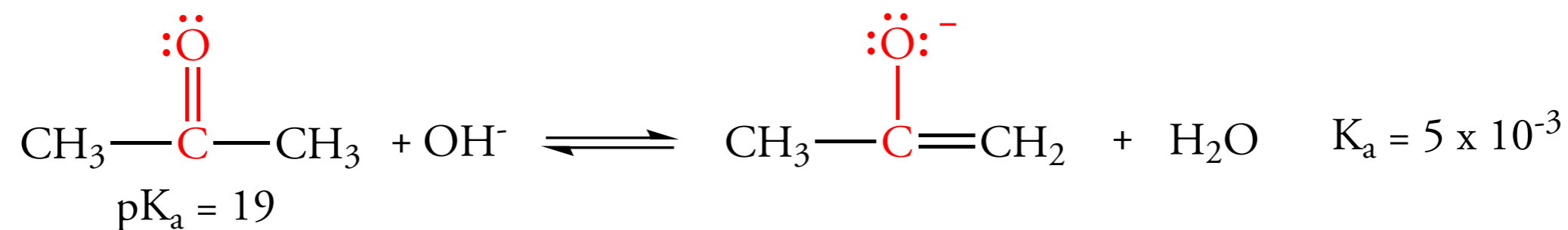
## 22.1 THE $\alpha$ CARBON ATOM OF ALDEHYDES AND KETONES

### Acidity of $\alpha$ Hydrogens



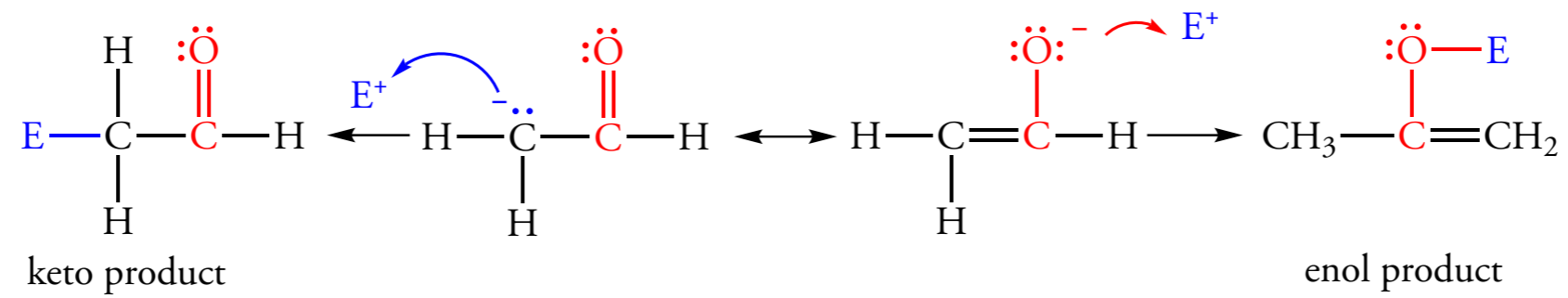
## 22.1 THE $\alpha$ CARBON ATOM OF ALDEHYDES AND KETONES

### Formation of Enolates



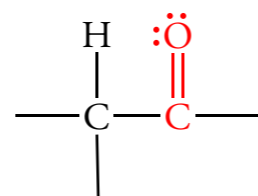
## 22.1 THE $\alpha$ CARBON ATOM OF ALDEHYDES AND KETONES

### Reactions of Enolates

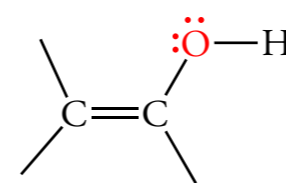


# 22.2 KETO-ENOL EQUILIBRIA OF ALDEHYDES AND KETONES

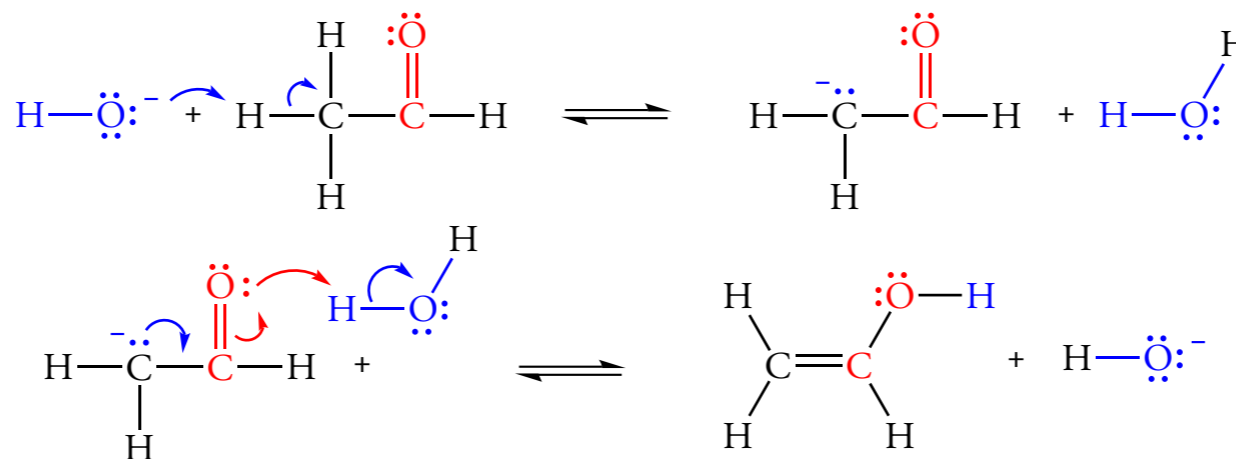
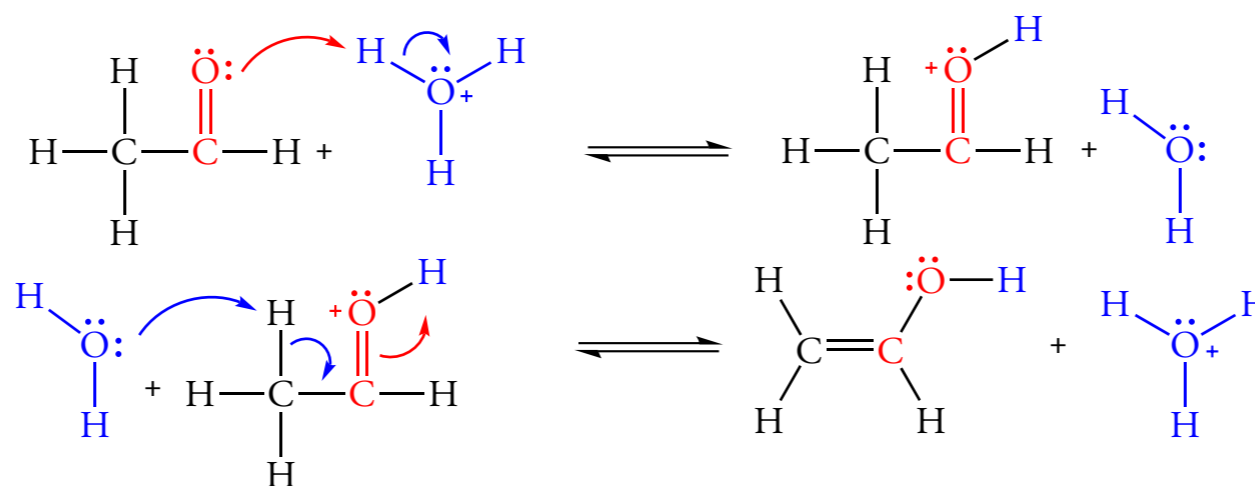
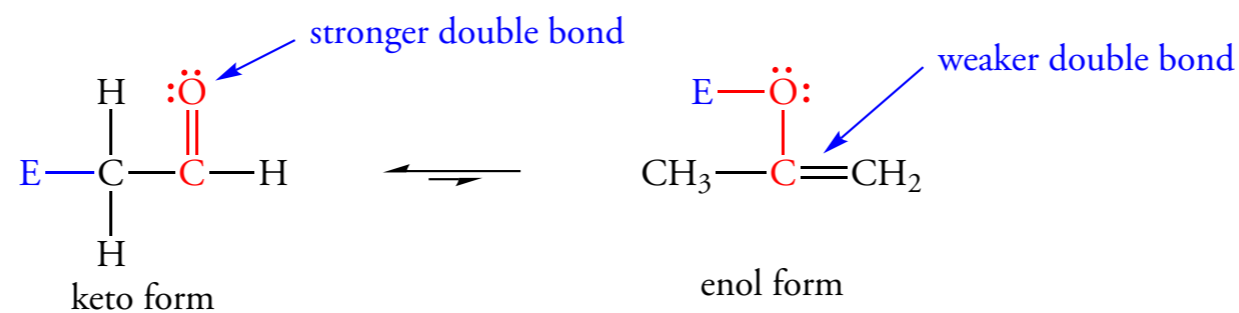
## Mechanism of Tautomerization



keto form

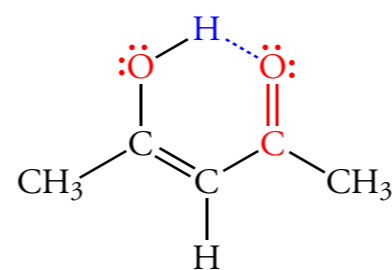
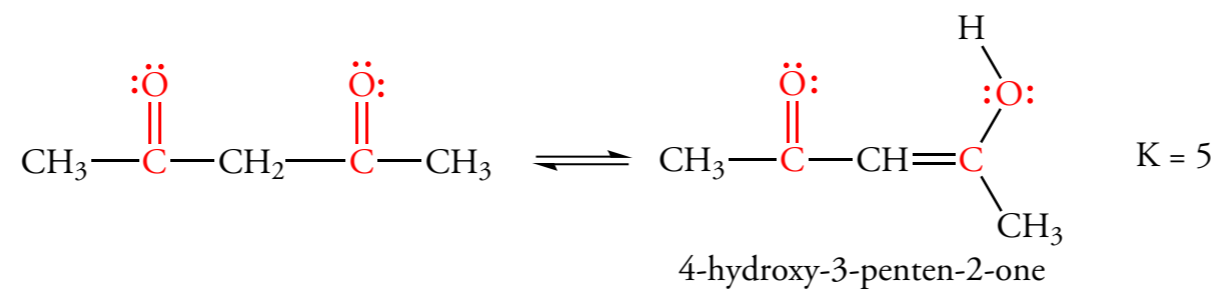
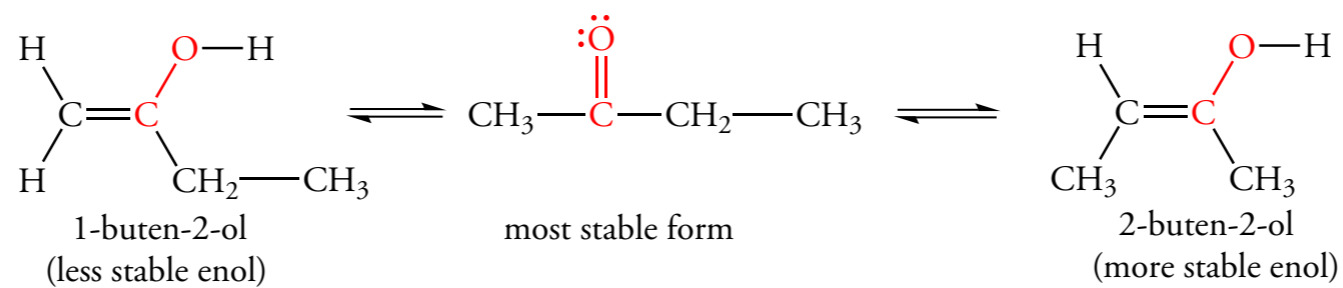
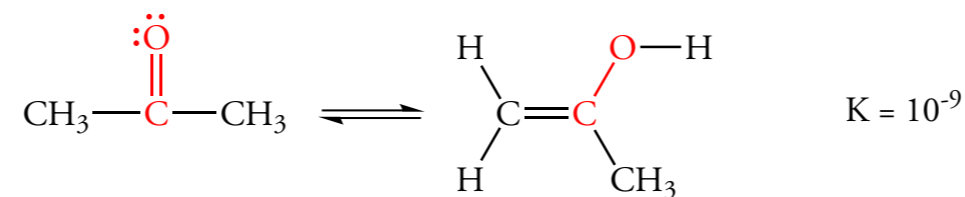
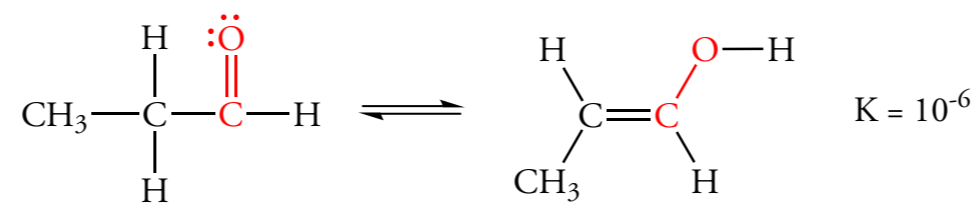


enol form



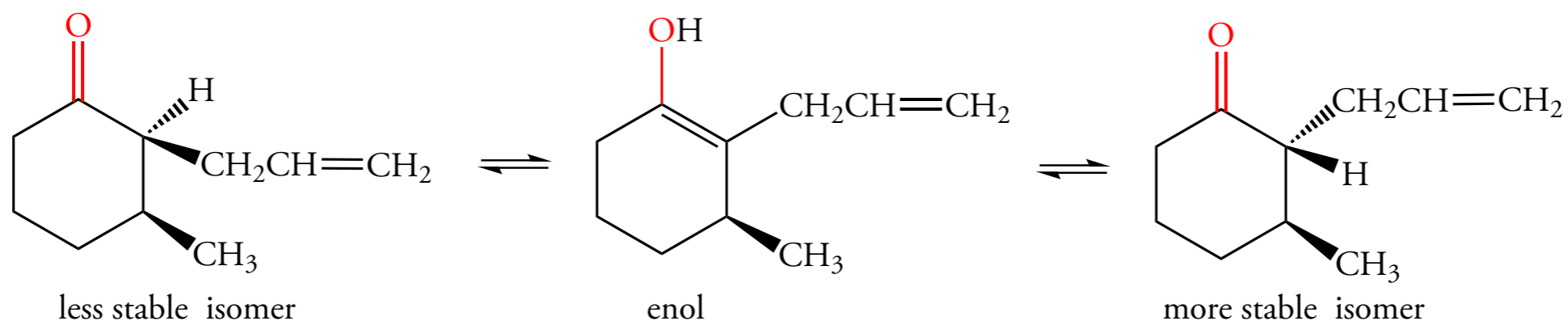
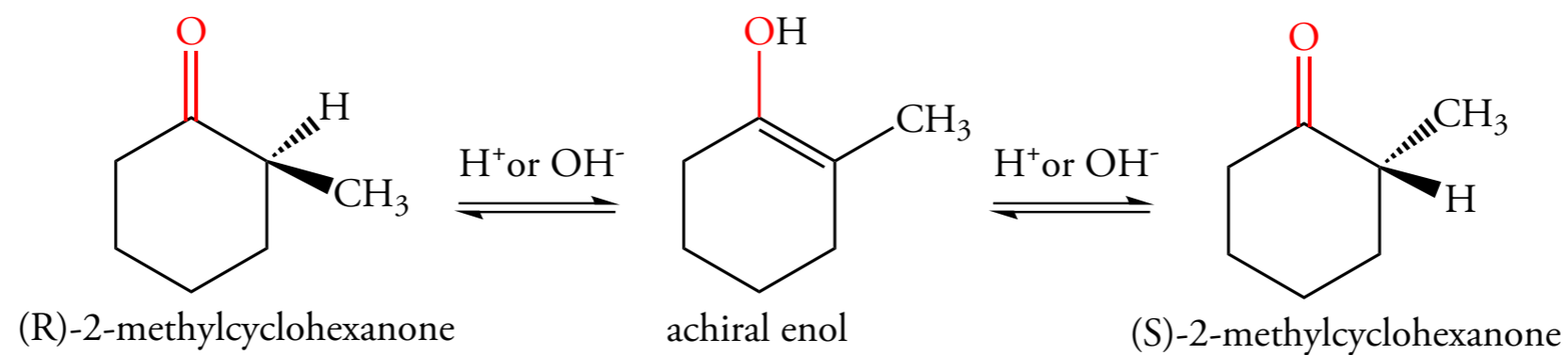
## 22.2 KETO-ENOL EQUILIBRIA OF ALDEHYDES AND KETONES

### Stability of Enols



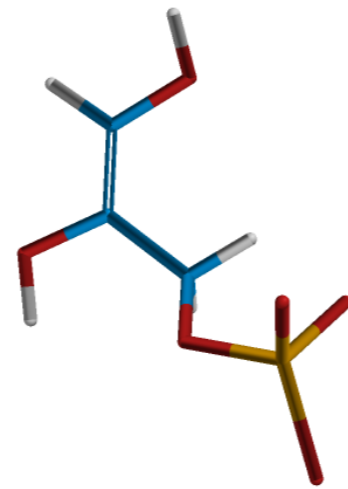
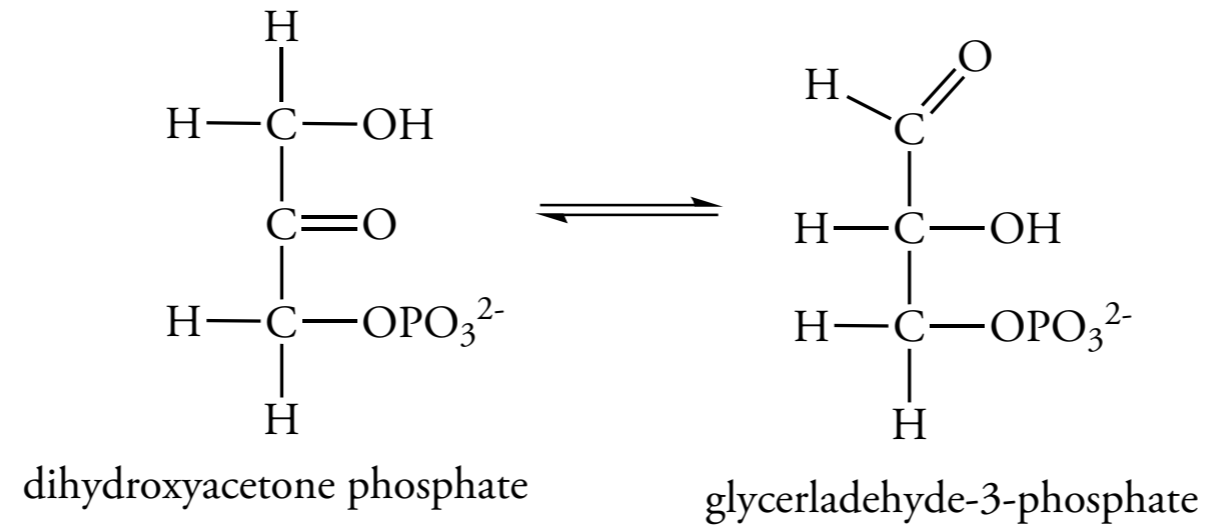
intramolecular hydrogen bond of an enol  
of a  $\beta$ -diketone

## 22.3 CONSEQUENCES OF ENOLIZATION

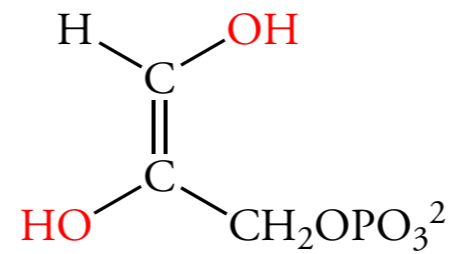


## 22.3 CONSEQUENCES OF ENOLIZATION

### Tautomerization in Metabolic Reactions

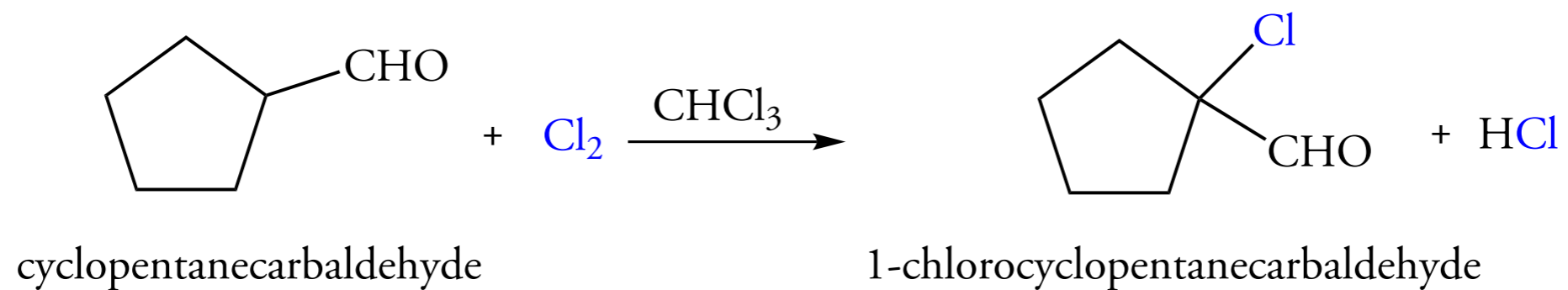
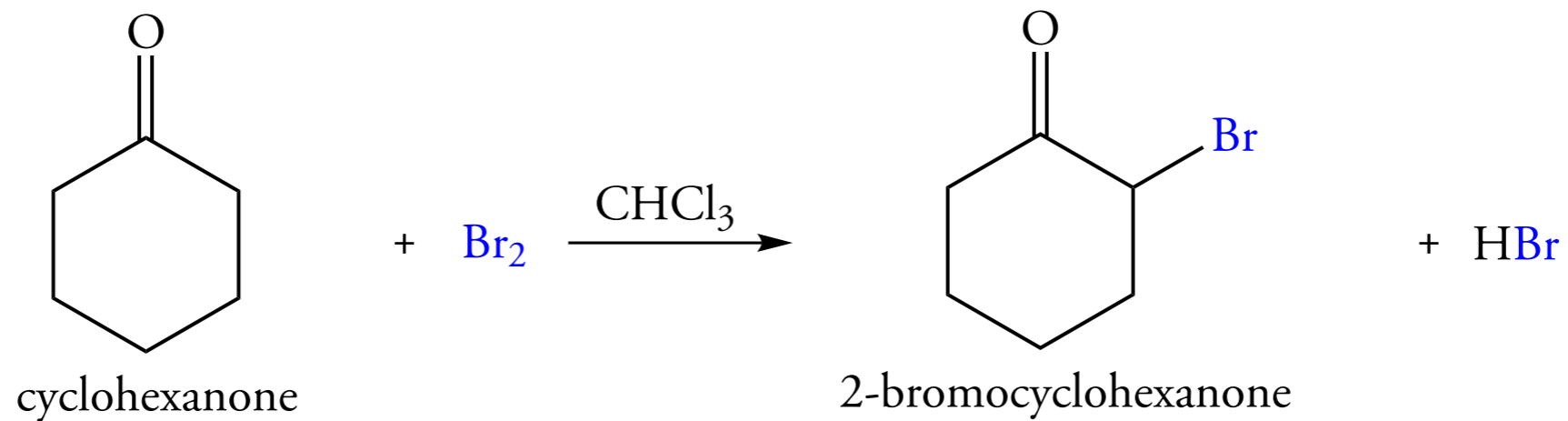


enediol intermediate



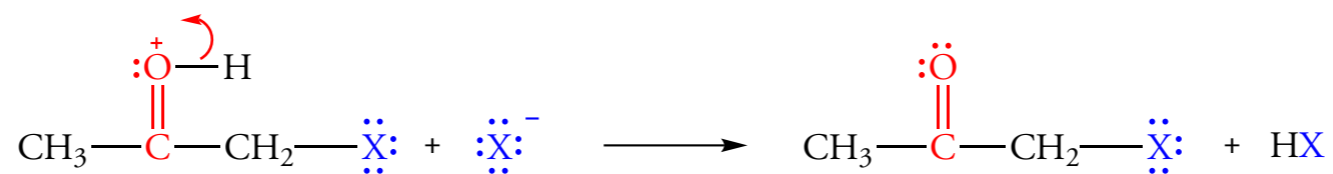
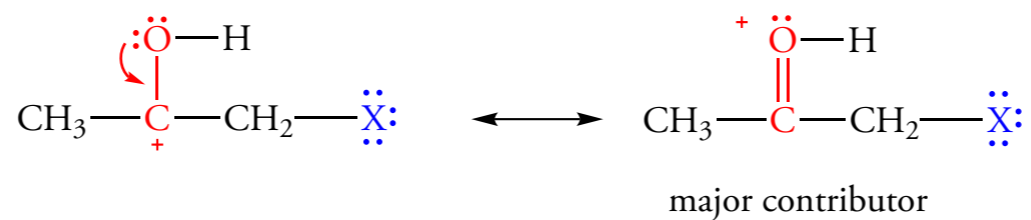
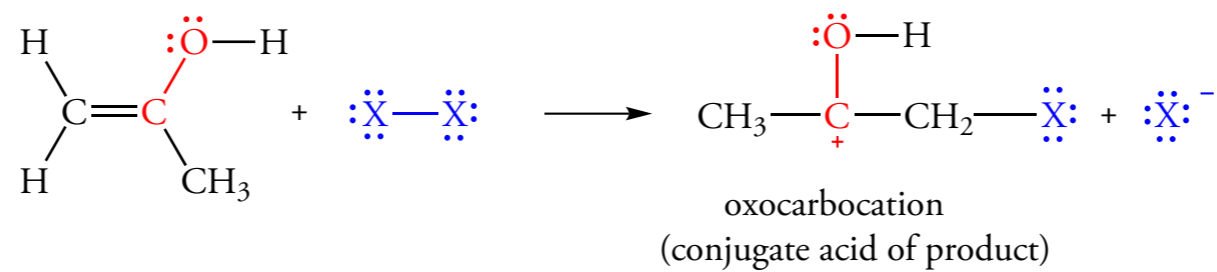
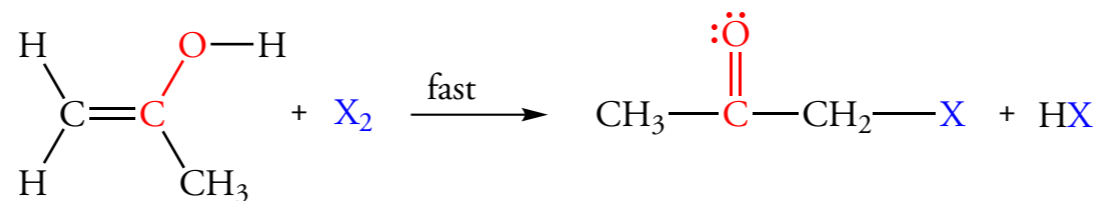
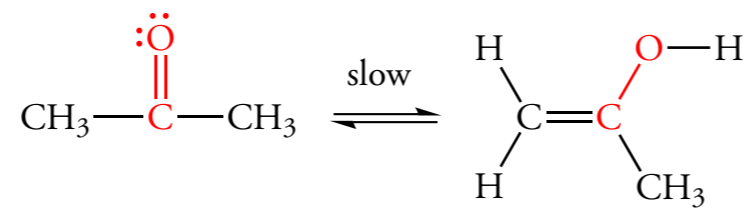


## 22.4 $\alpha$ HALOGENATION REACTIONS OF ALDEHYDES AND KETONES



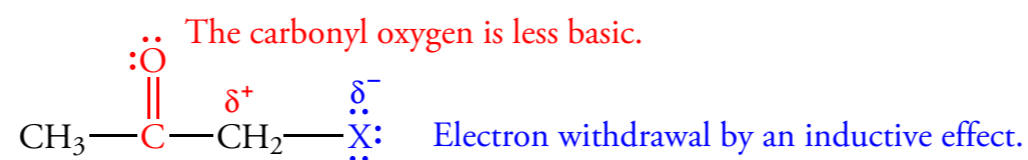
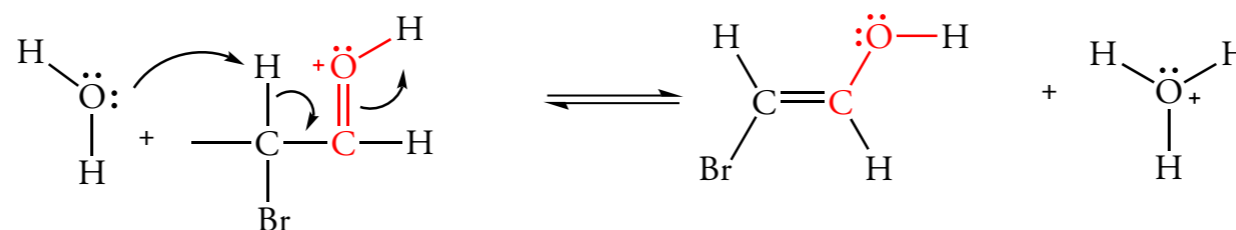
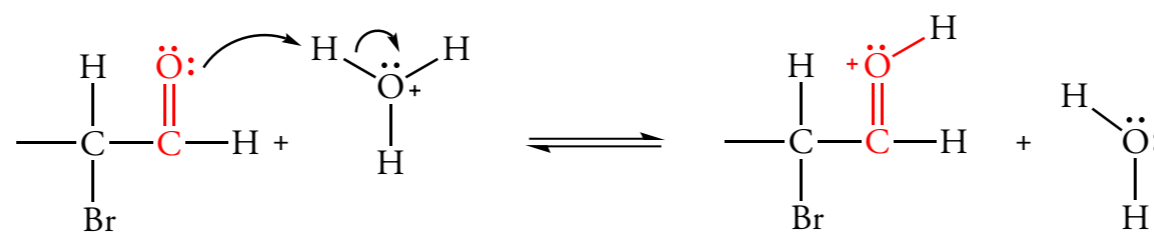
## 22.4 $\alpha$ HALOGENATION REACTIONS OF ALDEHYDES AND KETONES

### Acid-Catalyzed Halogenation

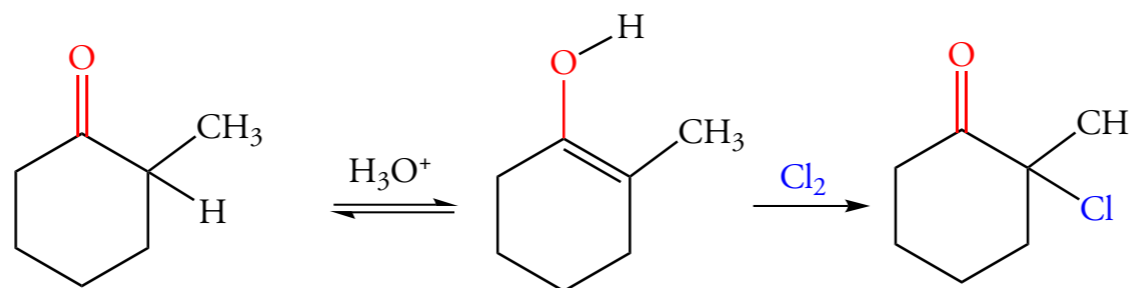


## 22.4 $\alpha$ HALOGENATION REACTIONS OF ALDEHYDES AND KETONES

### Acid-Catalyzed Halogenation, II

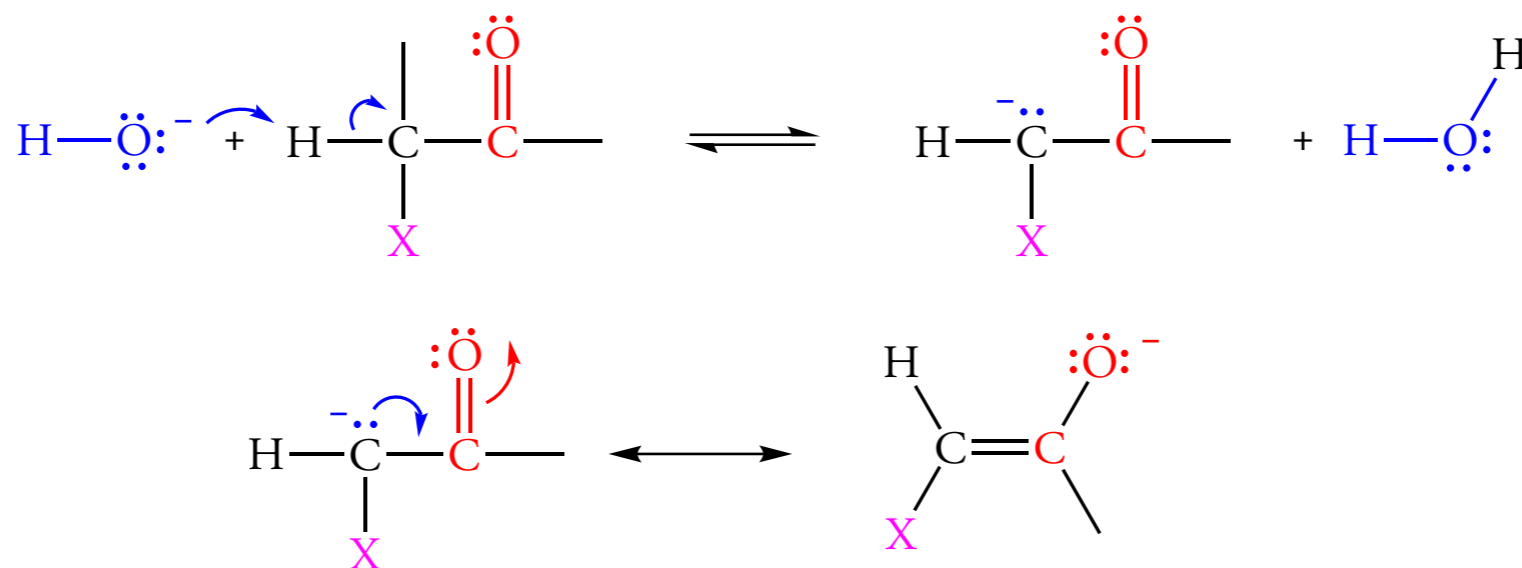
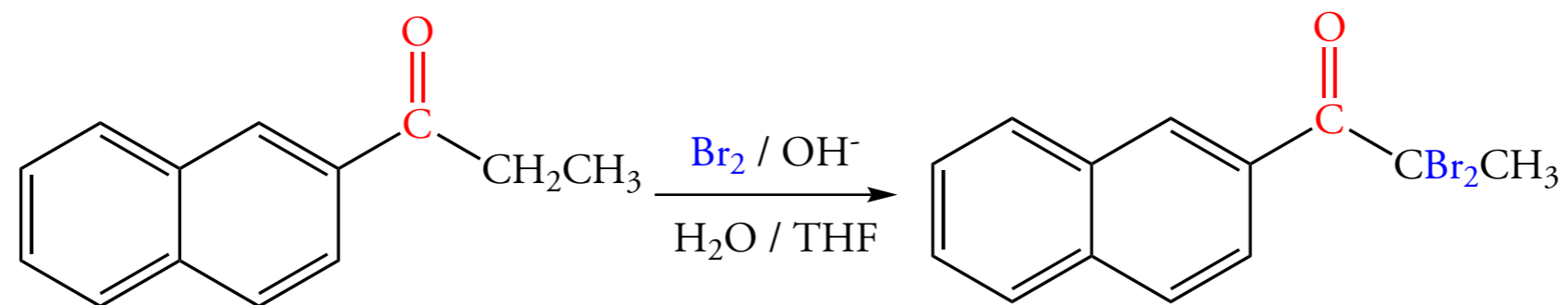


This resonance form is destabilized by the electron-withdrawing halogen atom.



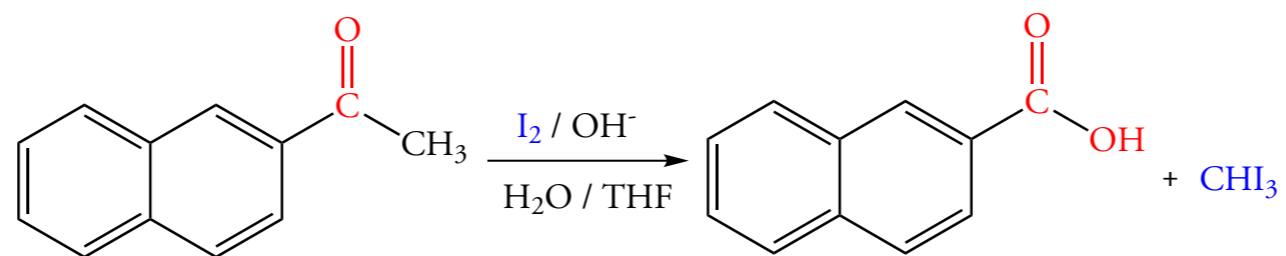
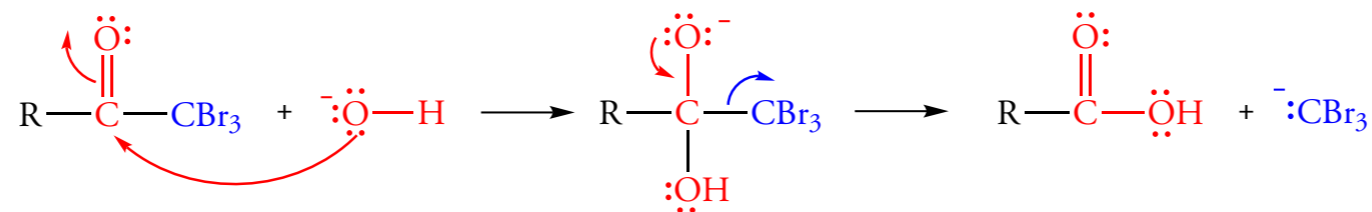
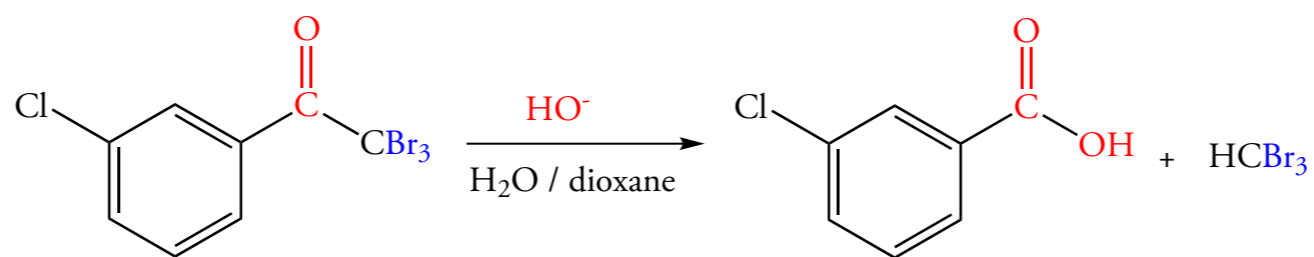
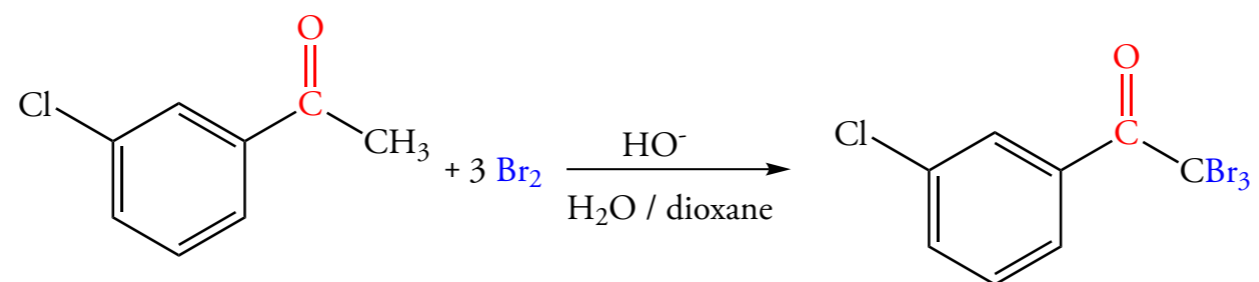
## 22.4 $\alpha$ HALOGENATION REACTIONS OF ALDEHYDES AND KETONES

### Base-Catalyzed Halogenation

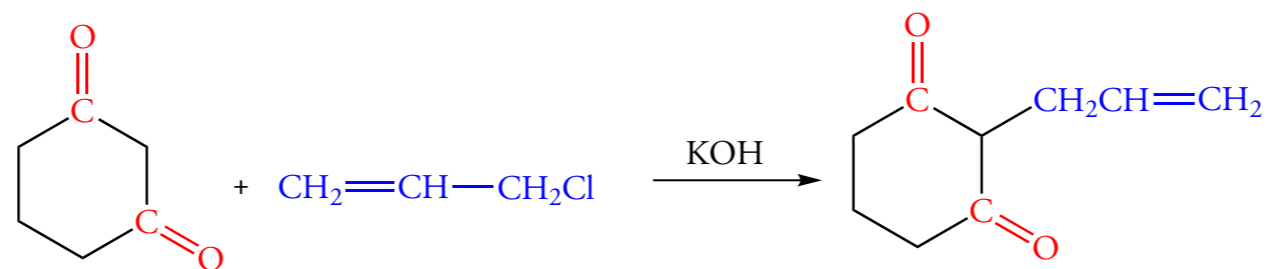
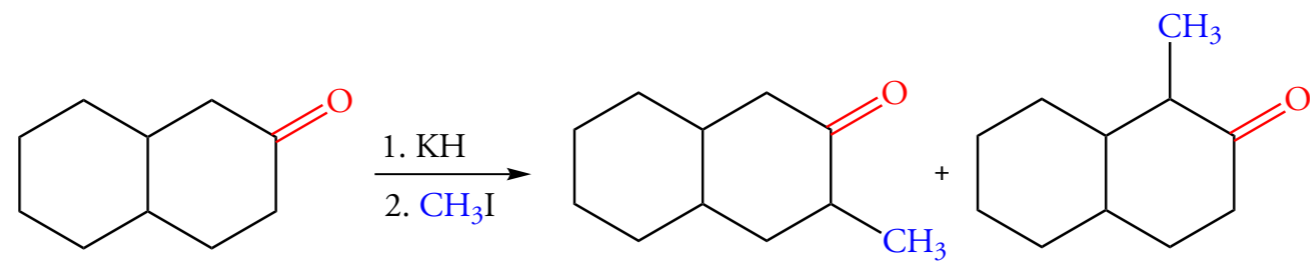
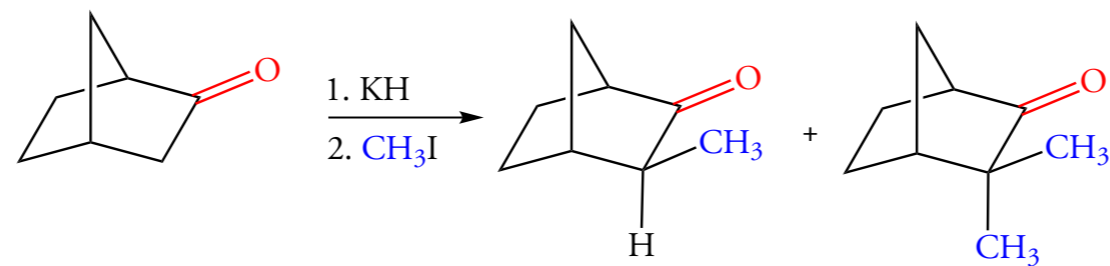
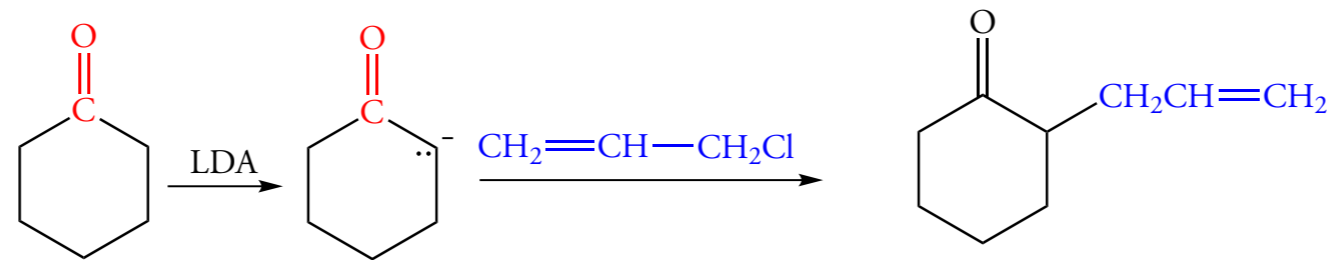
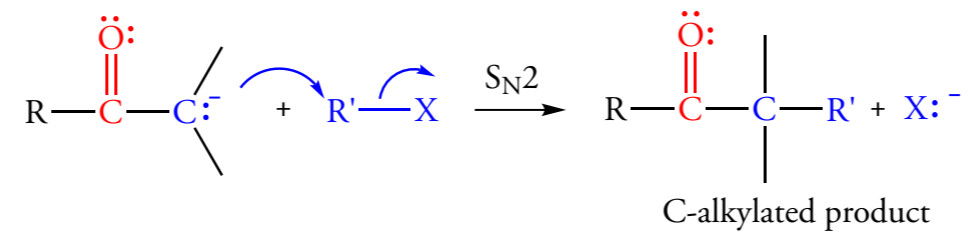


## 22.4 $\alpha$ HALOGENATION REACTIONS OF ALDEHYDES AND KETONES

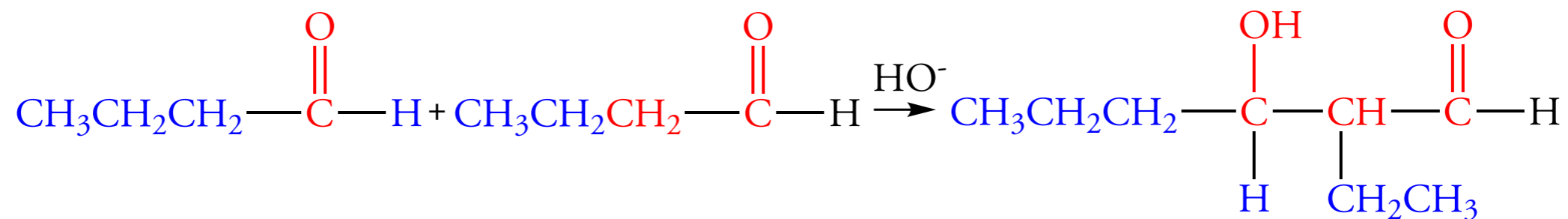
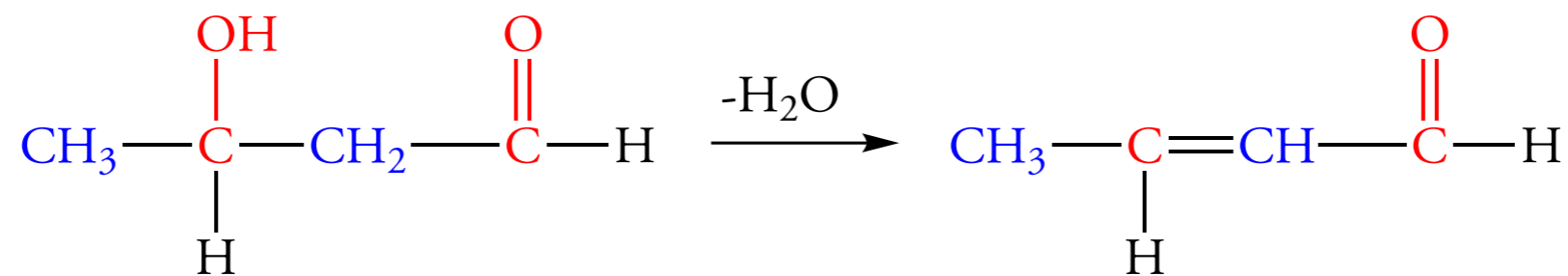
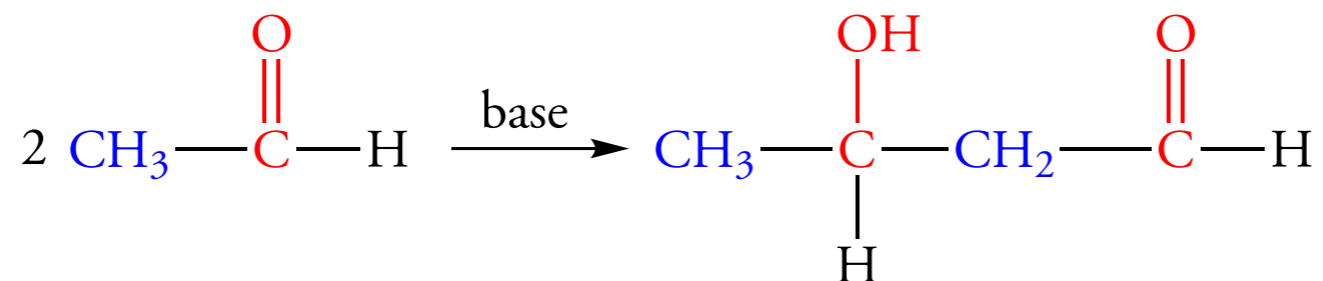
### The Haloform Reaction



## 22.5 ALKYLATION OF ENOLATE IONS

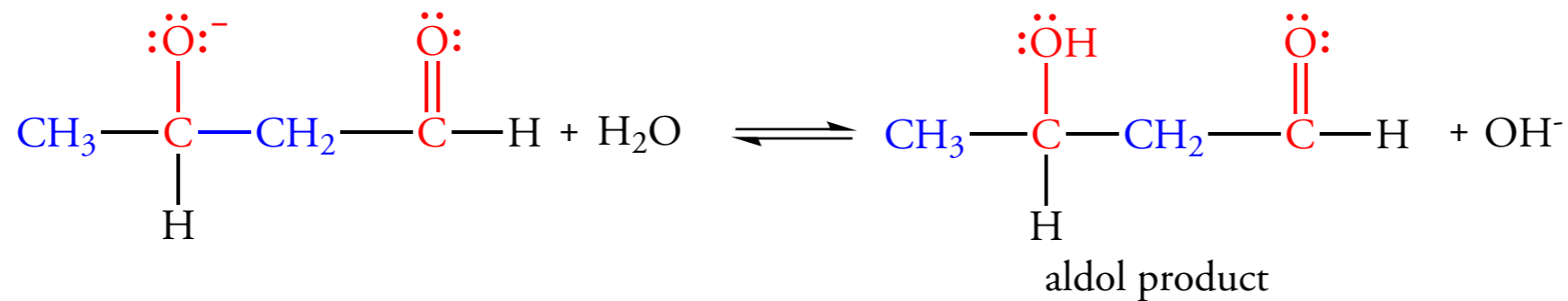
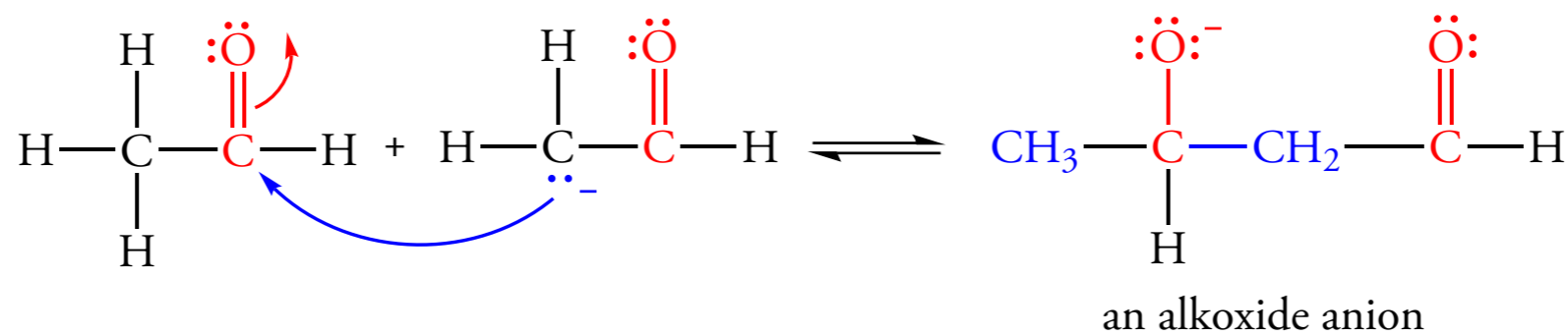
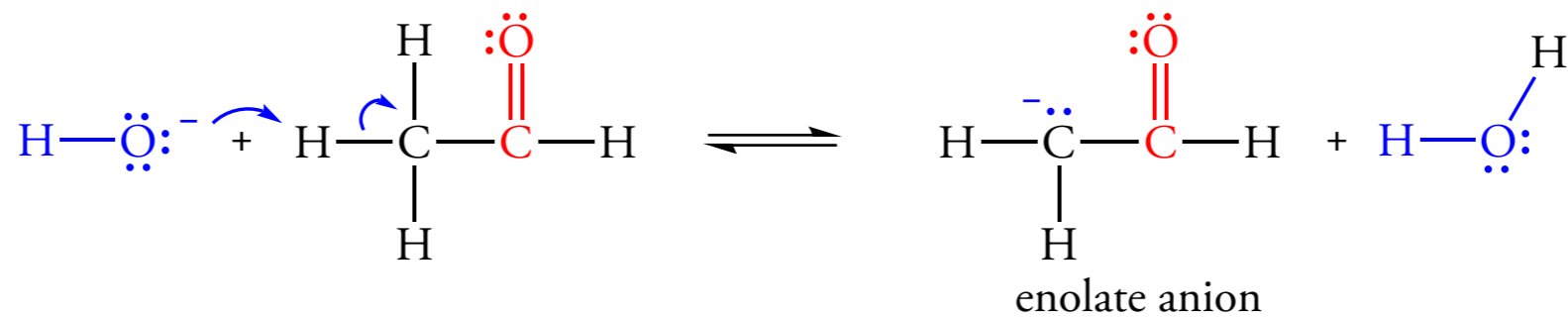


## 22.6 THE ALDOL CONDENSATION OF ALDEHYDES



## 22.6 THE ALDOL CONDENSATION OF ALDEHYDES

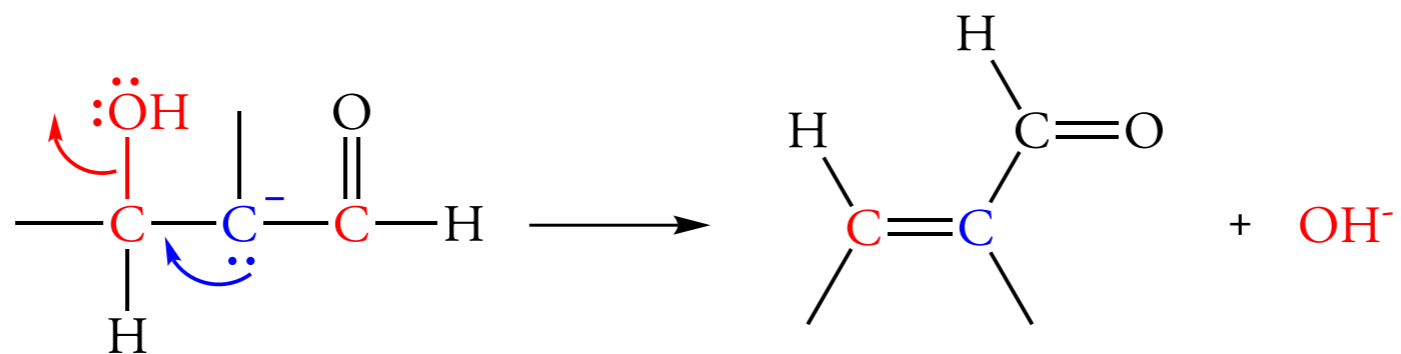
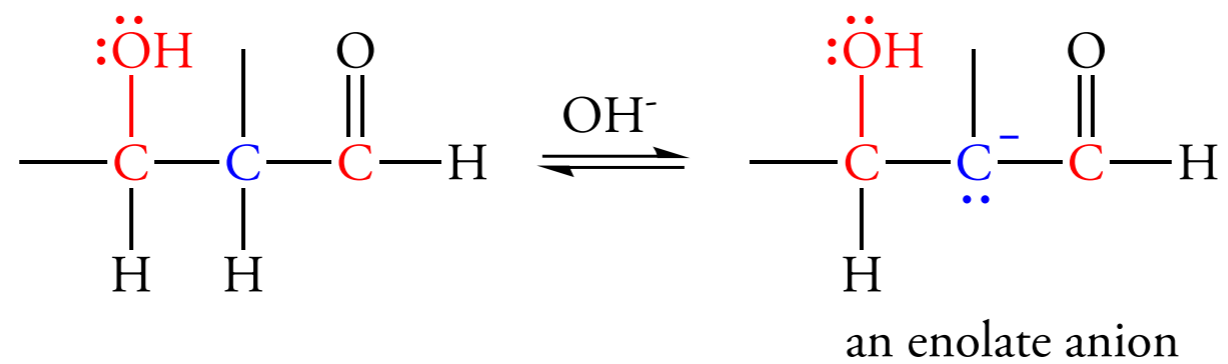
### Mechanism of the Addition Reaction



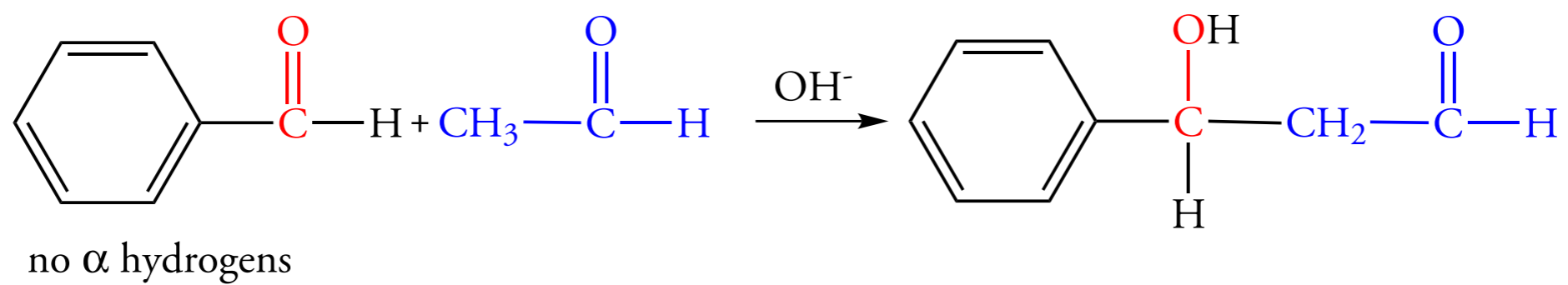


## 22.6 THE ALDOL CONDENSATION OF ALDEHYDES

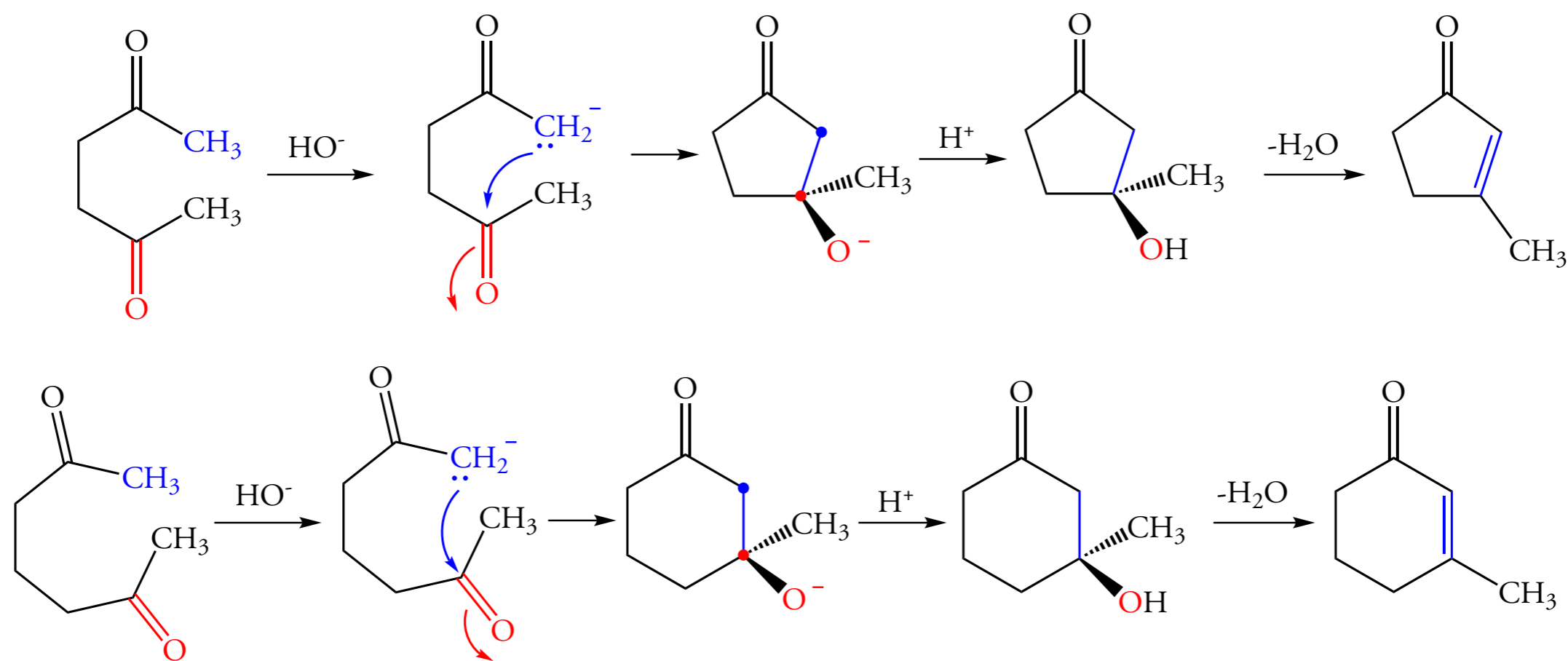
### Dehydration of Aldols



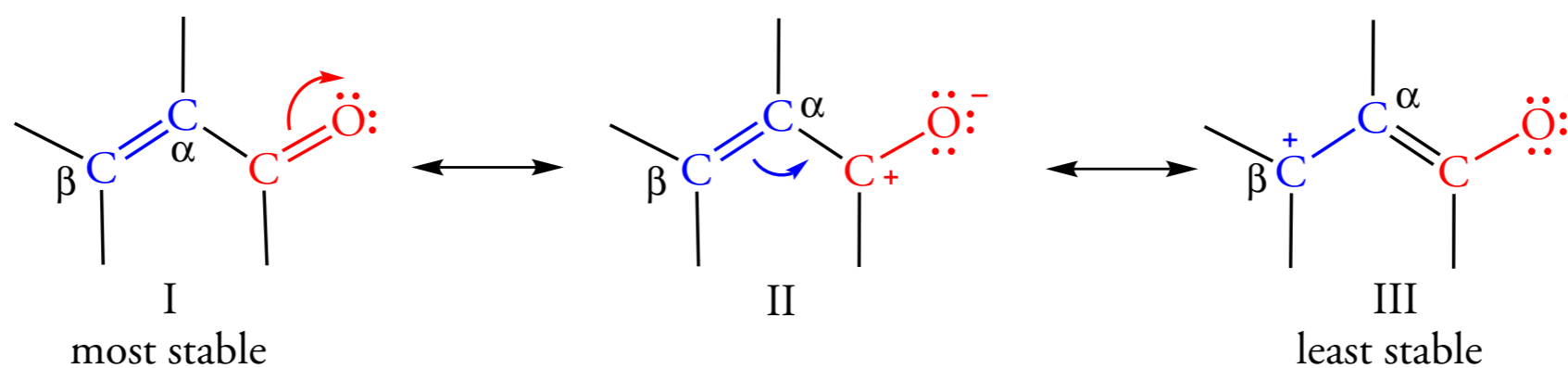
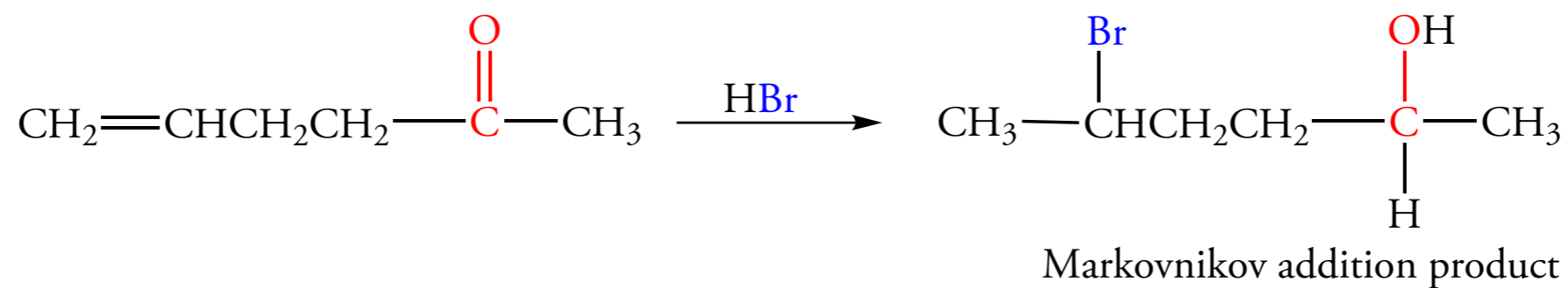
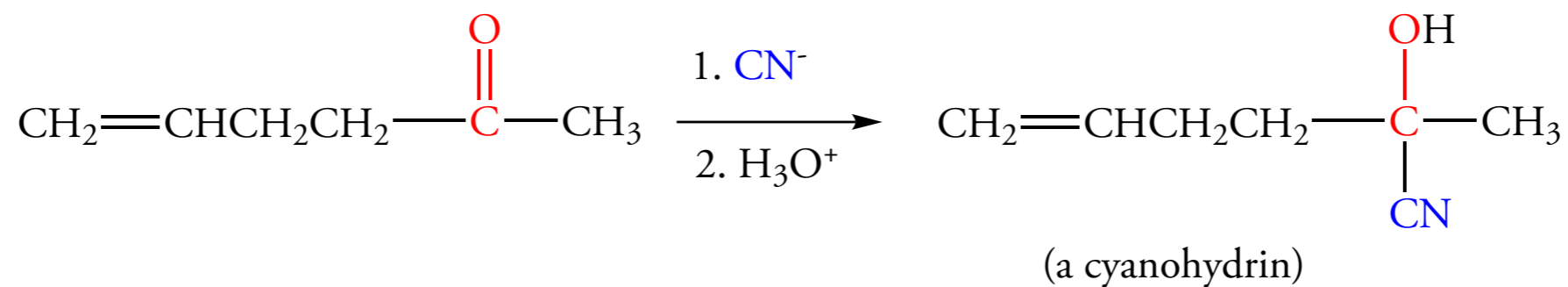
## 22.7 MIXED ALDOL CONDENSATION REACTIONS



## 22.8 INTRAMOLECULAR ALDOL CONDENSATION REACTIONS

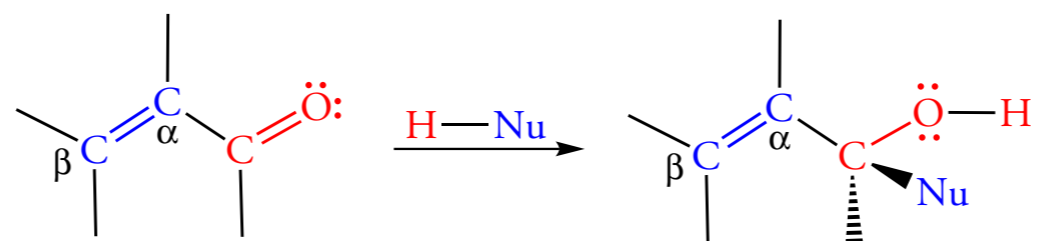


## 22.9 CONJUGATION IN $\alpha$ - $\beta$ -UNSATURATED ALDEHYDES AND KETONES

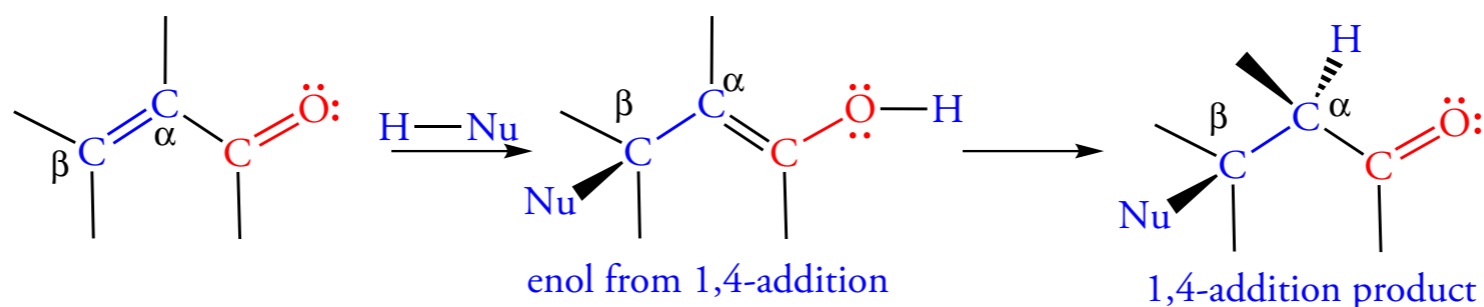


## 22.10 CONJUGATE ADDITION REACTIONS

### 1,2- and 1,4-Addition Reactions

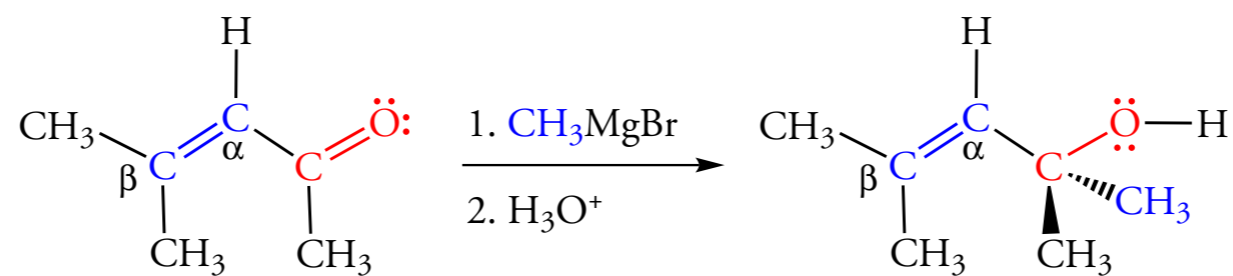
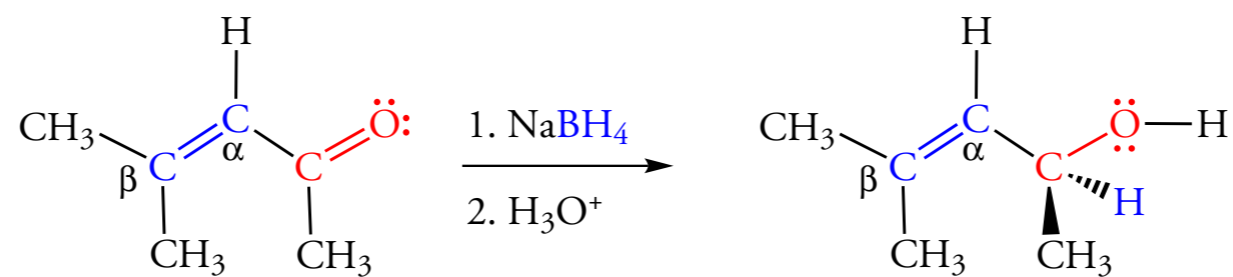


1,2-addition product



enol from 1,4-addition

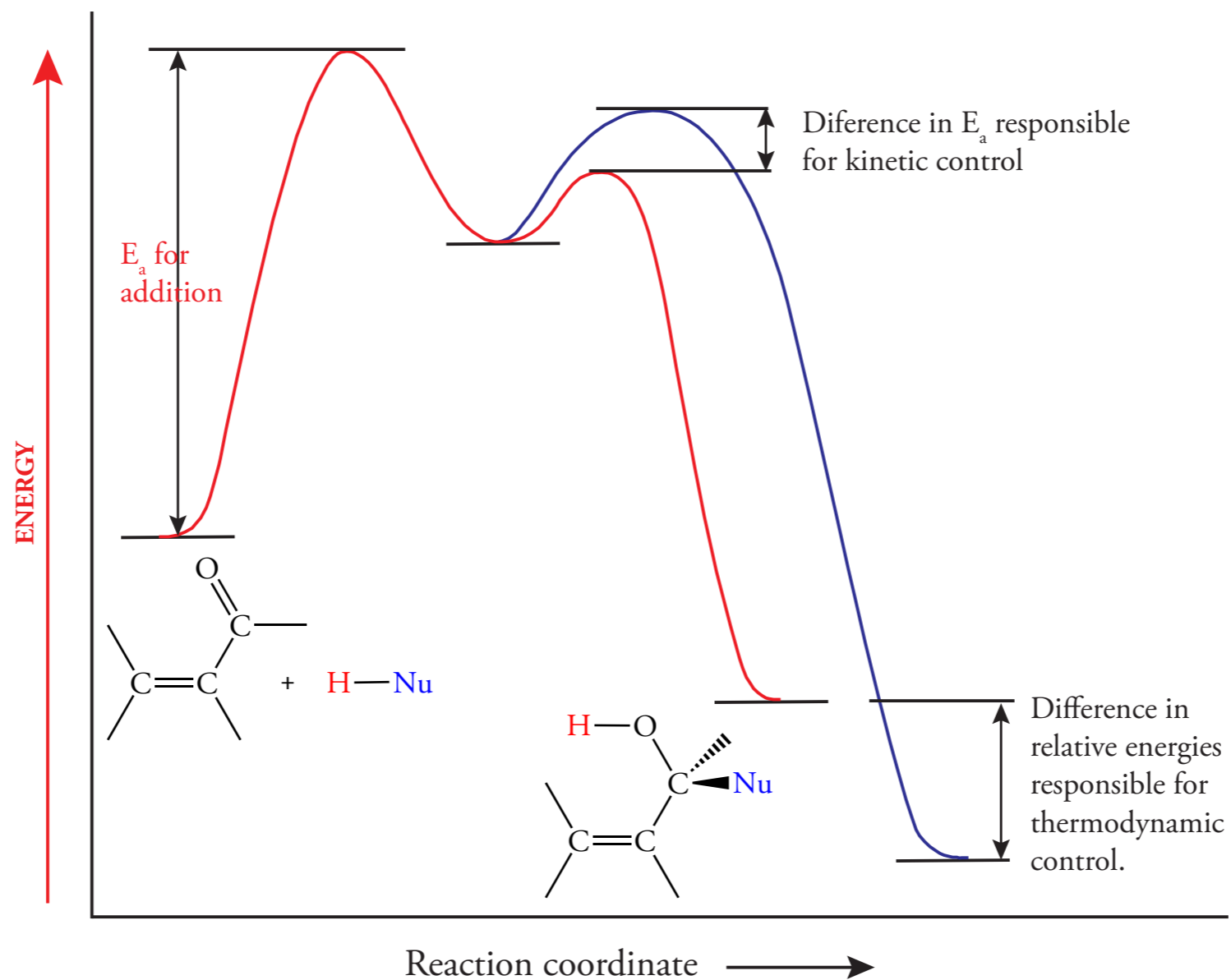
1,4-addition product



## 22.10 CONJUGATE ADDITION REACTIONS

### 1,2- and 1,4-Addition Reactions

**Figure 22.1 Kinetic vs. Thermodynamic Control of 1,2- and 1,4-Addition Reactions**  
Direct 1,2-addition occurs faster than 1,4-conjugate addition, but gives a less stable product. The 1,4-addition product isomerizes to give a more stable product that retains the carbonyl group.

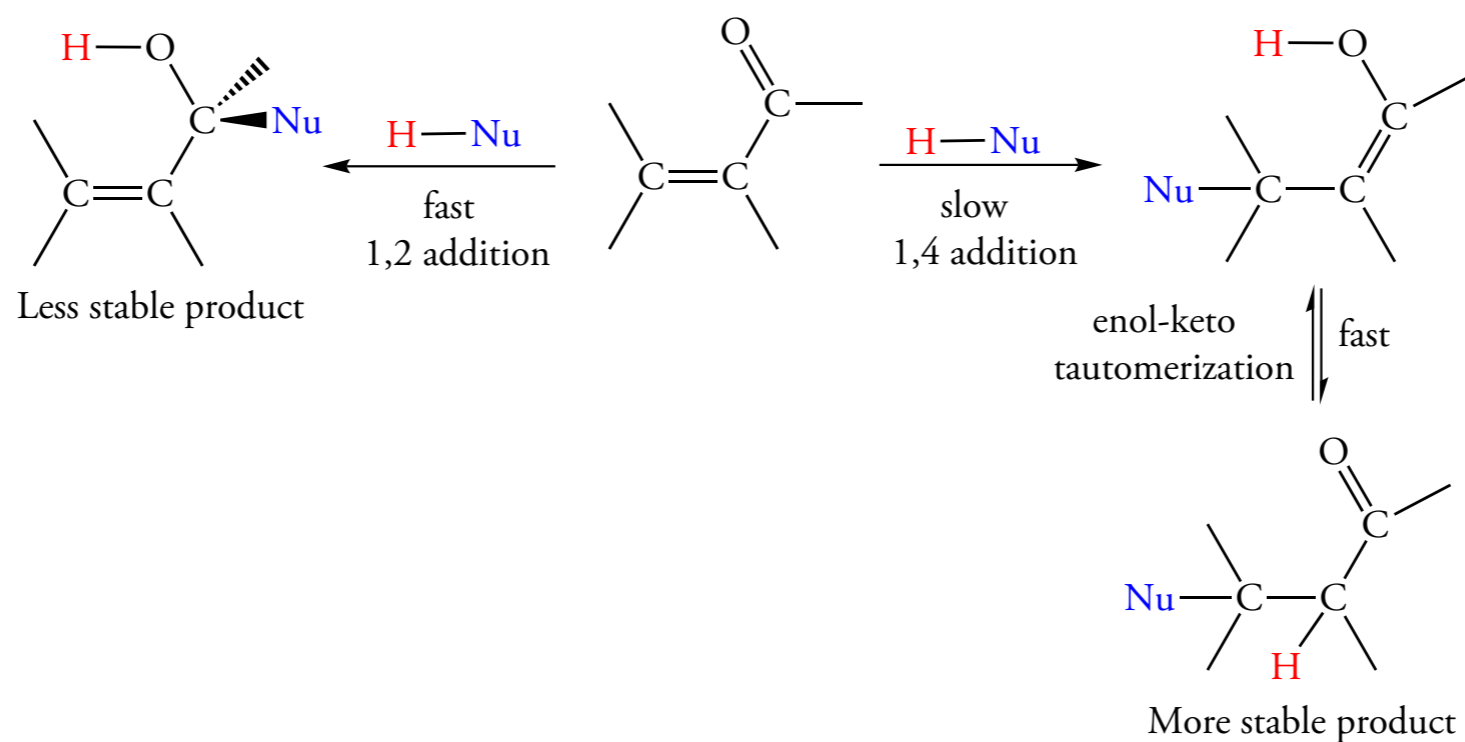


## 22.10 CONJUGATE ADDITION REACTIONS

### 1,2- and 1,4-Addition Reactions

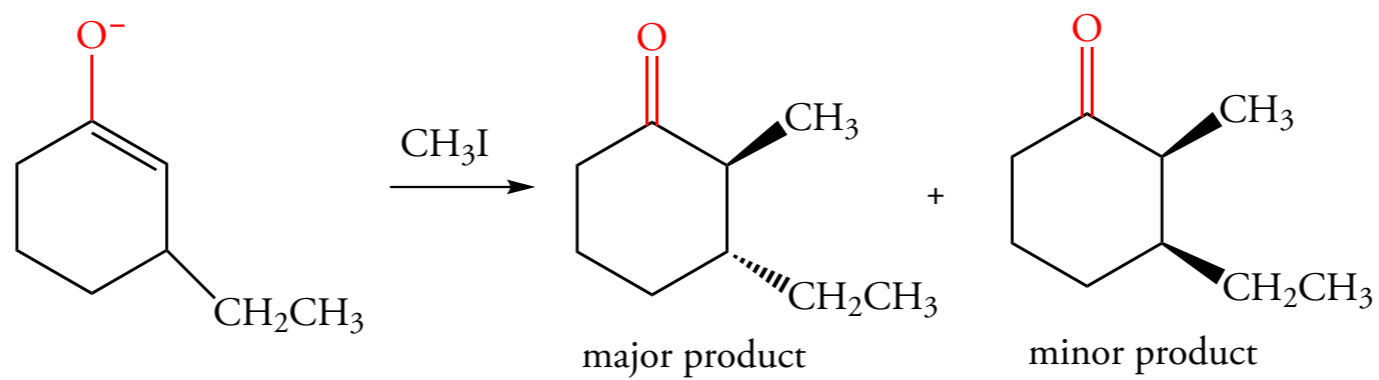
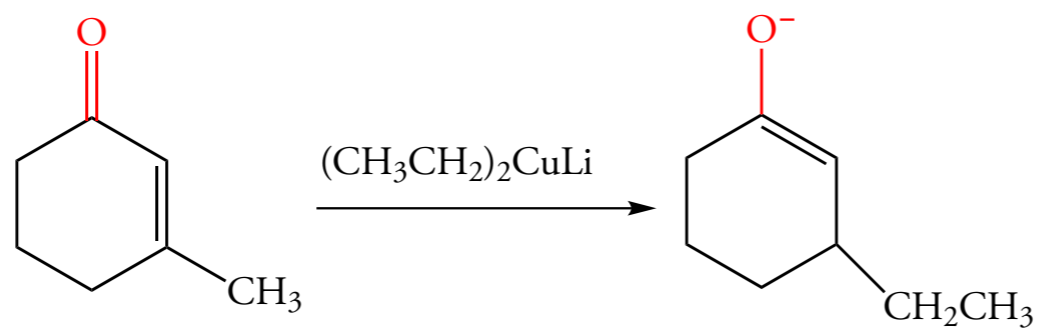
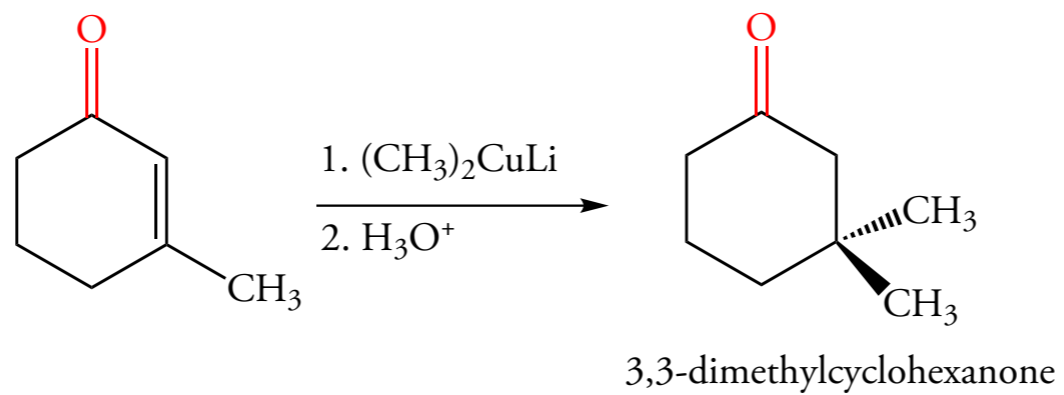
#### Figure 22.1 Kinetic vs. Thermodynamic Control of 1,2- and 1,4-Addition Reactions

Direct 1,2-addition occurs faster than 1,4-conjugate addition, but gives a less stable product. The 1,4-addition product isomerizes to give a more stable product that retains the carbonyl group.



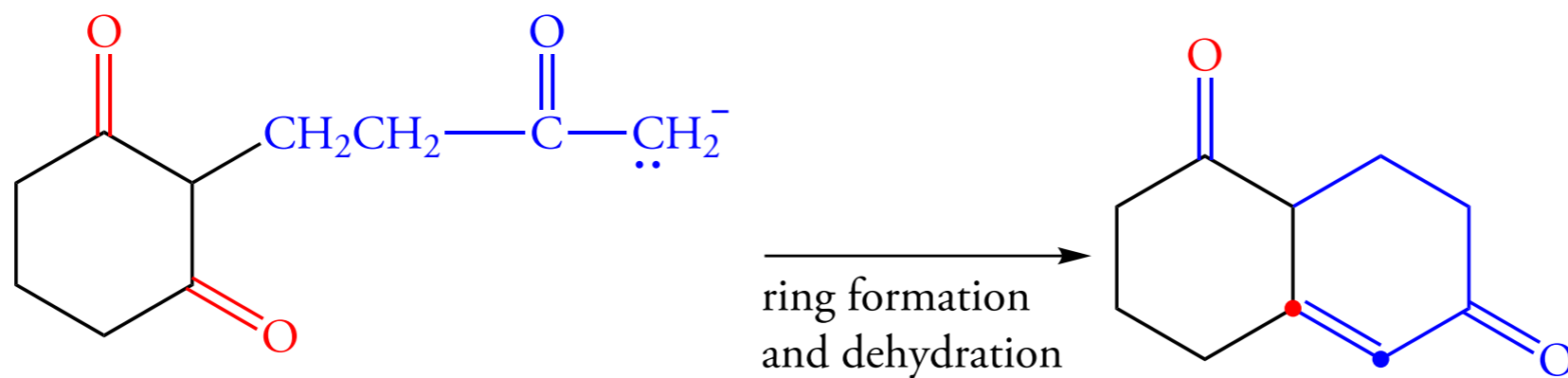
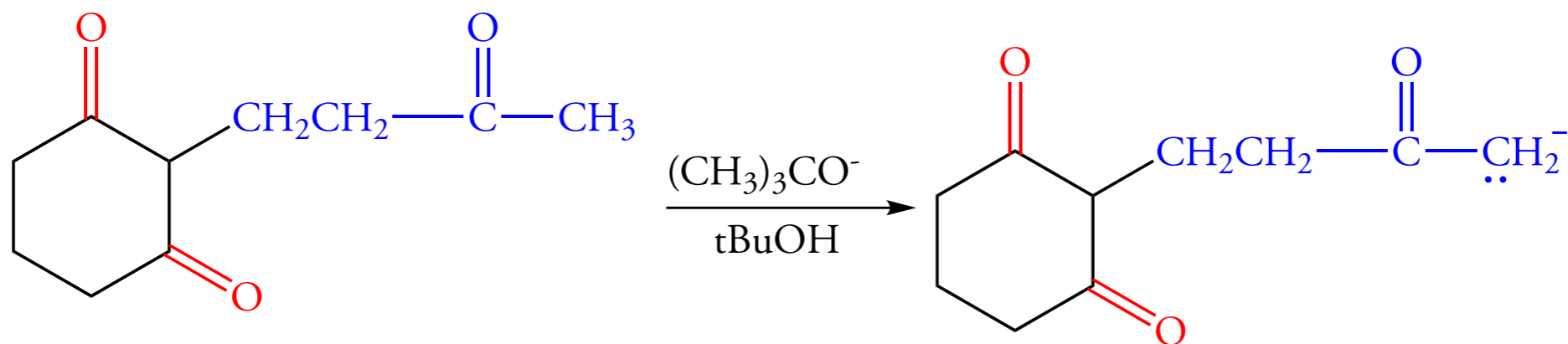
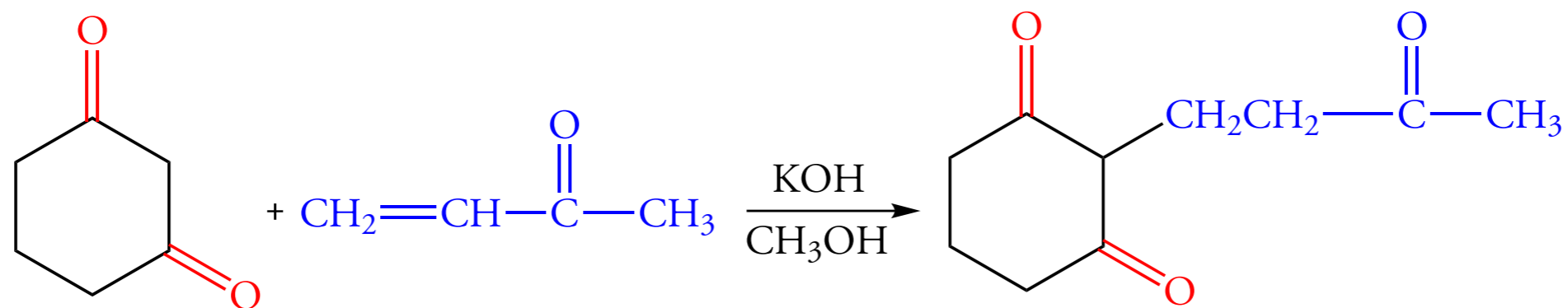
## 22.10 CONJUGATE ADDITION REACTIONS

### Conjugate Addition of Organometallic Reagents





## 22.11 THE MICHAEL REACTION AND ROBINSON ANNULATION



## 22.12 THE $\alpha$ HYDROGEN ATOMS OF ACID DERIVATIVES

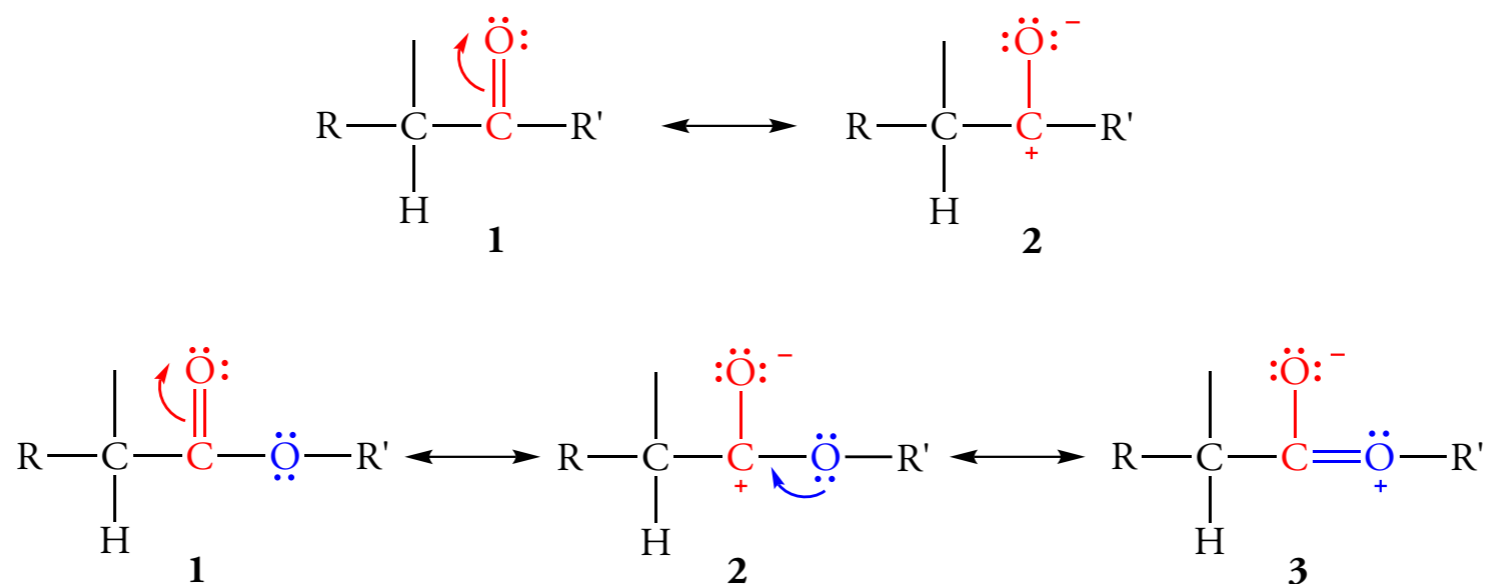
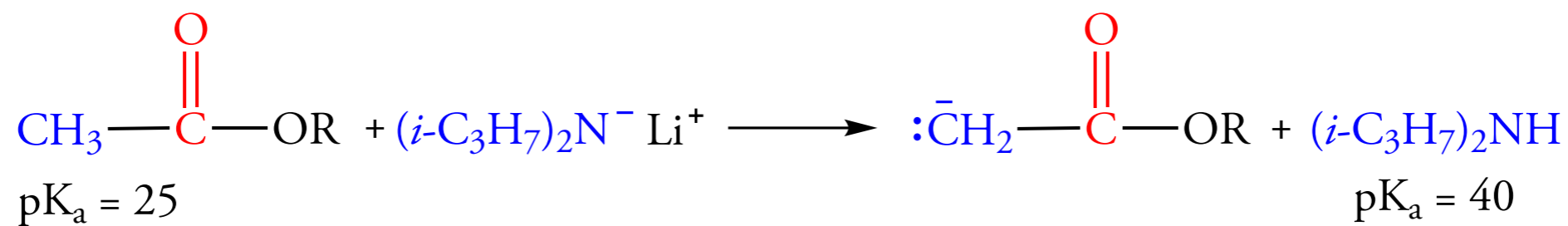
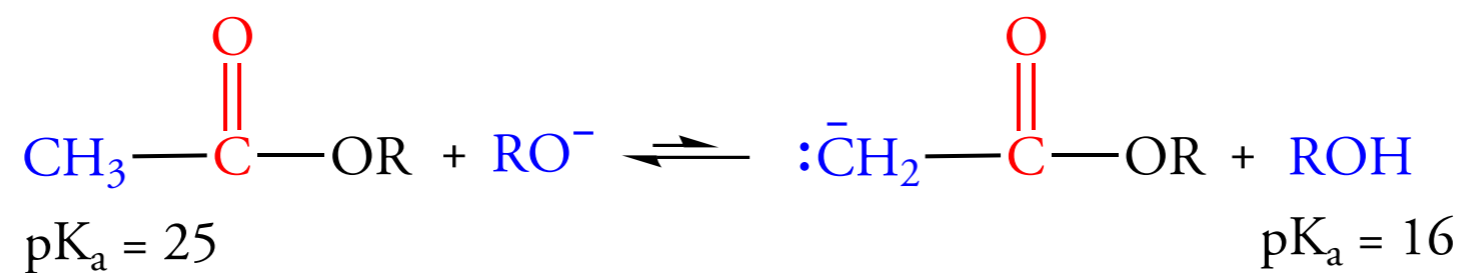


Table 22.1 Acidity of  $\alpha$  Hydrogen Atoms

| Compound  | $pK_a$ |
|---|--------|
| $\text{CH}_3-\overset{\text{O}}{\parallel}{\text{C}}-\text{Cl}$               | 16     |
| $\text{CH}_3-\overset{\text{O}}{\parallel}{\text{C}}-\text{CH}_3$             | 19     |
| $\text{CH}_3-\overset{\text{O}}{\parallel}{\text{C}}-\text{OCH}_3$            | 25     |
| $\text{CH}_3-\text{C}\equiv\text{N}$  | 25     |
| $\text{CH}_3-\overset{\text{O}}{\parallel}{\text{C}}-\text{N}(\text{CH}_3)_2$ | 30     |

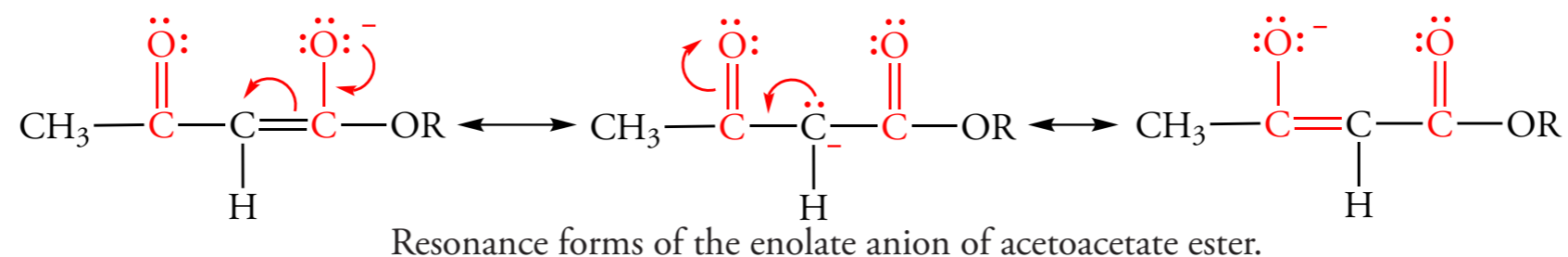
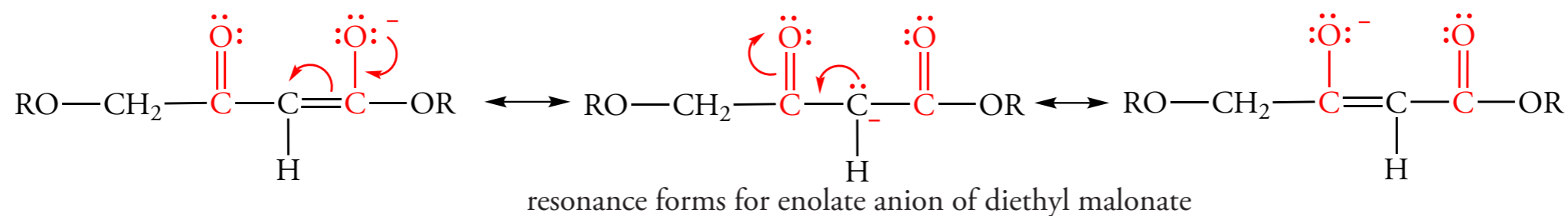
## 22.12 THE $\alpha$ HYDROGEN ATOMS OF ACID DERIVATIVES

### Formation of Ester Enolates



## 22.12 THE $\alpha$ HYDROGEN ATOMS OF ACID DERIVATIVES

### Enolates of $\beta$ -Dicarbonyl Compounds

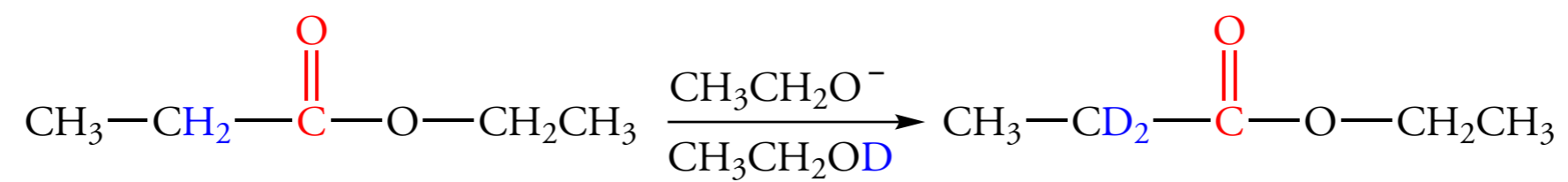


**Table 22.2 Acidity of  $\alpha$  Hydrogen Atoms**

| <i>Compound</i>  | $pK_a$ | <i>Common name</i> |
|--|--------|--------------------|
| $\text{CH}_3-\overset{\text{O}}{\parallel}{\text{C}}-\text{CH}_2-\overset{\text{O}}{\parallel}{\text{C}}-\text{CH}_3$  | 9      | acetylacetone      |
| $\text{CH}_3-\overset{\text{O}}{\parallel}{\text{C}}-\text{CH}_2-\overset{\text{O}}{\parallel}{\text{C}}-\text{O}-\text{CH}_2-\text{CH}_3$                       | 11     | ethyl acetoacetate |
| $\text{N}\equiv\text{C}-\text{CH}_2-\overset{\text{O}}{\parallel}{\text{C}}-\text{CH}_2-\overset{\text{O}}{\parallel}{\text{C}}-\text{O}-\text{CH}_2\text{CH}_3$ | 9      | ethyl cyanoacetate |
| $\text{CH}_3\text{CH}_2-\text{O}-\overset{\text{O}}{\parallel}{\text{C}}-\text{CH}_2-\overset{\text{O}}{\parallel}{\text{C}}-\text{O}-\text{CH}_2\text{CH}_3$    | 13     | diethyl malonate   |

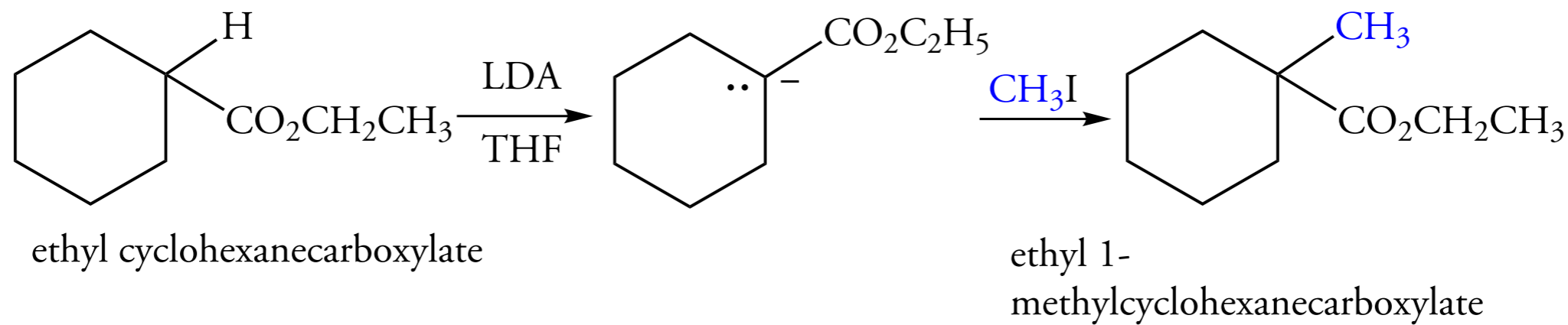
## 22.13 REACTION AT THE $\alpha$ CARBON OF ACID DERIVATIVES

### Deuterium Exchange



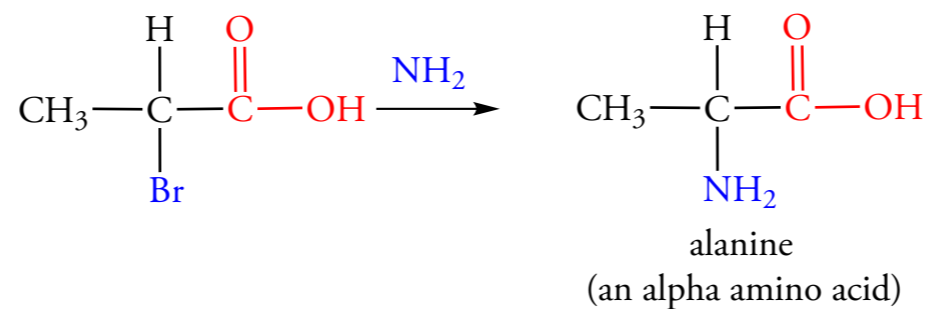
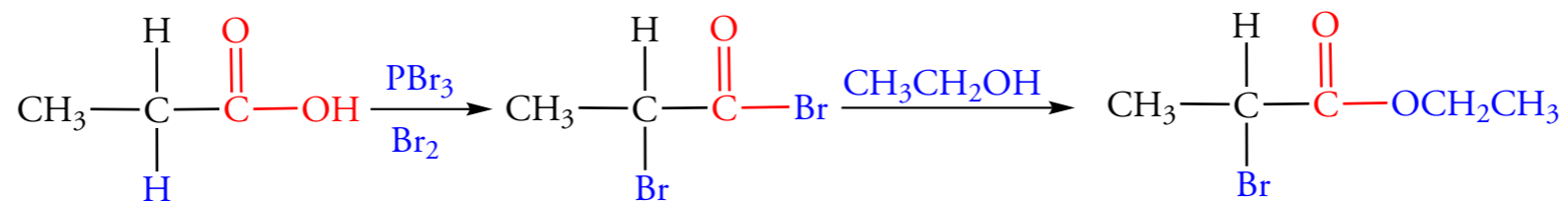
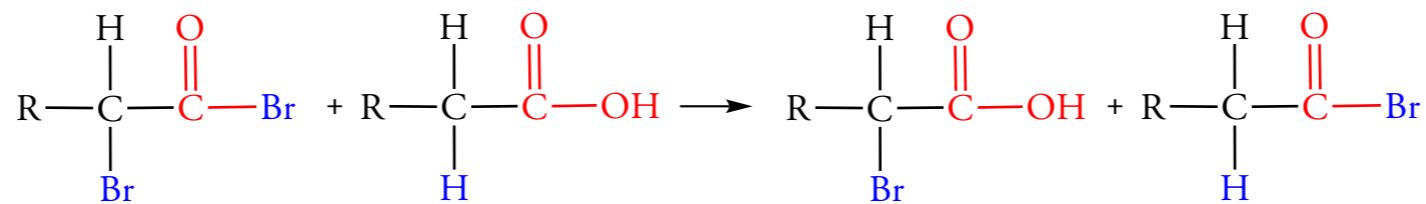
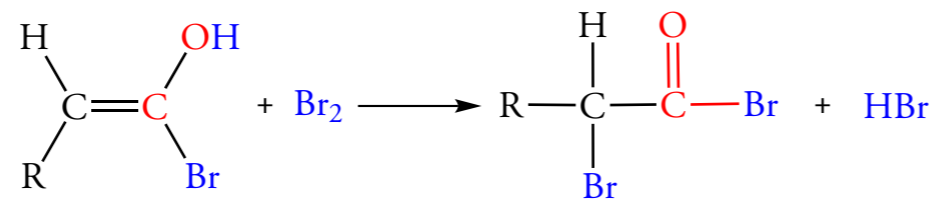
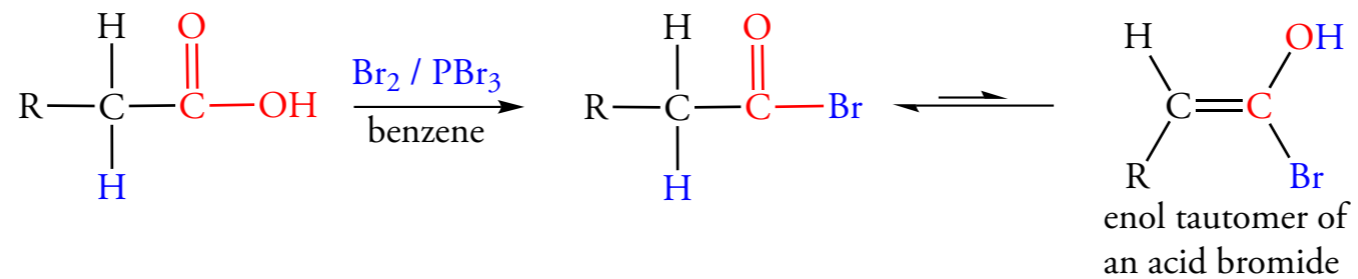
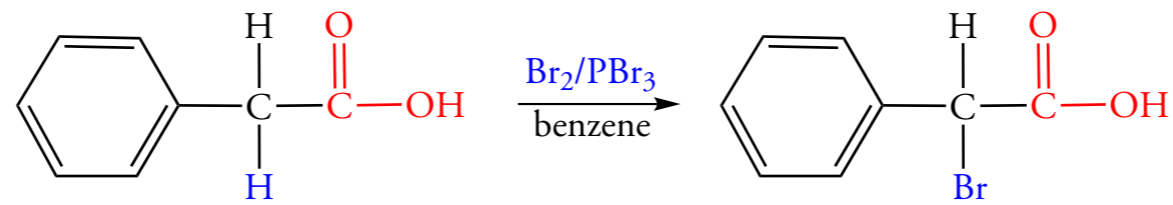
## 22.13 REACTION AT THE $\alpha$ CARBON OF ACID DERIVATIVES

### Alkylation of Esters

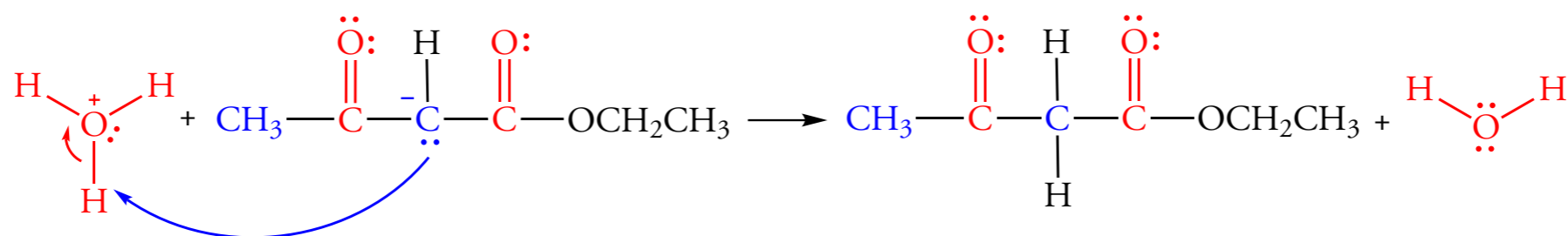
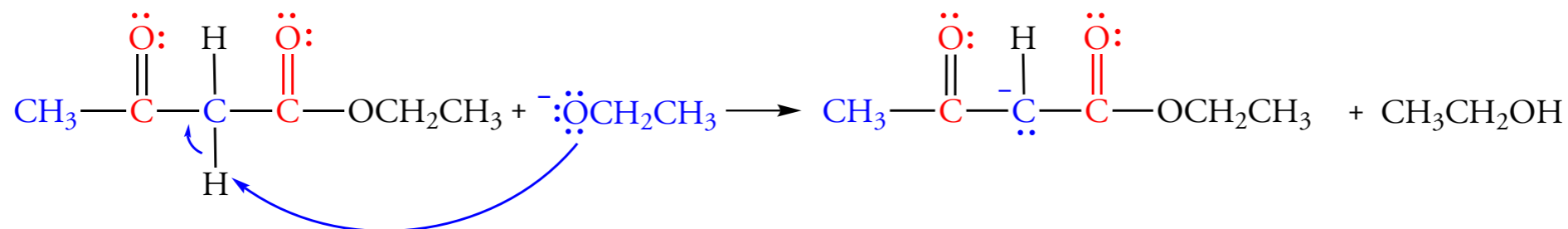
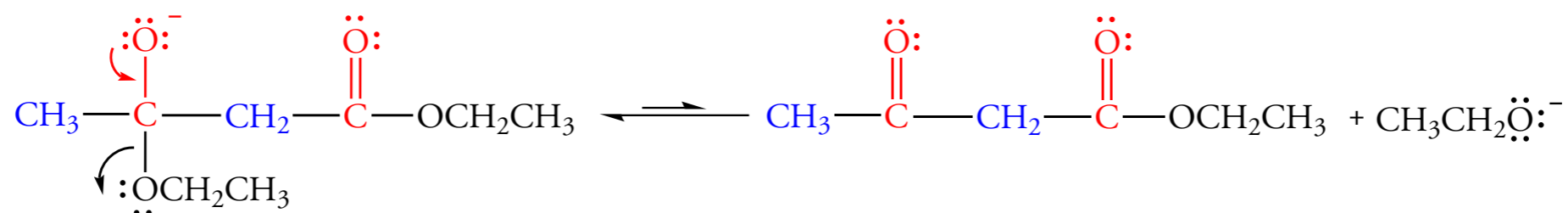
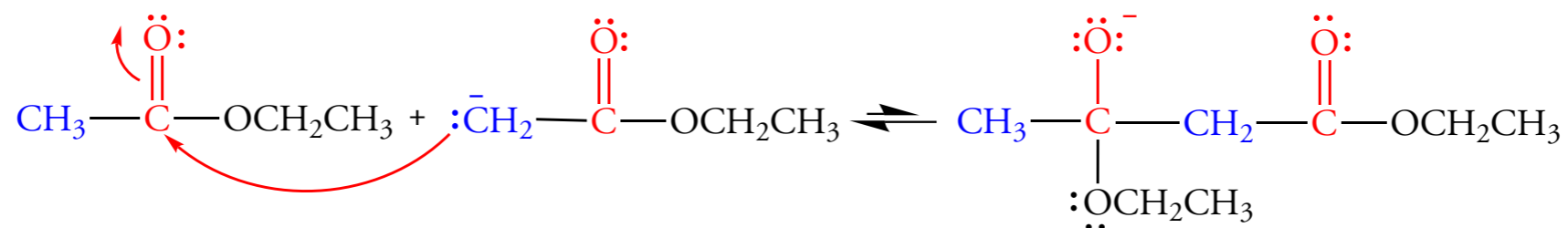
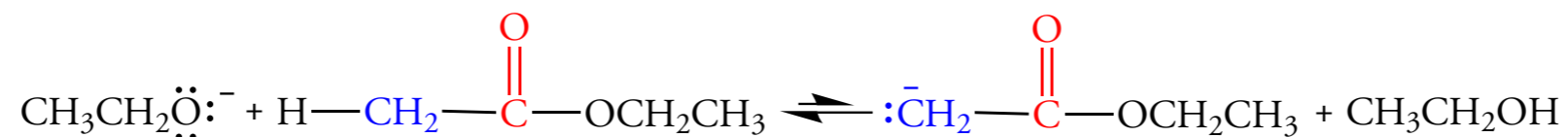
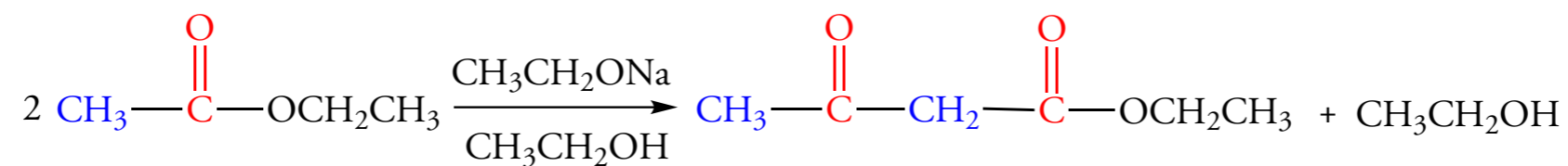


## 22.13 REACTION AT THE $\alpha$ CARBON OF ACID DERIVATIVES

### $\alpha$ Bromination



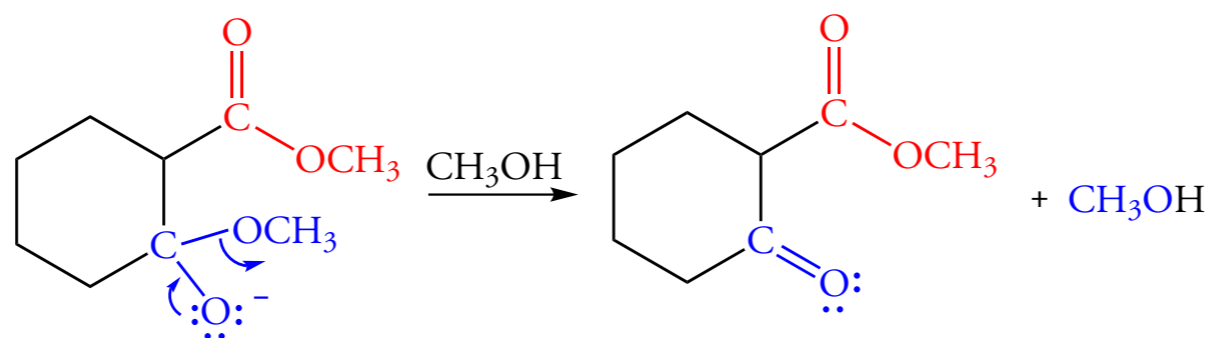
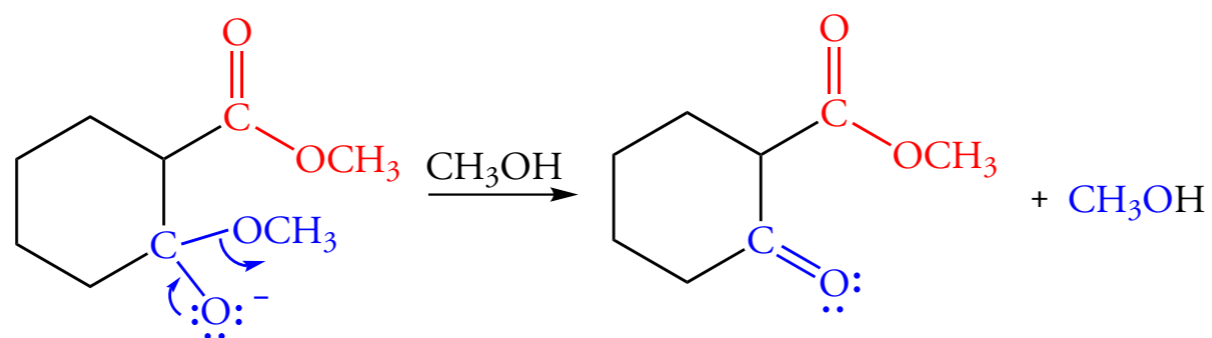
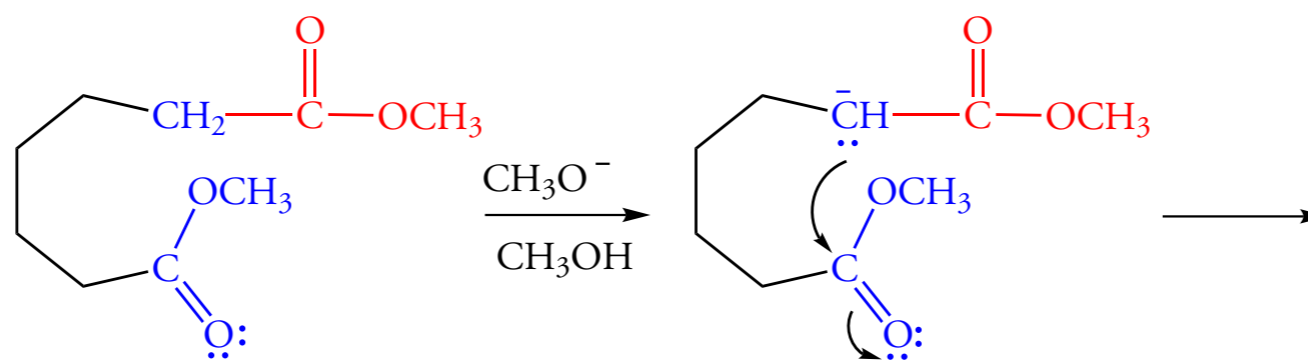
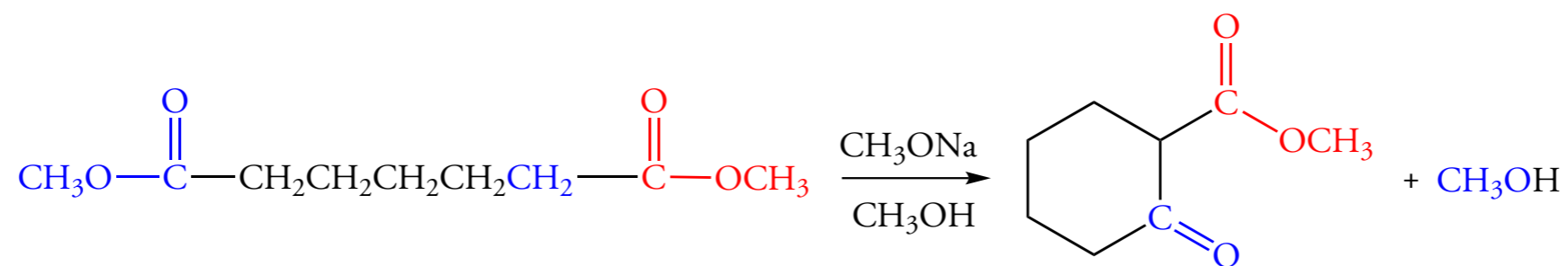
## 22.14 THE CLAISEN CONDENSATION





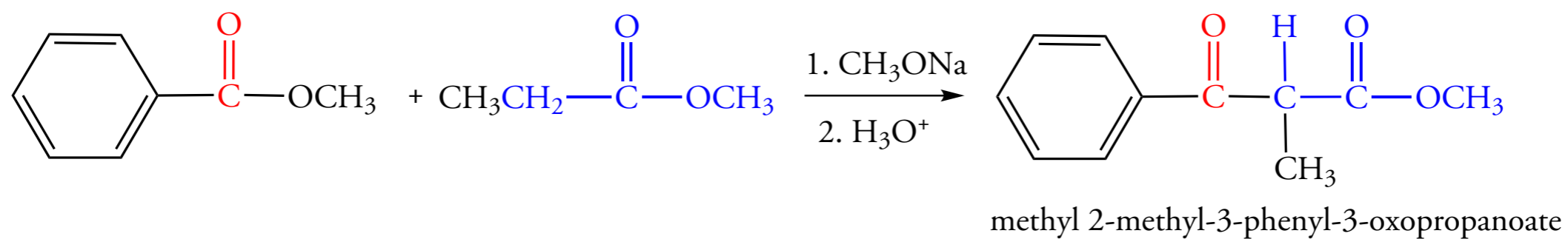
## 22.14 THE CLAISEN CONDENSATION

### Dieckmann Condensation



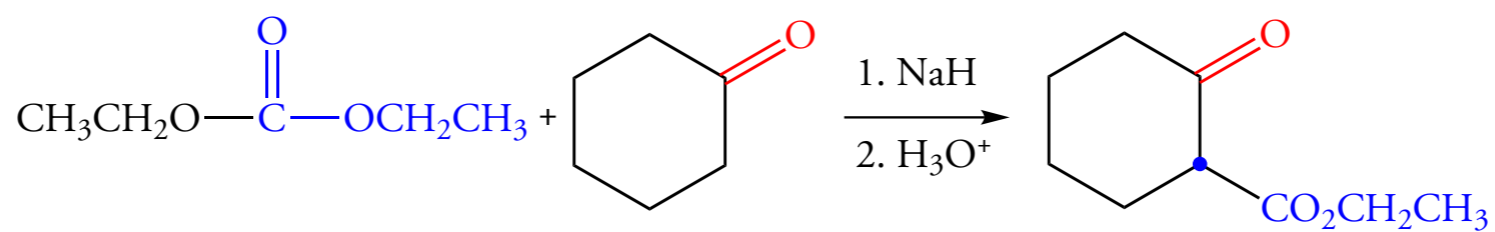
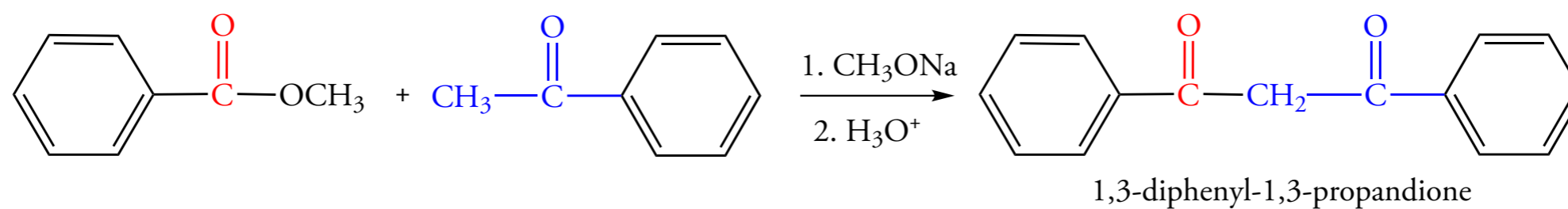
## 22.14 THE CLAISEN CONDENSATION

### Mixed Claisen Condensations



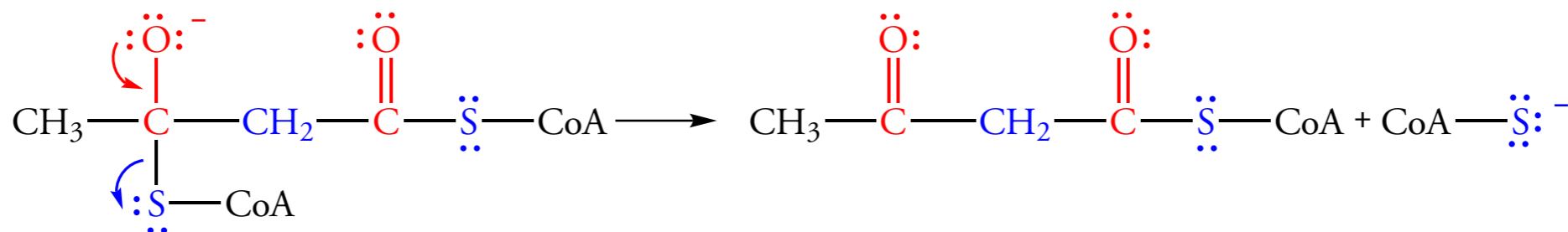
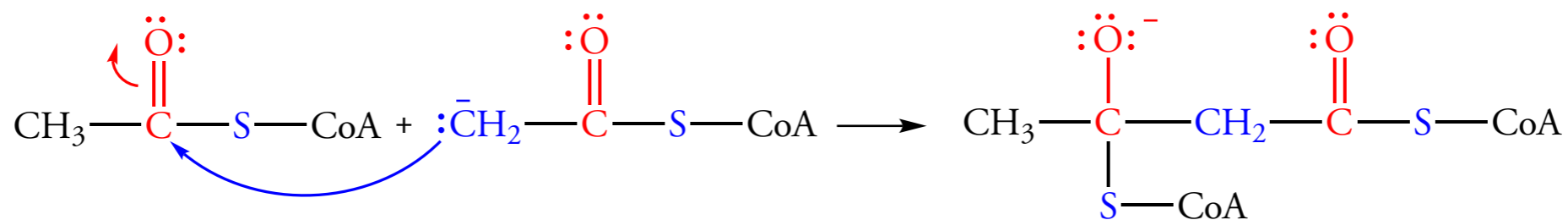
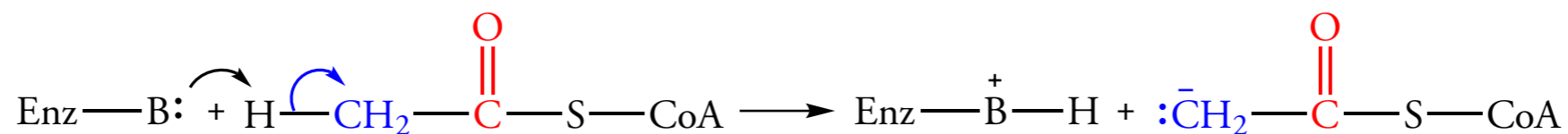
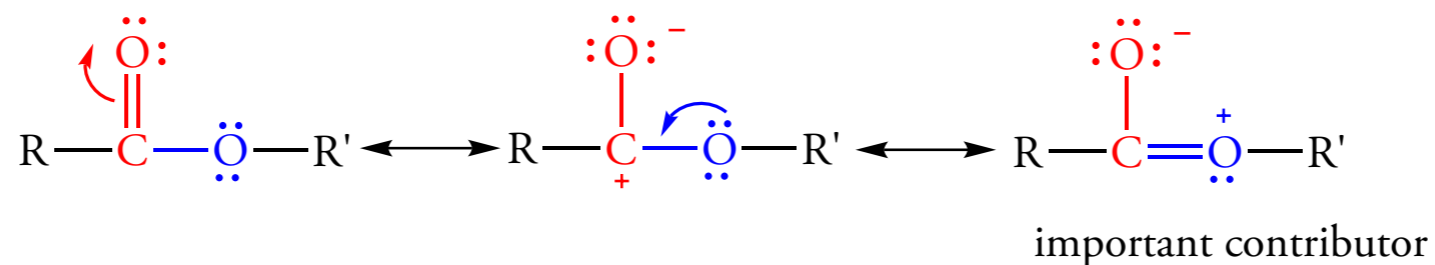
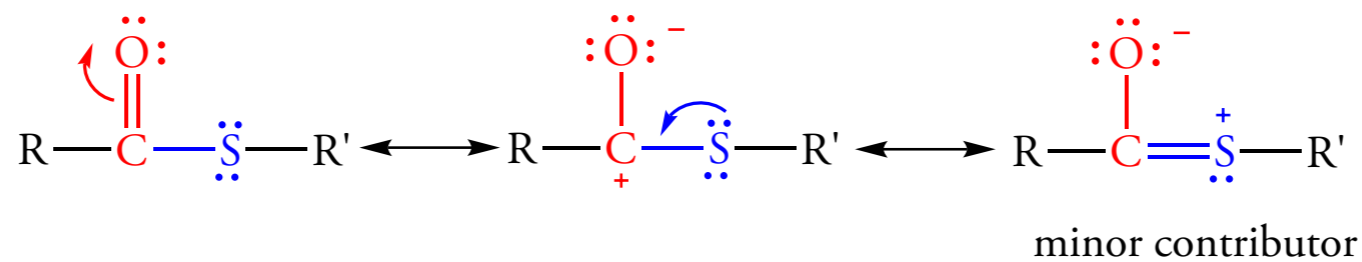
## 22.14 THE CLAISEN CONDENSATION

### Acylation of Ketones with Esters



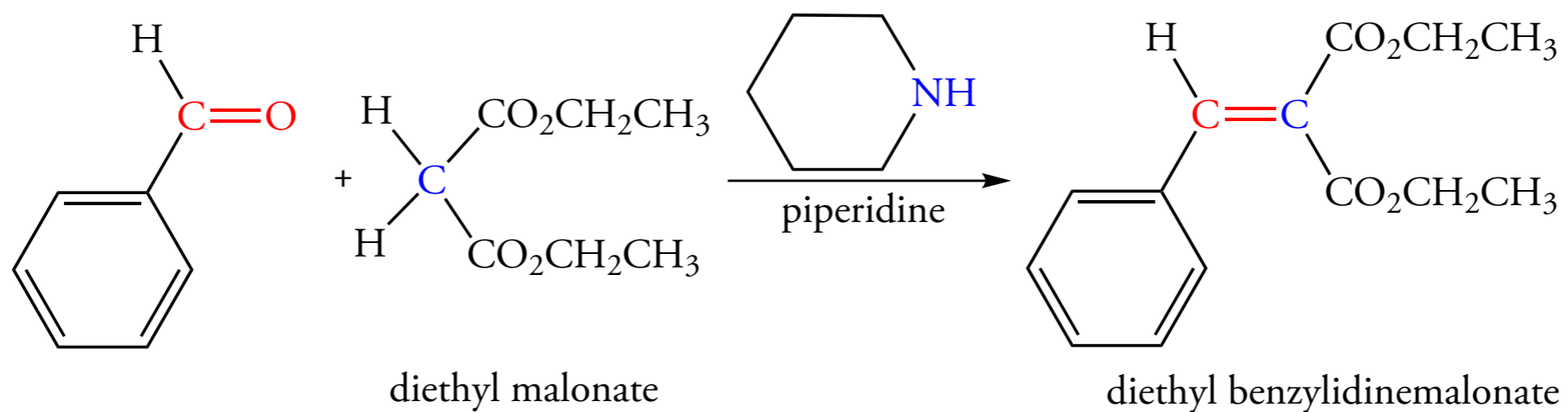
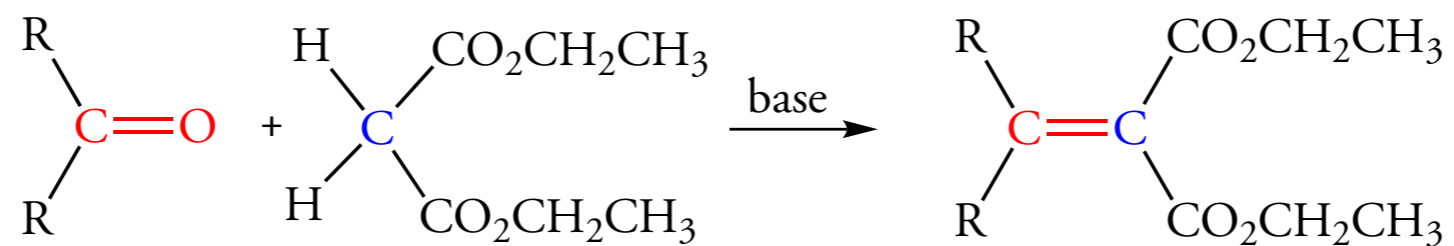
## 22.14 THE CLAISEN CONDENSATION

### Claisen Condensation of Thioesters: A Biochemical Process



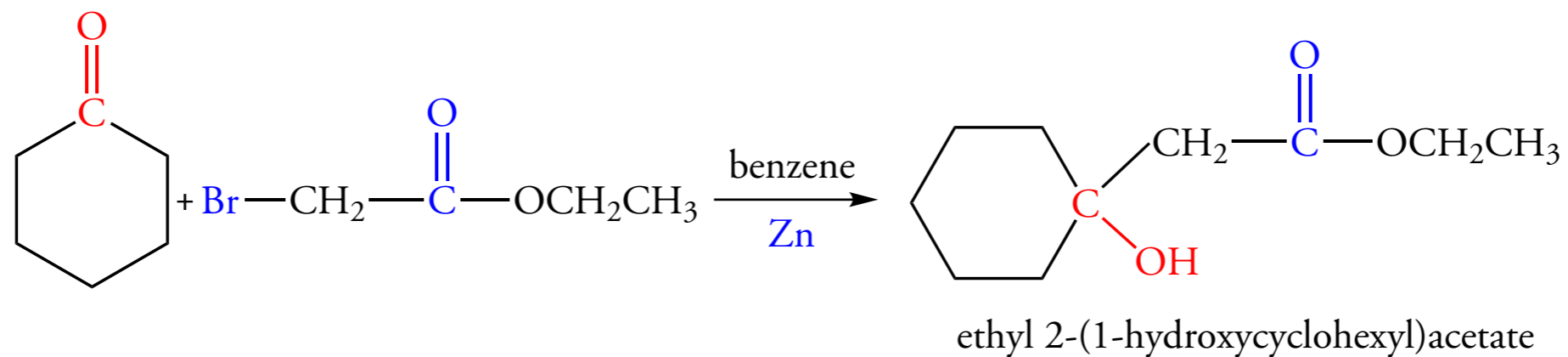
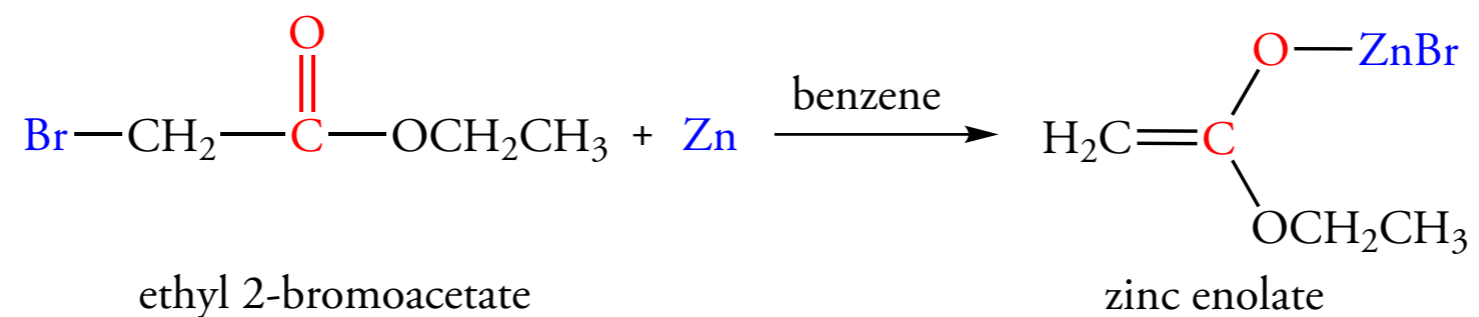
## 22.15 ALDOL-TYPE CONDENSATIONS OF ACID DERIVATIONS

### Knoevenagel Condensation



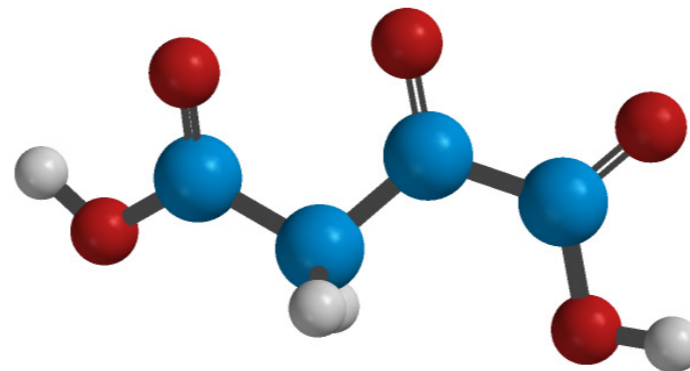
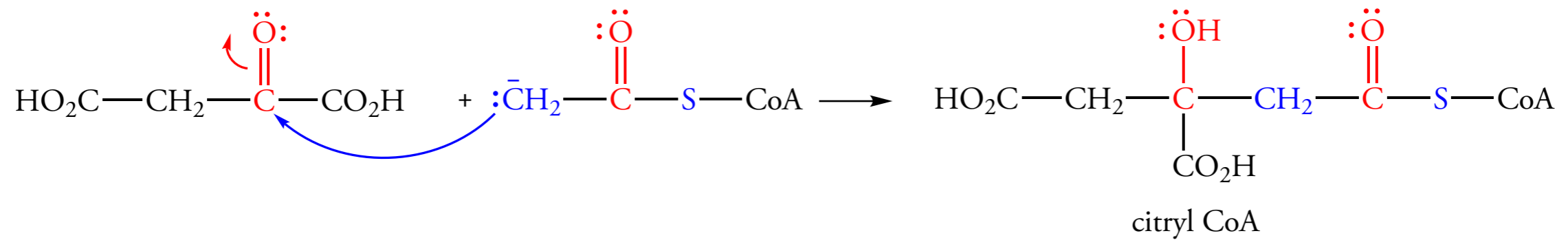
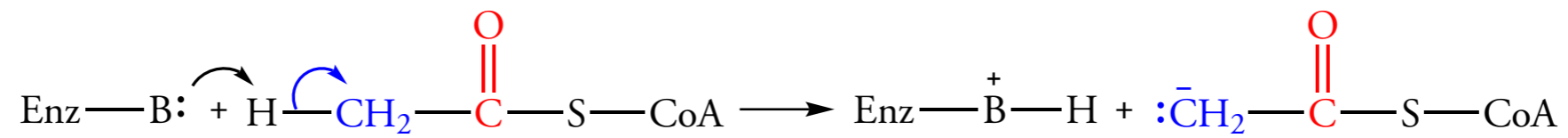
## 22.15 ALDOL-TYPE CONDENSATIONS OF ACID DERIVATIONS

### Reformatskii Reaction



## 22.15 ALDOL-TYPE CONDENSATIONS OF ACID DERIVATIONS

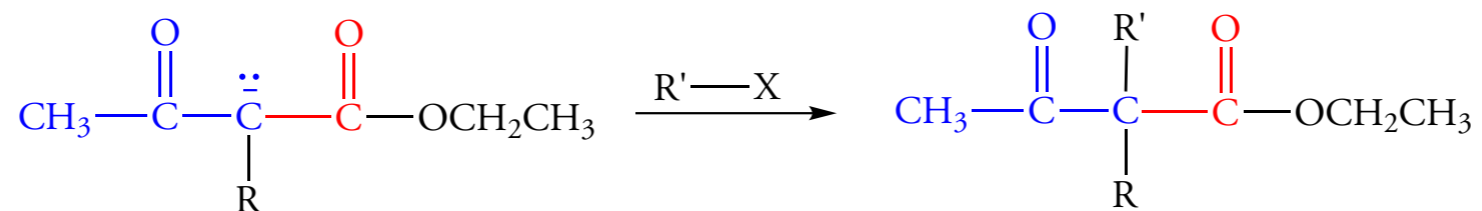
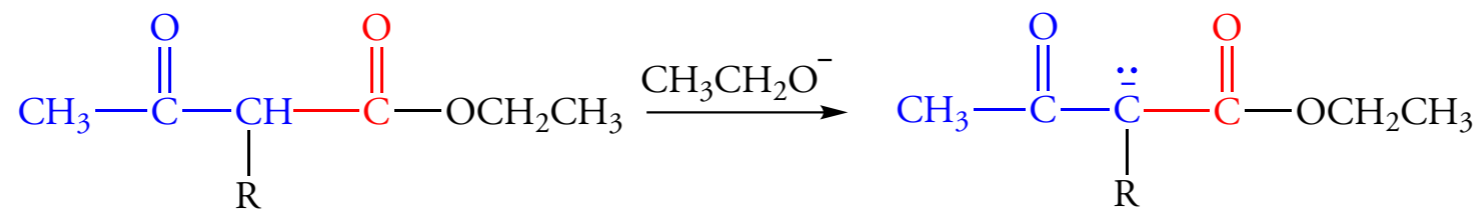
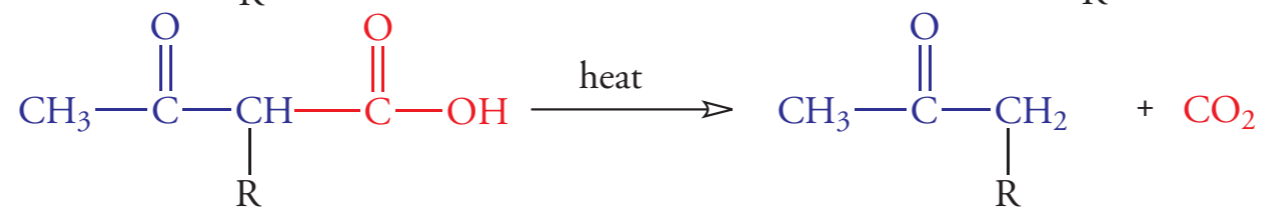
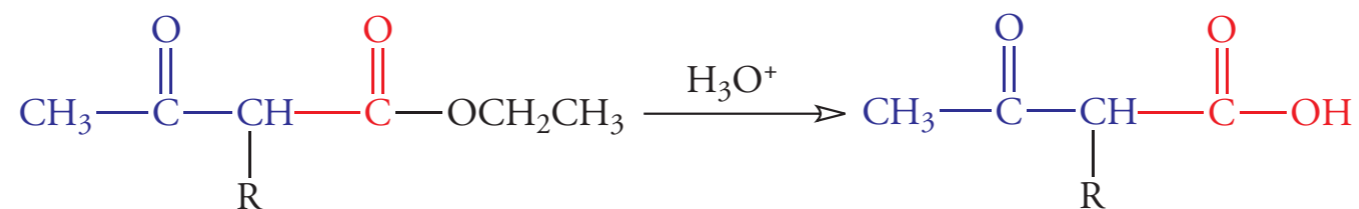
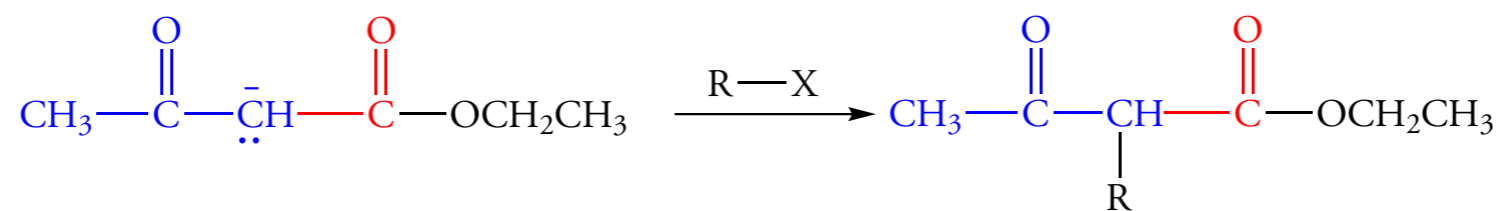
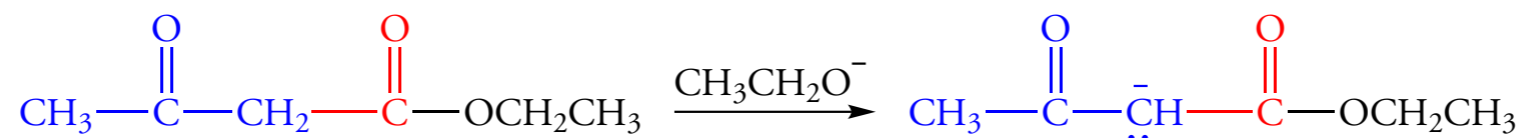
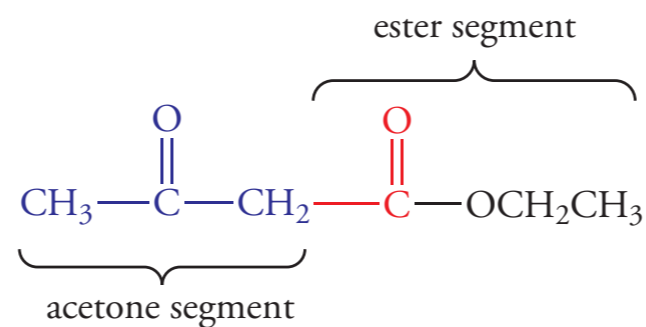
### Biochemical Condensation Reactions, II



oxaloacetic acid

## 22.16 $\beta$ -DICARBONYL COMPOUNDS IN SYNTHESIS

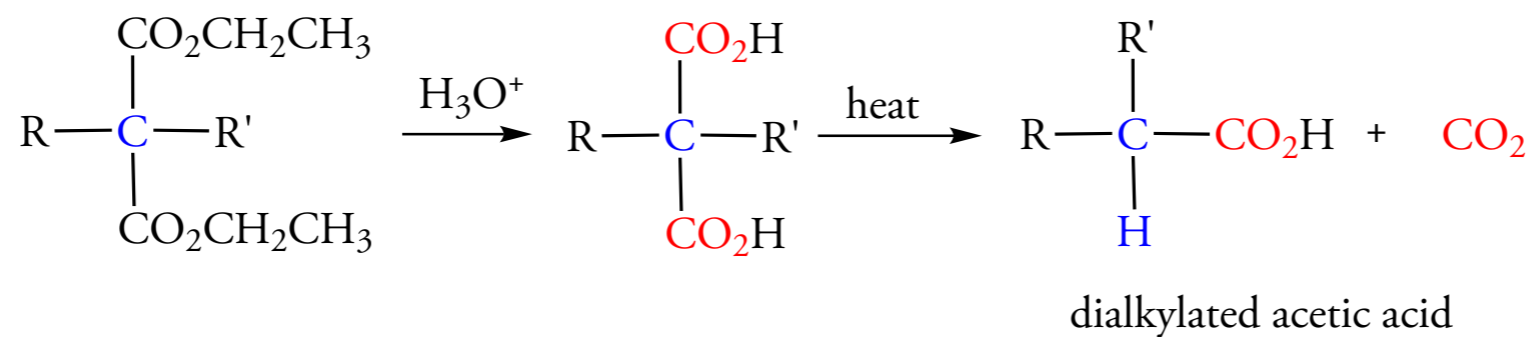
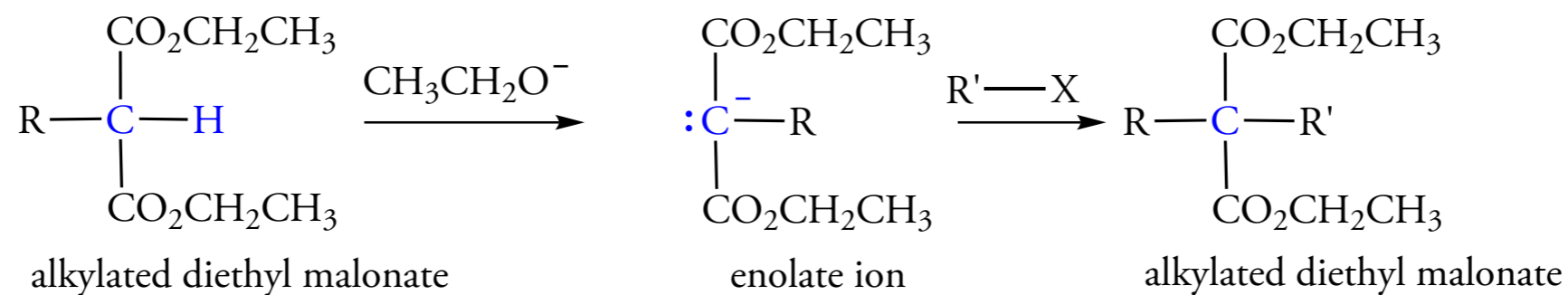
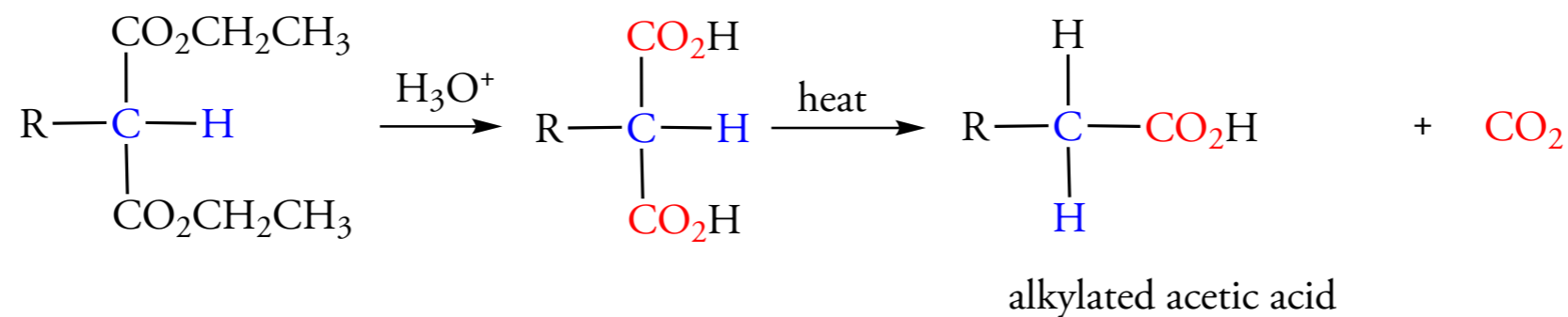
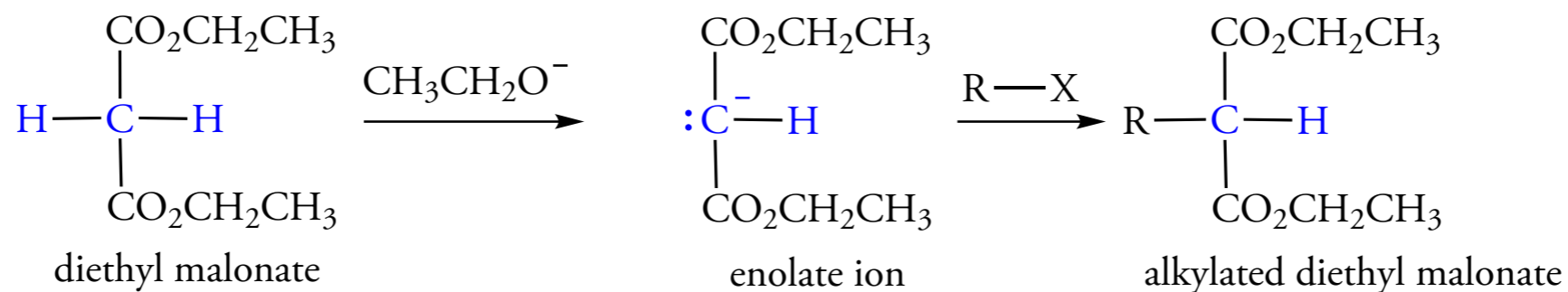
### Acetoacetate Ester Synthesis



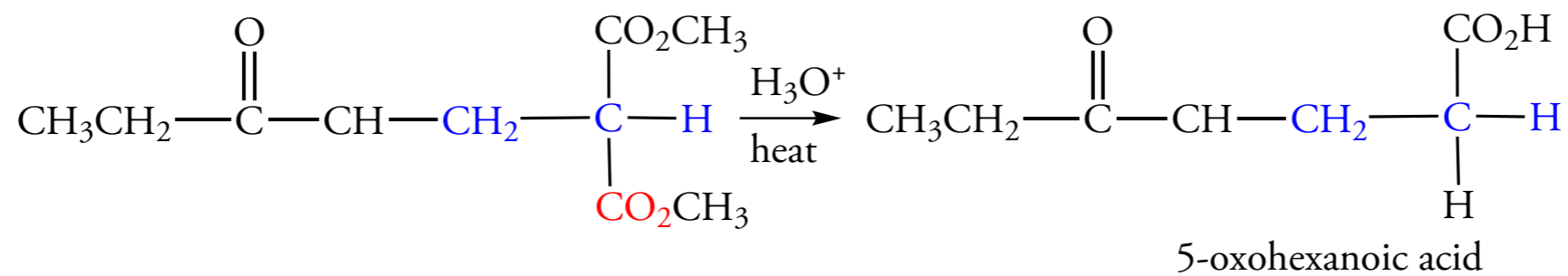
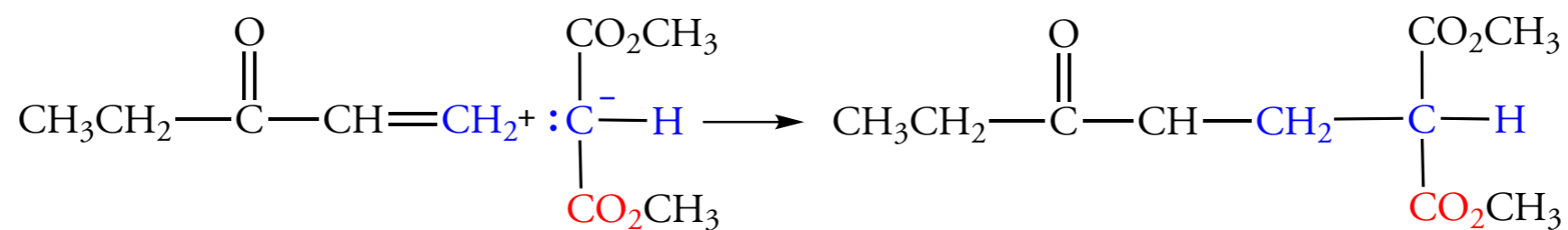
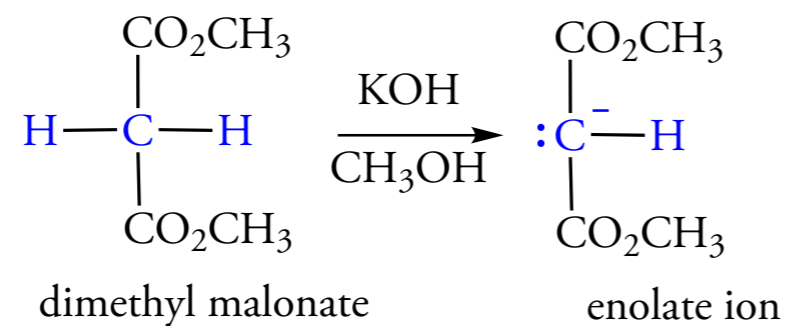


## 22.16 $\beta$ -DICARBONYL COMPOUNDS IN SYNTHESIS

### Malonate Ester Synthesis



## 22.17 MICHAEL CONDENSATIONS OF ACID DERIVATIVES



## 22.10 CONJUGATE ADDITION REACTIONS

### 1,2- and 1,4-Addition Reactions

