18.11
Effects of Conjugation in
α,β-Unsaturated Aldehydes and Ketones
Relative Stability

Aldehydes and ketones that contain a carbon-carbon double bond are more stable when the double bond is conjugated with the carbonyl group than when it is not. Compounds of this type are referred to as $\alpha,\beta$ unsaturated aldehydes and ketones.
Relative Stability

\[
\begin{align*}
\text{CH}_3\text{CH} & \equiv \text{CHCH}_2\text{CCH}_3 & (17\%) \\
& ^\gamma & ^\beta & ^\alpha \\
\end{align*}
\]

\[
K = 4.8
\]

\[
\begin{align*}
\text{CH}_3\text{CH}_2\text{CH} & \equiv \text{CHCCH}_3 & (83\%) \\
& ^\gamma & ^\beta & ^\alpha \\
\end{align*}
\]
Acrolein

\[ \text{H}_2\text{C} \equiv \text{CHCH} \]

[Chemical structure of Acrolein]
Acrolein

H₂C=CHCH₂
Acrolein

\( \text{H}_2\text{C}==\text{CHCHCH} \)
Resonance Description

\[ \text{C} = \text{C} - \text{C} = \text{C}^+ \text{O} \quad \leftrightarrow \quad \text{C} = \text{C} - \text{C} = \text{C}^+ \text{O}^- \]
Properties

α,β-Unsaturated aldehydes and ketones are more polar than simple aldehydes and ketones.

α,β-Unsaturated aldehydes and ketones contain two possible sites for nucleophiles to attack:

- carbonyl carbon
- β-carbon
α,β- Unsaturated aldehydes and ketones are more polar than simple aldehydes and ketones.

α,β- Unsaturated aldehydes and ketones contain two possible sites for nucleophiles to attack.

carbonyl carbon

β-carbon
Dipole Moments

\[ \mu = 2.7 \text{ D} \]
Butanal

greater separation of positive and negative charge

\[ \mu = 3.7 \text{ D} \]
trans-2-Butenoral
18.12
Conjugate Addition to
$\alpha,\beta$- Unsaturated Carbonyl Compounds
Nucleophilic Addition to \( \alpha,\beta \)-Unsaturated Aldehydes and Ketones

1,2-addition (direct addition)

nucleophile attacks carbon of C=O

1,4-addition (conjugate addition)

nucleophile attacks \( \beta \)-carbon
Kinetic versus Thermodynamic Control

attack is faster at C=O

attack at β-carbon gives the more stable product
formed faster major product under conditions of kinetic control (i.e. when addition is not readily reversible)
enol

goes to keto form

under reaction

conditions
keto form is isolated product of 1,4-addition is more stable than 1,2-addition product
C=O is stronger than C=C
observed with *strongly* basic nucleophiles

Grignard reagents

LiAlH$_4$

NaBH$_4$

Sodium acetylide

strongly basic nucleophiles add irreversibly
Example

\[
\text{CH}_3\text{CH}≡\text{CHCH} + \text{HC≡CMgBr} \\
\begin{align*}
1. & \quad \text{THF} \\
2. & \quad \text{H}_3\text{O}^+ \\
\text{OH} \\
\text{CH}_3\text{CH}≡\text{CHCHC≡CH} \\
\text{(84%)}
\end{align*}
\]
1,4-Addition

observed with weakly basic nucleophiles

cyanine ion (CN⁻)
thiolate ions (RS⁻)
ammonia and amines
azide ion (N₃⁻)

weakly basic nucleophiles add reversibly
Example

\[
\text{KCN} \quad \text{ethanol, acetic acid} \\
\]

\[
\begin{align*}
\text{C}_6\text{H}_5\text{CH} &= \text{C} = \text{CH} \quad \text{C} = \text{CC}_6\text{H}_5 \\
\text{O} & \quad \text{O} \\
\text{C}_6\text{H}_5\text{CHCHCH}_2\text{CC}_6\text{H}_5 \\
\text{CN} & \quad (93-96\%) \\
\end{align*}
\]
Example

\[ \text{C}_6\text{H}_5\text{CH}==\text{CHCC}_6\text{H}_5 \]

KCN, ethanol, acetic acid

\[ \text{C}_6\text{H}_5\text{CHCHCH}_2\text{CC}_6\text{H}_5 \]

(93-96\%)
Example

\[
\begin{array}{c}
\text{C}_6\text{H}_5\text{CH}_2\text{SH} \quad \text{HO}^-, \text{H}_2\text{O} \\
\downarrow \\
\text{SCH}_2\text{C}_6\text{H}_5
\end{array}
\]

(58%)
Example

\[
\begin{align*}
\text{C}_6\text{H}_5\text{CH}_2\text{SH} & \rightarrow \text{HO}^-, \text{H}_2\text{O} \\
\text{HO}^- & \rightarrow \text{SCHR}_2\text{C}_6\text{H}_5
\end{align*}
\]

(58%)
18.13
Addition of Carbanions to
\( \alpha,\beta \)-Unsaturated Carbonyl Compounds:
The Michael Reaction
Stabilized carbanions, such as those derived from β-diketones undergo conjugate addition to α,β-unsaturated ketones.
Example

\[
\text{KOH, methanol} \quad \xrightarrow{\text{KOH, methanol}} \quad \text{(85%)}
\]

\[
\text{CH}_3\text{CH}_2\text{CH}_2\text{CCH}_3
\]

\[
\text{H}_2\text{C}=\text{CHCCH}_3
\]
The Michael reaction is a useful method for forming carbon-carbon bonds.

It is also useful in that the product of the reaction can undergo an intramolecular aldol condensation to form a six-membered ring. One such application is called the Robinson annulation.
Example

\[
\text{NaOH} \xrightarrow{\text{heat}}
\]

not isolated; dehydrates under reaction conditions
Example

\[ \text{NaOH heat} \]

\( \text{(85%)} \)
18.14

Conjugate Addition of Organocopper Reagents to α,β-Unsaturated Carbonyl Compounds
The main use of organocopper reagents is to form carbon-carbon bonds by conjugate addition to $\alpha,\beta$-unsaturated ketones.

Addition of Organocopper Reagents to $\alpha,\beta$-Unsaturated Aldehydes and Ketones
Example

\[
\text{Ketone + LiCu(CH}_3\text{)}_2\rightarrow\text{Product (98%)}
\]

1. diethyl ether
2. H₂O
18.15
Alkylation of Enolate Anions
Enolate ions are nucleophiles and react with alkyl halides.

However, alkylation of simple enolates does not work well.

Enolates derived from β-diketones can be alkylated efficiently.
Example

\[
\text{CH}_3\text{CCH}_2\text{CCH}_3 + \text{CH}_3\text{I} \xrightleftharpoons[\text{K}_2\text{CO}_3]{\text{(75-77\%)}} \text{CH}_3\text{CCHCHCCH}_3
\]