25 Conjugate Additions

from chapter(s) ______ in the recommended text

A Introduction

B Polarization Of $\alpha,\beta$-Unsaturated Carbonyl Compounds

is always on the $\beta$-carbon

LUMO

more / less stable
C Mechanism Of Conjugate Addition

**enolate**

**enol**

**OMe**
**Examples Of Conjugate Additions**

**Amines And Thiols**

the *nucleophile* adds to the 4-position

the *proton* adds to the oxygen

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**Enolate Intermediate**

**1,4-addition product**

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**Enolate Intermediate**

**1,4-addition product**
Enzyme-mediated Conjugate Additions

\[ \cdot\text{O}_2\text{C} \equiv \text{CO}_2^- + \text{NH}_3 \xrightarrow{\beta\text{-methylaspartase}} \cdot\text{O}_2\text{CH}\text{CO}_2^- \]

\[ \cdot\text{O}_2\text{C} \equiv \text{CO}_2^- + \text{OH}_2 \xrightarrow{\text{fumarase}} \cdot\text{O}_2\text{CH}\text{CO}_2^- \]

\[ \text{S-product} \]

\[ \text{enzyme} \cdot\text{SH} + \cdot\text{O}_2\text{C} \xrightleftharpoons{\text{rotation about this bond}} \text{enzyme} \cdot\text{C} \text{O}_2^- \]

\[ \text{adduct} \]

\[ \text{retro-1,4-addition}\]

\[ \text{rotamer of initial adduct} \]

\[ \text{isomerized product} \]
Stabilized C-Anion Nucleophiles

the base is required in \textit{stoichiometric} quantities.
Organometallic Agents In Laboratory Chemistry

Ph₃CuLi + PhC≡N → PhCH=CHCN

enolate intermediate

1,4-addition product
**Conjugate Addition Then Aldol Condensation**

- Conjugate addition product

- An enolate that can cyclize easily

- Cyclization product

- Cyclic aldol/dehydration product
Predict the products of the following reactions.

\[
\text{enolate from conjugate addition} \quad \text{terminal enolate}
\]

\[
\text{intramolecular cyclization product} \quad \text{enone}
\]
intramolecular cyclization product

enone
F Nucleophilic Epoxidation

α-effect

more acidic than water

It is not possible
G Addition Elimination Reactions

![Reaction 1](image1)

![Reaction 2](image2)

![Reaction 3](image3)
Formation Of α-Bromo Enones

\[
\begin{align*}
\text{enolate} & \quad \rightarrow \quad \text{intermediate} \\
\text{enolate} & \quad \rightarrow \quad \text{product}
\end{align*}
\]
Nucleophilic Aromatic Substitution

$S_{N}Ar$ processes.

They involve rate-limiting addition

anionic intermediates

$sp^3$ hybridized C-atom.

2-chloropyridine

3-chloropyridine
2- isomer.
Addition occurs fastest for the 2- and 4-isomers

2-chloro-1,3-pyrimidine reacted with cyanide

4-bromo-1,3-pyrimidine reacted with azide

chlorobenzene reacted with phenoxide