17.12
The Wittig Reaction
Some reactions of aldehydes and ketones progress beyond the nucleophilic addition stage

- Acetal formation
- Imine formation
- Compounds related to imines
- Enamines
- The Wittig reaction
Some reactions of aldehydes and ketones progress beyond the nucleophilic addition stage

- Acetal formation
- Imine formation
- Compounds related to imines
- Enamines
- The Wittig reaction
The Wittig Reaction

Synthetic method for preparing alkenes.

One of the reactants is an aldehyde or ketone.

The other reactant is a phosphorus ylide.
Phosphorus ylides

R is usually C₆H₅ (phenyl)

key point is that carbon is negatively polarized and nucleophilic

\[(\text{C}_6\text{H}_5)_3\text{P} ≈ \text{C} : \text{B} \quad \text{versus} \quad (\text{C}_6\text{H}_5)_3\text{P} \equiv \text{C} \text{A} \]

\[(\text{C}_6\text{H}_5)_3\text{P} \text{ is usually C} ≈ \text{C} \text{B} \text{, negatively polarized and nucleophilic.} \]
Figure 17.9 Charge distribution in a ylide
The Wittig Reaction

\[
\begin{align*}
\text{R} & \quad \text{R}' \\
\text{C}=\text{O} & \quad \text{+} \quad (\text{C}_6\text{H}_5)\text{P}^+\text{C}^- \\
\text{R} & \quad \text{R}' \\
\text{C} \quad \text{=} \quad \text{C} & \quad \text{+} \quad (\text{C}_6\text{H}_5)\text{P}^+\text{O}^- \quad \text{B}
\end{align*}
\]
Example

\[
\text{Cyclic ketone} + (\text{C}_6\text{H}_5)_3\text{P} \overset{\text{CH}_2}{\text{O}} \quad \text{DMSO}
\]

\[
\text{Enyne} + (\text{C}_6\text{H}_5)_3\text{P} \overset{\text{O}}{\text{O}}
\]

(86%)

dimethyl sulfoxide (DMSO) or tetrahydrofuran (THF) is the customary solvent
Mechanism

Step 1

\[
\begin{align*}
R & \quad \text{C} \quad \text{P(C}_6\text{H}_5)_3 \\
R' & \quad \text{C} \quad \text{O} \\
A & \quad \text{C} \\
B & \quad \text{P(C}_6\text{H}_5)_3
\end{align*}
\]

\[
\begin{align*}
R & \quad \text{C} \quad \text{O} \\
R' & \quad \text{C} \\
A & \quad \text{C} \\
B & \quad \text{P(C}_6\text{H}_5)_3
\end{align*}
\]
Mechanism

Step 2

\[ \text{Step 2} \]

\begin{align*}
R & \quad R' \\
\text{C} & \quad \text{C} \\
A & \quad B
\end{align*}

\begin{align*}
+:O:- & \quad + \\
P(C_6H_5)_3 & \quad P(C_6H_5)_3
\end{align*}

\[ \text{Step 2} \]

\begin{align*}
R & \quad R' \\
\text{C} & \quad \text{C} \\
A & \quad B
\end{align*}

\begin{align*}
+:O:- & \quad + \\
P(C_6H_5)_3 & \quad P(C_6H_5)_3
\end{align*}
17.13
Planning an Alkene Synthesis via the Wittig Reaction
There will be two possible Wittig routes to an alkene.

Analyze the structure retrosynthetically.

Disconnect the doubly bonded carbons. One will come from the aldehyde or ketone, the other from the ylide.
Retrosynthetic Analysis of Styrene

\[ \text{C}_6\text{H}_5\text{CH} == \text{CH}_2 \]

\[ \Downarrow \]

\[ \text{O} \]

\[ \text{C}_6\text{H}_5\text{CH} + (\text{C}_6\text{H}_5)_3\text{P} --\text{CH}_2 \]
Retrosynthetic Analysis of Styrene

\[
\begin{align*}
\text{C}_6\text{H}_5\text{CH} &= \equiv \text{CH}_2 \\
\text{(C}_6\text{H}_5)_3\text{P} &\quad \text{CHC}_6\text{H}_5 \\
\text{HCH} &\quad + \\
\end{align*}
\]
Retrosynthetic Analysis

Both of the routes are acceptable.
Ylides are prepared from alkyl halides by a two-stage process.

The first step is a nucleophilic substitution. Triphenylphosphine is the nucleophile.
Ylides are prepared from alkyl halides by a two-stage process. The first step is a nucleophilic substitution. Triphenylphosphine is the nucleophile.

\[
(C_6H_5)_3P : + \text{CH} - X \xrightarrow{\text{A}} \xrightarrow{\text{B}} (C_6H_5)_3P^+ \text{CH} \xrightarrow{\text{B}} \quad \text{CH}^- \xrightarrow{\text{X}^-} 
\]
In the second step, the phosphonium salt is treated with a strong base in order to remove a proton from the carbon bonded to phosphorus.
In the second step, the phosphonium salt is treated with a strong base in order to remove a proton from the carbon bonded to phosphorus.

\[
(C_6H_5)_3P^+ \xrightarrow{\text{base-H}} C^:: \xleftarrow{\text{base}} C-H
\]
Typical strong bases include organolithium reagents (RLi), and the conjugate base of dimethyl sulfoxide as its sodium salt [NaCH₂S(O)CH₃].