Stereospecific Synthesis of Alkenes
Motive for the Stereospecific Synthesis of Alkenes

If an alkene is required for a specific application, it needs to be synthesized stereospecifically.
The Wittig reaction is a common method for the synthesis of alkenes from aldehydes or ketones. The synthetic disadvantage of the Wittig reaction is that it gives a mixture of E/Z-diastereomers of the alkene. Although one of the diastereomers may predominate in the mixture, the separation of the mixture is tedious.
Stereospecific Synthesis of Z-Alkenes
Catalytic Hydrogenation

Since E/Z diastereomers often have different bioactivities, it is essential that they be synthesized stereospecifically.

Partial Reduction of Alkynes to (Z)-Alkenes

\[
\begin{align*}
\text{Alkyne} & \quad \xrightarrow{\text{H}_2} \quad \text{Lindlar catalyst} & \quad \text{Fast} & \quad \text{Z-Alkene} & \quad \xrightarrow{\text{H}_2} \quad \text{Lindlar catalyst} & \quad \text{Slow} & \quad \text{Alkane}
\end{align*}
\]

Since alkynes are more reactive to catalytic hydrogenation than alkenes, controlled/ selective reduction of alkynes to alkenes without over-reduction is possible by employing a poisoned palladium catalyst (Lindlar’s catalyst).
Stereospecific Synthesis of Z-Alkenes

Catalytic Hydrogenation

Partial Reduction of Alkynes to (Z)-Alkenes

Lindlars catalyst consists of 5% palladium on a calcium carbonate support poisoned with lead acetate and a small amount of quinoline.

\[
\text{Me} \equiv \equiv \text{Me} \quad \xrightarrow{\text{H}_2} \quad \text{Me} \quad \equiv \quad \text{Me}
\]

\[
\text{Pd/ CaCO}_3 \quad \text{Pb(OAc)}_2 \quad \text{Quinoline}
\]

Z-Alkene

Lindlar catalyst

Due to environment concerns of the use of lead (Pb), other catalysts such as PdSO_4 poisoned with quinoline are found to be equally effective in this partial reduction.
Stereospecific Synthesis of Z-Alkenes

Catalytic Hydrogenation

Chemisorption of the hydrogen and the alkyne takes place first on a metal (Pd) surface:

\[ \text{H}_2 + \text{Pd} \rightarrow \text{Chemisorbed } \text{H}_2 \text{ on metal catalyst} \]

Chemisorbed Alkyne on metal catalyst surface:

Addition:

Catalyst regenerated Z-Alkene
Stereospecific Synthesis of Z-Alkenes

Catalytic Hydrogenation

Synthesis of (Z)-9-Tricosene (Muscalure)

\[
\begin{align*}
\text{CH}_3(\text{CH}_2)_6\text{CH}_2 & \quad \text{CH}_2(\text{CH}_2)_{11}\text{CH}_3 \\
\text{H} & \quad \text{H} \\
\text{Muscalure}
\end{align*}
\]

The synthesis of Muscalure ((Z)-9-tricosene), the pheromone of the female domestic housefly *Musca domestica*, was accomplished through a stereospecific partial reduction of an appropriate alkyne.
Stereospecific Synthesis of E-Alkenes

Dissolving Metal Reduction

Partial Reduction of Alkynes to (E)-Alkenes

\[ R-\text{C≡C} \rightarrow \text{Na} \rightarrow \text{NH}_3 \rightarrow R-\text{C}=\text{C} \]

Alkyne \hspace{2cm} Blue solution \hspace{2cm} E-Alkene

The reduction of alkynes under dissolving-metal conditions occurs through radical anion intermediates initiated by successive electron and proton-transfer processes.

Bright blue solutions of group 1 metals (Na or Li) in ammonia are used as the reducing mixture.

Example

\[ \text{Me-} \text{C≡C} \rightarrow \text{Na} \rightarrow \text{NH}_3 \rightarrow \text{Me-} \text{C}=\text{C} \]

Alkyne \hspace{2cm} Blue solution \hspace{2cm} E-Alkene
Stereospecific Synthesis of E-Alkenes
Dissolving Metal Reduction

Mechanism

\[ \text{Na} \rightarrow \text{Na}^+ + \text{e}^- \]

Repulsion between electrons in orbitals

\[ \text{R-} \text{C≡C-R} \rightarrow \text{C}=\text{C} \rightarrow \text{C}=\text{C} \]

\[ \text{cis-radical anion} \]

Disfavoured

\[ \text{Na}^+ \]

\[ \text{ trans-radical anion} \]

Less repulsion between electrons in orbitals

\[ \text{H} \text{C=C} \text{R} \text{R} \text{NH}_2 + \text{Na}^+ \]

\[ \text{ vinyl anion} \]
The biologically inactive stereoisomer (E-9-tricosene) of Muscalure, the pheromone of the female housefly *Musca domestica*, can be prepared stereospecifically by partial reduction of an alkyne under dissolving-metal conditions.