Directed aldol reaction is a variation of crossed aldol reaction.

crossed aldol reaction:

If a mixture of two enolizable aldehydes, two enolizable ketones, or an enolizable aldehyde and an enolizable ketone were subjected to the conditions of crossed aldol reaction, two enolate ions would form.

e.g.,

\[
\begin{align*}
\text{enolizable aldehyde (1)} & \quad \longrightarrow \quad \text{enolate ion 1e} \\
\text{enolizable ketone (2)} & \quad \longrightarrow \quad \text{enolate ion 2e}
\end{align*}
\]

Each enolate ion would react with unreacted 1 and 2, giving, after protonation by water, an aldol.

Since the overall reaction results in four aldols, it would not be an effective approach to synthesizing any of the aldols; the yield of each aldol
would be poor and purification would be difficult. Aldols 3 and 6 can be prepared readily using aldol reaction. Directed aldol reaction provides a method to synthesize aldols 4 and 5 in high yield.

desired aldol = 4:

\[
\text{CH}_3\text{CHO} \quad 1 \quad \xrightarrow{1. \text{LDA} (1 \text{ eq}) \text{, THF}} \quad \text{OH} \\
\text{2. (CH}_3)_2\text{CO (2)} \\
\text{3. aq. HCl} \\
\text{CH}_3\text{CHO} \quad 4
\]

mechanism:

desired aldol = 5:

\[
\text{CH}_3 \quad 2 \quad \xrightarrow{1. \text{LDA} (1 \text{ eq}) \text{, THF}} \quad \text{OH} \\
\text{2. CH}_3\text{CHO (1)} \\
\text{3. aq. HCl} \\
\text{CH}_3\text{CHO} \quad 5
\]

mechanism:

see also diisopropylamide ion

Contributors

- Gamini Gunawardena from the OChemPal site (Utah Valley University)