Enolates can act as a nucleophile in $S_{N2}$ type reactions. Overall an $\alpha$ hydrogen is replaced with an alkyl group. This reaction is one of the more important for enolates because a carbon-carbon bond is formed. These alkylations are affected by the same limitations as $S_{N2}$ reactions previously discussed. A good leaving group, Chloride, Bromide, Iodide, Tosylate, should be used. Also, secondary and tertiary leaving groups should not be used because of poor reactivity and possible competition with elimination reactions. Lastly, it is important to use a strong base, such as LDA or sodium amide, for this reaction. Using a weaker base such as hydroxide or an alkoxide leaves the possibility of multiple alkylation's occurring.

**Example 1: Alpha Alkylation**

1) Enolate formation

```
\begin{align*}
\text{H}_2\text{C} & \text{C} \text{H} \\
\text{H} & \text{H}
\end{align*}
```

2) $S_{N2}$ attack

```
\begin{align*}
\text{H}_2\text{C} & \text{C} \text{H} \\
\text{H} & \text{H}
\end{align*}
```

**Mechanism**

1) Enolate formation

```
\begin{align*}
\text{H}_2\text{C} & \text{C} \text{H} \\
\text{H} & \text{H}
\end{align*}
```

2) $S_{N2}$ attack

```
\begin{align*}
\text{H}_2\text{C} & \text{C} \text{H} \\
\text{H} & \text{H}
\end{align*}
```

**Alkylation of Unsymmetrical Ketones**

Unsymmetrical ketones can be regioselectively alkylated to form one major product depending on the reagents.

Treatment with LDA in THF at $-78^\circ$C tends to form the less substituted kinetic enolate.
Using sodium ethoxide in ethanol at room temperature forms the more substituted thermodynamic enolate.

Problems

1) Please write the structure of the product for the following reactions.

Answers

1)
Contributors

- Prof. Steven Farmer (Sonoma State University)