The McMurry Olefination Reaction. An important alternative to the acyloin condensation is the McMurry olefination which is a free radical coupling reaction initiated by Ti\(^{IV}\) generated from TiCl\(_3\) and a suitable reducing agent (K\(^{-}\), LAH, Li\(^{I}\) are the most commonly used).

\[
\begin{align*}
\text{R}1\text{O} & \quad \text{R}2\text{O} \quad \text{TiCl}_3 / \text{K}^{\cdot} \\
\rightarrow & \quad \text{R}1\text{R}2\text{R}2 \\
\end{align*}
\]

Due to the statistical problems of product mixtures in intermolecular and unsymmetrical McMurry coupling reactions, this reaction has been used primarily for intramolecular cyclization reactions. This is nicely illustrated in the total synthesis of taxol by Nicolaou and co-workers as shown below.

![Chemical structures](images)

The mechanism for the McMurry olefination is illustrated below on the Nicolaou taxol synthesis intermediate. Mechanistic studies have suggested that this reaction is heterogeneous occurring on the surface of the reduced titanium metal. The ultimate by-product of this reaction is TiO\(_2\).

![Mechanistic diagram](images)

While the reaction typically yields the olefin as the major product, the reaction can be attenuated to give the 1,2-diol products (Pinacol products) as shown below.

![Pinacol products](images)
The Ramberg-Backlund Reaction. The general reaction, which takes place via \(-\)-chlorosulfones, is shown below:

\[
\begin{align*}
\text{R}_{1}S\text{O} & \overset{\text{base}}{\rightarrow} \text{R}_{1}S\text{O}\text{R}_{2}Cl \quad \text{R}_{2}\text{O} \quad \text{SO}_{2} \\
\text{R}_{1}S\text{O} & \quad \quad \text{R}_{2}\text{O} \\
\end{align*}
\]

The Ramberg-Backlund reaction has proven useful for the synthesis of cyclic olefins since, it is more difficult to control the stereochemistry of the olefin in acyclic systems. Typically, a cyclic sulfide will first be formed followed by chlorination \(-\)- to the sulfur, followed by oxidation of the sulfide to the sulfone and finally, the olefin-forming step induced by base. Some examples are shown below.

The Eschenmoser Sulfide Contraction. The total synthesis of vitamin B\textsubscript{12}, achieved by the Eschenmoser and Woodward groups in 1973, required that a critical coupling reaction between two sectors of the pre-corrin ring system be devised. Many traditional methods failed to effect the joining of these two lactams; the Eschenmoser group developed the sulfide contraction reaction shown below.

Eschenmoser sulfide contraction

The mechanism for the Eschenmoser sulfide contraction is illustrated below. Note the incipient formation of the episulfide intermediate that is desulfurized to give the olefin by triethylphosphite.
Dehydration of alcohols. Alcohols can be dehydrated to alkenes, usually by the E₁ elimination mechanism by treatment with hot 85% H₃PO₄ or hot 20% (or more concentrated) H₂SO₄. The reaction typically obeys the Saytzeff rule giving the most stable alkene isomer. The general reaction is shown below:

Thus, the dehydration of 2-methyl-1-cyclohexanol, gives the trisubstituted alkene which is the expected and observed major product.

A nice illustration of this reaction is found in the total synthesis of longifolene by McMurry and co-workers:

**Carbocation Rearrangements: The Wagner-Meerwein Rearrangement.** Since the $E_1$ elimination proceeds through carbocations, it is quite common to observe the production of carbocation rearrangement products (depending on the exact nature and structure of the substrate and reaction conditions). Thus, the attempted dehydration of 2,2-dimethyl-1-cyclohexanol, gives a significant amount of 1,2-dimethylcyclohexene. This type of carbocation rearrangement is a 1,2-shift and is called a **Wagner-Meerwein rearrangement**.

\[
\begin{align*}
\text{Carbocation} & \quad \xrightarrow{\text{H}^+} \quad \text{Cyclohexene} \\
\text{OH} & \quad \xrightarrow{-\text{H}_2\text{O}} \quad \text{OH}
\end{align*}
\]

Wagner-Meerwein rearrangements can also lead to ring-expansion rearrangements such as that depicted below:

An example of a Wagner-Meerwein rearrangement in the synthesis of rhoeadine by Irie and co-workers illustrates the ring-expansion potential:

\[
\begin{align*}
\text{O} & \quad \xrightarrow{\text{MsCl, TEA}} \quad \text{NMe} \\
\text{OH} & \quad \xrightarrow{-\text{H}_2\text{O}} \quad \text{NMe}
\end{align*}
\]


The Wagner-Meerwein rearrangement is also a very common skeletal reorganization process in biosynthesis. For example, the natural product longifolene is constructed by a Wagner-Meerwein rearrangement of the initially formed $2^\circ$ carbocation generated by pyrophosphate dissociation from the substrate shown below. The Wagner-Meerwein rearrangement of the $2^\circ$ to $3^\circ$ carbocation is terminated by an $E_1$-type elimination giving the exocyclic alkene longifolene.

**Selenoxide eliminations.** Aryl selenides can be introduced into organic structures by a variety of methods. The phenylselenide can be oxidized to the corresponding selenoxide under very mild conditions (NaIO$_4$, H$_2$O$_2$, mCPBA, etc.). Selenoxides bearing an [$\equiv$]-hydrogen atom are unstable to a mild thermal syn-elimination yielding an olefin. The phenylselenic acid generated as a by-product, spontaneously dimerizes to the diselenoxide species (a polar substance). The general reaction is shown below:
Thus, enolates can be selenated with either PhSeBr or PhSeSePh (diphenyl diselenide) and then eliminated to yield the corresponding \( \text{unsaturated carbonyl derivative} \).

Mesylates, tosylates, and halides can also be readily displaced with the phenylselenide anion and then processed to the olefin. The selenoxide elimination usually occurs at room temperature or below depending on the specific substrate.

**Sulfoxide eliminations.** The sulfur analogy to the selenoxide method discussed above has been an important olefin-forming reaction in synthetic organic chemistry for many years. Compared to the selenium system, the corresponding sulfoxides are synthesized in much the same way from the corresponding sulfides with peracids oxidation being the most commonly employed method. The elimination of the sulfoxide requires elevated temperatures, typically above 100°C compared to the much milder selenoxide elimination (which can considered to be a draw back to the sulfoxide method compared to the selenium system). On the other hand, for industrial uses, the much more toxic and costly selenium reagents will rarely, if ever, be deemed suitable and the economical sulfur-based chemistry has enjoyed the commensurate popularity. The general reaction is shown below:

Several examples are shown below:

\[ \text{MOMO} \text{Me} \text{Me} \text{OH} \text{py.} \text{MOMO} \text{Me} \text{Me} \text{OMs} \text{DMF} \text{PhSeNa} \text{MOMO} \text{Me} \text{Me} \text{SPh} \]

\[ \text{MeCO}_2\text{H}, \text{CH}_2\text{Cl}_2 \text{NaOAc}, \text{HOAc} \text{MOMO} \text{Me} \text{Me} \text{SPh} \text{[CaCO}_3\text{ decaline} \text{MOMO} \text{Me} \text{Me} \text{Me} \text{Me} \text{Me} \text{Me} \text{Me} \text{Me} \text{Me} \text{Me} \text{Me} \text{Me} \]

The Shapiro Reaction

Tosylhydrazones and related species, when treated with strong base, undergo a fragmentation reaction giving a vinyl lithium species that can be trapped (alkylated) or protonated. This is a net reductive olefination of a ketone.

The Shapiro Reaction

Tetrahedron Lett., 1984, 25, 4901 (this example)