Welcome to the Bachelor of Science third year program in the subject of chemistry, semester six for the course CHC 110 section A organic chemistry. I'm Dr. Durga Kamat, assistant professor at DCT's, Dhempe College of Arts and Science, and I'm going to take up a module on reaction and mechanism Darzen's glycidic ester condensation.

In this module, after a brief introduction on Darzen's glycidic ester condensation, we will discuss some of the examples of Darzen's glycidic ester condensation, mechanism of Darzen's glycidic ester condensation and its application. At the end of this module you will be able to give the reaction for Darzen's glycidic ester condensation, explain the mechanism of Darzen's glycidic ester condensation and discuss its application. Darzen's glycidic ester condensation is the condensation of a carbonyl compound such as an aldehyde or a ketone with alpha halo ester in presence of a base to form alpha beta epoxy esters, also called as glycidic esters.

This is an alpha carbon atom and this is the beta carbon atom of the epoxide ring. Any alkoxide base can be used for this reaction, however generally potassium tertiary butoxide is used as a base for this reaction. Potassium tertiary butoxide is a hindered, bulky base. A hindered base is preferred for this reaction in order to avoid SN2 displacement of the halide ion. Aromatic aldehydes and ketones
give good yield of the product, but aliphatic aldehydes react poorly. However, the yield of the reaction for aliphatic aldehydes can be improved by using certain lithium bases, and the yield can go up to 80%.

Now let's see an example of Darzen's glycidic ester condensation. Ethyl chloroacetate on condensation with acetophenone in presence of potassium tertiary butoxide base produces alpha beta epoxy ester.

Now let us understand the mechanism of Darzen's glycidic ester condensation. Initially, Base abstracts, an acidic alpha proton from the alpha halo ester to give the enolate ion. We can draw the resonance contributor for this. That is the carbanion. So the carbanion formed then undergoes nucleophilic addition. There is nucleophilic addition of the carbanion to the carbonyl group of the carbonyl compound that is an aldehyde or ketone. So we get an oxyanion, also called as halo alkoxide. Then there is displacement of the halide ion by internal SN2 reaction which gives glycidic ester.

Now the halo alkoxide formed in this reaction could be isolated in case of fluoro esters or chloro esters. Thus, providing evidence that carbene intermediate is not a part of this mechanism. Glycidic ester formed as a product of Darzen's glycidic ester condensation can be converted to glycidic acid by hydrolysis. Alkaline hydrolysis can be carried out and then on treatment with acid it undergoes decarboxylative rearrangement to give Aldehyde.

Let me explain the steps with the help of curved arrows. So initially there is decarboxylation. So this is the decarboxylative rearrangement to give enol. Now there is tautomerization. So the enol will form the corresponding aldehyde or ketone. So there is addition of one more carbon atom giving the longer chain homologue of the carbonyl compound. So we can call this as chain extension reaction. For example cyclohexanone on reaction with ethyl chloroacetate in presence of potassium tertiary butoxide gives glycidic ester which on hydrolysis and decarboxylative rearrangement gives cyclohexane carbaldehyde.

Here we can see that in cyclohexane carbaldehyde that is the product there is addition of one more carbon atom that is homologation. Darzen's condensation of methyl chloroacetate and beta ionone gives the corresponding glycidic ester. This glycidic ester or apha beta epoxy ester on subsequent hydrolysis and decarboxylative rearrangement gives the corresponding aldehyde which on treatment with base gives alpha beta unsaturated aldehyde which is used for synthesis of vitamin A. This is a very important application of Darzen's glycidic ester condensation.

In the past, Darzen's methodology was primarily used for homologation reaction that means for the synthesis of aldehydes and ketones without any consideration of stereocontrol in the epoxide formation.

Now, let us revisit the mechanism by considering the stereo chemistry aspects. So we can note here that anti and syn oxyanion diastereomers are formed when the alpha chloro ester initially undergoes deprotonation and then adds to the carbonyl compound. So the syn diastereomer will undergo displacement of the halide to give the cis epoxide whereas the anti diastereomer will undergo displacement of halide to give trans epoxide.

Typically cis to trans ratio of epoxide formation lies between one is to one and one is to two. So now let's summarize Darzen's glycidic ester condensation with help of this example.

Reaction of carbonyl compound in this case cyclohexanone with alpha halo ester in this case ethyl chloroacetate with the base potassium tertiary butoxide gives alpha beta epoxy ester or glycidic ester.

The key steps in the mechanism are deprotonation of the alpha halo ester to form carbanion, nucleophilic addition of the carbanion to the carbonyl group of carbonyl compound and then displacement of the halide ion by internal SN2 reaction which gives this glycidic ester.

These are my references.

Thank you.