# Synthetic Strategies: Aldehydes and Ketones

## Transcript

00:00:00:00 - 00:00:16:40
**Dr.Jessie Key:** Hello again, Dr. Jessie Key here to talk to you about synthetic strategies with aldehydes and ketones by going through a few examples. Please consider solving the examples on your own first by stopping the video as needed and comparing your answer to the solution presented in the video.

00:00:16:40 - 00:00:41:69
**Dr.Jessie Key:** Note, there are multiple correct answers possible, but only one will be presented for each of the two examples. In our first example, we are going to propose a multi-step synthesis of propylidenecyclohexane from the starting material cyclohexylmethanol. Pause now to work on this on your own and return back when you're ready.

00:00:46:70 - 00:01:00:16
**Dr.Jessie Key:** Welcome back! To approach this problem, you should first determine what kind of changes have occurred between the starting material and the product. Has there been a change to the carbon skeleton?

00:01:00:16 - 00:01:15:62
**Dr.Jessie Key:** Yes, two additional carbons have been added. Has there been a change in functional groups? Yes, the starting material has a primary alcohol and the final product has an alkene.

00:01:16:71 - 00:01:36:43
**Dr.Jessie Key:** This analysis tells you that you'll need to conduct some sort of carbon-carbon bond forming reaction somewhere in the synthesis. Two likely candidates are the Grignard reaction and the Wittig reaction. Let's try designing a synthesis around the Grignard reaction using a forward synthesis approach.

00:01:39:05 - 00:02:00:61
**Dr.Jessie Key:** If you oxidize the primary alcohol using either PCC, Swern, or DMP methods, you'll get an aldehyde. I've written down the conditions for PCC oxidation, the reagent PCC

insolvent dichloromethane. With aldehyde now installed, it can be used in a Grignard reaction to add the two additional carbons.

00:02:00:61 - 00:02:24:61
**Dr.Jessie Key:** The reagents used for this transformation are the Grignard reagent ethyl magnesium bromide in a first step followed by water in a second step. Now the carbon skeleton is in place, but there's an alcohol present instead of the alkene. If you remember back to organic one, you learned a reaction to go from an alcohol to an alkene elimination.

00:02:24:61 - 00:03:16:15
**Dr.Jessie Key:** In this case, we can use some sulfuric acid, H2SO4 and heat to perform an E1 style elimination to obtain the desired final product propylidenecyclohexane. It should be noted that there are other correct answers possible for the synthesis, including the use of different oxidation methods or different reaction conditions to accomplish the elimination. In our second example, we're going to propose a multi-step synthesis of (6E)-9,9-dimethyldec-6-en-4-one from the starting material 1-hydroxyhexan-3-one.

00:03:16:15 - 00:03:35:73
**Dr.Jessie Key:** Feel free to pause and try this problem on your own and join us again when you're ready. Okay, welcome back! To approach this problem, you should first determine what kinds of changes have occurred between the starting material and the product.

00:03:35:73 - 00:03:46:69
**Dr.Jessie Key:** Has there been a change to the carbon skeleton? Yes, the parent chain is going 6 to 10 carbons. Has there been a change in functional groups?

00:03:46:69 - 00:04:04:79
**Dr.Jessie Key:** Yes, the starting material has a primary alcohol. And the final product has an alkene. This analysis tells you that you'll need to conduct some carbon-carbon bond forming reaction somewhere in the synthesis.

00:04:04:79 - 00:04:19:69
**Dr.Jessie Key:** The appearance of the product screens out Wittig reaction, having two larger groups connected by an alkene. Let's see how we can accomplish this transformation using the Wittig reaction. And this time, let's approach it retrosynthetically.

00:04:26:16 - 00:05:00:11
**Dr.Jessie Key:** The final product could be obtained from the intermediates obtained if we cleave the alkene and make one side an aldehyde and the other side a phosphorane ylide Wittig reagent. We can access the aldehyde easily by oxidizing the primary alcohol at the one position of our starting material. But wait, there's a problem with this approach.

00:05:00:11 - 00:05:20:77
**Dr.Jessie Key:** How can we make sure that it is the aldehyde that reacts with our Wittig reaction and not the ketone? If we protect the ketone as a cyclic acetal, we can mask it while

we conduct the Wittig reaction and deprotect to regain the ketone functionality at the end. Our synthesis should look like this.

00:05:24:77 - 00:06:01:21
**Dr.Jessie Key:** First, protect the starting material as a cyclic acetal using ethane-1,2-diol with some acid catalyst and a Dean-Stark trap to remove water. Next, the alcohol at carbon one can be oxidized using either PCC, DCM, or Swern conditions - for simplicity, I'll use PCC and dichloromethane. Next, the Wittig reaction can be performed with the phorphorane ylide Wittig reagent derived from 1-bromo-3,3,-dimethylbutane.

00:06:10:53 - 00:06:23:97
**Dr.Jessie Key:** After the Wittig reaction is complete, deprotection can be done using acidic water to regenerate the ketone and get to the desired final product, (6E)-9,9-dimethyldec-6-en-4-one