TRU
Open Press

Synthetic Strategies: Aldehydes and Ketones

Transcript

Instructor: Jessie Key

00:00:00:00 - 00:00:23:80
Instructor: Hello again, Doctor 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. Note, there are multiple correct answers possible, but only one will be presented for each of the two examples.

00:00:26:49 - 00:01:03:90
Instructor: In our first example, we're going to propose a multi-step synthesis of propylene cyclohexene from the starting material cyclohexyl methanol. Pause now to work on this on your own and return back when you're ready. Welcome back. To approach this problem, you should first determine what changes have occurred between the starting material and the product. Has there been a change to the carbon skeleton? Yes, two additional carbons have been added.

00:01:04:34 - 00:01:24:99
Instructor: Has there been a change in functional groups? 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 sort of carbon carbon bond forming reaction somewhere in the synthesis.

00:01:24:99 - 00:01:47:11
Instructor: Two likely candidates are the Grignard reaction and the VIG reaction. Let's try designing a synthesis around the Grignard reaction using a Ford synthesis approach. If you oxidize the primary alcohol using either PCC, Swern or DMP methods, you'll get an aldehyde.

00:01:47:11 - 00:02:08:69
Instructor: 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. The reagents used for this transformation are the Grignard reagent ethyl magnesium bromide in a first step followed by water in a second step.

00:02:10:97 - 00:02:36:45
Instructor: 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. In this case, we can use some sulfuric acid, HSO four and heat to perform an E one style elimination to obtain the desired final product propylene cyclohexane.

00:02:38:85 - 00:03:23:21
Instructor: 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 6e99 dimethyl 6n4o from the starting material one hydroxy hexane 3,0. Feel free to pause and try this problem on your own and join us again when you're ready.

00:03:26:87 - 00:03:38:85
Instructor: Okay, welcome back. To approach this problem, you should first determine what kinds of changes have occurred between the starting material and the product. Has there been a change to the carbon skeleton?

00:03:38:85 - 00:03:50:71
Instructor: Yes, the parent chain is going 6-10 carbons. Has there been a change in functional groups? Yes, the starting material has a primary alcohol.

00:03:51:77 - 00:04:11:51
Instructor: 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. The appearance of the product screens out wittig reaction, having two larger groups connected by an alkene.

00:04:11:51 - 00:04:37:84
Instructor: Let's see how we can accomplish this transformation using the wittig reaction. And this time, let's approach it retro synthetically. 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 phosphene ylide wittig reagent.

00:04:45:73 - 00:05:08:21
Instructor: 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. How can we make sure that it is the aldehyde that reacts with our wittig reaction and not the ketone?

00:05:08:21 - 00:05:34:17
Instructor: 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. First, protect the starting material as a cyclic acetal using ethane 12 dial with some acid catalyst and a diene trap to remove water.

00:05:37:25 - 00:06:01:21
Instructor: Next, the alcohol at carbon one can be oxidized using either PCC, DCM, or sworn conditions. For simplicity, I'll use PCC and dichlomethane. Next, the wittig reaction can be performed with the phosphorne ylide wittig reagent derived from one bromo 33 dimethyl butane.

00:06:10:53 - 00:06:23:97
Instructor: After the wittig reaction is complete, deprotection can be done using acidic water to regenerate the ketone and get to the desired final product, 6e99 dimethyl 6n4o.