Synthesizing a Polysubstituted Benzene Derivative

Transcript

Instructor: Jessie Key

00:00:00:84 - 00:00:30:16
Instructor: Hello, again, Doctor Jessie Key here. In this video, you'll be exploring two examples where complex poly substitute benzene derivatives are synthesized from benzene. In our first example, we'll plan a synthesis of one chloro, four isopropyl, two nitrobenzene, from the string material benzene.

00:00:30:16 - 00:00:53:80
Instructor: There are many ways you could approach this problem, including strategies that could be classified as either forward or retrosynthesis. Forward synthesis places emphasis on going forward from the string material one step at a time until you reach the final desired product. Retro synthesis is the opposite where you focus on the final product and work backwards one step at a time until you reach the starting material.

00:00:53:80 - 00:01:07:46
Instructor: I find that both strategies have merit and some people prefer one over another. But usually the way my mind works, I often end up using some combination of the two. Let me walk you through how I would approach this.

00:01:07:46 - 00:01:28:44
Instructor: First, I look at the functional groups present in the final product and classify them according to both their directing effects and their activation deactivation effects. At carbon one, there's a chloro group, which is weekly deactivating and ortho para directing. It could be added by chlorination.

00:01:32:46 - 00:01:55:74
Instructor: At carbon two, there's a nitro group, which is strongly deactivating and meta directing. It could be added by nitration. Finally, at carbon four, there's an isopropyl group, which is weakly activating and ortho para directing.

00:01:55:74 - 00:02:18:21
Instructor: It could be added by Friedel-Crafts alkylation. Next, I'd look for the relative position of each group. The chloro group is ortho to the nitro and Para to the isopropyl.

00:02:18:85 - 00:02:44:93
Instructor: The nitro group is ortho to the chloro group and meta to the isopropyl. The isopropyl

group is Para to the chloro group and meta to the nitro group. Now with this information in hand, I can plan my synthetic root.

00:02:46:25 - 00:03:17:25
Instructor: Knowing that Friedel-Crafts alkylations do not work with strongly deactivate groups present, this suggests that nitration should be a later step or the last step in the synthesis. I'll focus on first placing the isopropyl or chloro groups onto the ring. The best order for doing this would probably be to first put the ortho para directing isopropyl group on the ring because its steric bulk would give a higher yield of the para chlorination product in the subsequent step.

00:03:18:50 - 00:03:41:26
Instructor: With the chloro group in place, it can direct the nitro group to the correct position ortho to the chloro group. My synthesis would start with benzene undergoing a Freel crafts alkylation reaction with two chloropropane in the presence of aluminum trichloride. This gives isopropyl benzene as an intermediate.

00:03:47:22 - 00:04:45:31
Instructor: Next, chlorination occurs with chlorine, CL two and aluminum trichloride, which gives one chloro for isopropyl benzene as an intermediate. The final step is nitration, using nitric acid and sulfuric acid to give the desired one chloro four isopropyl two nitrobenzene. In our second example, let's see how we can synthesize one bromo three ethyl benzene from benzene.

00:04:46:35 - 00:05:10:55
Instructor: Feel free to pause and give this a try on your own, and when you're comfortable, we can go through it together. Welcome back. Again, let's analyze the substituents present in the desired final product and classify based on the activating, deactivating and directing effects.

00:05:10:63 - 00:05:46:38
Instructor: The ethyl group is a weak activator and ortho para directing and could be added to the ring by Friedel-Crafts alkylation. While the bromo group is a weak deactivator, there's also ortho para directing, and could be added by bromination. Given this information, it does not immediately make sense how the two substituents can be positioned relatively meta to each other.

00:05:46:38 - 00:06:12:23
Instructor: We'll need to look at this from a broader retrosynthetic viewpoint. How else can we get to the final product? The ethyl group could be obtained by Clemensen reduction of acetophenone.

00:06:12:23 - 00:06:59:57
Instructor: The ketone of acetophenone would be a moderate deactivator and meta directing. With this knowledge, it now becomes clear that we can obtain the meta arrangement of the two substituents by first performing a Friedel-Crafts acylation with ethanol chloride and aluminum trichloride to generate acetophenone. Bromination can then be performed with bromine and iron tribromide to give meta substitution of the bromine with three bromo acetophenone.

00:07:07:01 - 00:07:18:49
Instructor: Finally, Clemens and reduction can be performed with zinc, mercury, amalgam, hydrochloric acid, and heat to get the desired product one bromo three ethyl benzene.