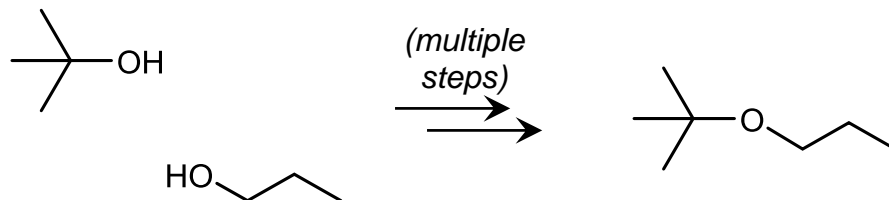


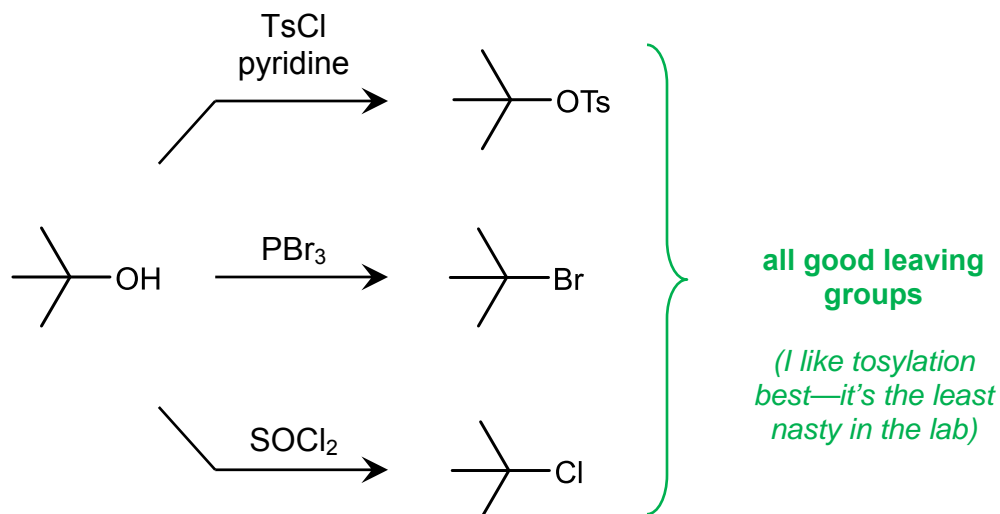
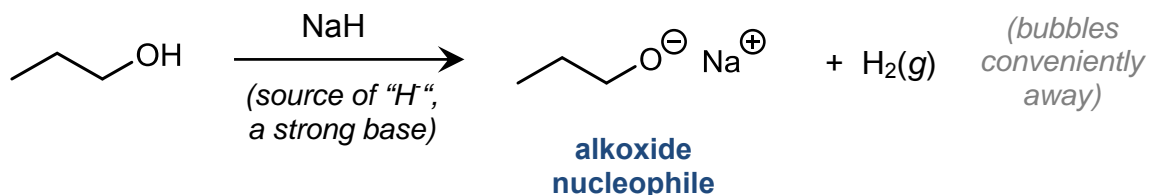
In-Class Solutions: Planning Multistep Organic Syntheses

1.

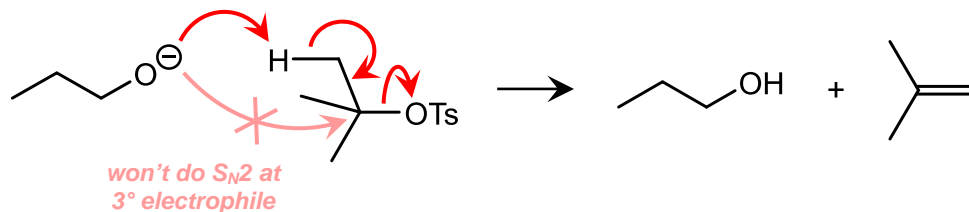


This synthesis is sometimes called the “Williamson ether synthesis”; unlike a lot of the synthesis problems you’ll be asked to solve in this class, where you will have to piece together syntheses on your own, the answer to this problem is entirely described by the Williamson method. In the Williamson ether synthesis, one side of the ether will come from an alkoxide (RO^-) nucleophile, and the other side will come from a molecule with a good leaving group. In principle, either of our starting molecules could be used for either purpose.

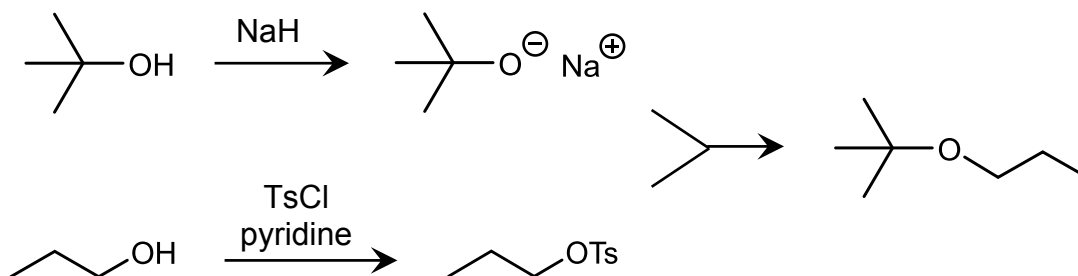
What happens if we set the right-hand starting material up as the alkoxide nucleophile, and the right-hand one as an electrophile with a leaving group?



The last step of this synthesis would be to combine the alkoxide nucleophile with the electrophile. But the way that we've set things up here, the tertiary electrophile is going to prefer E2 elimination rather than S_N2 substitution. And that's not what we want.



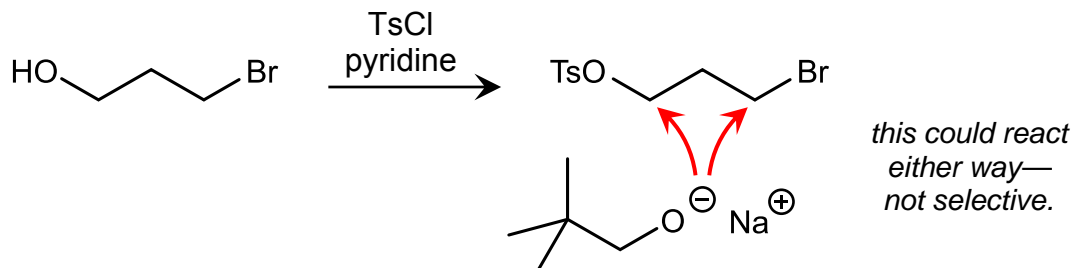
Instead, we can solve this problem by switching the parts of the molecule that serve as the nucleophile and electrophile. Here's how we might do that:



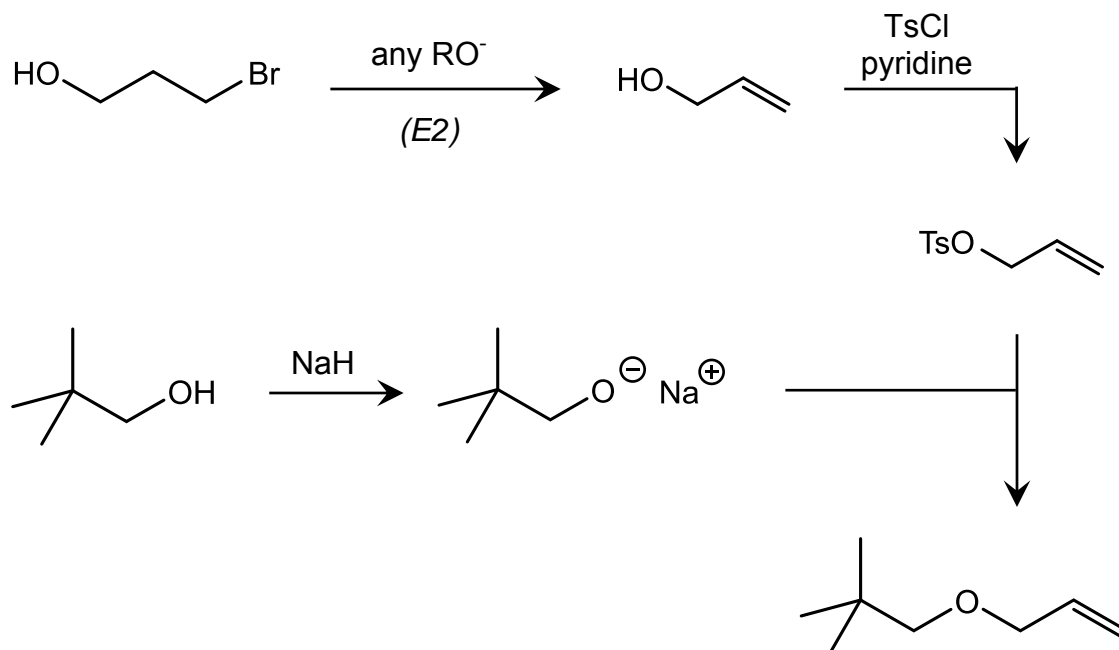
Even this route will have a little bit of E2 competing with S_N2 in the final step, but tosylates naturally favor S_N2 , and the fact that the leaving group is attached to a primary carbon also favors S_N2 . So this should be pretty selective for S_N2 .

2. Here, things are a little more complicated. Not only do we have to make an ether, we also have to convert an alkyl halide into an alkene. So which do we do first?

I think we can't make the ether first, because the alcohol that will have a leaving group already has a leaving group:



But doing the sequence elimination-first solves this problem:



There are a number of correct answers to this problem, but any answer has to address a central question to all syntheses: does my route generate my proposed product selectively, or are there other, inadvertent products that also get made?