Chemistry 2331H

Workshop 18 Solutions: More Multistep Organic Synthesis

A challenge in both of these problems is to use the few reactions you know to make what you want. (You might imagine this issue could be resolved for professional chemists by knowing lots of reactions, but in the end, even they get stuck—there are never enough reactions to make everything.) Here, I've given you the hint that you should go through an epoxide, which makes good sense; you learned that SN2 reactions on epoxides can generate products with two different functional groups attached

the only thing you know to do with a hydrocarbon is to halogenate it, and you only know how to do mono-halogenation and multi-halogenation, always at the more substituted/more stabilized position. Here, that is at the benzylic carbon. Dihalogenation here generates something that can be eliminated to yield the product.



This problem is a bit harder, because chemistry clearly has to happen—a CN has to be added—at a position that's not the most substituted. So, although we have to start with halogenation again (we don't know anything else to do with propane), it's clear we're going to have to do some trickery to translate halogenation at the most substituted position to substitution at the least substituted position. One thing we can't do is just say "I'll halogenate to get the material I want":



Yes, if you were to expose propane to chlorine gas for a while, you would get this molecule, but you'd get hundreds of other molecules too. (Monochlorinated, other dichlorinated, with chlorines all over the place.) A central goal of these synthesis problems is to propose ways of making the products *selectively*.

An obvious way to approach these problems is to go forward from starting materials after all, that's what a chemist would physically do in the lab—but another way to think about synthesis is backwards from the end. Given a product, from what materials might we start? Our product has two functional parts to it, an alkene and a cyano (CN) group. How might we get to those functional groups? The CN could be introduced via $S_N 2$ by cyanide (CN⁻), or the alkene could be made by elimination:



The bottom, elimination route would require that the leaving group be on the end of the molecule, because elimination of either of the other bromides would lead to the more substituted alkene in resonance with the CN group. It would be awfully tricky to put the Br there...so let's look at the other route. For the top route we would need an allylic bromide, which...hmmm...we can make via allylic bromination:



Now we just need a way to make propene from propane, and we've finished. Here's a total route:

