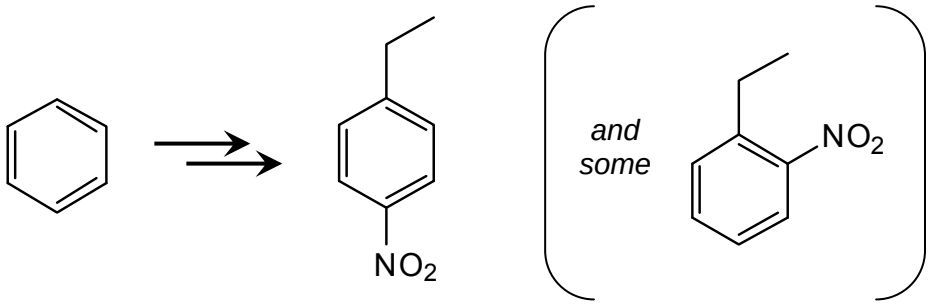
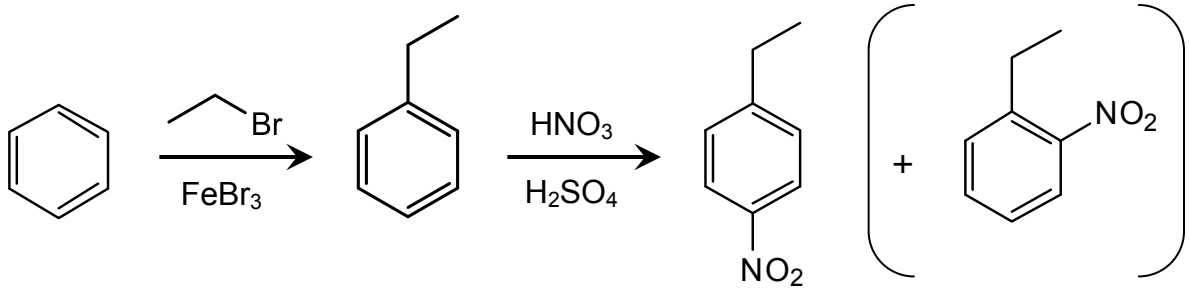
Chemistry 2302

Workshop 7 Solutions
Synthesizing Complex Aromatic Products

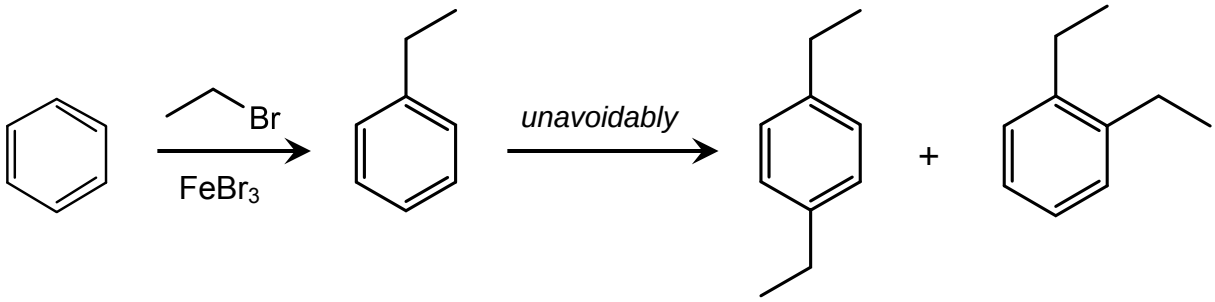


Here we need to introduce two groups onto the benzene ring: a nitro group, and an ethyl group. These can both be introduced via electrophilic aromatic substitution reactions. However, if we put the nitro group on first, introduction of an alkyl group via Friedel-Crafts reaction won't work. So we have to make the carbon-carbon bond first, before we put on the nitro group.

One way to do this would be via sequential Friedel-Crafts alkylation and nitration:

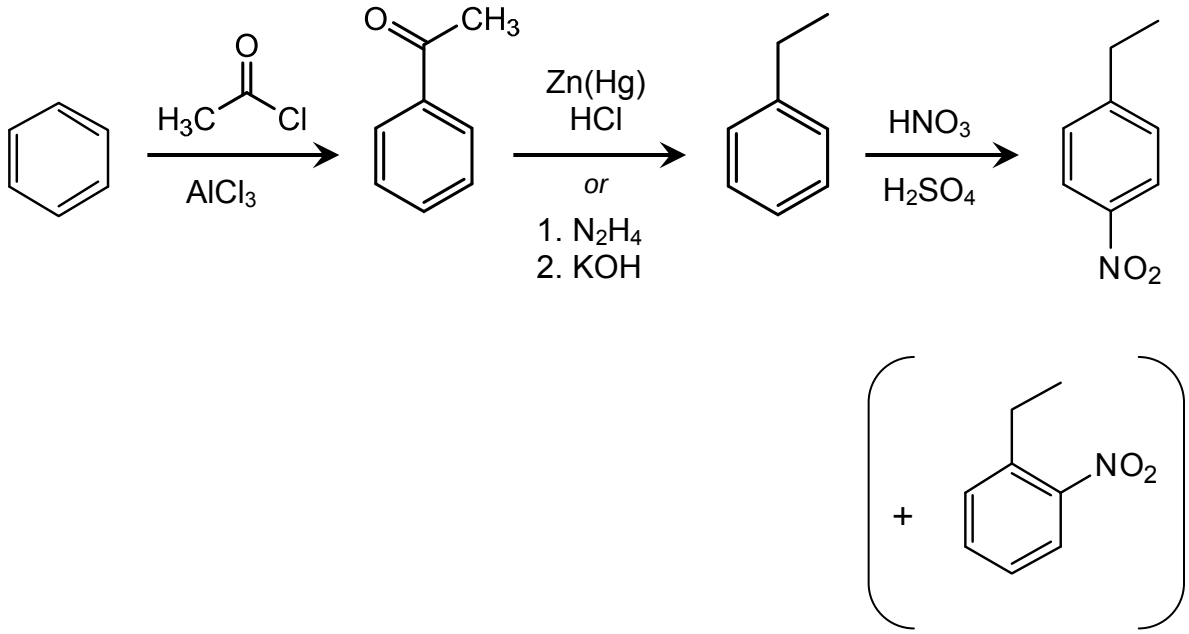


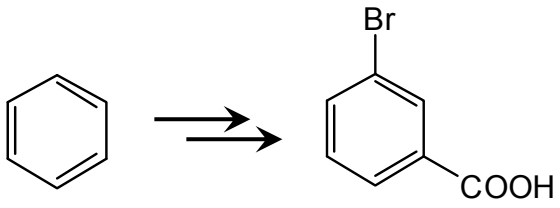
This synthesis looks OK, but it does have a minor flaw: the first, Friedel-Crafts alkylation reaction is subject to over-alkylation because it introduces an activating group.



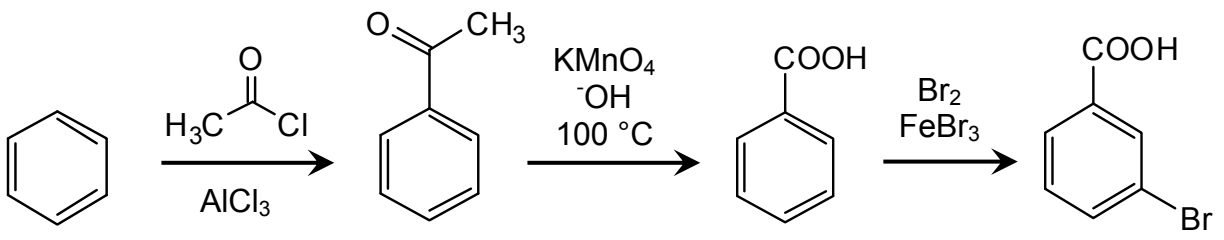
(If this were an exam question, this answer would probably get most of the credit for the problem, but not all of it.)

So how do we fix that problem? In class, we said that sequential Friedel-Crafts acylation and benzylic reduction aren't subject to those same limitations:

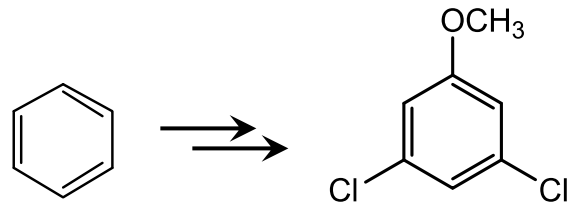




Once again we have two groups to introduce, and once again we don't know how to introduce one of them (-COOH) directly. We do know, however, that we can convert a benzylic, carbon-containing substituent to –COOH with $KMnO_4$. Br is *ortho*-/*para*-directing, so we'd better not put it on first; wiser to introduce the carbon substituent first, and then oxidize:



You could also have switched the last two steps; the ketone is electron-withdrawing and *meta*-directing, just like the carboxylic acid.



All three of the substituents in the product are *ortho*-/*para*-directing, so none of them can be used directly to introduce the others. But the synthesis could work if we could introduce a *meta*-director first, and then convert that into one of the other groups: