3.12: SYNTHESIS OF POLYSUBSTITUTED BENZENES

OBJECTIVES

After completing this section, you should be able to

- Design a multistep synthesis which may involve reactions in the alkyl side chain of an alkylbenzene and the electrophilic substitution reactions discussed in this chapter. You should pay particular attention to
  - carrying out the reactions in the correct order.
  - using the most appropriate reagents and conditions.
  - the limitations of certain types of reactions.
- Analyze a proposed multistep synthesis involving aromatic substitution to determine its feasibility, point out any errors in the proposal and identify possible problem areas.

STUDY NOTES

As you can see, designing a multistep synthesis requires an analytical mind and an ability to think logically, as well as a knowledge of organic reactions. The best way to become an expert in designing such syntheses is to get lots of practice by doing plenty of problems.

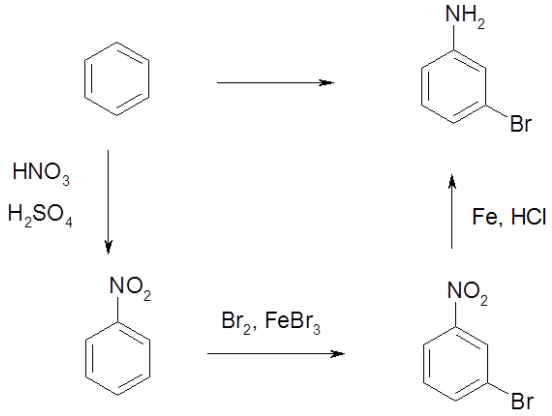
The ability to plan a successful multi step synthesis of complex molecules is one of the goals of organic chemists. It requires a working knowledge of the uses and limitations of many organic reactions - not only which reactions to use, but when. A few examples follow:

FROM BENZENE MAKE *M*-BROMOANILINE

In this reaction three reactions are required.

1. A nitration
2. A conversion from the nitro group to an amine
3. A bromination

Because the end product is meta a meta directing group must be utilized. Of the nitro, bromine, and amine group, only the nitro group is meta direction. This means that the first step need to be the nitration and not the bromination. Also, the conversion of the nitro group to an amine must occur last because the amine group is ortho/para direction.

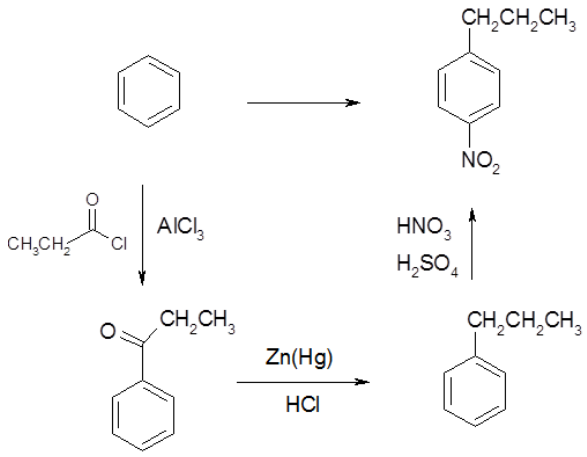


FROM BENZENE MAKE *P*-NITROPROPYLBENZENE :

In this reaction three reactions are required.

1. A Friedel Crafts acylation
2. A conversion from the acyl group to an alkane
3. A nitration

Because the propyl group has more than two carbons, it must be added in two steps. A Friedel Crafts acylation followed by a Clemmensen Reduction. Remember that Friedel Crafts reactions are hindered if the benzene ring is strongly deactivated. This means that the acyl group must go on first. Because the end product is para a para directing group must be utilized. Of the nitro, acyl, and alkane group, only the alkane group is meta direction. This means that the acyl group must be converted to an alkane prior to the nitration step.



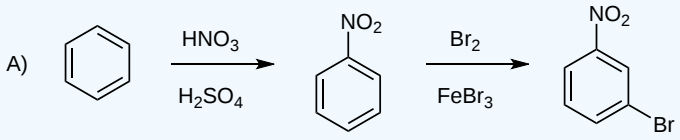
EXERCISE 3.12.1

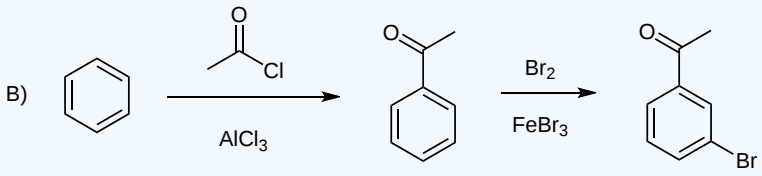
How would make the following compounds from benzene?

a. *m*-bromonitrobenzene
b. *m*-bromoethylbenzene

Answer

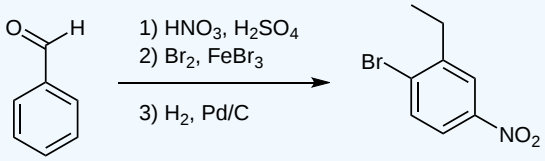
Only one possible synthesis is shown for each compound. There are multiple possibilities.





EXERCISE 3.12.2

There is something wrong with the following reaction, what is it?



Answer

The bromine should be in the meta position. Right now it is in the ortho position, from perhaps having the ethyl group present first and then the having it substituted there. BUT the ethyl group is last to form, and the aldehyde and nitro groups would both encourage a meta substitution.