Montogue

Quiz CH205

Organic Chemistry

Electrophilic Aromatic Substitution

Lucas Monteiro Nogueira

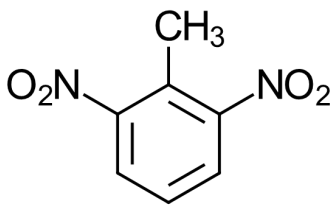
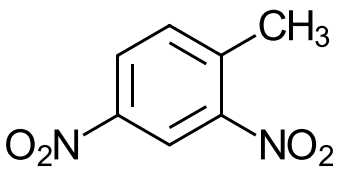
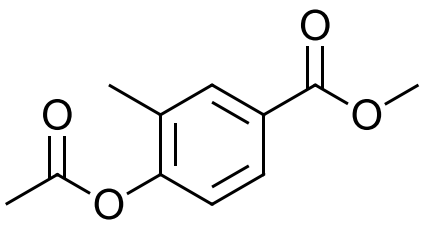
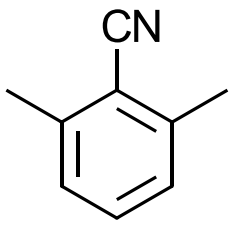
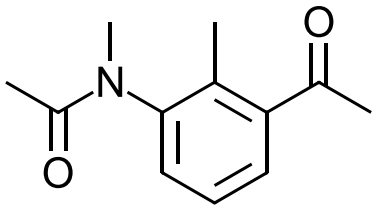
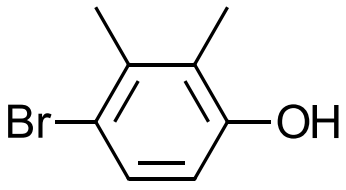
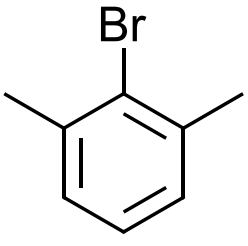
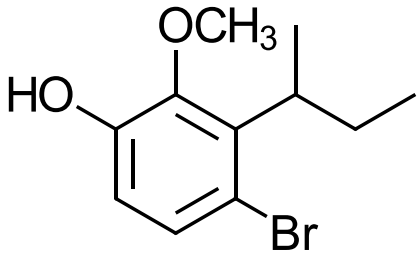
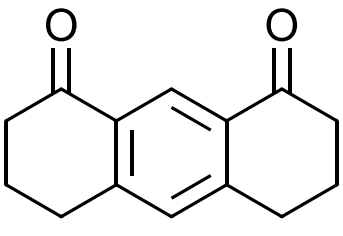
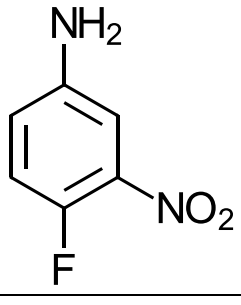
PROBLEMS

Problem 1 (McMurry, 2008, w/ permission)

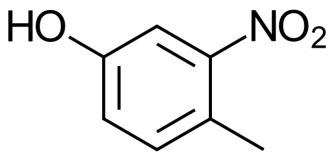
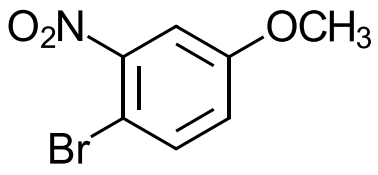
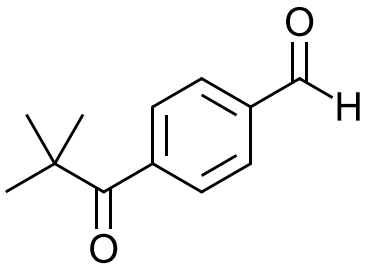
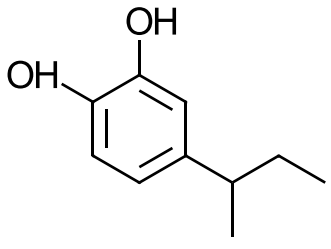
1.1. Write resonance structures for chlorobenzene to show the electron-withdrawing effect of the chloro group.
1.2. Write resonance structures for nitrobenzene to show the electron-donating effect of the nitro group.

Problem 2 (Klein, 2017, w/ permission)

For each compound below, identify which position(s) is/are most likely to undergo an electrophilic aromatic substitution reaction. In problems 2.1 - 10, ignore steric hindrance.

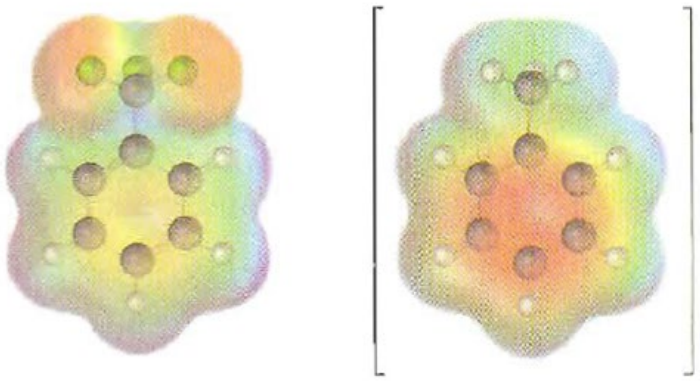
2.1. 	**2.2.** 
2.3. 	**2.4.** 
2.5. 	**2.6.** 
2.7. 	**2.8.** 
2.9. 	**2.10.** 

In Problems 2.11 – 14, considering steric effects, indicate the position that is most likely to be the site of an electrophilic aromatic substitution reaction.

2.11. 	**2.12.** 
2.13. 	**2.14.** 

▶ Problem 3 (McMurry, 2008, w/ permission)

An electrostatic potential map of (trifluoromethyl)benzene, $C_6H_5CF_3$, is shown below. Also shown is an electrostatic potential map of toluene. Would you expect (trifluoromethyl)benzene to be more reactive or less reactive than toluene toward electrophilic substitution? Explain.

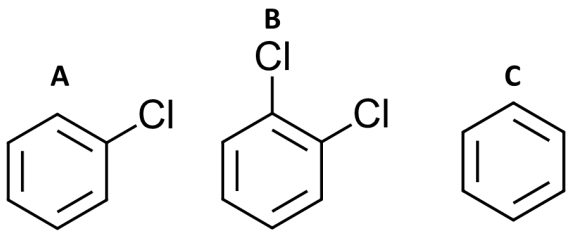


(Trifluoromethyl)benzene Toluene

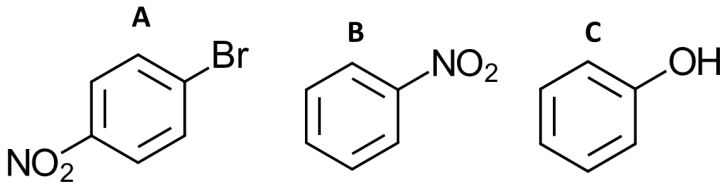
▶ Problem 4

Rank the following compounds in order of decreasing reactivity for EAS.

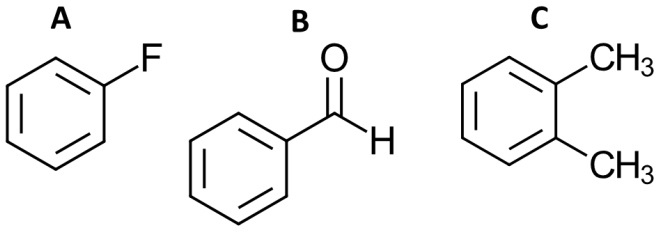
4.1: Chlorobenzene, *o*-dichlorobenzene, benzene



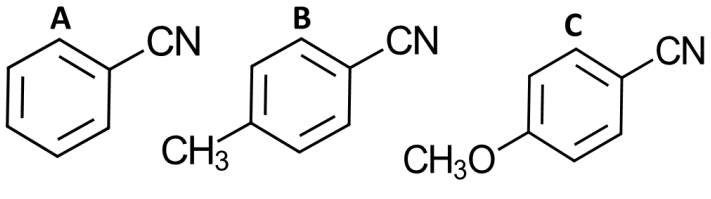
4.2: *p*-Bromonitrobenzene, nitrobenzene, phenol



4.3: Fluorobenzene, benzaldehyde, *o*-xylene



4.4: Benzonitrile, *p*-methylbenzonitrile, *p*-methoxybenzonitrile



▶ Problem 5 (Carey, 2008, w/ permission)

How many products are capable of being formed from toluene in each of the following reactions?

5.1. Mononitration (HNO_3, H_2SO_4, 40°C)
5.2. Dinitration (HNO_3, H_2SO_4, 80°C)
5.3. Trinitration (HNO_3, H_2SO_4, 110°C)
5.4. The explosive TNT (trinitrotoluene) is the major product obtained on trinitration of toluene. Which trinitrotoluene isomer is TNT?

▶ Problem 6

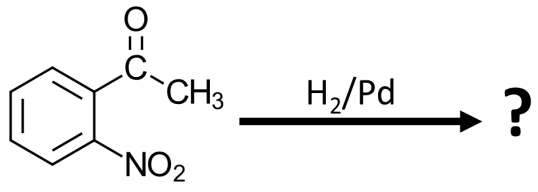
Predict the major product(s) of nitration of the following substances.

6.1. Bromobenzene
6.2. Benzonitrile
6.3. Benzoic acid
6.4. Nitrobenzene
6.5. Benzenesulfonic acid
6.6. Methoxybenzene

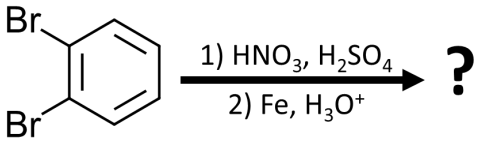
▶ Problem 7

What product(s) would you expect to obtain from the following reactions?

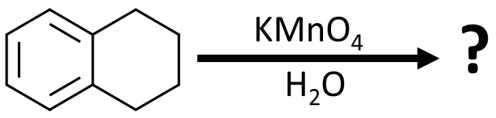
7.1.



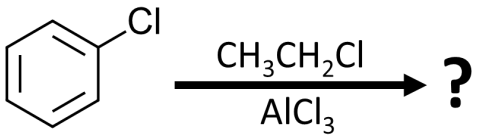
7.2.



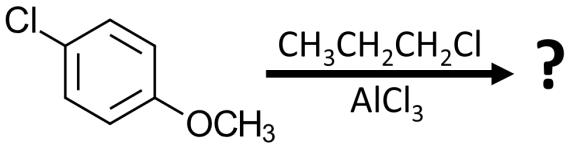
7.3.



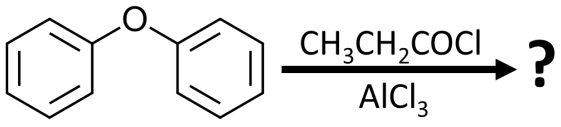
7.4.



7.5.



7.6.



▶ Problem 8 (McMurry, 2008, w/ permission)

Predict the major monoalkylation products you would expect to obtain from reaction of the following substances with chloromethane and $AlCl_3$.

8.1. Bromobenzene
8.2. *m*-Bromophenol
8.3. *p*-Chloroaniline
8.4. 2,4-Dichloronitrobenzene

8.5. 2,4-Dichlorophenol
8.6. Benzoic acid
8.7. *p*-Methylbenzenesulfonic acid
8.8. 2,5-Dibromotoluene

▶ Problem 9 (Carey, 2008, w/ permission)

Write equations showing how you could prepare each of the following from anisole and any necessary organic or inorganic reagents. If an *ortho-para* mixture is formed in any step of your synthesis, assume that you can separate the two isomers.

9.1. *p*-Methoxybenzenesulfonic acid
9.2. 2-Bromo-4-nitroanisole
9.3. 4-Bromo-2-nitroanisole
9.4. *p*-Methoxystyrene

▶ Problem 10 (Carey, 2008, w/ permission)

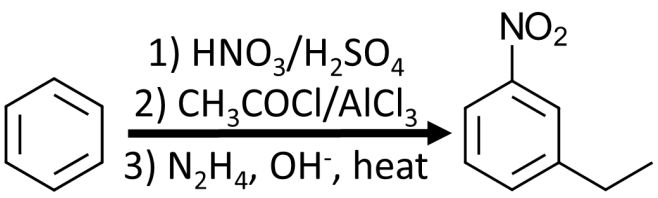
Write equations showing how to prepare each of the following from benzene or toluene and any necessary organic or inorganic reagents. If an *ortho-para* mixture is formed in any step of your synthesis, assume that you can separate the two isomers.

10.1. Isopropylbenzene
10.2. *p*-Isopropylbenzenesulfonic acid
10.3. 2-Bromo-2-phenylpropane
10.4. 4-*Tert*-butyl-2-nitrotoluene
10.5. *m*-Chloroacetophenone
10.6. *p*-Chloroacetophenone
10.7. 3-Bromo-4-methylacetophenone
10.8. 3-Bromo-4-ethyltoluene
10.9. 1-Bromo-3-nitrobenzene
10.10. 1-Bromo-2,4-dinitrobenzene
10.11. 3-Bromo-5-nitrobenzoic acid
10.12. 2-Bromo-4-nitrobenzoic acid
10.13. Diphenylmethane
10.14. 1-Phenyloctane
10.15. 1-Phenyl-1-octene
10.16. 1-Phenyl-1-octyne

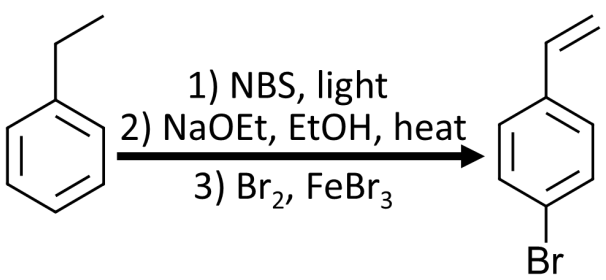
▶ Problem 11 (Solomons *et al.*, 2014, w/ permission)

Both of the following syntheses will fail. Explain what is wrong with each one.

11.1.

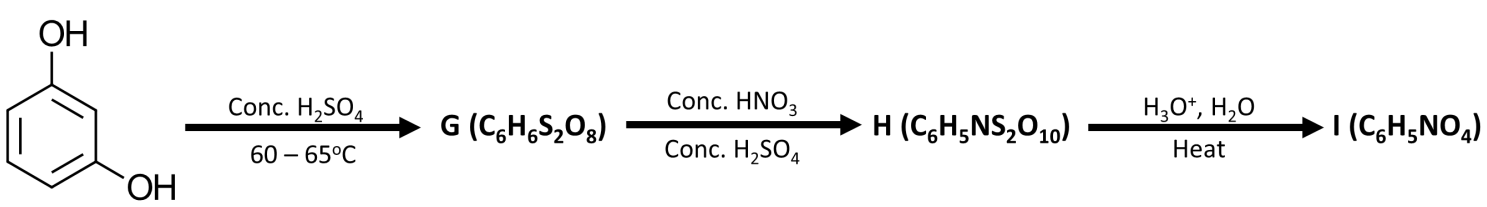


11.2.



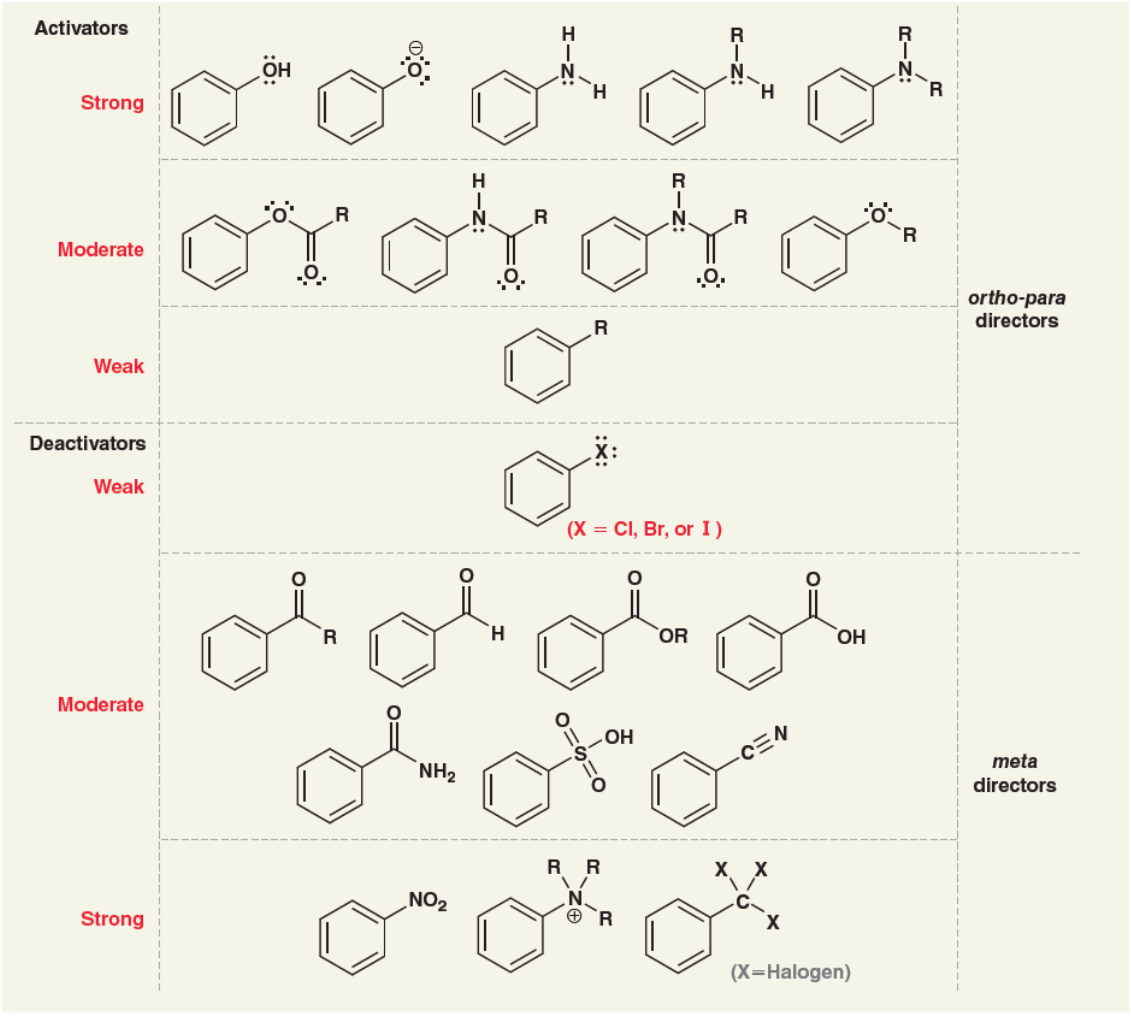
▶ Problem 12 (Solomons *et al.*, 2014, w/ permission)

Propose structures for compounds **G** – **I**.



ADDITIONAL INFORMATION

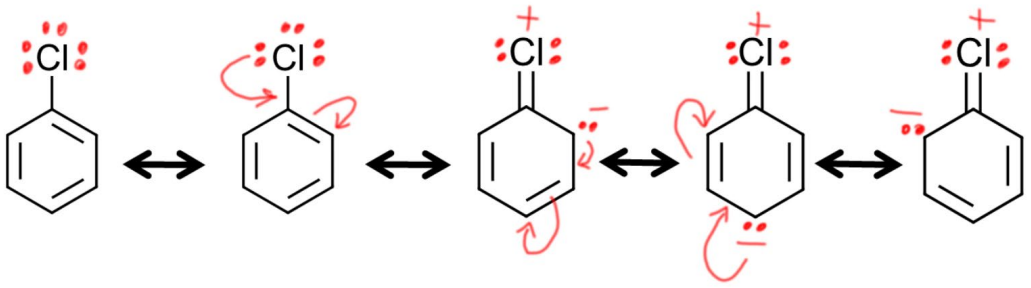
Table 1 A list of activators and deactivators by category.



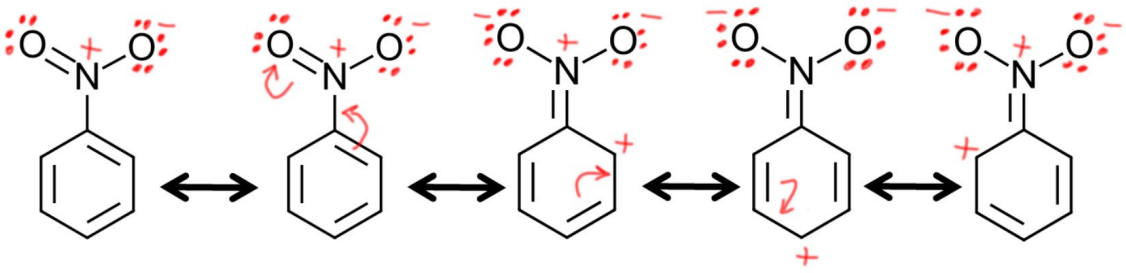
SOLUTIONS

P.1 ➡ *Solution*

1.1: The resonance structures are shown below.

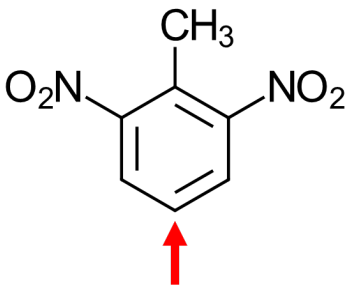


1.2: The resonance structures are shown below.

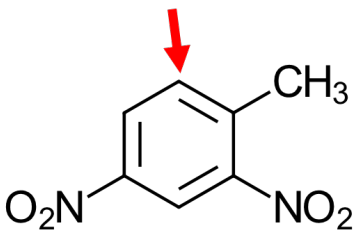


P.2 ➡ *Solution*

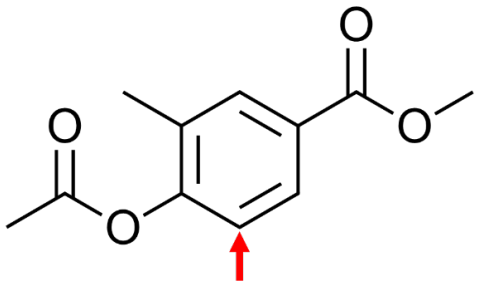
2.1: The methyl group is weakly activating and the nitro groups are strongly activating. The directing effects are controlled by the most strongly activating group. Therefore, in this case the methyl group controls the directing effects. As an activator, the methyl group is an *ortho-para* director. Since the two *ortho* positions are already occupied (by nitro groups), an electrophilic aromatic substitution reaction is likely to occur at the position that is *para* to the methyl group.



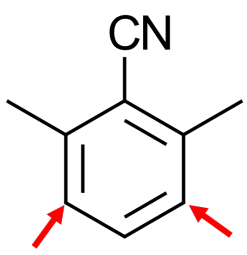
2.2: The methyl group is weakly activating and the nitro groups are strongly activating. The directing effects are controlled by the most strongly activating group. Therefore, in this case the methyl group controls the directing effects. As an activator, the methyl group is an *ortho-para* director. Since the *para* position and one of the *ortho* positions are already occupied (by nitro groups), an electrophilic aromatic substitution reaction is likely to occur at the remaining *ortho* position relatively to the methyl group.



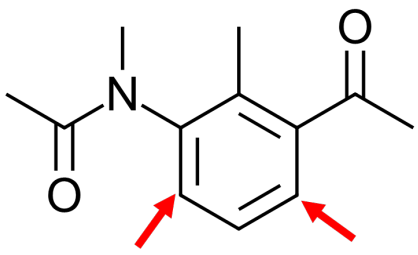
2.3: This aromatic ring has three substituents. The methyl group is weakly activating. The other two groups are both esters, but they differ in the way they are connected to the ring. One group is moderately activating (the oxygen atom connected to the ring) and the other is moderately deactivating (the carbonyl group connected to the ring). The directing effects are controlled by the most strongly activating group. Therefore, in this case the ester group connected to the ring by an oxygen atom controls the directing effects. As an activator, this group is an *ortho-para* director. Since the *para* position and one of the *ortho* positions are already occupied by other substituents, an electrophilic aromatic substitution reaction is most likely to occur at the position that is *ortho* to the moderately activating group.



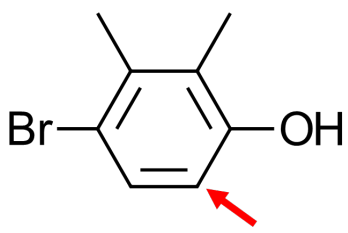
2.4: The methyl groups are weakly activating and the cyano group is moderately deactivating. The directing effects are controlled by the most strongly activating group. Therefore, in this case the methyl groups control the directing effects. Both of the methyl groups are directing to the same two locations (*ortho* and *para* to the methyl groups), as shown below. These two locations are identical because of symmetry.



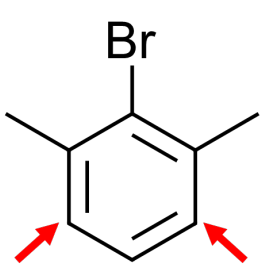
2.5: This aromatic ring has three substituents. The methyl group is weakly activating, the carbonyl group (C=O) is moderately deactivating, and the amide group is moderately activating. The directing effects are controlled by the most strongly activating group. Therefore, in this case the amide group controls the directing effects. As an activator, this group is an *ortho-para* director. Since one of the *ortho* positions is already occupied (by a methyl group), an electrophilic aromatic substitution reaction is likely to occur in the remaining *ortho* position or the *para* position relatively to the amide group.



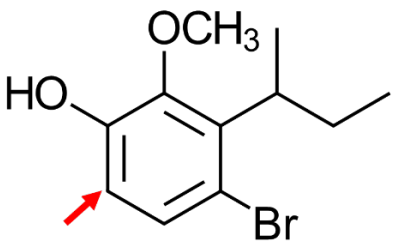
2.6: The aromatic ring has three substituents. A halogen such as bromide is weakly deactivating, a methyl group is weakly activating, and a hydroxyl group is strongly activating. The directing effects are controlled by the most strongly activating group. Therefore, in this case the hydroxyl group controls the directing effects. As an activator, this group is an *ortho-para* director. Since one of the *ortho* positions and the *para* position are already occupied by other substituents, an electrophilic aromatic substitution reaction is likely to occur in the remaining *ortho* position relatively to the hydroxyl group.



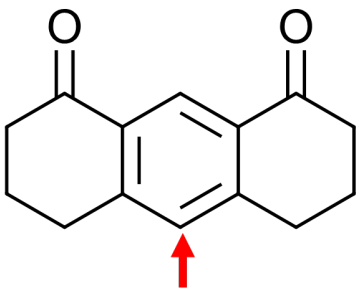
2.7: The methyl groups are weakly activating and the bromo group is weakly deactivating. The directing effects are controlled by the most strongly activating group. Therefore, in this case the methyl groups control the directing effects. Both of the methyl groups are directing to the same two locations, *ortho* and *para* relatively to these substituents, as shown below. These two locations are identical because of symmetry.



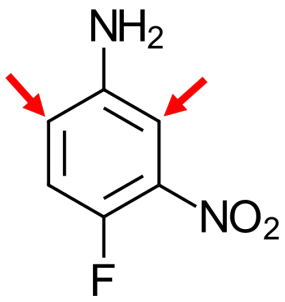
2.8: The directing effects are controlled by the most strongly activating group. Hydroxyl is a strong activator and prevails over the methoxy group, which is a moderate activator. As an activator, the OH group is an *ortho-para* director. Since one of the *ortho* positions and the *para* position are already occupied by other substituents, an electrophilic aromatic substitution reaction is most likely to occur at the remaining *ortho* position relatively to the hydroxyl group.



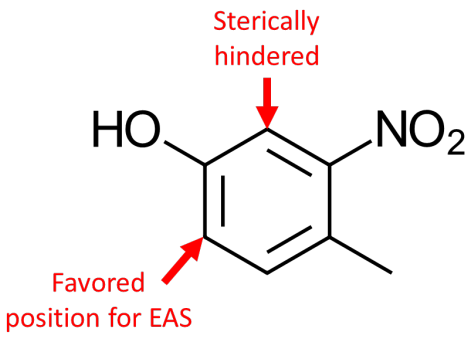
2.9: This aromatic ring has four substituents, two electron-donating alkyl groups and two electron-withdrawing carbonyl groups. The directing effects are controlled by the most strongly activated group. Therefore, in this case the alkyl substituents are directing to the same location, *ortho* relatively to these substituents, as shown below.



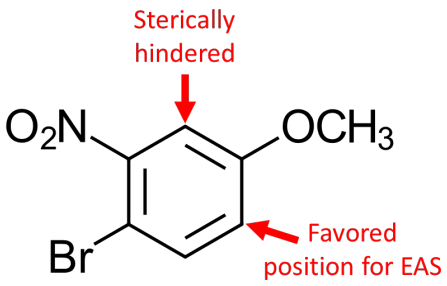
2.10: The aromatic ring has three substituents. A halogen such as fluoride is weakly deactivating, an amine group is strongly activating, and a nitro group is strongly deactivating. The directing effects are controlled by the most strongly activating group. Therefore, in this case the amine group controls the directing effects. As an activator, this group is an *ortho-para* director. Since the *para* position is already occupied by another substituent (a fluoride group), an electrophilic aromatic substitution reaction is likely to occur in the remaining *ortho* positions relatively to the amine group.



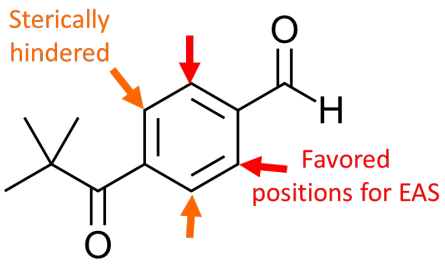
2.11: The directing effects are controlled by the most strongly activating group. In this case, the hydroxyl group (a strong activator) controls the directing effects. As an activator, the OH group is an *ortho-para* director. Since the *para* position is already occupied (by a methyl group), an electrophilic aromatic substitution reaction should occur at one of the *ortho* positions. Among the two *ortho* positions, one of them is sterically hindered and we do not expect the reaction to occur at that location. This leaves us with only one favored site for electrophilic substitution, as shown below.



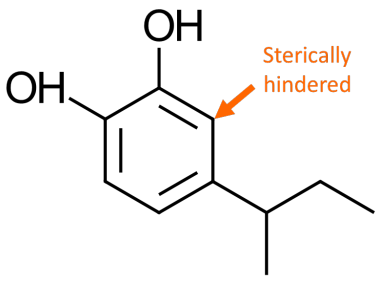
2.12: The directing effects are controlled by the most strongly activating group. In this case, the methoxy group (a moderate activator) controls the directing effects. As an activator, the methoxy group is an *ortho-para* director. Since the *para* position is already occupied (by a bromine atom), an electrophilic substitution reaction should occur at one of the *ortho* positions. Among the two *ortho* positions, one of them is sterically hindered and we do not expect the reaction to occur at that location. This leaves us with only one favored site for electrophilic substitution, as shown below.



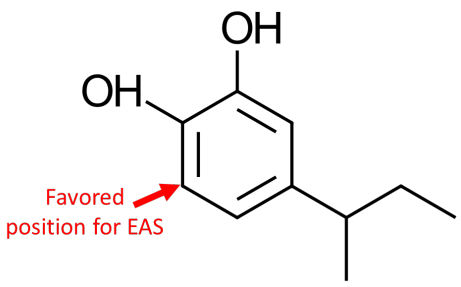
2.13: The directing effects are controlled by the most strongly activating group. However, this aromatic ring lacks an activating substituent. Both substituents are deactivators, and they are competing with each other (as each group directs to the positions that are *meta* to itself). So electronically, the four aromatic positions are equally likely to undergo an electrophilic aromatic substitution reaction. The larger group (left) is more sterically bulky and should block the positions closest to it. The reaction therefore occurs in one of the two positions indicated in red below. The two locations are identical because of symmetry.



2.14: As usual, the directing effects are controlled by the most strongly activating group. Therefore, in this case the hydroxyl groups (strong activators) control the directing effects. However, each OH group directs to different locations (*ortho* and *para* to itself), so all available positions are activated. To differentiate between them, we note that the following position is too sterically hindered for a reaction to occur at this location.



Among the two remaining positions, one is less sterically hindered and should be the optimal site for an electrophilic aromatic substitution reaction.



P.3 ➡ *Solution*

(Trifluoromethyl)benzene is less reactive toward electrophilic substitution than toluene. The electronegativity of the three fluorine atoms causes the trifluoromethyl group to be electron-withdrawing and deactivating toward electrophilic substitution. The electrostatic potential map shows that the aromatic ring of (trifluoromethyl)benzene is more electron-poor, and thus less reactive, than the ring of toluene shown in the problem statement.

P.4 ➡ *Solution*

4.1: Chlorobenzene has a weakly deactivating group, and hence should be less reactive for electrophilic substitution than benzene. *o*-Dichlorobenzene has two such weakly deactivating groups, and hence should be less reactive than chlorobenzene. The correct order, from most reactive to least reactive, is **C** > **A** > **B**.

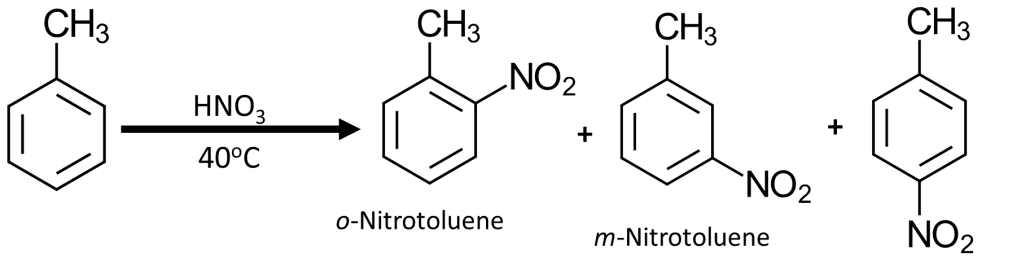
4.2: Nitrobenzene has a strongly deactivating group, and hence should be poorly reactive for electrophilic substitution. In addition to a nitro group, *p*-bromonitrobenzene has a bromine group, which is weakly deactivating and renders the molecule less reactive than nitrobenzene. Phenol contains hydroxyl, a strong activator, and should be more reactive than both preceding molecules. The correct order, from most reactive to least reactive, is **C** > **B** > **A**.

4.3: Fluorobenzene contains fluorine, a weakly deactivating group. Benzaldehyde contains an aldehyde group, which is a moderately deactivating group. *o*-Xylene contains two methyl groups, which are weakly activating. The correct order, from most reactive to least reactive, is **C** > **A** > **B**.

4.4: All three molecules contain a cyano group, so we should distinguish their reactivity on the basis of substituents different from CN. *p*-Methylbenzonitrile contains a methyl substituent, which is a weakly activating group. *p*-Methoxybenzonitrile contains a methoxy substituent, which is a moderately activating group. The correct order, from most reactive to least reactive, is **C** > **B** > **A**.

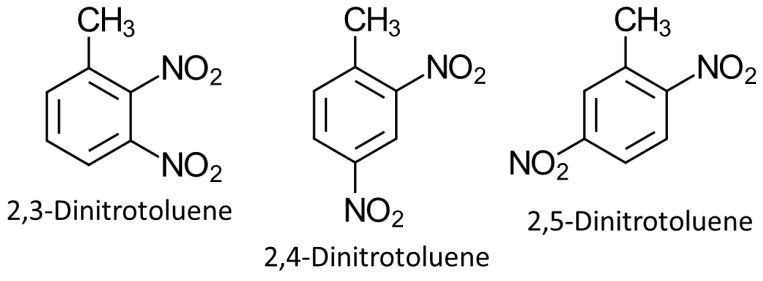
P.5 ➡ *Solution*

5.1: Methyl is an *ortho-para*-directing substituent, so mononitration of toluene yields mainly *o*-nitrotoluene and *p*-nitrotoluene on mononitration; some *m*-nitrotoluene may also be formed. Thus, there are three possible products of mononitration of toluene.

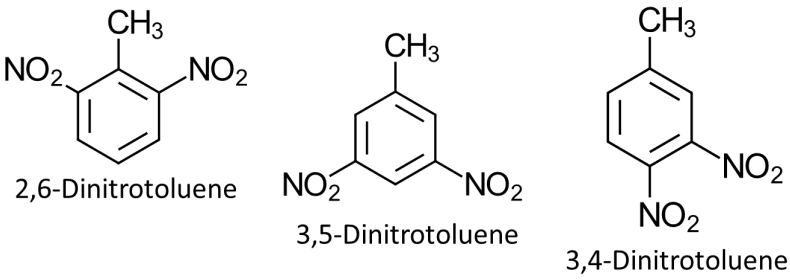


o-Nitrotoluene *m*-Nitrotoluene *p*-Nitrotoluene

5.2: There are six isomeric dinitrotoluenes. The least likely product is 3,5-dinitrotoluene because neither of its nitro groups is *ortho* or *para* to the methyl group.

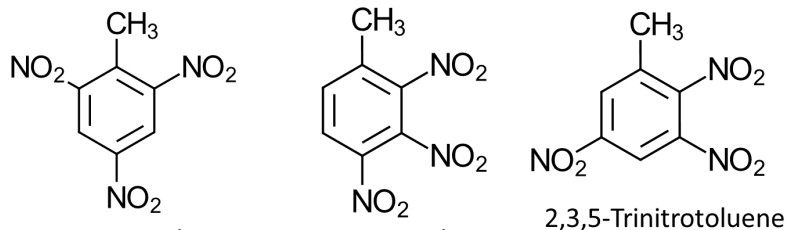


2,3-Dinitrotoluene 2,4-Dinitrotoluene 2,5-Dinitrotoluene

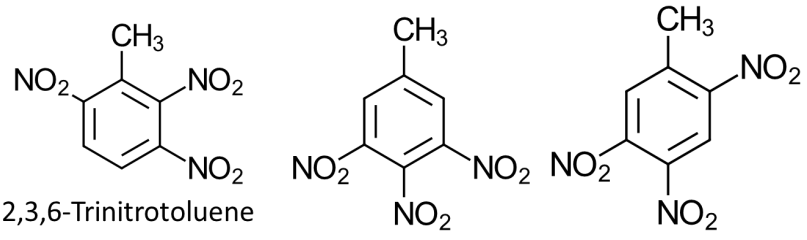


2,6-Dinitrotoluene 3,5-Dinitrotoluene 3,4-Dinitrotoluene

5.3: There are six isomeric trinitrotoluenes.



2,4,6-Trinitrotoluene 2,3,4-Trinitrotoluene 2,3,5-Trinitrotoluene

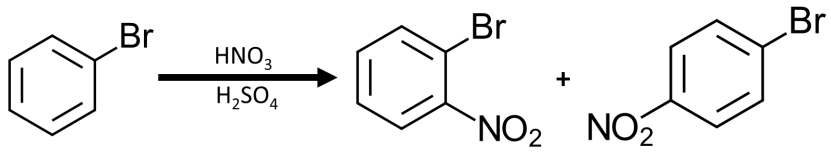


2,3,6-Trinitrotoluene 3,4,5-Trinitrotoluene 2,4,5-Trinitrotoluene

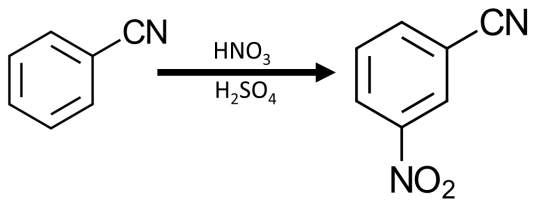
5.4: The most likely major product of trinitration of toluene is 2,4,6-trinitrotoluene, for all the *ortho* and *para* positions activated by the methyl group are occupied by nitro groups. Thus, TNT is 2,4,6-trinitrotoluene.

P.6 ➡ *Solution*

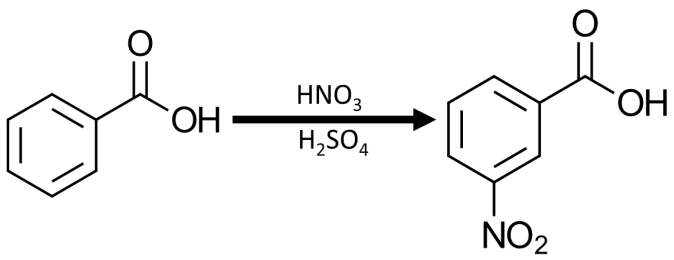
6.1: Bromine, a halogen, is a weak deactivator, but nonetheless acts as an *ortho-para* director. Thus, nitration of bromobenzene yields *o*-bromonitrobenzene and *p*-bromonitrobenzene.



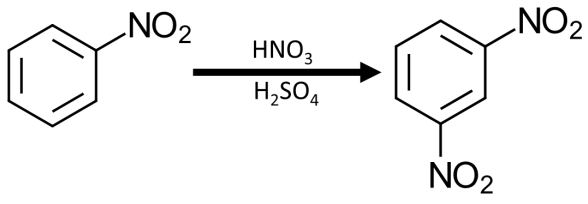
6.2: A cyano group is moderately deactivating and acts as a *meta* director. Thus, nitration of benzonitrile yields *m*-nitrobenzonitrile.



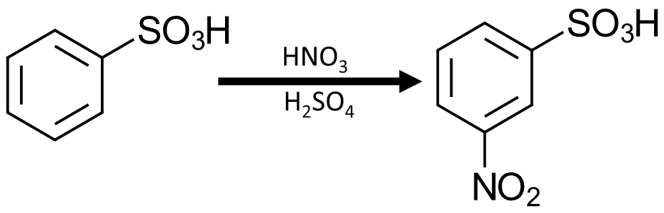
6.3: A carboxylic acid group is moderately deactivating and acts as a *meta* director. Thus, nitration of benzoic acid yields *m*-nitrobenzoic acid.



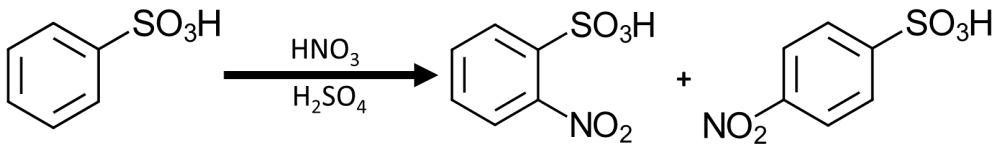
6.4: A nitro group is strongly deactivating and acts as a *meta* director. Thus, nitration of nitrobenzene yields *m*-dinitrobenzene.



6.5: A sulfo group is moderately deactivating and acts as a *meta* director. Thus, nitration of benzenesulfonic acid yields *m*-nitrobenzenesulfonic acid.

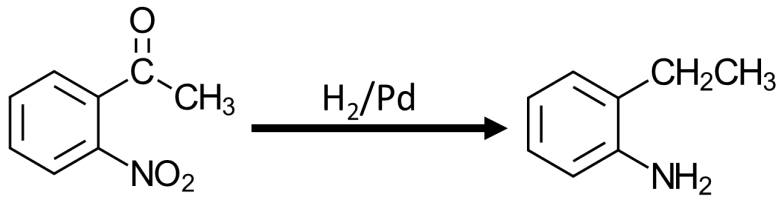


6.6: A methoxy group is a moderately activating group and acts as an *ortho-para* director. Thus, nitration of methoxybenzene yields *o*-methoxynitrobenzene and *p*-methoxynitrobenzene.

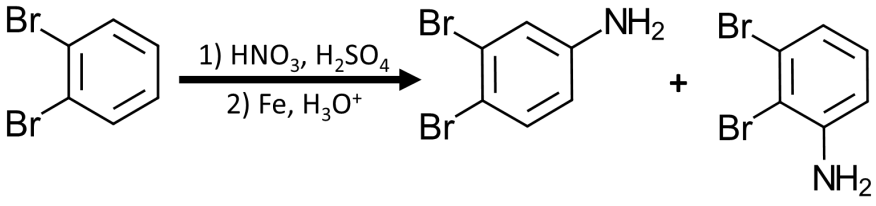


P.7 ➡ *Solution*

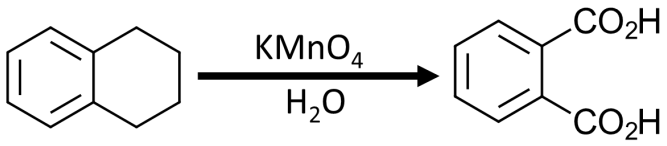
7.1: Catalytic hydrogenation reduces the aromatic ketone and the nitro group, ultimately yielding *o*-ethylaniline.



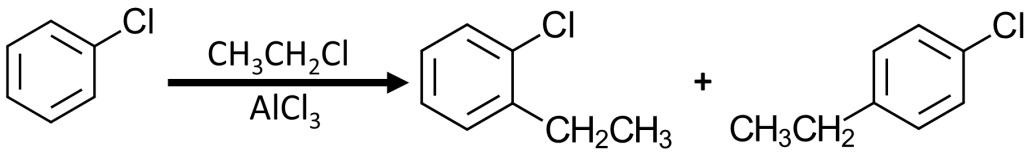
7.2: Step 1 nitrates the aromatic ring, while reduction with Fe reduces the nitro groups to amines.



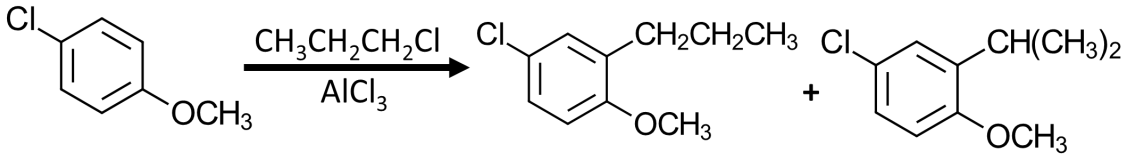
7.3: Aqueous $KMnO_4$ oxidizes alkyl side chains to benzoic acids. The product, in this case, is phthalic acid.



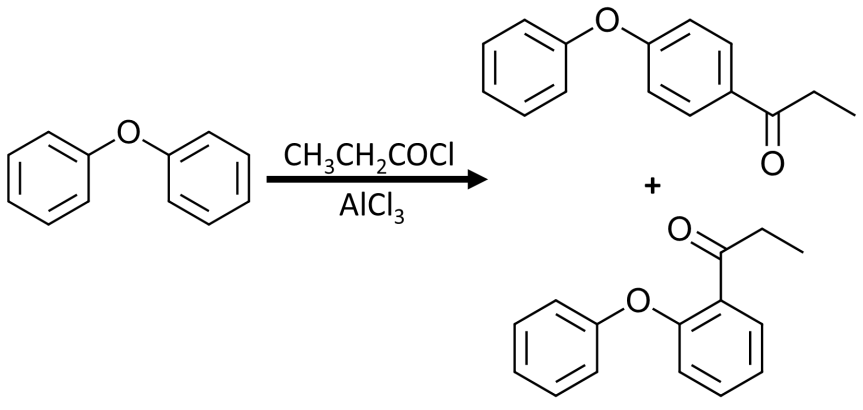
7.4: This is a Friedel-Crafts alkylation reaction. Chlorine, a halogen, is an *ortho-para* director. The products of the reaction are shown below.



7.5: As before, this is a Friedel-Crafts alkylation reaction. The methoxy group directs substitution because it is a more powerful activating group. Rearranged and unrearranged products are formed.

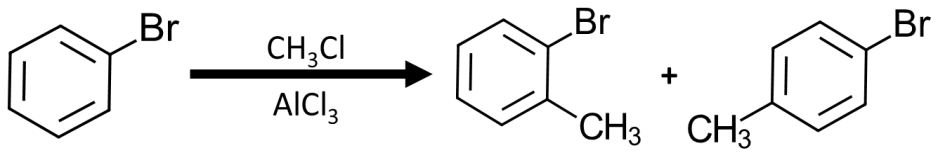


7.6: Phenoxybenzene is acylated to yield *ortho* and *para* products, as shown.

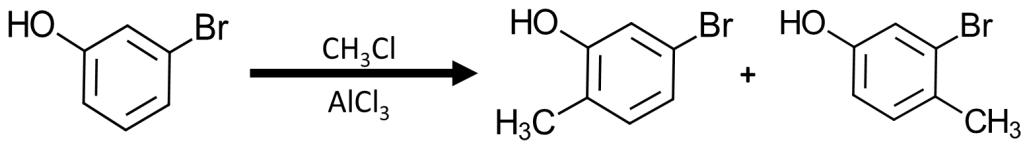


P.8 ➡ *Solution*

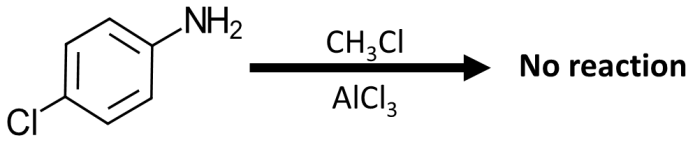
8.1: Bromine is a weakly deactivating group, but nonetheless acts as an *ortho-para* director. Accordingly, monoalkylation of bromobenzene should yield *o*-bromotoluene and *p*-bromotoluene.



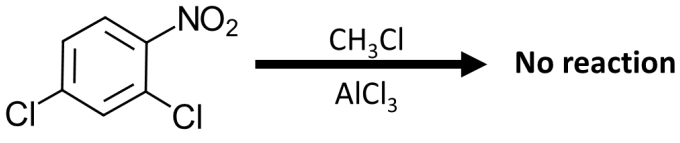
8.2: In addition to bromine, *m*-bromophenol contains hydroxyl, which is also an *ortho-para* director. Monoalkylation of *m*-bromophenol should yield 5-bromo-2-methylphenol and 3-bromo-4-methylphenol.



8.3: $AlCl_3$ combines with $-NH_2$ to form a complex that deactivates the ring toward Friedel-Crafts alkylation.

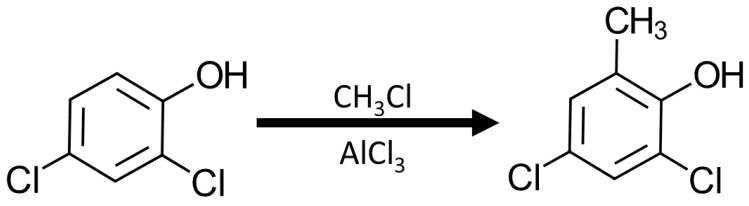


8.4: There is no reaction because the ring is deactivated.

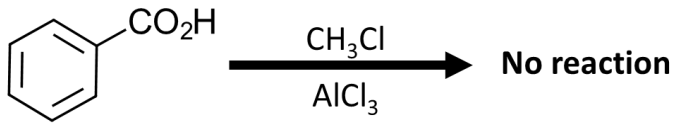


8.5: In this case, alkylation is directed by the hydroxyl group, which is a strongly activating director. Since one of the *ortho* positions and the *para*

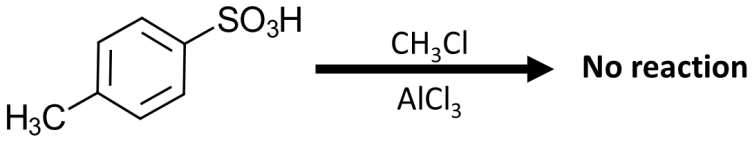
position are already occupied, methylation should occur in the remaining *ortho* position, yielding 2,4-dichloro-6-methylphenol.



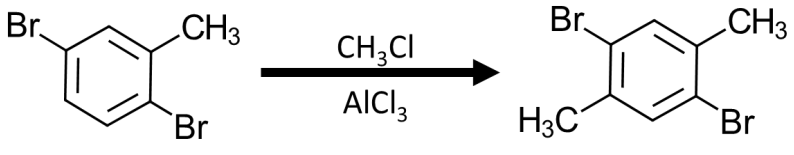
8.6: There is no reaction because the ring is deactivated.



8.7: There is no reaction because the ring is deactivated.

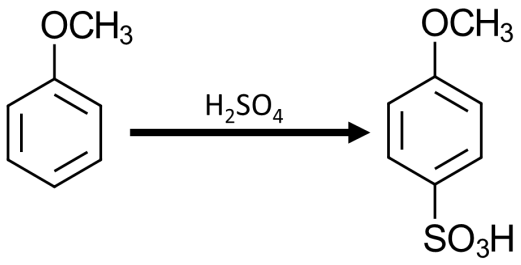


8.8: In this case, alkylation is directed by the methyl group, which is weakly activating. One *ortho* position and the *para* position are available, but, in view of the fact that substitution rarely occurs between two substituents because of steric hindrance, only the *para* position should be substituted. The product is 1,4-dibromo-2,5-dimethylbenzene.

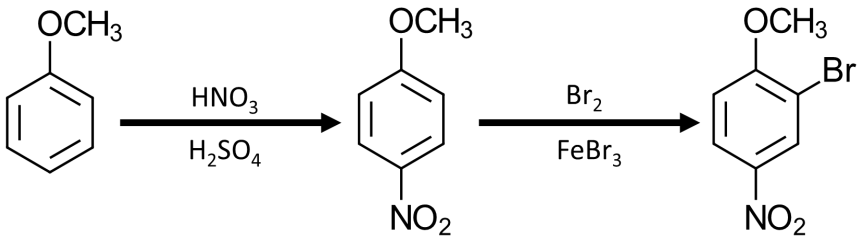


P.9 ➡ *Solution*

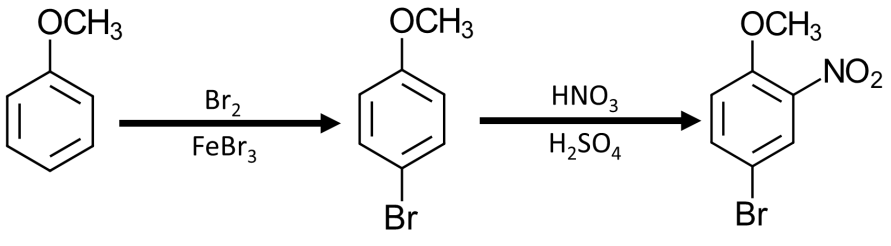
9.1: Methoxy is an *ortho-para* directing substituent. All that is required to prepare *p*-methoxybenzenesufonic acid is to sulfonate anisole.



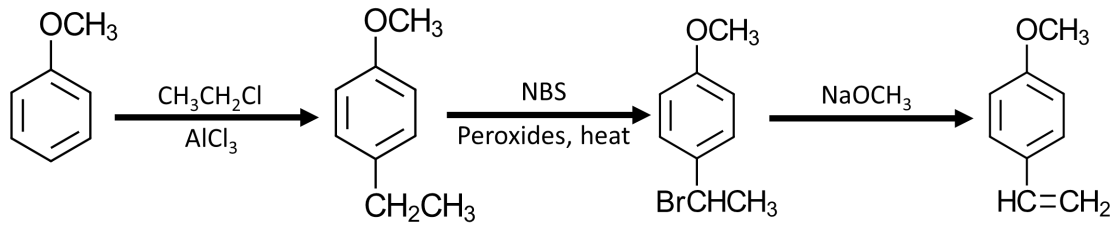
9.2: In reactions involving disubstitution of anisole, a good strategy is to introduce the *para* substituent first. The methoxy group is *ortho-para* directing, but *para* substitution predominates.



9.3: Reversing the order of steps in the previous problem should yield 4-bromo-2-nitroanisole.

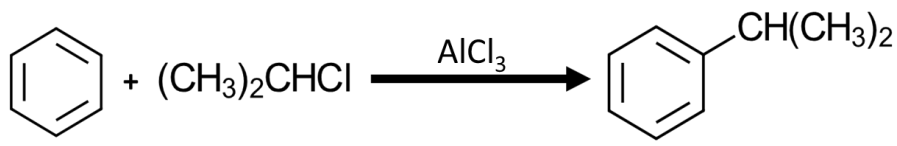


9.4: Direct introduction of a vinyl substituent onto an aromatic ring is not a feasible reaction. *p*-Methoxystyrene must be prepared in an indirect way by adding an ethyl side chain and then taking advantage of the reactivity of the benzylic position by bromination (e.g., with *N*-bromosuccinimide) and dehydrohalogenation.

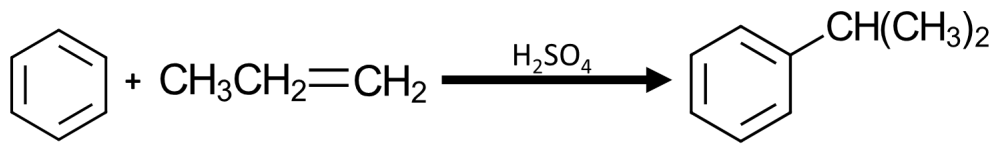


P.10 ➡ *Solution*

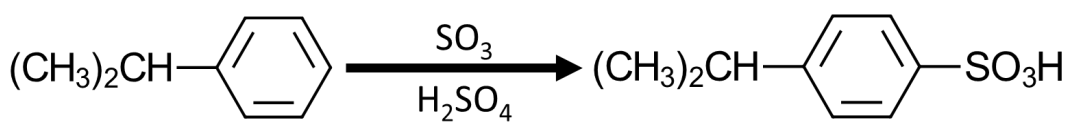
10.1: Isopropylbenzene may be prepared by a Friedel-Crafts alkylation of benzene with isopropyl chloride (or bromide, or iodide).



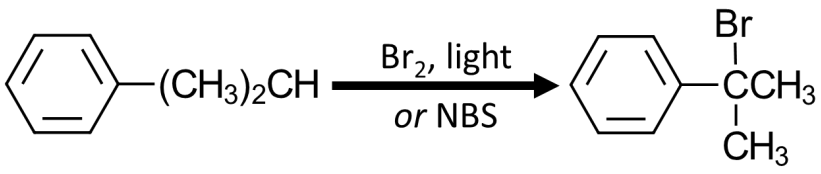
It would not be appropriate to use propyl chloride and trust that a rearrangement would lead to isopropylbenzene, because a mixture of propylbenzene and isopropylbenzene would be obtained. Isopropylbenzene may also be prepared by alkylation of benzene with propene in the presence of sulfuric acid.



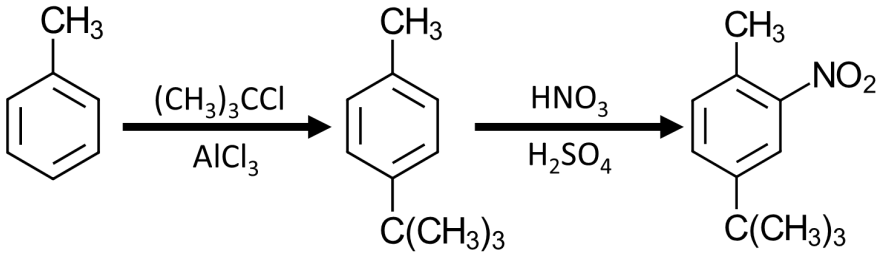
10.2: Since the isopropyl and sulfonic acid groups are *para* to each other, the first group introduced on the ring must be the *ortho-para* director, that is, the isopropyl group. We may therefore use the product of Problem 10.1, isopropylbenzene, in this synthesis. Since an isopropyl group is a fairly bulky *ortho-para* director, sulfonation of isopropylbenzene should yield *p*-isopropylbenzenesulfonic acid as the main product.



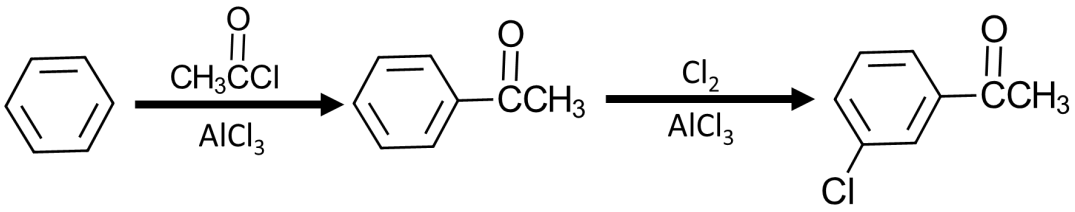
10.3: We begin by preparing isopropylbenzene as we did in Problem 10.1. This is followed by free-radical bromination of isopropylbenzene. Free-radical halogenation of isopropylbenzene occurs with high regioselectivity at the benzylic position. *N*-Bromosuccinimide (NBS) is a good reagent to use for benzylic bromination reactions.



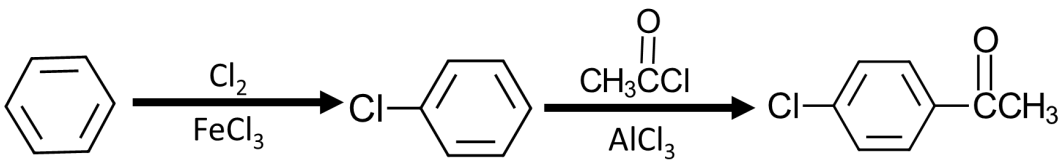
10.4: Toluene is an obvious starting material for the preparation of 4-*tert*-butyl-2-nitrotoluene. Two possibilities, both involving nitration and alkylation of toluene, present themselves; the problem to be addressed is in what order to carry out the two steps. Introduction of the nitro group as the first step is an unsatisfactory approach since Friedel-Crafts reactions cannot be carried out on nitro-substituted aromatic compounds. Friedel-Crafts alkylation must precede nitration.



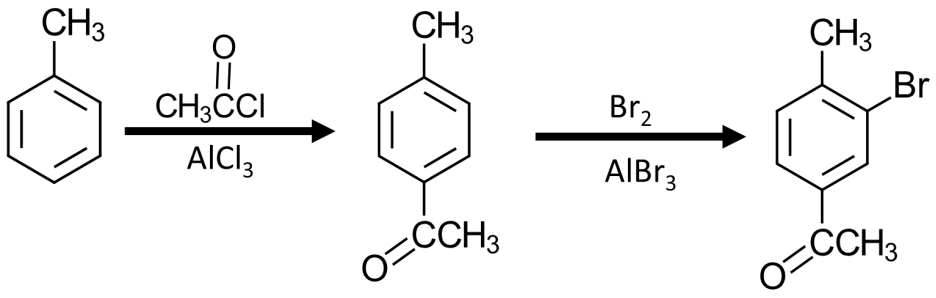
10.5: Two electrophilic substitution reactions need to be performed: chlorination and Friedel-Crafts acylation. The order in which the reactions are carried out is important; chlorine is an *ortho-para* director, and the acetyl group is a *meta* director. Since the groups are *meta* in the desired compound, introduce the acetyl group first.



10.6: To synthesize *p*-chloroacetophenone, we employ the same reactions used in the previous problem, but the order of steps is reversed. Friedel-Crafts reactions can be carried out on halobenzenes but not on arenes that are more strongly deactivated.

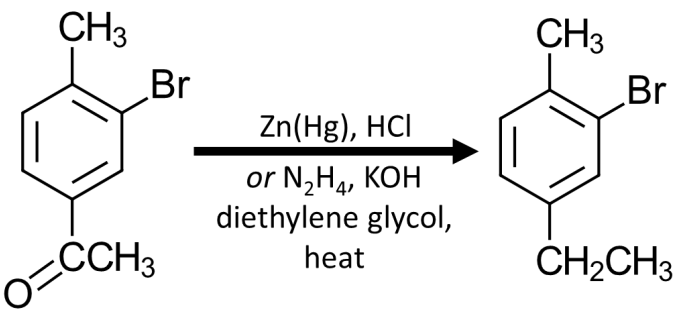


10.7: Here again the problem involves two successive electrophilic aromatic substitution reactions, this time using toluene as the initial substrate. The proper sequence is Friedel-Crafts acylation first, followed by bromination of the ring.

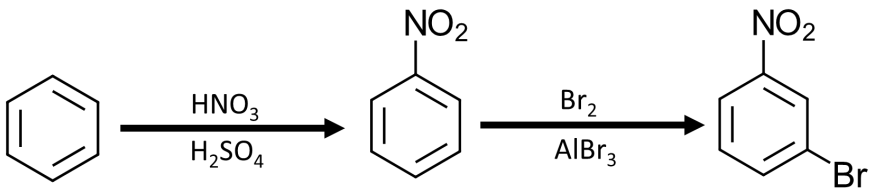


Carey notes that, if the sequence of steps had been reversed, with halogenation preceding acylation, the first intermediate would be *o*-bromotoluene. Friedel-Crafts acylation of this product would give a complex mixture of products because both groups are *ortho-para* directing. On the other hand, the orienting effects of the two groups in *p*-methylacetophenone reinforce each other, so that its bromination is highly regioselective and in the desired direction.

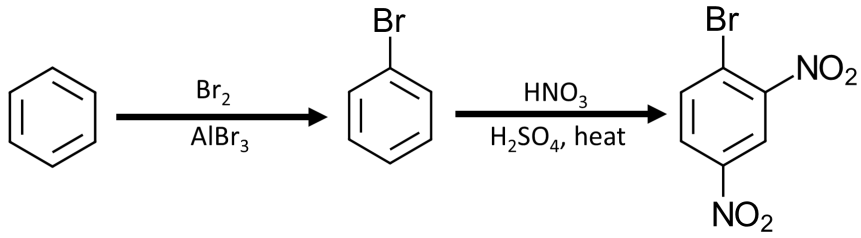
10.8: We proceed as we did in the previous problem to produce 3-bromo-4-methylacetophenone. Then, we reduce the ketone group by dint of a Clemmensen or Wolff-Kishner procedure, yielding 2-bromo-4-ethyltoluene.



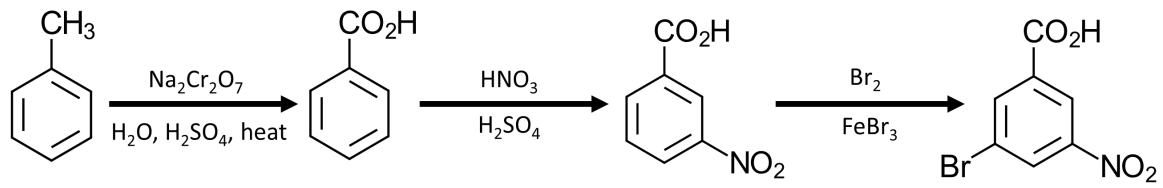
10.9: This is a relatively straightforward synthetic problem. Bromine is an *ortho-para* directing substituent, while nitro is *meta* directing. Nitrate first, then brominate to give 1-bromo-3-nitrobenzene.



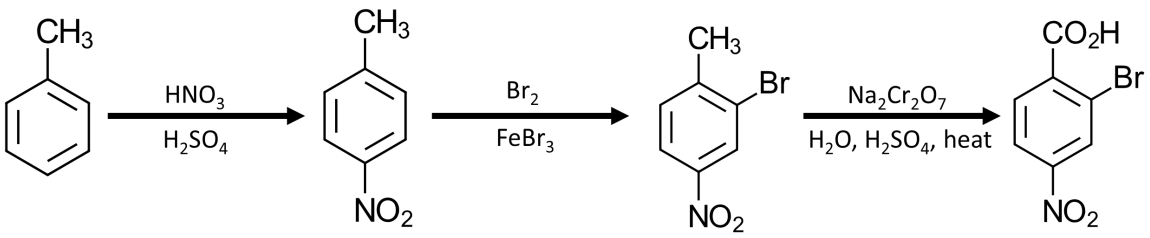
10.10: Take advantage of the *ortho-para* directing properties of bromine to prepare 1-bromo-2,4-dinitrobenzene. Brominate first, and then nitrate under conditions that lead to disubstitution. The nitro groups are introduced at positions *ortho* and *para* to the bromine group.



10.11: Carey notes that, although bromo and nitro substituents are readily introduced by electrophilic aromatic substitution, the only methods we have available so far to prepare carboxylic acids is oxidation of alkyl side chains. The appropriate starting material, then, is toluene, which is oxidized to have its methyl group converted to a carboxylic acid group. Nitrate next, and brominate lastly. Nitro and carboxyl are both *meta*-directing groups, so that the bromination in the last step occurs with the proper regioselectivity. If bromination is performed prior to nitration, the bromine substituent will direct an incoming electrophile to positions *ortho* and *para* to itself, giving the wrong orientation of substituents in the product.

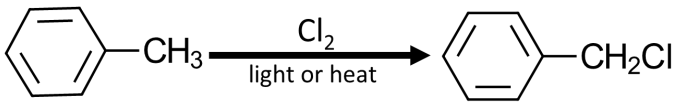


10.12: Again toluene is a suitable starting material, with its methyl group serving as the source of the carboxyl substituent. The orientation of the substituents in the final product requires that the methyl group (an *ortho-para* director) be retained until the final step. As we did in the previous problem, nitration must precede bromination in order to prevent the formation of an undesired mixture of isomers.

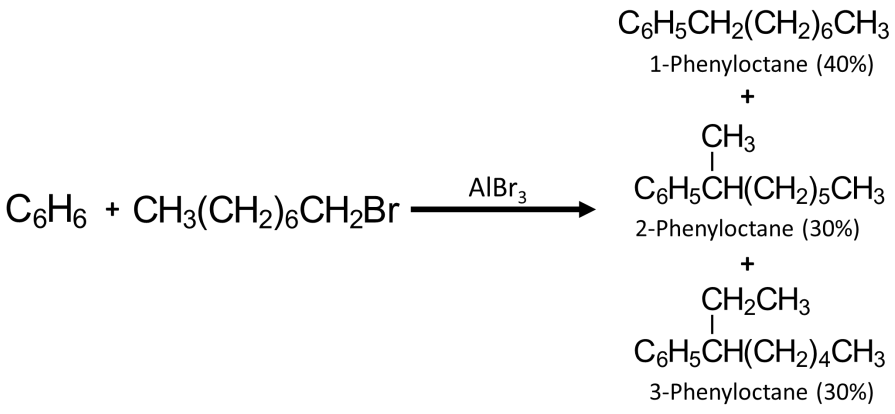


10.13: Friedel-Crafts alkylation of benzene with benzyl chloride (or benzyl bromide) is a satisfactory route to diphenylmethane.

Benzyl chloride is prepared by free-radical chlorination of toluene.

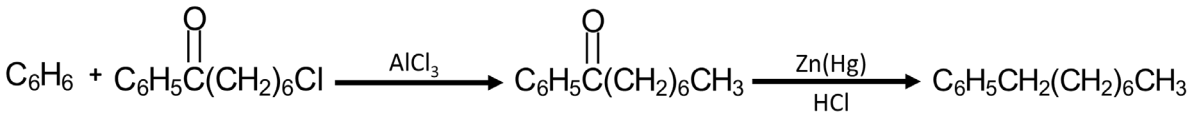


10.14: 1-Phenyloctane cannot be prepared efficiently by direct alkylation of benzene, because of the probability that rearrangement will occur. Indeed, Friedel-Crafts alkylation of benzene with 1-bromooctane yields a mixture of 1-phenyloctane, 2-phenyloctane, and 3-phenyloctane.

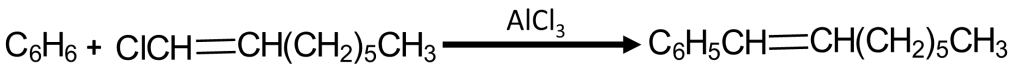


A method that permits the synthesis of 1-phenyloctane free of isomeric compounds is acylation with octanoyl chloride followed by reduction. Instead of reducing the ketone with a Clemmensen procedure as indicated below, a

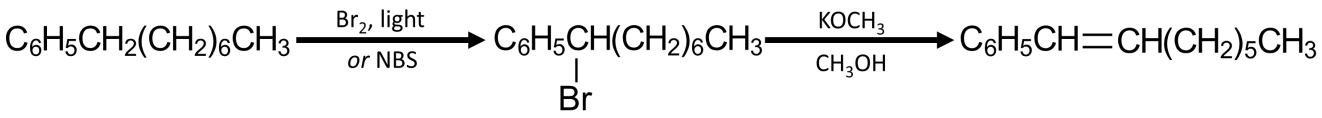
Wolff-Kishner process (hydrazine, potassium hydroxide, diethylene glycol) may be used.



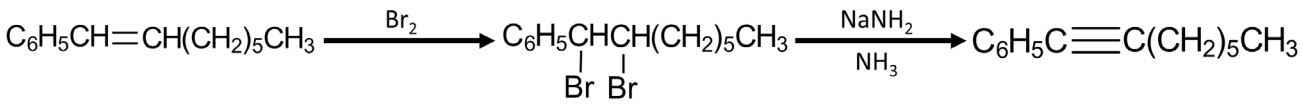
10.15: Direct alkenylation of benzene under Friedel-Crafts reaction conditions does not take place, because this kind of reaction only works with alkyl halides, not 1-haloalkenes. That is, 1-phenyl-1-octene cannot be prepared by the following reaction.



Having already prepared 1-phenyloctane in the previous problem, however, we can functionalize the benzylic position by bromination and then carry out a dehydrohalogenation to obtain the target compound.

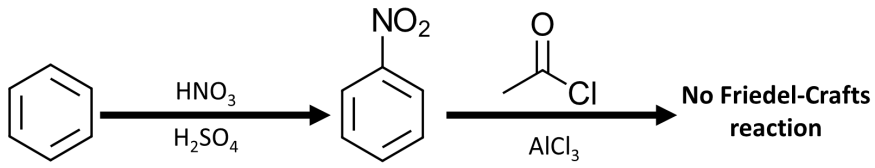


10.16: 1-Phenyl-1-octyne cannot be prepared in one step with benzene because 1-haloalkynes are unsuitable reactants for a Friedel-Crafts process. However, alkynes may be produced from the corresponding alkene by bromination followed by double elimination with sodium amine. Thus, we may produce 1-phenyl-1-octene as we did in the previous problem, then synthesize the desired molecule using the pathway just described.

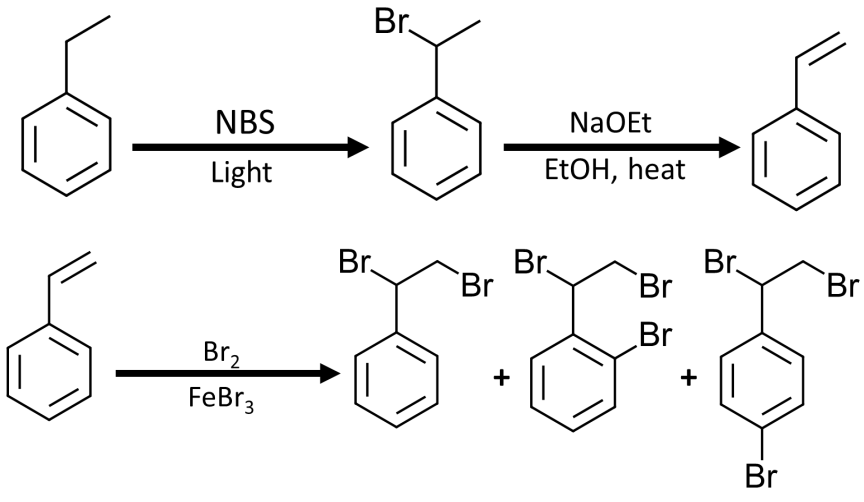


P.11 ➡ *Solution*

11.1: Step 2 will fail because a Friedel-Crafts alkylation will not take place on a ring that bears a nitro group (or any *meta* director, for that matter).

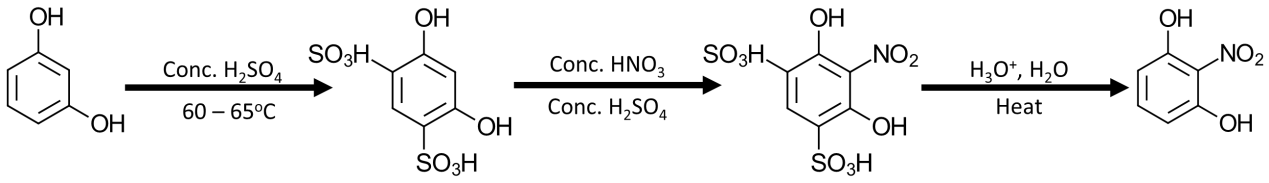


11.2: The last step will fail because the last step will likely brominate the double bond created in step 2 before it brominates the aromatic ring.



P.12 ➡ *Solution*

Reaction of the initial aromatic diol with concentrated sulfuric acid should add two sulfonic acid groups to the ring, one in the less hindered *ortho* position and one in the *para* position relatively to the hydroxyl groups, yielding compound G. Reaction of compound G with HNO_3/H_2SO_4 should nitrate the remaining *ortho* position relatively to the hydroxyl groups, yielding compound H. Lastly, removal of sulfo groups in an acidic medium with heat yields compound I.



REFERENCES

- CAREY, F. (2008). *Organic Chemistry*. 7th edition. New York: McGraw-Hill.
- KLEIN, D. (2017). *Organic Chemistry*. 3rd edition. Hoboken: John Wiley and Sons.
- MCMURRY, J. (2008). *Organic Chemistry*. 7th edition. Belmont: Thomson.
- SOLOMONS, G., FRYHLE, C. and SNYDER, S. (2014). *Organic Chemistry*. 11th edition. Hoboken: John Wiley and Sons.

Got any questions related to this quiz? We can help!
Send a message to contact@montogue.com and we'll
answer your question as soon as possible.