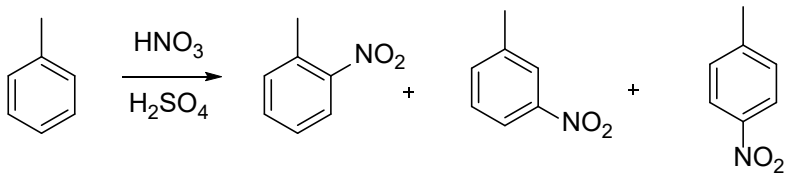
THE VIRTUAL ARYL NITRATION AND ACYLATION

- Benzene Nitration
  - Methyl-benzene
  - Benzaldehyde
- Friedel-Crafts
  - Methyl-benzene
  - Benzaldehyde
  - Acetyl chloride

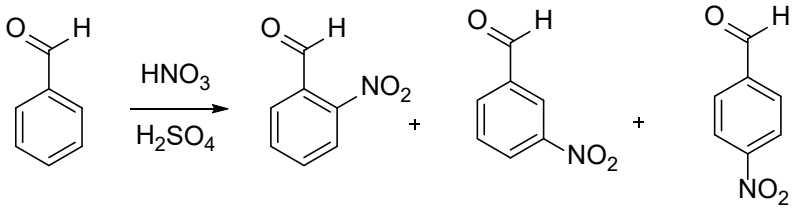
In this virtual experiment, you will explore two electrophilic aromatic substitution (EAS) reactions (Nitration and Friedel-Crafts Acylation), using two different substrates: toluene and benzaldehyde. You will also explore variables that affect reaction rates, and compare the effects of the methyl and aldehyde substituents on product distribution (ortho/para vs. meta), described as the "directing effect," and their effects on reaction rates.

Introduction

The rate of an electrophilic substitution reaction on a substituted benzene ring can either be faster or slower than that of benzene, depending upon the nature of the inductive and resonance effects of the attached group. In addition, the attached group will preferentially direct an incoming substituent primarily ***ortho/para*** or ***meta***, depending on the nature of the attached group. Review the appropriate chapters from your textbook to ensure that you understand the reasons for the activating/deactivating, and directing effects of various groups, including the resonance structures of the intermediates formed during the course of the reaction.

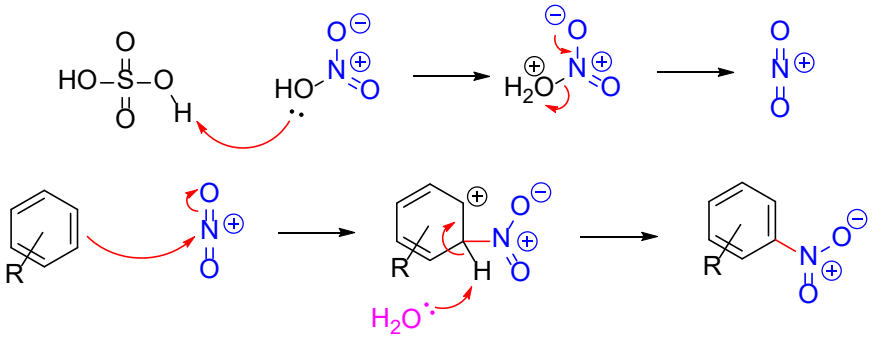


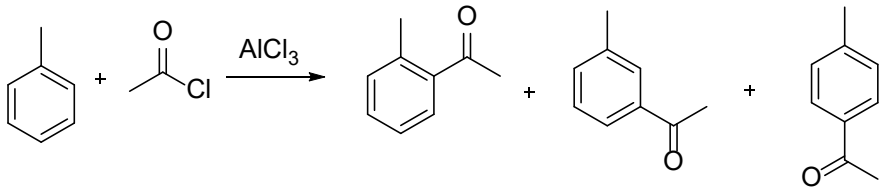
Reaction #1:



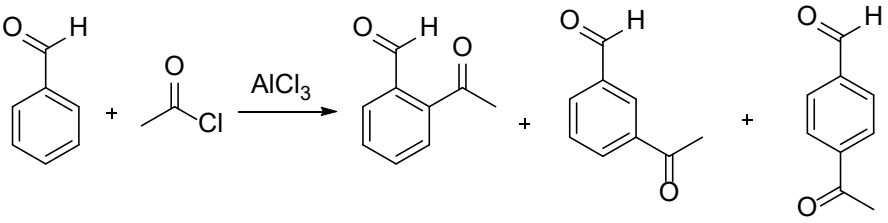
Reaction #2:

The nitration mechanism involves protonation of nitric acid followed by the loss of water to form a nitronium ion, which acts as an electrophile for the nucleophilic double bond of the arene. This momentarily breaks the aromaticity of arene, but water readily removes the acidic proton to re-establish aromaticity.



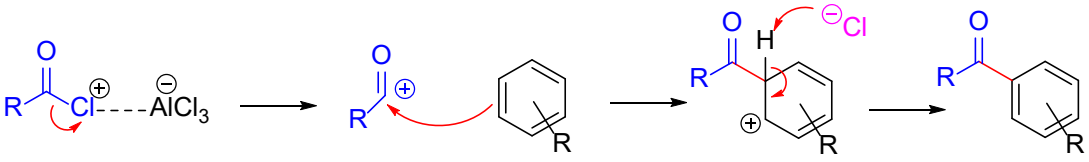


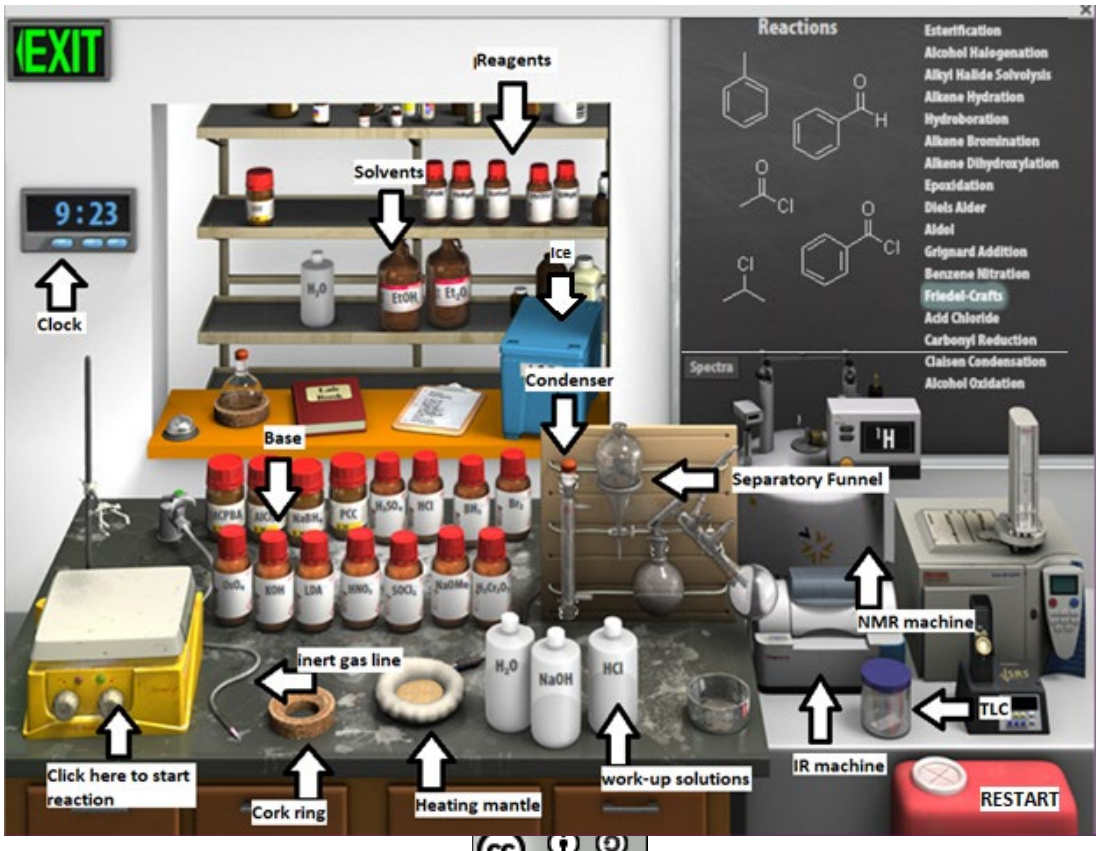
Reaction #3:



Reaction #4:

The Friedel-Crafts acylation is sensitive to substrate reactivity. Benzene or "activated" aromatic substrates (those with electron-donating groups on them) can be acylated, but Friedel-Crafts reactions fail on deactivated substrates. The mechanism involves coordination of the acyl chloride to $AlCl_3$, a Lewis acid, followed by loss of the chloride to form an acylium ion, which acts as an electrophile for the nucleophilic double bond of the arene. This momentarily breaks the aromaticity of arene, but a chloride ion readily removes the acidic proton to re-establish aromaticity.





Procedure

Reactions 1 & 2: Nitration (using two different substrates: **Methylbenzene** and **Benzaldehyde**)

Using the BeyondLabz platform, go to the Virtual ChemLab – Organic Synthesis. From the Stockroom list, click on **Benzene Nitration** to load the reaction-specific reagents onto the stockroom shelves. Click on a substrate, and click on ether (Et_2O) from the Solvents list at the top of the Stockroom list. Confirm that both have been added to the round bottom flask, by going to the Live Data tab (or hover over the flask to see the contents drawn on the chalkboard). Double-click on the flask to clamp it above the stir plate. Add an ice bath and inert gas line before adding a nitric/sulfuric acid mixture (bottle is labelled HNO_3). Use the virtual Lab Book to record the time (from the clock below the exit sign) and turn on the stir plate to start the reaction. You may fast forward in time by clicking on the buttons attached to the clock. Periodically check the progress of your reaction by TLC and try to stop the reaction before multiple nitrations occur. If multiple nitrations occur, you will have to restart by clicking on the chemical waste bin on the bottom left corner.

After the reaction has been completed, double click on the separatory funnel and add NaOH to work up the reaction. Drag the organic layer (top or bottom layer?) to the cork ring to evaporate the solvent (rotatory evaporator), leaving you with just the product(s) in the flask. Analyze by ^1H NMR and IR (by clicking on the NMR or FTIR spectrometer and dragging it to the round bottom flask), and save the spectra to your Lab Book.

Varying Reaction Conditions (Nitration of Methylbenzene)

Let's explore the effects of **concentration** and **temperature** on reaction rate! For each trial below, advance the reaction time in 1-hour increments, and monitor the progress of the reaction by viewing the Flask Contents in the Live Data tab. Record your observations in your Lab Book. Note how quickly the nitration reaction takes place, and how quickly a second nitration reaction occurs (to give dinitromethylbenzene).

- **Rate Trial 1:** run the experiment as described above (dilute, 0 °C)
- **Rate Trial 2:** repeat the experiment, but without adding any solvent, aka "neat" (concentrated, 0 °C)
- **Rate Trial 3:** repeat the experiment, but without solvent or ice bath (concentrated, room temp.)
- **Rate Trial 4:** repeat the experiment with solvent, but without the ice bath (dilute, room temp.)

<u>Reactions 3 & 4: Friedel-Crafts Acylation</u> (using two different substrates: **Methylbenzene** and **Benzaldehyde**)

From the Stockroom list, click on **Friedel-Crafts** to load the reaction-specific reagents onto the stockroom shelves. Click on a substrate and the desired acid chloride (acetyl chloride), and click on ether (Et_2O) from the Solvents list at the top of the Stockroom list. Confirm that all three have been added to the round bottom flask, by going to the Live Data tab (or hover over the flask to see the contents drawn on the chalkboard). Double-click on the flask to clamp it above the stir plate. Click and drag each required solvent and reagent to the round bottom flask before moving the flask to the stir plate. Add an inert gas line before adding $AlCl_3$. Record the time (from the clock below the exit sign) and turn on the stir plate to start the reaction. You may fast forward in time by clicking on the buttons attached to the clock. You may periodically check the progress of your reaction by TLC (Recall: not every Friedel-Crafts reaction is expected to be successful!).

After the reaction has been completed, double click on the separatory funnel and add NaOH to work up the reaction. Drag the organic layer (top or bottom layer?) to the cork ring to evaporate the solvent (rotatory evaporator), leaving you with just the product(s) in the flask. Analyze by ^{1}H NMR and IR (by clicking on the NMR or FTIR spectrometer and dragging it to the round bottom flask), and save the spectra to your Lab Book.

Results

- Attach the ^{1}H NMR and IR spectra of the compounds you virtually synthesized. Label all relevant peaks in the IR, and match the NMR peaks to labeled protons on a drawing of each product. **Show your work!**
- Some reactions give a mixture of products, and in those cases, both products are present in the NMR spectrum. To analyze these spectra, first draw both products and identify all unique H's with distinct labels for the two products (e.g., use 1/2/3 labels for one product and a/b/c for the other). Next, determine the expected integration and multiplicity of each of these unique H's. Finally, use these labels to identify the peaks for each of these compounds in the ^{1}H NMR spectrum. Try to estimate the ratio of the two products (are they formed in roughly equimolar amounts, or is one major and the other minor?).

Discussion

1. For some reactions, an acidic aqueous workup is used, and in other cases a basic workup is used. What factors would you consider when selecting a suitable workup? Why was aq. NaOH required in the reaction workups for the electrophilic aromatic substitution procedures in this virtual lab?
2. Consider the results of the various nitration reaction conditions. Which was the fastest reaction, and which was the slowest? Discuss the effects of concentration and temperature on reaction rates.
3. Was there a difference in the rate of nitration for the two substrates? Were both Friedel-Crafts acylation reactions successful? Explain the observed differences in substrate reactivity.
4. Why is it difficult to do three successive nitration reactions on toluene to get to trinitrotoluene (TNT)?
5. What kind of directing group is on toluene? Briefly explain, using drawings to support your answer.
6. What kind of directing group is on benzaldehyde? Briefly explain, using drawings to support your answer.