

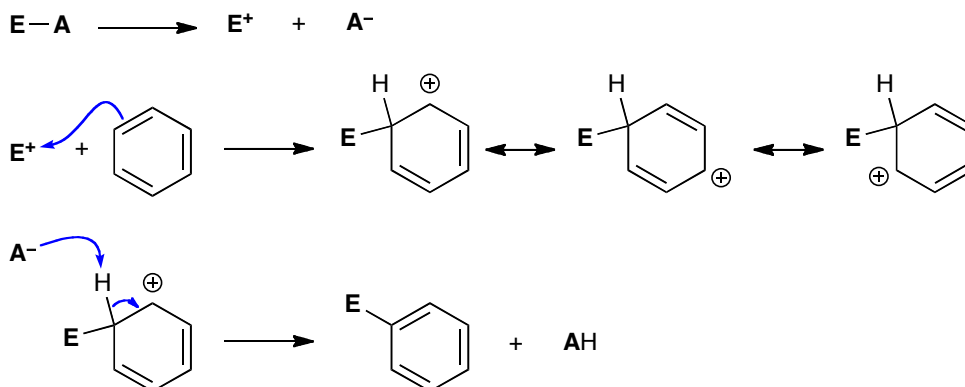
EXPERIMENT 5: Electrophilic Aromatic Substitution – A Friedel-Crafts Acylation Reaction

Relevant Sections in the text (Wade, 7th ed.)

- 17.1-17.2 (p. 751-755) Electrophilic aromatic substitution
- 17.6-17.8 (p. 761-770) Substituent effects in EAS
- 17.11 (p. 777-782) Friedel-Crafts acylation

General Concepts

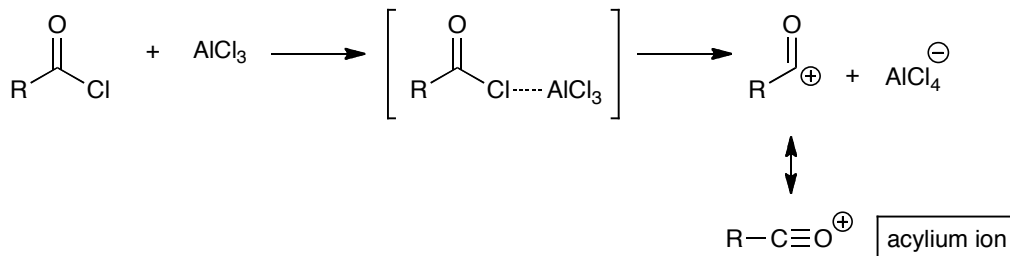
A very important class of molecules in nature and in medicine is substituted benzene rings, also known as aryl rings. Consequently, chemically synthesizing benzene with varying substituents is quite common. Unlike alkyl compounds, which undergo *nucleophilic* substitution, aromatic systems involve substitution reactions by an *electrophilic* pathway. Electrophilic Aromatic Substitution (EAS) reactions involve the generation of an electrophile in one or more steps, leading to the two-step addition/elimination process. In EAS reactions, a carbocation intermediate is formed when the nucleophilic π electrons of the aromatic ring attack the electrophile reagent, E^+ . This carbocation intermediate then reforms the aromatic system in the elimination step, with the loss of H^+ . The overall result is the substitution of an aromatic hydrogen with the electrophile (E^+), as shown in Scheme 1.



Scheme 1. General Mechanism for electrophilic aromatic substitution

Pre-existing substituents on aromatic rings affect the reactivity and regioselectivity of the EAS reaction. Electron-donating substituents cause an accelerated reaction where the strong electrophile preferentially binds in the *ortho*- or *para*- positions. This preferred position is due to resonance (and inductive) stabilization of the cation intermediate. Aromatic electron withdrawing groups however react less rapidly and direct the external electrophile to the favored *meta*- position. *Why?*

The EAS reaction you will be performing is a Friedel-Crafts acylation, where the electrophile is an acylium ion ($R-C\equiv O^+$). This reactive ion is formed by the reaction of an acid chloride (acetyl chloride, CH_3CO-Cl) with aluminum chloride ($AlCl_3$) acting as the Lewis acid catalyst (see Scheme 2).



Scheme 2. Generation of the acylium ion electrophile

You will be given an unknown mono-substituted aromatic compound which may yield any or all of the disubstituted benzenes (where the electrophile gets added *ortho*, *meta* or *para* to the substituent). After performing the reaction, the identity and structure of the product (and therefore the starting material) may be determined by IR and NMR spectroscopy. A proposed mechanism for the reaction will also be required, accounting for any regioselectivity. All the necessary background will be discussed in lecture, however you will need to read ahead in Chapter 17.

In addition to the NMR analysis, disubstituted benzenes can be distinguished by the location of the out-of-plane (oop) C-H bending bands in the IR spectrum. The frequency decreases with the number of adjacent hydrogens (see Table 1)

Table 1: Frequencies of C-H (OOP) Bending Bands in the IR for Aromatic Rings

Number of Adjacent Hydrogens	Frequency Range/ cm^{-1}
1	900 – 860, weak
2 (<i>para</i>)	850 – 810
3 (<i>meta</i>)	810 – 750, 690
4 (<i>ortho</i>)	770 – 735 (usually one strong band near 750)
5 (monosubstituted)	Strong band at 690 and 770 – 730

***NOTE*:** Pre-lab calculations are required before beginning the lab. Read over the procedure on the next page, and make the necessary calculations!

PART A: PREPARATION OF A DISUBSTITUTED AROMATIC COMPOUND

***HAZARDS*:** Always work in the fumehood. Please wear gloves for this experiment. Aluminum chloride is water sensitive, an irritant, and corrosive. It will react with the moisture in the atmosphere or on your skin to liberate HCl. Weigh it in a fumehood and make sure the container is covered when you transport it back to your own hood. Acetyl chloride is also corrosive so keep it in the hood. Keep all reagent bottles tightly capped. Discard aqueous waste down the drain with lots of water. Collect organic waste into the appropriate waste containers.

Make the necessary pre-lab calculations before beginning the lab!!

- Transfer the appropriate amount of anhydrous aluminum chloride, AlCl_3 , (MW = 133.3 g/mol, 0.055 mol) to a 100 mL round bottomed flask with 15 mL of dry dichloromethane, CH_2Cl_2 . Add a stir bar, Claisen head, addition funnel, and reflux condenser to the flask (see Fig. 1). *Weigh out the AlCl_3 in the fumehood and transport it to your fumehood tightly capped!*
- While cooling the mixture to 0 °C in an ice water bath, add the appropriate amount of acetyl chloride, CH_3COCl (0.055 mol, density = 1.14 g/mL) to 10 mL of dry dichloromethane into the addition funnel. Add this mixture drop wise over 10 min into the reaction flask containing the AlCl_3 solution. Record all observations.
- Add your unknown aromatic compound (0.050 mol = x g) as a solution in 10 mL of dichloromethane from the addition funnel over 10 min (*do not* wash the funnel). Ensure that the solution does not boil excessively. HCl gas is being liberated. Test this by briefly removing the drying tube above the condenser and holding a piece of pH paper near the opening. Record all observations.

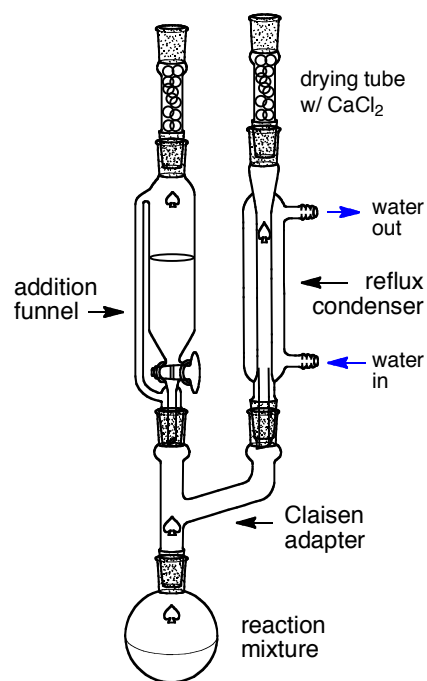


Figure 1. Reaction setup

***Note*:** Each unknown aromatic is anhydrous. Consequently, the reagent bottles are sealed and they always have a stream of nitrogen over them. Your TA will show you how to properly obtain these sensitive reagents. Pay careful attention bearing in mind that this is a common and important skill in synthetic chemistry.

The unknown is one of the following:

- A (MW = 92.1, density = 0.867 g/mL),
- B (MW = 108.2, density = 0.996 g/mL),
- C (MW = 106.17, density = 0.867 g/mL) or
- D (MW = 120.2, density = 0.864 g/mL).

- Remove the ice bath after the addition is complete and bring the flask to room temperature. Stir for another 15 minutes and then slowly pour the contents (while stirring) into about 25 g of ice and 15 mL of conc. HCl in a large beaker.

PART B: PURIFICATION AND ANALYSIS

- After transferring the solution to a separatory flask, the organic layer is collected. The aqueous layer is extracted 2 x 20 mL of dichloromethane, CH₂Cl₂. Combine the organic layers and wash with 2 x 50 mL of saturated aqueous sodium bicarbonate (NaHCO₃).
- Dry the organic layer over anhydrous MgSO₄ and gravity filter the drying agent, collecting the product in a **tared** round bottomed flask. Remove the CH₂Cl₂ by rotary evaporation.
- Weigh the crude product. Obtain an IR spectrum of your product. Also prepare an NMR sample of your product using deuterated CDCl₃ as a solvent and give it to your TA properly labeled. Review the procedures from experiment 3 in Chem 2273a if necessary.
- If your product is a solid, make sure to obtain a melting point.
- Run a TLC plate of your crude product directly against your unknown aromatic on the same TLC plate, using 2:1 petroleum ether: ethyl acetate as the eluent. Visualize with UV and iodine. If your sample is a solid, get a melting point.

You will have to work up your ¹H and ¹³C NMR data and analyze it. Obtain an accurate integration of your ¹H NMR spectrum, including any “impurities”. If you suspect that your product is contaminated with starting material, carefully integrate the starting material peaks separately so you can calculate an approximate percent of each.

- Calculate a percent yield of your crude product.
- Analyze all spectra.

EXPERIMENT 5: Electrophilic Aromatic Substitution – A Friedel-Crafts Acylation Reaction – DATA SHEET

NAME:	
LAB SECTION:	
DEMONSTRATOR(S):	

DUE DATE: _____

UNKNOWN Aromatic (circle) **A B C D**

After determining the identity of your unknown aromatic draw the reaction equation showing the structures of starting material and possible products. Name the compounds using IUPAC rules:

Calculate your yield:

Acetyl chloride: Molecular Weight = _____ Grams used = _____
 Volume used = _____ Moles used = _____

Unknown Aromatic (____): Molecular Weight = _____ Grams used = _____
 Volume used = _____ Moles used = _____

Limiting reagent? _____

Product: Molecular Weight = _____ (*hint: MW of your unknown + 42*)
 Moles Expected = _____
 Grams expected = _____ (*theoretical yield*)

Mass of round bottom flask and stopper = _____

Mass of round bottom flask, stopper and products = _____

Net Mass of products obtained = _____

Percentage Yield: = _____ (*Show calculations on reverse*)

Analysis of NMR Spectrum of Product:

Attach your NMR spectra to this Data Sheet. Assign a structure of your product by completely analyzing your ^1H and ^{13}C NMR spectra. In some cases it may be possible to see more than one of the disubstituted benzene products. Be sure to integrate all peaks and assign a relative proportion of the products.

Analysis of Infrared Spectrum:

Attach and analyze the IR spectrum of your products, assigning appropriate peaks. Compare and comment on it compared to the IR spectrum of the starting material (provided in the laboratory). Also use Table 1 in experiment 4 to try to determine (confirm) the substitution pattern of your product (*ortho*, *meta* or *para*).

Draw a *complete mechanism* of the reaction on your unknown aromatic with acetyl chloride + AlCl_3 accounting for any regiochemistry.