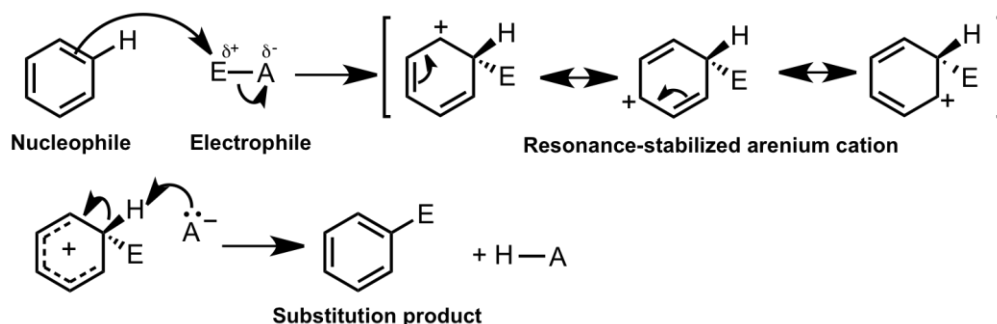


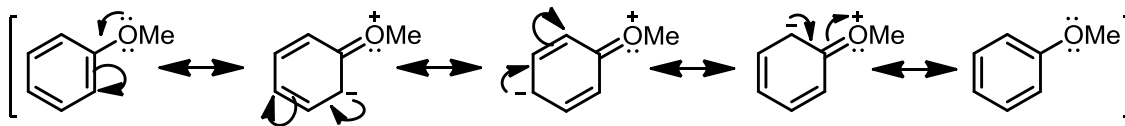
13 Friedel-Crafts Acylation of Anisole

13.1 Introduction

A benzene ring is rich in π -electrons, making it susceptible to **electrophilic aromatic substitution** (EAS) reactions. These reactions proceed by initial attack of the π -electrons of the ring at the electrophile (E^+ or EA) leading to an **arenium cation** intermediate in which the electrophile has added to one of the positions of the ring. The arenium cation intermediate contains an sp^3 -hybridized carbon atom. Removal of an H-atom from the sp^3 hybridized carbon atom restores aromaticity and neutrality, resulting in a net substitution of E in place of an H-atom on the ring.



It is possible to direct the regiochemistry of electrophilic substitution on an aromatic ring by employing electron withdrawing or electron donating substituents. In the following example, several resonance structures are shown where a methoxy group (OMe) is attached to the ring.

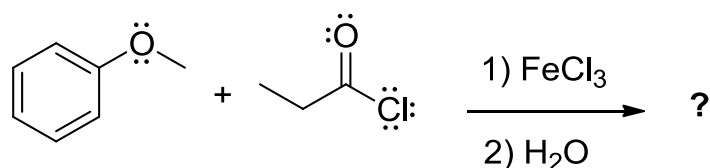


The p-rich orbital containing one of the O-atom lone pairs conjugates to the π -system of the benzene ring allowing the OMe group to donate electron density into the benzene ring, thus making the ring more reactive toward an electrophile relative to benzene. As is evident from the above resonance structures, the electron density is not evenly distributed about the ring; instead, it is localized on the C-atoms that are *ortho* and *para* to the OMe group. Recall that resonance structures do not exist independently but are simply a way of using Lewis structures to represent the electron distribution around a π -system.

Understanding the principles of activating and deactivating groups is critical to understanding EAS reactions. Consult your CHEM 343/345 notes and Loudon p. 740-772 for detailed discussion of aromaticity and EAS reactions.

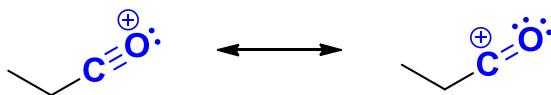
Friedel-Crafts alkylations and acylations are a special class of EAS reactions in which the electrophile is a carbocation, specifically an **acylium cation**. Such carbon-carbon bond formation reactions are useful because they allow alkyl or acyl groups to be substituted directly onto an aromatic ring.

In this lab, you will use $^1\text{H-NMR}$ data to determine the regiochemistry of the product resulting from acylation of anisole (methoxybenzene) by propionyl chloride. The molecular and electronic structure of the electrophilic propionylium cation will be explored by computational chemistry.



13.2 Pre-lab questions

- 1) Draw an electron-pushing mechanism for the formation of the propionylium cation resulting from the reaction of propionyl chloride and FeCl_3 . Show all lone pairs, formal charges, and appropriate arrows.
- 2) Two resonance structures of the propionylium cation are typically drawn in textbooks or on websites. For each resonance structure, identify how many electrons are shared between the C-atom and O-atom highlighted in the functional group.



If the actual structure of the propionylium cation is an equally-weighted resonance hybrid of these two resonance structures, how many electrons are shared between the C-atom and O-atom?

13.3 Procedure

Friedel-Crafts acylation of anisole

To a 25 mL round bottom flask containing a stir bar and fitted with a Claisen adaptor was added FeCl_3 (0.66 g, 4.0 mmol), CH_2Cl_2 (6 mL), and propionyl chloride (0.41 mL, 4.6 mmol, dispense via Eppendorf pipette). A solution of anisole (0.43 mL, 4.6 mmol, dispense via Eppendorf pipette) in CH_2Cl_2 (3 mL) was added slowly drop-wise to the reaction mixture over ~ 5 min *via* a Pasteur pipette threaded through a thermometer adaptor (see Figure 13.1). The mixture was stirred for a further 10 min upon complete addition. After this time the reaction was quenched by slow addition of ice-cold water (5 mL, add the first 1 mL drop-wise), stirred for a further 5 min, and the mixture transferred to a separatory funnel. Water (10 mL) was added to the separatory funnel and the aqueous layer extracted with CH_2Cl_2 (2 x 5 mL). The combined organic layers were washed with 5% aq. NaOH solution (10 mL) and stirred over anhydrous MgSO_4 for ~ 5 min. Following gravity filtration, the filtrate was transferred to a weighed beaker and the solvent removed by evaporation on a hot plate on a low heat setting (what do you need to add to the beaker before heating it?). When all solvent had evaporated the beaker was cooled to room temperature and its mass recorded. Calculate the weight and % yield of the crude product. Obtain an IR spectrum and submit a sample for $^1\text{H-NMR}$ analysis.

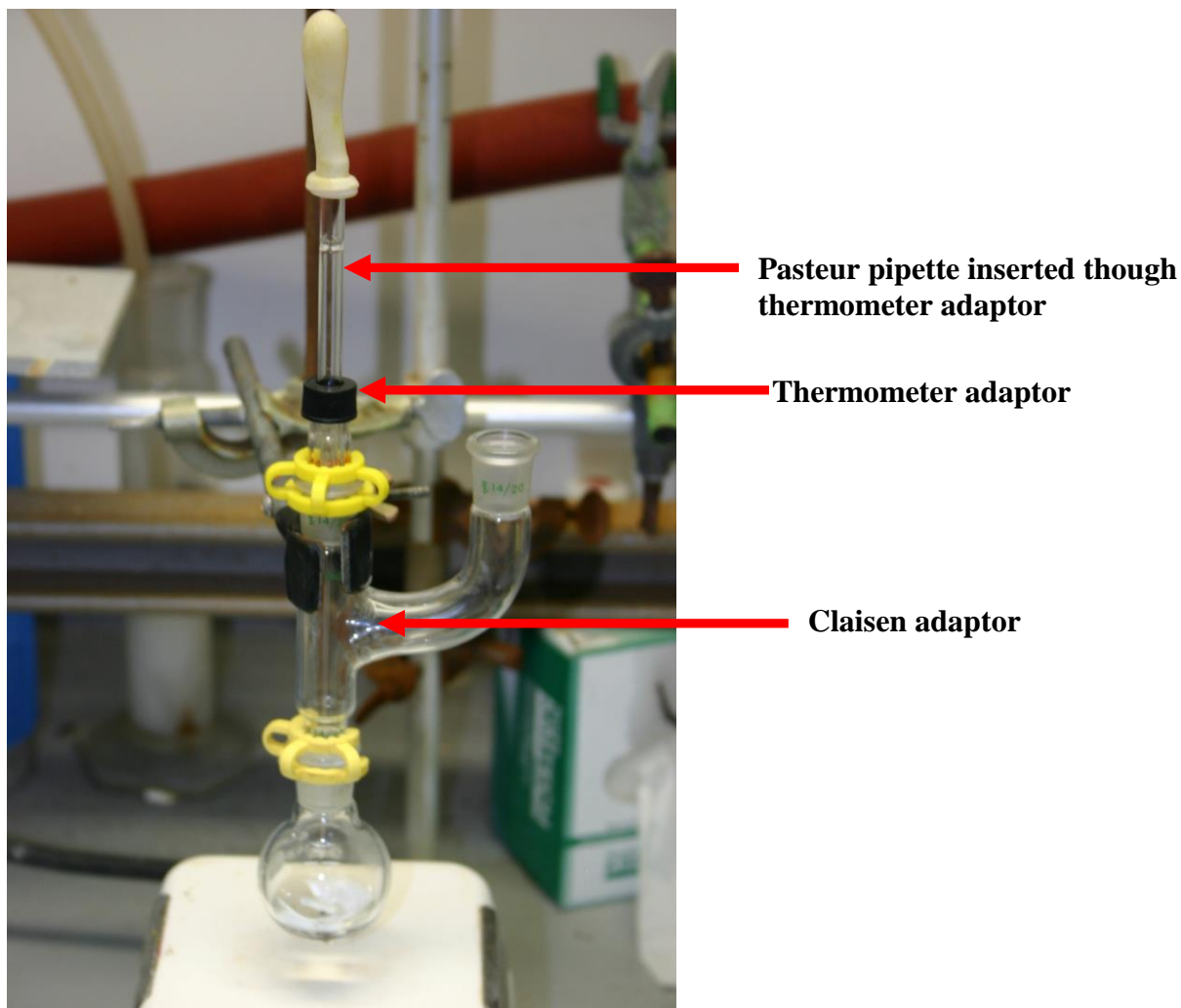


Figure 13.1 Equipment setup for the Friedel-Crafts acylation reaction.

13.4 Lab Report

In addition to answering the post-lab questions shown on the next page, you should fully assign the ^1H -NMR spectrum of the product(s) obtained from this reaction.

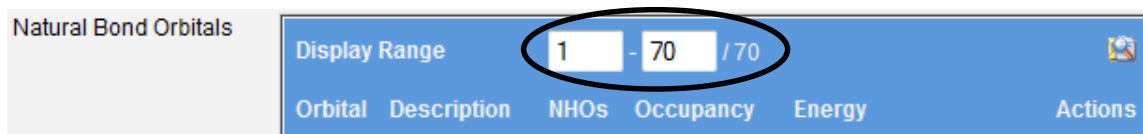
13.5 Post-lab questions

Molecular structure of propionylium cation

- 1) Use WebMO/Gaussian09 to obtain an optimized geometry (**B3LYP/6-31G(d)**) for the propionylium cation (symmetry point group C_s). Provide a screen-capture image of the molecular structure in your notebook.

Electronic structure of propionylium cation

- 2) Using the optimized geometry obtained above, perform an NBO calculation and show the NPA charges on each atom in the cation. Based upon the NPA charges, state which atom you expect to be the most electrophilic. Explain whether or not the computational charge data are supported by the reactivity of this species.
- 3) Use the *Natural Bond Orbitals* list to find and visualize all of the bonding orbitals of the carbon-oxygen bond (they will be displayed as BD(#)CX-OY, where # is the number of the bond and X and Y are the numbers of the atoms). Provide a color screen-capture image of the orbitals in your lab report, labeling each with its electron occupancy and symmetry (σ or π). Using this information, comment on whether or not the electronic structure is more similar to one resonance structure or a hybrid of the two.
- 4) Electrophiles such as the propionylium cation are electron pair acceptors (Lewis acids). The acceptor orbital(s) of the propionylium cation are the CX-OY π^* anti-bonding orbital(s) and can be viewed in the *Natural Bond Orbitals* list. Find the π^* orbitals at the end of the NBO list (they will have the notation BD*(#)CX-OY). Provide a color screen-capture of the orbitals in your lab report, labeling each as π^* and identifying the largest lobes of each π^* orbitals. You may need to expand the display range of available *Natural Bond Orbitals* in WebMO (see below).



Natural Bond Orbitals					
Display Range					
1 - 70 / 70					
Orbital	Description	NBOs	Occupancy	Energy	Actions

- 5) Draw an electron-pushing mechanism for the Friedel-Crafts acylation reaction and use Hammond's Postulate to rationalize the observed regiochemistry of the product. Show all lone pairs and formal charges.

CHEM 344 Friedel-Crafts Acylation of Anisole

Name:

Lab Partner:

TA:

Weight of FC acylation product _____

% Yield of FC acylation product (show calculation below) _____

Propionylium cation WebMO job numbers: _____ (Opt+Vib Freq)
_____ (NBO)

Name

Friedel-Crafts Acylation of Anisole

Prelab

Descriptive title

Balanced reaction

Answers to pre-lab questions

Reagent table

Outline of procedure

Total ____/5

Report

Observations ____/3

Discretionary pts (legibility, organization etc.) ____/2

Total ____/5

Pre-lab + Report Total ____/10

Results

Interpretation of ¹H-NMR data ____/8

Post-lab question 1 ____/4

Post-lab question 2 ____/4

Post-lab question 3 ____/4

Post-lab question 4 ____/4

Post-lab question 5 ____/6

Results Total ____/30

Final Total ____/40