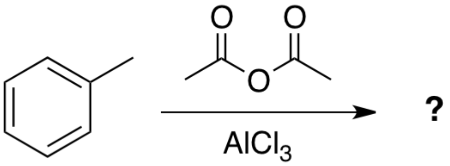
12 Electrophilic Aromatic Substitution

Friedel-Crafts Acylation of Toluene

12.1 Introduction

Friedel-Crafts alkylations and acylations are a special class of EAS reactions in which the electrophile is a carbocation or an **acylium cation**. These reactions are useful in that they involve carbon-carbon bond formation and allow alkyl and acyl groups to be substituted onto aromatic rings. In this lab, you will use ^{1}H-NMR data to determine the regiochemistry of the product resulting from acylation of toluene by acetic anhydride under microwave heating conditions. The molecular and electronic structure of the electrophillic acylium cation will be explored by computational chemistry.



Concepts relevant to this lab are covered in Loudon. pp.759-761. EAS reactions are discussed pp. 740-772 and have been covered extensively in CHEM 345 lecture.

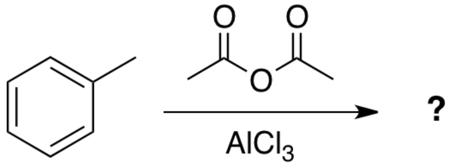
Aluminum chloride ($AlCl_3$) is a strong Lewis acid. It reacts vigorously and exothermically with air and water forming HCl vapor. Any spills must be cleaned up immediately and disposed of in the labeled $AlCl_3$ waste container. Do not put $AlCl_3$ in the sinks. The cap on the bottle of $AlCl_3$ must be replaced immediately after the desired amount has been weighed out.

12.2 Pre-lab question

Draw an electron-pushing mechanism for the formation of the acylium cation by reaction of acetic anhydride with $AlCl_3$. Draw 2 resonance structures of the acylium cation, clearly showing all H-atoms, lone pairs, and formal charges.

12.3 Procedure

Friedel-Crafts acylation of toluene



Read p. 67 to review the procedure for preparation of microwave samples.

Work individually.

To a microwave vial add $AlCl_3$ (0.50 g, 3.75 mmol), toluene (3 mL), anhydride (250 μL via an Eppendorf pipette) and a stir bar, then cap the vial and tighten with the torque wrench. Place the microwave vial in the sample carousel and note the slot number. The TA will place the carousel into the microwave instrument and begin the heating program.

Once the microwave program is complete allow the vials to cool. **In the fume hood** open the microwave vial and add water (6 mL), then recap the vial and shake the mixture vigorously for ~30 sec. Remove the stir bar and pour the mixture into a 60 mL separatory funnel. Rinse the microwave vial with ethyl acetate (2 mL) and add the washings to the funnel. Allow the phases to separate.

Extract the aqueous layer with ethyl acetate (4 mL). Combine the organic phases and wash with sat. aq. NaCl solution (5 mL), then with sat. aq. $NaHCO_3$ solution (5 mL). Stir the organic phase over anhydrous $MgSO_4$ for ~5 min, vacuum filter the mixture and pour the filtrate into a pre-weighed beaker. Evaporate the solvent on a hotplate until boiling ceases (what do you need to add to the beaker before heating it?). Allow the beaker to cool to room temperature, record the mass of the beaker, and prepare a sample for ^{1}H-NMR spectroscopy (use all of the product to prepare your NMR sample). You do not need to calculate a % yield.

12.4 Lab Report

In addition to answering the post-lab questions shown on the next page, you should fully assign the ^{1}H-NMR spectrum of the product(s) obtained from this reaction. Calculate the ratio product:by-product or product:starting material if the NMR spectrum shows that there is more than one compound in your reaction product.

12.3 Post-lab questions

Molecular structure of acylium cation

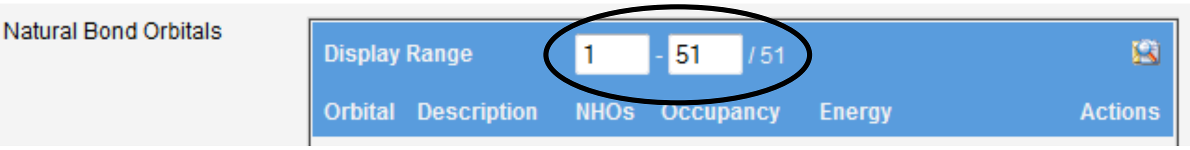
1) Use WebMO/Gaussian09 to obtain an optimized geometry (**B3LYP**/**6-31G(d)**) for the acylium cation you generated in the experiment. State the symmetry of the molecule and the hybridization at each carbon atom, and provide a sketch or screen capture of the molecular structure in your notebook (4 pts).

Electronic structure of acylium cation

2) Using the structure obtained above, perform an NBO calculation and list the NPA charges on each atom in the acylium cation. Comment on whether the calculated charge distribution of the acylium cation matches the formal charges you predicted in the pre-lab question (3 pts).

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(#)C2-O3, where # is the number of the bond and 2 and 3 are the numbers of the atoms). Draw or provide a screen capture of the orbitals in your laboratory notebook, labeling each with its electron occupancy and symmetry (sigma σ or pi π). Using this information, comment on which resonance structure of the acylium cation you drew in the pre-lab question best matches the calculated C-O bonding orbitals (4 pts).

4) Electrophiles such as the acylium cation are electron pair acceptors (Lewis acids). The acceptor orbital(s) of the acylium cation are the C2-O3 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*(#)C2-O3). Draw or provide a screen capture of the orbitals in your laboratory notebook labeling each as π* and identify the largest lobes of the π* orbitals. You may need to expand the display range of available *Natural Bond Orbitals* in WebMO (see below) (3 pts).



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5) Use the calculated NPA charges and π* orbital(s) to explain which atom in the acylium cation is the most electrophilic. Discuss whether the computational results agree with the experimentally observed reactivity of the acylium cation toward toluene (3 pts).

Name

Friedel-Crafts Acylation of Toluene

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 ^{1}H-NMR data	_____/8
Post-lab question 1	_____/4
Post-lab question 2	_____/3
Post-lab question 3	_____/4
Post-lab question 4	_____/3
Post-lab question 5	_____/3

Results Total____/25

Final Total ____/35