

Nitration of Aromatic Compounds: Preparation of methyl-*m*-nitrobenzoate



Purpose

- Study electrophilic aromatic substitution reaction (EAS)
- Study regioselectivity for EAS reactions

Chemicals

Methyl benzoate
Sulfuric acid (conc.)
Nitric acid (conc.)
Ice
Methanol

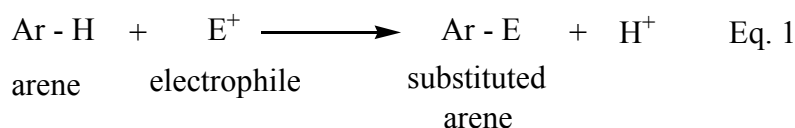
Materials

150 – mL beaker
400-mL beaker
125-mL flask
Stirring rod
Mel-temp
Suction filtration funnel

Introduction

Unlike nucleophilic substitutions, which proceed via several different mechanisms, electrophilic aromatic substitutions (EAS) generally occur via the same process. Because of the high electron density of the aromatic ring, during EAS reactions electrophiles are attracted to the ring's π system and protons serve as the leaving groups.

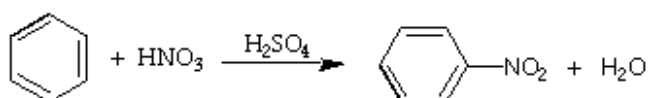
Equation 1. During S_N1 reactions, however, nucleophiles attack an aliphatic carbon and weak Lewis bases serve as leaving groups.



Generally, EAS reactions occur in three steps, Scheme I. During Step I, the electrophile is produced, Scheme I

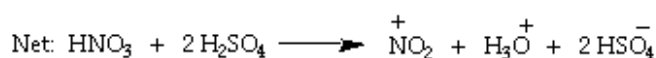
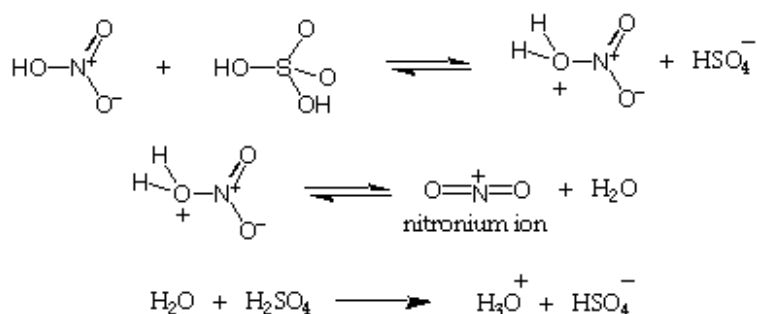
Electrophilic Aromatic Substitution

Nitration of Benzene:

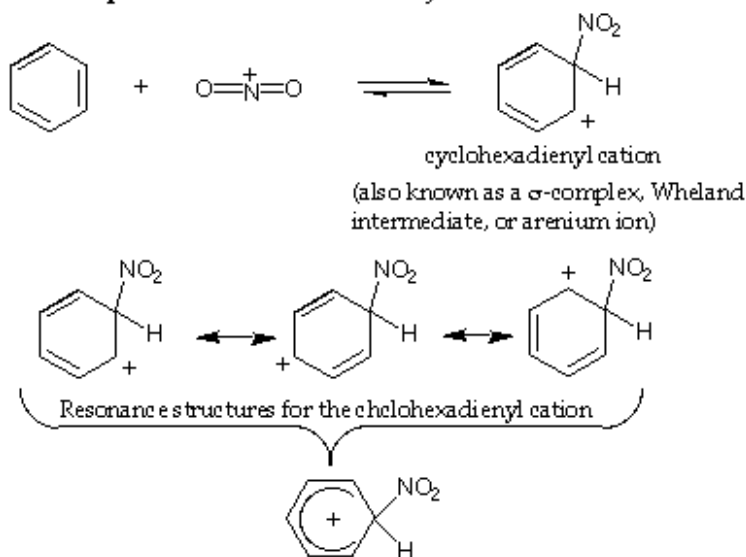


Mechanism:

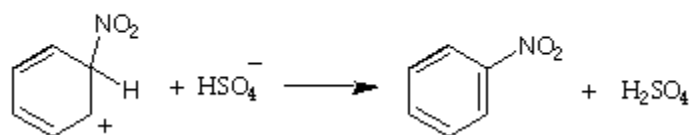
Step 1: Generation of the Electrophile:



Step II: Electrophilic Attack on Aromatic π System:



Step II: Re-aromatization



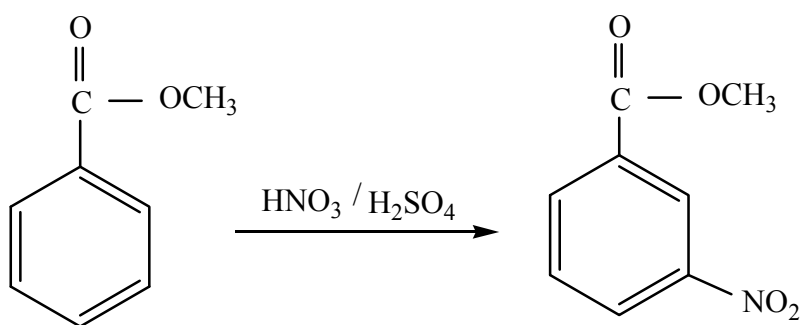
Usually, by the interaction of a compound containing the potential electrophile and a catalyst. During Step II, the aromatic π system donates an electron pair to the electrophile, forming a σ bond (an arenium cation) followed by deprotonation in step III in the present of a base (HSO_4^-) affording the substituted arene. EAS reactions are generally second-order processes, i.e., first order in electrophile and first order in arene. Thus, Step II. is the rate-determining step (rds); $\text{rate} = k_2 [\text{arene}][\text{electrophile}]$.

Electrophilic Aromatic Substitution: Nitration of Methyl Benzoate

Benzene rings are components of many important natural products and other useful organic compounds. Therefore, the ability to put substituents on a benzene ring, at specific positions relative to each other, is a very important factor in synthesizing many organic compounds. The two main reaction types used for this are both substitutions: Electrophilic Aromatic Substitution (EAS) and Nucleophilic Aromatic Substitution (NAS). The benzene ring itself is electron-rich, which makes NAS difficult, unless there are a number of strongly electron-withdrawing substituents on the ring. EAS, on the other hand, is a very useful method for putting many different substituents on a benzene ring, even if there are other substituents already present. Electrophilic Aromatic Substitution chapter describes the factors involved in the regioselectivity for EAS reactions using benzene rings, which already have substituents on them.

In this experiment you will put a nitro (—NO_2) group on a benzene ring, which already has an ester group, attached to it (methyl benzoate). The actual electrophile in the reaction is the nitronium ion (NO_2^+), which is generated *in situ* ("in the reaction mixture" $\text{HNO}_3/\text{H}_2\text{SO}_4$) using concentrated nitric acid and concentrated sulfuric acid.

Reaction:



Methyl Benzoate

MW = 136.15 g/mol
Density = 1.094 g/ml
B.P. = 198-199 °C
M.P. = -12 °C

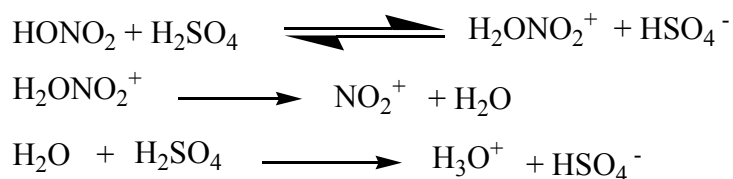
Methyl *m*-nitrobenzoate

MW = 181.14 g/mol
B.P. = 279 °C
M.P. = 78-80 °C

Reaction mechanism

The carbomethoxy group ($\text{—CO}_2\text{CH}_3$) directs the aromatic substitution reaction to the position that are meta to it. As a result the *m*-nitrobenzoate is the principal product from this reaction. Formation of dinitro products from this reaction is unlikely under the conditions in which you carry out your reaction. The reason for this is that both carbomethoxy groups as well as the nitro group (on the mono nitrated product) are deactivating groups making the second nitration less favorable.

Concentrated sulfuric acid is the solvent for this reaction and is involved in the formation of nitronium ion (NO_2^+) from concentrated nitric acid. Water has a retarding effect on the nitration since it interferes with the nitric acid-sulfuric acid equilibrium (shown below) that generates the required nitronium ion (NO_2^+).



Overall reaction:



Temperature also has an effect on the product distribution from this reaction. Higher the temperature, greater will be the amounts of dinitration products formed from this reaction.

Safety Note

Caution: Avoid contact with the acids used in this experiment and the reaction product. Prevent contact with the skin, eyes, and clothing; work in the hood. An acid spill is neutralized using solid sodium carbonate or bicarbonate. The reaction is highly exothermic. A vigorous reaction will occur if the acid mixture is added too rapidly to the methyl benzoate.

Concentrated nitric acid and concentrated sulfuric acid are both strong oxidizers, and strongly corrosive--wear gloves while handling them, and avoid breathing their vapors. Methyl benzoate and methyl *m*-nitrobenzoate are irritants -- wear gloves while handling them. Methanol is a flammable liquid, and is toxic -- no flames will be allowed in lab, wear gloves while handling it, and avoid breathing its vapors.

Experimental Procedure

In a 125-mL Erlenmeyer flask mix 1.5 mL of methyl benzoate and approximately 4.0 mL of concentrated sulfuric acid (drop-wise), and chill it in an ice bath. Continue to cool the mixture in the ice bath to reduce the heat, which produced in the reaction. After complete addition of sulfuric acid, add approximately 2.0 mL concentrated nitric acid (measured in 10- mL graduated cylinder) drop- wise using a small graduated plastic pipette and mix by gentle swirling. Continue to cool the reaction mixture. Allow the reaction mixture to stand at room temperature for about five minutes.

Float the 125-mL flask in a 400-ml beaker hot water bath. Remove the flask occasionally and swirl the content carefully. After fifteen minutes heating pour the reaction mixture in 100-ml of ice water contained in a 150- mL beaker, with stirring.

Product Isolation- Isolate the product by vacuum filtration, wash the product with (ice) cold water (20 mL).

Note - Proper washing removes the more soluble *ortho* isomer. The crude material may be purified by recrystallization from a small volume (~ 10 mL) of hot methanol (**optional**). The crude product is pressed dry. You may need to air dry (or hand dry using paper towels) the product. Discard the aqueous filtrate down the drain with lots of water.

Determine the **weight**, **melting point**, and **percentage yield**. Pure methyl *m*-nitrobenzoate melts at 78.5°C.

Submit the product to your instructor in a paper wrapped and labeled including your name(s).

EXPERIMENT 3 (Organic Chemistry II)

Nitration of Aromatic Compounds: Preparation of methyl-*m*-nitrobenzene

REPORT FORM

Name _____

Instructor _____

Date _____

Calculation

(please show your calculations on results of laboratory report)

1. Weight of methyl benzoate _____ g _____ moles

2. Theoretical yield of methyl *m*-nitrobenzoate _____ g _____ moles

3. Weight of methyl *m*-nitrobenzoate _____ g _____ moles

4. Percentage yield of methyl *m*-nitrobenzoate _____ %

5. Melting point range of product _____ °C

6. Literature melting point of methyl *m*-nitrobenzoate _____ °C

Pre-Laboratory Questions–EXP 3 Name: _____

Nitration of Aromatic Compounds

Due before lab begins. Answer in space provided.

1. Which is nitrated faster? toluene or nitrobenzene? Explain.
2. Indicate the product formed on (mono) nitration of each of the following compounds:
 - a) Cyanobenzene (benzonitrile)
 - b) toluene
 - c) benzoic acid.
3. Why is methyl *m*-nitrobenzoate formed in this reaction instead of *o*- and *p*-? What product would you expect if methyl benzoate underwent dinitration?
4. Methyl-*m*-nitrobenzoate is an excellent (identification) derivative of methyl benzoate. What are the properties of methyl-*m*-nitrobenzoate that makes it an excellent derivative of the starting ester? .
5. List three combinations of reagents used for nitration of aromatic compounds?

Post-Laboratory Questions–EXP 3 Name:

Nitration of Aromatic Compounds

Due after completing the lab.

1. Why is concentrated sulfuric acid employed in this reaction? What is the electrophile that is produced by the reaction of sulfuric acid and nitric acid?
2. Why is it important to maintain the reaction temperature low and the addition of nitric acid-sulfuric acid mixture carried out slowly?
3. Explain why concentrated H_2SO_4 , not concentrated HCl , was used in this experiment?
4. Which ring of phenyl benzoate would you expect to undergo nitration more easily? Explain.
5. Which is nitrated faster, toluene or phenol? Explain.