March 28th, 2014

Experiment 6: Regioselective Nitration of Acetanilide

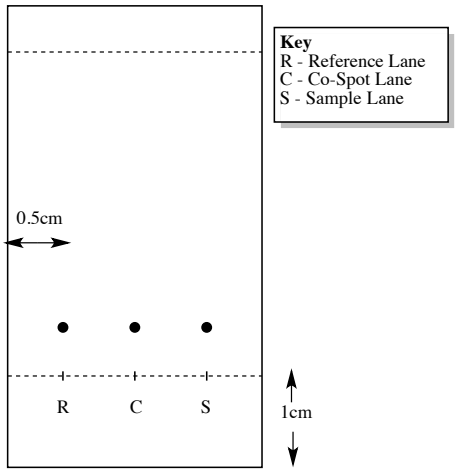
Intro:

Purpose: To carry out the nitration of acetanilide in order to demonstrate electrophilic aromatic substitution.

Procedure:

1. 1.01g of acetanilide and a small stir bar were placed into a 25.0mL round bottom flask. The flask was clamped over a magnetic stir plate.
2. 3.00mL of H_2SO_4 were added to the reaction mixture. The reaction mixture was stirred gently for approximately two minutes.
3. The reaction flask was placed in an ice bath over the magnetic stir plate. The reaction mixture was allowed to cool and stir gently for approximately 10 minutes.
4. 0.70mL of concentrated nitric acid and 1.30mL of sulphuric acid were added to a 50.0mL Erlenmeyer flask. The reaction mixture added to the 25.0mL reaction flask in drop wise fashion and allowed to sit for approximately 10 minutes.
5. A TLC plate was (using Hexane:EtOAc 5:5 as the solvant) was preformed (see figure 1)
6. The reaction flask was removed from the magnetic stir plate. The magnetic stirrer was removed from the reaction flask.
7. Approximately 20.0mL of cold water, 4 small ice cubes and a magnetic stir bar were placed in a 125.0mL Erlenmeyer flask. The 125.0mL Erlenmeyer flask was placed on the magnetic stir plate, and the reaction mixture contained in the 25.0mL flask was added to the this flask. The reaction mixture contained within the 125.0mL Erlynmeyer flask was gently stirred until all the ice had melted.
8. The solid that formed in the reaction mixture was extracted using cold water suction filtration.
9. A TLC plate was was prepared using the crude solid product (dissolved in acetone) as the sample. See figure 1.
10. TLC plates were prepared using samples of the ortho and 2,4 - dinitro product isomers (using ether:hexanes 9:1 as the solvent) and the meta and para isomers (using Hexane:EtOAc 5:5 as the solvent). See figure 1.
11. The remaining solid product was dissolved in a minimum amount of boiling ethanol within a 50.0mL Erlenmeyer flask. A stir bar was added to the flask.

Figure 1.



12. Once all the solid product dissolved, the flask was removed from the heat and allowed to sit at room temperature until crystal formation occurred.
13. The crystals were collected using suction filtration and the purified product collected was used along with the crude product to spot a TLC plate (using ether:hexanes 9:1) as the solvent. See figure 1.
14. A TLC plate was prepared and spotted using the mother liquor. See figure 1.

Observations/Data

Experimental Procedure and Observations:

- Table 1: Reagent Table

Compound	Molecular Weight (g/mol)	Density (g/mL)	Amount (g or mL)	Moles (mmol)
Acetanilide	135.16	1.129	1.01g	7.4
Sulphuric Acid	98.079	1.84	4.30mL	43.8
Nitric Acid	63.01	1.5129	0.70mL	11.1

- *Table 2: Qualitative Observations of Reactions and Compounds*

Compound / or Reaction	Qualitative Description
Acetanilide	Odourless solid, flakey and off white in colour.
Sulfuric Acid	Clear, colourless liquid, mild to strong odour.
Nitric Acid	Clear, colourless liquid, mild to strong odour.
Ether:Hexanes 9:1	Clear, colourless liquid. No odour.
Hexanes:EtOAc 5:5	Clear, colourless liquid. No odour.
Ethanol	Clear, colourless liquid. Mild Odour
Initial addition of H_2SO_4 to Acetanilide (see Procedure Step #2).	Acetanilide flakes were slow to dissolve in sulphuric acid.
Addition of conc. H_2SO_4 + conc. HNO_3 solution to H_2SO_4/Acetanilide mixture (see Procedure Step #3).	The drop wise addition of the concentrated acid mixture causes the reaction solution to turn a dark brownish green, and an increase in temperature was also observed.
Addition of Water and Ice to Reaction Mixture (see Procedure Step #7)	The reaction mixture quickly became yellow in colour, resembling mustard. No odour or temperature change observed.

- *Table 3: Peak Intensity Measurement for Ortho TLC Plate*

TLC Lane	Number of Peaks		Area of Peaks	Total Area of Peaks	Percentage Peak Intensity
1	1	Area peak 1	12914.217	12914.217	100%
2	2	Area peak 1	12791.388	16644.048	76.85%
		Area peak 2	3852.660		23.25%
3	2	Area peak 1	2133.640	5543.099	39.20%
			3309.459		60.80%

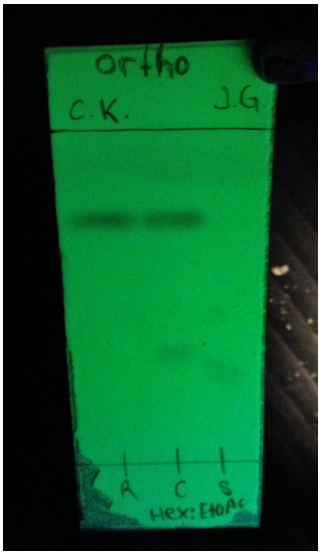
- *Table 4: Peak Intensity Measurement for Meta TLC Plate*

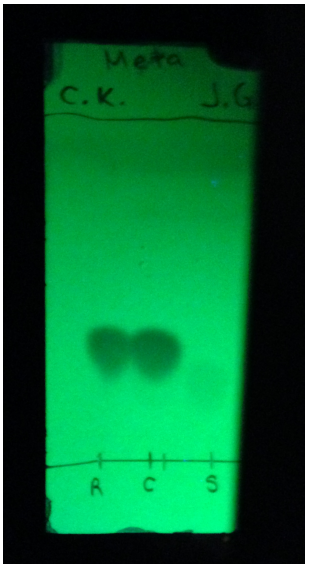
TLC Lane	Number of Peaks		Area of Peaks	Total Area of Peaks	Percentage Peak Intensity
1	1	Area peak 1	15826.220	15826.22	100%
2	2	Area peak 1	32083.726	32083.726	100%
		Area peak 2	insignificant		insignificant
3	1	Area peak 1	3063.823	3063.823	100%

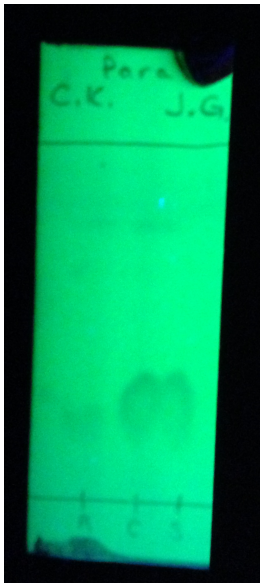
- *Table 5: Peak Intensity Measurement for Para TLC Plate*

TLC Lane	Number of Peaks		Area of Peaks	Total Area of Peaks	Percentage Peak Intensity
1	1	Area peak 1	14299.011	14299.011	100%
2	2	Area peak 1	5673.439	40762.328	13.92%
		Area peak 2	35088.889		86.08%
3	2	Area peak 1	5913.702	26309.37	22.48%
		Area of peak 2	20395.668		77.52%

- *Figures 1, 2 & 3: Images of TLC Plates spotted with Ortho, Meta and Para Isomers Respectively, under UV Light.*

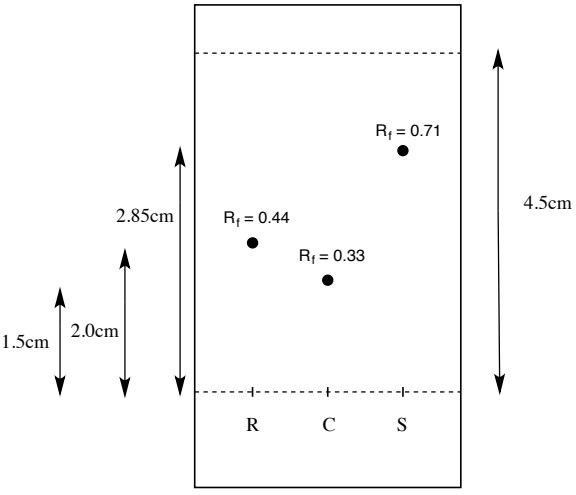






TLC Plates

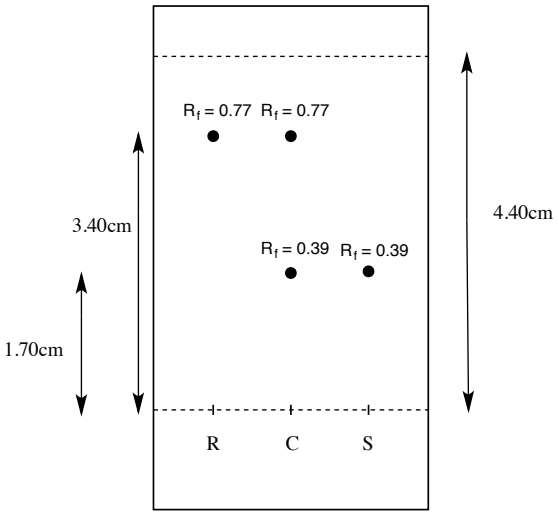
TLC Plate #1 - Verification of Reaction Completion (See procedural step #5)



Lane Key
R - Acetanilide
C - Acetanilide + rxn' mixture
S - Rxn' mixture

Eluent: Hexanes:EtAOc 5:5

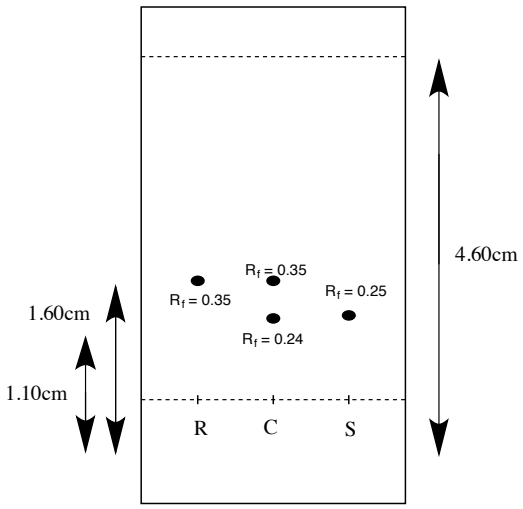
TLC Plate #2 - Spotted with Ortho Isomer (See procedural step #10)



Lane Key
R - Ortho - nitroacetenalide
C - Ortho - nitroacetenalide + crude product
S - Crude product

Eluent: Ether:Hexanes 9:1

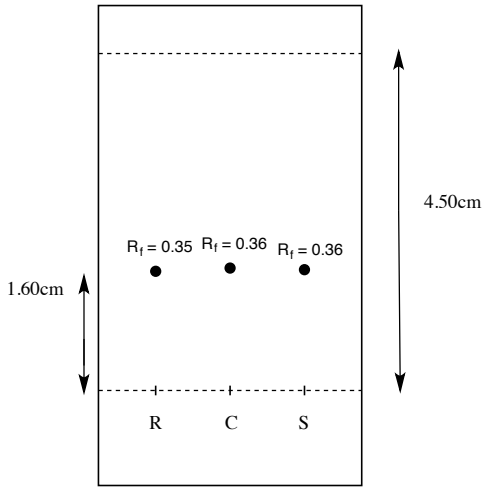
TLC Plate #3 - Spotted with Meta Isomer (See procedural step #10)



Lane Key
R - Meta - nitroacetenalide
C - Meta - nitroacetenalide + crude product
S - Crude product

Eluent: Ether:Hexanes 9:1

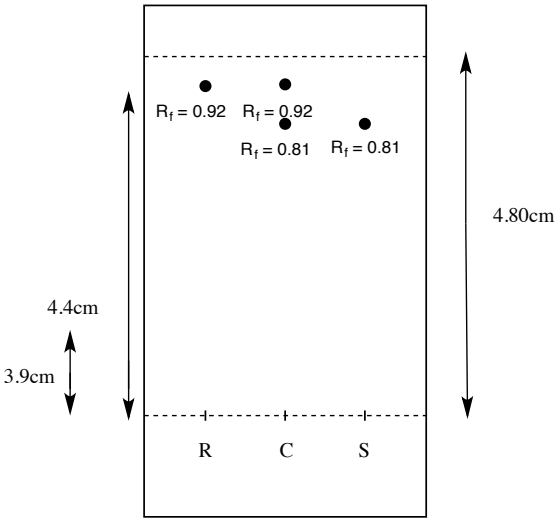
TLC Plate #4 - Spotted with Para Isomer (See procedural step #10)



Lane Key
R - Para - nitroacetenalide
C - Para - nitroacetenalide + crude product
S - Crude product

Eluent: Ether:Hexanes 9:1

TLC Plate #5 - Purified Product Vs. Crude Product

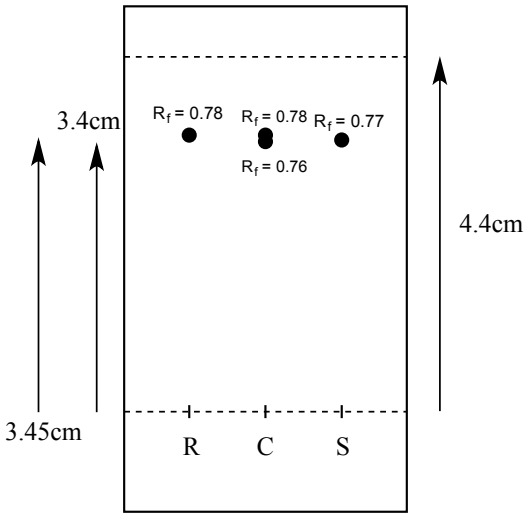


Lane Key
R - Crude Product
C - Crude Product + Pure Product
S - Pure product

Eluent: Ether:Hexanes 9:1

1.

TLC Plate #6 - Pure product Against Mother Liquor

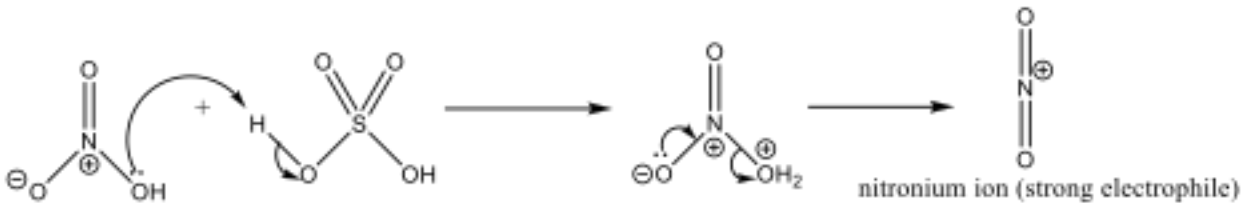


Lane Key
R - Mother Liquor
C - Mother Liquor + Pure Product
S - Pure product

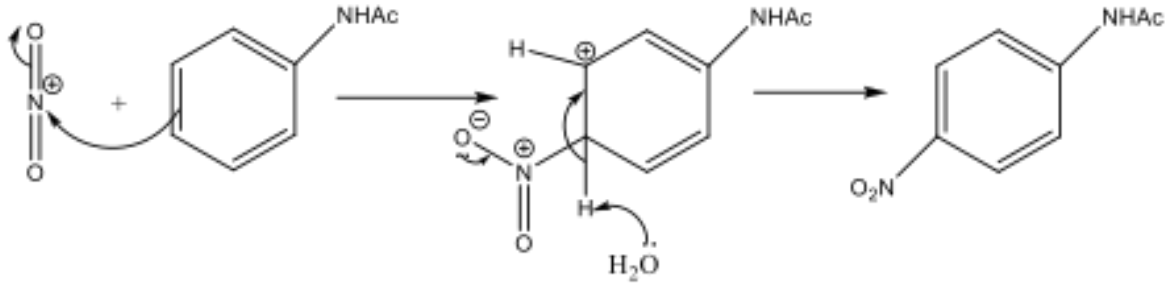
Eluent: Ether:Hexanes 9:1

Mechanisms

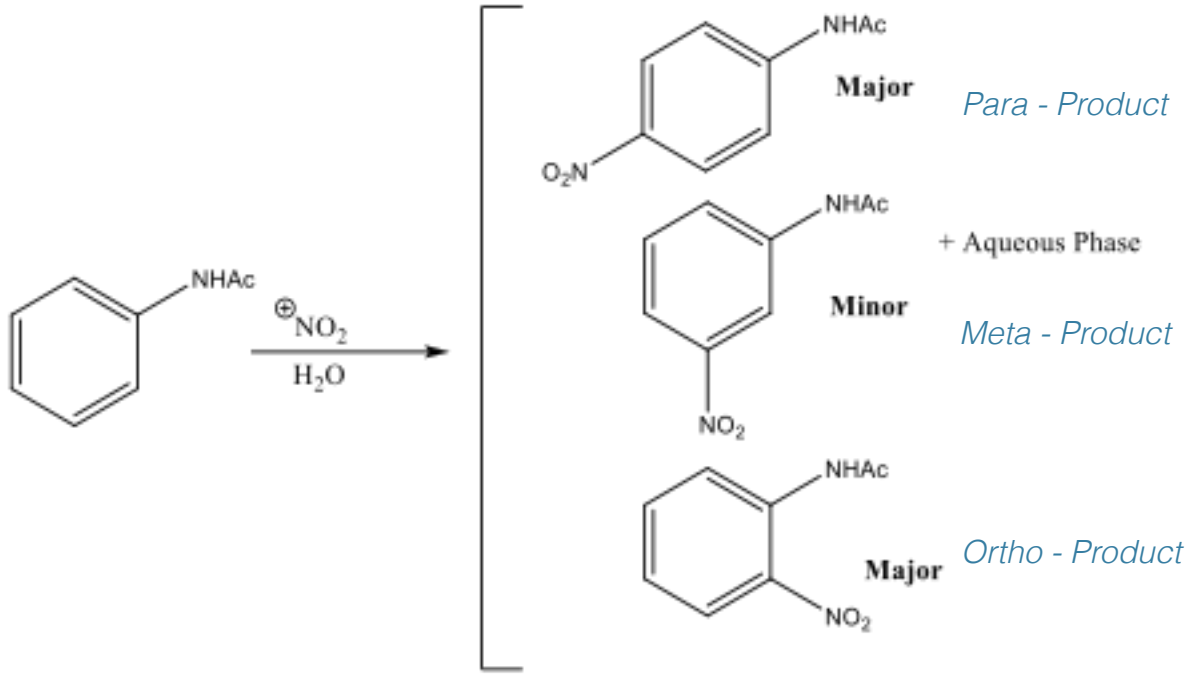
- Preparation of the Strong Electrophile using Nitric and Sulphuric Acid



- Nitration of Acetanilide with the use of a Strong Electrophile



- *Flow Chart of the Nitration of Acetanilide*



1.

Yield of NO_2-Ph - $NHAc_{(aq)}$

Reaction is given by:

Ph - $NHAc_{(aq)}$ + $HNO_{3(aq)}$ + H2SO4(aq) —> NO_2-Ph - $NHAc_{(aq)}$ + H2SO4(aq)
*Catalyst in Red

*Note that acetenalide is the limiting reagent, as all reactants and products are in 1:1 ratio, and acetenalide is the lowest in amount of mols.

Actual Yield = mol of NO_2-Ph - $NHAc_{(aq)}$ = mass collected/molar mass
= 2.33g/180.2g/mol
=$1.29x10^{-2}$ mol

Theoretical yield = mols of acetenalide = mols of NO_2-Ph - $NHAc_{(aq)}$ (due to 1:1 ratio)
= $7.4x10^{-3}$mol

Percent yield = Actual yield/theoretical x 100%
= $1.29x10^{-2}$ mol/ $7.4x10^{-3}$mol x 100%
= 174%

**See* Error Discussion *for explanation regarding the very high percent yield.*

Discussion*:*

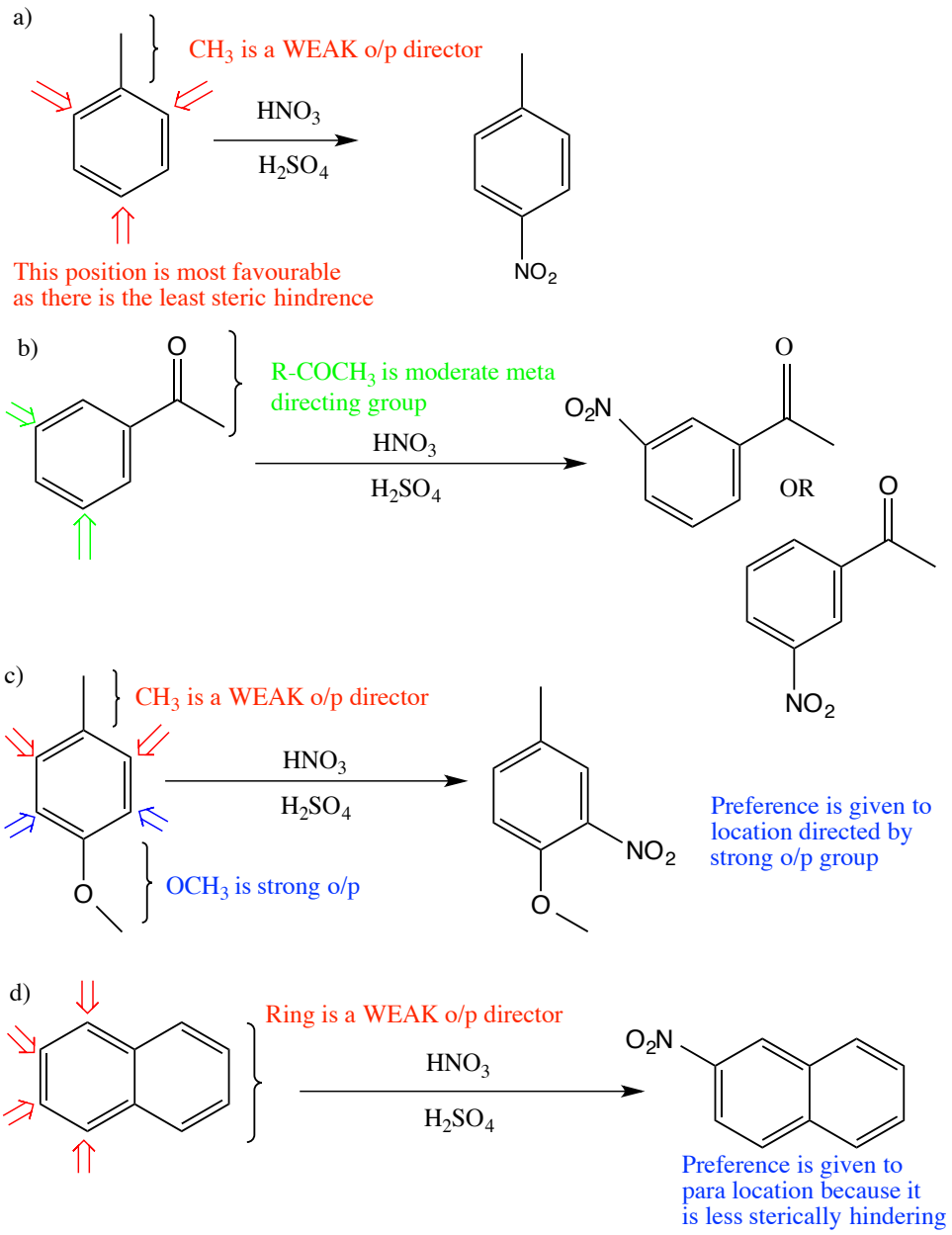
Discussion Questions

1. By examining the TLC plates of the *ortho* and *para* isomers of nitroacetanilide, it is evident that the *ortho* isomer is more polar. This can be explained by the fact that the charges on the *para* isomer are on opposite sides of the molecule, and so exhibit a cancelling effect on each other. This decreases the polarity significantly - and so explains why the *para* isomer moves up the plate further than the *ortho* isomer - as its attraction to the charged silica gel is lesser than that of the *ortho* isomer.
2. The explanation of the relative solubility of *ortho* and *para* isomers begins by noting the *relatively* high polarity of ethanol. By applying the "*like dissolves like"* principle, and our comparison of relative polarities between the isomers in questions deduced in question 1, it is obvious that the *para* isomer will have a low solubility in ethanol. Conversely, the high polarity of the *ortho* isomer translates to high solubility in ethanol.
3. It is important to first note that nitro groups are strong meta deactivators, and consequently strongly electron withdrawing. The first addition of a nitro group moves the molecule to a lowered energetic level, due to the electron withdrawing

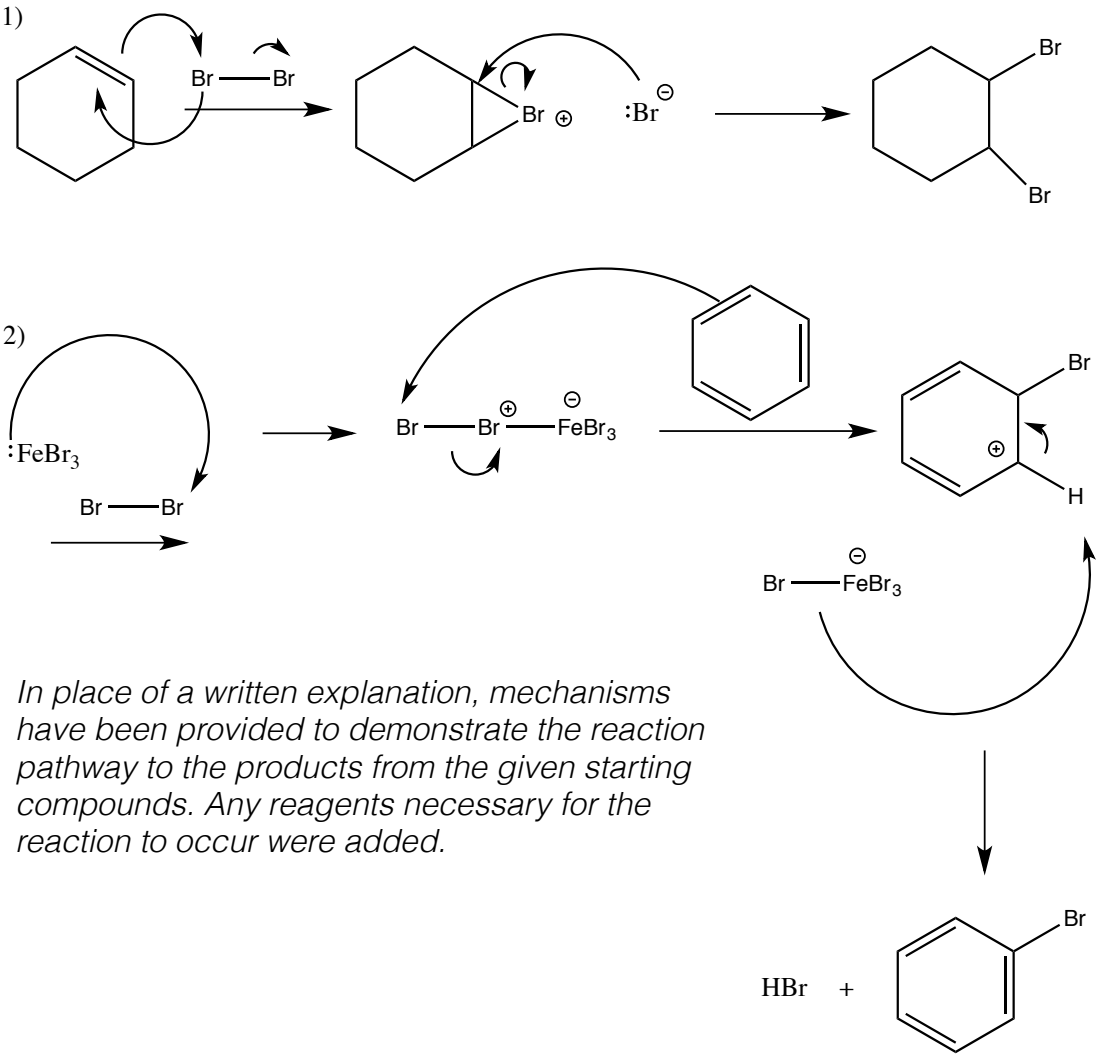
effect of the nitro group. Therefore, the second addition of a nitro group is an attack on a less reactive molecule, and so the reaction proceeds much slower.

4. Simply put, *para* isomers experience less steric hindrance based on their substituents positions on the ring. *Para* isomers have functional groups on opposite sides of the ring, while substituents on the *ortho* isomer are on adjacent carbons. Less steric hindrance translates to less destabilizing behaviour between substituents, and therefore a molecule with a more energetically favourable state.

5.



6.



In place of a written explanation, mechanisms have been provided to demonstrate the reaction pathway to the products from the given starting compounds. Any reagents necessary for the reaction to occur were added.

7.

a) Limiting reagent:

number of moles of **benzene** = 780g/ 78g/mol = 10 mols
number of moles of **HNO_3** = 0.750L*16 mol/L = 12 mols
number of moles of **H_2SO_4** = 0.750L* 18 mol/L = 13.5 mols

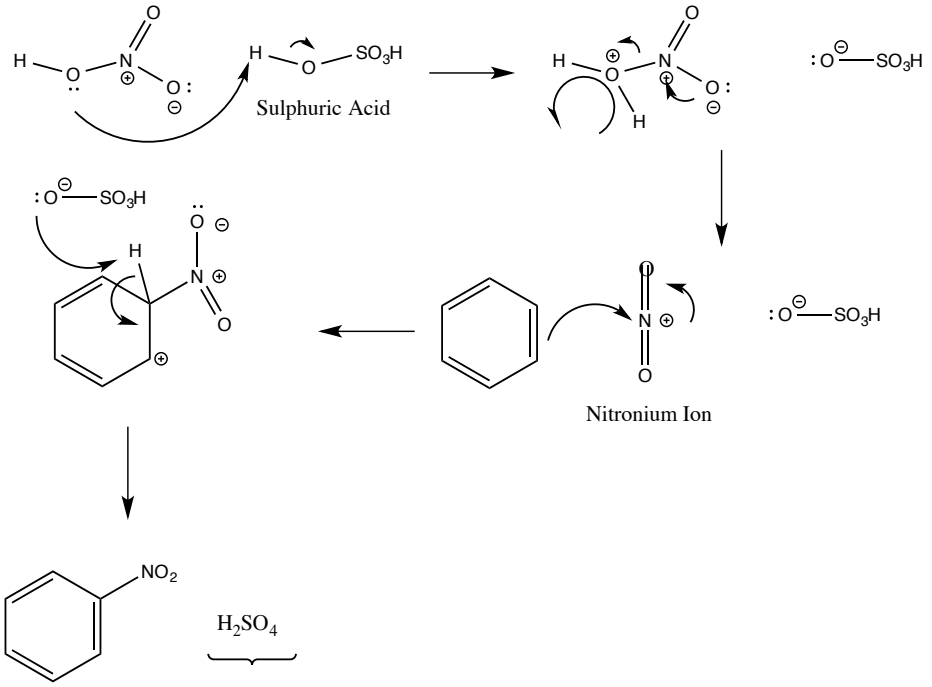
*Because all compounds are in a 1:1 ratio, **benzene** is the limiting reagent

so, theoretical yield of nitro benzene = 10 mols * (123g/mol)
= 1230g

b) %yield = actual/theoretical * 100%
= 1000g/1230g * 100%
= 81.30%

c) The most likely side product, X, is sulphuric acid. It is used as a catalyst in this reaction, and also has a boiling point 337 degrees celsius. Making it the most probable side product. (*see mechanism in part d))

d) Sulphuric acid is used as at catalyst in the reaction (acid hydrolysis), specifically to coax the formation of a positively charged nitronium ion. The following mechanism severs to demonstrate sulphuric acid's use in the formation of the nitronium ion and as a proof that the side product, X, was in fact sulphuric acid (from part c)):



Note the reformation of Sulphuric Acid

e)

	C_6H_6	NO_2^+	–>	$C_6H_5NO_2$	$C_6H_4N_2O_4$
Mass(g)	780	310.54		830.25	1134.73
Molar Mass (g/mol)	78	46.0055		123	168.11
Moles (mol)	10	6.7500		6.7500	6.7500

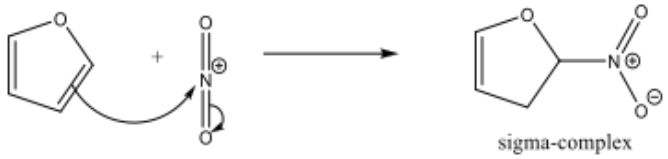
The above table calculates the number of mols for the compounds involved in the RXN. Note NO_2^+ *is the limiting reagent.*

% yield = actual/theoretical * 100%
= 250g/1134.73g * 100%
= 22%

Therefore, the percent yield of $C_6H_4N_2O_4$ is 22%

1.

8. Mechanism:



The 1-nitrofuran isomer is preferred because of the ability of the molecule to better stabilize its charges when the nitronium attacks that carbon. Due to the inductive effect, and the induced dipoles present on the molecule (delta positive on the carbon and delta negative on the oxygen), the molecule has a better chance of stabilizing itself. Therefore, the 1-nitrofuran isomer is more common and is more preferred than the 2-nitrofuran.

General Discussion:

The execution of the procedural steps were carried out with the intent of causing the nitration of acetanilide. As we know, the aromatic substitution of benzene has the possibility of producing three distinct isomers. These are known as the ortho, para and meta products. In this lab particularly, TLC plates were used to determine which aforementioned isomer was produced (i.e. Was the nitro group added to the para, ortho or meta position on the acetanilide molecule).

By examining the TLC plates (**See **observations** TLC plates*) it is clear that we produced, in the greatest amount, the **para** isomer of NO_2-Ph - $NHAc_{(aq)}$. To clarify, this conclusion was arrived upon by noting the extreme similarity in Rf values of the spotted sample of our crude product vs the spotted sample of the para isomer.

An explanation for *why* the para isomer seems to be the most favourable isomer of the 3 is simply. With two functional groups on the ring, the para position places them in the further possible location from each other on the ring. This reduces the steric hindrance the functional groups exert on each other when compared to the ortho and meta isomers. Less steric hindrance results in a lower activation state for this para isomer and therefore make its *more energetically favourable* compared to the other isomers, and so explains the preference for the formation of the para isomer.

Error Discussion:

We achieved an unrealistic percent yield of NO_2-Ph - $NHAc_{(aq)}$ 174%. We believe this extremely high yield can be easily explained by the fact that the product was still wet when we weighed it (unfortunately due to time constraints, we had no choice but to weigh without allowing for ample the product to dry).

Conclusion:

2.33g of *NO_2-Ph - $NHAc_{(aq)}$* was synthesized from *acetanilide* in this experiment, giving us a percent yield of **174%**.

1.