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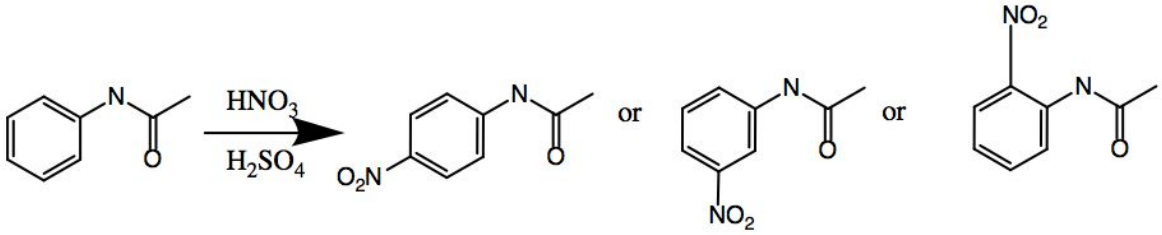
Lab Day (T/W/Th/F): W
Lab Week (even/odd): even
Lab time: 10:00

Experiment 6. Regioselective Nitration of Acetanilide

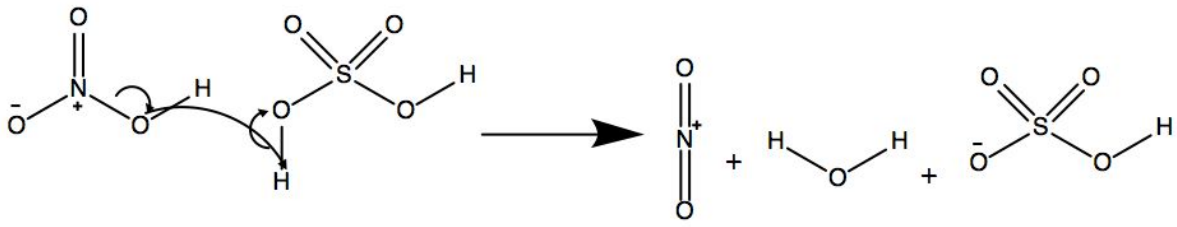
Initials: H.P.

Introduction:

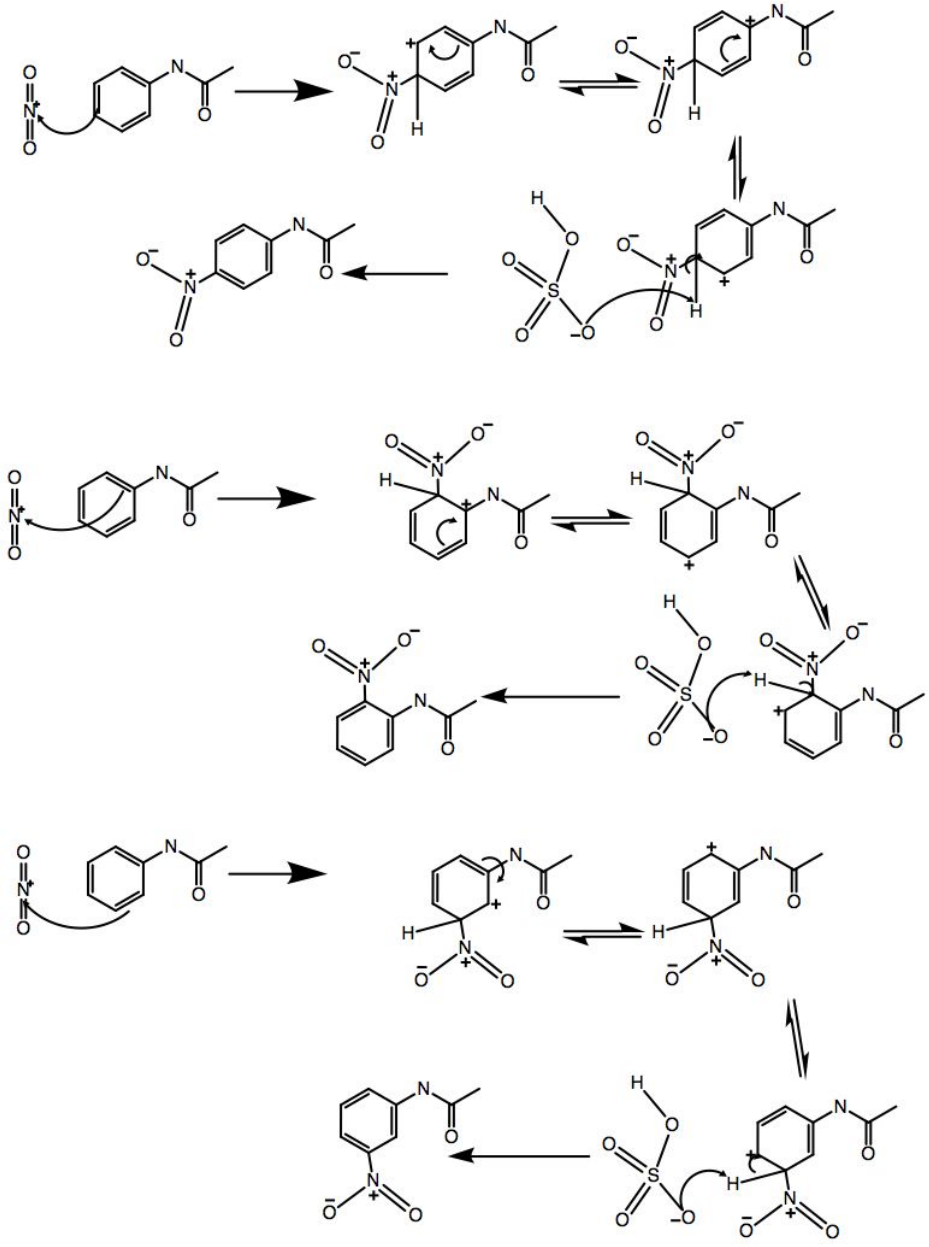
The nitration of acetanilide goes as such:



This requires the formation of nitronium as the electrophile. This is formed by the acid-base reaction of nitric and sulfuric acid, which goes as such:



The nitronium ion attacks the benzene ring, resulting into a multitude of isomers.



It is possible for a second nitration can occur in this reaction. However, this only affects 2- and 4-nitroacetanilide due to the strong deactivating effect of the nitro group direct the second nitro group towards a carbon position that is *meta* to it (which may be *ortho* or *para* relative to the acetamide group depend on the position of the first nitro group). The mechanism of the reaction of 4-nitroacetanilide into 2,4-dinitroacetanilide goes as such:

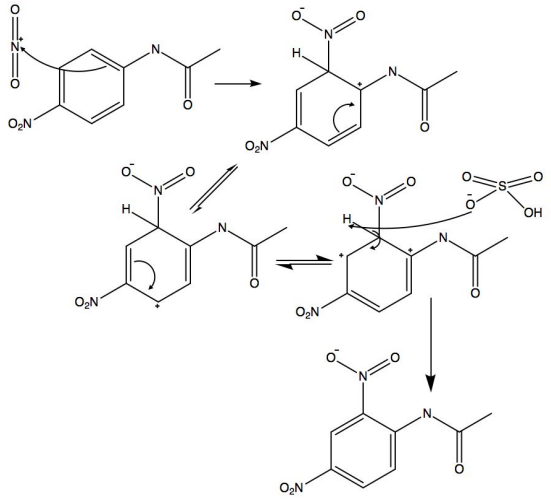


Table of Reagents

Compound	Mol. Wt (g/mol)	Amount	Density (g/mL)	mmol
Acetanilide	135.17	1 g		7.40
Sulfuric acid (solvent)	98.08	5 mL	1.84	
Sulfuric acid (reagent)	98.08	1.2 mL	1.84	
Nitric acid	63.01	0.9 mL	1.5129	
Water	18.01	20 mL	1	
Dichloromethane	84.927	2 mL	1.3255	
Ethanol (99%)	46.06		0.7893	

Procedure: (Refer to lab manual**)**

- 1 g of acetanilide was placed into a 50 mL round-bottom flask and clamped over a magnetic stirrer
- A stir bar was inserted into the flask
- 5 mL of concentrated sulfuric acid was carefully measured with a graduated cylinder and poured slowly into the flask. There was a brown colour
- The flask was stirred for one minute
- 1.2 mL of concentrated sulfuric acid and 0.9 mL of concentrated nitric acid was measured in separate graduated cylinders and carefully combined in a 50 mL Erlenmeyer flask. Heat was produced
- The acid mixture was carefully added to the reaction flask. Heat was produced
- The mixture was stirred for 10 minutes. The mixture became a dark brown colour.
- A TLC was taken of the reaction mixture with the original mixture as the reference and EtOAc:Hexanes 5:5 as the eluent solvent. This is to verify the completion of the reaction
- The stir bar was removed
- 4 small ice cubes were placed into 200 mL beaker along with 20 mL of cold water. The sit bar was inserted into the flask. The mixture was stirred.
- The content of the reaction flask was poured into the 125 mL flask and stirred until the ice melted
- The solid product was collected using suction filtration. 4.5 g of solid, yellow product was obtained. The filtered liquid was transparent and yellow.
- 2 small pieces of solid product was dissolved in 2 mL of dichloromethane.
- A TLC was taken with the dissolved product as the sample and 2-, 3-, 4- nitroacetanilide and 2,4 -dinitroacetanilide as the reference in a EtOAc:Hexanes 5:5 solvent system
- The TLC plates were developed and visualized under a UV lamp
- The remaining product was dissolved in a small volume of boiling ethanol. The ethanol boiled on a hot plate
- The flask was cooled to room temperature
- The crystals were collected suing suction filtration. 0.45 g of a yellow solid was obtained.
- TLCs were taken with the pure product (dissolved in acetone) as the sample and the mother liquor and dissolved crude product as the reference.
- The TLC plates were developed and visualized under a UV lamp

Data:

Table 1: Experimental data of TLC to verify completion of reaction

Measurement (cm)	Displacement
Solvent front (R_s)	4
Displacement of Reference	1.7
Displacement of Co-spot	N/A
Displacement of Reaction Mixture	2.9

Figure 1: TLC plate for the verification of the completion of reaction

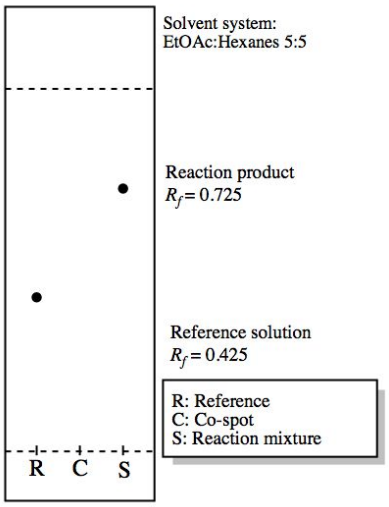


Table 2: Experimental data of TLC of crude product compared with 2-nitroacetanilide, 3-nitroacetanilide. 4-nitroacetanilide and 2,4-dinitroacetanilide references

Measurement (cm)	**Displacement**			
	2-nitroacetanilide reference	**3-nitroacetanilide reference**	**4-nitroacetanilide reference**	**2,4-dinitroacetanilide reference**
Solvent front (R_s)	4.2	4.0	4.0	4.1
Displacement of Reference	2.8	1.8	2.2	3.0
Displacement of Co-spot	1.2/2.3/2.9	1.7/2.6	2.2/2.75	1.75/3.0
Displacement of Reaction Mixture	1.3/2.3/2.8	1.7/2.6	2.2/2.7	1.75

Figure 2: TLC plate of crude product compared with o-nitroacetanilide, m-nitroacetanilide, p-nitroacetanilide and 2,4-dinitroacetanilide reference solution

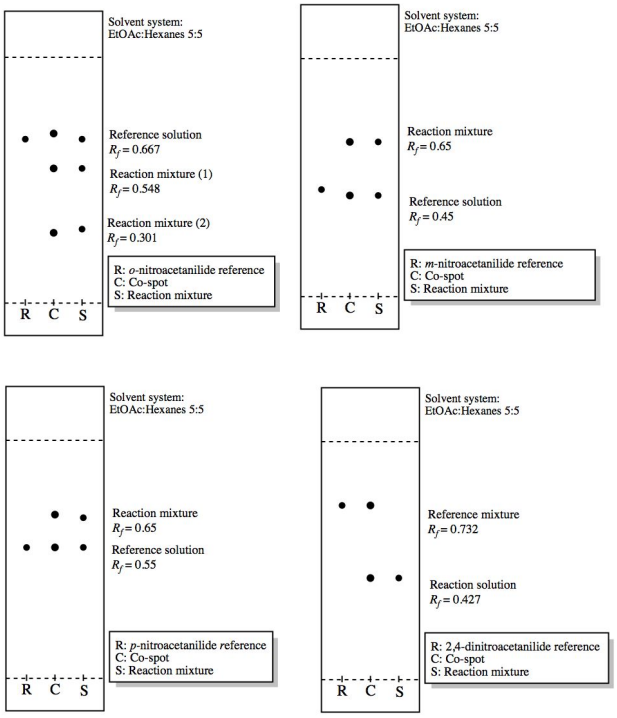
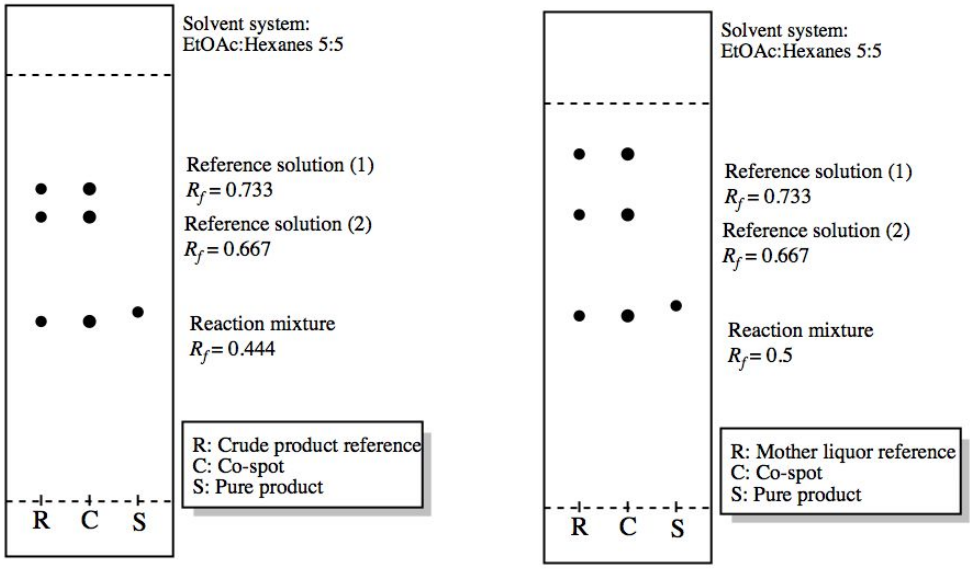


Table 2: Experimental data of TLC of pure product compared with crude product and mother liquor

Measurement (cm)	**Displacement**	
	Crude product reference	**Mother liquor reference**
Solvent front (R_s)	4.5	4.0
Displacement of Reference	1.9/3.0/3.3	1.9/2.9/3.5
Displacement of Co-spot	1.9/3.0/3.3	1.9/2.9/3.5
Displacement of Reaction Mixture	2	2

Figure 3: TLC plate comparing pure and crude product and mother liquor



Calculation:

Retention Factor:

TLC 1

Retention factor of Reference

$R_f = \frac{Displacement\ of\ Substance}{Displacement\ of\ solvent\ front} = \frac{1.7\ cm}{4.0\ cm} = 0.425$

Retention factor of Reaction mixture

$R_f = \frac{Displacement\ of\ Substance}{Displacement\ of\ solvent\ front} = 0.725$

TLC 2

Retention factor of Reference

$R_f = \frac{Displacement\ of\ Substance}{Displacement\ of\ solvent\ front} = \frac{2.8\ cm}{4.2\ cm} = 0.667$

Retention factor of Co-spot

$R_f = \frac{Displacement\ of\ Substance}{Displacement\ of\ solvent\ front} = 0.286/0.548/0.69$

Retention factor of Reaction mixture

$R_f = \frac{Displacement\ of\ Substance}{Displacement\ of\ solvent\ front} = 0.301/0.548/0.667$

TLC 3

Retention factor of Reference

$R_f = \frac{Displacement\ of\ Substance}{Displacement\ of\ solvent\ front} = \frac{1.8\ cm}{4.0\ cm} = 0.45$

Retention factor of Co-spot

$R_f = \frac{Displacement\ of\ Substance}{Displacement\ of\ solvent\ front} = 0.425/0.65$

Retention factor of Reaction mixture

$R_f = \frac{Displacement\ of\ Substance}{Displacement\ of\ solvent\ front} = 0.425/0.65$

TLC 4

Retention factor of Reference

$R_f = \frac{Displacement\ of\ Substance}{Displacement\ of\ solvent\ front} = \frac{2.2\ cm}{4.0\ cm} = 0.55$

Retention factor of Co-spot

$R_f = \frac{Displacement\ of\ Substance}{Displacement\ of\ solvent\ front} = 0.55/0.6875$

Retention factor of Reaction mixture

$R_f = \frac{Displacement\ of\ Substance}{Displacement\ of\ solvent\ front} = 0.55/0.675$

TLC 5

Retention factor of Reference

$R_f = \frac{Displacement\ of\ Substance}{Displacement\ of\ solvent\ front} = \frac{3.0\ cm}{4.1\ cm} = 0.732$

Retention factor of Co-spot

$R_f = \frac{Displacement\ of\ Substance}{Displacement\ of\ solvent\ front} = 0.427/0.732$

Retention factor of Reaction mixture

$R_f = \frac{Displacement\ of\ Substance}{Displacement\ of\ solvent\ front} = 0.427$

TLC 6

Retention factor of Reference

$R_f = \frac{Displacement\ of\ Substance}{Displacement\ of\ solvent\ front} = 0.422/0.667/0.733$

Retention factor of Co-spot

$R_f = \frac{Displacement\ of\ Substance}{Displacement\ of\ solvent\ front} = 0.422/0.667/0.733$

Retention factor of Reaction mixture

$R_f = \frac{Displacement\ of\ Substance}{Displacement\ of\ solvent\ front} = 0.444$

TLC 7

Retention factor of Reference

$R_f = \frac{Displacement\ of\ Substance}{Displacement\ of\ solvent\ front} = 0.475/0.725/0.875$

Retention factor of Co-spot

$R_f = \frac{Displacement\ of\ Substance}{Displacement\ of\ solvent\ front} = 0.475/0.725/0.875$

Retention factor of Reaction mixture

$R_f = \frac{Displacement\ of\ Substance}{Displacement\ of\ solvent\ front} = 0.5$

Percent yield

Acetanilide is the limiting reagent. For every one mole of acetanilide, one mole of acetanilide derivative is produced. Hence, the theoretical yield is 7.40 mmol. Since the *para* isomer is the major product, the theoretical yield is of that of 4-nitroacetanilide. The reaction product is composed of bi-substituent nitro-derivatives of benzene, hence, molar mass of the product is 180.16 g/mol. 0.45 g of pure product was obtained. 2.5 mmol was obtained.
As a result, there is a 33.78% yield of 4-nitroacetanilide crystals.

Composition (Crude product):

Absorbance of ortho: 20811

Absorbance of meta: 32212

Absorbance of para: 141589

%Absorption (ortho): $\frac{Absorption\ of\ isomer}{\Sigma Absorption} \times 100\% = 10.70$

%Absorption (meta): $\frac{Absorption\ of\ isomer}{\Sigma Absorption} \times 100\% = 16.55$

%Absorption (para): $\frac{Absorption\ of\ isomer}{\Sigma Absorption} \times 100\% = 72.75$

Mole percentage (o:p):

x = %Absorption (ortho) = 10.70%

$Y = 0.0079391x^2 + 0.15962x + 3.3788 = 6$

Mole percentage of *ortho*: 6%

Mole percentage (m:o):

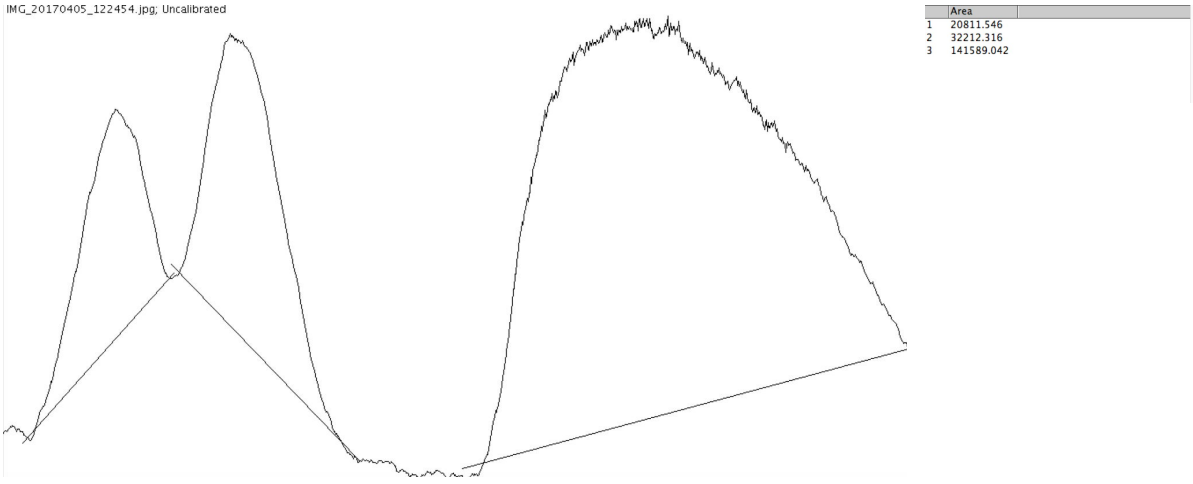
x = %Absorption (meta) = 16.55%

$Y = 0.007757x^2 + 0.067612x + 1.6469 = 4.89$

Mole percentage of *meta*: 4.89%

Mole percentage of *para*: 100% - 4.89% - 6% = 89.11%

Figure 4: ImageJ analysis data of crude product lane



Composition (Mother liquor):

Absorbance of ortho: 20811
Absorbance of meta: 52166
Absorbance of para: 57264

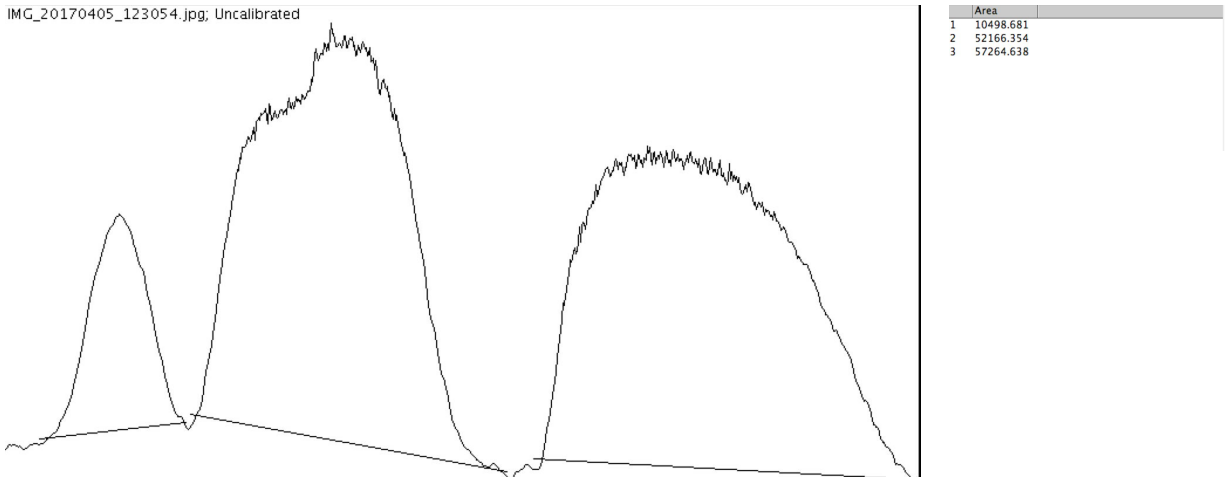
%Absorption (ortho): $\frac{Absorption\ of\ isomer}{\Sigma Absorption} \times 100\% = 16$
%Absorption (meta): $\frac{Absorption\ of\ isomer}{\Sigma Absorption} \times 100\% = 40$
%Absorption (para): $\frac{Absorption\ of\ isomer}{\Sigma Absorption} \times 100\% = 44$

Mole percentage (o:p):
x = %Absorption (ortho) = 16%
$Y = 0.0079391x^2 + 0.15962x + 3.3788 = 7.97$
Mole percentage of *ortho*: 7.97%

Mole percentage (m:o):
x = %Absorption (meta) = 40%
$Y = 0.007757x^2 + 0.067612x + 1.6469 = 16.76$
Mole percentage of *meta*: 16.76%

Mole percentage of *para*: 100% - 7.97% - 16.76% = 75.27%

Figure 5: ImageJ analysis data of mother liquor lane



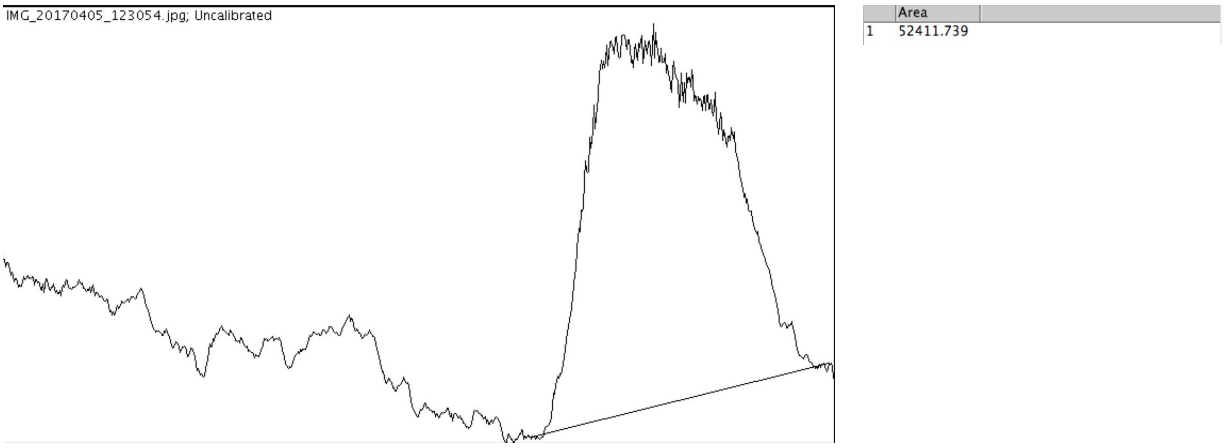
<u>Composition (Pure product):</u>
Absorbance of ortho: 0

Absorbance of meta: 0
Absorbance of para: 52411

%Absorption (ortho): $\frac{Absorption\ of\ isomer}{\Sigma Absorption} \times 100\% = 0\%$
%Absorption (meta): $\frac{Absorption\ of\ isomer}{\Sigma Absorption} \times 100\% = 0\%$
%Absorption (para): $\frac{Absorption\ of\ isomer}{\Sigma Absorption} \times 100\% = 100\%$

Mole percentage of *para*: 100%

Figure 6: ImageJ analysis data of pure product lane



Discussion:

The reaction is likely complete considering that the retention factors of the reference lane and the reaction product lane are completely different.

Based on the obtained retention factors of the crude product and the reference solutions, the reaction mixture is likely composed of *o-, m-,* and *p*-nitroacetanilide since the spots of reaction mixture possess retention factors that are similar to the retention factors of those isomers: 0.667 to 0.667, 0.45 to 0.425, and 0.55 to 0.55 respectively. The analysis of the TLC lanes of the crude product and the mother liquor through ImageJ indicates that *p*-nitroacetanilide is the major product and *o, m*-nitroacetanilide are the minor products. This is consistent with the

concept of the direct effect of the substituent in the sense that the secondary amine attached to the benzene is a strong activator by stabilizing the sigma complex through induction, which means that the major product should be in the *ortho-para* configuration. In addition, the comparison between the crude product and mother liquor indicates that the process of suction filtration showed some success in the extraction of the *para* isomer as seen in the decrease in the mole percentage of the *para* isomer. However, it is not a complete extraction of the *para* isomer from the liquor since a spot indicating the presence of that isomer is on the mother liquor lane. It appears that the process of recrystallization is successful in removing the impurities but had limits in prevent some of the desired product from dissolving into the solvent. Alterations to the temperature of the solvent may be recommended.

The percent yield of the major product is relatively low with 33.78%. This is correlated by the minor decrease in mole percentage of *p*-nitroacetanilide between the crude product and the mother liquor.

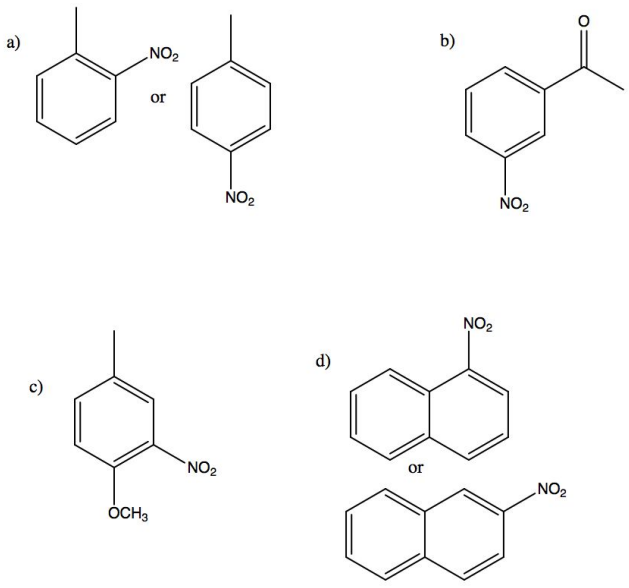
One potential issue that may arise during the experiment stemmed from the addition of the acid mixture to the dissolved acetanilide, where the heat produced by the reaction of the mixture with the acetanilide has the potential to cause some of the reactants to evaporate, limiting the mass of product obtained and hence, the percent yield. This can be solved through the slow addition of the mixture to allow time for the reaction container to cool down so that vaporization will less likely occur. Another issue that is derived from the heat of the reaction container is that with that increased temperature, there is more kinetic energy that can contribute to the reaction, meaning that alternative reactions may occur if the activation energy is low enough. This may explain the production of a *meta* product, which has a greater activation energy due to the relative instability of the sigma complex. This can be resolved through the slow addition of the acid mixture into the flask of dissolved acetanilide.

Question:

1. Based on the observations of the TLC plates, it appears that the *para* isomer has a greater polarity than the *ortho* isomer since the *para* isomer has a lesser retention factor and displacement, implying that the *para* isomer experiences greater resistance due to the polarity of the silica gel. The lesser resistance towards the *ortho* isomer is due the steric interference on the nitro group by the adjacent substituent. This interference may limit the interactions between the charged nitro group and the surface of polar silica gel. While for the *para* isomer, there is minimal interference from the other group, allows a greater potential for the nitro group to interact with the silica gel.
2. The addition of a second nitro group in this reaction much slower than the first nitration of the reagent due to how the nitro group acts as a strong deactivator in electrophilic aromatic substitutions. The nitro group is a strong deactivator because in the nitro group,

the nitrogen atom has a positive charge, which causes the atom to have an electron-withdrawing effect on the aromatic molecule. That withdrawing of electron density causes the destabilization of the positively charged sigma complex, which increases the activation energy of the reaction. This decreases the overall rate of reaction.

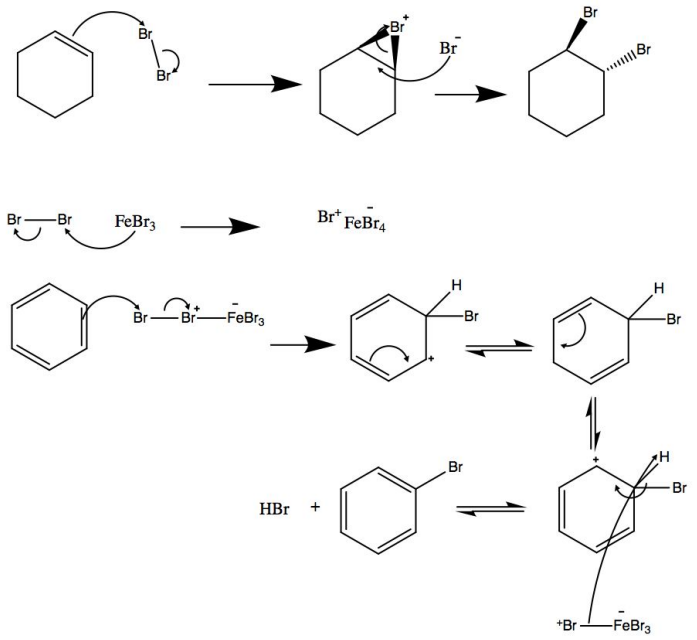
3. *Para* isomers are favoured over *ortho* isomers in electrophilic aromatic substitutions because when forming the *ortho* isomer, there is steric hindrance from the other substituent group while in the formation of the *para* isomer, there is no steric hindrance from the other substituent group.



4.

5. For the reaction with cyclohexene, the bromides perform an *anti* electrophilic addition on the pi bond of the cyclohexene. However, this will not occur with the benzene as a result of the aromatic stability of the ring from the resonance and delocalization of electrons that are of a low energy state. Instead, an electrophilic aromatic substitution occurs in which, after the formation of a iron (III) bromide complex, a bromide ion attacks a pi bond of the benzene, resulting in a sigma complex. The electron density within the sigma complex then undergoes alterations that result in the expulsion of a hydrogen atom and

the subsequent formation of a pi bond.



6. a) Moles of benzene: 10 mol Moles of HNO_3: 12 mol Moles of H_2SO_4: 12.5 mol
Hence, benzene is the limiting reagent.

b) For every one mole of benzene reacted with, one mole of nitrobenzene would be produced. Hence, theoretically, 10 mol of nitrobenzene is produced.

Moles of nitrobenzene (experimentally): 1000 g of nitrobenzene/123 g/mol = 8.13 mol

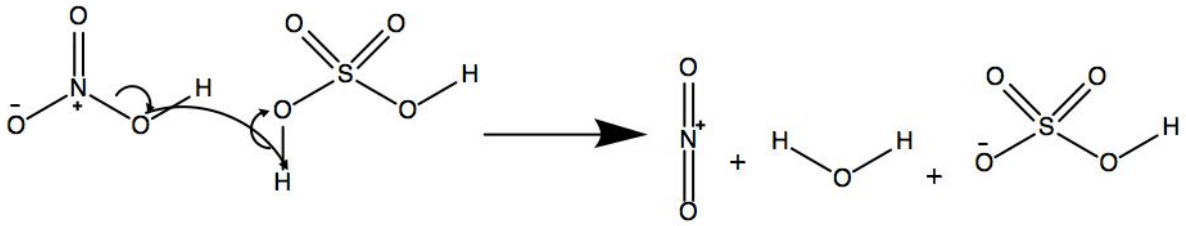
Percent Yield = $\frac{Experimental\ Yield}{Theoretical\ Yield} \times 100\%$

$= \frac{8.13\ moles\ of\ nitrobenzene}{10\ moles\ of\ nitrobenzene} \times 100\% = 81.3\%.$

Therefore, the percent yield is 81.3%.

c) The side product is most probably dinitrobenzene.

d) The role of sulfuric acid is to serve to produce the nitronium ions along with nitric acid. Through the production of nitronium ions, there is an electrophile that can perform the electrophilic aromatic substitution of benzene.



e) Based on a), there is, in theory, 1.87 moles of side product. Molar mass = 168.11 g/mol. Theoretical mass = 314.37 g. Experimental mass = 250 g.

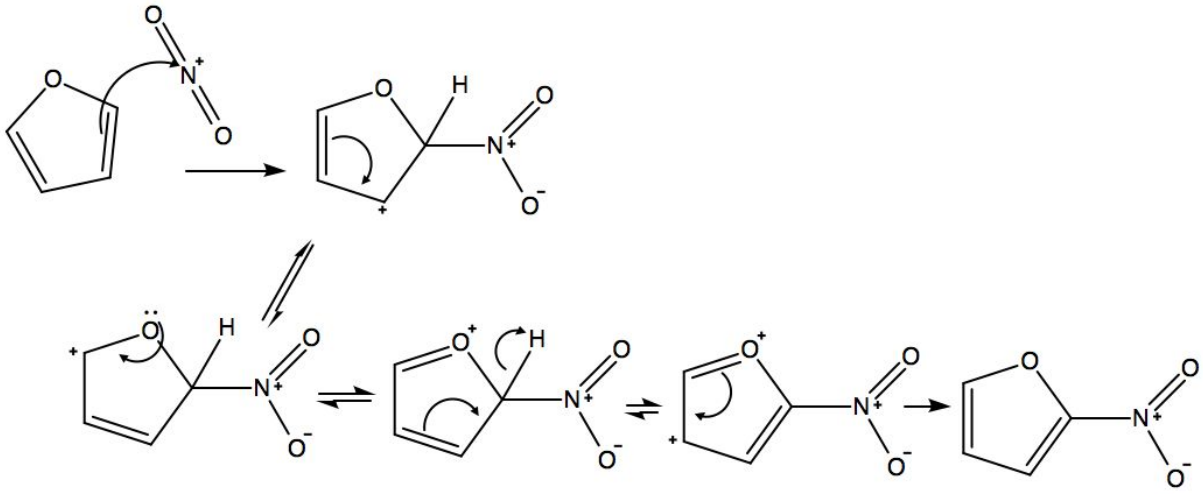
Percent Yield = $\frac{Experimental\ Yield}{Theoretical\ Yield} \times 100\%$

$= \frac{250\ g}{314.37\ g} \times 100\% = 79.5\%.$

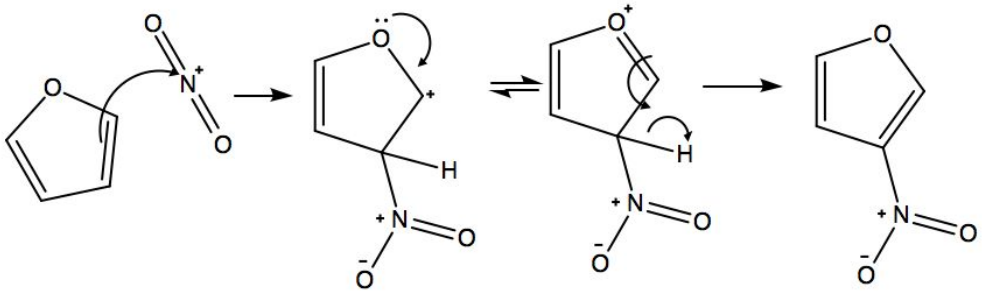
Therefore, the percent yield is 79.5%.

7. The nitration of furn into 1-nitrofuran is more preferable than into 2-nitrofuran due to how the formation of 1-nitrofuran has a more stable (a result of having more resonance structures) sigma complex than that of 2-nitrofuran.

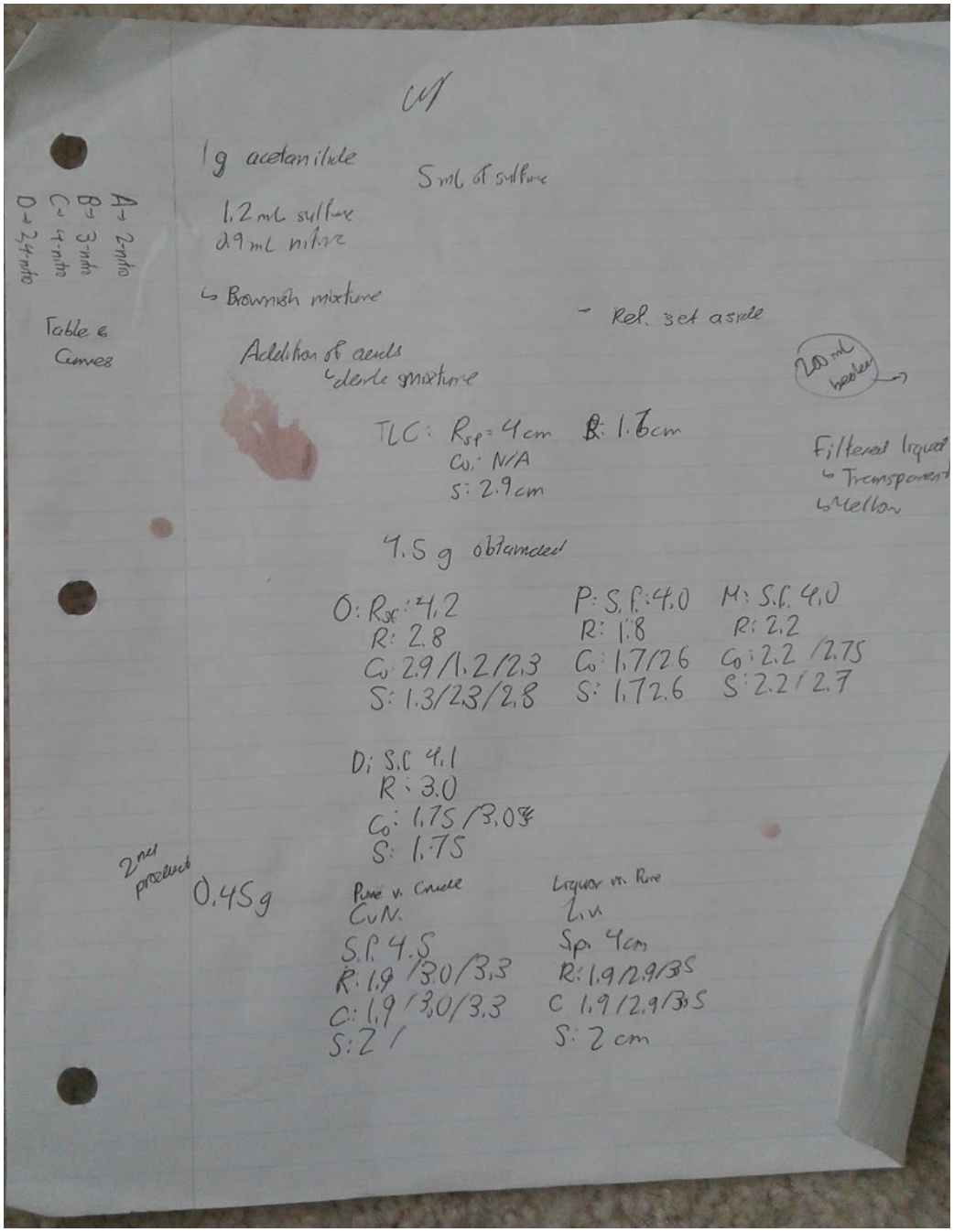
Formation of 1-nitrofuran



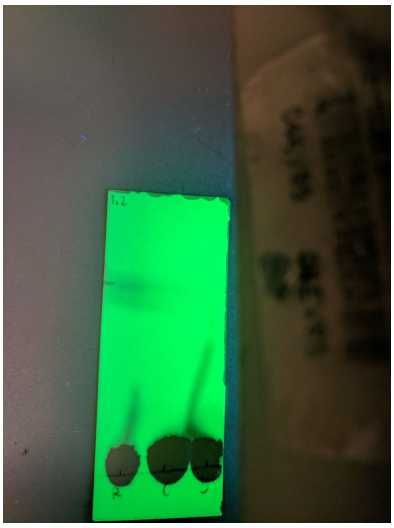
Formation of 2-nitrofuran

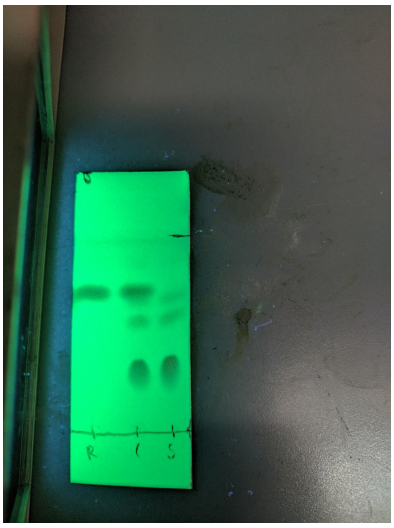


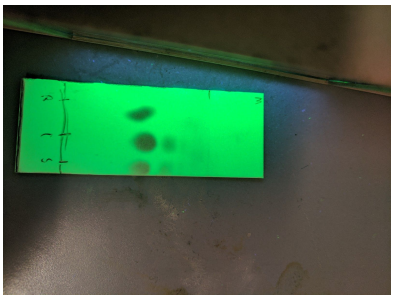
Raw Data:

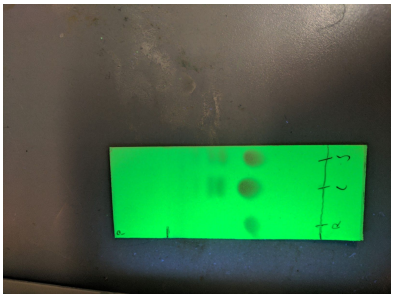

1g acetanilide
5mL of sulfuric
1.2mL sulfuric
2.9mL nitric
Brownish mixture
Ref. set aside
Addition of acids
Table & Curves
TLC: Rsf = 4cm B: 1.6cm
Co: N/A
S: 2.9cm
Filtered liquid
Transparent
Yellow
4.5g obtained
O: Rsf: 4.2
R: 2.8
Co: 2.9/1.2/2.3
S: 1.3/2.3/2.8
P: S.f.: 4.0
R: 1.8
Co: 1.7/2.6
S: 1.7/2.6
M: S.f. 4.0
R: 2.2
Co: 2.2/2.75
S: 2.2/2.7
D: S.f. 4.1
R: 3.0
Co: 1.75/3.0
S: 1.75
2nd product
0.45g
Pure v. Crude
Co.N.
S.f. 4.5
R: 1.9/3.0/3.3
C: 1.9/3.0/3.3
S: 2/
Liquor vs. Pure
L.v.
Sp. 4cm
R: 1.9/2.9/3.5
C 1.9/2.9/3.5
S: 2cm

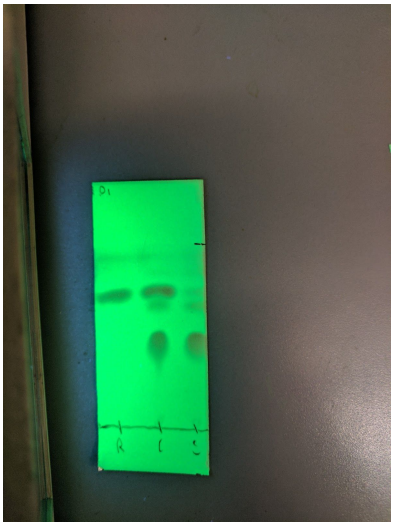
TLC Photos

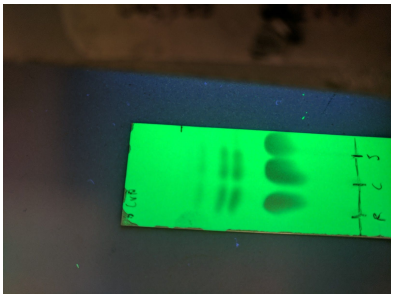


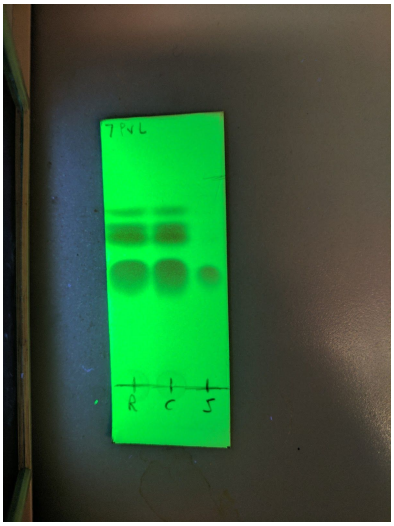












Calibration Curves