LAB 6:

REGIOSELECTIVE NITRATION OF ACETANILIDE

Submitted by:

[redacted]	[redacted]
[redacted]	[redacted]

Submitted to: Vimarsha

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uOttawa

Faculté des sciences
Faculty of Science

CHM1321 - Z05

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Procedure

See lab manual Experiment 6: Regioselective Nitration of Acetanilide (pg 1-7) .

Mechanism

Figure 1.0 Mechanism for the formation of the nitronium ion

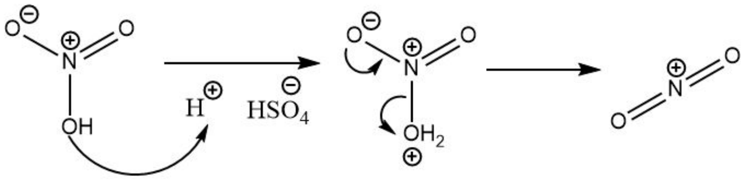


Figure 1.1 Mechanism for the ortho isomer. B represents a protonating base

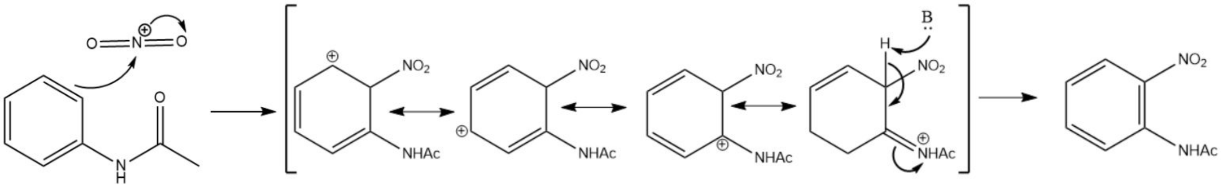


Figure 1.2 Mechanism for the meta isomer. B represents a protonating base

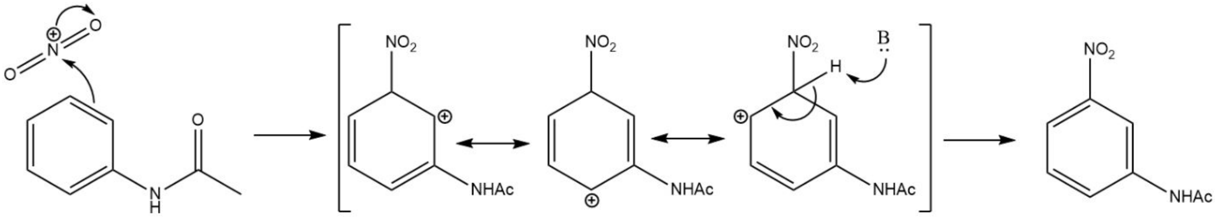
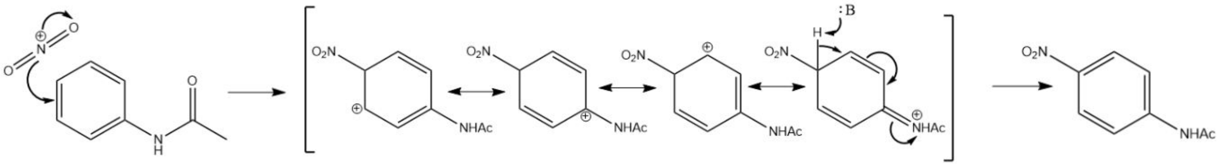


Figure 1.3 Mechanism for the meta isomer. B represents a protonating base



Qualitative Observations

- Acetanilide was a greyish brown flaky crystal.
- H2SO4 was a clear colourless solution
- Once the H2SO4 was added to the acetanilide some of the crystals dissolved, but not all. There was no change in the colour of the solution.
- After placing the mixture in an ice bath with a stir bar for 10 minutes more of the acetanilide dissolved. There was no visible change in the mixture.
- The nitric acid and sulfuric acid mix was then added. This mixture was clear and colourless, as well.
- After the entire mixture was stirred for 10 minutes, there was a noticeable difference in the colour of the mixture. The mixture was a dark brown colour and only a few specks of acetanilide crystals had not dissolved.
- When a TLC of the reaction mixture was taken before eluting the TLC the reaction mixture stained the plate a dark brown colour. During the TLC a yellow streak could be seen going up the TLC plate with the eluent from the dark brown spot. The yellow stain remained on the TLC plate after drying.
- Once the reaction mixture was in contact with the ice and water, it becomes yellow immediately. There is a yellow solid that has also precipitated out of the solution.
- This precipitate was more clearly seen to be an orange-yellow colour upon filtering it. This was the crude product
- Boiling ethanol had to be added to the crude product. Ethanol was a clear colourless liquid. Ethanol was added until the solution turned clear. The solution was now a dark red orange colour.
- Upon boiling down the mixture, it became an even darker red colour.
- The mixture was then cooled until precipitate formed. This precipitate was then filtered to obtain the final product. The final product was an orange coloured powdery crystal.

Quantitative Observations

Table 1.0. Reagents involved in the reaction

Reagent	Amount (g or ml)	Molecular Weight (g/mole)*	Moles (mmol)	Density (g/ml)
Acetanilide	1.01 g	135.166	7.47	-
H2SO4 (first time)	5.0 ml	98.072	108.82	1.84
H2SO4 (second time)	0.8 ml			
HNO3	0.6 ml	63.012	14.38	1.51

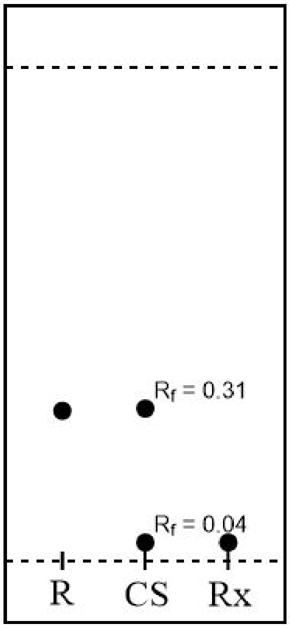
*Molecular weights for reagents from (National Center for Biotechnology Information. PubChem Compound Database; CID=904, CID=11184, CID)

TLC's

Legend:

d_s = displacement between former and new solvent line
d_X= displacement between starting solvent line and molecule
● = 1 Spot visible under UV light

Figure 2.0. TLC testing whether or not the reaction was complete using acetanilide as a reference

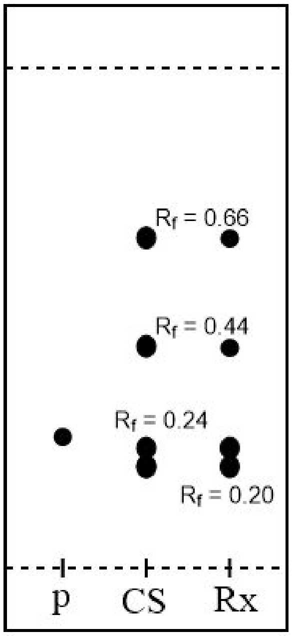


Solvent System:
EtOAc:hex
5:5

displacements:
d_s= 5 cm
Rf = 0.31→
dx = 1.6 cm
Rf = 0.04 →
dx = 0.2 cm

Ref = reference
CS = Co-Spot
Rx= reaction product

Figure 2.1 TLC of crude product and the para isomer as a reference

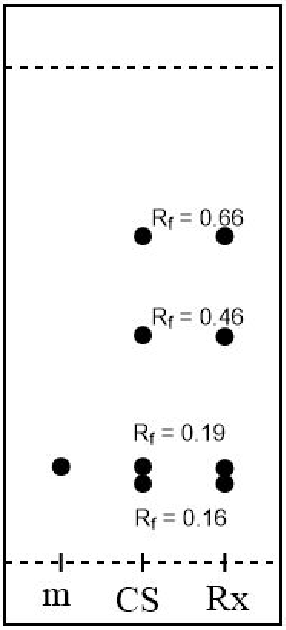


Solvent System:
EtOAc:hex
5:5

displacements:
d_s= 5 cm
Rf = 0.66→
dx = 3.3 cm
Rf = 0.44 →
dx = 2.2 cm
Rf = 0.24 →
dx = 1.2 cm
Rf = 0.20 →
dx = 1.0 cm

P= para isomer
CS = Co-Spot
Rx= reaction product

Figure 2.2. TLC of crude product and the meta isomer as a reference

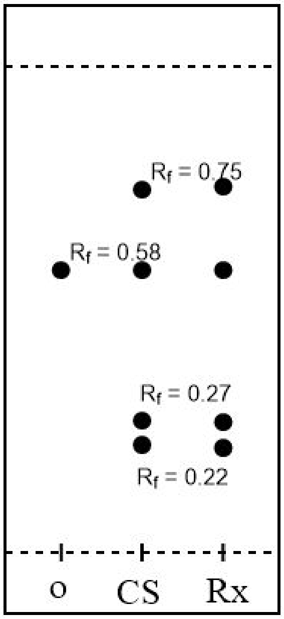


Solvent System:
EtOAc:hex
5:5

displacements:
d_s= 4.8 cm
Rf = 0.66→
dx = 3.2 cm
Rf = 0.46 →
dx = 2.2 cm
Rf = 0.19 →
dx = 0.9 cm
Rf = 0.16 →
dx = 0.8 cm

M = meta isomer
CS = Co-Spot
Rx= reaction product

Figure 2.3. TLC of crude product and the ortho isomer as a reference

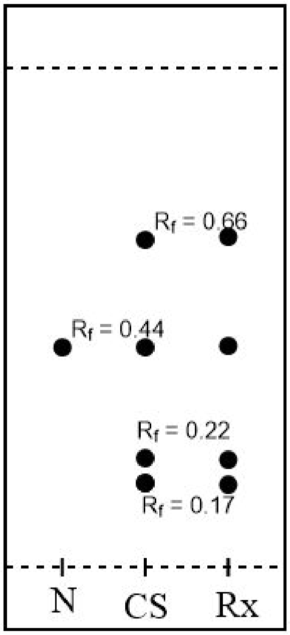


Solvent System:
EtOAc:hex
5:5

displacements:
d_s= 4.5 cm
Rf = 0.75→
dx = 3.6 cm
Rf = 0.58→
dx = 2.8 cm
Rf = 0.27 →
dx = 1.3 cm
Rf = 0.22 →
dx = 1.0 cm

o = ortho isomer
CS = Co-Spot
Rx= reaction product

Figure 2.4. TLC of crude product and the 2,4-dinitro isomer as a reference

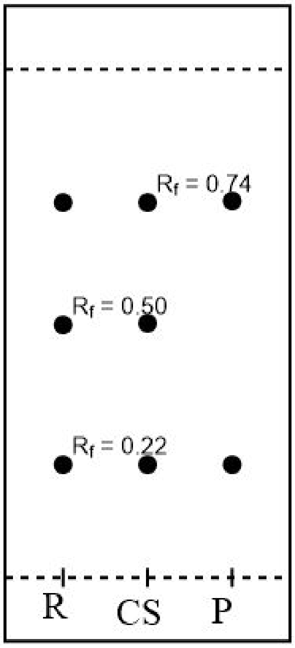


Solvent System:
EtOAc:hex
5:5

displacements:
d_s= 4.5 cm
Rf = 0.66→
dx = 3.0 cm
Rf = 0.44→
dx = 2.0 cm
Rf = 0.22 →
dx = 1.0 cm
Rf = 0.17 →
dx = 0.8 cm

N = 2,4- dinitro
CS = Co-Spot
rm = reaction product

Figure 2.5. TLC of purified product vs the crude product (reference)

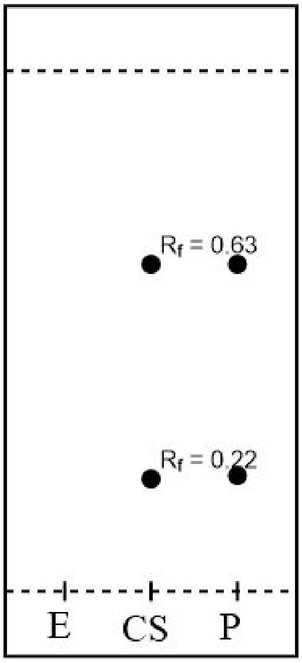


Solvent System:
EtOAc:hex
5:5

displacements:
d_s= 4.6 cm
Rf = 0.74→
dx = 3.4 cm
Rf = 0.50→
dx = 2.3 cm
Rf = 0.22 →
dx = 1.0 cm

Ref = reference
CS = Co-Spot
P = Product of reaction

Figure 2.6. TLC of purified product using ethanol as a reference



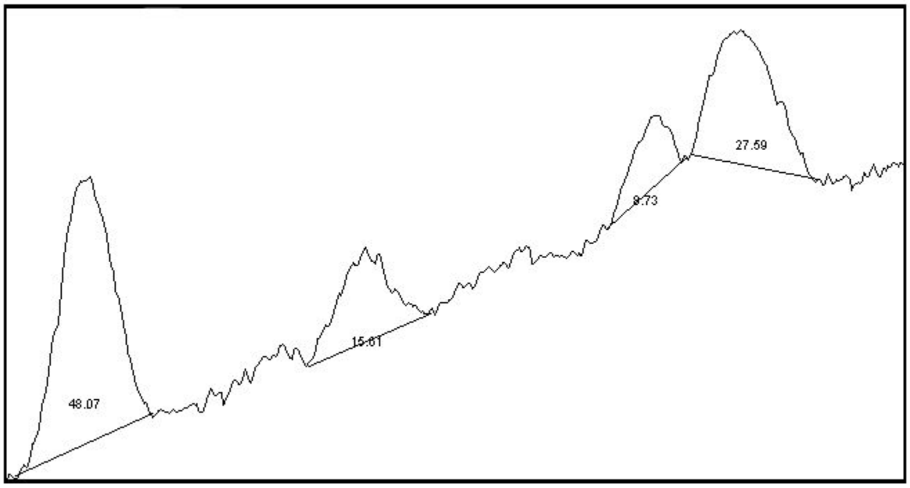
Solvent System:
EtOAc:hex
5:5

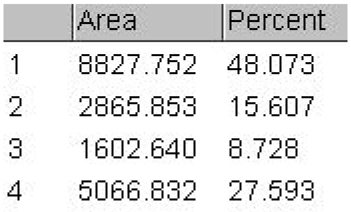
displacements:
d_s= 4.9 cm
Rf = 0.63→
dx = 3.1 cm
Rf = 0.22→
dx = 1.1 cm

E= ethanol
CS = Co-Spot
P = Product of reaction

ImageJ Analysis

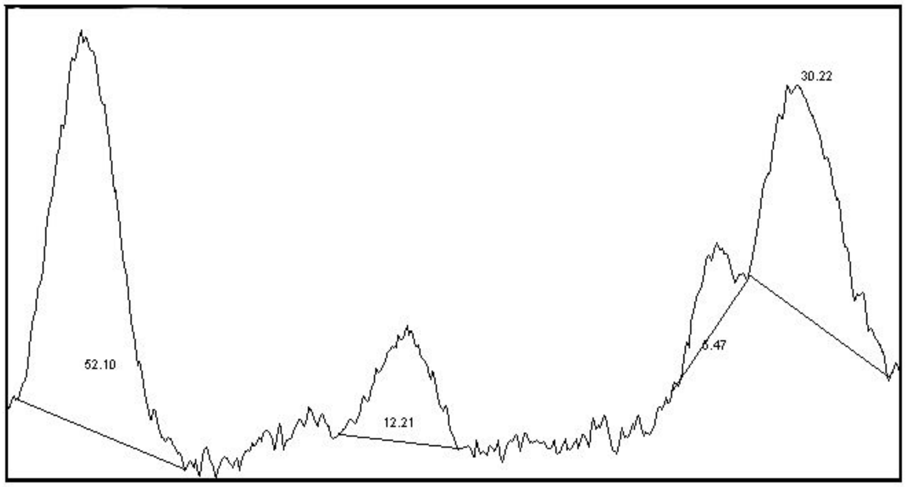
Fig 3.1: Analysis of TLC from figure 2.1





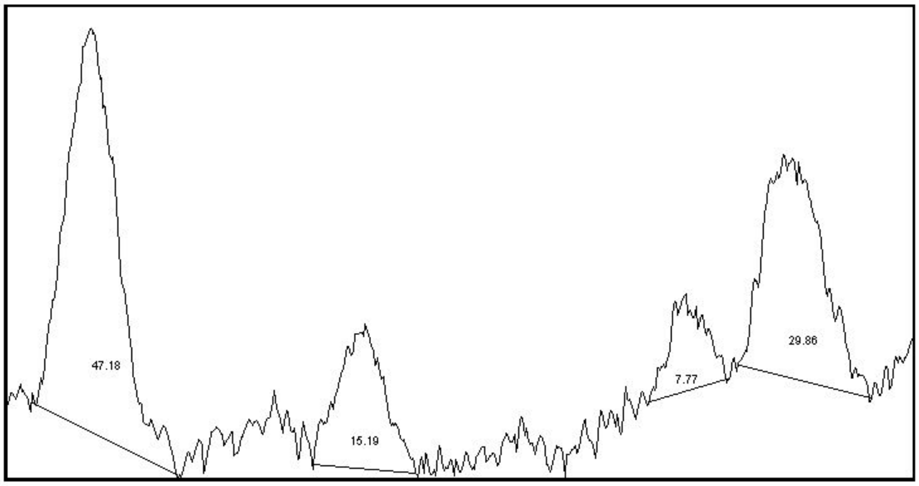
	Area	Percent
1	8827.752	48.073
2	2865.853	15.607
3	1602.640	8.728
4	5066.832	27.593

Fig 3.2: Analysis of TLC from figure 2.2



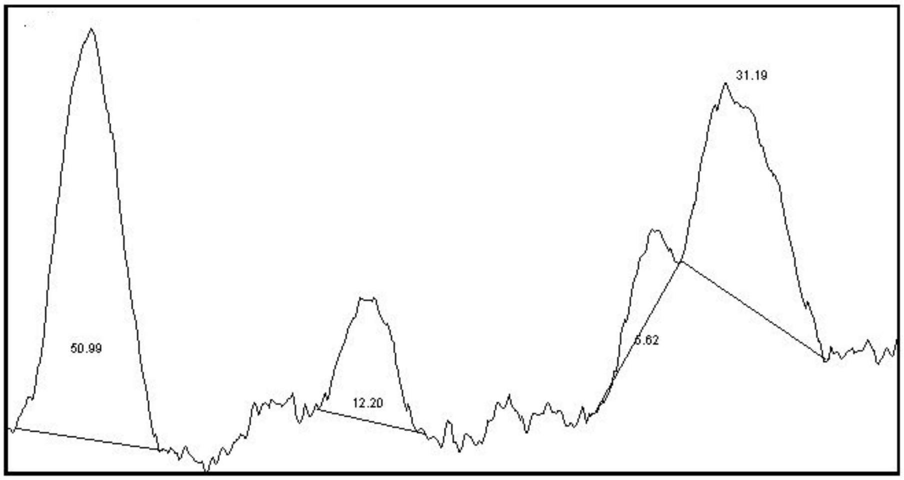
	Area	Percent
1	15615.208	52.100
2	3658.882	12.208
3	1639.640	5.471
4	9057.915	30.222

Fig 3.3: Analysis of TLC from figure 2.3



	Area	Percent
1	15201.673	47.184
2	4893.518	15.189
3	2502.154	7.766
4	9620.510	29.861

Fig 3.4: Analysis of TLC from figure 2.4



	Area	Percent
1	15328.853	50.991
2	3666.690	12.197
3	1690.518	5.623
4	9375.915	31.189

Table 2.0. Ratios of substances (% composition) in the crude product from the ImageJ and Calibration curves

	Ortho %	**Para %**	**Meta %**	**2,4-dinitro%**
From TLC 2.1	15.52	62.07	1.72	20.69
From TLC 2.2	16.82	63.29	5.99	13.99
From TLC 2.3	16.72	66.87	2.72	13.70
From TLC 2.4	16.50	62.07	1.83	19.60

Table 3.0. Results regarding the final product

Product	**Amount (g or ml)**	**Molecular Weight (g/mole)***	**Moles (mmol)**	**% Yield**
nitroacetanilide	0.50	180.163	2.8	37.5

* Molecular weights for reagents from (National Center for Biotechnology Information. PubChem Compound Database; CID=7691)

Calculations

Sample Rf Calculation, Figure 2.0

Given:	*Calculation:*
d_s= 5.0 cm $d_{R,\ CS(highest)}$ = 1.6 cm $d_{Rx,\ CS(Lowest)}$ = 0.2 cm	**$Rf = d_x/d_s$** $Rf_{R,\ CS(highest))}$ = 5.0 cm / 1.6 cm = 0.31 $Rf_{Rx,\ CS(Lowest)}$ = 0.2 cm / 5.0 cm = 0.04

Calculation of the percent yield of benzoic acid product

For every one mole of acetanilide one mole of product (derivatives of nitroacetanilide is formed). This means that in theory there should have been a yield of 7.47 mmol. Furthermore, the para isomer is the major product, thus the molar mass of the product is that of p-nitroacetanilide giving an actual yield of 2.8 mmol.

$$\% \text{ Yield} = \frac{\text{actual yield (in mmol)}}{\text{theoretical yield (in mmol)}} \times 100$$

$$\% \text{ Yield} = \underline{\text{\# of mol of product}} \times 100$$

# of mol of starting material

$$\% \text{ Yield} = \frac{2.8 \text{ mmol}}{7.47 \text{ mmol}} \times 100$$

% Yield = 37.5%

Sample Calculation to find ratios of Crude Product using ImageJ using results from fig 3.1

From ImageJ
Ortho % = 27.593
Para % = 48.073
Meta % = 15.607
Dinitro % = 8.728

Now all three calibration curves must be used to find the exact percentage from a standard sample

For Ortho:Para
Excluding Dinitro and Meta

Ortho% = (27.593) x 100 / (27.593 + 48.073) = 36.71
Para% = (48.073) x 100 / (27.593 + 48.073) = 63.29

Actual % (y) using calibration curve formula where x = 36.71
$y = 0.0079391x^2 + 0.15962x + 3.3788$
y = 20% ⇒ Actual Ortho%

So, actual Para % = 100-20=80

So the ratio of o:p is 1:4

For Meta:Ortho
Excluding Dinitro and Para

Meta% = (15.607) x 100 / (15.607+27.593) = 28.77
Ortho% = (27.593) x 100 / (27.593+15.607) = 71.23

Actual % (y) using calibration curve formula where x = 28.77
$y = 0.007757x^2 + 0.067612x + 1.6469$
y = 10% ⇒ Actual Meta%

So, actual Ortho % = 100-10=90

So the ratio of m:o is 1:9

For Dinitro:Para
Excluding Ortho and Meta
Dinitro% = (8.728) x 100 / (48.073+8.728) = 9.50
Para% = (48.073) x 100 / (48.073+8.728) = 90.50

Actual % (x) using calibration curve formula where y = 9.50
$y = 0.0227x^2-1.6809x+37.421$
Using quadratic formula we get :
x = 25% ⇒ Actual Dinitro%

So, actual Para % = 100-25=75

So the ratio of d:p is 1:3

Finally the ratio of o:p:m:d = 9:36:1:12
Which gives the final % values as:
Ortho % composition =15.52%
Para % composition = 62.07%
Meta % composition = 1.72%
Dinitro % composition = 20.69%

Discussion

In this experiment, acetanilide, a benzene ring compound with an amide functional group (NHAc) was nitrated through electrophilic aromatic substitution in order to observe regioselectivity. Acetanilide has an electron donating group attached as a functional group. This is the amide, NHAc. We know this because Nitrogen is relatively less electronegative and thus, won't hold on to electrons, instead preferring to give them away or donate them. This means that it will lower the Energy of the arenium ion, which is an intermediate in the nitration of acetanilide (“Experiment 6 : Regioselective Nitration of Acetanilide,” 2014). Due to a lower energy, the arenium ions are stabilized and the positive charge can be dispersed through resonance. This theoretically means that the final product will contain more ortho and para products. This is better seen as the mechanism for ortho and para products have 1 more resonance form than the meta products and these forms also have all atoms with full octets. Between ortho and para products, the para products are more preferred and therefore, are the major products. This is because of steric interaction. Due to the close proximity of the functional groups in the ortho products, they will interact (“Experiment 6 : Regioselective Nitration of Acetanilide,” 2014). This can cause changes to the structure of the ortho-acetanilide, whereas in para-acetanilide there can be no interaction because the functional groups are on opposite ends of the benzene ring and, so can be considered more stable.

For the nitration reaction, the nitronium ion was produced from the reaction of sulfuric acid (H2SO4) and nitric acid (HNO3) (see figure mech). Which is why both acids were required in this experiment. During the experiment, the reaction mixture was kept cold and the acid mixture was added very slowly because adding the reaction would be very exothermic and adding the acid slowly would prevent any sudden outbursts of bubbling or even an explosion due to the large excess of nitric acid with benzene providing fuel and the nitro groups as oxidizers. The cooling would also have allowed for the exothermic reaction to slow down a bit and decrease the amount of 2,4-dinitroacetanilide being produced. 2,4-dinitroacetanilide is formed by the overreaction of the para-acetanilide products with excess amounts of the nitronium ion.

TLC and Imagej analysis

The first TLC (figure 2.0) was taken to check whether or not the reaction was complete, which it was as none of the starting material (the reference) was showing in the reaction material. The next 4 TLCs were taken to see which isomers were in the crude product. All of which showed to be there (ortho, meta, para and dinitro) because the R_f values of the references are similar to some of the spots in the crude product lane. Then the next purification happened and the crude product which previously showed all isomers was tested as a reference to the final product. In figure 2.5 it is seen how the final product is actually mostly para isomers. Which makes sense para has more resonance and therefore the charges are delocalized and the isomers will therefore be preferred (For resonance structures look at figures 1.2 and 1.3). The last TLC was using ethanol as a reference which unfortunately did not show despite putting a decent amount on the TLC. This could have been for a number of reasons like it evaporating, it not being bright enough against UV light and so on. There is a second spot higher than the para isomer; however, the origin of this spot could not be determined and is likely a form of contamination. Although this is a dark spot, it could not be used in the calculation of the composition of the final product because it’s origin cannot be determined, so the percent yield is calculated assuming only p-nitroacetanilide.

In order to determine the ratios of products produced ImageJ was used. ImageJ works by measuring the amount of UV light absorbed by each spot which in turn is proportional to the amount of compound present on that spot as well as the the ability of the compound to absorb UV light. This works because the energy from UV is absorbed easily by organic compounds and thus, can be compared with bond energy (“Experiment 6 : Regioselective Nitration of Acetanilide,” 2014).

Because different compounds absorb light differently, a calibration curve is used to standardize the measurement to yield an accurate ratio of products. A calibration curve is a useful method to generate the concentration of substances in a mixture using standard samples with known concentrations. A sample calculation depicts the method used to determine the ratios of materials in the crude product.

From Imagej we can conclude that the the crude product contained about 16-17% o-nitroacetanilide, 62 - 66% p-nitroacetanilide, 14 - 20% of 2,4-dinitroacetanilide and 2-6% of m-nitroacetanilide. This is not a surprise because the para isomer is the major product as it composes most of the crude product. The next highest ratio is that of the ortho isomer which is the second most preferred form of nitroacetanilide. Finally we have the least preferred product in the smallest amount (the meta product) and the dinitroacetanilide product is in the third smallest ratio which makes sense because the dinitro product was formed from the overreaction of the para product which was present in a relatively large quantity. Therefore, the actual ratios of the substances present in the crude product is an accurate representation of the theory discussed.

Sources of Error

One major source of error for this lab was the addition of Ethanol. There was no specified amount of ethanol to be added and it was recommended that we add enough that the crude product mixture becomes clear, unfortunately this meant that the ethanol added also needed to be boiled away which in turn could have caused us to lose some product in the boiling process. It was also very time consuming. If the experiment were to be be repeated, the manual should be changed to say a maximum amount of ethanol that can be added (20 ml).

Because the crude product was so sticky and wet, it was impossible to obtain all of the crude product from the buchner funnel. Each time the crude product had to be transferred from one vessel to another there was loss of product. On the beakers and the filter. Using some other kind of tool to transfer it might have helped.

Conclusion

The crude product was composed of 16-17% o-nitroacetanilide, 62 - 66% p-nitroacetanilide, 14 - 20% of 2,4-dinitroacetanilide and 2-6% of m-nitroacetanilide

The final product had a mass of 0.50 g and this was a yield of 37.4%.

Questions

1. Nitration is an electrophilic reaction, therefore, the more electron dense the aromatic ring, the faster the process. The addition of an electron withdrawing nitro group will remove electron density on the aromatic ring, whereas, the addition of acetamides will add to it. In the first reaction, the nitro group will react with a very electron dense ring

and the reaction process is fast. In the second reaction, there is already a nitro group on the ring, decreasing electron density, so the addition of a second electron group will be slower than the first.

2.

a)

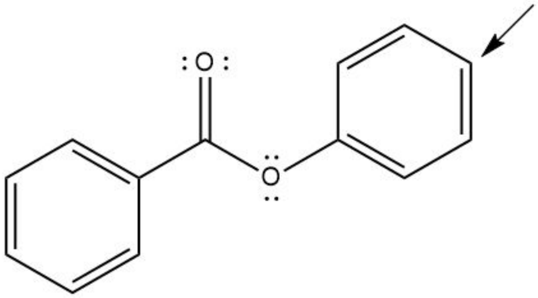


Figure 4.0. The preferred position will be on the right benzene ring due to that ring being more electron rich and oxygen is an electron donating group therefore it will prefer either ortho or para position. Although para is preferred since it's less sterically hindered

b)

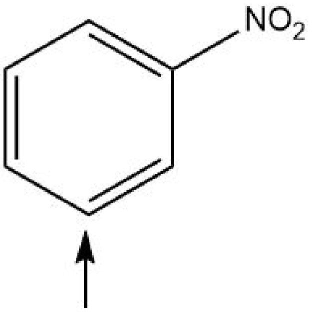


Figure 4.1. NO_2 is an electron withdrawing group therefore it will prefer the meta position

c)

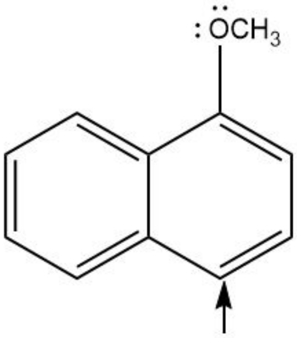


Figure 4.2. Due to OMe being an electron donating group it will prefer the para or ortho configuration. Although para is preferred since it's less sterically hindered

d)

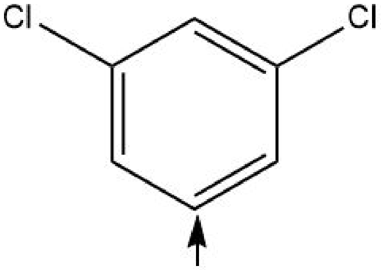


Figure 4.3. Cl is an electric withdrawing group therefore it will prefer the meta position, there is only one place in the ring were the nitration would be meta to both of the Cls.

3.

Figure 5.0. Reaction bellow and mechanism explaining it's products

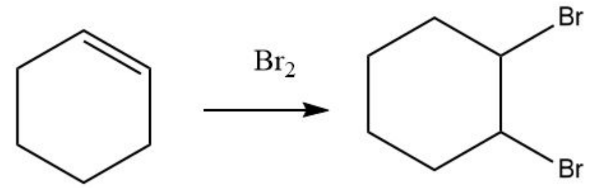
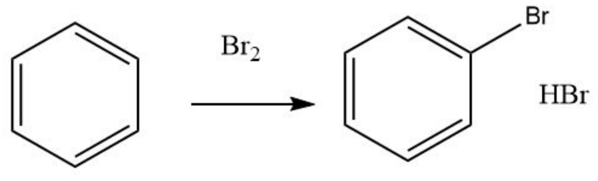
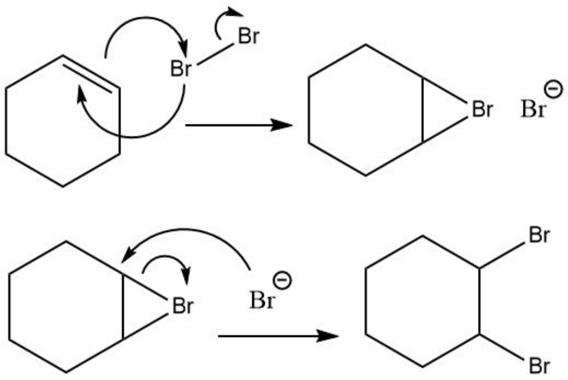
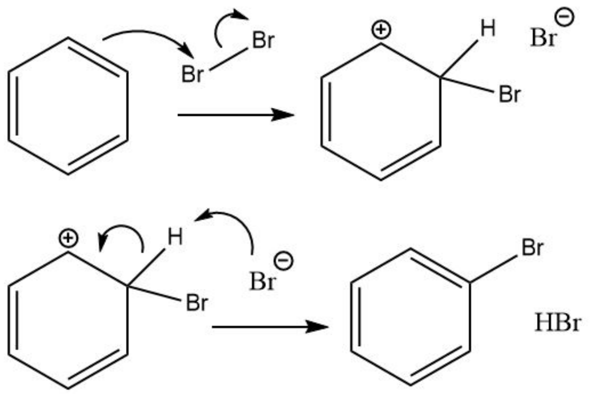


Figure 5.1. Reaction bellow and mechanism explaining it's products



Mechanism:





4.

a)

Benzene	=	$10g \times \frac{1\,mol}{78\,g}$ = 0.13 mol	H_2SO_4 (0.16 mol) > HNO_3 (0.14 mol) > Benzene (0.13 mol) **Therefore benzene is the limiting reagent**
HNO_3	=	$9\,ml \times \frac{1L}{1000\,ml} \times \frac{16\,mol}{1L}$ =0.14 mol	
H_2SO_4	=	$9\,ml \times \frac{1L}{1000\,ml} \times \frac{18\,mol}{1L}$ = 0.16 mol	

b)

Percent yield = actual yield/theoretical yield × 100%
= (moles of nitro benzene/moles of benzene) *100
= ((8.1g*(mol/123g)/ 0.13mol) *100 = 51 % yield

Therefore there is a 51 % yield of nitro benzene

c) Dinitrobenzene is the most probable side product. Because benzene is the limiting reagent, there will be left over free nitronium ions that will react with the nitrobenzene, undergoing a second nitration. The melting point of dinitrobenzene is 174°C

d) The role of sulfuric acid is to act as a catalyst to activate the electrophilic nitric acid to produce a nitronium ion. Refer to mechanism depicted in figure 1.0

e) Molecular weight = 168.108 g/mol
Theoretical Mass = 10 mol × 168.108 g/mol = 1681.08 g
Percent Yield = 250 g/1681.08 g × 100% = 14.87 %

5.

Figure 6.0. 2-nitrofuran isomer formation

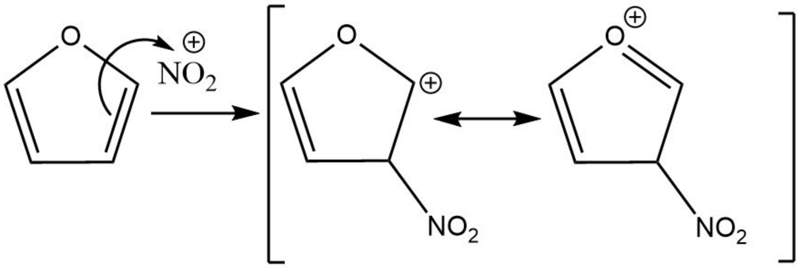
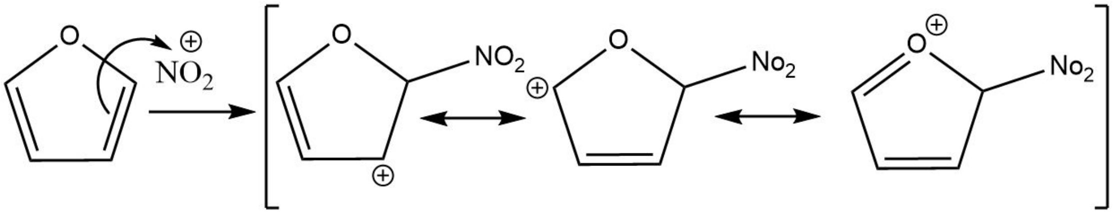


Figure 6.1. 1-nitrofuran isomer formation



→ 1-nitrofuran isomer is the preferred position as more resonance is possible and it delocalized the charge better

6.

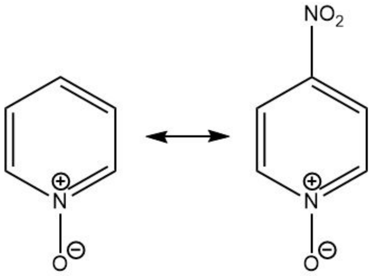
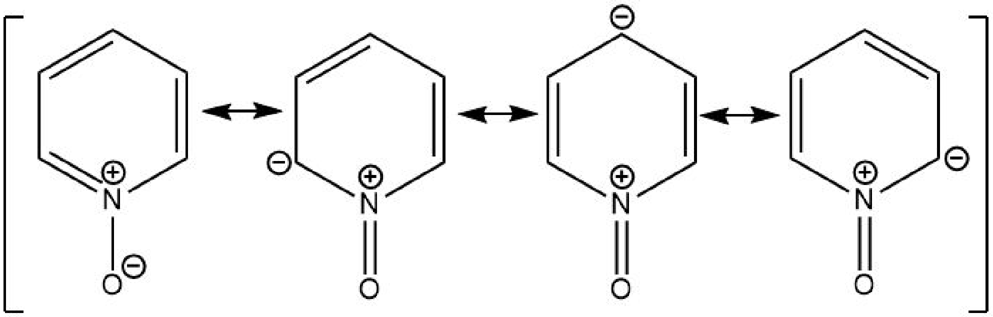


Figure 7.0. Reaction given in question 6 of the procedure

Figure 7.1. The resonance structure of Pyridine N-oxides in electrophilic aromatic substitutions



→ The structure on the most left is prefered because all carbons have full octets and the charges - and + are close to each other, balancing the pulls. Oxygen is an electron donating group so you are getting on ortho/para directing group which is why you would get para isomer as a product. Ortho isn’t preferred due to steric hindrance.

References

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Experiment 6 : Regioselective Nitration of Acetanilide. (2014), (September), 1–7

National Center for Biotechnology Information. PubChem Database. Acetanilide, CID=904, https://pubchem.ncbi.nlm.nih.gov/compound/904 (accessed on Mar. 31, 2019)

National Center for Biotechnology Information. PubChem Database. Sulfuric acid, CID=1118, https://pubchem.ncbi.nlm.nih.gov/compound/1118 (accessed on Mar. 31, 2019)

National Center for Biotechnology Information. PubChem Database. Nitric acid, CID=944, https://pubchem.ncbi.nlm.nih.gov/compound/944 (accessed on Mar. 31, 2019)

National Center for Biotechnology Information. PubChem Database. N-(4-Nitrophenyl)acetamide, CID=7691, https://pubchem.ncbi.nlm.nih.gov/compound/7691 (accessed on Apr. 3, 2019)

[redacted]

MARIA PIMENOVA
300065365

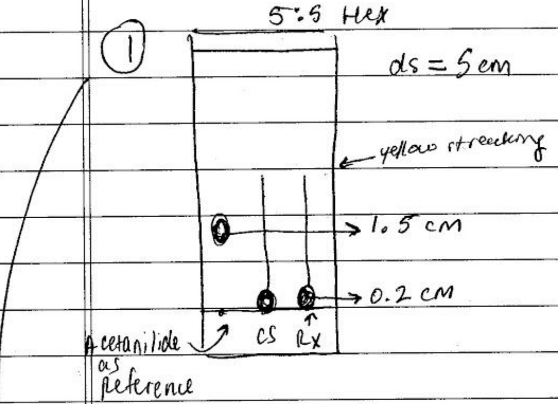
LAB 6 RAW DATA

1. g of acetanilide + H_2SO_4 (5 ml)
→ looked like brown sugar, but fluffy dissolved a bit, no bubbles.
→ cooled
→ nitric acid 0.6 ml + sulfuric 0.8 ml (given by TA)
→ acetanilide dissolved more but not entirely.
↳ yellowish specks on top of otherwise clear solution
↳ when doing the TLC though the whole solution looked very dark brown.

FIRST TLC of REACTION: Is it complete? [✓ Y] or N

5:5 Hex

①



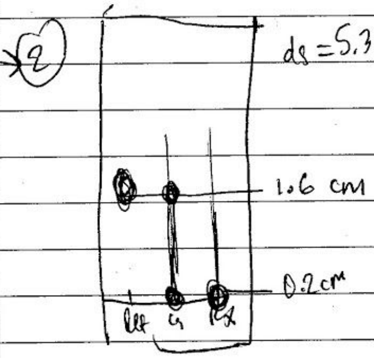
ds = 5 cm

- In TLC, the Rx looked brown & yellow & there were yellow streaks as the TLC was developing.

- Ret ~~the~~ did not show but no Ret is seen in Rx so ∴ complete.

→ Reaction mix is a <u>very</u> dark brown

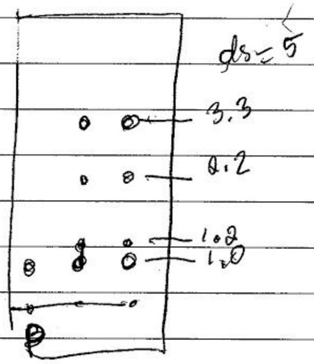
②

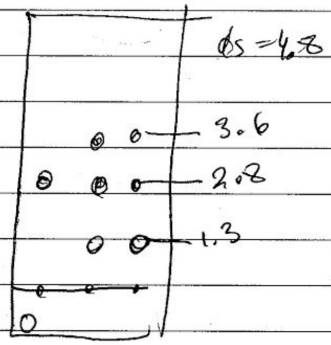


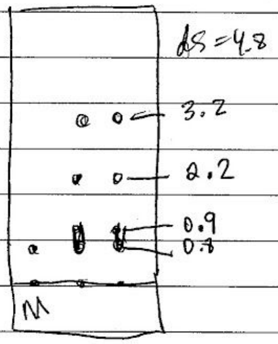
ds = 5.3

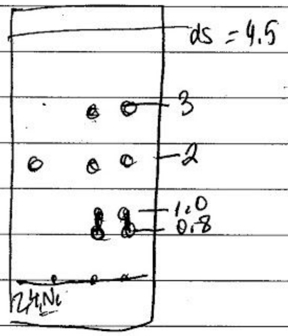
- when water was added to Rx, yellow Tumeric like perciptate formed

TLC'S ~~C-C-PP~~ 5:5 rxn





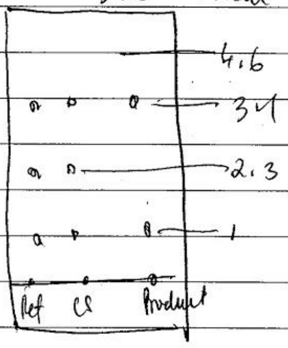




boiling ethanol added turned red/brown & clear

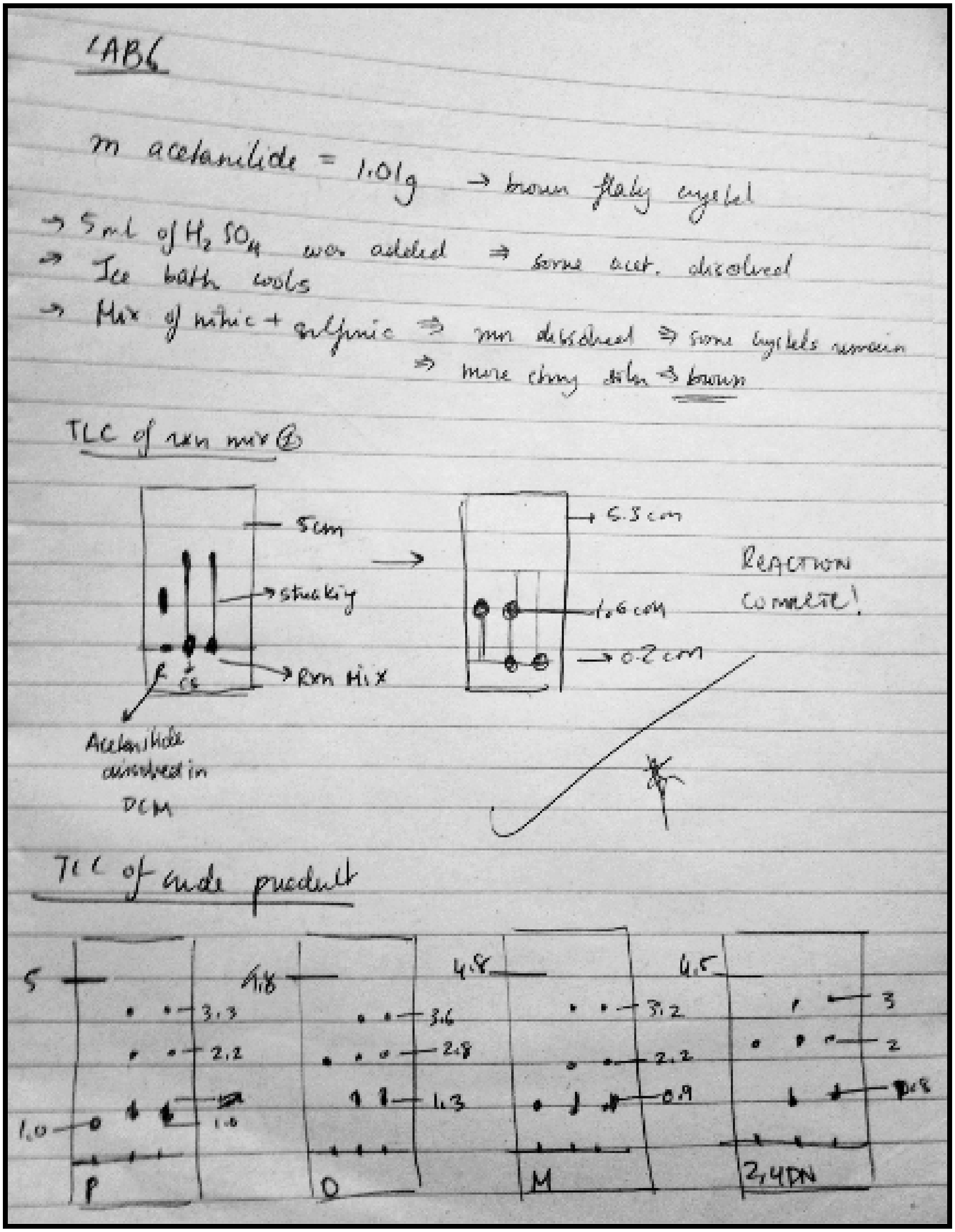
5:5 Final TLC.

Product weight = 0.50g.



↓ Lunch

[redacted]



LAB 6

m acetanilide = 1.01g → brown flaky crystal

→ 5 ml of H_2SO_4 was added ⇒ some acet. dissolved

→ Ice bath cools

→ Mix of nitric + sulfuric ⇒ mn dissolved ⇒ some crystals remain

⇒ more clear soln ⇒ brown

TLC of rxn mix ①

5cm

streaking

Rxn Mix

CS

Acetanilide dissolved in DCM

5.3 cm

1.6 cm

0.2 cm

REACTION COMPLETE!

TLC of crude product

5

3.3

2.2

1.0

1.0

P

4.8

3.6

2.8

1.3

O

4.8

3.2

2.2

0.9

M

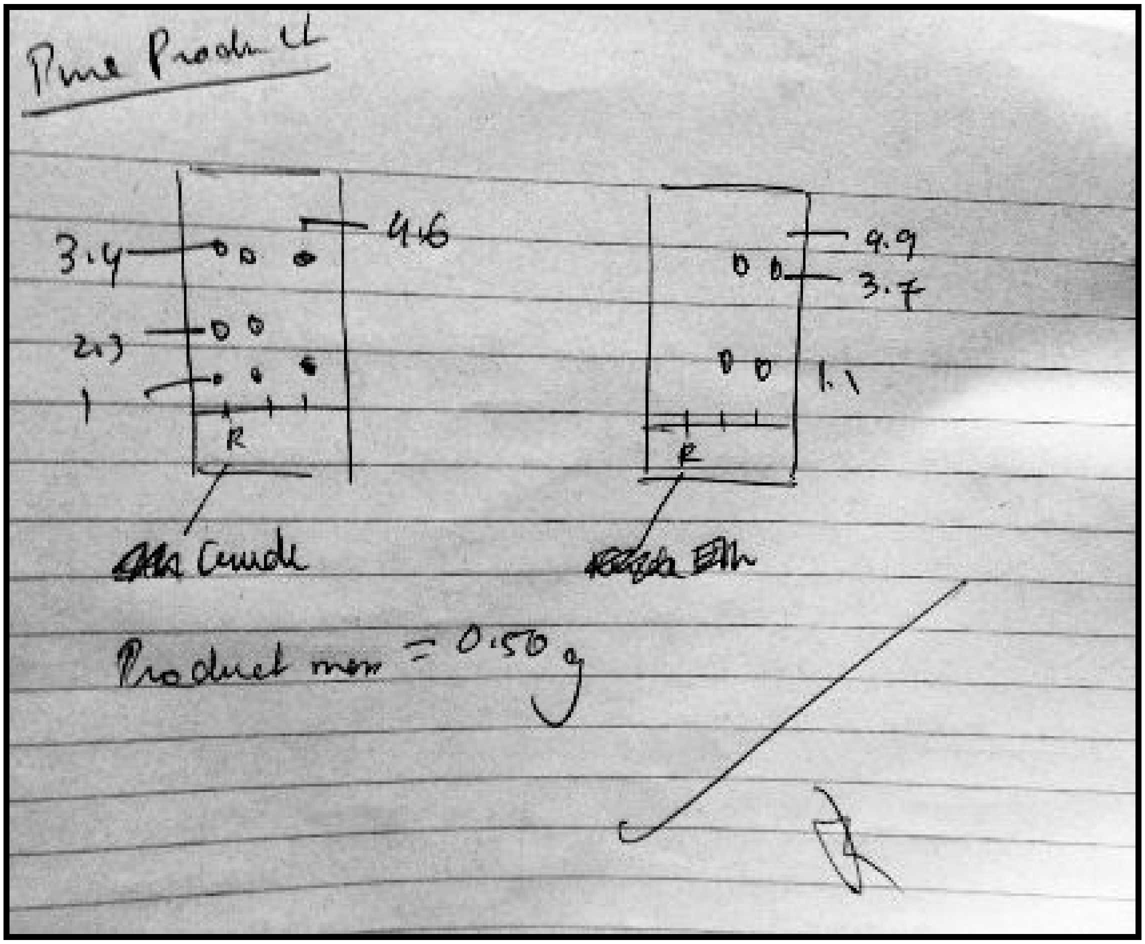
4.5

3

2

0.8

2,4DN



Pure Product

Product mass = 0.50 g

TLC Pictures from Lab

→ corresponding to their figure drawing in the lab report

Fig 2.0

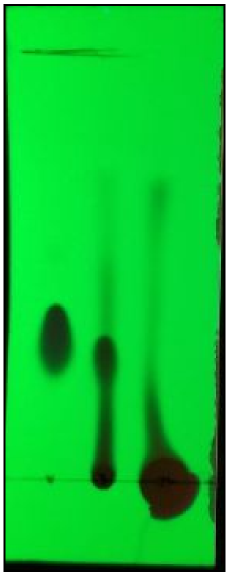


Fig 2.1

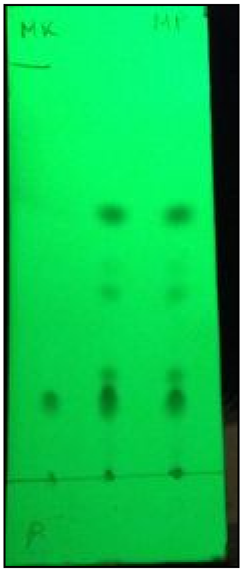


Fig 2.2

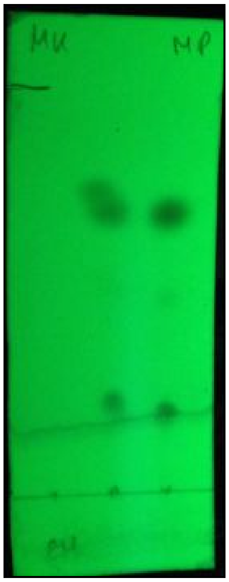


Fig 2.3

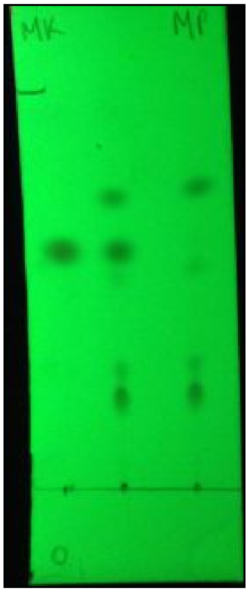


Fig 2.4

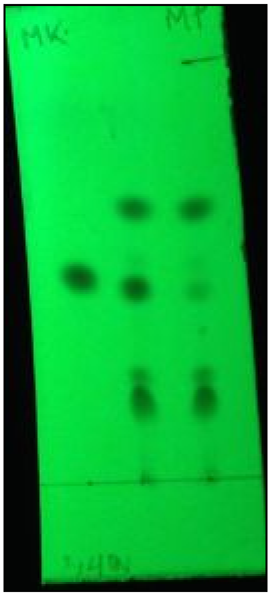


Fig 2.5

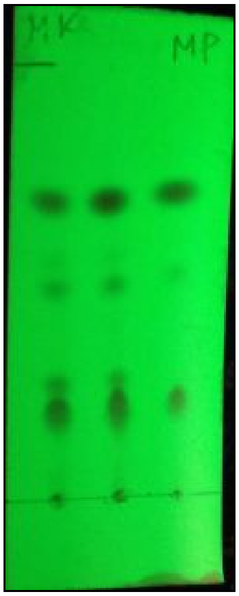


Fig 2.6