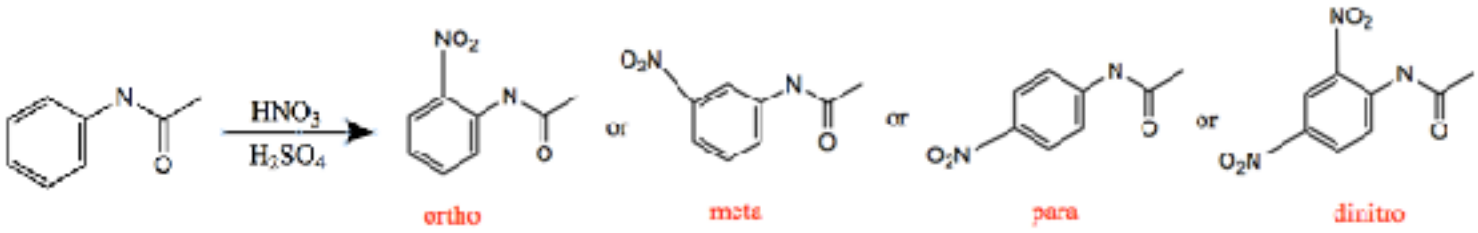
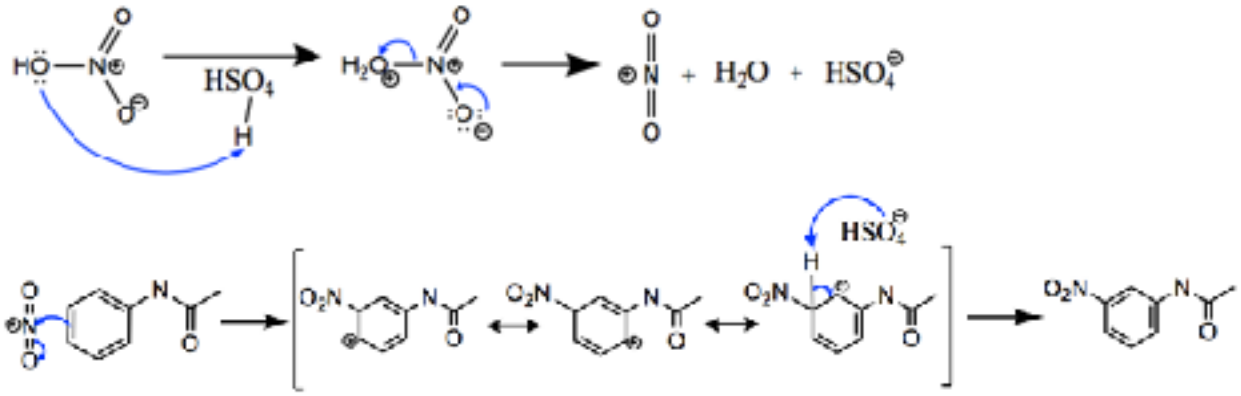
Regioselective Nitration of Acetanilide

Electrophilic Aromatic Substitution



Introduction:

The mechanisms for the nitration of acetanilide in the *meta* position.



Procedure:

As described in the Organic Chemistry Laboratory Manual on pages 53 to 54.

Data and Observations:

Acetanilide: light brown/beige solid, odourless, resembles oats

Sulfuric acid: Transparent, colourless solution with a strong odour

Nitric acid: Transparent, colourless solution with a strong odour

Dichloromethane: Transparent, colourless liquid with a faint odour

Ethanol: Transparent, colourless solution with a strong odour

5:5 ethyl acetate and hexane (eluent): Transparent, colourless liquid with a mild odour that resembles nail polish remover

- Mixing the acids gave off heat therefore it was an exothermic reaction
- The reaction mixture was so dark that it appeared black in colour however the sides of the round bottom flask were actually yellow from the sulfur
- This reaction had a mild odour
- When the mixture was added to the beaker with ice and water, the solution got cloudy, opaque and had a mustard yellow colour
- While on the stir plate, a lot of yellow frothy looking foam was being produced
- After suction filtration the precipitate was a thick yellow, sticky paste
- When the boiling ethanol was added to the crude product the solution turned very red but it was still transparent, a minimal amount of crystals formed at the top of the solution

Table 1: Table of Reagents

Reagent	Molecular Weight (g/mol)	Amount (Mass or Volume)	Moles (mol)	Density (g/mL)
Acetanilide	**135.17**	**1.0g**	**0.0074**	**1.22**
Sulfuric Acid (solvent)	98.08	5mL	0.0938	1.84
Sulfuric Acid (reagent)	**98.08**	**1.2mL**	**0.0225**	**1.84**
Nitric Acid	**63.01**	**0.9mL**	**0.0216**	**1.51**
Water	18.01	~ 20mL	—	1.00
Ethanol	46.06	~ 1mL	0.0171	0.789

TLC:

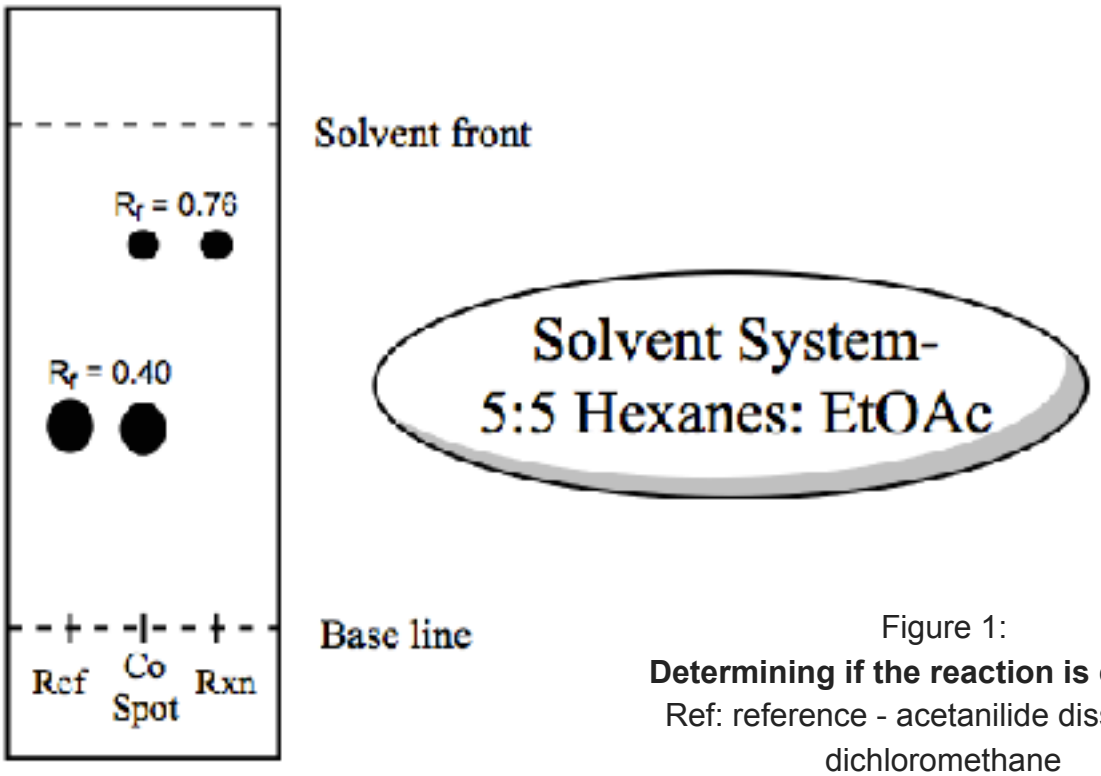


Figure 1:
Determining if the reaction is complete
Ref: reference - acetanilide dissolved in dichloromethane
Co spot: reference + reaction mixture
Rxn: reaction mixture + dichloromethane

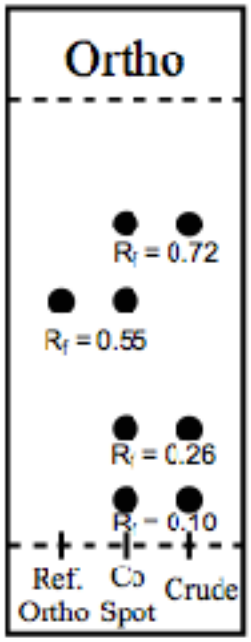


Figure 2:
Comparing the crude product to the *ortho* isomer
Ref: reference: *ortho*-acetanilide
Co spot: reference + crude
Crude: crude product dissolved in dichloromethane

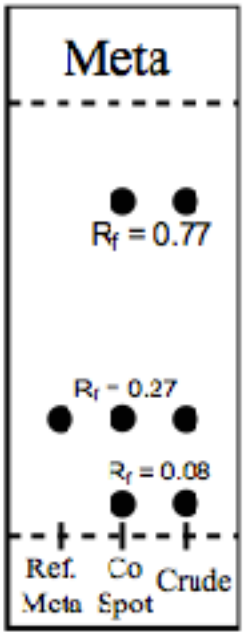


Figure 3:
Comparing the crude product to the *meta* isomer
Ref: reference: *meta*-acetanilide
Co spot: reference + crude
Crude: crude product dissolved in dichloromethane

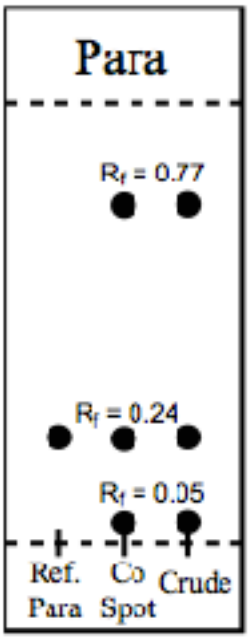


Figure 4:
Comparing the crude product to the *para* isomer
Ref: reference: *para*-acetanilide
Co spot: reference + crude
Crude: crude product dissolved in dichloromethane

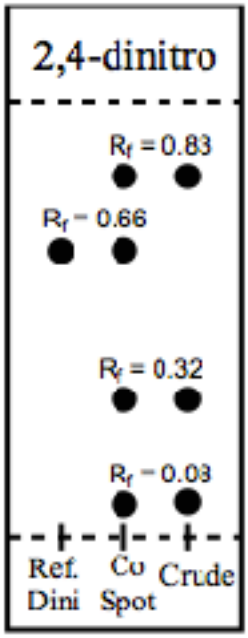


Figure 5:
Comparing the crude product to the *2,4-dinitro* isomer
Ref: reference: 2,4-dinitro-acetanilide
Co spot: reference + crude
Crude: crude product dissolved in dichloromethane

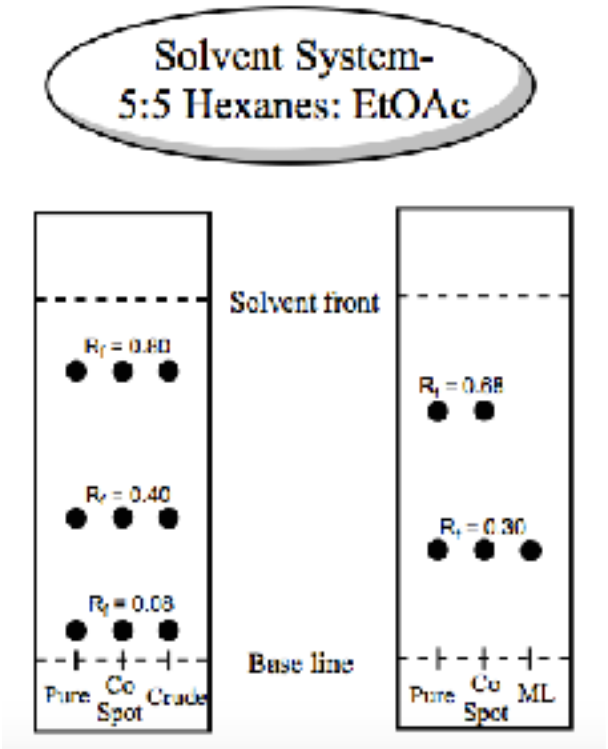


Figure 6:
Comparing the crude product to pure product
Pure: crystals disolved in dichloromethane
Co spot: pure product + crude product
Crude: crude product dissolved in dichloromethane

Figure 7:
Comparing the pure product to the mother liquor
Pure: crystals disolved in dichloromethane
Co spot: pure product + mother liquor
ML: mother liquor

Table of Results-

Table 2: Results for pure nitroacetanilide

Product	Mass (g)	Molecular weight	Moles (mol)	Percent Yield
Pure Product	0.80	180.2 g/mol	0.0044	60%

Table 3: R_f values for the TLC plates (Figures 1-7)

Spot # (bottom to top)	R_f values for Figure 1	R_f values for Figure 2	R_f values for Figure 3	R_f values for Figure 4	R_f values for Figure 5	R_f values for Figure 6	R_f values for Figure 7
1	0.40	0.10	0.08	0.05	0.08	0.08	0.30
2	0.40	0.10	0.08	0.05	0.08	0.08	0.30
3	0.76	0.26	0.27	0.24	0.32	0.08	0.30
4	0.76	0.26	0.27	0.24	0.32	0.39	0.68
5	—	0.55	0.27	0.24	0.66	0.39	0.68
6	—	0.55	0.77	0.77	0.66	0.39	—
7	—	0.72	0.77	0.77	0.89	0.89	—
8	—	0.72	—	—	0.89	0.89	—
9	—	—	—	—	—	0.89	—

Calculations:

Percent Yield = (# mol of product) ÷ (# mol of starting material) x 100

= (# mol of pure nitroacetanilide) ÷ (# mol of acetanilide) x 100

= (0.0044 ÷ 0.0074) x 100%

= 60%

ImageJ- I would have done calculations similar to those listed below, but this data is only an example

Absorbance (Meta) = 6464.037

Absorbance (Para) = 5523.128

% Absorbance (meta) = [(absorbance meta) ÷ (absorbance meta + absorbance para)] x 100

= [6464.037 ÷ (6464.037 + 5523.128)] x 100

= 53.9%

% Absorbance (para) = 100 - [% Absorbance (meta)]

= 100 - 53.9

= 46.1%

<u>Calculating the mole %</u>

y = 0.976x + 0.804

53.9 = 0.976x + 0.804

53.9 - 0.804 = 0.976x

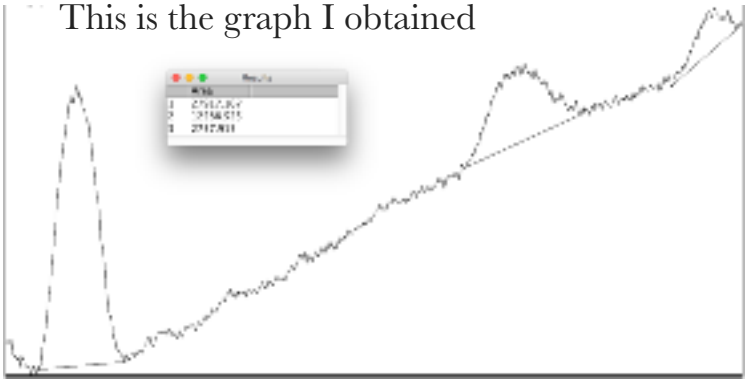
53.096 ÷ 0.976 = x

54.4% = x (mole% meta)

100 - x = mole% para

100 - 54.4 = 45.6%

This is the graph I obtained



Discussion:

In this experiment 1g of acetanilide was dissolved in sulfuric acid. The instructions said to use approximately 1g, accurately weighed. This meant that we had to use a scale and measure 1g rather than just estimating the weight without actually measuring it. It was okay to go slightly above or below (i.e. 1.01g or 0.99g), but the measurement had to be accurate and noted in the report. Once the acetanilide was dissolved, we added two strong acids. Sulfuric acid as a reagent was the nucleophile and the nitric acid was the electrophile. Prior to adding the acids, the reaction had to be cooled so that the nitration could occur at a low temperature. When everything was mixed together, heat was produced which meant that there was a lot of energy in the system and the reaction was exothermic. If there is too much energy, the reaction will take the highest energy pathway which would lead to more *meta* isomers. This is what mostly likely happened in our case because the *meta* product was observed in the TLC, Figure 3.

Several TLCs were prepared during this lab. The first TLC, Figure 1, demonstrates that the reaction is complete. We know this because the R_f values for the starting material and the reaction mixture are very different (0.40 vs 0.76 respectively). In this section, dichloromethane was mixed with the reaction mixture to prevent streaks/smudging from appearing on the TLC plate. By mixing the solution with dichloromethane it pushes the mixture to the organic phase so that the ions in the aqueous phase will not interact with the silica gel on the TLC plate to create a smudge of spots in the polar region. The next set of TLCs were used to determine the regiochemistry of the product that was formed. Typically there are 3 options for regiochemistry of a molecule: *ortho*, *para*, *meta*. However, in this case 2,4-dinitro is also another option because the *para* product may over react and another nitration will occur. The final TLCs were spotted using the pure product; in Figure 6 and 7 we compared the pure product to the crude product as well as the mother liquor. In Figure 6 all the spots line up and the R_f values are the same across the rows which means that the crude product and the pure product are composed of the exact same things; this should not have been the case however.

For ImageJ I was unable to do real calculations due to the fact that my data and TLCs were inconclusive. The mixture contained too many impurities to distinguish between the components. My results show that I either have only the *meta* isomer, only the *para* isomer, or a combination of both. *Meta* and *para* have extremely similar R_f values so I am not able to distinguish between the two with a naked eye. To test which isomer is present I could have ran a TLC with my product in the middle and the *meta* and *para* isomers as references on either side. That way I could compare them all at once to calculate the percent composition of my product. If the *para* isomer was present, I would assume that the spot further up on the TLC was 2,4-dinitro or even *ortho*, and then I would be able to use the calibration curves given to calculate my percent composition as well as the mole percent. Since none of the reference spots lined up with the non polar spot on the TLC plates, I am unable to identify what that spot refers to. The bottom spot, the most polar one in Figures 2-6, is probably some of the starting material still in the solution, or it could be more polar impurities. Therefore my TLC plates did not give me enough information to do all the calculations and determine which isomer is present.

The percent yield for the pure product was 60%. Initially a lot of precipitate formed when creating the crude product, but there were not as many crystals during the recrystallization process. To increase our percent yield we could have added slightly more ethanol and allowed the mixture to cool off for a longer period of time.

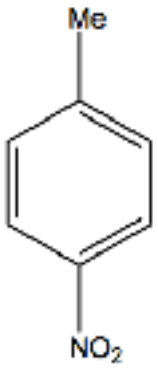
Sources of Error—

Some sources of error could come from the recrystallization process, such as not allowing enough time for the solution to cool off so that crystals can form, as well as disturbing the flask by moving it or mixing the mixture. It was also important that everything was correctly labeled during this experiment because there were a lot of TLCs and it is easy to mix up solutions if they are not properly labelled. Finally, human error could involve not getting the correct amounts of acid and not knowing which is the reagent vs solvent.

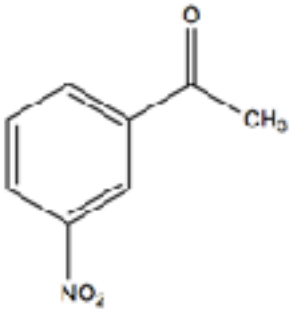
Questions:

1. The TLCs show that the *ortho* isomer is less polar than the *para* isomer so it travelled farther on the TLC plate and its R_f value was larger. The *para* isomer would have interacted more with the silica gel causing a slower movement and it to travel a shorter distance.
2. Nitro groups are strong deactivating electron withdrawing groups, which means they are *meta* directors. Therefore there is a large difference in energy when it comes to adding a second nitro group. A catalysts is necessary because it requires more energy to break the bonds in order to add the substituent to the benzene molecule which is already stable on it's own. Thus the rate of the reaction will be slower because it requires more energy to occur.
3. The *para* isomer is favoured in electrophilic aromatic substitution because of steric interactions; the functional groups are spread out and farthest from each other when they are located *para* to one another. When the substituent is placed at the *para* position, the charge is spread out over the whole molecule thus it is more stable. On the other hand, having two functional groups right next to each other is not favourable, which is what happens in the case of *ortho* isomers.
4. The nitration would occur at each of the following positions.

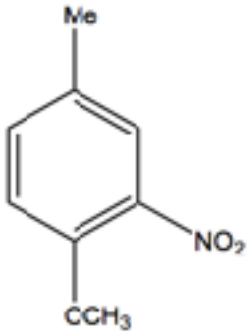
a.



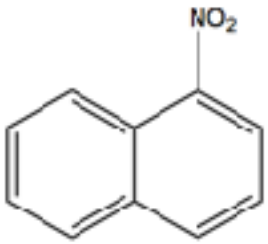
b.



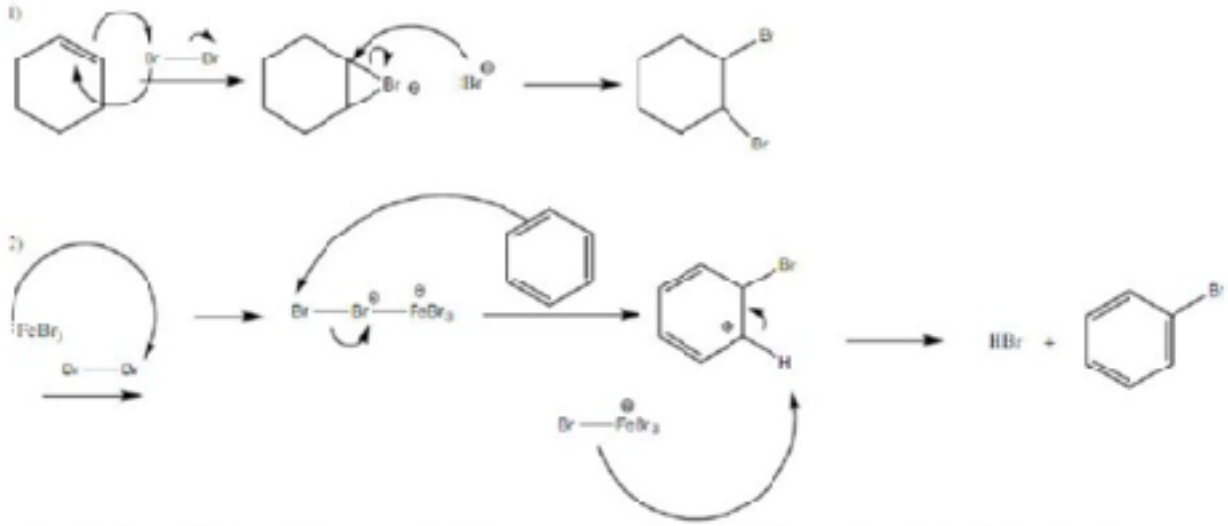
c.



d.



5. The first reaction is an anti electrophilic bromide addition to the pi bond of a cyclohexene. The second reaction is an electrophilic aromatic substitution of bromine to form bromobenzene.



6. a) Benzene is the limiting reagent (10mol) [nitric acid (12mol) and sulfuric acid (13.5mol)]

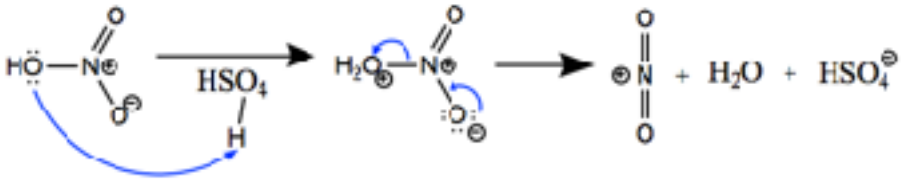
b) Percent yield = (# mol of experimental nitrobenzene) ÷ (# mol of theoretical nitrobenzene) x 100

= (8.13 mol ÷ 10 mol) x 100

= 81.3%. Therefore the percent yield of nitrobenzene is 81.3%

c) Dinitrobenzene is the most probably side product with a high melting point.

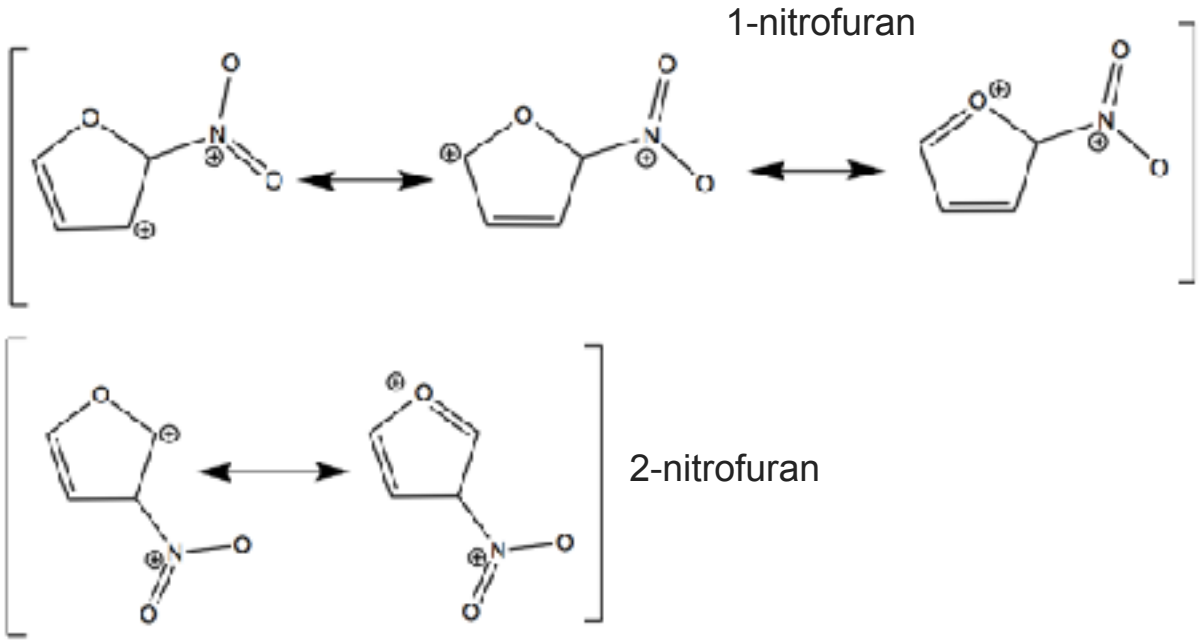
d) As shown in the introduction, the role of sulfuric acid is used as a catalyst to protonate the nitric acid so that it forms nitronium ions and hydrogen sulfate ions. This allows the nitronium ions to act as electrophiles and begin the aromatic substitution.



e) Percent yield = (1.487 mol ÷ (10mol - 8.13mol)) x 100

= 79.5%. Therefore the percent yield of side product is 79.5%

7. The nitration of 1-nitrofuran is preferred because it has more resonance structures and is thus more stable than 2-nitrofuran.



Raw Data