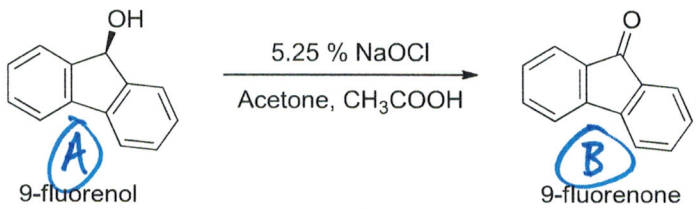
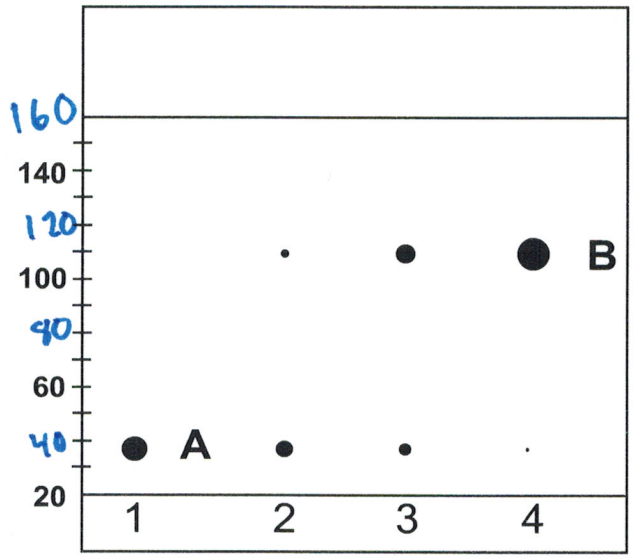
1) A sample of 50 mg of 9-fluorenol is dissolved in 3 mL of acetone in a 10-mL round-bottom flask. To the 9-fluorenol, 0.12 mL of glacial acetic acid is added, followed by the addition of 0.4 mL of 5.25 % sodium hypochlorite solution (commercial bleach). After 5 minutes the progress of the reaction is determined by normal phase TLC and additional bleach is added in 0.4 mL increments as needed. Once TLC indicates completion of the reaction, the reaction mixture is extracted twice with 2 mL of hexane and then washed with 1 mL of 5% $NaHCO_3$ solution and 2 mL of water. Recrystallization is carried out using a small portion of hexane and the product is characterized by ^{1}H-NMR, ^{13}C-NMR, and IR spectroscopy. **(34 pts total)**



a) The progress of the reaction was tracked using TLC, shown below. Spot 1 shows the starting material and spots 2-4 are at 5 min intervals after the reaction was started. Showing all work, calculate the R_f values (as decimals) for compounds A and B. **(6 pts)**



$R_{fA} = \frac{35-20}{160-20} = 0.11$

$R_{fB} = \frac{110-20}{160-20} = 0.64$

b) What can be concluded from the TLC plate at the final time point 4? Explain, how you would proceed. **(4 pts)**

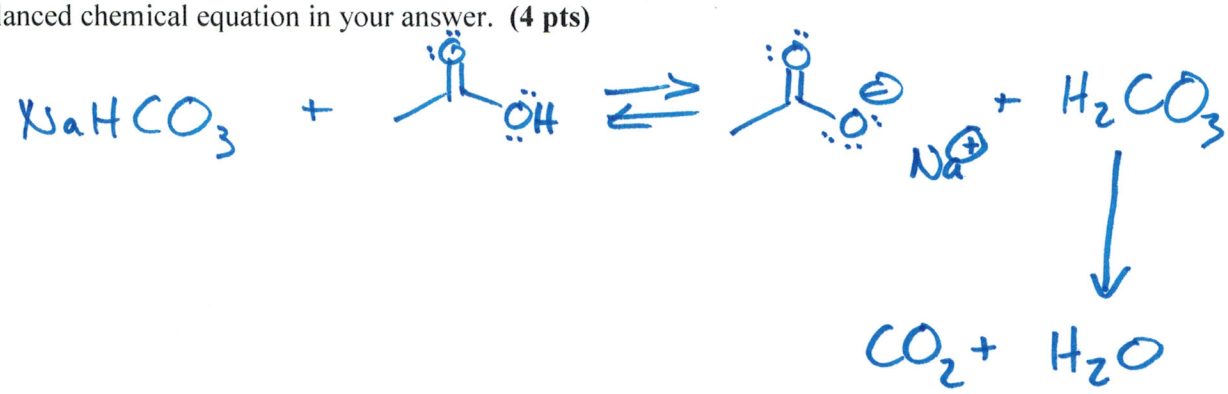
Not all of Reactant A has been used up in the reaction. Add more NaOCl and wait a short while. Then retest.

c) Provide the balanced chemical equation that accounts for the production of the active oxidizing agent. **(2 pts)**

$NaOCl + 2H^{\oplus} \rightleftharpoons Na^{\oplus} + H_2OCl^{\oplus}$

(or some acceptable variant)

d) What is the purpose of washing the crude product with 1 mL of 5 % $NaHCO_3$ solution? Include a balanced chemical equation in your answer. **(4 pts)**



$H_2CO_3 \rightarrow CO_2 + H_2O$

Sodium bicarbonate is used to remove any excess acetic acid.

$H_a = 7.36 + 0.45 + 0.07 = 7.88$

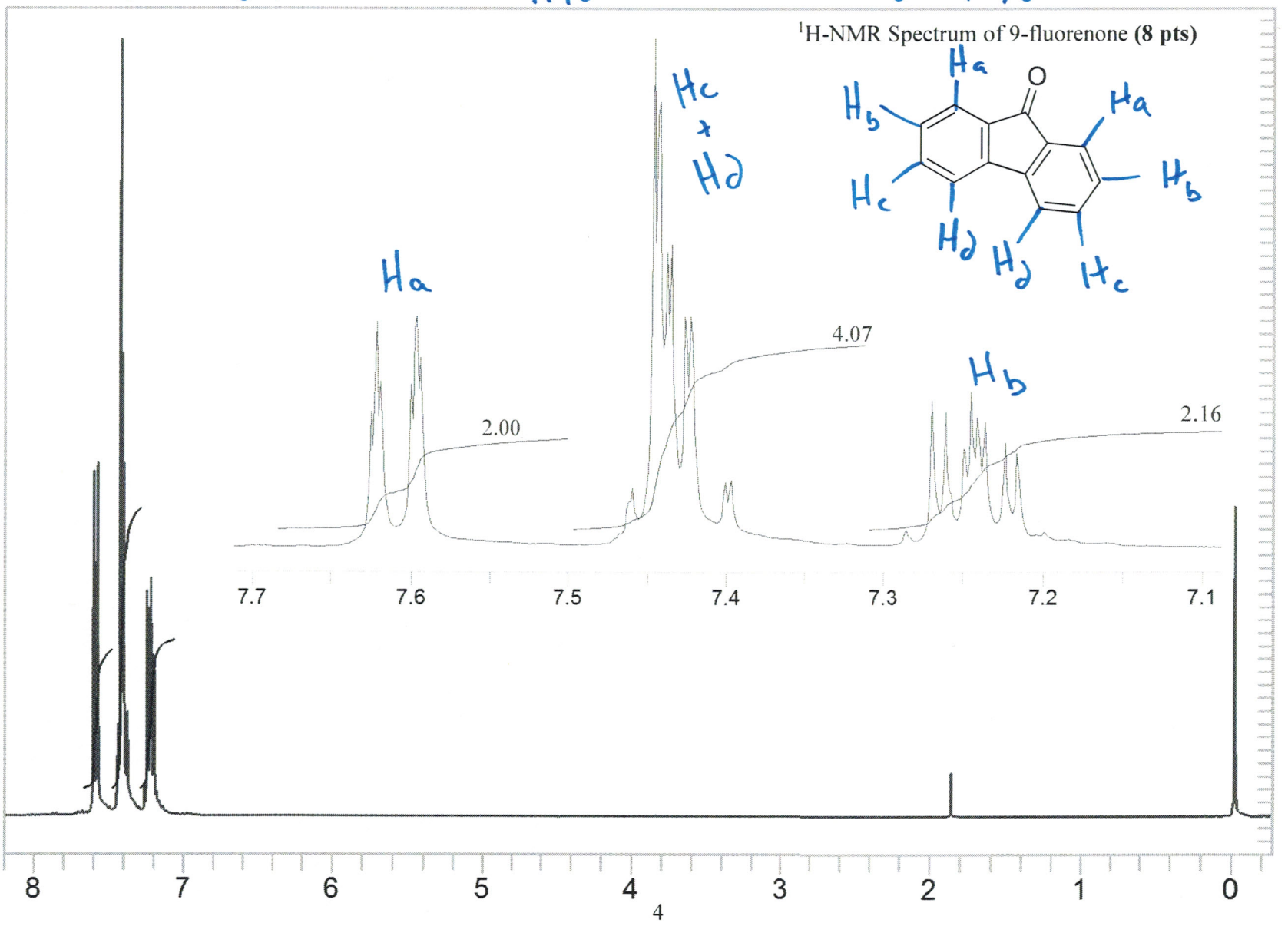
$H_c = 7.36 + 0.23 + 0.07 = 7.66$

$H_b = 7.36 + 0.12 + -0.02 = 7.46$

$H_d = 7.36 + 0.12 + 0.23 = 7.71$

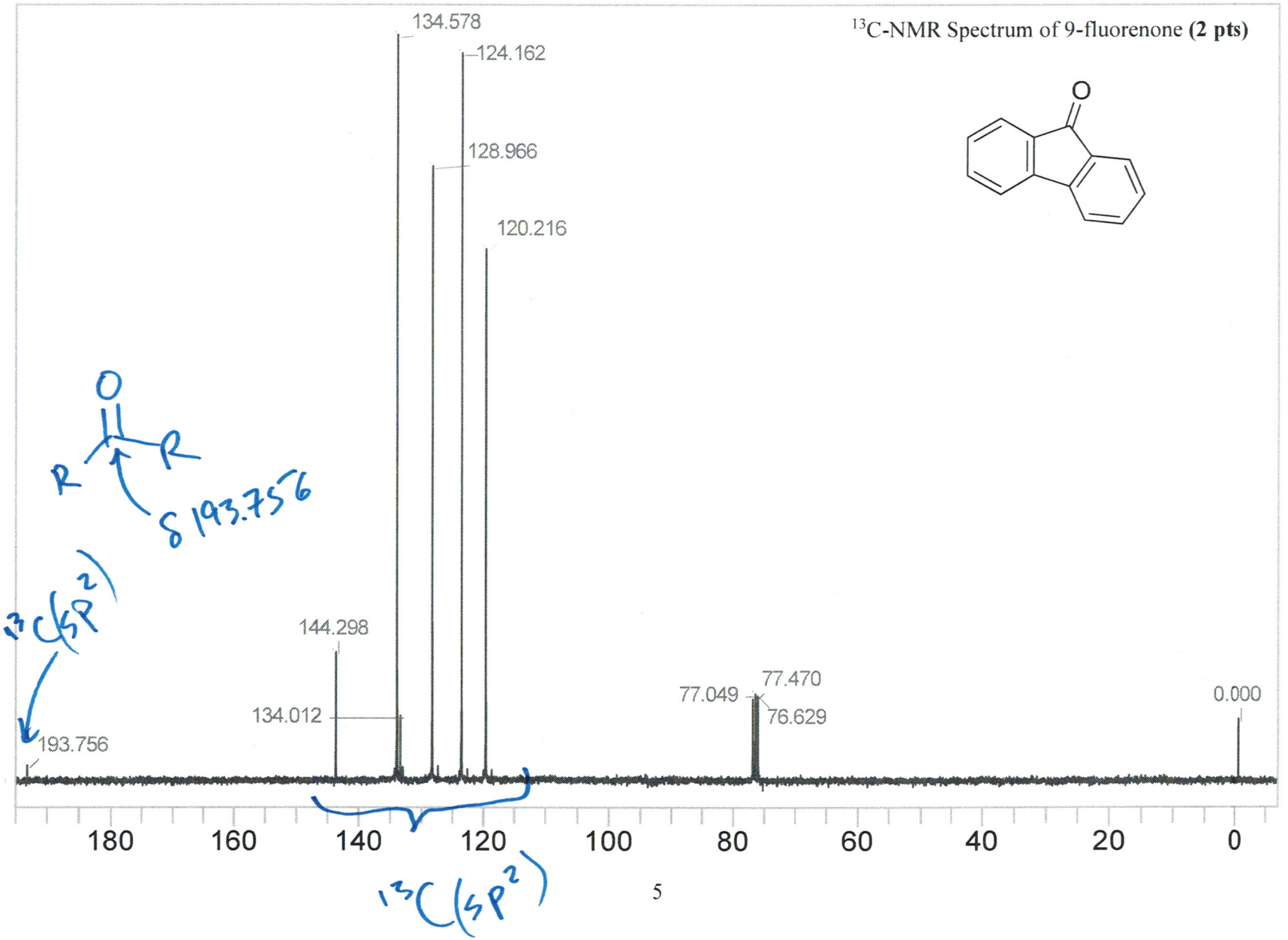
300 MHz ^{1}H NMR

In CDCl3

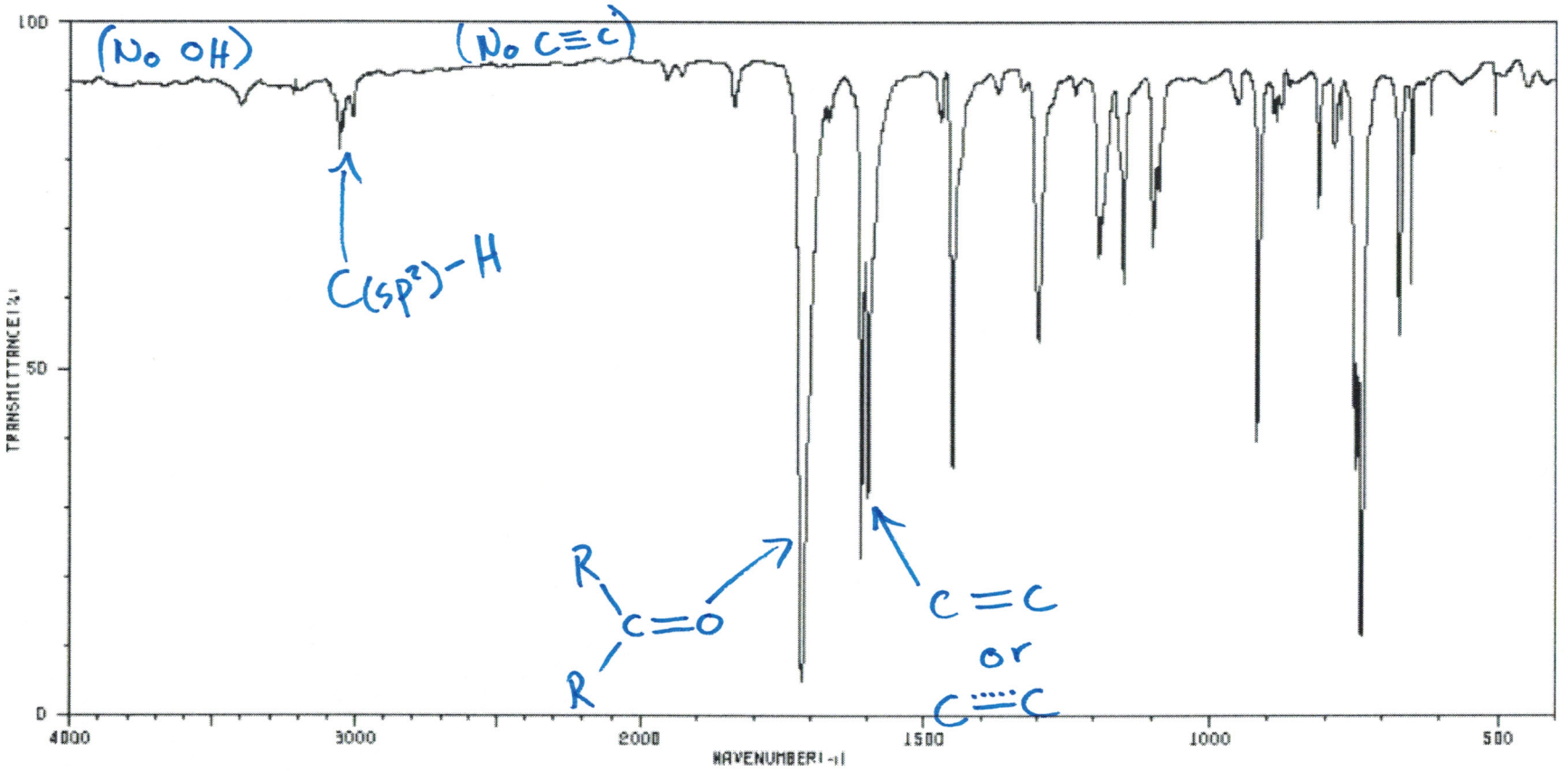


75 MHz ^{13}C NMR

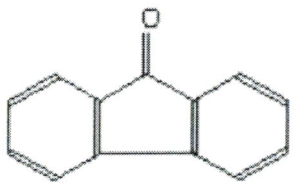
In CDCl3



IR Spectrum of 9-fluorenone **(2 pts)**

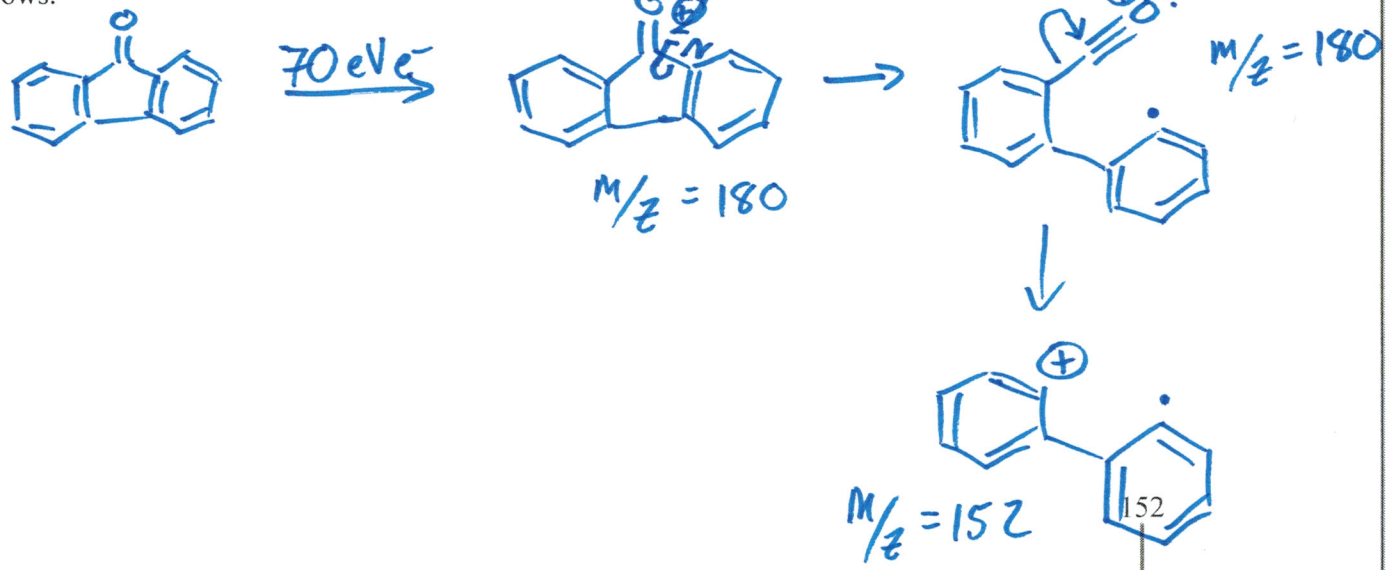


3401	84	1666	84	1236	86	962	84	774	84
3061	79	1612	21	1194	64	920	37	745	34
3047	81	1600	30	1167	88	893	84	736	10
3013	84	1476	84	1158	77	887	81	672	62
1834	84	1471	81	1151	60	879	84	651	60
1715	4	1451	34	1098	84	815	70	617	64
1671	81	1299	62	1090	72	786	79	607	84

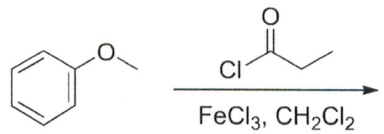


EI-Mass Spectrum of 9-fluorenone **(6 pts)**

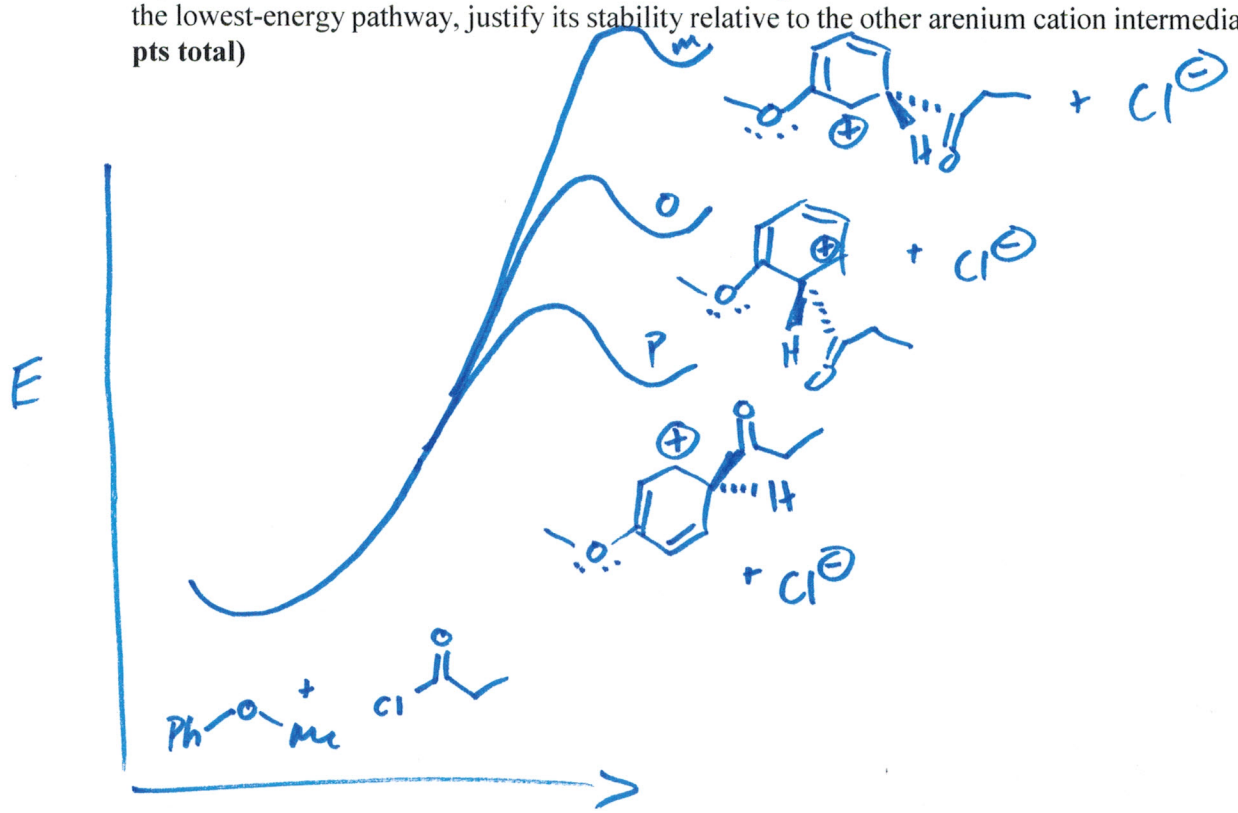
Provide a fragmentation mechanism which accounts for the generation of the ion responsible for the signal at *m/z* = 152 from the ion responsible for the signal at *m/z* = 180. Show all lone pairs, formal charges, and electron-pushing arrows.



2) Anisole can react with propionyl chloride in the presence of a Lewis acid catalyst in an electrophilic aromatic substitution to produce one or more anisole derivatives. **(18 pts total)**

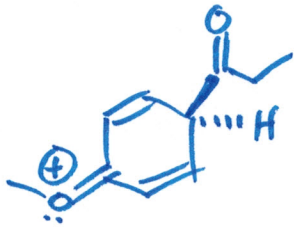


b) The regiochemical outcome of the reaction is governed by the kinetic favorability of one reaction pathway over another. Draw a potential energy surface showing the formation of the possible regioisomeric arenium intermediates from the starting material. For the arenium intermediate on the lowest-energy pathway, justify its stability relative to the other arenium cation intermediates. **(8 pts total)**



These factors stabilize the para arenium relative to the meta and ortho.

1) Charge is delocalized by -ÖMe.



2) No steric interactions between ring substituents.

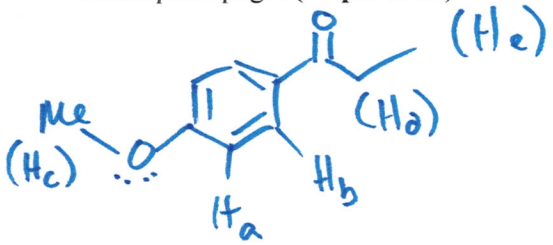
3) The ipso carbons are not adjacent reducing the polarity effect.

$H_a = 7.36 + -0.45 + 0.10 = 7.01$ $H_c = 0.90 + 2.95 = 3.85$

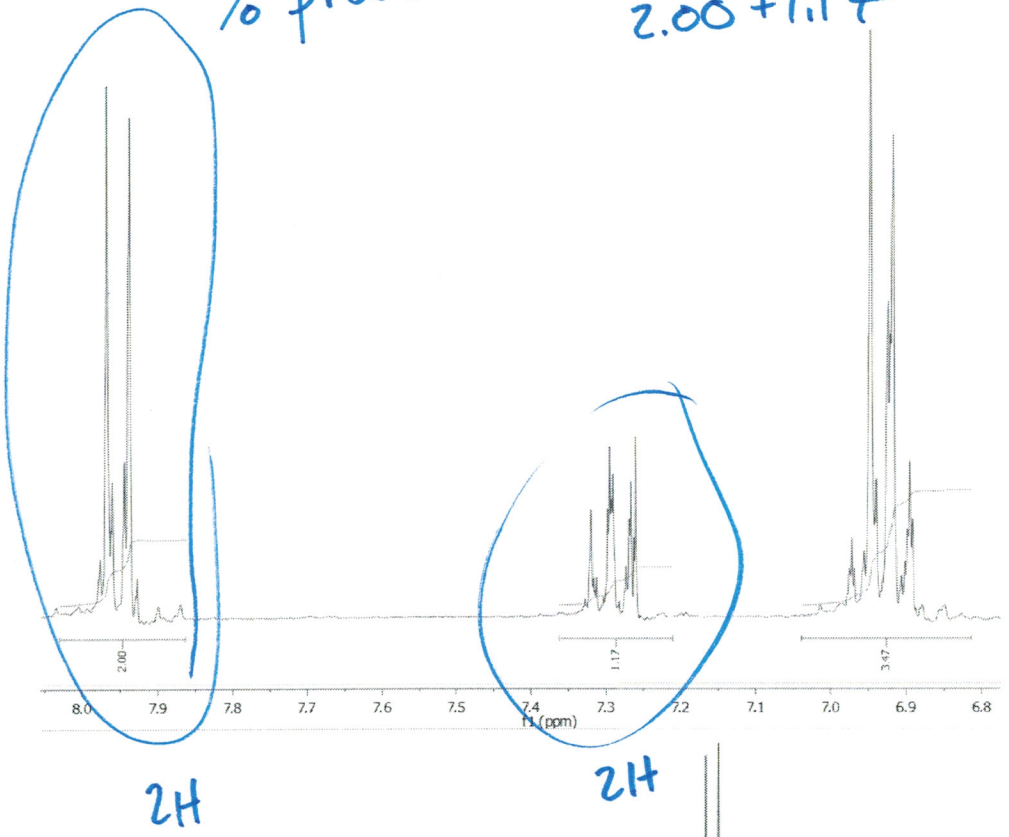
$H_b = 7.36 + -0.07 + 0.44 = 7.73$ $H_d = 1.20 + 1.64 = 2.84$

b) An authentic reaction sample may contain more than one molecule as evidenced by the ^{1}H-NMR spectrum. Using the spectrum, determine the % of the mixture that is the major product of the reaction and assign all integrated NMR signals as per the instructions on the cover page. Place the calculation and assignments directly on this ^{1}H-NMR spectrum. Expansions are provided on the subsequent page. **(10 pts total)**

$H_e = 0.90 + 0.28 = 1.18$

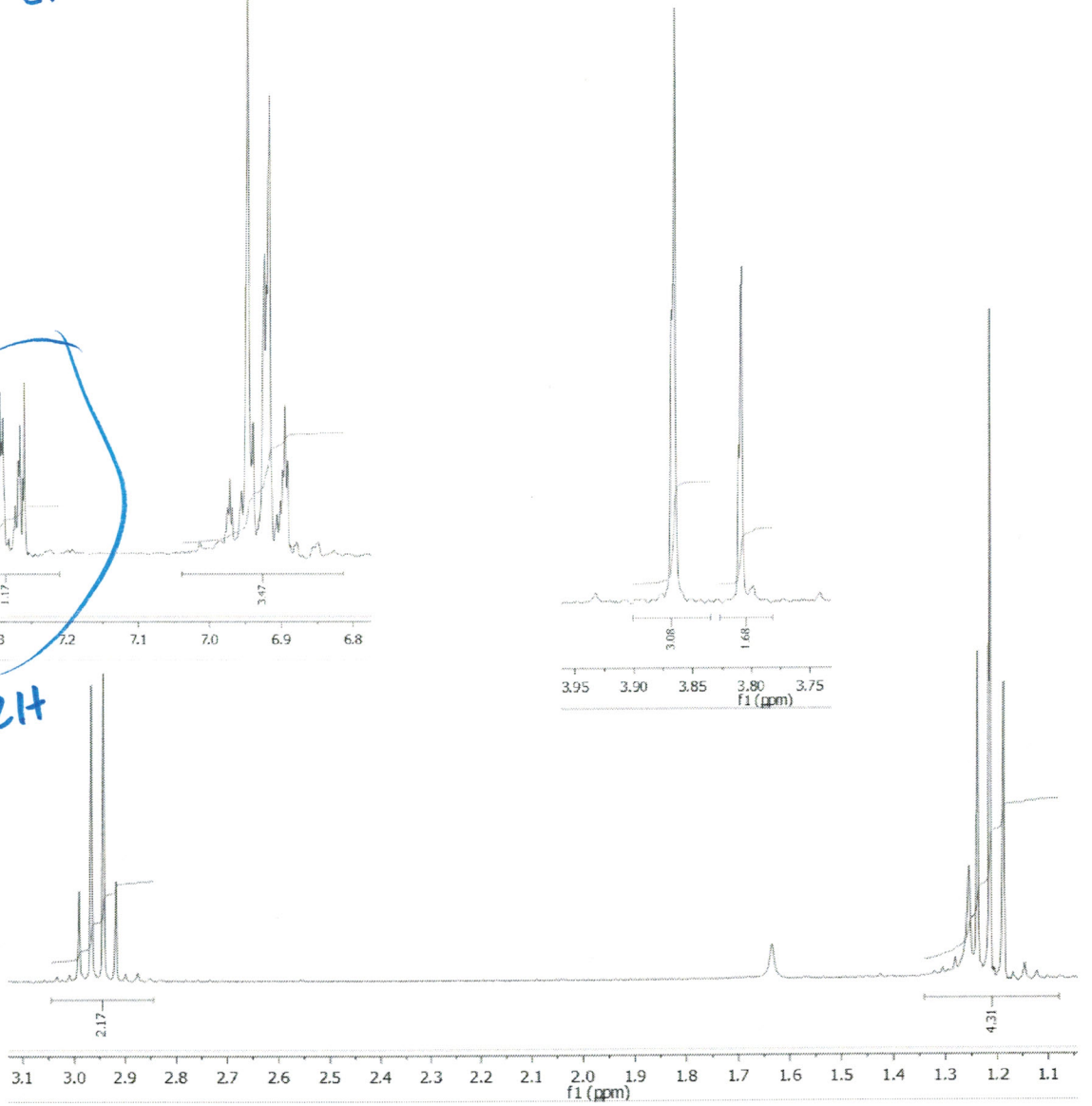


$$\% \text{ product} = \frac{2.00}{2.00 + 1.17} = 63.09\ \%$$

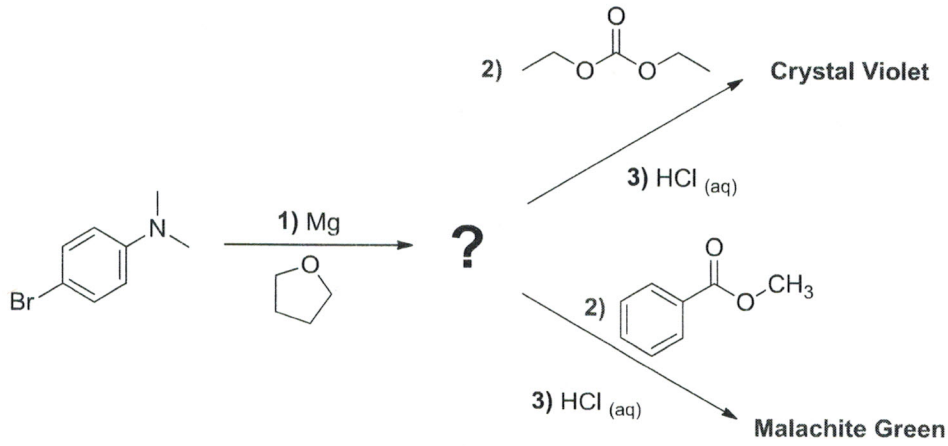


2H

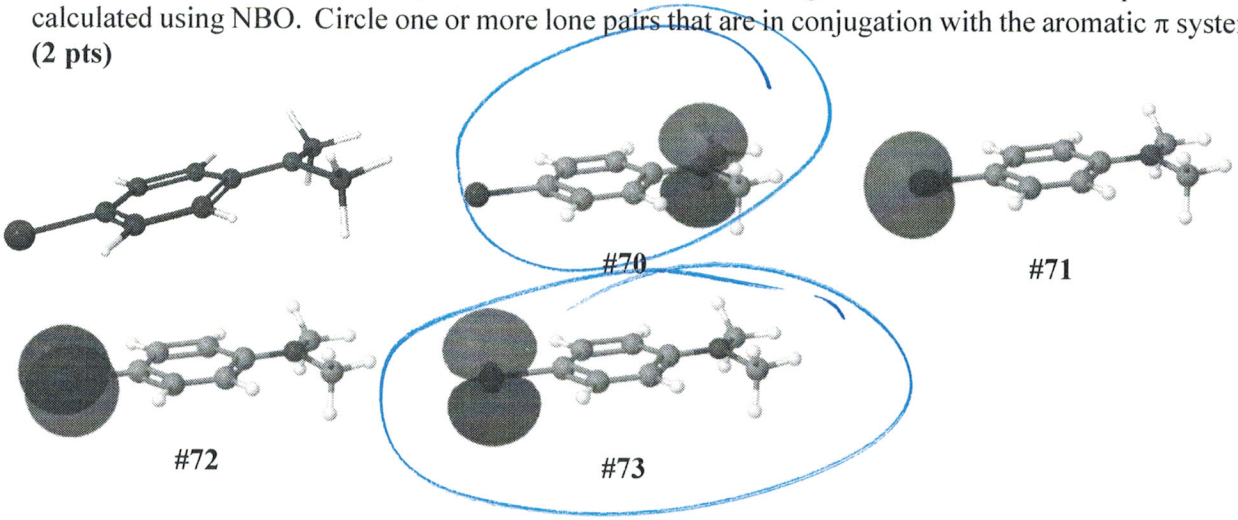
2H



3) A Grignard synthesis can be used to make triarylmethane dyes such as **Malachite Green** and **Crystal violet** in reasonable yield and is shown in the synthetic route below. Crystal violet has a varied usage history including high school and undergraduate kinetic experiments, treating athlete's foot, staining gram-positive bacteria, and ink-jet printers. Malachite green is a controversial antifungal used in commercial aquaculture that has been used to dye bacteria, silk, leather, and paper. **(24 pts total)**



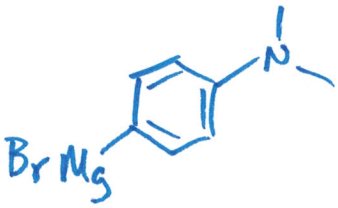
a) The B3LYP/6-31G(d) optimized 4-bromo-N,N-dimethylaniline (precursor to both **Crystal Violet** and **Malachite Green**) structure is presented below along with images of all four of its lone pair orbitals calculated using NBO. Circle one or more lone pairs that are in conjugation with the aromatic π system. **(2 pts)**



70 LP(1)N2 s(2.10%)p46.66(97.89%)d0.01(0.01%)
71 LP(1)Br15 s(86.27%)p0.16(13.73%)d0.00(0.00%)
72 LP(2)Br15 s(0.00%)p1.00(99.99%)d0.00(0.01%)
73 LP(3)Br15 s(0.00%)p1.00(99.98%)d0.00(0.02%)

Step 1 of the dye preparation is carried out in a 250-mL round bottomed flask equipped with a reflux condenser. The flask and condenser are rinsed with a few milliliters of anhydrous THF, then the flask is charged with magnesium (0.80 g), anhydrous THF (45 mL), 4-bromo-N,N-dimethylaniline (5.0 g), and a few drops of 1,2-dibromoethane. The mixture is warmed gently to reflux, and maintained there for 30 min, during which time the original dark color changes to the typical "dirty dishwater" shade of the Grignard reagent. In **step 2**, the flask is cooled to room temperature (ice- water bath), then diethyl carbonate (0.49 g) to make **crystal violet** or methyl benzoate (0.85 g) to make **malachite green** in 5mL of THF is added in one portion. The mixture is warmed to reflux for an additional 5 min, then cooled again to room temperature (ice-water bath). In **step 3**, Aqueous hydrochloric acid (15mL of a 10% solution) is added slowly (the reaction with the remaining magnesium is vigorous). The result is a muddy purple (**crystal violet**) or cloudy green (**malachite green**) mixture. The product was prepared for ^{1}H-NMR, ^{13}C-NMR, IR, and UV/VIS analysis.

b) Draw the Grignard reagent that forms by reaction of magnesium to 4-bromo-N,N-dimethylaniline. Provide an additional halogentated starting material that would likely work as well for this reaction and one that would not work effectively for this reaction. Justify your selections. **(5 pts)**



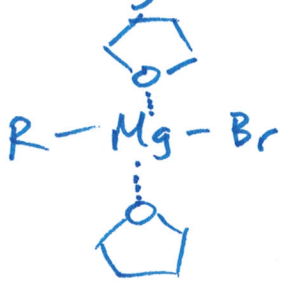
:Cl–Ar = ok

:F–Ar = not ok

The C-F bond is too strong for Mg insertion.
C-Br, C-Cl, and C-I are all more reactive.

c) The glassware is rinsed with a few milliliters of anhydrous THF and 45 mL is used for the reaction. Why is THF an effective solvent for Grignard reagent formation and Grignard reactions? Why does it need to be anhydrous? **(4 pts)**

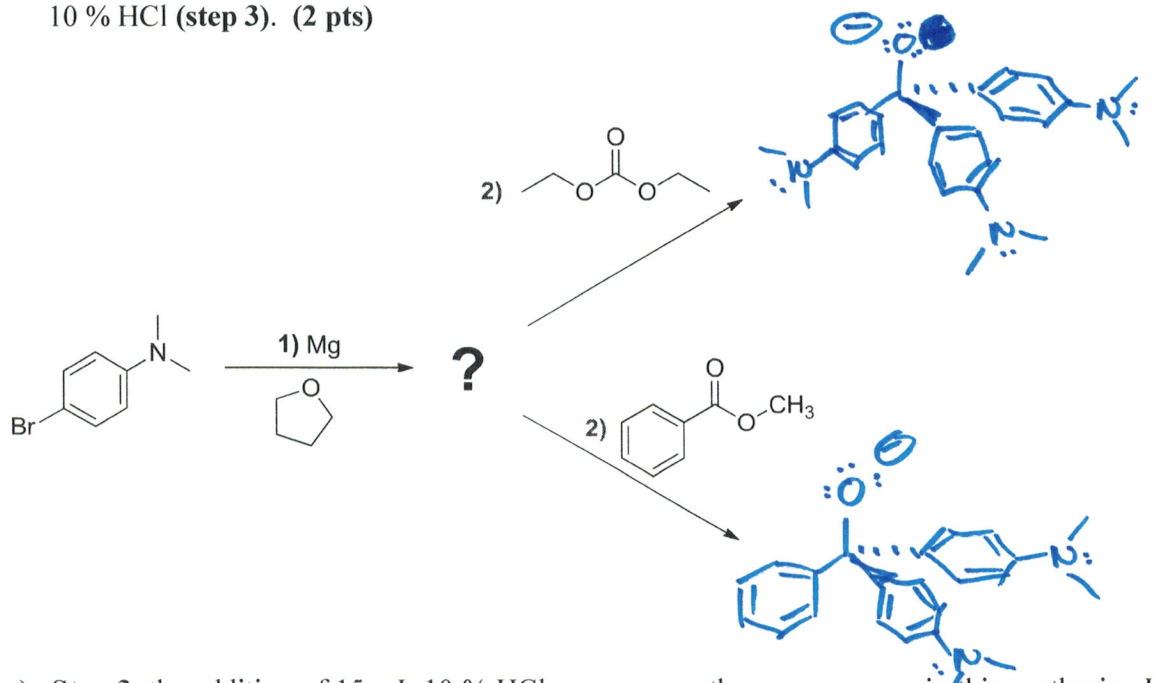
THF stabilizes the Grignard reagent and is NOT acidic.



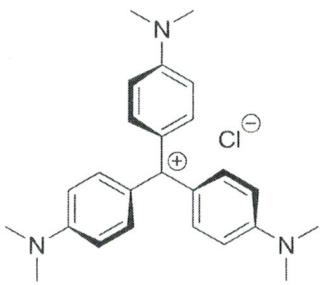
$RMgBr + H_2O \longrightarrow R-H + {}^{\ominus}OH + {}^{\oplus}MgBr$

pka ≈ 15.7 pka ≈ 55

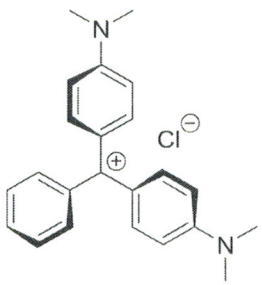
d) The esters (diethyl carbonate or methyl benzoate) allow for three or two additions of the Grignard reagent respectively. For each case, show the product at the **end of step 2** before the addition of 15 mL 10 % HCl **(step 3). (2 pts)**



e) **Step 3**, the addition of 15 mL 10 % HCl serves more than one purpose in this synthesis. It is used to workup the reaction mixture and to protonate and dehydrate the product at the end of step two. This dehydrated product is crystal violet or malachite green depending on the synthesis. Show an electron-pushing mechanism depicting how this protonation and dehydration occurs for **crystal violet**. You may use –Ar for aromatic substituents not involved in a specific mechanistic step. **(4 pts)**



Crystal Violet



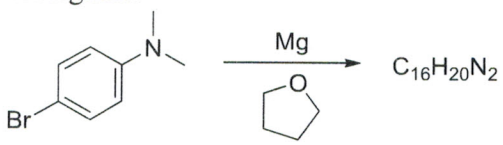
Malachite Green

f) The extended conjugated π systems of triarylmethane dyes are responsible for the most intense absorption features in their UV/Vis spectra and their bright colors. For **crystal violet** and **malachite green**, identify the total number of atoms in π conjugation. **(2 pts)**

Crystal Violet = 22

Malachite Green = 21

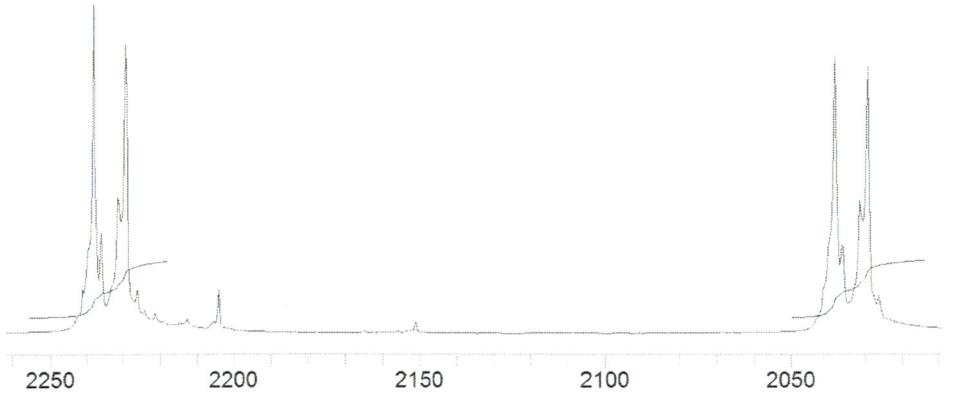
g) A common byproduct of Grignard reagent formation, highlighting that the mechanism is more complicated than often depicted, is a combination of two Grignard reagents. Use the provided ^{1}H-NMR spectrum to determine the byproduct of this Grignard reaction. Place your final answer directly on the spectrum and assign the ^{1}H-NMR signals.

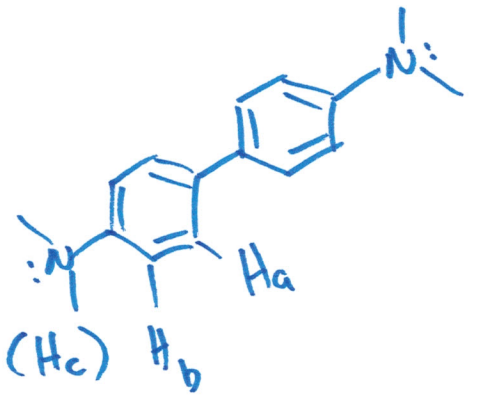


300 MHz ^{1}H NMR

In CDCl3

$C_{16}H_{20}N_2$ **(5 pts)**



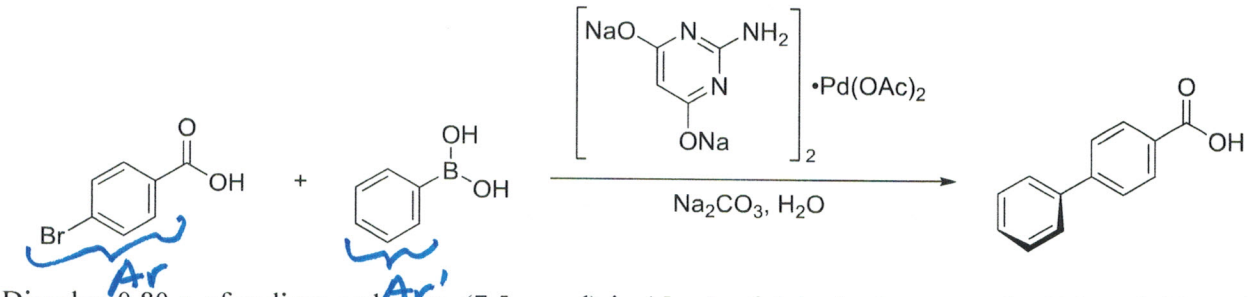


$H_a = 7.36 + 0.23 + -0.18$
$= 7.41$

$H_b = 7.36 + 0.07 + -0.66$
$= 6.77$

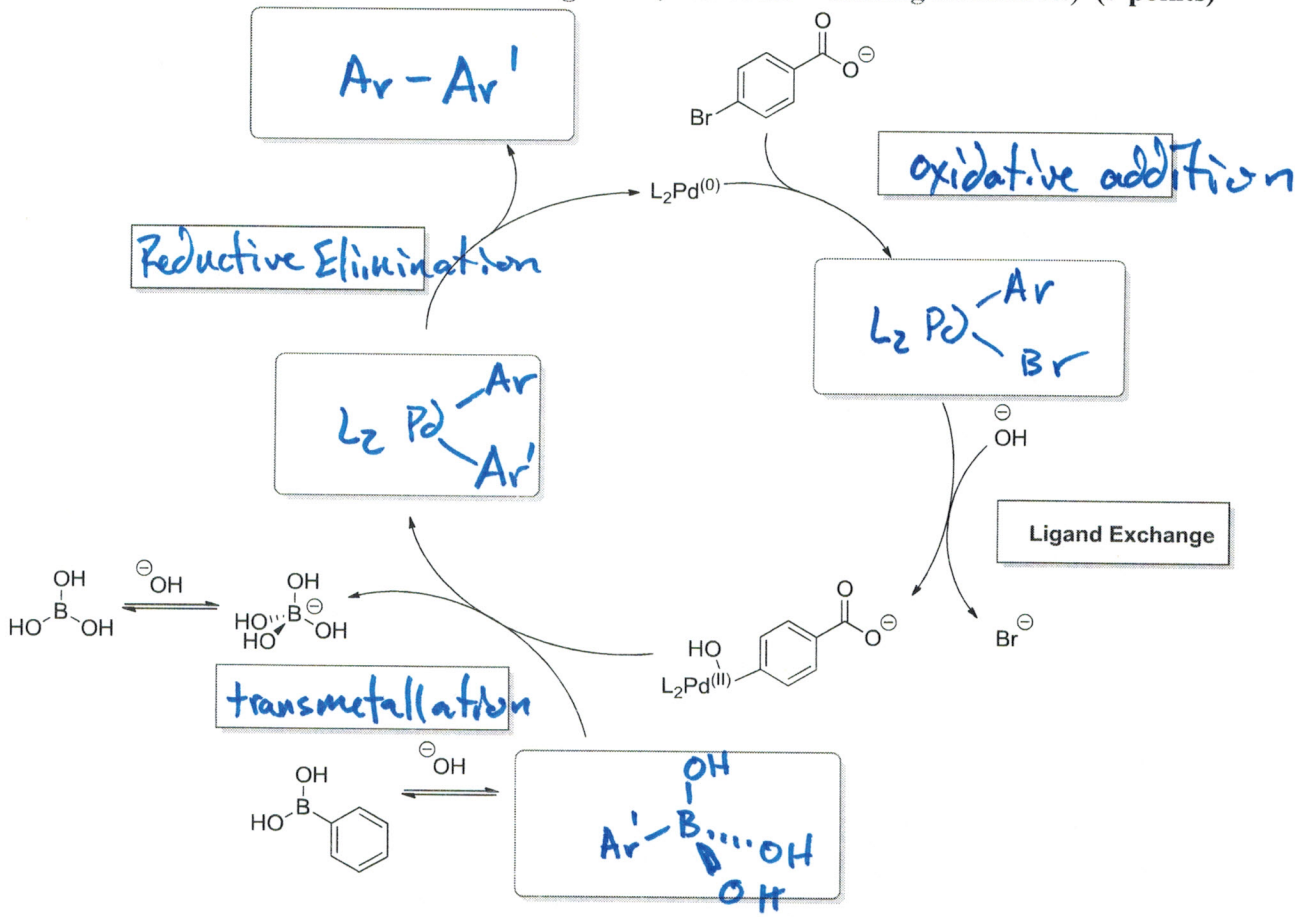
$H_c = 0.90 + 2.08$
$= 2.98$

4) Described as an operationally simple aqueous Suzuki-Miyaura cross-coupling reaction, 4-phenylbenzoic acid can be synthesized in greater than 50% yield from phenylboronic acid and *para*-bromobenzoic acid. **(24 points total)**

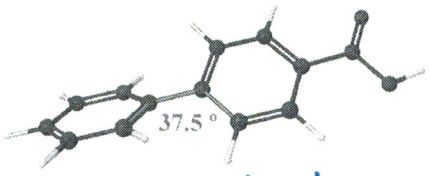


Dissolve 0.80 g of sodium carbonate (7.5 mmol) in 15 mL of deionized water and add it to 0.50 g of 4-bromobenzoic acid (2.5 mmol) and 0.37 g of phenylboronic acid (3.0 mmol) to a 125 mL Erlenmeyer flask containing a stirring bar. After 10 min. of stirring add 1.0 mL palladium (0.01 mol %) catalyst solution. Heat the reaction to a temperature of about 70 °C for 30 minutes. Allow the reaction cool to room temperature and place it in an ice bath. Position the flask and ice bath so that the mixture is still stirred efficiently. Add 25 mL of 1M HCl dropwise and stir for 5 minutes. Isolate the crude product by vacuum filtration and recrystallize in a 1 to 10 ratio of 1M HCl and EtOH. Prepare the sample for IR, ^{1}H-NMR, and ^{13}C-NMR analysis.

a) An incomplete catalytic cycle for this Suzuki-Miyuara coupling is shown below. Fill in the missing terms and molecules. (**Blue boxes = missing terms; red boxes = missing structures.**) **(7 points)**



b) The B3LYP/6-31G(d) optimized structure of the carboxylic acid product is shown below with the inter-ring dihedral angle labeled. Clearly explain the factor or factors that result in this 37.5 ° dihedral angle. **(4 points)**

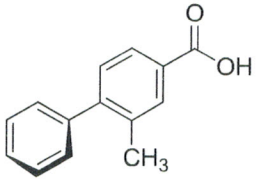


steric repulsions between C-H bonds are min at 90° and max a 0°

π Conjugation is max at 0° and min at 90°

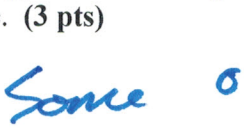
the angle of 37.5°C is a dihedral angle the reduces the steric interaction and allows some conjugation.

c) Would you expect the dihedral angle to be greater or lesser in the molecule below compared to the product of the reaction shown above in 2b. Justify your answer. **(2 points)**

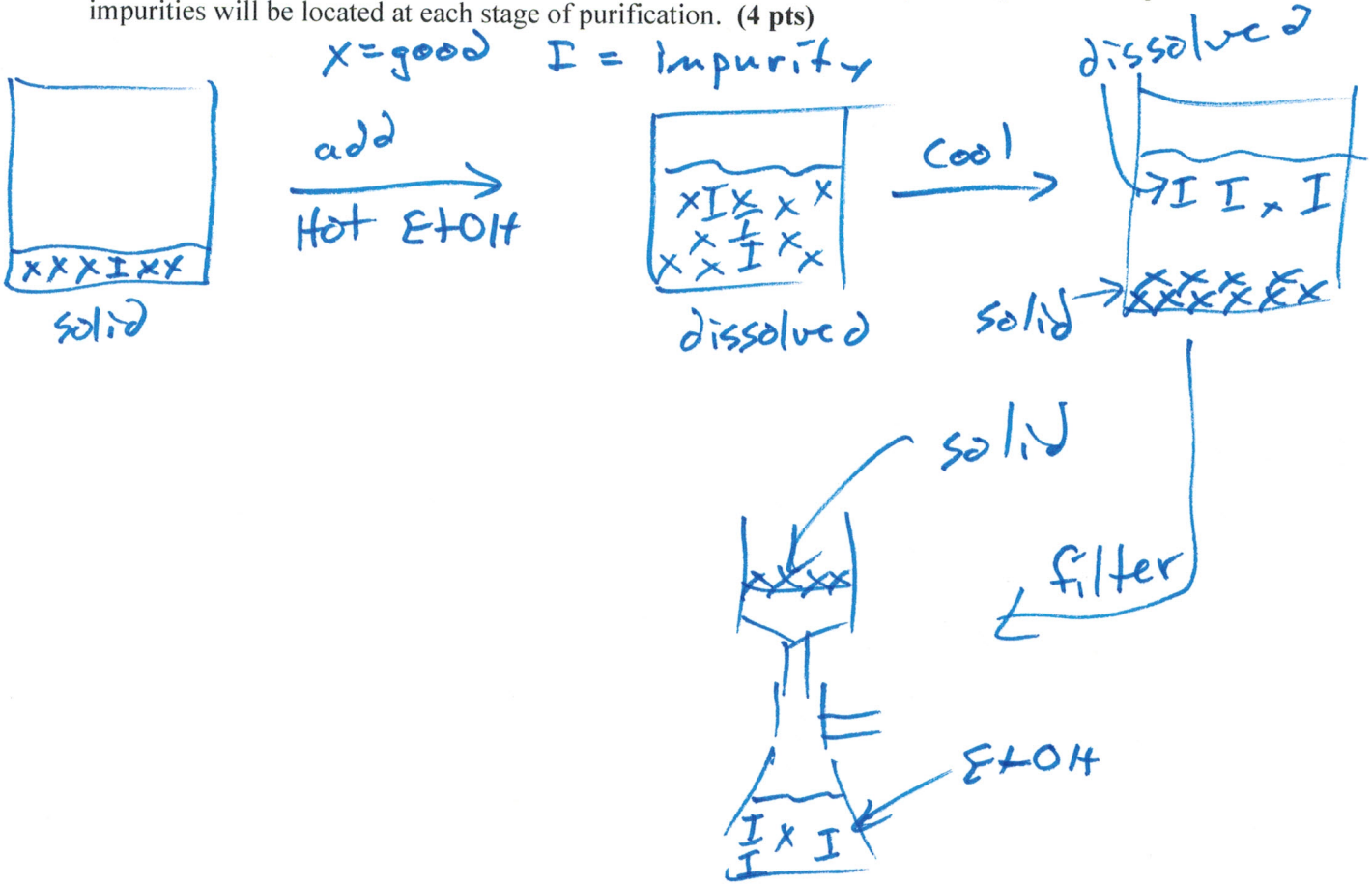


If should be greater due to the increased repulsion of the C—CH3 compared to C—H

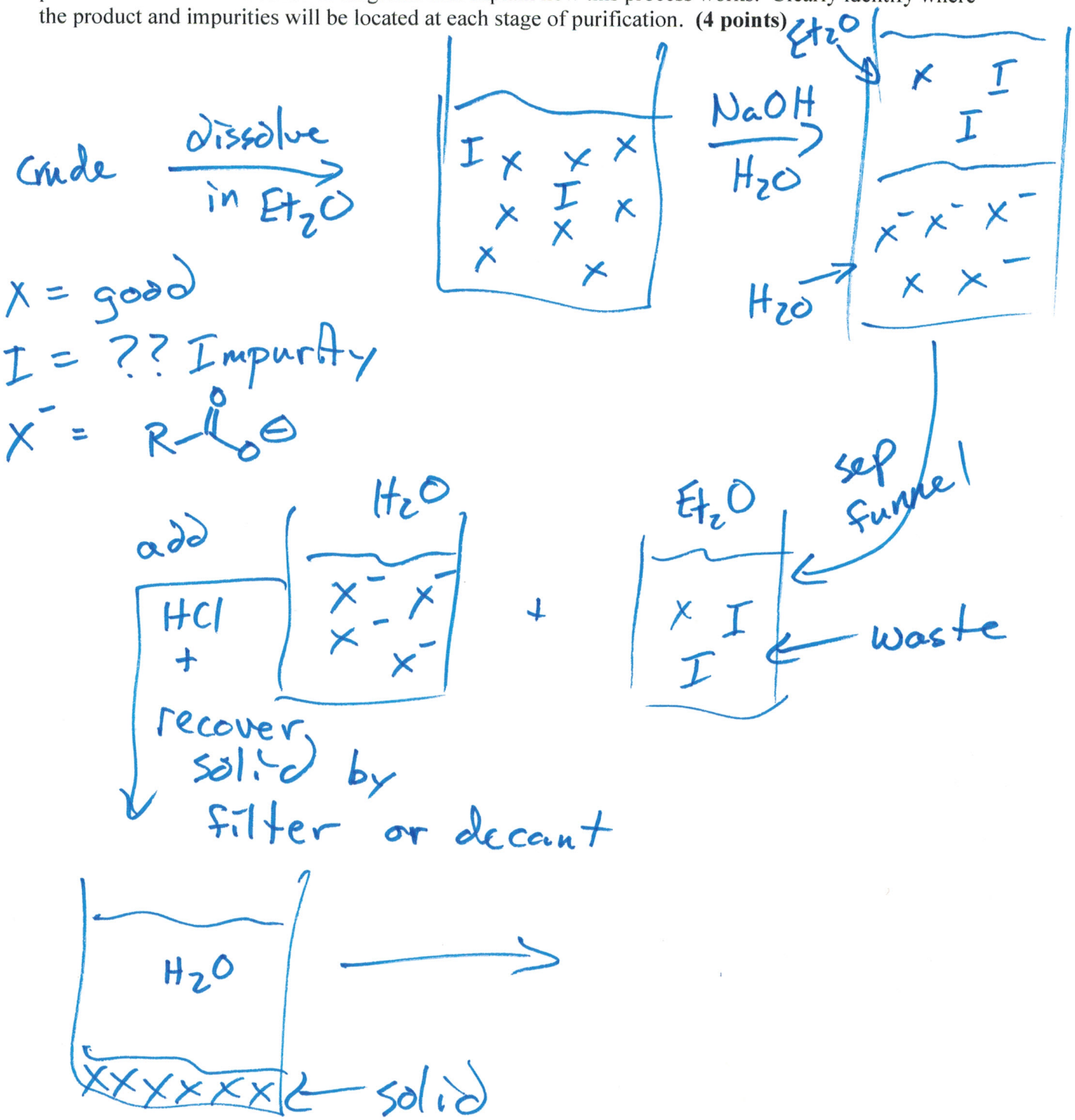
d) The ^{1}H-NMR Spectrum in $CDCl_3$/DMSO-d_6 of the product (on the subsequent page) contains a signal at δ 13.0 ppm with an integration of 0.89. Provide a rationale for why this signal has an integration less than one. **(3 pts)**

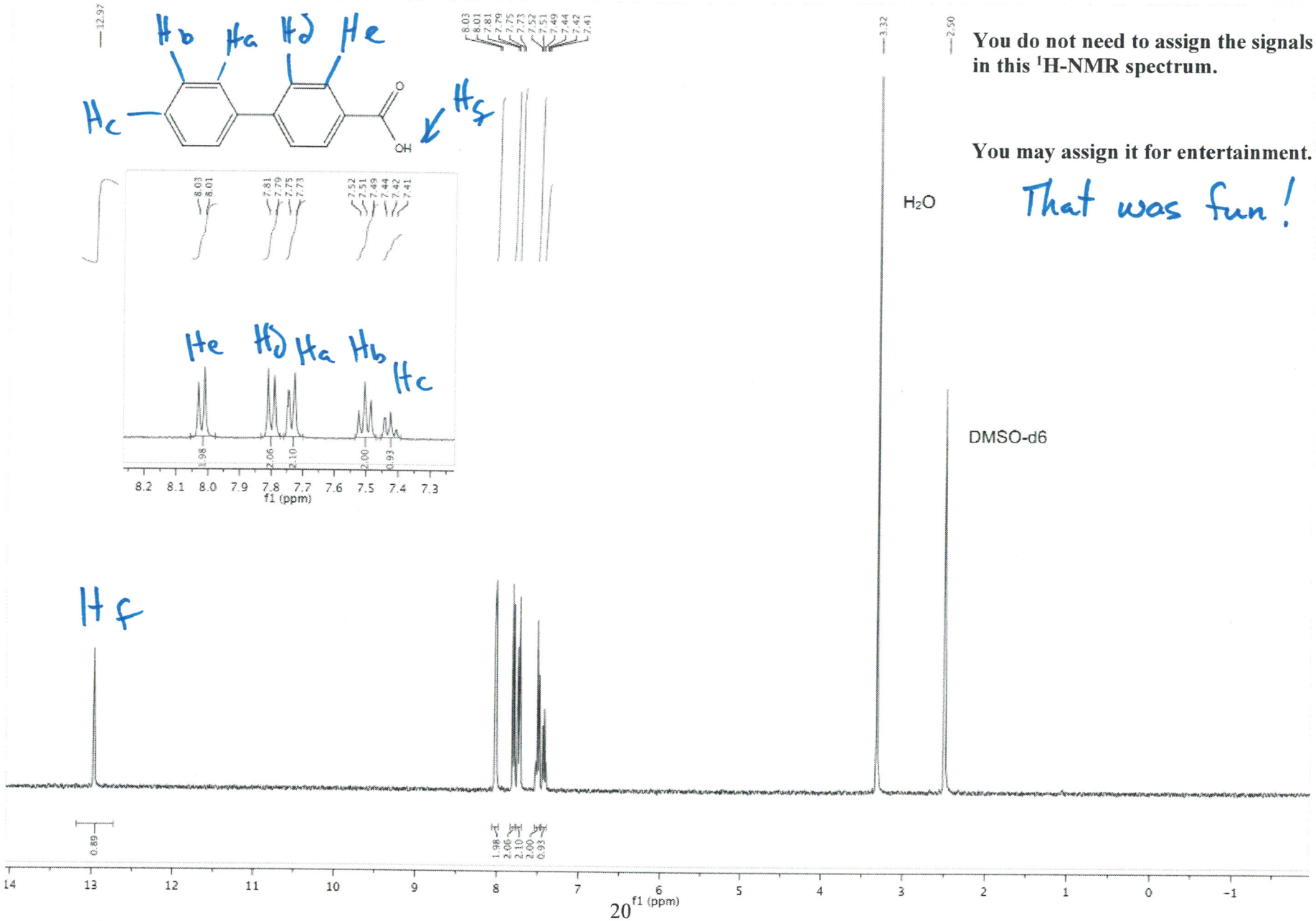
Some of the  has converted to  with reaction/exchange with $CDCl_3$

e) The crude biaryl product can be purified by recrystallization in acidic ethanol and vacuum filtration. Draw a series of diagrams that explain how this process works. Clearly identify where the product and impurities will be located at each stage of purification. **(4 pts)**



f) The crude biaryl product could be purified readily by another method. Suggest an alternate method of purification and draw a series of diagrams that explain how this process works. Clearly identify where the product and impurities will be located at each stage of purification. **(4 points)**





You do not need to assign the signals in this ^{1}H-NMR spectrum.

You may assign it for entertainment.

That was fun!

CHEM 344 Summer 2014 Final Quiz (100 pts)

Name:

TA Name:

1) _____ /34

Page 2	**_____ /10**
Page 3	**_____ /6**
Page 4	**_____ /8**
Page 5 – 7	**_____ /10**

2) _____ /18

Page 8	**_____ /8**
Page 9 – 10	**_____ /10**

3) _____ /24

Page 11	**_____ /2**
Page 12	**_____ /9**
Page 13	**_____ /6**
Page 14 – 15	**_____ /7**

4) _____ /24

Page 16	**_____ /7**
Page 17	**_____ /6**
Page 18	**_____ /7**
Page 19	**_____ /4**

Total = _____ /100

Total = _____ /100 (math double-check)