Lab 3

THE WITTIG REACTION[1]

Background

Reading Assignments
Techniques:
- TLC: Mohrig,[2] Chp. 18.1-18.6 (on Sakai)
- Labflow: "Running a TLC analysis" video.

Chemistry:
- Wittig Reaction: Loudon,[3] p. 918-920
- *J* constant : Loudon,[3] p. 629

In CHEM 202, you will see several reactions that result in new carbon-carbon bond formations. You previously performed the Diels-Alder reaction, which resulted in the formation of two new C-C bonds when the cyclohexene product was formed. Another example of a reaction that leads to new C-C bonds is the Wittig alkene synthesis, a useful method for the preparation of alkenes from aldehydes and ketones.

One of the most important features of the Wittig synthesis is that it is *regioselective*, meaning little or no unwanted regioisomers are formed. This aids in synthesizing alkenes that might be difficult to prepare by other mechanisms, such as regioselective formation of alkenes by alcohol dehydration. Another feature of the Wittig reaction is that alkene formation tends to favor the *Z*- or *cis*-isomer. However, in some cases it is possible to control the ratio of (E/Z) products by changing solvents or adding salts.

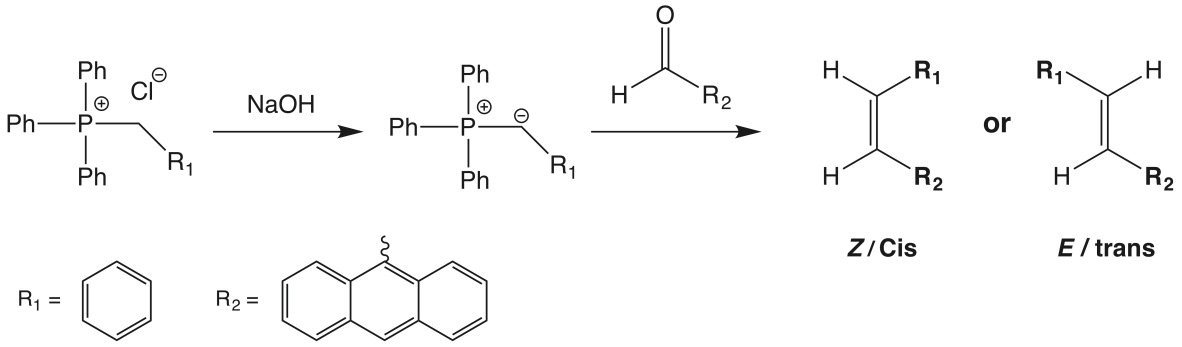


Figure 1. The Wittig reaction for the preparation of 9-styrylanthracene. (The squiggly line on the anthracene molecule signifies the "9" carbon position.

The scheme for today's reaction is shown in Figure 1. The first step involves deprotonating benzyltriphenylphosphonium chloride with a relatively strong base (NaOH) to yield the reactive ylid species. The ylid is generated *in situ* (i.e., in the reaction mixture) due to its unstable nature. Once formed, the ylid acts as a nucleophile and reacts with the electrophilic carbon of the aldehyde group. Along with the final product, triphenylphosphine oxide (Ph_3PO) is formed as a byproduct.

The formation of either *Z* or *E* isomers is sometimes based on the intermediate pathway that occurs. There are two theoretical pathways to the formation of the final product (Figure 2).

1. **[2+2] Cycloaddition:** This pathway is the faster of the two, and the intermediate species formation is concerted, like the S_N2 reaction. The intermediate species of this pathway is a four-membered ring known as an *oxaphosphetane*. Most literature shows evidence that this mechanism is the most likely to take place in the Wittig reaction.

2. **Betaine formation:** Betaine formation occurs via a S_N1-type reaction. The carbanion of the ylid first attacks the carbonyl carbon. This leads to the formation of the betaine structure shown in Figure 2. Once formed, the betaine structure reacts intramolecularly to form the four-membered oxaphosphetane species, which fragments to afford the final alkene.

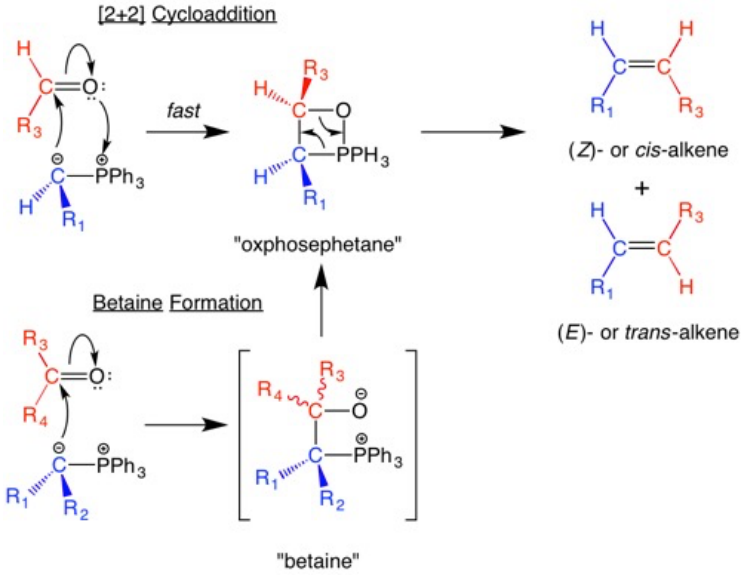
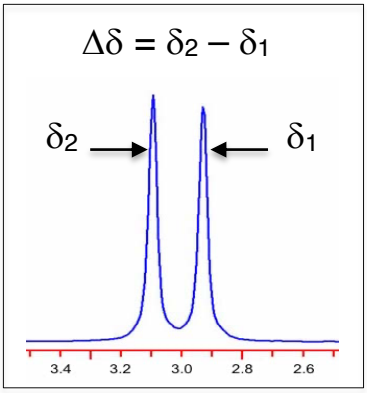
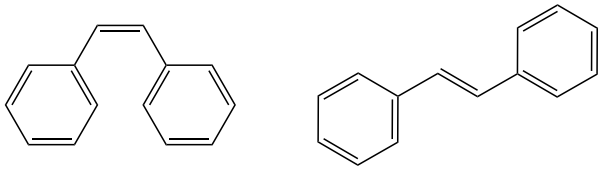


Figure 2. The two proposed reaction pathways for the Wittig reaction.

In today's experiment you will prepare 9-styrylanthracene. Using spectral data, you will determine which isomer (*Z* or *E*) was isolated from your reaction. Considering the structural properties of the starting materials, can you guess which isomer is most likely to form? Would this alkene be the expected isomer? Looking at Table 1 below, you can see that (*Z*)- and (*E*)-stilbene (1,2-diphenylethene), a diaryl alkene like that of this lab's product, exhibit differences in their ^{1}H NMR spectra. (*E*)-stilbene alkene protons appear further downfield than those for (*Z*)-stilbene. The coupling constant, *J*, determined by multiplying the chemical shift difference between signal peaks (Figure 3) by the resonance frequency of the NMR magnet, yields different value ranges for (*Z*) and (*E*)-stilbene. Similarly, differences are seen in FT-IR spectroscopy, where fingerprint-region frequencies associated with the alkene C-H bend differ between the two isomers.





(*Z*)-1,2-diphenylethene (*E*)-1,2-diphenylethene

	(*Z*) Ph-C*H*=C*H*-Ph	(*E*) Ph-C*H*=C*H*-Ph
NMR δ (ppm)	**6.57**	**7.15**
J (Hz)	**4 – 12**	**14 – 19**
IR ν (cm^{-1})	**675 – 727**	**960 – 990**

Figure 3. Determining Δδ for calculation of the coupling constant *J* (left), and NMR and IR data for the *Z*- and *E*-stilbene (right)

An interesting property of 9-styrylanthracene is its ability to undergo chemiluminescence. Chemiluminescence is the emission of light during a chemical reaction, with limited emission of heat. Examples of products that have chemiluminescent properties include Glowsticks and luminol (used to detect blood at crime scenes). In the second half of this lab, you will briefly explore the chemiluminescent properties of your product.

SAFETY PRECAUTIONS – GLOVES AND GOGGLES MUST BE WORN AT ALL TIMES!

- **Benzyltriphenylphosphonium chloride** and **sodium acetate** are **hygroscopic** and **irritants**.
- **Propanol, hexane,** and **ethyl acetate** are **highly flammable**. Keep these solvents away from high-heat sources!
- ***N,N*-dimethylformamide (DMF)** is a **suspected carcinogen** and **irritant**.
- **50% w/w NaOH (aq**) is **highly corrosive.** Can cause burns to skin, eyes, and clothing! **HANDLE IN THE HOOD ONLY!**
- **9-Anthraldehyde and bis[2-(methoxycarbonyl)phenyl] oxalate (MCPO)** are mild irritants.
- **30% w/w H_2O_2 (aq)** can cause **burns to skin and eyes**!

Procedure

PART ONE: Preparation of 9-Styrylanthracene

1. In a 10-mL round bottom flask, add **200 mg** of benzyltriphenylphosphonium chloride, **115 mg** of 9-anthraldehyde, and **0.7 mL** of DMF. Add a stir bar to your flask and proceed to vigorously stir the solution.

2. While stirring, carefully add **0.25 mL (6 - 8 drops) of 50% w/w NaOH solution dropwise** to the solution (*ask your TA for this*!). If necessary, wash any solids on the walls of the flask with additional DMF (about 5 drops). Continue vigorously stirring the solution for **30 minutes**. Note any color changes that occur during this time.

3. After the 30-minute period, add **4 mL** of a **1:1 propanol/H_2O mixture** to precipitate your product. Collect the crude product by vacuum filtration on a Hirsch funnel. Rinse the product with 1-2 mL of **ice-cold** 1:1 propanol/H_2O and allow to air dry under vacuum for 10 minutes.

4. Next, prepare a TLC chamber using 4:1 hexane/ethyl acetate. Prepare dilute solutions (~ 1 mL) of 9-anthraldehyde and your crude product using acetone. On your silica gel plate, prepare lanes for: **1)** 9-anthraldehyde**, 2)** a co-spot of 9-anthraldehyde and the crude product, and **3)** the crude product. Once the TLC plate is ready, visualize the results using the UV lamp and circle the apparent spots. What do you notice about the spot of your product under the UV lamp? Calculate the R_f values for the starting aldehyde and the product and record them in your notebook. Also include a drawing of your TLC plate with spot locations circled.

5. Determine the **mass** of your crude product and determine the **melting point range**. Using the mass, calculate your **percent yield** of your product.

6. The **IR & ^{1}H-NMR spectra** of the product are at the end of this lab handout. Submit all **analyzed** spectra with your post-lab report. **You will not take an IR of your product this week!**

PART TWO: Chemiluminescence of 9-Styrylanthracene

***Your TA will demonstrate this part of the experiment for the class**

1. In a 25-mL Erlenmeyer flask dissolve **20 mg** of **MCPO** and approximately **5-10 mg** of the product in **15 mL** of ethyl acetate (masses of solids can be approximate; using the balance is not necessary). Next, in a large test tube combine **100 mg** of sodium salicylate and **1 mL** of 30% hydrogen peroxide and mix the contents well.
2. With the room darkened, add the peroxide suspension to the flask containing the MCPO and product, and plug the flask snuggly with a rubber stopper. Swirl the flask gently to mix the contents. **If no luminescence is seen or is difficult to see, add a few drops of acetone**. Record your observations in your notebook. Note the length of time the mixture displayed luminescence.

Pre-Lab Assignments

- **Pre-reading** – Read the sections pertaining to the new techniques and chemistry in this lab (see first page). **For a TLC refresher, read the TLC section of the Mohrig text under the Lab Resources and watch any videos posted under Lab 3 on Labflow.**
- **Prelab Notebook**
  - ✓ **Objective:**
    - Include a brief statement describing the goals of the experiment.
    - Include the proposed reaction mechanisms for this week's experiment, starting with benzyltriphenylphosphonium chloride and 9-anthraldehyde, and ending with 9-styrylanthracene. Draw the structures of the (*Z*) and (*E*) isomers of 9-styrylanthracene.
    - Hypothesize which isomer you think will form (*Z*, *E*, or both?). Briefly explain your reasoning.
    - Include a Table of Reagents like the one shown below.

Chemical	MW (g/mol)	mp (°C)	Density (g/mL)	Actual Mass (g)	Actual Vol. (mL)	Actual Moles
9-Anthraldehyde	206.24	103-105	-----		-----	
Benzyl (PPh_3)Cl	388.87	> 300	-----		-----	
50% NaOH (w/v)	40.00	-----	1.515			
DMF	73.09	153 (bp)	0.944	-----		-----
(E)-9-Styrylanthracene	280.37	132	-----		-----	
(Z)-9-Styrylanthracene	280.37	111	-----		-----	

  - ✓ **Reaction + separation scheme:** Include a scheme beginning with benzyltriphenylphosphonium chloride, 9-anthraldehyde, 50% NaOH (aq), and DMF, and ending with 9-styrylanthracene.
  - ✓ **Procedure:** Write out a brief summary of the experimental steps for **Part 1 only**. The written procedure should have enough detail that your TA can understand it without referring to the lab handout.

In-Lab Notebook

Observations – Record EXACT amounts of reagents used (redraw and use a table like the one shown on the previous page), observations, and any changes you have made to the written procedure. Also include all physical data (appearance & melting point, TLC results). This should be written directly in your notebook while you are in the lab.

All information *above* should be written *directly into your lab notebook*. The duplicate pages will be turned in to your TA at the end of the lab.

All information *below* will be *included on the Post-Lab Report* and does NOT have to be written separately in the notebook. You may choose to work through your calculations or organize your ideas for the discussion, etc. in the notebook, but this information is not required in the notebook.

Post-Laboratory Report

Complete as directed on the following pages.

References

[1] Part One adapted from: Jaworek, C.; Iacobucci, S. *J. Chem. Ed.* **2002**, *79* (1), 111. Part Two adapted from: Williams, K. L. *Organic Experiments, 9th Ed*. Houghton Mifflin Company, 2004, p. 558-563.

[2] Mohrig, J.R. et. al, *Laboratory Techniques in Organic Chemistry, 4th Ed.* W. H. Freeman & Company: New York, NY, 2014

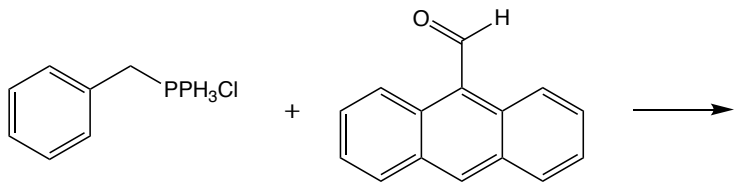
[3] Loudon, G.M.; Parise, J. *Organic Chemistry, 6th Ed*. Roberts & Company Publishers, 2016.

Chemistry 202L – Post-lab Report for the Wittig Reaction (Lab 3)

Name:_____ **TA name/Section Number:**_____

1. Draw the reaction product & balance the chemical equation using the ***theoretical*** amounts of reagents.

Show correct stereochemistry!



_____ _____ _____

2. Calculate the ***actual*** amount (in moles) of benzyltriphenylphosphonium chloride used in the reaction.

3. Calculate the ***actual*** amount (in moles) of 9-anthraldehyde used in the reaction.

4. What is the **limiting reagent**? _____

5. Calculate the **theoretical yield** (in milligrams) of 9-styrylanthracene for the reaction.

6. Calculate the **actual** amount (in moles) of **9-styrylanthracene** you obtained in the reaction.

7. Calculate the **percent yield** of your crude product using moles or milligrams.

8. Draw your ***revised Reaction & Separation scheme***, beginning with benzyltriphenylphosphonium chloride, 9-anthraldehyde, 50% NaOH (aq), and DMF; and ending with crude 9-styrylanthracene.

9. Draw the curved-arrow reaction mechanism based on **the [2+2] cycloaddition pathway**, starting with benzyltriphenylphosphonium chloride & 9-anthraldehyde, and ending with 9-styrylanthracene.

10. Fill in the following table with your experimental data and literature values.

	Literature	Experimental
Appearance		
Melting point range (°C)		

11. ***TLC Analysis of the Reaction Mixture***

Indicate the approximate **location, shape, and size** of each of the spots on the TLC plate. To the right of the plate, indicate **UV activity** and R_f **value** of each of the spots you recorded (**show calculations**!). Did you notice anything unique about your product spots under UV light?

1 = 9-Anthraldehyde
2 = co-spot (9-anthraldehyde + crude reaction)
3 = crude reaction

Spot	UV Activity (Y/N?)	R_f values	Unique Observation?
1			
2			
3			

Additionally:

- Attach a copy of the analyzed ^{1}H NMR spectrum of 9-styrylanthracene (**on the next page**). **On the spectrum, draw the correct product isomer and match the *alkene* hydrogens to their corresponding chemical shifts.** Using the data on the spectrum, calculate the *J values* ***(show your calculations on the spectrum!).*** Analyze ONLY the alkene protons, not the entire molecule.

- Attach a copy of the analyzed IR spectrum (**on last page**), indicating the functional group vibrations responsible for **at least four important peak, including any peak(s) that confirm isomer stereochemistry**!

- For your typed discussion, assimilate the answers the following questions into a careful analysis of the experimental results.

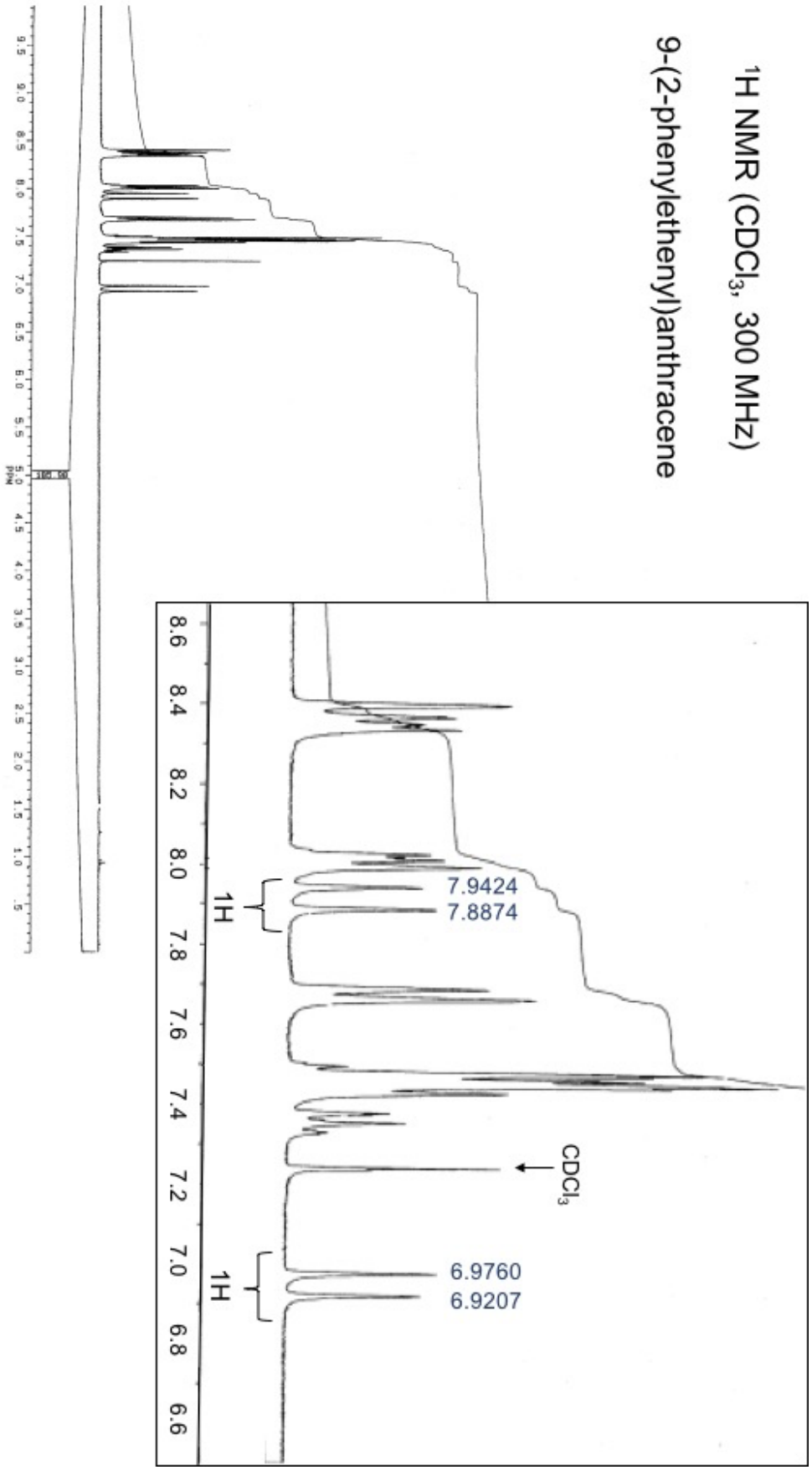
    1. Which isomer was obtained in the reaction? How do you know based on physical appearance and m.p data? Why was this specific isomer obtained and not the other isomer or a mixture of the two?

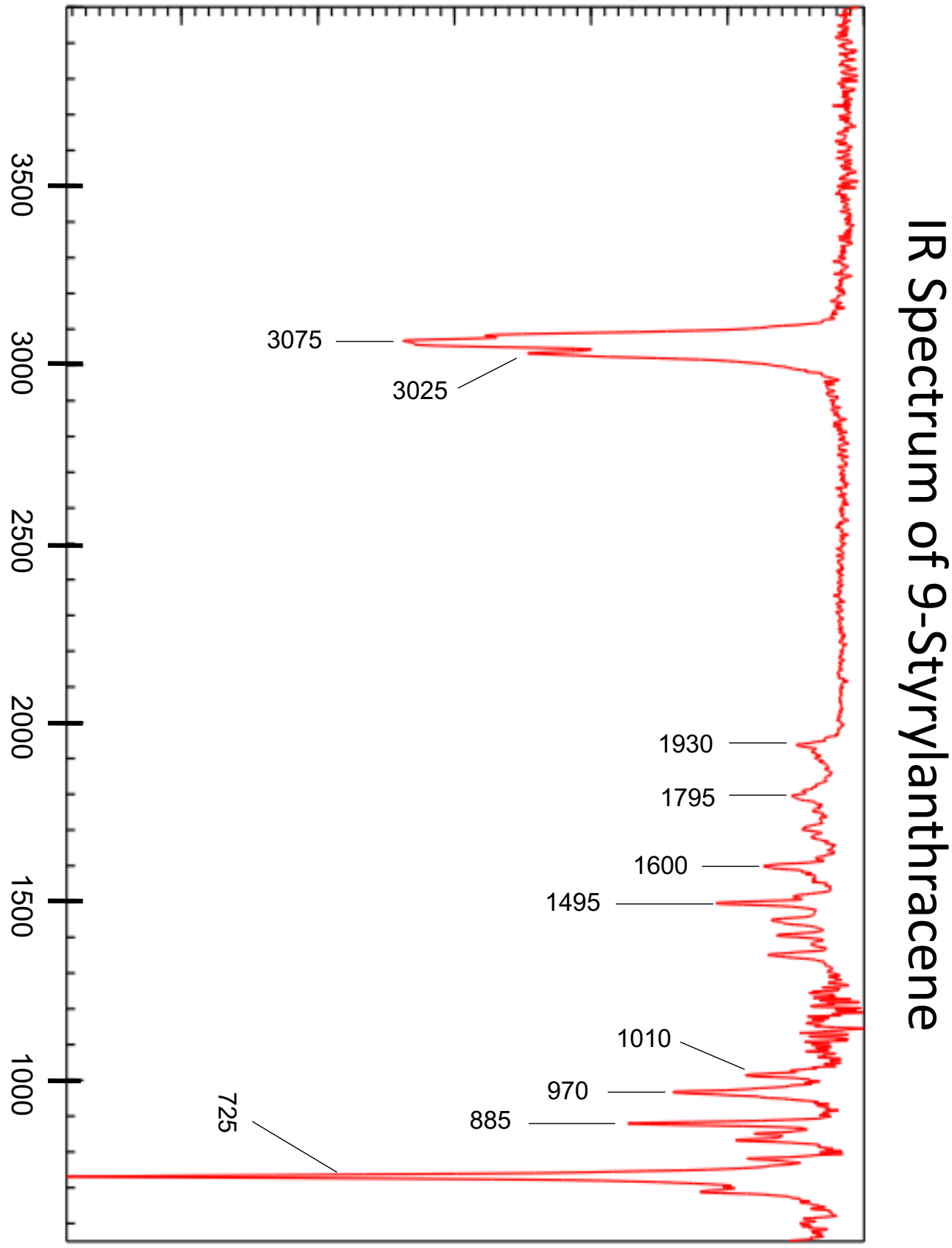
    2. Based on the IR and NMR data, how do you know you obtained a specific isomer? Discuss specific IR peaks/wavenumbers and *J* values that provide evidence for your claim.

    3. How pure was your final product? Use your TLC & m.p. data to support your claim. (Do **not** include IR or NMR data here since the spectra are of your actual product obtained in lab)

    4. What was your percent yield? What steps might you take to increase your percent yield.

    5. Include a thorough error analysis and explain at which steps product was most likely lost. Consider the procedural steps of the reaction to determine the most probable areas of loss. What steps might you take to reduce product loss during the procedure?


^{1}H NMR ($CDCl_3$, 300 MHz)
9-(2-phenylethenyl)anthracene
7.9424
7.8874
1H
$CDCl_3$
6.9760
6.9207
1H



IR Spectrum of 9-Styrylanthracene