Kinetic Vs. Thermodynamic Control: The Friedel-Crafts Reaction

There is no coversheet for this reaction, each group should fill out the worksheet at the end of the lab.

Note: The first half of the course is in this investigative format, though some labs are designed to lead you through the format without you being totally aware of it, so you will get used to what to include. Though we do synthesis at the end of the course, all those labs have a worksheet to follow. We will not use the preparative format till next semester. All labs are done individually except the spectroscopy lab and the Friedel-Crafts.

Very important: You are also responsible for keeping a notebook. Keeping your notebook is a separate and distinct exercise from writing your report. Some people write their reports in their notebooks, but this should be done on separate pages. You can also write the report on your computer, but the notebook is your daily record of what you plan to do and what you actually do and it is extremely important. So much so that we will collect these pages every week. The components for the notebook are listed repetitively on the main page of the on-line notebook. Don't forget observations! Note: what you do depends on what you are doing. The guidelines for the notebook are based on synthesis, some of these components are not included on a given week if you are doing an investigative report or just collecting data for a multi week procedure.

Please note: that this lab is a group lab report. There is a form that must be completed by each group. (the form is at the end of the lab). Note again that the keeping of your notebook is separate and distinct from keeping your lab notebook. You keep your lab notebook up to date every week regardless of your lab report status. The lab report can be written in either your note book or on the form or in the computer. For this lab, I would suggest using the form to write your report.

The first week will be used for completing experimental work. The second week for analyzing data in groups and filling out the worksheet. One is due per group.
Kinetic Vs. Thermodynamic Control: The Friedel-Crafts Reaction

General Safety Considerations

1. AlCl₃ reacts violently with H₂O liberating HCl gas. Be careful when you open AlCl₃ bottle (keep your nose out of it). Make sure you tightly cap the bottle when you are finished. Do not allow your AlCl₃ to sit around exposed to the atmosphere. It will react with the atmospheric H₂O and deactivate. When you measure out the AlCl₃ you should immediately transfer it into a very dry round-bottom (the reaction flask) and immediately cover the aluminum chloride with the p-xylene. The p-xylene will create a barrier to the atmospheric H₂O. Generally, wear gloves and goggles. In the event of a spill, consult your instructor immediately.

2. p-Xylene, 1-bromobutane and 1-bromopropane are irritants and toxic. Take all the normal precautions to avoid exposure. Keep the chemicals in the hood as much as possible. Wear gloves and goggles. In the event of a major spill, consult your instructor. If you come in contact with these substances, flush the exposed area for fifteen minutes with cold water.
Kinetic Friedel's Craft
Flow Chart

One or two groups in each class will be assigned to carry out the kinetic version of lab.

Flow Chart For Experiment 11a

Apparatus shown in procedure

1. Add 0.5 g of aluminum chloride to round-bottom
2. Add 6.3 mL of dry p-xylene to round-bottom
3. Slowly add bromopropane over 15 minutes
4. Stir for thirty minutes
5. Dump reaction in about 5 g of ice
6. Allow ice to melt and separate layers in micro separatory funnel or 125 mL separatory funnel.

organic layer

1. dry over calcium chloride
2. wait five minute
3. decant into vial or small Erlenmeyer
4. Analyze by GC

aqueous

discard down drain
Experiment 11a

Aromatic Substitution: Friedel-Crafts Alkylation

“Science repulses the indefinite.”

Claude Bernard (1813-78), Introduction
L’Etude de la Medecine Experimentale
(1865)

In preparation for this investigation, carefully study the Friedel-Crafts Reaction in your textbook, view any provided Youtube videos.

This exercise is an excellent example of the kind of experiments that are done in order to investigate the mechanism of a reaction. Your objectives are to carry out the Friedel-Crafts alkylation of p-xylene with 1-bromopropane and analyze the products by GC. The expected products are n-propyl-p-xylene and iso-propyl-p-xylene. You will determine the ratio of these products by GC. The extent of isomerization of the alkyl group from n-propyl to iso-propyl gives information on the rate of rearrangement versus the rate of alkylation. You will compare that information with the ratio of products found in the alkylation of benzene.
A. Procedure:

1. Set up the apparatus shown on the top of the next page in the hood using drierite in the curved adapter. The method to pack the drying tube (the curved adapter filled with drierite) is as follows. Wearing gloves, put a small amount of glass wool in the curved adapter. Add enough drierite using a spatula to nearly fill the tube. Then place a small piece of glass wool at the end of the tube. If the drierite is dry, the colored drierite will be blue. If it has absorbed significant water, it will take on a reddish/pink color. If the drierite becomes wet during the reaction, it should be replaced. In building your apparatus, you should be using your 14/20 micro glassware and the round-bottom should be a 25 mL round-bottom. Set a magnetic stirrer under the round-bottomed flask. Take the addition funnel to the hood and add to it 0.025 mole of 1-bromopropane. Stopper the funnel with an appropriate septum cap and reconnect it to the apparatus. Place a small magnetic stirring bar in the 25 mL roundbottom flask and bring it and a small septum cap to the hood. Place 0.5 g of aluminum chloride in the flask and immediately cover it with 6.3 mL of dry p-xylene (the point is to minimize exposure of AlCl₃ to moisture in the air). Quickly reconnect the flask to the apparatus.

2. With the stirrer on, add the 1-bromopropane dropwise (1 drop or less per second – you may have to close the stopcock occasionally). After addition is complete (about 15 minutes), allow the mixture to react an additional 30 minutes.
3. Pour the mixture into a 50 mL beaker containing about 5 g of ice. Stir until the ice has melted, then transfer to a 25 or 30-mL separatory funnel, separate the layers, and discard the aqueous layer. Dry the organic layer over anhydrous CaCl₂ for about 5 minutes.

4. Filter or decant the solution into a small Ehrlemeyer flask or vial and carry out a preliminary GC analysis of the solution. If you have sensitivity problems with the GC, adjustment of the concentration of the sample may be necessary. Please see your instructor if you are having trouble with the GC.
The Thermodynamic Friedel-Crafts Reaction (Thermodynamically Controlled) : A Discovery Based Lab. All groups will carry this lab out except the two groups that will do the kinetic. Those two kinetic groups will also be assigned to a thermo group.

This project will involve doing a Friedel-Crafts alkylation of xylene similar to the kinetically controlled reaction described earlier in the prior pages, but at elevated temperature and extended time so that the reaction will be under thermodynamic control. The product mixture will be analyzed using GC/Mass Spectrometry (GCMS). Our GCMS is a robotic instrument and you need only do the reaction and prepare the sample, the staff from the course will set up the run and collect your data. You should work in groups of three on this project.

Please do the following to prepare for your project. All students should be prepared to do either the kinetic or the thermodynamic.

Go over the kinetic Friedel-Crafts procedure in your lab book (the prior procedure) and adapt it so that the reaction will be done at 50°C in a sand or oil bath for two hours rather than the given time at room temperature. You should also consider using 1-bromobutane in lieu of 1-bromopropane in the reaction because it gives better resolved products on the GCMS. Though it is not a perfect control the kinetic with 1-bromopropane gives nearly identical ratios as the kinetic with 1-bromobutane. This seems a bit odd, but the kinetic is analyzed on our normal lab GCs and the butyl products are simply not volatile enough and get on the GCMS they give better resolution. I hope this makes some sense. With your group, work out a plan for how you are going to do a thermodynamic reaction (assume the reaction will take much longer than you think to set up, particularly because it takes a long time to regulate a sand or oil bath to 50°C) in a group and a two groups will do kinetic reactions as described above and then will join a thermodynamic group. For the thermo, you want to think about raising the temperature, having a longer time. Everything else should be the same, except you might want to add a reflux condenser to the reaction. Only use mineral spirit thermometers for the measurement of your baths. The two different types of reactions are quenched and the product isolated in exactly the same way. Please use the kinetic as your model for the thermodynamic. If the instructor has preset the sand or oil baths with them do not radically change the step control to adjust the temp. Think about cooking if your pot is a little too hot you do not turn it off to cool it down. Temperature adjustments are little “tweaks” of the voltage or the addition of more of the medium being used to heat (say to cool it a bit).

In addition to having your notebook prepared for both these reactions, prepare by reading up on the mass spectroscopy in your text book – Chapter 14 of Bruice and on the web if necessary go over the mass spectral fragmentation of aromatics. The mass spectral behavior of aromatics will also be gone over in lab lecture. Please attend lab lecture. It is clear that students who attend lecture do better.

Also it is good to ponder the following questions: What is kinetic control? Think about the fact that kinetics are dictated by what happens fastest and this relates to transition states and which are lower. Under kinetic conditions there is no ability of the reaction to reverse. Under what conditions does this occur. What is a thermodynamic control? Thermodynamics has to do with the formation of the lowest energy ground state molecules. To do this the reaction normally has to be equilibrating – going back and forth with a crop up of molecules occurring
in the lower energy states. IN these conditions, one is not focused on the energy of the transition states. It is assumed there is enough energy to surmount higher, but reasonable transition states in both directions.

Note the following: Carbocations are kinetic – they are models of transition states (Hammond Postulate). Carbocation stability may have nothing to do with the stability of ground state molecules. The compound with the rearrangement is not necessarily the most stable molecule.

You must make a distinction between the reaction – what happens there and what the mass spectrometer does to the molecules. The process is as follows. You do a reaction. The reaction is allowed to equilibrate through raised temperature and longer time. You produce a large number of molecules. The most dominant or the molecules that are building up over time are presumably the most thermodynamically stable molecules – you do not know which will be most stable. These molecules are separated on the GC part of the GSMS. GC separation is largely based on boiling point as on our small GCs in our lab. This gives rise to a series of peaks. Each of these peaks is a different compound with different boiling points. The compounds as they leave the GC column are bombarded with electrons and they fragment in characteristic ways according to their structure and functional groups. The fragments are charged and deflected in the magnetic field of the spectrometer according to their mass/charge ratio. They are detected and recorded over time. Each mass spectrum is a fingerprint of the way one of those peaks fragmented after being hit with an electron beam and was deflected and detected. Really think about the fact that the mass spectral destruction helps give us the structures of the compounds that came off on the GC that were formed in your reaction. Ultimately, we want to use the GCMS info to tell us through the structures that are formed about the mechanism that occurred in the flask. Try not to confuse the mechanism in the spectrometer with the mechanism that you carried out in your flask.

Thermodynamic reaction gives rise to multiple compounds reflecting molecular stability. The Reaction is stopped at a certain point in time by dumping reaction in ice, thus destroying the aluminum chloride. The resulting compounds are separated by boiling point on GC and the compounds as they come off are analyzed for molecular weight and structure by Mass Spec.
B. Lab Worksheet:

The following worksheet should be completed by each group. One worksheet will be expected by from group. The second week of the lab is devoted to interpreting all the data. Please use this time to complete the worksheet. If you wait on it, it becomes difficult to do.

-- Formyl benzene
by Liza Donlon & Heather Campbell
Kinetic vs. Thermodynamic Control, The Friedel-Crafts Reaction
Form Write-up

Name: ___________________________________ Exp. name: ________________________________

T.A. Name ______________________________ Date: ________________________________

Please turn in one worksheet per group. Time will be provided during the second week of
this lab to thoroughly understand this lab and work on worksheet during lab. Please use
this time and the human resources that are available. Ask lots of questions, discuss. : )

I. Introductory Questions

A. Why is it essential to use a gas trap and to work in the hood while carrying out these
reactions? (5 points)

B. Why is a drying tube used in these reactions? (5 points)

C. What side reaction will occur if the glassware used is not dry in these
reactions? (5 points).

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D. Why is an excess of p-xylene used in these reactions? (5 points)
II. Experiment and Results

Kinetic and Thermodynamic Friedel-Crafts – everyone is responsible for this, even if you just get the data from the one or two groups who were assigned to carry it out.

A. Attach the required GC for the kinetic reaction or a copy to the back of the report. Assign a structure to each peak on the GC. (10 points)

B. Report the ratio of products in percent form for the kinetic reaction excluding unreacted p-xylene. (8 points)

C. Attach all the GCMS data from the Thermodynamic Friedel Crafts. Even if you did the Kinetic, you will also be assigned to a thermodynamic group. This data can include the assignments of the peaks that we focus on and will be determined in the rest of the report. (20 points)
III. Analysis of Data:

A. For Kinetic Reaction: Discussion of Rate of Rearrangement vs. Rate of Substitution. This is very important and should include structures and consider the timeline of the reaction and the reactivity of the substrate. What was faster rearrangement or substitution. How can you tell and can you explain why considering the mechanism of Friedel-Crafts. (20 points)
B. For the Kinetic Reaction: Write a complete mechanism (arrow formalism, resonance structures) explaining the formation of the two products. (8 points)

C. For both Reactions: Why was the reaction mixture poured on ice at the end of the reaction, Write equations to describe any chemistry occurring in this step. (4 points)
C. For the Kinetic Reaction: Approximately what ratio of rearranged to unrearranged products do you expect if toluene (methyl benzene) is subjected to the reaction carried out in this lab? (8 points)

D. For the Thermodynamic: What changes in apparatus, procedure were used in the thermodynamic reaction. How do these conditions allow for equilibration. (12 points)
E. After you have put a decent effort into the previous section of the lab, please ask your instructor to orient you to your GCMS data for the Thermodynamic version of the reaction. It takes a while to follow the data. For your general edification, the top of each sheet is a GC of your reaction products. Yes, there are many more products than the kinetic. The bottom of each page is the mass spectrum of a given product that came off the gc column. They are classified by time and are in order of their retention time and they are likewise in order of molecular weights. Get used to it before you start interpreting.

F. What are the molecular ions (molecular weight of the GC peaks for which you have data) of the compounds eluted off the GC column. In other words, look at the mass spec you are given for the compounds in order of molecular weight and time and find the molecular ion and establish each molecular weight. Aromatics always give a molecular ion that corresponds to the original molecule made in the reaction minus one electron. If different peaks give rise to molecular ions that have the same mass, then they are isomers. Do this below or on the printout itself. (20 points)

G. From this reaction, you will only obtain compounds that have methyls and butyls on benzene. This has to do with the temperature of the reaction and the fact that there are limits as to what bonds can break in the reaction (even at 50 degrees the reaction is a Friedel-Crafts only). Based on molecular weight, which peaks correspond to compounds that have two methyls and one butyl on a benzene ring. This can be determined by molecular weight. Which peaks correspond to compounds that have some other combination – what are those combinations? Note, you are not working
blind, you only obtain compounds with butyls and methyls on benzene. What is different among the groups are the number of these groups and where they are on the ring, also, whether they are arranged or rearranged. Please ask during the workshop for help if you are struggling. (20 points)

H. How many peaks can you see that correspond in terms of molecular weight to products having one butyl and two methyls on a benzene ring? (8 points)

I. Can you write a series of isomers that might correspond to number of peaks you have that have the molecular weight of a benzene with two methyls and one butyl. You have to use your imagination here. Avoid compounds that have all three groups ortho and that have exotic side chain rearrangements. Sec-butyls and n-buyls are most likely at 50 degrees. The side chains are not doing wild things, the Friedel-Crafts is equilibrating and there is some simple rearrangement that is all. Groups can be in new positions on the ring, however. (20 points)
J. Using the formation of a tropylium ion as discussed in class (your instructor will discuss this again) can you figure out which of your products with one butyls\ and two methyl groups, have which type of butyl? Again, sec-butyl and n-butyl are most possible. Note which groups of peaks correspond to which type of butyl. (12 points)

1. Assign the GC. Divide the products isolated by type of butyl group, then within each group, assign the four compounds by boiling points. You can look up the proposed compounds boiling points on chem spider or another data base. Alternatively, You will be given some model boiling points of related compounds from a very good reference called. Rossini, Pitzer, Arnett, Braun, Pimentel, Selected Values of Physical and Thermodynamic Properties of Hydrocarbons and Related Compounds. You can use propylxylene boiling points as models for butylxlenes. Using this reference, arrange the proposed isomers in order of boiling points. Realize the compounds should elute of the GC of the GCMS in order of boiling point. This is very helpful with such a complex mixture. (20 points)

J. Compare data with you friends in lab and decide who has the most extreme data compared with the kinetic reaction. What does your data and this extreme data data telling you about thermodynamic stability of aromatics with three groups. Remember under thermodynamic conditions – conditions of equilibration – the product that is most stable is dominant or over time because dominant. (12 points)
K. Can you write a mechanism for the formation (principle of microscopic reversibility) of your most unexpected product that has a molecular weight of 168. (20 points)