

Chemistry 125 Final Examination
May 7, 2003

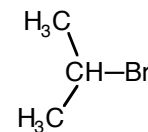
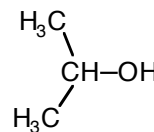
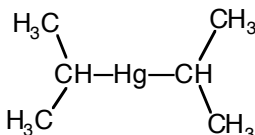
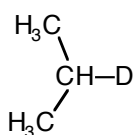
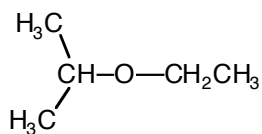
Name _____

This exam is budgeted for 150 minutes, but you may have a full 180 minutes to complete it.

I.A (10 min) Suggest a method to prepare each of the following compounds from **propane** in **high yield**.

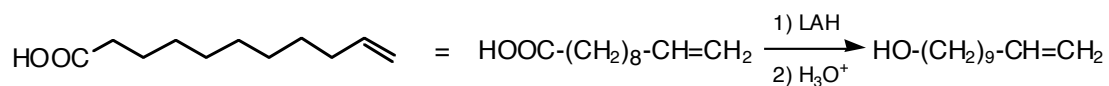
You may use any other reagents, but the atoms of the propyl groups must come from propane.

You may use a product prepared in one synthesis as a starting material for preparing another.

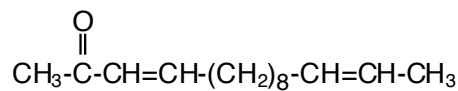
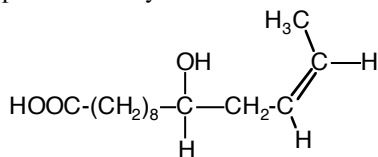


N.B. in 2003 we talked more about halogen-metal interchange, which we mentioned only in passing this year.

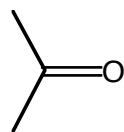
I.B (10 min) In practical organic synthesis it is important to know what starting materials are cheap and readily available. For example, heating ricinoleic acid, which constitutes about 80% of castor oil, gives a high yield of 10-undecenoic acid, shown below. Since carboxylic acids can be reduced to primary alcohols with LAH, this makes undec-10-en-1-ol readily available.



Propose practical a multi-step method for preparing **ONE (ONE ONLY!)** of the following two compounds from 10-undecenoic acid, or undec-10-en-1-ol and any other reagent with 4 or fewer carbons. Be sure to count carbons and to use protecting groups if necessary.

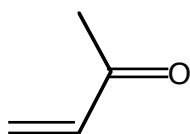


I.C (6 min) **Draw straight lines** to connect each of the following functional groups with its characteristic strong absorption frequency (cm^{-1}) in the IR spectrum.



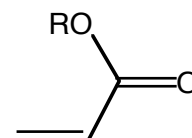
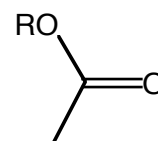
1675

1715



1720

1735

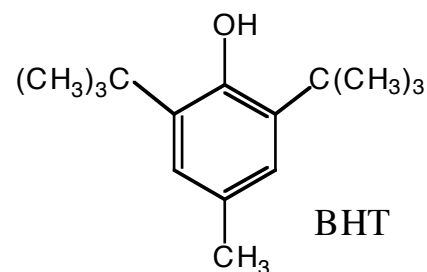


II. Last night while preparing this exam I bought a candy bar. The wrapper said it contained “BHT”, which stands for butylated hydroxy toluene.

BHT is added to foods to protect their fats, especially the unsaturated ones, from reacting with oxygen in a free-radical chain reaction. Oxygen radicals abstract one H-atom, then another, from BHT rather than abstracting an H-atom from the fat.

Fats are called “triglycerides” because they contain glycerin (1,2,3-propanetriol).

Here are some questions about these compounds:



A. Consider butylating para-hydroxytoluene (**pHT**) to make BHT via **electrophilic aromatic substitution**.

1) (3 min) What would be a reasonable source of the two butyl groups? In what form would they react with pHT?

2) (6 min) Give a plausible electronic (not steric) explanation about why butylation takes place next to the OH group rather than next to the CH₃ group of pHT.

B. (4 min) Rank ALL four kinds of hydrogen atoms in BHT in order of their expected ease of abstraction by an R-O-O• free radical. Explain your ranking.

C. (4 min) Draw a plausible structure for an **natural fat**.

N.B. in 2003 we had talked a little more about fatty acids.

D. (6 min) **Draw** a **Claisen** condensation of **Acetyl-S-coA**, and **explain** what this reaction has to do with how you decided to draw the fat in the preceding question (C).

E. (10 min) **Explain** why Pearl Martin was **smart to use lye** rather than muriatic acid to convert lard to soap and why she did **not fear to wash her hair** with this soap. In answering this question **use specific pKa values** to estimate the equilibrium constant for saponification.

N.B. in 2003 we had talked about Pearl Martin, a folk “chemist”, who made soap by hydrolyzing fat.

Emil Fischer's Osazones

Just 100 years ago Emil Fischer won the second Nobel Prize in Chemistry “in recognition of the extraordinary services he has rendered by his work on sugar and purine syntheses.” It is informative to look back on this work to see that everything wasn't as clear as it went along as it appears in retrospect. The rest of the exam has a number of questions relating one way or another to Fischer's work.

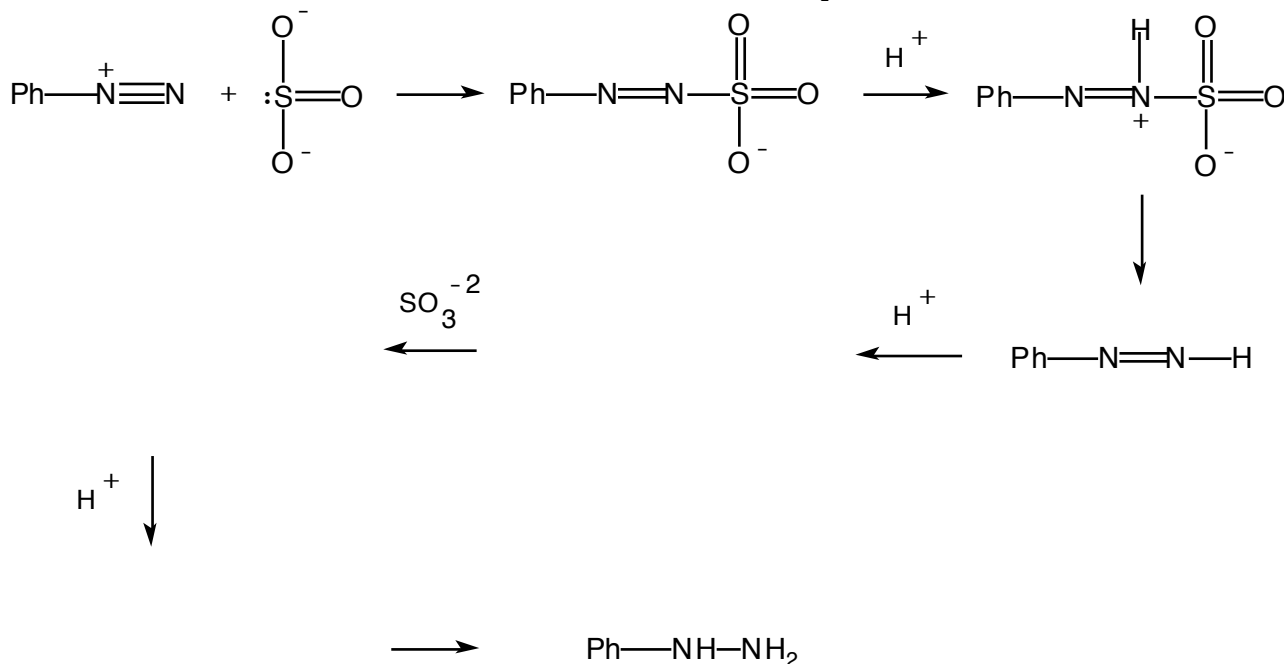
- III.** Fischer earned his Ph.D. under Adolf Baeyer, who a dozen years or so later developed both the Baeyer strain theory and the Baeyer-Villiger oxidation of ketones with peroxycarboxylic acids.
- A.** (7 min) Cite **specific experimental evidence** supporting the **Baeyer strain theory**, and give a very brief **molecular orbital explanation** of the phenomenon.
- B.** (8 min) Draw the mechanism of the **Baeyer-Villiger oxidation**, complete with **curved arrows**.
- IV.** As a graduate student in Strasbourg in 1875, 22-year-old Fischer was the first to prepare phenylhydrazine (Ph-NH-NH₂) and invented the name “hydrazine” for this class of compounds. Although he suffered greatly from poisoning by phenylhydrazine, he later described it as his “first and most lasting chemical love.”
- A.** (3 min) In 1874 a 22-year-old Dutch chemist, who would be awarded the first Nobel Prize in Chemistry, made a monumental proposal in organic structural theory, that was overwhelmingly confirmed by Fischer's work on the sugars. **Who** was the chemist, and **what** was his proposal?

B. Fischer's preparation of Ph-NH-NH₂ involved reducing the "benzenediazonium" cation with sulfite (SO₃⁻²).

- 1) (4 min) Sulfite is called an "ambident" nucleophile. **Explain** this term by giving the products for reactions of SO₃⁻² with a **proton** and with **CH₃I**.

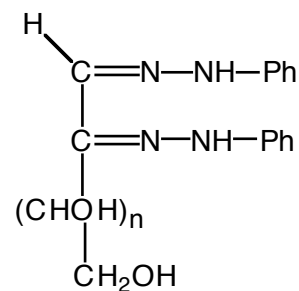
N.B. in 2003 we had talked explicitly about "ambident" nucleophiles in which more than one atom can act as a nucleophile.

- 2) (10 min) Complete the following scheme with **intermediate structures** and **curved arrows** to show a mechanism for reduction of benzenediazonium ion to Ph-NH-NH₂ by sulfite and HCl.



- 3) (3 min) For the **very first step** in the scheme above (addition of sulfite to benzenediazonium ion) label atomic **oxidation states** on relevant atoms of **starting material and product**. Label **only the atoms that change** oxidation state during this reaction step.
- 4) (8 min) Draw the **mechanism** for oxidation of 2-propanol by Br₂, **and** explain the **analogy** with the above conversion of Ph-N₂⁺ to Ph-N=NH.

- V. In 1884, nine years after discovering his chemical love, Fischer wrote a paper entitled *Compounds of Phenylhydrazine with the Sugars. Part I*. In this paper he described how to make derivatives of various sugars by reacting them with phenylhydrazine. He coined the name “osazones” for these high-melting, crystalline derivatives, which finally made it possible to separate and purify the components of sugar mixtures. He soon decided that the osazone functional group has the structure shown on the right.



Among the seven sugars he tested were sucrose, dextrose, and levulose. The last two (now called glucose and fructose) are components of “invert” sugar, which can be made by treating sucrose with acid and water.

Fischer was especially excited because “in many cases one may use these derivatives to recognize and distinguish among the individual sugars.”

- A. (3 min) The names “dextrose”, “levulose”, and “invert” are still used in food technology. What do these names mean?

N.B. in 2003 we had talked about the source of these names.

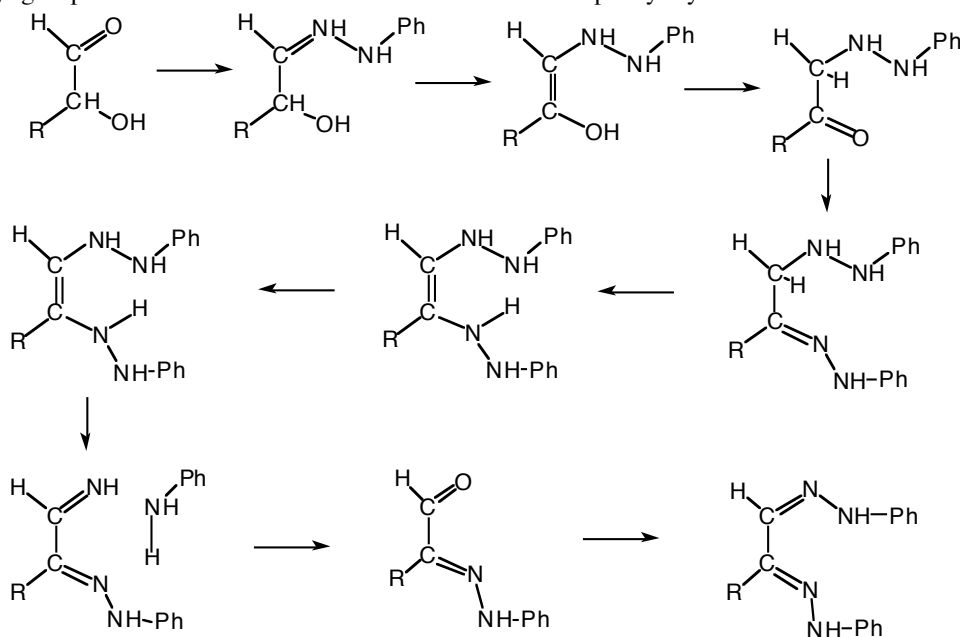
- B. (4 min) Fischer was probably disappointed to have to report in 1885 that “This hydrazine test is not appropriate to distinguish between dextrose and levulose,” since both of their osazones melted at 204°C. Four years later Kiliani proved the constitutional difference between dextrose (glucose) and levulose (fructose), an aldohexose and a ketohexose, respectively. Explain how this is consistent with Fischer’s earlier observation. [Do not give Kiliani’s proof.]
- C. (6 min) Today one might use NMR spectroscopy to distinguish fructose from glucose. Assuming the sugars to exist in the open chain (non-cyclic) form, and assuming that you do not have authentic spectra for comparison, describe as specifically as you can what distinguishing feature you would look for in the NMR spectrum, and what that feature would look like.

- D. (5 min) What sort of **functional group** holds glucose and fructose together in the disaccharide sucrose, and **why** may it be cleaved by **acid**, but not by **base**?

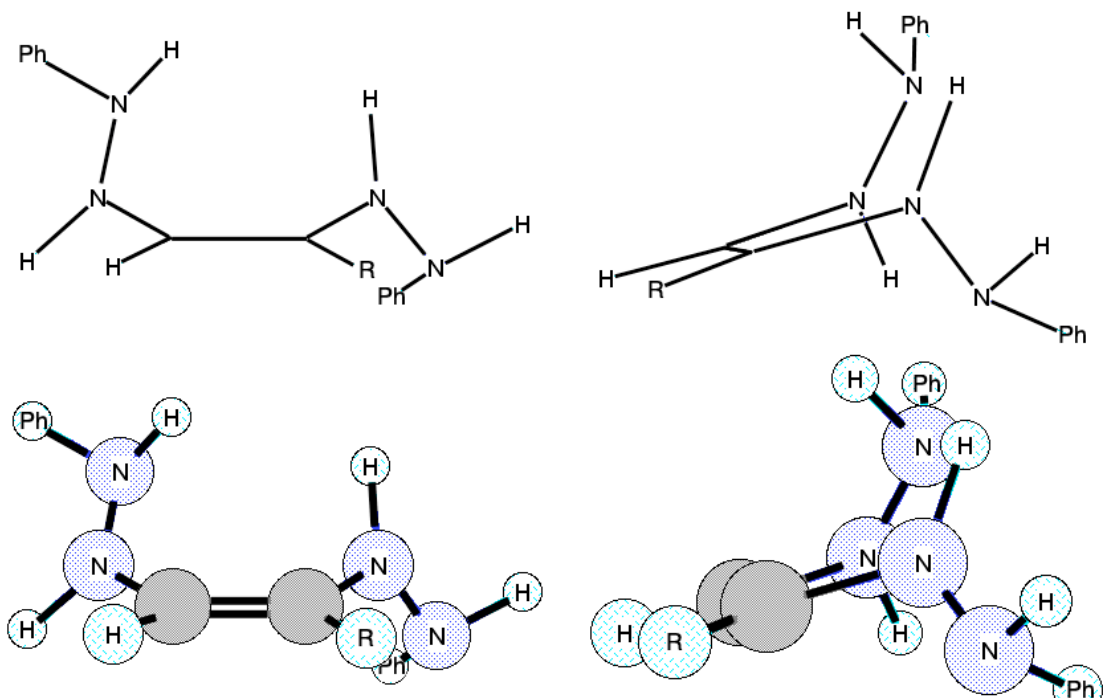
N.B. in 2003 we had talked about disaccharides, in which sugars are linked together as acetals or hemiacetals.

- E. (10 min) Fischer put off reporting on the osazone of mannose until 1888, four years after the original osazone paper. In 1888 he wrote, “[mannosazone] differs from glucosazone in its somewhat higher melting point, near 210°, and a considerably greater solubility in acetone.” In an 1889 paper he changed his tune, deciding that the previous samples had been insufficiently purified and that the **mannosazone was indeed identical with glucosazone**. **Explain** how the **identity of these two osazones**, and the fact that the **reduction product** of mannose is **chiral**, played a key role in Fischer’s determination of the configuration of glucose in 1891. [Don’t give the whole argument, just explain how mannosazone fits in.]

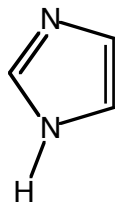
- F. Fischer originally reported that he needed only two moles of phenylhydrazine to form the osazone from glucose. It later developed that three moles were needed, although only two appear in the final osazone. **One of the phenylhydrazine molecules** that first is linked to the sugar as an imine **is transformed into PhNH₂** and a simple imine (lower left corner of the following proposed scheme), from which NH₃ is lost to generate a carbonyl group. This carbonyl group then forms an imine with the third molecule of phenyl hydrazine:



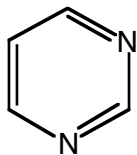
- (2 min) In the scheme above **circle every arrow that represents an allylic rearrangement**.
- (2 min) **Draw curved arrows on the leftmost structure in the middle row above** to show the rearrangement that releases PhNH₂.
- (2 min) **Circle the preferred connectivity** for the rearrangement in Question 2: **Hückel** or **Möbius**
- (5 min) **On the two stick models below**, which represent this same structure in two views, **draw the relevant sigma and pi atomic orbitals, the ones involved** in the rearrangement of Question 2. Include atomic orbital **signs** and use lines to join adjacent orbitals into a ring with the **appropriate connectivity**. [The corresponding structures with balls are to help visualize the third dimension in the stick models.]



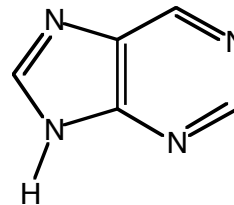
- G. (9 min) Purine, which shares a place with sugars in Fischer's Nobel Prize citation, also figures prominently in the "purine bases", adenine and guanine, of the nucleic acids. **Think carefully about the number of hydrogen atoms and of sigma and pi electrons** on each ring atom of the following structure of this **flat** molecule to decide whether one might reasonably expect that it would profit from "**aromatic stabilization**". First answer for its five-membered ring (**imidazole**) and its six-membered ring (**pyrimidine**), considered in isolation, then answer for the 9-membered ring that constitutes the periphery of the **purine** molecule. Explain your thinking.



Imidazole



Pyrimidine



Purine