Chemistry 125 Second Semester Name _____

May 7, 2010 Final Examination

This exam is budgeted for 150 minutes, but you may have 180 minutes to finish it. Good Luck.

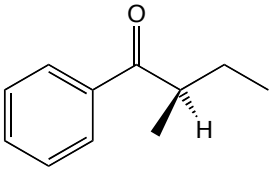
1. (32 minutes) Give as realistic an example as you can **for each of 8** of the following 14 reactions (use front and back of this sheet)
OMIT SIX (only your first 8 answers will be graded) NO MECHANISMS REQUIRED, JUST REAGENTS AND PRODUCTS

a) a Friedel-Crafts acylation
b) CH_2 insertion by the Arndt-Eistert Reaction
c) a Claisen condensation
d) O insertion by the Baeyer-Villiger Reaction
e) a Hunsdiecker (Borodin) reaction
f) a reaction involving a *o*,*p*-directing, deactivating substituent
g) an epoxidation
h) a reaction involving periodate (IO_4^-)
i) cross-linking a polymer
j) reduction (rather than addition) by a Grignard reagent
k) a reaction involving a carbene
l) a reaction involving N-bromosuccinimide (NBS)
m) a Mitsunobu inversion
n) a Wittig reaction

2. (3 min) Nitrogen-based fertilizer has been in the news since last weekend. The most common nitrogen fertilizers are ammonia, ammonium nitrate, and urea. **ABOVE EACH ATOM** in the formulae below write its oxidation state. Then **CIRCLE** the substance which is best suited to be an oxidizing agent.

NH_3 NH_4NO_3 H_2NCONH_2

3. (5 min) When treated with aqueous NaOH the optically active ketone shown below racemizes. If Br_2 is present in the basic solution, racemic α-bromoketone is formed. The rates of these two reactions (with and without Br_2) turn out to be identical. Explain this seeming coincidence.

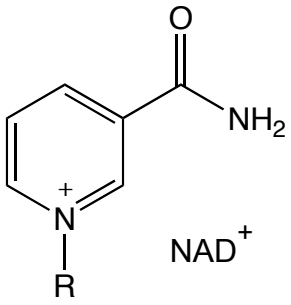


4. Explain contributions A and B below:

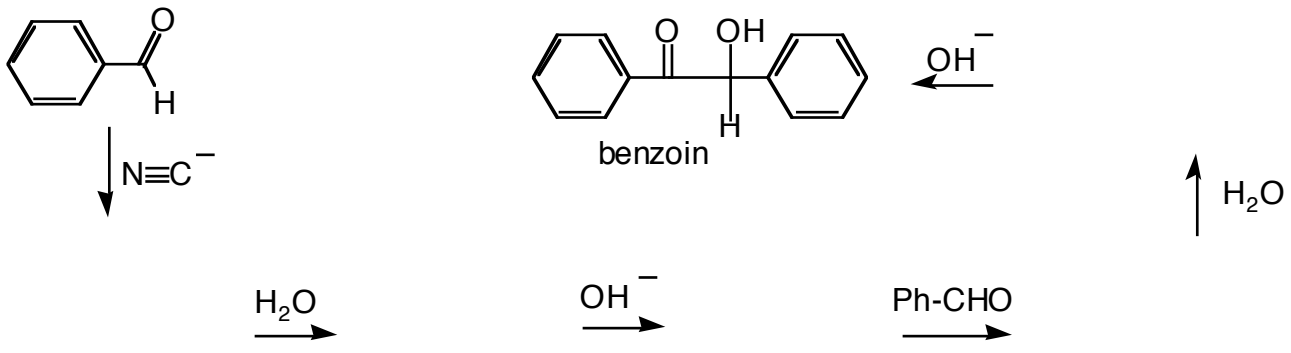
A. (4 min) How in 1894 Victor Meyer developed a **new concept in stereochemistry** on the basis of a **failure of Fischer esterification** with certain benzoic acids.

4 B. (4 min) How Melvin Newman (Yale '29, Ph.D.'32) devised **an alternative way** to succeed in making these challenging esters.

5. (4 min) Explain how NAD^+ is well suited for its role as a biological oxidant.

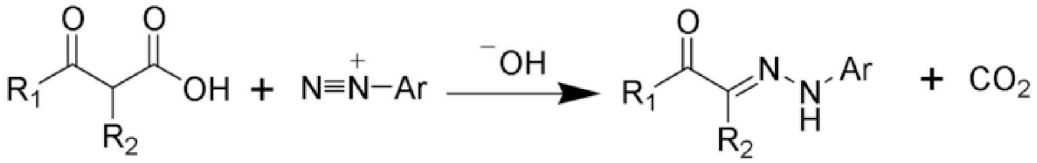


6. (10 min) **Complete** the following scheme for the benzoin condensation, and **say why cyanide is so well suited** to catalyze it.
(**No curved arrows** necessary, just **draw the five intermediate structures**.)



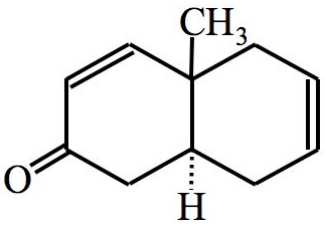
7. (10 min) Explain how the reduction of the aldopentose **arabinose to arabitol** together with Kiliani-Fischer synthesis of a mixture of **glucose and mannose from arabinose (not xylose)** helped Fischer establish the configuration of the aldohexose glucose. (It would probably help to draw Rosanoff projections of the four sugars mentioned.)

8. (8 min) Organic chemists delight in knowing reactions by the names of their discoverers, often obscure 19th century chemists. I was impressed that Prof. Ziegler knew by name the "**Japp-Klingemann**" reaction (discovered in 1887). Below are the starting materials, products and catalyst for the J-K reaction. **Propose a mechanism** for this transformation and draw **at least two intermediate** molecules**. Use curved arrows to show the analogy of one step** to a characteristic reaction of malonic acids, $R_2C(COOH)_2$.

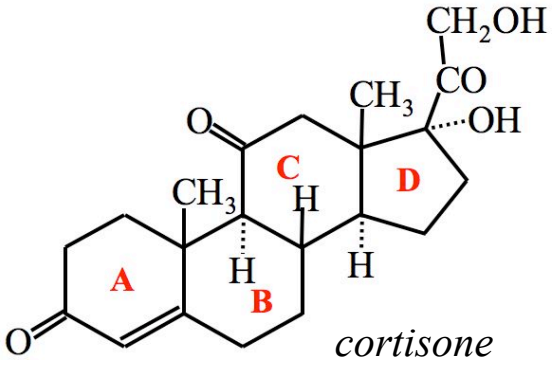


9. Woodward began his total synthesis of cortisone by converting readily available ***A*** by several steps into intermediate ***B***.

A. (5 min) Label the rings in ***B*** to show how it fits into the ultimate cortisone molecule, and explain what structural features make it suitable for subsequent transformations toward cortisone?



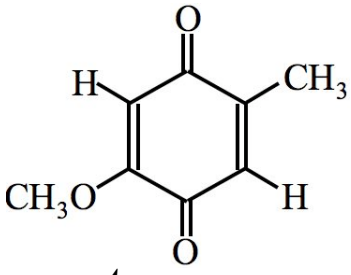
B



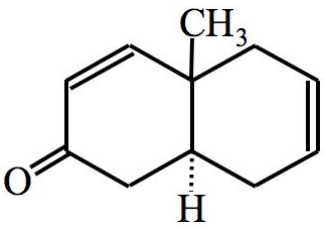
cortisone

B. (16 min) **Sketch at least four intermediates** involved in converting A into B.
Show reagents, but curved arrows are **not** required.

The reagents used were chosen from this alphabetical list:
acetic anhydride, acid, base, butadiene, lithium aluminum hydride, water, zinc



A

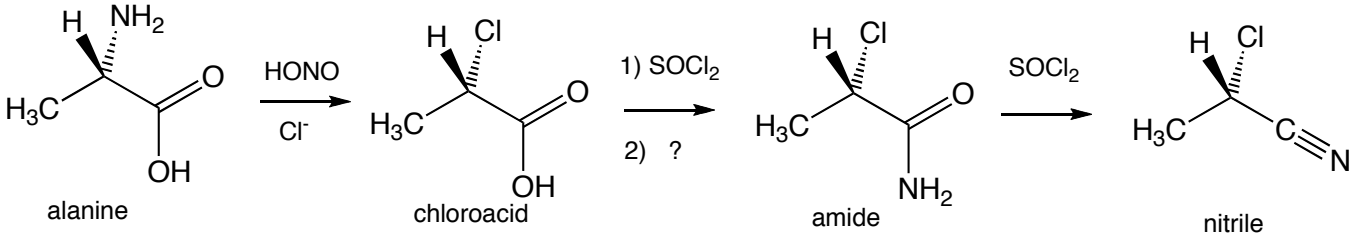


B

Your Name _____

The Rest of the Exam Concerns Professor Wiberg's Problem

Professor Wiberg is deeply involved in the kind of research he described in his guest lecture last semester. He is attempting to prepare a single enantiomer of 1-chloro-1-cyano-1-deuteromethane in order to measure its optical activity at various wavelengths in hopes of resolving differences between calculated and observed values for the undeuterated analogue. He had already prepared the undeuterated analogue by the following scheme:



Wiberg's synthesis begins with a single enantiomer of the amino acid alanine (available from nature). The first transformation replaces NH_2 by Cl stereospecifically.

A) (1 min) What seems surprising about the stereochemistry of the chloroacid intermediate?

B) (6 min) How does HONO help NH_2 become a leaving group? In answering this question refer to the analogous use of HONO for performing "Sandmeyer" type aromatic substitutions (remember the little box labeled "OHNO" in the photo of the Yale chemistry class of 1898).

The explanation of the **curious stereochemistry** of the chloroacid is that an unstable intermediate intervened that was subsequently attacked by the chloride anion to give the chloroacid. Its formula is $C_3H_4O_2$, and if it lasted long enough be observed by IR, it would have shown a strong peak at about 1900 cm^{-1}. Analogous compounds prepared by adding carbenes to CO_2 have in fact been observed by IR near that frequency and are found to disappear with a rate constant of about 10^4/sec.

C) (4 min) **Draw** the structure of the intermediate, **explain** its instability, and **estimate** the activation energy for its decomposition.

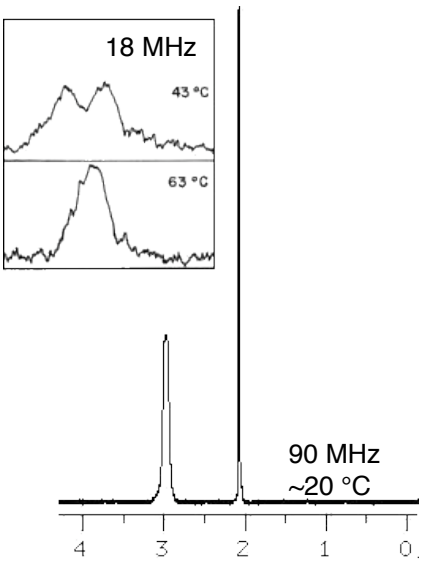
D) (3 min) Explain how the unusual IR frequency at **1900 cm^{-1}** can be understood, at least in part, in terms of unusual **hybridization** in a bond between C and O.

E) (3 min) In conversion of the chloroacid to the amide, **what is the intermediate** formed by reaction with $SOCl_2$, **and what reagent** would be used for the second step to form the amide? (No mechanism necessary, just the two structures)

F) (5 min) Actually Prof. Wiberg is frustrated right now. He has prepared 40 g of the deuterated chloroacid, a precious substance that he wants to convert to the nitrile in the highest possible yield. But organic chemistry remains an empirical science. He finds that the reaction of his acid with $SOCl_2$, which is usually a very reliable reagent, gives only a low yield of the desired intermediate with which to form the amide. The principal product is one that shows two strong IR absorptions at about 1810 and 1740 cm^{-1}. **Suggest a reasonable identity** for this product and **explain the IR frequencies and** what you would anticipate about their relative **intensities.**

The following questions should help prepare you for discussing conversion of the amide to the nitrile.

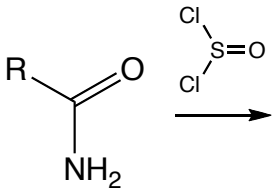
G) (5 min) On the right is the proton NMR spectrum of N,N-dimethylacetamide, CH_3-CO-N(CH_3)$_2$, measured with modern 90 MHz spectrometer. The peak at 3 ppm is rather broad, and the inset shows this peak measured in 1956 in the weaker field of an early 18 MHz spectrometer. At 43°C there are two peaks (2.9 and 3.2 ppm), but at 63° there is a single peak. **What can you infer** from these signals near 3 ppm?

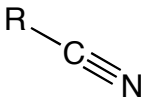


H) (6 min) The amide functional group could be protonated at two sites. **Draw** the two protonated forms and explain **from an orbital point of view** which site should be favored for protonation. (An explanation in terms of resonance structures will earn partial credit.)

I) (5 min) **Explain** how the following observation confirms your answer to Question H: When **acid** is added to a solution of N,N-dimethylacetamide, coalescence of the NMR peaks near 3 ppm begins at a **higher temperature** than without acid.

J) (6 min) The last step in Wiberg's synthesis involves losing the elements of water from the amide to form the desired nitrile. He actually uses a different reagent (P_2O_5) to accomplish this dehydration, but I would like you to **draw a detailed mechanism with accurate curved arrows** to show how it could be accomplished with $SOCl_2$. Draw as many intermediates as you need. (The previous two questions should help prepare you for this one.)





K) (5 min) At the end of his synthesis of the nitrile, Wiberg may want to check that his synthesis involved no racemization by converting a small amount of the nitrile back into the chloroacid and confirming that the optical rotation is unchanged. He might do this with **EITHER acid- or basic catalysis**. Draw a mechanism with **careful curved arrows** for **ONE** (1 only) of these two catalysts **and explain** whether there is **any risk** that this reaction itself might lead to some racemization.