Name: _____ Student Number: _____

Chemistry 2600 Final Exam (Version A)
April 22nd, 2009

INSTRUCTIONS

1) Read the exam carefully before beginning. There are 11 questions on pages 2 to 11 followed by a periodic table and a blank page for rough work. You are also provided with an NMR Data Package and a page with pi MOs. **Please ensure that you have a complete exam. If not, let an invigilator know immediately**. All pages must be submitted.
2) You are allowed to bring one index card (maximum size 3"x5") into the exam with you as a "cheat sheet". This card must be submitted with your exam.
3) You are allowed to bring a ruler and a molecular model kit.
4) No electronic devices of any kind (including calculators) are permitted.
5) If your work is not legible, it will be given a mark of zero.
6) Marks will be deducted for incorrect information added to an otherwise correct answer.
7) When drawing molecules, clearly show any relevant stereochemistry. If a mixture of diastereomers is produced, draw both/all of them.
8) IF YOU USE RESONANCE ARGUMENTS AS PART OF YOUR REASONING, THEN DRAW THE RELEVANT STRUCTURES.
9) If you think that you see another student cheating, write a note on your exam paper and raise your hand to show an invigilator so that we can investigate the situation.
10) **DO NOT OPEN THE EXAM UNTIL YOU ARE TOLD TO BEGIN.**
Beginning prematurely will result in removal of your exam paper and a mark of 0.
11) You have **3 hours** to complete this exam. Nobody may leave the exam room during the first hour or the last 15 minutes of the exam.

Confidentiality Agreement:
I agree not to discuss (or in any other way divulge) the contents of this exam with or in the presence of any CHEM 2600 student who has not yet written their final exam. *(The last official exam timeslot ends at 5pm on Saturday, April 25th, 2009.)*

Signature: _____ Date: _____
Course: CHEM 2600 (Organic Chemistry II)
Semester: Spring 2009
The University of Lethbridge

Q	Mark
1	/ 10
2	/ 10
3	/ 4
4	/ 4
5	/ 2
6	/ 3

Q	Mark
7	/ 4
8	/ 5
9	/ 7
10	/ 15
11	/ 1

Total	/ 65

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1. **[10 marks]**

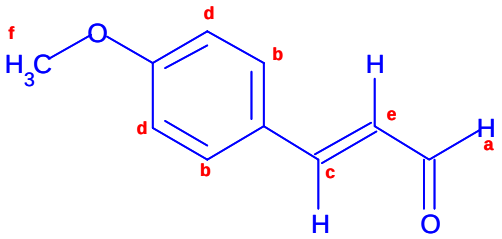
(a) Deduce the structure of the molecule, $C_{10}H_{10}O_2$, that gives the following proton NMR (400 MHz) and IR spectra.

(b) Assign all signals on the proton NMR, and assign two meaningful IR bands.

(c) Measure the coupling constants for the signal at 6.55 ppm, and indicate what this information tells you about the structure of this molecule.

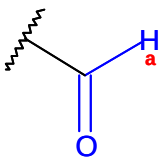
(a)

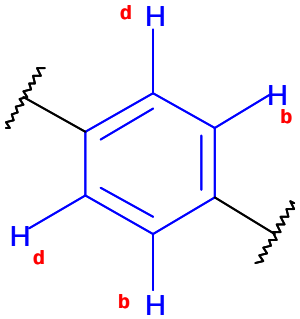
chemical shift	multiplicity	integration	assignment
9.6 ppm	doublet (can't measure J from top spectrum)	1 H	H_a
7.48 ppm	doublet (J = 8 Hz)	2 H	H_b
7.38 ppm	doublet (J = 16 Hz)	1 H	H_c
6.90 ppm	doublet (J = 8 Hz)	2 H	H_d
6.55 ppm	doublet of doublets (J = 16 Hz, 8 Hz)	1 H	H_e
3.8 ppm	singlet	3 H	H_f

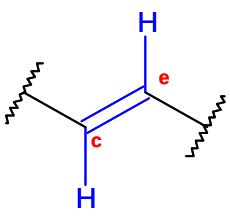


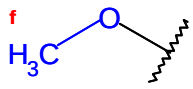
	Evidence	Conclusion
	$C_{10}H_{10}O_2$	DU = 6
IR:	Strong peak at ~1680 cm^{-1}	C=O (not amide since no N; must therefore be conjugated)
^{1}H NMR:	doublet (1H) at 9.6 ppm	aldehyde H (next to CH since it's a doublet)
	Two doublets each integrating to 2H in aromatic region (6.5-9ppm)	1,4-disubstituted benzene
	Wide doublet (J = 16 Hz) at 7.38 ppm	vinyl H; *trans* to another H; unusually far downfield likely due to resonance
	Doublet of doublets (J = 16 Hz, 8 Hz)	vinyl H; *trans* to 7.38 ppm H; also coupling to another H
	Singlet (3H) at ~3.8 ppm	CH_3 next to a heteroatom; likely $-OCH_3$ given molecular formula

Pieces:









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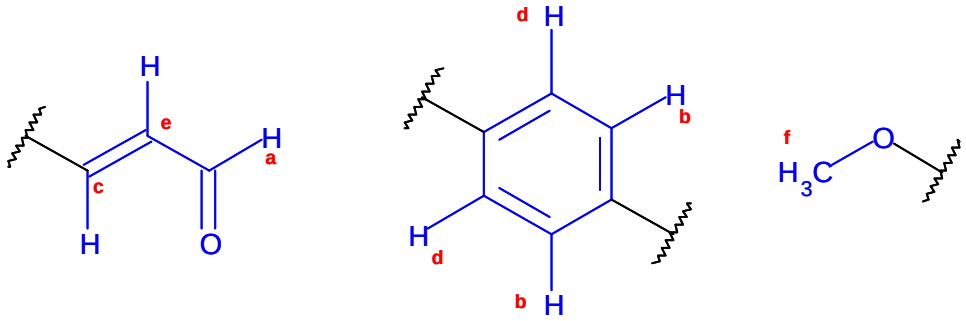
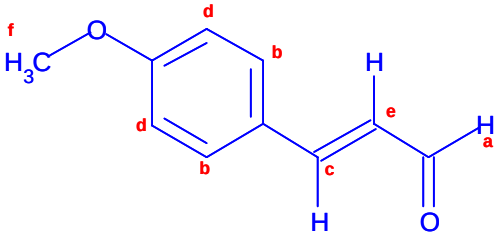
Assembly:

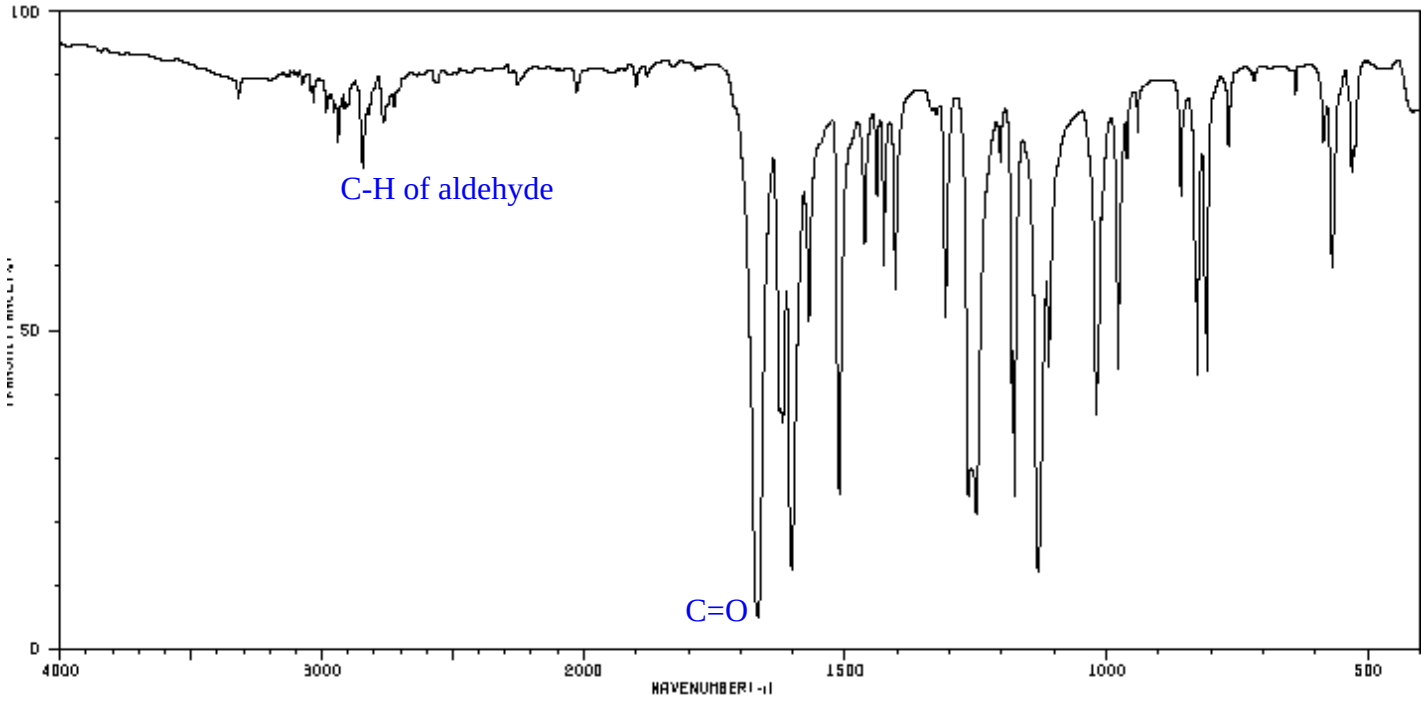
We noted that the hydrogen atom producing the wide doublet at 7.38ppm was unusually far downfield. This is likely due to deshielding by resonance. As such, it is very likely that the vinyl group and aldehyde are attached:



This gives us two terminal groups and one middle group, and there is therefore only one way to assemble them:



(b)



(c) As noted in part A, the coupling constants for the signal at 6.55 ppm are 16 Hz and 8 Hz. The 16 Hz coupling constant tells us that the C=C double bond is *trans* disubstituted.

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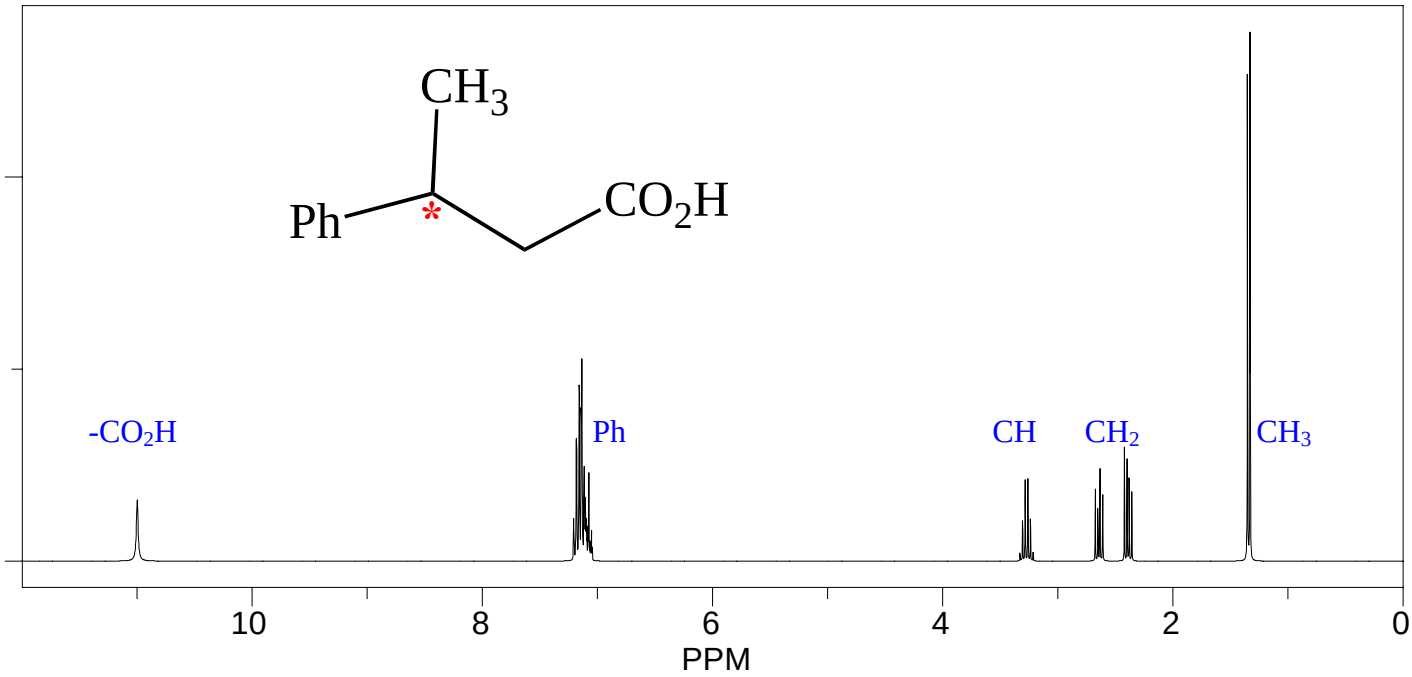
2. The 400 MHz proton NMR spectrum of 3-phenylbutanoic acid appears below. Assign all signals and account for the two signals between 2 and 3 ppm. **[10 marks]**



- Carboxylic acid H are always downfield of 10 ppm, so the peak at 11 ppm must be $-CO_2H$.
- Aromatic H usually appear between 6.5 and 9 ppm, so the messy peak at ~7.1 ppm must be due to the phenyl group.
- The CH_3 group is next to CH (so has one vicinal H). Thus, it should appear as a doublet. These are the least deshielded H of the molecule, so would be expected to give the most upfield signal. Both of these points are consistent with the assignment of the CH_3 signal as the doublet at 1.2 ppm.

That leaves three hydrogen atoms and three signals. At first glance, we would expect one signal from the CH (appearing as a sextet since it has five vicinal H) and one signal from the CH_2 (appearing as a doublet since there is one vicinal H). Careful consideration of the molecule, however, shows that the two hydrogens of the CH_2 group are, in fact, **diastereotopic**. This is due to the fact that there is a **chiral centre** in the molecule (marked with a * on the diagram above). Thus, the two hydrogen atoms of the CH_2 group are in different chemical environments and therefore give **different chemical shifts**. This explains why they give different signals on the spectrum. Their multiplicities can be explained by recalling that, since they are diastereotopic, they **couple to each other**. As such, each signal is a **doublet of doublets**!

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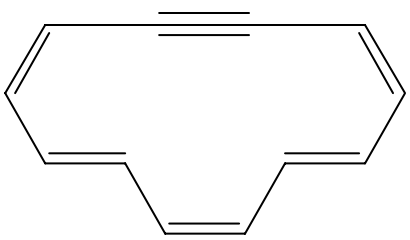
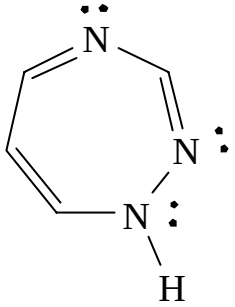
3. Identify whether each of the following molecules is aromatic, nonaromatic or antiaromatic **in the planar conformation**. If it is a factor in your decision, you must also indicate the number of electrons in the pi system. **[4 marks]**

(a)



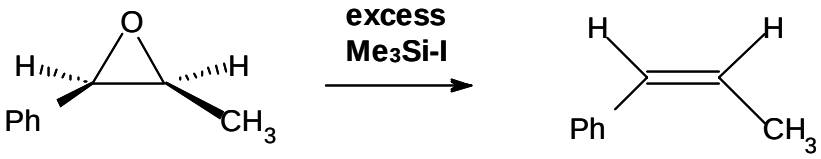
12 π electrons in cyclic π system
antiaromatic

(b)



8 π electrons in cyclic π system
antiaromatic

4. You are studying the following reaction. It gives only the product shown. Does this result mean that this reaction is stereospecific? If not, what experiment might you do to test whether it is stereospecific or not, and what other information might be useful? **[4 marks]**



It does NOT mean that the reaction must be stereospecific. It might just be highly stereoselective.

In order to determine whether or not the reaction is stereospecific, it will be necessary to work out the mechanism.

If the same reaction were performed on the *trans* epoxide and the same product (*cis* alkene) obtained, we would know that the reaction is NOT stereospecific. If the same reaction were performed on the *trans* epoxide and the *trans* alkene was obtained, it would seem more likely that the reaction was stereospecific.

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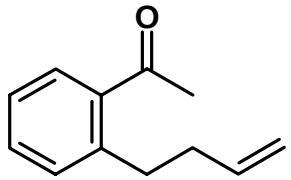
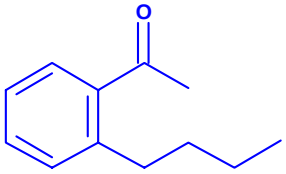
5. Consider the following molecule: **[2 marks]**

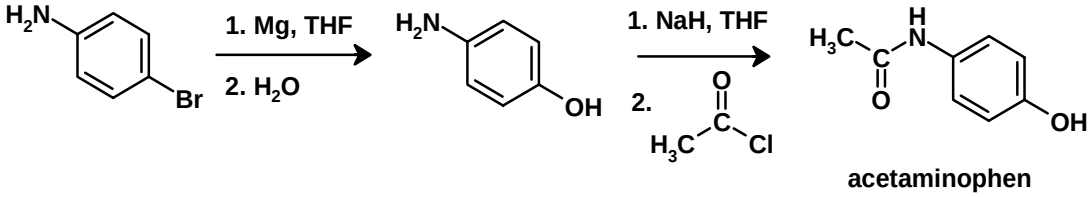


When treated with 1 equivalent of H_2 in the presence of Pd/C, what is the product? Briefly explain why reaction occurs at the site you have chosen.



The C=C double bond that is not part of the benzene ring reacts. The aromatic C=C π system is too strong to be hydrogenated under these conditions. The same is true of the C=O π bond.

6. A student proposed the following synthesis of acetaminophen:



acetaminophen

Identify **three** problems with this synthetic route. **[3 marks]**

1. It is not possible to make Grignard reagents in the presence of acidic H (like the NH_2 group).
2. The electrophilic sites in a water molecule are the H not the O so, even if the Grignard could be generated, reacting it with water would give Ar-H not Ar-OH.
3. NaH will deprotonate the phenol H not the aniline H. This will give O^- which is a better nucleophile than neutral N. Thus, the acetyl chloride will be attacked by O not N and the product will be the ester not the amide.

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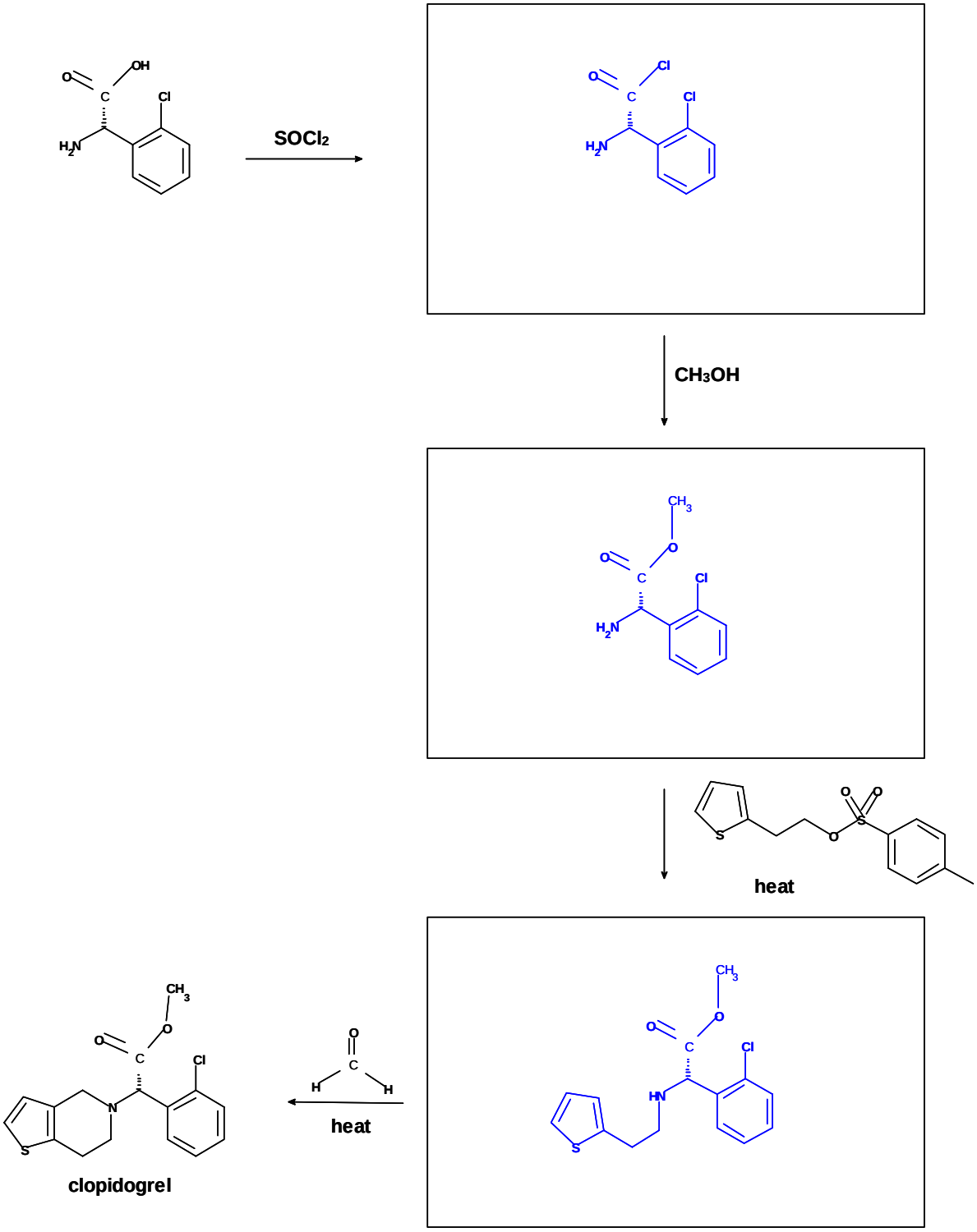
7. Clopidogrel (marketed as Plavix®) is an antithrombotic drug that inhibits platelet aggregation. **[4 marks]**

(a) Fill in the blanks in the following synthesis of Plavix®. *[3 marks]*
Some reaction conditions have been simplified for clarity. You do not need to show mechanisms.



(b) Which enantiomer of clopidogrel is shown in the diagram above? *[1 mark]*

S

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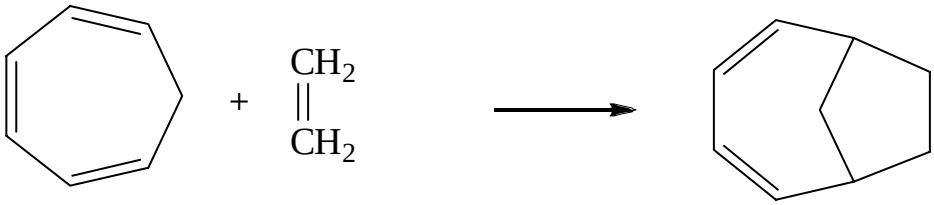
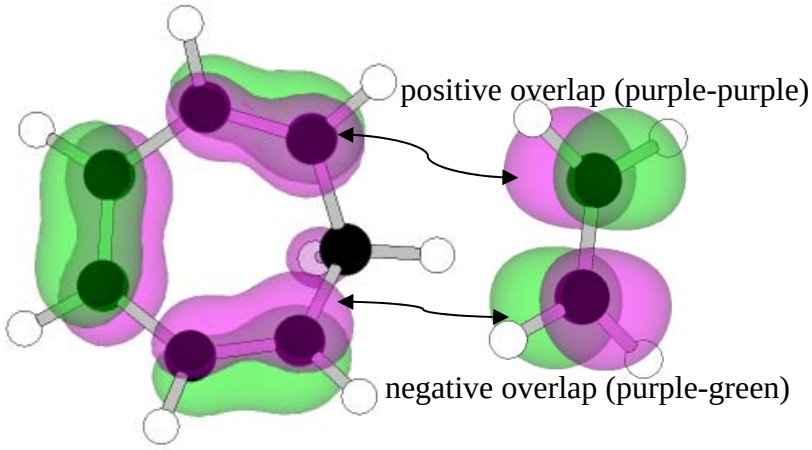
8. **[5 marks]**

(a) Showing the appropriate pi molecular orbitals, indicate whether the following reaction is thermally allowed. You may assume that the reaction involves the HOMO of the triene.





(ignore the purple blip on the C-H bond of the CH_2 group)

For a cycloaddition reaction to proceed, the two π systems need to be able to sit one on top of the other such that there is positive overlap at both ends.

This reaction is NOT thermally allowed. While we can get positive overlap between one end of each π system, the other ends will have negative overlap. As such, the HOMO of the triene and LUMO of the alkene cannot react in a cycloaddition and the reaction does not occur.

(b) Come up with a rule, similar to the Huckel rule, that relates the number of pi electrons involved in a cycloaddition reaction to whether it is thermally allowed. You may name it after yourself if you wish.

A cycloaddition is thermally allowed when the total number of π electrons involved is equal to 4n+2 where 'n' is any integer.

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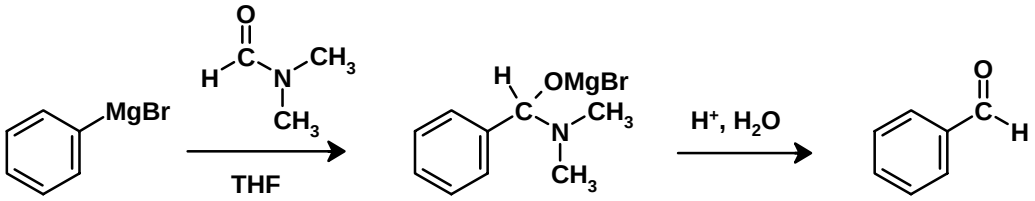
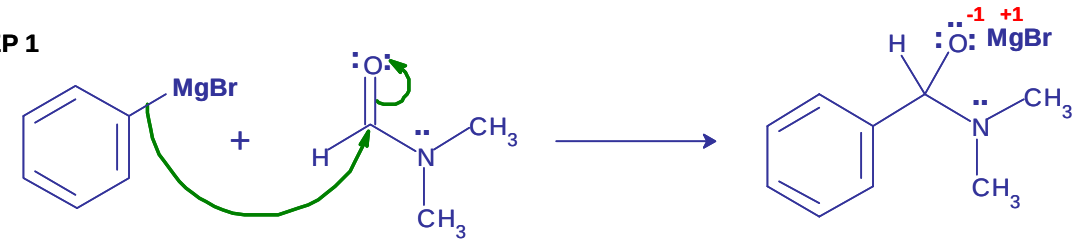
9. When phenylmagnesium bromide is reacted with N,N-dimethylformamide (DMF), the final product (after work-up with aqueous acid) is benzaldehyde: **[7 marks]**

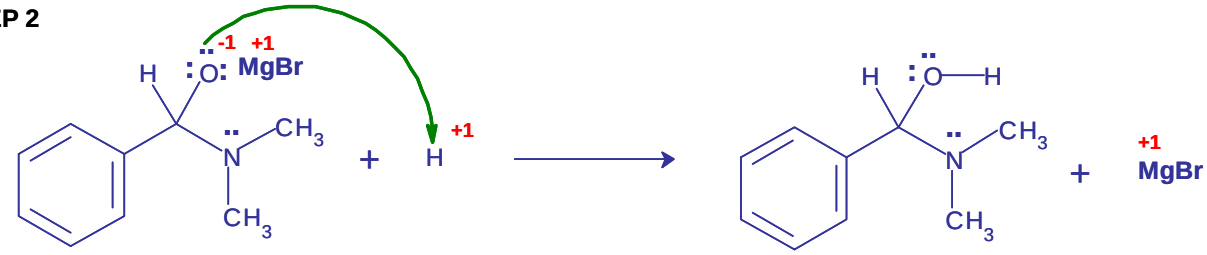


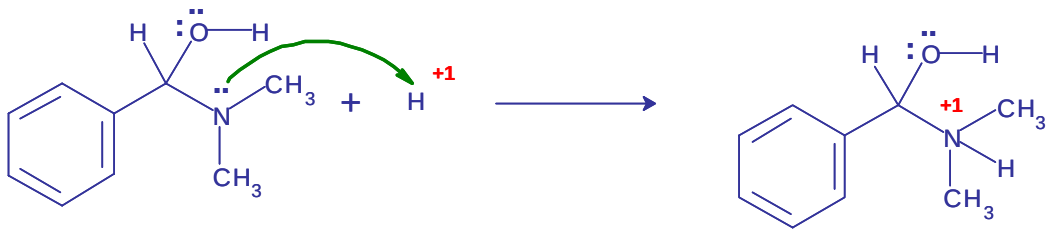
(a) Propose a mechanism for this reaction **<u>including the work-up</u>**. *[5 marks]*

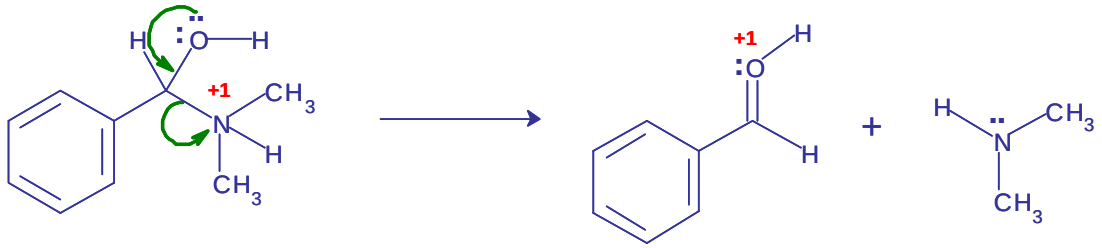
STEP 1

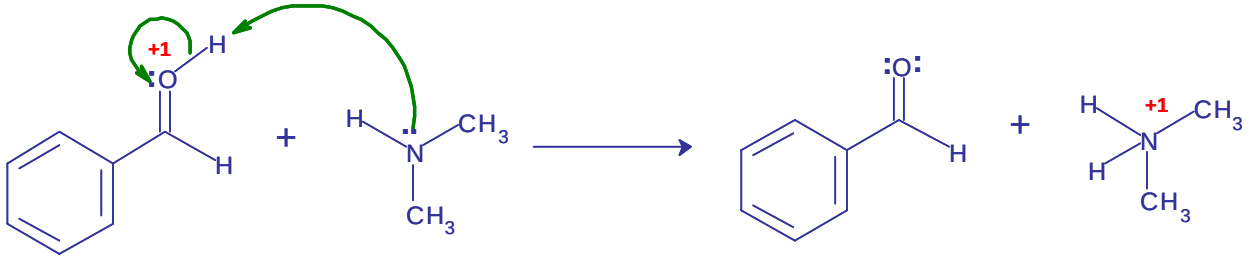


STEP 2



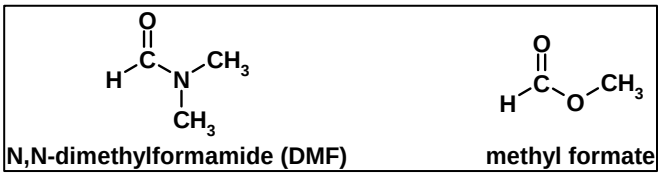




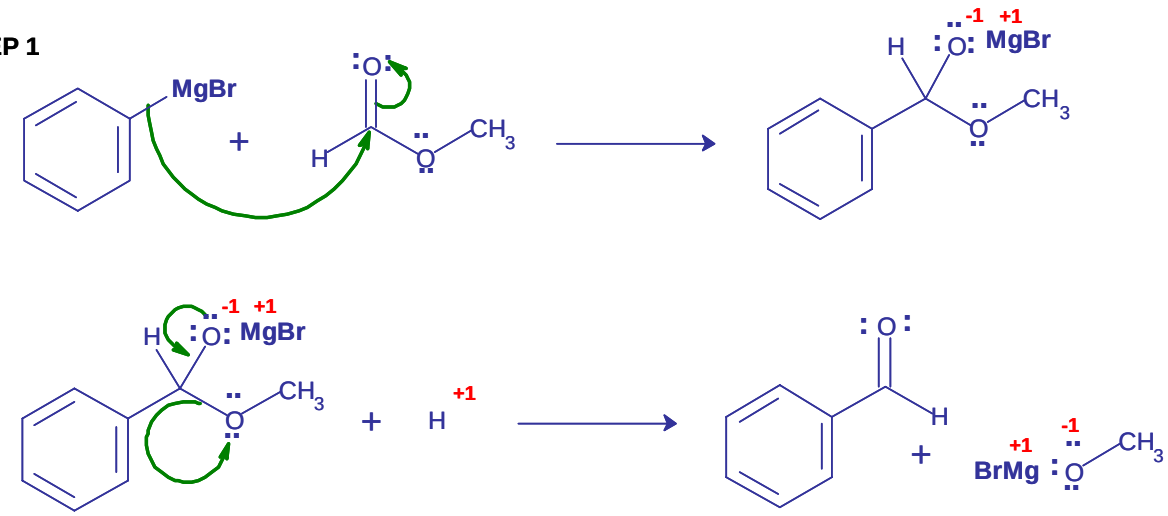


Name: _____ Student Number: _____

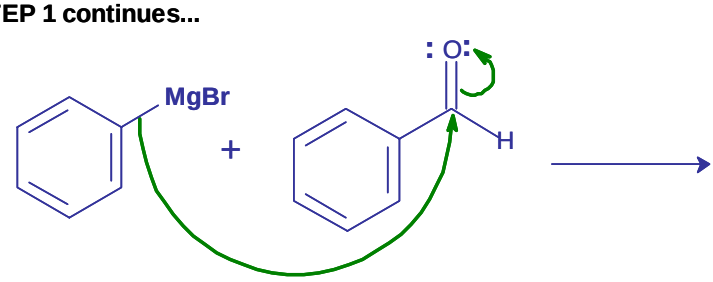
(b) If methyl formate is used instead of DMF, a different product is obtained. Draw this product and explain why DMF gives benzaldehyde but methyl formate does not. *[2 marks]*



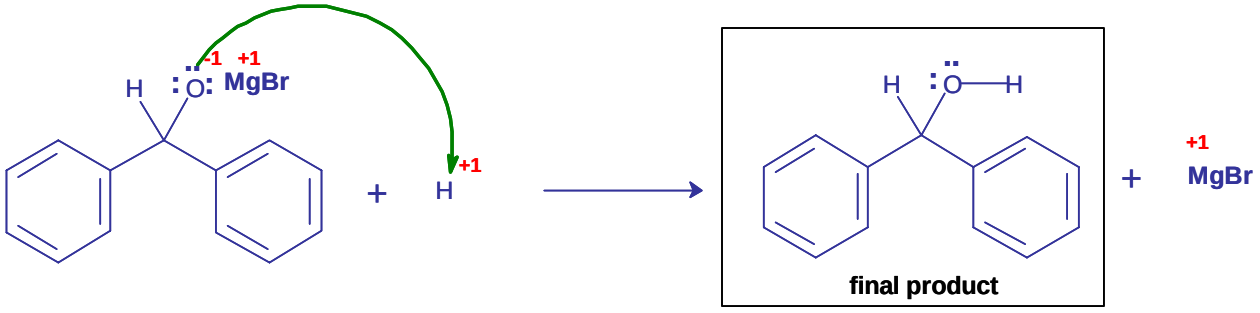
STEP 1



STEP 1 continues...



THEN STEP 2 (work-up)



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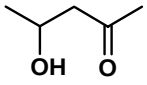
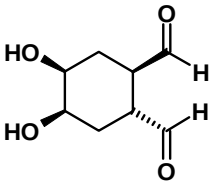
10. Choose any **three** of the molecules below and propose a synthesis of each. **[15 marks]**

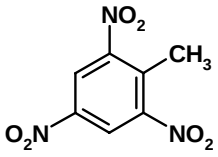
- Your organic reactants must be stable compounds that contain no more than five carbon atoms. **They may be hydrocarbons, alkyl halides or alcohols and may contain C=C or C≡C bonds.** You are also allowed to use benzene, bromobenzene or phenol.
- If you wish to use an organic reactant (including Grignard reagent) that does not meet these requirements, you must show how to make it from starting materials that do.
- You may use any inorganic reagents, acids, bases, catalysts, etc.
- Acids, bases, catalysts, etc. do not need to meet the "organic reactant" requirements if the organic part will not be present in the final product.
- Clearly indicate stereochemistry of reaction products where appropriate. Assume that all stereochemistry shown is relative and that you are to make racemic product.
- You are not required to show mechanisms for this question.
- If you work out syntheses for more than three of the molecules, clearly indicate which three you want marked by circling those compounds. Otherwise, I will mark the first three syntheses given.
- If you run out of space on this page, continue your work on the next page.



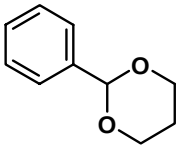
A



B



C

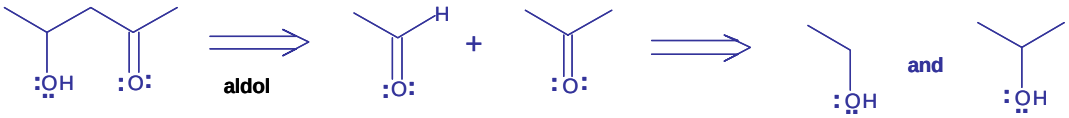


D

Note the sentence in bold red type above. If your starting materials do not fall into this category (or the benzene/bromobenzene/phenol exceptions), your synthesis is considered to be missing the steps required to get from a material that does to the starting material you actually used. As such, only partial credit can be given.

There are many valid routes to each target compound. Only one is shown for each.

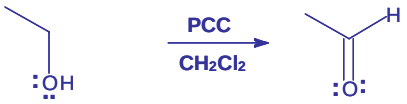
A: **RETROSYNTHETIC ANALYSIS**



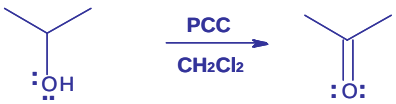
oxidize alcohols to ketone and aldehyde

PROPOSED SYNTHESIS

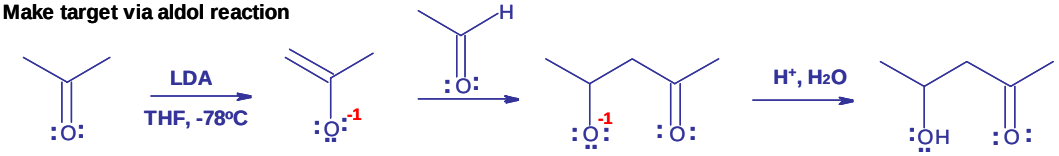
1a. Make ethanal



1b. Make 2-propanone

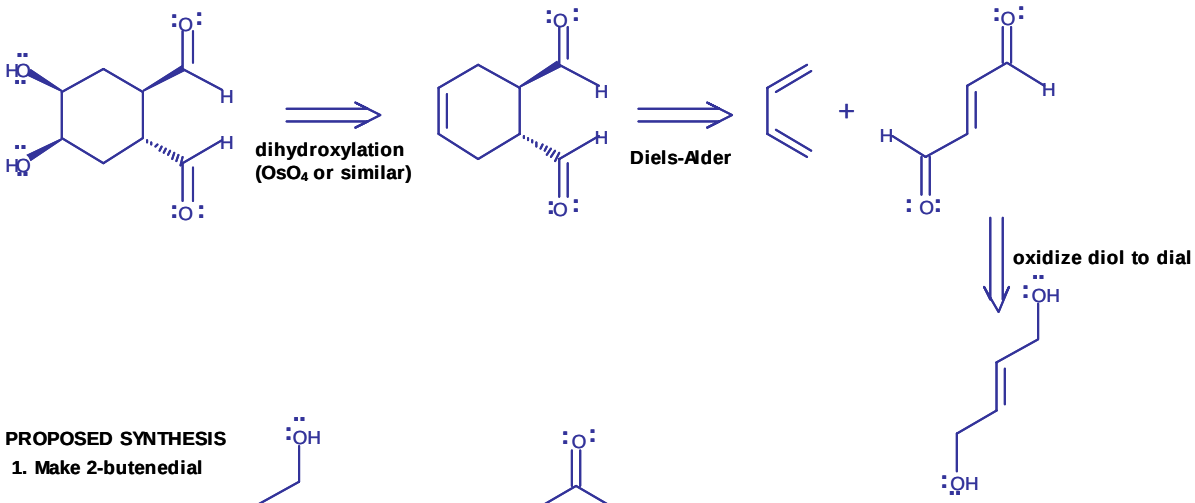


2. Make target via aldol reaction



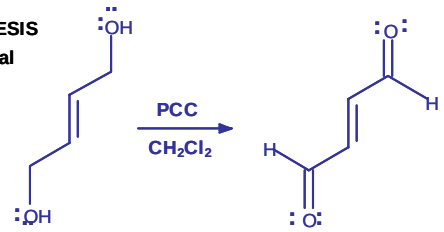
Name: _____ Student Number: _____

B: **RETROSYNTHETIC ANALYSIS**

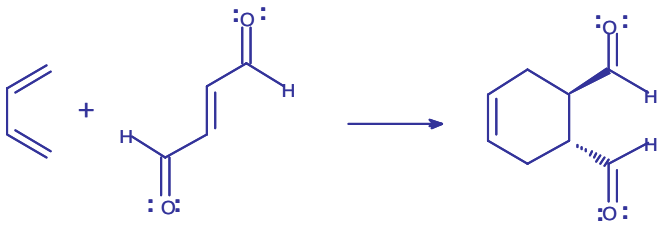


PROPOSED SYNTHESIS

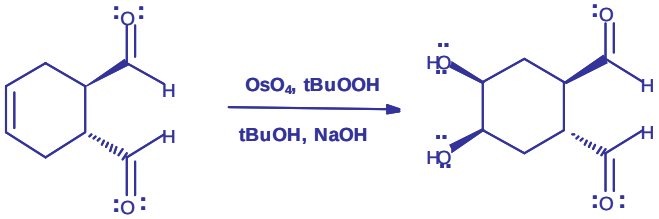
1. Make 2-butenedial



2. Make ring via Diels-Alder reaction (*trans* dienophile gives *trans* cyclohexene)

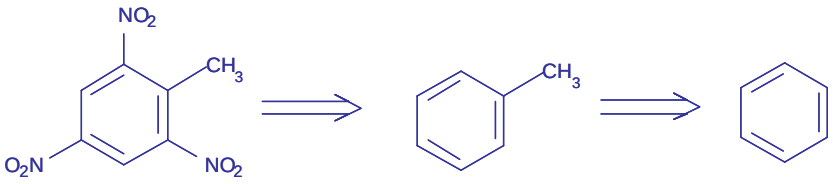


3. Introduce alcohol groups via dihydroxylation (choose stereospecific reaction conditions to get *cis* diol)



Name: _____ Student Number: _____

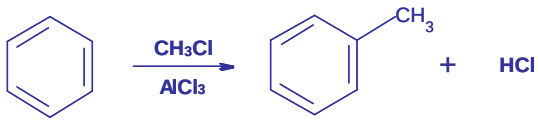
C: **RETROSYNTHETIC ANALYSIS**



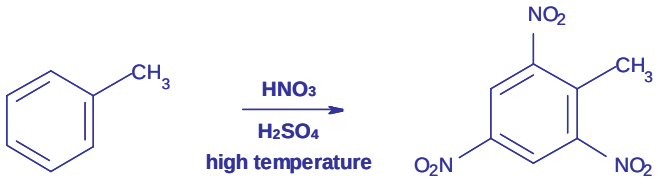
nitration **Friedel-Crafts**

PROPOSED SYNTHESIS

1. Make toluene (methylbenzene)



2. Add nitro groups (methyl group directs ortho/para; nitro groups direct meta)

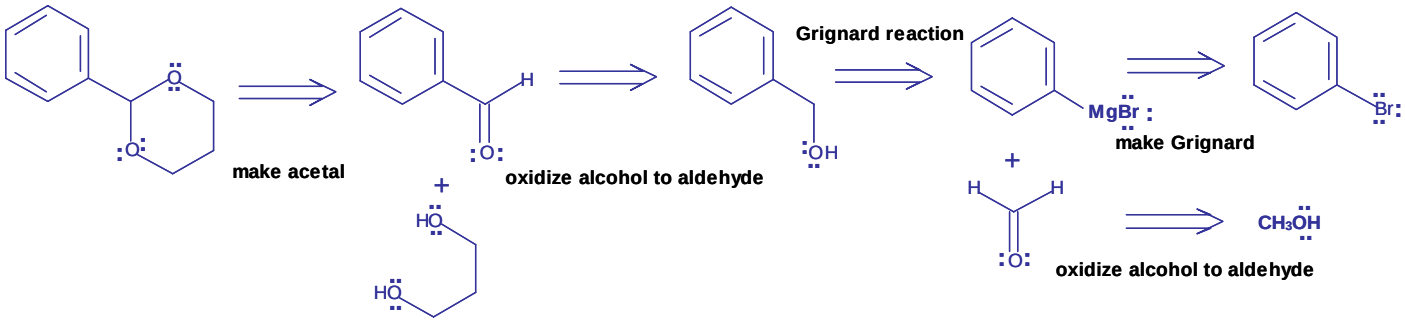


This synthesis is not recommended without appropriate protective equipment.
The product is TNT!

Name: _____ Student Number: _____

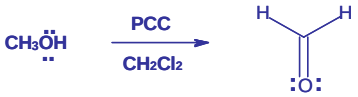
D:

RETROSYNTHETIC ANALYSIS

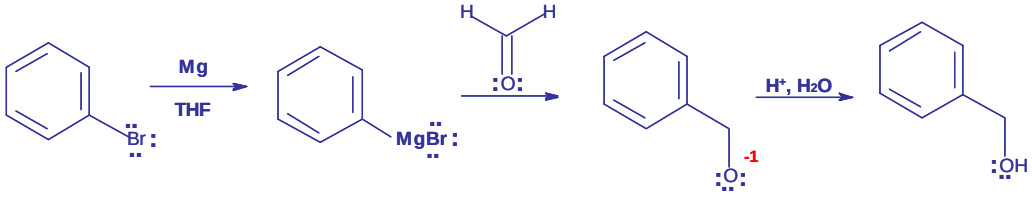


PROPOSED SYNTHESIS

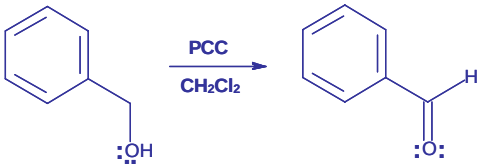
1. Oxidize methanol to methanal



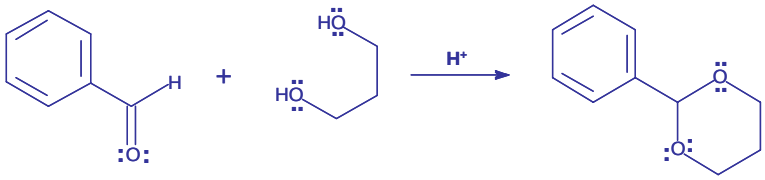
2. Prepare Grignard reagent and react it with methanal



3. Oxidize benzyl alcohol to benzaldehyde



4. Make acetal



11. What was the most interesting and/or useful thing you learned in CHEM 2600? **[1 mark]**

…AND THAT'S ALL FOR CHEM 2600.
HAVE A GREAT SUMMER!

DATA SHEET/SCRAP PAPER

Chem 2000 Standard Periodic Table

1												13	14	15	16	17	18
1.0079 **H** 1	2																4.0026 **He** 2
6.941 **Li** 3	9.0122 **Be** 4											10.811 **B** 5	12.011 **C** 6	14.0067 **N** 7	15.9994 **O** 8	18.9984 **F** 9	20.1797 **Ne** 10
22.9898 **Na** 11	24.3050 **Mg** 12	3	4	5	6	7	8	9	10	11	12	26.9815 **Al** 13	28.0855 **Si** 14	30.9738 **P** 15	32.066 **S** 16	35.4527 **Cl** 17	39.948 **Ar** 18
39.0983 **K** 19	40.078 **Ca** 20	44.9559 **Sc** 21	47.88 **Ti** 22	50.9415 **V** 23	51.9961 **Cr** 24	54.9380 **Mn** 25	55.847 **Fe** 26	58.9332 **Co** 27	58.693 **Ni** 28	63.546 **Cu** 29	65.39 **Zn** 30	69.723 **Ga** 31	72.61 **Ge** 32	74.9216 **As** 33	78.96 **Se** 34	79.904 **Br** 35	83.80 **Kr** 36
85.4678 **Rb** 37	87.62 **Sr** 38	88.9059 **Y** 39	91.224 **Zr** 40	92.9064 **Nb** 41	95.94 **Mo** 42	(98) **Tc** 43	101.07 **Ru** 44	102.906 **Rh** 45	106.42 **Pd** 46	107.868 **Ag** 47	112.411 **Cd** 48	114.82 **In** 49	118.710 **Sn** 50	121.757 **Sb** 51	127.60 **Te** 52	126.905 **I** 53	131.29 **Xe** 54
132.905 **Cs** 55	137.327 **Ba** 56	**La-Lu**	178.49 **Hf** 72	180.948 **Ta** 73	183.85 **W** 74	186.207 **Re** 75	190.2 **Os** 76	192.22 **Ir** 77	195.08 **Pt** 78	196.967 **Au** 79	200.59 **Hg** 80	204.383 **Tl** 81	207.19 **Pb** 82	208.980 **Bi** 83	(210) **Po** 84	(210) **At** 85	(222) **Rn** 86
(223) **Fr** 87	226.025 **Ra** 88	**Ac-Lr**	(261) **Rf** 104	(262) **Db** 105	(263) **Sg** 106	(262) **Bh** 107	(265) **Hs** 108	(266) **Mt** 109	(281) **Dt** 110	(283) **Rg** 111							

138.906 **La** 57	140.115 **Ce** 58	140.908 **Pr** 59	144.24 **Nd** 60	(145) **Pm** 61	150.36 **Sm** 62	151.965 **Eu** 63	157.25 **Gd** 64	158.925 **Tb** 65	162.50 **Dy** 66	164.930 **Ho** 67	167.26 **Er** 68	168.934 **Tm** 69	173.04 **Yb** 70	174.967 **Lu** 71
227.028 **Ac** 89	232.038 **Th** 90	231.036 **Pa** 91	238.029 **U** 92	237.048 **Np** 93	(240) **Pu** 94	(243) **Am** 95	(247) **Cm** 96	(247) **Bk** 97	(251) **Cf** 98	(252) **Es** 99	(257) **Fm** 100	(258) **Md** 101	(259) **No** 102	(260) **Lr** 103

Developed by Prof. R. T. Boeré