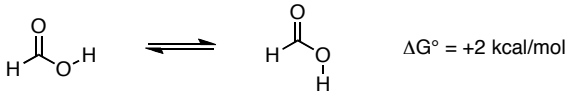
Name: _____

CHEM 633: Advanced Organic Chem: Physical
Problem Set 2. Due 9/22/16. *Do <u>not</u> look up references until after you have turned in the problem set!*

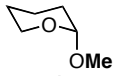
1. Using FMO arguments, please explain why the *Z* acid conformation is more stable than then *E* conformation.



(*Z*) (*E*)

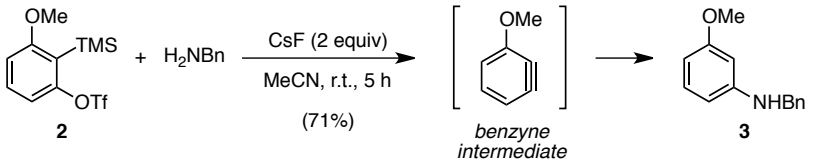
2. Please predict the lowest energy conformation of 2-chlorotetrahydropyran. Explain your answer using pictures and less than 10 words.

3. Where is the methyl group in the lowest energy conformation of ketal **1**? Please use Newman projections to clearly illustrate the position of the methyl group. Also, please explain your reasoning. You may use steric, electronic and/or stereoelectronic arguments.

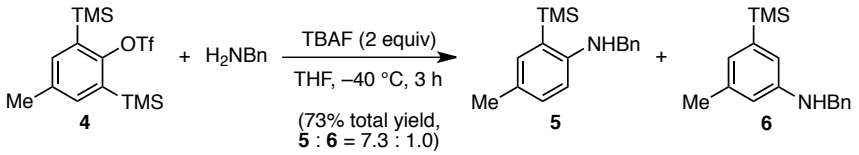


1

4. *ortho*-Silylaryl triflates, such as **2**, are useful substrates for generating benzyne intermediates. Larock et al. found that *meta*-substituted product **3** was the only observed product in the addition of benzyl amine to **2**. In contrast, Akai et al. observed that *ortho*-substituted aniline **5** was the major product in the reaction of **4**.



Liu, Z.; Larock, R. C. *J. Org. Chem.* **2006**, *71*, 3198.

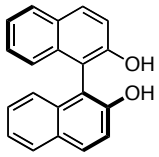


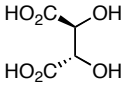
Ikawa, T.; Nishiyama, T.; Shigeta, T.; Mohri, S.; Morita, S.; Takayanagi, S.; Terauchi, Y.; Morikawa, Y.; Takagi, A.; Ishikawa, Y.; Fujii, S.; Kita, Y.; Akai, S. *Angew. Chem. Int. Ed.* **2011**, *50*, 5674.

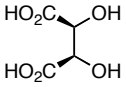
(a) Please draw a reasonable arrow-pushing mechanism for the transformation of **2** to **3**.

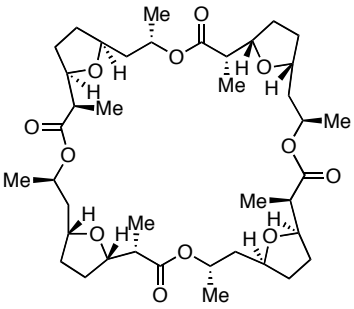
(b) Please rationalize the observed regiochemistry in both of these reactions. Specifically address why *meta* substitution is favored in one case and *ortho* in the other.

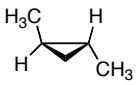
5. Are the following molecules chiral? Circle the ones that are chiral.

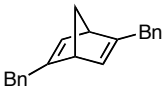




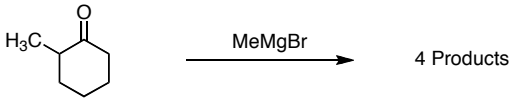






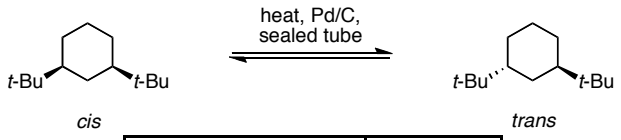


6. (a) Please draw the 4 possible products from the reaction of 2-methylcyclohexanone and methyl magnesium bromide.



(b) What are the stereochemical relationships between these products?

7. The temperature-dependent ratio of isomers of 1,3-di-*tert*-butylcyclohexane has been examined at equilibrium (*J. Am. Chem. Soc.* **1960**, *82*, 2393).



cis *trans*

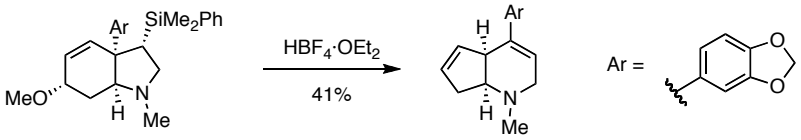
Temperature (K)	% *trans*
492.6	2.69
522.0	3.61
555.0	5.09
580.0	6.42
613.0	8.23

(a) Are the *cis* and *trans* conformations enantiomers or diastereomers?

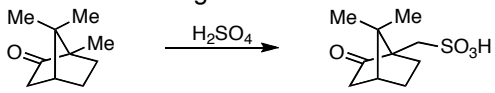
(b) Determine $\Delta H°$ and $\Delta S°$ for this process in kcal/mol and eu, respectively. Please attach your Excel worksheet and graph to the end of your problem set.

(c) Compare the measured value of $\Delta S°$ with those determined for other alkyl substituents by NMR spectroscopy (Me = –0.03 eu, Et = 0.64, *i*-Pr = 2.31), and provide an explanation for the sign and magnitude of the observed value in the *t*-Bu case.

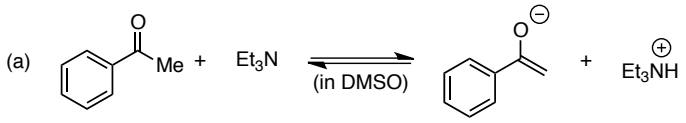
8. Propose an arrow-pushing mechanism for the following transformation.

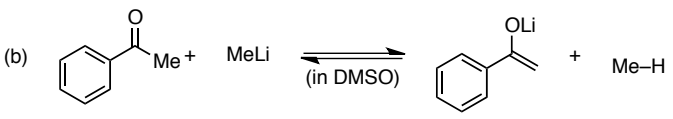


9. Propose an arrow-pushing mechanism for the following transformation.

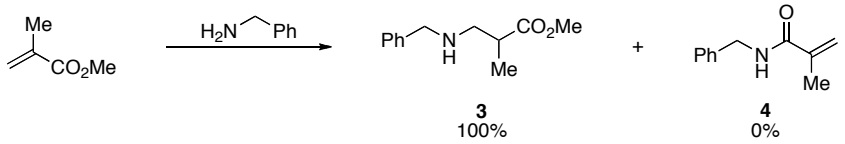


10. Please circle which side of the following equilibria will be favored. Please report the relevant pK_a's and give K_{eq} for both equations.





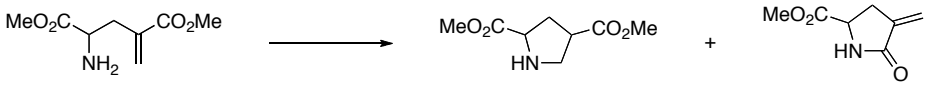
11. (a) The reaction of benzylamine and methyl methylacrylate results exclusively in the formation of product **3**. Please explain the selectively for product **3** over **4**.



3
100%

4
0%

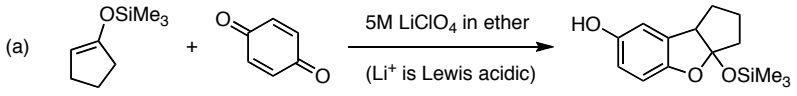
(b) In contrast, product **6** is the exclusive product in the intramolecular addition of an amine to a similar electrophile (Baldwin, J.; Cutting, J.; Dupont, W.; Kruse, L.; Silberman, L.; Thomas, R. *J. Chem. Soc., Chem. Commun.* **1976**, 736). Please explain the selectivity for product **6** over **5**.

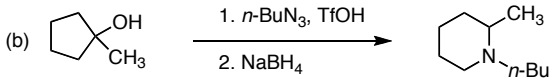


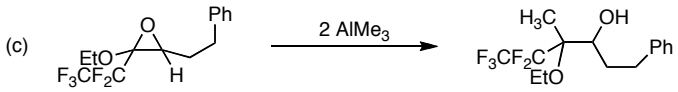
5
0%

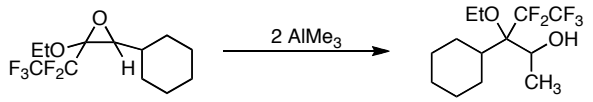
6
100%

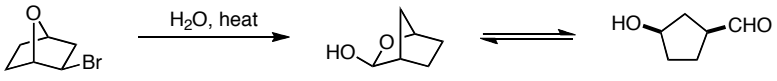
12. (Grossman, Ch 2, #4) Draw reasonable arrow-pushing mechanisms for the following reactions.

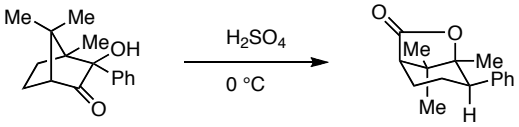
(a) 

(b) 

(c) 

(d) 
EtO
F3CF2C
O
H
2 AlMe3
EtO
CF2CF3
OH
CH3

(e) 
O
Br
H2O, heat
HO
O
HO
CHO

(f) 
Me
Me
Me
OH
Ph
O
H2SO4
0 °C
O
O
Me
Me
Ph
Me
H