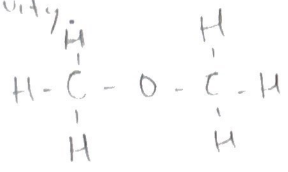
Your Name:

Isomer Relationships, Conformational Stability, and Reaction Selectivity

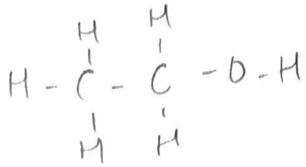
Instructions:
Read the instructions carefully and answer the following questions in the space provided. Then attach the PDF file on Discussion Board for peer discussion and peer review.

1. In a few sentences define each of the three main classes of isomers below. Configurational Isomers can be further classified as either enantiomers or diastereomers and should also be discussed. Your descriptions should enable your peers to quickly and easily compare and contrast the differences between the different classes of isomers.
    - A. Constitutional Isomers (or Structural Isomers)
    - B. Conformational Isomers
    - C. Configurational Isomers (or Stereoisomers)
        - I. Enantiomers
        - II. Diastereomers

A. Type of isomers in which the difference lies on atomic connectivity.

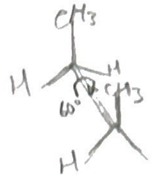


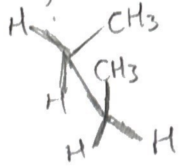
C_2H_6O



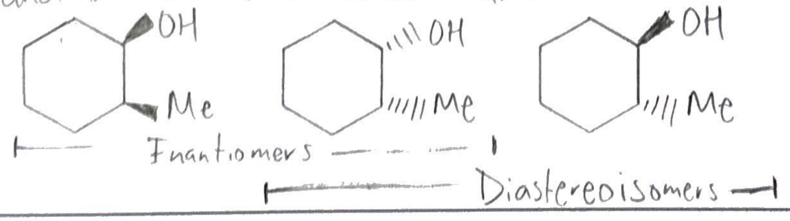
C_2H_6O

B. "Stereoisomers produced by rotation about σ bonds"[1]





C. "Enantiomers are stereoisomers that are image mirrors of one another. Diastereomeres are not mirror images of one another."[2]



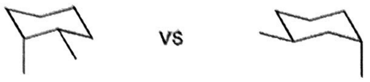
[1] Reference from University of Calgary where they have a short description of conformational isomers

[2] From the book required by the class; Organic chemistry Chapter 5.5, where it specifies the distinction between enantiomers and diastereoisomers.

2. Analyze each pair of compounds below. Identify which class of isomers each pair of structures represent. Your choices are: ***(i) constitutional, (ii) conformational, (iii) enantiomers, or (iv) diastereomers or (v) identical (non-isomers).*** Only one label for each pair should be used. For each case show work (drawings, (R)/(S), rotation of bonds, chair-flips, etc) which led you to each answer for the pairs below. [During your peer review, any differences of answers between you and your peers can be discussed and corrected as needed.]

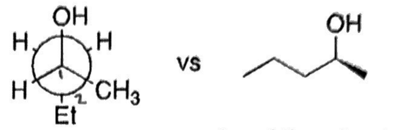
Note: Various projections may be used when drawing chemical structures including bond-line structures (using proper dash/wedge bonds), Newman projections, chair structures (for cyclohexane derivatives), Haworth projections, and Fischer projections. These projections just represent different vantage points of visualizing a chemical structure and can be interconverted from one projection to another. Each different projection has been labeled for you below. These are all utilized throughout the text book.

(a)



Both are chair structures

(b)



Newman projection

bond-line structure (dash/wedge shown)

(c)

bond-line structure (dash/wedge shown)

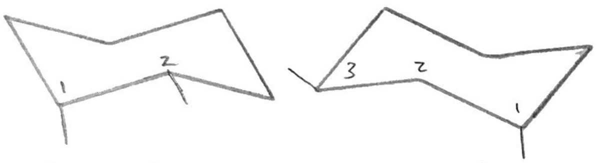
chair structure

(d)

bond-line structure (dash/wedge shown)

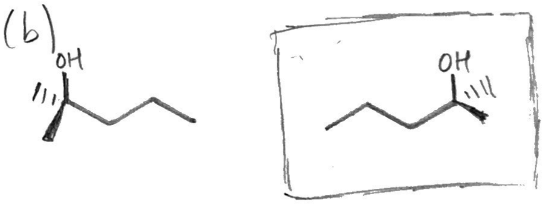
bond-line structure (dash/wedge shown)

(a)



(i) Constitutional isomers since they have the same molecular formula, but differ in atomic connectivity

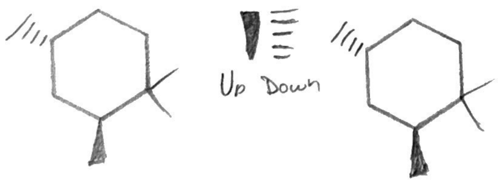
(b)



Mirror next to molecule

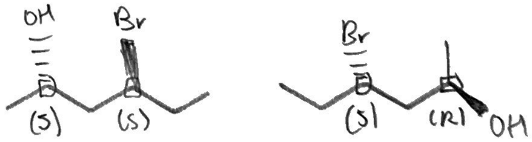
(iii) Enantiomers

(c)



Identical compounds

(d)

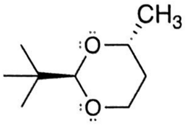


Since they are not mirror images, we can detect they are (iv) diastereoisomers

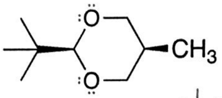
3. Analyze the structures for **Compound A** and **Compound B** shown below. Answer and discuss each question (a) and (b), respectively.

   a. What type of isomers do these represent?
   b. Which compound is more stable? (Hint: You will need to draw the chair structures for each compound (4 total chairs, two for each compound) and compare/contrast/analyze the various 1,3-diaxial interactions in order to justify this answer. Show your work clearly.

Compound A



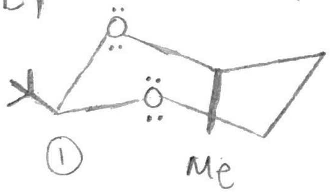
Compound B



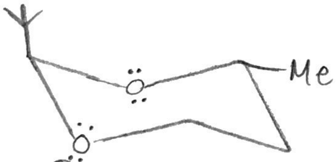
More stable

a) These compounds are constitutional isomers since the CH_3 is connected to a different carbon number in each compound.

b) A



①

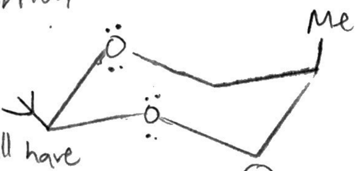


②

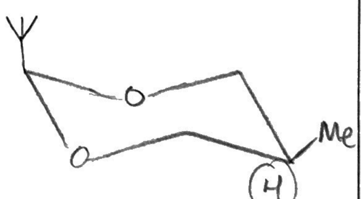
However, we could use chair conformations to checn which one is more stable

B

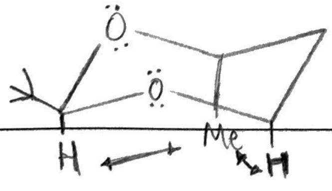
As we saw on the lab portion R groups have different energy differences in their axial forms. A tert butyl on the axial will have more energy than a methyl. Remind for this case more energy = less stable meaning ① and ③ will be more stable.



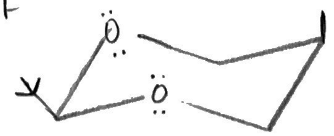
③



④

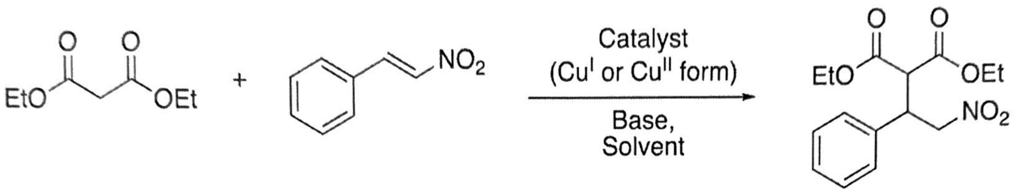


Now in terms of ① vs ③, ① has 1,3 diaxial interaction and ③ has not.



Therefore, ③ is more stable

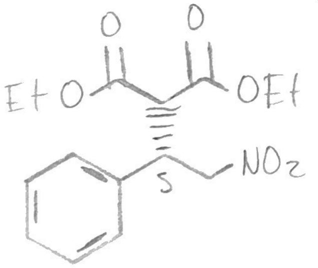
4. Chiral catalysts can be designed to favor the formation of one enantiomer over another in reactions where a new chiral center is formed. The example shown below was recently reported in the chemical literature (*J. Am. Chem. Soc.* **2012,** *134*, 8054–8057) where a new type of chiral copper (Cu) catalyst was developed. When the Cu^I catalyst was used, the (S)-enantiomer of the product predominated, and the (R)-enantiomer of the product was selectively formed when Cu^{II} catalyst was used instead.

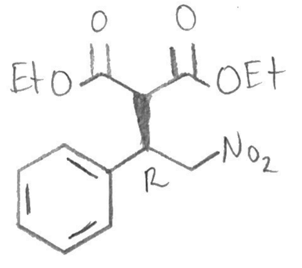


Answer part (a) and (b) below. You aren't required to understand the chemistry to answer correctly and discuss the experimental results.

a. The product has been shown on the right of the reaction scheme above but the absolute stereochemistry of the product has been excluded. Draw the **major enantiomer** formed when each form of the catalyst is used. You need to be sure to show the stereochemistry clearly using appropriate dash/wedge bonds at the stereocenter and indicate which catalyst (Cu^I or Cu^{II}) was used for each of the two individual enantiomers you draw.

"When the Cu^I catalyst was used, the (S)-enantiomer of the product predominated"





"the (R)-enantiomer of the product was selectively formed when Cu^{II} catalyst was used"

b. The chart below reports the data when the (S)-selective catalyst was used in various solvents. The enantiomeric excess (reported as % ee) is shown for each case.

Solvent	% ee of (S)-product	% Yield of total product	% S	% R
Toluene	24	55	62	38
THF	48	33	74	26
Acetonitrile	72	55	86	14
Chloroform	30	40	65	35
Dichloromethane	46	44	73	27
Hexane	51	30	75.5	24.5

Complete the table above by calculating the % (S) and % (R) formed when the (S)-selective reaction was repeated in the various solvents. How are these values calculated? Illustrate this by showing a complete calculation for the toluene case. For the others, you can simply just write in the values. If your values do not match your peers', you will need to discuss this and correct as needed. Also, discuss which solvent gives the optimal results in terms of both enantioselectivity and overall total product yield. What experimental data led you to make this conclusion? Where any other solvents comparable? What solvent gave the worst results?

$$\% ee = \frac{|S-R|}{S+R} \cdot 100\%$$

$$24\% = |S-R|$$

$$24\% = S - (100\% - S)$$

$$\begin{aligned} 24\% &= 2S - 100\% \\ +100\% & \qquad\quad +100\% \end{aligned}$$

$$\frac{124\%}{2} = \frac{\cancel{2}S}{\cancel{2}} \qquad \boxed{\% S = 62}$$

$$S + R = 100\%$$

$$S = 100\% - R$$

$$R = 100\% - S$$

$$R = 100\% - 62\%$$

$$\boxed{\% R = 38}$$

% Yield or total product from Toluene and Acetonitrile are 55. However, % S is higher in Acetonitrite meaning is slightly a better solvent.

The worst results are the ones from hexane since % yield is 30.