

Practice Problems in Biomedical Organic Chemistry:
*Self-Guided Problems and Answers for Students in Bioorganic and
Organic Chemistry, Volume I*

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About this problem set

This problem set was developed to assist undergraduate students taking a one semester or two semester, non-majors course in organic chemistry. Students in these courses often come to organic chemistry from diverse backgrounds including biology, microbiology, and a variety of medical-related fields (e.g., pre-medical, pre-nursing, pre-pharmacy, and others). If you are one of these students, these problems were made for you. We have generated a series of questions and answers dealing with major topics in organic chemistry as they apply to biology, medicine, and cell biology. In addition, we have included questions related to important analytical chemistry tools that students might encounter during their professional careers.

Our plan is to release sets of organic chemistry problems in a three volume series. The problems are intended to serve as self-directed learning tools, which students can use at a pace that meets their individual educational needs. We have created three types of problems (i.e., **C, I, A**) for each topic:

- **C: *Core concepts*.** These problems define major terms and ideas pertaining to a particular topic.
- **I: *Integrated*.** These problems require the assimilation and integration of multiple core concepts to arrive at the correct solution to the problem.
- **A: *Applied*.** These problems test understanding of core concepts by applying them to data-driven and real-world problems in biology and other life science disciplines.

While I-type and A-type problems are multidimensional, they should not be automatically perceived as ‘more difficult.’ Instead, students should use these problems to test how well integrated chemistry concepts have become in terms of relating this knowledge to practical, everyday problems. It is unfortunate that organic chemistry has been distorted in many peoples’ minds to become a roadblock obstructing their way to a degree. Instead of ‘doing time’ in organic, we hope that students will embrace this opportunity to learn new ways of viewing the world around them and use this new-found knowledge to better understand problems and assist patients.

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The authors would like to acknowledge financial support from the University of Oklahoma Libraries for an Alternative Textbook Initiative grant, which helped offset the cost of producing this work. We are also grateful for assistance from C. Coker who helped format and organize the problems in this volume. We hope this problem set will assist you as you enter into the world of organic chemistry. We would like to hear from you. If you have ideas for topics to be included in future volumes or have suggestion or corrections, you can email the authors at rhcichewicz@ou.edu. Additional problem sets in this series will be archived in SHAREOK (<https://shareok.org/>), a digital repository for open access publications. Be sure to check this site for updates and new additions to the series.

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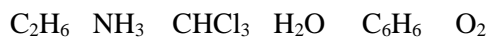
ANSWERS TO PROBLEM SETS

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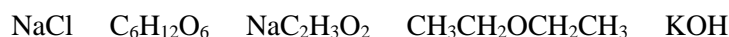
PROBLEM SET 1: GENERAL CHEMISTRY PRINCIPLES

a. Electrons and Bonds

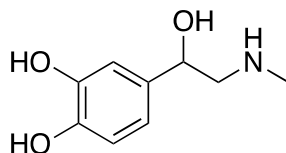
1. (C) Which of the following compounds exhibits a molecular dipole moment?



2. (C) For the following compounds, determine if they are covalent or ionic in nature.



3. (I) Identify and draw each of the dipole moments for the C-O and C-N bonds present in adrenaline (pictured below).



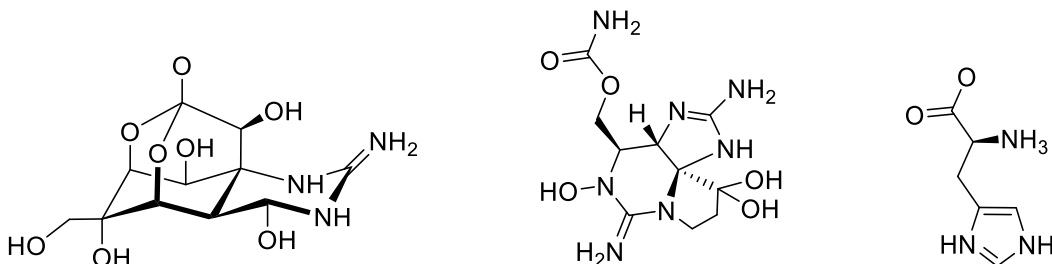
4. (I) What is the hybridization of the carbon atom in an amide, nitrile, alkane, and isocyanate functional group?

5. (A) Proteins are made up of amino acids that are joined together by amide functional groups. What is the hybridization of the nitrogen atom in an amide functional group? Explain your reasoning for your answer. Would you expect this hybridization to make a polypeptide chain more flexible or rigid in structure?

6. (C) Determine if the following bonds are polar or nonpolar:



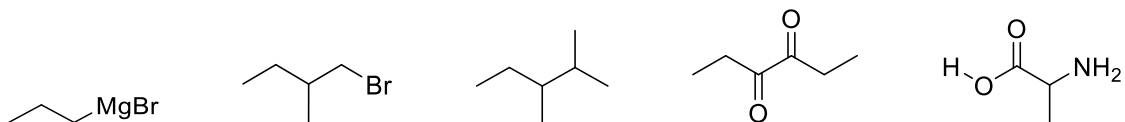
7. (C) Tetrodotoxin (left) is a potent neurotoxin found in pufferfish. Neosaxitoxin is another neurotoxin found in some shellfish after harmful algal blooms, but it has also been investigated for anesthetic purposes. It is shown in its protonated form (middle). Histidine (right) is an essential amino acid. Add formal charges the structures.



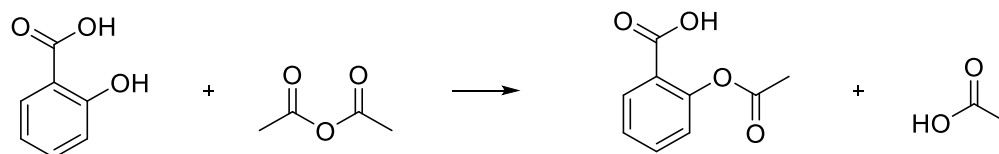
8. (I) Draw all possible structures for the following formulae:



9. (I) Assign partial positive (δ^+) and partial negative (δ^-) charges to the following structures. Are these compounds polar or nonpolar?

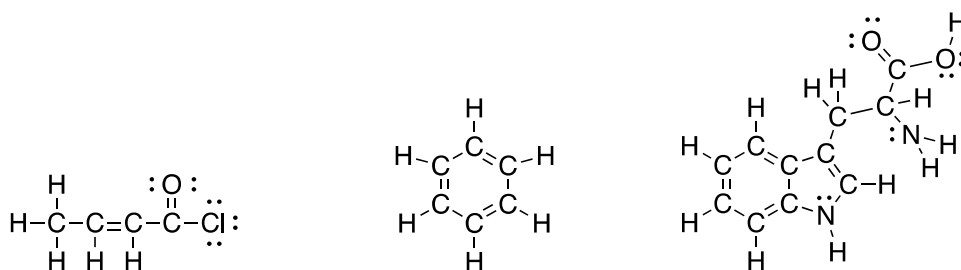


10. (A) Aspirin, also known as acetylsalicylic acid, can be produced by reacting salicylic acid with acetic anhydride. In the reaction shown, a partially positive (δ^+) carbon will be attacked by an anion ($R-O^-$). Identify the partially positive carbons in the reactants and the products.

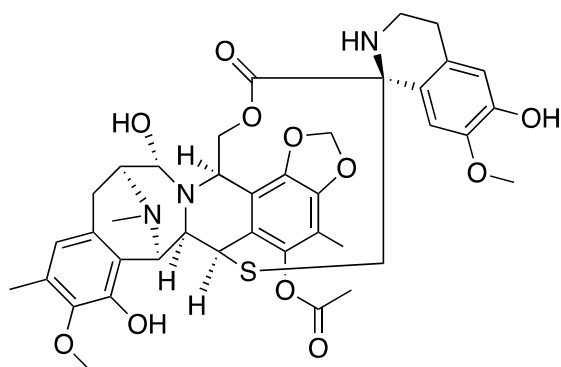


b. Structure and Molecular Representations

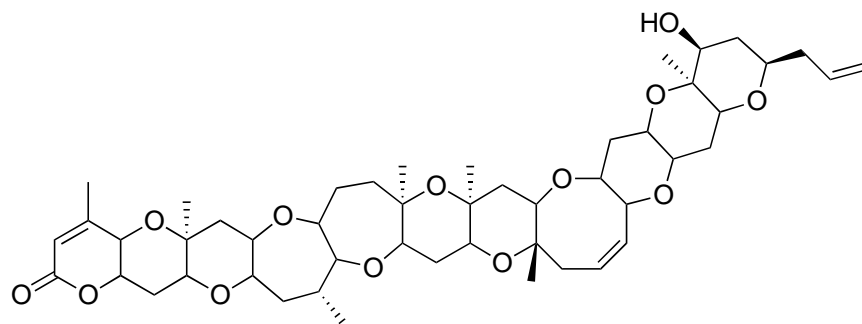
11. (C) Draw a bond-line structure for the Lewis structures shown below.



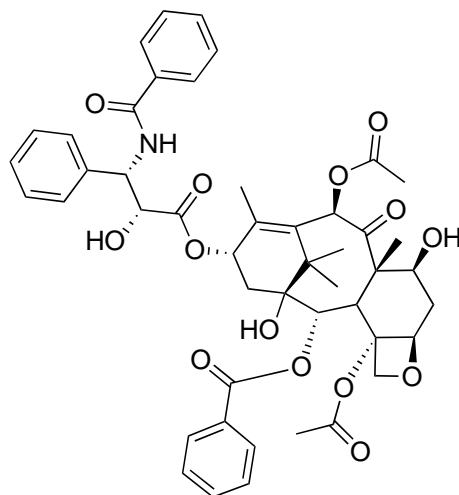
12. (C) Unlike Lewis structures, bond-line structures do not show lone pairs. However these lone pairs are still there and should not be forgotten. Show all lone pairs on any heteroatoms (atoms other than carbon) of trabectedin, an anti-tumor drug derived from a marine tunicate.



13. (C) Determine the molecular formula of brevetoxin A, a neurotoxin produced by dinoflagellates that can cause fish kills during red tides.



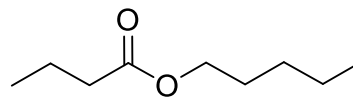
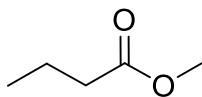
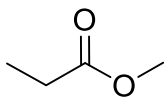
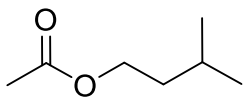
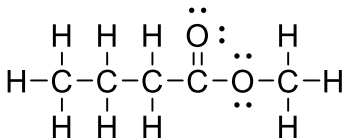
14. (I) Paclitaxel is another anticancer drug from a natural source, the bark of the Pacific yew tree. Identify the hybridization of each carbon in the molecule. How many hydrogen atoms are present on each carbon atom?



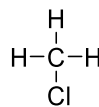
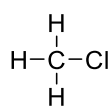
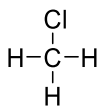
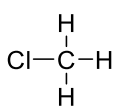
15. (I) Draw all significant resonance structures for the molecules shown below:



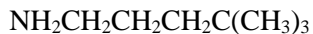
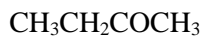
16. (C) Identify which of the line drawings corresponds to the Lewis structure:



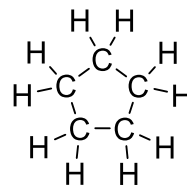
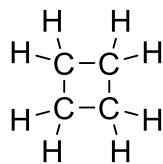
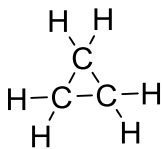
17. (C) Explain whether these Lewis structures represent the same compound or different compounds. What is the hybridization of the central atom?



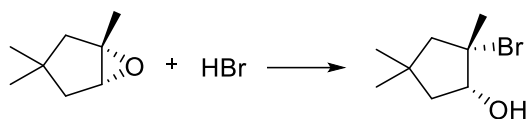
18. (I) Draw the line drawings for the following compounds.



19. (A) Which of the following is least stable and why?

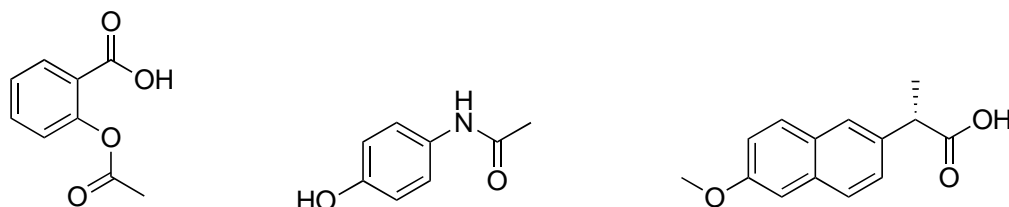


20. (A) In the reaction below, is the hybridization of any carbon atom changed? Would you expect the products or reactants be more favorable?

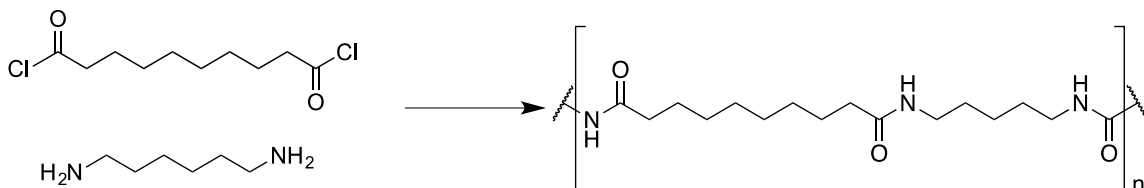


c. Organic Molecules and Functional Groups

21. (C) Which functional groups are present in the over-the-counter pain medications aspirin, Tylenol, and Aleve?



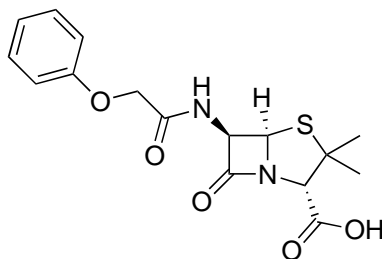
22. (C) Nylon 6,10 can be made through the reaction shown below. What functional groups are present in the starting materials and the product?



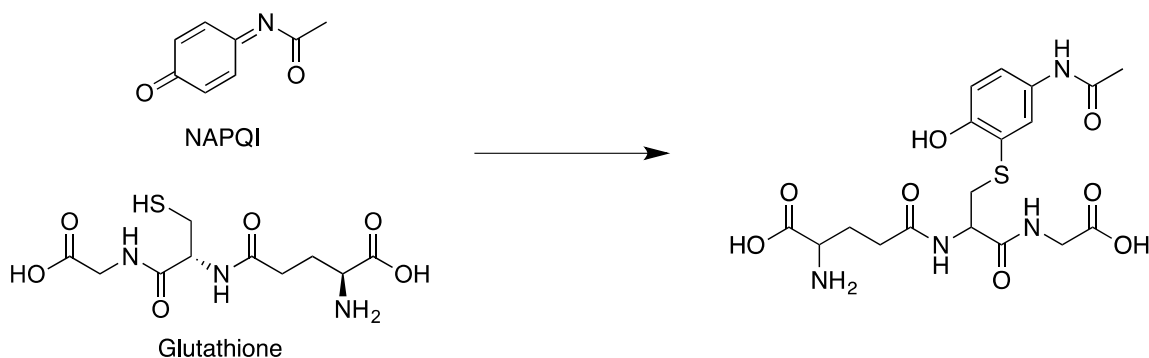
23. (I) Which of the following functional groups can participate in hydrogen bonding? If a functional group can participate in hydrogen bonding, draw a figure showing hydrogen bonding between two molecules containing this functional group.

Alkanes, alcohols, carboxylic acids, amides, thiols, alkynes, haloalkanes

24. (I) Identify each functional group present in penicillin V. What is the hybridization of each atom within these functional groups?



25. (A) Tylenol, when used in excessive amounts, can result in liver damage and even death. When Tylenol is metabolized, NAPQI is formed. This metabolite undergoes detoxification in the body through reaction with glutathione. When glutathione is depleted, detoxification cannot occur resulting in damage to the liver by NAPQI. What functional groups are present in each molecule? What functional groups change in the reaction?



26. (C) What functional groups are always found in the twenty common amino acids? What *additional* functional groups are found in: alanine, phenylalanine, aspartic acid, lysine, threonine, cysteine, and glutamine?

27. (C) Solanine is a toxin found in plants of the nightshade family, which includes some edible vegetables such as potatoes and tomatoes. How many of the following functional groups are present in the structure of solanine?

Primary alcohols:

Secondary alcohols:

Tertiary alcohols:

Primary amines:

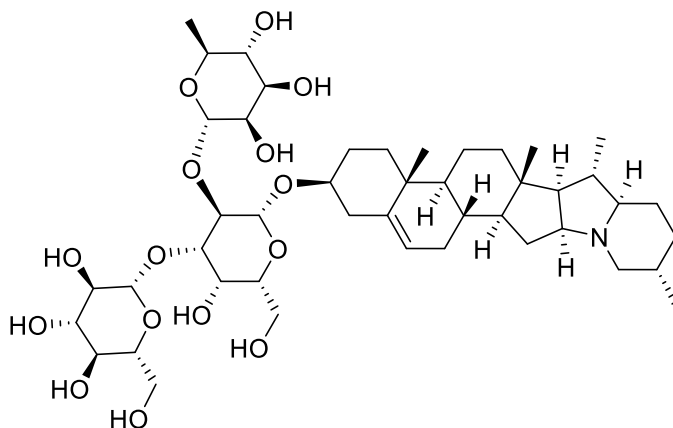
Secondary amines:

Tertiary amines:

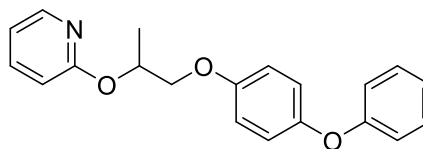
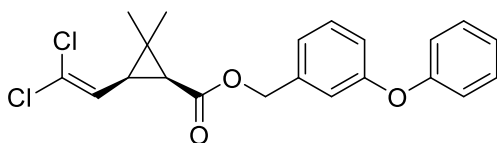
Esters:

Ethers:

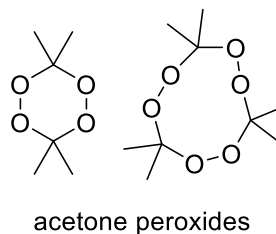
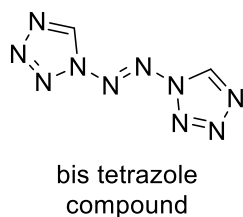
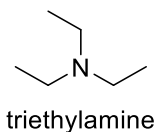
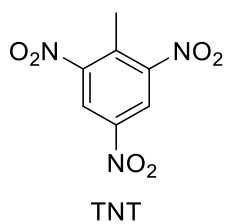
Double bonds:



28. (I) What functional groups are present in permethrin (left) that are **not** present in pyriproxyfen (right), both used as insecticides?

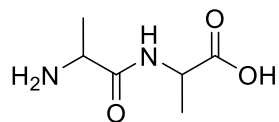


29. (I) Compounds that contain a high proportion of nitrogen, such as TNT, are often explosive because they produce the very stable nitrogen gas, while the nitrogen-containing triethylamine is stable. The bis tetrazole compound on the right is extremely explosive. Acetone peroxide is also explosive. Which functional group(s) would you expect to give a compound the *potential* to be explosive?



amine	R-NH ₂
nitro	R-NO ₂
azo	R-N=N-R
nitrite	R-O-N=O
amide	R-CONH ₂
peroxide	R-O-O-R

30. (A) Peptides – and proteins – are made up of amino acids joined by peptide bonds. Two alanines are shown below. What is the name of the functional group that make up a peptide bond? How many would be present in the A chain of insulin (sequence in 3 letter code below)?



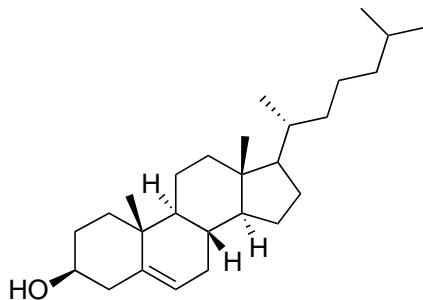
GLY-ILE-VAL-GLU-GLN-CYS-CYS-THR-SER-ILE-CYS-SER-LEU-TYR-GLN-LEU-GLU-ASN-TYR-CYS-ASN

d. Intermolecular Forces

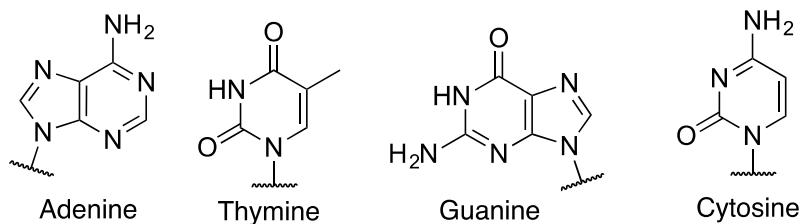
31. (C) Based on the strength of intermolecular forces present, rank the following from lowest to highest boiling point: methane, propane, octane, butane, hexane

32. (C) Define ion-dipole, hydrogen bonding, dipole-dipole and dispersion intermolecular forces.

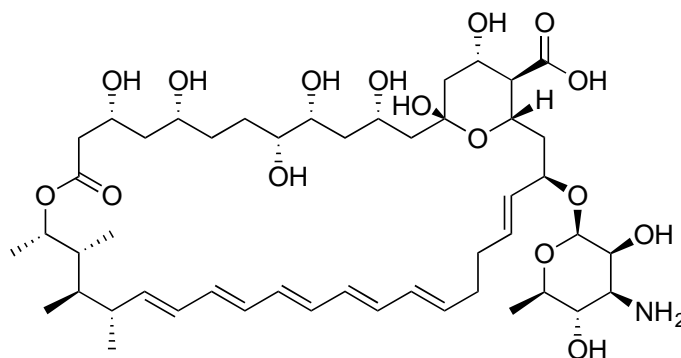
33. (I) Which intermolecular forces would you expect to occur between two molecules of cholesterol? Which portions of the molecule will interact with each other through these intermolecular forces?



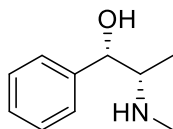
34. (I) DNA contains the bases adenine, thymine, cytosine, and guanine. Adenine pairs with thymine, and cytosine pairs with guanine. What intermolecular force is predominant in this base pairing? Which pair of bases would you expect to be bound more strongly to one another?



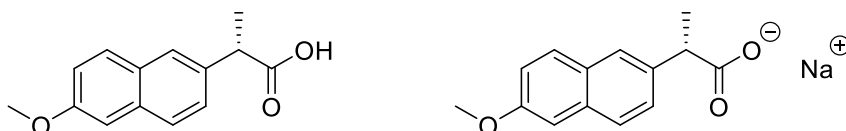
35. (A) Amphotericin B (shown below) is an antifungal drug typically used for serious infections. One mechanism by which it is believed to act is by formation of channels through incorporation of multiple amphotericin B molecules into the fungal membrane. Which portion of amphotericin B do you expect to interact with the lipids of the membrane? What kind of intermolecular force does this represent?



36. (C) What intermolecular forces would be present in pseudoephedrine, a component of many cough syrups?

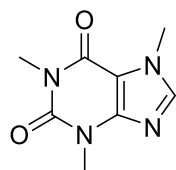


37. (I) Naproxen is a nonsteroidal anti-inflammatory drug (NSAID). It is often sold as its sodium salt, naproxen sodium. What intermolecular forces would be present in an aqueous solution of naproxen (left)? What would be present in naproxen sodium (right)?

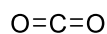


38. (A) Determine whether the vitamins A, B3, C, D, E, and K would be more soluble in water or lipids and give your reasoning.

39. (A) Various methods are employed in order to remove the caffeine from coffee beans to make decaffeinated or “decaf” coffee. Some older methods used organic solvents like dichloromethane or chloroform. A solvent which is still sometimes used is water, but now a common method is extraction by carbon dioxide as a supercritical fluid. When using the latter method, water is used as a co-solvent. How would you expect adding the water to affect the amount of caffeine extracted??

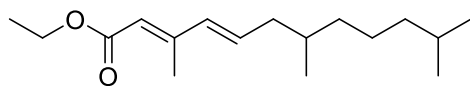


caffeine

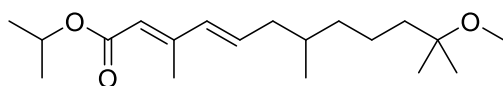


carbon dioxide

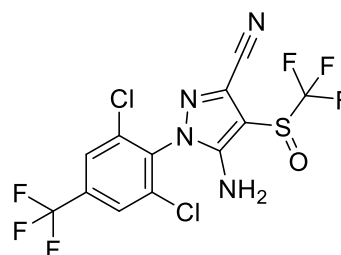
40. (A) Many people use insecticides on their pets to kill and prevent fleas and ticks. Fipronil and methoprene are two common ingredients in flea and tick medications for pets. Fipronil is an insecticide, while methoprene and hydroprene are insect growth regulators. Which of these would be most soluble in water? Least?



hydroprene



methoprene

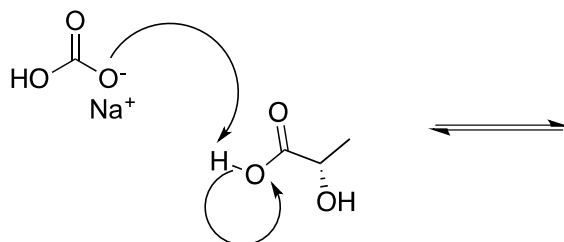


fipronil

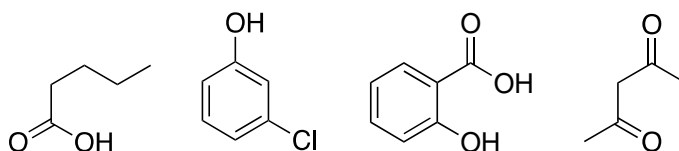
PROBLEM SET 2: ACIDS AND BASES

a. What is a chemical reaction?

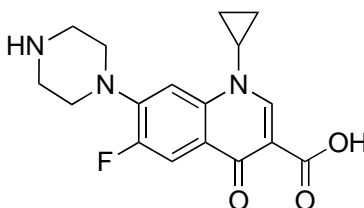
1. (C) Given the curved arrow drawing below, draw the two resulting products formed.



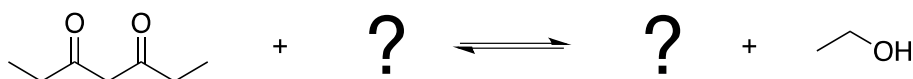
2. (C) Write an equation for the most likely proton transfer reaction that occurs when each of the following is added to sodium methoxide.



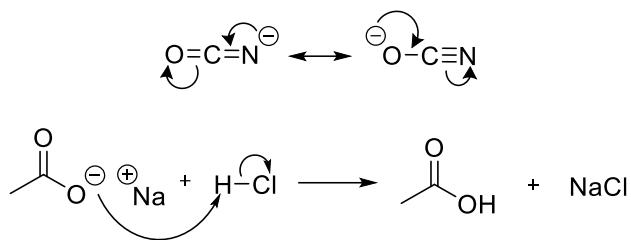
3. (I) Identify the most acidic proton in the antibiotic ciprofloxacin. Draw a curved arrow representation of the reaction that occurs when sodium hydroxide is added to a solution of ciprofloxacin. Is sodium hydroxide a sufficiently strong base to perform this deprotonation?



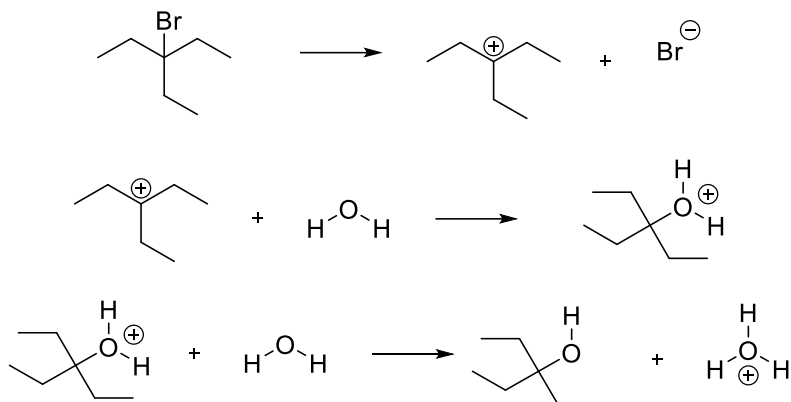
4. (A) One common transformation encountered in organic synthesis is the malonic ester synthesis. In the first step of this reaction a base is used to deprotonate diethyl malonate. Complete the reaction below, and draw a curved arrow representation of the reaction that is occurring. What is the pKa of the most acidic proton in diethyl malonate? What is the pKa of ethanol? What will be the ratio of reactants to products for this acid-base reaction?



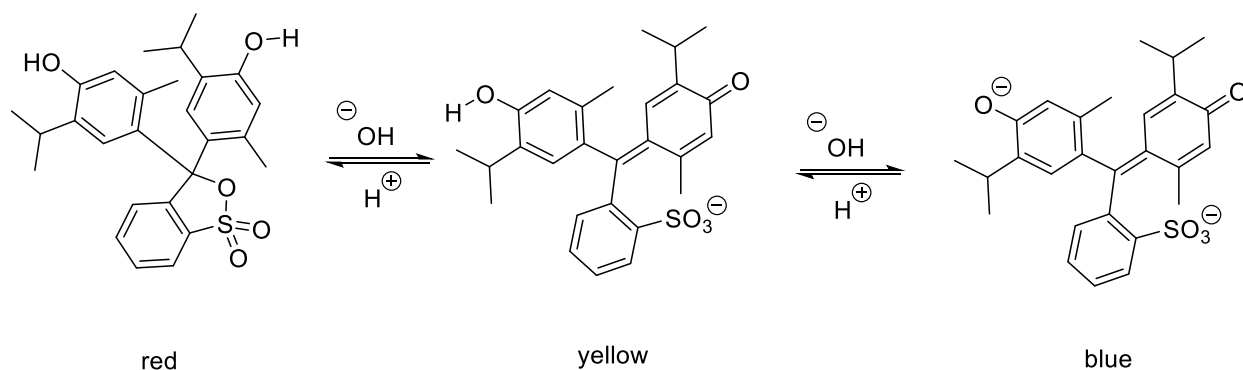
5. (C) Which of the following represents a chemical reaction?



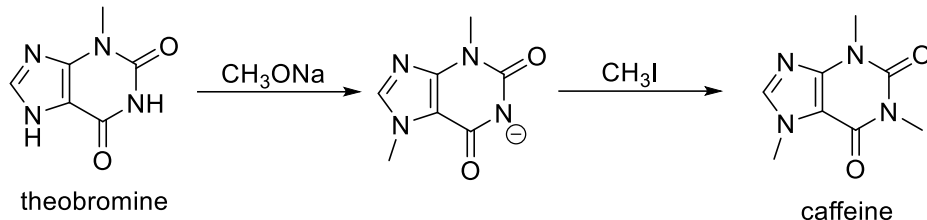
6. (C) Draw in the curved arrows for the steps of the reaction shown below.



7. (I) Thymol blue is a pH indicator. It changes colors from red to yellow at pH 1.2-2.8 and from yellow to blue at pH 8.0-9.6. Add curved arrows to show the reaction from neutral (yellow) to basic (blue) conditions and the reverse reaction.

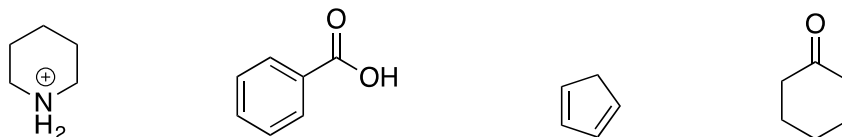


8. (A) Caffeine and theobromine are found in chocolate and are structurally similar. Caffeine can be synthesized from theobromine. A possible synthesis in methanol is shown below (add reference Calderon 2015). Draw the curved arrows for the reaction. Assuming each step goes to completion, what would the other products be?

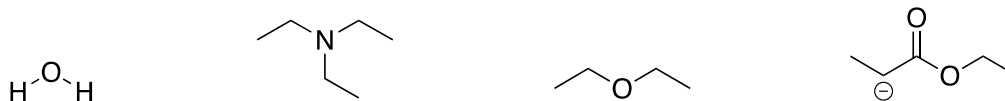


b. Brønsted-Lowry Definition

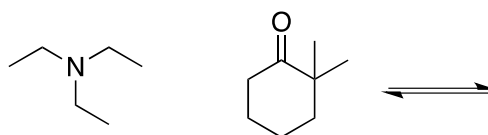
9. (C) Draw the conjugate base for each of the following.



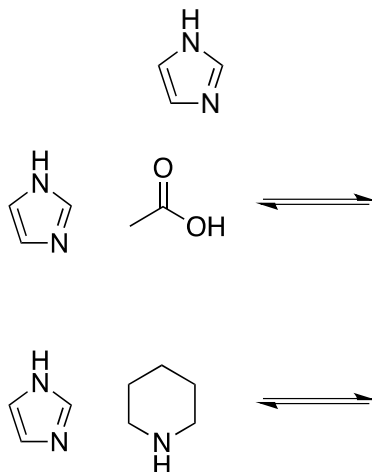
10. (C) Draw the conjugate acid for each of the following.



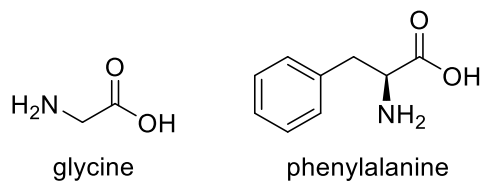
11. (I) For the pair of acid and base below, identify which is an acid and which is a base. Draw a curved arrow drawing of the reaction that occurs, and draw the resulting products. Finally, determine whether the equilibrium favors the reactants or the products of the reaction.



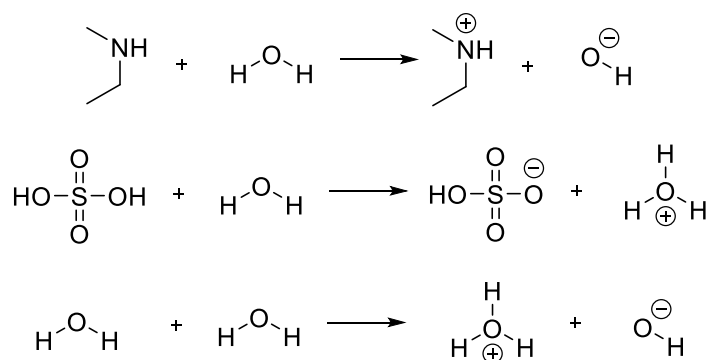
12. (A) Imidazoles, such as that found in the amino acid histidine, are capable of acting as acids and bases. Identify which portion of the imidazole ring shown below can act as an acid, and which can act as a base. Draw a curved arrow representation of how this imidazole would react if combined with acetic acid. Draw another representation to show the reaction of the imidazole with piperidine.



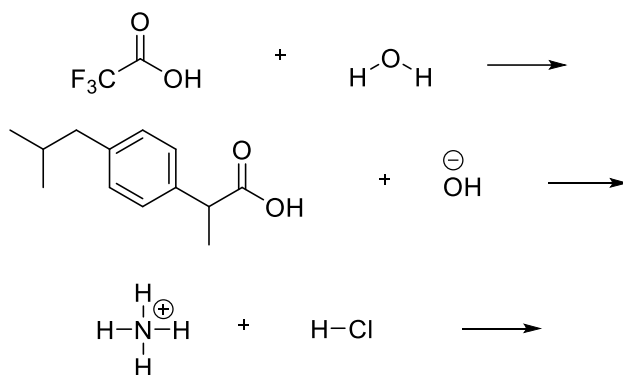
13. (C) Draw the conjugate acid(s) and base(s) for glycine and phenylalanine.



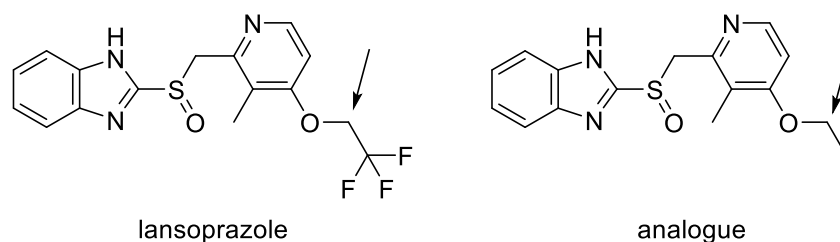
14. (I) Is water acting as a Brønsted-Lowry acid, base, both, or neither in the following reactions? Explain your reasoning.



15. (I) For each problem below, determine if the compounds would act as an acid or a base. What would be the products for each proton transfer reaction? Label the conjugate acid and base. Use NR to indicate no reaction.

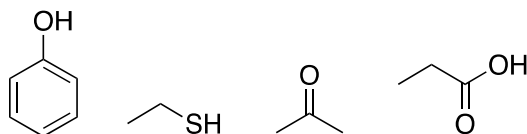


16. (A) Medicinal chemists make slight modifications to molecules in the attempt to increase the efficacy of the potential drug while also decreasing toxicity and side effects. Lansoprazole (Prevacid) is a proton-pump inhibitor that is used in the treatment of ulcers. Would the proton indicated in lansoprazole be more or less acidic than the proton indicated in the analogous compound? Would these compounds be more likely to act as an acid or a base?

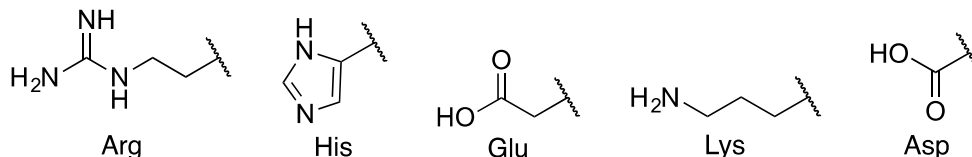


c. pK_a

17. (C) What is the ratio of protonated vs. deprotonated species for the following compounds at pH 2, 5, 9, and 14?

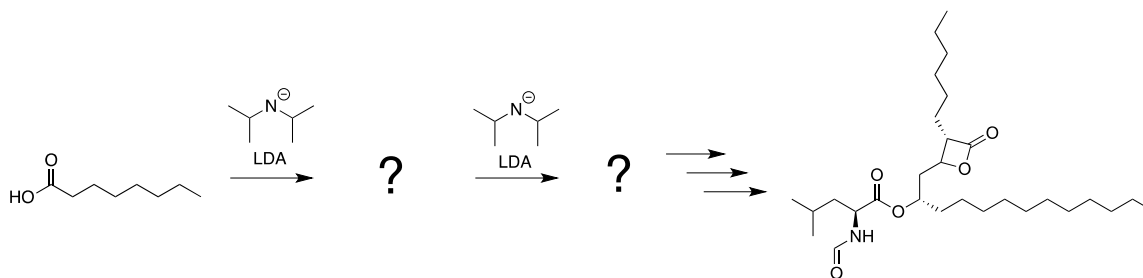


18. (I) Side chains of amino acids may be charged depending on the pH of their environment. These charges can affect how a protein folds, and therefore how it functions. For the peptide chain Ala-Arg-His-Gly-Glu-Pro-Lys-Asp-Ser-Asp, what is its charge at pHs of 1, 3, 5, 7, 9, 11, and 13? The pK_a s and structures of relevant side chains are given below.

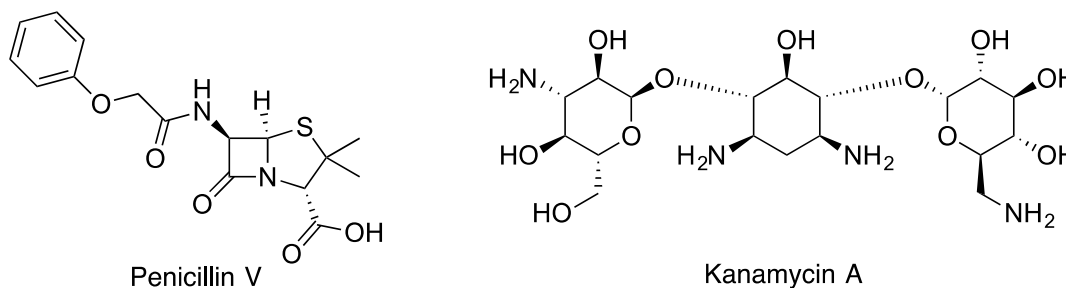


Arg	12.48 (conjugate acid)
His	6.04 (conjugate acid)
Glu	4.07
Lys	10.54 (conjugate acid)
Asp	3.90

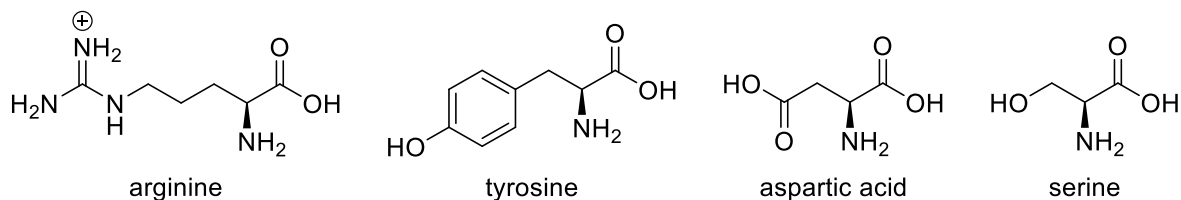
19. (A) Orlistat (commonly sold over the counter as Alli) is a drug used to assist in weight loss by inhibiting lipase enzymes in the body. An early synthesis of this drug uses the base lithium diisopropylamide (LDA) in one of its steps to promote the formation of a carbon-carbon bond. What is the most acidic proton found in the starting material? Draw the resulting anion if one deprotonation occurs (1 equivalent of LDA used). What is the second most acidic proton in the starting material? Draw the resulting dianion if two deprotonations occur (2 equivalents of LDA used). (*J. Org. Chem.* **1988**, 53, 1218-1221)



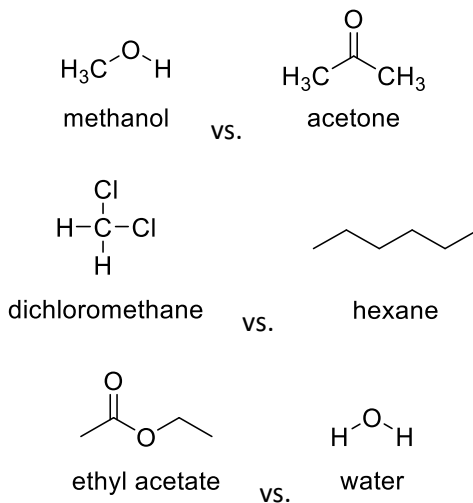
20. (A) In order for a molecule of a drug to be absorbed in the body, it should be neutral in charge. For this reason, drugs are often administered through different routes to optimize their absorption in the body. If penicillin V ($pK_a=2.8$) and kanamycin A ($pK_a=7.2$) are taken orally, draw the resulting species for both drugs under the acidic conditions of the stomach (assume the pH in the stomach is 2). Which of the drugs will more easily be absorbed?



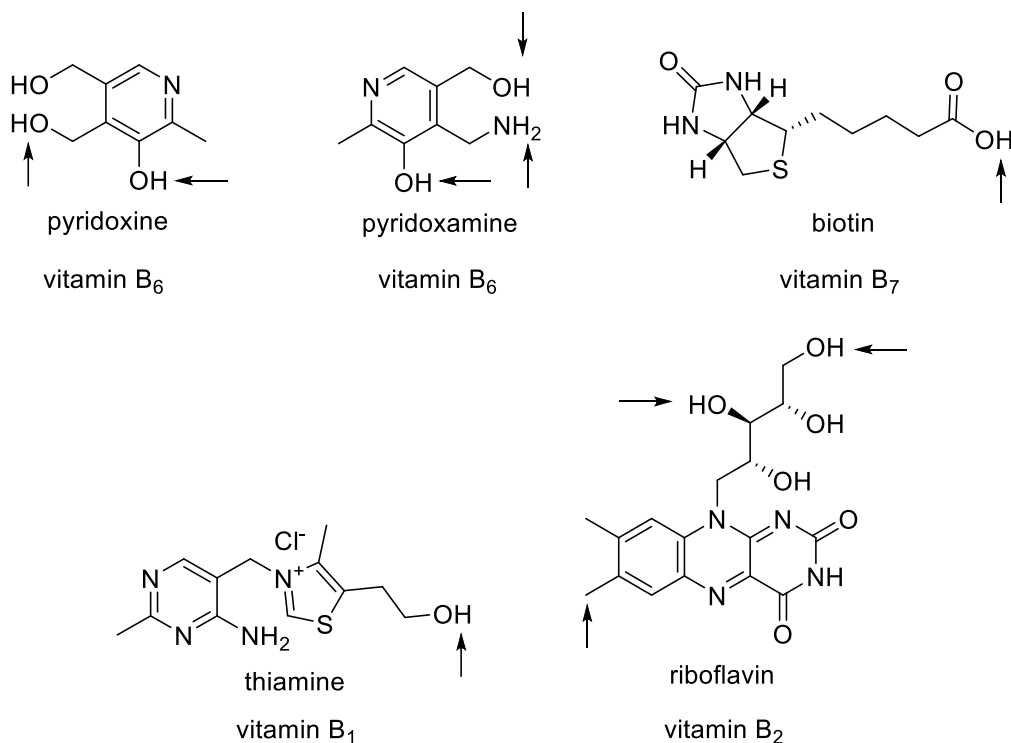
21. (C) Place the following amino acids in order from least acidic to most acidic based on the pK_a of the side chain.



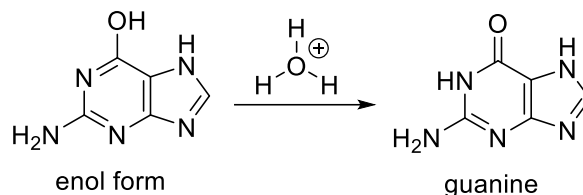
22. (C) For each set of common laboratory solvents, identify the compound that is more acidic.



23. (I) Assign approximate pK_a values (5, 10, 15, 20, etc.) to the indicated protons of the B vitamins below. Which of these B vitamins is most acidic?

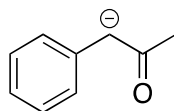


24. (A) An alcohol group on a double bond (known as an enol) can be converted to a ketone through either an acid- or base-catalyzed reaction. Guanine is a component of DNA and RNA. The acid-catalyzed reaction from its enol form to its stable (ketone) form is shown below. Assign approximate pK_a s to the alcohol and amino groups (enol form) and the hydronium ion. Which proton would be lost? Is the enol form acting as an acid or a base?



d. Concepts on Resonance

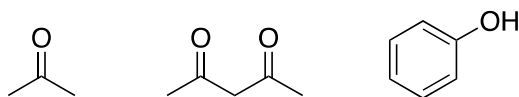
25. (C) For the conjugate base shown below, show all resonance structures that contribute to its stability.



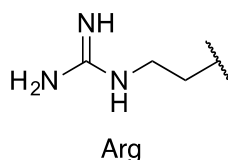
26. (C) What are the pK_a 's of phenol and ethanol? Draw the conjugate base of both molecules. Using your drawings, rationalize why the pK_a of phenol is lower than that of ethanol.



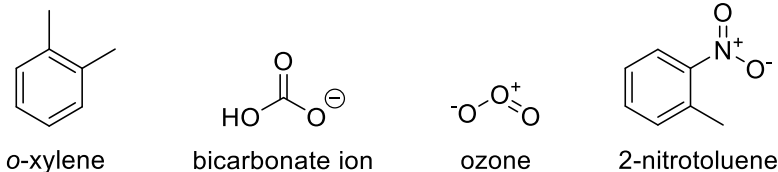
27. (I) Which of the following acids has the most stable conjugate base? Explain your reasoning with any necessary drawings. Which of the following is the strongest acid?



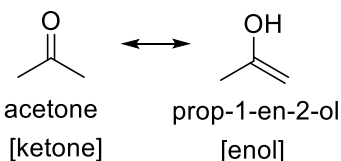
28. (A) Typically, nitrogen atoms that can participate in resonance, such as that in aniline, are less basic than an amine that cannot due to their electrons being more delocalized. The amino acid arginine can undergo resonance, but is relatively more basic than many amines that do not undergo resonance. Draw the conjugate acid of the guanidinium side chain of arginine and use this to rationalize the stability of the conjugate acid. Given that arginine is often found in the active site of enzymes that bind to molecules containing phosphates, why might this basicity be helpful?



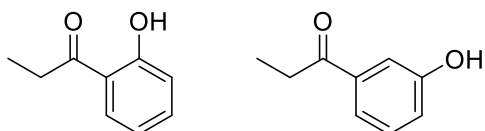
29. (C) Draw major resonance structures for the following compounds.



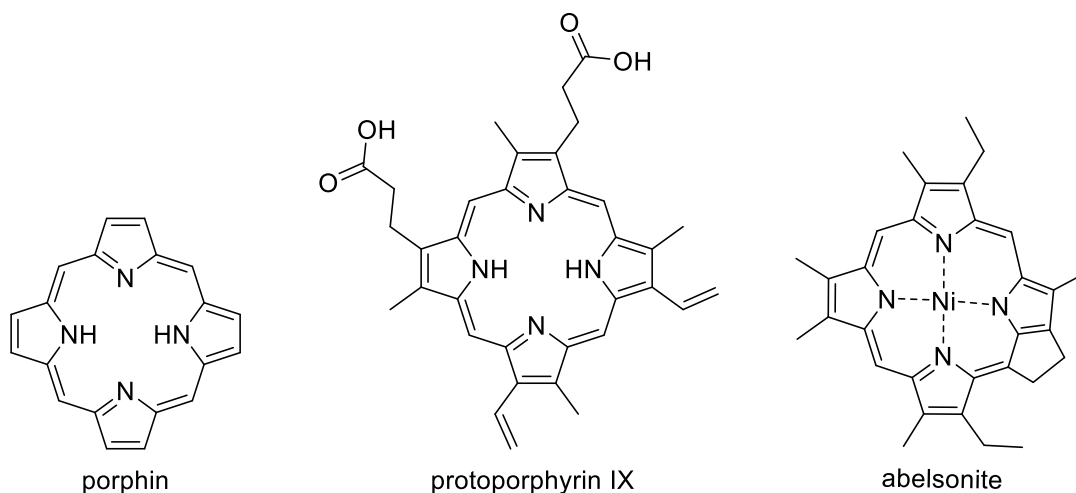
30. (C) Keto-enol tautomerization was mentioned earlier in this problem set. Acetone may also undergo tautomerization to an enol, although the enol is not stable. Explain why this is not considered resonance.



31. (I) Determine which of the conjugate bases for the two compounds below is more stable. Which of the following would be most acidic?



32. (A) Porphyrins are found in the active sites of some enzymes, including hemoglobin. Porphin is a simple porphyrin. Protoporphyrin IX is incorporated into hemoglobin as heme B (where an Fe^{2+} is replaced by two H^+ in the pocket of the structure). Porphyrins may sometimes be found in oil shale and sedimentary rocks. Abelsonite is a geoporphyrin mineral with a nickel in the center of the porphyrin ring. Show the resonance structures of porphin, protoporphyrin IX, and abelsonite. What is the structure of heme B?

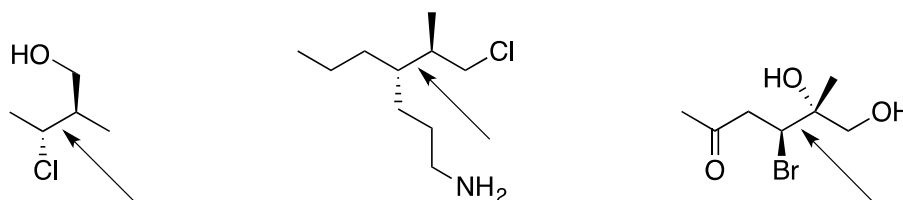


PROBLEM SET 3: ALKANES AND CYCLOALKANES

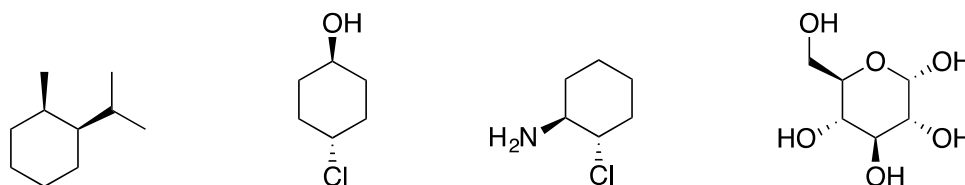
a. Drawing Organic Compounds

1. (C) Draw all possible alkanes with the following molecular formulas: C_6H_{14} and C_4H_{10} .

2. (C) Draw a Newman projection for each of the following substituted alkanes, looking down the indicated bond.



3. (I) Draw both chair conformations for the following compounds. Be sure to observe the wedge and dash bonds for the substituents.



4. (I) Draw an alkane that meets the following conditions:

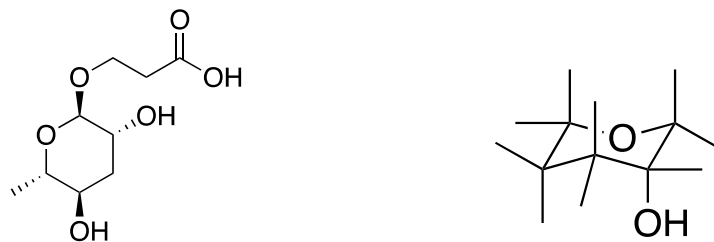
a. Has 7 total carbons; 6 carbons are secondary; 1 carbon is primary

b. Has 14 hydrogens total; has 4 primary carbons

c. Contains an ethyl substituent; contains an ether functional group; has 6 total carbons; has no tertiary or quaternary carbons

5. (I) Draw all molecules with the formula $C_4H_{10}O$ (There will be a total of 7). Name the oxygen-containing functional group present in each of your drawings.

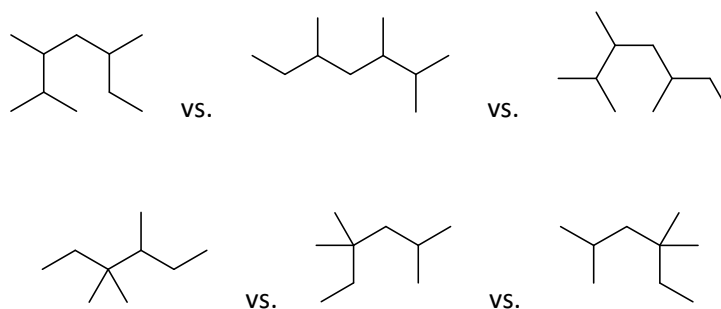
6. (A) Ascarosides are molecules produced by a variety of nematodes that are used as signaling molecules. These ascarosides are made up of an ascarylose sugar as well as a fatty acid tail. Given the drawing of ascaroside C3 shown below, complete the chair conformation drawing on the right. Indicate if the substituents are axial or equatorial in the chair conformation. (*Proc. Natl. Acad. Sci. U.S.A.* **2008**, *105*, 14288-14292)



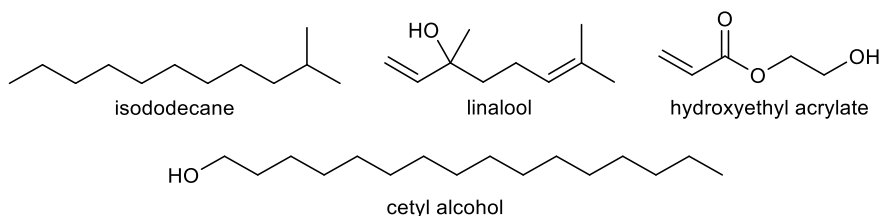
7. (C) Draw all possible alkanes with the following formulae:



8. (C) Identify whether the compounds in the following sets are identical or different.

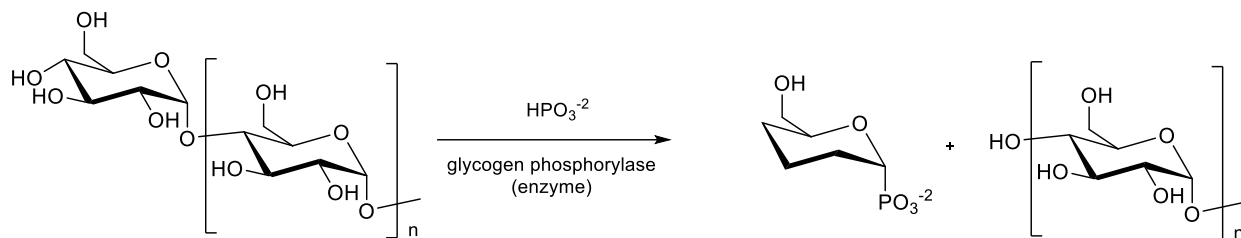


9. (I) The following compounds (common names given) are often found in soaps, lotions, or other similar products. Determine if these are alkanes and what functional groups are present.



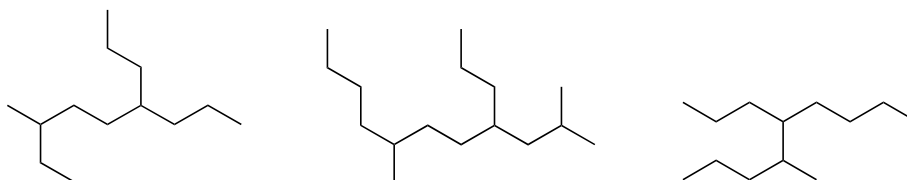
10. (I) How many alkanes with at least one 4° carbon could be drawn from the formula C_5H_{12} ? C_6H_{12} ?

11. (A) Glycogen is one of the ways the body can store glucose. It is broken down by an enzyme, glycogen phosphorylase, into a compound known as glucose-1-phosphate, which is then converted by another enzyme into glucose-6-phosphate. Add the missing substituents to the ring in the products and draw the other chair conformation for glucose-1-phosphate.

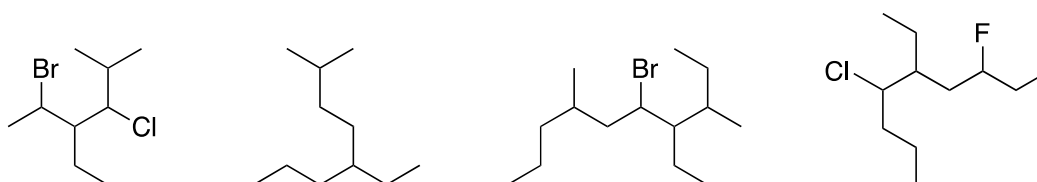


b. Parent Chain and Substituents

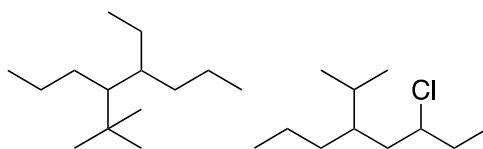
12. (C) For the following alkanes, identify the parent chain. How many carbon atoms are within each of these parent chains?



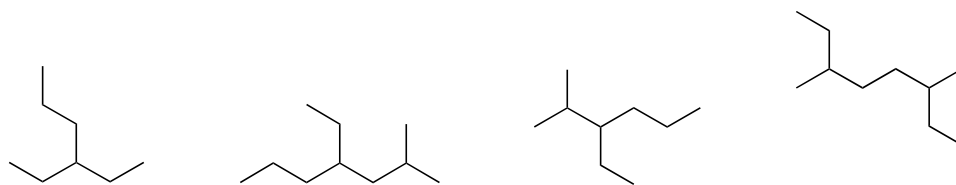
13. (C) For each of the following alkanes, identify and name any substituents (including numbering) attached to the parent chain.



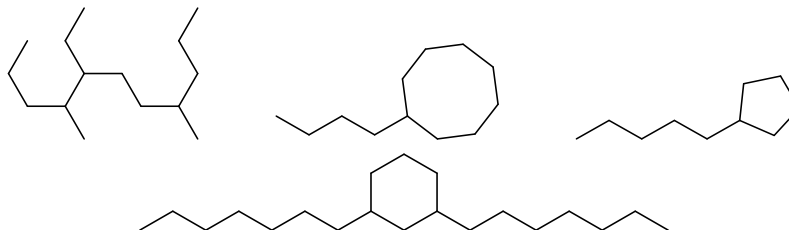
14. (I) Name the following compounds with complex substituents. How many hydrogens are present on each carbon?



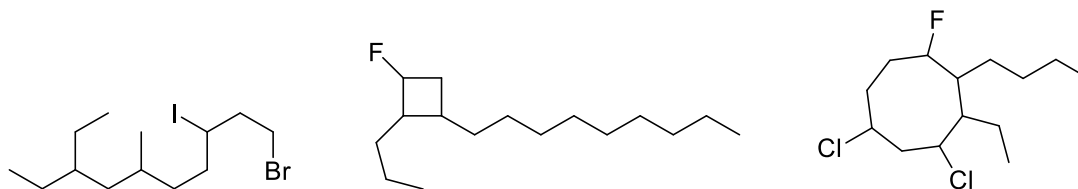
15. (I) Which of the following compounds have the same number of carbons in their parent chains? Do these parent chains have the same number of hydrogen atoms present?



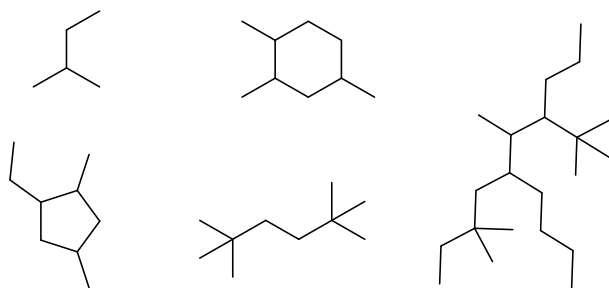
16. (C) Identify the parent chain in the following compounds.



17. (C) Identify the substituents present in the following compounds.



18. (C) Match the following structures to the descriptions. Descriptions may be used more than once.

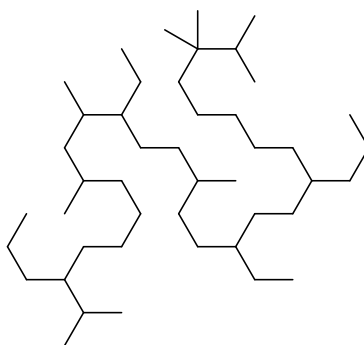


Descriptions

- A. 2 quaternary carbons
- B. 3 tertiary carbons
- C. 3 primary carbons
- D. 6 C in parent chain
- E. 4 total C in substituents
- F. 3 total substituents
- G. 3 different substituents

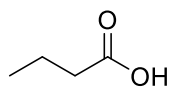
19. (I) What is the maximum number of methyl substituents that could be present on a parent chain of butane? Of pentane?

20. (I) How many R-CH₃ groups are present in the following compound? Which of these would be considered methyl substituents?

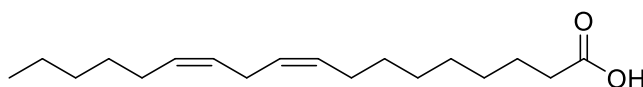


21. (A) The American Heart Association recommends reducing the amount of saturated fat and *trans*-fat in diets for people who need to lower the “bad” LDL cholesterol. The following are fatty acids found in food.

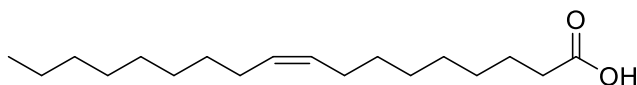
- What is the number of carbons in the parent chain?
- Is the carbon chain an alkane?
- Would the fatty acid be classified as saturated or unsaturated?



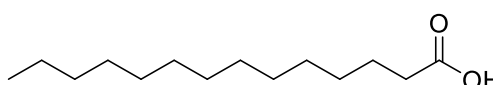
butyric acid
butter



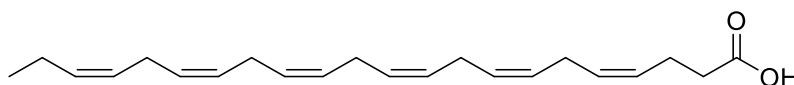
linoleic acid
corn and peanut oil, almonds



oleic acid
butter



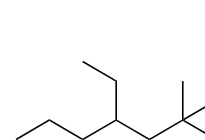
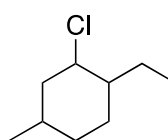
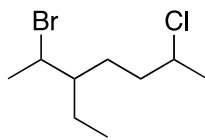
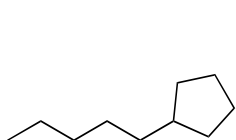
myristic acid
dairy



docosahexaenoic acid (DHA)
fish

c. Introduction to Naming Organic Compounds and IUPAC Nomenclature

22. (C) Name the following organic compounds using IUPAC nomenclature.



23. (C) Draw the following organic compounds based on the given IUPAC name.

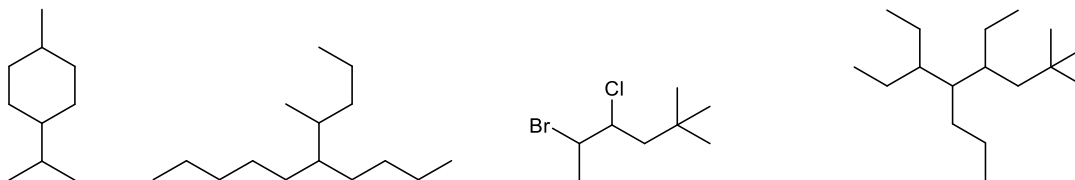
- 2-methylheptane
- 1-bromo-2-chloro-5-ethylcycloheptane
- 4-(1,1-dimethylethyl)-5-propylnonane

24. (I) Are the following names correct according to IUPAC nomenclature? If not, change them such that they are correct.

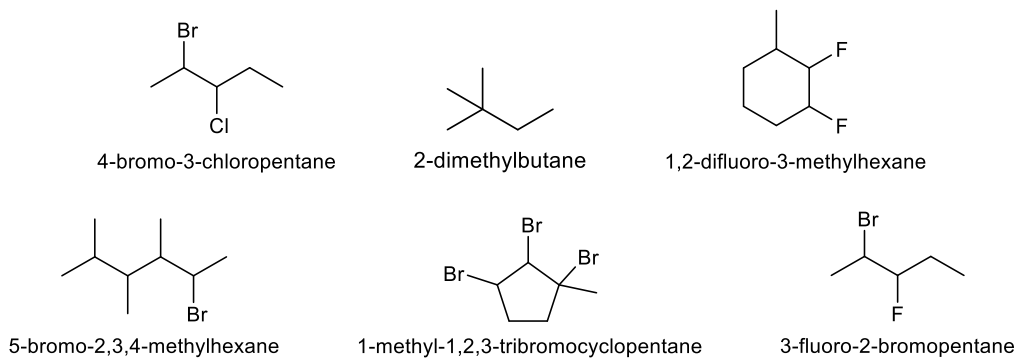
- 4-bromo-5-chlorocyclohexane
- 1,3-dimethyl-2-ethyloctane
- 3-pentylheptane
- 2-methyl-7-propyldecane

25. (I) Draw all possible alkanes with the molecular formula C_5H_{12} and give the IUPAC name for each.

26. (C) Name the following compounds.



27. (C) There is one error in each of the following names. Identify and correct the problem with the names.



28. (C) Draw the structures that correspond to the following names.

1,3-dibromobutane

3,4,5-triethylheptane

3-chloro-4-isopropyl-2,5-dimethylhexane

3-chloro-5-ethyl-2-methyl-5-pentylcycloheptane

29. (I) Draw the structures that correspond to the given names. Are these the correct names for the structures? If not, give the correct name.

3,4-diethylhexane

1-methylhexane

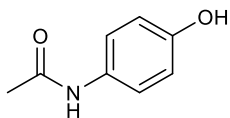
9-fluoro-5,5-dimethyl-4-propylnonane

6-methylcyclohexane

2-iodo-1,1,1-methylethane

2-propyl-4-chloro-3-bromopentane

30. (A) A compound is often called by a “common” name rather than by its name under IUPAC nomenclature. Sometimes, compounds are known by multiple common names. Acetaminophen is an example of this: in some countries (e.g. the U.S.) it is called acetaminophen but in other countries it is known as paracetamol. Its IUPAC name is *N*-(4-hydroxyphenyl)acetamide, or *N*-(4-hydroxyphenyl)ethanamide [“acet” is a historical but accepted alternate for derivatives of acetic or ethanoic acid]. Para explains how the benzene ring is substituted. Determine how the IUPAC name(s) correspond to the compound and how acetaminophen and paracetamol were derived.



IUPAC
N-(4-hydroxyphenyl)acetamide
N-(4-hydroxyphenyl)ethanamide

Other Names
N-acetyl-*p*-aminophenol
para-acetylaminophenol

Common names
acetaminophen
paracetamol

31. (A) Rubbing alcohol is often used as a disinfectant and sometimes as a component of hand sanitizers. If you were to purchase a bottle of rubbing alcohol at a store, it would most likely say isopropyl alcohol or isopropyl rubbing alcohol, although it is also called isopropanol. Ethyl alcohol is also used in hand sanitizers, and is actually more commonly used. Draw the structures for both compounds. What are the IUPAC names for each? Why would a hand sanitizer whose major component is ethyl alcohol evaporate more quickly than one whose major component is rubbing alcohol?

PROBLEM SET 4: STEREOCHEMISTRY, CONFORMATION, AND CONFIGURATION

a. More on Bond Line Structures, Drawing, and Isomers

1. (C) Determine if the following sets of compounds are identical or isomers of one another.

a.



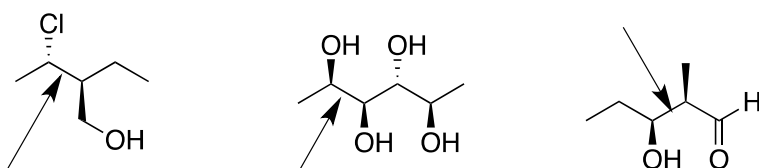
b.



c.



2. (C) Draw a Newman and Fischer projection for the following molecules. For your Newman projections, draw as viewed along the indicated carbon-carbon bond.

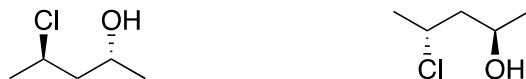


3. (I) Determine if the following sets of molecules are identical, enantiomers, diastereomers, meso compounds, or constitutional isomers.

a.



b.



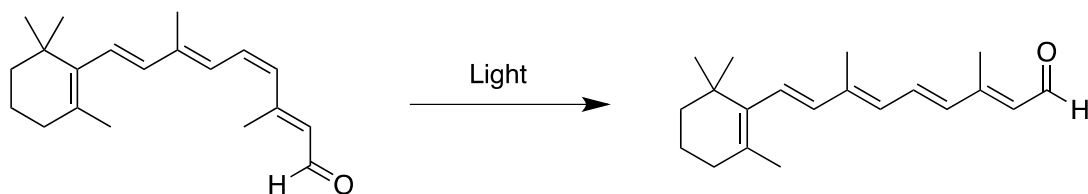
c.



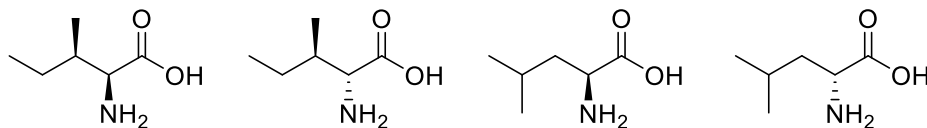
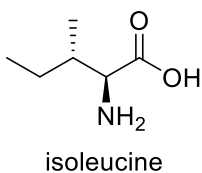
d.



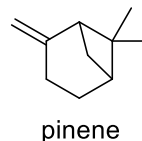
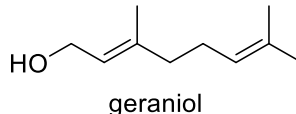
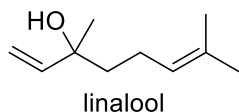
4. (A) Retinal is a molecule that is essential for vision. One crucial transformation that this molecule undergoes is the transition from its 11-*cis* state to its all-*trans* state after absorbing light (shown below). Label each alkene for both states of retinal as being either E or Z.



5. (C) Determine if the following compounds are constitutional isomers, stereoisomers, or identical to isoleucine.



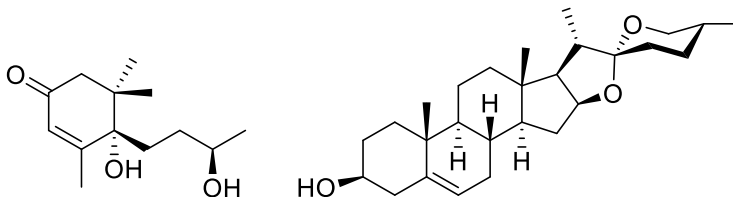
6. (C) Draw all possible stereoisomers for the following structures.



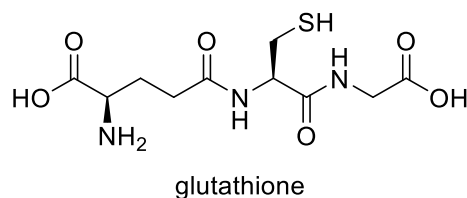
7. (I) Determine if it would be possible for the following to have a stereoisomer.



8. (I) Label the compounds with E or Z for double bonds and R or S for chiral centers.

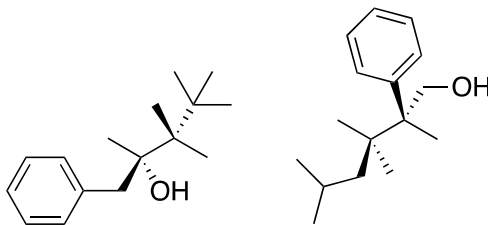


9. (A) Glutathione is a tripeptide antioxidant. Identify the functional groups present in glutathione. What amino acids make up glutathione? How many stereoisomers are possible for glutathione?

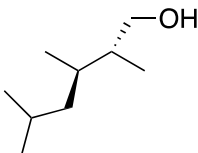


b. Bond Rotation Energy

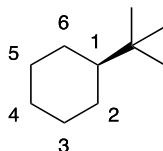
10. (C) Draw all possible staggered and eclipsed conformations for the following molecules using Newman projections.



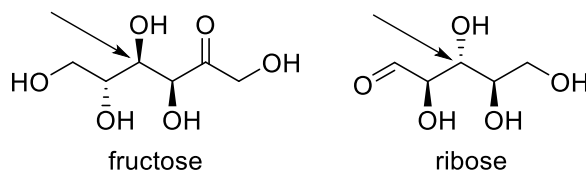
11. (C) Draw each staggered conformation for the molecule below using Newman projections. Indicate which conformation is lowest in energy.



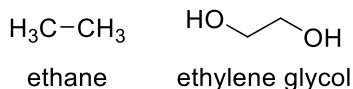
12. (I) As you have seen previously, substituted cyclohexanes can take on two different chair conformations. In the case of *t*-butylcyclohexane, one of these conformations is heavily favored with respect to the other. Draw both chair conformations for this molecule as well as their Newman projections looking down the C₁-C₂ and C₄-C₅ bonds. Which conformation is lower in energy with respect to the other? Which conformation do you expect is more heavily favored?



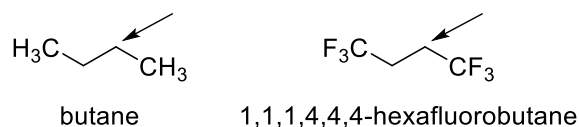
13. (C) Draw the Newman and Fischer projections for the compounds. For the Newman projection, draw looking down the indicated bond.



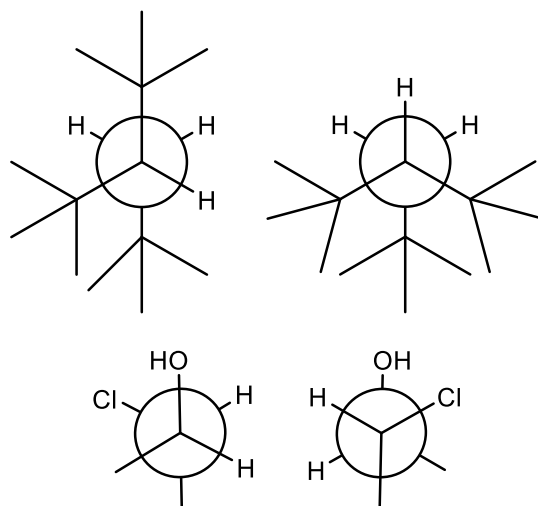
14. (I) Draw the staggered and eclipsed Newman projections for ethane and ethylene glycol. For each, determine which of the projections are degenerate.



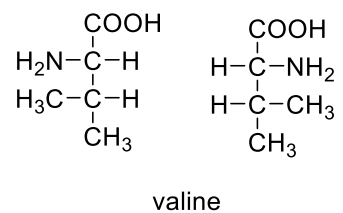
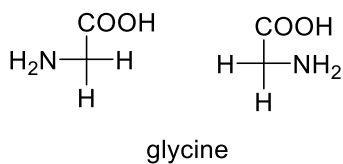
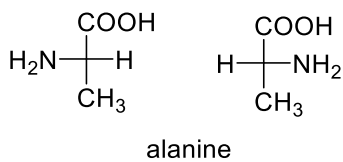
15. (I) Which compound would you expect to have more steric hindrance with respect to rotation about the indicated bond?



16. (I) Are the following pairs of compounds rotamers or identical?

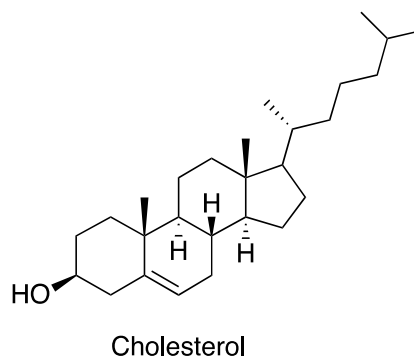
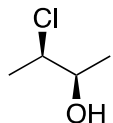
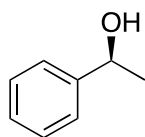


17. (A) Draw the line bond drawings for the Fischer projections of amino acids below. For each amino acid, do these represent the same structures or stereoisomers?

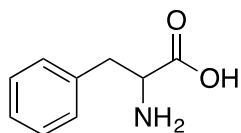


c. Chirality and Stereocenters

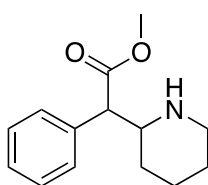
18. (C) Draw the enantiomers of the following molecules.



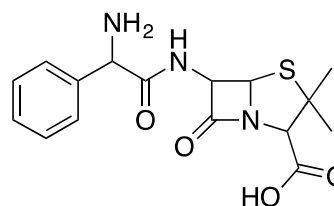
19. (C) Draw all possible stereoisomers for the following compounds. How many chiral centers do you expect for each?



Phenylalanine

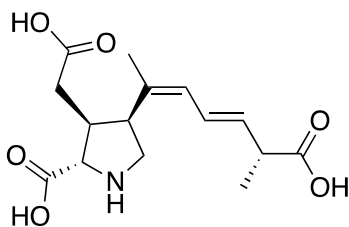


Methylphenidate

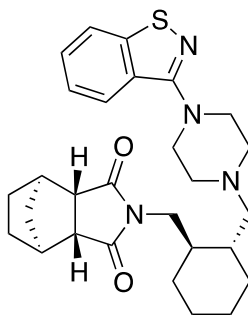


Ampicillin

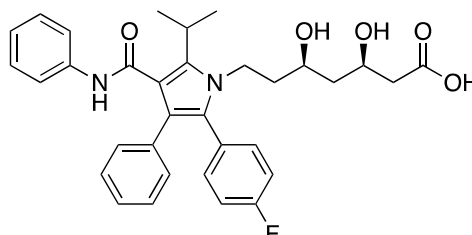
20. (I) How many chiral centers are present in the following molecule? Assign configurations for each chiral center.



Domoic Acid

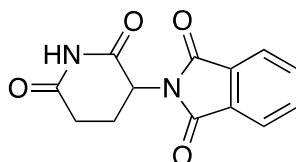


Lurasidone



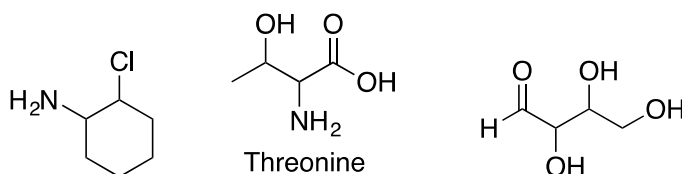
Atorvastatin

21. (A) Thalidomide was a drug that was used primarily in the 1950s and 1960s to treat morning sickness in pregnant women. The drug was pulled from the market due to its link with an increase in birth defects, and has led to tougher regulations for the approval of drugs. It has been suggested that this side effect of thalidomide could be due to the presence of its enantiomer (the (S) enantiomer). Draw both stereoisomers and label as (R) or (S) isomers.



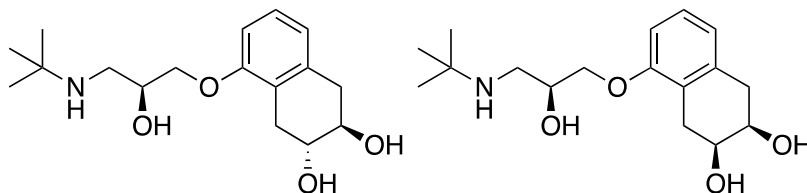
Thalidomide

22. (C) Draw all possible diastereomers for the following compounds.



23. (I) Determine the relationship between the following pairs of compounds. If they are enantiomers or diastereomers, assign configuration of any chiral centers.

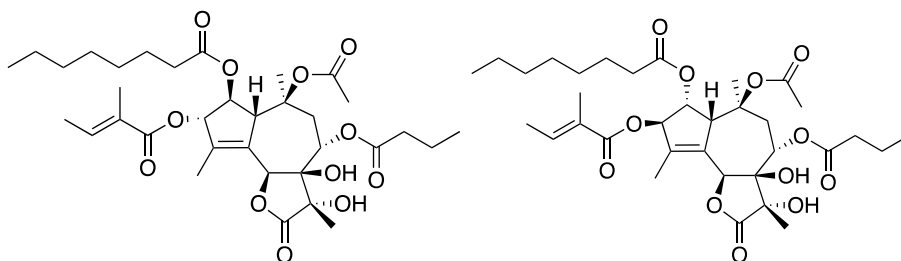
a.



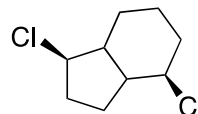
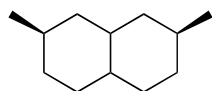
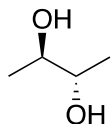
b.



c.

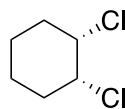
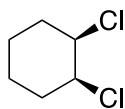


24. (C) Determine if the following compounds contain an internal plane of symmetry.

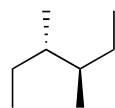
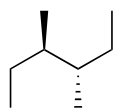


25. (C) Are the following compounds enantiomers, diastereomers, or identical?

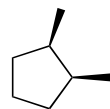
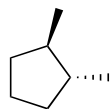
a.



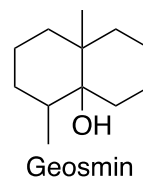
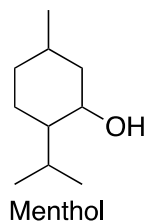
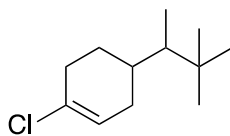
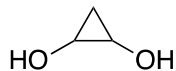
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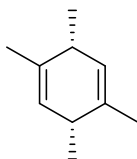
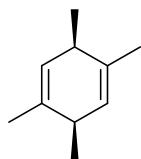
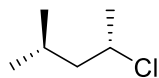
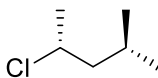
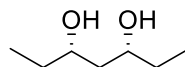
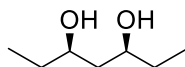
c.



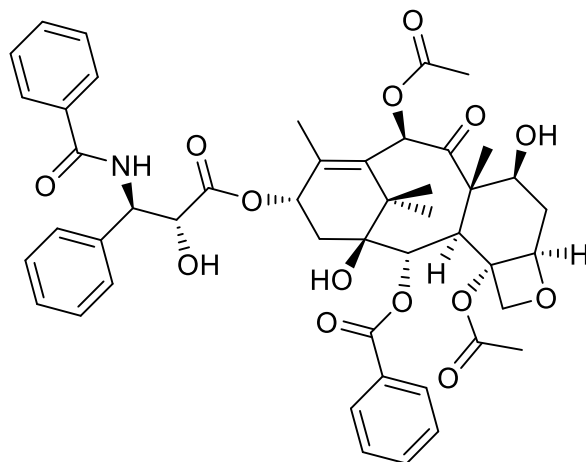
26. (I) Draw all possible stereoisomers of the following compounds. Are there any sets of meso compounds?



27. (C) Determine if the pairs of compounds are enantiomers or meso.

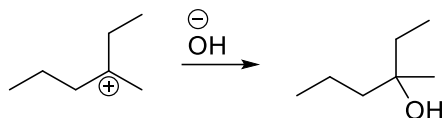


28. (C) Paclitaxel is a natural product used in the treatment of some cancers. How many chiral carbons are present? Label these as R or S. Would paclitaxel have an enantiomer?

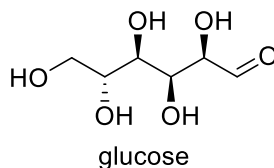


29. (I) Most of the twenty common amino acids have stereocenters (chiral carbons). How many stereocenters are present? How many possible structures for the twenty amino acids would there be?

30. (A) The reaction below will have two major products differing only in their stereochemistry. Draw the products. Given that the carbocation is planar, would you expect one stereoisomer to be favored over the other?

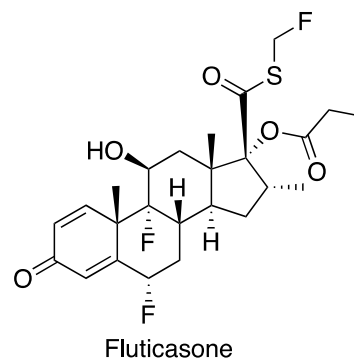
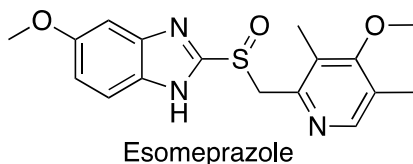
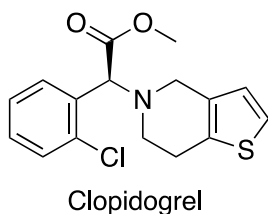


31. (A) Draw all possible stereoisomers of glucose. Label the stereocenters as R or S. Label the compounds as enantiomers, diastereomers, or meso.

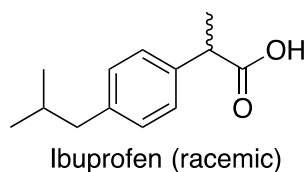


d. Racemic Mixtures and Optical Activity

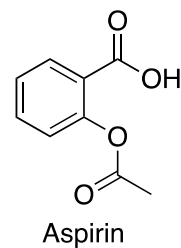
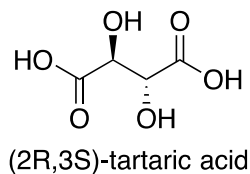
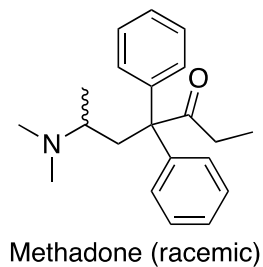
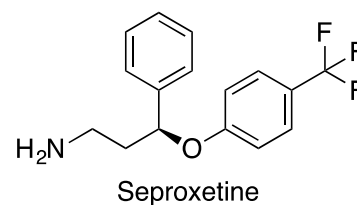
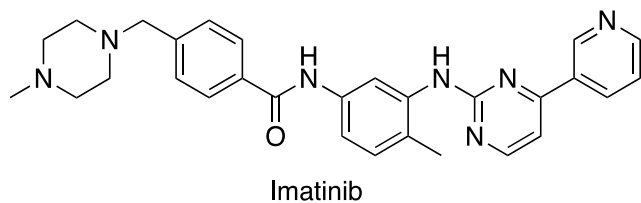
32. (C) Determine if the following molecules are optically active.



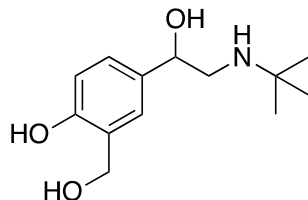
33. (C) Ibuprofen is an example of a drug that is administered as a racemic mixture. If you were to measure the specific rotation of ibuprofen, would you expect your sample to be optically active? Why or why not?



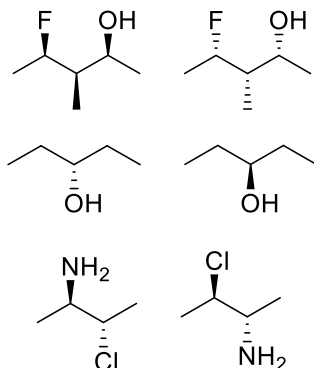
34. (I) Determine if the following compounds are optically active or inactive.



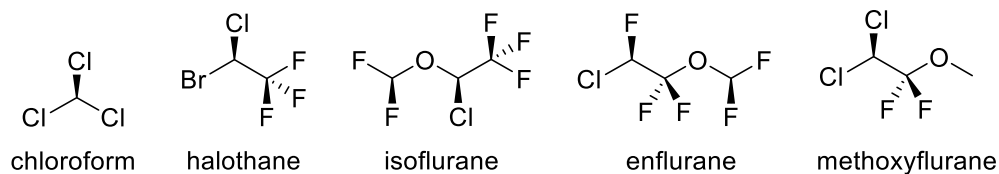
35. (A) Salbutamol is a drug that is used to open airways in the event of asthma attacks. This drug is administered as a racemate (racemic mixture), but the (R)-enantiomer is pharmacologically active. Suppose that you performed a synthesis resulting in a mixture of the enantiomers of salbutamol. Draw both enantiomers of salbutamol and label as (R) or (S). If the specific rotation of the (R)-enantiomer is -32.2° and the specific rotation of the mixture is -12.3° , what is the enantiomeric excess of the (R)-enantiomer?



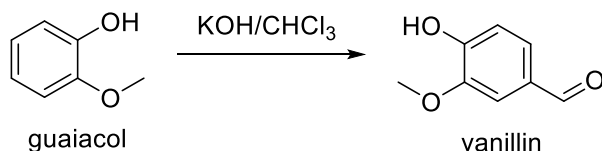
36. (C) Determine if a 50:50 mixture of the following sets of compounds would be considered a racemic mixture.



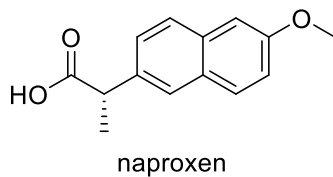
37. (C) Which of the following anesthetics would have optical activity?



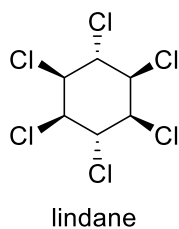
38. (I) Would optical rotation be useful to determine if the product was made in the following reaction?



39. (I) Naproxen is a single enantiomeric drug that is sold under the brand name Aleve. Its specific rotation is $+66^\circ$ in chloroform. After attempting a new synthesis of the drug, you found the optical rotation to be -64° in chloroform. Did you produce naproxen or its enantiomer?



40. (A) Lindane is a pesticide formerly used in agriculture that is occasionally used to treat lice and scabies. Its use has been greatly restricted due to its environmental persistence and possible human health effects. Draw both chair conformations of lindane. What is the formula for lindane? Is lindane optically active? Does lindane have 2^n stereoisomers?



PROBLEM SET 5: SPECTROSCOPY, PART 1

a. The Electromagnetic Spectrum and Organic Compounds

- 1. (C)** What are the types of electromagnetic radiation used for infrared and UV-VIS spectroscopy? What are the approximate ranges of wavelengths that these types of radiation cover? Which type is higher in energy?
- 2. (I)** If a molecule exhibits absorbance at a wavelength of 450nm, what is the energy of a photon of this wavelength? Likewise, if a molecule exhibits absorbance in IR spectroscopy at a wavenumber of 1700 cm^{-1} , what is the energy of a photon of this radiation?
- 3. (A)** If a carbon-carbon stretching is observed at a wavenumber of 1650 cm^{-1} for alkenes and 2180 cm^{-1} for alkynes using IR spectroscopy, which bond requires more energy to observe bond stretching? Does this agree with your expectations from previous knowledge? Explain.
- 4. (C)** What are the wavelength ranges for red, orange, yellow, green, blue, and violet light? Which is highest in energy and which is lowest in energy?
- 5. (C)** What is the frequency and energy associated with a photon with a wavelength of 254 nm?
- 6. (C)** Place the following classifications of the electromagnetic spectrum in order from lowest to highest wavelength. Which has the highest frequency, lowest frequency, highest energy, and lowest energy?
UV IR X-rays visible radio γ -rays microwave
- 7. (A)** Rhodopsin is a light-sensitive protein involved in vision that is found in the rods of the eye. Baylor et al. used rods from toads to show that it is possible for rods to respond to a single photon. The maximum absorption of rhodopsin is about 500 nm, and they tested wavelengths of 460 nm, 580 nm, and 700 nm. What is the energy of a single photon for each of these wavelengths? Hecht et al. found that it takes about 90 photons for the majority of people to respond to a flash of light (510 nm) in a dark room. What is the energy of this flash of light? (*J. Physiol.* **1979**, DOI: 10.1113/jphysiol.1979.sp012716 & *J. Opt. Soc. Am.* **1942**, DOI: 10.1364/JOSA.32.000042).

b. Infrared Spectroscopy

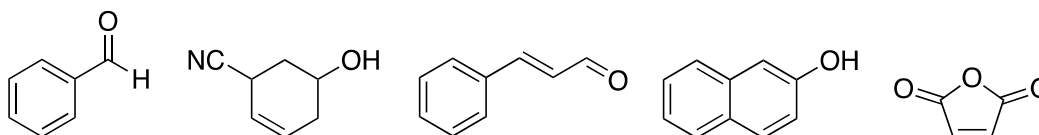
8. (C) For the following functional groups, what approximate IR absorptions would you expect to observe?

Nitrile, ester, alkene, aldehyde, carboxylic acid, alcohol, alkane

9. (I) Match the following IR absorptions with the appropriate compound(s). One compound may match with multiple absorptions and each absorption value may be used more than once.

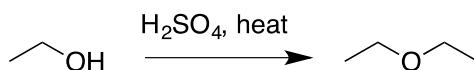
Absorptions (cm^{-1}): 3400, 2800, 2250, 1700, 1500

Compounds:

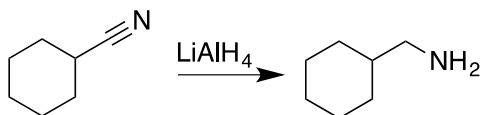


10. (A) How might one use IR spectroscopy to observe the progress of the following reactions?

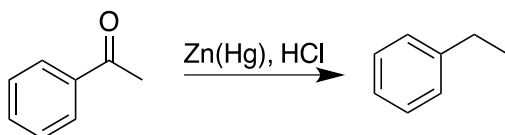
a.



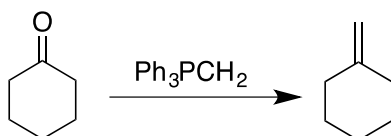
b.



c.

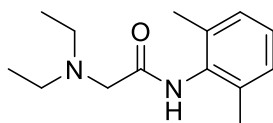


d.



11. (C) An O-H bond typically appears in an IR spectrum between 3200 and 3600 cm^{-1} . Would you expect an O-D bond have a higher or lower IR absorption? Why?

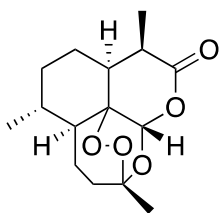
12. (I) What peaks in the diagnostic region of the IR spectrum would you expect to see for lidocaine, a topical analgesic? Would you expect any of these peaks to overlap?



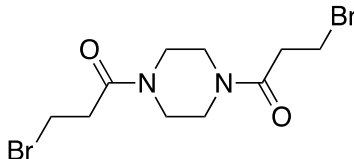
lidocaine

13. (A) You and your lab partner are analyzing a product from a reaction using IR spectroscopy. Your lab partner dissolved the compound in water for the analysis. From other data collected, you know that the compound is very pure and that its chemical formula is $C_4H_6Cl_2$, but you are seeing a very strong absorption around 3500 cm^{-1} . You compared your results with another group who used mineral oil to dissolve the same product, and they reported no such peak in their IR spectrum. What is causing the strong absorbance at 3500 cm^{-1} ?

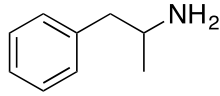
14.(C) Which bonds in the following compounds do you expect to have absorbance in the fingerprint region of an IR spectrum? Estimate the wavenumber for each absorbance.



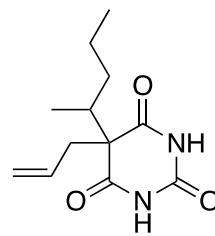
Artemisinin



Pipobroman



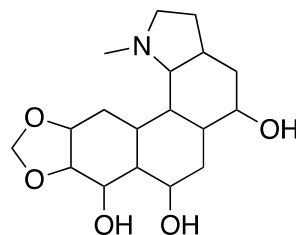
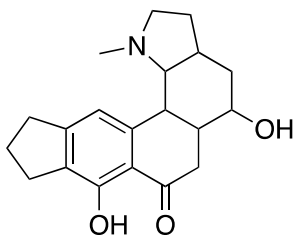
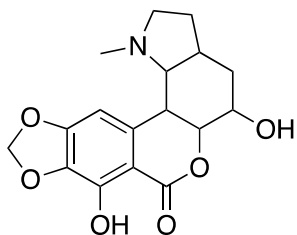
Amphetamine



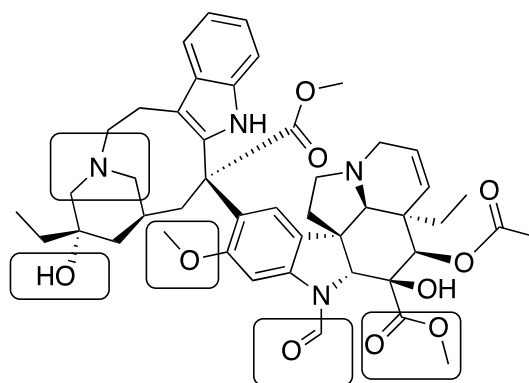
Secobarbital

15. (I) A compound exhibits the following peaks when analyzed with IR spectroscopy. Deduce which compound matches with this IR spectrum, and explain your reasoning.

IR Absorption Peaks (cm^{-1}): 3400, 2925, 2357, 1683, 1636, 1507, 1489, 1274, 1079, 1029, 468



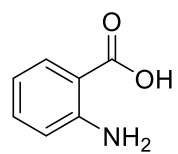
16. (A) Vincristine is a vinca alkaloid anticancer drug that was first isolated from the Madagascar periwinkle. Approximate the wavenumbers for the IR absorptions of the indicated functional groups.



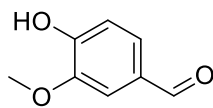
17. (I) What IR absorptions would you expect to see for hydrogen cyanide? Would these peaks be in the diagnostic region or the fingerprint region?

18. (I) The following compounds are the possible structures of “unknowns” given to you in a lab. Which of the following could you rule out based on the given IR absorptions? Were the absorptions in the diagnostic region or the fingerprint region more helpful in determining this?

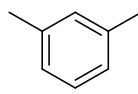
IR absorptions (cm^{-1}): 3400, 2800, 1620, 1580, 1500, 1450, 1420, 1300, 1280, 1200, 1190, 1020, 730, 680, 600



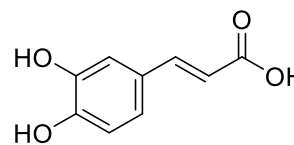
anthranilic acid



vanillin



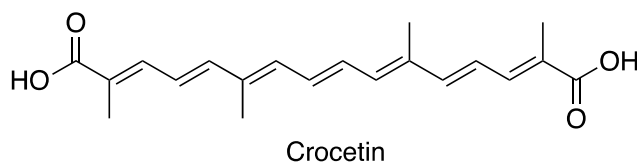
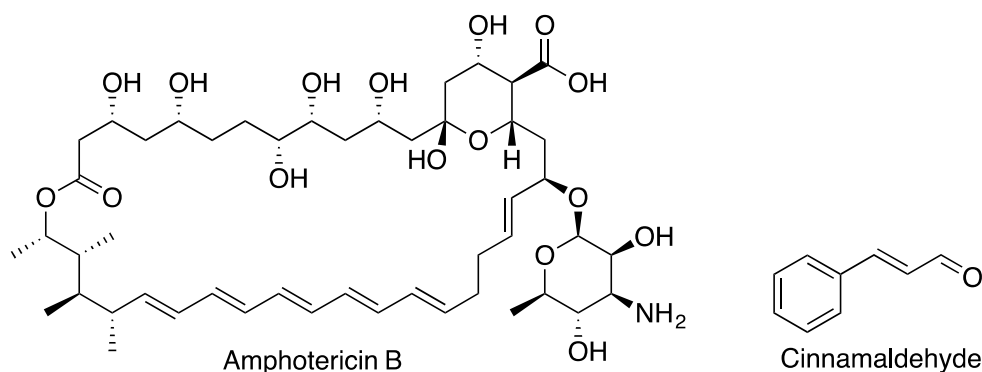
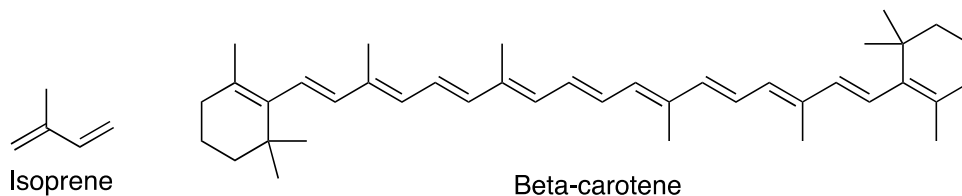
m-xylene



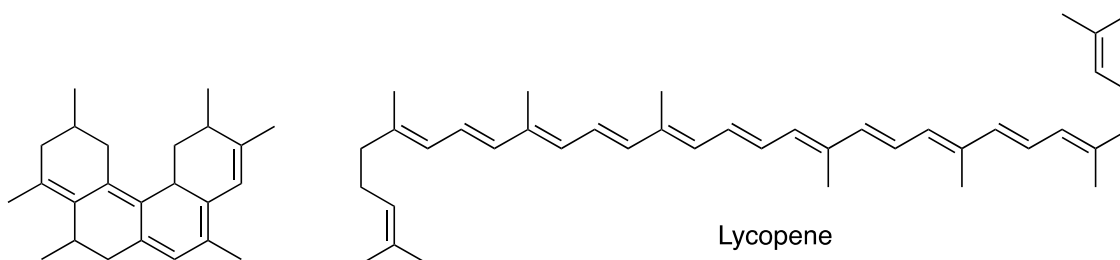
caffeic acid

c. UV Spectroscopy

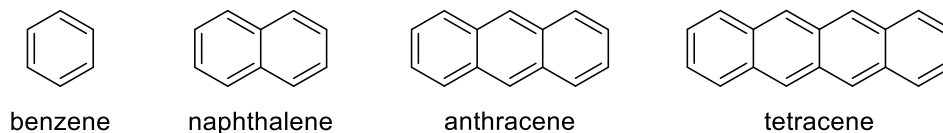
19.(C) Which of the following compounds shown below do you expect to have the largest wavelength for maximum absorbance by UV-Vis spectroscopy? Explain your answer.



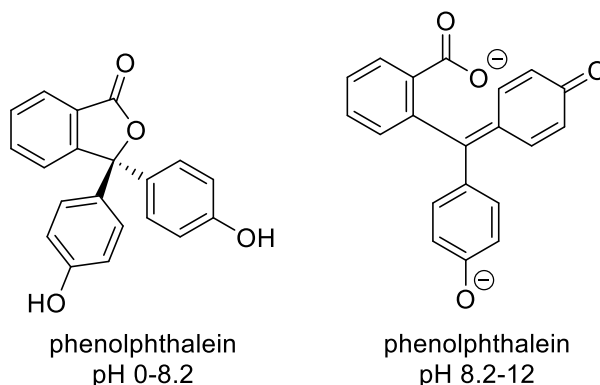
20. (I) In the following compounds, identify the chromophore and auxochromes. For each chromophore, use the Woodward-Fieser rules to estimate the wavelength of maximum absorbance. What are the limitations of the Woodward-Fieser rules for estimating this value? Given this information, which prediction do you think will be more accurate?



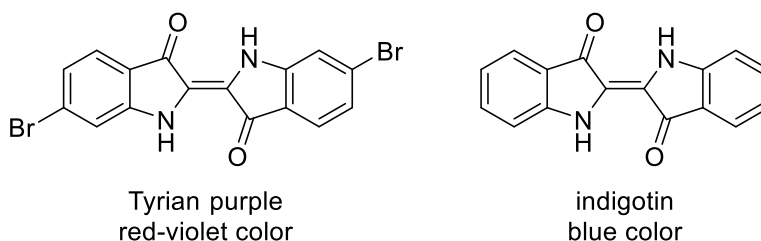
21. (C) Which benzene derivative would you expect to have the largest λ_{\max} ?



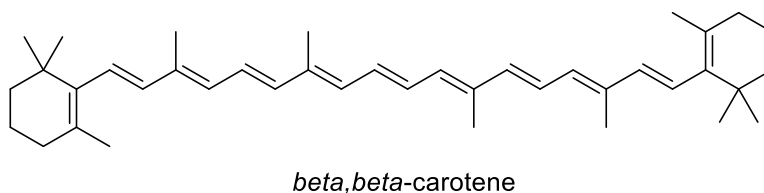
22. (A) Phenolphthalein is a pH indicator. It is colorless from a pH of 0-8.2, while it is a pink color from a pH of about 8.2-12. How does this change affect the conjugation of the molecule? In what region (UV or visible) do each of these structures absorb?



23. (I) Two dyes, Tyrian purple and indigotin, are shown below. The color we observe is listed under each compound. What range of wavelengths do these compounds absorb strongly? Does the loss of bromine in indigotin cause the compound to absorb light of a higher or lower energy?



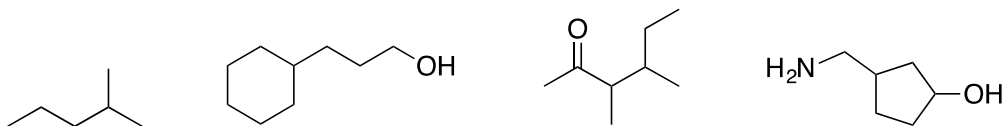
24. (A) Carrots are well-known for containing *beta,beta*-carotene, which is a provitamin A carotenoid. The carrots commonly found in grocery stores are usually orange in color, but carrots come in a variety of colors including white and purple. Use the Woodward-Feiser rules to approximate the λ_{\max} of *beta,beta*-carotene. Do you expect this approximation to be accurate? Would this absorb in the visible or UV region? Would you expect white carrots or orange carrots contain more of this compound?



d. Mass Spectrometry

25. (C) Explain the events that occur to a molecule starting from its entry into the mass spectrometer and ending at its arrival at the detector. Is charge necessary for separation to occur? Why or why not?

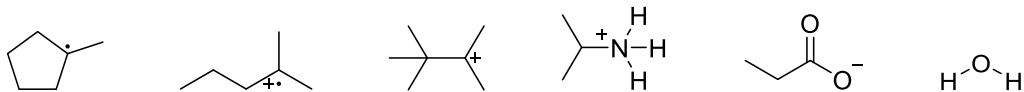
26. (I) For each molecule shown below, give three potential fragments that may form. For each fragment, determine the value of m/z for the resulting ion and the mass loss for each.



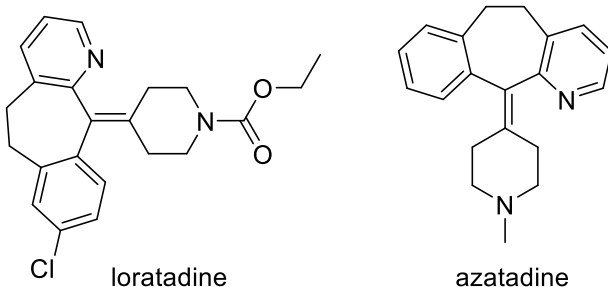
27. (I) Calculate the HDI for each of the following molecular formulas.

- a. C_6H_5Cl b. $C_5H_{10}O$ c. $C_6H_{15}N$ d. $C_6H_{10}O$ e. $C_7H_{13}Br$
f. $C_{47}H_{51}NO_{14}$ g. $C_6H_8O_6$ h. $C_{16}H_{24}O_4$ i. $C_7H_5N_3O_6$

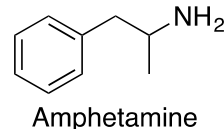
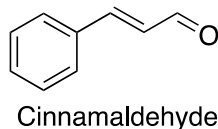
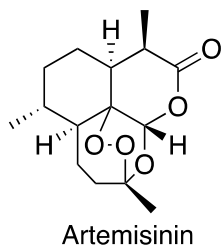
28. (C) Which of the following could be detected in a mass spectrometer?



29. (I) What would $[M]^+\bullet$ be for the following compounds after ionization by EI? If you would expect them to be above 5%, estimate the relative abundances of $[M+1]^+\bullet$ and $[M+2]^+\bullet$. What is the HDI for each compound?



30. (C) For each of the molecules below, determine the molecular formula and expected mass for the molecular ion in its mass spectrum.



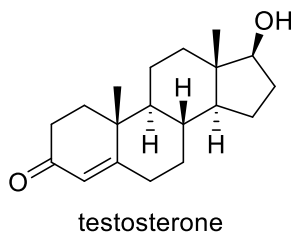
31. (I) Propose a molecular formula for a molecule that fits the following data:

- A hydrocarbon with a molecular ion peak at $m/z=94$.
- A compound with IR absorption at 3400 and 1720 cm^{-1} and exhibits a molecular ion peak at $m/z=128$
- A compound with a molecular ion peak at $m/z=118$ and $(M+2)$ peak at $m/z=120$ that is about one-third the height of the molecular ion peak.

32. (I) Estimate what the significant peaks in the molecular ion region (e.g. $[M]^+\bullet$, $[M+2]^+\bullet$, $[M+4]^+\bullet$) would look like for the following compounds. Do you see the 3:1 ratio indicative of chlorine or the 1:1 ratio indicative of bromine in each compound?



33. (I) You were given a mass spectrum of testosterone and asked whether EI or ESI was used as the ionization source. The mass spectrum has a base peak at 289 m/z , and the only fragment observed is a loss of water. Which ionization source was used, and how could you tell?



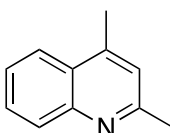
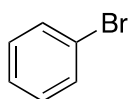
34. (C) Investigate three different ionization methods used for mass spectrometry. Explain the basic idea behind how they work and list any advantages and disadvantages for each.

35. (I) Describe how you could distinguish the following molecules from one another using mass spectrometry.

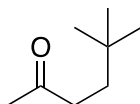
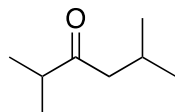
a.



b.



c.

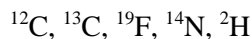


36. (A) GC-MS is used in medicine, forensics, drug testing, and security. What advantage does GC-MS have for analyzing a mixture of compounds? What are some instances in which GC-MS is used?

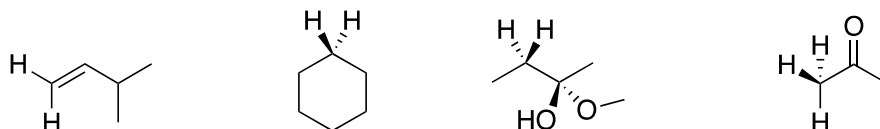
PROBLEM SET 6: SPECTROSCOPY, PART II: NMR SPECTROSCOPY

a. Principles of Operation

1. (C) What is the requirement for a nucleus to be analyzed by nuclear magnetic resonance (NMR) spectroscopy? Knowing this, can the following nuclei be observed with NMR?



2. (I) Determine if the following sets of protons shown are homotopic, enantiotopic, or diastereotopic. Explain your reasoning. For homotopic protons, do you expect to see a single signal or multiple signals?



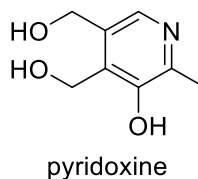
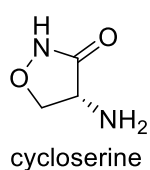
3. (I) If you are using a 300-MHz instrument, what is the difference, in hertz, between the frequency of absorption of TMS and the frequency of absorption of a proton with a δ value of 7.4 ppm. What is the difference if using a 400-MHz instrument?

4. (C) Define shielded and deshielded. Would the following terms be more similar with shielded or deshielded?

upfield downfield higher chemical shift lower chemical shift

5. (I) Most journals today have NMR spectra with scales reported in ppm instead of Hertz, with the instrument used (e.g. 300 MHz, 400 MHz) reported in the figure or table caption and in the methods. Is it necessary for the spectra to be reported in ppm? Why would ppm be more common? If the spectra were reported in Hertz, why would the instrument need to be mentioned?

6. (I) What are the chemical formulae for cycloserine and pyridoxine? For each set of protons, determine if they are chemically equivalent (homotopic or enantiotopic) or not chemically equivalent (diastereotopic).

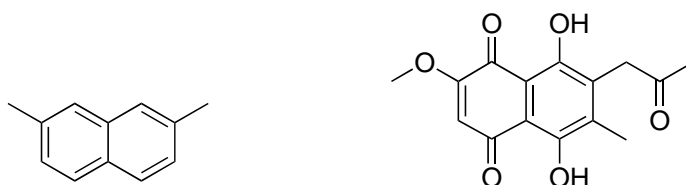


b. ^1H NMR

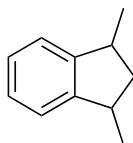
7. (C) What do the following pieces of information tell you about a signal in a ^1H NMR spectrum?

- The location of the signal
- The area under the signal
- The shape of signal

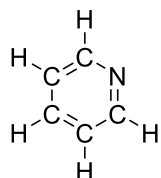
8. (I) For the following molecules, how many signals do you expect to see in a ^1H NMR spectrum? How many protons does each of these signals represent? What property of the spectrum should relate to these numbers of protons?



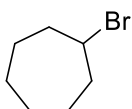
9. (A) Draw the expected ^1H NMR of the following compound. Indicate which peaks you have drawn correspond to which protons on your structure.



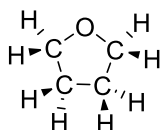
10. (C) Indicate in the following molecules which nuclei you would be able to detect using ^1H NMR.



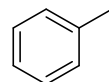
pyridine



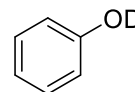
bromocycloheptane



tetrahydrofuran

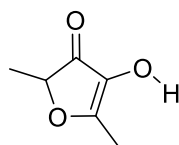


toluene

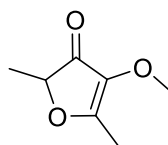


phenol-*d*

11. (A) Furanol and methoxyfuranol contribute to the smell of strawberries. In lab, you were given a sample of each and have to identify which is which, but you only have access to an NMR to help you. Would you expect any of the peaks to be similar? How would you be able to tell which sample is which compound?

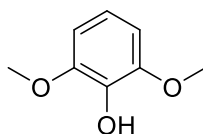


furaneol



methoxyfuranol

12. (A) Draw the expected ^1H NMR spectrum for the following compound. Should you have three, four, or six peaks in your spectrum?



syringol

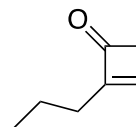
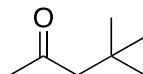
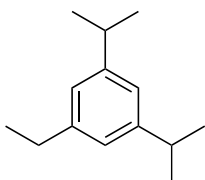
c. Signal Strength and Intensity

13. (C) For the following compounds, determine the number of protons giving rise to each signal.

a. The compound has a molecular formula of $\text{C}_7\text{H}_8\text{O}_3$. The ^1H NMR has signals at 8.04, 7.56, 6.77, 4.38, and 1.35 ppm with integration values of 23.1, 24.2, 23.7, 48.2, and 73.2 respectively.

b. The compound has a molecular formula of $\text{C}_{16}\text{H}_{26}$. The ^1H NMR has signals at 7.48, 7.23, 7.18, 6.98, 2.31, 2.18, and 0.89 ppm with integration values of 10.1, 11.0, 10.5, 10.2, 31.2, 11.2, and 183.3 respectively.

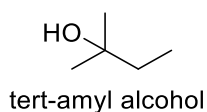
14. (I) For the following compounds, draw the expected ^1H NMR spectrum. State the expected integration for each of your signals based on the number of protons they represent.



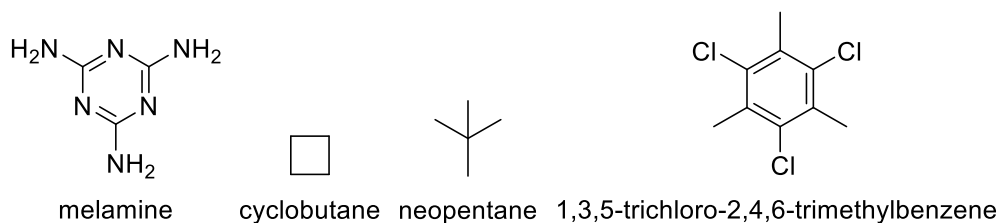
15. (A) Suppose you have a molecule with formula $\text{C}_{17}\text{H}_{36}$. This molecule when analyzed by ^1H NMR spectroscopy only shows one singlet. Based on this information, deduce the structure of the compound. How many ^{13}C NMR signals do you expect?

16. (I) You have a compound with 5 carbons, 2 oxygens, and must find the number of protons from the NMR spectrum. You have peaks with the following integrations: 0.89 ppm (84.9), 1.11 ppm (85.0), 1.46 ppm (56.5), 3.40 ppm (28.6), 3.60 ppm (28.3), 5.37 ppm (28.4), and 5.40 ppm (28.2). What is the chemical formula? What is the HDI?

17. (I) After integrating your spectrum, you find the following peaks and integrations for tert-amyl alcohol: 0.9 ppm (1.5 H), 1.2 ppm (3 H), 1.4 ppm (1 H), 4.5 ppm (0.5 H). Was the integration done correctly? If not, how would you fix this? Assign the peaks to the protons in the compound.

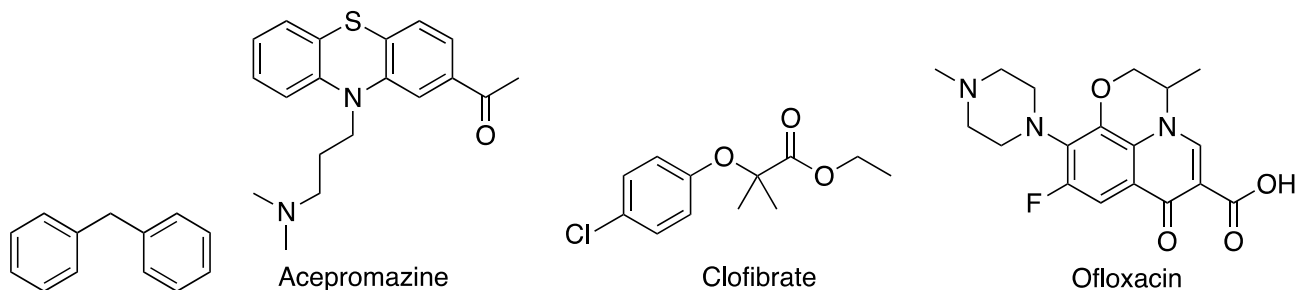


18. (I) Explain why each of the following compounds would NMR spectra with one peak integrating to one. How many protons are actually accounted for in that peak?



d. Coupling

19. (C) Predict the multiplicity of each signal in the ^1H NMR spectrum of the following compounds.



20. (I) Propose the structure of a compound that exhibits the following ^1H NMR data.

a. Molecular formula= C_8H_{10}

7.43 δ (1H, triplet); 7.34 δ (1H, singlet); 6.98 δ (2H, doublet); 2.31 (6H, singlet)

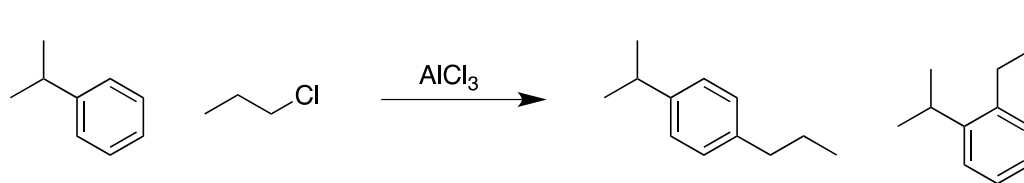
b. Molecular formula= C_{10}H_8

7.67 δ (4H, doublet); 7.32 δ (4H, doublet of doublets)

c. Molecular formula= $\text{C}_{12}\text{H}_{16}\text{O}$

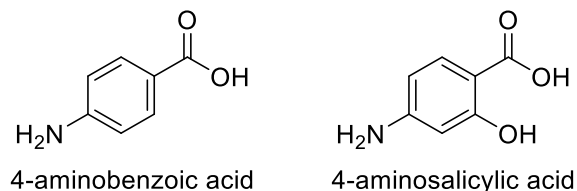
6.90 δ (2H, doublet); 6.80 δ (2H, doublet); 3.54 δ (2H, quartet); 2.61 δ (2H, triplet); 1.64 δ (2H, sextet); 1.22 δ (3H, triplet); 0.94 δ (3H, triplet)

21. (A) In the following Friedel-Crafts alkylation, there are two possible products formed. Predict the ^1H NMR spectra for the two products. How do these spectra differ from one another? Based on this information, how could you use ^1H NMR to distinguish between the two products?

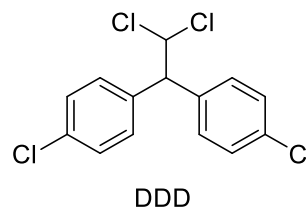
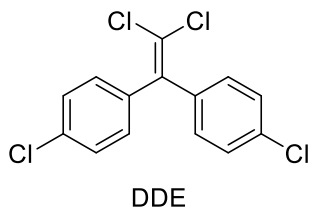
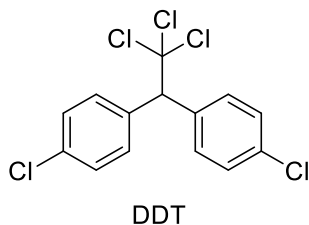


22. (C) The $n+1$ rule can be used to predict the number of neighboring protons, and Pascal's triangle can be used to predict the relative intensities of the peaks. Draw Pascal's triangle to the seventh row. Use these tools to predict what the signal would look like for protons with 0, 1, 2, 3, 4, 5, and 6 neighbors.

23. (I) Draw the NMR spectrum – including approximate shift, integration, and splitting pattern – for 4-aminobenzoic acid (also called PABA, a former active ingredient of sunscreens) and 4-aminosalicylic acid (used in the treatment of tuberculosis).

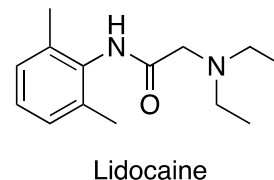
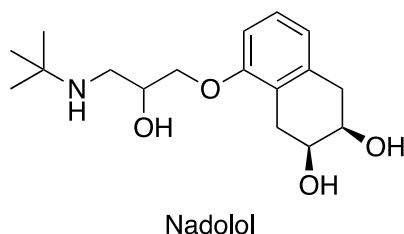
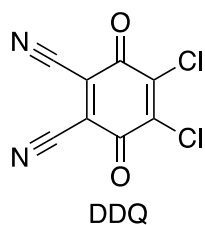


24. (A) Dichlorodiphenyltrichloroethane, more commonly known as DDT, is an insecticide and a persistent environmental pollutant. Its use was banned due to environmental concerns. Two of its breakdown products, DDE (dichlorodiphenyldichloroethylene) and DDD (dichlorodiphenyldichloroethane), are environmental breakdown products with similar properties. Predict the ^1H NMR spectrum for each compound (including chemical shift, splitting pattern, and integration) and explain how you could distinguish these structurally-similar compounds based on their proton NMR spectra.



e. ^{13}C NMR

25. (C) How many signals do you expect to see in a ^{13}C NMR spectrum of the following compounds?



26. (I) Using the following DEPT spectral data, how many primary, secondary, tertiary and quaternary carbons do you expect in these compounds? Based on chemical shifts of the signals, what functional groups do you believe may be contained in the structure? What is the HDI for each molecule? What can this tell you about the structure?

a. Molecular formula: $\text{C}_9\text{H}_{11}\text{NO}_2$

^{13}C NMR: 165.9, 152.7, 130.7, 114.1, 60.9, 14.1

DEPT 135: 130.7(+), 114.1(+), 60.9(-), 14.1(+)

DEPT 90: 130.7(+), 114.1(+)

b. Molecular formula: $\text{C}_{17}\text{H}_{17}\text{Cl}_2\text{N}$

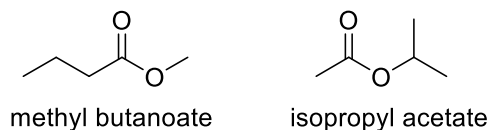
^{13}C NMR: 145.5, 139.6, 138.0, 132.5, 130.9, 130.7, 129.4, 127.7, 126.4, 126.0, 124.9, 125.1, 59.9, 44.7, 34.6, 27.7, 21.9

DEPT 135: 130.7(+), 129.4(+), 127.7(+), 126.4(+), 126.0(+), 124.9(+), 125.1(+), 59.9(+), 44.7(+), 34.6(+), 27.7(-), 21.9(-)

DEPT 90: 130.7(+), 129.4(+), 127.7(+), 126.4(+), 126.0(+), 124.9(+), 125.1(+), 59.9(+), 44.7(+)

27. (A) Suppose you are synthesizing trinitrobenzenes to be used as potential explosives. You have three possible isomers that could be made and wish to distinguish between them. What are the possible isomers? How many ^{13}C signals do you expect to see for each? Could ^{13}C NMR be used to distinguish between them? Why or why not?

28. (C) Describe how the signals for each of the carbons would appear in a typical ^{13}C NMR spectrum, a DEPT-90 spectrum, and a DEPT-135 spectrum. Also include the approximate chemical shift.



29. (I) Determine the structure of the compound based on the following information.

$\text{C}_{10}\text{H}_{10}\text{O}_2$

IR (cm^{-1}): 3030, 2990, 2950, 1720, 1640, 1600, 1500, 1450, 1380, 980, 710, 690

EI-MS (m/z): 162, 131 (base peak), 103, 77, 51

Note: only reported if >20% of base peak.

^1H (ppm [splitting, integration]): 3.80 (s, 3H); 6.31 (d, 1H); 7.33 (t, 1H); 7.38 (t, 2H); 7.48 (d, 1H); 7.54 (d, 2H)

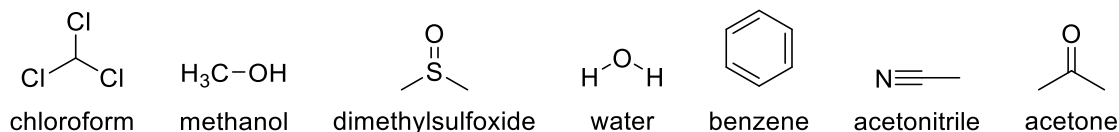
*NOTE: some peaks overlap in the spectrum, it has been simplified for you.

^{13}C (ppm): 52.0, 115.1, 127.9, 128.5 (2 carbons), 128.6 (2 carbons), 135.2, 143.6, 166.5

DEPT-135: 52.0 (+), 115.1 (+), 127.9 (+), 128.5 (+, 2 carbons), 128.6 (+, 2 carbons), 135.2 (+), 143.6 (+), 166.5 (+)

DEPT-90: 115.1 (+), 127.9 (+), 128.5 (+, 2 carbons); 128.6 (+, 2 carbons); 143.6 (+)

30. (A) Solvent peaks often show up in NMR spectra as impurities, because the solvent was not 100% deuterated, or through a proton exchange between the compound and the solvent. For each of the common, undeuterated solvents, determine the splitting pattern and approximate chemical shift for the protons. For carbon-containing solvents, also determine the approximate chemical shift for the carbon(s).



PROBLEM SET 7: FOUNDATIONS OF CHEMICAL REACTIVITY AND MECHANISMS

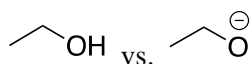
a. Chemical Reaction Components

i. Reactants and substrates

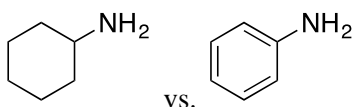
1. (C) Define reactant and substrate. Where do you find these in a chemical reaction equation?

2. (I) Which of the following is more nucleophilic?

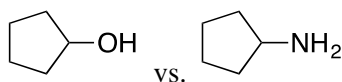
a.



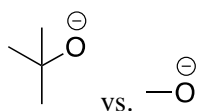
b.



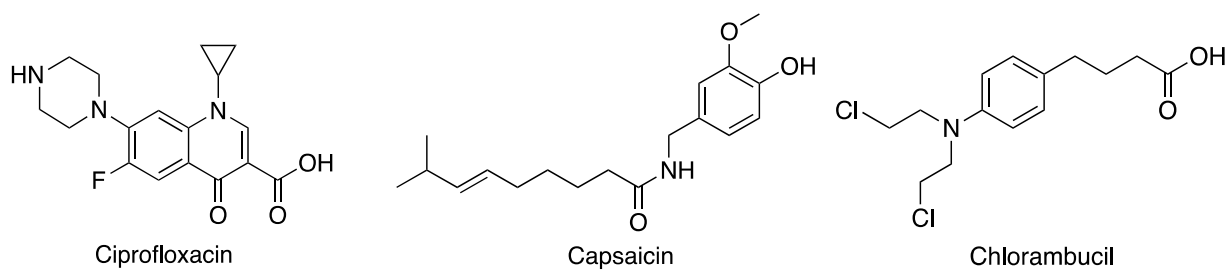
c.



d.



3. (A) For the following molecules, identify any nucleophilic sites. If you select more than one site, which do you expect is more nucleophilic? Explain your reasoning.

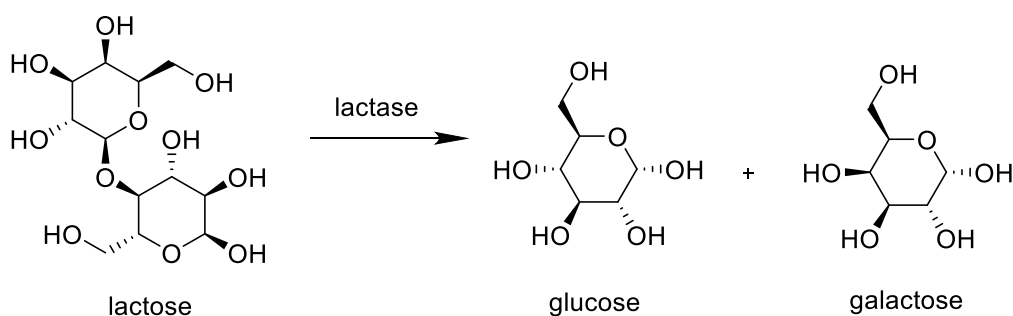


4. (C) What are steric effects? What is steric hindrance?

5. (I) Identify and draw the structure for each reactant in the situations below.

- The combustion of propane in the presence of oxygen producing carbon dioxide and water.
- The decomposition of hydrogen peroxide into water and oxygen gas.
- The synthesis of aspirin from acetic anhydride and salicylic acid.

6. (A) Lactose intolerance is the inability of a person to digest lactose, a sugar found in milk. Lactase is an enzyme that breaks down lactose into glucose and galactose. Would lactose be considered a reactant, substrate, neither, or both? Explain. What is needed to balance the reaction?



ii. Reagents

7.(C) Define reagent. Where are reagents indicated in a chemical reaction equation? How do reagents differ from reactants?

8. (I) A wide variety of reagents are used to perform reductions in organic synthesis due to the fact that different reagents affect different functional groups. For this reason, it is very important to choose a proper reducing agent to achieve the desired transformation in a synthesis.

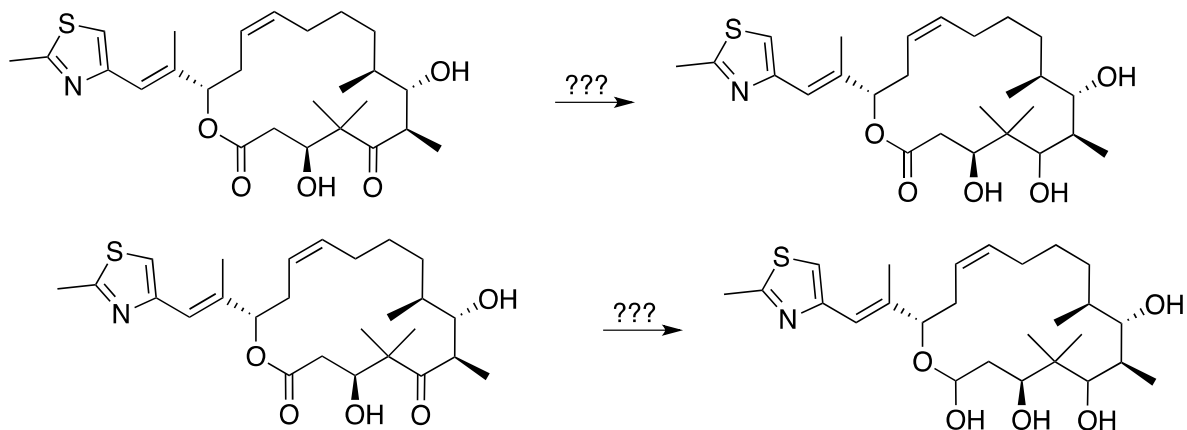
a. What functional groups can the following reagents be used to reduce?

i. NaBH_4

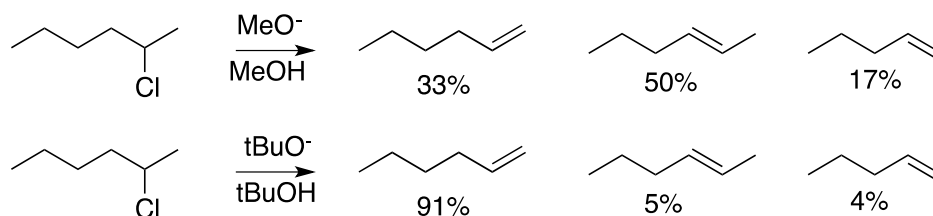
ii. Lithium aluminum hydride

iii. H_2 , Pd

b. Which reagent would you use to perform the following transformations of epothilone C, a natural product with anticancer activity?



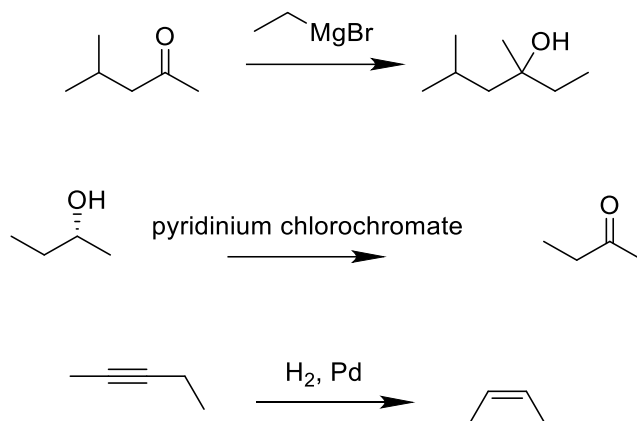
9. (A) When performing an elimination reaction, the base used can play a role in the product that is formed. In the case of the example below, the use of tert-butoxide results in the formation of 1-hexene preferentially, while the use of methoxide results in preferential formation of 2-hexene. Draw a mechanism for each elimination reaction. Provide an explanation for the difference in preference depending on the reagent used. (*J. Am. Chem. Soc.* **1967**, *91*, 1376)



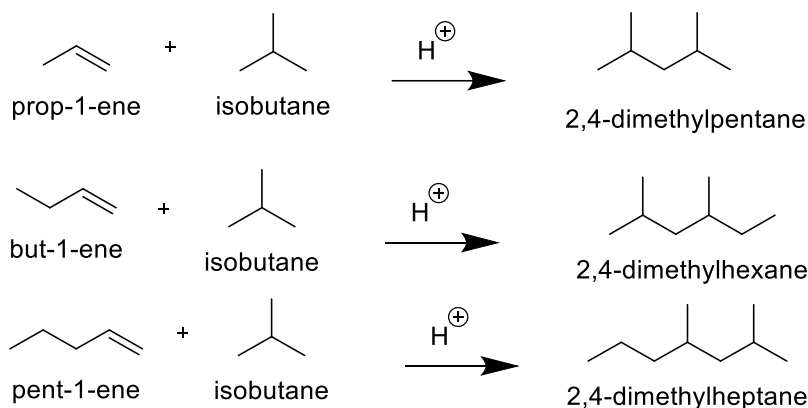
10. (C) Describe what you expect would generally happen with the following types of reagents:

- alkylating agent
- fluorinating agent
- dehydrating agent
- oxidizing agent
- reducing agent

11. (I) Reagents are used to oxidize as well as to reduce organic compounds. For each reaction below, identify the reagent and determine if it oxidized or reduced the substrate.



12. (A) The petroleum industry uses alkylation to produce high-octane components of gasoline. This is often done using isobutene and a strong acid catalyst such as sulfuric acid. For each of the reactions below, assign the terms reactant, reagent, and substrate. Identify what part of the product is from isobutene and the new carbon-carbon bond formed. (Alkylation is an important source for octane in gasoline. U.S. Energy Information Administration. Eia.gov)

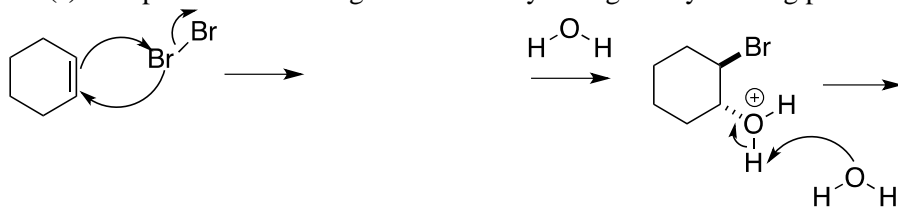


iii. Product

13. (C) Define product. Where are products indicated in a chemical reaction equation?

14. (I) What is a kinetic product? What is a thermodynamic product? Draw energy diagrams showing both types of products of a reaction.

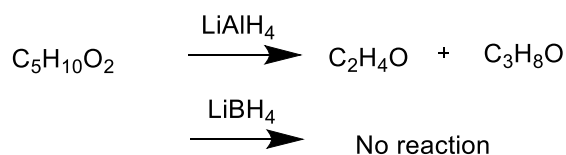
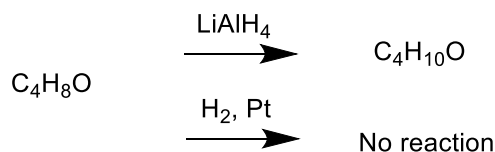
15. (I) Complete the following mechanism by filling in any missing products or curved arrows.



16. (C) What is the difference between a transition state and an intermediate? Would either of these be considered products?

17. (I) Draw a reaction diagram with only one transition state. Draw a reaction diagram with one intermediate. Label each diagram with reactant, transition state, intermediate, and product.

18. (I) Some reactions are performed in order to determine what functional groups are present in the starting material or to get an idea of the possible structure. For each set of reactions below, determine a possible structure for the reactant and products.

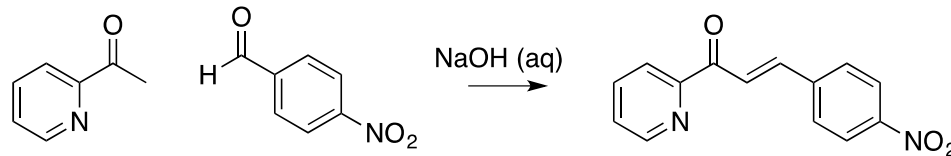


iv. Reaction conditions

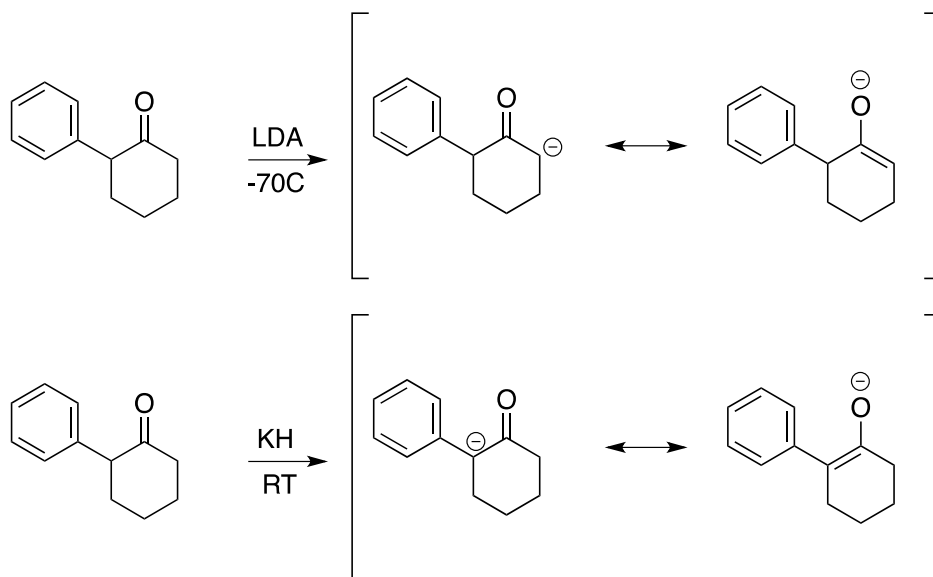
19. (C) Name three examples of variables that could be considered reaction conditions?

20. (I) While $\text{S}_{\text{N}}2$ reactions are typically more favorable in polar aprotic solvents, the use of polar protic solvents can result in $\text{S}_{\text{N}}2$ reactions as well. What variables in your reaction could you alter to achieve an $\text{S}_{\text{N}}2$ substitution reaction in a polar protic solvent? How would you change these conditions?

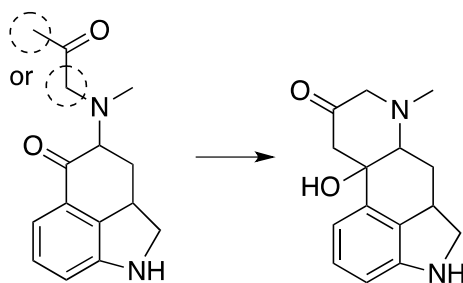
21. (A) In green organic chemistry, the focus is development of more environmentally friendly processes of preparation of organic compounds. One way that this can be achieved is through the minimal use of organic solvents. In the following reaction, an aldol condensation results in the formation of the product along with water. Would you expect the use of water as the solvent to increase or decrease the yield of the product? If the product is insoluble in water, does this change? (*J. Chem. Educ.* **2007**, *84*, 475-476)



22. (A) When performing an aldol addition, reaction conditions can dictate whether a kinetic or thermodynamic enolate forms. An example of this is shown below (kinetic top, thermodynamic bottom). (*J. Am. Chem. Soc.* **1974**, *96*, 5944)

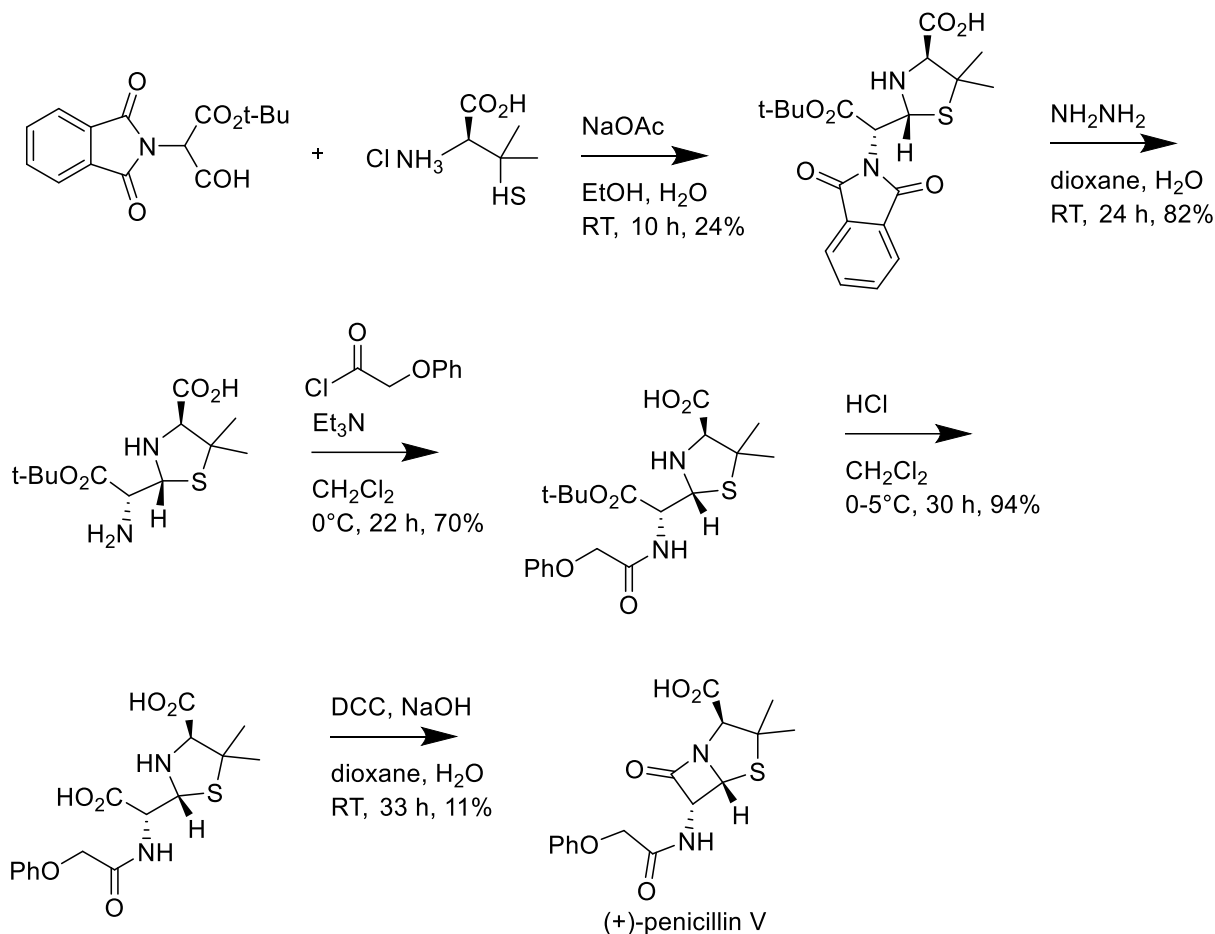


- Which product is lower in energy?
- Why is a larger base used to form the kinetic enolate?
- Given the following reactant and desired product, which enolate should be formed?

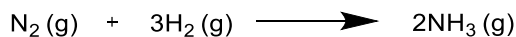


23. (C) Explain whether it would be better to alter one condition at a time or change multiple conditions when trying to find the best set of conditions for a reaction. How would you determine which set of reaction conditions were best?

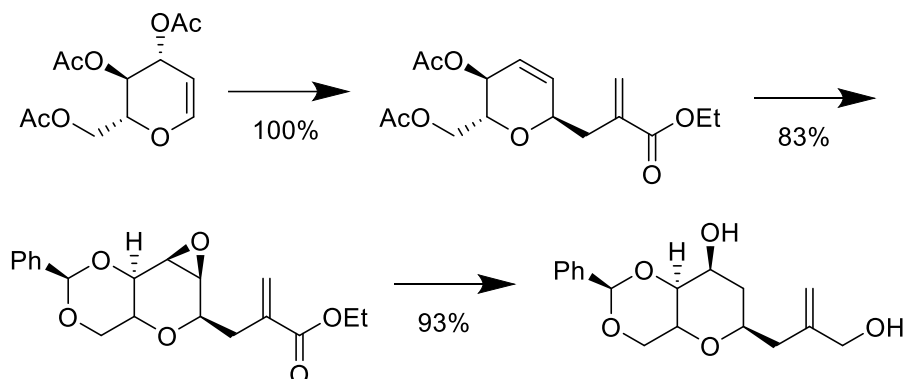
24. (I) A total synthesis of penicillin V is shown below. For each step, identify the reaction conditions. (*J. Am. Chem. Soc.* **1957**, DOI: 10.1021/ja01562a063 & *J. Am. Chem. Soc.* **1957**, DOI: 10.1021/ja01521a044).



25. (A) Pressure and temperature are important conditions to consider for some reactions, such as the Haber Bosch Process used to produce ammonia. Why would pressure be important for this reaction but not for the reaction between acetic acid and sodium hydroxide? Would increasing the temperature favor the forward (exothermic) or reverse (endothermic) reaction for the Haber Bosch Process?



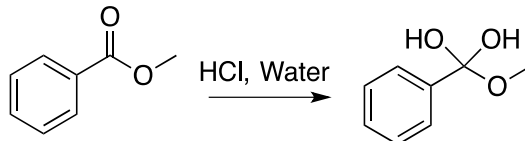
26. (A) Determine the overall yield for the selected steps from the convergent synthesis of hemibrevetoxin B, a marine neurotoxin. If you were able to find reaction conditions that would improve the percent yield of the second step to 89% and the third step to 95%, how would the overall yield improve? (*J. Am. Chem. Soc.* **2002**, DOI: 10.1021/ja029225v)



v. Catalyst

27. (C) Define catalyst. Is a catalyst consumed in a reaction? What is the catalyst's role in a reaction?

28. (I) Draw a mechanism for the following reaction. Is there a catalyst present? If so, what is acting as a catalyst.



29. (A) 2,4-dinitrophenylhydrazine, or Brady's reagent, is used to test compounds for the presence of an aldehyde or ketone functional group. The 2,4-dinitrophenylhydrazine reacts with the aldehyde or ketone group of the compound, in the presence of an acid catalyst, to form an insoluble dinitrophenylhydrazone. You perform Brady's test using both concentrated hydrochloric acid and acetic acid. For the hydrochloric acid, you observe immediate formation of the hydrazone, but do not see formation of the hydrazone for the acetic acid. After 15 minutes, you begin to see formation of the hydrazone. Why does the acid used result in differing rates of reaction? (*J. Chem. Educ.* **1959**, 36, 575)

30. (C) Does the presence of a catalyst have an effect on the change in free energy of a reaction?

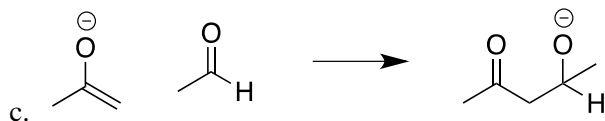
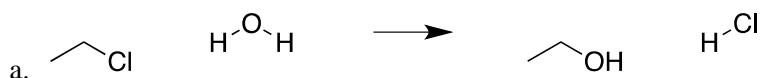
31. (C) What is the difference between a heterogeneous catalyst and a homogenous catalyst?

32. (I) Carbonic anhydrase catalyzes the reaction from carbonic acid to carbon dioxide and water in the lungs, where there the carbon dioxide concentration is low. Carbonic anhydrase is also present in other tissues; in the tissues with high concentrations of carbon dioxide, would you expect the enzyme to catalyze the decomposition of carbonic acid?

33. (A) Catalase is an important enzyme for protecting cells from damage from reactive oxygen species by catalyzing the decomposition of hydrogen peroxide into water and oxygen. The uncatalyzed decomposition is thermodynamically favorable, but it is slow enough that hydrogen peroxide is fairly stable at room temperature and can be bought at grocery stores. It has many uses; it is often used for cleaning wounds, and in microbiology it can aid in identifying catalase-positive bacteria. What causes the bubbling observed when it is applied to a wound? Why would this not be observed if it applied to uncut skin? What would be the observable difference between catalase-positive and catalase-negative bacteria when it comes into contact with hydrogen peroxide?

vi. The role of energy

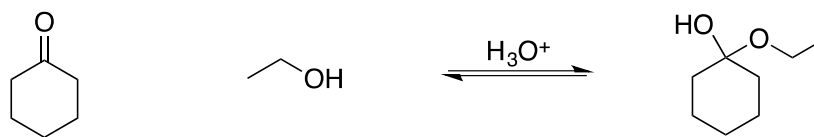
34. (C) Estimate ΔH for the following reactions. Are they exothermic or endothermic? Is the entropy, ΔS , positive, negative or approximately zero for these reactions? Identify any reactions that you expect to be spontaneous at any temperature.



35. (C) Determine whether the reactants, products or neither are favored in the following equilibrium reactions.

- A reaction with a $K_{eq}=3$
- A reaction with $K_{eq}=0.5$
- A reaction with $\Delta G=0$
- An endothermic reaction with negative entropy
- An exothermic reaction with positive entropy

36. (I) In the following equilibrium, will more products form at a higher or lower temperature? Explain why this occurs.



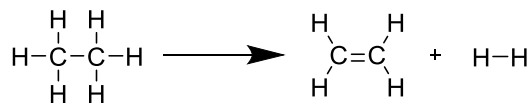
37. (A) One method used to reduce alkenes and alkynes to alkanes is a combination of palladium and hydrogen gas. If one wants to reduce an alkyne to an alkene, one cannot use this system, but must use a modified (poisoned) version of the palladium catalyst so that the reaction stops at the alkene.

- What is the enthalpy for the reduction of 2-butyne to 2-butene?
- What is the enthalpy for the reduction of 2-butene to butane?
- Explain why the normal palladium catalyzed reduction does not stop at the alkene, but continues to the alkane.

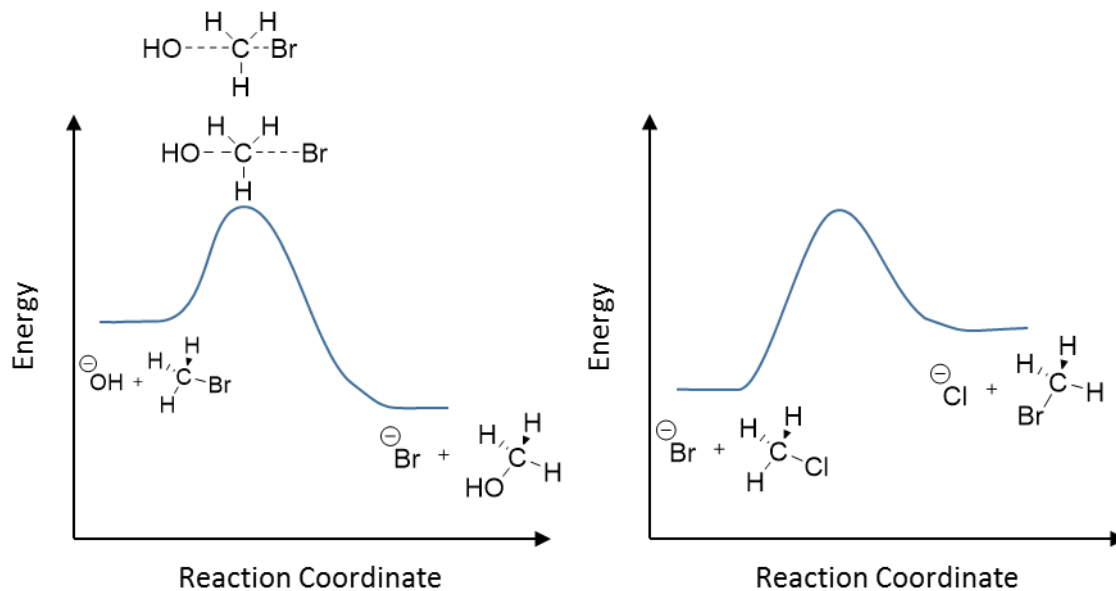
38. (C) Define enthalpy, entropy, Gibb's free energy, exothermic, endothermic, exergonic, and endergonic.

39. (C) What are the units for a reaction rate? What are the units for the rate constant of a first order, second order, and third order reaction?

40. (I) Is this reaction spontaneous room temperature (~21°C)? Above what temperature would this reaction become spontaneous? $\Delta S = + 120 \text{ J/mol}\cdot\text{K}$



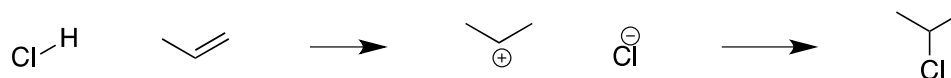
41. (I) Use the Hammond Postulate to determine which of the structures is a better representation of the transition state for the exothermic reaction. Use this information to predict the transition state for the endothermic reaction. What generalization can you make about the transition state for an exothermic reaction and an endothermic reaction with only one transition state?



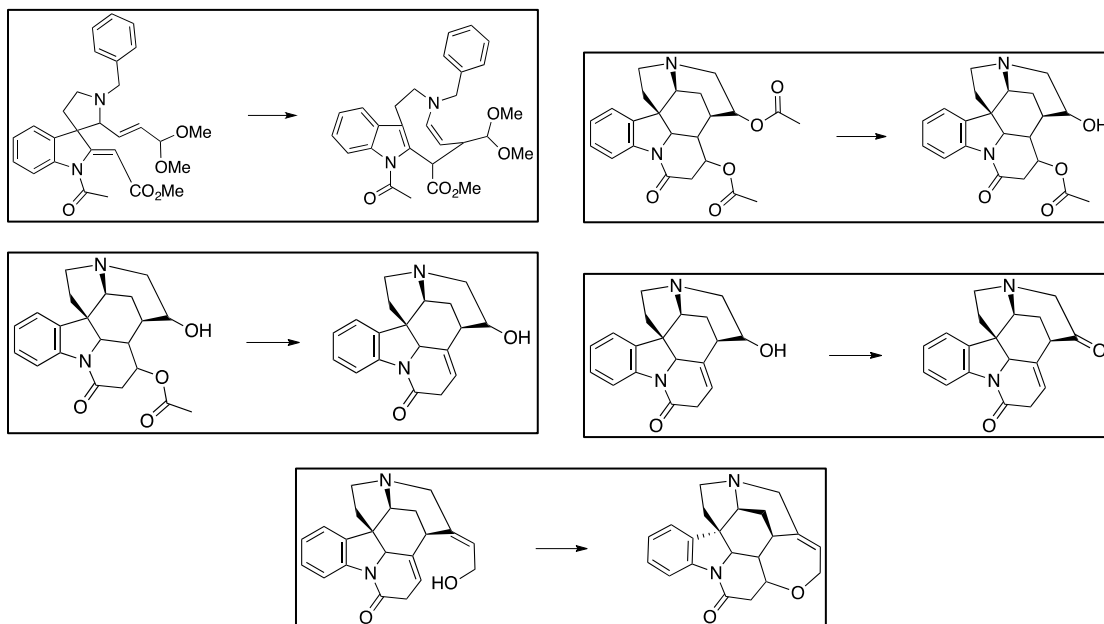
b. Basic Classes of Reactions

i. Addition

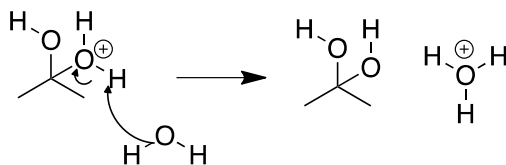
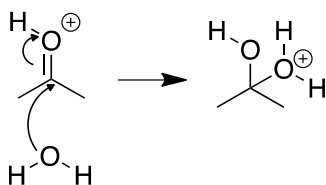
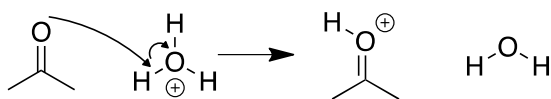
42. (C) Complete the following addition reaction mechanism by including curved arrows for each transformation step.



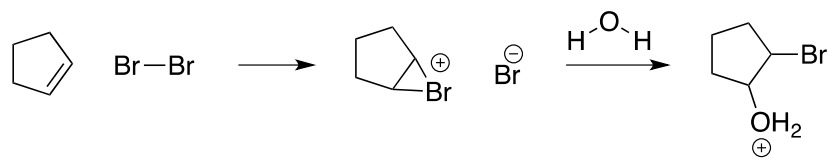
43. (C) Which of the following transformations from the total synthesis of strychnine represents an addition reaction?



44. (I) Determine if the following arrow pushing patterns are a nucleophilic attack, loss of a leaving group, proton transfer, or rearrangement. There may be multiple patterns in a reaction sequence.



45. (I) Estimate the enthalpy changes for each step of the following addition reaction. Using these estimated values, draw an energy diagram for the chemical reaction.

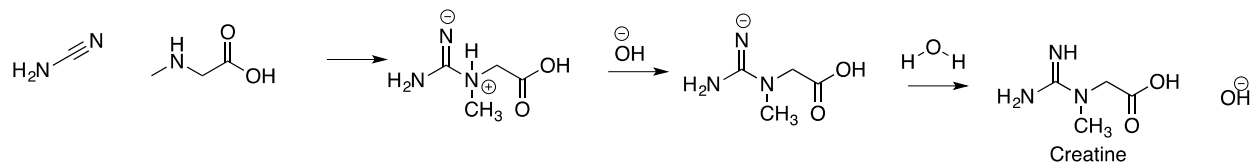


46. (A) Creatine is a small molecule that is naturally found in vertebrates with the purpose of providing the cells of the body with energy. Since this molecule acts primarily on muscle cells in the body, it has become a popular supplement for athletes.

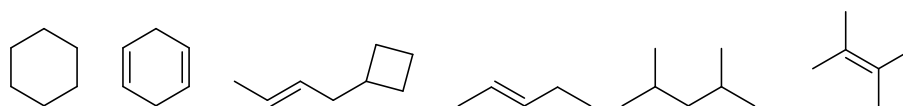
a. In the synthesis of creatine shown below, complete the arrow pushing mechanism (*J. Chem. Educ.*, 2006, 83, 1654.).

b. Which arrow pushing patterns are present with each step?

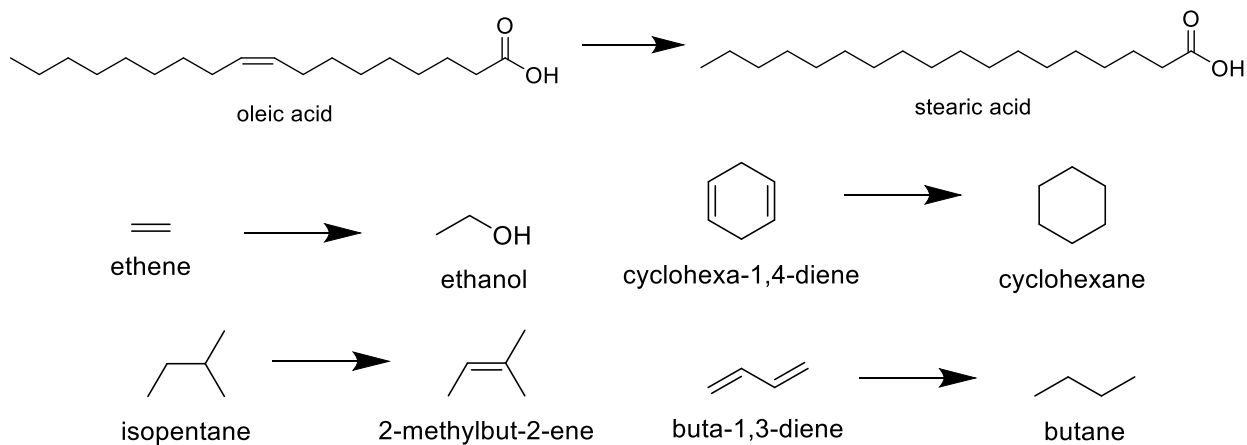
c. For any nucleophilic attacks, identify the nucleophile and the electrophile.



47. (C) Where on the following compounds could an addition reaction take place?

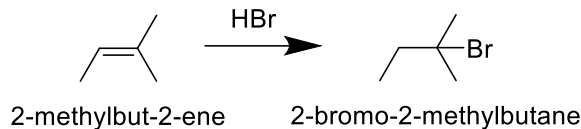


48. (C) Which of the following represents a hydrogenation reaction?

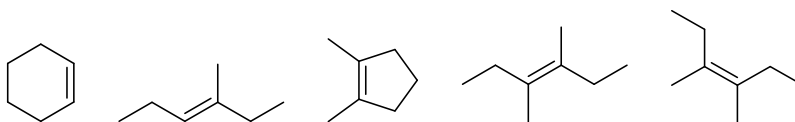


49. (I) What is Markovnikov addition? Anti-Markovnikov addition? Why – without an additive such as a peroxide – would Markovnikov addition be favored?

50. (I) Draw the mechanism for the Markovnikov addition of HBr. Would you expect the anti-Markovnikov addition to also have a carbocation intermediate?

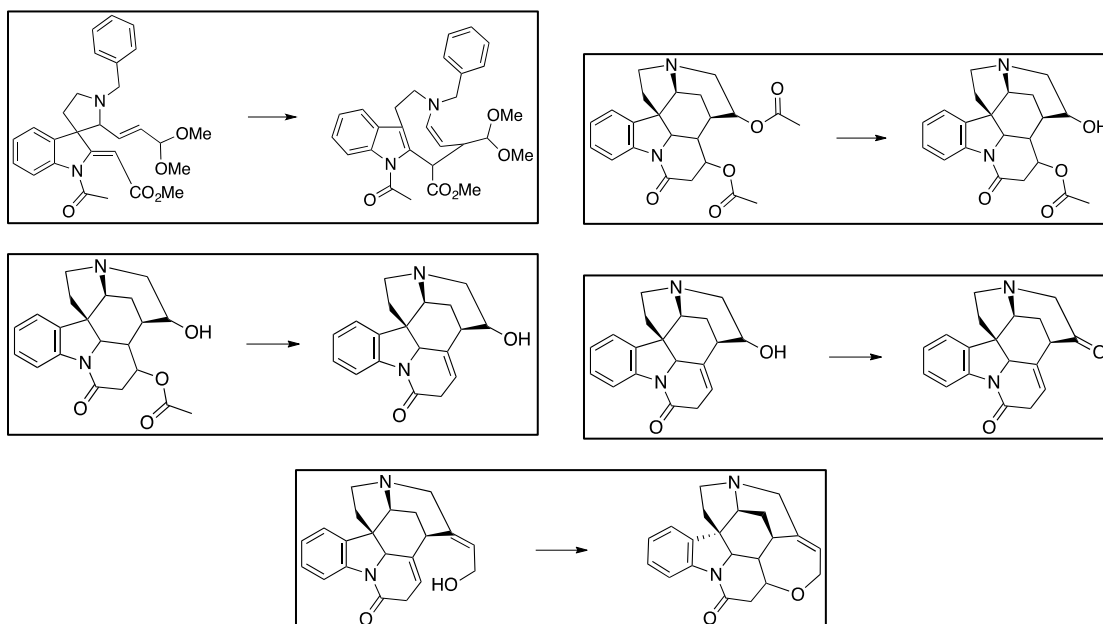


51. (A) The reaction of an alkene with hydrogen gas and a catalyst such as platinum, palladium, or nickel (among many others) is known as catalytic hydrogenation. During this process, the H atoms are added *syn* across the double bond, which may result in a chiral center in the molecule. Draw the expected products for catalytic hydrogenation, taking into account stereochemistry, and indicate if the product is achiral, meso, diastereomers, or enantiomers. Identify the carbons in the starting materials below that became chiral centers. Assuming the reaction goes to completion (and no side reactions or byproducts) which of the reactions would require separation to achieve a single product?



ii. Elimination

52. (C) Which of the following transformations from the total synthesis of strychnine represents an elimination reaction?

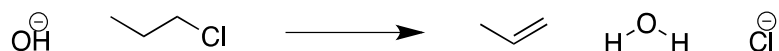


53. (C) The two main categories of elimination reactions are E1 and E2 eliminations. Compare and contrast these two elimination reaction types.

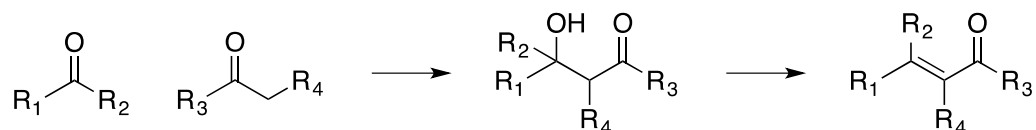
54. (I) Elimination reactions typically require the presence of a base to perform a deprotonation. Will the following conditions result in an elimination?

- a. NaBr b. NaOH c. NaN₃ d. NaOMe

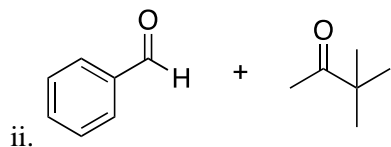
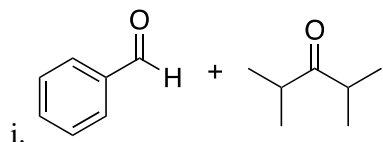
55. (I) Draw curved arrows to show the mechanism of the following elimination reaction. Based on the transformations occurring from reactants to products, estimate the enthalpy of the reaction and predict whether the entropy of the reaction will be positive or negative.



56. (A) The Aldol condensation is a useful reaction in organic chemistry, due to its utility in forming carbon-carbon bonds. Additionally, the resulting alkene is useful for carrying out further reactions. The reaction has two steps, which are shown below.



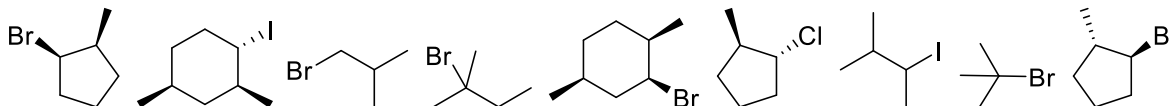
- a. Identify the elimination step of the reaction.
 b. Will the following sets of reactants result in the Aldol condensation product? Explain.



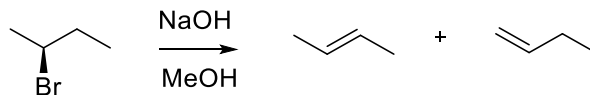
- c. What types of reactions could be carried out on the resulting product?

57. (C) What is the Zaitsev rule? What is Hofmann's rule?

58. (C) Which of the following compounds would have the same major product from an elimination reaction?

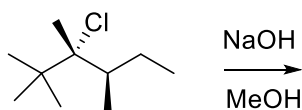
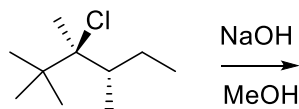


59. (I) Determine which would be the major product and draw the mechanism for it.



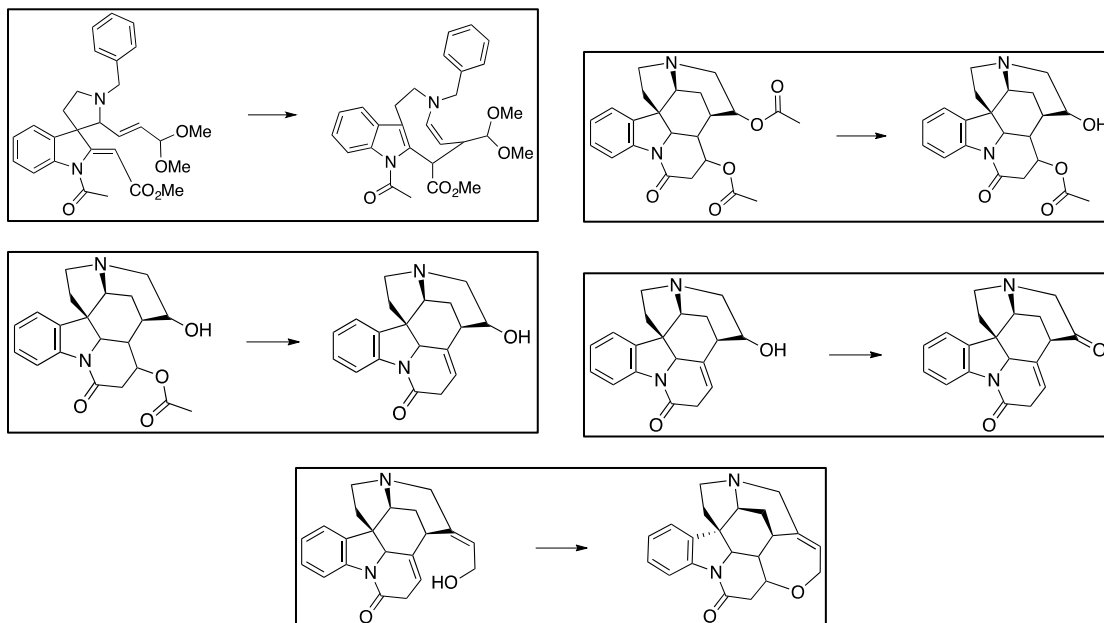
60. (I) Draw an example of a hydride shift and an alkyl shift and explain why they are often referred to as 1,2-hydride shift or 1,2-alkyl shift. Would this be observed with E1 or E2 reaction mechanisms?

61. (A) Many chemicals are sold as racemic mixtures. If you needed to produce a *cis* alkene as a product, would you be able to use the racemic mixture, need to use only one enantiomer, or not be able to use either of the compounds (i.e. would need a diastereomer)?

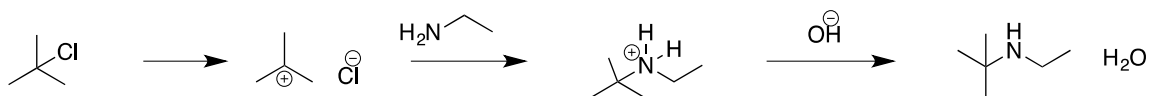


iii. Substitution

62. (C) Which of the following transformations from the total synthesis of strychnine represents a substitution reaction?



63. (C) Draw curved arrows for the following substitution reaction.



64. (I) Estimate the enthalpy change for the reaction of an acid halide, amide, and acid anhydride with an alcohol to form an ester. Is the entropy change of this reaction expected to be positive or negative. Which of these reactions do you expect to be more likely to occur spontaneously? Draw a reaction equation for each transformation.

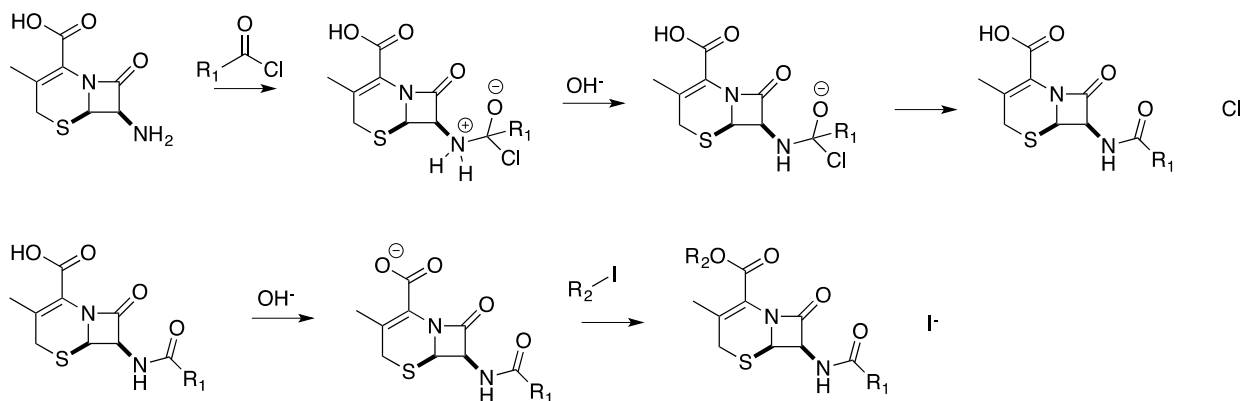
65. (A) In the Fischer esterification of carboxylic acids, an acid is used as a catalyst. Draw curved arrows to complete the mechanism for the Fischer esterification of acetic acid with ethanol. Is the protonated or non-protonated carboxylic acid more electrophilic? Why is the acid necessary for the reaction to proceed?

66. (A) In medicinal chemistry, chemists often perform structure-activity relationship (SAR) studies, where they compare the medicinal effect of a variety of closely related molecules to determine how the structure of the molecule affects its medicinal properties. An example of a synthetic transformation used in a SAR study of β lactams against tuberculosis is shown below (*J. Med. Chem.*, DOI: 10.1021/acs.jmedchem.5b01833).

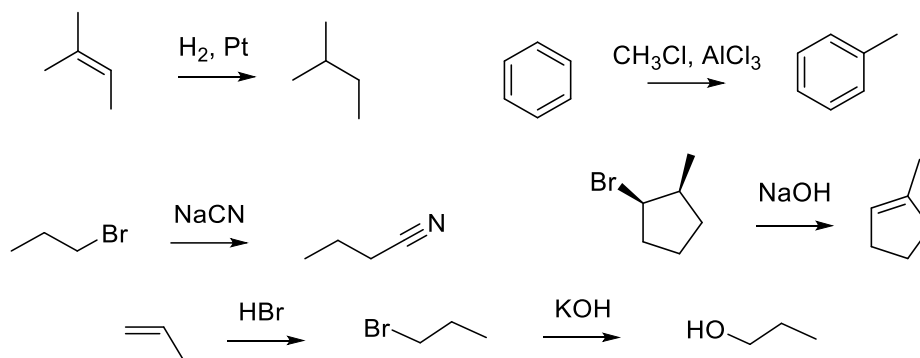
a. Complete the arrow pushing mechanism for the two reactions.

b. In each reaction, what is the nucleophile and electrophile?

c. Which of these nucleophiles do you expect is more nucleophilic? Offer a possible explanation for this increased nucleophilicity.



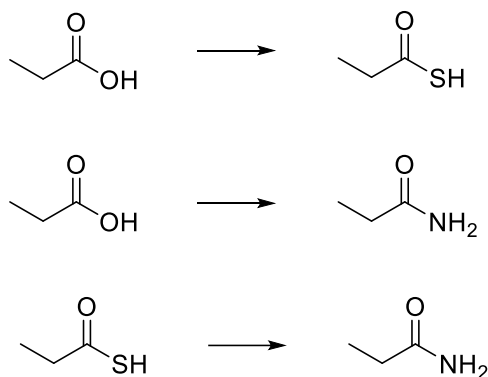
67. (C) Determine if the following reactions are substitution reactions.



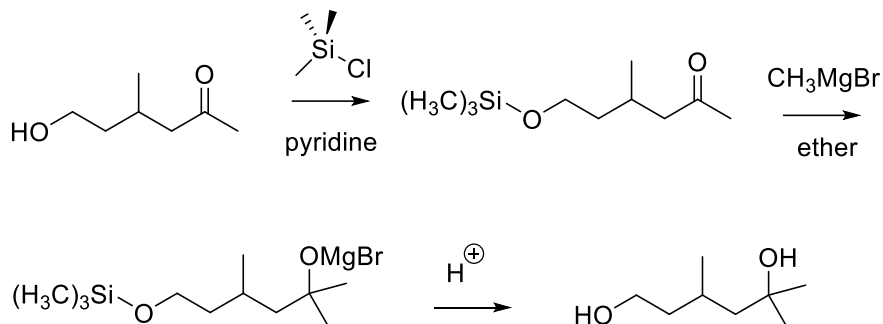
68. (C) Describe the general reaction mechanism for S_N1 and S_N2 reactions. Why is “umbrella flip” sometimes used to describe an S_N2 reaction?

69. (I) Theoretically, the S_N1 reaction should result in a racemic mixture. Observations, however, point to a slight favoring of the inversion of stereochemistry over the retention of stereochemistry. What might cause this observation?

70. (I) Would you expect $K > 1$ or $K < 1$ for the following substitution reactions?

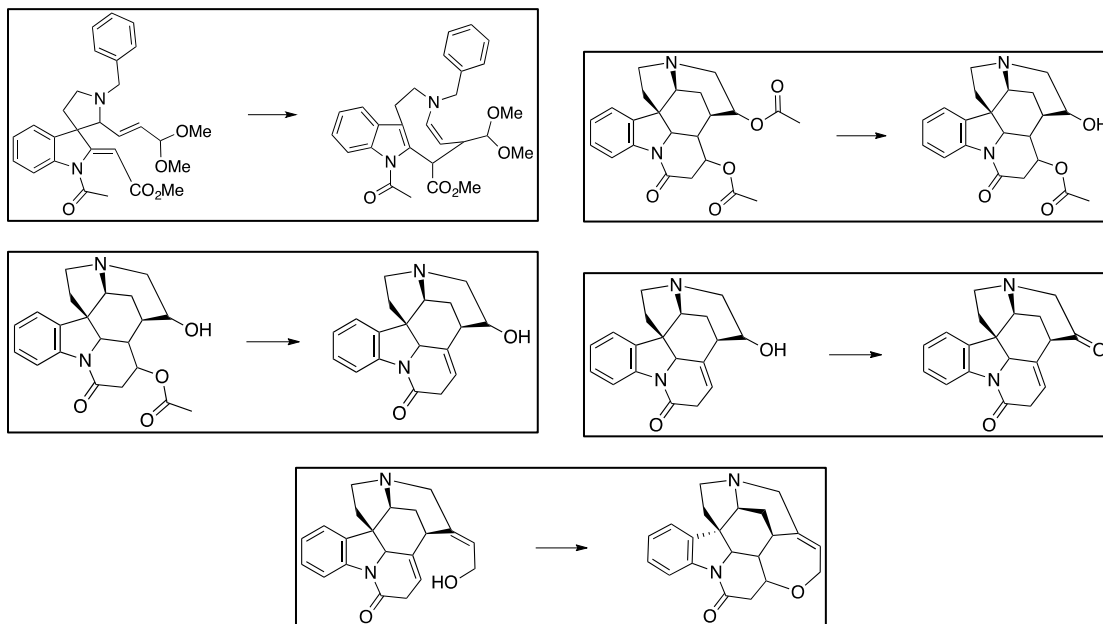


71. (A) Protecting groups are used to prevent the reaction of a functional group when it is not wanted. Trimethylsilyl chloride (abbreviated TMSCl) is often used to protect alcohols and proceeds through the S_N2 mechanism. In the reaction below, draw the mechanism for the protection step. What would the transition state for the S_N2 mechanism look like?

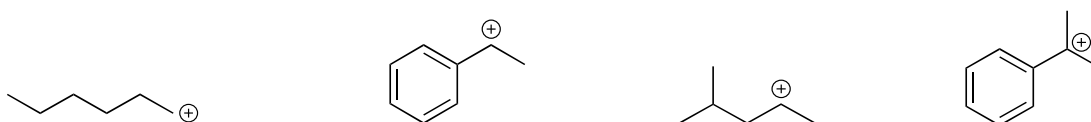


iv. Rearrangement

72. (C) Which of the following transformations from the total synthesis of strychnine represents a rearrangement reaction?



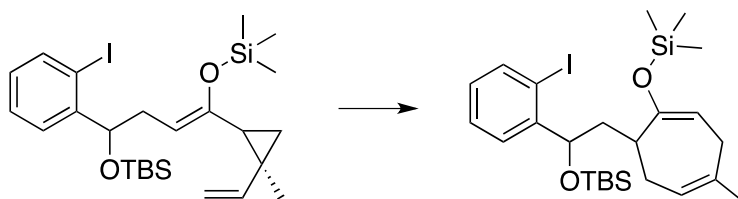
73. (C) Rank the following carbocations from most stable to least stable.



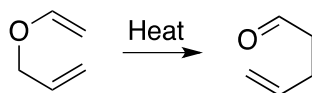
74. (C) Do you expect the following carbocations to undergo rearrangements? If so, draw the resulting carbocation.



75. (I) Draw a curved arrow mechanism for the following rearrangement reaction.

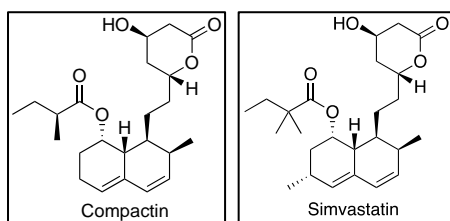
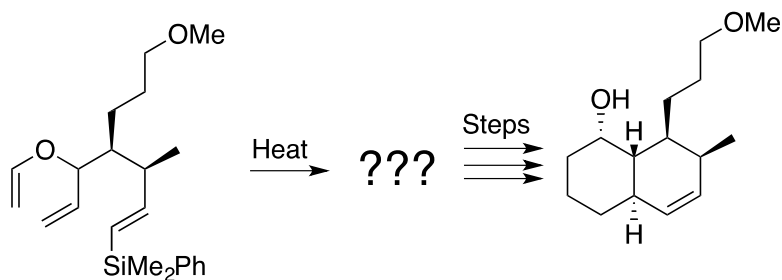


76. (A) Dihydrocompactin is a compound made by fungi that was found to have cholesterol lowering activity, and along with other related compounds, inspired many of that statins (i.e. Simvastatin) used to lower cholesterol in the clinic. In its partial synthesis, a special kind of rearrangement known as a Claisen rearrangement is used. The general reaction is shown below, and occurs due to a movement of electrons resulting in the rearrangement of two pi bonds and one sigma bond.



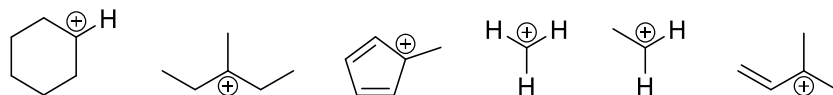
a. Draw curved arrows to show the movement of electrons.

b. Propose a mechanism for the Claisen rearrangement step for the partial synthesis of dihydrocompactin. What is the resulting product? (*Tetrahedron Lett.* **1985**, 26, 1131)

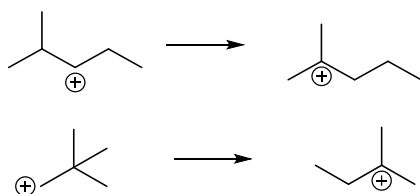


77. (C) What is the common hybridization of a carbocation? Why is a tertiary carbocation more stable than a primary carbocation? Would an allylic or a vinylic carbocation be stable?

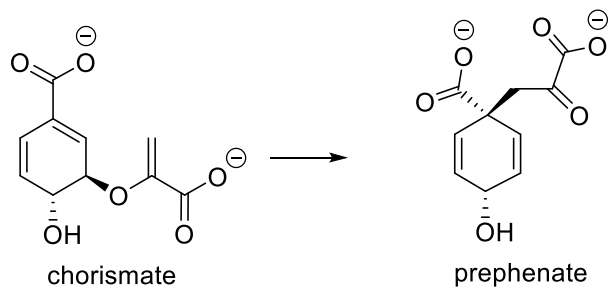
78. (C) Rank the following carbocations in order of increasing stability.



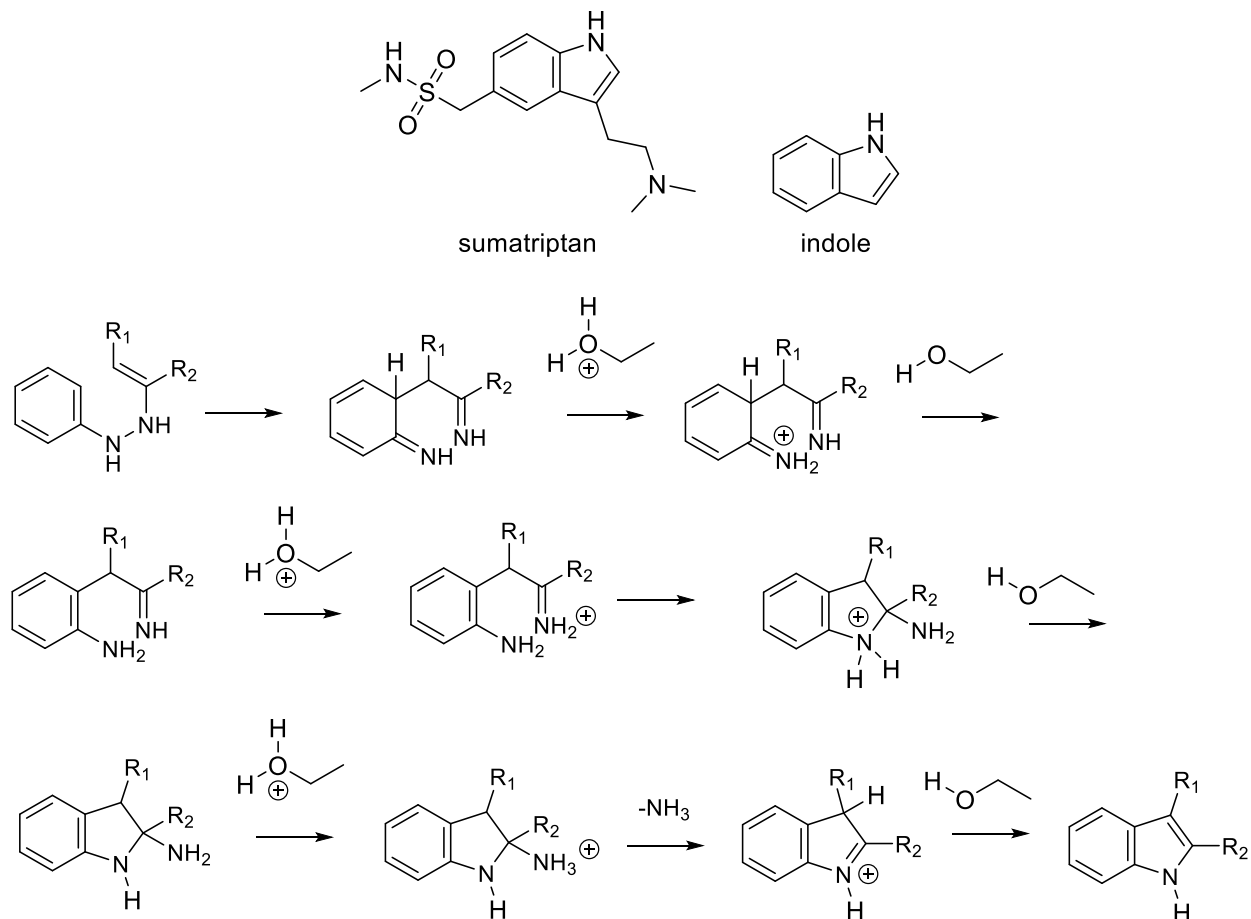
79. (C) Determine what kind of carbocation rearrangement is observed. Draw a reaction energy diagram representing the carbocation rearrangement.



80. (I) Draw the curved arrows for the rearrangement of chorismate into prephenate.

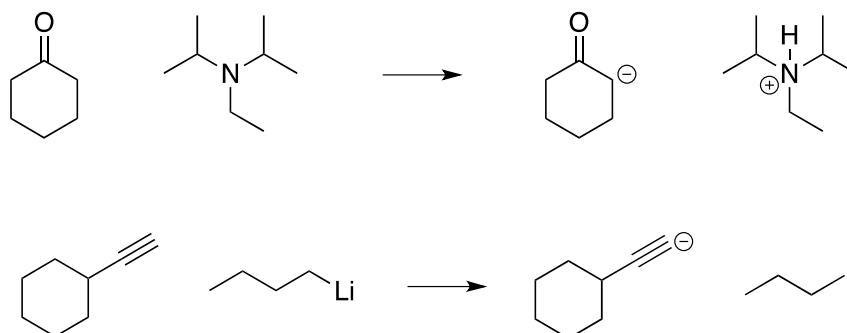


81. (A) Sumatriptan is in the triptan class of drugs, which are used in the treatment of migraines. Triptans are synthetic drugs, and they are often synthesized using the Fischer indole synthesis. Identify the indole core of sumatriptan. Draw in the curved arrows for the Fischer indole mechanism. (*Beilstein J. Org. Chem.* **2011**, DOI: 10.3762/bjoc.7.57)



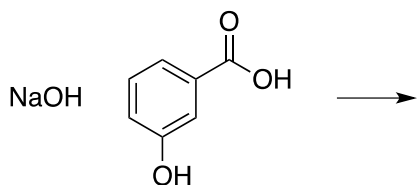
v. Acids and Bases

82. (C) Identify the acid and base in each pair of reactants.

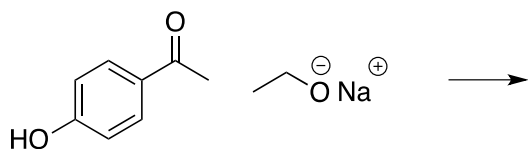


83. (I) Identify the acid and base in the following reactions. Predict the products of the reaction by drawing the conjugate acid and conjugate base of the two reactants.

a.

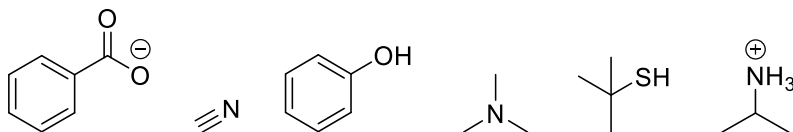


b.

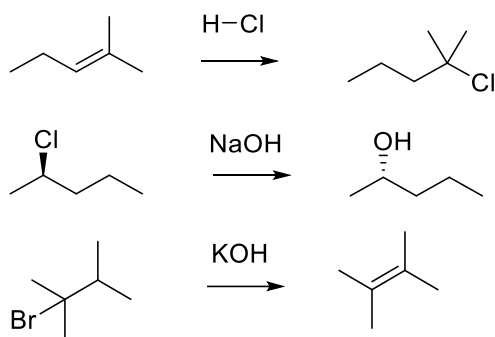


84. (C) Explain why a carbocation would not act as a Brønsted-Lowry acid nor base but could be considered a Lewis acid.

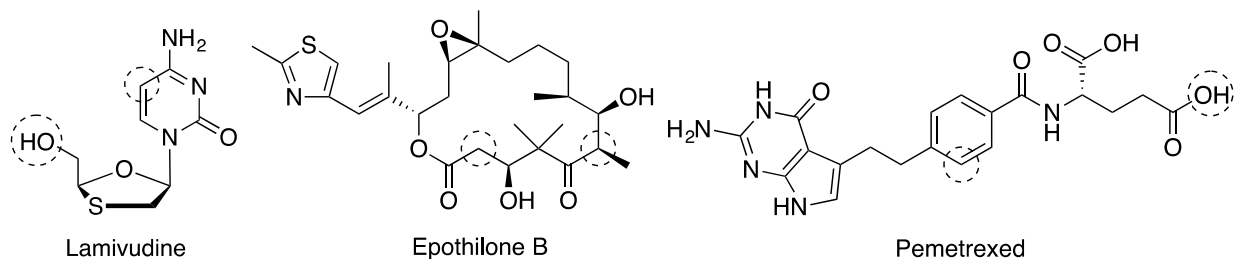
85. (C) Would the following compounds be more likely to act as a Brønsted-Lowry acid or base? Draw the conjugate acid/base.



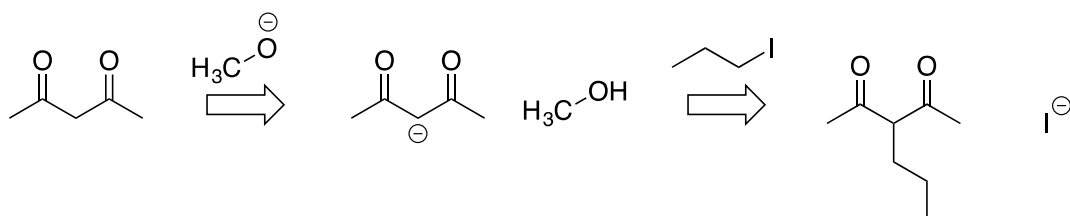
86. (I) Do the following reactions have a proton transfer step? If so, state what is acting as a Brønsted-Lowry acid and what is acting as the base.



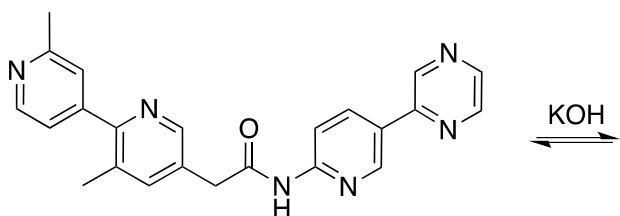
87. (C). What is the approximate pKa of the indicated protons of the following molecule?



88. (I) Complete the following reaction mechanism by including curved arrows. Determine if each step in the mechanism is reversible or irreversible and include the appropriate reaction arrows.



89. (I) Identify the conjugate acids and conjugate bases and complete the reaction. What will be the ratio of reactants to products for the following equilibrium? Can this reaction be considered essentially irreversible?

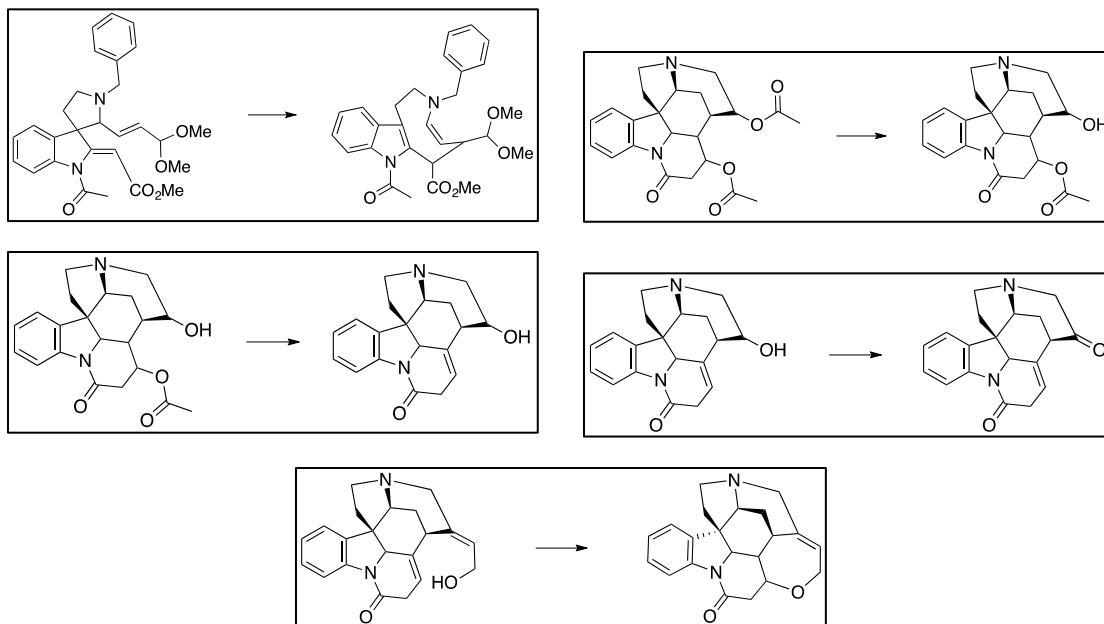


90. (C) Use the Henderson-Hasselbalch equation to prove that the concentration of formic acid and formate are equal when the pH is equal to 3.75. Would this also be true for acetic acid and acetate? If not, what would the

91. (I) Define isoelectric point. What is the isoelectric point of arginine (a basic amino acid), glutamic acid (an acidic amino acid), and valine?

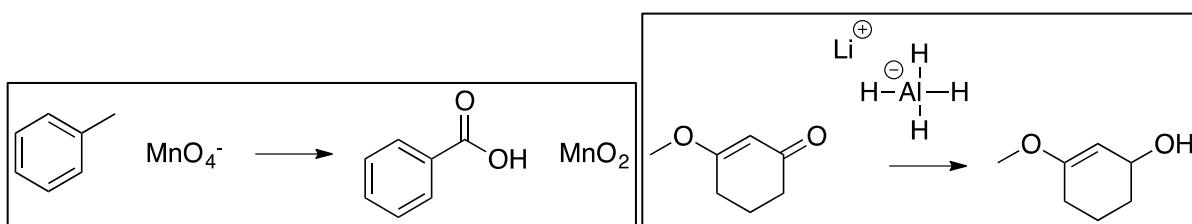
vi. Oxidation and Reduction

92. (C) Which of the following transformations from the total synthesis of strychnine represents an oxidation or reduction reaction?

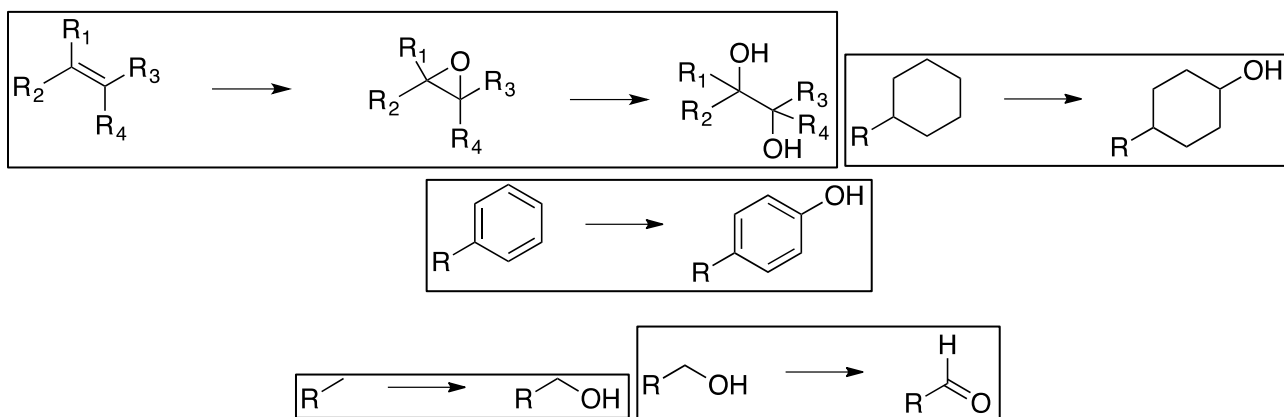


93. (C) Define oxidation and reduction. List three reagents commonly used for these types of reactions.

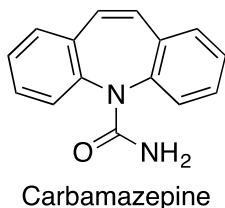
94. (I) In the following reactions, which molecule is oxidized and which molecule is reduced?



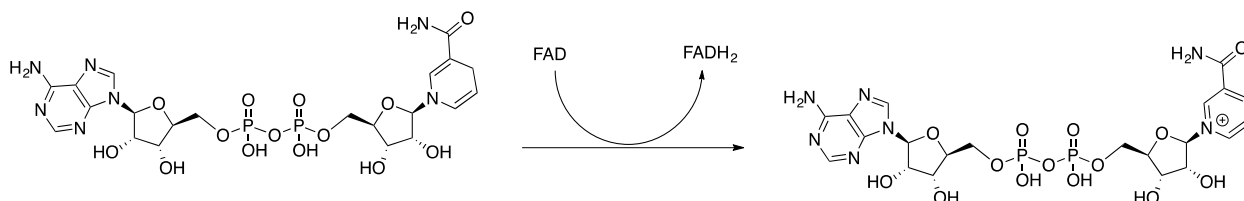
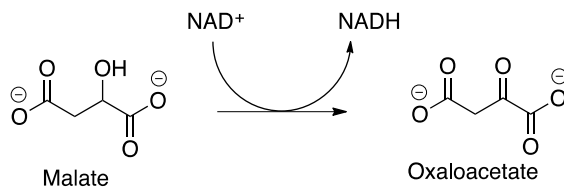
95. (A) In drug metabolism, enzymes in the liver, such as cytochrome P450, carry out reactions as a means of detoxification. Examples of such reactions are shown below.



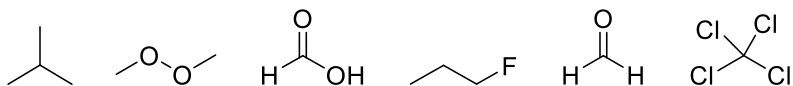
- Are the reactions above examples of oxidation or reduction reactions?
- Draw 3 possible metabolic products for the following drug molecule



96. (A) Many oxidation and reduction reactions occur in biological systems. These are often facilitated by molecules such as nicotinamide adenine dinucleotide and flavin adenine dinucleotide. For the following reactions that occur in biological systems, which molecule is being reduced and which molecule is being oxidized?



97. (C) What is the oxidation state of each atom in the following compounds?



98. (C) Many redox reactions in organic chemistry are given more specific descriptors than “oxidation” or “reduction,” but it is important to recognize what these terms mean as they are ubiquitous. Determine if the following terms would be considered oxidation or reduction. (*J. Chem Ed.* **1997**, DOI: 10.1021/ed074p69)

Addition of hydrogen

Loss of hydrogen

Dehydrogenation

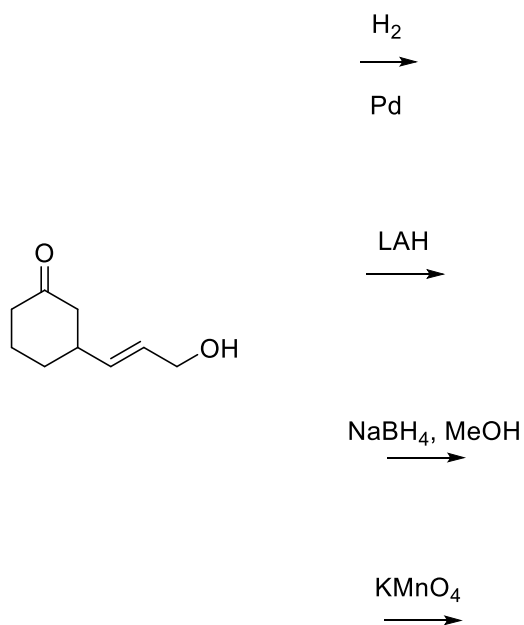
Hydrogenation

Addition of oxygen

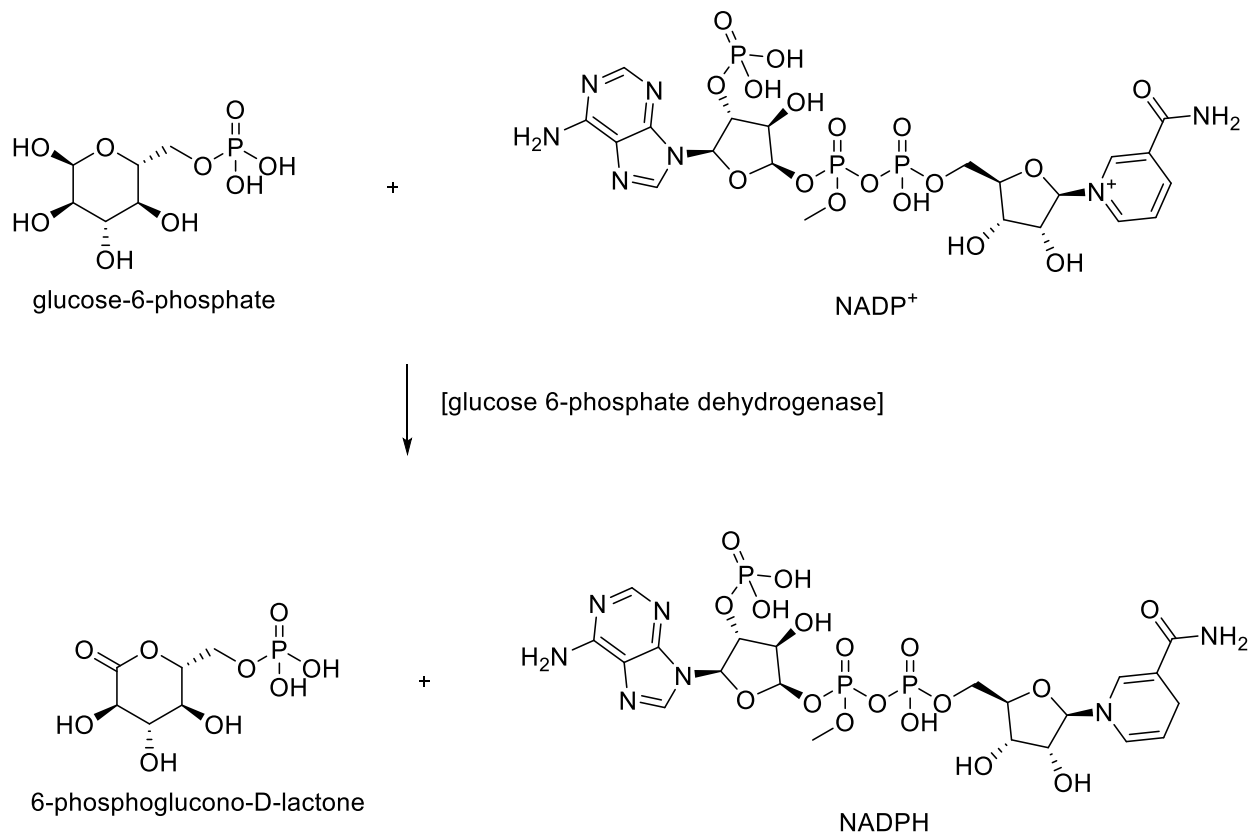
Loss of oxygen

99. (C) What is the most highly oxidized state and the most highly reduced state for carbon? Give an example of a carbon in each state.

100. (I) Predict the product of the following reactions. Are the reagents oxidizing agents or reducing agents?



101. (A) Nicotinamide adenine dinucleotide phosphate, or NADP^+ , is a cofactor for some enzymes in both plants and animals. In animals, NADPH may be produced from the pentose phosphate pathway, as pictured below. Determine what is oxidized and what is reduced. Does NADP^+ act as an oxidizing agent or a reducing agent? What is the role of glucose 6-phosphate dehydrogenase?

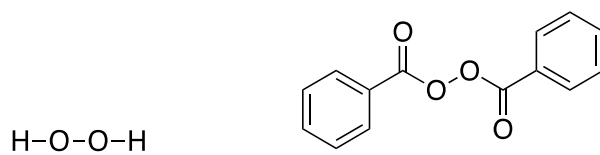


vii. Radicals

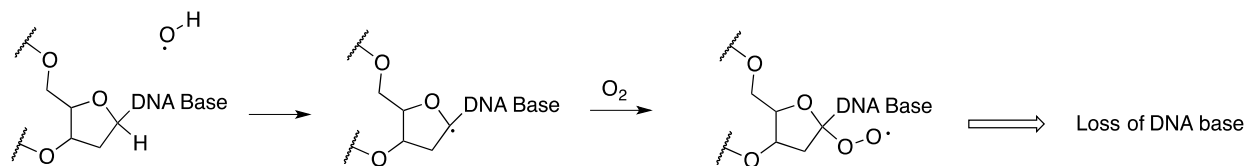
102. (C) Define homolytic and heterolytic bond cleavage. Which type of bond cleavage results in the formation of radicals?

103.(C) What are the three typical steps for a radical reaction mechanism? What occurs during each of these steps?

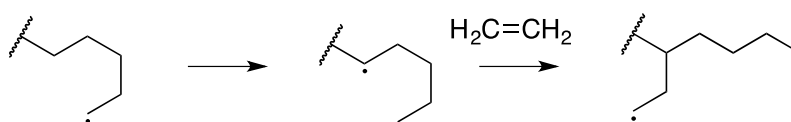
104.(I) For the following common radical initiators, which bond is cleaved to give a radical? Draw a mechanism for the initiation step reaction.



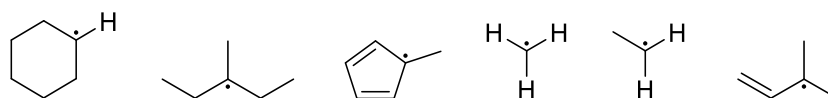
105. (A) As a result of metabolism, free radicals are produced in the body that can cause damage to DNA. One way in which this can occur is through a radical reaction that results in the loss of a DNA base. Complete the following mechanism by drawing curved arrows.



106. (A) Many polymers are made through radical polymerization reactions. Polyethylene, when made through radical polymerization, is considered low density polyethylene (LDPE). This is due to back biting that can occur, leading to branching of the polymer chain. Draw a mechanism for the following back-biting reaction of polyethylene. Why would this back-biting lead to low-density polyethylene?



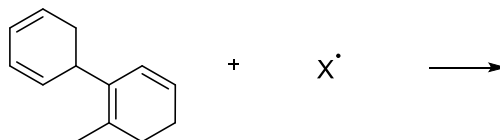
107. (C) Rank the following radicals in increasing order of stability. How does this compare to carbocations?



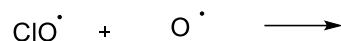
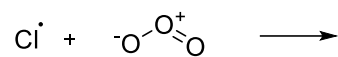
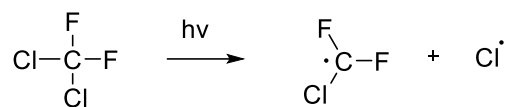
108. (C) What is the only step in a radical reaction that does not result in the formation or propagation of a radical species? Draw a representation of this.

109. (I) Define chain reaction, initiation, propagation, and termination (with respect to chemical reactions). Why might this both be good/useful and harmful?

110. (I) Which carbon is most likely to become a radical due to a hydrogen being abstracted by a radical?



111. (A) Chlorofluorocarbons, or CFCs, are organic compounds known to damage the ozone layer and have been phased out as part of the Montreal Protocol. A study in 2016 showed that the ozone hole above Antarctica has started to shrink, and that the “healing” is due to waning levels of chlorine and bromine in the atmosphere. Complete the reactions below (include arrows). Why would the ozone hole grow during the “winter” months in the Northern Hemisphere (the article reported September)? (*Science* **2016**, DOI: 10.1126/science.aae0061)



ANSWERS TO PROBLEMS

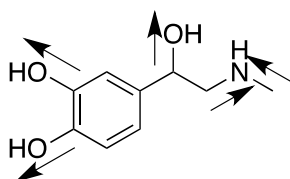
ANSWERS FOR PROBLEM SET 1: GENERAL CHEMISTRY PRINCIPLES

a. Electrons and Bonds

1. (C) 1. NH_3 , CHCl_3 , H_2O

2. NaCl is made up of sodium cations and chloride anions, so it is ionic. $\text{C}_6\text{H}_{12}\text{O}_6$ is made up entirely of covalent bonds and is therefore covalent in nature. While $\text{NaC}_2\text{H}_3\text{O}_2$ has covalent bonds occurring within the acetate anion, it is ionic in nature since the sodium is a cation and the acetate is an anion. $\text{CH}_3\text{CH}_2\text{OCH}_2\text{CH}_3$ is made up entirely of covalent bonds and is covalent in nature. KOH is ionic in nature as it is composed of K^+ and OH^- ions.

3.



4. Amide- sp^2 ; nitrile- sp ; alkane- sp^3 ; isocyanate- sp

5. The hybridization of the nitrogen atom in an amide functional group is sp^2 . This is due to the possibility of resonance as shown by the resonance structures below. The presence of the second resonance structure restricts free rotation about the C-N bond, making polypeptide chains more rigid in nature.

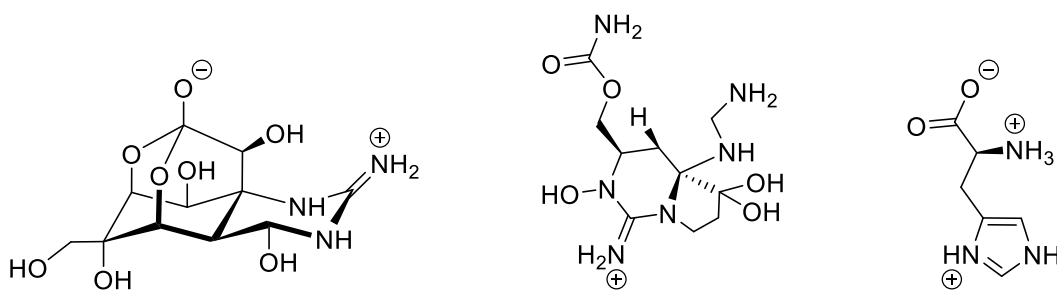


6.

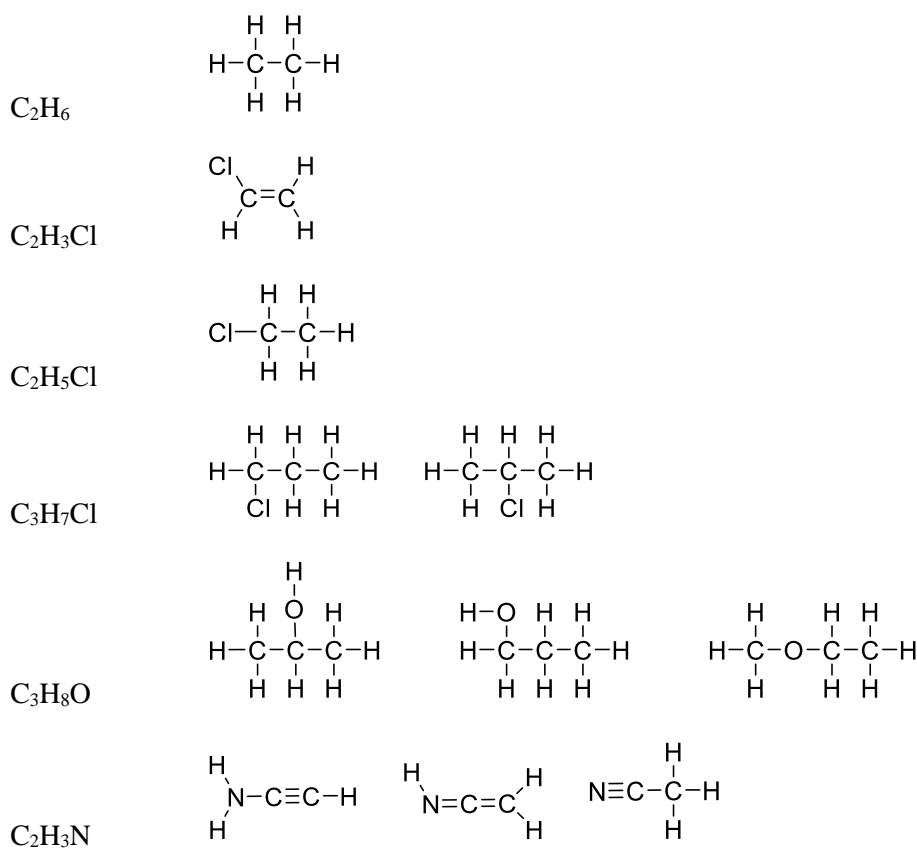
C-H	C-B	C-C	C-N	C-O	C-F	C-P	C-S	C-Cl	C-Br	C-I
NP	NP	NP	NP	P	P	NP	NP	P	P	P

*Based on the Pauling electronegativity scale and common cutoffs ($\Delta\text{EN} = 0.5\text{-}1.7$ is polar), C-Br and C-I would be nonpolar, but these are typically considered polar bonds.

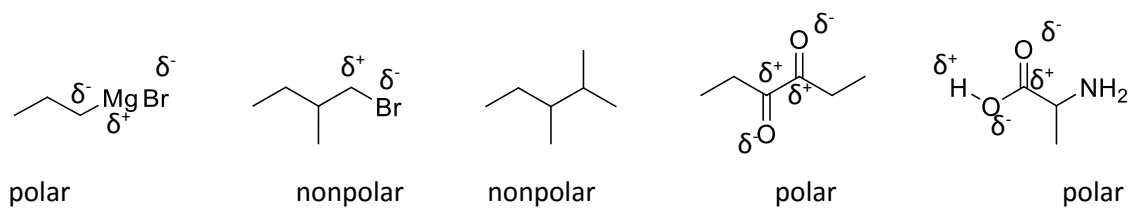
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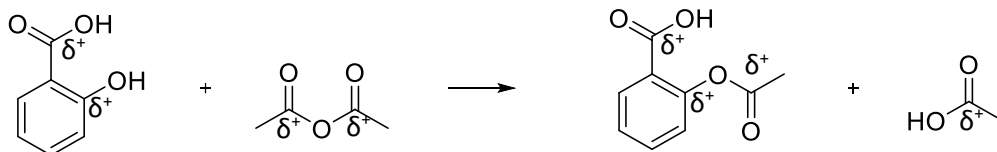
8.



9.

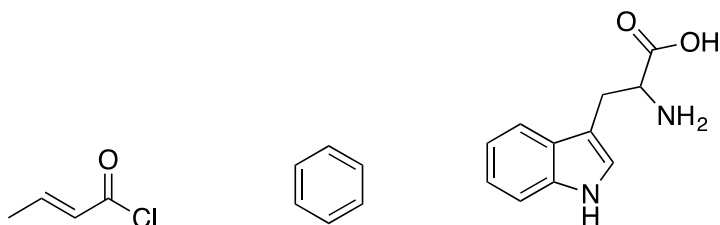


10.

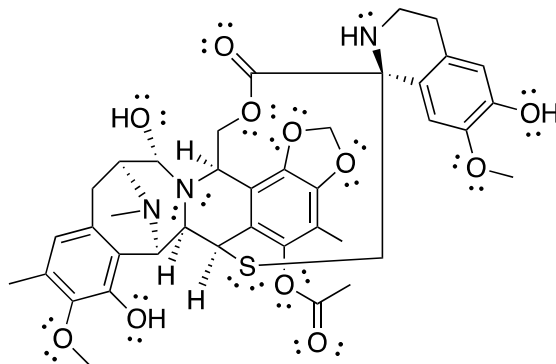


b. Structure and Molecular Representations

11.

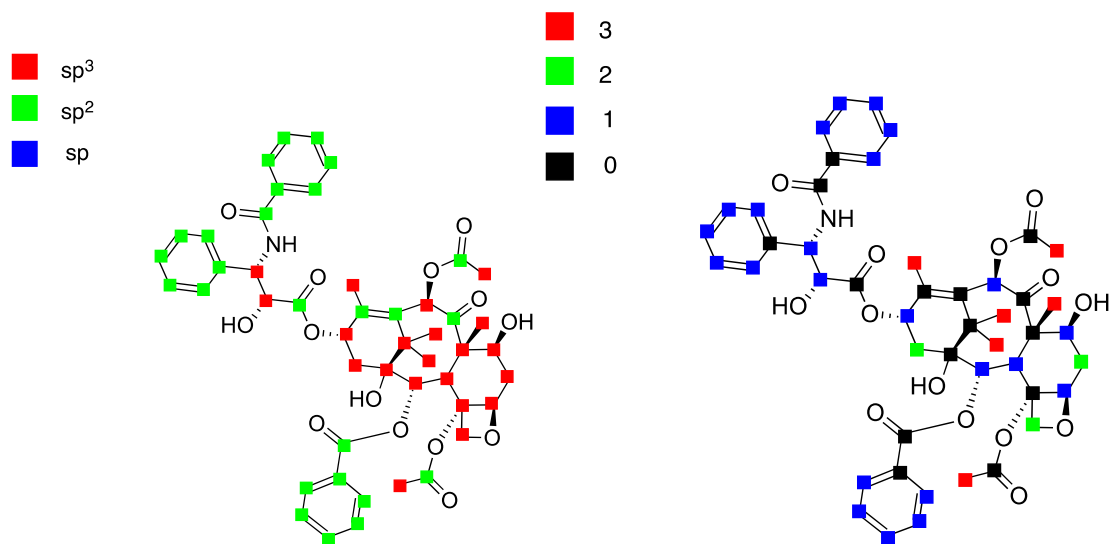


12. Each oxygen and sulfur shown has 2 lone pairs. Each nitrogen shown has 1 lone pair.

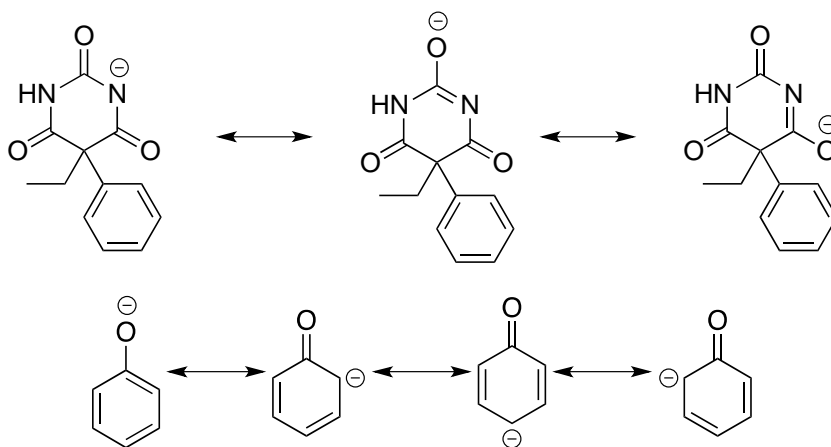


13. The molecular formula for brevetoxin A is $C_{49}H_{70}O_{13}$.

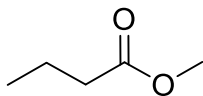
14.



15.

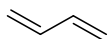
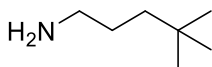
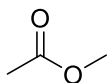
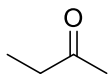
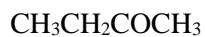
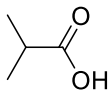


16.

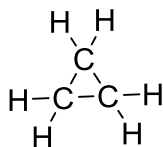


17. These are all the same compound, chloromethane, and it does not matter in which position the chlorine is shown in the Lewis structure. The hybridization of the central atom is sp^3 .

18.



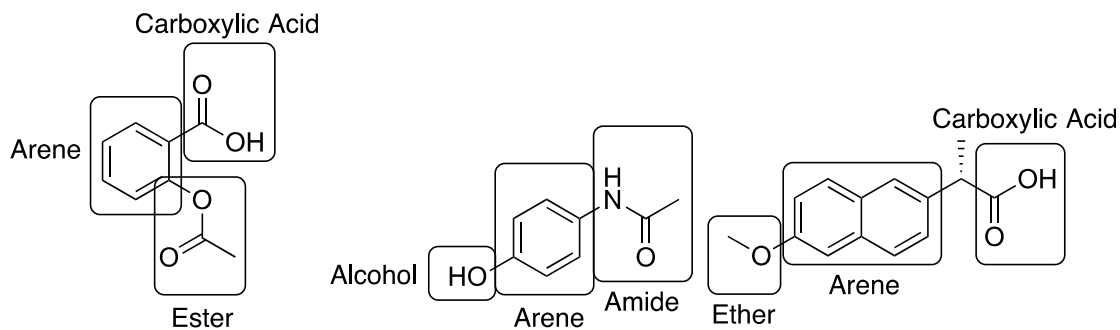
19. The molecule on the left is the least stable because of ring strain.



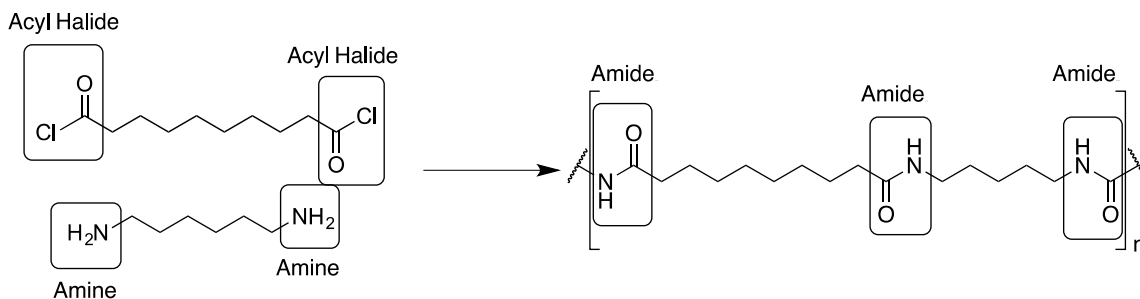
20. The hybridization of the carbon atoms remain the same. The product is more favorable because the ring strain is alleviated.

c. Organic Molecules and Functional Groups

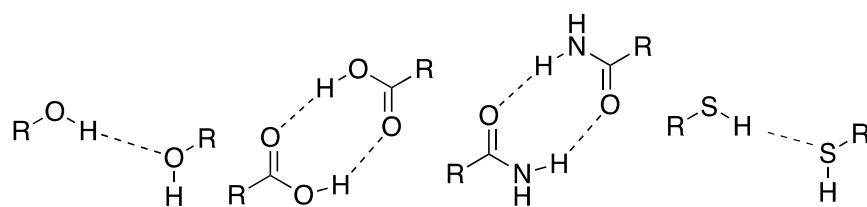
21.



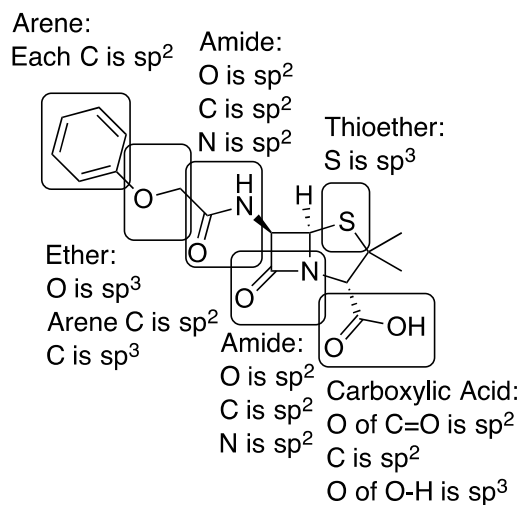
22.



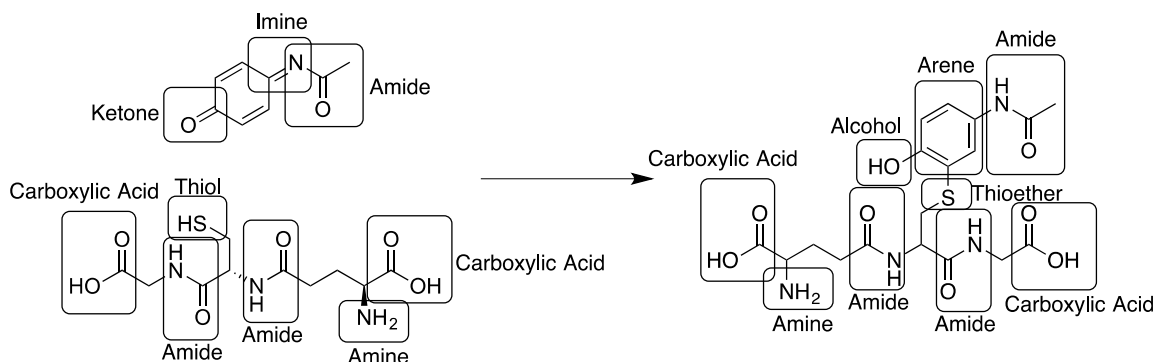
23. Alcohols, carboxylic acids, amides, thiols can participate in hydrogen bonding.



24.



25.



26. All amino acids contain an amine (or amino group) and a carboxylic acid. Depending on the source, you might also say that all amino acids also contain hydrocarbon components. Alanine has no additional functional groups. Phenylalanine has a phenyl (benzene) group. Aspartic acid has an additional carboxylic acid group. Lysine has an additional amino group. Threonine has an alcohol. Cysteine has a thiol group. Glutamine has an amide functional group.

27.

Primary alcohols: 2

Secondary alcohols: 7

Tertiary alcohols: 0

Primary amines: 0

Secondary amines: 0

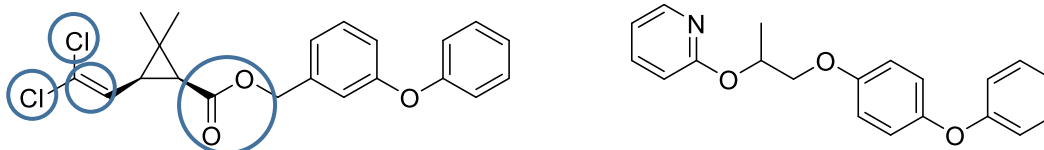
Tertiary amines: 1

Esters: 0

Ethers: 6

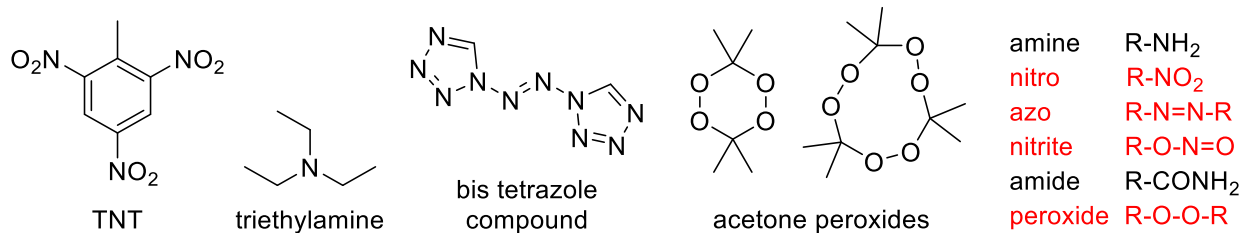
Double bonds: 1

28.



Permethrin has an ester, a double bond (that is not part of a ring), and two chlorines (halides).

29.



The nitro, azo, nitrite, and peroxide groups have the potential to make a compound explosive. They are sometimes called explosophores for this reason.

30. A peptide bond is an amide. There would be 20 amides from the peptide bonds, 2 from the glutamines (GLN), and 2 from the asparagines (ASN) for a total of 24.

d. Intermolecular Forces

31. Lowest to highest boiling point: Methane < propane < butane < hexane < octane

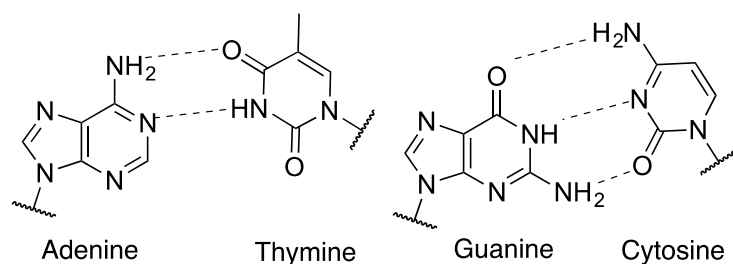
32. Ion-dipole: an attractive force that results from electrostatic forces between an ion and a neutral molecule with a dipole

Hydrogen bonding: a special type of dipole-dipole force that occurs between an electronegative atom and hydrogen that is attached to another electronegative atom

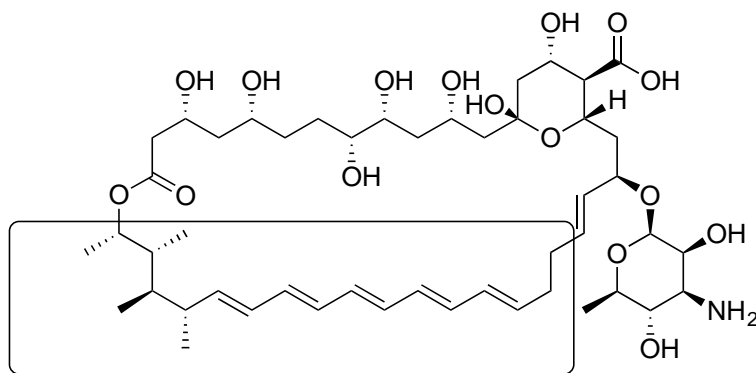
Dispersion forces: an attractive force that occurs as a result of induced dipoles on two molecules.

33. Dispersion forces and hydrogen bonding. Dispersion forces could occur between the atoms of the four rings as well as the alkyl tail of the molecule. Hydrogen bonding could occur between the alcohol functional groups of two cholesterol molecules.

34. Hydrogen bonding is predominant in the pairing of DNA bases. Adenine and thiamine form 2 hydrogen bonds, while cytosine and guanine form 3 hydrogen bonds. Therefore, cytosine and guanine are bound more strongly to one another.



35. The interaction between amphotericin B and the lipids of the cell membrane are dispersion forces. These occur between the fatty acid tails of the lipids of the membrane and the alkene and alkane functional groups of amphotericin B.



36. London-dispersion, dipole-dipole, and hydrogen bonding.

37. Aqueous naproxen would have London dispersion, dipole-dipole, and hydrogen bonding. Aqueous naproxen sodium would have London dispersion, dipole-dipole, hydrogen bonding, and ion-dipole.

38. Vitamins A, D, and E would be more soluble in lipids because they are fairly nonpolar. These (along with K) are known as the “fat-soluble” vitamins. Vitamins B3 and C would be soluble in water as they are very polar. The B vitamins and vitamin C are known as the “water-soluble” vitamins.

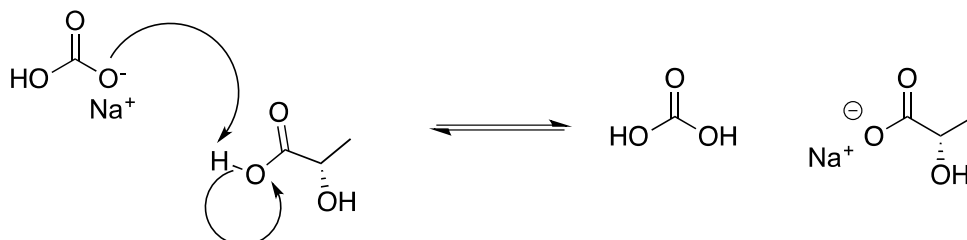
39. Carbon dioxide is nonpolar, so adding a more polar co-solvent such as water will increase the amount of caffeine (moderately polar) extracted.

40. Fipronil would be the most soluble in water, while hydroperene would be least soluble in water.

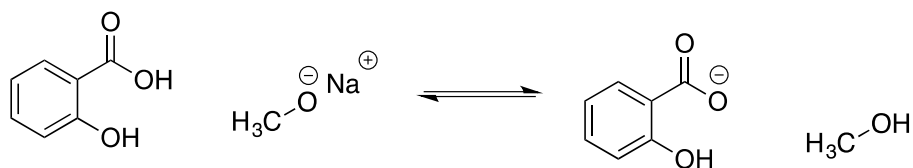
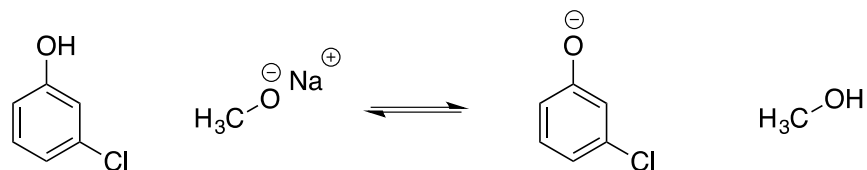
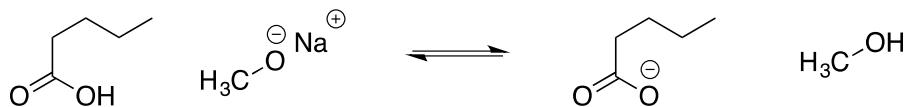
ANSWERS FOR PROBLEM SET 2: ACIDS AND BASES

a. What is a chemical reaction?

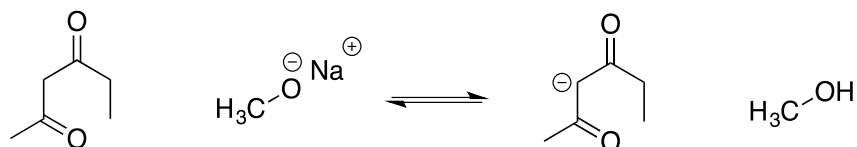
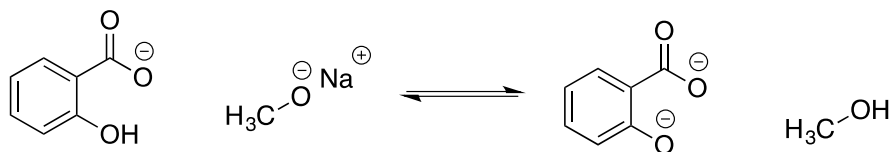
1. The reaction of sodium bicarbonate and lactic acid results in the formation of carbonic acid and lactate.



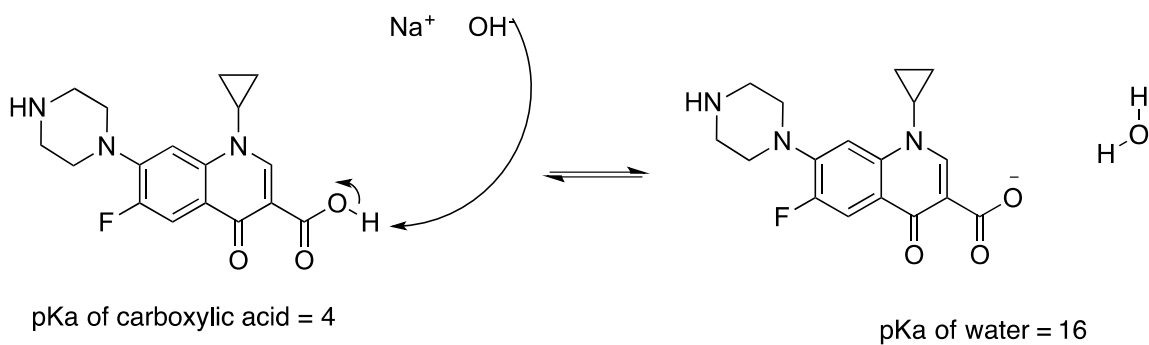
2. All four compounds will act as acids in the presence of sodium methoxide.



(Second deprotonation possible if more base is present)

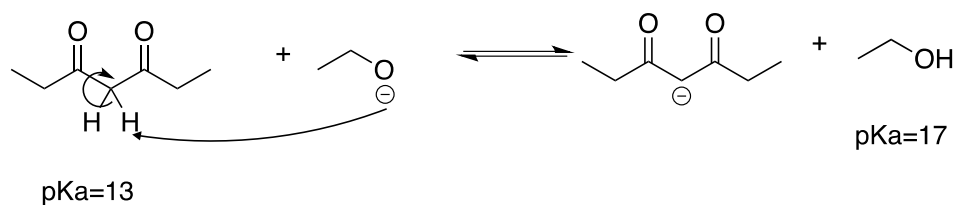


3.



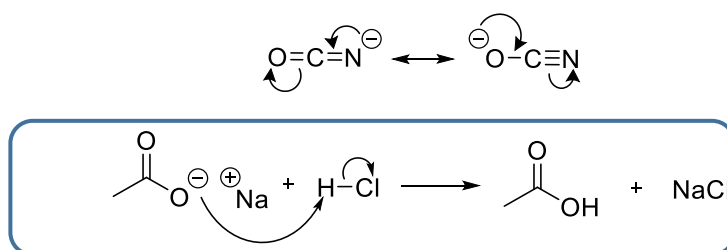
Water is a weaker base than the carboxylic acid of ciprofloxacin, meaning that products will be favored in the equilibrium. Sodium hydroxide is a sufficiently strong base.

4.



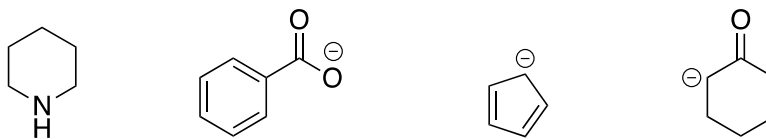
The pKa difference between the reactant and product is 4 pKa units. According to the Henderson-Hasselbalch equation, the ratio of reactants to products will be 1:10,000.

5.



b. Brønsted-Lowry Definition

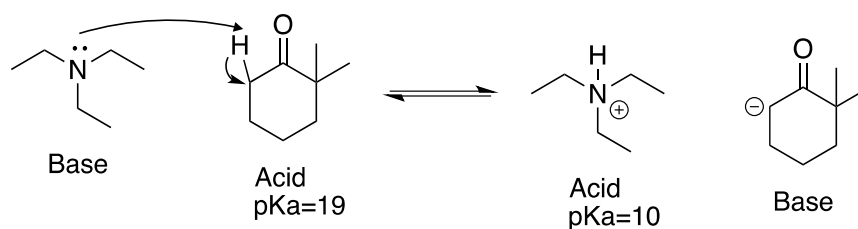
9.



10.

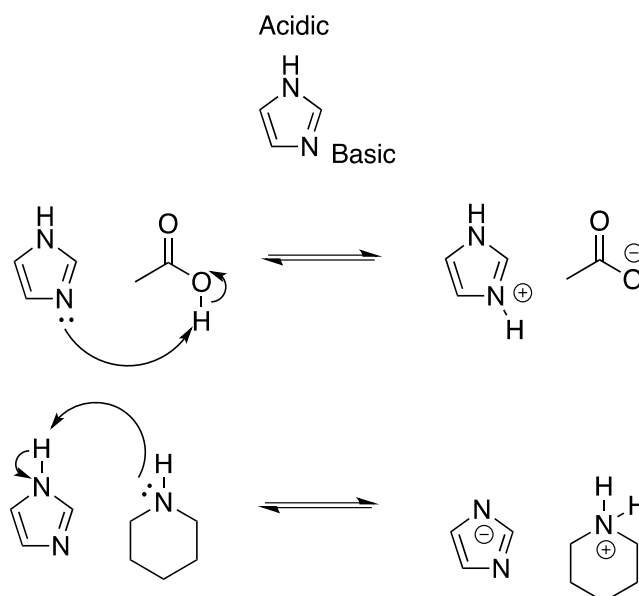


11.

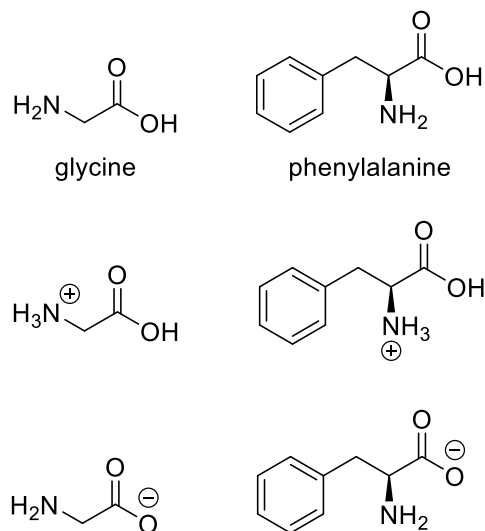


The lower pKa of the protons adjacent to the ketone versus the protonated amine suggest that the reactants are more stable, and therefore, the equilibrium favors the reactants (by a ratio of $10^9:1$).

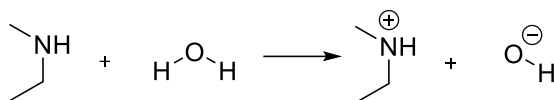
12.



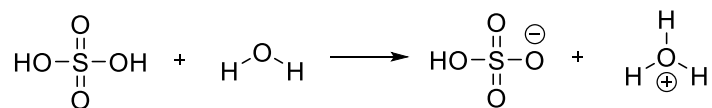
13.



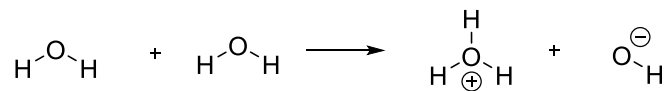
14.



Water donates a proton; acid.

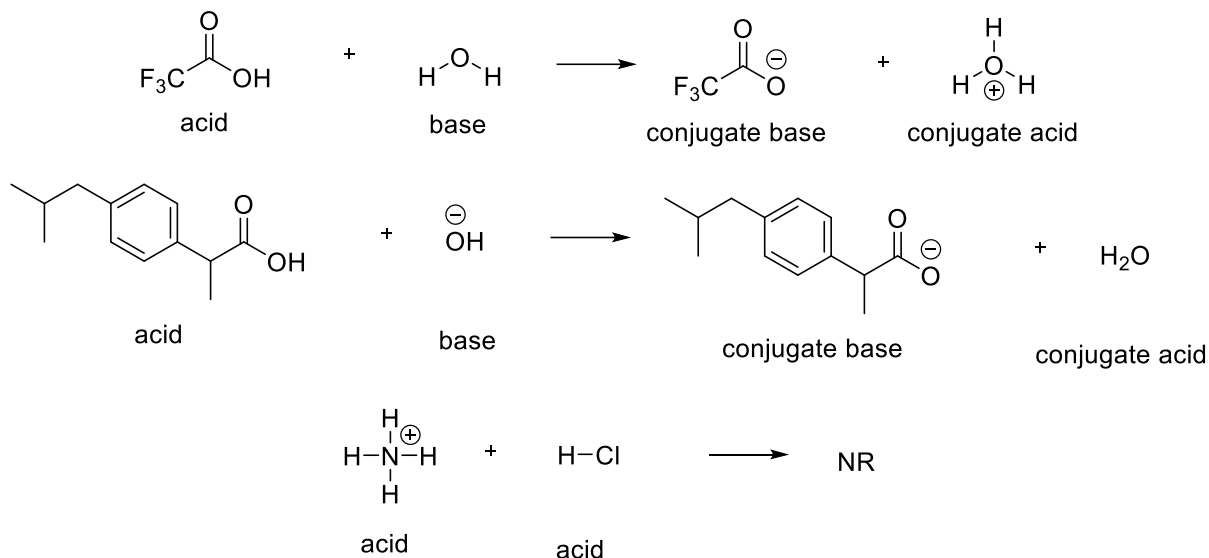


Water accepts a proton; base.

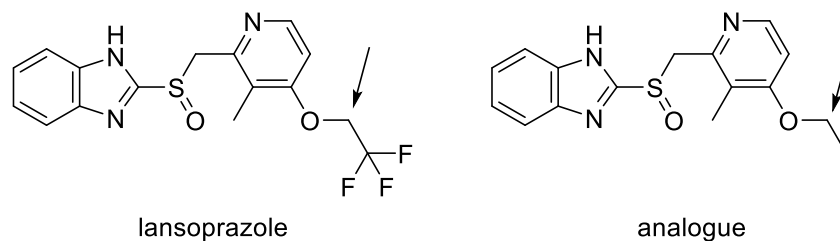


One water molecule accepts a proton and the other water molecule donates a proton; both.

15.



16.



The indicated proton in lansoprazole would be more acidic. Both compounds would be more likely to act as a base (accept a proton) than as an acid (donate a proton).

c. pKa

17. The ratios of protonated to deprotonated species at pH=2, 5, 9, and 14 are:

Compound	pKa	pH=2	pH=5	pH=9	pH=14
Phenol	10	10 ⁸ :1	10 ⁵ :1	10:1	1:10 ⁴
Thiol	13	10 ¹¹ :1	10 ⁸ :1	10,000:1	1:10
Ketone	19	10 ¹⁷ :1	10 ¹⁴ :1	10 ¹⁰ :1	10 ⁵ :1
Carboxylic Acid	4	100:1	1:10	1:10 ⁵	1:10 ¹⁰

18. At pH of 1, all side chains will be protonated ($\text{pH} < \text{pK}_a$ for all side chains). Therefore Arg, His, and Lys will be +1 charge and Glu and Asp will be neutral in charge. Total charge of protein = +3

At pH=3, all will be protonated. Charge = +3

At pH=5, Asp and Glu will be deprotonated (-1 charge each). Total charge = 0

At pH=7, Asp, Glu and His will be deprotonated. Total charge = -1

At pH=9, Asp, Glu and His will be deprotonated. Total charge = -1

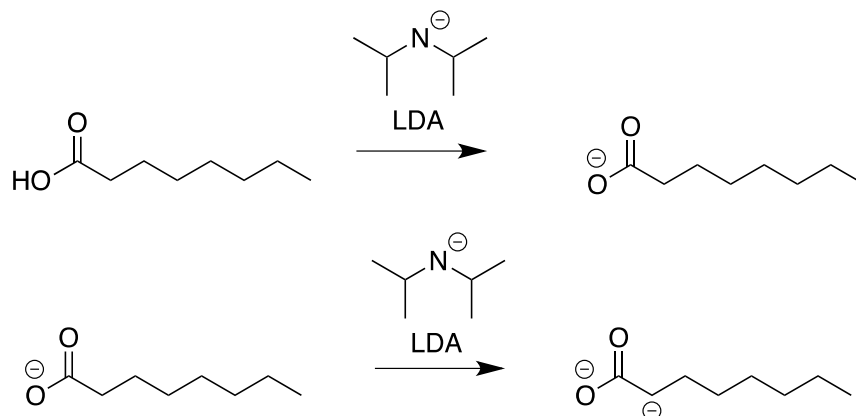
At pH=11, all but Arg are deprotonated. Total charge = -2

At pH=13, all are deprotonated. Total charge = -3

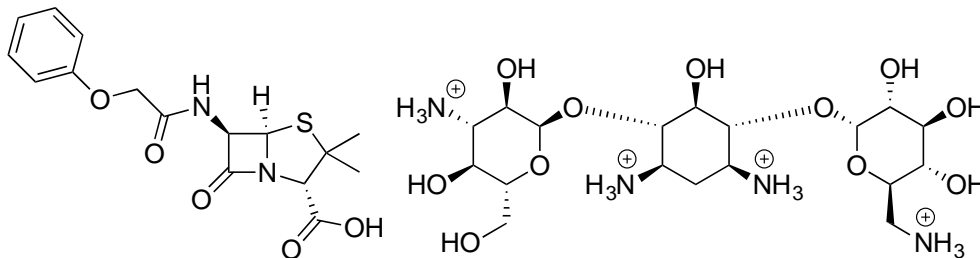
The charges on each amino acid at each pH are shown in the following table

	Ala	Arg	His	Gly	Glu	Pro	Lys	Asp	Ser	Asp	Total
pH=1	0	+1	+1	0	0	0	+1	0	0	0	+3
pH=3	0	+1	+1	0	0	0	+1	0	0	0	+3
pH=5	0	+1	+1	0	-1	0	+1	-1	0	-1	0
pH=7	0	+1	0	0	-1	0	+1	-1	0	-1	-1
pH=9	0	+1	0	0	-1	0	+1	-1	0	-1	-1
pH=11	0	+1	0	0	-1	0	0	-1	0	-1	-2
pH=13	0	0	0	0	-1	0	0	-1	0	-1	-3

19.

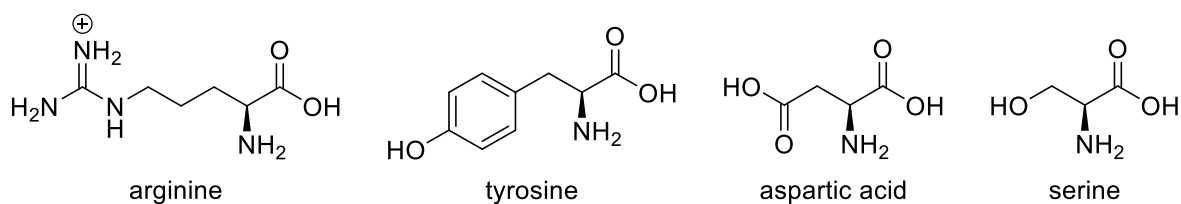


20. At pH=2, the following species will predominate.



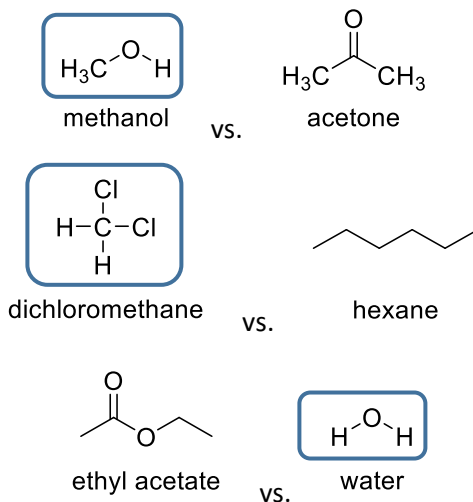
Since penicillin V is uncharged, and kanamycin A has positive charges present, penicillin V will be more easily absorbed under these conditions.

21.

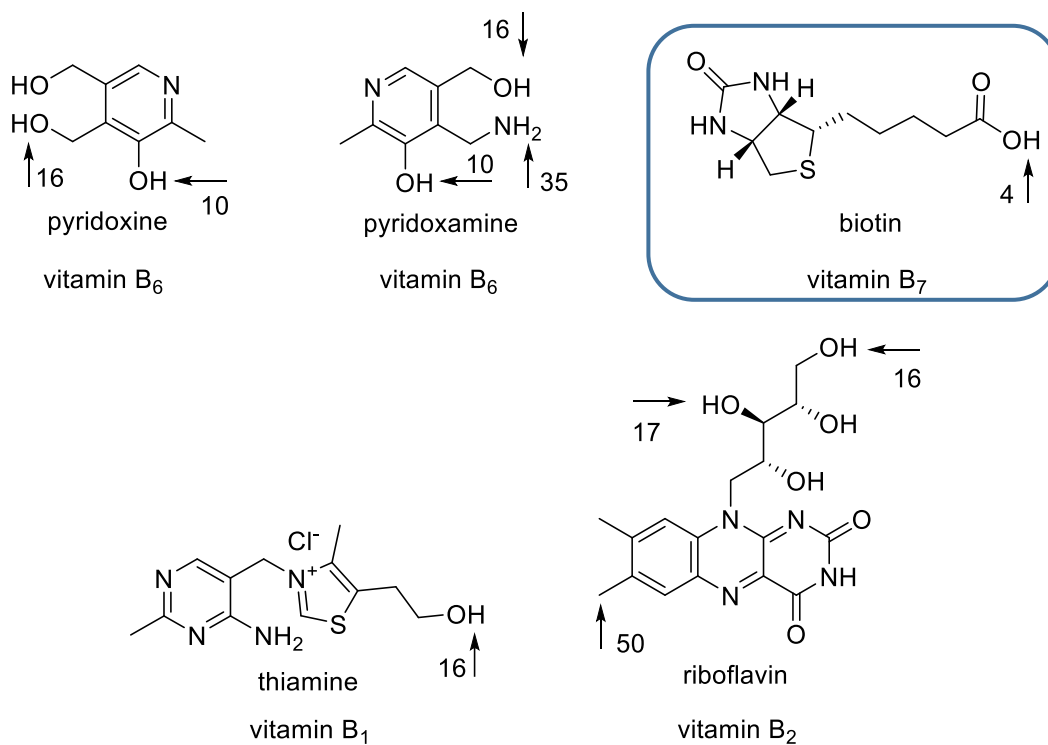


[least acidic] serine (~16) < arginine (12.1) < tyrosine (10.1) < aspartic acid (3.7) [most acidic]

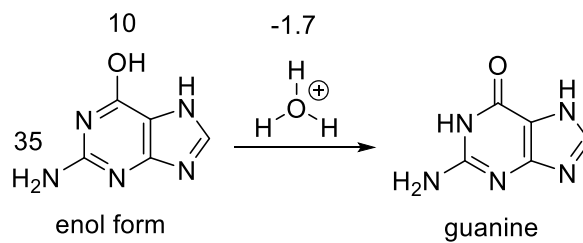
22.



23.



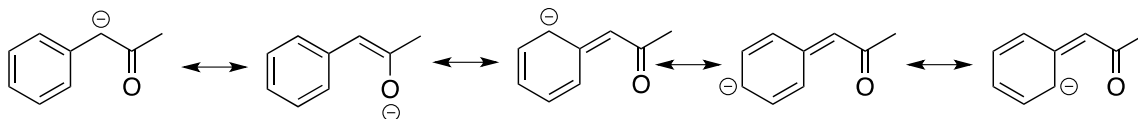
24.



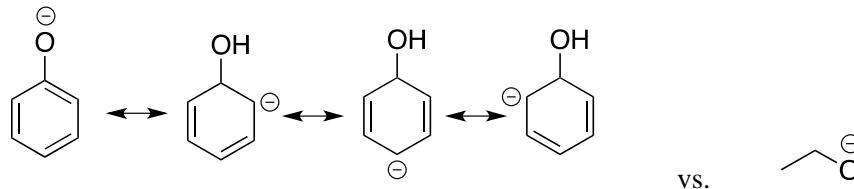
A proton would be lost from the hydronium (H_3O^+) ion. The enol form will accept a proton, so it is acting as a base.

d. Concepts on Resonance

25.



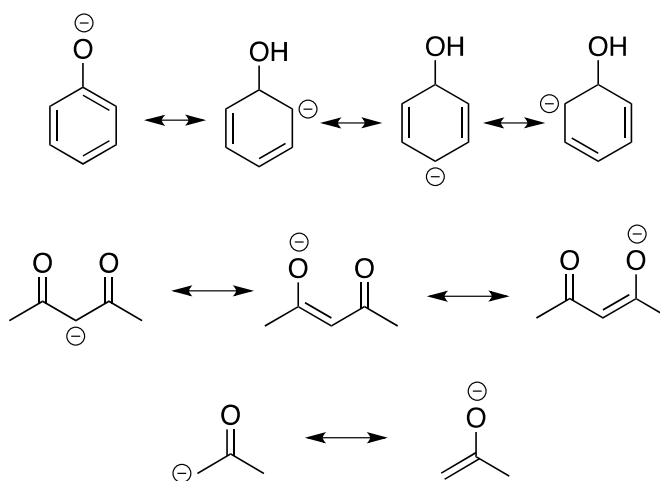
26. pKa of phenol is about 10, while the pKa of ethanol is about 17. The conjugate bases of phenol and ethanol are shown below. Phenol has a lower pKa because its conjugate base is stabilized through resonance while that of ethanol is not.



27.

From most stable to least stable conjugate base: , ,

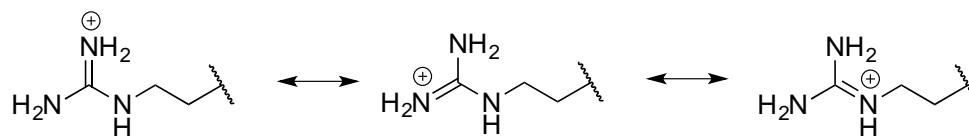
This is due to resonance contributions for stabilize the conjugate base.



28.

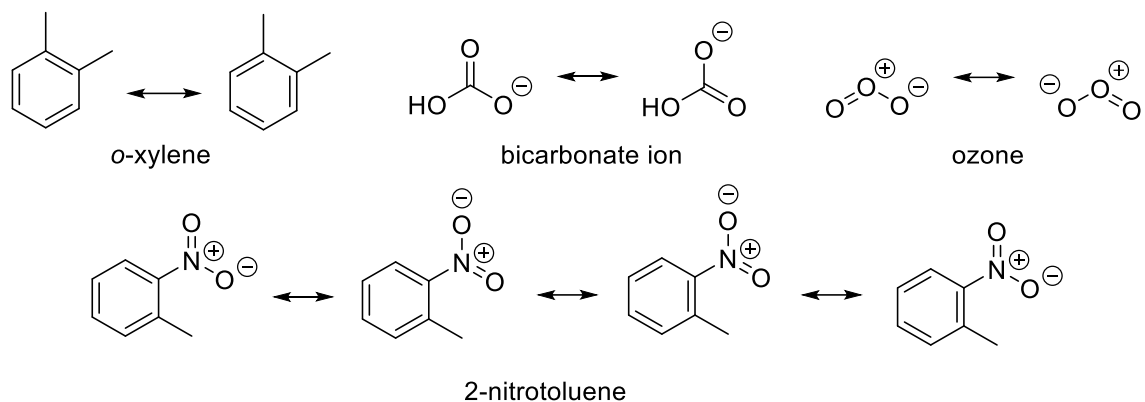
The conjugate acid of the guanidinium side chain is

This can undergo resonance to stabilize the cation as follows.

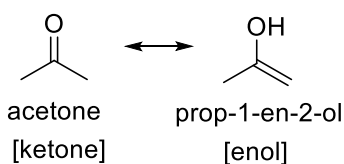


Since phosphates are negatively charged, having a very basic amino acid in the active site would be beneficial due to its being protonated and positively charged at a wide range of pH.

29.

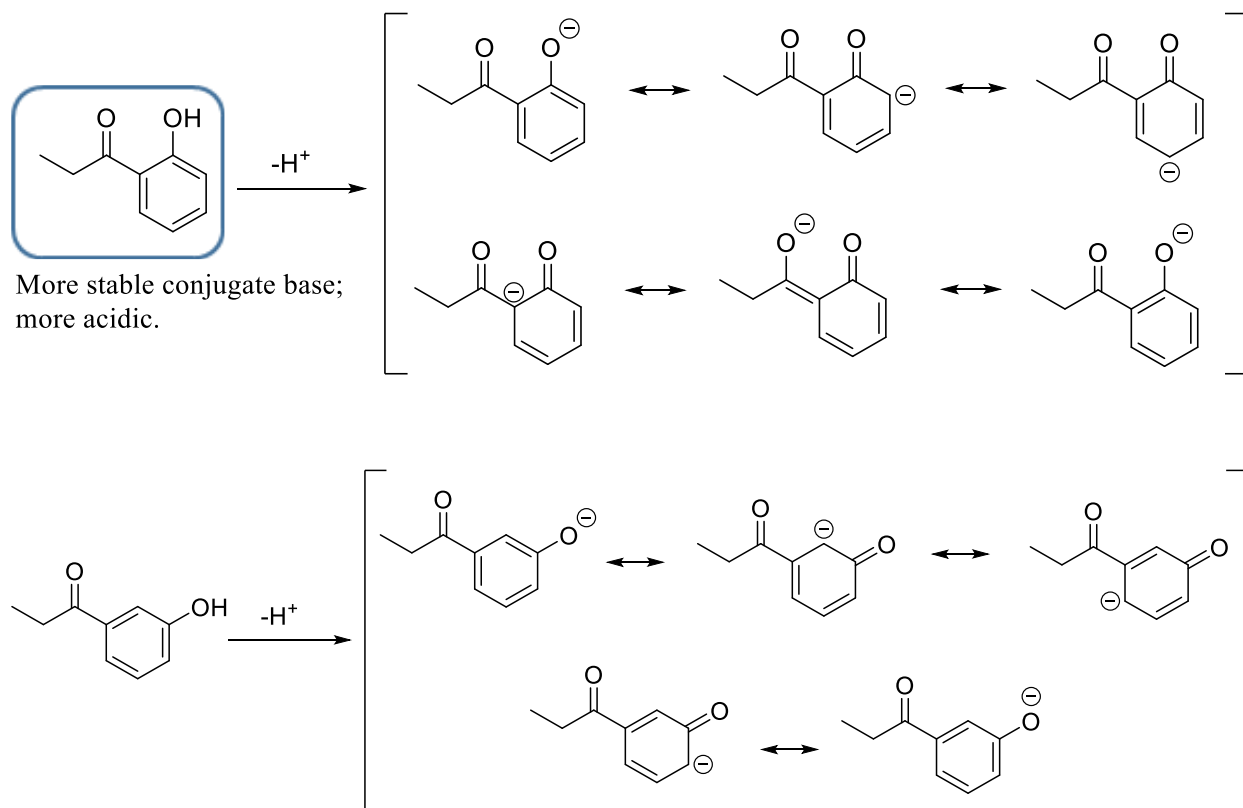


30.

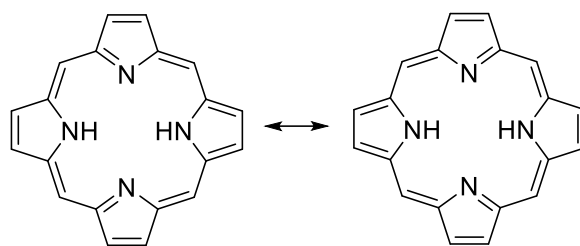


Resonance structures will have the same connectivity while showing the delocalization of electrons. Acetone and prop-1-en-2-ol differ in the connectivity of the atoms; these show isomerism not resonance.

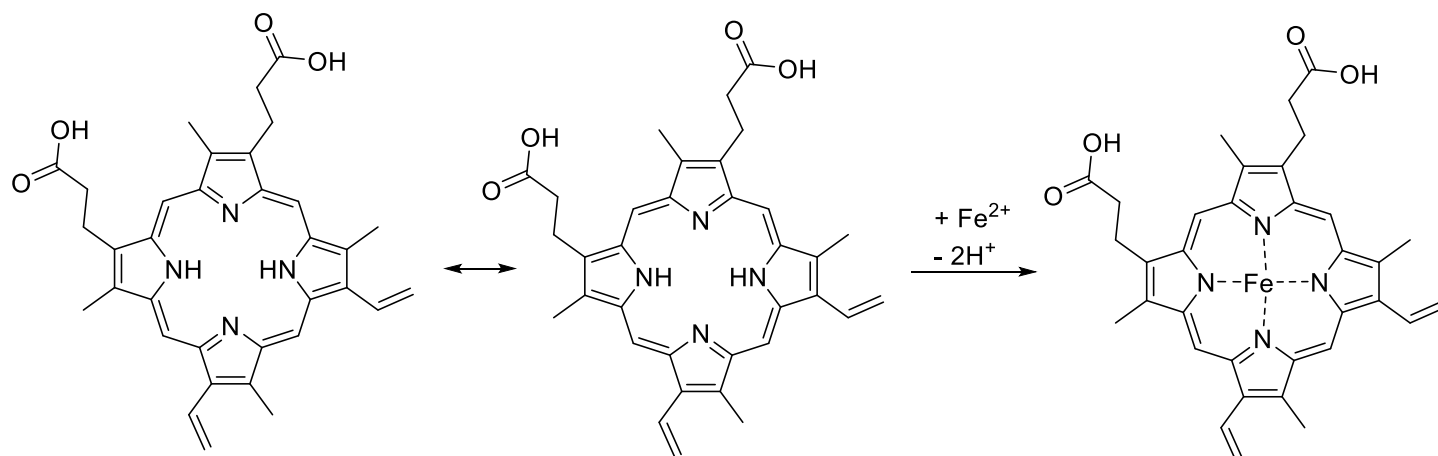
31.



32.

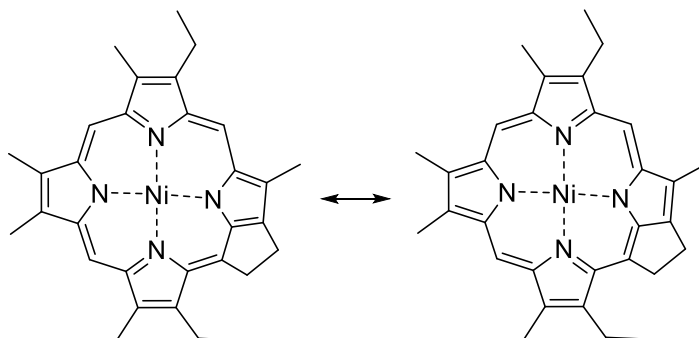


porphin



protoporphyrin IX

heme B

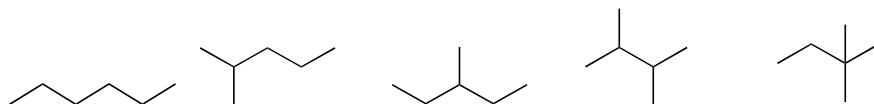


abelsonite

ANSWERS FOR PROBLEM SET 3: ALKANES AND CYCLOALKANES

a. Drawing Organic Compounds

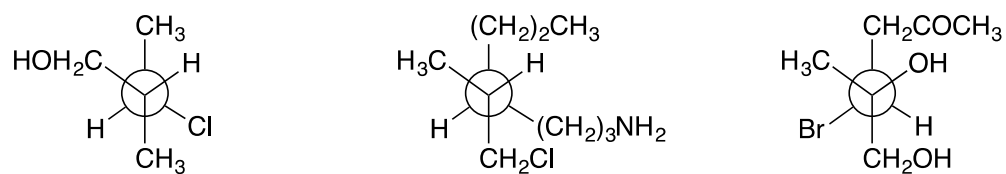
1. C_6H_{14}



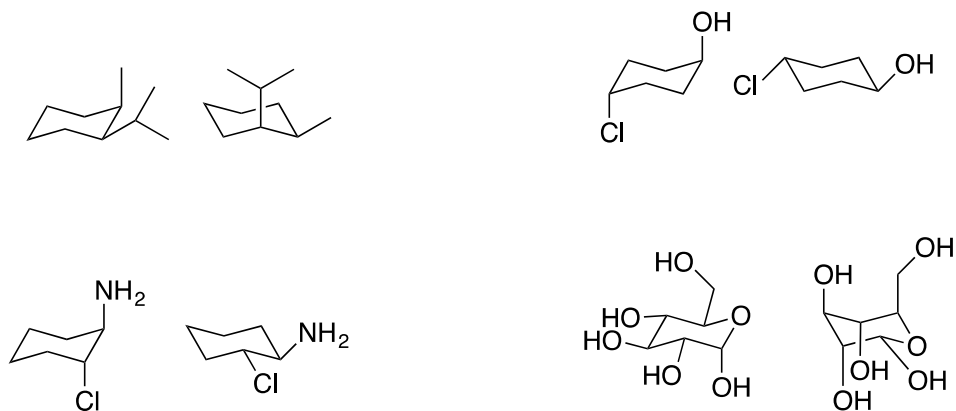
C_4H_{10}



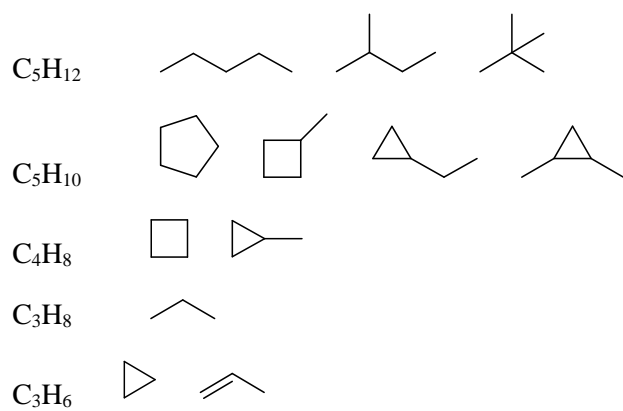
2.



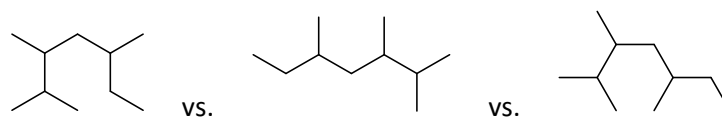
3.



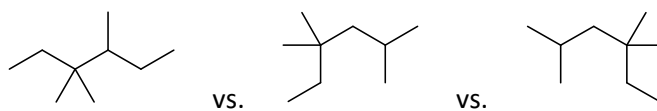
7.



8.

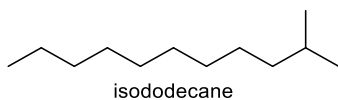


All are the same.

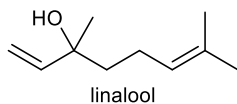


The left compound is different. The middle and the right are the same.

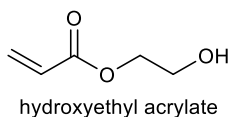
9.



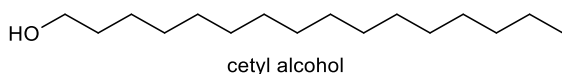
Isododecane is an alkane and has no additional functional groups.



Linalool is an alkene and has an alcohol group.

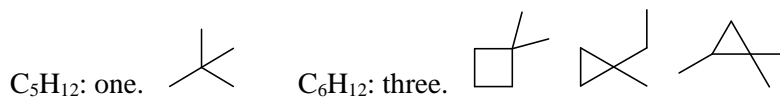


Hydroxyethyl acetate is an alkene and has an ester and an alcohol group.

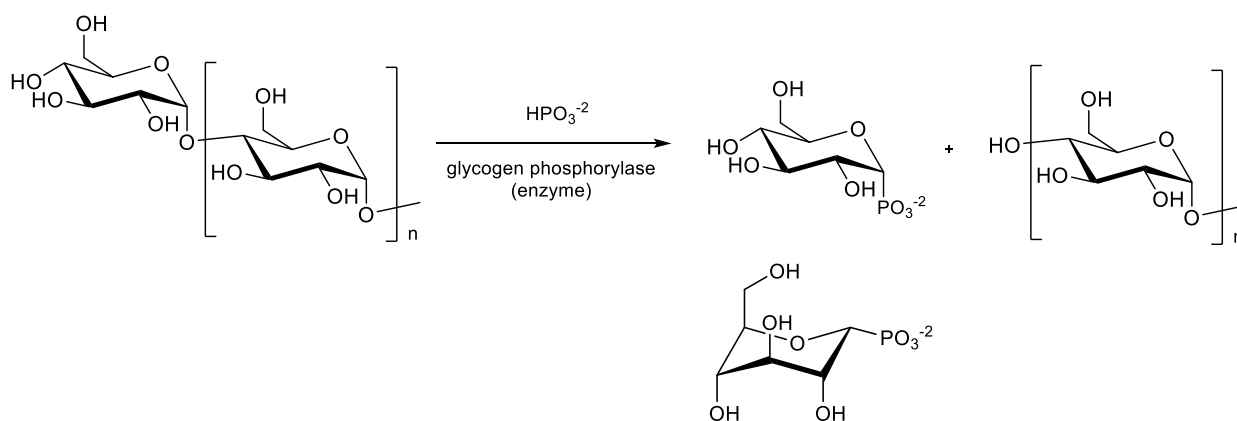


Cetyl alcohol is an alkane with an alcohol group.

10.

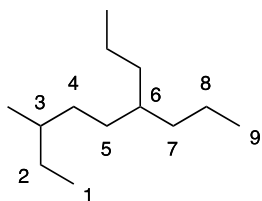


11

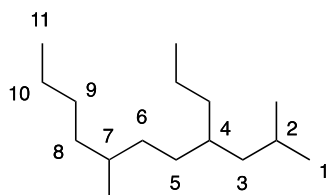


b. Parent Chain and Substituents

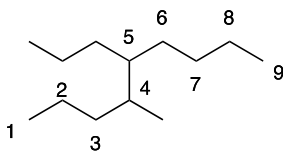
12.



Parent chain = 9 carbons

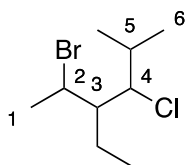


Parent chain = 11 carbons

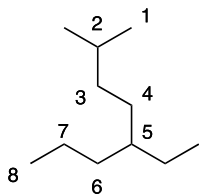


Parent chain = 9 carbons

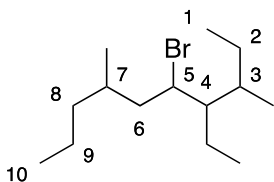
13.



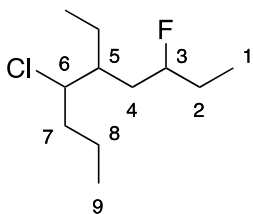
2-bromo; 4-chloro; 3-ethyl; 5-methyl



2-methyl; 5-ethyl

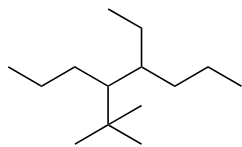


3-methyl; 4-ethyl; 5-bromo; 7-methyl

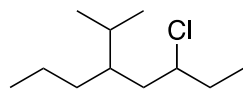
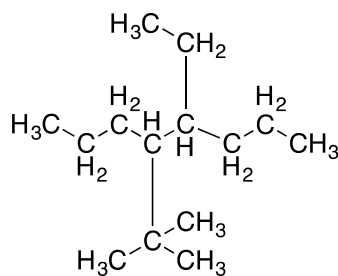


3-fluoro; 5-ethyl; 6-chloro

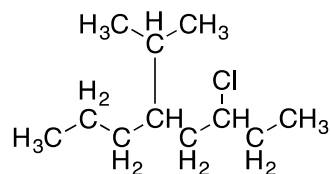
14.



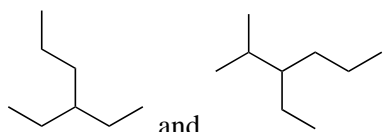
4-(*tert*-butyl)-5-ethyloctane



3-chloro-5-isopropyloctane

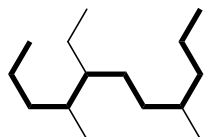


15.

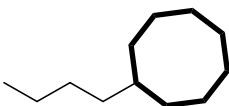


and . Both have 6 carbons in their parent chains. The parent chain of the first contains 13 hydrogens. The parent chain of the second contains 12 hydrogens. This is due to the presence of 1 substituent on the first parent chain versus 2 substituents present on the second parent chain.

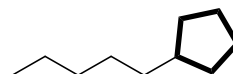
16.



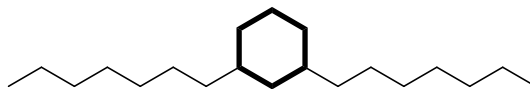
11 C = undecane



8 C in ring = cyclooctane

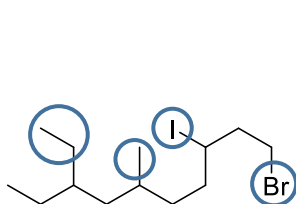


5 C in ring = cyclopentane

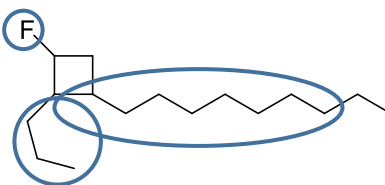


6 C in ring = cyclohexane

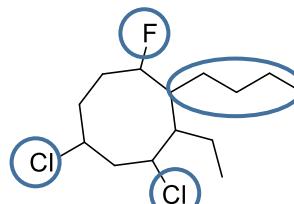
17.



1-bromo
8-ethyl
3-iodo
6-methyl

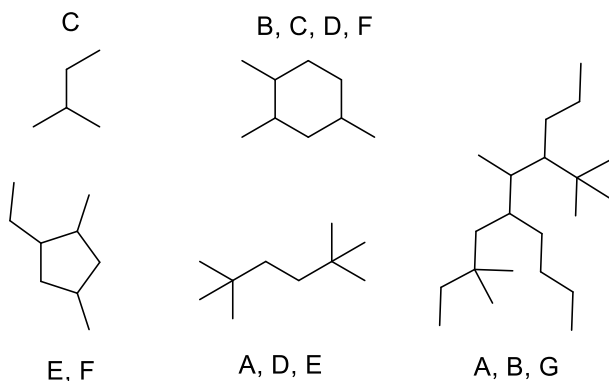


1-fluoro
3-nonyl
2-propyl



2-butyl
4,6-dichloro
3-ethyl
1-fluoro

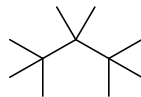
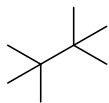
18.



Descriptions

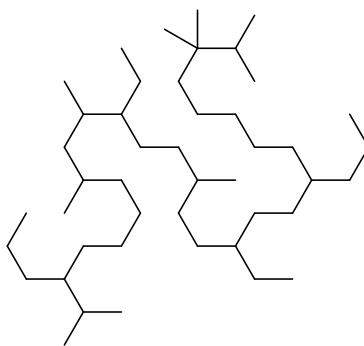
- A. 2 quaternary carbons
- B. 3 tertiary carbons
- C. 3 primary carbons
- D. 6 C in parent chain
- E. 4 total C in substituents
- F. 3 total substituents
- G. 3 different substituents

19. 4 on a parent chain of butane and 6 on a parent chain of pentane.



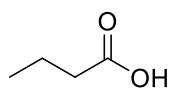
2,2,3,3-tetramethylbutane 2,2,3,3,4,4-hexamethylpentane

20.

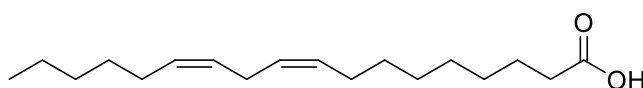


There are 13 R-CH₃ groups; 6 are methyl substituents.

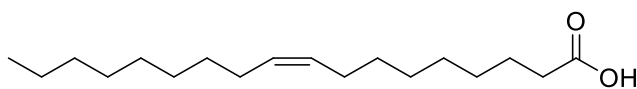
21.



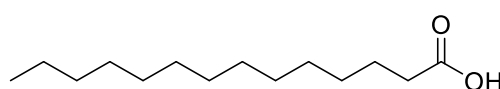
butyric acid
butter



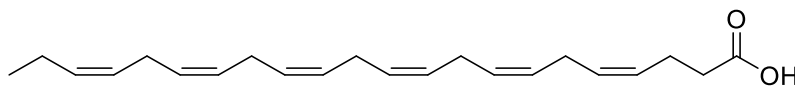
linoleic acid
corn and peanut oil, almonds



oleic acid
butter



myristic acid
dairy



docosahexaenoic acid (DHA)
fish

Butyric acid has 4 C in the parent chain, is an alkane, and would be classified as saturated.

Linoleic acid has 18 C in the parent chain, is an alkene, and would be classified as unsaturated.

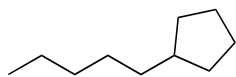
Oleic acid has 18 C in the parent chain, is an alkene, and would be classified as unsaturated.

Myristic acid has 14 C in the parent chain, is an alkane, and would be classified as saturated.

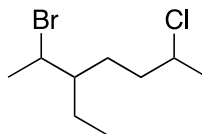
DHA has 22 C in the parent chain, is an alkene, and would be classified as unsaturated.

c. Introduction to Naming Organic Compounds and IUPAC Nomenclature

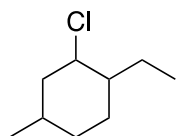
22.



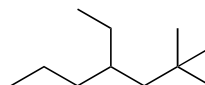
pentylcyclopentane



2-bromo-6-chloro-3-ethylheptane

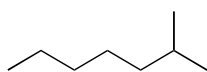


2-chloro-1-ethyl-4-methylcyclohexane

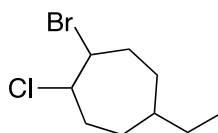


4-ethyl-2,2-dimethylheptane

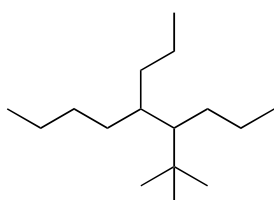
23.



a. 2-methylheptane



b. 1-bromo-2-chloro-5-ethylcycloheptane



c. 4-(1,1-dimethylethyl)-5-propylnonane

24.

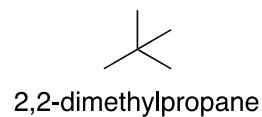
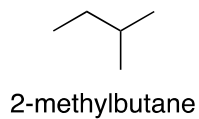
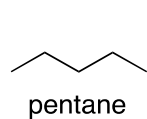
a. Should be 1-bromo-2-chlorocyclohexane. Numbers corresponding to substituents should be minimized as much as possible.

b. Should be 3-ethyl-4-methylnonane. Parent chain is nine carbons long instead of eight.

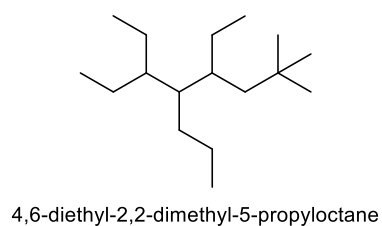
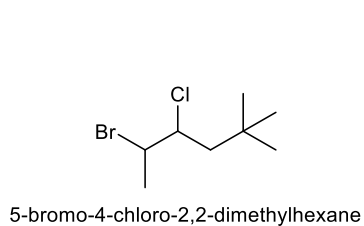
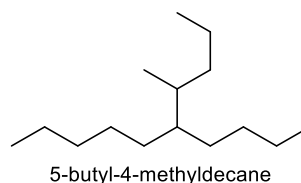
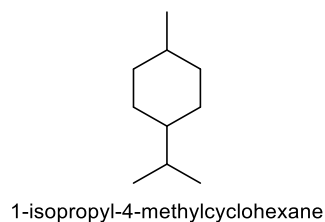
c. Should be 5-ethyldecane. Parent chain is 10 carbons long, not six carbons long.

d. This is the correct name.

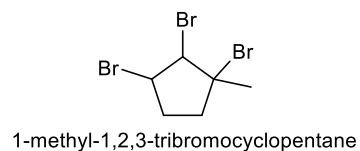
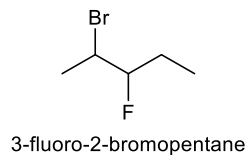
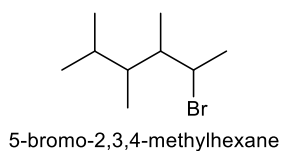
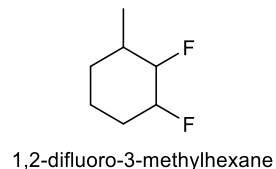
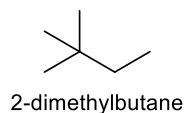
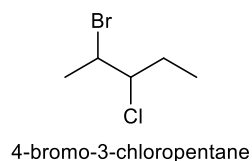
25.



26.



27.



Substituents should have lowest possible numbers: 2-bromo-3-chloropentane.

Locants must be given for both methyl groups: 2,2-dimethylbutane

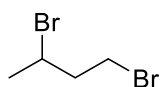
The parent chain is a ring: 1,2-difluoro-3-methylcyclohexane

The number of substituents must be stated with a prefix: 5-bromo-2,3,4-trimethylhexane

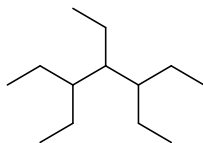
Substituents should be in alphabetical order: 2-bromo-3-fluoropentane.

Substituents should be in alphabetical order (ignoring prefixes): 1,2,3-tribromo-1-methylcyclopentane.

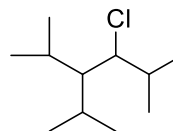
28.



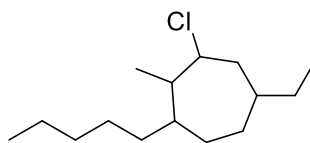
1,3-dibromobutane



3,4,5-triethylheptane

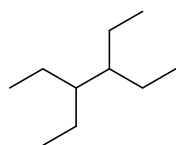


3-chloro-4-isopropyl-2,5-dimethylhexane

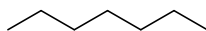


3-chloro-5-ethyl-2-methyl-1-pentylcycloheptane

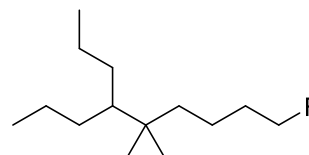
29.



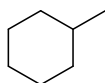
Given: 3,4-diethylhexane
Corrected: name is correct



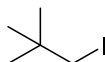
1-methylhexane
heptane



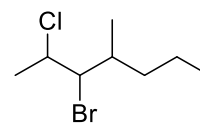
9-fluoro-5,5-dimethyl-4-propylnonane
1-fluoro-5,5-dimethyl-6-propylnonane



Given: 6-methylcyclohexane
Corrected: methylcyclohexane

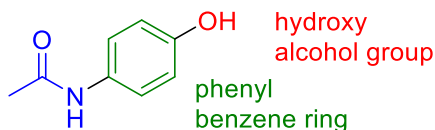


2-iodo-1,1,1-trimethylethane
1-iodo-2,2-dimethylpropane



2-propyl-4-chloro-3-bromopentane
3-bromo-2-chloro-4-methylheptane

30.



ethanamide/acetamide
2C and an amide

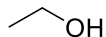
hydroxy
alcohol group

phenyl
benzene ring

"N" means that the phenyl group is attached to the N in the amide. 4-hydroxy means that the alcohol is on the 4th C in the ring from where it is attached to the amide

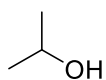
Acetaminophen comes from para-acetylaminophenol. Paracetamol comes from para-acetylaminophenol.

31.



Common: ethyl alcohol

IUPAC: ethanol



isopropyl alcohol

propan-2-ol

Ethyl alcohol and isopropyl alcohol both have similar intermolecular forces (London dispersion, dipole-dipole, and hydrogen bonding). Ethyl alcohol will evaporate faster because it has a lower molar mass.

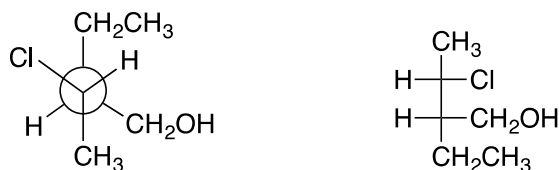
ANSWERS FOR PROBLEM SET 4: STEREOCHEMISTRY, CONFORMATION, AND CONFIGURATION

a. More on Bond Line Structures, Drawing, and Isomers

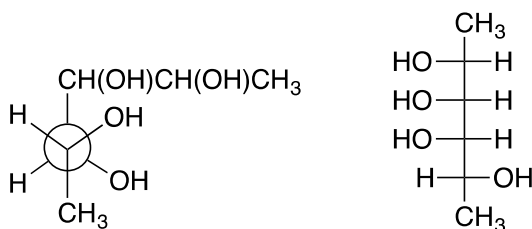
1. a. Both compounds 4-ethyl-2-methylhexane. Therefore they are identical compounds.
b. The first compound is 2,3,5-trimethylheptane, and the second is 3-ethyl-2,5-dimethylhexane. Therefore these are isomers of one another.
c. The first compound is 2,3,3-trimethylpentane, and the second is also 2,3,3-trimethylpentane. Therefore these are identical.

2.

a.



b.



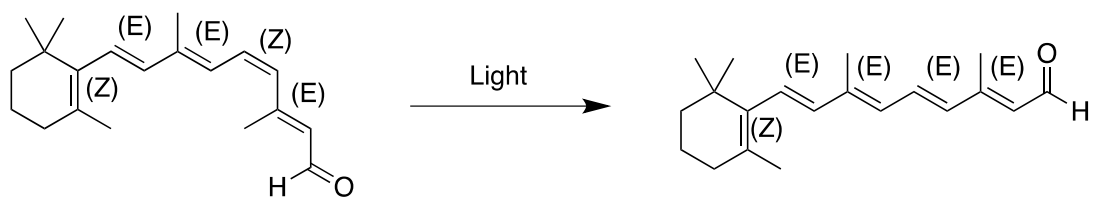
c.



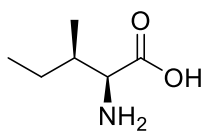
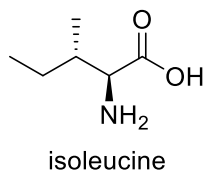
3.

- a. Both contain a plane of symmetry and are therefore meso compounds.
b. Rotating the second structure yields the first structure. Therefore these are identical.
c. The configuration of one of the two stereocenters is different. Therefore, these are diastereomers.
d. The configuration of the chiral center is different. These are enantiomers.

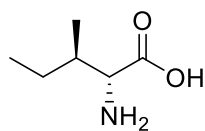
4.



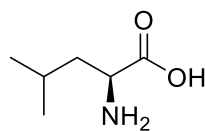
5.



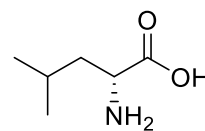
stereoisomer



stereoisomer

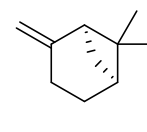
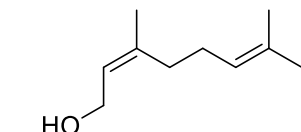
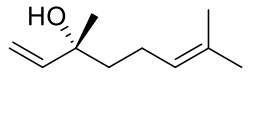
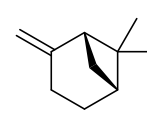
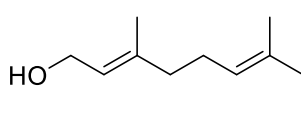
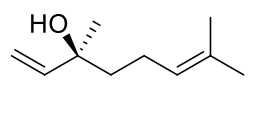
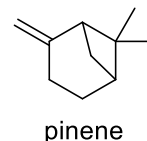
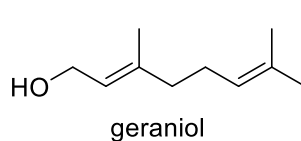
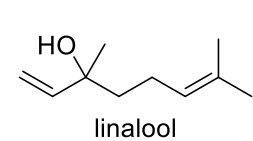


constitutional isomer

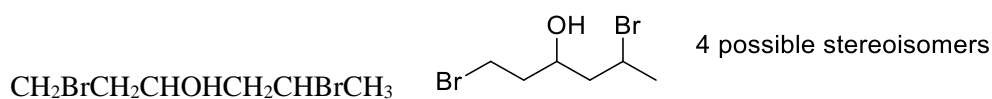
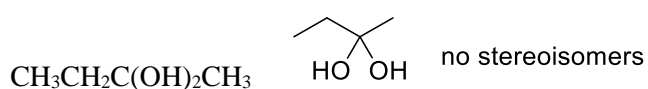
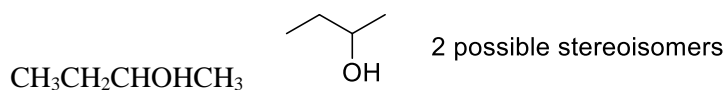
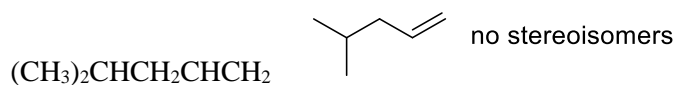


constitutional isomer

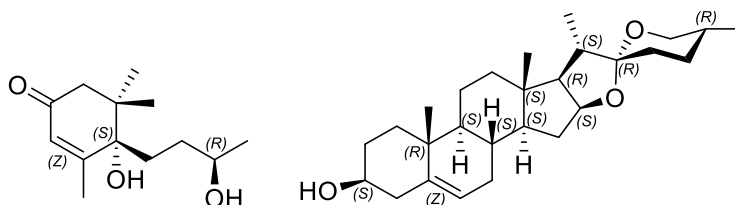
6.



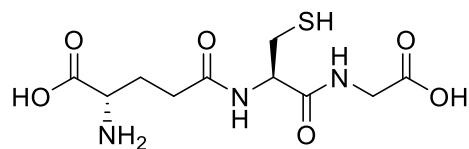
7.



8.



9.



glutathione

Functional groups: carboxylic acid, amine, amide, thiol

Amino acids: glutamate/glutamic acid, cysteine, glycine

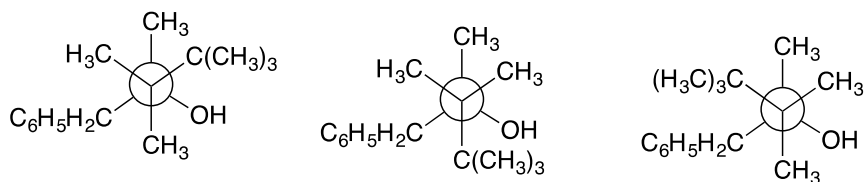
Stereoisomers: two stereocenters, $2^2 = 4$ stereoisomers

b. Bond Rotation Energy

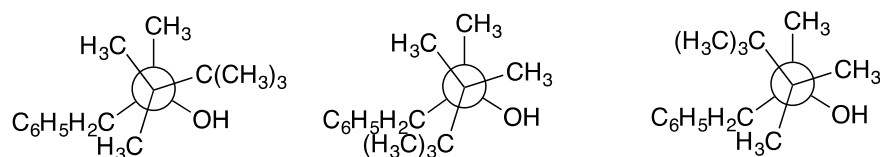
10.

a.

Staggered

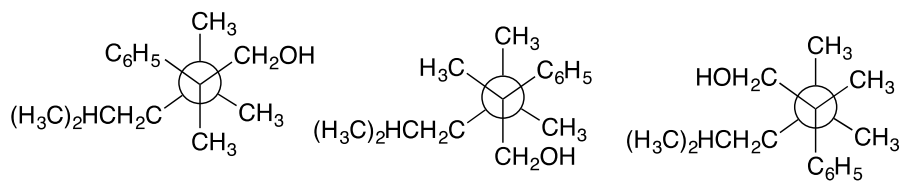


Eclipsed

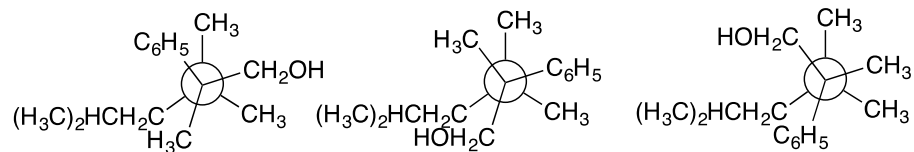


b.

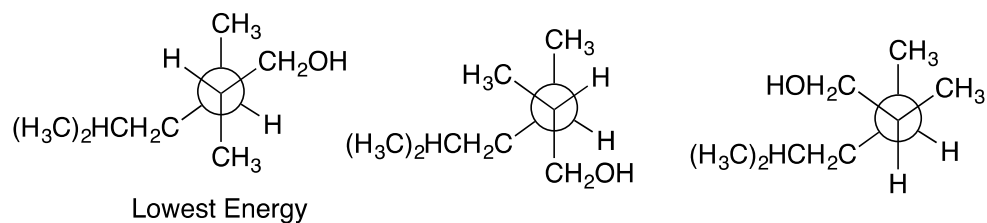
Staggered



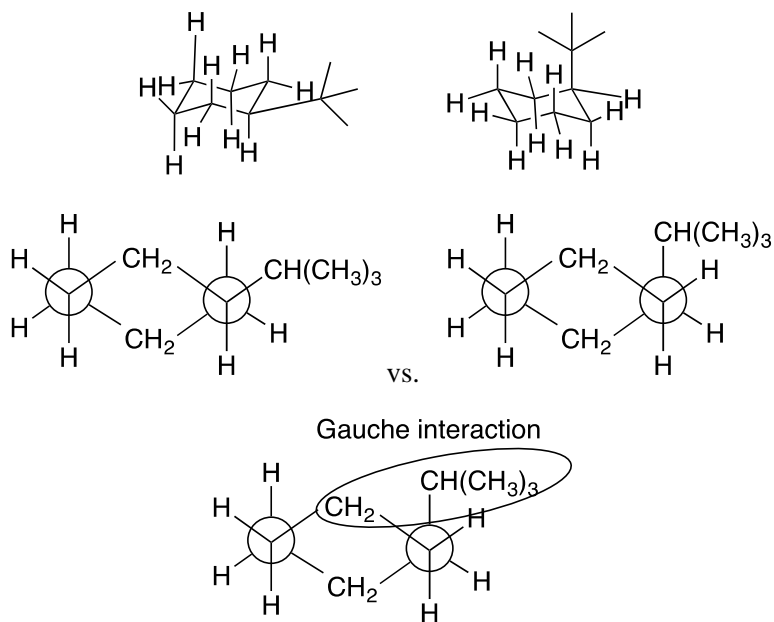
Eclipsed



11.

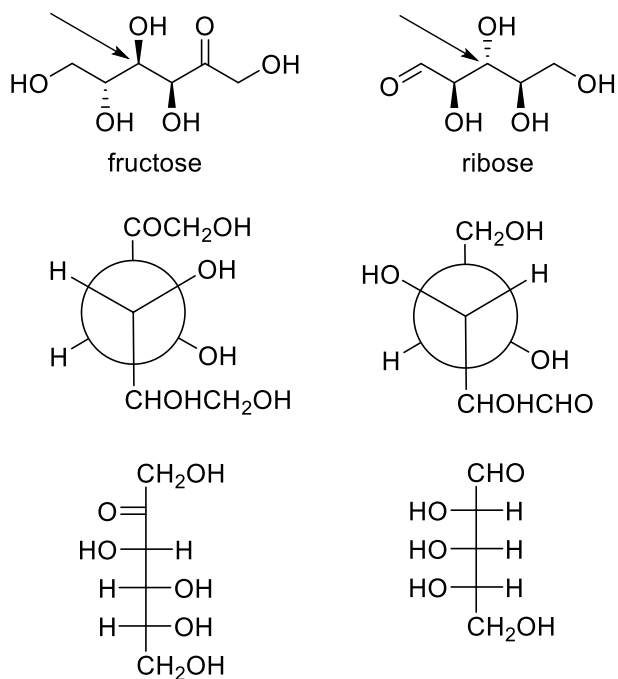


12.

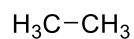


The first chair shown is the favored configuration (tert-butyl equatorial). This is due to the gauche interaction of the CH₂ and tert-butyl groups when it is positioned axially.

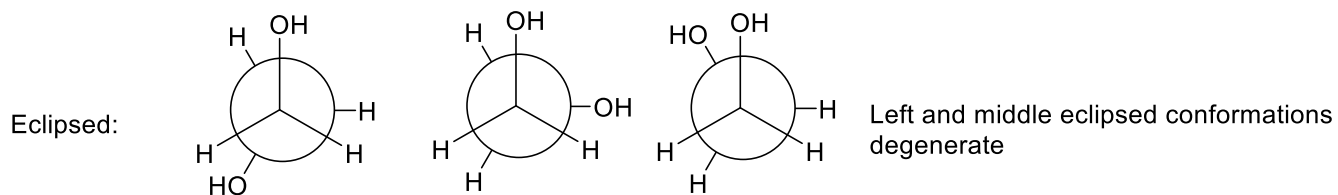
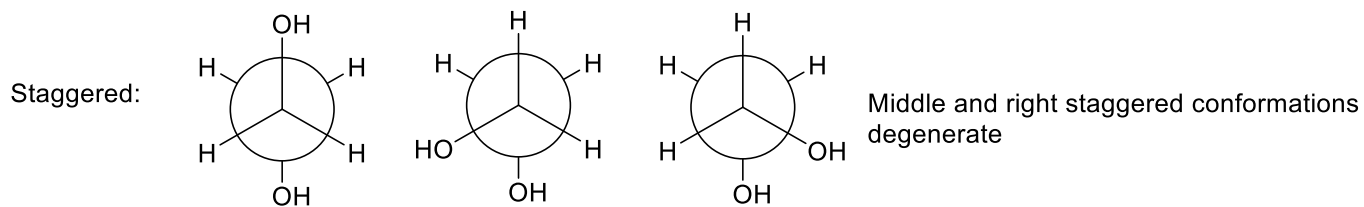
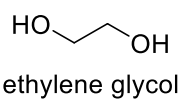
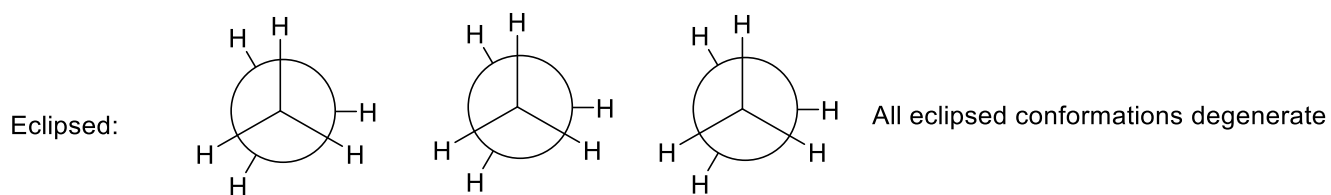
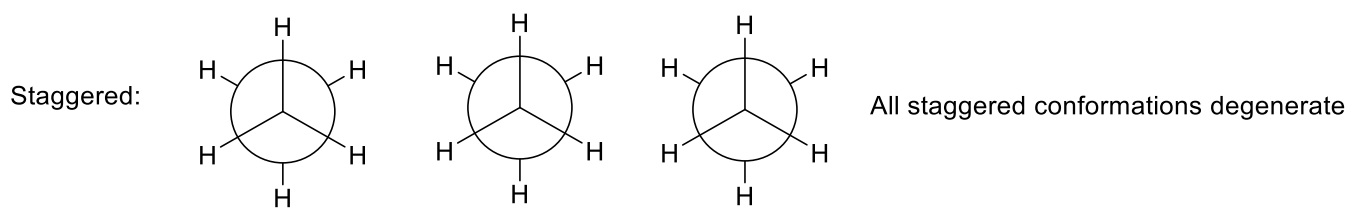
13.



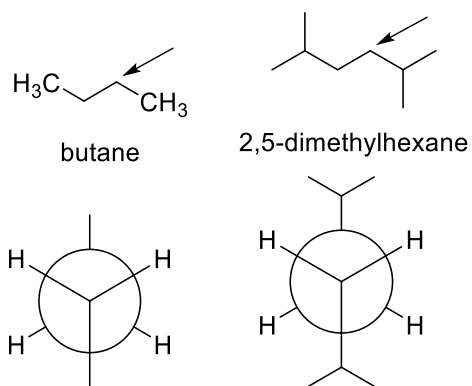
14.



ethane

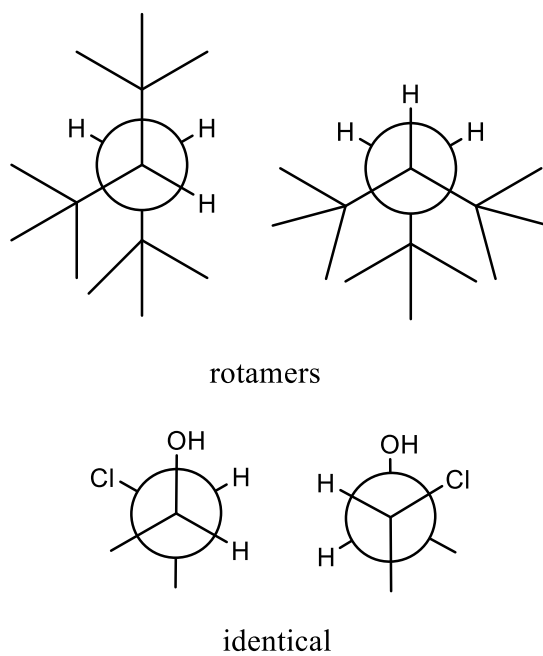


15.

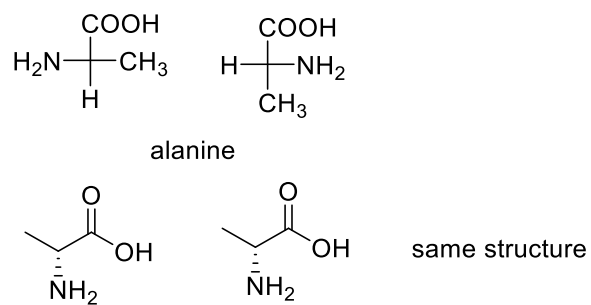


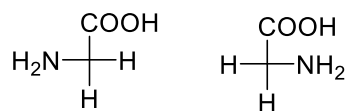
2,5-Dimethylhexane will have more steric hindrance.

16.

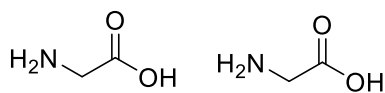


17.

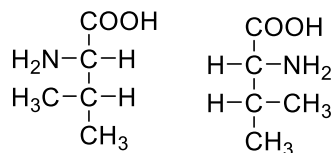




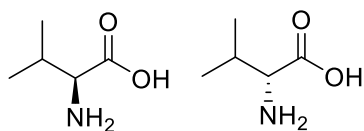
glycine



same structure



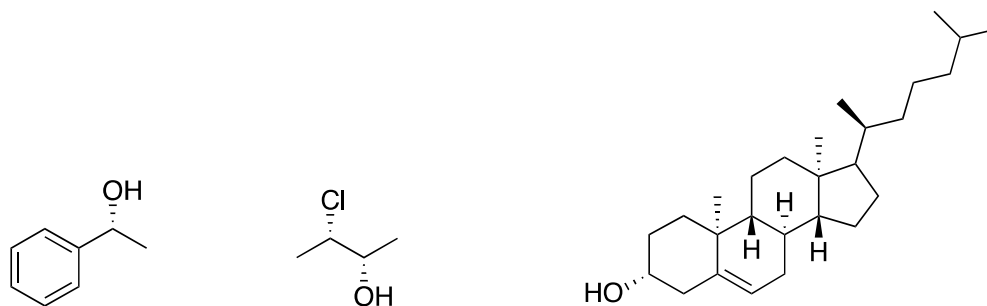
valine



stereoisomers

c. Chirality and Stereocenters

18.

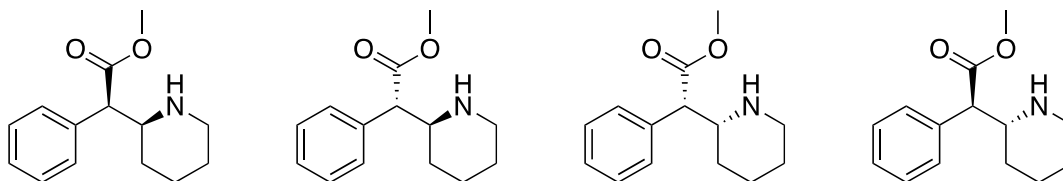


19.

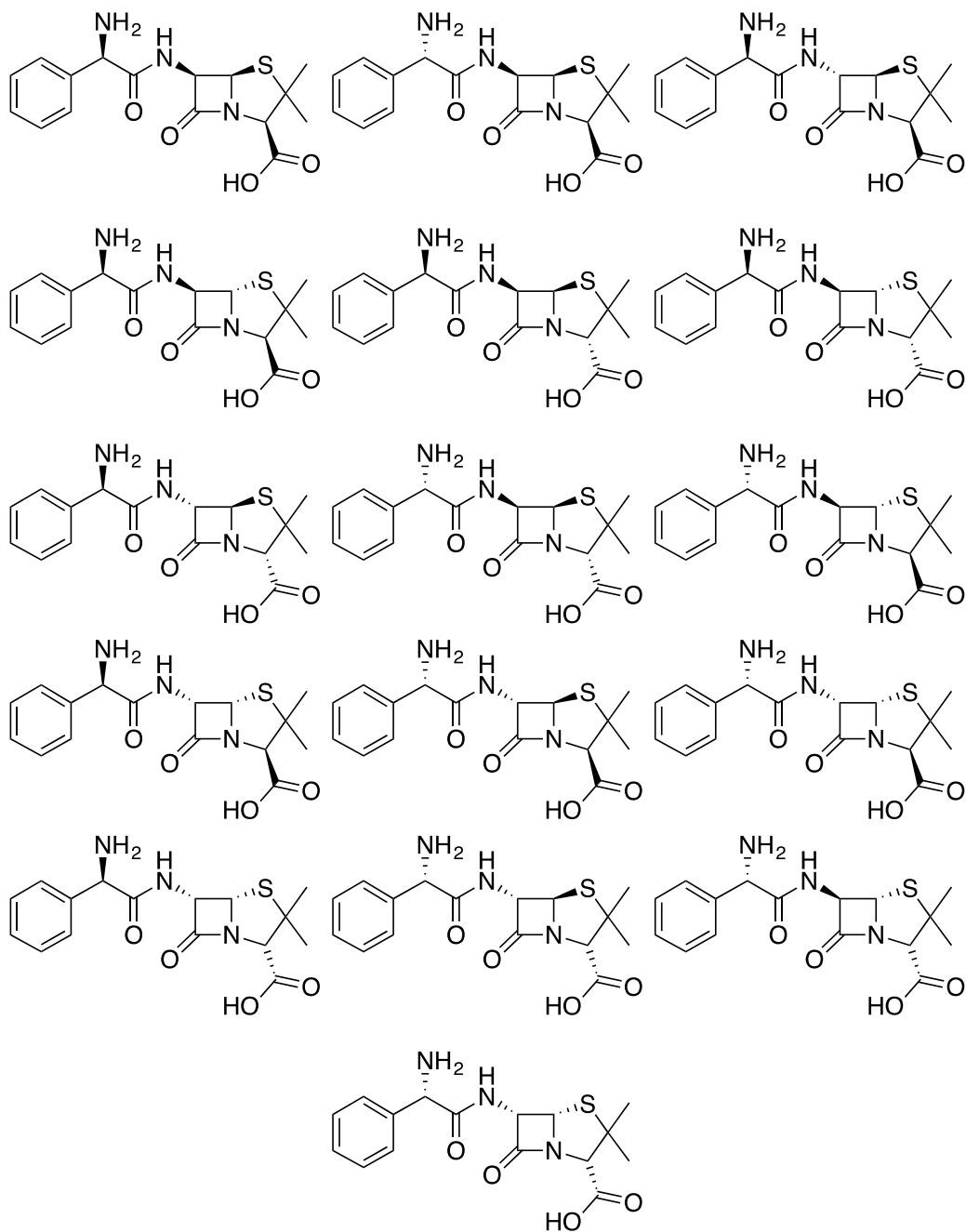
Phenylalanine has 1 chiral center. (2 possible stereoisomers)



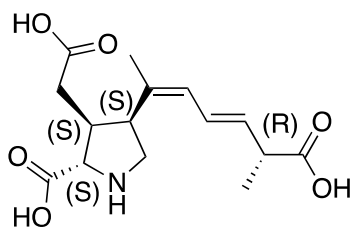
Methylphenidate has 2 chiral centers (4 possible stereoisomers)



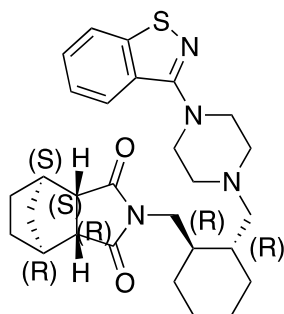
Ampicillin has 4 chiral centers (16 possible stereoisomers)



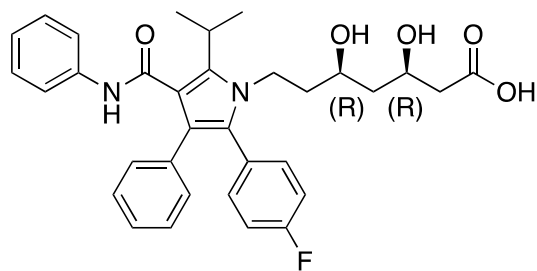
20.



Lurasidone has 6 chiral centers.

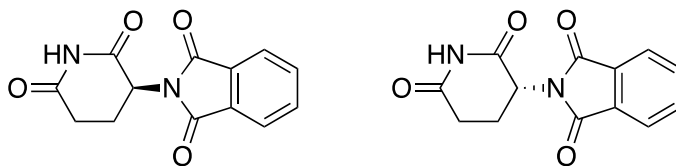


Atorvastatin has 2 chiral centers.

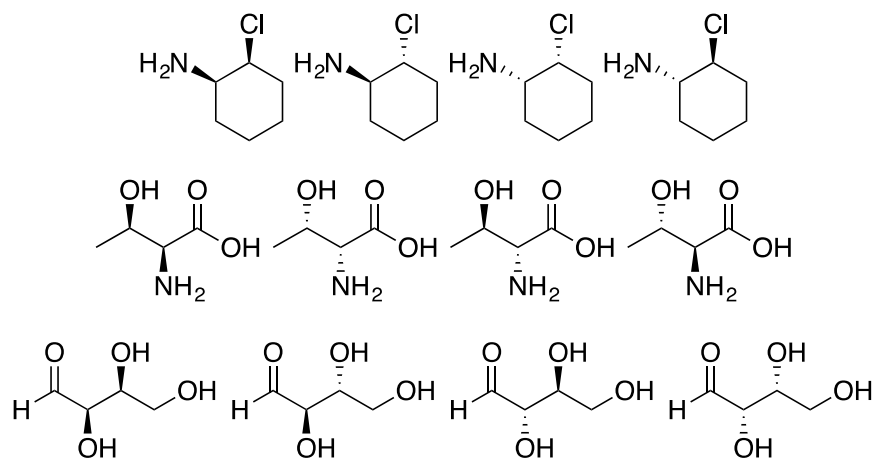


Atorvastatin

21.

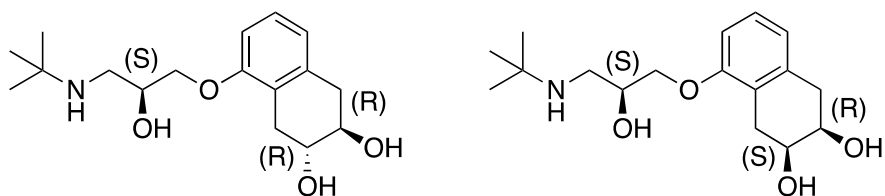


22.

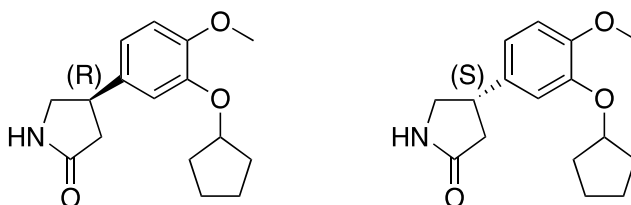


23.

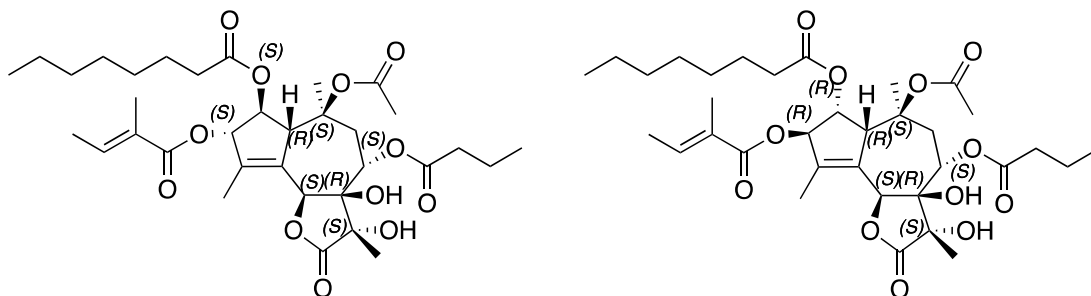
a. The pair of compounds are diastereomers.



b. The pair of compounds are enantiomers.

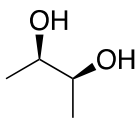


c. The pair of compounds are diastereomers.

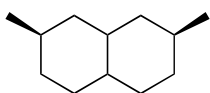


24.

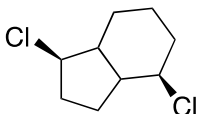
a. The molecule shown redrawn contains an internal plane of symmetry.



b. This molecule also has an internal plane of symmetry.



c. This molecule does not contain an internal plane of symmetry.



25.

a. This pair of compounds is identical. The compounds contain an internal plane of symmetry, making them meso compounds.

b. The pair of compounds are enantiomers. Both chiral centers are different configurations in the first and second structures.

c. The pair of compounds are diastereomers. The configuration of one of the chiral centers is unchanged.

26.

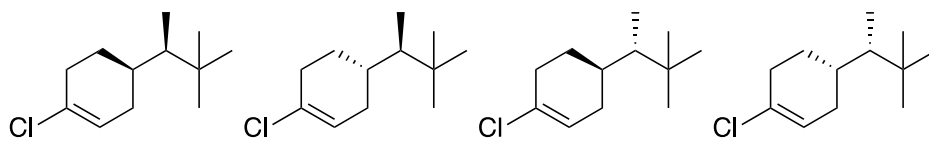
Meso compounds:



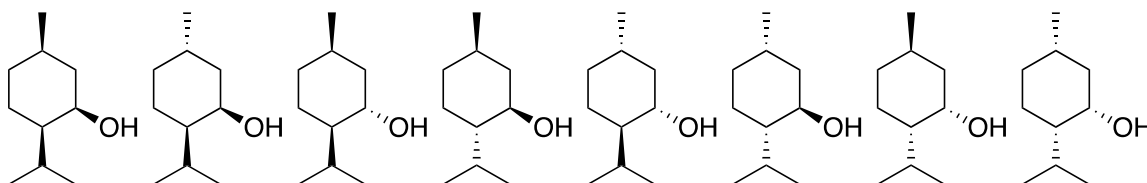
Other stereoisomers:



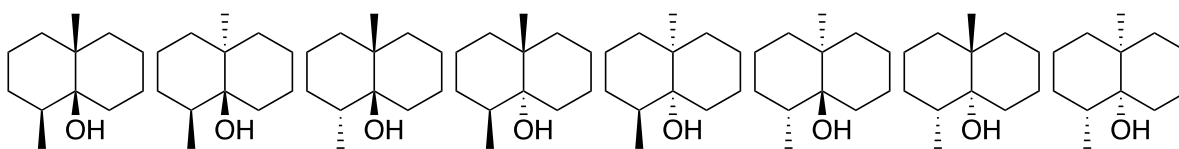
No meso compounds.



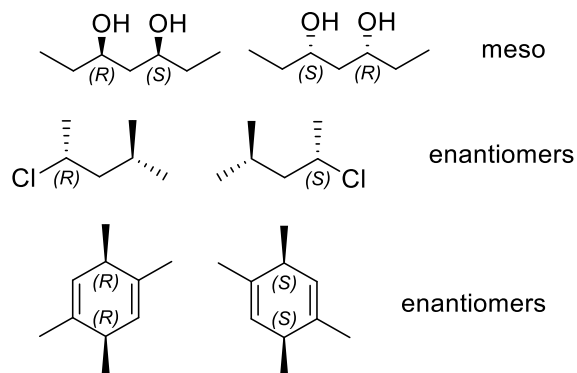
No meso compounds.



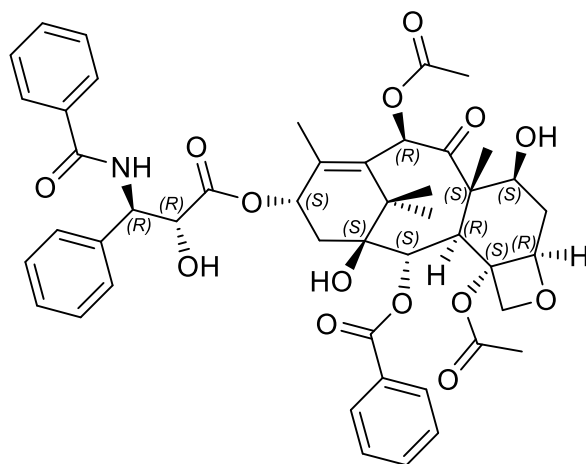
No meso compounds.



27.



28.

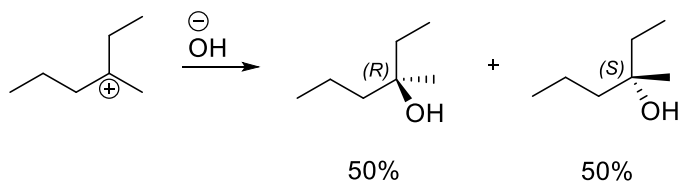


There are 11 chiral carbons. Paclitaxel would have an enantiomer (it is not a meso compound).

29.21 chiral carbons: all have one chiral carbon except isoleucine and threonine (each have two chiral carbons) and glycine (no chiral carbons)

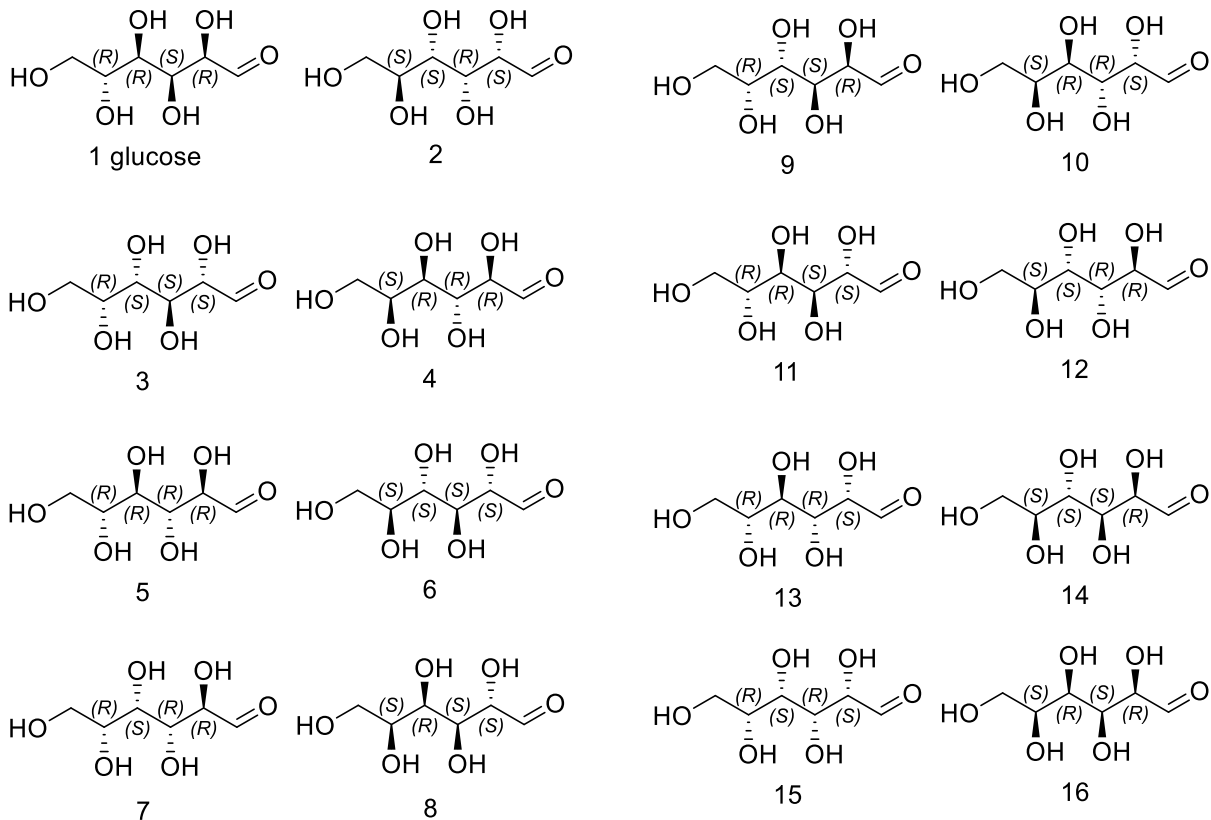
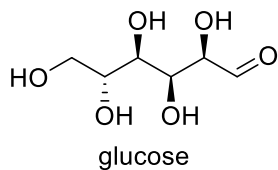
41 structures: Arg ($2^1 = 2$ possible structures), His (2), Lys (2), Asp (2), Glu (2), Ser (2), Thr (4), Asn (2), Gln (2), Cys (2), Gly (1), Pro (2), Ala (2), Ile (4), Leu (2), Met (2), Phe (2), Trp (2), Tyr (2), Val (2)

30.



Since the carbocation is planar, there will be an equal mix of both stereoisomers.

31.



1 is d-glucose and 2 is its enantiomer (l-glucose). 3-16 are diastereomers of glucose, and 3&4, 5&6, 7&8, 9&10, 11&12, 13&14, and 15&16 are sets of enantiomers.

d. Racemic Mixtures and Optical Activity

32. Clopidogrel and fluticasone contain chiral centers and therefore will show optical activity. Esomeprazole has no chiral centers and will not be optically active.

33. Ibuprofen as a racemic mixture should not exhibit optical activity. This is because racemic mixtures do not exhibit optical activity.

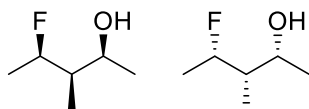
34. Imatinib, aspirin, methadone (racemic mixture), and (2R, 3S)-tartaric acid are not optically active due to their lack of a chiral center (imatinib and aspirin), being a racemic mixture (methadone) and being a meso compound ((2R, 3S)-tartaric acid). Siproxetine is the only optically active compound.

35.

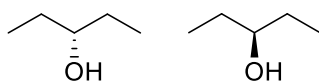
$$\% ee = \frac{|\text{observed } \alpha|}{|\alpha \text{ of pure enantiomer}|} \times 100\%$$

$$\% ee = \frac{12.3}{32.2} \times 100\% = 38.2\%$$

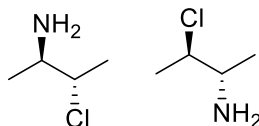
36.



Yes; these are enantiomers.

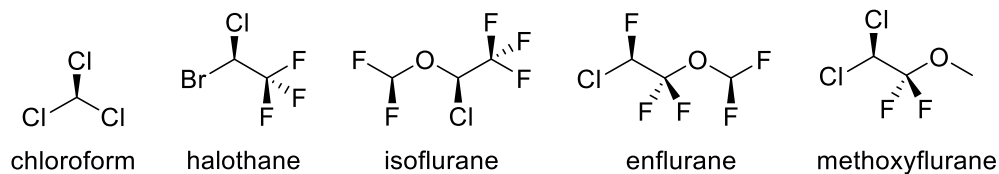


No; these are the same molecule, and it is not chiral.



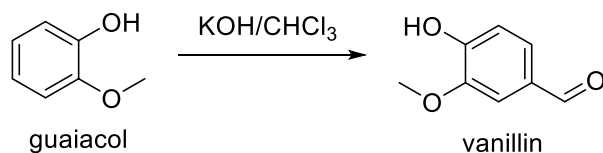
Yes; these are enantiomers.

37.



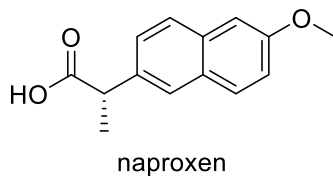
Halothane, isoflurane, and enflurane would have optical activity. Chloroform and methoxyflurane are achiral and so would not exhibit optical activity.

38.



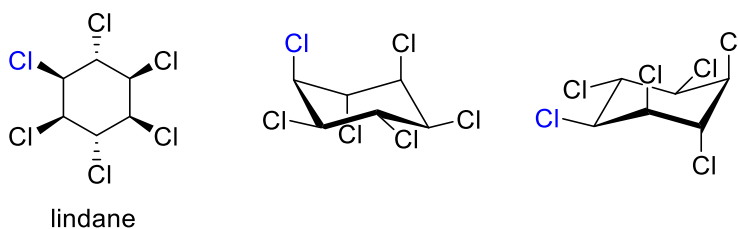
No, optical activity would not be useful to determine if the product was made because vanillin is optically inactive. The reactant, guaiacol, is also optically inactive, so the reaction could not be tracked by loss of the reactant. Another method of analysis would be necessary.

39.



A pure sample of the enantiomer would have a specific rotation of -66° in chloroform, so the enantiomer was produced.

40.



The formula for lindane is $C_6H_6Cl_6$. Lindane is optically inactive because it is a meso compound. Because it is meso, lindane would have fewer than 2^n ($2^6 = 64$) stereoisomers.

ANSWERS FOR PROBLEM SET 5: SPECTROSCOPY, PART 1

a. The Electromagnetic Spectrum and Organic Compounds

1.

	Type of Radiation	Wavelength range	Relative Energy
Infrared	Infrared light	700 nm – 50 μ m	Lower energy
UV-Vis	UV and visible light	200 nm – 700 nm	Higher energy

2.

$$E = \frac{hc}{\lambda} = \frac{(6.626 \times 10^{-34} \text{ J s}) \left(3 \times 10^8 \frac{\text{m}}{\text{s}}\right)}{(450 \times 10^{-9} \text{ m})} = 4.4 \times 10^{-19} \text{ J}$$

$$E = hc(\text{wavenumber}) = (6.626 \times 10^{-34} \text{ J s}) \left(3 \times 10^{10} \frac{\text{cm}}{\text{s}}\right) (2180 \text{ cm}^{-1}) = 4.3 \times 10^{-20} \text{ J}$$

3. Since wavenumber is directly proportional to energy, the stretching for an alkyne requires more energy. This makes sense because carbon-carbon triple bonds are shorter and stronger than carbon-carbon double bonds.

4.

Note: You may see the delineations for these vary.

Red	Orange	Yellow	Green	Blue	Violet
750 – 620 nm	620 – 590 nm	590 – 570 nm	570 – 495 nm	495 – 450 nm	450 – 380 nm
Lowest energy					Highest energy

5.

$$\nu = \frac{c}{\lambda} = \frac{2.998 \times 10^8 \text{ m/s}}{2.54 \times 10^{-7} \text{ m}} = 1.18 \times 10^{15} \text{ Hz}$$

$$E = \frac{hc}{\lambda} = \frac{(6.626 \times 10^{-34} \text{ J} \cdot \text{s})(2.998 \times 10^8 \text{ m/s})}{2.54 \times 10^{-7} \text{ m}} = 7.82 \times 10^{-19} \text{ J}$$

6.

UV IR X-rays visible radio γ -rays microwave

Lowest to highest wavelength: γ -rays < X-rays < UV < visible < IR < microwaves < radio

Highest frequency: γ -rays

Lowest frequency: radio waves

Lowest energy: radio waves

7.

$$E_{460 \text{ nm}} = \frac{hc}{\lambda} = \frac{(6.626 \times 10^{-34} \text{ J} \cdot \text{s})(2.998 \times 10^8 \text{ m/s})}{4.60 \times 10^{-7} \text{ m}} = 4.32 \times 10^{-19} \text{ J}$$

$$E_{500 \text{ nm}} = \frac{hc}{\lambda} = \frac{(6.626 \times 10^{-34} \text{ J} \cdot \text{s})(2.998 \times 10^8 \text{ m/s})}{5.00 \times 10^{-7} \text{ m}} = 3.97 \times 10^{-19} \text{ J}$$

$$E_{580 \text{ nm}} = \frac{hc}{\lambda} = \frac{(6.626 \times 10^{-34} \text{ J} \cdot \text{s})(2.998 \times 10^8 \text{ m/s})}{5.80 \times 10^{-7} \text{ m}} = 3.42 \times 10^{-19} \text{ J}$$

$$E_{700 \text{ nm}} = \frac{hc}{\lambda} = \frac{(6.626 \times 10^{-34} \text{ J} \cdot \text{s})(2.998 \times 10^8 \text{ m/s})}{7.00 \times 10^{-7} \text{ m}} = 2.84 \times 10^{-19} \text{ J}$$

$$E_{510 \text{ nm}} = \frac{hc}{\lambda} = \frac{(6.626 \times 10^{-34} \text{ J} \cdot \text{s})(2.998 \times 10^8 \text{ m/s})}{5.10 \times 10^{-7} \text{ m}} = 3.90 \times 10^{-19} \text{ J}$$

$$E_{\text{flash}} = n_{\text{photons}} \times E_{510 \text{ nm}} = 90 \text{ photons} \times 3.90 \times 10^{-19} \text{ J} = 3.50 \times 10^{-17} \text{ J}$$

b. Infrared Spectroscopy

8. Nitriles: 2200-2300 cm^{-1}

Esters: 1700-1750; 1250-1350 cm^{-1}

Alkene: 1600-1700; 3000-3100 cm^{-1}

Aldehyde: 2750-2850; 1680-1750 cm^{-1}

Carboxylic acid: 2200-3600; 1700-1750 cm^{-1}

Alcohol: 3200-3600; 1000-1100 cm^{-1}

Alkane: 2850-3000 cm^{-1}

9. From the IR data, it appears that the compound should contain a hydroxyl group, leaving options 2 and 4. The presence of the nitrile functional group in option 2 agrees well with the observed signal at 2250 cm^{-1} suggesting that this is probably the correct compound.

10. a. Loss of signal at 3200-3600 cm^{-1}
 b. Loss of signal at 2200-2300 cm^{-1} , and gain at 1000-1200 cm^{-1}
 c. Loss of signal at 1680-1750 cm^{-1}
 d. Loss of signal at 1680-1750 cm^{-1} , gain at 1600-1700 cm^{-1} and 880-900 cm^{-1}

11. The isotope deuterium (D) is heavier than hydrogen (H), so the O-D bond would vibrate at a lower frequency and thus have a lower IR absorption. This is based on the change in reduced mass (symbol μ or m_{red}) in the following equations:

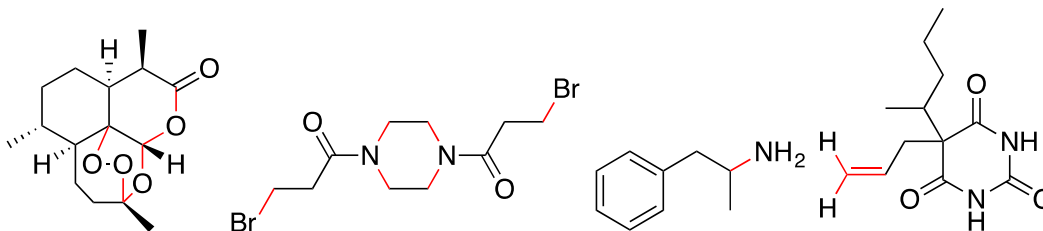
$$\tilde{\nu} = (1/2\pi c) (f/\mu)^{1/2} \quad \mu = (m_1 m_2)/(m_1 + m_2)$$

where $\mu_{\text{OD}} = 1.78$ and $\mu_{\text{OH}} = 0.94$, which will make $\tilde{\nu}_{\text{OD}} < \tilde{\nu}_{\text{OH}}$.

12. 3250 cm^{-1} (NH, secondary amide)
 3010 cm^{-1} (sp^2 CH)
 2800-2970 cm^{-1} (sp^3 CH)
 1670 cm^{-1} (C=O, amide)
 1590 and 1500 cm^{-1} (aromatic C=C)
 The sp^3 CH and sp^2 CH would overlap some, but are still distinguishable

13. The water your lab partner used as the solvent is causing the absorption at 3500 cm^{-1} (–OH stretch). The other group did not see this absorption because they used mineral oil, which is a mixture of alkanes.

14. The bonds with expected fingerprint region absorbances are highlighted in red.



15. With the peaks at 1683 and 1274 cm^{-1} one could expect the possibility of an ester being present. Additionally, the peaks at 1079 and 1029 cm^{-1} may be indicative of an ether and/or amine functional group. Based on this information the first option should be the correct molecule.

16. Hydroxyl group: $3200\text{-}3600\text{ cm}^{-1}$ (O-H bond); $1000\text{-}1100\text{ cm}^{-1}$ (C-O bond)

Amine: $1000\text{-}1200\text{ cm}^{-1}$ (C-N bond)

Ether: $1000\text{-}1100\text{ cm}^{-1}$ (C-O bond)

Aldehyde: $1680\text{-}1750\text{ cm}^{-1}$ (C=O bond); $2750\text{-}2850\text{ cm}^{-1}$ (C-H bond)

Ester: $1700\text{-}1750\text{ cm}^{-1}$ (C=O bond); $1250\text{-}1350\text{ cm}^{-1}$ (C-O bond); $1000\text{-}1100\text{ cm}^{-1}$ (O-CH₃ bond)

17. Hydrogen cyanide (HCN) would be expected to have absorptions around 2100 cm^{-1} (CN stretch), 3300 cm^{-1} (CH stretch), and 700 cm^{-1} (bend). The CN stretch and the CH stretch would be in the diagnostic region while the bending would be in the fingerprint region.

NOTE: You may be asked to calculate the number of vibrational modes using degrees of freedom. For linear molecules, this is $3N-5$ which will give four vibrational modes for 3 atoms; hydrogen cyanide would have two equivalent vibrational modes corresponding to the bending on the molecule, which accounts for this discrepancy.

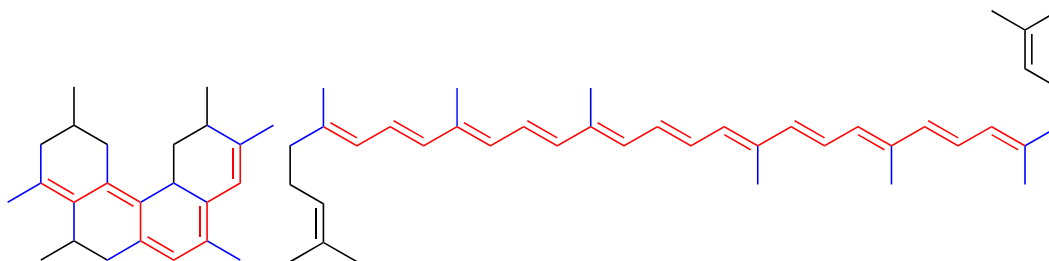
18. The IR absorption at 3400 cm^{-1} indicates the presence of an -OH. Since xylene is the only compound without an alcohol (or carboxylic acid), it can be ruled out. The diagnostic region was more helpful in ruling out one of the compounds than the fingerprint region.

The unknown compound is vanillin, although from the information given this would be very hard to determine.

c. UV Spectroscopy

19. The greater extent of conjugation, the longer the wavelength for absorbance will be. Of the given options, beta-carotene has the greatest extent of conjugation and therefore will have the largest wavelength of maximum absorbance by UV-Vis spectroscopy.

20. The chromophores of the molecules are indicated in red, while the auxochromes are indicated in blue.



Estimated maximum wavelength:

#1: diene+3 additional double bonds+8 auxochromic alkyl groups+2 exocyclic double bonds+1 homoannular diene

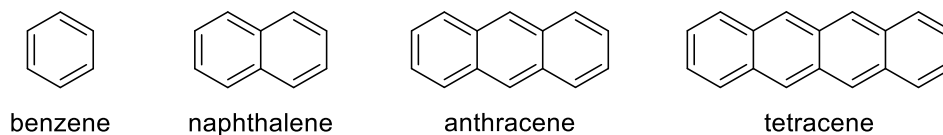
$$217+3(30)+8(5)+2(5)+39=396\text{ nm}$$

#2: diene+9 additional double bonds+8 auxochromic alkyl groups

$$217+9(30)+8(5)=527 \text{ nm}$$

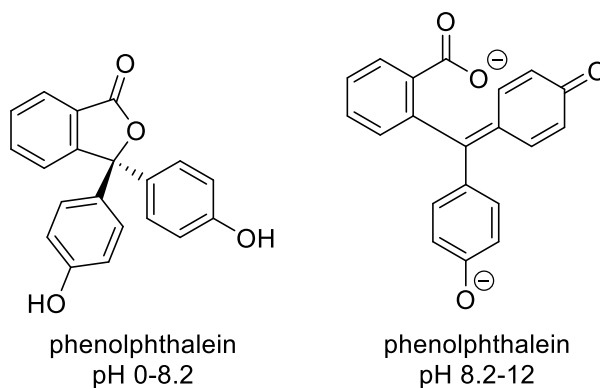
The Woodward-Fieser rules are not very reliable for compounds with more than 6 double bonds in conjugation. Based on this, it should be more reliable for the first compound than the second.

21.



Tetracene will have the largest λ_{\max} because it has a larger conjugated π system.

22.



The increase in pH results in a structure (pH 8.2-12) that is highly conjugated. Both forms of phenolphthalein absorb in the UV region, but the pH 8.2-12 structure will also absorb in the visible region (approximately 553 nm (green), contributing to the pink/magenta color).

23. The absence of the bromine in indigotin causes the compound to absorb a higher wavelength, which would be a lower frequency and lower energy. This would be a bathochromic shift because it is to a higher wavelength.

24. λ_{\max} calculated = 214 nm (base) + 270 nm (9 extending olefins x 30 ea.) + 50 nm (10 alkyl groups x 5 ea.) = 534 nm

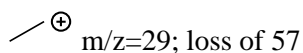
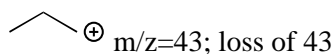
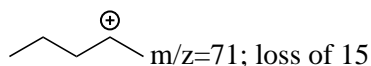
Since this is a highly conjugated system (11 double bonds), this calculation is not expected to be very accurate; the actual λ_{\max} is about 470 nm. This compound would absorb in the visible region, and it would appear orange to red-orange. As this pigment lends to the color of orange carrots, orange carrots would have more than white carrots.

d. Mass Spectrometry

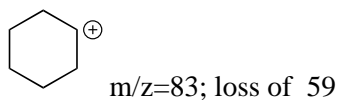
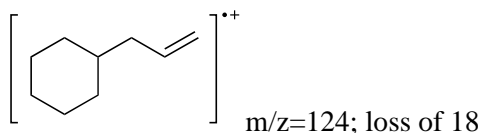
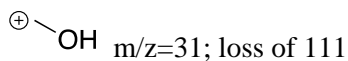
25. Once a compound enters the mass spectrometer, it vaporized and made into ions first. This ionization can vary from instrument to instrument (For example, electron ionization involves bombardment of the compound with high-energy electrons). The resulting ions are then accelerated and separated through the use of electric and magnetic fields respectively. The ions then reach the detector which provides a signal to the computer that is collecting the data.

26.

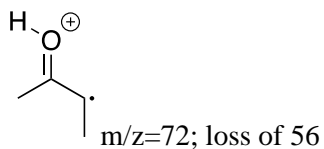
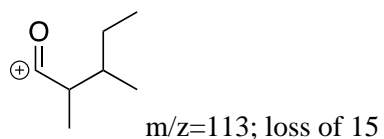
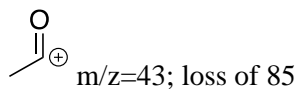
a.



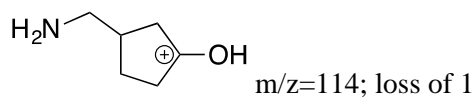
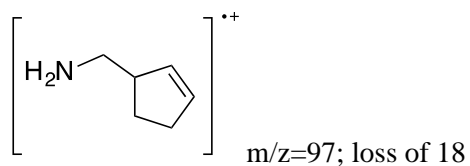
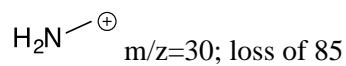
b.



c.



d.



27.

a. $\text{HDI}=0.5 \cdot (2C+2-H-X+N)=0.5 \cdot (12+2-5-1+0)=4$

b. $\text{HDI}=0.5 \cdot (10+2-10-0+0)=1$

c. $\text{HDI}=0.5 \cdot (12+2-15-0+1)=0$

d. $\text{HDI}=0.5 \cdot (12+2-10-0+0)=2$

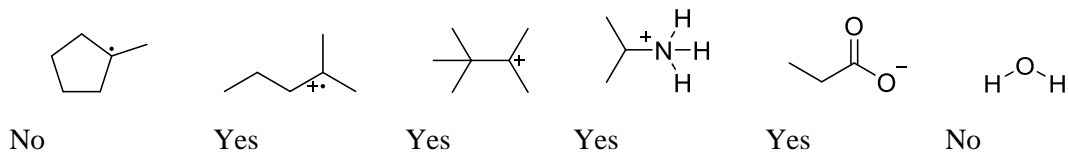
e. $\text{HDI}=0.5 \cdot (14+2-13-1+0)=1$

f. $\text{HDI}=0.5 \cdot (94+2-51-0+1)=23$

g. $\text{HDI}=0.5 \cdot (12+2-8-0+0)=3$

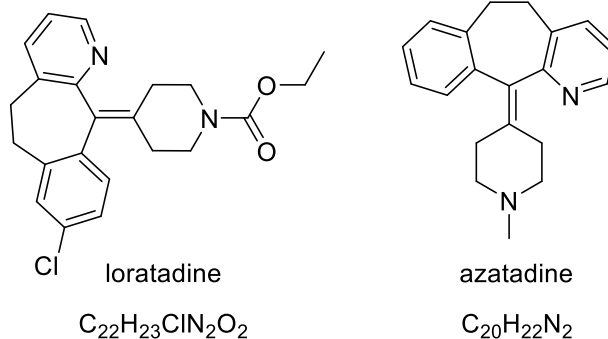
h. $\text{HDI}=0.5 \cdot (14+2-5-0+3)=7$

28.



A mass spectrometer detects ions, so it will only detect compounds carrying a charge.

29.



Loratadine: $[M]^{+•} = 382$ (100%) $[M+1]^{+•} = 383$ (24%) $[M+2]^{+•} = 384$ (32%)

$$\text{HDI} = \frac{1}{2}(2C - 2H - X + N) = 12$$

Azatadine: $[M]^{+•} = 290$ (100%) $[M+1]^{+•} = 291$ (22%) $[M+2]^{+•} = 292$ (less than 5%)

$$\text{HDI} = \frac{1}{2}(2C - 2H - X + N) = 11$$

The relative abundance (i.e. percent intensity of the base peak) for M+1 can be estimated by the relative abundance of ^{13}C (1.1%) as compared to ^{12}C (100%). This is done by multiplying 1.1% by the number of carbons.

The relative abundance of M+2 can be estimated by the relative abundance of the chlorine isotopes: ^{35}Cl (100%) and ^{37}Cl (32%). This is the “3:1” ratio observed in a mass spectrum when a single chlorine is present.

30.

Artemisinin: $C_{15}H_{22}O_5$; $m/z=282$

Cinnamaldehyde: C_9H_8O ; $m/z=132$

Amphetamine: $C_9H_{13}N$; $m/z=135$

31.

a. The molecule is a hydrocarbon, so it will only contain carbons and hydrogens. The molecular ion peak is 94, so the molar mass should be 94. Based on this, the molecular formula should be C_7H_{10} .

b. According to the IR spectroscopy data, the compound may contain a hydroxyl group as well as a carbonyl group (probably a carboxylic acid). Subtracting the mass of this functional group (45) from the mass of the compound (128), this leaves C_6H_{11} as the remaining portion of the molecular formula. Therefore, the formula is $C_7H_{12}O_2$.

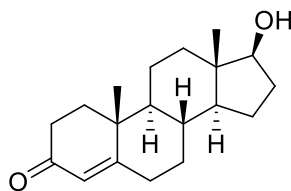
c. The presence of an $(M+2)$ peak with 1/3 the height suggests the presence of a chlorine atom. Knowing this, the mass of the remaining portion of the molecule must be 83. This leaves C_6H_{11} as the remaining portion of the molecule. Therefore, the molecular formula is $C_6H_{11}Cl$.

32.

	$[M]^+$	$[M+2]^+$	$[M+4]^+$
CH_2ClF	100%	32%	n/a
CH_2Cl_2	100%	64%	10%
CH_2BrCl	77%	100%	24%
CH_2BrF	100%	100%	n/a
CH_2Br_2	50%	100%	50%

The clear $M+2$ peak with 3:1 and 1:1 ratios for chlorine and bromine, respectively, are only observed when there is one chlorine or one bromine present. Having more than one present (e.g. two bromines) means that the possibility of having ^{79}Br (A) and ^{81}Br (B) for each must be taken into account: AA, AB, BA, and BB. Since there is a 50% possibility for each and since BA is equivalent to AB, we get the 1:2:1 ratio seen in the table above.

33.



testosterone

ESI was used. This is indicated by m/z 289 being an $[M+H]^+$ peak and the lack of significant fragmentation observed. ESI is known as a “soft” ionization technique due to the minor fragmentation, while EI is considered “hard” ionization since there is extensive fragmentation.

34. The following is just an example. Your answers may vary.

	How does it work?	Advantages	Disadvantages
Electrospray Ionization	Sample is sprayed from an electrically charged needle, leading to eventual ionization of the compound	Less fragmentation leads to simpler spectra, can be used for higher mass compounds, sample doesn't need to be volatile	Multiply charged ions can make spectra more difficult to interpret, does not ionize all types of molecules
Electron Ionization	High energy electrons impact the molecule, leading to ionization	Very reproducible, can get structural information from fragmentation, provides a fingerprint for molecule	May not be able to see the molecular ion peak (can't always get the mass of your compound)
Chemical Ionization	A reagent gas is ionized by electron impact, and the resulting ion acts to ionize the compound being analyzed	More often leads to a visible molecular ion peak, less fragmentation/simpler spectrum	Don't get a fingerprint (harder to use with a database to search for matches), more variables (reagent gas, reaction time, pressure)

35.

a. The molecular formulas for these compounds differ and therefore their masses differ. The first compound should result in a molecular ion peak at $m/z=78$, whereas the second compound should result in a molecular ion peak at $m/z=79$.

b. The molecular ion peaks for these two compounds will be seen at $m/z=157$. Therefore, they cannot be distinguished by mass (unless one is obtaining an accurate mass of the two). The presence of the bromine however, will result in an isotope pattern with an M peak at $m/z=158$ and (M+2) peak at $m/z=160$. These peaks will appear at a 1:1 ratio.

c. Both compounds have the same molecular formulas and therefore cannot be distinguished by mass. However, the first compound can undergo a McLafferty rearrangement, while the second cannot. Therefore, one would expect a fragment with $m/z=86$ for the first compound. Additionally, the alpha cleavage for these two compounds will result in fragments of differing masses.

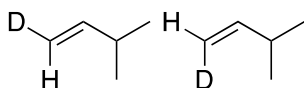
36. GC-MS has the advantage of separation of compounds prior to detection by the MS. This separation can give an indication of the number of compounds present in a mixture and aid in identifying compounds (by comparison to a standard). GC-MS is often used for drug testing and forensics, environmental analyses, and food/beverage analyses (among many other uses).

ANSWERS FOR PROBLEM SET 6: SPECTROSCOPY, PART II: NMR SPECTROSCOPY

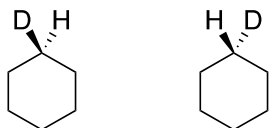
a. Principles of Operation

1. A nucleus must have nuclear spin, which requires that the nucleus has an odd number of protons and/or an odd number of neutrons. Therefore, ^{13}C , ^{19}F , ^{14}N , and ^2H can be detected by NMR spectroscopy.

2.



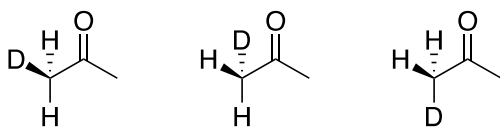
By the replacement test, one does not get the same compound, and therefore the protons are not homotopic. Additionally, these protons are not interchangeable by reflectional symmetry and therefore are not enantiotopic. They are diastereotopic, and should produce two separate signals.



After performing the replacement test, one can obtain the same molecule by rotating one by 180 degrees. Therefore, the protons are homotopic and will produce one signal by ^1H NMR.



When performing the replacement test, one produces a pair of diastereomers. Therefore, the protons are diastereotopic and will produce two signals in a ^1H NMR spectrum.



Rotation of the $\text{CH}_3\text{-CO}$ bond can be performed to create identical compounds. Therefore, the protons are homotopic and will be represented by one signal in a ^1H NMR spectrum.

3. 300 MHz instrument: $\text{Frequency} = (7.4 \times 10^{-6})(300 \times 10^6 \text{ Hz}) = 2220 \text{ Hz}$

400 MHz Instrument: $\text{Frequency} = (7.4 \times 10^{-6})(400 \times 10^6 \text{ Hz}) = 2960 \text{ Hz}$

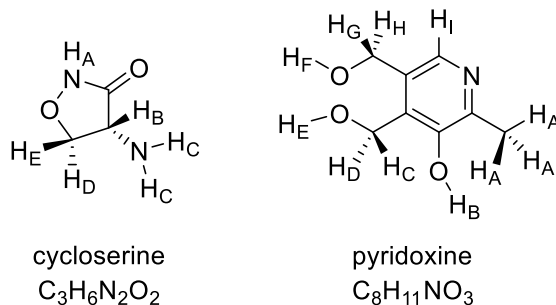
4. Shielded means that the nucleus has high electron density (more “shielded” from the magnetic field). The more shielded the nuclei, the lower the chemical shift. Upfield is an oft-used term to describe the location of the chemical shift.

Deshielded means that the nucleus has poor electron density (less “shielded” from the magnetic field). The less shielded the nuclei, the higher the chemical shift. Downfield is an oft-used term to describe the location of the chemical shift.

NOTE: These are qualitative terms used to describe the relative environment and chemical shifts of nuclei.

5. It is not necessary for the spectra to be reported in ppm, and you may find some articles where the spectrum is given in Hertz (these are typically older). Since the instrument used is reported, the chemical shift could be calculated from the difference reported in Hertz and the instrument. It is more common to report in ppm because the information is more useful; for example, the protons of an aliphatic methyl group will always appear about 1 ppm, but this would be 300 Hz on a 300 MHz instrument, 400 Hz on a 400 MHz instrument, and so on.

6.



NOTE: Although the protons H_C and H_D are diastereotopic, their chemical environments are similar enough that only one signal would be seen in an NMR spectrum (i.e. they are essentially – though not technically – chemically equivalent). The same can be said for H_G and H_H. NMR prediction software will also show that H_E and H_F would be in similar enough environments to have the same chemical shift.

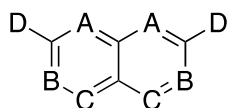
b. ¹H NMR

7. The location of the signal is indicative of the electronic environment of the protons responsible for the signal.

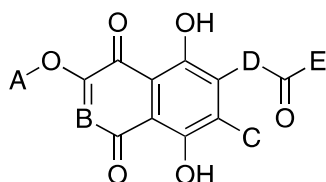
The area under the signal is proportional to the number of protons responsible for the signal.

The shape of the signal is indicative of the number of protons adjacent to the protons responsible for the signal.

8. For both, the area under the signal for each set of protons will indicate the number of protons responsible for the signal.

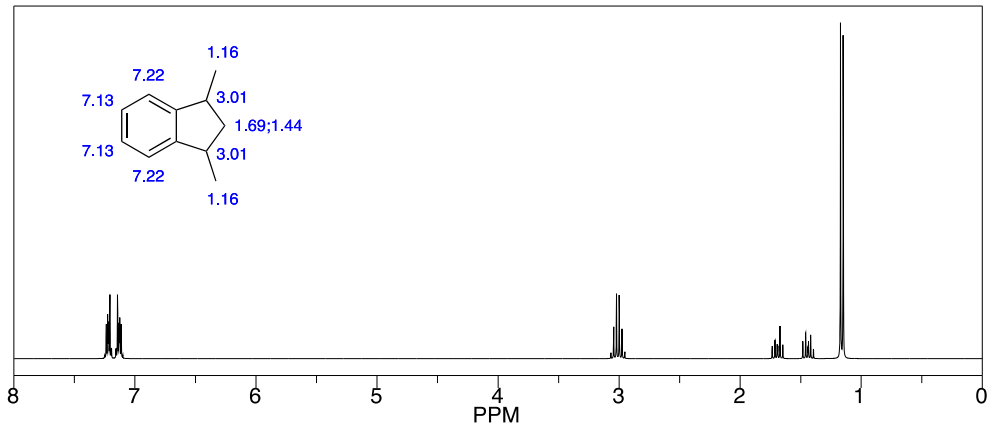


The spectrum should contain a total of 4 signals, representing protons at the carbons labeled, A, B, C, and D. Therefore, one should expect the signals from A, B, and C should represent 2 protons, while those for D represent 6 protons.

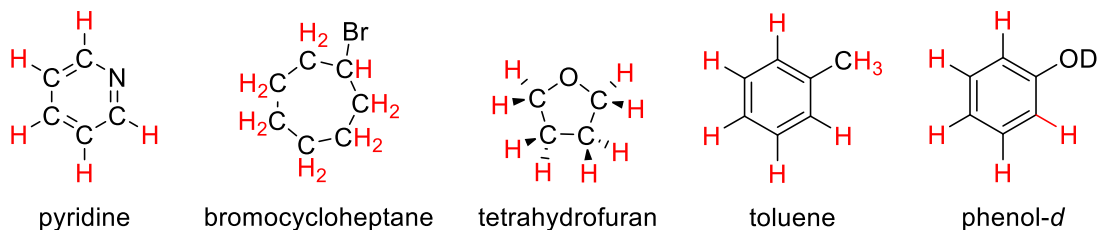


The spectrum for this molecule could contain 5 or 7 signals depending on the solvent. This is due to the fact that the hydroxyl protons are exchangeable, meaning that their appearance in a ^1H NMR spectrum is dependent on the solvent used. If only 5 signals are seen, the signal for A would represent 3 protons, B would represent 1 proton, C would represent 3 protons, D would represent 2 protons, and E would represent 3 protons. If the hydroxyl protons are visible, each would have a signal representative of one proton.

9.



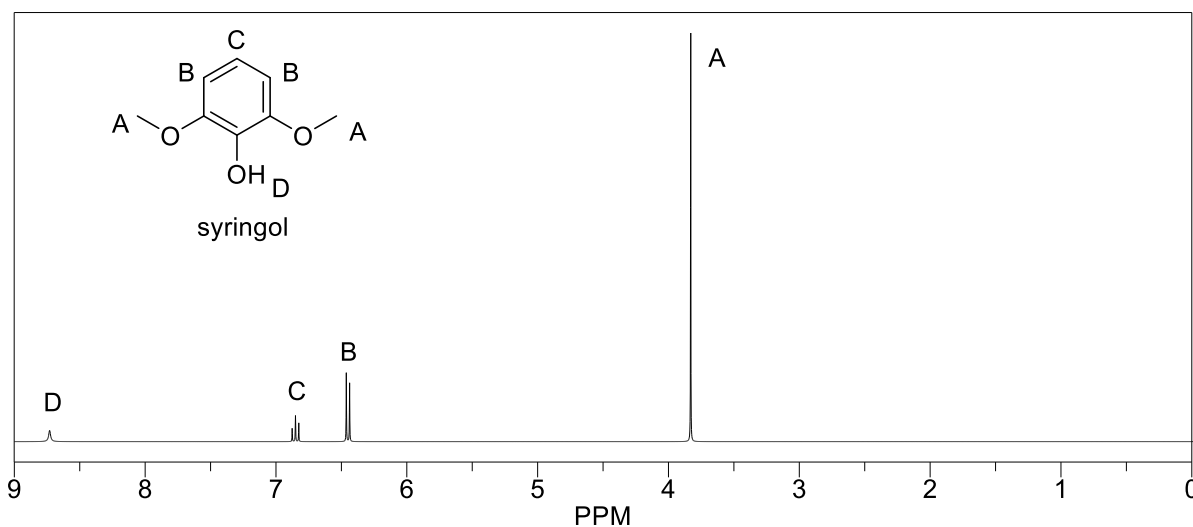
10.



Hydrogen-1 (shown in red) can be detected using ^1H NMR. Phenol-*d* has an isotope of hydrogen, deuterium, which would not be observed (although an alcohol can exchange a D for an H, which could be observed).

11. Furaneol and methoxyfuraneol would have highly similar spectra for most of the peaks. You would be able to distinguish between the two by determining if the spectrum contains a signal indicative of an alcohol or a methoxy.

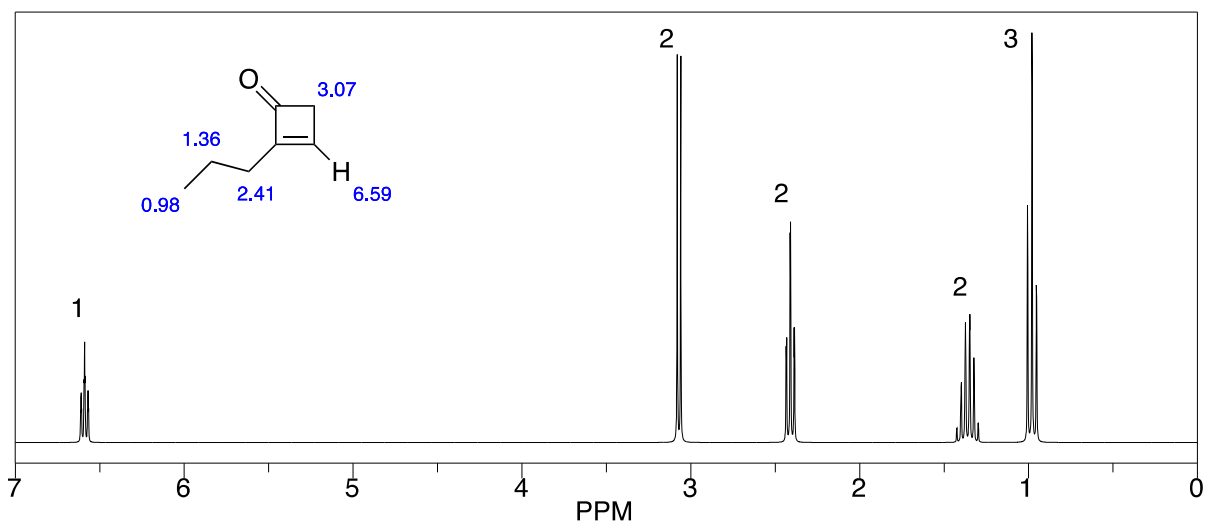
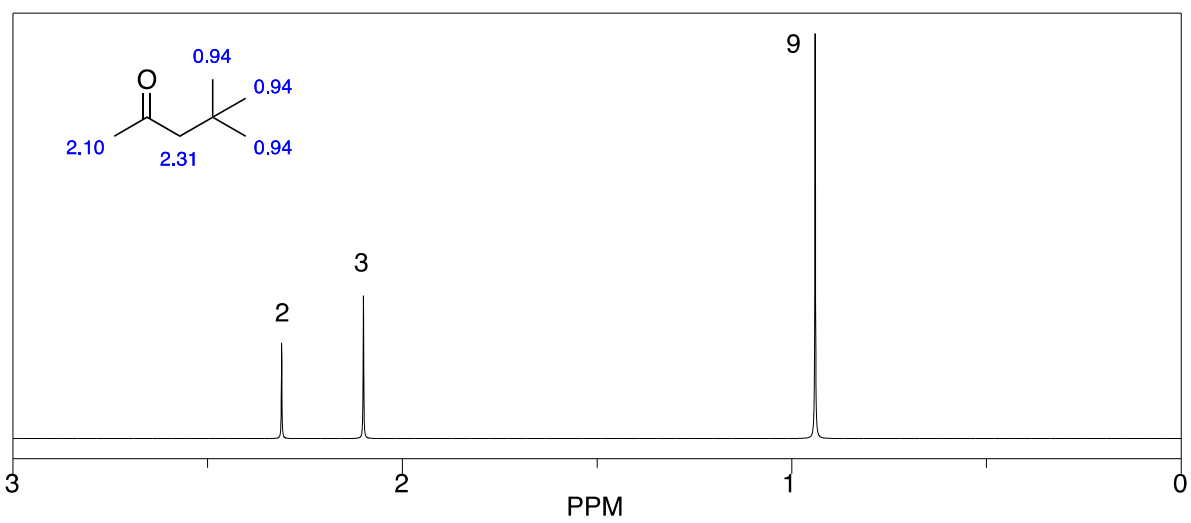
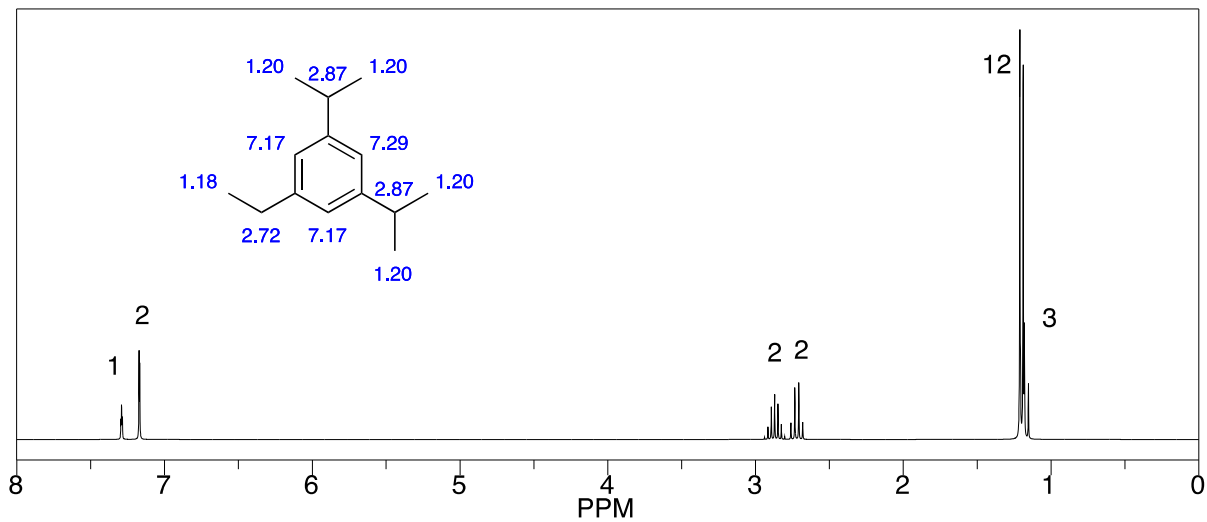
12.



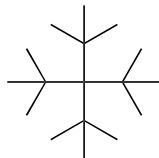
c. Signal Strength and Intensity

13. a. Adding up the integration values, one obtains a total of 192.4. Since the compound has a total of 8 protons, this means that each proton should correspond to about 24 integration units. Therefore, the signals represent 1, 1, 1, 2 and 3 protons respectively.
- b. Adding up the integration values, one obtains a total of 267.5. Since the compound has 26 protons, this means that each proton should correspond to about 10 integration units. Therefore, the signals represent 1, 1, 1, 1, 3, 1, and 18 protons respectively.

14. Integrations are shown above peaks.



15. If the NMR spectrum of this compound is one singlet, this means that all protons in the compound must be chemically equivalent, and no protons are neighboring each other. Since there are 36 protons total, this could be representative of 12 equivalent methyl groups. Since there are no neighboring protons to these methyl groups, tert-butyl groups would be a reasonable starting point. Each tert-butyl group is made up of 9 protons, so 4 tert-butyl groups are needed. This results in the following structure. This structure would yield a total of 3 signals in a ^{13}C NMR spectrum.



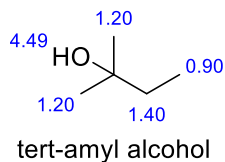
16. Find the number of hydrogens for each signal: $84.9 / 28.2 = 3\text{H}$

Add up the hydrogen: $3\text{H} + 3\text{H} + 2\text{H} + 1\text{H} + 1\text{H} + 1\text{H} + 1\text{H} = 12\text{H}$

Chemical formula: $\text{C}_5\text{H}_{12}\text{O}_2$

$$\text{HDI} = \frac{1}{2}(2C + 2 + N - X - H) = \frac{1}{2}(10 + 2 - 12) = 0$$

17.

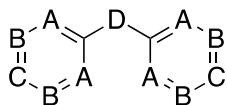


The integration was not done correctly; each integration should be doubled: 0.9 ppm (3 H), 1.2 ppm (6 H), 1.4 ppm (2 H), 4.5 ppm (1 H).

18. Each of these compounds have protons that are all chemically equivalent. Melamine would have 6 H accounted for in the peak, cyclobutane 8 H, neopentane 12 H, and the chlorobenzene compound would have 9H.

d. Coupling

19.

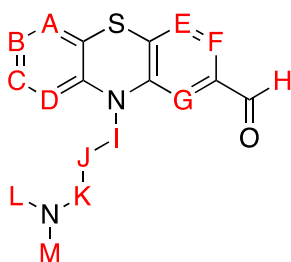


A=1 neighboring proton=doublet

B=2 neighboring protons= triplet

C=2 neighboring protons= triplet

D=0 neighboring protons= singlet



A=1 neighboring proton=doublet

B=2 neighboring protons= triplet

C=2 neighboring protons=triplet

D=1 neighboring protons=doublet

E=1 neighboring protons=doublet

F=1 neighboring protons=doublet

G=0 neighboring protons=singlet

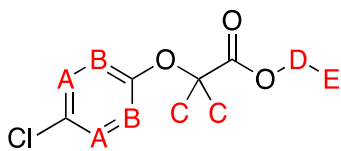
H=0 neighboring protons=singlet

I=2 neighboring protons=triplet

J=4 neighboring protons=quintet

K=2 neighboring protons=triplet

L/M=0 neighboring protons=singlet



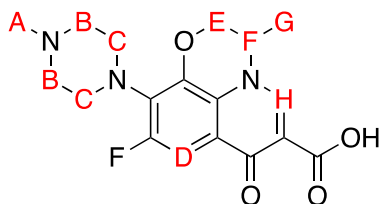
A=1 neighboring proton=doublet

B=1 neighboring proton=doublet

C=0 neighboring protons=singlet

D=3 neighboring protons=quartet

E=2 neighboring protons=triplet



A=0 neighboring protons=singlet

B=2 neighboring protons=triplet

C=2 neighboring protons=triplet

D=0 neighboring protons=singlet

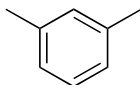
E(protons are not chemically equivalent)=2 neighboring protons=doublet of doublets

F=2 neighboring protons=triplet

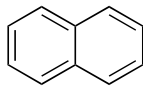
G=1 neighboring proton=doublet

H=0 neighboring protons=singlet

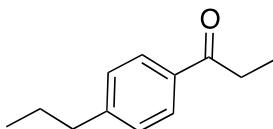
20. a. Based on the molecular formula, the HDI=4. The presence of peaks at 7.43, 7.34 and 6.98 suggests an aromatic ring. These account for a total of 4 protons, meaning that this could be a disubstituted benzene ring. There is also a singlet that accounts for the remaining 6 protons, which could be due to two chemically equivalent methyl groups. Since one of the protons on the benzene ring appears as a singlet, this means that it cannot have any neighboring protons. This could be accomplished by the placement of the methyl groups on each side of this proton, leading to the following structure.



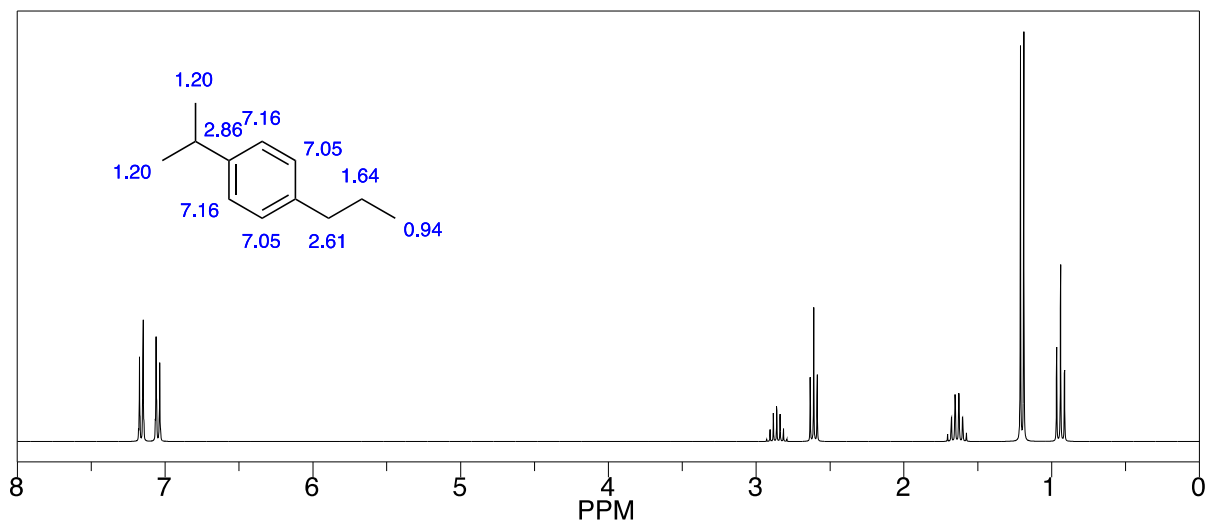
b. Based on the molecular formula, the HDI=7. The presence of peaks at 7.67 and 7.32, suggests that all protons are probably attached to an aromatic ring. Since 1 benzene ring has an HDI of 4, there are probably multiple aromatic rings present. The following structure has an HDI of 7 and matches the expected ^1H NMR spectrum.

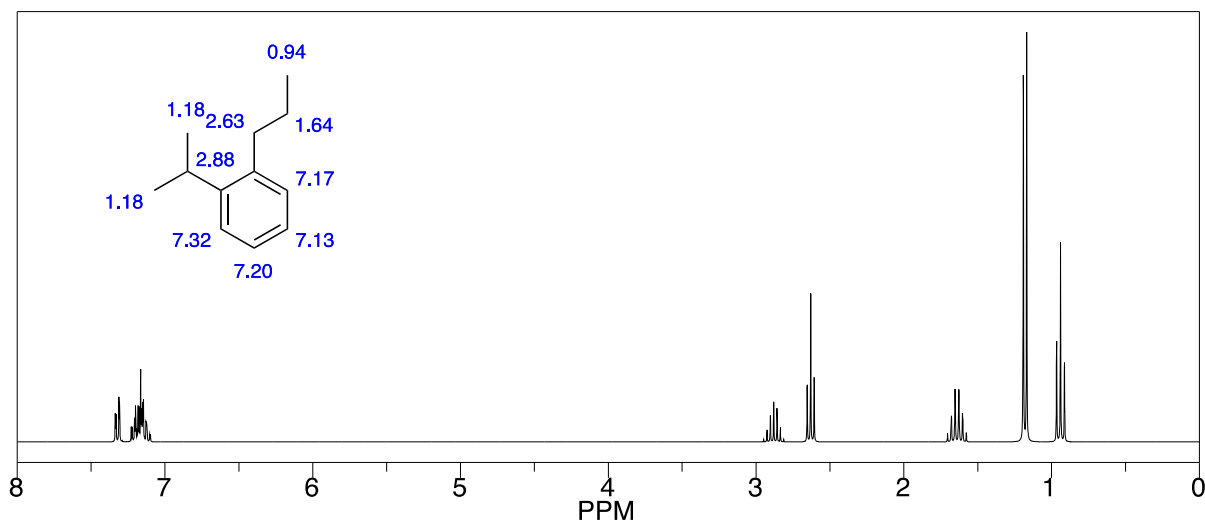


c. Based on the molecular formula, the HDI=5. The peaks at 6.90 and 6.80 are probably aromatic and account for a total of 4 protons. The splitting for these peaks suggests 2 substituents on the aromatic ring on opposite sides of the ring (para). The peak at 3.54 is suggestive of protons adjacent to an oxygen or a carbonyl group. Since the HDI is 5, a carbonyl group would give the additional double bond needed. Since both methyl peaks are triplets, this means that they must both be adjacent to CH_2 groups. Since one of the CH_2 groups appear as a sextet (1.64 ppm), this must also neighbor a CH_2 group (2.61 ppm) (5 neighboring protons total), leading to the presence of a propyl chain. The other CH_2 group (3.54 ppm) is a quartet, meaning that the other alkyl chain must be an ethyl chain. This yields the following structure.



21.





While the peaks from 0-3 ppm remain very similar to one another, the main difference is in the peaks in the region of 7-8 ppm. In the first product, one can expect 2 doublets in this region, while in the second product, one can expect 4 separate peaks with varying splitting patterns in this region of the spectrum. For this reason, one could use ^1H NMR to differentiate between these products.

22.

				1										
				1		1								
			1		2		1							
		1		3		3		1						
	1		4		6		4		1					
		1	5		10		10		5	1				
			1	6		15		20		15		6		1

Protons with 0 neighbors would be a singlet.

Protons with 1 neighbor would be a doublet with the ratio of peaks at 1:1.

Protons with 2 neighbors would be a triplet with the ratio of peaks at 1:2:1.

Protons with 3 neighbors would be a quartet with the ratio of peaks at 1:3:3:1.

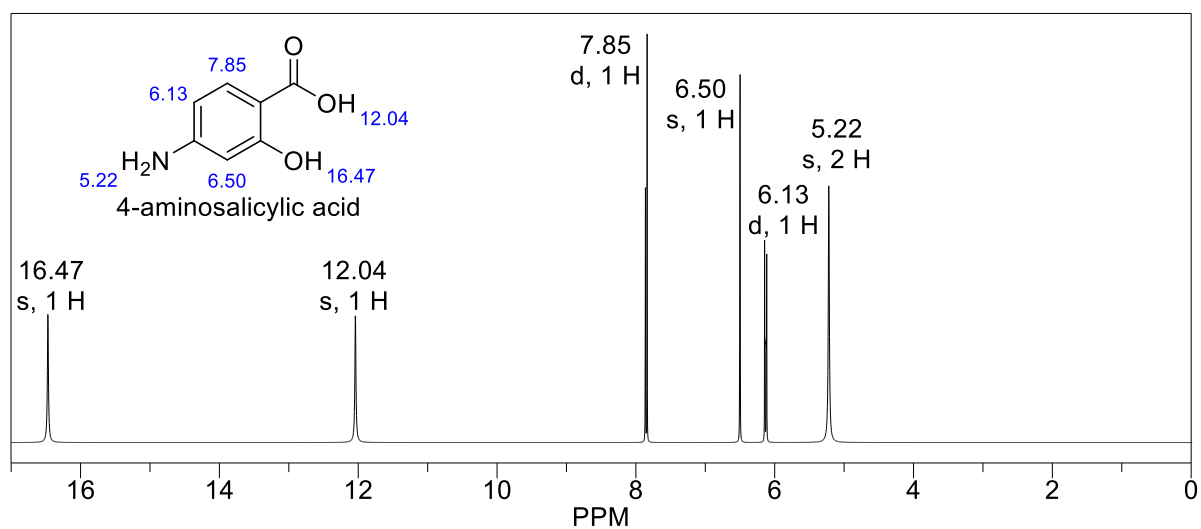
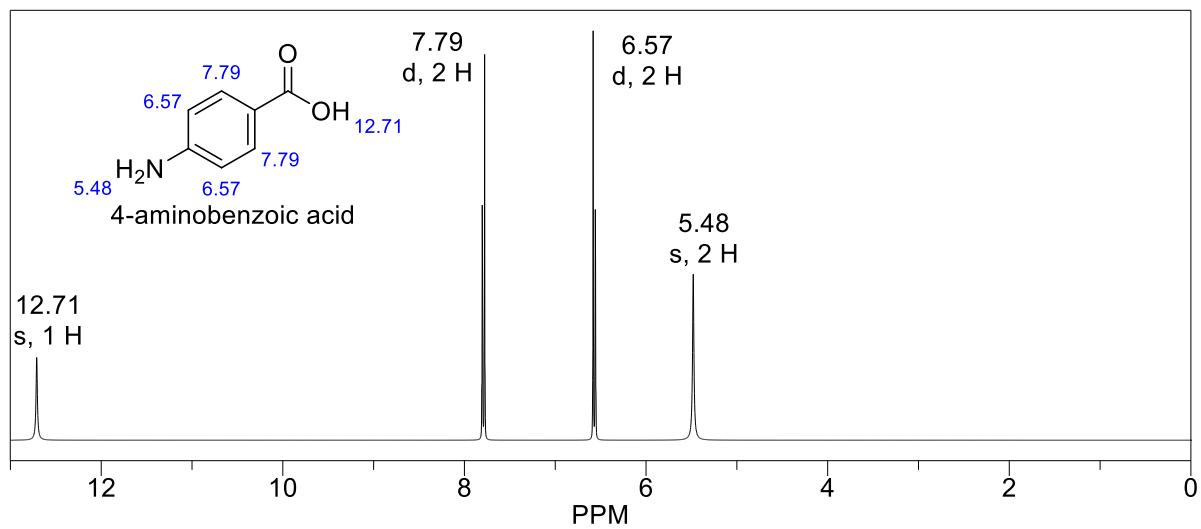
Protons with 4 neighbors would be a quintet with the ratio of peaks at 1:4:6:4:1.

Protons with 5 neighbors would be a sextet with the ratio of peaks at 1:5:10:10:5:1.

Protons with 6 neighbors would be a heptet with the ratio of peaks at 1:6:15:20:15:6:1.

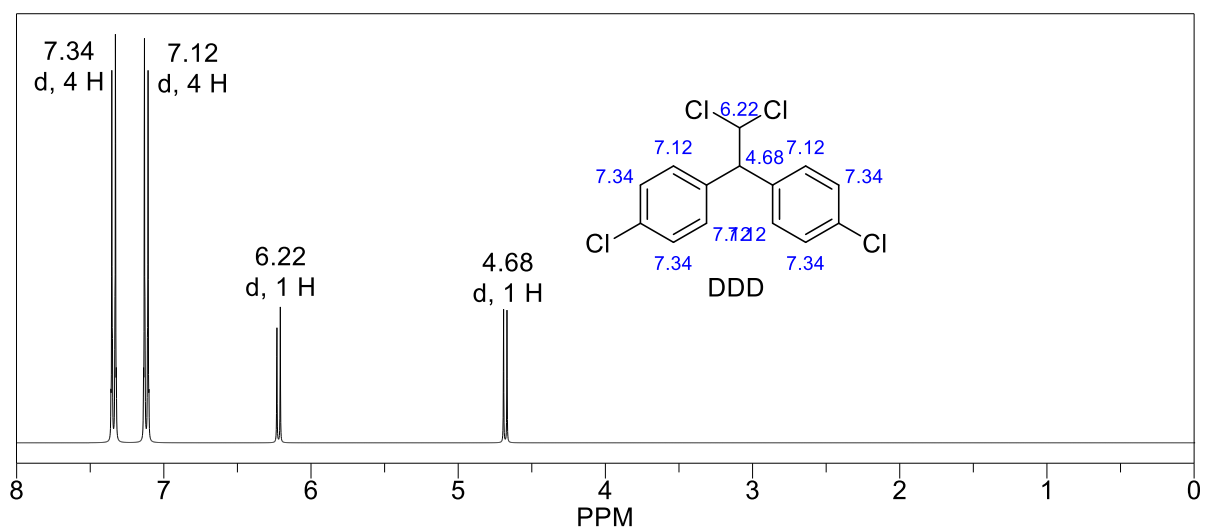
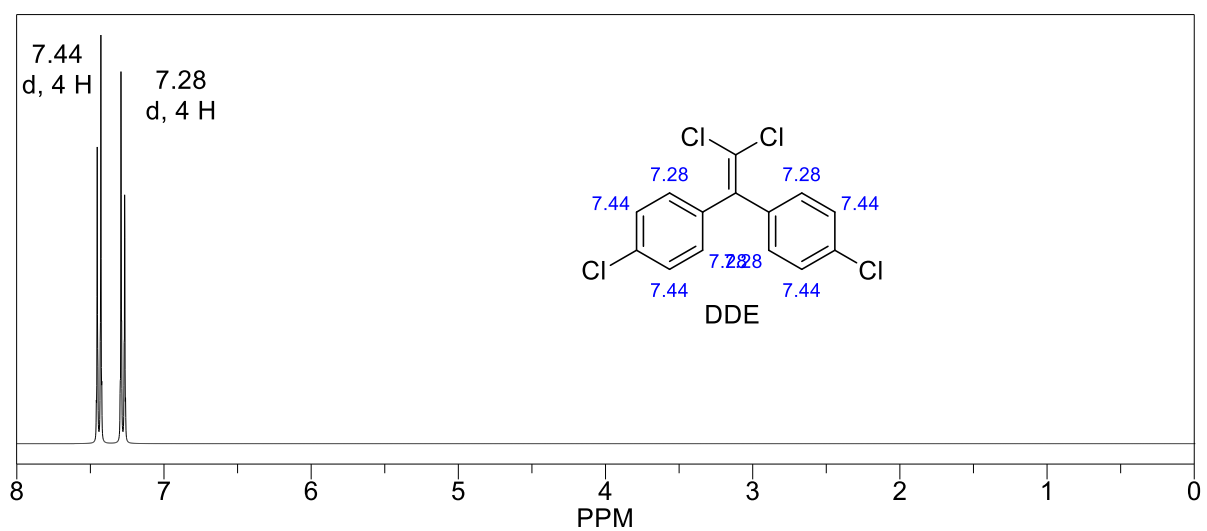
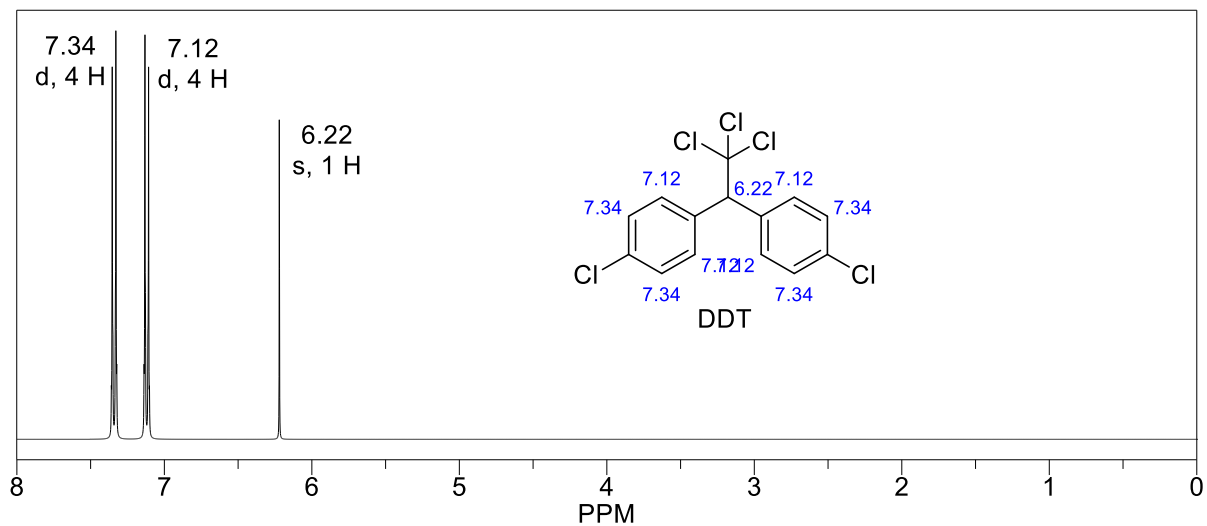
NOTE: You will also see “multiplet” used when the splitting pattern is unclear. Also notice that the outer peaks of splitting patterns such as sextet and heptet may be hard (or in some cases nearly impossible) to distinguish from the baseline.

23.



NOTE: Phenolic protons typically appear between 4 and 8 ppm, but is shifted downfield (more deshielded) due to intramolecular hydrogen bonding with the carboxylic acid.

24.

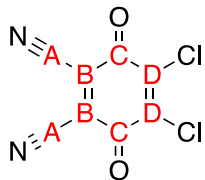


All of the compounds have aromatic rings with similar substituents, but the non-aromatic protons can be used to distinguish between the compounds: DDE has no other protons, DDT has a proton that would appear as a singlet, and DDD has two protons that would appear as doublets.

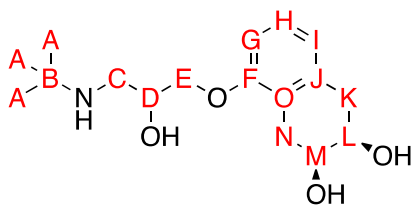
e. ^{13}C NMR

25.

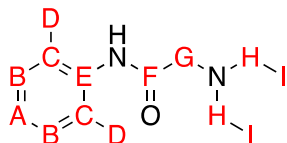
One can expect a total of 4 peaks.



One can expect a total of 15 peaks.



One can expect a total of 9 peaks.

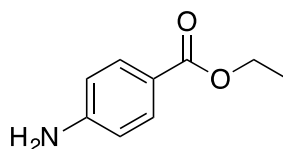


26. a. 1 secondary carbon signal (- in DEPT 135); 2 tertiary carbon signals (+ in DEPT 90); 1 primary carbon signal (+ in DEPT 135, 0 in DEPT 90); 2 quaternary carbon signals (not in either DEPT)

Peak at 165.9 ppm could be a carbonyl carbon. 152.7 and 130.7 ppm are probably aromatic carbons (symmetry possible since less than 9 signals are seen).

HDI=5 (4 from aromatic ring and 1 from carbonyl=5)

Structure (for your information):

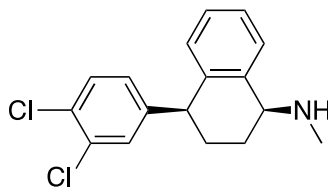


b. 2 secondary carbon signals; 9 tertiary carbon signals; 1 primary carbon signal; 5 quaternary carbon signals

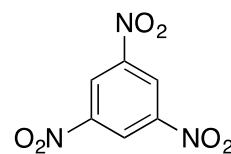
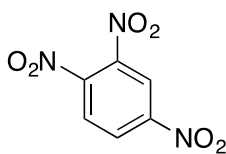
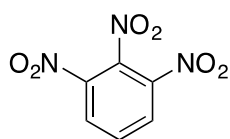
Peaks from 150-125 ppm are probably from aromatic rings. Based on the number of signals (12), it could be two benzene rings.

HDI=9 (each benzene ring contributes 4, so if 2 are present, one more ring should be present)

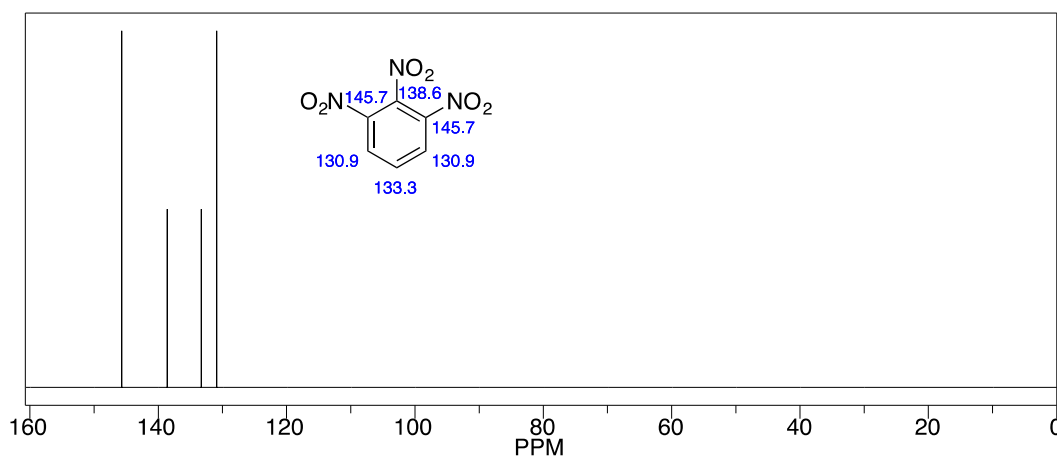
Structure (for your information):

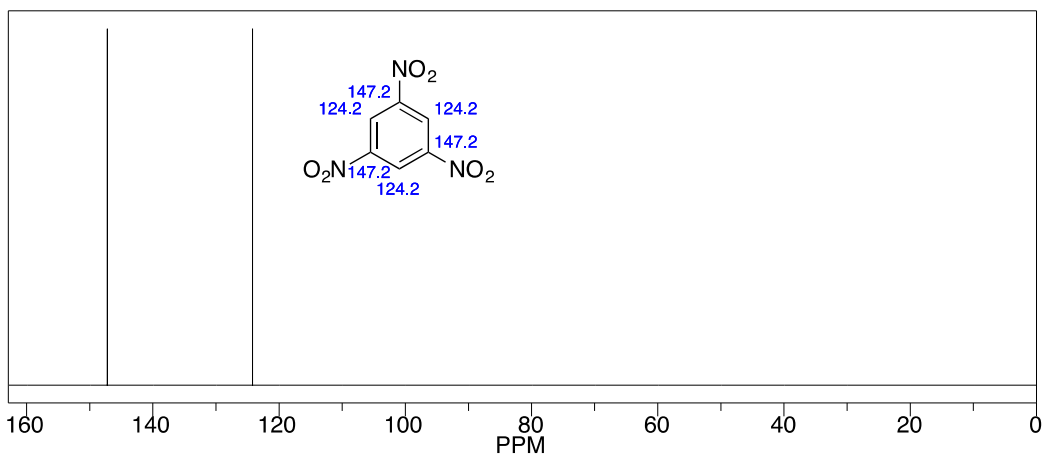
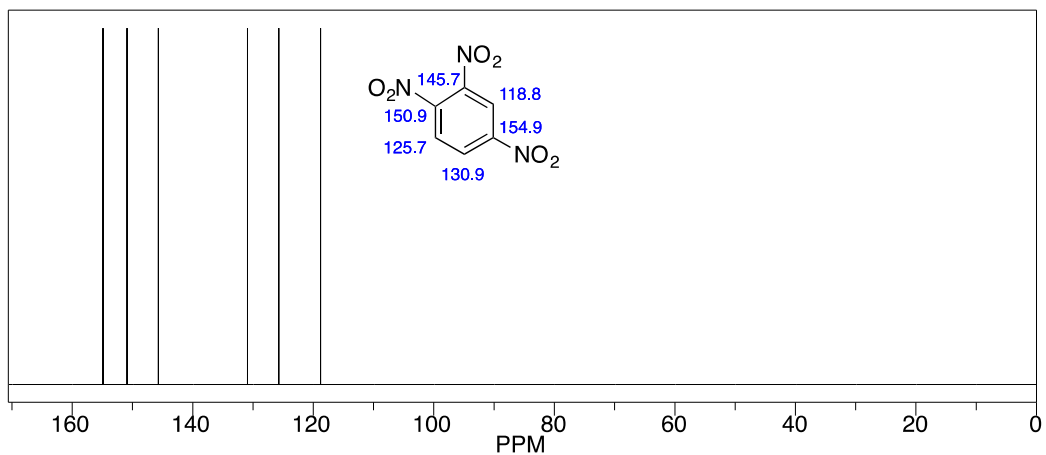


27.

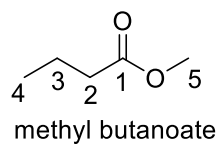


I would expect to see 4, 6, and 2 respectively. Therefore, one can use ^{13}C NMR to differentiate between isomers.

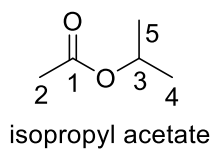




28.

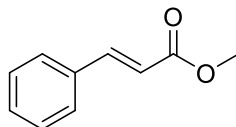


	Type	δ (ppm)	13C	DEPT-135	DEPT-90
1	C	173	positive	null	null
2	CH ₂	36	positive	negative	null
3	CH ₂	18	positive	negative	null
4	CH ₃	14	positive	positive	null
5	CH ₃	52	positive	positive	null



	Type	δ (ppm)	^{13}C	DEPT-135	DEPT-90
1	C	173	positive	null	null
2	CH_3	36	positive	negative	null
3	CH	18	positive	negative	null
4	CH_3	14	positive	positive	null
5	CH_3	52	positive	positive	null

29.



methyl cinnamate

30.

Solvent	^1H NMR	^{13}C NMR
chloroform	7.24 ppm, s, 1 H	77.2 ppm
methanol (CH_3)	3.31 ppm, s, 3 H	49.15 ppm
methanol (OH)	4.78 ppm, s, 1 H	n/a
dimethylsulfoxide	2.50 ppm, s, 6 H	39.51 ppm
water	3.30 ppm, s, 2 H	n/a
benzene	7.16 ppm, s, 6 H	128.39 ppm
acetonitrile (CH_3)	1.94 ppm, s, 3 H	1.39 ppm
acetonitrile (C)	n/a	118.69 ppm
acetone (CH_3)	2.05 ppm, s, 6 H	29.92 ppm
acetone (C)	n/a	206.68 ppm

NOTE: Values obtained from NMR Solvent Data Chart (Cambridge Isotope Laboratories, Inc.) and/or ChemBioDraw Ultra NMR Prediction Software (CambridgeSoft Corp., PerkinElmer, Inc.).


ANSWERS FOR PROBLEM SET 7: FOUNDATIONS OF CHEMICAL REACTIVITY AND MECHANISMS

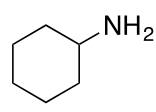
a. Chemical Reaction Components

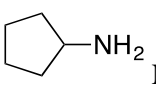
i. Reactants and substrates

1. Reactant/Substrate—a substance that takes part in and is changed in the course of a chemical reaction. These are found on the left side of the arrow in a chemical reaction equation.

2.

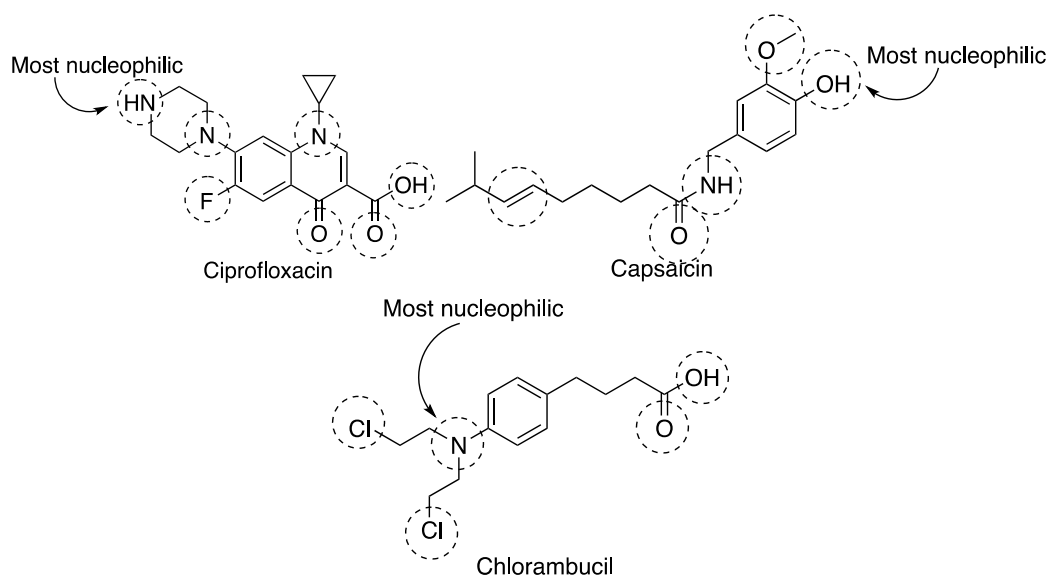
a.  Negatively charged, more nucleophilic

b.  No resonance with nitrogen, more nucleophilic

c.  Nitrogen is less electronegative, more nucleophilic

d.  Less steric hindrance, more nucleophilic

3.

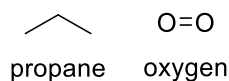


4. Steric effects: the consequences on a reaction or a molecule due to the size of atoms or groups (e.g. size: t-Bu > CH₃ > H and steric effects: t-Bu > CH₃ > H)

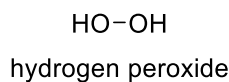
Steric hindrance: the slower reaction rate or prevention of a chemical reaction due to the increase in energy from having larger/bulkier groups (e.g. S_N2 reactivity: 3° < 2° < 1°)

5.

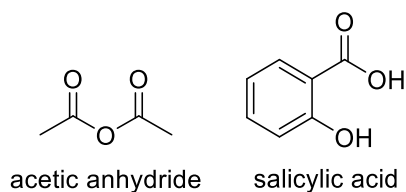
a.



b.



c.



6. Lactose would be considered both a reactant and a substrate. It is changed in the reaction and is the species converted by an enzyme. Water is needed as a reactant to balance the reaction.

ii. Reagents

7. Reagent-substance added to cause a chemical reaction to occur

Reagents are usually indicated above the reaction arrow in the chemical reaction equation.

Reactants are typically the substance that the desired transformation is being performed on, while reagents are used to achieve those transformations.

8.

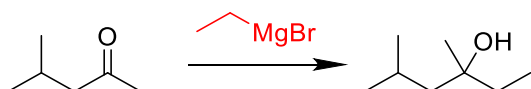
a. NaBH_4 can be used to reduce ketones and aldehydes. Lithium aluminum hydride can be used to reduce aldehydes, ketones, esters and carboxylic acids. H_2 and palladium can be used to reduce alkenes, aldehydes and ketones.

b. For the first transformation, we want a reagent that will convert the ketone without affecting the ester or alkenes. For this reason we would want to use NaBH_4 to accomplish this reduction. For the second, we want to reduce the ketone and the ester, but not the alkenes. Therefore, we will use lithium aluminum hydride.

9. The main difference between the two reactions is in the size of the base used. In the first reaction, a smaller base is used allowing for easier deprotonation to give the more substituted 2-hexene products. In the second, a more bulky base is used, lowering the yield of the 2-hexene products in favor of the 1-hexene.

- 10.
- a. alkylating agent: transfers an alkyl group from one molecule to another (alkylation; e.g. alkyl halides can be used to alkylate aromatic substrates, as in the Friedel-Crafts reactions)
 - b. fluorinating agent: adds fluorine to the molecule (e.g. HF-pyridine can be used to convert alcohols into alkyl fluorides)
 - c. dehydrating agent: results in a loss of H₂O from the molecule (e.g. sulfuric acid can be used as a dehydrating agent to remove H₂O from sucrose)
 - d. oxidizing agent: oxidizes the molecule (e.g. bleach, sodium hypochlorite, can be used with a catalyst to produce an epoxide from an alkene)
 - e. reducing agent: reduces the molecule (e.g. lithium aluminum hydride can be used to reduce a nitrile to an amine)

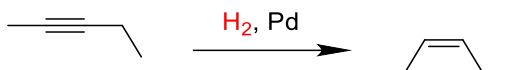
11.



The reagent is ethylmagnesium bromide, and it reduced the ketone to an alcohol.

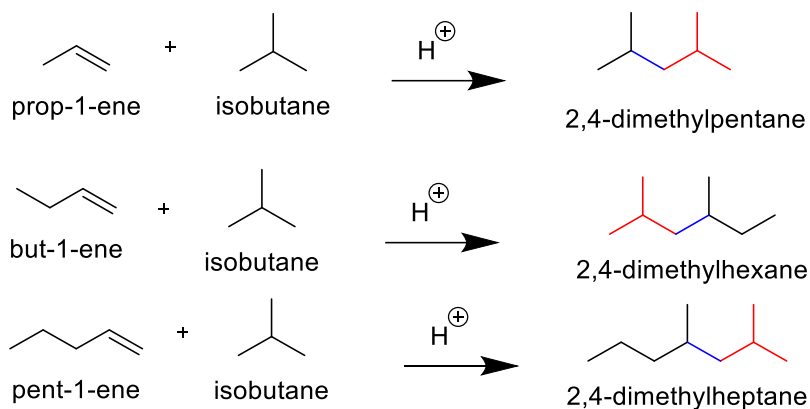


The reagent is pyridinium chlorochromate, and it oxidized the alcohol to a ketone.



The reagent is hydrogen (palladium is a catalyst), and it reduced the alkyne to an alkene.

12.



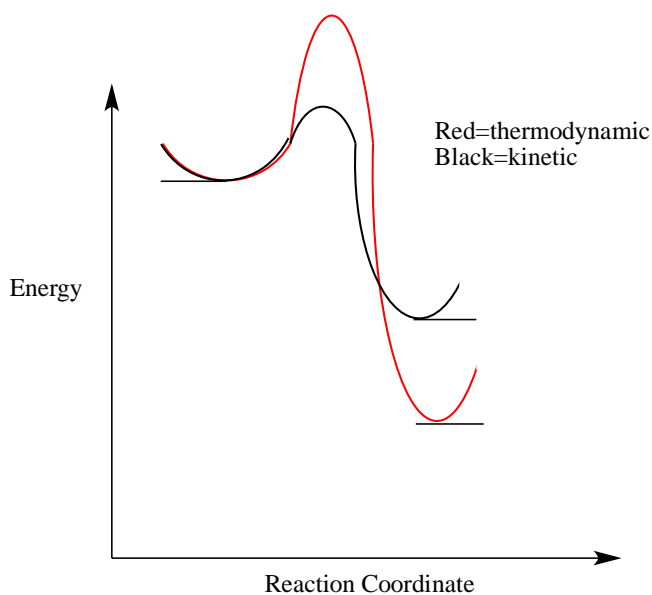
Prop-1-ene, but-1-ene, and pent-1-ene would each be considered a reactant and a substrate. Isobutane would be considered a reactant as well as a reagent. The new C-C bond formed is shown in blue, and the added isobutene unit is shown in red.

iii. Product

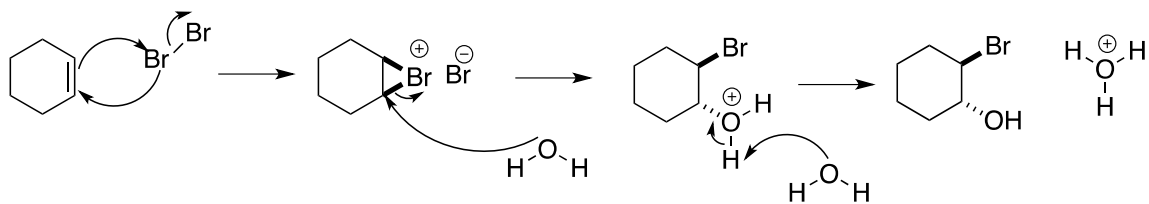
13. Product-the chemical compound that results from a chemical reaction. Products are indicated on the right side of the arrow in a chemical reaction equation.

14. Kinetic product-the product of a chemical reaction that is favored by the reaction rate

Thermodynamic product-the product of a chemical reaction that is favored by the lower energy of the product.

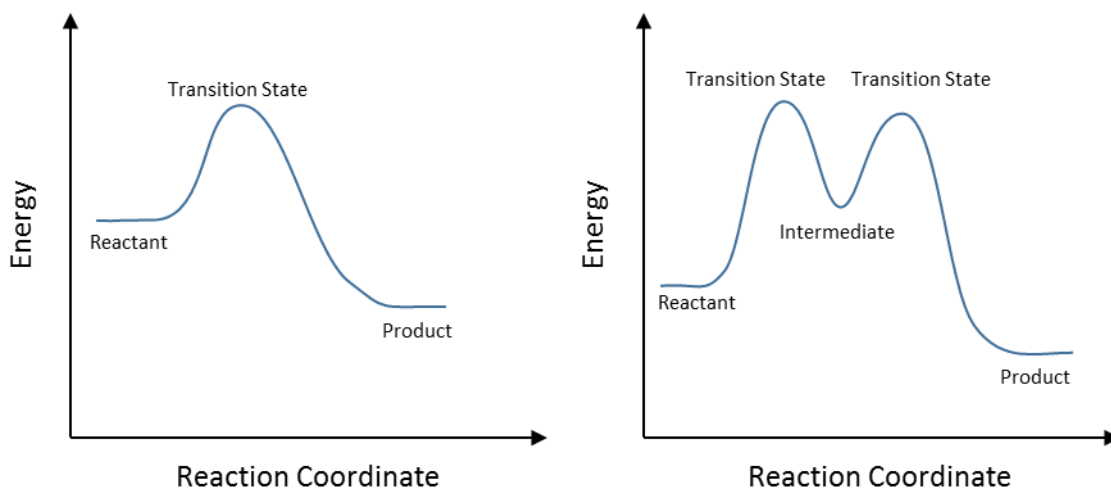


15.

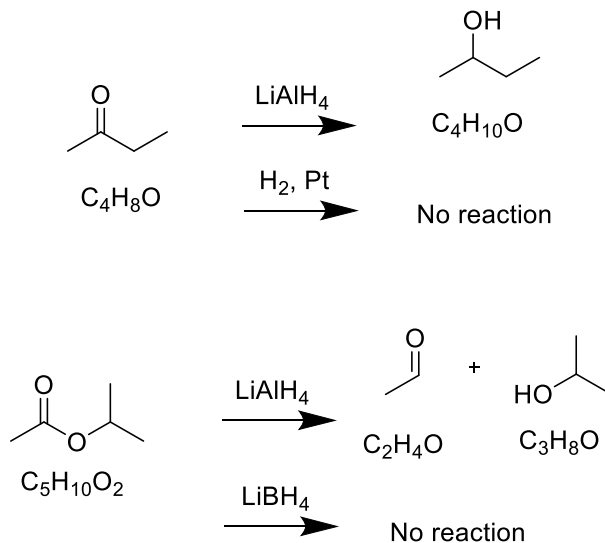


16. A transition state is a high-energy configuration through which the reaction coordinate progresses, while an intermediate forms and then reacts as the reaction coordinate progresses. An intermediate does not have any bonds forming or breaking, but is highly reactive and so will have a short lifespan (e.g. a carbocation). Neither the transition state nor the intermediate would be considered a product, as they are not the final outcome of the reaction

17.



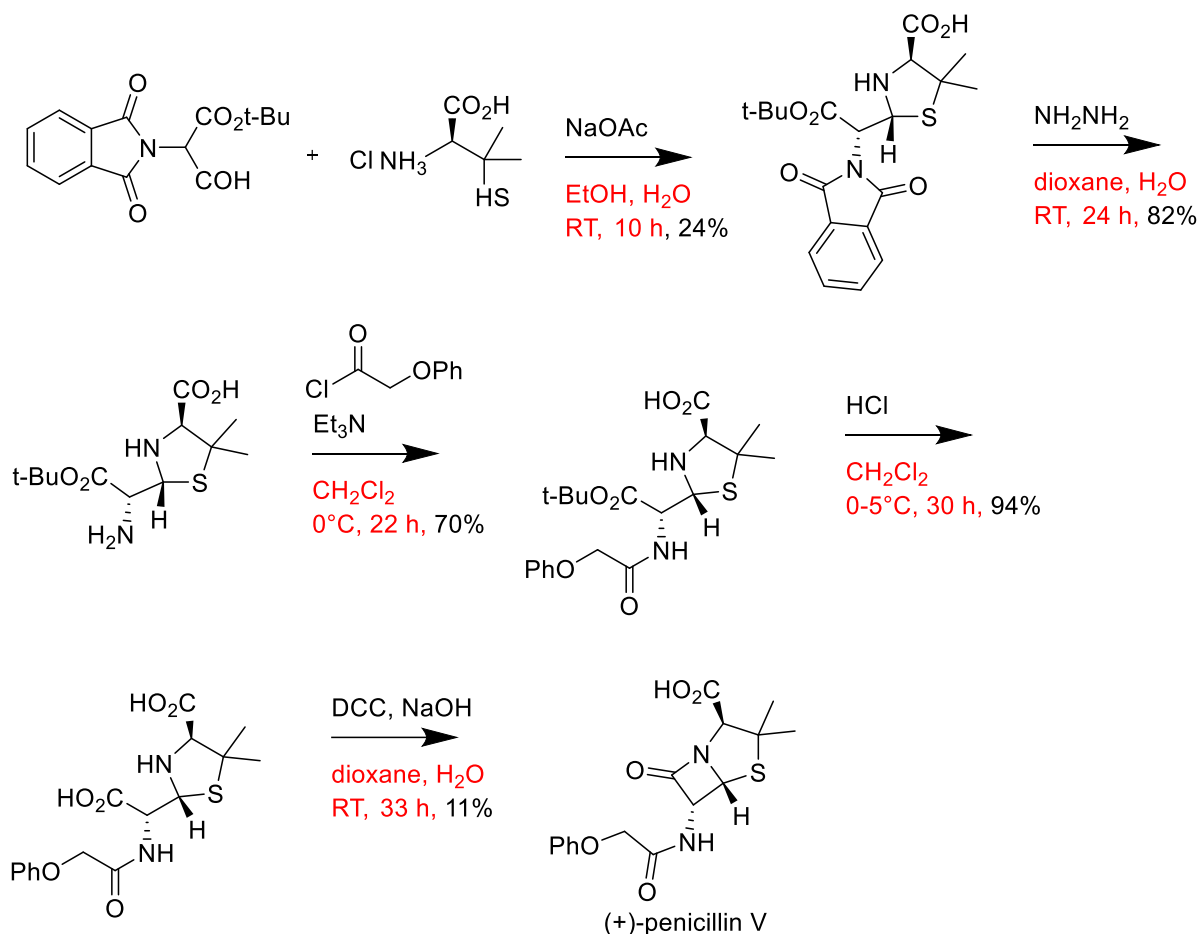
18.



iv. Reaction conditions

- 19.** Three variables that could be considered reaction conditions are temperature, solvent used, reaction time.
- 20.** Conditions that could be changed are the substrate used, the nucleophile used, and the leaving group. In order to favor an S_N2 reaction, one could use a methyl or primary substrate if possible and a good, charged nucleophile.
- 21.** Based on Le Chatelier's Principle, I would expect that additional water, a product of the reaction, would cause reactants to be favored and lower the yield. If the product is insoluble in water, however, this would change as the concentration of product will be low due to its being insoluble, causing products to be more favored.
- 22.**
- a. The thermodynamic (bottom) product is lower in energy.
 - b. A larger base has more difficulty deprotonating the carbon necessary to form the thermodynamic enolate, causing the kinetic enolate to be favored. This proton is more open and easily taken away by a base.
 - c. The kinetic enolate should be formed to give the desired product.
- 23.** Only one condition – the variable – should be changed at a time to give the best indication of what is causing the change. The sets of reaction conditions can be compared by determining which has the best percent yield.

24. (I) A total synthesis of penicillin V is shown below. For each step, identify the reaction conditions. (*J. Am. Chem. Soc.* **1957**, DOI: 10.1021/ja01562a063 & *J. Am. Chem. Soc.* **1957**, DOI: 10.1021/ja01521a044).



Reaction conditions are shown in red. These indicate the solvent(s) used, the temperature, and the reaction time. The percent yield of each reaction is also shown below the arrow, but this is a result of the reaction and not a condition. The reagents used in the reaction are indicated above the arrow.

25. Pressure is very important for reactions that involve gases (as reactants, products, or both), but is relatively unimportant for reactions involving only liquids and solids (such as the example of acetic acid and sodium hydroxide). Increasing the temperature will favor the reverse, or endothermic, reaction because the additional heat will affect the equilibrium (Le Chatlier's Principle).

26. Overall yield = $1.00 \times 0.83 \times 0.93 = 77\%$

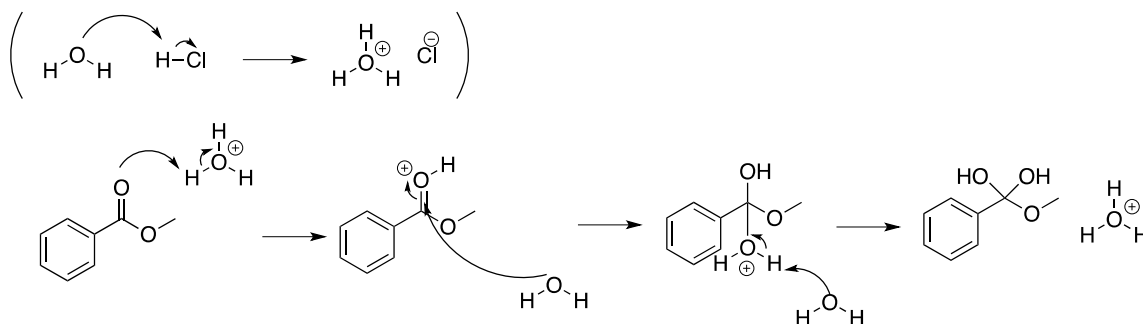
Improved yield = $1.00 \times 0.89 \times 0.95 = 85\%$

The improved yields for the second and third steps result in an increase of 9.5% for the overall yield.

v. Catalyst

27. Catalyst-an additive in a reaction that makes the reaction occur more quickly; catalysts are not consumed in the reaction; catalysts serve to lower the activation energy, causing the rate of the reaction to be increased.

28.



Yes, a catalyst is present. The catalyst is the hydronium ions present from the dissociation of HCl in water.

29. In the case of the hydrochloric acid, product forms immediately. This is due to the fact that HCl is a strong acid and therefore dissociated completely in water, allowing for more catalyst to be present for the reaction. In the case of acetic acid, a weak acid, there is less catalyst present and therefore the rate of reaction is slower.

30. The presence of a catalyst has no effect on the difference in free energy of the reactants or products; it lowers the energy of activation needed to reach the transition state in a reaction.

31. A homogenous catalyst is in the same phase as the reactants, while a heterogeneous catalyst is in a different phase than the reactants.

32. Enzymes lower the activation energy and allow the reaction to proceed more quickly, but they do not affect equilibrium. In tissues where there the concentration of carbon dioxide is high, the enzyme will catalyze the reverse reaction (i.e. the reaction between carbon dioxide and water to form carbonic acid).

33. The bubbling is due to the production of oxygen gas from the reaction. Uncut skin means the cells are intact, so there is no catalase present to catalyze the reaction.

A catalase-positive bacterium would be indicated by the bubbles formed from the decomposition reaction, while a catalase-negative microorganism would not show the characteristic bubbling.

vi. The role of energy

34. Your values for bond dissociation energies may vary some.

a. Bonds broken: C-Cl; O-H = $339 \text{ kJ/mol} + 498 \text{ kJ/mol} = +837 \text{ kJ/mol}$

Bonds formed: C-O; H-Cl = $-381 \text{ kJ/mol} + -431 \text{ kJ/mol} = -812 \text{ kJ/mol}$

Enthalpy of reaction = $+837 \text{ kJ/mol} - 812 \text{ kJ/mol} = +25 \text{ kJ/mol}$

Reaction is endothermic.

Entropy is approximately 0.

Not spontaneous at all temperatures.

b. Bonds broken: C=C (3); C-C = $+602 (3) + 356 \text{ kJ/mol} = +2162 \text{ kJ/mol}$

Bonds formed: C-C (5); C=C = $-356 (5) + -602 \text{ kJ/mol} = -2382 \text{ kJ/mol}$

Enthalpy of reaction = -220 kJ/mol

Reaction is exothermic.

Entropy of reaction is negative.

Spontaneous at some (lower) temperatures.

c. Bonds broken: C=C; C=O; C-O = $+602 + 799 + 358 \text{ kJ/mol} = +1759 \text{ kJ/mol}$

Bonds formed: C-C (2); C=O; C-O = $-356(2) + -799 + -358 \text{ kJ/mol} = -1869 \text{ kJ/mol}$

Enthalpy of reaction = -110 kJ/mol

Reaction is exothermic.

Entropy is negative.

Spontaneous at some (lower) temperatures.

35.

a. Products are favored.

b. Reactants are favored.

c. Neither is favored.

d. Reactants are favored.

e. Products are favored.

36. Bonds broken: C=O; O-H = +799 + 459 kJ/mol=1258 kJ/mol
Bonds formed: C-O (2); O-H = -358(2) + -459 kJ/mol= -1175 kJ/mol
Enthalpy of reaction= +83 kJ/mol

This reaction is endothermic. Therefore, the equilibrium will favor products if more heat is put into the reaction (higher temperature).

37.

- a. Bonds broken: C-C triple bond = +962 kJ/mol
Bonds formed: C=C; C-H (2) = -682 + (2)(-427 kJ/mol) = -1536 kJ/mol
Enthalpy=+962 – 1536 kJ/mol = -574 kJ/mol

- b. Bonds broken: C=C = +682 kJ/mol
Bonds formed: C-C; C-H (2) = -356 + (2)(-410 kJ/mol) = -1176 kJ/mol
Enthalpy=682 – 1176 kJ/mol = -494 kJ/mol

c. Palladium acts as a catalyst in this reaction, meaning that it lowers the activation energy. This combined with the fact that the reaction is exothermic, makes the reduction of the alkene very favorable with the typical hydrogenation conditions.

38. Enthalpy:

Entropy:

Gibb's free energy:

Exothermic: a process in which the net transfer of energy is to the surroundings from the system (ΔH is negative)

Endothermic: a process in which the net transfer of energy is from the surroundings to the system (ΔH is positive)

Exergonic: a process which has a negative ΔG , and so is spontaneous

Endergonic: a process which has a positive ΔG , and so is nonspontaneous

39.

Rate: M/s

First order: s^{-1}

Second order: $M^{-1}s^{-1}$

Third order: $M^{-2}s^{-1}$

40. Bonds broken: $2 \text{ C-H} + 1 \text{ C-C} = (2 \cdot 464 \text{ kJ/mol}) + (1 \cdot 368 \text{ kJ/mol}) = 1296 \text{ kJ/mol}$

Bonds formed: $1 \text{ C=C} + 1 \text{ H-H} = (1 \cdot 632 \text{ kJ/mol}) + (1 \cdot 435 \text{ kJ/mol}) = 1067 \text{ kJ/mol}$

$\Delta H = 1296 \text{ kJ/mol} - 1067 \text{ kJ/mol} = +229 \text{ kJ/mol}$

$\Delta G_{294 \text{ K}} = 229 \text{ kJ/mol} - 294 \text{ K} (0.120 \text{ kJ/mol} \cdot \text{K}) = +193 \text{ kJ/mol}$, so this reaction is nonspontaneous at room temperature.

The reaction will be spontaneous when $\Delta G < 0$:

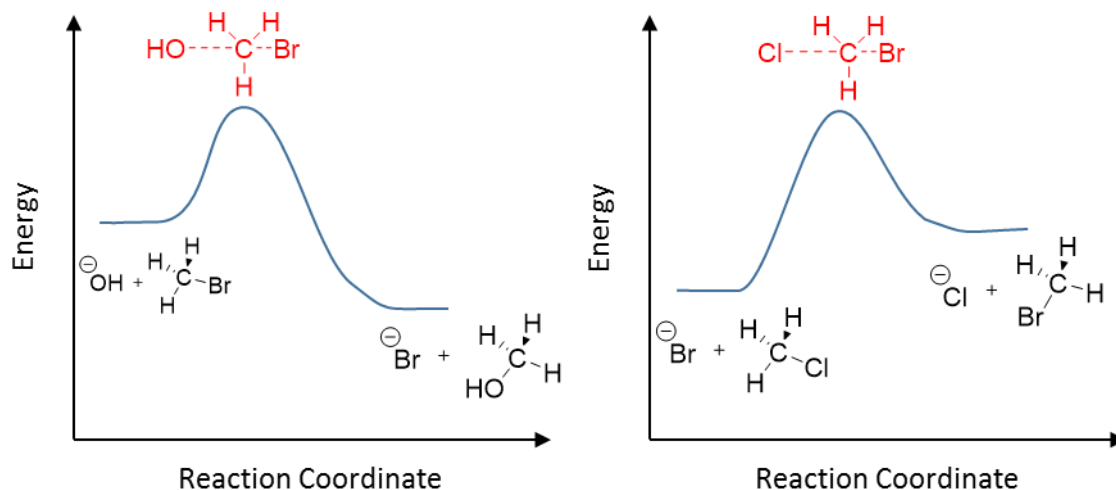
$0 < 229 \text{ kJ/mol} - T (0.120 \text{ kJ/mol} \cdot \text{K})$

$-229 \text{ kJ/mol} < (0.120 \text{ kJ/mol} \cdot \text{K}) T$

$1908 \text{ K} < T$

The reaction will be spontaneous when the temperature is greater than 1908 K (1635°C).

41.

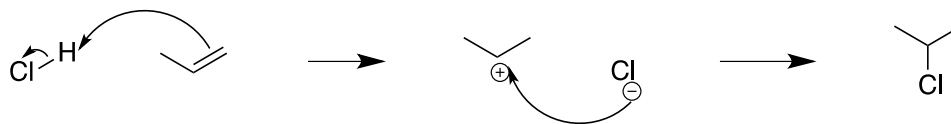


For an exothermic reaction, the transition state will more closely resemble the reactants, while it will more closely resemble the products for an endothermic reaction.

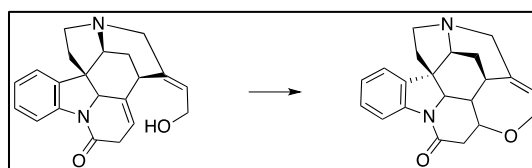
b. Basic Classes of Reactions

i. Addition

42.



43.



44. a. Proton transfer

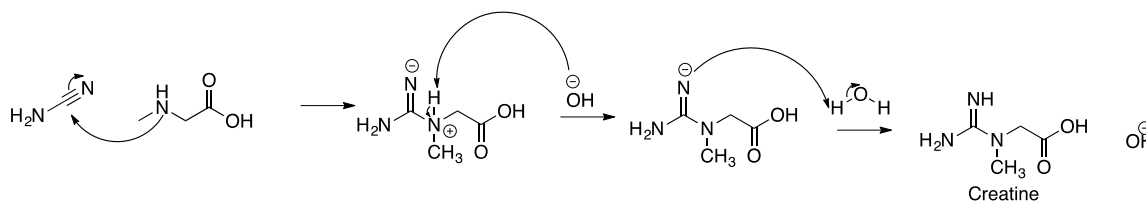
b. Nucleophilic attack

c. Proton transfer

45. 1st step = -124 kJ/mol; 2nd step = -73 kJ/mol

Energy diagram should show a difference of 124 kJ/mol between the reactant and the 1st product, followed by a difference of 73 kJ/mol between the 1st and 2nd product.

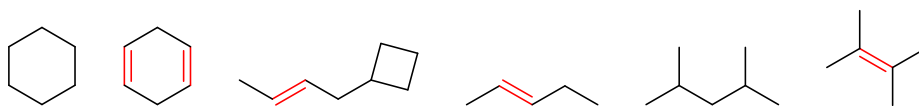
46. a.



b. The first step is a nucleophilic attack. This is followed by two proton transfer steps.

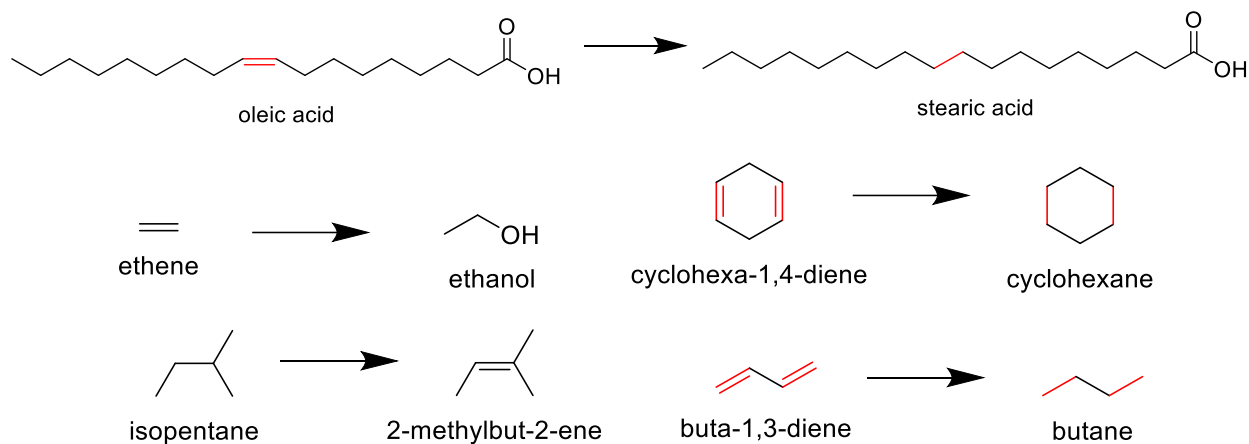
c. The nucleophile is the amine of the second reagent. The electrophile is the carbon of the nitrile functional group of the first reagent.

47.



The possible locations of an addition reaction are shown in red. Cyclohexane and 2,4-dimethylpentane do not have a double bond, so there cannot be an addition reaction performed on these compounds.

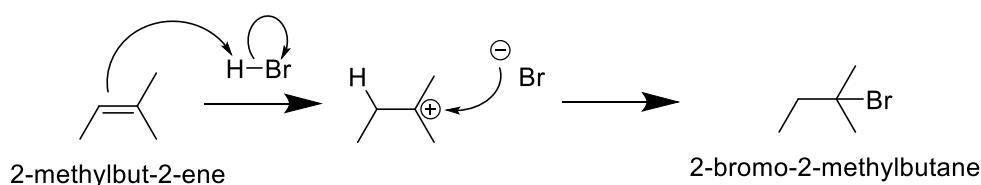
48.



Oleic acid to stearic acid, cyclohexa-1,4-diene to cyclohexane, and buta-1,3-diene to butane are hydrogenation reactions. Ethene to ethanol is a hydration addition reaction. Isopentane to 2-methylbut-2-ene is an elimination reaction.

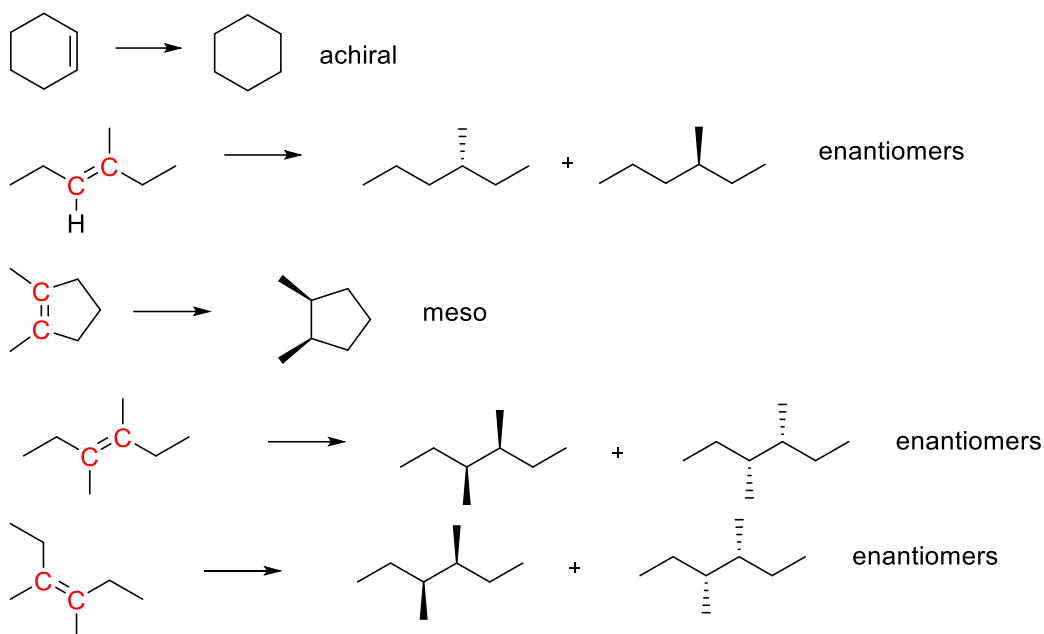
49. Markovnikov addition is the observation that in addition reactions with HBr, the H will end up on the less substituted carbon while the Br (or other group) will be on the more substituted carbon. Anti-Markovnikov addition is where the H is observed to be on the more substituted carbon and the Br on the less substituted carbon. In these reactions, a carbocation is formed when the alkene is protonated. Since the stability of the carbocation increases with substitution, it is more likely that the more substituted carbon will be a carbocation while the less substituted carbon will have the H. The Br anion will then attack the carbocation, resulting in the observed trend.

50.



No, we would not expect the anti-Markovnikov addition to have the same intermediate because it would result in a different product.

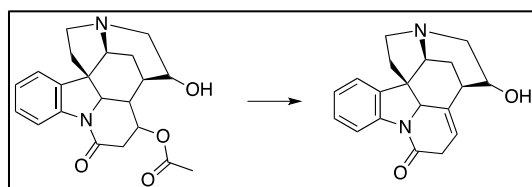
51.



The carbons in red became chiral centers, although the cyclopentene compound's product is meso. The enantiomers would need to be separated in order to obtain a single product.

ii. Elimination

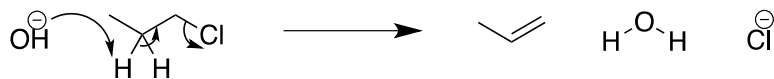
52.



53. E1 eliminations proceed by loss of a leaving group, followed by deprotonation and formation of the alkene. E2 eliminations are concerted, meaning that the loss of the leaving group and the deprotonation occur simultaneously.

54. NaOH and NaOMe are both bases and will result in eliminations. NaBr and NaN₃ do not act as bases and therefore do not result in elimination.

55.



Bonds broken: C-H; C-Cl; C-C = $+411 + 327 + 346 \text{ kJ/mol} = 1084 \text{ kJ/mol}$

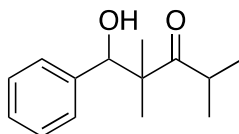
Bonds formed: O-H; C=C = $-459 + -602 \text{ kJ/mol} = -1061 \text{ kJ/mol}$

Enthalpy of reaction = $1084 - 1061 = +23 \text{ kJ/mol}$

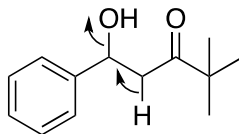
Entropy will be positive.

56. a. The second step is the elimination step of the reaction.

b. The first reaction will not result in a condensation product. The product does not have a proton that can give the elimination step.



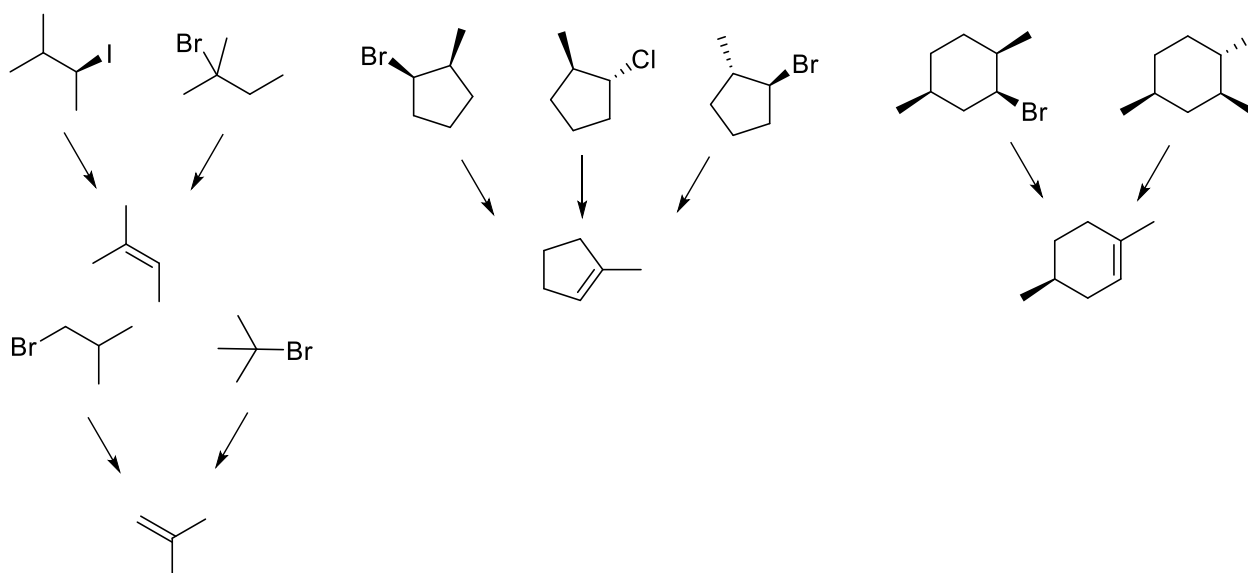
The second reaction will result in a condensation product. There are protons present to allow the elimination to occur.



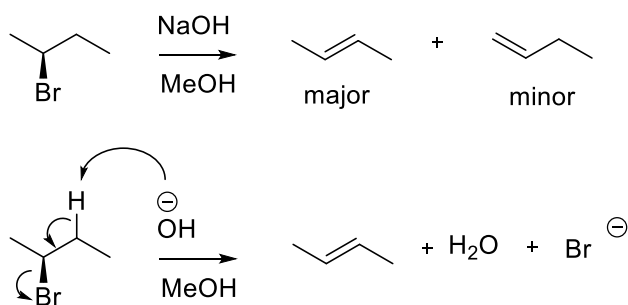
c. The resulting alkene could then undergo a variety of addition reactions to the carbon-carbon double bond.

57. Zaitsev's rule predicts that the product of an elimination reaction will favor the more substituted alkene. Hofmann's rule predicts that the product of an elimination reaction will favor the less substituted alkene.

58.

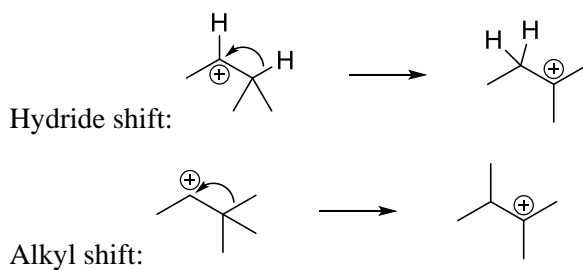


59.



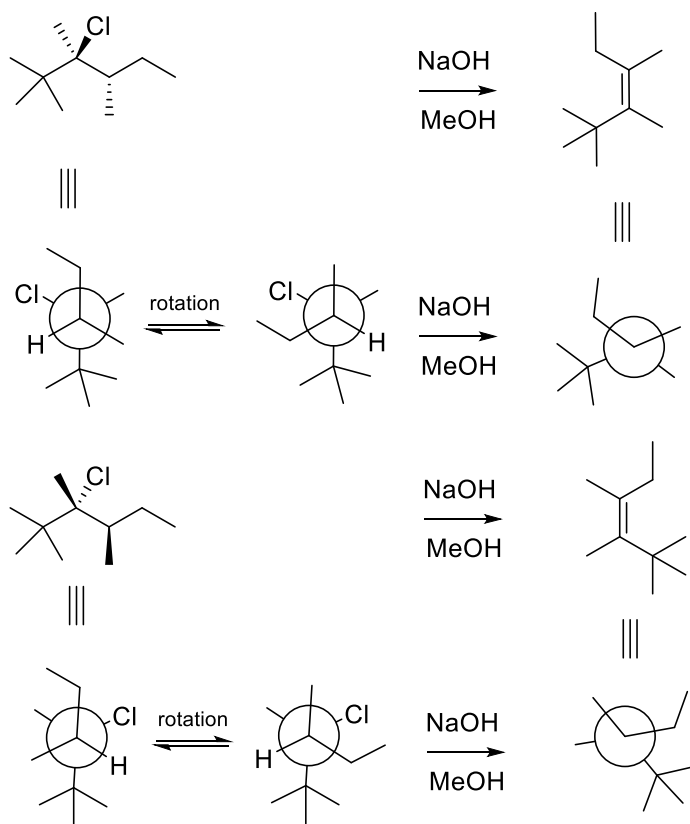
This is a dehydrohalogenation proceeding through an E2 reaction mechanism

60.



Hydride shifts and alkyl shifts are called 1,2-hydride/alkyl shifts to denote that the group has moved to an adjacent carbon. This would only be observed with the E1 reaction mechanism because there is no carbocation intermediate in the E2 mechanism.

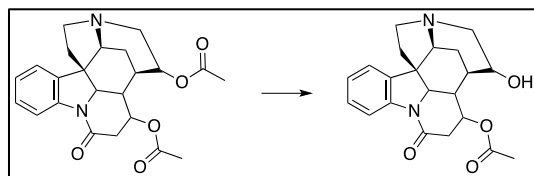
61.



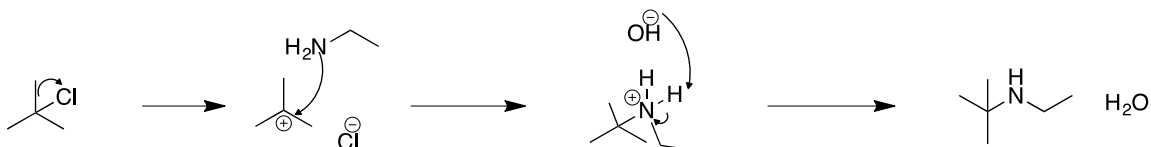
If a *cis* alkene is the desired product, you would be able to use the racemic mixture since the enantiomers gave the same product. You would get the same result with an optically pure sample of the starting material, but the additional cost would not be worth it. The diastereomers would give the *trans* alkene.

iii. Substitution

62.

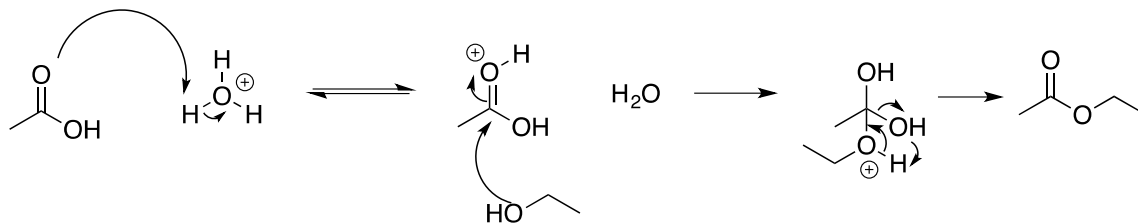


63.



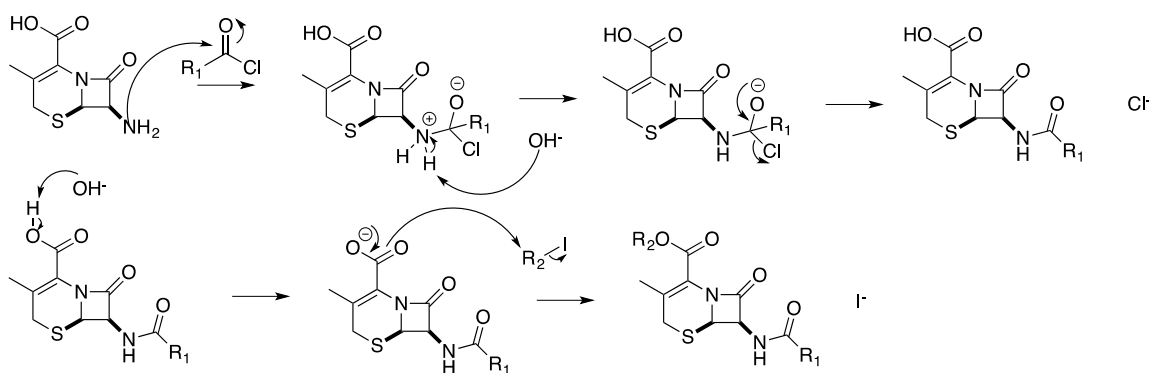
64. For this problem, the reaction of the acid halide and acid anhydride should be more exothermic than that of the amide. Entropy for these reactions should be approximately zero for these reactions. Ultimately, the reaction with the acid halide and acid anhydride should be more likely to occur spontaneously.

65.



66.

a.

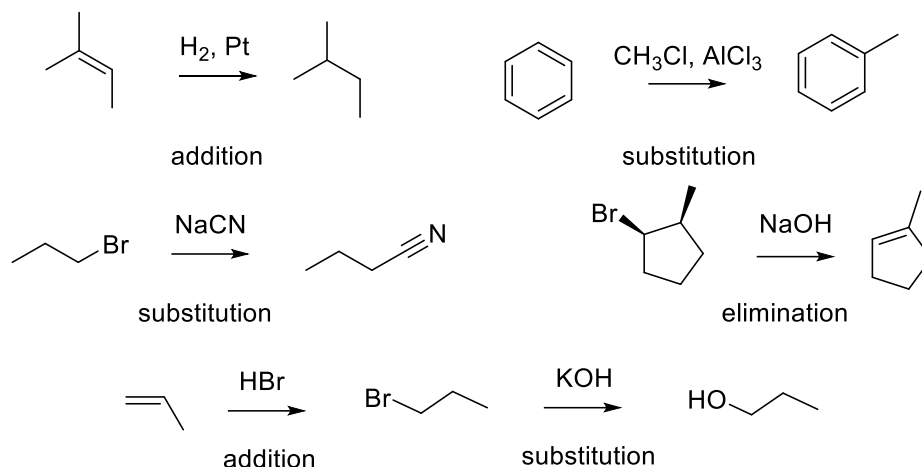


b. First Reaction: Nucleophile is amine functional group. Electrophile is carbonyl carbon of acid chloride.

Second Reaction: Nucleophile is oxygen of carboxylate functional group. Electrophile is alkyl iodide.

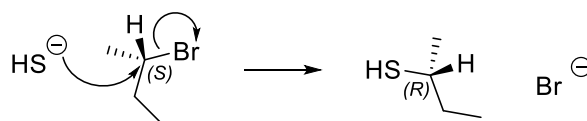
c. The amine should be more nucleophilic. Nitrogen is less electronegative than oxygen, as well as the fact that the electrons on the oxygen are distributed more by resonance, while those of the nitrogen do not participate in resonance.

67.

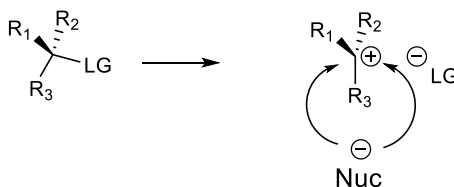


68. The S_N1 reaction mechanism is a stepwise mechanism where a leaving group is lost then there is a nucleophilic attack on the carbocation intermediate. Carbocation rearrangement may occur before the nucleophilic attack.

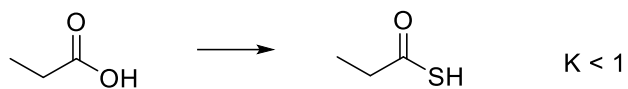
The S_N2 reaction mechanism is a concerted mechanism where the nucleophilic attack and loss of the leaving group occur simultaneously, resulting in an inversion of configuration. “Umbrella flip” is a term sometimes used to describe the inversion of stereochemistry observed in the S_N2 reaction: the “umbrella” made of H, Me, and Et in the example below “flips” to the opposite configuration, much like an umbrella may be turned inside out by strong winds.



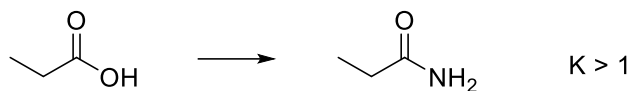
69. The carbocation is planar, but can interact with the leaving group (anion) and solvent molecules. In very polar solvents, ions are completely separated, e.g. NaCl in an aqueous solution. In less polar solvents, the cation and anion may retain some interaction as a solvent-separated ion pair or a tight ion pair. This concept, known as the intimate ion pair, can explain the tendency for the nucleophile to attack the opposite side of the leaving group and the slight preference for inversion.



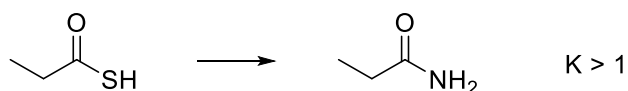
70.



The reactants are favored (SH⁻ is a better leaving group than OH⁻)

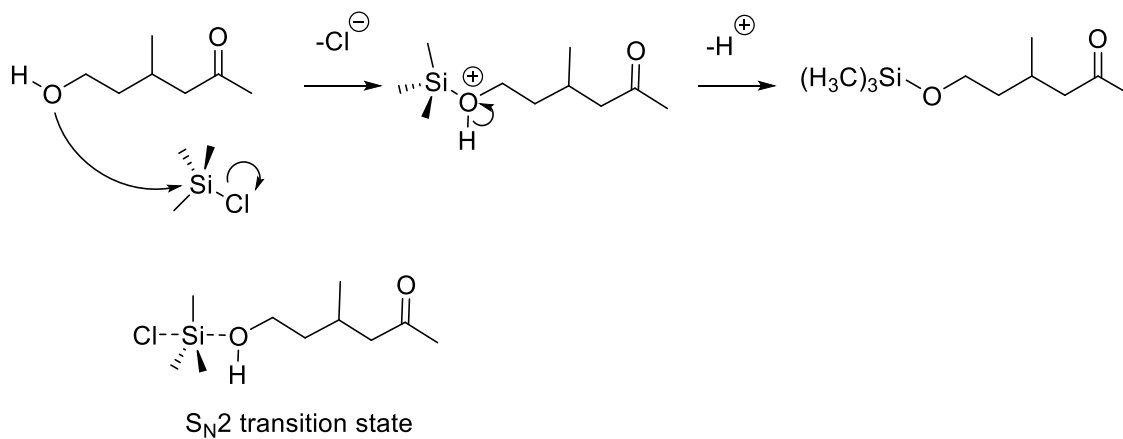
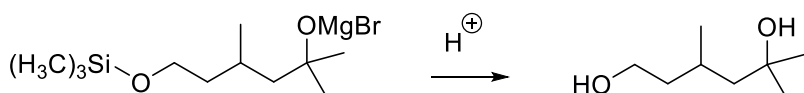
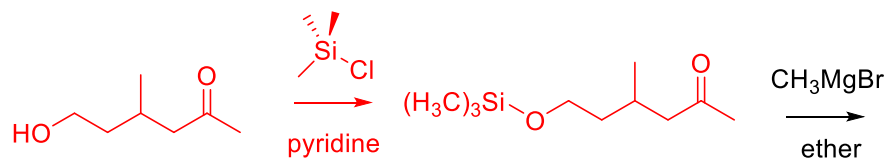


The products are favored (OH⁻ is a better leaving group than NH₂⁻)



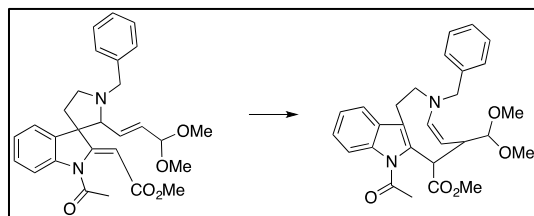
The products are favored (SH⁻ is a better leaving group than NH₂⁻)

71.

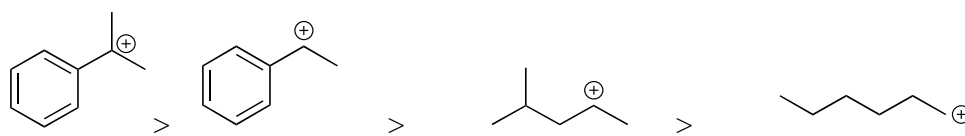


iv. Rearrangement

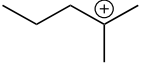
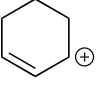
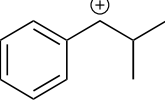
72.



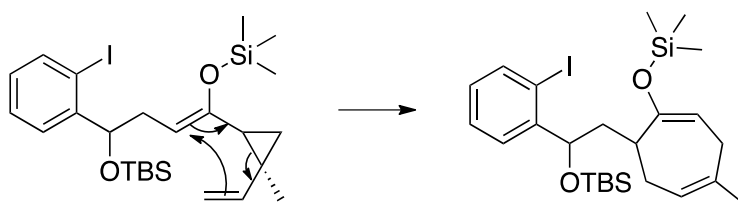
73.



74.

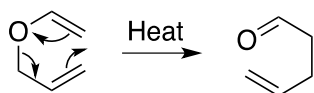
- a. Yes. 
- b. Yes. 
- c. Yes. 
- d. No.

75.

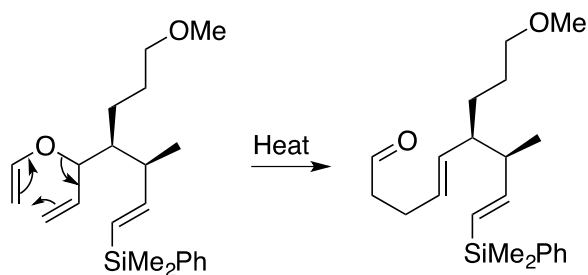


76.

a.

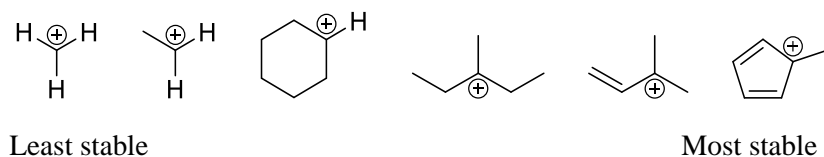


b.

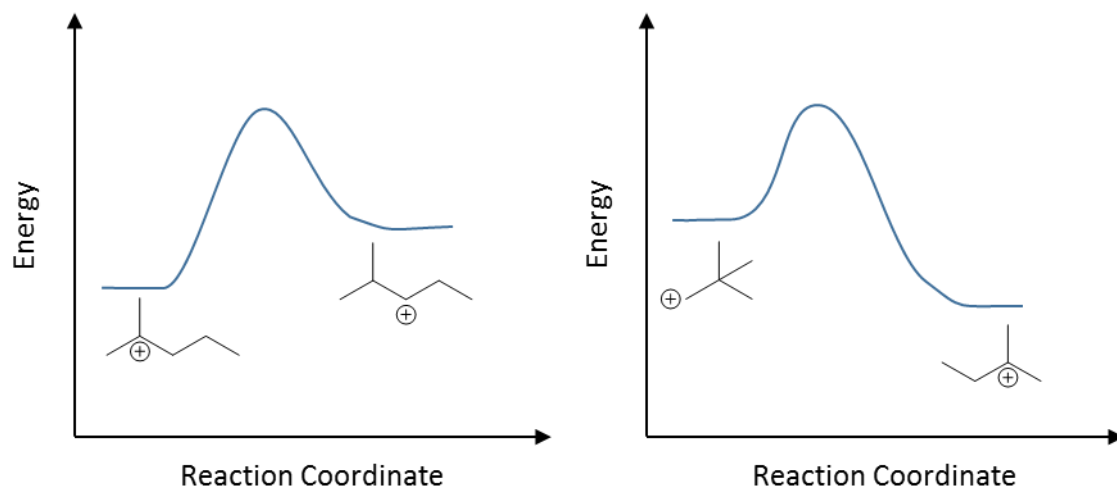


77. The most common hybridization of a carbocation is sp^2 , with the third p orbital vacant. Tertiary carbocations are more stable than primary carbocations due to the inductive effects of the alkyl groups (also meaning that a methenium ion, CH_3^+ , is less stable than a primary carbocation). An allylic carbocation is relatively stable due to the delocalization (resonance stabilization) of the positive charge, and the same is true of benzylic carbocations. Vinylic (and by extension aryl) carbocations are not stabilized by delocalization (the orbitals do not overlap) and the carbocation has sp hybridization (more s character is less stable).

78.

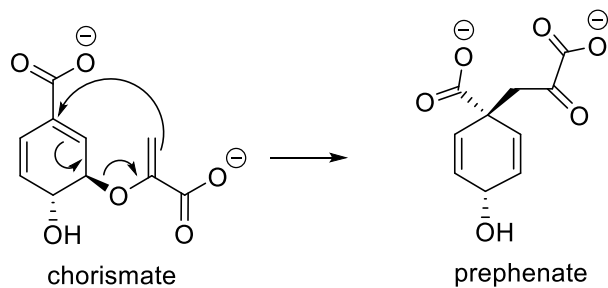


79.

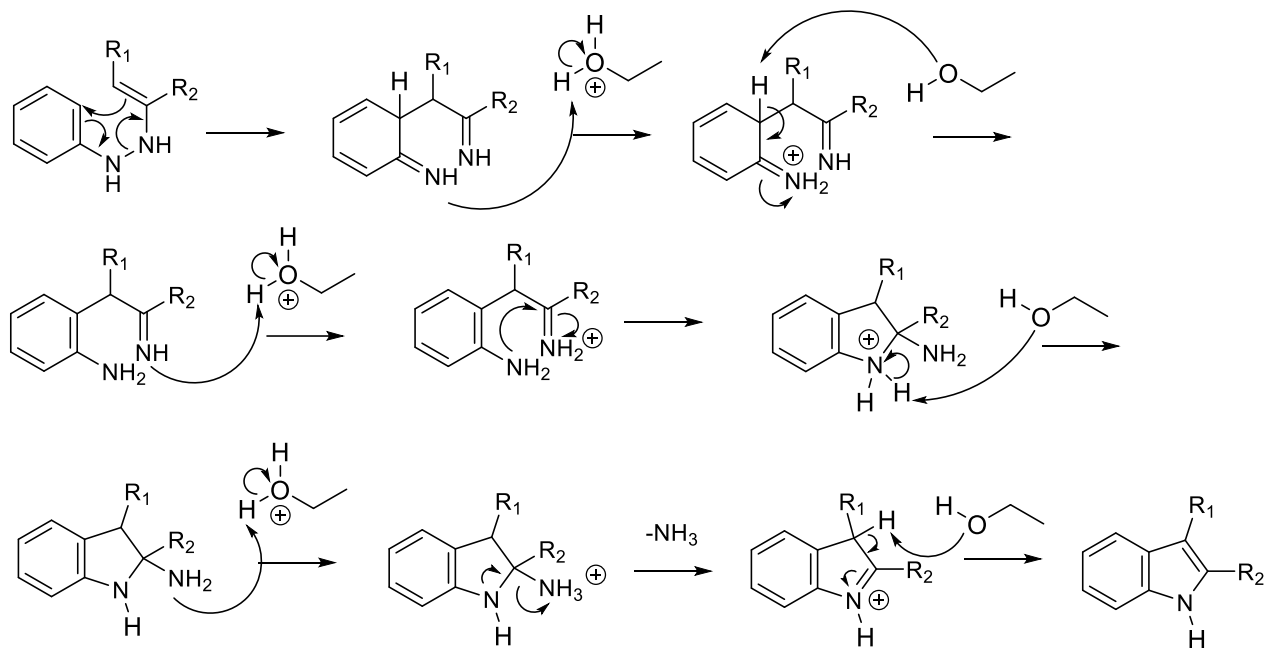
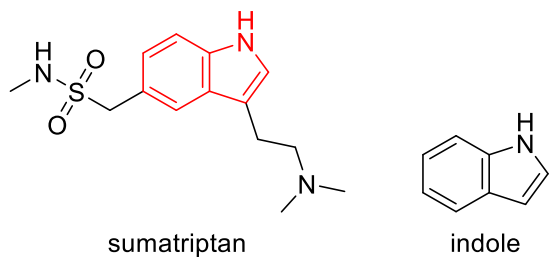


The first rearrangement is a 1,2-hydride shift, but the indicated rearrangement is unfavorable because the carbocation on the left is more stable. The second rearrangement is a 1,2-alkyl or 1,2-methyl shift, and the rearrangement is favorable because the carbocation on the right is more stable.

80.

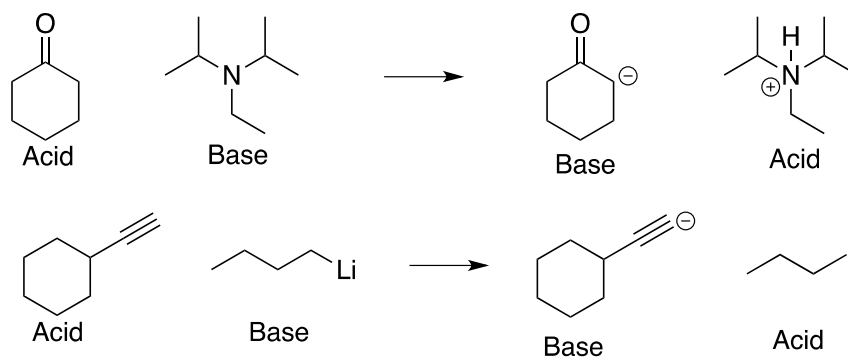


81.



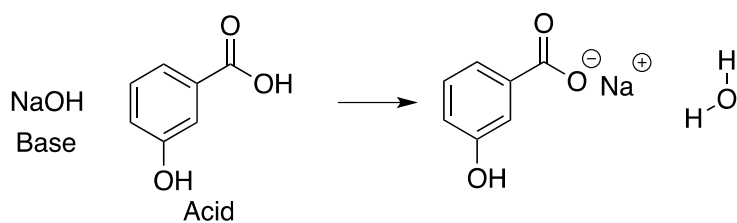
v. Acids and Bases

82.

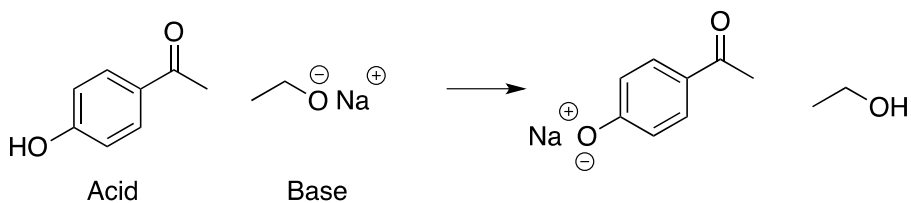


83.

a.

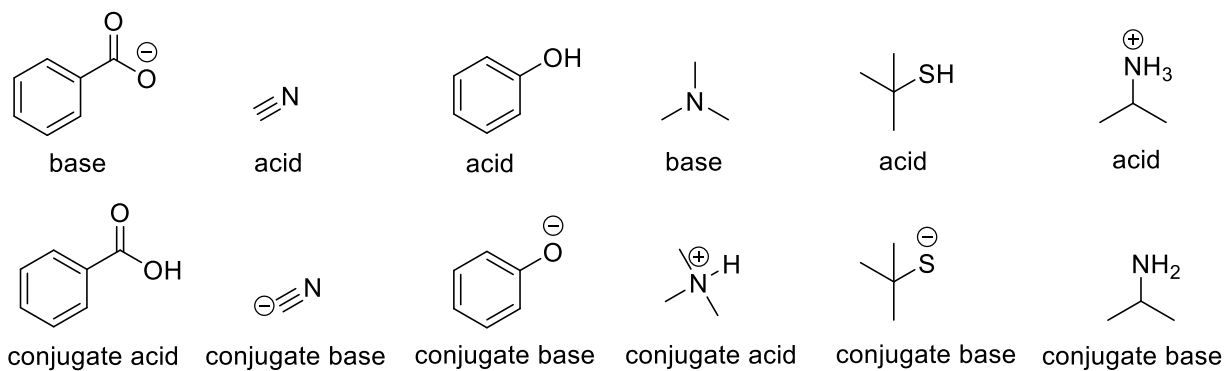


b.

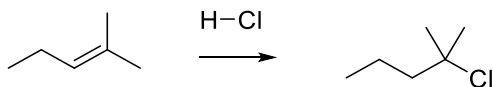


84. A Brønsted-Lowry acid is a proton donor, and a Brønsted-Lowry base is a proton acceptor. A carbocation would not donate nor accept an H^+ . A carbocation may accept a pair of electrons, so it can be considered a Lewis acid.

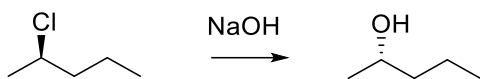
85.



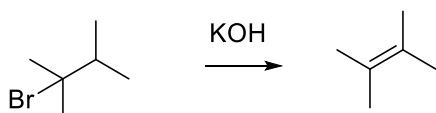
86.



Yes, this reaction would involve a proton transfer from the HCl (Brønsted-Lowry acid) to the alkene (Brønsted-Lowry base).

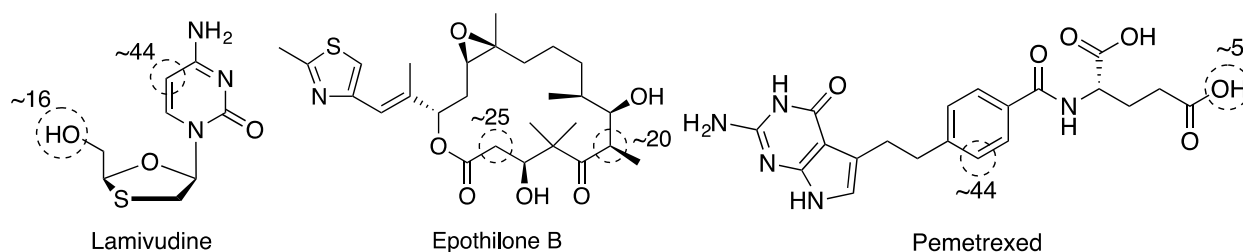


No, this substitution reaction (S_N2) does not involve a proton transfer step, so neither compound is acting as a Brønsted-Lowry acid/base.

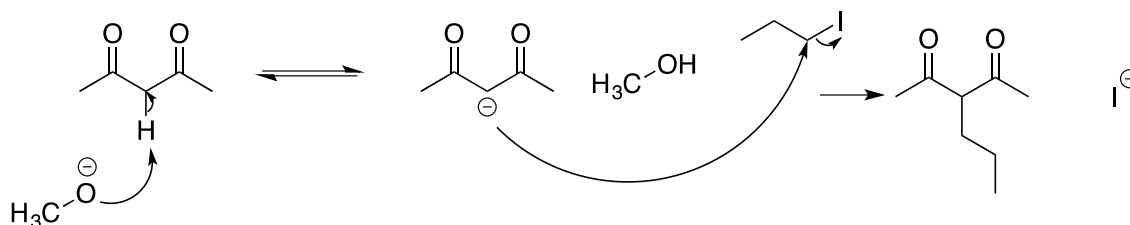


Yes, this elimination reaction (E2) would involve a proton transfer from the brominated alkane (Brønsted-Lowry acid) to the potassium hydroxide (Brønsted-Lowry base).

87.

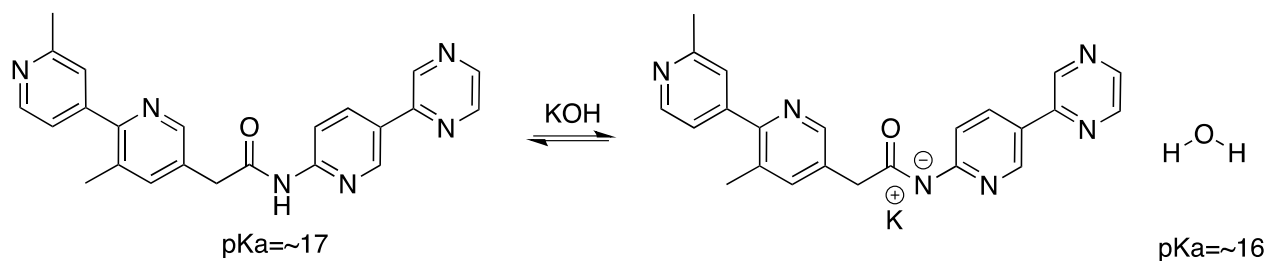


88.



The protonated carboxylic acid is more electrophilic than the non-protonated carboxylic acid due to the presence of the positive charge. The acid acts as a catalyst, making the carboxylic acid more readily react with the alcohol to form the ester.

89.



The difference in pK_a is about 1 unit, so the ratio will be 10:1 in favor of the reactants. Since the difference is 1 unit, the reaction is reversible.

90.

The Henderson-Hasselbalch equation is: $\text{pH} = \text{pK}_a + \log\left(\frac{[A^-]}{[HA]}\right)$

The pK_a of formic acid is 3.75, so $3.75 = 3.75 + \log\left(\frac{[A^-]}{[HA]}\right)$

$$0 = \log\left(\frac{[A^-]}{[HA]}\right)$$

$$1 = \frac{[A^-]}{[HA]}$$

$$[HA] = [A^-]$$

The pK_a of acetic acid is 4.75, so $3.75 = 4.75 + \log\left(\frac{[A^-]}{[HA]}\right)$

$$-1 = \log\left(\frac{[A^-]}{[HA]}\right)$$

$$0.1 = \frac{[A^-]}{[HA]}$$

$$[HA] \neq [A^-]$$

The concentration of acetic acid and acetate would be equal when $\text{pH} = \text{pK}_a = 4.75$.

91. Isoelectric point is the point at which there is no net charge on a molecule. For many acids (e.g. formic acid) and bases (e.g. ammonia) this is when there is no charge at all (HCOOH and NH₃, respectively), but for some compounds – such as amino acids – this will be the zwitterionic form (e.g. NH₃⁺-R-COO⁻).

The isoelectric point of arginine is:

$$pI = \frac{9.00 + 12.10}{2} = 10.55$$

The isoelectric point of glutamic acid is:

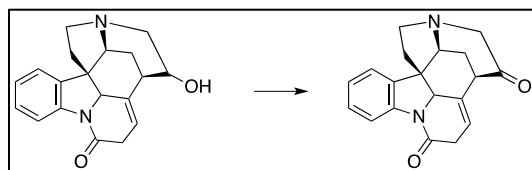
$$pI = \frac{2.16 + 4.15}{2} = 3.16$$

The isoelectric point of valine is:

$$pI = \frac{2.27 + 9.52}{2} = 5.90$$

vi. Oxidation and Reduction

92.



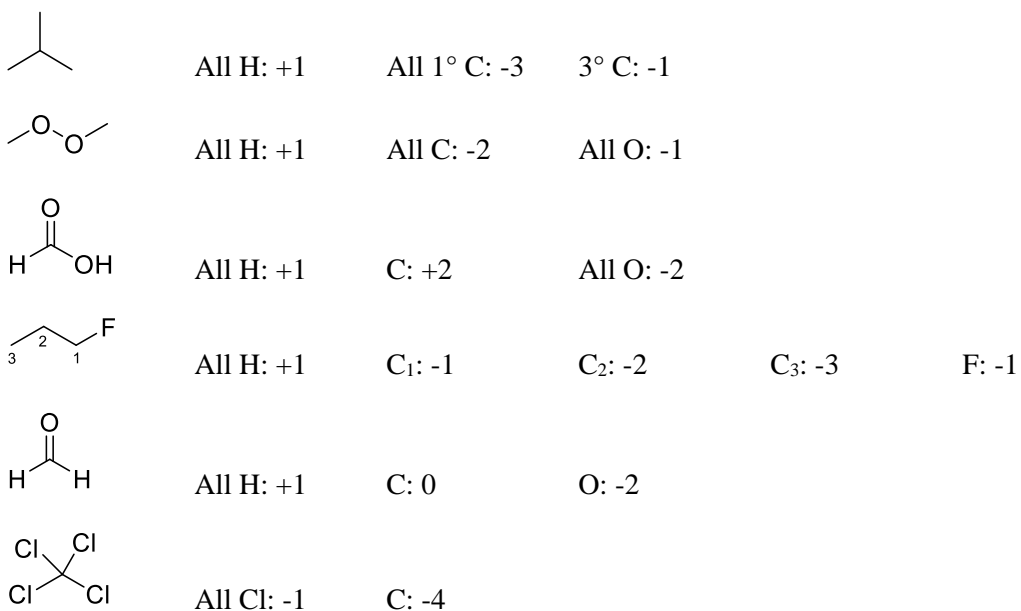
93. Oxidation-a reaction in which a compound undergoes an increase in oxidation state (loss of electrons)

Reduction-a reaction in which a compound undergoes a decrease in oxidation state (gain of electrons)

Oxidizing agents- PCC, OsO₄, KMnO₄

Reducing agents- NaBH₄, LAH, H₂/Pd

97.



98. Addition of hydrogen: reduction

Loss of hydrogen: oxidation

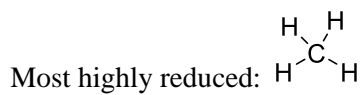
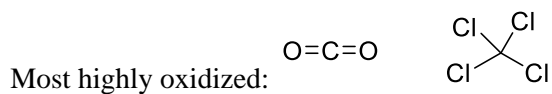
Dehydrogenation: oxidation

Hydrogenation: reduction

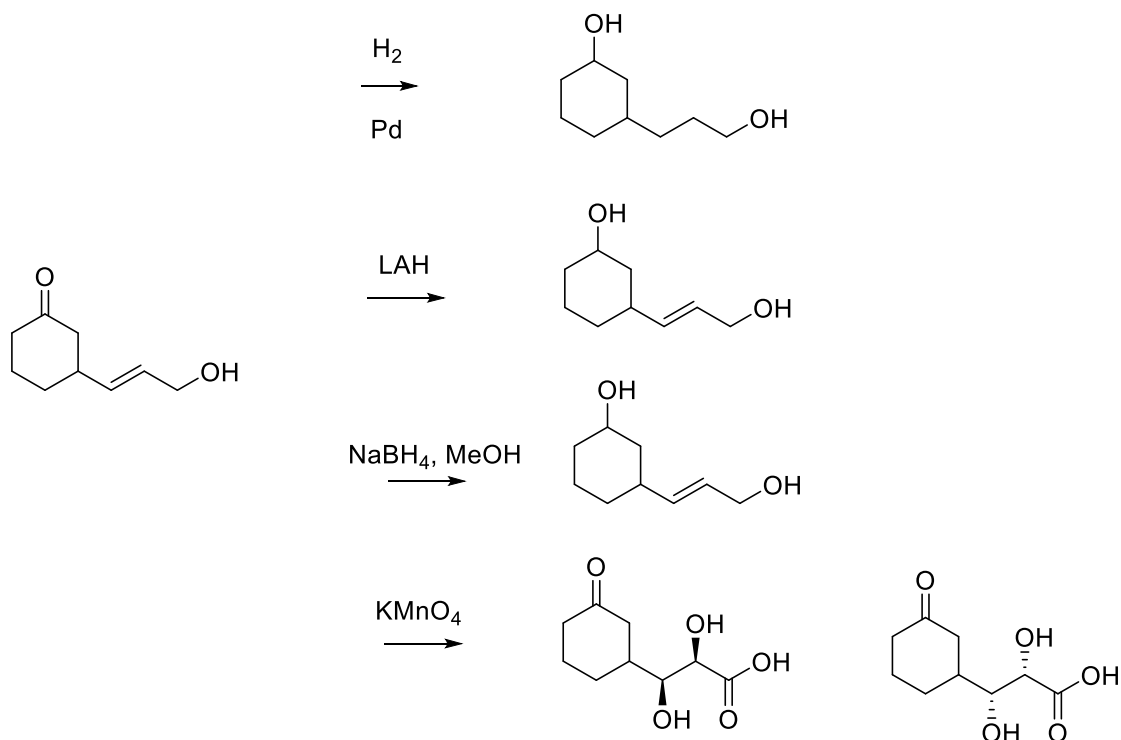
Addition of oxygen: oxidation

Loss of oxygen: reduction

99. The most highly oxidized state carbon can obtain is +4. The most reduced state is -4.



100.



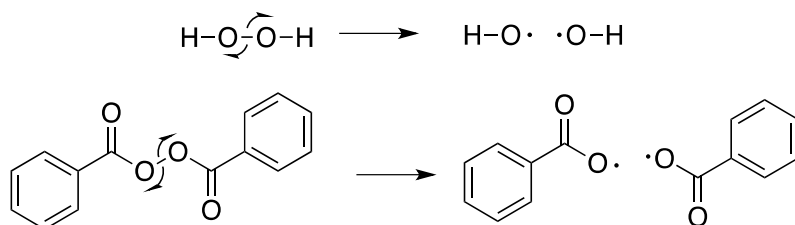
101. Glucose-6-phosphate is oxidized to 6-phosphoglucono-D-lactone, while NADP^+ is reduced to NADPH. NADP^+ acts as an oxidizing agent. Glucose 6-phosphate dehydrogenase is an enzyme, and its role is to catalyze the reaction.

vii. Radicals

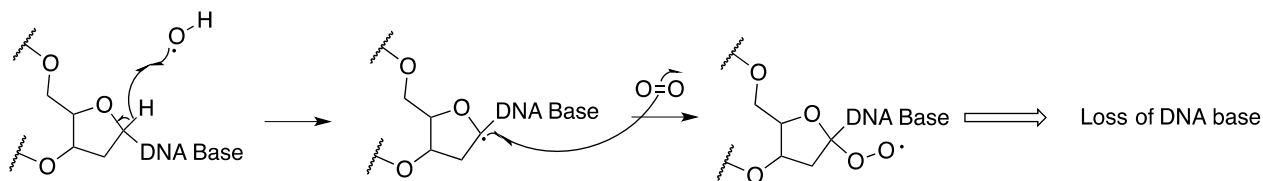
102. Heterolytic bond cleavage—bond breaking that results in the formation of ions. Homolytic results in radical formation.

103. Initiation, propagation, termination. Initiation involves the formation of radical species. In the propagation step, the net chemical reaction takes place. In termination, two radicals join together to give a compound with no unshared electrons.

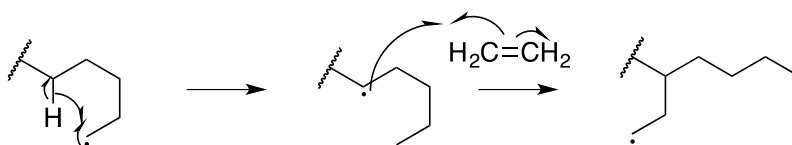
104.



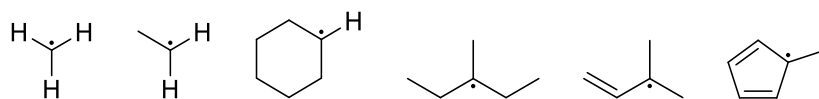
105.



106.



107.

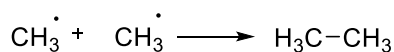
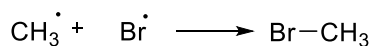
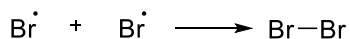


Least stable

Most stable

The order of stability for radicals and carbocations are the same.

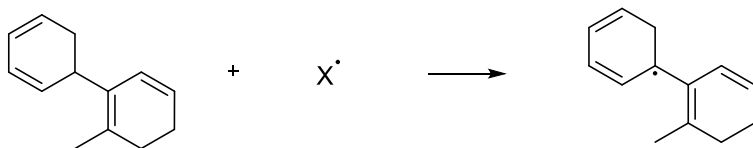
108. Coupling results in the termination of the radicals.



109. Chain reaction: chemical reaction in which the mechanism involves at least one step where an intermediate/product (e.g. radical species) may continue the reaction until the reactants are used up or the chain is terminated.

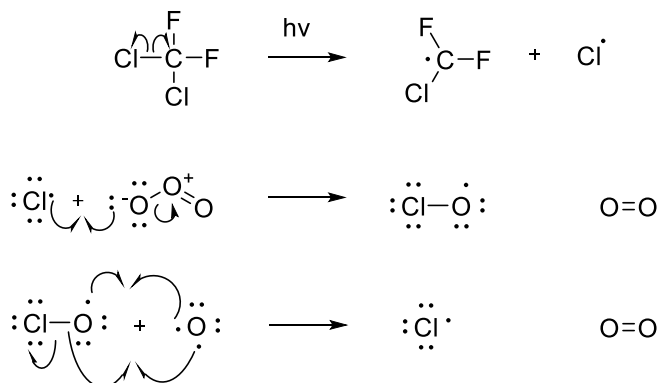
This could be useful in some scenarios, such as energy production in nuclear reactors (nuclear fission chain reaction), but can also be harmful, such as the depletion of the ozone layer by chlorine and bromine free radicals from chlorofluorocarbons and bromofluorocarbons, respectively.

110.



This is the weakest C-H bond, and the radical is stabilized by inductive effects as well as resonance.

111.



The homolytic cleavage of the C-Cl bond requires energy (light, $h\nu$). Antarctica is dark during their winter (Northern Hemisphere summer), and starts to receive more light as it turns to their summer (Northern Hemisphere winter).

THIS IS THE END FOR VOLUME I