Chemistry 210
"Organic Chemistry I"
Fall Semester 2000
Dr. Rainer Glaser

Examination #2
"Alkyl Halides: Their Synthesis by Halogenation of Alkanes and Their Nucleophilic Substitution Reactions."

Friday, October 20, 2000, 9:00 - 9:50

Name:

Question 1. Radicals I. Radical Chain Halogenation.	20	
Question 2. Radicals II. Stability and Hammond. (IAE)	20	
Question 3. Stereochemistry. (News #5 and IAE)	20	
Question 4. Nucleophilic Substitution I. Mechanisms.	20	
Question 5. Nucleophilic Substitution II. Reactions.	20	
Total	100	

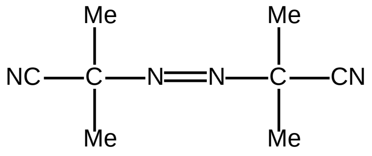
Question 1. Radicals I. Radical Chain Halogenations. (20 points)

(a) Consider the **monochlorination** of butane. Write down the structures of all possible products. Circle the product that is **statistically** most likely to be produced. (5 points)

(b) Consider the **monobromination** of butane. Write down the structures of all <u>possible</u> products. Circle the product that is produced as the **major product**. (5 points)

(c) Suppose you use azobisisobutyronitrile (AIBN) to initiate the radical chain **chlorination of ethane**. Show the structure of the initiator and the reactions that create chlorine radicals. Then show the reactions that make up the "radical chain reaction". Finally, show one of the possible chain termination reactions. (10 points)

Initiation Reaction:



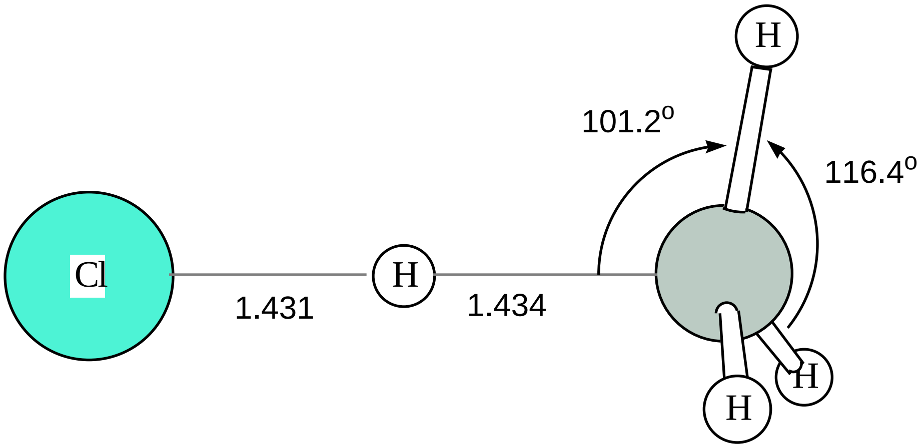
$\mathrm{NC{-}C(Me)_2{-}N{=}N{-}C(Me)_2{-}CN}$

Chain Reactions:

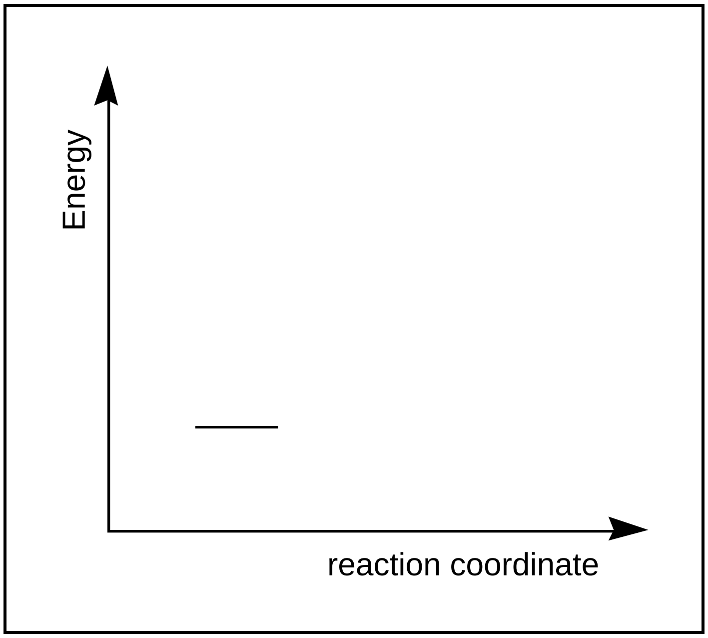
One Termination Reaction:

Question 2. Radicals II. Stability and Hammond. (20 points)

(a) The transition state structure is shown for the **H-atom abstraction by chlorine from methane**. The values shown are the values you analyzed in the online exercise on the application of the Hammond Postulate to H-atom abstraction reactions. For every value given for the chlorine case, indicate whether the respective value would be "**smaller"** or "**larger"** for the case of the bromine reaction. (8 points)



(b) The photochemical radical chain halogenation of alkanes involves two propagation steps. The first propagation step involves the abstraction of a hydrogen-atom from the alkane by a halogen radical and this step is rate-determining. The differences in the selectivities in the radical chain chlorination and bromination of alkanes has to do with the differences in this first propagation step. In the diagram on the right, show the potential energy profile for the first propagation step of the chlorination and the bromination of **methane**. Your drawing should reflect the thermochemistry and the kinetics of the step. (8 points)



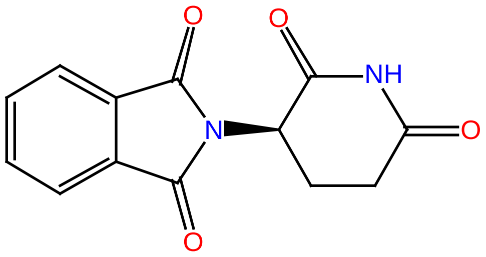
(c) The homolytic bond dissociation energies of methane, of ethane, of the allylic position of propene, and of benzene are <u>in increasing order</u>: (I) 87, (II) 98, (III) 104, and (IV) 110 kcal/mol.

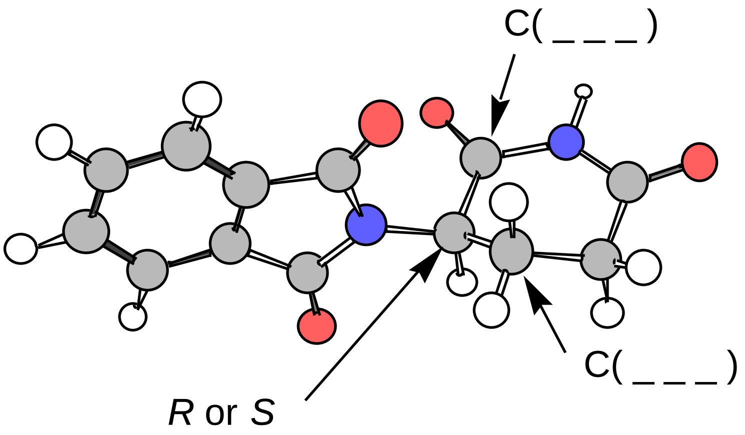
Which bond dissociation energy is that of the allylic C—H bond in propene? ______ (2 points)

Which bond dissociation energy is that of an aromatic C—H bond in benzene? _______ (2 points)

Question 3. Stereochemistry. (20 points)

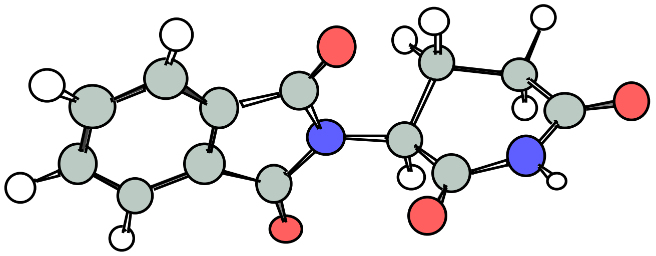
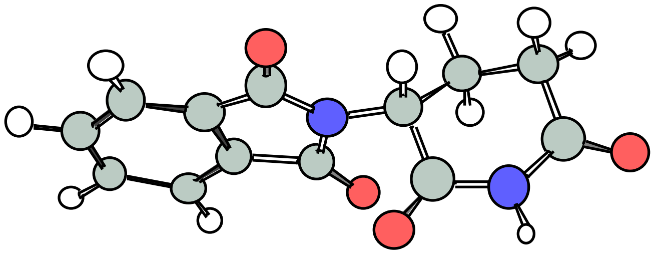
(a) The article “BRISTOL-MYERS TAXOL WINS FDA NOD FOR KAPOSI’S SARCOMA” (*Bloomberg News*, Aug. 7, **1997**) talked about the importance of the right chirality for the desired drug action to occur. The enantiomers of **thalidomide** were discussed in this context and one of these enantiomers is shown as a molecular model. Name this enantiomer according to the R/S nomenclature; **circle *R* or *S***, and **fill in the blanks** in the lists “C(_ _ _)” you use in applying the **sequence rules**. Clearly indicate the **priorities** of the four substitutents.



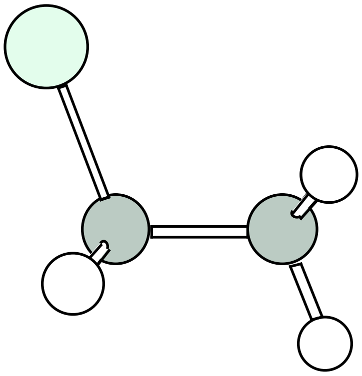
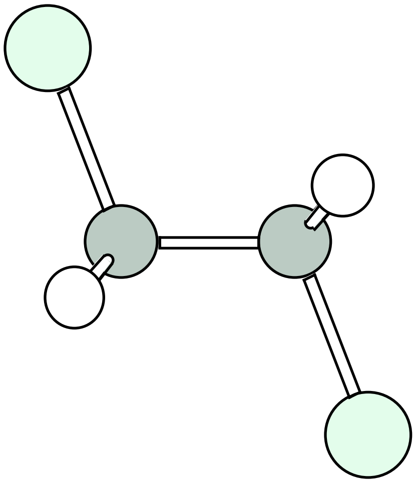


The enantiomers of thalidomide bind to different receptors. Receptors are themselves chiral. **Chiral recognition** occurs because the aggregates formed between the enantiomers and a given receptor are ______________ (enantiomers, diastereomers) and they have _____ (the same, different) energies. (6 points.)

For each of the following structures, decide whether it is the same stereoisomer as the one shown above or whether it is the enantiomer. (4 points)

	Same as above or enantiomer?
	Same as above or enantiomer?

(b) The structures are shown of one conformation of chloroethane (left) and of one conformation of 1,2-dichloroethane (right). Identify the symmetry elements of these molecules. (10 points)

		
Is the paper plane a symmetry plane?		
Consider the plane that is perpendicular to the paper plane and <ins>horizontal</ins>. Is this plane a symmetry plane?		
Consider the plane that is perpendicular to the paper plane and <ins>vertical</ins>. Is this plane a symmetry plane?		
Does the molecule contain an inversion center? [1]		
Does the molecule contain a C_3 symmetry axis? [2]		
How many C_2 symmetry axes are there? [2]		

[1] If the molecule contains an inversion center, then indicate the location of the inversion center by a big cross in the molecular model.

[2] If the molecule contains rotational axes, then indicate the rotational axes by drawing lines directly into the molecular models.

Question 4. Nucleophilic Substitutions I. Mechanisms. (20 points)

(a) Which statement describes the reaction order of the bimolecular nucleophilic substitution? (3 p.)

- a. First-order in alkyl halide, zero-order in nucleophile, zero-order overall
- b. First-order in alkyl halide, first-order in nucleophile, zero-order overall
- c. First-order in alkyl halide, first-order in nucleophile, first-order overall
- d. First-order in alkyl halide, first-order in nucleophile, second-order overall
- e. Second-order in alkyl halide, zero-order in nucleophile, second-order overall

(b) Consider the nucleophilic substitution reaction between methyl bromide and hydroxide. How does the reaction rate change if the concentrations of methyl bromide and hydroxide are doubled? (2 points)

a. No change. b. Rate X 2. c. Rate X 4. d. Rate X 8. e. Rate X 16.

(c) Identify the correct formula of the solvent DMSO. (3 points)

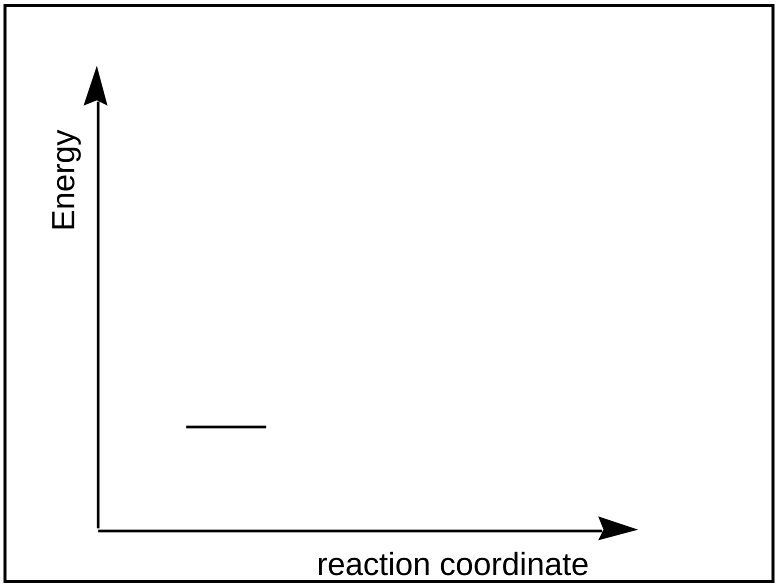
a. CH_3SOCH_3. b. $CH_3SO_2CH_3$. c. $(CH_3)_2S(OH)_2$. d. CH_3SO_3H e. CH_3SO_4H

(d) Which type of alkyl halide substrate shows the highest reactivity in SN2 reactions? (2 points)

a. Methyl halide. b. Prim. alkyl halide. c. Secondary alkyl halide. d. Tertiary alkyl halide

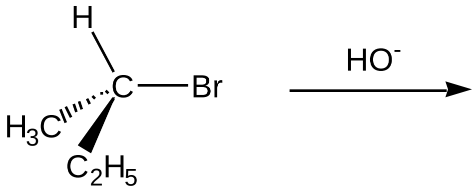
(e) Leaving groups. Draw the structure of the tosylate anion. No need to draw resonance forms, just draw one structure. (2 points)

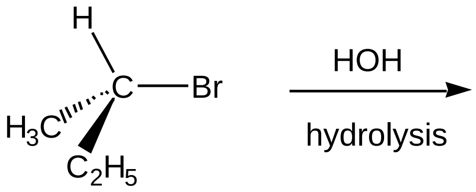
(f) Consider the solvent effects on the **unimolecular nucleophilic substitution**. Draw a typical potential energy diagram for an SN1 reaction. Then draw a second line into this same diagram assuming that the reaction is carried out in **a more polar and aprotic solvent**. Clearly indicate how this change in solvent polarity affects the energy of the intermediate and the energies of both transition states. (8 points)



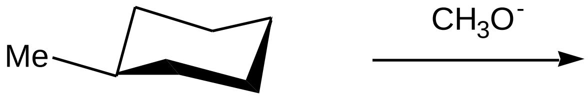
Question 5. Nucleophilic Substitutions II. Reactions. (20 points)

(a) Determine the configuration of the chiral C-atom (*R* or *S*). This substrate is a ____ (prim., sec., tert.) alkyl halide and it can undergo SN1 or SN2 reactions depending on the reaction conditions. Draw the products obtain under the two reaction conditions indicated. If only one stereoisomer is formed, then draw only one stereoisomer. If two stereoisomers are formed, then draw both stereoisomers and indicate which one is the major product or whether they are formed in equal amounts. (10 points)





(b) *Cis*-1-bromo-4-methylcyclohexane undergoes a stereospecific SN2 reaction with methoxide ion, CH_3O^-, to form 1-methoxy-4-methylcyclohexane. Complete the structure of the substrate (add the Br to the right C-atom). Draw the product. The product is ______ (*cis, trans*). (10 points)



The **substrate** ____ (contains, does not contain) a symmetry plane and it ___ (is, is not) optically active.
The **product** ____ (contains, does not contain) a symmetry plane and it ___ (is, is not) optically active.