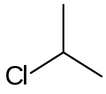
Chem 201, 2009
HW #6, due M, Nov 16, 12 PM

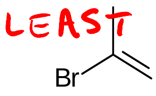
ANSWERS

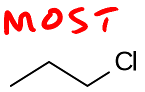
#1. (from 50 minute exam #3, Fall 2000)

5. *(6 points)* For each group of 3 compounds, identify the compound that expresses the indicated property the "MOST" and the compound that expresses it the "LEAST"

a) reactivity towards NaI in DMSO







NaI contains a strong nucleophile (and I^- is not basic at all) and DMSO is an aprotic polar solvent, a perfect combination for S_N2 reactions. If the leaving groups are identical, the reactivity order is $CH_3X > 1^o$ RX $> 2^o$ RX. Although Br is a better leaving group than Cl, the middle compound contains a CX bond involving an sp^2 hybridized C, so this compound is not reactive at all.

b) reactivity towards H_2O in aqueous acetone

3-chloro-1-propene

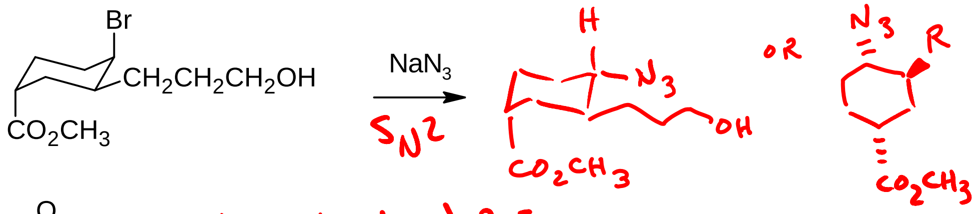
1-chloropropane

2-chloropropene

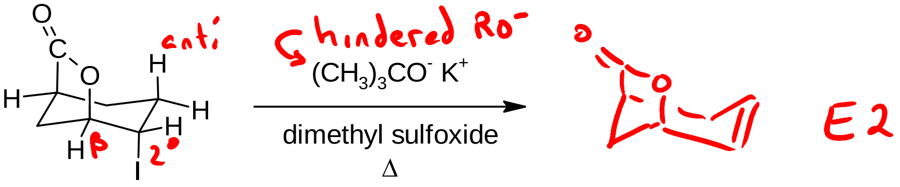
H_2O is a weak nucleophile (and not basic at all) and aqueous acetone is a reasonable medium for forming ions, so this is a good combination for S_N1 and E1 reactions. The reactivity order in these reactions is determined by the stability of the carbocation that is produced by dissociation of Cl^- (Hammond postulate). The reactivity order is 3^o RX $> 2^o$ RX. Now at this point it gets a little confusing because there are two 1^o RX compounds and a 2^o RX in which Cl is bonded to an sp^2 hybridized C. It might seem that no reaction should occur with any of these compounds, but not so. Allyl chloride, the compound on the left, liberates allyl cation which has comparable stability to a 2^o RX (go back to lecture #12 for a comparison of allyl cation, benzyl cation, and alkyl carbocation energies). This compound is the most reactive. The other two compounds cannot undergo S_N1/E1 reactions, but the 1^o RCl (middle compound) can undergo a very slow S_N2 reaction with H_2O. The compound on the right does not undergo any reaction with water.

#2. Draw the most likely reaction products:

a.



b.



a. N_3^- is an effective nucleophile, but not very basic. Br is a good leaving group and is attached to a 2^o alkyl C. Expect S_N2 and inversion of configuration (Note: only one conformation of the starting material and product have been drawn. To anticipate the stereochemistry of the product, note whether spectator groups are cis or trans to the leaving group and assume that this relationship will switch relative to the nucleophile in the product.)

b. Although the iodide is 2^o (and I is a good leaving group!), branching at the beta C slows down S_N2. Alkoxides should always be viewed as bases when the halide is the least bit hindered, and hindered alkoxides should be viewed as bases in almost every situation. Therefore, the iodide and alkoxide both offer steric factors that slow down S_N2 and favor E2. The presence of a H anti to I in this molecule makes this a no-brainer. (Note: both beta C possess H, but 1) only one is anti to I, and 2) elimination to a bridgehead C violates Bredt's rule – see chapter 7.)

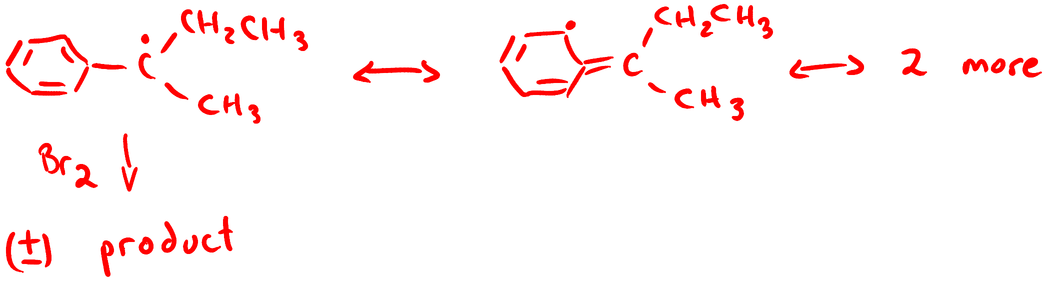
#3. Loudon, chapter 8: **44B, 56, 59B**

44B *2-chloroethanol < 3-chloro-1-propanethiol < 2-chloro-1-propanethiol (**most acidic**)*

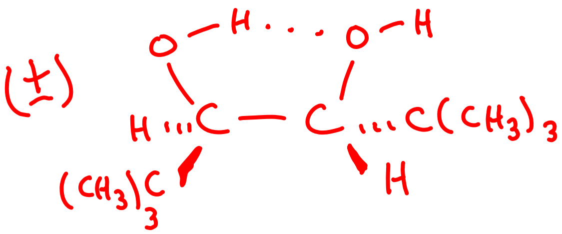
Alkanethiols (pK_a ~10) are much more acidic than alcohols (pK_a ~18) so the least acidic compound must be the alcohol. The two alkanethiols can be differentiated by considering polar (field/inductive) effects of the Cl. The C-Cl bond is polar and C lies at the positive end of the bond dipole. See chapter 3 for more.

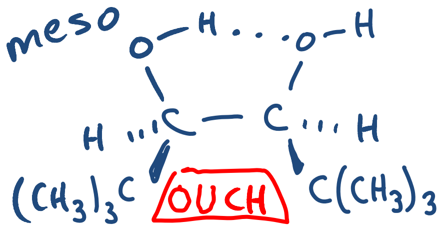
56 *sec-Butylbenzene is a chiral molecule. The problem says that we start with optically active material and when you see these words you can usually assume that you are working with a single enantiomer (of course, this is not necessarily the case, but the reasoning process that is based on a single enantiomer leads to valid answers for other cases too).*

The free radical intermediate is trigonal planar (sp^2 hybridized) at the benzylic (free radical) carbon. Note: this is generally true for radicals, just as it is for carbocations, but it is especially true for benzyl radicals where the free radical carbon is connected to the benzene ring by a partial pi bond. Because the unpaired electron "lives" in a 2p orbital, the next step can occur at either lobe with equal probability (note: this intermediate is achiral) and the product will be a racemic mixture. **No optical activity.**



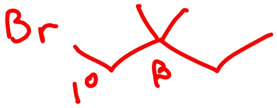
59B *The molecules in the racemate must adopt an eclipsed (or nearly eclipsed) conformation to create an intramolecular hydrogen bond. This isn't possible in the meso stereoisomer because of steric repulsion between the bulky tert-butyl groups.*





#4. Loudon, chapter 9: **34D, 62, 70 (draw mechanism for B → C)**

34D *1-bromo-2,2-dimethylbutane is the least reactive of the bunch. It is important to realize that NaOCH$_3$ can bring about S$_N$1 and E2 reactions, so the "least reactive" molecule is the one that resists <u>both</u> of these reactions. 1-Bromo-2,2-dimethylbutane cannot undergo E2 because C beta lacks hydrogens, and it cannot easily undergo S$_N$2 because the C beta is highly branched (quarternary). This molecule belongs to the family of "neopentyl-like" compounds that have been shown to be relatively unreactive in S$_N$2. (Note: 3-bromo-3-methylpentane is a 3^o RBr and also resists S$_N$2, but it readily undergoes E2 reactions.)*



62 *These compounds are stereoisomers so any difference in reactivity is due to some kind of geometry issue.* ***Compound B*** *undergoes elimination more rapidly because one conformer puts a hydrogen on a beta C <u>anti</u> to bromine.*

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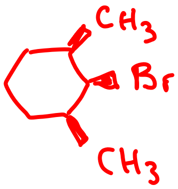
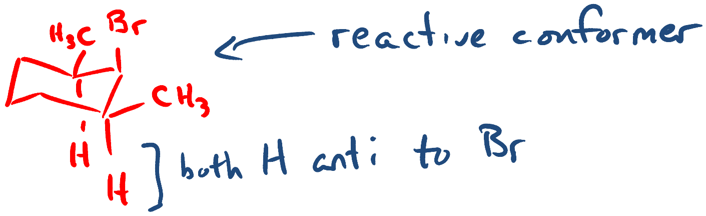
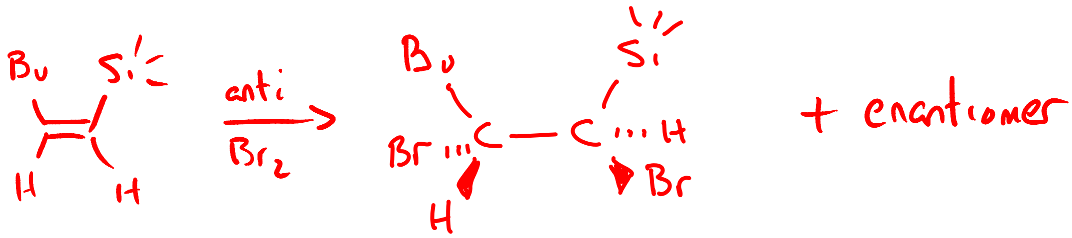
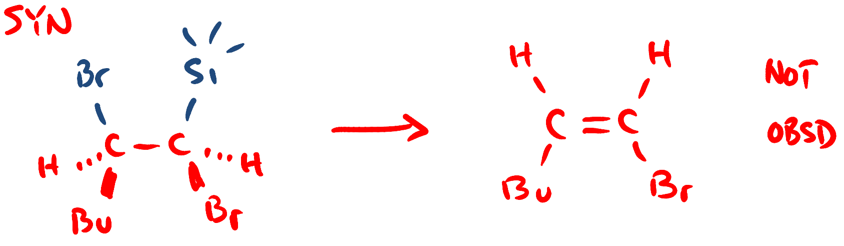


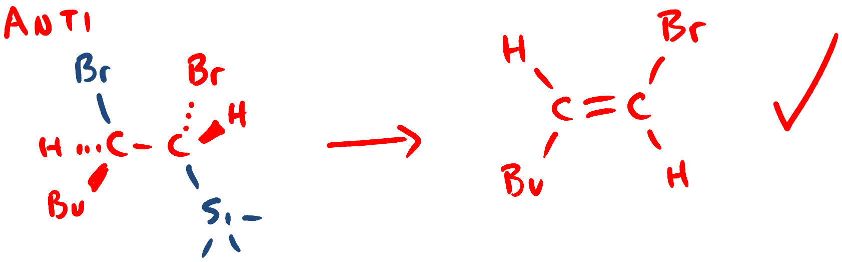


70A *Draw whatever conformer is most convenient to draw.*



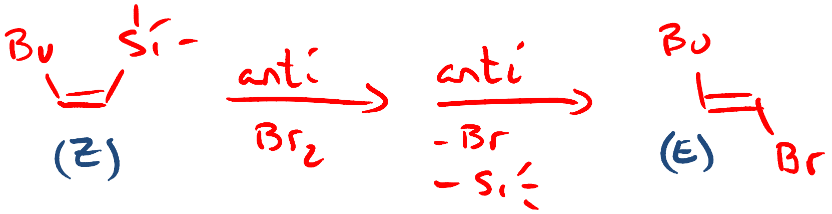
70B *Br and Si(CH*$_3$*)*$_3$ *are the two groups that are removed during B → C. To work out the stereochemistry of this reaction, draw TWO conformers, one in which the groups are eclipsed (leads to syn addition) and one in which they are anti (leads to anti addition). Then draw the products that are obtained from each process (remove Br and Si(CH*$_3$*)*$_3$ *and flatten C alpha and C beta). When both drawings are correctly made, it becomes obvious that only* ***anti elimination*** *produces the observed product.*

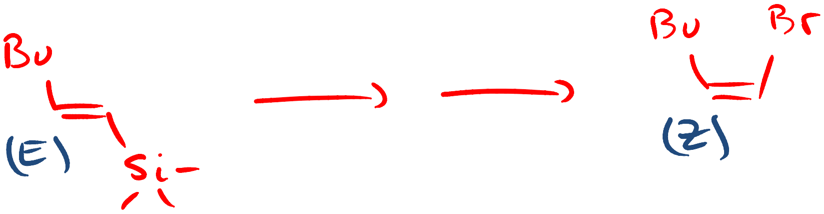




70C *The sequence investigated in parts A and B involved the Z stereoisomer of compound A. The most reliable way to work the behavior of the E stereoisomer is to make the same drawings that were made in parts A and B and assume that the same geometrical rules are followed by each reaction, i.e., anti addition of Br*$_2$ *and anti elimination of Br and Si(CH*$_3$*)*$_3$*.*

Fortunately, there is a short-cut. The Z and E stereoisomers of compound A differ by changing the configuration at one stereocenter in compound A. Therefore, instead of making drawings, we can simply imagine inverting the configuration of this stereocenter in compound B and again in compound C. So, instead of an E product, we will obtain a Z product.





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70 Mechanism *Remember the "rules" for thinking about mechanisms. First, they can't be proven, only disproven. Second, confidence in a mechanism builds when it fits a lot of data and/or looks like other mechanisms that we already have confidence in ("plausibility" test). We know two mechanisms for elimination already: E2 and E1. Only E2 has a geometry (anti CH and CLg) requirement. And this requirement is enforced by breaking the CH and CLg bonds at the same time that the CC pi bond forms. Since B → C has a similar geometry requirement, we might suppose that CBr and CSi bonds break at the same time as the CC pi bond forms. A "one-step bimolecular" mechanism can account for this nicely (see below), but other, more complicated mechanisms can also be drawn (not shown).*