Chemistry 125   Fifth Examination Answers   **February 4, 2011**

1. (10 min) The following molecules were carefully designed to answer particular questions about reaction mechanisms.

CIRCLE ONE (**ONE ONLY**) of the molecules and **explain**
(A) What question(s) it was designed to answer.
**(B)** What features of the molecule were relevant to the experimental design.
(C) What answer study of this molecule provided to the question(s) in part **A**.

$(CH_3)_3C-N$
$N-C(CD_3)_3$
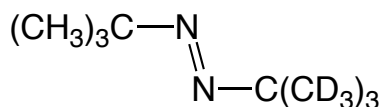
Question: Can subtle, short-range motion such as rotation constitute the rate-limiting step in an organic reaction?

Features: This molecule can be decomposed photolytically to generate an N_2 molecule between two t-butyl radicals, which will react very quickly with each other by H-transfer (disproportionation) NOT by coupling (because of steric hindrance). The choice between H and D allows for observing a deuterium kinetic isotope effect on the product ratio, if H-transfer is rate limiting.

Answer: An isotope effect (more H- than D-transfer) was observed in fluid solvents, but in a viscous solvent there was no preference showing that another process (presumably rotation) was rate limiting in collapse of the pair of t-butyl radicals. [Lecture 47]
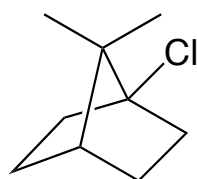

Questions: (1) Can there be frontside displacement in S_N2 nucleophilic substitution? and (2) can S_N1 substitution take place via a non-planar cation?

Features: The bridgehead carbon to which Cl is attached cannot be attacked backside (because it is sterically inaccessible and the inverted product would be impossibly strained), and it cannot become planar (also because of ring strain). Furthermore the competing process of E2 elimination is not possible because the product "alkene" would have a severely twisted bridgehead C=C double bond and contravene Bredt's Rule.

Answer: The chloride survived very strenuous nucleophilic substitution conditions without undergoing either substitution or elimination showing that frontside displacement is much more than 10^6 times slower than backside displacement, and that cation formation is more that 10^9 times slower than an analogous acyclic tertiary chloride. (Actually Bartlett and Knox prepared the chloride by a substitution presumably involving the bridgehead cation, generated by loss of a superb leaving group, N_2.) [Lecture 44]

$CH_3O \quad OCH_3$
$CH_3O \quad \overset{+}{C} \quad OCH_3$
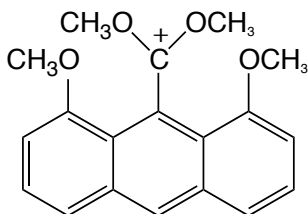
Question: Is the pentavalent carbon species on the SN2 reaction coordinate a transition state or an intermediate. *i.e.* are there bonds with restoring force to the nucleophile and the leaving group?

Features: the three rings of anthracene hold the "nucleophile" and the "leaving group" (both $Ar-O-CH_3$) on opposite faces of the trivalent cationic carbon, so that the assembly, even if only barely metastable, cannot fall apart and can be studied by x-ray diffraction. The O-C distances are somewhat longer than expected for even abnormally long bonds, so if there is a restoring force, these atoms should experience an attraction, shortening the O-C distances.

Answer: The Ar-O bonds are indeed bent toward the central C^+, as expected for an attractive force, but the difficulty is in knowing what distortion to expect without an attractive force. Using H, or even O, as the central atom also resulted in similar distortion, suggesting that it is due not to attraction to the central atom, but rather to repulsion between the CH_3 groups and the adjacent ring H atoms. There was no compound in which attraction to a central carbon cation shortened both "bonds" significantly compared to clearly non-bonding models, so the conclusion (supported by quantum mechanical models) is that there is no significant restoring force to such "bonds" and the S_N2 mechanism involves a transition state, not an intermediate. [Lecture 46]

2. (5 min) It is frequently said that the stability order of carbon radicals is tertiary > secondary > primary.

   A. What evidence supports this contention?

   The Blanksby-Ellison R-H bond dissociation energies increase in the order tertiary < secondary < primary < CH_4 [96, 99, 101, 105 kcal/mole – Frame 13 Lecture 38].
   Similarly the rate of abstraction of tertiary H atoms (e.g. by Br or Cl atoms) increases in the order primary < secondary < tertiary. [Most impressive if you can reproduce the per-atom reactivity ratios. See Problem 1 and Frames 2-5 Lecture 40]

   B. What experimental and computational evidence shows that there is more to this series than simply "radical stability"?

   When dissociation energies for bonds to groups other than H are compared (*e.g.* other alkyl groups), and correction is applied for steric strain in the starting material (calculated by molecular mechanics), it is found that there is no significant difference among primary, secondary, and tertiary radicals. For these compounds the only difference seems to be due to strain in the starting bonds, not to difference in the radical stability. In fact the trend for C-X bonds, where X is halogen seems to be in the opposite direction. [Frames 14-22, Lecture 39]

3. (2.5 min) What is curious about the hydrogen bond in the hydrated hydroxide ion ($H_3O_2^-$)?

   At 28 kcal/mole in the gas phase (frame 2 of Lecture 43) the HOH-OH$^-$ association is unusually strong for an H-bond (mostly because of charge-dipole and charge-induced dipole forces. But the most curious feature is that although the reaction coordinate for bouncing the central H between OH groups is a double minimum, the central H spends most of its time near the symmetrical structure, because the barrier is so low, and the mass of H so small that the lowest vibrational quantum level tunnels and maximize near the center. (frame 15 of Lecture 42) That is, the double-minimum potential gives a symmetrical minimum-energy structure. The barrier is unusually low because of genuine bonding (HOMO-LUMO mixing between the unshared pair of HO$^-$ and σ^* H-OH), which is not the case for most H-bonds (but is true for H_2O-H-OH_2^+).

4. (2.5 min) Why is HBr the only hydrogen halide that undergoes free-radical addition to alkenes?

   To sustain a free-radical-chain reaction all propagation steps must be fast, because otherwise termination reactions will destroy the radicals.   In this case both steps must be exothermic to be rapid. This is true only of HBr, since addition of I• to C=C in endothermic, and abstraction of H from HF or HCl by R• is endothermic. [Frame 7 of Lecture 40]

5. (2 min) List four factors that can be important in determining the **pKa** for an organic acid (just name, no explanation)

   Here are eight factors that could be invoked:

   Bond dissociation energy of the X-H bond (this includes overlap)

   Energy mismatch between H and A (same as electronegativity, nuclear charge)

   Resonance stabilization of the A$^-$ anion.

   Inductive electron withdrawal in the A- anion.

   Solvent stabilization (e.g. H-bonding) of H$^+$ and/or A$^-$.

   Electrostatic change in the acid (e.g. H_3O^+ strong; ^-O_2C-CO_2H weak)

   Field effect from a dipole within the molecule.
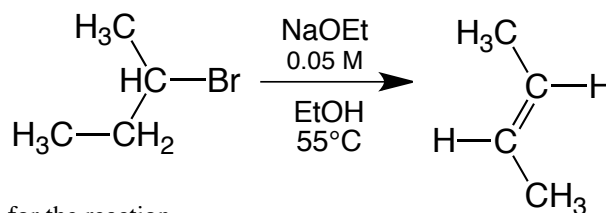
   Polarizability of substituent groups or solvent.

6. (6 min) Fill in the table by drawing two pairs of related acids **with their pKa values** (if you wish, one acid can appear in both pairs, in which case you would have a series of three acids), and **explain** below how their relative pKa values relate to factors you listed question 5

PAIR I			PAIR II	
Structure	pK$_a$		Structure	pK$_a$
1			1	
2			2	
Lesson(s):			Lesson(s):	

This question is obviously too open-ended for a standard answer.

7. Consider these influences on the rate of this elimination reaction:

A) Increasing [NaOEt] to 0.1 M doubles the rate

B) Using of *i*-PrI instead of *i*-PrBr increases the rate

C) Using (CD$_3$)$_2$CHBr instead of *i*-PrBr slows the rate about 7-fold

$$H_3C\text{—}\underset{H_3C\text{—}CH_2}{HC}\text{—Br} \xrightarrow[\substack{EtOH \\ 55°C}]{\substack{NaOEt \\ 0.05\ M}} \underset{H\text{—}C\text{—}CH_3}{H_3C\diagdown C\text{—}H}$$

A. (7.5 min) Below are five possible reaction coordinate diagrams for the reaction.
The first two involve initial loss of bromide with formation a carbon cation intermediate.
The second two involve initial abstraction of a proton by ethoxide with formation of a carbon anion intermediate.
Put an **X** in the box for each mechanism that **IS consistent** with the corresponding experimental observation (A-C) above.

Mechanism	cation	cation	anion	anion	
(A) 0.1M NaOEt		X	X	X	X
(B) I for Br	X	X		X	X
(C) D for H		X	X		X

[Remember that changes that shift an initial, rapid eqilibrium toward the intermediate (*e.g.* I for Br with a cation intermediate, or increasing ethoxide with an anion intermediate) accelerate the reaction even when the second step is rate limiting (because they make the rate-determining transition state closer in energy to the starting material, or, which is the same thing, increase the concentration of "starting material" for the second step).]

B. (1.5 min) This elimination is said to follow "Saytzeff Rule" regiochemistry. What would have been the product if it had followed the "Hoffman Rule"?

[Just draw the structure, no explanation necessary]

$$\underset{H_2C}{H_2C}\diagup C\text{—}H \diagdown CH_3$$
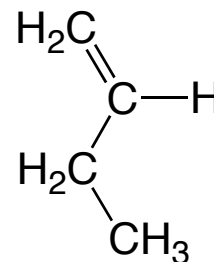
C. (3 min) **Explain** which mechanism (or pair of mechanisms) in part **A** would be most strongly favored by using a more polar solvent (*e.g.* water containing only enough EtOH to achieve dissolution).

   A more polar solvent favors the formation or concentration of charge. In the concerted reaction and the reaction that involves formation of the anion in the rate-determining step, the charge that was initially concentrated on EtO⁻ is spread out in the transition state, losing solvent stabilization and slowing the reaction. The same is true at the transition state in which halide is leaving from the anion in the transition state (part of the negative charge is on halide, part on carbon). In the reations with a cation intermediate a material that was initially uncharged is developing (or has developed) charges, carbon +, halide -, in the transition state (or in the preequilibrium), so that a polar solvent will accelerate the reaction.

D. (10 min) Assuming that this is an **E2** reaction, **draw as accurate a diagram as you are able** showing the starting 2-bromobutane and ethoxide molecules **properly situated in space** for reaction. Include **carefully drawn curved arrows** showing electron pair shifts. Clearly **show the proper conformation** of the 2-bromobutane.
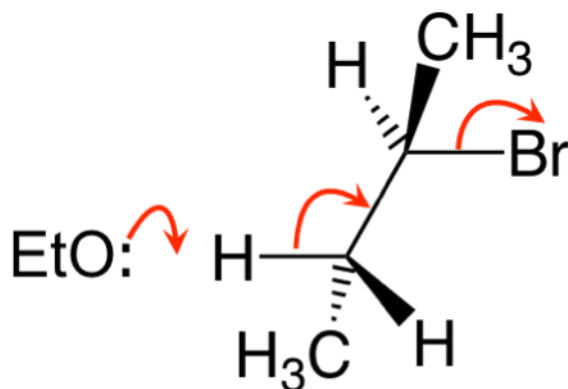
   Note that lines, dashes, and wedges are drawn so that the bonds in individual carbons appear tetrahedral (109° bond angles).

   Note *anti* arrangement of H-C-C-Br to allow overlap in formation of new C=C.

   Note *anti* arrangement of H₃C-C-C-CH₃ to minimize steric repulsion between methyl groups (and to generate the product with trans methyl groups as H⁺ and Br⁻ are lost). There is no way for C number 4 to be other than *gauche* to the Br atom, if the proton to be lost is in the required *anti* orientation.

   Note that every curved arrow originates where there is a non-bonded or bonding pair of electrons in the starting material and ends where there is to be a non-bonded or bonding pair of electrons in the product.