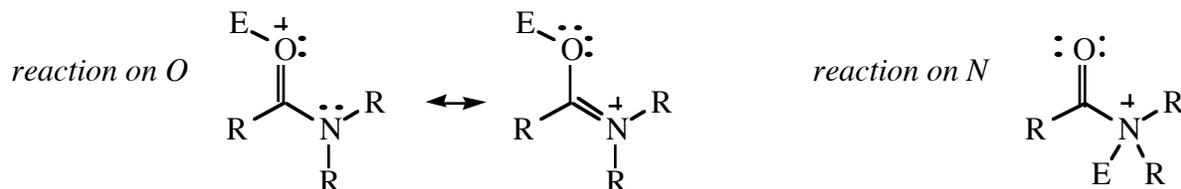## Answers To Chapter 1 Problems.

1. (a) Both N and O in amides have lone pairs that can react with electrophiles. When the O reacts with an electrophile E$^+$, a product is obtained for which two good resonance structures can be drawn. When the N reacts, only one good resonance structure can be drawn for the product.

*reaction on O*

reaction on N

(b) Esters are *lower in energy* than ketones because of resonance stabilization from the O atom. Upon addition of a nucleophile to either an ester or a ketone, a tetrahedral intermediate is obtained for which resonance is not nearly as important, and therefore the tetrahedral product from the ester is nearly the same energy as the tetrahedral product from the ketone. As a result it costs more energy to add a nucleophile to an ester than it does to add one to a ketone.

(c) Exactly the same argument as in (b) can be applied to the acidity of acyl chlorides versus the acidity of esters. Note that Cl and O have the *same* electronegativity, so the difference in acidity between acyl chlorides and esters cannot be due to inductive effects and must be due to resonance effects.

(d) A resonance structure can be drawn for **1** in which charge is separated. Normally a charge-separated structure would be a minor contributor, but in this case the two rings are made aromatic, so it is much more important than normal.
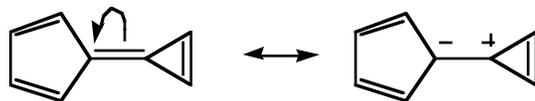

(e) The difference between **3** and **4** is that the former is cyclic. Loss of an acidic H from the γ C of **3** gives a structure for which an aromatic resonance structure can be drawn. This is not true of **4**.
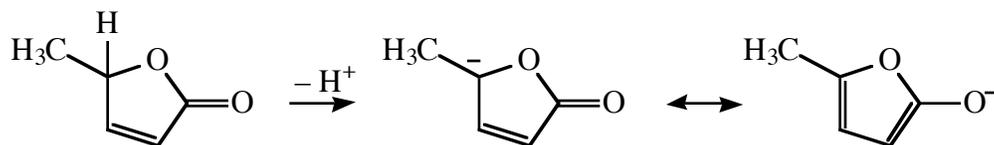
(f) Both imidazole and pyridine are aromatic compounds. The lone pair of the H-bearing N in imidazole is required to maintain aromaticity, so the other N, which has its lone pair in an sp^2 orbital that is perpendicular to the aromatic system, is the basic one. Protonation of this N gives a compound for which two equally good aromatic resonance structures can be drawn. By contrast, protonation of pyridine gives an aromatic compound for which only one good resonance structure can be drawn.
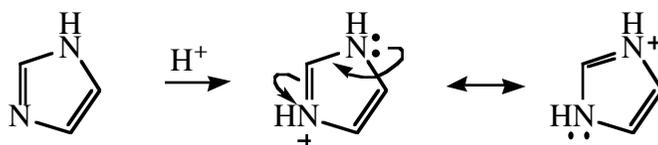
(g) The C=C π bonds of simple hydrocarbons are usually nucleophilic, not electrophilic. However, when a nucleophile attacks the exocyclic C atom of the nonaromatic compound fulvene, the electrons from the C=C π bond go to the endocyclic C and make the ring aromatic.
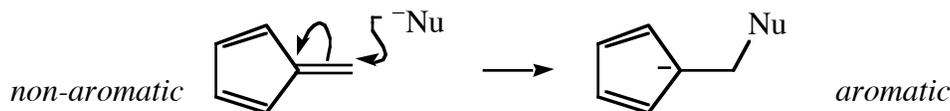
(h) The tautomer of 2,4-cyclohexadienone, a nonaromatic compound, is phenol, an aromatic compound.

(i) Carbonyl groups C=O have an important resonance contributor $\overset{+}{C}-\overset{-}{O}$. In cyclopentadienone, this resonance contributor is antiaromatic.

[**Common error alert:** Many cume points have been lost over the years when graduate students used cyclohexadienone or cyclopentadienone as a starting material in a synthesis problem!]

(j) PhOH is considerably more acidic than EtOH (pK_a= 10 vs. 17) because of resonance stabilization of the conjugate base in the former. S is larger than O, so the S(p)–C(p) overlap in PhS⁻ is much smaller than

the O(p)–C(p) overlap in PhO⁻. The reduced overlap in PhS⁻ leads to reduced resonance stabilization, so the presence of a Ph ring makes less of a difference for the acidity of RSH than it does for the acidity of ROH.

(k) Attack of an electrophile E⁺ on C2 gives a carbocation for which three good resonance structures can be drawn. Attack of an electrophile E⁺ on C3 gives a carbocation for which only two good resonance structures can be drawn.
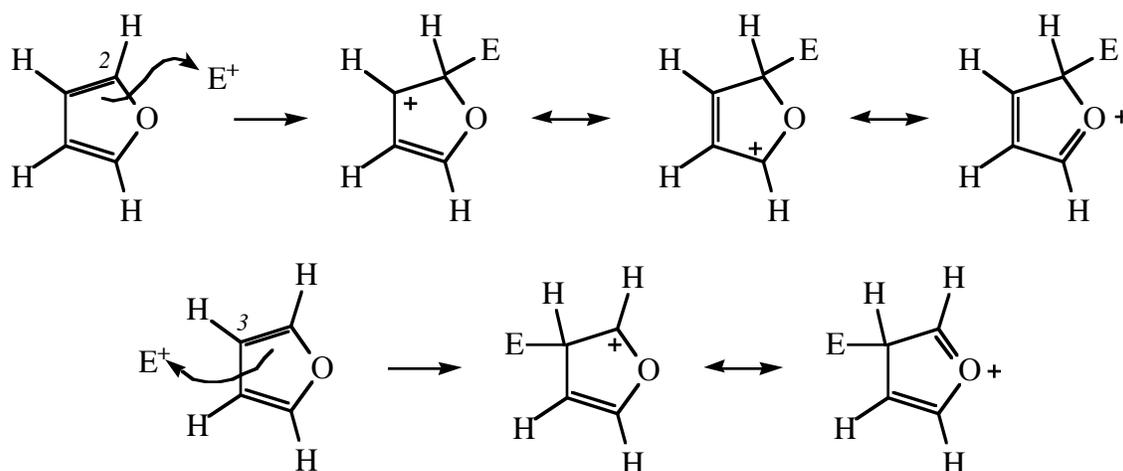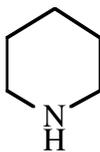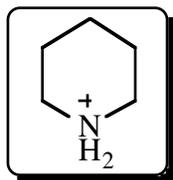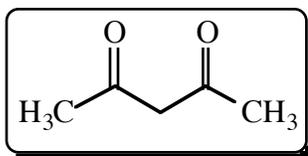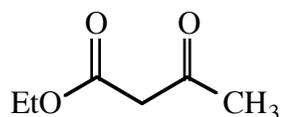

2. (a)
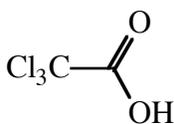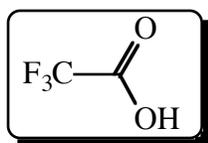
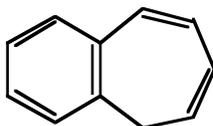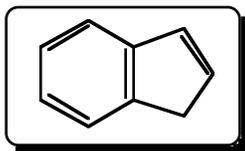inductive electron-withdrawing effect of F is greater than Cl

(b)
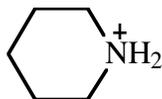

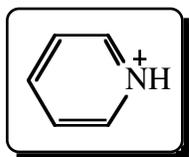In general, AH⁺ is more acidic than AH

(c)

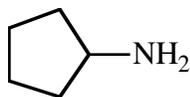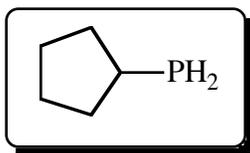Ketones are more acidic than esters

(d)

Deprotonation of 5-membered ring gives aromatic anion; deprotonation of 7-membered ring gives anti-aromatic anion.
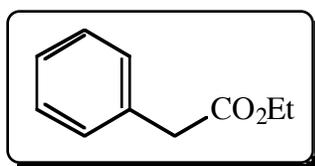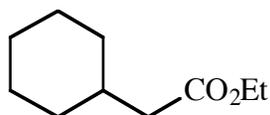
(e)

The $N(sp^2)$ lone pair derived from deprotonation of pyridine is in lower energy orbital, hence more stable, than the $N(sp^3)$ lone pair derived from deprotonation of piperidine.
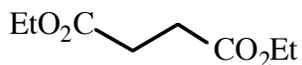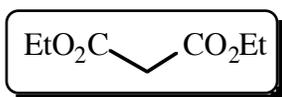
(f)

Acidity increases as you move down a column in the periodic table due to increasing atomic size and hence worse overlap in the A–H bond
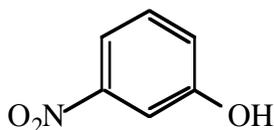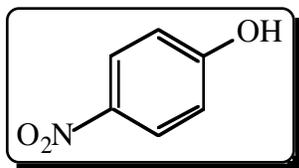
(g)

The anion of phenylacetate is stabilized by resonance into the phenyl ring.
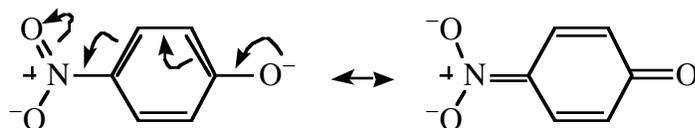
(h)

Anions of 1,3-dicarbonyl compounds are stabilized by resonance into *two* carbonyl groups
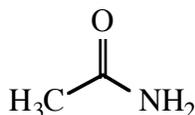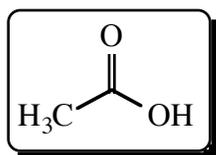
(i)

The anion of 4-nitrophenol is stabilized by resonance directly into the nitro group. The anion of 3-nitrophenol can't do this. Draw resonance structures to convince yourself of this.

(j)

More electronegative atoms are more acidic than less electronegative atoms in the same row of the periodic table

(k)

Ph—≡—CH₃   Ph—≡—H
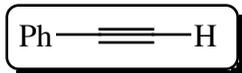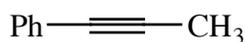
C(sp) is more acidic than C(sp³), even when the anion of the latter can be delocalized into a Ph ring.

(ℓ)
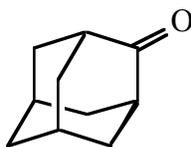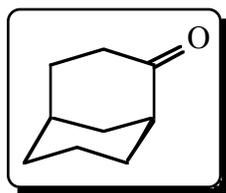
The anion of the latter cannot overlap with the C=O π bond, hence cannot delocalize, hence is not made acidic by the carbonyl group.

(∓)

this C atom

this C atom
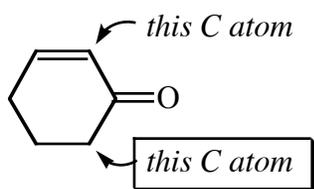
The C(sp²)–H bond on the upper atom is the plane of the paper, orthogonal to the p orbitals of the C=O bond, so the C=O bond provides no acidifying influence. The C(sp³)–H bonds on the lower atom are in and out of the plane of the paper, so there is overlap with the C=O orbitals.

3.

(a) Free-radical. (Catalytic peroxide tips you off.)

(b) Metal-mediated. (Os)

(c) Polar, acidic. (Nitric acid.)

(d) Polar, basic. (Fluoride ion is a good base. Clearly it's not acting as a nucleophile in this reaction.)

(e) Free-radical. (Air.) Yes, an overall transformation can sometimes be achieved by more than one mechanism.

(f) Pericyclic. (Electrons go around in circle. No nucleophile or electrophile, no metal.)

(g) Polar, basic. (LDA is strong base; allyl bromide is electrophile.)

(h) Free-radical. (AIBN tips you off.)

(i) Pericyclic. (Electrons go around in circle. No nucleophile or electrophile, no metal.)

(j) Metal-mediated.

(k) Pericyclic. (Electrons go around in circle. No nucleophile or electrophile, no metal.)
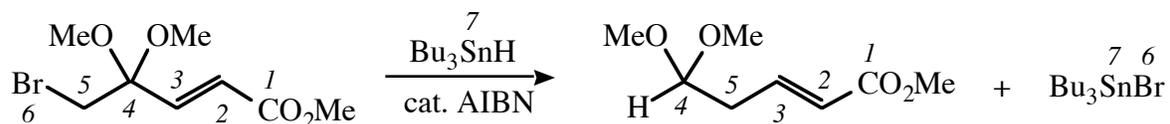
(l) Polar, basic. (Ethoxide base. Good nucleophile, good electrophile.)

(m) Pericyclic. (Electrons go around in circle. No nucleophile or electrophile, no metal.)

4. (a) The mechanism is free-radical (AIBN). Sn7 and Br6 are missing from the product, so they're probably bound to one another in a by-product. Made: C5–C3, Sn7–Br6. Broken: C4–C3, C5–Br6.

(b) Ag^+ is a good Lewis acid, especially where halides are concerned, so polar acidic mechanism is a reasonable guess, but mechanism is actually pericyclic (bonds forming to both C10 and C13 of the furan and C3 and C7 of the enamine). Cl8 is missing from the product; it must get together with Ag to make insoluble, very stable AgCl. An extra O appears in the product; it must come from H_2O during workup. One of the H's in H_2O goes with the BF_4^-, while the other is attached to N1 in the by-product. Made: C3–C10, C7–C13, C2–O (water), Ag–Cl. Broken: N1–C2, C7–Cl8.
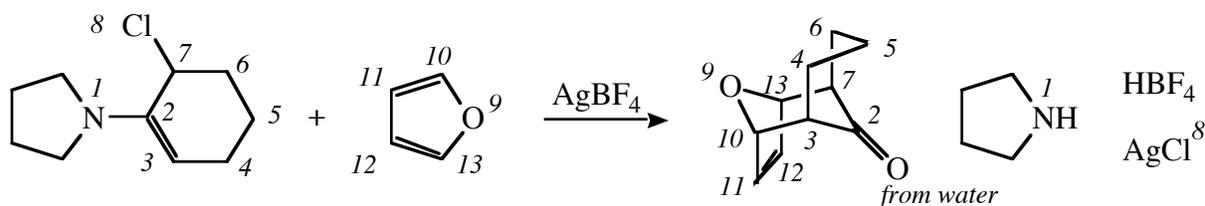
(c) This mechanism is also pericyclic. Use the carbonyl, Me₃SiO, and CH₃ groups as anchors for numbering the atoms. Made: C2–C12, C3–C11. Broken: C2–C8.
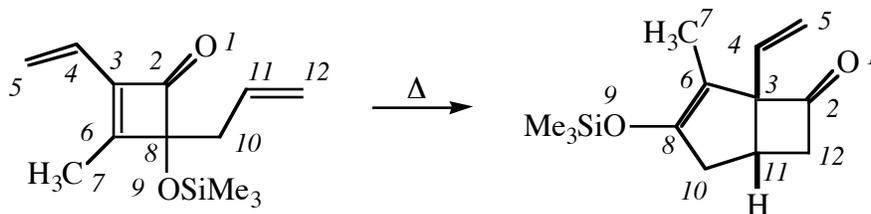
(d) Ph₃P is a Lewis base. The mechanism is polar under basic conditions. Made: C1–C7, O2–C4, O3–C6. Broken: O3–C4.
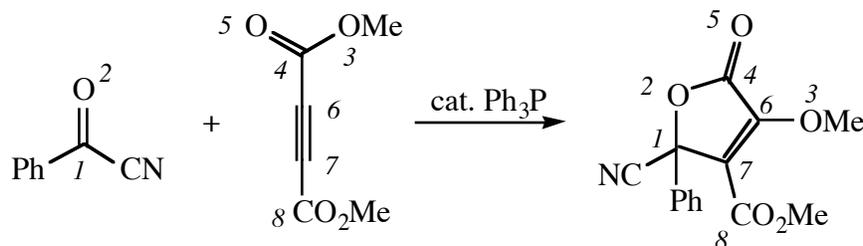
(e) The mechanism is polar under acidic conditions due to the strong acid RSO₃H. Made: C13–C6. Broken: C13–C8.
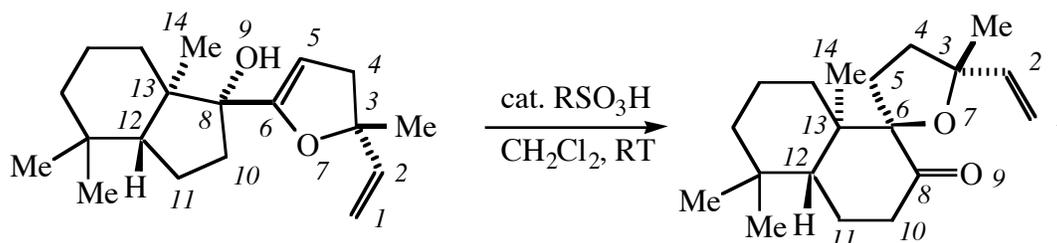
(f) The mechanism is polar under basic conditions (NaOEt). Two equivalents of cyanoacetate react with each equivalent of dibromoethane. One of the CO₂Et groups from cyanoacetate is missing in the product

and is replaced by H. The H can come from EtOH or HOH, so the CO_2Et is bound to EtO or HO. The two products differ only in the location of a H atom and a π bond; their numbering is the same. Made: C2–C5, C2'–C6, C2'–C3, C1'–OEt. Broken: C1'–C2', C5–Br, C6–Br.

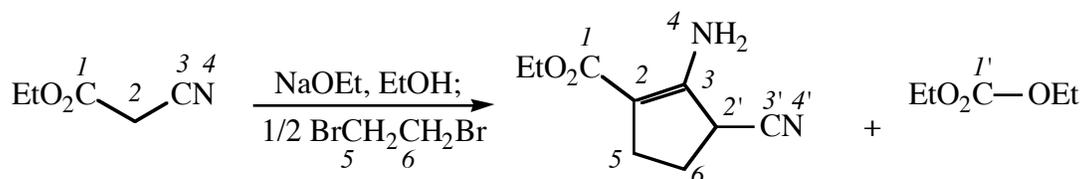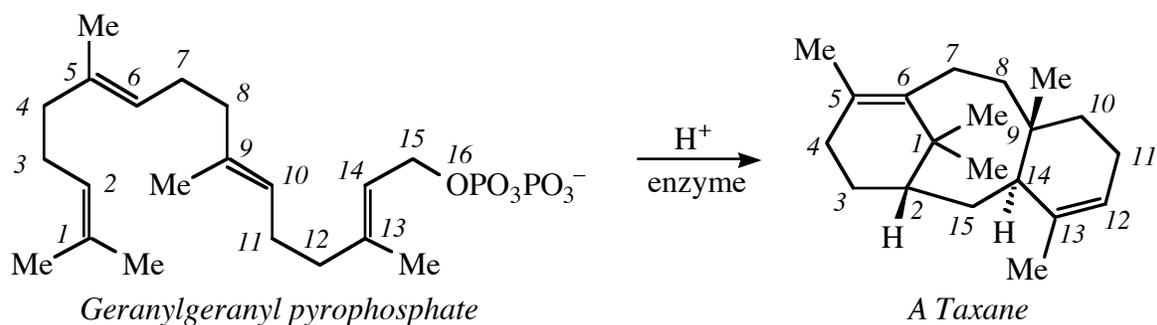(g) Polar under acidic conditions. The enzyme serves to guide the reaction pathway toward one particular result, but the mechanism remains fundamentally unchanged from a solution phase mechanism. The Me groups provide clues as to the numbering. Made: C1–C6, C2–C15, C9–C14. Broken: C15–O16.

Geranylgeranyl pyrophosphate   *A Taxane*

(h) Two types of mechanism are involved here: First polar under basic conditions, then pericyclic. At first the numbering might seem very difficult. There are two CH_3 groups in the starting material, C5 and C16, and two in the product. Use these as anchors to decide the best numbering method. Made: C1–C14, C2–C12, C12–C15. Broken: C3–C12, O7–Si8.
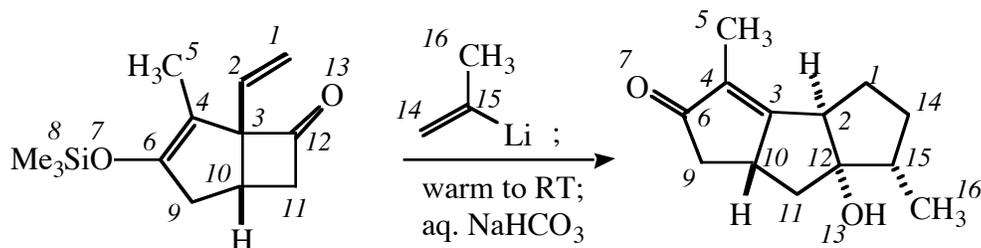
(i) The carboxylic acid suggests a polar acidic mechanism. Made: C2–C7, C2–O3, C4–O6. Broken: O3–C4.
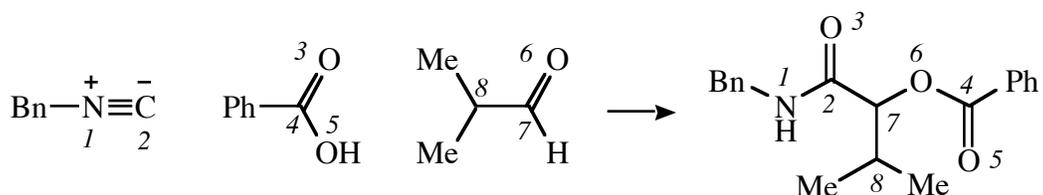
(j) Free-radical mechanism (AIBN). Both Br7 and Sn11 are missing from the product, so they are probably connected to one another in a by-product. H12 appears connected to C10 in the product, as C10 is the only C that has a different number of H's attached in S.M. and product. Made: C1–C9, C2–C6, Br7–Sn11. Broken: C6–Br7.
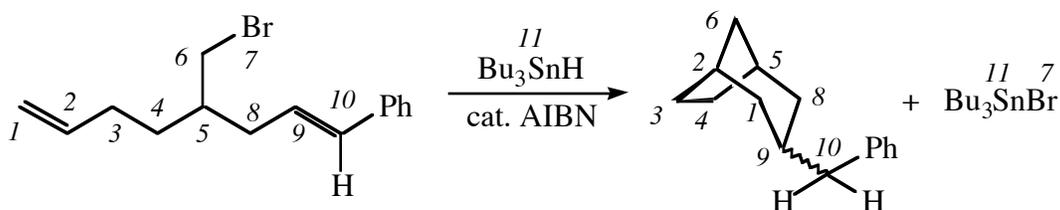
(k) No acid or base is present, and the reaction involves changes in π bonds. This is a pericyclic mechanism. Use C8 with its two Me groups as an anchor to start numbering. Ozone is a symmetrical molecule, but the middle O is different from the end O's; it's not clear which O in ozone ends up attached to which atom in the product. However, it is clear where O4 ends up, as it remains attached to C3. Made: C1–O11, C1–O4, C2–O9, C2–O10. Broken: C1–C2, O9–O10.
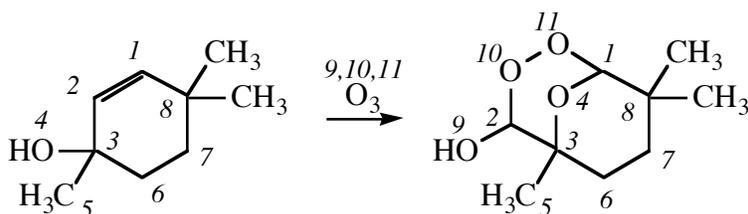
(ℓ) Polar mechanism under basic conditions. Again, use C11 with its two Me groups as an anchor to start numbering. C7 remains attached to C8 and O6 in the product. C2 leaves as formate ion; the two O's attached to C2 in the S.M. remain attached to it in the formate product. O4 is still missing; it's probably lost as H_2O, with the two H's in H_2O coming from C8. Made: C5–C8. Broken: C2–C7, O3–O4, O4–C5, C5–O6.
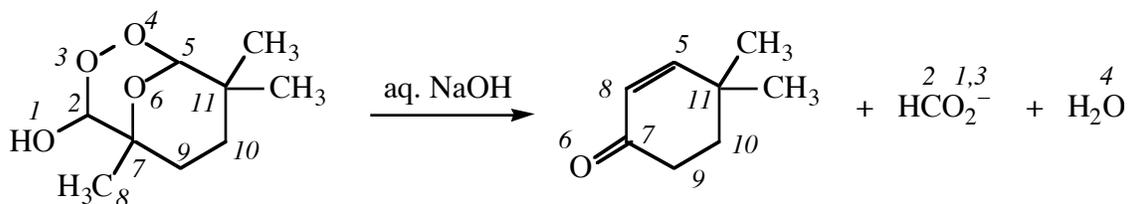
(m) Bromine undergoes electrophilic (polar acidic) reactions in the absence of light. Use C6 as an anchor to begin numbering. In the S.M. there are two CH_2 groups, C4 and C7. The one CH_2 group in the product must be either C4 or C7. C7 is next to C6 in the S.M., while C4 is not; since the CH_2 group in the product is not next to C6, it is probably C4. Made: C2–C7, C3–Br. Broken: Br–Br.
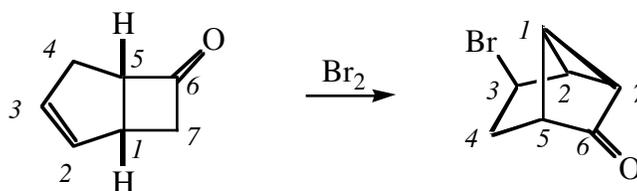
5. N= nucleophilic, E= electrophilic, A= acidic.

(a) E	(b) none*	(c) E	(d) A	(e) A**	(f) E
(g) none†	(h) N	(i) none	(j) N	(k) A	(l) E
(m) none**	(n) E	(o) A	(p) N	(q) none	(r) N
(s) A, N	(t) E	(u) E	(v) none	(w) none	(x) N
(y) A	(z) E	(aa) A	(bb) N	(cc) N, A	(dd) N
(ee) none	(ff) N	(gg) E, A	(hh) N	(ii) none	(jj) N
(kk) N	(ll) E	(mm) slightly A?			

*See text (Section B.1) for an explanation.

**The O atom still has a lone pair, but if it were to use it in a nucleophilic reaction, it would acquire a very unfavorable +2 formal charge.

†The fact that an elimination reaction can occur upon removal of H^+ from this atom (with loss of the leav-

ing group next door) is irrelevant to the question of the *acidity* of this atom. Acidity is a measure of the difference in energy between an acid and its conjugate base. The conjugate base formed by removing H^+ from this atom would be very high in energy.