

The Study of Chemical Reactions

Reading: Wade chapter 4, sections 4-12- 4-16

Study Problems: 4-39, 4-41, 4-43, 4-44, 4-46, 4-48, 4-49

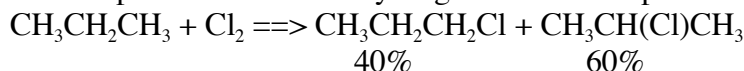
Key Concepts and Skills:

- Use energy diagrams to discuss transition states, activation energies, intermediates, and the RDS of a multistep reaction.
- Use the Hammond postulate to predict whether a transition state will be reactant-like or product-like.
- Describe the structures and reactivities of carbocations, carbanions, free radicals, and carbenes, and the structural features that stabilize them.

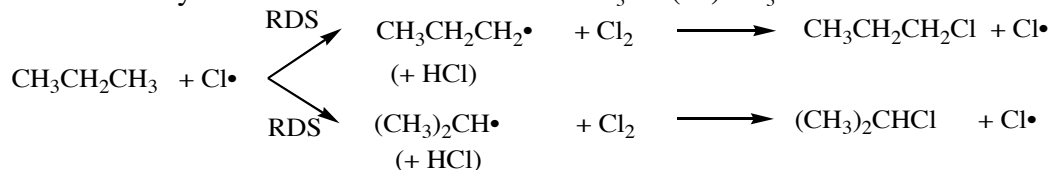
Lecture Topics:

I. Halogenation of Higher Alkanes

Propane has both primary (1°) and secondary (2°) hydrogen atoms that can be replaced upon chlorination. The product ratio upon reaction with Cl_2 (g) in the presence of light as an initiator is 40% chlorine replacement of a 1° hydrogen and 60% replacement of a 2° hydrogen:

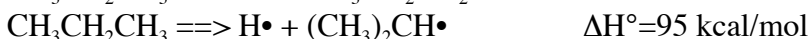


In the rate-determining step of the reaction (first propagation step), generation of a primary radical leads ultimately to formation of $\text{CH}_3\text{CH}_2\text{CH}_2\text{Cl}$; alternatively, generation of a secondary radical leads to formation of $\text{CH}_3\text{CH}(\text{Cl})\text{CH}_3$:

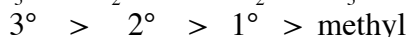
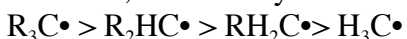


Apparently, the secondary radical is formed preferentially (at a faster rate)

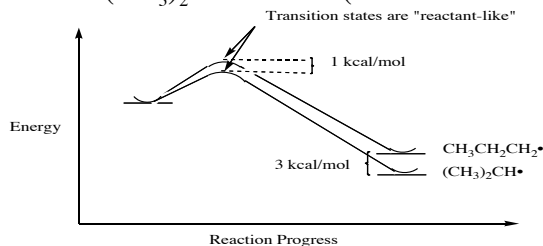
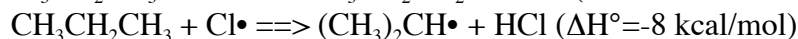
Analysis of bond dissociation energies (BDE's) shows that more highly substituted radicals are more stable:



And thus, the stability order for radicals is



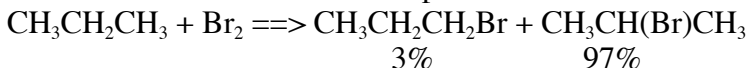
Abstraction of the 2° H atom is 3 kcal/mol more exothermic than abstraction of the 1° H atom: $\text{CH}_3\text{CH}_2\text{CH}_3 + \text{Cl}\cdot \rightleftharpoons \text{CH}_3\text{CH}_2\text{CH}_2\cdot + \text{HCl}$ ($\Delta H^\circ = -5$ kcal/mol)



Relative rates of chlorination: 2° (4.5 x faster than 1°); 3° (5.5 x faster than 1°)

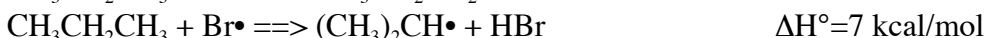
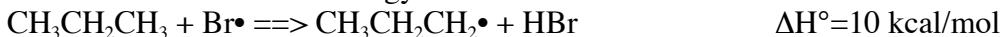
II. Bromination of Propane

Bromination is a more selective process:



the 2° H's are 97 x more reactive than the 1° H's !

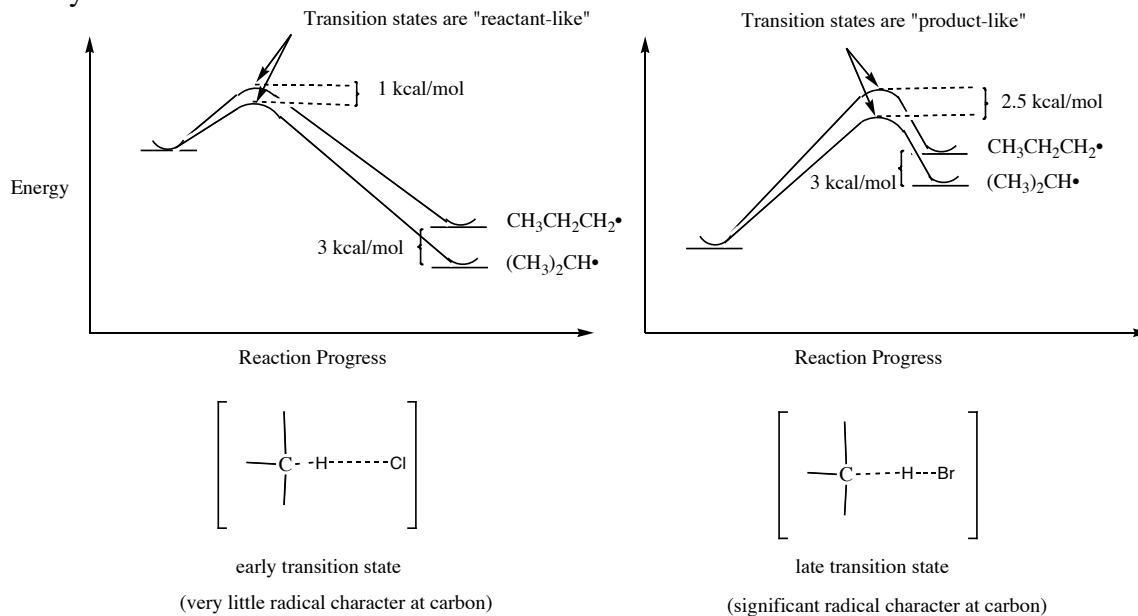
The energetics of this reaction show that, similar to the chlorination reaction, there is a 3 kcal/mol difference in energy of the intermediate radicals



Yet this process is endothermic in both cases, unlike chlorination!

Although the energy differences of the intermediate radicals are the same in the chlorination and bromination, the **transition state energies** are different. For chlorination, the difference in energy for the two transition states is 1 kcal/mol; for bromination, the difference in transition state energies is 2.5 kcal/mol. Why is this so?

In an **endothermic** reaction, the transition state is closer to the products in energy and structure, and this is termed a "late transition state". In an **exothermic reaction**, the transition state is closer in structure and energy to the reactants, and this is termed an "early transition state"



The **Hammond Postulate** summarizes this important concept for organic chemical reactions: *related species that are closer in energy are also closer in structure. The structure of a transition state resembles the structure of the closest stable species*. Thus, endothermic reactions have product-like transition states, and exothermic reactions have reactant-like transition states.

In general, exothermic processes are less selective than endothermic processes. Chlorination is not very selective, whereas bromination is quite site-selective.

III. Reactive intermediates in Chemical Reactions

In general, carbon atoms with less than four bonds react quickly to give more stable tetravalent species. Most mechanisms involve some kind of reactive intermediates.

Trivalent carbon atoms include the carbocation, R_3C^+ , the radical, R_3C^\bullet , and the carbanion, R_3C^- . Divalent carbon species are called carbenes, $R_2C:$.

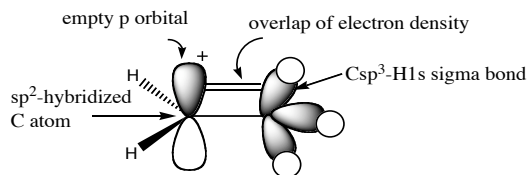
- a. Carbocations** have no non-bonding electrons, and are positively charged with six valence electrons. Their hybridization is sp^2 with a vacant p orbital perpendicular to the bonding plane.

Carbocations are powerful **electrophiles** (=Lewis acids = acceptor of electron pairs) that react with nucleophiles (=Lewis bases = donors of electron pairs)

Like radicals, carbocations are **electron deficient** (lacking an octet), and are stabilized by alkyl substitution.

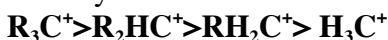
There are three modes of alkyl group stabilization of carbocations

1. Inductive donation of electron density through the sigma bonds of the molecule. The positive charge on carbon withdraws electron-density from the alkyl group
2. Orbital overlap (“hyperconjugation”) from a nearby filled sp^3 orbital of the alkyl group. This spreading out of charge from a sigma bond is a type of through-space resonance. Free rotation about the sigma bond allows all three sigma bonds on the attached methyl group to participate in hyperconjugative donation to the carbocation.

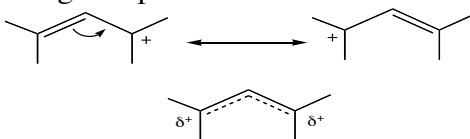


Hyperconjugative overlap stabilizes carbocations

An additive effect is observed for increasing alkyl group substitution, and thus the stability order for carbocations is $3^\circ > 2^\circ > 1^\circ > \text{methyl}$

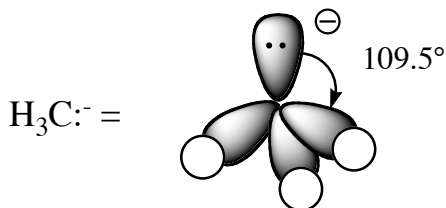


3. Resonance (pi-orbital overlap) is a third mode of stabilization of carbocations in which the positive charge is spread out over two or more carbon atoms:

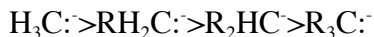


- b. Radicals** are also sp^2 hybridized with a p-orbital perpendicular to the bonding plane containing a single unpaired electron; they are electron-deficient species stabilized by electron donation from alkyl groups in the same manner as for carbocations. Pi-bond resonance also stabilizes radicals.

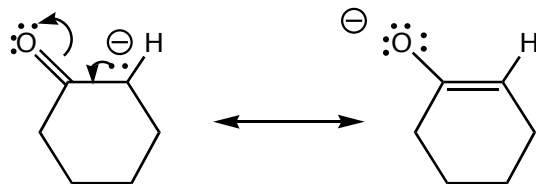
- c. **Carbanions** resemble NH_3 in structure, they are sp^3 hybridized with the lone pair occupying an sp^3 orbital. Their structure is very nearly tetrahedral.



Carbanions are electron rich and thus act as nucleophiles (Lewis bases). The stability order is the opposite that for radicals and carbocations: methyl $>$ $1^\circ >$ $2^\circ >$ 3°

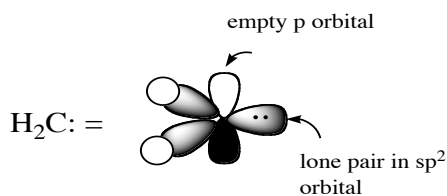


Resonance (charge delocalization) through pi bonds also stabilizes carbanions:

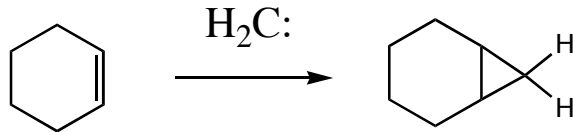




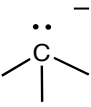

note: the carbanion must rehybridize to sp^2 (negative charge in p-orbital) in order for efficient overlap with the $\text{C}=\text{O}$ to occur!

d. **Carbenes** are uncharged reactive intermediates with a divalent carbon atom: $\text{H}_2\text{C}:$, methylene; $\text{Br}_2\text{C}:$, dibromocarbene. Carbenes are sp^2 hybridized with a pair of electrons occupying an sp^2 orbital, and an empty p-orbital is perpendicular to the plane of sp^2 -orbitals:



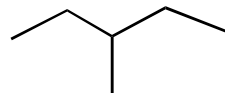
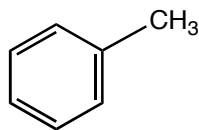
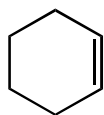
Carbenes can react as both nucleophiles and electrophiles; they can thus simultaneously accept and donate electrons to form 2 bonds to the carbene carbon atom:



Structure	Stability	Reactivity
	$3^\circ > 2^\circ > 1^\circ > \text{methyl}$	electrophilic; Lewis acid
	$3^\circ > 2^\circ > 1^\circ > \text{methyl}$	electron-deficient
	$\text{methyl} > 1^\circ > 2^\circ > 3^\circ$	nucleophilic
		both nucleophilic and electrophilic

Additional Problems for practice:

- 1.) Draw a reaction profile (graph of energy versus reaction coordinate) for a one step reaction with a late transition state. State whether the transition state resembles the starting material or the product. Repeat the process for a one step reaction with an early transition state.
- 2.) Draw out the structure of a tertiary alkyl carbocation and a primary alkyl carbocation and explain in detail why a tertiary carbocation is more stable than a primary carbocation. Do the same for the corresponding radical species.
- 3.) Indicate the preferred site(s) of monobromination ($\text{Br}_2, h\nu$) for the following molecules. Use bond dissociation energies in table 4-2 in your text as a guide. Remember that bromination is more selective than chlorination.



- 4.) Draw the structures of the three possible monochlorination products for the following molecule. Predict the ratios in which these monochlorination products are formed, remembering that a chlorine atom abstracts a 2° H atom 4.5 x as fast as a 1° H atom, and a 3° H atom is abstracted 5.5 x as fast as a 1° H atom.

