Organic Chemistry 1
Lecture 8

Instructor: Prof. Duncan Wardrop

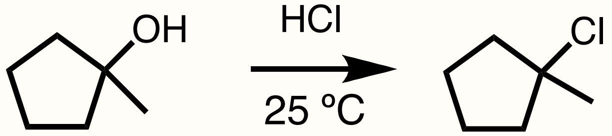
Time/Day: T & R, 12:30-1:45 p.m.

February 04, 2010

Self Test Question

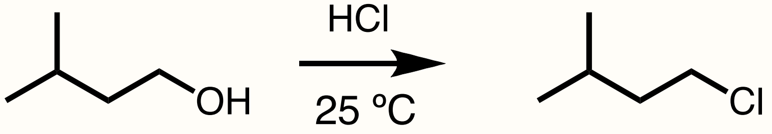
Which of the following transformations is unlikely to generate the product indicated?

a.

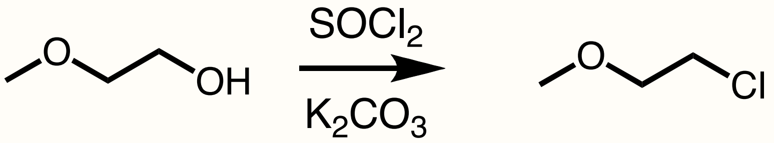


primary alcohols and HCl are insufficiently reactive

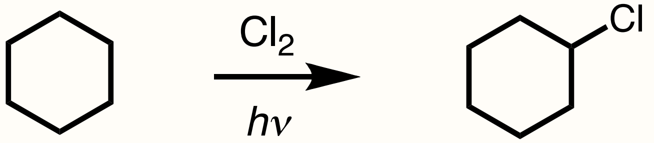
✗ b.



c.



d.



A. a.

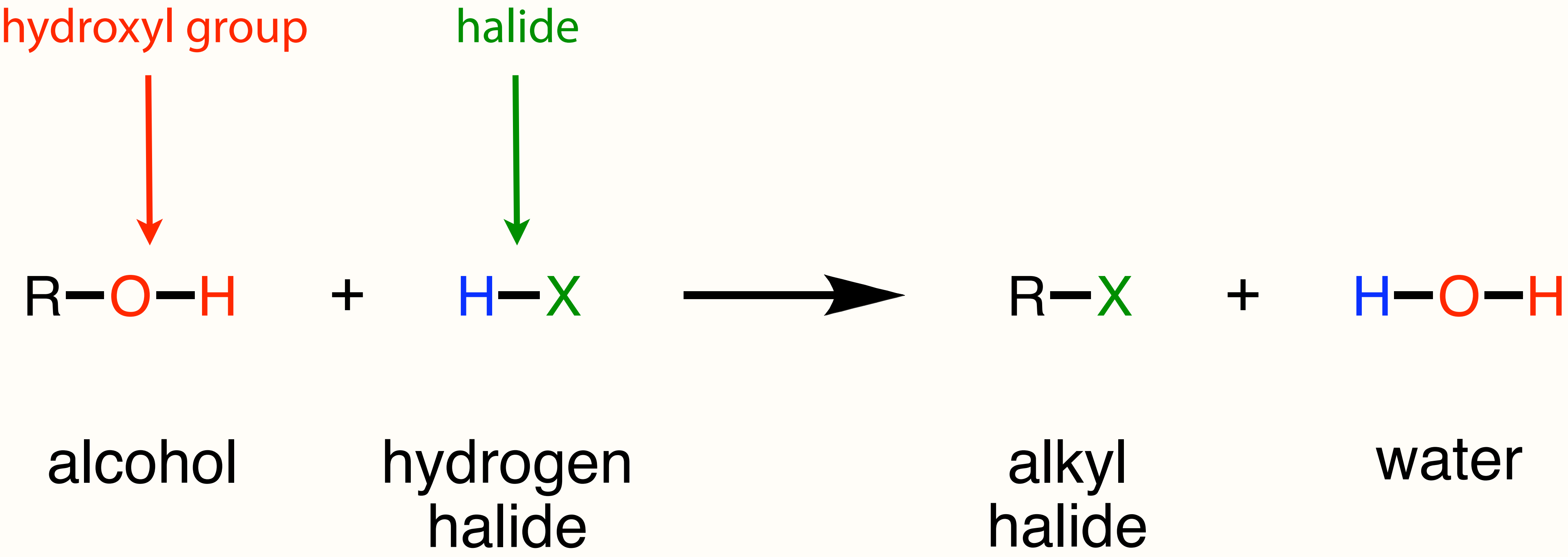
B. b.

C. c.

D. d.

Compound "b." is a primary alcohol, which are insufficiently reactive to undergo reaction with hydrogen chloride. Primary alcohols do, however, react with thionyl chloride (SOCl2) to form chlorides and so the transformation shown in "c" will proceed successfully Compound "a" is tertiary alcohol and consequently reacts with HCl.

Substitution Reaction



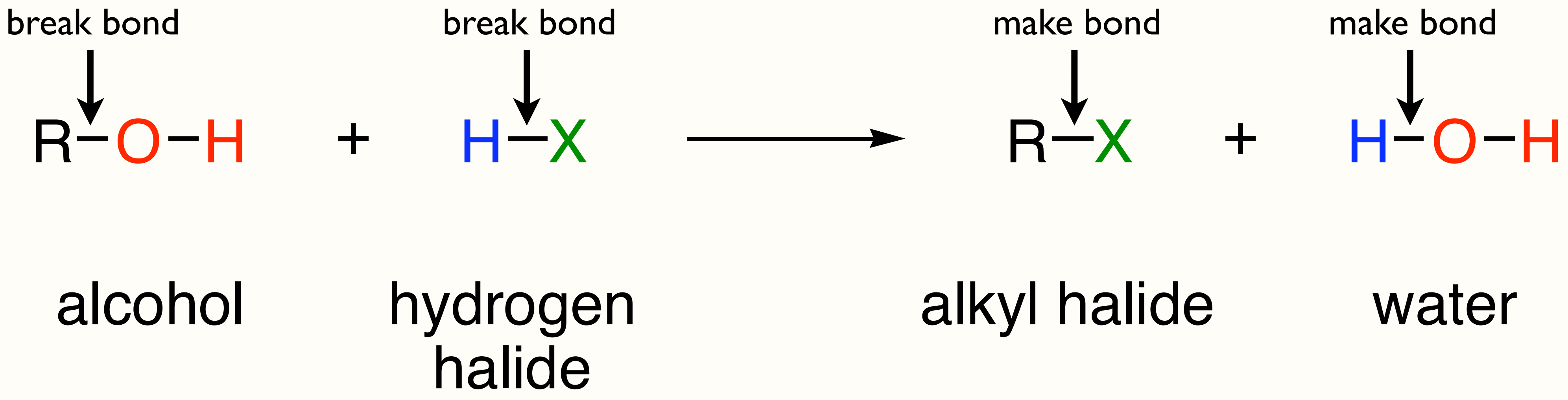
$$R{-}O{-}H + H{-}X \longrightarrow R{-}X + H{-}O{-}H$$

Hydroxyl group is being substituted (replaced with) a halide

Mechanisms of Substitution Reactions

Sections: 4.8-4.11

Substitution: How Does it Happen?

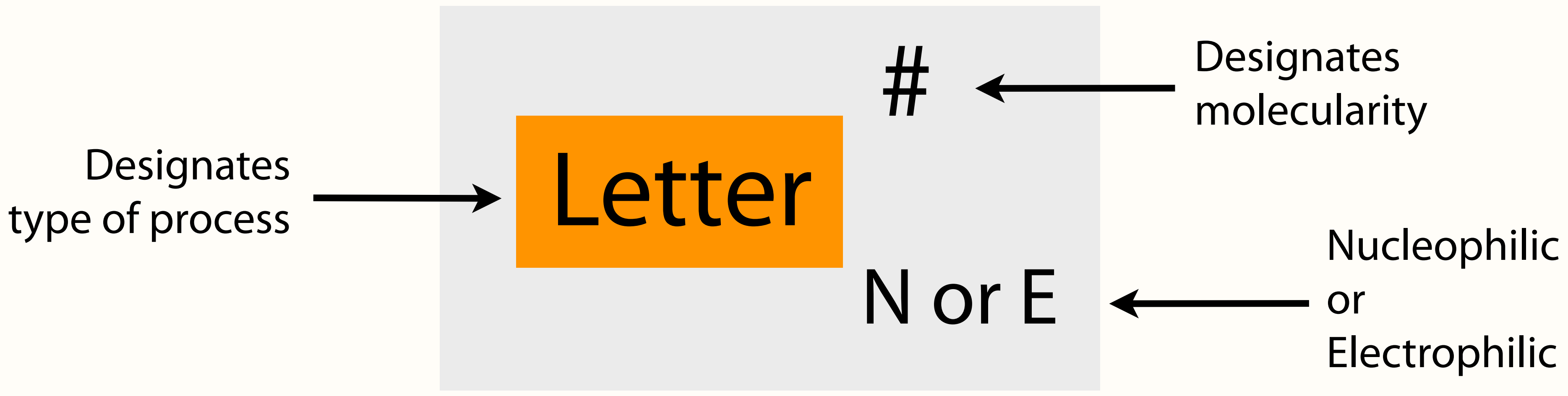


$$\text{R–O–H} + \text{H–X} \longrightarrow \text{R–X} + \text{H–O–H}$$

mechanism: a generally accepted series of elementary steps that show the order of bond breaking and bond making

elementary step: a bond making and/or bond breaking step that only involves one transition state

Ingold-Hughes Mechanistic Designators

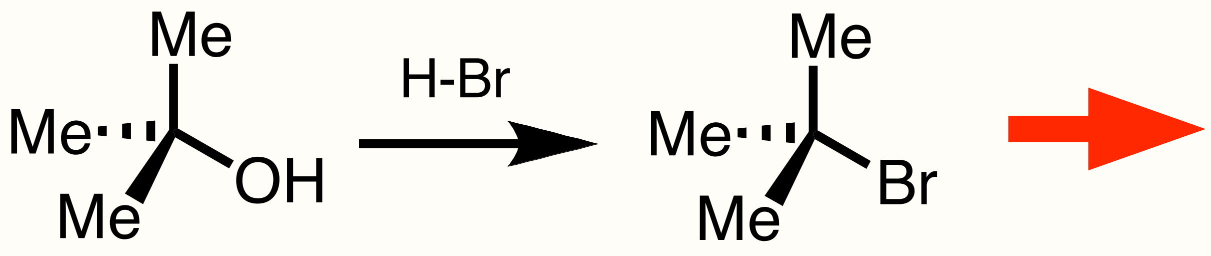


Designates type of process → Letter

← Designates molecularity

N or E ← Nucleophilic or Electrophilic

Example



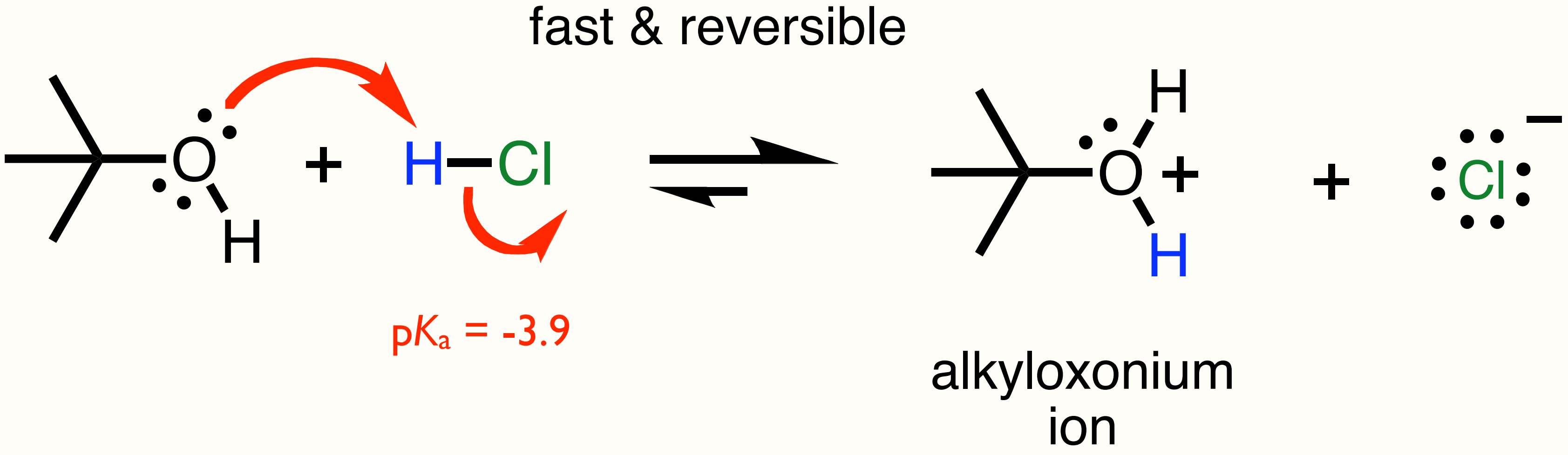
S_N1 Substitution, nucleophilic, 1st order

Rate = k x [*t-BuOH*]

Nucleophilic Substitution (S_N1)

Step One

Proton Transfer (Protonation)



this is an acid–base reaction; product is an alkoxonium ion

exothermic and fast (proton transfer is among the fastest processes in organic chemistry)

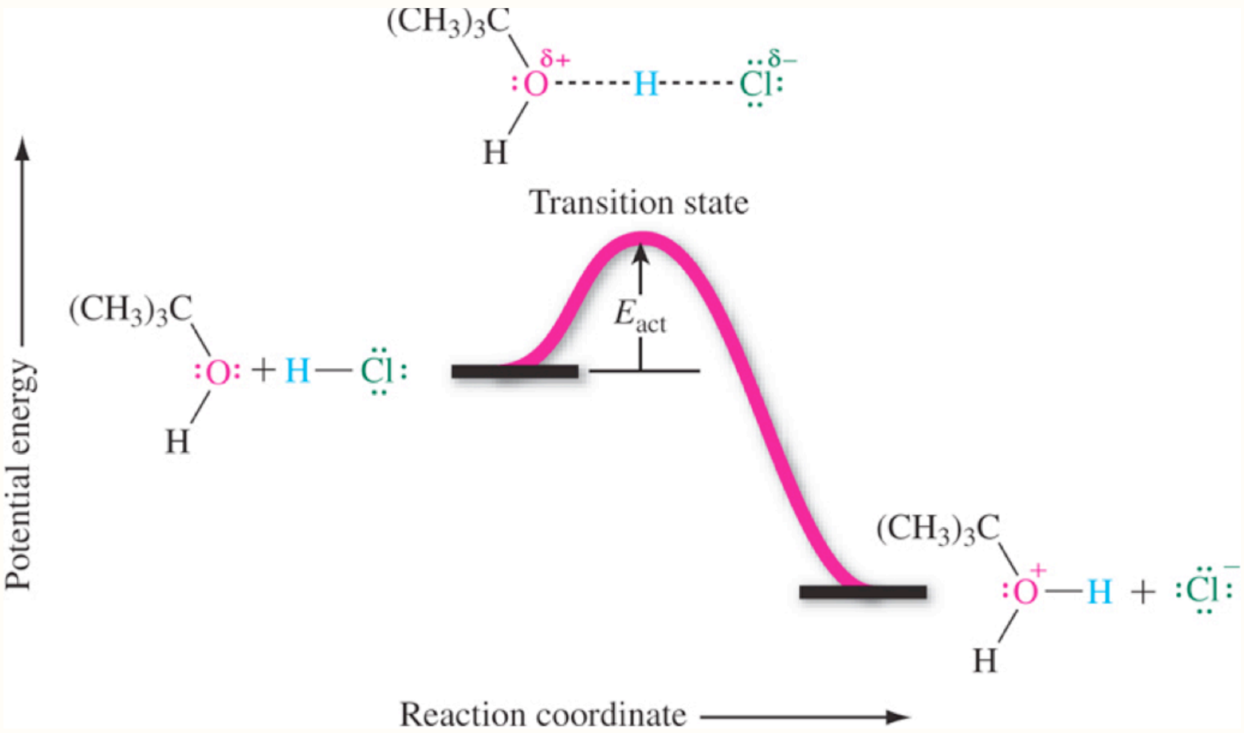
rate of individual step =k x [alcohol] x [HX]; two reactants = bimolecular (2nd order)

oxonium ion is an intermediate in the overall reaction

Step One Potential Energy Diagram

Step One

Proton Transfer (Protonation)



transition state: energy maximum along reaction coordinate for one elementary step; usually involves partial bond making and partial bond breaking

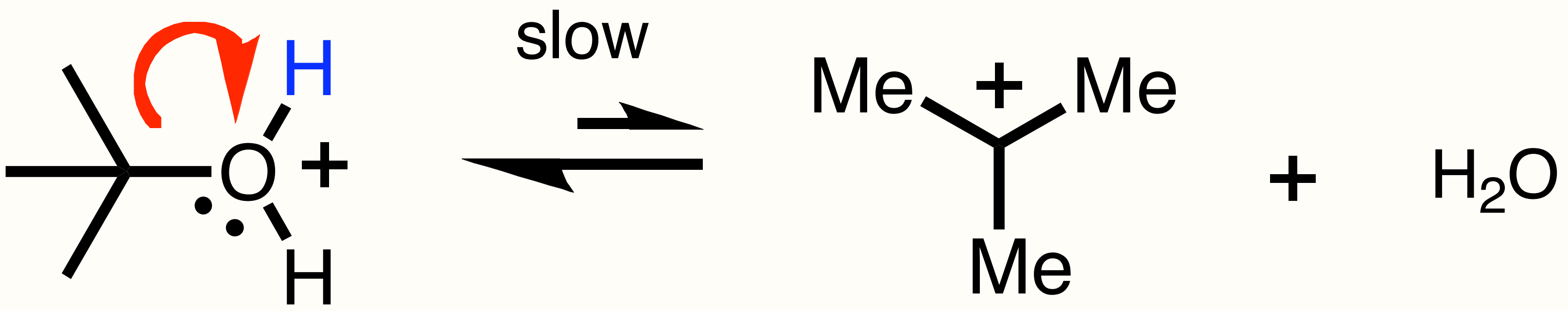
intermediate: energy minimum along the reaction coordinate; species with a finite lifetime; neither reactant, nor product

Hammond Postulate: structure of the transition state "looks" most like its closest energy reactant or intermediate

Mechanism: Nucleophilic Substitution (S_N1)

Step Two

Dissociation (Ionization)



carbocation
(*t*-butyl cation)

breaking a carbon–oxygen bond

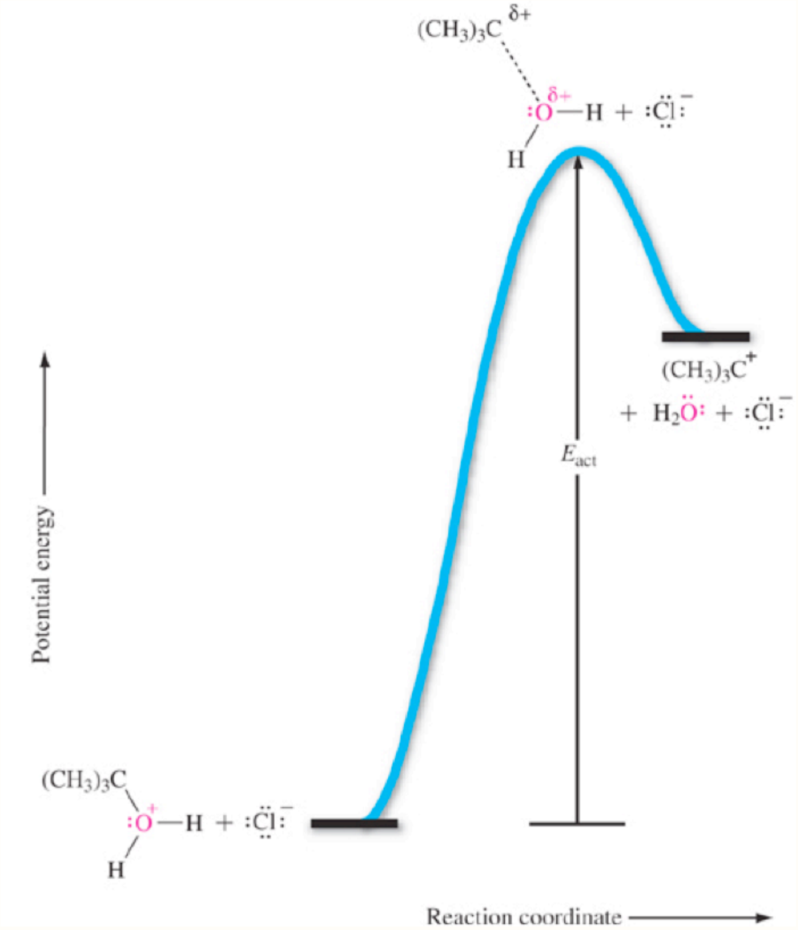
slowest (rate determining) step in entire mechanism; endothermic

rate=k[oxonium ion]; one reactant = unimolecular (1st order)

Step Two Potential Energy Diagram

Step Two

Dissociation (Ionization)

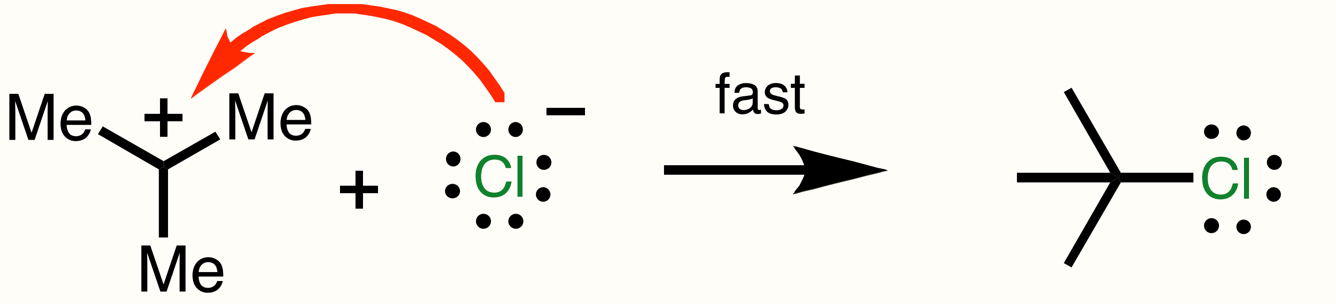


- largest activation energy (Ea)
- endothermic, slowest
- carbocation intermediate is much higher in energy than an oxonium ion
- carbocations do not have a full octet, whereas oxonium ions do
- structure of transition state most resembles the closest energy neighbor, the carbocation (Hammond Post.)

Mechanism: Nucleophilic Substitution (S_N1)

Step Three

Carbocation Capture



carbocation
(*t*-butyl cation)

t-butyl chloride

Cation = Electrophile

Anion = Nucleophile

exothermic and fast; neutral products much lower in NRG

small activation energy; negative charge to positive charge

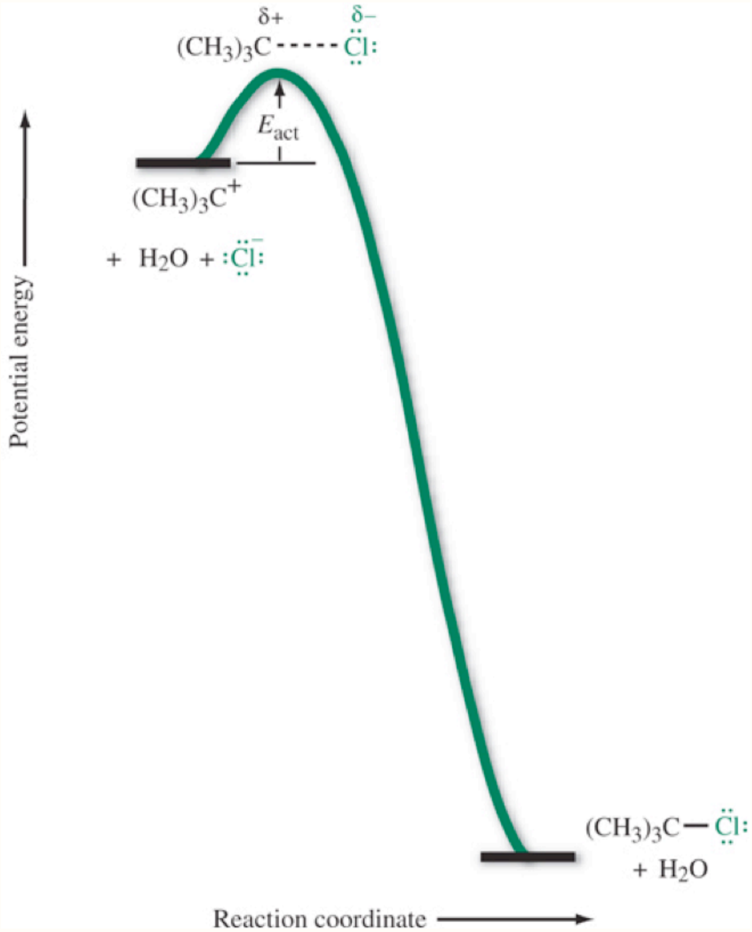
transition state looks most like carbocation since they are closest in energy

rate = k x [carbocation][halide]; two reactants = bimolecular

Step Three Potential Energy Diagram

Step Three

Carbocation Capture

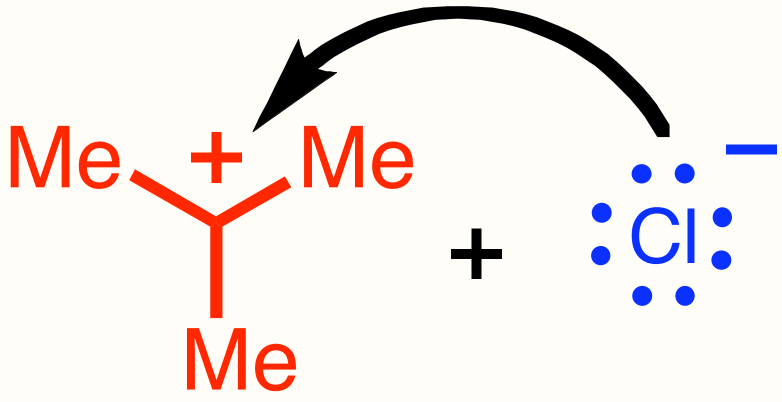


- fast step because small activation energy; positive and negative atoms bond fast
- products are much lower in energy since they are neutral; exothermic reaction
- transition state looks most like its closest neighbor, the carbocation intermediate (very little C-Cl bond formation at transition state) (Hammond Postulate)

Nucleophiles Add to Electrophiles

nucleophile: nucleus loving; Lewis base; electron pair donor; forms bonds with a nucleus that can accept electrons; does not necessarily have to be negatively charged; has available, filled orbitals!

electrophile: electron loving; Lewis acid; electron pair acceptor; forms bonds by accepting electrons from other atoms; does not necessarily have to be positively charged; has available, empty orbitals!



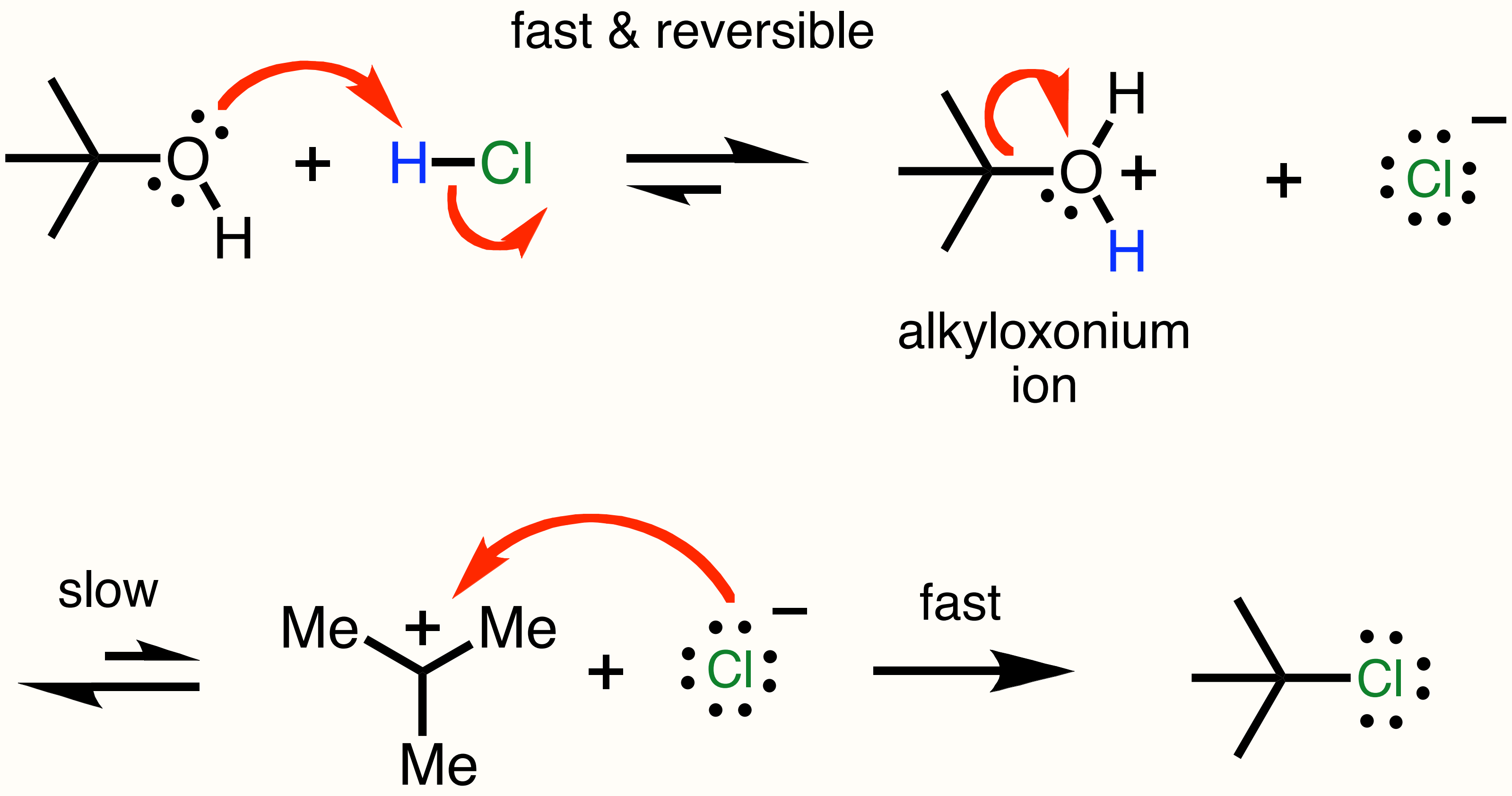
Cation is Electrophile

empty $2p_z$ orbital

Chloride is Nucleophile

filled *n* orbital (: = lone pair)

Complete Mechanism

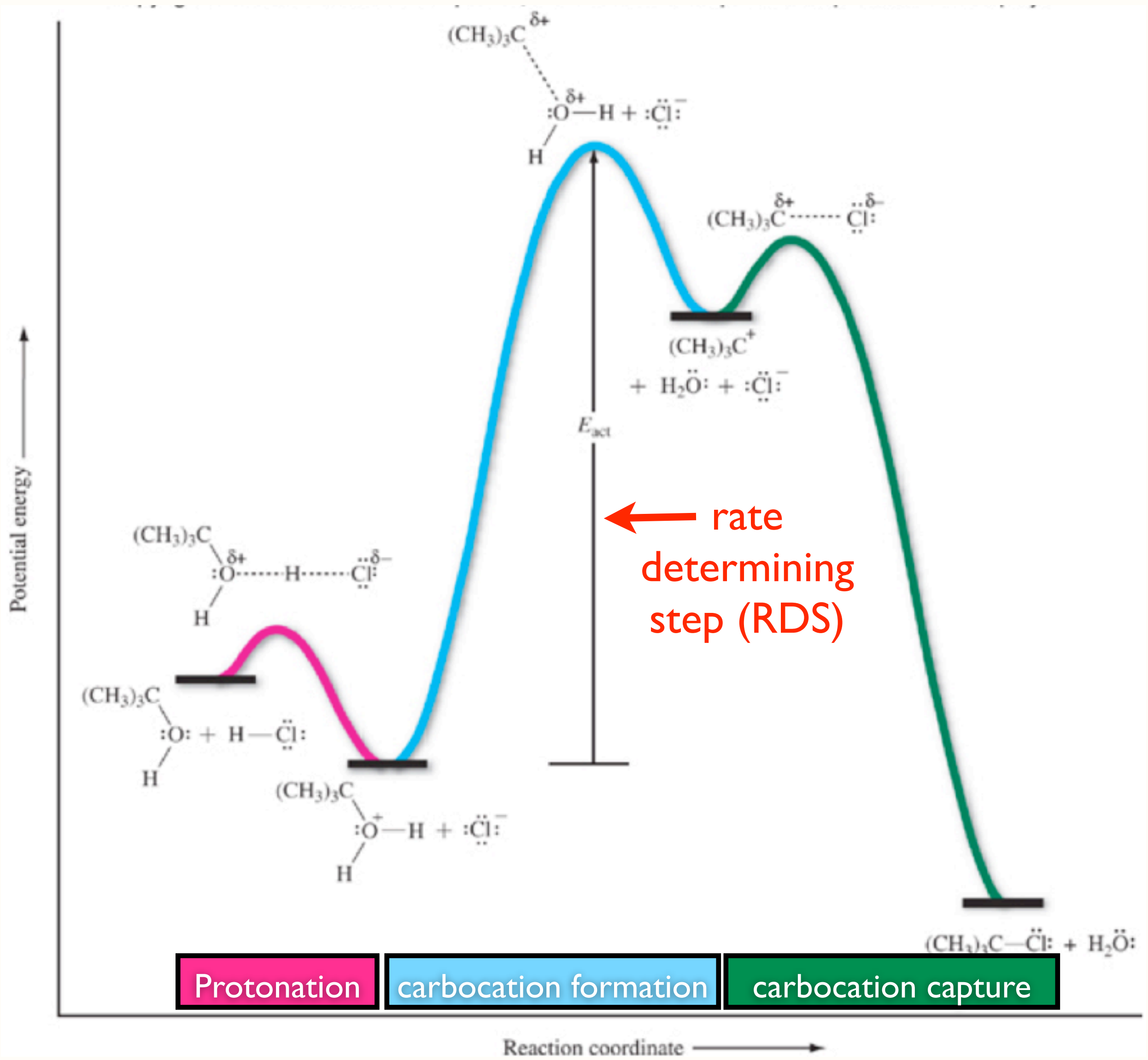


alkyloxonium ion

carbocation (*t*-butyl cation) + H_2O

t-butyl chloride

Complete Potential Energy Diagram



- mechanism only valid for 3° & 2° alcohols
- reaction is only as fast as its slowest step
- slowest step (largest Ea) = rate determining step (RDS)
- here, slowest step is carbocation formation
- here, RDS is unimolecular

Naming the Mechanism: Ingold Notation

$$\mathrm{R{-}O{-}H} \quad + \quad \mathrm{H{-}X} \longrightarrow \mathrm{R{-}X} \quad + \quad \mathrm{H{-}O{-}H}$$

$\mathrm{R{-}O{-}H}$	$\mathrm{H{-}X}$	$\mathrm{R{-}X}$	$\mathrm{H{-}O{-}H}$
alcohol	hydrogen halide	alkyl halide	water

S_N1

S: Substitution

the alcohol functional groups is being substituted with a halide

N: Nucleophilic

the halide doing the substitution is a nucleophile

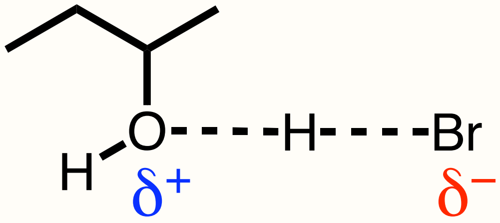
1: 1st order (unimolecular)

the RDS is carbocation formation; this step is unimolecular (1st order)

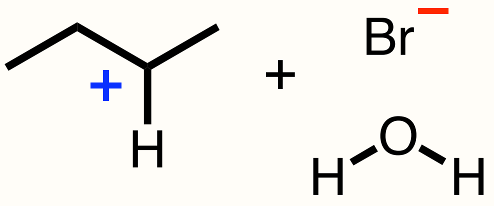
Self Test Question

Consider the S_N1 mechanism for the formation of 2-bromobutane. Which structure best represents the highest energy *transition state* in this mechanism?

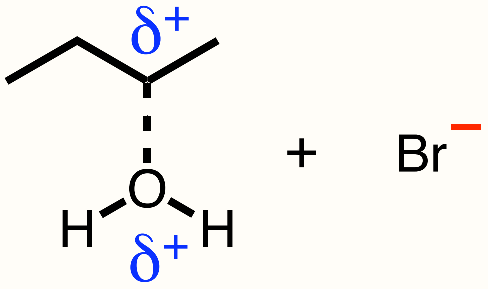
a.



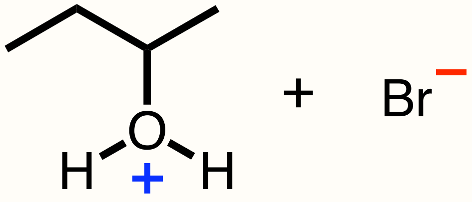
c.



b.



d.



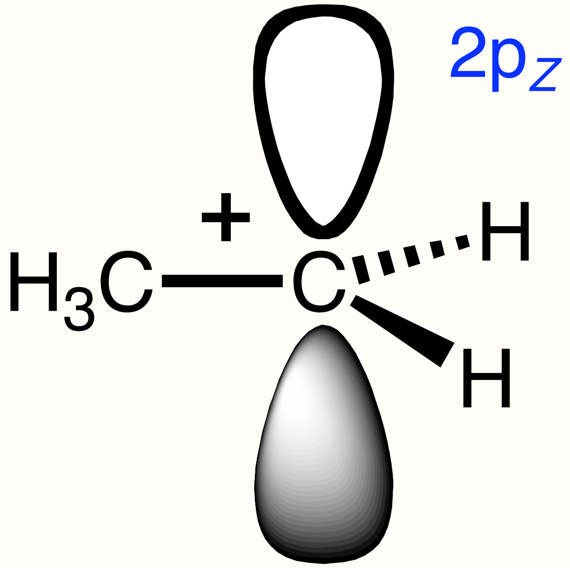
A. a.

B. b.

C. c.

D. d.

Structure of Carbocations



carbocations can be stabilized by inductive effects and hyperconjugation

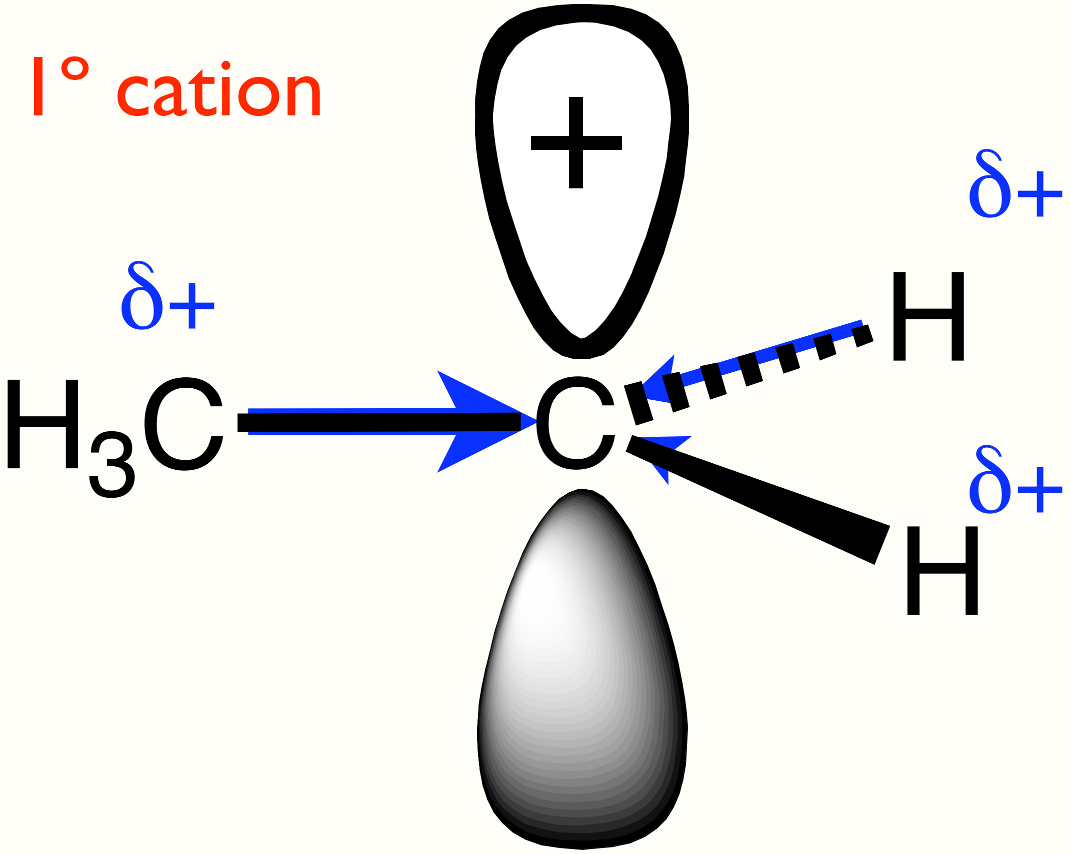
- carbocations are high energy *intermediates*; hard, but not impossible to isolate
- carbon is sp^2-hybridized with a single, unoccupied $2p_z$ orbital; 6 valence electrons
- planar structure : three bonds to carbon are at 120° angles from each other and 90° to empty *p*-orbital; VSEPR
- nucleophiles add to either lobe of the empty *p*-orbital; since it is flat, there is no preference to which side nucleophile adds

Stability of Carbocations

1. Inductive Effects

electron withdrawal or electron donation that is transmitted through σ-bonds; polarization of σ-bonds

1° cation

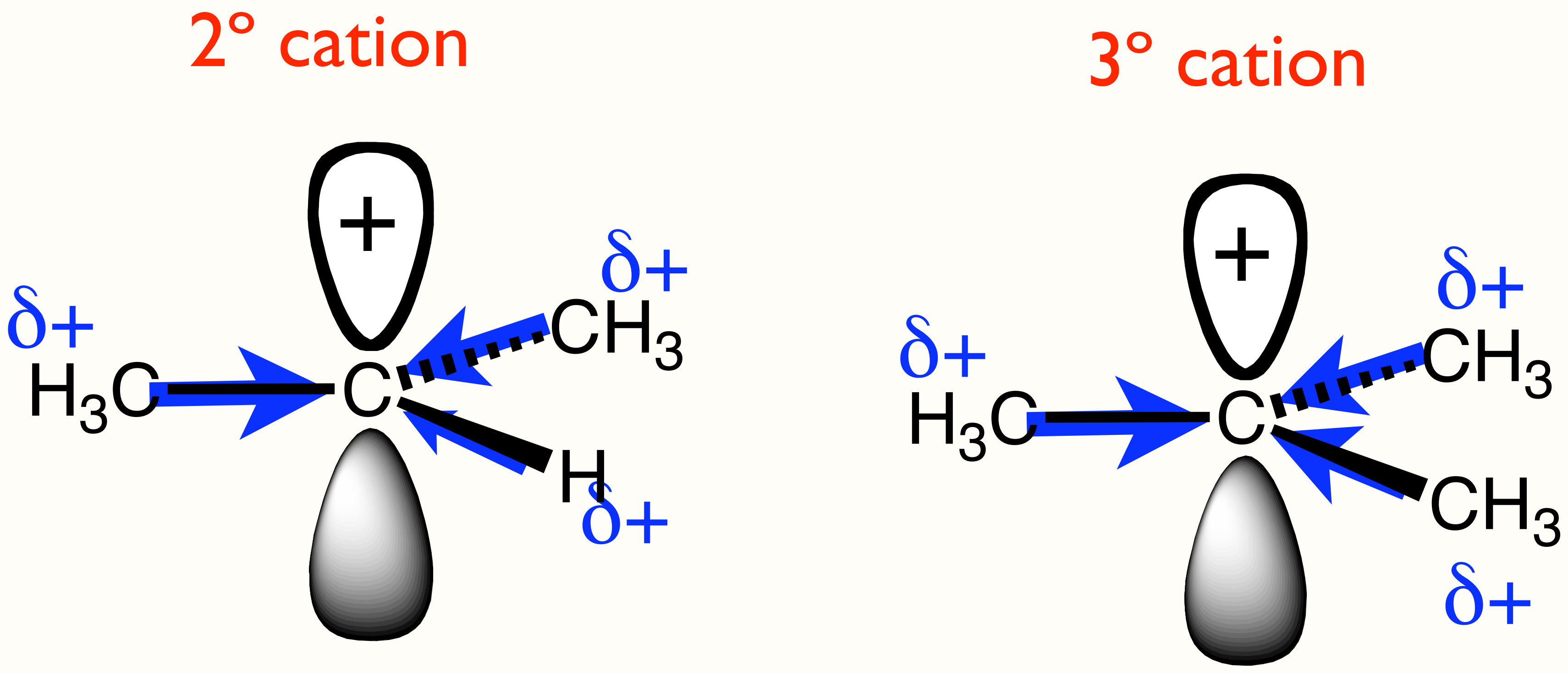


- electron donation through σ-bonds toward carbocation delocalizes charge (spreads out)
- C-C σ-bonds are more polarizable, therefore donate more electron density through σ-bonds
- more C-C σ-bonds = more stable carbocation

Stability of Carbocations

1. Inductive Effects

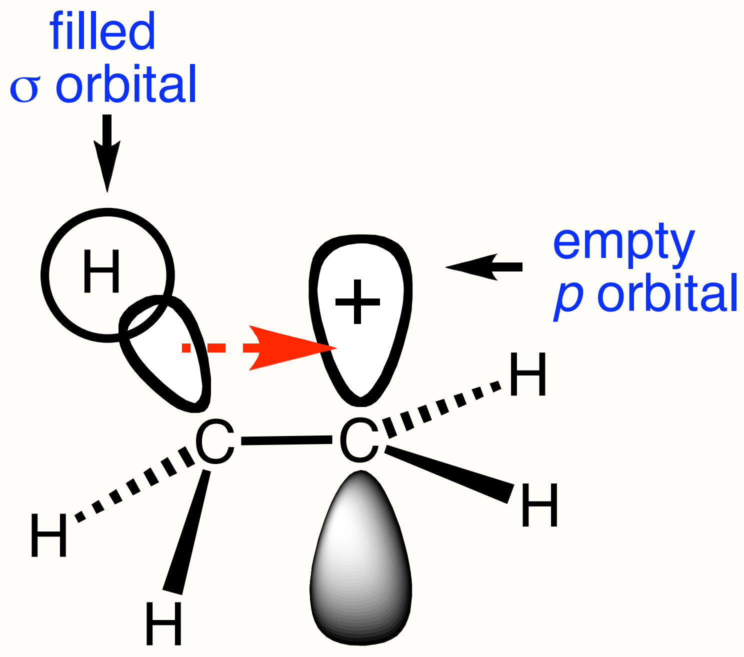
Since C-C σ-bonds are more polarizable than C-H bonds, the additional of more alkyl groups leads to stabilization of the cation



Stability of Carbocations

2. Hyperconjugation

stabilizing interaction that results from the interaction of the electrons in a σ-bond (C–H or C–C bond) with an adjacent empty (or partially filled) orbital. Leads to the formation of an extended molecular orbital that increases the stability of the system

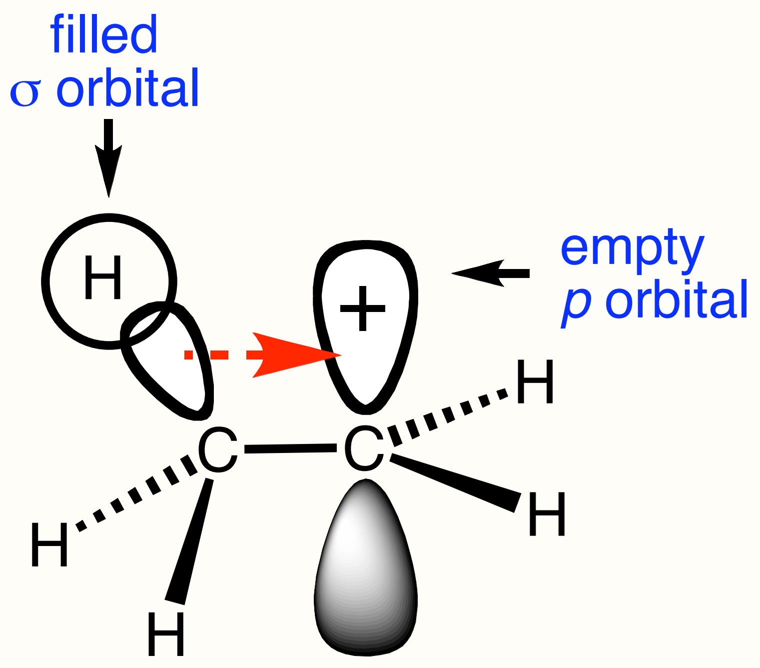


1° cation

- stabilization results from σ-donation to empty p orbital of planar carbocation
- electron donation through σ-bonds toward carbocation delocalizes charge (spreads out)
- methyl cations cannot be stabilized by hyperconjugation since σ-bonds are perpendicular to the empty p orbital

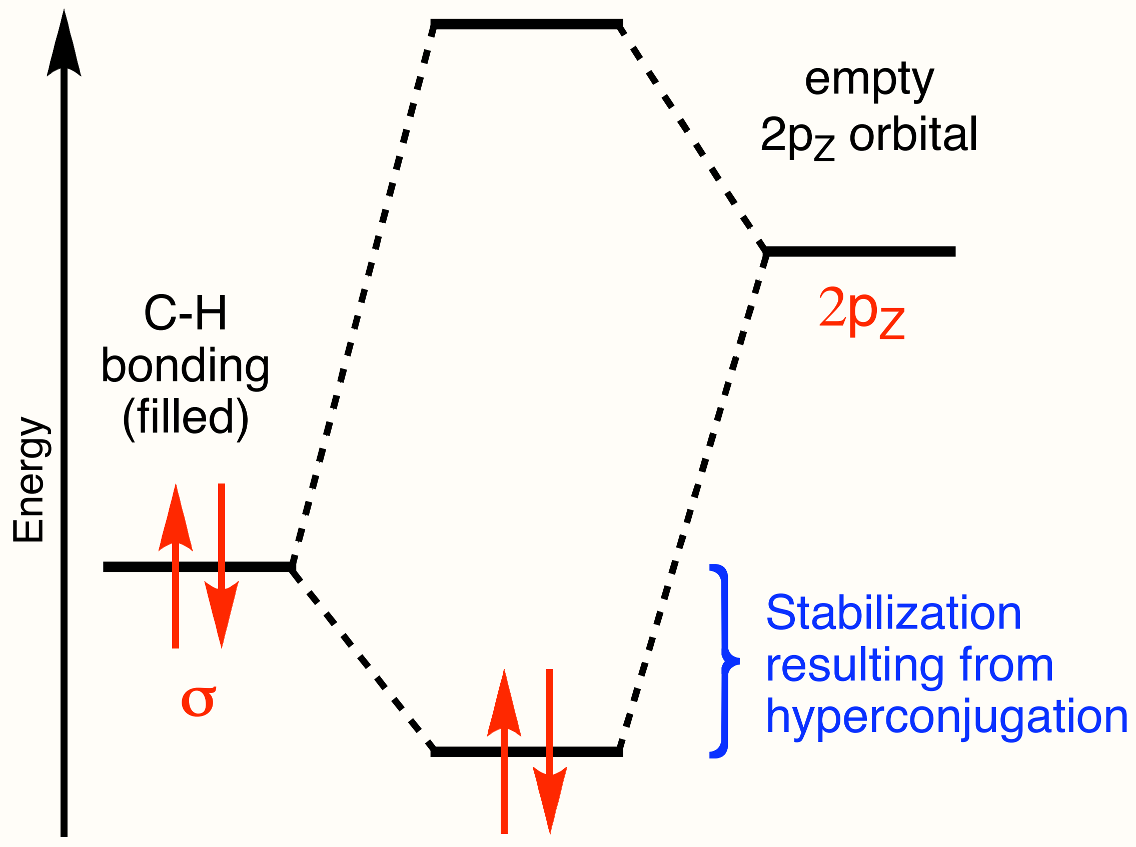
Stability of Carbocations

2. Hyperconjugation



filled
σ orbital

empty
p orbital



C-H
bonding
(filled)

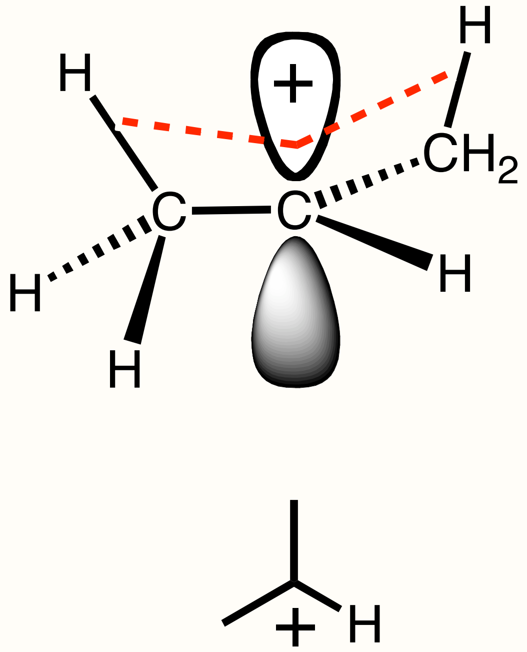
σ

empty
$2p_Z$ orbital

$2p_Z$

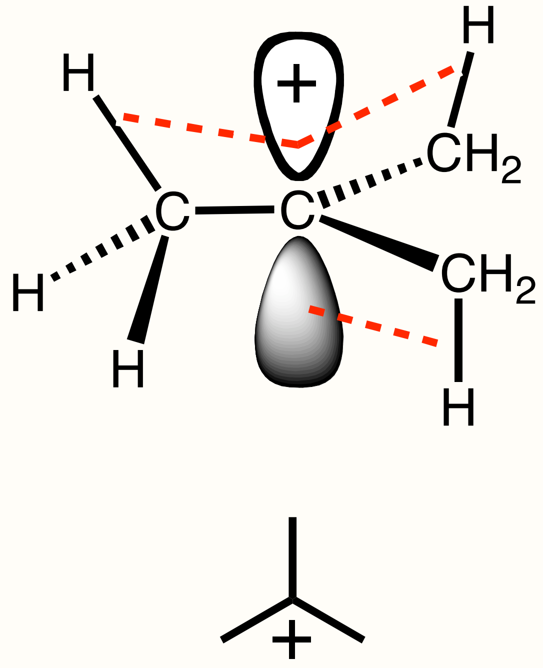
Stabilization
resulting from
hyperconjugation

Stability of Carbocations



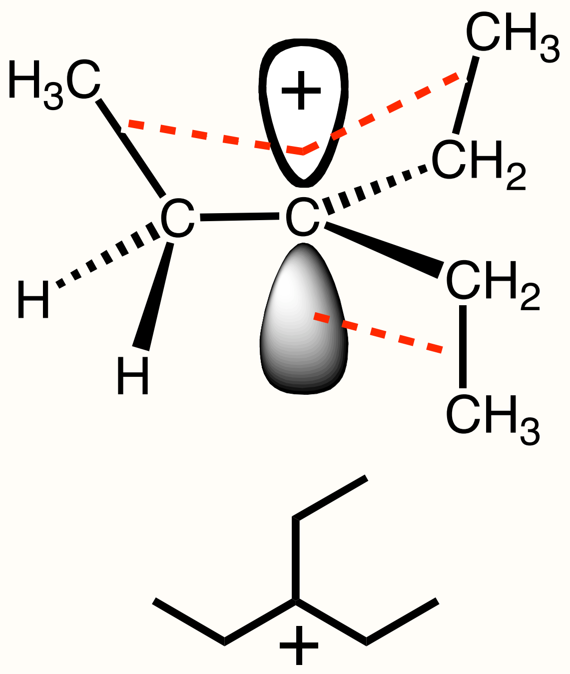
2° carbocation

2 C-H bond hyperconjugative donors



3° carbocation

3 C-H bond hyperconjugative donors



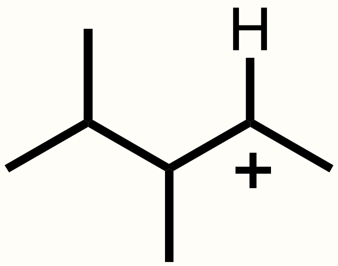
3° carbocation

3 C-C *or* C-H bond hyperconjugative donors

i>Clicker Question

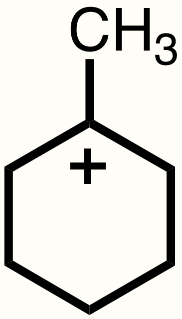
Rank the following carbocations in order of increasing stability?

a.



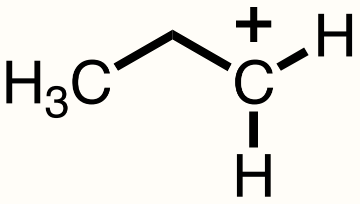
2°

b.



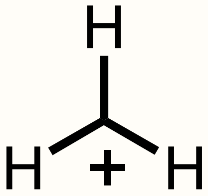
3°

c.



1°

d.



methyl

A. a,b,c,d

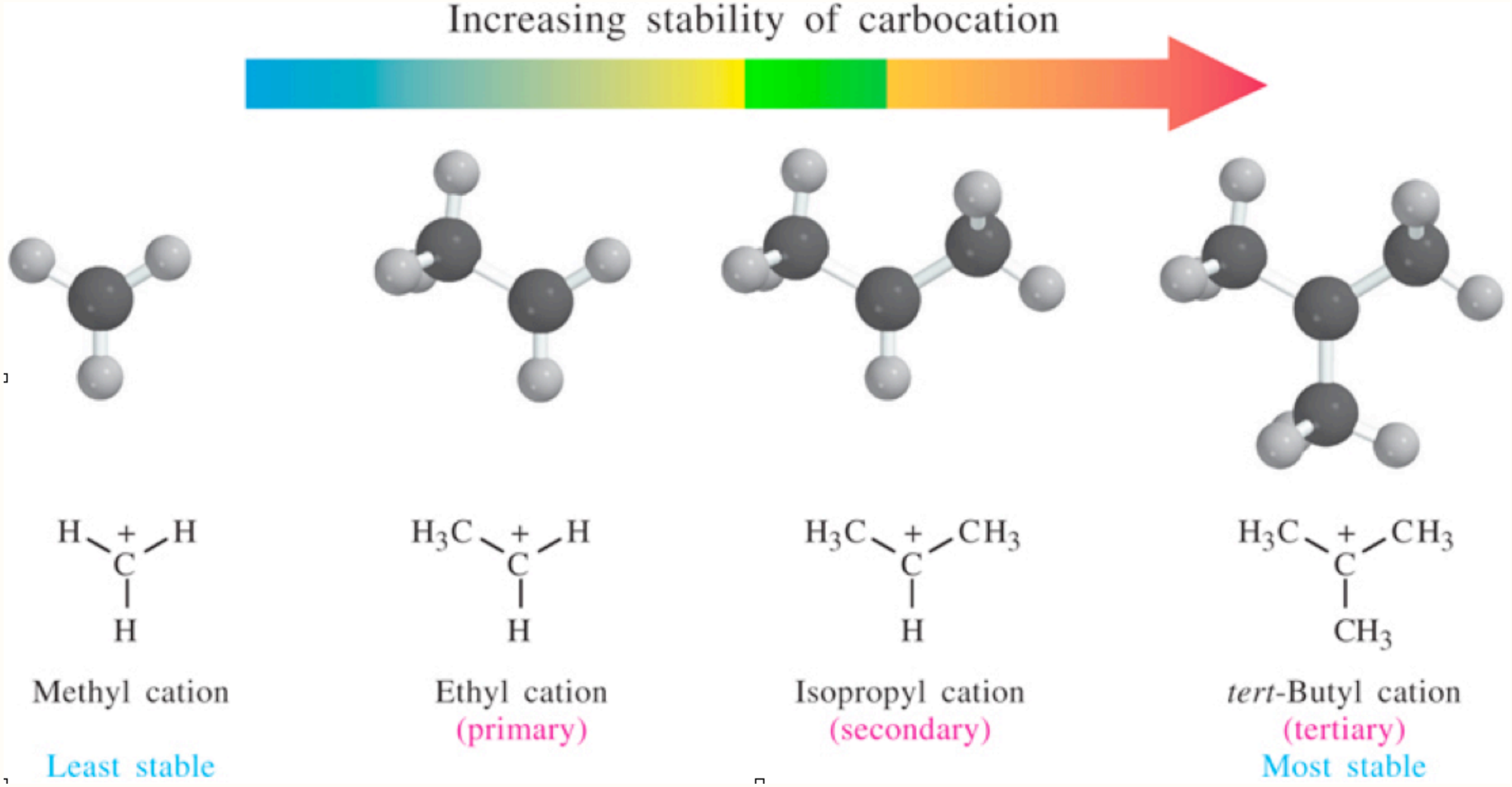
B. c,d,b,a

C. d,c,a,b

D. b,c,a,d

E. d,a,c,b

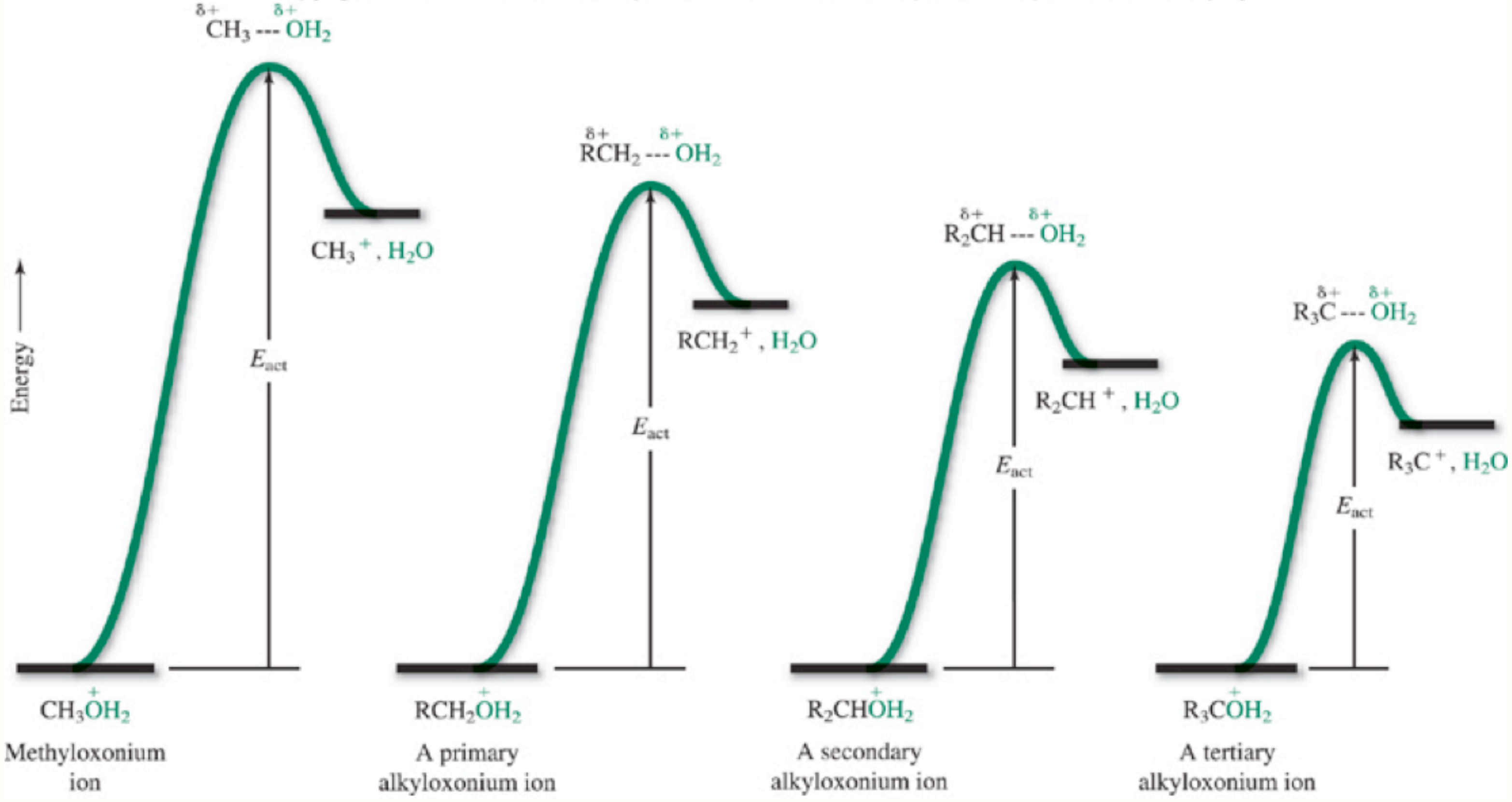
Stabilizing Effects on Carbocations



- smallest inductive effect
- no hyperconjugation

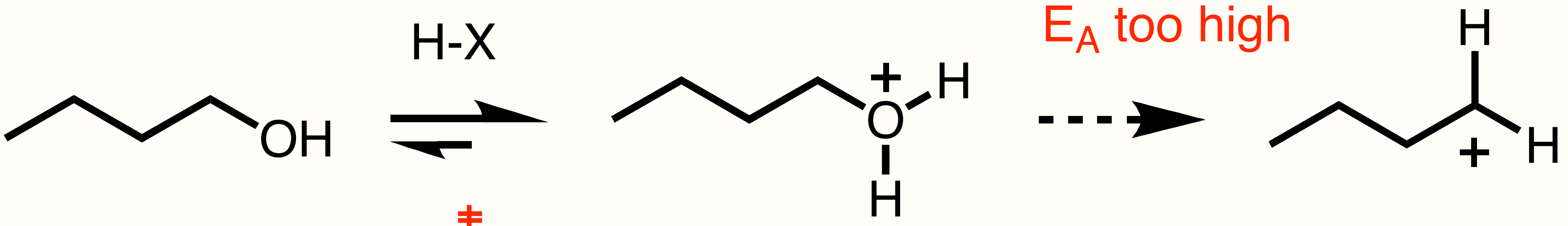
- largest inductive effect
- most hyperconjugation

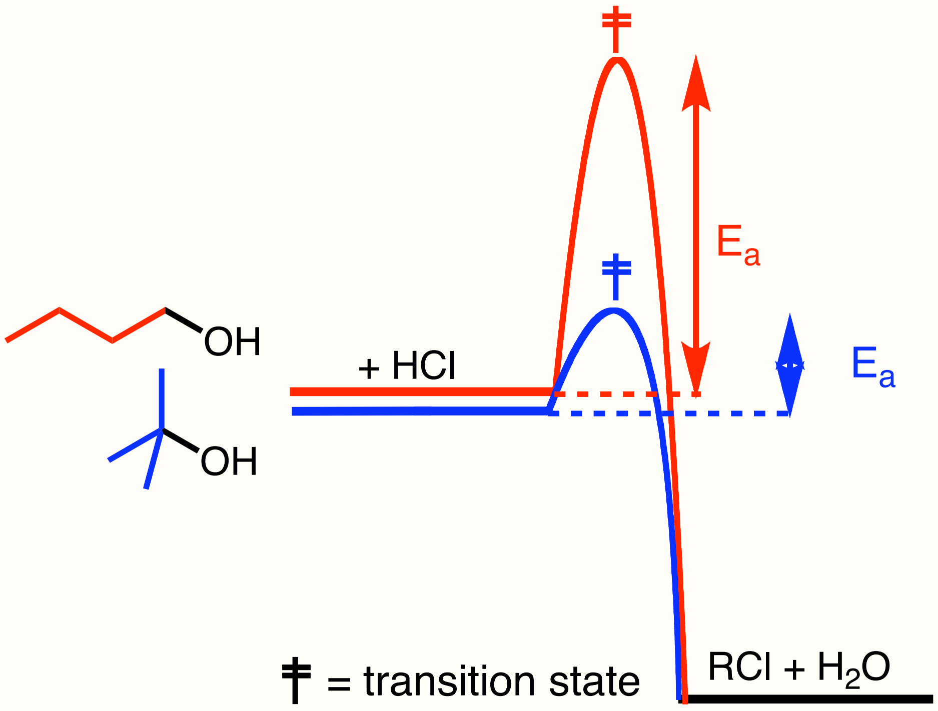
How Carbocation Stability Effects Rate of Reaction



- more stable (lower energy) carbocation =
- more stable (lower energy) transition state (Hammond Post.) =
- lower activation energy (Ea) =
- faster reaction

Why are 1° & 2° Alcohols Less Reactive?

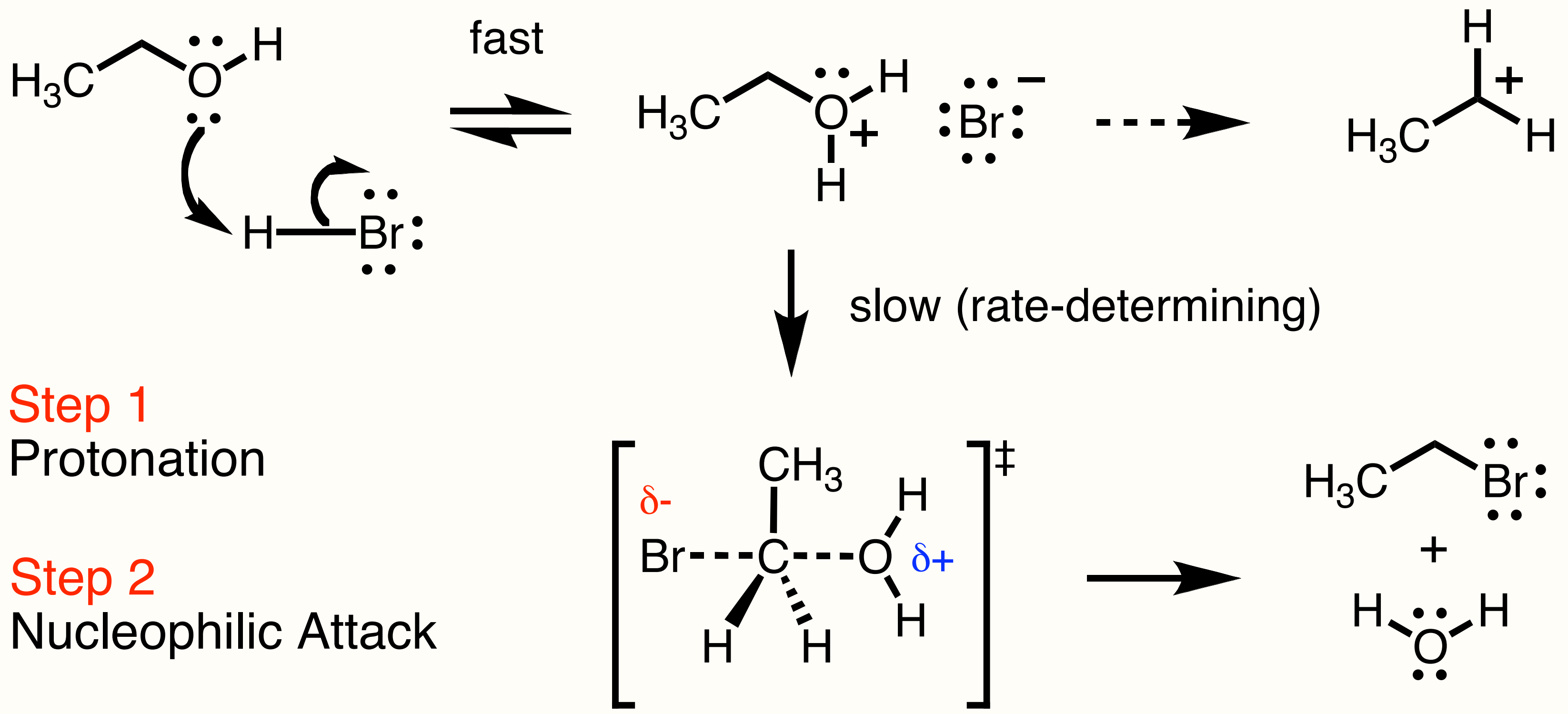




simple 1° and 2° alcohols do not undergo substitution by the S_N1 mechanism since methyl and primary carbocations are too high in energy to be intermediates in nucleophilic substitution reactions

an alternative mechanism is required.......

Bimolecular Substitution - S_N2 Mechanism



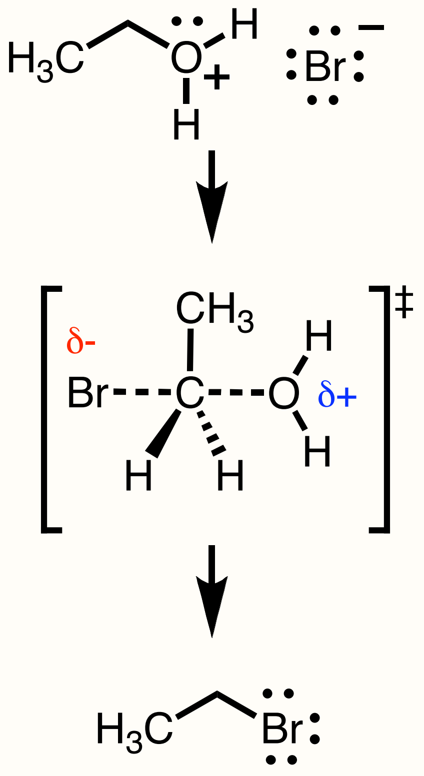
Step 1
Protonation

Step 2
Nucleophilic Attack

- C-O bond breaks at the **same time** the nucleophile (Br) forms the C-X bond
- RDS is nucleophilic attack; bimolecular, therefore Ingold notation = **S_N2**
- fewer steps does not mean faster reaction

Self Test Question

Which rate equation below best describes the rate determining step (RDS) in an S_N2 mechanism?



A. rate = k[oxonium ion]

B. rate = k[carbocation]

C. rate = k[oxonium ion][halide]

D. rate = k[carbocation][halide]

E. rate = k[alcohol][HX]

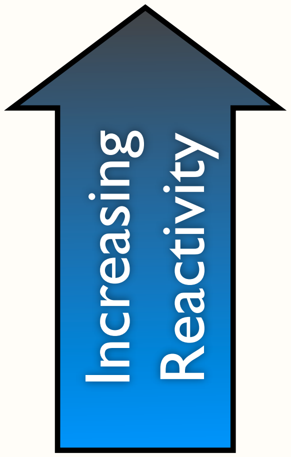
Halogenation of Alkanes
Methods and Mechanism

Sections: 4.14-4.17
You are responsible for Section 4.16 & 4.18
(Be able to perform this calculation!)

Halogenation of Alkanes

$$\underset{\text{Alkane}}{R{-}H} + \underset{\text{Halogen}}{X_2} \longrightarrow \underset{\text{Alkyl halide}}{R{-}X} + \underset{\text{Hydrogen halide}}{H{-}X}$$

$$\underset{\text{Ethane}}{CH_3CH_3} + \underset{\text{Chlorine}}{Cl_2} \xrightarrow{420°C} \underset{\substack{\text{Chloroethane (78\%)}\\ \text{(ethyl chloride)}}}{CH_3CH_2Cl} + \underset{\text{Hydrogen chloride}}{HCl}$$



Fluorination (F_2): Highly Exothermic (Explosive !)

Chlorination (Cl_2): Exothermic

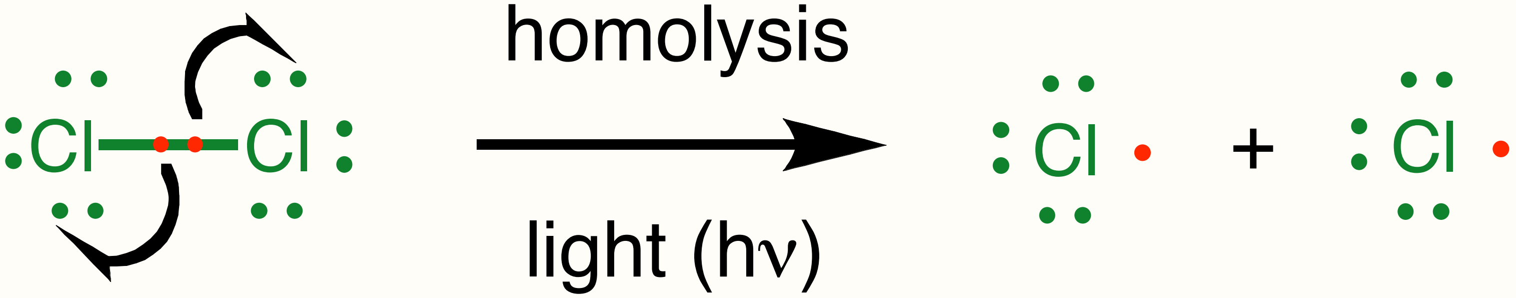
Bromination (Br_2): Slightly Exothermic

Iodination (I_2): Endothermic

Radical Chain Mechanism

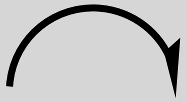
Step One

Initiation via Homolysis



half-headed arrow "fishhook"

movement of a single electron, not a pair



homolysis (homolytic cleavage)

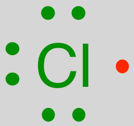
cleavage of a covalent bond so that each atom in the bond retains one electron

heterolysis (heterolytic cleavage)

cleavage of a covalent bond so that one atom in the bond retains both electron

free radical

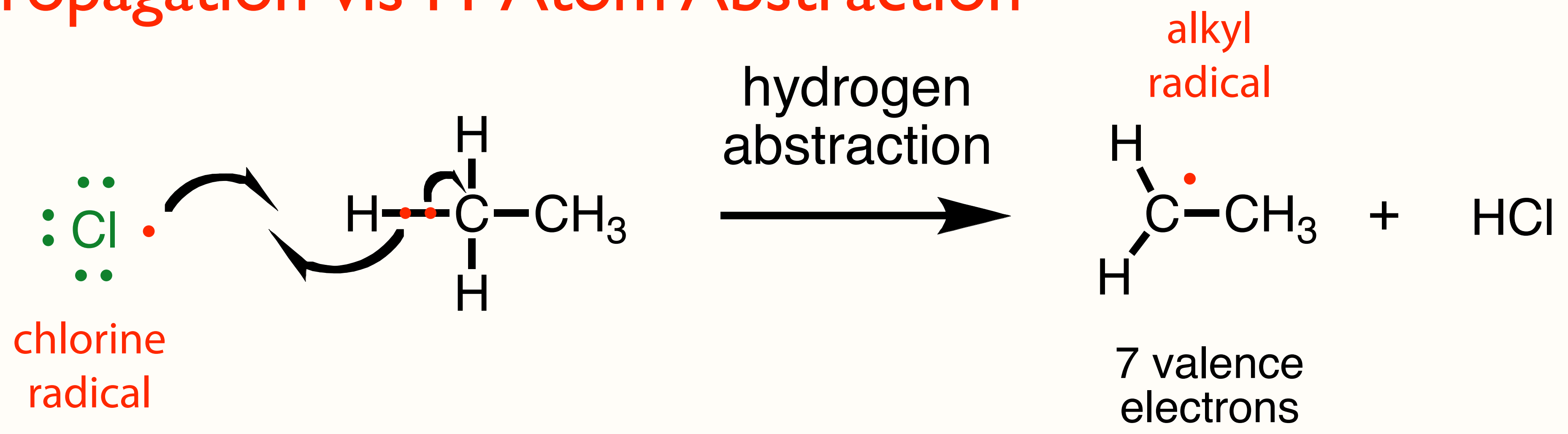
unpaired electron; stabilized by same factors that stabilized carbocations



Radical Chain Mechanism

Step Two

Propagation vis H-Atom Abstraction

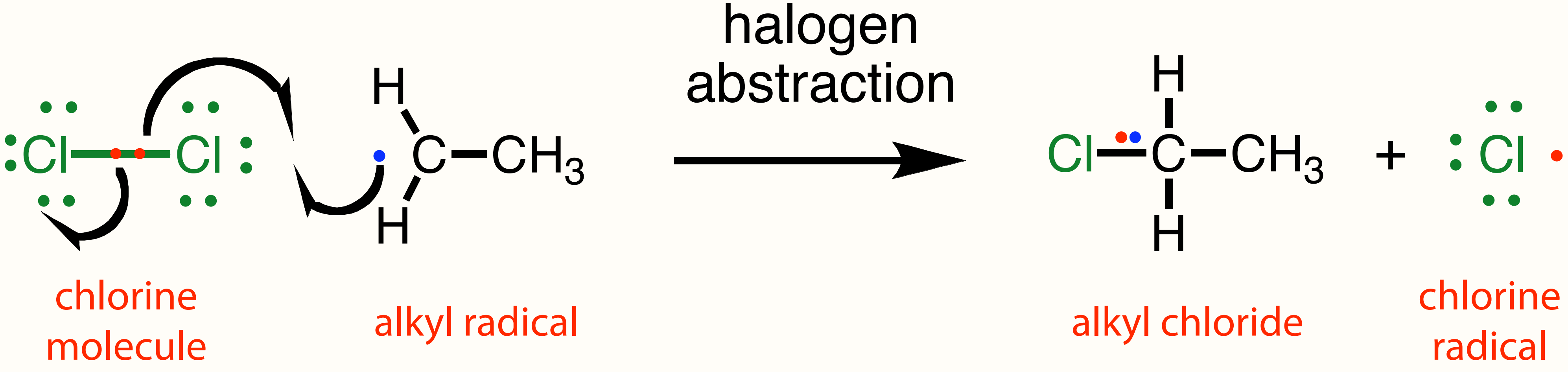


- Cl radical abstracts H atom from most substituted C atom
- alkyl radical is an intermediate in the mechanism
- alkyl radicals are stabilized by same factors that stabilize carbocations
- note that radical is generated - propagation!

Radical Chain Mechanism

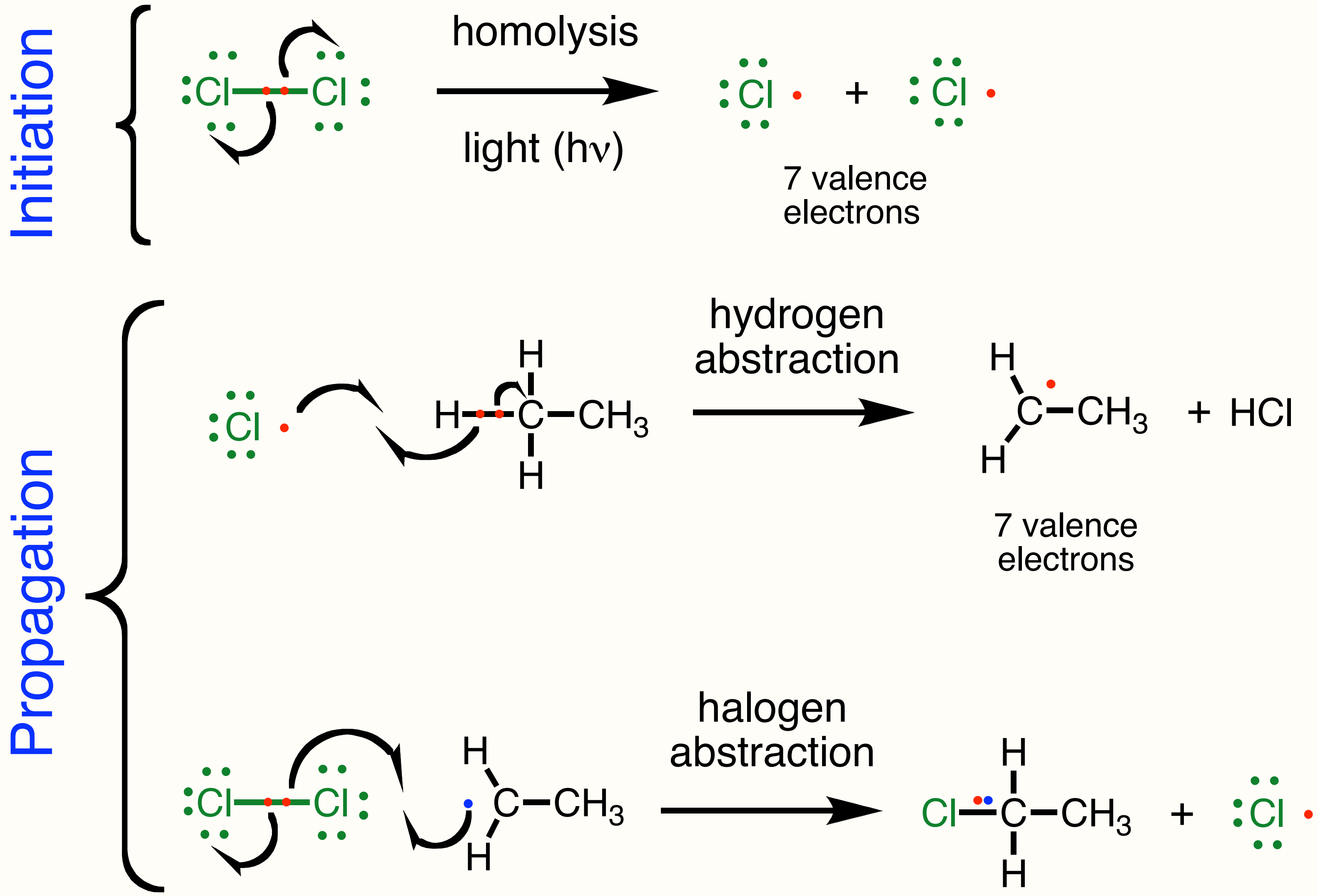
Step Three

Propagation vis Cl-Atom Abstraction

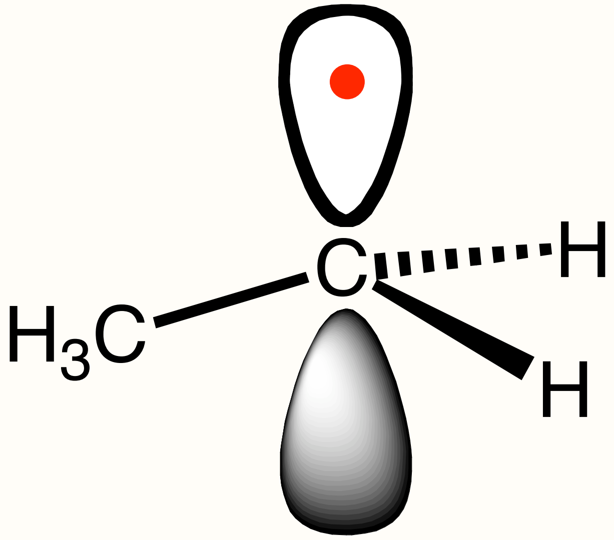


- alkyl radical abstract a halogen from a 2nd X_2 molecule
- chlorine radical product continues on in chain; starts the cycle over again by abstracting hydrogen from another alkane
- radical chain mechanisms are faster than a stepwise mechanism which would require initiation in each step

Complete Mechanism



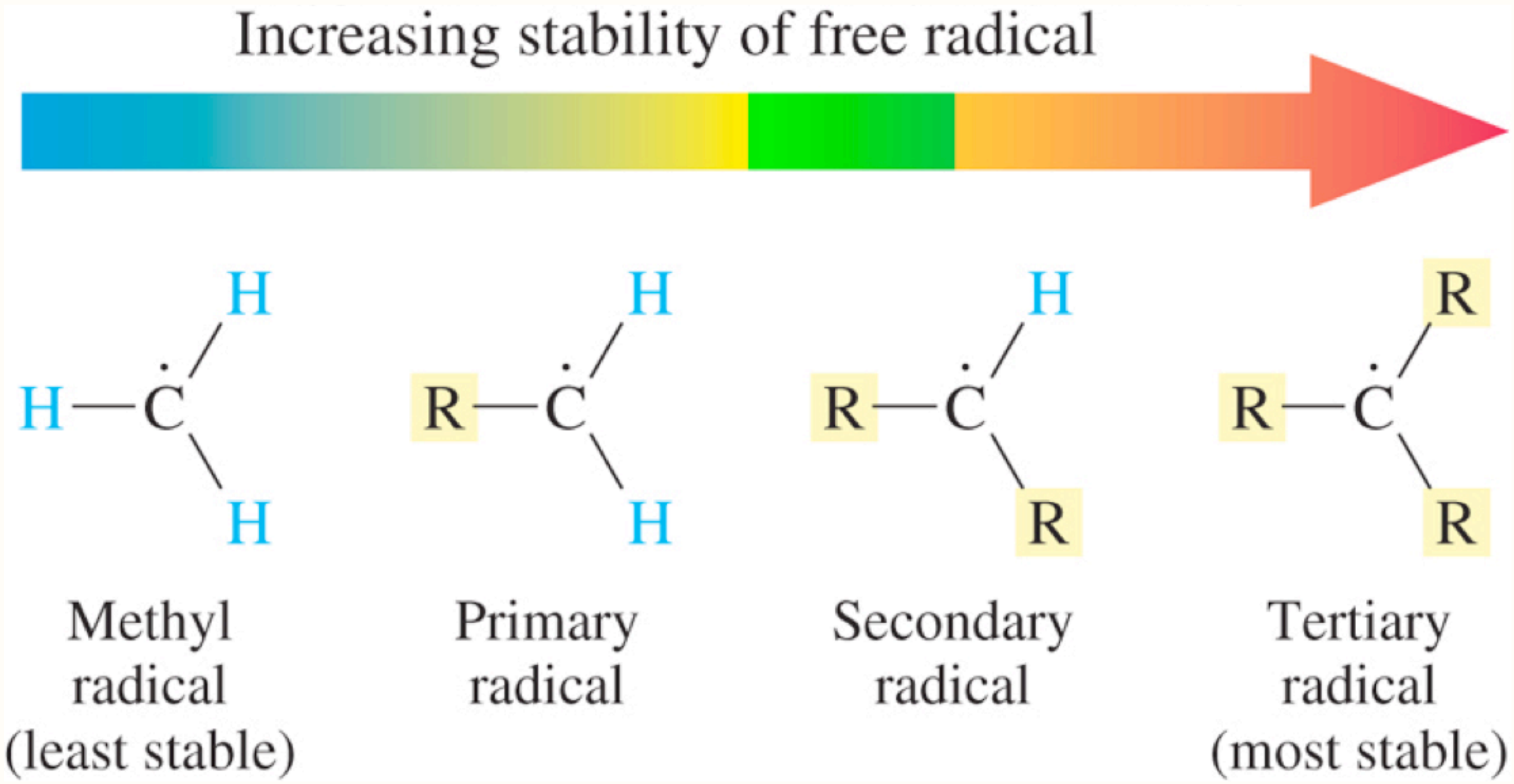
Structure of Alkyl Radical Intermediates



alkyl radicals can be stabilized by inductive effects and hyperconjugation; similar to carbocations

- radicals are high energy intermediates; 7 valence electrons; cannot be isolated
- sp^2-hybridized; contain one empty p-orbital; unpaired electron in the p-orbital;
- approximately planar: three bonds to carbon are at ~120° angles from each other and ~90° to half-filled p-orbital
- stabilized by inductive effects and hyperconjugation
- Stability: $3^\circ > 2^\circ >> 1^\circ > CH_3$

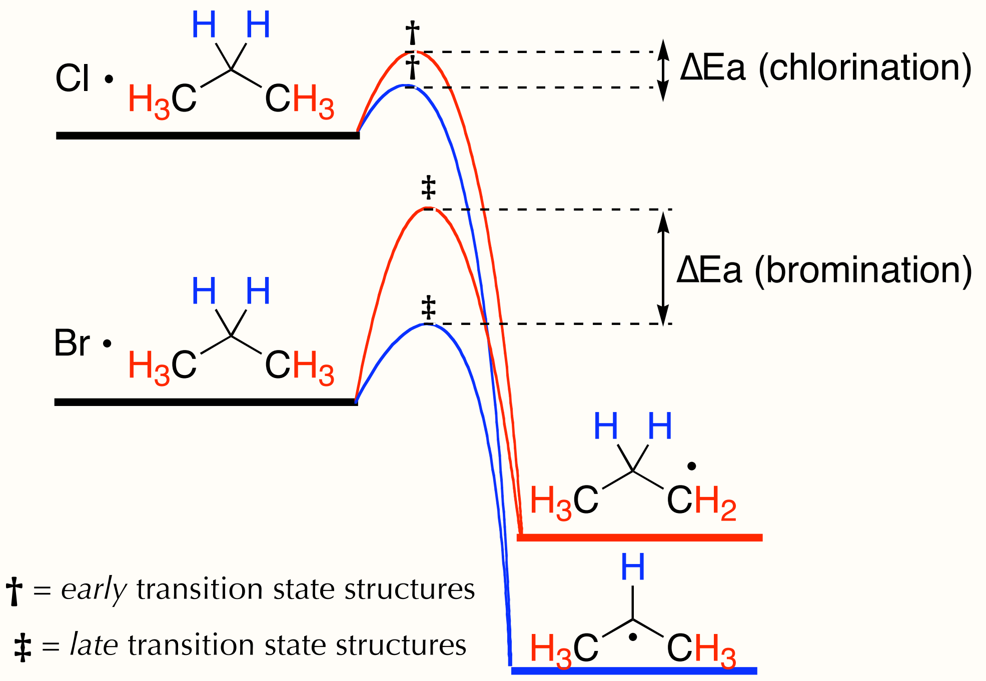
Stabilizing Effects on Alkyl Radicals



- smallest inductive effect
- no hyperconjugation

- largest inductive effect
- most hyperconjugation

Bromination is More Selective Than Chlorination



ΔEa (bromination) > ΔEa (chlorination)
Bromination is <u>more</u> selective.

Relative Rates (k_{rel}) of Halogenation

	R_3CH (tertiary, 3°)	R_2CH_2 (secondary, 2°)	RCH_3 (primary, 1°)
chlorination	***5.2***	***3.9***	***1.0***
bromination	***1640***	***82***	***1.0***

Hammond Postulate

- chlorine radicals are higher in energy than bromine radicals =
- transition states in chlorination are earlier=
- look <u>more like</u> reactants =
- less difference in TS energy =
- less selective =
- greater mixture

- bromine radicals are lower in energy than chlorine radicals =
- transition states in bromination are later=
- look <u>more like</u> products (radical interm.) =
- greater difference in TS energy =
- more selective =
- less of a mixture

Quantifying Selectivity

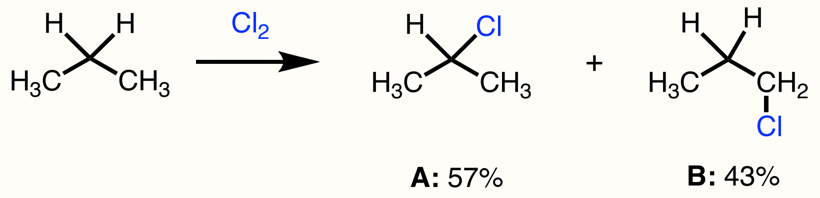
Relative Rates (k_{rel}) of Halogenation

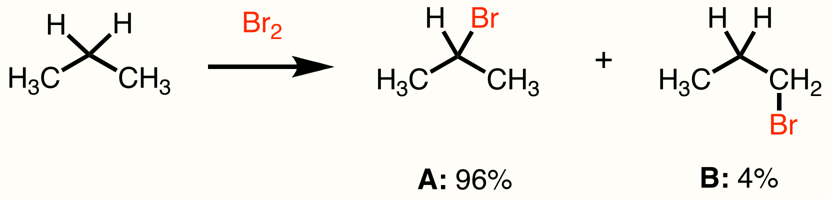
	R_3CH (tertiary, 3°)	R_2CH_2 (secondary, 2°)	RCH_3 (primary, 1°)
chlorination	***5.2***	***3.9***	***1.0***
bromination	***1640***	***82***	***1.0***

$$\% = \frac{(krel) \times (\text{statistical factor})}{\text{total}}$$

Predicted Product Ratios

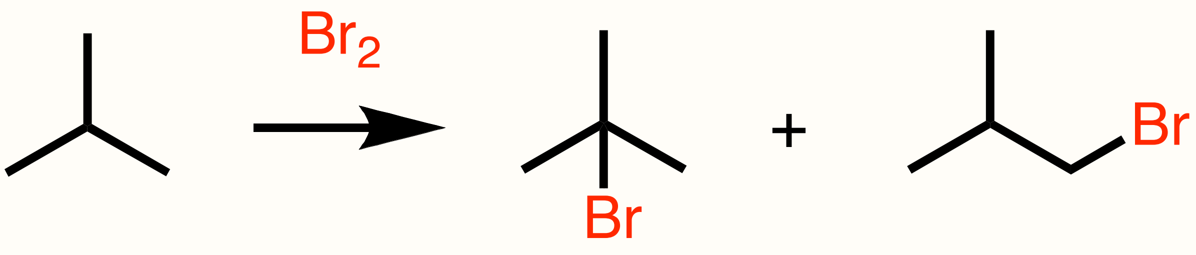
	Product	Relative Yield	Absolute Yield
chlorination	A (2 2° H's)	2 x ***3.9*** = 7.8	7.8/13.8 = 57%
	B (6 1° H's)	6 x ***1*** = 6.0	6.0/13.8 = 43%
	Sum	13.8	100%
bromination	A (2 2° H's)	2 x ***82*** = 164	164/170 = 96%
	B (6 1° H's)	6 x ***1*** = 6.0	6.0/170 = 4%
	Sum	170	100%





Self Test Question

Determine the predicted product distribution for **A** in the following clorination.



A **B**

A. 99%
B. 97%
C. 95%
D. 93%
E. 91%

Relative Rates (k_{rel}) of Halogenation

	R_3CH (tertiary, 3°)	R_2CH_2 (secondary, 2°)	RCH_3 (primary, 1°)
chlorination	*5.2*	*3.9*	*1.0*
bromination	*1640*	*82*	*1.0*

Next Lecture. . .

Chapter 5: Sections 5.1-5.9