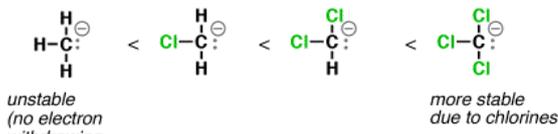


## Types of Reactions

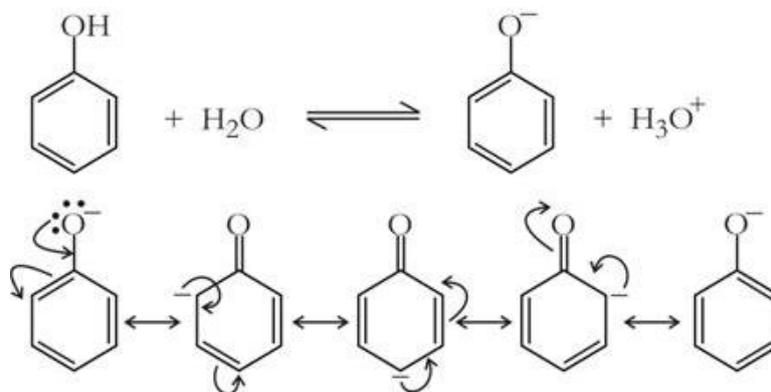
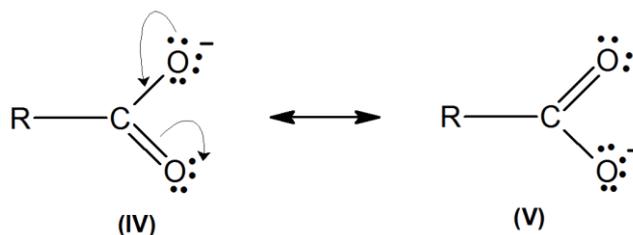
1. Acid-base: Transfer of protons, H<sup>+</sup>
2. Substitution
3. Addition
4. Elimination
5. Oxidation and reduction: Loss and gain of O/H

## Acid-Base Reactions

- Acids: Proton donors, e<sup>-</sup> pair acceptor
  - HA + H<sub>2</sub>O ⇌ A<sup>-</sup> + H<sub>3</sub>O<sup>+</sup>
  - Acidity higher with:
    - Weaker X-H bond → H<sup>+</sup> more easily dissociates
    - Higher stability of anion → higher acidity as unlikely to react w/ H<sup>+</sup> → stays in dissociated form
  - Strength of X-H bond:
    - Higher electronegativity of X in X-H → more dipole, weaker bond → higher acidity
      - i.e. e<sup>-</sup> easily removed from H and H<sup>+</sup> readily dissociates
      - C-H < N-H < O-H, Cl-H
    - Higher length of bond → weaker bond → higher acidity
      - E.g. HI > HF in acidity despite F being more electronegative due to large radius → weaker bond
  - Stability of anion:
    - Electron withdrawing groups on side → greater delocalisation of -ve charge
      - Electron withdrawing groups:
        - Electronegative atoms (can be bonded to atom next to -ve charge)
          - 

unstable (no electron withdrawing groups)

more stable due to chlorines
        - Formal +ve or δ+ve charge
      - Electron donating groups:
        - Have lone pairs and not too electronegative/double or triple bonded to more electronegative atoms
        - E.g. OH, NH<sub>2</sub>, NO<sub>2</sub>, OCl
    - Resonance stabilisation w/ delocalisation of -ve charge → higher stability
      - R-OH < phenol < R-COOH
      - Phenol less acidic than -COOH because delocalised over 1 O atom and less electronegative carbon atoms (vs 2 electronegative O)
        - Resonance structures of phenoxide ion → -ve charge on C as well

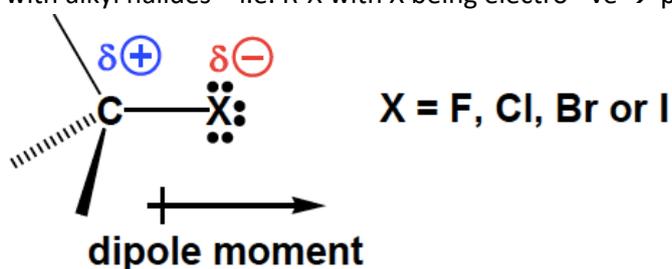


- Bases: Proton acceptor, e- pair donor

### Substitution Reactions

*Nucleophilic substitution: Nucleophile e.g. OH- (-ve charge, lone pair) substitutes with atom attached to electrophile*

- Usually with alkyl halides – i.e. R-X with X being electro -ve → polar C-X bond



- o Dipole moment due to both diff in electronegativity (bond strength) and size of halogen (bond length)
  - Higher diff in electronegativity and longer bond length → higher dipole moment w/ C more  $\delta^+$
  - → C as electrophile, X as nucleophile
- Types of alkyl halides:
  - o Primary: 1 alkyl group attached to C bonded to halogen
  - o Secondary: 2 alkyl groups...
  - o Tertiary: 3 alkyl groups...

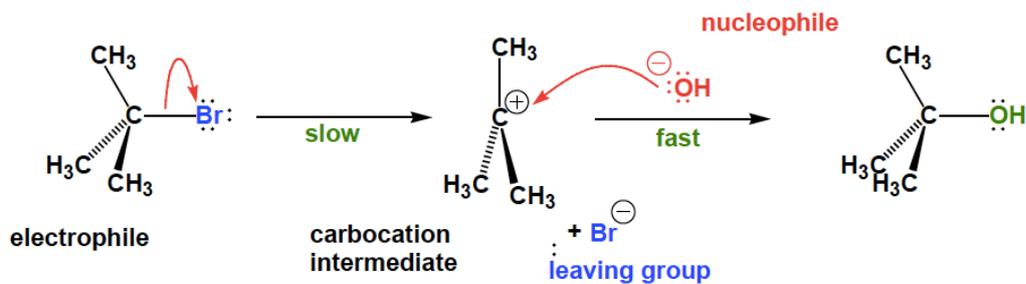
*Range of nucleophiles and substitutions:*

- OH- → alcohol
- RO- → ether
- C≡N- → nitrile
- R-C≡C- → alkyne
- H<sub>2</sub>N- → amine

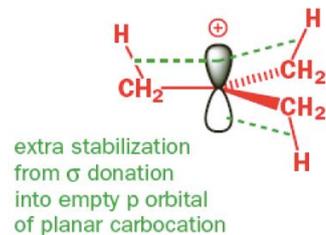
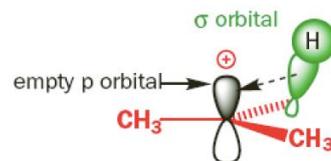
- $R_3N \rightarrow$  tetraalkylammonium salt  $H_3C-NR_3^+$

### Paths to $S_N$

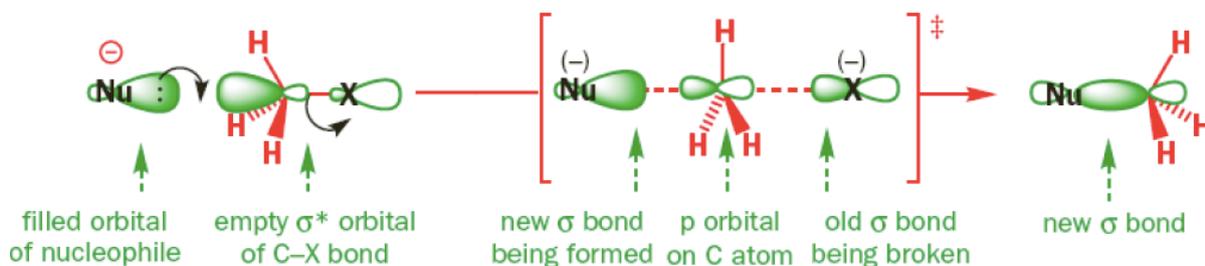
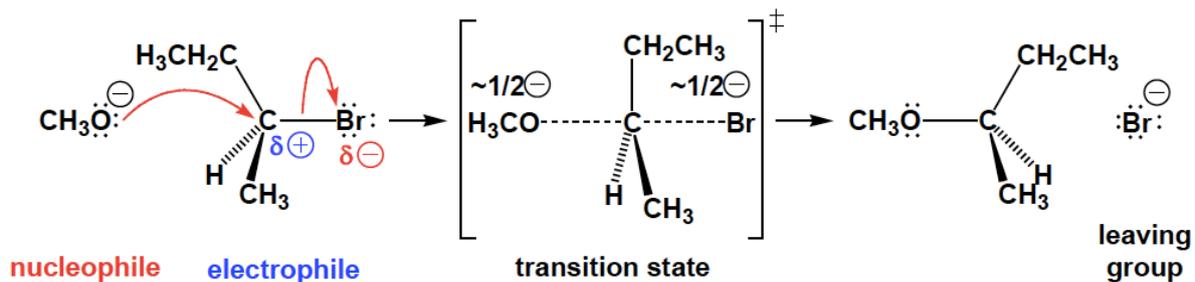
- $S_N1$ : Nucleophilic substitution – first order i.e. unimolecular, stepwise
  1. Group leaves  $\rightarrow$  carbocation intermediate
    - C is  $sp^2$  hybridised; trigonal planar
  2. Nucleophile joins from either top or bottom  $\rightarrow$  racemic



- Rate determining step: Electrophile leaving
- $S_N1$  barrier: Carbocation stability – determined by hyperconjugation (sigma bond of C-H donates  $e^-$  to empty p orbital of carbocation)
  - Methyl < Primary < Secondary < Tertiary

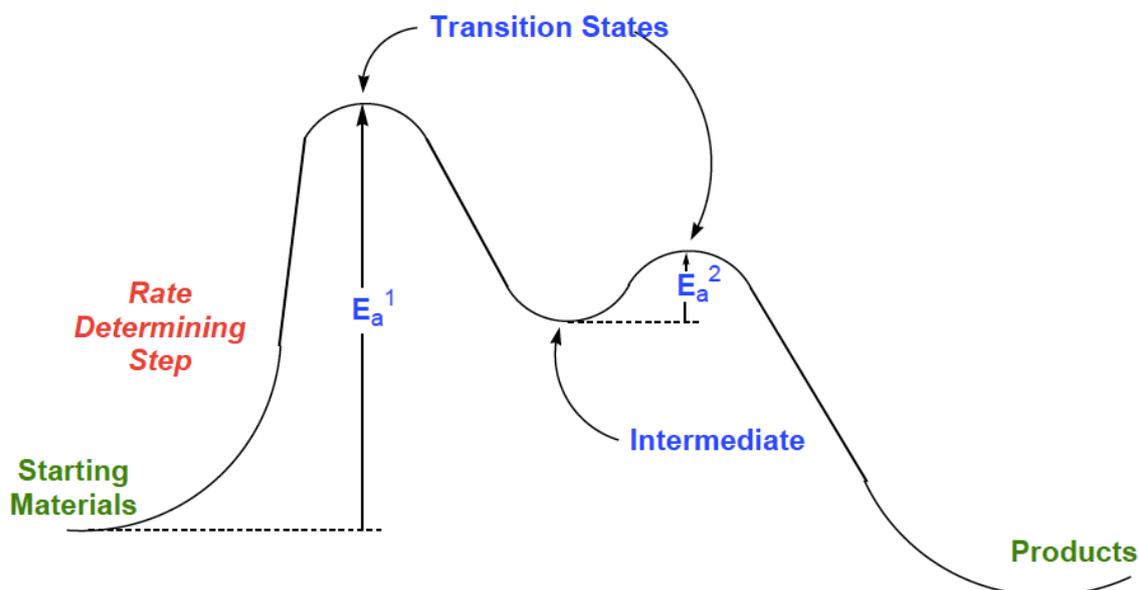


- $S_N2$ : Nucleophilic substitution – second order i.e. bimolecular, concerted
  1. Nucleophile attacks LUMO; an anti-bonding orbital  $\rightarrow$  transition state w/  $\frac{1}{2}$  bond to Nu and  $\frac{1}{2}$  bond to halogen
    - Backside attack: 180 degrees from most polarised, C-X orbital (anti-bonding orbital)
    - Change in concavity as  $e^-$  density of new sigma bond repels other bonds  $\rightarrow$  change in absolute configuration i.e. enantiomer if chiral centre



- Rate determining step: Nucleophile adding, forcing group to leave
- $S_N2$  barrier: Steric hindrance
  - Tertiary < Secondary < Primary < Methyl
- Intermediate vs Transition State:
  - Transition state doesn't exist – cannot be isolated like intermediate

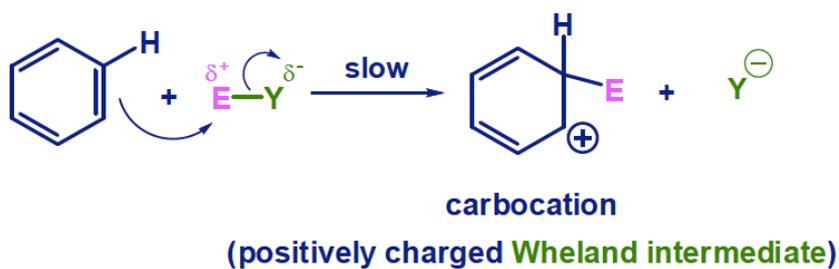
#### Energy Diagram for $S_N1$



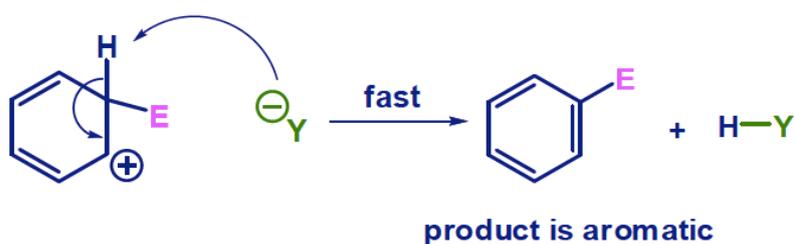
1. Electrophile leaving  $\rightarrow$  increasing polarisation  $\rightarrow$  higher energy
2. Transition state: Highest energy species; cannot be isolated
3. Generating carbocation and ion  $\rightarrow$  fall in energy
4. Intermediate: Local energy minimum (carbocation + ion); can be isolated
5. Nucleophile approaches carbocation  $\rightarrow$  steric repulsion  $\rightarrow$  higher energy
6. Transition state: Highest energy where steric repulsion maximised
7. Electrostatic attraction > steric repulsion  $\rightarrow$  fall in energy  $\rightarrow$  lower energy products

### Electrophilic Aromatic Substitution ( $S_EAr$ )

1. Addition: Pi system attacks electrophile (slow, RDS, bimolecular)  $\rightarrow$  carbocation and anion



2. Elimination: Loss of  $H^+$  restores aromaticity (fast)  $\rightarrow$  aromatic product +  $H-Y$



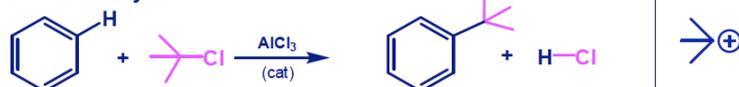
Possible electrophiles:

- Halogens
- Alkyl halides
- Acyl groups (has C=O carbonyl)

#### Halogenation



#### Friedel-Crafts Alkylation

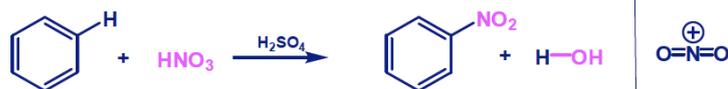


#### Friedel-Crafts Acylation

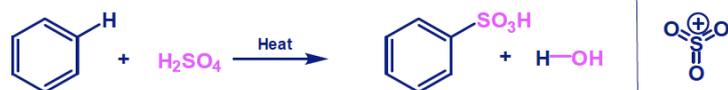


- Lewis acids e.g.  $NO_2^+$ ,  $SO_3^+$

#### Nitration



#### Sulfonation

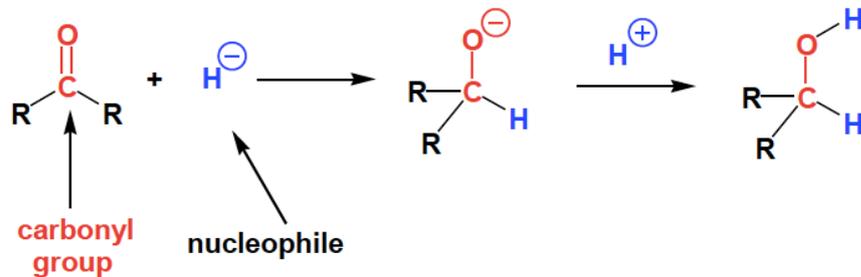


## Addition Reactions

- Break double bond  $\rightarrow$  single bond

### Nucleophilic Addition

- Nucleophile attracted to  $\delta+$  C in C=O group
- Alkoxide anion intermediate

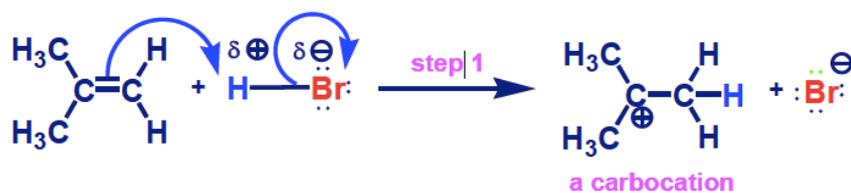


### Electrophilic Addition

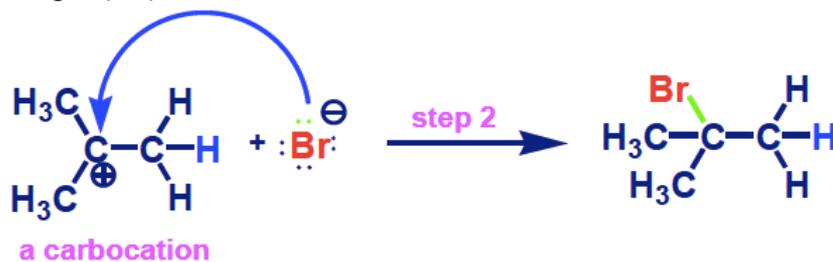
- Electrophiles attracted to e<sup>-</sup> density in pi bond; Usually in alkenes
  - o In non-polar molecule, a dipole is induced
- Carbocation intermediate  $\rightarrow$  racemic mixture
- E.g. Hydrohalogen, halogen, H<sub>2</sub>O

### Hydrohalogenation

1. Double bond breaks and H<sup>+</sup> adds  $\rightarrow$  carbocation + halogen (-ve)



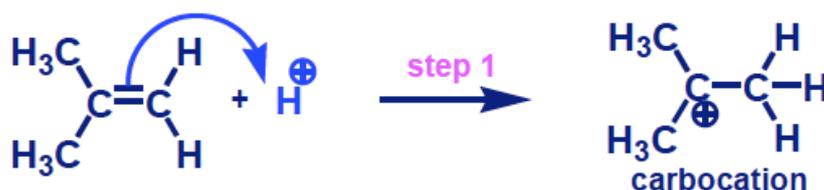
2. Halogen (-ve) adds



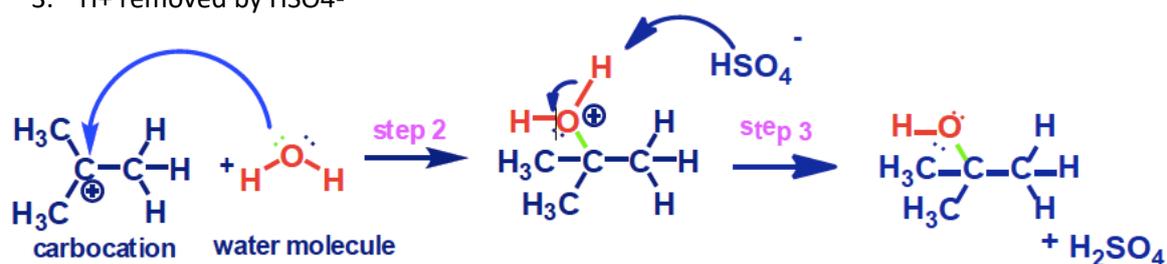
### Hydration

\*\*H<sup>+</sup> catalyst needed as H<sub>2</sub>O not electrophilic enough

1. H<sup>+</sup> adds  $\rightarrow$  carbocation



2. H<sub>2</sub>O adds using lone pair e<sup>-</sup> of O
3. H<sup>+</sup> removed by HSO<sub>4</sub><sup>-</sup>

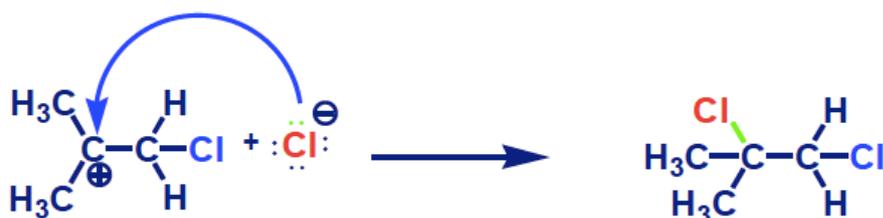


### Halogenation

1. Halogen polarized by alkene (induced)
2. One end of halogen reacts w/ alkene → carbocation + anion



3. Halogen ion adds to carbocation



### Hydrogenation

\*\*Catalyst: Palladium powder on charcoal

\*\*Always cis product produced → racemic mixture of enantiomers if unsymmetrical alkene

1. H<sub>2</sub> adsorbed onto surface and H-H bond broken
2. Reagent adsorbed onto surface and pi bond broken
3. H<sub>2</sub> adds onto reagent and leaves surface

### Product Isomers

- No isomers when HX adds to symmetrical alkene
- Isomers if unsymmetrical alkene – major and minor product
- Markovnikov's Rule: H of unsymmetrical reagent adds to end of double bond w/ greater no. of H atoms
  - o Due to greater stability of carbocation intermediate
  - o Primary (one alkyl group) < secondary (2 alkyl groups) < tertiary (3 alkyl groups)
  - o Sigma-conjugation/hyperconjugation: E- density in adjacent C-H bonds (in CH<sub>3</sub> alkyl group) overlaps w/ empty p orbital of carbocation

### Alkynes

- Addition reactions to both pi bonds
- Markovnikov's rule applies

- Hydrogenation used to make alkene (poisoned catalyst → alkene intermediate won't adsorb) or alkane (Pd/C catalyst)

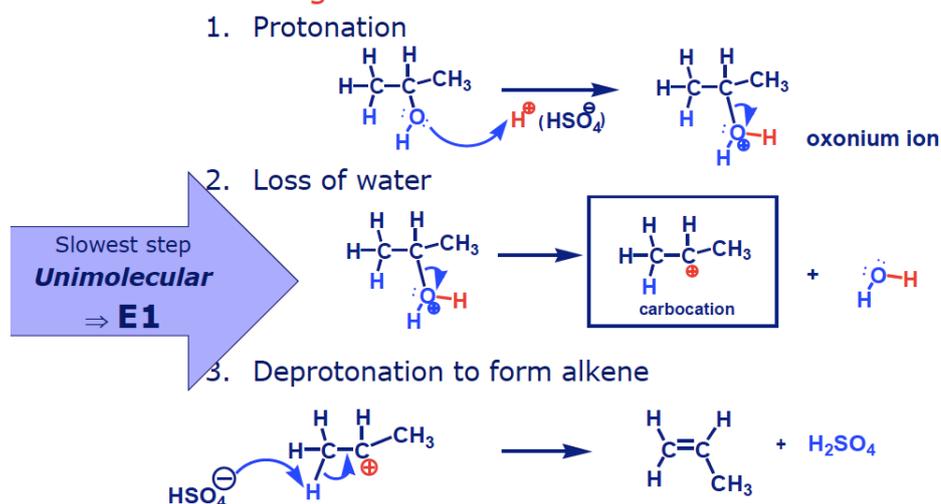
## Elimination Reactions

Opposite of addition; remove atom(s), creates double bonds

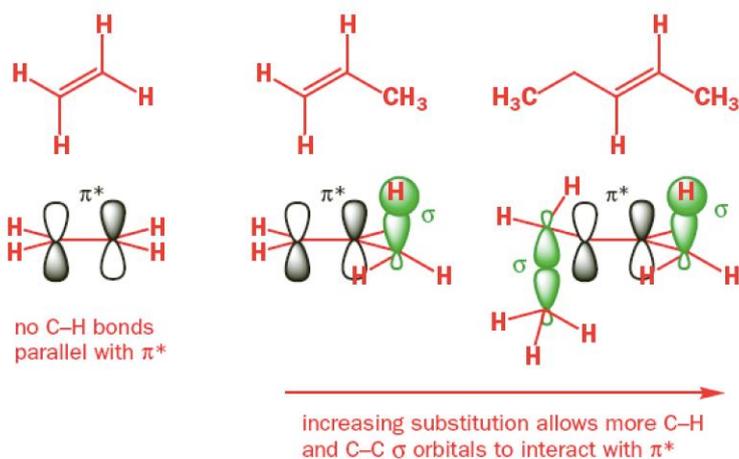
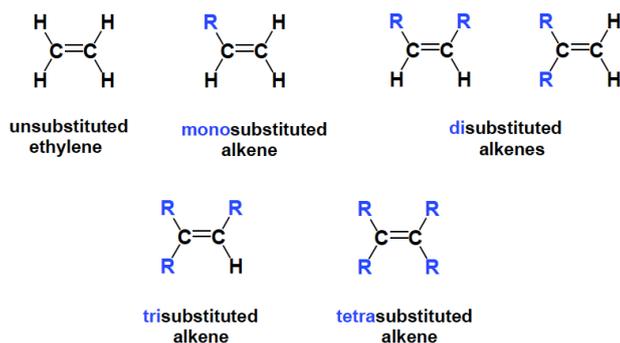
\*Needs heat

*E1 reactions: One molecule involved in rate determining step*

- Acid-catalysed dehydration: Concentrated H<sub>2</sub>SO<sub>4</sub> + heat needed



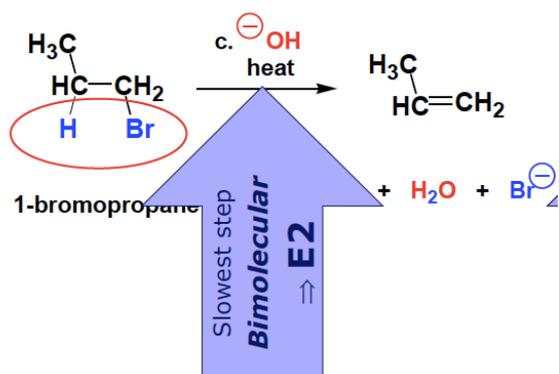
- Two steps, carbocation intermediate
- E or Z isomers equally likely to form if product has isomers
- Regioselectivity in E1: More substitution → more adjacent C-H bonds overlap w/  $\pi^*$  (antibonding) orbital
  - Similar to hyperconjugation w/ overlap of C-H bonds w/ empty p orbital



- Zaitsev's Rule: More substituted alkene forms major product as more stable w/ regioselectivity  $\rightarrow$  lower activation energy barrier to form

*E2 reactions: Two molecules involved in rate determining step*

- Dehydrohalogenation: Use base e.g. KOH or bulky base  $\text{KO}^t\text{B}^u$  + heat
  - One step, no intermediate, transition state



- Base  $\text{OH}^-$  removes  $\text{H}^+$   $\rightarrow$  double bond  $\rightarrow$  nucleophile removed  $\rightarrow$   $\text{H}_2\text{O}$  and  $\text{Br}^-$
- Regioselectivity in E2:
  - When bulky base  $\text{KO}^t\text{B}^u$  is used w/ cyclic rings, proton not on the ring/tertiary carbon is removed as less sterically crowded
  - Hofmann's Rule: Less substituted alkene forms

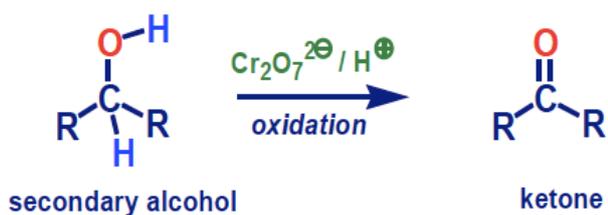
*Oxidation-Reduction Reactions*

- Oxidation: Increasing O content/no. bonds to O & reducing H content/no. bonds to H

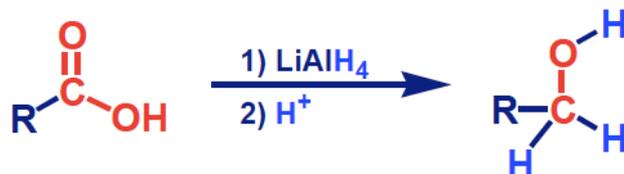
- Uses dichromate ions  $\text{Cr}_2\text{O}_7^{2-}$  and  $\text{H}^+$
- Primary alcohol (C-OH has one alkyl group attached)  $\rightarrow$  aldehyde  $\rightarrow$  carboxylic acid (cannot stop aldehyde  $>$  carboxylic acid as carboxylic acid more stable since lone pair of  $e^-$  on O in carboxylic donates to C)



- Secondary alcohol (C-OH has 2 alkyl groups attached)  $\rightarrow$  ketone



- Reduction: Reducing O content/no. bonds to O and increasing H content/no. bonds to H
  - Uses  $\text{LiAlH}_4$  or  $\text{NaBH}_4$  (milder) and then  $\text{H}^+$
  - Carboxylic acid  $\rightarrow$  primary alcohol
    - Does not stop at aldehyde as aldehyde is very reactive



- Aldehydes  $\rightarrow$  primary alcohol
- Ketone  $\rightarrow$  secondary alcohol

