Chapter Definitions

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Nucleophile: nucleus loving, donates a pair of electrons

Electrophile: electron loving, accepts a pair of electrons

Leaving Group: any group departs a molecule with a pair of electrons

Thermodynamics: study of how favorable a reaction will be

Kinetics: how fast a reaction proceeds

Rate determining step: in a multistep reaction the rate determining step is the slowest step (highest activation energy) rate of reaction is affected by the molecules in this step of the mechanism only

Activation energy: the amount of energy it takes for the starting materials to reach their transition state.

Transition state: proposed highest energy arrangement of atoms. Structure is somewhere between the starting material and the products

Carbocation: a reactive intermediate which is isolable: carbon has empty p-orbital and is sp² hybridized

Reactions of Alkyl Halides: Substitution and Elimination Reactions



Elimination Reaction: A base (B) removes a proton (H) adjacent to the leaving group (LG) $H \xrightarrow{H}_{LG} \xrightarrow{:B}_{HB} HB + \underbrace{-}_{+} LG^{\ominus}$

There are two subsets of each substitution and elimination reaction, for a total of 4 types of these reactions

Polarized Bonds

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Difference in electronegativity leads to polarized bond. The polarized bond is reactive.



Super Bowl of Chemistry

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Brendan (twitter handle @ChemScrapes)

Unimolecular Reactions, S_N1 and E1





Examples of SN₁



Carbocations are sp2 hybridized and the nucleophile can attack from top or bottom

More Examples SN1



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E₁ **Examples**



Bimolecular Reactions, S_N^2 and E2





SN2 Examples



E2 examples



Dehydrohalogenation

Dehydrohalogenation

Dehydrohalogenation Two different adjacent protons. Only the blue is deprotonated to give the most stable alkene (Zaitsev's rule)

Dehalogenation

Deciding Between Substitution Elimination Reactions



The Leaving Group

- Good leaving groups are weak bases
- The stronger the acid the weaker its conjugate base
 - We can use a pka table to determine relative stability of conjugate bases!



http://www.masterorganicchemistry.com/2011/04/12/what-makes-a-good-leaving-group/

Practice Questions

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Place the following leaving groups in order from best to worst.

 $H^{\ominus} H_2 \overset{\cdot\cdot}{O} \colon \overset{\ominus}{O} H \ I^{\ominus} \ CI^{\ominus} : NH_3$

Place the following leaving groups in order from best to worst. Explain why the best leaving group is the best.

$$\stackrel{\bigcirc}{=} O_{- \underset{O}{\overset{O}{\overset{}}{_{\scriptscriptstyle 0}}} - CH_3} \stackrel{\bigcirc}{=} O_{- \underset{O}{\overset{O}{\overset{}}{_{\scriptscriptstyle 0}}} - \underset{O}{\overset{O}{\overset{}}{_{\scriptscriptstyle 0}}} - CH_3 \stackrel{\bigcirc}{=} O_{- \underset{O}{\overset{O}{\overset{}}{_{\scriptscriptstyle 0}}} - CF_3}$$

Making a bad leaving group Into a good leaving group

 Hydroxyl and ether groups can be made into good leaving groups by treating them with acid
Good LG



Example



Deciding Between Substitution Elimination Reactions



The Electrophile

- Recall that electrophile means "electron- loving."
- When considering substitution and elimination reactions we must consider the carbon attached to the leaving group. Is it a primary, secondary, or tertiary carbon?

Electrophile Type	Favors	Disfavors
Methyl	S _N 2	S _N 1, E1, E2
Primary	S _N 2, E2	S _N 1,E1
Secondary	S _N 1, S _N 2, E1, E2	
Resonance Stabilized Primary	S _N 1, S _N 2	E1, E2
Tertiary	S _N 1, E2, E1	S _N 2



The Electrophile: S_N^1 and E1 Reactions, Carbocation Stability

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- The first step in a S_N^1 and E1 reaction is to form a carbocation. If the carbocation is too unstable, then regardless of how good the leaving group is the carbocation will not form.
- To determine the stability of a carbocation we must consider inductive and resonance effects



Examining the Leaving Group and Electrophile

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The Leaving Group and the Electrophile: Examples

The leaving group here would be OH⁻, a **bad** leaving group No reaction is likely to take place here without further modifying the the substrate.

The leaving group here would be Cl⁻, a **good** leaving group The electrophile is a secondary electrophile, SN1, SN2, E1, and E2 are all possible



Haloalkane produced by red algea

The leaving group here would be Br⁻, a **good** leaving group. However, it is attached to an Sp2 carbon, no substitution or elimination reaction will occur here.

Practice Question

Which substrate will undergo the fastest ${\rm S}_{\rm N}2$ reaction?



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Deciding Between Substitution Elimination Reactions



The Nucleophile

- Recall that nucleophile means "nucleus loving" or "positive-charge loving"
- Nucleophiles donate a pair of electrons to an electrophile. (Lewis base!)
- When the nucleophile donates a pair of electrons to a proton it is called a Bronsted base or simply a base. The proton is acting like an electrophile.

Nucleophile Type	Favors	Disfavors
Strong Nuc/Strong Base	S _N 2, E2	S _N 1, E1
Strong Nuc/ Weak Base	S _N 2	S _N 1, E1, E2
Weak Nuc/ Strong Base	E2	S _N 1, S _N 2, E1
Weak Nuc/Weak Base	S _N 1,E1	S _N 2, E2

The Nucleophile: Factors That Affect Nucleophilicity and Basicity

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How do we know if a nucleophile is acting as a nucleophile or a base?



The Nucleophile: Charge and Electronegativity

Charge

- The greater the electron density on the nucleophile the greater its nucleophilicity
- Increased electron density results in an increased desire to donate those electrons; ie: increased nucleophilicity



- Electronegativity
 - Electronegativity relates how "tightly" held a pair of electrons are. The more tightly they are held the less the ability for them to be donated is.

$$H_{3}C^{\bigcirc} > H_{2}\overset{\bigcirc}{N^{\bigcirc}} > H\overset{\bigcirc}{O^{\bigcirc}} > \overset{\bigcirc}{F^{\bigcirc}} > \overset{\bigcirc}{F^{\bigcirc}} > H^{\bigcirc}_{2}\overset{\bigcirc}{N^{\bigcirc}} > H^{\bigcirc}_{2}\overset{\bigcirc}{N^{\bigcirc}} > H^{\bigcirc}_{2}\overset{\bigcirc}{P^{\bigcirc}} > H^{\bigcirc}_{1}\overset{\bigcirc}{F^{\bigcirc}} > H^{\bigcirc}_{2}\overset{\bigcirc}{P^{\bigcirc}} > H^{\bigcirc}_{1}\overset{\bigcirc}{F^{\bigcirc}} > H^{\bigcirc}_{1}\overset{\bigcirc}{P^{\bigcirc}} > H^{\bigcirc}_{2}\overset{\bigcirc}{P^{\bigcirc}} > H^{\bigcirc}_{2}\overset{O}{P^{\bigcirc}} > H^{\bigcirc}_{2}\overset{O}{P^{O}} > H^{O}_{2}\overset{O}{P^{O}} > H^{O}_{2} > H^{O}_{2}\overset{O}{P^{O}} > H^{O}_{2} >$$



Rank the Following Nucleophiles in Order of Increasing Nucleophilicity (1 being the weakest 5 being the strongest)

→O →OH →OH

The Nucleophile: Steric Hindrance

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- Nucleophilicity decreases with increasing steric bulk



Practice Question

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 \Box t-butoxide has the following structure. $--o^{\ominus}$



Based on what you know about nucleophilicity what type of reaction or reactions are favored?

- A. Both $S_N 1$, E1
- B. Both $S_N 2$, E2
- C. Primarily E1
- D. Primarily E2

Deciding Between Substitution Elimination Reactions



Solvent Effects: The Electrophile

Solvent Type	Favors	Disfavors
Polar Protic	S _N 1, E1	
Polar Aprotic	S _N 2	S _N 1, E1
Non-Polar		S _N 1, S _N 2, E1, E2

- \Box S_N1 and E1 reactions proceed more quickly in polar protic solvents
 - Intermediates are solvated through hydrogen bonding

Polar protic solvents favour S_N^1 and E1 reactions because the intermediates are **solvated**

Solvent effects: The Nucleophile

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- Nucleophilicity can be affected by solvent.
- Delar protic solvents cause nucleophilicity to increase going down the periodic table

Polar aprotic solvents cause nucleophilicity to decrease going down the periodic table

Solvent Effects: The Nucleophile

Hydrogen bonding between lone pairs and polar protic solvents result in dispersion of negative charge. Lone pairs are tied up in H-bond and less available to be donated

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Polar aprotic

Acetone N, N-Dimethylformamide (DMF) Acetonitrile (MeCN)

 $H_3C-C\equiv N$:

Dimethyl sulfoxide (DMSO)

Polar aprotic solvents have dipoles present which could interact with the nucleophile, however the partial positive charge created from the dipole is sterically hindered and therefore the nucleophile is unable to interact with these solvent.

Polar aprotic solvents help in the solvolysis of cations which result in "naked" anions

Non-polar solvent

hexane

Recall that "like dissolves like." as many nucleophiles are charged or very polar they will not dissolve in non-polar solvents

Can you rank the following nucleophiles in order of increasing nucleophilicity? (1 being the weakest 5 being the strongest)

How would the rate of the reaction change if the solvent was changed from methanol to DMF.

Deciding Between Substitution Elimination Reactions

Temperature Effects

When all else is equal increased temperatures will favor elimination reactions over substitution reactions

Mind Map

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Practice Question

- What is the most likely reaction to occur under the following conditions?
- What is the most likely product of the following reaction.

С

Substitution and Elimination Reactions

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Additional Practice Questions

- Textbook Problems Solomons+Fryhle+Snyder (12 edition)
- Leaving Group and Electrophile
 - **Q**. 6.20, 6.22
- Nucleophile and Solvent Effects
 - **Q**.6.21, Q6.29
- Deciding between SN1 and SN2
 - **Q**. 6.28, 6.35, 6.40
- Challenge Problems

6.41, 6.42, 6.46, 6.47

Group Discussion Problems