



Substitution-Elimination Study Guide

[Link to Series on jOeCHEM](#)

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Hi, gang, and welcome to the Substitution-Elimination study guide on jOeCHEM! If this is your **first** study guide (hey, welcome—glad you're here), let me provide some background for what I envision these guides to be and how they are supposed to help you kick organic butt.

For every series on jOeCHEM (aka "Gen Chem Boot Camp", for example), I want these study guides to be a central summary point. If you're starting to study for an exam, and you want to have a general idea of what is contained within a given unit, I hope you can turn to these study guides and get that overview.


Of course jOeCHEM can't be a perfect substitute for every Organic Chemistry class (each teacher/class is different), but I'll aim to include:

1. Terms you need to know + their definitions
2. An overview of all the key concepts in a given series
3. A summary of all the reactions specific to that series (this will be a thing when we start learning reactions)
4. Tips & Tricks I think could be helpful and may not necessarily fit in the other sections

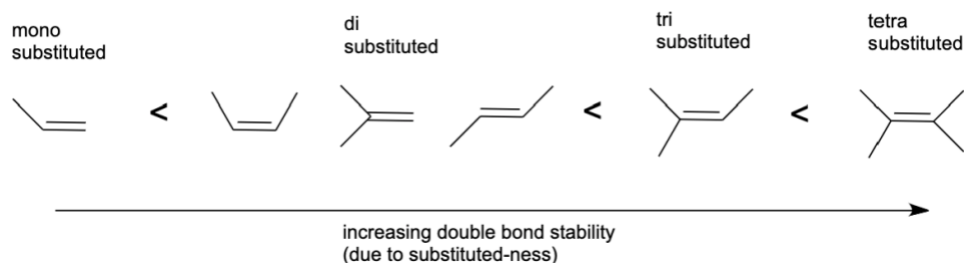
Terms to Know (with some concepts mixed in)

Below is a list of terms that you should have a working understanding of. There's a lot of science-y jargon in Organic Chemistry, so to be able to walk-the-walk (do reactions and stuff), we have to have to be able to talk-the-talk (talk and stuff).

*Note: In this particular study guide, gang, I think it helps to have examples/some more explanation alongside the definitions, so that is why this section is a bit large.

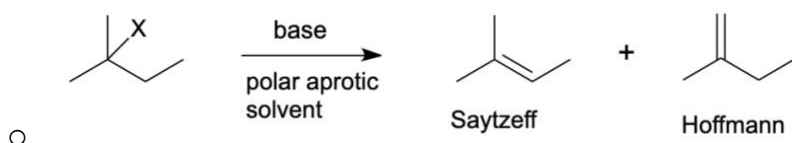
- **Nucleophile (nuc:)** – a “lover of positive charge”. Nucleophiles are molecules that are either net negative or partially negative. As a result, they will have an affinity for interacting with net positive or partially positive molecules.
 - For example: H_2O , OH^- , CN^- , Br^-
- **Electrophile** – a “lover of negative charge”. Electrophiles are molecules that are either net positive or partially positive. As a result, they will have an affinity for interacting with net negative or partially negative molecules.
 - For example: CH_3Br (partial positive carbon is electrophilic),  (t-butyl carbocation)
 - We will talk a LOT about nucleophiles seeking out and attacking electrophiles.
- **Substrate** – a generic term to describe an atom/molecule “being operated on” or attacked. I include this here because the word ‘substrate’ ends up getting used often to describe electrophiles when they are attacked by nucleophiles.
- **Solvent** – a substance (typically a liquid) that is used to dissolve one or more things. For our purposes, we will use solvents to dissolve compounds in order for a reaction to take a place.
- **Non-Polar Solvent** – a solvent that has no net dipole moment. This could be due to the solvent having no polar bonds in it or being symmetrical and having individual dipole moments cancelling each other out overall.
 - For example: hexane, cyclohexane, diethyl ether
- **Polar-Protic Solvent** – a solvent that has a net dipole moment AND has one or more **very** strongly partially positive hydrogens (aka has ≥ 1 H bonded to a very electronegative atom).
 - For example: H_2O , CH_3OH , NH_3 , acetic acid, etc
- **Polar-Aprotic Solvent** – a solvent that has a net dipole moment BUT DOES NOT have a ‘protic’ hydrogen (aka an H bonded to a very electronegative atom).
 - For example: acetone, DMSO, DMF, acetonitrile

- **Leaving Group** – a group that leaves! For a leaving group to be ‘good’, it needs to be a weak, stable conjugate base.
 - The reason being is that when something leaves, it will accept electrons and could even take on a negative charge. Nature likes stability, so it will only allow/tolerate atoms/molecules to leave if they can handle the extra negativity (aka are stable).
- ‘**How substituted a carbon is**’ – when someone refers to how ‘substituted’ a carbon is, they are referring to **how many other carbons** that carbon is attached to. For example, the least substituted a carbon can get is if it is methyl—it’s not attached to any other carbons. The following indented bullet shows substituted-ness going up left to right
 - methyl < primary (1°) < secondary (2°) < tertiary (3°) < quaternary (4°)
- ‘**How substituted a double bond is**’ – when someone refers to how ‘substituted’ a double bond is, they are referring to **the total number of other carbons** the two carbons within the double bond are attached to. For example, the least substituted a carbon can get is if it is methyl—it’s not attached to any other carbons. The following indented bullet shows increasing stability due to substituted-ness from left to right:

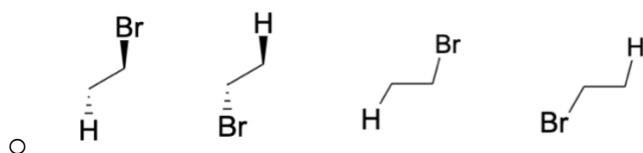


- The more substituted a double bond is, the more stable it is.
- **Solvent Caging** – when a protic solvent surrounds a base or nucleophile, creating a cage around it and preventing the nuc./base from performing its job.
- **Substitution Reaction** – a generic phrase to describe a reaction where a new atom/molecule is added to an existing one and an atom/molecule is removed (as a result of the newly added entity).
- **Elimination Reaction** – a generic phrase to describe a reaction where an atom/molecule is ejected by a newly created double bond.
- **S_N2** – a substitution reaction that has the following characteristics/is carried out in certain conditions:
 - is a concerted process (concerted process = 1 step reaction)
 - has 2nd order kinetics (rate law depends on both the concentrations of the substrate & nucleophile): Rxn Rate = k[substrate][nuc:]

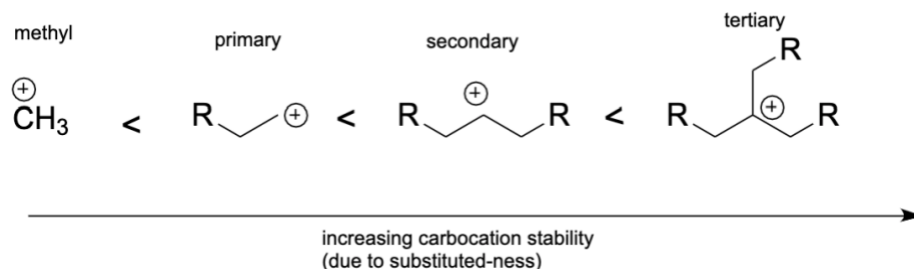
- 'k' is a generic rate constant (a blast from Gen-Chem past—in most OChem courses, you shouldn't need to remember anything more about it than just knowing it's part of the rate law)
 - involves a good nucleophile attacking a substrate/electrophile, bonding to the substrate, and ejecting a good leaving group (from the substrate)
 - is best conducted in a **polar aprotic** solvent to avoid solvent caging
 - results in stereochemical inversion (original stereochem of attacked carbon gets flipped) of the substrate carbon being attacked IF it is chiral
 - is more effective/favorable on sterically available carbons (methyl & primary)
 - S_N2 CANNOT occur on tertiary carbons (too much steric hindrance prevents backside attack from occurring)
- **“Backside Attack”** – a nickname for S_N2 since the nucleophile approaches & attacks the carbon in the substrate from the backside of where the leaving group is.
- **Saytzeff Product** (there are different spellings) – an elimination product where, of the possible double bonds that could be created, the **most substituted** option is made. This can be a major or minor product (depends on base size).
- **Hoffmann Product** – an elimination product where, of the possible double bonds that could be created, the **least substituted** option is made. This can be a major or minor product (depends on base size).
- **E2** – an elimination reaction that has the following characteristics/is carried out in certain conditions:
 - is a concerted process (concerted process = 1 step reaction)
 - has 2nd order kinetics (rate law depends on both the concentrations of the substrate & base): Rxn Rate = k[substrate][base]
 - involves the following steps **happening all at once**:
 - good base abstracts (aka “picking up”) a proton (aka an “H”) from a carbon NEXT TO a carbon with a good leaving group
 - electrons swing down and form a new carbon-carbon double bond (between the carbon w/ the good leaving group and the carbon that lost the H)
 - the good leaving group is ejected
 - is best conducted in a **polar aprotic** solvent to avoid solvent caging
 - is more favorable on sterically hindered (aka more substituted) carbons since E2 is in competition with S_N2



- when using a **small** base, E2 results in a major Saytzeff & minor Hoffmann product mixture
 - when using a **big** base, E2 results in a minor Saytzeff & major Hoffmann product mixture
 - if the carbon attached to the leaving group is chiral, the anti-peri planar requirement must be honored/followed
- anti-periplanar requirement** – when performing E2, if the substrate carbon is chiral, the Leaving Group (LG) and the H being eliminated must be anti to one another (anti in the Newman Projection sense). Meaning if the leaving group is “up”, the H must be “down”, as shown in the various scenarios below with a bromine LG:



- Carbocation Stability** – due to hyperconjugation, carbocations (while always unstable) become more stable the more substituted they are. The bullet below shows (from left to right) carbocation stability increasing due to increased substituted-ness:



- Solvolysis** – the process by which a polar protic solvent coaxes a leaving group off of a carbon, causing it to leave (aka the bond between carbon and leaving group breaks).
 - After the leaving group leaves, the attached carbon loses electrons & its full octet, transforming into a carbocation. As a result, solvolysis is a **slow** reaction step that causes molecules to increase in energy, becoming less stable.
 - S_N1** – a substitution reaction that has the following characteristics/is carried out in certain conditions:
 - is a multi-step process (≥ 1 steps in the reaction)
 - has 1st order kinetics (rate law ONLY depends on the concentration of the substrate): $\text{Rxn Rate} = k[\text{substrate}]$
 - solvolysis **is** the slow, rate determining step & only involves the substrate

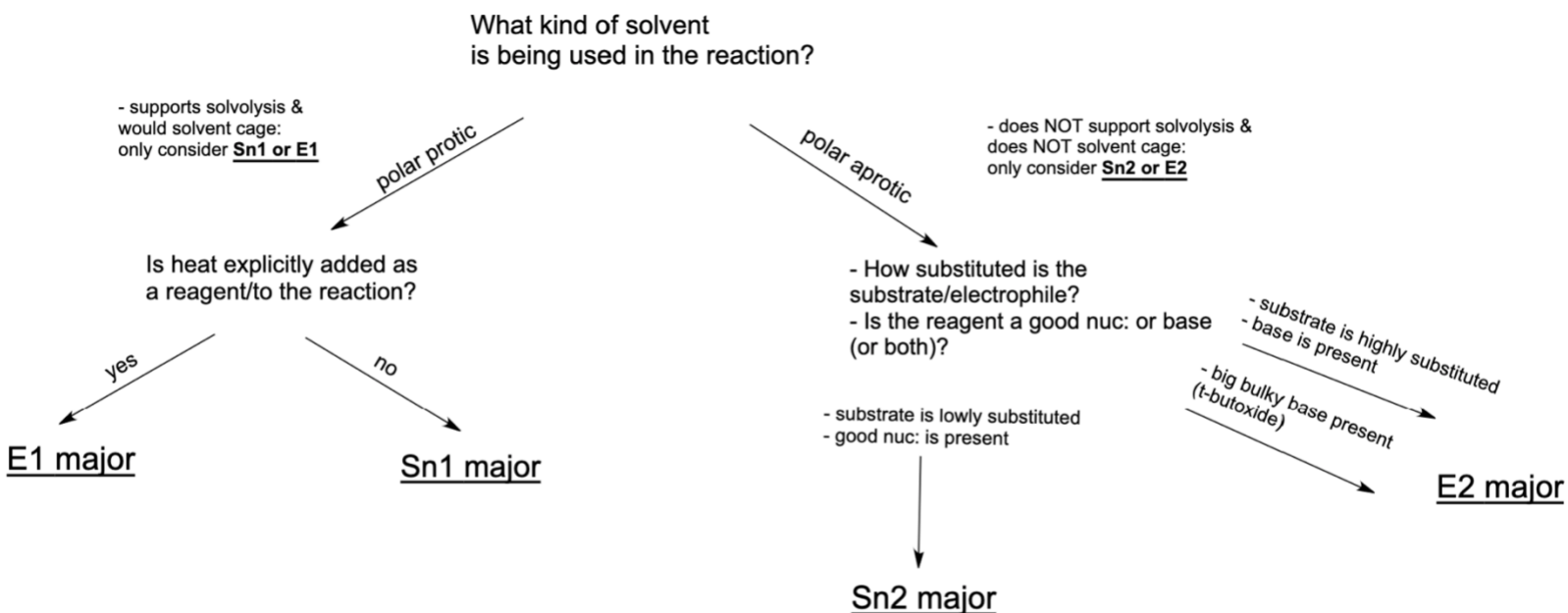
- is best conducted in a **polar protic solvent** to support solvolysis, the “weaning off” of the leaving group by the solvent—creating a carbocation
- involves a weak nucleophile (aka the molecule that doubles as the solvent) attacking a substrate/electrophile after it has undergone solvolysis. S_N1 nucs: must be weak to allow time for solvolysis to occur, and while that’s not great for substitution to take place, the substrate will make up for the lack of reactivity since it will have a carbon lacking a full octet (aka a carbocation)
- is prone to carbocation rearrangements/shifts, both hydride and methyl shifts
- is more effective/favorable on sterically hindered (aka more substituted) since that will yield more stable carbocations (after solvolysis occurs)
- if the carbon being attacked is chiral after the fact, the product mixture will show 50% wedge and 50% dash attachment to the nuc: since carbocations are sp^2 , trigonal planar
- **E1 “the minor product”** – an elimination reaction that has the following characteristics/is carried out in certain conditions:
 - is a multi-step process (≥ 1 steps in the reaction)
 - has 1st order kinetics (rate law ONLY depends on the concentration of the substrate): $\text{Rxn Rate} = k[\text{substrate}]$
 - solvolysis is the slow, rate determining step & only involves the substrate
 - is best conducted in a **polar protic solvent** to support solvolysis, the “weaning off” of the leaving group by the solvent—creating a carbocation
 - involves a weak base (aka the molecule that doubles as the solvent) abstracting a proton off of the carbon next to the carbon attached to the good leaving group, creating a new carbon-carbon double bond. E1 nucs: must be weak to allow time for solvolysis to occur, otherwise if the base was stronger E2 would occur instead.
 - Polar protic solvents are better weak nucs: than they are weak bases, so as a result, S_N1 dominates the competition against E1 (*except if additional heat is added to the reaction)
 - *E1 product yield can be increased if additional heat is added to the reaction since E1 has a positive (favorable) entropy change
 - is prone to carbocation rearrangements/shifts, both hydride and methyl shifts
 - is more effective/favorable on sterically hindered (aka more substituted) since that will yield more stable carbocations (after solvolysis occurs)
 - forms the most stable/substituted double bond possible (Saytzeff major product)

- **Hydride Shift** – a rearrangement where a hydride atom (hydrogen with 2 electrons aka H^-) physically moves and attaches to a carbocation from a neighboring carbon—this effectively shifts the carbocation to the carbon next door (and only does so when the new carbocation location is more substituted aka more stable).
- **Methyl Shift** – a rearrangement where a whole $-\text{CH}_3$ group physically moves and attaches to a carbocation from a neighboring carbon—this effectively shifts the carbocation to the carbon next door (and only does so when the new carbocation location is more substituted aka more stable).

Overview of Concepts

With the detail provided in the Terms section, this section will only contain the following flow chart below:

- Deciding whether a reaction is Sn2, E2, Sn1, and E1
 - Below is a flow chart that will *hopefully* provide a process to help you categorize unknowns reaction given to you.

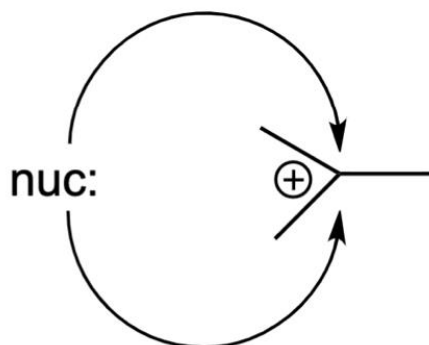


Summary of Reactions

Reaction:	Rxn/Reagent Conditions:	Characteristics
Sn2	<ul style="list-style-type: none"> • good nucleophile • lowly substituted (not sterically hindered) substrate/electrophile • polar aprotic solvent • good leaving group 	<ul style="list-style-type: none"> • concerted process • 2nd order kinetics • Rate = $k[\text{substrate}][\text{nuc:}]$ • stereochemical inversion if substrate carbon being attacked is chiral
E2	<ul style="list-style-type: none"> • strong base • highly substituted (sterically hindered) substrate/electrophile • polar aprotic solvent • good leaving group 	<ul style="list-style-type: none"> • concerted process • 2nd order kinetics • Rate = $k[\text{substrate}][\text{base}]$ • Creates double bond <ul style="list-style-type: none"> ○ Large base = Saytzeff (major) ○ Small base = Hoffmann (major) • Must honor anti-periplanar requirement if chiral
Sn1	<ul style="list-style-type: none"> • weak nucleophile • highly substituted (sterically hindered) substrate/electrophile—produces stable carbocations • polar protic solvent • good leaving group 	<ul style="list-style-type: none"> • multi-step process • 1st order kinetics • Rate = $k[\text{substrate}]$ • Involves carbocation intermediate—rearrangements <ul style="list-style-type: none"> ○ Methyl + Hydride • If the attack creates a stereocenter, result will be racemic since an sp², trigonal planar (flat) carbon is being attacked
E1	<ul style="list-style-type: none"> • weak base • highly substituted (sterically hindered) substrate/electrophile—produces stable carbocations • polar protic solvent • good leaving group • HEAT (to drive more E1 product) 	<ul style="list-style-type: none"> • multi-step process • 1st order kinetics • Rate = $k[\text{substrate}]$ • Involves carbocation intermediate—rearrangements <ul style="list-style-type: none"> ○ Methyl & Hydride • Creates most substituted double bond available as major product

Tips, Tricks & General Advice

- Be very comfortable with:
 - Identifying weak and strong bases as well as weak and strong nucleophiles.
 - You'll need to lean on your acid/base knowledge for bases, but nucleophiles (luckily) are more straight forward: the more negative, the better.
 - Having and applying a mental process for picking out characteristics of a reaction when trying to identify whether it's Sn2, E2, Sn1, and E1.
 - I provided the flow chart above, but go with the mental process that works best for you. However, I strongly recommend getting problems like this, putting your notes away, and trying to identify them as if you were taking a test
 - **Know your solvents.** Understanding and identifying polar protic and aprotic solvents will help you tremendously.
 - Carbocation shifts. Nature loves stability, and nature loves it so much that it will encourage bonds to pick up and move to achieve a better energetic state.
 - Anytime you form a carbocation from here on out, be suspicious and look for shifts.
 - Identifying "small" and "big" bases + the anti-periplanar requirement.
 - E2 can be confusing, but it gets even hairier when you have to consider the anti-periplanar requirement and base size when determining *where* the elimination is going to happen.
 - Stereochem.
 - Sn2: invert the stereochem if you're attacking a stereocenter
 - Sn1: reflect a racemic result from nucleophilic attack if the product is chiral.



Since carbocations are sp² (trigonal planar aka flat) attack from a nuc: happens above and below in equal, 50/50 amounts.