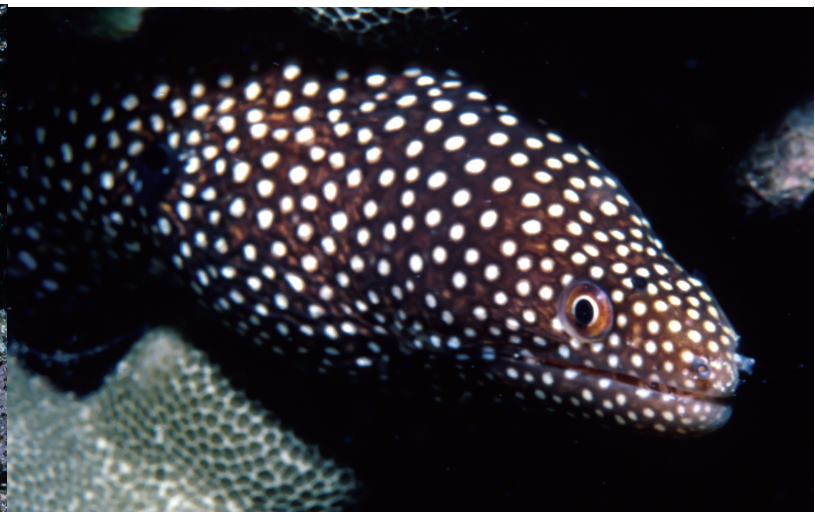
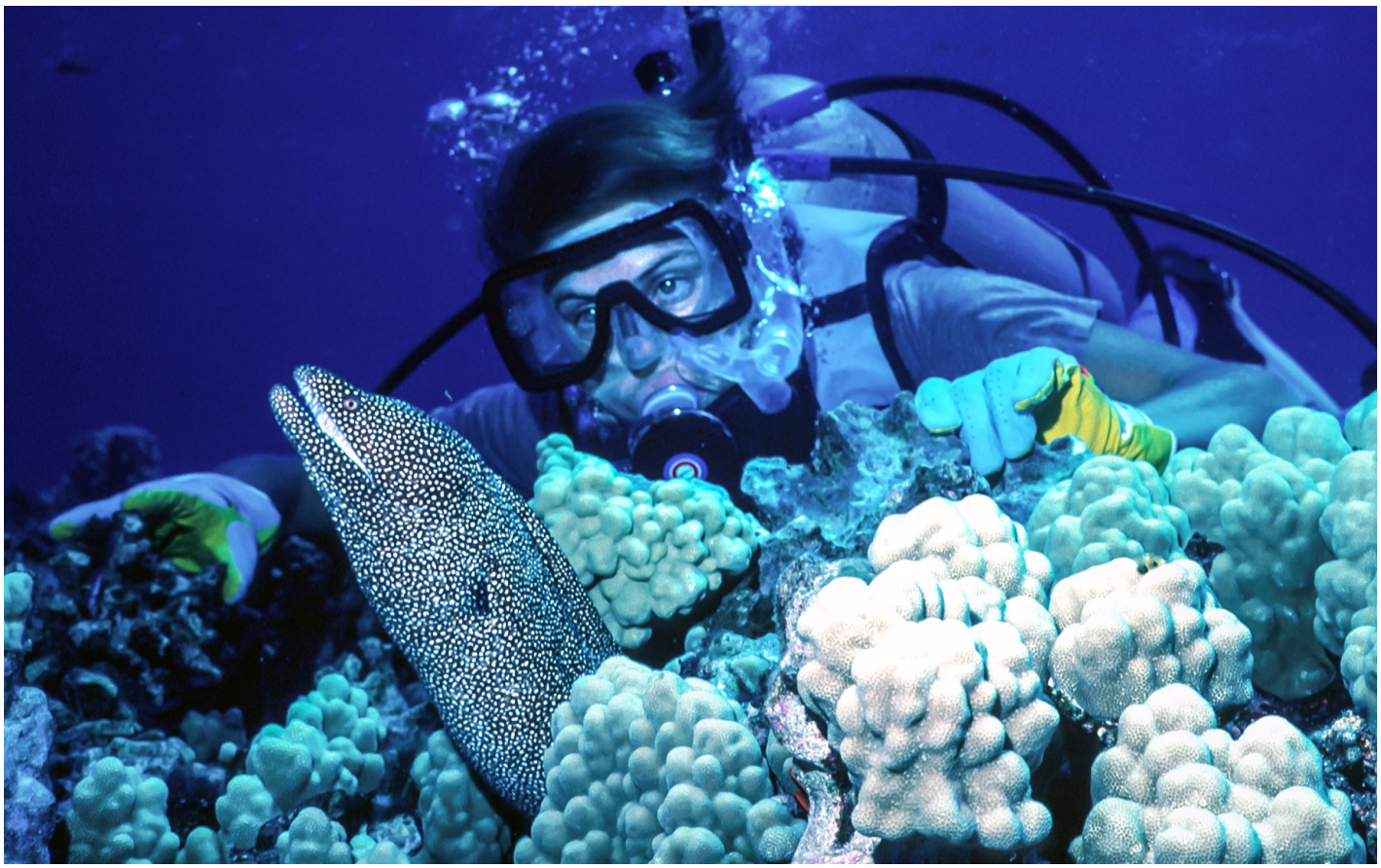




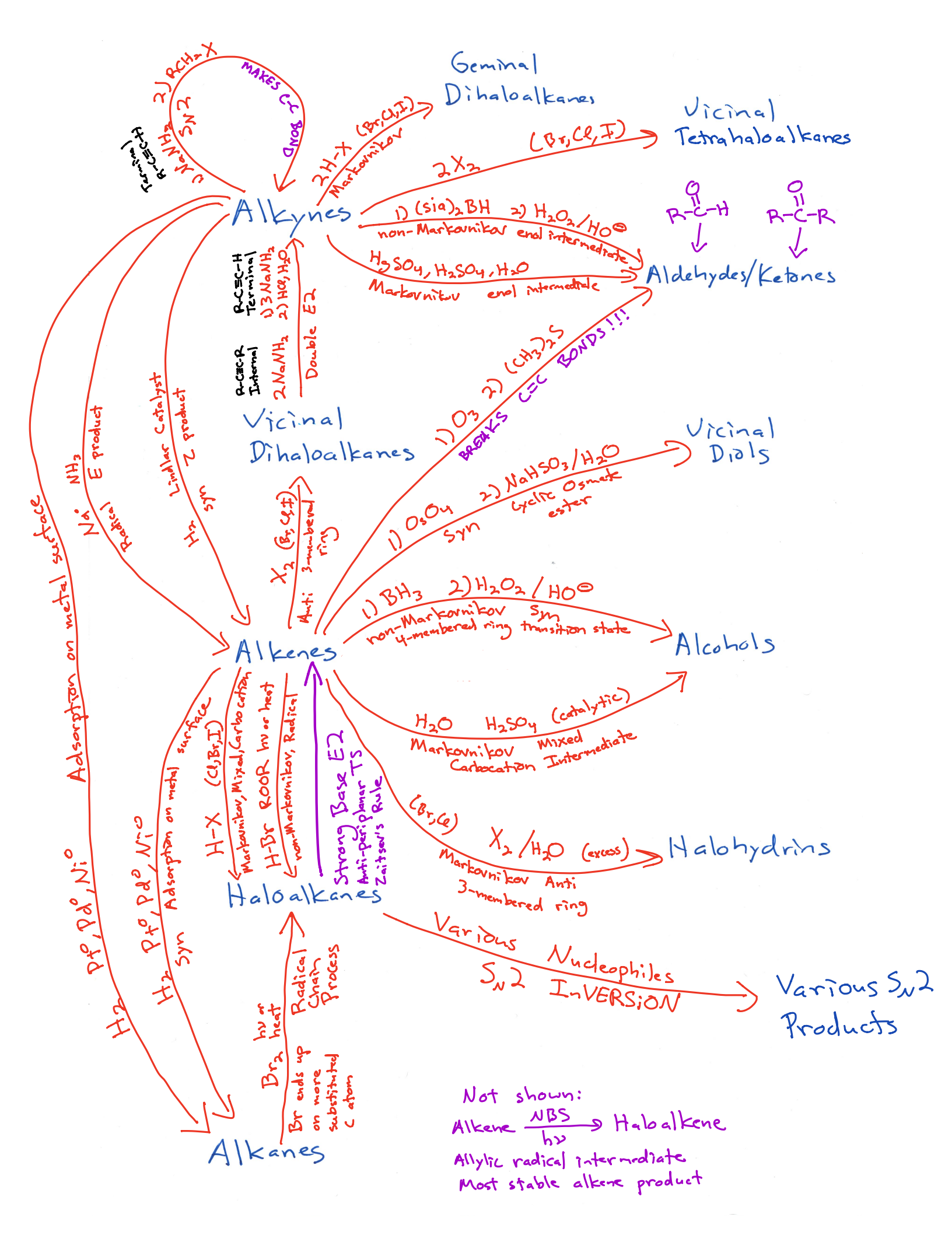


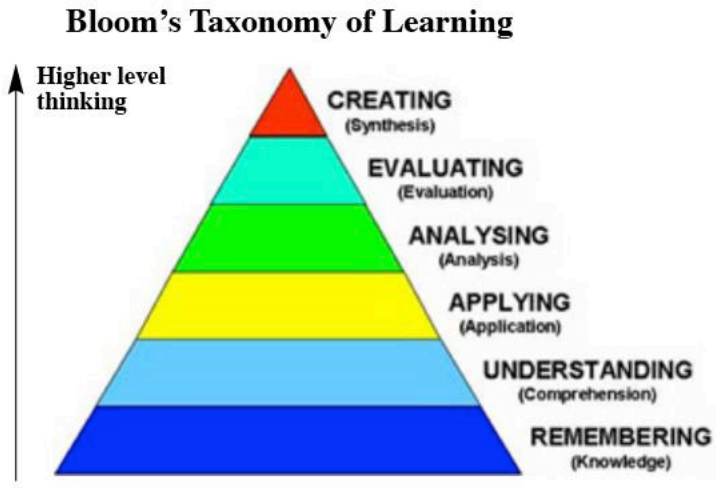


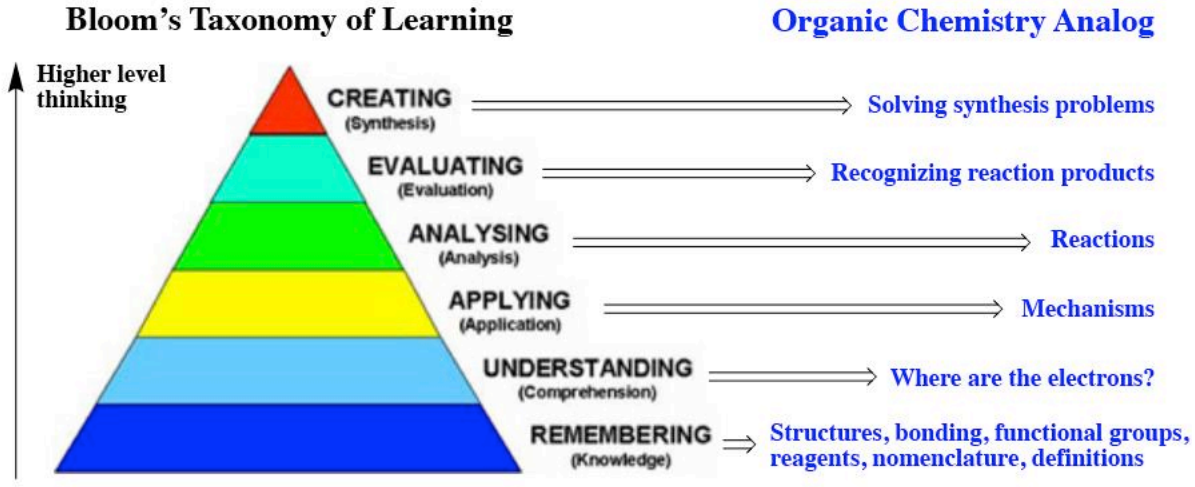







Alkynes
Terminal R-C≡C-H
1) NaNH2 2) RCH2X SN2
MAKES C-C
ANOTHER
2H-X (Br,Cl,I) Markovnikov
Geminal Dihaloalkanes
2X2 (Br,Cl,I)
Vicinal Tetrahaloalkanes
1) (sia)2BH 2) H2O2/HO⊖ non-Markovnikov enol intermediate
H2SO4, H2SO4, H2O Markovnikov enol intermediate
Aldehydes/Ketones
R-C(=O)-H
R-C(=O)-R
R-C≡C-H Terminal 1) 3NaNH2 2) HCl, H2O
R-C≡C-R Internal 2NaNH2
Double E2
Vicinal Dihaloalkanes
1) O3 2) (CH3)2S BREAKS C=C BONDS!!!
1) OsO4 2) NaHSO3/H2O syn cyclic Osmate ester
Vicinal Diols
X2 (Br, Cl, I) Anti 3-membered ring
Alkenes
1) BH3 2) H2O2/HO⊖ non-Markovnikov syn 4-membered ring transition state
Alcohols
H2O H2SO4 (catalytic) Markovnikov Mixed Carbocation Intermediate
(Br,Cl) X2/H2O (excess) Markovnikov Anti 3-membered ring
Halohydrins
H-X (Cl,Br,I) Markovnikov, Mixed, Carbocation
H-Br ROOR hv or heat non-Markovnikov, Radical
Strong Base E2 Anti-periplanar TS Zaitsev's Rule
Haloalkanes
Various Nucleophiles SN2 INVERSION
Various SN2 Products
Adsorption on metal surface
Pt°, Pd°, Ni°
H2 syn
Ni° NH3 Radical E product
Lindlar Catalyst H2 syn Z product
Br2 hv or heat Radical Chain Process
Br ends up on more substituted C atom
Alkanes
Not shown:
Alkene NBS hv Haloalkene
Allylic radical intermediate
Most stable alkene product





A) **You must have your entire roadmap learned** so you can recite the NIRRS parameters for each reagent, i.e. Nature of overall transformation ("locations" on the roadmap), the Intermediate or transition state (carbocation, anti-periplanar etc.), the Reagents and how to designate them, as well as any Regiochemistry (Markovnikov, etc.) and any appropriate Stereochemistry (syn, anti, InVERSiON, scrambled, etc).

B) **Work backwards** (learn to RECOGNIZE the appropriate reagents and starting materials by looking at the products) from the final product. DO NOT try to work forward from the starting materials. Please trust me on this.

C) **Count carbons** in the starting material(s) and product(s) to see if any carbon-carbon bonds need to be broken or made, thereby zeroing in on key steps. This will be far more important next semester, so you should get used to doing this now.

D) **Pretty much all synthesis problems in OChem 1 involve traveling "north or south" on the so-called "I-35"** reactions (alkanes SA, haloalkanes NB/SM, alkenes ATX, vicinal dihaloalkanes Waco, alkynes DFW) at least part way at some point during the synthesis. This is not a promise or a rule, just an observation.





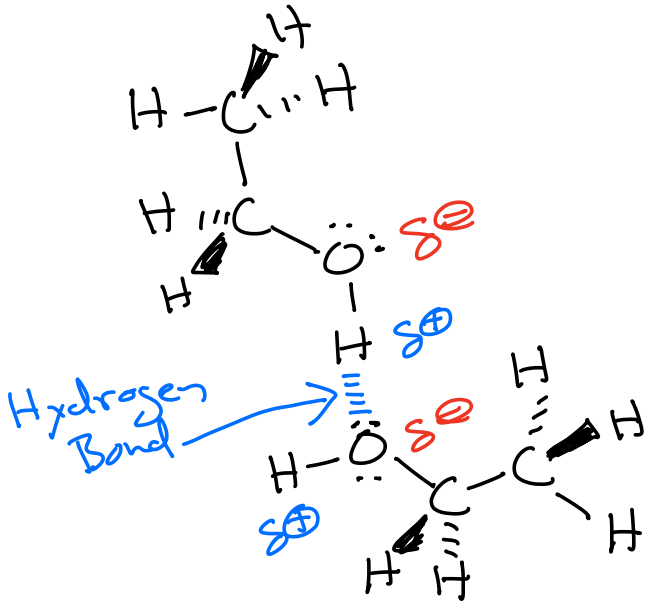
"You can't stop the waves, but you can learn to surf"

Jon Kabat-Zinn


Alkanes
Alkenes
Alkynes
Haloalkanes
Vicinal dihaloalkanes
Ketones and Aldehydes
Carboxylic Acids
Alcohols
Where Electrons Are
Mechanisms
Roadmaps
Stereochemistry
Regiochemistry
ROTD
NIRRS
Motive
Opportunity
Carbocation
Radical
Pi-ways
Golden Rules
Make a Bond
Break a Bond
Add a Proton
Take a Proton
Nucleophiles and Electrophiles
Charge Delocalization
Hyperconjugation
Steric strain
Angle and Torsional Strain
Epoxides
Vicinal Diols
Radical Chain
SN2 vs. E2
SN1 and E1
Anti-periplanar
Markovnikov
Zaitsev

Alcohols → R–Ö–H

↳ The O–H bond is very polar ⇒ Hydrogen bonds!



Consequences of Hydrogen Bonds →

These molecules are "sticky"

⇒ High boiling points

Table 10.1 Boiling Points and Solubilities in Water of Five Groups of Alcohols and Hydrocarbons of Similar Molecular Weight

Structural Formula	Name	Molecular Weight (g/mol)	Boiling Point (°C)	Solubility in Water
CH_3OH	Methanol	32	65	Infinite
CH_3CH_3	Ethane	30	−89	Insoluble
CH_3CH_2OH	Ethanol	46	78	Infinite
$CH_3CH_2CH_3$	Propane	44	−42	Insoluble
$CH_3CH_2CH_2OH$	1-Propanol	60	97	Infinite
$CH_3CH_2CH_2CH_3$	Butane	58	0	Insoluble
$CH_3CH_2CH_2CH_2OH$	1-Butanol	74	117	8 g/100 g
$CH_3CH_2CH_2CH_2CH_3$	Pentane	72	36	Insoluble
$HOCH_2CH_2CH_2CH_2OH$	1,4-Butanediol	90	230	Infinite
$CH_3CH_2CH_2CH_2CH_2OH$	1-Pentanol	88	138	2.3 g/100 g
$CH_3CH_2CH_2CH_2CH_2CH_3$	Hexane	86	69	Insoluble

General Rules of Solvents

Polar Protic

Has polar O-H bonds

Has a proton

"Like dissolves like"

Polar protic solvents dissolve other polar molecules → especially salts or molecules that can hydrogen bond

Polar protic solvents → cannot dissolve molecules unless that molecule can disrupt the strong interactions between solvent molecules.

⇒ See the POTD for today for the main messages here

1) Solvation of cations and anions
2) Solvation of carbocations / anions in S_N1 / E1 reactions
3) Methanol dissolved in water
4) Why pentane and water do not mix

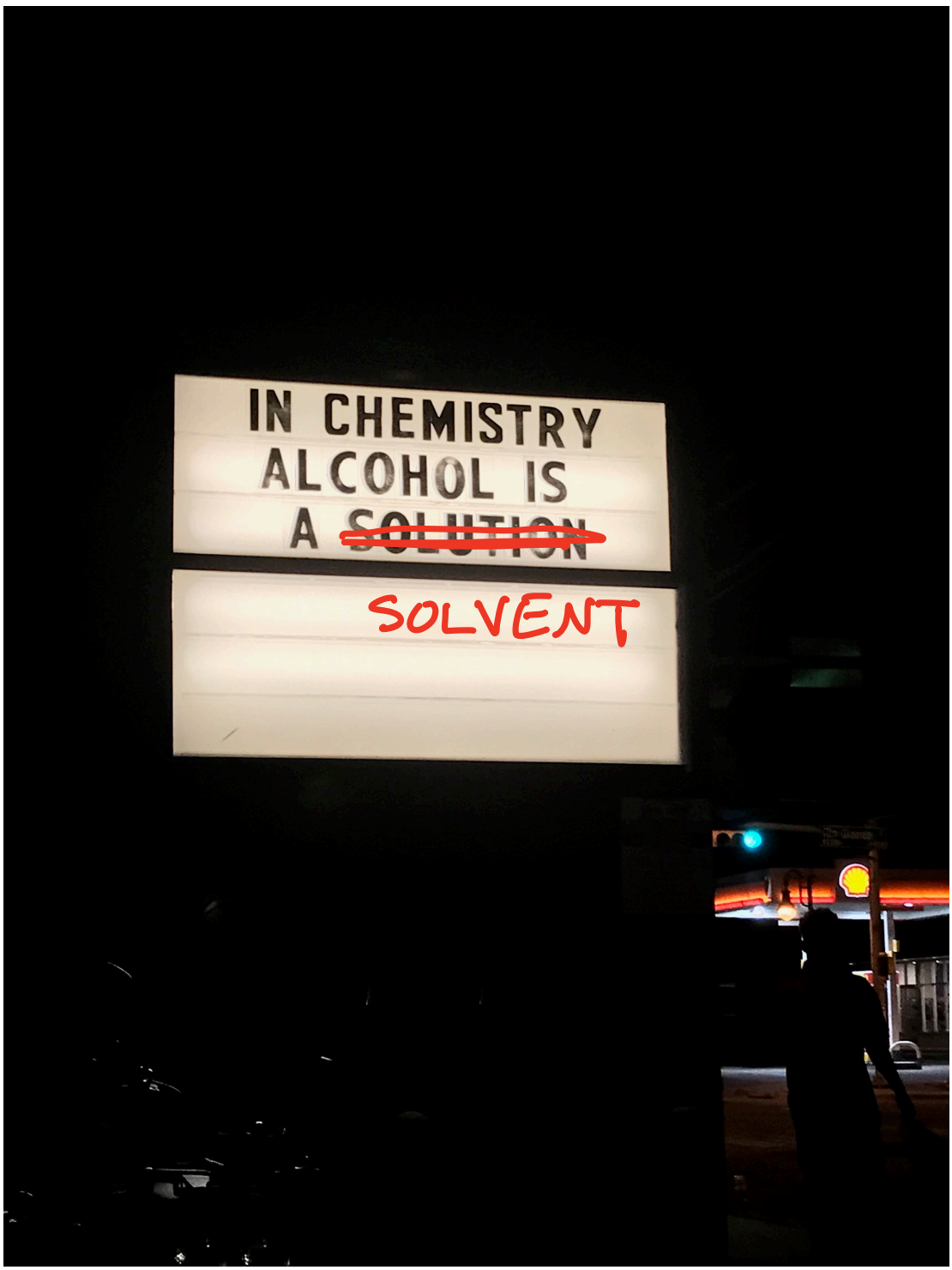

IN CHEMISTRY
ALCOHOL IS
A SOLUTION
SOLVENT

Table of Nucleophiles

Strong Nucleophiles

Br^-, I^-, $R\text{-}S^-$, $H\text{-}S^-$, $N{\equiv}C^-$, N_3^-

$R\text{-}C{\equiv}C^-$, $R\text{-}O^-$, $H\text{-}O^-$ **Strong Bases**

Medium Nucleophiles

$R\text{-}CO_2^-$, R-S-H, R_2S,
NH_3, RNH_2, R_2NH, NR_3

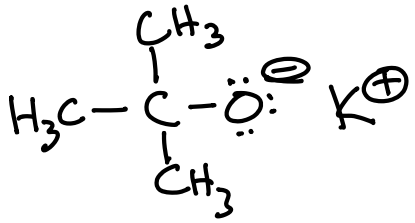
Weak Nucleophiles

$R\text{-}CO_2H$, R-O-H, H_2O **Very Weak Bases**

Used as solvents!

Special Case

***Tert*-Butoxide ($tBuO^-$) is a strong base, but is not a nucleophile due to steric hindrance.**



"KOtBu"
or
"$tBuO^-$"

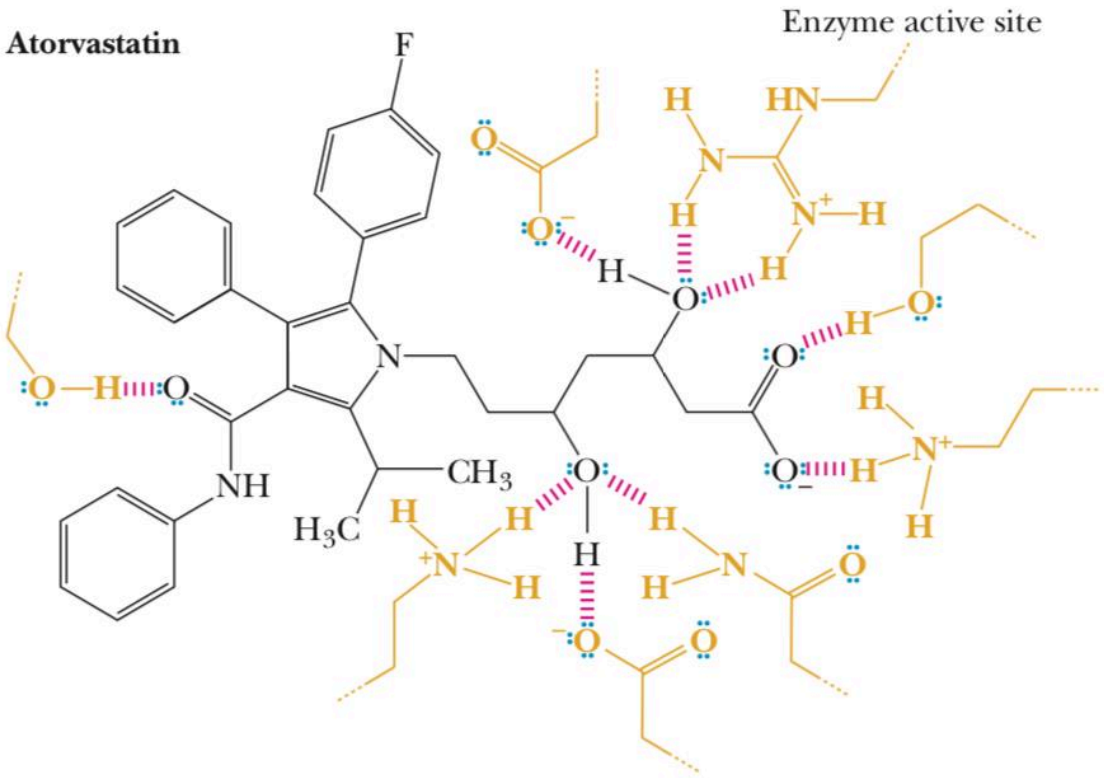


Figure 2

Hydrogen bonding (shown in red) between atorvastatin and the functional groups at the active site of the enzyme HMG-CoA reductase. The nine hydrogen bonds (shown in red), many of which involve hydroxyl groups on atorvastatin or the enzyme surface, help to provide the specificity that directs the binding of the drug to its target enzyme.

Hydrogen bonds between drug molecules and key amino acids of the protein target → Designed on purpose to keep the drug "stuck" to the protein

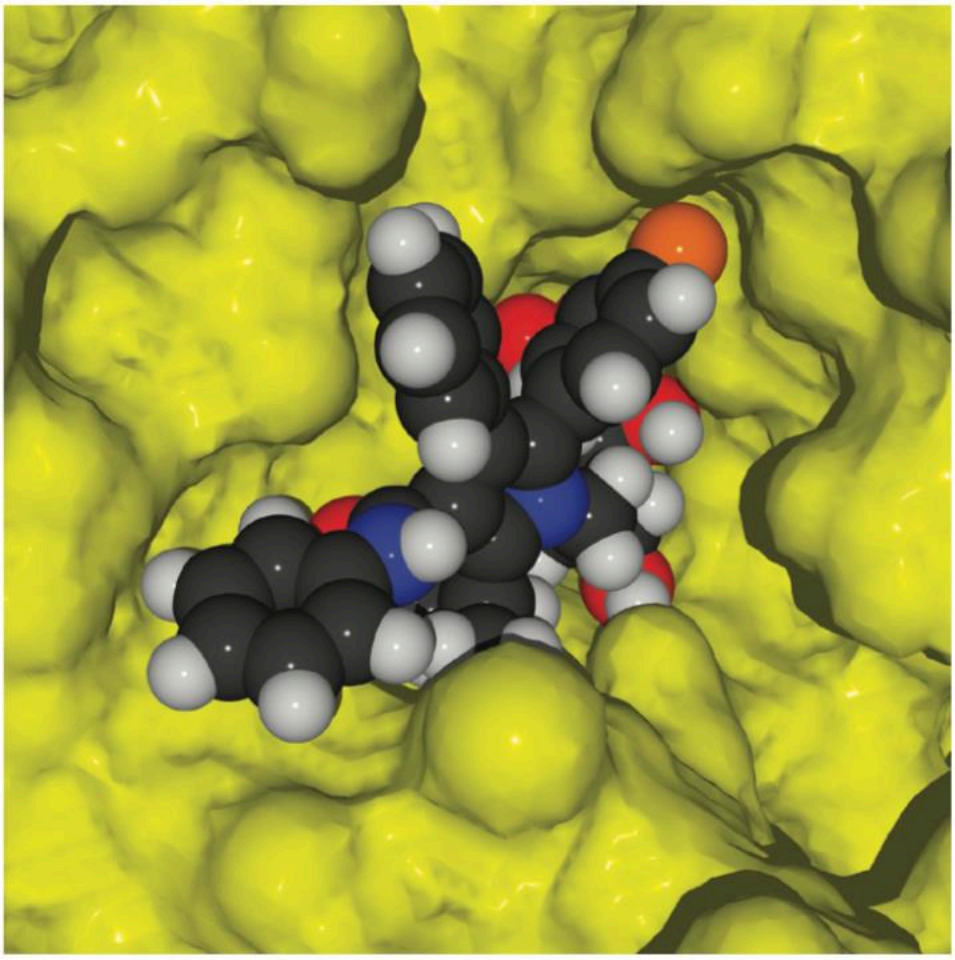


Figure 1

A space-filling model of the cholesterol-lowering drug atorvastatin (Lipitor) bound to the active site of its enzyme target HMG-CoA reductase (shown as a yellow surface). The shape of the drug is complementary to the active site of the enzyme.

The drug molecule must fit perfectly in three-dimensional space → like a key fits in a lock

<u>Organic Chemistry</u> is the study of carbon-containing molecules.

This class has two points.

The first point of the class is to understand the organic chemistry of living systems. We will teach you how to think about and understand the most amazing things on the planet!!

Water is essential for life, you will learn why water has such special properties. 8/25/26

You will learn the secret structural reason proteins, the most important molecular machines in our bodies, can support the chemistry of life. 9/9/26

You will learn why when you take Advil for pain, exactly half of what you take works, and the other half does nothing.

You will learn how toothpaste works. 9/21/26 9/30/26

You will learn how a single chlorofluorocarbon refrigerant molecule released into the atmosphere can destroy many, many ozone molecules, leading to an enlargement of the ozone hole. 10/26/26

You will learn how medicines like Benadryl, Seldane, and Lipitor work. 11/9/26

You will learn how Naloxone is an antidote for an opioid overdose.

You will learn why Magic Johnson is still alive, decades after contracting HIV.

You will learn how MRI scans work.

The second point of organic chemistry is the synthesis of complex molecules from simpler ones by making and breaking specific bonds.

You will learn how to understand movies of reaction mechanisms like alkene hydration. 10/5/26

You will learn reactions that once begun, will continue reacting such that each product molecule created starts a new reaction until all the starting material is used up. 10/26/26

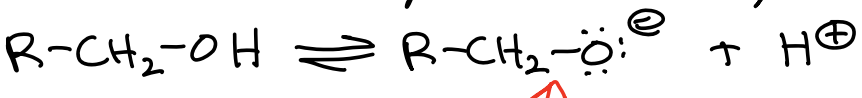
You will learn reactions that can make antifreeze from vodka.

You will learn a reaction that can make nail polish remover from rubbing alcohol.

You will learn how to look at a molecule and accurately predict which atoms will react to make new bonds, and which bonds will break during reactions.

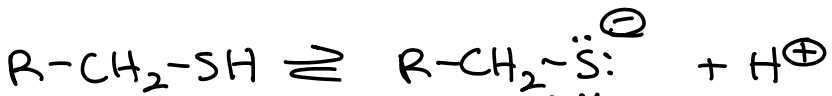
You will learn how to analyze a complex molecule's structure so that you can predict ways to make it via multiple reactions starting with less complex starting molecules.

Alcohols → Acidity and Basicity



$pK_a \cong 16\text{-}17$

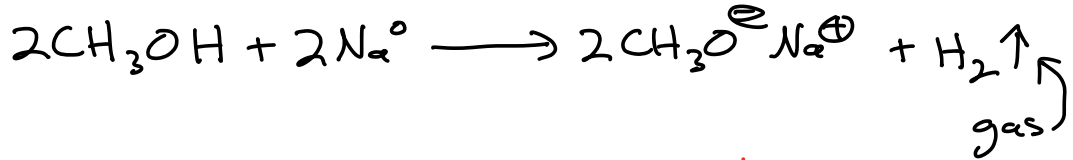
Strong Base



$pK_a \cong 8\text{-}12$

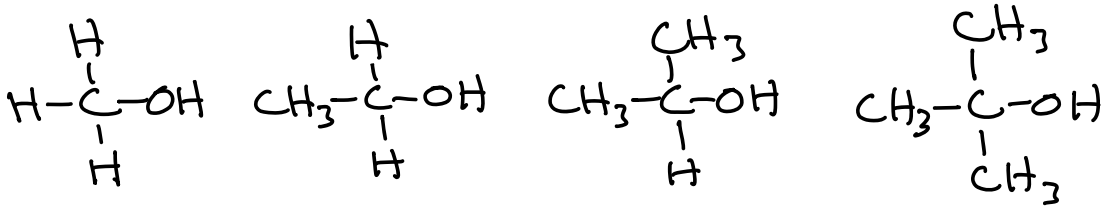
Weaker base

Notice This → $Na^\circ, K^\circ, Li^\circ$



→ Useful to make alkoxides!

Alcohols → Reaction mechanisms depend on the number of alkyl groups attached on the C atom of C-OH bond.



Methyl 1° 2° 3°

☆ The -OH is not a leaving group but several reactions involve conversion of the -OH group into a good leaving group

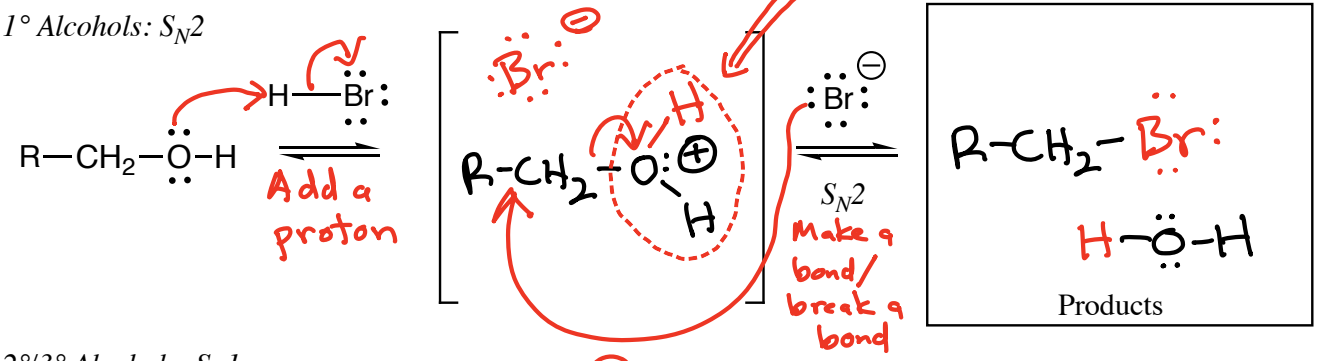
⟹ Recall, the -OH group is a weak nucleophile and weak base (in strong acid)

X = Cl, Br, I

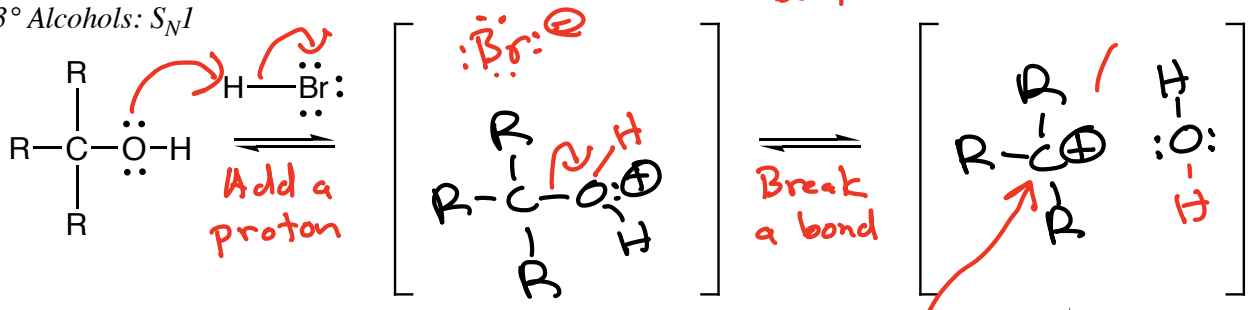
Alcohols + H-X

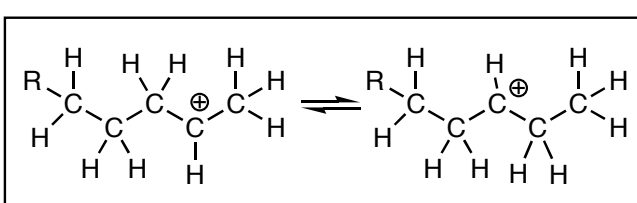
Good leaving group

1° Alcohols: S_N2

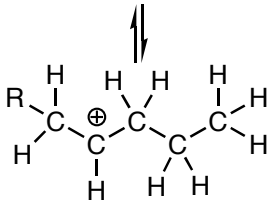


2°/3° Alcohols: S_N1

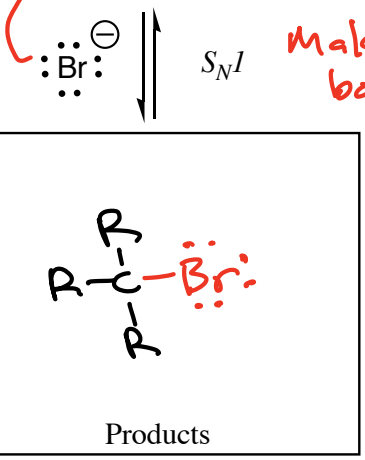




Under these acidic conditions, rearrangements are a particular problem with 2°carbocations



Note → The highly acidic nature of this reaction prevents any E1 before the S_N1 is finished

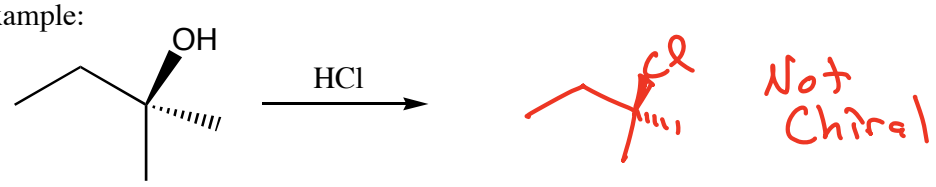


Summary: Reaction of primary alcohols → S_N2
Reaction of secondary/tertiary alcohols → S_N1
The -OH group is converted to a good leaving group by being protonated, followed by S_N2 or S_N1 substitution

Regiochemistry: N/A

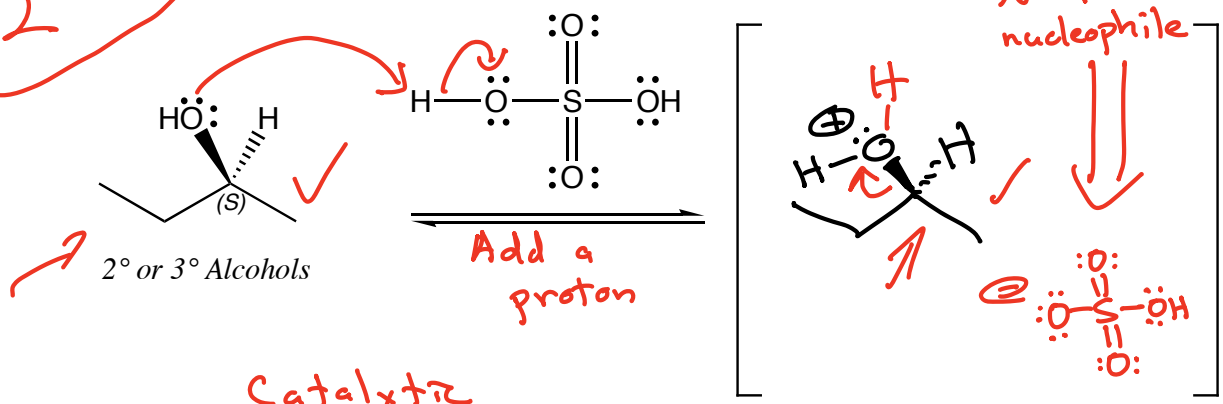
Stereochemistry: Chiral tertiary alcohols give scrambled products ← S_N1

Example:

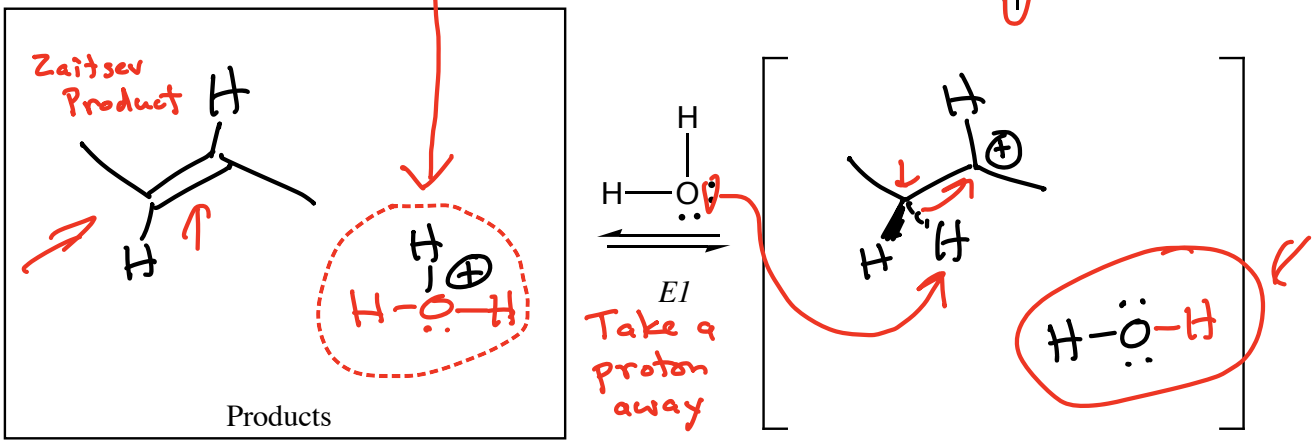


1° alcohols react via E2

2° or 3° Alcohol Dehydration → E1



Catalytic in acid

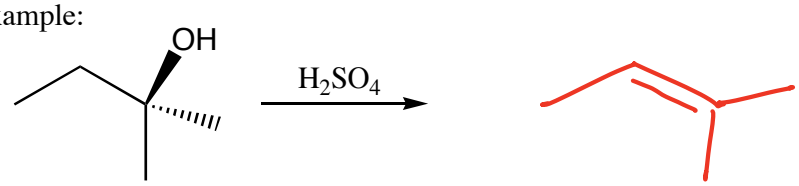


Summary: The OH group is protonated in strong acid to make a good leaving group, water, which breaks a bond to give a carbocation that has a proton taken away to give the product alkene

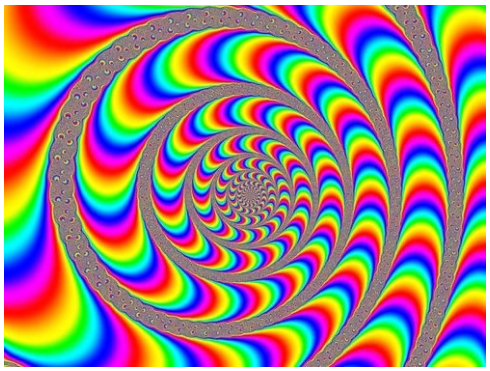
Regiochemistry: Zaitsev's Rule

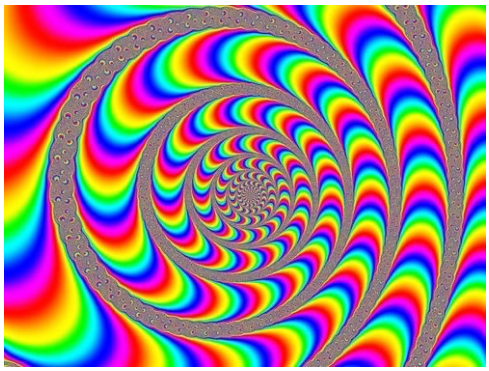
Stereochemistry: N/A

Example:

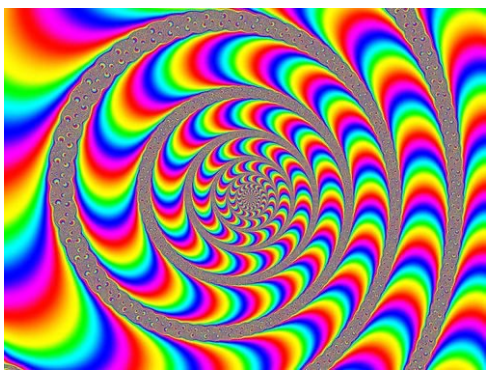


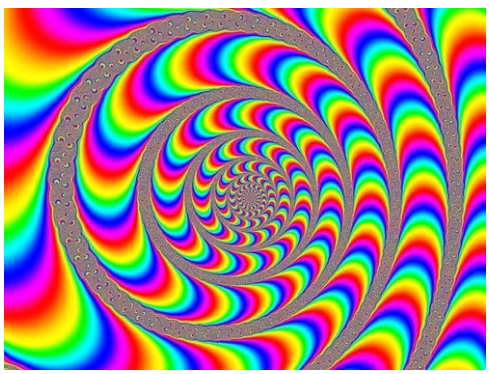
Flashback!!





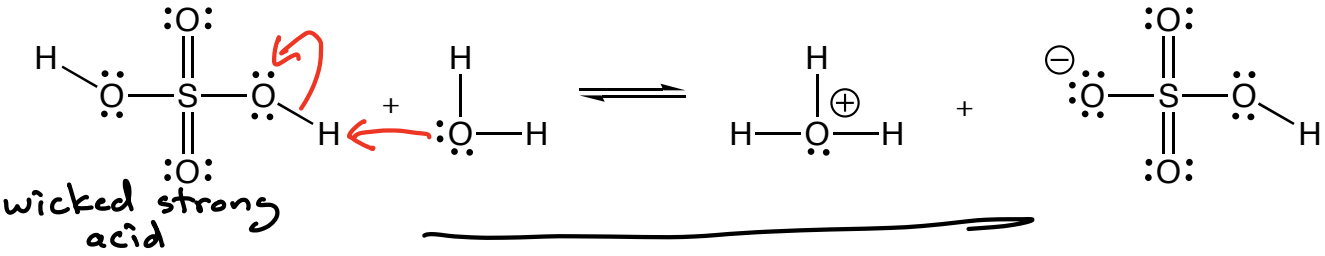


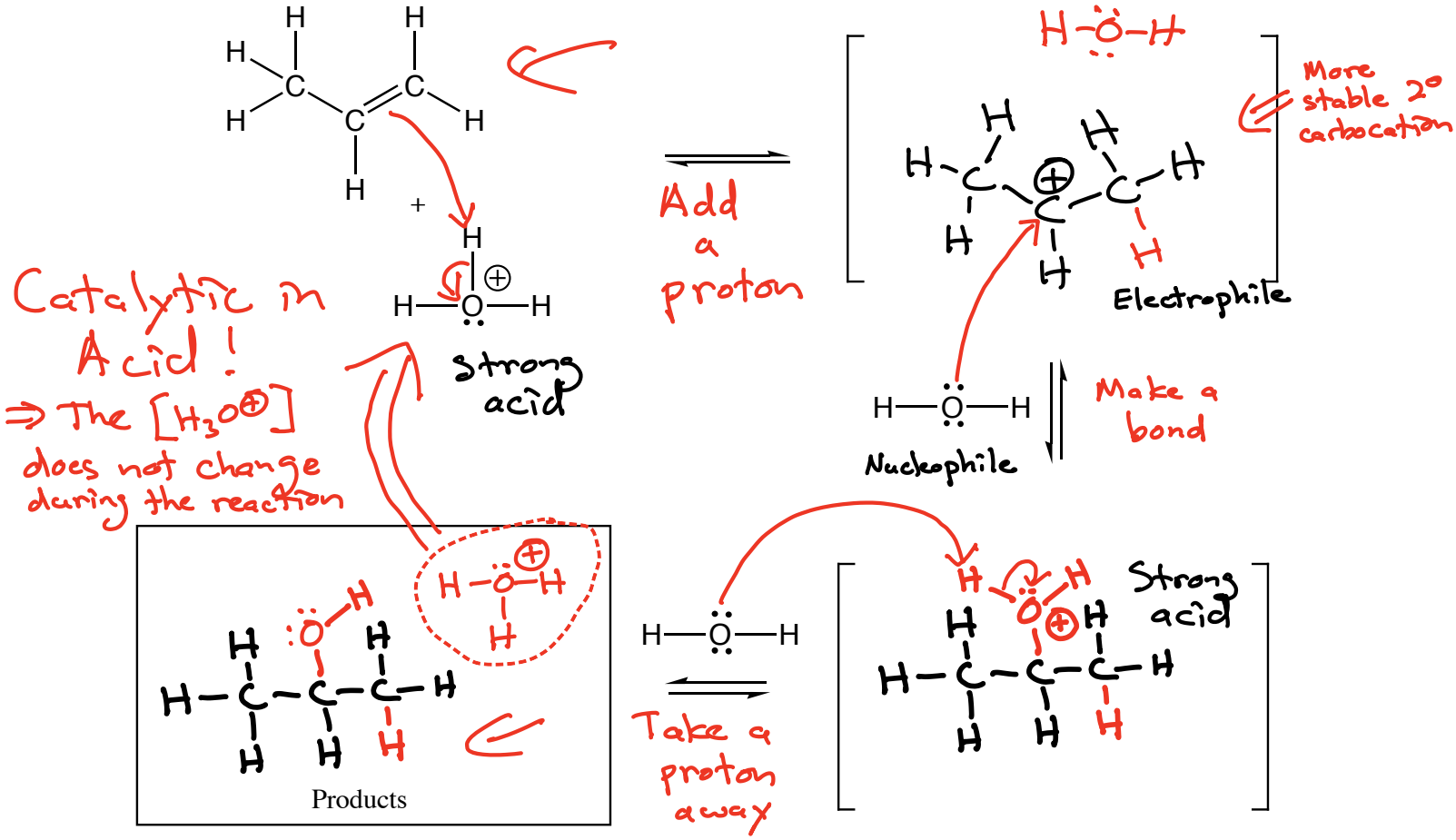




Flashback!!

Acid-catalyzed Hydration of an Alkene



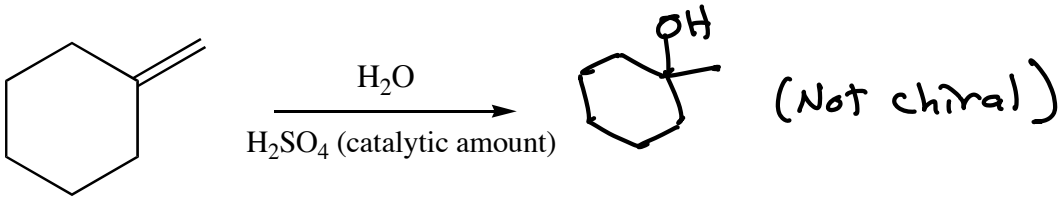


Summary: Proton adds to make a carbocation intermediate, water attacks to make a new bond, take a proton away to make the product alcohol. Catalytic in $H_3O^{\oplus}$

Regiochemistry: Markovnikov's Rule

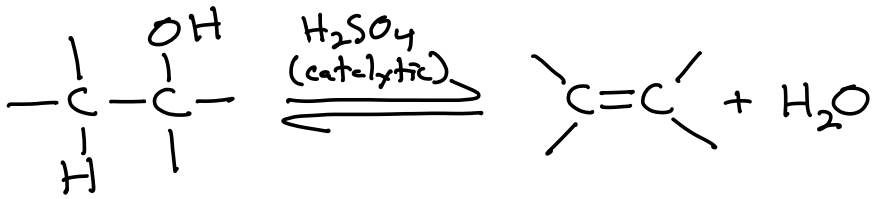
Stereochemistry: Mixed (time capsule)

Example:



-OH on more substituted C atom ⇒ Markovnikov's Rule

Microscopic Reversibility → Reversible reaction mechanisms have the same intermediates in both directions. → Compare the last two mechanisms!



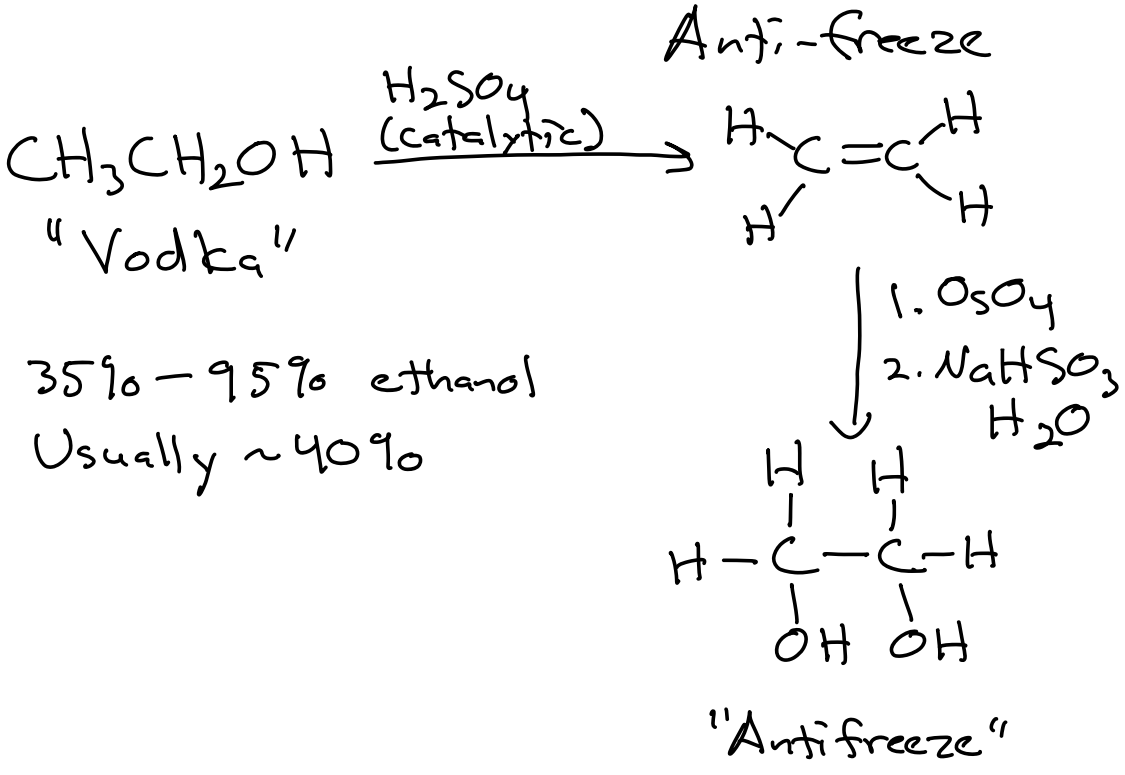
This reaction is REVERSIBLE!

Le Chatlier's Principle ⇒

If we add water → we drive the reaction to the alcohol product

If we remove the water as it is formed → we drive the reaction to the alkene product

Anti-freeze



35% – 95% ethanol

Usually ~40%

<u>Organic Chemistry</u> is the study of carbon-containing molecules.

This class has two points.

The first point of the class is to understand the organic chemistry of living systems. We will teach you how to think about and understand the most amazing things on the planet!!

Water is essential for life, you will learn why water has such special properties. 8/25/26

You will learn the secret structural reason proteins, the most important molecular machines in our bodies, can support the chemistry of life. 9/9/26

You will learn why when you take Advil for pain, exactly half of what you take works, and the other half does nothing.

You will learn how toothpaste works. 9/21/26 9/30/26

You will learn how a single chlorofluorocarbon refrigerant molecule released into the atmosphere can destroy many, many ozone molecules, leading to an enlargement of the ozone hole. 10/26/26

You will learn how medicines like Benadryl, Seldane, and Lipitor work. 11/9/26

You will learn how Naloxone is an antidote for an opioid overdose.

You will learn why Magic Johnson is still alive, decades after contracting HIV.

You will learn how MRI scans work.

The second point of organic chemistry is the synthesis of complex molecules from simpler ones by making and breaking specific bonds.

You will learn how to understand movies of reaction mechanisms like alkene hydration. 10/5/26

You will learn reactions that once begun, will continue reacting such that each product molecule created starts a new reaction until all the starting material is used up. 10/26/26

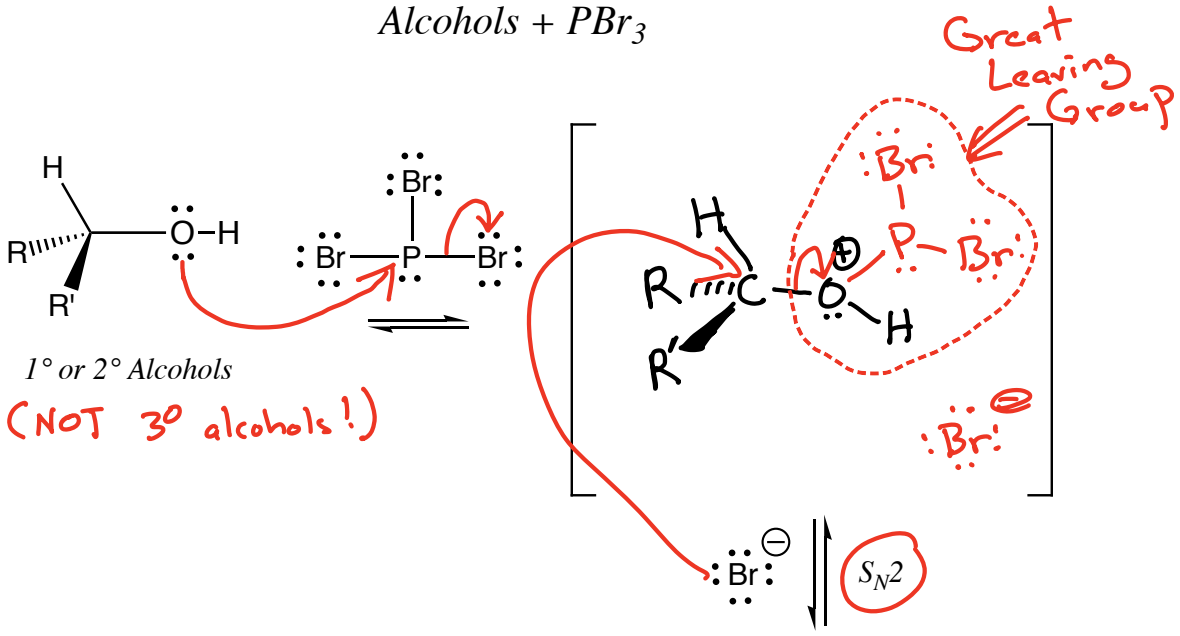
You will learn reactions that can make antifreeze from vodka. 11/9/26

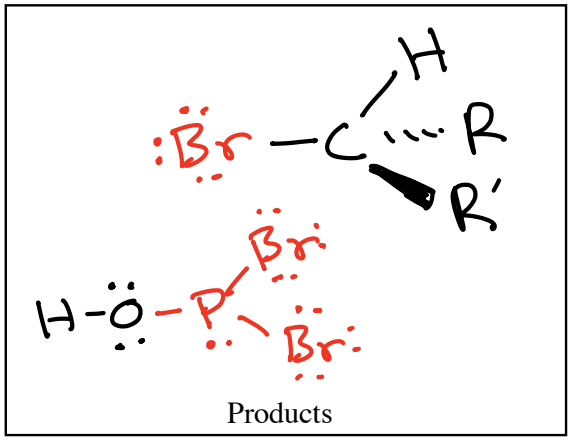
You will learn a reaction that can make nail polish remover from rubbing alcohol.

You will learn how to look at a molecule and accurately predict which atoms will react to make new bonds, and which bonds will break during reactions.

You will learn how to analyze a complex molecule's structure so that you can predict ways to make it via multiple reactions starting with less complex starting molecules.

Alcohols + PBr_3





Summary: 1° or 2° alcohols react with PBr_3 via an S_N2 reaction at the P atom to create a great leaving group that undergoes an S_N2 reaction with $Br^{\ominus}$ at the C atom

Regiochemistry:

Stereochemistry:

Example:

