



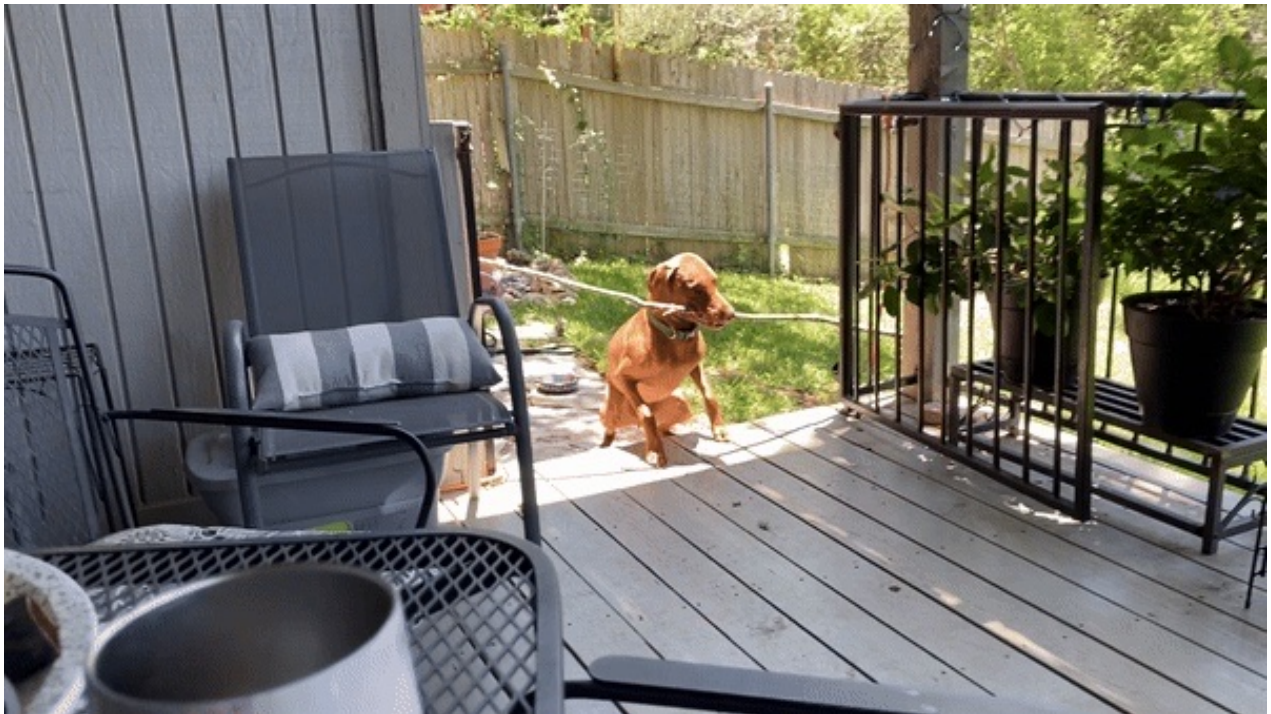
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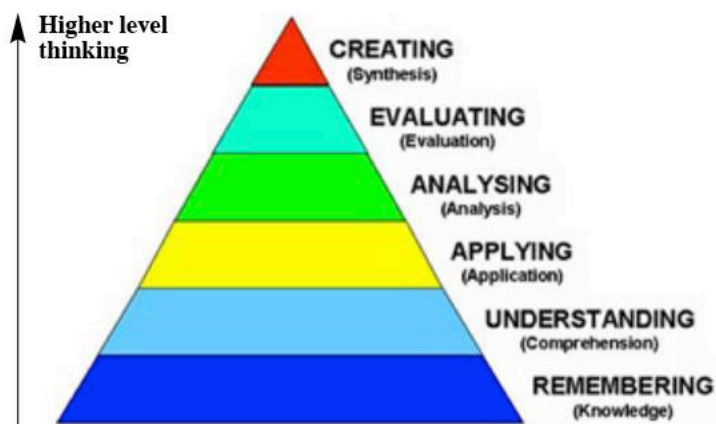


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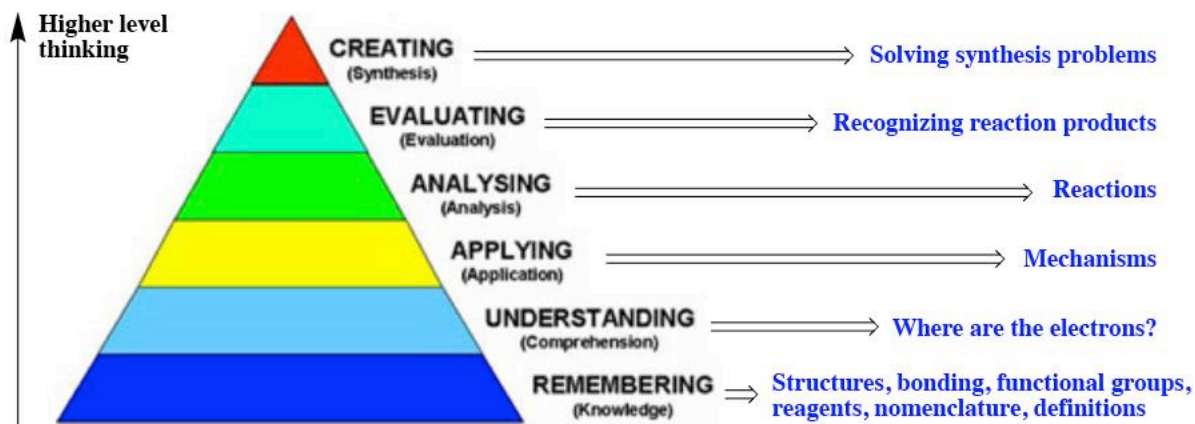


Bloom's Taxonomy of Learning



Bloom's Taxonomy of Learning

Organic Chemistry Analog

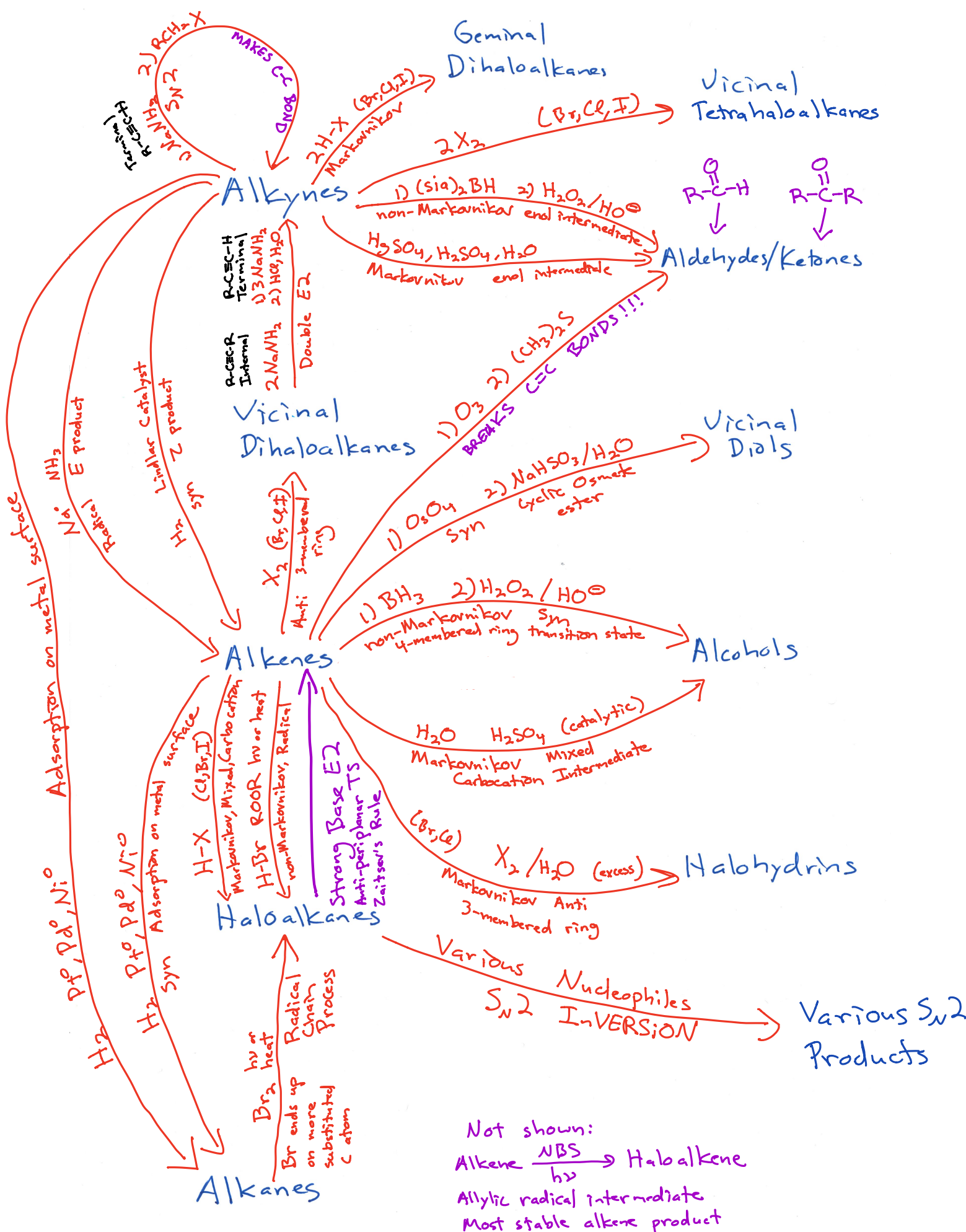


A) **You must have your entire roadmap learned** so you can recite the NIRRS parameters for each reagent, i.e. Nature of overall transformation ("locations" on the roadmap), the Intermediate or transition state (carbocation, anti-periplanar etc.), the Reagents and how to designate them, as well as any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

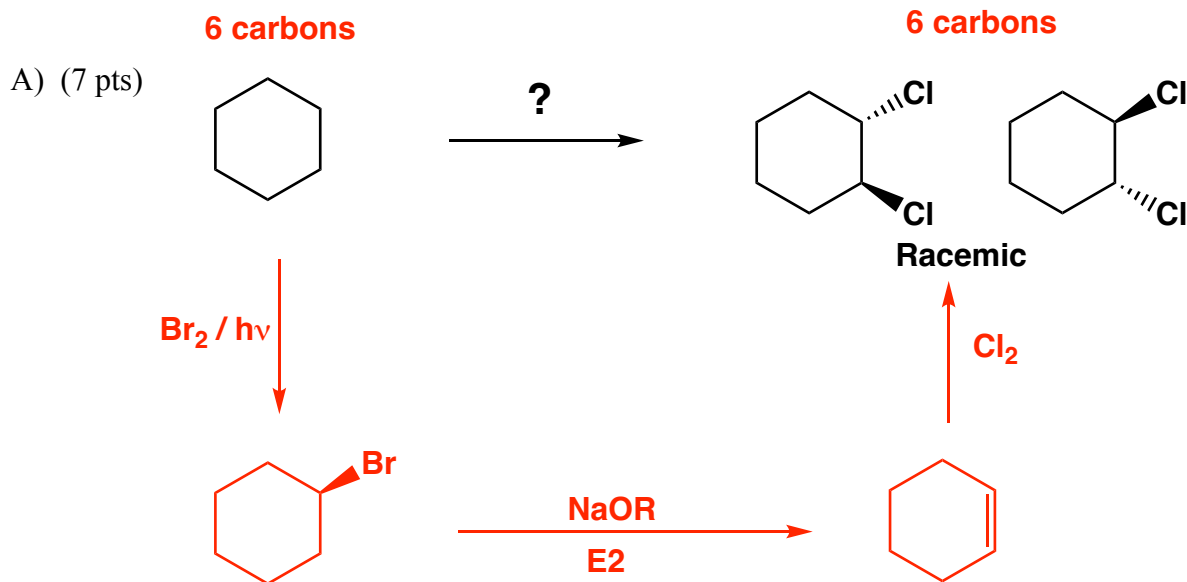
B) **Work backwards** (learn to RECOGNIZE the appropriate reagents and starting materials by looking at the products) from the final product. DO NOT try to work forward from the starting materials. Please trust me on this.

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.

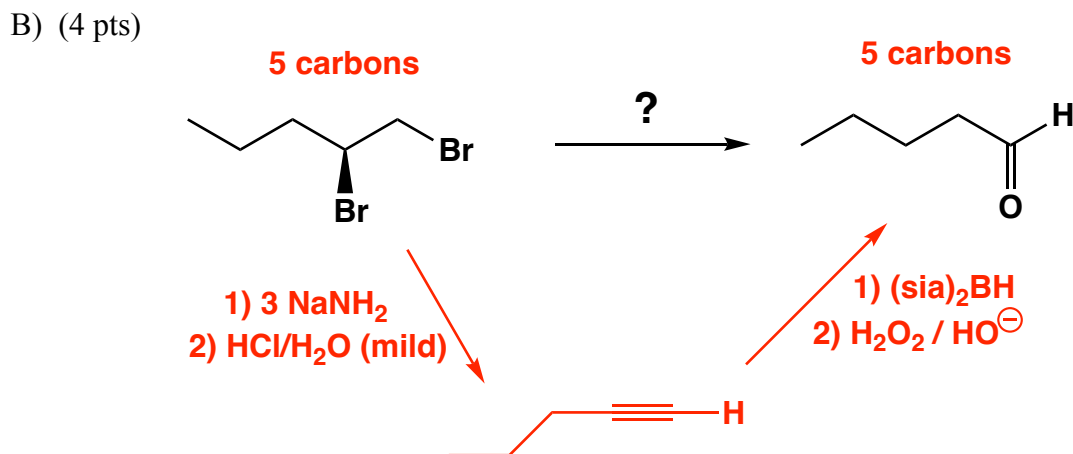
D) **Pretty much all synthesis problems in OChem 1 involve traveling "north or south" on the so-called "I-35"** reactions (alkanes SA, haloalkanes NB/SM, alkenes ATX, vicinal dihaloalkanes Waco, alkynes DFW) at least part way at some point during the synthesis. This is not a promise or a rule, just an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



20. These are synthesis questions. You need to show how the starting material can be converted into the product(s) shown. You may use any reactions we have learned provided that the product(s) you draw for each step is/are the predominant one(s). Show all the reagents you need. Show each molecule synthesized along the way and be sure to pay attention to the regiochemistry and stereochemistry preferences for each reaction. You must draw all stereoisomers formed, and use wedges and dashes to indicate chirality at each chiral center. Write racemic when appropriate. **All the carbons of the product must come from carbons of the starting material.**



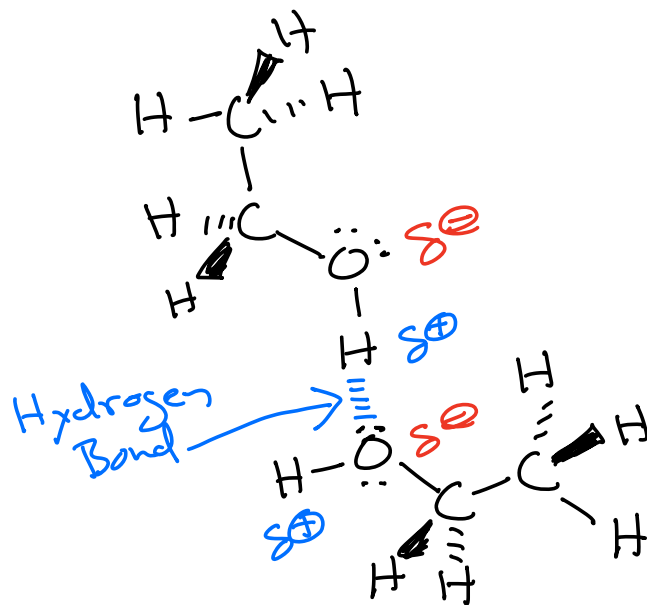
Recognize: The product is a *trans* dichlorocyclohexane that must result from the reaction of an alkene (cyclohexene) with Cl₂. **Recognize:** The cyclohexene comes from the usual “1-35” combination of halogenation of an alkane with light (the only reaction that uses an alkane starting material) followed by an E2 in strong base such as an alkoxide (NaOR).



Recognize: The product is an aldehyde that can be made from a primary alcohol, ozonolysis of an alkene (breaks carbon-carbon bond so not possible here) or from an alkyne. Choose the latter because an alkyne can be made from the starting vicinal dihaloalkane using base, in this case three equivalents of NaNH₂ followed by mild acid workup because the product is a terminal alkyne.



\hookrightarrow The O-H bond is very polar \Rightarrow Hydrogen bonds!



Consequences of Hydrogen Bonds \rightarrow
These molecules are "sticky"
 \Rightarrow 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
<u>CH₃OH</u>	Methanol	32	65	Infinite
<u>CH₃CH₃</u>	Ethane	30	-89	Insoluble
CH ₃ CH ₂ OH	Ethanol	46	78	Infinite
CH ₃ CH ₂ CH ₃	Propane	44	-42	Insoluble
CH ₃ CH ₂ CH ₂ OH	1-Propanol	60	97	Infinite
CH ₃ CH ₂ CH ₂ CH ₃	Butane	58	0	Insoluble
CH ₃ CH ₂ CH ₂ CH ₂ OH	1-Butanol	74	117	8 g/100 g
CH ₃ CH ₂ CH ₂ CH ₂ CH ₃	Pentane	72	36	Insoluble
HOCH ₂ CH ₂ CH ₂ CH ₂ OH	1,4-Butanediol	90	230	Infinite
CH ₃ CH ₂ CH ₂ CH ₂ CH ₂ OH	1-Pentanol	88	138	2.3 g/100 g
CH ₃ CH ₂ CH ₂ CH ₂ CH ₂ CH 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

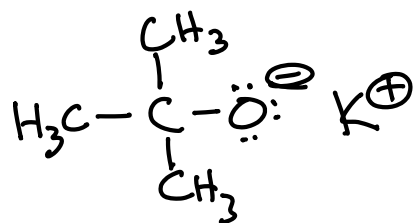
Table of Nucleophiles

<p>Strong Nucleophiles</p> <p>Br^-, I^-, R-S^-, H-S^-, $\text{N}\equiv\text{C}^-$, N_3^-</p> <p>$\text{R-C}\equiv\text{C}^-$, R-O^-, H-O^- Strong Bases</p>
<p>Medium Nucleophiles</p> <p>R-CO_2^-, R-S-H, R_2S, NH_3, RNH_2, R_2NH, NR_3</p>
<p>Weak Nucleophiles</p> <p>$\text{R-CO}_2\text{H}$, R-O-H, H_2O Very Weak Bases</p>

Used as solvents!

Special Case

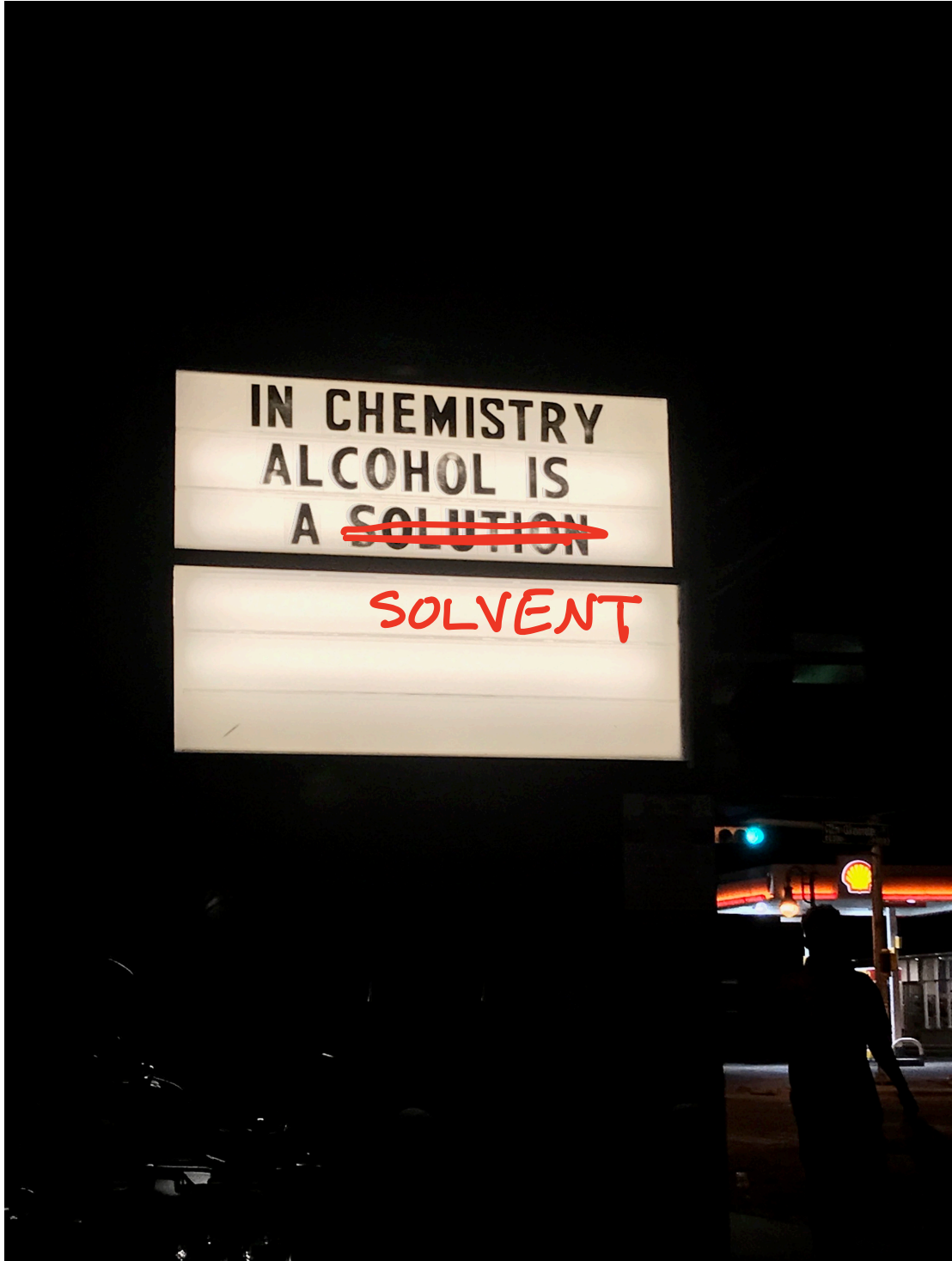
Tert-Butoxide (tBuO^-) is a strong base, but is not a nucleophile due to steric hindrance.



" KOtBu "
or
" tBuO^- "

IN CHEMISTRY
ALCOHOL IS
A ~~SOLUTION~~

SOLVENT



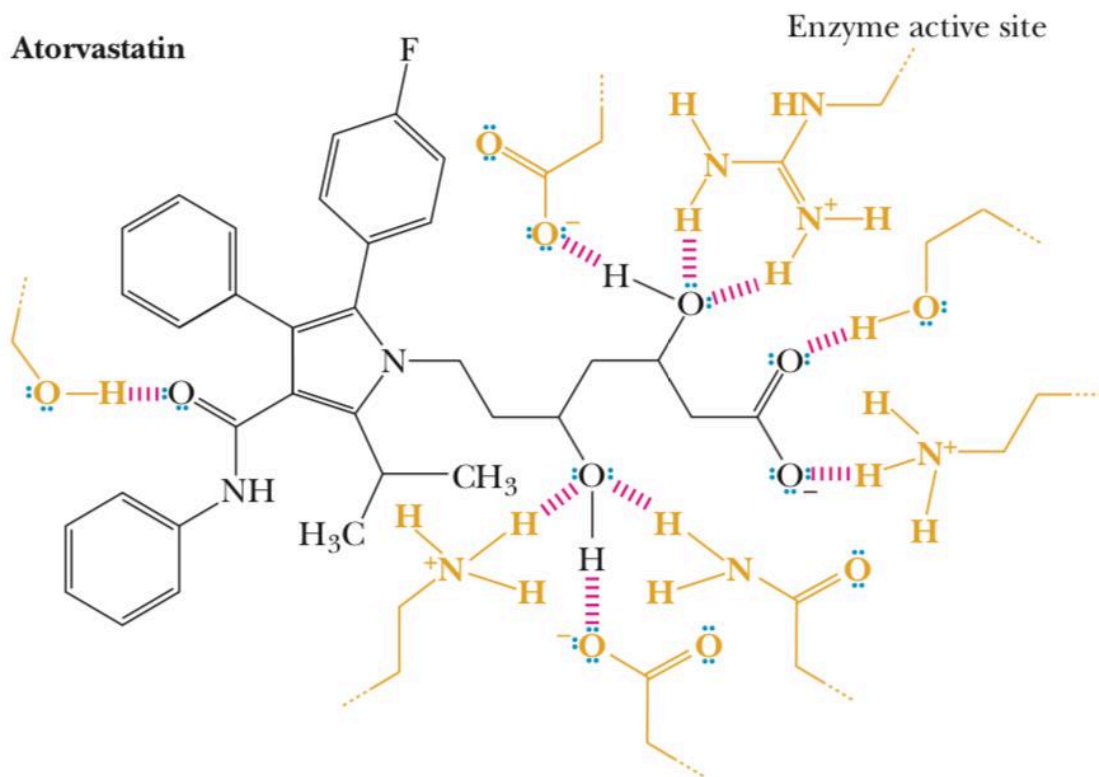


Figure 2

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

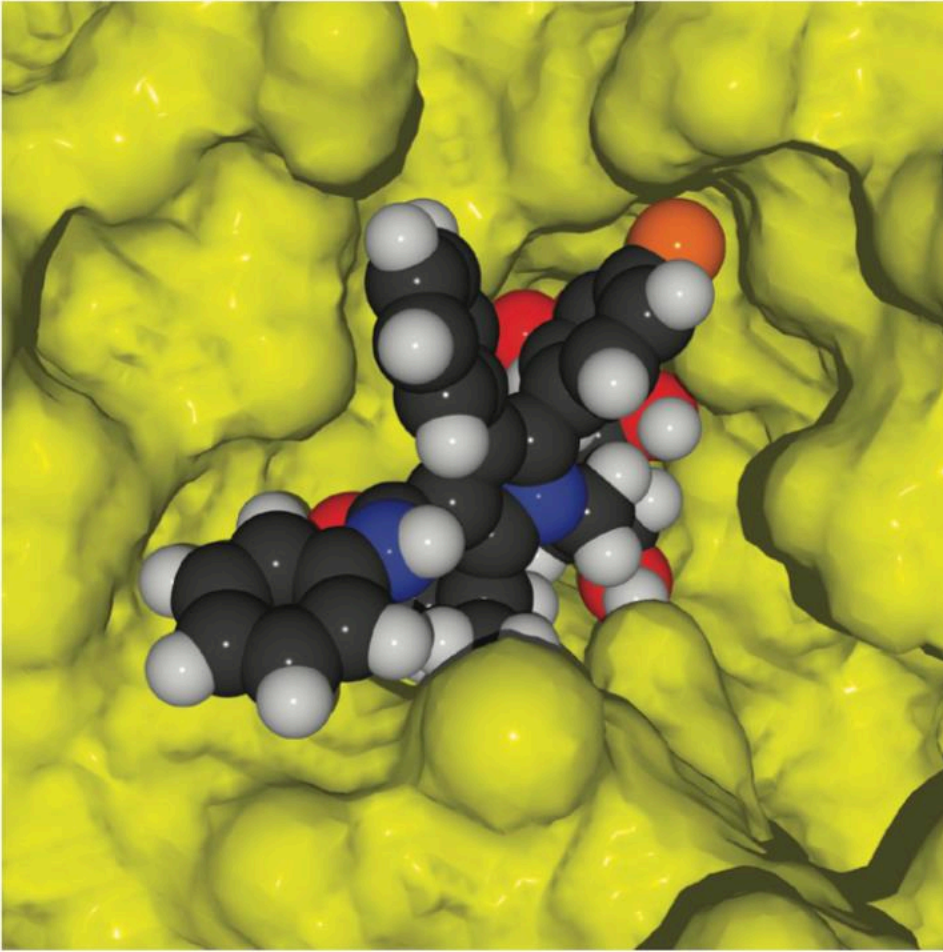


Figure 1

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

Organic Chemistry 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. 8/25/2022

You will learn the secret structural reason proteins, the most important molecular machines in our bodies, can support the chemistry of life. 9/6/22

You will learn why when you take Advil for pain, exactly half of what you take works, and the other half does nothing. 9/20/22

You will learn how toothpaste works. 9/29/22

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. 10/27/22

You will learn how medicines like Benadryl, Seldane, and Lipitor work. 11/10/22

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. 10/4/22

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. 10/27/22

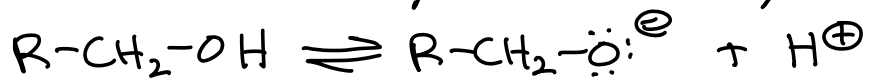
You will learn reactions that can make antifreeze from vodka. 11/10/22

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 \rightarrow Acidity and Basicity



$pK_a \cong 16-17$

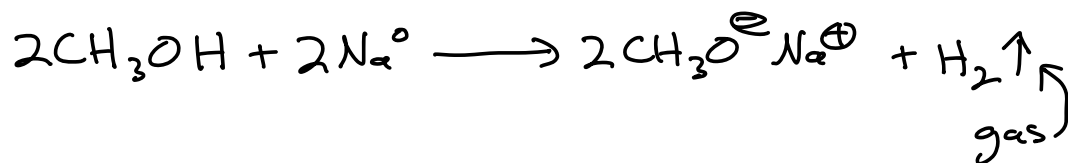
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Strong Base



$pK_a \cong 8-12$

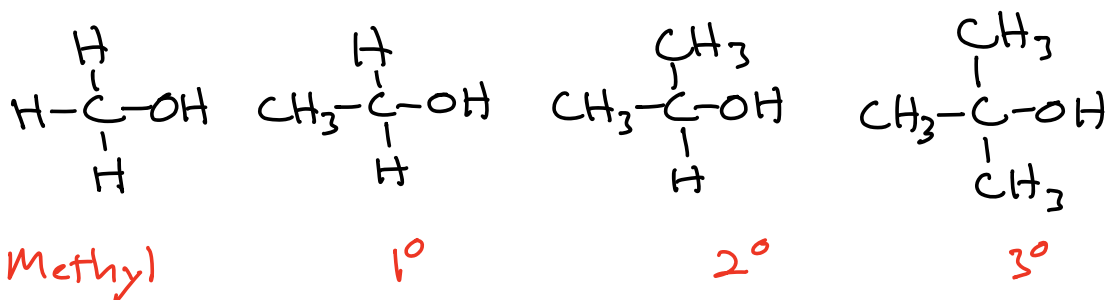
\uparrow
Weaker base

Notice This $\rightarrow \text{Na}^{\circ}, \text{K}^{\circ}, \text{Li}^{\circ}$



\rightarrow Useful to make alkoxides!

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



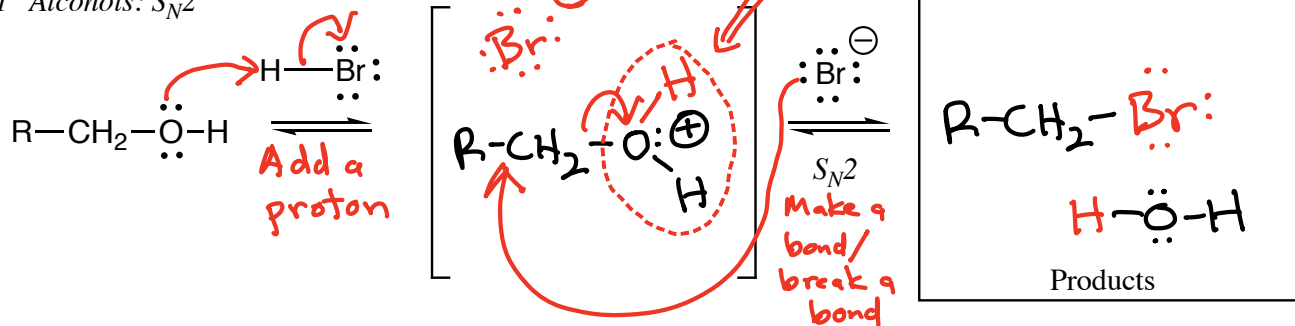
★ The -OH is not a leaving group but several reactions involve conversion of the -OH group into a good leaving group

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

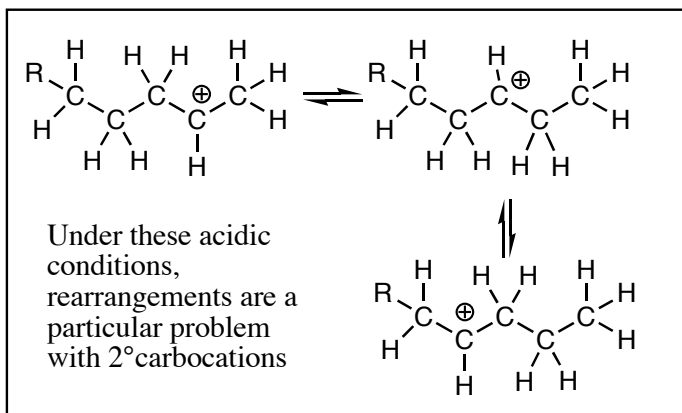
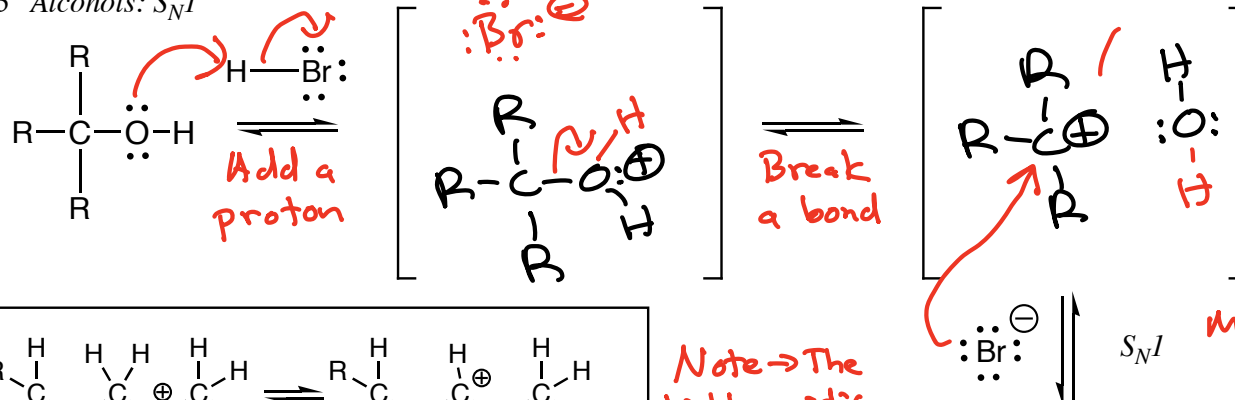


Alcohols + H-X Good leaving group

1° Alcohols: S_N2



2°/3° Alcohols: S_N1

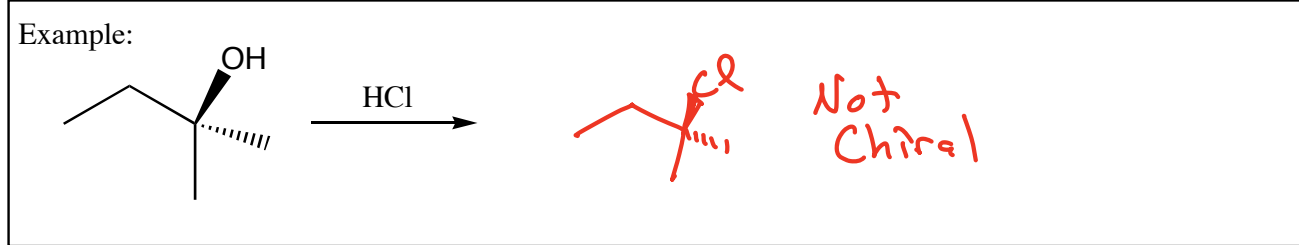


Note → The highly acidic nature of this reaction prevents any E1 before the S_N1 is finished

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

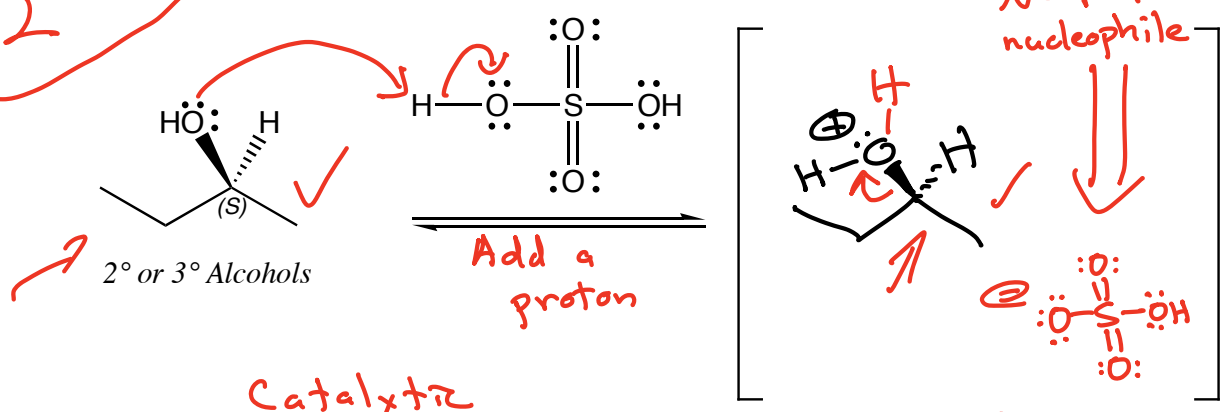
Regiochemistry: N/A

Stereochemistry: Chiral tertiary alcohols give scrambled products ← S_N1

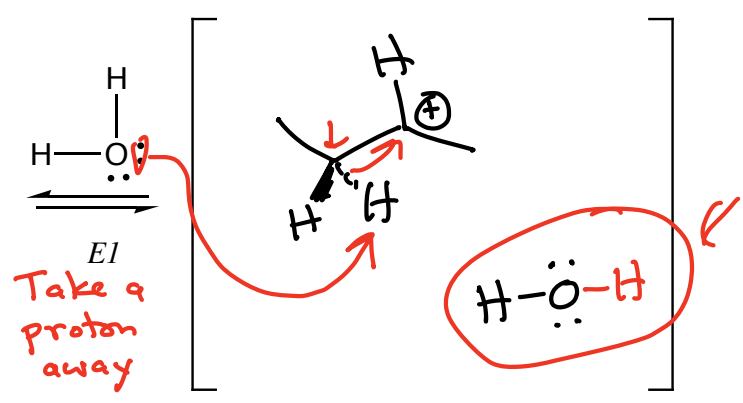
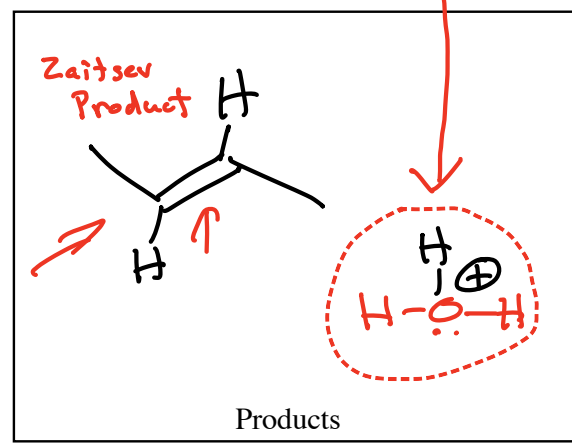


1° alcohols react via E2

2° or 3° Alcohol Dehydration → E1



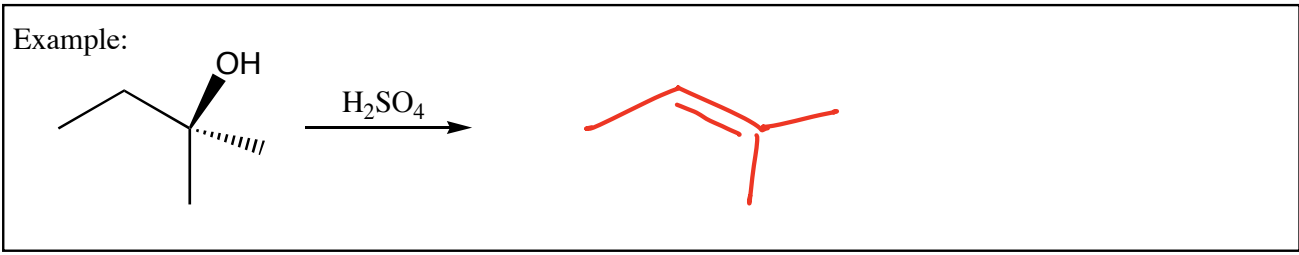
Catalytic in acid



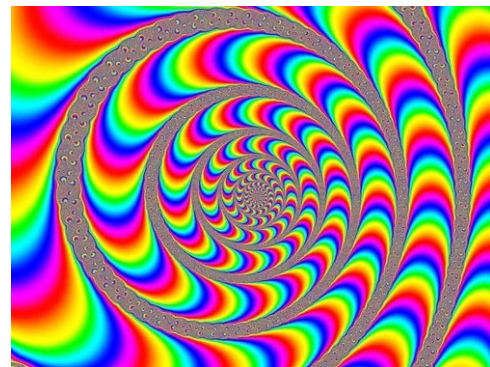
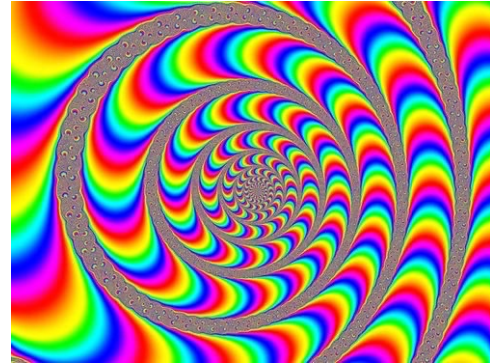
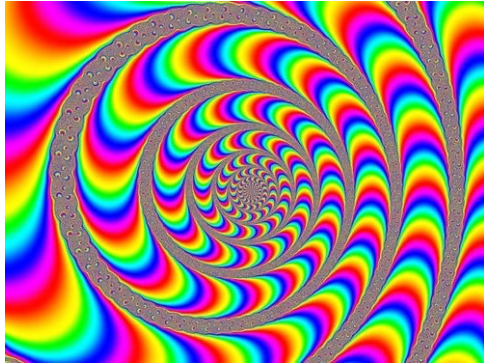
Summary: The OH group is protonated in strong acid to make a good leaving group, water, which breaks a bond to give a carbocation that has a proton taken away to give the product alkene

Regiochemistry: Zaitsev's Rule

Stereochemistry: N/A

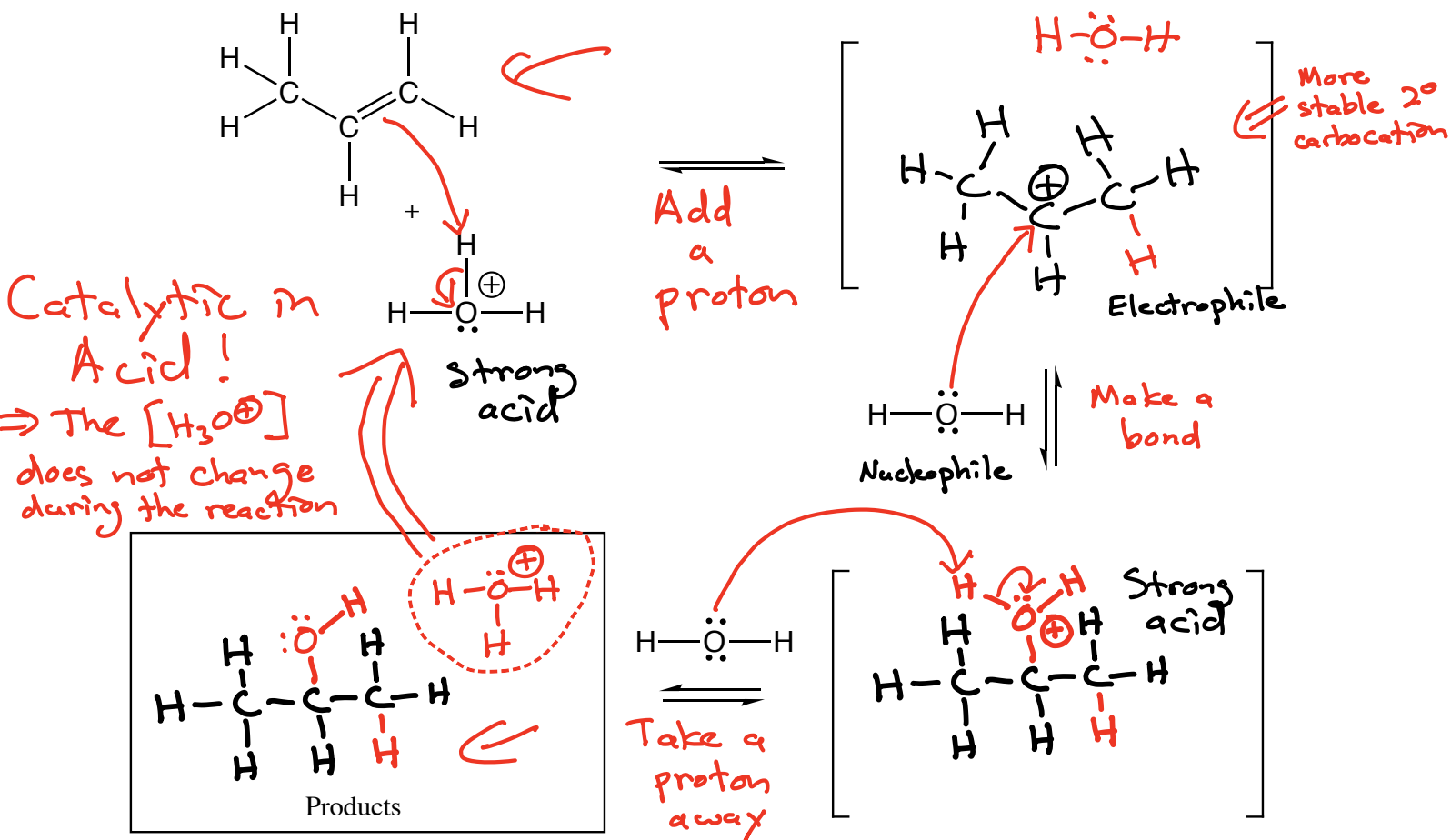
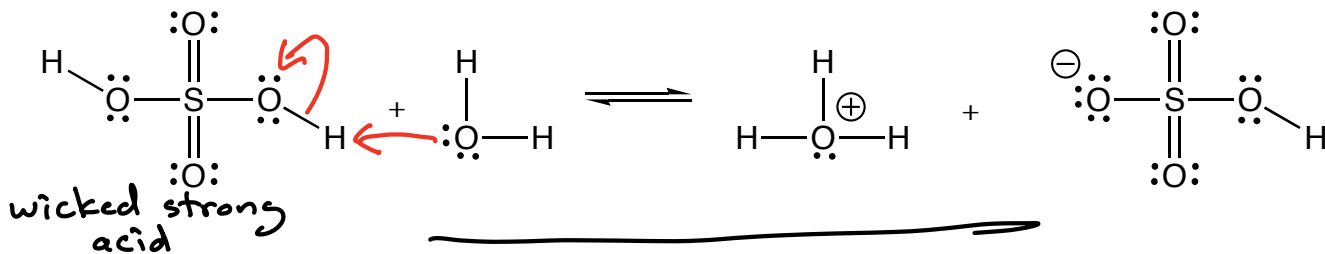


Flashback!!



Flashback!!

Acid-catalyzed Hydration of an Alkene

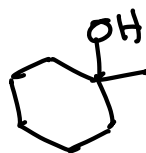
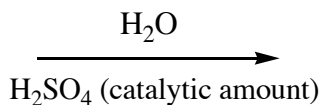
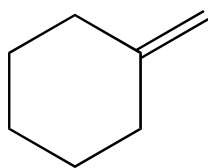


Summary: Proton adds to make a carbocation intermediate, water attacks to make a new bond, take a proton away to make the product alcohol. Catalytic in H_3O^+

Regiochemistry: Markovnikov's Rule

Stereochemistry: Mixed (time capsule)

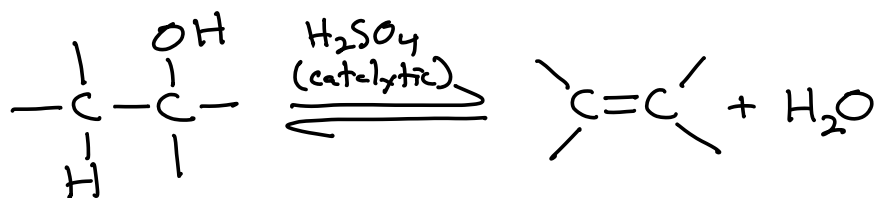
Example:



(Not chiral)

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

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

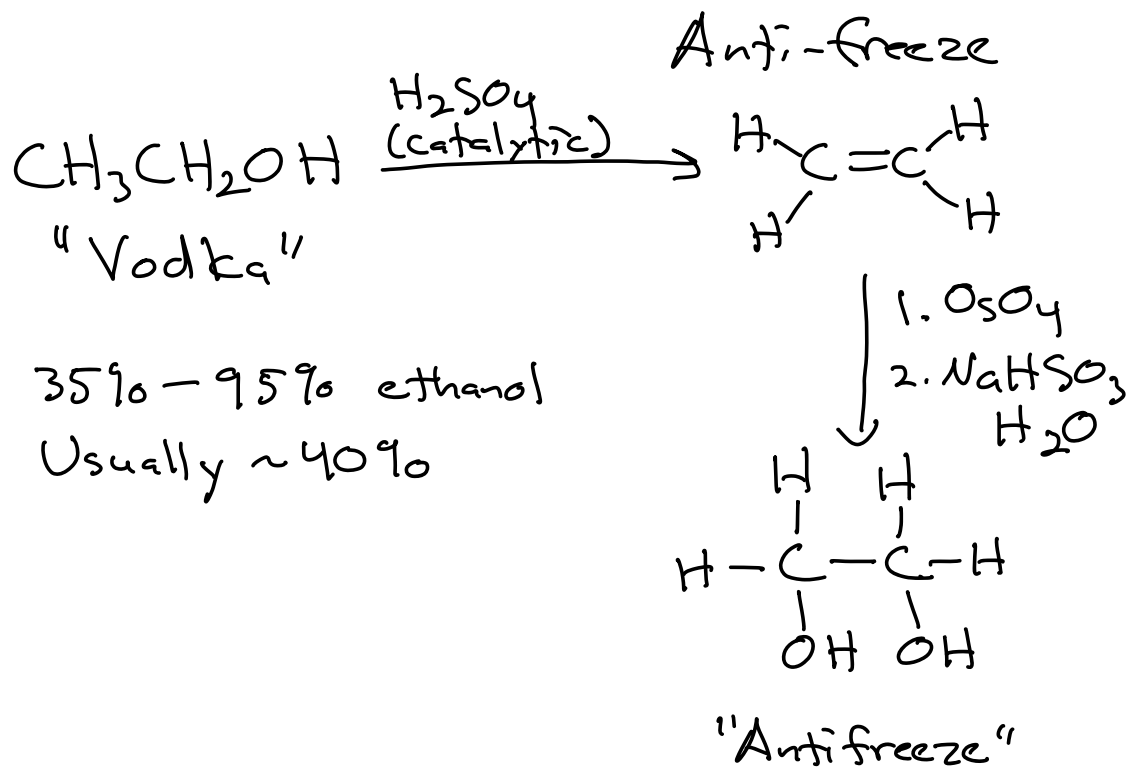


This reaction is **REVERSIBLE!**

Le Chatlier's Principle \Rightarrow

If we add water \rightarrow we drive the reaction to the alcohol product

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



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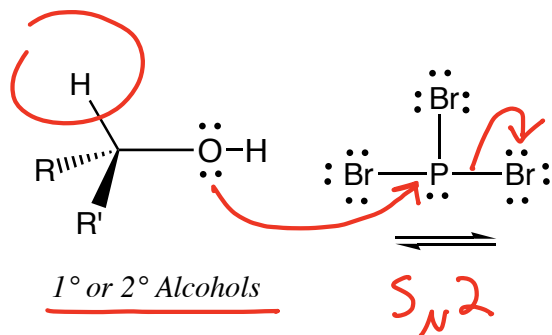
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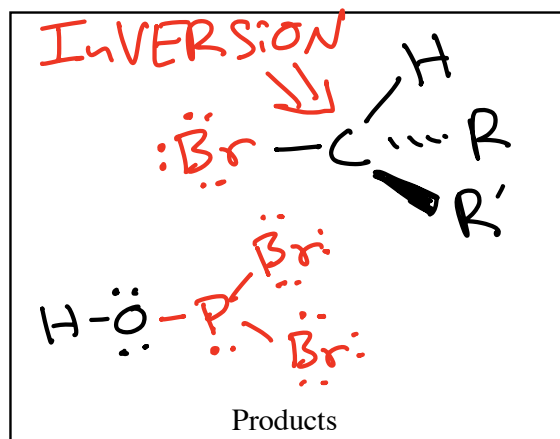
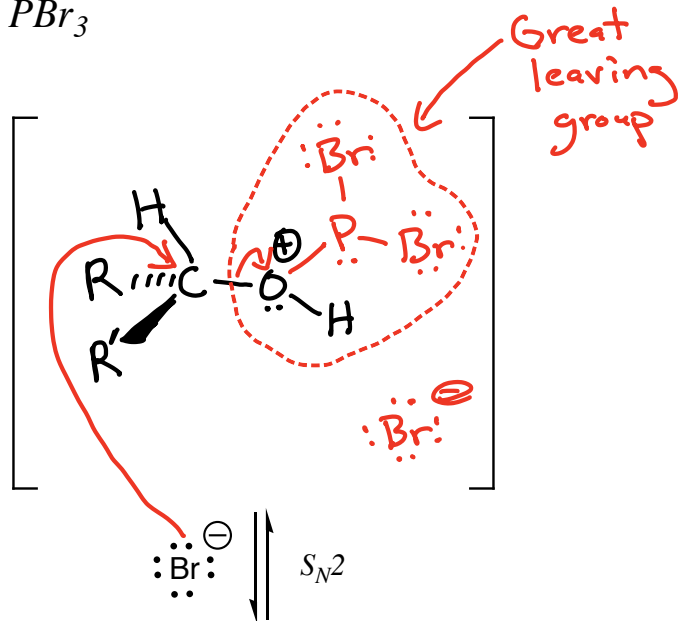
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Alcohols + PBr₃



Does NOT work with 3° alcohols



Summary:

Regiochemistry:

Stereochemistry:

Example:

