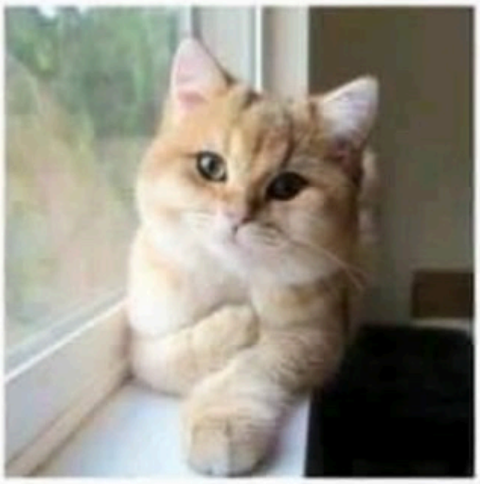


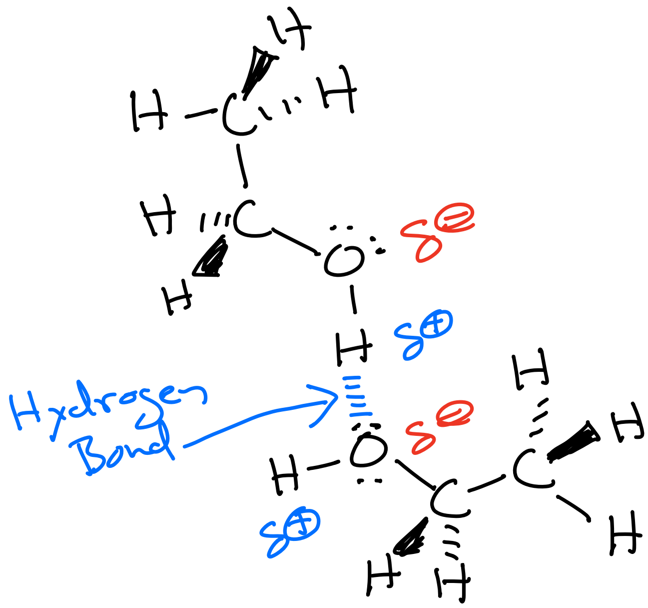
ions

are

sitive

Alcohols → $R{-}\ddot{O}{-}H$

↳ 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

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

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

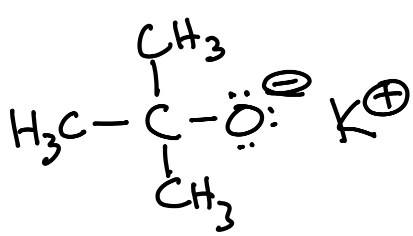
Weak Nucleophiles

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

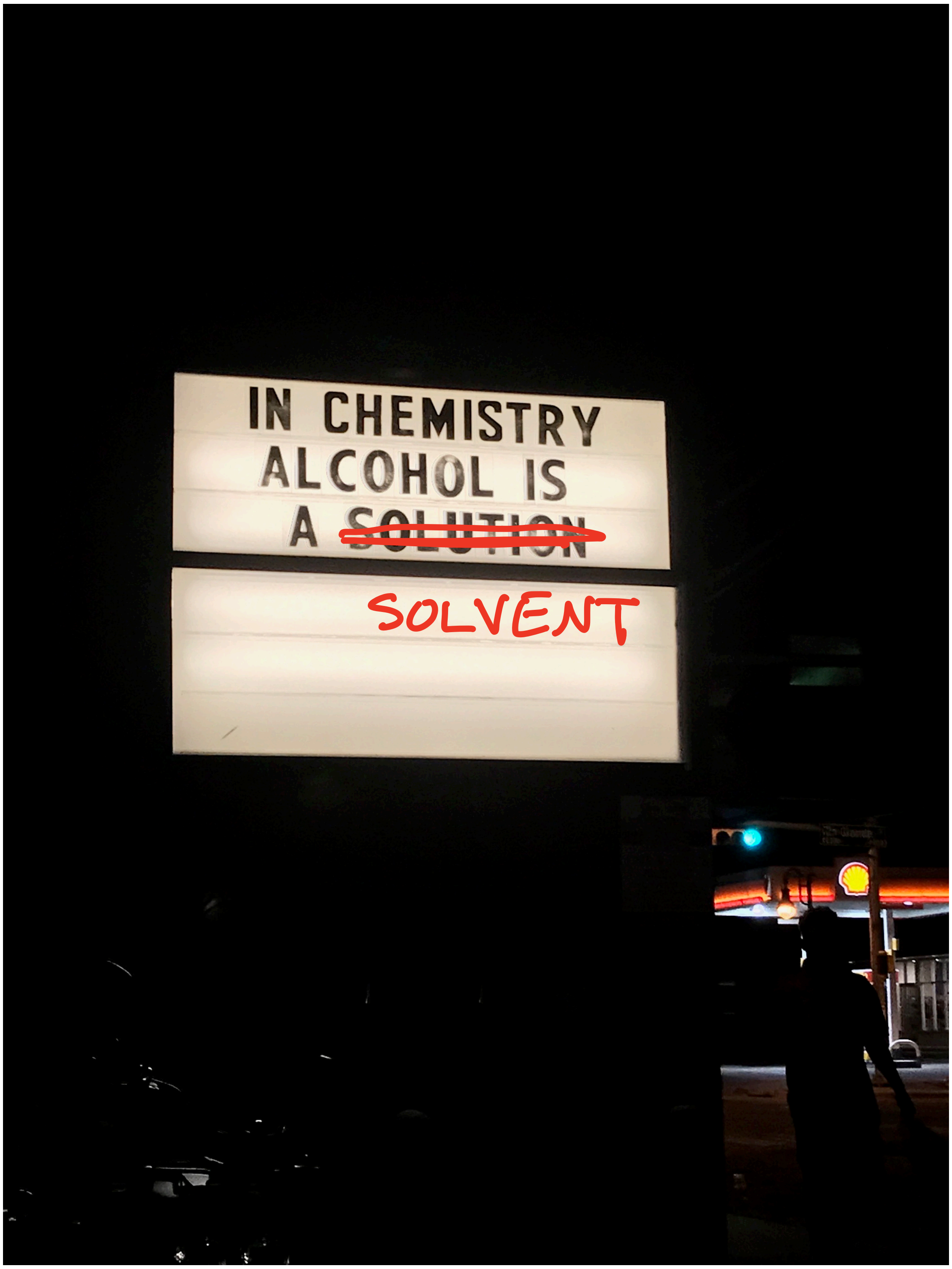
Used as solvents!

Special Case

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



"KOtBu"
or
"$tBuO^{\ominus}$"


IN CHEMISTRY
ALCOHOL IS
A ~~SOLUTION~~
SOLVENT

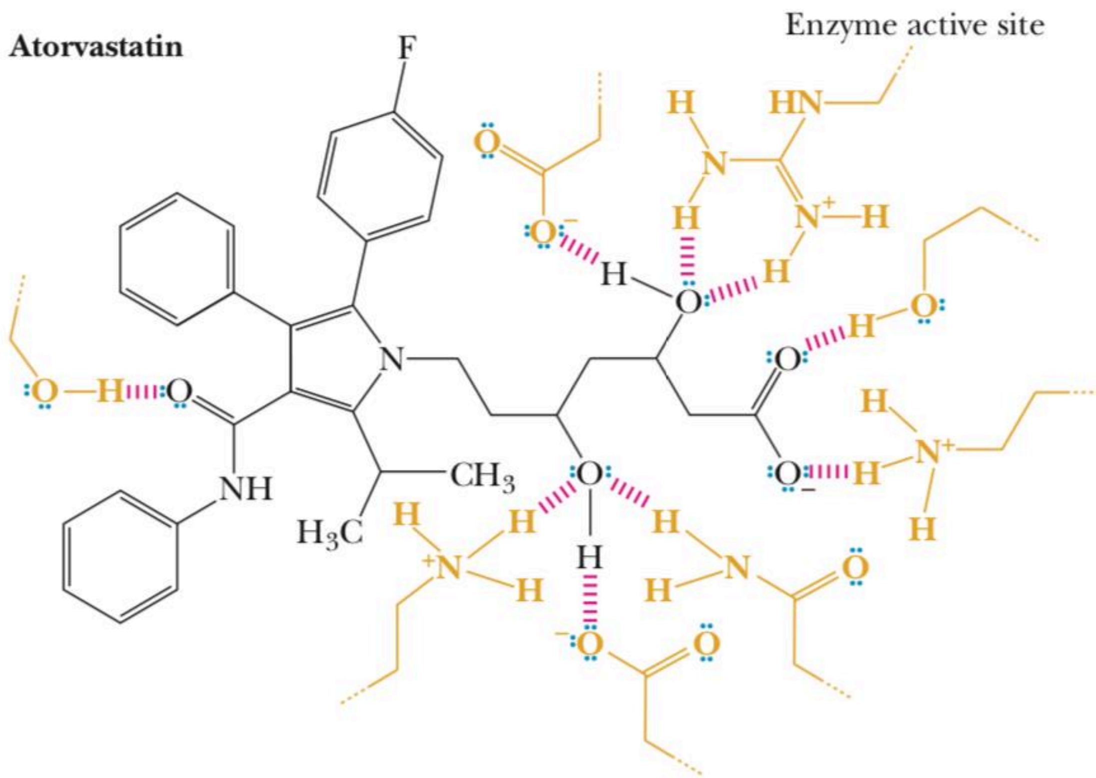


Figure 2

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

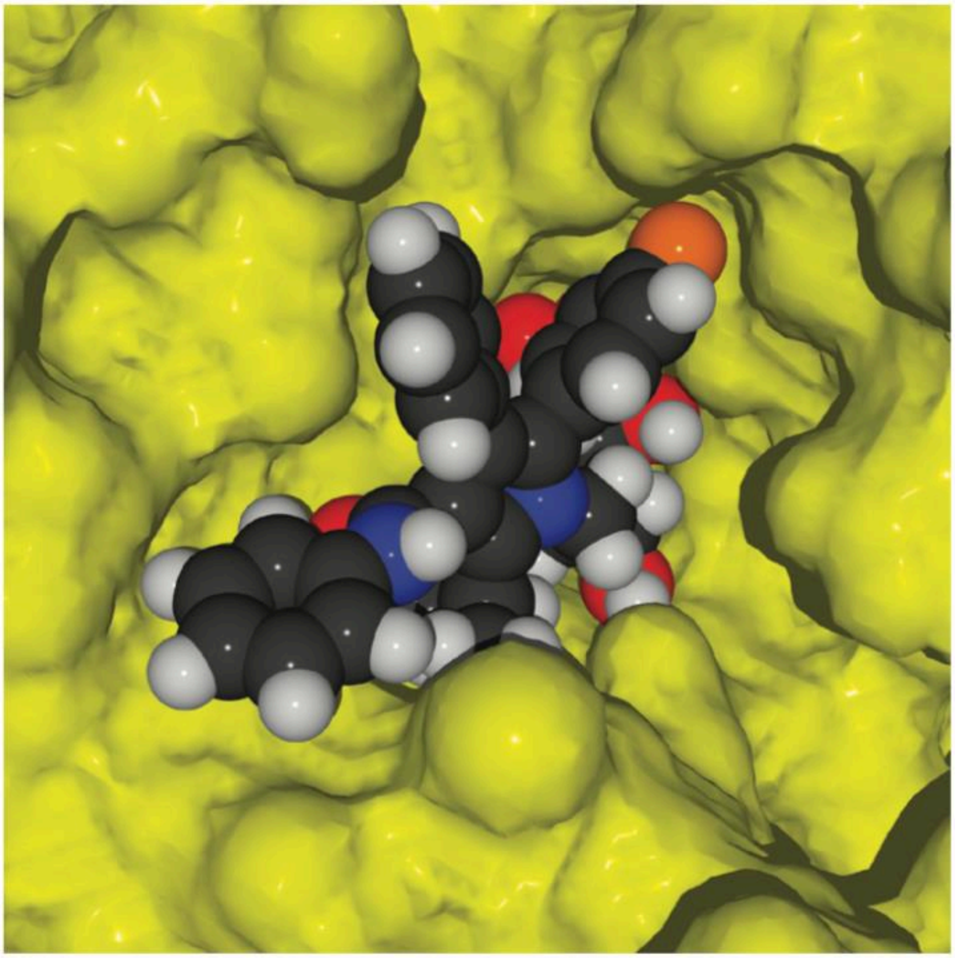


Figure 1
A space-filling model of the cholesterol-lowering drug atorvastatin (Lipitor) bound to the active site of its enzyme target HMG-CoA reductase (shown as a yellow surface). The shape of the drug is complementary to the active site of the enzyme.

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

<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. 8/25/2022

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 → Acidity and Basicity

$$R-CH_2-OH \rightleftharpoons R-CH_2-\ddot{\underset{..}{O}}:^{\ominus} + H^{\oplus}$$

$pK_a \cong 16-17$

Strong Base

$$R-CH_2-SH \rightleftharpoons R-CH_2-\ddot{\underset{..}{S}}:^{\ominus} + H^{\oplus}$$

$pK_a \cong 8-12$

Weaker base

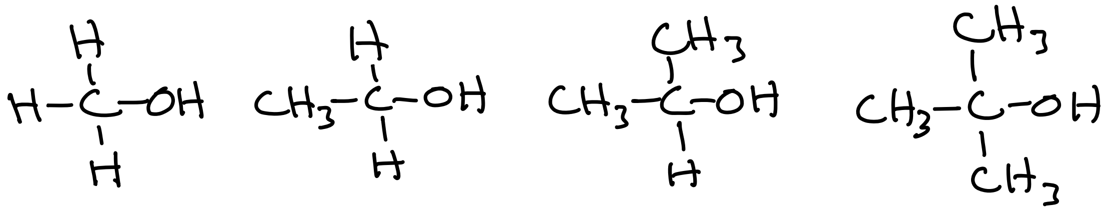
<u>Notice This</u> → $Na^{\circ}, K^{\circ}, Li^{\circ}$

$$2CH_3OH + 2Na^{\circ} \longrightarrow 2CH_3O^{\ominus}Na^{\oplus} + H_2\uparrow$$

gas

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°

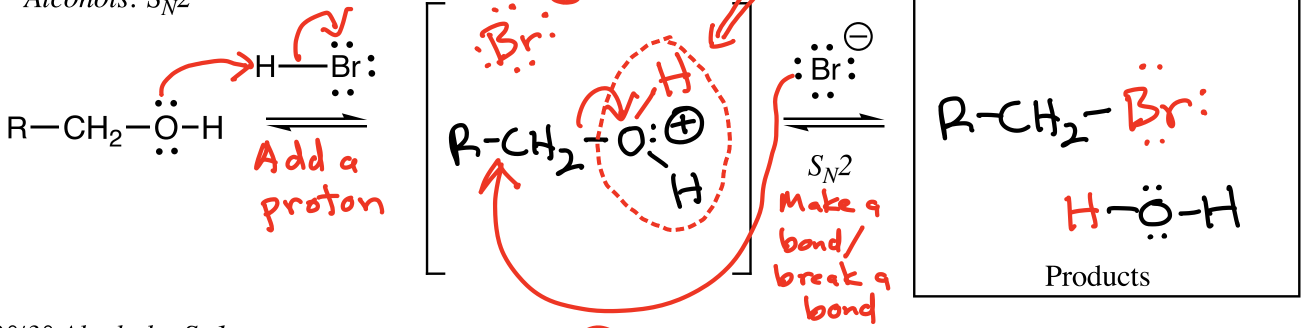
☆ The -OH is not a leaving group but several reactions involve conversion of the -OH group into a good leaving group

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

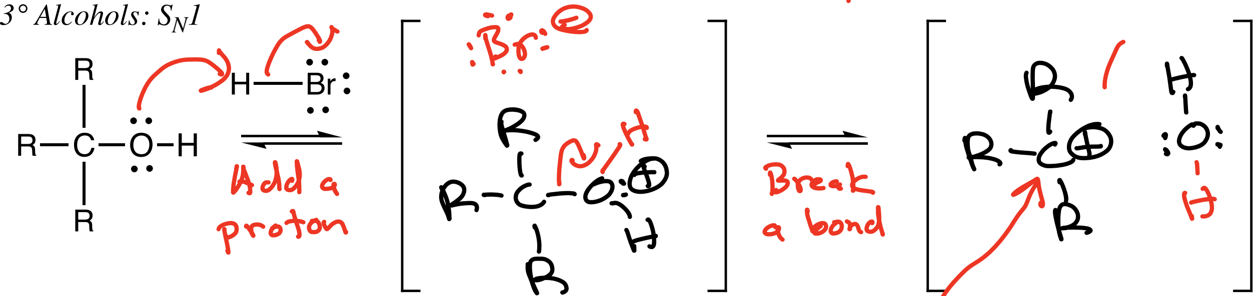
X = Cl, Br, I

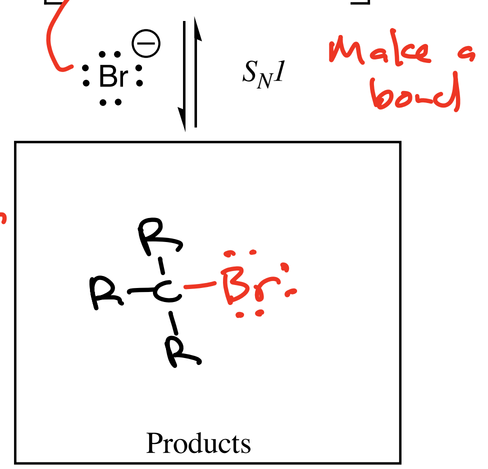
Alcohols + H-X

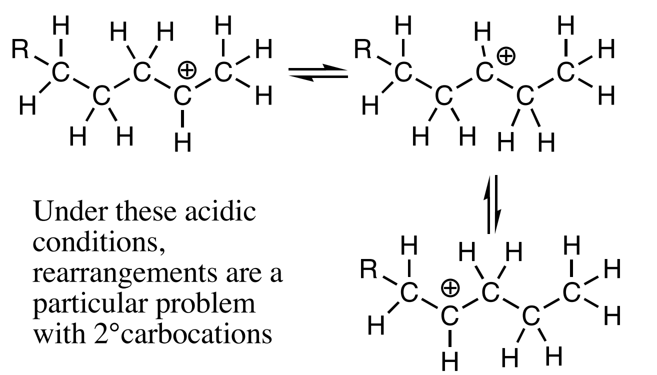
1° Alcohols: S_N2



2°/3° Alcohols: S_N1







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

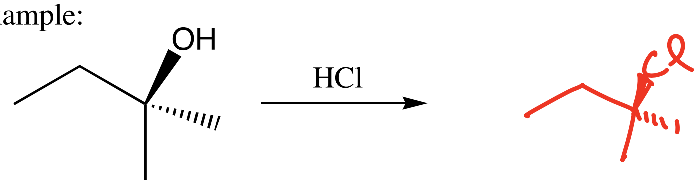
Note → The highly acidic nature of this reaction prevents any E1 before the S_N1 is finished

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

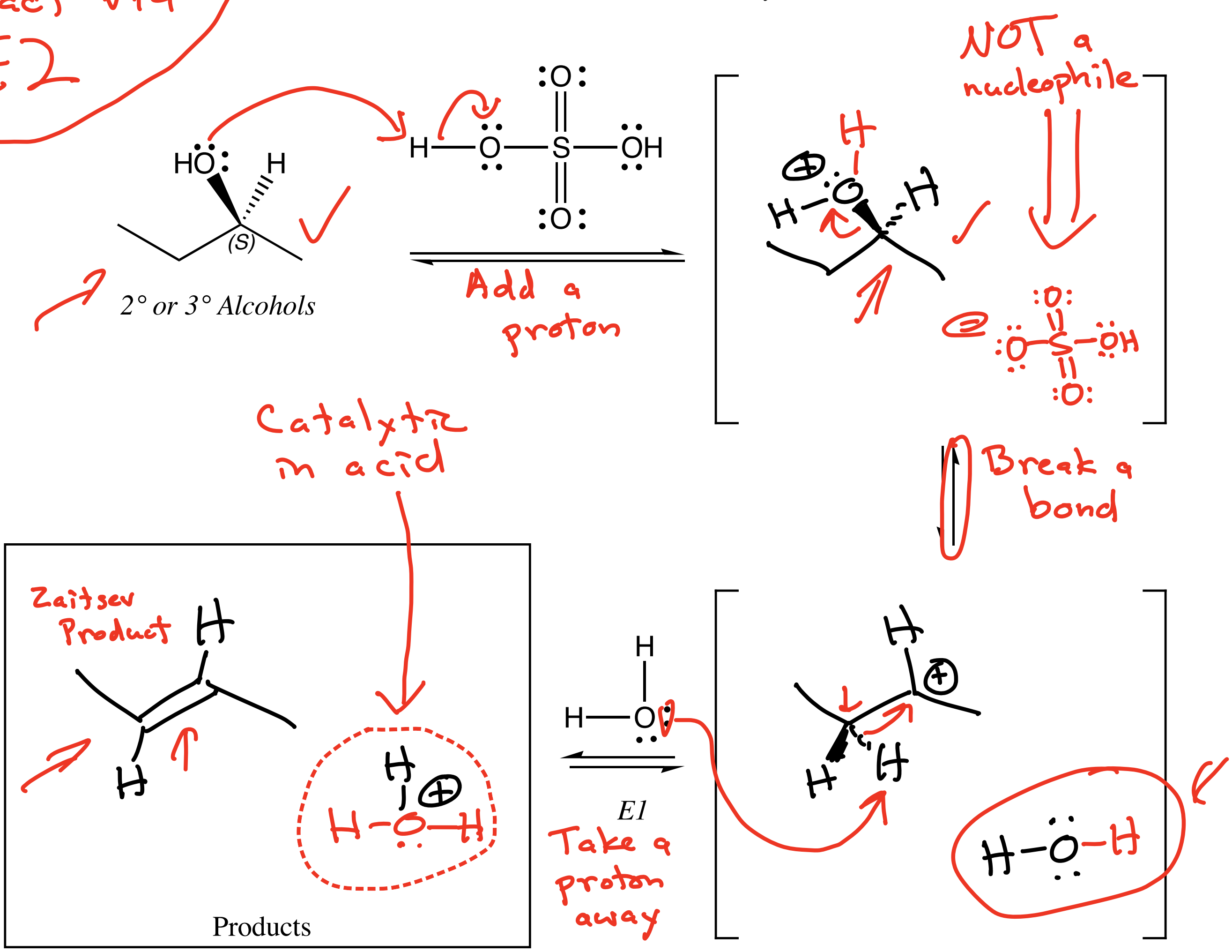
Example:



Not Chiral

1° alcohols react via E2

2° or 3° Alcohol Dehydration → E1

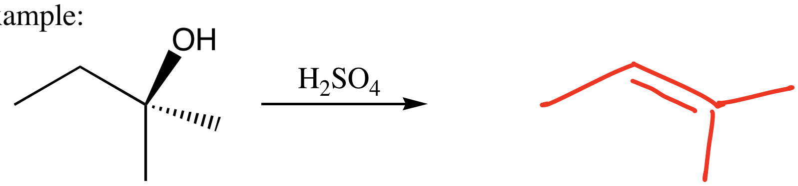


Summary: The OH group is protonated in strong acid to make a good leaving group, water, which breaks a bond to give a carbocation that has a proton taken away to give the product alkene

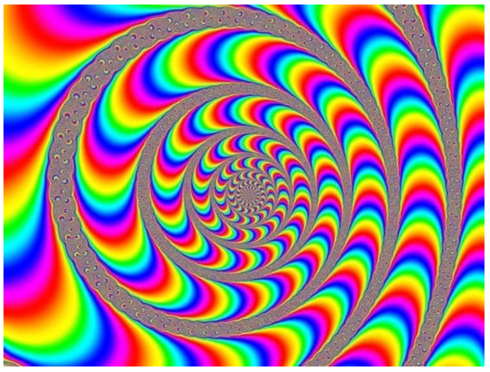
Regiochemistry: Zaitsev's Rule

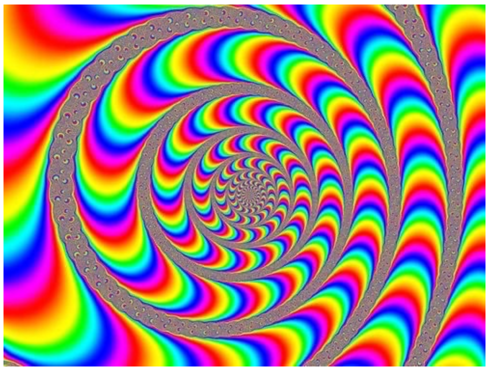
Stereochemistry: N/A

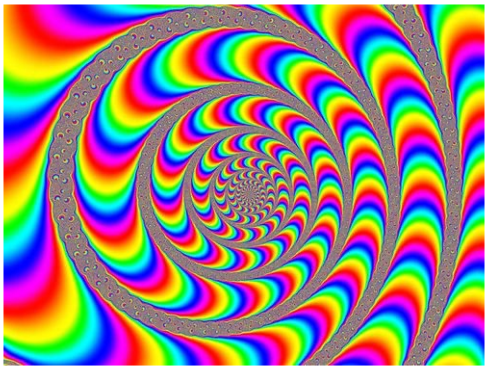
Example:

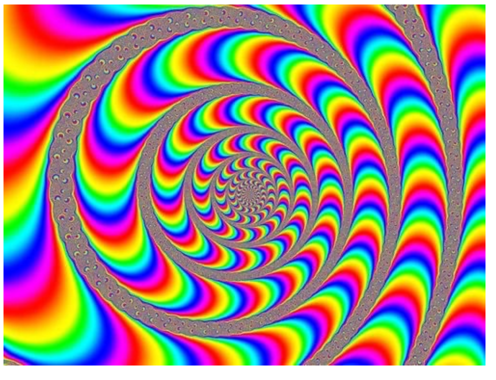


Flashback!!



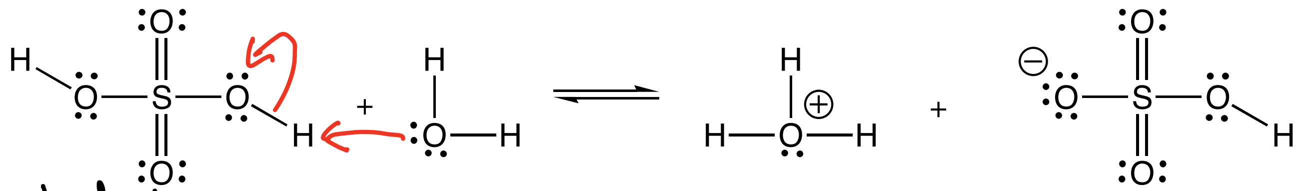




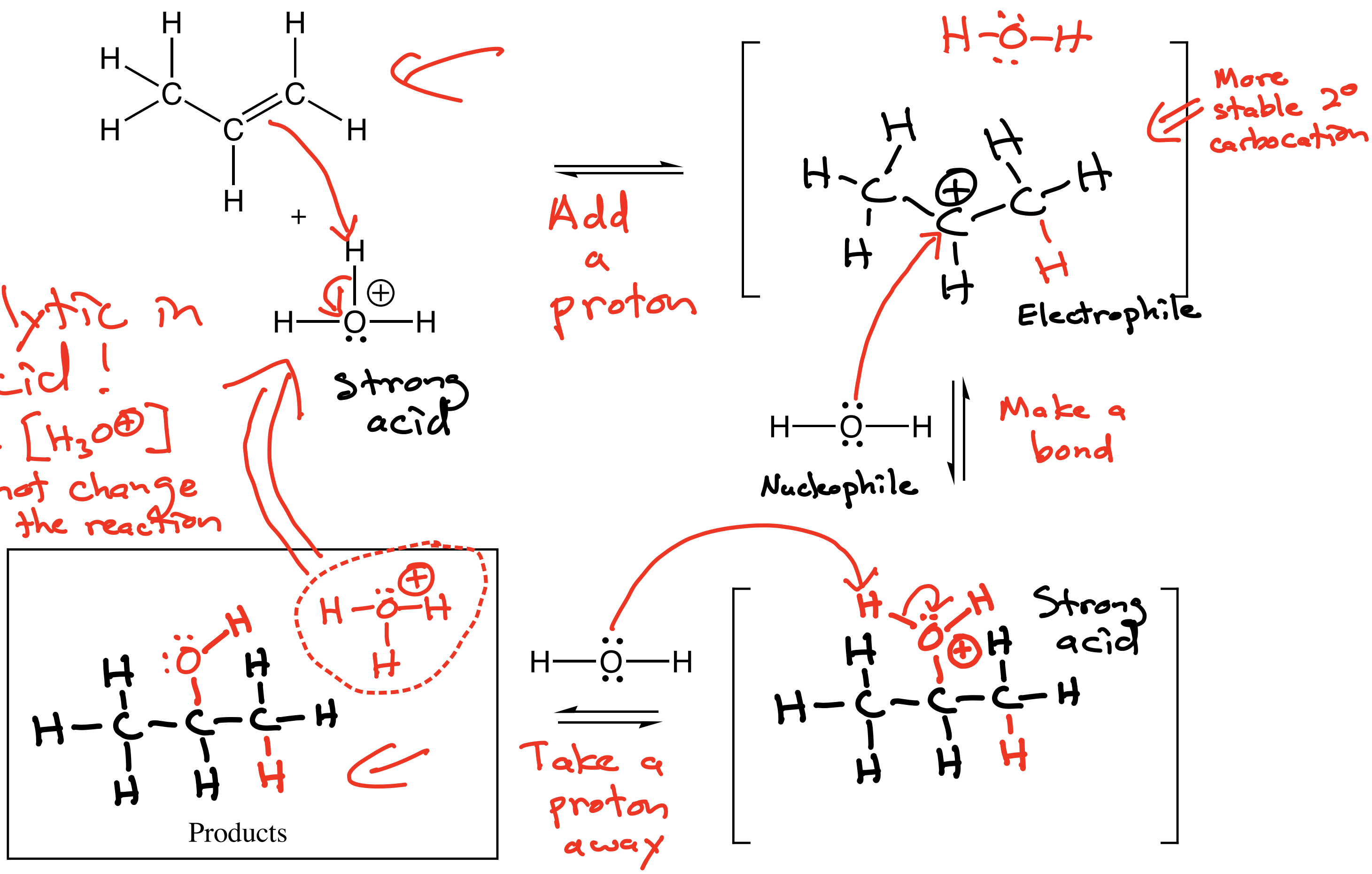


Flashback!!

Acid-catalyzed Hydration of an Alkene



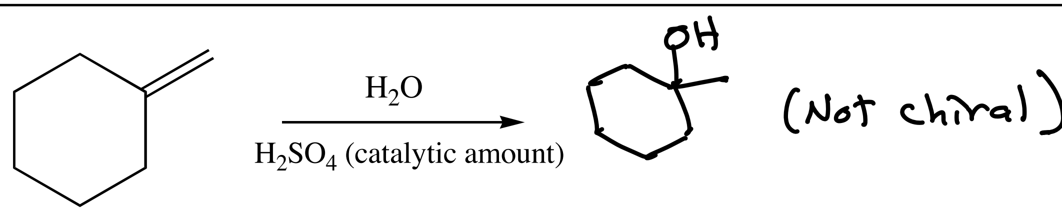
wicked strong acid



Catalytic in Acid!
⇒ The [$H_3O^{\oplus}$] does not change during the reaction

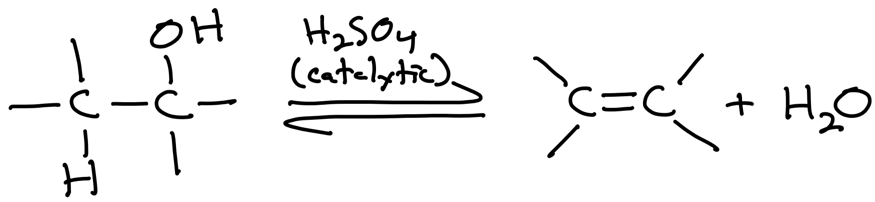
Summary:	Proton adds to make a carbocation intermediate, water attacks to make a new bond, take a proton away to make the product alcohol. Catalytic in $H_3O^{\oplus}$
Regiochemistry:	Markovnikov's Rule
Stereochemistry:	Mixed (time capsule)

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 ⇒

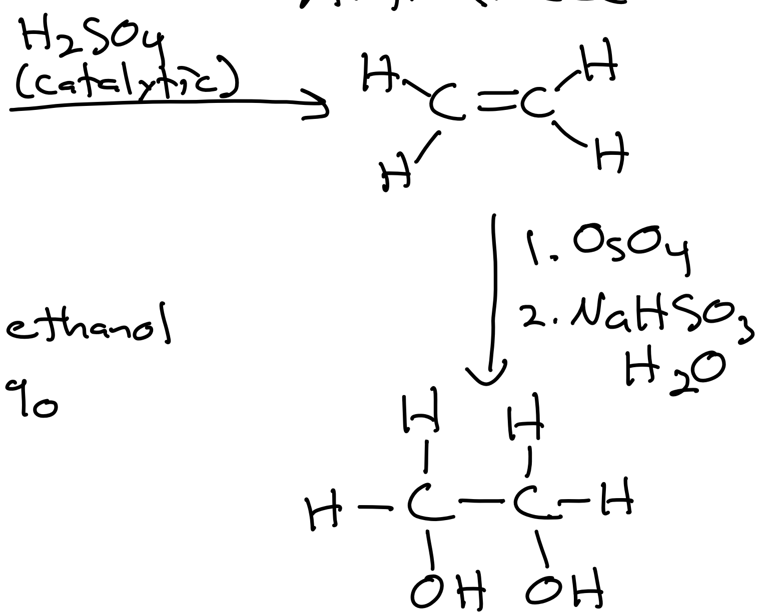
If we add water → we drive the reaction to the alcohol product

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

Anti-freeze

CH_3CH_2OH

"Vodka"

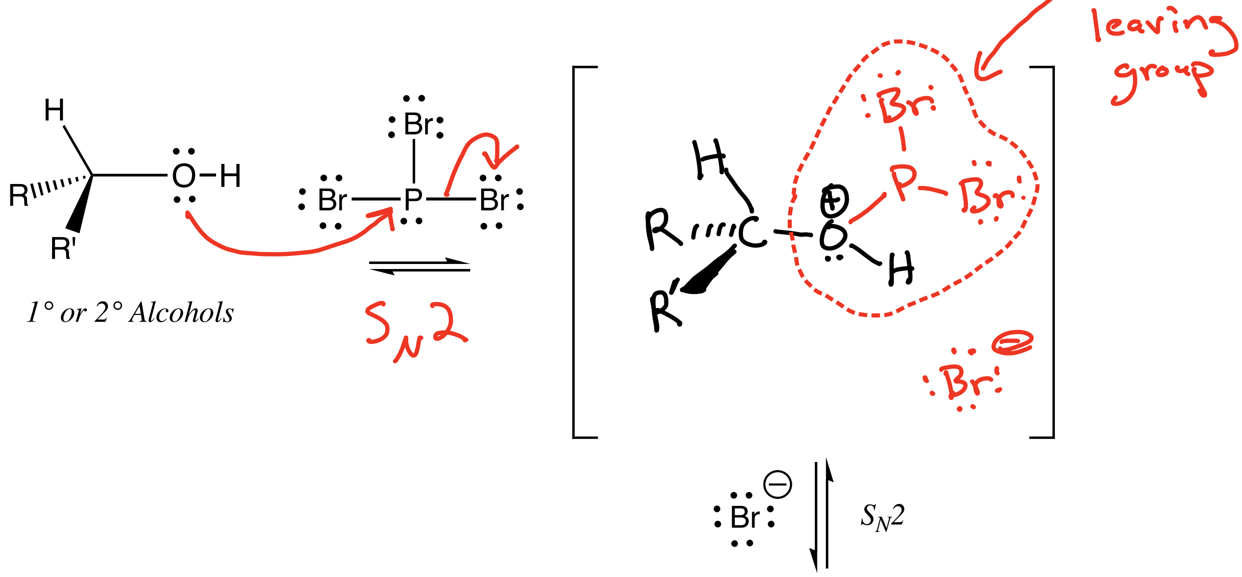


"Antifreeze"

35% – 95% ethanol

Usually ~40%

Alcohols + PBr_3



Products

Summary:

Regiochemistry:

Stereochemistry:

Example: