

Chapter 5

Alcohols and Alkyl Halides

Alcohols and alkyl halides are very important functional groups. A functional group is an atom or group of atoms that undergoes certain reactions that are typical of that functional group. It is important to recognize functional groups since it makes the organization and learning of organic chemistry much easier. There are several million organic compounds that are known and more are discovered or synthesized everyday but there is a limited number of functional groups.

Functional groups we have already seen:

Alkanes – essentially have no functional group. They contain only C and H single bonds.

Alkenes – have the carbon-carbon double bond as the functional group.

Alkynes – have the carbon-carbon triple bond as the functional group.

Arenes – have the benzene ring as a functional group.

New functional groups in this chapter:

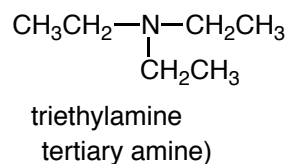
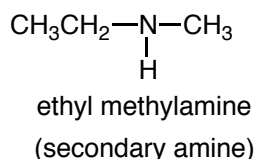
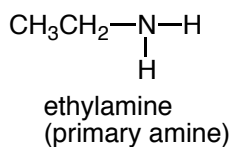
Alcohols – contain the hydroxyl group, -OH.

Alkyl halides – contain a halide. We use the symbol X to stand for any halogen (I, Br, Cl, F).

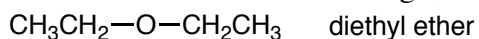
“R” is used to refer to any alkyl group regardless of size. It can be primary, secondary or tertiary, so a generalized alcohol is written as ROH and a generalized alkyl halide is written as RX.

Other functional groups that will be studied throughout the rest of the course include:

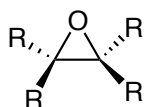
Amines – contain a nitrogen, N. The amine may be primary (RNH_2), secondary (R_2NH), or tertiary (R_3N) where the R groups can be the same or different.



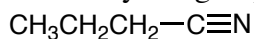
Ethers – contain a C-O-C linkage, R-O-R', where R and R' can be the same or different.



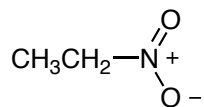
Epoxides – these are special 3-membered ring ethers.



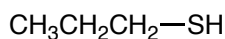
Nitriles – these contain the CN functional group, RCN. This functional group is also called a cyano-group.



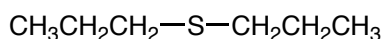
Nitroalkanes – these contain the nitro group, $-\text{NO}_2$.



Thiols – these contain an $-\text{SH}$ group RSH.

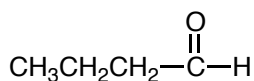


Sulfide – these are thio ethers, R-S-R'.

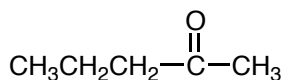


Carbonyl Derivatives – all contain the carbonyl group, $\text{C}=\text{O}$

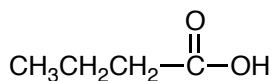
Aldehydes – have the carbonyl group at the end of the chain, $-\text{CHO}$.



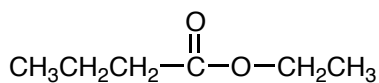
Ketones – have the carbonyl group attached to two other carbons, one on each side, RCOR'.



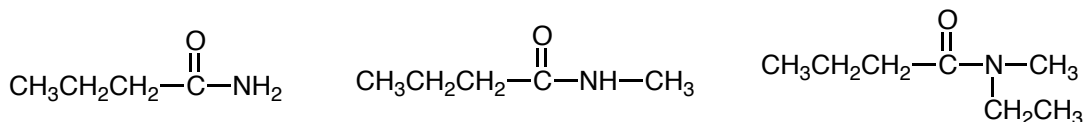
Carboxylic Acid – contain the functional group $-\text{CO}_2\text{H}$.



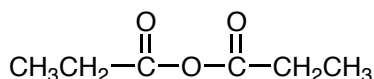
Carboxylic Acid Esters (or Esters) – contain the functional group $-\text{CO}_2\text{R}$.



Amides – contain the functional group $-\text{CONR}'_2$



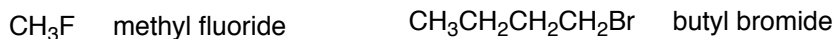
Carboxylic Acid Anhydrides – contain the functional group $\text{RCO}_2\text{COR}'$



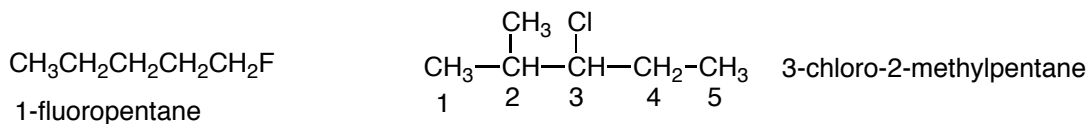
Nomenclature

Alkyl halides: There are two ways to name alkyl halides.

1. Name the alkyl group first, then as a separate word name the halide.



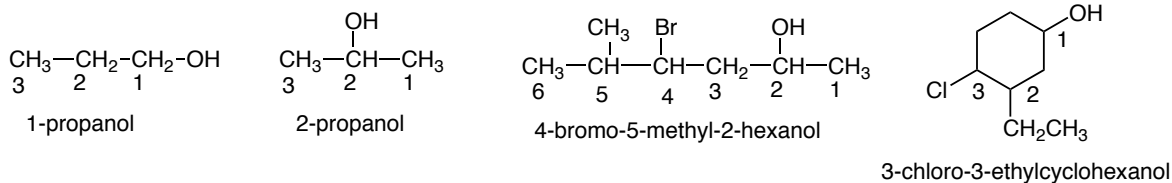
2. The systematic IUPAC name is to treat the halide as a substituent on the longest alkyl chain that contains the halide. Alphabetize it along with any other substituents. Number the chain so that the substituents get the lowest number at the first point of difference between the two possible directions for numbering.



Alcohols:

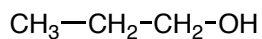
For the systematic IUPAC name, identify the parent alkane as the longest chain that contains the hydroxyl group. Drop the “e” from the alkane and add the suffix “-ol”. The alcohol group takes precedence over alkyl and halide substituents so number the parent chain in the direction that gives the alcohol the lowest number, giving the terminal carbon the number one. List the other substituents alphabetically, specifying their locations by number.

In cyclic alcohol, the hydroxyl group always gets number one, though the number is not written. Number the other substituents so as to obtain the lowest number at the first point of difference between the two possible numbering directions.

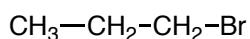


Classes of Alcohols and Alkyl Halides

A primary alcohol has a hydroxyl group attached to a primary carbon and a primary alkyl halide has a halogen attached to a primary carbon.

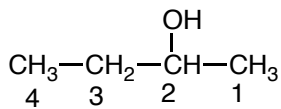


primary alcohol

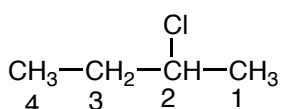


primary alkyl halide

A secondary alcohol has a hydroxyl group attached to a secondary carbon and a secondary alkyl halide has an alkyl group attached to a secondary carbon.

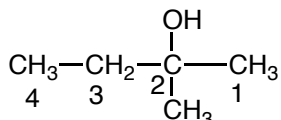


secondary alcohol

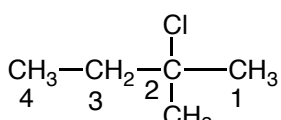


secondary alkyl halide

A tertiary alcohol has a hydroxyl group attached to a tertiary carbon and a tertiary alkyl halide has a halide attached to a tertiary carbon.

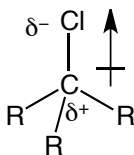
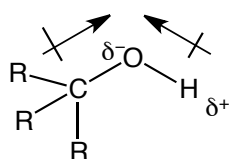


tertiary alcohol

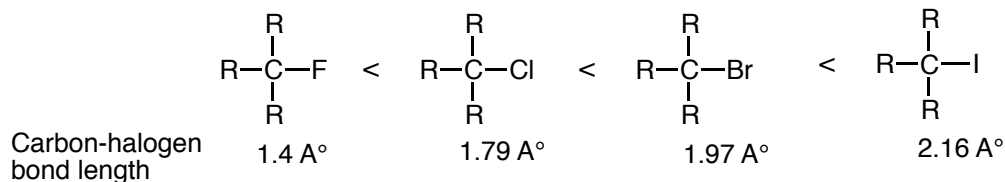


tertiary alkyl halide

Both alcohols and alkyl halides have fairly large dipole moments.

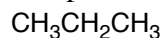


For alkyl halides, note the trend in bond lengths. The C-F bond is the shortest and the C-I bond is the longest as one would expect based on the much larger size of iodine versus fluorine.

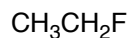


Physical Properties:

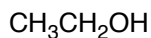
Compare boiling points:



b.p. -42°C

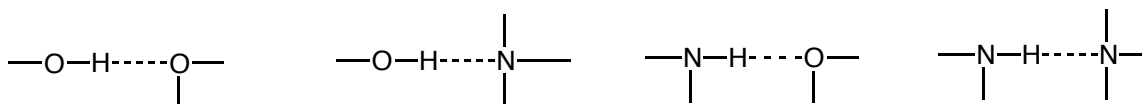
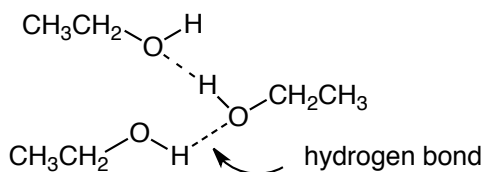


b.p. -32°C



b.p. 78°C

Fluoroethane is more polar than propane and has a slightly higher boiling point due to increases in dipole-induced dipole interactions but the alcohol has a much higher boiling point due to intermolecular hydrogen bonding. In order for hydrogen bonding to occur a hydrogen must be attached to an electronegative atom like oxygen or nitrogen or fluorine that has a lone pair. Each hydrogen bond is worth about 20 KJ/mol or ~ 5 Kcal/mol in energy. Carbon-hydrogen bonds are not polarized enough to engage in hydrogen bonding.



For alkyl halides, the boiling point increases with the increasing size of the halogen.

	$\text{CH}_3\text{-F}$	$\text{CH}_3\text{-Cl}$	$\text{CH}_3\text{-Br}$	$\text{CH}_3\text{-I}$
boiling point $^{\circ}\text{C}$	-78	-24	3	42

This is because the larger halogens are more polarizable. In the very large iodine, the electrons are much farther from the nucleus and more easily distorted. Therefore, there are stronger induced dipole-induced dipole interactions.

The boiling point also increases with the increasing number of halogens.

	CH_3Cl	CH_2Cl_2	CHCl_3	CCl_4
boiling point $^{\circ}\text{C}$	-24	40	61	77

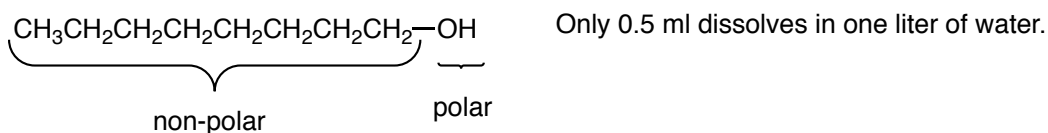
Again, this is due to increased induced dipole-induced dipole interactions.

But fluorine is an exception due to the fact that fluorine is not very polarizable, though CF_3CF_3 still has a higher boiling point than ethane, CH_3CH_3 , since it is more polar.

	$\text{CH}_3\text{CH}_2\text{F}$	CH_3CHF_2	CH_3CF_3	CF_3CF_3	CH_3CH_3
boiling point, $^{\circ}\text{C}$	-32	-25	-47	-78	-89

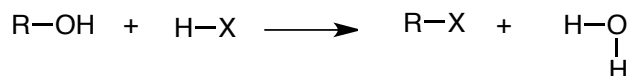
Water solubility:

All alkyl halides are insoluble in water, like alkanes. Low molecular weight alcohols (methanol, ethanol, 1-propanol, 2-propanol) are miscible with water. Miscible means they are soluble in all proportions and form one layer with water. This is due to intermolecular hydrogen bonding. As the hydrocarbon chain gets longer, the solubility decreases.

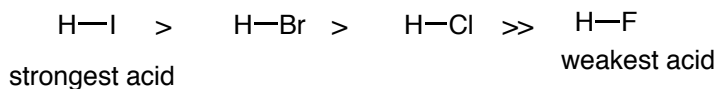


Preparation of Alkyl Halides from Alcohols and HX

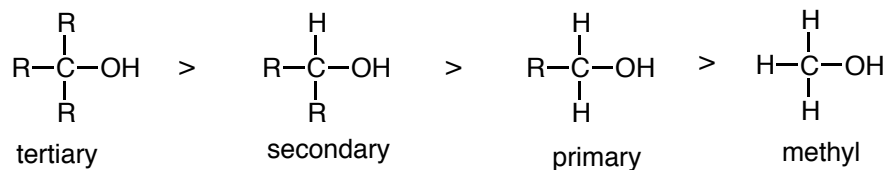
General reaction:



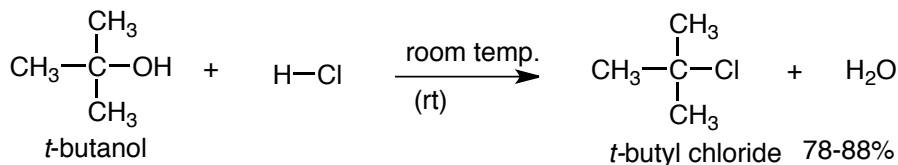
The reactivity order for the hydrogen halides parallels their acidity:



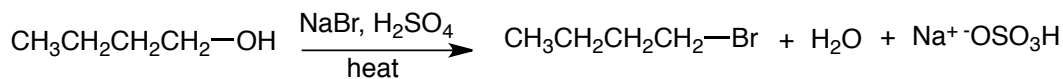
The reactivity order for the alcohols is:



Ex:



Sometimes we write the reagents over the arrow in order to save space.

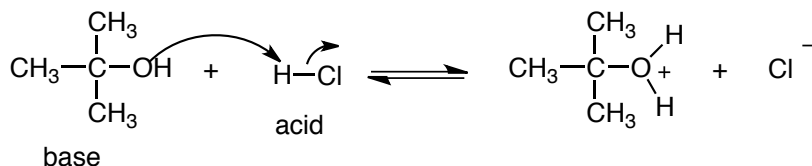


Mechanism of the Reaction of *t*-Butanol and HCl

When *t*-butanol reacts with hydrochloric acid to form *t*-butyl chloride, this is a substitution reaction. We substitute the hydroxyl group with the chlorine. The mechanism is a Nucleophilic Substitution Unimolecular or S_N1 mechanism. The mechanism of a chemical reaction is a detailed, step-by-step description of how the reaction occurs. As chemists, we can never actually observe a reaction occurring and so we have to infer the actual

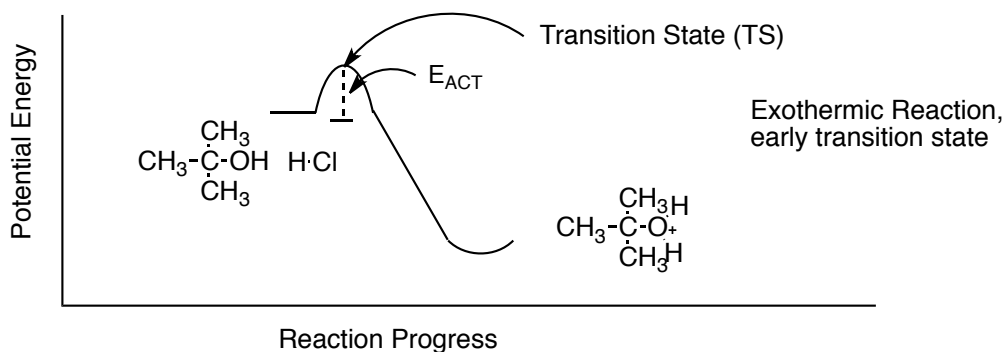
mechanism based on what intermediates are formed and based on our understanding of chemical principles. Generally most chemists will agree on a mechanism and it is critical in the study of organic chemistry to learn the proper mechanism and to keep track of how the electrons are moving in a given reaction by means of the curved arrow formalism.

Step One: The S_N1 mechanism under consideration here involves three separate steps. Step one is proton transfer from the hydrochloric acid to the oxygen lone pair of the alcohol. We protonate the hydroxyl group to make it into a good leaving group in step 2.



This is a simple acid-base reaction. It is a very fast reaction and therefore has a low activation energy (E_{ACT}). The rate of the reaction is determined by the height of energy barrier. In general, proton transfer reactions are the fastest reactions in chemistry. The reaction is exothermic, which means heat is given off and it is favorable. The H-Cl bond is weak and easily broken. The hydrogen forms a stronger bond with oxygen.

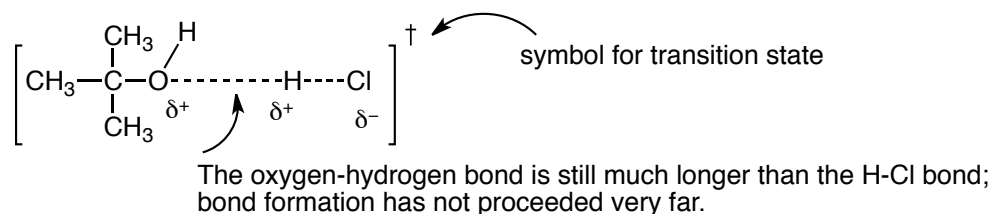
If we make a graph of what happens to the potential energy as the reaction proceeds we see that initially the potential energy increases slightly. This is the activation energy or energy barrier to the reaction. The potential energy then reaches a maximum. We define this maximum as the transition state or TS. This literally is the point of transition between starting materials and the product.



We cannot actually isolate the transition state to study its structure. It has a very short lifetime and is an unstable structure that is literally making the transition from starting material to product. It is very important to understanding the full mechanism to have some sense of the structure of the transition state because it is the height of the maximum point of the transition state, the activation energy, that determines the rate and the more stable the transition state the lower it is in energy.

Hammond's Postulate: this is a theory or postulate that predicts the structure of the transition state based on whether a reaction is exothermic or endothermic. It states that if two species are similar in energy, they are similar in structure. In general:

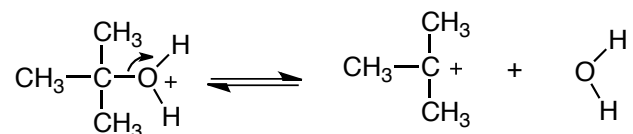
For an exothermic reaction, the transition state is similar in energy to the starting materials so it resembles the starting materials in structure. Bond breaking and bond formation have not proceeded very far. We call this an early transition state and show it using dotted lines for the bonds that are breaking and forming.



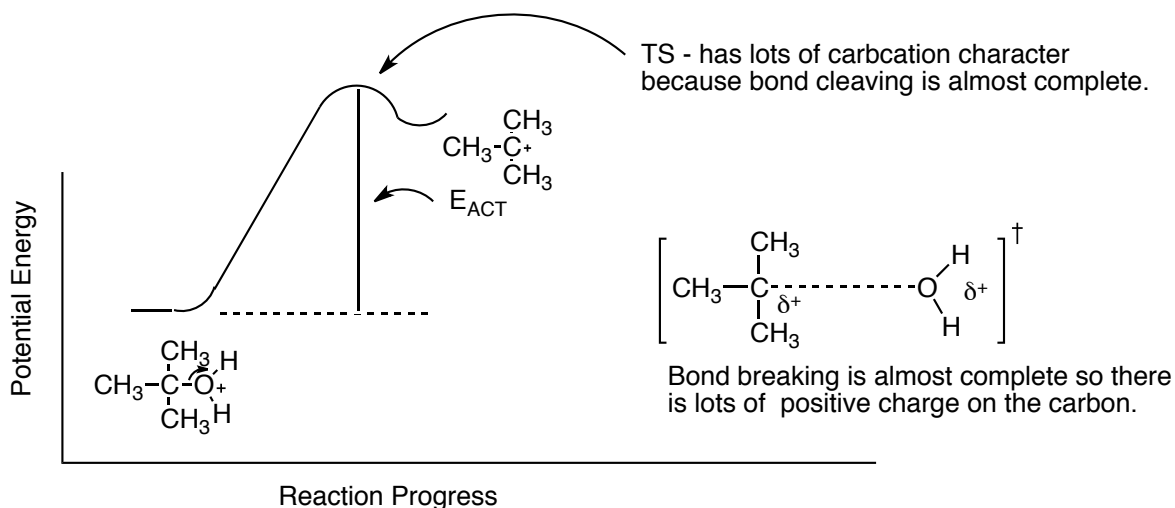
For an endothermic reaction, we have a late transition state. Bond breaking and bond formation is nearly complete and the transition state resembles the product.

We will see an example of an endothermic reaction and a late transition state in step two of our S_N1 mechanism.

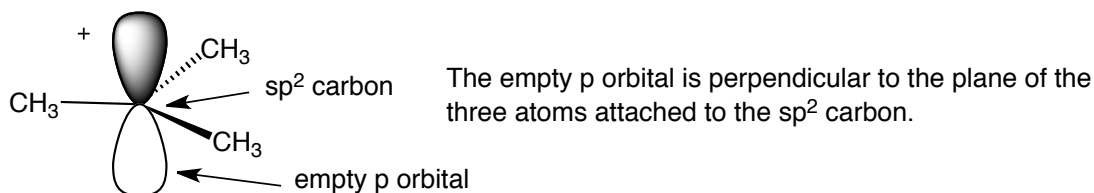
Step Two: Step two is the slow, rate-determining step. It is a unimolecular reaction in which the protonated alcohol from step one leaves as the neutral water to form a carbocation.



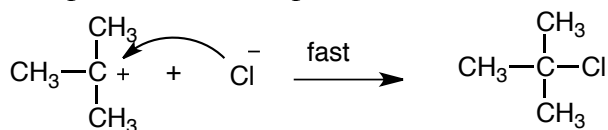
This step is endothermic since a bond is being broken but no bond is being formed. It requires energy to break a bond. The carbocation product of this reaction is a high energy intermediate. The potential energy versus reaction progress diagram shows that the transition state is similar in energy to the carbocation product. So there is lots of positive charge on the carbocation intermediate.



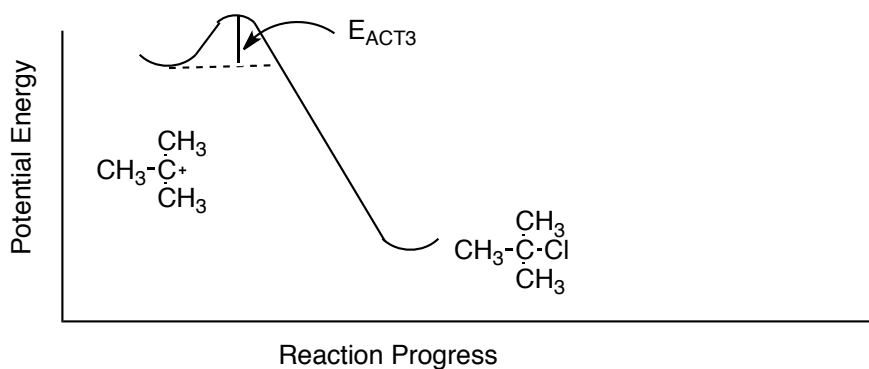
Carbocations are planar, trigonal structures with an sp^2 carbon that has an empty p-orbital perpendicular to the plane of the carbon atom and its three substituents. The carbocation has only six electrons around it so it is a Lewis Acid. Another term for a Lewis acid is electrophile. An electrophile is a species that “loves” (from the Greek *philos*) electrons.



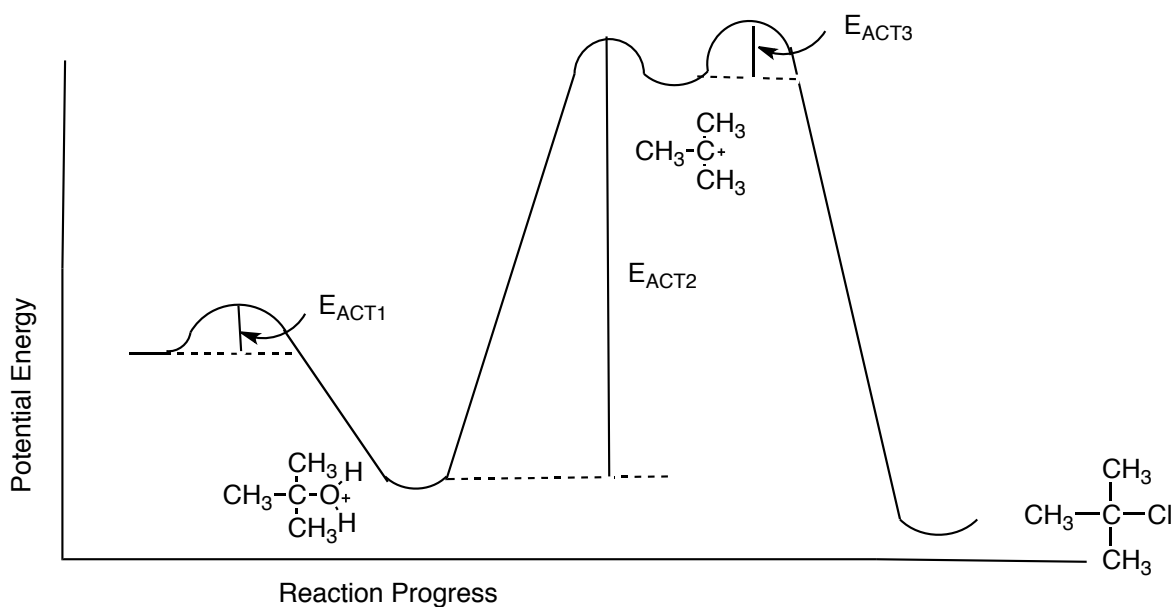
Step 3: The chlorine attacks the empty p orbital on the carbocation to form a new Cl-C bond. This step is very fast and thermodynamically very favorable since a bond is being formed and no bond is being broken. The chlorine is a nucleophile. Nucleophiles are Lewis bases that have a lone pair and/or a minus charge. They donate electrons to the electrophile. We always show the arrow for the electrons as moving from the nucleophile lone pair to the electrophile.



This step is fast and has a low activation energy. It is exothermic.



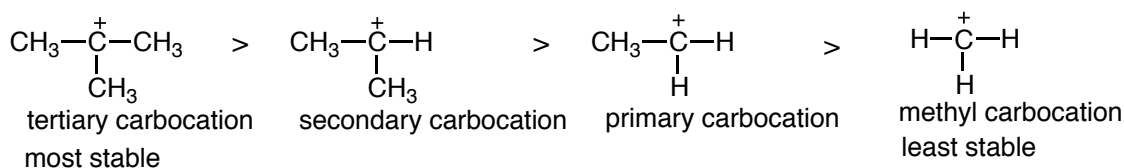
The overall potential energy diagram for all three steps is as follows:



The second step, the formation of the carbocation has the highest activation energy and therefore it is the slowest step and determines the overall rate of the reaction.

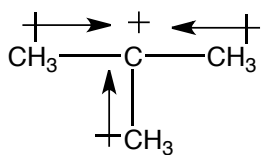
Carbocation Stability

Alkyl groups stabilize a carbocation by donating electrons and helping to spread out the positive charge.

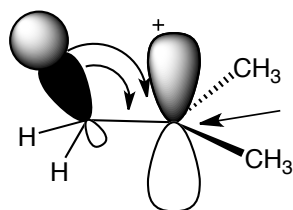


There are two ways that the alkyl groups release electrons.

(1) The Inductive Effect: This is due to the polarization of sigma bonds. The electrons in a C-C bond are more polarizable than the electrons in a C-H bond. So replacing H's with alkyl groups has the effect of increasing the polarizability of the bonds to the carbocation and allows for better electron donation through the sigma bonds. This has the result of making the carbocation less electron deficient and therefore more stable and lower in energy.

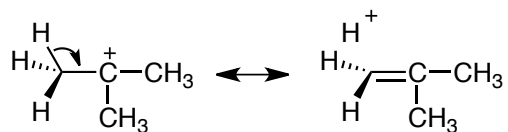


(2) Hyperconjugation: This is a resonance effect due to overlap of the six C-H bonds with the empty p orbital of the carbocation. For this overlap to be effective the C-H bonds must be on the carbon directly connected to the carbocation.



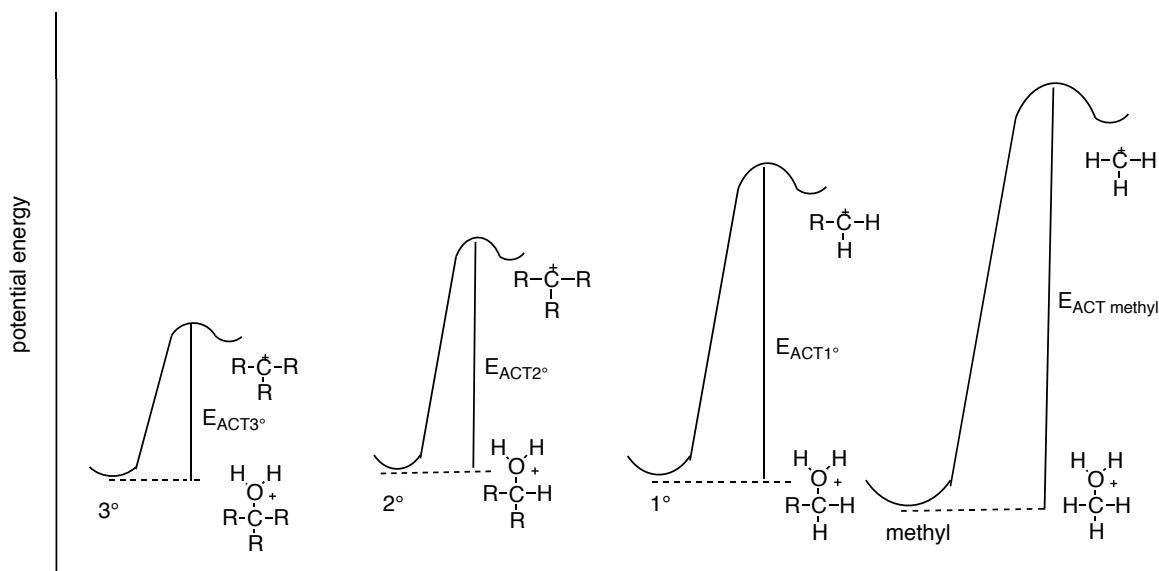
The two electrons from the C-H bond on the alkyl group attached to the carbocation can donate into the empty p orbital of the carbocation. The two C-H electrons are partially delocalized onto the p orbital. The more alkyl groups that are attached to the carbocation, the more electron donation there is.

Another representation of this effect that is sometimes shown is as follows:



Now we can understand why tertiary alcohols react faster than secondary alcohols and why secondary alcohols react faster than primary ones. It is due to the fact that the tertiary alcohols, upon protonation and loss of water, form the more stable tertiary carbocations. Tertiary carbocations are lower in energy than secondary and primary and methyl carbocations and form faster.

A graphical comparison of the relative energies of the various carbocations shows that the tertiary is much lower in energy and furthermore has a lower activation energy (E_{ACT3°) so that it forms much faster.

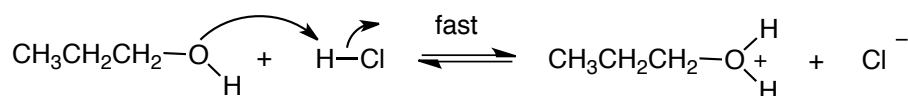


Generally speaking, the primary and methyl carbocations are too high in energy to be formed and are never observed. So with primary and methyl alcohols there is a different mechanism.

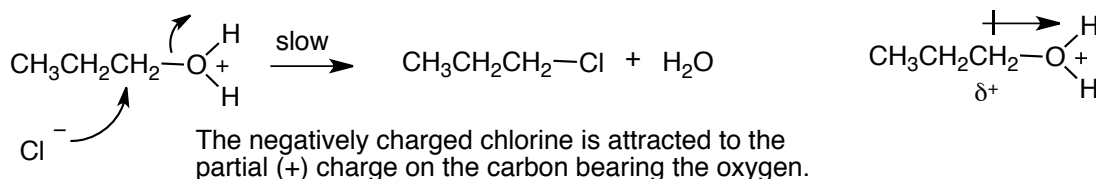
S_N2 Mechanism: Nucleophilic Substitution Bimolecular

With methyl alcohol and primary alcohol we have a different mechanism called the S_N2 mechanism, where the "2" refers to the fact that the rate determining step has two molecules coming together (i.e. bi-molecular).

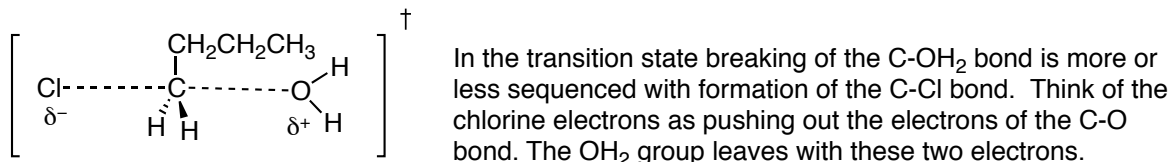
The first step is the same as in the tertiary alcohol case: the alcohol oxygen is protonated so as to make it into a good leaving group.



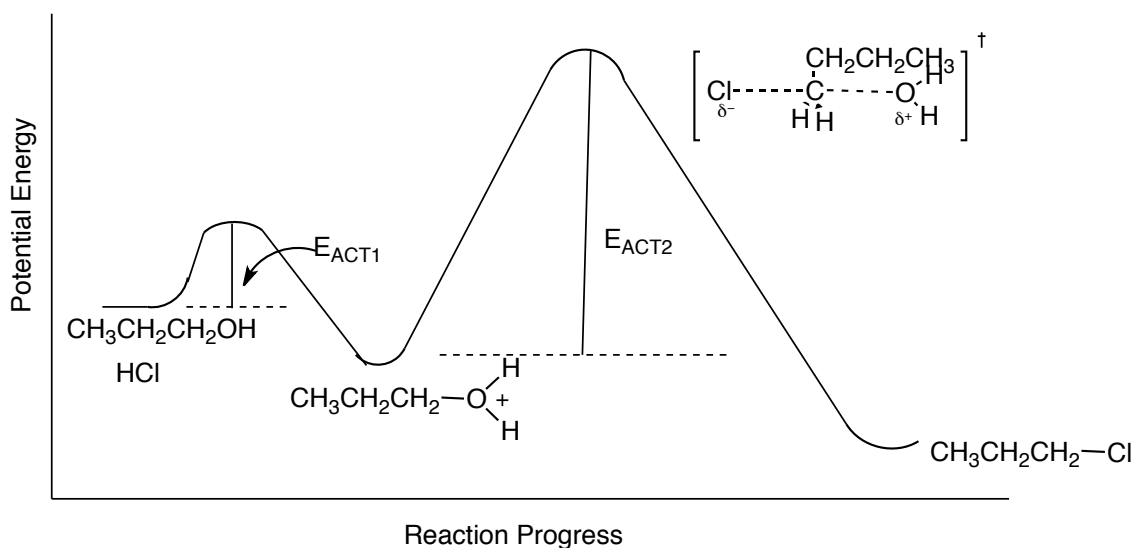
In the second step, the chlorine anion produced in the first step directly attacks the carbon bearing the protonated hydroxyl group to replace it. The carbon bearing the oxygen has a partial positive charge since the oxygen is more electronegative than carbon.



As will be discussed in much more detail in Chapter 8, the attack by the nucleophilic chlorine occurs from the backside. The transition state is pictured below.

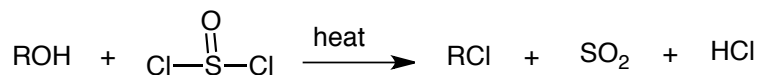


The potential energy versus reaction progress diagram shows two transition states corresponding to the two steps. The second step has the higher activation energy and is therefore the slow step and overall rate-determining step.

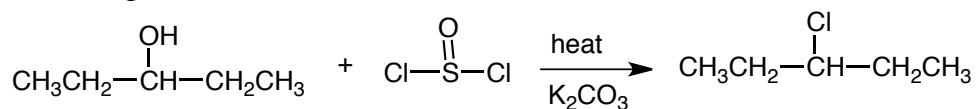


Other ways to convert alcohols to alkyl halides

(1) **Thionyl Chloride:** We can treat alcohols with boiling thionyl chloride (SOCl₂) to convert the alcohol to an alkyl chloride. This method is considerably milder than using concentrated hydrochloric acid and is useful when the molecule contains sensitive functional groups that would react with the strong acid. This is usually used with primary and secondary alcohols since, as we have seen, tertiary alcohols react easily at low temperatures with hydrochloric acid. Often a weak base such as potassium carbonate (K₂CO₃) or pyridine (C₅H₅N) is used to neutralize the HCl that is produced.

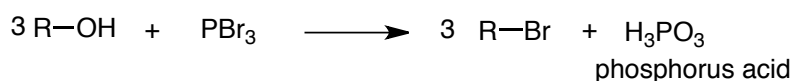


For example:



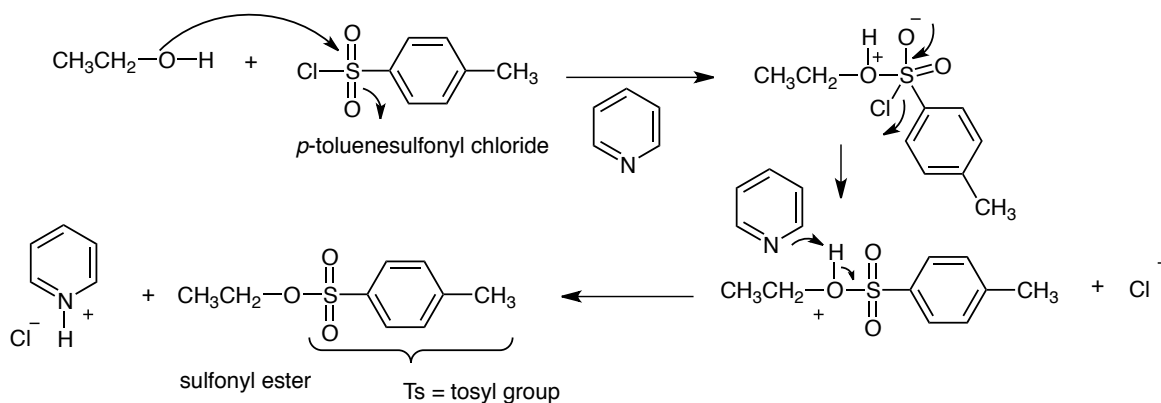
(2) Phosphorus Tribromide:

A mild way to convert alcohols to alkyl bromides involves the treatment of the alcohol with phosphorus tribromide, PBr_3 . One equivalent of phosphorus tribromide will convert three molecules of the alcohol.

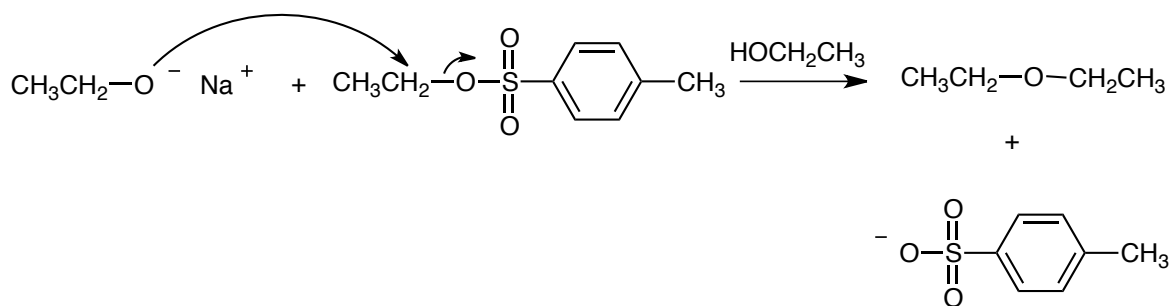


Sulfonate Esters

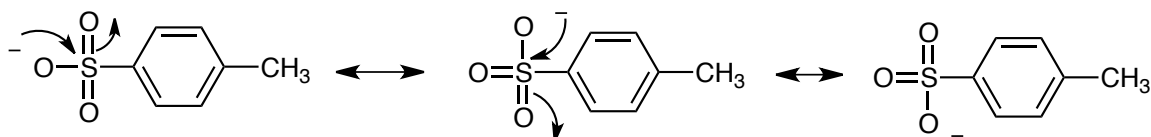
Alkyl sulfonate esters are also very good leaving groups, similar in leaving group ability to halogens. They are prepared from alcohols by reaction with a sulfonyl chloride. A common sulfonyl chloride is *p*-toluene sulfonyl chloride. Generally a mild, non-nucleophilic base such as pyridine or triethyl amine is used to neutralize the HCl that is formed in the reaction.



The sulfonate ester can then be attacked by strongly basic nucleophiles to give substitution products with loss of the tosyl group.

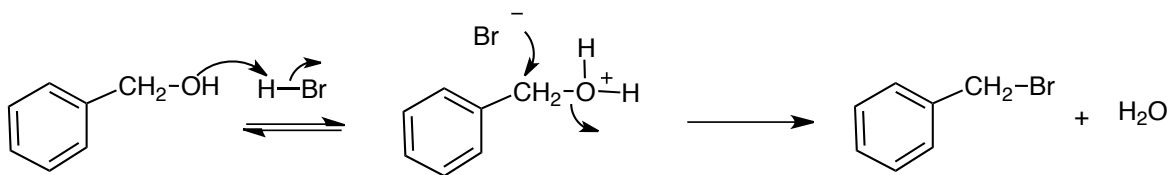


The tosyl group is a very good leaving group, equivalent to a halogen, because it forms a resonance-stabilized anion that is a weak base. Remember, by definition, a good leaving group is a weak base.



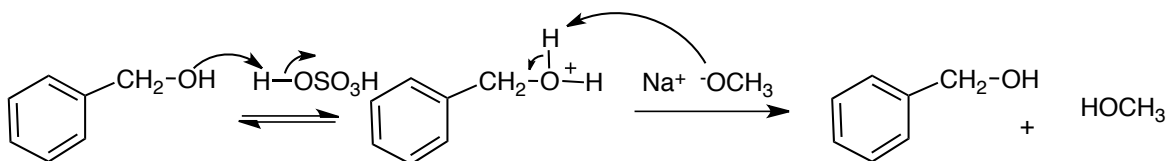
The (-) charge is spread out over all three oxygens and is thereby stabilized.

Note that the overall effect of making the alcohol into the tosylates is to convert the OH group into a good leaving group under mild, non-acidic conditions. As we have learned, we can convert the OH group into a good leaving group by protonation but this restricts the nucleophiles we can use to those that are very weakly basic such as the halogens.

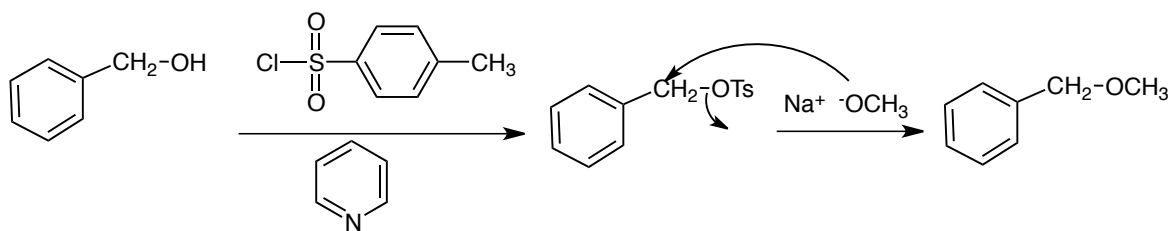


The Br⁻ is a very weak base and will not deprotonate the oxygen.

If we tried to do this same type of reaction with a more basic nucleophile like CH₃O⁻, we would simply deprotonate the hydroxyl group in an acid-base reaction rather than a substitution reaction. Recall that the fastest reactions are always the proton transfer reactions.



So, if we first make the tosylates we can safely react it with the basic sodium methoxide and get an excellent yield of the substitution product.



Note that the stereochemistry of the C-O bond does not change when the tosylate is made but it does undergo inversion in the subsequent S_N2 reaction.

