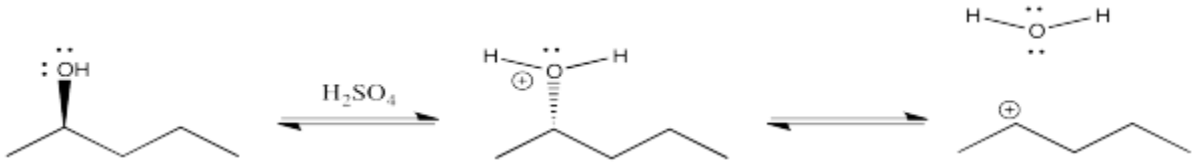
LEAVING GROUP FORMATION

Aliphatic Nucelophilic Substitutions can be useful reactions. A minor drawback is the low natural occurrence of alkyl halides. Alcohols are much more common.

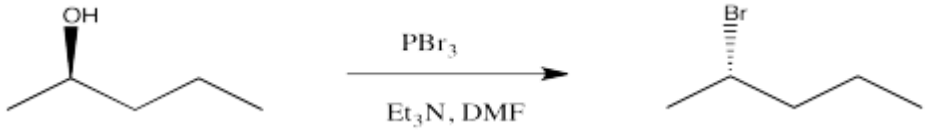
We could do nucleophilic substitutions on alcohols. The trouble is, oxygens are less polarizable than halides. A hydroxide ion is less stable, and harder to form than a halide ion. They don't make very good leaving groups, comparatively.

One way around that problem would be to protonate the oxygen. Attached to the carbon, it is a cation. Once it leaves, it becomes a neutral. The issue of ion stability is sidestepped. The trouble is, plunking a compound into concentrated acid is not always a reliable way to get things done.



For that reason, it is pretty helpful to be able to turn alcohols into alkyl halides, or otherwise turn hydroxyls into stable, anionic leaving groups.

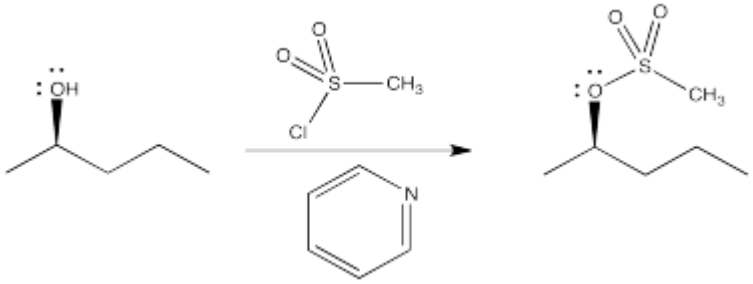
One of the most common synthetic methods of converting alcohols into good candidates for nucleophilic substitution is to convert the hydroxyl into a halide through the use of a phosphorus reagent. Phosphorus tribromide is frequently used to make alkyl bromides from alcohols.



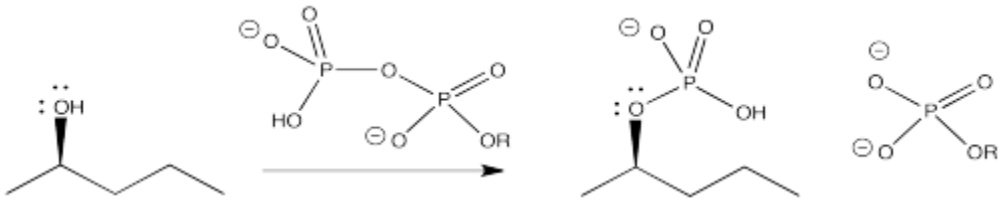
This reaction itself involves a sequence of nucleophilic substitution reactions. In the first, the oxygen atom in a hydroxyl group acts as the nucleophile and replaces a bromide on phosphorus. In the second, the displaced bromide ion rebounds to displace the oxygen atom from the tetrahedral carbon. This mechanism is aided by the strength of the strong phosphorus-oxygen bond that is formed. The phosphite that forms is a very good leaving group.

Another common method is to turn the hydroxyl into a sulfonate ester, such as a mesylate or tosylate. Again, the oxygen atom acts as a nucleophile, displacing a halide from the sulfur in a sulfonyl chloride. This is very similar to the bromination

with phosphorus tribromide, but the sulfonate ester waits, poised to be displaced by a nucleophile. In fact, tosylates are generally even better leaving groups than halides.



Biologically, something very similar to both of these processes sometimes happens. The alcohol unit is converted into a phosphate. The alcohol can be phosphorylated by a molecule of ATP. Again, the phosphate portion of the molecule is a very good leaving group.



Source: http://employees.csbsju.edu/cschaller/Reactivity/nusub/NSOLGp.htm