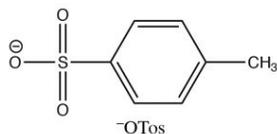
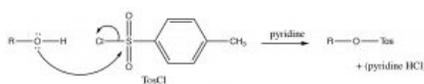


## 6.3: O O , S S , and N N as Leaving Groups

Recall that a good leaving group should be able to accept (in a stable form) the pair of electrons from the bond that breaks. Typically, good leaving groups are weak bases. For this reason, hydroxide ( $^-OH$ ) and amide ( $^-NH_2$ ) are unlikely to be produced during a nucleophilic substitution reaction. However, as noted earlier, alcohols can be converted into good leaving groups by protonation, which results in  $H_2O$  as the leaving group.

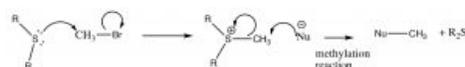


Alcohols can also be modified (or derivatized) to produce better leaving groups. This is particularly useful when we need to carry out a reaction that is sensitive to acidic conditions when the method we have used earlier (protonation of the OH) cannot be used. The most common derivative used to make the OH group into a good leaving group is the Tosyl group (para-toluenesulphonate). It can be formed by reacting an alcohol with p-toluenesulfonylchloride (TosCl) in the presence of a base (such as pyridine) that acts to remove the HCl that is produced).



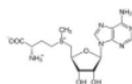
We can consider the derivatization reaction as mechanistically similar to other nucleophilic substitutions we have considered, except that it takes place at an S instead of a C.

The resulting OTos group is a very good leaving group, making the molecule reactive to nucleophilic substitution reactions. In effect, we have changed the leaving group from  $^-OH$ , which is a relatively strong base, to  $^-OTos$  which is a very weak base—it is the organic equivalent of sulfate, the conjugate base of sulfuric acid. The negative charge on  $^-OTos$  becomes delocalized to the other oxygens bound to the S, thereby stabilizing the base.



In a similar manner, sulfides can be transformed into leaving groups, most commonly through the methylation of the sulfide, which produces a powerful reagent that can be used to methylate other species.

In biological systems, a common methylating agent, S-adenosylmethionine (SAM  $\rightarrow$ ), uses this mechanism



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