

## Tips for Drawing Mechanisms

### General Advice

Always be sure that your structures are correct; formal charges, number of bonds etc. It is easy when first learning mechanisms to forget some of these basics while in the throes of getting the mechanistic arrows right.

Don't forget about resonance forms! When a structure can have resonance forms, it is important to draw several of the more important ones. A different "view" (= resonance form) may give you some new ideas about how to proceed with your mechanism. By the way, a mechanism should work for all resonance forms.

Remember that the double-headed arrow, mechanistic arrows and the equilibrium arrows each have very specific and non-overlapping uses. Know them.

Be sure you know how to identify nucleophiles, electrophiles, and leaving groups, and what factors make a good nucleophile etc. Also, understand Bronsted and Lewis acid concepts, they are related to these categories.

Know your acid-base chemistry. Remember that proton transfers can occur before, during and at the end of a mechanism. Remember that there are often options about the proton transfer details, all of which may be correct. For instance, do you use  $H^+$  or  $H_3O^+$ ? If water is present, a purist would say to use  $H_3O^+$ , but most people would be satisfied with either. If the conditions are specifically anhydrous, then you must use  $H^+$ .

A classic beginner's mistake is to have all sorts of arrows going in all sorts of directions. A few reactions are this fancy, but 95% proceed via intermediates. So, generally, one or two arrows gives rise to an intermediate, then that intermediate gets more arrows and becomes another intermediate or the product, etc. No atom should have two arrows leading to it at the same time, or away from it at the same time.

### Specific Advice:

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$\sigma$  bonds are rarely nucleophiles.

*Note: the following do not apply to reactions at enzyme active sites where pKa's can be rather different than they are in free solution.*

Don't postulate acidic species, including Lewis acids, when the reactions conditions are basic. Remember that a carbonium ion is a Lewis acid.

Don't postulate basic species when the reaction conditions are acidic.

### How to Get Started When You Are Flummoxed

When reaction conditions are acidic, a good "first move" in a mechanism is to protonate something basic, and see where that leads. Try an N or O first, but even alkenes can be protonated.

Compare the structures of the starting materials and products, with an eye to which bonds have been broken, which have been made, and which are untouched. For instance, if you have a new C-O bond formed, as some point an oxygen nucleophile must have attacked that carbon.

Really stuck? Identify all possible nucleophiles and all possible electrophiles. Consider mechanistic options in which each possible nucleophile attacks each possible electrophile. Do any of these lead to the desired product?