Understanding how the number of equivalents of base used will affect an aldol or Claisen reaction

1) **Remember that the amount of carbonyl compound present is defined to be 1.0 equivalent, so the number of equivalents of base are really describing a ratio of the amount of base to the amount of carbonyl compound added at the beginning of the reaction. 0.5 equivalents of base means there only half as many base molecules as carbonyl compound molecules added to the reaction.**

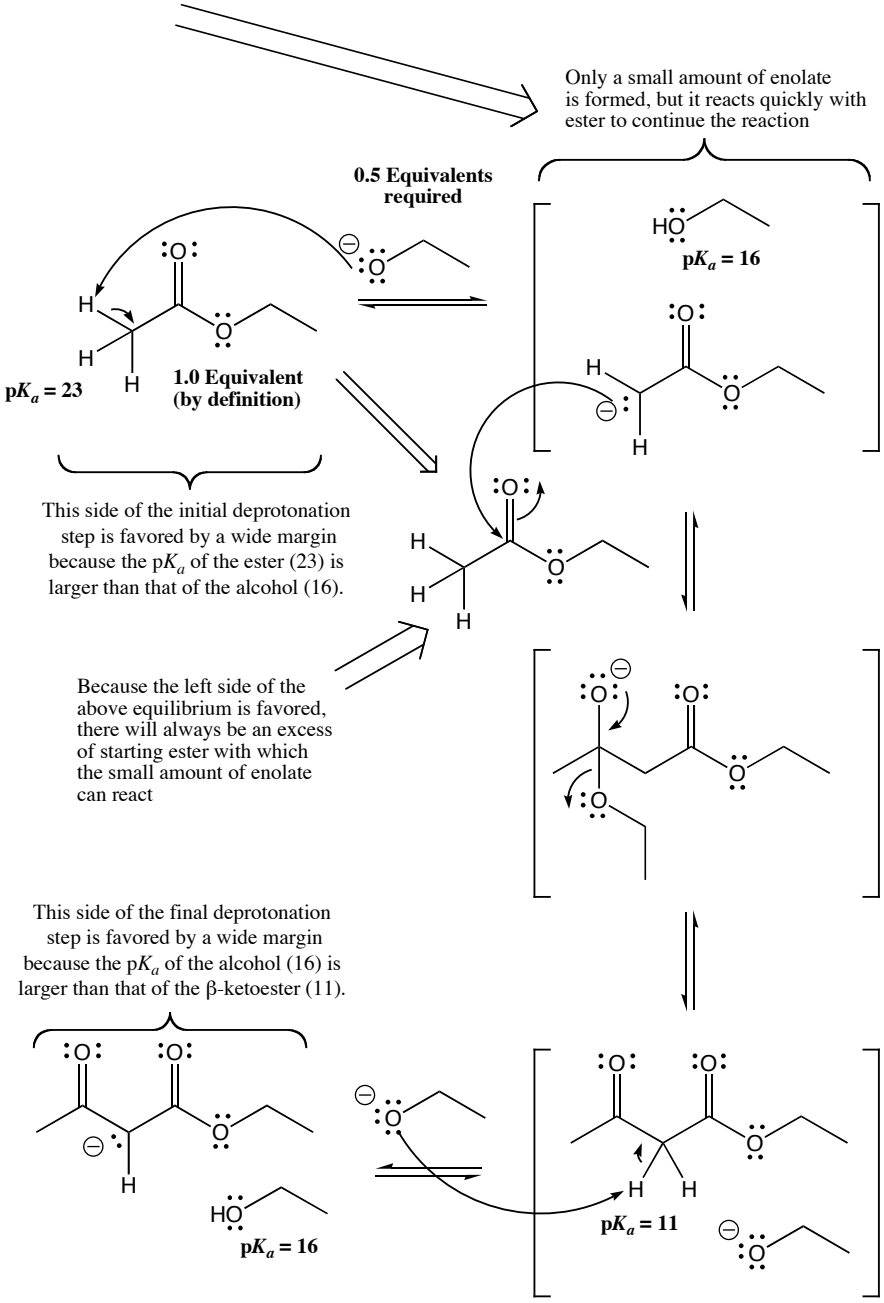
2) **Determine how much base is consumed in the overall reaction mechanism (i.e. is a catalytic amount or are 0.5 equivalents required?) by seeing if base is consumed (i.e. the last step of the Claisen condensation) or not (i.e. aldol mechanism). If base is consumed, calculate the ratio of number of molecules of base consumed versus the number of starting carbonyl compounds consumed in the reaction. For example, in the Claisen condensation, one molecule of base is consumed for every product molecule created (due to the last step). However, each product molecule requires two ester molecules. Therefore, the ratio of base to ester consumed 1 molecule of base for every two molecules of ester. Since the amount of ester is by definition 1.0 equivalents, this means you need at minimum of 0.5 equivalents of base.**

3) **Analyze the initial deprotonation step of the mechanism to see which side predominates at equilibrium based on a comparison of the pK_a values of the carbonyl species and conjugate acid of the base. The side with the weaker acid (higher pK_a value) predominates.**

    A) If the side with the starting carbonyl compound predominates at equilibrium (because a weaker base is used), there will always be excess carbonyl compound present with which the small amount of enolate formed will react. In this scenario, adding excess base does not change the reaction outcome, so long as there is at least enough base to satisfy the requirements of the reaction mechanism. Any excess base serves to increase the rate of the reaction, and is simply left over after the reaction is completed.

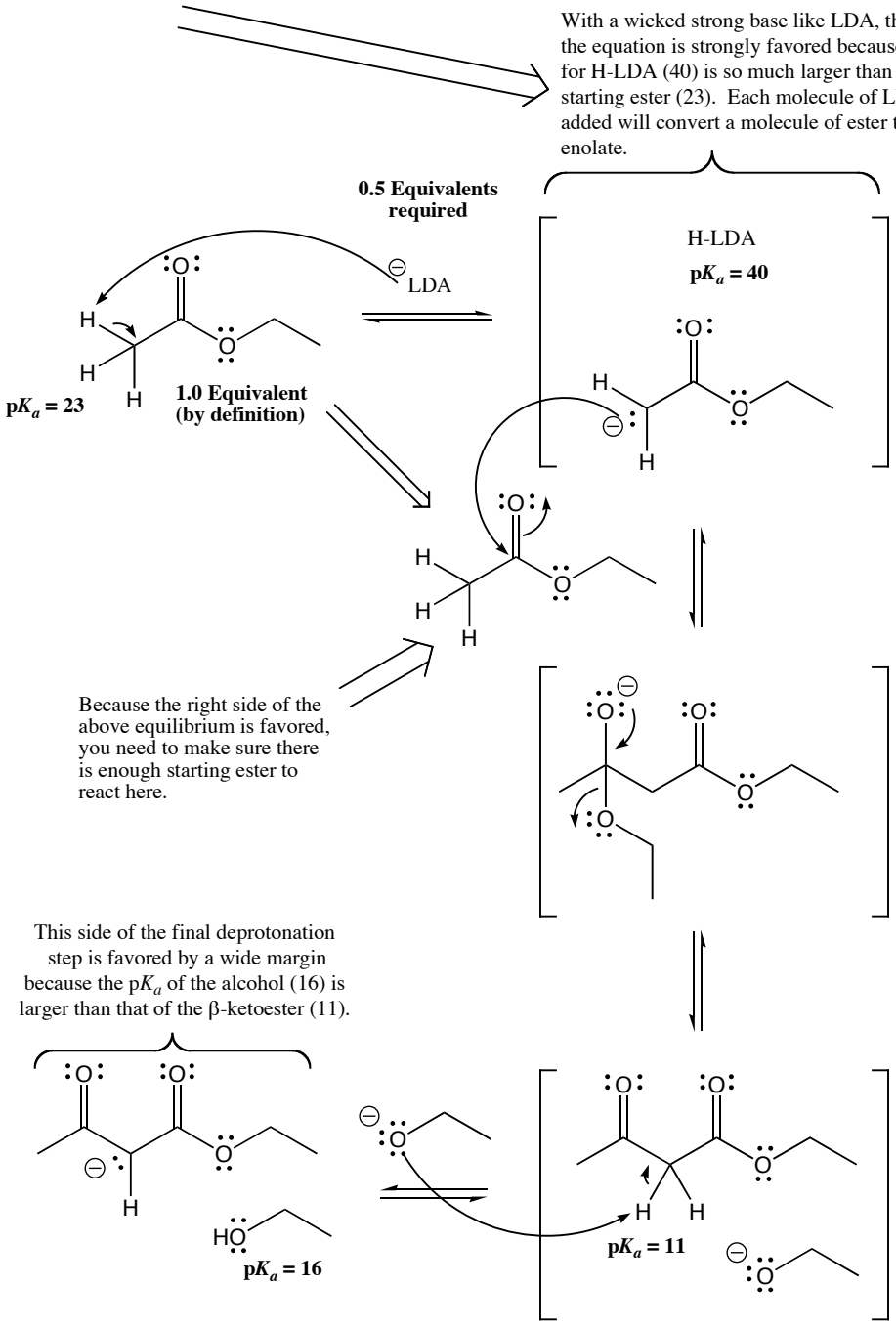
    B) IF the side with the enolate is favored (by using a very strong base like LDA), adding too much can stop the reaction. For example, if 1.0 equivalent of LDA is used, the entire sample of carbonyl compound is converted to the enolate, which now has no carbonyl compound to react with so further reaction does not take place until the chemist opens the flask and adds a second carbonyl reactant (i.e. for a directed aldol or Claisen reaction).

If more than 0.5 equivalents of ethoxide is used, because equilibrium favors the left side of this equation, there is still going to be an excess of starting ester around for the small amount of enolate to react with. Thus, adding excess ethoxide only serves to speed up the reaction, it still goes to completeion.



Because of this last step, one of these ethoxide molecules is consumed for every product molecule made. It takes 2 starting ester molecules to make a single product molecule, therefore, there is a two to one ratio of ester to base used. Because by definition 1.0 equivalent of ester is used in the reaction, the minimum amount of base required is 0.5 equivalents.

If more than 0.5 equivalents of LDA is used, because equilibrium strongly favors the right side of this equation, there will not be enough starting ester around for the enolate to react with. Thus, adding more than one equivalent of LDA will lower the yield of the reaction.



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