Crossed Claisen Condensations

So the next logical question is to whether Claisen Condensations can be done between two different esters, or employing one non-ester, and have the reaction work well. These reactions would be called crossed Claisen Condensations. They, in fact can be done in some cases, but some conditions must be met normally. They are indicated below:

a) The electrophilic ester should be more electrophilic (than the enolizing one), and not enolizable. Good examples of this include:









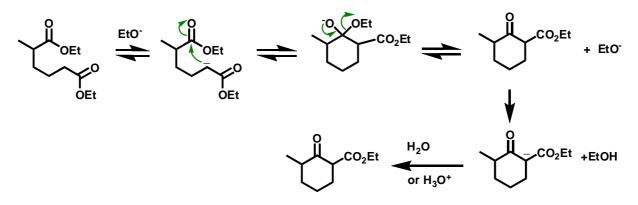
diethyl oxalate reactive since each ester has an EWG on it

ethyl formate reactive - H is the least sterically hindered group

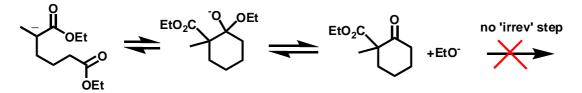
diethyl carbonate with one OEt as a +M group the second functions more as a -I group

ethyl benzoate included in Clayden without a reason perhaps just used in excess

b) In intramolecular cases, especially where the ring being formed is a 5- or 6- membered ring. Oddly enough, this reaction is normally recognized by a different name – the **Dieckmann Condensation**. In the example below, the esters have been made different, and the Claisen/Dieckmann in one direction is heavily favoured.

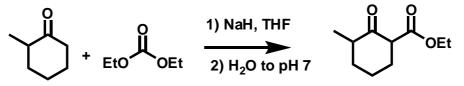


Note: The reaction doesn't go the 'other way' because of the lack of the functionally irreversible step



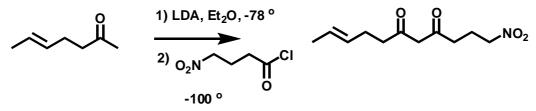
Corrollary: A general corollary to this last point is that α, α -disubstituted esters don't normally function as the C-H acid in Claisen or Dieckmann condensations, because the functionally irreversible step isn't possible.

- c) This raises the question as to whether ketones can even be the C-H acid in a Claisen condesnation. The answer is *yes*, with some conditions.
 - We don't want the aldol competing , so normally one chooses a strong base (to convert 'all' the ketone molecules to their enolates). NaH has been used traditionally for this purpose.



ii)

Sometimes one can resort to true discrete kinetic enolate generaton, but then it is usually a more reactive ester replacement that is used as the electrophile, such as an acid chloride. You will have to be wary of the possibility of O-acylation in these cases, so the solvent polarity has been dropped intentionally a bit here to minimize that.



Final points:

The β - keto esters that one forms from Claisens (or Dieckmanns) often exist with a high content of the enol tautomer, relative to normal ketones especially.

OH DEt

significant enol content