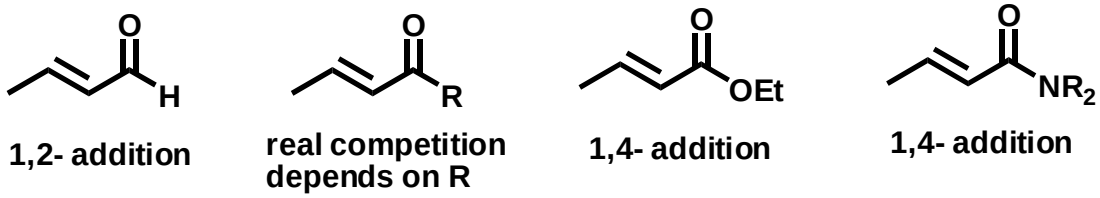
Michael Reaction with Kinetic/Stoichiometric Enolates

Michael reactions with kinetic enolates (or stoichiometrically generated enolates) can be done in some cases, but on the whole are less reliable that those based on highly activated malonic esters or β-keto esters. The problem is that there is competition from 1,2- addition (aldol type addition) that is too tough a competition in many of the cases. Nevertheless, the 1,2- versus 1,4- addition preferences are fairly logical, given the ease of attack trend of nucleophiles at carbonyl centres. Recall the order is…

Aldehydes > ketones >esters > amides

As a result, it follows that

- Aldehydes 'always' favour 1,2- addition
- Ketones are the functional group where there's a real competition; small and medium R's favour 1,2- addition, while large groups favour 1,4- / conjugate addition. For the purposes of **large versus small** for this course, we'll set the **barrier at an A value of 2**; groups larger than ethyl ketones favour 1,4- addition (i.e., *i*-Pr, Ph, *t*-Bu), while ethyl or methyl ketones favour 1,2- addition. This is susceptible to the effects of additional substitution elsewhere, but we will use that as a general guideline.
- Esters and tertiary amides favour 1,4- addition.



Some examples: