

ORGANIC CHEMISTRY 2 LECTURE GUIDE 2019

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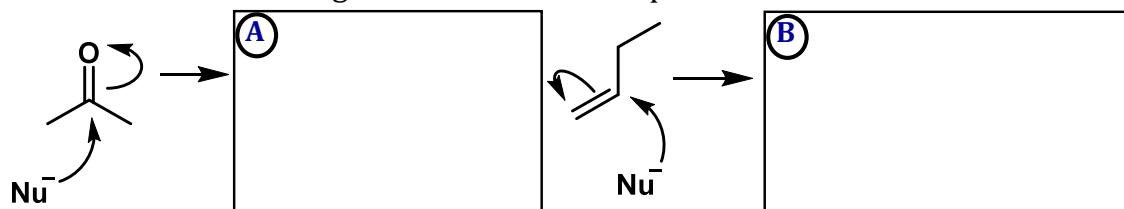
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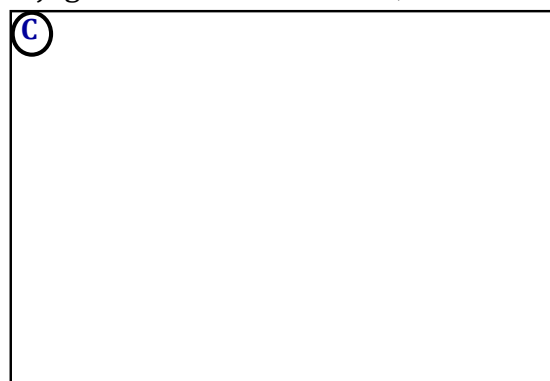
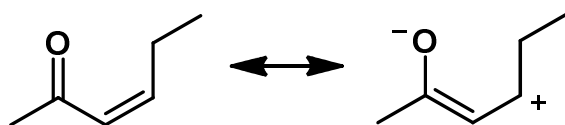
ISBN 978-0578415017 (IQ-Proton Guru)

Lesson VI.20. Addition of Nucleophiles to α,β -Unsaturated Carbonyls*Electrophilic sites*

We have seen enough examples to know how carbonyls react with nucleophiles and how an alkene might react with a nucleophile:



If the carbonyl and the alkene are in pi-conjugation with one another, what might the impact be?



Notes

Lesson VI.20. Addition of Nucleophiles to α,β -Unsaturated Carbonyls

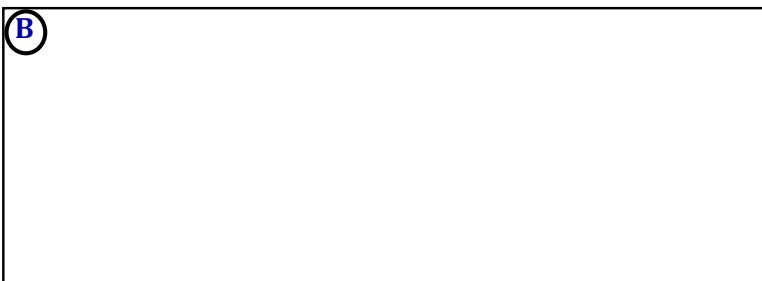
Direct addition versus conjugate addition in unsaturated carbonyls

As a result of the **two electrophilic sites** present in an α,β -unsaturated carbonyl, there are two potentially competing pathways for reaction with a nucleophile:

**1,2-addition
(direct addition)**



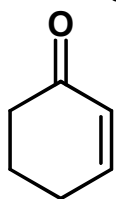
**1,4-addition
(direct addition)**



Notes

Lesson VI.20. Addition of Nucleophiles to α,β -Unsaturated Carbonyls*Direct addition versus conjugate addition in unsaturated carbonyls*

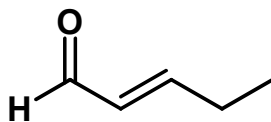
Fortunately, the type of addition depends in large extent on whether the attacking nucleophile is a strong or weak base. Strong bases do 1,2-addition.



1. RMgBr
2. acidic workup



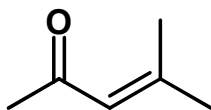
(A)

1. LiAlH₄

2. acidic workup



(B)



1. Ph—C≡C—Na

2. acidic workup

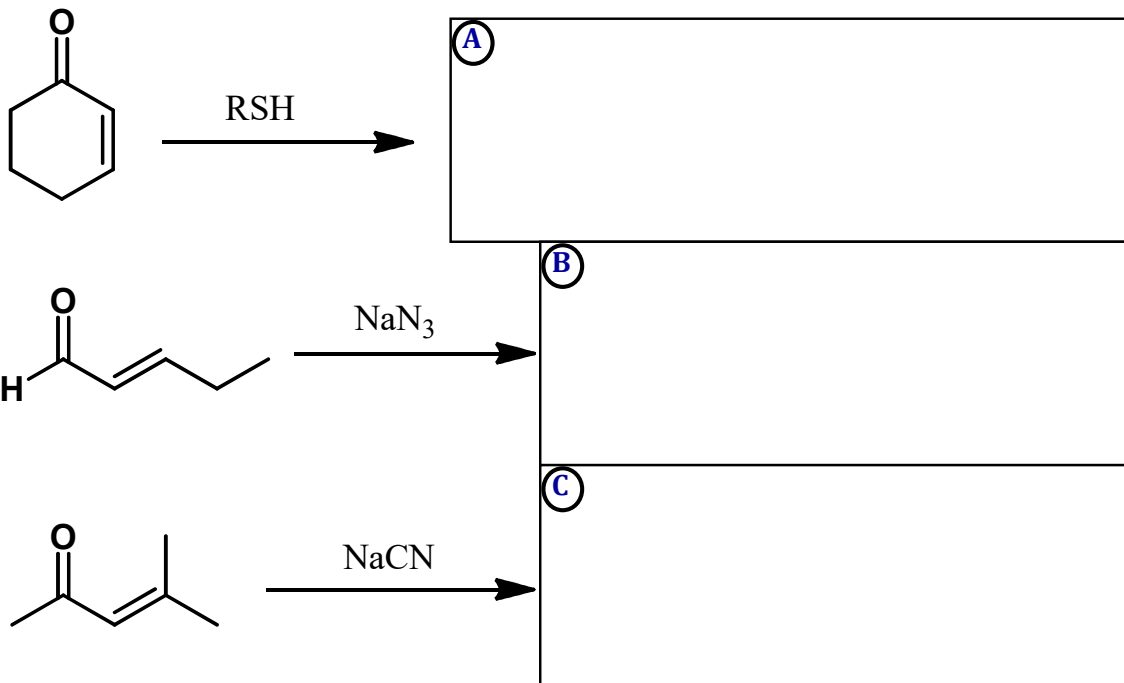


(C)

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Lesson VI.20. Addition of Nucleophiles to α,β -Unsaturated Carbonyls*Direct addition versus conjugate addition in unsaturated carbonyls*

Weak bases (stable anions) tend to do 1,4-addition:

Notes

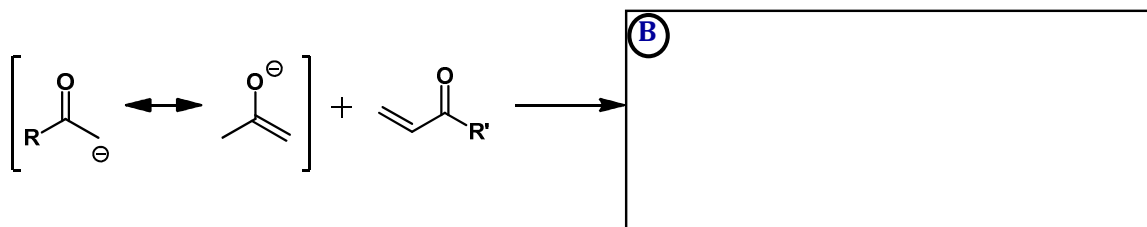
Lesson VI.20. Addition of Nucleophiles to α,β -Unsaturated Carbonyls*Michael Addition*

Let us use our newfound knowledge of how unsaturated carbonyls tend to react to predict what might happen if an unsaturated carbonyl reacts with an enolate.

First, evaluate the enolate's relative base strength:

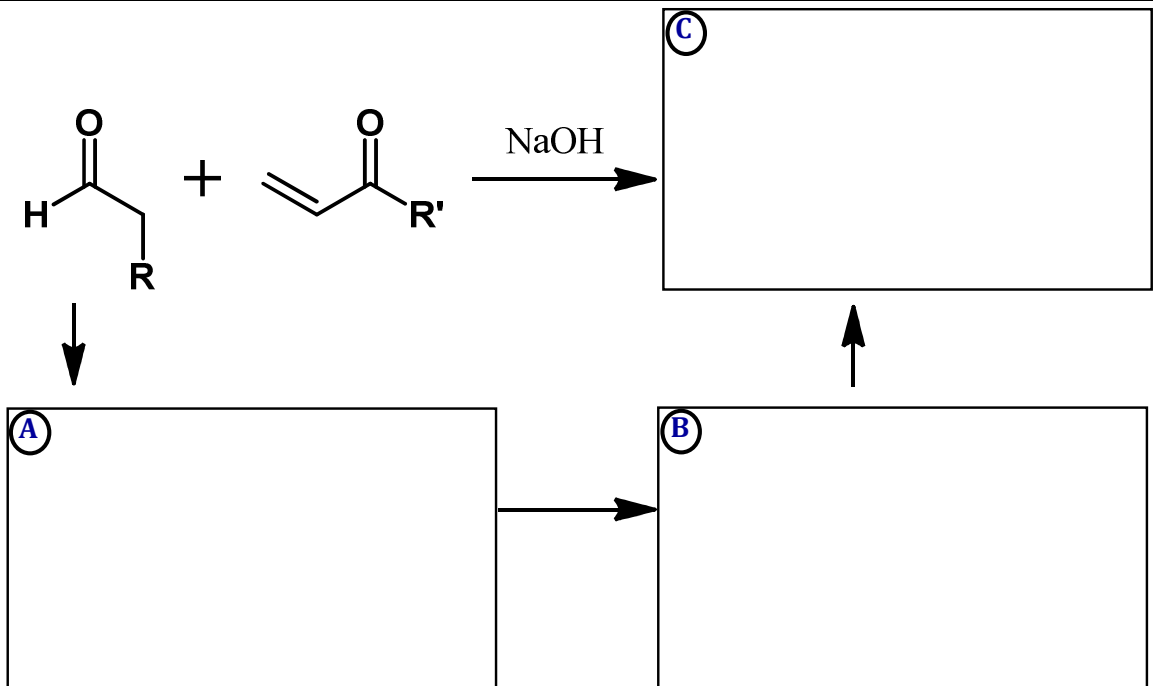


Now we should be able to predict what an enolate nucleophile would tend to do upon reaction with an α,β -unsaturated carbonyl:



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Lesson VI.20. Addition of Nucleophiles to α,β -Unsaturated Carbonyls
Michael Addition

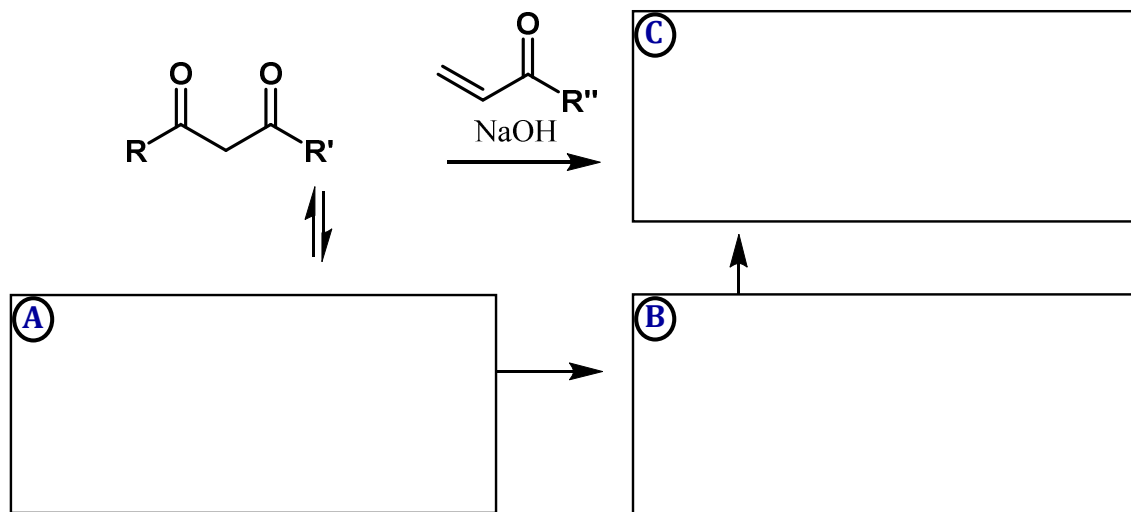


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Lesson VI.20. Addition of Nucleophiles to α,β -Unsaturated Carbonyls

Michael Addition

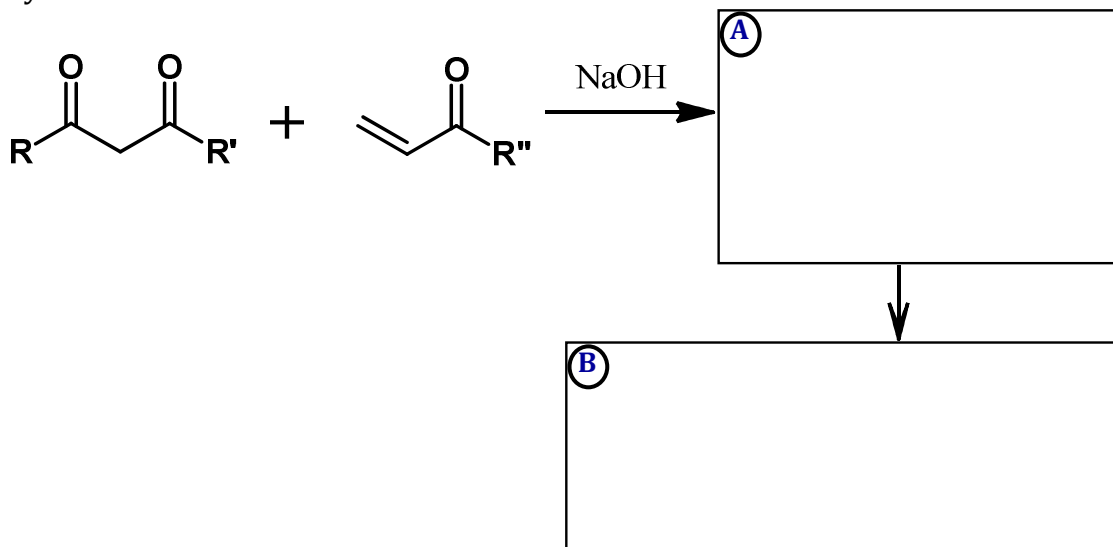
The conditions for the Michael reaction are the same type of conditions used for the Aldol condensation. For this reason, the reactions can be in competition with each other. The Michael reaction can be made more favorable if we use β -diketones as the enolate component of a Michael addition:



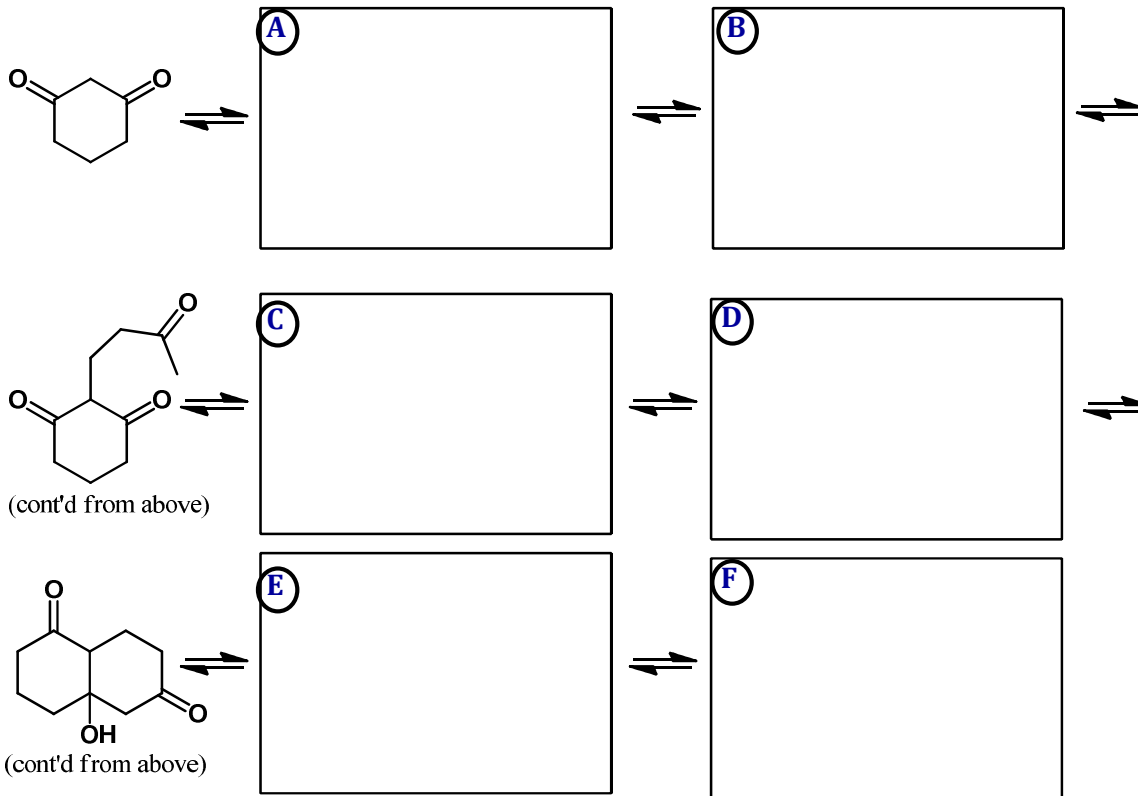
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Lesson VI.20. Addition of Nucleophiles to α,β -Unsaturated Carbonyls*Robinson Annulation:**Aldol Condensation then Intramolecular Michael Addition*

You may notice that the product of a Michael reaction is a species that contains at least two carbonyls in it. This means that we can do an intramolecular aldol condensation reaction *between* the carbonyls on the initial Michael product. This is called **Robinson Annulation**, an important route for making substituted cyclohexanones:

Notes

Lesson VI.20. Addition of Nucleophiles to α,β -Unsaturated Carbonyls
Robinson Annulation



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