

CH 318 N

LECTURE 10

Textbook Assignment: Chapter 16

Homework (for credit): POW 5 posted

Today's Topics: Aldehydes & Ketones

Notice & Announcements:

Exam 1-Grades posted

ORGANIC LECTURE SERIES

Aldehydes And Ketones

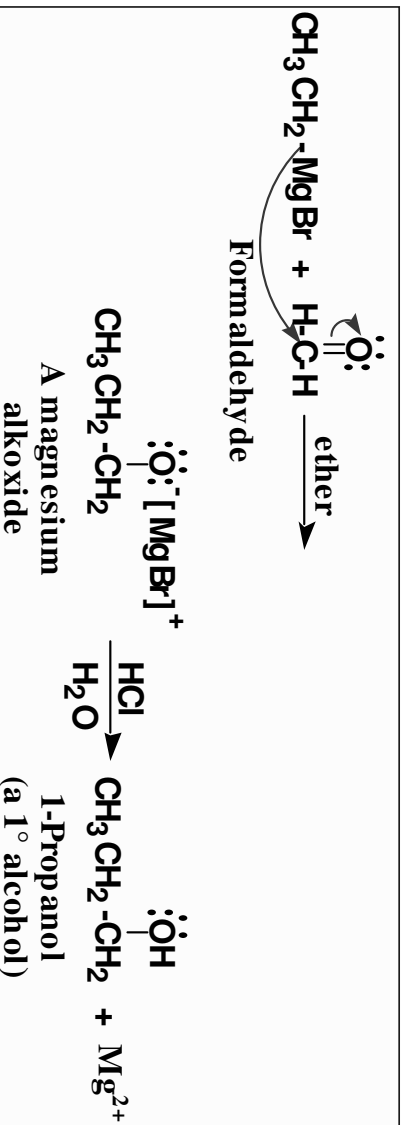
Drawing Mechanisms

- Use double-barbed arrows to indicate the flow of pairs of e⁻
- Draw the arrow from higher e⁻ density to lower e⁻ density i.e. from the nucleophile to the electrophile
- Removing e⁻ density from an atom will create a formal + charge
- Adding e⁻ density to an atom will create a formal - charge
- Proton transfer is fast (kinetics) and usually reversible

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Grignard Reagents

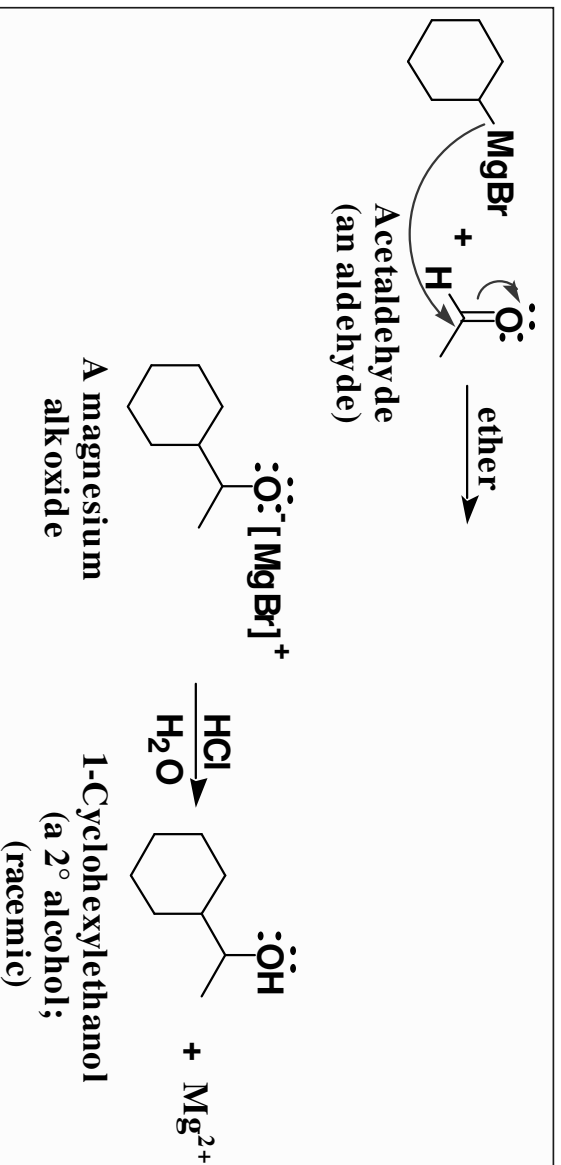
– addition of a Grignard reagent to formaldehyde followed by H₃O⁺ gives a 1° alcohol



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Grignard Reagents

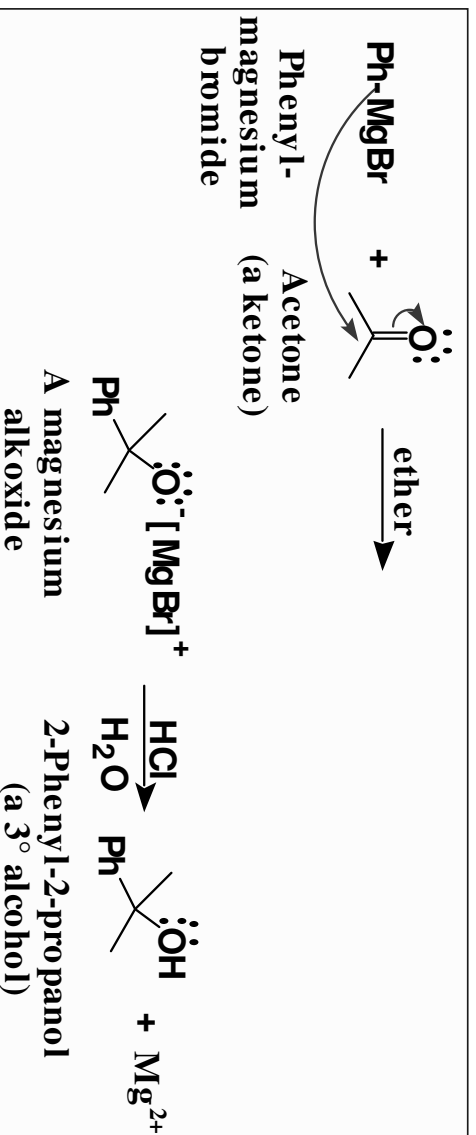
— addition to any other RCHO gives a
2° alcohol



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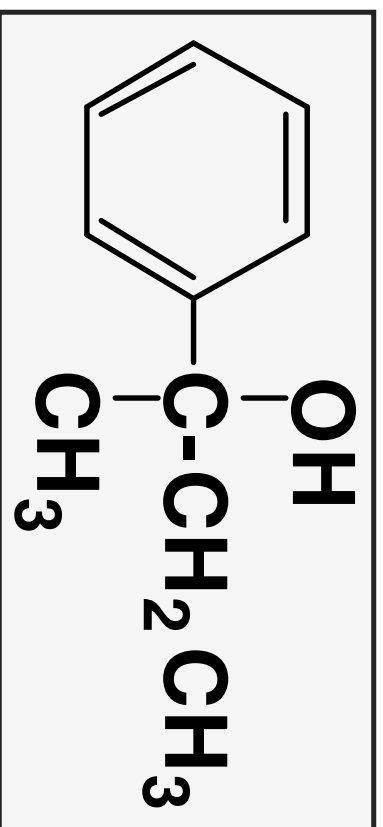
Grignard Reagents

— addition to a ketone gives a 3° alcohol



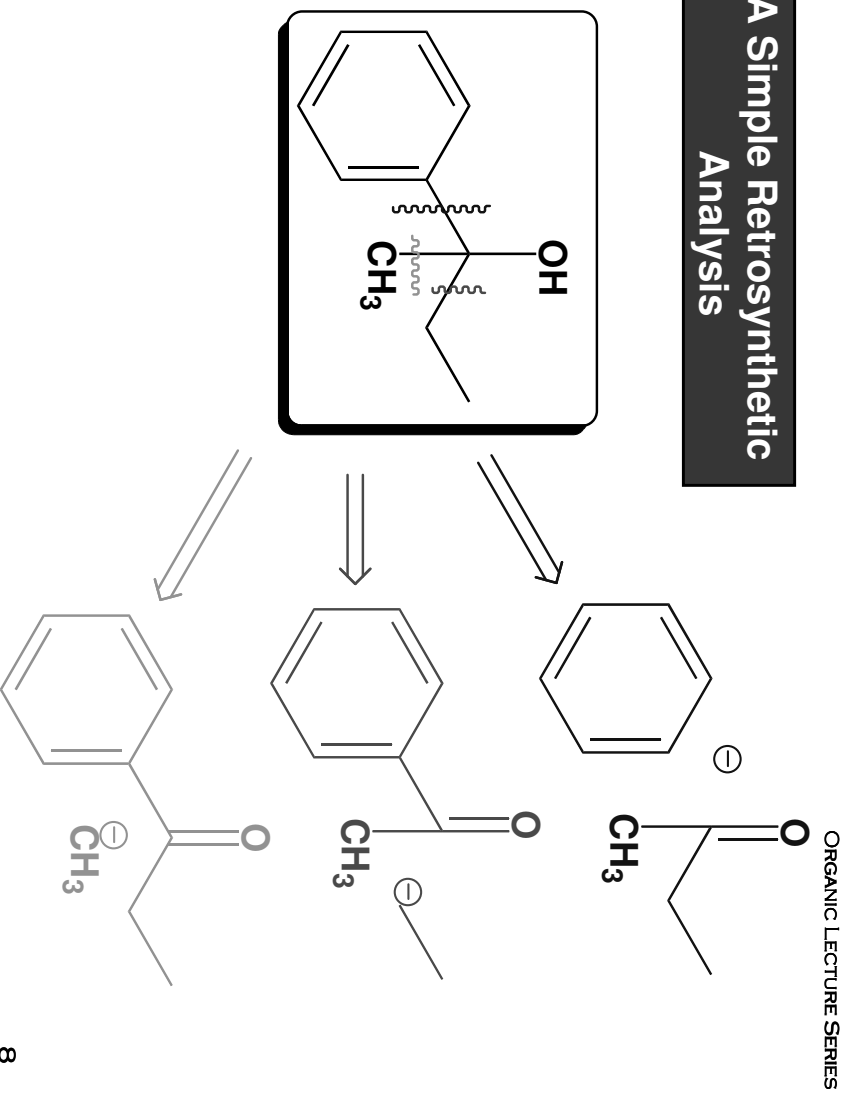
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Problem: 2-phenyl-2-butanol can be synthesized by three different combinations of a Grignard reagent and a ketone. Show each combination.

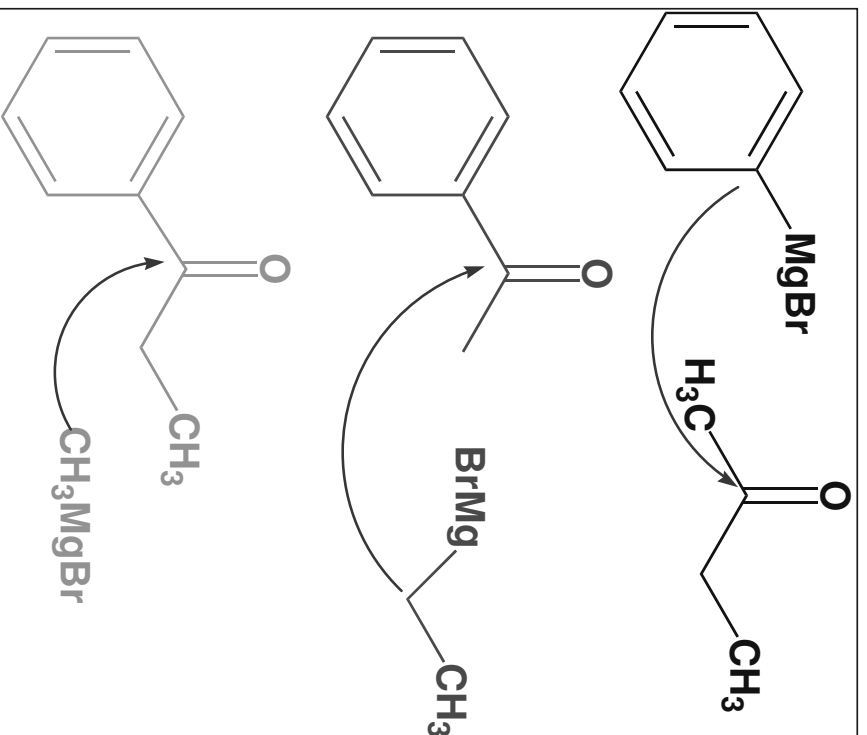


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A Simple Retrosynthetic Analysis



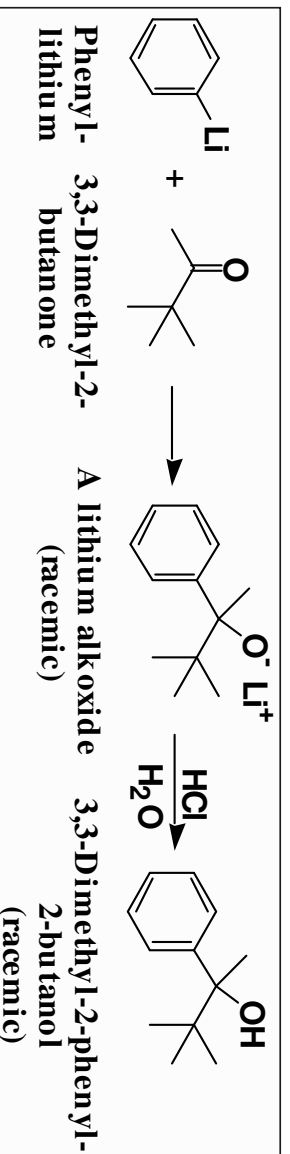
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Organolithium Reagents

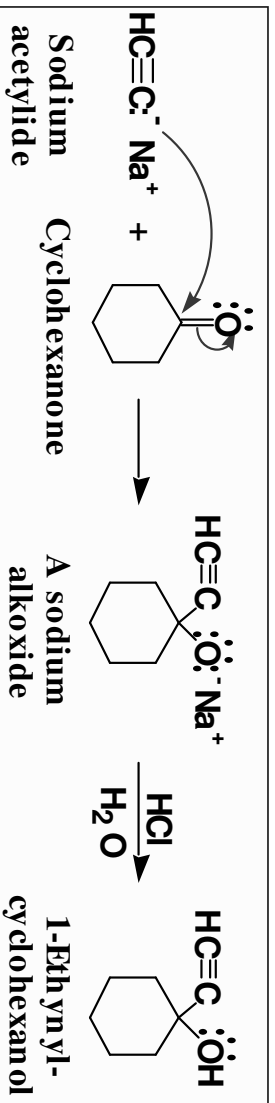
Organolithium compounds are generally more reactive in $\text{C}=\text{O}$ addition reactions than RMgX , and typically give higher yields



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Salts of Terminal Alkynes

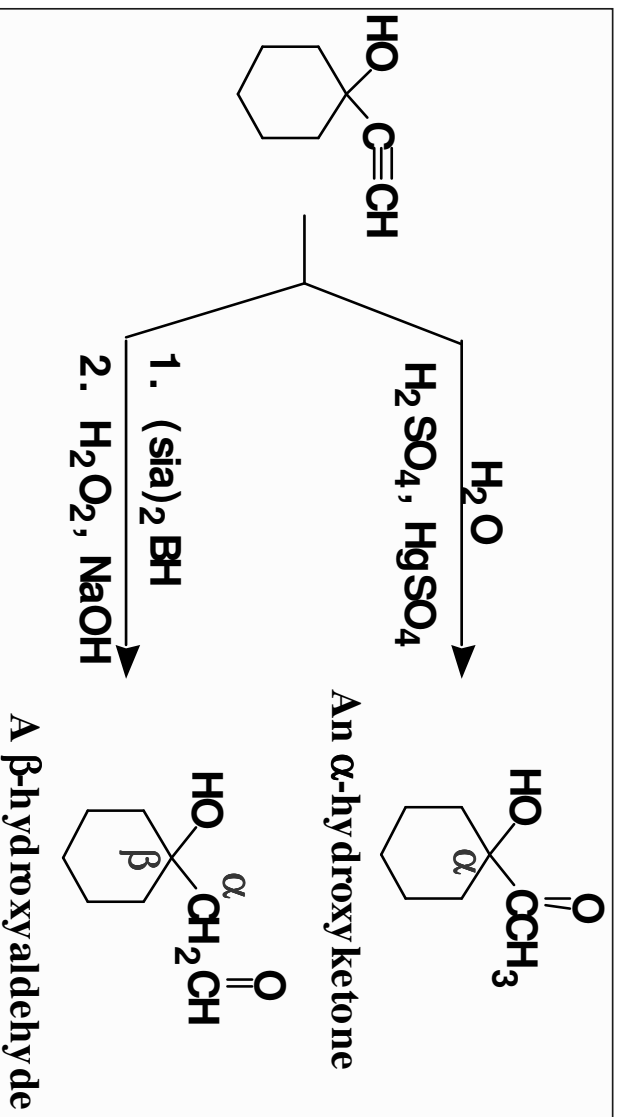
- Addition of an alkyne anion followed by H_3O^+ gives an α -acetylenic alcohol
- Note: this is a 2-C homologation



Homologation is a term used for extending a carbon chain

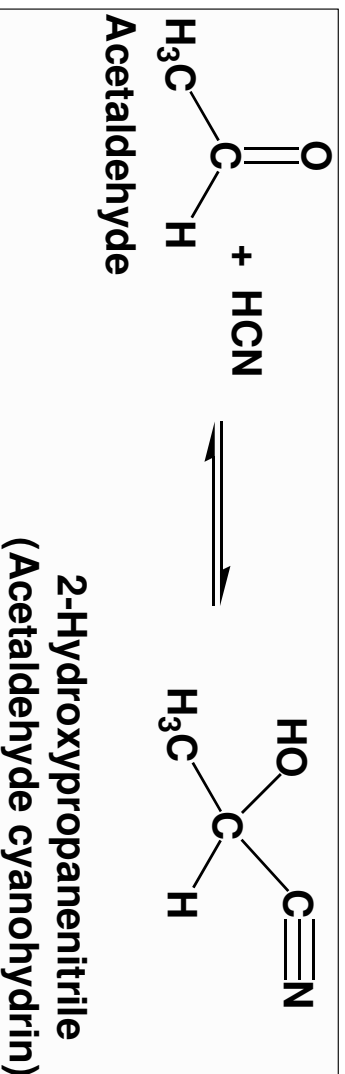
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Oxidation of Terminal Alkynes



Addition of HCN

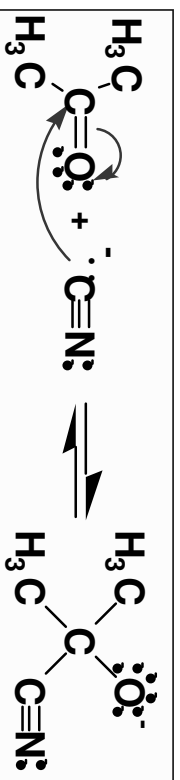
- HCN adds to the C=O group of an aldehyde or ketone to give a cyanohydrin
- Cyanohydrin: a molecule containing an -OH group and a -CN group bonded to the same carbon



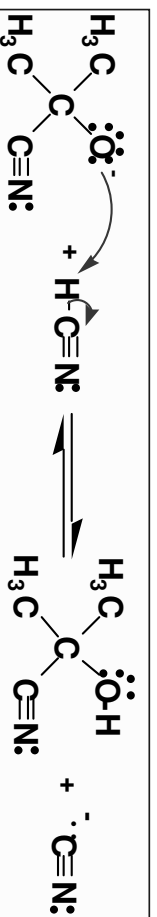
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Addition of HCN

- Mechanism of cyanohydrin formation
 - Step 1: nucleophilic addition of cyanide to the carbonyl carbon



- Step 2: proton transfer from HCN gives the cyanohydrin and regenerates cyanide ion

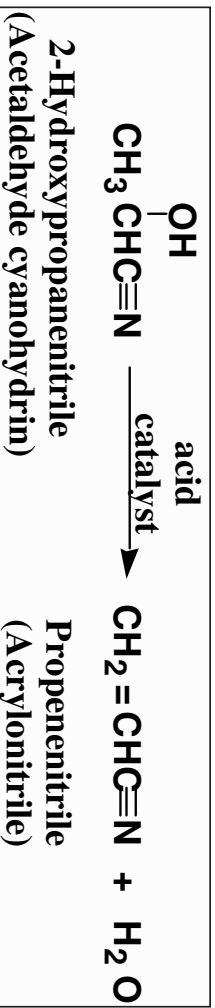


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Cyanohydrins

- The value of cyanohydrins
 - acid-catalyzed dehydration of alcohol gives an alkene

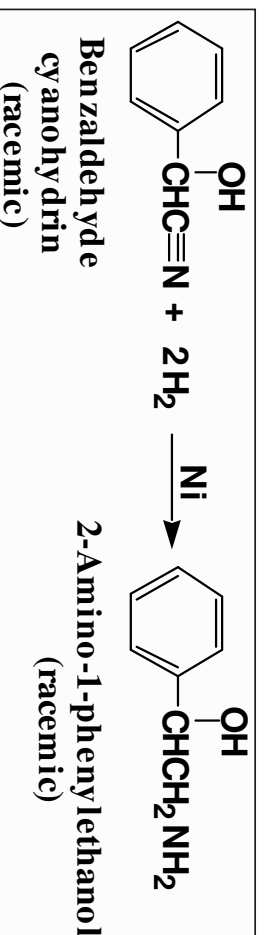
Monomer for polymers



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Cyanohydrins

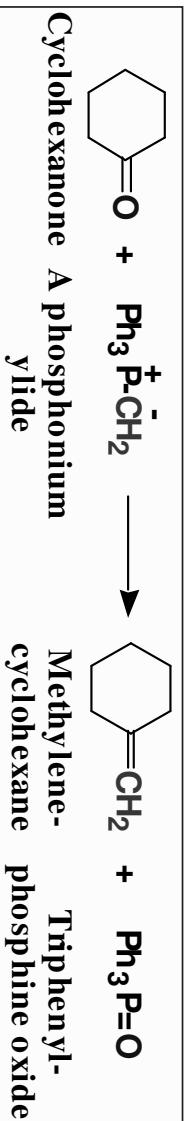
- catalytic reduction of the cyano group gives a 1° amine



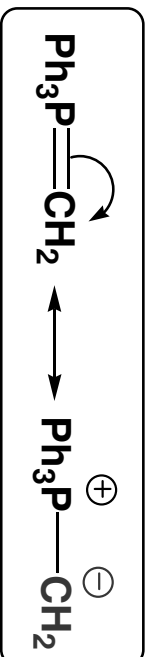
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Wittig Reaction

The Wittig reaction is a very versatile synthetic method for the synthesis of alkenes (olefins) from aldehydes and ketones

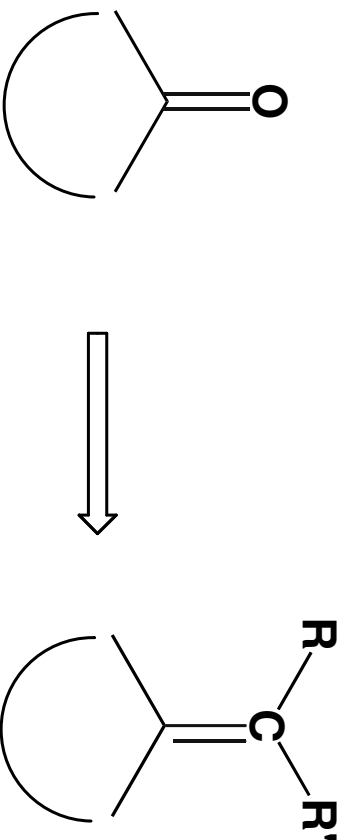


Ylides are reagents (or reactive intermediates) which have adjacent charges:



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Overall Synthetic Transformation of Wittig Reagents & Its Variations



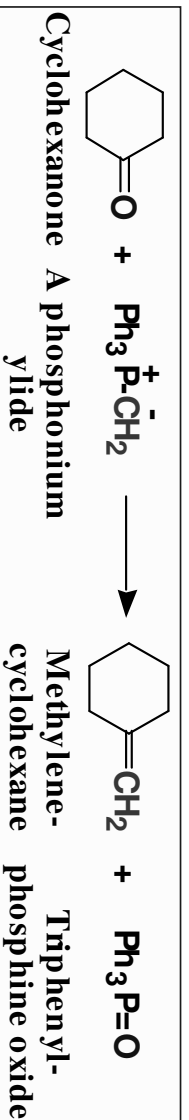
**KETONE
CAN BE
CYCLIC**

**ALKENES
OR
OLEFINS**

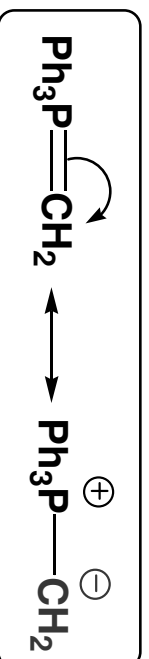
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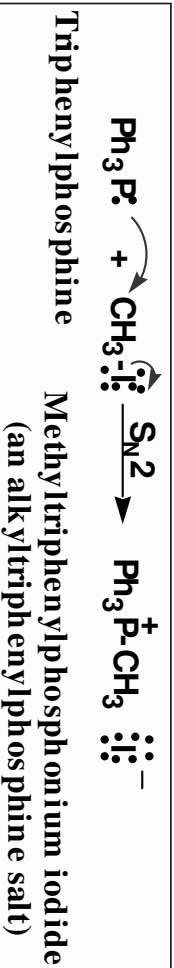


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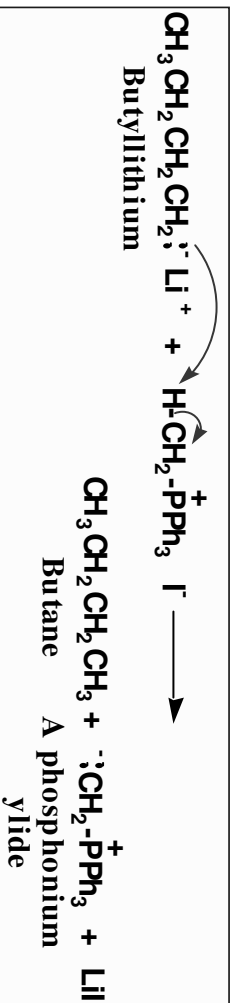
Phosphonium ylides

ORGANIC LECTURE SERIES

Phosphonium ylides are formed in two steps:
Step 1: nucleophilic displacement of iodine by triphenylphosphine



Step 2: treatment of the phosphonium salt with a very strong base, most commonly BuLi, NaH, or NaNH₂

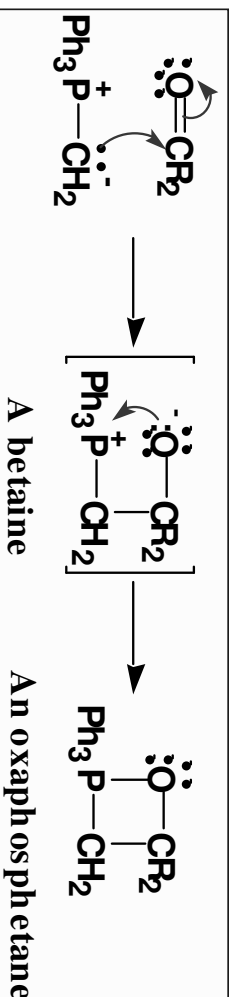


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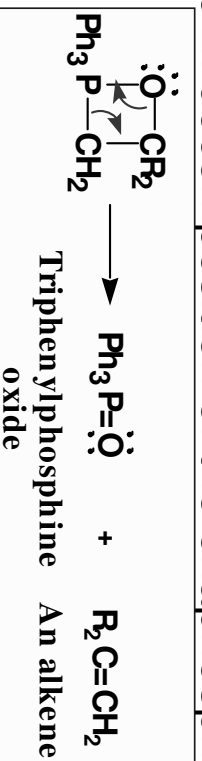
Wittig Reaction

Phosphonium ylides react with the C=O group of an aldehyde or ketone to give an alkene

Step 1: nucleophilic addition of the ylide to the electrophilic carbonyl carbon

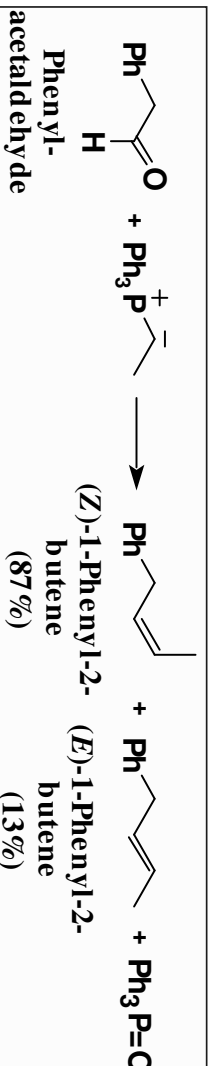
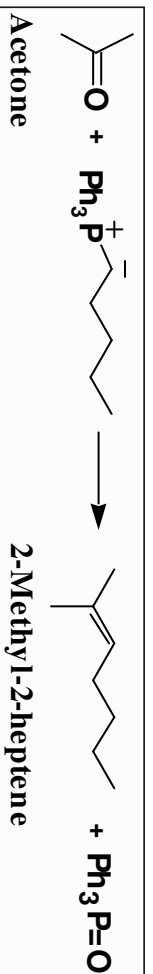


Step 2: decomposition of the oxaphosphetane

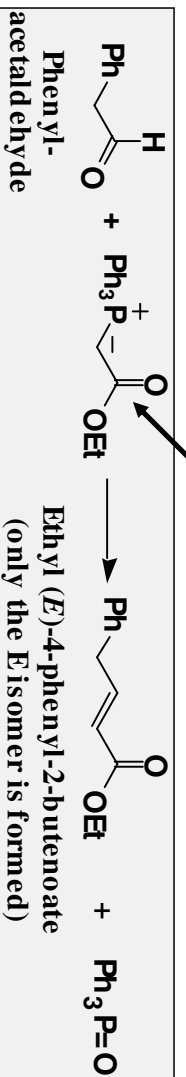


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Wittig Reaction



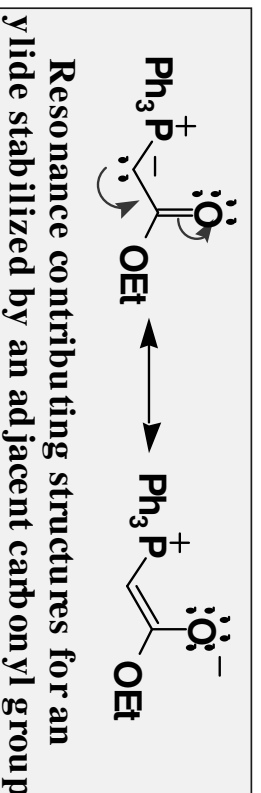
Resonance stabilized Wittig reagent:



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Wittig Reaction

- some Wittig reactions are *Z* selective, others are *E* selective
- Wittig reagents with an anion-stabilizing group, such as a carbonyl group, adjacent to the negative charge are generally *E* selective



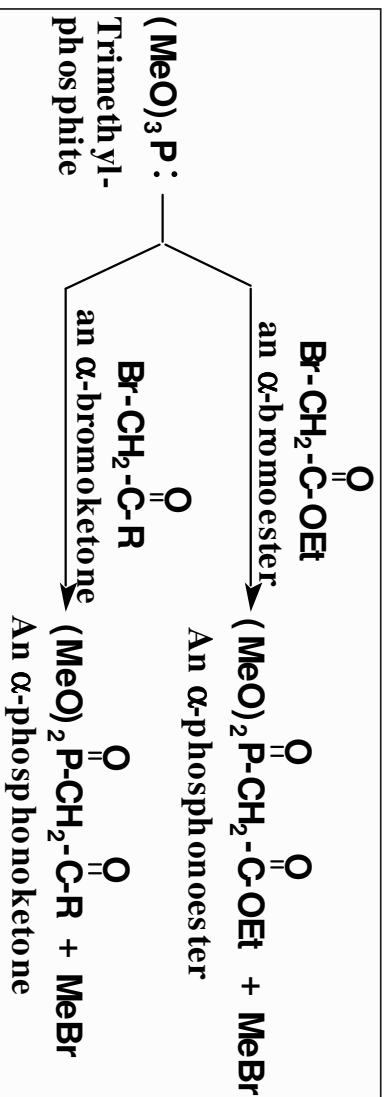
- Wittig reagents without an anion-stabilizing group are generally *Z* selective

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A Variant of the Wittig Reagent

Horner-Emmons-Wadsworth modification

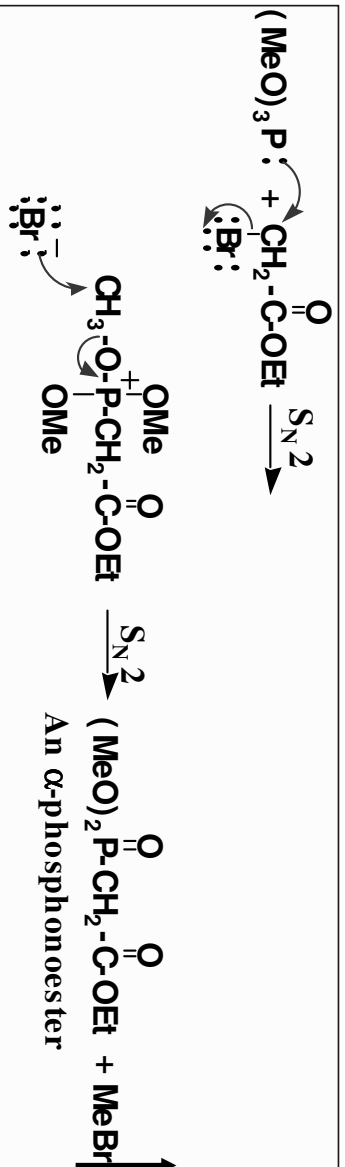
- uses a **phosphonoester**



These reagents are usually isolated.

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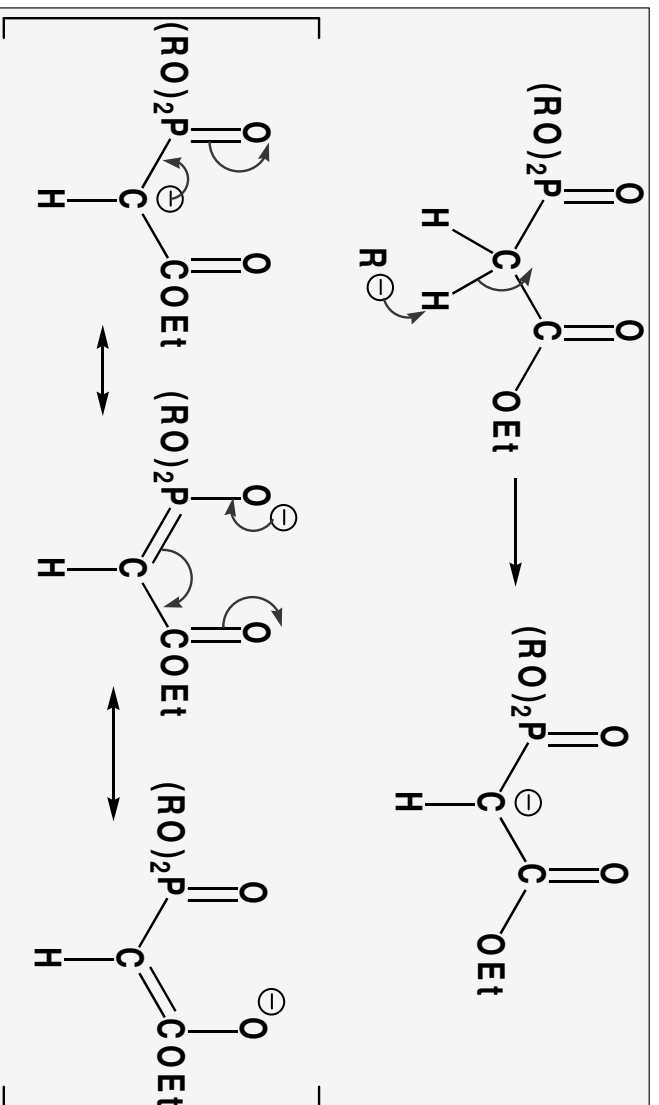
–phosphonoesters are prepared by successive S_N2 reactions



Very exothermic as MeBr is boiled from the reaction mixture

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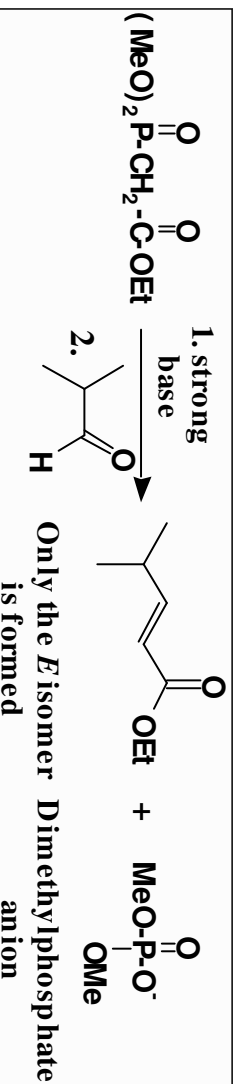
Resonance Stabilization:



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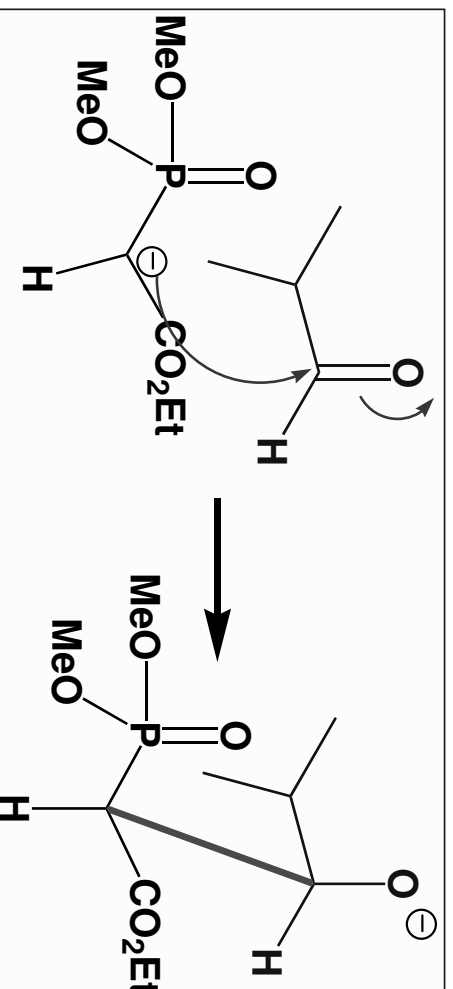
The Use of Phosphonoesters

1. treatment of a phosphonoester with a strong base followed by an aldehyde or ketone gives an alkene
2. a particular value of using a phosphonoester-stabilized anion is that they are almost exclusively *E* selective



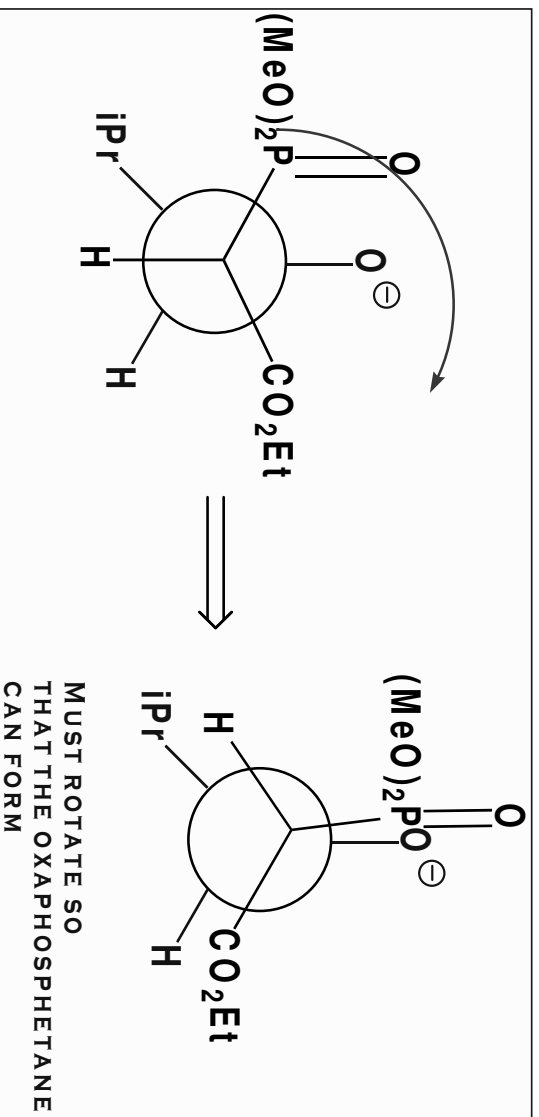
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Why do Stabilized Horner-Emmons-Wadsworth Reagents give the *E* olefin?



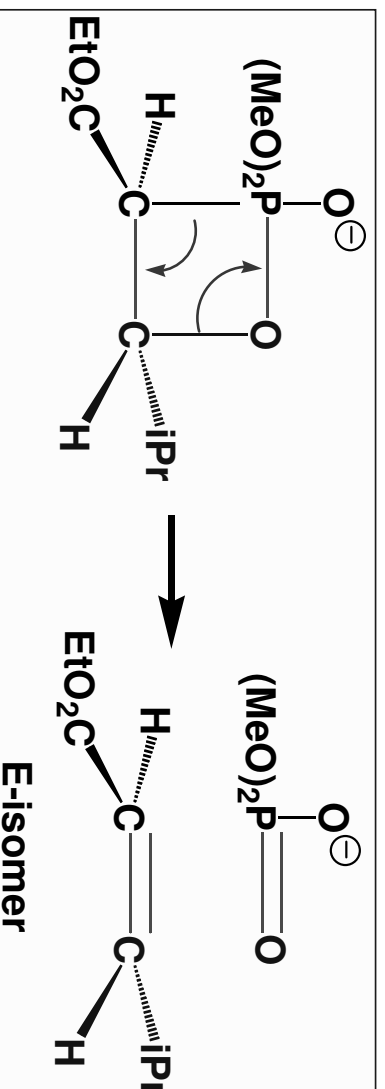
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Why do Stabilized Horner-Emmons-Wadsworth Reagents give the E olefin?



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Why do Stabilized Horner-Emmons-Wadsworth Reagents give the E olefin?



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