

4 Electron Rich Carbons with Attached Heteroatoms

- Heteroatoms are non-metallic atoms other than carbon. The effect of heteroatoms on an electron rich carbon system can be divided into two general areas:
 - stabilisation of carbon charge (e.g. enolate etc., § 3.4)
 - **change the reaction product**

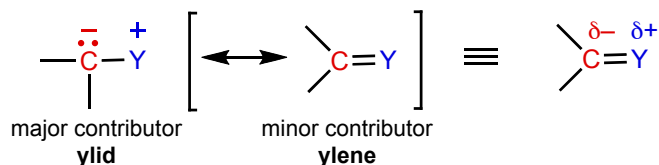
The second type of effect is the focus of this section.

- Usually these reactions involve two steps:
 - nucleophilic addition of carbon nucleophiles
 - neutralisation of the anionic intermediate
 - often by elimination of the heteroatom

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4.1 Electron Rich Carbon – Ylids

- Wide variety of possible electrophilic partners but the most common and useful reactions are those carried out with *carbonyl compounds as the electrophile*.
- Largest area of interest is the use of **ylids** (ylides):

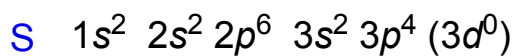


- Ylids are substances that can be formally drawn as a carbanion directly bound to a positively charged heteroatom (Y).
- The most stable and useful ylids are those where Y can stabilise the molecule by accepting some negative charge from the carbanion to give a multiply-bonded contributor to the resonance hybrid which involves a higher valency of Y.
- Best achieved if Y is from the elements below the first short period of the periodic table and has suitable **d orbitals for participation**. The most common heteroatoms are **sulfur and phosphorus**.

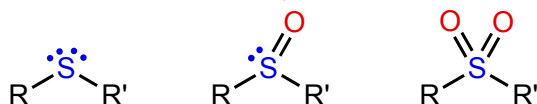
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4.2 Sulfur Ylids

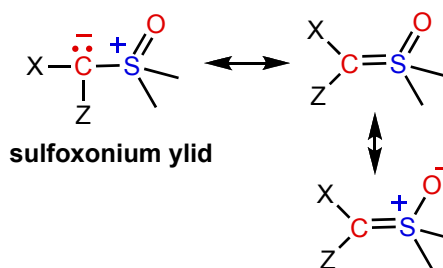
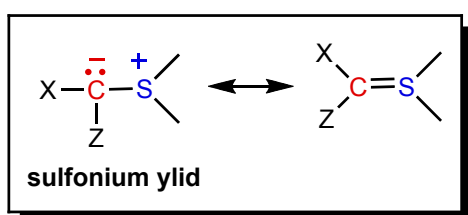
Electronic configuration of sulfur:



Has 6 valence electrons and forms divalent sulfur compounds (sulfides) and can be oxidised to sulfoxides, then sulfones



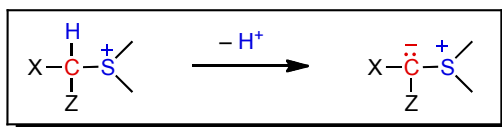
Sulfur ylids:



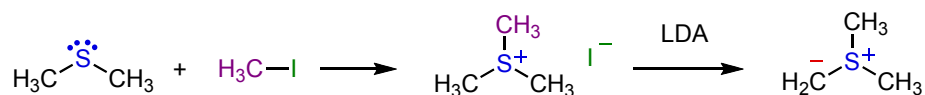
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4.2 Sulfur Ylids – Preparation

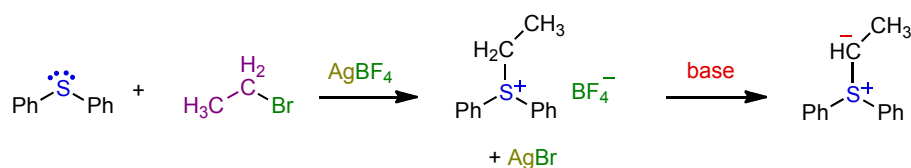
Treat a sulfonium salt with a base:



Sulfonium salts are made from sulfides and alkylating agents:



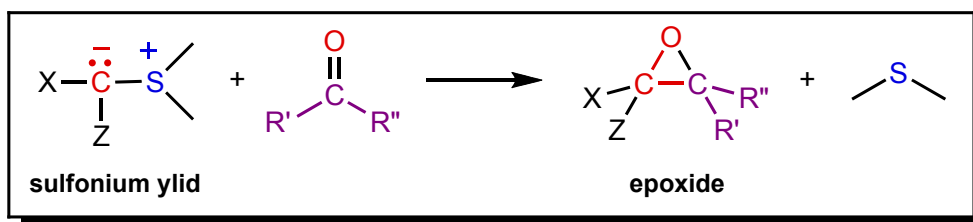
For unsymmetrical cases, Ph-S-Ph is used, with activating conditions as diphenyl sulfide is a poor nucleophile:



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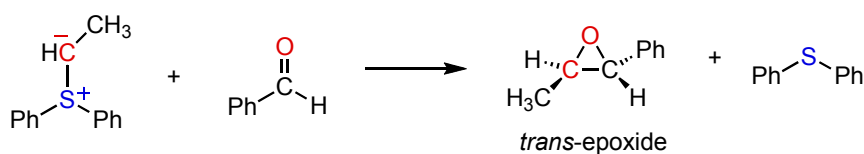
4.2 Sulfur Ylids – Reactions

Sulfur ylids react with carbonyl compounds to yield **epoxides**:



General, convergent method for preparing a wide range of epoxides.

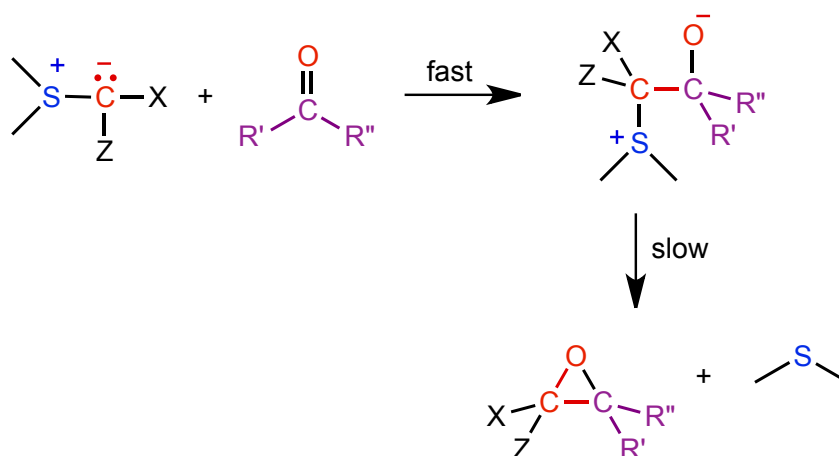
➤ *trans* products formed



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4.2 Sulfur Ylids – Mechanism

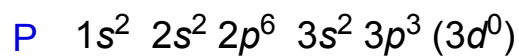
The nucleophilic addition of the sulfonium ylid carbon to the carbonyl carbon is fast and **irreversible** → kinetic control



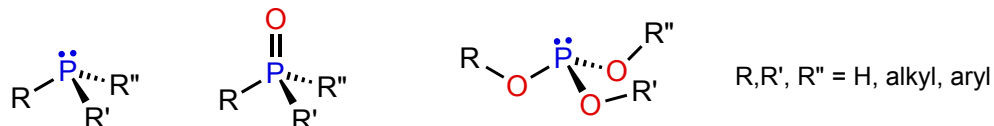
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4.3 Phosphorus Ylids

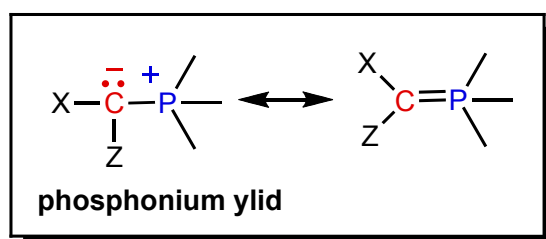
Electronic configuration of phosphorus:



Has 5 valence electrons and forms trivalent phosphorus compounds (phosphines) and can be oxidised to phosphine oxides



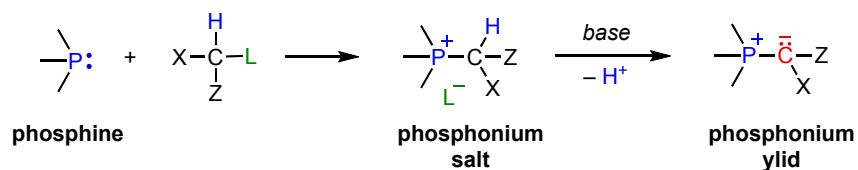
Phosphorus ylids:



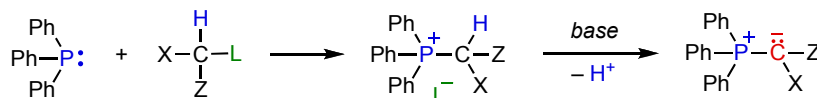
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4.3 Phosphorus Ylids – Preparation

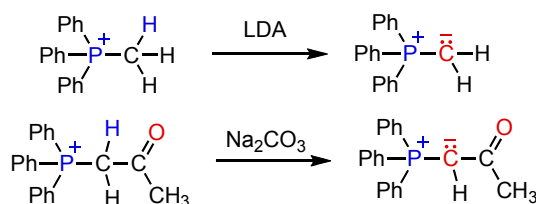
All P ylids are obtained by deprotonation of phosphonium salts:



usually

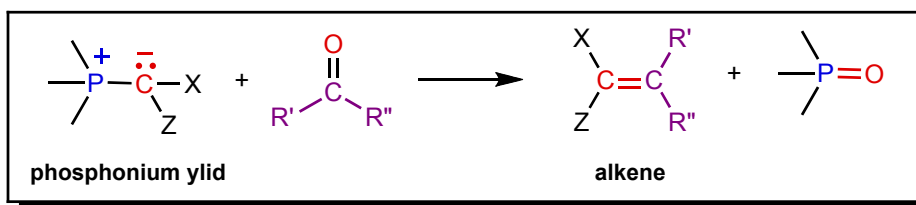


Strength of base depends on electron withdrawing ability of X, Z

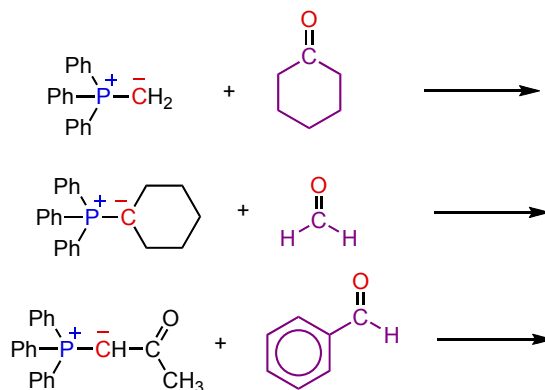


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4.3 Phosphorus Ylids – Reaction



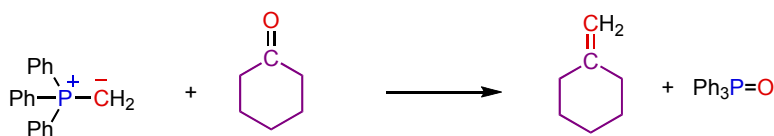
This is known as the **Wittig reaction**, and is a general method for converting carbonyls (aldehydes, ketones) into alkenes



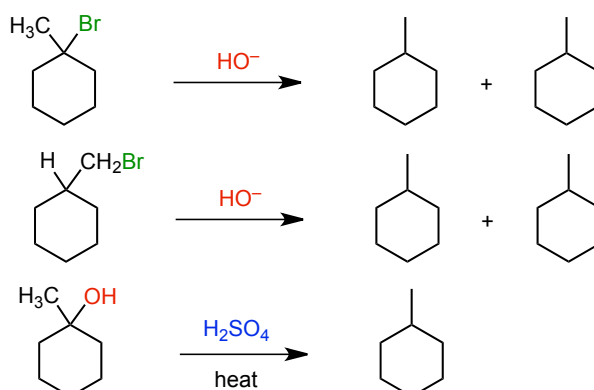
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4.3 Phosphorus Ylids – Wittig vs Other Methods

The **Wittig reaction** is regioselective. Compare:



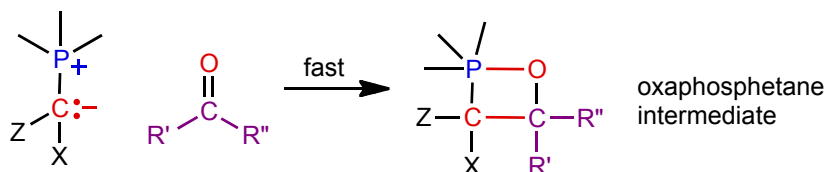
Generation of the alkene by elimination would yield a terminal alkene as the minor product (or not at all):



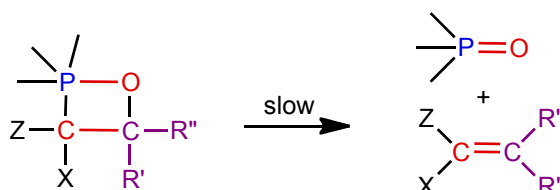
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4.3 Phosphorus Ylids – Mechanism

Step 1: the nucleophilic ylid carbon attacks the carbonyl carbon, and the carbonyl oxygen attacks the electrophilic phosphorus



Step 2: elimination of phosphine oxide forms the alkene product



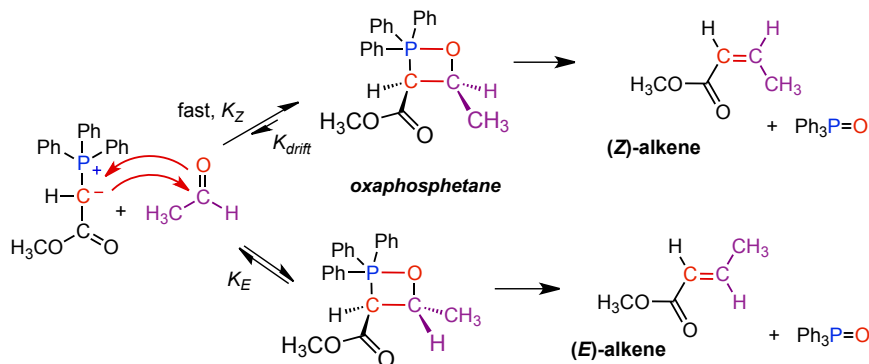
- if the ylid is **unstabilised**, the first step is irreversible
→ **kinetic** control
- if the ylid is **stabilised** (X, Z electron withdrawing), the first step is reversible → **thermodynamic** control

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4.3 Phosphorus Ylids – Stereochemistry

The stereochemistry is determined by the stereostructure of the oxaphosphetane intermediate

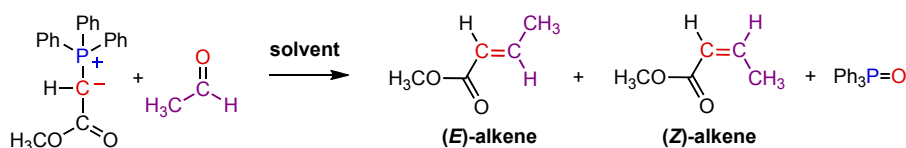
- if the first step is irreversible → get **(Z)-alkene** (kinetic product)
- if the intermediate is stabilised or collapses to the alkene is inhibited, then equilibrium of the first step occurs → get **(E)-alkene** as the major product (thermodynamic control)



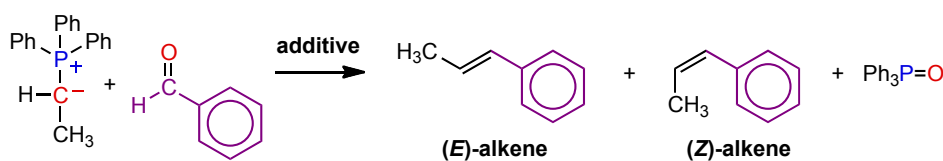
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4.3 Phosphorus Ylids – Stereochemistry 2

- **solvents** or the presence of **salts** can affect the stereochemical outcome



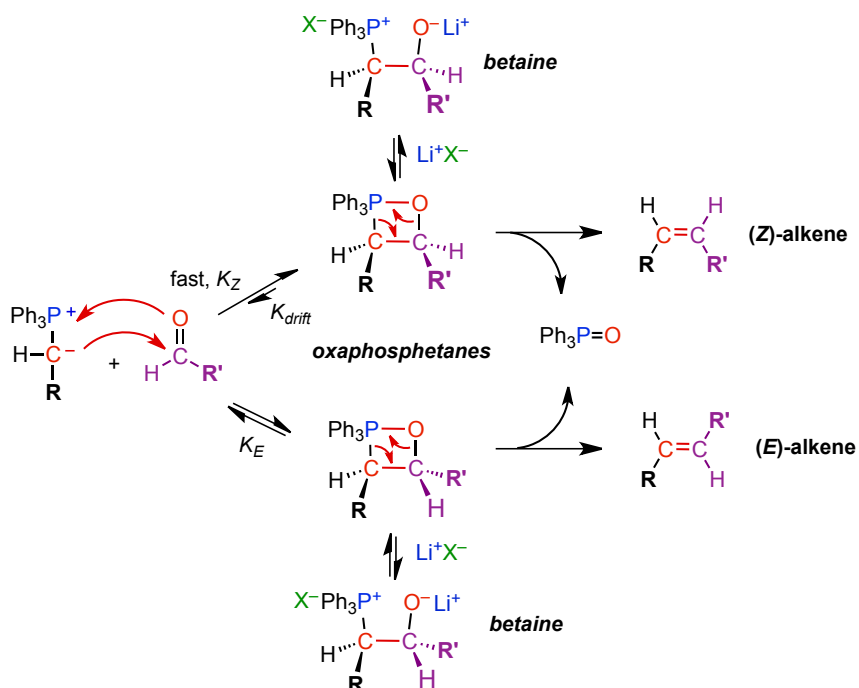
solvent	(E)	(Z)
CH ₂ Cl ₂	94	6
CH ₃ OH	62	38



conditions	(E)	(Z)
no salts		
Lil		

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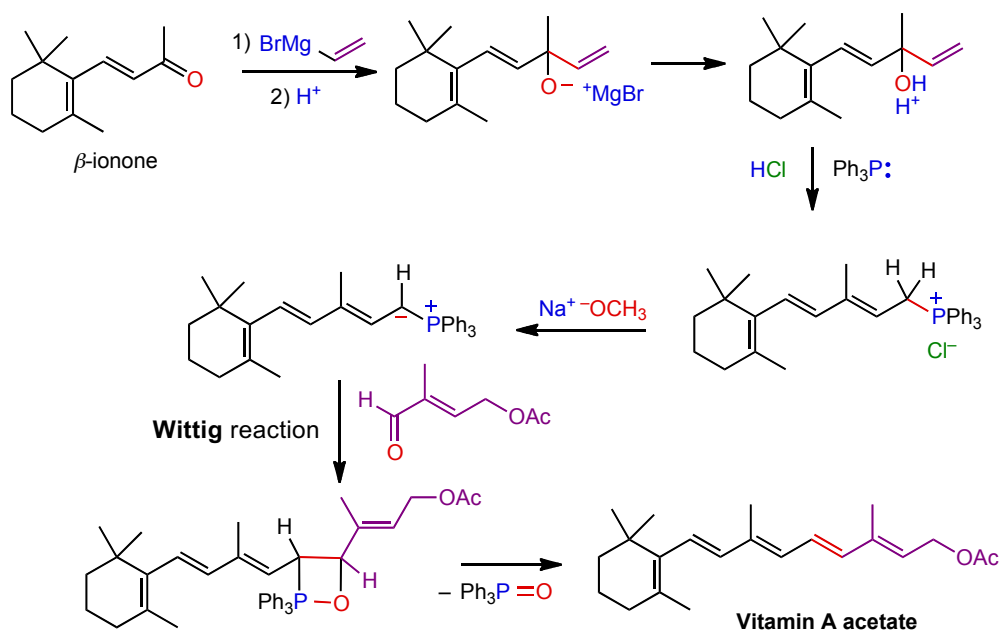
4.3 Wittig equilibrium with salt



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4.3 Phosphorus Ylids – Application Examples

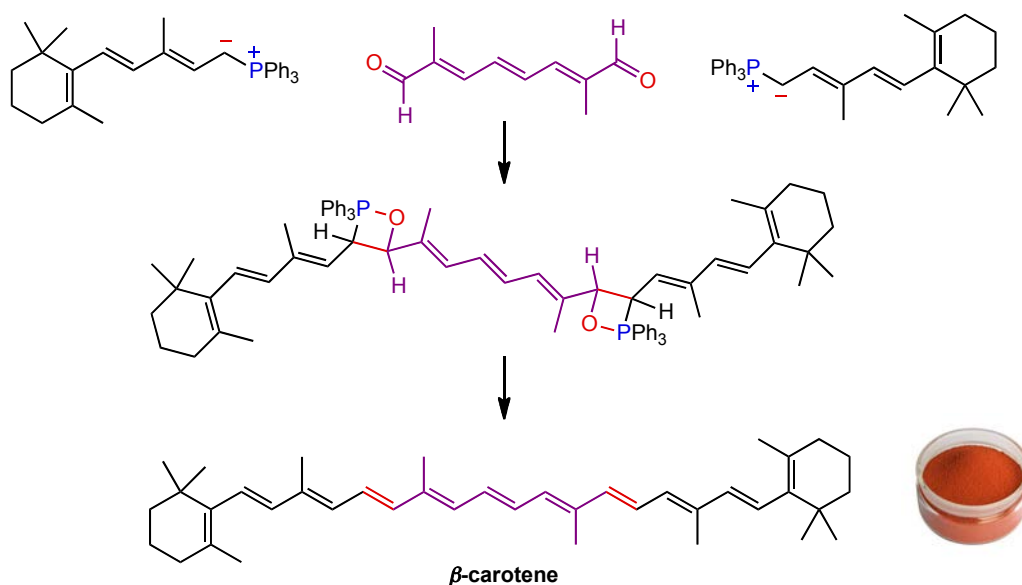
Synthesis of Vitamin A acetate:



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4.3 Phosphorus Ylids – Application Examples

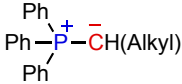
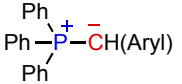
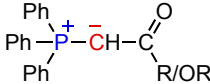
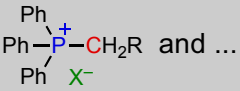
Synthesis of β -carotene:



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4.3 Phosphorus Ylids – Summary

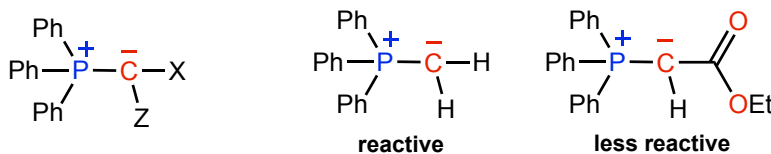
P-Ylids: Nomenclature, Preparation and Stereoselectivity of the Wittig reaction

P-Ylid			
Ylid type			
Ylid is prepared...	... <i>in situ</i> <i>in situ</i> in prior reactions...
...from 	<i>n</i> -BuLi or Na ⁺ -NH ₂ or K ⁺ -O ^{<i>tert</i>} Bu	NaOEt or aqueous NaOH	aqueous NaOH
1,2 disubstituted olefins typically result with ≥ 90% <i>Z</i> -selectivity	... as an <i>E</i> -, <i>Z</i> -mixture	... with > 90% <i>E</i> -selectivity

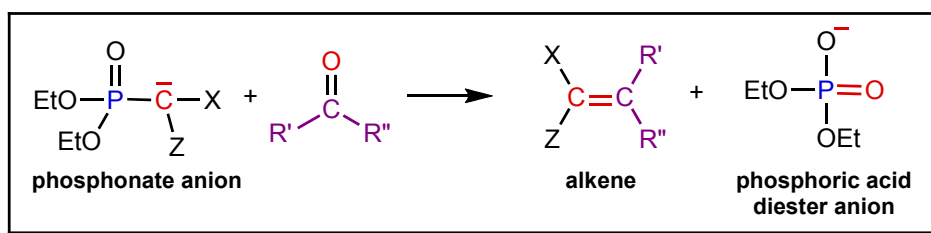
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4.4 Other Phosphorus-stabilised Carbanions

The reactivity of phosphorus ylids varies quite widely depending on the electron withdrawing ability of X and Z



Wittig-type reactions with electron-withdrawing X, Z can be achieved by using



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4.4 Other Phosphorus-stabilised Carbanions

The phosphonate ester anion is more reactive than phosphorus ylids, and produces the (*E*)-alkene product (**thermodynamic** control)

