## 16.10   *The Addition of Ylides: The Wittig Reaction*

● Aldehydes and ketones react with phosphorus ylides to yield alkenes and triphenylphosphine oxide (a by-product). This reaction is known as the **Wittig reaction**.
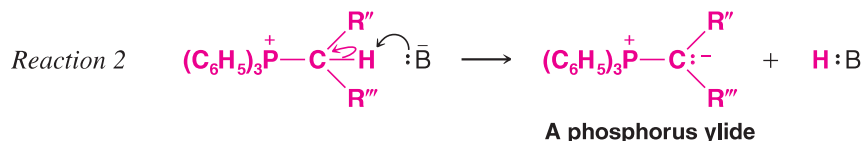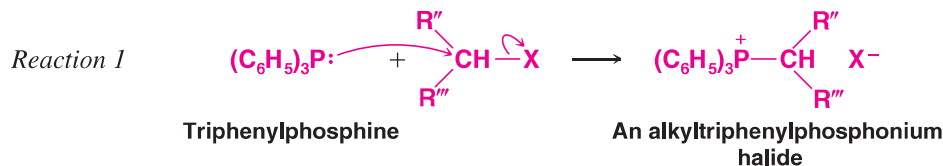
The Wittig reaction has proved to be a valuable method for synthesizing alkenes. The **ylide** required for the reaction is a molecule with no net charge but which has a negative carbon atom adjacent to a positive heteroatom, which in the Wittig reaction is a phosphorus atom. Phosphorus ylides are also called phosphoranes.

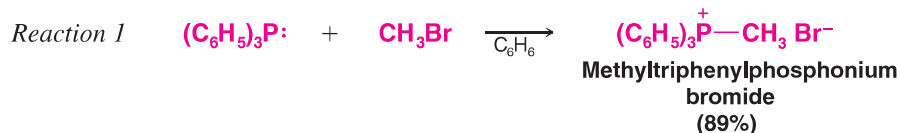| Aldehyde or ketone | Phosphorus ylide (or phosphorane) | Alkene [(*E*) and (*Z*) isomers] | Triphenyl-phosphine oxide |
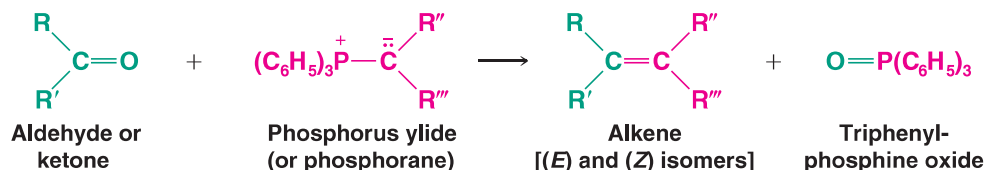
The Wittig reaction is applicable to a wide variety of compounds, and although a mixture of (*E*) and (*Z*) isomers may result, the Wittig reaction offers a great advantage over most other alkene syntheses in that *no ambiguity exists as to the location of the double bond in the product*. (This is in contrast to E1 eliminations, which may yield multiple alkene products by rearrangement to more stable carbocation intermediates, and both E1 and E2 elimination reactions, which may produce multiple products when different β hydrogens are available for removal.)

Phosphorus ylides are easily prepared from triphenylphosphine and primary or secondary alkyl halides. Their preparation involves two reactions:
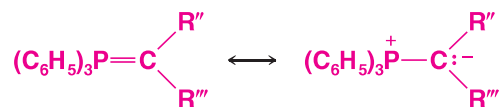
General Reaction

Reaction 1

Triphenylphosphine   **An alkyltriphenylphosphonium halide**

Reaction 2

A phosphorus ylide

Specific Example

Reaction 1 $(C_6H_5)_3P\colon$ + CH_3Br $\xrightarrow{C_6H_6}$ $(C_6H_5)_3\overset{+}{P}-CH_3\ Br^-$

Methyltriphenylphosphonium bromide (89%)

Reaction 2 $(C_6H_5)_3\overset{+}{P}-CH_3$ + C_6H_5Li $\longrightarrow$ $(C_6H_5)_3\overset{+}{P}-CH_2\colon^-$ + C_6H_6 +   LiBr
                   Br^-

The first reaction is a nucleophilic substitution reaction. Triphenylphosphine is an excellent nucleophile and a weak base. It reacts readily with 1° and 2° alkyl halides by an S_N2 mechanism to displace a halide ion from the alkyl halide to give an alkyltriphenylphosphonium salt. **The second reaction is an acid–base reaction**. A strong base (usually an alkyllithium or phenyllithium) removes a proton from the carbon that is attached to phosphorus to give the ylide.

Phosphorus ylides can be represented as a hybrid of the two resonance structures shown here. Quantum mechanical calculations indicate that the contribution made by the first structure is relatively unimportant.

$$(C_6H_5)_3P{=}C\overset{R''}{\underset{R'''}{\diagup\hspace{-0.4em}\diagdown}} \longleftrightarrow (C_6H_5)_3\overset{+}{P}{-}\overset{..}{C}{:}^{-}\overset{R''}{\underset{R'''}{\diagup\hspace{-0.4em}\diagdown}}$$

Studies by E. Vedejs (University of Michigan) indicate that the Wittig reaction takes place in two steps. In the first step (below), the aldehyde or ketone combines with the ylide in a cycloaddition reaction to form the four-membered ring of an oxaphosphetane. Then in a second step, the oxaphosphetane decomposes to form the alkene and triphenylphosphine oxide. The driving force for the reaction is the formation of the very strong ($DH° = 540 \text{ kJ mol}^{-1}$) phosphorus–oxygen bond in triphenylphosphine oxide.
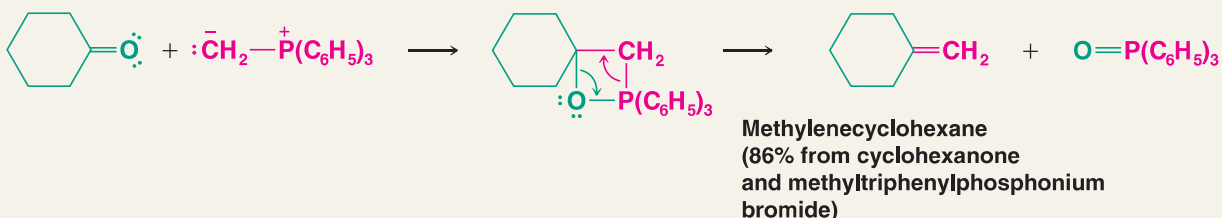
A MECHANISM FOR THE REACTION

The Wittig Reaction

| Aldehyde or ketone | Ylide | Oxaphosphetane | Alkene (+ diastereomer) | Triphenylphosphine oxide |

Specific Example
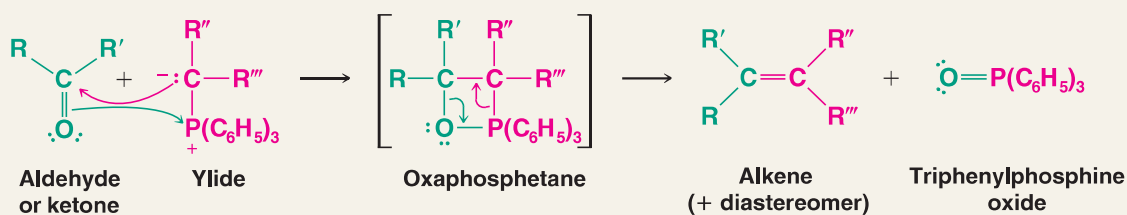
Methylenecyclohexane
(86% from cyclohexanone
and methyltriphenylphosphonium
bromide)
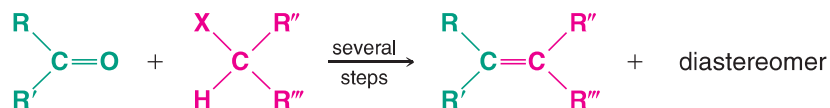
While Wittig syntheses may appear to be complicated, in practice they are easy to carry out. Most of the steps can be carried out in the same reaction vessel, and the entire synthesis can be accomplished in a matter of hours.

The overall result of a Wittig synthesis is

$$\overset{R}{\underset{R'}{\diagup\hspace{-0.4em}\diagdown}}C{=}O \;+\; \overset{X\;\;\;R''}{\underset{H\;\;\;R'''}{\diagup\hspace{-0.4em}C\hspace{-0.4em}\diagdown}} \xrightarrow[\text{steps}]{\text{several}} \overset{R}{\underset{R'}{\diagup\hspace{-0.4em}\diagdown}}C{=}C\overset{R''}{\underset{R'''}{\diagup\hspace{-0.4em}\diagdown}} \;+\; \text{diastereomer}$$

16.10A   How to Plan a Wittig Synthesis

Planning a Wittig synthesis begins with recognizing in the desired alkene what can be the aldehyde or ketone component and what can be the halide component. Any or all of the R groups may be hydrogen, although yields are generally better when at least one group is hydrogen. The halide component must be a primary, secondary, or methyl halide.
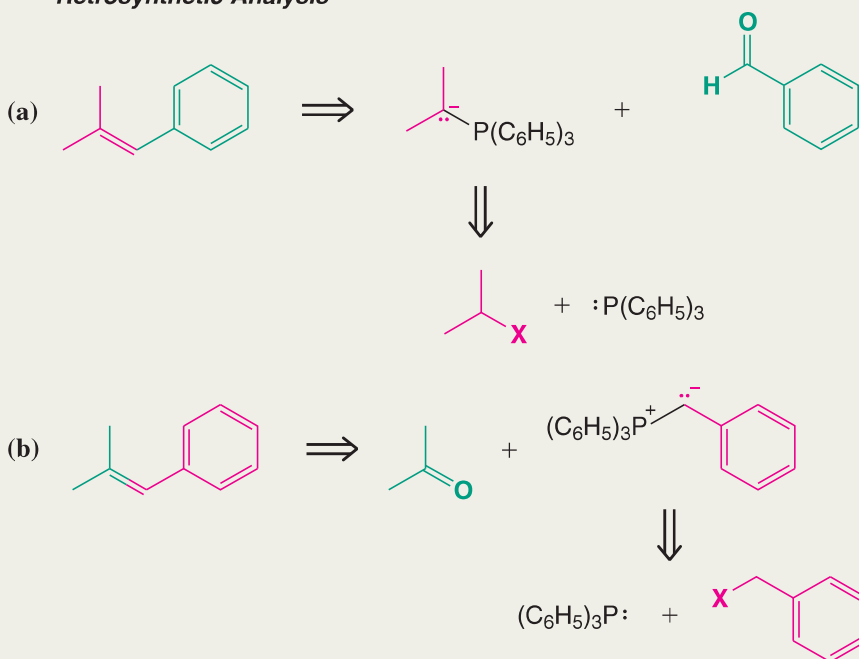
Synthesize 2-methyl-1-phenylprop-1-ene using a Wittig reaction. Begin by writing a retrosynthetic analysis.

STRATEGY AND ANSWER We examine the structure of the compound, paying attention to the groups on each side of the double bond:
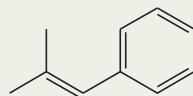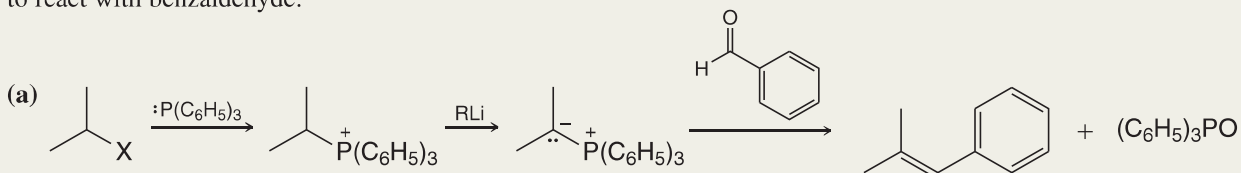
2-Methyl-1-phenylprop-1-ene

We see that two retrosynthetic analyses are possible.

Retrosynthetic Analysis

(a)

(b)

Synthesis

Following retrosynthetic analysis (a), we begin by making the ylide from a 2-halopropane and then allow the ylide to react with benzaldehyde:

(a)

Following retrosynthetic analysis (b), we make the ylide from a benzyl halide and allow it to react with acetone:

(b)