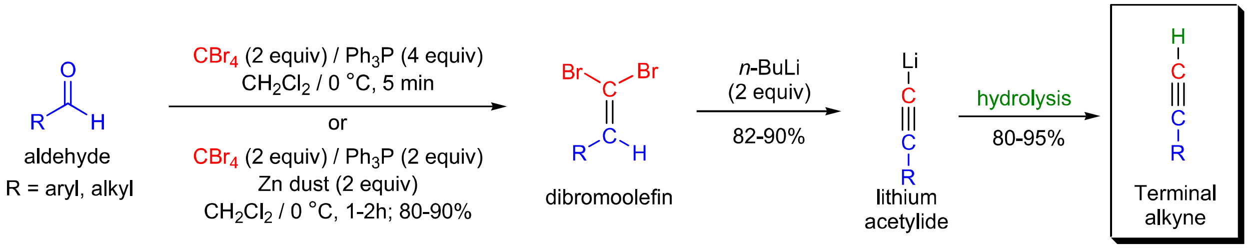
COREY-FUCHS ALKYNE SYNTHESIS

(References are on page 566)

Importance:

[*Seminal Publication*[1]; *Reviews*[2]; *Modifications and Improvements*[3-5]]

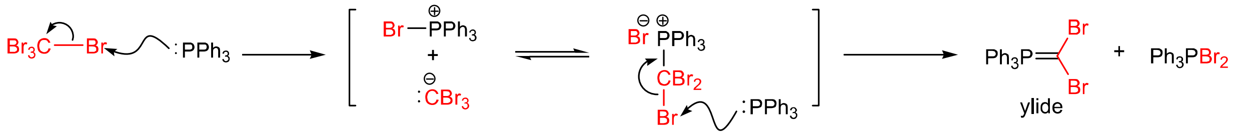
The one-carbon homologation of aldehydes to the corresponding terminal alkynes using carbon tetrabromide and triphenylphosphine is known as the *Corey-Fuchs alkyne synthesis*. In 1972, E.J. Corey and P.L. Fuchs examined the synthetic possibility of transforming aldehydes to the corresponding one-carbon chain-extended alkynes.[1] The first step of their procedure involved the conversion of the aldehyde to the corresponding homologated dibromoolefin in two possible ways: **I**) addition of the aldehyde (1 equivalent) to a mixture of triphenylphosphine (4 equivalents) and carbon tetrabromide (2 equivalents) in CH_2Cl_2, at 0 °C in 5 minutes;[6] or **II**) addition of the aldehyde to a reagent, which is prepared by mixing zinc dust (2 equivalents) with Ph_3P (2 equivalents) and CBr_4 (2 equivalents) in CH_2Cl_2 at 23 °C for 24-30h (the reaction time to form the alkyne is 1-2h). Yields are typically 80-90% for this first Wittig-type step. Procedure **II**, using zinc dust and less Ph_3P, tends to give higher yields of dibromoolefins and simplifies the isolation procedure. In the second step, the conversion of the prepared dibromoolefins to the corresponding terminal alkynes is accomplished by treatment with 2 equivalents of *n*-butyllithium at -78 °C (*lithium-halogen exchange* and elimination), followed by simple hydrolysis. The intermediate is a lithium acetylide, which can be treated with a number of electrophiles to produce a wide variety of useful derivatives. Recently, a one-pot modified procedure using *t*-BuOK/(Ph_3PCHBr_2)Br followed by the addition of excess *n*-BuLi was published.[5]



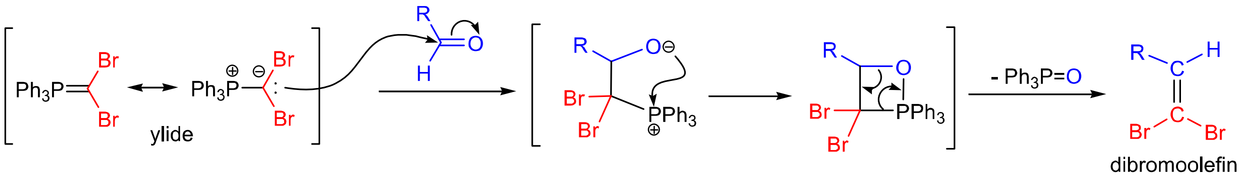
Mechanism: [6,1]

The mechanism of dibromoolefin formation from the aldehyde is similar to the mechanism of the *Wittig reaction*. However, there is very little known about the formation of the alkyne from the dibromoolefin. The mechanism below is one possible pathway to the observed product.

Generation of the phosphorous ylide:



Reaction of the phosphorous ylide with the aldehyde:



Conversion of dibromoolefin to terminal alkyne: