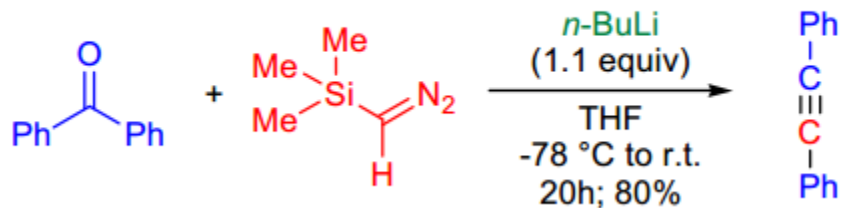
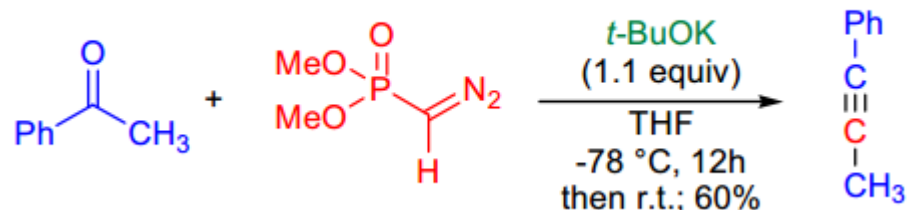


Seyferth-Gilbert homologation

Colvin & Hamill (1973):



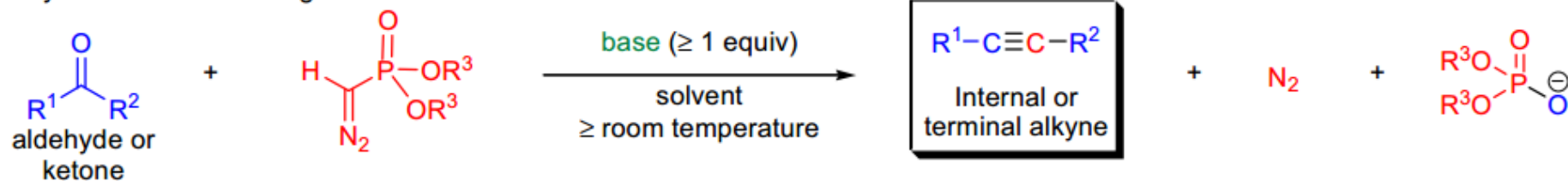
Gilbert & Weerasooriya (1979):



only for non-enolizable carbonyl compounds
such as diaryl ketones and aromatic aldehydes
with electronwithdrawing groups.

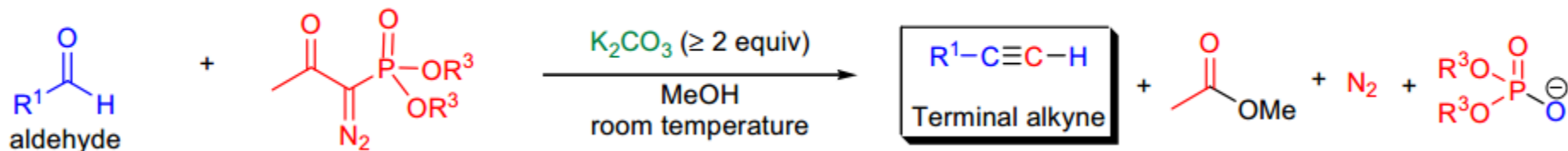
Dramatically increased the
scope of the reaction.

Seyferth-Gilbert homologation:



R¹ = alkyl, aryl, heteroaryl; R² = H, aryl, heteroaryl; R³ = Me, Et; base: *n*-BuLi, KO-*t*Bu

Modification for the synthesis of terminal alkynes (Ohira & Bestmann):

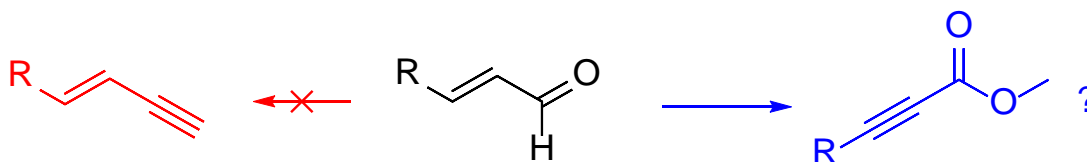


The general features

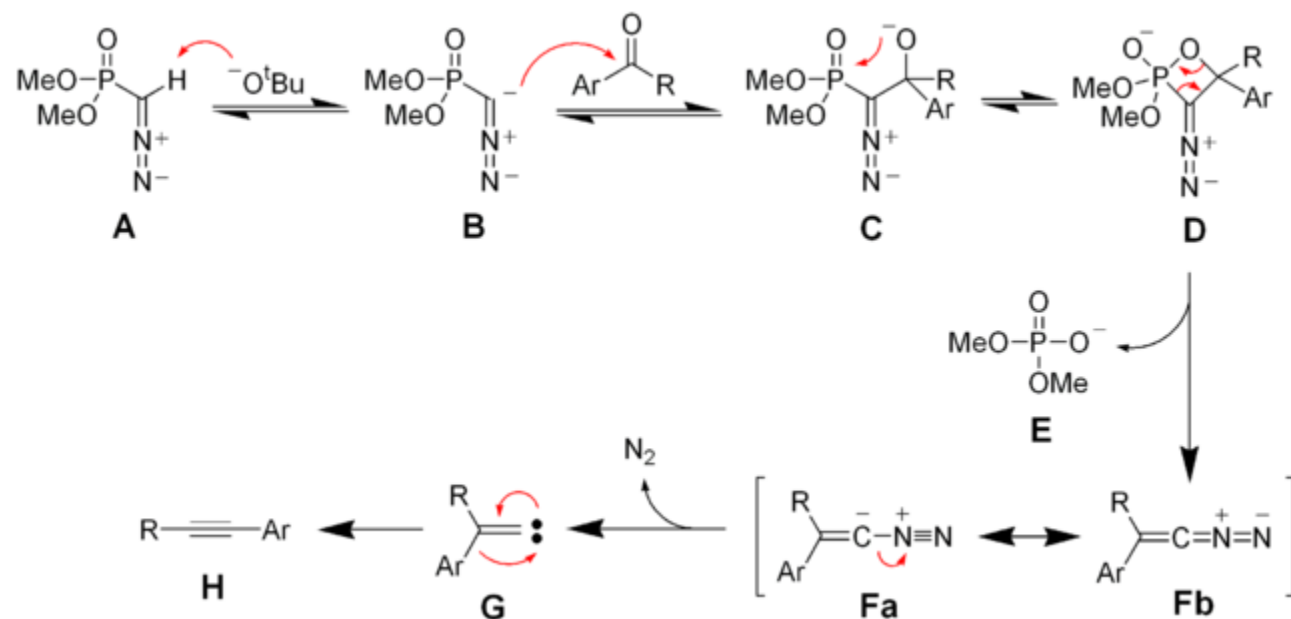
- 1) the phosphonate reagents are not commercially available, but they can be prepared readily;
- 2) in the original procedure developed by Gilbert, the dialkylphosphonodiazomethane (DAMP) was deprotonated with a **strong base** such as an alkyllithium or potassium tert-butoxide, and the carbonyl compound was added at **low temperature** under an inert atmosphere. The product alkyne was isolated upon a simple aqueous work-up (this procedure is only **rarely used**, since base-sensitive substrates do not tolerate the strongly basic conditions);
- 3) in the Ohira-Bestmann modification the dimethyl-1-diazo-2-oxopropylphosphonate is added to a solution of **K₂CO₃** and the aldehyde in methanol at **room temperature**. After several hours of stirring, the product is isolated upon aqueous work-up in excellent yield (this modified procedure is by far **the most popular**).

The key features of the Ohira-Bestmann protocol

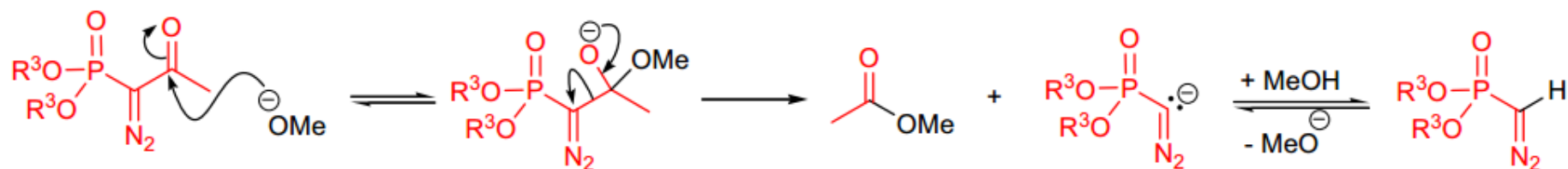
- 1) the reaction conditions are **mild**, and most functional groups are tolerated;
- 2) highly sensitive **enantiopure** α -alkoxy aldehydes do not undergo racemization;
- 3) aliphatic, aromatic, as well as arylalkyl aldehydes are homologated to the corresponding terminal alkynes in **excellent yields**;
- 4) substrates containing highly **C-H acidic bonds** are homologated in high yields;
- 5) α,β -unsaturated aldehydes do not undergo the transformation and the expected enynes are not formed (rather the **homopropargylic methyl esters** are obtained).



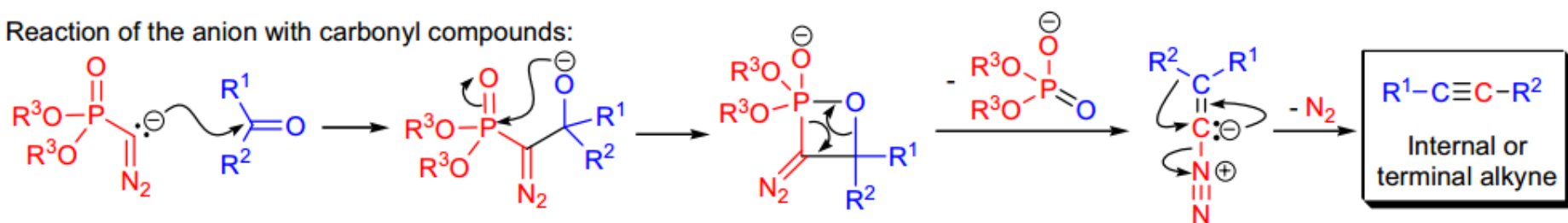
Mechanism:



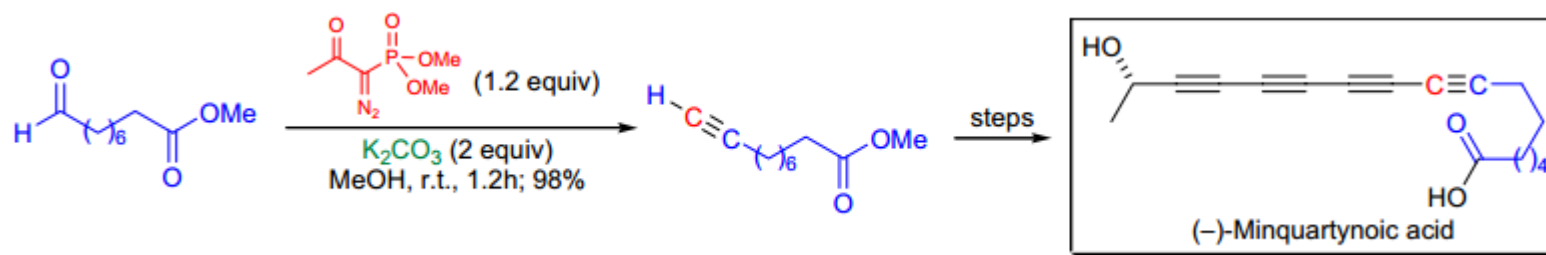
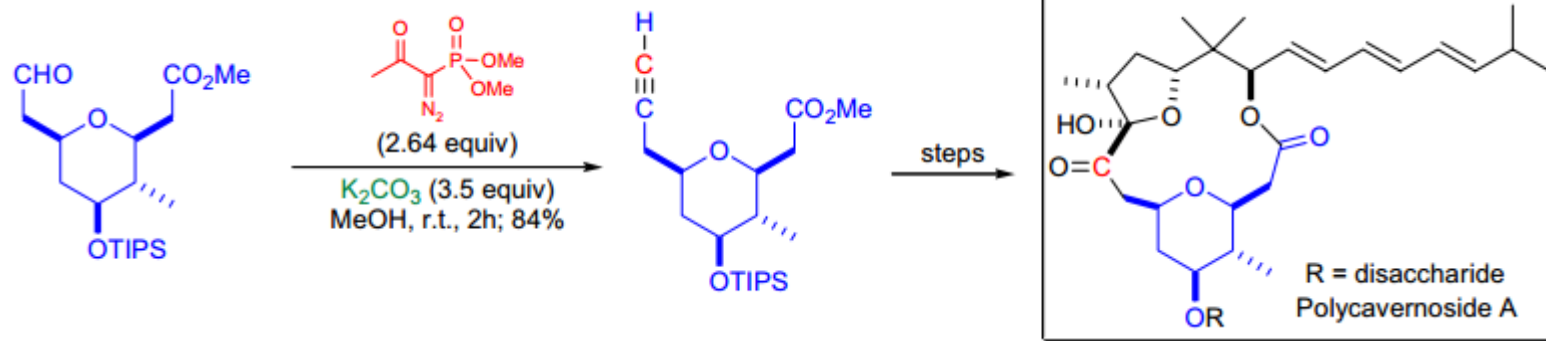
Formation of the dialkylphosphonodiazomethane from dialkyl-1-diazo-2-oxopropylphosphonate:



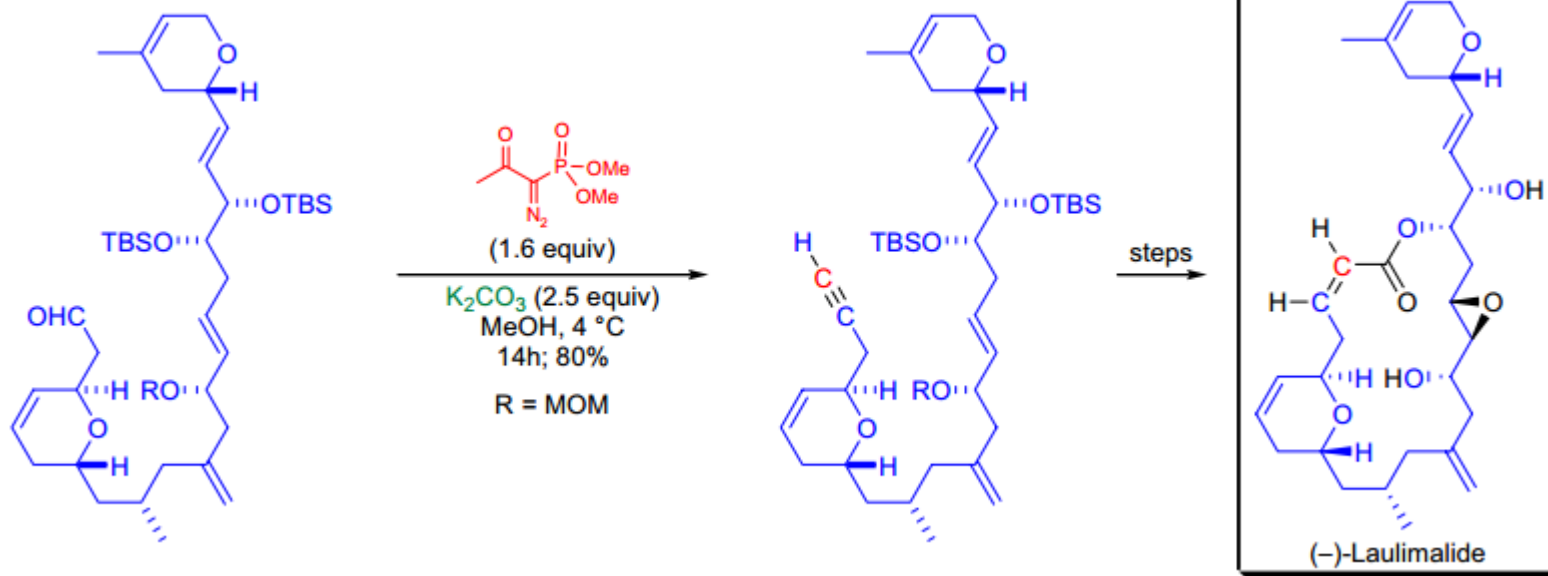
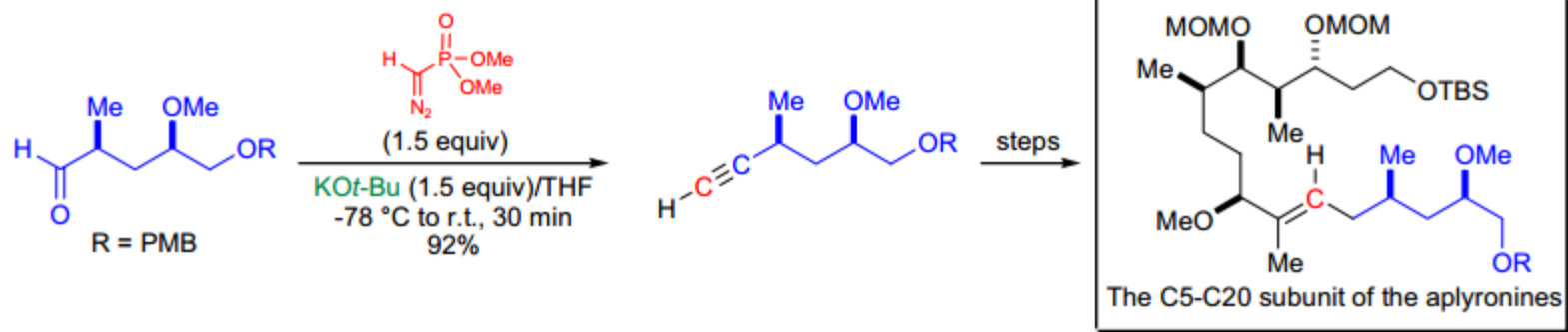
Reaction of the anion with carbonyl compounds:



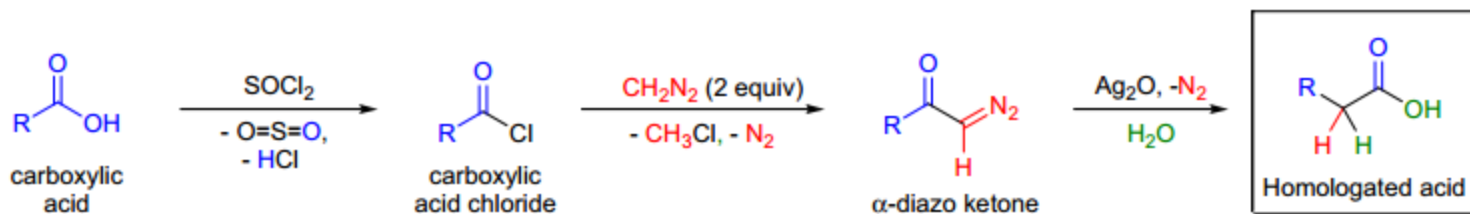
Synthetic Applications:



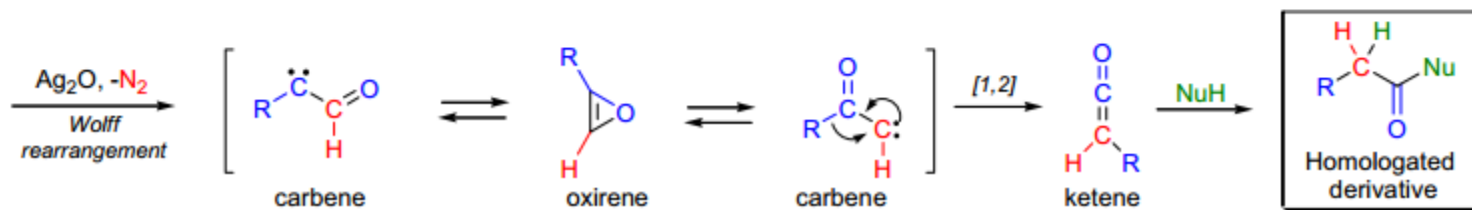
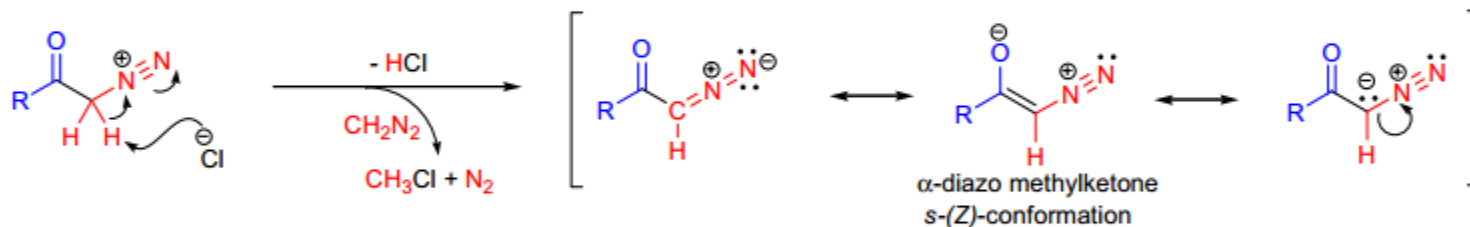
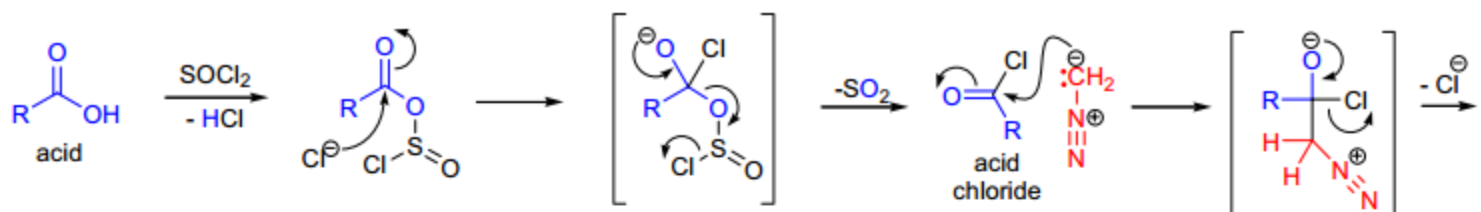
Synthetic Applications:



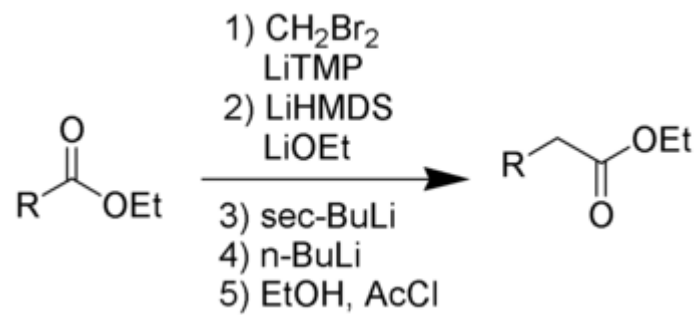
ARNDT-EISSERT HOMOLOGATION / SYNTHESIS



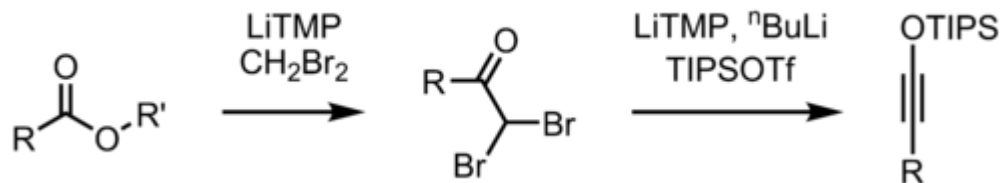
Mechanism:



Kowalski ester homologation



Mechanism:



The mechanism is disputed.

thanks