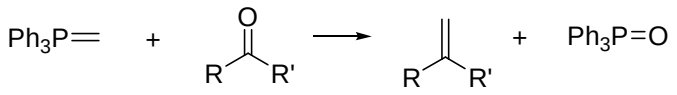
Methylenation reactions

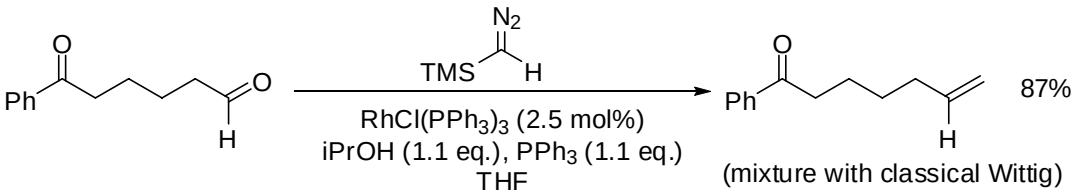
The transformation of carbonyl compounds to terminal olefins is an important transformation, particularly with the recent exploitation of the metathesis reaction in organic synthesis. The reaction can be loosely divided into two general classes:

1) "Metal free" reactions
a) Phosphorus reagents



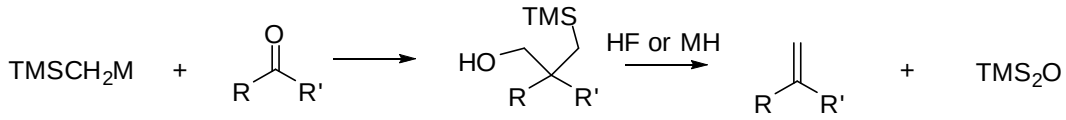
-Wittig and Horner ($Ph_2P(O)CH_2M$) reagents
-driven by P=O bond formation
-low reactivity with hindered substrates
-largely confined to aldehydes and ketones
-basic, possible epimerisation/chemoselectivity issues

In 2001 Lebel reported a Rh-catalysed salt-free variant:[1]



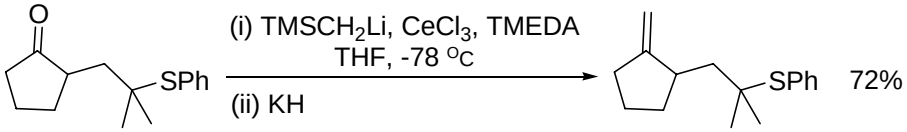
-often higher yields than classical Wittig reaction
-tolerant to a wide range of protecting groups
-mild, non-basic
-chemoselective for aldehydes

b) Peterson reagents[2]



-driven by Si-O bond formation
-volatile disiloxane by-product readily removed (*cf.* Ph_3PO)
-basic, possible epimerisation/chemoselectivity issues

Johnson modification:

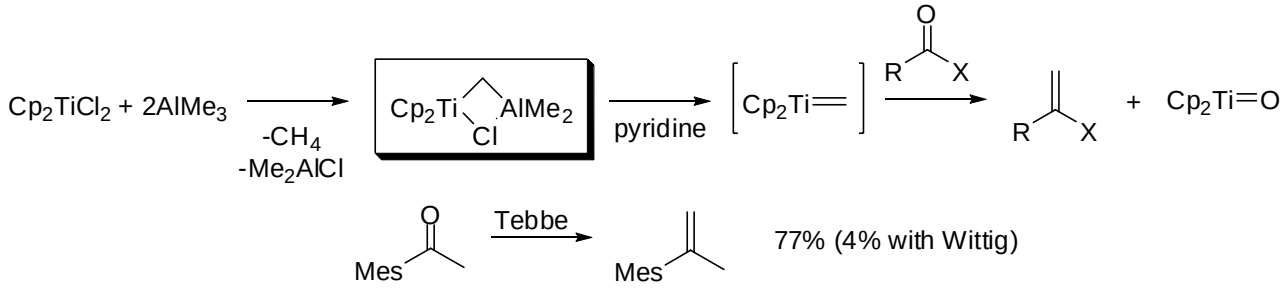


-Generally higher yields
-non-basic

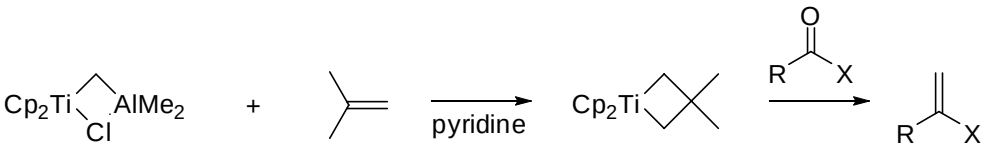
NB: range of similar reagents based on other elements *e.g.* R_2MCH_2Li M=B, As, Sb, Bi; R_3MCH_2Li M=As, Sb, Bi

2) Transition metal-mediated processes
a) Ti carbenes
-driven by Ti=O bond formation

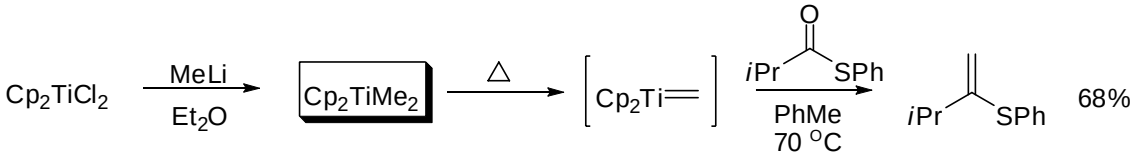
(i) Tebbe



-aldehydes, ketones, esters, amides
-ketones react in the presence of esters
-non-basic
-commercially available as toluene solution
-Al-free reagent is more readily handled (Grubbs):

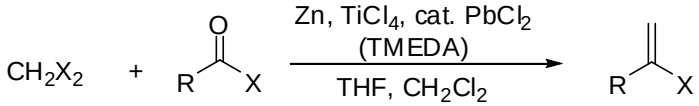


(ii) Petasis

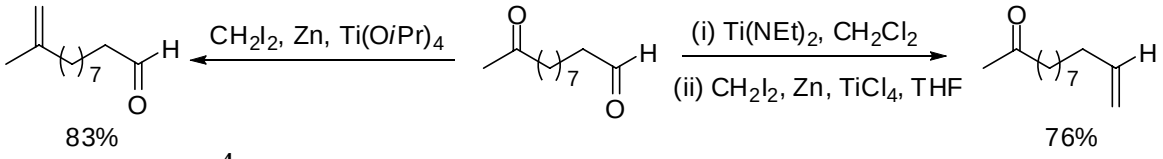


-aldehydes, ketones, esters, lactones, amides, anhydrides, carbonates, imides
-tolerant of air and moisture
-light sensitive

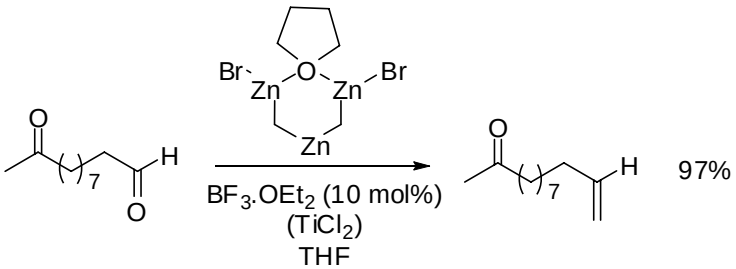
(iii) Oshima-Lombardo-Takai



-similar substrate scope to Tebbe/Petasis (requires TMEDA for esters/lactones)
-compatible with enolisable aldehydes/ketones
-tuning of conditions to obtain chemoselective reactions possible:



b) Zn reagent – Nysted[4]



-aldehydes/ketones
-commercially available as THF solution
-non-basic

References

1. ACIE **2001**, 2887
2. For a review see: Chem. Soc. Rev. **2002**, 195
3. For a review on Ti reagents see: JCS Perkin Trans 1, **2002**, 2763
4. Synlett **1998**, 313