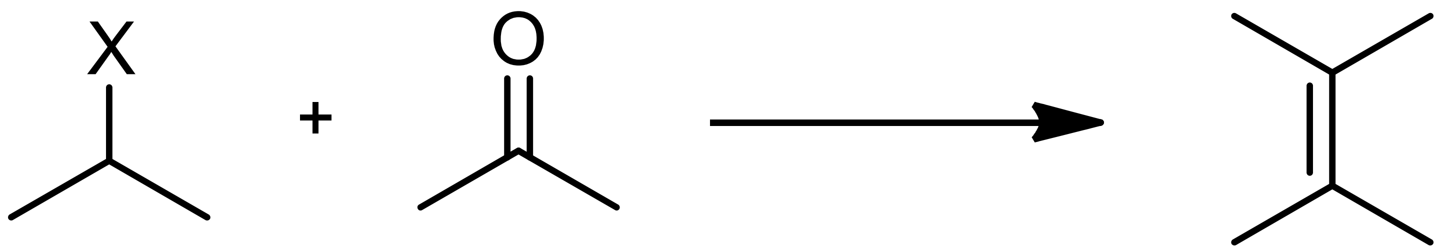
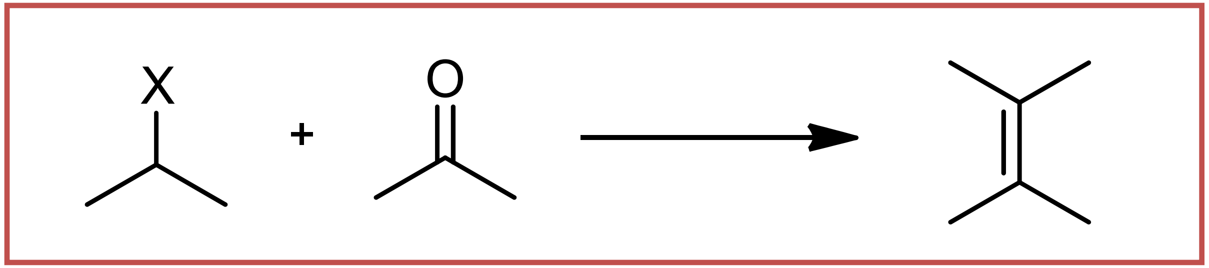
Olefination Reactions



Olefination Reactions

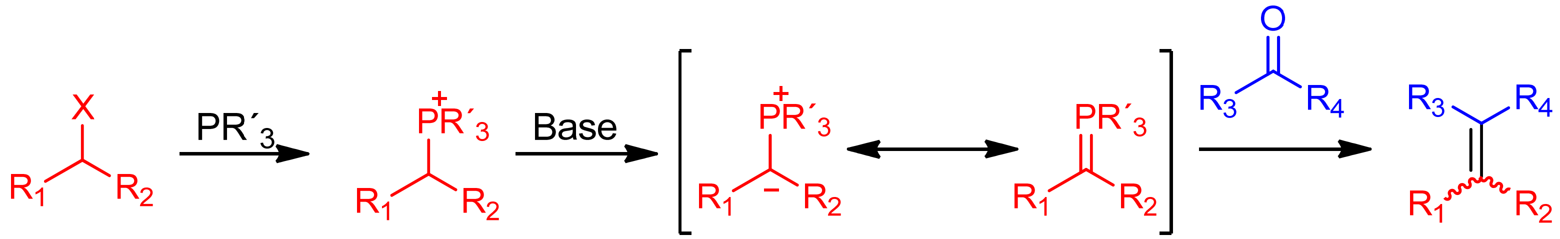


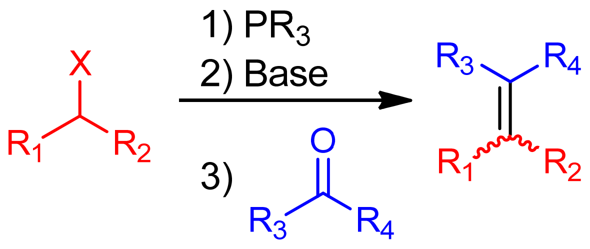
- Wittig Reaction (Phosphorous ylides)
- Horner-Wadsworth-Emmons Reaction (Phosphonates)
- Peterson Olefination (Silanes)
- Julia-Lythgoe (Sulphones)
- McMurry Coupling (Titanium complexes)
- Petasis / Tebbe Olefination (Carbene complexes)

Mechanism
Stereochemistry (*Z* / *E*)
Experimental Examples

Olefination Reactions

Wittig Reaction



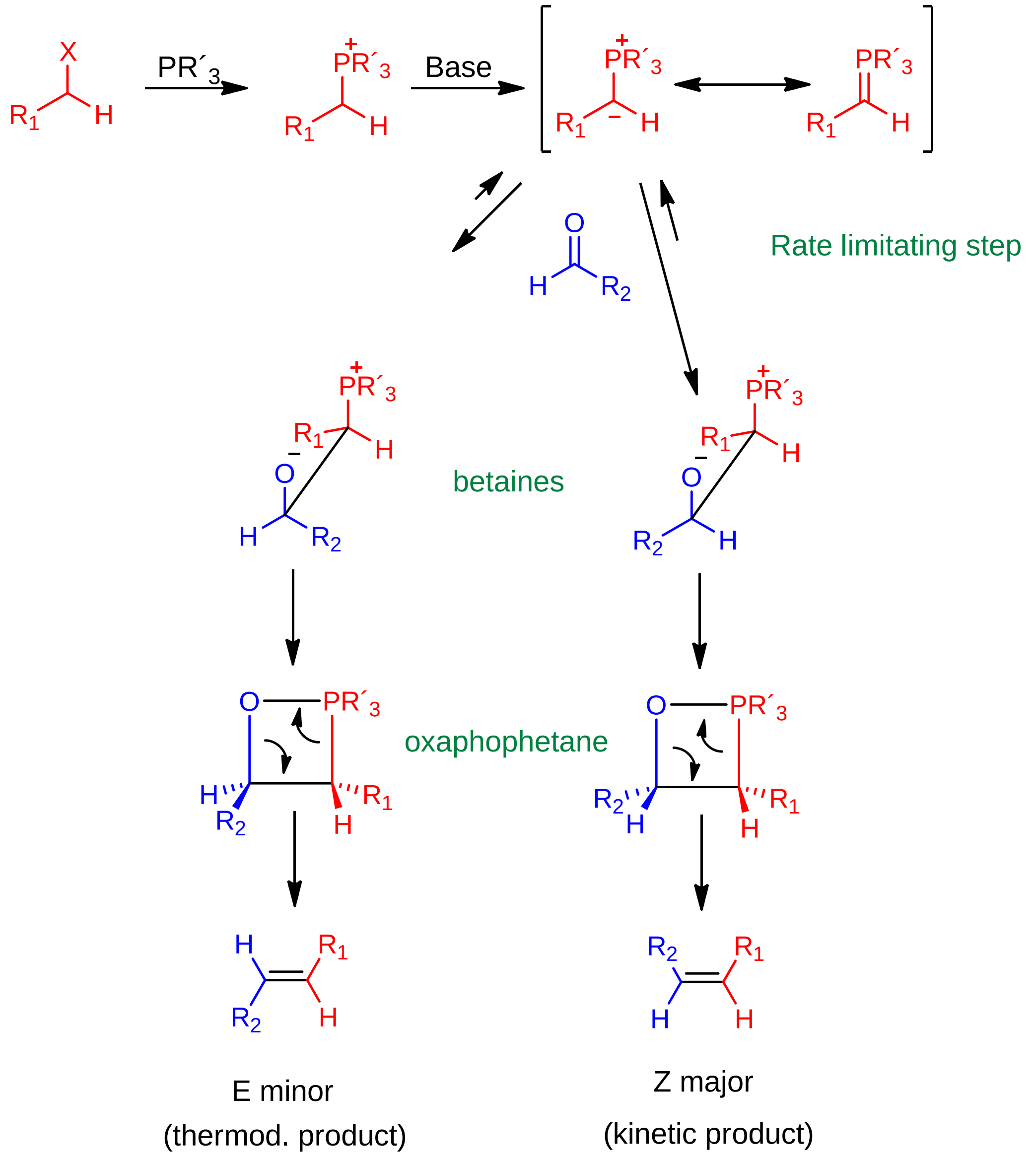


X: Cl, Br, I, OTs

R_3, R_4: alkyl, aryl

Olefination Reactions

Wittig Reaction



Mechanism:

1.Deprotonation

2.Coupling of the ylide to the carbonyl compound (RL step) to form the betaine

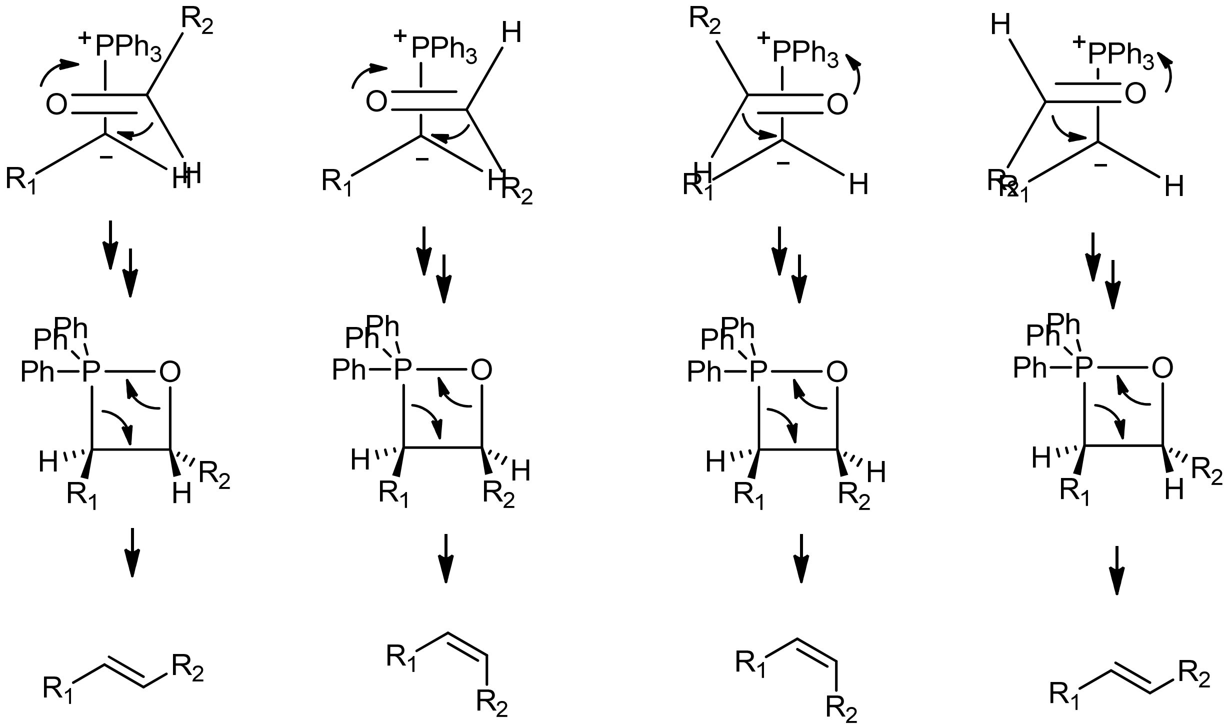
3.Cyclation to the oxaphosphetane

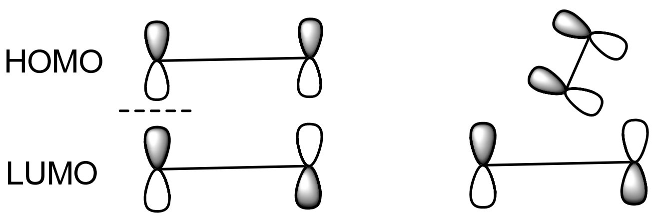
4.Rearrangement to the olefins

Olefination Reactions

Stereochemistry:

1.the *cis* product is favoured due to steric inderance during the attack of the carbonyl to the ylide.





Supra-supra
forbidden

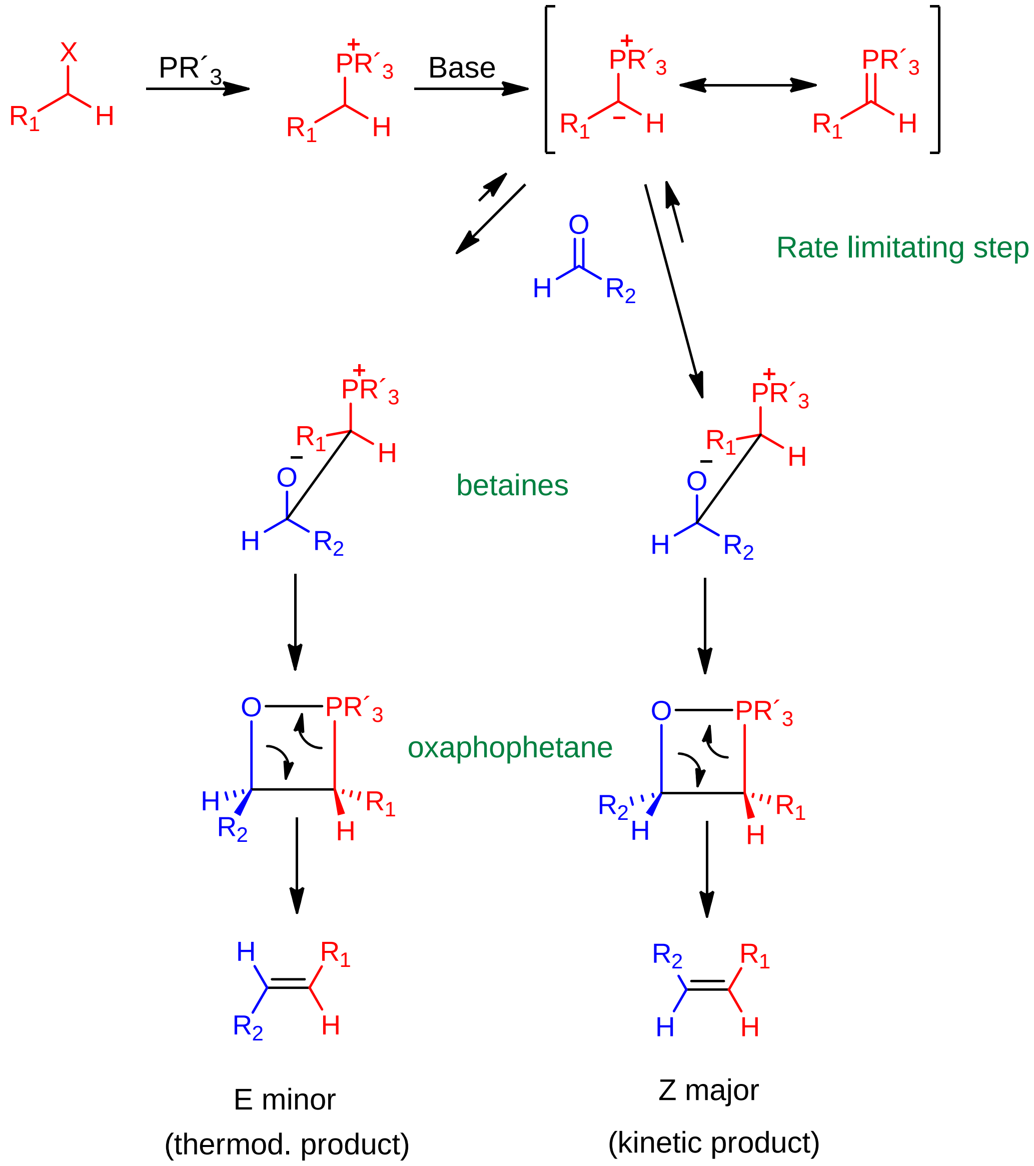
Antara-supra
Constricted
(higher selectivity)

Olefination Reactions

Stereochemistry:

1.the *cis* product is favoured due to steric inderance during the attack of the carbonyl to the ylide.

2.Non polar solvents and salt free conditions induce Z-olefin formation due to the destabiliyation of the betaines.



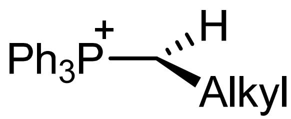
Olefination Reactions

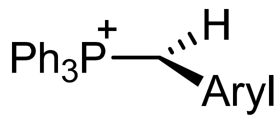
Stereochemistry:

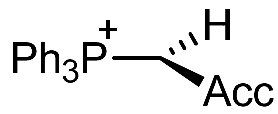
1.the *cis* product is favoured due to steric inderance during the attack of the carbonyl to the ylide.

2.Non polar solvents and salt free conditions induce Z-olefin formation due to the destabiliyation of the betaines.

3.By increasing the stability of the ylide, the proportion of *E*-olefin increases.





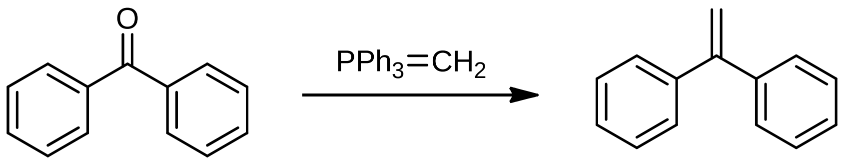


	Labile ylide	**Semistable ylide**	**Stable ylide**
Preparation	In situ	In situ	isolated
Base used	${}^{n}BuLi$ $NaNH_2$ $K^{t}BuO$	NaEtO Aq. NaOH	NaOH
Selectivity	$\geq$ 90% *cis*	*cis, trans*	$\geq$ 90% *trans*

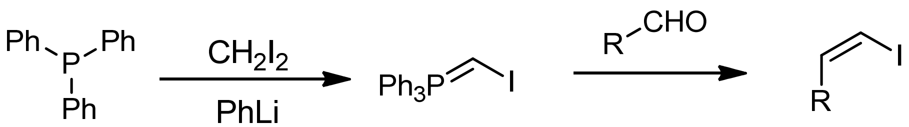
Olefination Reactions

Wittig Reaction

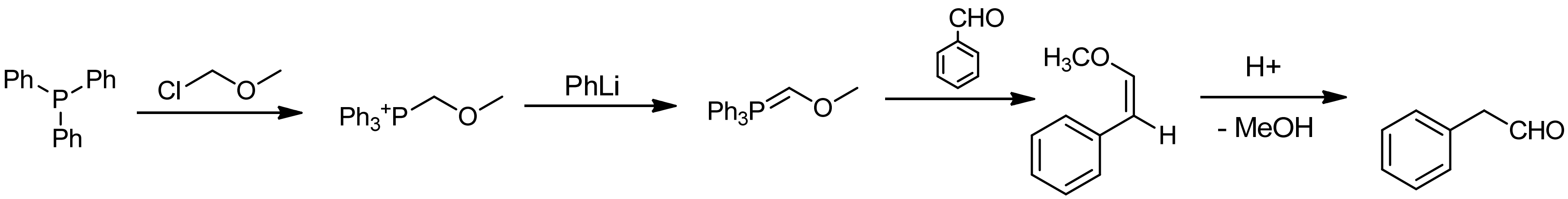
Examples:



Wittig, 1950´s



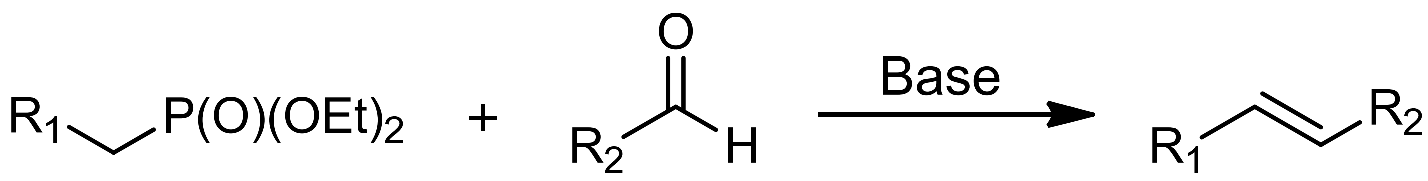
Wittig-Stork



Wittig Homologation

Olefination Reactions

Horner-Wadsworth-Emmons Reaction

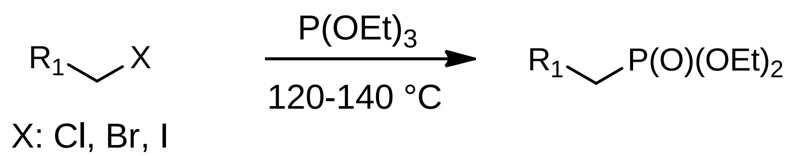


E product

R_1 is an electronwithdrawing group

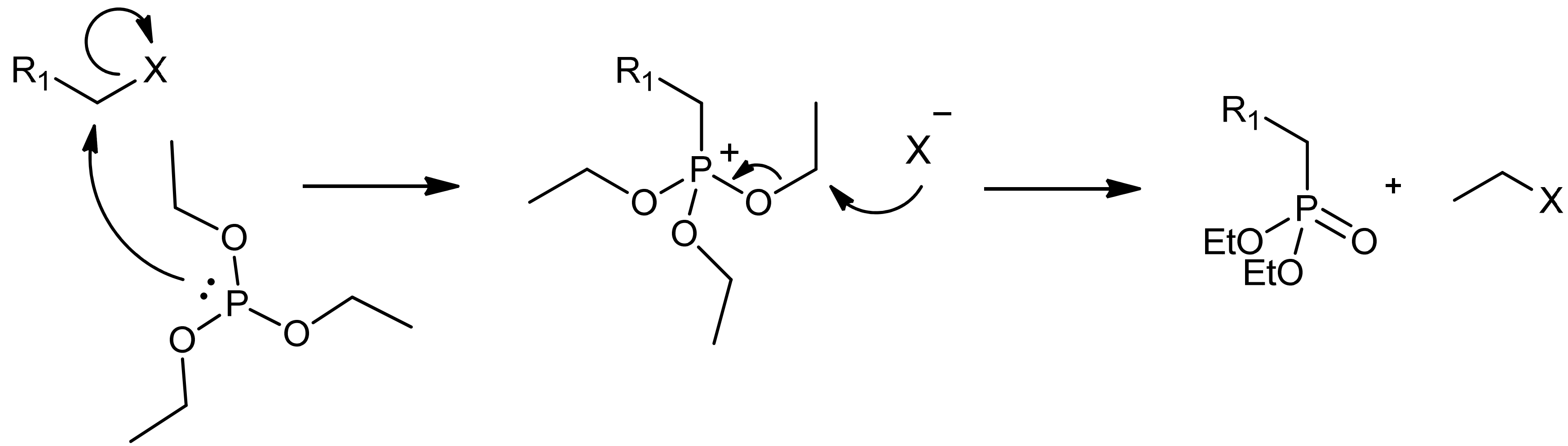
Olefination Reactions

Arbuzov Reaction



Mechanism

1. nucleophilic subs.
2. dealkylation



Olefination Reactions

Horner

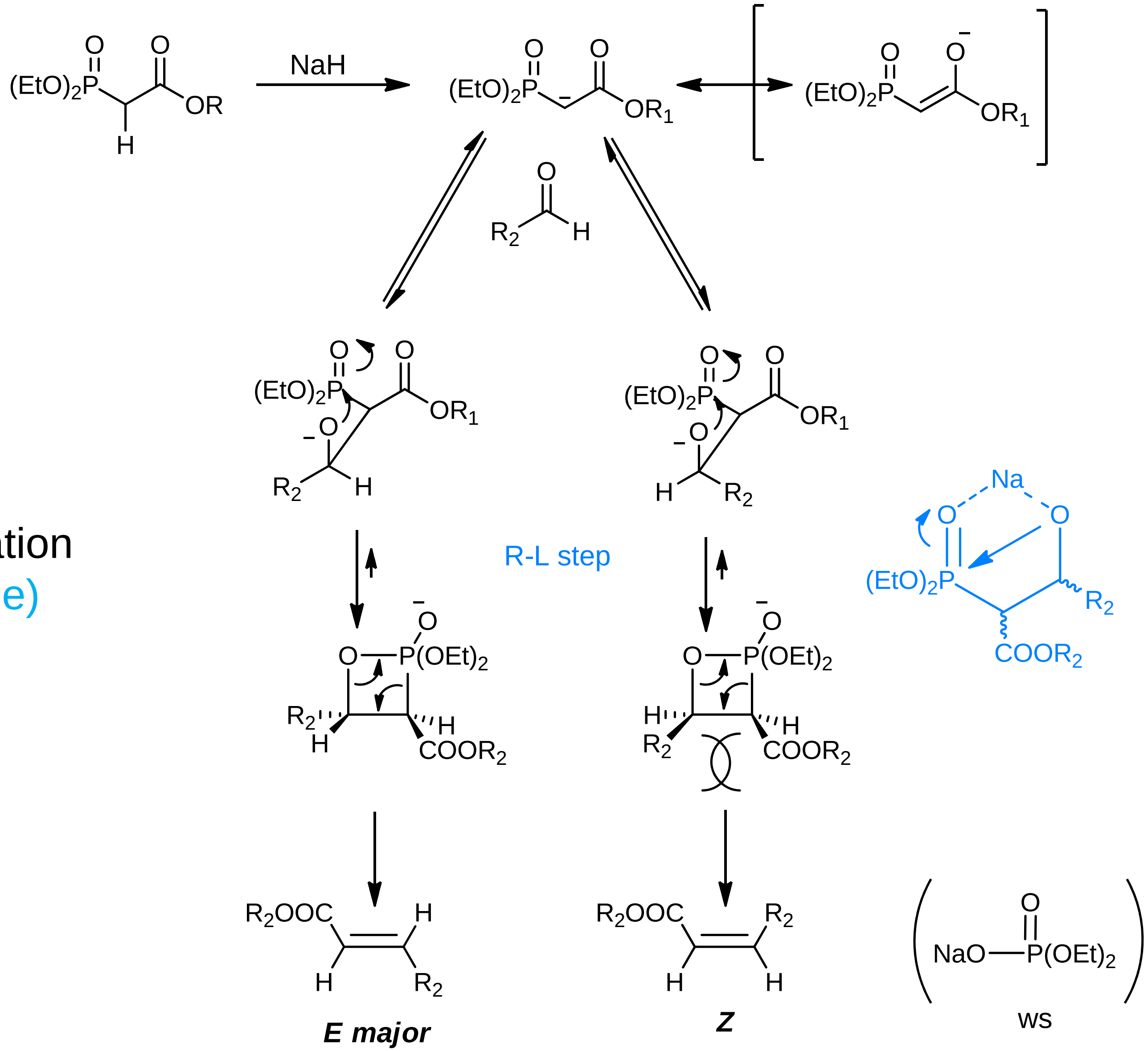
Mechanism

1. deprotonation.

2. Coupling with the aldehyde and formation of the betaine (stable)

3. Evolution to the oxaphosphetane

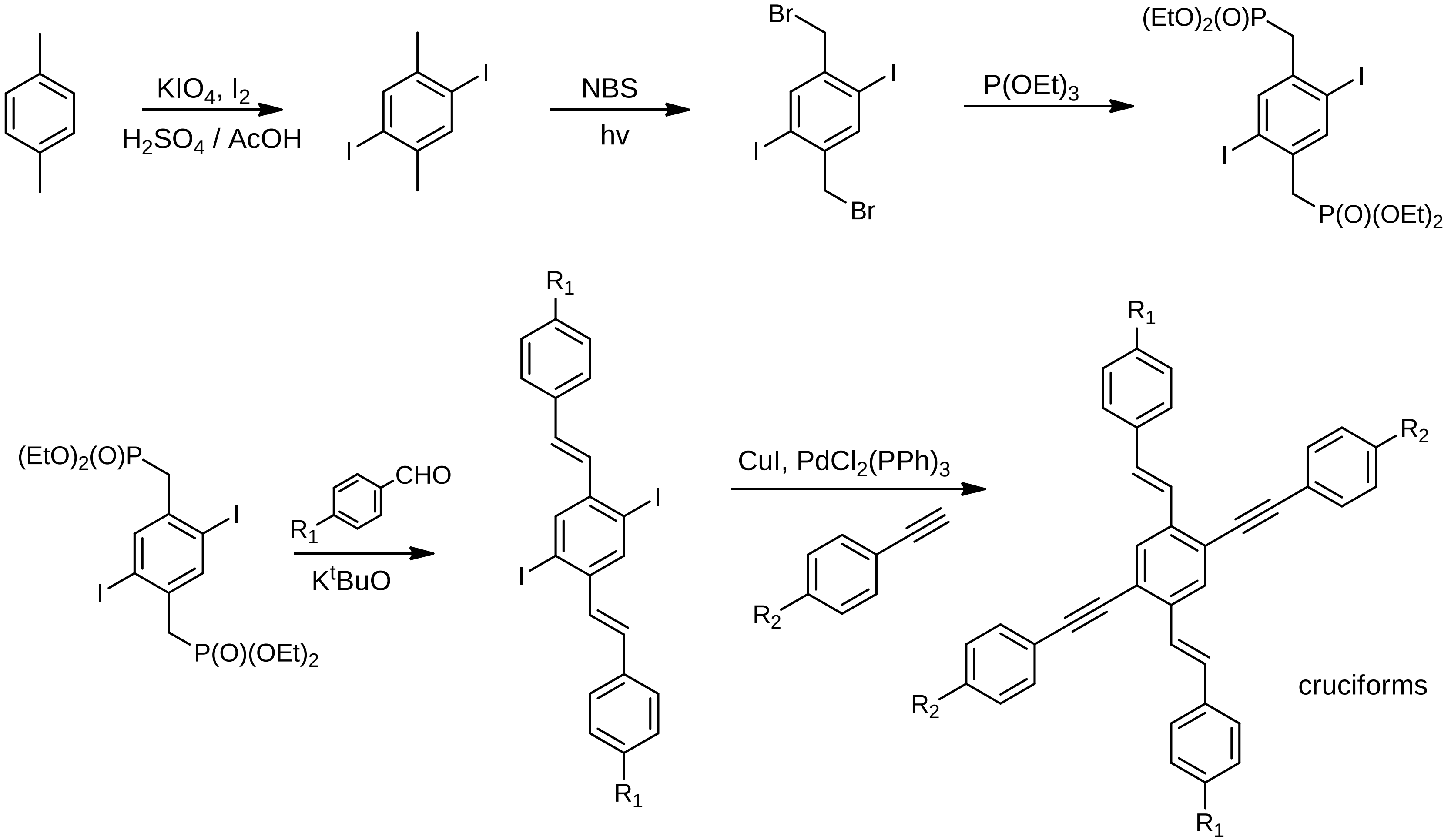
4. Rearrangement



Olefination Reactions

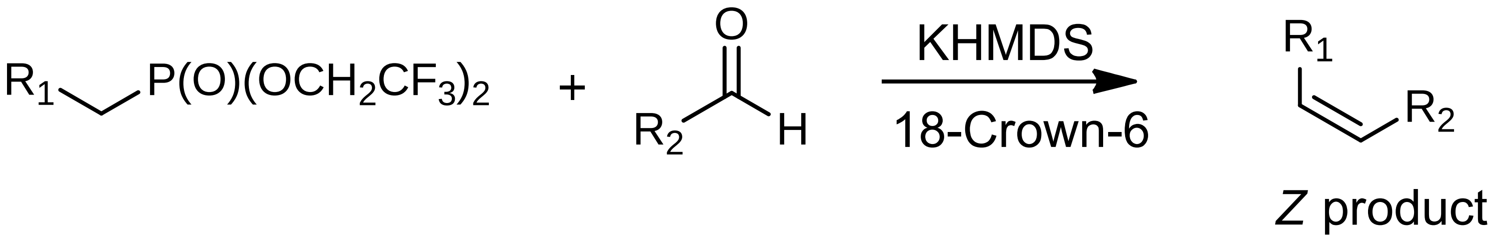
Horner

Example



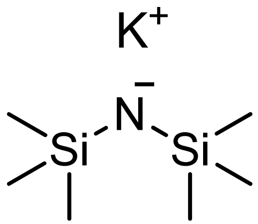
Olefination Reactions

Still-Gennari modification:



Highly dissociative media

KHMDS:



Olefination Reactions

Still-Gennari

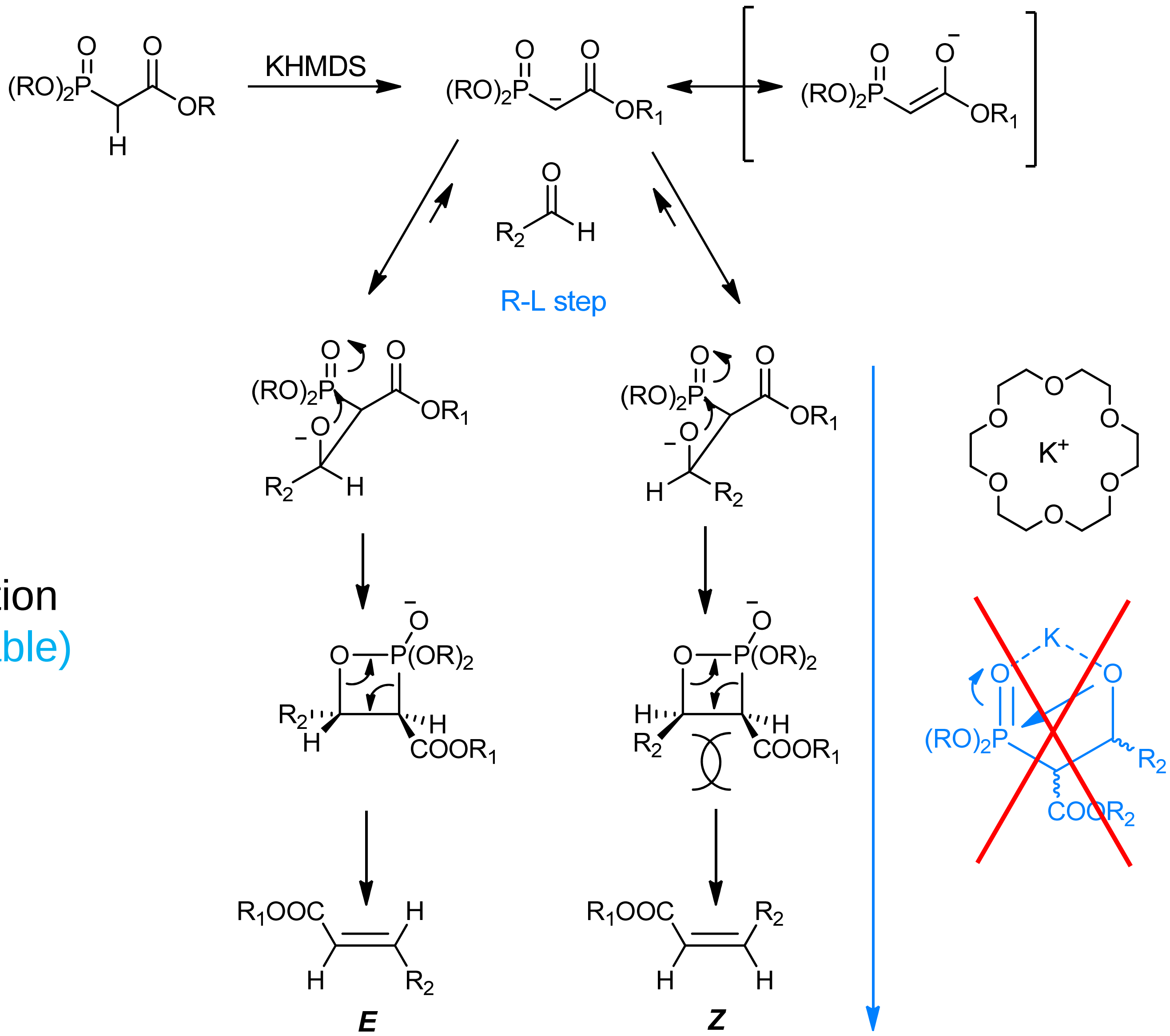
Mechanism

1. Deprotonation (with KHMDS).

2. Coupling with the aldehyde and formation of the betaine (unstable)

3. Evolution to the oxaphosphetane

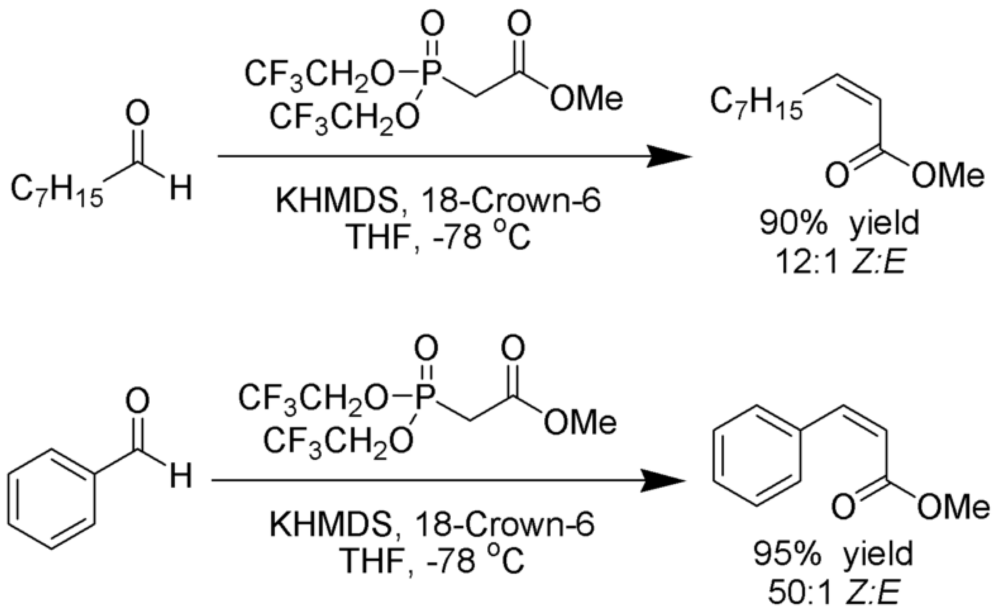
4. Rearrangement



Olefination Reactions

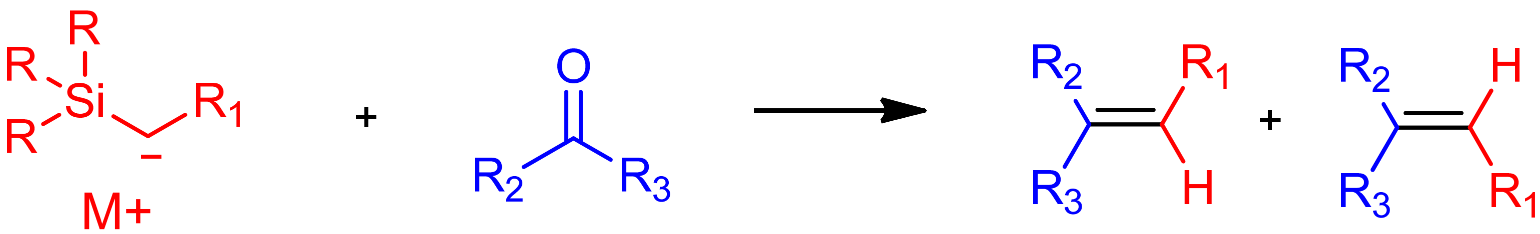
Still-Gennari

Example



Olefination Reactions

Peterson Olefination



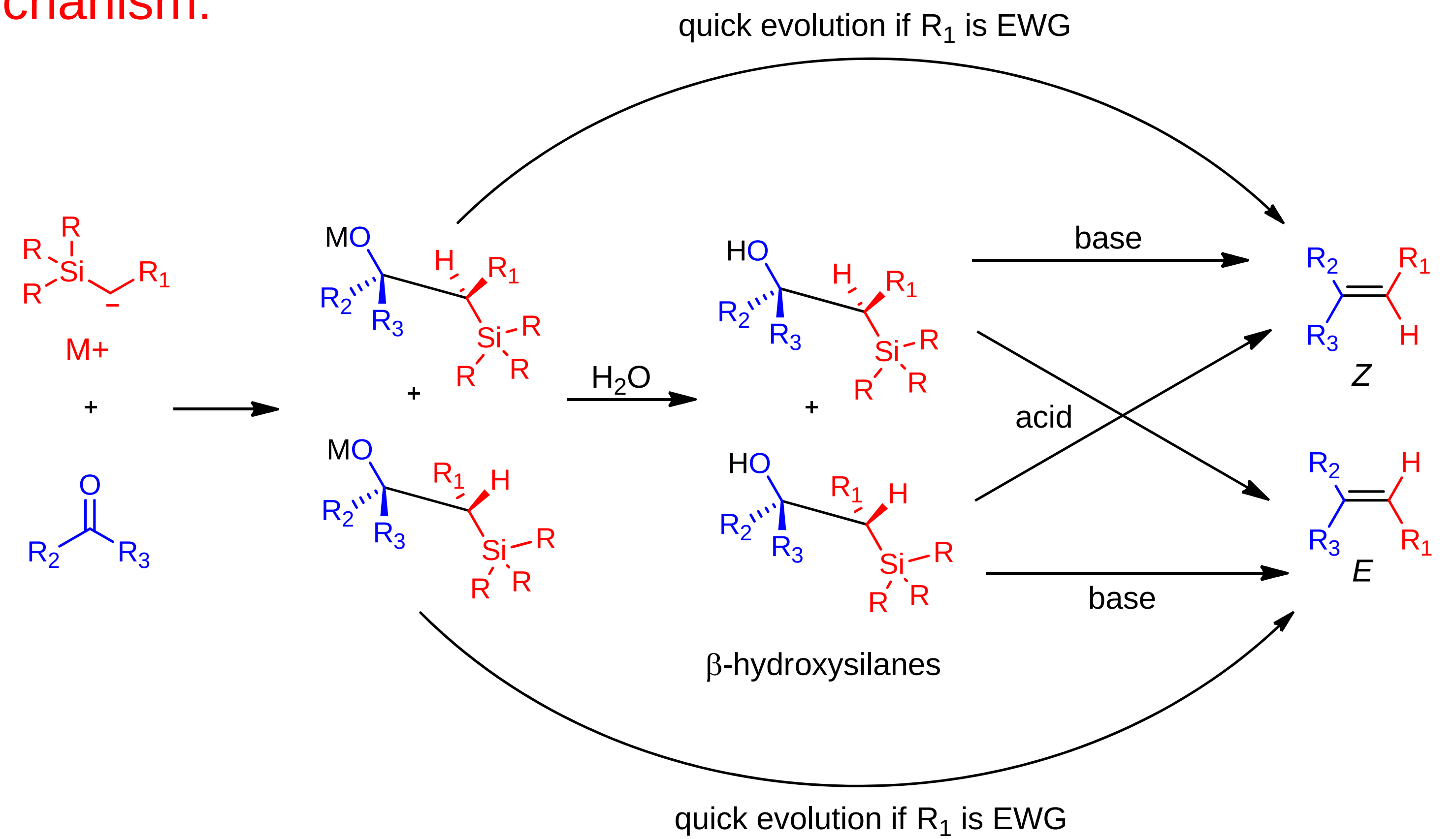
R_2, R_3: alkyl, aryl

R_1: alkyl, aryl, ester, cyano, amide…

Highly versatile

Olefination Reactions

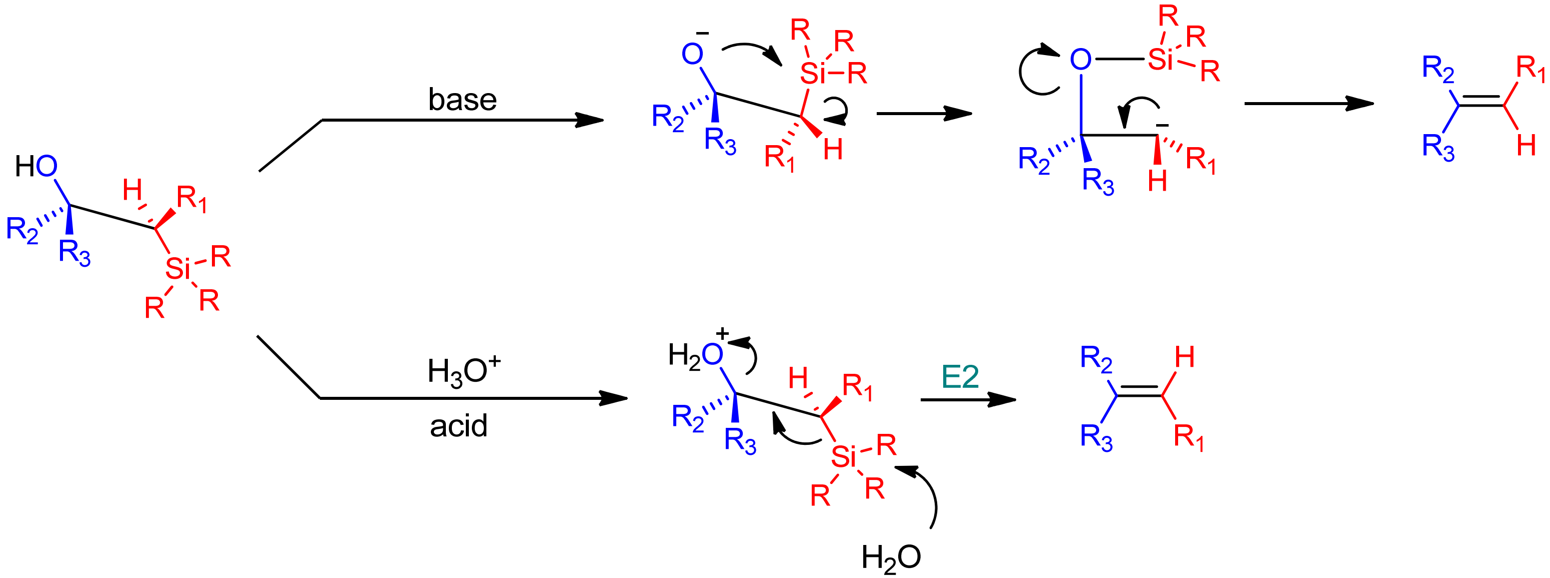
Mechanism:



1. Adition of the carbonyl
2. Formation of the β-hydroxysilanes. Isolable only if R_1 is a donor
3. Elimination to the olefins. *Syn* or *anti* depending on the conditions

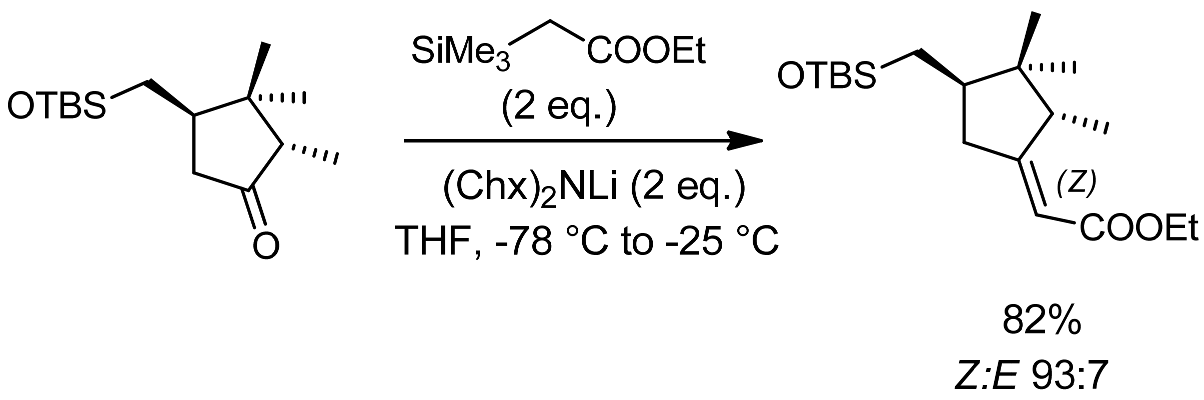
Olefination Reactions

Mechanism:



Olefination Reactions

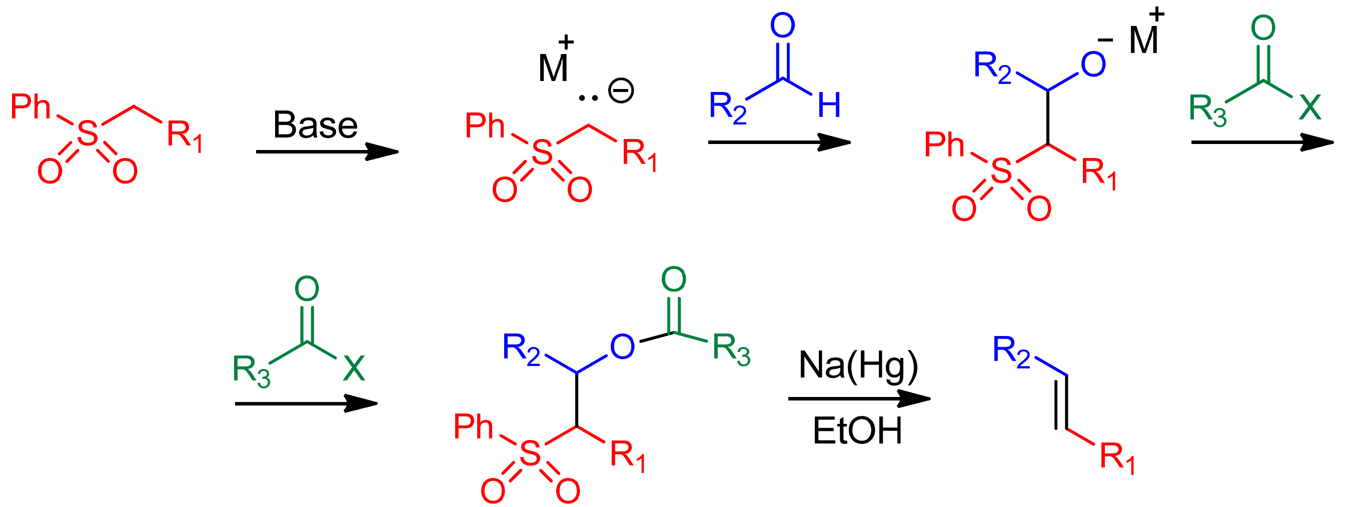
Example:



This is the only methodology to intruduce this (Z)-alkene moiety

Olefination Reactions

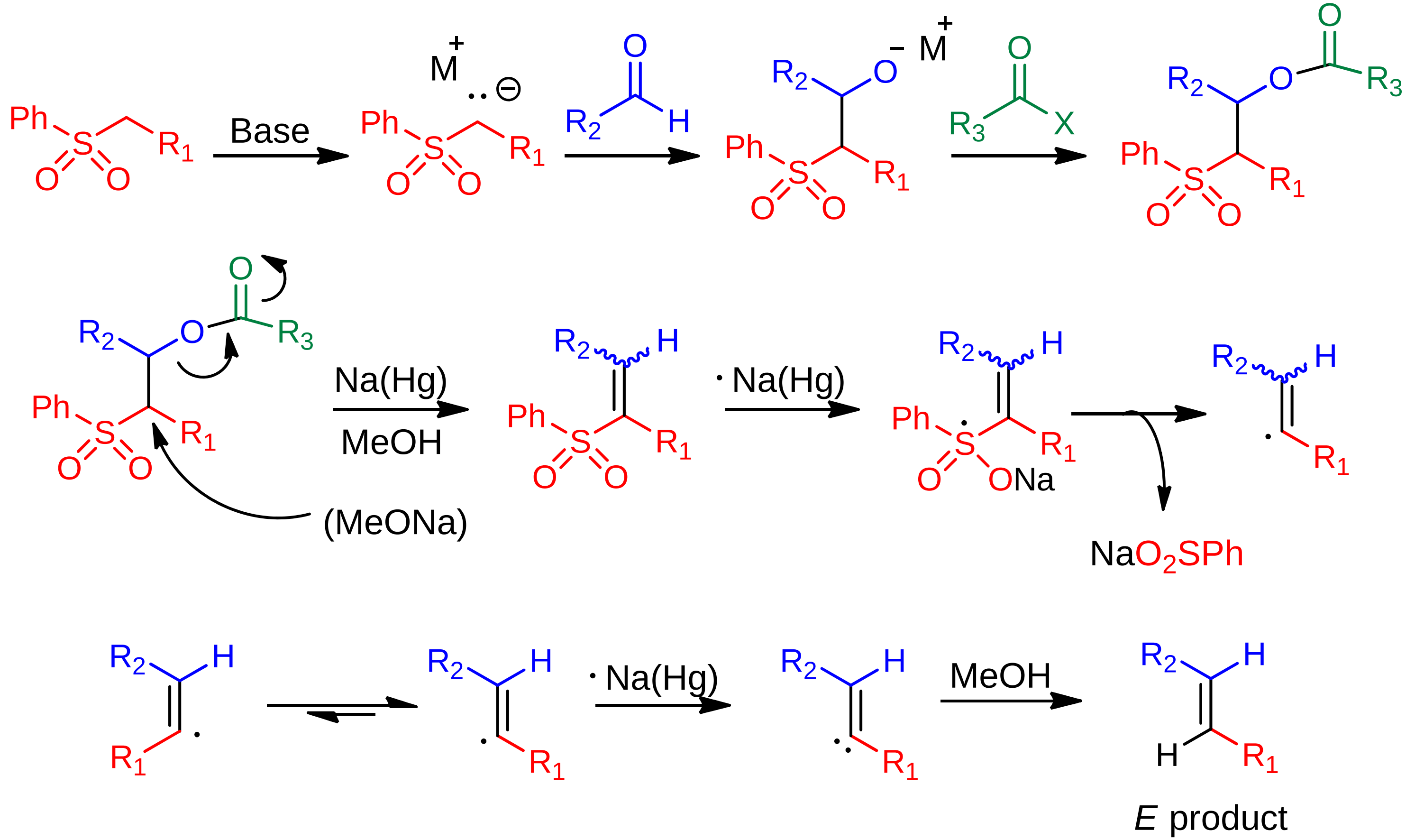
Julia-Lythgoe Olefination



X: Cl, Br, OCOR$_3$
R$_1$: H, alkyl, aryl
R$_2$: H, alkyl, aryl, alkenyl

Olefination Reactions

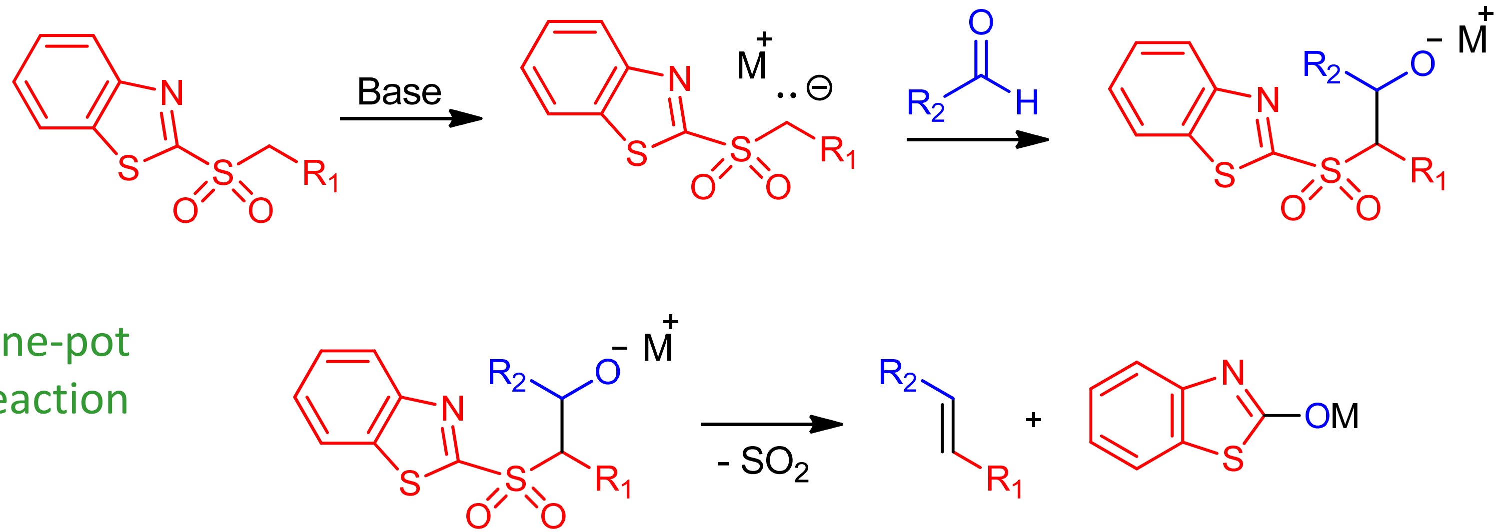
Julia-Lythgoe Olefination

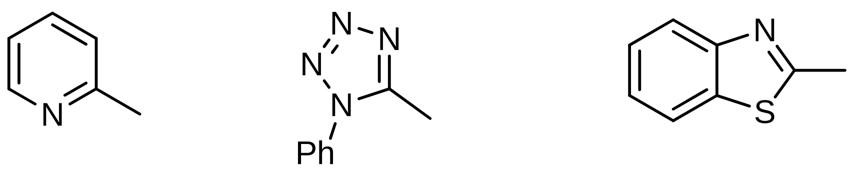


Olefination Reactions

Modified Julia-Lythgoe

One-pot reaction





PYR

pyridin-2yl-

PT

1-phenyl-1H-tetrazol

BT

benzothiazol-2yl-

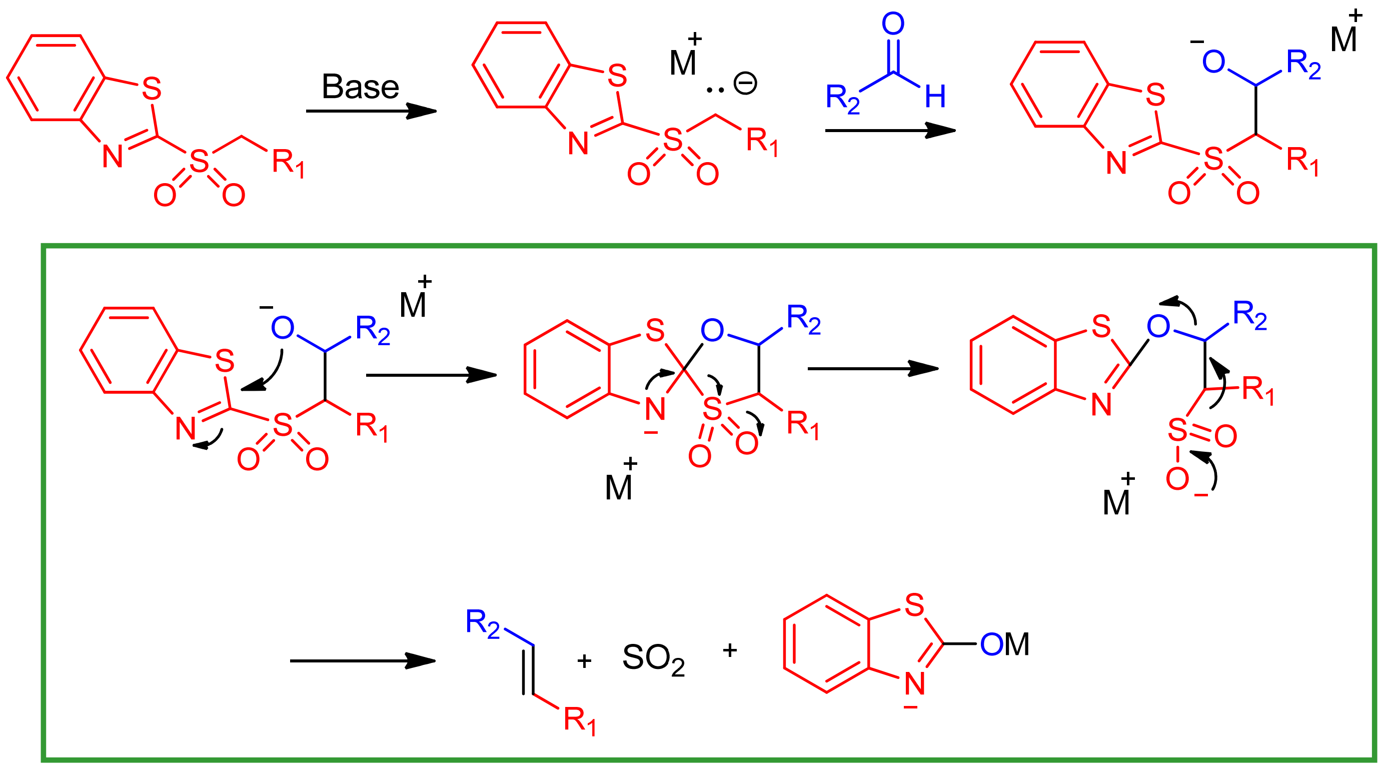
R_1: H, alkyl, aryl

R_2: H, alkyl, aryl, alkenyl

Olefination Reactions

Modified Julia-Lythgoe

Mechanism

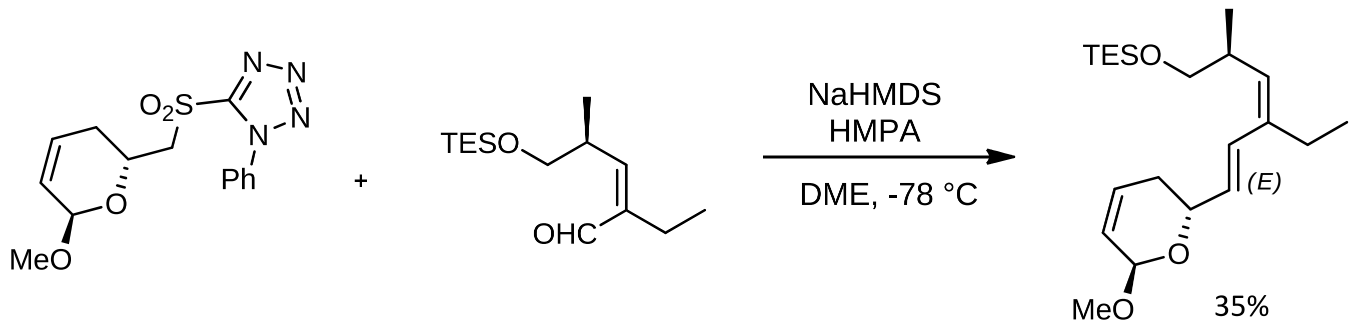


Smiles rearrangement

Olefination Reactions

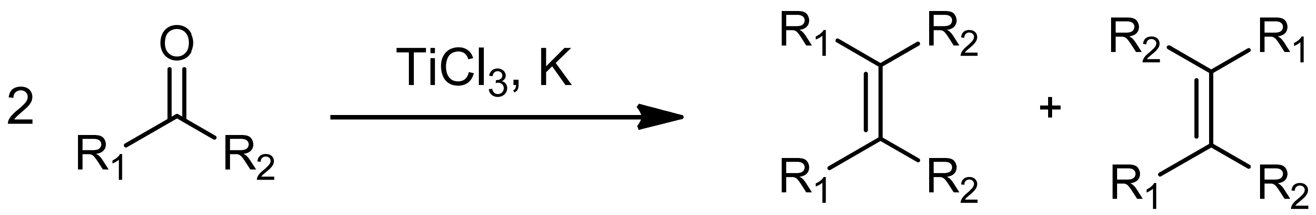
Modified Julia-Lythgoe

Example



Olefination Reactions

McMurry Coupling



R: H, alkyl, aryl

Uncontrolled reaction. Random stereochemistry

Olefination Reactions

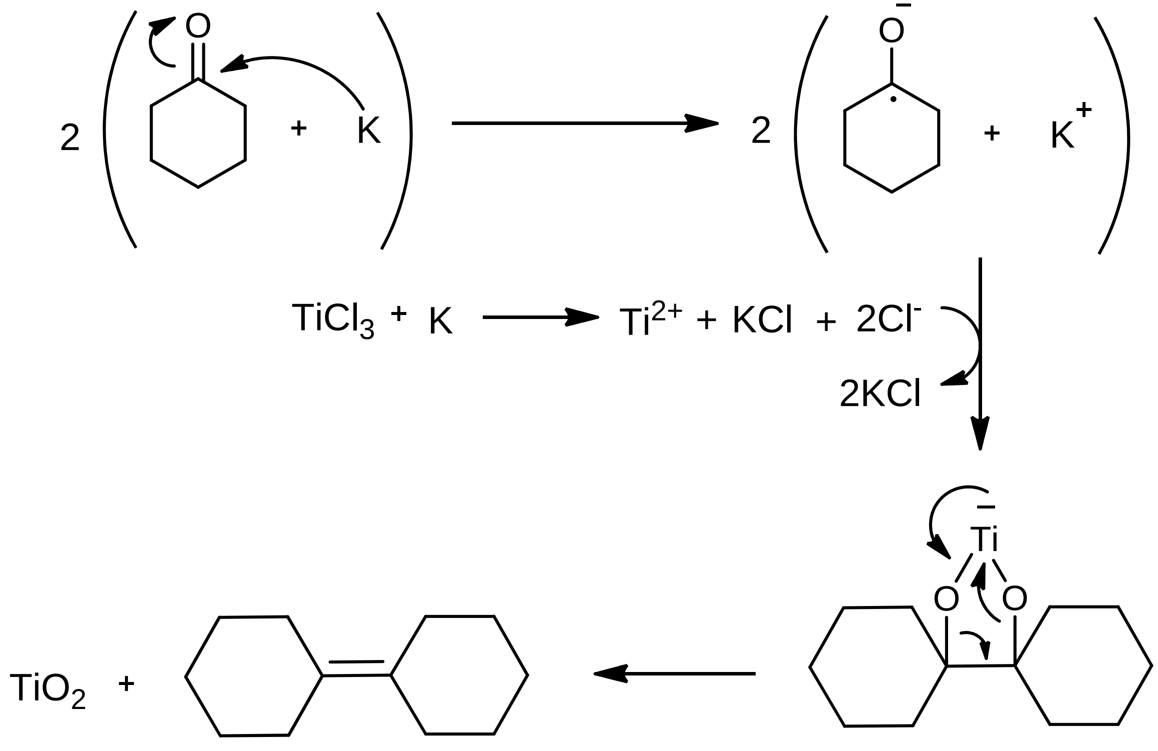
McMurry Coupling

Mechanism

1. Re-dox over the carbonyl group.

2. Coupling of the radicals (Ti^{2+} mediated).

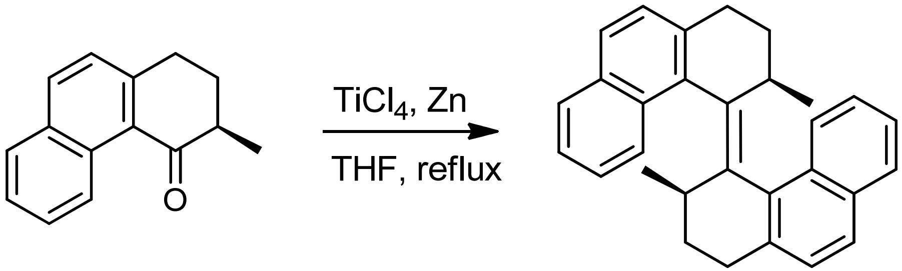
3. Rearrangement with re-oxidation of Ti(II) to Ti(IV)

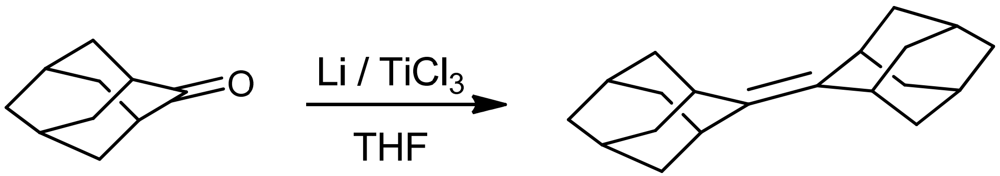


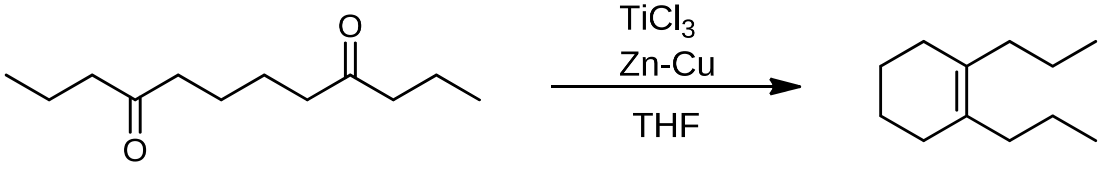
Olefination Reactions

McMurry Coupling

Exmaple

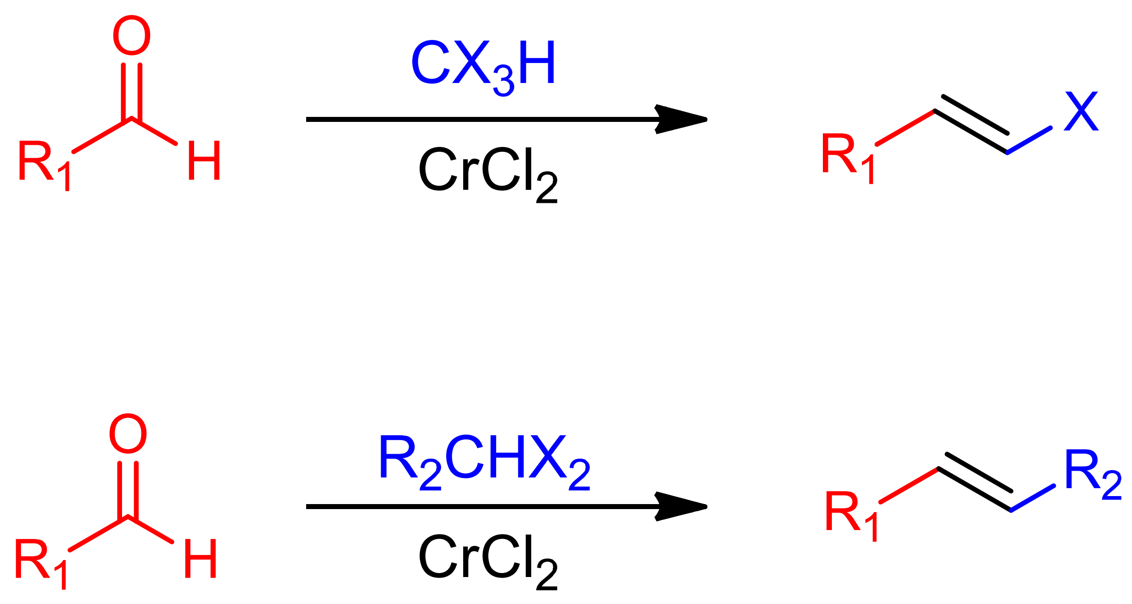






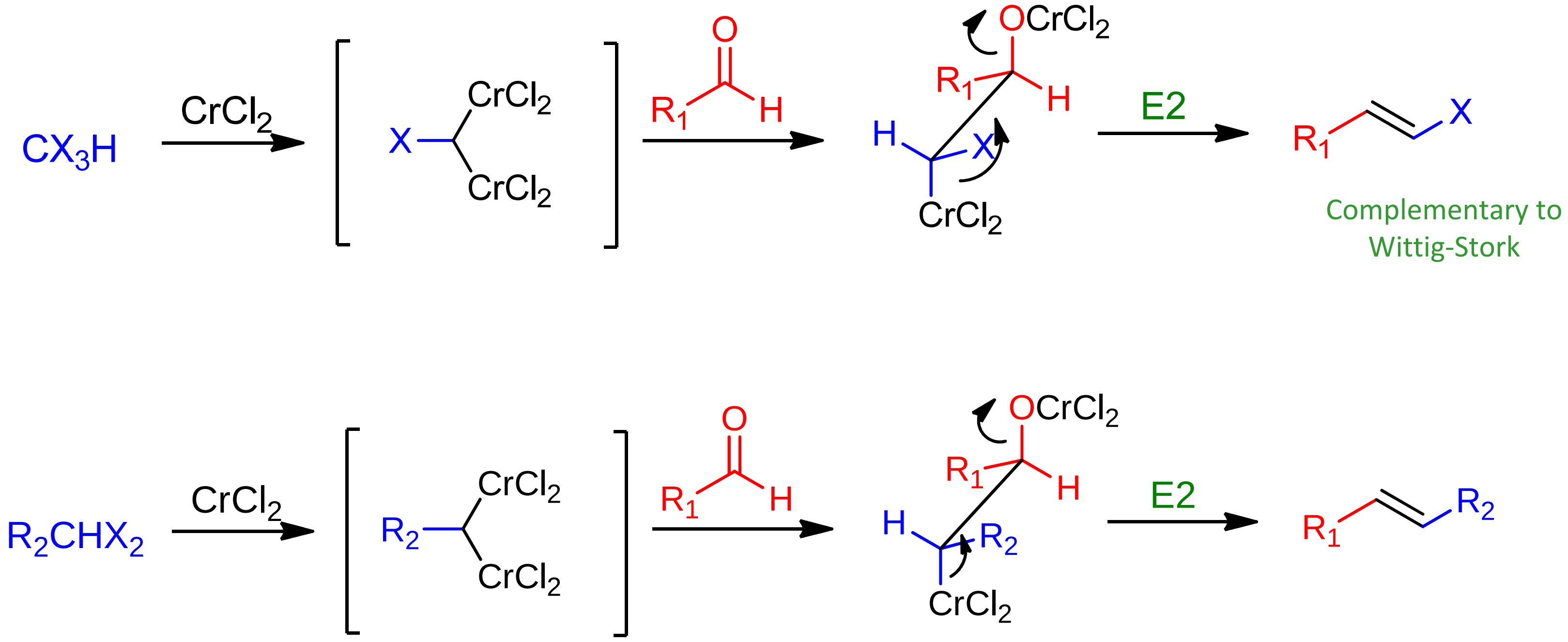
Olefination Reactions

Takai Olefination



Olefination Reactions

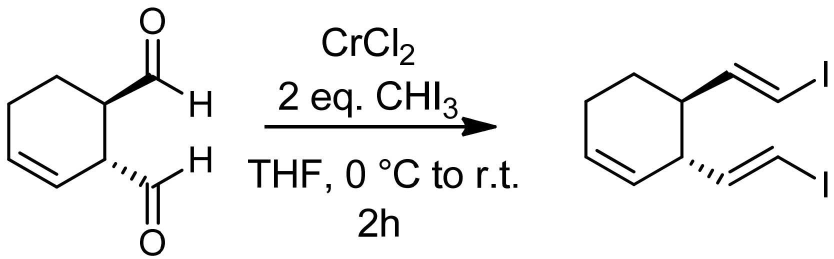
Takai Olefination

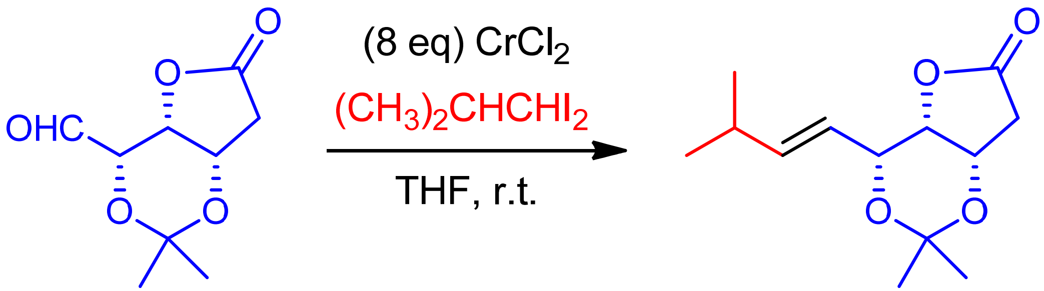


Olefination Reactions

Takai Olefination

Example

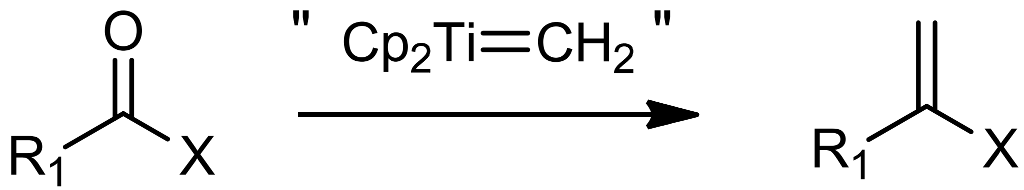




29 %

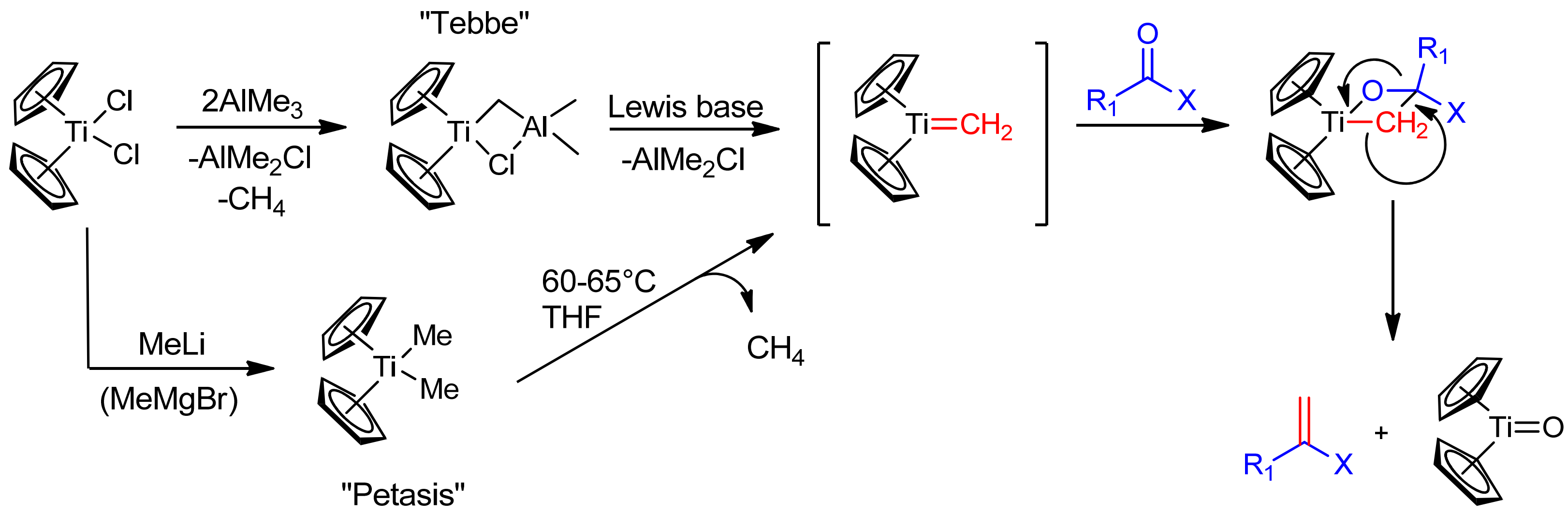
Olefination Reactions

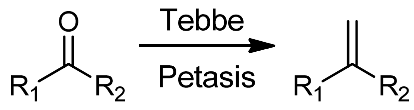
Tebbe/Petasis reaction



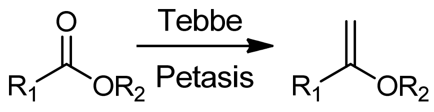
Olefination Reactions

Tebbe/Petasis reaction

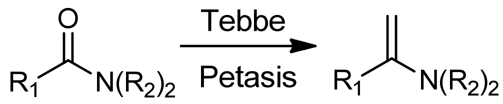




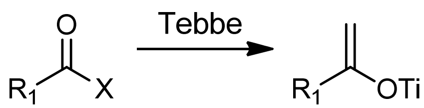
aldehydes and ketones



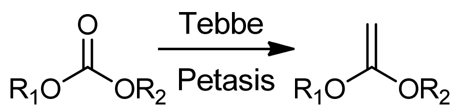
esters and lactones



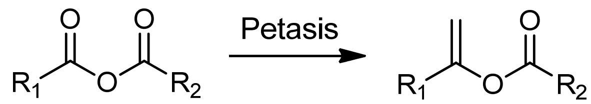
amides or lactams



acid halides and anhydrides



carbonates



anhydrides

Olefination Reactions

Tebbe/Petasis reaction

Example: