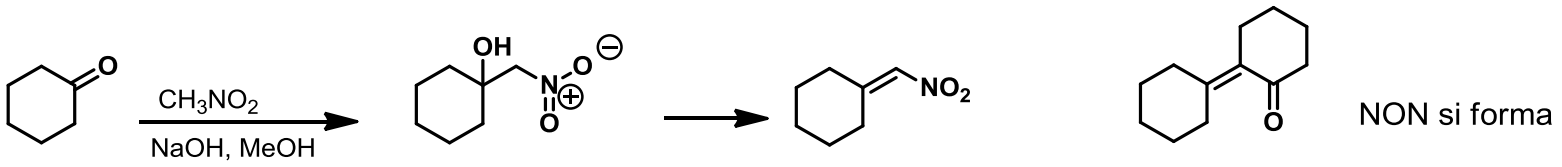
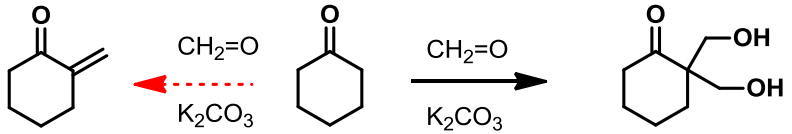
impiego dell'anione del nitrometano come Nu

Louis Henry
26 December 1834 – 9 March 1913
Belgian, b. Marche, Belgium
Henry reaction
Henry, L., Compt. Rend. 1895, 120, 1265

il Nitrometano dà facilmente il corrispondente enolato
incapace tuttavia di autocondensare
.....pertanto, nonostante entrambi i reagenti possano enolizzare
è la condensazione incrociata a prevalere



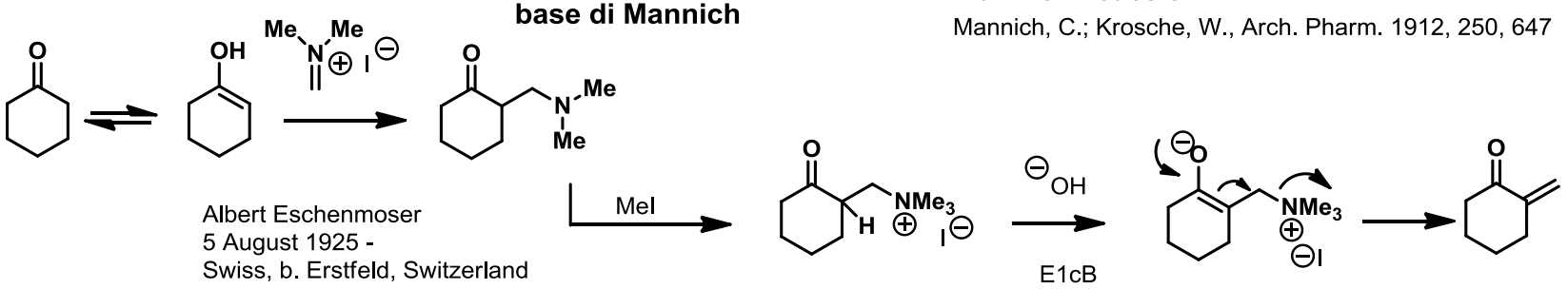
strategie alternative per direzionare reazioni aldoliche



impiegando K_2CO_3 si evita lo step riduttivo (Cannizzaro)
tuttavia c'è doppia condensazione

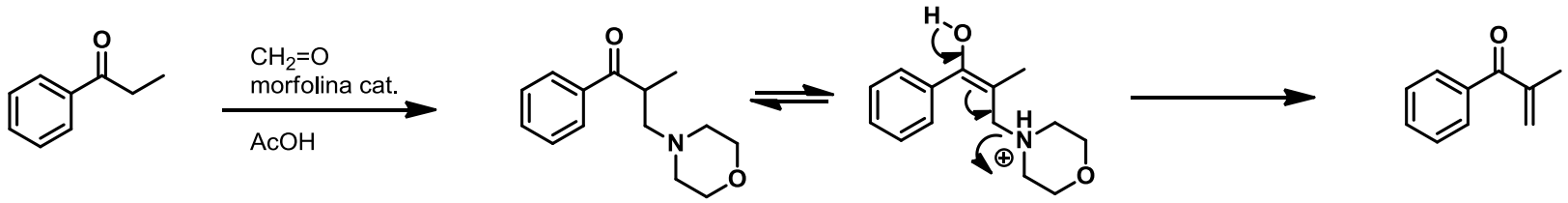
sale di Eschenmoser
equivalente sintetico
della formaldeide

base di Mannich



Albert Eschenmoser
5 August 1925 -
Swiss, b. Erstfeld, Switzerland

Carl Ulrich Franz Mannich
8 March 1877 - 5 March 1947
German, b. Breslau, Germany, now Wroclaw, Poland
Mannich reaction
Mannich, C.; Krosche, W., Arch. Pharm. 1912, 250, 647

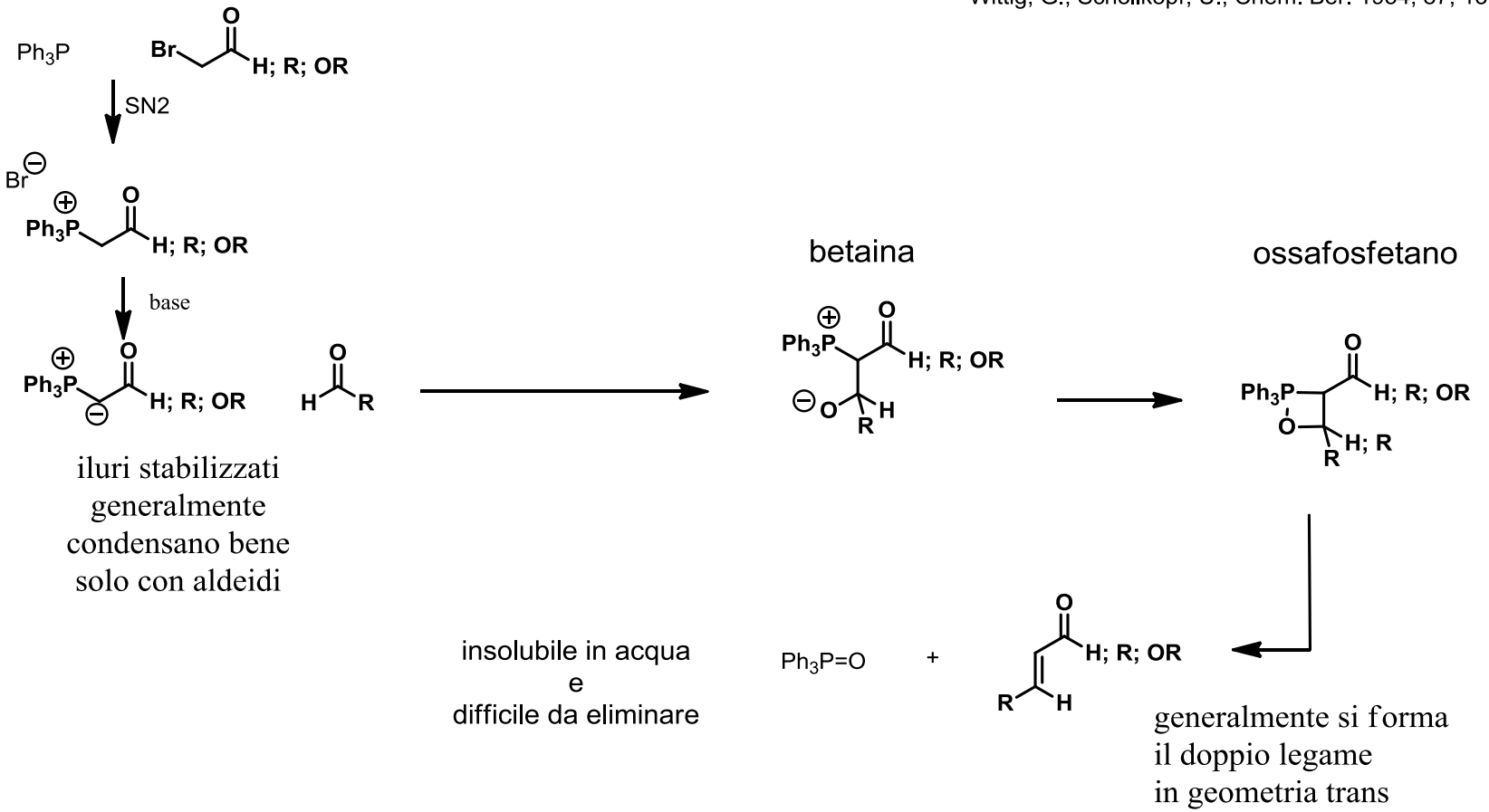


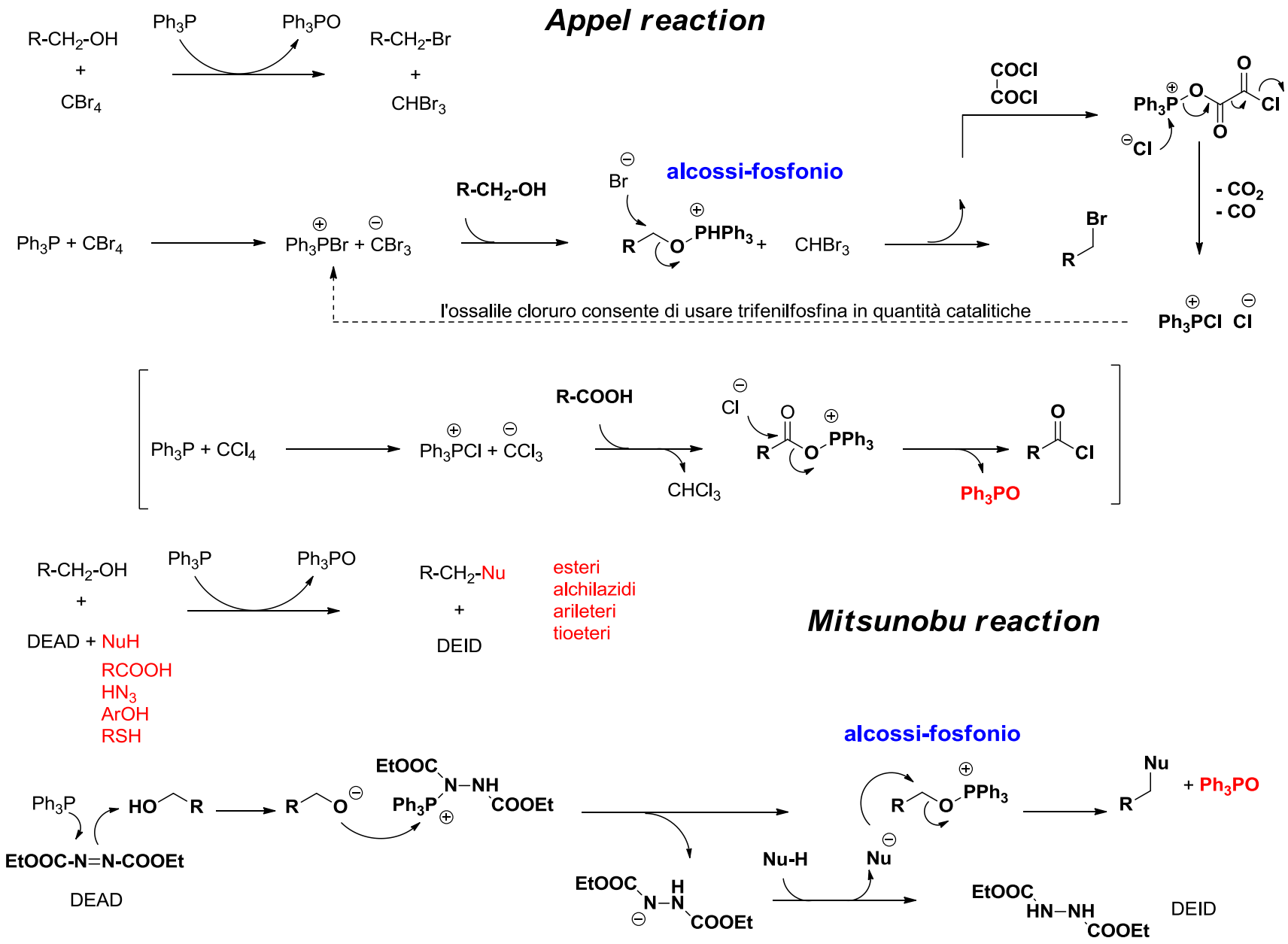
strategie alternative per preparare composti carbonilici α,β-insaturi

(prodotti della condensazione aldolica)

impiego di iluri di fosfonio stabilizzati (anche commerciali)

Georg F.K. Wittig
German, b. Berlin, Germany
Nobel Prize Chemistry 1979
Wittig reaction
Wittig, G.; Schöllkopf, U., Chem. Ber. 1954, 87, 1318




Appel reaction
R-CH2-OH
+
CBr4
Ph3P
Ph3PO
R-CH2-Br
+
CHBr3
alcossi-fosfonio
R-CH2-OH
Ph3P + CBr4
Ph3PBr + CBr3
CHBr3
COCl
COCl
- CO2
- CO
l'ossalile cloruro consente di usare trifenilfosfina in quantità catalitiche
Ph3PCl Cl
Ph3P + CCl4
Ph3PCl + CCl3
R-COOH
CHCl3
Ph3PO
Mitsunobu reaction
R-CH2-OH
+
DEAD + NuH
RCOOH
HN3
ArOH
RSH
Ph3P
Ph3PO
R-CH2-Nu
+
DEID
esteri
alchilazidi
arileteri
tioeteri
EtOOC-N=N-COOEt
DEAD
alcossi-fosfonio
Nu-H
+ Ph3PO
DEID

strategie alternative per preparare composti carbonilici α,β-insaturi

(prodotti della condensazione aldolica)

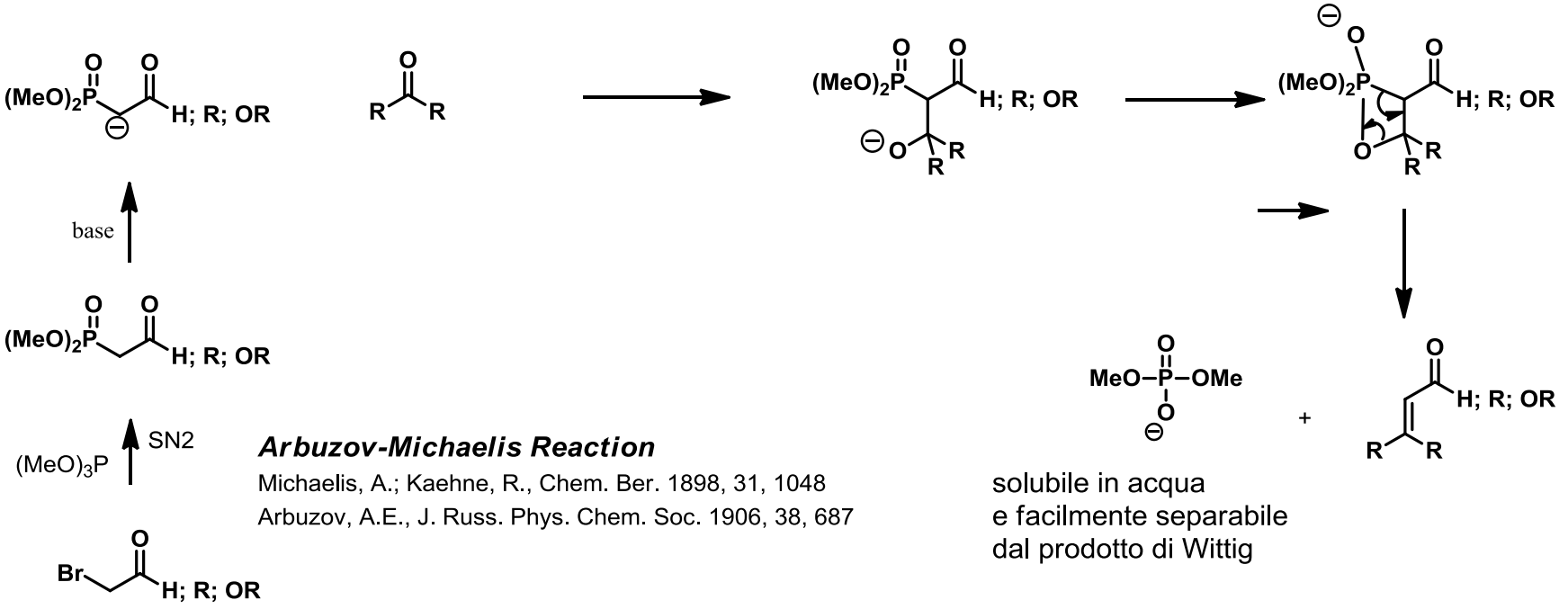
impiego di anioni fosfonato stabilizzati (anche commerciali)

William David Emmons
18 November 1924 - 8 December 2001
American, b. Minneapolis, Minnesota, USA

Horner-Wadsworth-Emmons reaction

Wadsworth, W.S., Jr.; Emmons, W.D., J. Am. Chem. Soc. 1961, 83, 1733

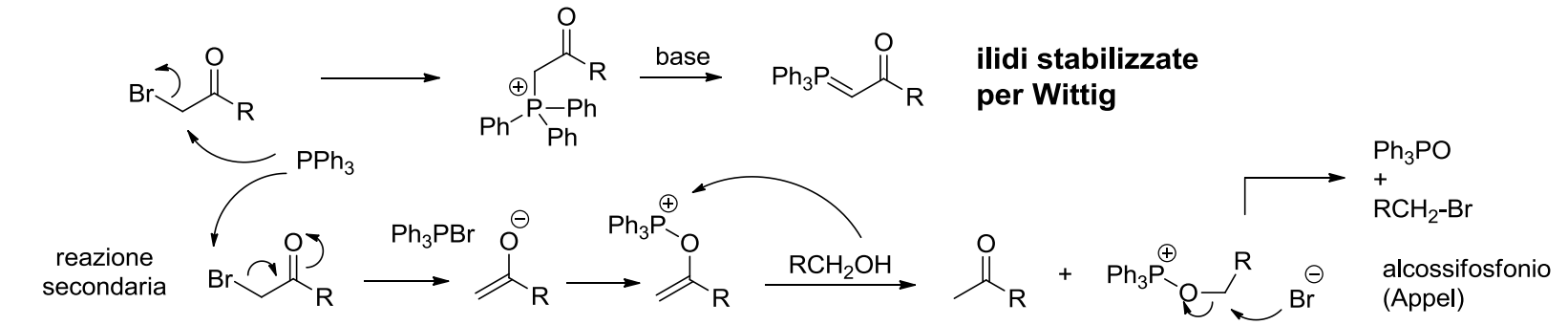
gli anioni fosfonato sono nucleofili
capaci di reagire anche con i chetoni

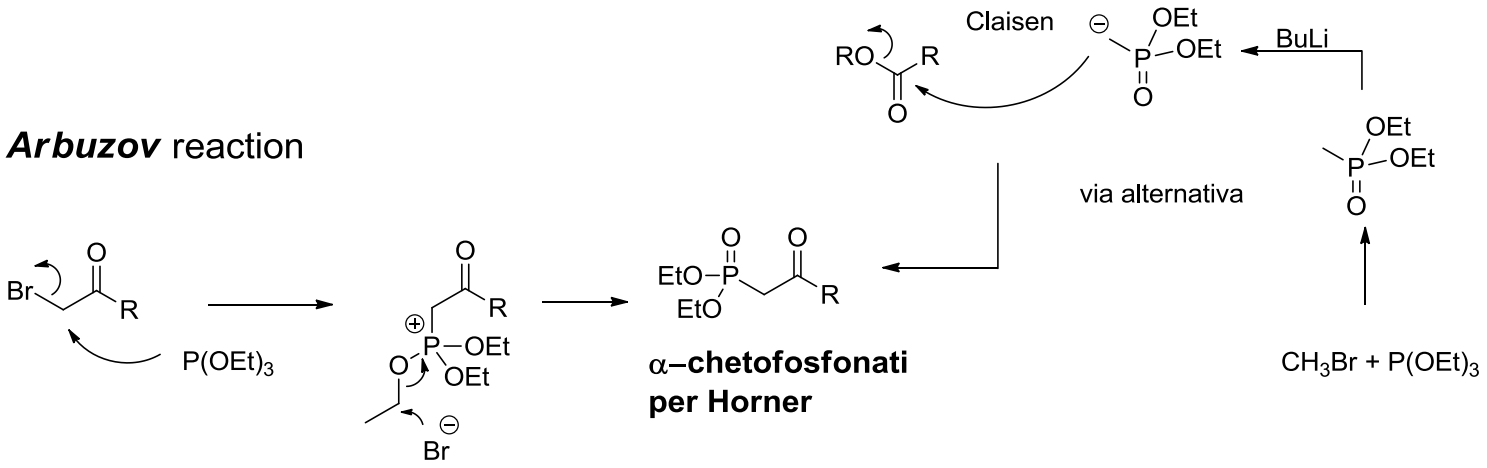


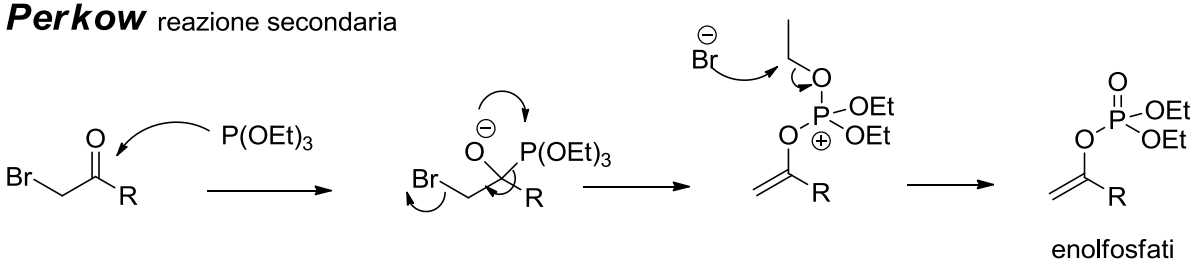
Arbuzov-Michaelis Reaction

Michaelis, A.; Kaehne, R., Chem. Ber. 1898, 31, 1048
Arbuzov, A.E., J. Russ. Phys. Chem. Soc. 1906, 38, 687

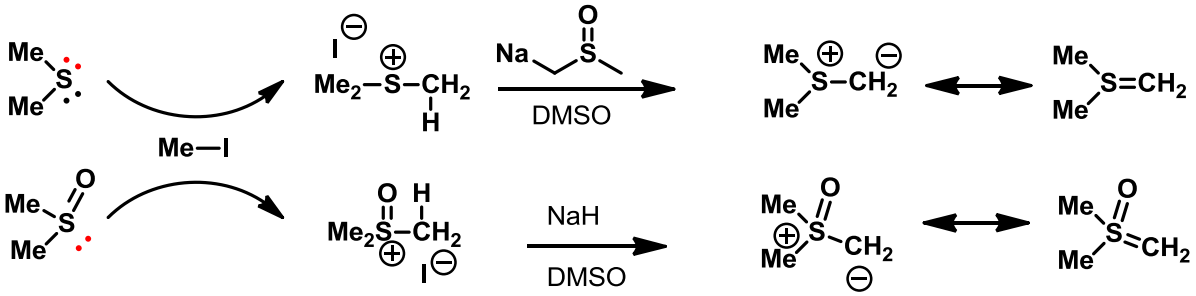
solubile in acqua
e facilmente separabile
dal prodotto di Wittig


base
ilidi stabilizzate
per Wittig
PPh3
reazione
secondaria
Ph3PBr
RCH2OH
Ph3PO
+
RCH2-Br
alcossifosfonio
(Appel)


Arbuzov reaction
Claisen
BuLi
via alternativa
P(OEt)3
α–chetofosfonati
per Horner
CH3Br + P(OEt)3


Perkow reazione secondaria
P(OEt)3
enolfosfati

comportamento degli ILURI di S con composti carbonilici

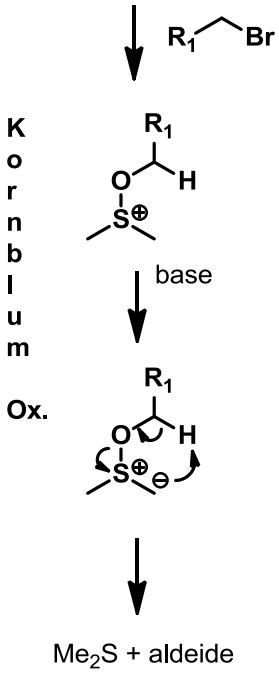


Dimetilsolfonio metilide

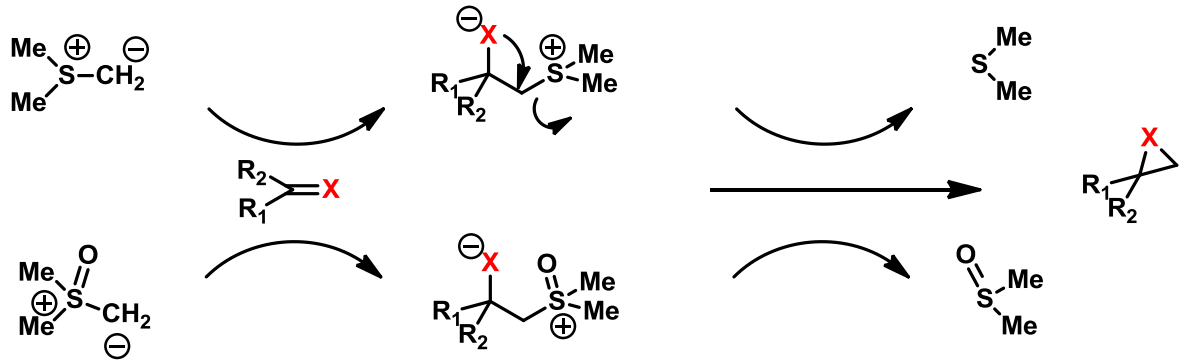
Dimetilsolfossonio metilide

Corey-Chaykovski sulfoxonium ylide

Elias James Corey
12 July 1928 -
American, b. Methuen, Massachusetts, USA
Nobel Prize Chemistry 1990



mentre gli iluri di fosforo reagiscono con carbonili per formare alcheni,
gli iluri di Zolfo reagiscono per dare epossidi

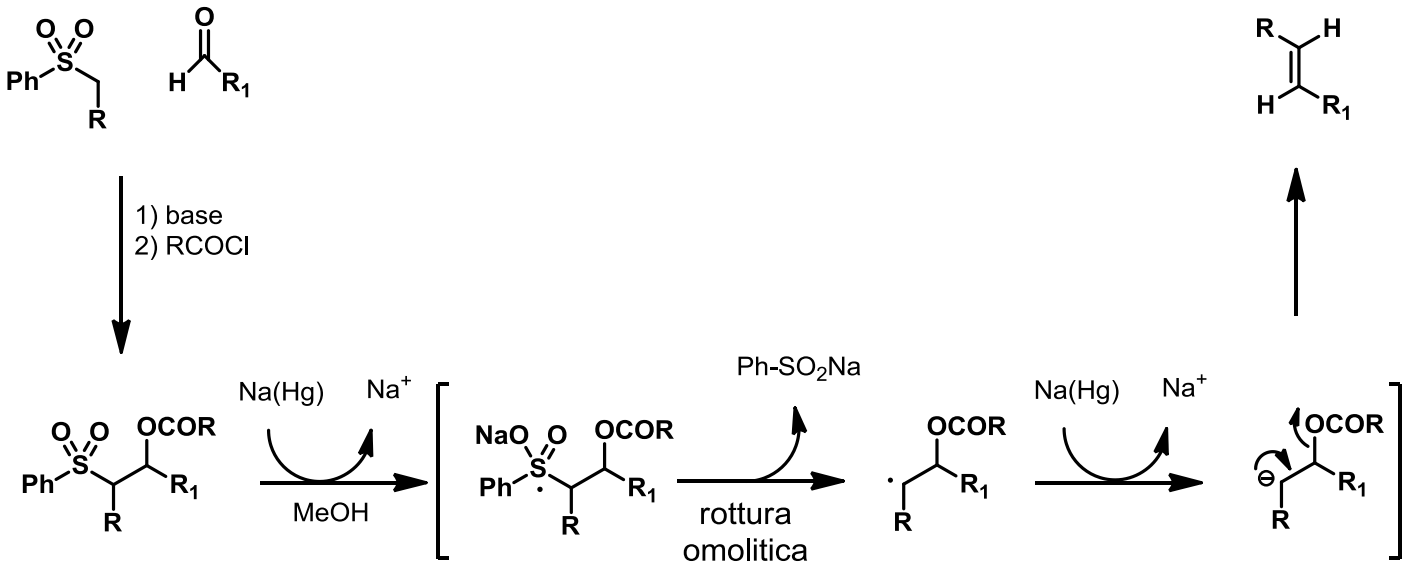


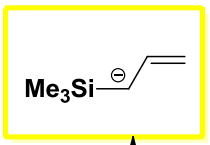
X = O Corey-Chaykovski epoxidation
X = NH Corey-Chaykovski aziridination

impiego di anioni solfonato stabilizzati

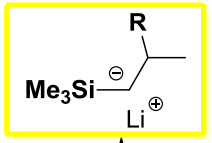
Marc Julia
1922 -
French, b. ?
Julia synthesis
Julia, M.; Paris, J.M., Tetrahedron Lett. 1973, 4933

Julia olefination





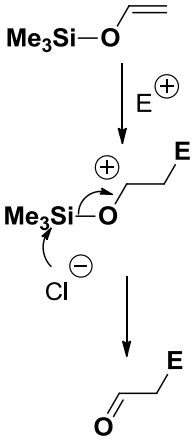
anioni stabilizzati per coinvolgimento orbitali **d** vuoti del Silicio

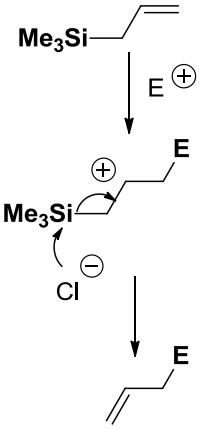


interazione stabilizzante con orbitali d vuoti di Si

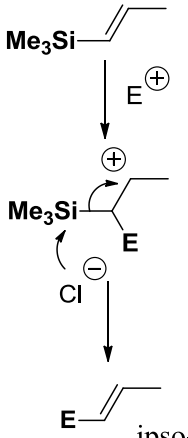
CHIMICA DEL SILICIO

Sililenoleteri — **Allil silani** — **Vinil silani**



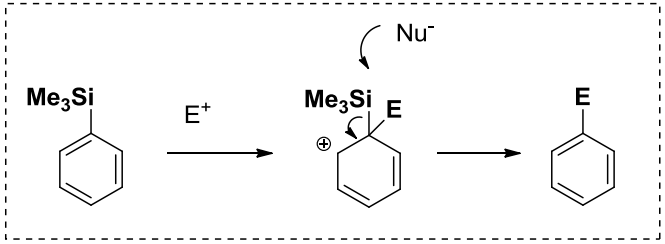


*allilazione

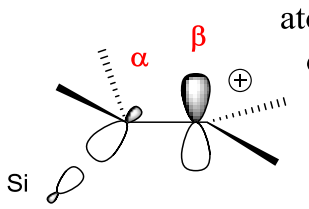


ipso-sostituzione

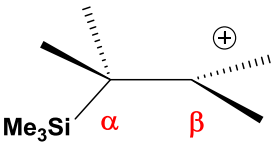
addizionano E^+ in modo da collocare la carica positiva su atomo in β al Si



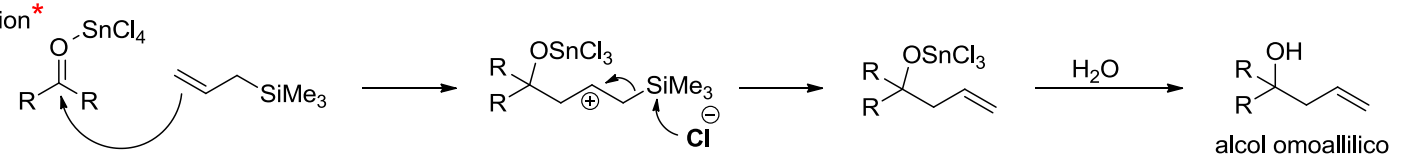
stabilizzazione intermedio per sovrapposizione fra p vacante su atomo β e σ di legame atomo α-Si



atomo α = **O** oppure **C**

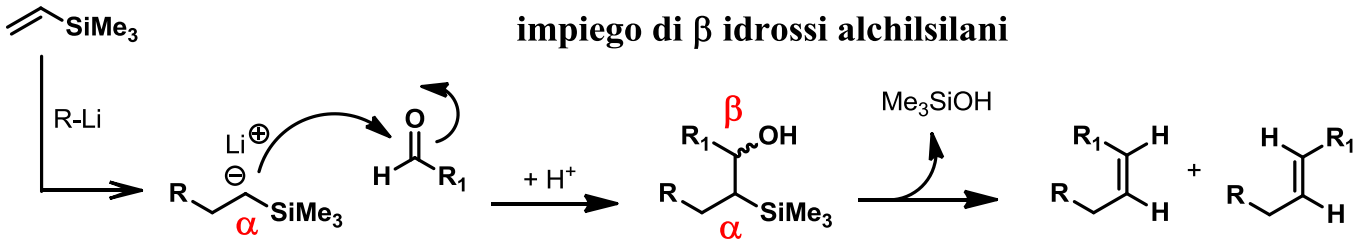


Sakurai reaction*

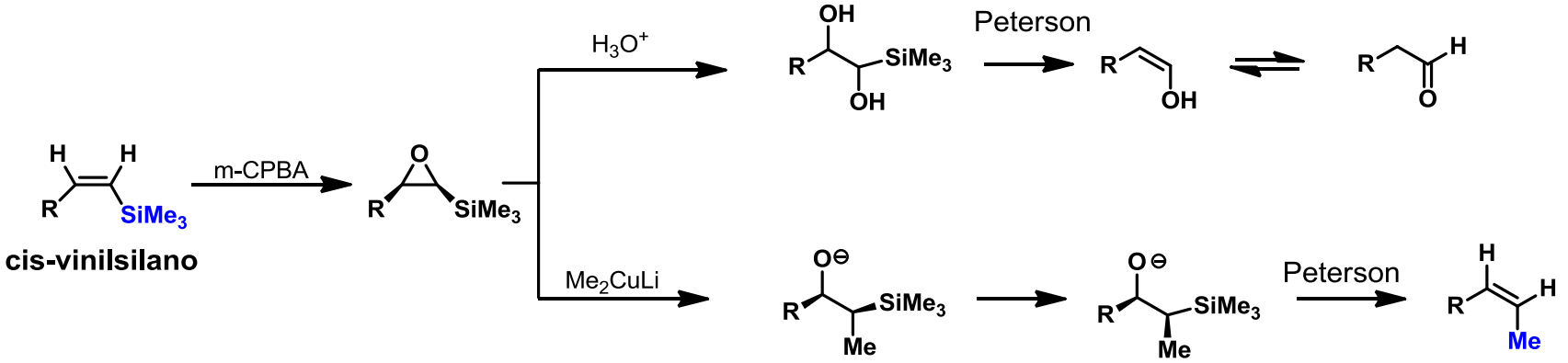


Peterson olefination

impiego di β idrossi alchilsilani

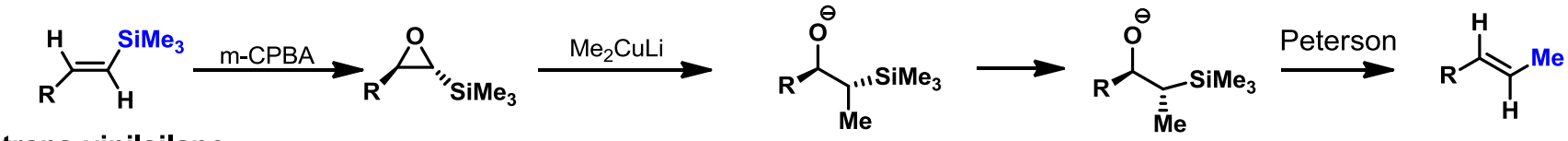


Donald J. Peterson
19 November 1935 -
American, b. Ladysmith, Wisconsin, USA
Peterson reaction
Peterson, D.J., J. Org. Chem. 1968, 33, 780



cis-vinilsilano

la Peterson è Stereospecifica

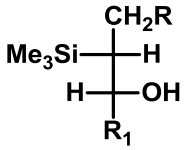


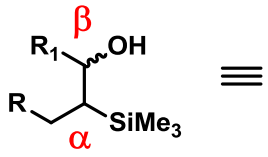
trans-vinilsilano

Stereoselettività della Peterson olefination

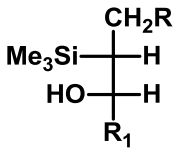
viene eliminato trimetilsilanolo:
in ambiente basico è un processo di sin-eliminazione e in ambiente acido è una E2 (anticoplanare)

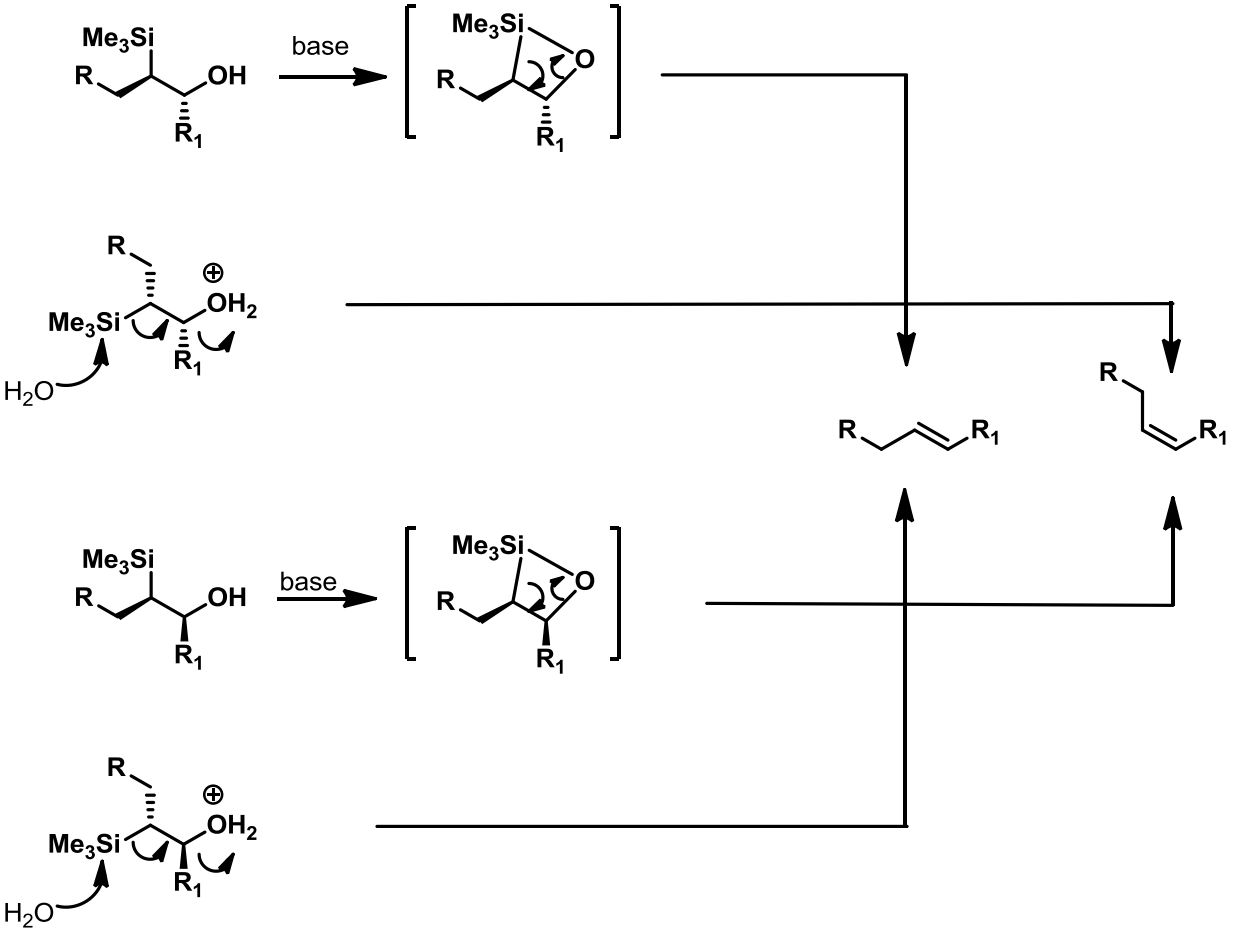
β-idrossialchilsilano
treo



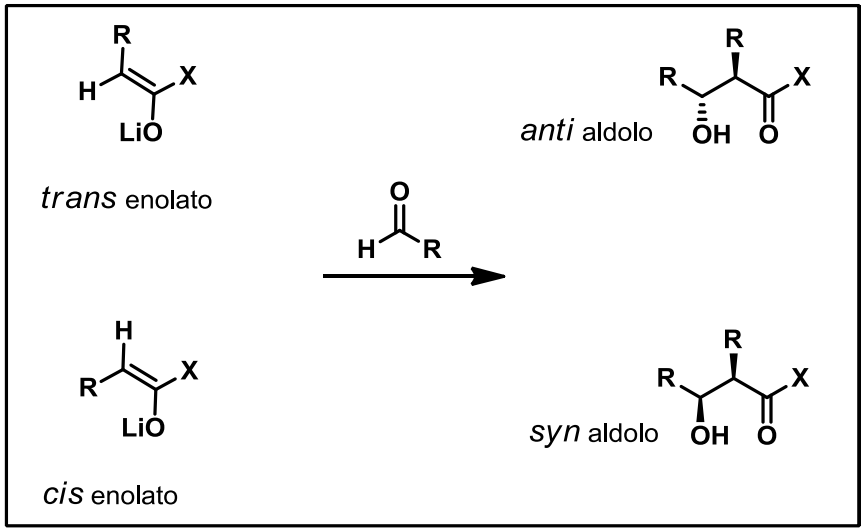


β-idrossialchilsilano
eritro

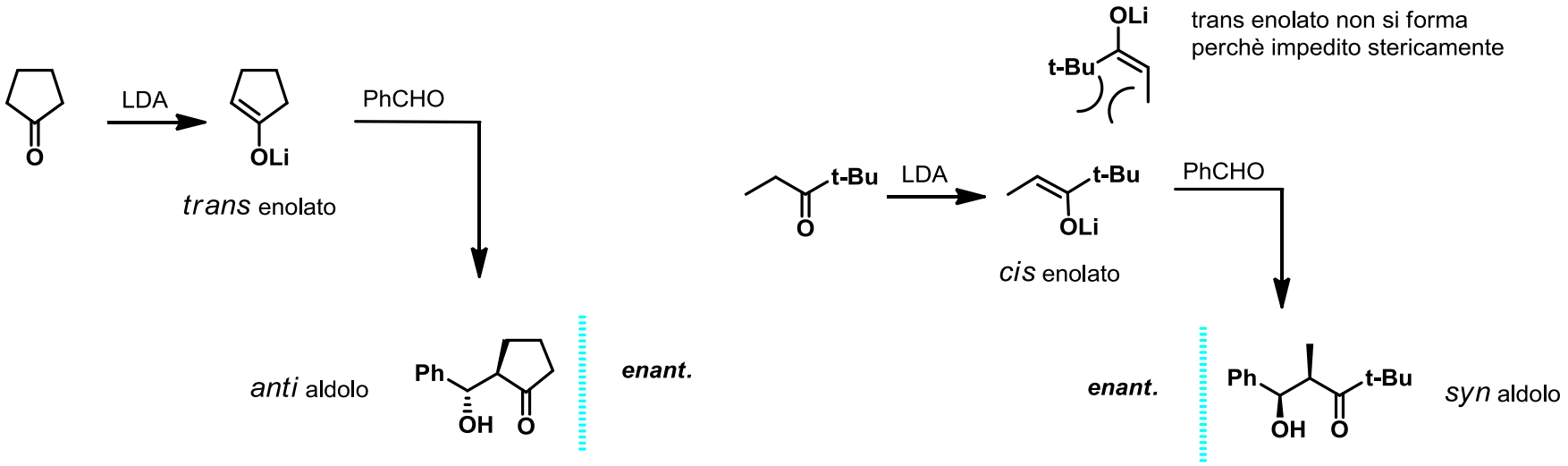




reazioni aldoliche: stereoselettività



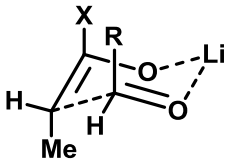
sperimentalmente si osserva



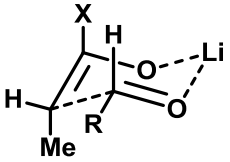
reazioni aldoliche: stereoselettività

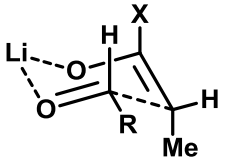
stato di transizione "chair like" di ***Zimmerman-Traxler***

cis enolato

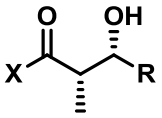


R pseudo ax. SFAVORITO

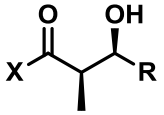




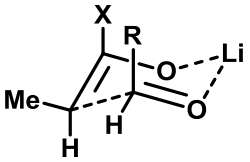
R pseudo eq. FAVORITO



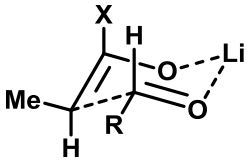
syn aldolo

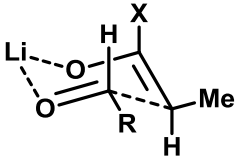


trans enolato

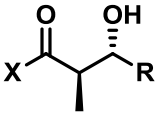


R pseudo ax. SFAVORITO

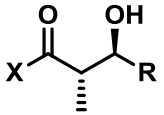




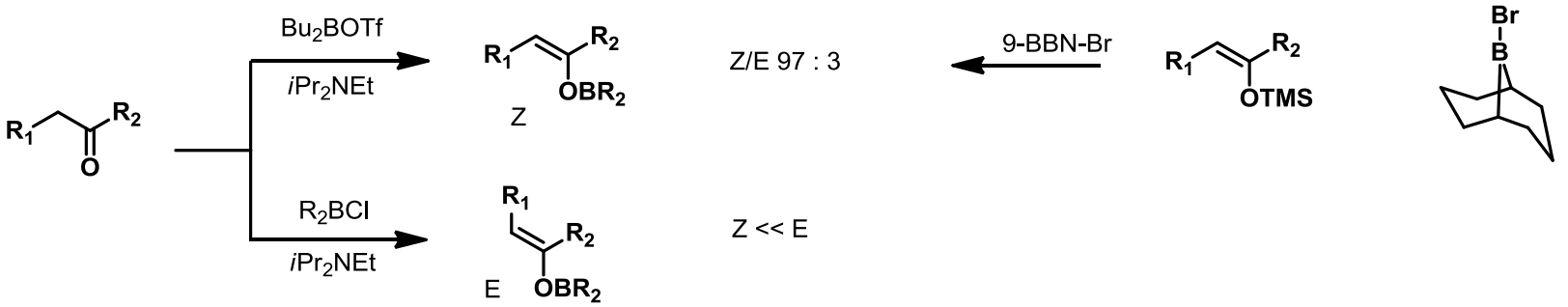
R pseudo eq. FAVORITO

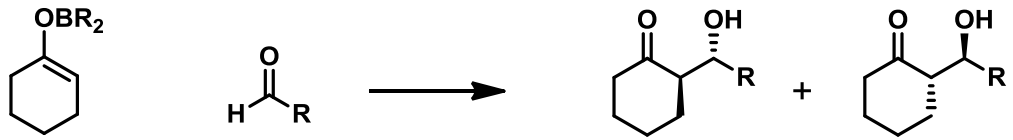


anti aldolo



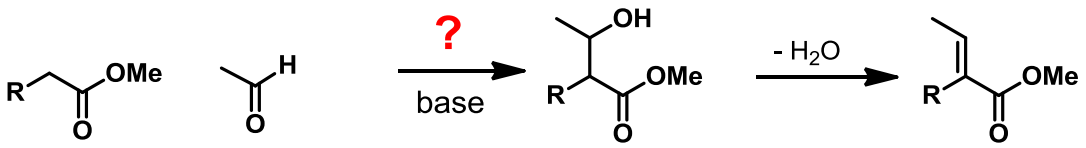
reazioni aldoliche: stereoselettività

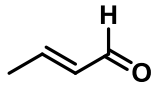




In generale
passando da Litio-enolati
a Boro-enolati
la stereoselettività
migliora

reazioni aldoliche impiegando enolati provenienti da esteri



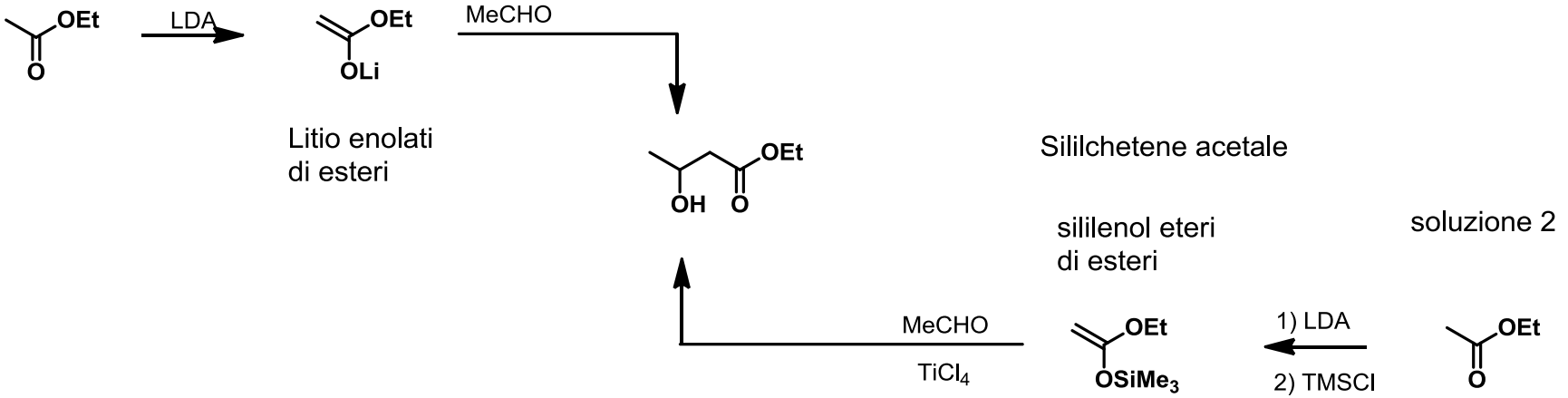


prodotto di autocondensazione dell'aldeide !!

si formerebbe in condizioni equilibranti

reazione aldolica incrociata difficile da realizzare in condizioni **Equilibranti** perchè non sono rispettati i punti **1)** e **2)** ma in condizioni **NON-Equilibranti**.....

soluzione 1

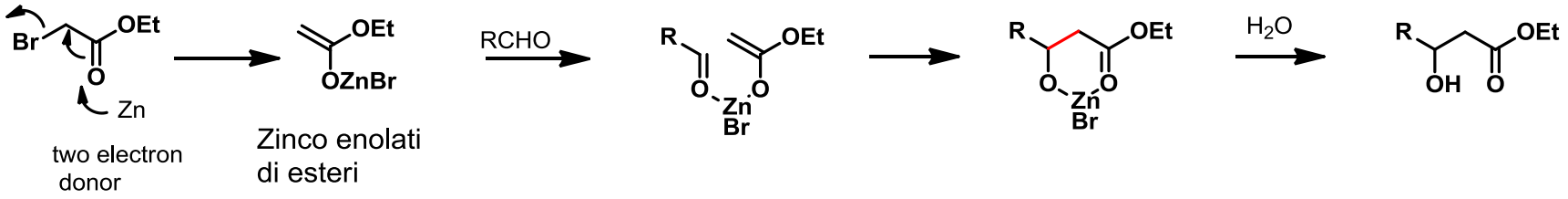


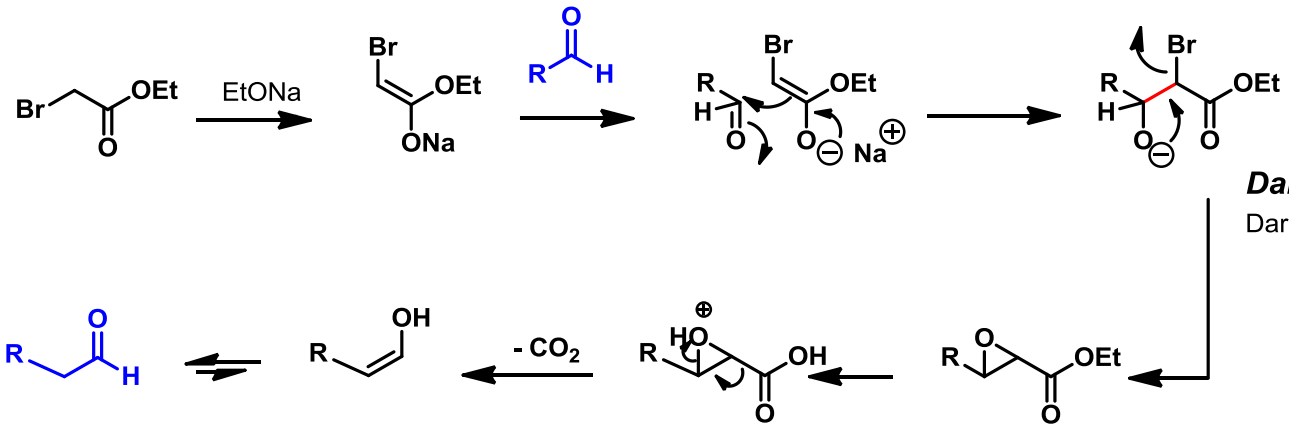
reazioni aldoliche impiegando enolati provenienti da esteri

Reformatskii reaction

Reformatskii, S., Chem. Ber. 1887, 20, 1210

Sergei Nikolaevich Reformatskii
1 April (20 March) 1860 - 28 July 1934
Russian, b. Borisoglebskoe, near Ivanovo, Russia



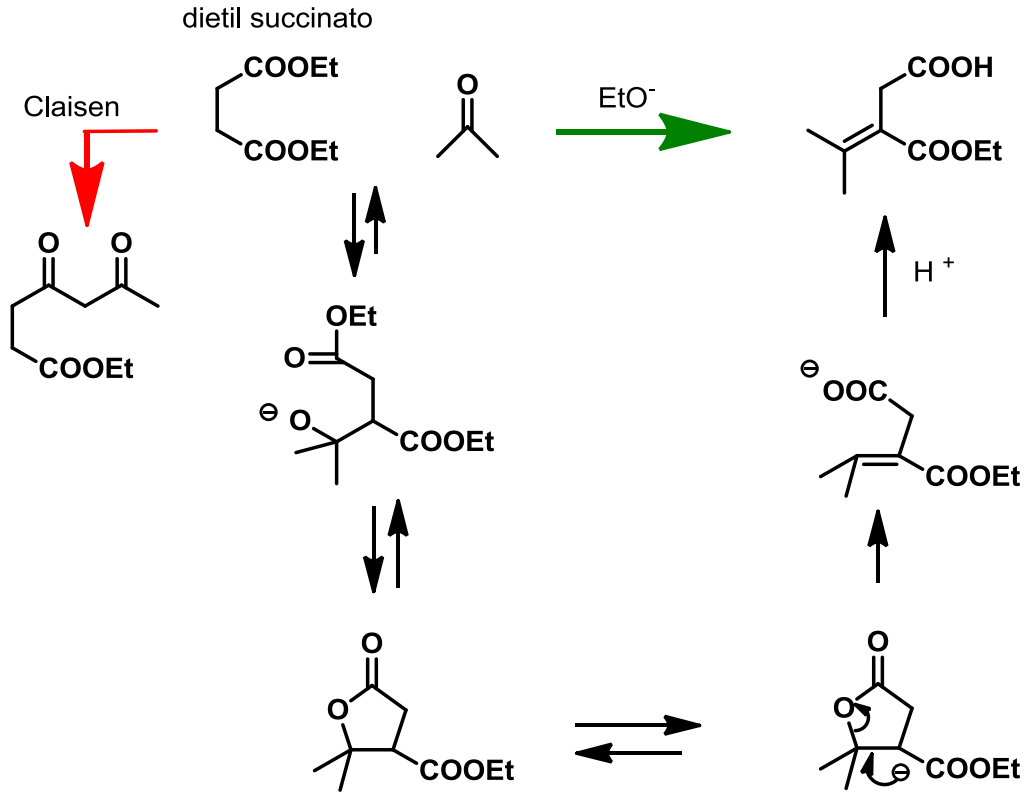


Darzens condensation

Darzens, G., Compt. Rend. 1904, 139, 1214

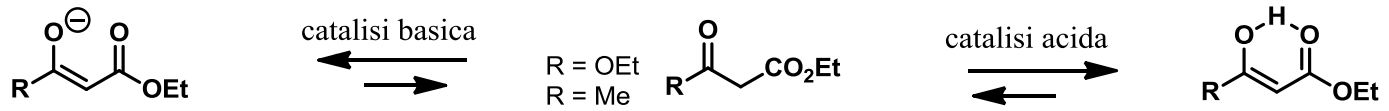
Auguste George Darzens
12 July 1867 - 10 September 1954
French, b. Moscow, Russia

reazioni aldoliche impiegando enolati provenienti da esteri



Johann Hans Hermann August Adolph Stobbe
9 June 1860 - 3 August 1938
German, b. Tiegenhof, near Danzig, Germany
Stobbe condensation
Stobbe, H., Chem. Ber. 1893, 26, 2312

reazioni aldoliche impiegando enolati provenienti da composti β-dicarbonilici



enolato stabile quindi poco nucleofilo

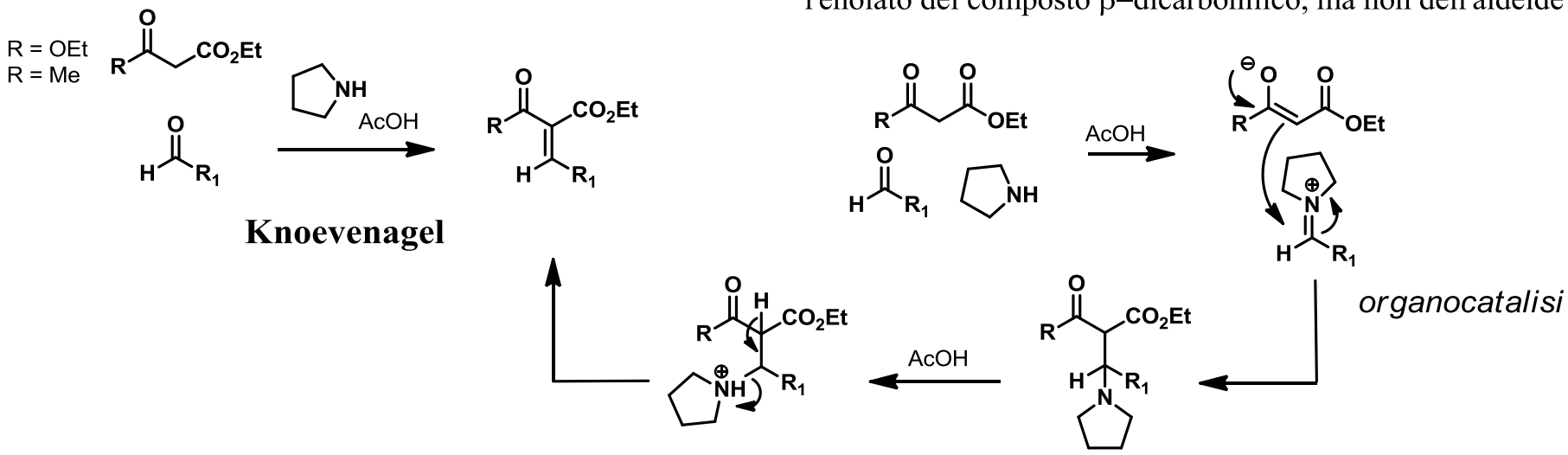
carbonili poco elettrofilici

enolo stabile quindi poco nucleofilo

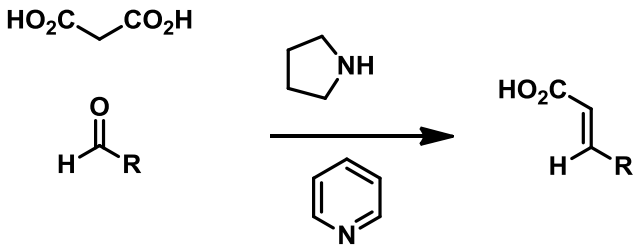
Questi composti pertanto non sono soggetti ad autocondensazione come invece lo sono aldeidi e chetoni

per avere una reazione aldolica incrociata è sufficiente
aggiungere un secondo composto carbonilico elettrofilico e una base debole o un acido debole o entrambi.

la pirrolidina è base sufficientemente forte per formare l'enolato del composto β–dicarbonilico, ma non dell'aldeide

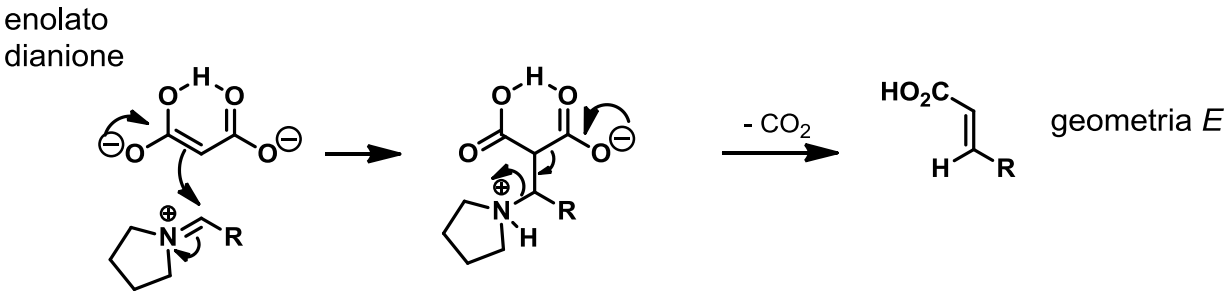


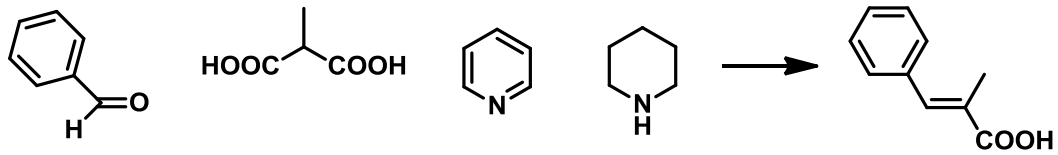
reazioni aldoliche impiegando enolati provenienti da composti β-dicarbonilici



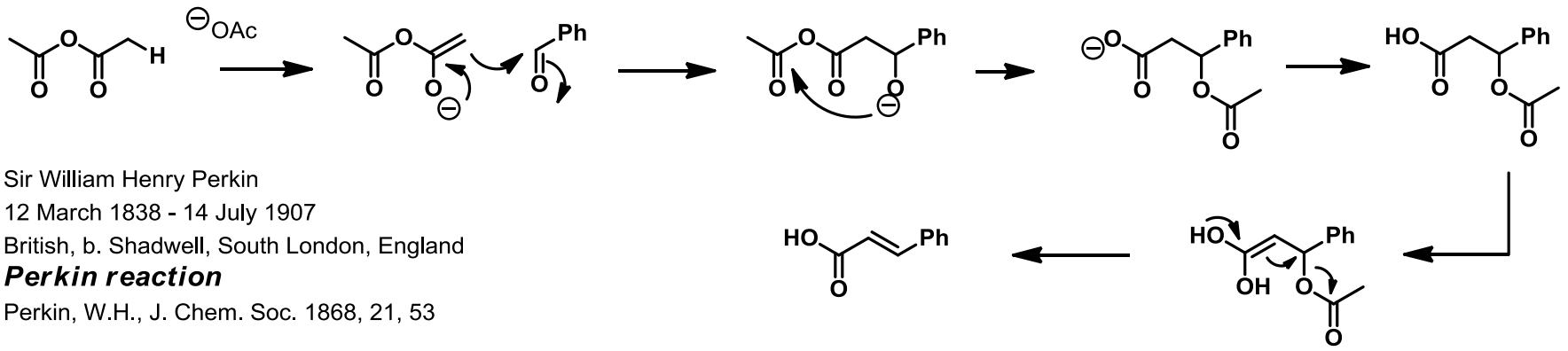
Heinrich Emil Albert Knoevenagel
18 June 1865 - 11 August 1921
German, b. Hannover-Linden, Germany
Knoevenagel condensation
Knoevenagel, E., Chem. Ber. 1898, 31, 2596

Doebner modification





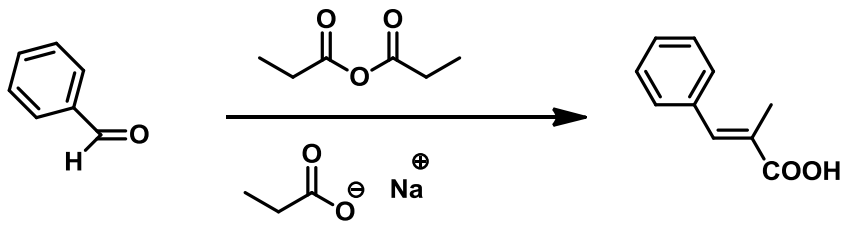
aldeide
non enolizzabile

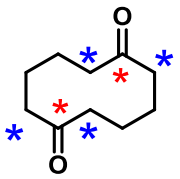


Sir William Henry Perkin
12 March 1838 - 14 July 1907
British, b. Shadwell, South London, England

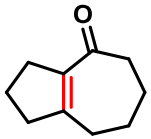
Perkin reaction

Perkin, W.H., J. Chem. Soc. 1868, 21, 53





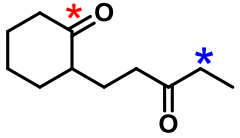
acido
o
base



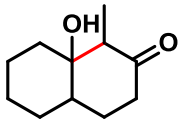
100%

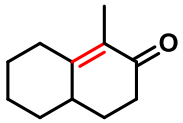
tutte le soluzioni
si equivalgono

reazioni aldoliche intramolecolari



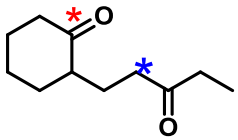
KOH



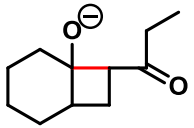


90%

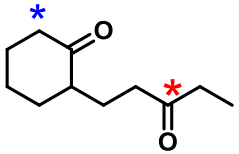
quattro opzioni, ma una vincente



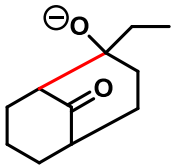
KOH



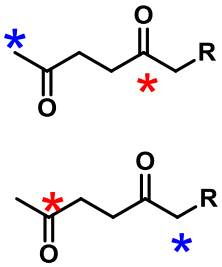
anello a quattro instabile
pertanto retroaldolica
al dichetone di partenza



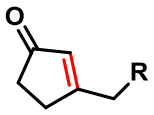
KOH



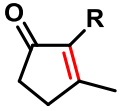
l'aldolo non può disidratare
pertanto retroaldolica
al dichetone di partenza



KOH



+



alchene tetrasostituito
prodotto termodinamicamente più stabile

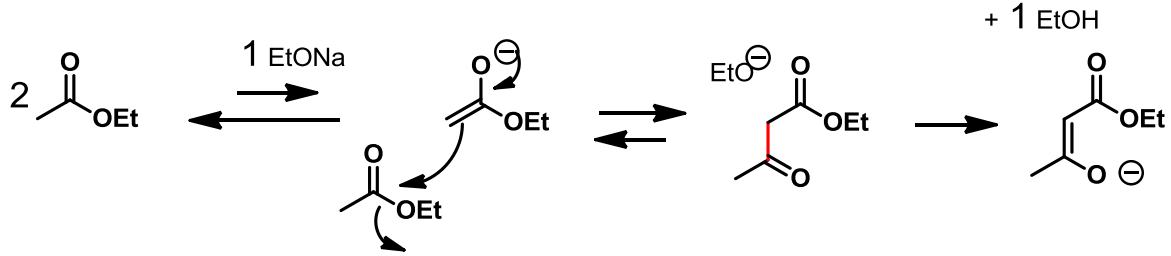
prevalente

Claisen condensation

Claisen, L.; Lowman, O., Chem. Ber. 1887, 20, 651

Rainer Ludwig Claisen
14 January 1851 - 5 January 1930
German, b. Cologne, Germany

autocondensazione gruppo elettrofilo è un carbonile di estere il nucleofilo è la specie enolato dello stesso estere

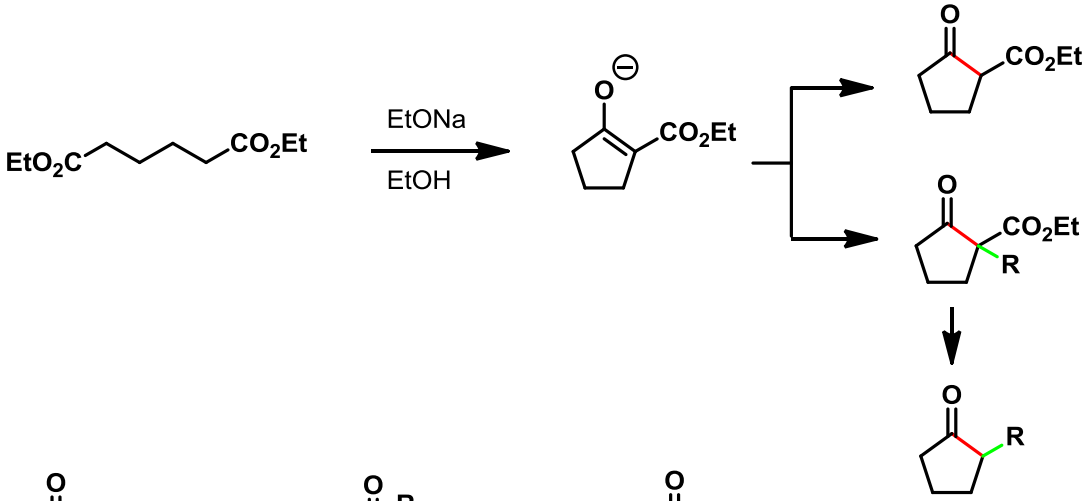


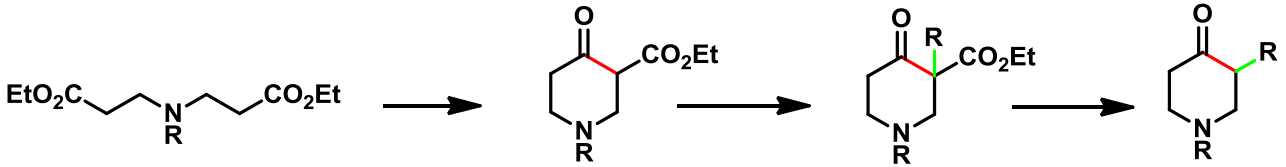
la condensazione aldolica è catalitica in base
la Claisen è stechiometrica

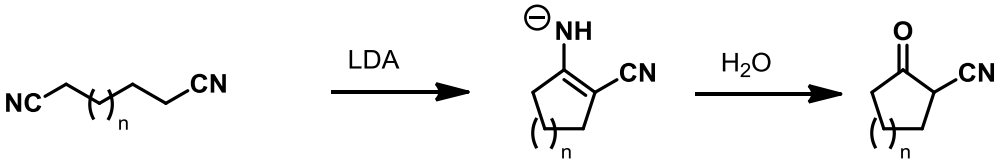
l'estere deve avere 2H in α
in modo da rendere possibile l'ultimo e irreversibile passaggio

Claisen intramolecolare

Walter Dieckmann
8 October 1869 - 12 January 1925
German, b. Hamburg, Germany
Dieckmann condensation
Dieckmann, W., Chem. Ber. 1894, 27, 102







reazione di ***Thorpe***

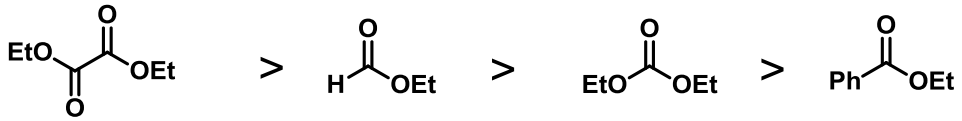
( )$_n$ = 1,2,3,4

Claisen incrociata ESTERE-ESTERE

si utilizzano come elettrofili (forti)
esteri non enolizzabili

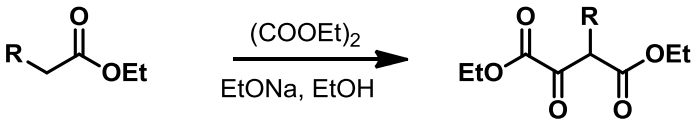
ordine di reattività come elettrofili

dietil ossalato > etil formiato > dietil carbonato > etil benzoato

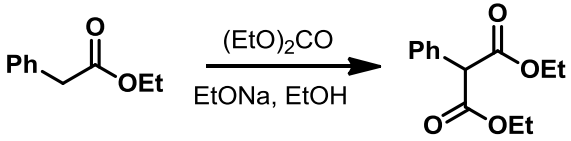


quattro orbitali p
LUMO abbassato

più reattivi di un normale estere
per il doppio effetto induttivo



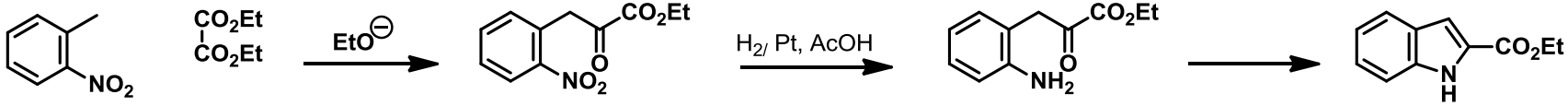
l'estere non auto-condensa poichè reagisce con l'elettrofilo più forte:
il dietilossalato



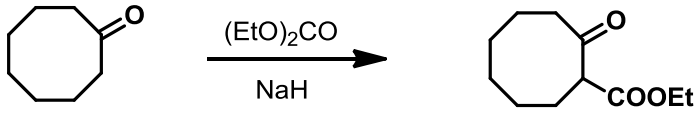
non ottenibile per alchilazione del malonato

Reissert Indole synthesis

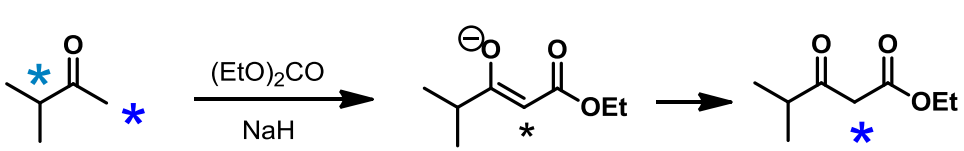
A. Reissert, Ber. 30, 1030 (1897)
vedi pag. 9 ETEROCICLI Arom.

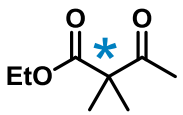


Claisen incrociata ESTERE-CHETONE



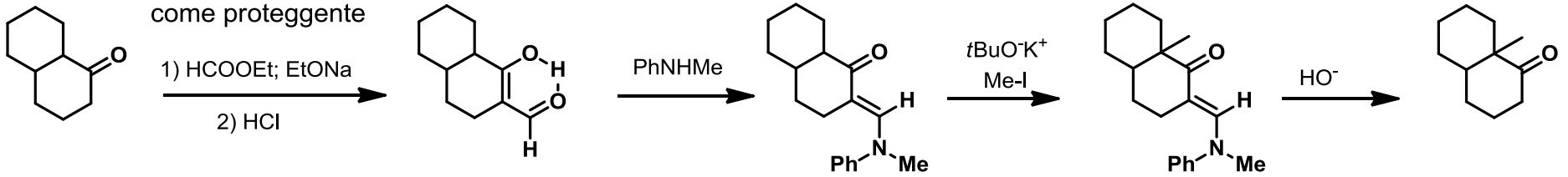
ragioni entropiche impediscono la sua preparazione via Dieckmann



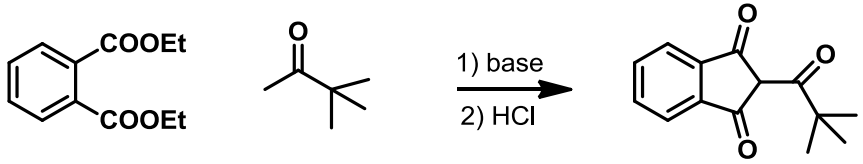


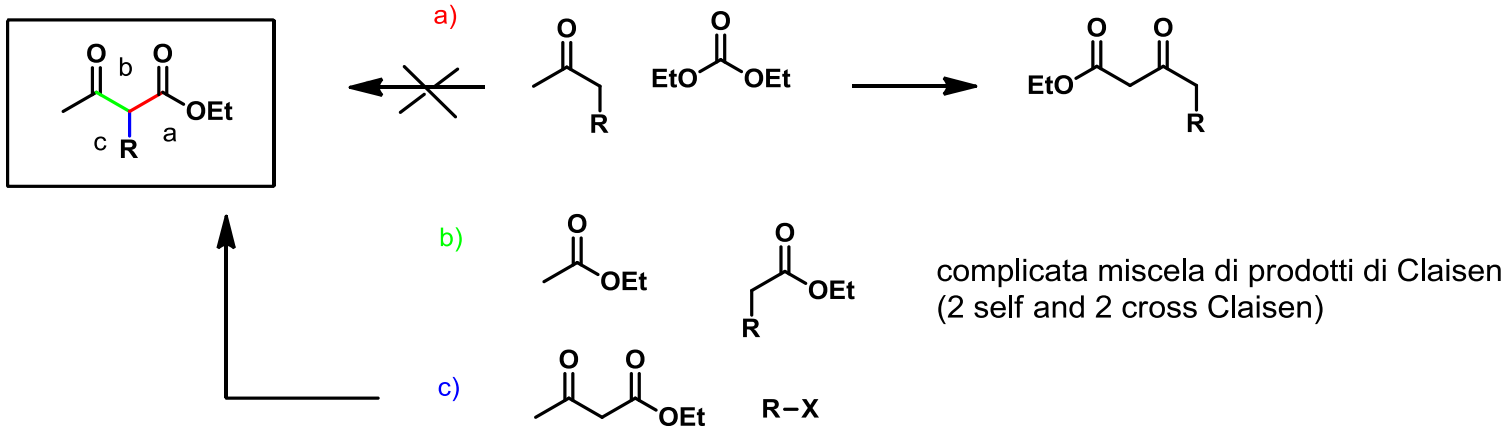
NON enolizzabile
NON si forma

Claisen regioselettiva

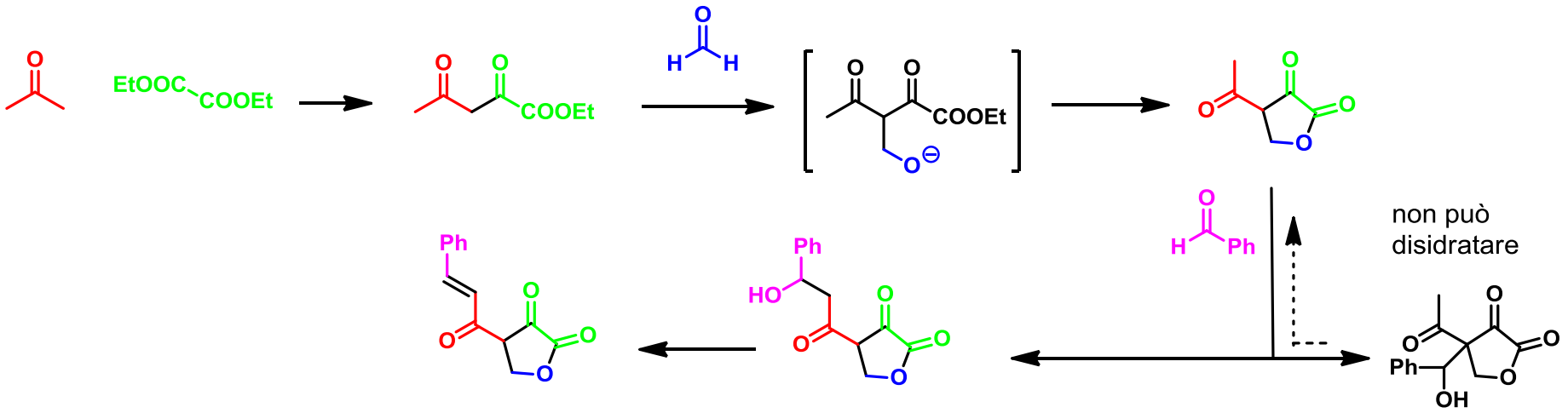


PIVAL topicida



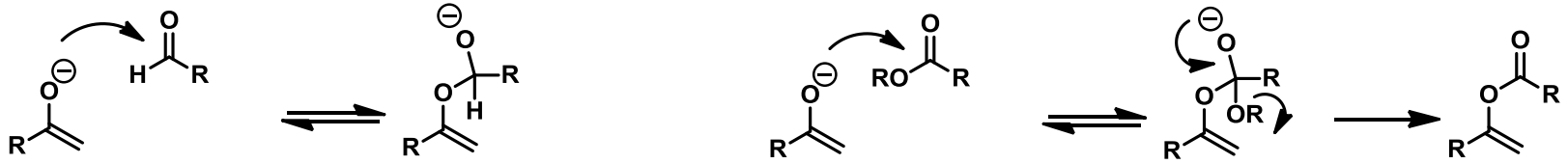


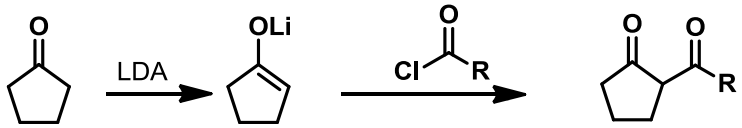
Applicazione alla sintesi



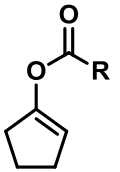
condensazioni quasi-Claisen il gruppo elettrofilo è un carbonile di acil cloruro

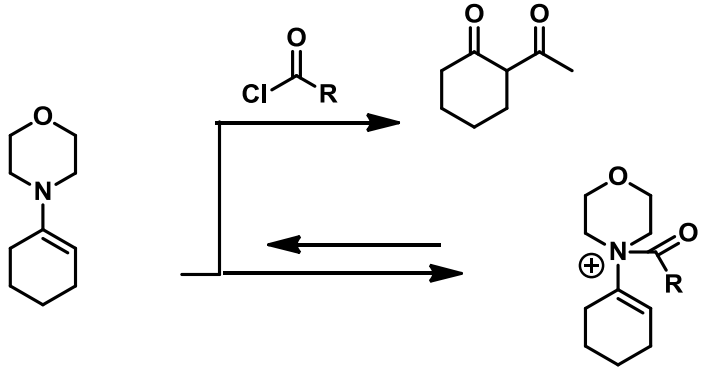
diversamente dalla condensazione aldolica, nella Claisen l'elettrofilia al dente *O* potrebbe costituire un problema



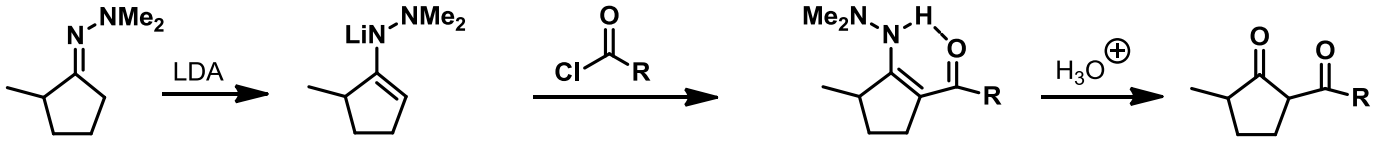


rischio *O*-acilazione
limitato dalla forte affinità Li-O



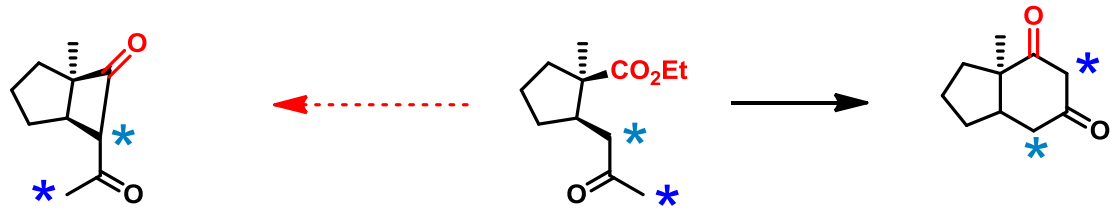


le enammine con elettrofili non adatti a SN_2 danno N-alchilazione irreversibile, evento che abbassa la resa
qui invece il prodotto di N-acilazione si forma reversibilmente e non costituisce un problema

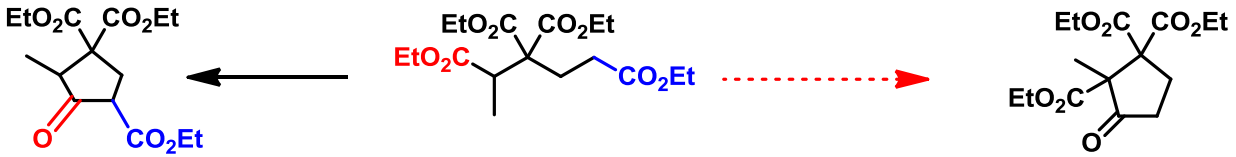


acilazione regioselettiva

Claisen incrociate intramolecolari

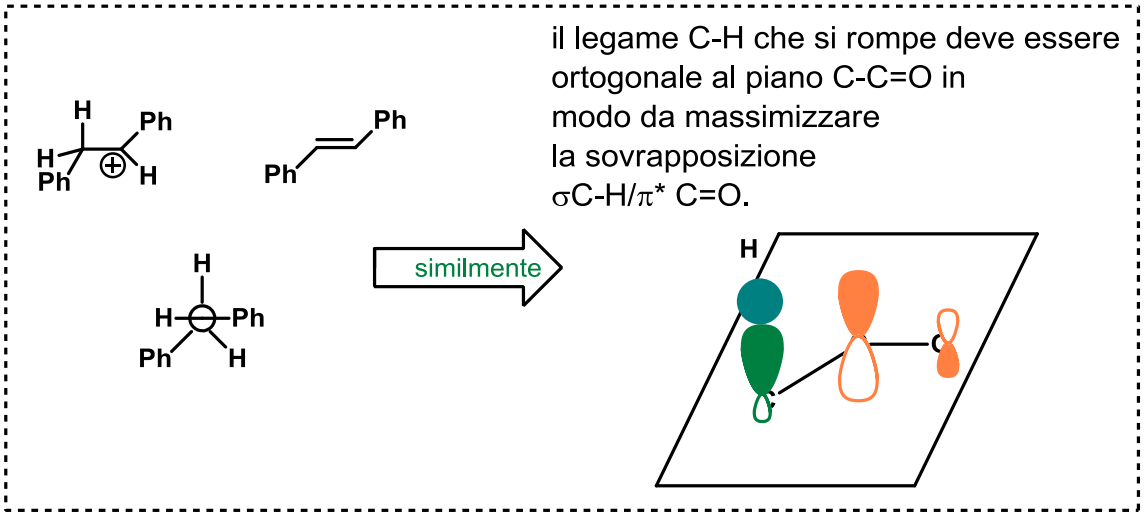


NO perchè vi è un anello
a 4 tensionato

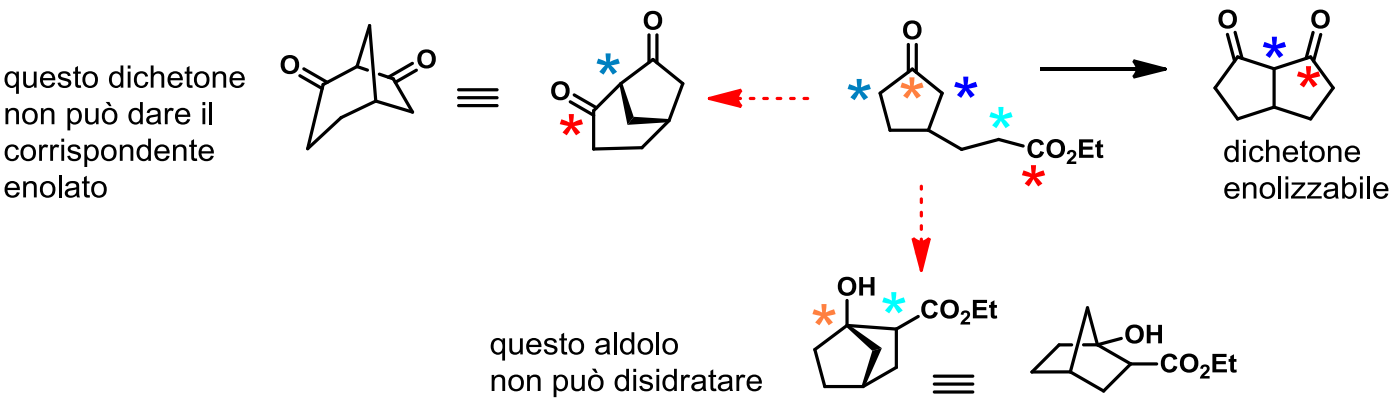


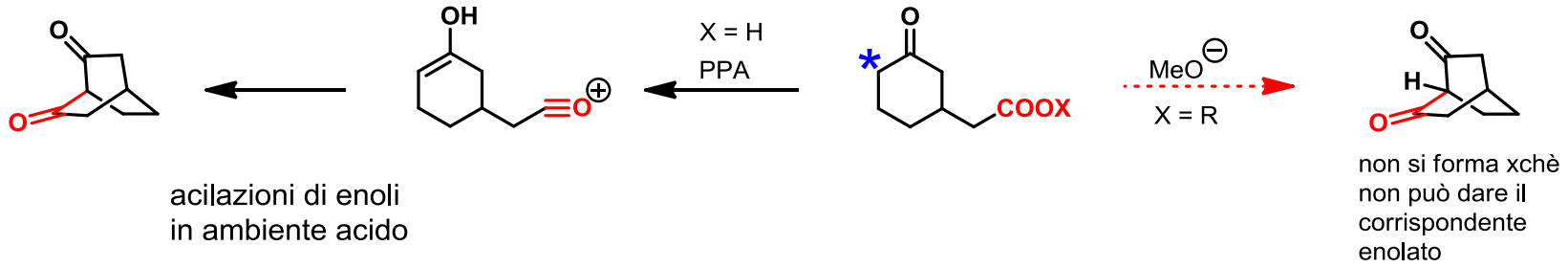
NO perchè non ci sono
due H in α e il composto
risultante non darebbe il
corrispondente enolato

Claisen incrociate intramolecolari

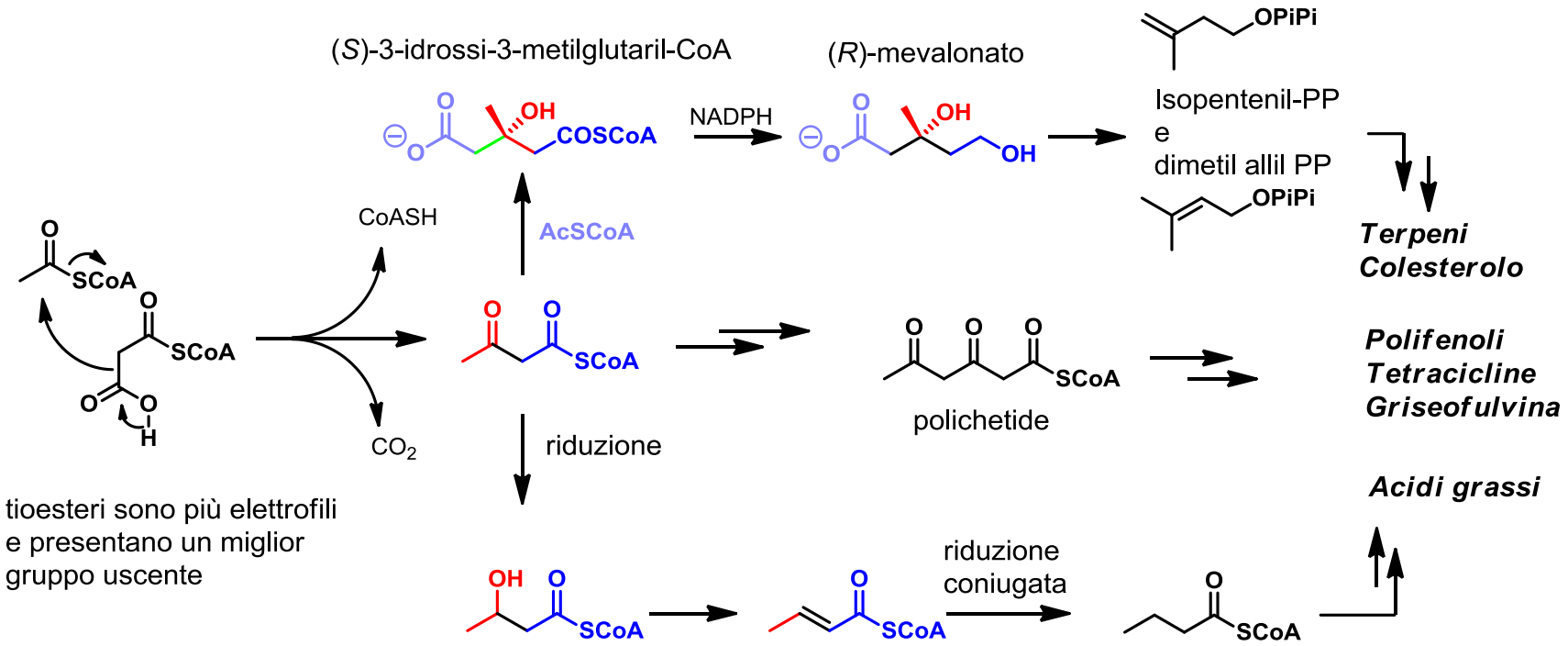


Claisen incrociate intramolecolari





Claisen a pH fisiologico e a 37°C



tappe iniziali nel processo di reticolazione del collagene nei tendini