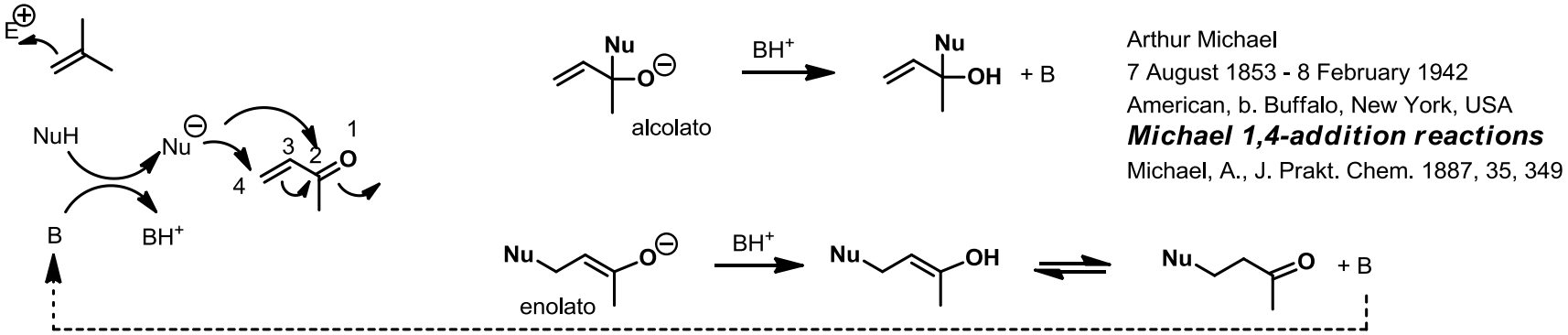
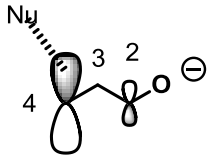
La coniugazione con gruppi elettronattrattori scarica gli alcheni e li rende elettrofili al Cβ

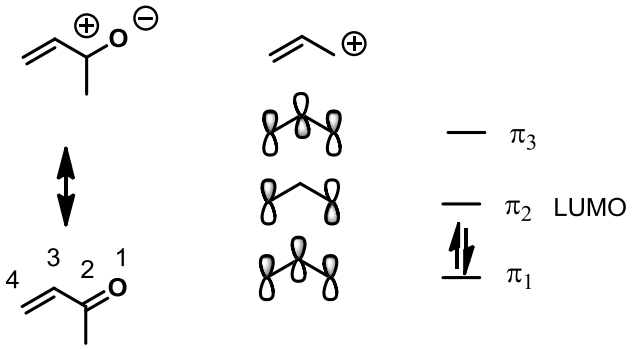


Arthur Michael
7 August 1853 - 8 February 1942
American, b. Buffalo, New York, USA
Michael 1,4-addition reactions
Michael, A., J. Prakt. Chem. 1887, 35, 349

Un accettore di Michael ha carattere carbocationico per la presenza del carbonile fortemente polarizzato C^+-O^-
Il segmento C2, C3, C4 assomiglia ad un allil catione.
Pertanto il LUMO di un accettore di Michael è isomorfo con il LUMO dell'allil catione

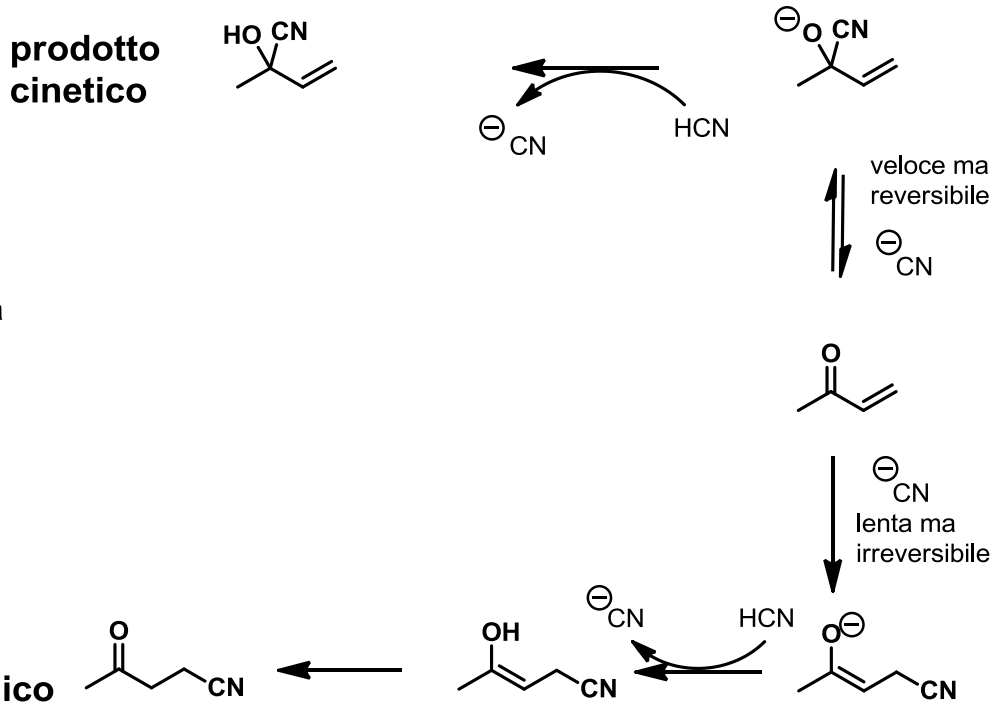


In π_2 (LUMO) il coefficiente dell'orbitale p al C4 è il maggiore.
HOMO del nucleofilo interagisce con efficacia legante al C4



Al C2 è più intensa la parzial positività,
interazioni Coulombiane dirigono l'attacco di nucleofili forti e carichi al C2

Addizione Michael: regioselettività



La Michael equivale alla rottura di un debole legame π e alla formazione di un robusto legame σ.

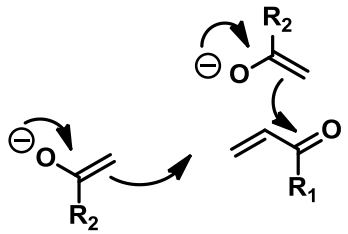
Temperatura: bassa T **controllo cinetico** alta T **controllo termodinamico**

natura alchene accettore: aldeidi α,β-insature addizionano 1,2 ma, ammidi, nitrili o esteri α,β-insaturi addizionano 1,4

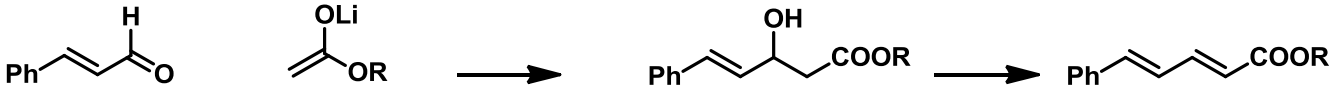
Addizione Michael: regioselettività

natura del nucleofilo: enolati stabili (soft)
R_2 = CH_2CO_2R β-chetoesteri o malonati
addizione coniugata 1,4

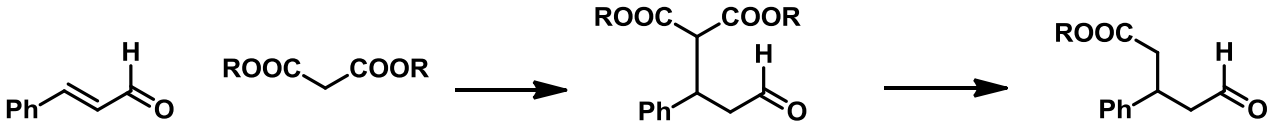
enolati non stabilizzati
R_2 = alchile
addizione 1,2 (reazione aldolica)



per **nucleofili organometallici** vale:
organocuprati (**reattivi Gilman**) addizione coniugata
organo-litio addizione 1,2.



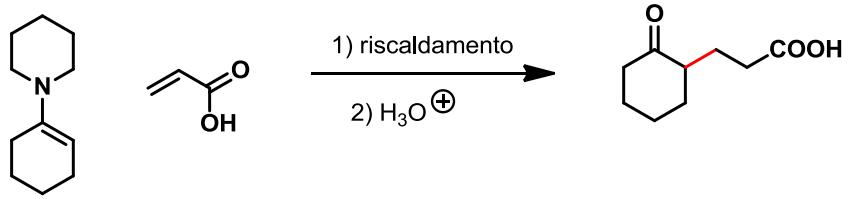
addizione 1,2



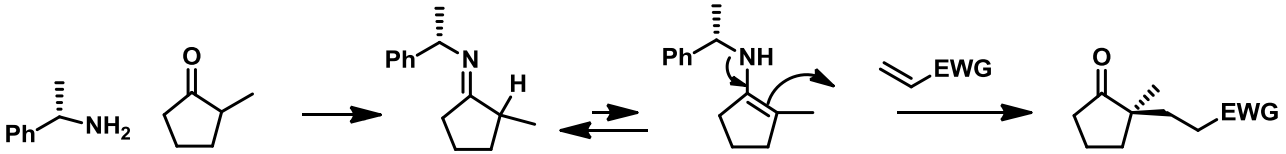
addizione 1,4

esempi di addizioni coniugate

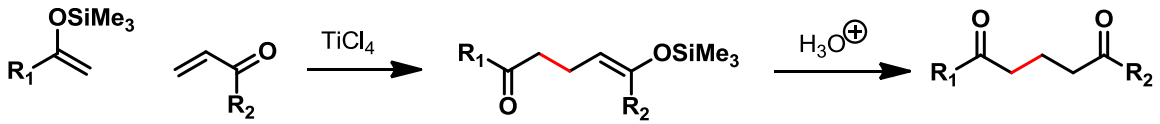
Enammine nucleofili neutri soft



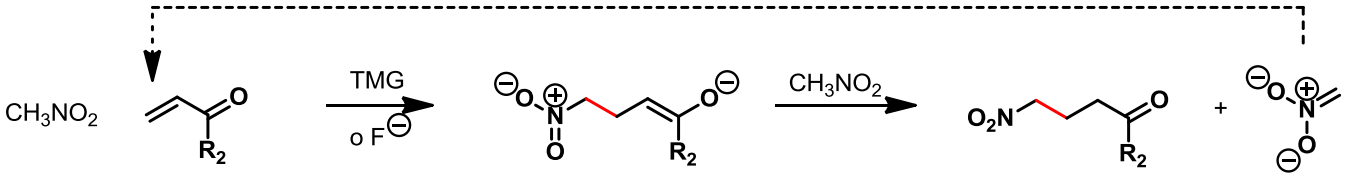
ma anche Immine



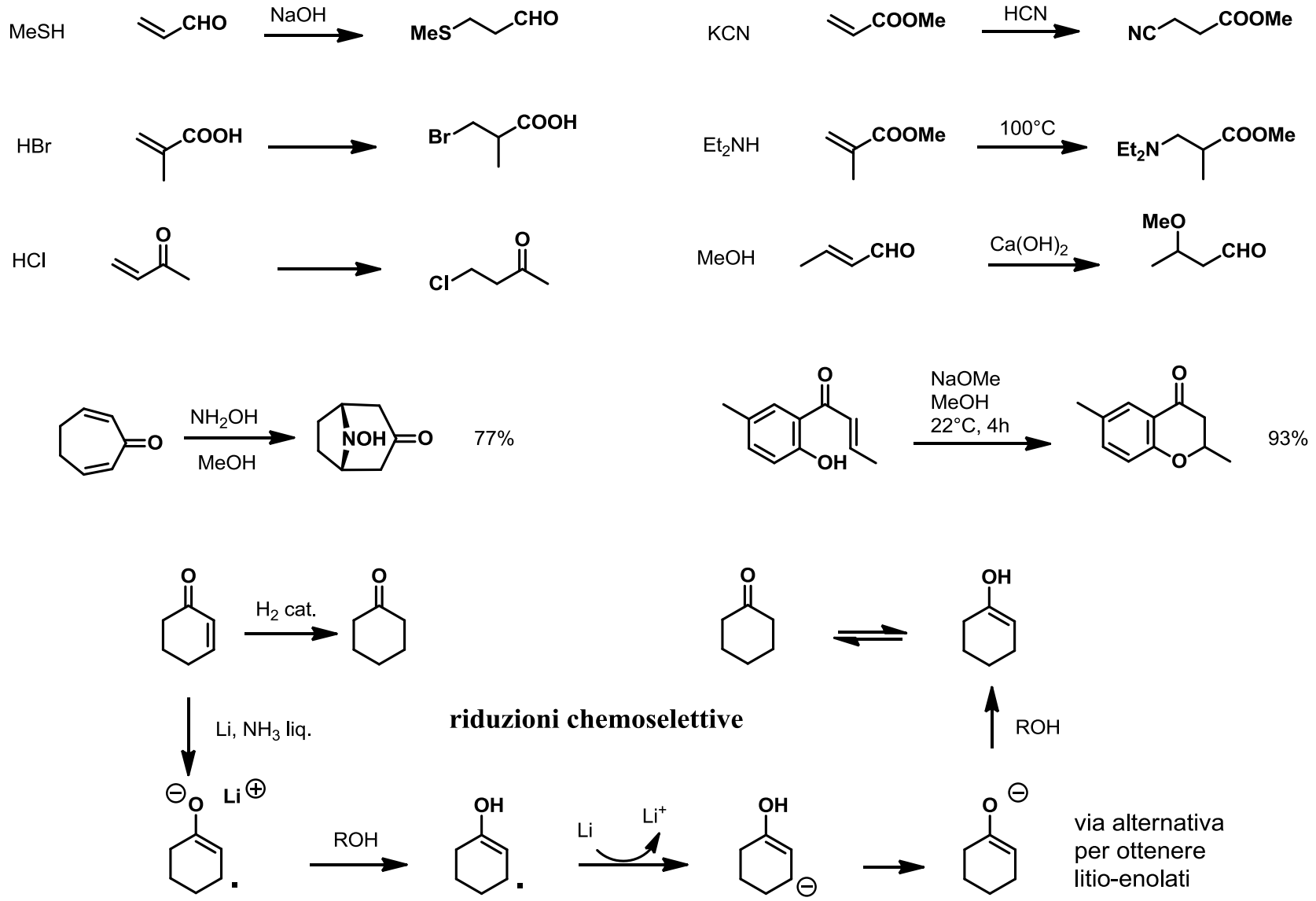
Silil enol eteri nucleofili neutri soft



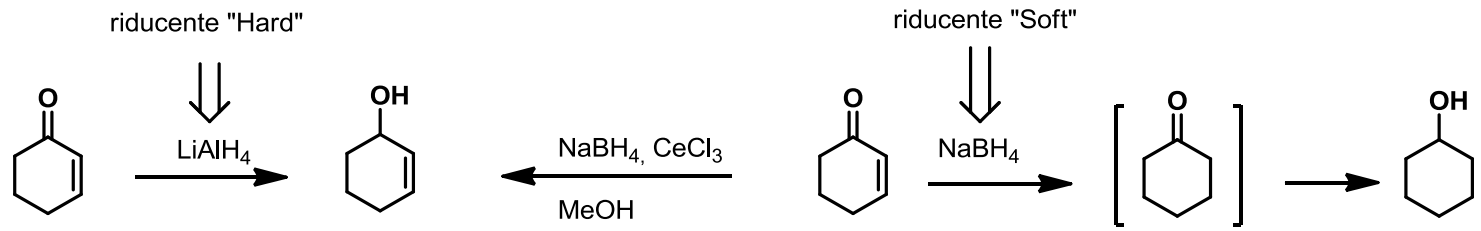
Nitroalcani



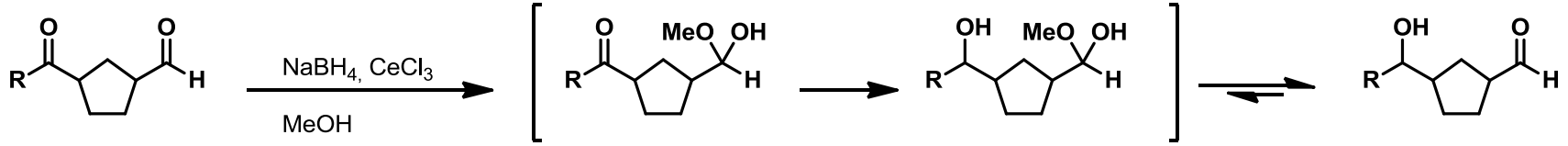
esempi di addizioni coniugate



riduzioni chemoselettive



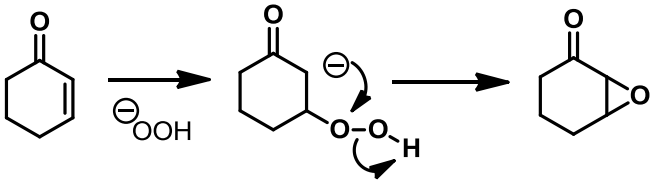
$NaBH_4 + CeCl_3 + MeOH = H_2 + NaB(OMe)_3H$ riducente "Hard" di **LUCHE**



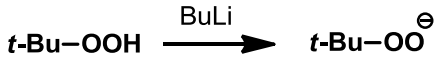
particolari addizioni coniugate

come epossidare olefine "scariche"

Weitz-Scheffer
epoxidation



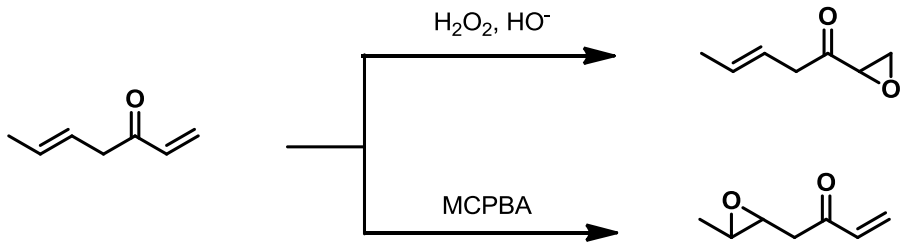
pKa H_2O_2 = 11.65 tuttavia
l'anione idroperossido è un
nucleofilo più forte dell'anione idrossido



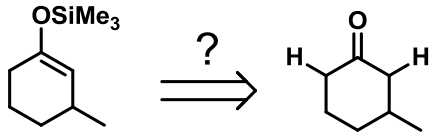
alternativamente si usa l'anione del ter-butilidroperossido
in solvente organico (THF)

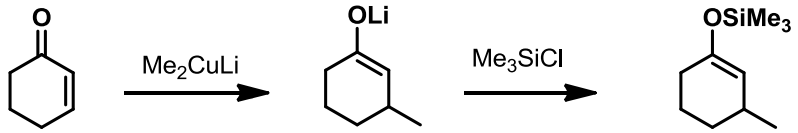
particolari addizioni coniugate

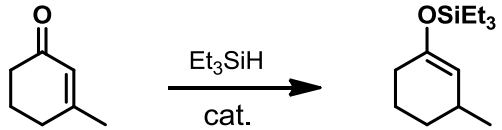
epossidazionii chemoselettive



formazione regioselettiva di sililenoleteri

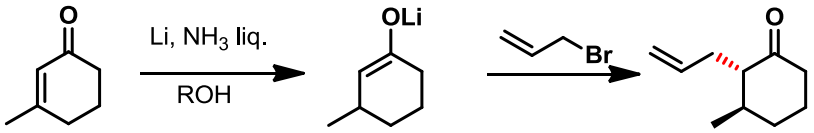




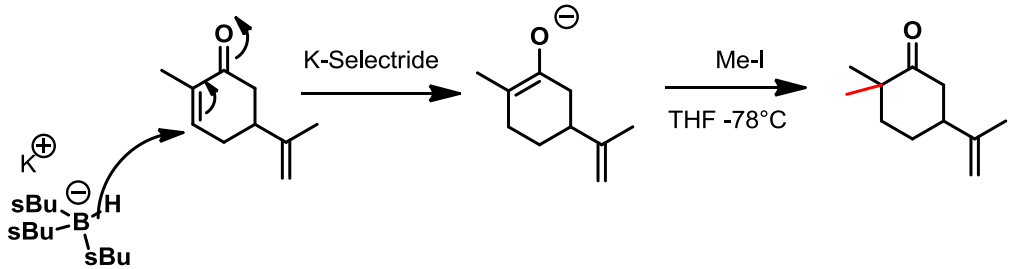


cat. = $(PPh_3)_3RhCl$ Wilkinson's catalyst
tris(triphenylphosphine)rhodium(I) chloride

Reazioni "Tandem" Michael - alchilazione

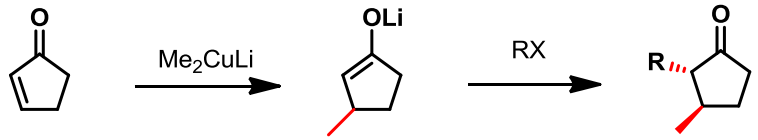


allilazione regio- e stereoselettiva via riduzione di enoni



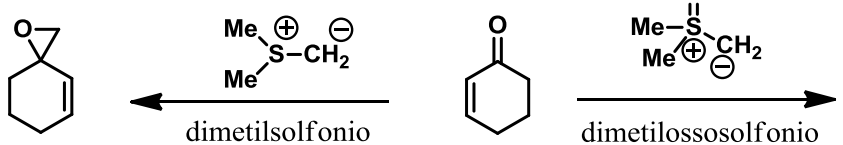
K-Selctride

metilazione regioselettiva via addizione coniugata di idruro

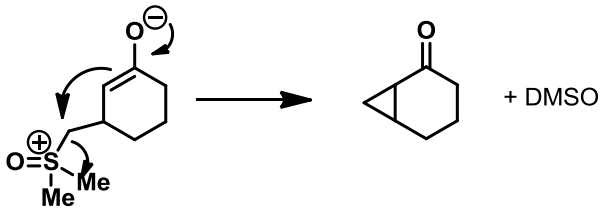


α,β alchilazione regio- e streoselettiva via addizione coniugata di reattivi di Gilman

Corey-Chaykovski epoxidation



Corey-Chaykovski cyclopropanation

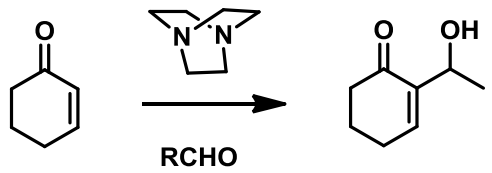


Reazioni "Tandem" Michael - aldolica
BAYLIS-HILLMAN

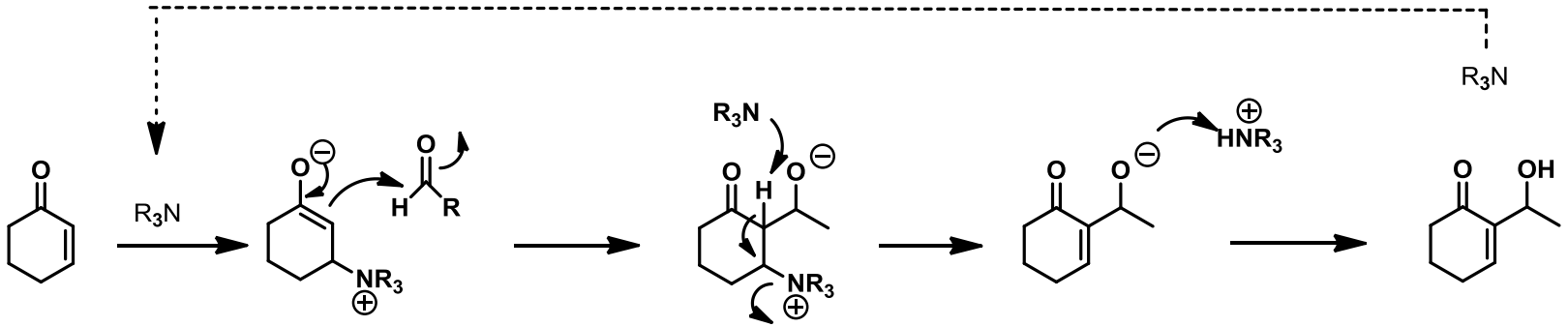
A.B. Baylis
German, b. ?

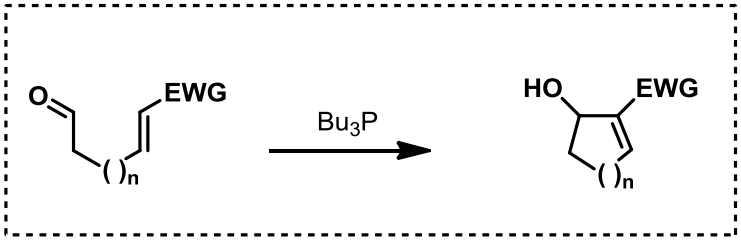
Baylis-Hillman reaction

Baylis, A.B.; Hillman, M.E.D.,
Celanese Corp., German patent 2155113, 1972
(Chem. Abs. 1972, 77, 34174q)

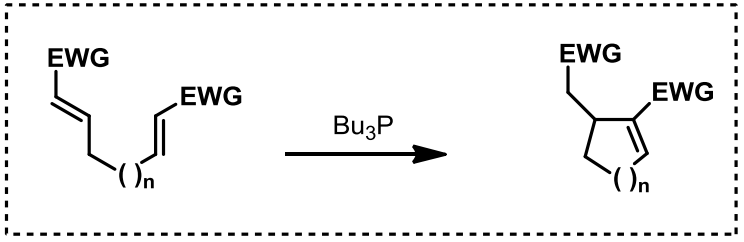


M.E.D. Hillman
German, b. ?





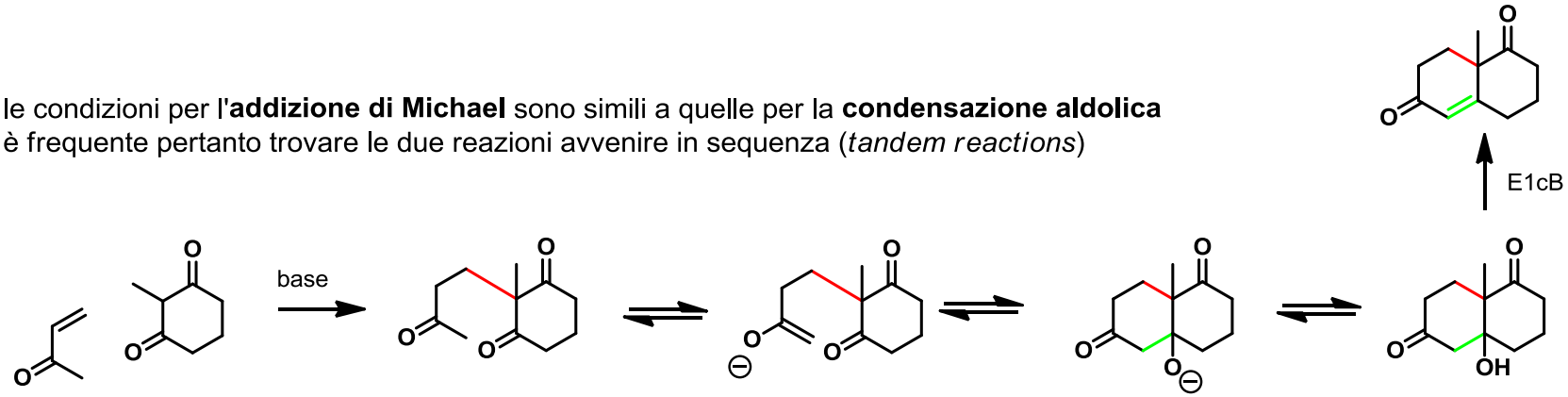
"Tandem" Michael - aldolica



"Tandem" Michael - Michael

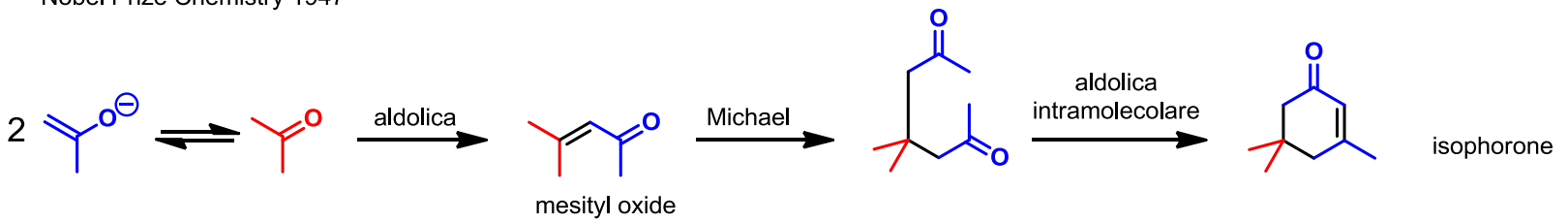
Reazioni "Tandem" Michael - aldolica intramolecolare

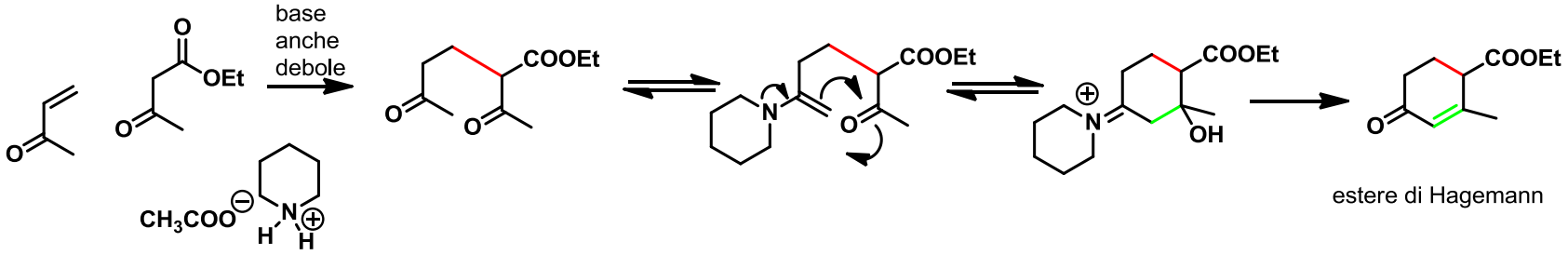
le condizioni per l'**addizione di Michael** sono simili a quelle per la **condensazione aldolica**
è frequente pertanto trovare le due reazioni avvenire in sequenza (*tandem reactions*)



Sir Robert Robinson
13 September 1886 - 8 February 1975
British, b. Bufford, near Chesterfield, Derbyshire, England
Nobel Prize Chemistry 1947

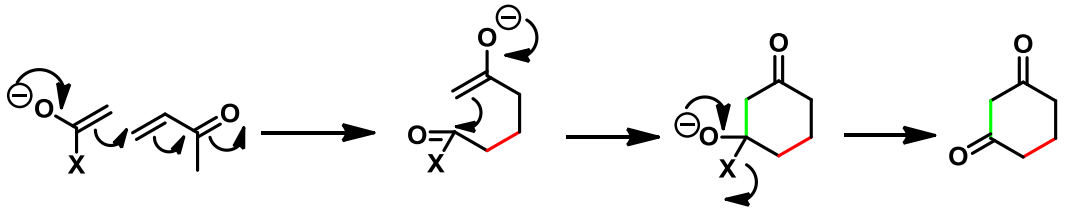
Robinson annulation
Rapson, W.S.; Robinson, R., J. Chem. Soc. 1935, 1285

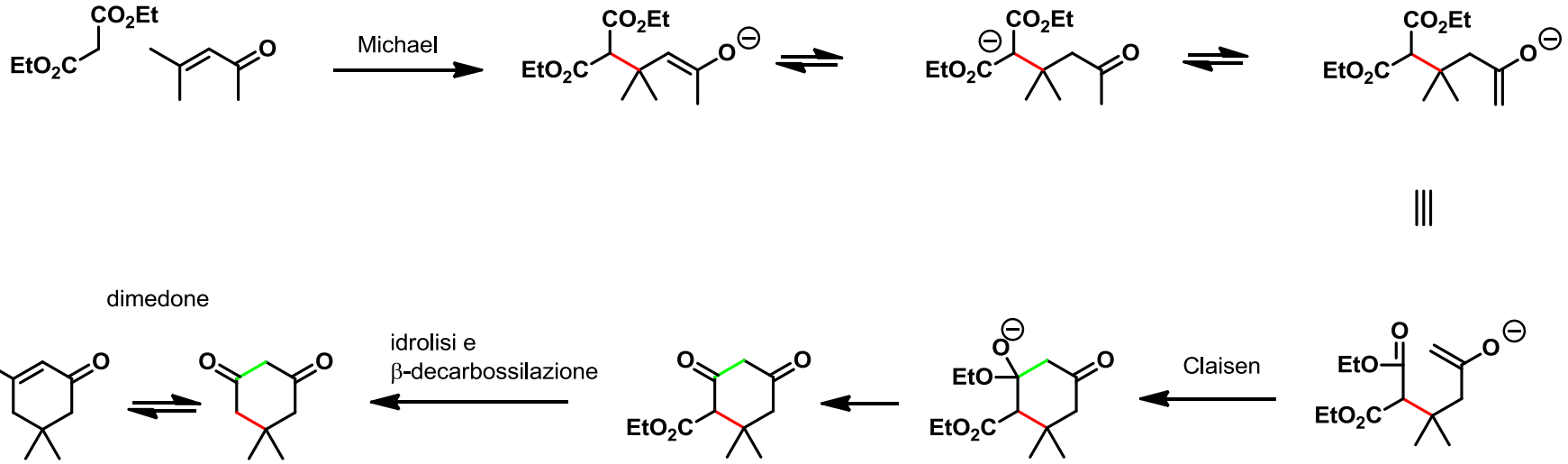




Reazioni "Tandem" Michael - Claisen intramolecolare

le condizioni per l'**addizione di Michael**
sono simili a quelle per la **Claisen**
è frequente pertanto trovare le due reazioni
avvenire in sequenza (tandem reactions)





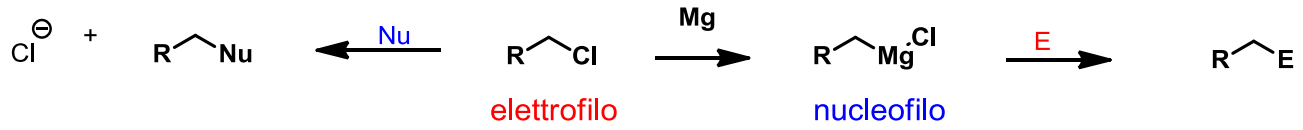
"UMPOLUNG"

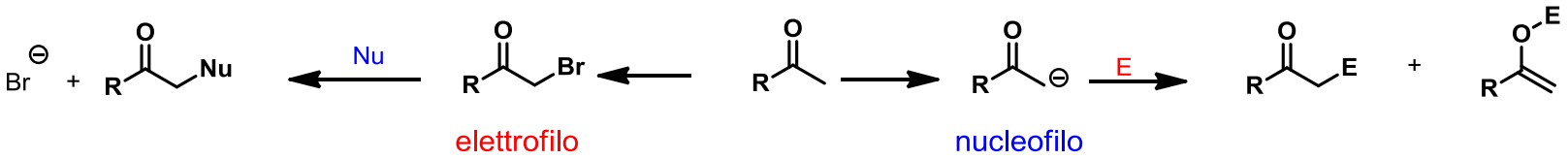
da Wikipedia

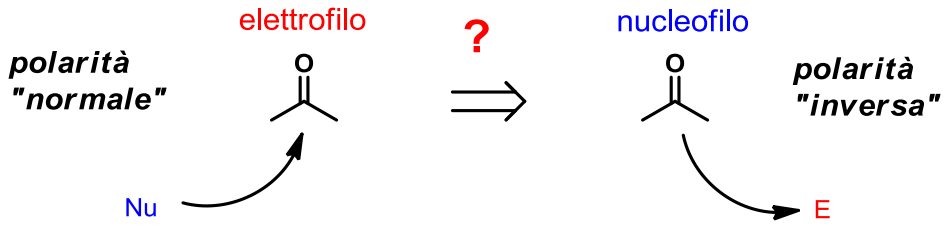
Umpolung or polarity inversion in organic chemistry is the chemical modification of a functional group with the aim of the reversal of polarity of that group.

This modification allows secondary reactions of this functional group that would otherwise not be possible.

*The concept was introduced by **D. Seebach** (hence the German word umpolung for reversed polarity) and **E.J. Corey**.*

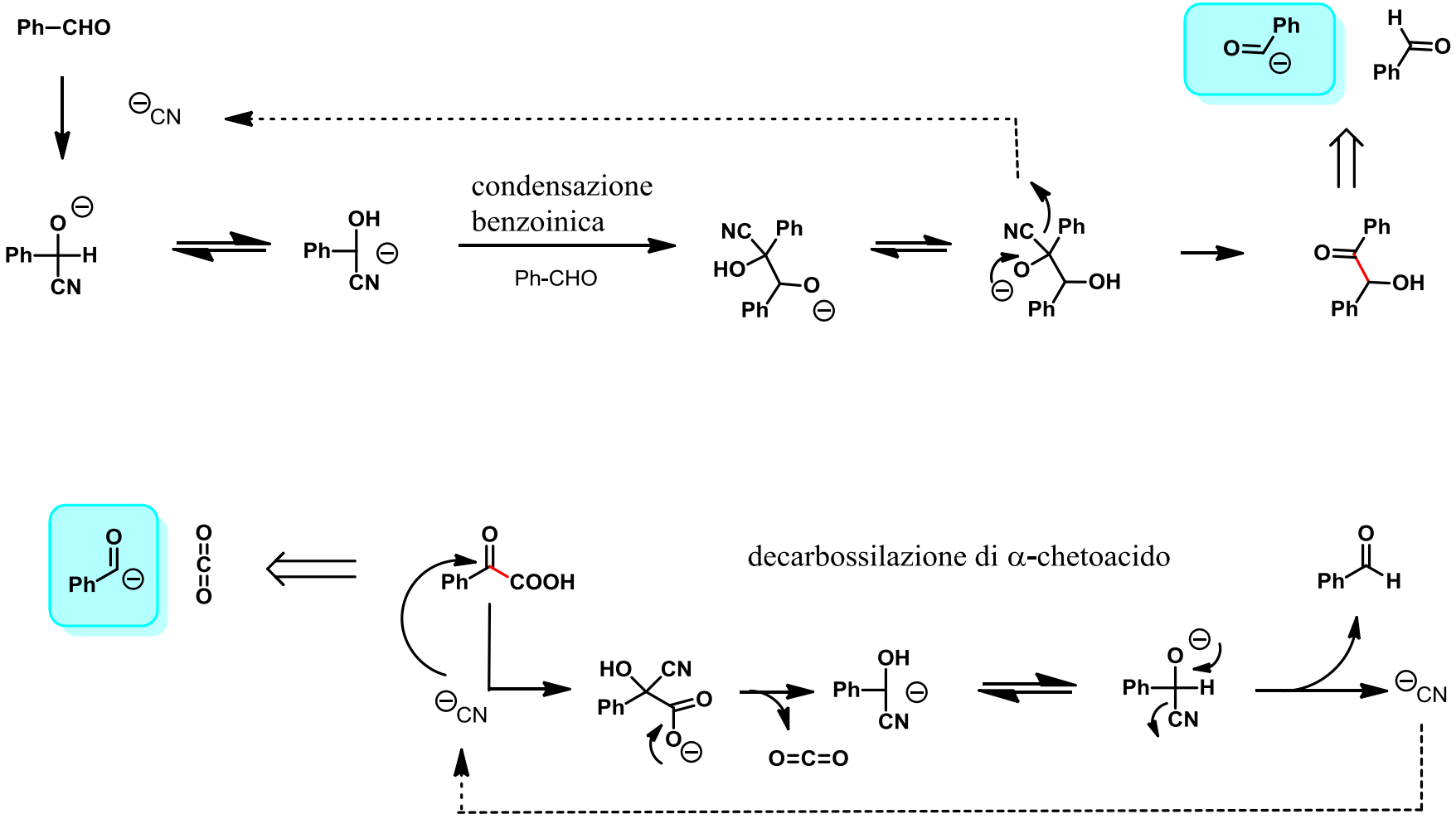


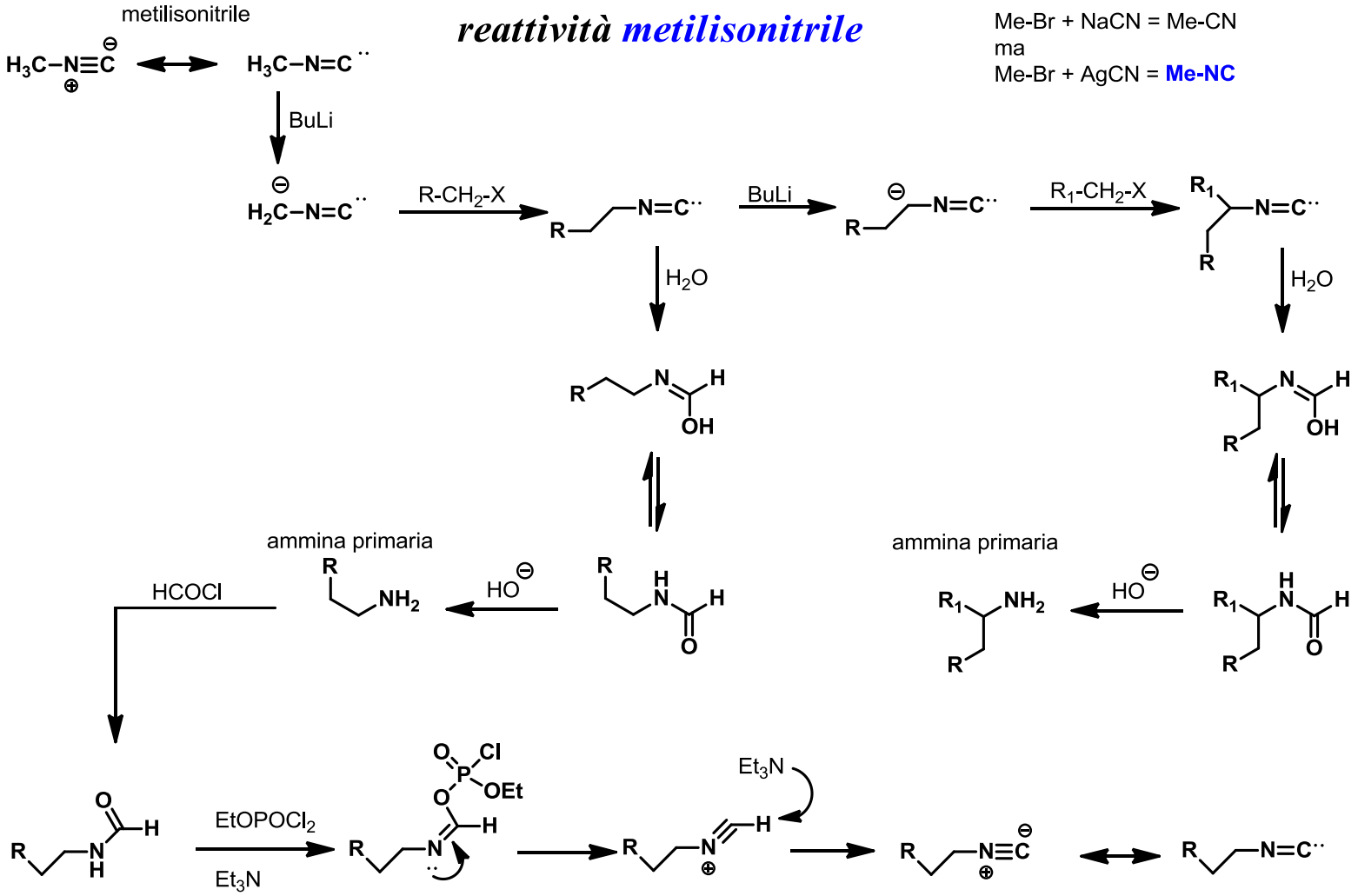


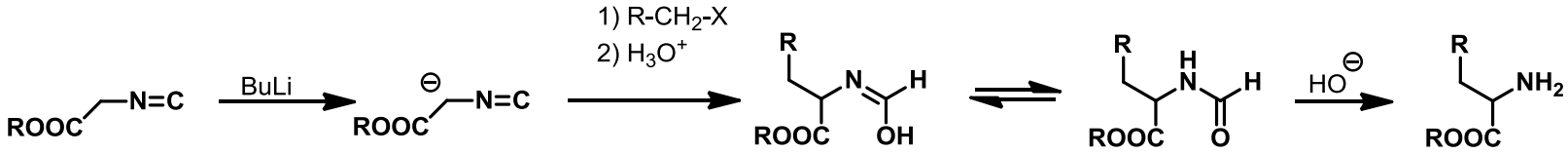


umpolung di carbonile

CN^- catalizzatore per invertire la polarità di carbonili

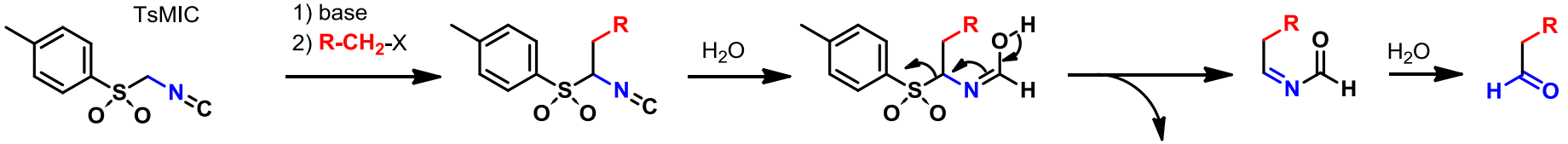



metilisonitrile
reattività metilisonitrile
Me-Br + NaCN = Me-CN
ma
Me-Br + AgCN = Me-NC
BuLi
R-CH2-X
H2O
BuLi
R1-CH2-X
H2O
ammina primaria
HO
HCOCl
ammina primaria
HO
EtOPOCl2
Et3N
Et3N

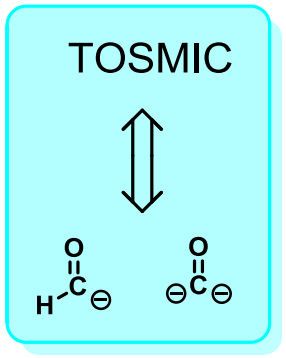


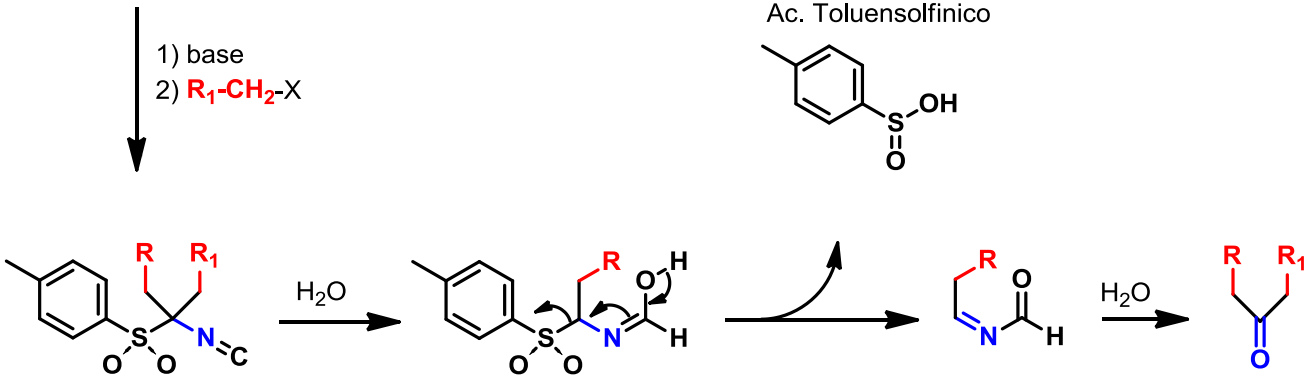
α-amminoacido

Toluensolfonilmetilisonitrile



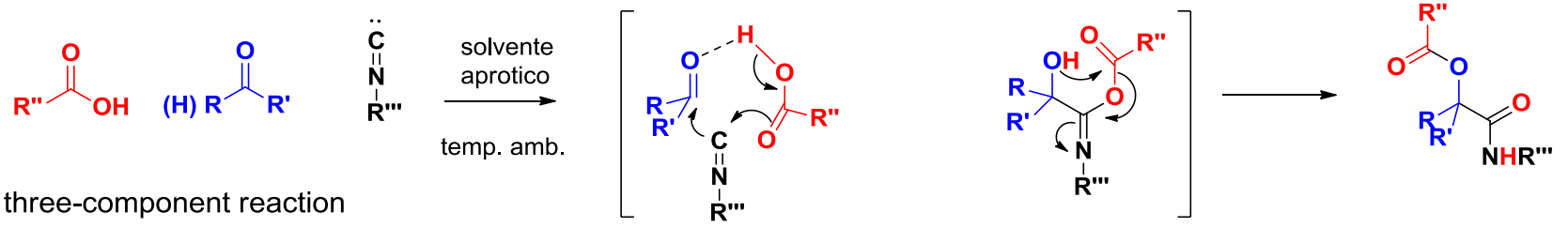
umpolung di carbonile





Ac. Toluensolfinico

il C carbenico di un isonitrile ha contemporaneamente carattere nucleofilo ed elettrofilo



three-component reaction

Passerini reaction

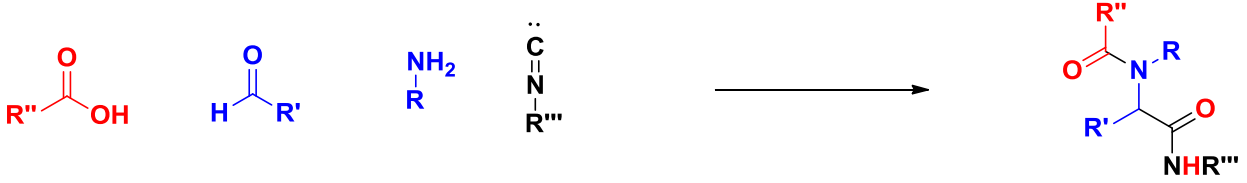
Mario Torquato Luigi Passerini
29 August 1891 - 1962
Italian, b. Scandicci, Italy
Passerini, M. Gazz. Chim. Ital. 1921, 51, 126; 181

Ivar Karl Ugi
5 September 1930 – 29 September 2005
German, b. Kuressaare, Estland, Germany

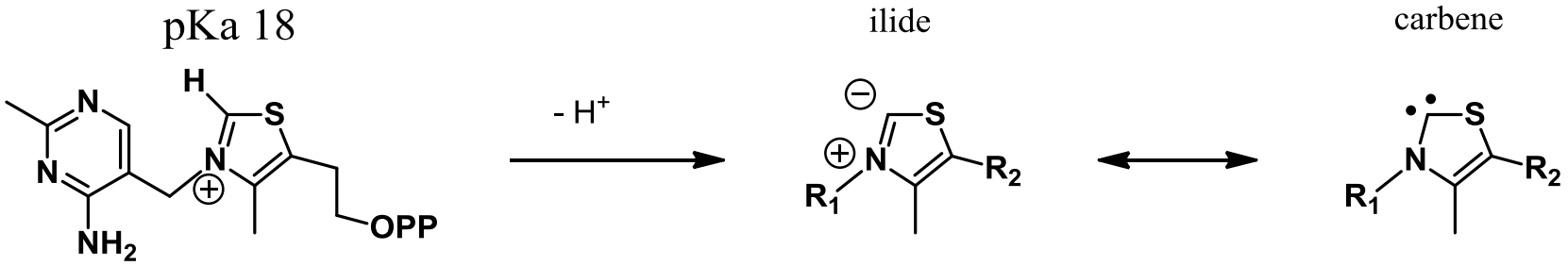
Ugi reaction (pronuncia ughi)

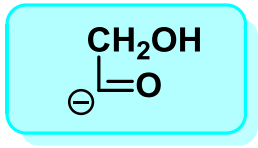
Ugi, I.; Meyr, R.; Fetzer, U.; Steinbrueckner, C. Angew. Chem. 1959, 71, 386
Urban, R.; Ugi, I., Angew. Chem. Int. Engl. Ed. 1975, 14, 61

four-component reaction

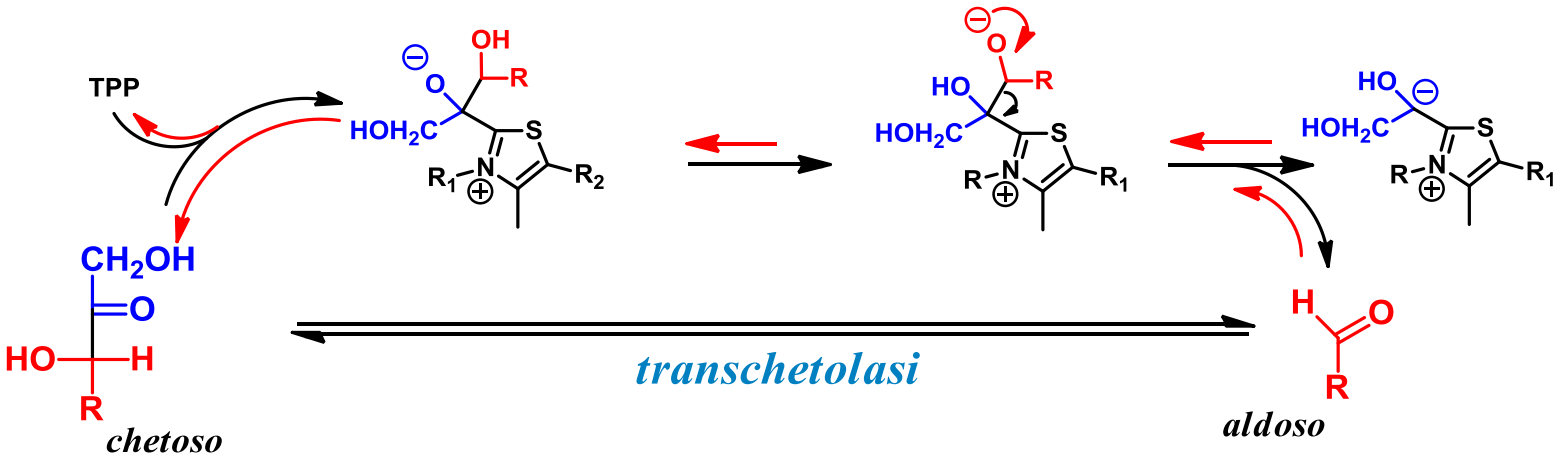


TPP: catalizzatore per invertire la polarità di carbonili

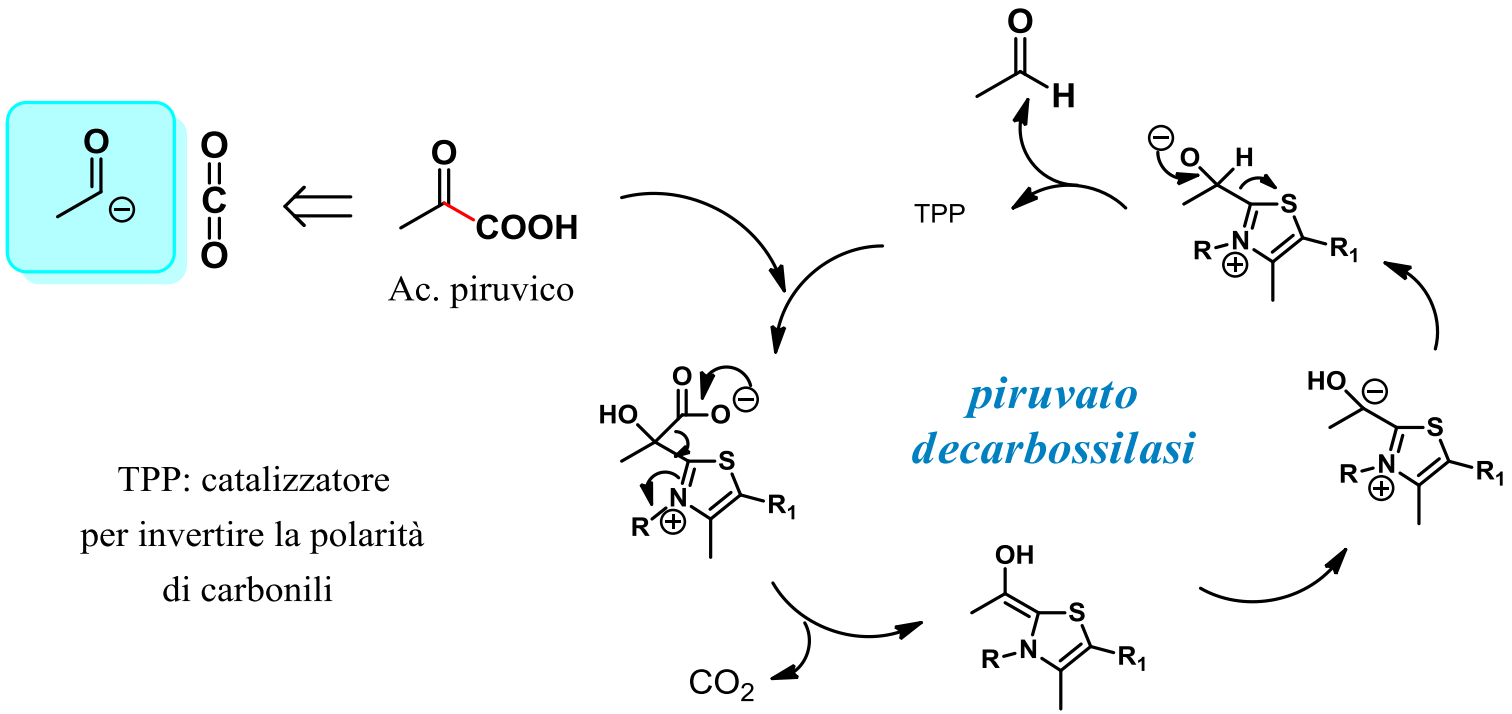




umpolung di carbonile

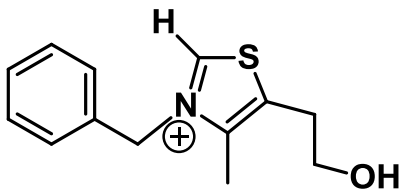


umpolung di carbonile



TPP: catalizzatore
per invertire la polarità
di carbonili

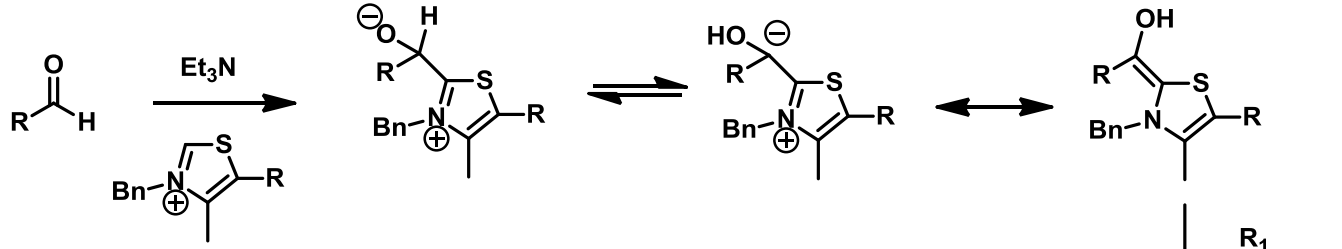
reattivo di **STETTER**
sale di tiazolio: catalizzatore per invertire la polarità di carbonili



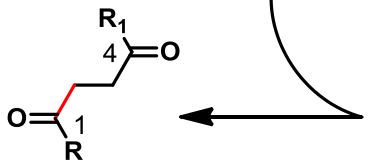
Hermann Stetter
16 May 1917 – 9 May 1993
German, b. Bonn, Germany
Stetter reaction
Stetter,H., Angew. Chem. Int. Engl. Ed. 1976, 15, 639

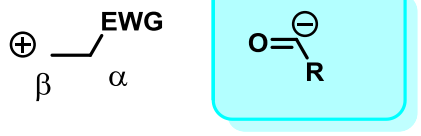
Breslow intermediate

reazione di Stetter



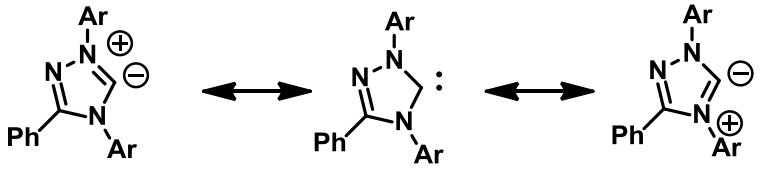
1,4-dicarbonile
vedi sintesi
eterocicli aromatici
pentaatomici

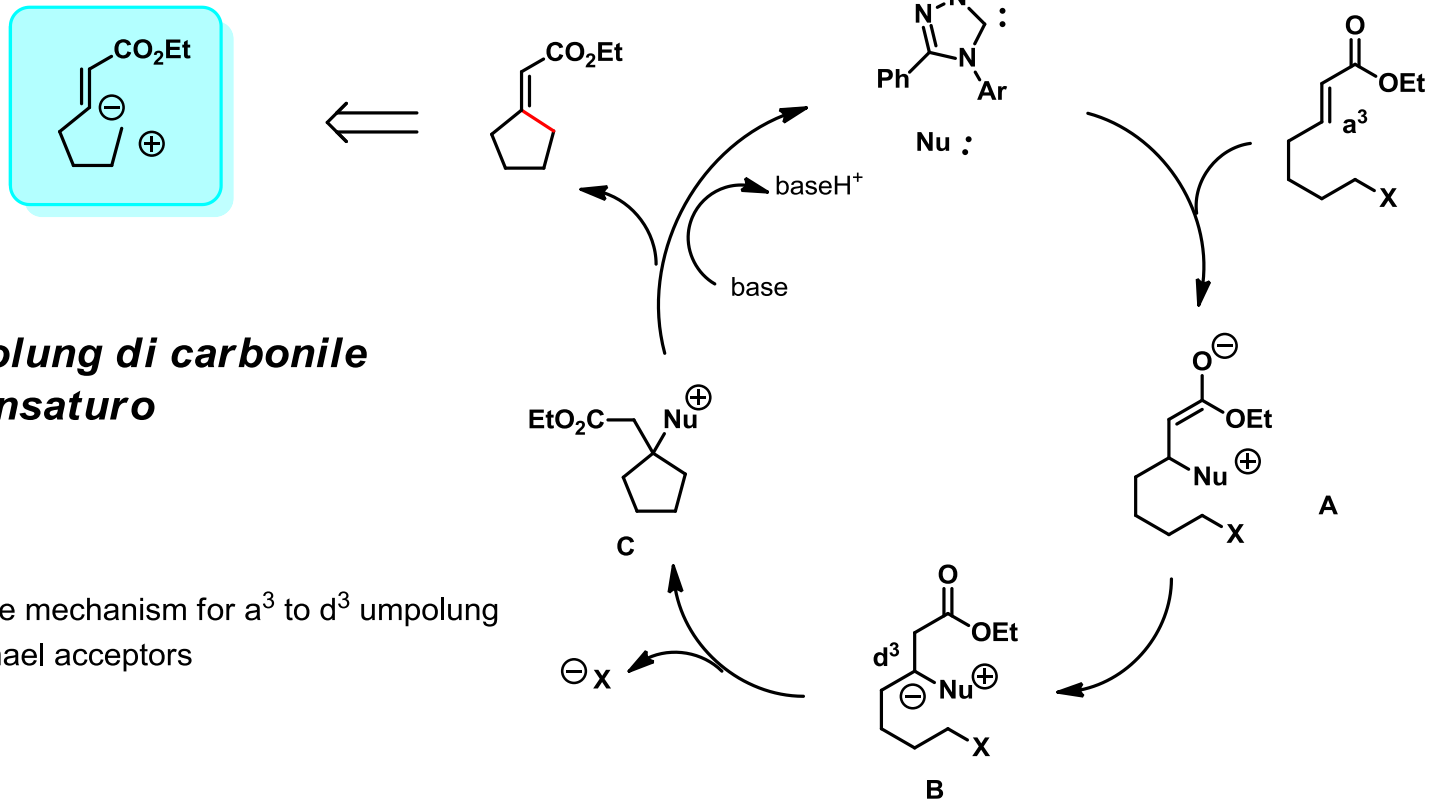




umpolung di carbonile

*N*itrogen *H*eterocyclic *C*arbene
NHC organo-catalizzatore
per invertire la polarità di enoni
***JACS* 2006**, *128*, 1472-1473





umpolung di carbonile
α,β-insaturo

possible mechanism for a^3 to d^3 umpolung of Michael acceptors