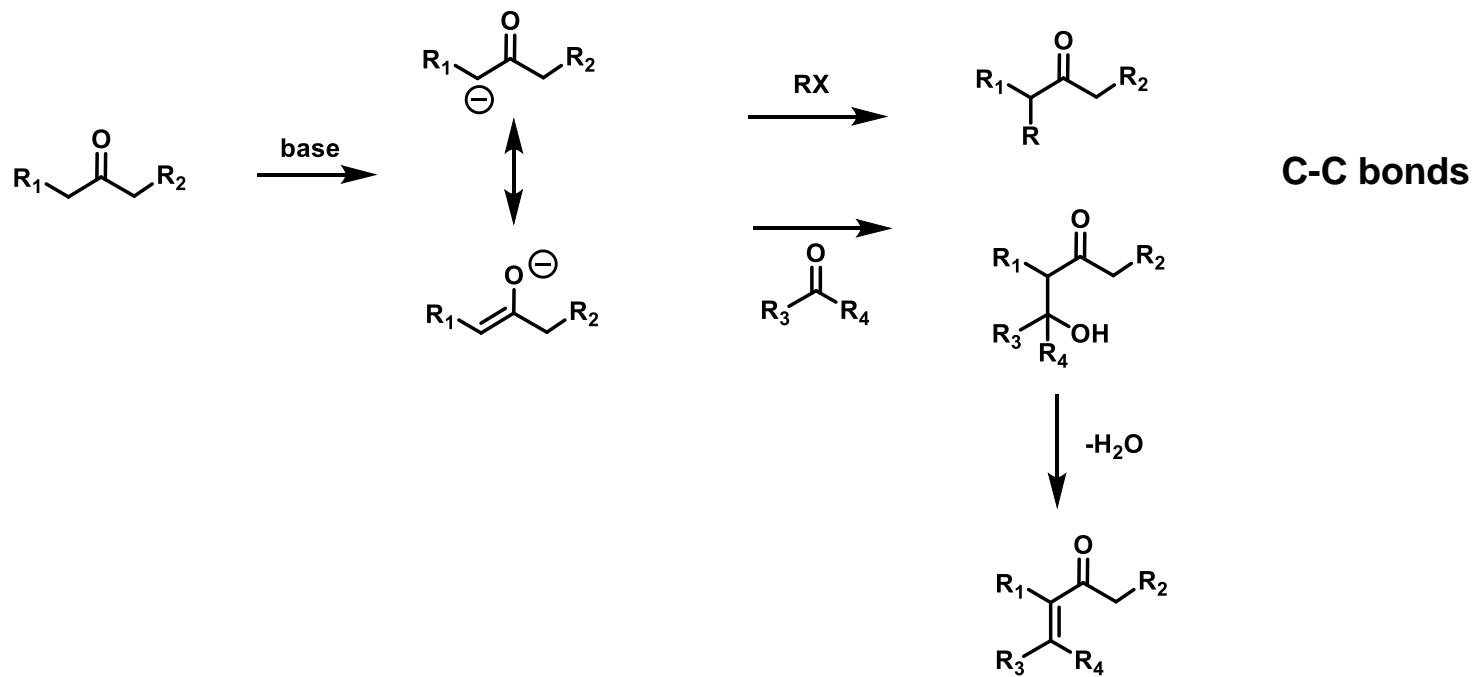
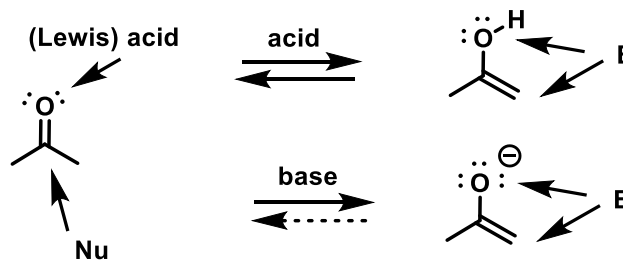


Organic synthesis

Kamil Paruch

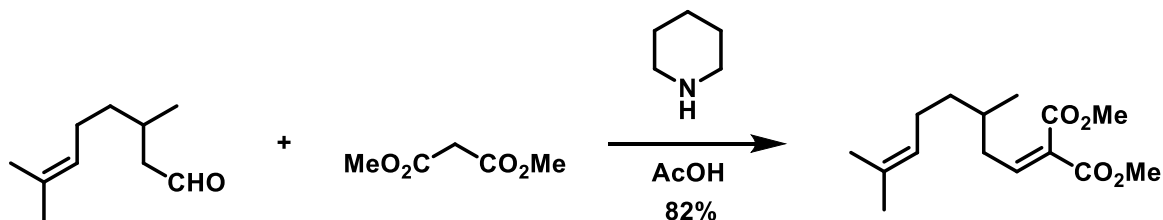
Masaryk University, Brno

Enols & enolates: formation, structure, reactivity

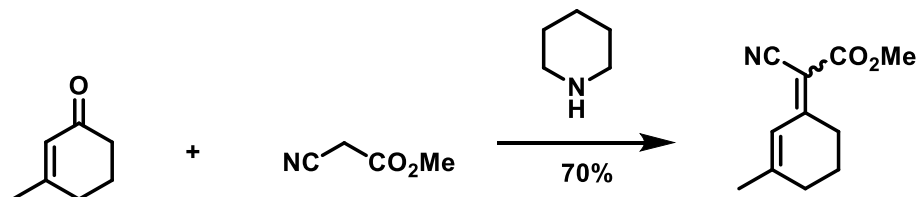


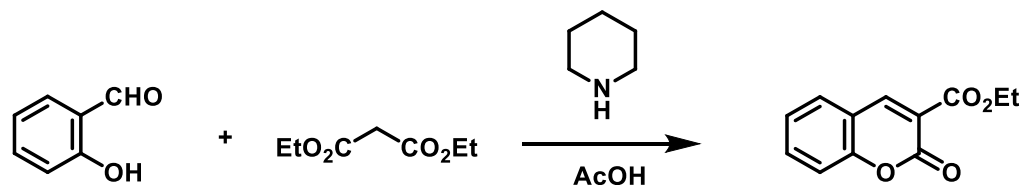
Knoevenagel condensations

- enolate attacks carbonyl C, subsequent elimination of H₂O



Tetrahedron Lett. **1986**, 27, 1767.

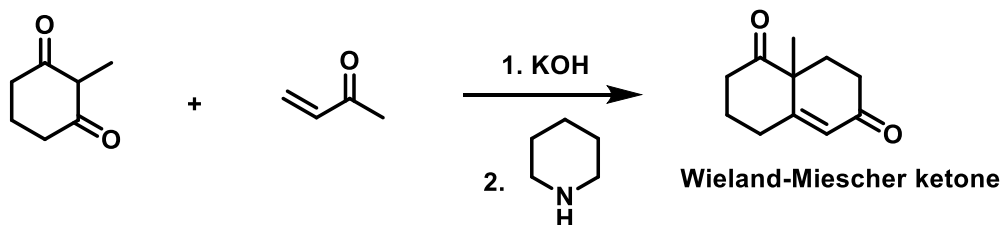




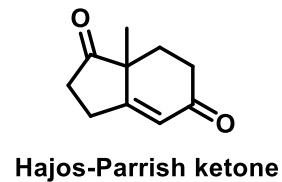
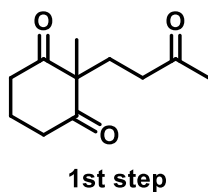
Org. Synth. Coll. Vol. 3, 1955, 165.

Robinson annulation

- Michael addition + aldol condensation

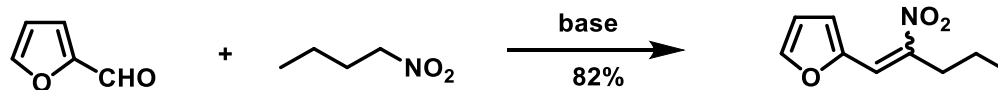
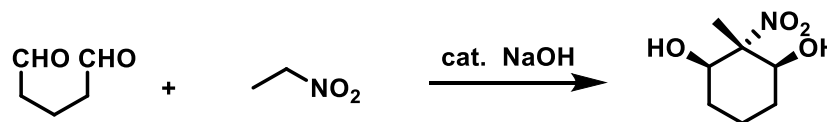


Helv. Chim. Acta 1950, 33, 2215.

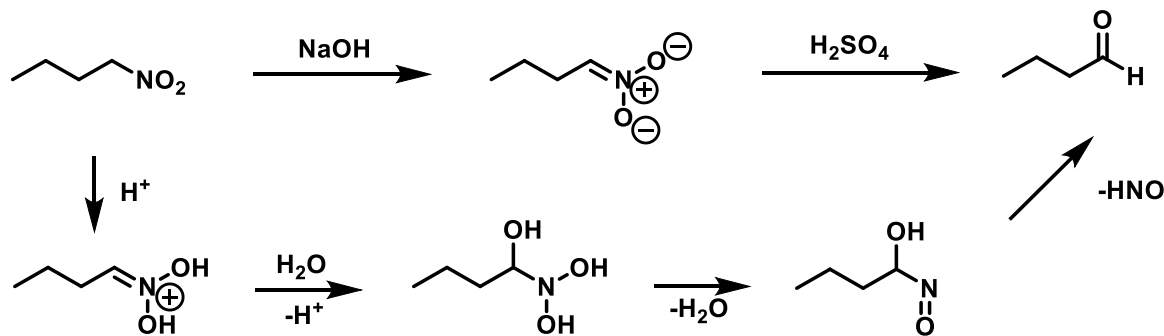


- both ketones can be prepared non-racemic by proline-catalyzed Robinson annulation

Henry reaction

*J. Org. Chem.* **1950**, 15, 8.*Helv. Chim. Acta* **1988**, 71, 1.

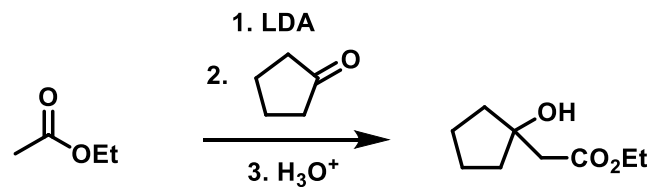
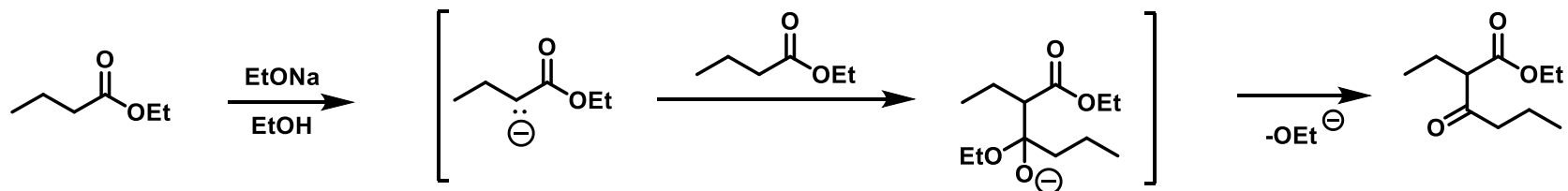
Nef reaction



modern version:

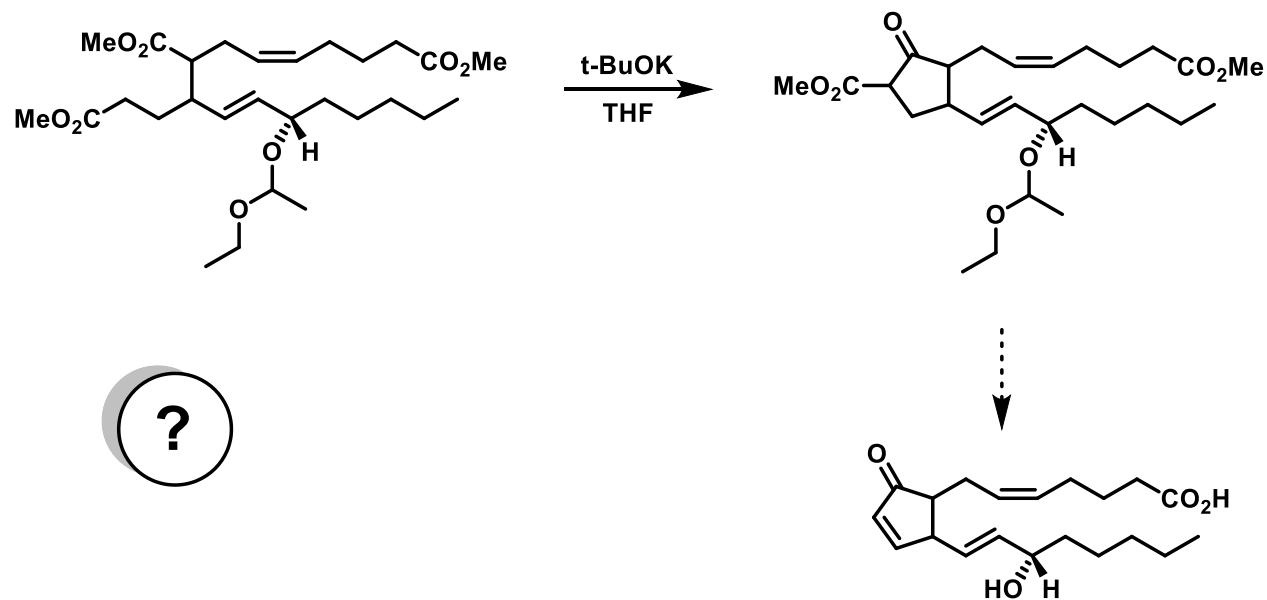
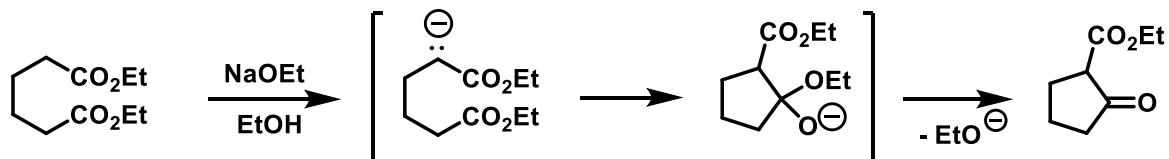
1. LDA 2. MoOPh
or TiCl₃
or 1. KOH 2. KMnO₄

Claisen condensation



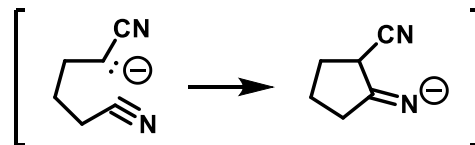
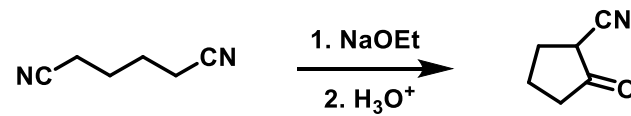
Dieckmann condensation

- intramolecular version of Claisen condensation

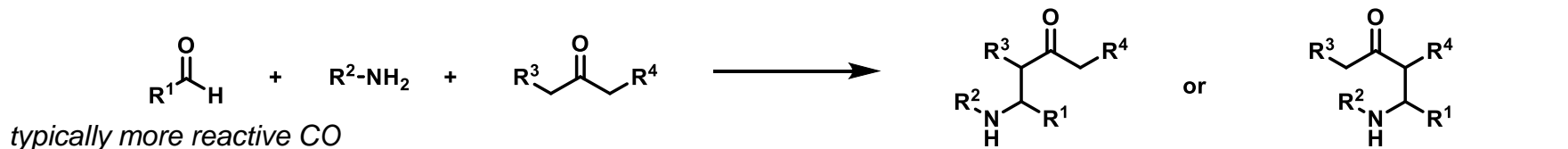


Thorpe reaction

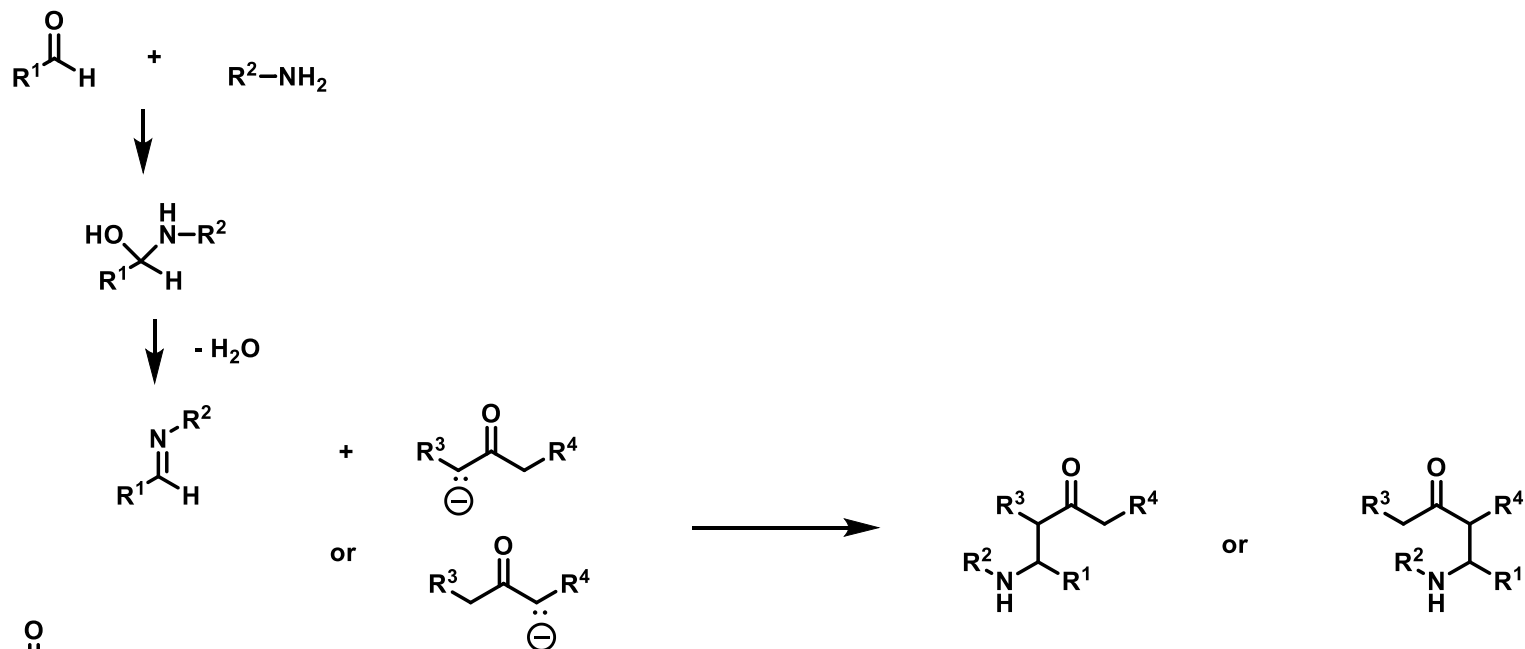
- „enolates“ of nitriles



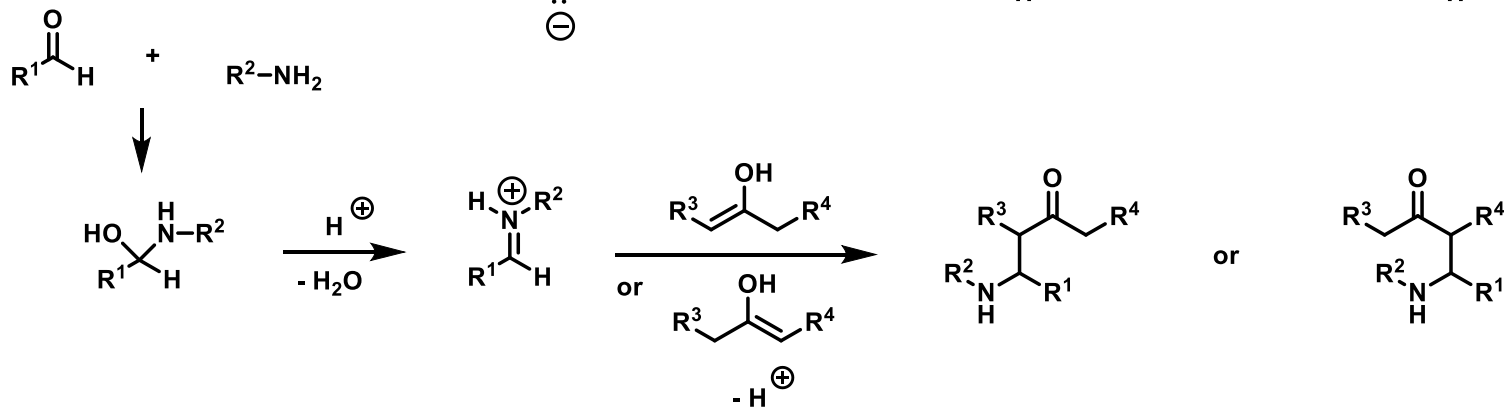
Mannich reaction • frequently used in assembly of cyclic N-containing systems

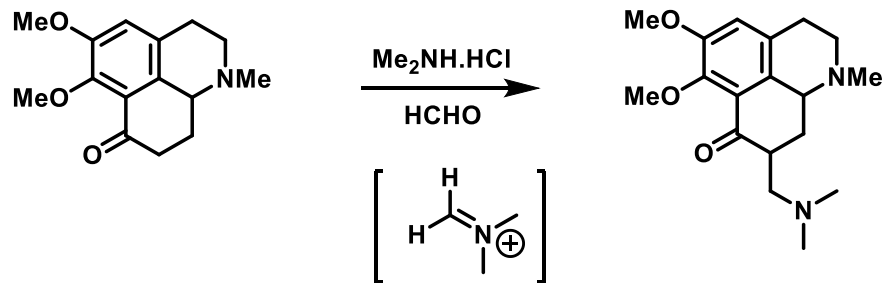


base-catalyzed



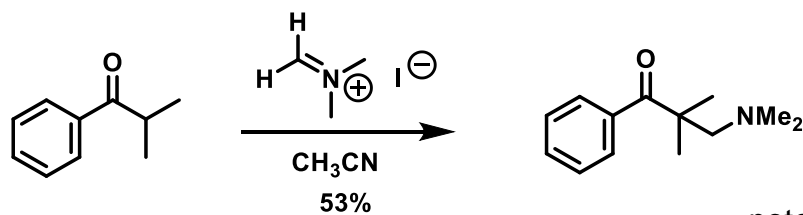
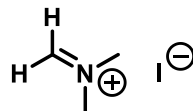
acid-catalyzed



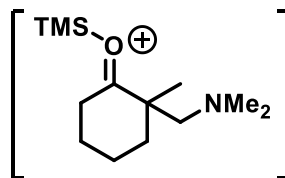
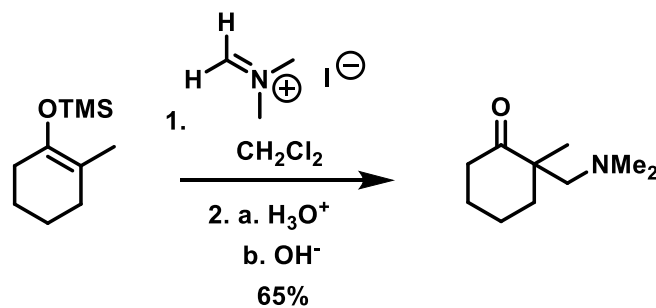


Chem. Pharm. Bull. **1991**, 39, 1349.

Eschenmoser's salt

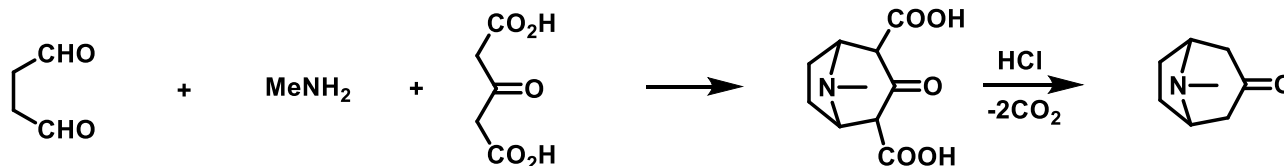


note: only 6% yield with $\text{HCHO} + \text{Me}_2\text{NH}$
(sterically hindered substrate)

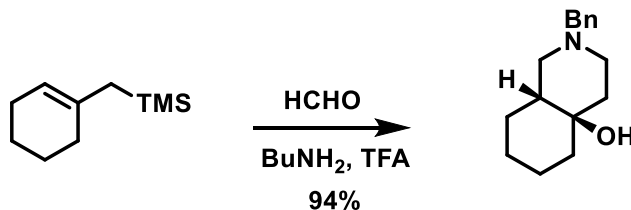


Mannich reaction is frequently used in assembly of cyclic N-containing systems

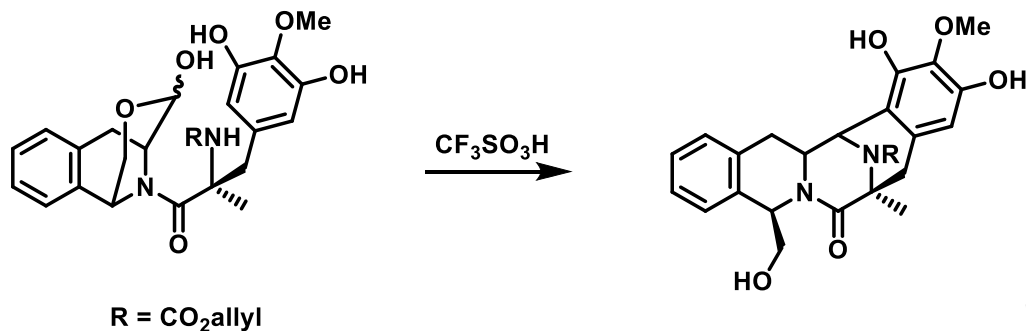
“*biomimetic approach*”



J. Chem. Soc. **1917**, 762.

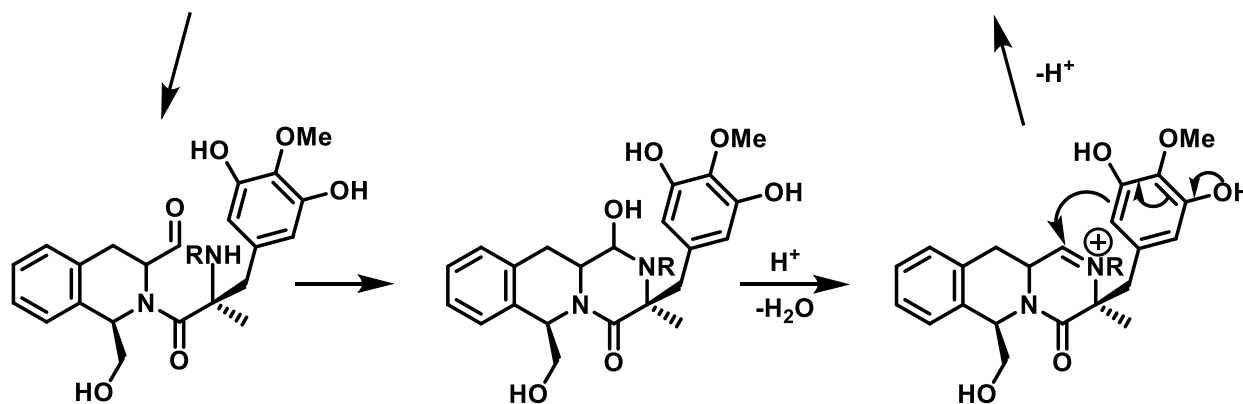


J. Am. Chem. Soc. **1986**, 108, 3512.



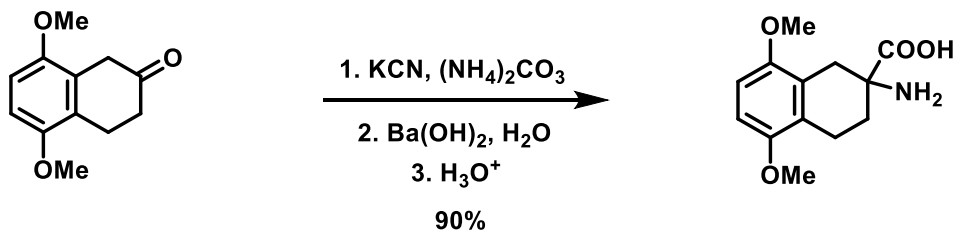
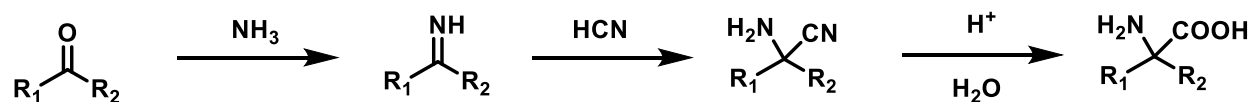
J. Am. Chem. Soc. **1996**, 118, 9202.

Org. Lett. **2000**, 2, 993.



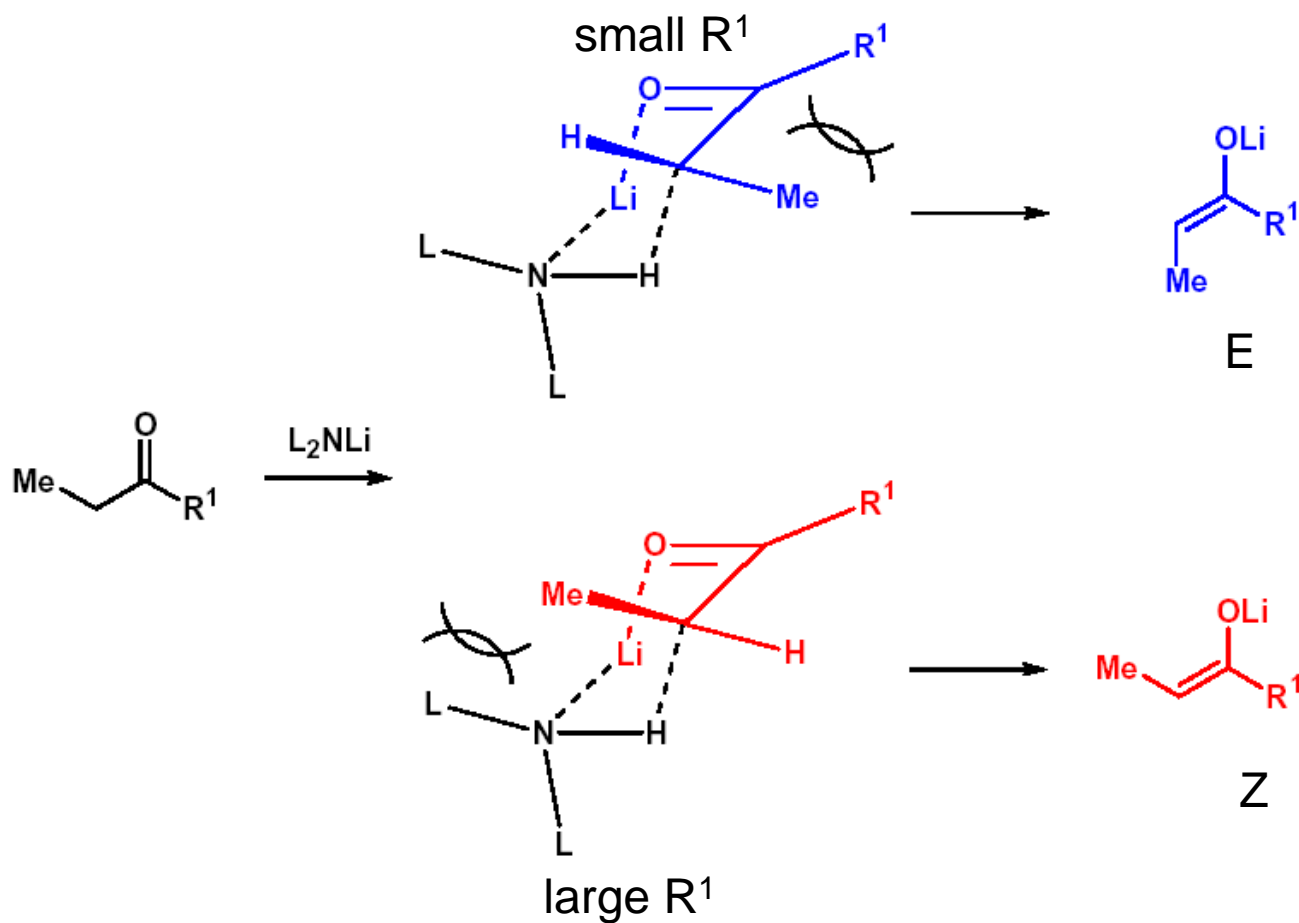
Strecker reaction

- synthesis of amino acids

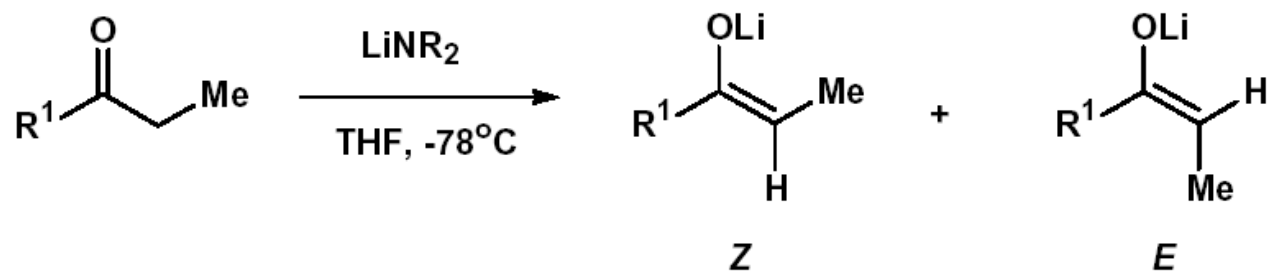


J. Org. Chem. **1987**, *52*, 4477.

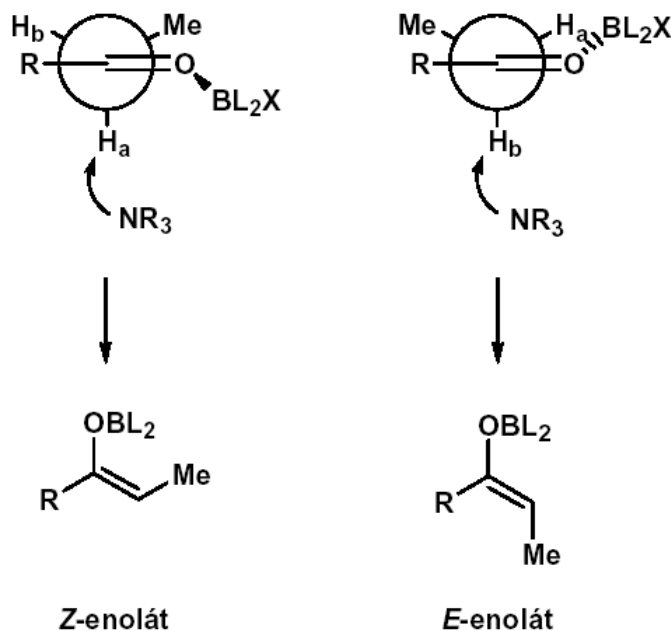
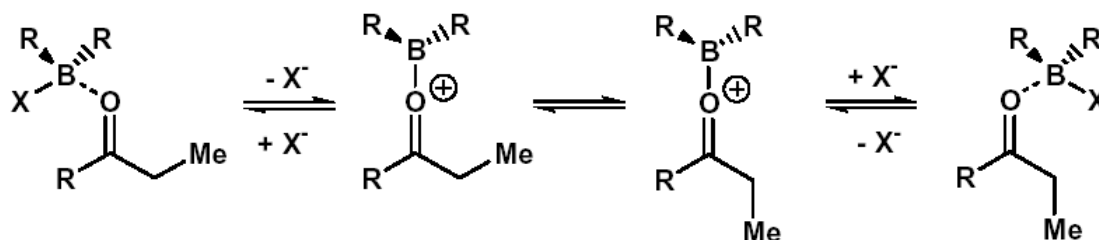
GEOMETRY OF ENOLATES - IRELAND MODEL



GEOMETRY OF ENOLATES - EFFECT OF BASE



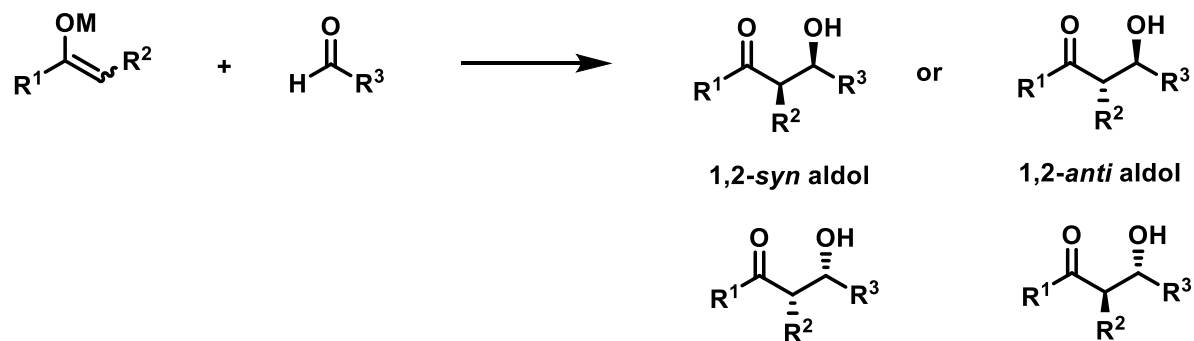
BÁZE	$R_1=Et$ (<i>Z</i> : <i>E</i>)	$R_1=cyklohexyl$ (<i>Z</i> : <i>E</i>)
$LiN(i-Pr)_2$	30 : 70	61 : 39
$LiN(SiMe_3)_2$	70 : 30	85 : 15
$LiN(SiEt_3)_2$	99 : 1	96 : 4
$LiN(SiMe_2Ph)_2$	100 : 0	100 : 0

SELECTIVE FORMATION OF *E* OR *Z* ENOL BORINATES

R_2BCl with large alkyls (e.g. cyclohexyl) + small base (Et_3N) \rightarrow *E* enolates

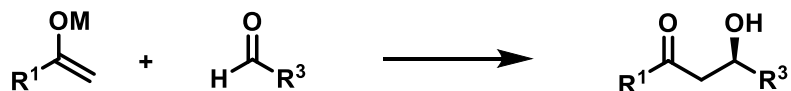
R_2BOTf with small alkyls (e.g. n-butyl) + large base (DIPEA) \rightarrow *Z* enolates

Aldol reaction: 2 new stereogenic centers can be created

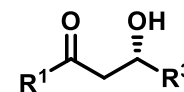


- stereochemistry of products depends on the configuration of the starting enolates
- stereochemistry can also depend on R³

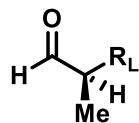
$R^2 = H$,
 R^1, R^3 achiral



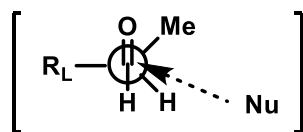
racemic mixture



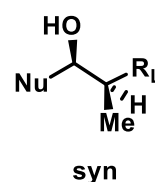
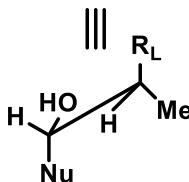
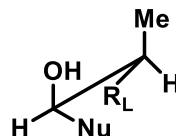
$R^2 = H$,
 R^1 achiral
 R^3 chiral



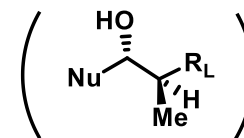
Felkin-Anh



Nu attacks C=O: 107° angle



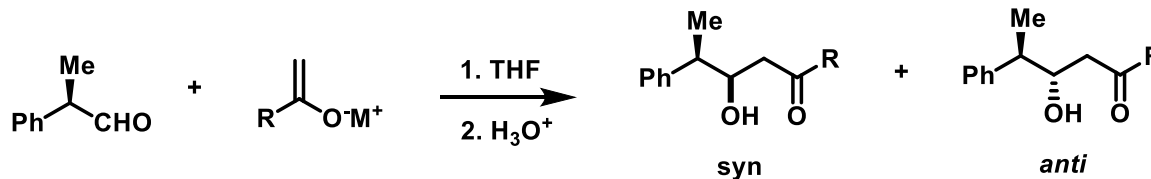
syn



anti

• stereoselective reactions with large Nu

mixture of diastereomers



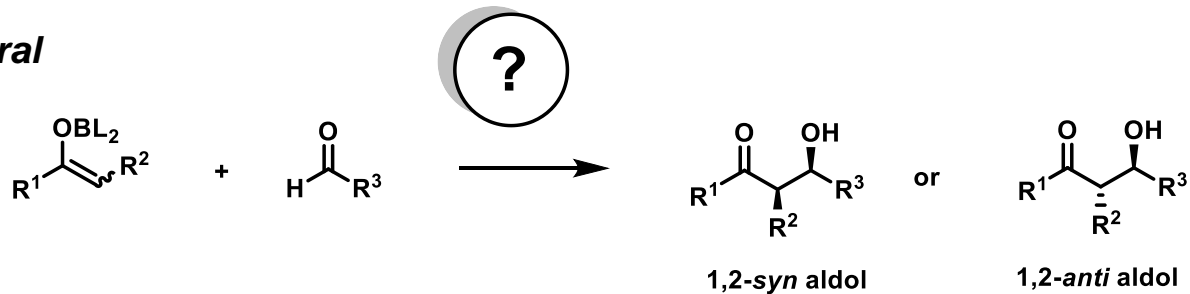
R: OMe 75 : 25

Me 76 : 24

t-Bu 80 : 20

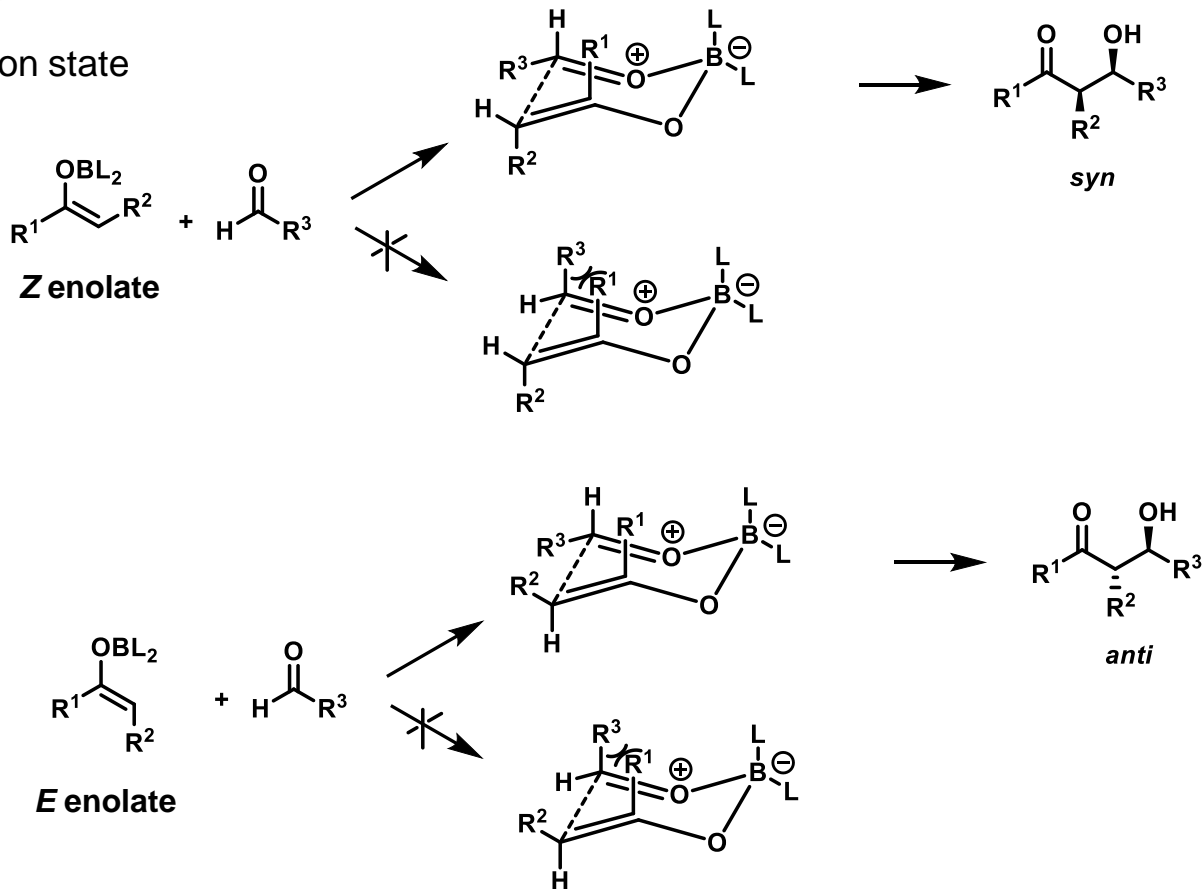
Aldol reaction: 2 new stereogenic centers can be created

R^2 is not H, R^3 achiral

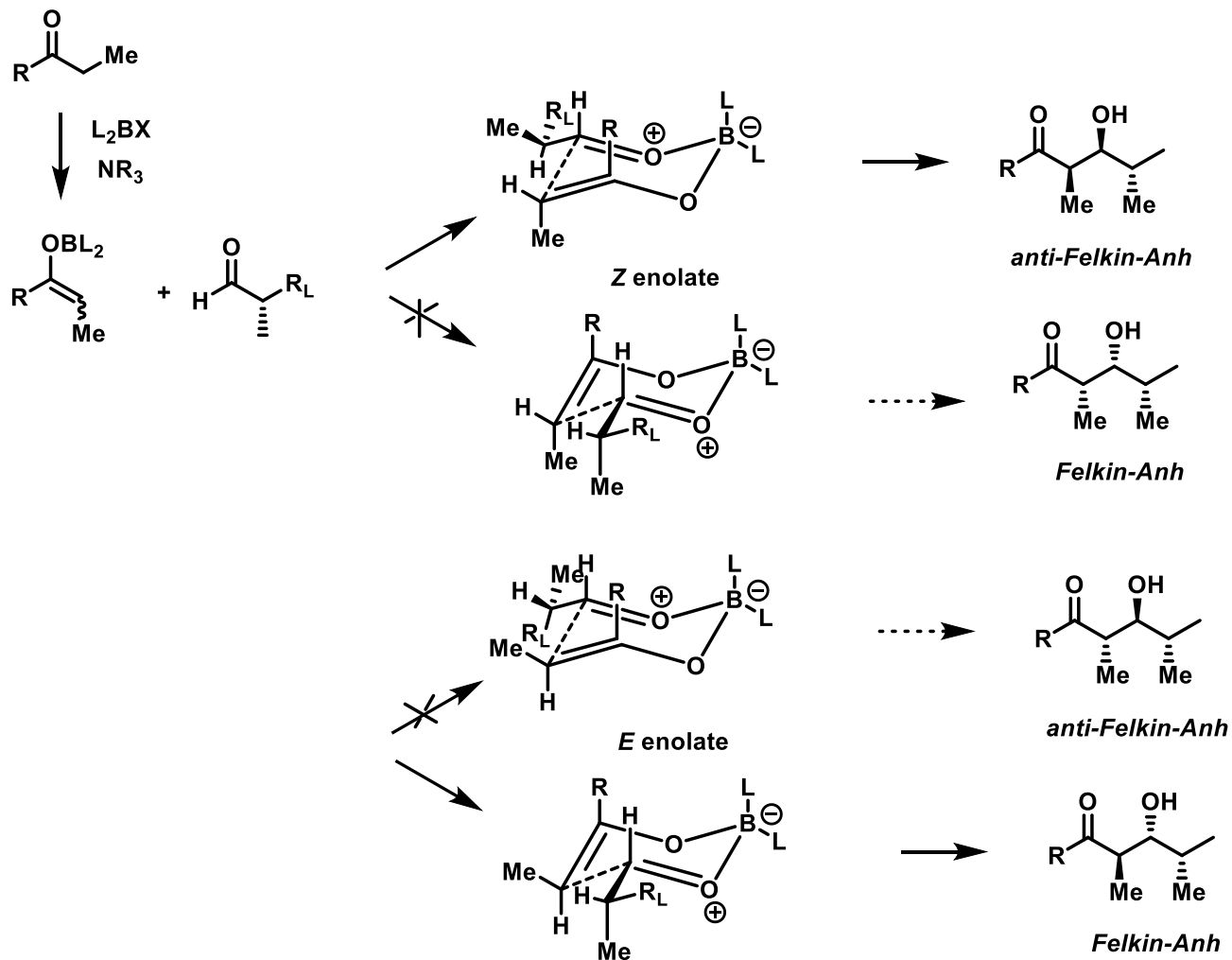


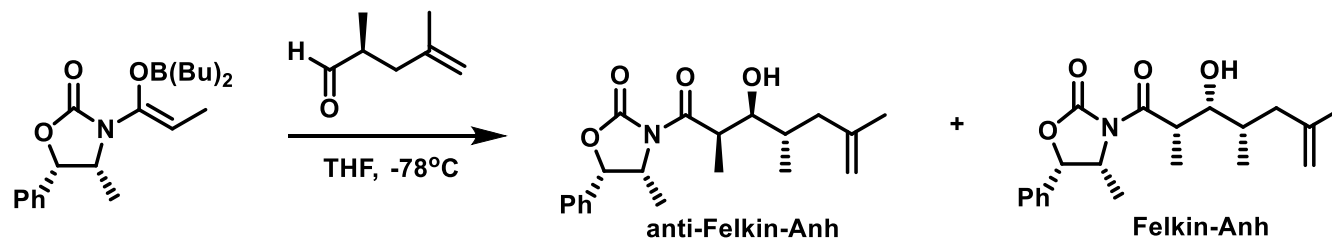
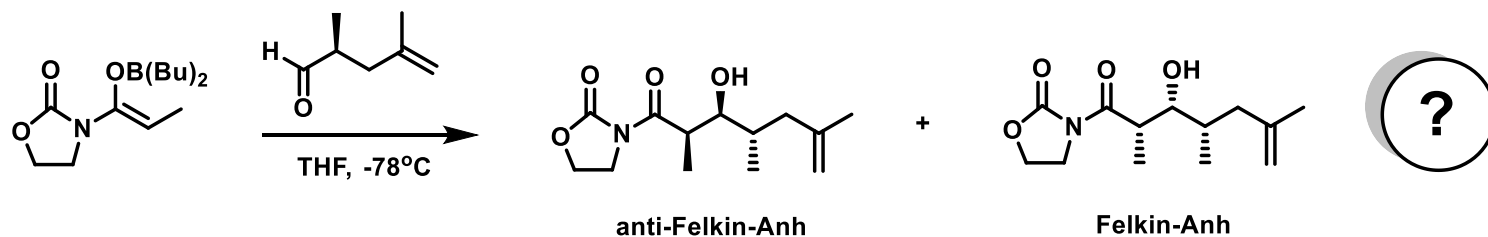
Zimmerman-Traxler

• cyclic transition state

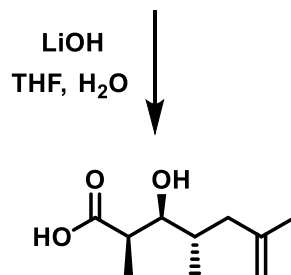


R^2 is not H, R^3 chiral

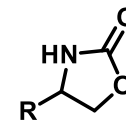
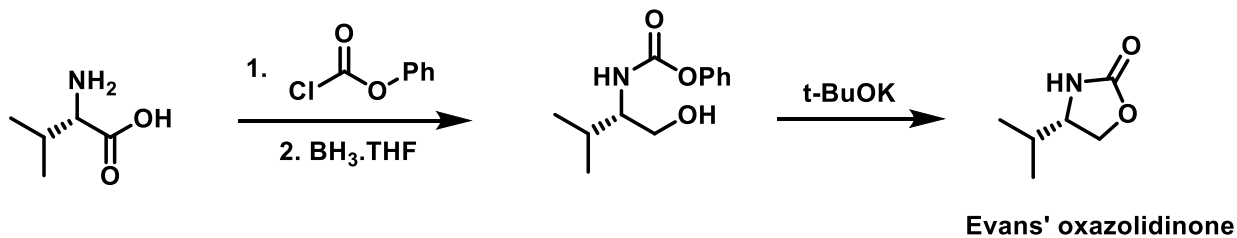




Evans' oxazolidinone

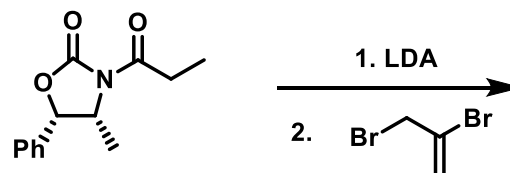


Tetrahedron Lett. 1982, 23, 807.

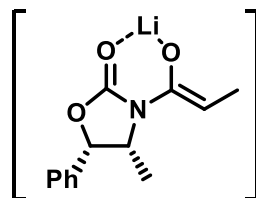


R : Bn, i-Pr, t-Bu ...

com. available

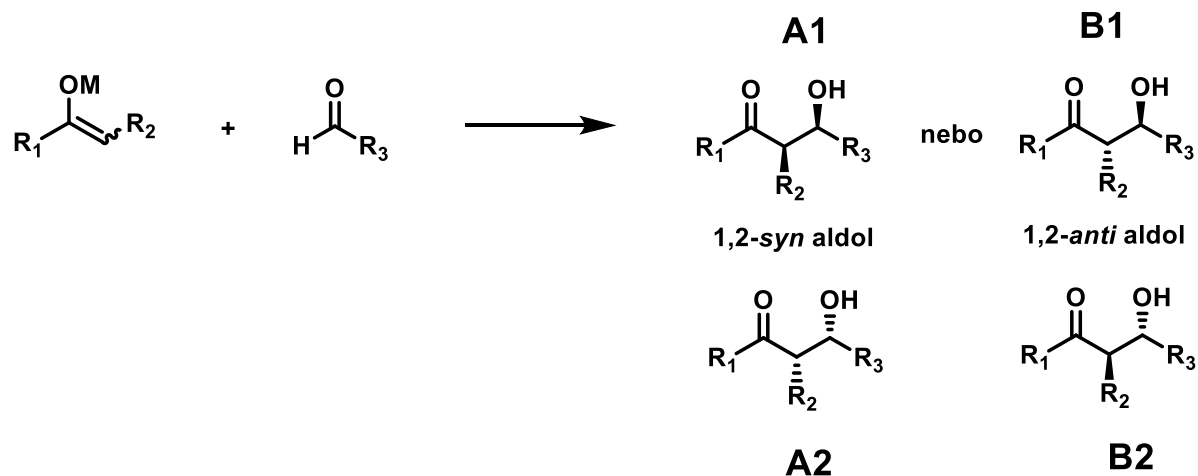


73%



J. Am. Chem. Soc. **1982**, *104*, 1737.

Aldol reaction: asymmetric induction



R₃ contains stereogenic center: typically, conditions can be adjusted so that the *syn*- or *anti*- product is predominant

