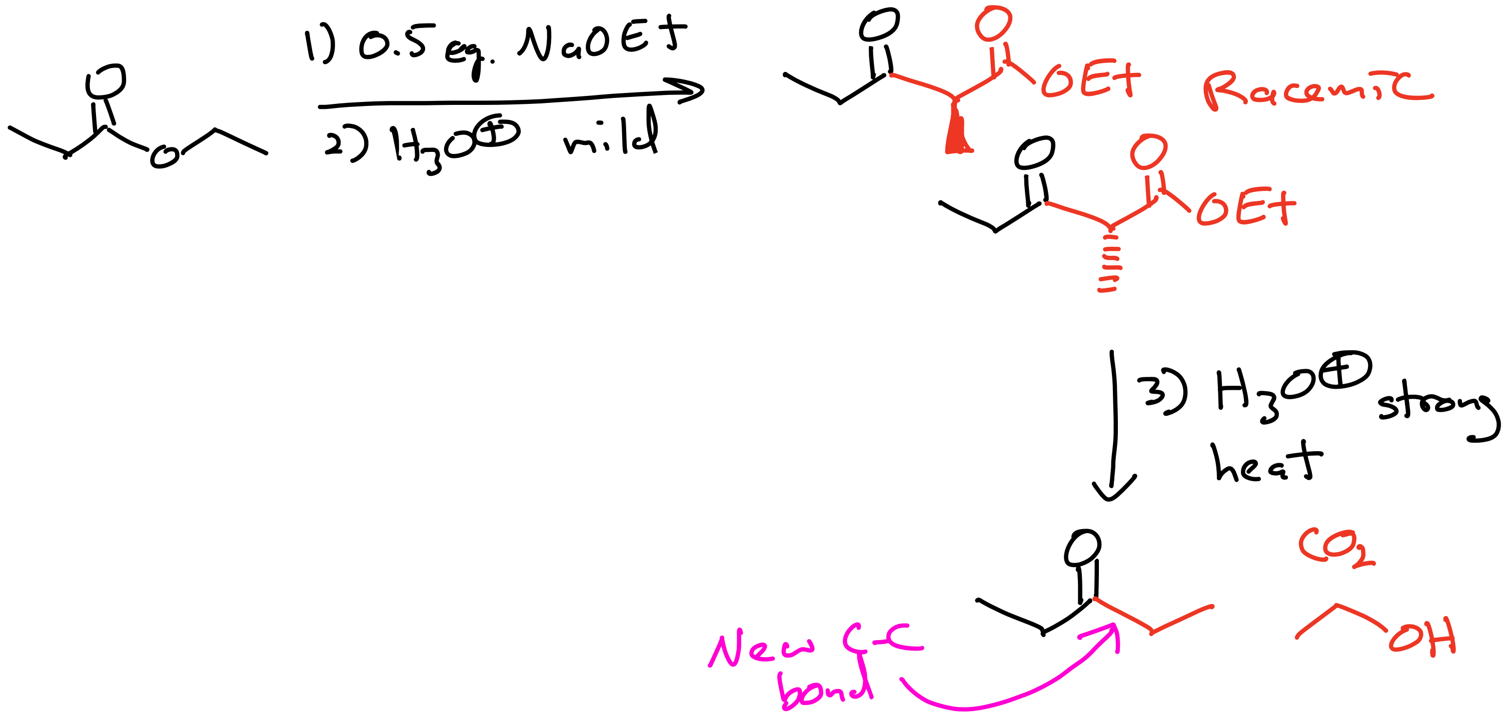
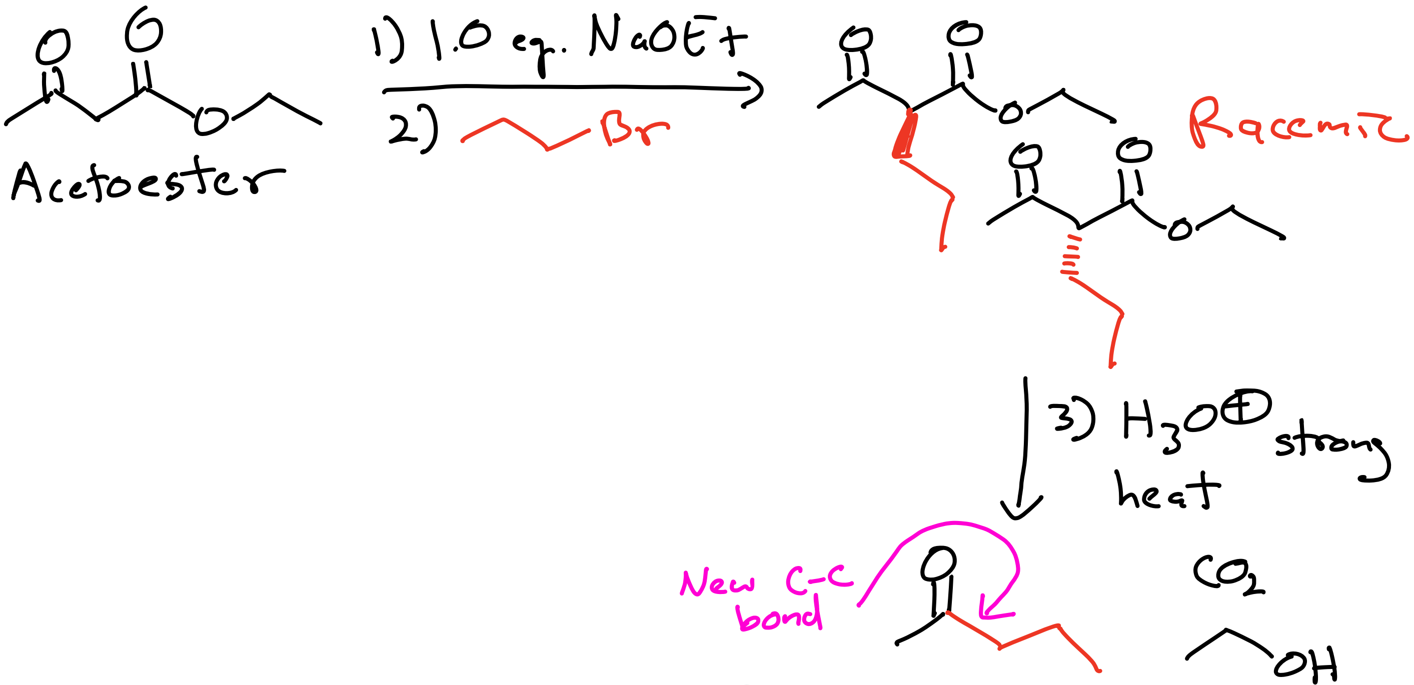
Claisen with Decarboxylation

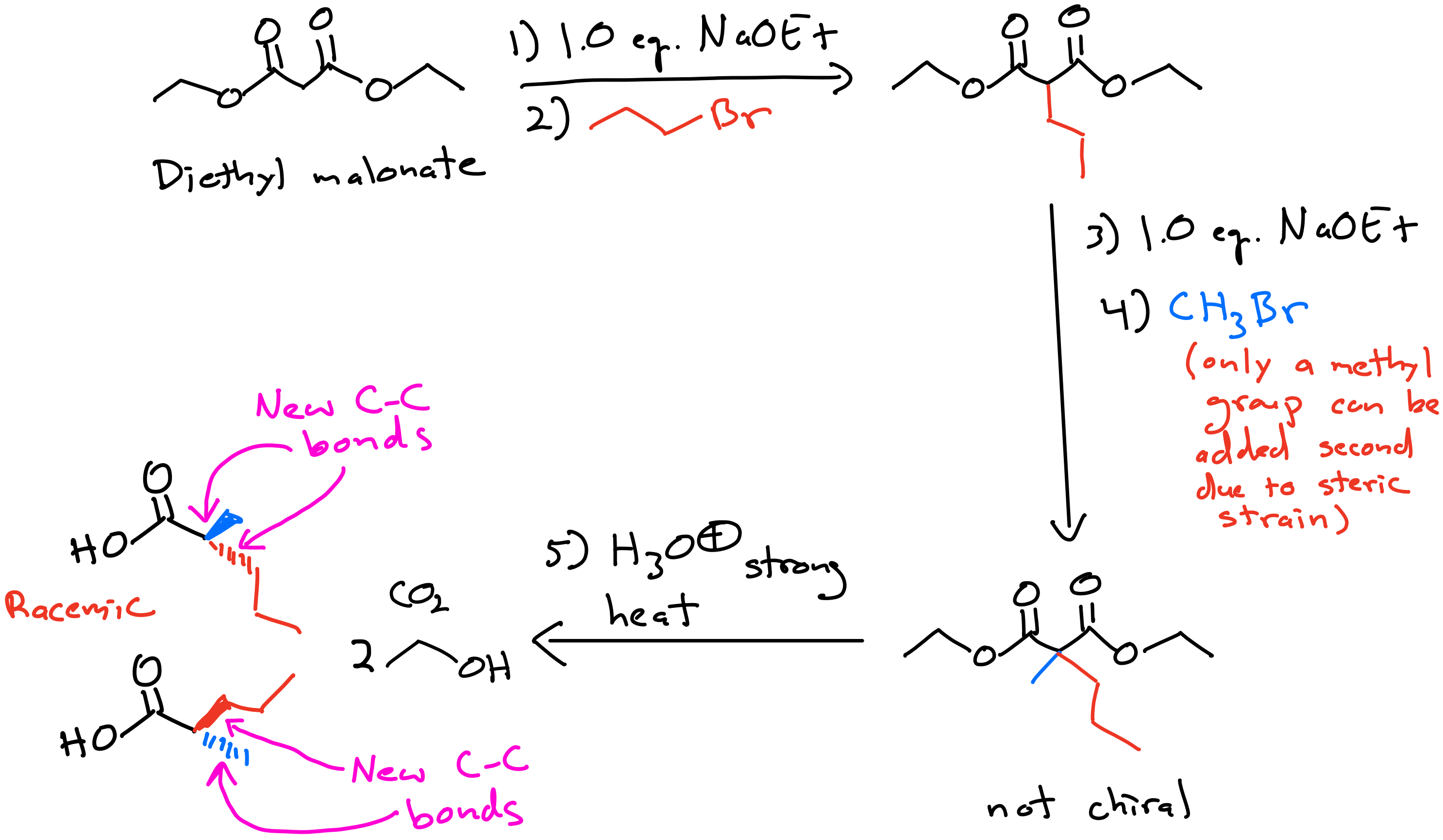


Acetoester Synthesis



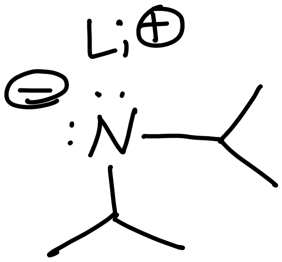
KRE → Methyl ketone

Malonic Ester Synthesis

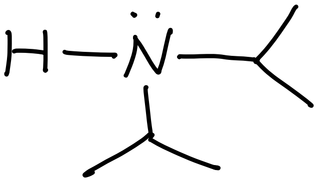


KRE → Carboxylic acid

The wicked strong base that changes things



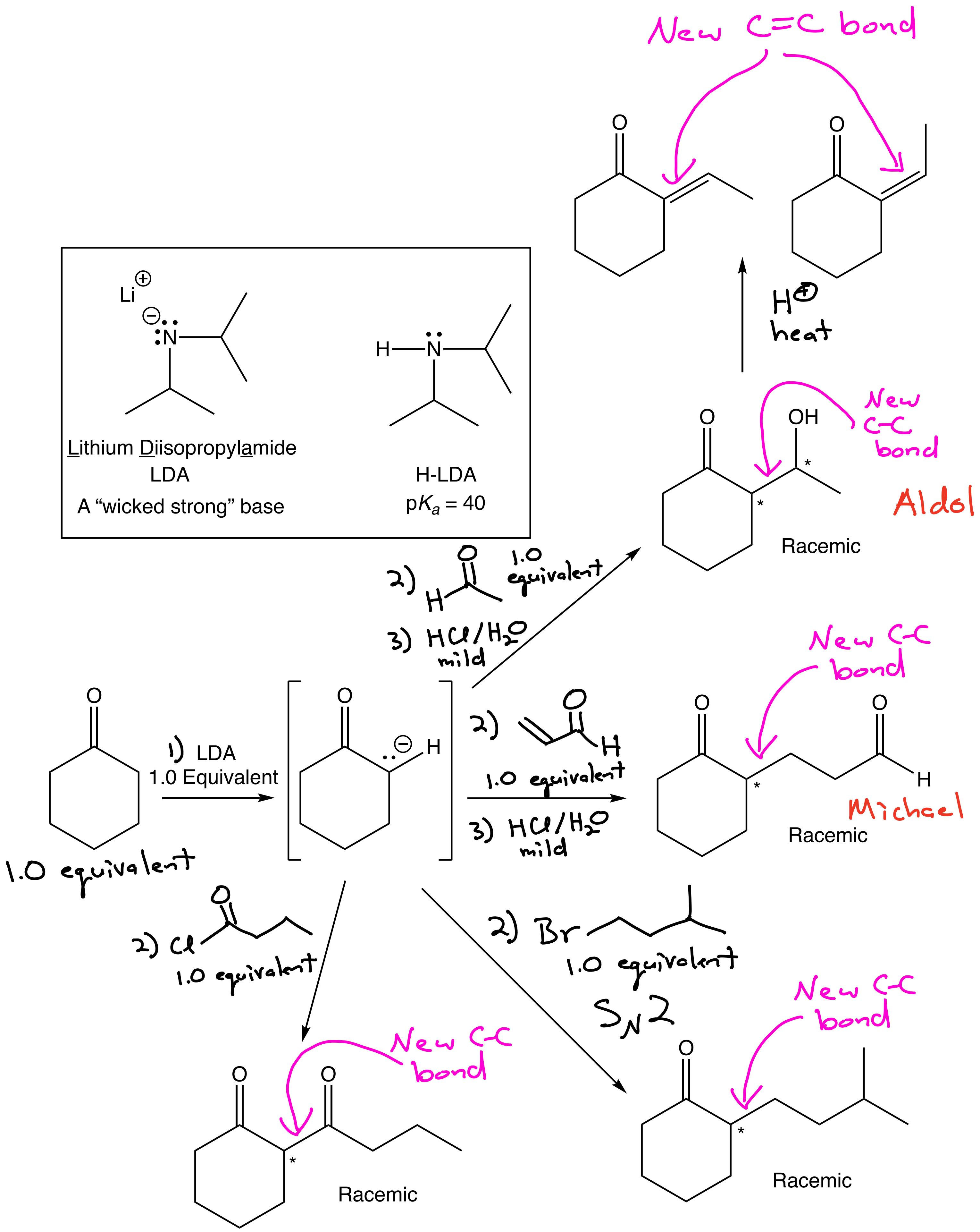
NOT a nucleophile



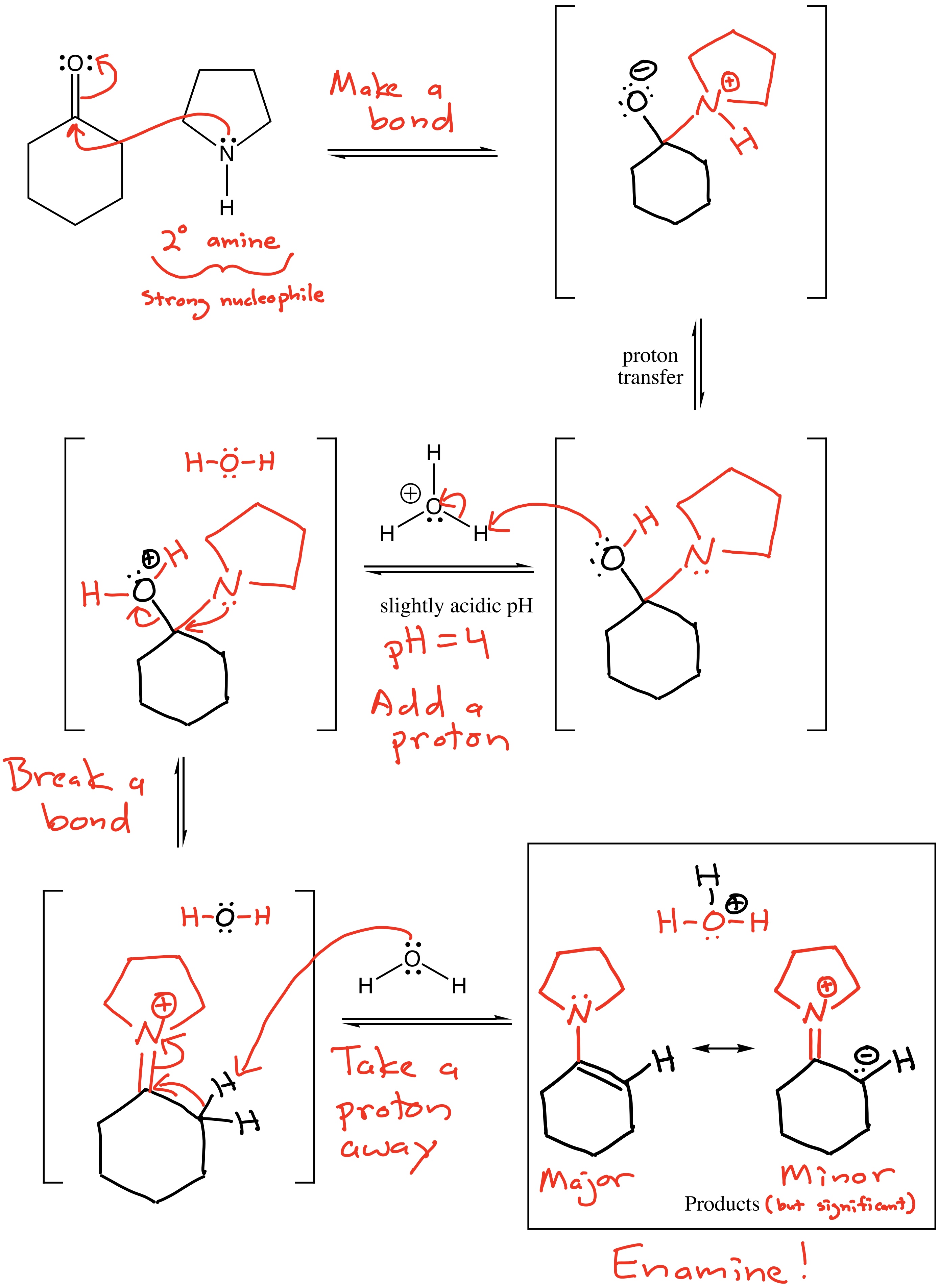
Lithium Diisopropylamide $pK_a \cong 40$

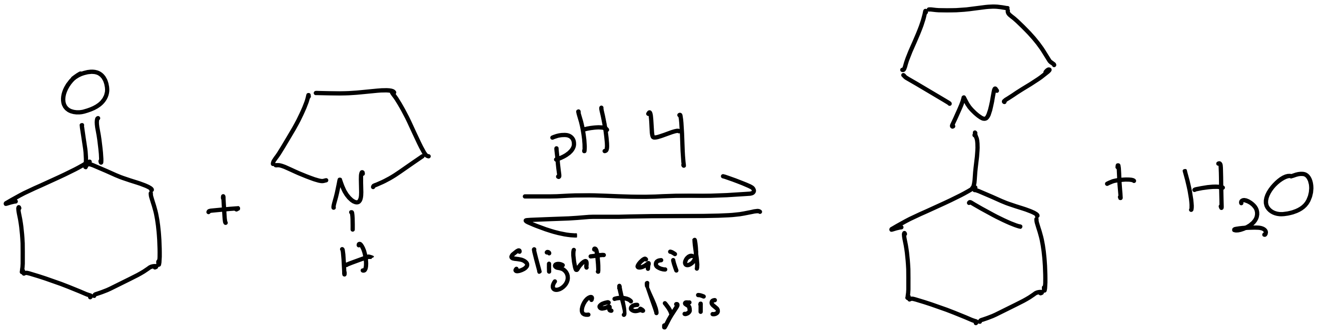
"LDA" "H-LDA"

LDA will quantitatively deprotonate aldehydes, ketones and esters to make enolates!


New C=C bond
O
O
H⊕
heat
Li⊕
⊖
N
H—N
Lithium Diisopropylamide
LDA
A "wicked strong" base
H-LDA
pK_a = 40
O
OH
*
*
New C–C bond
Aldol
Racemic
2) H
1.0 equivalent
3) HCl/H$_2$O mild
O
O
⊖
H
1) LDA
1.0 Equivalent
1.0 equivalent
2) H
1.0 equivalent
3) HCl/H$_2$O mild
New C–C bond
O
O
H
*
Michael
Racemic
2) Cl
1.0 equivalent
2) Br
1.0 equivalent
S$_N$2
New C–C bond
O
O
*
Racemic
New C–C bond
O
*
Racemic

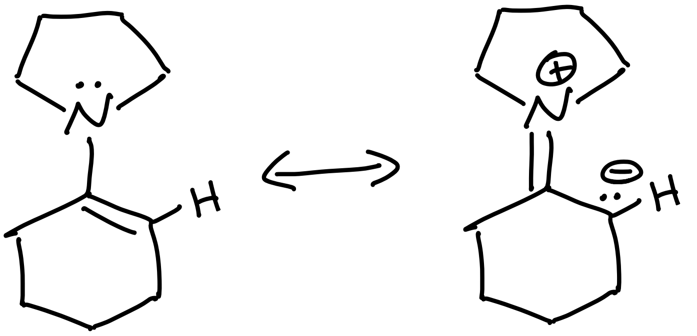
Enamine Formation





Enamine

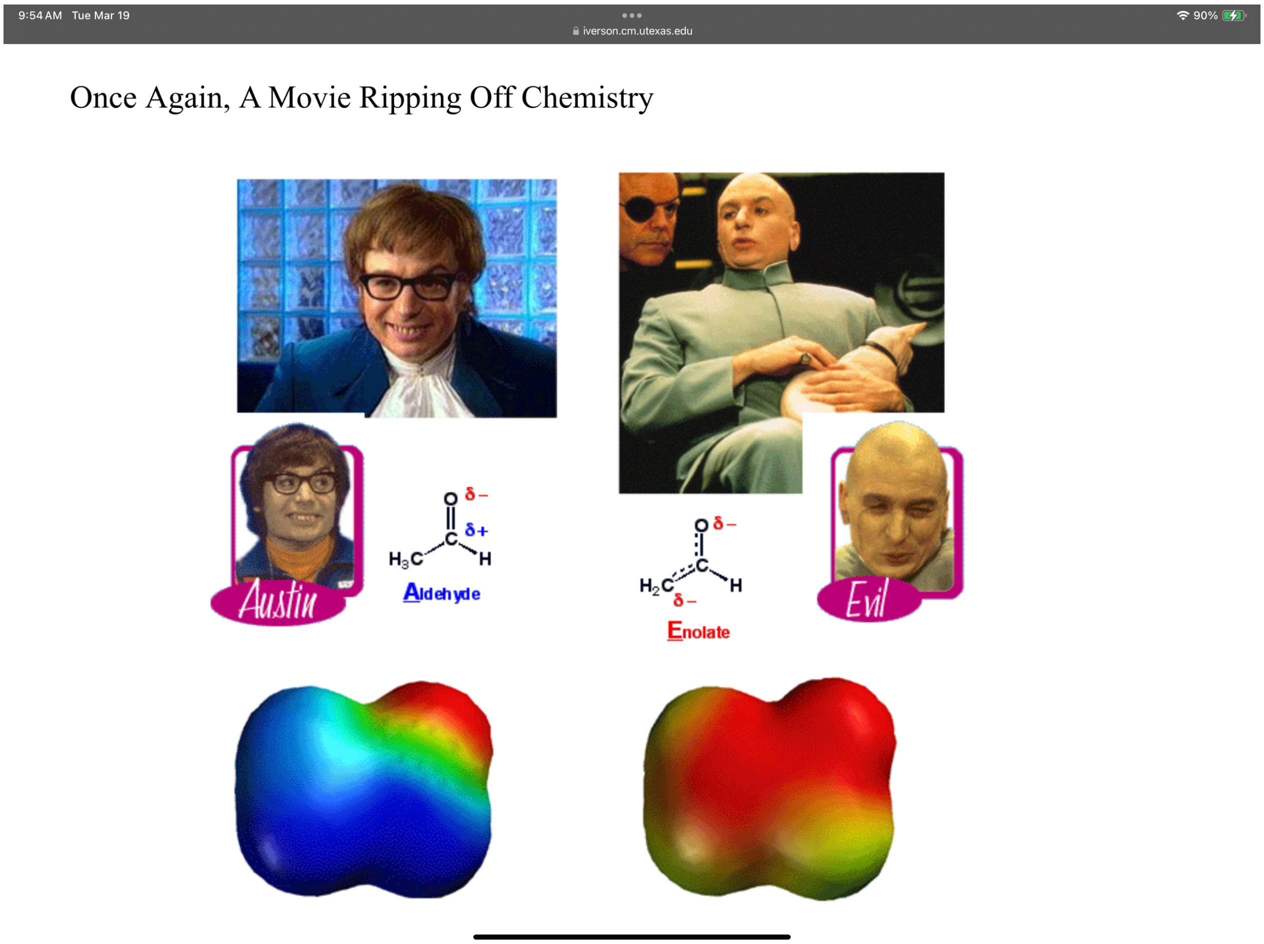
This process is reversible → adding H_2O drives it to the left (ketone) and taking H_2O away drives it to the right (enamine)



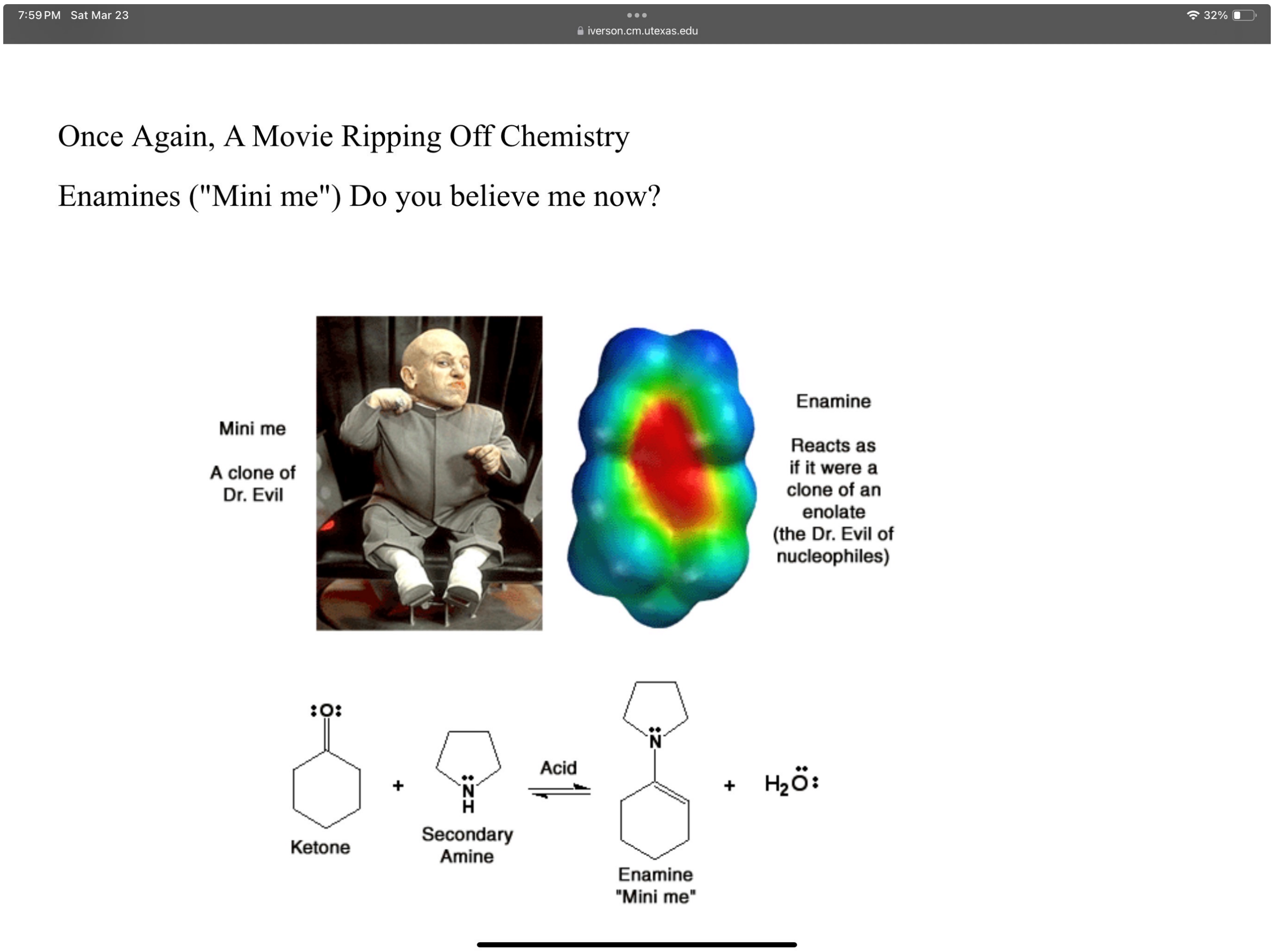
Major Contributor

Minor Contributor (but still significant)

⇒ A "smaller" (i.e. less reactive) version of an enolate ⇒ α C is a nucleophile!!



Once Again, A Movie Ripping Off Chemistry



Once Again, A Movie Ripping Off Chemistry

Enamines ("Mini me") Do you believe me now?

Mini me

A clone of Dr. Evil

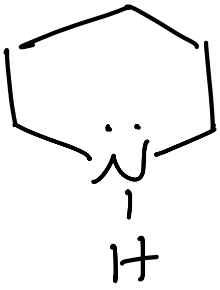
Enamine

Reacts as if it were a clone of an enolate (the Dr. Evil of nucleophiles)

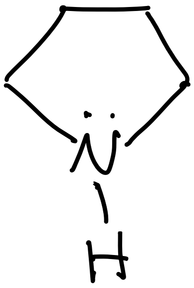
Note the relatively mild conditions used to make the enamine → pH 4, no harsh acid or base required.

It takes strong base to make an enolate

For this class we will only use the following two secondary amines to make an enamine:

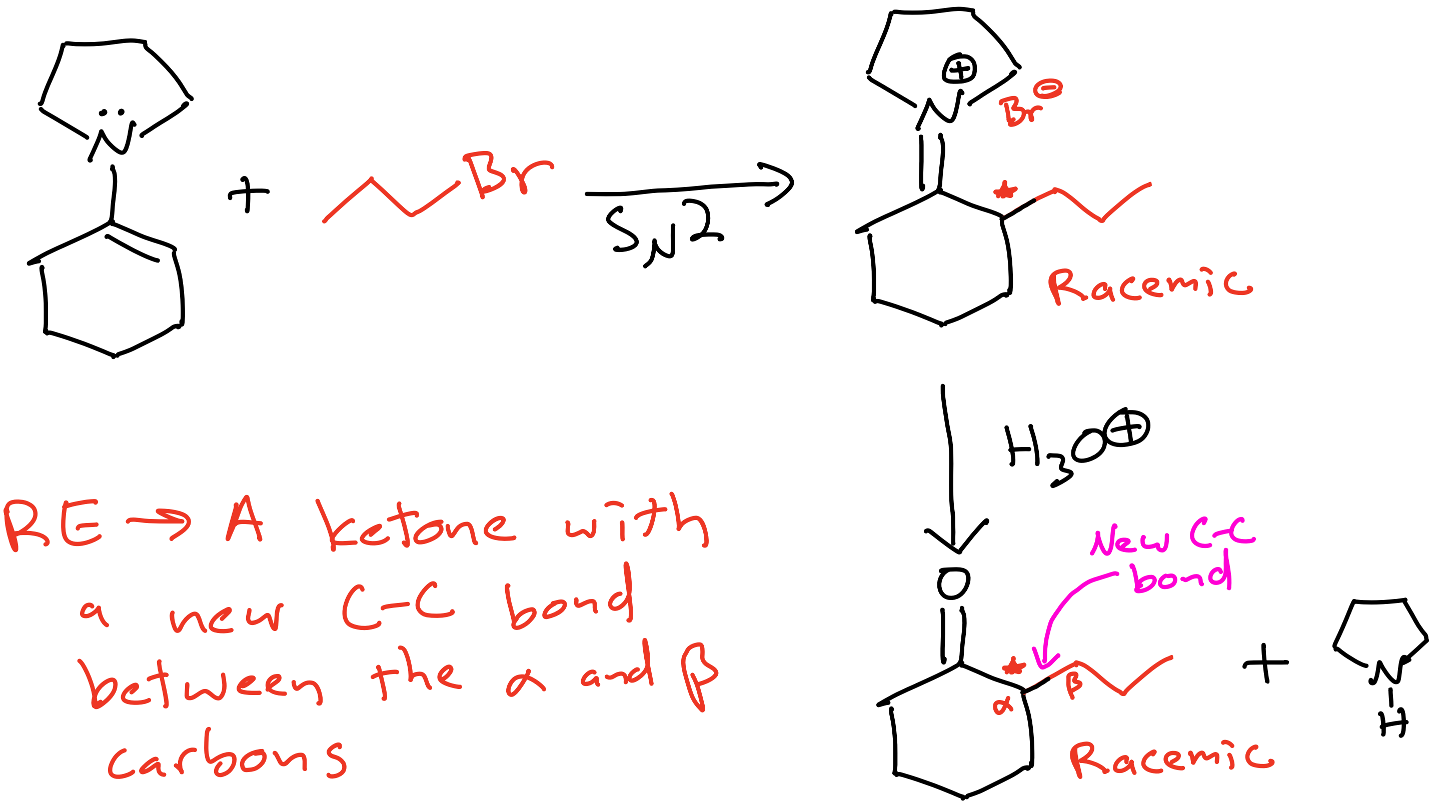


or



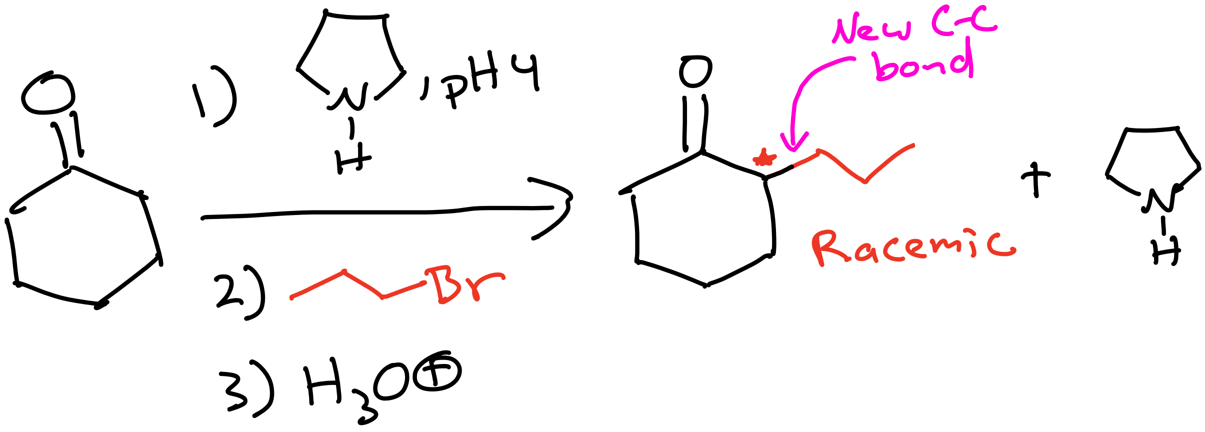
Reactions of enamines

1) Primary haloalkanes (S_N2)

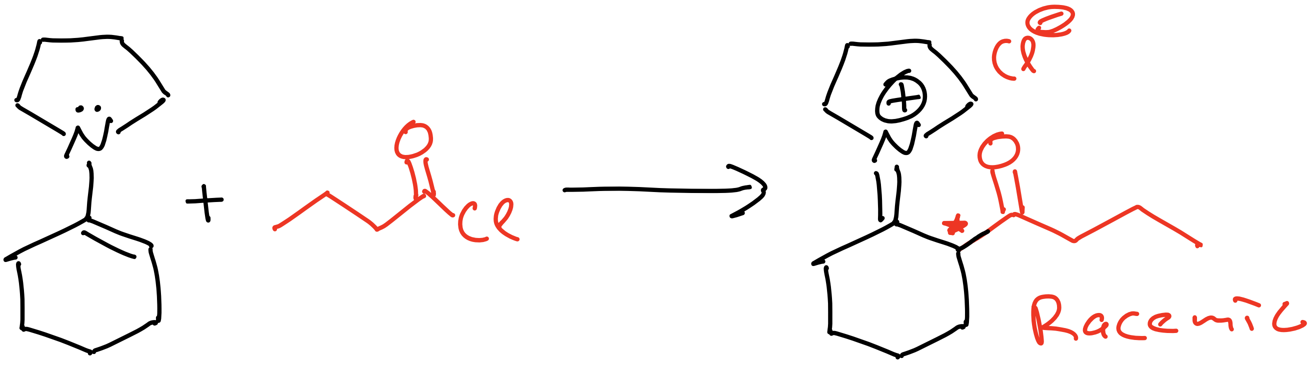


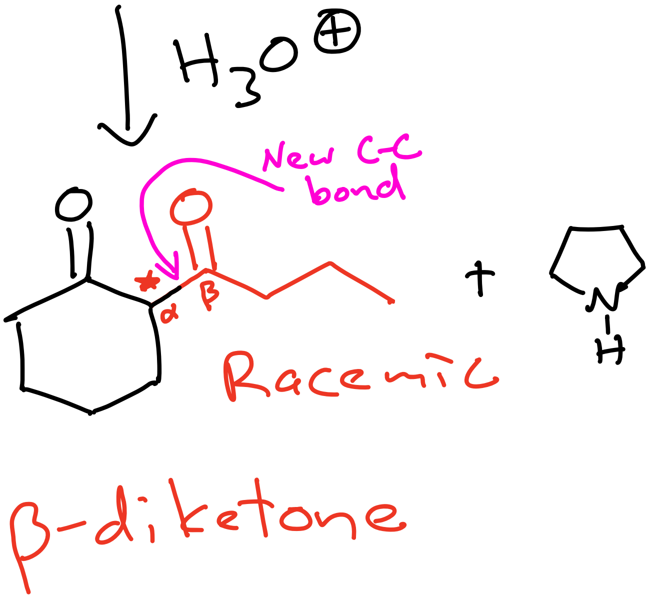
KRE → A ketone with a new C-C bond between the α and β carbons

Overall Reaction



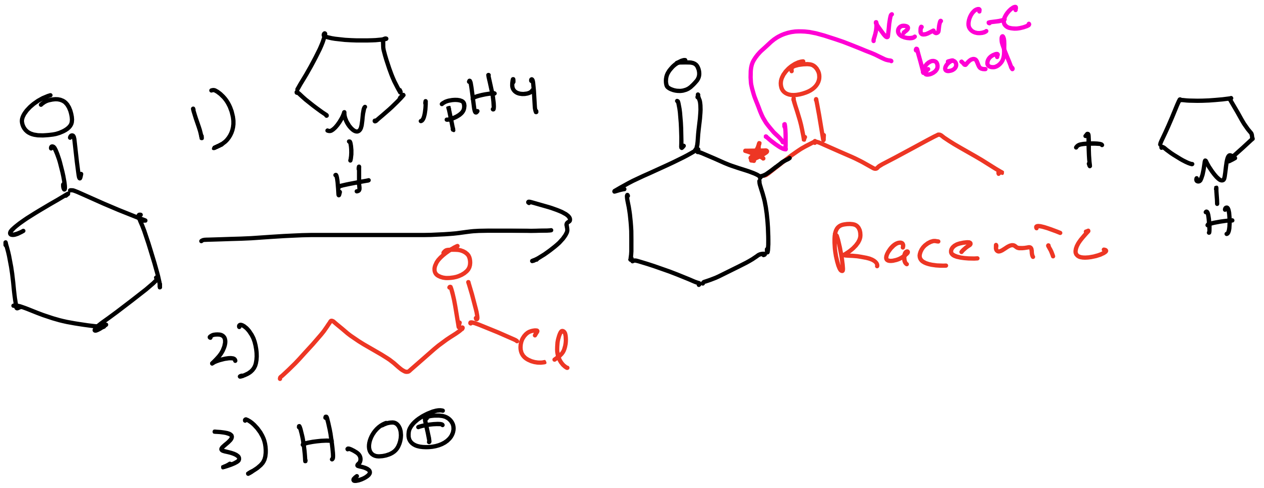
2) Acid chlorides ⇒ β-diketones





KRE → A β-diketone with a new C-C bond between the α and β carbons

Overall Reaction



β-Substituted aldehydes, nitriles, ketones, or esters

α,β-Unsaturated, nitriles, ketones, or esters

β-Keto esters

α,β-Unsaturated aldehydes

Acid Chlorides

β-Hydroxy aldehydes

Aldehydes

Ketones

Carboxylic esters

β-Ketoaldehyde

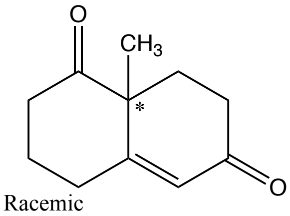
β-Diketone

Carboxylic acids

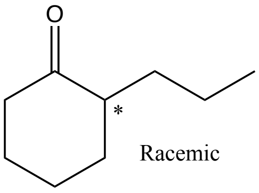
Substituted aldehyde

Substituted ketone

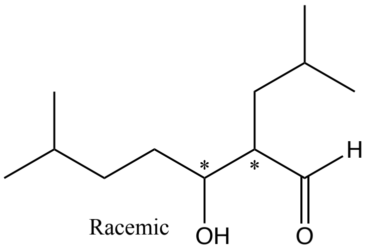
β-Diester



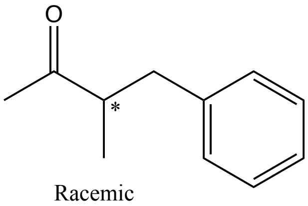
Racemic



Racemic



Racemic



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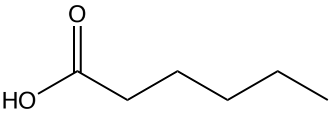

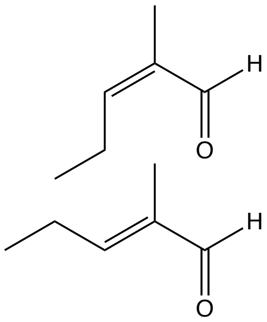

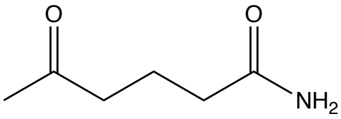

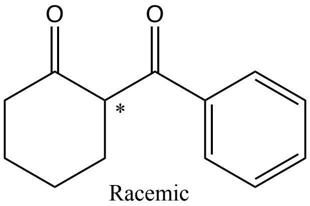

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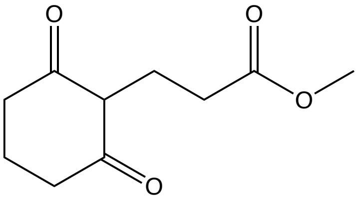

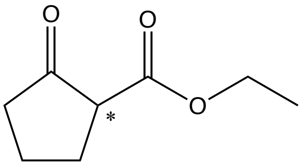

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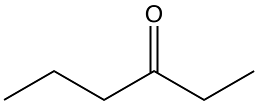

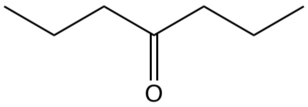

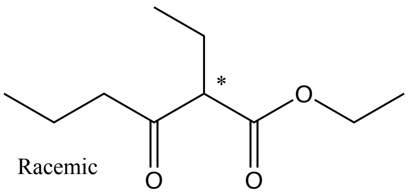

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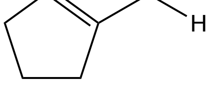
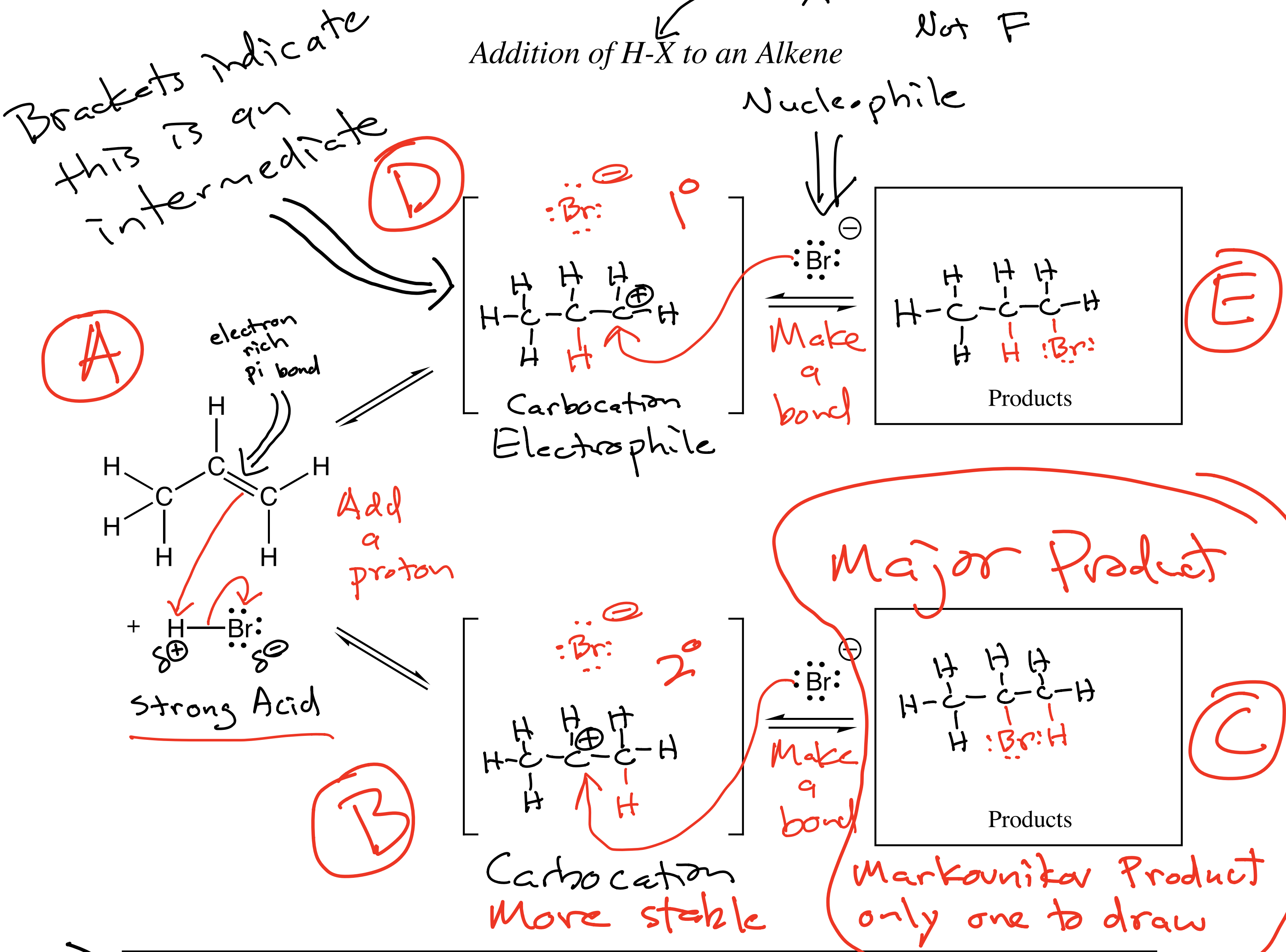



WAYNE'S WORLD

"X" can be Cl, Br, I
Not F

Addition of H-X to an Alkene



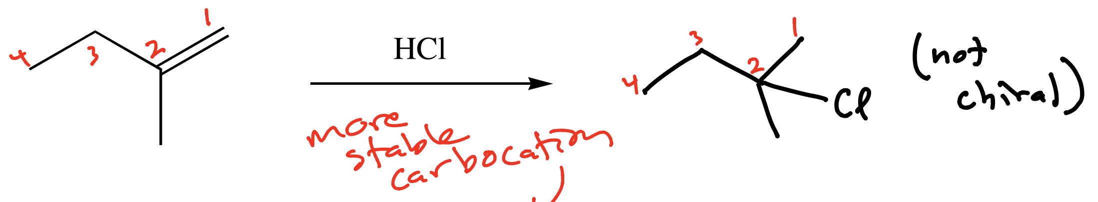
Summary: Alkene pi bond reacts with H-X to add a proton to create a carbocation intermediate that makes a bond with X⊖ to give the product

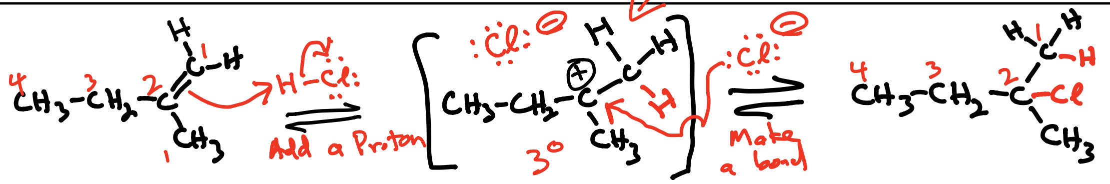
Which constitutional isomer is formed?

Regiochemistry: Markovnikov's Rule

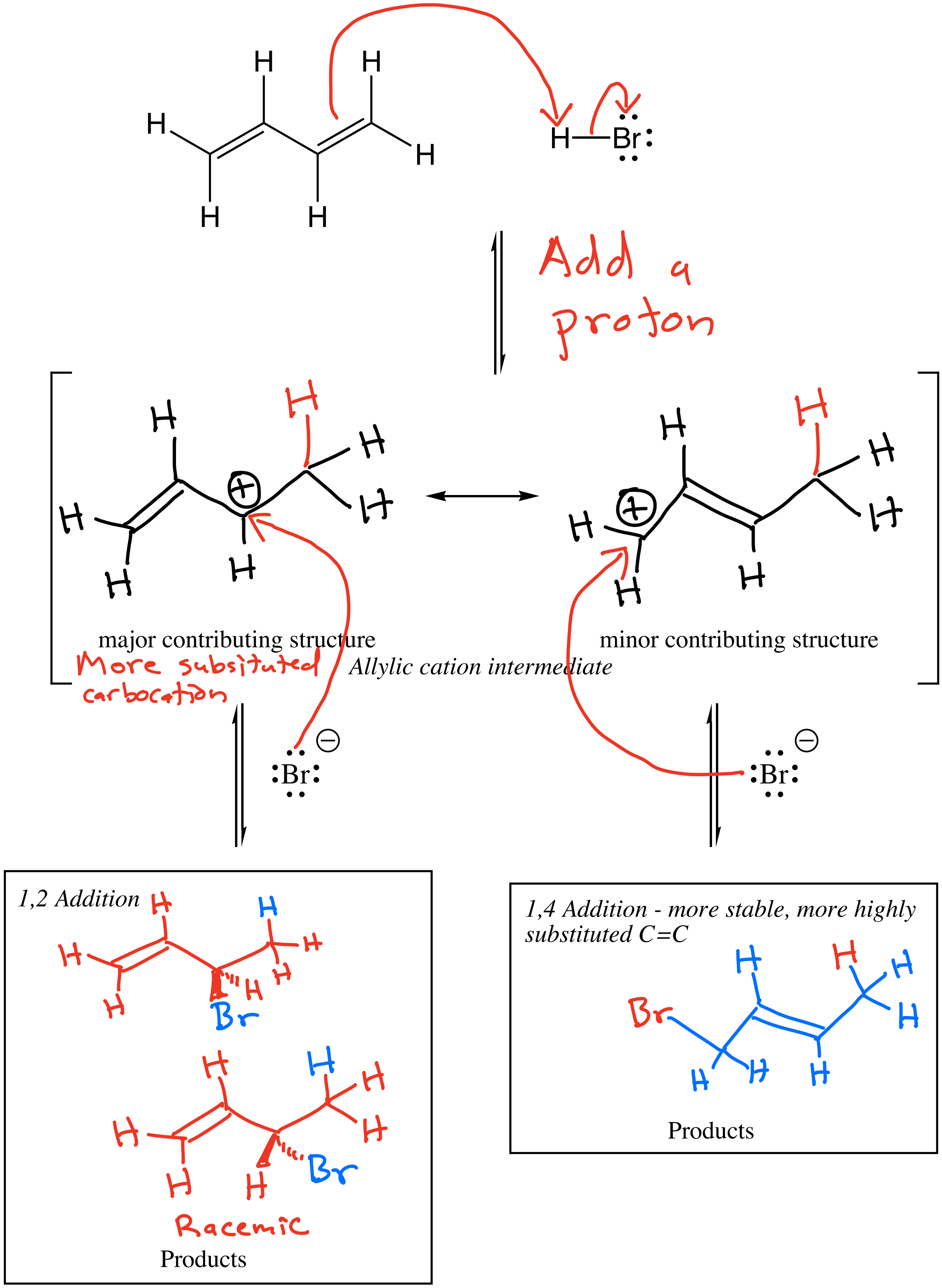
Stereochemistry: Mixed (time capsule) → Racemic Product

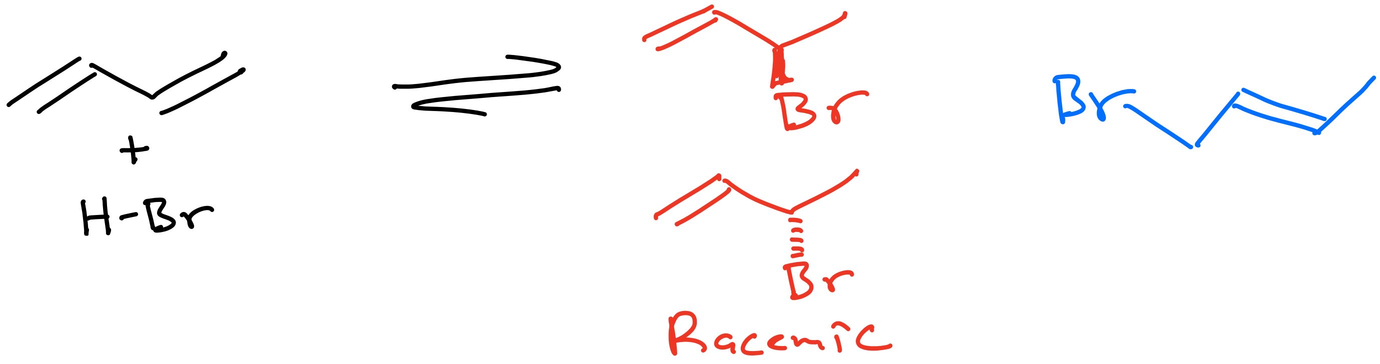
Example:



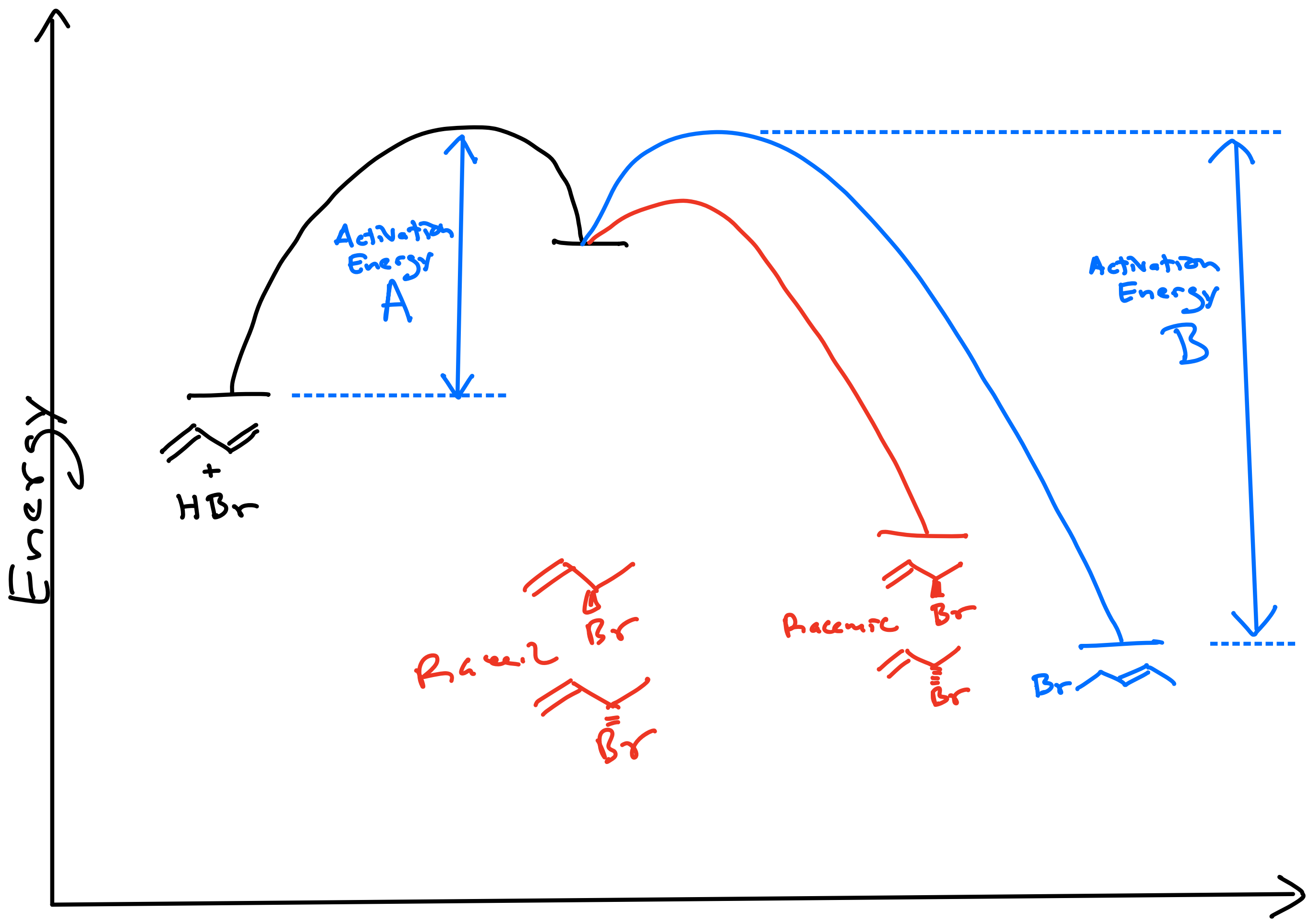


H-X reacting with conjugated dienes





Temperature of Reaction	1,2 addition	1,4 addition
-78° C	90%	10%
+40° C	15%	85%



Low temperature → Molecules have enough energy to get over activation energy A, but not enough energy to get over activation energy B.

Kinetic Control

"Fastest" wins

High temperature → Molecules have enough energy to get over activation energy A <u>and</u> activation energy B

Thermodynamic Control

Most stable product wins

Electrons should be thought of as waves.

Orbitals are described by wave equations.

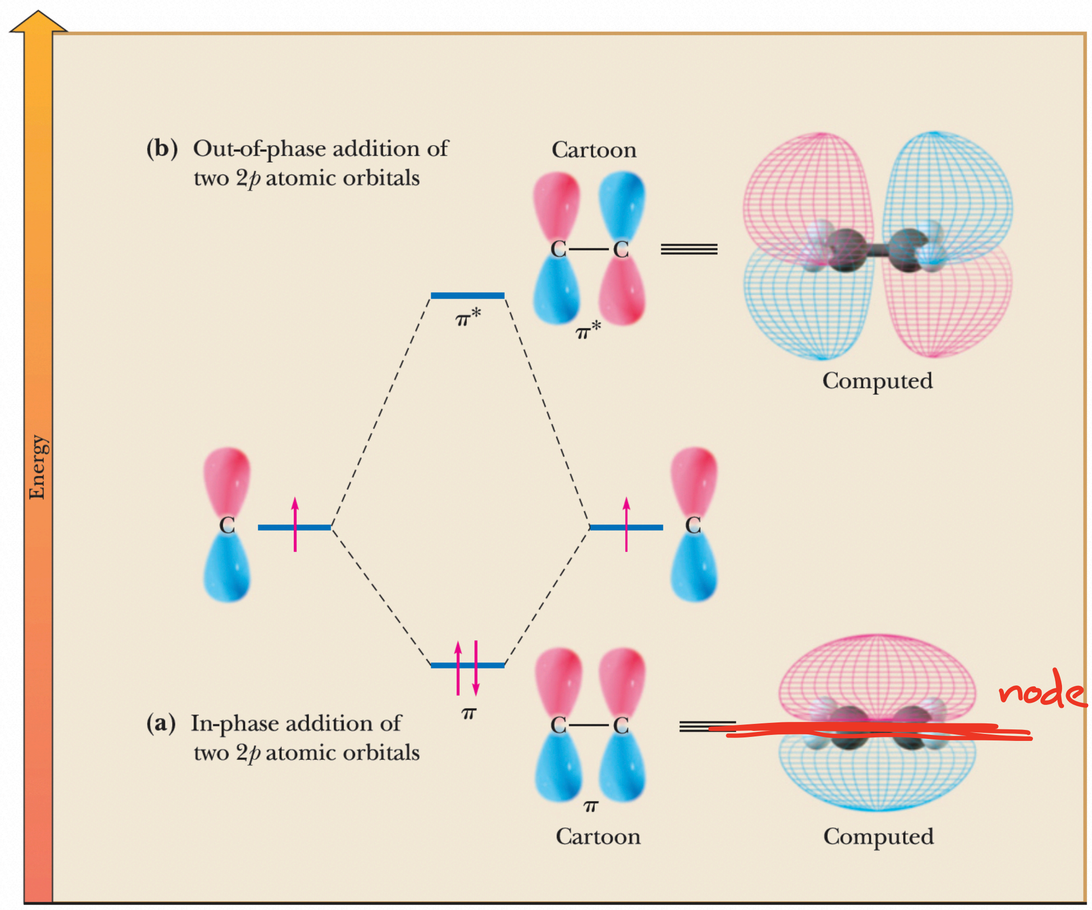
Like waves → orbitals can add constructively and destructively

When adding atomic orbitals, you get as many new molecular orbitals as there are component atomic orbitals

→ Half of these are bonding molecular orbitals.

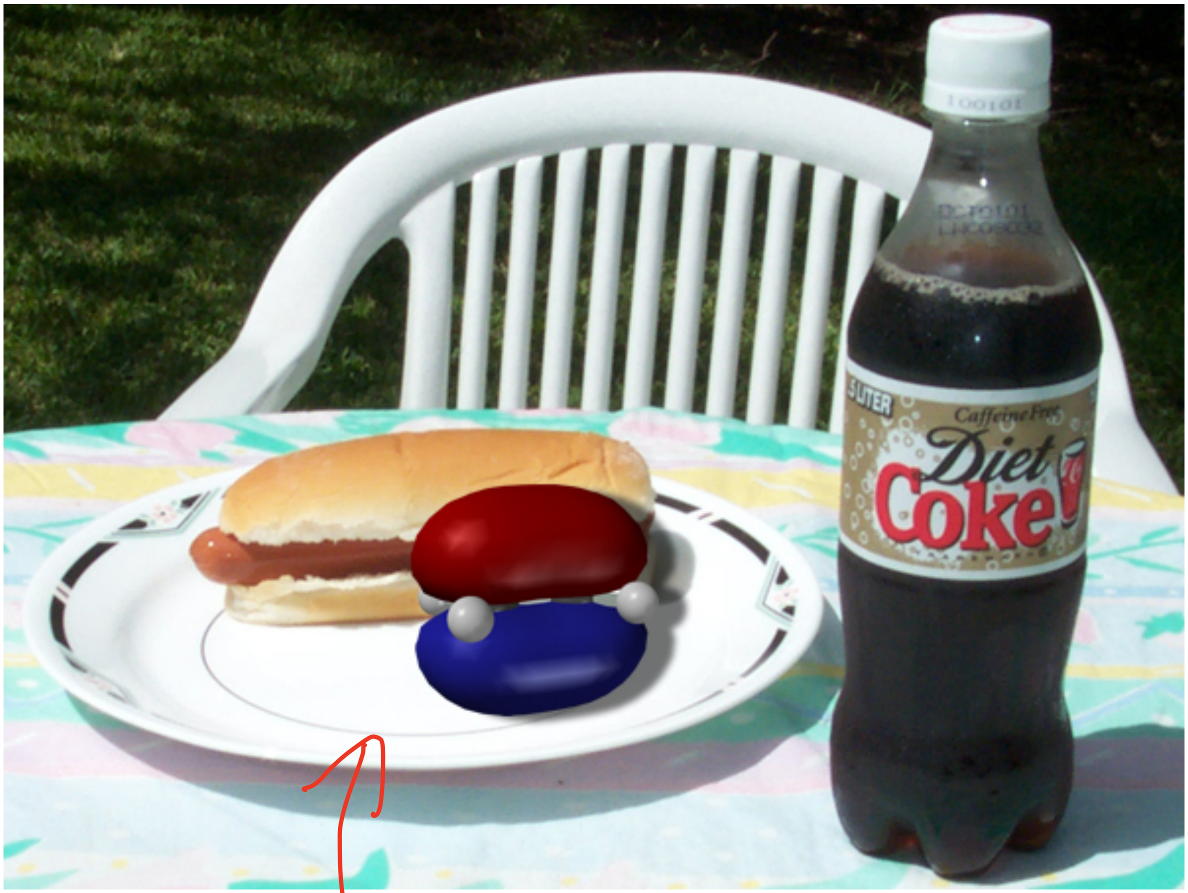
→ Half of these are antibonding molecular orbitals.

For molecules with adjacent 2p orbitals that overlap the resulting molecular orbitals extend over all of the atoms!



Watch a video explanation

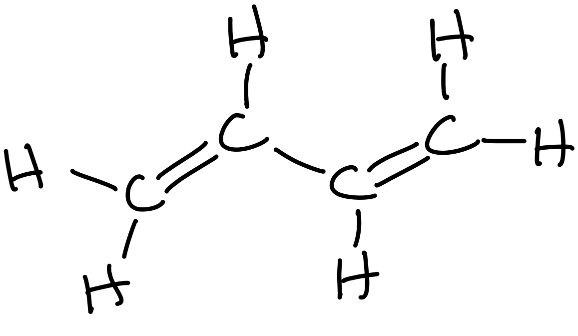
FIGURE 1.21 Molecular orbital mixing diagram for the creation of any C—C π bond. (a) Addition of two p atomic orbitals in phase leads to a π orbital that is lower in energy than the two separate starting orbitals. When populated with two electrons, the π orbital gives a π bond. (b) Addition of the p orbitals in an out-of-phase manner (meaning a reversal of phasing in one of the starting orbitals) leads to a π* orbital. Population of this orbital with one or two electrons leads to weakening or cleavage of the π bond, respectively.



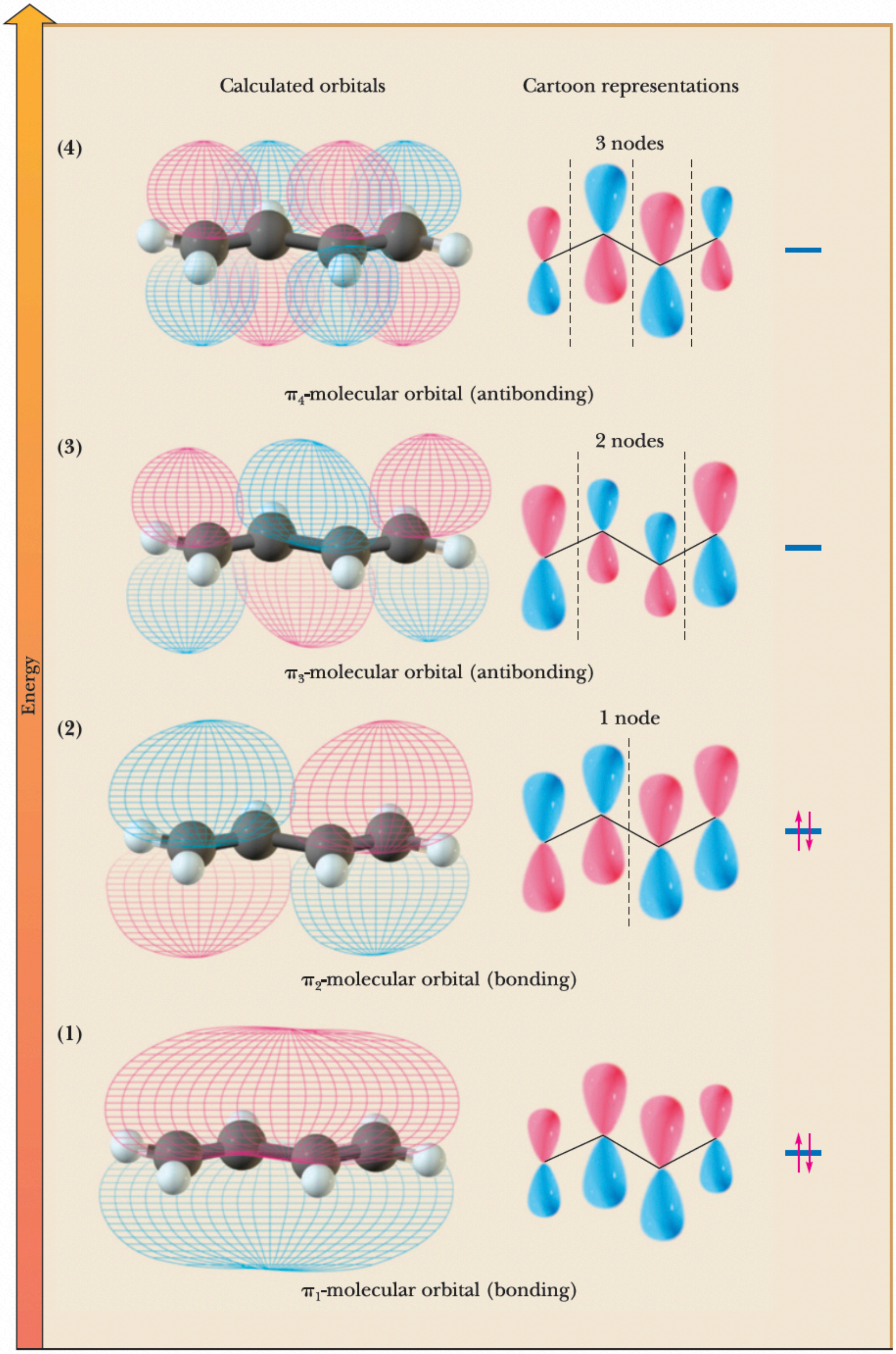
π bonding orbitals look like hot dog buns → formed from the overlap of 2p orbitals.

If you drink a lot of this you have 2p

The same applies when there are 4 atoms, each with an overlapping 2p orbital:



1,3-Butadiene

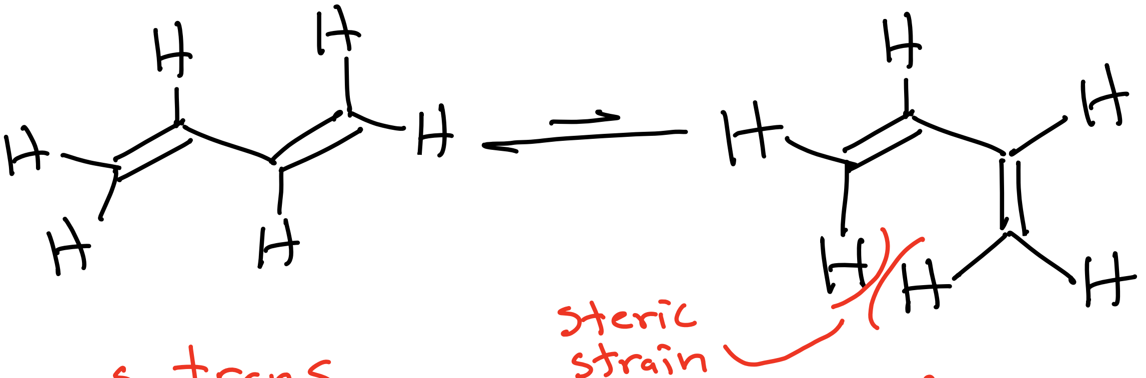


Watch a video explanation

FIGURE 20.2 Structure of 1,3-butadiene—molecular orbital model. Combination of four parallel $2p$ atomic orbitals gives two π-bonding MOs and two π-antibonding MOs. In the ground state, each π-bonding MO is filled with two spin-paired electrons. The π-antibonding MOs are unoccupied.

Consequence of the "π-way" molecular orbital → The bond between the middle 2 carbon atoms is not a normal sigma bond.

⇒ partial double bond because of lowest energy molecular orbital (π way)



s-trans

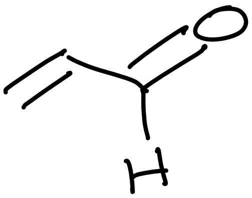
More stable

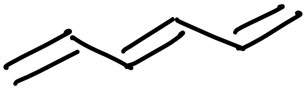
s-cis

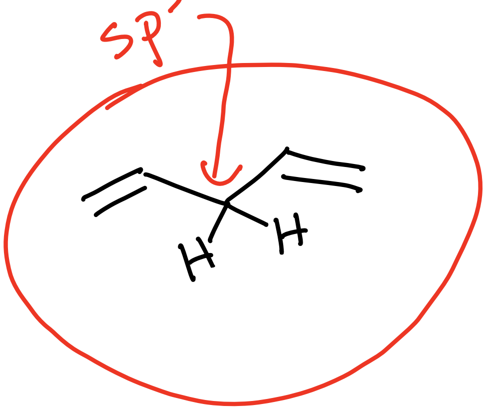
Less stable due to some steric strain

Conjugation → "π way" → 3 or more atoms

→ Also when one or more π bonds are adjacent to each other.







NOT conjugated because sp^3 C atom is between the π bonds